Applications of Phosphonium- and Sulfonium Bromide & Silica Supported Perchloric Acid for Developing New Synthetic Methodologies

A Thesis Submitted

in Partial Fulfillment of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

By

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November 20, 2006

Dedicated to my

Parents

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI

DEPARTMENT OF CHEMISTRY

INDIA

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This is to certify that Md Lokman Hakim Choudhury has satisfactorily completed all the courses required for the Ph. D degree programme.

These courses include:

CH 603	Supramolecules: Concepts and Applications
CH 611	Bioinorganic Chemistry
CH 627	New Reagents in Organic Chemistry
CH 630	A Fundamental Approach to Physical Chemistry

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This is to certify that Md Lokman Hakim Choudhury has been working in my research group since October 10, 2003 as a regular registered Ph. D. student. I am forwarding his thesis entitled "Applications of Phosphonium- and Sulfonium Bromide & Silica Supported Perchloric Acid for Developing New Synthetic Methodologies" being submitted for the Ph. D. (Science) Degree of this Institute. I certify that he has fulfilled all the requirements according to the rules of this Institute regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

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STATEMENT

I do hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology Guwahati, India under the guidance of Professor Abu T. Khan.

In keeping with the general practice of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the findings of other investigators.

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CH 603	Supramolecules: Concepts and Applications	6	BB
CH 630	A Fundamental Approach to Physical Chemistry	6	BB

Semester Performance Index (S.P.I.) : 8.00
Cumulative Performance Index (C.P.I.): 8.00

Semester II (January–May) 2004

Course	Course Name	Credit	Grade
CH 611	Bioinorganic Chemistry	6	AB
CH 627	New Reagents in Organic Chemistry	6	AA

Semester Performance Index (S.P.I.) : 9.50
Cumulative Performance Index (C.P.I.) : 8.75

Date: November, 2006

Asst. Registrar (Academic)

Acknowledgements

I take this opportunity to express my deep sense of gratitude to my research guide and architect of this thesis, Prof. Abu T. Khan, for his continuous inspiration and constructive guidance, which has helped me profoundly during the course of my work. His enthusiasm decisive approach to scientific methods has instilled a sense of confidence in me to reach the destination through dedication.

I am grateful to Dr. A. K. Saikia, Chairman of Doctoral Committee, and other members Prof. B. K. Patel and Dr. S. Ghosh for their valuable suggestions.

I am grateful to CSIR for providing my research fellowship and to IIT Guwahati for general facilities to carry out my research work.

I remain obliged to Dr. A. Ramesh, IIT Guwahati and my senior Dr. Gopal Bose for their selfless help and active co-operation.

I also express my sincere thanks to all faculty members, Department of Chemistry, IIT Guwahati.

My senior, Dr. Subrata Ghosh will always be remembered for the spontaneous help and co-operation on various matters at different stages of my thesis work.

I wish to acknowledge for the help and co-operation rendered by Paporoi di, Priti di, Tasneem, Kalpana and Asif for their direct and indirect help. I thank my all lab mates as well as friends for their help and co-operation.

I am thankful to all research scholars and M.Sc students of the Department of Chemistry, IIT Guwahati for their help.

I want to express my thanks to our technical staff Avilasha, Lipika-ba, Parikshit, Panchanan-da, Jagannath, and office staff Santunu, Dipumani-da, as well as Subal for their help.

I indebted to my parents, brother, and sister for their constant encouragement and incessant support in all my odd times. Their kind co-operation helped in completing my Ph.D degree and no words are enough to acknowledge them.

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SUMMARY

This dissertation describes the successful efforts on the development of new synthetic methodologies in protection-deprotection chemistry as well as α-bromination of β-keto esters and 1,3-diketones employing mainly three versatile reagents acetonyl-triphenylphosphonium bromide (ATPB), bromodimethylsulfonium bromide (BDMS) and silica supported perchloric acid.

The thesis contains mainly three chapters. Each chapter is subdivided into two parts viz. Part I and Part II.

Part I describes a general review on the usefulness of that particular reagent in various organic transformations and a brief literature survey from the year 1990 to till to date for dealing with that particular transformation investigated. **Part II** of the each chapter is subdivided into two sections: Section A and Section B, which will describe an account of work carried out by the candidate.

Chapter I, Part I describes a brief literature review on the application of acetonyl-triphenylphosphonium bromide (ATPB) in various organic transformations and a brief survey on desilylation and acetylation.

Part II of **Chapter I** illustrates the usefulness of catalytic amount of acetonyltriphenyl-phosphonium bromide for desilylation of TBS ethers in **Section A**. The significant features of the present method include the ease of operations, high efficiency and mild conditions, which may be useful extensively in organic synthesis. In addition, the chemoselectivity, for example, the selective deprotection of alkyl *tert*-butyldimethylsilyl ether can be achieved in the presence of aryl-*tert*-butyldimethylsilyl ethers. Moreover, a wide variety of other protecting groups are survived such as acetyl, benzyl, benzoyl, thioketals, esters and isopropylidene under the experimental conditions.

Similarly, **Section B** of this chapter describes the efficient catalytic activity of the reagent ATPB for acylation of a wide variety of alcohols, phenols, thiols and aldehydes at room temperature. The reaction of alcohol, phenol and thiol or amine with 1.5-2.0 equivalent amount of acetic anhydride in presence of 5 mol% ATPB at room temperature provide their corresponding acetate within a very short time in good yields. The notable advantages of this protocol are: ease of operations, high efficiency and mild conditions.

which may be useful extensively in organic synthesis. Moreover, a wide variety of other protecting groups are survived such as benzyl, benzoyl, -TBS, -TBDPS, isopropylidene, methoxy- and thio group at the anomeric position under the experimental conditions. In addition tertiary as well as hindered alcohols also undergo acetylation under the experimental conditions.

Part I of **Chapter II** demonstrates a literature review on the application of bromodimethylsulfonium bromide and peroxovanadium mediated *in situ* bromonium ion in organic synthesis as well as a brief survey on the α-bromination of β-keto esters and 1,3-ketones.

Part II of **Chapter II** describes two new synthetic methodologies for α-bromination of β-keto esters and 1,3-diketones in Section A and Section B.

Section A illustrates a new method for regioselective α-bromination of β-keto esters and 1,3-diketones using a versatile reagent bromodimethylsulfonium bromide. The notable advantages of this protocol are: mild, clean and simple reaction conditions, very good yields, no need of chromatographic separations as well as no need of any base or Lewis acid as an additive, which is invariably required by NBS methods. Furthermore, this method is also expected to have much better application in organic synthesis because of the low cost, easy accessibility and less hazardous nature of the reagent. We believe this methodology will be a valuable addition to modern synthetic methodologies.

Section B gives an account of a simple and environmentally acceptable method for the same transformation using a combination of V_2O_5-H_2O_2-NH_4Br, avoiding the use of the conventional reagent NBS or hazardous molecular bromine. Interestingly, all these reagents are environmentally acceptable and we have suggested that vanadium pentoxide plays a dual role: i) formation of peroxo complexes, which oxidize bromide ion to the bromonium ion and ii) promotion of enol formation by chelating with the two carbonyl groups of the β-keto esters or 1,3-diketones as a result this combination exhibits selectivity under the experimental conditions.

Part I of **Chapter III** describes a review of literature on the application of silica-supported perchloric acid in organic synthesis and literature survey on *gem*-diacylation, oxathioacetalization, thioacetalization and tetrahydropyranylation.

Section A of Part II demonstrates the potentiality of silica-supported perchloric acid for protection of aldehydes as *gem*-diacetates. Silica supported perchloric acid is a highly effective and cheap reusable catalyst for 1,1-diacylation of aldehydes. The significant features of this protocol are: mild conditions, chemoselectivity, tolerable to a wide variety of other protecting groups such as benzoyl and TBS ethers and no cyclotrimerization observed for aliphatic aldehydes. In addition, this method is very simple, cost effective and the reaction times are very short as well as it provides very good yields.

Section B of **Part II** illustrates the versatility of the same reagent ($HClO_4$-SiO_2) for the protection of carbonyl and hydroxyl compounds as oxathioacetals, thioacetals and tetrahydropyranyl ethers respectively. The notable advantages of this protocol are no aqueous work-up, very rapid and simple procedure, very good yields as well as the catalyst is reusable.

In conclusion, the thesis describes some new and effective synthetic methodologies on protection /deprotection chemistry as well as selective α-bromination of β-keto esters and 1,3-diketones. Due to the advantages of these methodologies over the existing methods, it is expected that these methodologies will be applicable in target-oriented synthesis as well as valuable additions in the arsenal of synthetic organic chemistry literature.

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GENERAL REMARKS

The present investigations were carried out in the Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati -781 039, Assam, from October 10, 2003 to November 17, 2006 as a research scholar under the supervision of Prof. Abu T. Khan.

The analytical samples were routinely dried *in vacuo* at 50 °C for 8 hours. Column chromatography was carried out with silica gel (60-120 mesh, Merck, SRL or Qualigen), for purifications of reaction mixture. After purification, the solvent was usually removed in rotavapor using Buechi R-114V instrument. In TLC experiments, silica gel G (SRL) or silica gel GF 254 (SRL) were employed as adsorbent and spots were detected by staining with iodine vapour or under UV light or charring 15% conc. H_2SO_4 in MeOH or MOSTAIN solution [by dissolving 20 g ammonium heptamolybdate and 0.4 g cerium (IV) sulphate in 400 mL 10% H_2SO_4 solution]. ^{1}H-Nuclear Magnetic Resonance spectra and ^{13}C-Nuclear Magnetic Resonance spectra were recorded either on Varian (400 MHz) or Bruker (300 MHz), or Jeol (400 MHz), instruments using tetramethylsilane (TMS) as an internal standard and $CDCl_3$ as solvent. The chemical shift values were expressed in δ scale and their multiplications were described using the following symbols: s-singlet, d-doublet, t-triplet, q-quartet, quin-quintet, *m*-multiplet, br-broad, brs-broad singlet.

The infrared spectra were recorded in KBr pellets or in liquid film on a Perkin Elmer 1330 and Nicolet Impact 410 instruments, respectively. Melting points were determined on a sulphuric acid bath or Buechi B-545 instrument and were uncorrected. Elemetal analysis has been done by Perkin Elmer CHNS/O-2400 instrument. All the solvents and reagents employed were purified using recommended procedures in literature.

X-ray diffraction data were collected with a Bruker Apex II smart diffractometer with CCD area detectors using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å).

Abbreviations

Ac_2O	Acetic anhydride
ATPB	acetonyltriphenylphosphonium bromide
BDMS	bromodimethylsulfonium bromide
Bz	benzoyl
Bn	benzyl
CAN	cericammonium nitrate
DIBALH	diisobutylaluminium hydride
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DHP	3,4-dihydro-*2H*-pyran
DMSO	dimethyl sulfoxide
DMF	N, N-dimethylformamide
EtOAc	Ethyl acetate
DMAP	4-(dimethylamino) pyridine
NBS	N-bromosuccinimide
NCS	N-chlorosuccinimide
MW	microwave
mp	melting point
PPTS	pyridinium *p*-toluenesulfonate
py	pyridine
rt	room temperature
SPB	sodium perborate
SPC	sodium percarbonate
TBS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TMSCl	trimethylchlorosilane
TBATB	tetrabutylammonium tribromide
PTSA	*p*-toluenesulfonic acid
THP	tetrahydropyranyl
Ts	*p*-toluenesulfonyl
Tr	trityl
TMS	trimethylsilyl

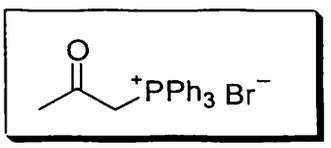
CHAPTER - I

PART I

REVIEW ON THE APPLICATION OF ACETONYLTRIPHENYLPHOSPHONIUM BROMIDE (ATPB) IN VARIOUS ORGANIC TRANSFORMATIONS AND A BRIEF SURVEY ON DESILYLATION AND ACETYLATION

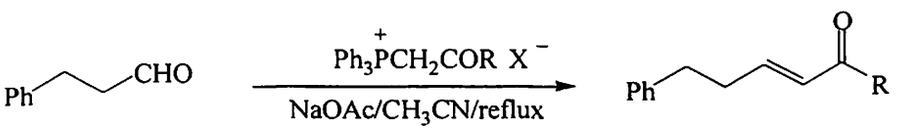
LITERATURE REVIEW

Acetonyltriphenylphosphonium bromide (ATPB) is an alkyl phosphonium salt, which can be easily prepared by stirring the reaction mixture of bromoacetone and triphenylphosphine in benzene at room temperature. It is a non-hygroscopic crystalline solid (mp 221-223 °C) and soluble in CH_2Cl_2, $CHCl_3$, MeOH, EtOH and CH_3CN, but not



ATPB

in THF, Et_2O, C_6H_6 and EtOAc. Conventionally, it has been used for the Wittig olefination reaction.[1] A few years later, Hon and his coworker reported[2] the olefination reaction using acetonyltriphenylphosphonium salts containing various counter anions as shown in Scheme 1. They have observed the effect of counteranion and their reactivity for the reaction of triphenylphosphonium or triphenylarsonium salts with aldehydes. From their study, it was observed that the reactivity of these salts for Wittig reaction is counteranion dependent. The observed reactivity order was as follows: p-TSO^-<Br^-<< CF_3COO^-<<$ClCH_2COO^-$<$PhCO_2^-$, HCO_2^-, $MeCO_2^-$.



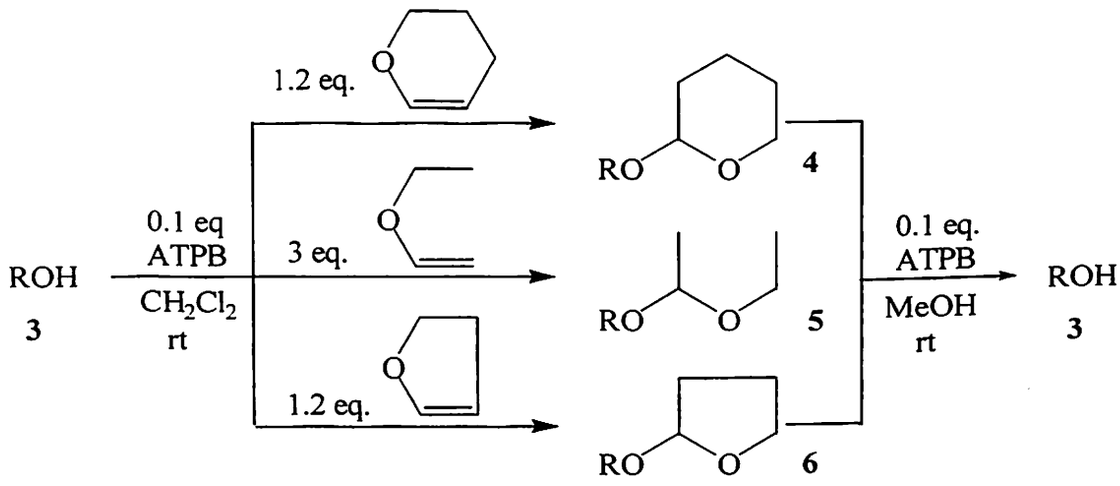
1 2

Scheme 1

To test the reactivity of different triphenylphosphonium salts, a mixture of triphenyl-phosphonium salts (1.1 mol equivalent) and 3-phenylpropanal was stirred at room temperature. Unfortunately, the triphenylphospnonium bromides or *p*-toluenesulfonates almost did not react with aldehyde at room temperature even after 24 h. However, the reaction took place within half an hour and provided excellent yields when the counteranions were acetates, benzoates or formats. This study clearly indicates that the reactivity of the phosphonium salts in Wittig reaction is counteranion dependent.

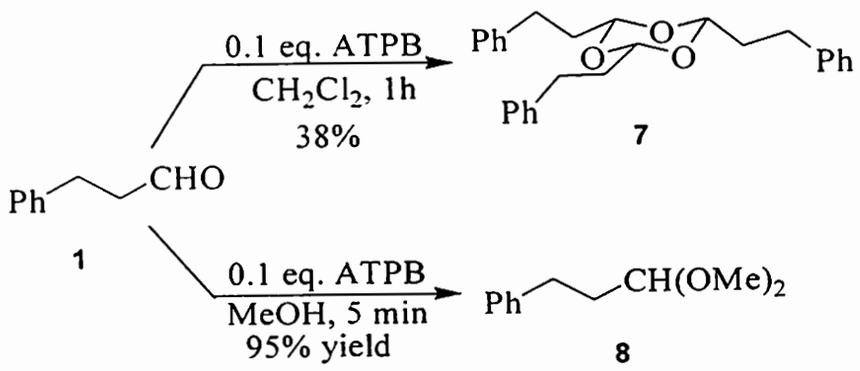
The reagent acetonyltriphenylphosphonium bromide as catalyst for organic synthesis was not explored much till 1999. The use of ATPB as a new pre-catalyst has been endorsed by the work of Hon and co-workers.[3] The catalytic activity of this reagent may be

attributed to the presence of two functionalities: one is the acidic proton α to the carbonyl group and the other one is the phosphonium center itself. They have found that it is an extremely efficient catalyst for the protection and deprotection of alcohols as alkyl vinyl ethers. Various hydroxyl compounds can be protected as THP, THF and EE (1-ethoxyethyl) ethers within a very short time in good yields in the presence of catalytic amount of acetonyltriphenylphosphonium bromide as shown in Scheme 2. The protocol is applicable to a wide range of substrates such as 1°, 2° and 3° alcohols. The advantages of this methodology are mild conditions, fast reaction rate, excellent yields and tolerance to acid-sensitive functionalities. In addition, the same catalyst can be used as well for deprotection of various ethers into the parent hydroxyl compounds.



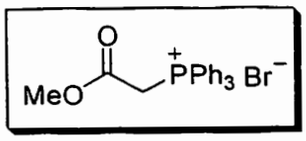
Scheme 2

Later on, the same research group exploited[4] the reagent for cyclotrimerization of various aldehydes under solvent-free conditions as shown in Scheme 3. The aldehydes tethered with a variety of functionalities, such as olefin, ether, ester, bromide, azide and diester could also be cyclotrimerized under the catalysis of ATPB. The notable advantages of this protocol are short reaction time, mild reaction conditions and very good yields.



Scheme 3

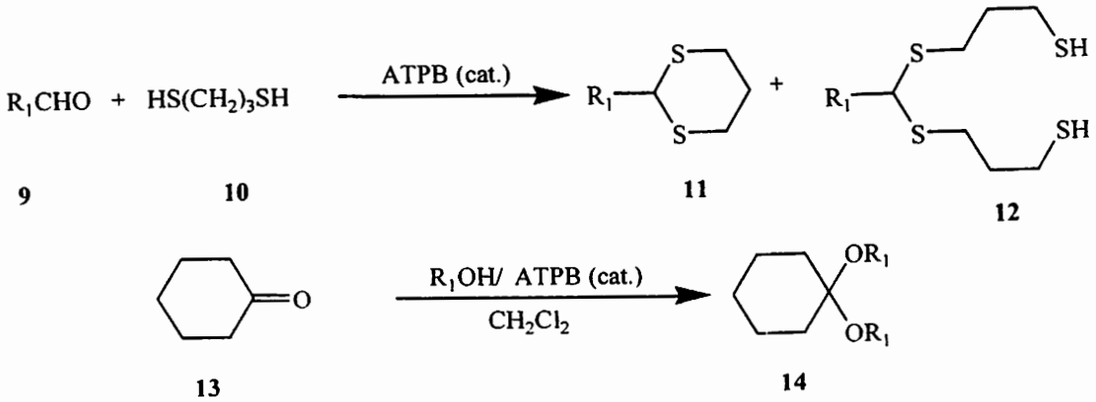
Moreover, they have noted that the substituent on the triphenylphosphonium salts affected the catalytic activity significantly for this transformation. By replacing the substituent from acetonyl (i.e. catalyst ATPB) to methoxycarbonylmethyl (i.e. catalyst **A**), the reaction was failure to provide any cyclotrimerized product.



Catalyst **A**

In continuation of their study on the application of acetonyltriphenylphosphonium bromide, they have reported explicitly about the polymer supported ATPB and their application for protection and deprotection of alcohols as alkyl vinyl ethers.[5] It has the sole advantage that only 1 mol% of the catalyst is required for the reactions.

Subsequently, in another communication Hon *et al.* demonstrated[6] that ATPB as well as poly-*p*-styryldiphenylacetonylphosphonium bromide (PATPB) is an excellent catalyst for the protection of aldehydes as acetals or thioacetals as shown in Scheme 4.



Scheme 4

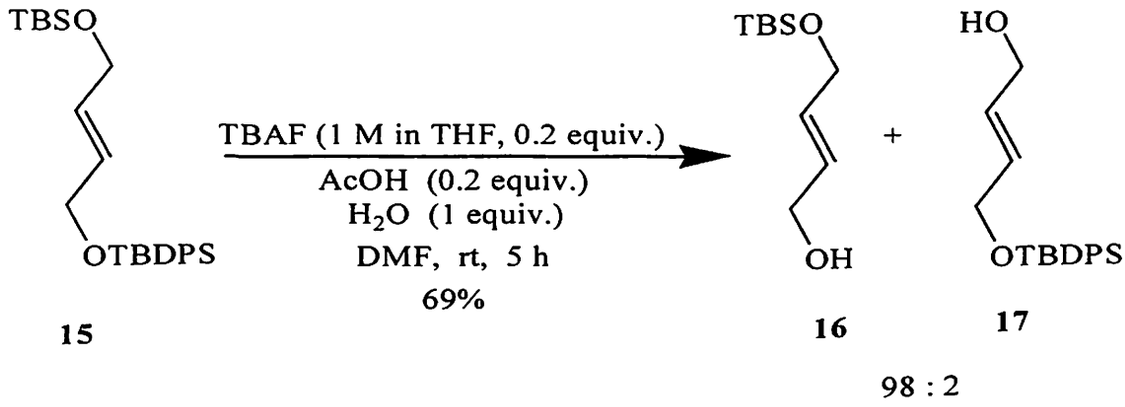
Interestingly, under the experimental condition 1,3-propandithiol reacts with aldehydes at room temperature and provides cyclic dithioacetals along with 5-10% protected dithiols **12.** Although this protocol is suitable for the protection of cyclohexanone as ketals but it is not suitable for other acyclic ketones such as acetophenone, α-tetralone and 4-phenyl-2-butanone. From the above literature survey, it seems to us that the reagent ATPB is a useful precursor for Wittig salt for the olefination reaction as well as a pre-catalyst for some organic transformations but its versatility has not been explored completely. Therefore, we were interested to explore further this reagent in various important transformations. Our research aim is to develop new methodologies for protection and deprotection chemistry by involving *in situ* generated HBr from ATPB in the reaction medium.

Protection/deprotection strategy is frequently employed for multi-steps target synthesis. The efficiency as well as effectiveness of a total synthesis directly depends on the chosen methodologies in each steps. It often requires either protection or deprotection the hydroxyl and carbonyl functionalities to manipulate other functionalities before achieving target molecule. Thus, protection and deprotection is an important transformation in organic synthesis.

Recently we have demonstrated various new methodologies particularly for protection/deprotection chemistry[7] by employing *in situ* generated dry HBr, which is actually obtained from bromodimethylsulfonium bromide. Our idea is to use generated HBr from ATPB for deprotection of *tert*-butyldimethylsilyl ethers (TBS) and acetylation of alcohols, phenol, thiols, amines and aldehydes. Therefore, the importance of the TBS ethers and the methods known for their cleavage into parent hydroxyl compounds are highlighted in the next part of the review as our intention to devise a new methodology by employing ATPB as pre-catalyst.

Among various functional groups, the protection and deprotection of hydroxyl compounds preferably alcohols play a key role in the organic synthesis of polyfunctional organic molecules and a large number of protecting groups have been used for this purpose. The ideal protecting group for an active-hydrogen moiety such as an alcohol or amine would be one that would mimic the hydrogen atom itself, but be much more flexible in its reactivity. It would readily provide high yield and be stable over a wide

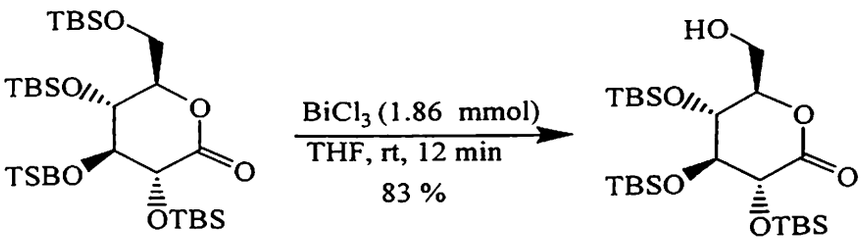
variety of reaction conditions and at the same time it should be selectively removable in the presence of other functional groups or other protecting groups. Among various protecting groups, *tert*-butyldimethylsilyl (TBS) ether is the most popular protecting group for alcohols because of its stability under a wide variety of reaction conditions, its clean NMR characteristics, and its ease of removal at the later stage. In addition, *tert*-butyl-dimethylsilyl (TBS) ether and *tert*-butyldiphenylsilyl (TBDPS) ether play a key role in carbohydrates and nucleosides due to its ease of preparation and inherent stability under basic and mild acidic conditions. Over the years, a large number of methods[8] have been developed for deprotection of TBS ethers. *n*-Tetrabutylammonium fluoride (TBAF) as a conventional reagent for desilylation of TBS ethers into hydroxyl compounds was first introduced by Corey and his co-worker.[9] Interestingly, *tert*-butyldiphenylsilyl (TBDPS) ethers can be cleaved in the presence of *tert*-butyldimethylsilyl (TBS) ethers with excellent selectivity, which are usually difficult by other methods, using a combination of a catalytic amount of TBAF, acetic acid and one equivalent amount of water in either THF or DMF[10] as shown in Scheme 5.



Scheme 5

However, TBAF has some drawbacks such as high cost as well as incompatibility with the base sensitive substrates because of the basic nature of fluoride ion and the reagent is highly moisture sensitive in nature, as a result it requires inert and dry reaction conditions. In addition, the phase transfer properties of the tetrabutylammonium cation often cause difficulties in work-up and purification of the products. After Corey's application of TBAF, many procedures have been developed for deprotection of TBS ethers using several fluoro compounds such as boron trifluoride etherate,[11] hydrofluoric acid,[12]

flurosilicic acid,[13] ammonium fluoride,[14] silicon fluoride,[15] *O*-(benzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium tetrafluoroborate (TBTU),[16] lithium tetrafluoroborate,[17] and zinc tetrafluoroborate.[18] Although these methods provide good yields still they suffer from some limitations such as incompatibility with the acid sensitive groups and requirement of longer reaction time as well as use of stoichiometric amount of reagent, dry reaction conditions etc. Similarly, literature enumerates several methods for deprotection of TBS ethers by employing chloro compounds such as cerium(III) chloride in combination with sodium iodide,[19] cerium(III) chloride alone,[20] $SnCl_2 \cdot 2H_2O$,[21] LiCl in DMF,[22] TMSCl in H_2O,[23] $ZrCl_4$[24] and CH_3COCl.[25] Similarly, BCl_3 in THF can be used for selective removal of primary TBS ethers in the presence of their secondary counterparts in carbohydrates as shown in Scheme 6.[26] The reaction condition does not affect benzyl group but isopropylidene acetal is incompatible under the experimental conditions.



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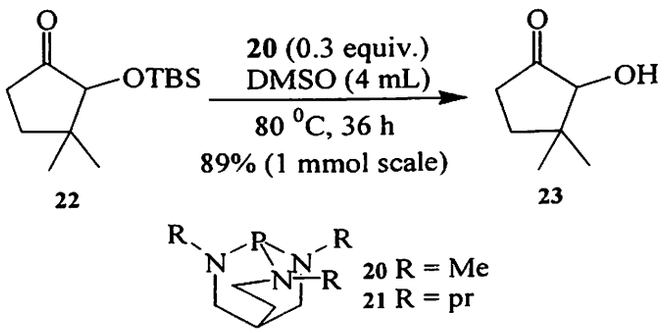
Scheme 6

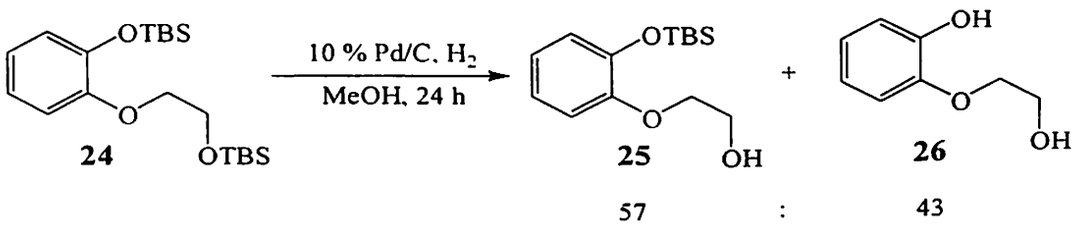
The TBS ethers of primary, secondary and tertiary alcohols as well as phenols can be deprotected with a catalytic amount of proazaphosphatranes **20** and **21** by heating at 80 °C in DMSO as shown in Scheme 7.[27] However, the reaction condition does not tolerate 1,4-dienes. Both catalysts are also much less effective (22–45% yield) for the desilylation of more hindered *tert*-butyldiphenylsilyl (TBDPS) ethers.



22 23

Scheme 7

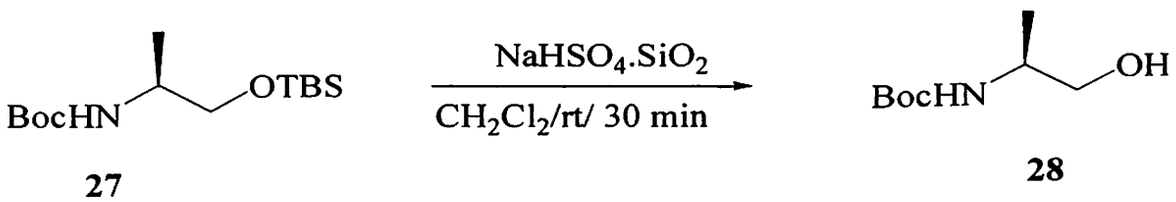
Interestingly, TBS ethers are labile under standard hydrogenations condition using 10% Pd/C in methanol[28] as shown in Scheme 8. For example, the *bis*-TBS ether **24** gives a mixture of **25** and **26** after 24 h. The reaction cannot be attributed due to acid or base contaminants since the cleavage did not take place in the absence of hydrogen. However, the unwanted cleavage can be completely suppressed by using a carbon-supported Pd–ethylenediamine complex as the catalyst.



Scheme 8

Likewise, several other methods are known in the literature for the regeneration of hydroxyl compounds from TBS ethers such as using ultrasonic cleavage in $MeOH/CCl_4$,[29] microwave heating in a mixture of acetic acid-THF and water,[30] $K_2CO_3/EtOH$,[31] Cs_2CO_3,[32] reductive cleavage by DIBAL-H,[33] DDQ,[34] CAN,[35] $I_2/MeOH$,[36] $DMSO/H_2O/90°C$,[37] $Sc(OTf)_3$,[38] $BiOClO_4$-xH_2O[39] etc. However, these methods involve either basic or high temperature conditions or oxidizing- or reducing agents, which give sometimes undesirable side products.

Recently solid supported reagent such as silica-supported sodium hydrogensulfate ($NaHSO_4$-SiO_2) has been demonstrated as an effective catalyst for selective cleavage of TBS ethers as shown in Scheme 9.[40]



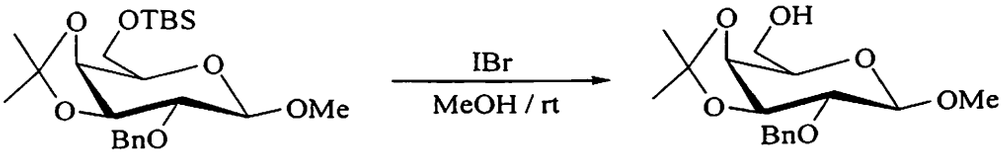
27 **28**

Scheme 9

In addition, high loading sulfonic acid-functionalized ordered nanoporous silica,[41] and phosphomolybdic acid supported on silica gel are effective catalysts for facile cleavage of TBS ethers.[42] The notable advantages of these methods are no need of aqueous work-up, and the supported catalyst as well as the solvent can be readily recovered and recycle

Very recently $TiCl_4$-Lewis base complexes has been used for selective deprotection of TBS ethers and this protocol has been utilized for the practical synthesis of 1-β-methyl-carbapenems.[43]

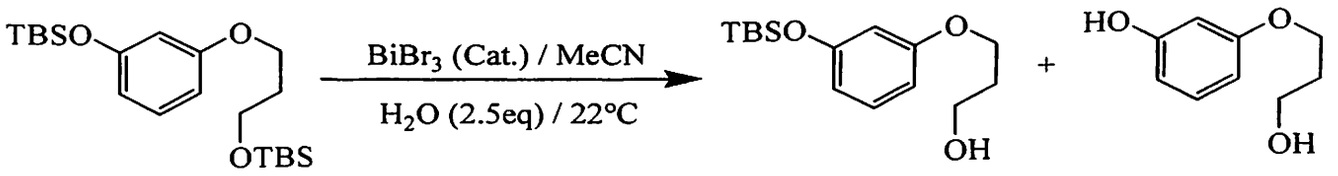
Besides these, numerous other methods are also known using bromo compounds for the same transformation eg. $ZnBr_2$,[44] CBr_4,[45] acetyl bromide,[46] *n*-tetrabutylammonium tribromide (TBATB),[47] molecular bromine[48] and bromodimethylsulfonium bromide[49] etc. Similarly, an interhalogen compound 'IBr' can be used for the deprotection of TBS ethers of simple alcohols, carbohydrates and nucleosides in methanol at room temperature.[50] A large number of sensitive functional groups such as acetals, PMB ethers, TBDPS ethers, esters and amides are stable under the experimental conditions as shown in Scheme 10. However, it fails to deprotect the substrate containing a thio group at the anomeric position of carbohydrate compounds.



29 **30**

Scheme 10

Likewise, catalytic amount of $BiBr_3$ in acetonitrile at ambient temperature is a mild and selective reagent for deprotection of TBS ethers (Scheme 11).[51] The notable advantages of this method are its chemoselectivity as well as mild reaction conditions. Prolonged reaction times lead to cleavage of aryl TBS ethers as well.



31 **32** **33**

Scheme 11

From this survey on desilylation, it is evident that most of these procedures suffer from some disadvantages such as requirement of relatively harsh reaction conditions, fail to deprotect aryl *tert*-butyldimethylsilyl ethers, require longer reaction times, use of

expensive reagent, incompatibility with other protecting groups such as thioketals or thio group at the anomeric position of the carbohydrate compounds, difficult to maintain stoichiometric ratio, difficult to handle, over oxidation, unwanted product acetate instead of alcohol and requirement of excess amount of reagents.

The cleavage of TBS ethers based on bromo reagents is primarily due to *in situ* generated HBr, which is actually responsible for cleavage of TBS ethers.[51] From the literature background on cleavage of TBS ethers, we perceived that there is a scope to devise a new methodology using ATPB as pre-catalyst. Our intention is to develop a better protocol, which will be applicable for a wide range of alkyl- and aryl TBS ethers. In addition, it might work for TBS- and TBDPS ethers under a mild reaction condition.

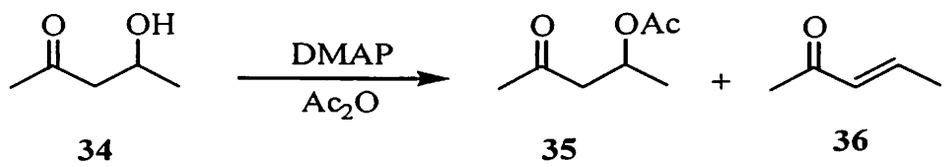
Next, the importance of acetylated products and their known method of preparation highlighted as our second goal is to find out a new methodology for acetylation of hydroxyl compounds. The acylation of alcohols, phenols, amines and thiols is another useful transformations in organic synthesis.[52] Of these, the conversion of hydroxyl group to the corresponding acetate is important due to its ease of introduction, stable under mild acidic reaction conditions and ease of removal by mild alkaline hydrolysis. The esterification is one of the most widely used techniques in organic synthesis due to the paramount importance of esters in our day to day life such as in chemicals, drugs, perfumes, food preservatives, cosmetics, pharmaceuticals and chiral auxiliaries. Among other esterification process the protection of hydroxyl compounds as their acetate derivatives i.e. acylation is one of the most vital and widely used transformations in organic synthesis. Many of the natural products of current biological importance and synthetic interest consist of highly oxygenated carbon skeleton. Most of the low molecular weight esters often have pleasant fruity smell and are often inherently responsible for odour of the fruits. One of the most common analgesics used frequently in our day-to-day life is 'aspirin' which is an acetate derivative of salicylic acid. Even Taxol, an anti cancer drug, also contains acyl ($OCOCH_3$) moiety.

On the other hand, acylation of hydroxyl compounds is one of the easy ways to protect its nucleophilicity or its other chemical reactivity, which is often requires in multi-step target oriented synthesis. Moreover, due to easy installation and tolerance to a wide variety of

reaction conditions acetylation is one of the preferred methods for the protection of hydroxyl moiety in organic synthesis.

Over the years new methods have been developed for this transformation and being added in the arsenal of Organic Chemistry literature. In this part a brief literature review on acetylation of hydroxyl functinality are highlighted.

The conventional method for acetylation of alcohols is using acetic anhydride or acetyl chloride in the presence of tertiary amine bases such as triethyl amine or pyridine. The role of the base is to activate the acylating reagent (nucleophilic activation) whereas in some cases the base e.g. triethyl amine is mainly used to trap the generated acid in the reaction medium. Pyridine is used as conventional catalyst as well as solvent for acetylation of hydroxyl compounds. Although this method is good still it suffers from some limitations such as longer reaction time, use of excess acetic anhydride and unpleasent smell of pyridine as well as tedious procedure to remove the pyridine from the reaction mixture after completion of reaction . Although DMAP (4-dimethylamino pyridine) is a better catalyst than pyridine for acylation of alcohols and phenols, it also suffers from some serious drawbacks such as for the acetylation of β-hydroxyl carbonyl compounds provides a mixture of acetates and α,β-unsaturated carbonyl compounds as shown in Scheme 12.[53]



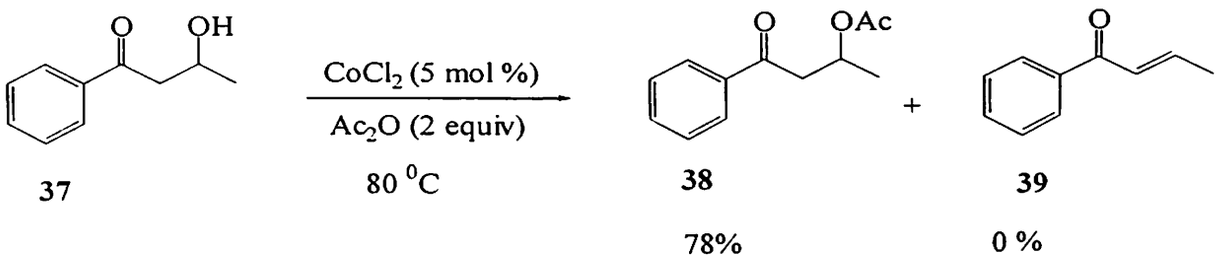
34 **35** **36**

Scheme 12

Sometimes tributylphosphine(Bu_3P) a less basic catalyst is used for the acetylation of hydroxyl functionality particularly for base sensitive substrates.[54] However, for the acetylation of tertiary alcohols it requires excess amount of catalyst (Bu_3P) and takes long reaction time. Therefore, basic catalysis is currently employed only for selective acylations.

A large number of acid catalyzed protocol are also known in the literature for acetylation reaction. Both Lewis acid and protic acids are effective for this transformation. Since these promoter strongly increases the electrophilicity of anhydrides, their action is

generally more efficient than base activation. Iqbal *et al.* demonstrated $CoCl_2$ as an effective catalyst for acylation of alcohols with acetic anhydride.[55] The β-hydroxy esters and ketones can be acylated without any elimination by employing this metal catalyst, which is difficult to get by DMAP method as shown in Scheme 13.



37 38 39

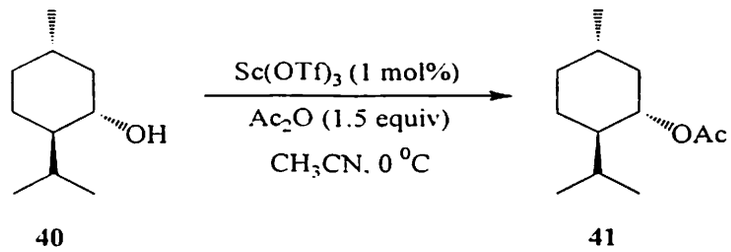
78% 0 %

Scheme 13

Although this method is applicable to a wide range of hydroxyl compounds but the major limitation of this protocol is for the acetylation of tertiary alcohols because it gives a mixture of ketones, acetoacetates, olefines, and diketene in addition to the acetate and requires harsh reaction conditions.

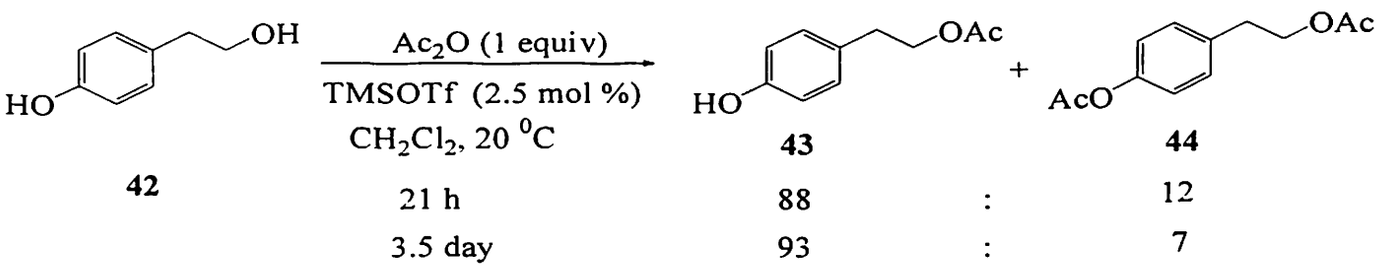
Likewise, various metal salts such as $ZnCl_2$,[56] $RuCl_3$,[57] bismuth(III) salts[58] and metal oxide such as ZnO[59] are reported as effective catalyst for acylation of alcohols with acetic anhydride. Recently, $ZrCl_4$,[60] Cp_2ZrCl_2,[61] $NbCl_5$,[62] $ZrOCl_2 \cdot 8H_2O$ using acetyl chloride[63] and $InCl_3$[64] have been introduced as effective catalyst for the same transformation. Although these methods fulfill to some extent the limitations of DMAP such as selectively primary hydroxyl group can be acylated in the presence of secondary and secondary hydroxyl group can be preferentially acylated in presence of tertiary group, but they also suffer from limitations such as cost-intensive catalyst, harsh reaction conditions, or longer reaction time etc.

Various triflates such as $Sc(OTf)_3$,[65] Me_3SiOTf,[66] $In(OTf)_3$,[67] $Cu(OTf)_2$,[68] $Ce(OTf)_3$[69] and recently $Bi(OTf)_3$[70] are reported as efficient catalyst for acylation of a wide range of hydroxyl compounds. Most of these triflates are very effective for acylation reactions and some of them are having additional advantages such the catalyst $Sc(OTf)_3$ is air stable and recyclable and acetic acid can be used instead of acetic anhydride or acetyl chloride as acetyl source as shown in Scheme 14.



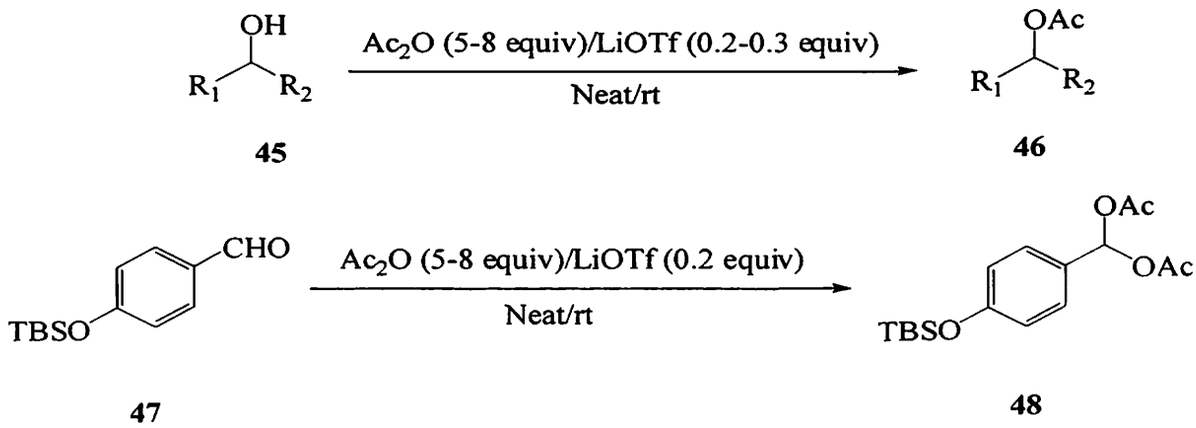
Scheme 14

The remarkable advantages of Me_3SiOTf protocol are: the procedure is clean and does not require chromatographic separation. Most of the functional groups are well tolerated under the experimental conditions. Moreover, high selectivity for acetylation of aliphatic versus phenolic hydroxyl group can be achieved by this protocol as shown in Scheme 15.



Scheme 15

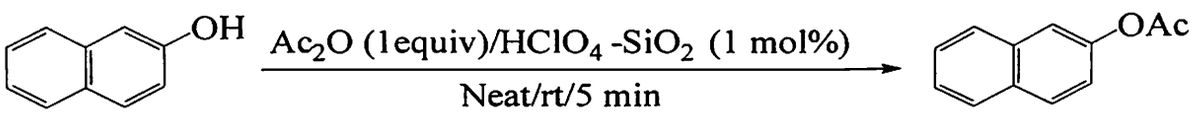
Karimi *et al.* demonstrated lithium trifluoromethanesulfonate (LiOTf)[71] as a recycleable catalyst for acetylation of alcohols and *gem*-diacylation of aldehydes under mild and neutral reaction conditions as shown in Scheme 16. Most of the acid sensitive protecting groups survive under the experimental condition.



Scheme 16

Aromatic aldehydes undergo protection as acylal at room temperature under solvent free conditions. Both hindered alcohol and highly deactivated aldehydes undergoes acylation without any difficulty using this protocol. The important drawbacks of this method are long reaction time and use of excess amount of acetic anhydride. Although triflates are efficient catalyst but due to their moisture sensitivity as well as high cost of the reagents they are inconvenient for general use.

Heterogeneous catalyst such a montmorillonite K-10 and KSF,[72] Zeolite under microwave irradiation,[73] silica sulfate,[74] $H_{14}[NaP_5W_{30}O_{110}$,[75] sulfated zirconia (SZ)[76] have gained considerable attention in recent years as effective catalysts for acetylation of alcohols, phenols and amines. Chakraborti *et al.* have shown heterogeneous catalyst perchloric acid absorbed on silica gel ($HClO_4$-SiO_2)[77] as highly efficient and versatile catalyst for acetylation of phenols, thiols, alcohols and amines. The reaction could be carried out with one equivalent of Ac_2O at room temperature in 5 to 30 minutes. $HClO_4$-SiO_2 is a better catalyst than most of the expensive metal triflates. Both acetic acid and acetic anhydride can be used for acetylation purpose by this protocol as depicted in Scheme 17. The low cost, ease of handling and solvent free conditions makes it as an environmentally friendly and industrial applicable protocol.



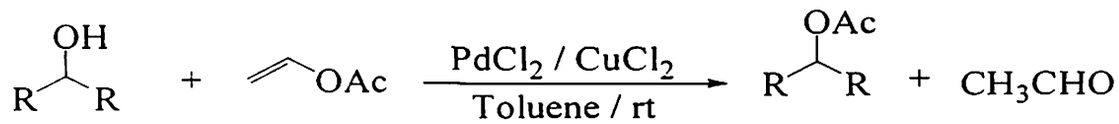
49 **50**

Scheme 17

Though perchlorates such as $TiCl_4$–$AgClO_4$,[78] $LiClO_4$,[79] $Mg(ClO_4)_2$,[80] $Zn(ClO_4)_2.6H_2O$[81] and $Cu(ClO_4)_2$[82] have been reported as effective catalysts for this transformation, but there are some serious drawbacks such as some of the perchlorates are highly explosive. In addition, $Mg(ClO_4)_2$ has to be anhydrous in order to obtain better yields.

Saikia *et al.* demonstrated vinyl acetate as an acylating reagent instead of acetic anhydride or acetic acid in presence of catalytic amount of palladium chloride[83] or molecular iodine[84] as shown in Scheme 18. As the byproduct of this method is acetaldehyde instead of acetic acid unlike other methods, thus there is a good scope that this method might be applicable for acid sensitive target molecule synthesis. But the

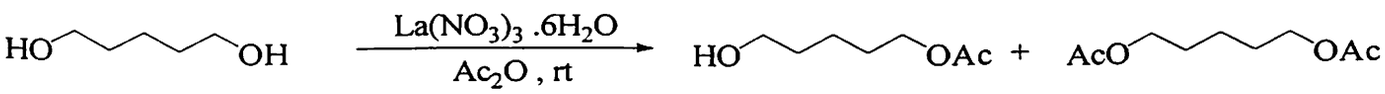
major drawback of this protocol is that tertiary alcohols, phenols, and amines are unaffected under the experimental conditions.



51 **52** **53** **54**

Scheme 18

Venkateswarlu, *et al.* showed the catalytic activity of lanthanum(III) nitrate hexahydrate[85] for effective acylation of a wide range of alcohols, phenols and amines as shown in Scheme 19. The method is compatible with acid sensitive hydroxyl protecting groups such as TBDMS, THP, OBz, OBn, Boc and some isopropylidenes and also offers excellent yields of the mono acetates of 1,3-, 1,4- and 1,5-diols.

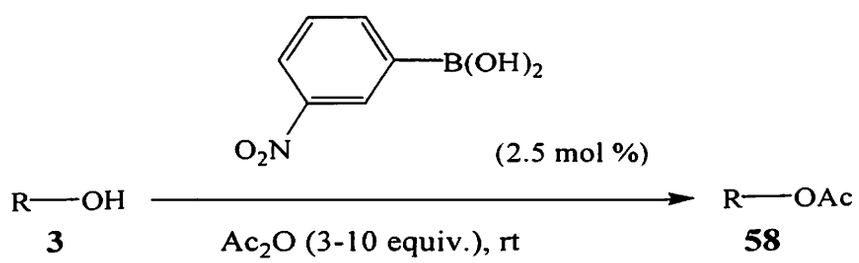


55 **80** : **20**

56 **57**

Scheme 19

Recently, 3-nitrobenzeneboronic acid[86] has been exploited as an effective catalyst for acetylation of hydroxyl compounds at room temperature under solvent free conditions (Scheme 20). The reactions are clean and the catalyst is mild such that highly sensitive functional groups including oximes are also stable to the reaction conditions.



3 **58**

Scheme 20

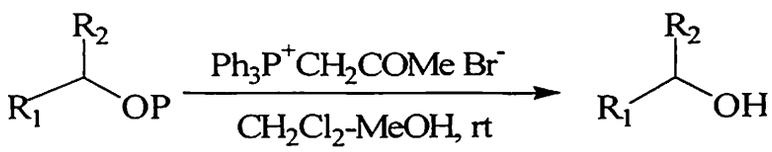
Phukan *et al.* showed the catalytic activity of molecular iodine[87] for the same transformation under solvent free conditions. Recently, molecular iodine in isopropenyl acetate[88] has been demonstrated as efficient catalyst for acylation reactions. Although literature enumerates these several methods for this fundamental transformations still some limitation remain such as long reaction times, harsh reaction conditions, the occurrence of side reactions, toxic reagents, and poor yields of the desired products and intolerance of other functional groups. Recently we have demonstrated bromodimethylsulfonium bromide (BDMS) is a useful pre-catalyst,[7a] which can generate *in situ* HBr, for acylation of alcohols, phenols, thiols and aldehydes. From the literature background as well as from our previous knowledge, we felt that a new methodology for acetylation can be developed using ATPB as new pre-catalyst.

SECTION A

PRESENT WORK ON THE DESILYLATION OF *TERT*- BUTYLDIMETHYLSILYL ETHERS USING A CATALYTIC AMOUNT OF ACETONYLTRIPHENYLPHOSPHONIUM BROMIDE (ATPB)

RESULTS AND DISCUSSION

The application of acetonyltriphenylphosphonium bromide (ATPB) and the reagents used so far for desilylation of *tert*-butyldimethylsilyl (TBS) ethers have been discussed in Part I of the Chapter I. From the literature survey, we realized that there is a scope to devise a better methodology for deprotection of TBS ethers by employing ATPB as new pre-catalyst. In continuation of our research for the development of new synthetic methodologies using a combination of new reagents[89] particularly in the field of protection/deprotection chemistry, we anticipated that acetonyltriphenylphosphonium bromide might be useful for deprotection of TBS ethers. In the present result and discussion part, our successful result for desilylation of various TBS ethers into parent hydroxyl compounds using ATPB as pre-catalyst is represented in Scheme 21.



R_1 = alkyl / aryl / sugar residue/ nucleoside residue;
R_2 = H, alkyl; P = TBS /TBDPS

Scheme 21

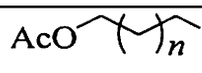
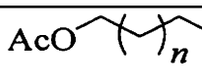
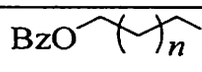
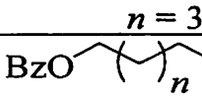
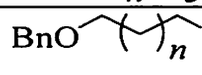
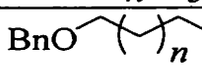
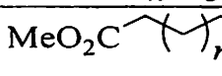
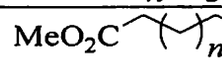
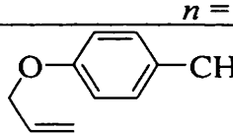
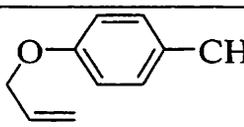
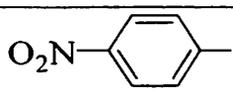
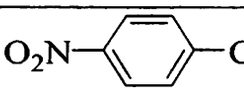
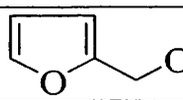
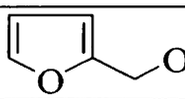
In order to verify our proposal we had to prepare a wide variety of *tert*-butyldimethylsilyl (TBS) ethers as well as *tert*-butyldiphenylsilyl (TBDPS) ethers by following the reported procedure.[9a] Next, we prepared the reagent acetonyltriphenylphosphonium bromide (ATPB) by reaction of triphenylphosphine with bromoacetone in benzene at room temperature following the literature procedure.[2] The solid ATPB was obtained by quick filtration followed by washing with benzene to remove the unreacted triphenylphosphine. First, we attempted the reaction of *tert*-butyldimethylsilyl ether **59** (1 equiv.) with 0.05 equivalents of acetonyltriphenylphosphonium bromide in dichloromethane/methanol (5:2) at room temperature. We noticed that the reaction was complete within three minutes and the pure product 5-acetoxy-1-pentanol (**56**) was obtained in 70% yield by passing the crude mixture through a silica gel column. The starting ether **59** and the product **56** was characterized by recording IR, ^{1}H NMR and ^{13}C NMR spectra which is given in (Fig **1-6**). The disappearance of the signals in the region δ 0.00 [s, 6H, $Si(CH_3)_2$], 0.85 [s, 9H, $SiC(CH_3)_3$], in ^{1}H NMR spectra clearly indicate the deprotection of *tert*-butyldimethyl silyl ether to their corresponding alcohols. In addition, the

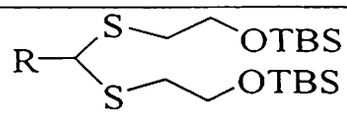
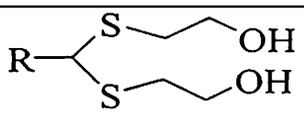
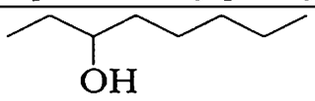
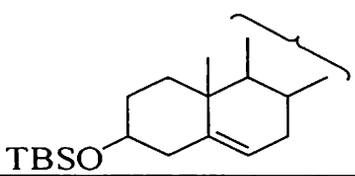
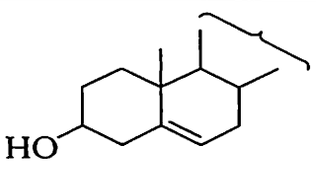
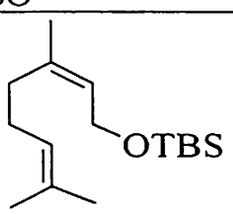
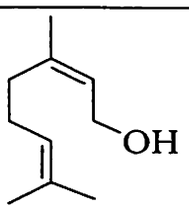
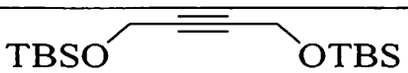
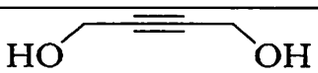
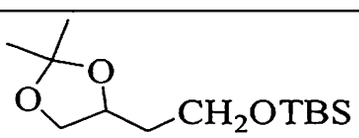
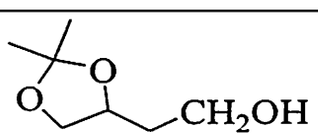
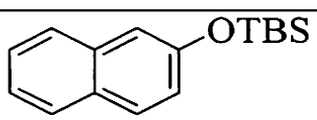
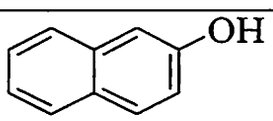
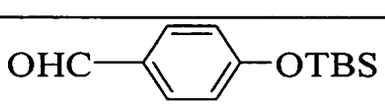
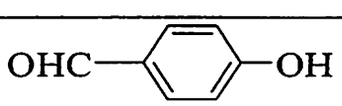
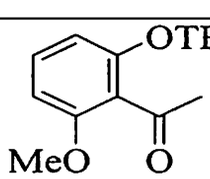
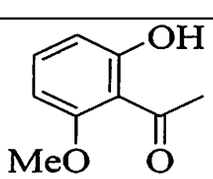
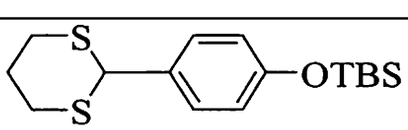
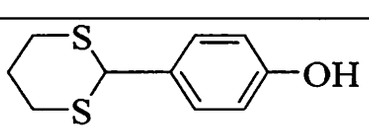
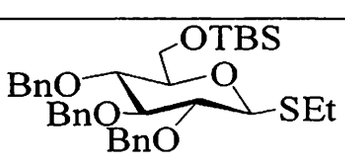
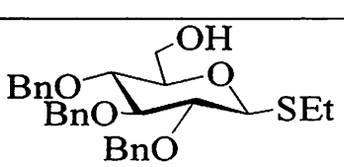
deprotected compound also exhibits a strong band at 3437 cm^{-1} in the IR spectrum which clearly indicates the presence of –OH group in the product. We found that various *tert*-butyldimethylsilyl ethers, such as **60-62** containing benzoyl, benzyl and ester groups, respectively, were smoothly deprotected to the corresponding alcohols **82-84** in good yields, without affecting these groups, under identical reaction conditions. It is worthwhile to mention that our protocol is more efficient in terms of reaction time than a recently reported procedure.[47] Similarly, other TBS ethers such as **63-65** were converted into the corresponding alcohols **85-87** in good yields by following the same procedure. It is interesting to note that no bromination occurs at the double bond or even in the furan ring under these experimental conditions. Likewise, the TBS ether **66** was easily transformed into the corresponding alcohol **88** without disturbing the thioketal group. Interestingly, the thioketal group is also cleaved when the same reaction is carried out with other bromo compounds such as tetrabutylammonium tribromide (TBATB), CBr_4 and molecular bromine. This result clearly indicates that our methodology has some additional advantages compared to the earlier reported procedures, especially those based on bromo reagents. In addition, various TBS ethers **67-68**, which were derived from secondary alcohols, were also cleaved to the corresponding alcohols **89-90** in good yields under identical reaction conditions. Again, we noticed that it took much less time for deprotection of **68** than the earlier procedures.[51] Moreover, by using our protocol, TBS ether **69** and an acetylenic TBS ether **70** were also deprotected to the desired alcohols **91** and **92** without bromination either at the double or at the triple bond. Remarkably, highly acid-sensitive TBS ether such as **71** can be cleaved to the corresponding alcohol **93** without losing the isopropylidene group.

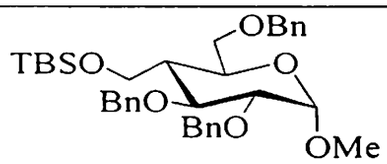
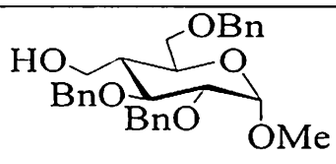
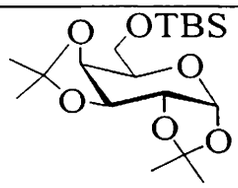
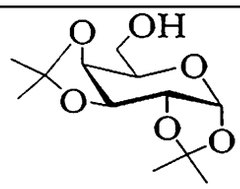
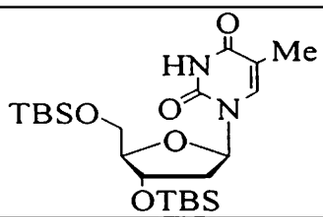
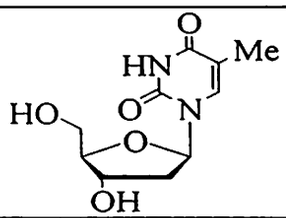
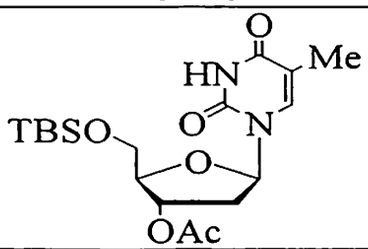
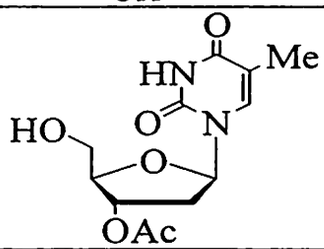
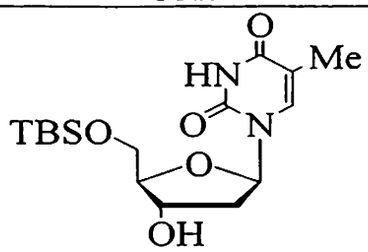
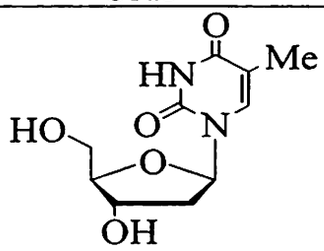
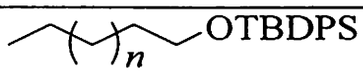
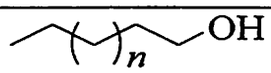
We also decided to study whether the same reagent can be employed for deprotection of aryl TBS ethers or not. We observed that various phenolic TBS ethers **72**, **47**, **73** and **74** could be converted into the respective phenolic compounds **49**, **94**, **95** and **96** without affecting a thioketal group. It is important to mention that no α-bromination was observed in the case of compound **73**, and neither was any cyclotrimerization observed in the case of the aromatic aldehyde **47**. The reactions with aryl TBS ethers take slightly longer reaction time than those with alcoholic TBS ethers. All the deprotected alcohols were characterized fully by IR and ^1H NMR spectroscopy and by elemental analysis; the spectra were compared with those of authentic samples.

We then turned our attention to whether this methodology could be further extended for deprotection of TBS ethers of carbohydrates and nucleosides. We found that various TBS ethers **75-80** can be cleaved easily to the corresponding parent hydroxyl compounds **97-101** in good yields under identical reaction conditions. Importantly, a thio group at the anomeric position usually affected by the earlier reported procedures[50] and OMe ether or an isopropylidene group at the anomeric position also survived under the experimental conditions. The reaction times and yields of all the products are summarized in Table 1. These results further encouraged us to study whether our methodology could be extended to the deprotection of *tert*-butyldiphenyl silyl (TBDPS) ethers. We found that TBDPS ether of 1-dodecanol (**81**) was also converted into the corresponding alcohol **102** in 88% yield in the presence of 0.2 equivalents of the same pre-catalyst although with a longer reaction time. The product was characterized by usual spectroscopic technique.

Table 1. Deprotection of various TBS ethers to the parent hydroxyl compounds using catalytic amount of acetonyltriphenylphosphonium bromide (ATPB) in dichloromethane-methanol

Substrate No.	Substrate	Time min/ [h]	Product[a]	Product No.	% Yield[b]
59		3		**56**	70
60		15		**82**	88
61		10		**83**	92
62		15		**84**	92
63		7		**85**	91
64		[2]		**86**	94
65		10		**87**	83

66	 R = *p*-methoxy phenyl	20	 R = *p*-methoxy phenyl	**88**	81
67		22		**89**	91
68		[2.5]		**90**	90
69		5		**91**	95
70		7		**92**	85
71		15		**93**	72
72		[6]		**49**	81
47		[5]		**94**	71
73		[3]		**95**	91
74		[4]		**96**	85
75		50		**97**	88

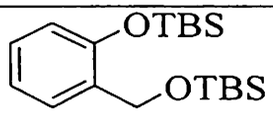
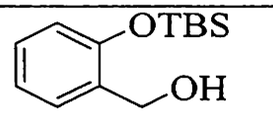
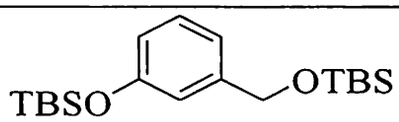
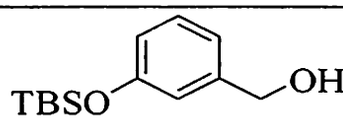
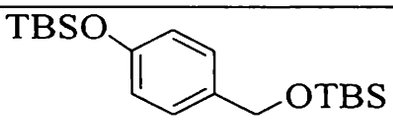
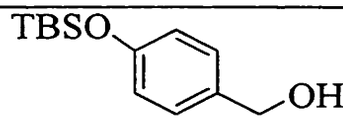
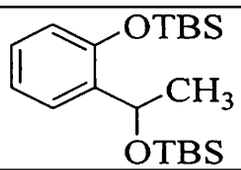
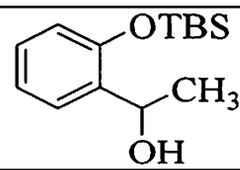
76		[2]		**98**	82
77		30		**99**	80
78		[6]		**100**	75
79		[3]		**101**	87
80		[3]		**100**	87
81	 $n = 8$	[5]	 $n = 8$	**102**	88

[a]All starting material and final products were characterized by IR, ^{1}H NMR, ^{13}C NMR and elemental analysis. [b]Isolated yield.

Interestingly, our protocol can also be further extended to the chemoselective deprotection of TBS ethers in the presence of TBDPS ether or aryl TBS ether. 1-*tert*-Butyldimethylsilyl-5-*tert*-butyldiphenylsilyl diether (**103**) and 1-*tert*-butyldimethylsilyl-8-*tert*-butyldiphenylsilyl diether (**104**) were smoothly converted into the corresponding mono TBDPS ethers chemoselectively, as shown in Table 2. Likewise, various alkyl *tert*-butyldimethylsilyl ethers **105-108** were converted into the desired mono aryl *tert*-butyldimethylsilyl ethers **111-114** in good yields. Moreover, the secondary TBS ether was also cleaved faster than the aryl TBS ether, as shown in Table 2. All the products were characterized by usual spectroscopic technique.^{1}H NMR spectrum of compound

105 is shown in figure **7** and IR, ^{1}H NMR and ^{13}C NMR spectrum of product **111** are given in figure **8-10** respectively.

Table 2. Deprotection of various TBS ethers to the parent hydroxyl compounds using catalytic amount of acetonyltriphenylphosphonium bromide (ATPB) in dichloromethane-methanol.

Substrate No	Substrate	Time min/ [h]	Product[a]	Product No.	Yield[b] [/%]
103	TBSO$(CH_2)_n$OTBDPS, $n = 3$	35	HO$(CH_2)_n$OTBDPS, $n = 3$	**109**	78
104	TBSO$(CH_2)_n$OTBDPS, $n = 6$	12	HO$(CH_2)_n$OTBDPS, $n = 6$	**110**	81
105		10		**111**	77
106		6		**112**	86
107		15		**113**	87
108		45		**114**	76

[a]All starting material and final products were characterized by IR, ^{1}H NMR, ^{13}C NMR and elemental analysis. [b]Isolated yield

The formation of the products can be rationalized as follows. We believe that HBr, generated in the reaction medium from the reaction of acetonyltriphenylphosphonium bromide with methanol, catalyzes the deprotection of TBS ethers to the corresponding alcohols. However, the same reaction failed when it was carried out with benzyltriphenylphosphonium bromide instead of acetonyltriphenylphosphonium bromide. This indicates that ATPB generates HBr much more easily than the other alkylphosphonium bromide.

In summary, we have devised a new, efficient, and regio as well as chemoselective protocol for the deprotection of TBS ethers and TBDPS ethers using a catalytic amount

of acetonyltriphenylphosphonium bromide in dichloromethane/methanol at room temperature under very mild conditions. The significant features of the present method include the ease of operation, high efficiency, mild conditions and chemoselectivity, which may be useful in organic synthesis. In addition, the selective deprotection of alkyl *tert*butyldimethylsilyl ether can be achieved in the presence of aryl-*tert*-butyldimethylsilyl ethers. We have found that a wide variety of other protecting groups, such as acetyl, benzyl, benzoyl, thioketals, esters and isopropylidene survive under the present experimental conditions.

SECTION A

DEPROTECTION OF *tert*-BUTYLDIMETHYLSILYL ETHERS INTO THE CORRESPONDING HYDROXYL COMPOUNDS USING ACETONYLTRIPHENYLPHOSPHONIUM BROMIDE (ATPB) AS A CATALYST

EXPERIMENTAL

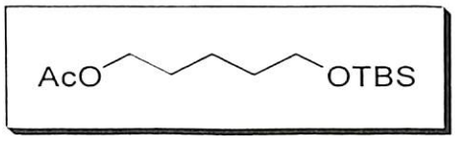
Preparation of the catalyst Acetonyltriphenylphosphonium bromide (ATPB):

To a stirred solution of triphenylphosphine (2.6 g, 10 mmol), in dry 10 mL benzene was added freshly prepared bromoacetone (1.2 g, 10 mmol) at ice-cold temperature. After 15 minute of stirring at the same temperature, the reaction mixture was allowed to stir for another 2h at room temperature. A white solid was precipitated out from the reaction mixture, which was filtered off through a Buchner funnel and the solid was washed with dry benzene to remove unreacted triphenylphosphine. The white solid was dried in desicator. The product was obtained 3.83 gm in 80 % yield. The melting point of the reagent was found to be 220-221 °C (Lit.[2] mp 221-223 °C)

General procedure for the preparation of *tert*-Butyldimethylsilyl ether of alcohols and phenols:

To a mixture of alcohol or phenol (2 mmol) and TBDMSCl (2.4 mmol) in dry CH_2Cl_2 or DMF (5 mL) was added imidazole (6 mmol) at room temperature. The reaction mixture was kept stirring until the reaction completed as shown in TLC at the same temperature. The reaction mixture was neutralized with 2N HCl solution and extracted with dichloromethane. The aqueous part was extracted once more with CH_2Cl_2. The combined organic part was dried over anhydrous Na_2SO_4 and it concentrated in rotavapor. Finally, the residue was passed through a silica gel column to obtain the desired silyl ether

5-*O*-Acetyl-1-*tert*-butyldimethylsilyloxy pentane (59):



Nature: Colourless liquid

Yield: 71% (0.37 g)

IR (Neat): 2960, 2935, 2868, 1747, 1475, 1373, 1250, 1112, 1045, 840, 779 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.36 (m, 2H, CH_2), 1.50 (m, 2H, CH_2), 1.60 (m, 2H, CH_2), 1.99 (s, 3H, $COCH_3$), 3.57 (t, 2H, J = 6.3 Hz, CH_2OTBS), 4.01 (t, 2H, J = 6.6 Hz, $AcOCH_2$) ppm.

^{13}C NMR (100MHz, $CDCl_3$): δ -5.4, 18.3, 20.9, 22.2, 25.9, 28.3, 32.3, 62.9, 64.5, 171.2 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{28}O_3Si$	C 59.95	C 59.72
260.45	H 10.83	H 10.75

Preparation of the catalyst Acetonyltriphenylphosphonium bromide (ATPB):

To a stirred solution of triphenylphosphine (2.6 g, 10 mmol), in dry 10 mL benzene was added freshly prepared bromoacetone (1.2 g, 10 mmol) at ice-cold temperature. After 15 minute of stirring at the same temperature, the reaction mixture was allowed to stir for another 2h at room temperature. A white solid was precipitated out from the reaction mixture, which was filtered off through a Buchner funnel and the solid was washed with dry benzene to remove unreacted triphenylphosphine. The white solid was dried in desicator. The product was obtained 3.83 gm in 80 % yield. The melting point of the reagent was found to be 220-221 °C (Lit.[2] mp 221-223 °C)

General procedure for the preparation of *tert*-Butyldimethylsilyl ether of alcohols and phenols:

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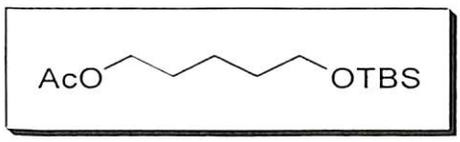
5-*O*-Acetyl-1-*tert*-butyldimethylsilyloxy pentane (59):



Nature: Colourless liquid

Yield: 71% (0.37 g)

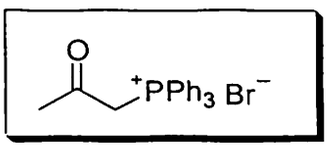
IR (Neat): 2960, 2935, 2868, 1747, 1475, 1373, 1250, 1112, 1045, 840, 779 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.36 (m, 2H, CH_2), 1.50 (m, 2H, CH_2), 1.60 (m, 2H, CH_2), 1.99 (s, 3H, $COCH_3$), 3.57 (t, 2H, J = 6.3 Hz, CH_2OTBS), 4.01 (t, 2H, J = 6.6 Hz, $AcOCH_2$) ppm.

^{13}C NMR (100MHz, $CDCl_3$): δ -5.4, 18.3, 20.9, 22.2, 25.9, 28.3, 32.3, 62.9, 64.5, 171.2 ppm.

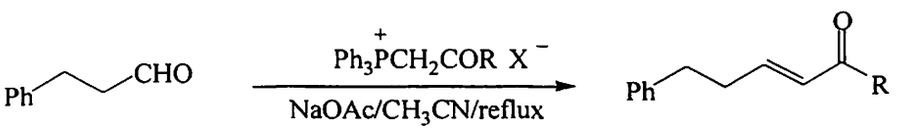
Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{28}O_3Si$	C 59.95	C 59.72
260.45	H 10.83	H 10.75

Acetonyltriphenylphosphonium bromide (ATPB) is an alkyl phosphonium salt, which can be easily prepared by stirring the reaction mixture of bromoacetone and triphenylphosphine in benzene at room temperature. It is a non-hygroscopic crystalline solid (mp 221-223 °C) and soluble in CH_2Cl_2, $CHCl_3$, MeOH, EtOH and CH_3CN, but not



ATPB

in THF, Et_2O, C_6H_6 and EtOAc. Conventionally, it has been used for the Wittig olefination reaction.[1] A few years later, Hon and his coworker reported[2] the olefination reaction using acetonyltriphenylphosphonium salts containing various counter anions as shown in Scheme 1. They have observed the effect of counteranion and their reactivity for the reaction of triphenylphosphonium or triphenylarsonium salts with aldehydes. From their study, it was observed that the reactivity of these salts for Wittig reaction is counteranion dependent. The observed reactivity order was as follows: p-TSO^-<Br^-<< CF_3COO^-<<$ClCH_2COO^-$<$PhCO_2^-$, HCO_2^-, $MeCO_2^-$.



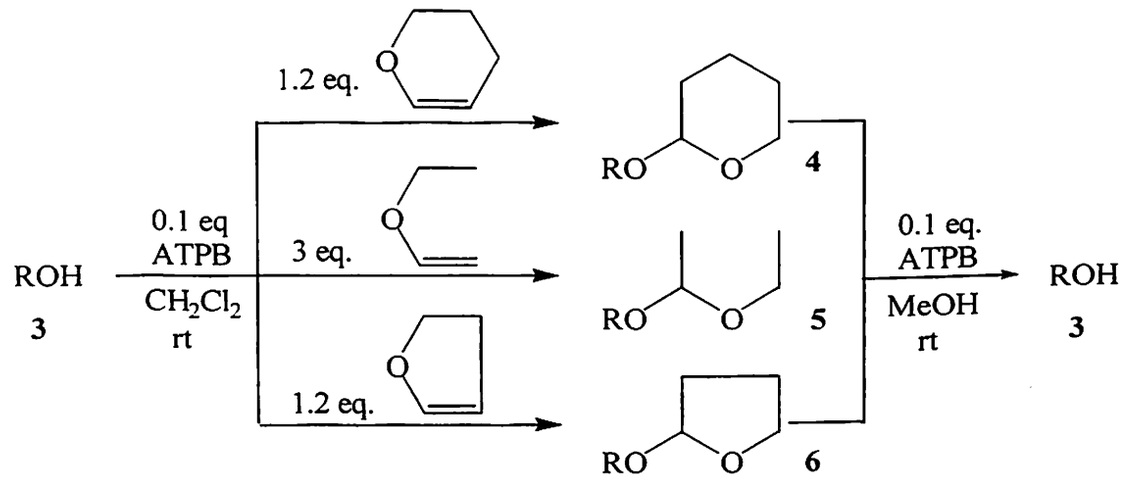
1 2

Scheme 1

To test the reactivity of different triphenylphosphonium salts, a mixture of triphenyl-phosphonium salts (1.1 mol equivalent) and 3-phenylpropanal was stirred at room temperature. Unfortunately, the triphenylphospnonium bromides or *p*-toluenesulfonates almost did not react with aldehyde at room temperature even after 24 h. However, the reaction took place within half an hour and provided excellent yields when the counteranions were acetates, benzoates or formats. This study clearly indicates that the reactivity of the phosphonium salts in Wittig reaction is counteranion dependent.

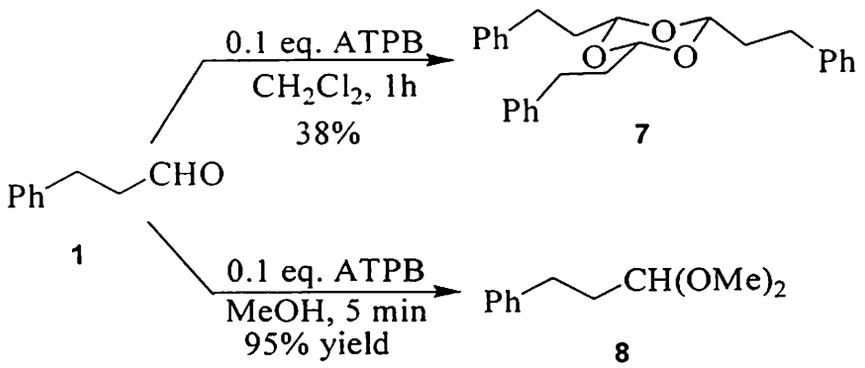
The reagent acetonyltriphenylphosphonium bromide as catalyst for organic synthesis was not explored much till 1999. The use of ATPB as a new pre-catalyst has been endorsed by the work of Hon and co-workers.[3] The catalytic activity of this reagent may be

attributed to the presence of two functionalities: one is the acidic proton α to the carbonyl group and the other one is the phosphonium center itself. They have found that it is an extremely efficient catalyst for the protection and deprotection of alcohols as alkyl vinyl ethers. Various hydroxyl compounds can be protected as THP, THF and EE (1-ethoxyethyl) ethers within a very short time in good yields in the presence of catalytic amount of acetonyltriphenylphosphonium bromide as shown in Scheme 2. The protocol is applicable to a wide range of substrates such as 1°, 2° and 3° alcohols. The advantages of this methodology are mild conditions, fast reaction rate, excellent yields and tolerance to acid-sensitive functionalities. In addition, the same catalyst can be used as well for deprotection of various ethers into the parent hydroxyl compounds.



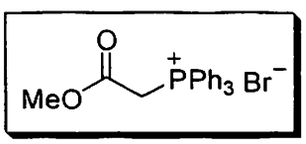
Scheme 2

Later on, the same research group exploited[4] the reagent for cyclotrimerization of various aldehydes under solvent-free conditions as shown in Scheme 3. The aldehydes tethered with a variety of functionalities, such as olefin, ether, ester, bromide, azide and diester could also be cyclotrimerized under the catalysis of ATPB. The notable advantages of this protocol are short reaction time, mild reaction conditions and very good yields.



Scheme 3

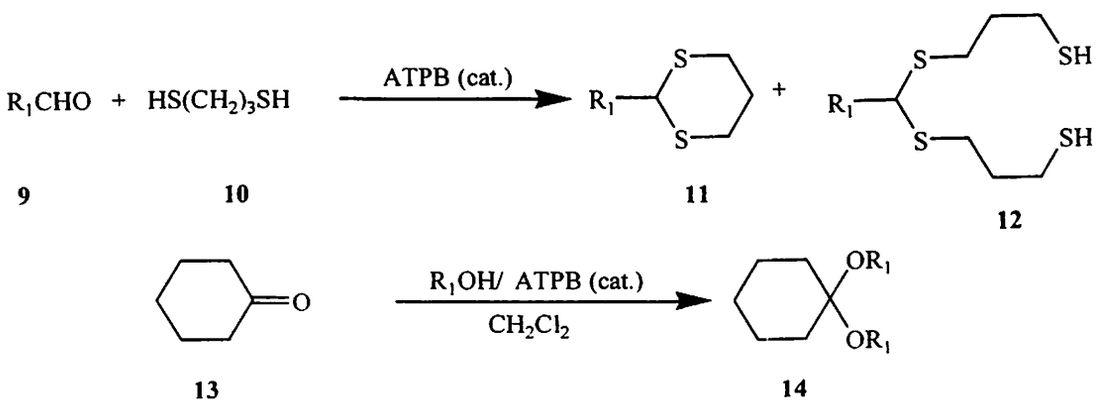
Moreover, they have noted that the substituent on the triphenylphosphonium salts affected the catalytic activity significantly for this transformation. By replacing the substituent from acetonyl (i.e. catalyst ATPB) to methoxycarbonylmethyl (i.e. catalyst **A**), the reaction was failure to provide any cyclotrimerized product.



Catalyst **A**

In continuation of their study on the application of acetonyltriphenylphosphonium bromide, they have reported explicitly about the polymer supported ATPB and their application for protection and deprotection of alcohols as alkyl vinyl ethers.[5] It has the sole advantage that only 1 mol% of the catalyst is required for the reactions.

Subsequently, in another communication Hon *et al.* demonstrated[6] that ATPB as well as poly-*p*-styryldiphenylacetonylphosphonium bromide (PATPB) is an excellent catalyst for the protection of aldehydes as acetals or thioacetals as shown in Scheme 4.



Scheme 4

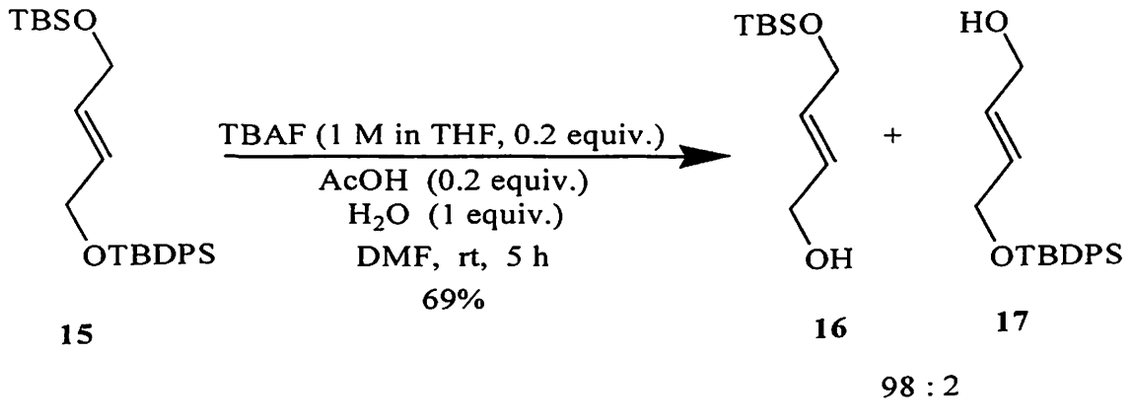
Interestingly, under the experimental condition 1,3-propandithiol reacts with aldehydes at room temperature and provides cyclic dithioacetals along with 5-10% protected dithiols **12.** Although this protocol is suitable for the protection of cyclohexanone as ketals but it is not suitable for other acyclic ketones such as acetophenone, α-tetralone and 4-phenyl-2-butanone. From the above literature survey, it seems to us that the reagent ATPB is a useful precursor for Wittig salt for the olefination reaction as well as a pre-catalyst for some organic transformations but its versatility has not been explored completely. Therefore, we were interested to explore further this reagent in various important transformations. Our research aim is to develop new methodologies for protection and deprotection chemistry by involving *in situ* generated HBr from ATPB in the reaction medium.

Protection/deprotection strategy is frequently employed for multi-steps target synthesis. The efficiency as well as effectiveness of a total synthesis directly depends on the chosen methodologies in each steps. It often requires either protection or deprotection the hydroxyl and carbonyl functionalities to manipulate other functionalities before achieving target molecule. Thus, protection and deprotection is an important transformation in organic synthesis.

Recently we have demonstrated various new methodologies particularly for protection/deprotection chemistry[7] by employing *in situ* generated dry HBr, which is actually obtained from bromodimethylsulfonium bromide. Our idea is to use generated HBr from ATPB for deprotection of *tert*-butyldimethylsilyl ethers (TBS) and acetylation of alcohols, phenol, thiols, amines and aldehydes. Therefore, the importance of the TBS ethers and the methods known for their cleavage into parent hydroxyl compounds are highlighted in the next part of the review as our intention to devise a new methodology by employing ATPB as pre-catalyst.

Among various functional groups, the protection and deprotection of hydroxyl compounds preferably alcohols play a key role in the organic synthesis of polyfunctional organic molecules and a large number of protecting groups have been used for this purpose. The ideal protecting group for an active-hydrogen moiety such as an alcohol or amine would be one that would mimic the hydrogen atom itself, but be much more flexible in its reactivity. It would readily provide high yield and be stable over a wide

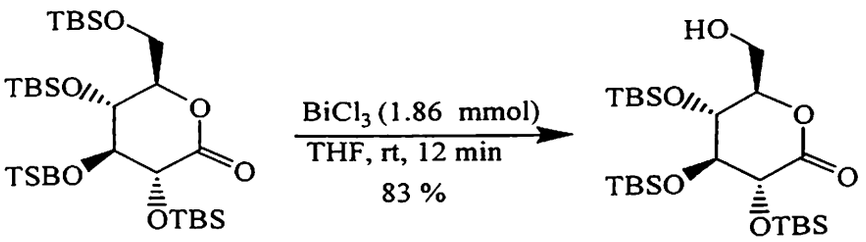
variety of reaction conditions and at the same time it should be selectively removable in the presence of other functional groups or other protecting groups. Among various protecting groups, *tert*-butyldimethylsilyl (TBS) ether is the most popular protecting group for alcohols because of its stability under a wide variety of reaction conditions, its clean NMR characteristics, and its ease of removal at the later stage. In addition, *tert*-butyl-dimethylsilyl (TBS) ether and *tert*-butyldiphenylsilyl (TBDPS) ether play a key role in carbohydrates and nucleosides due to its ease of preparation and inherent stability under basic and mild acidic conditions. Over the years, a large number of methods[8] have been developed for deprotection of TBS ethers. *n*-Tetrabutylammonium fluoride (TBAF) as a conventional reagent for desilylation of TBS ethers into hydroxyl compounds was first introduced by Corey and his co-worker.[9] Interestingly, *tert*-butyldiphenylsilyl (TBDPS) ethers can be cleaved in the presence of *tert*-butyldimethylsilyl (TBS) ethers with excellent selectivity, which are usually difficult by other methods, using a combination of a catalytic amount of TBAF, acetic acid and one equivalent amount of water in either THF or DMF[10] as shown in Scheme 5.



Scheme 5

However, TBAF has some drawbacks such as high cost as well as incompatibility with the base sensitive substrates because of the basic nature of fluoride ion and the reagent is highly moisture sensitive in nature, as a result it requires inert and dry reaction conditions. In addition, the phase transfer properties of the tetrabutylammonium cation often cause difficulties in work-up and purification of the products. After Corey's application of TBAF, many procedures have been developed for deprotection of TBS ethers using several fluoro compounds such as boron trifluoride etherate,[11] hydrofluoric acid,[12]

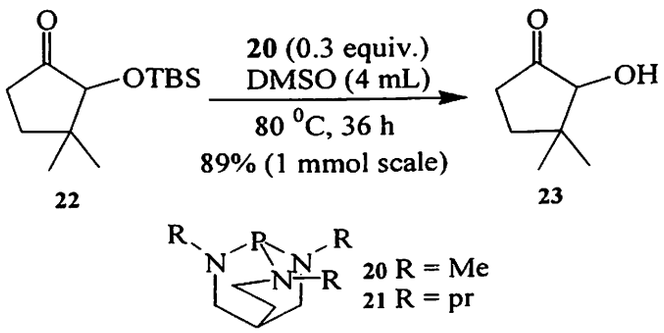
flurosilicic acid,[13] ammonium fluoride,[14] silicon fluoride,[15] *O*-(benzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium tetrafluoroborate (TBTU),[16] lithium tetrafluoroborate,[17] and zinc tetrafluoroborate.[18] Although these methods provide good yields still they suffer from some limitations such as incompatibility with the acid sensitive groups and requirement of longer reaction time as well as use of stoichiometric amount of reagent, dry reaction conditions etc. Similarly, literature enumerates several methods for deprotection of TBS ethers by employing chloro compounds such as cerium(III) chloride in combination with sodium iodide,[19] cerium(III) chloride alone,[20] $SnCl_2 \cdot 2H_2O$,[21] LiCl in DMF,[22] TMSCl in H_2O,[23] $ZrCl_4$[24] and CH_3COCl.[25] Similarly, BCl_3 in THF can be used for selective removal of primary TBS ethers in the presence of their secondary counterparts in carbohydrates as shown in Scheme 6.[26] The reaction condition does not affect benzyl group but isopropylidene acetal is incompatible under the experimental conditions.



18 19

Scheme 6

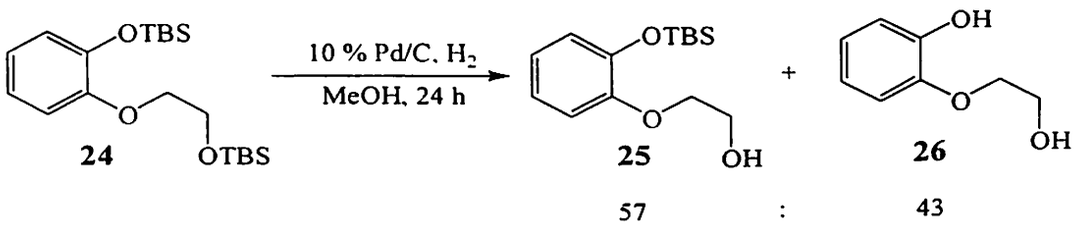
The TBS ethers of primary, secondary and tertiary alcohols as well as phenols can be deprotected with a catalytic amount of proazaphosphatranes **20** and **21** by heating at 80 °C in DMSO as shown in Scheme 7.[27] However, the reaction condition does not tolerate 1,4-dienes. Both catalysts are also much less effective (22–45% yield) for the desilylation of more hindered *tert*-butyldiphenylsilyl (TBDPS) ethers.



22 23

Scheme 7

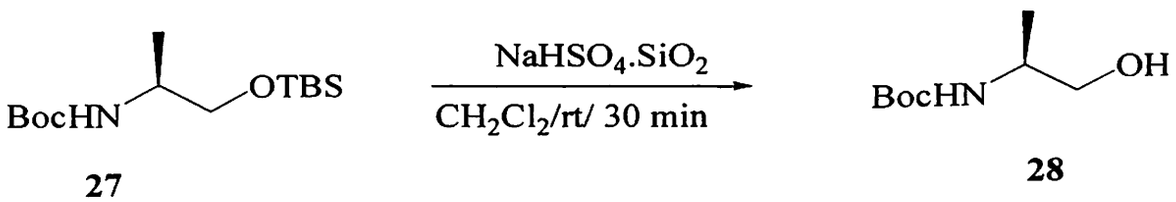
Interestingly, TBS ethers are labile under standard hydrogenations condition using 10% Pd/C in methanol[28] as shown in Scheme 8. For example, the *bis*-TBS ether **24** gives a mixture of **25** and **26** after 24 h. The reaction cannot be attributed due to acid or base contaminants since the cleavage did not take place in the absence of hydrogen. However, the unwanted cleavage can be completely suppressed by using a carbon-supported Pd–ethylenediamine complex as the catalyst.



Scheme 8

Likewise, several other methods are known in the literature for the regeneration of hydroxyl compounds from TBS ethers such as using ultrasonic cleavage in $MeOH/CCl_4$,[29] microwave heating in a mixture of acetic acid-THF and water,[30] $K_2CO_3/EtOH$,[31] Cs_2CO_3,[32] reductive cleavage by DIBAL-H,[33] DDQ,[34] CAN,[35] $I_2/MeOH$,[36] $DMSO/H_2O/90°C$,[37] $Sc(OTf)_3$,[38] $BiOClO_4$-xH_2O[39] etc. However, these methods involve either basic or high temperature conditions or oxidizing- or reducing agents, which give sometimes undesirable side products.

Recently solid supported reagent such as silica-supported sodium hydrogensulfate ($NaHSO_4$-SiO_2) has been demonstrated as an effective catalyst for selective cleavage of TBS ethers as shown in Scheme 9.[40]



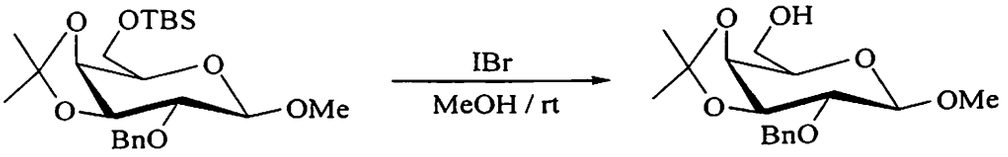
27 **28**

Scheme 9

In addition, high loading sulfonic acid-functionalized ordered nanoporous silica,[41] and phosphomolybdic acid supported on silica gel are effective catalysts for facile cleavage of TBS ethers.[42] The notable advantages of these methods are no need of aqueous work-up, and the supported catalyst as well as the solvent can be readily recovered and recycle

Very recently $TiCl_4$-Lewis base complexes has been used for selective deprotection of TBS ethers and this protocol has been utilized for the practical synthesis of 1-β-methyl-carbapenems.[43]

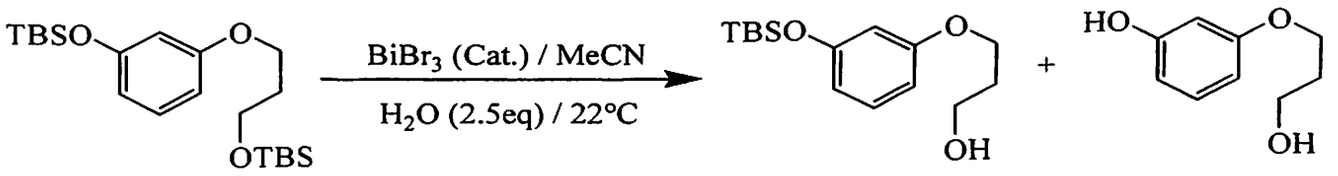
Besides these, numerous other methods are also known using bromo compounds for the same transformation eg. $ZnBr_2$,[44] CBr_4,[45] acetyl bromide,[46] *n*-tetrabutylammonium tribromide (TBATB),[47] molecular bromine[48] and bromodimethylsulfonium bromide[49] etc. Similarly, an interhalogen compound 'IBr' can be used for the deprotection of TBS ethers of simple alcohols, carbohydrates and nucleosides in methanol at room temperature.[50] A large number of sensitive functional groups such as acetals, PMB ethers, TBDPS ethers, esters and amides are stable under the experimental conditions as shown in Scheme 10. However, it fails to deprotect the substrate containing a thio group at the anomeric position of carbohydrate compounds.



29 **30**

Scheme 10

Likewise, catalytic amount of $BiBr_3$ in acetonitrile at ambient temperature is a mild and selective reagent for deprotection of TBS ethers (Scheme 11).[51] The notable advantages of this method are its chemoselectivity as well as mild reaction conditions. Prolonged reaction times lead to cleavage of aryl TBS ethers as well.



31 **32** **33**

Scheme 11

From this survey on desilylation, it is evident that most of these procedures suffer from some disadvantages such as requirement of relatively harsh reaction conditions, fail to deprotect aryl *tert*-butyldimethylsilyl ethers, require longer reaction times, use of

expensive reagent, incompatibility with other protecting groups such as thioketals or thio group at the anomeric position of the carbohydrate compounds, difficult to maintain stoichiometric ratio, difficult to handle, over oxidation, unwanted product acetate instead of alcohol and requirement of excess amount of reagents.

The cleavage of TBS ethers based on bromo reagents is primarily due to *in situ* generated HBr, which is actually responsible for cleavage of TBS ethers.[51] From the literature background on cleavage of TBS ethers, we perceived that there is a scope to devise a new methodology using ATPB as pre-catalyst. Our intention is to develop a better protocol, which will be applicable for a wide range of alkyl- and aryl TBS ethers. In addition, it might work for TBS- and TBDPS ethers under a mild reaction condition.

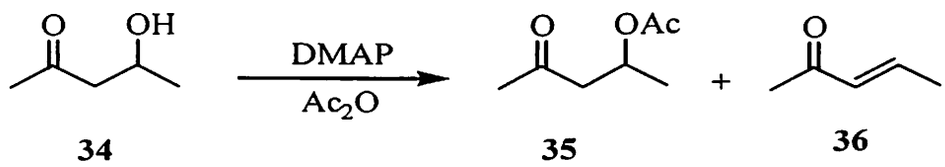
Next, the importance of acetylated products and their known method of preparation highlighted as our second goal is to find out a new methodology for acetylation of hydroxyl compounds. The acylation of alcohols, phenols, amines and thiols is another useful transformations in organic synthesis.[52] Of these, the conversion of hydroxyl group to the corresponding acetate is important due to its ease of introduction, stable under mild acidic reaction conditions and ease of removal by mild alkaline hydrolysis. The esterification is one of the most widely used techniques in organic synthesis due to the paramount importance of esters in our day to day life such as in chemicals, drugs, perfumes, food preservatives, cosmetics, pharmaceuticals and chiral auxiliaries. Among other esterification process the protection of hydroxyl compounds as their acetate derivatives i.e. acylation is one of the most vital and widely used transformations in organic synthesis. Many of the natural products of current biological importance and synthetic interest consist of highly oxygenated carbon skeleton. Most of the low molecular weight esters often have pleasant fruity smell and are often inherently responsible for odour of the fruits. One of the most common analgesics used frequently in our day-to-day life is 'aspirin' which is an acetate derivative of salicylic acid. Even Taxol, an anti cancer drug, also contains acyl ($OCOCH_3$) moiety.

On the other hand, acylation of hydroxyl compounds is one of the easy ways to protect its nucleophilicity or its other chemical reactivity, which is often requires in multi-step target oriented synthesis. Moreover, due to easy installation and tolerance to a wide variety of

reaction conditions acetylation is one of the preferred methods for the protection of hydroxyl moiety in organic synthesis.

Over the years new methods have been developed for this transformation and being added in the arsenal of Organic Chemistry literature. In this part a brief literature review on acetylation of hydroxyl functinality are highlighted.

The conventional method for acetylation of alcohols is using acetic anhydride or acetyl chloride in the presence of tertiary amine bases such as triethyl amine or pyridine. The role of the base is to activate the acylating reagent (nucleophilic activation) whereas in some cases the base e.g. triethyl amine is mainly used to trap the generated acid in the reaction medium. Pyridine is used as conventional catalyst as well as solvent for acetylation of hydroxyl compounds. Although this method is good still it suffers from some limitations such as longer reaction time, use of excess acetic anhydride and unpleasent smell of pyridine as well as tedious procedure to remove the pyridine from the reaction mixture after completion of reaction . Although DMAP (4-dimethylamino pyridine) is a better catalyst than pyridine for acylation of alcohols and phenols, it also suffers from some serious drawbacks such as for the acetylation of β-hydroxyl carbonyl compounds provides a mixture of acetates and α,β-unsaturated carbonyl compounds as shown in Scheme 12.[53]



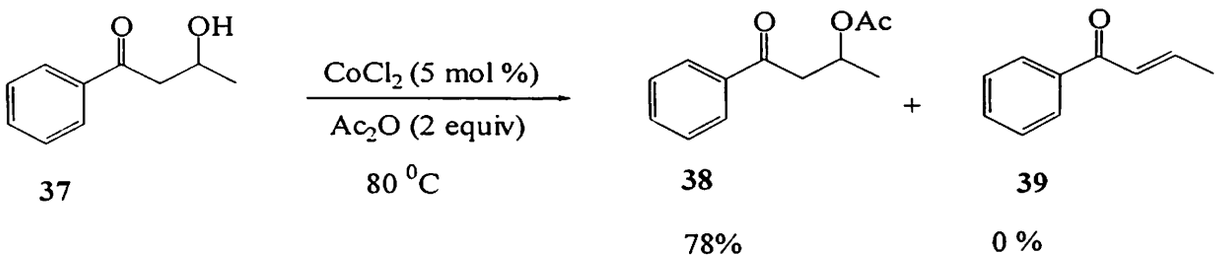
34 **35** **36**

Scheme 12

Sometimes tributylphosphine(Bu_3P) a less basic catalyst is used for the acetylation of hydroxyl functionality particularly for base sensitive substrates.[54] However, for the acetylation of tertiary alcohols it requires excess amount of catalyst (Bu_3P) and takes long reaction time. Therefore, basic catalysis is currently employed only for selective acylations.

A large number of acid catalyzed protocol are also known in the literature for acetylation reaction. Both Lewis acid and protic acids are effective for this transformation. Since these promoter strongly increases the electrophilicity of anhydrides, their action is

generally more efficient than base activation. Iqbal *et al.* demonstrated $CoCl_2$ as an effective catalyst for acylation of alcohols with acetic anhydride.[55] The β-hydroxy esters and ketones can be acylated without any elimination by employing this metal catalyst, which is difficult to get by DMAP method as shown in Scheme 13.



37 38 39

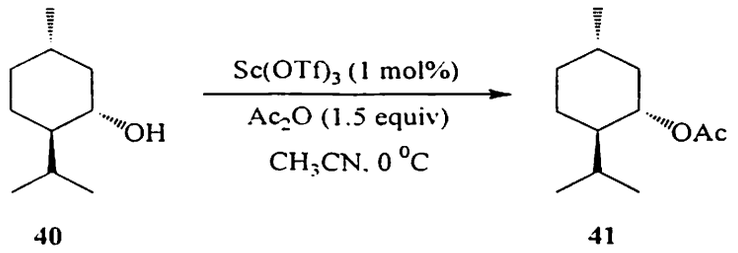
78% 0 %

Scheme 13

Although this method is applicable to a wide range of hydroxyl compounds but the major limitation of this protocol is for the acetylation of tertiary alcohols because it gives a mixture of ketones, acetoacetates, olefines, and diketene in addition to the acetate and requires harsh reaction conditions.

Likewise, various metal salts such as $ZnCl_2$,[56] $RuCl_3$,[57] bismuth(III) salts[58] and metal oxide such as ZnO[59] are reported as effective catalyst for acylation of alcohols with acetic anhydride. Recently, $ZrCl_4$,[60] Cp_2ZrCl_2,[61] $NbCl_5$,[62] $ZrOCl_2 \cdot 8H_2O$ using acetyl chloride[63] and $InCl_3$[64] have been introduced as effective catalyst for the same transformation. Although these methods fulfill to some extent the limitations of DMAP such as selectively primary hydroxyl group can be acylated in the presence of secondary and secondary hydroxyl group can be preferentially acylated in presence of tertiary group, but they also suffer from limitations such as cost-intensive catalyst, harsh reaction conditions, or longer reaction time etc.

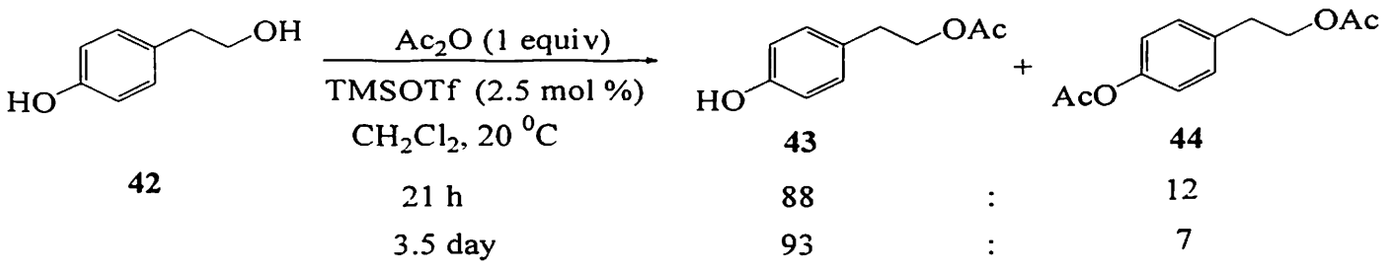
Various triflates such as $Sc(OTf)_3$,[65] Me_3SiOTf,[66] $In(OTf)_3$,[67] $Cu(OTf)_2$,[68] $Ce(OTf)_3$[69] and recently $Bi(OTf)_3$[70] are reported as efficient catalyst for acylation of a wide range of hydroxyl compounds. Most of these triflates are very effective for acylation reactions and some of them are having additional advantages such the catalyst $Sc(OTf)_3$ is air stable and recyclable and acetic acid can be used instead of acetic anhydride or acetyl chloride as acetyl source as shown in Scheme 14.



40 41

Scheme 14

The remarkable advantages of Me_3SiOTf protocol are: the procedure is clean and does not require chromatographic separation. Most of the functional groups are well tolerated under the experimental conditions. Moreover, high selectivity for acetylation of aliphatic versus phenolic hydroxyl group can be achieved by this protocol as shown in Scheme 15.

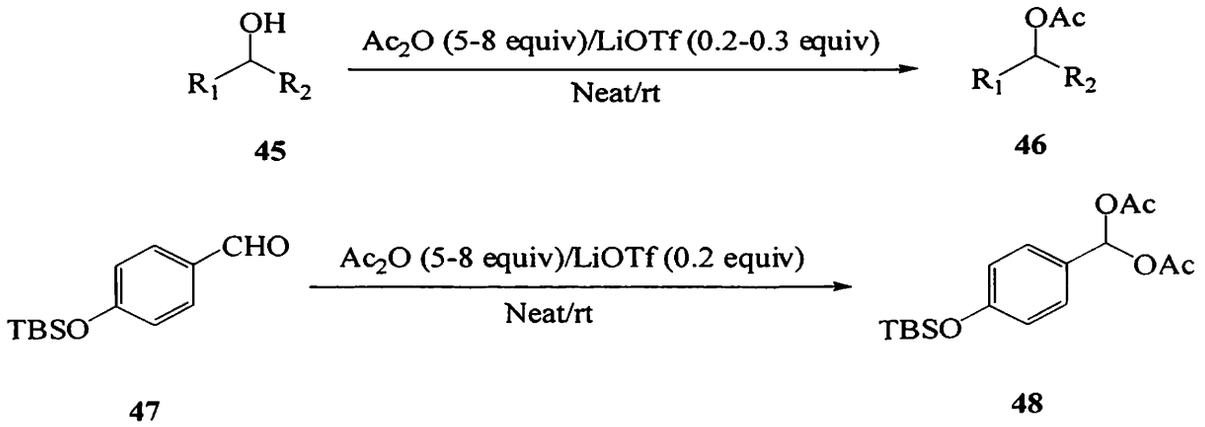


42 43 44

21 h	88	:	12
3.5 day	93	:	7

Scheme 15

Karimi *et al.* demonstrated lithium trifluoromethanesulfonate (LiOTf)[71] as a recycleable catalyst for acetylation of alcohols and *gem*-diacylation of aldehydes under mild and neutral reaction conditions as shown in Scheme 16. Most of the acid sensitive protecting groups survive under the experimental condition.



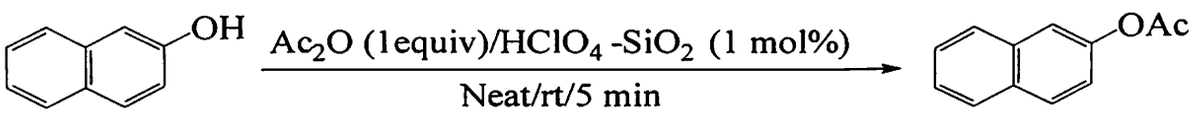
45 46

47 48

Scheme 16

Aromatic aldehydes undergo protection as acylal at room temperature under solvent free conditions. Both hindered alcohol and highly deactivated aldehydes undergoes acylation without any difficulty using this protocol. The important drawbacks of this method are long reaction time and use of excess amount of acetic anhydride. Although triflates are efficient catalyst but due to their moisture sensitivity as well as high cost of the reagents they are inconvenient for general use.

Heterogeneous catalyst such a montmorillonite K-10 and KSF,[72] Zeolite under microwave irradiation,[73] silica sulfate,[74] $H_{14}[NaP_5W_{30}O_{110}$,[75] sulfated zirconia (SZ)[76] have gained considerable attention in recent years as effective catalysts for acetylation of alcohols, phenols and amines. Chakraborti *et al.* have shown heterogeneous catalyst perchloric acid absorbed on silica gel ($HClO_4$-SiO_2)[77] as highly efficient and versatile catalyst for acetylation of phenols, thiols, alcohols and amines. The reaction could be carried out with one equivalent of Ac_2O at room temperature in 5 to 30 minutes. $HClO_4$-SiO_2 is a better catalyst than most of the expensive metal triflates. Both acetic acid and acetic anhydride can be used for acetylation purpose by this protocol as depicted in Scheme 17. The low cost, ease of handling and solvent free conditions makes it as an environmentally friendly and industrial applicable protocol.



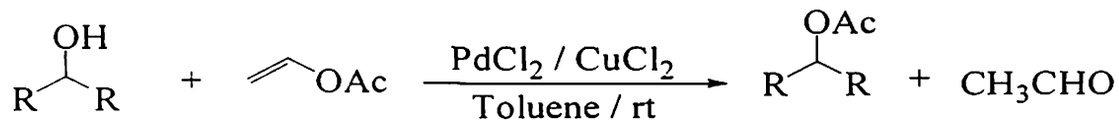
49 **50**

Scheme 17

Though perchlorates such as $TiCl_4$–$AgClO_4$,[78] $LiClO_4$,[79] $Mg(ClO_4)_2$,[80] $Zn(ClO_4)_2.6H_2O$[81] and $Cu(ClO_4)_2$[82] have been reported as effective catalysts for this transformation, but there are some serious drawbacks such as some of the perchlorates are highly explosive. In addition, $Mg(ClO_4)_2$ has to be anhydrous in order to obtain better yields.

Saikia *et al.* demonstrated vinyl acetate as an acylating reagent instead of acetic anhydride or acetic acid in presence of catalytic amount of palladium chloride[83] or molecular iodine[84] as shown in Scheme 18. As the byproduct of this method is acetaldehyde instead of acetic acid unlike other methods, thus there is a good scope that this method might be applicable for acid sensitive target molecule synthesis. But the

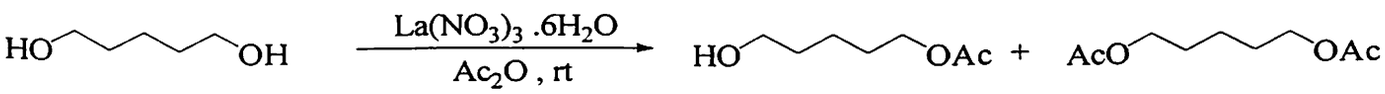
major drawback of this protocol is that tertiary alcohols, phenols, and amines are unaffected under the experimental conditions.



51 **52** **53** **54**

Scheme 18

Venkateswarlu, *et al.* showed the catalytic activity of lanthanum(III) nitrate hexahydrate[85] for effective acylation of a wide range of alcohols, phenols and amines as shown in Scheme 19. The method is compatible with acid sensitive hydroxyl protecting groups such as TBDMS, THP, OBz, OBn, Boc and some isopropylidenes and also offers excellent yields of the mono acetates of 1,3-, 1,4- and 1,5-diols.

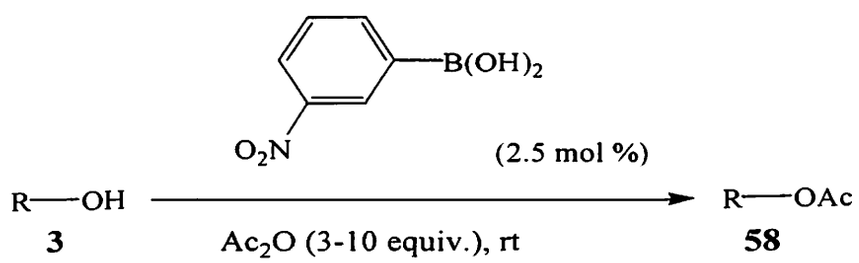


55 **80** : **20**

56 **57**

Scheme 19

Recently, 3-nitrobenzeneboronic acid[86] has been exploited as an effective catalyst for acetylation of hydroxyl compounds at room temperature under solvent free conditions (Scheme 20). The reactions are clean and the catalyst is mild such that highly sensitive functional groups including oximes are also stable to the reaction conditions.



3 **58**

Scheme 20

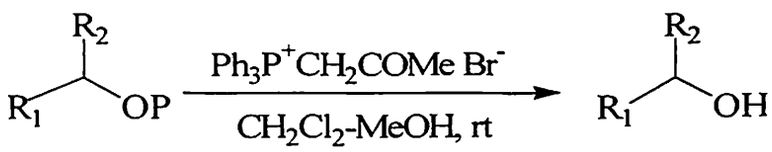
Phukan *et al.* showed the catalytic activity of molecular iodine[87] for the same transformation under solvent free conditions. Recently, molecular iodine in isopropenyl acetate[88] has been demonstrated as efficient catalyst for acylation reactions. Although literature enumerates these several methods for this fundamental transformations still some limitation remain such as long reaction times, harsh reaction conditions, the occurrence of side reactions, toxic reagents, and poor yields of the desired products and intolerance of other functional groups. Recently we have demonstrated bromodimethylsulfonium bromide (BDMS) is a useful pre-catalyst,[7a] which can generate *in situ* HBr, for acylation of alcohols, phenols, thiols and aldehydes. From the literature background as well as from our previous knowledge, we felt that a new methodology for acetylation can be developed using ATPB as new pre-catalyst.

SECTION A

PRESENT WORK ON THE DESILYLATION OF *TERT*- BUTYLDIMETHYLSILYL ETHERS USING A CATALYTIC AMOUNT OF ACETONYLTRIPHENYLPHOSPHONIUM BROMIDE (ATPB)

RESULTS AND DISCUSSION

The application of acetonyltriphenylphosphonium bromide (ATPB) and the reagents used so far for desilylation of *tert*-butyldimethylsilyl (TBS) ethers have been discussed in Part I of the Chapter I. From the literature survey, we realized that there is a scope to devise a better methodology for deprotection of TBS ethers by employing ATPB as new pre-catalyst. In continuation of our research for the development of new synthetic methodologies using a combination of new reagents[89] particularly in the field of protection/deprotection chemistry, we anticipated that acetonyltriphenylphosphonium bromide might be useful for deprotection of TBS ethers. In the present result and discussion part, our successful result for desilylation of various TBS ethers into parent hydroxyl compounds using ATPB as pre-catalyst is represented in Scheme 21.



R_1 = alkyl / aryl / sugar residue/ nucleoside residue;
R_2 = H, alkyl; P = TBS /TBDPS

Scheme 21

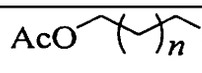
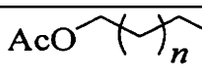
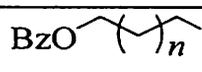
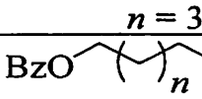
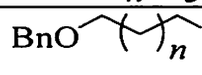
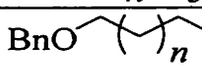
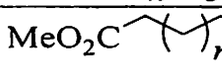
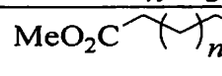
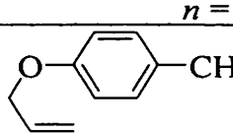
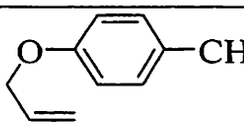
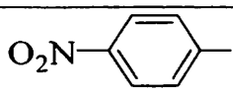
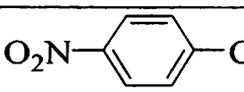
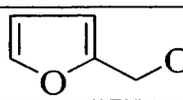
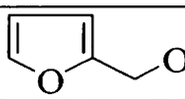
In order to verify our proposal we had to prepare a wide variety of *tert*-butyldimethylsilyl (TBS) ethers as well as *tert*-butyldiphenylsilyl (TBDPS) ethers by following the reported procedure.[9a] Next, we prepared the reagent acetonyltriphenylphosphonium bromide (ATPB) by reaction of triphenylphosphine with bromoacetone in benzene at room temperature following the literature procedure.[2] The solid ATPB was obtained by quick filtration followed by washing with benzene to remove the unreacted triphenylphosphine. First, we attempted the reaction of *tert*-butyldimethylsilyl ether **59** (1 equiv.) with 0.05 equivalents of acetonyltriphenylphosphonium bromide in dichloromethane/methanol (5:2) at room temperature. We noticed that the reaction was complete within three minutes and the pure product 5-acetoxy-1-pentanol (**56**) was obtained in 70% yield by passing the crude mixture through a silica gel column. The starting ether **59** and the product **56** was characterized by recording IR, ^{1}H NMR and ^{13}C NMR spectra which is given in (Fig **1-6**). The disappearance of the signals in the region δ 0.00 [s, 6H, $Si(CH_3)_2$], 0.85 [s, 9H, $SiC(CH_3)_3$], in ^{1}H NMR spectra clearly indicate the deprotection of *tert*-butyldimethyl silyl ether to their corresponding alcohols. In addition, the

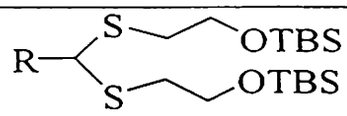
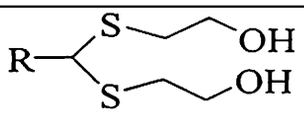
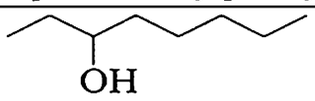
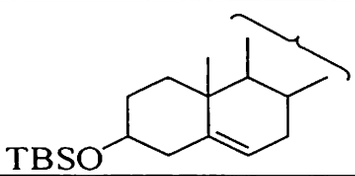
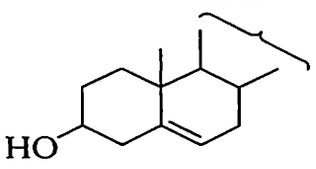
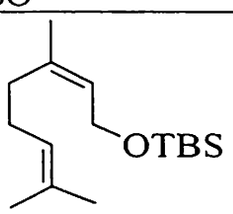
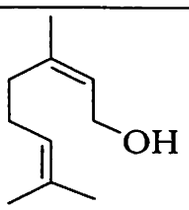
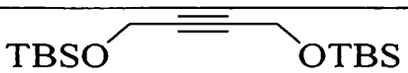
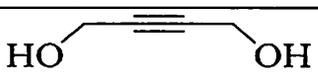
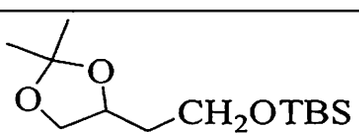
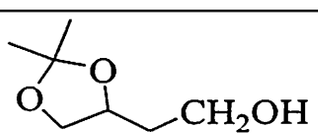
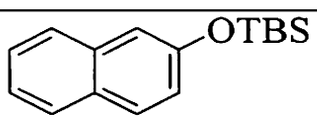
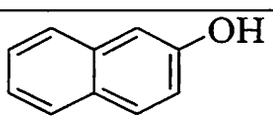
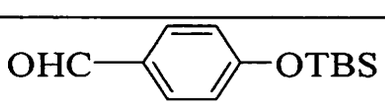
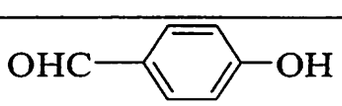
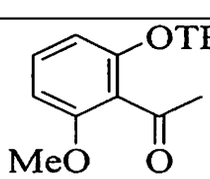
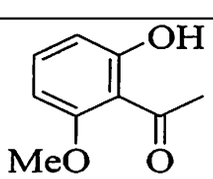
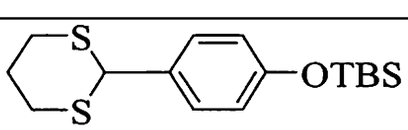
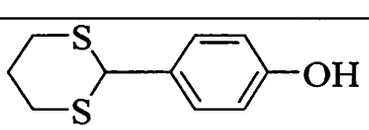
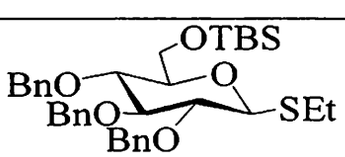
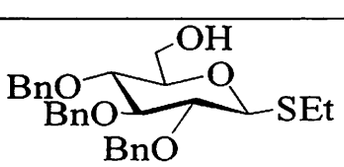
deprotected compound also exhibits a strong band at 3437 cm^{-1} in the IR spectrum which clearly indicates the presence of –OH group in the product. We found that various *tert*-butyldimethylsilyl ethers, such as **60-62** containing benzoyl, benzyl and ester groups, respectively, were smoothly deprotected to the corresponding alcohols **82-84** in good yields, without affecting these groups, under identical reaction conditions. It is worthwhile to mention that our protocol is more efficient in terms of reaction time than a recently reported procedure.[47] Similarly, other TBS ethers such as **63-65** were converted into the corresponding alcohols **85-87** in good yields by following the same procedure. It is interesting to note that no bromination occurs at the double bond or even in the furan ring under these experimental conditions. Likewise, the TBS ether **66** was easily transformed into the corresponding alcohol **88** without disturbing the thioketal group. Interestingly, the thioketal group is also cleaved when the same reaction is carried out with other bromo compounds such as tetrabutylammonium tribromide (TBATB), CBr_4 and molecular bromine. This result clearly indicates that our methodology has some additional advantages compared to the earlier reported procedures, especially those based on bromo reagents. In addition, various TBS ethers **67-68**, which were derived from secondary alcohols, were also cleaved to the corresponding alcohols **89-90** in good yields under identical reaction conditions. Again, we noticed that it took much less time for deprotection of **68** than the earlier procedures.[51] Moreover, by using our protocol, TBS ether **69** and an acetylenic TBS ether **70** were also deprotected to the desired alcohols **91** and **92** without bromination either at the double or at the triple bond. Remarkably, highly acid-sensitive TBS ether such as **71** can be cleaved to the corresponding alcohol **93** without losing the isopropylidene group.

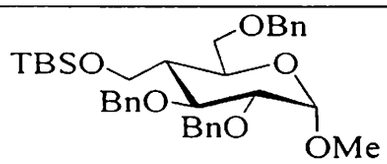
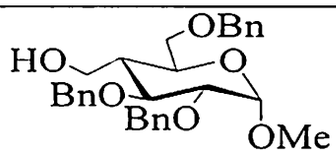
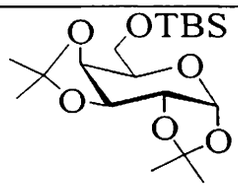
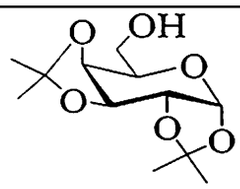
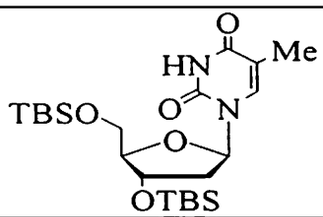
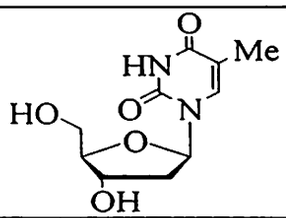
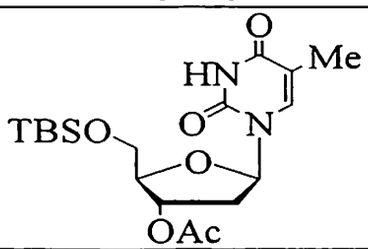
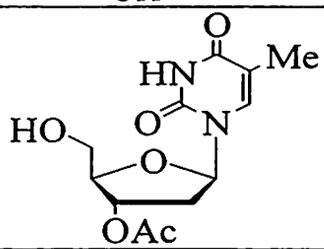
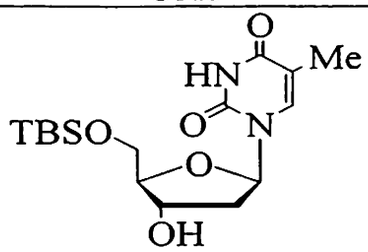
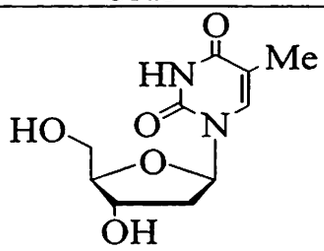
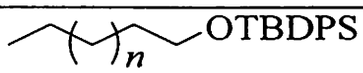
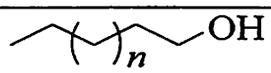
We also decided to study whether the same reagent can be employed for deprotection of aryl TBS ethers or not. We observed that various phenolic TBS ethers **72**, **47**, **73** and **74** could be converted into the respective phenolic compounds **49**, **94**, **95** and **96** without affecting a thioketal group. It is important to mention that no α-bromination was observed in the case of compound **73**, and neither was any cyclotrimerization observed in the case of the aromatic aldehyde **47**. The reactions with aryl TBS ethers take slightly longer reaction time than those with alcoholic TBS ethers. All the deprotected alcohols were characterized fully by IR and ^1H NMR spectroscopy and by elemental analysis; the spectra were compared with those of authentic samples.

We then turned our attention to whether this methodology could be further extended for deprotection of TBS ethers of carbohydrates and nucleosides. We found that various TBS ethers **75-80** can be cleaved easily to the corresponding parent hydroxyl compounds **97-101** in good yields under identical reaction conditions. Importantly, a thio group at the anomeric position usually affected by the earlier reported procedures[50] and OMe ether or an isopropylidene group at the anomeric position also survived under the experimental conditions. The reaction times and yields of all the products are summarized in Table 1. These results further encouraged us to study whether our methodology could be extended to the deprotection of *tert*-butyldiphenyl silyl (TBDPS) ethers. We found that TBDPS ether of 1-dodecanol (**81**) was also converted into the corresponding alcohol **102** in 88% yield in the presence of 0.2 equivalents of the same pre-catalyst although with a longer reaction time. The product was characterized by usual spectroscopic technique.

Table 1. Deprotection of various TBS ethers to the parent hydroxyl compounds using catalytic amount of acetonyltriphenylphosphonium bromide (ATPB) in dichloromethane-methanol

Substrate No.	Substrate	Time min/ [h]	Product[a]	Product No.	% Yield[b]
59		3		**56**	70
60		15		**82**	88
61		10		**83**	92
62		15		**84**	92
63		7		**85**	91
64		[2]		**86**	94
65		10		**87**	83

66	 R = *p*-methoxy phenyl	20	 R = *p*-methoxy phenyl	**88**	81
67		22		**89**	91
68		[2.5]		**90**	90
69		5		**91**	95
70		7		**92**	85
71		15		**93**	72
72		[6]		**49**	81
47		[5]		**94**	71
73		[3]		**95**	91
74		[4]		**96**	85
75		50		**97**	88

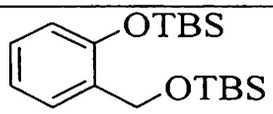
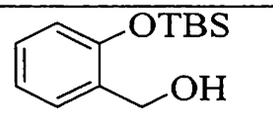
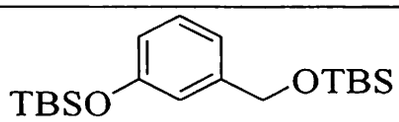
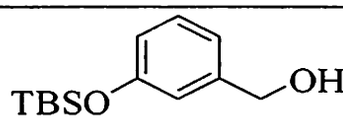
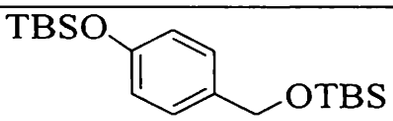
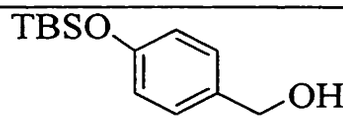
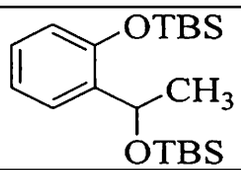
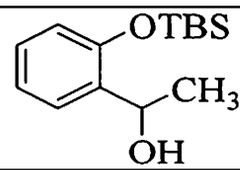
76		[2]		**98**	82
77		30		**99**	80
78		[6]		**100**	75
79		[3]		**101**	87
80		[3]		**100**	87
81	 $n = 8$	[5]	 $n = 8$	**102**	88

[a]All starting material and final products were characterized by IR, ^{1}H NMR, ^{13}C NMR and elemental analysis. [b]Isolated yield.

Interestingly, our protocol can also be further extended to the chemoselective deprotection of TBS ethers in the presence of TBDPS ether or aryl TBS ether. 1-*tert*-Butyldimethylsilyl-5-*tert*-butyldiphenylsilyl diether (**103**) and 1-*tert*-butyldimethylsilyl-8-*tert*-butyldiphenylsilyl diether (**104**) were smoothly converted into the corresponding mono TBDPS ethers chemoselectively, as shown in Table 2. Likewise, various alkyl *tert*-butyldimethylsilyl ethers **105-108** were converted into the desired mono aryl *tert*-butyldimethylsilyl ethers **111-114** in good yields. Moreover, the secondary TBS ether was also cleaved faster than the aryl TBS ether, as shown in Table 2. All the products were characterized by usual spectroscopic technique.^{1}H NMR spectrum of compound

105 is shown in figure **7** and IR, ^{1}H NMR and ^{13}C NMR spectrum of product **111** are given in figure **8-10** respectively.

Table 2. Deprotection of various TBS ethers to the parent hydroxyl compounds using catalytic amount of acetonyltriphenylphosphonium bromide (ATPB) in dichloromethane-methanol.

Substrate No	Substrate	Time min/ [h]	Product[a]	Product No.	Yield[b] [/%]
103	TBSO$(CH_2)_n$OTBDPS, $n = 3$	35	HO$(CH_2)_n$OTBDPS, $n = 3$	**109**	78
104	TBSO$(CH_2)_n$OTBDPS, $n = 6$	12	HO$(CH_2)_n$OTBDPS, $n = 6$	**110**	81
105		10		**111**	77
106		6		**112**	86
107		15		**113**	87
108		45		**114**	76

[a]All starting material and final products were characterized by IR, ^{1}H NMR, ^{13}C NMR and elemental analysis. [b]Isolated yield

The formation of the products can be rationalized as follows. We believe that HBr, generated in the reaction medium from the reaction of acetonyltriphenylphosphonium bromide with methanol, catalyzes the deprotection of TBS ethers to the corresponding alcohols. However, the same reaction failed when it was carried out with benzyltriphenylphosphonium bromide instead of acetonyltriphenylphosphonium bromide. This indicates that ATPB generates HBr much more easily than the other alkylphosphonium bromide.

In summary, we have devised a new, efficient, and regio as well as chemoselective protocol for the deprotection of TBS ethers and TBDPS ethers using a catalytic amount

of acetonyltriphenylphosphonium bromide in dichloromethane/methanol at room temperature under very mild conditions. The significant features of the present method include the ease of operation, high efficiency, mild conditions and chemoselectivity, which may be useful in organic synthesis. In addition, the selective deprotection of alkyl *tert*butyldimethylsilyl ether can be achieved in the presence of aryl-*tert*-butyldimethylsilyl ethers. We have found that a wide variety of other protecting groups, such as acetyl, benzyl, benzoyl, thioketals, esters and isopropylidene survive under the present experimental conditions.

SECTION A

DEPROTECTION OF *tert*-BUTYLDIMETHYLSILYL ETHERS INTO THE CORRESPONDING HYDROXYL COMPOUNDS USING ACETONYLTRIPHENYLPHOSPHONIUM BROMIDE (ATPB) AS A CATALYST

EXPERIMENTAL

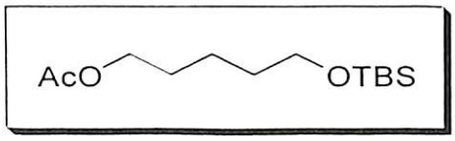
Preparation of the catalyst Acetonyltriphenylphosphonium bromide (ATPB):

To a stirred solution of triphenylphosphine (2.6 g, 10 mmol), in dry 10 mL benzene was added freshly prepared bromoacetone (1.2 g, 10 mmol) at ice-cold temperature. After 15 minute of stirring at the same temperature, the reaction mixture was allowed to stir for another 2h at room temperature. A white solid was precipitated out from the reaction mixture, which was filtered off through a Buchner funnel and the solid was washed with dry benzene to remove unreacted triphenylphosphine. The white solid was dried in desicator. The product was obtained 3.83 gm in 80 % yield. The melting point of the reagent was found to be 220-221 °C (Lit.[2] mp 221-223 °C)

General procedure for the preparation of *tert*-Butyldimethylsilyl ether of alcohols and phenols:

To a mixture of alcohol or phenol (2 mmol) and TBDMSCl (2.4 mmol) in dry CH_2Cl_2 or DMF (5 mL) was added imidazole (6 mmol) at room temperature. The reaction mixture was kept stirring until the reaction completed as shown in TLC at the same temperature. The reaction mixture was neutralized with 2N HCl solution and extracted with dichloromethane. The aqueous part was extracted once more with CH_2Cl_2. The combined organic part was dried over anhydrous Na_2SO_4 and it concentrated in rotavapor. Finally, the residue was passed through a silica gel column to obtain the desired silyl ether

5-*O*-Acetyl-1-*tert*-butyldimethylsilyloxy pentane (59):



Nature: Colourless liquid

Yield: 71% (0.37 g)

IR (Neat): 2960, 2935, 2868, 1747, 1475, 1373, 1250, 1112, 1045, 840, 779 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.36 (m, 2H, CH_2), 1.50 (m, 2H, CH_2), 1.60 (m, 2H, CH_2), 1.99 (s, 3H, $COCH_3$), 3.57 (t, 2H, J = 6.3 Hz, CH_2OTBS), 4.01 (t, 2H, J = 6.6 Hz, $AcOCH_2$) ppm.

^{13}C NMR (100MHz, $CDCl_3$): δ -5.4, 18.3, 20.9, 22.2, 25.9, 28.3, 32.3, 62.9, 64.5, 171.2 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{28}O_3Si$	C 59.95	C 59.72
260.45	H 10.83	H 10.75

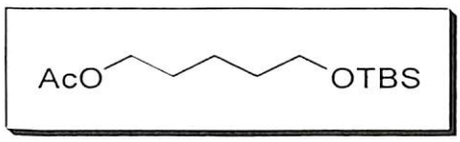
Preparation of the catalyst Acetonyltriphenylphosphonium bromide (ATPB):

To a stirred solution of triphenylphosphine (2.6 g, 10 mmol), in dry 10 mL benzene was added freshly prepared bromoacetone (1.2 g, 10 mmol) at ice-cold temperature. After 15 minute of stirring at the same temperature, the reaction mixture was allowed to stir for another 2h at room temperature. A white solid was precipitated out from the reaction mixture, which was filtered off through a Buchner funnel and the solid was washed with dry benzene to remove unreacted triphenylphosphine. The white solid was dried in desicator. The product was obtained 3.83 gm in 80 % yield. The melting point of the reagent was found to be 220-221 °C (Lit.[2] mp 221-223 °C)

General procedure for the preparation of *tert*-Butyldimethylsilyl ether of alcohols and phenols:

To a mixture of alcohol or phenol (2 mmol) and TBDMSCl (2.4 mmol) in dry CH_2Cl_2 or DMF (5 mL) was added imidazole (6 mmol) at room temperature. The reaction mixture was kept stirring until the reaction completed as shown in TLC at the same temperature. The reaction mixture was neutralized with 2N HCl solution and extracted with dichloromethane. The aqueous part was extracted once more with CH_2Cl_2. The combined organic part was dried over anhydrous Na_2SO_4 and it concentrated in rotavapor. Finally, the residue was passed through a silica gel column to obtain the desired silyl ether

5-*O*-Acetyl-1-*tert*-butyldimethylsilyloxy pentane (59):



Nature: Colourless liquid

Yield: 71% (0.37 g)

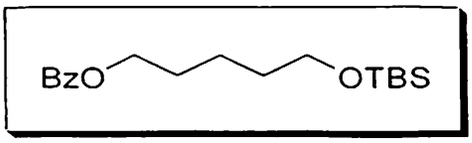
IR (Neat): 2960, 2935, 2868, 1747, 1475, 1373, 1250, 1112, 1045, 840, 779 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.36 (m, 2H, CH_2), 1.50 (m, 2H, CH_2), 1.60 (m, 2H, CH_2), 1.99 (s, 3H, $COCH_3$), 3.57 (t, 2H, J = 6.3 Hz, CH_2OTBS), 4.01 (t, 2H, J = 6.6 Hz, $AcOCH_2$) ppm.

^{13}C NMR (100MHz, $CDCl_3$): δ -5.4, 18.3, 20.9, 22.2, 25.9, 28.3, 32.3, 62.9, 64.5, 171.2 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{28}O_3Si$	C 59.95	C 59.72
260.45	H 10.83	H 10.75

5-*O*-Benzoyl-1-*tert*-butyldimethylsilyloxy pentane (60):



Nature: Colourless liquid

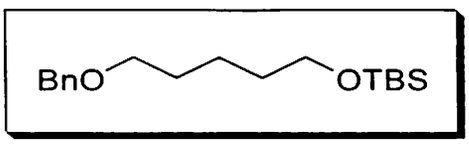
Yield: 73% (0.471 g)

IR (Neat): 2940, 2858, 1721, 1583, 1429, 1337, 1301, 1112, 943 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ -0.02 (s, 6H, $Si(CH_3)_2$), 0.83 (s, 9H, $SiC(CH_3)_3$), 1.47 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.74 (m, 2H, CH_2), 3.57 (t, 2H, J = 6.3 Hz, CH_2OTBS), 4.26 (t, 2H, J = 6.6 Hz, $PhCOOCH_2$), 7.39 (t, 1H, J = 7.8 Hz, ArH), 7.44 (t, 1H, J = 7.8 Hz, ArH), 7.54 (m, 1H, ArH), 8.00 (dd, 1H, J = 1.2 Hz, J = 7.3 Hz, ArH), 8.09 (dd, 1H, J = 1.2 Hz, J = 7.1 Hz, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{18}H_{30}O_3Si$	C 67.03	C 66.91
322.52	H 9.38	H 9.25

5-*O*-Benzoyl-1-*tert*-butyldimethylsilyloxy pentane (61):



Nature: Colourless liquid

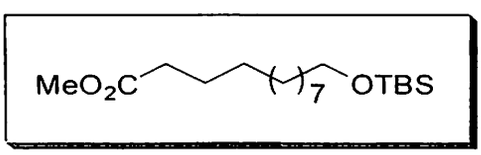
Yield: 72% (0.427 g)

IR (Neat): 2960, 2935, 2858, 1506, 1470, 1460, 1368, 1255, 1102, 1009, 840 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ -0.01 (s, 6H, $Si(CH_3)_2$), 0.83 (s, 9H, $SiC(CH_3)_3$), 1.50 (m, 6H, CH_2), 3.43 (t, 2H, J = 6.5 Hz, CH_2OTBS), 3.57 (t, 2H, J = 6.4Hz, $PhCH_2OCH_2$), 4.46 (s, 2H,OCH_2Ph), 7.31 (m, 5H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{17}H_{32}O_2Si$	C 68.86	C 68.79,
296.52	H 10.88	H 10.80

12-Carbomethoxymethylate-1-*tert*-butyldimethylsilyloxy dodecane (62):



Nature: Colourless liquid

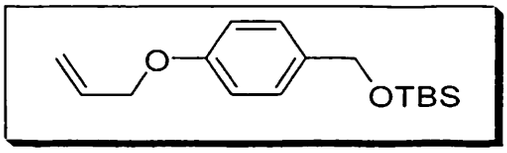
Yield: 69% (0.476 g)

IR (Neat): 2945, 2858, 1752, 1470, 1255, 1178, 1107 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.22 (m, 18H, CH_2), 2.25 (t, 2H, *J* = 7.3 Hz, $COCH_2$), 3.55 (t, 2H, *J* = 6.3Hz, CH_2OTBS), 3.62 (s, 3H,OCH_3) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{19}H_{40}O_3Si$	C 66.22	C 65.98
344.61	H 11.70	H 11.75

***tert*-Butyldimethylsilyl ether of 4-allyloxybenzyl alcohol (63):**



Nature: Colourless liquid

Yield: 78 % (0.434 g)

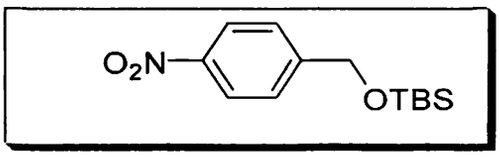
IR (Neat): 2955, 2929, 2863, 1655, 1615, 1516, 1470, 1250, 1096, 1034, 855 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.08 (s, 6H, $Si(CH_3)_2$), 0.93 (s, 9H, $SiC(CH_3)_3$), 4.52 (d, 2H, *J* = 1.2 Hz, $OCH_2CH{=}CH_2$), 4.66 (s, 2H, CH_2OTBS), 5.27 (dd, 1H, *J* = 1.0 Hz, *J* = 10.5 Hz, $OCH_2CH{=}CH_2$), 5.40 (dd, 1H, *J* = 1.4 Hz, *J* = 15.8 Hz, $OCH_2CH{=}CH_2$), 6.06 (m, 1H, $OCH_2CH{=}CH_2$), 6.88 (d, 2H, *J* = 8.6 Hz, ArH), 7.22 (d, 2H, *J* = 8.3 Hz, ArH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.2, 18.4, 25.9, 64.7, 68.9, 114.5, 117.6, 127.5, 133.4, 133.8, 157.7 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{26}O_2Si$	C 69.01	C 68.82
278.47	H 9.41	H 9.47

***tert*-Butyldimethylsilyl ether of 4-nitrobenzyl alcohol (64):**



Nature: Yellowish liquid

Yield: 65 % (0.348 g)

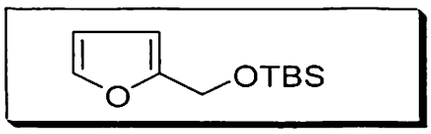
IR (Neat): 2955, 2935, 2863, 1614, 1521, 1475, 1352, 1265, 1102, 1020, 856 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.13 (s, 6H, Si $(CH_3)_2$), 0.96 (s, 9H, SiC $(CH_3)_3$), 4.83 (s, 2H, CH_2OTBS), 7.49 (d, 2H, *J* = 8.7 Hz, ArH), 8.20 (d, 2H, *J* = 9.0 Hz, ArH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.4, 18.3, 25.8, 64.0, 123.5, 126.3, 146.0, 149.0 ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{21}O_3NSi$	C 58.39	C 58.15
267.40	H 7.92	H 7.84
	N 5.24	N 5.08

***tert*-Butyldimethylsilyl ether of furfuryl alcohol (65)**



Nature: Colourless liquid

Yield: 69 % (0.293 g)

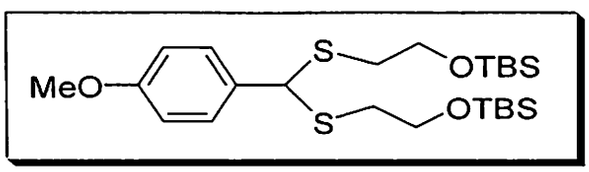
IR (Neat): 2960, 2935, 2863, 1603, 1506, 1470, 1255, 1158, 1076, 1015, 840 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.08 (s, 6H, $Si(CH_3)_2$), 0.88 (s, 9H, $SiC(CH_3)_3$), 4.62 (s, 2H, CH_2OTBS), 6.14 (d, 1H, J = 3.2 Hz, 3-H), 6.23 (dd, 1H, J = 1.7 Hz, J = 3.2 Hz, 4-H), 7.28 (dd, 1H, J = 0.9 Hz, J = 1.7 Hz, 5-H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ -5.3, 18.4, 25.9, 58.1, 107.2, 110.2, 142.0,154.3 ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{20}O_2Si$	C 62.22	C 61.97
212.36	H 9.49	H 9.42

Compound (66):



Nature: Colourless liquid

Yield: 69 % (0.694 g)

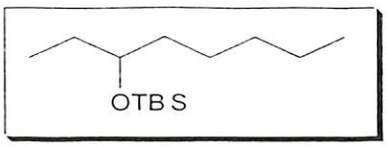
IR (Neat): 2955, 2930, 2863, 1609, 1516, 1470, 1255, 1091, 1040, 902, 840 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 12H, 2 x $Si(CH_3)_2$), 0.84 (s, 18H, 2x $SiC(CH_3)_3$), 2.54-2.61 (m, 4H, SCH_2), 3.66 (m, 4H, OCH_2), 3.76 (s, 3H, OCH_3), 5.01 (s, 1H, SCHS), 6.82 (d, 2H, J = 9.5 Hz, ArH), 7.33 (d, 2H, J = 9.8 Hz, ArH) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ -5.3, 18.3, 25.9, 34.6, 53.4, 55.3, 63.2, 113.9, 128.9, 132.5, 159.2 ppm.

Elemental Analysis	Calculated	Found
$C_{24}H_{46}O_3S_2Si_2$	C 57.32	C 57.08
502.93	H 9.22	H 9.15
	S 12.75	S 12.63

***tert*-Butyldimethylsilyl ether of Octan-3-ol (67):**



Nature: Colourless liquid

Yield: 74% (0.362 g)

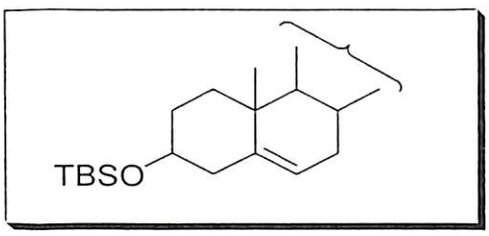
IR (Neat): 2960, 2940, 2863, 1475, 1378, 1255, 1132, 1061, 835 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.83 (t, 6H, J = 7.6 Hz, 2 x CH_3), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.22-1.30 (m, 6H, CH_2), 1.34-1.43 (m, 4H, CH_2), 3.53 (quin, 1H, J = 5.9 Hz, CH_2CHCH_2) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ -4.5, -4.5, 9.6, 14.0, 18.1, 22.6, 25.0, 25.9, 29.7, 32.0, 36.5, 73.5 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{14}H_{32}OSi$	C 68.78	C 68.91
244.49	H 13.19	H 13.06

***tert*-Butyldimethylsilyl ether of Cholesterol (68):**



Nature: White solid; mp: 151-153 °C

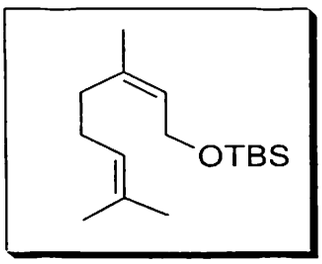
Yield: 58% (0.581 g)

IR (KBr): 2930, 2858, 1665, 1460, 1378, 1255, 1112 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.06 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$), 0.82 (s, 6H, 2x - CH_3), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.85 (d, 3H, J = 6.3 Hz, $CHCH_3$), 0.94 (s, 6H, 2x CH_3), 1.00-1.50 (m, 22H, CH and CH_2), 1.75 (m, 2H, CH2), 1.94 (m, 2H, CH_2), 2.12 (m, 1H, CH), 2.20 (m, 1H, CH), 3.42 (q, 1H, J = 6.Hz, OCH), 5.25 (m, 1H, = CH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{33}H_{60}OSi$	C 79.13	C 79.09
500.92	H 12.07	H 12.11

tert-Butyldimethylsilyl ether of Geraniol (69):



Nature: Colourless liquid

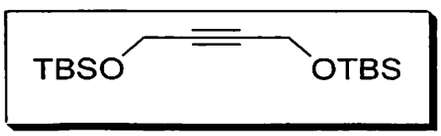
Yield: 73% (0.392 g)

IR (Neat): 2955, 2930, 2858, 1665, 1465, 1383, 1255, 1096, 1061, 835 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 6H, $Si(CH_3)_2$), 0.84 (s, 9H, $SiC(CH_3)_3$), 1.53 (s, 6H, $C(CH_3)_3$), 1.61(s, 3H, CH_3), 1.88-2.03 (m, 4H, $CHCH_2$), 3.54-3.59 (m, 1H, OCH_2), 4.12-4.13 (m, 1H, OCH_2), 5.01-5.05 (m, 1H, CH), 5.22-5.25 (m, 1H, CH)ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{32}OSi$	C 71.57	C 71.75
268.51	H 12.01	H 12.09

Bis (_tert_-Butyldimethylsilyl) ether of 1,4-butyne-diol (70):



Nature: Yellowish liquid

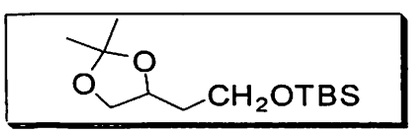
Yield: 68 % (0.428 g)

IR (Neat): 2955, 2934, 2863, 1465, 1357, 1255, 1137, 1070, 840 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.12 (s, 12H, 2x $Si(CH_3)_2$), 0.91 (s, 18H, 2x $SiC(CH_3)_3$), 4.34 (s, 4H, OCH2) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{34}O_2Si_2$	C 61.08	C 61.10
314.61	H 10.89	H 10.85

TBS ether of 2,3-_O_-isopropylidene-_D_-(±)-glycerol (71):



Nature: Colourless liquid

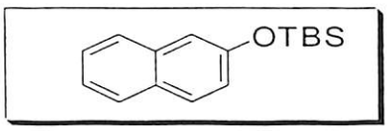
Yield: 72% (0.32 g)

IR (Neat): 2945, 2863, 1460, 1378, 1255, 1148, 1107, 846, 784 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.12 (s, 6H, $Si(CH_3)_2$), 0.91 (s, 9H, $SiC(CH_3)_3$), 1.37 (s 3H, CH_3), 1.42 (s, 3H, CH_3), 3.75 (dd, J = 6.2 Hz, J = 8.2 Hz, 1H, CH_2), 4.05-4.10 (m, 2H, -CH_2), 4.18 (dd, J = 4.8 Hz, J = 11.6 Hz, 1H, CH_2), 4.32-4.37 (m, 1H, CH) ppm.

Elemental Analysis	Calculated	Found
$C_{10}H_{26}O_3Si$	C 54.01	C 54.12
222.40	H 11.78	H 11. 83

***tert*-Butyldimethylsilyl ether of 2-naphthol (72):**



Nature: Colourless liquid

Yield: 59% (0.305 g)

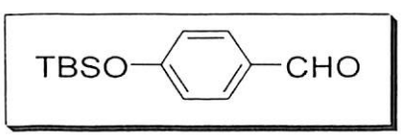
IR (Neat): 3058, 2966, 2940, 2863, 1634, 1603, 1506, 1470, 1363, 1260, 1230, 1173, 1132, 1015, 933, 851 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.25 (s, 6H, $Si(CH_3)_2$), 1.02 (s, 9H, $SiC(CH_3)_3$), 7.07(dd, 1H, *J* = 3.2 Hz, *J* = 8.7 Hz, 3-ArH), 7.19 (d, 1H, *J* = 2.4 Hz,1-ArH), 7.30(t, 1H, *J* = 7.0 Hz, 6-ArH), 7.38 (t, 1H, *J* = 7.0 Hz, 7-ArH), 7.68 (d, 1H, *J* = 8.7 Hz, ArH, 4-ArH), 7.72 (d, 1H, *J* = 9.0 Hz, 5-ArH), 7.76 (d, 1H, *J* = 8.1 Hz, 8-ArH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ -4.3, 18.3, 25.7, 114.9, 122.1, 123.7, 126.1, 126.7, 127.6, 129.3, 134.6, 153.5 ppm.

Elemental Analysis	Calculated	Found
$C_{16}H_{22}OSi$	C 74.36	C 74.10
258.43	H 8.58	H 8.50

***tert*-Butyldimethylsilyl ether of 4-hydroxy benzaldehyde (47):**



Nature: Yellowish liquid

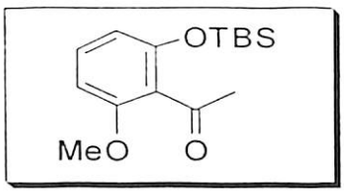
Yield: 71% (0.336 g)

IR (Neat): 2945, 2858, 1705, 1603, 1511, 1270, 1157, 912, 845 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.25 (s, 6H, $Si(CH_3)_2$), 0.99 (s, 9H, $SiC(CH_3)_3$), 6.95 (d, 2H, *J* = 8.4 Hz, ArH), 7.81 (d, 2H, *J* = 8.4 Hz, ArH), 9.89 (s, 1H, CHO) ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{20}O_2Si$	C 66.06	C 65.37
236.39	H 8.53	H 8.58

***tert*-Butyldimethylsilyl ether of 2-methoxy-5-hydroxy acetophenone (73):**



Nature: Colourless liquid

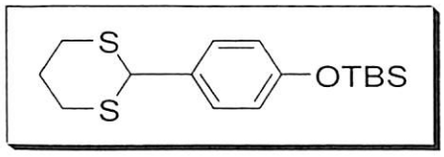
Yield: 68% (0.381 g)

IR (Neat): 2966, 2935, 2863, 1711, 1593, 1470, 1255, 1107, 974, 840 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.19 (s, 6H, $Si(CH_3)_2$), 0.94 (s, 9H, $SiC(CH_3)_3$), 2.47 (s, 3H, $COCH_3$), 3.77 (s, 3H, OCH_3), 6.37 (d, 1H, J = 8.3 Hz, ArH), 6.51 (d, 1H, J = 8.3 Hz, ArH), 7.15 (t, 1H, J = 8.3 Hz, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{15}H_{24}O_3Si$	C 64.24	C 64.45
280.44	H 8.63	H 8.58

***tert*-Butyldimethylsilyl ether of 2-[4′-hydroxyphenyl]-1,3-dithiane (74):**



Nature: White solid, mp: 82.6 °C

Yield: 73% (0.477 g)

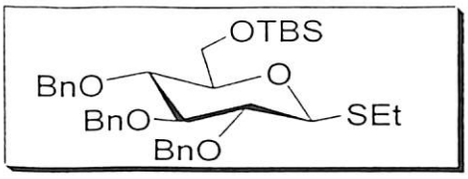
IR (Neat): 2955, 2929, 2893, 2852, 1608, 1511, 1470, 1419, 1255, 1168, 912, 845 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.09 (s, 6H, $Si(CH_3)_2$), 0.97 (s, 9H, $SiC(CH_3)_3$), 1.84-1.88(m, 1H, SCH_2CH_2), 1.91-1.97(m, 1H, SCH_2CH_2), 2.85-2.92 (m, 2H, SCH_2CH_2), 2.99-3.09 (m, 2H, SCH_2CH_2), 5.12 (s, 1H, CH), 6.79 (d, 2H, J = 8.4 Hz, ArH), 7.32(d, 2H, J = 8.4 Hz, ArH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ -4.5, 18.1, 25.0, 25.6, 32.1, 50.8, 120.1, 128.8, 131.8, 155.7 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{26}OS_2Si$	C 58.84	C 58.72
326.60	H 8.02	H 8.09
	S 19.64	S 19.85

Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (75):



Nature: Gummy liquid

Yield: 74% (0.901 g)

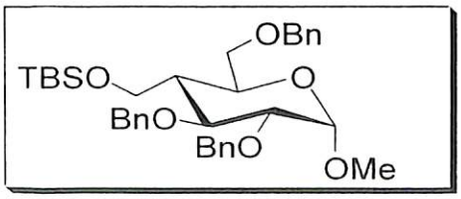
IR (Neat): ν 3037, 2960, 2930, 2873, 1619, 1496, 1460, 1255, 1158, 1096, 846 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 3H, $Si(CH_3)_2$), 0.02 (s, 3H, $Si(CH_3)_2$), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.25 (t, 3H, J = 7.3 Hz, SCH_2CH_3), 2.63-2.71 (m, 2H, SCH_2CH_3), 3.21-3.24 (m, 1H, H-5), 3.46 (t, 1H, J = 9.0 Hz, H-3), 3.56 (t, 1H, J = 9.3 Hz, H-2), 3.61 (t, 1H, J = 9.0 Hz, H-4), 3.75 (dd, 1H, J = 3.8 Hz, J = 11.2 Hz, H-6), 3.80 (dd, 1H, J = 2.0 Hz, J = 11.7 Hz, H-6′), 4.38 (d, 1H, J = 9.8 Hz, H-1), 4.62 (d, 1H, J = 10.2 Hz, O*CH*Ph), 4.68 (d, 1H, J = 10.2 Hz, O*CH*Ph), 4.79 (dd, 2H, J = 4.6 Hz, J = 10.7 Hz, OCH_2Ph), 4.85 (dd, 2H, J = 4.0 Hz, J = 10.3 Hz, OCH_2Ph), 7.19-7.33 (m, 15 H, ArH) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = -5.4, -5.0, 15.2, 18.3, 24.3, 25.9, 62.3, 75.1, 75.5, 75.9, 77.7, 80.0, 81.8, 84.4, 86.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 128.5, 138.2, 138.3, 138.5 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{35}H_{48}O_5SSi$	C 69.04	C 69.22
608.91	H 7.95	H 7.87
	S 5.27	S 5.12

4-Methyl-*O*-*tert*-butyldimethylsilyl-2,3,6-tri-*O*-benzyl-1-β-D-methylglucopyranoside (76):



Nature: Colourless liquid

Yield: 71% (0.845 g)

IR (Neat): ν 2929, 2858, 1603, 1459, 1362, 1260, 1106, 1060, 845, 742, 701 cm^{-1}.

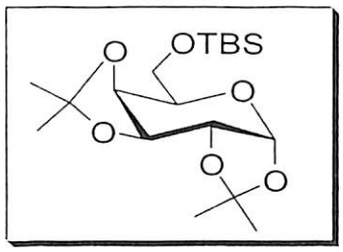
^{1}H NMR (300 MHz, $CDCl_3$): δ -0.12(s, 3H,$SiCH_3$), -0.05 (s, 3H,$SiCH_3$), 0.83 (s, 9H,$Si(CH_3)_3$), 1.86 (t, 1H, J = 10.8 Hz, H-4), 3.38 (s, 3H, OCH_3), 3.39-3.44 (m, 1H, H-1), 3.53-3.66(m, 3H, CH_2 & H–2), 3.88 (dd, 1H, J = 1.8 Hz, J =10.5 Hz, H′- 6), 3.95 (d , 1

H, J = 10.8 Hz H- 5), 4.06 (t, 1H,J = 9.9 Hz , H- 3), 4.43 (d ,1H, J= 12.3 Hz , OCH_2) , 4.61 (m, 3H ,OCH_2 & H- 6), 4.65 (d, 1H, J = 12.6 Hz, OCH_2) , 4.77(d , 1H , J = 12.0 Hz, OCH_2), 5.01 (d, 1H, J =12.0 Hz, OCH_2), 7.26-7.37(m ,15 H , ArH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ -5.8, -5.5, 18.1, 25.8, 44.8, 55.0, 58.3, 68.3, 69.3, 73.0, 73.4, 75.3, 75.7, 81.7, 98.5, 127.6, 127.7, 127.8, 127.9, 128.2, 128.4, 138.2, 138.4, 139.1 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{35}H_{48}O_6Si$	C 70.91	C 70.68
592.84	H 8.16	H 8.24

6-*O*-*tert*-Butyldimethylsilyl-1,2, 3,4-di-isopropylidene galactose (77):



Nature: Yellowish liquid

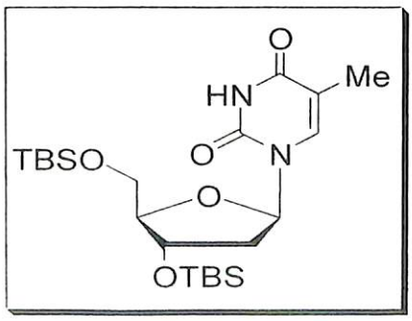
Yield: 73% (0.547 g)

IR (Neat): 2986, 2935, 2858, 1475, 1378, 1312, 1255, 1214, 1112, 1071, 1004, 840 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.07 (s, 6H, -Si(CH_3)$_2$), 0.90 (s, 9H, -SiC(CH_3)$_3$), 1.33 (s, 6H, =C(CH_3)$_2$), 1.44 (s, 3H, =CCH_3), 1.54 (s, 3H, =CCH_3), 3.70-3.86 (m, 3H, H-2, H-3, H-5), 4.30 (dd, 2H, J = 2.3 Hz, J = 7.2 Hz, H-4, H-6), 4.60 (dd, 1H, J = 1.6 Hz, J = 7.9 Hz, H-6′), 5.52 (d, 1H, J = 4.9 Hz, H-1) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{18}H_{34}O_6Si$	C 57.72	C 57.89
374.55	H 9.15	H 9.02

Bis (*tert*-butyldimethylsilyl) ether of thymidine (78):



Nature: White solid, mp:115 °C

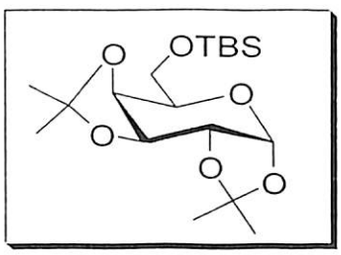
Yield: 69% (0.517 g)

H, J = 10.8 Hz H- 5), 4.06 (t, 1H,J = 9.9 Hz , H- 3), 4.43 (d ,1H, J= 12.3 Hz , OCH_2) , 4.61 (m, 3H ,OCH_2 & H- 6), 4.65 (d, 1H, J = 12.6 Hz, OCH_2) , 4.77(d , 1H , J = 12.0 Hz, OCH_2), 5.01 (d, 1H, J =12.0 Hz, OCH_2), 7.26-7.37(m ,15 H , ArH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ -5.8, -5.5, 18.1, 25.8, 44.8, 55.0, 58.3, 68.3, 69.3, 73.0, 73.4, 75.3, 75.7, 81.7, 98.5, 127.6, 127.7, 127.8, 127.9, 128.2, 128.4, 138.2, 138.4, 139.1 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{35}H_{48}O_6Si$	C 70.91	C 70.68
592.84	H 8.16	H 8.24

6-*O-tert*-Butyldimethylsilyl-1,2, 3,4-di-isopropylidene galactose (77):



Nature: Yellowish liquid

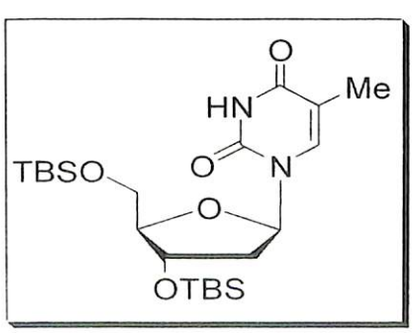
Yield: 73% (0.547 g)

IR (Neat): 2986, 2935, 2858, 1475, 1378, 1312, 1255, 1214, 1112, 1071, 1004, 840 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.07 (s, 6H, $-Si(CH_3)_2$), 0.90 (s, 9H, $-SiC(CH_3)_3$), 1.33 (s, 6H, $=C(CH_3)_2$), 1.44 (s, 3H, $=CCH_3$), 1.54 (s, 3H, $=CCH_3$), 3.70-3.86 (m, 3H, H-2, H-3, H-5), 4.30 (dd, 2H, J = 2.3 Hz, J = 7.2 Hz, H-4, H-6), 4.60 (dd, 1H, J = 1.6 Hz, J = 7.9 Hz, H-6′), 5.52 (d, 1H, J = 4.9 Hz, H-1) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{18}H_{34}O_6Si$	C 57.72	C 57.89
374.55	H 9.15	H 9.02

Bis (*tert*-butyldimethylsilyl) ether of thymidine (78):



Nature: White solid, mp:115 °C

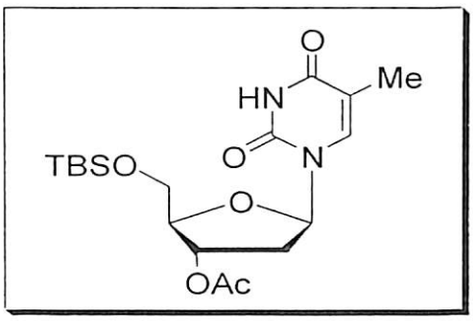
Yield: 69% (0.517 g)

IR (KBr): 3180, 3057, 2950, 2929, 2858, 1700, 1465, 1362, 1270, 1101, 1065, 1029, 835, 778 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.06(s, 3H, $SiCH_3$), 0.07(s, 3H, $SiCH_3$), 0.10 (s, 6H, $SiCH_3$), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.91 (s, 9H, $SiC(CH_3)_3$), 1.91 (s, 3H, CH_3) 1.94- 2.03(m, 1H , H-2) , 2.21-2.28 (m , 1H, H′-2), 3.75 (dd, 1H , J =2.3 Hz , J = 13.7 Hz , H-4), 3.84-3.92 (m, 2H , OCH_2) , 4.37-4.41 (m, 1H , H-3), 6.30-6.35(m, 1H , H –1),7.46 (s, 1H, CH), 9.01(s,1H, NH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{22}H_{42}O_5N_2Si_2$	C 56.13	C 56.34
374.55	H 8.99	H 8.89
	N 5.95	N 6.12

Compound (79):



Nature: White solid, mp:145 °C

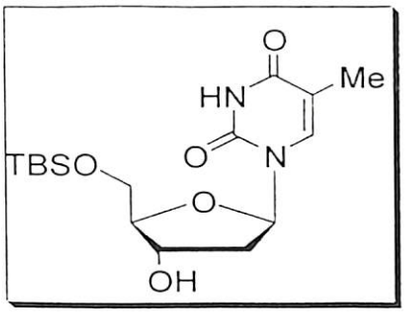
Yield: 68% (0.271 g)

IR (KBr): 3247, 3083, 2940, 2863, 1736, 1700, 1467, 1372, 1255,1203,1121,1014 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.14 (s, 6H, Si $(CH_3)_2$), 0.93 (s, 9H, $SiC(CH_3)_3$), 1.93 (S, 3H, CH_3), 2.11 (s, 3H, $COCH_3$), 2.12 (m, 2H, H-2, H-2′), 2.41 (dd, 1H, J = 5.2 Hz, J = 13.7 Hz), 3.92 (d, 2H, J = 1.8 Hz, CH_2OTBS), 4.10 (d, 1H, J = 1.1 Hz, 5.25 (d, 1H, J = 5.9 Hz), 6.38 (dd, 1H, J = 5.2 Hz, J = 9.2 Hz), 7.55 (d, 1H, J = 1.1 Hz, ArH), 9.12 (s, 1H, NH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{18}H_{30}O_6N_2Si$	C 54.25	C 54.16
398.53	H 7.59	H 7.49
	N 7.03	N 7.11

Compound (80):



Nature: White solid

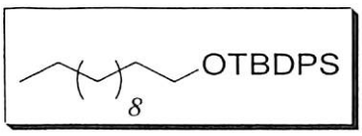
Yield: 54% (0.385 g)

IR (KBr): 3478, 3421, 3180, 3057, 2950, 2929, 2858, 1700, 1465, 1362, 1270, 1101, 1065, 1029,835, 778 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.12 (s, 6H, $Si(CH_3)_2$), 0.91 (s, 9H, $SiC(CH_3)_3$), 1.92 (s, 3H, CH_3), 2.01-2.04 (m, 1H, CH_2), 2.36-2.38 (m, 1H, CH_2), 3.14 (s, 1H, OH), 3.85-3.88 (m, 2H, OCH_2), 4.05-4.07(m, 1H, OCH), 4.46(m, 1H, OCH), 6.40 (m, 1H, OCH), 7.52 (m, 1H, =CH), 9.40 (s, 1H, NH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{28}O_5N_2Si$	C 53.91	C 53.70
356.491	H 7.92	H 7.78
	N 7.86	N 7.89

***tert* -butyldiphenylsilyl ether of dodecanol (81):**



Nature: Colourless liquid

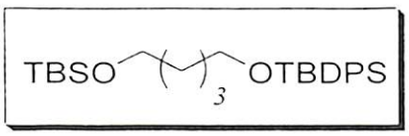
Yield: 71% (0.646 g)

IR (neat): 3063, 2925, 2858, 1460 1388, 1107,825,702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, J = 6.1 Hz, CH_3), 1.05 (s, 9H, $SiC(CH_3)_3$, 1.06 (m, 2H, CH_2CH_3), 1.25 (m, 16H, CH_2), 1.55 (m, 2H, OCH_2CH_2), 3.65 (t, 2H, J = 6.4Hz,OCH_2), 7.42 (m, 5H, ArH), 7.66(m, 5H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{28}H_{44}OSi$	C 80.55	C 80.63
454.74	H 9.75	H 9.80

1-*tert*- Butyldimethylsilyl-5-*tert*-butyldiphenylsilyl diether (103):



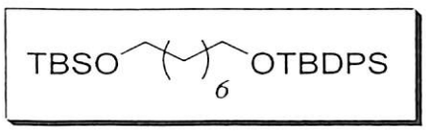
Nature: Yellowish liquid

Yield: 74% (0.676 g)

IR (Neat): 2965, 2929, 2858, 1599, 1475, 1424, 1260, 1101, 835 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.04(s, 6H, $Si(CH_3)_2$), 0.89 (s, 9H, $SiC(CH_3)_3$), 1.04 (s, 9H, $SiC(CH_3)_3$), 1.49 (m, 6H, CH_2), 3.60 (t, 2H, *J* = 6.3 Hz, OCH_2CH_2), 3.66 (t, 2H, *J* = 6.6 Hz, OCH_2CH_2), 7.39(m, 5H, ArH), 7.68 (m, 5H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{27}H_{44}O_2Si_2$	C 70.99	C 70.90
456.81	H 9.71	H 9.65

1-*tert*-butyldimethylsilyl-8-*tert*-butyldiphenylsilyl diether (104):



Nature: Yellowish liquid

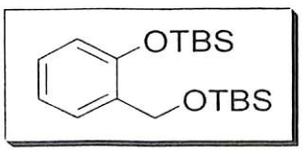
Yield: 71% (0.708 g)

IR (Neat): 3073, 2940, 2863, 1588, 1481, 1434, 1388, 1260, 1107, 840 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ 0.02(s, 6H, $Si(CH_3)_2$), 0.87 (s, 9H, $SiC(CH_3)_3$), 1.02 (s, 9H, $SiC(CH_3)_3$), 1.25 (m, 8H, CH_2), 1.53 (m, 4H, CH_2), 3.57 (t, 2H, *J* = 6.4 Hz OCH_2CH_2), 3.62 (t, 2H, *J* = 6.4 Hz OCH_2CH_2), 7.38(m, 5H, ArH), 7.66 (m, 5H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{30}H_{50}O_2Si_2$	C 72.22	C 72.50
498.90	H 10.10	H 10.22

Di-*tert*- butyldimethylsilyl ether of 2-hydroxybenzyl alcohol (105):



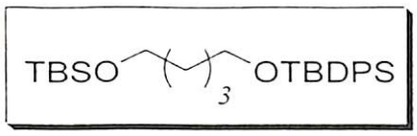
Nature: Yellowish liquid

Yield: 67% (0.478)

IR (Neat): 2945, 2858, 1598, 1485, 1459, 1377, 1260, 1116, 1070, 932, 840 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): 0.09 (s, 6H, $Si(CH_3)_2$), 0.20 (s, 6H, $Si(CH_3)_2$), 0.94 (s, 9H, $SiC(CH_3)_3$), 0.99 (s, 9H, $SiC(CH_3)_3$), 4.75 (s, 2H, OCH_2), 6.73 (d, 1H, *J* = 8.0 Hz, ArH),

1-*tert*- Butyldimethylsilyl-5-*tert*-butyldiphenylsilyl diether (103):



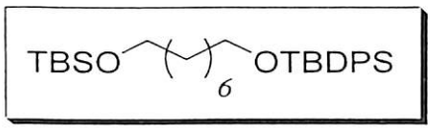
Nature: Yellowish liquid

Yield: 74% (0.676 g)

IR (Neat): 2965, 2929, 2858, 1599, 1475, 1424, 1260, 1101, 835 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.04(s, 6H, $Si(CH_3)_2$), 0.89 (s, 9H, $SiC(CH_3)_3$), 1.04 (s, 9H, $SiC(CH_3)_3$), 1.49 (m, 6H, CH_2), 3.60 (t, 2H, J = 6.3 Hz, OCH_2CH_2), 3.66 (t, 2H, J = 6.6 Hz, OCH_2CH_2), 7.39(m, 5H, ArH), 7.68 (m, 5H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{27}H_{44}O_2Si_2$	C 70.99	C 70.90
456.81	H 9.71	H 9.65

1-*tert*-butyldimethylsilyl-8-*tert*-butyldiphenylsilyl diether (104):



Nature: Yellowish liquid

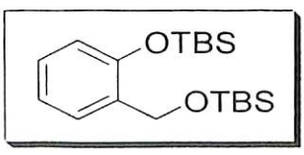
Yield: 71% (0.708 g)

IR (Neat): 3073, 2940, 2863, 1588, 1481, 1434, 1388, 1260, 1107, 840 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ 0.02(s, 6H, $Si(CH_3)_2$), 0.87 (s, 9H, $SiC(CH_3)_3$), 1.02 (s, 9H, $SiC(CH_3)_3$), 1.25 (m, 8H, CH_2), 1.53 (m, 4H, CH_2), 3.57 (t, 2H, J = 6.4 Hz OCH_2CH_2), 3.62 (t, 2H, J = 6.4 Hz OCH_2CH_2), 7.38(m, 5H, ArH), 7.66 (m, 5H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{30}H_{50}O_2Si_2$	C 72.22	C 72.50
498.90	H 10.10	H 10.22

Di-*tert*- butyldimethylsilyl ether of 2-hydroxybenzyl alcohol (105):



Nature: Yellowish liquid

Yield: 67% (0.478)

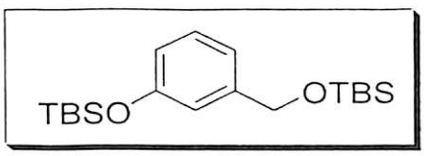
IR (Neat): 2945, 2858, 1598, 1485, 1459, 1377, 1260, 1116, 1070, 932, 840 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): 0.09 (s, 6H, $Si(CH_3)_2$), 0.20 (s, 6H, $Si(CH_3)_2$), 0.94 (s, 9H, $SiC(CH_3)_3$), 0.99 (s, 9H, $SiC(CH_3)_3$), 4.75 (s, 2H, OCH_2), 6.73 (d, 1H, J = 8.0 Hz, ArH),

6.96 (t, 1H, *J* = 7.6 Hz, ArH), 7.10 (t, 1H, J = 8.0 Hz, ArH), 7.44 (d, 1H, J = 6.8 Hz, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{19}H_{36}O_2Si_2$	C 64.71	C 64.80
356.66	H 10.29	H 10.32

Di-*tert*- butyldimethylsilyl ether of 3-hydroxybenzyl alcohol (106):



Nature: Colourless liquid

Yield: 68% (0.480 g)

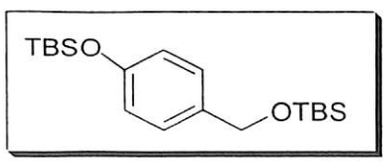
IR (Neat): 2959, 2934, 2860, 1597, 1479, 1370, 1282, 1163, 1104, 1015, 971, 848, 705 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.10 (s, 6H, $Si(CH_3)_2$), 0.20 (s, 6H, $Si(CH_3)_2$), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.89 (s, 9H, $SiC(CH_3)_3$), 4.60 (s, 2H, CH_2OTBS), 6.51 (dd, 1H, *J* = 2.4, J = 7.8 Hz, ArH), 6.65 (s, 1H, ArH), 6.69 (d, 1H, *J* = 7.6 Hz, ArH), 6.98 (t, 1H, *J* = 7.8 Hz, ArH) ppm.

^{13}C NMR (100MHz, $CDCl_3$): δ -5.3, -4.4, 18.2, 18.4, 25.7, 25.9, 64.7, 117.6, 118.6, 118.8, 129.1, 143.1, 155.7 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{19}H_{36}O_2Si_2$	C 64.71	C 64.82
352.66	H 10.29	H 10.32

Di-*tert*- butyldimethylsilyl ether of 4-hydroxybenzyl alcohol (107):



Nature: Colourless liquid

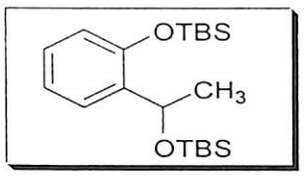
Yield: 71% (0.501 g)

IR (Neat): 2960, 2945, 2899, 2868, 1614, 1516, 1475, 1255, 1091, 922, 851, 779 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.08 (s, 6H, $Si(CH_3)_2$), 0.18 (s, 6H, $Si(CH_3)_2$), 0.93 (s, 9H, $SiC(CH_3)_3$), 0.98 (s, 9H, $SiC(CH_3)_3$), 4.66 (s, 2H, CH_2OTBS), 6.79 (d, 2H, *J* = 8.4 Hz, ArH), 7.17 (d, 2H, *J* = 8.4 Hz, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{19}H_{36}O_2Si_2$	C 64.71	C 64.83
352.66	H 10.29	H 10.35

Di-*tert*- butyldimethylsilyl ether of 2-hydroxy-1′-methyl-benzyl alcohol (108):



Nature: Colourless liquid

Yield: 60% (0.440 g)

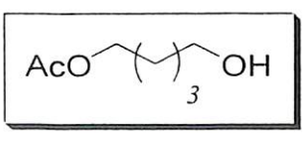
IR (Neat): 2960, 2935, 2863, 1609, 1588, 1496, 1470, 1368, 1260, 1107, 1086, 1040, 927, 846, 789 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.01(s, 3H, $SiCH_3$), 0.03(s, 3H, $SiCH_3$), 0.26 (s, 3H, $SiCH_3$), 0.30 (s, 3H, $SiCH_3$), 0.93 (s, 9H, Si $C(CH_3)_3$), 1.05 (s, 9H, Si $C(CH_3)_3$), 1.38 (d, 3H, J = 6.2 Hz, $CHCH_3$), 5.25 (q, 1H, J = 6.2 Hz, $OCHCH_3$), 6.75 (d, 1H, ArH), 6.96 (t, 1H, ArH), 7.06 (t, 1H, ArH), 7.55 (d, 1H, ArH).

Elemental Analysis	Calculated	Found
$C_{20}H_{38}O_2Si_2$	C 65.51	C 65.62
366.69	H 10.44	H 10.50

General procedure for the deprotection of tert-Butyldimethylsilyl ethers to the parent hydroxyl compounds: To a well stirred solution of *tert*-butyldimethylsilyl ether (1 mmol) in 2 mL of dichloromethane-methanol mixture (5:2) was added a catalytic amount of acetonyltriphenylphosphonium bromide (20 mg, 0.05 mmol) except for **81** at room temperature and kept for stirring. After completion of the reaction as monitored by TLC, it was concentrated in rotavapor. The crude residue was subjected to silica gel column chromatography to isolate the desired alcohols in good yields.

5-Acetoxy-1-pentanol (56):



Nature: Colourless liquid

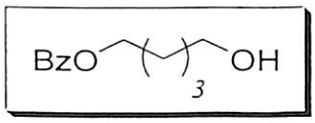
Yield: 70% (0.103 g)

IR (Neat): 3437, 2940, 1737, 1603, 1460, 1363, 1245, 1035 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35-1.74 (m, 7H, CH_2 & OH), 2.05 (s, 3H, $COCH_3$), 3.67 (t, 2H, J = 6.4 Hz, CH_2OH), 4.08 (t, 2H, J = 6.6 Hz, $AcOCH_2$) ppm.

Elemental Analysis	Calculated	Found
$C_7H_{14}O_3$	C 57.52	C 57.63
146.18	H 9.65	H 9.71

5-Benzoyloxy-1-pentanol (82):



Nature: Colourless liquid

Yield: 88% (0.184 g)

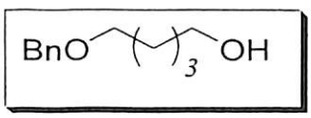
IR (Neat): 3421, 3068, 2940, 2868, 1726, 1614, 1460, 1393, 1281, 1122, 717 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.48 (m, 3H, CH_2 & OH), 1.59 (m, 2H, CH_2), 1.75 (m, 2H, CH_2), 3.62 (t, 2H, J = 6.4 Hz, CH_2OH), 4.27 (t, 2H, J = 6.6 Hz, PhCOOCH_2), 7.37 (t, 2H, J = 7.8 Hz, ArH), 7.49 (t, 1H, J = 7.6Hz, ArH), 7.96 (d, 2H, J = 7.1 Hz ArH) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.4, 28.6, 32.3, 62.7, 64.9, 128.3, 129.5, 130.5, 132.9, 166.7 ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{16}O_3$	C 69.21	C 69.32
208.26	H 7.74	H 7.83

5-Benzyloxy-1-pentanol (83):



Nature: Colourless liquid

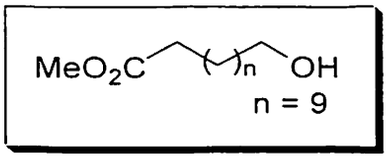
Yield: 92% (0.179 g)

IR (Neat): 3416, 2935, 2863, 1609, 1501, 1455, 1368, 1265, 1209, 1096, 1055 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31-1.70 (m, 7H, CH_2 & OH), 3.47 (t, 2H, J = 6.4 Hz, CH_2OH), 3.63 (t, 2H, J = 6.4Hz, PhCH$_2$OCH_2), 4.48 (s, 2H, OCH_2Ph), 7.32 (m, 5H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{18}O_2$	C 74.19	C 74.32
194.27	H 9.34	H 9.41

12-Carboxymethylate-1-dodecanol (84):



Nature: Colourless liquid

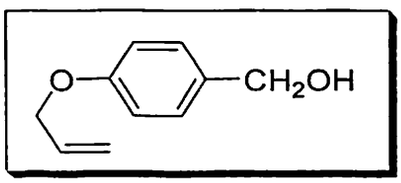
Yield: 92% (0.212 g)

IR (Neat): 3442, 2925, 2858, 1737, 1460, 1358, 1255, 1209, 1055, 1112, 876 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.45 (m, 18H, -CH_2-), 1.61 (bs, 1H, -OH), 2.30 (t, 2H, *J* = 6.8 Hz, -C*H*$_2$OH), 3.64 (t, 2H, *J* = 5.9 Hz, -$COCH_2$-), 3.67 (s, 3H, -OCH_3) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{26}O_3$	C 67.79	C 67.56
230.35	H 11.38	H 11.23

4-Allyloxy benzyl alcohol (85):



Nature: Colourless liquid

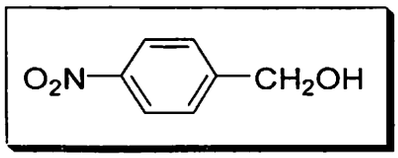
Yield: 91% (0.150 g)

IR (Neat): 3350, 2930, 2879, 1619, 1511, 1460, 1424, 1373, 1301, 1240, 1189, 1122, 1009, 1034, 938, 825 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60 (s, 1H, -OH), 4.53-4.55 (m, 2H, -O*C*H_2CH=CH_2), 4.56 (s, 2H, -C*H*$_2$OH), 5.27 (dd, 1H, *J* = 1.0 Hz, *J* = 10.5 Hz, OCH_2CH=*C*H_2), 5.40 (dd, 1H, *J* = 1.4 Hz, *J* = 15.8 Hz, OCH_2CH=*C*H_2), 6.04 (m, 1H, OCH_2*C*H=CH_2), 6.89 (d, 2H, *J* = 8.5 Hz, ArH), 7.30 (d, 2H, *J* = 8.6 Hz, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{12}O_2$	C 73.15	C 72.90
164.20	H 7.37	H 7.17

4-Nitro benzyl alcohol (86):



Nature: Colourless liquid

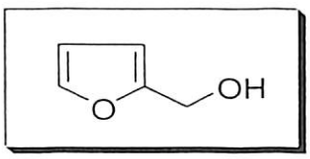
Yield: 94% (0.144 g)

IR (Neat): 2955, 2935, 2863, 1614, 1521, 1475, 1352, 1265, 1102, 1020, 856 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.09 (s, 1H, -OH), 4.84 (s, 2H, -*C*H_2OH), 7.54 (d, 2H, *J* = 9.0 Hz, ArH), 8.22 (d, 2H, *J* = 9.0 Hz, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_7H_7O_3N$	C 54.90	C 54.73
153.14	H 4.61	H 4.86
	N 9.15	N 9.32

Furfuryl alcohol (87):



Nature: Colourless liquid

Yield: 83% (.082 g)

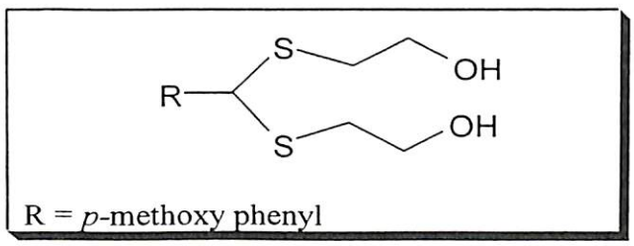
IR (Neat): 3375, 2940, 2879, 1634, 1501, 1429, 1158, 1009, 922, 815, 748 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.02 (bs, 1H), 4.59 (s, 2H), 6.28 (d, 1H, *J* =3.2 Hz), 6.32 (d, 1H, *J* =3.2 Hz), 7.38 (d, 1H, *J* = 2.0 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 57.5, 107.8, 110.3, 142.6, 153.9 ppm.

Elemental Analysis	Calculated	Found
$C_5H_6O_2$	C 61.22	C 61.47
98.10	H 6.16	H 6.23

Compound (88):



Nature: White solid

Yield: 81% (0.223 g)

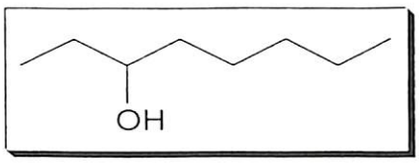
IR (Neat): 3334, 2914, 2848, 2745, 1609, 1516, 1455, 1255, 1173, 1076, 1020, 830 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 2.58-2.90 (m, 6H, SCH_2 & OH), 3.71 (m, 4H, OCH_2), 3.80 (s, 3H, OCH_3), 5.06 (s, 1H, SCHS), 6.87 (d, 2H, *J* = 8.6 Hz, ArH), 7.38 (d, *J* = 8.6 Hz, ArH) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 36.1, 33.2, 55.9, 99.5, 114.7, 129.5, 132.0, 160.0 ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{18}O_3S_2$	C 52.53	C 53.58
274.40	H 6.61	H 6.73
	S 23.37	S 23.40

3-Octanol (89):



Nature: Colorless liquid

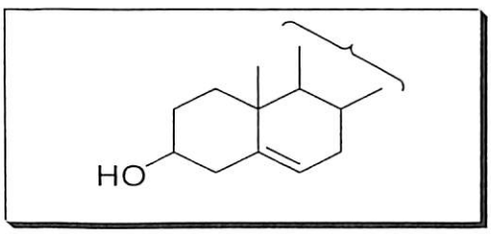
Yield: 91% (0.119 g)

IR (Neat): 3350, 2930, 1460, 1010 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J* = 7.2 Hz), 0.92 (t, 3H, *J* = 7.2 Hz), 1.28-1.58 (m, 10H), 1.72 (s, 1H), 3.49 (m, 1H) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_8H_{18}O$	C 73.78	C 73.92
130.23	H 13.93	H 13.87

Cholesterol (90):



Nature: White solid, mp: 148 ^{0}C

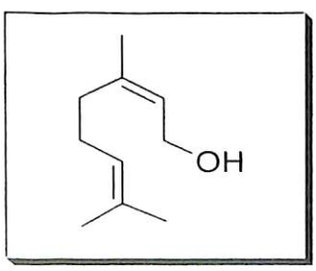
Yield: 90% (0.348 g)

IR (KBr): 3342, 2930, 2863, 1619, 1465, 1378, 1137, 1061, 1030, 963, 810 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.68 (s, 3H), 0.86 (d, 3H, *J* = 1.68 Hz), 0.87 (d, 3H, *J* = 1.72 Hz), 0.91 (d, 3H, *J* = 6.6 Hz), 1.01 (s, 3H), 1.07-1.22 (m, 4H), 1.23-1.51 (m, 2H), 1.56 (bs, 17H), 1.78-1.87 (m, 2H), 1.95-2.03 (m, 2H), 2.20-2.31 (m, 2H), 3.49-3.55 (m, 1H), 5.35-5.36 (t, 1H, *J* = 2.7 Hz) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{27}H_{46}O$	C 83.87	C 84.02
386.66	H 11.99	H 12.08

Geraniol (91):



Nature: Colorless liquid

Yield: 95% (0.147 g)

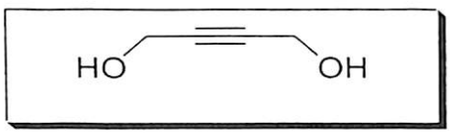
IR (Neat): 3380, 2970, 2925, 2868, 1670, 1465, 1385,1020 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.58 (s, 3H), 1.66 (s, 3H), 1.73 (s, 3H), 1.92-2.15 (m, 5H), 4.20 (d, 2H, J = 6.4 Hz), 5.07 (t, 1H, J = 6.6 Hz), 5.34 (t, 1H, J = 6.4 Hz,) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 17.7, 29.6, 30.7, 39.6, 59.8, 124.0, 124.8, 131.6, 140.2 ppm.

Elemental Analysis	Calculated	Found
$C_{10}H_{18}O$	C 77.87	C 77.62
154.25	H 11.76	H 11.85

Butyne-1,4-diol (92):



Nature: Low melting solid

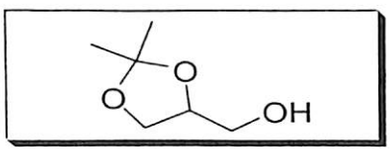
Yield: 85% (0.073 g)

IR (Neat): 3370, 2925, 2868, 1639, 1434, 1358, 1230, 1132, 1015 cm^{-1}.

^{1}H NMR (400 MHz, Acetone-d_6): δ 4.23 (bs, 4H, 2 x CH_2OH), 4.39 (bs, 2H, 2 x OH) ppm.

Elemental Analysis	Calculated	Found
$C_4H_6O_2$	C 55.81	C 55.73
86.09	H 7.02	H 7.16

2,3-*O*-isopropylidene-*D*-(±)-glycerol (93):



Nature: Liquid

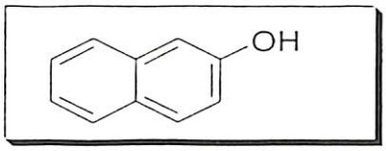
Yield: 72% (0.095 g)

IR (Neat): 3365, 2925, 2868, 1460, 1123, 1011 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 1.39 (s 3H, CH_3), 1.46(s, 3H, CH_3), 2.60 (bs, 1H, OH), 3.63-3.77(m, 1H, CH_2) 3.62-3.72(m, 1H, CH_2), 3.79 (dd, J = 4.8 Hz, J = 11.4 Hz 1H, CH_2), 4.05-4.12 (dd, J = 4.6 Hz, J = 11.6 Hz, 1H, CH_2), 4.24-4.36 (m, 1H, CH) ppm

Elemental Analysis	Calculated	Found
$C_6H_{12}O_3$	C 54.53	C 54.43
132.16	H 9.15	H 9.08

β-Naphthol (49):



Nature: Solid, mp: 121-122 °C.

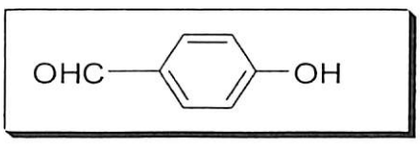
Yield: 81% (0.117 g)

IR (KBr): 3291, 2937, 2848, 1642, 1602, 1506, 1471, 1362, 1234, 935, 854, 748 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.08 (dd, 1H, *J* = 3.1 Hz, *J* = 8.7 Hz, 3-ArH), 7.20 (d, 1H, *J* = 2.4 Hz), 7.30 (t, 1H, *J* = 7.0 Hz, ArH), 7.38 (t, 1H, *J* = 7.0 Hz, ArH), 7.68 (d, 1H, *J* = 8.7 Hz, ArH, ArH), 7.72 (d, 1H, *J* = 9.0 Hz, ArH), 7.76 (d, 1H, *J* = 8.1 Hz, ArH), 9.48 (bs, 1H, OH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_8O$	C 83.31	C 83.39
144.17	H 5.59	H 5.53

4-hydroxy benzaldehyde (94):



Nature: Solid, mp: 117 °C

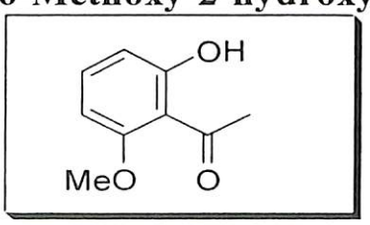
Yield: 71% (0.086 g)

IR (KBr): 3383, 2948, 2856, 1706, 1603, 1511, 1270, 1157, 912, 845 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.62 (bs, 1H, -OH), 7.33(d, 2H, *J* = 8.32 Hz, ArH), 7.88 (d, 2H, J = 8.04 Hz, ArH), 9.96 (s, 1H, -CHO) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_7H_6O_2$	C 68.85	C 68.65
122.12	H 4.95	H 5.05

6-Methoxy-2-hydroxy acetophenone (95):



Nature: Liquid

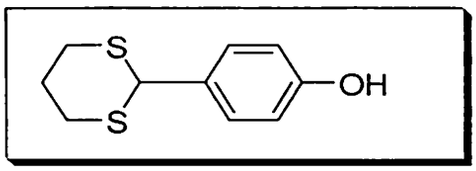
Yield: 91% (0.151 g)

IR (Neat): 3343, 3017, 2981, 2935, 2805, 1706, 1627, 1595, 1459, 1434, 1347, 1238, 1183, 1103, 1025, 854, 795, 730, 636 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.67 (s, 3H, $COCH_3$), 3.90 (s, 3H, OCH_3), 6.39 (d, 1H, *J* = 8.3 Hz, ArH), 6.58 (d, 1H, *J* = 8.4 Hz, ArH), 7.34 (t, 1H, *J* = 8.3 Hz, ArH), 13.24 (bs, 1H, OH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_9H_{10}O_3$	C 65.05	C 65.01
166.18	H 6.07	H 6.02

2-[4′-Hydroxyphenyl]-1,3-dithiolane (96):



Nature: White solid

Yield: 85% (0.180 g)

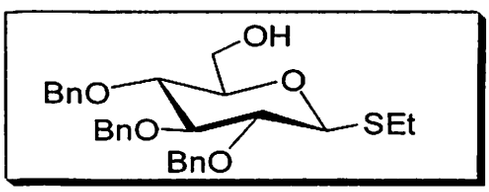
IR (KBr): 3396, 2914, 1603, 1511, 1450, 1368, 1250, 1178, 1102, 851 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.31-3.37 (m, 2H), 3.45-3.52 (m, 2H), 5.23 (s, 1H), 5.62 (s, 1H), 6.75 (d, 2H, *J* = 7.8 Hz), 7.39 (d, 2H, *J* = 8.5 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 40.18 (2C), 56.03, 115.34 (2C), 129.40 (2C), 131.96, 155.30 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{12}OS_2$	C 56.57	C 56.63
212.32	H 5.70	H 5.68
	S 30.20	S 30.24

Ethyl-2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (97):



Nature: White solid

Yield: 88% (0.435)

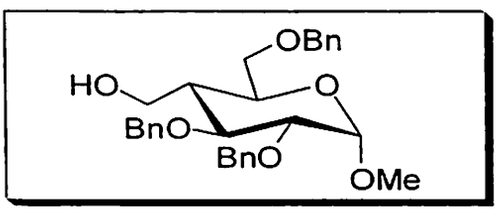
IR (Neat): 3355, 3032, 2909, 2863, 1608, 1459, 1362, 1219, 1080, 1034, 1004, 845, 747, 701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (t, 3H, *J* = 7.3 Hz), 1.95 (bs, 1H), 2.71-2.80 (m, 2H), 3.35-3.39 (m, 1H), 3.41 (t, 1H, *J* = 9.3 Hz), 3.58 (t, 1H, *J* = 9.3 Hz), 3.70 (t, 1H, *J* = 8.8 Hz), 3.87 (d, 1H, *J* = 11.5 Hz), 4.50 (d, 1H, *J* = 9.8 Hz), 4.65 (d, 1H, *J* = 11 Hz), 4.74 (d, 1H, *J* = 11 Hz), 4.86 (d, 2H, *J* = 12.4 Hz), 4.89 (d, 1H, *J* = 10.0 Hz), 4.92 (dd, 2H, *J* = 6.8 Hz, *J* = 11 Hz), 7.25-7.38 (m, 15 H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.16, 25.20, 62.15, 75.17, 75.57, 75.74, 75.76, 77.69,79.27, 81.77, 85.27, 86.47, 127.71, 127.77, 127.89, 127.96, 128.07, 128.29, 128.41,128.46, 128.52, 137.90 (2C), 138.41 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{29}H_{34}O_5S$	C 70.42	C 70.64
494.65	H 6.93	H 7.08
	S 6.48	S 6.10

Methyl-2,3,6-tri-*O*-benzyl-4-hydroxymethyl-α-D-glucopyranoside (98):



Nature: Gummy liquid

Yield: 82% (0.393 g)

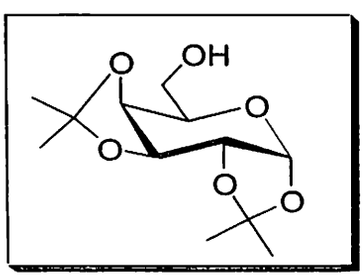
IR (Neat): 3457, 3032, 2930, 2894, 1609, 1455, 1358, 1096, 1050, 743, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.68 (bs, 1H), 1.86 (m, 1H), 3.37 (s, 3H), 3.55 (d, 1H, *J* = 3.4 Hz), 3.58 (t, 2H, *J* = 2.4 Hz), 3.61 (m, 2H), 3.68 (dd, 1H, *J* = 3.4 Hz, *J* = 11.4 Hz), 3.83 (m, 1H), 3.58 (t, 1H, *J* = 10.24 Hz), 4.47 (d, 1H, *J* = 11.96 Hz), 4.61 (d, 1H, *J* = 11.96 Hz), 4.66 (m, 1H), 4.69 (d, 1H, *J* = 3.2 Hz), 4.77 (d, 1H, *J* = 11.96 Hz), 4.99 (d, 1H, *J* = 11.2 Hz), 7.32 (m, 15H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 46.07, 55.19, 59.50, 68.20, 70.48, 72.88, 73.53, 75.19, 75.44, 81.49, 98.45, 127.76, 127.87, 128.09, 128.35, 128.39, 128.43, 128.51, 137.66, 138.18, 138.42 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{29}H_{34}O_6$	C 72.78	C 72.57
478.58	H 7.16	H 7.25

1,2,3,4-Di-*O*-isopropylidene-D-galactose (99):



Nature: Yellowish gummy liquid

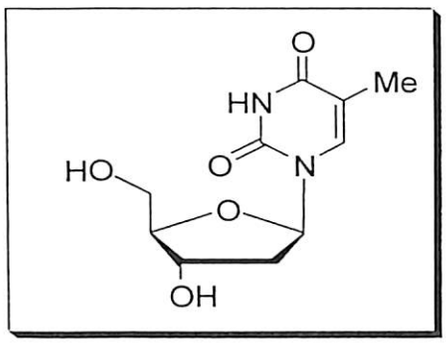
Yield: 80% (0.208 g)

IR (Neat): cm^{-1} 3493, 2991, 2935, 1460, 1383, 1255, 1219, 1173, 1076, 1009, 892

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (s, 6H), 1.46 (s, 3H), 1.54 (s, 3H), 2.28 (bs, 1H), 3.75 (t, 1H, *J* = 7.3 Hz), 3.82-3.90 (m, 2H), 4.27 (d, 1H, *J* = 7.9 Hz), 4.34 (dd, 1H, *J* = 2.3 Hz, *J* = 4.9 Hz), 4.62 (dd, 1H, *J* = 2.3 Hz, *J* = 7.9 Hz), 5.57 (d, 1H, *J* = 5.0 Hz) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{20}O_6$	C 55.38	C 55.46
260.28	H 7.74	H 7.68

Thymidine (100):



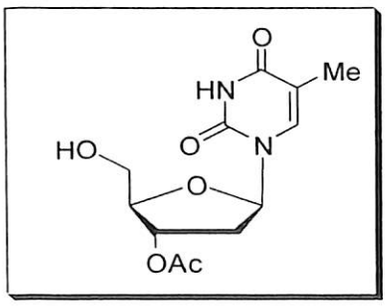
Nature: White solid; mp: 187 °C

Yield: 87% (0.211 g)

IR (Neat): 3324, 3165, 3032, 2843, 1711, 1481, 1445, 1286, 1117, 1071, 1020, 968, 897 cm^{-1}.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{14}O_5N_2$	C 49.59	C 49.67
242.23	H 5.83	H 5.98
	N 11.57	N 11.36

Mono acetate of Thymidine (101):



Nature: White solid, mp: 174 °C

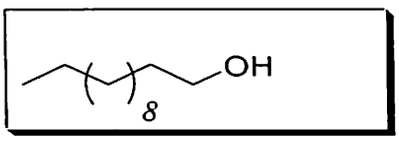
Yield: 87% (0.247 g)

IR (KBr): 3472, 3201, 3068, 2929, 1738, 1710, 1669, 1475, 1249, 1111, 1075, 1024,881, 788, 576 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.92 (s, 3H, CCH_3), 2.11 (s, 3H, $COCH_3$), 2.40 (bs, 3H, CH_2 & OH), 3.92 (s, 2H, OCH_2), 4.10 (bs, 1H, H-3), 5.36 (bs, 1H, H-4), 6.27 (bs, 1H, H-1), 7.55 (s, 1H,= CH), 9.50 (s, 1H, NH) ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{16}O_6N_2$	C 50.70	C 50.81
284.27	H 5.67	H 5. 61
	N 9.85	N 9.01

Dodecanol (102):



Nature: Liquid

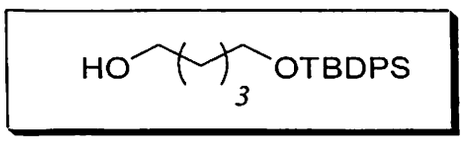
Yield: 88% (0.164 g)

IR (Neat): 3396, 2925, 2848, 1460, 1050, 758, 728 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J* = 6.9 Hz, -CH_2CH_3), 1.26 (bs, 18H, -CH_2), 1.57 (m, 2H, -CH_2CH_2OH), 1.67 (s, 1H, -OH), 3.64 (t, 2H, *J* = 6.6 Hz, -CH_2OH) ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{26}O$	C 77.35	C 77.12
186.34	H 14.07	H 13.89

5-*tert*-butyldiphenylsilyl pentane 1-ol (109):



Nature: Colourless liquid

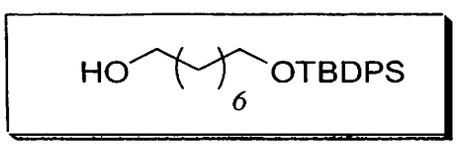
Yield: 78 % (0.267 g)

IR (Neat): 3396, 3068, 3053, 2930, 2863, 1598, 1470, 1424, 1393, 1112, 1045, 1004, 943, 825 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (s, 9H, $SiC(CH_3)_3$), 1.56 (m, 7H, CH_2 & OH), 3.62 (t, 2H, *J* = 6.4 Hz OCH_2CH_2), 3.67 (t, 2H, *J* = 6.2 Hz OCH_2CH_2), 7.40(m, 5H, ArH), 7.68 (m, 5H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{21}H_{30}O_2Si$	C 73.63	C 73.53
342.55	H 8.81	H 8.69

8-*tert*-butyldiphenylsilyl octane-1-ol (110):



Nature: Yellowish liquid

Yield: 81 % (0.312 g)

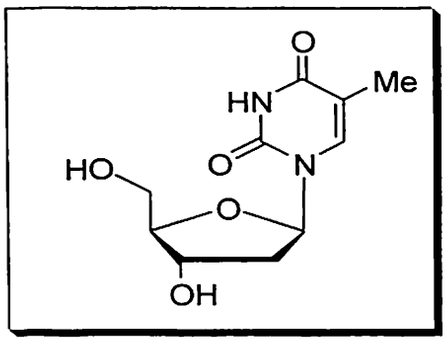
IR (Neat): 3355, 3073, 3053, 2935, 2868, 1593, 1475, 1429, 1399, 1117, 835 cm^{-1}.

IR (Neat): cm^{-1} 3493, 2991, 2935, 1460, 1383, 1255, 1219, 1173, 1076, 1009, 892

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (s, 6H), 1.46 (s, 3H), 1.54 (s, 3H), 2.28 (bs, 1H), 3.75 (t, 1H, *J* = 7.3 Hz), 3.82-3.90 (m, 2H), 4.27 (d, 1H, *J* = 7.9 Hz), 4.34 (dd, 1H, *J* = 2.3 Hz, *J* = 4.9 Hz), 4.62 (dd, 1H, *J* = 2.3 Hz, *J* = 7.9 Hz), 5.57 (d, 1H, *J* = 5.0 Hz) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{20}O_6$	C 55.38	C 55.46
260.28	H 7.74	H 7.68

Thymidine (100):



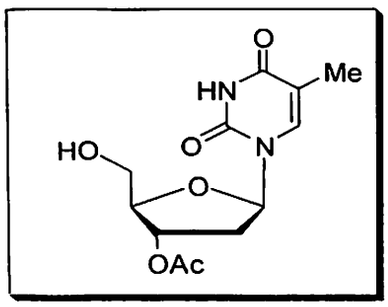
Nature: White solid; mp: 187 °C

Yield: 87% (0.211 g)

IR (Neat): 3324, 3165, 3032, 2843, 1711, 1481, 1445, 1286, 1117, 1071, 1020, 968, 897 cm^{-1}.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{14}O_5N_2$	C 49.59	C 49.67
242.23	H 5.83	H 5.98
	N 11.57	N 11.36

Mono acetate of Thymidine (101):



Nature: White solid, mp: 174 °C

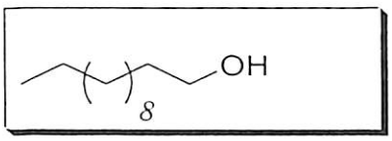
Yield: 87% (0.247 g)

IR (KBr): 3472, 3201, 3068, 2929, 1738, 1710, 1669, 1475, 1249, 1111, 1075, 1024,881, 788, 576 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.92 (s, 3H, CCH_3), 2.11 (s, 3H, $COCH_3$), 2.40 (bs, 3H, CH_2 & OH), 3.92 (s, 2H, OCH_2), 4.10 (bs, 1H, H-3), 5.36 (bs, 1H, H-4), 6.27 (bs, 1H, H-1), 7.55 (s, 1H,= CH), 9.50 (s, 1H, NH) ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{16}O_6N_2$	C 50.70	C 50.81
284.27	H 5.67	H 5. 61
	N 9.85	N 9.01

Dodecanol (102):



Nature: Liquid

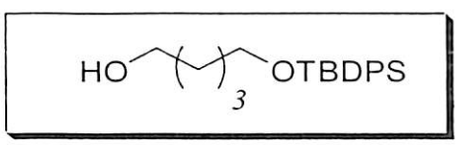
Yield: 88% (0.164 g)

IR (Neat): 3396, 2925, 2848, 1460, 1050, 758, 728 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, J = 6.9 Hz, -CH_2CH_3), 1.26 (bs, 18H, -CH_2), 1.57 (m, 2H, -CH_2CH_2OH), 1.67 (s, 1H, -OH), 3.64 (t, 2H, J = 6.6 Hz, -CH_2OH) ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{26}O$	C 77.35	C 77.12
186.34	H 14.07	H 13.89

5-*tert*-butyldiphenylsilyl pentane 1-ol (109):



Nature: Colourless liquid

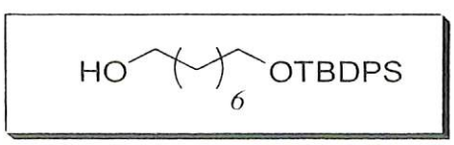
Yield: 78 % (0.267 g)

IR (Neat): 3396, 3068, 3053, 2930, 2863, 1598, 1470, 1424, 1393, 1112, 1045, 1004, 943, 825 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (s, 9H, $SiC(CH_3)_3$), 1.56 (m, 7H, CH_2 & OH), 3.62 (t, 2H, J = 6.4 Hz OCH_2CH_2), 3.67 (t, 2H, J = 6.2 Hz OCH_2CH_2), 7.40(m, 5H, ArH), 7.68 (m, 5H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{21}H_{30}O_2Si$	C 73.63	C 73.53
342.55	H 8.81	H 8.69

8-*tert*-butyldiphenylsilyl octane-1-ol (110):



Nature: Yellowish liquid

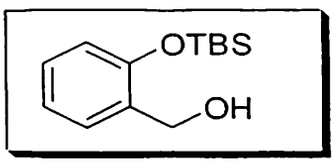
Yield: 81 % (0.312 g)

IR (Neat): 3355, 3073, 3053, 2935, 2868, 1593, 1475, 1429, 1399, 1117, 835 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.02 (s, 9H, $SiC(CH_3)_3$), 1.28 (m, 8H, CH_2), 1.54 (m, 5H, CH_2 & OH), 3.60 (t, 2H, J = 6.6 Hz, OCH_2CH_2), 3.64 (t, 2H, J = 6.3 Hz, OCH_2CH_2), 7.37 (m, 5H, ArH), 7.67 (m, 5H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{24}H_{36}O_2Si$	C 74.95	C 74.89
384.63	H 9.43	H 9.48

2′-*tert*-butyldimethylsilyloxy benzyl alcohol (111):



Nature: Yellowish liquid

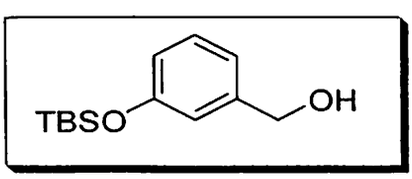
Yield: 77% (0.184 g)

IR (Neat): ν 3370, 2976, 2940, 2873, 1609, 1588, 1491, 1460, 1393, 1368, 1265, 1194, 1117, 1040, 922, 840 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.24 (s, 6H, $Si(CH_3)_2$), 1.00 (s, 9H, $SiC(CH_3)_3$), 2.01 (s, 1H, OH, D_2O exchangeable), 4.65 (s, 2H, CH_2OH), 6.79 (d, 1H, J = 8.1 Hz, ArH), 6.93 (t, 1H, J = 7.3 Hz, ArH), 7.15 (t, 1H, J = 7.6 Hz, ArH), 7.27 (d, 1H, J = 7.6 Hz, ArH) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ -4.2, 18.2, 25.7, 61.9, 118.4, 121.3, 128.6, 128.8, 131.4, 153.5 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{22}O_2Si$	C 65.50	C 65.54
238.40	H 9.30	H 9.36

3′-*tert*-butyldimethylsilyloxy benzyl alcohol (112):



Nature: Colourless liquid

Yield: 86% (0.205 g)

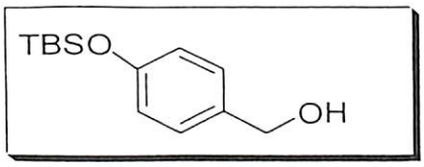
IR (Neat): 3334, 2960, 2935, 2863, 1598, 1496, 1445, 1378, 1281, 1255, 1153, 1020, 953, 851, 784, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.79 (s, 9H, $SiC(CH_3)_3$), 1.46 (s, 1H, OH, D_2O exchangeable), 4.44 (s, 2H, CH_2OH), 6.56 (dd, 1H, J = 2.4, J = 8.0 Hz, ArH), 6.66 (s, 1H, ArH), 6.75 (d, 1H, J = 7.3 Hz, ArH), 7.03 (t, 1H, J = 7.8 Hz, ArH) ppm.

^{13}C NMR (100MHz, $CDCl_3$): δ -4.5, 18.2, 25.7, 65.2, 118.6, 119.2, 119.7, 129.5, 142.5, 155.9 ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{22}O_2Si$	C 65.50	C 65.55
238.40	H 9.30	H 9.38

4′-*tert*-butyldimethylsilyloxy benzyl alcohol (113):



Nature: Colourless liquid

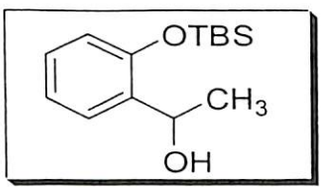
Yield: 87% (0.207 g)

IR (Neat): ν 3365, 2970, 2945, 2863, 1618, 1521, 1485, 1260, 1019, 916, 840, 783 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.19 (s, 6H, $Si(CH_3)_2$), 0.98 (s, 9H, $SiC(CH_3)_3$), 1.62 (s, 1H, OH, D_2O exchangeable), 4.60 (s, 2H, CH_2OH), 6.82 (d, 2H, J = 8.4 Hz, ArH), 7.23 (d, 2H, J = 8.4 Hz, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{22}O_2Si$	C 65.50	C 65.47
238.40	H 9.30	H 8.29

Compound (114) :



Nature: Colourless liquid

Yield: 76% (0.192 g)

IR (Neat): 3396, 2960, 2940, 2858, 1603, 1491, 1460, 1255, 1127, 1071, 1015, 927, 835, 784 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.28 (s, 6H, $Si(CH_3)_2$)), 1.02 (s, 9H, $SiC(CH_3)_3$), 1.48 (d, 3H, J = 6.5 Hz, $CHCH_3$), 2.35(bs, 1H, OH, D_2O exchangeable), 5.21 (q, 1H, J = 6.5 Hz, CH(OH)), 6.75 (d, 1H, ArH), 6.96 (t, 1H, J = 7.3 Hz, ArH), 7.06 (t, J = 7.06 Hz, 1H, ArH), 7.55 (d, J = 7.06 Hz, 1H, ArH) ppm.

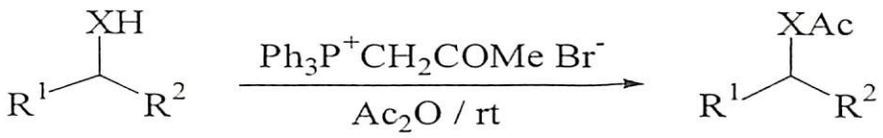
Elemental Analysis	Calculated	Found
$C_{14}H_{24}O_2Si$	C 66.61	C 66.80
252.43	H 9.58	H 9.54

SECTION B

PRESENT WORK ON ACETYLATION OF ALCOHOLS, PHENOLS, THIOLS, THIOPHENOLS AND AMINES AND 1,1-DIACYLATION OF ALDEHYDES CATALYZED BY ACETONYLTRIPHENYLPHOSPHONIUM BROMIDE (ATPB)

RESULTS AND DISCUSSION

We have disclosed the catalytic activity of acetonyltriphenylphosphonium bromide for selective deprotection of TBS ethers in the previous section of Chapter I. Next we paid our attention to explore the same reagent for other important transformations. From the literature survey on acylation of hydroxyl, amines and thiols as stated in Part I, we realized that still there is a scope to develop an improved and better protocol for acylation using stoichiometric amount of acetic anhydride and catalytic conditions. In continuation of our research for the development of new synthetic methodologies we perceived that the reagent acetonyltriphenylphosphonium bromide might be useful for acetylation. In the present result and discussion part, our successful results for acylation of various alcohols, phenols, thiols, and amines using ATPB as pre-catalyst are represented in Scheme 22.



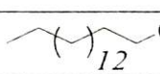
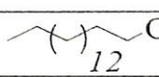
X = O / NH / S
R^1 = alkyl / aryl / sugar residue/ nucleoside residue;
R^2 = H, alkyl, aryl

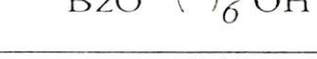
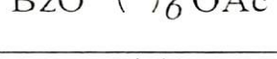
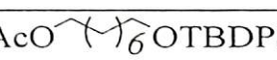
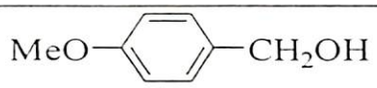
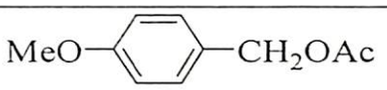
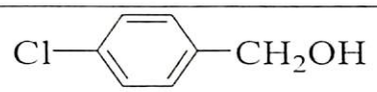
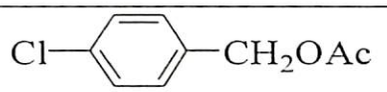
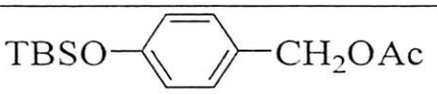
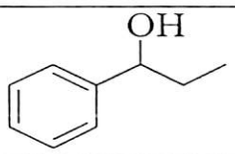
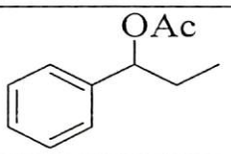
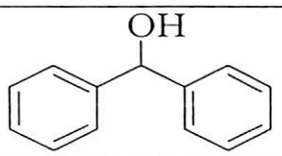
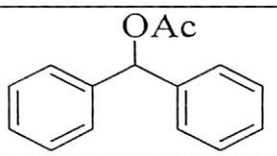
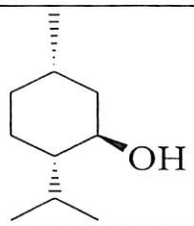
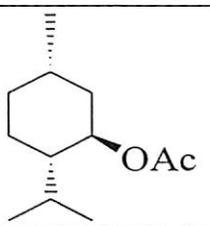
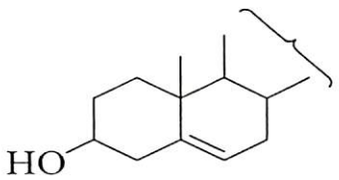
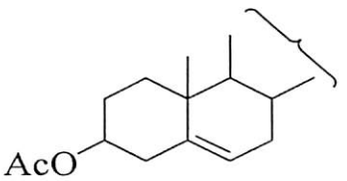
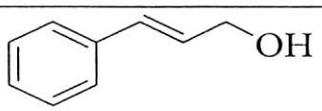
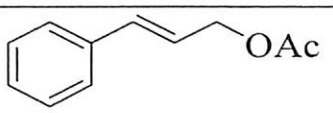
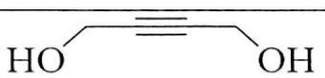
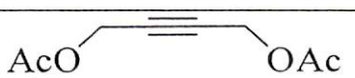
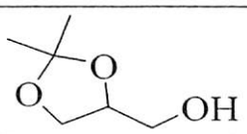
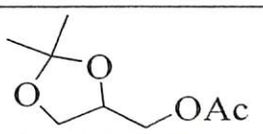
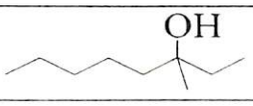
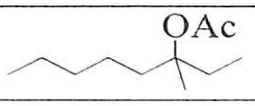
Scheme 22

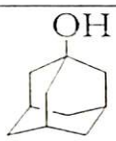
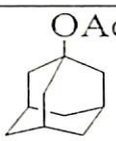
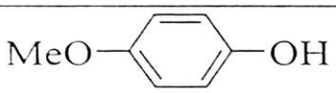
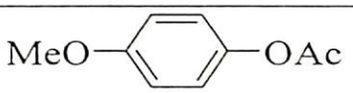
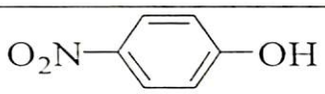
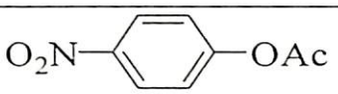
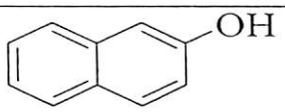
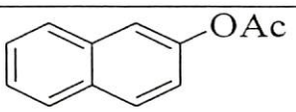
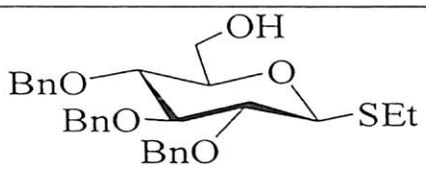
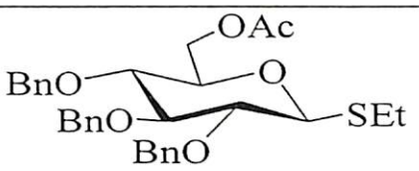
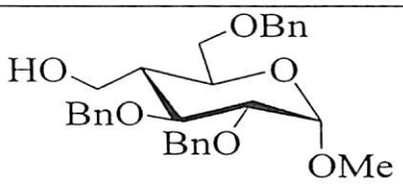
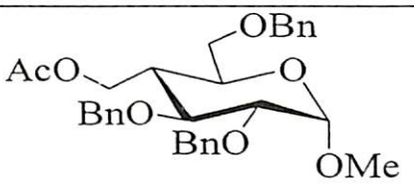
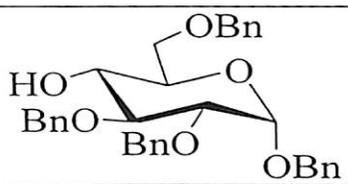
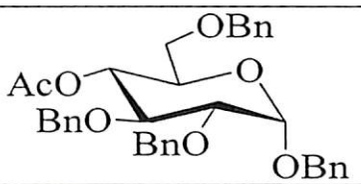
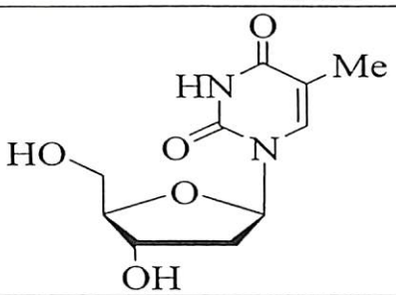
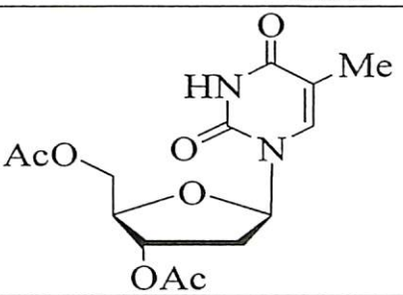
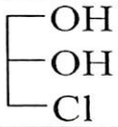
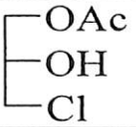
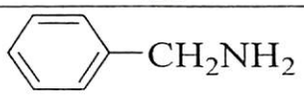
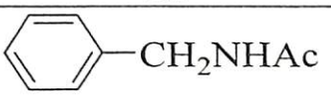
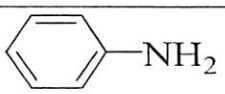
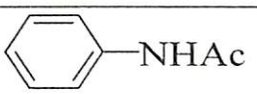
First, we attempted the acylation reaction of cetyl alcohol (**115**) with acetic anhydride in the presence of 5 mol% acetonyltriphenylphosphonium bromide at room temperature. The reaction was completed within 25 min and the pure acetate derivative of cetyl alcohol (**135**) was obtained in 96% yield after chromatographic separation. The product was characterized by recording IR, ^{1}H NMR spectra (Fig **11** and **12**) and elemental analysis and is agreeable with the acetate. The appearance of the signal at δ 2.04 (s, 3H, -$COCH_3$), in ^{1}H NMR spectra as well as IR absorption at 1739 (CO), clearly indicates the protection of alcohol to their corresponding acetate. Next, we examined benzoyl, *tert*-butyldimethyl silyl and *tert*-butyldiphenylsilyl protected alcohols (**116-118**), and were smoothly converted to the corresponding acetates **136-138** in good yields without affecting the protecting groups by following identical reaction conditions. Likewise, various benzylic alcohols (**113, 119, 120**), secondary alcohols (**121-123** and **90**), allyl alcohol (**124**) and 1,4-butynediol (**92**) were also converted to the corresponding acetate

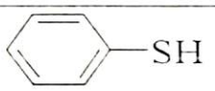
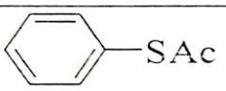
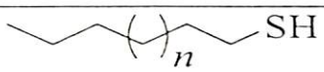
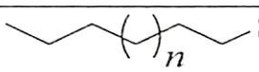
derivatives **139-147,** respectively in very good yields in a similar manner. It is interesting to mention that neither alkyl bromide formation nor HBr addition took place at the double bond or even in the triple bond during the experimental conditions. It was observed that the TBS group was difficult to survive during acetylation reaction by using $Ce(OTf)_3$. However, our protocol has some advantages because the TBS group was unaffected during the reaction conditions. It is also worthwhile to point out that our protocol is more efficient, for example, the acetylation of cholesterol (entry **90**) was completed much faster as compared to the recently reported procedure.[69] Notably, chiral alcohol such as menthol (entry **123**) was acetylated easily with complete retention of optical activity in high yields. Remarkably, an isopropylidene protected alcohol **93** can also be acetylated under identical conditions without cleavage of the isopropylidene group. A tertiary alcohol (**125**) and a sterically hindered tertiary alcohol, adamentanol (**126**) were also smoothly converted to the corresponding acetate derivatives **149** and **150** respectively without any difficulty. We have noticed that the present method is more efficient in terms of reaction timing as compared to the ruthenium(III) chloride method[57] particularly for the preparation of **126**. Then, we interested whether the same reagent can be employed for acetylation of phenolic compounds or not. By using the same protocol, various phenolic compounds **127-128** and **49** were transformed easily to the corresponding acetate derivatives **151-153**. Again, we observed that 4-nitrophenol (**128**) and 2-naphthol (**49**) were converted to the corresponding acetate derivatives much quicker than the recently reported procedure.[57] Next, we turned our attention whether our methodology could be extended further for acetylation of carbohydrates as well as for nucleosides or not. We have found that various carbohydrate molecules such as **97**, **98**, **129** and thymidine (**100**) were converted to the corresponding acetate derivatives **154-157** in good yields under similar reaction conditions. Importantly, a thio group and a methoxy group at the anomeric position were unaffected during experimental conditions. The reaction times and yields of the products are summarized in the Table 3.

Table 3. Acetylation of alcohols, phenols, amines and thiols using acetonyltriphenyl-phosphonium bromide as pre-catalyst at room temperature

S. No.	Substrate	Time min/[h]	Product[a]	Product No	% Yield[b]
115		25		**135**	96

116		30		**136**	92
117		30		**137**	89
118		30		**138**	91
119		40		**139**	96
120		40		**140**	90
113		35		**141**	85
121		30		**142**	95
122		50		**143**	93
123		35		**144**	94
90		3.5		**145**	94
124		40		**146**	92
92		30		**147**	90
93		30		**148**	75
125		[2.0]		**149**	63

126		[1.5]		**150**	87
127		55		**151**	94
128		[2]		**152**	80
49		[3]		**153**	72
97		55		**154**	72
98		55		**155**	74
129		[1.2]		**156**	78
100		[3.5]		**157**	77
130		35		**158**	65
131		35		**159**	86[c]
132		45		**160**	85

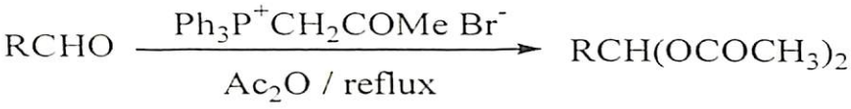
133		[1]		**161**	90
134	 $n = 7$	45	 $n = 7$	**162**	82

[a]All the acetylated compounds were characterized by recording IR, ^{1}H NMR and elemental analyses. [b]Isolated yield. [c]Acetic anhydride was used 3-5 equivalent instead of 1.5-2.0 equivalent.

All these acetylated products were characterized by recording IR, ^{1}H NMR and elemental analyses. IR and ^{1}H NMR of spectra of compound **141**, **146** and **154** are shown in Fig.**13-18** Interestingly, it is also possible that a primary OH group can be acetylated chemoselectively (**130**) under similar reaction conditions. By using our protocol, both aliphatic and aromatic amines (**131-132**) as well as thiols (**133** and **134**) were transformed to the corresponding acetate derivatives **159-162** in good yields by employing the same pre-catalyst.

Subsequently, we paid our attention to study whether the same pre-catalyst is useful for 1,1-diacetylation of aldehydes. The formation of geminal diesters from the corresponding aldehydic compound is an important organic transformation because they serve as building blocks for asymmetric allylic alkylation[90] and Diels-Alder reaction.[91] Moreover, acylals are more oftently used as protecting groups for aldehydes because they are stable under neutral and basic conditions. The formation of 1,1-diacetate is usually achieved by the reaction of aldehydic compound with acetic anhydride in the presence of an acid or Lewis acid, which act as a catalyst. In the literature, there are several methods reported by employing various reagents for similar transformation such as LiOTf,[71] ceric ammonium nitrate,[92] $InCl_3$,[93] H_2NSO_3H,[94] $LiBF_4$,[95] H_2SO_4,[96] PCl_3,[97] NBS,[98] I_2,[99] TMSCl-NaI,[100] $FeCl_3$[91] and $Bi(NO_3)_3.5H_2O$.[101] Some metal triflates e.g. $Cu(OTf)_2$[102] and $Sc(OTf)_3$[103] have also been utilized as catalysts for the preparation of 1,1-diacetate derivatives from the corresponding aldehydes. A brief survey on *gem*-diacylation has been illustrated in part I of Chapter III. Some of these methods have certain drawbacks such as requirement of longer reaction time, involvement of expensive reagents and sometimes it fails to obtain acylals from an aliphatic aldehyde or from an aromatic aldehyde having electron donating groups in the aromatic ring.[101] Therefore, there is a scope to find out an alternative method.

By using the same pre-catalyst, various aldehydes can be converted smoothly to the corresponding 1,1-diacetates as shown in Scheme 23.

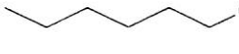
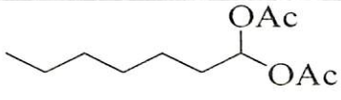


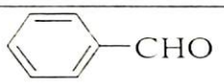
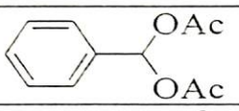
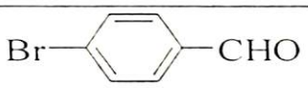
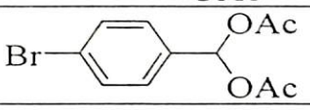
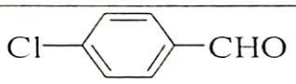
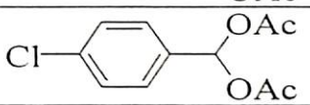
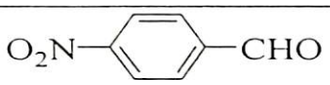
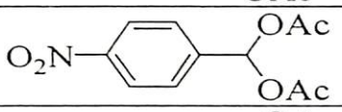
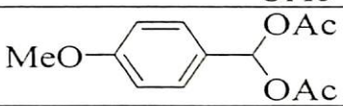
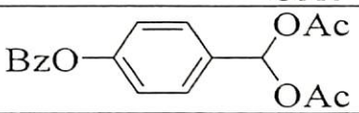
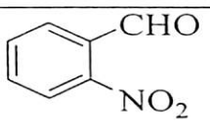
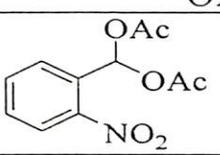
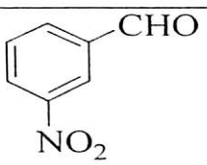
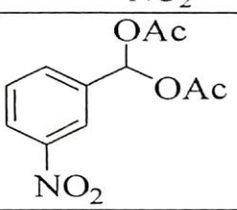
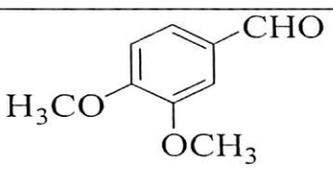
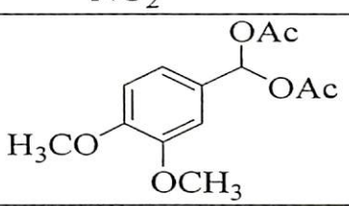
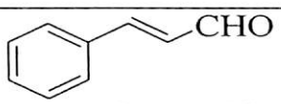
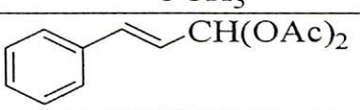
R = alkyl / aryl

Scheme 23

When an aliphatic aldehyde was treated with acetic anhydride in the presence of 10 mol% ATPB at room temperature, the reaction was very sluggish and yield was also low. However, on refluxing the same reaction mixture provided the corresponding *gem*-diacetate derivative in good yield. Then, we have realized for the formation of 1,1-diacetates require more activation energy by our protocol. Various aliphatic and aromatic aldehydes were smoothly converted to the corresponding *gem*-diacetates in good yields using the same pre-catalyst under reflux conditions. The reaction times and yields of the 1,1-diacetates are mentioned in Table 4. The products were characterized by checking melting point and recording IR, ^{1}H NMR spectra and elemental analyses as well as by comparison the compounds data with the reported data. It is important to mention that neither α-bromination nor cyclotrimerization was noticed during the experimental conditions. The present method is relatively harsher for the formation of *gem*-diacetates than the earlier reported methods. Nevertheless, both aliphatic and aromatic aldehydes can be converted to the corresponding diacetates in good yields. Like earlier reported method, the present protocol did not provide any 1,1-diacetates from the ketones under identical reaction conditions. For example, when acetophenone was treated with acetic anhydride in the presence of the same pre-catalyst under reflux conditions, it did not give the corresponding 1,1-diacetate derivatives.

Table 4. Formation of *gem*-diacetates from the corresponding aldehydes using 10 mol% ATPB as pre-catalyst under solvent free conditions

Substrate No.	Substrate	Time /h	Product[a]	Product No	Yield[b] [/%]
163		9		**174**	88

164		5		**175**	85
165		6		**176**	78
166		7		**177**	78
167		11		**178**	75
168		6		**179**	82
169		10		**180**	72
170		15		**181**	69
171		14		**182**	71
172		5		**183**	79
173		5		**184**	90

[a]All the products were characterized by recording melting point, IR, ^{1}H NMR and elemental analysis. [b]Isolated yield

The formation of the product can be rationalized as follows. We believe that HBr is generated in the reaction medium from the reaction of acetonyltriphenylphosphonium bromide with alcohol, which catalyzes the acetylation of the alcohols to the corresponding acetates. However, the same reaction was failure while it was carried out with benzyltriphenylphosphonium bromide instead of acetonyltriphenylphosphonium bromide. This indicates that ATPB generates HBr much more easily as compared to the other alkylphosphonium bromide.

In conclusion, we have devised a new, efficient and chemoselective protocol for the acetylation of alcohols, phenols, amines and thiols using a catalytic amount of acetonyltriphenylphosphonium bromide as pre-catalyst at room temperature under very mild conditions. In addition, both aliphatic and aromatic aldehydes can be converted to the *gem*-diacetates by employing the same catalyst under reflux conditions. The significant features of the present method include the ease of operations, high efficiency, mild conditions and chemoselectivity, which may be useful extensively in organic synthesis. Moreover, a wide variety of other protecting groups are survived such as benzyl, benzoyl, TBS, TBDPS, isopropylidene, methoxy- and thio group at the anomeric position under the experimental conditions.

SECTION B

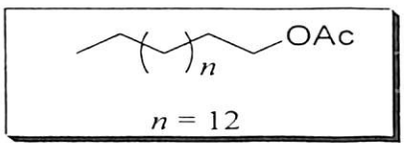
ACETYLATION OF ALCOHOLS, PHENOLS, THIOLS AND *GEM*-DIACYLATION OF ALDEHYDES CATALYZED BY ACETONYLTRIPHENYLPHOSPHONIUM BROMIDE (ATPB)

EXPERIMENTAL

General procedure for acetylation of alcohols, phenols, amines and thiols:

To a mixture of the alcohol or phenol or amine or thiol (1 mmol) and acetic anhydride (1.5-2.0 mmol) was added acetonyltriphenylphosphonium bromide (0.05 mmol) and kept for stirring at room temperature. After complete disappearance of the starting material as monitored by TLC, it was quenched with a saturated bicarbonate solution (2 mL). Finally, the reaction mixture was extracted with ethyl acetate (20 mL x 3). The combined organic extract was washed with water and dried over anhydrous sodium sulfate. After removal of the organic solvent in a rotary evaporator, the crude residue was subjected to silica gel column to isolate the desired pure acetate.

Cetyl acetate (135):



Nature: Colourless liquid

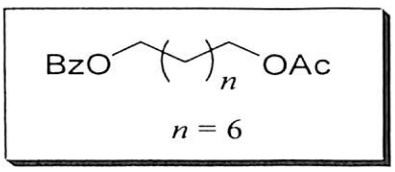
Yield: 96% (0.273 g)

IR (Neat): 2919, 2858, 1747 (CO), 1465, 1368, 1235, 1045 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J* = 7.2 Hz, $-CH_3$), 1.22-1.36 (m, 26H, $-CH_2$), 1.48-1.62 (m, 2H, $-CH_2$), 2.04 (s, 3H, $-COCH_3$), 4.04 (t, 2H, *J* = 7.2 Hz, $-OCH_2$) ppm.

Analysis	**Calculated**	**Found**
$C_{18}H_{36}O_2$	C 76.00	C 75.82
284.48	H 12.75	H 12.69

8-*O*-benzoyloxy octyl acetate (136):



Nature: Colourless liquid

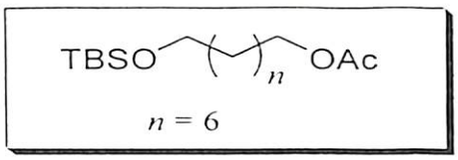
Yield: 92% (0.269 g)

IR (Neat): 3063, 2930, 2858, 1731 (CO), 1593, 1455, 1378, 1271, 1240, 1112 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30-1.50 (m, 8H, $-CH_2$), 1.60-1.70 (m, 2H, $-CH_2$), 1.72-1.80 (q, 2H, $-CH_2$), 2.04 (s, 3H, $-COCH_3$), 4.05 (t, 2H, *J* = 7.2 Hz, $-OCH_2$), 4.32 (t, 2H, *J* = 6.8 Hz, $-OCH_2$), 7.44 (t, 2H, *J* = 8.0 Hz, ArH), 7.55 (t, 1H, *J* = 8.0 Hz, ArH), 8.04 (d, 2H, *J* = 7.6 Hz, ArH) ppm.

Analysis	Calculated	Found
$C_{17}H_{24}O_4$	C 69.84	C 69.70
292.37	H 8.27	H 8.21

8-*O-tert*-butyldimethylsilyloxy octyl acetate (137):



Nature: Colourless liquid

Yield: 89% (0.269 g)

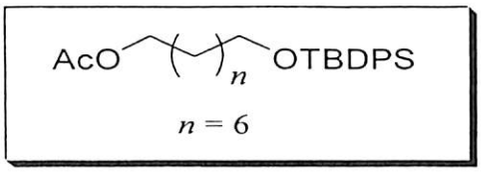
IR (Neat): 3056, 2920, 2848, 1740 (CO), 1475, 1433, 1373, 1245, 1112, 1035 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ -0.01(s, 3 H, -Si$(CH_3)_2$), 0.00 (s, 3H, -Si$(CH_3)_2$), 0.85 (s, 9 H,-SiC$(CH_3)_3$), 1.26-1.40 (m, 8 H, -CH_2), 1.44-1.55 (m, 2 H. -CH_2), 1.57-1.61(m, 2H, -CH_2), 2.00 (s, 3 H, -$COCH_3$), 3.54 (t, J = 6.8 Hz, 2 H, -OCH_2), 4.00 (t, J = 6.8 Hz, 2 H, -OCH_2) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ -5.3, 0.0, 18.3, 21.0, 25.7, 25.8, 26.0 (3C), 29.2, 29.3, 32.3, 32.8, 63.2, 64.6, 171.2 ppm.

Analysis	Calculated	Found
$C_{16}H_{34}O_3Si$	C 63.52	C 63.34
302.53	H 11.33	H 11.24

8-*O-tert*-butyldiphenylsilyloxy octyl acetate (138):



Nature: Colourless liquid

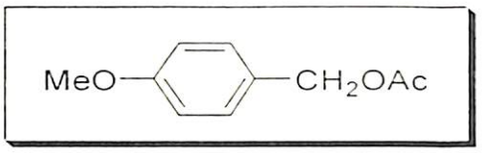
Yield: 91% (0.388 g)

IR (Neat): 3058, 2925, 2848, 1742 (CO), 1475, 1434, 1373, 1245, 1112, 1035 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (s, 9H. -SiC$(CH_3)_3$), 1.20-1.40 (m, 8H, CH_2), 2.01(s, 3 H, $COCH_3$), 3.65 (t, *J* = 6.4 Hz, 2H, OCH_2), 4.05 (t, *J* = 6.8 Hz, 2H, OCH_2), 7.36 –7.42 (m, 6 H, ArH), 7.66-7.68 (dd, *J* = 1.6 Hz, J = 7.6 Hz, 4 H, ArH) ppm.

Analysis	Calculated	Found
$C_{26}H_{38}O_3Si$	C 73.19	C 73.01
426.67	H 8.98	H 8.91

4-Methoxy benzyl acetate (139):



Nature: Colorless liquid

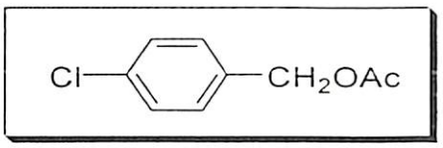
Yield: 96% (0.173 g)

IR (Neat): 2949, 1736, 1492, 1379, 1226, 1096, 1019 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ δ 2.15 (s, 3H, $COCH_3$), 3.15 (s, 3H, OCH_3), 5.02 (s, 2H, OCH_2), 7.41 (d, 2H, J =7.2Hz, ArH), 8.12 (d, 2H, J = 8.4Hz, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{12}O_3$	C 66.65	C 66.38
180.20	H 6.71	H 6.69

4-Chloro benzyl acetate (140):



Nature: Colorless liquid

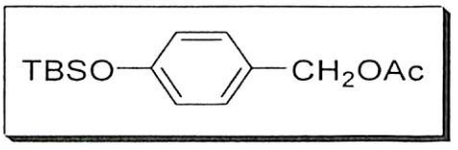
Yield: 90% (0.166 g)

IR (Neat): 2950, 1736, 1495, 1383, 1229, 1096, 1019, 973, 819, 609, 543 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 3H, -$COCH_3$), 5.06 (s, 2H, OCH_2), 7.28 (d, J = 8.4 Hz, ArH), 7.32 (d, J = 8.8 Hz, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_9H_9O_2Cl$	C 58.55	C 57.98
184.62	H 4.91	H 4.89

4-*O-tert*-butyldimethylsilyloxy benzyl acetate (141):



Nature: Colourless liquid

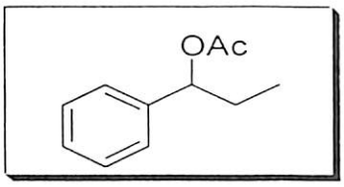
Yield: 85% (0.238 g)

IR (Neat): 2954, 2930, 2888, 2859, 1747 (CO), 1610, 1521, 1237, 1229, 913 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.19 (s, 6H, $Si(CH_3)_2$), 0.98 (s, 9H, -$SiC(CH_3)_3$), 2.08 (s, 3H, -$COCH_3$), 5.02 (s, 2H, -OCH_2), 6.81 (d, 2H, J = 8.0 Hz, ArH), 7.22 (d, 2H, J = 8.0 Hz, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{15}H_{24}SiO_3$	C 64.24	C 64.59
280.44	H 8.63	H 8.55

Acetate of 1-phenyl propan-1-ol (142):



Nature: Colourless liquid

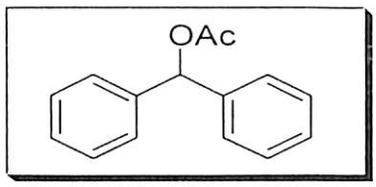
Yield: 95% (0.170 g)

IR (Neat): 3063, 3022, 2976, 2925, 2879, 1742 (CO), 1491, 1460, 1378, 1055 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, 3H, *J* = 7.2 Hz, CH_3), 1.81-195 (m, 2H, CH_2), 2.07 (s, 3H, $COCH_3$), 5.66 (t, 1H, *J* = 7.2 Hz, CHOAc), 7.20-7.37 (m, 5H, ArH) ppm.

Analysis	Calculated	Found
$C_{11}H_{14}O_2$	C 74.13	C 74.01
178.23	H 7.92	H 7.85

Acetate of benzhydrol (143):



Nature: Colourless gummy liquid

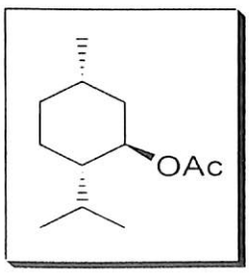
Yield: 93% (0.210 g)

IR (Neat): 3073, 3037, 2935, 1747 (CO), 1598, 1496, 1445, 1373, 1235, 1020 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 3H, -$COCH_3$), 6.88 (s, 1H, -CHOAc), 7.32-7.34 (m, 10H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{15}H_{14}O_2$	C 79.62	C 79.41
226.27	H 6.24	H 6.18

Acetate of menthol (144):



Nature: Low melting solid

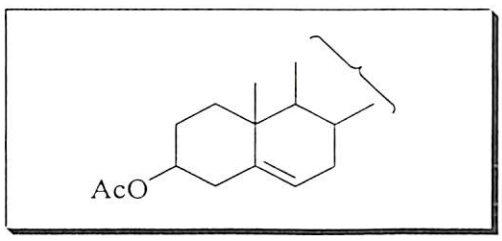
Yield: 94% (0.186 g)

IR (Neat): 1737 (CO) cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): 0.76 (d, J = 6.8 Hz, 3H, CH_3), 0.89 (d, J = 6.8 Hz, 3H, CH_3), 0.90 (d, J = 6.8 Hz, 3H, CH_3), 0.95-1.07 (m, 1H, CH_2), 1.30-1.39 (m, 1H, CH_2), 1.41-1.50 (m, 2H, CH_2), 1.65-1.70 (m, 2H, CH_2), 1.82-1.89 (m, 2H, CH_2), 1.97-2.01 (m, 1H, CH_2), 2.04 (s, 3H, $COCH_3$), 4.67 (dt, J = 7.6 Hz, J = 4.4 Hz, 1H, OCH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{22}O_2$	C 72.68	C 72.71
198.30	H 11.18	H 11.15

Acetate of Cholesterol (145):



Nature: White Solid, mp:113 ^{0}C

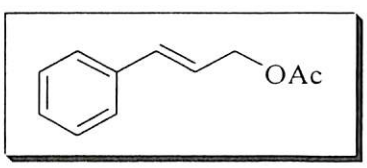
Yield: 94% (0.403 g)

IR (Neat): 2923, 2850, 1736, 1465, 1391, 1230, 1021 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.68 (s, 6H, CH_3), 0.86 (d, 6H, J = 6.4 Hz, $CHCH_3$), 0.91(d, 3H, J = 7.2 Hz, CH_3), 0.94-1.00 (m, 16H, CH_2), 1.02 (s, 3H, CH_3), 1.04-1.69 (m, 2H, CH_2), 1.41-1.60 (m, 2H, CH2), 1.79-2.00 (m, 1H, CH_2), 2.03 (s, 3H, $COCH_3$), 2.31 (d, J = 6.4 Hz, 4H, CH_2), 4.60 (m, 1H, CHOAc), 5.37 (d, J = 4.8 Hz, 1H, =CH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{29}H_{48}O_2$	C 81.25	C 81. 18
428.70	H 11.28	H 11.23

Cinnamyl acetate (146):



Nature: Colourless liquid

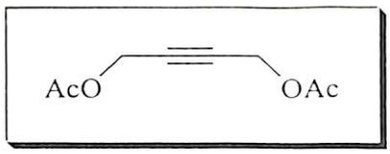
Yield: 92% (0.162 g)

IR (Neat): 2936, 2842, 1739, 1614, 1232, 1146, 782 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 3H, -$COCH_3$), 4.72 (dd, J = 1.2 Hz, J = 6.4 Hz, 2H, -OCH_2), 6.28 (m, 1H, =CH), 6.65 (d, J = 16.0 Hz, 1H, =CH), 7.26 (d, J = 6.8 Hz, 1H, ArH), 7.33 (t, J = 7.2 Hz, 2H, ArH), 7.39 (d, J = 7.2 Hz, 2H, ArH) ppm.

Analysis	Calculated	Found
$C_{11}H_{12}O_2$	C 75.03	C 75.12
176.10	H 6.87	H 6.85

Di-acetate of butyne-1, 4-diol (147):



Nature: Colourless low melting solid

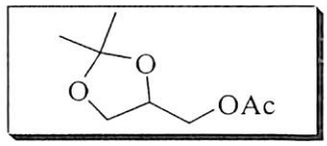
Yield: 90% (0.153 g)

IR (Neat): 2949, 1752 (CO), 1435, 1383, 1222, 1156, 1038 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 6H, 2 x -$COCH_3$), 4.71 (s, 4H, 2 x -OCH_2) ppm.

Elemental Analysis	Calculated	Found
$C_8H_{10}O_4$	C 56.47	C 56.19
170.16	H 5.92	H 5.85

Acetate of 2,3-*O*-isopropylidene-*D*-(±)-glycerol (148):



Nature: Colourless liquid

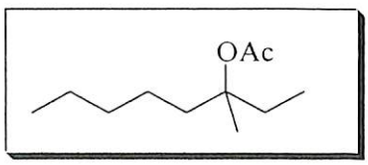
Yield: 75% (0.131 g)

IR (Neat): 1737 (CO) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (s 3H, CH_3), 1.44(s, 3H, CH_3), 2.10 (s, 3H, -$COCH_3$, 3.74 (dd, J = 6.0 Hz, J = 8.4 Hz, 1H, CH_2), 4.05-4.10 (m, 2H, -CH_2), 4.18 (dd, J = 4.8 Hz, J = 11.6 Hz, 1H, CH_2), 4.30-4.35 (m, 1H, CH) ppm.

Elemental Analysis	Calculated	Found
$C_8H_{14}O_4$	C 55.16	C55.23
174.19	H 8.10	H 8.14

Acetate of 3-methyl-3-octanol (149):



Nature: Colourless liquid

Yield: 63% (0.117 g)

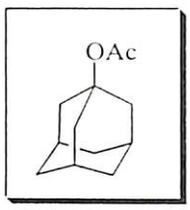
IR (Neat): 2935, 2873, 1737 (CO), 1465, 1373, 1250, 1143, 1025 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, 3H, J = 8.0 Hz, CH_3), 0.89 (t, 3H, J = 7.2 Hz, CH_3), 1.24-1.34 (m, 6H, CH_2), 1.37 (s, 3H, CH_3), 1.62-1.90 (m, 4H, CH_2), 1.97 (s, 3H, $COCH_3$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 8.13, 14.17, 22.48, 22.72, 23.37 (2C), 30.91, 32.25, 37.81, 85.13, 170.18 ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{22}O_2$	C 70.92	C 70.76
186.29	H 11.90	H 11.85

Acetate of adamentanol (150):



Nature: Low melting solid

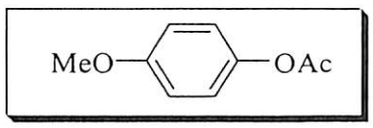
Yield: 87% (0.169 g)

IR (Neat): 2940, 2852, 1746 (CO), 1365, 1243, 1095, 1042 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60-1.70 (bs, 6H, $-CH_2$), 1.96 (s, 3H, $-COCH_3$), 2.10 (bs, 6H, $-CH_2$), 2.15 (bs, 3H, -CH) ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{18}O_2$	C 74.19	C 74.01
194.27	H 9.34	H 9.28

Acetate of 4-methoxyphenol (151):



Nature: Viscous liquid

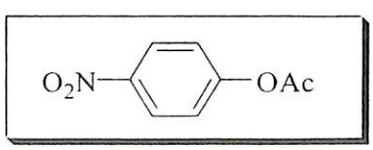
Yield: 94% (0.156 g)

IR (Neat): 2933, 2852, 1746 (CO), 1363, 1243, 1093, 1044 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 3H, $-COCH_3$), 3.79 (s, 3H, $-OCH_3$), 6.88 (d, J = 9.2 Hz, 2H, ArH), 7.99 (d, J = 9.6 Hz, 2H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_9H_{10}O_3$	C 65.06	C 65.02
166.15	H 6.06.	H 6.40

Acetate of 4-nitrophenol (152):



Nature: Low melting solid

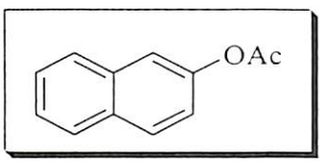
Yield: 80% (0.145 g)

IR (Neat): 2939, 2855, 1749 (CO), 1550, 1363, 1243, 1084, 1042 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H, -$COCH_3$), 7.28 (d, J = 9.6 Hz, 2H, ArH), 8.27 (d, J = 8.8 Hz, 2H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_8H_7O_4N$	C 53.05	C 53.06
181.10	H 3.89	H 3.74

Acetate of β-naphthol (153):



Nature: Solid, mp: 68 ^{0}C.

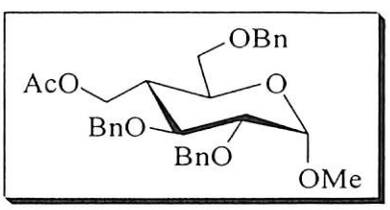
Yield: 72% (0.134 g)

IR (KBr): 1757 (CO) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H, $COCH_3$), 7.23 (dd, J = 2.4 Hz, J = 8.4 Hz, 1H, ArH), 7.47(dt, J = 8.0 Hz, J = 2.0 Hz, 2H, ArH), 7.55 (d, 1H, J = 2.0 Hz,1-ArH) , 7.80 (dd, J = 2.0 Hz, J = 7.2 Hz, 1H, ArH), 7.84 (d, J = 8.8 Hz, 2H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{10}O_2$	C 77.40	C 77.46
186.21	H 5.41	H 5.39

Acetate of methyl 2, 3, 6-tri-*O*-benzyl-1-*β*-D-glucopyranoside (154):



Nature: Colorless liquid

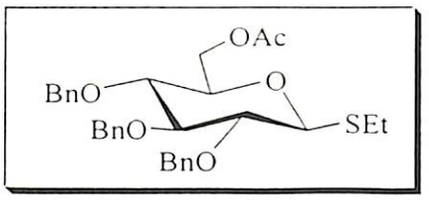
Yield: 74% (0.385 g)

IR (Neat): 3032, 2899, 1742 (CO), 1455, 1363, 1240, 1091, 1055 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.94 (s, 3H, -$COCH_3$), 2.07 (m, 1H, H-4), 3.39 (s, 3H, -OCH_3), 3.59-3.63 (m, 3H), 3.82-3.88 (m, 1H, H-5), 3.90 (t, 1H, J = 9.2Hz, H-3), 4.01 (dd, 1H, J = 2.4 Hz, J = 11.4 Hz, H-6), 4.32 (dd, 1H, J = 2.8 Hz, H-6′), 4.47 (d, 1H, J = 12.0 Hz, -OCHPh), 4.58 (d, 1H, J = 10.8 Hz, -OCHPh), 4.60 (d, 1H, J = 12.0 Hz, -OCHPh), 4.66 (d, 1H, J = 12.0 Hz, -OCHPh), 4.69 (d, 1H, J = 3.6 Hz, H-1), 4.78 (d, 1H, J = 12.0 Hz, -OCHPh), 4.96 (d, 1H, J = 10.8 Hz, -OCHPh), 7.22-7.40 (m, 15H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{31}H_{36}O_7$	C 71.52	C 71.25
520.62	H 6.97	H 6.90

Acetate of 2,3,4-tri-O-benzyl-ethyl-β-D-thioglucopyranoside (155):



Nature: viscous liquid

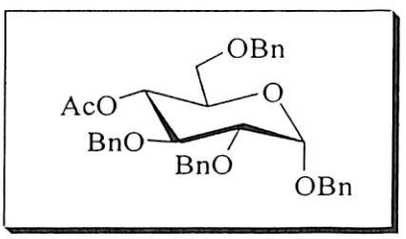
Yield: 72% (0. 386 g)

IR (Neat): cm^{-1} 3063, 3027, 2925, 2868, 1737 (CO), 1455, 1363, 1235, 1071

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (t, 3H, J = 7.6 Hz, -SCH_2CH_3), 2.03 (s, 3H, -$COCH_3$), 2.64-2.80 (m, 2H, -SCH_2CH_3), 3.44 (t, 1H, J = 9.2 Hz), 3.50-3.52 (m, 1H, H-5), 3.54 (t, 1H, J = 9.6 Hz), 3.71 (t, 1H, J = 8.8 Hz), 4.19 (dd, 1H, J = 4.4 Hz, J = 11.6 Hz, H- 6), 4.33 (dd, 1H, J = 1.6 Hz, J = 12.0 Hz, H- 6′), 4.47 (d, 1H, J = 9.6 Hz, H-1), 4.57 (d, 1H, J = 11.2 Hz, -OCHPh), 4.74 (d, 1H, J = 10.4 Hz, -OCHPh), 4.85 (d, 1H, J = 10.8 Hz, -OCHPh), 4.86 (d, 1H, J = 10.8 Hz, -OCHPh) 4.92 (d, 1H, J = 10.4 Hz, -OCHPh), 4.95 (d, 1H, J = 10.8 Hz, -OCHPh), 7.26-7.36 (m, 15H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{31}H_{36}O_6S$	C 69.38	C 69.23
536.68	H 6.76	H 6.70
	S 5.97	S 5.70

Acetate of 2,3,6-tri-O-benzyl-benzyl-α-D-glucopyranoside (156):



Nature: viscous liquid

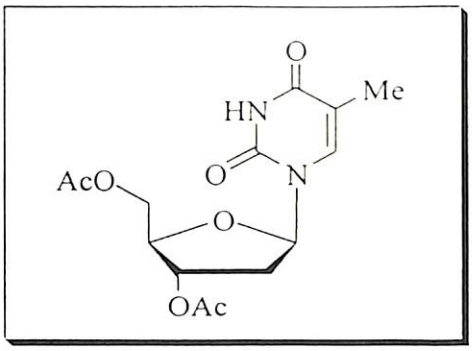
Yield: 78% (0.454 g)

IR (Neat): 3065, 3030, 2918, 2867, 1748 (CO), 1503, 1457, 1376, 1234, 1101, 1045 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 11.83 (s, 3H, -$COCH_3$), 3.40-3.44 (m, 2H), 3.59 (dd, 1H), 3.83-3.87 (m, 1H), 3.97 (t, 1H), 4.46-4.56 (m, 4H), 4.62-4.71 (m, 3H), 4.82 (d, 1H, J = 3.6 Hz, H-1), 4.90 (d, 1H, J = 12.0 Hz), 5.04 (t, 1H, J = 8.0 Hz), 7.25-7.40 (m, 20H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{36}H_{38}O_7$	C 71.52	C 71.25
582.69	H 6.57	H 6.60

Diacetate of thymidine (157):



Nature: Solid, mp: 127 ^{0}C.

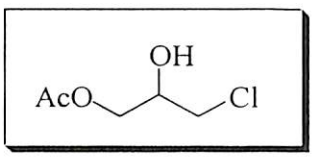
Yield: 77% (0.251 g)

IR (Neat): cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.95(s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.48 (dd, 2H, *J* = 5.2 Hz, 13.7Hz), 4.20 (dd, 1H, *J* = 2Hz, *J* = 4.8 Hz), 4.26 (dd, 1H, *J* = 3.2 Hz, *J* = 6.4 Hz), 4.36 (dd, 1H, *J* = 4 Hz, *J* = 7.2 Hz), 5.21-5.25 (m, 1H), 6.34 (dd, 1H, *J* = 5.6 Hz, *J* = 8.4 Hz), 7.29 (s, 1H), 9.70 (bs, 1H) ppm

Elemental Analysis	**Calculated**	**Found**
$C_{14}H_{18}O_7N_2$	C 51.53	C 50.66
326.30	H 5.56	H 5.45
	N 8.59	N 8.66

Mono acetate of 3-chloro glycerol (158):



Nature: Colourless liquid

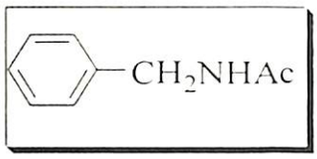
Yield: 65% (0.100 g)

IR (Neat): 3437 (OH), 2960,1737 (CO),1424, 1240, 1045, 933 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 1.71(bs, 1H, OH, D_2O exchangeable), 2.12 (s, 3H, -$COCH_3$), 3.60-3.64(m, 2H, -OCH_2), 4.07-4.09(m, 1H, -OCH), 4.21(d, *J* = 5.2 Hz, CH_2Cl) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_5H_9ClO_3$	C 39.35	C 39.10
152.62	H 5.94	H 5.86

Acetamide of benzylamine (159)



Nature: Solid; mp: 61-62 °C

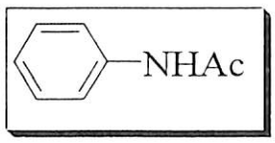
Yield: 86% (0.165g)

IR (Neat): 3298, 3068, 3027, 2925, 2884, 1650 (CO), 1557, 1455, 1383, 1281, 1081, 1009 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.01 (s, 3H, $-COCH_3$), 4.41 (d, 2H, J = 5.2 Hz, $-NCH_2Ar$), 5.92 (bs, 1H, -NH), 7.22-7.40 (m, 5H, ArH) ppm .

Elemental Analysis	Calculated	Found
$C_9H_{11}NO$	C 72.46	C 72.19
192.26	H 7.43	H 7.36

Acetamide of aniline (160):



Nature: Solid; mp: 113-114 °C

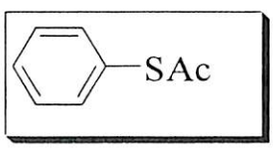
Yield: 85 % (0.115g)

IR (Neat): 3300, 1660, 1600 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 2.12(s, 3H, $COCH_3$), 7.01(t, 1H, J = 8.0 Hz), 7.35 (t, 2H, J = 8.0 Hz, ArH), 7.63 (d, 2H, J = 8.0 Hz, ArH) ppm.

Elemental Analysis	Calculated	Found
C_8H_9ON	C 71.07	C 70.70
135.08	H 6.71	H 6.22
	N 10.36	N 9.86

Acetate of thiophenol (161):



Nature: viscous liquid

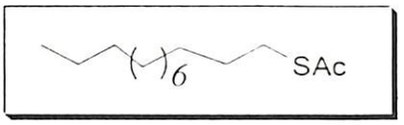
Yield: 90 % (0.137 g)

IR (Neat): 1710 (CO) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 2.33 (s, 3H, $-COCH_3$), 7.38-7.40 (m, 5H, ArH) ppm.

Elemental Analysis	Calculated	Found
C_8H_8SO	C 63.13	C 63.12
152.07	H 5.26	H 5.21
	S 21.04	S 20.20

Acetate of dodecanethiol (162):



Nature: Colourless liquid

Yield: 82 % (0.200 g)

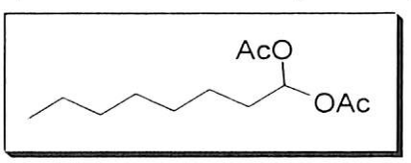
IR (Neat): 2940, 2853, 1692 (CO), 1460, 1342, 1132, 948 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, J = 7.2 Hz, -CH_3), 1.20-1.40 (m, 18H, -CH_2), 1.45-1.60 (m, 2H, -CH_2), 2.32 (s, 3H, -$COCH_3$), 2.86 (t, 2H, J = 7.6 Hz, -SCH_2) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{14}H_{28}SO$	C 68.79	C 68.49
244.44	H 5.26	H 11.49
	S 13.12	S 12.97

General procedure for 1,1-diacetylation of aldehydes: A mixture of aldehyde (1 mmol) and acetic anhydride (4 mmol) was placed in a 10 mL round-bottomed flask fitted with a reflux condenser. The acetonyltriphenylphosphonium bromide precatalyst (0.1 mmol) was then added and the mixture was stirred under reflux conditions. After completion of the reaction as monitored by TLC, it was quenched with a saturated solution of sodium hydrogencarbonate (2 mL) and the mixture was extracted with ethyl acetate (20 mL×2). The combined organic layer was dried over anhydrous sodium sulfate and was concentrated in vacuo. Finally, the crude residue was passed through a silica gel column to provide the desired 1,1-diacetate derivatives.

1,1-diacetate of heptanal (174):



Nature: gummy liquid

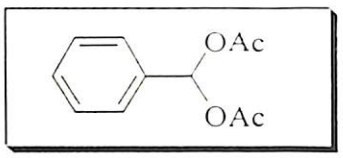
Yield: 88% (0.190 g)

IR (Neat): 2930, 2863, 1762 (CO), 1465, 1378, 1250, 1214, 1112, 1015, 968 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (t, 3H, J = 6.8 Hz, CH_3), 1.22-1.40 (m, 8H, -CH_2), 1.66-1.80 (m, 2H, -CH_2), 2.07 (s, 6H, 2 x $COCH_3$), 6.77 (t, 1H, CH(OAc)$_2$ ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{20}O_4$	C 61.09	C 60.89
216.28	H 9.32%	H 9.27

1,1-diacetate of benzaldehyde (175):



Nature: Solid, mp: 45 °C

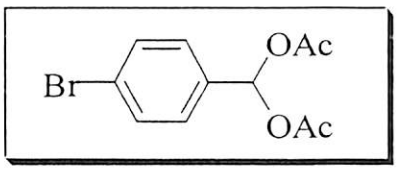
Yield: 85% (0.167 g)

IR (Neat): 3068, 2991, 2940, 1752 (CO), 1383, 1250, 1204, 1055, 1009, 974 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 6H, -$COCH_3$), 7.40-7.43 (m, 3H, ArH), 7.51-7.56 (m, 2H, ArH), 7.71 (s, 1H. C*H*$(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{12}O_4$	C 61.11	C 60.76
196.10	H 6.16	H 5.76

1,1-diacetate of 4- bromobenzaldehyde (176):



Nature: White solid; mp: 84 °C

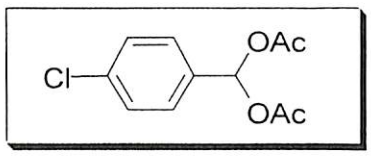
Yield: 78% (0.224 g)

IR (Neat): 3063, 2986, 2930, 1762 (CO), 1593, 1486, 1378, 1245, 1214, 1076, 968 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 6H, 2 x -$COCH_3$), 7.39 (d, 2H, *J* = 8.4 Hz, ArH), 7.53 (d, 2H, *J* = 8.8 Hz, ArH), 7.61 (s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{11}BrO_4$	C 46.02	C 46.21
287.10	H 3.86	H 3.80

1,1-diacetate of 4- chlorobenzaldehyde (177):



Nature: White solid; mp: 80 °C.

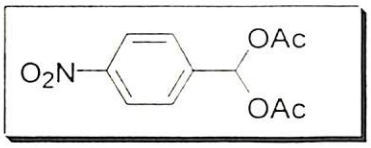
Yield: 78% (0.189 g)

IR (Neat): 1748, 1611, 1492, 1421, 1379, 1261, 1199, 1072, 939, 826 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 6H, -$COCH_3$), 7.37 (d, *J* = 8.8 Hz, 2H, ArH), 7.45 (d, *J* = 8.8 Hz, 2H, ArH), 7.63(s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{11}O_4Cl$	C 54.41	C 54.12
242.59	H 4.57	H 4.50

1,1-diacetate of 4- nitrobenzaldehyde (178):



Nature: Yellow crystalline; mp:125 ^{0}C

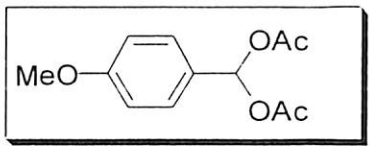
Yield: 75% (0.190 g)

IR (Neat): 3124, 3072, 3010, 1760 (CO), 1611, 1535, 1379, 1351, 1237, 1067, 972 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.16 (s, 6H, -$COCH_3$), 7.69(s, 1H, C*H*$(OAc)_2$), 7.72 (d, *J* = 6.4 Hz, 2H, ArH), 8.27(d, *J* =8.4 Hz, 2H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{11}O_6N$	C 52.18	C 51.95
253.21	H 4.38	H 4.29
	N 5.53	N 5.49

1,1-diacetate of 4- methoxybenzaldehyde(179)



Nature: Solid, mp: 68 ^{0}C

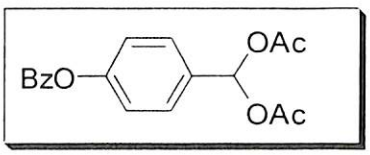
Yield: 91% (0.217 g)

IR (Neat): 3068, 3017, 2976, 2838, 1752, 1619, 1527, 1434, 1373, 1260, 1209, 1173, 1066, 933 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 6H, -$COCH_3$), 3.81 (s, 3H, OCH_3), 6.89 (d, *J* = 8.8 Hz, 2H, ArH), 7.43 (d, *J* = 8.8 Hz, 2H, ArH) 7.60(s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{14}O_5$	C 60.50	C 60.55
238.24	H 5.92	H 5.89

1,1-diacetate of 4- benzoyloxybenzaldehyde (180):



Nature: Solid, mp: 97-98 ^{0}C

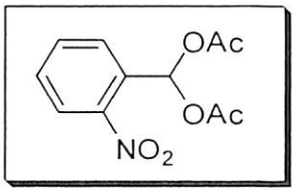
Yield: 91% (0.299 g)

IR(KBr): 1688, 1754 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.14 (s, 6H, -$COCH_3$), 7.26 (d, *J* = 8.4 Hz, 2H, ArH), 7.52 (t, *J* = 8.0 Hz, 2H, ArH), 7.59 (d, *J* = 8.4 Hz, 2H, ArH), 7.65 (t, *J* = 7.2 Hz, 1H, ArH), 7.70 (s, 1H, C*H*$(OAc)_2$), 8.20 (dd, *J* = 8.4 Hz, *J* = 1.2 Hz 2H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{18}H_{16}O_6$	C 65.85	C 65.92
328.32	H 4.91	H 4.89

1,1-diacetate of 2-nitrobenzaldehyde (181):



Nature: Solid, mp: 85-86 °C.

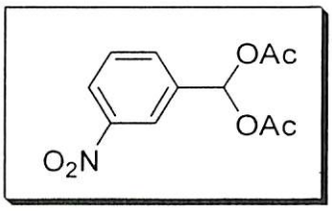
Yield: 69% (0.175 g)

IR (KBr): 1771, 1587, 1525, 1454, 1377, 1351, 1244, 1208, 1105, 1075, 1025 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 6H, 2 x $COCH_3$), 7.57-7.61 (m, 1H, ArH), 7.67-7.74 (m, 2H, ArH) 8.05 (dd, 1H, *J* = 0.8 Hz, *J* = 7.6 Hz, ArH), 8.20 (s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{11}NO_6$	C 52.18	C 51.93
253.21	H 4.38	H 4.30
	N 5.53	N 5.38

1,1-diacetate of 3-nitrobenzaldehyde (182):



Nature: Solid, mp: 85-86 °C.

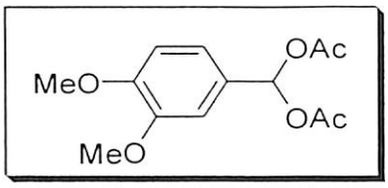
Yield: 71% (0.180 g)

IR (KBr): 1773, 586, 1521, 1454, 1372, 1349, 1244, 1208, 1105, 1067, 1069, 1024 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 6H, 2 x $COCH_3$), 7.60 (t, *J* = 8.0 Hz, 1H, ArH), 7.73 (s, 1H, C*H*$(OAc)_2$), 7.83 (d, *J* = 8.0 Hz, 1H, ArH), 8.27 (d, *J* = 8.0 Hz, 1H, ArH), 8.40 (s, 1H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{11}NO_6$	C 52.18	C 51.94
253.21	H 4.38	H 4.28
	N 5.53	N 5.47

1,1-diacetate of 3,4-dimethoxybenzaldehyde (183):



Nature: Solid, mp: 63-64 °C

Yield: 79% (0.212 g)

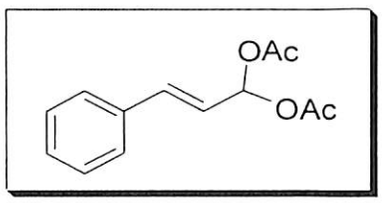
IR (KBr): 2965, 2847, 1751, 1602, 1525, 1464, 1387, 1346, 1254, 1208, 1152, 1064, 998 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 (s, 6 H, 2x $COCH_3$), 3.88 (s, 3 H), 3.92 (s, 3 H), 6.88 (d, *J* = 8.0 Hz, 1H, ArH), 7.05 (s, 1 H, ArH), 7.11 (d, *J* = 8.0 Hz, 1H, ArH), 7.62 (s, 1 H, C*H*$(OAc)_2$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7 (2C0, 55.9 (2C), 89.8, 109.6, 111.5,119.5, 128.0, 149.1, 150.1, 168.7 (2C) ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{16}O_6$	C 58.21	C 57.95
268.26	H 6.01	H 5.96

1,1-diacetate of cinnamaldehyde (184):



Nature: Solid, mp: 84 ^{0}C.

Yield: 90% (0.211 g)

IR (Neat): 3065, 3032, 2930, 1749 (CO), 1602, 1486, 1426, 1271, 1207, 1086 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.16 (s, 3H, -$COCH_3$), 6.20 (dd, *J* = 16Hz, *J* = 6.8Hz, 1H, =CH), 6.87(d, *J* = 16.4Hz, 1H, =CH), 7.30-7.34 (m, 4H, ArH & $CH(OAc)_2$), 7.42 (d, J = 8.4 Hz, 2H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{14}O_4$	C 66.63	C 66.12
234.12	H 6.02	H 6.00

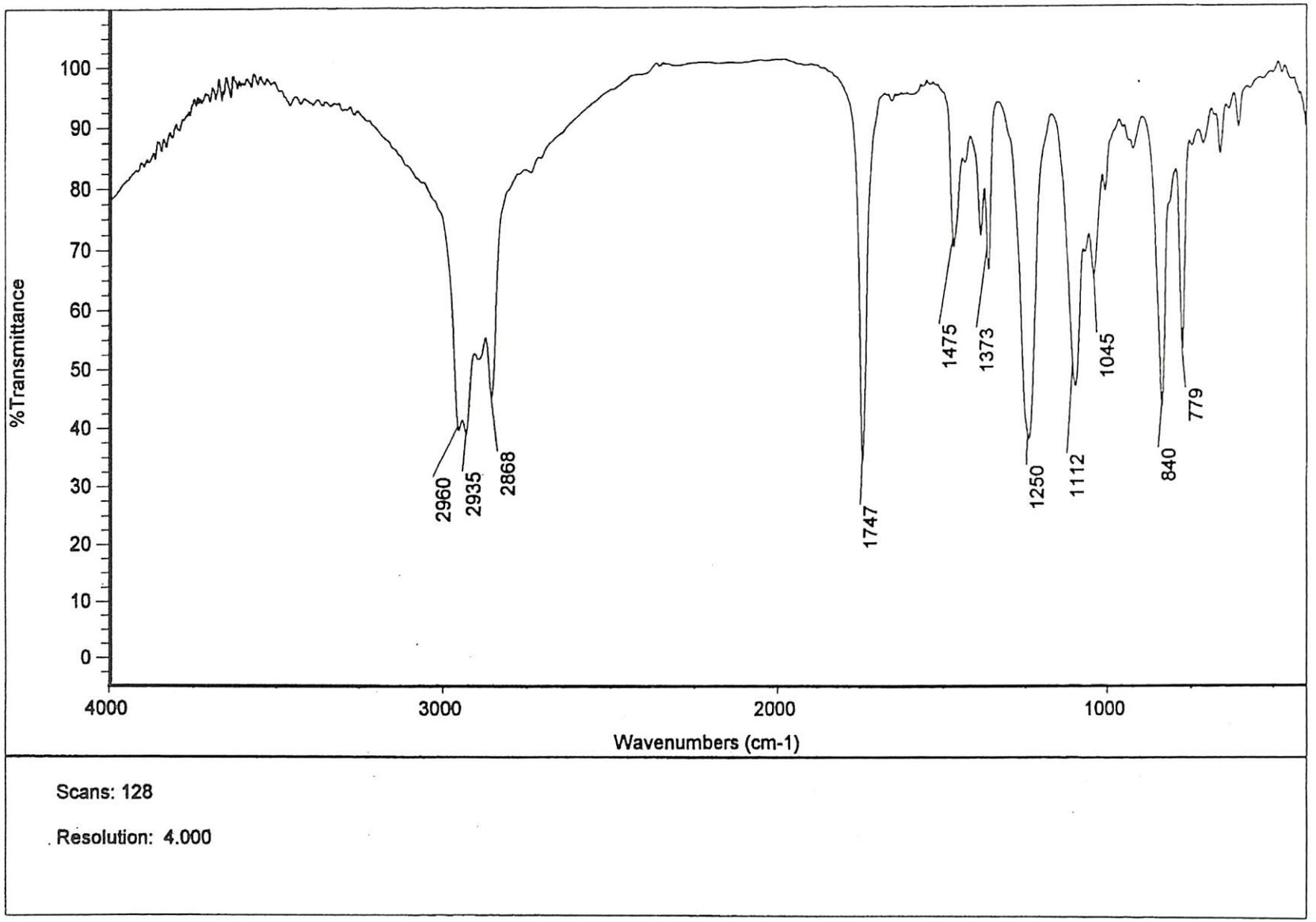


Figure 1: IR spectrum of 5-*O*-acetyl-1-*tert*-butyldimethylsilyloxy pentane **(59)**

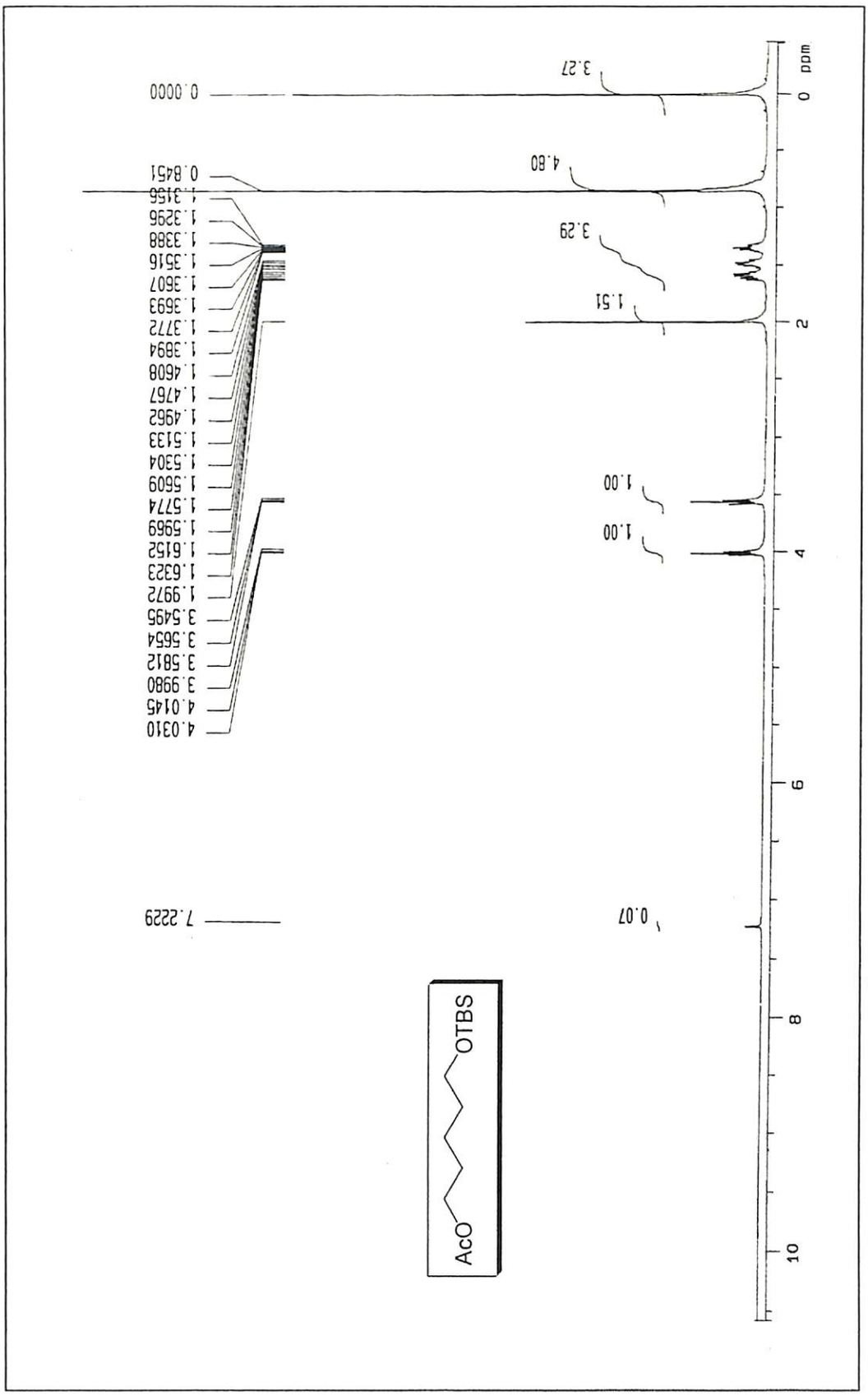


Figure 2: ^{1}H NMR spectrum of 5-*O*-acetyl-1-*tert*-butyldimethylsilyloxy pentane **(59)**

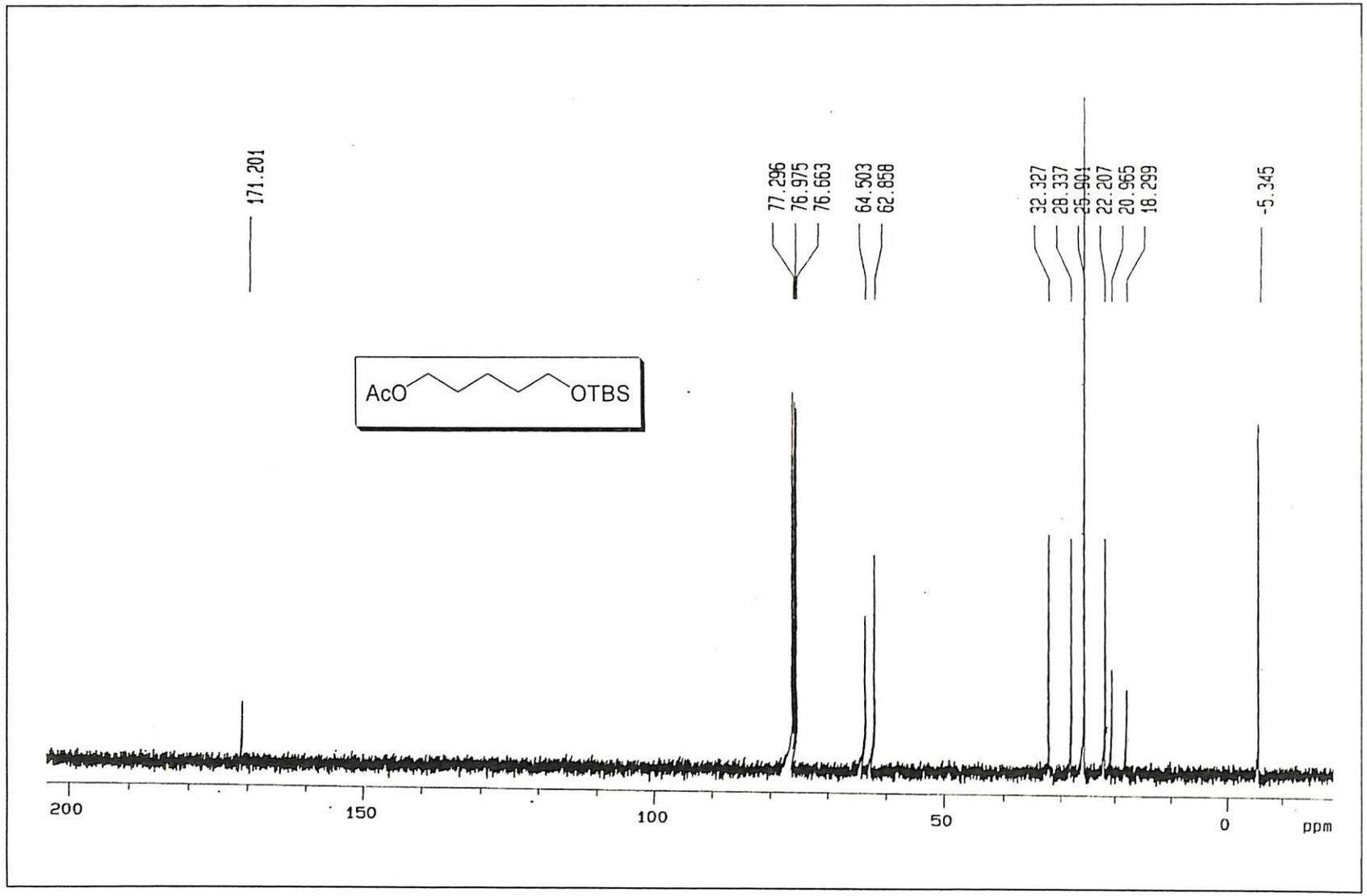


Figure 3: ^{13}C NMR spectrum of 5-*O*-acetyl-1-*tert*-butyldimethylsilyloxy pentane **(59)**

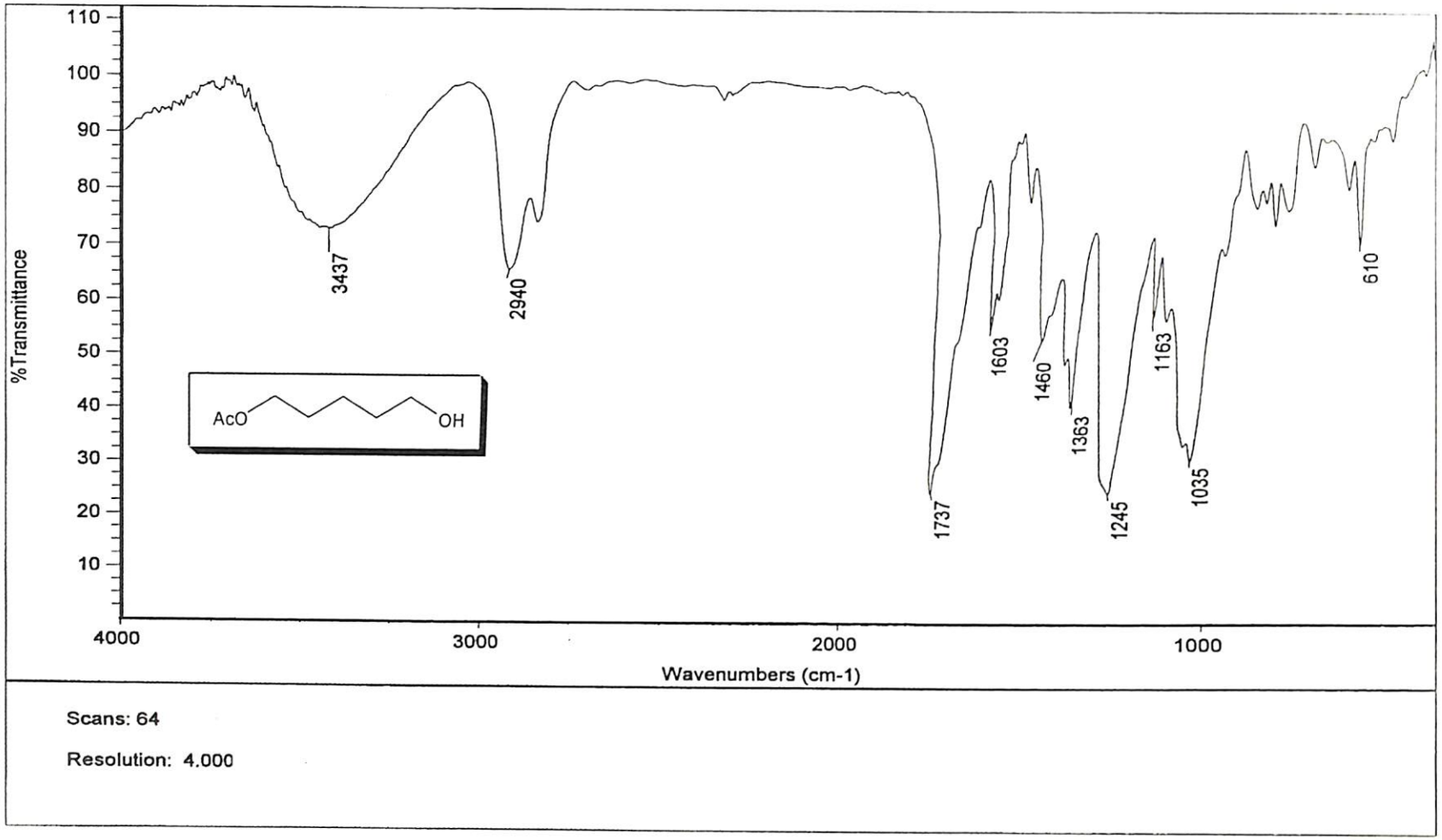


Figure 4: IR spectrum of 5-acetoxy-1-pentanol **(56)**

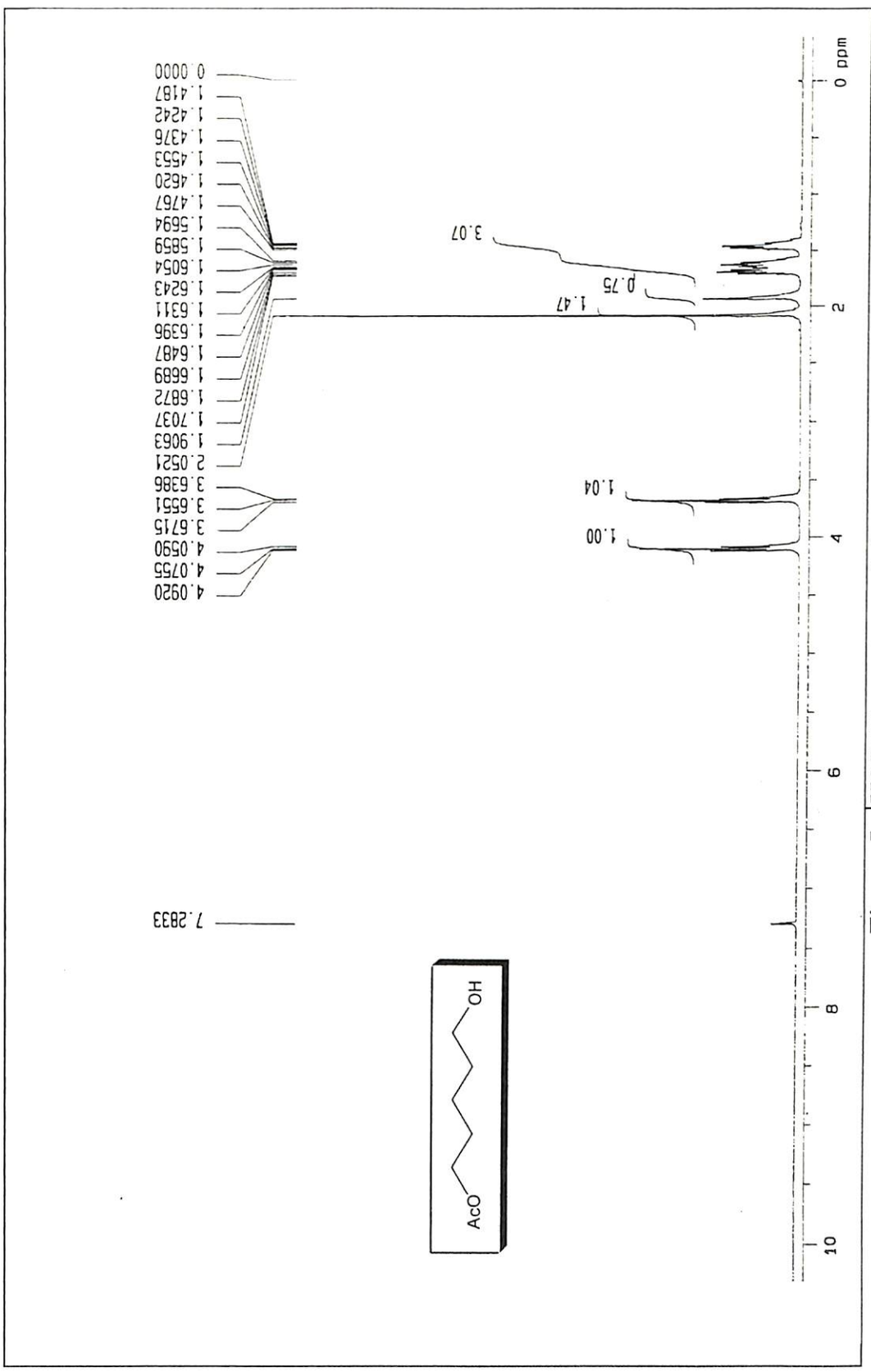


Figure 5: ^{1}H NMR spectrum of 5-acetoxy-1-pentanol (**56**)

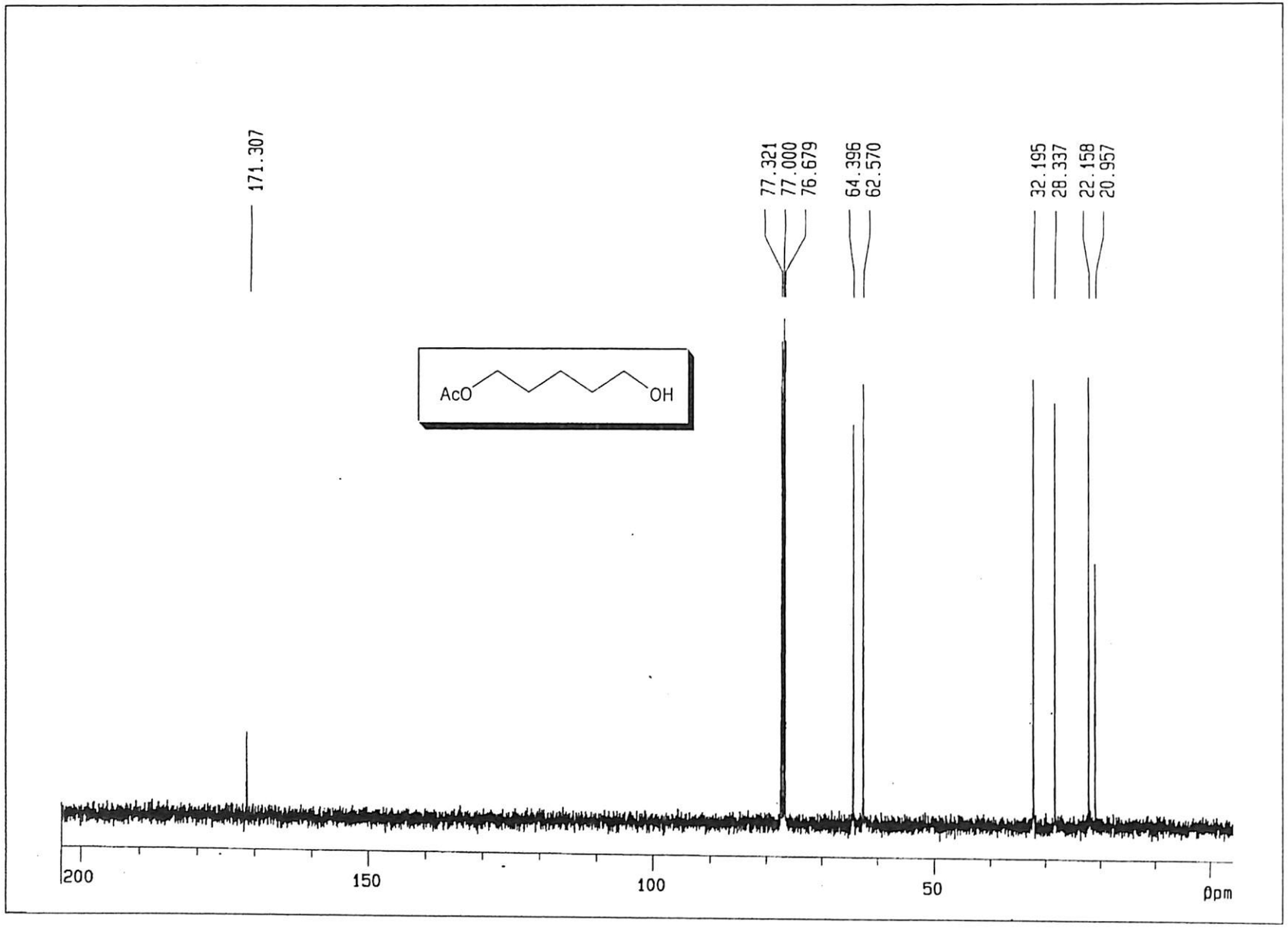


Figure 6: ^{13}C NMR spectrum 5-acetoxy-1-pentanol **(56)**

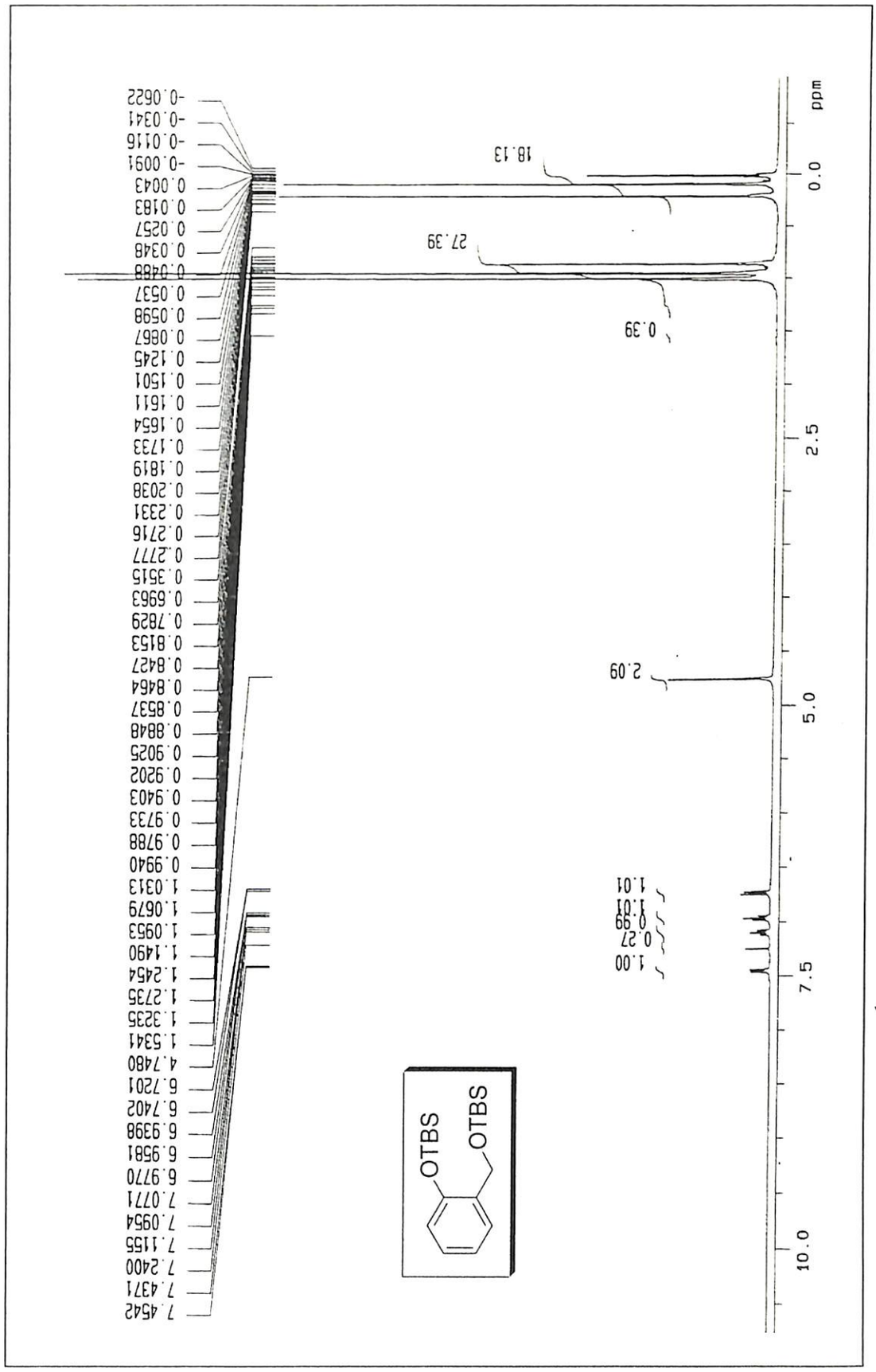


Figure 7: ^{1}H NMR spectrum of *tert*- butyldimethylsilyl ether of 2-hydroxybenzyl alcohol **(105)**

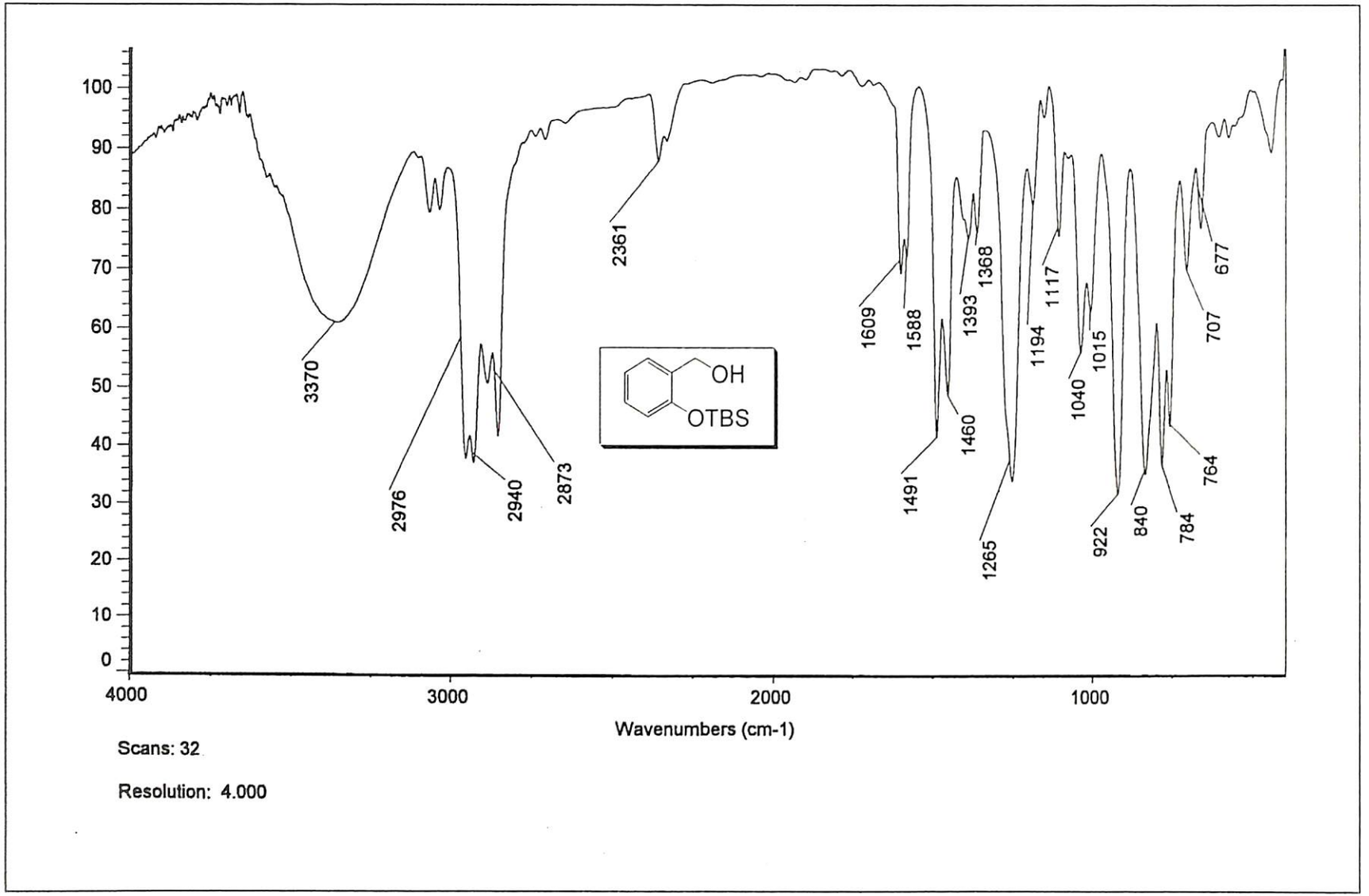


Figure 8: IR spectrum of 2′-*tert*-butyldimethylsilyloxy benzyl alcohol **(111)**

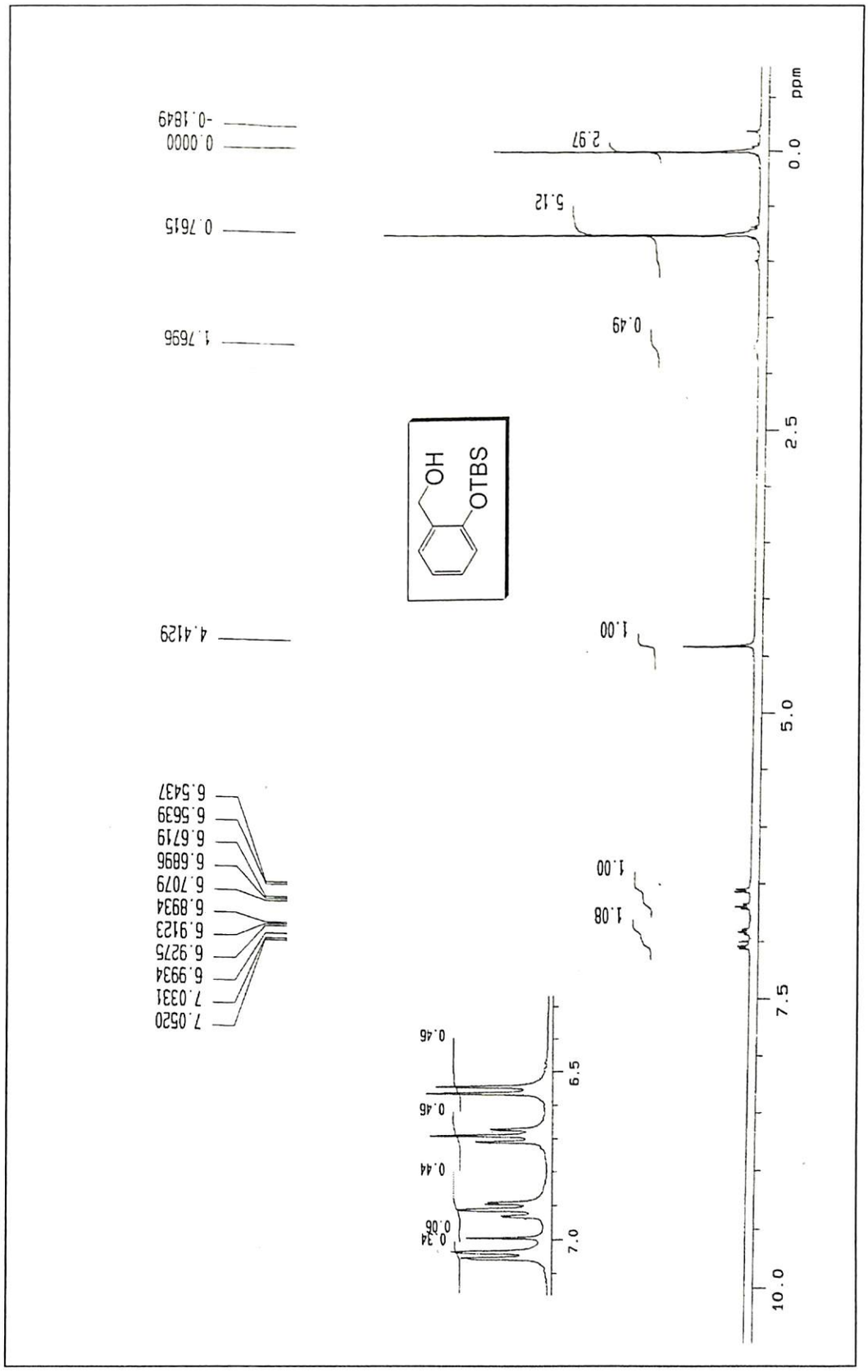


Figure 9: ^{1}H NMR spectrum of 2′-*tert*-butyldimethylsilyloxy benzyl alcohol **(111)**

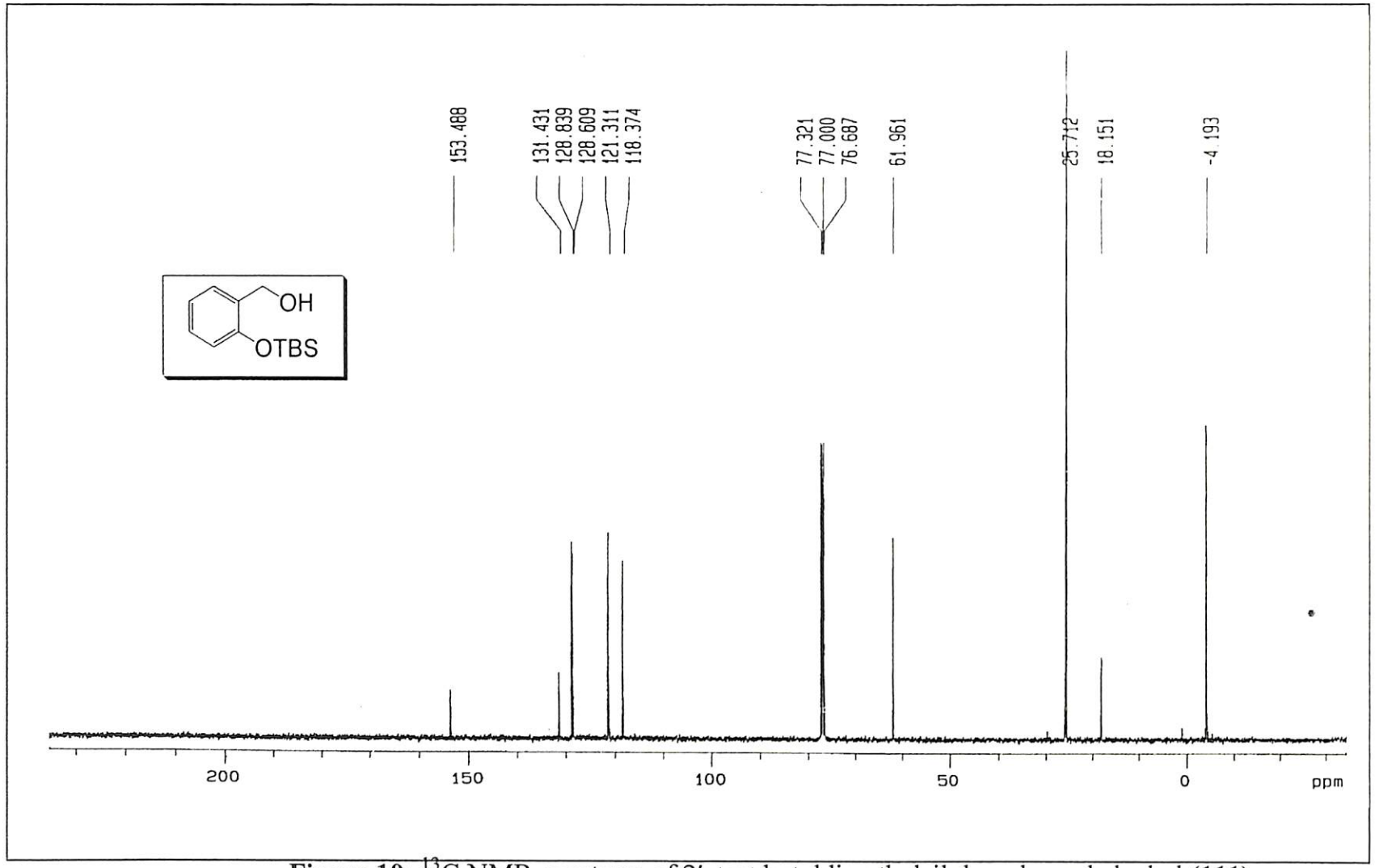


Figure 10: ^{13}C NMR spectrum of 2′-*tert*-butyldimethylsilyloxy benzyl alcohol **(111)**

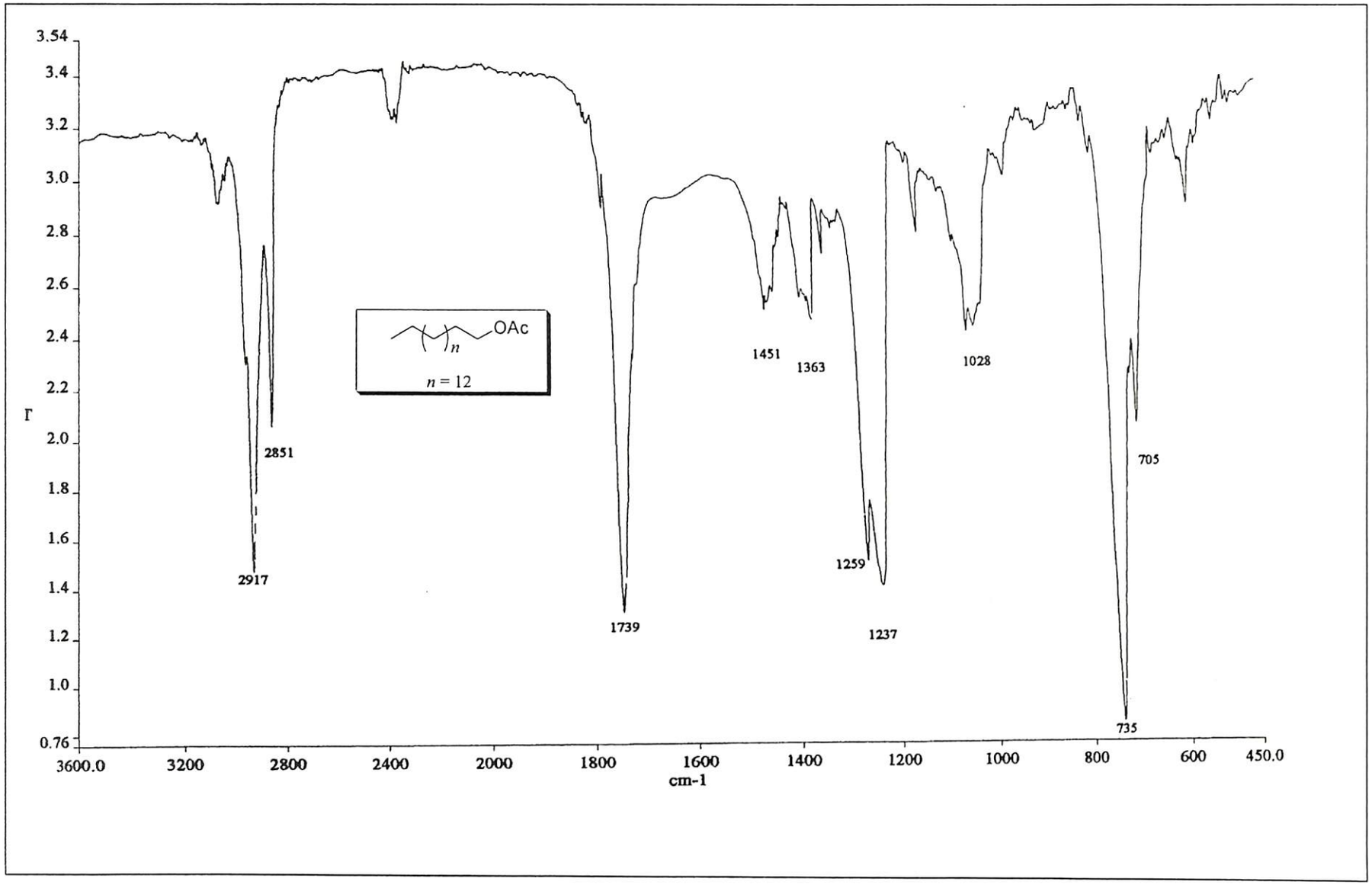


Figure 11: IR spectrum of acetate of cetyl alcohol **(135)**

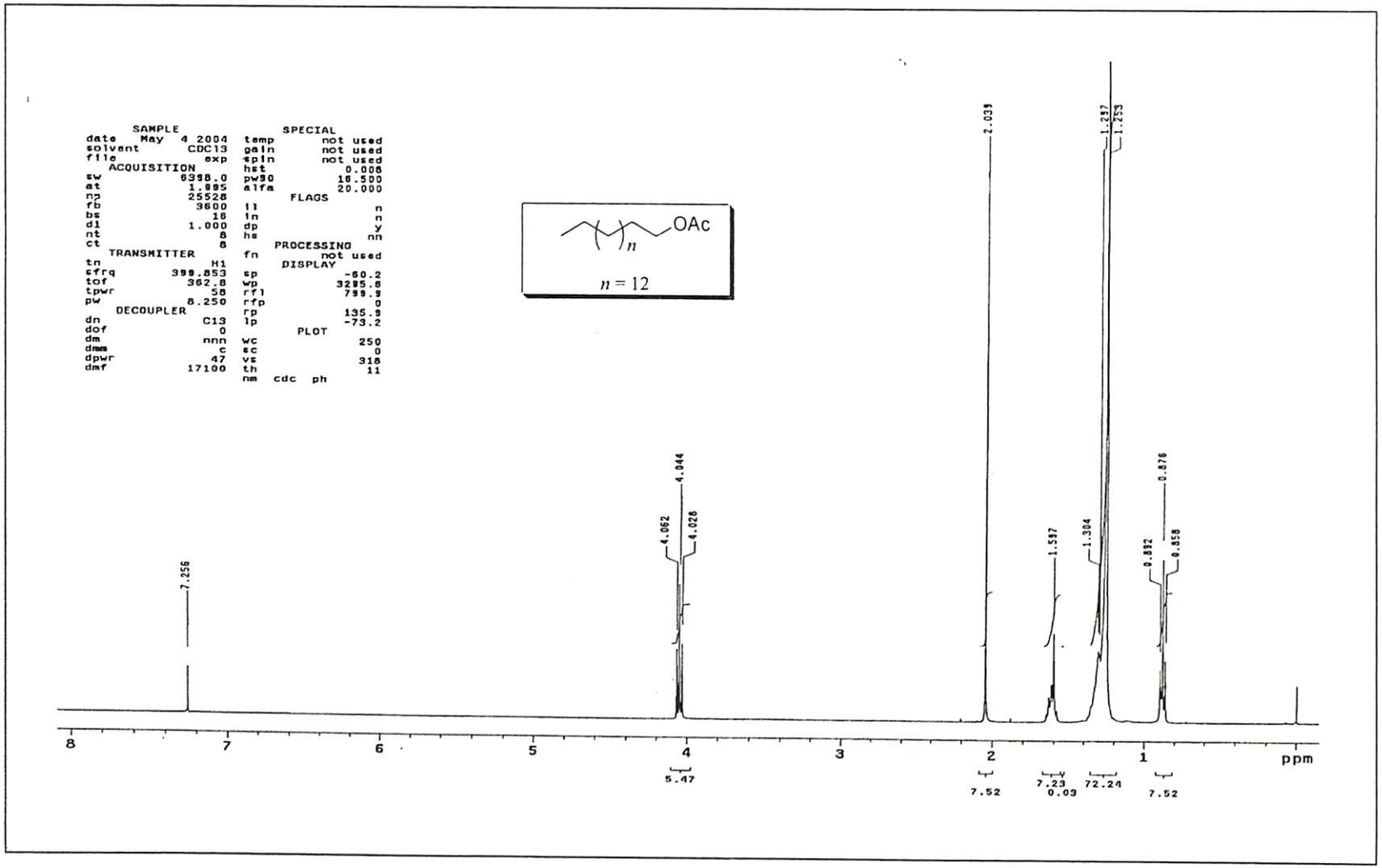


Figure 12: ^{1}H NMR spectrum of acetate of cetyl alcohol **(135)**

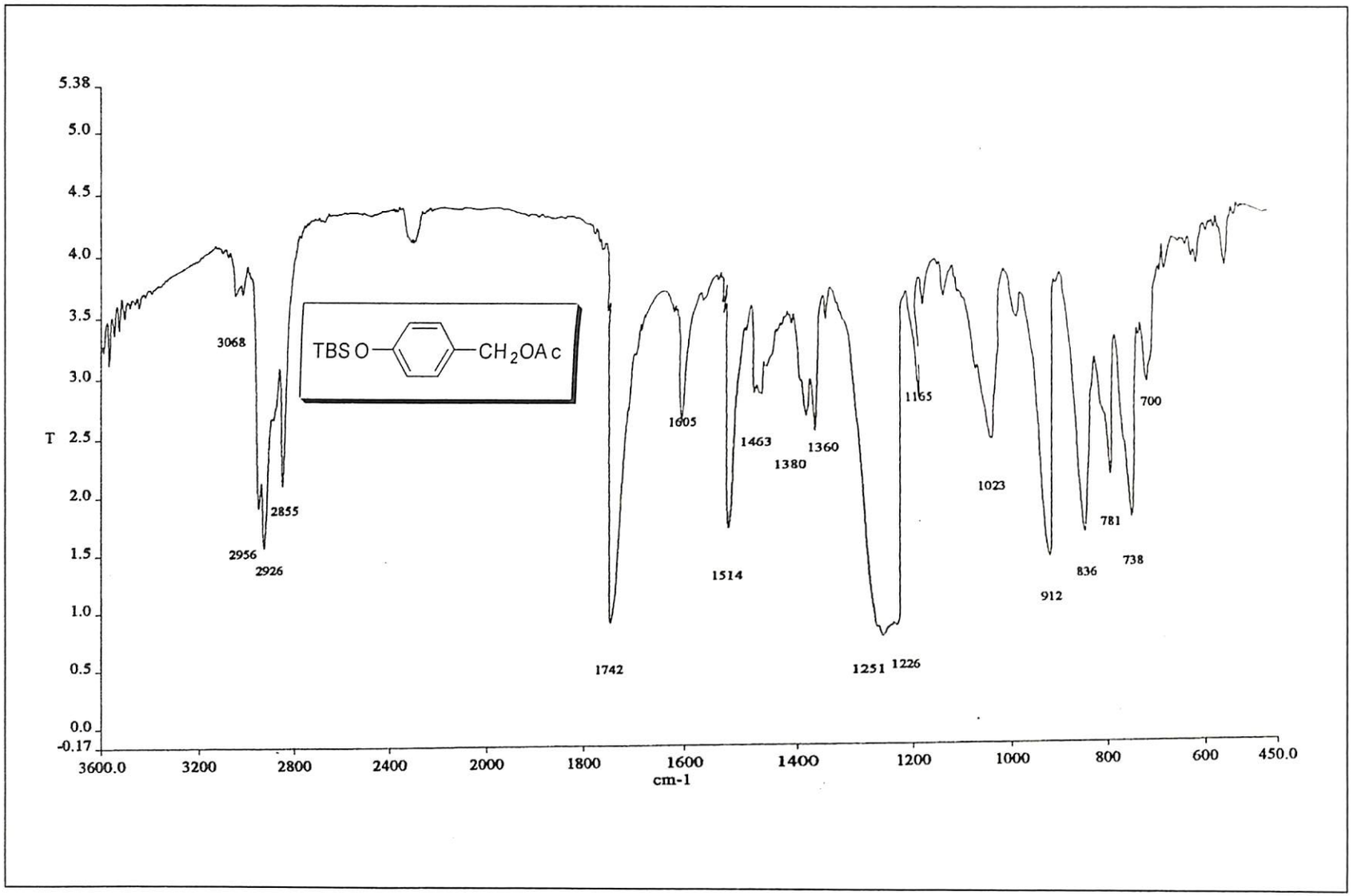


Figure 13: IR spectrum of 4-*O*-*tert*-butyldimethylsilyloxy benzyl acetate **(141)**

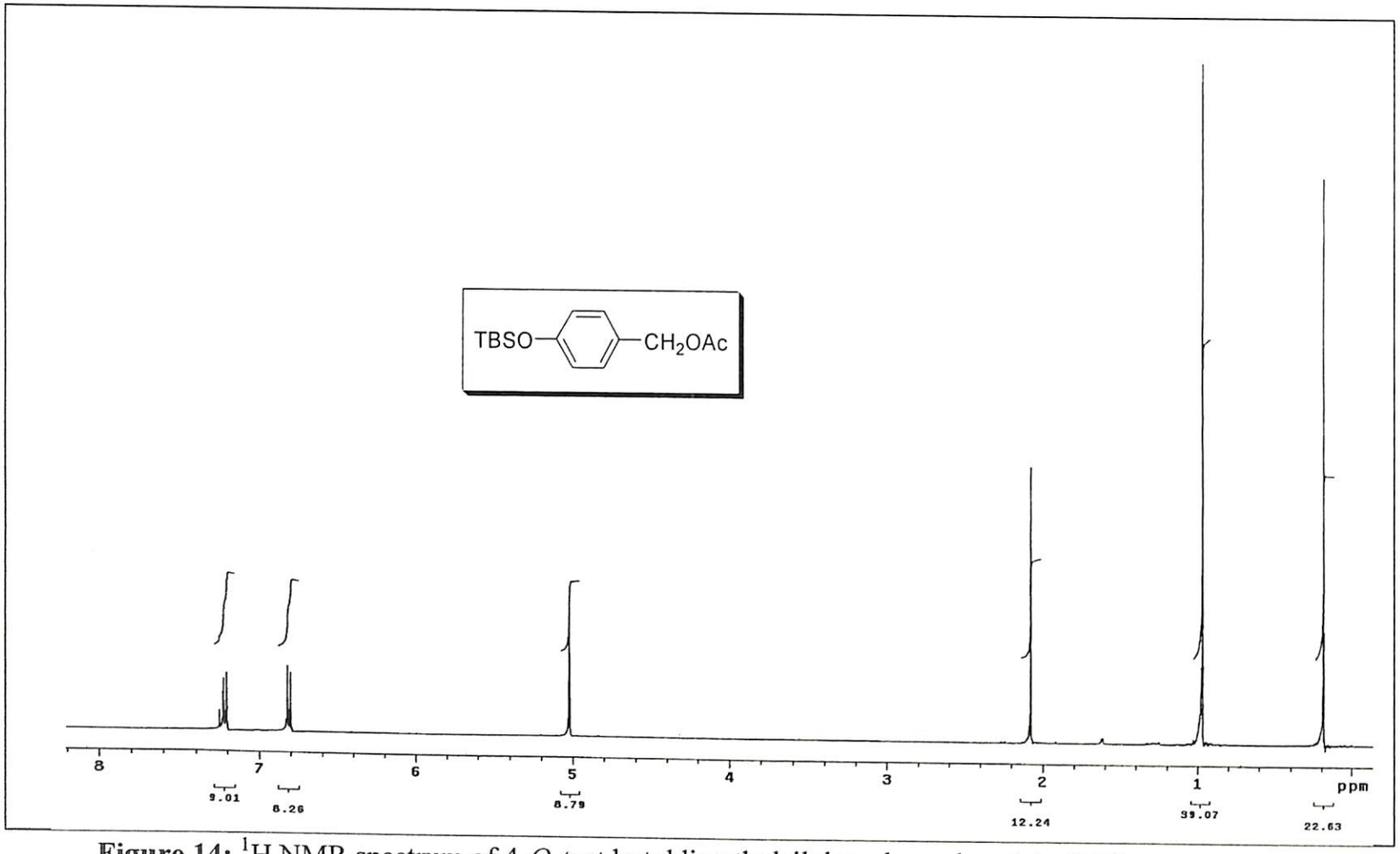


Figure 14: ^{1}H NMR spectrum of 4-*O*-*tert*-butyldimethylsilyloxy benzyl acetate **(141)**

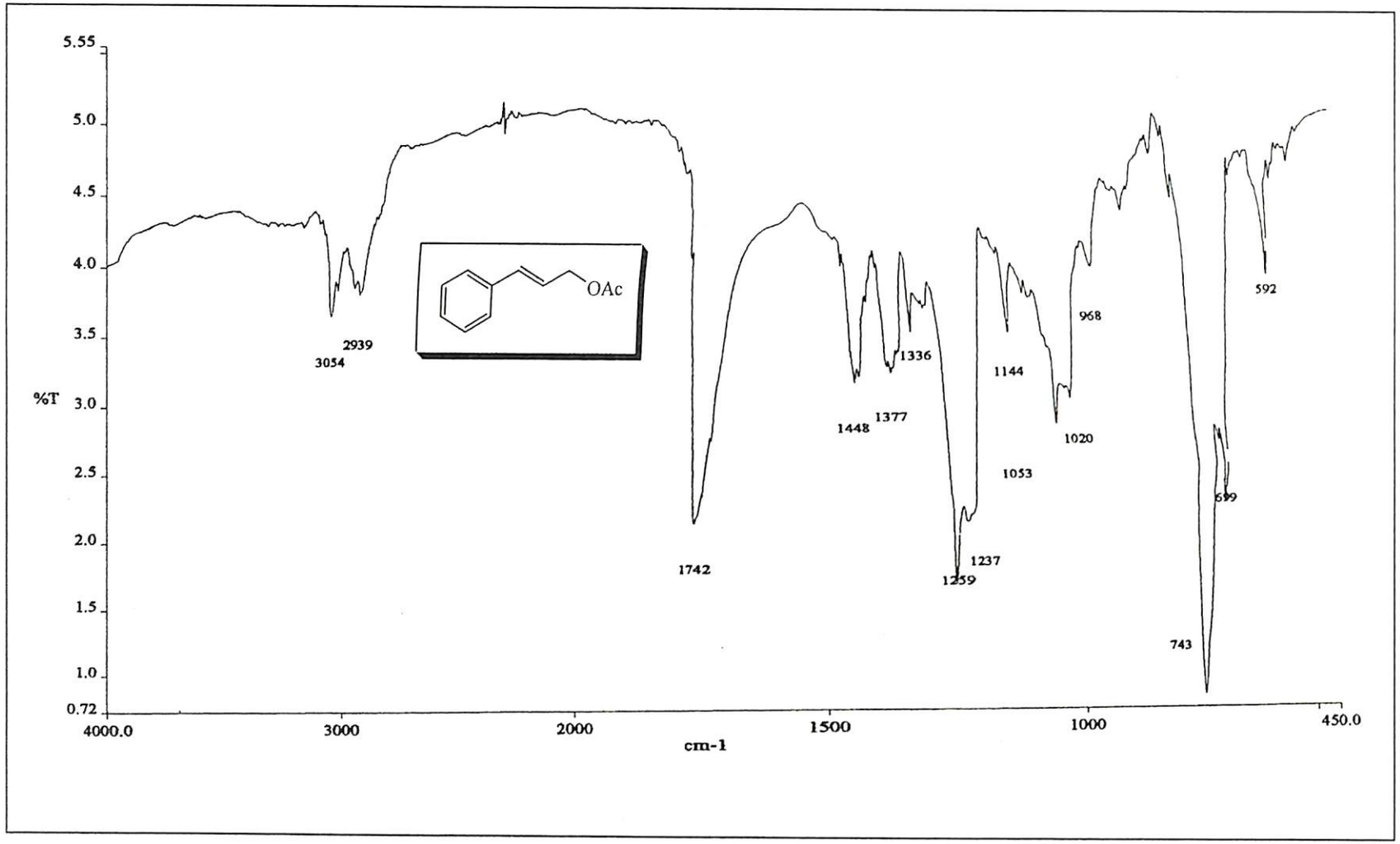


Figure 15: IR spectrum of cinnamyl acetate **(146)**

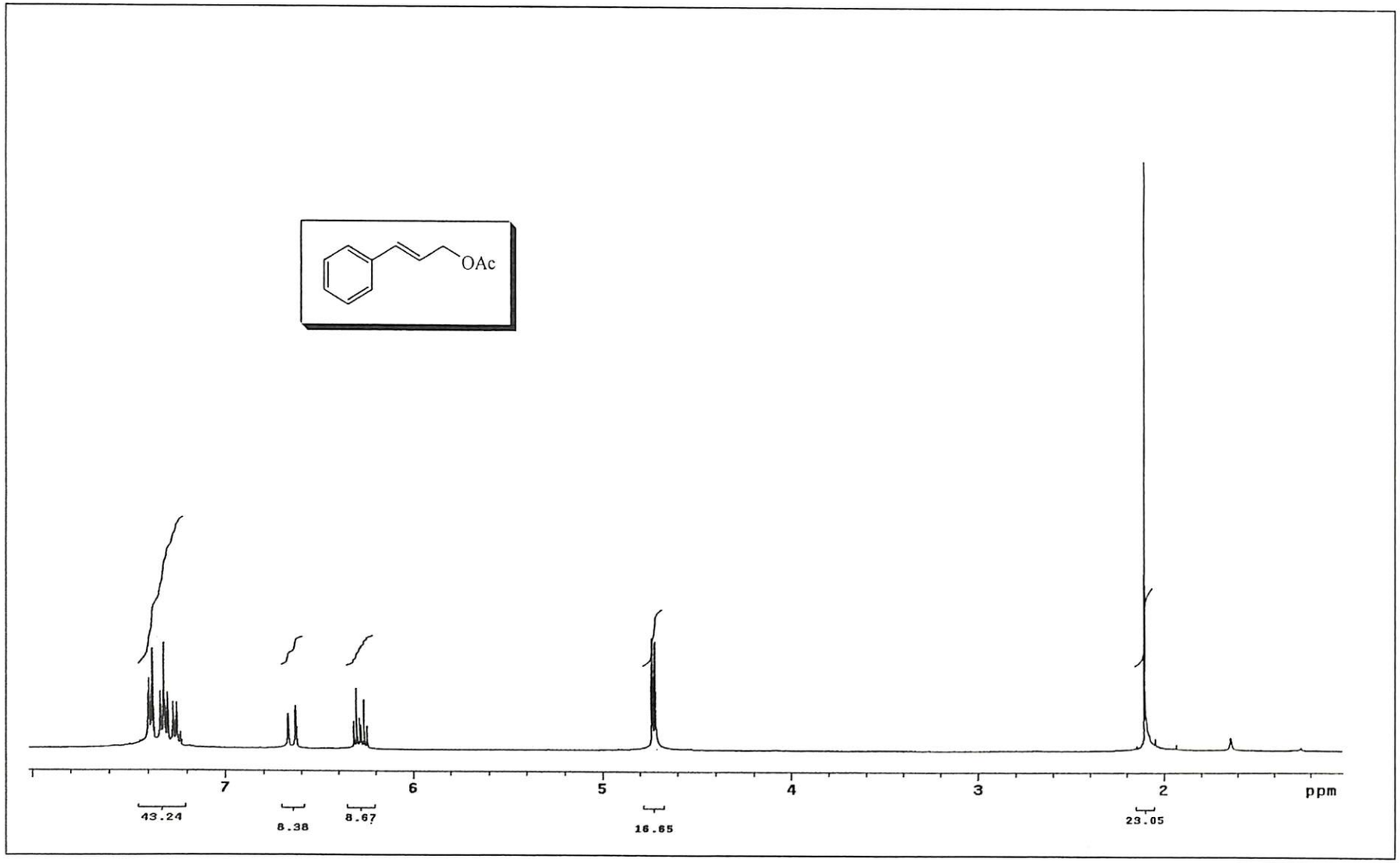


Figure 16: ^{1}H NMR spectrum of cinnamyl acetate **(146):**

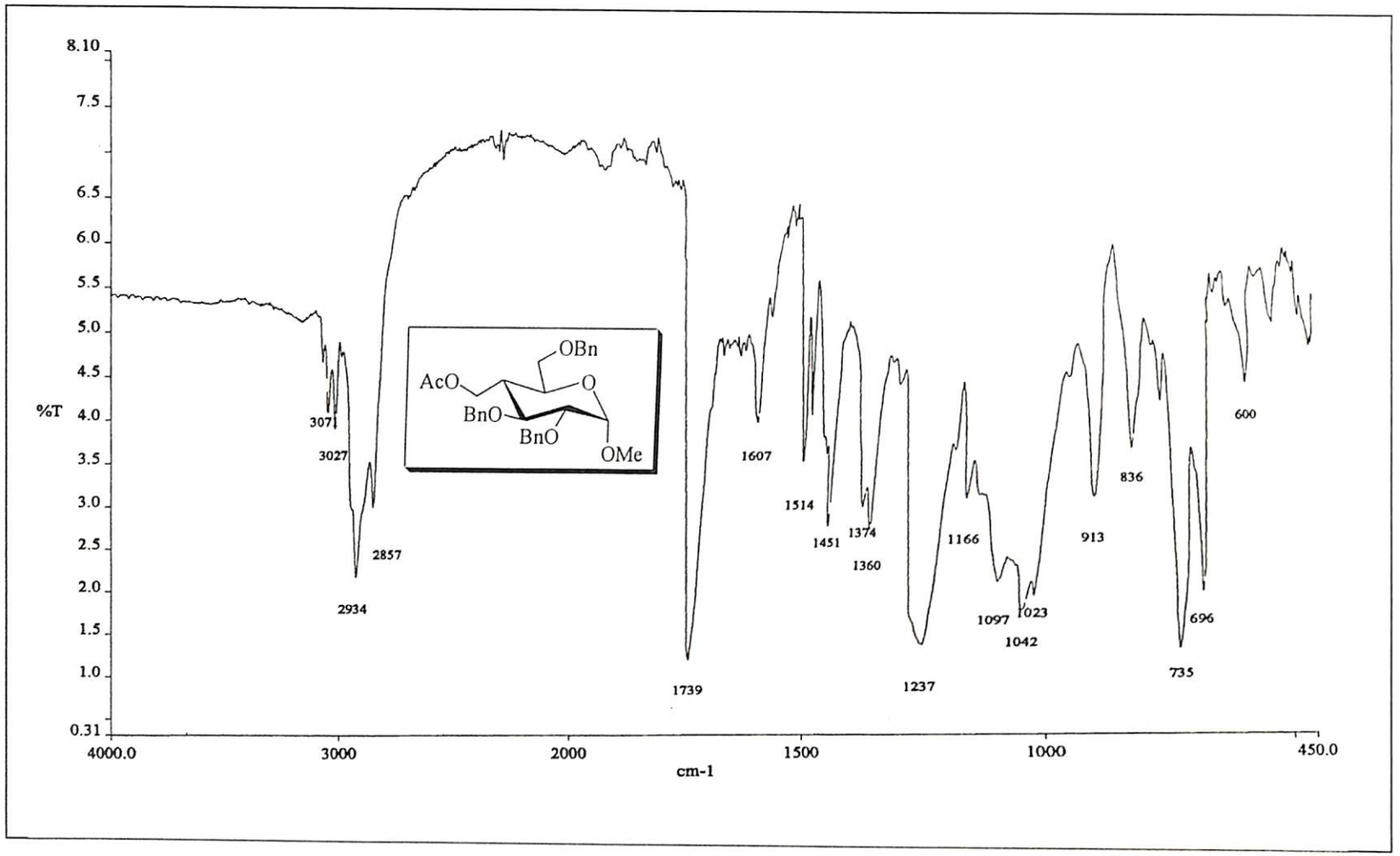


Figure 17: IR spectrum of acetate of methyl 2, 3, 6-tri-*O*-benzyl-1-β-D-glucopyranoside **(154)**

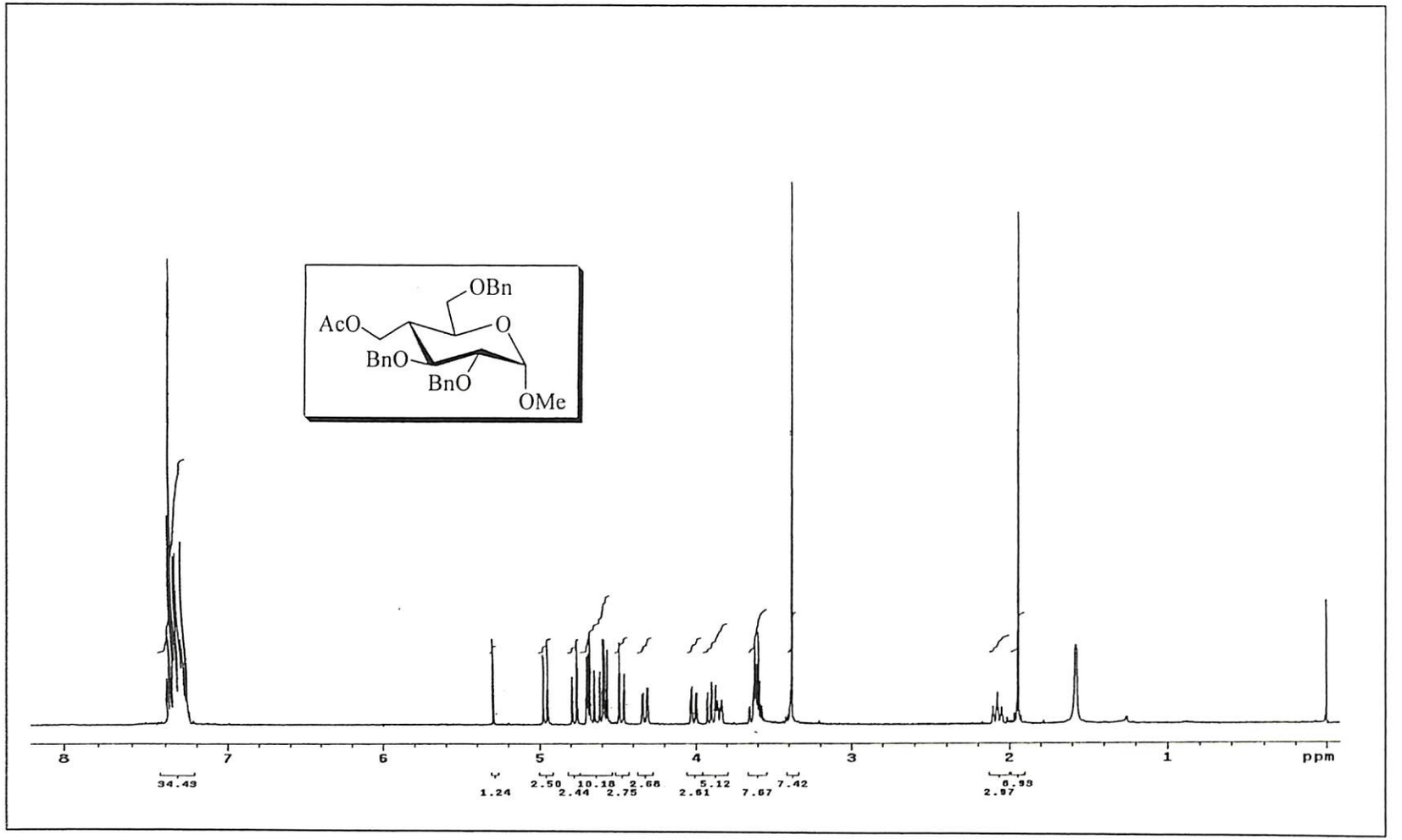


Figure 14: ^{1}H NMR spectrum of acetate of methyl 2, 3, 6-tri-*O*-benzyl-1-*β*-D-glucopyranoside **(154)**

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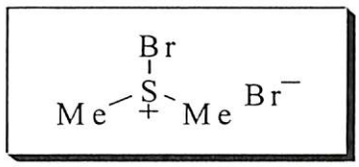
CHAPTER - II

PART I

LITERATURE SURVEY ON THE APPLICATION OF BROMODIMETHYLSULFONIUM BROMIDE AND PEROXOVANADIUM MEDIATED *IN SITU* BROMONIUM ION IN ORGANIC SYNTHESIS AS WELL AS ON α-BROMINATION OF β-KETO ESTERS AND 1,3-DIKETONES

LITERATURE REVIEW

Bromodimethylsulfonium bromide (BDMS) is a light orange solid, which can be easily prepared from molecular bromine and dimethylsulfide.[1] Interestingly, it can also be generated *in situ* by treating aqueous HBr with dimethylsulfoxide.[2] The product BDMS, which is obtained from the reaction of dimethylsulfide and molecular bromine, is reaction condition dependent. If it is prepared at room temperature, it can exist as charge transfer form $[(CH_3)_2S\rightarrow Br_2]$ as evident from the Raman spectroscopy. On the other hand, addition of the two reagents at –30 ^{0}C provide an orange compound, which can exist in ionic form $(CH_3)_2SBr^+Br^-$. The structure of BDMS is confirmed by powder X-ray diffraction study.[3] The ionic form is metastable towards the charge transfer form. Upon storage of metastable form for a period of one week at room temperature, it transforms into the charge transfer form. The reagent BDMS can be considered as a convenient storage of bromine molecule or source of **bromonium** ion by analogy with hypobromite, N-bromosuccinimide or bromoazide. It is safer and easier to handle as compared to hazardous molecular bromine. In addition, due to its fascinating features such as efficient catalytic properties and unique behaviour as a brominating reagent, it has gained substantial interest in current organic chemistry.

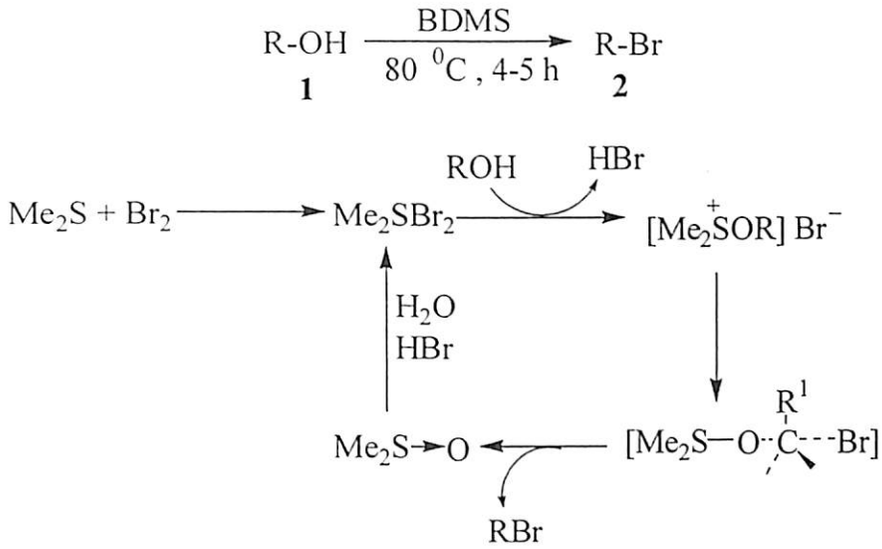


BDMS

The dawn of halodimethylsulfonium halide began[4] from the discovery of Meerwein's bromodimethylsulfonium bromide in 1965 and subsequent use of chlorodimethyl-sulfonium chloride[5] by Corey *et al.* Over the years, bromodimethylsulfonium bromide has been used extensively in organic synthesis. A brief survey on the application of bromodimethylsulfonium bromide as a versatile reagent as well as an effective pre-catalyst is illustrated below.

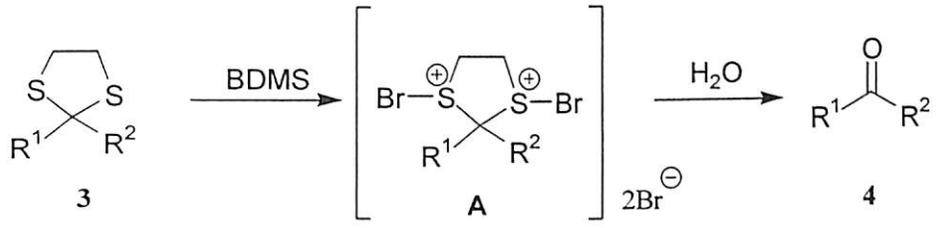
Furukawa *et al.* first demonstrated the application of this reagent for the conversion of alcohols to bromides in high yields.[6] The reaction mainly proceeds through an inversion process i.e. optically active alcohol provides the corresponding bromide with inversion of configuration. During the course of the reaction the generation of DMSO was not detected which might form from the decomposition of intermediate sulfoxonium salt.

This may be due to the reaction of DMSO and HBr to produce BDMS again as shown in Scheme 1.



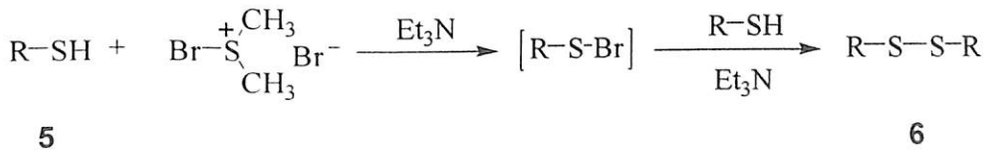
Scheme 1

Later on, Olah *et al.* had shown the applicability of this reagent for the cleavage of dithioacetals.[1] As BDMS is considered as a storage of bromonium ion, thus 'soft' electrophile Br^+ can combine with the 'soft' sulfur atoms of the dithioacetals to give a *bis*-sulfonium ion intermediate (**A**), which can be finally hydrolyzed to regenerate the parent carbonyl compounds as shown in Scheme 2.



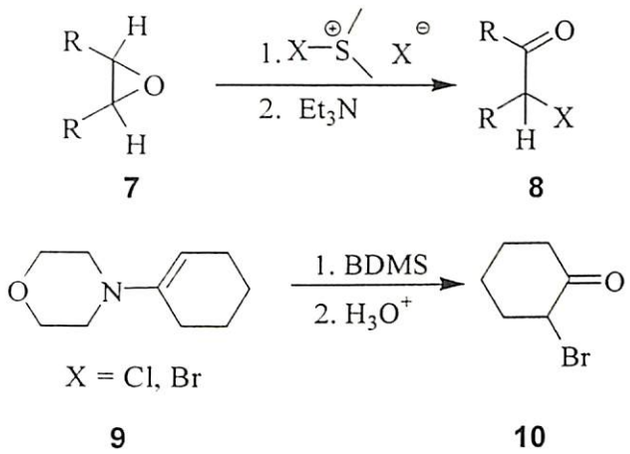
Scheme 2

Subsequently, Olah *et al.* demonstrated that bromodimethylsulfonium bromide efficiently oxidized thiols into the corresponding disulfides[7] as shown in Scheme 3. The reaction takes place in the presence of triethylamine at room temperature affording good yields. This method for the preparation of disulfide is milder and efficient in comparison to the other methods reported in the literature.



Scheme 3

In continuation of their research work[8] on the utilization of BDMS for various transformations, they reported that epoxides upon treatment with halodimethylsulfonium halides (chloride/bromide) in the presence of triethylamine afforded α-halo ketones in high yields. The reaction proceeds well with alkene oxides and cycloalkene oxides of small ring sizes. In case of medium and large ring sized epoxides, it underwent transannular rearrangements giving a mixture of products. Similarly, enamines react with BDMS to give α-bromoketones as shown in Scheme 4.



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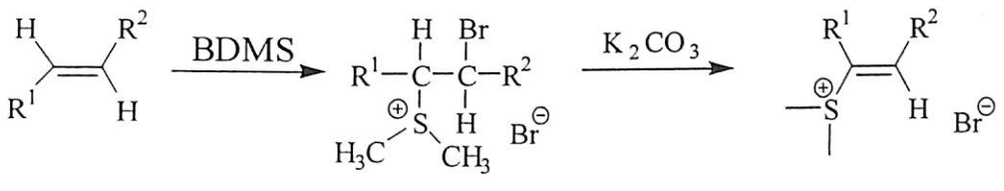
Scheme 4

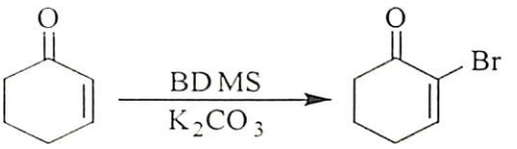
Chow *et al.* demonstrated that bromdimethylsulfonium bromide reacts with various alkenes and provides corresponding addition product sulfonium bromides **12** instead of the expected dibromides in good yields.[9] The resultant sulfonium bromide on treatment with aqueous potassium carbonate affords dehydrobrominated products **13** as shown in Scheme 5.



11 12 13

Scheme 5

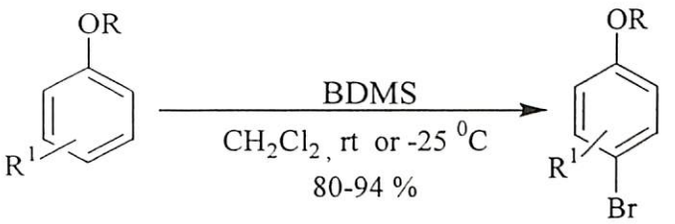
Subsequently, Chow *et al.* reported that it can react with conjugated enones at 0 °C and give α-bromo-β-sulfonium carbonyl compounds, which on subsequent treatment with aqueous K_2CO_3 give α-bromo enones in excellent yields[10] as depicted in Scheme 6.



14 15

Scheme 6

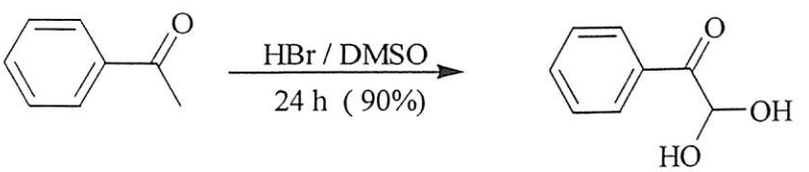
Olah *et al.* further shown that bromodimethylsulfonium bromide as well as its chloro analogue is an efficient regioselective halogenating agent for activated aromatics such as phenols, anisole, diphenyl ether and N-alkyl anilines[11] as shown in Scheme 7. The observed high *para* selectivity is a consequence of the transfer of halogens going through a "late" arenium ion like transition state and of the bulky nature of the halogenating agents. Unfortunately, it fails to halogenate *para* substituted aromatics



16 17

Scheme 7

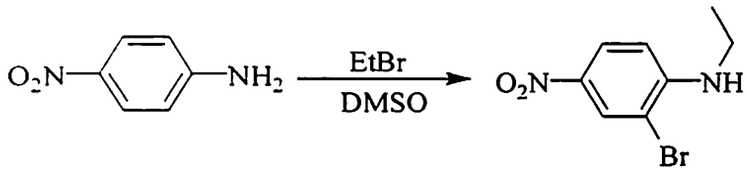
Floyd and co workers[12] achieved the oxidation of acetophenone to glyoxal hydrate **19** using BDMS, which was generated *in situ* from the aqueous hydrobromic acid in DMSO as shown in Scheme 8.



18 19

Scheme 8

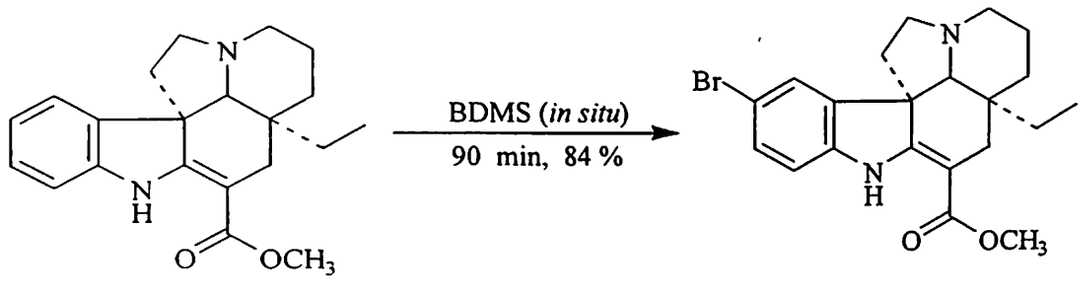
Interestingly Fletcher and Pan noted the bromination of aromatic amines on heating with ethyl bromide in DMSO during an investigation of alkylation reaction[13] as depicted in Scheme 9.



20 21

Scheme 9

Megyeri and Keve found that indole alkaloids could also be brominated using this versatile reagent bromodimethylsulfonium bromide (Scheme 10).[14]



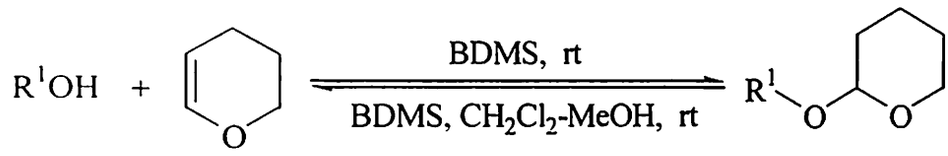
22 23

Scheme 10

Due to the enormous synthetic utility of bromoarenes, bromination is one of the most important transformations in organic synthesis. In continuation of the use of bromo-dimethylsulfonium bromide in various transformations, Majetich *et al.* demonstrated that BDMS generated *in situ* by treating DMSO with aqueous HBr, is a milder and selective reagent for electrophilic aromatic bromination than elemental bromine.[2] The activated arenes such as aniline or N,N-dimethylaniline undergoes mono bromination without any side products. In contrast, molecular bromine provided benzylic brominated products for the substrates such as *o*-cresol. Although it offers a wealth of advantages but it also suffers from some limitations: acid sensitive functionality such as acetals or ketals did not survive under the experimental conditions. Inactivated arenes containing electron-withdrawing substituent such as carboxylic acid, halogen substituent, nitro group, aldehyde or ketone without α-protons did not react even under forcing conditions.

Despite the broad scope of this versatile reagent both as a catalyst and a safer brominating reagent, its catalytic property was unexplored until last decade. Our group (Khan and co-workers) demonstrated that bromodimethylsulfonium bromide is an effective catalyst for protection of hydroxyl compounds such as tetrahydropyranyl ether as well as the same reagent is useful for depyranylation. This protocol is applicable to a

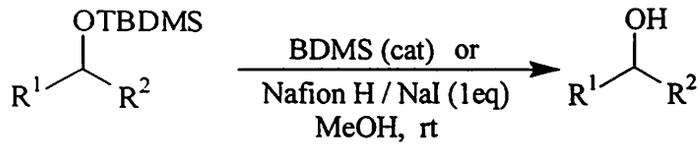
wide range of alcohols and phenols (Scheme 11). The notable advantages of this protocol are: excellent yield, no aqueous workup and rapid process.[15]



24 25

Scheme 11

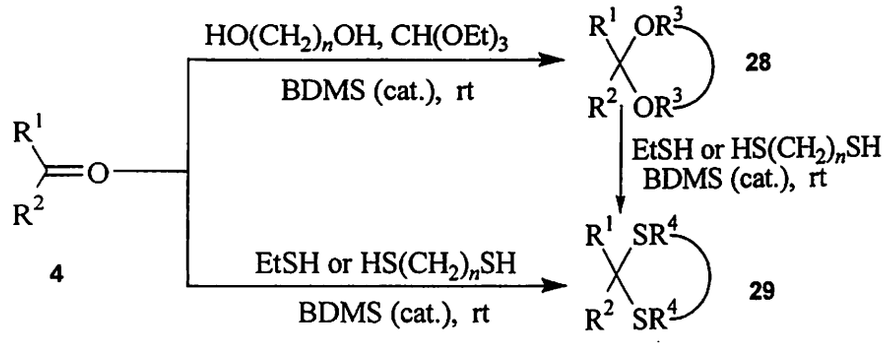
Vankar *et al.* reported that catalytic amount of bromodimethylsulfonium bromide, or Nafion-H along with NaI (1 equiv.) in methanol cleave a variety of TBDMS ethers readily in high yields (Scheme12).[16] Alkyl TBDMS ethers cleave more chemoselectively as compared to the phenolic TBDMS ethers, benzyl, and methyl ethers.



26 27

Scheme 12

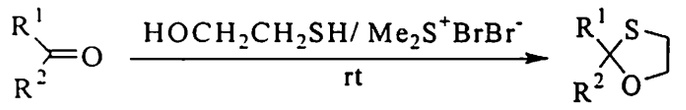
Subsequently, our group demonstrated that the thioacetalization, acetalization as well as transthioacetalization of carbonyl compounds can be accomplished in an effective manner in high yields using a catalytic amount of bromodimethylsulfonium bromide as shown in Scheme in 13.[17]



Scheme 13

Similarly, a wide variety of aldehydes and ketones can be transformed into the corresponding oxathioacetals in presence of catalytic amount of bromodimethylsulfonium bromide (BDMS) in high yields (Scheme 14). Large-scale reaction can also be performed

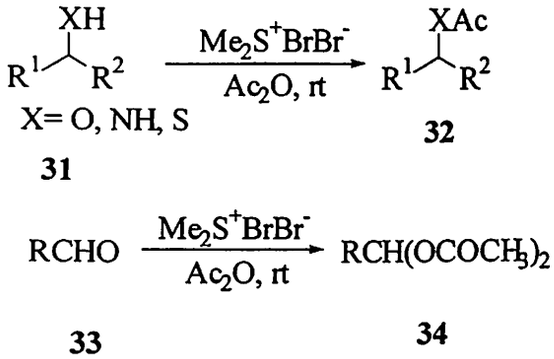
as well as pure products can be isolated just by distillation of the crude reaction mixture avoiding any aqueous work-up and column chromatography using this protocol. [18]



4 30

Scheme 14

Later on, we also noted[19] that in presence of catalytic amount of bromodimethylsulfonium bromide, alcohols, phenols, amines, thiols and thiophenols undergo acylation with quantitative amount of acetic anhydride under solvent-free conditions at room temperature. Acylal of both aliphatic and aromatic aldehydes can also be accomplished at room temperature using the same catalyst.

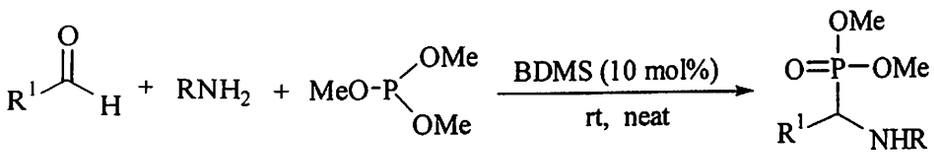


31 32

33 34

Scheme 15

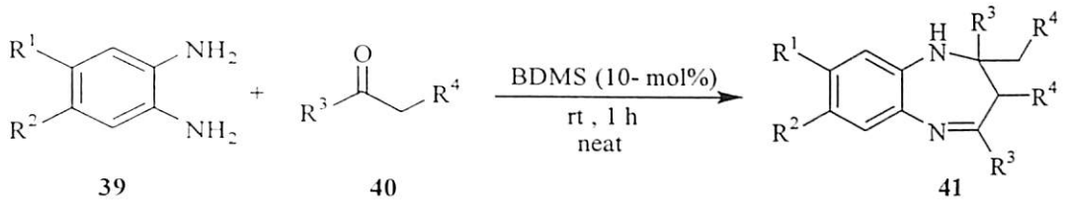
Bommena *et al.* demonstrated that solvent-free one pot synthesis of α-aminophosphonate in presence of catalytic amount of bromodimethylsulfonium bromide in good to excellent yields.[20] The method is applicable for aromatic as well as α,β-unsaturated aldehydes and products are obtained in very good yields.



35 36 37 38

Scheme 16

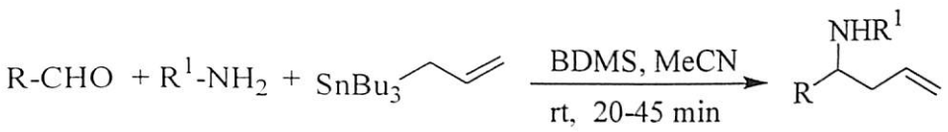
Bromodimethylsulfonium bromide is an efficient catalyst for the solvent-free synthesis of 1,5-benzodizepines by condensation of *o*-phenylinediamine with enolizable ketones[21] as shown in Scheme 17. The reaction takes place at room temperature and provided very good yields.



39 40 41

Scheme 17

Das *et al.* demonstrated that bromodimethylsulfonium bromide catalyses multi-component reaction of aldehydes, amines and allyltributylstanane affording the corresponding homoallylic amines in excellent yields in short reaction time.[22]



33 42 43 44

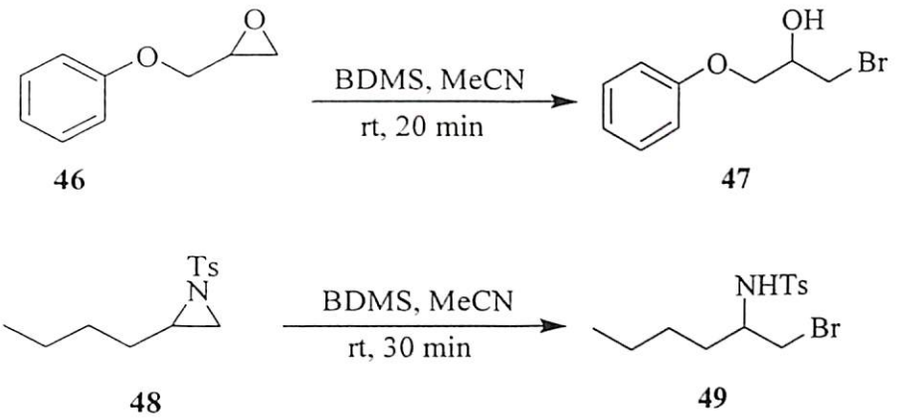
Scheme 18

Further, Das *et al.* reported[23] that bromodimethylsulfonium bromide is an effective catalyst for efficient one-pot synthesis of α-amino nitriles from the three-component condensation of carbonyl compounds, amines and trimethylsilyl cyanide as shown in Scheme 19. The reaction takes place in short reaction time with high yields.

33 42 45

Scheme 19

Subsequently, Das *et al.* demonstrated that on treatment of bromodimethylsulfonium bromide with Baylis-Hillman adducts in MeCN provided (*Z*)- and (*E*)-allyl bromides stereoselectively. The reaction is rapid at room temperature with high yields and high stereoselectivity.[24] In addition, recently they have reported[25] that epoxides and aziridines undergo ring opening efficiently with BDMS at room temperature affording the corresponding β-bromohydrins and β-bromoamines, respectively (Scheme 20). The conversions are highly regioselective and provided excellent yields.



46 47

48 49

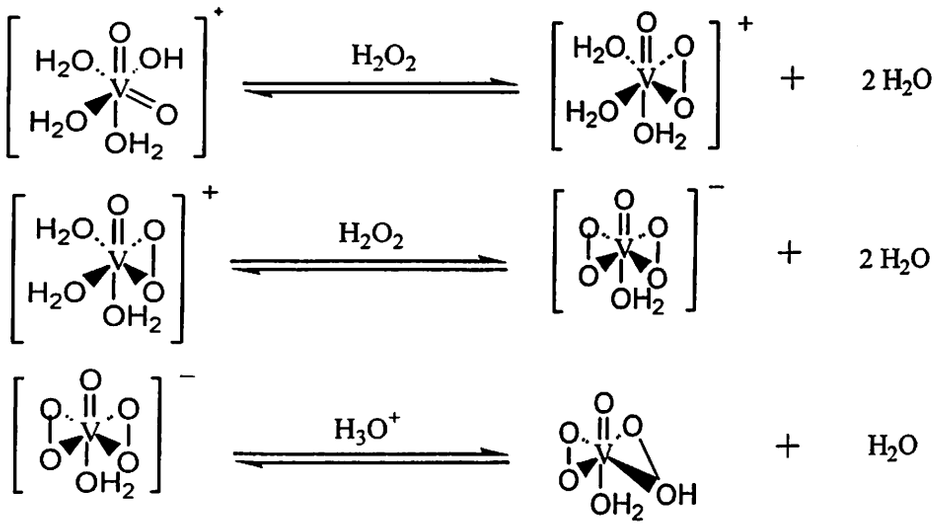
Scheme 20

From this literature survey it is quite clear that bromodimethylsulfonium bromide (BDMS) is a versatile reagent[26] which acts both as an effective catalyst as well as a mild brominating reagent. In continuation of our work on bromo organics as well as on the development of new synthetic methodologies by employing BDMS and other new reagents, we wanted to explore this reagent to device a new and effective protocol for the regioselective bromination of β-keto esters and 1,3-diketones, which is eventually a challenging and important organic transformation. The results of our observation will be described in Section A of this Chapter.

As our research goal was the bromination of β-keto esters, so we were looking for safer and environmentally acceptable alternative brominating agent or a combination to replace the current methodologies. Thus we found in the literature that the peroxovanadium complexes can oxidize bromide ion to their corresponding bromonium ion and can mimic the activity of vanadium haloperoxidases (an enzyme which catalyzes the oxidation of halide[27] ion by hydrogen peroxide and also responsible for the production of bromo-organics).[28] As a part of our ongoing project to develop new synthetic methodologies so

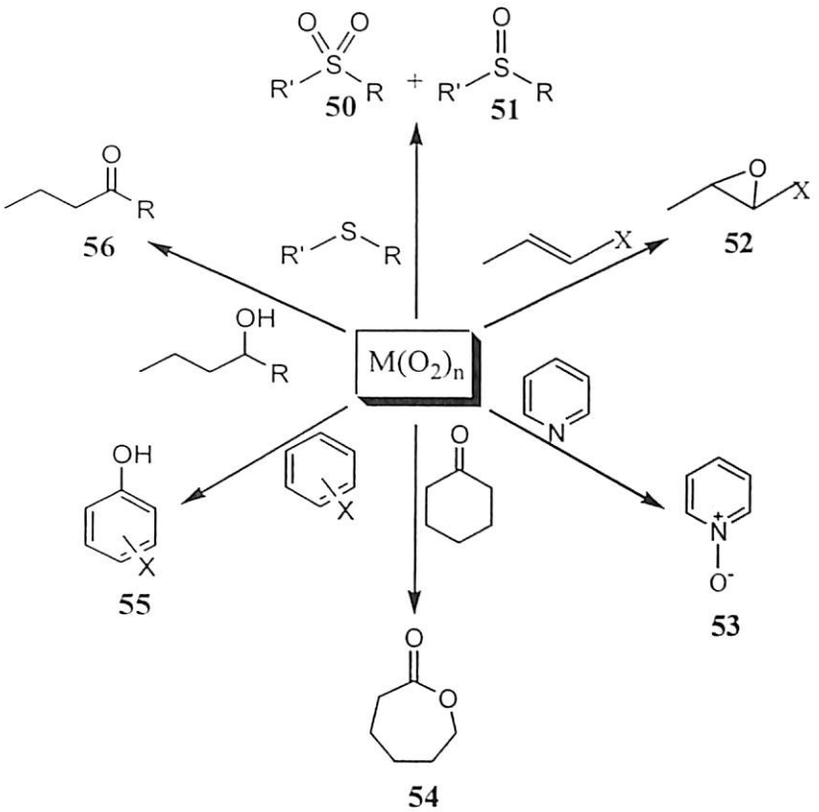
far we have used the combination of V_2O_5-H_2O_2 and bromide source e.g. NH_4Br for some of the important transformations. A brief history as well as some of the applications of this combination is highlighted below.

Peroxovanadium complex obtained from the reaction of vanadium pentoxide or ammonium vanadate with hydrogen peroxide has gained considerable interest in recent years due to its strong oxidizing properties.[29, 30] The dissolution of vanadium pentoxide in aqueous hydrogen peroxide or the addition of hydrogen peroxide to the acidic solution of vanadium(V) gives red peroxo complexes in which oxygen atoms on the vanadate ions are replaced by one or more O_2^{2-} groups. Howarth and Hunt investigated the structure of the intermediates,[29] which are formed in the solution by ^{51}V-NMR and proposed that in solution following intermediates are formed, such as $[VO(O_2)]^+$, $[HVO_2(O_2)_2]^{2-}$, $[H_2VO_2(O_2)_2]^-$, $[VO(O_2)_3]^{3-}$, $[HVO(O_2)_3]^{2-}$ and $[V(O_2)_4]^{3-}$ etc. Di Furia *et al.* proposed on the basis of *ab initio* calculation[30,31] and ^{51}V-NMR Spectroscopy study,[32,33] that depending on pH and the amount of H_2O_2 added in acidic solution, it exist as diperoxovanadium complexes, $[VO(O_2)]^+$ or $[VO(O_2)_2]^-$. However, a fundamental aspect concerning the nature of the first coordination sphere of the peroxovanadium derivatives in solution is still uncertain.



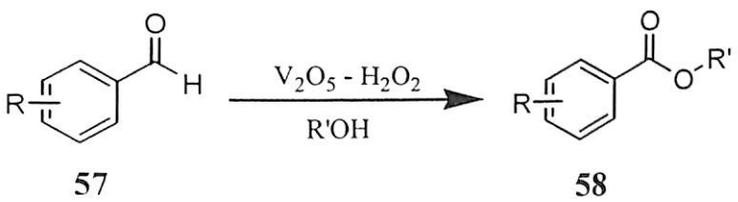
Scheme 21

It is well known in the literature that the peroxometal complexes are stronger oxidant as compared to H_2O_2 with much more reactivity.[34-37] The versatility of peroxometal complexes have already been studied as strong oxidants for various valuable organic transformations, as shown in Scheme 22.



Scheme 22

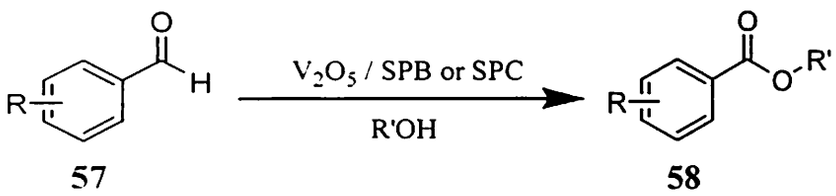
By taking into consideration of the oxidative property of peroxovanadium complexes, Patel *et al.* reported[38] a combination of V_2O_5 and H_2O_2 as a better oxidant than hydrogen peroxide in the controlled oxidation of aldehydes to the corresponding esters as depicted in Scheme 23.



Scheme 23

Later on, they have also demonstrated[39] a new method for the oxidative transformation of various aldehydes to the corresponding esters by using sodium perborate (SPB) or

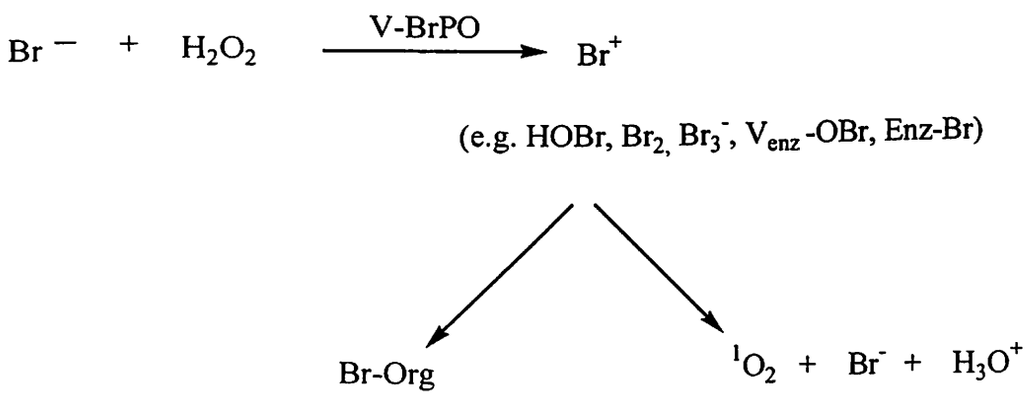
sodium percarbonate (SPC) as the alternative sources of hydrogen peroxide as shown in Scheme 24.



57 58

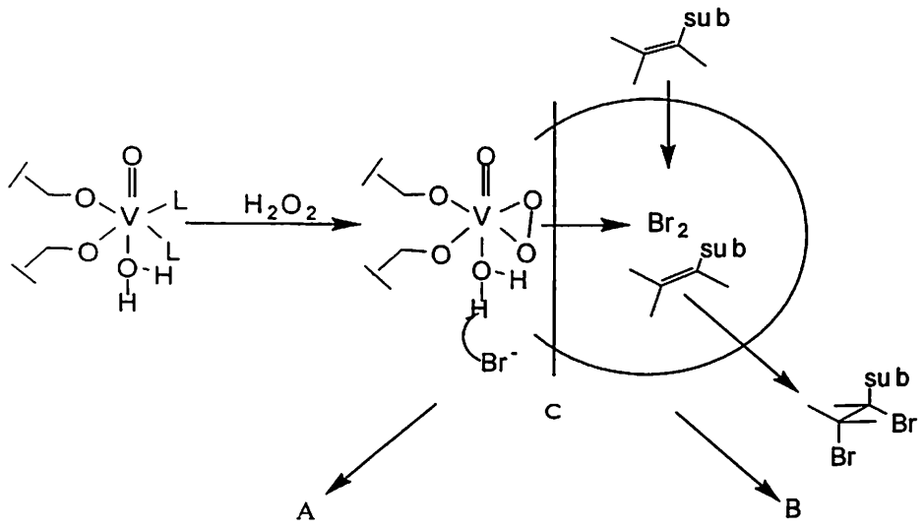
Scheme 24

There was a breakthrough in peroxovanadium chemistry after the discovery and isolation of vanadium haloperoxidases.[40, 41] In addition, peroxovanadium chemistry is important as the complex peroxovanadium species can serve as a clinical alternative of insulin for the treatment of diabetes.[42, 43] The exact mechanism of halogenation of the organic substrates by haloperoxidases is still not very clear. However, Butler and her group proposed a mechanism for the oxidation of chloride, bromide and iodide ion by H_2O_2 to their corresponding halonium ion.[41] Vanadium exists in the +5 oxidation state in the vanadium dependent bromoperoxidase (V-BrPO), which bind with hydrogen peroxide to produce a peroxo species as the reactive intermediate. This oxidizes the halide, keeping the oxidation state of the metal unaltered during the bromination step. According to them, in the first step the enzyme catalyses the oxidation of the halide by hydrogen peroxide producing an intermediate, which is a two electron oxidized halogen species such as hypohalous acid or its equivalent. In the second step, the oxidized halogen species can halogenate the organic substrate or oxidize a second equivalent of hydrogen peroxide to give singlet oxygen, as shown in Scheme 25.



Scheme 25: Proposed mechanism of bromoperoxidase activity catalysed by V-BrPO.

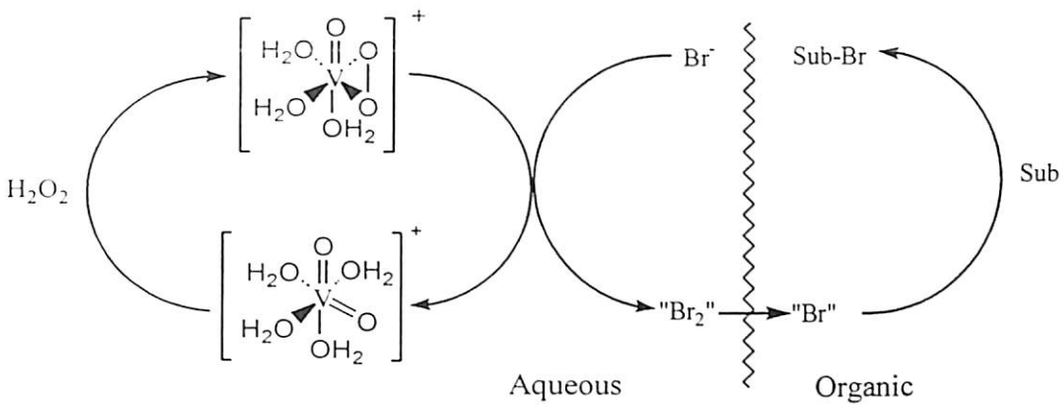
Later on, Di Furia *et al* investigated the bromination reaction of various organic substrates and alkenes by mimicking the vanadium bromoperoxidases reactions.[44] They proposed a model for the mechanism that the bromide oxidation takes place in the hydrophilic portion of the enzyme and then the intermediate migrates to the hydrophobic portion where the bromination occur, as described in Scheme 26, on the basis of Neumann's observation.[45]



A = hydrophilic portion B = lipophilic portion

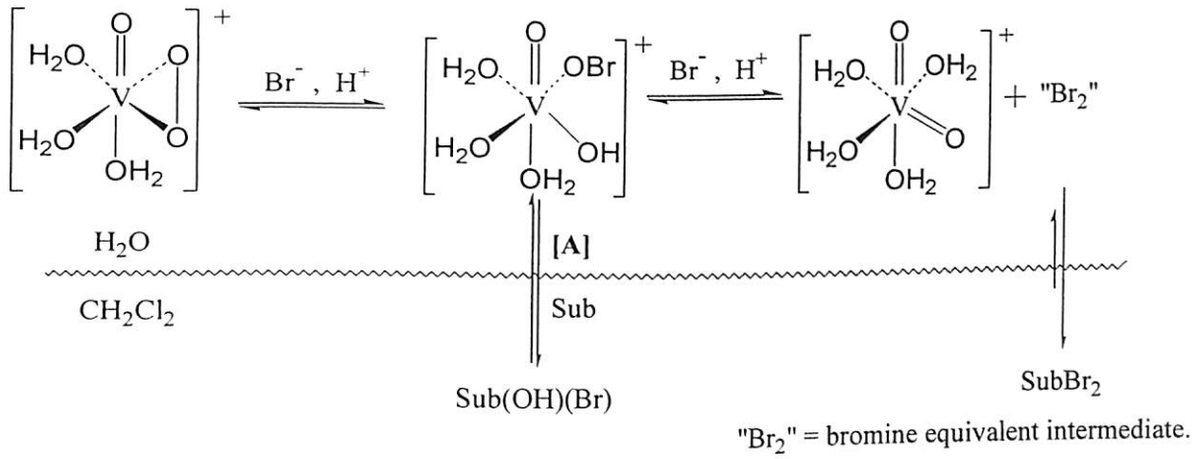
Scheme 26

On this basis of the above concept, along with the oxidation of bromide ion by hydrogen peroxide, Di Furia and his co-worker thought that a two-phase system (H_2O/CH_2Cl_2 or $H_2O/CHCl_3$) could be a better model for the reactivity of V-BrPO, which led them to develop a synthetic procedure for the bromination of a series of aromatic compounds and olefins.[46] They found that in the absence of vanadium only a trace amount of brominated products were formed. According to them, the formation of monoperoxovanadium complex by the interaction of vanadium salt and hydrogen peroxide occurred in aqueous phase, which oxidizes the bromide ion to bromine equivalent and transfers it into the organic phase where the bromination of the substrate takes place as depicted in Scheme 27.



Scheme 27

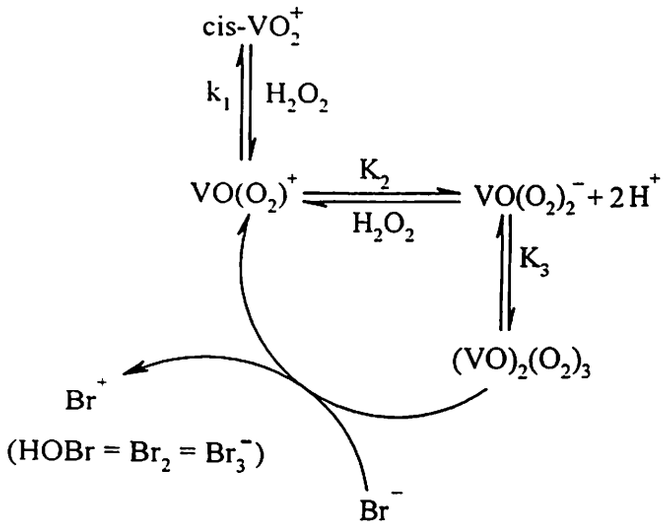
In order to expand the scope of the procedure, Di Furia and his group examined the bromination of some olefins. They observed that along with the bromo derivative, bromohydrin was also formed in some cases.[46] The formation of bromohydrin derivative not only depends upon the nature of the substrate but also on the nature of the brominating reagent and the rate of stirring. From the above observation, they concluded that the interaction of the peroxovanadium complex with the bromide ion produces an intermediate **[A]**, which resembles hypobromous acid and is also responsible for the formation of the bromohydrin derivative. Further reaction of the intermediate **[A]** with bromide ion gives the bromine, which brominates the organic substrate as shown in Scheme 28.



Scheme 28

Successively, Buttler and Clague studied the mechanism and reactivity of *cis*-dioxovanadium(V) catalyzed oxidation of bromide ion by hydrogen peroxide.[47] They have proposed a model that under acidic condition addition of hydrogen peroxide to *cis*

VO_2^+ gives the red oxomonoperoxo $VO(O_2)^+$ and yellow diperoxo $(VO)_2(O_2)^-$ species. Under more acidic conditions, neutral dioxotriperoxodivanadium complexes $(VO)_2(O_2)_3$ is also formed by the dimerisation of $VO(O_2)^+$ and $(VO)_2(O_2)^-$. From the kinetic and spectroscopic result, they concluded that the binuclear oxotriperoxovanadium(V) complex is responsible for the oxidation of bromide ion and also they proposed the following mechanism as depicted in Scheme 29.



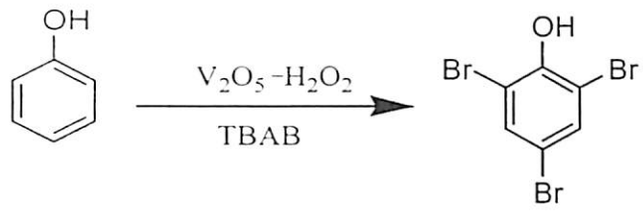
Scheme 29

Taking cues from the knowledge of the reactivity of vanadium bromoperoxidase, which catalyzes the bromination of marine natural products as well as from the reactivity of peroxovanadium complex towards organic substrates, Chaudhuri *et al.* reported a new method for the oxidative transformation of organic ammonium bromide (OAB) to the corresponding organic ammonium tribromide (OATB), for example TBATB, using V_2O_5 as the promoter and hydrogen peroxide as the oxidant as shown in Scheme 30.[48]

$$\underset{\textbf{59}}{Bu_4NBr} \xrightarrow{V_2O_5\text{-}H_2O_2} \underset{\textbf{60}}{Bu_4NBr_3\ (TBATB)}$$

Scheme 30

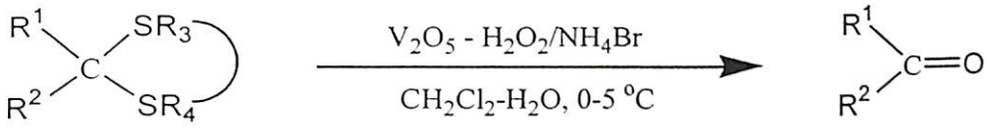
Later on, they have shown[49] that the *in situ* generated active brominating species Br_3^- is responsible for the bromination of a wide variety of organic substrates as represented in Scheme 31.



61 **62**

Scheme 31

The discovery of vanadium bromoperoxidase (VBrPO),[40] and its activities encouraged us to study the reactivity of the *in situ* generated reactive bromonium ion for valuable organic transformations. Keeping this goal in mind, we have successfully demonstrated some of the organic transformations. Our group has reported[50] that various dithioacetals and dithioketals can be converted smoothly to the parent carbonyl compounds by using catalytic oxidation of ammonium bromide by V_2O_5-H_2O_2 as shown in Scheme 32.

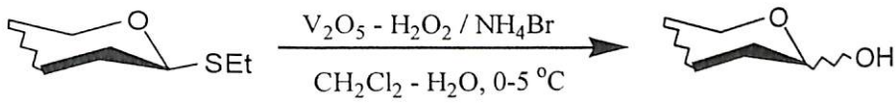


63 **4**

R^1 = aryl, alkyl, sugar residue
R^2 = H, aryl; R_3 = Et, -$(CH_2)_3$-

Scheme 32

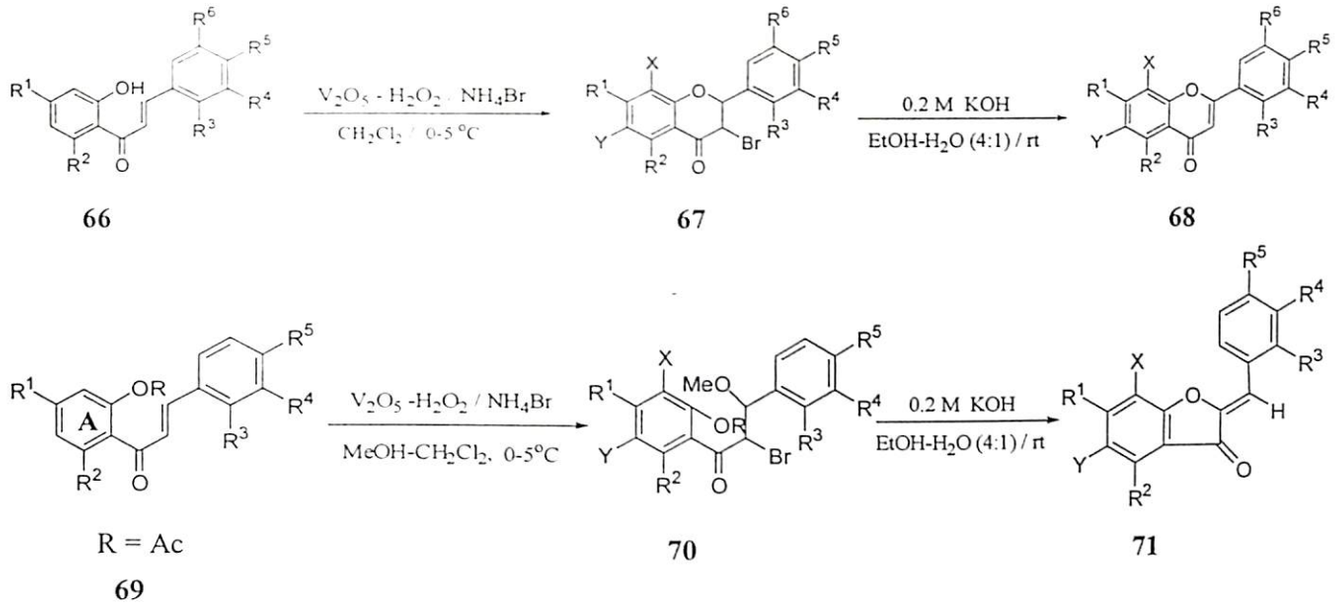
Successively, the same combination was utilized for other important transformations. By employing the *in situ* generated bromonium ion, from the combination of V_2O_5-H_2O_2-NH_4Br, our group has reported that various thioglycosides can be hydrolyzed[51] smoothly to the corresponding 1-hydroxy sugars, as shown in Scheme 33.



64 **65**

Scheme 33

By using the same combination recently our group has reported[52] that 6,8-dibromoflavones, 8-bromoflavones, 5,7-dibromoaurones and 7-bromoaurones can be synthesized easily from 2'-hydroxychalcones in good yields as shown in Scheme 34.

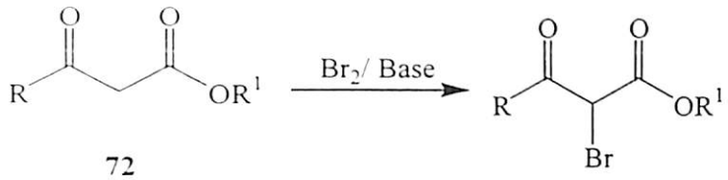


Scheme 34

The above successful results of the use of peroxovanadium complexes in organic transformation prompted us to develop some more new synthetic methodologies in organic synthesis. Keeping this in mind, we wanted to investigate the peroxovanadium-mediated oxidation of bromide ion to the bromonium ion and its further use for α-bromination of β-keto esters and 1,3-diketones.

As my research objective was to study the bromination of β-keto esters and 1,3-diketones using new reagent(s), then we looked for what are the methods available in the literature for the selective α-bromination of β-keto esters and 1,3-diketones. A brief survey on the bromination of β-keto esters and 1,3-diketones with various reagents are highlighted below.

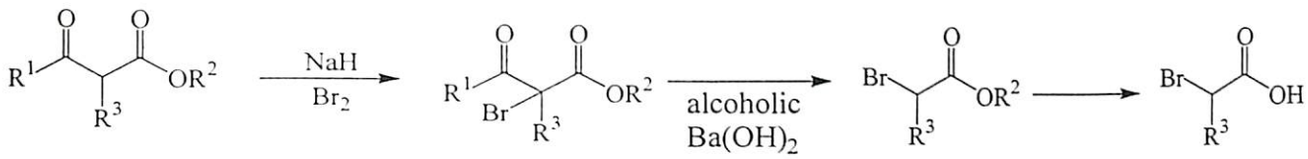
The regioselective α-bromination of β-keto esters and 1,3-diketones is a useful transformation in organic synthesis.[53] These brominated products serve as valuable building blocks for the synthesis of both natural- and non-natural products.[54] Over the years, several methods have been developed for the bromination of 1,3-dicarbonyl compounds.[53] Usually, molecular bromine[55] and bromine/NaH[54a] are used for this transformation as shown in Scheme 35.



72 73

Scheme 35

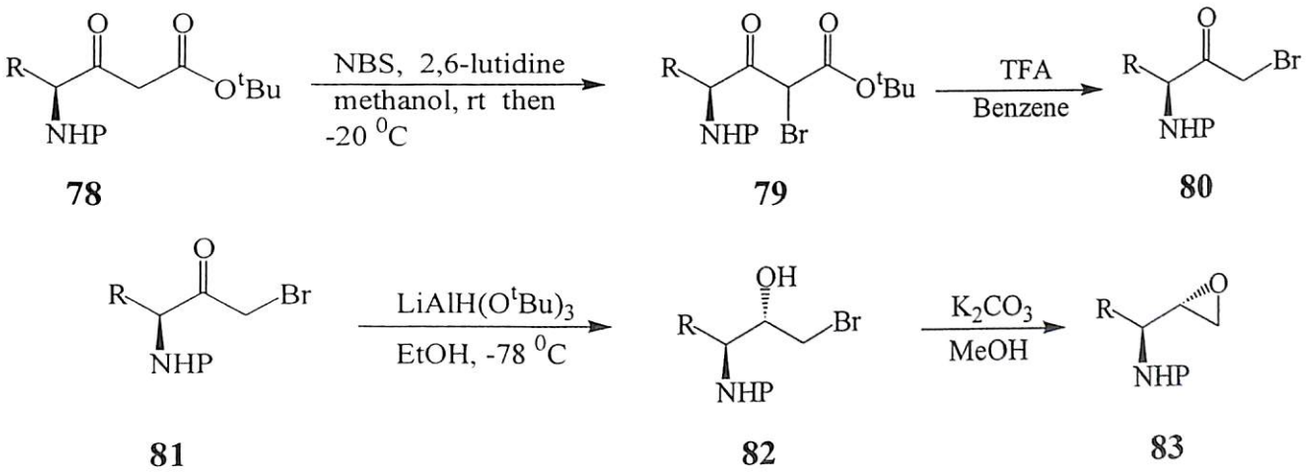
Stotter *et al.* demonstrated[54a] that monobrominated product of α-alkylacetoacetates obtained by NaH/Br_2 method can be utilized for the preparation of α-bromo esters and α-bromo acids as shown in Scheme 36.



74 75 76 77

Scheme 36

The most widely used brominating reagent for this transformation is *N*-bromo succinimide (NBS). NBS in combination with a base such as NaH[56] or NEt_3[54d] or various additives are also used for regioselective bromination of β-keto esters and 1,3-diketones. For example, Hoffmann *et al.* used 2,6-lutidine as a base for this transformation and they have demonstrated a new way to synthesize stereoselective *anti*-N-protected-α-amino epoxides as shown in Scheme 37.[57]

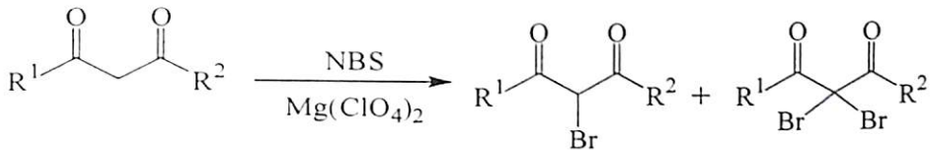


78 79 80

81 82 83

Scheme 37

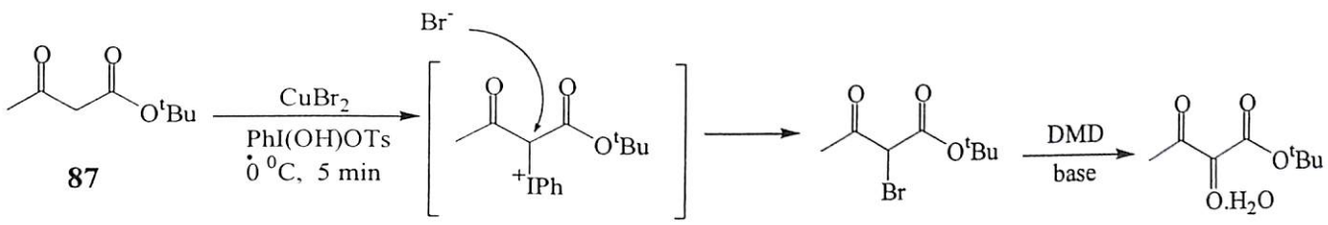
Tongi *et al.* used Ti(TADDOLato) complex catalyzed enantioselective α-halogenation of α-substituted β-keto esters.[58] Similarly, Yang *et al.* reported that NBS in combination with a Lewis acid $Mg(ClO_4)_2$ in CH_3CN and EtOAc is a mild protocol for α-bromination of β-keto esters (Scheme 38).[59] The same protocol is applicable for α-chlorination and α-iodination of 1,3-dicarbonyl compounds with NCS and NIS respectively. It is reported that chelation of the Lewis acid with two carbonyl groups of β-keto esters promotes the enol formation and thus changes the electronic property of the α-carbon.



84 **85** **86**

Scheme 38

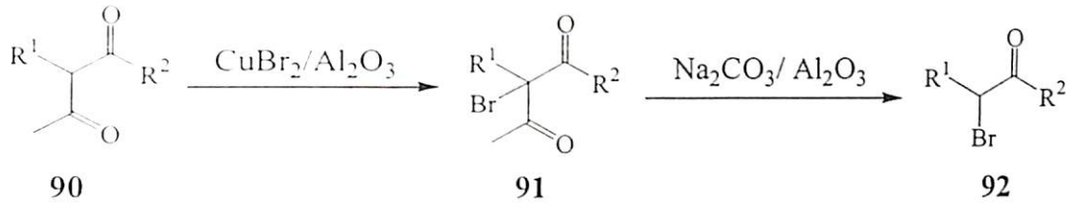
Wasserman *et al.* demonstrated [hydroxy (tosyloxy)iodo] benzene, Koser's reagent, in the presence of excess $CuBr_2$ in acetonitrile at 0 °C as a good combination for α-bromination of β-keto esters as shown in Scheme 39.[54c] In addition, this brominated compound can be used for the preparation of vicinal tricarbonyl compounds.



87 **88** **89**

Scheme 39

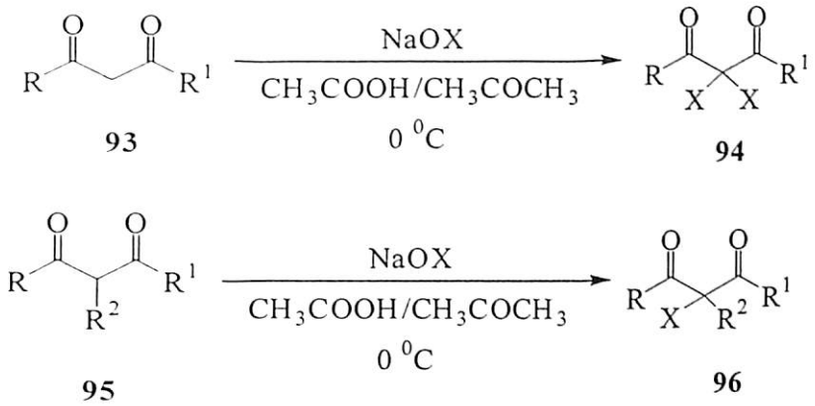
Aoyama *et al.* demonstrated[60] that one-pot synthesis of α-bromo esters and ketones are possible from β-keto esters and diketones using a supported reagent system as shown in Scheme 40. Alumina supported $CuBr_2$ in benzene medium at 50 °C is used to obtain the product **90** and subsequent treatment with alumina-supported sodium carbonate at the same temperature provided the product **92** in good yield.



90 91 92

Scheme 40

Weinreb *et al.* reported an efficient method for the halogenation of β-dicarbonyl compounds under mildly acidic condition as shown in Scheme 41. But the main draw back of this method is that it gives dibrominated products of unsubstituted β-keto esters instead of monobrominated product.[61]

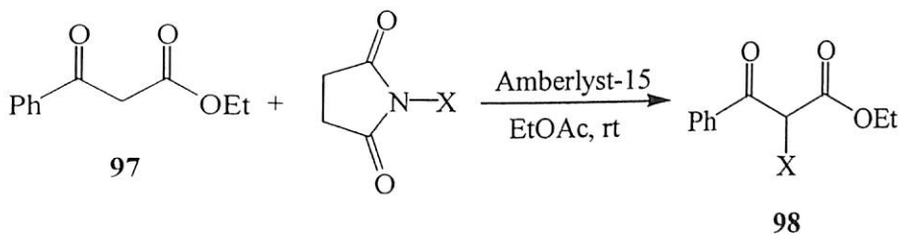


93 94

95 96

Scheme 41

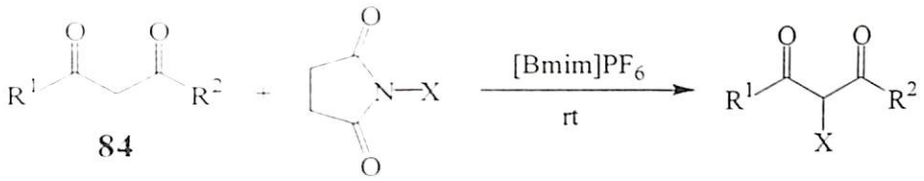
Recently a number of new methods for this transformation are available employing NBS along with various additives such as silica-supported $NaHSO_4$[62] or Amberlyst-15[63] (Scheme 42) or sulfonic acid functionalized silica,[64] or TMSOTf.[65]



97 98

Scheme 42

In addition, α-halogenation of 1,3-dicarbonyls can also be accomplished in ionic liquids using N-halosuccinimide as shown in Scheme 43.[66]



Scheme 43

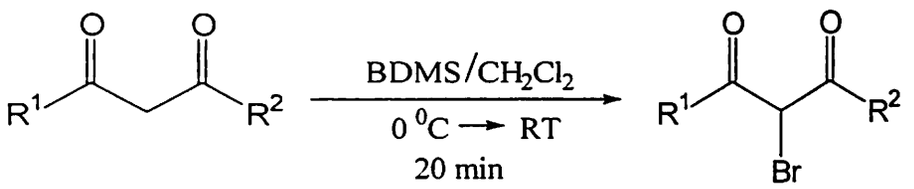
Although literature enumerates several methods but most of them suffer from one or the other limitations, for examples, molecular bromine is hazardous and difficult to handle, and use of Lewis acid as an additive or strong bases. Moreover, sometimes the reaction needs to be performed under dry and inert atmospheric conditions. From the literature it is apparent that the chemoselective α-monobromination of unsubstituted β-ketoesters or 1,3-diketones is a very challenging task since some of the monobrominated products are reported to be unstable and also undergoes disproportionations to dibromo and debrominated products.[57] In continuation of our effort in the field of new synthetic methodologies using new reagents, we were in search of new and improved synthetic protocol for chemo- and regioselective α- monobromination of β-keto esters and 1,3-diketones, which can be applied to a wide range of substituted and unsubstituted β-keto esters and 1,3-diketones. The successful results of our study for α-bromination of β-keto esters and 1,3-diketones using a combination of V_2O_5, H_2O_2 and NH_4Br will be presented in Section B of this Chapter.

SECTION A

NEW SYNTHETIC METHOD FOR SELECTIVE α- MONOBROMINATION OF β- KETO ESTERS AND 1,3-DIKETONES USING BROMODIMETHYLSULFONIUM BROMIDE (BDMS)

RESULTS AND DISCUSSION

From the literature survey on the reagent bromodimethylsulfonium bromide as described in the review part of Chapter II, it is evident that bromodimethylsulfonium bromide can be used either as a safer brominating reagent or an effective catalyst for various organic transformations. In continuation of our research in the field of new synthetic methodologies employing various new reagents as well as in exploration of bromodimethylsulfonium bromide to replace current chemical process by better synthetic protocols we noticed that α-monobromination of β-keto esters is an important and challenging transformation due to the importance of the brominated products. Although several methods are known in the literature for this transformation, which is already mentioned in the Part I of this Chapter, still there is a need to find out a new, simple and selective method, which can overcome some of the limitations of the existing methods. Therefore, we wanted to explore BDMS for this selective α-bromination of β-keto esters and 1,3-diketones as shown in Scheme 44.



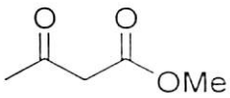
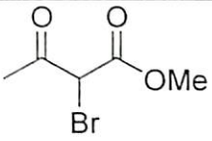
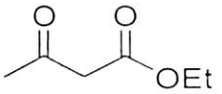
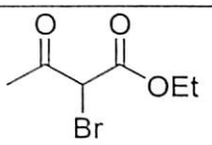
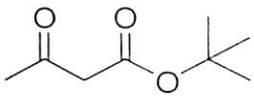
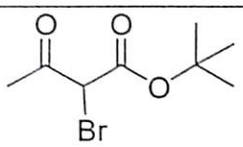
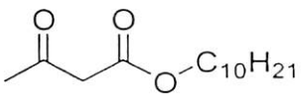
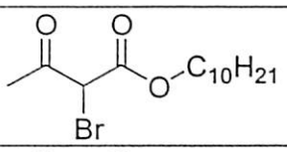
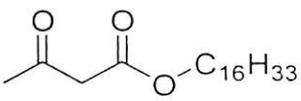
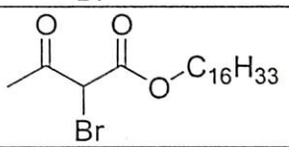
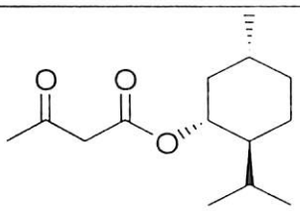
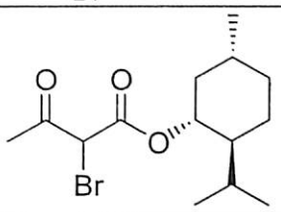
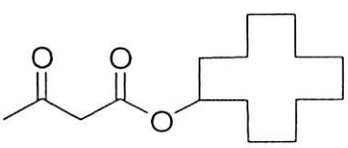
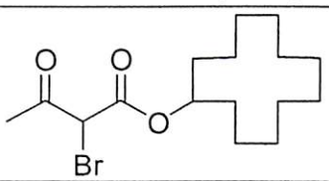
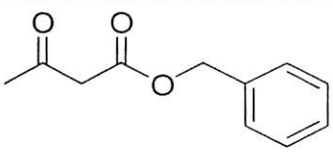
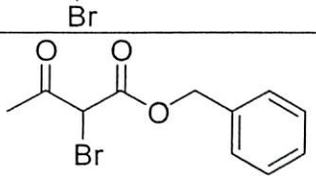
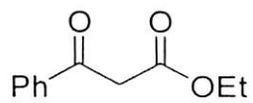
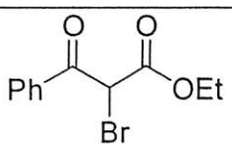
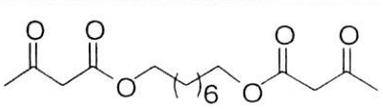
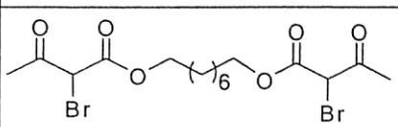
Scheme 44

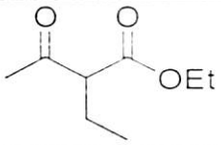
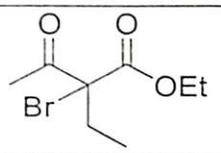
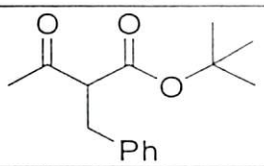
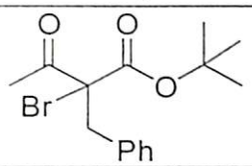
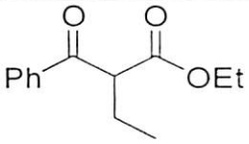
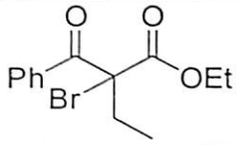
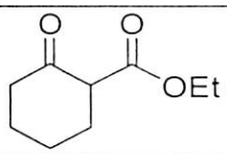
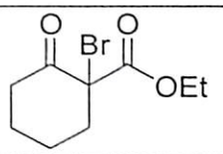
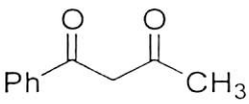
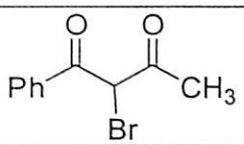
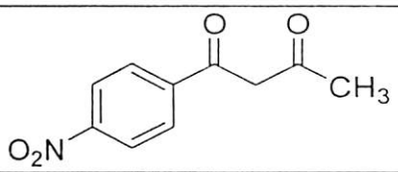
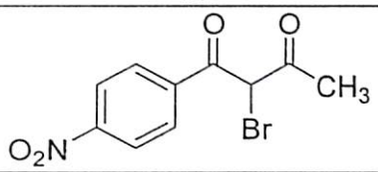
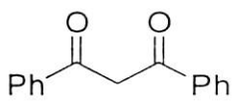
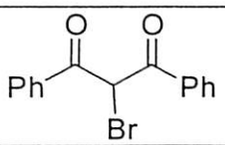
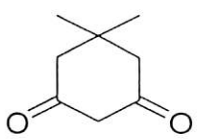
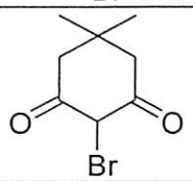
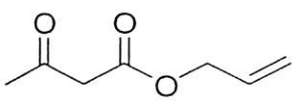
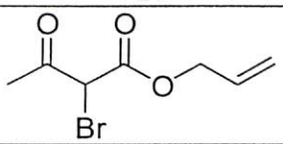
For the present study, the catalyst bromodimethylsulfonium bromide (BDMS) was prepared by following the literature procedure.[1] In the preliminary experiment, when methyl acetoacetate (**100**) (1 mmol) was treated with bromodimethylsulfonium bromide (1.25 mmol) in dichloromethane (5 mL) at 0-5 ^{0}C, it provided exclusively monobrominated product within 20 min in 85% yield. The product **117** was characterized by recording ^{1}H, ^{13}C-NMR spectra and elemental analysis. Interestingly, we did not observe any detectable amount of dibrominated product under the experimental conditions while recording ^{1}H NMR spectrum of the crude product. Encouraged by this result, we tried to explore this protocol to a wide range of β-keto esters. Similarly, other unsubstituted β-keto esters (**101** and **87**) underwent α-bromination smoothly under similar conditions and afforded exclusively monobrominated product **118** and **88** respectively in excellent yields. For characterization of this products we have compared the data with literature reported data e.g. for the substrate ethyl acetoacetate (**101**) the methyl signal attached with the

carbonyl group resonated at δ 2.27, whereas in the monobrominated product it appeared at δ 2.44 as shown in (Figure **1**). The disappearance of signal at 2.27 and appearance of new peak at δ 4.74 in the ^{1}H NMR of crude reaction mixture clearly indicates the formation of the mono-brominated product. In addition, the appearance of characteristic ^{13}C NMR signal at 49.3 due to α-brominated carbon atom (Figure **2**) supports the formation of mono brominated product (**118**).

For further investigation, a wide variety of β-keto esters **102-106** were prepared by transesterification of methyl acetoacetate with their corresponding alcohols using silica supported perchloric acid method.[67] By following identical reaction procedure, various substrates **102-106** and **97** were converted to the desired α-monobrominated products **119-123** and **98** respectively in very good yields. Next, di-keto ester of octanediol **107** was treated with 2.5 equivalent amounts of BDMS and the desired monobrominated product **124** was found in very good yield. The notable advantages of this protocol over the other existing methods are: the conversion takes place within a very short time without using any catalyst as well as no need of chromatographic separation as it gives full conversion of the starting material with single product. NMR spectra of all the products were recorded from crude product just after aqueous work-up without any further purifications and it shows high purity without of any detectable byproducts. To explore further, mono substituted β-keto esters **108-110** were prepared by alkylation of β-keto esters using K_2CO_3 as base by following a standard procedure. Subsequently, the substrates **108-110** were treated with BDMS following the same experimental procedure and provided the monobrominated products **125-127,** respectively, in good yields at room temperature. As there is no probability for dibromination, we performed the reactions at room temperature instead of ice-bath temperature. Similarly, a cyclic β-keto ester **111** underwent α-bromination smoothly in good yield at room temperature. Likewise, various 1,3-diketones (**112-114**) provided α-monobrominated products **129-131** exclusively with very good yields under the given experimental conditions. ^{1}H NMR and ^{13}C NMR spectrum for compound **128** and **129** are given in Figure **3-6** respectively.

Table 1. α-Bromination of β-Keto Esters and 1,3-Diketones using BDMS[a]

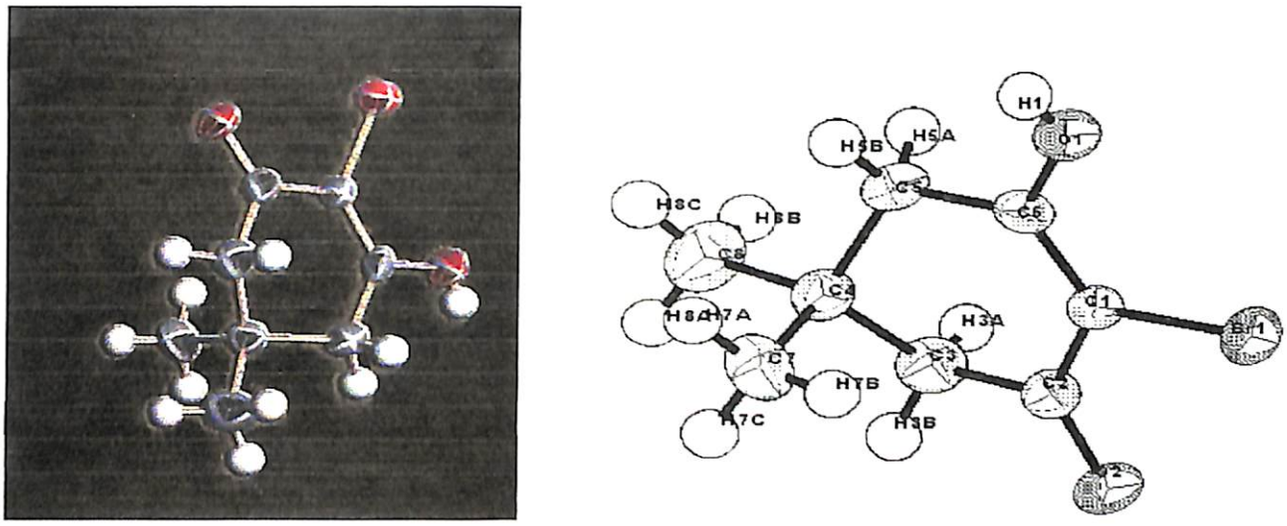
Substrate	Substrate No.	Product[a]	Product No.	% Yield[b]
	**100**		**117**	85
	**101**		**118**	84
	**87**		**88**	91
	**102**		**119**	95
	**103**		**120**	90
	**104**		**121**	93
	**105**		**122**	92
	**106**		**123**	94
	**97**		**98**	94
	**107**		**124**	97[d]

	**108**		**125**	89[c]
	**109**		**126**	96[c]
	**110**		**127**	95[c]
	**111**		**128**	99[c]
	**112**		**129**	97
	**113**		**130**	86
	**114**		**131**	98
	**115**		**132**	91[c,e]
	**116**		**133**	81

[a] Reaction conditions: β-keto ester/1,3 diketone (1 mmol), BDMS (0.278 g, 1.25 mmol), 0 °C -rt, 20-30 min. [b] Reactions were carried out at 0 °C, [c] Reactions were performed at room temperature. [d] Bromodimethyl sulfonium bromide was used 2.5 equiv., [e] Reaction time was 30 min.

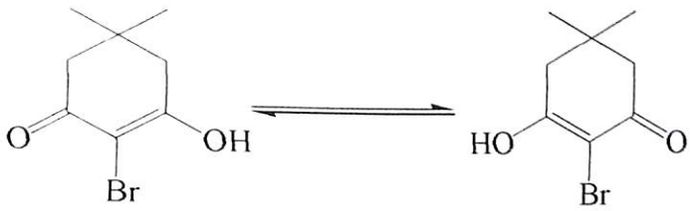
Interestingly dimedone **(115)** provided exclusive mono brominated product at room temperature, which is sometimes difficult to achieve by some of the reported methods. Surprisingly, we could not find the proton attached with the α-brominated carbon atom of compound **132** in the ^{1}H NMR spectrum. We observed only two signals at 1.12 (s) and 2.48 (s), respectively. Also, in the IR spectrum, we did not observe any carbonyl peak of

this product. Therefore, to further confirm the structure of compound **132** whether the product is either mono or dibrominated, we intended to record a single crystal XRD.



ORTEP Plot of α-Mono bromo Dimedone with Atom numbering Scheme

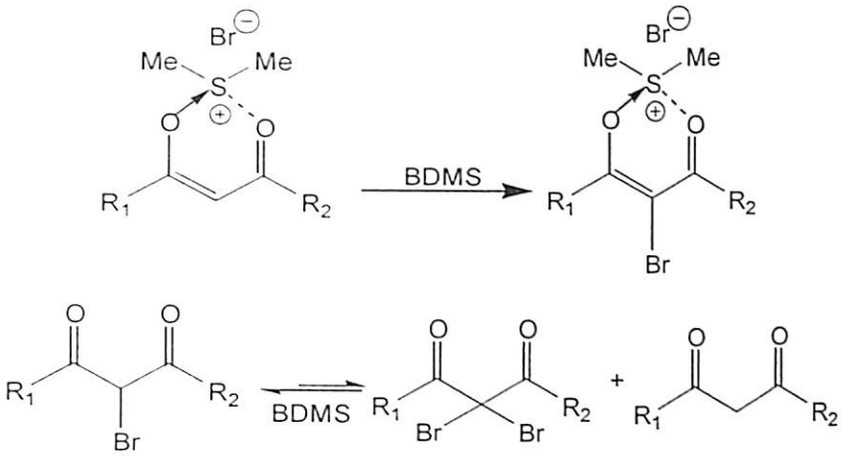
Accordingly, the product was recrystallized from (ethyl acetate/hexane, 7:3) and a single crystal XRD was recorded. Interestingly, we found that in solid state it exists in enol form as shown in the ORTEP picture as shown above. It shows intermolecular hydrogen bonding of O-H of enol and ketonic CO of the other unit. We believe that in solution state it undergoes rapid keto-enol tautomerization as shown in Scheme 45, for which we do not observe the proton signal for the α-hydrogen associated with the brominated carbon.



Scheme 45. Rapid Keto-enol Tautomerization in Solution

Next to exemplify further the applicability of this protocol; the substrate **116** was treated under the experimental conditions. Interestingly, the allylic double bond survives under the given conditions and provided the desired product **133** in good yields.

A probable mechanism portraying the mechanistic illustration is depicted in Scheme 46. We believe that bromodimethylsulfonium bromide facilitates the enol formation of β-keto esters or 1,3-diketones.



Scheme 46. Probable mechanism for selective mono bromination

In addition, bromodimethylsulfonium ion may also bind with the enol form of the mono brominated product, which provides extra stability of the monobrominated product as a result it makes the process sluggish for further bromination or disproportionation.

In conclusion, we have devised a simple and efficient synthetic protocol for highly selective α-monobromination of β-keto esters and 1,3-diketones using a versatile reagent bromodimethylsulfonium bromide. The notable advantages of this protocol are: mild, clean and simple reaction conditions, very good yields, no need of chromatographic separations as well as no need of any base or Lewis acid as an additive which is invariably required by NBS methods. Furthermore, this method is also expected to have much better application in organic synthesis because of the low cost, easy accessibility and less hazardous nature of the reagent. We believe this methodology will be a valuable addition to modern synthetic methodologies.

SECTION A

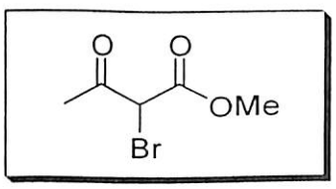
α-BROMINATION OF β-KETO ESTERS AND 1,3-DIKETONES USING BROMOMODIMETHYLSULFONIUM BROMIDE (BDMS)

EXPERIMENTAL

Preparation of Bromodimethylsulfonium bromide (BDMS): Dimethyl sulfide (1.83 mL, 25 mmol) was taken in 5 mL of dry dichloromethane into a 150 mL standard joint conical flask. Then, 1.3 mL of bromine (25 mmol) was dissolved in 5 mL of dry dichloromethane and added slowly into the above solution at ice-bath temperature over a period of 5 min. During the addition, light orange crystals of bromodimethylsulfonium bromide begin to separate out. After the addition of bromine was completed, the crystals of bromodimethylsulfonium bromide were collected by filtration. The solid material was then washed with dry hexane and dried under vacuum. The crystalline product was obtained 4.3 g in 77% yield, m.p. 80 °C.

General Procedure for α-Bromination of β-Keto esters and 1,3-Diketones: Bromodimethylsulfonium bromide (BDMS) (1.25 mmol, 0.278 g), was added to a stirred solution of β-keto ester or 1,3-diketone (1 mmol) in CH_2Cl_2 (5 mL) at 0-5 °C or room temperature. After 20 min, the reaction mixture was washed with water (10 mL x 2) and extracted with CH_2Cl_2 (10 mL x 2). The organic layers were combined, dried over anhydrous Na_2SO_4 and solvents were removed by evaporation in a rotary evaporator to get the crude product. All the products were characterized without any further purification.

Compound (117):



Nature: Liquid

Yield: 85% (0.166 g)

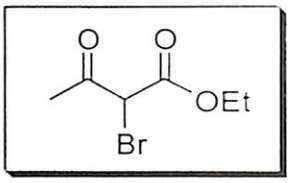
IR (Neat): 1751, 1716 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.45 (s, 3H), 3.84 (s, 3H), 4.77 (s, 1H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.7, 48.9, 54.0, 165.6, 196.1 ppm.

Elemental Analysis	Calculated	Found
$C_5H_7BrO_3$	C 30.80	C 30.55
195.01	H 3.62	H 3.53

Compound (118):



Nature: Liquid

Yield: 84% (0.176g)

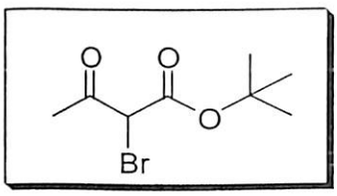
IR (Neat): 1742, 1721 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (t, J = 7.2 Hz, 3H), 2.44 (s, 3H), 4.28 (q, J = 7.2 Hz, 2H), 4.74 (s, 1H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 26.6, 49.3, 63.3, 165.0, 196.1 ppm.

Elemental Analysis	Calculated	Found
$C_6H_9BrO_3$	C 34.48	C 34.29
209.04	H 4.34	H 4.26

Compound (88):



Nature: Liquid

Yield: 91% (0.216 g)

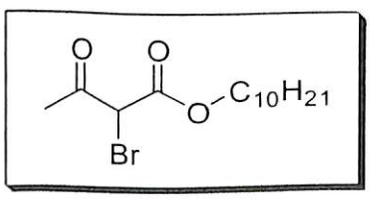
IR (Neat): 1745, 1726 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.49 (s, 9H), 2.42 (s, 3H), 4.67 (s, 1H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.2, 27.5 (3C), 50.6, 84.1, 163.5, 195.9 ppm.

Elemental Analysis	Calculated	Found
$C_8H_{13}BrO_3$	C 40.53	C 40.60
237.09	H 5.53	H 5.59

Compound (119):



Nature: Liquid

Yield: 95% (0.305 g)

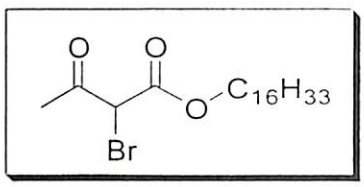
IR (Neat): 1743, 1718 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.87 (t, J = 6.8 Hz, 3H), 1.26 (bs, 14 H), 1.66 (quin, J = 6.8 Hz, 2H), 2.43 (s, 3H), 4.20 (t, J = 6.8 Hz, 2H), 4.74 (s, 1H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 23.0, 26.0, 26.7, 28.6, 29.4, 29.6, 29.8 (2C), 32.2, 49.4, 67.5, 165.2, 196.2 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{14}H_{25}BrO_3$	C 52.34	C 52.11
321.25	H 7.84	H 7.89

Compound (120):



Nature: Liquid

Yield: 90% (0.365 g)

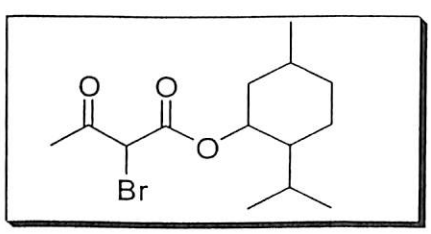
IR (Neat): 1742, 1716 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J = 7.2 Hz, 3H), 1.26 (bs, 26H), 1.67 (quin, J = 6.8Hz, 2H), 2.44 (s, 3H), 4.21(t, J = 6.8 Hz, 2H), 4.74 (s, 1H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.5, 23.0, 26.0, 26.7, 28.6, 29.4, 29.7 (2C), 29.8 (2C), 29.9 (2C), 30.0 (3C), 32.2, 49.3, 67.5, 165.2, 196.2 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{20}H_{37}BrO_3$	C 59.25	C 59.01
405.41	H 9.20	H 9.15

Compound (121):



Nature: Liquid (mixture of diastereomer)

Yield: 93% (0.297 g)

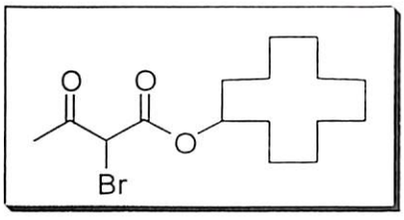
IR (Neat): 1742, 1716 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.77 (d, J = 7.6 Hz, 3H), 0.78 (d, J = 7.6 Hz, 3H), 0.83-0.93 (m, 12H), 1.00-1.10 (m, 2H), 1.40-1.51 (m, 4H), 1.65-1.75 (m, 4H), 1.70-1.80 (m, 4H), 2.00-2.20 (m, 4H), 2.42 (s, 6H), 4.72 (s, 1H), 4.73 (s, 1H), 4.74-4.78 (m, 2H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.3, 16.4, 21.0 (2C), 22.2 (2C), 23.5, 23.6, 26.3, 26.4, 26.7 (2C), 31.7 (2C), 34.3 (2C), 40.5 (2C), 47.1, 47.1, 49.8, 49.9, 77.8 (2C), 164.7 (2C), 196.2 (2C) ppm.

Elemental Analysis	Calculated	Found
$C_{14}H_{23}BrO_3$	C 52.67	C 52.47
319.24	H 7.26	H 7.35

Compound (122):



Nature: Liquid

Yield: 92% (0.320 g)

IR (Neat): 1740, 1726 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.30-1.50 (bs, 18H), 1.52-1.60 (m, 2H), 1.70-1.80 (m, 2H), 2.43 (s, 3H), 4.72 (s, 1H), 5.07-5.10 (m, 1H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.1 (2C), 23.4 (2C), 23.6 (2C), 24.1, 24.3 (2C), 26.7, 29.1 (2C), 49.8, 76.1, 164.8, 196.3 ppm.

Elemental Analysis	Calculated	Found
$C_{16}H_{27}BrO_3$	C 55.34	C 55.10
347.29	H 7.84	H 7.75

Compound (123):

Nature: Liquid

Yield: 94% (0.255 g)

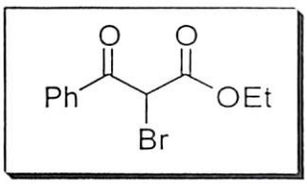
IR (Neat): 1746, 1725 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.39 (s, 3H), 4.78 (s, 1H) 5.23 (s, 2H), 7.31-7.35 (bs, 5H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.7, 49.3, 68.8, 128.4 (2C), 128.7 (2C), 128.8, 134.5, 164.9, 196.0 ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{11}BrO_3$	C 48.73	C 48.79
271.11	H 4.09	H 4.15

Compound (98):



Nature: Liquid

Yield: 94% (0.255 g)

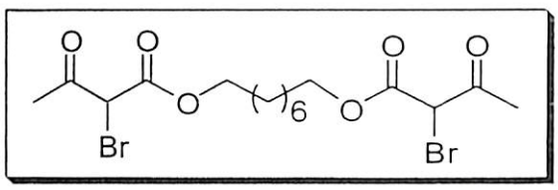
IR (Neat): 1752, 1690 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.25 (t, J = 7.2 Hz, 3H), 4.27 (q, J = 7.2 Hz, 2H), 5.64 (s, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.97 (d, J = 8.0 Hz, 2H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.8, 46.3, 63.0, 128.6 (2C), 128.8 (2C), 133.0, 133.9, 164.7, 187.7 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{11}BrO_3$	C 48.73	C 48.46
271.11	H 4.09	H 4.02

Compound (124):



Nature: Liquid

Yield: 97% (0.458 g)

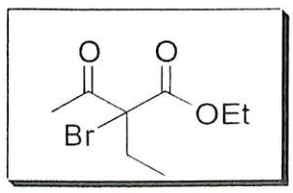
IR (Neat): 1747, 1727 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (bs, 8H), 1.67 (quin, J = 6.4 Hz, 4H), 2.44 (s, 6H), 4.21 (t, J = 6.8 Hz, 4H), 4.75 (s, 2H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.8 (2C), 26.8 (2C), 28.5 (2C), 29.2 (2C), 49.3 (2C), 67.3 (2C), 165.2 (2C), 196.3 (2C) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{24}Br_2O_6$	C 40.70	C 40.48
472.17	H 5.12	H 5.19

Compound (125):



Nature: Liquid

Yield: 89% (0.211 g)

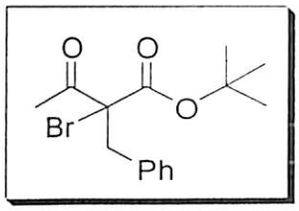
IR (Neat): 1747, 1716 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.01 (t, J = 7.2 Hz, 3H), 1.30 (t, J = 7.2 Hz, 3H), 2.22-2.27 (m, 2H), 2.34 (s, 3H), 4.27 (q, J = 7.2 Hz, 2H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.2, 14.3, 26.6, 30.9, 63.3, 70.9, 167.5, 197.6 ppm.

Elemental Analysis	Calculated	Found
$C_8H_{13}BrO_3$	C 40.53	C 40.59
237.09	H 5.53	H 5.48

Compound (126):



Nature: Liquid

Yield: 96% (0.314 g)

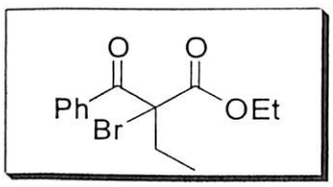
IR (Neat): 1743, 1721 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.41 (s, 9H), 2.34 (s, 3H), 3.49 (d, J = 14.4 Hz, 1H), 3.59 (d, J = 14.8 Hz, 1H), 7.20-7.41 (bs, 5H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 27.2, 27.9 (3C), 42.7, 70.3, 84.7, 127.2, 128.2 (2C), 129.6 (2C), 135.0, 165.7, 198.0 ppm.

Elemental Analysis	Calculated	Found
$C_{15}H_{19}BrO_3$	C 55.06	C 54.85
327.22	H 5.85	H 5.77

Compound (127):



Nature: Liquid

Yield: 95% (0.284 g)

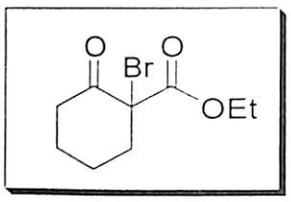
IR (Neat): 1751, 1722 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.08 (t, J = 7.2 H, 6H), 2.41-2.48 (m, 2H), 4.16 (q, J = 7.2 Hz, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.53 (t, J = 6.4 Hz, 1H), 7.98 (d, J = 7.2 Hz, 2H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 9.7, 14.0, 32.2, 63.3, 68.4, 128.4 (2C), 129.4 (2C), 133.2, 133.9, 168.0, 189.1 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{15}BrO_3$	C 52.19	C 52.01
299.16	H 5.05	H 5.11

Compound (128):



Nature: Liquid

Yield: 99% (0.247 g)

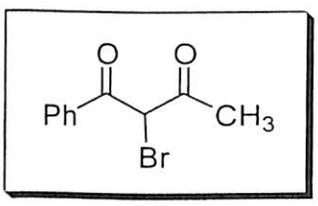
IR (Neat): 1752, 1716 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (t, J = 6.8 Hz, 3H), 1.71-1.92 (m, 4H), 2.20-2.22 (m, 1H), 2.42 –2.50 (m, 1H), 2.85- 2.96 (m, 2H), 4.29 (q, J = 7.2 Hz, 2H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.8, 23.1, 26.7, 30.8, 40.5, 62.8, 67.4, 167.1, 198.6 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_9H_{13}BrO_3$	C 43.40	C 43.15
249.10	H 5.26	H 5.20

Compound (129):



Nature: Viscous liquid

Yield: 97% (0.234 g)

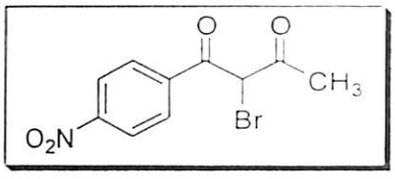
IR (Neat): 1731, 1680 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.45 (s, 3H), 5.60 (s, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.62 (t, J = 6.8 Hz, 1H), 7.95 (d, J = 7.6 Hz, 2H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 27.5, 53.3, 129.2 (2C), 129.4 (2C), 133.9, 134.6, 190.0, 198.2 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_9BrO_2$	C 49.82	C 49.59
241.08	H 3.76	H 3.69

Compound (130):



Nature: Liquid

Yield: 86% (0.246 g)

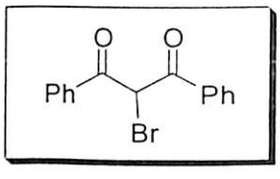
IR (Neat): 1715, 1688 1530, 1348 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.51 (s, 3H), 5.54 (s, 1H), 8.11 (d, J = 8.4 Hz, 2H), 8.32 (d, J = 8.4 Hz, 2H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 27.7, 52.3, 124.1 (2C), 130.4 (2C), 138.2, 150.8, 188.8, 197.6 ppm.

Elemental Analysis	Calculated	Found
$C_{10}H_8BrNO_4$	C 41.98	C 41.79
286.08	H 2.82	H 2.85
	N 4.90	N 4.78

Compound (131):



Nature: Solid, mp: 89 ^{0}C.

Yield: 98% (0.294 g)

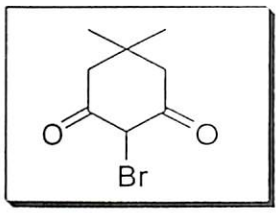
IR (KBr): 1689 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.54 (s, 1H), 7.45 (t, J = 7.6 Hz, 4H), 7.58 (t, J = 7.6 Hz, 2H), 7.96 (d, J = 7.2 Hz, 4H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 52.6, 128.8 (4C), 129.0 (4C), 133.6 (2C), 134.1 (2C), 188.9 (2C) ppm.

Elemental Analysis	Calculated	Found
$C_{15}H_{11}BrO_2$	C 59.43	C 59.18
303.15	H 3.66	H 3.58

Compound (132):



Nature: Solid, mp: 156 ^{0}C.

Yield: 91%(0.199 g)

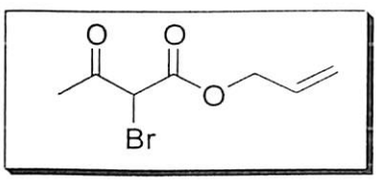
IR (KBr): 1636, 1574, 1370, 1323 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.12 (s, 6H), 2.48 (s, 4H) ppm.

^{13}C NMR ($CDCl_3$ + CD_3OD, 100 MHz): δ 27.9 (2C), 32.1, 47.3 (2C), 98.4, 182.0 (2C) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_8H_{11}BrO_2$	C 43.86	C 43.92
219.08	H 5.06	H 5.09

Compound (133):



Nature: Viscous Liquid

Yield: 81% (0.179 g)

IR (Neat): 1738, 1718, 1650, 1491, 1425, 1359, 1273, 1224, 1143 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.44(s, 3H), 4.69 (dd, J =1.2 Hz, J = 5.6 Hz, 2H), 4.78 (s, 1H), 5.30 (dd, J = 1.2 Hz, J = 10.4 Hz, 1H), 5.37 (dd, J = 1.2 Hz, J = 16.0 Hz, 1H), 5.90 (m, 1H) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_7H_9BrO_3$	C 38.04	C 37.78
221.05	H 4.10	H 4.06

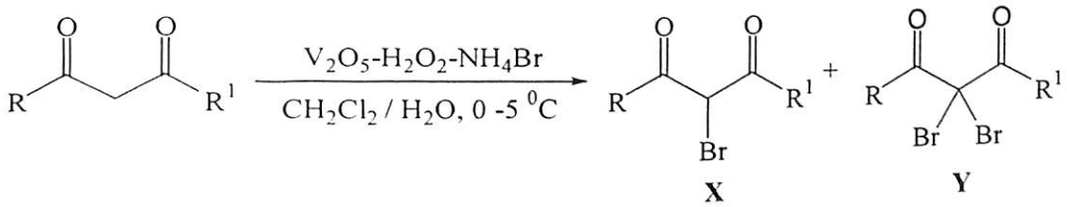
SECTION B

PRESENT WORK ON CHEMOSELECTIVE α-BROMINATION OF β-KETO ESTERS AND 1, 3-DIKETONES USING A COMBINATION OF V_2O_5-H_2O_2-NH_4Br

RESULTS AND DISCUSSION

We have successfully demonstrated the application of bromodimethylsulfonium bromide (BDMS) for selective bromination of β-keto esters and 1,3-diketones.[68] Incidentally, the main drawback is molecular bromine is required for the preparation of the reagent. Therefore, we looked for an alternative source of bromonium ion without involving molecular bromine. From our earlier knowledge on the application of V_2O_5-H_2O_2-NH_4Br, it seems to us that the same combination is an environmentally benign alternative for bromination of organic compounds. Therefore, we thought that *in situ* generated bromonium ion from the combination of V_2O_5-H_2O_2-NH_4Br can be explored further for selective bromination of β-keto esters and 1,3-diketones.

Although literature enumerates several methods for this transformation, still most of them suffer from one or other disadvantage. From the Green Chemistry point of view, the use of molecular bromine has several drawbacks: the reagent itself is harmful, hazardous and there are difficulties in handling and maintaining the stoichiometric ratio during the reaction. In addition, the conventional reagent NBS has also some limitations: the reaction needs to be carried out under a dry and inert atmosphere and also uses expensive NaH as well as sometimes require harsh reaction conditions. Selective monobromination at the α position of β-keto esters is a challenging problem, since some of the α-monobrominated β-keto esters are unstable and readily disproportionate to dibrominated and debrominated products.[57a] Therefore, there is scope to find an alternative methodology that would be environmentally benign, clean and efficient. In this section we would like to discuss a new and environmentally acceptable protocol for α-monobromination of β-keto esters and 1,3-diketones as shown in Scheme 47.



R = Me/ Ph

R^1= OMe, OEt, OBn

Scheme 47

For the present study, ethyl acetoacetate (**101**) was chosen as a model substrate to find optimal conditions, as shown in Table 2. We noted that a (1:1.5:0.5:19) substrate

/ammonium bromide/vanadium pentoxide/hydrogen peroxide ratio, in dichloromethane-water (1:1, 2.5 mL per mmol of the substrate), provided the best results. For the same substrate, a combination of V_2O_5, NH_4Br and H_2O_2 (0.25:1.5:19) gave only a 40% conversion (calculated from the ^1H NMR spectrum) after 3.5 h with only α-monobrominated product **118**. The chemical yield was 92% based on recovery of starting material. The percent of conversion as well as the ratio of mono- and dibrominated product were calculated directly from the integrations of NMR signals obtained from the crude reaction mixture. For the substrate ethyl acetoacetate the methyl signal attached with the carbonyl group resonated at δ 2.27, whereas in the monobrominated product it appeared at δ 2.44. Based on integration, we calculated the percentage conversion to products. Next we varied the amount of V_2O_5. Using 0.5 equivalents of V_2O_5 led to an increase in conversion from 40% to 92% within the same time interval (Table 2, run 2). The chemical yield of monobrominated product was 85% and dibrominated product was less than 1%. When the amount of ammonium bromide was increased from 1.5 equivalents to 2.0 equivalents, there was a total conversion of 86% within 2 h with same chemical yield (run 3). It is clear that the reaction can be completed in shorter time if the amount of vanadium pentoxide, ammonium bromide and hydrogen peroxide are increased.

Table 2. Optimization of the reaction conditions for selective α-bromination of ethyl acetoacetate (**101**)

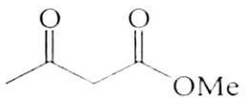
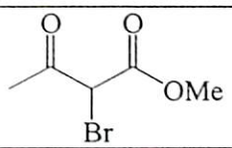
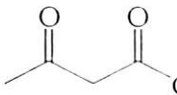
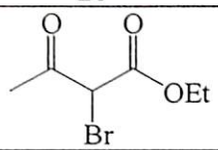
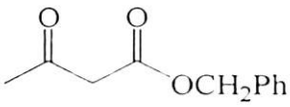
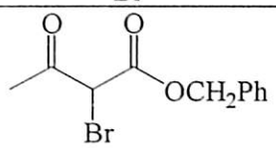
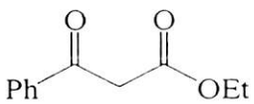
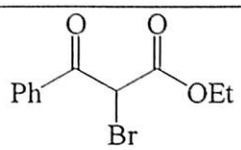
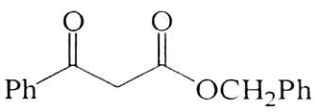
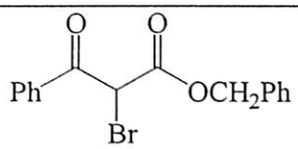
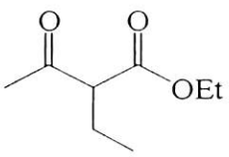
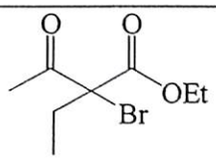
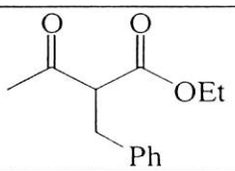
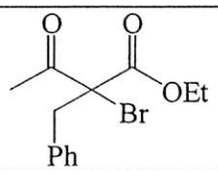
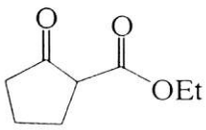
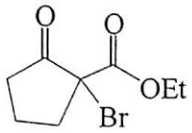
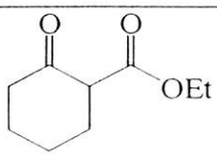
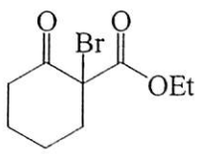
Run	V_2O_5 mmol	NH_4Br (mmol)	50% H_2O_2 (mL)	Time/ h	Conversion[a] %	Yield[b] of product **X** (%)	ratio of **X: Y**[c]
1	0.25	1.5	1.3	3.5	40	92	100:0
2	0.50	1.5	1.3	3.5	92	85	10: 1
3	0.50	2	1.3	2	86	84	9:1
4	0.75	6	2.1	9	100	13	1:9

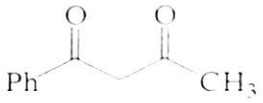
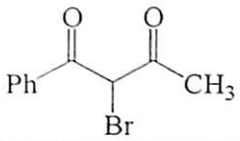
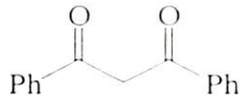
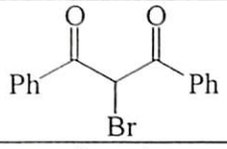
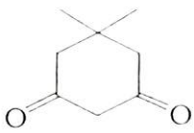
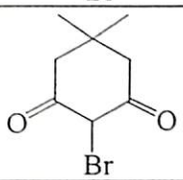
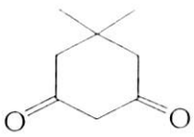
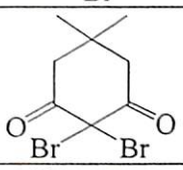
[a]The table represents for 1 mmol of ethyl acetoacetate, however, all reactions were carried out with 3.8 mmol scale of the substrate. [b]Isolated yield. [c]Conversion and product ratio were determined using ^1H NMR.

Using the typical reaction protocol, methyl acetoacetate (**100**) also reacted smoothly to give the α-monobrominated product **117** in 83% yield along with 7% dibrominated product based on starting material recovery. Other unsubstituted β-keto esters **106**, **97**

and **134** underwent selective bromination exclusively to their corresponding α-mono-brominated products **123**, **98** and **137** respectively in good yields.

Table 3. Selective α- bromination of β-keto esters and 1,3-diketones using V_2O_5/NH_4Br/ 50% H_2O_2

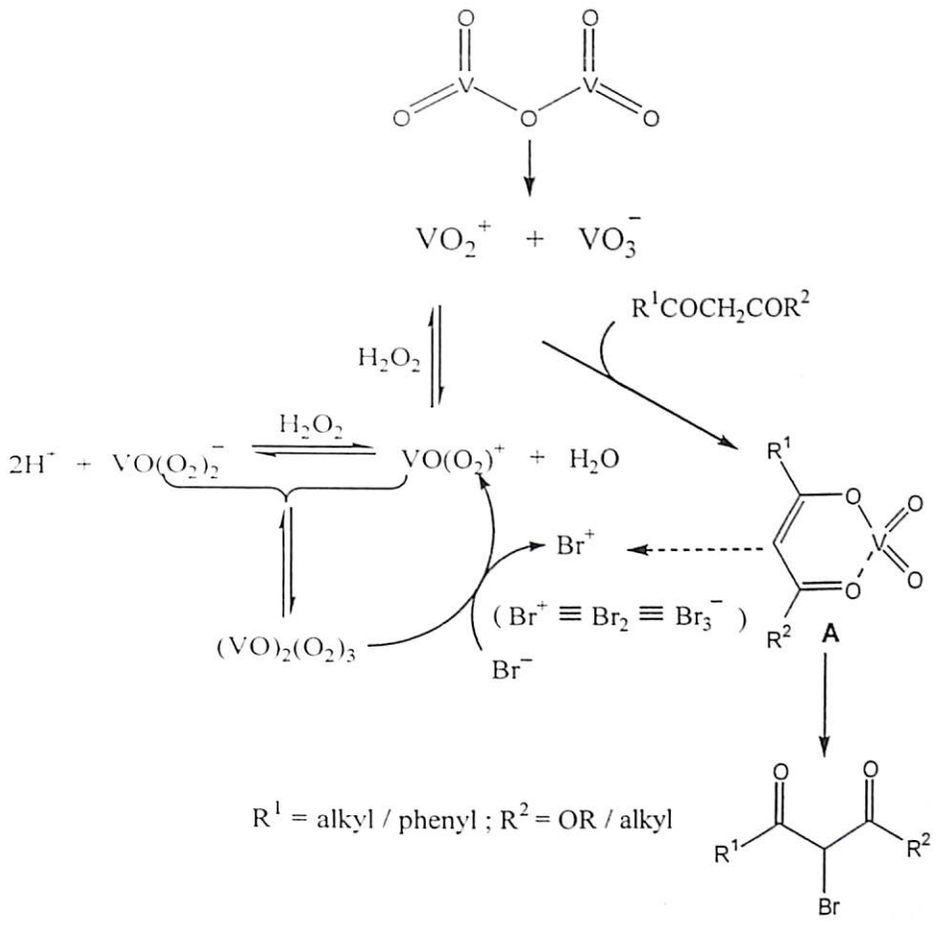
S. No.	Substrate	Reaction time/h	Product[a]	Product No.	% Yield[b, c]
100		3.0		**117**	83[c]
101		3.5		**118**	85[c]
106		4.0		**123**	90
97		4.0		**98**	98
134		4.5		**137**	91
108		3.0		**125**	94
135		3.5		**138**	92
136		3.5		**139**	87
111		3.0		**128**	90

112		2.5		**129**	92
114		3.0		**131**	95
115		2.5		**132**	89
115		4.0		**140**	90

[a]Products were characterised by recording ^{1}H NMR, ^{13}C NMR spectra and elemental analysis. [b]Isolated yield. [c]Yield was calculated based on starting material recovery.

Various monoalkyl substituted β-keto esters **108, 135**,**136** and **111** were also treated under the experimental condition and provided the corresponding brominated product chemoselectively at the α-position. Following identical reaction conditions, 1-benzoylacetone **112** was smoothly converted to the corresponding α-monobrominated product **129** in good yield. Likewise, dibenzoylmethane **114** and dimedone **115** were transformed chemoselectively to the corresponding α-monobrominated products, respectively in good yields. It is important to point out that α,α-dibromodimedone (**140**) can be obtained exclusively by increasing the amount of ammonium bromide from 1.5 equivalents to 3.0 equivalents.

We believe that the promoter (V_2O_5) is used not only for the oxidation of ammonium bromide by H_2O_2 but also acts as a Lewis acid for chelation with the two carbonyl groups present in β-keto esters or 1,3-diketones as shown in Scheme 48. This promotes enol formation for chemoselective mono bromination.



Scheme 48: Plausible mechanism for α-bromination of β-keto esters showing the dual role of vanadium.

In conclusion, we have developed a general method for mild α-bromination of β-keto esters and 1,3-diketones using a combination of V_2O_5-H_2O_2-NH_4Br, avoiding the use of the conventional reagent NBS for this transformation. Additionally, all these reagents are environmentally acceptable. We suggest that vanadium pentoxide plays the dual role: i) formation of peroxo complexes, which oxidize bromide ion to the bromonium ion and ii) promotion of enol formation by chelating with the two carbonyl groups of the β-keto ester or 1,3-diketone. We also noted, that the ester functionality does not undergo hydrolysis under the experimental conditions. We believe our protocol will find a position in the arsenal of synthetic organic chemistry because of its high selectivity, high yields, simplicity and economic viability.

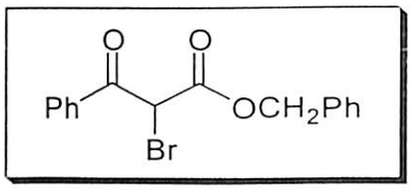
SECTION B

α-BROMINATION OF β-KETO ESTERS AND 1,3-DIKETONES USING A COMBINATION OF V_2O_5-H_2O_2-NH_4Br

EXPERIMENTAL

General Procedure for α-bromination of β-keto esters and 1,3-diketones: Into a stirred solution of vanadium pentoxide (1.9 mmol, 345 mg) in water (5 mL) was added 50% hydrogen peroxide (5 mL, 73.5 mmol) at ice-bath temperature with stirring. The colour changed from light orange to deep red after 25-30 min. Then, ammonium bromide (5.7 mmol, 560 mg) was added and the reaction mixture was stirred for another 10 min. Subsequently, ethyl acetoacetate (495 mg, 3.8 mmol) in CH_2Cl_2 (5 mL) was added and the reaction mixture was then stirred for a further 3.0 h at the same temperature. After completion of the reaction as monitored by TLC, it was extracted with dichloromethane (25 mL x 2) and the organic layer was washed with saturated sodium metabisulfite solution to destroy unreacted molecular bromine. Finally, it was washed with water and dried over anhydrous sodium sulfate. Removal of the organic layer provided a crude residue, which was finally purified by short path distillation. Some of the compounds were purified through silica gel column (60-120 mesh, SRL) chromatography by eluting with a mixture of (2% ethylacetate in hexane) to obtain the pure products.

Compound (137):



Nature: Liquid

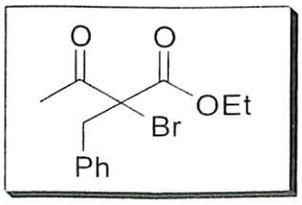
Yield: 91% (1.152 g)

IR(Neat): 1695, 1742 cm^{-1}

^{1}H NMR (400 MHz): δ 4.32 (s, 2H), 5.68 (s, 1H), 7.31-7.38 (bs, 5H), 7.48 (t, J = 7.6 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.97 (d, J = 8 Hz, 2H), ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{13}BrO_3$	C 57.68	C 57.59
333.18	H 3.93	H 3.98

Compound (138):



Nature: Liquid

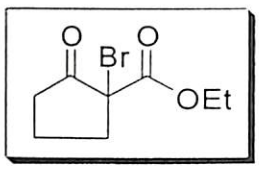
Yield: 92% (1.046 g)

IR(Neat): 1742, 1723 cm^{-1}.

^{1}H NMR (400 MHz): 1.35 (t, J = 7.2 Hz, 3H), 2.40 (s, 3H), 3.45 (d, J = 14.4 Hz, 1H), 3.57 (d, J = 14.8 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 7.25-7.46 (bs, 5H) ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{15}BrO_3$	C 52.19	C 52.25
299.16	H 5.05	H 5.10

Compound (139):



Nature: Liquid

Yield: 87% (0.777 g)

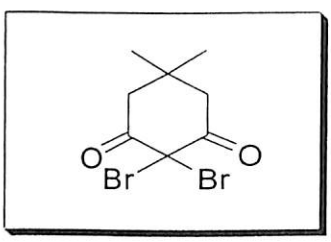
IR(Neat): 2981, 1757, 1721, 1455, 1245, 1143, 1020 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 1.31 (t, J = 7.2 Hz, 3H), 2.08-2.15 (m, 2H, CH_2), 2.16-2.56 (m, 2H, CH_2), 2.71-2.79 (m, 2H, CH_2), 4.25 (q, J = 6.8 Hz, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): 7.01, 12.18, 17.10, 27.82, 31.46, 55.81, 159.37, 198.25 cm^{-1}.

Elemental Analysis	Calculated	Found
$C_8H_{11}BrO_3$	C 40.87	C 40.79
235.08	H 4.72	H 4.78

Compound (140):



Nature: Solid, mp:

Yield: 90% (1.020 g)

IR(KBr): 2960, 1721, 1603, 1373, 1194, 1055, 707 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 1.02 (s, 6H), 3.00 (s, 4H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): 27.79, 30.60, 48.19, 66.41, 192.47 ppm.

Elemental Analysis	Calculated	Found
$C_8H_{10}Br_2O_2$	C 32.25	C 32.29
297.97	H 3.38	H 3.34

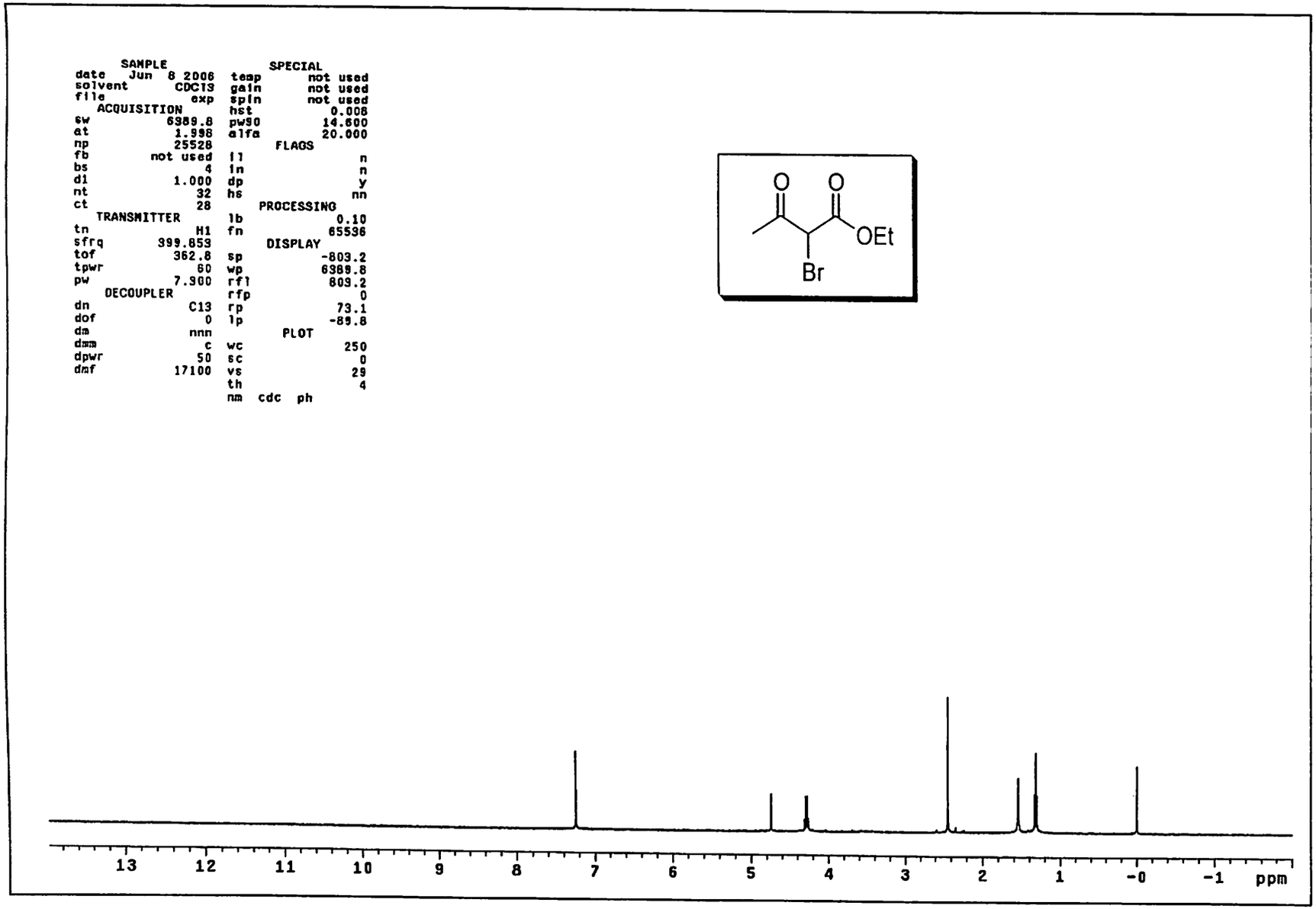


Figure 1: ^{1}H NMR spectrum of compound **(118)**

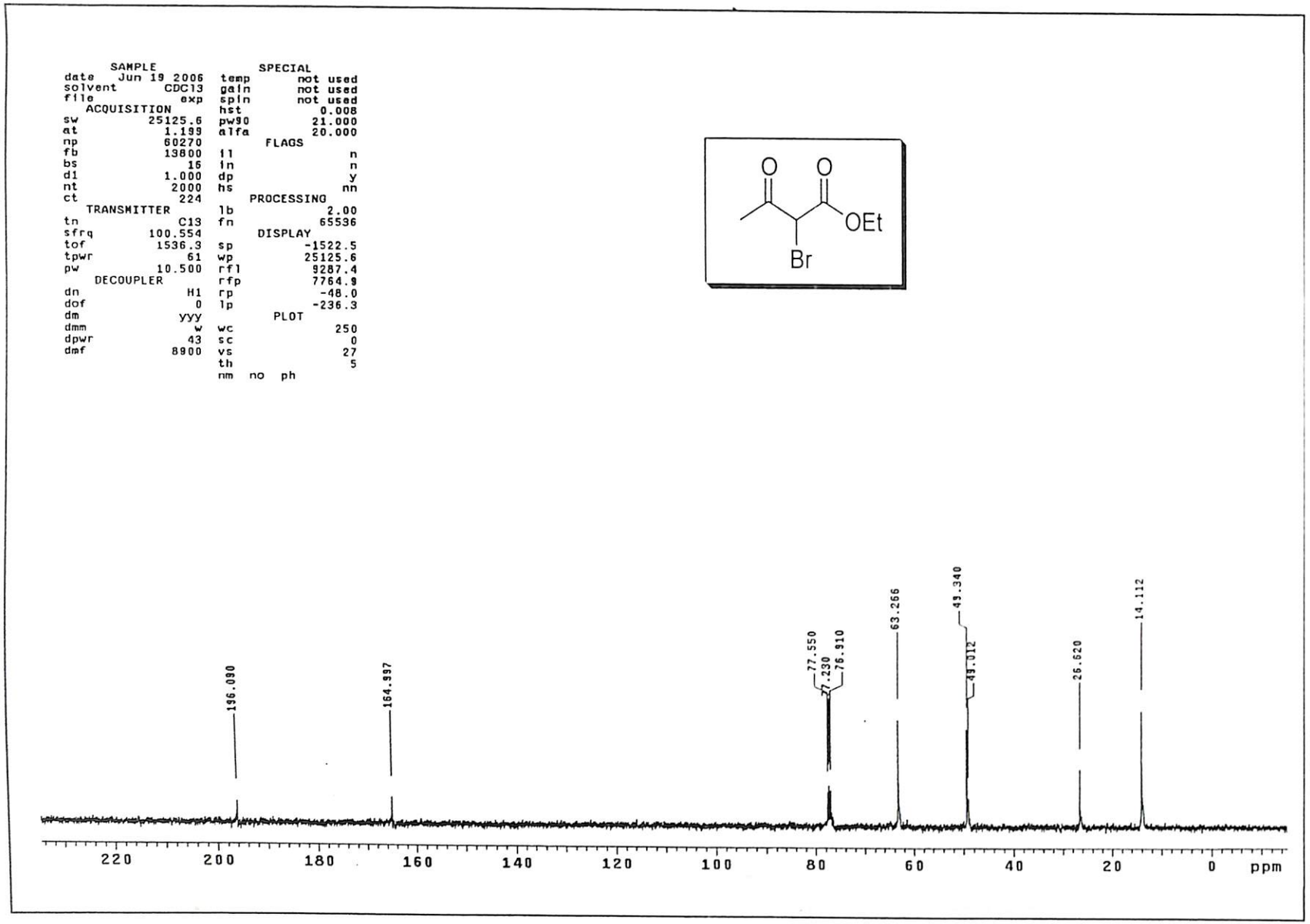


Figure 2: ^{13}C NMR spectrum of compound **(118)**

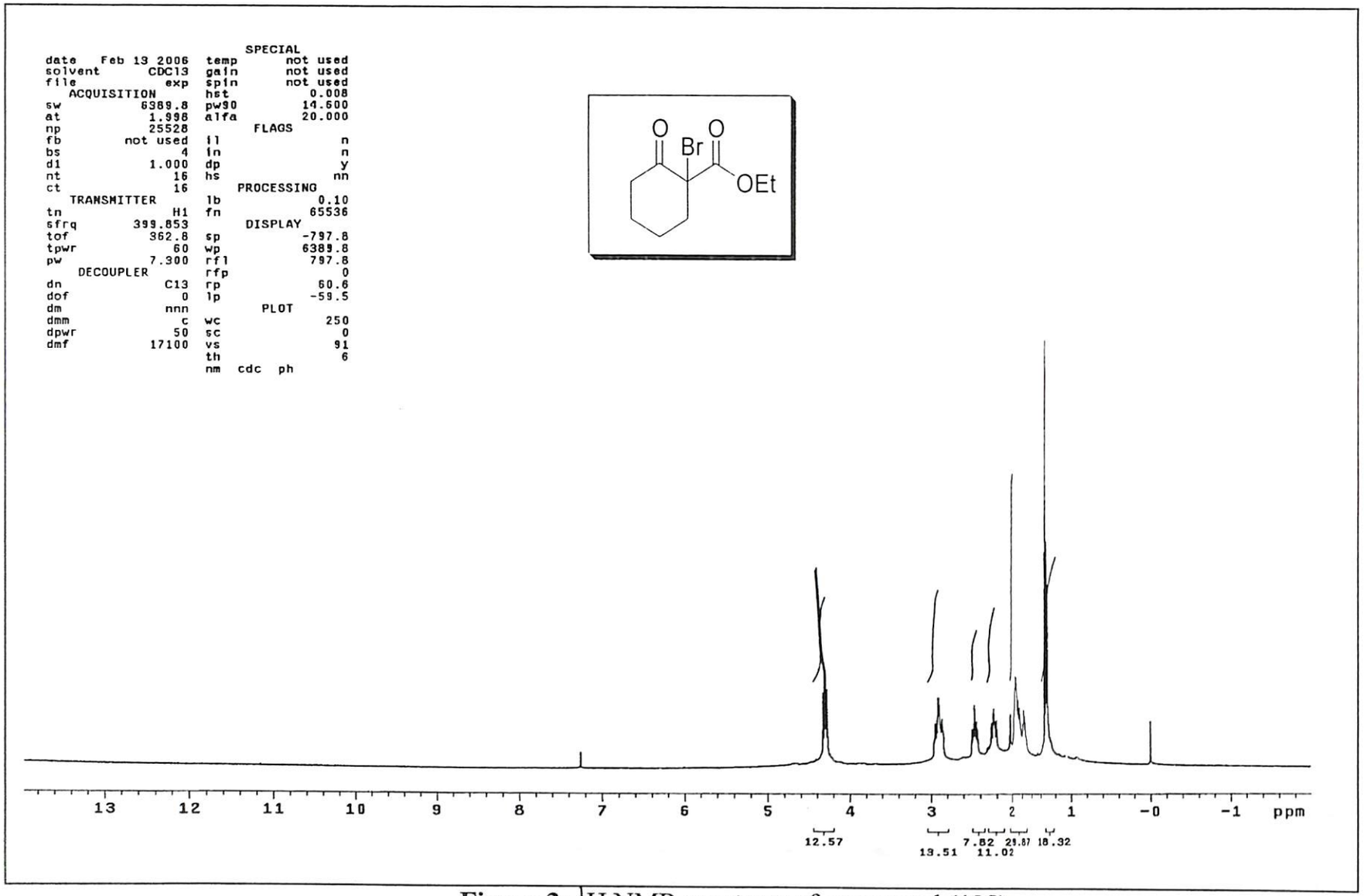


Figure 3: ^{1}H NMR spectrum of compound **(128)**

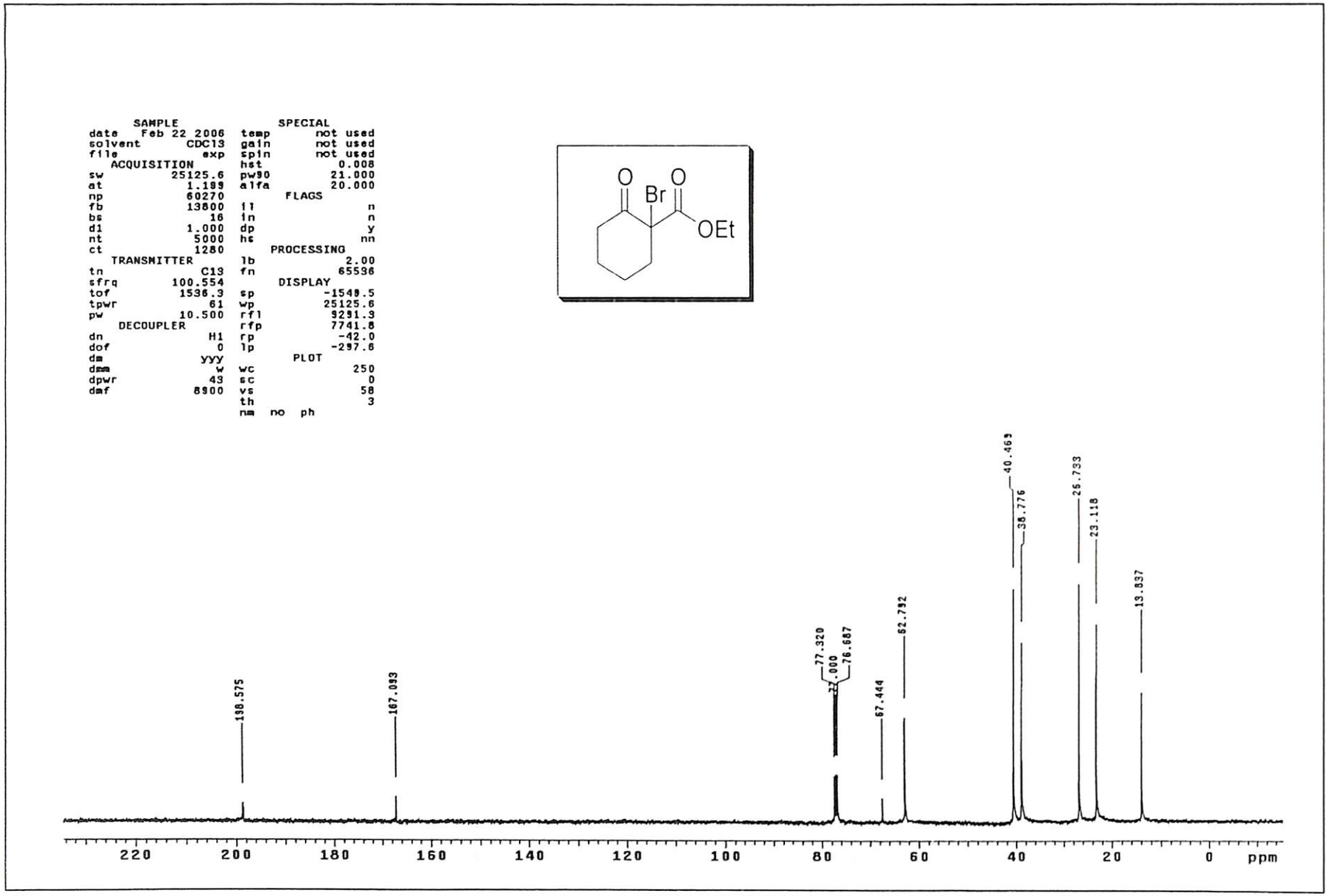


Figure 4: ^{13}C NMR spectrum of compound **(128)**

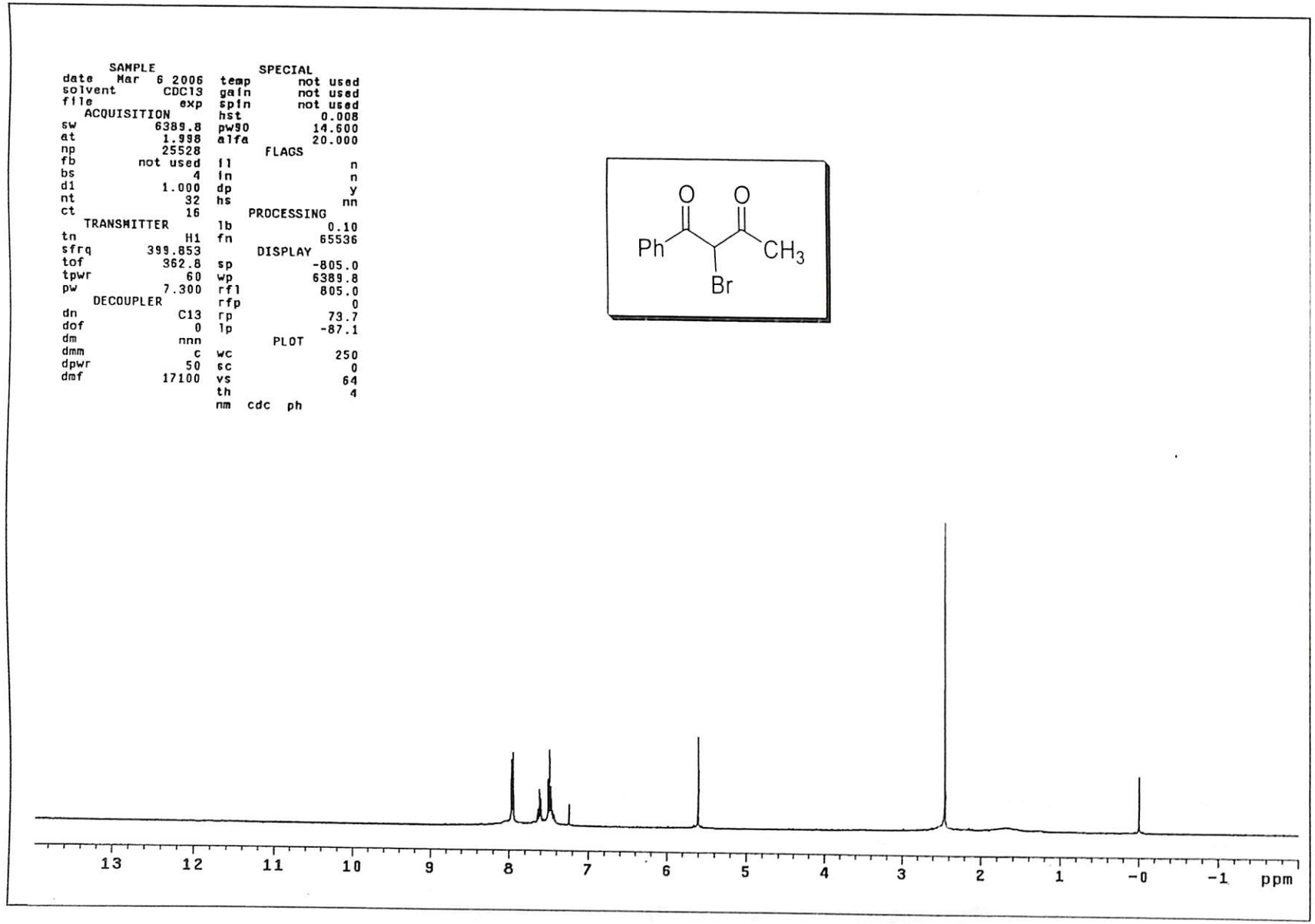


Figure 5: ^{1}H NMR spectrum of compound **(129)**

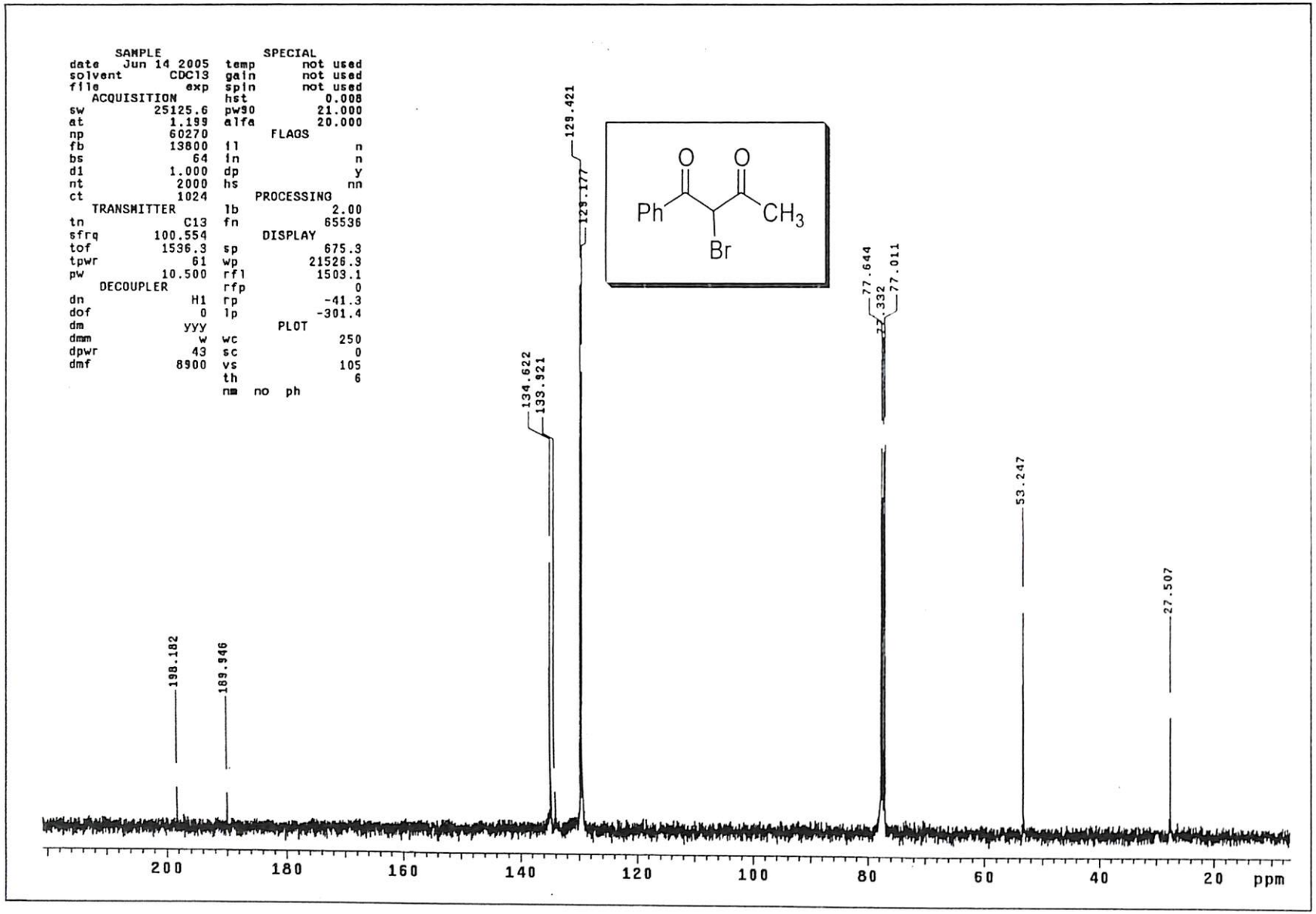


Figure 6 : ^{13}C NMR spectrum of compound **(129)**

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CHAPTER - III

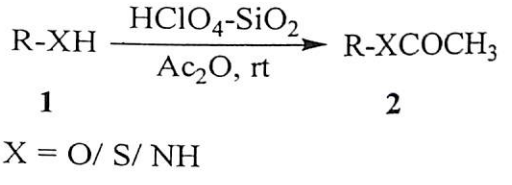
Part I

A BRIEF LITERATURE SURVEY ON THE APPLICATION OF SILICA SUPPORTED PERCHLORIC ACID ($HClO_4$-SiO_2) IN ORGANIC SYNTHESIS AND *GEM*-DIACYLATION, THIOACETALIZATION, OXATHIOACETALIZATION AND TETRAHYDROPYRANYLATION

LITERATURE REVIEW

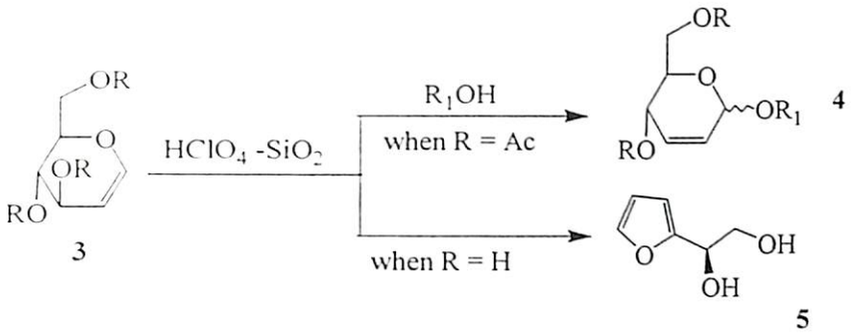
Silica supported reagents[1] have gained substantial interest in modern organic chemistry due to their unique properties such as high efficiency because of more surface area, extra stability, greater selectivity, ease of handling and reusability. Recently, $HClO_4$-SiO_2 has been used extensively for acid catalyzed organic transformations. Due to free flowing nature of the catalyst, it is an effective, cheap and reusable, eco-friendly versatile catalyst in organic synthesis and can be readily prepared by mixing 70% perchloric acid with silica gel in ether solution, followed by drying under vacuum condition.[1a] Though perchloric acid is slightly weaker acid than TfOH, it is still the second strongest protic acid according to its p*K*a value. The first application of silica supported perchloric acid was shown by Chakraborti *et al.*[1a] and it has gained extensive application in current organic chemistry. Recently our group (Khan and co-worker) as well as several others had shown the versatility and scope of this catalyst by employing this catalyst in several organic transformations. In this part a brief literature survey on the application of this versatile reagent ($HClO_4$-SiO_2) is addressed below.

The importance and usefulness of silica supported perchloric acid as an effective catalyst was first started by Chakraborti and his co-worker.[1a] They demonstrated that perchloric acid impregnated on silica gel ($HClO_4$-SiO_2) is a highly efficient and reusable catalyst for acetylation of a wide variety of alcohols, phenols, thiols and amines under solvent-free condition as shown in Scheme 1.



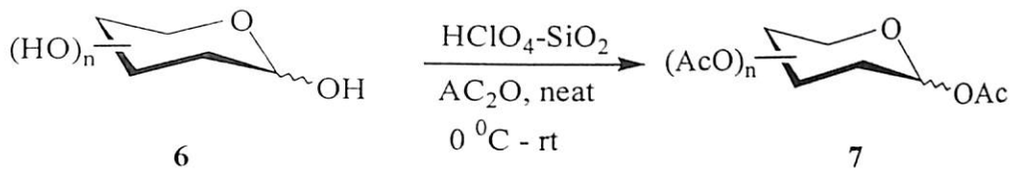
Scheme 1

Vankar *et al.* introduced[2] silica-supported perchloric acid as an efficient catalyst for synthesis of 2,3-unsaturated-*O*-glucosides and a chiral furan diol from 2,3-glycals in good to excellent yields. The notable features of this protocol are: the reaction time is very short and exhibits good α selectivity. Alcohols such as primary, secondary, allylic alcohols, phenols and thiols react with 3,4,6-tri-*O*-acetyl glucal in presence of catalytic amount of $HClO_4$-SiO_2 to provide corresponding 2,3-unsaturated-*O*-glucosides.



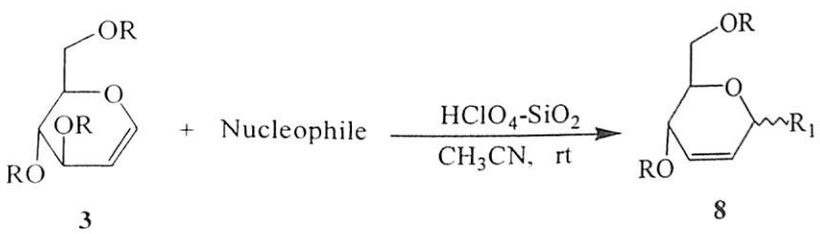
Scheme 2

Misra *et al.* revealed that silica-supported perchloric acid $HClO_4$-SiO_2 is an efficient and effective catalyst for per-*O*-acetylation of carbohydrates using a stoichiometric amount of acetic anhydride avoiding the pyridine or excess amount of acetic anhydride (Scheme 3).[3] The method is very fast, simple and convenient for the preparation of peracetylated carbohydrate derivatives. A large number of protecting groups survive under the experimental condition.



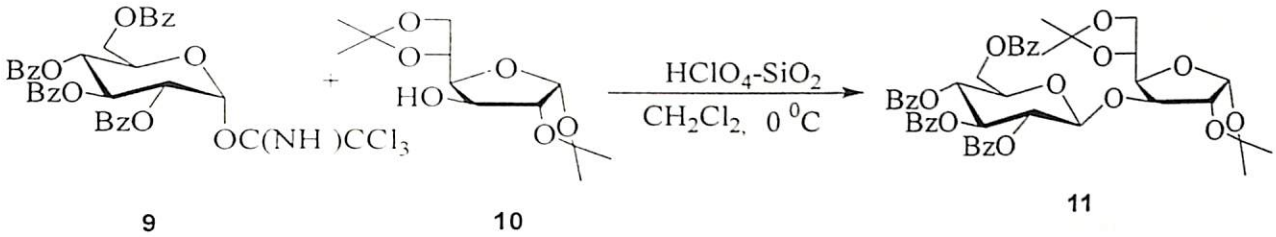
Scheme 3

Soon after, the same group reported that $HClO_4$-SiO_2 can be used for the synthesis of 2,3-unsaturated *C*-glycosides by Ferrier rearrangement of glycals (Scheme 4).[4] Allyltrimethylsilane, TMSCN and 1,3-diketone reacts with *O*-acylated or *O*-alkylated glycals at room temperature and provided 2,3-unsaturated *C*-glycosides in good yields. The advantages of $HClO_4$–SiO_2 as catalyst for this transformation: high yield of products, simplicity in operation, cleaner reaction profiles, short reaction times and exceptionally high selectivity. In addition, this method does not require any additive or stringent reaction conditions. There is no need to take any special precautions in either handling the catalyst or excluding moisture from the reaction medium.



Scheme 4

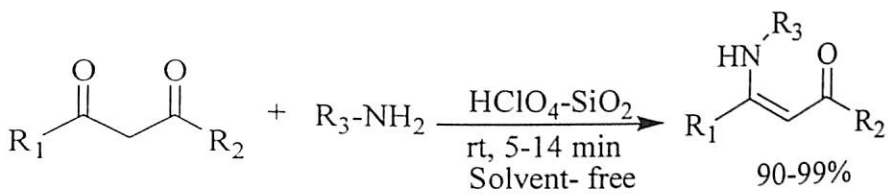
Du and Lindhardt *et al.* reported[5] that silica-supported perchloric acid ($HClO_4$-SiO_2) is an efficient promoter as well as a replacement for TMSOTf, in various glycosylation reactions using sugar trichloroacetimidates as glycosyl donors as shown in Scheme 5. The notable advantages of this protocol are: operational simplicity, low cost, short reaction time, high yields and low toxicity.



9 10 11

Scheme 5

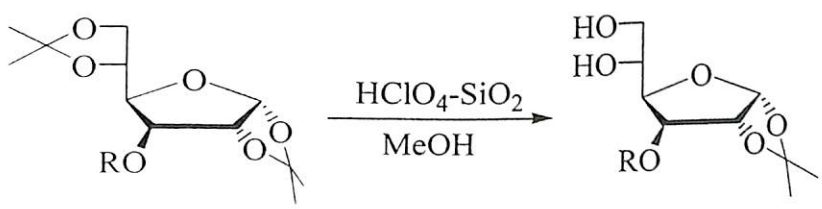
The catalyst $HClO_4$-SiO_2 can be used for chemo-and stereoselective conversion of β-dicarbonyl compounds into β-enaminones and β-enamino esters by treatment with amines as show in Scheme 6. The reaction gives very good yields at room temperature under solvent-free conditions.[6]



12 **13** **14**

Scheme 6

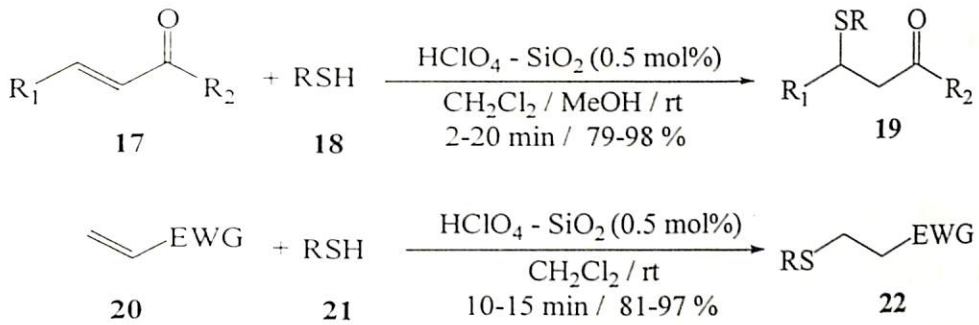
Vankar *et al.* showed[7] the catalytic activity of this versatile reagent for selective deprotection of isopropylidene acetals as depicted below (Scheme 7). Similarly, primary trityl ethers can also be cleaved selectively to the corresponding hydroxyl compounds in presence of a sensitive isopropylidene group using the same catalyst. The work-up involves merely filtration of the reagent followed by purification of the product.



15 **16**

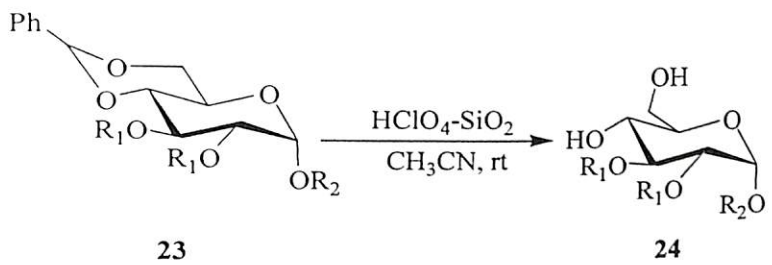
Scheme 7

Recently our group has demonstrated[8] that silica supported perchloric acid is a highly efficient and versatile catalyst for Michael addition of thiols to electron deficient alkenes. A wide variety of α,β-unsaturated ketones, nitiles, esters and amides undergo 1,4-addition within a very short reaction time and provide good yields in presence of catalytic amount of $HClO_4$-SiO_2 (Scheme 8).



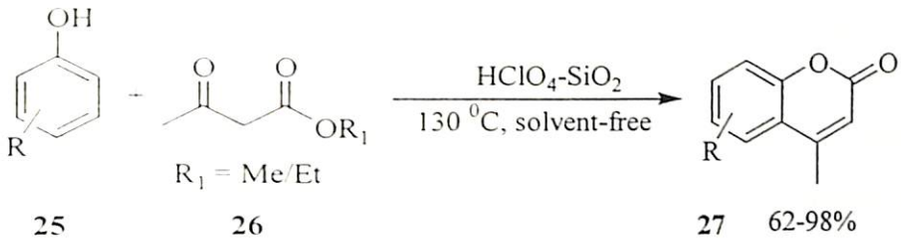
Scheme 8

Silica supported perchloric acid is a mild and useful catalyst for the cleavage of benzylidine acetals as well as for the direct conversion of acetals to acetates.[9] This method can be considered as a green protocol as the reaction is very clean and without involvement of any toxic reagent as well as no need of chromatographic purification (Scheme 9).



Scheme 9

Recently Rao *et al*. have shown[10] that $HClO_4$-SiO_2 is an effective catalyst for solvent-free synthesis of coumarin derivatives **27** *via* Pechmann condensation as shown in Scheme 10. Various substituted phenols reacts with methyl acetoacetate or ethyl acetoacetate under solvent-free conditions and provide very good yields of oxygen heterocycle coumarins. The notable advantages of this protocol are: simple procedure, cost-effective as well as short reaction times.



Scheme 10

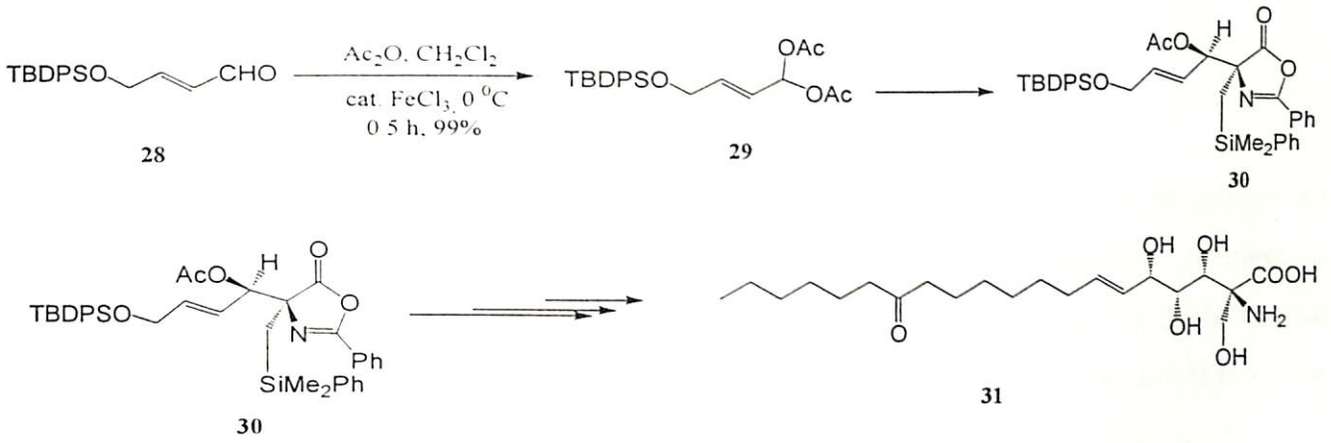
Similarly, Chakraborti *et al.* reported that perchloric acid adsorbed on silica gel is a highly efficient catalyst for chemoselective N-*tert*-butoxycarbonylation of amines at room temperature and under solvent-free conditions.[11]

In addition, there are numerous synthetic applications of this versatile catalyst in organic synthesis such as: synthesis of 1,5-benzodiazepines,[12] synthesis of 2-benzoxepines from Morita-Baylis-Hillman adducts,[13] selective removal of anomeric *O*-acetate groups in carbohydrates[14] and one-pot synthesis of polyhydroquinoline derivatives *via* Hantzsch condensation.[15] All these valuable transformation have notable contribution in organic synthesis.

From the above survey it is evident that perchloric acid impregnated on silica gel is a multidimensional catalyst for various transformations.[16] By taking cues from this and from our earlier experience on the catalytic activity of aqueous perchloric acid,[17] we wanted to explore the potentiality of $HClO_4$-SiO_2 for other valuable transformation in organic synthesis. In continuation of our research for the development of new synthetic methodologies using various reagents in the field of protection and deprotection chemistry,[18] we observed that there are still lots of drawbacks of existing methods. Therefore, we thought that there is some scope to device new methodologies for the protection of carbonyl and hydroxyl functionalities. As a result a brief survey on the recent methods available in the literature for the protection of aldehydes as acylal and thioacetals, oxathioacetals as well as tetrahydropyranylation of hydroxyl compounds are described below.

The protection of aldehydes as acetal or oxathioacetal or dithioacetal or acylal is a common practice for manipulation of other functional groups during multi-step synthesis. Sometimes the protection of aldehydic compounds as acylal is usually preferred due to ease of preparation and their stability towards basic and neutral conditions.[19] In addition, the preparation of 1,1-diacetates from the corresponding aldehydes can be achieved very

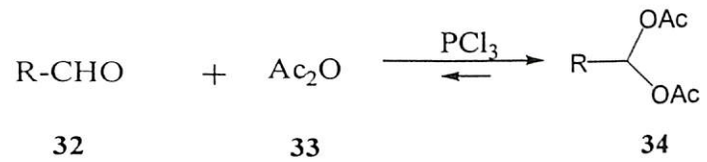
easily in the presence of ketones. Moreover, they also serve as valuable precursors for asymmetric allylic alkylation, for example, Trost *et al.* demonstrated that *gem*-diacetates of carbonyl compounds are surrogates for asymmetric synthesis and they have shown that natural product Sphingofungin E (**31**) can be synthesized from the allylic *gem*-diacetate **29** as shown in Scheme 11. [20]



Scheme 11

In addition, *gem*-diacetates are considered as the precursor for the synthesis of 1-acetoxydienes for Diels-Alder reactions.[21] The preparation of acylal is usually performed from the reaction of an aldehyde with acetic anhydride in the presence of protonic acids e.g. sulfuric acid[22] or methanesulfonic acid/phosphoric acid[23] or by employing a Lewis acid, which acts as a catalyst.

Michie *et al.* introduced phosphorous trichloride as an effective catalyst for the preparation of *gem*-diacetates as shown in Scheme 12.[24]

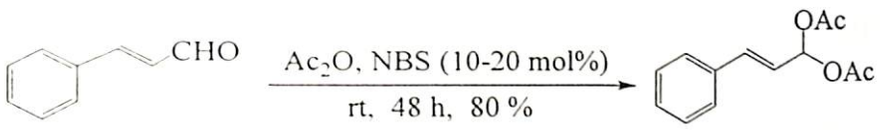


Scheme 12

This method provides good yields for aromatic aldehydes. Unfortunately, this method is not suitable for aldehydes having electron withdrawing substituent such as nitro as well as for α,β-unsaturated aldehydes e.g. cinnamaldehyde as it provides very low yield. In addition the major drawback of this method is that the reaction time is too long.

Later on, Karimi *et al.* demonstrated that NBS is an effective catalyst for the same transformation.[25] This method provides good yields for aromatic aldehydes but for

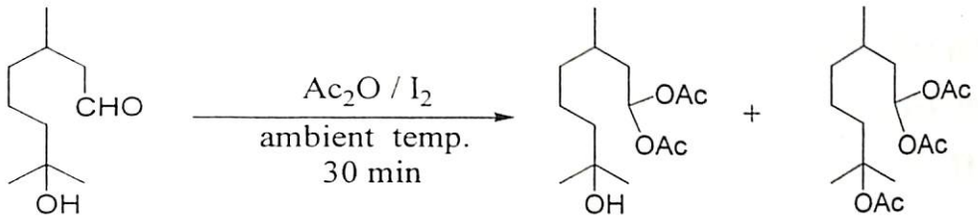
aliphatic and α,β- unsaturated aldehydes the reaction time is too long and excess amount (1 mL per mmol of aldehyde) of acetic anhydride is required under this experimental condition (Scheme 13).



35 36

Scheme 13

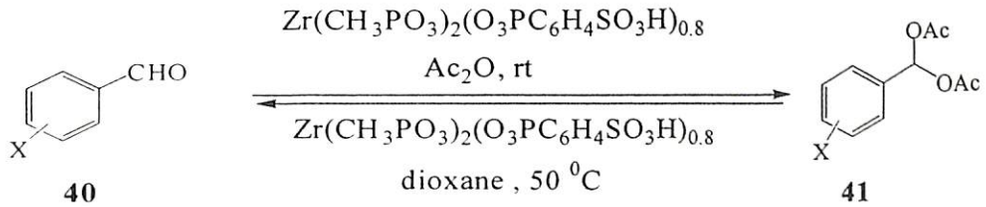
Subsequently, Sarma *et al.* reported molecular iodine as an efficient and mild catalyst for the protection of aldehydes as *gem*-diacetates.[26] The present method exhibits no effect on the substituent of aromatic ring unlike PCl_3 method. Both 4-nirobenzaldehyde and cinnamaldehyde undergo protection in good yields under the experimental condition. For the substrate **37** this method provides a mixture of products as shown in Scheme 14.



37 38 39

Scheme 14

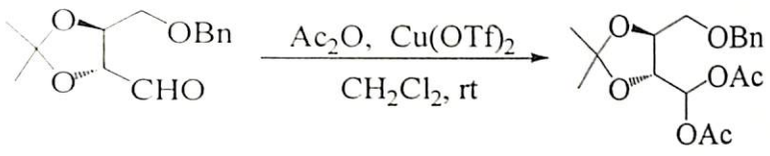
Similarly, Curini *et al.* introduced zirconium sulfophenyl phosphonate as an effective catalyst both for the protection of aldehydes as *gem*-diacetates as well as for the deprotection as depicted in Scheme 15.[27] Even though this method provides good yields for the deprotection of *gem*-diacetate of aromatic and α,β-unsaturated aldehydes but in case of deprotection of aliphatic acylals this protocol is not useful and provide very low yields.



40 41

Scheme 15

Singh *et al.* reported the efficacy of $Cu(OTf)_2$ for the formation of *gem*-diacetates of a wide variety of aldehydes (Scheme 16) with good yields.[28] Acid sensitive protecting group such as isopropylidine also survives under the experimental condition. Likewise, other metal triflates such as $Sc(OTf)_3$[29] and $Bi(OTf)_3$[30] have also been utilized as catalysts



42 **43**

Scheme 16

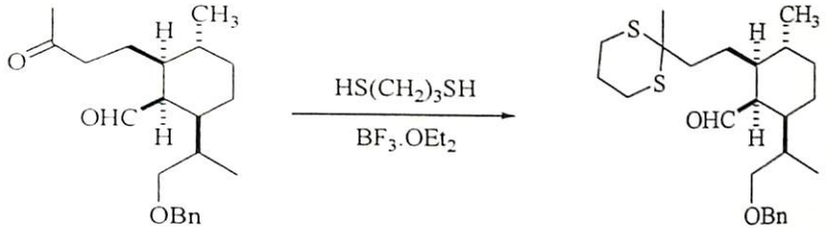
for the preparation of 1,1-diacetate derivatives from the corresponding aldehydes. Unfortunately, many of these methods have drawbacks such as harsh reaction conditions, requirement of excess amount of acetic anhydride, tedious work-up procedure, and involvement of expensive and moisture sensitive catalyst.

Over the years, a large number of methods have been developed for the preparation of 1,1-diacetates from the corresponding aldehydes by employing various new reagents such as LiOTf,[31] ceric ammonium nitrate,[32] $InCl_3$,[33] H_2NSO_3H,[34] $LiBF_4$,[35] TMSCl-NaI,[36] $FeCl_3$,[37] $CoCl_2$,[38] $Bi(NO_3)_3 \cdot 5H_2O$,[39] Wells-Dawson acid ($H_6P_2W_{18}O_{62} \cdot 24H_2O$),[40] n-tetrabutylammonium tribromide (TBATB),[41] and heterogeneous catalysts such as aluminum dodecatungstophosphate ($AlPW_{12}O_{40}$)[42] and zirconium sulfophenyl phosphonate [$Zr(CH_3PO_3)_{1.2}(O_3PC_6H_4SO_3H)_{0.8}$][27] etc.

Recently few more new methods are also reported in the literature for the same transformation using various new reagents such as: Heteropolyacid encapsulated into mesoporous silica framework,[43] cupric sulfate pentahydrate,[44] acidic alumina,[45] silica sulfate,[46] $KHSO_4$,[47] lithium perchlorate,[48] Envirocat EPZG [49] environmentally benign Mo/TiO_2-ZrO_2 solid acid catalyst,[50] and Amberlyst-15[51] are notable.

Though these methods are quite efficient, but most of the currently available methods encounter some limitations such as strong acidic condition, difficulty in preparing an acylal from furfural[42] and longer reaction times particularly for aliphatic and α,β-unsaturated aldehydes.[27] Therefore, a new methodology by using an inexpensive and mild catalyst, which might overcome these drawbacks in the preparation of acylals from the corresponding aldehydes, is still required.

Similarly, the oxathioacetalization or thioacetalization of aldehydes or ketones is an important and valuable organic transformation in organic synthesis. Some times thioacetalization of carbonyl compounds are preferred due to their inherent stability under both acidic and basic reaction conditions as compared to *O,O*-acetals/ketals or *O,S*-acetals/ketals. From the literature we found several methods are being developed over the years for protection of carbonyl functionality as thioacetals, and oxathioacetals. The conventional reagent for the protection of carbonyl compounds as thioacetals is either protic acid HCl[52] or $BF_3.OEt_2$ [53] Generally most of the methods demonstrate that chemo selective protection of aldehyde functionality is possible in presence of ketone. But if steric factor play a vital role, then some times it is possible to protect a ketone in presence of aldehyde functionality as shown in Scheme 17.[54]

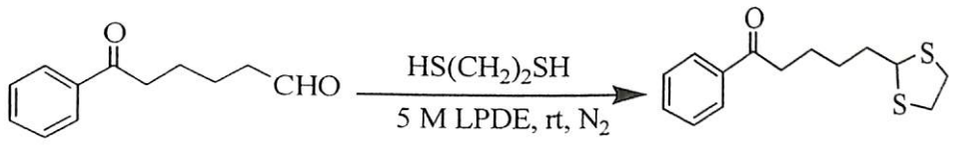


44 **45**

Scheme 17

The method that uses $BF_3.OEt_2$ is a superior one than the HCl method but the major drawback is that it needs stoichiometric amount of the catalyst, which makes the method inconvenient for acid sensitive functional groups such as TBS ethers.

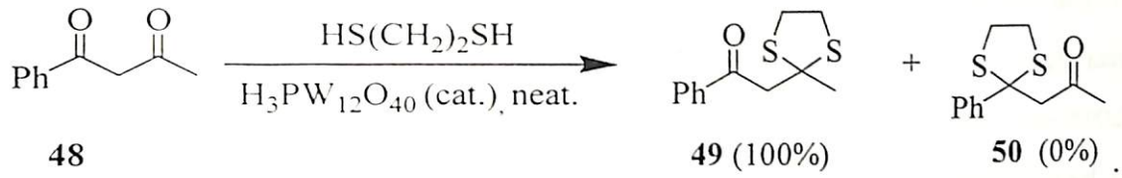
Sankararaman *et al.* have reported[55] that the chemoselective dithioacetalization of carbonyl compounds could be achieved by employing lithium perchlorate in diethyl ether medium as depicted in Scheme 18. The limitation of this method is that it fails to give dithioacetal derivatives from 4-methoxybenzaldehyde and acetophenone. Moreover, the reaction has to be performed under inert atmospheric conditions.



46 **47**

Scheme 18

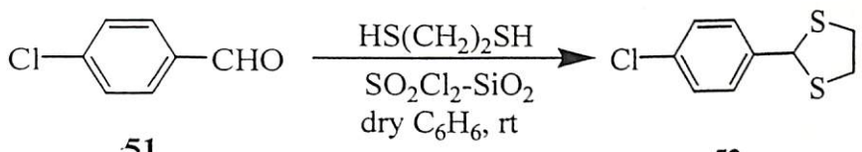
Firouzabadi *et al.* have reported the usefulness of tungstophosphoric acid in its solid state as catalyst for the thioacetalization reactions.[56] In this protocol aliphatic ketones are more reactive than aromatic ketones and as a result this method can be used for the chemoselective protection of aliphatic ketones in presence of an aromatic ketone as shown in Scheme 19.



48 **49** (100%) **50** (0%)

Scheme 19

Hojo *et al.* have reported[57] the thioacetalization of carbonyl compounds by using a solid supported reagent (SO_2Cl_2-SiO_2) as shown in Scheme 20. Aromatic, aliphatic and α,β-unsaturated aldehydes undergo thioacetalization smoothly by employing this catalyst at room temperature. Interestingly, ketones are less reactive under similar reaction conditions and do not provide dithioacetals even at refluxing temperature. However, they have overcome the difficulties by using excess amount of reagent and by refluxing the reaction mixture.



51 **52**

Scheme 20

Similarly other supported reagents such as $Cu(OTf)_2$-SiO_2,[58] $ZrCl_4$-SiO_2,[59] $TaCl_5$-SiO_2,[60] and $CoBr_2$-SiO_2[61] are also used as effective catalyst for the protection of carbonyl compounds as thioacetals.

Over the years, a large number of methods have been developed by using various Lewis acids viz. $AlCl_3$,[62] $TiCl_4$,[63] $LaCl_3$,[64] LiBr,[65] $InCl_3$,[66] $LiBF_4$,[67] and by our group $NiCl_2$[68] for the same transformation. Similarly, some new catalysts, for examples, molecular I_2,[69] NBS,[70] $Sc(OTf)_3$[71] have been utilized for thioacetalisation reaction. Moreover, our group also demonstrated that bromodimethylsulfonium bromide ($Me_2S^+BrBr^-$)[72] and acetyl chloride[18c] are effective catalysts for thioacetalization of carbonyl compounds. Some of

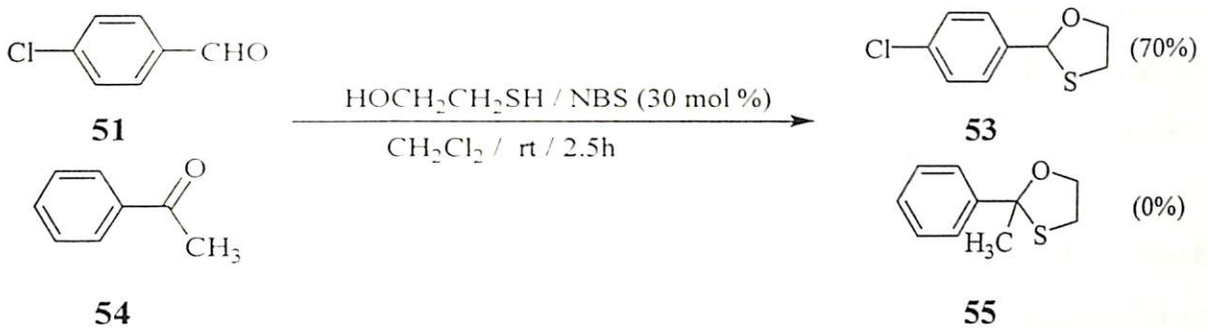
the recent methods for thioacetalization are: copper (II) tetrafluoroborate,[73] ruthenium(III) chloride,[74] *p*-TSA/SiO_2,[75] silica supported polyphosphoric acid.[76] Although literature enumerate so many methods still some drawbacks remain. As for example some of the methods involve: tedious work-up,[62, 63] inert atmospheric reaction conditions,[66, 69] harsh reaction conditions,[65] incompatibility with other protecting group such as TBS ether,[67] involve relatively more expensive reagents[74] and fail to provide cyclic dithioketals.[68] In an endeavor to gradually change the current working practices to greener alternatives and to meet environmental demands,[77] we realized there is a need to develop catalytically efficient alternative which will overcome existing drawbacks for protection of carbonyl compounds as dithioacetals.

Similarly from the literature we found a large number of methods are available for oxathioacetalization of carbonyl compounds. The common procedures for the protection of carbonyl compounds to the corresponding 1,3-oxathiolanes involve the use of strong protonic acid or Lewis acids. Ralls *et al.* reported the preparation of various 1,3-oxathiolane by using HCl as the proton source.[78] Unfortunately, this method has some drawbacks such as low yield as well as highly acidic reaction conditions, which is not suitable for a acid sensitive substrate.

Later on, Djerassi *et al* developed a new method for the preparation of oxathioacetals by using ketonic compounds and 2-mercaptoethanol in presence of *p*-tolunesulfonic acid as catalyst under reflux conditions by employing an azeotropic distillation set-up.[79] After that, Edwin Wilson *et al* reported borontrifluoride-etherate (BF_3-OEt_2) as an effective method for oxathioacetalization.[80] Although this procedure gives the desired product in good yield but this method has also some drawbacks such as longer reaction time.

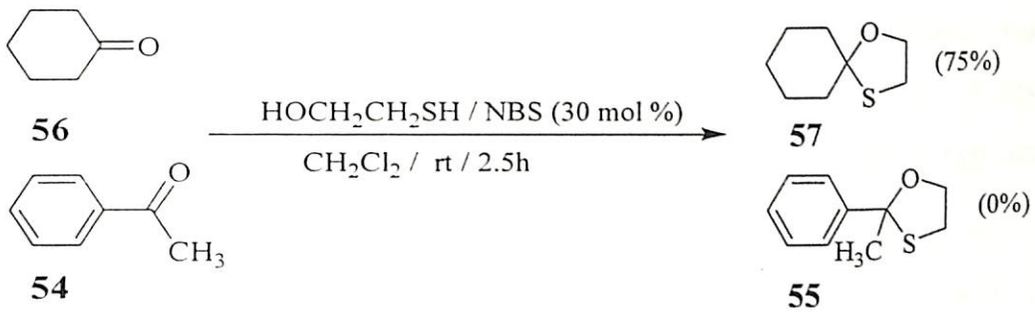
Similarly, $ZnCl_2$,[81] trimethylsilyl triflate (TMSOTf)[82] and $LiBF_4$[67] are reported as effective catalysts for the conversion of various carbonyl compounds to the corresponding 1,3-oxathiolane derivatives.

Kamal *et al.* reported that *N*-bromosuccinimide (30 mol%) as a catalyst for the preparation of various 1,3-oxathiolane of carbonyl compounds in dichloromethane.[83] They have shown that the selective protection of aldehyde might be possible in presence of a ketone as shown in Scheme 21.



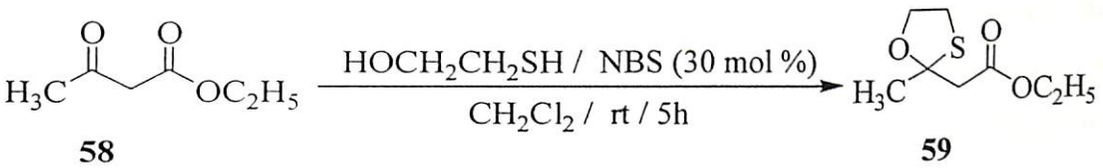
Scheme 21

They have also shown the selective protection of a cyclic ketone in presence of an aromatic ketone as shown in Scheme 22.



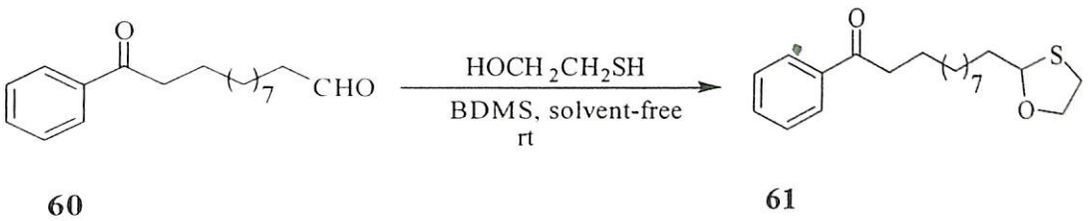
Scheme 22

In addition by using this protocol keto functionality of various keto-esters can be chemoselectively protected without *trans*-esterification as shown in Scheme 23.



Scheme 23

Very recently our group has demonstrated BDMS as a highly efficient catalyst for oxathioacetalization of carbonyl compounds as shown in Scheme 25.[18d] The notable advantages of this method are: mild reaction conditions, no aqueous work-up, avoidance of columchromatographic separation as well as chemoselectivty as shown in Scheme 24.



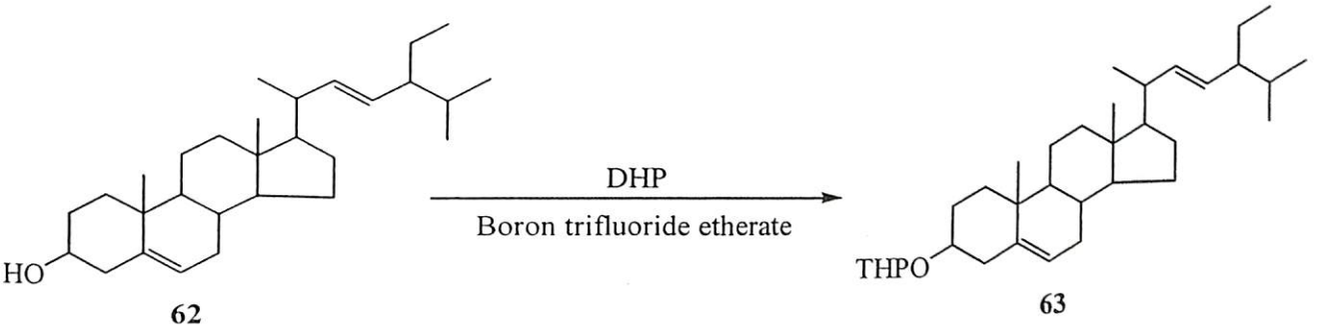
Scheme 24

Although all the reported methods are useful for oxathioacetalization yet most of them suffer from some limitations such as longer reaction times, low yields and involvement of expensive catalyst as well as requirement of halogenated solvent such as dichloromethane. Therefore, our endeavor was to overcome the existing limitations.

Similarly, we looked for the available literature methods for tetrahydropyranylations. As we know that the hydroxyl group is present in a number of biologically active compounds such as nucleosides, carbohydrates, steroids, macrolides, polyethers, peptides and amino acids. Sometimes the protection-deprotection strategy for a free hydroxyl group becomes an essential job to manipulate other functional groups particularly in polyfunctional natural and non-natural product synthesis. Therefore, high selectivity is frequently desired for a given hydroxyl group in polyol chemistry. Several protecting groups have been cited in the literature for the protection of hydroxyl groups. Among them, tetrahydropyranyl (THP) ether[84] is often used for protection of hydroxyl groups in organic synthesis.

The particular advantages for using THP group as protecting group are: its ease of introduction, the low cost of dihydropyran, stability under a variety of reaction conditions such as reaction with metal hydrides, metal triflates, Grignard reagents, acylating agents, oxidative reagents and alkylating agents. In addition it can be easily deprotected at a later stage.

Tetrahydropyranylation of alcohols and phenols are traditionally carried out in presence of *p*-TSA,[85] PPTS,[86] or K-10 clay.[87] Boron trifluoride etherate[88] as a convenient catalyst for tetrahydropyranylation of stigmasterol is shown in Scheme 25. Although this method gives satisfactory results but it needs excess amount of dihydropyran (DHP).

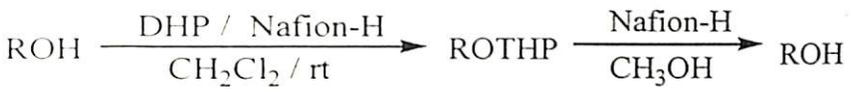


62 **63**

Scheme 25

Similarly, Olah and his group demonstrated[89] that Nafion-H, a solid superacid, can be utilized as catalyst for tetrahydropyranylation/depyranylation of alcohols and phenols as

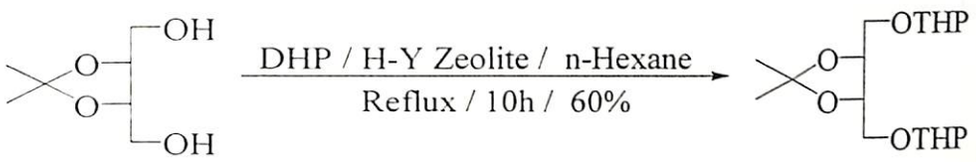
shown in Scheme 26. This method is very good in terms of yield but it takes relatively much longer time for completion.



64 65 64

Scheme 26

Kumar *et al* showed that H-Y Zeolite[90] is also a good and reusable catalyst for tetrahydropyranylation of alcohols and phenols as shown in Scheme 27. This method requires reflux condition and longer reaction time.

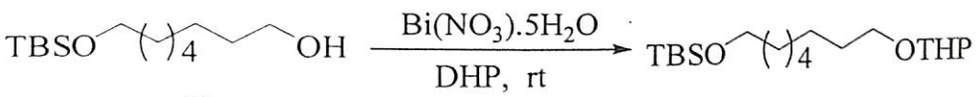


66 67

Scheme 27

Over the years, a huge number of methods have been developed and being added in the arsenal of organic synthesis literature for the same transformation. Among them, some of the recently reported methods are: $ZrCl_4$,[91] I_2,[92] LiBr,[93] acetonyltriphenylphosphonium bromide,[94] n-tetrabutylammonium tribromide (TBATB),[95] aluminium chloride hexahydrate,[96] $Bi(OTf)_3$,[97] dialkylimidazolium tetrachloroaluminates,[98] $InCl_3$ immobilized in ionic liquids,[99] H_2O,[100] bromodimethylsulfonium bromide[101] and cupric sulfate pentahydrate.[18f]

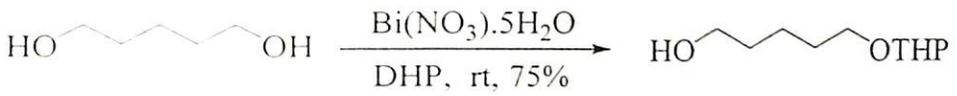
Very recently, we have shown bismuth nitrate pentahydrate as an efficient catalyst for the same transformation as shown in Scheme 28.[18a]



68 69

Scheme 28

The notable advantages of this method are non-aqueous work-up, compatability in presence of a large number of other protecting groups. In addition selective mono protection of symmetric diols can be achieved using the same protocol as shown below (Scheme 29).



70 71

Scheme 29

Very recently Bartoli *et al.* reported that a combination of $CeCl_3 \cdot 7H_2O$/NaI is an effective combination for tetrahydropyranylation of hydroxyl group under solvent-free conditions.[102] Although most of the methods provide good yields, still some of them encounter one or the other difficulties such as requirement of harsh reaction conditions, longer reaction times, involvement of more expensive and moisture sensitive catalysts. Therefore, development of new synthetic methods for tetrahydropyranylation of hydroxyl compounds is still in demand.

From the above literature survey, we realized that $HClO_4$-SiO_2 is a cheap, readily accessible and highly efficient as well as reusable catalyst in organic synthesis. Moreover, there are some scope to devise new methodologies for the protection of aldehydes and hydroxyl functionalities as acylal, thioacetal, oxathioacetal and THP ethers. Therefore, we perceived that the supported reagent $HClO_4$-SiO_2 might be useful to overcome some of the existing limitations. The successful results for the protection of carbonyl group as *gem*-diacetate will be discussed in Section A and thioacetalisation and oxathioacetalisation and pyranylation will be addressed in Section B of this Chapter.

SECTION A

PRESENT WORK ON *GEM*-DIACYLATION OF ALDEHYDES USING SILICA SUPPORTED PERCHLORIC ACID ($HClO_4$-SiO_2)

RESULTS AND DISCUSSION

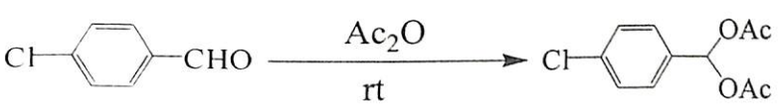
The application of solid supported reagent $HClO_4$-SiO_2 as well as literature survey on *gem*-diacylation of aldehydes and its further scope are already highlighted in the review section. Therefore, we thought that the reagent $HClO_4$-SiO_2 could be further explored as a versatile reagent both from its catalytic activity and economic point of view. In addition, we found the shortcomings of existing methodologies for the protection of carbonyl and hydroxyl functionalities, as *gem*-diacetates, dithioacetals, oxathioacetals and tetrahydropyranyl ethers respectively during literature survey. The protection of aldehydes as acetal or oxathioacetal or dithioacetal or acylal is a common practice for manipulation of other functional groups during multi-step synthesis. Sometimes the protection of aldehydic compounds as *gem*-diacetate is usually preferred due to ease of preparation and their stability towards basic and neutral conditions. In addition, the preparation of 1,1-diacetates from the corresponding aldehydes can be achieved very easily in the presence of ketones. As a part of our ongoing research project to develop newer synthetic methodologies particularly in protection and deprotection chemistry we perceived that silica-supported perchloric acid ($HClO_4$-SiO_2) might be a useful, effective, versatile and reusable catalyst for chemoselective protection of aldehydes as acylals. Interestingly as per our speculation, perchloric acid immobilized on silica gel was found to be an efficient and expedient catalyst for geminal diacylation of aldehydes as shown in Scheme 30.

$$RCHO \xrightarrow[\text{rt, 2 -10 min, 85-98\%}]{Ac_2O,\ HClO_4\text{-}SiO_2\ (0.5\ mol\%)} RCH(OAc)_2$$

R = aliphatic / aromatic

Scheme 30

For our requirements, we initially prepared the catalyst silica supported perchloric acid by following the literature procedure.[1a] To prove the better catalytic activity of this supported reagent over the aqueous perchloric acid, we have carried out a model study with 4-chlorobenzaldehyde (**51**) and acetic anhydride using various catalytic conditions as shown in Table 1.



Scheme 31

Table 1. The results of the reaction of 4-chlorobenzaldehyde (**51**) with acetic anhydride in different catalytic conditions at room temperature.

Run	Catalyst	Time	% Yield[a,b]
1.	No catalyst	12 h	0
2	SiO_2 (10 mg/ mmol)	12 h	43
3.	Aqueous $HClO_4$ (0.5 mol%)	20 min	93
4.	$HClO_4$-SiO_2 (10 mg/mmol, 0.5 mol %)	2 min	98

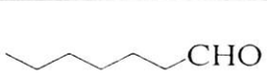
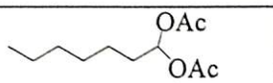
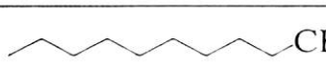
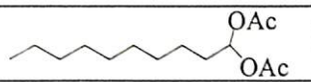
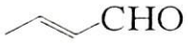
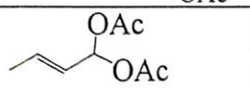
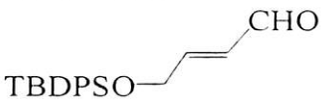
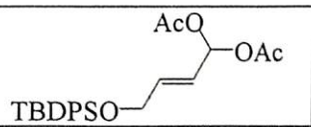
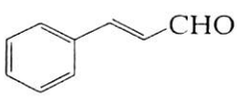
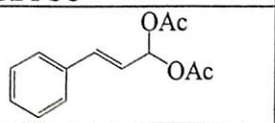
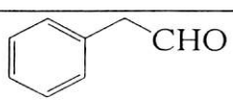
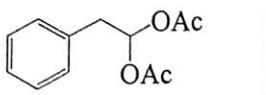
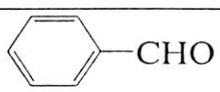
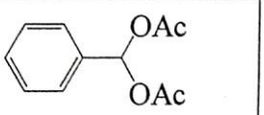
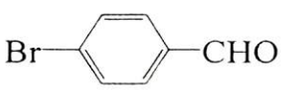
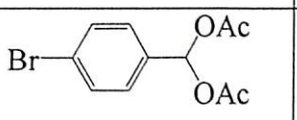
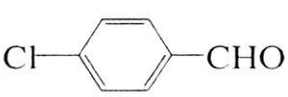
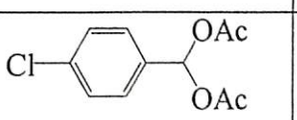
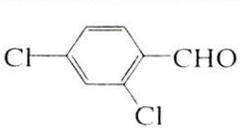
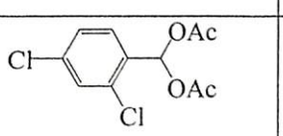
[a]Isolated yields, [b]All the reactions were carried out in 5-mmol scales with 2 equivalents of acetic anhydride under solvent free conditions.

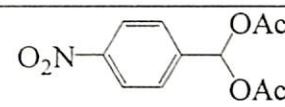
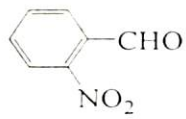
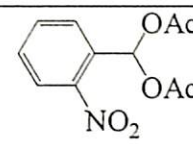
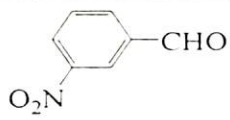
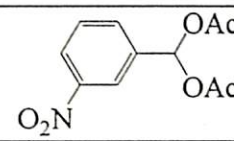
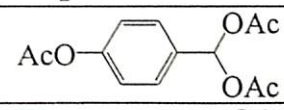
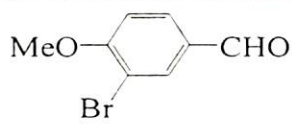
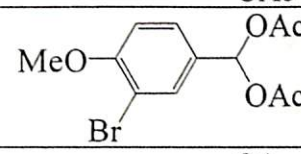
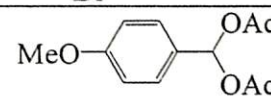
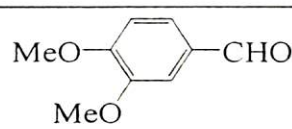
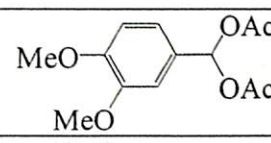
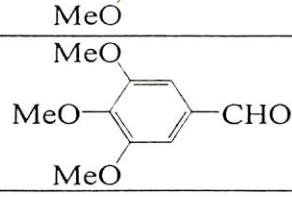
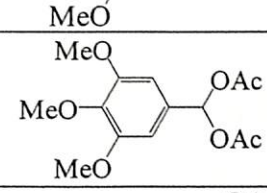
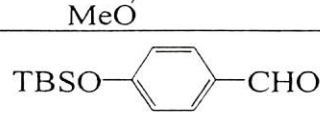
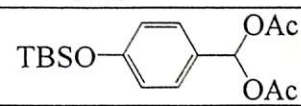
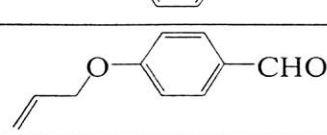
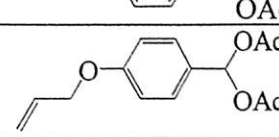
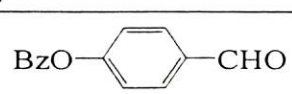
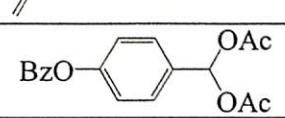
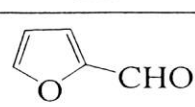
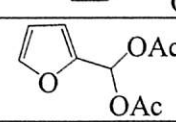
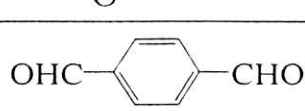
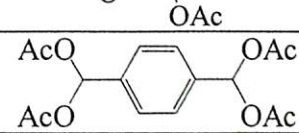
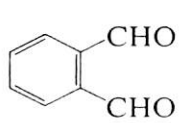
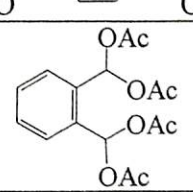
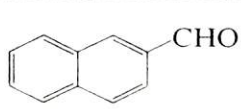
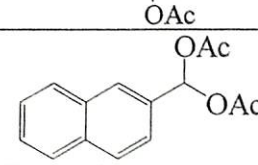
The product **102** was characterized by recording IR, ^{1}H NMR spectrum as well as by elemental analysis. The disappearance of CHO absorption at 1705 cm^{-1} as well as appearance of a strong peak at 1748 cm^{-1} in IR spectrum indicates the formation of product. Again in ^{1}H NMR spectrum absence of aldehydic proton at δ 9.98 as well as the presence of two singlet peaks at δ 2.12 (s, 6H, 2 x $COCH_3$) and 7.63 (s, 1H, C*H*$(OAc)_2$) respectively clearly indicates the formation of product. After confirmation of the formation of the product, we turned our attention to see the efficacy of the supported reagent $HClO_4$-SiO_2 over the aqueous $HClO_4$. The results of the Table 1 clearly demonstrate that silica-supported perchloric acid is an effective catalyst in terms of reaction time and yield obtained. Then, we attempted the reaction of 1-heptanal (**72**) with two equivalents of acetic anhydride in presence of catalytic amount of $HClO_4$–SiO_2 at room temperature. The reaction was complete within 5 min and the pure acylal (**96**) was obtained in 86% yield just passing through a small silica gel column. Similarly, 1-decanal and crotyl aldehyde (**73, 74**, **28** and **35**) provided the corresponding acylals under the similar reaction conditions. It is noteworthy to mention that substrate **28** undergoes *gem*-diacylation within shorter time than the reported method[37] with good yields by keeping intact the acid sensitive protecting group *tert*-butyldiphenylsilyl ethers and the corresponding product **29** is a valuable key ingredient for the synthesis of a potent antifugal agent sphingofungin F.[20] In the same manner phenacyl aldehyde (**75**) was also converted to the corresponding *gem*-diaceates using the same catalyst within a short while. Interestingly, we did not observe any cyclotrimerization for aliphatic aldehydes (**72**, **73** and **75**) under the experimental conditions. Likewise, a wide variety of aromatic aldehydes containing both electron-donating and electron-withdrawing substituents underwent *gem*-diacylation within a very short reaction time and the results are

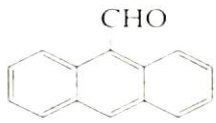
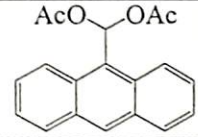
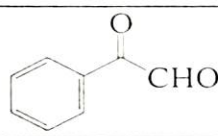
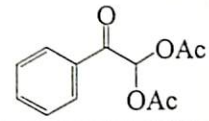
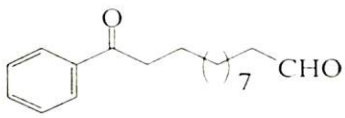
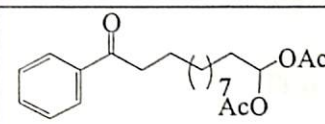
summarized Table 2. It is important to point out that the formation of acylals from the aldehydes containing electron-donating group such as methoxy, are failure by some of the reported procedures whereas by using this protocol it can be easily achieved (substrates **84-86**) without any difficulty in good yields.

Likewise, various aldehydes containing other protecting groups such as TBS (**87**), allyl (**88**) and benzoyl (**89**) were smoothly converted to the desired acylals by keeping the protecting groups intact in good yields. Moreover, acid sensitive aldehyde (**90**) and

Table 2. Formation of acylals from the corresponding aldehydes catalyzed by $HClO_4$-SiO_2

S. No	Substrate	Time / min	Product	Product No.	% Yield
72		5		**96**	86
73		5		**97**	91
74		2		**98**	83
28		10		**29**	95
35		5		**36**	98
75		5		**99**	85
76		2		**100**	97
77		2		**101**	96
51		2		**102**	98
78		5		**103**	95

79		5		**104**	96
80		5		**105**	93
81		5		**106**	96
82		5		**107**	82
83		5		**108**	94
84		5		**109**	91
85		5		**110**	93
86		5		**111**	96
87		3		**112**	87
88		5		**113**	93
89		5		**114**	91
90		2		**115**	90
91		5		**116**	90
92		5		**117**	95
93		5		**118**	94

94		5		**119**	96
95		10		**120**	93
60		10		**121**	94

[a] Isolated yields, melting point and the reference for spectroscopic data

dialdehydes (**91-92**) can also be transformed to the required diacylals (**116-117**) without any difficulty. Furthermore, polycyclic aromatic aldehydes (**93** and **94**) were also provided the desired acylals in very good yields. IR, ^{1}H NMR and ^{13}C NMR spectra of the compounds **109** and **119** are given in Figure **1-6**, respectively.

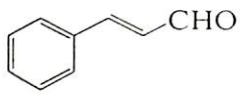
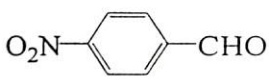
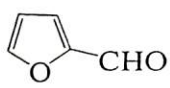
Interestingly, the aldehyde functionality of the keto aldehydes (substrates **95** and **60**) can be chemoselectively achieved in good yields under identical conditions. Remarkably, it is also possible to carry out the same transformation in a 50-mmol scale or even more without any difficulty.

Next for checking the reusability of the catalyst, we have performed the reaction in the following way. The reaction of 4-nitrobenzaldehyde (**79**) with acetic anhydride was carried out using 0.5 mol% $HClO_4$-SiO_2 in 50 mmol scale, after completion of the reaction the catalyst was filtered off and washed with dry ether and finally it was dried under vacuum for 30 min, which was reused for the next cycle. The recovered catalyst was reused for another two more consecutive times for acylation of 4-nitrobenzaldehyde with acetic anhydride and it provided the desired acylal in 89 % and 87 % yield within 10 min.

The generality and the scope of the reagent can be easily reflected from the comparison Table 3. The superiority of silica supported perchloric acid over the metal triflates and some of the recently reported heterogeneous catalyst can be easily visualized at a glance by comparing the results of some of the substrates. Here, we have chosen some of the substrates as model substrate and the comparison is made with respect to the % of yields, reaction time and mol % of the catalyst used. It is noteworthy to mention that cinnamaldehyde and 4-nitrobenzaldehyde provide the desired acylal within 5 min with

much better yield than other reported methods. Again, the present protocol is much more effective for the substrate furfural in terms of reaction timing as well as % of yield, which is usually difficult to achieve by some of the reported procedures.[42]

Table 3. Comparison of $HClO_4$- SiO_2 with other catalyst for gem-diacylation of aldehydes

Substrate	Catalyst	Catalyst mol %	Reaction time	% Yields[a]
	NBS	20	48 h	80[25]
	$Bi(OTf)_3$	0.1	15 min	70[30]
	TBATB	10	5.2 h	87[41]
	$AlPW_{12}O_{40}$	0.1	5 min	92[42]
	$Cu(OTf)_2$	2.5	3 h	76[28]
	$H_6P_2W_{18}O_{62}\cdot 24\ H_2O$	1	30 min	98[40]
	$HClO_4$-SiO_2	0.5	5 min	98
	NBS	10	8 h	98[25]
	TBATB	10	22 h	78[41]
	$AlPW_{12}O_{40}$	0.1	45 min	89[42]
	$H_6P_2W_{18}O_{62}\cdot 24\ H_2O$	1	30 min	92[40]
	$HClO_4$-SiO_2	0.5	5 min	96
	NBS	10	24 h	81[25]
	TBATB	10	7 h	80[41]
	$AlPW_{12}O_{40}$	0.1	30 min	0[42]
	$H_6P_2W_{18}O_{62}\cdot 24\ H_2O$	1	30 min	88[40]
	$HClO_4$-SiO_2	0.5	2 min	90

[a] Reference for earlier methods.

In conclusion, we believe that silica-supported perchloric acid is a highly effective, cheap and reusable catalyst for *gem*-diacylation of aldehydes. A wide variety of aromatic and aliphatic aldehydes can be easily transformed into the corresponding acylals using 0.5 mol% $HClO_4$-SiO_2 within 2-10 min under solvent-free conditions at room temperature. The notable advantages of this protocol are: require less reaction time and stoichiometric amount of acetic anhydride, highly economic and the catalyst is recyclable.

SECTION A

A RAPID AND MILD METHOD FOR *GEM*-DIACYLATION OF ALDEHYDES USING SILICA SUPPORTED PERCHLORIC ACID ($HClO_4$-SiO_2)

EXPERIMENTAL

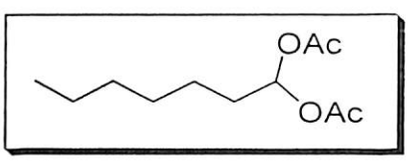
Preparation of silica supported perchloric acid ($HClO_4$-SiO_2):

$HClO_4$ (1.8 gm, 12.5 mmol, as a 70% aq solution) was added to a suspension of SiO_2 (230-400 mesh, 23.7 g) in Et_2O (70.0 mL). The mixture was concentrated and the residue was heated at 100 ^{0}C for 72 hours under vacuum to furnish $HClO_4$-SiO_2 (0.5 mmol/g) as a free flowing powder (50 mg = 0.025 mmol of $HClO_4$).

Typical procedure for the preparation of acylals from 4-nitrobenzaldehyde:

To a mixture of 4-nitrobenzaldehyde (5 mmol, 0.750 g) and freshly distilled acetic anhydride (10 mmol, 0.92 mL), the catalyst $HClO_4$-SiO_2 (50 mg, 0.025 mmol) was added and the mixture was stirred at room temperature. When the reaction was complete as judged by TLC, diethyl ether (2 x 25 mL) was added into it. The ether layer was separated, washed with saturated solution of $NaHCO_3$ (5 mL), water (2 x 10 mL) and finally dried over anhydrous $MgSO_4$. After removal of ether, the residue was obtained as almost pure acylal, which was recrystallized from hexane. The desired product was obtained as yellowish crystalline solid (1.22 g) in 96% yield

1,1-diacetate of 1-heptanal (96):



Nature: Gummy liquid

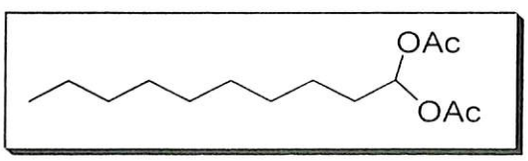
Yield: 86% (0.930 g)

IR (Neat): 2930, 2863, 1762, 1465, 1378, 1250, 1214, 1112, 1015, 968 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (t, 3H, J = 6.8 Hz, CH_3), 1.22-1.40 (m, 8H, CH_2), 1.66-1.80 (m, 2H, CH_2), 2.07 (s, 6H, 2 x $COCH_3$), 6.77 (t, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{20}O_4$	C 61.09	C 60.89
216.28	H 9.32	H 9.27

1,1-diacetate of 1-decanal (97):



Nature: Gummy liquid

Yield: 91% (1.176 g)

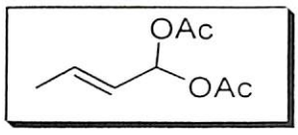
IR (Neat): 2930, 2858, 1767, 1470, 1370, 1250, 1209 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J = 6.8 Hz, 3H, CH_3), 1.26 (bs, 14H, CH_2), 1.72-1.76 (m, 2H, CH_2), 2.07 (s, 6H, $COCH_3$), 6.75 (t, 1H, J = 5.6 Hz, $CH(OAc)_2$) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): 14.2, 20.9 (2C), 22.7, 23.5, 29.2, 29.3, 29.4, 29.5, 31.9, 33.2, 90.5, 168.8 (2C) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{14}H_{26}O_4$	C 65.09	C 64.89
258.36	H 14.14	H 14.06

1,1-diacetate of 1-crotonaldehyde (98):



Nature: Gummy liquid

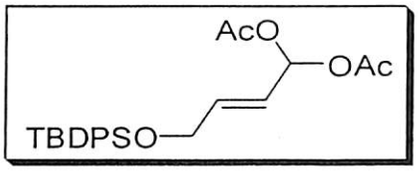
Yield: 83% (0.715 g)

IR (Neat): 1752, 1637, 1214, 1135, 1011 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.75 (dd, J = 8.4 Hz, J = 2.4 Hz, 3H, CH_3), 2.08 (s, 6H, $COCH_3$), 5.55 (dd, J = 8.4 Hz, J = 15.6 Hz, 1H, =CH), 6.03 (m, 1H, $=CHCH_3$), 7.06 (d, 1H, J = 6.4 Hz, $CH(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_8H_{12}O_4$	C 55.81	C 55.78
172.18	H 7.02	H 7.09

1,1-diacetate of *4-tert*-butyldiphenylsilyloxy-but-2-ene 1-al (29):



Nature: Gummy liquid

Yield: 95% (2.026 g)

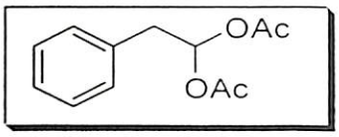
IR (Neat): 3073, 2970, 2940, 2863, 1762, 1434, 1372, 1244, 1208, 1121, 1009, 707 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.07 (s, 9H, $Si(CH_3)_3$), 2.10 (s, 6H, 2 x $-COCH_3$), 4.23 (bs, 2H, OCH_2), 5.91 (ddt, 1H, J = 2.0 Hz, J = 6.4 Hz, J = 15.6 Hz, =CH), 6.06 (dt, 1H, J = 2.8 Hz, J = 15.6 Hz, =CH), 7.17 (d, 1H, J = 6.4 Hz, $CH(OAc)_2$), 7.34-7.41 (m, 6H, ArH), 7.63 (dd, 4H, J = 1.2 Hz, J = 7.6 Hz, ArH) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): 19.4, 21.0 (2C), 26.9 (3C), 62.8, 89.2, 122.0, 127.6 (4C), 129.6 (2C), 133.0, 135.3 (4C), 135.8 (2C), 168.5 (2C) ppm.

Elemental Analysis	Calculated	Found
$C_{24}H_{30}O_5Si$	C 67.58	C 67.38
426.58	H 7.09	H 7.01

1,1-diacetate of phenylacetaldehyde (99):



Nature: Gummy liquid

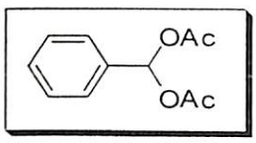
Yield: 85% (0.945 g)

IR (Neat): 3063, 3032, 2930, 1757, 1603, 1496, 1424, 1273, 1209, 1086 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.94 (s, 6H, 2 x $COCH_3$), 2.97 (d, 2H, J = 5.7 Hz, CH_2Ph), 6.84 (t, 1H, J = 5.7 Hz, C*H*$(OAc)_2$), 7.07-7.26 (m, 5H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{14}O_4$	C 64.85	C 64.78
222.24	H 6.35	H 6.29

1,1-diacetate of benzaldehyde (100):



Nature: Solid, mp: 45 °C

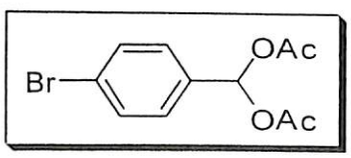
Yield: 97% (1.010 g)

IR (KBr): 3068, 2991, 2940, 1752, 1383, 1250, 1204, 1055, 1009, 974 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 6H, 2 x $COCH_3$), 7.40-7.43 (m, 3H ArH), 7.51-7.56 (m, 2H, ArH), 7.71 (s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{12}O_4$	C 63.46	C 63.57
208.21	H 5.81	H 5.79

1,1-diacetate of 4-bromobenzaldehyde (101):



Nature: Solid, mp: 84 °C

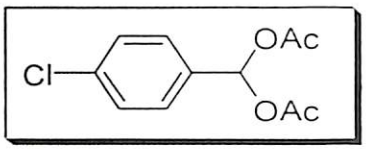
Yield: 96% (1.378 g)

IR (KBr): 3063, 2986, 2930, 1762, 1593, 1486, 1378, 1245, 1214, 1076, 1015, 968 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 6H, 2 x $COCH_3$), 7.39 (d, 2H, J = 8.4 Hz, ArH), 7.53 (d, 2H, J = 8.8 Hz, ArH), 7.61 (s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{11}BrO_4$	C 46.02	C 46.21
287.10	H 3.86	H 3.80

1,1-diacetate of 4-chlorobenzaldehyde (102):



Nature: White Solid, mp: 80 °C

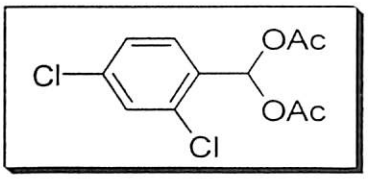
Yield: 98% (1.189 g)

IR (KBr): 1748, 1611, 1492, 1421, 1379, 1261, 1199, 1072, 937, 826 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 6H, 2 x $COCH_3$), 7.37 (d, 2H, J = 8.8 Hz, ArH), 7.45 (d, 2H, J = 8.8 Hz, ArH), 7.63 (s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{11}ClO_4$	C 54.41	C 54.12
242.59	H 4.57	H 4.50

1,1-diacetate of 2,4-dichlorobenzaldehyde (103):



Nature: Solid, mp: 100-102 °C.

Yield: 95% (1.316 g)

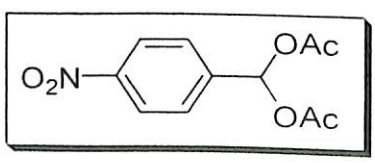
IR (KBr): 3088, 3022, 2945, 1757, 1434, 1378, 1235, 1199, 1081 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.14 (s, 6H, 2 x -$COCH_3$), 7.31 (d, J = 7.6 Hz, 1H, ArH), 7.43 (s, 1H, ArH), 7.50 (d, J = 7.9 Hz, 1H, ArH), 7.91 (s, 1H, C*H*$(OAc)_2$) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7 (2C), 87.7, 127.4, 128.8, 129.9, 132.0, 133.9, 136.3, 168.3 (2C) ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{10}Cl_2O_4$	C 47.68	C 47.49
277.10	H 3.64	H 3.59

1,1-diacetate of 4-nitrobenzaldehyde (104):



Nature: Yellow crystals. mp: 125°C.

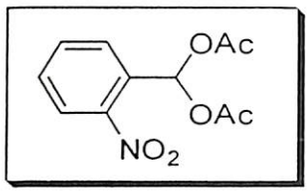
Yield: 96% (1.215 g)

IR (KBr): 3124, 3072, 3010, 1760, 1611, 1535, 1379, 1351, 1237, 1029, 1067, 972 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.16 (s, 6H, 2 x $COCH_3$), 7.69 (s, 1H, C*H*$(OAc)_2$), 7.72 (d, J = 6.4 Hz, 2H, ArH), 8.27 (d, J = 8.4 Hz, 2H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{11}NO_6$	C 52.18	C 51.96
253.21	H 4.38	H 4.31
	N 5.53	N 5.48

1,1-diacetate of 2-nitrobenzaldehyde (105):



Nature: Solid, mp: 85-86 °C.

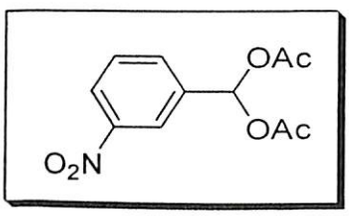
Yield: 93% (1.18 g)

IR (KBr): 1771, 1587, 1525, 1454, 1377, 1351, 1244, 1208, 1105, 1075, 1025 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 6H, 2 x $COCH_3$), 7.57-7.61 (m, 1H, ArH), 7.67-7.74 (m, 2H, ArH) 8.05 (dd, 1H, J = 0.8 Hz, J = 7.6 Hz, ArH), 8.20 (s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{11}NO_6$	C 52.18	C 51.93
253.21	H 4.38	H 4.30
	N 5.53	N 5.38

1,1-diacetate of 3-nitrobenzaldehyde (106):



Nature: Solid, mp: 65 °C.

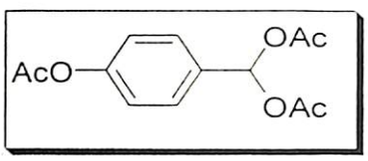
Yield: 96% (1.215 g)

IR (KBr): 1773, 586, 1521, 1454, 1372, 1349, 1244, 1208, 1105, 1067, 1069, 1024 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 6H, 2 x $COCH_3$), 7.60 (t, J = 8.0 Hz, 1H, ArH), 7.73 (s, 1H, C*H*$(OAc)_2$), 7.83 (d, J = 8.0 Hz, 1H, ArH), 8.27 (d, J = 8.0 Hz, 1H, ArH), 8.40 (s, 1H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{11}H_{11}NO_6$	C 52.18	C 51.94
253.21	H 4.38	H 4.28
	N 5.53	N 5.47

1,1-diacetate of 4-acetoxybenzaldehyde (107):



Nature: Solid. mp: 57 °C.

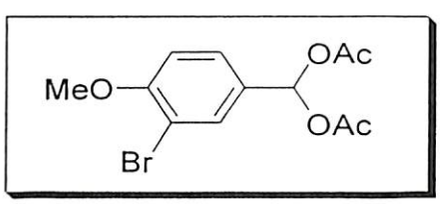
Yield: 82% (1.091 g)

IR (KBr): 2948, 2889, 2854, 1755, 1735, 1451, 1369, 1240, 1081, 910 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.01 (s, 6H, 2 x $COCH_3$), 2.21 (s, 3H, $COCH_3$), 6.90 (d, J = 8.0 Hz, 2H, ArH), 7.40 (d, J = 8.0 Hz, 2H, ArH), 7.51(s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{14}O_6$	C 58.67	C 58.61
266.12	H 5.30	H 5.34

1,1-diacetate of 3-bromo-4-methoxybenzaldehyde (108):



Nature: Solid, mp: 81-83 °C.

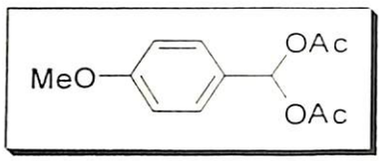
Yield: 94% (1.491 g)

IR (KBr): 3077, 3015, 2967, 1762, 1605, 1505, 1360, 1258, 936 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.12 (s, 6H, 2 x -$COCH_3$), 3.91 (s, 3H, OCH_3), 6.89 (d, J = 8.5 Hz, 1H, ArH), 7.42 (dd, J = 8.5 Hz, J = 2.2 Hz, 1H, ArH), 7.57 (s, 1H, C*H*$(OAc)_2$) 7.71 (d, J = 2.2 Hz, 1H, ArH) ppm.

Elemental Analysis	Calculated	Found
$C_{12}H_{13}BrO_5$	C 45.45	C 45.21
317.13	H 4.13	H 4.06

1,1-diacetate of 4-methoxybenzaldehyde (109):



Nature: Solid, mp: 66 ^{0}C

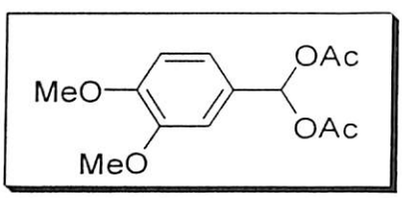
Yield: 82% (1.084 g)

IR (Neat): 3068, 3017, 2976, 2838, 1752, 1619, 1527, 1434, 1373, 1260, 1209, 1173, 1066, 933 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 6H, -$COCH_3$), 3.81 (s, 3H, OCH_3), 6.89 (d, J = 8.8 Hz, 2H, ArH), 7.43 (d, J = 8.8 Hz, 2H, ArH) 7.60(s, 1H, CH($OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{14}O_5$	C 60.50	C 60.55
238.24	H 5.92	H 5.89

1,1-diacetate of 3,4-dimethoxybenzaldehyde (110):



Nature: Solid, mp: 64 °C

Yield: 93% (1.247 g)

IR (KBr): 2965, 2847, 1751, 1602, 1525, 1464, 1387, 1346, 1254, 1208, 1152, 1064, 998 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 (s, 6 H, 2x $COCH_3$), 3.88 (s, 3 H), 3.92 (s, 3 H), 6.88 (d, J = 8.0 Hz, 1H, ArH), 7.05 (s, 1 H, ArH), 7.11 (d, J = 8.0 Hz, 1H, ArH), 7.62 (s, 1 H, CH($OAc)_2$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7 (2C), 55.9 (2C), 89.8, 109.6, 111.5,119.5, 128.0, 149.1, 150.1, 168.7 (2C) ppm.

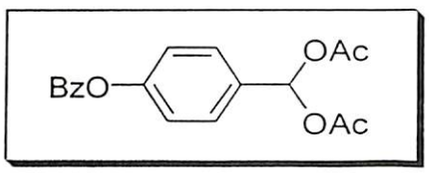
Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{16}O_6$	C 58.21	C 57.95
268.26	H 6.01	H 5.96

OCH_2), 5.29 (d, J = 10.2 Hz, 1H), 5.41 (d, J = 17.3 Hz, 1H), 5.98-6.10 (m, 1H), 6.92 (d, J = 8.6 Hz, 2H, ArH), 7.44 (d, J = 8.6 Hz, 2H, ArH), 7.61(s, 1H, $CH(OAc)_2$) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): 20.9 (2C), 68.9, 89.8, 114.8 (2C), 117.9, 127.9, 128.2 (2C), 132.9, 158.5, 168.8 (2C) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{14}H_{16}O_5$	C 63.63	C 63.45
264.28	H 6.10	H 6.05

1,1-diacetate of 4-benzoyloxybenzaldehyde (114):



Nature: Solid, mp: 97-98 ^{0}C

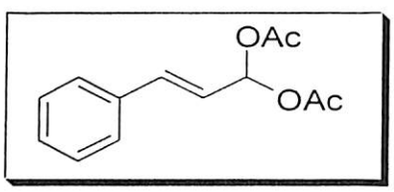
Yield: 72% (1.182 g)

IR (KBr): 1688, 1754 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.14 (s, 6H, $COCH_3$), 7.26 (d, J = 8.4 Hz, 2H, ArH), 7.52 (t, J = 8.0 Hz, 2H, ArH), 7.59 (d, J = 8.4 Hz, 2H, ArH), 7.65 (t, J = 7.2 Hz, 1H, ArH), 7.70 (s, 1H, C*H*$(OAc)_2$), 8.20 (dd, J = 8.4 Hz, J = 1.2 Hz, 2H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{18}H_{16}O_6$	C 65.85	C 65.92
328.32	H 4.91	H 4.89

1,1-diacetate of cinnamaldehyde (36):



Nature: Solid, mp: 84 °C.

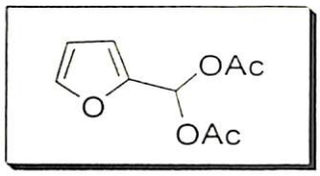
Yield: 98% (0.229 g)

IR (KBr): 3065, 3032, 2930, 1749, 1602, 1486, 1426, 1271, 1207, 1086 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.16 (s, 6H, $COCH_3$), 6.20 (dd, J =16.0 Hz, J = 6.8 Hz, 1H, =CH), 6.87 (d, J = 16.4 Hz, 1H, =CH), 7.30-7.34 (m, 4H, ArH & $CH(OAc)_2$), 7.42 (d, J = 8.4 Hz, 2H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{13}H_{14}O_4$	C 66.66	C 66.70
234.25	H 6.02	H 5.99

1,1-diacetate of furfuraldehyde (115):



Nature: Solid, mp: 54 ^{0}C

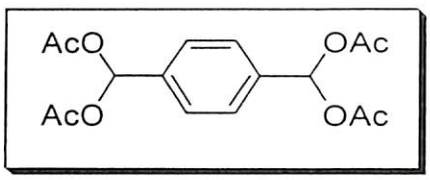
Yield: 90% (0.892 g)

IR (KBr): 1757, 1373, 1242, 1201, 1152, 1012, 930, 750, 602 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.13 (s, 6H, $COCH_3$), 6.38 (m, 1H), 6.53 (d, J = 3.3 Hz, 1H), 7.45 (d, J = 2.0 Hz, 1H,), 7.71 (s, 1H, $CH(OAc)_2$) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_9O_5H_{10}$	C 54.55	C 54.52
198.17	H 5.09	H 5.05

1,1-diacetate of terephthaldehyde (116):



Nature: Solid, mp: 174-175 °C.

Yield: 90% (1.522 g)

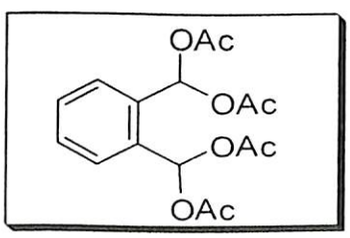
IR (KBr): 3119, 3032, 2940, 1752, 1603, 1434, 1378, 1250, 1076, 963, 861 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.13 (s, 12 H, 4 x $COCH_3$), 7.57 (s, 4H, ArH), 7.68 (s, 2H, $C\underline{H}(OAc)_2$)ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.8 (2C), 89.3 (2C), 127.1 (4C), 137.0 (2C), 168.7 (2C) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{18}O_8$	C 56.80	C 56.69
338.31	H 5.36	H 5.28

1,1-diacetate of phthaldehyde (117):



Nature: Solid, mp: 137-139 °C.

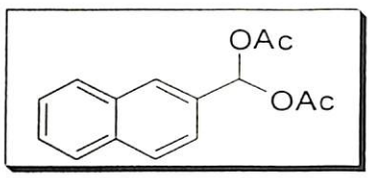
Yield: 95% (1.607 g)

IR (KBr): 3086, 2953, 1766, 1605, 1434, 1377, 1258, 1116 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.11 (s, 12 H, 4 x $COCH_3$), 7.46-7.49 (m, 2H, ArH), 7.61-7.63 (m, 2H, ArH), 8.00 (s, 2H, 2 x $CH(OAc)_2$) ppm.

Elemental Analysis	Calculated	Found
$C_{16}H_{18}O_8$	C 56.80	C 56.64
338.31	H 5.36	H 5.26

1,1-diacetate of naphthaldehyde (118):



Nature: Solid, mp: 101 ^{0}C

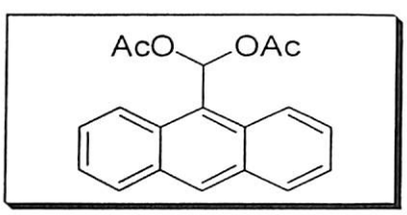
Yield: 94% (1.214 g)

IR (KBr): 3068, 2991, 2940, 1752, 1383, 1250, 1204, 1055, 1009, 974, 943, 820 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.16 (s, 6H, $COCH_3$), 7.26 (d, J = 2.6 Hz, 1H, ArH), 7.53 (d, J = 4.5 Hz, 1H, ArH), 7.62 (d, J = 8.4 Hz, 1H, ArH), 7.85-7.90 (m, 4H, ArH), 7.99 (s, 1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	Calculated	Found
$C_{15}H_{14}O_4$	C 69.76	C 69.70
258.27	H 5.46	H 5.41

1,1-diacetate of anthranaldehyde (119):



Nature: Solid, mp: 197^{0}C

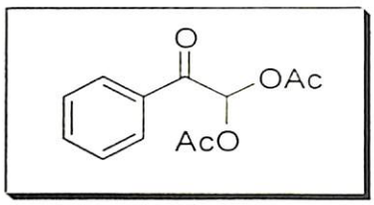
Yield: 96% (1.480 g)

IR (KBr): 3053, 2853, 2776, 1762, 1665, 1552, 1440, 1240, 1050, 958, 902, 723 cm^{-1}

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.12 (s, 6H, -$COCH_3$), 7.48 (t, J = 9.2 Hz, 2H, ArH), 7.59 (t, J = 8.0 Hz, 2H, ArH), 7.80 (d, J = 11.2 Hz, 2H, ArH), 8.52 (s, 1H, ArH), 8.69 (d, J = 11.6 Hz ,2H, ArH), 9.24 (s,1H, C*H*$(OAc)_2$) ppm.

Elemental Analysis	Calculated	Found
$C_{19}H_{16}O_4$	C 74.01	C 74.06
308.33	H 5.23	H 5.26

1,1-diacetate of phenyl glyoxal (120):



Nature: Solid, mp: 50-51 °C.

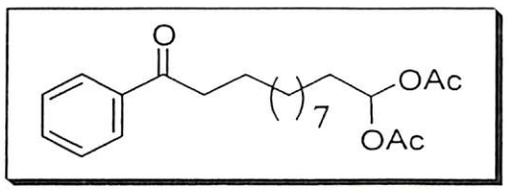
Yield: 93% (1.098 g)

IR (KBr): 3068, 2950, 1762, 1711, 1598, 1445, 1378, 1230, 1061, 963, 892, 774 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.18 (s. 6H, $COCH_3$), 7.49 (t, J = 6.4 Hz, ArH), 7.62 (s + t, 2H, J = 6.4 Hz, $CH(OAc)_2$ + ArH), 7.93 (t, J = 6.2 Hz, 2H, ArH) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{12}O_5$	C 61.06	C 61.11
236.22	H 5.12	H 5.12

1,1-diacetate of ketoaldehyde (121):



Nature: Solid, mp: 39-40 °C.

Yield: 94% (0.354g)

IR (KBr): 2919, 2858, 1752, 1680, 1455, 1378, 1271, 1209, 1112, 1020, 979 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.21-1.27 (m, 16H, $-CH_2$), 1.64-1.69 (m, 2H, $-CH_2$), 2.00 (s, 6H, $-COCH_3$), 2.89 (t, J = 7.6 Hz, 2H, $-CH_2$), 6.70 (t, J = 5.6 Hz, 1H, $CH(OAc)_2$), 7.39 (dd, J = 8.0 Hz, J = 1.4 Hz, 2H, ArH), 7.46 (dd, J = 7.3 Hz, J = 1.4 Hz, 1H, ArH), 7.89 (dd, J = 1.2 Hz, J = 8.2 Hz, 2H, ArH)ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): 20.83 (2C), 23.36, 24.35, 29.13, 29.36 (2C), 29.40 (3C), 33.15, 38.60, 90.55, 128.03 (2C), 128.53 (2C), 132.85, 137.08, 169.05 (2C), 200.60 ppm.

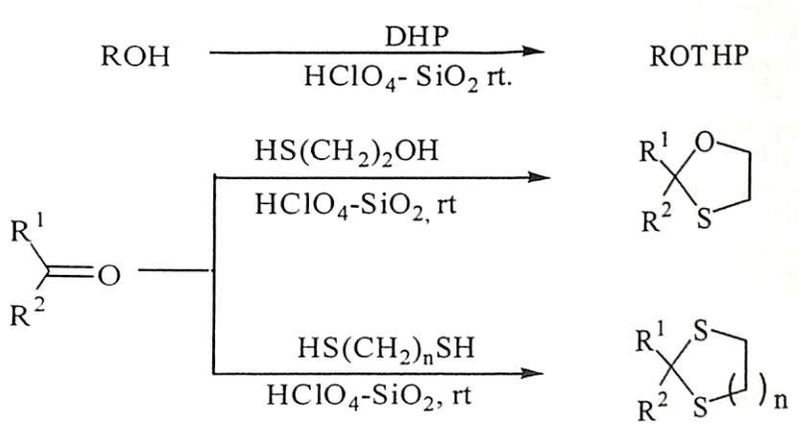
Elemental Analysis	**Calculated**	**Found**
$C_{22}H_{32}O_5$	C 70.19	C 70.01
376.49	H 8.57	H 8.49

SECTION B

PRESENT WORK ON TETRAHYDROPYRANYLATION, OXATHIOACETALIZATION AND THIOACETALIZATION OF HYDROXYL AND CARBONYL COMPOUNDS USING A CATALYTIC AMOUNT OF SILICA SUPPORTED PERCHLORIC ACID

RESULTS AND DISCUSSION

In Section A of this Chapter we have disclosed the catalytic activity of silica-supported perchloric acid, for the protection of aldehydes as *gem*-diacetates.[103] Again recently we have revealed that the same catalyst is highly efficient for the Michael addition of thiols to the electron deficient alkenes.[8] Moreover, in our earlier preliminary communication,[17] we reported that 70% aqueous perchloric acid is an effective catalyst for oxathioacetalization of carbonyl compounds. In continuation of our work on solvent-free conditions and utilization of heterogeneous catalysis, then we wanted to explore this versatile catalyst for other important transformation in protection deprotection chemistry such as tetrahydropyranylation, oxathioacetalization and thioacetalization. As a part of our ongoing project for the development of new synthetic methodologies using various new reagents, recently we have developed two new synthetic methodologies for the protection of hydroxyl compounds as THP ethers using $Bi(NO_3)_3.5H_2O$[18a] and $CuSO_4.5H_2O$[18f] as catalyst. In addition we have revealed that and acetyl chloride is an effective catalyst for thioacetalization of carbonyl compounds.[18c] We have described in the review section on tetrahydropyranylation, oxtathioacetalization, and thioacetalization and we realized that there is a scope to develop a new methodology though there are a large number of methods available in the literature. Some of the drawbacks of existing methods are: longer reaction time, harsh reaction conditions, poor yields, incompatible with other acid sensitive functional groups and cumbersome work-up procedure. Therefore we sought to explore the versatile reagent $HClO_4$-SiO_2 for these important transformations.

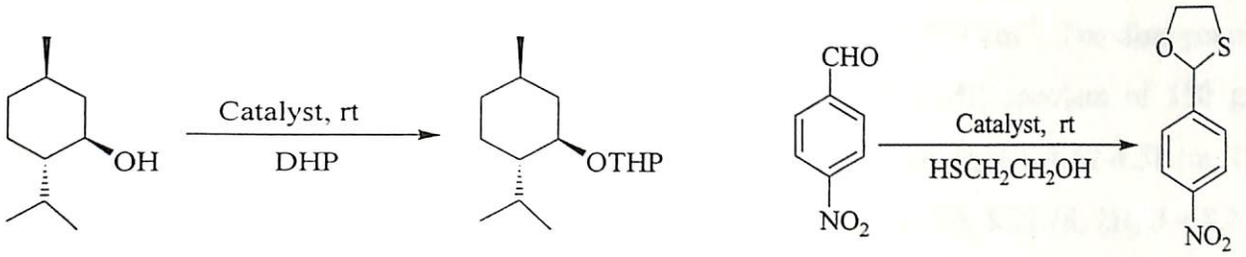


R = alkyl, aryl ; R^1= alkyl/ aryl ; R^2 = H/ alkyl /aryl; n = 1, 2

Scheme 32

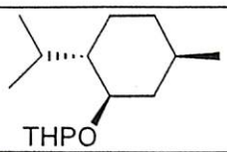
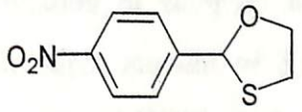
As per our speculation, a wide variety of alcohols and carbonyl compounds undergo tetrahydropyranylation, oxathioacetalization and thioacetalization at room temperature under mild reaction conditions using catalytic amount of $HClO_4$-SiO_2 as shown in Scheme 32.

For our study the catalyst $HClO_4$-SiO_2 was prepared by following the literature procedure.[1a] Next, to prove the better catalytic activity of silica supported perchloric acid over aqueous perchloric acid as well as to find out an optimal condition for both the transformations, *i.e.* tetrahydropyranylation and oxathioacetalization a set of reactions were studied under different catalytic conditions. Menthol and 4-nitrobenzaldehyde were chosen as the model substrates for tetrahydropyranylation and oxathioacetalization, respectively. For both the transformations the same sets of experiments were carried out and the results are summarized in Table 4.



Scheme 33

Table 4 The results of tetrahydropyranylation of menthol and oxathioacetalization of 4 nitrobenzaldehyde under different catalytic conditions at room temperature.

Run	Catalyst				
		Time	% Yield[a]	Time	% Yield[b]
1	No catalyst	12 h	0	12 h	0
2	SiO_2 (20 mg /mmol)	12 h	5	12 h	10
3	Aqueous $HClO_4$ (10 mol %)	10 min	76	1h	35[b]
4	$HClO_4$-SiO_2 (20mg/mmol, 1 mol %)	5 min	91[c]	30 min	65

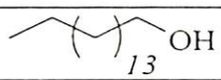
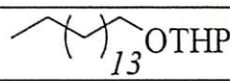
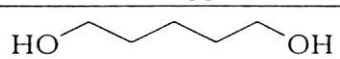
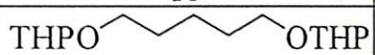
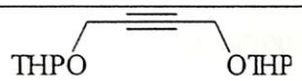
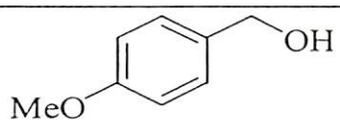
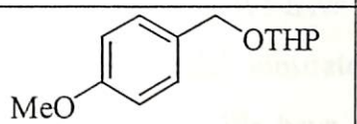
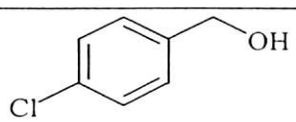
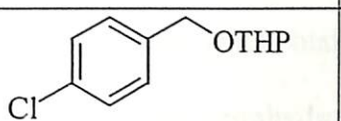
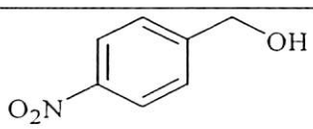
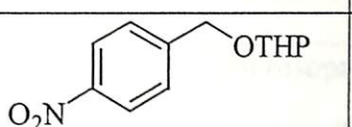
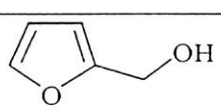
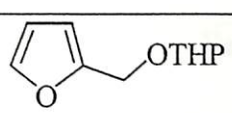
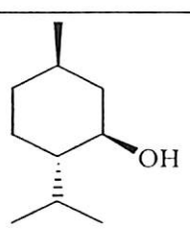
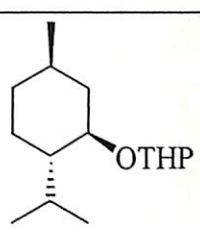
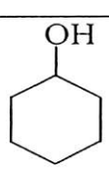
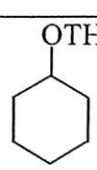
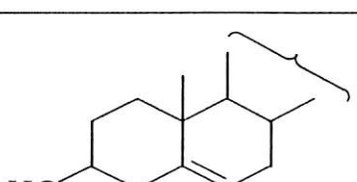
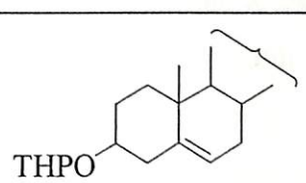
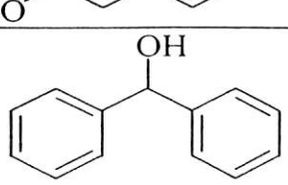
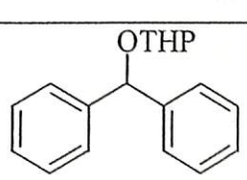
[a]Isolated yield. [b]Ref.17. [c] The catalyst can be recycled three consecutive cycles without lose of its activity and provided 85, and 82 % of yield within 5 and 10 min., respectively for THP protection.

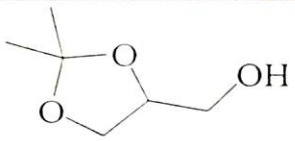
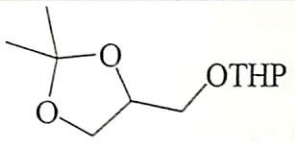
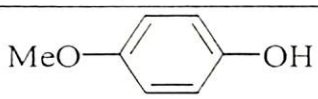
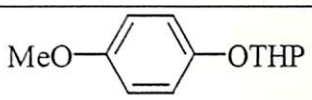
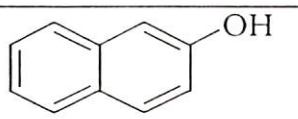
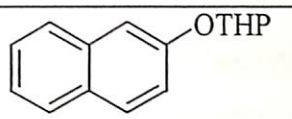
The formation of the THP ether of menthol (**142**) was confirmed by recording IR and ^{1}H NMR spectrum, as well as by elemental analysis. In IR spectrum, it exhibits absorbance values at 2955, 2879, 1465, 1383, 1189, 1137, 1035 cm^{-1}. The disappearance of hydroxyl absorption frequency in the IR spectrum clearly indicates the formation of THP ether. Similarly, ^{1}H NMR spectrum gives the signals at (mixture of diastereomers): δ 0.76-1.10 (m, 12H), 1.19-1.78 (m, 10H), 2.05-2.37 (m, 2H), 3.28-3.50 (m, 2H), 3.82-4.00 (m, 1H), 4.54-4.80 (m, 1H) ppm. The characteristic signal at δ 4.54-4.80 clearly indicates the formation of THP ether. In ^{13}C NMR spectrum, it shows peaks at δ 15.57, 16.23, 19.66, 20.23, 21.15, 21.20, 22.22, 22.34, 23.20, 25.14, 25.47, 25.58, 31.14, 31.28, 31.38, 31.60, 34.37, 34.53, 40.09, 43.52, 45.05, 48.12, 48.86, 50.10, 62.36, 63.01, 74.06, 79.88, 94.29, 101.26 ppm. The appearance of a new signal at δ 101.26 in the ^{13}C NMR spectrum support the formation of THP ether. Similarly, the product **150** exhibits absorbance values in the IR spectrum at 1603, 1526, 1347, 1070, 866, 717 cm^{-1}. The disappearance of carbonyl peak gives the indication of protection. ^{1}H NMR spectum of **150** gives signals at δ 3.21-3.30 (m, 2H, -SCH_2), 3.99-4.06 (m, 1H, -OCH_aH_b), 4.52-4.58 (m, 1H, -OCH_aH_b), 6.13 (s, 1H, -SCHO-), 7.60 (d, 2H, J = 8.7 Hz, ArH), 8.21 (d, 2H, J = 8.7 Hz, ArH) ppm. The appearance of new signals at 3.21-3.30 (m, 2H, -SCH_2), 3.99-4.06 (m, 1H, -OCH_aH_b), 4.52-4.58 (m, 1H, -OCH_aH_b), 6.13 (s, 1H, -SCHO-) clearly support the formation of the oxathioacetal.

Next to verify the scope of this reagent for tetrahydropyranylation of alcohols and phenols, firstly cetyl alcohol (**122**) was treated with 1.1 equivalent amount of 3,4-dihydro-2*H*-pyran (DHP) under solvent-free conditions with 1 mol% of $HClO_4$-SiO_2 at room temperature, it was smoothly converted to the corresponding THP ether (**135**) within 5 min in 95% yield. Similarly, a wide variety of other aliphatic as well as benzyl alcohols also gave desired THP ethers within a very short time. It is worthwhile to mention that this protocol is much faster in terms of reaction timing and also provide better yields as compared to the recently reported methods. Likewise, various secondary alcohols such as cyclohexanol (**129**), cholesterol (**130**) and even hindered alcohol benzhydrol (**131**) also underwent tetrahydropyranylation without any difficulty. Moreover, isopropylidine protected glycerol (**132**) provided desired THP ethers under similar experimental conditions keeping acid sensitive protecting group intact. Next, we were interested to see whether our protocol is applicable for phenolic substrates or not.

As per our expectation substrates like 4-methoxyphenol(**133**) and β-naphthol (**134**) were also converted to the required THP ethers **147** and **148** respectively in good yields.

Table 4. Tetrahydropyranylation of alcohols and phenols using $HClO_4$-SiO_2 as catalyst

S. No	Substrate	Time /min	Product	Product No	% Yield[a]
122		5		**135**	91
70		5		**136**	90
123		5		**137**	87
124		5		**138**	95
125		5		**139**	92
126		5		**140**	83
127		15		**141**	96
128		5		**142**	91
129		5		**143**	91
130		15		**144**	97
131		5		**145**	95

132		15		**146**	84
133		5		**147**	80
134		30		**148**	83

The generality and scope of this reagent for tetrahydropyranylation of alcohols and phenols can be rationalized at a glance from the comparison Table 5. We have chosen menthol (**128**) and 2,3-*O*-isopropylidene-*D*-(±)-glycerol(**132**) as the model substrates for comparison of this protocol with some of the recently reported methods. We have done the comparison with respect to mol % of catalyst used, reaction timing and yields obtained

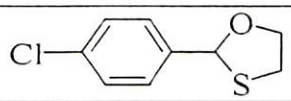
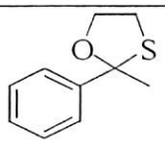
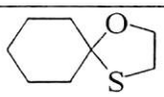
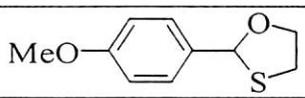
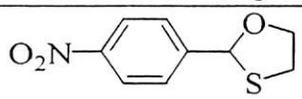
Table 5 Comparison of some of the recent methods for tetrahydropyranylation with $HClO_4$-SiO_2 protocol.

Catalyst[Ref]	Mol %	Menthol		2,3-*O*-isopropylidene-*D*-(±)-glycerol	
		Time	% Yields[a]	Time	% Yields[a]
$CuSO_4.5H_2O$[18f]	20	1 h	89	50 min	85
TBATB[95]	0.1	1 h	74	-	-
$Bi(OTf)_3.4H_2O$[97]	0.1	2 h	74	3.25 h	78
$Bi(NO_3)_3.5H_2O$[18a]	5	22 min	90	20 min	84
$HClO_4$-SiO_2	1	5 min	91	10 min	86

Subsequently, we were keen to see the usefulness of this reagent for other organic transformations such as masking of the carbonyl functionality as oxathioacetals and dithioacetals. Protection of carbonyl group as oxathioacetal or thioacetal is quite often necessary requirement in the synthesis of multifunctional organic molecules because of their stability under both acidic and basic conditions as well as they serve as acyl carbanion equivalents in *C-C* bond-forming reactions. Though over the years several methods are known in the literature for both oxathioacetalization and thioacetalization, still there is a need to find out better alternative, which might work efficiently under mild conditions. It is noteworthy to mention that in our preliminary communication[17] we had shown the catalytic activity of 70% aq. perchloric acid for the same transformation.

Notably, we got relatively low yield in case of 4-nitrobenzaldehyde as mentioned in Table 6. Therefore, we realized that silica-supported perchloric acid might provide better result as compared to aq. perchloric acid. To show our working hypothesis that $HClO_4$-SiO_2 is a better catalyst we have shown the comparison in Table 6. From the results, it is obvious that $HClO_4$-SiO_2 is much more effective catalyst in terms of reaction timing as well as % of yield obtained. Both aromatic aldehydes and ketones can be protected as oxathioacetals using this protocol without any difficulty as shown in Table 6. All the products were isolated by distillation under reduced pressure.

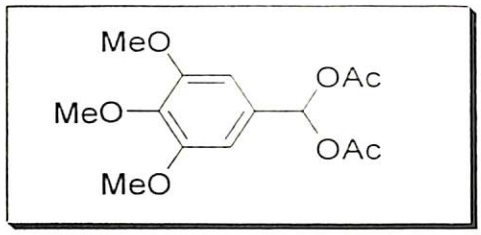
Table 6 Oxathioacetalization of carbonyl compounds using catalytic amount of $HClO_4$-SiO_2 versus aq $HClO_4$ under solvent-free conditions

Product No	Product	Method **A**		Method **B**	
		Time	% yield[a,b]	Time	% yield[a,b]
53		-	-	25 min	90
55		90 min	60	60 min	75
57		30 min	76	30 min	85
149		20 min	68	10 min	74
150		60 min	35	30 min	65

Method A = reactions were carried out using 10 mol% aq. $HClO_4$, Method B = reactions were carried out using 1 mol% $HClO_4$-SiO_2.

Then we sought to explore the same reagent further for thioacetalization of carbonyl compounds. As we have seen in our literature survey on the various available methods for thioacetalization of carbonyl compounds, though all this methods are useful but many of these methods encounter either one or the other difficulties such as long reaction time, harsh reaction conditions, and involvement of expensive catalyst. Moreover, the methods based on using Lewis acids encounter difficulties such as they are generally destroyed in the work-up procedure and cannot be recovered as well as reused. Therefore, we envisioned that this catalyst could over come these drawbacks. Interestingly, a large

1,1-diacetate of 3,4,5-trimethoxybenzaldehyde (111):



Nature: Solid, mp:114-116 °C.

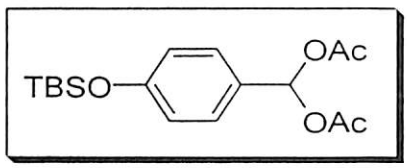
Yield: 96% (1.432 g)

IR (KBr):3017, 2976, 2950, 2848, 1757, 1603, 1506, 1470, 1424, 1368, 1209, 1076 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.14 (s, 6H, 2 x $COCH_3$), 3.85 (s, 3H, OCH_3), 3.89 (s, 6H, 2 x OCH_3), 6.75 (s, 2H, ArH), 7.59 (s, 1H C*H*$(OAc)_2$).

Elemental Analysis	**Calculated**	**Found**
$C_{14}H_{18}O_7$	C 56.37	C 56.09
298.29	H 6.08	H 6.01

1,1-diacetate of 4-*tert*-butyldimethylsilyloxybenzaldehyde (112):



Nature: Solid, mp: 57-59 °C.

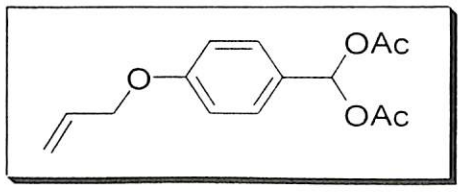
Yield: 87% (1.472 g)

IR (KBr): 2950, 2889, 2858, 1757, 1614, 1416, 1481, 1368, 1250, 1081 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.00 (s, 6H, $Si(CH_3)_2$), 0.78 (s, 9H, $SiC(CH_3)_3$), 1.91 (s, 6H, 2 x $COCH_3$), 6.64 (d, J = 8.4 Hz, 2H, ArH), 7.18 (d, J = 8.4 Hz, 2H, ArH), 7.42 (s, 1H, C*H*$(OAc)_2$).

Elemental Analysis	**Calculated**	**Found**
$C_{17}H_{26}O_5Si$	C 60.30	C 60.27
338.30	H 7.74	H 6.78

1,1-diacetate of 4-allyloxybenzaldehyde (113):



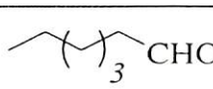
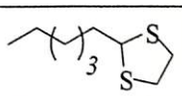
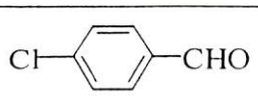
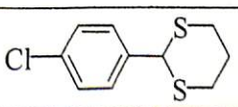
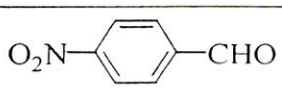
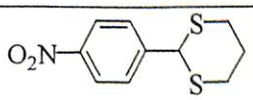
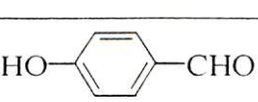
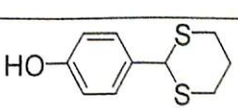
Nature: Solid, mp: 40-41 °C.

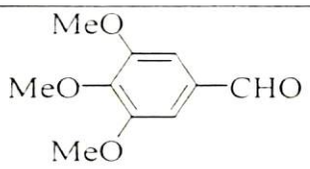
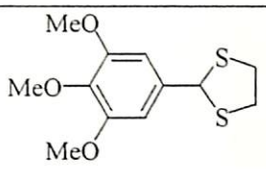
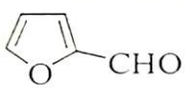
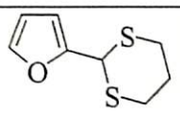
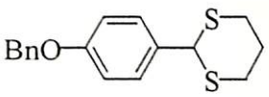
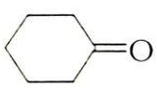
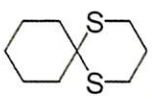
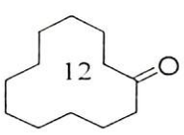
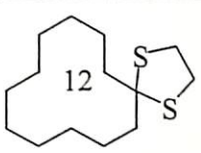
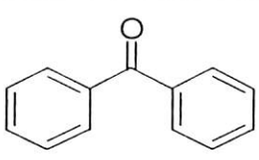
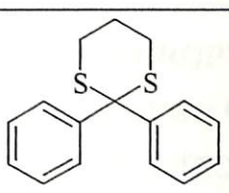
Yield: 93% (1.229 g)

IR (KBr): 3104, 2986, 2950, 1757, 1615, 1527, 1429, 1373, 1245, 1209, 1066, 1004, 922 cm^{-1}. **^{1}H NMR ($CDCl_3$, 400 MHz):** δ 2.11 (s, 6H, $COCH_3$), 4.54 (d, J = 4.9 Hz, 2H,

number of carbonyl compounds underwent dithioacetalization using 1 mol % $HClO_4$-SiO_2 under solvent-free conditions at room temperature. Most of the reaction was completed within 2-30 min in very good yields as shown in Table 7. Remarkably, various aldehydes having electron donating or withdrawing substituents in the aromatic ring underwent thioacetalization smoothly in good yields although the yield for 1,3-dithiane of 4-nitrobenzaldehyde is lesser as compared to the other protected aldehydes. It is noteworthy to mention that the same procedure is applicable to aliphatic aldehydes also. The acid sensitive aldehyde such as furfuraldehyde (**90**) can also be protected to the desired 1,3-dithiane derivative **160** without any difficulty. All the products were fully characterized by recording ^1H NMR, ^{13}C NMR and elemental analysis. Some of the compound's spectral data such as compound **139**, **146**, **150** and **159** are shown in Figure **7-18,** respectively. Remarkably, all solid dithioacetals can be obtained by direct recrystallisation after filtering the catalyst. The generality and scope of this catalyst can be ascertained from its recyclability, which we have tested by the following way. For example, the mixture of 4-hydroxybenzaldehyde (10 mmol) with 1,3-propanedithiol (11 mmol) was treated with $HClO_4$-SiO_2 (200 mg). After completing the reaction, dry diethyl ether was added to the reaction mixture and the catalyst was filtered off, dried and used for second time. The recovered catalyst can be recycled for another two more cycles without any loss of its catalytic activity and yield were obtained 92% and 90% respectively after 2 and 5 min.

Table 7. Thioacetalisation of carbonyl compounds using a catalytic amount of $HClO_4$-SiO_2 under solvent- free conditions.

S. No	Substrate	Time/ min	Product[a]	Product No.	% Yield[b]
72		15		**154**	98
51		10		**155**	81
79		30		**156**	61
82		2		**157**	94

86		15		**158**	98
90		15		**159**	96
151		5		**160**	98
56		30		**161**	93
152		5		**162**	91
153		40		**163**	96

[a]All products were characterized by recording ^{1}H NMR, ^{13}C NMR and elemental analysis.
[b]Isolated Yield.

In conclusion we have devised a simple and efficient methodology for tetrahydropyranylation, oxathioacetalisation and thioacetalisation using a very cheap, readily accessible and recyclable catalyst. The notable advantages of this protocol are no aqueous work-up; very simple procedure i.e avoiding tedious column chromatography, very good yields and reaction time is very less. Therefore, we believe this methodology will be a new addition in organic synthesis.

SECTION B

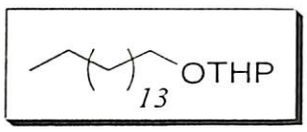
NEW SYNTHETIC METHOD FOR TETRAHYDROPYRANYLATION, OXATIOACETALIZATION AND THIOACETALIZATION OF HYDROXYL AND CARBONYL COMPOUNDS USING SILICA SUPPORTED PERCHLORIC ACID ($HClO_4$-SiO_2)

EXPERIMENTAL

General procedure for tetrahydropyranylation of alcohols and phenols using $HClO_4$-SiO_2:

Into a mixture of alcohol or phenol (1 mmol) and 2, 3-dihydropyran (DHP) (1.1 mmol) was added $HClO_4$-SiO_2 (0.01 mmol, 20 mg) and the mixture was stirred at room temperature. After completion of the reaction as checked by TLC, the crude reaction mixture was directly passed through a short basic alumina column to get the desired pure THP ether

THP ether of 1-hexadecanol (135):



Nature: Colorless liquid

Yield: 91% (0.297g)

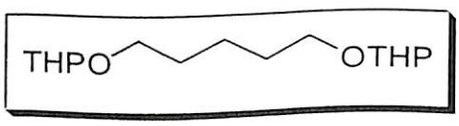
IR (Neat): cm^{-1} 2930, 2858, 1460, 1358, 1209, 1132, 1081, 1040, 989

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, 3H, *J* = 6.6 Hz), 1.22-1.32 (m, 26H), 1.47-1.58 (m, 6H), 1.65-182 (m, 2H), 3.35 (dt, 1H, *J* = 6.6 Hz, *J* = 13.4 Hz), 3.44-3.49 (m, 1H), 3.69 (dt, 1H, *J* = 6.8 Hz, *J* = 13.9 Hz), 3.81-3.87 (m, 1H), 4.54 (dd, 1H, *J* = 2.7 Hz, *J* = 7.0 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.05, 19.63, 22.64, 25.46, 26.19, 29.31, 29.44, 29.57 (2C), 29.62 (3C), 29.64 (3C), 29.71, 30.73, 31.87, 62.24, 67.62, 98.76 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{21}H_{42}O_2$	C 77.24	C 77.08
326.56	H 12.96	H 12.87

THP ether of pentane-1, 5-diol (136):



Nature: Colourless viscous liquid.

Yield: 90% (0.245 g)

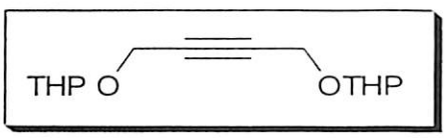
IR (Neat): 2940, 2879, 1455, 1445, 1352, 1265, 1204, 1132, 1035 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42-1.88 (m, 18 H, CH_2), 3.39 (dt, 2 H, J = 6.8 Hz, *J* = 9.6 Hz, -OCH_2), 3.46-3.53 (m, 2 H, OCH_2), 3.74 (dt, 2 H, *J* = 6.8 Hz, *J* = 9.6 Hz, -OCH_2), 3.83-3.90 (m, 2 H, OCH_2), 4.56 (dd, 2 H, *J* = 6.8 Hz, *J* = 9.6 Hz, -OCH-) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.71 (2C), 23.00, 25.55 (2 C), 29.61 (2 C), 30.79 (2 C), 62.23 (2 C), 67.41 (2 C), 98.67 (2 C) ppm.

Elemental Analysis	Calculated	Found
$C_{15}H_{28}O_4$	C 66.14	C 66.21
272.38	H 10.36.	H 10.40.

Di-THP ether of butyne 1, 4-diol (137):



Nature: Colorless liquid

Yield: 87% (0.221 g)

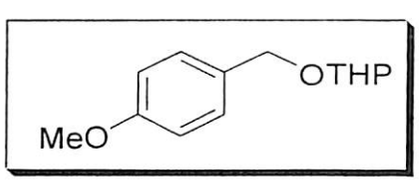
IR (Neat): cm^{-1} 2940, 2873, 1445, 1399, 1352, 1271, 1209, 1127, 1025, 968

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46-1.79 (m, 12H), 3.43-3.48 (m, 2H), 3.73-3.79 (m, 2H), 4.24 (d, 4H, *J* = 15.3 Hz), 4.74 (t, 2H, *J* = 3.4 Hz) ppm.

^{13}C NMR (100 MHz, CDCl3): δ 18.9(2C), 25.2(2C), 30.1(2C), 54.2(2C), 61.8(2C), 81.8(2C), 96.7(2C) ppm.

Elemental Analysis	Calculated	Found
$C_{14}H_{22}O_4$	C 66.12	C 66.21
254.32	H 8.72	H 8.69

THP ether of 4-methoxybenzyl alcohol (138):



Nature: Colorless liquid

Yield: 95% (0.211 g)

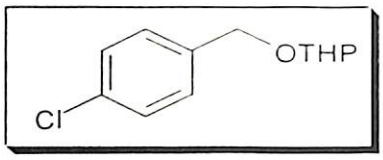
IR (Neat): 2940, 2858, 1619, 1516, 1460, 1358, 1255, 1132, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.48-1.90 (m, 6H), 3.51-3.57 (m, 1H), 3.79 (s, 3H), 3.88-3.93 (m, 1H), 4.43 (d, 1H, *J* = 12.0 Hz), 4.66-4.69 (m, 1H), 4.71 (d, 1H, *J* = 11.2 Hz), 6.87 (d, 2H, *J* = 8.4 Hz), 7.29 (d, 2H, *J* = 8.8 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.9, 25.9, 31.0, 55.6, 62.5, 68.8, 97.7, 113.9 (2C), 129.7 (2C), 130.5, 159.2 ppm.

Elemental Analysis	Calculated	Found
$C_{13}H_{18}O_3$	C 70.25	C 70.02
222.28	H 8.16	H 8.04

THP ether of 4-chlorobenzyl alcohol (139):



Nature: Colorless liquid

Yield: 92% (0.209 g)

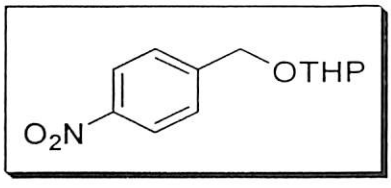
IR (Neat): 2942, 2865, 1595, 1465, 1357, 1130, 1075, 1038 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.51-1.87 (m, 6H), 3.51-3.55 (m, 1H), 3.86-3.91 (m, 1H), 4.46 (d, 1H, *J* = 12.0 Hz), 4.68-4.69 (m, 1H), 4.74 (d, 1H, *J* = 12.0 Hz), 7.30 (bs, 4H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4, 25.5, 30.6, 62.1, 68.0, 97.7, 128.3 (2C), 128.9 (2C), 133.0, 136.7 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{15}ClO_2$	C 63.58	C 63.38
226.70	H 6.67	H 6.59

THP ether of 4-nitrobenzyl alcohol (140):



Nature: Yellowish liquid

Yield: 83% (0.197 g)

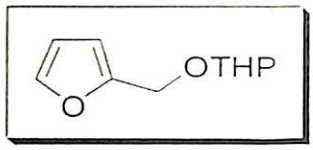
IR (Neat): 2943, 2869, 1605, 1522, 1346, 1202, 1127, 1036 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52-1.92 (m, 6H), 3.51-3.59 (m, 1H), 3.86-3.92 (m, 1H), 4.61 (d, 1H, *J* = 13.6 Hz), 4.73-4.74 (m, 1H), 4.89 (d, 1H, *J* = 13.2 Hz), 7.53 (d, 2H, *J* = 9.2 Hz), 8.20 (d, 2H, *J* = 8.8 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4, 25.4, 30.5, 62.3, 67.6, 98.2, 123.4 (2C), 127.6 (2C), 145.9, 147.3 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{15}NO_4$	C 60.75	C 60.54
237.25	H 6.37	H 6.29
	N 5.90	N 5.78

THP ether of furfuryl alcohol (141):



Nature: Colorless liquid

Yield: 96% (0.175 g)

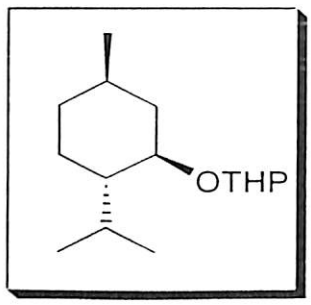
IR (Neat): 2945, 2873, 1506, 1450, 1347, 1209, 1158, 1127, 1025, 984 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50-1.88 (m, 6H), 3.51-3.56 (m, 1H), 3.87-3.92 (m, 1H), 4.48 (d, 1H, *J* =13.2Hz), 4.66 (d, 1H, *J* = 12.8 Hz), 4.69-4.71 (m, 1H), 6.31 (bs, 2H), 7.39 (d, 1H, *J* =1.2 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 25.5, 30.4, 60.6, 61.9, 97.1, 109.1, 110.1, 142.5, 151.5 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{14}O_3$	C 65.92	C 65.67
182.22	H 7.74	H 7.64

THP ether of menthol (142):



Nature: Colorless liquid

Yield: 91% (0.219 g)

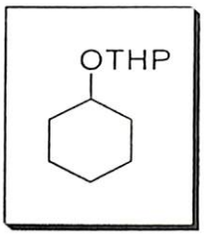
IR (Neat): 2955, 2879, 1465, 1383, 1189, 1137, 1035 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ 0.76-1.10 (m, 12H), 1.19-1.78 (m, 10H), 2.05-2.37 (m, 2H), 3.28-3.50 (m, 2H), 3.82-4.00 (m, 1H), 4.54-4.80 (m, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.57, 16.23, 19.66, 20.23, 21.15, 21.20, 22.22, 22.34, 23.20, 25.14, 25.47, 25.58, 31.14, 31.28, 31.38, 31.60, 34.37, 34.53, 40.09, 43.52, 45.05, 48.12, 48.86, 50.10, 62.36, 63.01, 74.06, 79.88, 94.29, 101.26 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{15}H_{28}O_2$	C 74.95	C 75.17
240.38	H 11.74	H 11.83

THP ether of cyclohexanol (143):



Nature: Colorless liquid

Yield: 91% (0.168 g)

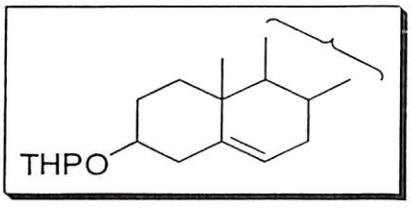
IR (Neat): 2934, 2867, 1454, 1362, 1203, 1132, 1116, 1024,1004 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07-1.36 (m, 5H), 1.46-1.52 (m, 5H), 1.58-1.86 (m, 6H), 3.38-3.44 (m, 1H), 3.49-3.56 (m, 1H), 3.79-3.88 (m, 1H), 4.64 (dd, 1H, J = 4.6 Hz, J = 7.3 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.95, 24.13, 24.40, 25.47, 25.68, 31.24, 31.72, 33.68, 62.67, 74.31, 96.52 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{20}O_2$	C 71.70	C 71.93
184.28	H 10.94	H 11.02

THP ether of cholesterol (144):



Nature: White solid. mp: 149 °C

Yield: 97% (0.457 g)

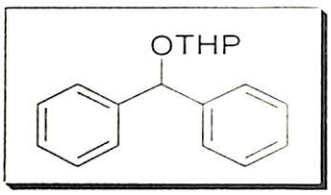
IR (KBr): 2945, 2868, 1470, 1373, 1117, 1030, 979 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ 0.70 (s, 3H), 0.83 (d, 3H, J = 2.0 Hz), 0.84 (d, 3H, J = 1.7 Hz), 0.88 (d, 3H, J = 6.7 Hz), 0.91-0.94 (m, 1H), 0.98 (s, 3H), 1.00-2.34 (m, 33H), 3.44-3.55 (m, 2H), 3.87-3.91 (m, 1H), 4.68-4.69 (m, 1H), 5.32 (t, 1H, J = 5.4 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 11.84, 18.70, 19.37, 20.02, 21.06, 22.55, 22.80, 23.81, 24.28, 25.49, 28.00 (2C), 28.22, 29.69, 31.27, 31.89, 35.77, 36.18, 36.76, 37.21, 39.51, 39.78, 40.25, 42.31, 50.16, 56.14, 56.76, 62.80, 76.02, 96.83, 121.48, 141.08 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{32}H_{54}O_2$	C 81.64	C 81.42
470.78	H 11.56	H 11.41

THP ether of benzhydrol (145):



Nature: White solid, mp: 50-51 ^{0}C.

Yield: 95% (0.255 g)

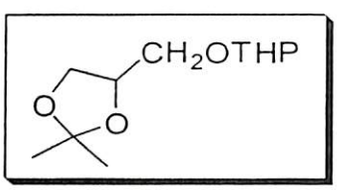
IR (KBr): 2942, 2903, 2877, 1490, 1199, 1121, 1025, 977, 916 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52-1.97 (m, 6H, CH_2), 3.47-3.51 (m, 1H, OCH_2), 3.85-3.91 (m, 1H, OCH_2), 4.66(t, 1H, *J* = 3.2 Hz, OCHO), 5.79 (s, 1H, ArCHAr), 7.17-7.36 (m, 10 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.27, 25.65, 30.66, 61.99, 78.07, 95.36, 126.67 (2C), 126.88 (2C), 127.43 (2C), 127.53 (2C), 128.03 (2C), 128.29 (2C).

Elemental Analysis	**Calculated**	**Found**
$C_{18}H_{20}O_2$	C 80.57	C 80.61
268.35	H 7.51	H 7.53.

THP ether of 2, 3-*O*-isopropylidene-*D*-(±)-glycerol (146):



Nature: Colorless liquid

Yield: 84% (0.182g)

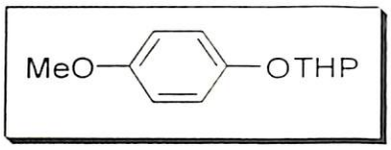
IR (Neat): cm^{-1} 2986, 2945, 2873, 1460, 1378, 1265, 1209, 1132, 1066, 1035

^{1}H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ 1.37 (s, 3H), 1.42 (s, 3H), 1.54-1.88 (m, 6H), 3.45-3.57 (m, 2H), 3.71-3.76 (m, 1H), 3.78-3.89 (m, 2H), 4.04-4.10 (m, 1H), 4.28-4.32 (m, 1H), 4.62-4.64 (m, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.6, 19.8, 25.7, 25.8, 25.9, 27.0, 27.1, 30.7, 62.3, 62.5, 67.0, 67.2, 68.2, 68.8, 74.9, 75.1, 99.1, 99.3, 109.4, 109.6 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{11}H_{20}O_4$	C 61.09	C 61.38
216.28	H 9.32	H 9.43

THP ether of 4-methoxyphenol (147):



Nature: Colorless liquid

Yield: 80% (0.167g)

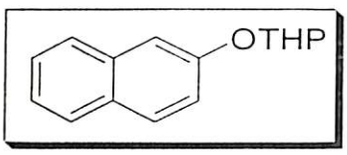
IR (Neat): cm^{-1} 2940, 2879, 1506, 1470, 1399, 1368, 1230, 1122, 1076, 1045, 968

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.61-2.01 (m, 6H), 3.58-3.61 (m, 1H), 3.77 (s, 3H), 3.91-3.97 (m, 1H), 5.29 (t, 1H, J = 3.6 Hz), 6.82 (d, 2H, J = 9.2 Hz), 6.99 (d, 2H, J = 9.6 Hz) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4, 25.7, 30.9, 56.0, 62.4, 97.6, 114.7 (2C), 117.9 (2C), 151.2, 158.8 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{16}O_3$	C 69.21	C69.48
208.26	H 7.74	H 7.82

THP ether of 2-naphthol (148):



Nature: Light yellow solid

Yield: 83% (0.189 g)

IR (Neat): 2919, 2854, 1469, 1354, 1218, 1127, 1037 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.60-1.73 (m, 3H), 1.89-1.92 (m, 2H), 1.99-2.08 (m, 1H), 3.62-3.66 (m, 1H), 3.91-3.97 (m, 1H), 5.56 (t, 1H, J = 3.3 Hz), 7.21-7.25 (m, 1H), 7.32 (d, 1H, J = 8.0 Hz), 7.39-7.43 (m, 2H), 7.72-7.76 (m, 3H) ppm.

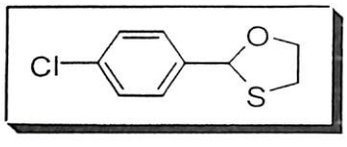
^{13}C NMR (75 MHz, $CDCl_3$): δ 18.7, 25.2, 30.4, 61.9, 96.4, 110.4, 119.1, 123.8, 126.2, 127.0, 127.5, 129.2, 129.4, 134.5, 154.8 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{15}H_{16}O_2$	C 78.92	C 78.71
228.29	H 7.06	H 6.98

General Procedure for Oxathioacetalization and Thioacetalization of Carbonyl Compounds using $HClO_4$-SiO_2:

A mixture of carbonyl compound (10 mmol) and 2- mercaptoethanol (12 mmol, 0.84 mL) was treated with $HClO_4$-SiO_2(200 mg, 0.1 mmol) and left for stirring at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the pure product was obtained directly by distillation. In case of dithioacetalization, the mixture of carbonyl compounds (5 mmol) and 1,2-ethanedithiol (**A**) or 1,3-propanedithiol (**B**) (6 mmol) treated with the same catalyst. After completion of reaction as checked by TLC, it was diluted with ethyl acetate and filtered off the catalyst. Then the filtrate was concentrated and either kept for recrystallization by adding hexane if the product is solid or purified by slica gel column chromatography.

2-[4′-Chlorophenyl]-1,3-oxathiolane (53):



Nature: Colourless liquid; **Boiling Point**: 125 ^{0}C/5mm

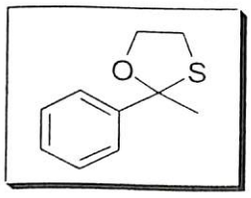
Yield: 90% (1.806 g)

IR (Neat): 1598, 1496, 1414, 1209, 1091, 1015 cm^{-1} .

^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ = 3.10-3.23 (m, 2H, -SCH_2), 3.82-3.92 (m, 1H, OCH_aH_b), 4.41-4.54 (m, 1H, OCH_aH_b), 5.94 (s, 1H, SCHO), 7.30 (d, 2H, J = 8.6 Hz, ArH), 7.44 (d, 2H, J = 8.4 Hz, ArH).

Elemental Analysis	**Calculated**	**Found**
C_9H_9ClOS	C 53.86	C 53.63
200.69	H 4.52	H 4.59
	S 15.98	S 15.77

[2-methyl 2-phenyl]-1,3-oxathiolane (55):



Nature: Liquid. **Boiling Point**: 110 ^{0}C/5 mm

Yield: 75% (1.352 g)

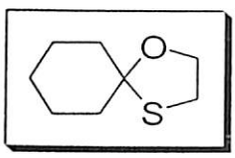
IR (Neat): 1496,1383,1219,1142, 1066,769 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 1.9 (s, 3H, CH_3), 3.05-3.10 (m, 1H, -SCH_aH$_b$), 3.20-3.26 (m, 1H, -SCH$_a$$H_b$), 4.00-4.06 (m, 1H, -OC$H_aH_b$), 4.33-4.38 (m, 1H, -OCH$_a$$H_b$), 7.30-7.47 (m, 3H, ArH), 7.48-7.50 (m, 2H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 32.36, 34.46, 70.66, 95.59, 124.84 (2C), 127.19, 128.14 (2C), 146.73.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{12}OS$	C 66.63	C 66.50
180.26	H 6.71	H 6.54
	S 17.79	S 17.53

1,4-Oxathiaspiro [4,5]decane (57):



Nature: Liquid

Yield: 85% (1. 35 g)

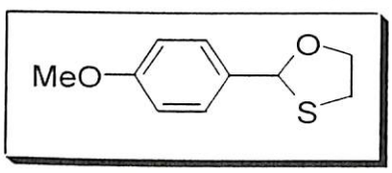
IR (Neat): 1449, 1270, 1239, 1145, 1075, 686 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.32-1.52 (m, 4H, CH_2), 1.74-1.89 (m, 6H, CH_2), 3.00 (t, 2H, J = 5.8 Hz, SCH_2), 4.14 (t, 2H, J = 5.9 Hz, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 24.83 (2C), 25.02, 32.86, 39.94 (2C), 69.46, 96.49

Elemental Analysis	**Calculated**	**Found**
$C_8H_{14}OS$	C 60.72	C 60.45
158.26	H 8.92	H 8.80
	S 20.26	S 20.02

2-[4′-Methoxyphenyl]-1,3-oxathiolane (149):



Nature: Liquid. **Boiling Point**: 135 ^{0}C/1mm.

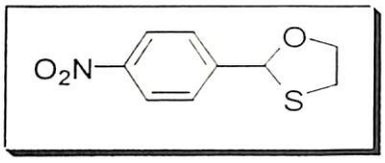
Yield: 68% (1.34 g)

IR (Neat): cm^{-1} 1613, 1516, 1260, 1175, 1029, 830.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 3.18-3.20 (m, 1H, SCH_aH$_b$), 3.26-3.30 (m, 1H, SCH$_a$$H_b$), 3.80 (s, 3H, OCH_3), 3.87-3.94 (m, 1H, OCH_aH$_b$), 4.49-4.54 (m, 1H, OCH$_a$$H_b$), 5.99 (s, 1H, SCHO), 6.87 (d, 2H, J = 8.6 Hz, ArH), 7.40 (d, 2H, J = 8.6 Hz, ArH).

Elemental Analysis	Calculated	Found
$C_{10}H_{12}O_2S$	C 61.20	C 60.99
196.26	H 6.16	H 6.18
	S 16.34	S 16.10

2-[4′-Nitrophenyl]-1,3-oxathiolane (150):



Nature: Light yellow solid. mp: 78 °C.

Yield: 65% (1. 37 g)

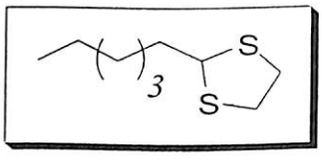
IR (KBr): 1603, 1526, 1347, 1070, 866, 717 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ 3.21-3.30 (m, 2H, -SCH_2), 3.99-4.06 (m, 1H, -OCH_aH_b), 4.52-4.58 (m, 1H, -OCH_aH_b), 6.13 (s, 1H, -SCHO-), 7.60 (d, 2H, J = 8.7 Hz, ArH), 8.21 (d, 2H, J = 8.7 Hz, ArH).

^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 34.08, 72.39, 85.33, 123.69 (3C), 127.12, 146.95, 147.76.

Elemental Analysis	Calculated	Found
$C_9H_9NO_3S$	C 51.17	C 51.29
211.24	H 4.29	H 4.22
	N 6.63	N 6.52
	S 15.18	S 15.00

2-Hexyl-1,3-dithiolane (154):



Nature: Liquid

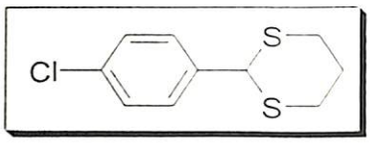
Yield: 98% (0.933g)

IR (Neat): 2930, 2858, 1465, 1378, 1281, 1117, 861, 728 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, 3H, J = 6.6 Hz, CH_3), 1.25-1.42 (m, 8H, CH_2), 1.76-1.82 (m, 2H, CH_2CHS), 3.14-3.25 (m, 4H, 2x SCH_2), 4.44 (t, 1H, J = 7.08 Hz, SCHS)

Elemental Analysis	Calculated	Found
$C_9H_{18}S_2$	C 56.78	C 56.49
190.37	H 9.53	H 9.46
	S 33.69	S 33.51

2-[4′-Chlorophenyl]-1,3-dithiane (155):



Nature: White solid, mp: 91 °C

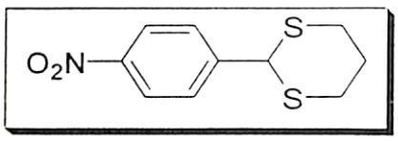
Yield: 81% (0.935g)

IR (KBr): 3048, 2904, 2822, 1598, 1486, 1424, 1281, 1178, 1091, 1009, 830, 769, 671 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.85-1.97 (m, 1H, -$SCH_2CHaHbCH_2S$-), 2.13- 2.18(m, 1H, -$SCH_2CHaHbCH_2S$-), 2.87-2.92 (m, 2H, -SCH_2-), 3.00-3.08 (m, 2H, -SCH_2-), 5.13 (s, 1H, ArCH-), 7.30 (d, 2H, J = 7.5 Hz, ArH), 7.41 (d, 2H, J = 7.5 Hz, ArH)

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{11}ClS_2$	C 52.05	C 52.21
230.78	H 4.80	H 4.73
	S 27.79	S 27.62

2-[4′-Nitrophenyl]-1,3-dithiane (156):



Nature: Light yellow solid; mp:148°C

Yield: 61% (0.736 g)

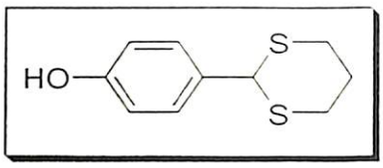
IR (KBr): cm^{-1} 3073, 2960, 2909, 2848, 1609, 1521, 1424, 1352, 1276, 1117, 861, 728

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.91- 2.02 (m, 1H, -$SCH_2CHaHbCH_2S$-), 2.16- 2.28 (m, 1H, -$SCH_2CHaHbCH_2S$-), 2.92- 2.98 (m, 2H, -SCH_2-), 3.05- 3.15 (m, 2H, -SCH_2-), 5.24 (s, 1H, ArCH-), 7.65 (d, 2H, J = 8.8 Hz, ArH), 8.20 (d, 2H, J = 8.8 Hz, ArH)

^{13}C NMR (100 MHz, $CDCl_3$): δ 24.9, 31.8, 50.4, 124.0, 129.0, 146.3,147.8

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{11}NO_2S_2$	C 49.77	C 49.87
241.33	H 4.59	H 4.53
	N 5.80	N 5.62
	S 26.57	S 26.71

2-[4′-Hydroxyphenyl]-1,3-dithiane (157):



Nature: White solid; mp:156-158 °C.

Yield: 94% (0.998 g)

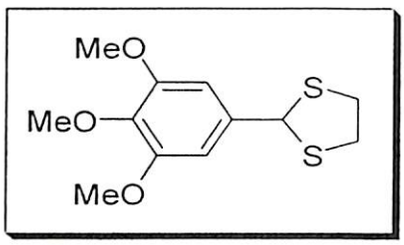
IR (KBr): 3370, 2940, 2894, 2807, 1609, 1516, 1450, 1363, 1250, 1173, 1112, 851, 774 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.85-1.96 (m, 1H, $SCH_2CHaHbCH_2S$), 2.12-2.19 (m, 1H, $SCH_2CHaHbCH_2S$), 2.86-2.92 (m, 2H, SCH_2), 3.01-3.08 (m, 2H, SCH_2), 5.12 (S, 1H, ArCH), 6.77 (d, 2H, J = 8.2 Hz, ArH), 7.31 (d, 2H, J = 8.3 Hz, ArH) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.06, 32.18 (2C), 50.74, 115.58 (2C), 129.18 (2C), 131.45, 155.61 ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{10}H_{12}OS_2$	C 56.56	C 56.34
212.34	H 5.70	H 5.63
	S 30.20	S 32.01

2-[3′,4′,5′- Trimethoxyphenyl]-1,3 -dithiolane (158):



Nature: White solid, mp: 53-54 ^{0}C

Yield: 98% (1.335 g)

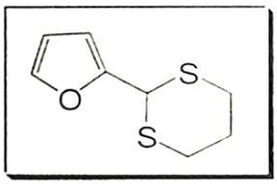
IR (KBr): 1586, 1505, 1127 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.31-3.38 (m, 2 H, SCH_2), 3.46-3.54 (m, 2 H, SCH_2), 3.82 (s, 3 H, OCH_3), 3.86 (s, 6 H, 2 x OCH_3), 5.60 (s, 1 H, ArCH-), 6.76 (s, 2 H, ArH) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 40.18 (2 C), 56.12 (2 C), 56.86, 60.78, 104.71, 104.85 (2 C), 135.14, 152.85 (2 C) ppm.

Elemental Analysis	**Calculated**	**Found**
$C_{12}H_{16}O_3S_2$	C 52.92	C 52.98
272.37	H 5.92	H 5.89
	S 23.54	S 23.61

2 –Furfuryl-1,3-dithiane (159):



Nature: Pale yellow liquid

Yield: 96% (0.894 g)

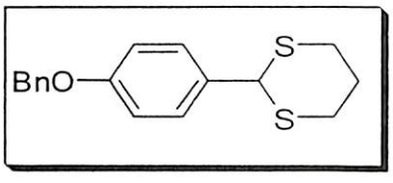
IR (Neat): cm^{-1} 2904, 1496, 1424, 1276, 1163, 1015, 943, 743

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.92-2.01 (m, 1H, -$SCH_2CHaHbCH_2S$-), 2.08- 2.16 (m, 1H, - $SCH_2CHaHbCH_2S$-), 2.88-2.93 (m, 4H, 2x -SCH_2-), 5.20 (s, 1H, -SCHS-), 6.32 (dd, 1H, J = 2.0 Hz, J = 3.2 Hz, H-4), 6.37 (d, 1H, J = 3.1 Hz, H-3), 7.34 (d, 1H, J = 1.9 Hz, H-5)

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.22, 30.24 (2C), 41.99, 107.83, 110.56, 142.27, 151.66

Elemental Analysis	Calculated	Found
$C_8H_{10}OS_2$	C 51.58	C 51.39
186.30	H 5.41	H 5.33
	S 34.42	S 34.23

2-[4′-Benzyloxyphenyl]-1,3-dithiane (160):



Nature: White solid; mp: 78 °C

Yield: 98% (1.482 g)

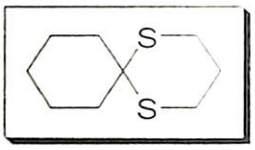
IR (KBr): 1609, 1511, 1393, 1245, 1189, 1009, 748 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 1.85-1.95 (m, 1H, -$SCH_2CHaHbCH_2S$-), 2.12-2.17 (m, 1H, -$SCH_2CHaHbCH_2S$-), 2.85-2.95 (m. 2H, -SCH_2-), 3.00-3.07(m. 2H, -SCH_2-), 5.04 (s, 2H, -OCH_2Ph), 5.12 (s, 1H, ArCH-), 6.92 (d, 2H, J = 8.52 Hz, ArH), 7.24-7.42 (m, 7H, ArH)

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 25.03, 32.13 (2C), 50.70, 69.98, 114.94 (2C), 127.42 (2C), 127.94, 128.54 (2C), 128.92 (2C), 131.53 (2C), 136.79

Elemental Analysis	Calculated	Found
$C_{17}H_{18}OS_2$	C 67.51	C 67.32
302.45	H 6.00	H 6.12
	S 21.20	S 21.25

1,4-Dithiaspiro[5.5]decane (161):



Nature: Colourless liquid

Yield: 93% (0.876 g)

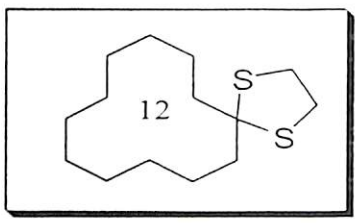
IR (Neat): 2930, 2853, 1440, 1265, 1127, 1015, 907, 861, 764 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43-1.49 (m, 2H, -CH_2-), 1.60-1.67 (m, 4H, -CH_2-), 1.96-2.02 (m, 6H, -$SCH_2CH_2CH_2S$- and 2 x -CH_2-), 2.79-2.83 (m, 4H, 2 x -SCH_2-)

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.97 (2C), 25.79 (2C), 25.87, 26.12, 37.86 (2C), 50.32

Elemental Analysis	Calculated	Found
$C_9H_{16}S_2$	C 57.39	C 57.14
188.36	H 8.56	H 8.50
	S 34.05	S 34.23

1,4-Dithiaspiro[4,11]hexadecane (162):



Nature: White solid, mp: 88 °C

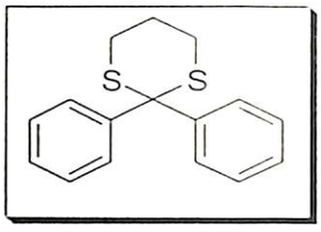
Yield: 91% (1.176 g)

IR (KBr): 2955, 2858, 1470, 1440, 1045, 799, 738, 687 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18-1.51 (m, 18 H, CH_2), 1.95 (dd, J = 7.6 Hz, J = 8.3 Hz, 4H, CH_2), 3.22 (s, 4H, SCH_2) ppm.

Elemental Analysis	Calculated	Found
$C_{15}H_{28}S_2$	C 66.11	C 66.03
272.52	H 10.35	H 10.34
	S 23.53	S 23.38

2,2-Diphenyl-1,3-dithiane (163):



Nature: White solid, mp: 107-109 °C

Yield: 96% (1.308 g)

IR (KBr): cm^{-1} 1598, 1496, 1445, 1286, 1158, 1009, 861, 753, 699

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 1.97-2.03 (m, 2H, -$SCH_2CH_2CH_2S$-), 2.78-2.79 (m, 4H, 2x-SCH_2-), 7.24-7.36 (m, 6H, ArH), 7.69 (m, 4H, ArH)

Elemental Analysis	**Calculated**	**Found**
$C_{16}H_{16}S_2$	C 70.54	C 70.67
272.44	H 5.92	H 5.75
	S 23.54	S 23.42

FIGURE

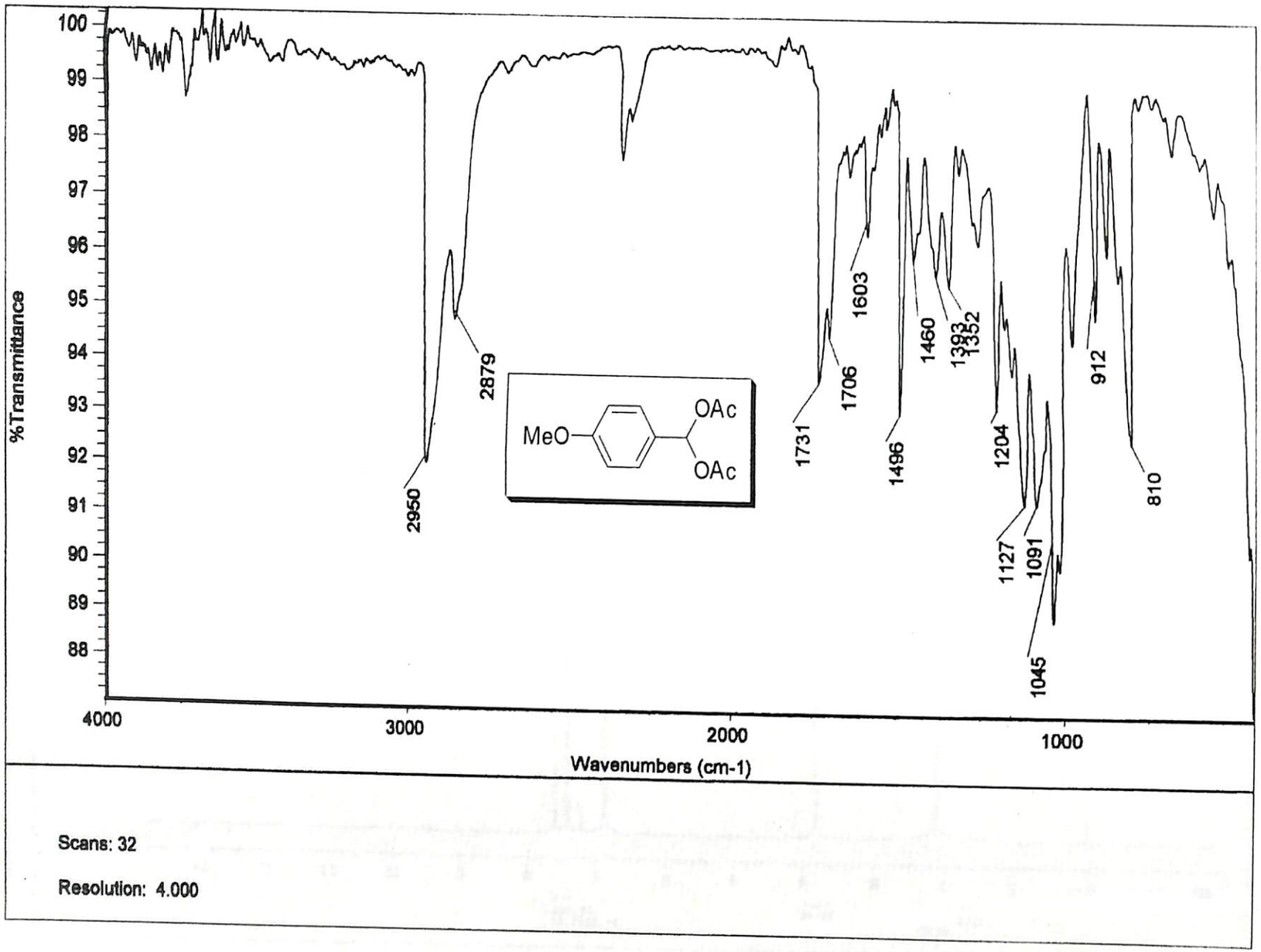


Figure 1: IR spectrum of 1,1-diacetate of 4-methoxybenzaldehyde **(109)**

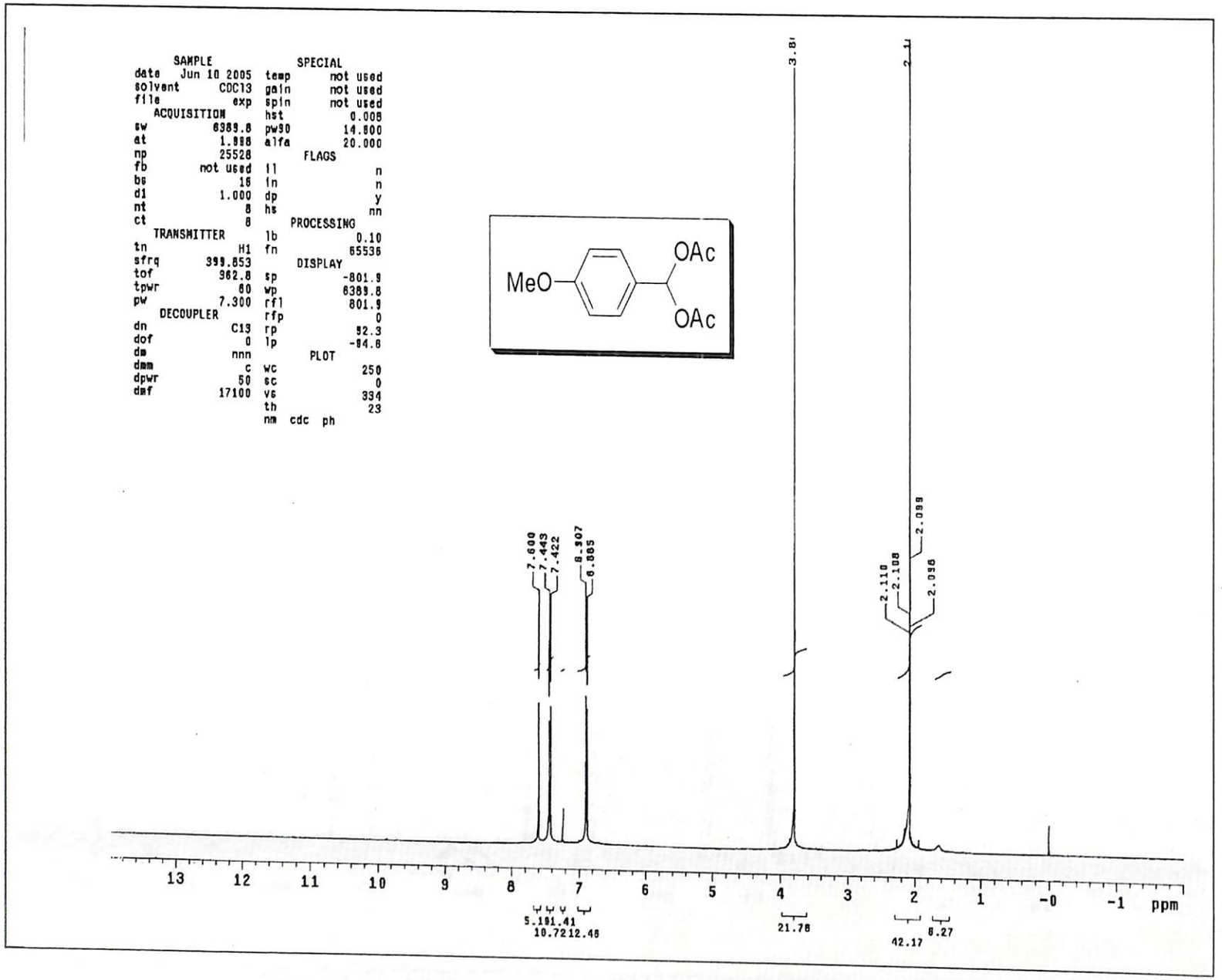


Figure 2: ^{1}H NMR spectrum of 1,1-diacetate of 4-methoxybenzaldehyde **(109)**

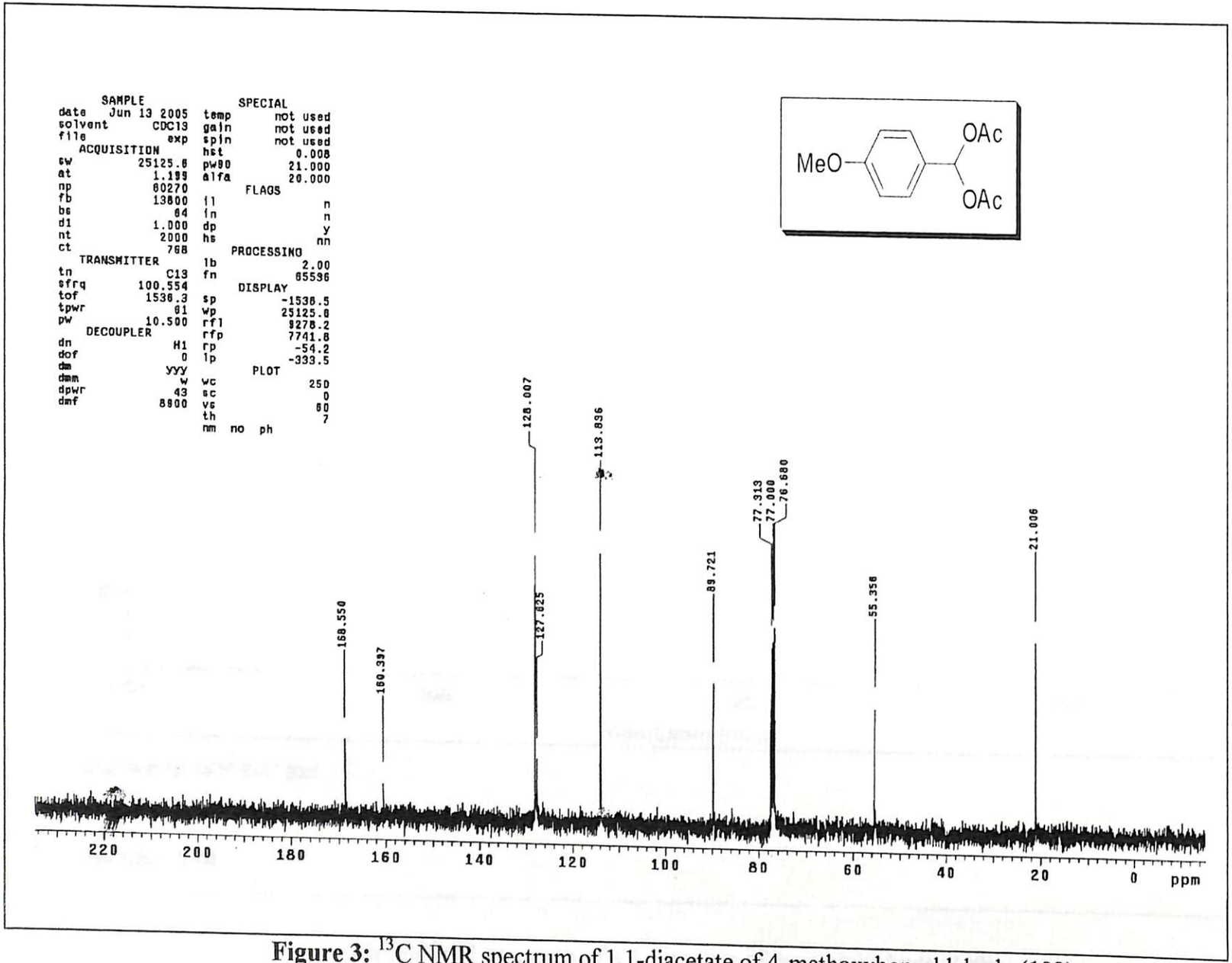


Figure 3: ^{13}C NMR spectrum of 1,1-diacetate of 4-methoxybenzaldehyde **(109)**

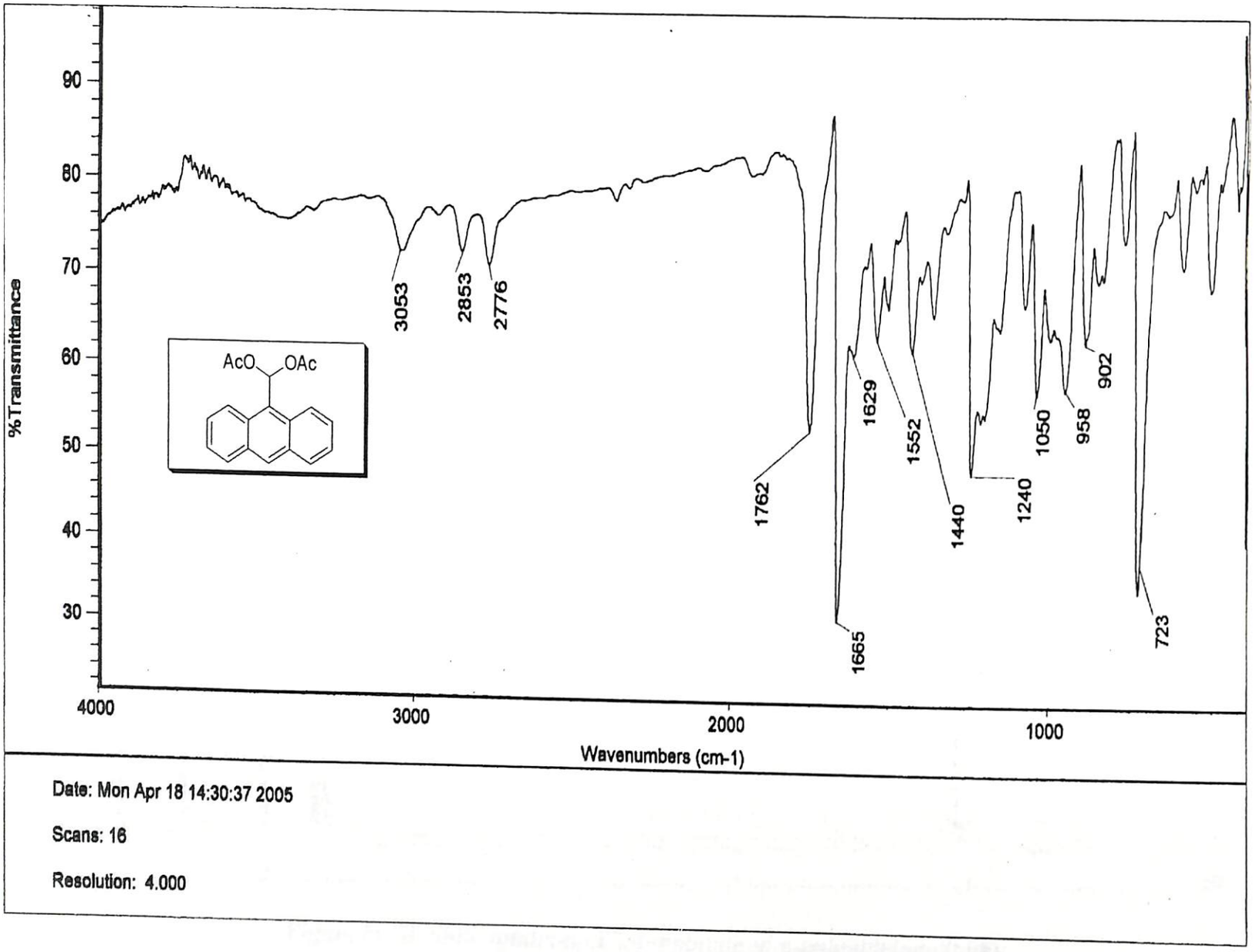


Figure 4: IR spectrum of 1,1-diacetate of 9-anthraldehyde **(119)**

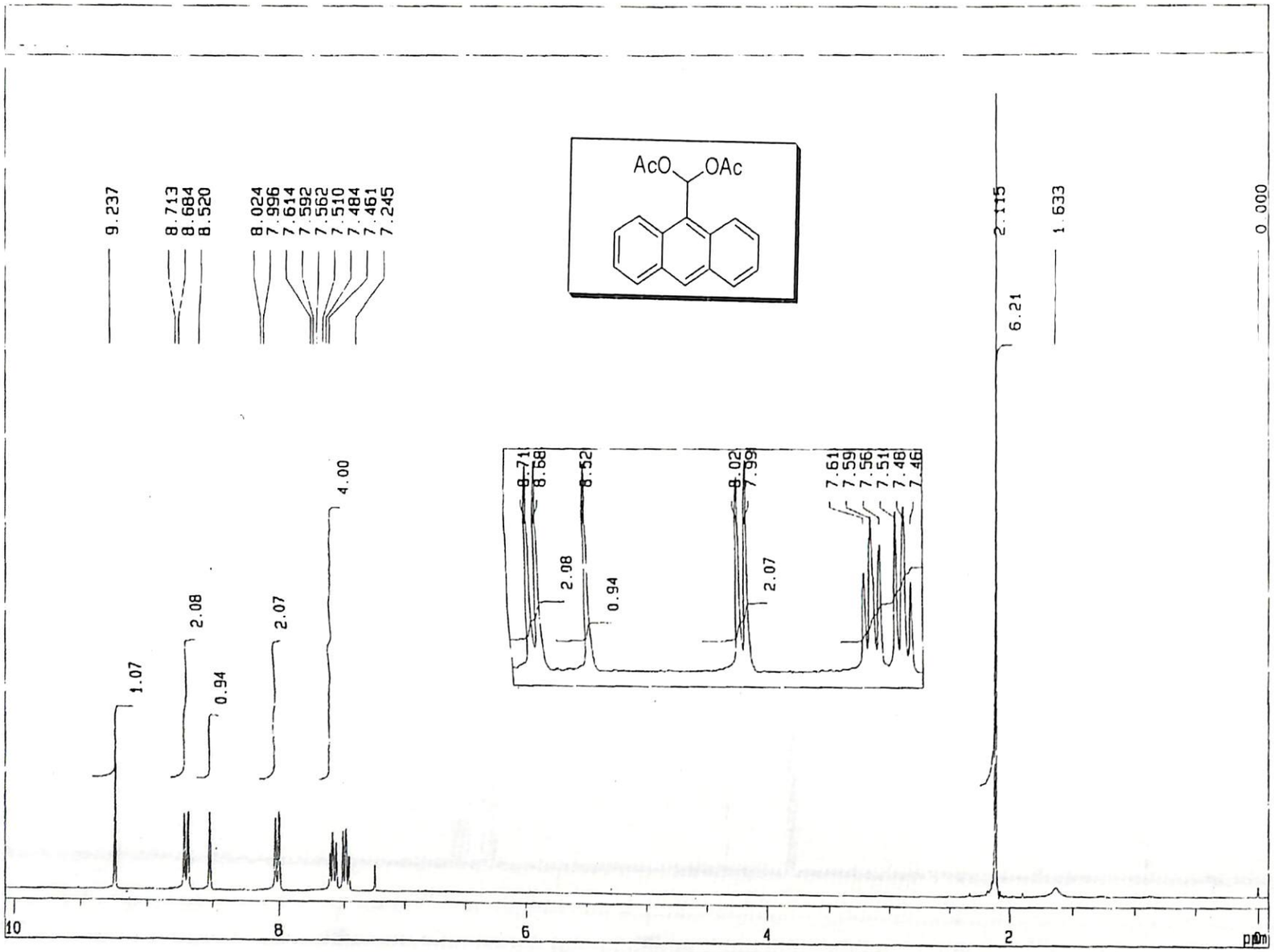


Figure 5: ^{1}H NMR spectrum of 1,1-diacetate of 9-anthraldehyde **(119)**

Figure 6: ^{13}C NMR spectrum of 1,1-diacetate of 9-anthraldehyde **(119)**

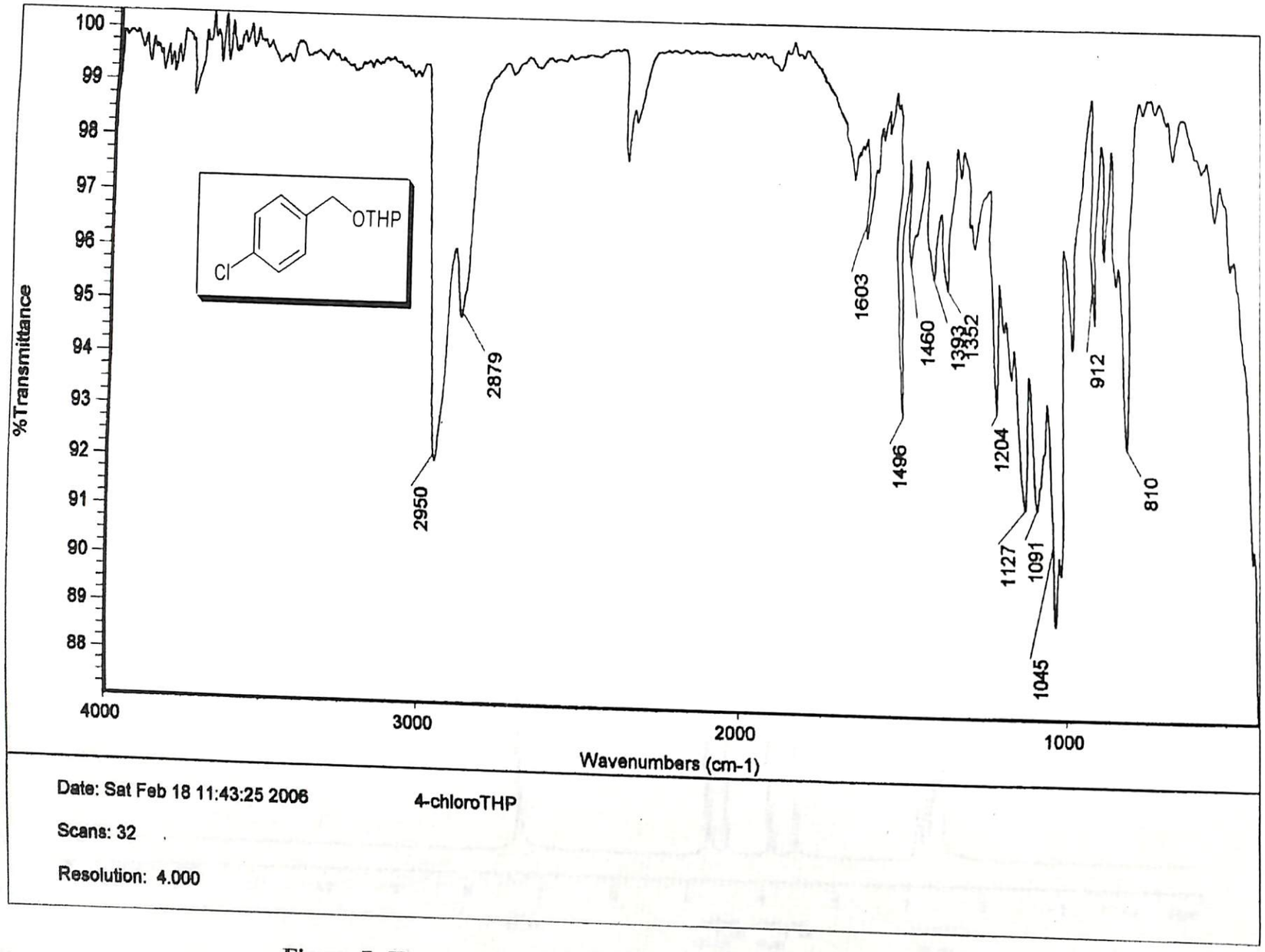


Figure 7: IR spectrum of THP ether of 4-chlorobenzyl alcohol **(139)**

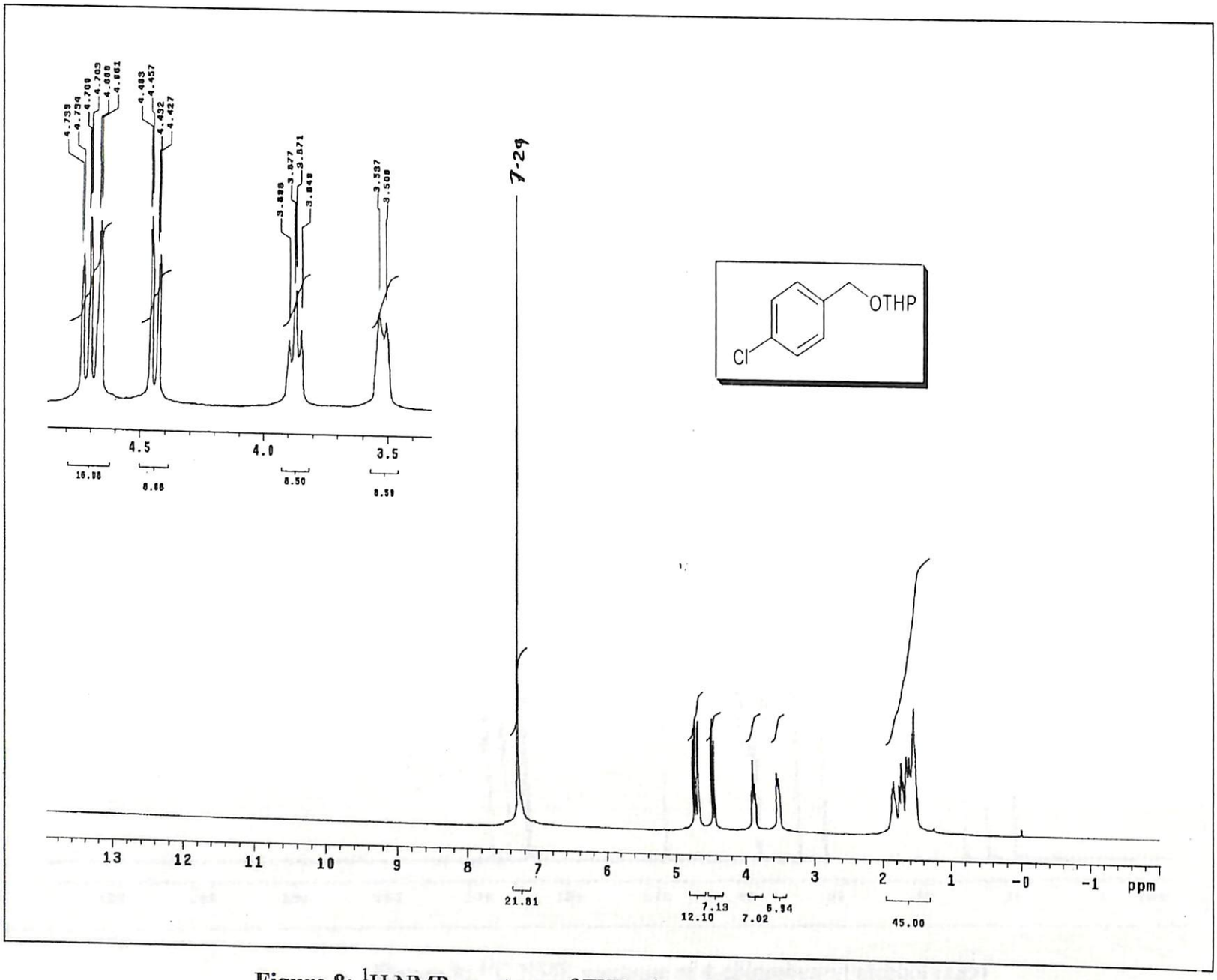


Figure 8: ^{1}H NMR spectrum of THP ether of 4-chlorobenzyl alcohol **(139)**

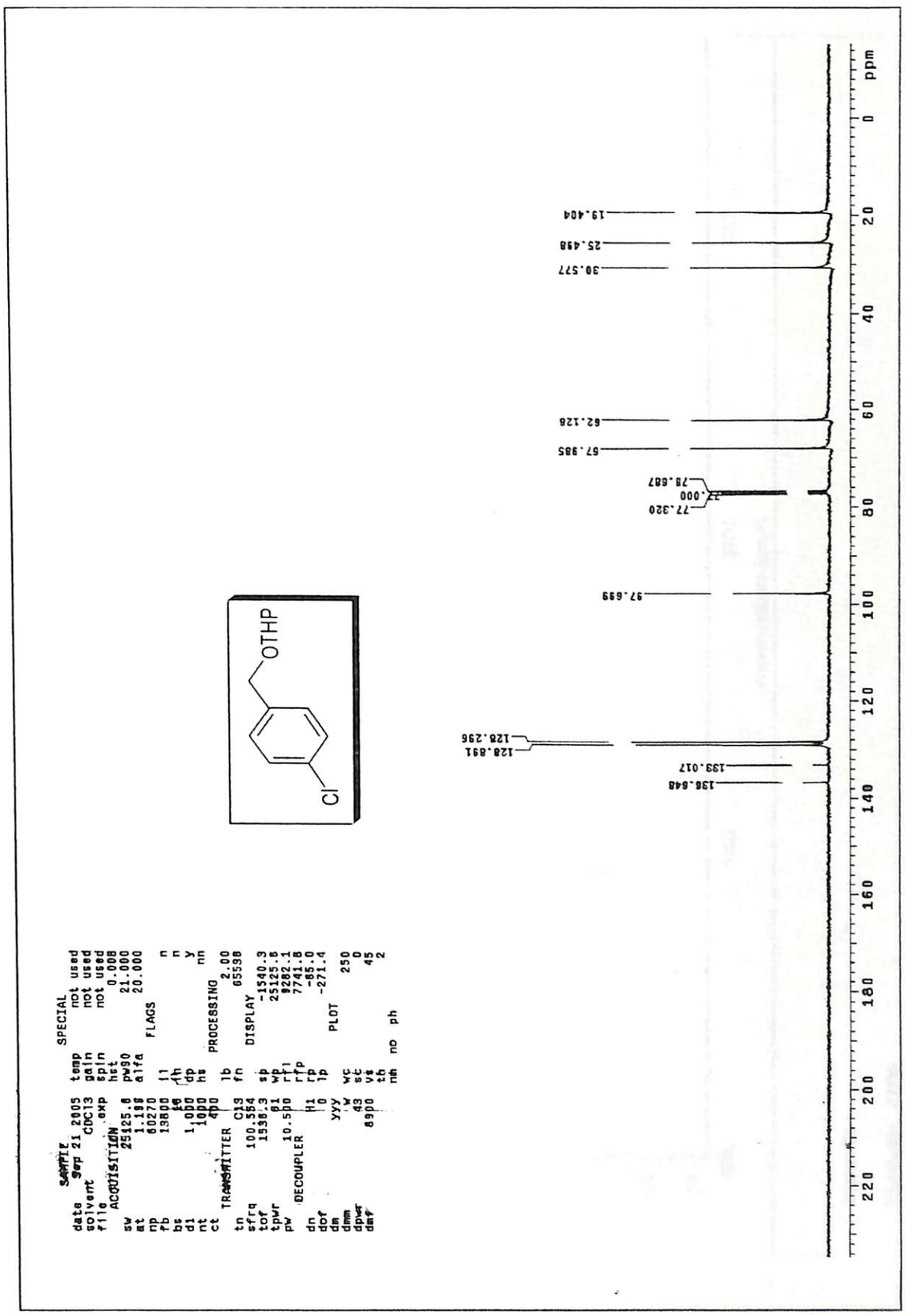


Figure 9: ^{13}C NMR spectrum of 4-chlorobenzyl alcohol **(139)**

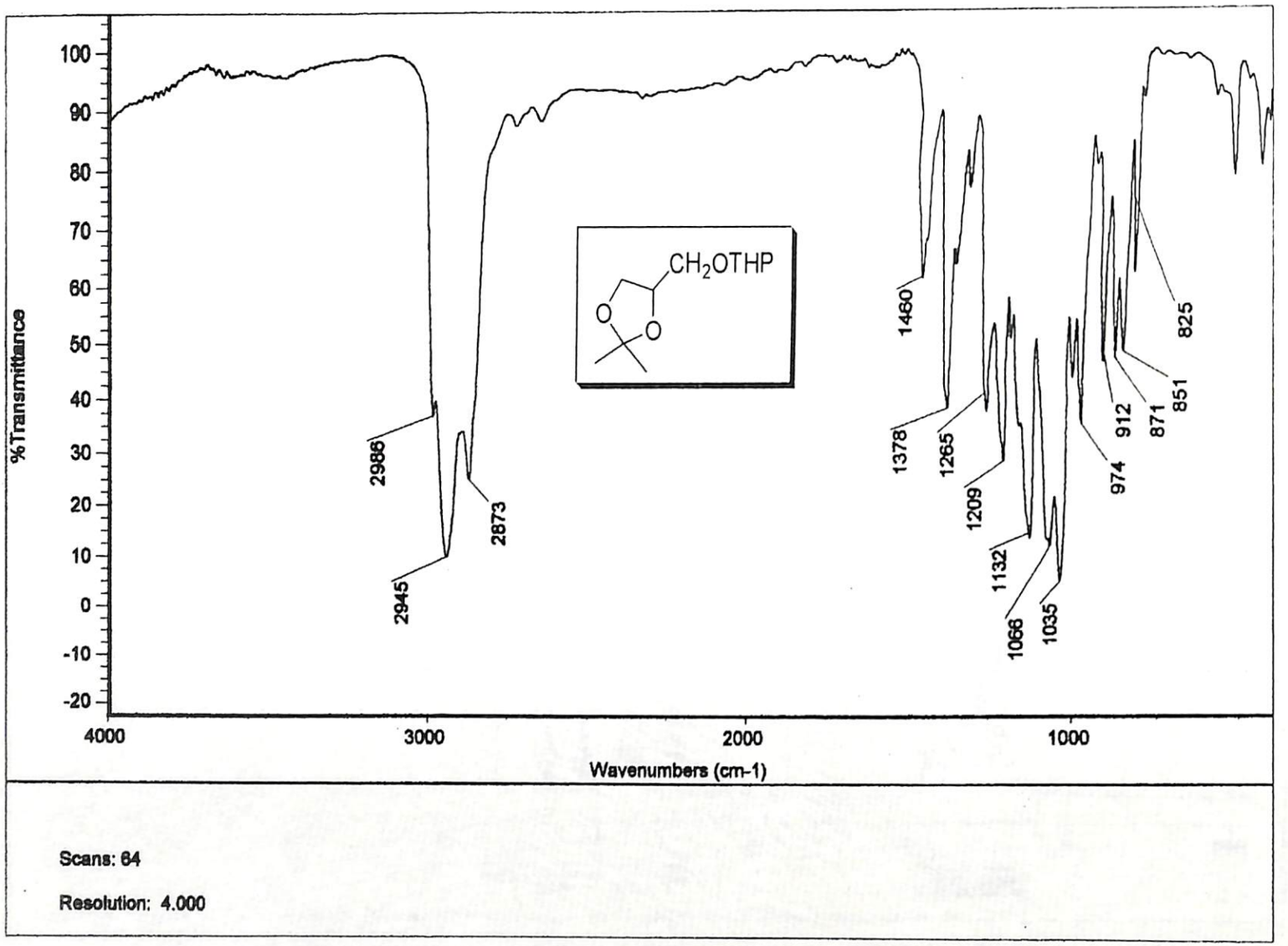


Figure 10: IR spectrum of THP ether of 2,3-*O*-isopropylidene-*D*-(±)-glycerol **(146)**

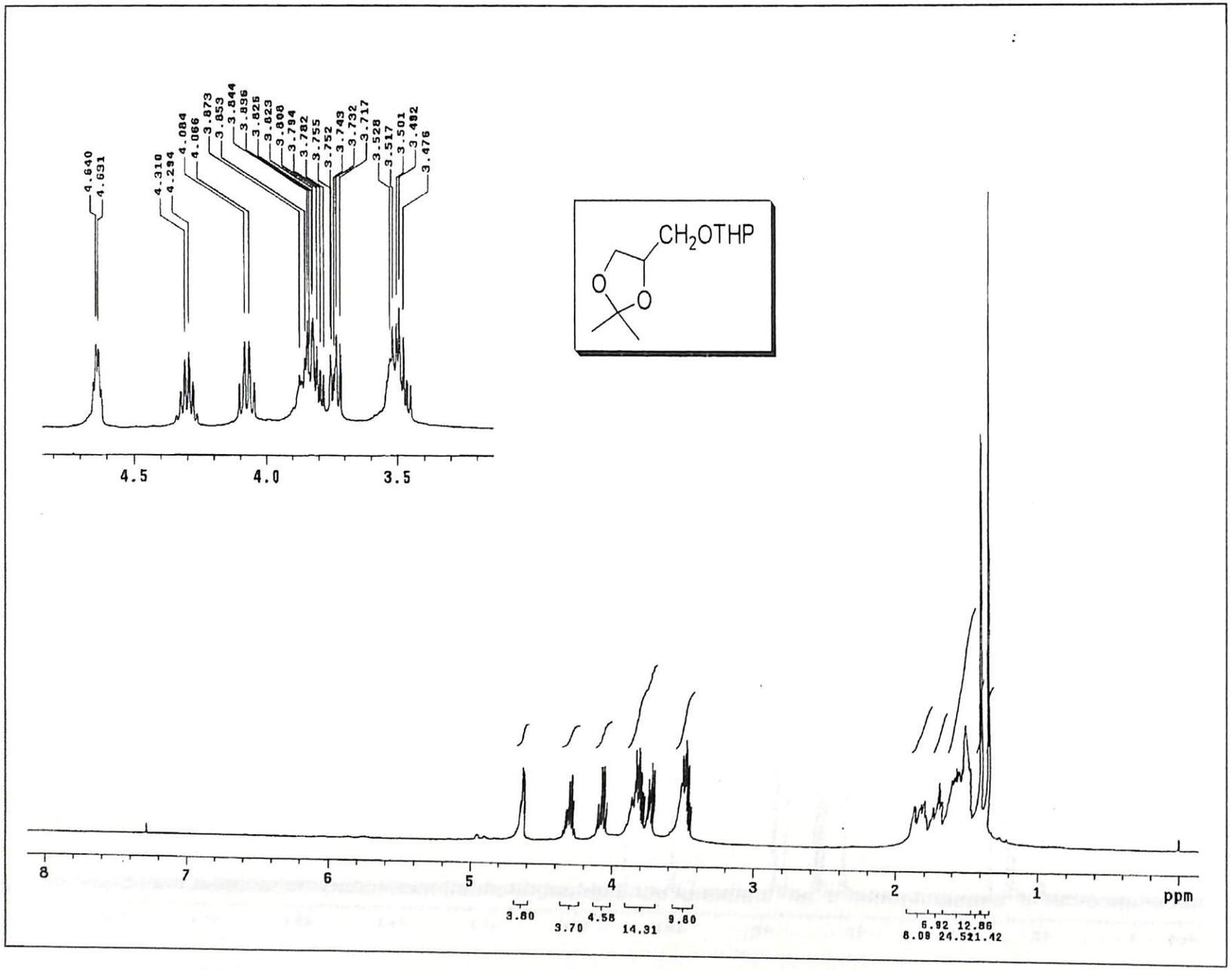


Figure 11: ^{1}H NMR spectrum of THP ether of 2,3-*O*-isopropylidene-*D*-(±)-glycerol **(146)**

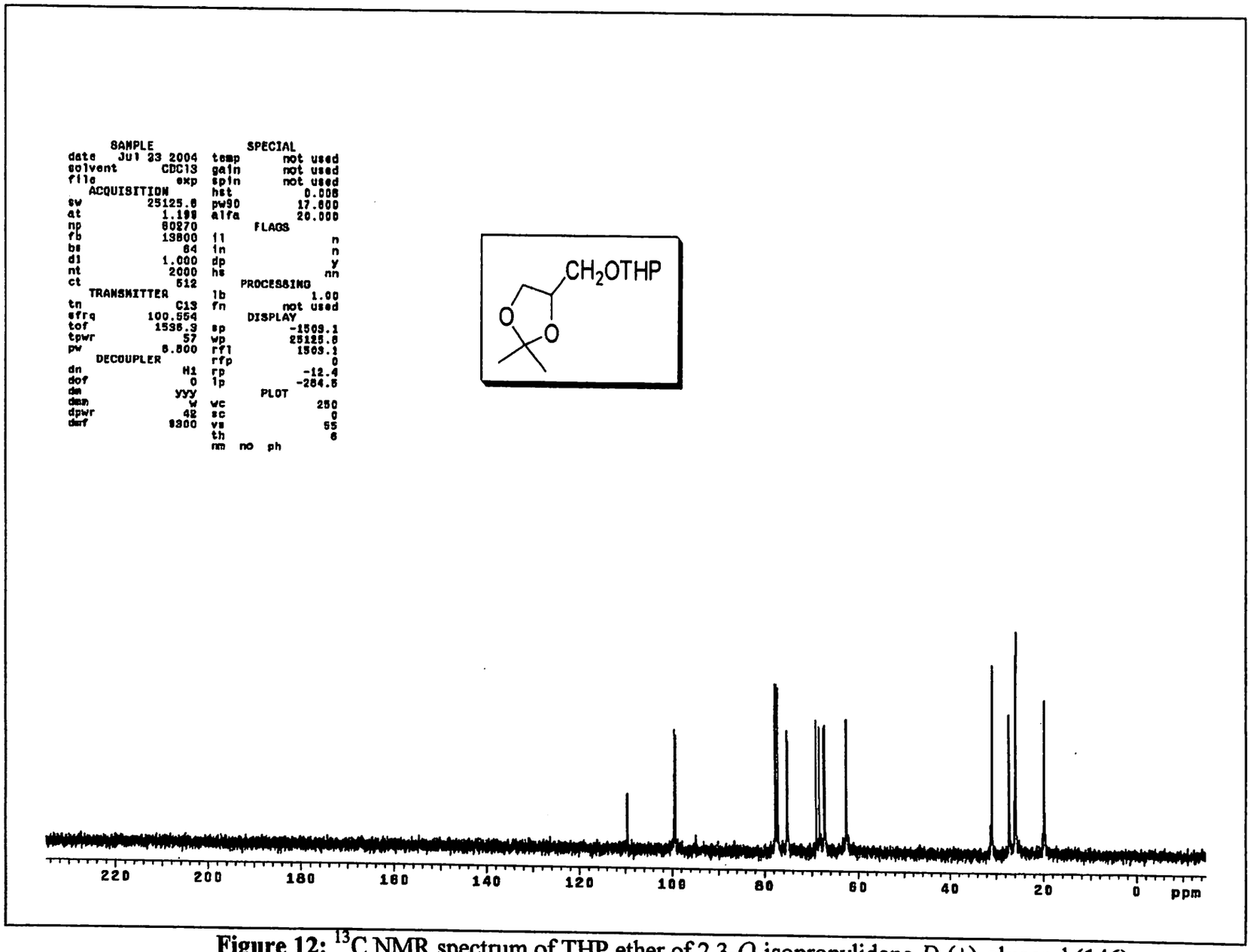


Figure 12: ^{13}C NMR spectrum of THP ether of 2,3-*O*-isopropylidene-*D*-(±)-glycerol **(146)**

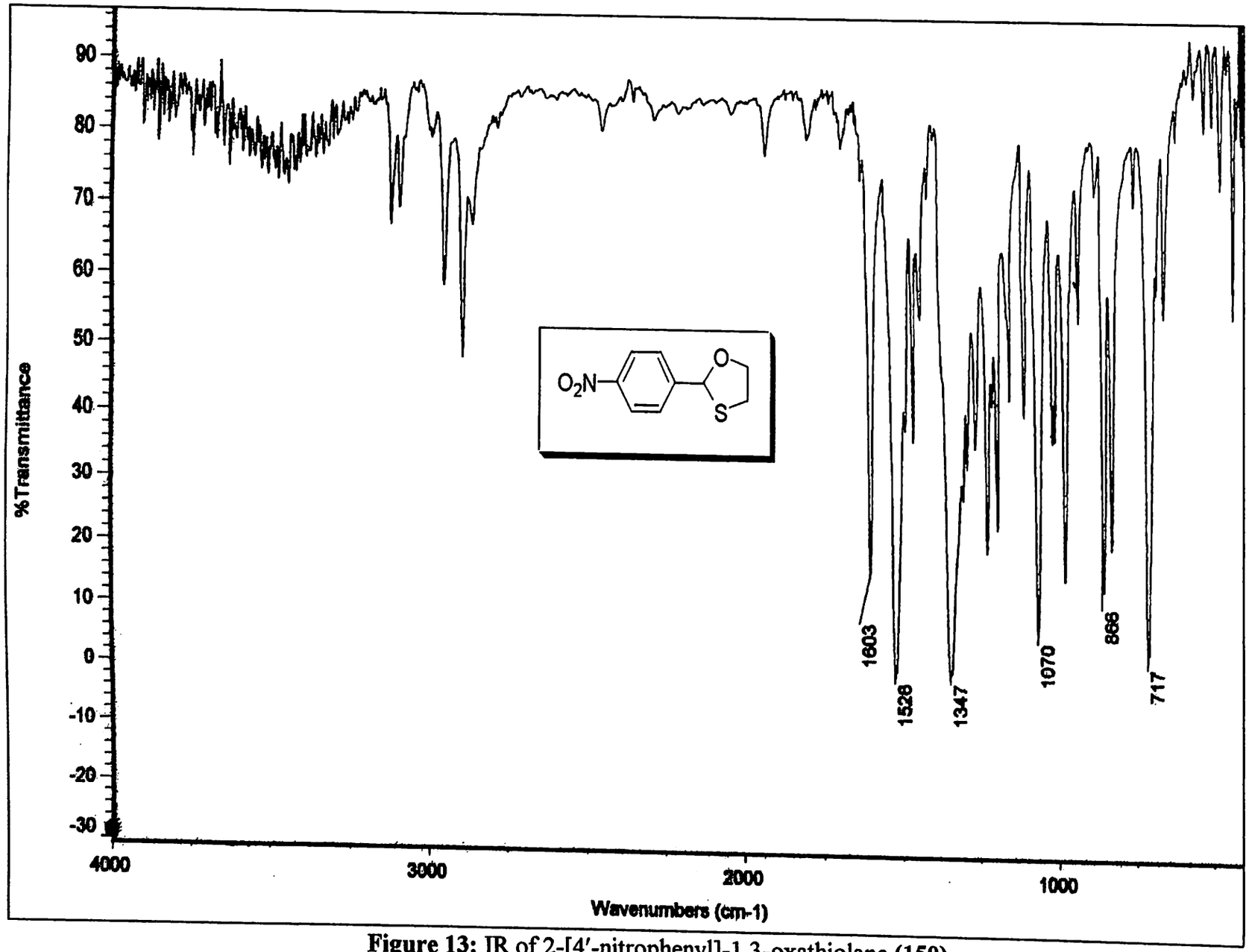


Figure 13: IR of 2-[4′-nitrophenyl]-1,3-oxathiolane **(150)**

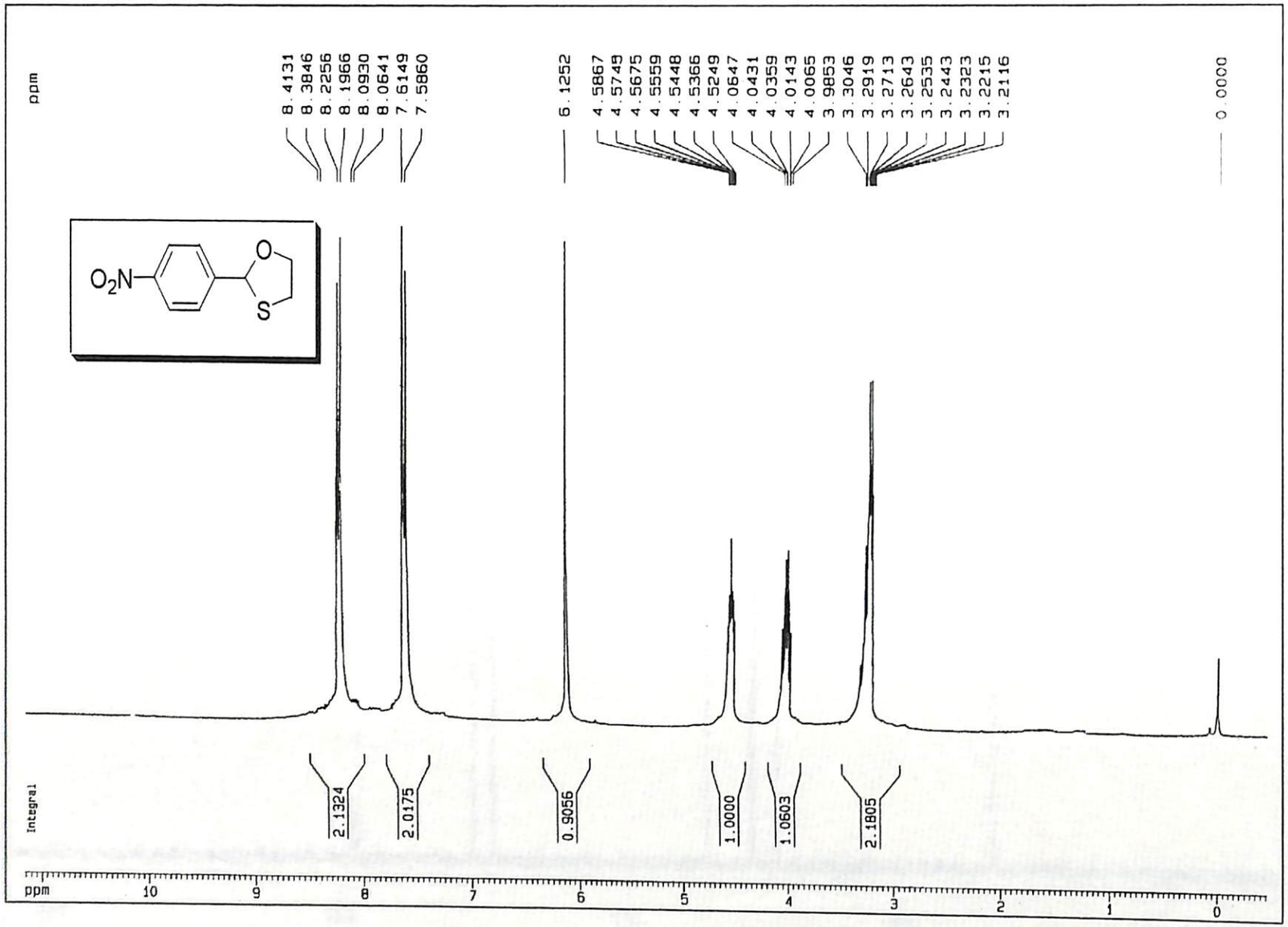


Figure 14: ^{1}H NMR spectrum of 2-[4′-nitrophenyl]-1,3-oxathiolane **(150)**

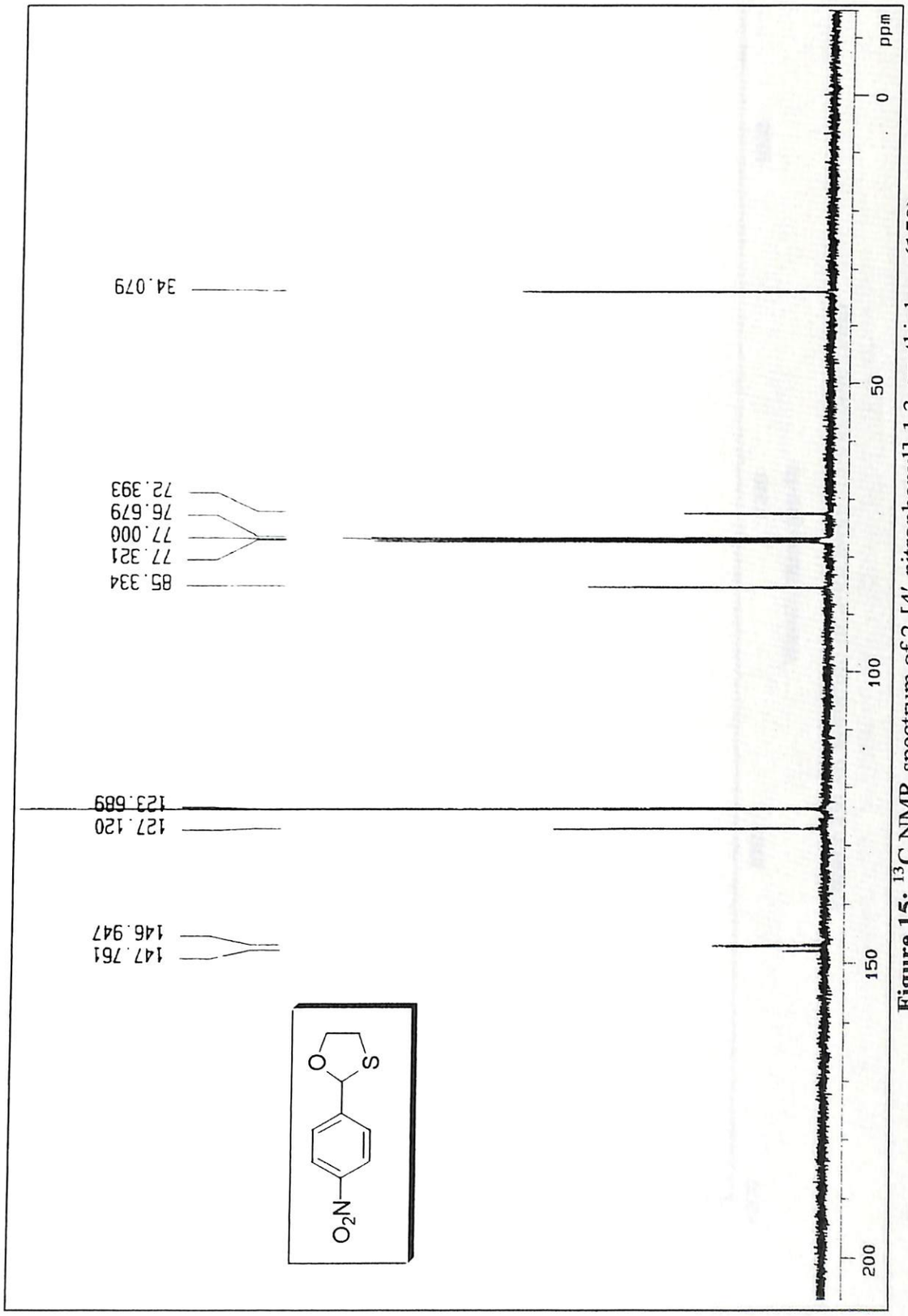


Figure 15: ^{13}C NMR spectrum of 2-[4′-nitrophenyl]-1,3-oxathiolane **(150)**

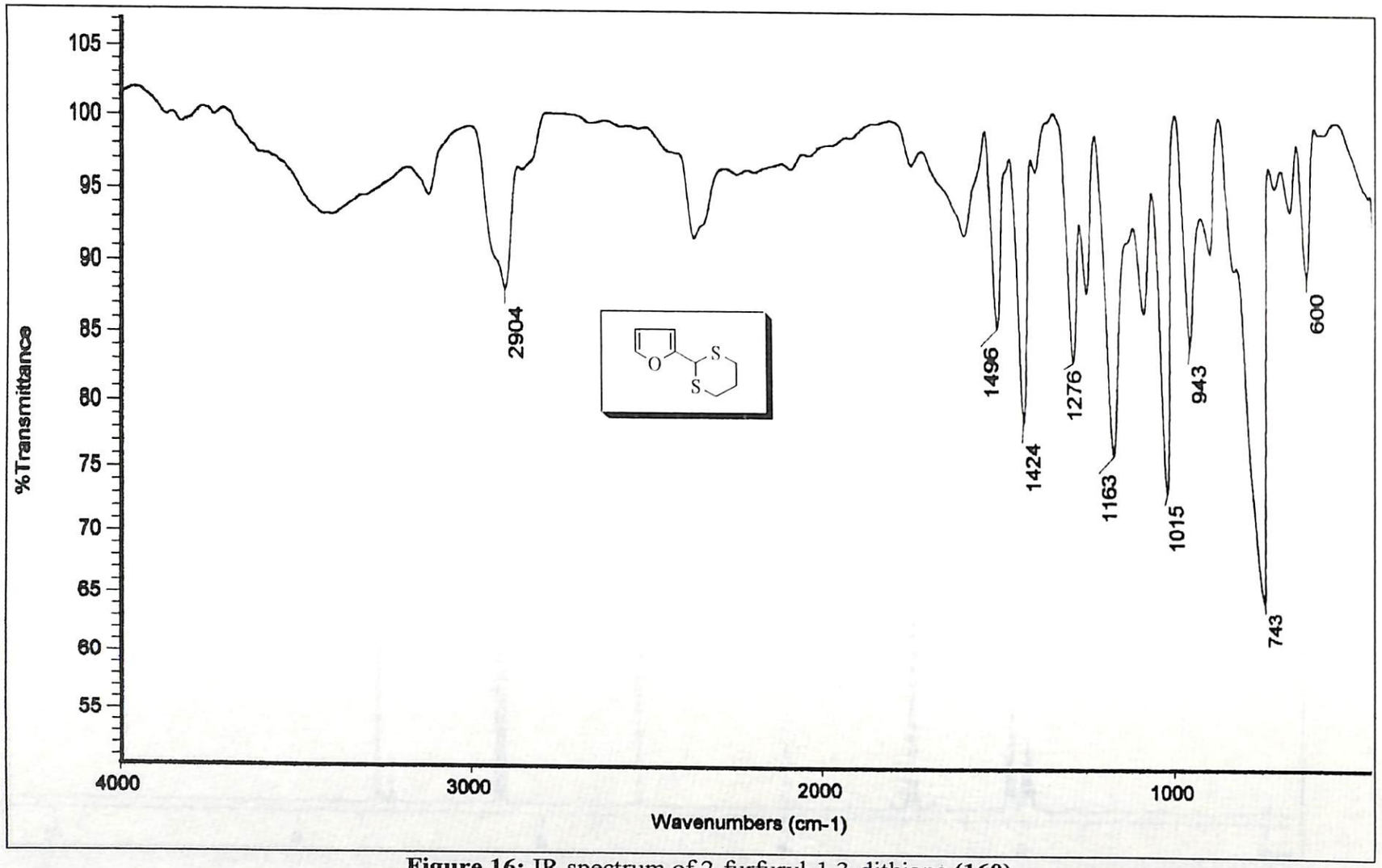


Figure 16: IR spectrum of 2-furfuryl-1,3-dithiane **(160)**

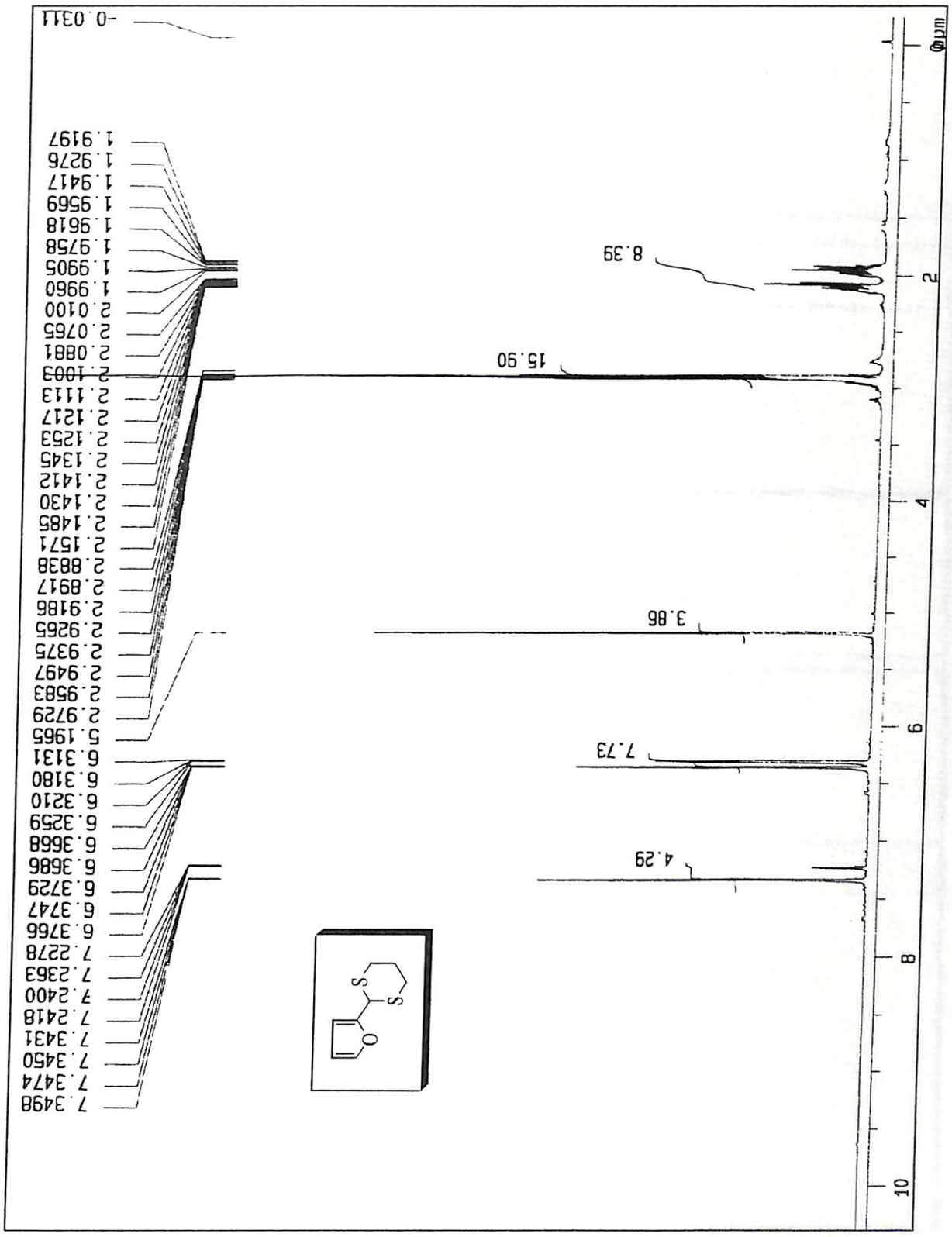


Figure 17: ^{1}H NMR spectrum of 2-furfuryl-1,3-dithiane **(160)**

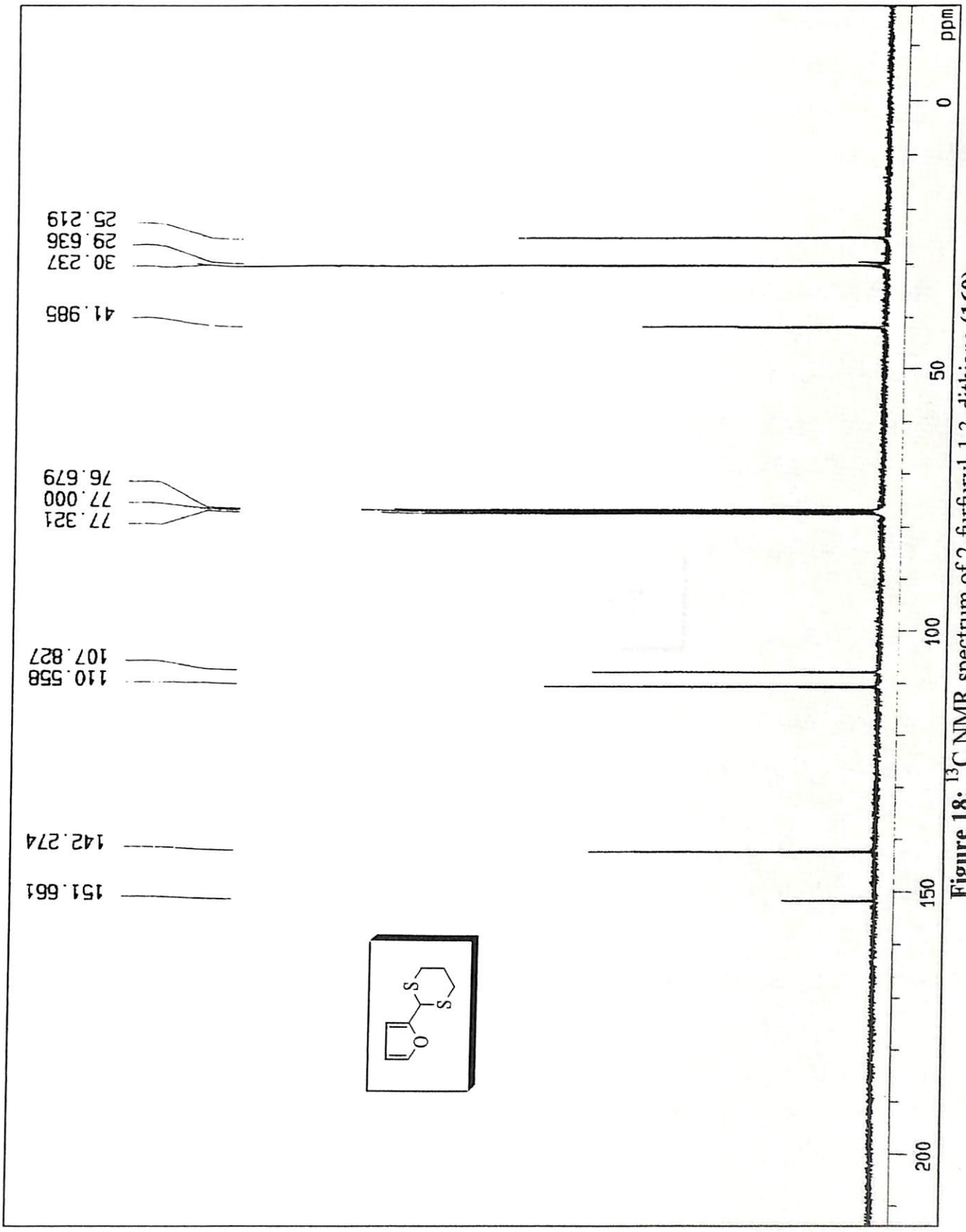


Figure 18: ^{13}C NMR spectrum of 2-furfuryl-1,3-dithiane **(160)**

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Conclusion and Future Scope

We have developed new methodologies for cleavage of TBS ethers and acetylation of alcohols, phenols, amines and thiols using acetonyltriphenylphosphonium bromide (ATPB). In addition, it is possible to achieve *gem*-diacylation of aldehydes using the same reagent. Due to harsh reaction conditions, we have devised another method for similar transformation by employing silica supported perchloric acid, which is milder as compared to other reported procedures as well as less expensive and environmentally benign. Moreover, we have further shown the applicability of silica-supported perchloric acid for tetrahydropyranylation, oxathioacetalization and thioacetalization. These are valuable contribution in protection and deprotection chemistry. Then, we have demonstrated two new methodologies for chemoselective α- monobromination of β-keto esters and 1,3-diketones. We expect that some of the protocols are valuable addition in modern organic synthesis.

The future scope of the work is to exploit further bromodimethylsulfonium bromide (BDMS) as well as other two reagents for some other valuable organic transformations. We would like to investigate glycosylation reaction using BDMS as promoter in presence of some activator. Moreover, we would like to utilize α-monobrominated product of β-keto esters and 1,3-diketones for the preparation of heterocyclic compounds, which is under progress. The future research work will be executed by another student and successful result will be reported in due time.

LIST OF AUTHOR'S PUBLICATIONS AND COMMUNICATIONS

1. A Simple and Useful Synthetic Protocol for Selective Deprotection of *tert*–Butyl dimethylsilyl (TBS) Ethers.
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A Simple and Useful Synthetic Protocol for Selective Deprotection of *tert*-Butyldimethylsilyl (TBS) Ethers

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Keywords: Deprotection / Ethers / Protecting groups / Synthesis design

A wide variety of *tert*-butyldimethylsilyl ethers **1** can be easily cleaved to the corresponding parent hydroxyl compound **2** in the presence of 5 mol % of acetonyltriphenylphosphonium bromide (ATPB) at room temperature. In addition, *tert*-butyldiphenylsilyl ethers can also be cleaved by using 20 mol % of the same catalyst. Alkyl *tert*-butyldimethylsilyl ethers can be deprotected to the hydroxyl compounds chemoselectively in the presence of aryl *tert*-butyldimethylsilyl ethers. Some of the major advantages are mild reaction conditions, no aqueous workup, high efficiency and chemoselectivity and compatibility with other protecting groups; no brominations occur in the aromatic ring under these experimental conditions.

Introduction

Protection and deprotection strategies are very common features of the manipulation of other functional groups in multi-step natural and non-natural product synthesis. Among the various functional groups, the protection of a hydroxyl group as a *tert*-butyldimethylsilyl (TBS) ether or *tert*-butyldiphenylsilyl (TBDPS) ether, first introduced by Corey and co-workers,[1] plays a key role in carbohydrate and nucleoside chemistry due to its ease of preparation and inherent stability under basic and mildly acidic conditions. Although a wide variety of reagents and recipes have been developed over the years for their removal,[2] there still is a need to find better alternatives that might work under milder reaction conditions with less-expensive reagents. The usual procedure for deprotection of *tert*-butyldimethylsilyl (TBS) ethers and *tert*-butyldiphenylsilyl (TBDPS) ethers involves the use of tetrabutylammonium fluoride.[1,3] However, this method has some serious drawbacks, such as high cost as well as incompatibility with base-sensitive substrates due to the basic nature of the fluoride ion, which causes side reactions.[4] Since then many other protocols have been developed that use other fluoro compounds such as, for example, boron trifluoride etherate,[5a] hydrofluoric acid,[5b] flurosilicic acid,[5c] ammonium fluoride,[5d] silicon fluoride,[5e] *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium tetrafluoroborate (TBTU),[5f] lithium tetrafluoroborate,[5g] and zinc tetrafluoroborate.[5h] However, these methods have some disadvantages, such as incompatibility with acid-sensitive groups,[5a–5e] and require relatively long reaction times[5g][5h] and harsh reaction conditions.[5g] Various methods have also been reported in the literature for the deprotection of TBS ethers with chloro compounds, such as cerium(III) chloride in combination with sodium iodide,[6a] cerium(III) chloride alone,[6b] LiCl in DMF,[6c] TMSCl in H_2O,[6d] $ZrCl_4$,[6e] and CH_3COCl.[6f] Likewise, a few methods have also been reported with TMSOTf,[7a] $Sc(OTf)_3$,[7b] I_2,[7c] oxone in aqueous methanol,[7d] 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[7e] decaborane,[7f] 1,1,3,3-tetramethylguanidine,[7g] and Cs_2CO_3.[7h] Moreover, the deprotection of TBS ethers has also been reported with several bromo compounds, for example CBr_4,[8a] $BiBr_3$,[8b] acetyl bromide,[8c] tetrabutylammonium tribromide,[8d] molecular bromine,[8e] and IBr.[8f] Unfortunately, some of these procedures have disadvantages such as relatively harsh reaction conditions,[7a–7c,8a] failure to deprotect aryl *tert*-butyldimethylsilyl ethers,[6c,7c,8b] require longer reaction times[6,7a–7d,8d] and much more expensive reagents,[6a,6b,8d] incompatibility with other protecting groups such as thioketals[8] or a thio group at the anomeric position of the carbohydrate compounds,[8f] difficulty in maintaining a stoichiometric ratio, difficult to handle,[7a,8c] over oxidation,[7e] unwanted product (acetate instead of alcohol),[8c] or require an excess amount of reagent.[7a–7c] Therefore, there is a need to develop other alternatives. As part of our ongoing research project to develop new synthetic methodologies, particularly in protection and deprotection chemistry,[9] we envisioned that acetonyltriphenylphosphonium bromide, which can generate HBr in situ on reaction with an alcohol,[10a] might be a useful catalyst for the deprotection of *tert*-butyldimethylsilyl ethers and *tert*-butyldiphenylsilyl ethers. So far acetonyltriphenylphosphonium bromide has been utilized mainly as a Wittig salt,[10b] for the tetrahydropyranylation/depyranylation of alcohols,[10c] and for the cyclotrimerization of aldehydes.[10d] However, the full

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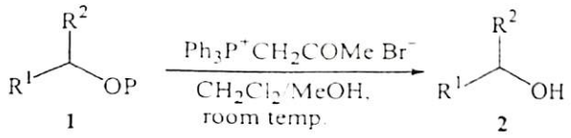
  DOI: 10.1002/ejoc.200400031

versatility of this reagent has not been investigated. Very recently, we demonstrated the utility of bromodimethylsulfonium bromide for the tetrahydropyranylation/depyranylation of alcohols and phenols and the thioacetalization of carbonyl compounds.[11] These results prompted us to investigate whether acetonyltriphenylphosphonium bromide could be used for the deprotection of TBS ethers or not. In this paper, we report for the first time a simple and useful synthetic protocol for the cleavage of various TBS ethers that involves acetonyltriphenylphosphonium bromide (ATPB) as a new pre-catalyst (Scheme 1).



R^1 = alkyl/aryl/sugar residue/nucleoside residue;
R^2 = H, alkyl; P = TBS/TBDPS

Scheme 1

Results and Discussion

In order to verify our proposal we had to prepare a wide variety of *tert*-butyldimethylsilyl (TBS) ethers as well as *tert*-butyldiphenylsilyl (TBDPS) ethers by following the reported procedure.[1,2] Next, we prepared the reagent acetonyltriphenylphosphonium bromide (ATPB) by reaction of triphenylphosphane with bromoacetone in benzene at room temperature following the literature procedure.[10d] The solid ATPB (m.p. 221−223 °C, ref. m.p. 221−223 °C) was obtained by quick filtration followed by washing with benzene to remove the unchanged triphenylphosphane. First, we attempted the reaction of *tert*-butyldimethylsilyl ether **1a** (1 equiv.) with 0.05 equivalents of acetonyltriphenylphosphonium bromide in dichloromethane/methanol (5:2) at room temperature. We noticed that the reaction was complete within three minutes and the pure product 5-acetoxy-1-pentanol (**2a**) was obtained in 70% yield by passing the crude mixture through a silica gel column. The product was characterized by recording IR and ^{1}H NMR spectra, which were then compared with the spectra of an authentic sample. We found that various *tert*-butyldimethylsilyl ethers, such as **1b**−**d**, containing benzoyl, benzyl and ester groups, respectively, were smoothly deprotected to the corresponding alcohols **2b**−**d** in good yields, without affecting these groups, under identical reaction conditions. All the products were characterized in a similar manner. It is worthwhile to mention that our protocol is more efficient in terms of reaction time than a recently reported procedure.[8d] Similarly, other TBS ethers such as **1e**−**g** were converted into the corresponding alcohols **2e**−**g** in good yield by following the same procedure. It is interesting to note that no bromination occurs at the double bond or even in the furan ring under these experimental conditions. Likewise, the TBS ether **1h** was easily transformed into the corresponding alcohol **2h** without disturbing the thioketal group. Interestingly, the thioketal group is also cleaved when the same reaction is carried out with other bromo compounds such as tetrabutylammonium tribromide (TBATB), CBr_4 and molecular bromine. This result clearly indicates that our methodology has some additional advantages compared to the other reported procedures, especially those based on bromo reagents. In addition, various TBS ethers **1i**−**j**, which are derived from secondary alcohols, were also cleaved to the corresponding alcohols **2i**−**j** in good yields under identical reaction conditions. Again, we noticed that it took much less time for deprotection of **1j** than the earlier procedures.[8b] Moreover, by using our protocol, TBS ether **1k** and an acetylenic TBS ether **1l** were also deprotected to the desired alcohols **2k** and **2l** without bromination either at the double or at the triple bond. Remarkably, a highly acid-sensitive TBS ether such as **1m** can be cleaved to the corresponding alcohol **2m** without losing the isopropylidene group.

We also decided to study whether the same reagent can be employed for deprotection of aryl TBS ethers or not. We observed that various phenolic TBS ethers **1n**−**q** can be converted into the respective phenolic compounds **2n**−**q** without affecting a thioketal group. It is important to men-

Table 1. Deprotection of various TBS ethers **1** to the parent hydroxyl compounds **2** in the presence of a catalytic amount of acetonyltriphenylphosphonium bromide (ATPB) in dichloromethane/methanol

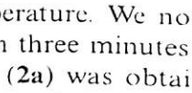
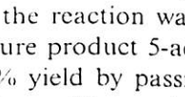
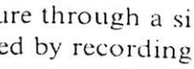
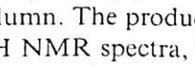
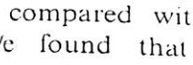
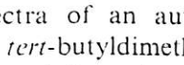
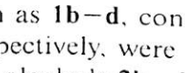
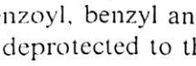
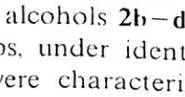
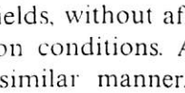
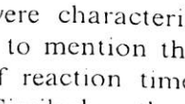
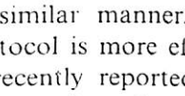
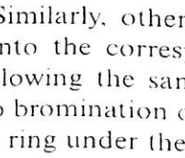
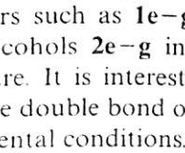
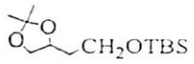
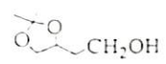
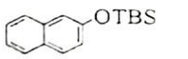
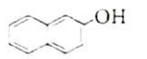
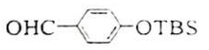
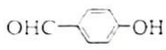
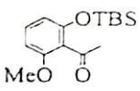
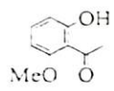
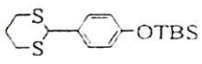
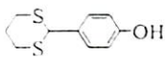
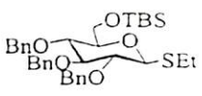
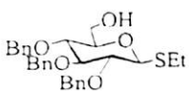
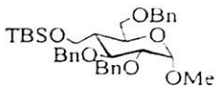
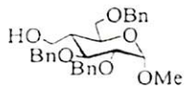
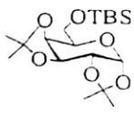
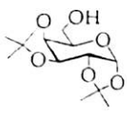
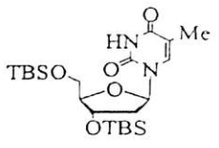
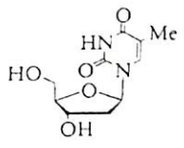
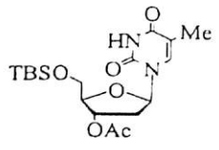
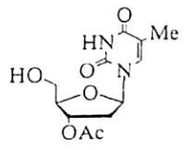
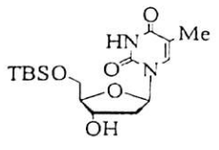
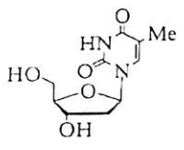
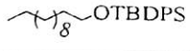
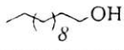
Entry	Substrate (1)	Time	Product[a] (2)	Yield[b][c] [%]
a	AcO(CH2)3OTBS	3 min	AcO(CH2)3OH	70
b	BzO(CH2)3OTBS	15 min	BzO(CH2)3OH	88
c	BnO(CH2)3OTBS	10 min	BnO(CH2)3OH	92
d	MeO2C(CH2)9OTBS	15 min	MeO2C(CH2)9OH	92[6f]
e		7 min		91[11a]
f		2 h		94[12]
g		10 min		83[12]
h	 R = *p*-methoxyphenyl	20 min	 R = *p*-methoxyphenyl	81
i		22 min		91[12]
j		2.5 h		90[12]
k		5 min		95[12]

Table 1. (continued)

Entry	Substrate (1)	Time	Product[a] (2)	Yield[b][c] [%]
l		7 min		85[12]
m		15 min		72[12]
n		6 h		81[12]
o		5 h		71[12]
p		3 h		91[12]
q		4 h		85
r		50 min		88[6f]
s		2 h		82
t		30 min		80[6f]
u		6 h		75[12]
v		3 h		87
w		3 h		87[12]
x		5 h		88[12]

[a] All starting materials and final products were characterized by IR, ^{1}H NMR and ^{13}C NMR spectroscopy, and elemental analysis. [b] Isolated yield.

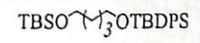
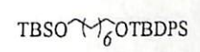
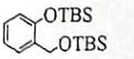
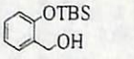
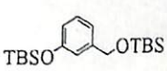
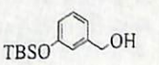
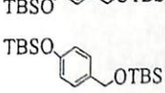
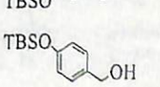
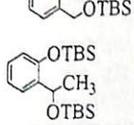
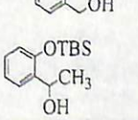
tion that no α-bromination was observed in the case of compound **1p**, and neither was any cyclotrimerization observed in the case of the aromatic aldehyde **1o**. The reactions with aryl TBS ethers take slightly longer than those with alcoholic TBS ethers. All the deprotected alcohols were characterized fully by IR and ^{1}H NMR spectroscopy and by elemental analysis; the spectra were compared with those of authentic samples.

We then turned our attention to whether this methodology could be further extended for deprotection of TBS ethers of carbohydrates and nucleosides. We found that various TBS ethers **1r**–**w** can be cleaved easily to the corresponding parent hydroxyl compounds **2r**–**w** in good yields under identical reaction conditions. Importantly, a thio group at the anomeric position usually affected by the earlier reported procedures.[8f] An OMe ether or an isopropylidene group at the anomeric position also survived under the experimental conditions. The reaction times and yields of all the products are summarized in Table 1.

These results further encouraged us to study whether our methodology could be extended to the deprotection of *tert*-butyldiphenyl silyl (TBDPS) ethers. We found that a TBDPS ether of 1-dodecanol (**1x**) was also converted into the corresponding alcohol **2x** in 88% yield in the presence of 0.2 equivalents of the same pre-catalyst although with a longer reaction time. The product was characterized as above.

Interestingly, our protocol can also be further extended to the chemoselective deprotection of TBS ethers in the presence of a TBDPS ether or an aryl TBS ether. 1-*tert*-Butyldimethylsilyl-5-*tert*-butyldiphenylsilyl diether (**1a′**) and 1-*tert*-butyldimethylsilyl-8-*tert*-butyldiphenylsilyl diether (**1b′**) were smoothly converted into the corresponding mono TBDPS ethers chemoselectively, as shown in Table 2. Likewise, various alkyl *tert*-butyldimethylsilyl ethers **1c′**–**f′** were converted into the desired mono aryl *tert*-butyldimethylsilyl ethers **2c′**–**f′** in good yields. Moreover, the secondary TBS ether was also cleaved faster than the aryl TBS ether, as shown in Table 2. All the products were characterized by the usual spectroscopic techniques.

Table 2. Deprotection of various TBS ethers **1** to the parent hydroxyl compounds **2** in the presence of a catalytic amount of acetonyltriphenylphosphonium bromide (ATPB) in dichloromethane/methanol

Entry	Substrate (1)	Time	Product[a] (2)	Yield[b] [%]
a′		35 min		78
b′		12 min		81
c′		10 min		77
d′		6 min		86
e′		15 min		87
f′		45 min		76

[a] All starting materials and final products were characterized by IR, ^{1}H NMR and ^{13}C NMR spectroscopy, and elemental analysis. [b] Isolated yield.

The formation of the products can be rationalized as follows. We believe that HBr, generated in the reaction medium from the reaction of acetonyltriphenylphosphonium bromide with methanol, catalyzes the deprotection of TBS ethers to the corresponding alcohols. However, the same reaction failed when it was carried out with benzyltriphenylphosphonium bromide instead of acetonyltriphenylphosphonium bromide. This indicates that ATPB generates HBr much more easily than the other alkylphosphonium bromide.

Conclusion

In summary, we have devised a new, efficient, and regioas well as chemoselective protocol for the deprotection of TBS ethers and TBDPS ethers using a catalytic amount of acetonyltriphenylphosphonium bromide in dichloromethane/methanol at room temperature under very mild conditions. The significant features of the present method include the ease of operation, high efficiency, mild conditions and chemoselectivity, which may be useful in organic synthesis. In addition, the selective deprotection of alkyl *tert*-butyldimethylsilyl ether can be achieved in the presence of aryl-*tert*-butyldimethylsilyl ethers. We have found that a wide variety of other protecting groups, such as acetyl, benzyl, benzoyl, thioketals, esters and isopropylidene survive under the present experimental conditions.

Experimental Section

Melting points were recorded on a Büchi B-545 melting point apparatus and are uncorrected. IR spectra were recorded in KBr or neat on a Nicolet Impact 410 spectrophotometer. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Bruker 200, Bruker 300 or Jeol 400 MHz spectrometer in $CDCl_3$ using TMS as internal reference. Elemental analyses were carried out with a Perkin–Elmer 2400 automatic carbon, hydrogen, nitrogen and sulfur analyzer. Column chromatographic separations were done on SRL silica gel (60–120 mesh).

General Procedure for the Deprotection: A catalytic amount of acetonyltriphenylphosphonium bromide (20 mg, 0.05 mmol) was added to a well-stirred solution of *tert*-butyldimethylsilyl ether **1** (1 mmol) in 2 mL of dichloromethane/methanol mixture (5:2) at room temperature (except for **1x**) and the mixture kept stirring. After completion of the reaction, as monitored by TLC, it was concentrated on a rotary evaporator. The crude residue was subjected to silica gel column chromatography to isolate the desired alcohols **2** in good yields.

Compound 1a: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2960, 2935, 2868, 1747, 1475, 1373, 1250, 1112, 1045, 840, 779 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.85 [s, 9 H, $SiC(CH_3)_3$], 1.36 (m, 2 H, CH_2), 1.50 (m, 2 H, CH_2), 1.60 (m, 2 H, CH_2), 1.99 (s, 3 H, $COCH_3$), 3.57 (t, J = 6.3 Hz, 2 H, CH_2OTBS), 4.01 (t, J = 6.6 Hz, 2 H, $AcOCH_2$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.4, 18.3, 20.9, 22.2, 25.9, 28.3, 32.3, 62.9, 64.5, 171.2 ppm. $C_{13}H_{28}O_3Si$ (260.45): calcd. C 59.95, H 10.83; found C 59.72, H 10.75.

Compound 1b: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2940, 2858, 1721, 1583, 1429, 1337, 1301, 1112, 943 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.02 [s, 6 H, $Si(CH_3)_2$], 0.83 [s, 9 H, $SiC(CH_3)_3$], 1.47 (m, 2 H, CH_2), 1.54 (m, 2 H, CH_2), 1.74 (m, 2 H, CH_2), 3.57 (t, J = 6.3 Hz, 2 H, CH_2OTBS), 4.26 (t, J = 6.6 Hz, 2 H, $PhCOOCH_2$), 7.39 (t, J = 7.8 Hz, 1 H, ArH), 7.44 (t, J = 7.8 Hz, 1 H, ArH), 7.54 (m, 1 H, ArH), 8.00 (dd, J = 1.2, J = 7.3 Hz, 1 H, ArH), 8.09 (dd, J = 1.2, J = 7.1 Hz, 1 H, ArH) ppm. $C_{18}H_{30}O_3Si$ (322.52): calcd. C 67.03, H 9.38; found C 66.91, H 9.25.

Compound 1c: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2960, 2935, 2858, 1506, 1470, 1460, 1368, 1255, 1102, 1009, 840 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.01 [s, 6 H, $Si(CH_3)_2$], 0.83 [s, 9 H, $SiC(CH_3)_3$], 1.50 (m, 6 H, CH_2), 3.43 (t, J = 6.5 Hz, 2 H, CH_2OTBS), 3.57 (t, J = 6.4 Hz, 2 H, $PhCH_2OCH_2$), 4.46 (s, 2 H, OCH_2Ph), 7.31 (m, 5 H, ArH) ppm. $C_{17}H_{32}O_2Si$ (296.52): calcd. C 68.86, H 10.88; found 68.79, H 10.80.

Compound 1e: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2955, 2929, 2863, 1655, 1615, 1516, 1470, 1250, 1096, 1034, 855 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08 [s, 6 H, $Si(CH_3)_2$], 0.93 [s, 9 H, $SiC(CH_3)_3$], 4.52 (d, J = 1.2 Hz, 2 H, $OCH_2CH{=}CH_2$), 4.66 (s, 2 H, CH_2OTBS), 5.27 (dd, J = 1.0, J = 10.5 Hz, 1 H, $OCH_2CH{=}CH_2$), 5.40 (dd, J = 1.4, J = 15.8 Hz, 1 H, $OCH_2CH{=}CH_2$), 6.06 (m, 1 H, $OCH_2CH{=}CH_2$), 6.88 (d, J = 8.6 Hz, 2 H, ArH), 7.22 (d, J = 8.3 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.2, 18.4, 25.9, 64.7, 68.9, 114.5, 117.6, 127.5, 133.4, 133.8, 157.7 ppm. $C_{16}H_{26}O_2Si$ (278.47): calcd. C 69.01, H 9.41; found C 68.82, H 9.47.

Compound 1f: Yellowish liquid. IR (neat): $\tilde{\nu}$ = 2955, 2935, 2863, 1614, 1521, 1475, 1352, 1265, 1102, 1020, 856 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.13 [s, 6 H, Si $(CH_3)_2$], 0.96 [s, 9 H, $SiC(CH_3)_3$], 4.83 (s, 2 H, CH_2OTBS), 7.49 (d, J = 8.7 Hz, 2 H, ArH), 8.20 (d, J = 9.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4, 18.3, 25.8, 64.0, 123.5, 126.3, 146.0, 149.0 ppm. $C_{13}H_{21}NO_3Si$ (267.40): calcd. C 58.39, H 7.92, and N 5.24; found C 58.15, H 7.84, N 5.08.

Compound 1g: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2960, 2935, 2863, 1603, 1506, 1470, 1255, 1158, 1076, 1015, 840 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08 [s, 6 H, $Si(CH_3)_2$], 0.88 [s, 9 H, $SiC(CH_3)_3$], 4.62 (s, 2 H, CH_2OTBS), 6.14 (d, J = 3.2 Hz, 1 H, 3-H), 6.23 (dd, J = 1.7, J = 3.2 Hz, 1 H, 4-H), 7.28 (dd, J = 0.9, J = 1.7 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.3, 18.4, 25.9, 58.1, 107.2, 110.2, 142.0, 154.3 ppm. $C_{11}H_{20}O_2Si$ (212.36): calcd. C 62.22, H 9.49; found C 61.97, H 9.42.

Compound 1h: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2955, 2930, 2863, 1609, 1516, 1470, 1255, 1091, 1040, 902, 840 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 [s, 12 H, 2 × $Si(CH_3)_2$], 0.84 [s, 18 H, 2 × $SiC(CH_3)_3$], 2.54–2.61 (m, 4 H, SCH_2), 3.66 (m, 4 H, OCH_2), 3.76 (s, 3 H, OCH_3), 5.01 (s, 1 H, SCHS), 6.82 (d, J = 9.5 Hz, 2 H, ArH), 7.33 (d, J = 9.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.3, 18.3, 25.9, 34.6, 53.4, 55.3, 63.2, 113.9, 128.9, 132.5, 159.2 ppm. $C_{24}H_{46}O_3S_2Si_2$ (502.93): calcd. C 57.32, H 9.22, S, 12.75; found C 57.08, H 9.15, S 12.63.

Compound 1i: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2960, 2940, 2863, 1475, 1378, 1255, 1132, 1061, 835 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.83 (t, J = 7.6 Hz, 6 H, 2 × CH_3), 0.85 [s, 9 H, $SiC(CH_3)_3$], 1.22–1.30 (m, 6 H, CH_2), 1.34–1.43 (m, 4 H, CH_2), 3.53 (quin., J = 5.9 Hz, 1 H, CH_2CHCH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −4.5, −4.5, 9.6, 14.0, 18.1, 22.6, 25.0, 25.9, 29.7, 32.0, 36.5, 73.5 ppm.

$C_{14}H_{32}OSi$ (244.49): calcd. C 68.78, H 13.19; found C 68.91, H 13.06.

Compound 1j: White solid, m.p. 151–153 °C. IR (KBr): $\tilde{\nu}$ = 2930, 2858, 1665, 1460, 1378, 1255, 1112 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.06 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.82 (s, 6 H, 2 × CH_3), 0.83 [s, 9 H, $SiC(CH_3)_3$], 0.85 (d, J = 6.3 Hz, 3 H, $CHCH_3$), 0.94 (s, 6 H, 2 × CH_3), 1.00–1.50 (m, 22 H, CH and CH_2), 1.75 (m, 2 H, CH_2), 1.94 (m, 2 H, CH_2), 2.12 (m, 1 H, CH), 2.20 (m, 1 H, CH), 3.42 (q, J = 6.0 Hz, 1 H, OCH), 5.25 (m, 1 H, =CH) ppm. $C_{34}H_{60}OSi$ (500.92): calcd. C 79.13, H 12.07; found C 79.09, H 12.11.

Compound 1k: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2955, 2930, 2858, 1665, 1465, 1383, 1255, 1096, 1061, 835 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.01 [s, 6 H, $Si(CH_3)_2$], 0.84 [s, 9 H, $SiC(CH_3)_3$], 1.53 [s, 6 H, $C(CH_3)_2$], 1.61 (s, 3 H, CH_3), 1.88–2.03 (m, 4 H, $CHCH_2$), 3.54–3.59 (m, 1 H, OCH_2), 4.12–4.13 (m, 1 H, OCH_2), 5.01–5.05 (m, 1 H, CH), 5.22–5.25 (m, 1 H, CH) ppm. $C_{16}H_{32}OSi$ (268.51): calcd. C 71.57, H 12.01; found C 71.75, H 12.09.

Compound 1l: Yellowish liquid. IR (neat): $\tilde{\nu}$ = 2955, 2934, 2863, 1465, 1357, 1255, 1137, 1070, 840 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.12 [s, 12 H, 2 × $Si(CH_3)_2$], 0.91 [s, 18 H, 2 × $SiC(CH_3)_3$], 4.34 (s, 4 H, OCH2) ppm. $C_{16}H_{34}O_2Si_2$ (314.61): calcd. C 61.08, H 10.89; found C 61.10, H 10.85.

Compound 1m: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2945, 2863, 1460, 1378, 1255, 1148, 1107, 846, 784 cm^{-1}. $C_{10}H_{26}O_3Si$ (222.40): calcd. C 54.01, H 11.78; found C 54.12, H 11.83.

Compound 1n: Colourless liquid. IR (neat): $\tilde{\nu}$ = 3058, 2966, 2940, 2863, 1634, 1603, 1506, 1470, 1363, 1260, 1230, 1173, 1132, 1015, 933, 851 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.25 [s, 6 H, $Si(CH_3)_2$], 1.02 [s, 9 H, $SiC(CH_3)_3$], 7.07 (dd, J = 3.2, J = 8.7 Hz, 1 H, 3-ArH), 7.19 (d, J = 2.4 Hz, 1 H, 1-ArH), 7.30 (t, J = 7.0 Hz, 1 H, 6-ArH), 7.38 (t, J = 7.0 Hz, 1 H, 7-ArH), 7.68 (d, J = 8.7 Hz, 1 H, ArH, 4-ArH), 7.72 (d, J = 9.0 Hz, 1 H, 5-ArH), 7.76 (d, J = 8.1 Hz, 1 H, 8-ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.3, 18.3, 25.7, 114.9, 122.1, 123.7, 126.1, 126.7, 127.6, 129.3, 134.6, 153.5 ppm. $C_{16}H_{22}OSi$ (258.43): calcd. C 74.36, H 8.58; found C 74.10, H 8.50.

Compound 1o: Yellowish liquid. IR (neat): $\tilde{\nu}$ = 2945, 2858, 1705, 1603, 1511, 1270, 1157, 912, 845 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.25 [s, 6 H, $Si(CH_3)_2$], 0.99 [s, 9 H, $SiC(CH_3)_3$], 6.95 (d, J = 8.4 Hz, 2 H, ArH), 7.81 (d, J = 8.4 Hz, 2 H, ArH), 9.89 (s, 1 H, CHO) ppm. $C_{13}H_{20}O_2Si$ (236.39): calcd. C 66.06, H 8.53; found C 65.37, H 8.58.

Compound 1p: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2966, 2935, 2863, 1711, 1593, 1470, 1255, 1107, 974, 840 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.19 [s, 6 H, $Si(CH_3)_2$], 0.94 [s, 9 H, $SiC(CH_3)_3$], 2.47 (s, 3 H, $COCH_3$), 3.77 (s, 3 H, OCH_3), 6.37 (d, J = 8.3 Hz, 1 H, ArH), 6.51 (d, J = 8.3 Hz, 1 H, ArH), 7.15 (t, J = 8.3 Hz, 1 H, ArH) ppm. $C_{15}H_{24}O_3Si$ (280.44): calcd. C 64.24, H 8.63; found C 64.45, H 8.58.

Compound 1q: White solid; m.p. 82.6 °C. IR (neat): $\tilde{\nu}$ = 2955, 2929, 2893, 2852, 1608, 1511, 1470, 1419, 1255, 1168, 912, 845 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 [s, 6 H, $Si(CH_3)_2$], 0.97 [s, 9 H, $SiC(CH_3)_3$], 1.84–1.88 (m, 1 H, SCH_2CH_2), 1.91–1.97 (m, 1 H, SCH_2CH_2), 2.85–2.92 (m, 2 H, SCH_2CH_2), 2.99–3.09 (m, 2 H, SCH_2CH_2), 5.12 (s, 1 H, CH), 6.79 (d, J = 8.4 Hz, 2 H, ArH), 7.32 (d, J = 8.4 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.5, 18.1, 25.0, 25.6, 32.1, 50.8, 120.1, 128.8, 131.8, 155.7 ppm. $C_{16}H_{26}OS_2Si$ (326.60): calcd. C 58.84, H 8.02; found C 58.72, H 8.09.

Compound 1r: Colourless liquid. IR (neat): $\tilde{\nu}$ = 3037, 2960, 2930, 2873, 1619, 1496, 1460, 1255, 1158, 1096, 846, 707 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.01 [s, 3 H, $Si(CH_3)_2$], 0.02 [s, 3 H, $Si(CH_3)_2$], 0.85 [s, 9 H, $SiC(CH_3)_3$], 1.25 (t, J = 7.3 Hz, 3 H, SCH_2CH_3), 2.63–2.71 (m, 2 H, SCH_2CH_3), 3.21–3.24 (m, 1 H, H-5), 3.46 (t, J = 9.0 Hz, 1 H, H-3), 3.56 (t, J = 9.3 Hz, 1 H, H-2), 3.61 (t, J = 9.0 Hz, 1 H, H-4), 3.75 (dd, J = 3.8, J = 11.2 Hz, 1 H, H-6), 3.80 (dd, J = 2.0, J = 11.7 Hz, 1 H, H-6′), 4.38 (d, J = 9.8 Hz, 1 H, H-1), 4.62 (d, J = 10.2 Hz, 1 H, $OCHPh$), 4.68 (d, J = 10.2 Hz, 1 H, $OCHPh$), 4.79 (dd, J = 4.6, J = 10.7 Hz, 2 H, OCH_2Ph), 4.85 (dd, J = 4.0, J = 10.3 Hz, 2 H, OCH_2Ph), 7.19–7.33 (m, 15 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.4, −5.0, 15.2, 18.3, 24.3, 25.9, 62.3, 75.1, 75.5, 75.9, 77.7, 80.0, 81.8, 84.4, 86.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 128.5, 138.2, 138.3, 138.5 ppm. $C_{35}H_{48}O_5SSi$ (608.91): calcd. C 69.04, H 7.95, S 5.27; found C 69.22, H 7.87, S 5.12.

Compound 1s: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2929, 2858, 1603, 1459, 1362, 1260, 1106, 1060, 845, 742, 701 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.12 (s, 3 H, $SiCH_3$), −0.05 (s, 3 H, $SiCH_3$), 0.83 [s, 9 H, $Si(CH_3)_3$], 1.86 (t, J = 10.8 Hz, 1 H, H-4), 3.38 (s, 3 H, OCH_3), 3.39–3.44 (m, 1 H, H-1), 3.53–3.66 (m, 3 H, CH_2 & H-2), 3.88 (dd, J = 1.8, J = 10.5 Hz, 1 H, H′-6), 3.95 (d, J = 10.8 Hz, 1 H H-5), 4.06 (t, J = 9.9 Hz, 1 H, H-3), 4.43 (d, J = 12.3 Hz, 1 H, OCH_2), 4.61 (m, 3 H, OCH_2 & H-6), 4.65 (d, J = 12.6 Hz, 1 H, OCH_2), 4.77 (d, J = 12.0 Hz, 1 H, OCH_2), 5.01 (d, J = 12.0 Hz, 1 H, OCH_2), 7.26–7.37 (m, 15 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.8, −5.5, 18.1, 25.8, 44.8, 55.0, 58.3, 68.3, 69.3, 73.0, 73.4, 75.3, 75.7, 81.7, 98.5, 127.6, 127.7, 127.8, 127.9, 128.2, 128.4, 138.2, 138.4, 139.1 ppm. $C_{35}H_{48}O_6Si$ (592.84): calcd. C 70.91, H 8.16; found C 70.68, H 8.24.

Compound 1t: Yellowish liquid. IR (neat): $\tilde{\nu}$ = 2986, 2935, 2858, 1475, 1378, 1312, 1255, 1214, 1112, 1071, 1004, 840 cm^{-1} ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.07 [s, 6 H, $Si(CH_3)_2$], 0.90 [s, 9 H, $SiC(CH_3)_3$], 1.33 (s, 6 H, 2 × CH_3), 1.44 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3), 3.70–3.86 (m, 3 H, H-2, H-3, H-5), 4.30 (dd, J = 2.3, J = 7.2 Hz, 2 H, H-4, H-6), 4.60 (dd, J = 1.6, J = 7.9 Hz, 1 H, H-6′), 5.52 (d, J = 4.9 Hz, 1 H, H-1) ppm. $C_{18}H_{34}O_6Si$ (374.55): calcd. C 57.72, H 9.15; found C 57.89, H 9.02.

Compound 1u: White solid; m.p. 115 °C. IR (KBr): $\tilde{\nu}$ = 3180, 3057, 2950, 2929, 2858, 1700, 1465, 1362, 1270, 1101, 1065, 1029, 835, 778 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), 0.10 (s, 6 H, $SiCH_3$), 0.88 [s, 9 H, $SiC(CH_3)_3$], 0.91 [s, 9 H, $SiC(CH_3)_3$], 1.91 (s, 3 H, CH_3) 1.94–2.03 (m, 1 H, H-2), 2.21–2.28 (m, 1 H, H′-2), 3.75 (dd, J = 2.3, J = 13.7 Hz, 1 H, H-4), 3.84–3.92 (m, 2 H, OCH_2), 4.37–4.41 (m, 1 H, H-3), 6.30–6.35 (m, 1 H, H-1), 7.46 (s, 1 H, CH), 9.01 (s, 1 H, NH) ppm. $C_{22}H_{42}N_2O_5Si_2$ (470.75): calcd. C 56.13, H 8.99, N 5.95; found C 56.34, H 8.89, N 6.12.

Compound 1v: White solid; m.p. 145 °C. IR (KBr): $\tilde{\nu}$ = 3247, 3083, 2940, 2863, 1736, 1700, 1467, 1372, 1255, 1203, 1121, 1014, 835 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.14 (s, 6 H, $Si(CH_3)_2$), 0.93 [s, 9 H, $SiC(CH_3)_3$], 1.93 (s, 3 H, CH_3), 2.11 (s, 3 H, $COCH_3$), 2.12 (m, 2 H, H-2, H-2′), 2.41 (dd, J = 5.2, J = 13.7 Hz, 1 H), 3.92 (d, J = 1.8 Hz, 2 H, CH_2OTBS), 4.10 (d, J = 1.1 Hz, 1 H, 5.25 (d, J = 5.9 Hz, 1 H), 6.38 (dd, J = 5.2, J = 9.2 Hz, 1 H), 7.55 (d, J = 1.1 Hz, 1 H, ArH), 9.12 (s, 1 H, NH) ppm. $C_{18}H_{30}N_2O_6Si$ (398.53): calcd. C 54.25, H 7.59, N 7.03; found C 54.16, H 7.49, N 7.11.

Compound 1w: White solid. IR (KBr): $\tilde{\nu}$ = 3478, 3421, 3180, 3057, 2950, 2929, 2858, 1700, 1465, 1362, 1270, 1101, 1065, 1029, 835, 778 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.12 [s, 6 H, $Si(CH_3)_2$], 0.91 [s, 9 H, $SiC(CH_3)_3$], 1.92 (s, 3 H, CH_3), 2.01–2.04 (m, 1 H, CH_2), 2.36–2.38 (m, 1 H, CH_2), 3.14 (s, 1 H, OH), 3.85–3.88 (m, 2 H, OCH_2), 4.05–4.07 (m, 1 H, OCH), 4.46 (m, 1 H, OCH), 6.40 (m, 1 H, OCH), 7.52 (m, 1 H, =CH), 9.40 (s, 1 H, NH) ppm. $C_{16}H_{28}N_2O_6Si$ (356.491): calcd. C 53.91, H 7.92, N 7.86; found C 53.70, H 7.78, N 7.89.

Compound 1x: Colourless liquid. IR (neat): $\tilde{\nu}$ = 3063, 2925, 2858, 1460 1388, 1107, 825, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.1 Hz, 3 H, CH_3), 1.05 [s, 9 H, $SiC(CH_3)_3$], 1.06 (m, 2 H, CH_2CH_3), 1.25 (m, 16 H, CH_2), 1.55 (m, 2 H, OCH_2CH_2), 3.65 (t, J = 6.4 Hz, 2 H, OCH_2), 7.42 (m, 5 H, ArH), 7.66 (m, 5 H, ArH) ppm. $C_{28}H_{44}OSi$ (454.74): calcd. C 80.55, H 9.75; found C 80.63, H 9.80.

Compound 1a′: Yellowish liquid. IR (neat): $\tilde{\nu}$ = 2965, 2929, 2858, 1599, 1475, 1424, 1260, 1101, 835 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.04 [s, 6 H, $Si(CH_3)_2$], 0.89 [s, 9 H, $SiC(CH_3)_3$], 1.04 [s, 9 H, $SiC(CH_3)_3$], 1.49 (m, 6 H, CH_2), 3.60 (t, J = 6.3 Hz, 2 H, OCH_2CH_2), 3.66 (t, J = 6.6 Hz, 2 H, OCH_2CH_2), 7.39 (m, 5 H, ArH), 7.68 (m, 5 H, ArH) ppm. $C_{29}H_{44}O_2Si_2$ (456.81): calcd. C 70.99, H 9.71; found C 70.90, H 9.65.

Compound 1b′: Yellowish liquid. IR (neat): $\tilde{\nu}$ = 3073, 2940, 2863, 1588, 1481, 1434, 1388, 1260, 1107, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.02 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.02 [s, 9 H, $SiC(CH_3)_3$], 1.25 (m, 8 H, CH_2), 1.53 (m, 4 H, CH_2), 3.57 (t, J = 6.4 Hz, 2 H OCH_2CH_2), 3.62 (t, J = 6.4 Hz, 2 H OCH_2CH_2), 7.38 (m, 5 H, ArH), 7.66 (m, 5 H, ArH) ppm. $C_{30}H_{50}O_2Si_2$ (498.90): calcd. C 72.22, H 10.10; found C 72.50, H 10.22.

Compound 1c′: Yellowish liquid. IR (neat): $\tilde{\nu}$ = 2945, 2858, 1598, 1485, 1459, 1377, 1260, 1116, 1070, 932, 840 cm^{-1}. $C_{19}H_{36}O_2Si_2$ (356.66): calcd. C 64.71, H, 10.29; found C 64.80, H 10.32.

Compound 1d′: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2959, 2934, 2860, 1597, 1479, 1370, 1282, 1163, 1104, 1015, 971, 848, 779, 705cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.10 [s, 6 H, $Si(CH_3)_2$], 0.20 [s, 6 H, $Si(CH_3)_2$], 0.85 [s, 9 H, $SiC(CH_3)_3$], 0.89 [s, 9 H, $SiC(CH_3)_3$], 4.60 (s, 2 H, CH_2OTBS), 6.51 (dd, J = 2.4, J = 7.8 Hz, 1 H, ArH), 6.65 (s, 1 H, ArH), 6.69 (d, J = 7.6 Hz, 1 H, ArH), 6.98 (t, J = 7.8 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.3, −4.4, 18.2, 18.4, 25.7, 25.9, 64.7, 117.6, 118.6, 118.8, 129.1, 143.1, 155.7 ppm. $C_{19}H_{36}O_2Si_2$ (352.66): calcd. C 64.71, H 10.29; found C 64.82, H 10.32.

Compound 1e′: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2960, 2945, 2899, 2868, 1614, 1516, 1475, 1255, 1091, 922, 851, 779 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.08 [s, 6 H, $Si(CH_3)_2$], 0.18 [s, 6 H, $Si(CH_3)_2$], 0.93 [s, 9 H, $SiC(CH_3)_3$], 0.98 [s, 9 H, $SiC(CH_3)_3$], 4.66 (s, 2 H, CH_2OTBS), 6.79 (d, J = 8.4 Hz, 2 H, ArH), 7.17 (d, J = 8.4 Hz, 2 H, ArH) ppm. $C_{19}H_{36}O_2Si_2$ (352.66): calcd. C 64.71, H 10.29; found C 64.83, H 10.3.

Compound 1f′: Colourless liquid. IR (neat): $\tilde{\nu}$ = 2960, 2935, 2863, 1609, 1588, 1496, 1470, 1368, 1260, 1107, 1086, 1040, 927, 846, 789 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$), 0.26 (s, 3 H, $SiCH_3$), 0.30 (s, 3 H, $SiCH_3$), 0.93 [s, 9 H, $SiC(CH_3)_3$], 1.05 [s, 9 H, $SiC(CH_3)_3$], 1.38 (d, J = 6.2 Hz, 3 H, $CHCH_3$), 5.25 (q, J = 6.2 Hz, 1 H, $OCHCH_3$), 6.75 (d, J = 8.0 Hz, 1 H, ArH), 6.96 (t, J = 7.6 Hz, 1 H, ArH), 7.06 (t, J) 7.3 Hz, 1 H, ArH), 7.55 (d, J = 6.9 Hz, 1 H, ArH) ppm. $C_{20}H_{38}O_2Si_2$ (366.69): calcd. C 65.51, H 10.44; found C 65.62, H 10.5.

Compound 2a: Yield: 0.102 g, 70%; colourless liquid. IR (neat): $\tilde{\nu}$ = 3447, 2935, 2868, 1742, 1465, 1404, 1368, 1235, 1045, 897, 851 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ = 1.35–1.74 (m, 7 H, CH_2 & OH), 2.05 (s, 3 H, $COCH_3$), 3.67 (t, J = 6.4 Hz, 2 H, CH_2OH), 4.08 (t, J = 6.6 Hz, 2 H, $AcOCH_2$) ppm. $C_7H_{14}O_3$ (146.18): calcd. C 57.52, H 9.65; found C 57.63, H 9.71.

Compound 2b: Yield: 0.183 g, 88%; colourless liquid. IR (neat): $\tilde{\nu}$ = 3421, 3068, 2940, 2868, 1726, 1614, 1460, 1393, 1281, 1189, 1122, 717 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.48 (m, 3 H, CH_2 & OH), 1.59 (m, 2 H, CH_2), 1.75 (m, 2 H, CH_2), 3.62 (t, J = 6.4 Hz, 2 H, CH_2OH), 4.27 (t, J = 6.6 Hz, 2 H, $PhCOOCH_2$), 7.37 (t, J = 7.8 Hz, 2 H, ArH), 7.49 (t, J = 7.6 Hz, 1 H, ArH), 7.96 (d, J = 7.1 Hz, 2 H ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.4, 28.6, 32.3, 62.7, 64.9, 128.3, 129.5, 130.5, 132.9, 166.7 ppm. $C_{12}H_{16}O_3$ (208.26): calcd. C 69.21, H 7.74; found C 69.32, H 7.83.

Compound 2c: Yield: 0.178 g, 92%; colourless liquid. IR (neat): $\tilde{\nu}$ = 3416, 2935, 2863, 1609, 1501, 1455, 1368, 1265, 1209, 1096, 1055, 1030, 805 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.31–1.70 (m, 7 H, CH_2 & OH), 3.47 (t, J = 6.4 Hz, 2 H, CH_2OH), 3.63 (t, J = 6.4 Hz, 2 H, $PhCH_2OCH_2$), 4.48 (s, 2 H, OCH_2Ph), 7.32 (m, 5 H, ArH) ppm. $C_{12}H_{18}O_2$ (194.27): calcd. C 74.19, H 9.34; found C 74.32, H 9.4%.

Compound 2h: Yield: 0.222 g, 81%; colourless liquid. IR (neat): $\tilde{\nu}$ = 3334, 2914, 2848, 2745, 1609, 1516, 1455, 1255, 1173, 1076, 1020, 830 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 2.58–2.90 (m, 6 H, SCH_2 & OH), 3.71 (m, 4 H, OCH_2), 3.80 (s, 3 H, OCH_3), 5.06 (s, 1 H, SCHS), 6.87 (d, J = 8.6 Hz, 2 H, ArH), 7.38 (d, J = 8.6 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.1, 33.2, 55.9, 99.5, 114.7, 129.5, 132.0, 160.0 ppm. $C_{12}H_{18}O_3S_2$ (274.40): calcd. C 52.53, H 6.61, S 23.37; found C 53.58, H 6.73, S 23.40.

Compound 2q: Yield: 0.180 g, 85%; White solid; m.p 155–158 °C. IR (KBr): $\tilde{\nu}$ = 3370, 2940, 2894, 1609, 1445, 1368, 1250, 1173, 1112 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.72–1.86 (m, 1 H, SCH_2CH_2), 2.02–2.07 (m, 1 H, SCH_2CH_2), 2.74–2.81 (m, 2 H, SCH_2CH_2), 2.89–2.98 (m, 2 H, SCH_2CH_2), 5.00 (s, 1 H, CH), 6.65 (d, J = 8.2 Hz, 2 H, ArH), 7.22 (d, J = 8.2 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.1, 32.2, 50.7, 115.6, 129.2, 131.5, 155.6 ppm. $C_{10}H_{12}OS_2$ (212.34): calcd. C 56.57, H 5.70; found C 56.63, H 5.68.

Compound 2v: Yield: 0.247 g, 87%; White solid; m.p 174 °C IR (KBr): $\tilde{\nu}$ = 3472, 3201, 3068, 2929, 1738, 1710, 1669, 1475, 1249, 1111, 1075, 1024, 881, 788, 576 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.92 (s, 3 H, CCH_3), 2.11 (s, 3 H, $COCH_3$), 2.40 (br. s, 3 H, CH_2 & OH), 3.92 (s, 2 H, OCH_2), 4.10 (br. s, 1 H, H-3), 5.36 (br. s, 1 H, H-4), 6.27 (br. s, 1 H, H-1), 7.55 (s, 1 H,= CH), 9.50 (s, 1 H, NH) ppm. $C_{12}H_{16}O_6N_2$ (284.27): calcd. C 50.70, H 5.67, N 9.85; found C 50.81, H 9.01.

Compound 2a′: Yield: 0.267 g, 78%; colourless liquid. IR (neat): $\tilde{\nu}$ = 3396, 3068, 3053, 2930, 2863, 1598, 1470, 1424, 1393, 1112, 1045, 1004, 943, 825 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05 [s, 9 H, $SiC(CH_3)_3$], 1.56 (m, 7 H, CH_2 & OH), 3.62 (t, J = 6.4 Hz, 2 H OCH_2CH_2), 3.67 (t, J = 6.2 Hz, 2 H OCH_2CH_2), 7.40 (m, 5 H, ArH), 7.68 (m, 5 H, ArH) ppm. $C_{21}H_{30}O_2Si$ (342.55): calcd. C 73.63, H 8.8; found C 73.53, H 8.69.

Compound 2b′: Yield: 0.311 g, 81%; Yellowish liquid. IR (neat): $\tilde{\nu}$ = 3355, 3073, 3053, 2935, 2868, 1593, 1475, 1429, 1399, 1117, 835 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 [s, 9 H, $SiC(CH_3)_3$], 1.28 (m, 8 H, CH_2), 1.54 (m, 5 H, CH_2 & OH), 3.60 (t, J = 6.6 Hz, 2 H, OCH_2CH_2), 3.64 (t, J = 6.3 Hz, 2 H, OCH_2CH_2), 7.37 (m, 5

H, ArH), 7.67 (m, 5 H, ArH) ppm. $C_{24}H_{32}O_2Si$ (384.63): calcd. C 74.95, H 9.43; found C 74.89, H 9.48.

Compound 2c′: Yield: 0.183 g, 77%; Yellowish liquid. IR (neat): $\tilde{\nu}$ = 3370, 2976, 2940, 2873, 1609, 1588, 1491, 1460, 1393, 1368, 1265, 1194, 1117, 1040, 922, 840 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.24 [s, 6 H, $Si(CH_3)_2$], 1.00 [s, 9 H, $SiC(CH_3)_3$], 2.01 (s, 1 H, OH, D_2O exchangeable), 4.65 (s, 2 H, CH_2OH), 6.79 (d, J = 8.1 Hz, 1 H, ArH), 6.93 (t, J = 7.3 Hz, 1 H, ArH), 7.15 (t, J = 7.6 Hz, 1 H, ArH), 7.27 (d, J = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −4.2, 18.2, 25.7, 61.9, 118.4, 121.3, 128.6, 128.8, 131.4, 153.5 ppm. $C_{13}H_{22}O_2Si$ (238.40): calcd. C 65.50, H 9.30; found C 65.54, H 9.36.

Compound 2d′: 1445, 1378, 1281, 1255, 1153, 1020, 953, 851, 784, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.79 [s, 9 H, $SiC(CH_3)_3$], 1.46 (s, 1 H, OH, D_2O exchangeable), 4.44 (s, 2 H, CH_2OH), 6.56 (d,d, J = 2.4, J = 8.0 Hz, 1 H, ArH), 6.66 (s, 1 H, ArH), 6.75 (d, J = 7.3 Hz, 1 H, ArH), 7.03 (t, J = 7.8 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −4.5, 18.2, 25.7, 65.2, 118.6, 119.2, 119.7, 129.5, 142.5, 155.9 ppm. $C_{13}H_{22}O_2Si$ (238.40): calcd. C 65.50, H 9.30; found C 65.55, H 9.38.

Compound 2e′: Yield: 0.207 g, 87%; colourless liquid. IR (neat): $\tilde{\nu}$ = 3365, 2970, 2945, 2863, 1618, 1521, 1485, 1260, 1019, 916, 840, 783 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.19 [s, 6 H, $Si(CH_3)_2$], 0.98 [s, 9 H, $SiC(CH_3)_3$], 1.62 (s, 1 H, OH, D_2O exchangeable), 4.60 (s, 2 H, CH_2OH), 6.82 (d, J = 8.4 Hz, 2 H, ArH), 7.23 (d, J = 8.4 Hz, 2 H, ArH) ppm. $C_{13}H_{22}O_2Si$ (238.40): calcd. C 65.50, H 9.30; found C 65.47, H 8.29.

Compound 2f′: Yield: 0.191 g, 76%; colourless liquid. IR (neat): $\tilde{\nu}$ = 3396, 2960, 2940, 2858, 1603, 1491, 1460, 1255, 1127, 1071, 1015, 927, 835, 784. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.28 [s, 6 H, $Si(CH_3)_2$], 1.02 [s, 9 H, $SiC(CH_3)_3$], 1.48 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 2.35 (br. s, 1 H, OH, D_2O exchangeable), 5.21 [q, J = 6.5 Hz, 1 H, CH(OH)], 6.75 (d, J = 8.1 Hz, 1 H, ArH), 6.96 (t, J = 7.3 Hz, 1 H, ArH), 7.06 (t, J = 7.6 Hz, 1 H, ArH), 7.55 (d, J = 7.6 Hz, 1 H, ArH) ppm. $C_{14}H_{24}O_2Si$ (252.43): calcd. C 66.61, H 9.58; found C66.80, H 9.54.

Acknowledgments

A. T. K. acknowledges the Department of Science and Technology (DST), New Delhi, for a research grant (Grant No. SP/S1/G-35/98). S. G. and L. H. C. are grateful to IITG for their research fellowships. We are also grateful to the Director of the IITG for general facilities to carry out our research work and to the referees for their valuable comments and suggestions.

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[12] ^{1}H NMR spectra of the products were compared with the Aldrich Spectral Library.

Received January 16, 2004

Acetonyltriphenylphosphonium Bromide (ATPB): A Versatile Reagent for the Acylation of Alcohols, Phenols, Thiols and Amines and for 1,1-Diacylation of Aldehydes under Solvent-Free Conditions

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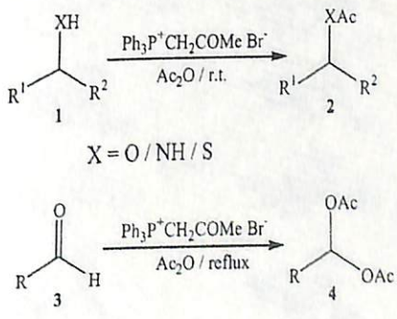
Dedicated to Professor K. C. Majumdar[‡]

Keywords: Acylations / Alcohols / Phenols / Amines / Thiols / Acetonyltriphenylphosphonium bromide

A wide variety of alcohols, phenols, amines and thiols may easily be converted into the corresponding acetate derivatives by treatment with acetic anhydride (1.5–2.0 equivalents) in the presence of acetonyltriphenylphosphonium bromide (ATPB; 5 mol %) in good yields at room temperature. With the same precatalyst, both aliphatic and aromatic aldehydes can also be transformed into the corresponding *gem*-diacetates under reflux conditions.

Introduction

The acylation of alcohols and phenols, amines and thiols is one of the most useful transformations in organic synthesis.[1] Of these, the conversion of a hydroxy group into the corresponding acetate is important due to its ease of introduction, stability under mild acidic reaction conditions and ease of removal by mild alkaline hydrolysis. The acylation of alcohols, phenols or amines is usually performed with acetic anhydride in the presence of amine bases such as triethylamine or pyridine, or pyridine together with 4-(dimethylamino)pyridine (DMAP), which acts as a cocatalyst, or 4-pyrrolidinopyridine (PPY).[2] It is also possible to use tributylphosphane (Bu_3P) as a less basic catalyst for acylation reactions, particularly for base-sensitive substrates.[3] Various metal salts such as $CoCl_2$,[4] $ZnCl_2$,[5] $RuCl_3$,[6] $TiCl_4$–$AgClO_4$,[7] $LiClO_4$,[8] $Mg(ClO_4)_2$,[9] $Zn(ClO_4)_2{\cdot}6H_2O$[10] and some triflates such as $Sc(OTf)_3$,[11] Me_3SiOTf,[12] $In(OTf)_3$,[13] $Cu(OTf)_2$,[14] $Ce(OTf)_3$[15] and $Bi(OTf)_3$[16] have also been employed for acylation reactions in recent years. Very recently, it was also shown that I_2 can be employed as a catalyst for the acetylation of alcohols under solvent-free conditions.[17] Though perchlorates[8–10] have been observed to be effective catalysts for this transformation, they have some serious drawbacks, such as some of them being highly explosive.[18] In addition, $Mg(ClO_4)_2$ has to be anhydrous in order to provide better yields.[9] Other methods based on triflates[11–16] or $RuCl_3$[6] also have some disadvantages: the reagents can be highly expensive or require longer reaction times and extremely dry reaction conditions. Although there are numerous known literature methods through which to obtain good yields of acetylated products, there is still a need for mild and effective catalysts applicable for acetylation reactions for a wide variety of substrates. As a part of our ongoing research project to develop newer synthetic methodologies, particularly in protection and deprotection chemistry,[19] we speculated that acetonyltriphenylphosphonium bromide (ATPB) might be a useful, effective and versatile precatalyst for acylation reactions. So far, acetonyltriphenylphosphonium bromide (ATPB) has been utilized mainly as a Wittig salt,[20a] for the tetrahydropyranylation/depyranylation of alcohols,[20b] and for the cyclotrimerization of aldehydes.[20c] Very recently, we have demonstrated the utility of ATPB for selective deprotection of *tert*-butyldimethylsilyl (TBS) ethers.[19c] Here we report the acetylation of alcohols, phenols, amines and thiols with acetic anhydride in the presence of catalytic amounts of acetonyltriphenylphosphonium bromide (ATPB) under solvent free-conditions, as shown in Scheme 1.



Scheme 1.

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  DOI: 10.1002/ejoc.200500066

Results and Discussion

For this study we first prepared the reagent acetonyltriphenylphosphonium bromide by the literature procedure.[20a] We then attempted the acylation of cetyl alcohol (**1a**) with acetic anhydride in the presence of acetonyltriphenylphosphonium bromide (5 mol%) at room temperature (Table 1). The reaction was complete within 25 min, and the pure acetate derivative of cetyl alcohol (**2a**) was obtained in 96% yield after chromatographic separation. We next examined benzoyl-, *tert*-butyldimethylsilyl- and *tert*-butyldiphenylsilyl-protected alcohols **1b–d** and found that they were smoothly converted into the corresponding acetates **2b–d** in good yields under identical reaction conditions, without the protecting groups being affected. Likewise, various benzylic alcohols (**1e–g**), secondary alcohols (**1h–k**), allyl alcohol (**1l**) and butyne-1,4-diol (**1m**) were converted in similar manner into the corresponding acetate derivatives **2e–m** in very good yields. It is interesting to mention that neither alkyl bromide formation nor HBr addition at double bonds or even triple bonds took place under the experimental conditions. It had been observed that the TBS group was unlikely to survive acetylation with use of $Ce(OTf)_3$,[15] while our procedure offered the advantage that the TBS group was unaffected under the reaction conditions. It is also worthwhile to point out that our procedure is more efficient: the acetylation of cholesterol (entry **1k**), for example, was completed much more quickly than in the recently reported procedure.[15] Notably, chiral alcohols such as menthol (entry **1j**) were easily acetylated in high yields and with complete retention of optical activity. Remarkably, an isopropylidene-protected alcohol **1n** could also be acetylated under identical conditions without cleavage of the isopropylidene group. A tertiary alcohol (**1o**) and a sterically hindered tertiary alcohol, adamentanol (**1p**), were also smoothly converted into the corresponding acetate derivatives **2o** and **2p**, respectively, without any difficulty. We have noticed that this method is more efficient than the ruthenium(III) chloride method[6] in terms of reaction times, particularly for the preparation of **2p**.

We next investigated whether or not the same reagent can be employed for acetylation of phenolic compounds. By the same procedure, various phenolic compounds **1q–s** were easily transformed into the corresponding acetate derivatives **2q–s**. Again, we observed that 4-nitrophenol (entry **1r**) and 2-naphthol (entry **1s**) were converted into the corresponding acetate derivatives much more quickly than in the recently reported procedure.[6] We next turned our attention to whether or not our methodology could be extended further, for acetylation of carbohydrates and nucleosides. We found that various carbohydrate molecules such as **1t–v** and thymidine (**1w**) were converted into the corresponding acetate derivatives **2t–w** in good yields under similar reaction conditions. Importantly, a thio group and a methoxy group at the anomeric position were unaffected under the experimental conditions. The reaction times and yields of the products are summarized in Table 1. Interestingly, it is also possible for a primary OH group to be acetylated chemose-

Table 1. Acetylation of alcohols, phenols, amines and thiols at room temperature in the presence of acetonyltriphenylphosphonium bromide as precatalyst.

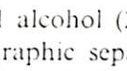
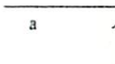
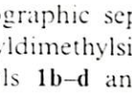
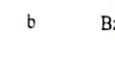
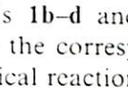
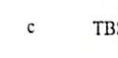
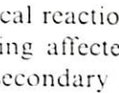
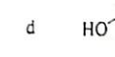
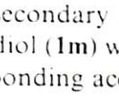
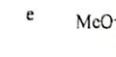
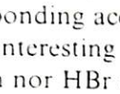
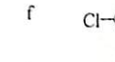
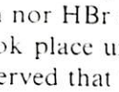
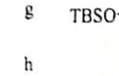
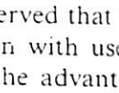
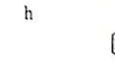
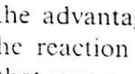
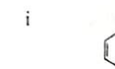
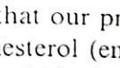
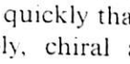
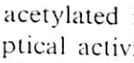
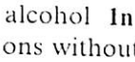
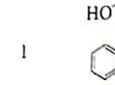
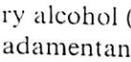
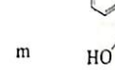
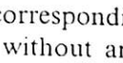
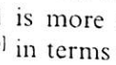
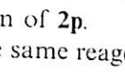
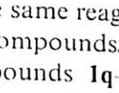
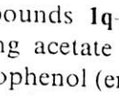
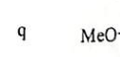
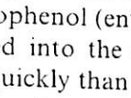
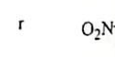
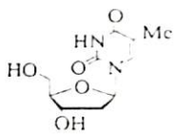
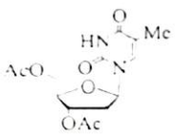
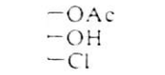
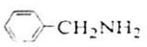
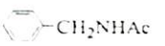
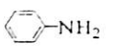
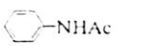
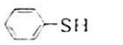
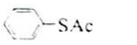
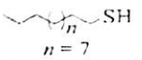
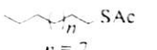
Entry	Substrate 1	Time	Product[a] 2	Yield[b] [%]
a	 $n = 12$	25 min	 $n = 12$	96
b	 $n = 6$	30 min	 $n = 6$	92
c	 $n = 6$	30 min	 $n = 6$	89
d	 $n = 6$	30 min	 $n = 6$	91
e		40 min		96[21]
f		40 min		90[22]
g		35 min		85
h		30 min		95
i		50 min		93
j		35 min		94[c]
k		3.5 min		94[d][12]
l		40 min		92[c]
m		30 min		90[d]
n		30 min		75[10]
o		2.0 h		63
p		1.5 h		87[23]
q		55		94[24]
r		2 h		80[c]
s		3 h		72[c]
t		55 min		74
u		55 min		72
v		1.2 h		78

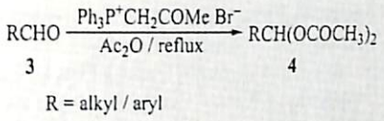
Table 1. (Continued)

Entry	Substrate 1	Time	Product[a] 2	Yield[b] [%]
w		3.5 h		77[d]
x		35 min		65[c]
y		35 min		86[c]
z		45 min		85[c]
a′		1 h		90[c]
b′	 $n = 7$	45 min	 $n = 7$	82

[a] All the acetylated compounds were characterized by IR, ^{1}H NMR and elemental analyses. [b] Isolated yield. [c] The data for the acetates were also compared with those for the authentic compounds. [d] Acetic anhydride (3–5 equivalents) was used instead of 1.5–2.0 equivalent. [e] Acetic anhydride (1 equivalent) was used.

lectively (entry **1x**) under similar reaction conditions. By our procedure, both aliphatic and aromatic amines (entry **1y–z**), as well as thiols (entry **1a′** and **1b′**), were transformed into the corresponding acetate derivatives **2y–b′** in good yields with the same precatalyst.

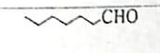
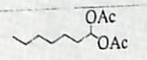
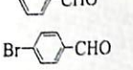
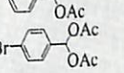
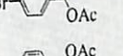
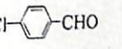
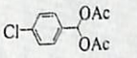
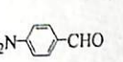
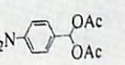
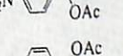
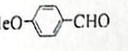
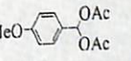
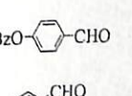
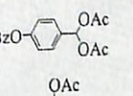
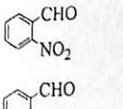
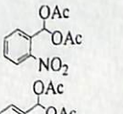
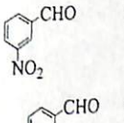
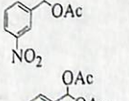
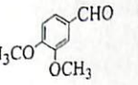
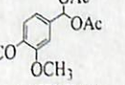
We next turned our attention to whether the same precatalyst would be useful for the 1,1-diacetylation of aldehydes. The formation of geminal diesters from the corresponding aldehyde compounds is an important organic transformation because they serve as building blocks for asymmetric allylic alkylation[25] and Diels–Alder reactions.[26] Moreover, acylals are commonly used as protecting groups for aldehydes because they are stable under neutral and basic conditions.[27] The formation of a 1,1-diacetate is usually achieved by treatment of an aldehyde compound with acetic anhydride in the presence of an acid or Lewis acid, acting as a catalyst. The literature includes several reported methods employing various reagents such as LiOTf,[28] ceric ammonium nitrate,[29] $InCl_3$,[30] H_2NSO_3H,[31] $LiBF_4$,[32] H_2SO_4,[33] PCl_3,[34] NBS,[35] I_2,[36] TMSCl·NaI,[37] $FeCl_3$,[38] and $Bi(NO_3)_3·5H_2O$ for similar transformations.[39] Some metal triflates (e.g., $Cu(OTf)_2$[40] and $Sc(OTf)_3$[41]) have also been utilized as catalysts for the preparation of 1,1-diacetate derivatives from the corresponding aldehydes. Some of these methods have certain drawbacks, such as requirements for longer reaction times or use of expensive reagents, and sometimes fail to provide acylals from aliphatic aldehydes or aromatic aldehydes possessing electron-donating groups in the aromatic ring,[39] so there would be scope for an alternative method. With our precatalyst, various aldehydes can be converted smoothly into the corresponding 1,1-diacetates, as shown in Scheme 2.



Scheme 2.

When an aliphatic aldehyde was treated with acetic anhydride in the presence of ATPB (10 mol%) at room temperature, the reaction was very sluggish and the yield was low. On heating at reflux, however, the same reaction mixture provided the corresponding *gem*-diacetate derivative in good yield by our procedure, more activation energy for the formation of 1,1-diacetates having been provided. Various aliphatic and aromatic aldehydes were smoothly converted into the corresponding *gem*-diacetates in good yields in the presence of the same precatalyst under reflux conditions; the reaction times and yields of the 1,1-diacetates are listed in Table 2. The products were characterized by checking of their melting points and by their IR and ^{1}H NMR spectra, and elemental analyses, as well as by comparison of the compounds' data with the reported data. It is important to mention that neither α-bromination nor cyclotrimerization under the experimental conditions were noticed. This method is relatively harsher than previously reported meth-

Table 2. Formation of *gem*-diacetates from the corresponding aldehydes in the presence of ATPB (10 mol%) as precatalyst under solvent-free conditions.

Entry	Substrate 3	Time	Product[a] 4	Yield[b] [%]	m. p. [°C] (lit.)
a		9 h		88	–
b		5 h		85[35]	–
c		6 h		78	84
d		7 h		78[36]	80 (79–80)
e		11 h		75[36]	126 (125)
f		6 h		82[36]	68 (67–68)
g		10 h		72[28]	97–98
h		15 h		69	85–86
i		14 h		71[38]	62–64 (64–66)
j		5 h		79	63–64
k		5 h		90[38]	85–86 (84–85)

[a] All the products were characterized by melting point, IR, ^{1}H NMR and elemental analysis. [b] Isolated yield.

ods for the formation of *gem*-diacetates, but both aliphatic and aromatic aldehydes can nevertheless be converted into the corresponding diacetates in good yields. Like a previously reported method,[7] this procedure did not provide any 1,1-diacetates from ketones under identical reaction conditions: when acetophenone, for example, was treated with acetic anhydride in the presence of the same precatalyst under reflux conditions, it did not give the corresponding 1,1-diacetate derivative.

The formation of the product can be explained as follows. We believe that HBr is generated in the reaction medium from the reaction between acetonyltriphenylphosphonium bromide and alcohol, and that this catalyses the acetylation of the alcohols to provide the corresponding acetates. However, the corresponding reaction failed when carried out with benzyltriphenylphosphonium bromide instead of acetonyltriphenylphosphonium bromide, indicating that ATPB generates HBr much more easily than the other alkylphosphonium bromide.

Conclusions

In conclusion, we have demonstrated a new, efficient and chemoselective procedure for the acetylation of alcohols, phenols, amines and thiols by use of a catalytic amount of acetonyltriphenylphosphonium bromide as precatalyst at room temperature under very mild conditions. In addition, both aliphatic and aromatic aldehydes can be converted into *gem*-diacetates by employing the same catalyst under reflux conditions. The significant features of this method include its ease of operation, high efficiency, mild conditions and chemoselectivity, which may prove widely useful in organic synthesis. Moreover, a wide variety of other protecting groups, such as benzyl, benzoyl, TBS, TBDPS and isopropylidene, survived under the experimental conditions, as did methoxy and thio groups at anomeric positions.

Experimental Section

Melting points were recorded on a Büchi B-545 melting point apparatus and were uncorrected. IR spectra were recorded in KBr or neat on a Nicolet Impact 410 spectrophotometer. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Jeol 400-MHz spectrometer in $CDCl_3$ with TMS as internal reference. Elemental analyses were carried out with a Perkin Elmer 2400 automatic carbon, hydrogen, nitrogen and sulfur analyzer. Column chromatographic separations were carried out on SRL silica gel (60–120 mesh).

General Procedure for Acetylation of Alcohols or Phenols or Amines and Thiols: Acetonyltriphenylphosphonium bromide (0.05 mmol) was added to a mixture of the alcohol, or phenol, or amine or thiol (1 mmol) and acetic anhydride (1.5–2.0 mmol) and the mixture was stirred at room temperature for ca. 0.5–3.5 h. After complete disappearance of the starting material as monitored by TLC, the mixture was quenched with a saturated hydrogencarbonate solution (2 mL). Finally, the reaction mixture was extracted with ethyl acetate (20 mL × 3). The combined organic extract was washed with water and dried over anhydrous sodium sulfate. After removal of the organic solvent in a rotary evaporator, the crude residue was subjected to silica gel column to isolate the desired pure acetate.

General Procedure for 1,1-Diacetylation of Aldehydes: A mixture of aldehyde (1 mmol) and acetic anhydride (4 mmol) was placed in a 10 mL round-bottomed flask fitted with a reflux condenser. The acetonyltriphenylphosphonium bromide precatalyst (0.1 mmol) was then added and the mixture was stirred under reflux conditions. After completion of the reaction as monitored by TLC, it was quenched with a saturated solution of sodium hydrogencarbonate (2 mL) and the mixture was extracted with ethyl acetate (20 mL × 2). The combined organic layer was dried over anhydrous sodium sulfate and was concentrated in vacuo. Finally, the crude residue was passed through a silica gel column to provide the desired 1,1-diacetate derivatives.

Compound 2a: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3 H, $-CH_3$), 1.22–1.36 (m, 26 H, $-CH_2$), 1.48–1.62 (m, 2 H, $-CH_2$), 2.04 (s, 3 H, $-COCH_3$), 4.04 (t, J = 7.2 Hz, 2 H, $-OCH_2$) ppm. IR (neat): $\tilde{\nu}$ = 2919, 2858, 1747 (CO), 1465, 1368, 1235, 1045 cm^{-1}. $C_{18}H_{36}O_2$ (284.48): calcd. C 76.00, H 12.75; found C 75.82, H 12.69%.

Compound 2b: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30–1.50 (m, 8 H, $-CH_2$), 1.60–1.70 (m, 2 H, $-CH_2$), 1.72–1.80 (q, 2 H, $-CH_2$), 2.04 (s, 3 H, $-COCH_3$), 4.05 (t, J = 7.2 Hz, 2 H, $-OCH_2$), 4.32 (t, J = 6.8 Hz, 2 H, $-OCH_2$), 7.44 (t, J = 8.0 Hz, 2 H, ArH), 7.55 (t, J = 8.0 Hz, 1 H, ArH), 8.04 (d, J = 7.6 Hz, 2 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3063, 2930, 2858, 1731 (CO), 1593, 1455, 1378, 1271, 1240, 1112, 1035 cm^{-1}. $C_{17}H_{24}O_4$ (292.37): calcd. C 69.84, H 8.27; found C 69.70, H 8.21%.

Compound 2c: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.01 [s, 3 H, $-Si(CH_3)_2$], 0.00 [s, 3 H, $-Si(CH_3)_2$], 0.85 [s, 9 H, $-SiC(CH_3)_3$], 1.26–1.40 (m, 8 H, $-CH_2$), 1.44–1.55 (m, 2 H, $-CH_2$), 1.57–1.61 (m, 2 H, $-CH_2$), 2.00 (s, 3 H, $-COCH_3$), 3.54 (t, J = 6.8 Hz, 2 H, $-OCH_2$), 4.00 (t, J = 6.8 Hz, 2 H, $-OCH_2$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.3, 0.0, 18.3, 21.0, 25.7, 25.8, 26.0 (3C), 29.2, 29.3, 32.3, 32.8, 63.2, 64.6, 171.2 ppm. IR (neat): $\tilde{\nu}$ = 3056, 2920, 2848, 1740 (CO), 1475, 1433, 1373, 1245, 1112, 1035 cm^{-1}. $C_{16}H_{34}O_3Si$ (302.53): calcd. C 63.52, H 11.33; found C 63.34, H 11.24%.

Compound 2d: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 [s, 9 H, $-SiC(CH_3)_3$], 1.20–1.40 (m, 8 H, $-CH_2$), 1.52–1.68 (m, 4 H, $-CH_2$), 2.01 (s, 3 H, $-COCH_3$), 3.65 (t, J = 6.4 Hz, 2 H, $-OCH_2$), 4.05 (t, J = 6.8 Hz, 2 H, $-OCH_2$), 7.36–7.42 (m, 6 H, ArH), 7.66–7.68 (dd, J = 1.6, J = 7.6 Hz, 4 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3058, 2925, 2848, 1742 (CO), 1475, 1434, 1373, 1245, 1112, 1035 cm^{-1}. $C_{26}H_{38}O_3Si$ (426.67): calcd. C 73.19, H 8.98; found C 73.01, H 8.91%.

Compound 2g: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.19 [s, 6 H, $Si(CH_3)_2$], 0.98 [s, 9 H, $-SiC(CH_3)_3$], 2.08 (s, 3 H, $-COCH_3$), 5.02 (s, 2 H, $-OCH_2$), 6.81 (d, J = 8.0 Hz, 2 H, ArH), 7.22 (d, J = 8.0 Hz, 2 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 2954, 2930, 2888, 2859, 1747 (CO), 1610, 1521, 1237, 1229, 913 cm^{-1}. $C_{15}H_{24}SiO_3$ (280.44): calcd. C 64.24, H 8.63; found C 64.59, H 8.55%.

Compound 2h: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 7.2 Hz, 3 H, $-CH_3$), 1.81–1.95 (m, 2 H, $-CH_2$), 2.07 (s, 3 H, $-COCH_3$), 5.66 (t, J = 7.2 Hz, 1 H, –CHOAc), 7.20–7.37 (m, 5 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3063, 3022, 2976, 2925, 2879, 1742 (CO), 1491, 1460, 1378, 1250, 1055 cm^{-1}. $C_{11}H_{14}O_2$ (178.23): calcd. C 74.13, H 7.92; found C 74.01, H 7.85%.

Compound 2i: Colourless gummy liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, $-COCH_3$), 6.88 (s, 1 H, –CHOAc), 7.32–7.34 (m, 10 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3073, 3037, 2935, 1747

(CO), 1598, 1496, 1445, 1373, 1235, 1020 cm^{-1}. $C_{14}H_{14}O_2$ (226.27): calcd. C 79.62, H 6.24; found C 79.41, H 6.18%.

Compound 2m: Colourless, low-melting solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (s, 6 H, 2×$COCH_3$), 4.71 (s, 4 H, 2×–OCH_2) ppm. IR (neat): $\tilde{\nu}$ = 2949, 1752 (CO), 1435, 1383, 1222, 1156, 1038 cm^{-1}. $C_8H_{10}O_4$ (170.16): calcd. C 56.47, H 5.92; found C 56.19, H 5.85%.

Compound 2o: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, J = 8.0 Hz, 3 H, CH_3), 0.89 (t, J = 7.2 Hz, 3 H, –CH_3), 1.24–1.34 (m, 6 H, CH_2), 1.37 (s, 3 H, CH_3), 1.62–1.90 (m, 4 H, –CH_2), 1.97 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.13, 14.17, 22.48, 22.72, 23.37 (2C), 30.91, 32.25, 37.81, 85.13, 170.18 ppm. IR (neat): $\tilde{\nu}$ = 2935, 2873, 1737 (CO), 1465, 1373, 1250, 1143, 1025 cm^{-1}. $C_{11}H_{22}O_2$ (186.29): calcd. C 70.92, H 11.90; found C 70.76, H 11.85%.

Compound 2t: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.94 (s, 3 H, –$COCH_3$), 2.07 (m, 1 H, 4-H), 3.39 (s, 3 H, –OCH_3), 3.59–3.63 (m, 3 H), 3.82–3.88 (m, 1 H, 5-H), 3.90 (t, J = 9.2 Hz, 1 H, 3-H), 4.01 (dd, J = 2.4, J = 11.4 Hz, 1 H, 6-H), 4.32 (dd, J = 2.8 Hz, 1 H, 6'-H), 4.47 (d, J = 12.0 Hz, 1 H, –OCHPh), 4.58 (d, J = 10.8 Hz, 1 H, –OCHPh), 4.60 (d, J = 12.0 Hz, 1 H, –OCHPh), 4.66 (d, J = 12.0 Hz, 1 H, –OCHPh), 4.69 (d, J = 3.6 Hz, 1 H, 1-H), 4.78 (d, J = 12.0 Hz, 1 H, –OCHPh), 4.96 (d, J = 10.8 Hz, 1 H, –OCHPh), 7.22–7.40 (m, 15 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3032, 2899, 1742 (CO), 1455, 1363, 1240, 1091, 1055 cm^{-1}. $C_{31}H_{36}O_7$ (520.62): calcd. C 71.52, H 6.97; found C 71.25, H 6.90%.

Compound 2u: Solid, m.p. 63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.6 Hz, 3 H, SCH_2CH_3), 2.03 (s, 3 H, –$COCH_3$), 2.64–2.80 (m, 2 H, –SCH_2CH_3), 3.44 (t, J = 9.2 Hz, 1 H), 3.50–3.52 (m, 1 H, 5-H), 3.54 (t, J = 9.6 Hz, 1 H), 3.71 (t, J = 8.8 Hz, 1 H), 4.19 (dd, J = 4.4, J = 11.6 Hz, 1 H, 6-H), 4.33 (dd, J = 1.6, J = 12.0 Hz, 1 H, 6'-H), 4.47 (d, J = 9.6 Hz, 1 H, 1-H), 4.57 (d, J = 11.2 Hz, 1 H, –OCHPh), 4.74 (d, J = 10.4 Hz, 1 H, –OCHPh), 4.85 (d, J = 10.8 Hz, 1 H, –OCHPh), 4.86 (d, J = 10.8 Hz, 1 H, –OCHPh), 4.92 (d, J = 10.4 Hz, 1 H, –OCHPh), 4.95 (d, J = 10.8 Hz, 1 H, –OCHPh), 7.26–7.36 (m, 15 H, ArH) ppm. IR (KBr): $\tilde{\nu}$ = 3063, 3027, 2925, 2868, 1737 (CO), 1455, 1363, 1235, 1071 cm^{-1}. $C_{31}H_{36}O_6S$ (536.68): calcd. C 69.38, H 6.76, S 5.97; found C 69.23, H 6.70, S 5.70%.

Compound 2v: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.83 (s, 3 H, –$COCH_3$), 3.40–3.44 (m, 2 H), 3.59 (dd, 1 H), 3.83–3.87 (m, 1 H), 3.97 (t, 1 H), 4.46–4.56 (m, 4 H), 4.62–4.71 (m, 3 H), 4.82 (d, J = 3.6 Hz, 1 H, 1-H), 4.90 (d, J = 12.0 Hz, 1 H), 5.04 (t, J = 8.0 Hz, 1 H), 7.25–7.40 (m, 20 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3065, 3030, 2918, 2867, 1748, 1503, 1457, 1376, 1234, 1101, 1045 cm^{-1}. $C_{36}H_{38}O_7$ (582.69): calcd. C 74.20, H 6.57; found C 74.01, H 6.60%.

Compound 2x: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.71 (br. s, 1 H, OH, D_2O exchangeable), 2.12 (s, 3 H, –$COCH_3$), 3.60–3.64 (m, 2 H, –OCH_2), 4.07–4.09 (m, 1 H, –OCH), 4.21(d, J = 5.2 Hz, 2 H, –CH_2Cl) ppm. IR (neat): $\tilde{\nu}$ = 3437 (OH), 2960,1737 (CO),1424, 1240, 1045, 933 cm^{-1}. $C_5H_9ClO_3$ (152.62): calcd. C 39.35, H 5.94; found C 39.10, H 5.86%.

Compound 2b': Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3 H, CH_3), 1.20–1.40 (m, 18 H, –CH_2), 1.45–1.60 (m, 2 H, CH_2), 2.32 (s, 3 H, $COCH_3$), 2.86 (t, J = 7.6 Hz, 2 H, SCH_2) ppm. IR (neat): $\tilde{\nu}$ = 2940, 2853, 1692 (CO), 1460, 1342, 1132, 948 cm^{-1}. $C_{14}H_{28}SO$ (244.44): calcd. C 68.79, H 11.55, S 13.12; found C 68.49, H 11.49, S 12.97%.

Compound 4a: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, J = 6.8 Hz, 3 H, CH_3), 1.22–1.40 (m, 8 H, –CH_2), 1.66–1.80 (m, 2 H, –CH_2), 2.07 (s, 6 H, 2×$COCH_3$), 6.77 [t, 1 H, $CH(OAc)_2$] ppm. IR (neat): $\tilde{\nu}$ = 2930, 2863, 1762, 1465, 1378, 1250, 1214, 1112, 1015, 968 cm^{-1}. $C_{11}H_{20}O_4$ (216.28): calcd. C 61.09, H 9.32; found C 60.89, H 9.27.

Compound 4c: Solid, m.p. 84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (s, 6 H, 2×$COCH_3$), 7.39 (d, J = 8.4 Hz, 2 H, ArH), 7.53 (d, J = 8.8 Hz, 2 H, ArH), 7.61 [s, 1 H, $CH(OAc)_2$] ppm. IR (KBr): $\tilde{\nu}$ = 3063, 2986, 2930, 1762, 1593, 1486, 1378, 1245, 1214, 1076, 1015, 968 cm^{-1}. $C_{11}H_{11}BrO_4$ (287.10): calcd. C 46.02, H 3.86; found C 46.21, H 3.80.

Compound 4h: Solid, m.p. 85–86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (s, 6 H, 2×$COCH_3$), 7.57–7.61 (m, 1 H, ArH), 7.67–7.74 (m, 2 H, ArH) 8.05 (dd, J = 0.8, J = 7.6 Hz, 1 H, ArH), 8.20 [s, 1 H, $CH(OAc)_2$] ppm. IR (KBr): $\tilde{\nu}$ = 1771, 1587, 1525, 1454, 1377, 1351, 1244, 1208, 1105, 1075, 1025 cm^{-1}. $C_{11}H_{11}NO_6$ (253.21): calcd. C 52.18, H 4.38, N 5.53; found C 51.93, H 4.30, N 5.38.

Compound 4j: Solid, m.p. 63–64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (s, 6 H, 2×$COCH_3$), 3.88 (s, 3 H), 3.92 (s, 3 H), 6.88 (d, J = 8.0 Hz, 1 H, ArH), 7.05 (s, 1 H, ArH), 7.11 (d, J = 8.0 Hz, 1 H, ArH), 7.62 [s, 1 H, $CH(OAc)_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (2C), 55.9 (2C), 89.8, 109.6, 111.5, 119.5, 128.0, 149.1, 150.1, 168.7 (2C) ppm. IR (KBr): $\tilde{\nu}$ = 2965, 2847, 1751, 1602, 1525, 1464, 1387, 1346, 1254, 1208, 1152, 1064, 998 cm^{-1}. $C_{13}H_{16}O_6$ (268.26): calcd. C 58.21, H 6.01; found C 57.95, H 5.96.

Acknowledgments

A. T. K. acknowledges to the Department of Science and Technology (DST), New Delhi for a research grant (Grant No. SP/S1/G-35/98). L. H. C. is grateful to the CSIR, Govt. of India, and S. G. to IITG for their research fellowships. We are also grateful to the Director, IITG for general facilities to carry out our research works. We are thankful to the referees for their valuable comments and suggestions.

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Received: January 27, 2005

JOC Note

A Mild and Regioselective Method for α-Bromination of β-Keto Esters and 1,3-Diketones Using Bromodimethylsulfonium Bromide (BDMS)

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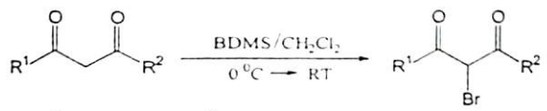
Received July 19, 2006



R^1 = alkyl/ Ph, R^2 = OR / Me/ Ph, R = alkyl

Bromodimethylsulfonium bromide has been found to be an effective and regioselective reagent for α-monobromination of β-keto esters and 1,3-diketones. A wide variety of β-keto esters and 1,3-diketones undergo chemoselective α-monobromination with excellent yields at 0−5 °C or room temperature. The notable advantages of this protocol are no need of chromatographic separation, use of less hazardous reagent than molecular bromine, and no added base, Lewis acid, or other catalyst.

The regioselective α-bromination of β-keto esters and 1,3-diketones is a useful transformation in organic synthesis.[1] These brominated products serve as valuable building blocks for the synthesis of both natural and non-natural products.[2] Over the years, several methods have been developed for the bromination of 1,3-dicarbonyl compounds.[1] Conventionally, molecular bromine,[3] bromine/NaH,[2a] NBS/Et_3N,[2d] and NBS/NaH[4] are used to access these compounds. In addition, other reagents such as $CuBr_2$ with [hydroxy(tosyloxy)iodo]benzene[2c] or NBS/$Mg(ClO_4)_2$[5] or NaOBr in acetone/acetic acid[6] or NBS in various combinations such as silica-supported $NaHSO_4$[7] or Amberlyst-15[8] or sulfonic acid functionalized silica[9] or in ionic liquids[10] are also utilized for similar transformation. Though several methods in the literature provide good yields, most of them suffer from limitations; for example, molecular bromine is hazardous and difficult to handle, the use of Lewis acid as an additive or strong bases may be required, and sometimes the reaction needs to be performed under dry and inert atmospheric conditions. From the literature it is apparent that the chemoselective α-monobromination of unsubstituted β-ketoesters or 1,3-diketones is a very challenging task since some of the monobrominated products are reported to be unstable and to undergo disproportionations to dibromo and debrominated products.[11] In continuation of our effort in the field of new synthetic methodologies using bromodimethylsulfonium bromide in various organic transformations,[12] we were in search of a new and improved synthetic protocol for chemo- and regioselective α-monobromination of β-keto esters and 1,3-diketones that could be applied to a wide range of substituted and unsubstituted β-keto esters and 1,3-diketones. So far, BDMS has been utilized for the transformations of alcohols to the corresponding bromides,[13] oxidation of thiols to disulfides,[14] deprotection of dithioacetals,[15] and preparation of α-bromoenones from the corresponding enones.[16] Recently, we have demonstrated that the peroxo vanadium mediated oxidation of bromide ion to bromonium ion can be utilized for selective α-monobromination of β-keto esters and 1,3-diketones.[17] Interestingly, we have noted by our earlier method that some of the substrates did not provide monobrominated product exclusively. However, by employing bromodimethylsulfonium bromide, it is possible to prepare selectively monobrominated products. In addition, it offers a wealth of advantages in comparison with the earlier reported methods, e.g., the reagent BDMS is readily accessible, can be considered a convenient storage of molecular bromine, is less hazardous and easy to handle, and facilitates maintaining the stoichiometric ratio while carrying out the reactions. In this note, we report that BDMS is a convenient and valuable reagent for highly selective α-bromination of β-keto esters and 1,3-diketones at 0−5 °C or room temperature under mild reaction conditions without using any base or Lewis acid or any other additive, as shown in Scheme 1.

For the present study, the catalyst bromodimethylsulfonium bromide (BDMS) was prepared by following the literature procedure.[15] In the preliminary experiment, when methyl

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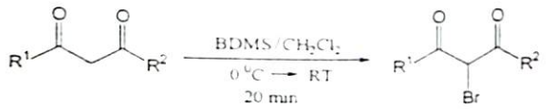
10.1021/jo061501r CCC: $33.50
Published on Web 10/11/2006

SCHEME 1. Selective α-Bromination of β-Keto Esters and 1,3-Diketones

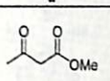
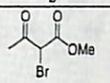
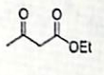
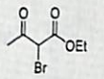
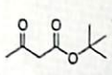
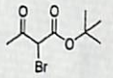
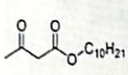
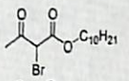
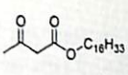
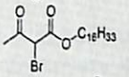
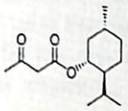
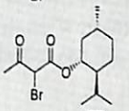
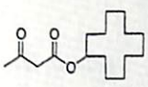
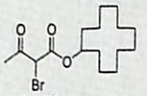
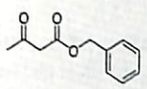
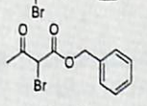
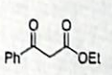
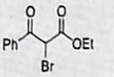
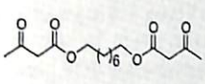
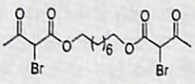
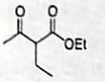
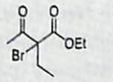
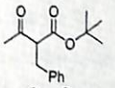
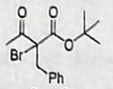
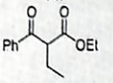
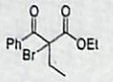
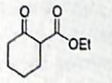
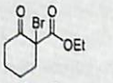
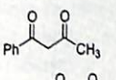
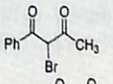
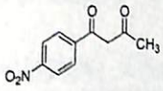
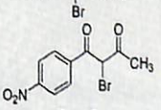
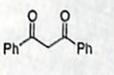
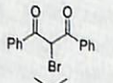
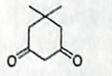
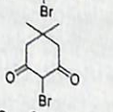
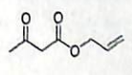
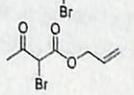


R^1 = alkyl/ Ph, R^2 = OR / Me/ Ph, R = alkyl

acetoacetate (1 mmol) was treated with bromodimethylsulfonium bromide (1.25 mmol) in dichloromethane (5 mL) at 0−5 °C, it provided exclusively monobrominated product within 20 min in 85% yield. The product **1b** was characterized by recording ^{1}H and ^{13}C NMR spectra and elemental analysis. Interestingly, we did not observe any detectable amount of dibrominated product under the experimental conditions while recording the ^{1}H NMR spectrum of the crude product. Encouraged by this result, we tried to apply this protocol to a wide range of β-keto esters. Similarly, other unsubstituted β-keto esters (Table 1, entries **2a** and **3a**) underwent α-bromination smoothly under similar conditions and afforded exclusively monobrominated product in excellent yields. For further investigation, a wide variety of β-keto esters (Table 1, entries **4a**−**8a** and **10a**) were prepared by transesterification of methyl acetoacetate with their corresponding alcohols using a silica-supported perchloric acid method.[18] By following the identical reaction procedure, various substrates **4a**−**9a** were converted to the desired α-monobrominated products in very good yields. Next, the di-keto ester of octanediol (**10a**) was treated with 2.5 equiv of BDMS, and the desired monobrominated product **10b** was found in very good yield. The notable advantages of this protocol over the other existing methods are that the conversion takes place within a very short time without using any catalyst and there is no need of chromatographic separation, as it gives full conversion of the starting material with a single product. NMR spectra of all the products were recorded from crude product just after aqueous workup without any further purifications and showed high purity without detectable byproducts. To explore further, monosubstituted β-keto esters (entries **11a**−**13a**) were prepared by alkylation of β-keto esters using K_2CO_3 as base by following a standard procedure. Subsequently, the substrates **11a**−**13a** were treated with BDMS following the same experimental procedure and provided the monobrominated products **11b**−**13b**, respectively, in good yields at room temperature. As there is no probability for dibromination, we performed the reactions at room temperature instead of ice-bath temperature. Similarly, a cyclic β-keto ester (entry **14a**) underwent α-bromination smoothly in good yield at room temperature. Likewise, various 1,3-diketones (Table 1, entries **15a**−**17a**) provided the desired α-monobrominated products **15b**−**17b** exclusively with very good yields under the given experimental conditions.

Interestingly, dimedone (entry **18a**) provided exclusive monobrominated product at room temperature, which is sometimes difficult to achieve by some of the reported methods.[9] Surprisingly, we could not find the proton attached with the α-brominated carbon atom of compound **18b** in the ^{1}H NMR spectrum. We observed only two signals at 1.12 (s) and 2.48 (s), respectively. Also, in the IR spectrum, we did not observe any carbonyl peak of this product. Therefore, to further confirm the structure of compound **18b**, whether the product is mono- or dibrominated, the product was recrystallized from ethyl acetate/hexane (7:3) and a single-crystal XRD was recorded. Interestingly, we found that in solid state it exists in enol form as shown

TABLE 1. α-Bromination of β-Keto Esters and 1,3-Diketones[a]

Entry	Substrate a	Product[a] b	% Yield[b]
1			85
2			84
3			91
4			95
5			90
6			93
7			92
8			94
9			94
10			97[d]
11			89[c]
12			96[c]
13			95[c]
14			99[c]
15			97
16			86
17			98
18			91[c,e]
19			81

[a] Reaction conditions: β-keto ester/1,3-diketone (1 mmol), BDMS (0.278 g, 1.25 mmol), 0 °C to rt, 20−30 min. [b] Reactions were carried out at 0 °C. [c] Reactions were performed at room temperature. [d] Bromodimethyl sulfonium bromide (2.5 equiv) was used. [e] Reaction time was 30 min.

(18) Khan, A. T., Goswami, P., Kalpana, K.; Choudhury, L. H. Unpublished work.

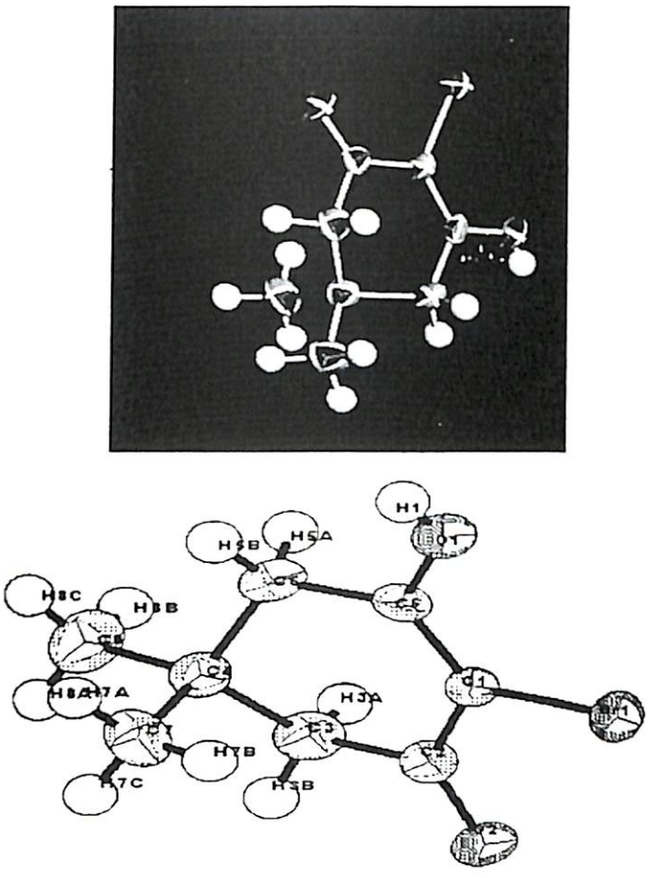


FIGURE 1. ORTEP plot of α-monobromo dimedone with atom numbering scheme.

SCHEME 2. Rapid Keto−Enol Tautomerization in Solution

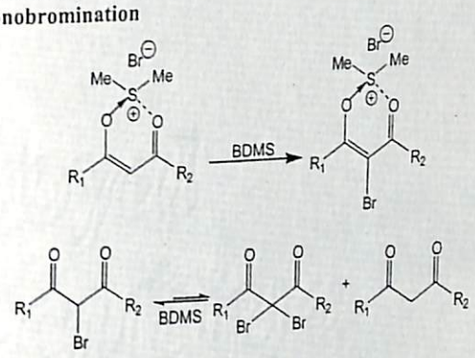
in the ORTEP diagram of Figure 1, which shows intermolecular hydrogen bonding of O−H of enol and ketonic CO of the other unit. We believe that in solution state it undergoes rapid keto−enol tautomerization as shown in Scheme 2, for which we do not observe the proton signal for the α-hydrogen associated with the brominated carbon.

Next, to exemplify further the applicability of this protocol, the substrate **19a** was treated under the experimental conditions. Interestingly, the allylic double bond survives under the given conditions and provided the desired product **19b** in good yields.

A probable mechanism is depicted in Scheme 3. We believe that bromodimethylsulfonium bromide facilitates the enol formation of β-keto esters or 1,3-diketones. In addition, bromodimethylsulfonium ion may also bind with the enol form of the monobrominated product, which provides extra stability of the monobrominated product and as a result makes the process sluggish for further bromination or disproportionation.

In conclusion, we have devised a simple and efficient synthetic protocol for highly selective α-monobromination of β-keto esters and 1,3-diketones using the versatile reagent bromodimethylsulfonium bromide. The notable advantages of this protocol are mild, clean, and simple reaction conditions; very good yields; no need of chromatographic separations; and

SCHEME 3. Probable Mechanism for Selective Monobromination



no need of any base or Lewis acid as an additive, which is invariably required by NBS methods. Furthermore, this method is also expected to have valuable application in organic synthesis because of the low cost, easy accessibility, and less hazardous nature of the reagent.

Experimental Section

Preparation of Bromodimethylsulfonium Bromide (BDMS).[15] Dimethyl sulfide (1.83 mL, 25 mmol) was taken in 5 mL of dry dichloromethane into a 150 mL standard joint conical flask. Then, 1.3 mL of bromine (25 mmol) was dissolved in 5 mL of dry dichloromethane and added slowly into the above solution at ice-bath temperature over a period of 5 min. During the addition, light orange crystals of bromodimethylsulfonium bromide begin to separate out. After the addition of bromine was completed, the crystals of bromodimethylsulfonium bromide were collected by filtration. The solid material was then washed with dry hexane and dried under vacuum. The crystalline product was obtained as 4.3 g in 77% yield, mp 80 °C.

General Procedure for α-Bromination of β-Keto Esters and 1,3-Diketones. Bromodimethylsulfonium bromide (BDMS) (1.25 mmol, 0.278 g) was added to a stirred solution of β-keto ester or 1,3 diketone (1 mmol) in CH_2Cl_2 (5 mL) at 0−5 °C or room temperature. After 20 min, the reaction mixture was washed with water (10 mL × 2) and extracted with CH_2Cl_2 (10 mL × 2). The organic layers were combined and dried over anhydrous Na_2SO_4, and solvents were removed by evaporation in a rotary evaporator to get the crude product. All products were characterized without any further purification.

Acknowledgment. P.G and L.H.C. are thankful to Council of Scientific and Industrial Research, New Delhi for their research fellowships. We also acknowledge Department of Science and Technology, New Delhi for providing single XRD facility under FIST program (sanction no. SR/FST/CSII-007/2003). The authors are also thankful to the Director, IIT Guwahati for the general facilities to carry out the research work and are grateful to the reviewers for their valuable comments and suggestions.

Supporting Information Available: Experimental details and analytical data of all products and ^1H and ^{13}C NMR spectra of unknown compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO061501R

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A mild and environmentally acceptable synthetic protocol for chemoselective α-bromination of β-keto esters and 1,3-diketones☆

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Received 17 January 2006; revised 7 February 2006; accepted 14 February 2006
Available online 3 March 2006

This letter is dedicated to my mentor Professor K. C. Majumdar, Department of Chemistry, Kalyani University on the occasion of his 60th birthday

Abstract—A wide variety of unsubstituted β-keto esters can be brominated chemoselectively to the corresponding α-monobromo-β-keto esters by using a combination of vanadium pentoxide, hydrogen peroxide and ammonium bromide in a biphasic system, dichloromethane–water at 0–5 °C. In addition, α-mono substituted β-keto esters, cyclic β-keto-esters and 1,3-diketones can also be brominated selectively using the same protocol.

The chemoselective α-bromination of β-keto esters is an important organic transformation[1] because the resulting α-brominated products are valuable building blocks in organic synthesis.[2] The transformation is usually achieved by using either molecular bromine,[3] or Br_2/NaH,[4] or NBS/Et_3N,[5] or NBS/NaH.[6] or $CuBr_2$ with [hydroxy(tosyloxy)iodo]benzene[7] or NBS/$Mg(ClO_4)_2$.[8] Recently, other methods have also been reported employing NBS in combination with silica-supported $NaHSO_4$,[9] Amberlyst-15[10] or in ionic liquids.[11] Though all these methods provide good yields, most suffer from one or more disadvantages. From the green chemistry point of view,[12] the use of molecular bromine has several drawbacks: the reagent itself is harmful and hazardous and there are difficulties in handling and maintaining the stoichiometric ratio during the reaction. In addition, the reaction needs to be carried out under a dry and inert atmosphere and also uses expensive NaH. Moreover, NBS has also some limitations such as the requirement for dry[7] and harsh reaction conditions,[9] and NBS and the required solvents, such as an ionic liquids,[11] are expensive. Selective monobromination at the α position of β-keto esters is a challenging problem, since some of the α-monobrominated β-keto esters are unstable and readily disproportionate to dibrominated and debrominated products.[13,14] Therefore, there is scope to find an alternative methodology that would be environmentally benign and efficient.

Recently we reported the synthesis of 6,8-dibromoflavone, 8-bromoflavone, 5,7-dibromoaurone and 7-bromoaurone using V_2O_5–H_2O_2 catalyzed oxidation of ammonium bromide.[15] We also demonstrated the usefulness of the same combination in various organic transformations such as cleavage of dithioacetals,[16] hydrolysis of 1-thioglycosides[17] and deprotection of oxathioacetals.[18] Based on a knowledge of the reactivity of peroxovandate(V) complexes for the oxidation of bromide,[19] we have now developed an environmentally acceptable protocol for α-monobromination of β-keto esters and 1,3-diketones as shown in Scheme 1.

For the present study, ethyl acetoacetate was chosen as a model substrate to find optimal conditions, as shown in Table 1. We noted that a (1:1.5:0.5:19) substrate/ammonium bromide/vanadium pentoxide/hydrogen peroxide ratio, in dichloromethane/water (1:1, 2.5 mL per mmol of the substrate), provided the best results. For the same substrate, a combination of V_2O_5, NH_4Br and H_2O_2 (0.25:1.5:19) gave only a 40% conversion (calculated from the ^1H NMR spectrum) after 3.5 h with only α-monobrominated product (Table 1, entry 1). The chemical yield was 92% based on recovery of the starting material. The percent of conversion and the ratio of

Keywords: β-Keto esters; α-Bromination; Vanadium pentoxide; Hydrogen peroxide; Ammonium bromide; α-Bromo-β-keto esters.
☆ Part of this work was presented at the conference 'Catalysis and Biocatalysis in Green Chemistry', Robinson College, Cambridge, UK, December 11–13, 2005.
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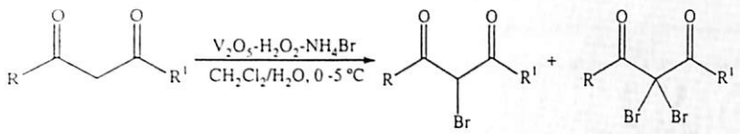
doi:10.1016/j.tetlet.2006.02.075



1 2 3

R = Me/Ph

R¹ = OMe, OEt, OBn

Scheme 1.

Table 1. Optimization of the reaction conditions for selective α-bromination of ethyl acetoacetate

Entry	V_2O_5 (mmol)	NH_4Br (mmol)	50% H_2O_2 (mL)	Time (h)	Conversion[a] (%)	Yield[b] of product **2** (%)	Ratio of **2**:**3**[c]
1	0.25	1.5	1.3	3.5	40	92	100:0
2	0.50	1.5	1.3	3.5	92	85	10:1
3	0.50	2	1.3	2	86	84	9:1
4	0.75	6	2.1	9	100	13	1:9

[a] Quantities in the table are based on 1 mmol of ethyl acetoacetate, however, all reactions were carried out with 3.8 mmol scale of the substrate **2**.
[b] Isolated yield.
[c] Conversion and product ratio were determined using ^1H NMR.

Table 2. Selective α-bromination of β-keto esters and 1,3-diketones using $V_2O_5/NH_4Br/50\%$ H_2O_2 (0.5:1.5:19)

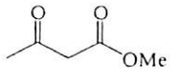
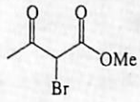
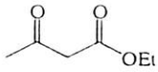
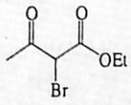
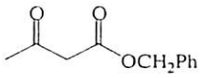
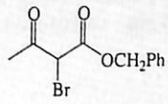
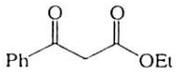
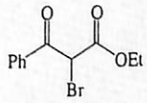
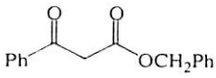
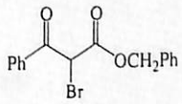
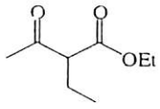
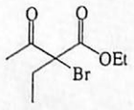
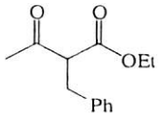
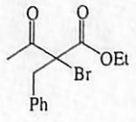
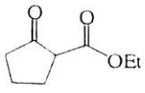
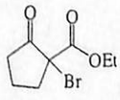
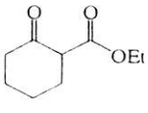
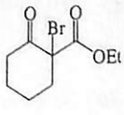
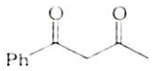
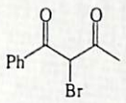
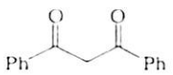
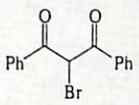
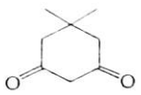
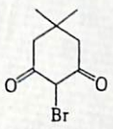
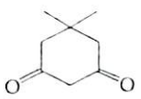
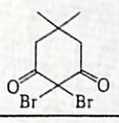
Entry	Substrate	Reaction time (h)	Product[a]	Yield[b,c] (%)
1		3.0		83[c]
2		3.5		85[c]
3		4.0		90
4		4.0		92
5		4.5		91
6		3.0		94
7		3.5		92
8		3.5		87
9		3.0		90

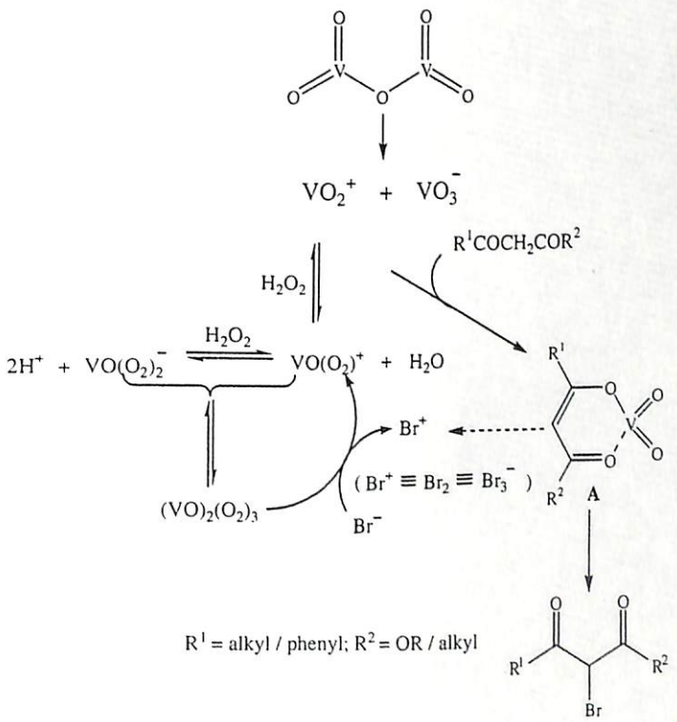
Table 2 (*continued*)

Entry	Substrate	Reaction time (h)	Product[a]	Yield[b,c] (%)
10		2.5		92
11		3.0		95
12		2.5		89
13		4.0		90

[a] Products were characterized by recording ^{1}H NMR, ^{13}C NMR spectra and elemental analysis.
[b] Isolated yield.
[c] Yield was calculated based on starting material recovery.

mono- and dibrominated products were calculated directly from the integrations of NMR signals obtained from the crude reaction mixture. For the substrate ethyl acetoacetate, the methyl signal attached to the carbonyl group resonated at δ 2.27, whereas in the monobrominated product it appeared at δ 2.44. Next we varied the amount of V_2O_5. Using 0.5 equiv of V_2O_5 led to an increase in conversion from 40% to 92% within the same time interval (Table 1, entry 2). The chemical yield of monobrominated product was 85% and dibrominated product was less than 1%. When the amount of ammonium bromide was increased from 1.5 to 2.0 equiv, the conversion was 86% within 2 h with almost the same chemical yield (entry 3). It is clear that the reaction can be completed in shorter time if the amount of vanadium pentoxide, ammonium bromide and hydrogen peroxide are increased.

Using the typical reaction protocol,[20] methyl acetoacetate (Table 2, entry 1) also reacted smoothly to give the α-monobrominated product in 83% yield along with 7% dibrominated product based on starting



Scheme 2. A plausible mechanism for the α-bromination of β-keto esters and 1,3-diketones showing the dual role of vanadium.

material recovery. Other unsubstituted β-keto esters (entries 3–5) were exclusively α-monobrominated in good yields.

Various monoalkyl substituted β-keto esters (entries 6–9) were also brominated chemoselectively at the α-position (Table 2). Following identical reaction conditions, 1-benzoylacetone (entry 10) was smoothly converted to the corresponding α-monobrominated product in good yield. Likewise, dibenzoylmethane (entry 11) and dimedone (entry 12) were transformed chemoselectively to the corresponding α-monobrominated products, respectively, in good yields. It is important to point out that α,α-dibromodimedone can be obtained exclusively by increasing the amount of ammonium bromide from 1.5 to 3.0 equiv.

We believe that the promoter (V_2O_5) is used not only for the oxidation of ammonium bromide by H_2O_2 but also acts as a Lewis acid for chelation with the two carbonyl groups present in β-keto esters or 1,3-diketones as shown in Scheme 2. This promotes enol formation for chemoselective monobromination.

In conclusion, we have developed a general method for mild α-bromination of β-keto esters and 1,3-diketones using a combination of V_2O_5–H_2O_2–NH_4Br, avoiding the use of the conventional reagent NBS for this transformation. Additionally, all these reagents are environmentally acceptable. We suggest that vanadium pentoxide plays the dual role in: (i) formation of peroxo complexes, which oxidize bromide ion to the bromonium ions and (ii) promotion of enol formation by chelating with the two carbonyl groups of the β-keto ester or 1,3-diketone. We also note, that the ester functionality does not undergo hydrolysis under the experimental conditions. We believe our protocol will find a position in the arsenal of synthetic organic chemistry because of its high selectivity, high yields, simplicity and economic viability.

Acknowledgements

The authors acknowledge financial support from the Council of Scientific and Industrial Research, New Delhi [Grant No. 01(1541)/98/EMR-II to A.T.K.]. P.G. and L.H.C. are thankful to the CSIR, New Delhi, for their research fellowships. The authors are grateful to the Director, IIT Guwahati for providing general facilities for this work. We are grateful to the referee for his valuable comments and suggestions.

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20. General procedure: To a stirred solution of vanadium pentoxide (1.9 mmol, 345 mg) in water (5 mL) was added 50% hydrogen peroxide (5 mL, 73.5 mmol) at ice-bath temperature with stirring. The colour changed from light orange to deep red after 25–30 min. Then, ammonium bromide (5.7 mmol, 560 mg) was added and the reaction mixture was stirred for another 10 min. Subsequently, ethyl acetoacetate (495 mg, 3.8 mmol) in CH_2Cl_2 (5 mL) was added and the reaction mixture was then stirred for a further 3.0 h at the same temperature. After completion of the reaction as monitored by TLC, it was extracted with dichloromethane (25 mL × 2) and the organic layer was washed with saturated sodium metabisulfite solution to destroy unreacted molecular bromine. Finally, it was washed with water and dried over anhydrous sodium sulfate. Removal of the organic layer provided a crude residue, which was purified by short path distillation. Some of the compounds were purified through silica gel column (60–120 mesh, SRL) chromatography by eluting with a mixture of (2% ethyl acetate in hexane) to obtain the pure products.
Spectroscopic data of the α-monobrominated product of benzyl acetoacetate: IR (neat): 1747, 1718 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 3H, $COCH_3$), 4.79 (s, 1H, CHBr), 5.23 (s, 2H, OCH_2Ph), 7.35 (bs, 5H, ArH). Anal. Calcd for $C_{11}H_{11}BrO_3$: C, 48.73; H, 4.09. Found: C, 48.52; H, 4.01. For α-monobrominated product of benzoylacetone: IR (neat): 1726, 1680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H, $COCH_3$), 5.61 (s, 1H, CHBr), 7.48 (t, 2H, $J = 7.6$ Hz, ArH), 7.61 (t, 1H, $J = 7.6$ Hz, ArH), 7.95 (t, 2H, $J = 7.2$ Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.5, 53.3, 127.2, 128.8, 129.2, 130.9, 133.9, 134.6, 190.0, 198.2. Anal. Calcd for $C_{10}H_9BrO_2$: C, 49.82; H, 3.76. Found: C, 49.56; H, 3.70.

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Journal of Molecular Catalysis A: Chemical 255 (2006) 230–235
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
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Silica supported perchloric acid ($HClO_4$-SiO_2): A highly efficient and reusable catalyst for geminal diacylation of aldehydes under solvent-free conditions

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Received 16 August 2005; received in revised form 1 April 2006; accepted 4 April 2006
Available online 22 May 2006

Abstract

Perchloric acid immobilized on silica gel has been found to be an efficient and expedient catalyst for geminal diacylation of aldehydes. A wide variety of aromatic and aliphatic aldehydes can be easily transformed into the corresponding acylals using 0.5 mol% $HClO_4$-SiO_2 within 2–10 min under solvent-free conditions at room temperature. The notable advantages of this protocol are: the reaction requires less reaction time and only stoichiometric amount of acetic anhydride being used, is highly economic and the catalyst is recyclable.

Keywords: Acetic anhydride; *gem*-Diacylation; Aldehydes; Silica supported perchloric acid; Catalytic synthetic protocol

1. Introduction

The protection of aldehydes as acetal or oxathioacetal or dithioacetal or acylal is a common practice for manipulation of other functional groups during multi-step synthesis. Sometimes the protection of aldehydic compounds as acylal is usually preferred due to ease of preparation and their stability towards basic and neutral conditions [1]. In addition, the preparation of 1,1-diacetates from the corresponding aldehydes can be achieved very easily in the presence of ketones. Moreover, they also serve as valuable precursors for asymmetric allylic alkylation [2a] and natural product synthesis [2b] as well as for the synthesis of 1-acetoxydienes for Diels–Alder reactions [3]. The preparation of acylal is usually performed from the reaction of an aldehyde with acetic anhydride in the presence of protonic acids, e.g. sulfuric acid [4] or methanesulfonic acid/phosphoric acid [5] or by employing a Lewis acid, which acts as a catalyst. Over the years, a large number of methods have been developed for the preparation of 1,1-diacetates from the corresponding aldehydes by employing various new reagents such as LiOTf [6], ceric ammonium nitrate [7], $InCl_3$ [8], H_2NSO_3H [9], $LiBF_4$ [10], NBS [11], I_2 [12], TMSCl-NaI [13], $FeCl_3$ [14], $CoCl_2$ [15], $Bi(NO_3)_3{\cdot}5H_2O$ [16], Wells–Dawson acid ($H_6P_2W_{18}O_{62}{\cdot}24H_2O$) [17] and tetrabutylammonium tribromide (TBATB) [18]. Some metal triflates, e.g. $Cu(OTf)_2$ [19], $Sc(OTf)_3$ [20] and $Bi(OTf)_3$ [21] have also been utilized as catalysts for the preparation of 1,1-diacetate derivatives from the corresponding aldehydes. Very recently, we have demonstrated the applicability of acetonyltriphenylphosphonium bromide (ATPB) [22] and bromodimethylsulfonium bromide (BDMS) [23] for acetylation of alcohols, phenols, amines and thiols and for 1,1-diacylation of aldehydes. Unfortunately, many of these methods have drawbacks such as harsh reaction conditions, requirement of excess amount of acetic anhydride, tedious work-up procedure and involvement of expensive and moisture sensitive catalyst. Some new methods are also known in the literature by involving heterogeneous catalysts, for examples, aluminum dodecatungstophosphate ($AlPW_{12}O_{40}$) [24] and zirconium sulfophenyl phosphonate [$Zr(CH_3PO_3)_{1.2}$ $(O_3PC_6H_4SO_3H)_{0.8}$] [25]. Though these methods are quite efficient, some of them encountered difficulties, e.g. difficulty in preparing an acylal from furfural [24] and longer reaction times particularly for aliphatic and α,β-unsaturated aldehydes [25]. Therefore, a new methodology by using an inexpensive and mild catalyst, which might overcome these drawbacks in the preparation of acylals from the corresponding aldehydes, is still required.

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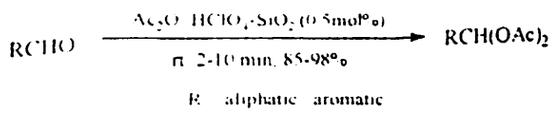
doi:10.1016/j.molcata.2006.04.008



Scheme 1.

In recent years, silica supported reagents are gaining considerable attention because of higher activity of the catalyst due to the larger surface area and better selectivity. In addition, silica supported reagents have high mechanical and thermal stabilities, easiness in handling, low toxicity, non-corrosiveity, easy separation of the catalyst after completing the reaction and reusability of the catalyst, which make it promising for both academic and industrial applications. From our recent result [26] as well as from the other results [27,28], we realized that perchloric acid adsorbed on silica gel has higher catalytic activity than most of the moisture sensitive and highly costly metal triflates. As a part of our ongoing research project to develop new synthetic methodologies particularly in protection and deprotection chemistry [29], we perceived that silica supported perchloric acid ($HClO_4$-SiO_2) might be a useful, effective, versatile and reusable catalyst for chemoselective protection of aldehydes as acylals. So far, silica supported perchloric acid ($HClO_4$-SiO_2) has been utilized mainly as catalyst for acetylation of phenols, thiols, alcohols and amines [27], peracetylation of carbohydrates [30], acetalization followed by acetylation [31] and Ferrier rearrangement of glucals [28]. Very recently, we have demonstrated that the same solid supported catalyst can be used for thia-Michael addition reactions [32]. Herein, we report silica supported perchloric acid as a highly efficient catalyst for *gem*-diacylation of aldehydes under solvent-free conditions as shown in Scheme 1.

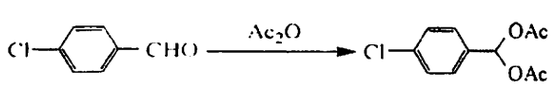
2. Result and discussion

We initially prepared the catalyst silica supported perchloric acid by following the literature procedure [27]. To prove the better catalytic activity of this supported reagent over the aqueous perchloric acid, we have carried out a model study with 4-chlorobenzaldehyde and acetic anhydride using various catalytic conditions as shown in Table 1 (Scheme 2).

Table 1
The results of the reaction of 4-chlorobenzaldehyde with acetic anhydride in different catalytic conditions at room temperature

Entry	Catalyst	Time	Yield[a,b] (%)
I	No catalyst	12 h	0
II	SiO_2 (10 mg/mmol)	12 h	43
III	Aqueous $HClO_4$ (0.5 mol%)	20 min	93
IV	$HClO_4$-SiO_2 (10 mg/mmol, 0.5 mol%)	2 min	98

[a] Isolated yields.
[b] All the reactions were carried out in 5-mmol scale with two equivalents of acetic anhydride under solvent-free conditions.



Scheme 2.

Table 1 clearly demonstrates that silica supported perchloric acid is an effective catalyst in terms of reaction time and yield obtained. Then, we attempted the reaction of 1-heptanal with two equivalent of acetic anhydride in the presence of catalytic amount of $HClO_4$-SiO_2 at room temperature. The reaction was complete within 5 min and the pure acylal was obtained in 86% yield by just passing through a small silica gel column. Similarly, 1-decanal and crotyl aldehyde (entries **1b** and **1c**) provided the corresponding acylals under similar reaction conditions. It is noteworthy to mention that **1d** undergoes *gem*-diacylation within shorter time than the reported method [14] with good yields by keeping intact the acid sensitive protecting group *tert*-butyldiphenylsilyl ether and the corresponding product **2d** is a valuable key ingredient for the synthesis of a potent antifugal agent sphingofungin F [2]. In a similar manner phenacyl aldehyde (**1e**) was also converted to the corresponding *gem*-diaceates using the same catalyst within a short while. Interestingly, we did not observe any cyclotrimerization for aliphatic aldehyde (entries **1a–1e**). Likewise, a wide variety of aromatic aldehydes containing both electron-donating and electron-withdrawing substituents underwent *gem*-diacylation within a very short reaction time, which is summarized in Table 2. It is important to point out that the formation of acylals from the aldehydes containing electron-donating groups such as methoxy and hydroxyl groups result in failure by some of the reported procedures [16] whereas by using this protocol it can be easily achieved (entries **1m–q**) without any difficulty in good yields.

Likewise, various aldehydes containing other protecting groups such as TBS, allyl and benzoyl (entries **1r–t**) were smoothly converted to the desired acylals with the protecting groups kept intact in good yields. Moreover, acid sensitive aldehyde (entry **1v**) and dialdehydes (entries **1w** and **1x**) can also be transformed to the required diacylals without any difficulty. Furthermore, polycyclic aromatic aldehydes (entries **1y** and **1z**) also provided the desired acylals in very good yields.

Interestingly, the aldehyde functionality of the keto aldehydes (entries **1a′** and **1b′**) can be chemoselectively transformed into the corresponding acylals in good yields under identical conditions. Remarkably, it is also possible to carry out the same transformation in a 50-mmol scale or even more without any difficulty. For checking the reusability of the catalyst, we have performed the reaction in the following way. The reaction of 4-nitrobenzaldehyde with acetic anhydride was carried out using 0.5 mol% $HClO_4$-SiO_2 in a 50 mmol scale; after completion of the reaction the catalyst was filtered off and washed with dry ether and finally it was dried under vaccum for 30 min, which was reused for the next cycle. The recovered catalyst was reused for two more consecutive runs for acylation of 4-nitrobenzaldehyde (entry **1j**) with acetic anhydride, providing the desired acylal in 89% and 87% yield within 10 min.

The generality and the scope of the reagent can be easily reflected from the comparison of the data in Table 3. The superiority of silica supported perchloric acid over the metal triflates and some of the recently reported heterogeneous catalyst can be easily visualized at a glance by comparing the results of some substrates. Here, we have chosen some model substrates and

Table 2
Formation of acylals from the corresponding aldehydes catalyzed by $HClO_4$-SiO_2

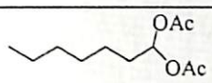
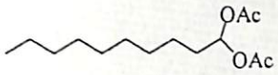
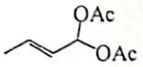
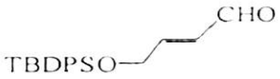
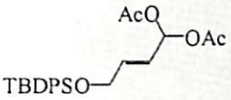
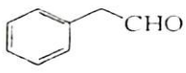
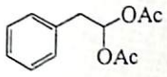
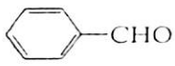
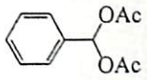
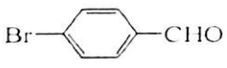
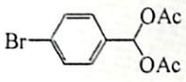
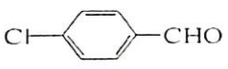
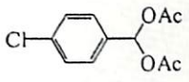
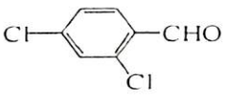
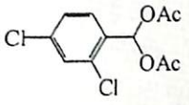
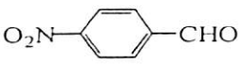
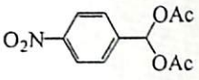
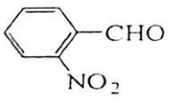
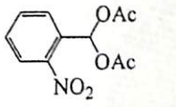
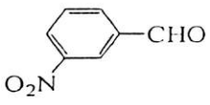
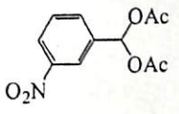
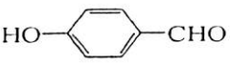
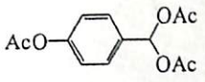
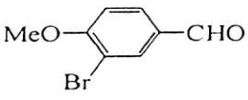
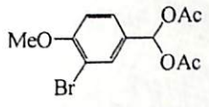
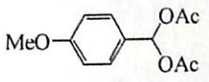
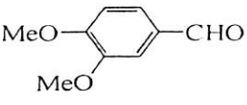
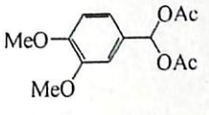
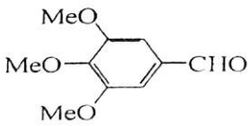
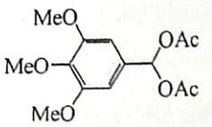
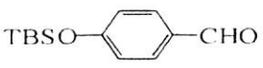
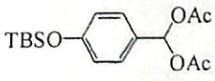
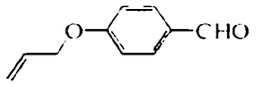
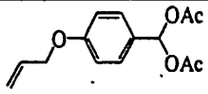
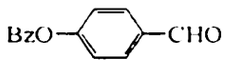
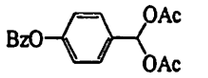
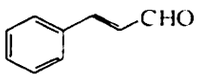
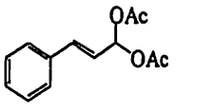
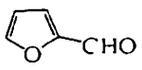
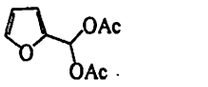
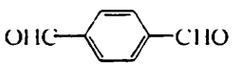
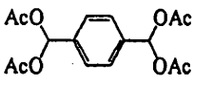
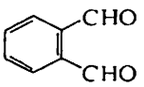
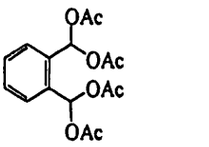
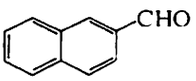
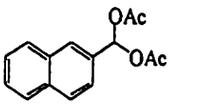
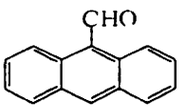
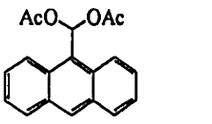
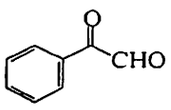
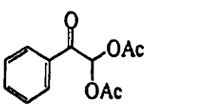
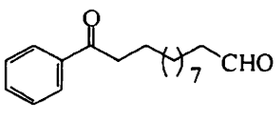
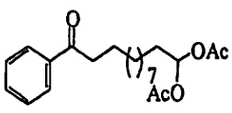
Entry	Substrate (1)	Time (min)	Product (2)	Yield[a] (%)	Mp (°C)
a		5		86 [22]	Gummy liquid
b		5		91	Gummy liquid
c		2		83 [12]	Gummy liquid
d		10		95	Gummy liquid
e		5		85 [23]	Gummy liquid
f		2		97 [14]	45 [lit.44–45]
g		2		96 [22]	84 [lit. 84]
h		2		98 [12]	80 [lit. 80]
i		5		95	100–102
j		5		96 [12]	125 [lit.125]
k		5		93 [22]	85-86 [lit. 85–86]
l		5		96 [14]	65 [lit. 64–66]
m		5		82 [15a]	57 [lit. 58]
n		5		94	81–83
o		5		91 [12]	66 [lit.67–68]
p		5		93 [22]	64 [lit. 63–64]
q		5		96	114–116
r		3		87 [6]	57–59

Table 2 (*Continued*)

Entry	Substrate (1)	Time (min)	Product (2)	Yield[a] (%)	Mp (°C)
s		5		93	40–41
t		5		91 [6]	98–99
u		5		98 [14]	84 [lit. 84–85]
v		2		90 [14]	54 [lit. 55]
w		5		90	174–175
x		5		95	137–139
y		5		94 [15b]	101 [lit.101–02]
z		5		96 [15b]	197 [lit.197–98]
a′		10		93 [10b]	50–51
b′		10		94	39–40

[a] Isolated yields, melting point and the reference for spectroscopic data.

the comparison is made with respect of yields, reaction time and mol% of the catalyst used. It is worthy to mention that cinnamaldehyde and 4-nitrobenzaldehyde provide the desired acylal within 5 min with much better yield than other reported methods. Again, the present protocol is much more effective for the substrate furfural in terms of reaction timing as well as yield, which is usually difficult to be diacylated by the reported procedures [24].

As a whole, we have revealed that silica supported perchloric acid is a highly effective, cheap and reusable catalyst for *gem*-diacylation of aldehydes.

3. Experimental

IR spectra were recorded in KBr or neat condition on a Nicolet Impact 410 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 400 MHz and Bruker 200 MHz spectrophotometers in $CDCl_3$ using TMS as internal reference. Elemental analyses were carried out in a Perkin-Elmer 2400 automatic carbon, hydrogen, nitrogen and sulfur analyzer.

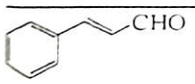
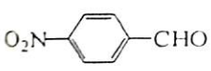
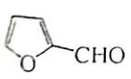
3.1. Preparation of silica supported perchloric acid ($HClO_4$-SiO_2) [27]

$HClO_4$ (1.8 gm, 12.5 mmol, as a 70% aq solution) was added to a suspension of SiO_2 (230–400 mesh, 23.7 g) in Et_2O (70.0 mL). The mixture was concentrated and the residue was heated at 100 °C for 72 h under vacuum to furnish $HClO_4$-SiO_2 (0.5 mmol/g) as a free flowing powder (50 mg = 0.025 mmol of $HClO_4$).

3.2. Typical procedure for the preparation of acylals from 4-nitrobenzaldehyde

To a mixture of 4-nitrobenzaldehyde (5 mmol, 0.750 g) and freshly distilled acetic anhydride (10 mmol, 0.92 mL), the

Table 3
Comparison of $HClO_4$-SiO_2 with other catalysts for *gem*-diacylation of aldehydes

Substrate	Catalyst	Catalyst (mol%)	Reaction time	Yields[a] (%)
	NBS	20	48 h	80 [11]
	$Bi(OTf)_3$	0.1	15 min	70 [21]
	TBATB	10	5.2 h	87 [18]
	$AlPW_{12}O_{40}$	0.1	5 min	92 [24]
	$Cu(OTf)_2$	2.5	3 h	76 [19]
	$H_6P_2W_{18}O_{62}{\cdot}24\ H_2O$	1.0	30 min	98 [17]
	$HClO_4$-SiO_2	0.5	5 min	98
	NBS	10	8 h	98 [11]
	TBATB	10	22 h	78 [18]
	$AlPW_{12}O_{40}$	0.1	45 min	89 [24]
	$H_6P_2W_{18}O_{62}{\cdot}24\ H_2O$	1.0	30 min	92 [17]
	$HClO_4$-SiO_2	0.5	5 min	96
	NBS	10	24 h	81 [11]
	TBATB	10	7 h	80 [18]
	$AlPW_{12}O_{40}$	0.1	30 min	0 [24]
	$H_6P_2W_{18}O_{62}{\cdot}24\ H_2O$	1	30 min	88 [17]
	$HClO_4$-SiO_2	0.5	2 min	90

[a] Reference for earlier methods.

catalyst $HClO_4$-SiO_2 (50 mg, 0.025 mmol) was added and the mixture was stirred at room temperature. When the reaction was complete as judged by TLC, diethyl ether (2 × 25 mL) was added into it. The ether layer was separated, washed with saturated solution of $NaHCO_3$ (5 mL), water (2 × 10 mL) and finally dried over anhydrous $MgSO_4$. After removal of ether, the residue was obtained as almost pure acylal, which was recrystallized from hexane. The desired product was obtained as yellowish crystalline solid (1.22 g) in 96% yield.

3.2.1. 1,1-Diacetate of 1-decanal (2c)

IR (Neat): 2930, 2858, 1767, 1470, 1370, 1250, 1209 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J = 6.8 Hz, 3H, CH_3), 1.26 (bs, 14H, CH_2), 1.72–1.76 (m, 2H, CH_2), 2.07 (s, 6H, $-COCH_3$), 6.75 (t, 1H, J = 5.6 Hz, $CH(OAc)_2$) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): 14.2, 20.9 (2C), 22.7, 23.5, 29.2, 29.3, 29.4, 29.5, 31.9, 33.2, 90.5, 168.8 (2C) ppm. Anal. Calcd for $C_{14}H_{26}O_4$ (258.36): C, 65.09; H, 14.14%. Found: C, 64.89; H, 14.06%.

3.2.2. 1,1-Diacetate of 4-tert-butyldiphenylsilyloxy but-2-ene-1-al (2d)

IR (Neat): 3073, 2970, 2940, 2863, 1762, 1434, 1372, 1244, 1208, 1121, 1009, 707 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.07 (s, 9H, $Si(CH_3)_3$), 2.10 (s, 6H, 2× $-COCH_3$), 4.23 (bs, 2H, $-OCH_2$), 5.91 (ddt, 1H, J = 2.0 Hz, J = 6.4 Hz, J = 15.6 Hz, =CH), 6.06 (dt, 1H, J = 2.8 Hz, J = 15.6 Hz, =CH), 7.17 (d, 1H, J = 6.4 Hz, $-CH(OAc)_2$), 7.34–7.41 (m, 6H, ArH), 7.63 (dd, 4H, J = 1.2 Hz, J = 7.6 Hz, ArH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 19.4, 21.0 (2C), 26.9 (3C), 62.8, 89.2, 122.0, 127.6 (4C), 129.6 (2C), 133.0, 135.3 (4C), 135.8 (2C), 168.5 (2C) ppm. Anal. Calcd for $C_{24}H_{30}O_5Si$ (426.58): C, 67.58; H, 7.09%. Found: C, 67.38; H, 7.01%.

3.2.3. 1,1-Diacetate of 2,4-dichlorobenzaldehyde (2i)

IR (KBr): 3088, 3022, 2945, 1757, 1434, 1378, 1235, 1199, 1081 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.14 (s, 6H, 2× $-COCH_3$), 7.31 (d, J = 7.6 Hz, 1H, ArH), 7.43 (s, 1H, ArH), 7.50 (d, J = 7.9 Hz, 1H, ArH), 7.91 (s, 1H, $CH(OAc)_2$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7 (2C), 87.7, 127.4, 128.8, 129.9, 132.0, 133.9, 136.3, 168.3 (2C) ppm. Anal. Calcd for $C_{11}H_{10}Cl_2O_4$ (277.10): C, 47.68; H, 3.64%. Found: C, 47.49; H, 3.59%.

3.2.4. 1,1-Diacetate of 3-bromo-4-methoxybenzaldehyde (2n)

IR (KBr): 3077, 3015, 2967, 1762, 1605, 1505, 1360, 1258, 936 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 2.12 (s, 6H, 2× $-COCH_3$), 3.91 (s, 3H, OCH_3), 6.89 (d, J = 8.5 Hz, 1H, ArH), 7.42 (dd, J = 8.5 Hz, J = 2.2 Hz, 1H, ArH), 7.57 (s, 1H, $CH(OAc)_2$) 7.71 (d, J = 2.2 Hz, 1H, ArH) ppm. Anal. Calcd for $C_{12}H_{13}BrO_5$ (317.13): C, 45.45; H, 4.13%. Found: C, 45.21; H, 4.06%.

3.2.5. 1,1-Diacetate of 3,4,5-trimethoxybenzaldehyde (2q)

IR (KBr): 3017, 2976, 2950, 2848, 1757, 1603, 1506, 1470, 1424, 1368, 1209, 1076 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.14 (s, 6H, 2× $-COCH_3$), 3.85 (s, 3H, $-OCH_3$), 3.89 (s, 6H, 2× $-OCH_3$), 6.75 (s, 2H, ArH), 7.59 (s, 1H $CH(OAc)_2$). Anal. Calcd for $C_{14}H_{18}O_7$ (298.29): C, 56.37; H, 6.08%. Found: C, 56.09; H, 6.01%.

3.2.6. 1,1-Diacetate of 4-allyloxybenzaldehyde (2s)

IR (KBr): 3104, 2986, 2950, 1757, 1615, 1527, 1429, 1373, 1245, 1209, 1066, 1004, 922 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.11 (s, 6H, $COCH_3$), 4.54 (d, J = 4.9 Hz, 2H, OCH_2), 5.29 (d, J = 10.2 Hz, 1H), 5.41 (d, J = 17.3 Hz, 1H), 5.98–6.10 (m, 1H), 6.92 (d, J = 8.6 Hz, 2H, ArH), 7.44 (d, J = 8.6 Hz, 2H, ArH), 7.61(s, 1H, $CH(OAc)_2$) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): 20.9 (2C), 68.9, 89.8, 114.8 (2C), 117.9, 127.9, 128.2 (2C), 132.9, 158.5, 168.8 (2C) ppm. Anal. Calcd for $C_{14}H_{16}O_5$ (264.28): C, 63.63; H, 6.10%. Found: C, 63.45; H, 6.05%.

3.2.7. 1,1-Diacetate of terephthaldehyde (2w)

IR (KBr): 3119, 3032, 2940, 1752, 1603, 1434, 1378, 1250, 1076, 963, 861 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.13 (s, 12H, 4× $-COCH_3$), 7.57 (s, 4H, ArH), 7.68 (s, 2H, $CH(OAc)_2$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) 20.8 (2C), 89.3 (2C), 127.1 (4C), 137.0 (2C), 168.7 (2C) ppm. Anal. Calcd for $C_{16}H_{18}O_8$ (338.31): C, 56.80; H, 5.36%. Found: C, 56.69; H, 5.28%.

3.2.8. 1,1-Diacetate of phthaldehyde (2x)

IR (KBr): 3086, 2953, 1766, 1605, 1434, 1377, 1258, 1116 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.11 (s, 12H, 4× $-COCH_3$), 7.46–749 (m, 2H, ArH), 7.61–7.63 (m, 2H, ArH), 8.00 (s, 2H, 2× $-CH(OAc)_2$) ppm. Anal. Calcd for $C_{16}H_{18}O_8$ (338.31): C, 56.80; H, 5.36%. Found: C, 56.64; H, 5.26%.

3.2.9. 1,1-Diacetate of ketoaldehyde (2b′)

IR (KBr): 2919, 2858, 1752, 1680, 1455, 1378, 1271, 1209, 1112, 1020, 979 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.21–1.27 (m, 16H, $-CH_2$), 1.64–1.69 (m, 2H, $-CH_2$), 2.00 (s, 6H, $-COCH_3$), 2.89 (t, J = 7.6 Hz, 2H, $-CH_2$), 6.70 (t, J = 5.6 Hz, 1H, $CH(OAc)_2$), 7.39 (dd, J = 8.0 Hz, J = 1.4 Hz, 2H, ArH), 7.46 (dd, J = 7.3 Hz, J = 1.4 Hz, 1H, ArH), 7.89 (dd, J = 1.2 Hz, J = 8.2 Hz, 2H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 20.83 (2C), 23.36, 24.35, 29.13, 29.36 (2C), 29.40 (3C), 33.15, 38.60, 90.55, 128.03 (2C), 128.53 (2C), 132.85, 137.08, 169.05 (2C), 200.60 ppm. Anal. Calcd for $C_{22}H_{32}O_5$ (376.49): C, 70.19; H, 8.57%. Found: C, 70.01; H, 8.49%.

4. Conclusion

In conclusion we have developed a rapid and mild synthetic protocol for *gem*-diacylation of aromatic and aliphatic aldehydes under solvent-free conditions. Interestingly aliphatic aldehydes did not show any other side reactions such as cyclotrimerization under the experimental conditions. The notable advantages of this protocol are very good yields, short reaction times, tolerance for a wide variety of other protecting groups. Furthermore due to the simplicity of the procedure and involvement of cheap and reusable catalyst, we believe this protocol will be a new addition in the field of modern organic synthesis.

Acknowledgements

A.T.K. acknowledges to the Department of Science and Technology (DST), New Delhi for research grant (Grant No. SP/S1/G-35/98). L.H.C. is thankful to the CSIR, Govt. of India and S.G. is grateful to IITG for their research fellowships. We are grateful to the Director, IIT Guwahati for providing general research facility.

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Silica-Supported Perchloric Acid ($HClO_4$-SiO_2): A Versatile Catalyst for Tetrahydropyranylation, Oxathioacetalization and Thioacetalization

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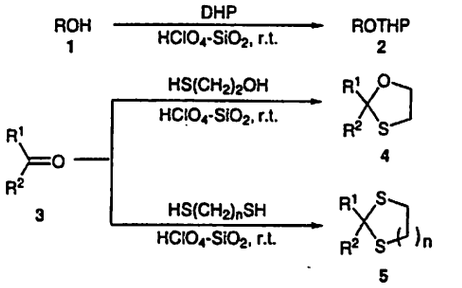
Received 10 February 2006; revised 27 March 2006

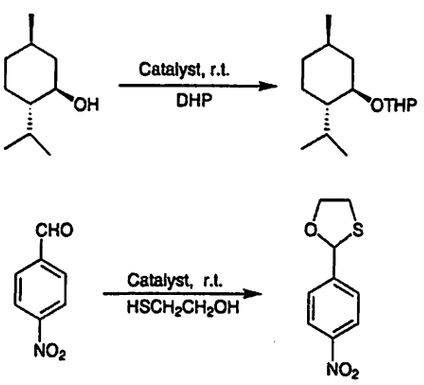
This work is dedicated to Prof. D. N. Buragohain, former Director of IITG, on the occasion of his 65th birthday.

Abstract: A simple and convenient synthetic protocol for the protection of hydroxyl group as tetrahydropyranyl ether as well as carbonyl functionality as oxathioacetal and thioacetal has been achieved using a catalytic amount of silica-supported perchloric acid under solvent-free conditions. This protocol has many advantages compared to currently available methodologies in terms of simplicity, yield, reaction time, reusability of the catalyst and economic viability.

Key words: alcohols, phenols, THP ethers, carbonyl compounds, oxathioacetals, thioacetals



Scheme 1



Scheme 2

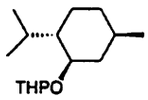
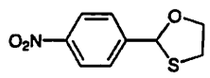
Recently silica-supported catalysts[1] as well as perchloric acid impregnated on silica gel has gained considerable attention in current organic synthesis due to its ease of preparation, high efficiency, reusability of the catalyst and its economic viability. The versatility and overall synthetic utility of this reagent is exemplified by the following applications such as acetylation of phenols, thiols, alcohols and amines,[2] peracetylation of carbohydrates,[3] acetalation followed by acetylation,[4] for glycosylation,[5] Ferrier rearrangement of glycals,[6] and synthesis of heterocycles[7] as well as selective cleavage of isopropylidene and trityl ethers.[8] Recently we found that the same catalyst is useful for *gem*-diacylation of aldehydes[9] as well as for Michael addition of thiols to the electron-deficient alkenes.[10] In our earlier preliminary communication,[11] we reported that 70% aqueous perchloric acid is an effective catalyst for oxathioacetalization of carbonyl compounds. In continuation of our work on solvent-free conditions and utilization of heterogeneous catalysis, herein report silica-supported perchloric acid as a catalyst for the protection of hydroxyl and carbonyl compounds as THP ethers and oxathioacetals or dithioacetals, respectively at room temperature under mild conditions as shown in Scheme 1.

The catalyst $HClO_4$-SiO_2 was prepared by following the literature procedure.[2] To prove the better catalytic activity of silica-supported perchloric acid over aqueous perchloric acid as well as to find out an optimal condition for both the transformations, i.e. tetrahydropyranylation and oxathioacetalization, a set of reactions were studied under different catalytic conditions. Menthol and 4-nitrobenzaldehyde were chosen as model substrates for tetrahydropyranylation and oxathioacetalization, respectively (Scheme 2). For both the transformations the same sets of experiments were carried out and the results are summarized in Table 1.

Sometimes the protection of hydroxyl group as its THP ether is preferred due to easy installation, low cost of the reagent DHP, stability towards a wide variety of reaction conditions as well as easy removal at the later stage. Tetrahydropyranylation of alcohols and phenols is traditionally carried out in the presence of PTSA,[12] PPTS,[13] K-10 clay[14] and $BF_3 \cdot OEt_2$.[15] Recent alternatives include $ZrCl_4$,[16] I_2,[17] LiBr,[18] acetonyltriphenylphosphonium bromide (ATPB),[19] tetrabutylammonium tribromide (TBATB),[20] aluminum chloride hexahydrate,[21] $Bi(OTf)_3$,[22] dialkylimidazolium tetrachloroaluminates,[23] $InCl_3$ immobilized in ionic liquid,[24] H_2O,[25] bromodimethylsulfonium bromide,[26] cupric sulfate pentahydrate,[27] and bismuth nitrate pentahydrate.[28] Although most of the methods provide

SYNTHESIS 2006, No. 15, pp 2497–2502
Advanced online publication: 04.07.2006
DOI: 10.1055/s-2006-942465; Art ID: P01506SS

Table 1 Tetrahydropyranylation of Menthol and Oxathioacetalization of 4-Nitrobenzaldehyde

Entry	Catalyst				
		Time	Yield (%)[a]	Time	Yield (%)[a]
1	No catalyst	12 h	0	12 h	0
2	SiO_2 (20 mg/mol)	12 h	5	12 h	10
3	Aqueous $HClO_4$ (10 mol%)	10 min	76	1 h	35[11]
4	$HClO_4$-SiO_2 (20 mg/mmol, 1 mol%)	5 min	91[b]	30 min	65

[a] Isolated yield.
[b] The catalyst can be recycled up to consecutive three cycles without lose of its activity and provided 85% and 82% yields within 5 and 10 min, respectively, for THP protection.

good yields, still some of them require harsh reaction conditions, long reaction times, involvement of expensive and moisture-sensitive catalysts. Hence cheap heterogeneous catalyst, which work under mild conditions are desirable.

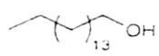
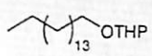
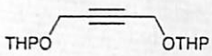
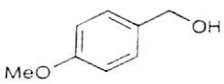
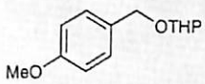
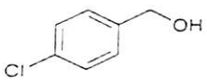
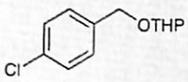
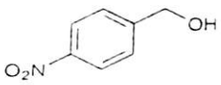
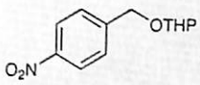
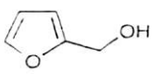
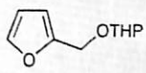
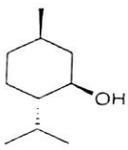
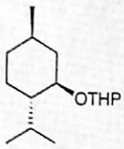
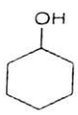
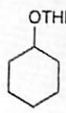
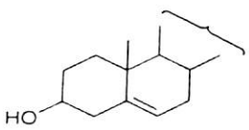
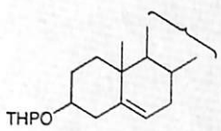
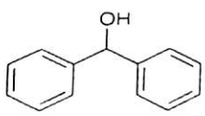
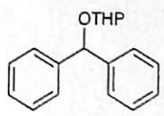
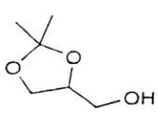
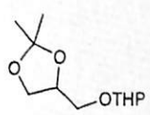
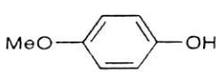
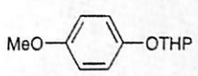
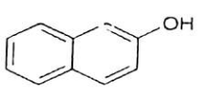
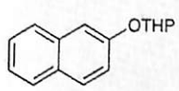
To verify the scope of this reagent for tetrahydropyranylation of alcohols and phenols, firstly cetyl alcohol was treated with 1.1 equivalents of 3,4-dihydro-2*H*-pyran (DHP) under solvent-free conditions with 1 mol% of $HClO_4$-SiO_2 at room temperature. It was smoothly converted to the corresponding THP ether within five minutes in 91% yield. Similarly, a wide variety of other aliphatic as well as benzyl alcohols also gave the THP ethers within a very short time. It is worthwhile to mention that this protocol is faster and provide better yields compared to recently reported methods. Likewise, various secondary alcohols such as menthol, cyclohexanol, cholesterol and even hindered alcohol benzhydrol also underwent tetrahydropyranylation without any difficulty. Moreover, isopropylidine-protected glycerol provided the desired THP ether under similar experimental conditions keeping the acid-sensitive protecting group intact. 4-Methoxyphenol and β-naphthol were also converted to the required THP ethers in good yields (Table 2).

In Table 3, menthol and 2,3-*O*-isopropylidene-D-(±)-glycerol are used as model substrates for comparison of this protocol with some of the recently reported methods. We have done the comparison with respect to mol% of catalyst used, reaction timing and yields obtained.

Several methods are known in the literature[29] for both oxathioacetalization and thioacetalization. Conventionally, oxathioacetals are prepared from the corresponding carbonyl compounds and 2-mercaptoethanol by using equimolar amount of Lewis acid such as $BF_3{\cdot}OEt_2$[30] or $ZnCl_2$.[31] Some of the recent procedures for similar transformation are: montmorillonite K-10,[32] bromodimethylsulfonium bromide[33] and silica-supported tungstophosphoric acid.[34] In our preliminary communication we reported the use of 70% aqueous perchloric acid for the same transformation.[11] Notably, we got relatively low yield in case of 4-nitrobenzaldehyde as mentioned in Table 1. $HClO_4$-SiO_2 is a better catalyst as shown in Table 4. It is much more effective in terms of reaction time and yield. Both aromatic aldehydes and ketones can be protected as oxathioacetals using this protocol without any difficulty. All the products were isolated by distillation under reduced pressure.

Various new methods have also been developed for thioacetalization of carbonyl compounds. Among them, some of the recent methods employ: *N*-bromosuccinimide,[35] bromodimethylsulfonium bromide,[36] acetyl chloride,[37] copper (II) tetrafluoroborate,[38] ruthenium(III) chloride,[39] PTSA/SiO_2,[40] silica-supported polyphosphoric acid[41] and other catalysts.[42] Interestingly, a large number of carbonyl compounds underwent dithioacetalization using 1 mol% $HClO_4$-SiO_2 under solvent-free conditions at room temperature. Most of the reactions were complete within 2–30 min in very good yields as shown in Table 5. Remarkably, aldehydes having electron-donating or -withdrawing substituents in the aromatic ring underwent thioacetalization smoothly in good yields although the yield for the 1,3-dithiane of 4-nitrobenzaldehyde is less than that of other protected aldehydes. It is noteworthy to mention that the same procedure is applicable to aliphatic aldehydes also. The acid-sensitive 2-furaldehyde can also be protected to the desired 1,3-dithiane derivatives without any difficulty. All the products were fully characterized by recording ^1H NMR, ^{13}C NMR and elemental analysis. Remarkably, all solid dithioacetals can be obtained by direct recrystallization after filtering the catalyst. The generality and scope of this catalyst can be ascertained from its recyclability, which we have tested by the following way. For example, a mixture of 4-hydroxybenzaldehyde and propane-1,3-dithiol was treated with $HClO_4$-SiO_2. After completion of the reaction, anhydrous diethyl ether was added to the mixture and the catalyst was filtered off, dried and used for a second time. The recovered catalyst can be recycled for another two more cycles without any loss of its catalytic activity: yields were 92% and 90% respectively after 2 and 5 minutes.

Table 2 Tetrahydropyranylation of Alcohols and Phenols Using $HClO_4$-SiO_2 as Catalyst

Entry	Substrate 1	Reaction time (min)	Product 2[a]	Yield (%)[b]
a		5		91[27]
b		5		90
c		5		87
d		5		95[25]
e		5		92
f		5		83[28]
g		15		96[13]
h		5		91[19]
i		5		91[13]
j		15		97[19]
k		5		95
l		15		84[25]
m		5		80[13]
n		30		83[28]

[a] Products were characterized by recording IR, ^1H and ^{13}C NMR spectra and elemental analysis.
[b] Isolated yield.

Table 3 Comparisons of Some of the Recent Methods for Tetrahydropyranylation with $HClO_4$-SiO_2 Protocol

Catalyst	Mol%	Menthol		2,3-*O*-Isopropylidene-D-(±)-glycerol	
		Time	Yield (%)[a]	Time	Yield (%)[a]
$CuSO_4 \cdot 5H_2O$[27]	20	1 h	89	50 min	85
TBATB[20]	0.1	1 h	74	–	–
$Bi(OTf)_3 \cdot 4H_2O$[22]	0.1	2 h	74	3.25 h	78
$Bi(NO_3)_3 \cdot 5H_2O$[26]	5	22 min	90	20 min	84
$HClO_4$-SiO_2	1	5 min	91	10 min	86

[a] Isolated yield.

In conclusion we have devised a simple and efficient methodology for tetrahydropyranylation, oxathioacetalization and thioacetalization using a very cheap, readily accessible and recyclable catalyst. The notable advantages of this protocol are non-aqueous work-up; very rapid and simple procedure, very good yields. Therefore, we believe this methodology will be a new addition in organic synthesis.

Melting points were recorded on a Büchi B-545 melting point apparatus and were uncorrected. IR spectra were recorded in KBr or neat on a Nicolet Impact 410 spectrophotometer. ^1H NMR spectra and ^{13}C NMR spectra were recorded on a Varian 400 MHz spectrometer in $CDCl_3$ using TMS as internal reference. Elemental analyses were carried out in a PerkinElmer 2400 automatic analyzer. Column chromatographic separations were done on SRL silica gel (60–120 mesh).

Silica-Supported Perchloric Acid ($HClO_4$-SiO_2)[2]

$HClO_4$ (1.8 g, 12.5 mmol, as a 70% aq solution) was added to a suspension of SiO_2 (230–400 mesh, 23.7 g) in Et_2O (70 mL). The mixture was concentrated and the residue was heated at 100 °C for 72 h under vacuum to furnish $HClO_4$-SiO_2 (0.5 mmol/g) as a free-flowing powder (50 mg = 0.025 mmol of $HClO_4$).

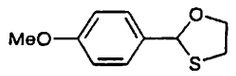
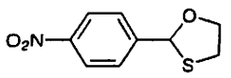
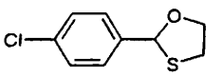
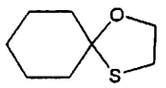
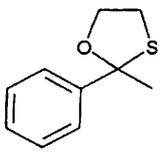
$HClO_4$-SiO_2 Catalyzed Tetrahydropyranylation of Alcohols and Phenols; General Procedure

To a mixture of alcohol or phenol **1** (1 mmol) and 2,3-dihydropyran (DHP) (1.1 mmol, 100 μL) was added $HClO_4$-SiO_2 (0.01 mmol, 20 mg) and the mixture was stirred at r.t. After completion of the reaction as checked by TLC, the crude mixture was directly passed through a short basic alumina column to obtain the desired pure THP ether **2** (Table 2).

$HClO_4$-SiO_2 Catalyzed Oxathioacetalization and Thioacetalization of Carbonyl Compounds; General Procedure

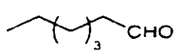
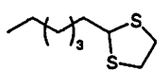
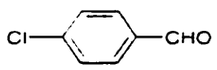
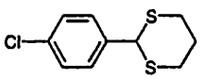
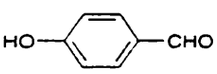
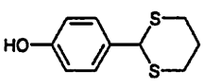
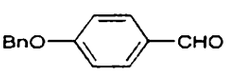
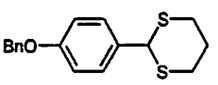
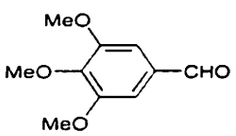
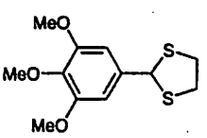
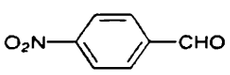
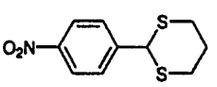
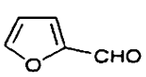
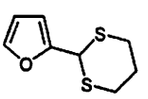
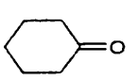
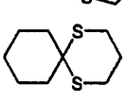
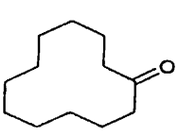
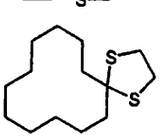
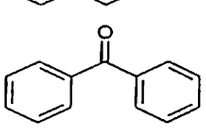
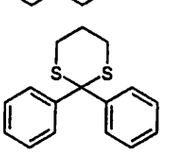
A stirred mixture of carbonyl compound **3** (10 mmol) and 2-mercaptoethanol (12 mmol, 0.84 mL) was treated with $HClO_4$-SiO_2 (200 mg, 0.1 mmol) at r.t. The progress of the reaction was monitored by TLC. After completion of the reaction, the pure product **4** was obtained directly by distillation (Table 4). In the case of dithioacetalization, a mixture of carbonyl compound **3** (5 mmol) and ethane-1,2-dithiol (A) or propane-1,3-dithiol (B) (6 mmol) was treated with the same catalyst. After completion of reaction as checked by TLC, it was diluted with EtOAc and the catalyst was fil-

Table 4 Oxathioacetalization of Carbonyl Compounds Using Catalytic Amount of $HClO_4$-SiO_2 versus Aqueous $HClO_4$ under Solvent-Free Conditions

Entry	Product 4	Method A[a]		Method B[b]		Bp (°C/mm Hg) or Mp (°C)
		Time (min)	Yield (%)[c,d]	Time (min)	Yield (%)[c,d]	
a		20	68	10	74[33]	135/1
b		60	35	30	65[33]	78
c		–	–	25[e]	90[33]	125/5
d		30	76	30	85[33]	85/5
e		90	60	60	75[33]	110/5

[a] Method A = reactions were carried out using 10 mol% aq $HClO_4$ (Ref. 11).
[b] Method B = reactions were carried out using 1 mol% $HClO_4$-SiO_2.
[c] Isolated yield.
[d] All the products were colorless oils, except **4b** (solid), and were characterized by recording ^1H NMR, ^{13}C NMR and elemental analysis.
[e] The catalyst was recycled up to consecutive three cycles without loss of its activity and it provided 80% and 78% yields within 25 and 30 min, respectively.

Table 5 Thioacetalization of Carbonyl Compounds Using Catalytic Amount of $HClO_4$-SiO_2 under Solvent-Free Conditions

Entry	Substrate 3	Thiol[a]	Reaction time (min)	Product 5[b]	Yield (%)[c]	Mp (°C)[d]
a		A	15		98[36]	liquid
b		B	10		81[35]	91
c		B	2		94[36]	157 (158)[36]
d		B	5		98[37]	77–78 (78)[37]
e		A	15		98	94
f		B	30		61[42b]	148 (141–142)[42b]
g		B	15		96[36]	liquid
h		B	30		93[36]	liquid
i		A	5		91[36]	88–89 (88)[36]
j		B	40		96[37]	109 (108–109)[37]

[a] A = ethane-1,2-dithiol, B = propane-1,3-dithiol.
[b] All products were solids, except 5a,g,h (liquids), and were characterized by recording ^{1}H NMR, ^{13}C NMR and elemental analysis.
[c] Isolated yield.
[d] Reported mps are given in parentheses.

tered off. Then the filtrate was concentrated and either kept for recrystallization by adding hexane if the product 5 is solid or purified by silica gel column chromatography (Table 5).

THP Ether of Pentane-1,5-diol 2b

Colorless viscous liquid; yield: 0.245 g (90%).

IR (neat): 2940, 2879, 1455, 1445, 1352, 1265, 1204, 1132, 1035 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42–1.88 (m, 18 H, CH_2), 3.39 (dt, *J* = 6.8, 9.6 Hz, 2 H, OCH_2), 3.46–3.53 (m, 2 H, OCH_2), 3.74 (dt, *J* = 6.8, 9.6 Hz, 2 H, OCH_2), 3.83–3.90 (m, 2 H, OCH_2), 4.56 (dd, *J* = 6.8, 9.6 Hz, 2 H, OCH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.71 (2 C), 23.00, 25.55 (2 C), 29.61 (2 C), 30.79 (2 C), 62.23 (2 C), 67.41 (2 C), 98.67 (2 C).

Anal. Calcd for $C_{15}H_{28}O_4$ (272.38): C, 66.14; H, 10.36. Found: C, 66.21; H, 10.40.

THP Ether of But-2-yne-1,4-diol 2c

Colorless viscous liquid, yield: 0.221 g (87%).

IR (neat): 2940, 2873, 1445, 1399, 1352, 1271, 1209, 1127, 1025, 968 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46–1.79 (m, 12 H, CH_2), 3.43–3.48 (m, 2 H, OCH_2), 3.73–3.79 (m, 2 H, OCH_2), 4.19 (d, *J* = 17.6 Hz, 1 H, OCH_2), 4.22 (d, *J* = 12.4 Hz, 2 H, OCH_2), 4.27 (d, *J* = 14.2 Hz, 1 H, OCH_2), 4.74 (t, *J* = 3.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.88 (2 C), 25.20 (2 C), 30.07 (2 C), 54.19 (2 C), 61.81 (2 C), 81.81 (2 C), 96.66 (2 C).

Anal. Calcd for $C_{14}H_{22}O_4$ (254.32): C, 66.12; H, 8.72. Found: C, 66.21; H, 8.69.

THP Ether of 4-Chlorobenzyl Alcohol 2e

Colorless viscous liquid; yield: 0.209 g (92%).

IR (neat): 2943, 2867, 1592, 1464, 1358, 1132, 1075, 1038 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54–1.89 (m, 6 H, CH_2), 3.52 (d, J = 11.2 Hz, 1 H, OCH_2), 3.87 (t, J = 8.4 Hz, 1 H, OCH_2), 4.44 (d, J = 12.0 Hz, 1 H, ArCH), 4.67 (br s, 1 H, OCHO), 4.72 (d, J = 12.4 Hz, 1 H, ArCH), 7.29 (br s, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.40, 25.50, 30.58, 62.13, 67.99, 97.70, 128.30 (2 C), 128.89 (2 C), 133.02, 136.65

Anal. Calcd for $C_{12}H_{15}ClO_2$ (226.70): C, 63.58; H, 6.67. Found: C, 63.38; H, 6.59.

THP Ether of Benzhydrol 2k
White solid; yield: 0.255 g (95%); mp 50–51 °C.

IR (KBr): 2942, 2903, 2877, 1490, 1199, 1121, 1025, 977, 916 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52–1.97 (m, 6 H, CH_2), 3.47–3.52 (m, 1 H, OCH_2), 3.85–3.91 (m, 1 H, OCH_2), 4.66 (t, J = 3.2 Hz, 1 H, OCHO), 5.79 [s, 1 H, $(Ar)_2CH$], 7.17–7.36 (m, 10 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.27, 25.65, 30.66, 61.99, 78.07, 95.37, 126.67 (2 C), 126.88 (2 C), 127.43 (2 C), 127.53 (2 C), 128.03 (2 C), 128.29 (2 C).

Anal. Calcd for $C_{18}H_{20}O_2$ (268.35): C, 80.57; H, 7.51. Found: C, 80.71, H, 7.59.

2-[3′,4′,5′- Trimethoxyphenyl]-1,3-dithiolane (5e)
White solid; yield: 1.335 g (98%); mp 53–54 °C.

IR (KBr): 1586, 1505, 1127 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.31–3.38 (m, 2 H, SCH_2), 3.46–3.54 (m, 2 H, SCH_2), 3.82 (s, 3 H, OCH_3), 3.86 (s, 6 H, 2 × OCH_3), 5.60 (s, 1 H, ArC*H*), 6.76 (s, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.18 (2 C), 56.12 (2 C), 56.86, 60.78, 104.71, 104.85 (2 C), 135.14, 152.85 (2 C).

Anal. Calcd for $C_{12}H_{16}O_3S_2$ (272.37): C, 52.92; H, 5.92; S, 23.54. Found: C, 52.98; H, 5.89; S, 23.61.

Acknowledgment

A.T.K. acknowledges to the Department of Science and Technology (DST), New Delhi for research grant (Grant No. SP/S1/G-35/98). L.H.C. is thankful to the CSIR, Govt. of India for a research fellowship. We are also grateful to the Director, IITG for providing general facilities to carry out our research work.

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