Peroxovanadium Catalysed Oxidative Transformations of Organic Functional Groups
&
Tetrabutylammonium Tribromide in Organic Synthesis

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A
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STATEMENT

I 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 Dr. Bhisma K. Patel.

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

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CERTIFICATE

This is to certify that Mr. R. Gopinath has been working under my supervision since September 1, 1997. I am forwarding his thesis entitled "Peroxovanadium Catalysed Oxidative Transformations of Organic Functional Groups & Tetrabutylammonium Tribromide in Organic Synthesis" being submitted for the Ph.D. degree of this Institute. I certify that he has fulfilled all the requirements according to the rules of this Institute, and regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

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COURSE CERTIFICATE

This is to certify that Mr. R. Gopinath has satisfactorily completed all the courses required for the Ph.D. degree programme. These courses include:

CHM 601	Physical Methods in Chemistry
CHM 610	Organometallics
CHM 620	Art in Organic Synthesis
CHM 621	Newer Reagents in Organic Synthesis

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CHM 610	Organometallics	6	BC
CHM 620	Art in Organic Synthesis	6	AA
CHM 621	Newer Reagents in Organic Synthesis	6	AB

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My honest regards to the faculty of the institute and friends for their motivation and encouragement which guided me upto this end.

I acknowledge to the Indian Institute of Technology, Guwahati for providing institute fellowship for the entire period of the Ph.D. programme.

R. Gopinath

Standard List of Abbreviations

Ac	acetyl	DMIPS	dimethylisopropylsilyl
acac	acetylacetonate	DMPS	dimethylphenylsilyl
AM1	Austin model 1	DMSO	dimethyl sulfoxide
anhy	anhydrous	DMT	dimethoxytrityl
Ar	aryl	DPIPS	dipheylisopropoxysilyl
Bn	benzyl	DPTBS	diphenyl-*tert*-butoxysilyl
Boc	*tert*-butoxycarbonyl	DTBS	di-*tert*-butylsilylene
br	broad	ee	enantiomeric excess
Bu	butyl	Et	ethyl
Bz	benzoyl	TEA	triethylamine
^{o}C	degrees Celsius	FAB	fast atom bombardment
calcd	calculated	FID	flame ionization detection
CAN	cerium(IV) ammonium nitrate	Fmoc	9-fluorenylmethoxy-carbonyl
CBz	benzyloxycarbonyl	FT	fourier transform
CSA	camphorsulfonic acid	g	grams(s)
δ	chemical shift in parts per million downfield from tetramethylsilane	GC	gas chromatography
		h	hour(s)
		HMPA	hexamethylphosphoric triamide
d	doublet (spectral)		
DBU	1,8-diazabicyclo[5/4/0]-undec-7-ene	Hz	hertz
		IR	infrared
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone	L	liter(s)
		μL	micro liter(s)
DEIPS	diethylisopropylsilyl	m	multiplet (spectral), milli
DMAP	4-*N*,*N*-dimethylamino-pyridine	MDIPS	methyldisopropylsilyl
		MDPS	methyldiphenylsilyl
DMF	dimethylformamide	Me	methyl

MHz	megahertz
mol	moles(s)
MTO	methyltrioxorhenium
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NMP	*N*-methylpyrrolidinone
NMR	nuclear magnetic resonance
PDC	pyridinium dichromate
Ph	phenyl
Piv	pivaloyl
PMB	*p*-methoxybenzyl
ppm	parts per million (in NMR)
PPTS	pyridinium *p*-toluenesulfonate
Pr	propyl
PTSA	*p*-tolunesulfonic acid
Py	pyridine
q	quartet (spectral)
rt	room temperature
s	singlet (spectral)
Salen	bis(salicylidene)ethylene-diamine
SPB	sodium perborate
SPC	sodium percarbonate
t	triplet (spectral)
TBAF	tetrabutylammonium fluoride
TBATB	tetrabutylammonium tribromide
TBS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TBHP	*tert*-butylhydroperoxide
TBMPS	*tert*-butylmethoxyphenyl-silyl
TBTU	*O*-(benzotriazol-1-yl)-*N,N,N',N'*-tetramethyl-uranium tetrafluoroborate
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluroacetic acid
TFAA	trifluroacetic anhydride
THF	tetrahydrofuran
THP	tetrahydropyran; tetrahydropyranyl
TIPS	trisopropylsilyl
TIPDS	1,1,3,3-tetra-isopropyldi-siloxane
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMATB	tetramethylammonium tribromide
TMS	trimethylsilyl
TMSCl	trimethylsilyl chloride
Tr	trityl
Ts	tosyl (*p*-tolunesulfonyl)
UHP	urea-hydrogen peroxide complex
UV	ultraviolet

Classification of Compounds

The compounds listed in the thesis are named according to their derivatives, which are classified as follows:

methyl esters	-	a
ethyl esters	-	b
hydroxy-ethyl esters	-	c
propyl esters	-	d
butyl esters	-	e
benzyl esters	-	f
hydroxy-ethoxy-ethyl esters	-	g
dimethyl acetals	-	h
diethyl acetals	-	i
1,3-dioxolanes	-	j
1,3-dioxanes	-	k
1,3-dioxepins	-	l
tert-butyldimethylsilyl ethers	-	m
tetrahydropyranyl ethers	-	n
4,4’-dimethoxytrityl ethers	-	o
tert-butyldiphenylsilyl ethers	-	p

Abstract

This thesis consists of two chapters, chapter I is about peroxovanadium catalysed oxidative transformations of organic functional groups and chapter II deals with tetrabutylammonium tribromide in organic synthesis. Each chapter contains four sections describing the introduction, present work, experimental section and spectral details.

CHAPTER I

Peroxovanadium Catalysed Oxidative Transformations of Organic Functional Groups

SECTION IA: Introduction

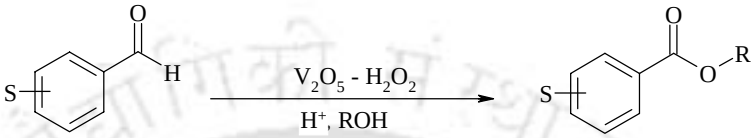
This chapter contains an overview of different oxidative esterifications of aldehydes, cyclic and acyclic acetals; and a brief review of peroxovanadium complexes in organic synthesis. This section also describes the use of hydrogen peroxide and its alternative sources such as sodium perborate (SPB) and sodium percarbonate (SPC) in organic synthesis.

SECTION IB: Present Work

IB.1 Catalytic Oxidative Esterification of Aldehydes Using V_2O_5-H_2O_2

This section describes peroxovanadium catalysed oxidative esterification of aldehydes. Organic esters represent an important class of compounds widely employed in the synthesis of fine chemicals, drugs, food preservatives, cosmetics, pharmaceuticals, solvents and chiral auxiliaries. Oxidative transformation of aldehydes to esters is often required in organic synthesis. Literature procedures often require large excess of reagents, expensive catalysts, dry solvents, inert atmosphere and photochemical conditions, causing severe economic problems upon scale up. Moreover, at times, poisonous and polluting reagents, mediators and co-catalysts are required along with longer reaction times and drastic reaction

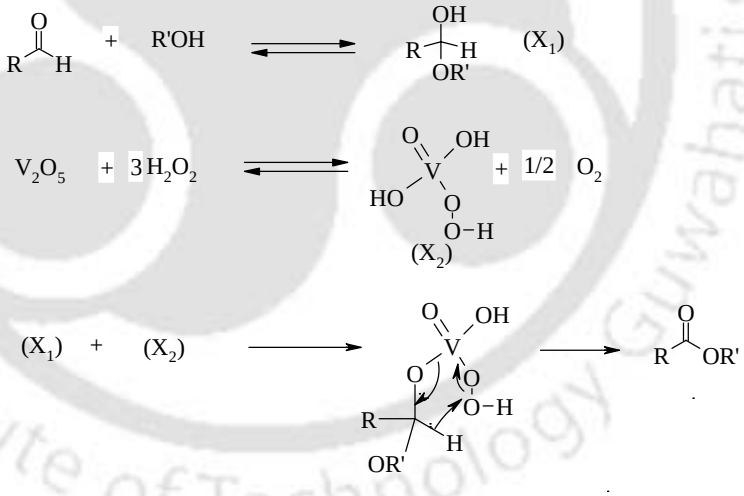
conditions. However, these reagents do not always prove to be satisfactory for specific oxidation of aldehydes in systems containing deactivating groups and olefinic functions. We have now developed a highly facile, cost-effective, and environmentally friendly catalytic route for esterification of aldehydes (Scheme 1).



S = Me, OMe, NO_2, OH, OBn, Br, Cl etc.,
R = Me, Et, Pr, Bu, Bz, $HOCH_2CH_2$-, $HOCH_2CH_2OCH_2CH_2$- etc.,

Scheme 1

In a typical reaction, to an ice cooled solution of aldehyde (1 mmol) in methanol (5 mL) containing 70% $HClO_4$ (0.6 mmol) was slowly added a solution of V_2O_5 (0.04 mmol) dissolved in H_2O_2 (4 mmol) at 5°C.



Scheme 2

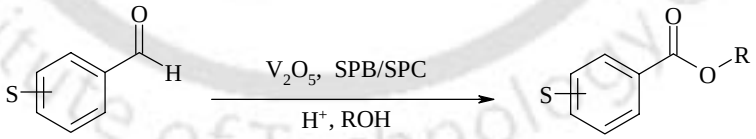
Mechanistically, it seems plausible that the aldehyde is oxidised by the peroxovanadium species to the corresponding acid, which is esterified immediately with an alcohol. However, when benzoic acid was used instead of benzaldehyde under identical conditions, no methylbenzoate could be obtained. In the above systems, H_2O_2 does not bring about esterification without the catalyst (V_2O_5) and the catalyst alone fails to bring about esterification. Aldehyde under acidic conditions reacts with alcohol to form hemiacetal. It is proposed that the hemiacetal thus formed reacts with oxoperoxovanadium species, which

results from the addition of H_2O_2 to vanadium(V) oxide to form a vanadium hemiacetal type intermediate. Subsequent elimination produces the desired product and releases the catalyst. A catalytic turnover number of >500 have been determined. This reaction can also be performed in the absence of any external acid but the reaction rates are slow. The proposed reaction mechanism is shown in Scheme 2.

The methodology works equally well for the synthesis of ethyl, propyl and butyl esters. Synthesis of glycol monoesters of diols has received considerable interest in view of widespread applications as intermediates for sex pheromones of lepidoptera; cross-linking agents for polyesters or fungicides. The major drawback for the preparation of these compounds from diols had been the concurrent formation of diester, necessitating a tedious separation. Alternatively they were prepared by the oxidation of the cyclic acetals using various oxidising agents. The present protocol has been successfully applied to the synthesis of monoesters of various diols including diethylene glycol.

IB.2 Catalytic Oxidative Esterification of Aldehydes Using V_2O_5-SPB/SPC

In this section peroxy salts such as sodium perborate (SPB) and sodium percarbonate (SPC) are used as an alternative source of hydrogen peroxide for the generation of peroxovanadium species for oxidative esterification of aldehyde in an acidic medium (Scheme 3).



S = Me, OMe, NO_2, OH, OBn, Br, Cl etc.,
R = Me, Et, Pr, Bu, Bz, $HOCH_2CH_2$-, $HOCH_2CH_2OCH_2CH_2$- etc.,

Scheme 3

The oxidation was carried out either by adding mineral acid to the mixture containing catalyst (V_2O_5), peroxy salt, aldehyde and alcohol (method A) or by adding peroxy salt to the rest (method B). For method A when perchloric acid was added in one lot, a considerable amount of over-oxidation of aldehyde to corresponding acid took place. Subsequent optimisation revealed that transformation is best achieved using drop wise addition of the

acid over a period of time. For both SPB and SPC the optimum stoichiometry was 3.5 per mmol of aldehyde. A higher concentration of acid was required for SPC as compared to SPB for the efficient release of hydrogen peroxide and for maintaining the catalytic activity of V_2O_5. This is because SPC is slightly more alkaline as compared to SPB.

UV spectral analysis confirmed the intermediacy of the peroxovanadium(V) species (λ = 430 nm) in solution. Though $VO(O_2)^+$ is a two-electron oxidant, it can function as a one-electron oxidant as well where no two electron pathway is accessible. In the previous section we have proposed a two-electron mechanism involving a hydride ion transfer in one of the step. To ascertain the importance of the cleavage of the aldehydic C-H bond in the rate-determining step, the oxidation of the [^{2}H] benzaldehyde (PhCDO) was studied. The result showed no significant kinetic isotope effect (K_H / K_D ≈1 at 273^o K), ruling out the possibility of a two-electron mechanism. The oxidation of benzaldehyde, under the reaction condition failed to induce polymerisation of methyl acrylate. Further the addition of methyl acrylate and a radical scavenger like benzophenone has no effect on the reaction rate. This however does not completely rule out a one-electron mechanism, since in oxygenated atmosphere the oxygen molecules either quench the radical before bringing about polymerisation of methyl acrylate or reaching to the radical inhibitor. Thus this reaction is expected to go *via* an intramolecular free radical mechanism. A catalytic turnover number of >500 were determined for both the methods. The methodology works equally well for the synthesis of other esters as described in the previous section.

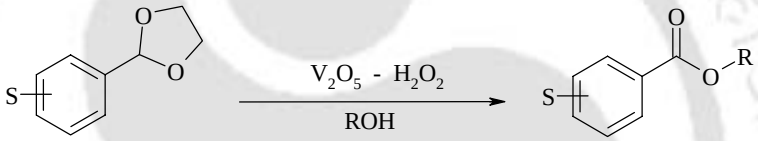
IB.3 Direct Oxidation of Acetals to Esters Using V_2O_5-H_2O_2

This section describes the direct oxidation of cyclic and acyclic acetals into a variety of esters using V_2O_5-H_2O_2.

The acetal functionality is one of the most commonly used protecting groups and the direct conversion of cyclic and acyclic acetals to the corresponding esters is a useful synthetic methodology in organic synthesis.

The intrinsic acidity (p*H ca.* 2.0) originating from dissolution of V_2O_5 in hydrogen peroxide is sufficient to deprotect acid-sensitive groups like acetals, THP and TBS ethers.

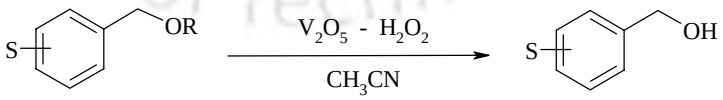
Thus, treatment of both cyclic and acyclic acetals with a mixture of V_2O_5-H_2O_2 in acetonitrile yields corresponding aldehydes. When the same reaction was performed in an alcoholic medium, esters of corresponding alcohols were obtained in excellent yields (Scheme 4). Cyclic acetals are known to get oxidise to the corresponding hydroxy esters only, with different oxidising agents, but by this method a wide varieties of esters can be synthesised from acetals by carefully choosing different alcohols for the reaction. The steps involved are deprotection of acetal to aldehyde followed by oxidative esterification as described in the earlier sections. Since, aldehyde was slowly generated in the medium from the acetal so no over-oxidised product was obtained. Efficacy of this methodology has been demonstrated with varieties of acetals.



S = OMe, NO_2,OH, Br etc.,

Scheme 4

The above methodology when applied to unsymmetrical acetals like tetrahydropyranyl (THP) ethers were cleanly deprotected into parent alcohols without any further oxidation of the resulting alcohol (Scheme 5). Other acid-sensitive ethers such as TBS could also be deprotected efficiently when treated with V_2O_5-H_2O_2. Thus this methodology is very useful for the deprotection of acid-sensitive protecting groups as well as in the transformation of acetals to esters.



S = H, Cl, NO_2
R = TBS, THP

Scheme 5

The other two sections namely, ***SECTION IC*** and ***SECTION ID*** deals with the experimental details and spectral pertaining to this chapter.

CHAPTER II

Tetrabutylammonium Tribromide in Organic Synthesis

SECTION IIA: Introduction

This chapter contains a brief review on deprotection of acid-sensitive groups such as DMT, THP, TBDPS, TBS etc., and describes various literature methods for the protection of carbonyl groups as acetals and their applications in organic synthesis. This chapter also contains a detailed account of organicammonium tribromides and their synthetic utility in general and tetrabutylammonium tribromide in particular.

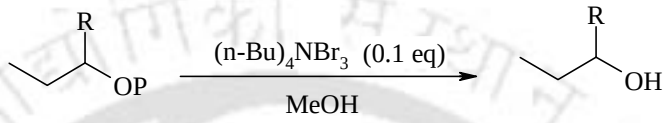
SECTION IIB: Present Work

IIB.1 Tetrabutylammonium Tribromide (TBATB)-Methanol as an Efficient Reagent for the Deprotection of Acid-Sensitive Groups

This part of the dissertation describes chemoselective deprotection of silyl, tetrahydropyranyl and dimethoxytrityl ethers with tetrabutylammonium tribromide in methanol.

The protection-deprotection of alcohol functionalities is important in synthetic organic chemistry, and a plethora of reagents and methods have been devised to this end. The importance of protecting the hydroxyl group frequently appears in the synthesis of biologically active molecules. Tetrahydropyranyl (THP) ethers in combination with silyl ethers have been used extensively for this purpose, and the 4,4'-dimethoxytrityl (DMT) group have been used widely for the protection of 5'-hydroxyl groups of nucleosides in oligonucleotide synthesis. However, many of the literature procedures require long reaction times, drastic reaction conditions, a large excess of phase transfer catalyst, and moisture-sensitive and expensive reagents causing serious problem for large-scale reaction. Most of these reagents are strongly acidic, basic, oxidising, or reducing in nature, a property that is not always desirable.

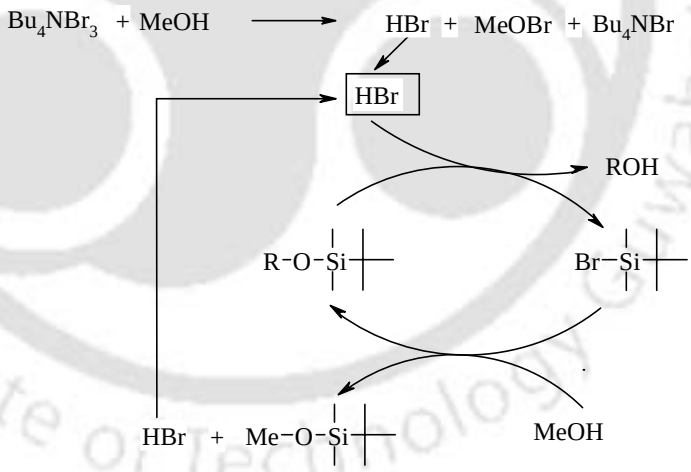
Tetrabutylammonium tribromide is known as an efficient brominating agent for a number of substrates in various solvents. It is also a good source of anhydrous HBr when dissolved in anhydrous alcohol (Scheme 7) though this property has not been exploited in the past. The HBr thus generated can be responsible for the deprotection of numbers of acid-sensitive ethers as shown below (Scheme 6).



R = H, alkyl or aryl
P = TBS, TBDPS, THP, DMT

Scheme 6

The results of solvent dependent cleavage of primary TBS ether with TBATB suggests that polar organic solvents are relatively more suitable for deprotection as compared to aprotic solvent and methanol turns out to be the best solvent for desilylation (Scheme 7).



Scheme 7

A wide spectrum of structurally varied TBS, THP, and DMT ethers were subjected to deprotection by this procedure. We also examined the inter and intramolecular chemoselective deprotection of TBS ethers in the presence of isopropylidene, Bn, Ac, Bz, THP, and TBDPS, and the results are very encouraging.

The reagent TBATB can selectively deprotect primary TBS ether in the presence of primary THP ether and secondary THP ether in the presence of secondary TBS ether. This

result indicates that TBATB can readily differentiate not only THP over TBS but also TBS over TBDPS ethers. The apparent order of stability as obtained from our present study is phenolic TBS > 1° OTBDPS > 2° TBS > 2° OTHP > 1° OTHP > 1° OTBS > 1° DMT.

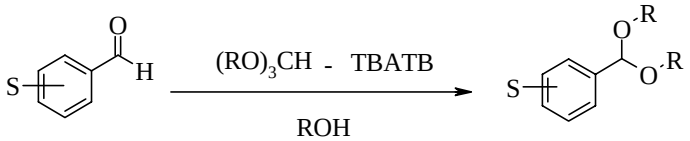
IIB.2 Tetrabutylammonium Tribromide (TBATB) as an Efficient Reagent for Acetalisation of Carbonyl Compounds

This chapter deals with the masking of carbonyl groups as acetals in presence of trialkyl orthoformate, alcohol, and tetrabutylammonium tribromide.

During a multistep synthesis, a carbonyl group may have to be protected against an attack by various reagents such as nucleophiles, oxidants, basic, catalytic or hydride reducing agents including organometallic reagents. Acetals are generally formed under acidic conditions and water formed during the reaction is removed either by physical or chemical methods. Orthoesters are used as one of the chemical methods for the removal of water, resulting in the equilibrium shifting to the right. Unfortunately, many of these procedures often require a large excess of reagents, longer reaction times, drastic reaction conditions, and moisture-sensitive and expensive reagents. Also, some of these reagents are not satisfactory for the acetalisation of cyclic and aromatic ketones.

The identification of tetrabutylammonium tribromide as a catalytic, mild and chemoselective reagent for the acetalisation of carbonyl compound is the basis of this investigation (Scheme 8).

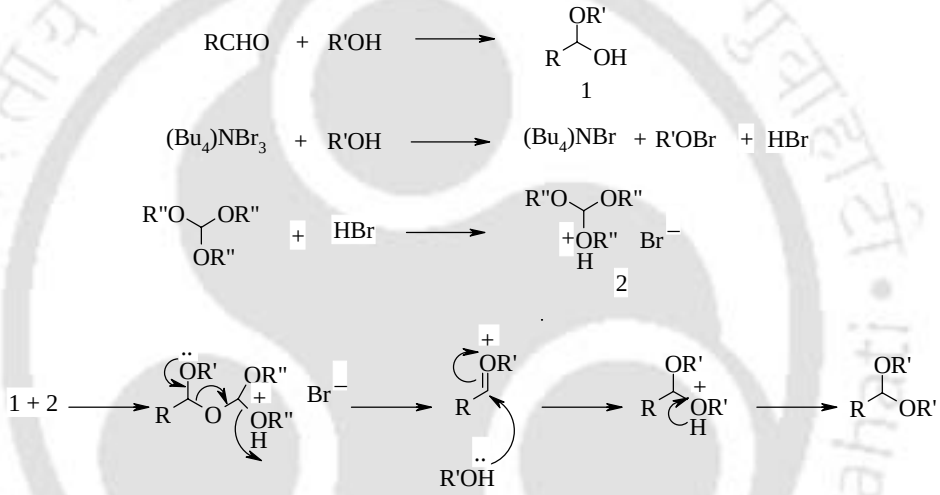
In a typical reaction to a solution of carbonyl compound (1 mmol), trialkyl orthoformate (1.1 mmol) in corresponding absolute alcohol (1 mL) was added tetrabutylammonium tribromide (0.01 mmol).



S = H, OH, OMe, NO_2, Cl

Scheme 8

Open chain acetals have frequently been subjected to special attention owing to their liability as compared with cyclic *O*,*O*-acetals. Under the experimental conditions, various carbonyl compounds can be acetalised to the corresponding *O*,*O*-acetals in excellent yields. HBr generated *in situ* from the reaction of TBATB with alcohol (Scheme 9) may catalyse the reaction. Solvent also plays a very important role in this reaction. This may be due to the fact that alcohol accelerates the formation of hemiacetal, which is further, facilitated by the HBr generated in the medium as shown in Scheme 9.



Scheme 9

Cyclic acetals such as 1,3-dioxolanes and 1,3-dioxanes are also important protecting groups for carbonyl compounds and are obtained in high to excellent yields by the present methodology. Acid-sensitive groups such as the phenolic TBS ethers are stable under the reaction condition. The methodology will be useful for chemoselective acetalisation of aldehyde in the presence of ketone. From the present study, the apparent order of acetal formation for different carbonyl groups is aldehyde-1,3-dioxanes > aldehyde-1,3-dioxolanes > ketone-1,3-dioxolanes > ketone-1,3-dioxanes.

This method is high yielding, safe, operationally simple under mild reaction conditions, fast, and cost-effective. The catalytic nature of this methodology makes it more suitable for practical organic synthesis.

The other sections namely, ***SECTION IIC*** and ***SECTION IID*** deals with the experimental details and spectra relating to this chapter.

Contents

Chapter I

Peroxovanadium Catalysed Oxidative Transformations of Organic Functional Groups

IA Introduction

IA.1 Green Chemical Processes

Modern life is dependent upon chemicals in a variety of ways as such it is almost impossible to live without them in the present days. Synthesis of new materials, dyes, agrochemicals, and pharmaceuticals has certainly contributed to the increase of the life expectancy. To ensure compatibility with conservation of global environment, chemical processes are required to be changed to "Green Processes", which includes the use of starting materials, reaction processes of low environmental loading and functional materials or additives without poisonous reagents. These are expected to aims at development of highly effective catalytic systems and catalysts suitable for green conditions that minimises the energy requirements and generates substances that possess little or no toxicity to human health and the environment.[1]

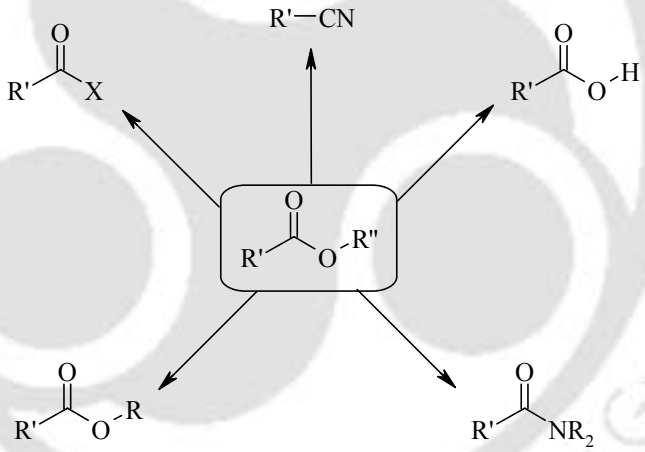
In spite of spectacular successes, organic synthesis has still a long way to go before achieving its ultimate goals *i.e*., being as or even more efficient than mother nature in terms of selectivity and capability of producing high yields of structurally varied complex molecules using processes which are simple, cheap, catalytic, and which do not destroy our environment. Efficiency and selectivity are essential characteristics of a good synthetic method and it is now become a major challenge for organic chemists. Catalytic reagents (as selective as possible) are found to be superior to stoichiometric reagents, while in search of newer environmentally benign methods.

IA.2 Organic Functional Group Transformations

Organic functional group transformations aims to present the vast subject of organic synthesis in terms of the introduction and interconversion of functional groups. Functionalisation reactions are emphasised which are of genuine practical utility, but others that are noteworthy and of potential synthetic significance. One of the pressing issues for chemists in the twenty-first century is the pursuit of 'clean' or 'green' chemical transformations.[1c] Based upon the principles of synthetic methodology and green chemistry

concern, the transformation of organic functional group has garnered more demand in present eco-conscious chemical processes and encouraged the development of several clean and practical alternatives and awaits further development of high yielding, clean, safe, and economical methods.

Many of the natural products of current biological importance and synthetic interest consist of highly oxygenated carbon skeletons. The desire to prepare these compounds and their analogs has lead to many impressive advances in synthetic technology. Within the realm of synthetic environment, organic esters represent an important family of intermediates widely employed in the synthesis of fine chemicals, drugs, perfumes, food preservatives, cosmetics, pharmaceuticals, and chiral auxiliaries. Esters can be transformed to several other functionalities as shown in Scheme 1.1.



Scheme 1.1

Esters are essential in our day-to-day life; for example (Figure 1.1) triglycerides **1**, in the form of fats and oils are produced in million ton quantities for a number of applications. Other esters, e.g., **2** and **3**, are olfactory components. Aspartame **5** is an important artificial sweetener, and pyrethrin **6** is the prototype of the pyrethroids, an unusually potent class of insecticides, which is chemically modified to **7** to prevent its degradation against sunlight.[2]

The monomer, methyl methacrylate **8**, is the building block of vinyl polymer poly(methyl methacrylate). The monomer, methyl α-cyanoacrylate **9**, is used in the adhesive, marketed under the trademark of "Superglue". The general class of cyanoacrylates **10** with

varying alkyl group is sold as contact adhesive. The addictive alkaloid cocaine **11** is an ester. Scopolamine **12** is used for protection against motion sickness. Due to the wide varieties of applications of esters in organic synthesis there is a great demand for the synthesis of esters.

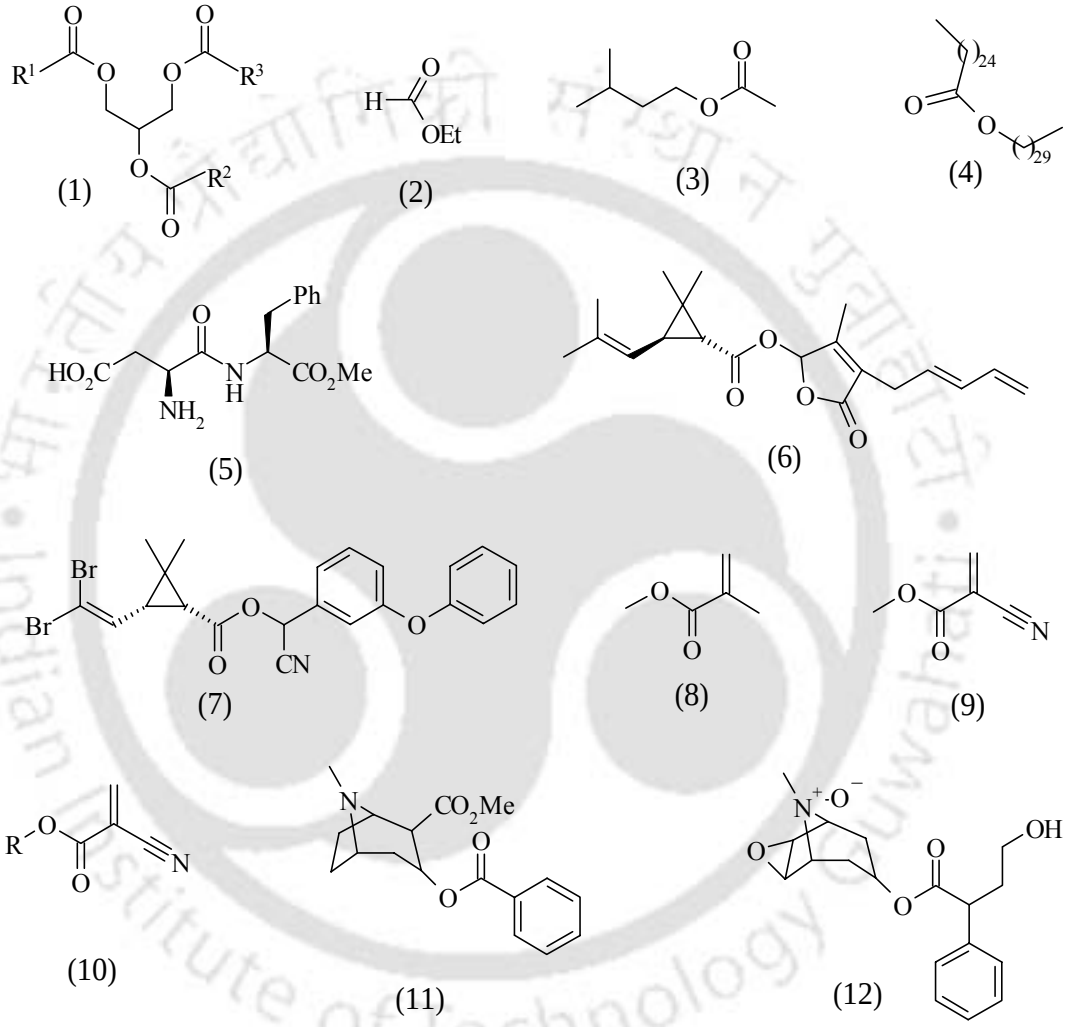


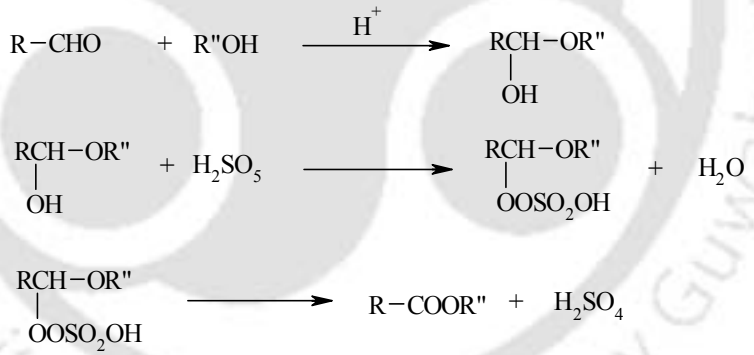
Figure 1.1

IA.2.1 Oxidative Esterification of Aldehydes

Esters are generally prepared by the following sequence: alcohol → aldehyde → acid → ester. Thus, the conversion of aldehydes to esters has traditionally been accomplished by a two-step reaction sequence (oxidation followed by esterification). Oxidative transformation of aldehyde to ester under mild conditions is often obligatory in organic synthesis and hence

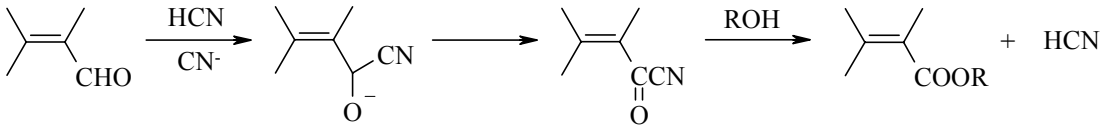
much effort has been devoted to find new methods or new reagents effective for this type of transformation. A brief literature review on the one-step transformation of aldehyde to ester is discussed below.

Smith and co-workers have reported the oxidation of acrolein in alcoholic medium with hydrogen peroxide in the presence of selenium dioxide as the catalyst.[3] Craig *et al.* have reported the oxidation of primary alcohol with dichromate and sulfuric acid to ester.[4] This reaction occurs by the reaction sequence: alcohol → aldehyde ⇌ hemiacetal → ester, rather than by the commonly accepted path: alcohol → aldehyde → acid → ester. Methyl methacrylate was obtained by the oxidation of methacrolein in methanol with *tert*-butyl hydroperoxide in the presence of metal salt catalyst, such as $FeCl_2$ and $FeCl_3$.[5] Nishihara and Kubota have demonstrated the oxidation of aldehydes with Caro acid in the presence of alcohols to esters.[6] This reaction proceeds through a hemiacetal peroxomonosulphate intermediate as shown in Scheme 1.2.



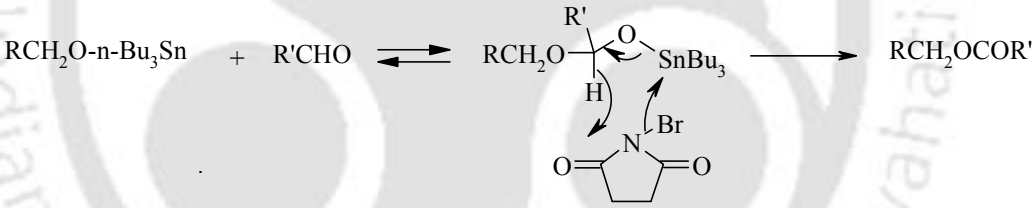
Scheme 1.2

Corey and co-workers[7] during the total synthesis of insect juvenile hormone have devised a simple method for the stereospecific conversion of conjugated aldehydes to esters. Conjugated aldehydes in the presence of MnO_2, HCN and alcohol lead to esters. This reaction involves oxidation of cyanohydrin intermediate to acyl cyanide, finally in an alcoholic medium leading to an ester. The proposed reaction mechanism for this transformation is shown in Scheme 1.3. This method was subsequently modified and applied to different reactions. Disadvantages of the reaction are the use of poisonous reagents, long reaction times and failure in the case of non-conjugated aldelydes.



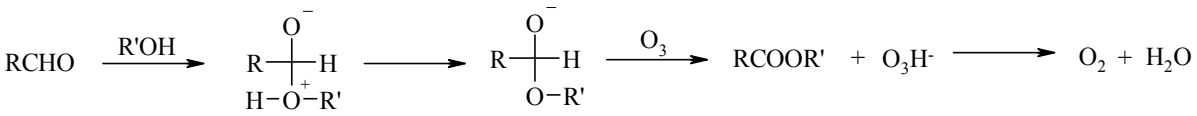
Scheme 1.3

Oxidation in an alkaline medium has been reported by Inch *et al.*[8] where aldehyde was oxidised with iodine in methanolic potassium hydroxide to afford methyl ester. Eliel group[9] later applied this method for a similar purpose. Ogawa and Matsui[10] have developed a procedure for the transformation of aldehyde to ester using NBS and R'OSn(*n*-Bu)$_3$. The method involves two successive operation: (i) stannylation of the alcohol, and (ii) NBS treatment of equimolar mixtures of aldehyde and stannylated alcohol, mechanism of the reaction is shown below, Scheme 1.4. In absence of added aldehyde, primary alcohols gave dimeric esters.



Scheme 1.4

Djerassi group[11] have achieved a single step transformation of esters from aldehydes by passing ozone into a methanolic potassium hydroxide solution at -78°C. Ethanol could be substituted for methanol to obtain the corresponding ethyl ester. Proposed mechanism has resemblance with Cannizaro and Tischenko reactions involving a hydride ion transfer to the corresponding electrophilic ozone from the hemiacetal, Scheme 1.5. However, they did not ruled out the mechanism involving ozone attack on the C-H bond of the hemiacetal with the



Scheme 1.5

production of hydrotrioxide decomposing into acid and ester. The disadvantage of the method is retroaldolisation followed by oxidation of substrates containing of α, β-unsaturated double bonds.

Yet another methodology for the one-pot esterification of aldehydes reported by Pinnick and co-workers, involved the addition of an aldehyde to silyl ether in the presence of NBS.[12] This reaction proceeds *via* a radical mechanism, hence, not suitable for substrates containing C-C double bonds. The other disadvantages are the use of expensive silyl ethers and photochemical conditions. Cheung has shown under photochemical conditions and in an inert atmosphere aldehyde reacts with NBS in presence of an alcohol to yield corresponding ester.[13] Benzylic positions are unaffected, however, it is apparently not selective enough to affect clean oxidation in the presence of olefinic functions.

Wilson *et al.*[14] have described selective conversion of aldehydes to acid chlorides with *tert*-butyl hypochlorite, which gave rise to esters in the presence of triethylamine and alcohol. This reaction probably involves *tert*-butoxy radical abstraction of the aldehydic hydrogen. Competition between free radical hydrogen abstraction and electrophilic chlorination results in a marked solvent effect.

Castells group[15] have reported a one-pot synthesis of methyl and ethyl esters from aldehydes (and the corresponding alcohols), using aromatic nitro compounds as oxidising agents under the catalytic action of cyanide ion or of a conjugate base of thiazolium ion. Requirement of inert atmosphere, long reaction times and along with the use of poisonous catalysts are some of the drawbacks of this method.

Stevens and co-workers[16] have described a method where sodium hypochlorite in acetic acid selectively oxidises secondary alcohols to ketones in the presence of primary alcohols, and in the presence of methanol converts aldehydes to methyl esters. Under the reaction conditions primary alcohols are converted to their corresponding dimeric esters. Although the yields are generally good, the limitations of the method are activated aromatic aldehydes give low yields due to the competing ring chlorination. Olefins are also susceptible to electrophilic attack by the reagent, which gave both multitude of chlorine containing by-products.

The catalyst benzyltrimethylammonium tetrabromomolybdate designed by Masuyama group[17] is an excellent chemoselective catalyst for the oxidation of secondary alcohols to ketones, primary alcohols to dimeric esters and aldehydes to acids or esters in the presence of *tert*-butyl hydroperoxide. The reaction rates are independent of the presence of radical scavengers like 2,6-di-*t*-butyl-4-methylphenol, which lead to postulate a hydride ion transfer to *tert*-butyl hydroperoxide.

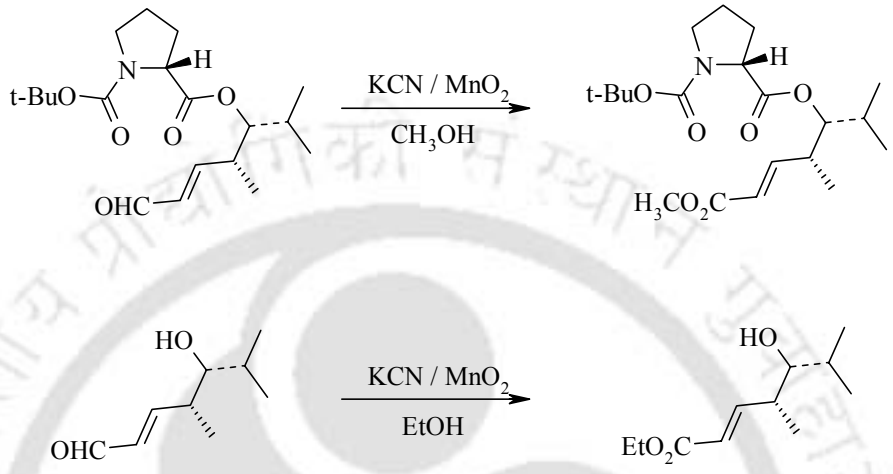
Different groups have reported several electrochemical oxidations of aldehydes. Shono and co-workers[18] have prepared methyl esters by passing a constant current at room temperature through a solution of aldehyde in methanol containing KI or KBr. Butyl esters has been prepared by electrochemical oxidation of aldehydes under the conditions of a two-phase system consisting of an aqueous layer containing KI or KBr and an organic one containing aldehyde and butanol, since the low dielectric conductivity of butanol did not allow its use as a sole solvent. In this method no special oxidising agent is required and the reaction conditions are mild, that substrates containing carbon-carbon double bond and an epoxy group can selectively be oxidised to the corresponding esters with these functional groups intact. However, this reaction is not suitable for large-scale reactions.

Nagashima *et al.* have reported a Pd salts catalysed oxidation of alcohols in the presence of K_2CO_3.[19] Primary alcohols are oxidised to the corresponding dimeric esters, and secondary alcohols to ketones. The reaction is considered to involve three elemental reactions: (i) oxidation of primary alcohol to aldehyde, (ii) formation of hemiacetal from aldehyde and alcohol, and (iii) oxidation of hemiacetal to ester.

Bisulfite adducts of aldehydes are conveniently oxidised to carboxylic acids and its derivatives by the action of DMSO and acetic anhydride followed by quenching the reaction mixture with water, or an alcohol or an amine.[20] The reaction mechanism involves oxidation of the hydroxyl of the bisulfite adduct with DMSO and Ac_2O to form α-ketosulfonate salt which when quenched with NaOMe / MeOH cleanly gave the methyl ester. Long reaction times, expensive solvents such as DMSO, Ac_2O and use of methoxide makes this method unattractive.

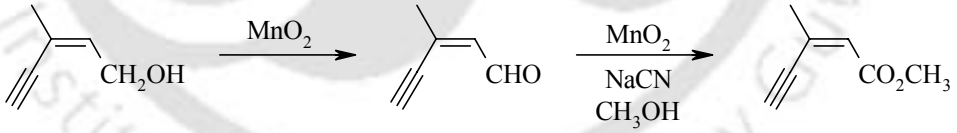
During the synthesis of virginiamycin M_2, a virginiamycin family of antibiotics,

Schlessinger and Iwanowicz[21] utilised the method of Corey *et al.*[7] for the following transformations, Scheme 1.6.



Scheme 1.6

Abscisic acid is a natural product extensively distributed in higher plants and has the important function of regulating the plants dormancy state, permitting survival in adverse conditions.[22] Principle of MnO_2 catalysed oxidations[7] has been further applied by Constantino group during the synthesis of a precursor of abscisic acid, Scheme 1.7.[23]

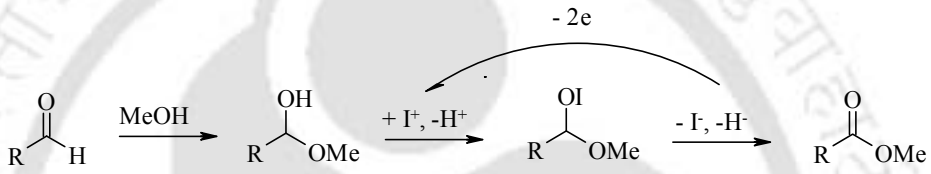


Scheme 1.7

Murahashi and co-workers have utilised dihydridotetrakis (triphenylphosphine)-ruthenium $RuH_2(PPh_3)_4$ for various oxidation reactions.[24] Primary alcohols are oxidised to dimeric esters with the evolution of molecular hydrogen when treated with $RuH_2(PPh_3)_4$. Under the identical conditions, 1,4 and 1,5- diols gave γ- and δ-lactones, respectively. The same principle was also extended to ester formation from aldehydes and alcohols. The disadvantages of this methodology are the use of expensive catalyst, requirement of hydrogen acceptor, dry solvents, and reaction in a sealed tube, and requirement of high temperature (180°C).

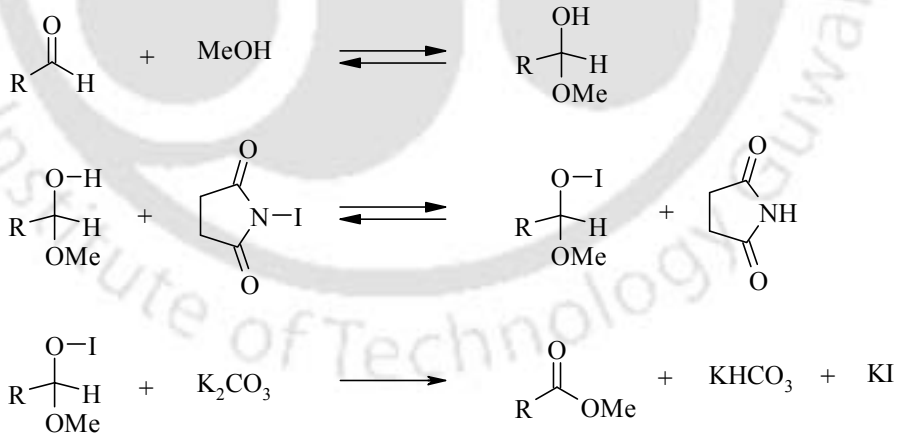
O'Connor and Just[25] have developed a single step transformation of aldehydes to methyl esters using PDC (pyridinium dichromate) in the presence of methanol.

Okimoto and Chiba have described another electrochemical oxidation of aldehydes to esters.[26] The electrooxidative preparation of methyl carboxylates from aldehydes was conducted in methanol containing NaOMe and a catalytic amount of KI. The electrolyses were carried out in a divided cell with a platinum anode under a constant current. The overall electrochemical reaction involves the *in situ* generation of positive iodine species, which then gets involved in the production of ester as shown in Scheme 1.8.



Scheme 1.8

NIS is also an effective reagent for the conversion of aldehydes to esters as described by McDonald's group.[27] The reaction is thought to proceed as indicated in Scheme 1.9.



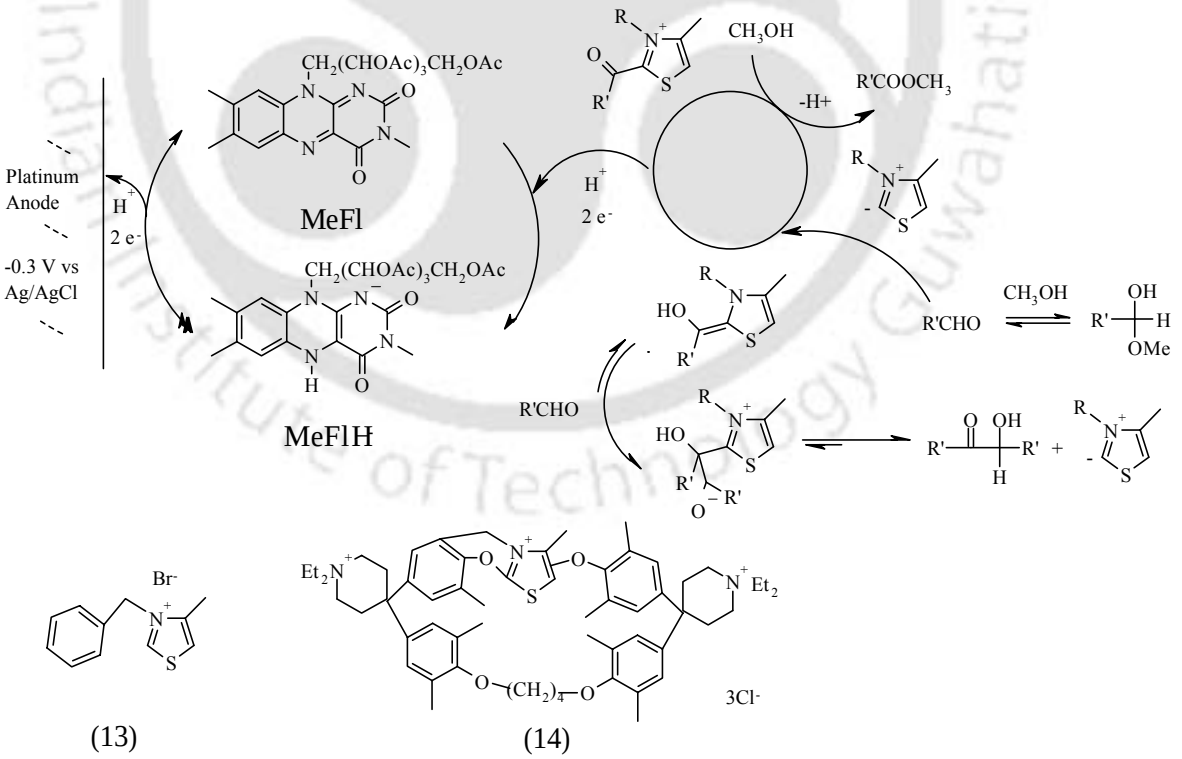
Scheme 1.9

The initially formed methyl hemiacetal is oxidised by NIS to the corresponding hemiacetal hypoiodite. Subsequent elimination of hydrogen iodide produces the observed product. The reaction is believed to be ionic in nature since moderately strong base is required. The reaction proceeds faster in polar solvents and light (or oxygen) has no effect on either the reaction rate or ultimate yield of the product. The success of the reaction is

dependent upon the selective oxidation of the methyl hemiacetal hydroxy moiety in the presence of a much higher concentration of methanol.

Molecular bromine with sodium hydrogen carbonate and sodium hypochlorite is an efficient reagent for the oxidation of aldehydes to esters.[28] Br_2-HMPT-$NaHCO_3$ in a two-phase system is yet another combination for such transformation as reported by Al Neirabeyeh and Pujol.[29] The key step in these oxidations is the formation of a hemiacetal intermediate between the aldehyde used, or formed in the reaction medium, and an alcohol. The use of HMPT accelerates considerably the oxidation by bromine and lowers the rate of halogenation, which is the main side reaction using halogens and halogen derivatives. The poor yield in the case of tertiary alcohol is due to difficulty in the formation of hemiacetal intermediate.

Yet another interesting electrochemical oxidation of aldehyde has been reported by Diederich group[30] where they have described an efficient, one-pot synthesis of aromatic

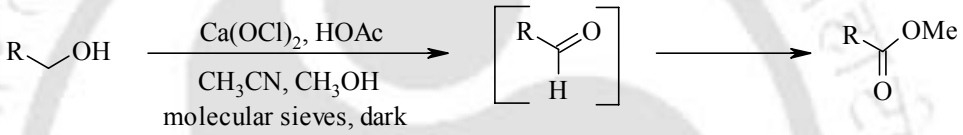


(13) (14)

Scheme 1.10

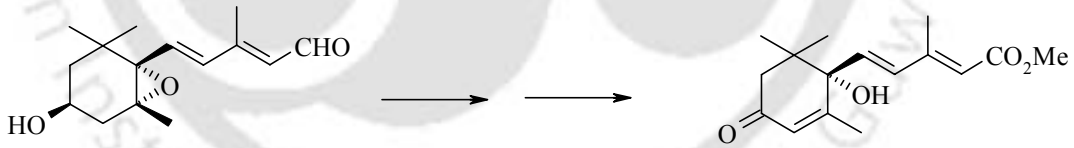
methyl esters by electrochemical oxidation of aldehydes, mediated by two-coenzyme catalysts: the thiazolium ions **13, 14** and flavin **MeFI**. The use of the macrocyclic catalyst **14** in electroorganic synthesis elegantly combines the principles of electrocatalysis with molecular recognition is shown in Scheme 1.10.

McDonald group[31] have reported yet another method for the synthesis of esters from alcohols using calcium hypochlorite as the oxidising agent as shown below in Scheme 1.11. The success of the reaction is dependent on the selective oxidation of the primary alcohol in the presence of much higher concentration of methanol. Hypochlorous acid generated from $Ca(OCl)_2$ is the actual oxidising species for this transformation.



Scheme 1.11

Yamamoto and Oritani[32] have utilised the method of Corey *et al.*[7] for the transformation of xanthoxin to abscisic acid methyl ester, Scheme 1.12.



Scheme 1.12

The method of O'Connor and Just[25] was applied to carbohydrates by Oscarson group[33] for the following transformation, Scheme 1.13.

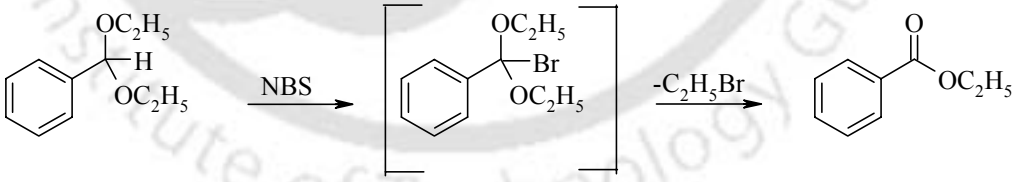
Scheme 1.13

By using Herrmann catalyst, (methyltrioxorhenium),[34a] Espenson[34b] group were able to transform aldehydes to esters using hydrogen peroxide as co-oxidant in the presence of co-catalyst such as chloride or bromide ions. But due to the requirement of co-catalysts and high cost of the catalyst, this method is not suitable for large-scale reactions.

IA.2.2 Oxidative Esterification of Acetals

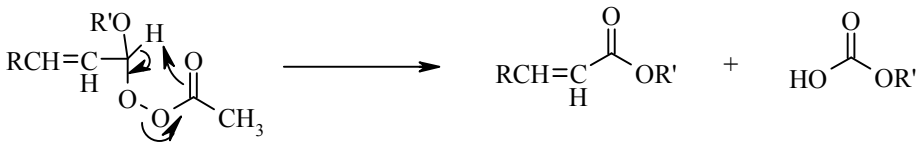
The acetal functionality is one of the most commonly used protecting group for aldehydes and the direct conversion of acyclic and cyclic acetals to the corresponding esters is a useful synthetic methodology in organic chemistry. Monoesters of ethylene glycol have been used as cross-linking agents for polyesters and fungicides.[35] They also find widespread applications as intermediates for sex pheromones of lepidoptera.[36] The major drawback for the preparation of monoesters of ethylene glycol is the simultaneous formation of diesters, necessitating a tedious separation procedure.[35] The following section described a detailed literature review on transformation of acetals to esters.

Marvell and Joncich have reported that benzaldehyde diethylacetal reacts with *N*-bromosuccinimide to give ethyl benzoate, Scheme 1.14.[37] Using the same principle Wright[38] was able to convert of α-ketoesters from dialkylacetals of α-ketoaldehydes.



Scheme 1.14

Heywood and Phillips[39] have described peracetic acid mediated oxidation of unsaturated acetals. This reaction is catalysed by sulphuric acid and proceeds through a hemiacetal peracetate intermediate as shown in Scheme 1.15.



Scheme 1.15

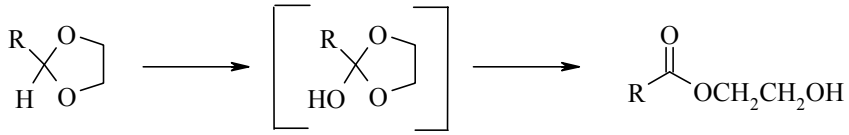
Huyser and Garcia[40] have reported a free radical oxidation of cyclic acetals mediated by di-*t*-butyl peroxide. Benzaldehyde 1,3-dioxolane was converted to ethyl benzoate by a peroxide induced reaction, Scheme 1.16.

Scheme 1.16

Hosokawa *et al.* have reported a range of Pd(II) catalysed oxidative ring cleavage of cyclic acetals with ^{t}BuOOH.[41] The homogeneous catalyst Pd(OCOCF$_3$)(OO^{t}Bu) in combination with anhydrous ^{t}BuOOH in dry benzene affords glycol monoesters in good yields.

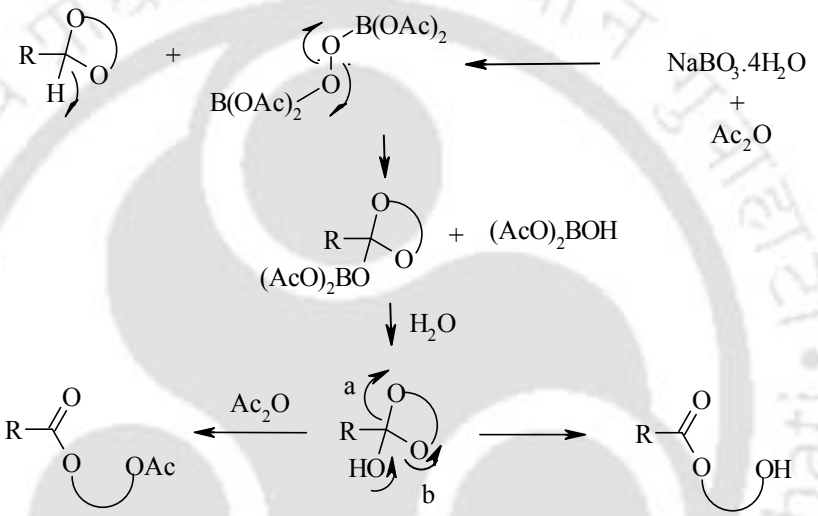
Oxygen[42] and ozone[42,43] are reported to be excellent reagents for the direct conversion of cyclic and acyclic acetals to the corresponding esters. Dinitrogen tetroxide (N_2O_5),[42] alkylhydroperoxide[42,44] and halogen-based reagents[45] are some of the reported methods for the direct conversion of acetals to esters. Masui and co-workers[46] have reported an electrochemical method for the oxidation of acetals to esters.

Chandrasekaran group[47] have utilised the oxidising agent pyridinium dichromate (PDC) and ^{t}BuOOH in the molar ratio (1:1.5) in dichloromethane for the conversion of acetals to esters. The hydroxy esters obtained from the oxidation of cyclic acetals are resistant to further oxidation. No selectivity was seen for the oxidation of the acyclic acetals. The reaction is believed to be a radical-assisted C-H bond cleavage of the acetal center, which gave hemi-orthoester, which on further cleavage yielded the desired product, Scheme 1.17.



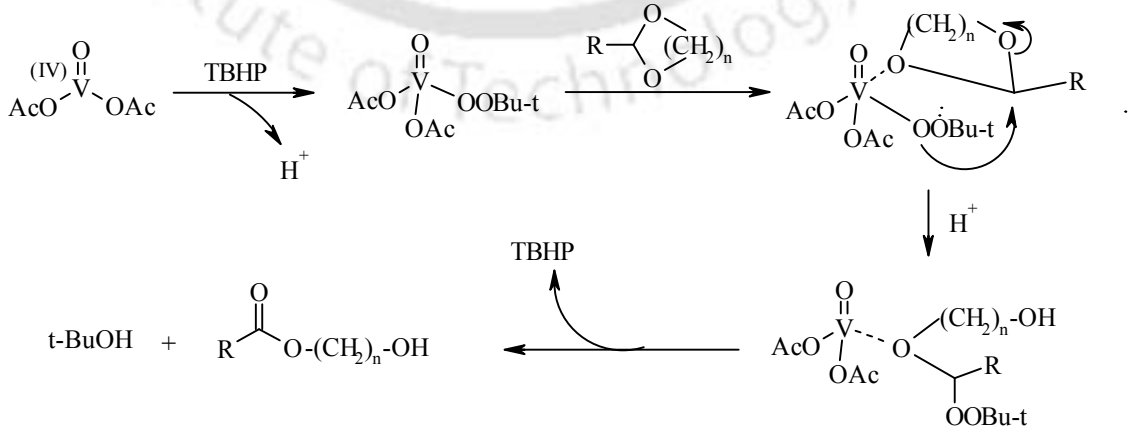
Scheme 1.17

In another report Chandrasekaran group have used inexpensive sodium perborate as oxidising agent in combination with acetic anhydride to achieve the conversion of cyclic acetals to esters.[48] This reaction was performed by adding sodium perborate, sodium carbonate, acetic anhydride and acetal in the molar ratio of 3:3:6:1, respectively, in dry benzene at 55°C. The authors have proposed the following reaction mechanism, Scheme 1.18.



Scheme 1.18

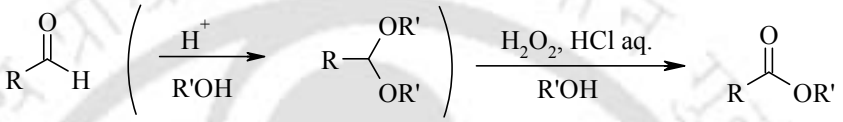
Choudary and Reddy[49] have used vanadyl acetate and *tert*-butyl hydroperoxide in dry benzene for the cleavage of cyclic acetals to glycol monoesters. The alkyl peroxovanadium



Scheme 1.19

complex $VO(OAc)_2(OO^tBu)$ generated in the medium is supposed to be the active oxidising species, Scheme 1.19.

A one-step conversion of acetal and aldehyde to ester was achieved with hydrogen peroxide and hydrochloric acid in an alcoholic medium.[50] In case of cyclic acetals; esters corresponding to solvent alcohol were obtained *via* a transesterification mechanism, Scheme 1.20.



Scheme 1.20

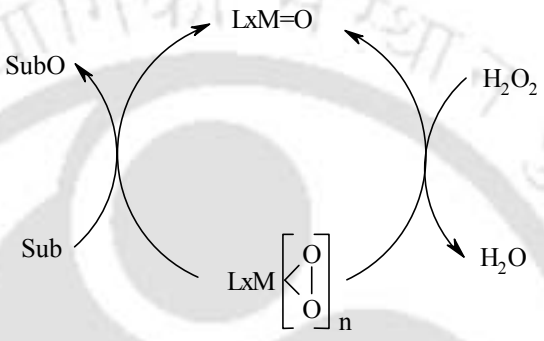
Recently, Curini and co-workers[51] have reported a methodology for the conversion of cyclic acetals to esters using Oxone® supported on wet alumina in chloroform.

The $MTO/H_2O_2/Br^-$ method of Espenson, when applied to 1,3-dioxolanes gave monoesters of ethylene glycol in excellent yields.[34b]

IA.3 Peroxometal Complexes in Organic Synthesis

Various transition metals have been applied for the synthesis of fine chemicals either catalytically or stoichiometrically. As a general rule in industry, catalytic routes are preferred over stoichiometric ones whenever it is possible. Oxidation reactions are extensively used in the synthesis of bulk and fine chemicals, including flame-retardants, disinfectants, antibacterial and antiviral drugs.[52] The majority of the processes employed industrially involve transition metal complexes in one or two electron reactions. In the past many stoichiometric oxidations were carried out with traditional oxidants like permanganate or dichromate producing vast amounts of inorganic effluents, which are difficult to dispose of. The search for alternative routes has generated a broad spectrum of catalytic oxidising agents. A number of oxidation reactions rely on the use of substrate-selective redox systems (often M^{n+2} / M^n) involving a two-electron oxidation. For a catalytic reaction it is necessary to reoxidise the reduced form of the redox system to its oxidised state. Attractive oxidants for this reoxidation are molecular oxygen, hydrogen peroxide and alkyl hydroperoxide.[53]

Unfortunately, hydrogen peroxide is a rather weak oxidant. Thus, in order to become stronger oxidant and synthetically significant, the oxidations by hydrogen peroxide need to be catalysed with metal ions.[54] Vanadium(V) oxide and the other metal oxides (Cr, Mo, Nb, Ta, Th, Ti, U, W, Zr) catalyse the reactions of hydrogen peroxide *via* the formation of inorganic peroxy acids *i.e.,* peroxometal complexes,[55] Scheme 1.21.

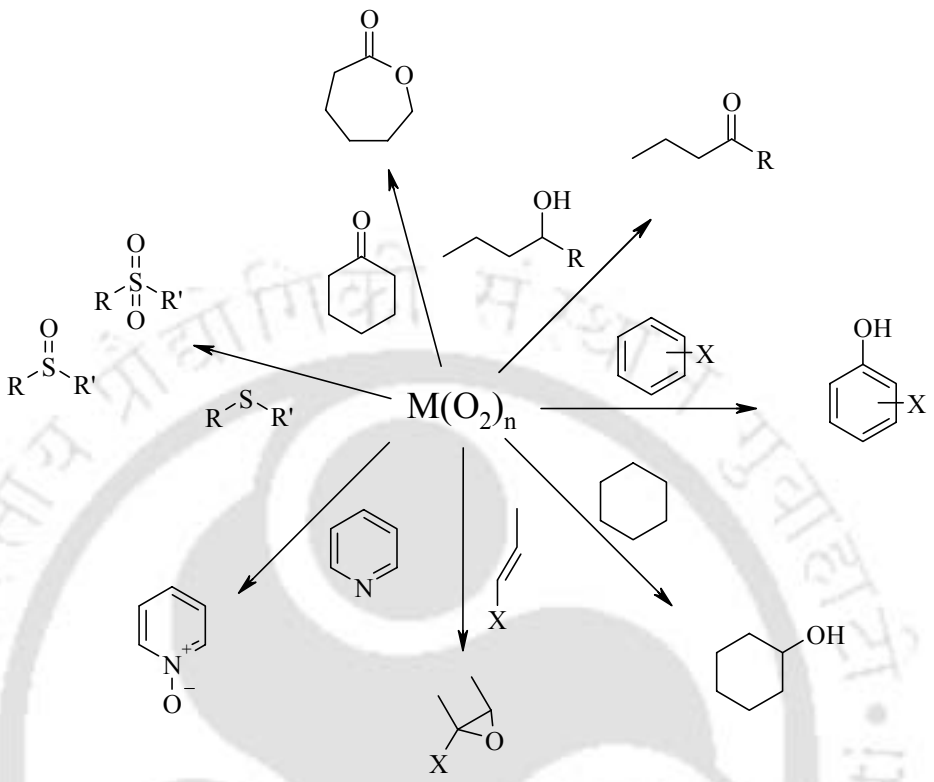


(15)

Scheme 1.21

These peracids **15** are hydroxy hydroperoxides, which result from the addition of hydrogen peroxide to an M═O group. The conjugate base of the peracid **15** is an excellent leaving group for nucleophilic displacement. Although inorganic peracids **15** closely resemble with organic peroxy acids, their peroxidic oxygen atoms are more electrophilic owing to the presence of the oxometal group (M═O). These are also much more efficient oxidants than hydrogen peroxide and in many cases its reactivity is many order of magnitude larger than that of the hydrogen peroxide so that the catalysed reactions are of remarkable synthetic significance.[53b,54,56] Its reduced form adds hydrogen peroxide again, thus accounting for the catalysis.[52a]

An interesting feature of these oxidants is their versatility, as demonstrated by the fact they are able to epoxidised substrates such as alkenes, and allylic alcohols;[57] sulfides can be oxidised to sulfoxides and sulfones;[58] benzene and other arenes and alkanes can be hydroxylated;[57f, 57g, 59] primary and secondary alcohols can be oxidised to aldehydes and ketones.[60] Ketones, phosphorous and nitrogen derivatives and even aromatic and aliphatic hydrocarbons[52b,e] can be oxidised as shown in Scheme 1.22.



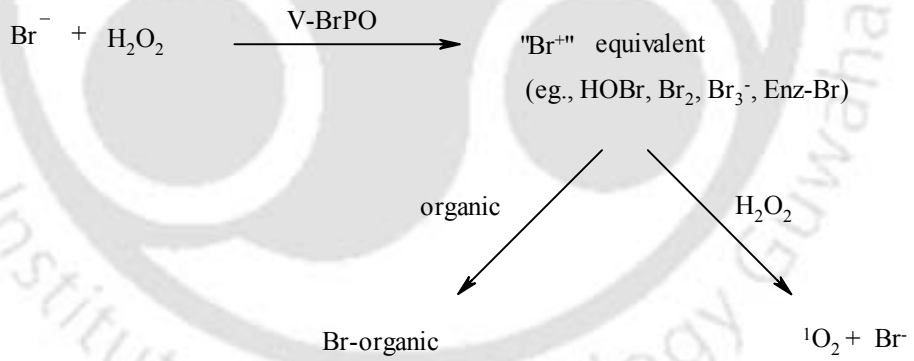
Scheme 1.22

IA.3.1 Peroxovanadium Complexes in Organic Synthesis

The propensity of vanadium(V) to coordinate peroxides is well known, as shown by the classic red spot test for vanadate, which is due to the formation of the red oxoperoxo vanadium(V) ion.[61] Depending on the p*H* of the medium vanadium(V) reacts with H_2O_2 to form mono (red), di (yellow), tri-(blue) and tetra-peroxovanadate (violet).[52] The redox potential of vanadium(V)-vanadium(IV) couple increases with acidity in the region from p*H* 1.5 to 2M acid.[62] Compounds of pentavalent vanadium are generally considered as two electron oxidants, it can function as a one electron oxidant in cases where no two electron pathway is accessible.[60] The reactive species in the aqueous solution is the VO_2^+ cation, which is stable in acidic medium and unstable in neutral medium.[62] In acidic solution ($[H^+]$ > 0.01 M), vanadium(V) exists as VO_2^+. Addition of hydrogen peroxide to VO_2^+ can give red monoperoxo- $VO(O_2)^+$ and yellow diperoxo- $VO(O_2)_2^-$ species.

In all these peroxo species a relatively weak O-O bond is present. During the oxidative process this bond is cleaved.[53b,63] Two main modes of cleavage has been envisaged. If the bond is cleaved heterolytically, polar oxidations take place, whereas if the cleavage is homolytic, radical oxidations are observed. The reactivity depends on the nature of the metal and especially on the nature of the ligand coordinated to the metal. Oxidation reactions by different vanadium compounds have been thoroughly reviewed by Freeman.[52b] In yet another review Butler group[52e] have discussed the structural reactivity of different vanadium complexes. Chaudhuri group have reported the synthesis of several interesting peroxovanadium complexes.[64]

Peroxometal chemistry has received much attention because of the inherent biological interest,[65] and catalytic activity.[57,65,66] With the discovery of vanadium bromoperoxidases, a vanadium(V) containing enzyme which is isolated primarily from marine algae and catalyses the oxidation of halides (Br^-, Cl^-, I^-) by hydrogen peroxide,[52e,65d–e,67] (Scheme 1.23), the reactivity of vanadium(V) peroxo complexes is receiving renewed attention.



Scheme 1.23

Several groups have attempted to mimic the activity of the vanadium bromo peroxidase reactions. Di Furia *et al.* have reported bromination of organic substrates using H_2O_2 and catalytic amount of NH_4VO_3, together with KBr in two phase (H_2O / $CHCl_3$) system.[68] Pandey group[69] have reported bromination of varieties of organic substrates in moderate to good yields using dilute hydrogen peroxide as an oxidising agent in the presence of bromide ions catalysed by ammonium metavanadate. They have observed ortho selectivity with electron-rich aromatics. Recently, Clark group[70] have studied the various

eco-efficient oxyhalogenation processes by examining various V and Mo salts as potential oxybromination catalysts.

A new vanadium complex, $VO(hoz)_2$ and $VO(hoz)_2Cl$ (hoz=2-(2'-hydroxyphenyl)-2-oxazoline), catalyse the epoxidation of allylic alcohol with *tert*-butyl hydroperoxide.[71] The later catalyst with the oxidation state (V) exhibits superior activity in comparison to the former. Pradilla and co-workers have reported the oxidation of several α-hydroxyalkyl α,β-unsaturated sulfoxides at sulfur followed by a highly regio- and stereoselective epoxidation at the electron deficient alkene by treatment with ^tBuOOH-$VO(acac)_2$.[72]

Skarzewski group have described enantioselective oxidation of sulfides using chiral vanadium catalyst.[73] Vanadium complex of chiral Schiff base with hydrogen peroxide oxidises bis-sulfides to the chiral mono- and bis-sulfoxides. Optically active bis-sulfoxides are formed in up to over 95% *ee*.

IA.4 Hydrogen Peroxide and its Alternatives

Hydrogen peroxide is one of the most versatile, dependable, and environmentally compatible oxidising agent. It is effective at treating both organic and inorganic pollutants, most notably the treatment of sulfur compounds found in wastewater for deodorisation, detoxification treatment of cyanide ions, oxidation of phenols and other organic pollutants. Hydrogen peroxide can be substituted for chlorine, hypochlorite, and potassium permanganate in many applications.

The use of hydrogen peroxide has many advantages: it is safe, cheap, the active oxygen content is high, it does not require a buffer, and it is clean, since the by-product formed is water. Hydrogen peroxide and the hydroxy peroxy anions are excellent nucleophilic in nature which can react with alkyl halides and other substrates having good leaving groups to furnish hydroperoxides. Hydrogen peroxide is a nucleophilic reagent capable of effecting substitution reactions and epoxidation of electron-deficient alkenes; a weak electrophile whose activity is enhanced in combination with transition metal oxides and a strong non-polluting oxidant, which can oxidise hydrogen halides.[74]

Aqueous hydrogen peroxide has been used widely in different oxidation reactions. It is used as a deacylating agent;[75] transformation of aromatic aldehydes to phenols (Dakin

reaction);[76] Baeyer-Villiger oxidation of ketones;[77] epoxidation of α,β-unsaturated ketones and acids;[78] synthesis of epoxides,[79] vicinal diols,[80] and ketones from alkenes; oxidation of alcohols and phenols,[81] organoboranes,[82] amines,[83] and sulfur containing compounds. [84]

Hydrogen peroxide is a photolabile and decomposed rapidly in the presence of trace amount of metal ion impurities, due to which it is stored in a dark colored plastic bottles. Concentrated hydrogen peroxide is not readily available and is, further more, very dangerous to handle. Since the exact strength of the hydrogen peroxide vary depending on the storage conditions, so, it is difficult to maintain the desired stoichiometry during a reaction. Further complications can arise from the transportation and storage of large quantities of hydrogen peroxide.

Sodium perborate (SPB) and sodium percarbonate (SPC) are peroxygen compounds and are convenient sources of alkaline hydrogen peroxide. These are available at a low price and extensively used in the detergent industry as bleaching and antiseptic agents.[85] SPB is a real persalt which has the formula, $NaBO_3.nH_2O$, n=1–4. Its crystal structure consists of a six-member heterocylic bisanion, Figure 1.2.[86]

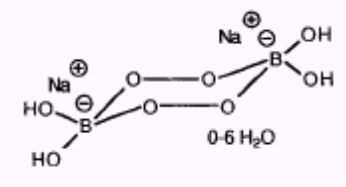


Figure 1.2

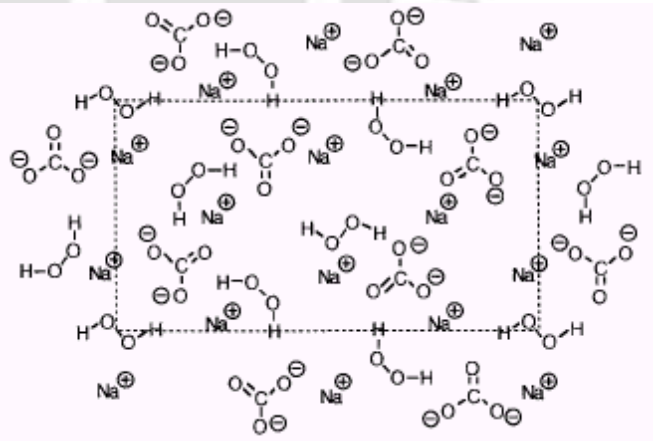


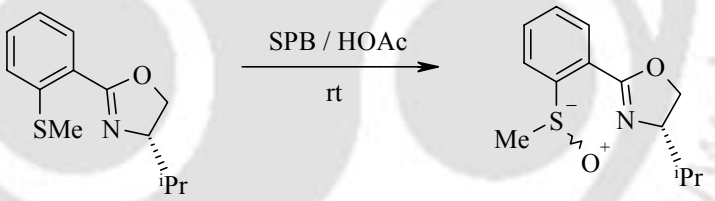
Figure 1.3

On the other hand, SPC is not a real peroxy salt, but a perhydrate, $Na_2CO_3.1.5H_2O_2$. The hydrogen peroxide is hydrogen bonded with carbonate ions as shown in Figure 1.3.[87] SPC is called as "sodium carbonate peroxyhydrate"[88] or "sodium carbonate perhydrate".[89] Both SPB and SPC are "solid form" or "portable form" of hydrogen peroxide.

In water, or in solvents with a significant aqueous component, both persalts functions as convenient sources of mild alkaline hydrogen peroxide.[90] SPB is a convenient source of such H_2O_2, the borate helps to buffer the medium that stabilise against decomposition, and activate towards nucleophilic oxidations, through associated species such as $[B(OH)_3(OOH)]^-$. SPC is slightly more alkaline, and solutions can contain minor amounts of a "true" percarbonate species, $[HOOC(O)O]^-$, which is electrophilic in nature.

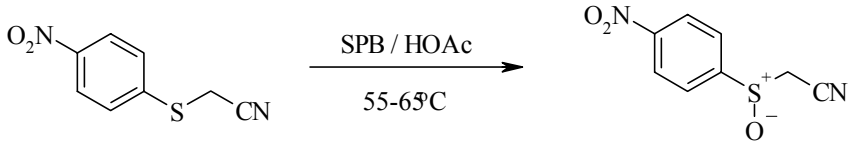
Consequently, the ability of SPB and SPC to release oxidative species in an organic medium has made them useful latent reagents in organic synthesis. Although the use of SPB was mention as an "excellent oxidising agent in organic chemical operations" in Chemical Abstracts as early as 1923, SPB and SPC have only recently emerged as interesting tools for the organic chemist, which now promise useful applications. The versatility of sodium perborate and sodium percarbonate has been reviewed by Muzard[91a] and McKillop *et al.* [91b–c]

Bower and co-workers[92] have reported chemoselective oxidation of sulfide to sulfoxide using SPB-acetic acid, Scheme 1.24.



Scheme 1.24

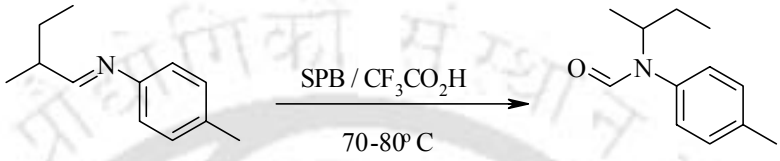
Yue and co-workers[88d] have reported oxidation of sulfides to sulfoxides and sulfalones in the presence of nitrile group by stepwise addition of SPB in acetic acid as shown in Scheme 1.25.



Scheme 1.25

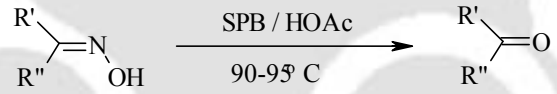
Amines, imines, N-heterocycles, oximes and hydrozones are oxidised by SPB and SPC. These oxidations are catalysed by metal ions such as hexacyanoferrate(III),[89b] Mo or

W(VI). Nongkunsarn and Ramsden have successfully used SPB in trifluoroacetic acid for oxidation of several C-aryl or -alkyl N-arylaldimines to N,N-disubstituted formamides, Scheme 1.26. The reaction is postulated to proceed through oxaziridine formation, followed by cleavage of the O-N bond.[93]



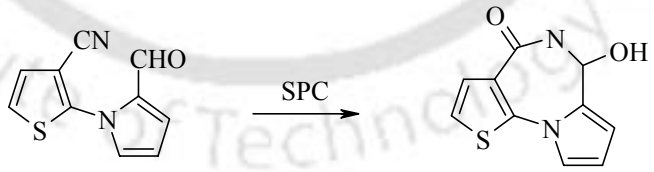
Scheme 1.26

Bandgar group have reported the conversion of oximes to carbonyl compounds.[94] Again, they have described the regeneration of aldehydes and ketones from their semicarbazones using SPB, Scheme 1.27.[95]



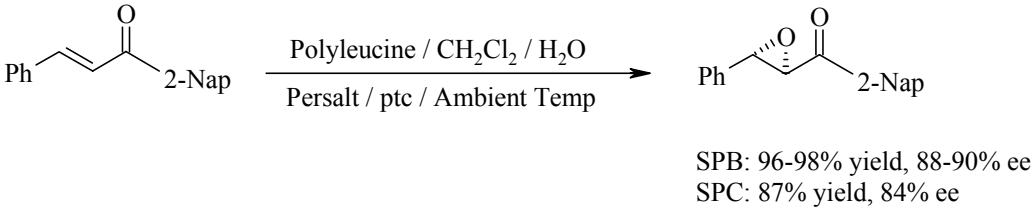
Scheme 1.27

Boulouard and co-workers[96] have used SPC during the synthesis of pyrrolothieno-[1,4]diazepines, Scheme 1.28.



Scheme 1.28

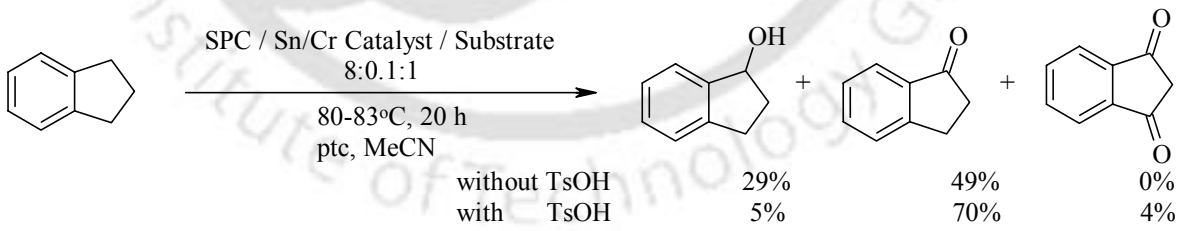
Roberts' group has explored the Julia asymmetric epoxidation reaction to enones other than chalcones. In the presence of polyleucine as catalyst, excellent yields and good enantiomeric excess (*ee*) values have been obtained for the following transformation, Scheme 1.29.[97]



Scheme 1.29

Kabalka and co-workers have published a method for dibromination of alkenes using a mixture of sodium bromide and SPB in acetic acid.[98] Ramsden *et al.* have described a method for the oxidative decarbonylation of β-aryl- and β-heteroaryl-pyruvic acids using SPB. In yet another report Kabalka's group has used SPC for oxidative cleavage of α-haloketones[99] and α-ketols or α-diketols[100] to carboxylic acids assisted by ultrasound.

It is well known that benzylic oxidations can be catalysed by cobalt acetate in the presence of bromide ion in acetic acid as solvent, using either air or hydrogen peroxide as the oxidant. Better selectivity to aldehyde can be obtained with the latter, and a further improvement has been demonstrated when SPB is used as the H_2O_2 source.[101] Muzard extended the method of alcohol oxidation for the benzylic system with SPC catalysed by chromium.[102] Indane gave indan-1-one as the main product along with 1-ol and 1,3-dione, Scheme 1.30.

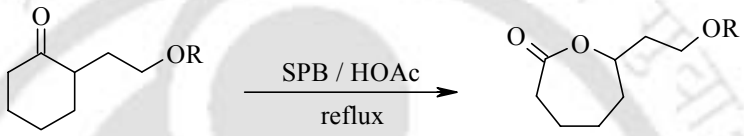


Scheme 1.30

Muzart group have used $MoO_2(acac)_2$ and phase transfer catalyst along with SPC in dichloromethane or acetonitrile for the oxidation of alcohols.[103] They have also studied the oxidation reaction using SPC with other metals such as Pd, Rh, and Ru.[104] Tao *et al.* have studied Baeyer-Villiger oxidation of ketones using persalts and acetic anhydride. SPC is said to perform well for cyclic ketones, with the yields of lactones being typically 80%, but

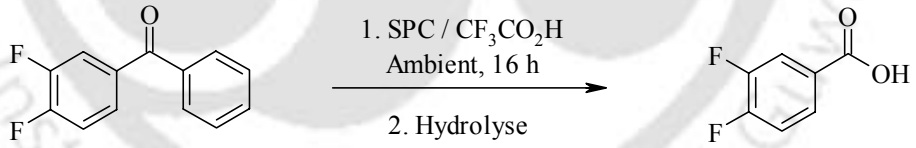
aromatic ketones only give good yields if the ring is activated. Reactions are accelerated by ultrasound.[105] SPB similarly gives good yields of lactones from cyclic ketones when used in acetic anhydride.[106]

A few patents have recently appeared on various Baeyer-Villiger oxidations, which include reference to use of SPB and/or SPC. BASF claim oxidation of 2-alkoxyethylcyclohexanone to the lactone of 8-alkoxy-6-hydroxyoctanoic acids with SPB-HOAc, for onward conversion to lipoic acids (Scheme 1.31). [107]



Scheme 1.31

Hoechst claim the production of halogenated benzoic acids by Baeyer-Villger oxidation of appropriately halogeneted benzophenones. For symmetrical benzophenones, the more electron-rich ring migrates, the electron deficient one retaining the carbonyl function, Scheme 1.32.[108]



Scheme 1.32

Selective monobromination of various deactivated anilines using KBr and sodium perborate has been reported.[109] The use of ammonium molybdate accelerating the rate of reaction.

What therefore emerge out of the above review is:

- To develop an efficient method for the oxidative transformation of aldehydes to esters using hydrogen peroxide as an oxidant and a catalytic quantity of relatively non toxic metal oxide such as V_2O_5. The other objective being direct preparation of monoesters of diols.

- Use of peroxy salts such as sodium percarbonate (SPC) and sodium perborate (SPB) as an alternative sources of hydrogen peroxide for the above transformation since they are dry carriers of hydrogen peroxide, readily available at low price and efficient release of hydrogen peroxide under mild conditions.
- Direct conversion of acetals to esters and deprotection of various acid-sensitive protecting groups such as THP, TBS ethers by utilising the intrinsic acidity originating from the dissolution of V_2O_5 with H_2O_2.

The results obtained from the above problems comprise Chapter I of the Ph.D dissertation.

IA.5 References

1. (a) Sato, K.; Aoki, M.; Noyori, R. *Science* **1998**, *281*, 1646. (b) Troste, B. M. *Science* **1991**, *254*, 1471. (c) Baker, R. T.; Tumas, W. *Science* **1999**, *284*, 1427.
2. Arlt, D.; Jautelat, M.; Lantzsch, R. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 703.
3. Smith, C. W.; Holm, R. T. *J. Org. Chem.* **1957**, *22*, 746.
4. Craig, J. C.; Horning, E. C. *J. Org. Chem.* **1960**, *25*, 2098.
5. Halcon International, Inc.; Netherlands Patent application, 1965, 6, 412, 904; *Chem. Abstr.* **1965**, *63*, 13085e.
6. Nishihara, A.; Kubota, I. *J. Org. Chem.* **1968**, *33*, 2525.
7. Corey, E. J.; Gilman, N. W.; Ganem, B. E. *J. Am. Chem. Soc.* **1968**, *90*, 5616.
8. Inch, T. D.; Ley, R. V.; Rich, P. *J. Chem. Soc. (C)* **1968**, 1693.
9. Eliel, E. L.; Clawson, L.; Knox, D. E. *J. Org. Chem.* **1985**, *50*, 2707.
10. Ogawa, T.; Matsui, M. *J. Am. Chem. Soc.* **1976**, *98*, 1629.
11. Sundaraman, P.; Walker, E. C.; Djerassi, C. *Tetrahedron Lett.* **1978**, *19*, 1627.
12. Pinnick, H. W.; Lajis, N. H. *J. Org. Chem.* **1978**, *43*, 371.
13. Cheung Y.-F. *Tetrahedron Lett.* **1979**, *20*, 3809.
14. Wilson, S. R.; Tofigh, S.; Misra, R. N. *J. Org. Chem.* **1982**, *47*, 1360.
15. Castells, J.; Pujol, F.; Llitjos, H.; Moreno-Manas, M. *Tetrahedron* **1982**, *38*, 337.
16. Stevens, R. V.; Chapman, K. T.; Weller, H. N. *J. Org. Chem.* **1980**, *45*, 2030.
17. Masuyama, Y.; Takahashi, M.; Kurusu, Y. *Tetrahedron Lett.* **1984**, *25*, 4417.

18. Shono, T.; Matsumura, Y.; Hayashi, J.; Inoue, K.; Iwasaki, F.; Itoh, T. *J. Org. Chem*. **1985**, *50*, 4967.
19. Nagashima, H.; Sato, K.; Tsuji, J. *Tetrahedron* **1985**, *41*, 5645.
20. Wuts, P. G. M.; Bergh, C. L. *Tetrahedron Lett.* **1986**, *27*, 3995.
21. Schlessinger, R. H.; Iwanowicz, E. J.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 3070.
22. Milborrow, B. V. *Annu. Rev. Plant Physiol.* **1974**, *25*, 259.
23. Constantino, M. G.; Donate, P. M.; Petragnani, N. *J. Org. Chem*. **1986**, *51*, 253.
24. Murahashi, S. -I.; Naota, T.; Ito, K.; Maeda, Y.; Taki, H. *J. Org. Chem.* **1987**, *52*, 4319.
25. O'Connor, B.; Just, G. *Tetrahedron Lett.* **1987**, *28*, 3235.
26. (a) Okimoto, M.; Chiba, T. *J. Org. Chem.* **1988**, *53*, 218. (b) Chiba, T.; Okimoto, M.; Nagai, H.; Takata, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 335.
27. McDonald, C.; Holcomb, H.; Kennedy, K.; Kirkpatrick, E.; Leathers, T.; Vanemon, P. *J. Org. Chem.* **1989**, *54*, 1213.
28. Williams, D. R.; Klingler, F. D.; Allen, E. E.; Lichtenthaler, F. W. *Tetrahedron Lett.* **1988**, *29*, 5087.
29. Neirabeyeh, M. Al.; Pujol, M. D. *Tetrahedron Lett.* **1990**, *31*, 2273.
30. Tam, S. -W.; Jimenez, L.; Diederich, F. *J. Am. Chem. Soc.* **1992**, *114*, 1503.
31. McDonald, C. E.; Nice, L. E.; Shaw, A. W.; Nestor, N. B. *Tetrahedron Lett.* **1993**, *34*, 2744.
32. Yamamoto, H.; Oritani, T. *Tetrahedron Lett*. **1995**, *36*, 5797.
33. Garegg, P. J.; Olsson, L.; Oscarson, S. *J. Org. Chem.* **1995**, *60*, 2200.
34. (a) Herrmann, W. A.; Fischer, R. W.; Marz, D. W. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1638. (b) Espenson, J. H.; Zhu, Z.; Zauche, T. M. *J. Org. Chem.* **1999**, *64*, 1191.
35. Babler, J. H.; Coghlan, M. J. *Tetrahedron Lett.* **1979**, 1971 and references therein.
36. (a) Leznoff, C. C. *Acc. Chem. Res.* **1978**, *11*, 327. (b) Henrick, C. A. *Tetrahedron* **1977**, *33*, 1845. (c) Rossi, R. *Synthesis* **1977**, *12*, 817.
37. Marvell, E. N.; Joncich, N. J. *J. Am. Chem. Soc.* **1951**, *73*, 973.

38. Wright, J. B. *J. Am. Chem. Soc.* **1955**, *77*, 4883.

39. Heywood, D. L.; Phillips, B. *J. Org. Chem.* **1960**, *25*, 1699.

40. Huyser, E. S.; Garcia, Z. *J. Org. Chem.* **1962**, *27*, 2716.

41. Hosokawa, T.; Imada, Y.; Murahashi, S. -I. *J. Chem. Soc., Chem. Commun.* **1983**, 1245.

42. Kuramshin, E. M.; Gumerova, V. K.; Dyachenko, V. A.; Kulak, L. G.; Molyavko, M. A.; Kochinashvili, M. V.; Mufteev, A. F.; Zlotskii, S. S.; Rakhmankulov, D. L. *Zh. Obshch. Khim.* **1988**, *58*, 1069.

43. (a) Kulak, L. G.; Kuramshin, E. M.; Zlotskii, S. S.; Rakhmankulov, D. L.; Paushkin, Ya. M. *Dokl. Akad. Nauk. SSSR.* **1987**, *293*, 369. (b) Deslongchamps, P.; Atlani, P.; Frehel, D.; Malaval, A.; Moreau, C. *Can. J. Chem.* **1974**, *52*, 3651. (c) Stork, G.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1987**, *109*, 1565.

44. (a) Rieche, A.; Bischoff, C. *Chem. Ber.* **1961**, *94*, 2722. (b) Rieche, A.; Schmitz, E.; Beyer, E. *Chem. Ber.* **1958**, *91*, 1935. *Chem. Ber.* **1958**, *91*, 1943. (c) Ramazanov, O. M.; Kalashnikov, S. M.; Skurko, M. R.; Pastushenko, E. V.; Karakhanov, R. A. *Izv. Akad. Nauk. SSSR Su Khim.* **1980**, 2635. (d) Kuhn, L. P.; Wellman, C. *J. Org. Chem.* **1957**, *22*, 774.

45. (a) Prugh, J. D.; McCarthy, W. C. *Tetrahedron Lett.* **1966**, 1351. (b) Pearson, R. G. *J. Chem. Soc.* **1960**, 1682.

46. Masui, M.; Kawaguchi, T.; Yoshida, S.; Ozaki, S. *Chem. Pharm. Bull.* **1986**, *34*, 1837.

47. Chidambaram, N.; Bhat, S.; Chandrasekaran, S. *J. Org. Chem.* **1992**, *57*, 5013.

48. Bhat, S.; Ramesha, A. R.; Chandrasekaran, S. *Synlett* **1995**, 329.

49. Choudary, B. M.; Reddy, P. N. *Synlett* **1995**, 959.

50. Takeda, T.; Watanabe, H.; Kitahara, T. *Synlett* **1997**, 1149.

51. Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Synlett* **1999**, 777.

52. (a) Sheldon, R. A.; Kochi, J. K. *Metal Catalysed Oxidations of Organic Compounds,* Academic Press: New York, 1981. (b) Freeman, F. *Organic Synthesis by Oxidation with Metal Compounds*, Mijs W. J., De Jonge C. H. R. I., Ed.; Plenum Press: New York, 1986. (c) Meunier, B. *Angew. Chem., Int. Ed.*

Engl. **1992**, *92*, 1411. (d) Beller, M.; Bolm, C. Ed., *Transition Metals for Organic Synthesis*, Wiley-VCH: New York, 1998. (e) Butler, A.; Clague, M. J.; Meister, G. *Chem. Rev.* **1994**, *94*, 625.

53. (a) Simandi, L. I. *Catalytic Activation of Dioxygen by Metal Complexes*, Kluwer: Dordrecht, The Netherlands, 1992. (b) Strukul, G. *Catalytic Oxidations with Hydrogen Peroxide as Oxidant*, Kluwer: Dordrecht, The Netherlands, 1992.

54. Di Furia, F.; Modena, G. *Rev. Chem. Intermed.* **1985**, *6*, 51.

55. (a) Schirmann, J. P.; Delavarenne, S. T. "*Hydrogen Peroxide in Organic Chemistry*", Informations Chimie: Paris, 1979. (b) Connors, J. A.; Ebsworth, E. A. V. *Adv. Inorg. Chem. Radiochem.* **1964**, *6*, 279. (c) Conte, V.; Di Furia, F.; Moro, S. *J. Phy. Org. Chem.* **1996**, *9*, 329. (d) Sels, B.; Vos, D. D.; Buntinx, M.; Pierard, F.; Mesmaeker, K. -D.; Jacobs, P. *Nature* **1999**, *400*, 855. (e) Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G. *J. Org. Chem.* **1986**, *51*, 2661.

56. (a) Patai, S. Ed.; *The Chemistry of Peroxides,* Wiley: Chichester, 1983. (b) Ando, W. Ed.; *Organic Peroxides,* Wiley: Chichester, 1992. (c) Di Furia, F.; Modena, G. *Pure Appl. Chem.* **1982**, *54*, 1853.

57. (a) Talsi, E. P.; Chinakov, V. D.; Babenko, V. P.; Zamaraev, K. I. *React. Kinet. Catal. Lett.* **1991**, *44*, 257. (b) Talsi, E. P.; Chinakov, V. D.; Babenko, V. P.; Zamaraev, K. I. *J. Mol. Catal.* **1993**, *81*, 235. (c) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. (d) Michaelson, R. C.; Palermo, R. E.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 1990. (e) Sharpless, K. B.; Verhoeven, T. R. *Aldrich Chemica Acta* **1979**, *12*, 63. (f) Mimoun, H.; Saussine, L.; Daire, E.; Postel, M.; Fischer, J.; Weiss, R. *J. Am. Chem. Soc.* **1983**, *105*, 3101. (g) Mimoun, H.; Chaumette, P.; Mignard, M.; Saussine, L.; Fischer, J.; Weiss, R. *Nouv. J. Chim.* **1983**, *7*, 467. (h) Mimoun, H.; Mignard, M.; Brechot, P.; Saussine, L. *J. Am. Chem. Soc.* **1986**, *108*, 3711. (i) Bortolini, O.; Di Furia, F.; Scrimin, P.; Modena, G. *J. Mol. Catal.* **1980**, *7*, 59.

58. (a) Nakajima, K.; Kojima, M.; Toriumi, K.; Saito, K.; Fujita, J. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 760. (b) Ballistreri, F. P.; Tomaselli, G. A.; Toscano, R. M.; Conte, V.; Di Furia, F. *J. Am. Chem. Soc.* **1991**, *113*, 6209. (c) Bortolini, O.; Di Furia,

F.; Modena, G. *J. Mol. Catal.* **1982**, *16*, 61. (d) Bonchio, M.; Conte, V.; Di Furia, F.; Modena, G.; Padovani, C.; Sivak, M. *Res. Chem. Intermed.* **1989**, *12*, 111.

59. (a) Shul'pin, G. B.; Attanasio, D.; Suber, L. *J. Catal.* **1993**, *142*, 147. (b) Attanasio, D.; Suber, L.; Shul'pin, G. B. *Bull. Russ. Acad. Sci., Div. Chem. Sci.* **1992**, *41*, 1502. (c) Bonchio, M.; Conte, V.; Di Furia, F.; Modena, G. *J. Org. Chem.* **1989**, *54*, 4368. (d) Bianchi, M.; Bonchio, M.; Conte, V.; Coppa, V.; Di Furia, F.; Modena, G.; Moro, S.; Standen, S. *J. Mol. Catal.* **1993**, *83*, 107.

60. (a) Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G. *Nouv. J. Chim.* **1985**, *9*, 147. (b) Conte, V.; Di Furia, F.; Modena, G. *J. Org. Chem.* **1988**, *53*, 1665.

61. Jeffery, G. H.; Bassett, J.; Mendham, J.; Denney, R. C. *Vogel's Textbook of Quantitative Chemical Analysis*, John Wiley & Sons: New York, 1989.

62. (a) Rosotti, F. J. C.; Rossetti, H. *Acta Chem. Scand.* **1956**, *10*, 957. (b) Ingri, N.; Brito, F. *Acta Chem. Scand.* **1959**, *13*, 1971. (c) Schwarzenbach, G.; Geier, G. *Helv. Chim. Acta.* **1963**, *46*, 906. (d) Mehrota, R. N. *J. Chem. Soc. B.* **1968**, 642. (e) Mishra, H. C.; Symons, M. C. R. *J. Chem. Soc.* **1962**, 4411. (f) LaSalle, M. J.; Cobble, J. W. *J. Phys. Chem.* **1955**, *59*, 519. (g) Latimer, W. M. *Oxidation Potentials,* 2nd ed., Prentice Hall: Englewood Cliffs, New Jersey, 1952. (h) Clark, R. J. H. in *Comprehensive Organometallic Chemistry,* Wilkinson, G. Ed., Pergamon Press: New York, 1981, Vol. 3, p. 491.

63. Curci, R.; Edwards, J. O. *Organic Peroxides,* Swern, D. Ed.; Wiley-Intescience: New York, 1970, Chapt. 4.

64. (a) Bhattacharjee, M.; Chaudhuri, M. K.; Paul, P. C. *Can. J. Chem.* **1992**, *70*, 2245. (b) Chaudhuri, M. K.; Ghosh, S. K. *Inorg. Chem.* **1982**, *21*, 4020. (c) Chaudhuri, M. K.; Ghosh, S. K. *Polyhedron* **1982**, *1*, 553. (d) Bhattacharjee, M. N.; Chaudhuri, M. K.; Islam, N. S. *Inorg. Chem.* **1989**, *28*, 2420. (e) Chaudhuri, M. K.; Islam, N. S. *Transition Met. Chem.* **1985**, *10*, 333.

65. (a) Ramasarma, T.; Crane, F. L. *Curr. Top. Cell. Regln.* **1981**, *20*, 247. (b) Schechter, Y.; Shisheva, A. *Endeavour New Ser.* **1993**, *17*, 27. (c) Amin, S. S.; Cryer, K.; Hang, B.; Dutta, S. K.; Eaton, S. S.; Anderson, O. P.; Miller, S. M.; Reul, B. A.; Brichard, S. M.; Crans, D. C. *Inorg. Chem.* **2000**, *39*, 406. (d) Vilter,

H. *Phytochemistry* **1983**, *23*, 1387. (e) Martinez, J. S.; Carroll, G. L.; Tschirret-Guth, R. A.; Altenhoff, G.; Little, R. D.; Butler, A. *J. Am. Chem. Soc.* **2001**, *123*, 3289.

66. (a) deBoer, E.; Tromp, M. G. M.; Plat, H.; Krenn, B. E.; Waver, R. *Biochem. Biophys. Acta.* **1986**, *104*, 872. (b) Hales, B. J.; Morningstar, J. E.; Case, E. E. *Red. Trav. Chim. Paxs-Bas.* **1987**, *106*, 872. (c) Richards, R. L. *Chem. Ber.* **1988**, *24*, 133. (d) Brand, S. G.; Hawkins, C. J.; Parry, D. L. *Inorg. Chem.* **1987**, *26*, 629. (e) Kustin, K.; McLeod, C. G.; Gilbert, T. R.; Briggs, Le B. R. *Struct. Bonding (Berlin)* **1983**, *53*, 139. (f) Chasteen, N. D. *Struct. Bonding (Berlin)* **1983**, *53*, 105. (g) Ravishankar, H. N.; Chaudhuri, M. K.; Ramasarma, T. *Inorg. Chem.* **1994**, *33*, 3788.

67. Butler, A.; Walker, J. V. *Chem. Rev.* **1993**, *93*, 1937.

68. Conte, V.; Di Furia, F.; Moro, S. *Tetrahedron Lett.* **1994**, *35*, 7429.

69. Dinesh, C. U.; Kumar, R.; Pandey, B.; Kumar, P. *J. Chem. Soc., Chem. Commun.* **1995**, 611.

70. Rothenberg, G.; Clark, J. H. *Green Chemistry* **2000**, *2*, 248.

71. Hwang, J. H.; Abu-Omar, M. M. *Tetrahedron Lett.* **1999**, *40*, 8313.

72. Paradilla, R. F. de la.; Mendez, P.; Priego, J.; Viso, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1247.

73. Skarzewski, J.; Ostrycharz, E.; Siedlecka, R. *Tetrahedron: Asymmetry* **1999**, *10*, 3457.

74. Paquette, L. A. *Encyclopedia of Reagents for Organic Synthesis*, John Wiley & Sons: Chichester, 1995, Vol. 4, p. 2731.

75. (a) Gage, J. R.; Evans, D. A. *Org. Synth.* **1990**, *68*, 83. (b) Evans, D. A.; Britton, T. C.; Ellman, J. A. *Tetrahedron Lett.* **1987**, *28*, 6141.

76. Matsumoto, M.; Kobayashi, H.; Hotta, Y. *J. Org. Chem.* **1984**, *49*, 4740.

77. Crimmins, M. T.; Jung, D. K.; Gray, J. L. *J. Am. Chem. Soc.* **1993**, *115*, 3146.

78. Corey, E. J.; Ensley, H. E. *J. Org. Chem.* **1973**, *38*, 3187.

79. Venturello, C.; D'Aloisio, R. *J. Org. Chem.* **1988**, *53*, 1553.

80. Warwel, S.; Rusch gen; Klaas, M.; Sojka, M. *J. Chem. Soc., Chem. Commun.* **1991**, 1578.

81. (a) Barak, G.; Dakka, J.; Sasson, Y. *J. Org. Chem.* **1998**, *53*, 3553. (b) Sakata, Y.; Ishii, Y. *J. Org. Chem.* **1991**, *56*, 6233.

82. Brown, H. C.; Mandal, A. K. *J. Org. Chem.* **1980**, *45*, 916.

83. Murahashi, S. I.; Oda, T.; Masui, Y. *J. Am. Chem. Soc.* **1989**, *111*, 5002.

84. Sedergran, T. C.; Dittmer, D. C. *Org. Synth.* **1984**, *62*, 210.

85. (a) Rémond, J. *Rev. Prod. Chim.* **1954**, *57*, 401. (b) Kirk-Othmer *Encyclopedia of Chemical Technology*, 3rd Ed.; Wiley: New York, 1978, Vol. 3, p. 944. (c) *Chem. Eng. News* 1980, *58* (July 21), 39. (d) Das, T. K.; Mandavawalla, A. K.; Datta, S. K. *Colourage* **1983**, *30*, 15. (e) Kuzel, P.; Lieser, T.; Dankowski, M. *Chim. Oggi.* **1986**, October, 60.

86. Hansson, A. *Acta Chem. Scand*. **1961**, *15*, 934.

87. (a) Adams, J. M.; Pritchard, R. G. *Acta Crystallogr. Sect. B.* **1977**, *33*, 3650. (b) Carrondo, M. A. A. F. de C. T.; Griffith, W. P.; Jones, D. P.; Skapski, A. C. *J. Chem. Soc., Dalton Trans.* **1977**, 2323.

88. (a) Comyns, A. E. *Peroxides and Peroxide Compounds-Inorganic,* in Kirk-Othmer *Encyclopedia of Chemical Technology,* 4th ed., John Wiley & Sons: London, 1996, Vol. 18, p. 202. (b) Bower, J. F.; Martin, C. J.; Rawson, D. J.; Slawin, A. M. Z.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 333. (c) Shimaziki, M.; Takahashi, M.; Komatsu, H.; Ohta, A.; Kajii, K.; Kodama, Y. *Synthesis* **1992**, 555. (d) Yue, G.; Wang, J.; Zhang, Z. *Yingynong Huaxue* **1995**, *12*, 93. (e) Quast, H.; Witzel, M.; Peters, E. -M.; Peters, K.; von Scherning, H. G. *Liebigs Ann. Chem.* **1995**, 725. (f) Kabilan, S.; Krishnasamy, K.; Sankar, P. *Oxid. Commun.* **1994**, *17*, 264. (g) Kabilan, S.; Pandiarajan, K.; Krishnasamy, K.; Sankar, P. *Int. J. Chem. Kinet.* **1995**, *27*, 443. (h) Karunakaran, C.; Gnanasekaran, K.; Alamelu, R. *Afinidad* **1995**, *52*, 245.

89. (a) Liu, Y.; Yang, Q.; Cheng, W. *Jingxi Huagong* **1996**, *13*, 27. (b) Karunakaran, C.; Palinasamy, P. N. *Pol. J. Chem.* **1996**, *70*, 1077.

90. Galwey, A. K.; Hood, W. J. *J. Chem. Soc., Faraday Trans. 1* **1982**, *78*, 2815.

91. (a) Muzart, J. *Synthesis* **1995**, 1325. (b) McKillop, A.; Sanderson, W. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 471. (c) McKillop, A.; Sanderson, W. R. *Tetrahedron* **1995**, *51*, 6145.
92. Bower, J. F.; Martin, C. J.; Rawson, D. J.; Slawin, A. M. Z.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, 555.
93. Nongkunsarn, P.; Ramsden, C. A. *Tetrahedron* **1997**, *53*, 3805.
94. Bandgar, B. P.; Shaikh, S. I.; Suresh, I. *Synth. Commun.* **1996**, *26*, 1163.
95. Bandgar, B. P.; Zirange, S. M. *Indian J. Chem., Sect. A: Inorg. Phys. Theor. Anal.* **1997**, *36*, 695.
96. Boulouard, M.; Rault, S.; Dallemagne, P.; Alsaidi, A.; Robba, M. *J. Heterocycl. Chem.* **1996**, *33*, 87.
97. Lasterra-Sanchez, M. E.; Felfer, U.; Mayon, P.; Roberts, S. M.; Thornton, S. R.; Todd, C. J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 343.
98. Kabalka, G. W.; Yand, K.; Reddy, N. K.; Narayana, C. *Synth. Commun.* **1998**, *28*, 925.
99. Yang, D. T. C.; Cao, Y. H.; Kabalka, G. W. *Synth. Commun.* **1995**, *25*, 3695.
100. Yang, D. T. C.; Cao, Y. H., Evans, T. T.; Kabalka, G. W. *Synth. Commun.* **1996**, *26*, 4275.
101. Jones, C. W.; Hackett, A.; Pattinson, I.; Johnstone, A.; Wilson, S. L. *J. Chem. Res. (S)* **1996**, 438; *J. Chem. Res. (M)* **1996**, 2501.
102. Muzart, J.; Ait-Mohand, S. *Tetrahedron Lett.* **1995**, *36*, 5735.
103. Maignien, S.; Ait-Mohand, S.; Muzart, S. *Synlett* **1996**, 439.
104. Ait-Mohand, S.; Lunak, S.; Muzart, J. *Chem. Ber./Recl.* **1997**, *130*, 1655.
105. Zhang, Y.; Hu, H.; Fang.;Y.; Ai, H.; Tao, F. *Youji Huaxe* **1996**, *16*, 64.
106. Yu, J.; Zhang, Y.; Ai, H.; Fang, Y.; Xie, G.; Tao, F.; Chen, M. *Huaxue Tongbao* **1995**, 35.
107. German Patent (DE) No 4229914, BASF 1994.
108. European Patent No 600317, Hoechst 1992.
109. Roche, D.; Prasad, K.; Repic, O.; Blacklock, T. J. *Tetrahedron Lett.* **2000**, *41*, 2083.

IB Present Work

IB.1 Catalytic Oxidative Esterification of Aldehydes Using V_2O_5-H_2O_2

Oxidative transformation of aldehydes to esters under mild conditions is often a requisite in organic synthesis and hence much effort has been devoted to find new methods and/or new reagents effective for this type of oxidative transformation.[1,2] Larock[1a] has compiled a comprehensive list of reagents for the one-step conversion of an aldehyde in the presence of an alcohol into ester, which includes: O_2; cat.HCl under photochemical conditions; O_3-KOH, ^{t}BuOOH-cat.($PhCH_2NMe_3$)$OMoBr_4$; $PhNO_2$-KCN-phase transfer catalyst; $NaHSO_3$-Ac_2O-DMSO; H_2SO_5; $(NH_4)_2S_2O_8$-H_2SO_4; HOCl; NaOCl-AcOH; $Ca(OCl)_2$-HOAc-CH_3CN-molecular sieves; ^{t}BuOCl-Et_3N or pyridine; Br_2-$NaHCO_3$; Br_2-HMPT-$NaHCO_3$; NBS-under photochemical conditions; NBS-R'$OSiMe_3$; NBS-R'OSn(*n*-Bu)$_3$; I_2-KOH; NIS-K_2CO_3; PDC-DMF; MnO_2-NaCN or KCN; Me_3SiCl-cat.ZnI_2-MnO_2-H^+; cat.$Ru_3(CO)_{12}$; cat.$H_2Ru(PPh_3)_4$; electrochemical oxidation mediated by KI, NaCN and biscoenzymes. Recently, such a transformation has been achieved with the peroxo species generated by the reaction of methyltrioxorhenium(VII) (MTO) with hydrogen peroxide in presence of co-catalysts such as chloride or bromide ions.[3]

Although several methods have been reported for the direct conversion of aldehydes to esters, unfortunately, many of these procedures often required a large amount of reagents, extremes of temperature, longer reaction times, inert atmosphere, photochemical conditions, poisonous and polluting reagents, mediators or co-catalysts, hydrogen acceptors, etc. Some of these reagents are also unsatisfactory for the specific oxidation of aldehydes containing activated, deactivated, hindered and double-bond-containing substrates resulting in over-oxidation, undesirable products, proceeds non selectively and gives poor to mediocre yields. Among all these methods, catalyst methyltrioxorhenium(VII), with hydrogen peroxide as oxidant, and a co-catalyst such as bromide or chloride ions is an efficient combination for the transformation of aldehydes to esters,[3] but causes a considerable economic problem upon scale-up.

In today's context, one of the challenging issues for chemist is to pursue of green chemical transformations.[4] Because of the amount of toxic wastes and by-products arising from chemical processes, due to environmental protection law, it has compelled to develop cost effective and environmentally friendly catalytic routes that minimises the hazardous waste. We have therefore sought to develop a highly facile, cost effective and environmentally friendly catalytic route for esterification of aldehydes.

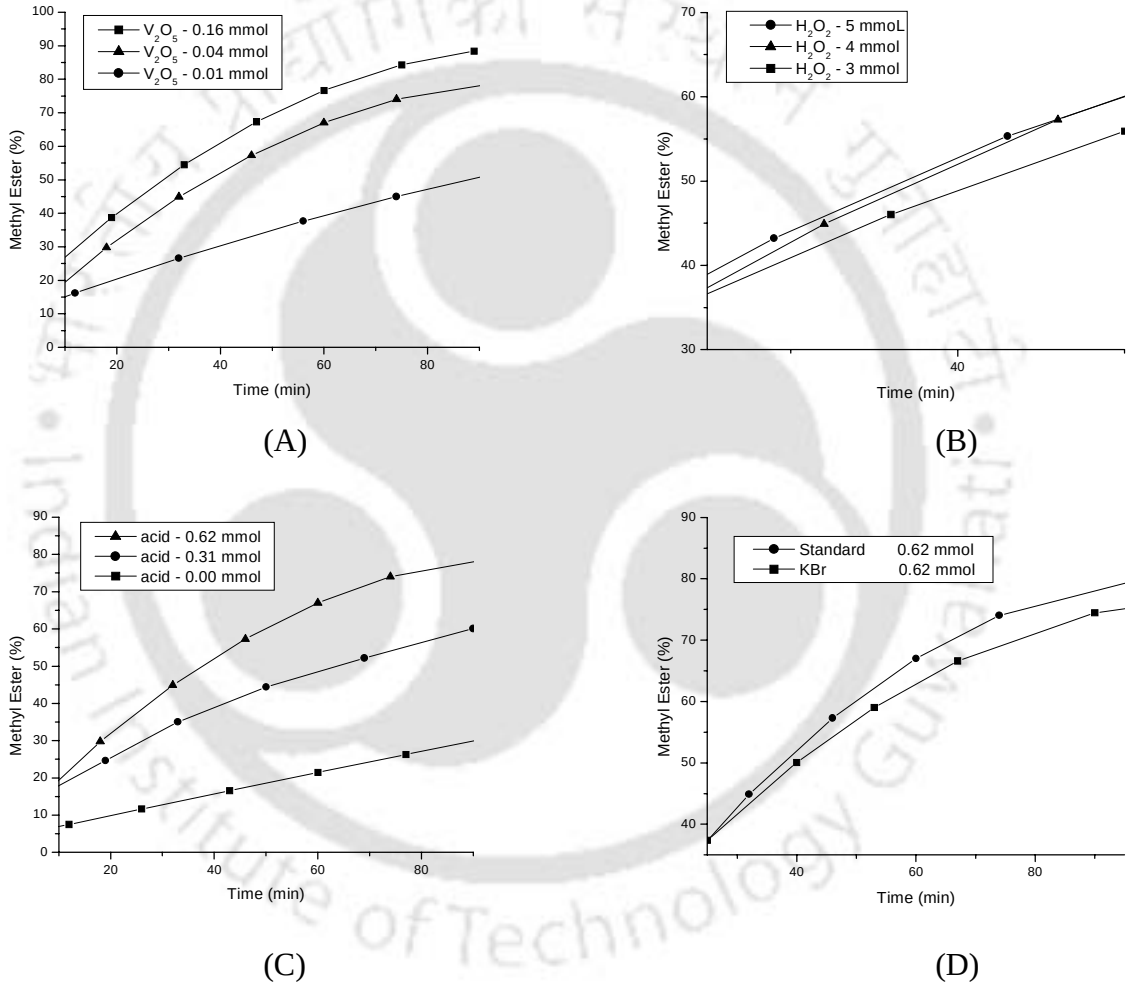
Recently, we have reported a method for the oxidative transformation of tetrabutylammonium bromide to the corresponding tribromide (Br_3^-) using V_2O_5 as a catalyst and H_2O_2 as an oxidant.[5] Utilising the *in situ* generated active brominating agent (Br_3^-) we have successfully brominated a wide spectrum of organic substrates.[6] Based on the versatility of the combination of V_2O_5–H_2O_2 as oxidant we chose to examine its efficacy in the controlled oxidation of aldehydes to esters in presence of an alcohol.

As a test substrate for the oxidative transformation of aldehydes to esters, benzaldehyde **1** was chosen to optimise the reaction conditions. Addition sequences of different components [catalyst (V_2O_5), oxidant (H_2O_2), methanol, aldehyde, acid] and their ratios were varied in order to achieve higher product conversion. Mineral acid such as $HClO_4$ was found to be better compare to acetic acid. Other mineral acids such as H_2SO_4, HCl, and HBr also worked equally well.

Effect of catalyst on the reaction rate was studied using different quantities of catalyst keeping the fixed concentrations of hydrogen peroxide (4 mmol), perchloric acid (0.6 mmol), aldehyde (1 mmol) and methanol (5 mL). As expected, reaction rates were accelerated with the increasing in quantities of the catalyst, which is shown in the following Graph 1.1 (A). However, an optimum of the catalyst (0.04 mmol) was used during the investigation. Catalytic turnover number, which is defined as the number of moles of substrate completely converted into product per mole of the catalyst was found to be >500.

While optimising the reaction, 4 mmol of the oxidant (H_2O_2) per mmole of the aldehyde was used. To see the effect of oxidant on the reaction rate, different concentrations of hydrogen peroxide such as 3, 4, and 5 mmol were used per mmole of the aldehyde keeping all other parameters constant, Graph 1.1 (B). No significant rate enhancement was observed using higher quantities of the oxidant.

As mentioned (Scheme 1.33), the reaction proceeds even without extraneous addition of the acid, but the reaction times are longer. Keeping all other parameters fixed, acid concentration was varied, and the reaction rate was found to increase with the increase in concentration of the acid, Graph 1.1 (C).



Graph 1.1. Effect of Catalyst (A), H_2O_2 (B), Mineral Acid (C), Co-catalyst (D) on the Reaction Rate

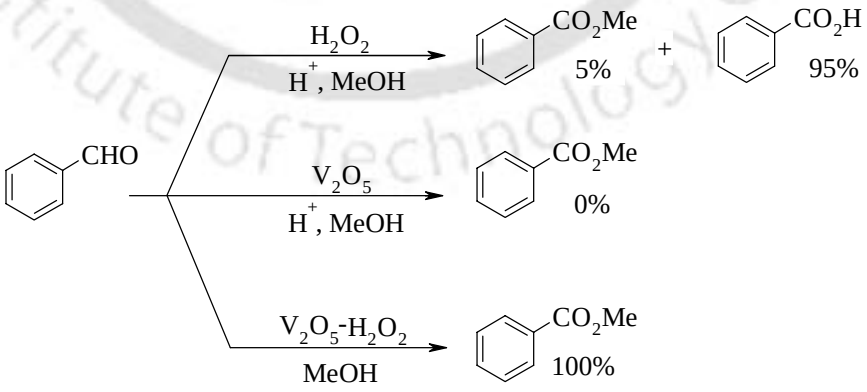
The increase in the reaction rate is because in acidic solution ($[H^+] > 0.01M$) vanadium(V) exists as VO_2^+, which is involved in the reaction. Addition of hydrogen peroxide to VO_2^+ can give the red monoperoxo- $VO(O_2)^+$ species and yellow diperoxo- $VO(O_2)_2^-$ species. These species are stable under acidic medium and unstable in neutral and

basic medium.[7] Acidic medium also prolongs the lifetime of the peroxo species of $MeReO_3$ against irreversible decomposition.[3]

Oxidation of aldehyde to ester using catalyst methyltrioxorhenium and hydrogen peroxide is negligible. However, addition of a catalytic quantity of bromide or chloride ion greatly enhances the rate. Since there is a great structural similarity between the rhenium and vanadium peroxo compounds, a similar rate enhancement is expected. Thus, when the reaction was performed in the presence of catalyst (V_2O_5) (0.04 mmol), hydrogen peroxide (4 mmol) and in absence of $HClO_4$, but in the presence of co-catalyst such as KBr the reaction rate was accelerated marginally. But in the presence of acid and absence of co-catalyst the rate enhancement was significant, Graph 1.1 (D). Thus, for our investigation we preferred to use catalytic quantity of acid rather than co-catalyst (KBr), since some of the activated substrates may undergo bromination.[3]

Thus, in a typical reaction, to an ice cold solution of aldehyde (5 mmol) in methanol (5 mL) containing 70% $HClO_4$ (3 mmol) was slowly added a solution of V_2O_5 (0.2 mmol) dissolved in H_2O_2 (20 mmol) *ca.* 5°C. Reaction mixture was left stirred for a specified period of time as shown against each substrate in Table 1.1.

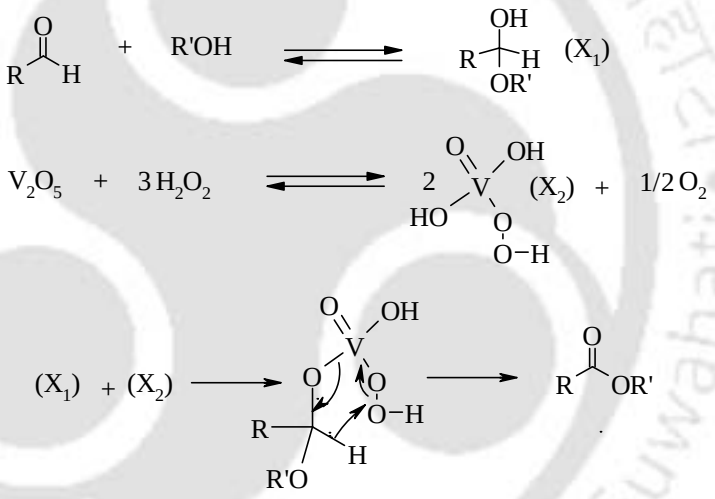
In this system, H_2O_2 does not bring about esterification without the catalyst (V_2O_5) and the catalyst alone fails to bring about esterification (Scheme 1.33). In presence of methanol and hydrogen peroxide, benzaldehyde gave poor yield of the ester (5%) and substa-



Scheme 1.33. A Control Reaction Showing the Role of Catalyst V_2O_5 and H_2O_2 on Oxidative Esterification

ntial amount of benzoic acid. The reactions can be carried out even in the absence of any external acid but reactions are rather sluggish.

Mechanistically, it seems plausible that the aldehyde was oxidised with V_2O_5–H_2O_2 to the corresponding acid, which was esterified immediately with alcohol. However, when benzoic acid was used instead of benzaldehyde **1** under identical conditions, no methyl benzoate **1a** could be obtained. It is most probable that the oxidation of aldehyde in an alcoholic medium proceeds through, a hemiacetal $\mathbf{X_1} \rightarrow$ vanadium hemiacetal intermediate $\mathbf{X_2} \rightarrow$ ester, as indicated in Scheme 1.34. UV spectral analysis confirmed the intermediacy of the peroxovanadium(V) species with the appearance of the peak at λ = 430 nm.



Scheme 1.34. Proposed Mechanism of Esterification

Aldehyde under acidic conditions reacts with alcohol to form hemiacetal $\mathbf{X_1}$. It is envisaged that the initially formed hemiacetal $\mathbf{X_1}$ reacts with peracid $\mathbf{X_2}$, which results from the addition of H_2O_2 to vanadium(V) oxide to from a vanadium hemiacetal type intermediate $\mathbf{X_2}$.[8] The conjugate base of the peracid $\mathbf{X_2}$ is an excellent leaving group for nucleophilic displacement.[8] Subsequent elimination produced the desired product and releases the catalyst. We believe that formation of the hemiacetal intermediate $\mathbf{X_1}$ is necessary. In the absence of alcohol, aldehydes are rapidly oxidised to their corresponding acids. The success of the reaction is dependent upon the selective oxidation of the hemiacetal hydroxy moiety $\mathbf{X_1}$ in the presence of much higher concentration of alcohol. Selective oxidation of more substituted

alcohol has been observed with other oxidising agents such as CrO_3[9] and NIS.[10] Primary alcohols are also selectively oxidised in presence of much higher concentration of methanol with oxidising agents such as calcium hypochlorite.[11]

Under similar experimental conditions activated, deactivated, conjugated and hindered aldehydes can all be oxidised to the corresponding methyl esters in excellent yields. Typically, V_2O_5–H_2O_2 catalysed reaction of benzaldehyde **1** with methanol, gave methyl benzoate **1a** in quantitative yield. Under similar experimental condition *m*-bromobenzaldehyde **2** and *p*-methylbenzaldehyde **3** produced the corresponding methyl esters, methyl *m*-bromobenzoate **2a** and methyl *p*-methylbenzoate **3a**, respectively, in very high yields in a short time. The reaction of aromatic aldehydes with the ortho substituted compounds such as *o*-hydroxybenzaldehyde **4** and *o*-methoxybenzaldehyde **5** to yield esters was more sluggish, as compared to the corresponding the para substituted substrates *p*-hydroxybenzaldehyde **6** and *p*-methoxybenzaldehyde **7**. This could be attributed to an unfavorable equilibrium to hemiacetal due to steric strain as proposed in Scheme 1.34.

Steric interaction could also be responsible for the slow reaction rate of tri-substituted aldehydes such as 4-hydroxy-3-methoxybenzaldehyde **8** and 3,4-dimethoxybenzaldehyde **9**. Aromatic aldehydes substituted with electron-withdrawing groups at the para position such as, *p*-chlorobenzaldehyde **10** and *p*-nitrobenzaldehyde **11** react slowly. Only 10% conversion to methyl *p*-nitrobenzoate **11a** was observed in 5 h for the deactivated substrate **11**, under the reaction conditions. However, refluxing the reaction in a water bath can accelerate the reaction rate as demonstrated in the case of *p*-nitrobenzaldehyde **11**. Importantly, no other side products are obtained during reflux. Substrate *p*-benzyloxybenzaldehyde **12** reacts slowly to give methyl *p*-benzyloxybenzoate **12a** in quantitative yield.

Principles of oxidative transformation can also be extended to the heterocyclic aldehydes as well. Thus, 2-furaldehyde **13** could be smoothly converted to methyl 2-furoate **13a** in quantitative yield. The efficacy of the methodology was further demonstrated by esterification of unsaturated aldehyde such as cinnamaldehyde **14**. Longer reaction times under the given conditions (30% in 7 h) can be due to an unfavorable equilibrium in hemiacetal formation, due to disruption of conjugation. Here again, refluxing the reaction mixture in a water bath can enhance the reaction rate and improve the yield (95% in 2 h).

Minor amount of carboxylic acid was also obtained for substrates, **2**, **5** and **9**. The esters formed do not hydrolyse under the reaction conditions to acids; thus the minor amounts of acids obtained are due to the over-oxidation of aldehydes.

Table 1.1. Oxidative Esterification[a] of Aldehydes to the Corresponding Methyl Esters with V_2O_5–H_2O_2

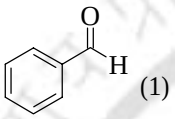
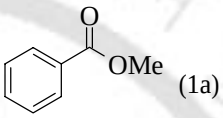
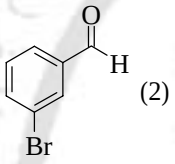
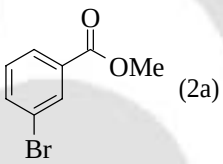
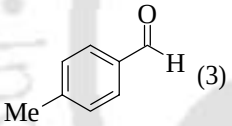
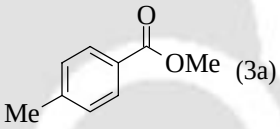
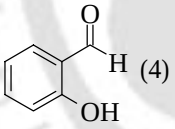
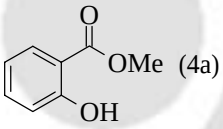
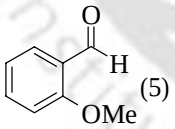
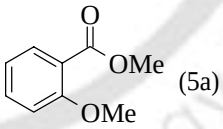
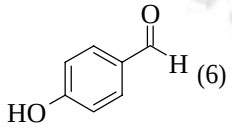
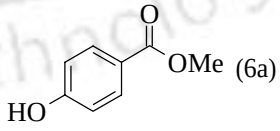
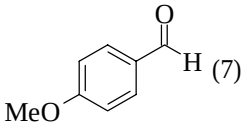
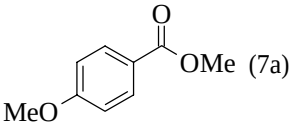
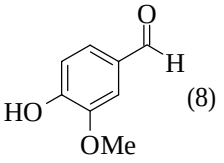
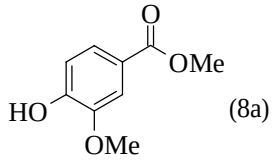
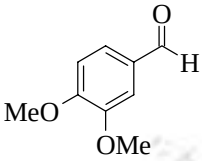
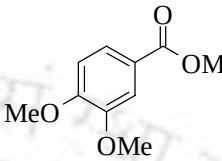
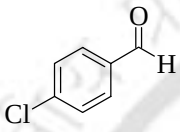
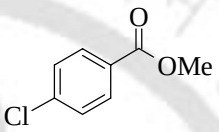
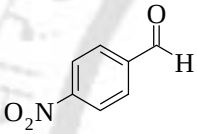
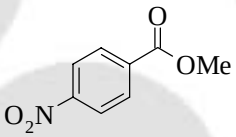
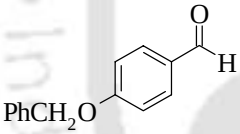
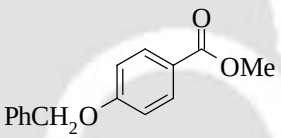
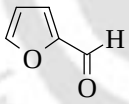
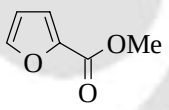
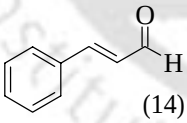
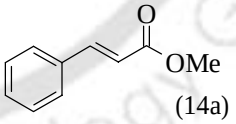
Substrate	Time/h	Product [b]	Yield (%)[c]	Ester (%)[c,d]
 (1)	3.0	 (1a)	100	100
 (2)	0.75	 (2a)	100	96
 (3)	0.5	 (3a)	100	100
 (4)	7.5	 (4a)	93	100
 (5)	5.0	 (5a)	100	91
 (6)	2.5	 (6a)	100	100
 (7)	3.0	 (7a)	100	100
 (8)	6.0	 (8a)	83	100

Table contd....

Table 1.1. Oxidative Esterification[a] of Aldehydes to the Corresponding Methyl Esters with V_2O_5–H_2O_2

Substrate	Time/h	Product[b]	Yield (%)[c]	Ester (%)[c,d]
 (9)	5.0	 (9a)	85	97
 (10)	5.5	 (10a)	100	100
 (11)	0.5[e]	 (11a)	100	100
 (12)	5.0	 (12a)	100	100
 (13)	2.0	 (13a)	100	100
 (14)	2.0[e]	 (14a)	95	100

[a]Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Determined by GC. [d]The balance is the carboxylic acid. [e]The reaction was performed at reflux temperature after addition of the reagent under ice cold condition.

Efficacy of this methodology was further applied to the preparation of other esters such as ethyl, propyl and butyl esters. Thus, various ethyl esters were prepared employing this method using ethanol instead of methanol and the results are shown in Table 1.2.

Table 1.2. Oxidative Esterification[a] of Aldehydes to the the Corresponding Ethyl Esters with V_2O_5–H_2O_2

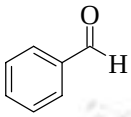
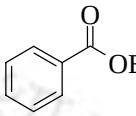
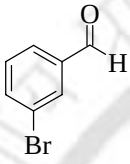
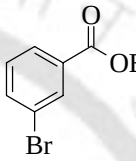
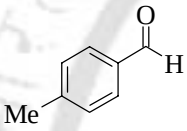
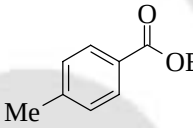
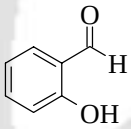
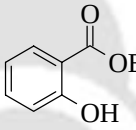
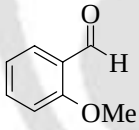
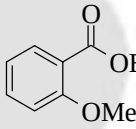
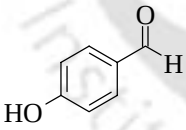
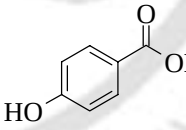
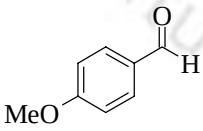
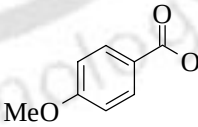
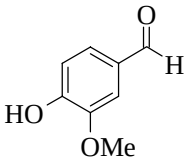
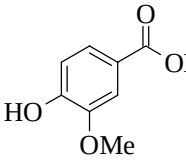
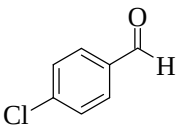
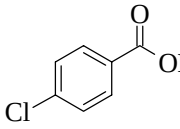
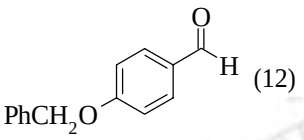
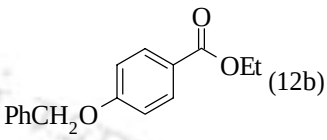
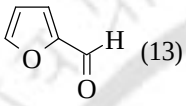
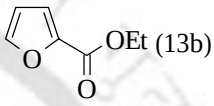
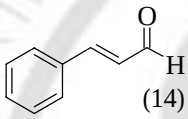
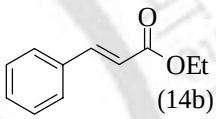
Substrate	Time/h	Product [b]	Yield (%)[c]
 (1)	1.5	 (1b)	95
 (2)	1.5	 (2b)	93
 (3)	0.75	 (3b)	94
 (4)	9.0	 (4b)	86
 (5)	6.5	 (5b)	89
 (6)	4.0	 (6b)	93
 (7)	3.5	 (7b)	90
 (8)	7.5	 (8b)	75
 (10)	6.5	 (10b)	92

Table contd…

Table 1.2. Oxidative Esterification[a] of Aldehydes to Corresponding Ethyl Esters with V_2O_5–H_2O_2

Substrate	Time/h	Product [b]	Yield (%)[c]
 (12)	3.0	 (12b)	85
 (13)	3.0	 (13b)	87
 (14)	2.5[d]	 (14b)	91

[a] Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Determined by GC. [d]The reaction was performed at reflux temperature after addition of the reagent under ice cold condition.

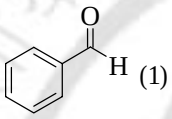
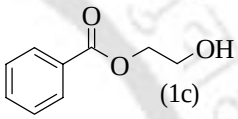
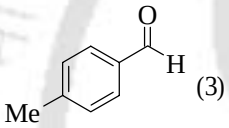
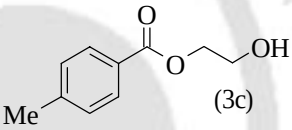
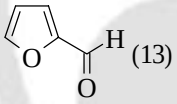
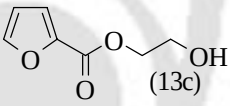
Here again, the reactions are favored for activated, unhindered substrates and disfavored for hindered, deactivated and conjugated substrates (Table 1.2). Reaction times were longer for the preparation of ethyl esters compared to the preparation of methyl esters.

Glycol monoesters have widespread applications as intermediates for sex pheromones of lepidoptera[12] and cross linking agents for polyesters or as fungicides.[13] The major drawback in the preparation of these compounds from the diols is the simultaneous formation of diesters along with the monoesters making the separation procedure a tedious one.[14] Alternatively, they have been prepared by the oxidation of the cyclic acetals using varieties of oxidising agents[1a] such as $VO(OAc)_2$-^{t}BuOOH, ^{t}BuOOH-PDC, ^{t}BuOOH-$Pd(OCOCF_3)(OO^tBu)$ and $NaBO_3.4H_2O$-Ac_2O-Na_2CO_3 etc. Few more methods are also available for the direct oxidation of the cyclic acetals to glycol monoesters using O_3,[15] $CuCl_2$,[16] DDQ,[17] $Ph_3P^+BF_3^-$,[18] and Oxone®.[19] These methods are not only two-step processes involving acetalisation followed by oxidation of cyclic acetals to hydroxy esters, but, also suffers from some disadvantages such as easy handling, longer reaction times, higher

amounts of reagents/catalysts etc. Therefore, there is a need to develop alternative methods for the direct transformation of aldehydes to hydroxy esters.

By employing above method, glycol monoesters can be directly obtained from the corresponding aldehydes along with ethylene glycol in good yields. Efficacy of the methodology has been tested with few substrates as shown in Table 1.3.

Table 1.3. Preparation of Glycol Monoesters[a] using V_2O_5–H_2O_2

Substrate	Time/h	Product [b]	Yield (%)[c]
 (1)	2.0	 (1c)	74
 (3)	1.5	 (3c)	80
 (13)	3.0	 (13c)	70

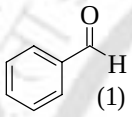
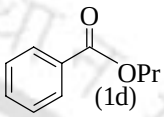
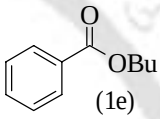
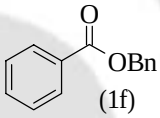
[a] Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Isolated yield.

Formation of diesters was not observed by this method. To the best of our knowledge this is the first successful synthesis of the glycol monoester directly from ethylene glycol and an aldehyde. The success of direct preparation of this type of ester is noteworthy, because such esters has only been prepared by the oxidation of 1,3-dioxolanes.[1a, 15–19]

The usefulness of this methodology was further demonstrated by oxidative esterification of benzaldehyde with other alcohols such as *n*-propanol, *n*-butanol, gave 94% and 93% of the corresponding esters **1d** and **1e** (Table 1.4). However, esters of branched alcohols such as *iso*-propanol and *tert*-butanol could not be obtained at all, which could be due to an unfavorable equilibrium in hemiacetal formation. Formation of benzyl esters was also not very successful by this methodology and gave a poor yield of benzyl benzoate **1f** (17%, 1.5 h). The poor yield in the case of benzyl esters was due to the oxidation of benzyl

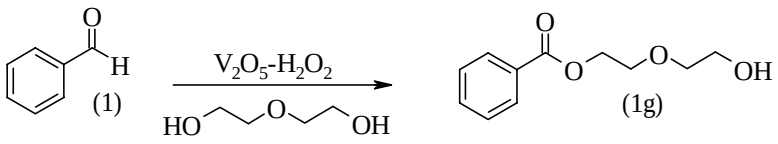
alcohol to benzaldehyde itself, which was subsequently oxidised to benzoic acid under the reaction conditions.

Table 1.4. Oxidative Esterification of Aldehydes to the Corresponding Propyl, Butyl and Benzyl Esters[a] with V_2O_5–H_2O_2

Substrate	Time/h	Product [b]	Yield (%)[c]
 (1)	1.5	 (1d)	94
	1.7	 (1e)	93
	1.5	 (1f)	17

[a] Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Isolated yield.

We further attempted to extend the above protocol for the preparation of monoesters of complex diols. Thus, reaction of benzaldehyde with diethylene glycol resulted in diethylene glycol monobenzoate (28%, 3 h). The ^{1}H and ^{13}C NMR spectrum of diethylene glycol monobenzoate is shown in (Figure 1.4). To the best of our knowledge, this is the first such ester prepared and would be difficult to prepare by any of the existing methods. Higher primary aliphatic diols gave lower yields because of the concurrent decomposition of active oxidising species and hydrogen peroxide at longer times. We believe that synthesis of monoesters of diethylene glycol of various aldehydes can be achieved by this method.



Scheme 1.35. Preparation of Monoesters of Diethylene Glycol

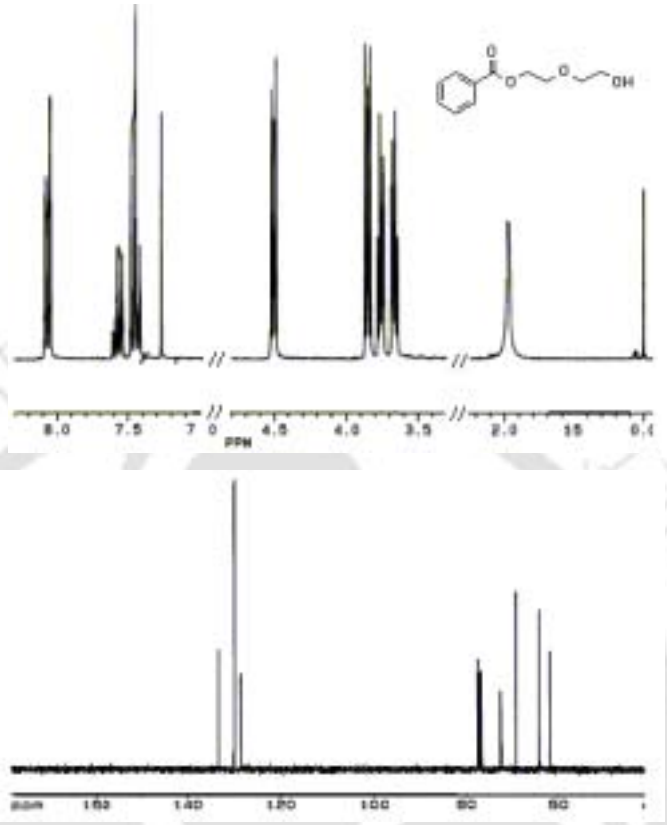


Figure 1.4. ^{1}H and ^{13}C NMR Spectrum of Diethylene Glycol Monobenzoate

In conclusion, the present method represents a simple, yet highly efficient method for the synthesis of esters from the corresponding aldehydes under mild conditions. The methodology equally works well for the synthesis of ethyl, propyl, butyl esters. Monoesters of various diols can be prepared directly. Although the simplicity and convenience of this oxidation procedure are appealing, the fact that the reaction proceeds in high yields without *cis-trans* isomerisation of the α,β-olefinic linkage is even more important. In particular, its use in aqueous media holds promises as the basis for process, which is environmentally safer and inexpensive. High catalytic turnover number combines with inexpensive, easily available reagents and innocuous side products in the reaction makes it a suitable alternative for practical application. Although literature enumerate a number of procedures for conversion of aldehydes to esters, the simplicity, environmental acceptability and inexpensiveness of our procedure makes it a practical alternative.

IB.1.1 References

1. (a) Larock, R. C. *Comprehensive Organic Transformation*, VCH: New York, 1999. (b) Williams, D. R.; Klingler, F. D.; Allen, E. E.; Lichtenthaler, F. W. *Tetrahedron Lett.* **1988**, *29*, 5087. (c) McDonald, C.; Holcomb, H.; Kennedy, K.; Kirkpatrick, E.; Leathers, T.; Vanemon, P. *J. Org. Chem.* **1989**, *54*, 1213.
2. (a) Corey, E. J.; Gilman, N. W.; Ganem, B. E. *J. Am. Chem. Soc.* **1968**, *90*, 5616. (b) Sakuragi, H.; Tokumaru, K. *Chem. Lett.* **1974**, 475. (c) Ogawa, T.; Matsui, M. *J. Am. Chem. Soc.* **1976**, *98*, 1629. (d) Sundararaman, P.; Walker, E. C.; Djerassi, C. *Tetrahedron Lett.* **1978**, *19*, 1627. (e) Chiba, T.; Okimoto, M.; Nagai, H.; Takata, Y. *Bull Chem. Soc. Jpn.* **1982**, *55*, 335. (f) Wilson, S. R.; Tofigh, S.; Misra, R. N. *J. Org. Chem.* **1982**, *47*, 1360. (g) Garegg, P. J.; Olsson. L.; Oscarson, S. *J. Org. Chem*. **1995**, *60*, 2200.
3. Espenson, J. H.; Zhu, Z.; Zauche, T. H. *J. Org. Chem.* **1999**, *64*, 1191.
4. (a) Anastas, P. T.; Williamson, T. C. Eds. *Green Chemistry: Frontiers in Benign Chemical Syntheses and Processes*; Oxford University Press: Oxford, 1998. (b) Clark, J. H. Ed. *Chemistry of Waste Minimisation*, Chapman & Hall: London, 1995.
5. Chaudhuri, M. K.; Khan, A. T.; Patel, B. K.; Dey, D.; Kharmawophlang, W.; Lakshmiprabha, T. R.; Mandal, G. C. *Tetrahedron Lett*. **1998**, *39*, 8163.
6. Bora, U.; Bose, G.; Chaudhuri, M. K.; Dhar, S. S.; Gopinath, R.; Khan, A. T.; Patel, B. K. *Org. Lett*. **2000**, *2*, 247.
7. Butler, A.; Clague, M. J.; Meister, G. E. *Chem. Rev*. **1994**, *94*, 625.
8. Freeman, F. *Organic Synthesis by Oxidation with Metal Compounds*, Mijs W. J., De Jonge C. H. R. I., Ed.; Plenum Press: New York, 1986, Chapter 1, p.2.
9. March, J. *Advanced Organic Chemistry*, John Wiley & Sons: New York, 1992, p. 1196.
10. McDonald, C.; Holcomb, H.; Kennedy, K.; Kirkpatrick, E.; Leathers, T.; Vanemon, P. *J. Org. Chem.* **1989**, *54*, 1213.

11. McDonald, C. E.; Nice, L. E.; Shaw, A. W.; Nestor, N. B. *Tetrahedron Lett.* **1993**, *34*, 2744.

12. (a) Leznoff, C. C. *Acc. Chem. Res.* **1978**, *11*, 327. (b) Henrick, C. A. *Tetrahedron* **1977,** *33*, 1845. (c) Rossi, R. *Synthesis* **1977**, 817.

13. Hosokawa, T.; Imada, Y.; Murahashi, S. -I. *J. Chem. Soc., Chem Commun.* **1983**, 1245.

14. Babler, J. H.; Coghlan, M. J. *Tetrahedron Lett.* **1979**, *20*, 1971 and references therein.

15. Stork, G.; Rychnovsky, S. D. *J. Am.Chem. Soc.* **1987**, *109*, 1565**.**

16. Sato, K. -I.; Igarashi, T.; Yanagisawa, Y.; Kawaichi, H.; Yoshimura, J. *Chem. Lett.* **1987**, *28*, 2835**.**

17. Sviridov, A. F.; Ermolenko, M. S.; Yashunsky, D. V.; Borodkin, V. S.; Kochetkov, N. K. *Tetrahedron Lett.* **1987**, *28*, 2835.

18. Hanessian, S. *Tetrahedron Lett.* **1973**, *14*, 3551.

19. Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Synlett* **1999**, 777.

IB.2 Catalytic Oxidative Esterification of Aldehydes Using V_2O_5-SPB/SPC

Despite of the distinct advantage of V_2O_5 catalysed oxidation of the aldehyde to ester using cheap and environmentally benign oxidant H_2O_2; the drawback of the previous methodology is the over-oxidation of some of the aldehydes to acids, instead of esters, and slow conversion due to the decomposition of active peroxovanadium species. As an alternative approach, to circumvent such side reactions by the V_2O_5–H_2O_2, we decided to use sodium perborate (SPB) and sodium percarbonate (SPC), instead of H_2O_2, for the direct oxidation of aldehydes to esters in presence of an alcohol. In this section, we describe the effectiveness of an optimised procedure that relies upon the anhydrous, stable and solid materials such as SPB or SPC in combination with a catalyst (V_2O_5) in an acidic medium.

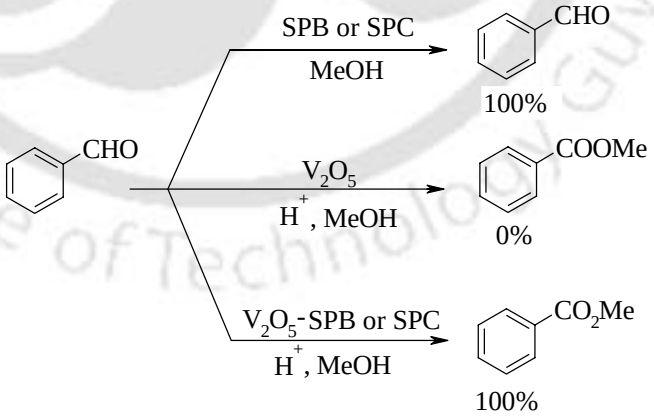
Our continued interest in developing new controlled oxidation procedures has prompted to use peroxy salts such as sodium perborate (SPB) and sodium percarbonate (SPC) which are inexpensive, readily available, safe and easy to handle and are convenient sources of active hydrogen peroxide especially for large scale reactions.[20] Concentrated hydrogen peroxide is not readily available and is, further more, very dangerous to handle. Consequently, the ability of SPB and SPC to release hydrogen peroxide in an aqueous or an organic medium has made them useful latent reagents in organic synthesis. Sodium perborate and reactions, catalysed by metals has been used for various organic functional group transformations. SPC in aqueous acetic acid activates the molybdate to peroxomolybdate species by acting as a source of hydrogen peroxide.[1] Urea-hydrogen peroxide, an addition complex, where hydrogen peroxide is present in 1:1 ratio has been employed as an alternative source of hydrogen peroxide for the oxyfunctionalisations catalysed by methyltrioxorhenium (MTO).[2] Peroxovanadium complex generated from the oxides of vanadium and hydrogen peroxide has specific catalytic activity towards organic synthesis especially in oxidation reactions.[3] An appealing feature of these oxidants is their versatility, as demonstrated by the fact that they are able to oxidise substrates such as alkenes, alcohols,

ketones, sulfur, phosphorous and nitrogen derivatives and even aromatic and aliphatic hydrocarbons.[3]

As a test substrate, for the oxidative transformation of aldehydes to esters, *p*-methoxybenzaldehyde **7** was chosen for optimising the reaction conditions. Addition sequences of different components and the ratios of substrate, catalyst, peroxy salts (SPB/ SPC) and mineral acid such as $HClO_4$ were varied in order to achieve higher product conversion. For both SPB and SPC the optimum stoichiometry was 3.5 per mmol of substrate, although H_2O_2 content in both the peroxy salts are different, 1 per molecule for the former and 1.5 per molecule for the latter. Both SPB and SPC have often been employed for the same purpose, unfortunately, the corresponding reports are separate and comparisons are lacking, but wherever available SPB is used in higher proportions compared to SPC.[20d] A different concentration of acid was required for the efficient release of hydrogen peroxide and maintaining the catalytic activity of the V_2O_5. This is because SPC is slightly more alkaline compared to SPB.[4] For SPB and SPC as an oxidants, the concentration of 70% perchloric acid required was (350 μL, 4.3 mmol) and (700 μL, 8.6 mmol), respectively, per 3.5 mmol of the peroxy salts. Thus for SPB reactions, the ratios of catalyst (V_2O_5) to oxidant (SPB) to substrate and acid were 0.04:3.5:1:4.3 and for SPC reactions, the ratio were 0.04:3.5:1:8.6, respectively. The oxidation was carried out either by adding acid to the mixture containing peroxy salt, aldehyde and alcohol (**Method A**) or by adding peroxy salt to the rest (**Method B**). For method A, when perchloric acid was added at once considerable amount of over-oxidation of aldehyde to the corresponding acid took place. However, we found upon adding acid in batches, less over-oxidised products were formed and yield ester as the exclusive product. Subsequent optimisation revealed that the transformation is best achieved using drop wise addition of the acid over a period of time. This could be due to slow liberation of H_2O_2 from the peroxy salt there by forming peroxovanadium compound, the active oxidising species for oxidative transformation. Again, for method B, when peroxy salt was added at once, considerable over-oxidation took place, and also catalytic decomposition and loss of hydrogen peroxide occurred which lead to a low conversion. In contrast, when peroxy salt was added over a period of time to the rest, excellent conversion was achieved; this is again due to a controlled release of H_2O_2 in an acidic reaction medium.

Both the methods minimises the generation of hydrogen peroxide either by controlling the addition of oxidant or acid. Also SPB and SPC help maintaining the catalytic activity owing to its lower water content. The p*H* of the medium progressively decreased from *ca.* 10.68 at the beginning of the reaction to *ca.* 0.10 after the complete addition of the mineral acid and remained almost constant for SPB mediated reactions and the change was from *ca.* 12.7 to *ca.* 1.0 when SPC was used as the oxidant.

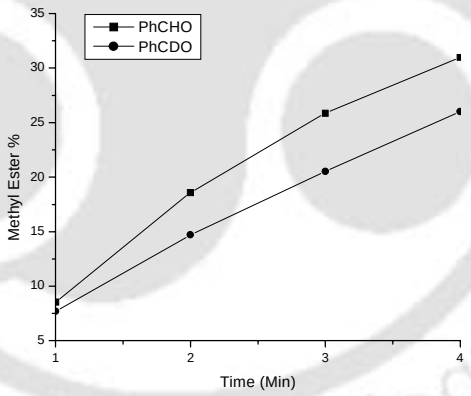
In either method, no oxidation was observed without V_2O_5 or combination of V_2O_5 and SPB/SPC unless acid was added to the medium (Scheme 1.36). Other mineral acids such H_2SO_4, HCl, HBr worked equally well. However, it is surprising to note that the reaction failed when acetic acid was used. This observation is in contrast to the MTO catalysed reaction where only acetic acid was used to activate the catalyst.[5] This could be because the activation of V_2O_5 requires low p*H* and sodium acetate/borate formed by the reaction of SPB and SPC with acetic acid might buffer the medium to a relatively higher p*H*. In acidic solution ($[H^+] > 0.01M$) vanadium(V) exist as VO_2^+. Addition of hydrogen peroxide to VO_2^+ can give the red monoperoxo- $VO(O_2)^+$ species and yellow diperoxo $VO(O_2)_2^-$ species. These species are stable under acidic medium and unstable in neutral and basic medium.[3] As discussed earlier the life time of these peroxo species are longer in acidic medium.



Scheme 1.36. A Control Reaction Showing the Role of Catalyst V_2O_5 and SPB/SPC and Acid on Oxidative Esterification

In order to further arrive at the optimum stoichiometry of the peroxy salt and hence the hydrogen peroxide, reactions were performed with different quantities of SPB and proportionate amounts of acid, keeping the catalyst and substrate concentration unchanged.

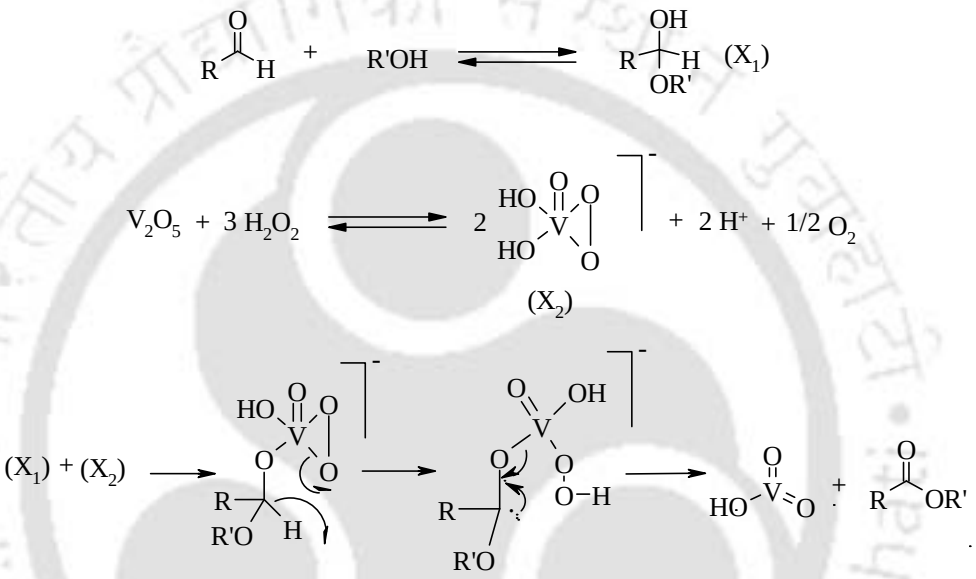
Increasing the ratio of SPB to aldehyde improves the yield of ester. Thus, when 1 equivalent of *p*-methoxybenzaldehyde **7** was allowed to react with one, two and three equivalents of SPB in the presence of V_2O_5 (0.04 mmol) and proportionate amounts of perchloric acid, the yield of ester obtained were respectively 32, 64 and 96% thus proving 1: 3 ratio of catalyst and hydrogen peroxide as proposed earlier (Scheme 1.34). UV spectral analysis confirmed the intermediacy of the peroxovanadium(V) species with the appearance of the peak at λ = 430 nm. Although $VO(O_2)^+$ is a two electron oxidant it can function as a one electron oxidant in cases where no two electron pathway is accessible.[3b] In our earlier work, we have proposed a two electron mechanism involving a hydride ion transfer in one of the steps (Scheme 1.34). To ascertain the importance of the cleavage of the aldehydic C-H bond in the rate-determining step, the oxidation of the [^{2}H] benzaldehyde (PhCDO) was studied. The result showed (Graph 1.2) no significant kinetic isotope effect ($K_H / K_D \approx 1$ at 273^o K), ruling out the possibilities of two electron mechanism.



Graph 1.2. Rate of Esterification of Benzaldehyde (PhCHO) vrs [^{2}H] Benzaldehyde (PhCDO)

The oxidation of benzaldehyde **1**, under the reaction condition failed to induce polymerisation of methyl acrylate. Further, the addition of methyl acrylate and radical scavenger like benzophenone has no effect on the reaction rate. This however does not completely rule out a one-electron mechanism, since in oxygenated atmosphere the oxygen molecules either quench the radical before bringing about polymerisation of methyl acrylate or reaching to the radical inhibitor. Thus, this reaction is expected to go *via* an intramolecular free radical mechanism as shown below in Scheme 1.37. Here also the success of the reaction

is dependent upon the selective oxidation of the hemiacetal hydroxy moiety in the presence of much higher concentration of alcohol. Such selectivity appears reasonable since more substituted alcohols are oxidised at a significantly faster rate by oxidising agents such as CrO_3[6], NIS,[7] and calcium hypochlorite.[8] A catalytic turnover number of >500 was determined for both the methods.



Scheme 1.37. Proposed Mechanism

Under these conditions wide range of aldehydes containing activated, deactivated, conjugated and hindered aldehydes can all be oxidised to the corresponding methyl esters in good to excellent yields. As could be seen from Table 1.5 most of the substrates gave excellent yields of the corresponding methyl esters. However, moderately deactivated substrate such as *m*-bromobenzaldehyde **2** and deactivated substrate *p*-nitrobenzaldehyde **11** gave poor yields of the corresponding esters 40 and 35% respectively by this method and gave corresponding acid as the major product. As an alternative approach we decided to add SPB or SPC to an acidic medium of aldehyde in methanol containing a catalytic amount of V_2O_5 at room temperature (Method B). The yield improved dramatically as shown in Table 1.5. This is because the redox potential of the vanadium(V)-vanadium(IV) couple increases with acidity in the region from p*H* 1.5 to 2 M acid, there by acting as a stronger oxidant for the deactivated substrates.[3d] It may be mentioned here, esterification of the deactivated

substrates such as *p*-nitrobenzaldehyde **11** is usually difficult and has been achieved under a reflux condition (Table 1.1). It is worth to note that, some of the activated substrates were over-oxidised by the later method. Slower reaction rates for the *o*-substituted substrate and conjugated system can be due to an unfavorable equilibrium in hemiacetal formation, due to disruption of conjugation. The efficacy of the methodology was demonstrated by the regioselective esterification of unsaturated aldehyde in 95% yield as shown in the case of cinnamaldehyde **14**. It is interesting to note that SPC mediated reactions are faster compared to the SPB mediated reactions (Table 1.5).

Table 1.5. Oxidative Esterification[a] of Aldehydes to the Corresponding Methyl Esters with V_2O_5–H_2O_2

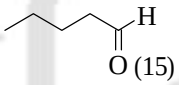
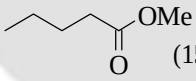
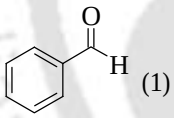
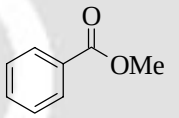
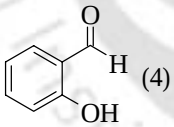
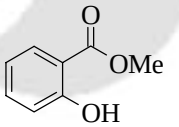
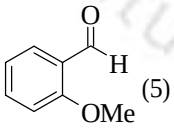
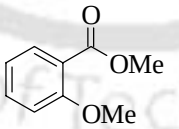
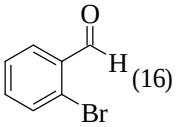
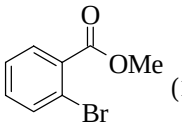
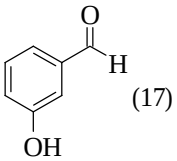
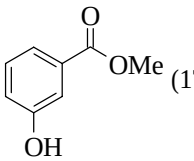
Substrate	Product	SPB		SPC	
		Time/h	Yield (%)[b]	Time/h	Yield (%)[b]
 (15)	 (15a)	0.3	96	0.3	97
 (1)	 (1a)	0.3	97	0.3	98
 (4)	 (4a)	1.5	94	1.0	96
 (5)	 (5a)	2.0	96	1.3	96
 (16)	 (16a)	2.0	96	1.3	96
 (17)	 (17a)	1.3	95[c]	1.3	96[c]

Table contd…

Table 1.5. Oxidative Esterification [a] of Aldehydes to the Corresponding Methyl Esters with V_2O_5–H_2O_2

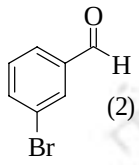
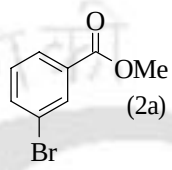
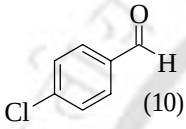
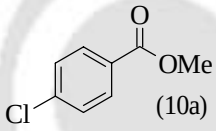
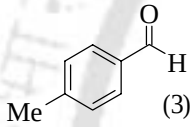
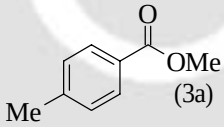
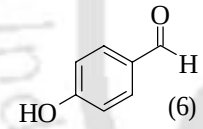
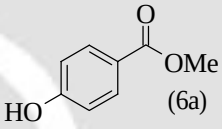
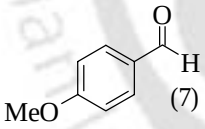
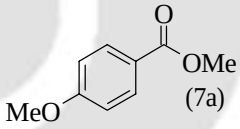
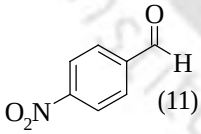
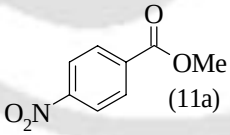
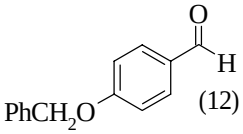
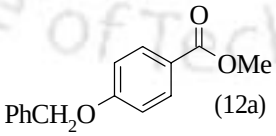
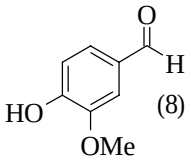
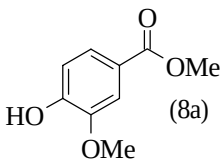
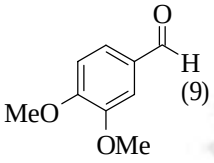
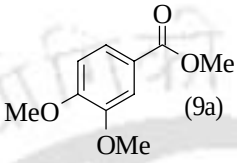
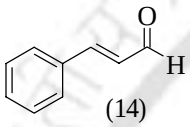
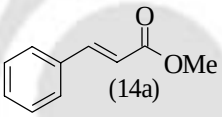
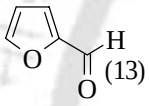
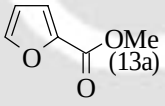
Substrate	Product	SPB		SPC	
		Time/h	Yield (%)[b]	Time/h	Yield (%)[b]
 (2)	 (2a)	0.75	98	1.3	98
 (10)	 (10a)	2.0	97	1.0	97
 (3)	 (3a)	0.75	98	0.75	98
 (6)	 (6a)	2.0	95	1.0	98
 (7)	 (7a)	1.3	90	0.3	92
 (11)	 (11a)	1.0	90 [c]	1.0	95 [c]
 (12)	 (12a)	3.3	85	1.0	95
 (8)	 (8a)	2.3	90	2.0	94

Table contd…

Table 1.5. Oxidative Esterification[a] of Aldehydes to the Corresponding Methyl Esters with V_2O_5–H_2O_2

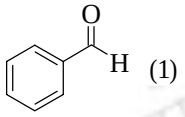
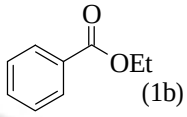
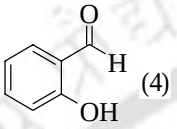
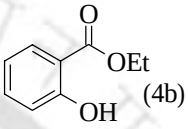
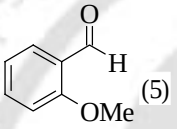
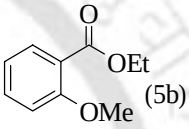
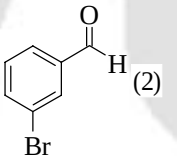
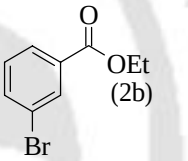
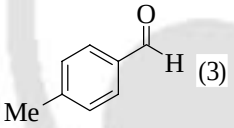
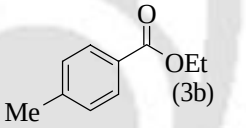
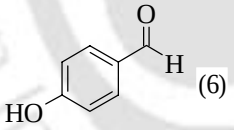
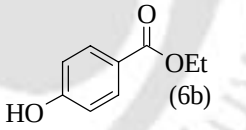
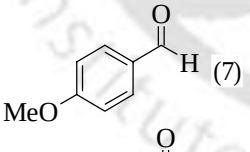
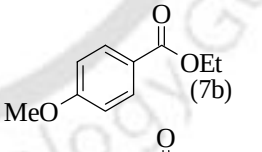
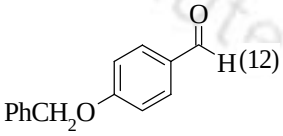
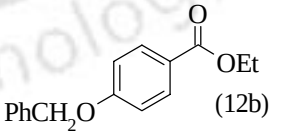
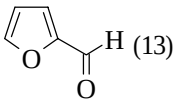
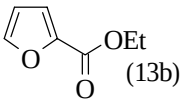
Substrate	Product	SPB		SPC	
		Time/h	Yield (%)[b]	Time/h	Yield (%)[b]
 (9)	 (9a)	3.3	80	0.45	97
 (14)	 (14a)	3.3	50[c]	0.3	97[c]
 (13)	 (13a)	1.0	85	0.35	95

[a]Reactions were monitored by TLC, GC. [b]Isolated yield. [c]The reaction was performed by method B. All the products are known in the literature and confirmed by comparison with IR and ^{1}H NMR of the authentic sample.

Other alcohols could be substituted for methanol to provide corresponding esters. With this end in view, reactions were performed in the presence of ethyl alcohol using SPC as the source of hydrogen peroxide under identical conditions as described for methyl ester. Thus, various ethyl esters can be prepared efficiently and in good yields by the present methodology as shown in Table 1.6.

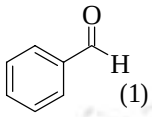
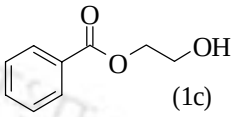
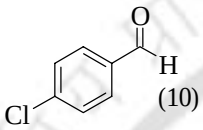
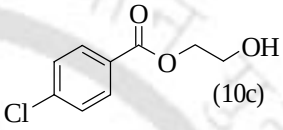
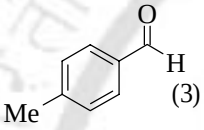
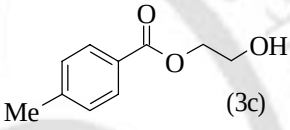
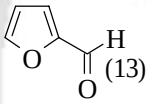
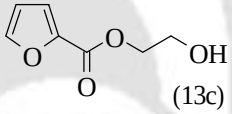
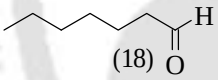
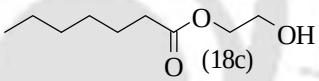
Monoesters of ethylene glycol can be prepared directly from aldehydes and ethylene glycol in good yields. The utility of the methodology has been tested with few substrates as shown in Table 1.7. Similar to V_2O_5–H_2O_2 mediated reactions, (Table 1.3), by the present method monoesters are the exclusive products. Formation of diesters was not observed by this method. These are single step esterification of aldehydes and ethylene glycol to hydroxy esters. Although procedures already exist for conversion of acetals to hydroxy esters by two-step procedures, the simplicity and low cost of single step esterification of present procedure allow it to compete as a practical alternative for the synthesis of hydroxy esters.

Table 1.6. Oxidative Esterification[a] of Aldehydes to the Corresponding Ethyl Esters with V_2O_5– SPC– H^+

Substrate	Time / h	Product	Yield (%)[b]
 (1)	1.0	 (1b)	95
 (4)	4.5	 (4b)	89
 (5)	5.0	 (5b)	90
 (2)	3.0	 (2b)	92[c]
 (3)	1.5	 (3b)	93
 (6)	3.0	 (6b)	95
 (7)	3.0	 (7b)	96
 (12)	5.5	 (12b)	88
 (13)	2.5	 (13b)	93

[a]Reactions were monitored by TLC, GC. [b]Isolated yield. [c]The reaction was performed by method B. All the products are known in the literature and confirmed by comparison with IR and ^{1}H NMR of the authentic sample.

Table 1.7. Oxidative Esterification[a] of Aldehydes to the Corresponding Hydroxy Esters with V_2O_5–SPB–H^+

Substrate	Time / h	Product	Yield (%)[b]
 (1)	2.0	 (1c)	78
 (10)	1.4	 (10c)	82
 (3)	3.0	 (3c)	72
 (13)	1.3	 (13c)	88
 (18)	2.2	 (18c)	75

[a] Reactions were monitored by TLC, GC. [b] Isolated yield. All the products are known in the literature and confirmed by comparison with IR and ^{1}H NMR of the authentic sample.

This method was further extended for the preparation of more complex glycol monoesters of diols. Thus, reaction of benzaldehyde with diethylene glycol resulted diethylene glycol monobenzoate (28%, 3 h). Higher primary aliphatic diols gave lower yields because of the concurrent decomposition of active oxidising species and hydrogen peroxide at longer times.

In conclusion, the two different methods represent a simple, rapid way to oxidise varieties of aldehydes containing activated, deactivated and double-bond-containing substrates to a wide range of esters. Method A being more suitable for activating substrates and Method B for deactivated aldehydes. Monoesters of various diols can be prepared directly. Although the simplicity and convenience of this oxidation procedure are appealing, the fact that the reaction proceeds in high yields without *cis-trans* isomerisation of the α,β-

olefinic linkage is even more important. In particular, its use in aqueous media holds promises as the basis for process, which is environmentally safe and inexpensive. High catalytic turnover number combined with inexpensive, easily available reagents and innocuous side products in the reaction makes it a suitable alternative for practical application.

IB.2.1 References

1. Karunakaran, C.; Gnanasekaran, K.; Sankar, P. *Int. J. Chem. Kinet.* **1995**, *27*, 443.
2. Adam, W.; Mitchell, C. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 533. (b) Adam, W.; Mitchell, C. M.; Saha-Möller. C. R.; Weichold, O. *J. Am. Chem. Soc.* **1999**, *121*, 2097.
3. (a) Butler, A.; Clague, M. J.; Meister, G. E. *Chem. Rev*. **1994**, *94*, 625. (b) Conte, V.; Di Furia, F.; Modena, G. *J. Org. Chem.* **1988**, *53*, 1165. (c) Hubert, M.; Lucien, S.; Eric, D.; Michele, P.; Jean, F.; Raymond, W. *J. Am. Chem. Soc.* **1983**, *105*, 3101. (d) Freeman, F. *Organic Synthesis by Oxidation with Metal Compounds*; Mijs W. J., De Jonge C. H. R. I., Ed.; Plenum Press: New York, 1986, Chapter 1, p.2.
4. Kirk-Othmer, *Encyclopedia of Chemical Technology*, 3rd ed.; Wiley: New York, 1982, Vol. 17, p.6.
5. Espenson, J. H.; Zhu, Z.; Zauche, T. H. *J. Org. Chem.* **1999**, *64*, 1191.
6. March, J. *Advanced Organic Chemistry*, John Wiley & Sons: New York, 1992, p. 1196.
7. McDonald, C.; Holcomb, H.; Kennedy, K.; Kirkpatrick, E.; Leathers, T.; Vanemon, P. *J. Org. Chem.* **1989**, *54*, 1213.
8. McDonald, C. E.; Nice, L. E.; Shaw, A. W.; Nestor, N. B. *Tetrahedron Lett.* **1993**, *34*, 2744.

IB.3 Direct Oxidation of Acetals to Esters Using V_2O_5-H_2O_2

Amongst the plethora of groups typically employed for protecting aldehydes, acetals enjoy a cardinal position, as exemplified by the numerous methods devised for their attachment and removal.[1] Direct conversion of cyclic and acyclic acetals to esters is a useful synthetic methodology in organic chemistry and numerous methods using a variety of reagents and conditions have been developed. A comprehensive list of reagents for the one-step transformation of an acetal to ester has been compiled by Larock.[2] These include O_2, O_2 under photochemical conditions in the presence of Na_2SO_3, O_3, H_2O_2 in the presence of $FeSO_4$, ROOH, $(^tBuO)_2$-$K_2Cr_2O_7$, ^{t}BuOOH, 3,3-dimethyldioxirane, NBS and N_2O_4. Other reagents are also effective for this type of transformation including peracetic acid,[3] DDQ,[4] ^{t}BuOOH-Pd(II) catalyst,[5] sodium perborate,[6] Oxone®,[7] Co(II) catalyst,[8] $VO(OAc)_2$,[9] H_2O_2 and HCl in alcohol,[10] electrochemical oxidation,[11] PPh_3^+ BF_3^-,[12] MTO-H_2O_2.[13] With a few exceptions, most of the methods suffer from disadvantages such as ease of operation, drastic conditions, long reaction times, use of excess and expensive reagents. Furthermore, some methods suffer from drawbacks like unsatisfactory yields in the case of aromatic aldehydes bearing an electron-withdrawing substituent in the aromatic ring, polymerisation of 2-furfural and are ineffective for aldehydes containing double bonds.

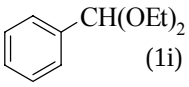
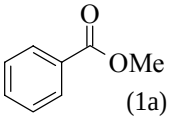
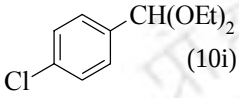
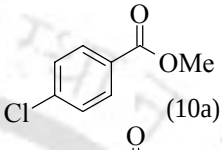
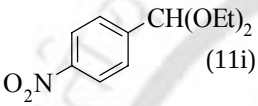
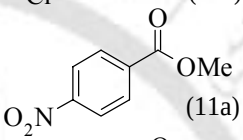
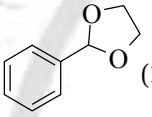
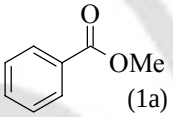
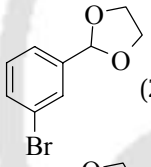
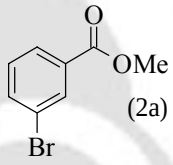
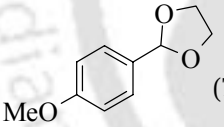
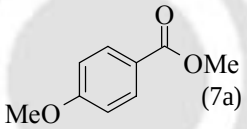
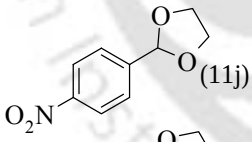
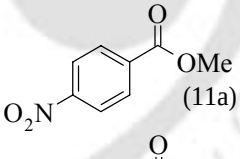
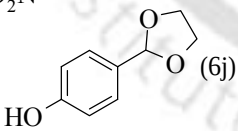
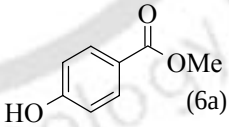
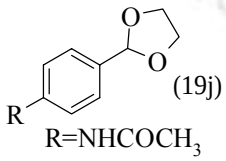
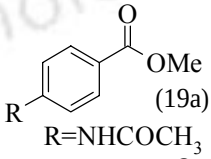
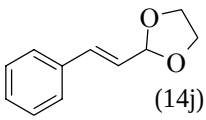
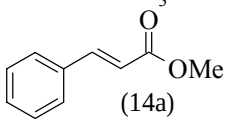
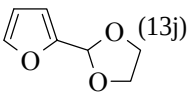
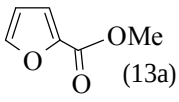
The peroxovanadium species generated upon treatment of oxides of vanadium with hydrogen peroxide is a stronger oxidant than either hydrogen peroxide or V_2O_5 and oxidises a variety of organic substrates.[14] This has been utilised for the oxidative transformation of aldehydes to esters, as discussed in the previous sections in which, in order to accelerate the reaction, a catalytic quantity of perchloric acid was added to the reaction medium. However, the inherent acidity[15] generated in the reaction medium by the reaction of V_2O_5 and H_2O_2 was apparently enough to bring about the esterification although the reaction rates were slow. We decided to test whether the intrinsic acidity originating from V_2O_5–H_2O_2 is sufficient to deprotect acid-sensitive protecting groups like acetals and to see if the resulting carbonyl compound, in an alcoholic medium, could be converted into the ester. We describe here a

mild and efficient method for the transformation of both cyclic and acyclic acetals to carbonyl compounds when acetonitrile was used as solvent and to esters when alcohol was used. We also describe deprotection of other acid-sensitive protecting groups such as THP and TBS ethers under similar conditions.

As a test substrate for the oxidative transformation of acetals to esters, benzaldehyde diethyl acetal **1i** was chosen. The reaction was performed by dissolving acetal (1 mmol) in methanol (3 mL) to which was added a solution of V_2O_5 (0.04 mmol) dissolved in 30% H_2O_2 (4 mmol) under ice-cold condition. The reaction times are indicated for each substrate in Table 1.8.

In most previous cases of acetal to ester transformations, the esters corresponding to the starting acetals were obtained. However, in H_2O_2–HCl mediated reactions,[10] esters corresponding to the solvent alcohol were obtained *via* a transesterification mechanism. In our case, esters derived only from the solvent, but not by a transesterification path. As expected, the acetal is first deprotected to the corresponding carbonyl compound and the resultant aldehyde is subsequently esterified by a mechanism similar to that proposed earlier (Scheme 1.34). Treatment of a wide variety of acetals with V_2O_5–H_2O_2 in methanol gave the corresponding methyl esters in high to excellent yields under mild reaction conditions. Acyclic acetals **1i** and **10i** were converted to the corresponding methyl esters, however, acetals **11i** and **11j** containing an electron-withdrawing group were reluctant to yield the ester, probably due to difficulty in regeneration of the aldehyde, and also a high activation energy for esterification (Table 1.8). However, good yields were achieved using a 10 fold excess of 30% H_2O_2 under reflux conditions. Cyclic 1,3-dioxolanes **1j**, **2j**, **7j**, **11j**, **6j**, **19j** were converted to the corresponding methyl esters in good yields. Double bond-containing-substrate **14j**, which is problematic and requires drastic conditions by other methods, yielded an ester by this method. Esterification of 2-furfural 1,3-dioxolane **13j** in good yields further demonstrates the efficacy of the methodology. In all the cases examined, reaction times were much longer than in our earlier methodology. The present one is a two-step process involving a deprotection step followed by an esterification.

Table 1.8. Oxidative Transformations of Acetals to Methyl Esters with V_2O_5–H_2O_2

Substrate	Time/h	Product	Yield (%)[a,b]
 (1i)	4.00	 (1a)	91
 (10i)	5.00	 (10a)	90
 (11i)	2.00	 (11a)	96[c]
 (1j)	4.00	 (1a)	92
 (2j)	6.00	 (2a)	82[d]
 (7j)	3.00	 (7a)	95
 (11j)	0.50	 (11a)	83[c,d]
 (6j)	3.50	 (6a)	95
 (19j)	1.50	 (19a)	98
 (14j)	2.50	 (14a)	94
 (13j)	9.00	 (13a)	82[d]

[a]Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]10 equiv. of 30% H_2O_2 and the reaction was performed at reflux. [d]The balance is aldehyde.

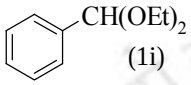
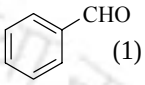
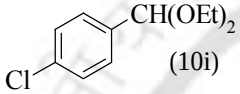
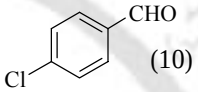
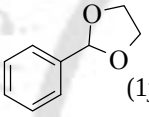
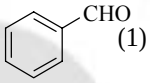
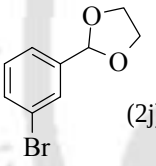
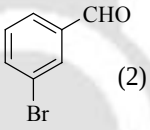
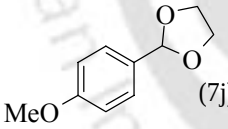
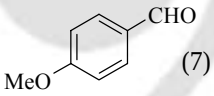
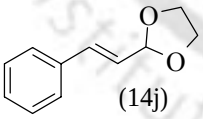
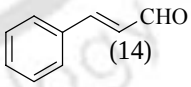
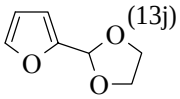
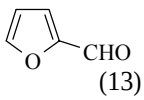
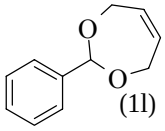
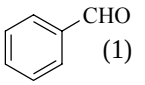
The p*H* values recorded at the beginning and after completion of the reaction were *ca.* 1.86 and 2.06, respectively. In our earlier methodology, the reaction times were relatively shorter, because esterification was directly from the aldehyde. In addition, external acid was also added to the medium because under acidic conditions, peroxovanadium species, the active oxidising agent is stable and active, Graph 1.1 (C) (p.37). An acidic medium also prolongs the lifetime of the peroxo species of $MeReO_3$ against irreversible decomposition.[13] One of the drawbacks of the previous methodology (Table 1.1) was the over-oxidation of some of the aldehydes giving acids instead of esters. By the present methodology aldehyde is slowly generated *in situ* from the acetal, and no over-oxidised products were detected.

Since aldehyde generated in the reaction medium and in the presence of methanol is converted to methyl ester, we reasoned that by changing the solvent to acetonitrile it should be possible to isolate the aldehyde. With this objective, acetals (1 mmol) of various aldehydes in acetonitrile (3 mL) were treated with a solution of V_2O_5 (0.04 mmol) dissolved in 30% H_2O_2 (4 mmol) under ice-cold conditions. Aldehydes were regenerated from both cyclic and acyclic acetals in less than 10 min. The results are shown in Table 1.9. It is interesting to note that the resultant aldehydes are not oxidised further under these conditions, however, after a longer period of time, aldehydes tended to be oxidised to the corresponding acids.

All the acetals described to this point were symmetrical and we thought it interesting to test the oxidation of unsymmetrical acetals such as tetrahydropyranyl derivatives of alcohols. It has been reported that THP ethers when treated with neutral or basic oxidising agents gave rise exclusively to the hydroxy esters[2,6] while treatment with other acidic oxidants[7,16] gave oxidative deprotection. When tetrahydropyranyl ethers of various alcohols were treated under identical conditions with V_2O_5–30% H_2O_2 very poor yields of alcohols were obtained. However, refluxing the reaction mixture can accelerate the deprotection as shown for different tetrahydropyranyl ethers in Table 1.10.

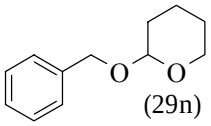
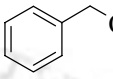
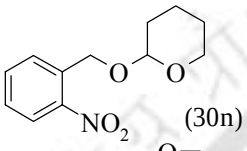
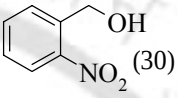
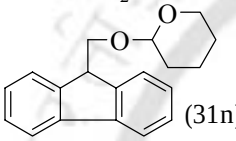
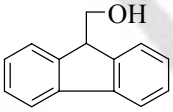
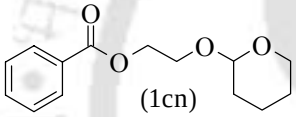
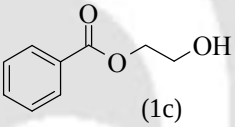
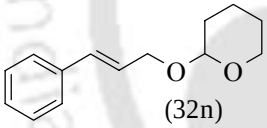
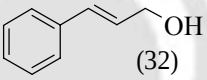
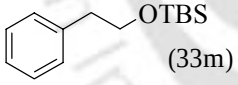
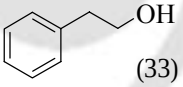
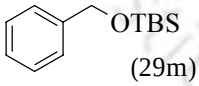
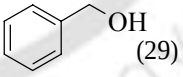
This observation shows that tetrahydropyranyl ethers are more stable compared to either cyclic or acyclic acetals. We further extended this methodology for the deprotection of other acid-sensitive protecting groups such as *tert*-butyldimethylsilyl (TBS) ethers.

Table 1.9. Deprotection of Acetals to Aldehydes and THP and TBS Ethers to the Corresponding Alcohols with V_2O_5–H_2O_2

Substrate	Time/h	Product	Yield (%)[a,b]
 (1i)	0.16	 (1)	95
 (10i)	0.16	 (10)	94
 (1j)	0.16	 (1)	94
 (2j)	0.16	 (2)	94
 (7j)	0.16	 (7)	96
 (14j)	0.16	 (14)	92
 (13j)	0.16	 (13)	93
 (1l)	2.00	 (1)	94

[a]Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]10 equiv. of 30% H_2O_2 and the reaction was performed at reflux. [d]The balance is aldehyde.

Table 1.10. Deprotection of Acetals to Aldehydes and THP and TBS Ethers to the Corresponding Alcohols with V_2O_5–H_2O_2

Substrate	Time/h	Product	Yield (%)[a,b]
 (29n)	0.25	 (29)	92[c]
 (30n)	0.25	 (30)	97[c]
 (31n)	0.25	 (31)	88[c]
 (1cn)	0.25	 (1c)	99[c]
 (32n)	0.25	 (32)	91[c]
 (33m)	2.00	 (33)	96
 (29m)	3.50	 (29)	80[d]

[a]Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]10 equiv. of 30% H_2O_2 and the reaction was performed at reflux. [d]The balance is aldehyde.

When TBS ethers **33m** and **29m** were treated with a solution of V_2O_5–30% H_2O_2, under ice-cold conditions, alcohols were regenerated in good yields. Surprisingly in the latter case along with the benzyl alcohol some benzaldehyde was also detected, which could originate from the over-oxidation of the resultant benzyl alcohol. The present study indicates that TBS ethers are more labile compared to THP ethers under acidic conditions, which is consistent with our subsequent observation (Chapter II).

In conclusion, the present method represents a simple, rapid way to oxidise acetals to esters and to deprotect THP and TBS ethers. The reagent, V_2O_5, is used in a catalytic quantity and hydrogen peroxide is a cheap and relatively safe oxidant, which produces only water as the side product. Acetals can be converted to other esters using different primary alcohols. Although procedures already exist for conversion of aldehydes to esters, the simplicity and low cost of our procedure allow it to compete as a practical alternative.

IB.3.1 References

1. (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; 3rd ed.; John Wiley & Sons: New York, 1999. (b) Kocieński, P. J. *Protecting Groups*, Georg Thieme Verlag: New York, 1994.
2. Larock, R. C. *Comprehensive Organic Transformation*, VCH: New York, 1999.
3. Heywood, D. L.; Philips, B. *J. Org. Chem.* **1960**, *25*, 1699.
4. Sviridov, A. F.; Ermolenko, M. S.; Yashunsky, D. V.; Borodkin, V. S.; Kochetkov, N. K. *Tetrahedron Lett*. **1987**, *28*, 2835.
5. Hosokawa, T.; Imada, Y.; Murahashi, S. -I. *J. Chem. Soc., Chem. Commun*. **1983**, 1245.
6. Bhat, S.; Ramesha, A. R.; Chandrasekaran, S. *Synlett* **1995**, 329.
7. Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Synlett* **1999**, 777.
8. Pei, Li.; Howard. A. *Can. J. Chem.* **1993**, *71*, 84.
9. Choudary, B. M.; Reddy, P. N. *Synlett* **1995**, 959.
10. Takeda, T.; Watanabe, H.; Kitahara, T. *Synlett* **1997**, 1149.
11. Masui, M.; Kawaguchi, T.; Yoshida, S.; Ozaki, S. *Chem. Pharm. Bull.* **1986**, *34*, 1837.
12. Babler, J. H.; Coghlan, M. J. *Tetrahedron Lett.* **1979**, *20*, 1971.
13. Espenson, J. H.; Zhu, Z.; Zauche, T. H. *J. Org. Chem.* **1999**, *64*, 1191.
14. Butler, A.; Clague, M. J.; Meister, G. E. *Chem. Rev*. **1994**, *94*, 625.
15. Bora, U.; Bose, G.; Chaudhuri, M. K.; Dhar, S. S.; Gopinath, R.; Khan, A. T.; Patel, B. K. *Org. Lett*. **2000**, *2*, 247.
16. (a) Raina, S.; Singh, V. K. *Synth. Commun.* **1995**, 2395; (b) Datta-Gupta, A.; Singh, R.; Singh, V. K. *Synlett* **1996**, 69.

IC Experimental

IC.1 General Experimental Section

All the solvents and reagents employed were of reagent grade (AR grade) and used as purchased without further purification, unless otherwise stated, and were obtained from E. Merck, Sigma-Aldrich, SRL, Qualigens. Organic extracts were dried over anhy. Na_2SO_4. Solvents were removed in a rotary evaporator under reduced pressure. Silica gel (60-120 mesh size) was used for column chromatography. Reactions were monitored by TLC on silica gel GF_{254} (0.25 mm). Gas liquid chromatography was performed using HP 6890 series II instrument with HP-1, a crosslinked methyl silicon gum capillary column (30 m × 0.32 mm × 0.25 μm) fitted with FID, and quantification was done using HP integrator

IC.2 Characterisation of Organic Substrates

Electronic spectra of solutions were recorded on Hitachi U-2001 UV-Vis spectrophotometer at 298^oK using spectroscopic grade solvents. Fourier transform-infra red (FT-IR) spectra were recorded on Nicolet Impact-410 instrument either as neat liquid or KBr pellets. Fast atom bombardment (FAB) mass were recorded using a JEOL SX-120/DA-6000 instrument using argon (6KV, 10mA) as the FAB gas. Elemental analyses were carried out in automatic C, H, and N analyser on 2400 Perkin Elmer Series II/CNO. Nuclear magnetic resonance (^1H NMR) spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (WM 400Bruker and Gemini Varian; 400 MHz and 200 MHz) or $CDCl_3$ as the internal standard for ^{13}C (100 MHz).

IC.3 Experimental Procedures

IC.3.1. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Methyl Esters Using V_2O_5–H_2O_2.

To an ice cold and stirred solution of aldehyde (5 mmol) in methanol (10 mL) was added 70% perchloric acid ($HClO_4$), 0.25 mL (3.1 mmol) and stirred for about 10 min. In a

separate flask, vanadium pentoxide (V_2O_5), 36.2 mg (0.2 mmol) was added to a solution of 30% hydrogen peroxide (H_2O_2), 2.25 mL (20 mmol) and left stirred in an ice cold condition until all the V_2O_5 dissolves and the solution becomes reddish brown colour (approx. 10 min). This was then added to the above aldehyde solution over a period of 40 min. The resulting homogeneous solution was allowed to stir at ~ 5°C until TLC and GC detected no starting material. The solvent was removed *in vacuo* and the residue was redissolved in ethyl acetate (20 mL). The organic layer was first washed with saturated solution of $NaHCO_3$ (2 × 5 mL) then with water (2 × 5 mL) and finally dried over anhy. Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel, hexane : ethyl acetate) to afford the product.

IC.3.2. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Methyl Esters Using V_2O_5–Peroxy salt (SPB or SPC). Method A:

To an ice cold and stirred solution of aldehyde (5 mmol) in methanol (10 mL) was added vanadium pentoxide (V_2O_5), 36.2 mg (0.2 mmol) and peroxy salt (sodium perborate (SPB), 2.64 g (17.5 mmol) or sodium percarbonate (SPC), 2.74 g (17.5 mmol)). To this heterogeneous reaction mixture was added 70% perchloric acid ($HClO_4$), (1.75 mL (21.7 mmol for SPB or 3.5 mL (43.4 mmol) for SPC), drop wise for over a period of 1 h. The reaction was stirred under an ice cold condition. The progress of the reaction was monitored by TLC and GC. After completion of the reaction, the solvent was removed *in vacuo* and the residue was redissolved in ethyl acetate (20 mL). The organic layer was first washed with saturated solution of $NaHCO_3$ (2 × 5 mL) then with water (2 × 5 mL) and finally dried over anhy. Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel, hexane : ethyl acetate) to afford the desired product.

IC.3.3. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Methyl Esters Using V_2O_5–Peroxy salt (SPB or SPC). Method B:

To an ice cold and stirred solution of aldehyde (5 mmol) in methanol (10 mL) was added vanadium pentoxide (V_2O_5), 36.2 mg (0.2 mmol) and 70% perchloric acid ($HClO_4$),

(1.75 mL (21.7 mmol) for SPB or 3.5 mL (43.4 mmol) for SPC). To this heterogeneous reaction mixture peroxy salt (sodium perborate (SPB), 2.64 g (17.5 mmol) or sodium percarbonate (SPC), 2.74 g (17.5 mmol)) was added portion wise over a period of 1 h. The reaction was left allowed to stirred at ice cold condition. The progress of the reaction was monitored by TLC and GC. After completion of the reaction, the solvent was removed *in vacuo* and the residue was redissolved in ethyl acetate (20 mL). The organic layer was first washed with saturated solution of $NaHCO_3$ (2 × 5 mL) then with water (2 × 5 mL) and finally dried over anhy. Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel, hexane : ethyl acetate) to afford the product.

IC.3.4. General Procedure for Oxidation of Acetals to Corresponding Methyl Esters Using V_2O_5–H_2O_2.

Vanadium pentoxide (V_2O_5), 36.2 mg (0.2 mmol) was added to a 30% hydrogen peroxide (H_2O_2), 2.25 mL (20 mmol) and left stirrring at 0°C until all the vanadium pentoxide dissolves and the solution becomes reddish brown colour (approx. 10 min). This was then added to an ice cold and stirred solution of acetal (5 mmol) in methanol (10 mL). The resulting solution was stirred at ~ 5°C until TLC and GC detected no starting material. The solvent was removed *in vacuo* and the residue was redissolved in ethyl acetate (20 mL). The organic layer was first washed with a saturated solution of $NaHCO_3$ (2 × 5 mL) then with water (2 × 5 mL) and finally dried over anhy. Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel, hexane : ethyl acetate) to afford the product.

IC.3.5. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Ethyl Esters Using V_2O_5–H_2O_2.

Similar to General Procedure IC.3.1 (p.68); ethanol was used instead of methanol.

IC.3.6. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Ethyl Esters using V_2O_5–SPC.

Similar to General Procedure IC.3.2 (p.69); ethanol was used instead of methanol.

IC.3.7. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Hydroxy-ethyl Esters Using V_2O_5–H_2O_2.

To an ice cold and stirred solution of aldehyde (5 mmol) in 1,2-ethanediol (5 mL) was added 70% perchloric acid ($HClO_4$), 0.25 mL (3.1 mmol) and stirred for about 10 min. In a separate flask, vanadium pentoxide (V_2O_5), 36.2 mg (0.20 mmol) was added to 30% hydrogen peroxide (H_2O_2), 2.25 mL (20 mmol) and left stirred in an ice cold temperature until all the V_2O_5 dissolves and the solution becomes reddish brown colour (approx. 10 min). This was then added to the above aldehyde solution over a period of 1 h. The resulting homogeneous solution was stirred at ~ 5 ^{0}C until TLC and GC detected no starting material. The solvent was removed *in vacuo* and the residue was redissolved in ethyl acetate (20 mL). The organic layer was washed with a saturated solution of $NaHCO_3$ (2 × 5 mL) then with water (2 × 5 mL) and finally dried over anhy. Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel, hexane:ethyl acetate) to afford the product.

IC.3.8. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Hydroxy-ethyl Esters Using V_2O_5–SPB.

To an ice cold and stirred solution of aldehyde (5 mmol) in 1,2-ethane diol (5 mL) was added vanadium pentoxide (V_2O_5), 36.2 mg (0.20 mmol) and sodium perborate (SPB), 2.625 g (17.5 mmol). To this heterogeneous reaction mixture 70% perchloric acid ($HClO_4$), 1.75 mL (21.7 mmol) was added over a period of 1 h. The reaction was allowed to stirred at ice cold temperature. The progress of the reaction was monitored by TLC and GC. After completion of the reaction, the reaction mixture was concentrated *in vacuo* and the residue was redissolved in ethyl acetate (20 mL). The organic layer was washed with saturated solution of $NaHCO_3$ (2 × 5 mL) then with water (2 × 5 mL) and finally dried over anhy. Na_2SO_4. The solvent removed *in vacuo* and the residue was purified by column chromatography (silica gel, hexane:ethyl acetate) to afford the product.

IC.3.9. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Propyl Esters Using V_2O_5–H_2O_2.

Similar to General Procedure IC.3.1(p.68); propanol was used instead of methanol.

IC.3.10. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Butyl Esters Using V_2O_5–H_2O_2.

Similar to General Procedure IC.3.1 (p.68); butanol was used instead of methanol.

IC.3.11. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Benzyl Esters Using V_2O_5–H_2O_2.

Similar to General Procedure IC.3.1(p.68); benzyl alcohol was used instead of methanol.

IC.3.12. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Hydroxy-ethoxy-ethyl Esters Using V_2O_5–H_2O_2.

Similar to General Procedure IC.3.7 (p.71); diethylene glycol was used instead of 1,2-ethanediol.

IC.3.13. General Procedure for Oxidative Esterification of Aldehydes to Corresponding Hydroxy-ethoxy-ethyl Esters Using V_2O_5–SPB.

Similar to General Procedure IC.3.8 (p.71); diethylene glycol was used instead of 1,2-ethanediol.

IC.3.14. Kinetic Isotopic Effect for Oxidative Esterification of Aldehydes to Corresponding Methyl Esters Using V_2O_5-H_2O_2.

To an ice cold and stirred solution of aldehyde (1 mmol) in methanol (5 mL) was added 70% perchloric acid ($HClO_4$), 0.05 mL (0.62 mmol) and stirred for about 10 min. In a separate flask, vanadium pentoxide (V_2O_5), 7.24 mg (0.04 mmol) was added to 30% hydrogen peroxide (H_2O_2), 0.45 mL (4 mmol) and left stirred in an ice cold temperature until all the V_2O_5 dissolves and the solution becomes reddish brown colour (approx. 10 min). This was then added to the above aldehyde solution in one lot. The resulting homogeneous solution was allowed to stirr at ~ 5^oC and the aliquots were collected every minute and quenched with saturated sodium bicarbonate solution. Percentage of product formed were determined by GC.

The same experiment was carried out under identical conditions using deuterated benzaldehyde in place of benzaldehyde. The rate of the reactions were determined from the plot in a graph with percentage of conversion (y-axis) against time (x-axis). Experimental results shows that there was not much difference between the rates of deuterated vrs undeuterated aldehydes during the oxidation. And thus, there is no significant kinetic isotopic effect ($K_H/K_D \approx 1$) at 273^{o}K.

IC.3.15. Catalytic Turnover Number of Oxidative Esterification of Aldehydes to Corresponding Methyl Esters Using V_2O_5–H_2O_2.

To an ice cold and stirred solution of *p*-methoxybenzaldehyde, 0.536 mL (20 mmol) in methanol (20 mL) was added 70% perchloric acid ($HClO_4$), 1 mL (12.4 mmol) and stirred for about 10 min. In a separate flask, vanadium pentoxide (V_2O_5), 7.24 mg (0.04 mmol) was added to 30% hydrogen peroxide (H_2O_2), 9 mL (80 mmol) and left stirred in an ice cold temperature until all the V_2O_5 dissolves and the solution becomes reddish brown colour (approx. 10 min). This was then added to the above aldehyde solution over a period of 40 min. The resulting homogeneous solution was allowed to stirred at ~ 5^{o}C and the progress of the reaction was monitored by GC. Catalytic turnover number, which is defined as the number of moles of substrate completely converted to product per mole of the catalyst. *p*-Methoxybenzaldehyde (20 mmol) was completely converted into methyl *p*-methoxybenzoate by a catalytic quantity of V_2O_5 (0.04 mmol) and hence the catalytic turnover number is: 20/0.04 = 500.

IC.3.16. Catalytic Turnover Number of Oxidative Esterification of Aldehydes to Corresponding Methyl Esters Using V_2O_5–SPB or SPC.

To a stirred solution of *p*-methoxybenzaldehyde, 0.536 mL (20 mmol) in methanol (20 mL) was added vanadium pentoxide (V_2O_5), 7.24 mg (0.04 mmol) and sodium perborate (SPB), 10.58 g (70 mmol) or sodium percarbonate (SPC), 10.99 g (70 mmol). To this heterogeneous reaction mixture 70% perchloric acid ($HClO_4$), [7 mL (86.8 mmol) for sodium perborate or 14 mL (173.6 mmol) for sodium percarbonate] was added drop wise over a period of 1 h. The reaction mixture was left allowed to stirred at ice cold condition. *p*-Methoxybenzaldehyde (20 mmol) was completely converted into methyl *p*-methoxybenzoate

by a catalytic quantity of V_2O_5 (0.04 mmol) and hence the catalytic turnover number is: 20/0.04 = 500.

IC.3.17. Effect of Induced Polymerisation during the Oxidation of Aldehyde by V_2O_5–SPB or SPC.

To a stirred solution of *p*-methoxybenzaldehyde, 121.7 μL (1 mmol) in methanol (5 mL) was added vanadium pentoxide (V_2O_5), 7.24 mg (0.04 mmol) and sodium perborate (SPB), 529 mg (3.5 mmol) or sodium percarbonate (SPC), 549 mg (3.5 mmol). To the reaction mixture 1 mL of methylacrylate was added. To this heterogeneous reaction mixture 70% perchloric acid ($HClO_4$), [0.350 mL (4.34 mmol) for sodium perborate or 0.7 mL (8.68 mmol) for sodium percarbonate] was added. The progress of the reaction was monitored by TLC and GC. There is no change of methyl acrylate during the oxidation of aldehyde under the reaction conditions. No induced polymerisation of methyl acrylate was observed during the oxidation. There was also no significant change in the reaction rates.

IC.3.18. Effect of Radical Scavenger during the Oxidation of Aldehyde by V_2O_5–SPB or SPC.

Similar to Procedure IC.3.17 (p.74); benzophenone 182.2 mg (1 mmol) was used instead of methyl acrylate. Benzophenone was not converted to diphenyl methanol under the reaction condition. Thus, there was no effect of radical scavenger on the reaction rates.

IC.3.19. General Procedure for Oxidative Deprotection of Acetals Using V_2O_5–H_2O_2.

Vanadium pentoxide (V_2O_5), 36.2 mg (0.2 mmol) was added to 30% hydrogen peroxide (H_2O_2), 2.25 mL (20 mmol) and left stirred in an ice cold temperature until all the V_2O_5 dissolves and the solution becomes reddish brown colour (approx. 10 min). This was then added to an ice cold and stirred solution of acetal, (5 mmol) in acetonitrile (10 mL). The resulting solution was stirred at ~ 5^oC until TLC and GC detected no starting material. The solvent was removed *in vacuo* and the residue was redissolved in ethyl acetate (20 mL). The organic layer was washed with saturated solution of $NaHCO_3$ (2 × 5 mL) then with water (2 × 5 mL) and finally dried over anhy. Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel, hexane:ethyl acetate) to afford the product.

IC.3.20. General Procedure for Oxidative Deprotection of Tetrahydropyranyl Ethers Using V_2O_5–H_2O_2.

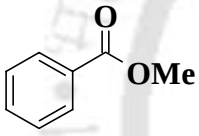
Similar to General Procedure IC.3.19 (p.74); tetrahydropyranyl ether was used instead of acetal and reaction mixture was refluxed.

IC.3.21. General Procedure for Oxidative Deprotection of *tert*-Butyldimethylsilyl Ethers Using V_2O_5–H_2O_2.

Similar to General Procedure IC.3.19 (p.74); *tert*-butyldimethylsilyl ether was used instead of acetal.

IC.4 Spectral Data

IC.4.1 Methyl esters

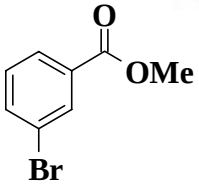


Methyl benzoate (1a)

IR (Neat): 2951, 1722, 1602, 1581, 1494, 1458, 1438, 1320, 1279, 1195, 1180, 1117, 1071, 1028, 968, 940, 823, 717 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 3H, -COOC$\underline{H}_3$), 7.42 (m, 2H, Ar$\underline{H}$), 7.54 (m, 1H, Ar$\underline{H}$), 8.05 (m, 2H, Ar$\underline{H}$)

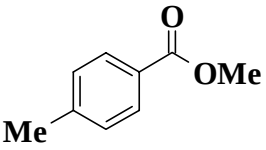
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.00, 128.30, 129.53, 130.21, 132.82, 166.99



Methyl 3-bromobenzoate (2a)

IR (Neat): 2960, 1731, 1572, 1444, 1424, 1291, 1265, 1193, 1122, 1086, 1070, 978, 901, 748, 717 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 3H, -COOC$\underline{H}_3$), 7.27 (t, 1H, Ar$\underline{H}$), 7.63 (d, 1H, Ar$\underline{H}$), 7.92 (d, 1H, Ar$\underline{H}$), 8.10 (s, 1H, Ar$\underline{H}$)

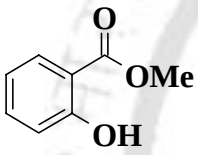


Methyl 4-methylbenzoate (3a)

IR (Neat): 2952, 1728, 1618, 1579, 1512, 1440, 1409, 1301, 1284, 1217, 1179, 1109, 1021, 970, 847, 760 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H, ArC$\underline{H}_3$), 3.89 (s, 3H, -COOC$\underline{H}_3$), 7.22 (d, 2H, Ar$\underline{H}$), 7.92 (d, 2H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.61, 51.89, 127.39, 129.01, 129.54, 143.46, 167.06

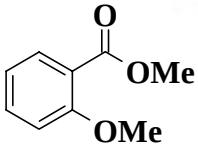


Methyl 2-hydroxybenzoate (4a)

IR (Neat): 3190, 2861, 1682, 1619, 1587, 1489, 1440, 1341, 1312, 1258, 1220, 1163, 1137, 1090, 1038, 968, 867, 858, 805, 771, 709 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.91 (s, 3H, -COOC$\underline{H}_3$), 6.85 (m, 1H, Ar$\underline{H}$), 6.96 (m, 1H, Ar$\underline{H}$), 7.42 (m, 1H, Ar$\underline{H}$), 7.80 (m, 1H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 52.23, 112.33, 117.50, 119.09, 129.85, 135.62, 161.54, 170.49

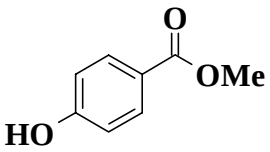


Methyl 2-methoxybenzoate (5a)

IR (Neat): 3000, 2852, 2842, 1730, 1600, 1581, 1496, 1463, 1444, 1305, 1260, 1185, 1178, 1143, 1088, 1045, 1020, 967, 826, 760, 709 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.88 (s, 6H, 2 x -OC$\underline{H}_3$), 6.95 (m, 2H, Ar$\underline{H}$), 7.45 (t, 1H, Ar$\underline{H}$), 7.78 (d, 1H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 51.90, 55.96, 112.06, 120.09, 120.12, 131.56, 133.40, 159.07, 166.62

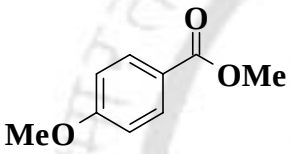


Methyl 4-hydroxybenzoate (6a)

IR (Neat): 3300, 2922, 2858, 1677, 1610, 1595, 1523, 1454, 1376, 1323, 1285, 1247, 1171, 1140, 1109, 1020, 857, 765, 700 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.9 (s, 3H, -COOC<u>*H*</u>$_3$), 6.88 (d, 2H, Ar<u>*H*</u>), 7.84 (d, 2H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 51.53, 115.26, 120.22, 131.35, 161.89, 165.96

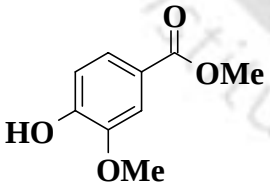


Methyl 4-methoxybenzoate (7a)

IR (Neat): 3000, 2942, 2823, 1720, 1604, 1581, 1518, 1445, 1438, 1323, 1280, 1260, 1175, 1120, 1104, 1023, 968, 854, 828, 768 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (s, 3H, -COOC<u>*H*</u>$_3$), 3.88 (s, 3H, ArOC<u>*H*</u>$_3$), 6.91 (d, 2H, Ar<u>*H*</u>), 7.99 (d, 2H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 51.81, 55.36, 113.54, 122.52, 131.52, 163.25, 166.77

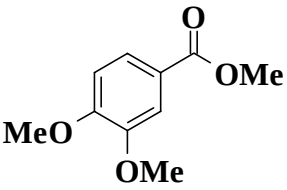


Methyl 4-hydroxy-3-methoxybenzoate (8a)

IR (Neat): 3540, 2918, 2850, 1700, 1600, 1518, 1375, 1295, 1282, 1260, 1190, 1120, 1028, 978, 875, 780, 767, 730 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 3H, -COOC<u>*H*</u>$_3$), 4.01 (s, 3H, ArOC<u>*H*</u>$_3$), 6.94 (d, 1H, Ar<u>*H*</u>), 7.54 (s, 1H, Ar<u>*H*</u>), 7.63 (d, 1H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 51.93, 56.08, 111.85, 114.15, 122.23, 124.18, 146.24, 150.11, 166.89

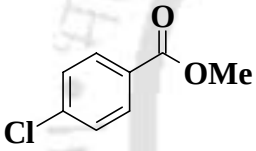


Methyl 3,4-dimethoxybenzoate (9a)

IR (Neat): 2960, 2929, 2856, 1722, 1698, 1620, 1523, 1468, 1438, 1417, 1298, 1269, 1236, 1190, 1166, 1140, 1111, 1040, 1023, 993, 743 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.88 (s, 3H, -COOC$\underline{H}_3$), 3.93 (s, 6H, 2 × ArOC$\underline{H}_3$), 6.88 (d, 1H, Ar$\underline{H}$), 7.53 (s, 1H, Ar$\underline{H}$), 7.67 (d, 1H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 51.91, 55.98, 110.30, 112.06, 122.70, 123.54, 148.63, 152.97, 166.75

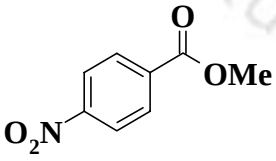


Methyl 4-chlorobenzoate (10a)

IR (Neat): 3000, 2951, 1726, 1600, 1591, 1438, 1400, 1283, 1277, 1198, 1179, 1128, 1099, 1020, 966, 851, 834, 763, 728, 682, 637, 529 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.90 (s, 3H, -COOC$\underline{H}_3$), 7.39 (d, 2H, Ar$\underline{H}$), 7.96 (d, 2H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 52.20, 128.66, 130.93, 139.32, 166.10

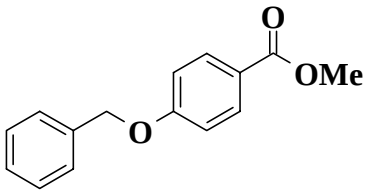


Methyl 4-nitrobenzoate (11a)

IR (KBr): 3118, 2980, 2925, 2857, 1720, 1610, 1605, 1524, 1443, 1356, 1280, 1120, 1238, 1190, 1180, 1120, 1028, 978, 875, 780, 767, 730 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.98 (s, 3H, -COOC$\underline{H}_3$), 8.20 (d, 2H, Ar$\underline{H}$), 8.29 (d, 2H, Ar$\underline{H}$)

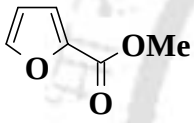
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.79, 123.50, 130.68, 135.51, 150.57, 165.10



Methyl 4-benzyloxybenzoate (12a)

IR (KBr): 1722, 1610, 1525, 1466, 1445, 1397, 1328, 1285, 1263, 1178, 1119, 1018, 858, 783, 752, 709, 666 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.93 (s, 3H, -COOC$\underline{H}_3$), 5.11 (s, 2H, -OC$\underline{H}_2$Ar), 7.00 (d, 2H, Ar$\underline{H}$), 7.38 (m, 5H, Ar$\underline{H}$), 8.00 (d, 2H, Ar$\underline{H}$)

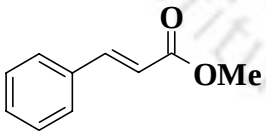


Methyl 2-furoate (13a)

IR (Neat): 3140, 3000, 2958, 1738, 1585, 1575, 1480, 1395, 1305, 1225, 1200, 1178, 1120, 1080, 1022, 976, 918, 885, 800, 765 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.90 (s, 3H, -COOC$\underline{H}_3$), 6.52 (dd, 1H, Ar$\underline{H}$), 7.19 (d, 1H, Ar$\underline{H}$), 7.59 (m, 1H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 51.86, 111.82, 117.88, 144.62, 146.27, 159.07

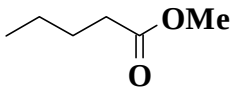


Methyl *trans*-cinnamate (14a)

IR (Neat): 3067, 3032, 2957, 2842, 1720, 1640, 1559, 1498, 1458, 1437, 1326, 1319, 1279, 1203, 1171, 1078, 1040, 980, 937, 928, 771, 717 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 3H, -COOC$\underline{H}_3$), 6.46 (d, 1H, ArCH=C$\underline{H}$-), 7.37 (m, 3H, Ar$\underline{H}$), 7.50 (m, 2H, Ar$\underline{H}$), 7.69 (d, 1H, ArC$\underline{H}$=CH-)

^{13}C NMR (100 MHz, $CDCl_3$): δ 51.64, 117.73, 128.00, 128.82, 130.22, 134.30, 144.77, 167.31

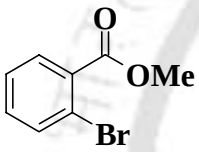


Methyl pentanoate (15a)

IR (Neat): 2960, 2878, 1743, 1440, 1363, 1260, 1178, 1116, 1020, 990, 838, 759 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, 3H, -$CH_2CH_2CH_3$), 1.28-1.42 (m, 2H, -$CH_2CH_2CH_3$), 1.60 (m, 2H, -$CH_2CH_2CH_3$), 2.31 (t, 2H, -CH_2COOCH_3), 3.68 (s, 3H, -$COOCH_3$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 13.69, 22.32, 27.11, 33.86, 51.36, 174.18

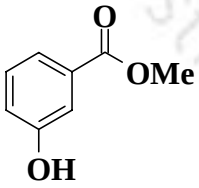


Methyl 2-bromobenzoate (16a)

IR (Neat): 2960, 1735, 1572, 1475, 1439, 1296, 1265, 1198, 1127, 1070, 978, 901, 835, 809, 748, 722 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.92 (s, 3H, -$COOCH_3$), 7.32 (m, 1H, Ar*H*), 7.68 (m, 1H, Ar*H*), 7.97 (m, 1H, Ar*H*), 8.18 (m, 1H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 52.4, 122.5, 128.2, 129.9, 132.1, 132.6, 135.9

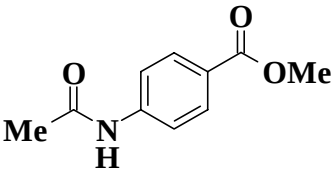


Methyl 3-hydroxybenzoate (17a)

IR (Neat): 3380, 2922, 2856, 1698, 1600, 1460, 1312, 1241, 1110, 975, 887, 799 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.90 (s, 3H, -$COOCH_3$), 7.08 (m, 1H, Ar*H*), 7.28 (m, 1H, Ar*H*), 7.57 (m, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 52.44, 116.44, 120.54, 121.75, 129.70, 131.11, 156.11, 167.78

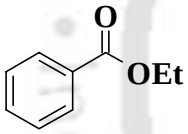


Methyl 4-*N*-acetamidobenzoate (19a)

IR (KBr): 3370, 2924, 1690, 1613, 1598, 1526, 1444, 1413, 1367, 1316, 1255, 1178, 1122, 999, 860, 804, 768, 702 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.22 (s, 3H, -NHCOC$\underline{H}_3$), 3.90 (s, 3H, -COOC$\underline{H}_3$), 7.60 (d, 2H, Ar$\underline{H}$), 8.00 (d, 2H, Ar$\underline{H}$)

IC.4.2 Ethyl esters

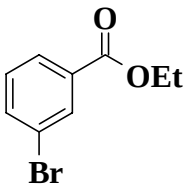


Ethyl benzoate (1b)

IR (Neat): 2891, 1720, 1604, 1583, 1456, 1397, 1371, 1318, 1279, 1179, 1109, 1072, 1031, 740, 877, 856, 716 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (t, 3H, -COOCH$_2$C$\underline{H}_3$), 4.37 (q, 2H, -COOC$\underline{H}_2$CH$_3$), 7.41 (m, 2H, Ar$\underline{H}$), 7.52 (m, 1H, Ar$\underline{H}$), 8.04 (m, 2H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.33, 60.88, 128.25, 129.49, 130.54, 132.71, 166.52



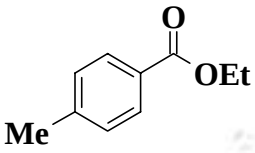
Ethyl 3-bromobenzoate (2b)

IR (Neat): 2981, 1724, 1571, 1478, 1368, 1298, 1261, 1121, 1094, 1070, 1020, 882, 750, 718, 677 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (t, 3H, -COOCH$_2$C$\underline{H}_3$), 4.36 (q, 2H, -COOC$\underline{H}_2$CH$_3$),

7.29 (t, 1H, Ar*H*), 7.64 (d, 1H, Ar*H*), 7.95 (d, 1H, Ar*H*), 8.17 (s, 1H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.27, 61.34, 122.33, 128.04, 129.81, 132.33, 132.45, 135.65, 165.11

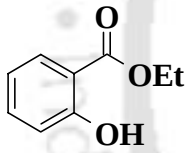


Ethyl 4-methylbenzoate (3b)

IR (Neat): 2985, 1726, 1613, 1562, 1511, 1459, 1367, 1275, 1178, 1106, 1024, 758 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (t, 3H, -$COOCH_2CH_3$), 2.38 (s, 3H, $ArCH_3$), 4.35 (q, 2H, -$COOCH_2CH_3$), 7.21 (d, 2H, Ar*H*), 7.93 (d, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.34, 21.61, 60.70, 127.74, 128.96, 129.50, 143.32, 166.60

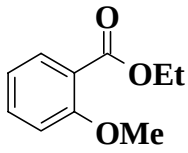


Ethyl 2-hydroxybenzoate (4b)

IR (Neat): 3150, 3182, 2983, 1679, 1619, 1587, 1489, 1400, 1379, 1330, 1309, 1256, 1220, 1160, 1139, 1097, 1038, 1019, 862, 820, 803, 760, 703 cm^{-1}

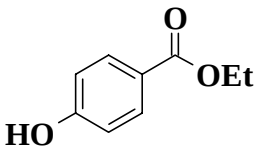
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50 (t, 3H, -$COOCH_2CH_3$), 4.40 (q, 2H, -$COOCH_2CH_3$), 6.85 (t, 1H, Ar*H*), 6.96 (d, 1H, Ar*H*), 7.45 (t, 1H, Ar*H*), 7.85 (d, 1H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.19, 61.36, 112.64, 117.51, 119.00, 129.86, 135.49, 161.68, 170.13



Ethyl 2-methoxybenzoate (5b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, 3H, -$COOCH_2CH_3$), 3.95 (s, 3H, $ArOCH_3$), 4.15 (q, 2H, -$COOCH_2CH_3$), 6.90 (m, 2H, Ar*H*), 7.45 (m, 1H, Ar*H*), 7.80 (m, 1H, Ar*H*)

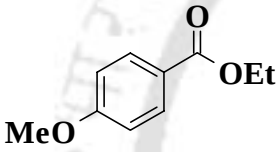


Ethyl 4-hydroxybenzoate (6b)

IR (Neat): 3220, 2922, 2859, 1675, 1610, 1597, 1523, 1451, 1377, 1320, 1289, 1243, 1176, 1140, 1108, 1022, 852, 776, 700 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, 3H, -$COOCH_2C\underline{H}_3$), 4.30 (q, 2H, -$COOC\underline{H}_2CH_3$), 5.42 (s, 1H, Ar$O\underline{H}$), 6.83 (d, 2H, Ar$\underline{H}$), 7.87 (d, 2H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.33, 60.17, 115.16, 121.20, 131.40, 161.78, 166.22

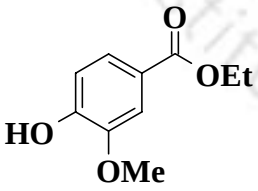


Ethyl 4-methoxybenzoate (7b)

IR (Neat): 2880, 1717, 1696, 1582, 1517, 1468, 1425, 1396, 1374, 1319, 1280, 1260, 1175, 1102, 1032, 852, 773, 700 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (t, 3H, -$COOCH_2C\underline{H}_3$), 3.83 (s, 3H, Ar$OC\underline{H}_3$), 4.33 (q, 2H, -$COOC\underline{H}_2CH_3$), 6.91 (d, 2H, Ar$\underline{H}$), 7.99 (d, 2H, Ar$\underline{H}$)

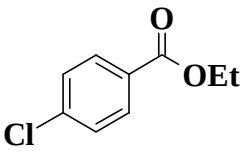
^{13}C NMR (100 MHz, $CDCl_3$): δ 14.38, 55.34, 60.59, 113.48, 122.87, 131.46, 163.18, 166.29



Ethyl 4-hydroxy-3-methoxybenzoate (8b)

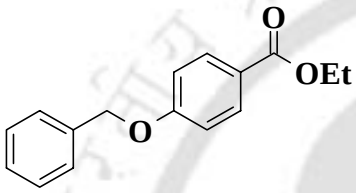
IR (Neat): 2980, 2842, 1721, 1608, 1511, 1465, 1419, 1372, 1347, 1296, 1270, 1229, 1178, 1137, 1106, 1024, 942, 881, 830, 773, 732 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (t, 3H, -$COOCH_2C\underline{H}_3$), 3.95 (s, 3H, Ar$OC\underline{H}_3$), 4.35 (q, 2H, -$COOC\underline{H}_2CH_3$), 5.6 (m, 2H, Ar$\underline{H}$), 6.85 (m, 1H, Ar$\underline{H}$), 7.6 (m, 1H, Ar$\underline{H}$)



Ethyl 4-chlorobenzoate (10b)

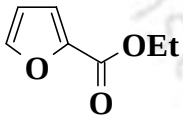
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (t, 3H, -COOCH$_2$C$\underline{H}_3$), 4.40 (q, 2H, -COOC$\underline{H}_2$CH$_3$), 7.45 (d, 2H, Ar$\underline{H}$), 8.00 (d, 2H, Ar$\underline{H}$)



Ethyl 4-benzyloxybenzoate (12b)

IR (KBr): 2980, 2934, 1713, 1606, 1583, 1560, 1540, 1511, 1456, 1422, 1384, 1370, 1315, 1281, 1258, 1174, 1108, 1024, 852, 774, 745, 699 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (t, 3H, -COOCH$_2$C$\underline{H}_3$), 4.33 (q, 2H, -COOC$\underline{H}_2$CH$_3$), 5.11 (s, 2H, - OC$\underline{H}_2$Ar), 6.96 (d, 2H, Ar$\underline{H}$), 7.31-7.53 (m, 5H, Ar$\underline{H}$), 7.99 (d, 2H, Ar$\underline{H}$)

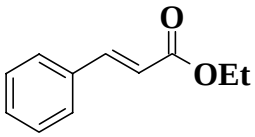


Ethyl 2-furoate (13b)

IR (Neat): 3152, 2981, 1732, 1591, 1478, 1402, 1391, 1368, 1300, 1233, 1183, 1120, 1079, 1014, 938, 886, 863, 764, 620, 598 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (t, 3H, -COOCH$_2$C$\underline{H}_3$), 4.37 (q, 2H, -COOC$\underline{H}_2$CH$_3$), 6.5 (dd, 1H, Ar$\underline{H}$), 7.18 (d, 1H, Ar$\underline{H}$), 7.57 (m, 1H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.34, 60.91, 111.73, 117.63, 144.98, 146.10, 158.67



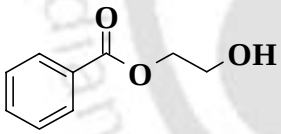
Ethyl *trans*-cinnamate (14b)

IR (Neat): 2980, 1717, 1640, 1580, 1496, 1451, 1368, 1318, 1272, 1202, 1181, 1098, 1039, 981, 867, 840, 771, 718, 686 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, 3H, -$COOCH_2CH_3$), 4.26 (q, 2H, -$COOCH_2CH_3$), 6.43 (d, 1H, ArCH=C*H*-), 7.35 (m, 3H, Ar*H*), 7.5 (m, 2H, Ar*H*), 7.57 (d, 1H, ArC*H*=CH-)

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.32, 60.44, 118.21, 127.97, 128.80, 130.14, 134.38, 144.48, 166.87

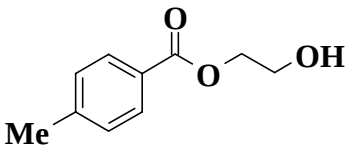
IC.4.3 Hydroxy-ethyl esters



Benzoic acid 2-hydroxy-ethyl ester (1c)

IR (Neat): 3418, 2953, 2882, 1718, 1601, 1452, 1373, 1316, 1277, 1177, 1123, 1070, 906, 711 cm^{-1}

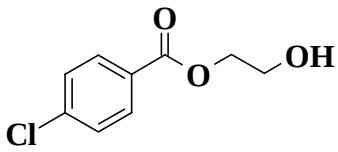
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.95 (s, 1H, -O*H*), 3.97 (t, 2H, -$COOCH_2CH_2$OH), 4.49 (t, 2H, -$COOCH_2CH_2$OH), 7.52 (m, 3H, Ar*H*), 8.09 (m, 2H, Ar*H*)



4-Methyl-benzoic acid 2-hydroxy-ethyl ester (3c)

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

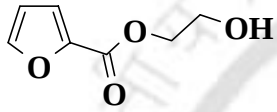
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H, ArCH_3), 3.91 (t, 2H, -$COOCH_2CH_2$OH), 4.42 (t, 2H, -$COOCH_2CH_2$OH), 7.29 (d, 2H, Ar*H*), 7.95 (d, 2H, Ar*H*)



4-Chloro-benzoic acid 2-hydroxy-ethyl ester (10c)

IR (Neat): 1724 cm^{-1}

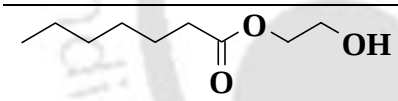
^1H NMR (400 MHz, $CDCl_3$): δ 3.98 (t, 2H, -$COOCH_2C\underline{H}_2OH$), 4.45 (t, 2H, -$COOC\underline{H}_2CH_2OH$), 7.45 (d, 2H, Ar$\underline{H}$), 8.00 (d, 2H, Ar$\underline{H}$)



Furan-2-carboxylic acid 2-hydroxy-ethyl ester (13c)

IR (Neat): 3391, 2954, 2885, 1722, 1647, 1455, 1380, 1258, 1087, 1044, 884 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 2.1 (s, 1H, -O$\underline{H}$), 3.82 (t, 2H, -$COOCH_2C\underline{H}_2OH$), 4.21 (t, 2H, -$COOC\underline{H}_2CH_2OH$), 6.53 (dd, 1H, Ar$\underline{H}$), 7.26 (d, 1H, Ar$\underline{H}$), 7.59 (m, 1H, Ar$\underline{H}$)

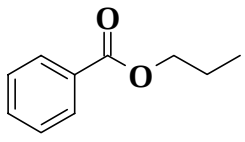


Heptanoic acid 2-hydroxy-ethyl ester (18c)

IR (Neat): 1734 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.9 (t, 3H, -$C\underline{H}_3$), 1.25-1.63 (m, 8H, -$(C\underline{H}_2)_4CH_3$), 2.30 (t, 2H, -$OCOC\underline{H}_2$-), 3.77 (t, 2H, -$COOCH_2C\underline{H}_2OH$), 4.18 (t, 2H, -$COOC\underline{H}_2CH_2OH$)

IC.4.4 Propyl ester



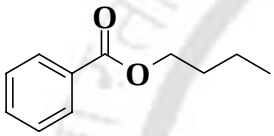
Propyl benzoate (1d)

IR (Neat): 2972, 1720, 1603, 1584, 1457, 1392, 1319, 1279, 1180, 1107, 1076, 1035, 942, 714 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.03 (t, 3H, -$COOCH_2CH_2CH_3$), 1.78 (m, 2H, -$COOCH_2CH_2CH_3$), 4.28 (t, 2H, -$COOCH_2CH_2CH_3$), 7.43 (m, 2H, Ar*H*), 7.53 (m, 1H, Ar*H*), 8.04 (m, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 10.53, 22.12, 66.49, 128.25, 129.47, 130.46, 132.73, 168.58

IC.4.5 Butyl ester



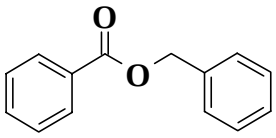
Butyl benzoate (1e)

IR (Neat): 2960, 2878, 1720, 1603, 1583, 1472, 1456, 1384, 1318, 1279, 1180, 1116, 1072, 1027, 942, 847, 718, 690 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, 3H, -COO-$(CH_2)_3CH_3$), 1.47 (m, 2H, -COO-$(CH_2)_2CH_2CH_3$), 1.75 (m, 2H, -COO-$CH_2CH_2CH_2CH_3$), 4.28 (t, 2H, -COO-$CH_2(CH_2)_2CH_3$), 7.42 (m, 2H, Ar*H*), 7.53 (m, 1H, Ar*H*), 8.05 (m, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 13.75, 19.30, 30.83, 64.79, 128.26, 129.50, 130.59, 132.70, 166.58

IC.4.6 Benzyl ester



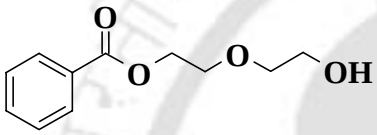
Benzyl benzoate (1f)

IR (Neat): 3065, 3038, 2955, 1720, 1603, 1586, 1498, 1454, 1379, 1317, 1270, 1176, 1108, 1072, 1029, 963, 917, 808, 757, 716 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35 (s, 2H, ArC*H*$_2$O-), 7.28-7.55 (m, 8H, Ar*H*), 8.06 (m, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 66.61, 128.07, 128.14, 128.28, 128.50, 129.61, 130.05, 132.92, 135.98, 166.27

IC.4.7 Hydroxy-ethoxy-ethyl Ester



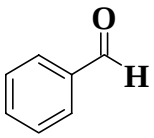
Benzoic acid 2-(2-hydroxy-ethoxy)-ethyl ester (1g)

IR (Neat): 3429, 2949, 2874, 1712, 1600, 1450, 1381, 1354, 1274, 1109, 1066, 1024, 938, 890, 714 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.00 (m, 1H, -O*H*), 3.66 (m, 2H, -OCH$_2$C*H*$_2$OH), 3.75 (m, 2H, -OC*H*$_2$CH$_2$OH), 3.86 (m, 2H, -COOCH$_2$C*H*$_2$O-), 4.53 (m, 2H, -COOC*H*$_2$CH$_2$O-), 7.40-7.62 (m, 3H, Ar*H*), 8.09 (m, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 61.79, 64.05, 69.28, 72.48, 128.4, 129.7, 133.1

IC.4.8 Aldehydes

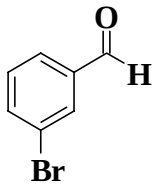


Benzaldehyde (1)

IR (Neat): 2820, 2738, 1702, 1599, 1584, 1458, 1395, 1396, 1205, 1168, 830, 749 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (m, 2H, Ar*H*), 7.63 (m, 1H, Ar*H*), 7.87 (m, 2H, Ar*H*), 10.2 (s, 1H, ArC*H*O)

^{13}C NMR (100 MHz, $CDCl_3$): δ 128.93, 129.64, 134.34, 136.44, 192.15

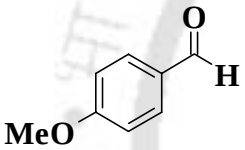


3-Bromobenzaldehyde (2)

IR (Neat): 2830, 2631, 1700, 1572, 1465, 1432, 1385, 1280, 1191, 1065, 880, 854, 788, 709, 673, 642 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (t, 1H, Ar*H*), 7.76 (dd, 2H, Ar*H*), 7.98 (s, 1H, Ar*H*), 9.95 (s, 1H, ArC*H*O)

^{13}C NMR (100 MHz, $CDCl_3$): δ 123.29, 128.25, 130.53, 132.21, 137.15, 137.99, 190.46

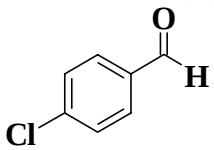


4-Methoxybenzaldehyde (7)

IR (Neat): 2840, 1700, 1682, 1600, 1580, 1516, 1460, 1428, 1396, 1318, 1262, 1220, 1142, 1111, 1030, 836, 768, 644, 610, 600, 520 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.97 (s, 3H, ArOCH_3), 6.98 (d, 2H, Ar*H*), 7.82 (d, 2H, Ar*H*), 9.87 (s, 1H, ArC*H*O)

^{13}C NMR (100 MHz, $CDCl_3$): δ 55.54, 114.29, 129.98, 131.88, 164.57, 190.60

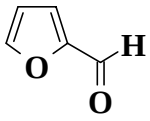


4-Chlorobenzaldehyde (10)

IR (Neat): 2838, 2738, 1705, 1597, 1570, 1485, 1386, 1299, 1286, 1210, 1164, 1095, 1017, 840, 820, 700, 545 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, 2H, Ar*H*), 7.82 (d, 2H, Ar*H*), 9.92 (s, 1H, ArC*H*O)

^{13}C NMR (100 MHz, $CDCl_3$): δ 129.39, 130.82, 137.74, 140. 86, 190.63

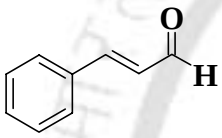


2-Furaldehyde (13)

IR (Neat): 3330, 2851, 2817, 1695, 1676, 1571, 1478, 1462, 1396, 1366, 1280, 1160, 1082, 1021, 932, 885, 757 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.63 (dd, 1H, Ar*H*), 7.28 (d, 1H, Ar*H*), 7.72 (m, 1H, Ar*H*), 9.67 (s, 1H, ArC*H*O)

^{13}C NMR (100 MHz, $CDCl_3$): δ 112.59, 121.05, 148.06, 152.95, 177.78



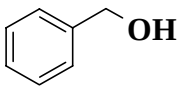
***trans*-Cinnamaldehyde (14)**

IR (Neat): 3060, 2820, 2740, 1680, 1628, 1578, 1498, 1454, 1296, 14257, 1123, 1009, 973, 750, 691, 607, 586 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.7 (dd, 1H, ArCH=C*H*-), 7,45 (m, 3H, Ar*H*), 7.50 (d, 1H, ArC*H*=CH-), 7.55 (m, 2H, Ar*H*), 9.68 (d, 1H, ArCH=CHC*H*O)

^{13}C NMR (100 MHz, $CDCl_3$): δ 128.41, 128.57, 129.03, 131.16, 134.01, 152.50, 193.39

IC.4.9 Alcohols

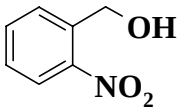


Benzyl alcohol (29)

IR (Neat): 3330, 3030, 2872, 1496, 1457, 1209, 1082, 1041, 1021, 915, 818, 756 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.85 (t, 1H, -O*H*), 4.84 (d, 2H, ArCH_2OH), 7.28 (m, 5H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 65.25, 127.18, 127.72, 128.68, 141.09

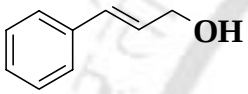


2-Nitrobenzyl alcohol (30)

IR (Neat): 3251, 2822, 2859, 1519, 1462, 1375, 1340, 1189, 1085, 1039, 860, 795 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 4.98 (brs, 2H, ArC*H*$_2$OH), 5.44 (brs, 1H, -O*H*), 7.46 (t, 1H, Ar*H*), 7.70 (t, 1H, Ar*H*), 7.89 (d, 1H, Ar*H*), 8.00 (d, 1H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 60.23, 124.04, 127.38, 128.26, 133.42, 138.48, 146.72

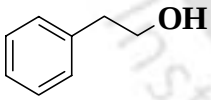


Cinnamyl alcohol (32)

IR (Neat): 3360, 3029, 2862, 1659, 1599, 1579, 1497, 1450, 1200, 1095, 1070, 1009, 968, 749, 737, 695 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 2.29 (brs, 1H, -O*H*), 4.28 (d, 2H, -C*H*$_2$OH), 6.34 (m, 1H, ArCH=C*H*-), 6.57 (d, 2H, ArC*H*=CH-), 7.28 (m, 5H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 63.50, 126.38, 127.57, 128.43, 128.50, 130.91, 136.58



Phenethyl alcohol (33)

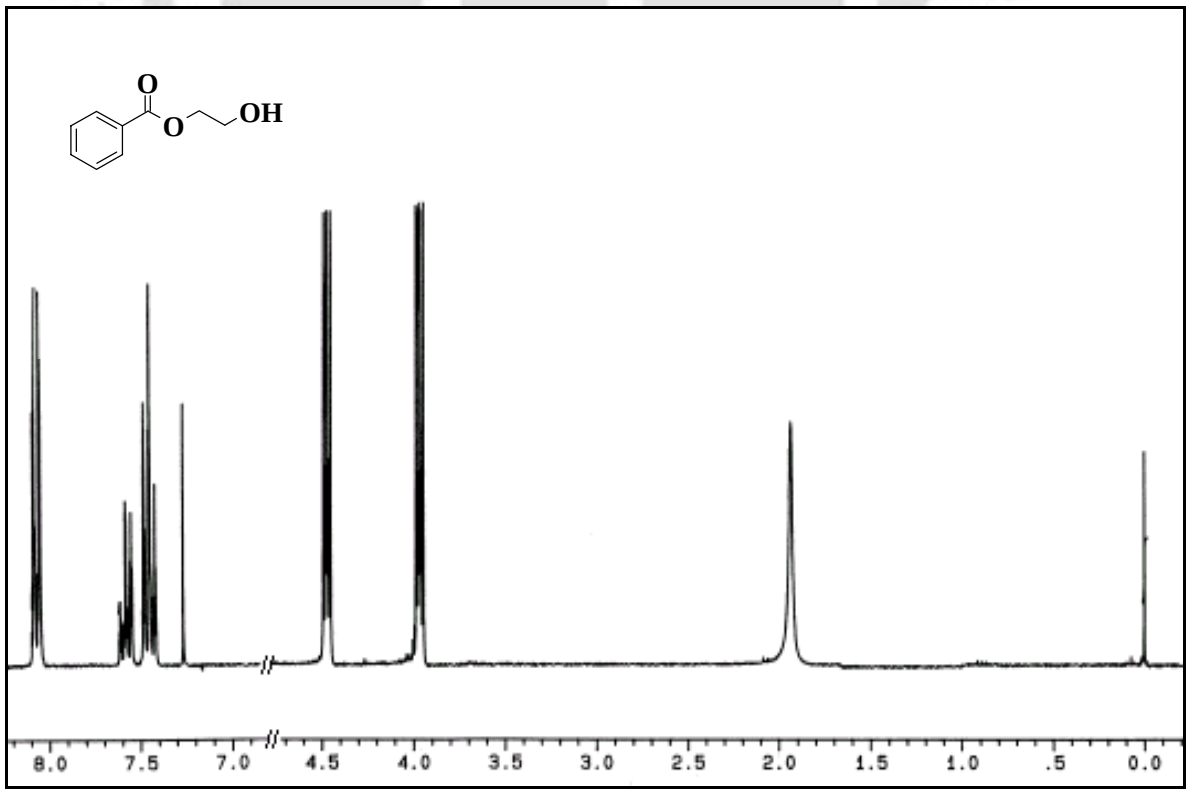
IR (Neat): 3340, 2940, 2878, 1604, 1500, 1455, 1180, 1047, 909, 856, 750, 700 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 2.17 (br, 1H, -O*H*), 2.82 (t, 2H, -C*H*$_2$OH), 3.77 (t, 2H, ArC*H*$_2$CH$_2$OH), 7.22 (m, 5H, Ar*H*)

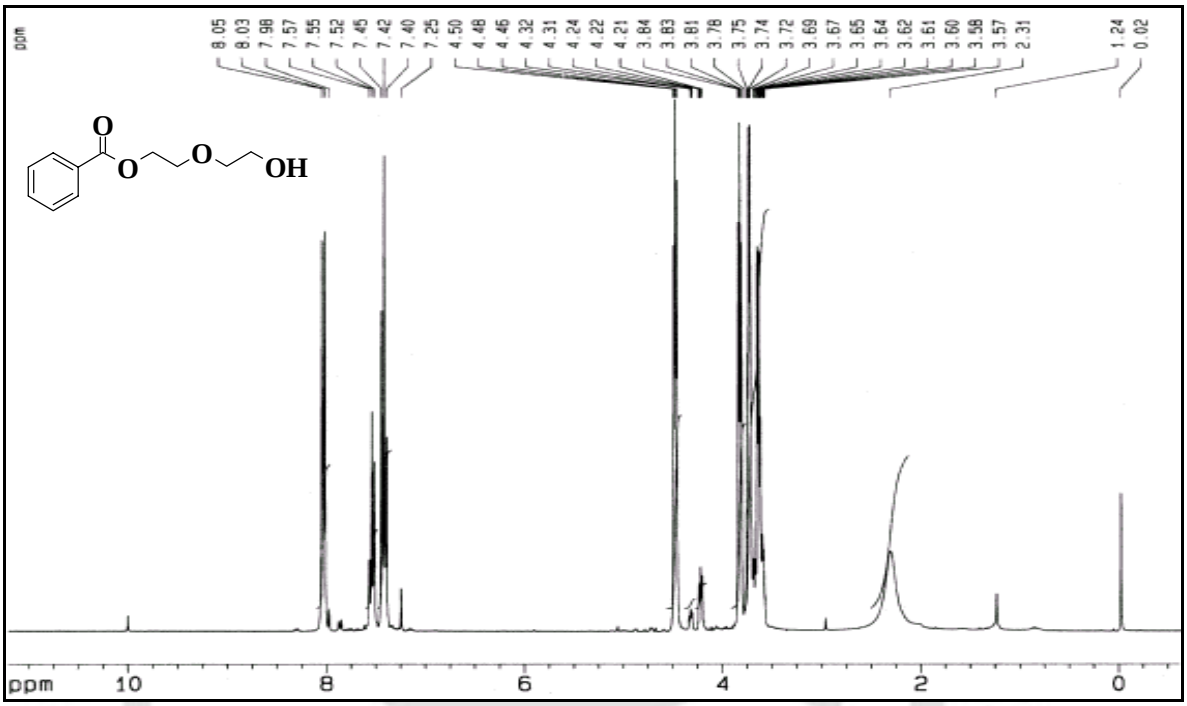
^{13}C NMR (100 MHz, $CDCl_3$): δ 39.12, 63.51, 126.31, 128.44, 128.94, 138.50

ID Spectra

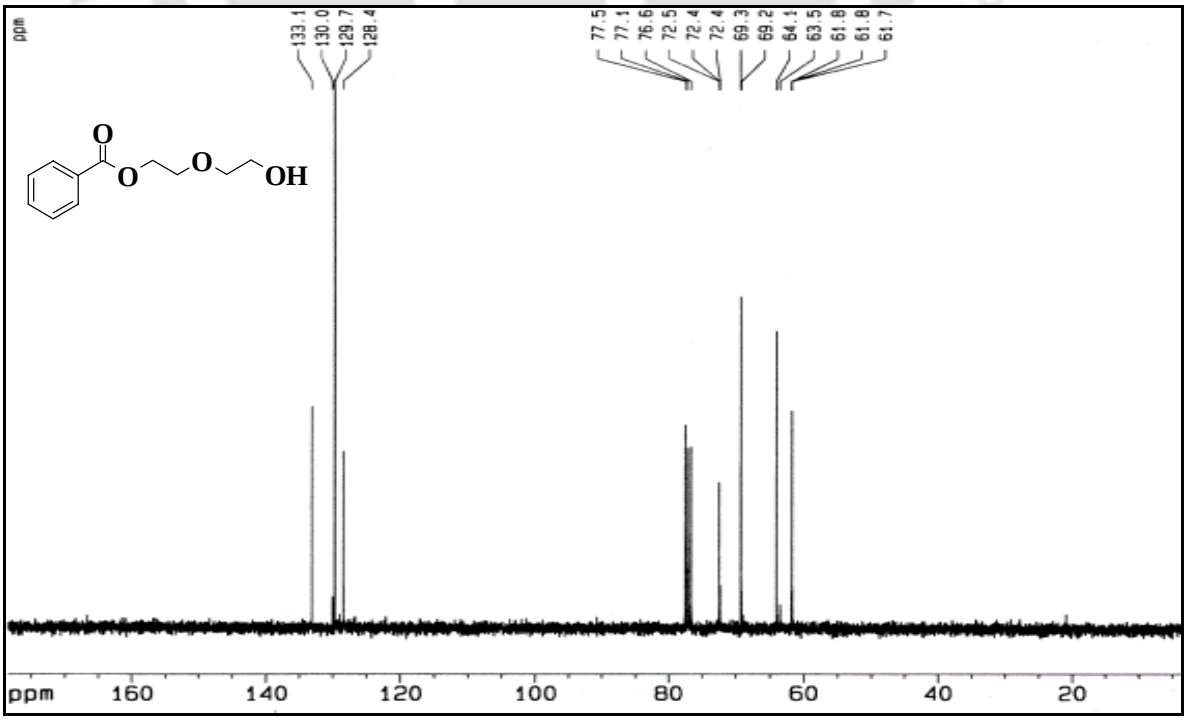
^{1}H NMR (200 MHz, $CDCl_3$): Benzoic acid 2-hydroxy-ethyl ester (1c)



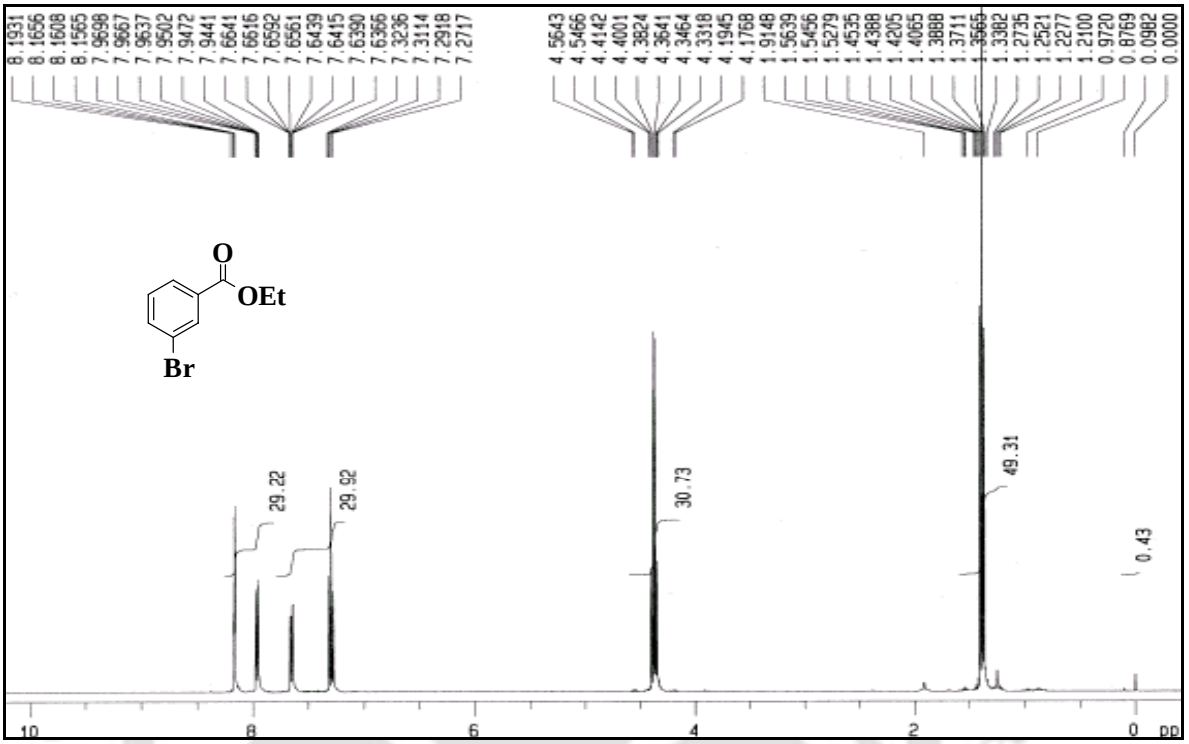
^{1}H NMR (400 MHz, $CDCl_3$): Diethylene glycol monobenzoate (1g)



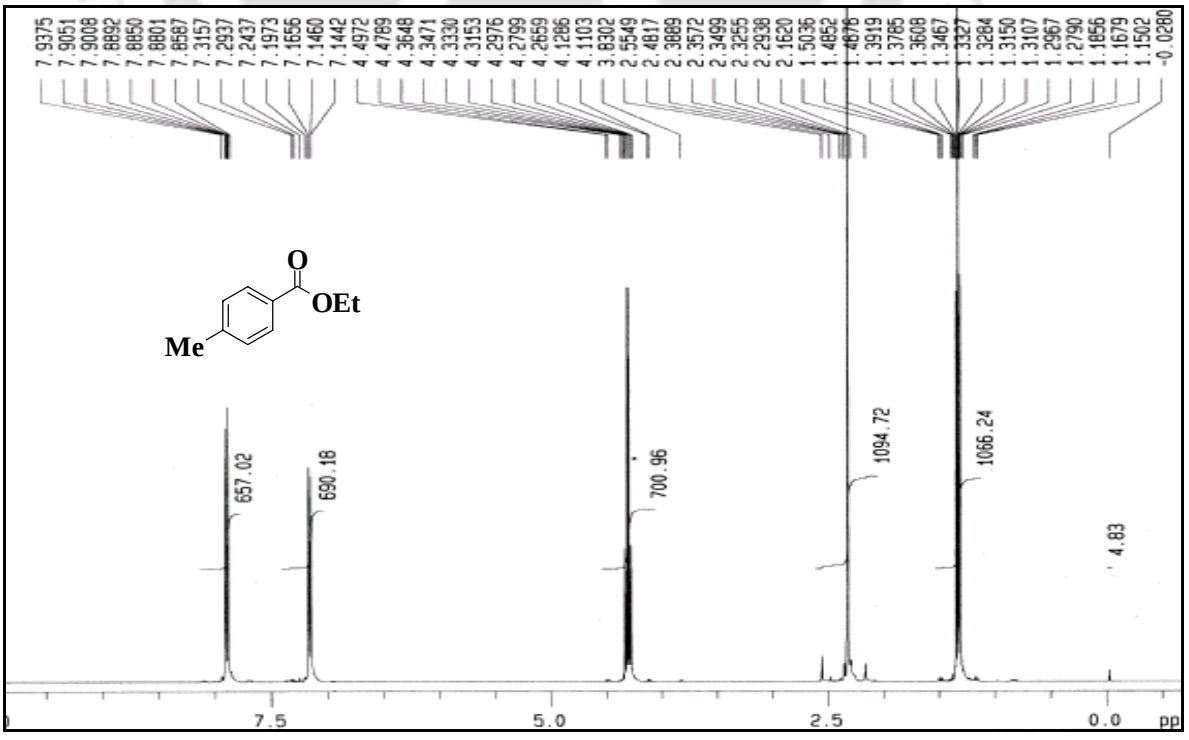
^{13}C NMR (100 MHz, $CDCl_3$): Diethylene glycol monobenzoate (1g)



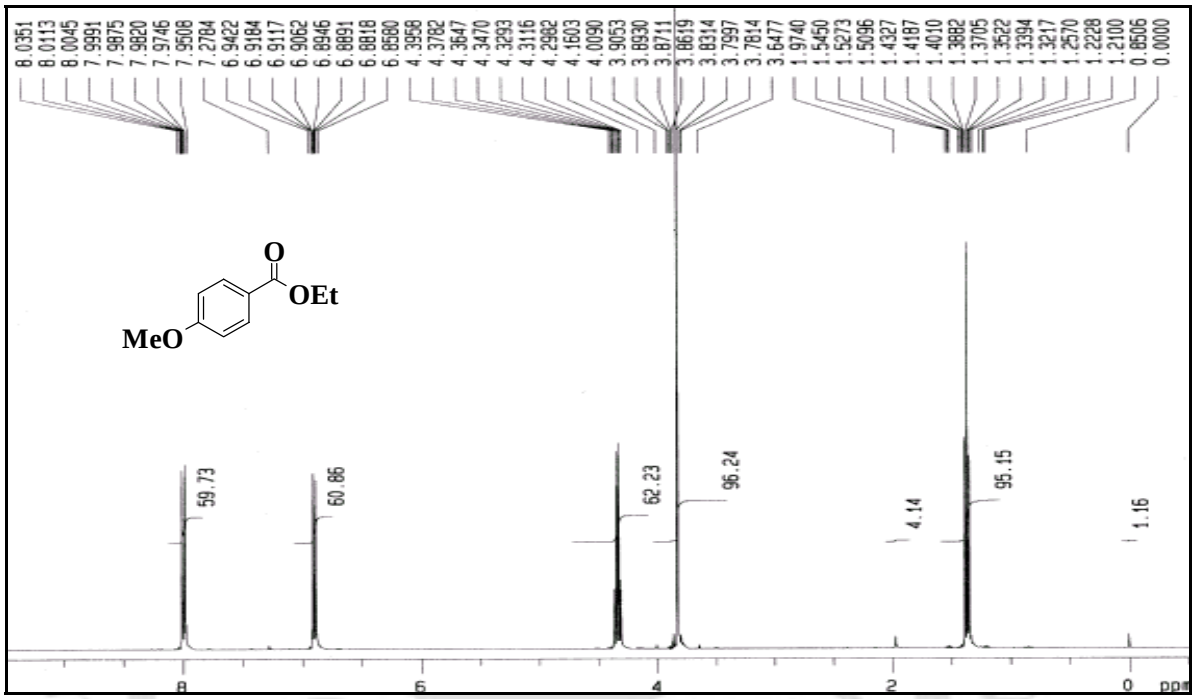
^{1}H NMR (400 MHz, $CDCl_3$): Ethyl 3-bromobenzoate (2b)



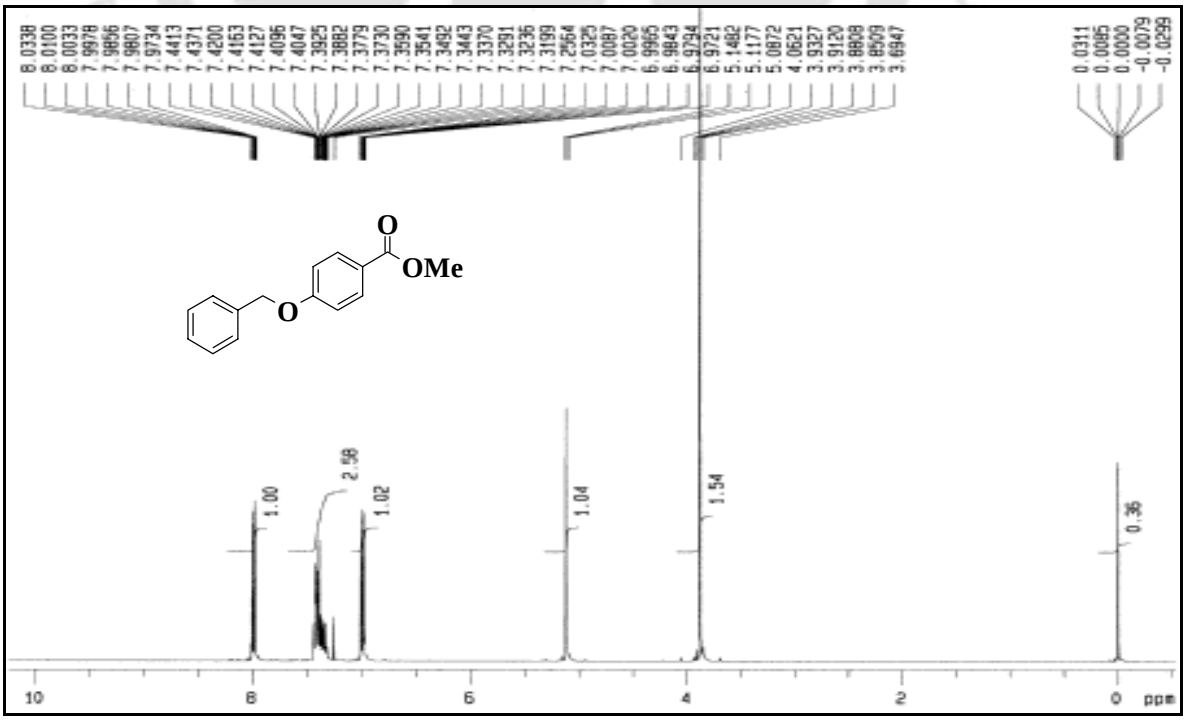
^{1}H NMR (400 MHz, $CDCl_3$): Ethyl 4-methylbenzoate (3b)



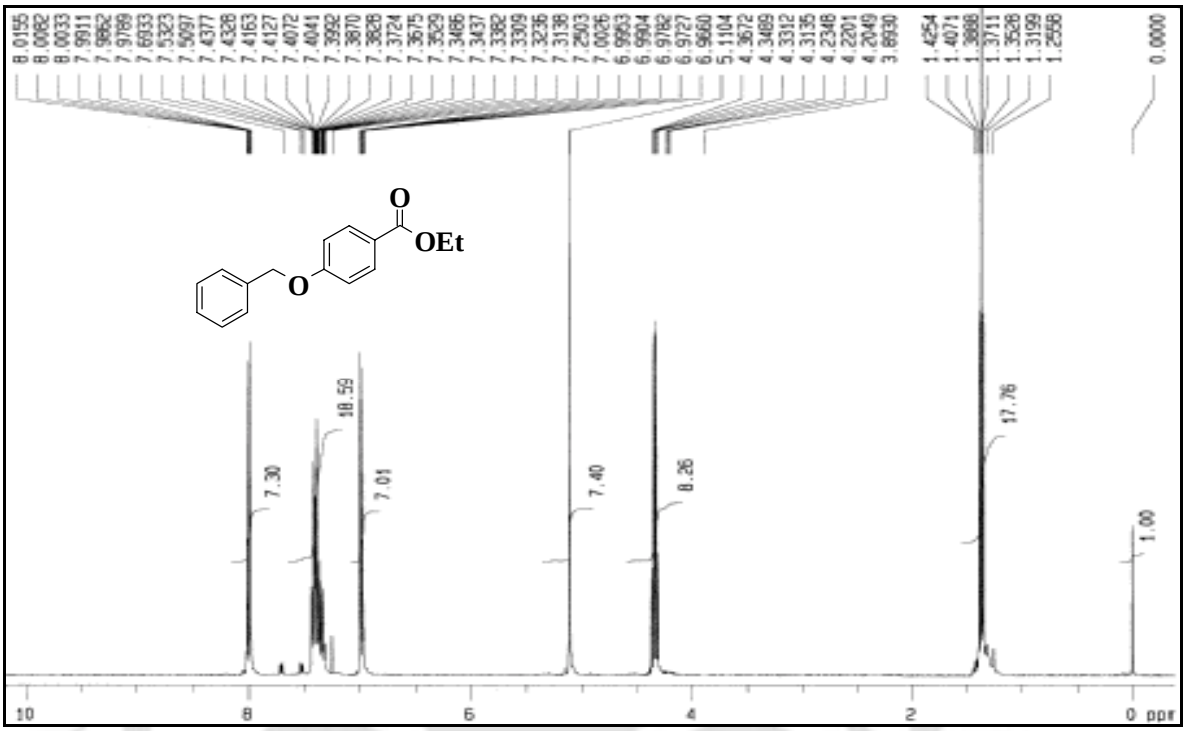
^{1}H NMR (400 MHz, $CDCl_3$): Ethyl 4-methoxybenzoate (7b)



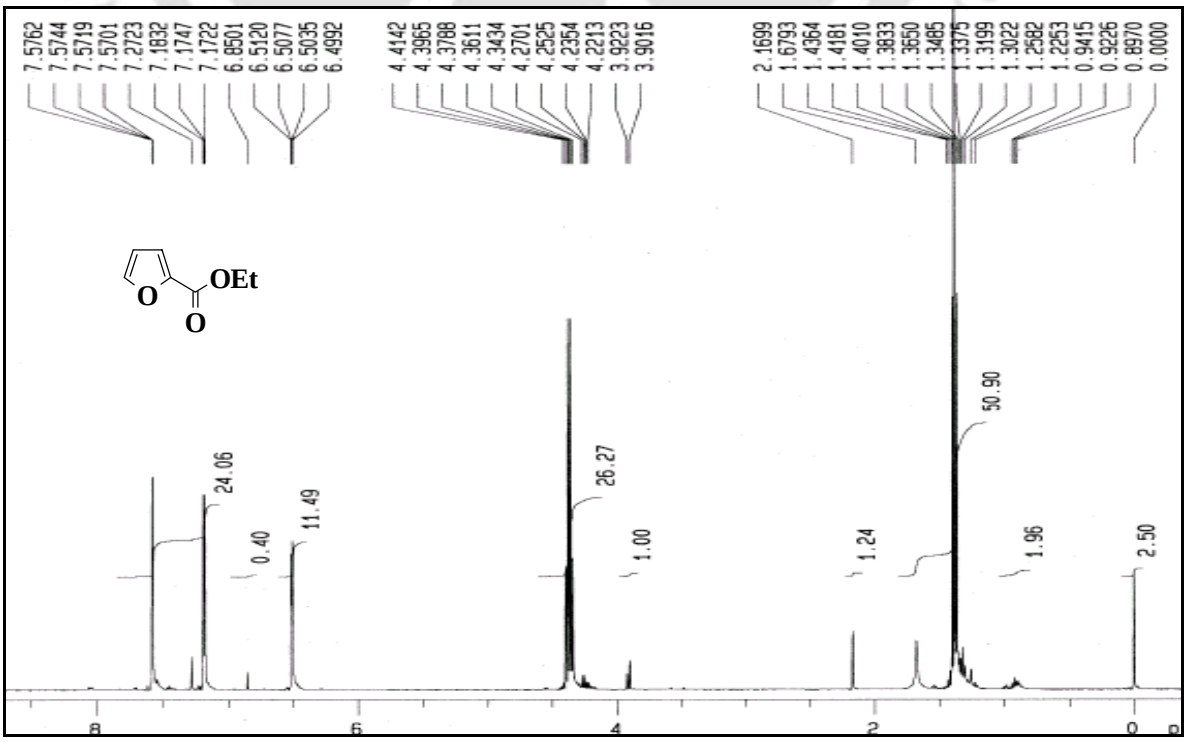
^{1}H NMR (400 MHz, $CDCl_3$): Methyl 4-benzyloxybenzoate (12a)



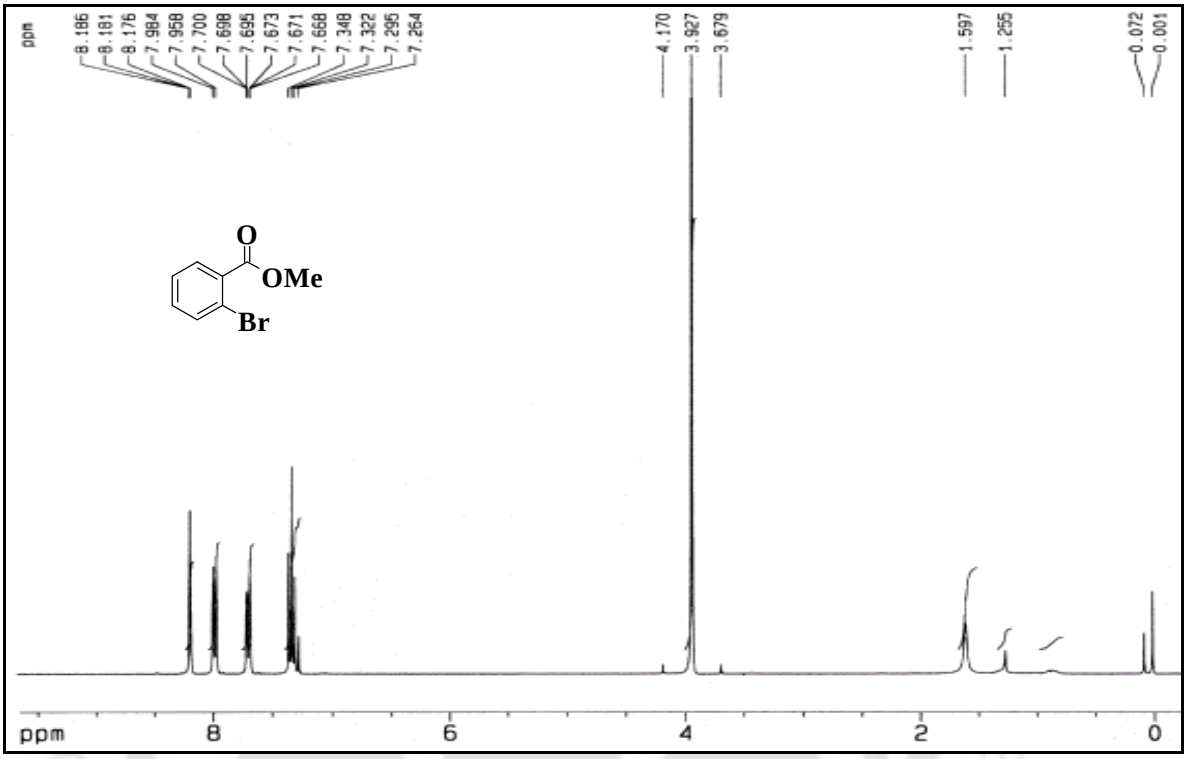
^{1}H NMR (400 MHz, $CDCl_3$): Ethyl-4-benzyloxybenzoate (12b)



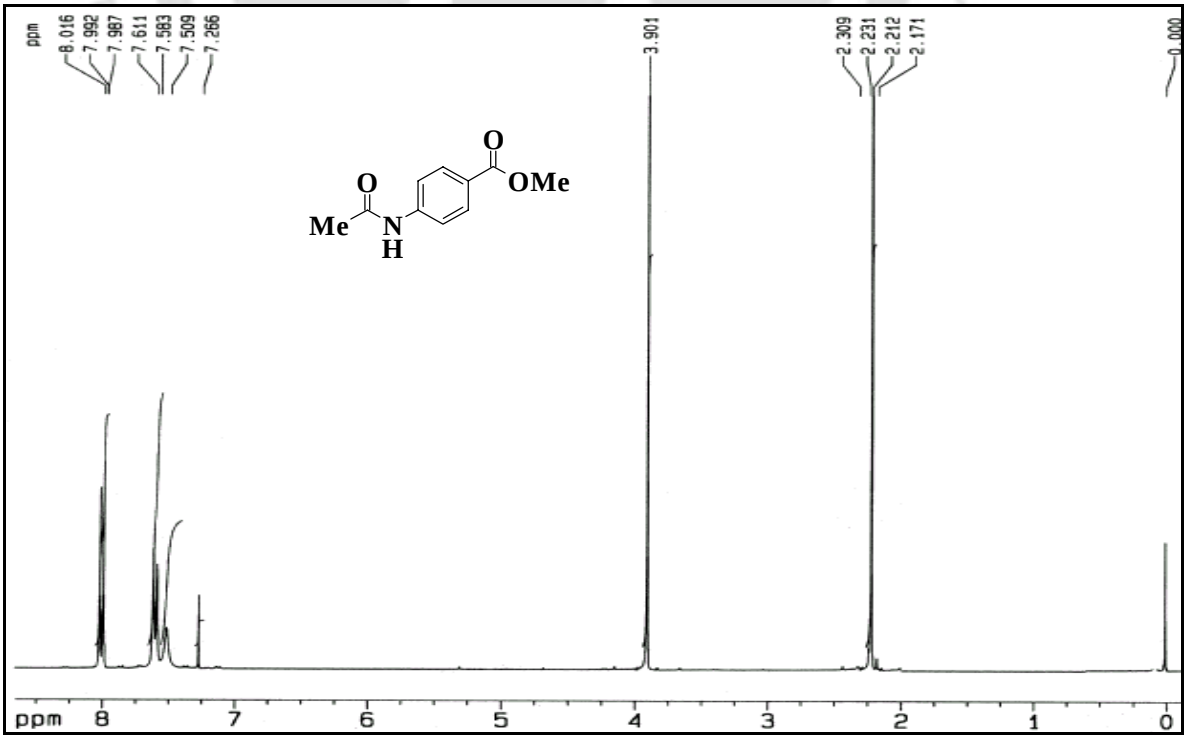
^{1}H NMR (400 MHz, $CDCl_3$): Ethyl 2-furoate (13b)



^{1}H NMR (400 MHz, $CDCl_3$): Methyl-2-bromobenzoate (16a)



^{1}H NMR (400 MHz, $CDCl_3$): Methyl 4-N-acetamidobenzoate (19a)



Chapter II

Tetrabutylammonium Tribromide in Organic Synthesis

IIA Introduction

IIA.1 Protecting Groups

Today, organic synthesis has reached a remarkable level of competence and even the most complex molecules are accessible. The prerequisites for this success are both the availability of a wide range of efficient synthetic methods and reagents and the fact that 'retrosynthetic analysis' can provide a framework for the design of a synthetic strategy leading to the desired product in the most efficient and logical way. The complex synthetic intermediates and products contain, in general, a multiplicity of functional groups, most of which must be protected, and at an appropriate point in the synthesis liberated. The correct choice of protecting groups is often decisive for the realisation of the overall operation.

Thus, a successful synthesis requires both basic retrosynthetic planning and a separate protecting group strategy that takes into account different requirements such as the ability of the intermediates and of the reagents to be used. The choice of protecting is one of the decisive factors in the successful realisation of a complex, and a demanding synthetic project. The protecting groups used influence the length and efficiency of the synthesis and are often responsible for its success or failure. A wide range of protecting groups are currently available for the different functional groups, however, an overall strategy combining these different masking techniques in an advantageous and reliable manner has never been proposed or at best only for individual cases.

For a protecting group to find wide applications in organic synthesis, it must fulfill several criteria. In particular it must be introduced into the molecule to be protected under mild conditions in a selective manner and in high yield; functional groups other than that to be protected must not be attacked, stable under all the conditions used during the synthesis, including those of the purification steps, up to the step in which the protecting group is removed, it should, as far as possible, have a stabilising effect on the molecule. It must be cleavable under very mild conditions in a highly selective manner and in high yield; other protecting groups present in the molecule and unprotected functionalities should not be affected by the cleavage conditions. In addition to these minimum requirements, the

protecting group should also be introduced and removed with the help of readily available reagents, such that in both transformations the products can be easily purified.

IIA.1.1 Hydroxyl Protecting Groups

Hydroxyl groups are present in a number of compounds of biological and synthetic interest, including nucleosides, carbohydrates, steroids, macrolides, polyethers, peptides, and amino acids. The protection-deprotection protocol of free hydroxyl groups has become a commonplace in organic synthesis. During oxidation, acylation, halogenation with phosphorus based reagents or hydrogen halides, or dehydration reactions of these compounds, a hydroxyl group must be protected. In polyfunctional molecules, selective protection of one functional group in the presence of others becomes an issue that has been addressed by the development of a number of new methods. Several protecting groups have been reported today, but of these, only comparatively small fractions are in common use. Ethers are among the most used protective groups in organic synthesis and vary from the simplest, most stable methyl to the more elaborate, substituted trityl ethers developed for use in nucleoside synthesis.[1]

IIA.1.1.1 Silyl Ethers

Amongst the entire hydroxyl protecting groups silyl ethers are used more than any other protecting groups in organic synthesis. *O*-Silylation of alcohols was first introduced in the late 1950's to increase volatility and stability of polar compounds during gas chromatography and mass spectrometry. Due to their easy and recently developed selectivity of attachment, a host of di- and trialkyl silyl groups have been commonly used as protection of free hydroxyl groups over the last three decades, Figure 2.1. The reason for the wide popularity of silicon protecting groups is because they are readily formed and cleaved under mild conditions and their relative stability can be finely tuned by simply varying the substituents on the silicon.[2] As a general rule, the bulkier the substituents, the greater the stability towards acid and base hydrolysis including organolithium and Grignard reagents, oxidations, reductions and column chromatography. Relative stability of the trialkyl silyl ethers towards acid catalysed hydrolysis are as follows.[2a]

TMS ≈ DMPS ≈ MDPS < TES ~ DMIPS ≈Pr_3Si ≈ Bu_3Si < TPS < MDIPS < TBS < TDS < TIPS < TBDPS < DTBMS.

Similarly, if the same protecting group is used to protect two or more hydroxyl groups, the silyl ether derived from less sterically encumbered alcohol is usually the first to be deprotected. In general, an increase in substituent size on either the silicon or the alcohol carbon decreases the rate of desilylation.[2a]

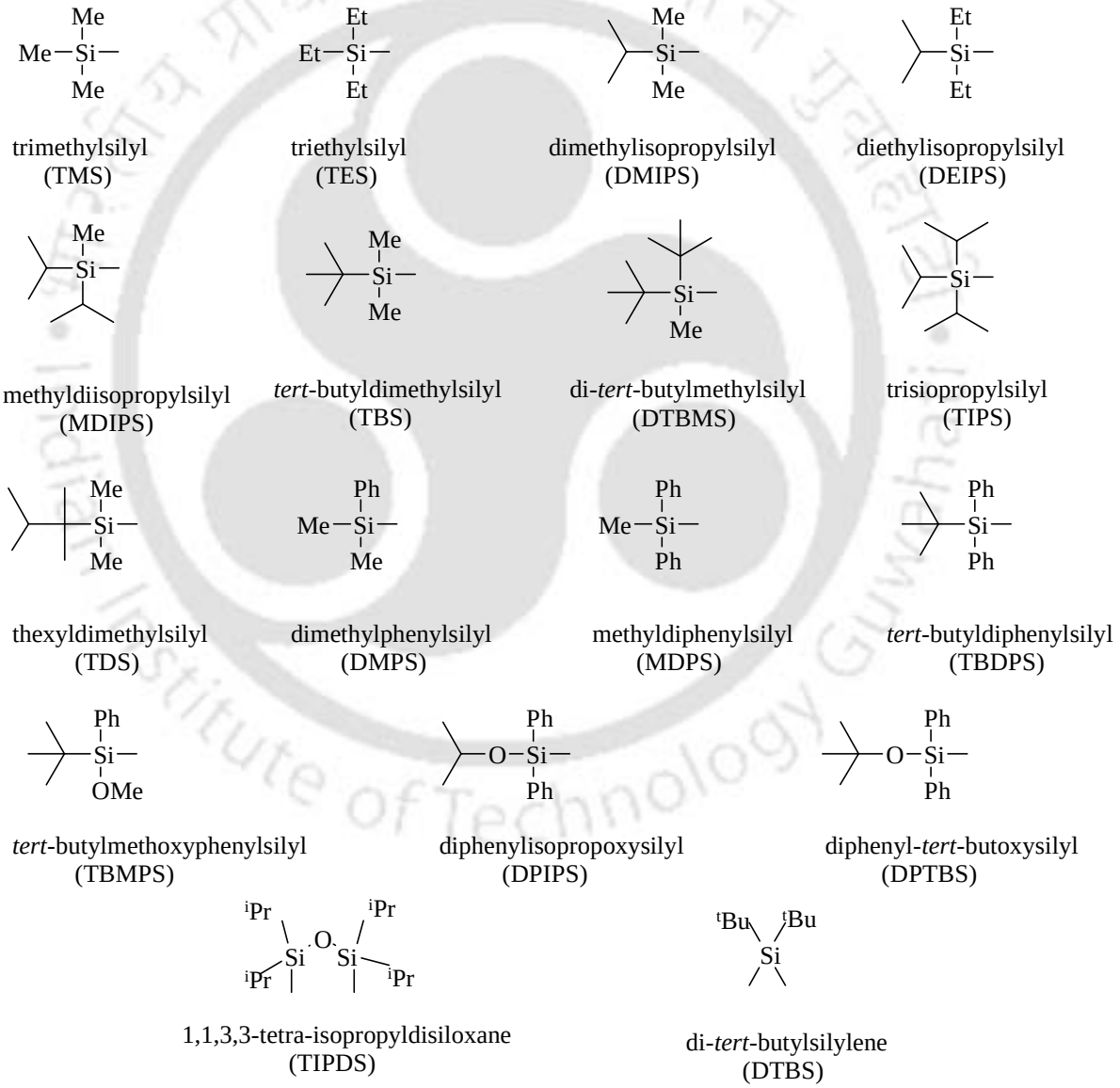


Figure 2.1

Electronic factors also play a crucial role in determining the stability, which can be exploited to differentiate stability under acidic or basic conditions. Generally electron-withdrawing substituents on silicon accelerate base catalysed hydrolysis of silyl ethers while electron donating groups accelerate acid catalysed hydrolysis.[2c] In both cases, the effect is more significant for groups attached to the oxygen rather than on silicon.[2d]

Among all the silyl ethers TBS ether has become one of the most popular silyl protective groups used in chemical synthesis. The TBS group first introduced by Stork[3] in 1968. It is easily introduced with a variety of reagents, has the virtue of being quite stable to a variety of organic reactions, and is readily removed under conditions that do not attack other functional groups. It has excellent stability towards basic reagents, but is relatively sensitive to acid. The easy of introduction and removal of the TBS ether are influenced by steric factors that often allow for its selective in polyfunctionalised, sterically differentiated molecules. The following section deals with the review pertaining to the different methods for the cleavage of TBS ether.

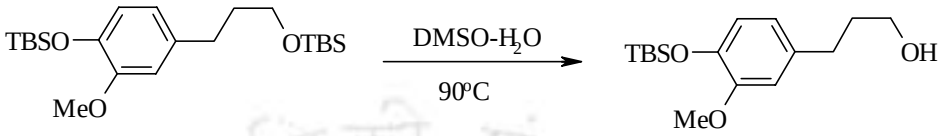
IIA.1.1.1.1 Cleavage of *tert*-Butyldimethylsilyl (TBS) Ethers

A plethora of methods are known for the deprotection of TBS ethers. Greene and Wuts[4] and Kocienski[1f] have compiled a list of reagents for the cleavage of TBS ethers. Nelson and Crouch[5] have thoroughly reviewed on the selective deprotection of silyl ethers in the presence of other like or unlike silyl ethers. This review will be focused on some of the very recent methods for the deprotection of TBS ethers.

One of the properties that have made silyl groups so popular is the fact that they are easily cleaved by fluoride ion, which is attributed to the high affinity that the fluoride ion has for silicon. The Si-F bond strength is 30 kcal/mol greater than the Si-O bond strength. Therefore several fluoride-based reagents are known for the cleavage of silyl ethers.[4] In addition other acidic reagents are also effective for the cleavage of TBS ethers.

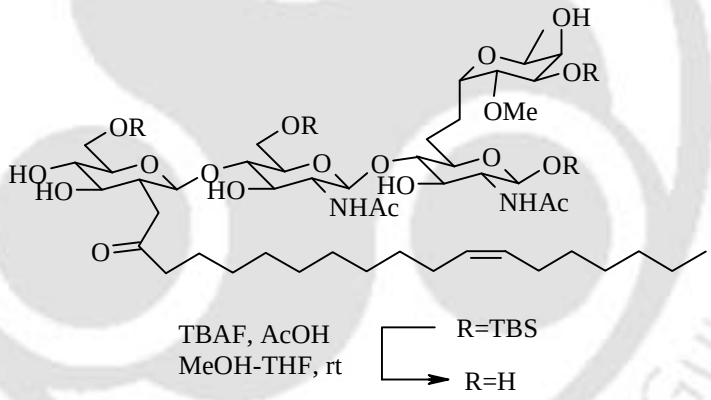
Maiti and Roy[6] have reported a selective method for the deprotection of primary allylic, benzylic, homoallylic and aryl TBS ethers using aqueous DMSO at 90^{o}C. Other TBS groups, THP ethers, methylenedioxy ethers, benzyl ethers, methyl esters and aldehyde

functionalities are unaffected under the reaction conditions. Benzyl TBS ether can be selectively deprotected in the presence of aryl TBS ether, Scheme 2.1.

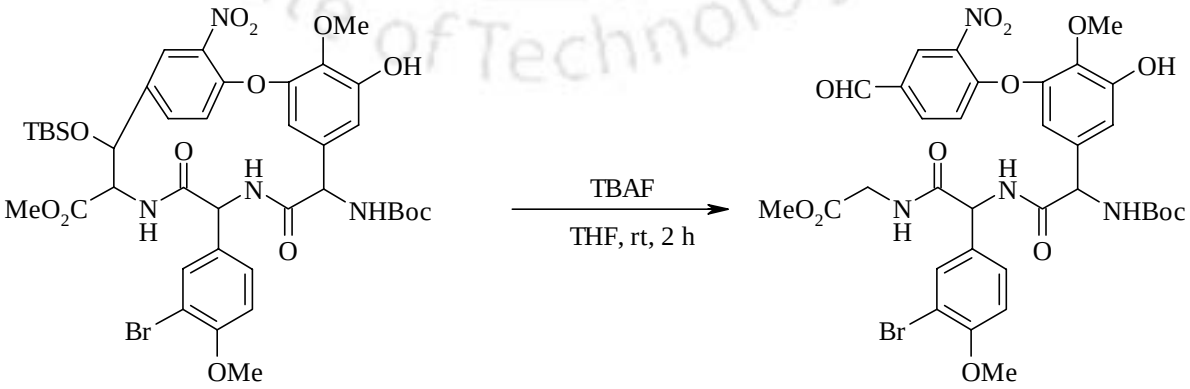


Scheme 2.1

One of the problems with the use of tetra-*n*-butylammonium fluoride is associated with the basicity of the fluoride. This is overcome by buffering the TBAF with acetic acid, as shown during the synthesis of the bacterial nodulation factor (NodRf-III),[7] Scheme 2.2 and Boger's synthesis of the vancomycin CD and DE ring system, Scheme 2.3.[8]

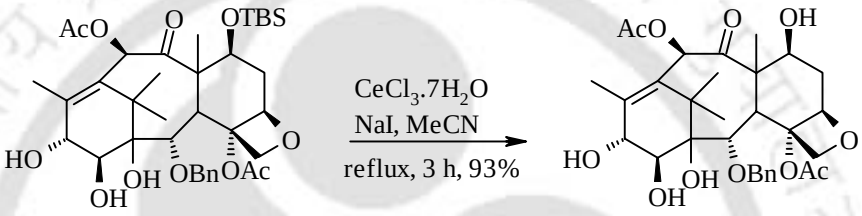


Scheme 2.2



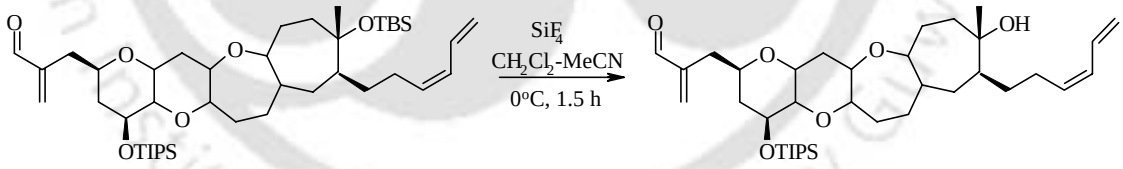
Scheme 2.3

Triethylsilyl (TES), *tert*-butyldimethylsilyl (TBS), trisopropylsilyl (TIPS) and *tert*-butyldiphenylsilyl (TBDPS) groups are deprotected by cerium(III) chloride heptahydrate and sodium iodide in acetonitrile.[9] A TBS ether can also be selectively deprotected in the presence of TBDPS ether. The reaction conditions do not affect acetate, benzyl, tetrahydropyranyl and *N*-Boc protecting groups but methoxymethyl ethers are incompatible. More complex molecules, *e.g.*, the baccatin derivative can also be deprotected without migration of the acetate group or detriment to the oxetane ring, Scheme 2.4.



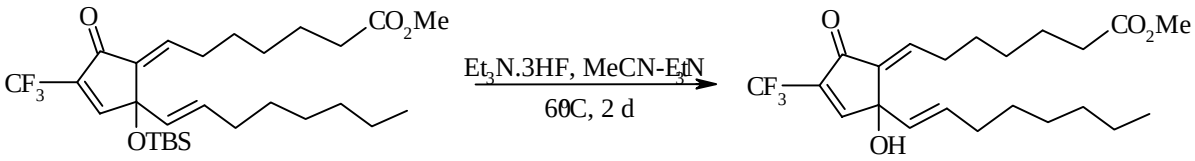
Scheme 2.4

The procedure of Corey and Yi[10] was applied in the final step of a synthesis of the hemibrevetoxin B.[11] The secondary TIPS and TBS ethers were removed by stirring a solution of the precursor under an atmosphere of gaseous silicon tetrafluoride, Scheme 2.5.



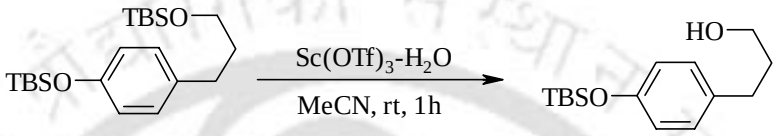
Scheme 2.5

The method of Westman and Stromberg[12] employing HF-triethylamine was applied in the final deprotection of the tertiary allylic TBS ether in the cross-conjugated prostanoid,[13] Scheme 2.6.



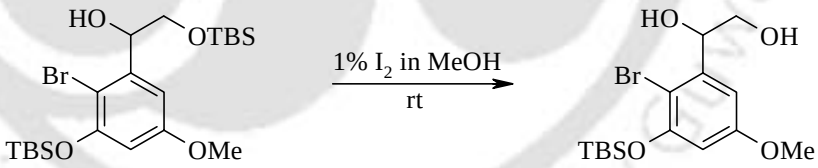
Scheme 2.6

Treatment of primary and secondary alkyl silyl ethers with a catalytic amount of scandium triflate (0.5 mol%) and water (5 equiv) in acetonitrile provide an efficient and practical method for deprotection.[14] Alkyl silyl ethers can be cleaved selectively in the presence of phenolic silyl ethers as illustrated in Scheme 2.7. TES, TMS and TBS ethers are all cleaved in shorter time, where as TIPS and TBDPS require longer times.



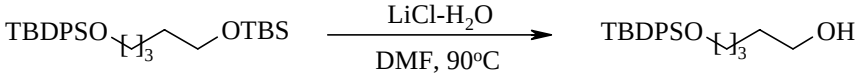
Scheme 2.7

Lipshutz and Keith[15] have reported that 1% iodine in methanol selectively cleaves alkyl silyl ethers in the presence of aryl silyl ethers as shown in Scheme 2.8. The reaction works equally well with TBS, TBDPS and TIPS ethers. The cleavage of TBDPS and TIPS ethers require longer time (14 h), where as TBS ether generally cleave in less than 6 h. The rate differential is sufficient to allow selective cleavage of a primary alkyl TBS ether in the presence of a primary TIPS ether.



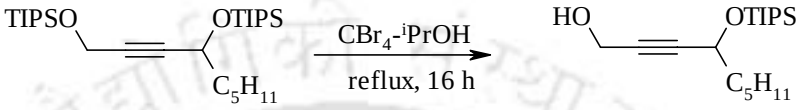
Scheme 2.8

The combination of lithium chloride (50 equiv) and water (5.5 equiv) in DMF selectively deprotects TBS ethers in the presence of TBDPS ethers, Scheme 2.9.[16] However, due to longer reaction times and requirement of higher temperature (90-120^{o}C) the method is unsuitable for thermally labile compounds.



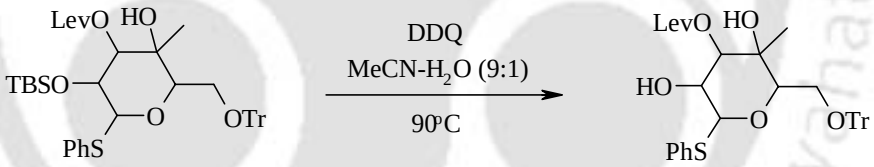
Scheme 2.9

Lee and co-workers[17] have reported a procedure for the cleavage of TBS, TBDPS and TIPS ethers using carbon tetrabromide (0.1 equiv) in refluxing methanol. In isopropanol, the rate of the reaction was much slower allowing the selective deprotection of a primary hydroxyl group in the presence of a secondary one, Scheme 2.10.



Scheme 2.10

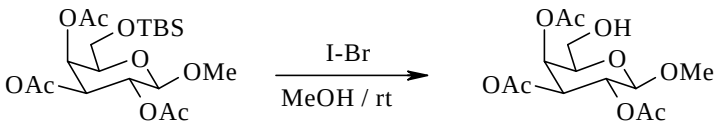
The reagent DDQ is an efficient oxidative deprotecting reagent for the allylic TBS ethers. This has been used by Paterson group[18] during the synthesis of aplyronine A. DDQ in wet acetonitrile is an effective reagent for the deprotection of TBS ether and trityl group in the presence of levulinate ester and an anomeric phenylthio acetal as demonstrated by Kakarla group during the synthesis of moenomycin intermediate Scheme 2.11.[19]



Scheme 2.11

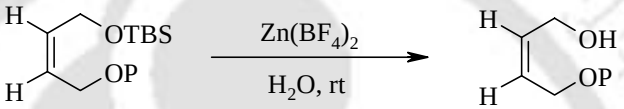
Aryl silyl ethers can be deprotected to yield phenols in good to excellent yields using a biphasic system of 10 equivalents of NaOH and catalytic Bu_4NHSO_4 in 1,4-dioxane.[20] Alkyl silyl ethers prepared using a variety of silyl protecting groups survive under these conditions, allowing selective deprotection of silyl protected phenols in the presence of silyl protected alcohols.

TBS ethers of simple alcohols, carbohydrates and nucleosides are efficiently deprotected on treatment with iodine monobromide in methanol at room temperature.[21] Acetals, PMB ethers, TBDPS ethers, esters and amides are unaffected under the reaction conditions, Scheme 2.12.



Scheme 2.12

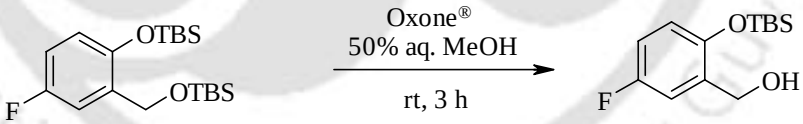
Ranu's group have used zinc tetrafluoroborate in water at room temperature for the cleavage of TBS ethers.[22] Aldehydes, esters and urethanes are not affected and also THP, allyl, benzyl and TBDPS ethers are inert under the reaction conditions, Scheme 2.13.



P=THP, allyl, benzyl and TBDPS

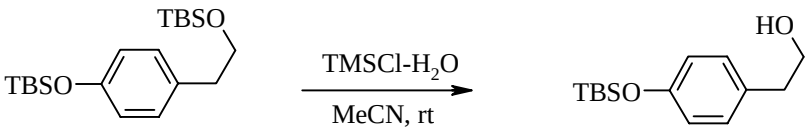
Scheme 2.13

Yadav and co-workers have reported the use of Oxone® in 50% methanol for the selective deprotection of the TBS ethers of primary alcohols in the presence of phenolic TBS ethers, Scheme 2.14.[23] Secondary TBS ethers and primary TBDPS ethers are unscratched. Inspite of p*H* being 2.8, THP and *N*-Boc groups are also unaffected.



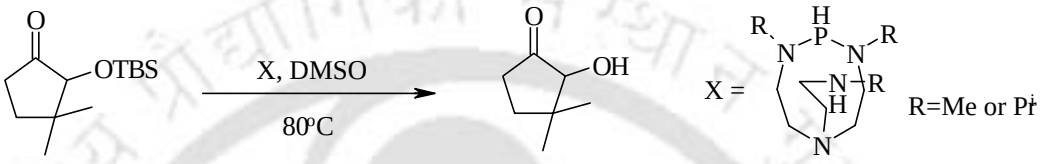
Scheme 2.14

Grieco and Markworth have used *in situ* generated HCl by the reaction of TMSCl in water for the selective deprotection of alkyl TBS ethers in the presence of aryl TBS ethers, Scheme 2.15.[24] The deprotection is accelerated by the addition of sodium iodide.



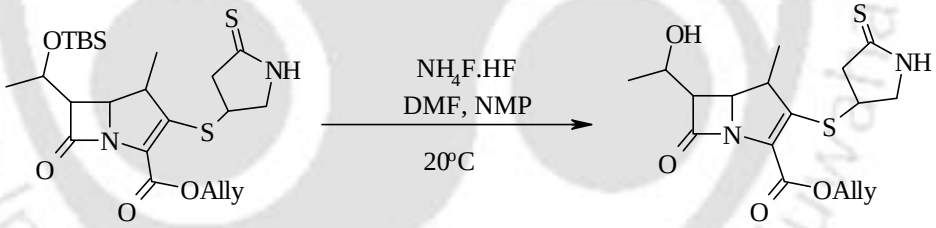
Scheme 2.15

Various alkyl and aryl TBS ethers can be deprotected with a catalytic amount of proazaphosphatranes (X), Scheme 2.16. Under the reaction conditions 1,4-dienes, rearrange to form the corresponding conjugated counterparts. Both the catalysts are less effective for the desilylation of more hindered TBDPS ethers. Use of expensive catalysts, higher temperature and longer reaction times are some of the drawbacks of the methodology.



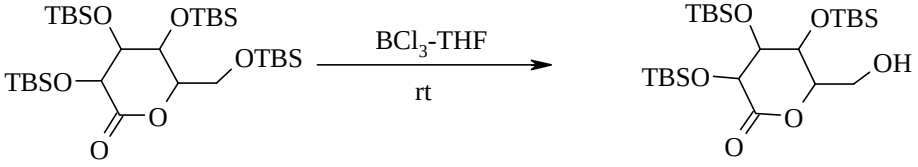
Scheme 2.16

During the synthesis of orally active 1-β-methylcarbapenem antibiotics TA-949, a selective deprotection of TBS ether was required, which was achieved using ammonium bifluoride in a mixture of DMF and NMP at room temperature, Scheme 2.17.[26]



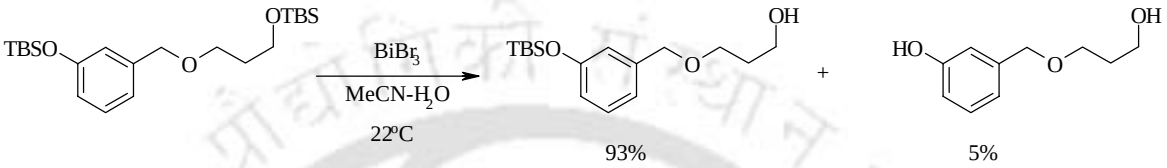
Scheme 2.17

Yang *et al*. have used BCl_3 in THF for the regioselective deprotection of primary TBS ethers in the presence of secondary TBS ethers in a series of TBS protected carbohydrates, Scheme 2.18.[27]



Scheme 2.18

Yet another method for the selective cleavage of alkyl TBS ethers has been achieved in the presence of aryl ethers using catalytic amount of bismuth bromide in wet acetonitrile at room temperature, Scheme 2.19.[28] The hydrolysis may be catalysed by HBr generated *in situ* from the reaction of bismuth bromide with water.



Scheme 2.19

Dommisse and co-workers[29] have reported a general method for the selective cleavage of phenolic TBS ethers ortho to a carbonyl group by sonication of 0.1 M solution of the substrate in equal proportion of CH_3OH and CCl_4 at 50-55^oC. Other phenolic *tert*-butyldimethylsilyl ethers are unaffected.

In another report Yadav *et al.*[30] have used indium(III) chloride for the cleavage of TBS ethers. Various TBS ethers are selectively deprotected to the corresponding alcohols in high yields when refluxed in aqueous acetonitrile in the presence of indium(III) chloride. Several functional groups like OBn, Boc, CBz, OBz, *O*-allyl, OTBDPS, OAc, OMe, ethers, esters and olefins present in the substrate remained unaffected. Alkyl TBS ether can be selectively deprotected in the presence of aryl TBS ether.

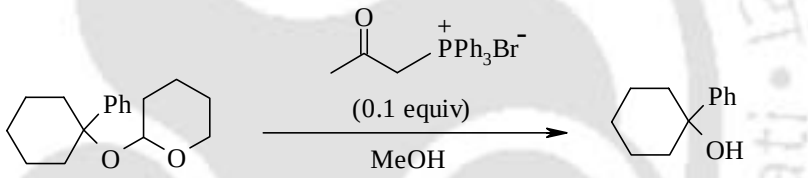
IIA.1.1.2 Tetrahydropyranyl Ethers

Tetrahydropyranyl ethers were one of the first generally useful protecting groups for alcohols.[31] The introduction of a THP ether onto a chiral molecule results in the formation of diastereomers because of the additional stereogenic center present in the tetrahydropyranyl ring (which can make the interpretation of NMR spectra somewhat troublesome at times). Inspite of this it is used extensively during chemical synthesis because of its low cost, easy installation, stability to most non-acidic reagents and easy of removal.

IIA.1.1.2.1 Cleavage of Tetrahydropyranyl Ethers

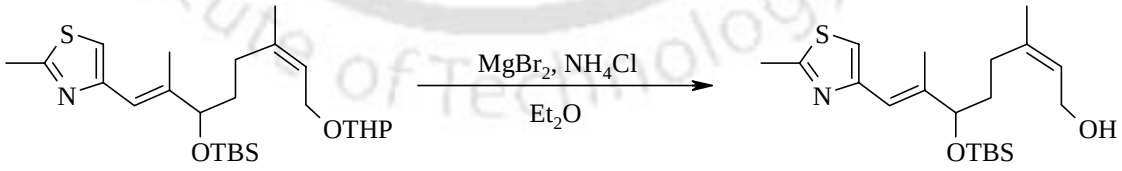
Genarally, most acidic reagents or any reagent that generates an acid *in situ* in an aprotic medium can be used to introduce the THP group and the same can be deprotected under acidic conditions in polar protic solvents. Several methods of deprotection of THP ethers have been compiled by Greene and Wuts[4] and by Kocienski.[1f] The following section deals with the some of the recent methods on the deprotection of THP ethers.

Hon and Lee[32] have used acetonyltriphenylphosphonium bromide, which catalyses the addition of alcohols to dihydropyran to form the corresponding THP ethers. The same reagent can also catalyses the deprotection when methanol is used as the solvent. The conditions are mild enough for the use with very acid-labile tertiary alcohol without significant dehydration, Scheme 2.20.



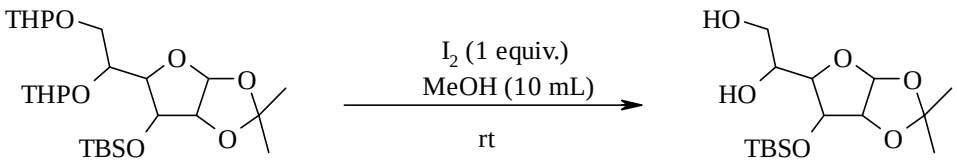
Scheme 2.20

The method of Kim and Park using magnesium bromide and ammonium chloride in ether was applied for the selective removal of the allylic THP ether in epothilone B intermediate, without detriment to the acid-sensitive allylic TBS ether, Scheme 2.21.[33]



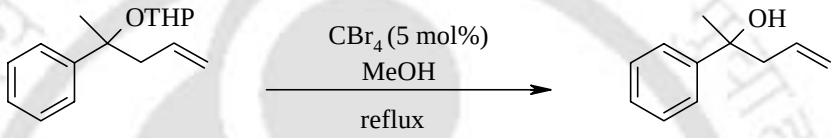
Scheme 2.21

Iodine in methanol deprotects tetrahydropyranyl (THP) and 4,4'-dimethoxytrityl (DMT) ethers in the presence of TBS groups.[34] Other protecting groups such as Bn, *N*-CBz, *N*-Boc and isopropylidine are compatible with the reaction conditions, Scheme 2.22.



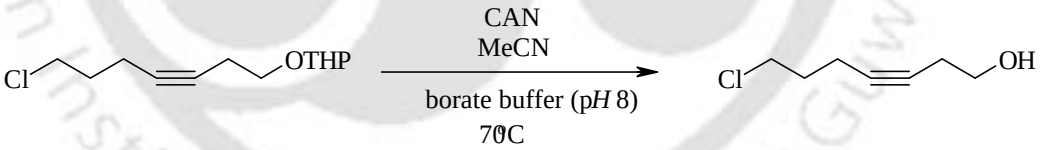
Scheme 2.22

Carbon tetrabromide in anhydrous methanol[35] is an effective combination for the cleavage of THP ethers, Scheme 2.23.[36]



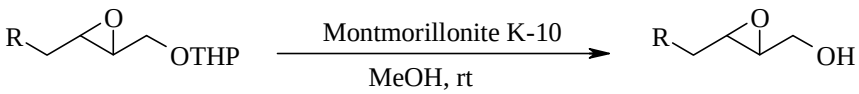
Scheme 2.23

A very mild method for the deprotection of THP and THF ethers has been achieved using CAN (3 mol%) in acetonitrile and borate buffer (p*H* 0.8), Scheme 2.24. Trityl ethers, esters, nitriles, ketones, enones, halides, sulfides, alkenes and alkynes are all compatible, however, ketone acetals do not survive under this condition.[37]



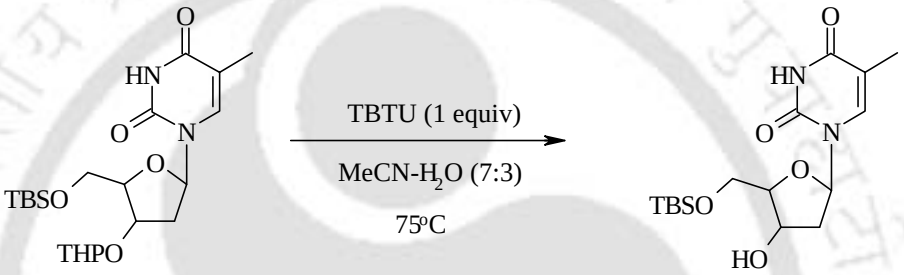
Scheme 2.24

Montmorillonite K-10 clay in methanol allows the smooth selective deprotection of both THP ethers containing an epoxide functionality, without affecting it, Scheme 2.25.[38] Methoxymethyl (MOM), *tert*-butyldiphenylsilyl (TBDPS) and acetoxy groups also remained intact under the reaction conditions but ketals, TBS ethers and 2,2,2-trichloroethylimidoxy [Cl_3CC (=NH)O-] functionalities are unstable.



Scheme 2.25

The reagent *O*-(benzotriazol-1-yl)-*N*,*N*,*N'*,*N'*-tetramethyluranium tetrafluoroborate (TBTU) selectively cleaves the THP and DMT ethers in the presence of TBS, isopropylidine, Bn, Boc and CBz groups.[39] The reaction is best conducted in acetonitrile-water (7:3) at 75°C. The hydrolysis is believed to be mediate by the production of HF and boric acid arising from the decomposition of the tetrafluoroborate anion. Selective deprotection of secondary THP group in the presence of primary TBS group has been achieved, Scheme 2.26. But due to the use of expensive reagent this method is not very attractive.

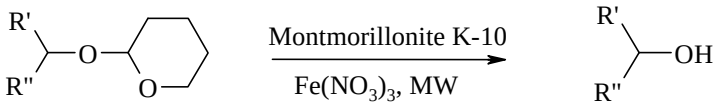


Scheme 2.26

In the presence of a catalytic amount of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), THP ethers are readily hydrolysed to their corresponding alcohols in wet acetonitrile under mild conditions.[40]

Deprotection of THP ethers in presence of NH_4Cl in methanol (p*H* 5.25) at reflux conditions afforded the corresponding alcohols in excellent yields.[41] Acid-sensitive groups like TBDPS, TBS, acetonoides and bromoalcohols are unaffected under these conditions.

Heravi group have reported[42] a convenient oxidative deprotection of THP ethers with $Fe(NO_3)_3$ and clay under microwave irradiation in solvent free conditions, Scheme 2.27.



Scheme 2.27

Kumar *et al.* have reported depyranylation of various THP protected alcohols using iodine in methanol.[43] The occurrence of this reaction is due to the *in situ* formation of HI by the interaction of alcohol and I_2. Other protecting groups such as OBn, OBz, *O*-allyl, *O*-TBS

remained unaffected during the process. The same principle was further extended but using microwave as the source of energy.[44]

Deprotection of several THP ethers has been effected using lithium bromide in methanol at reflux temperature.[45] Protecting groups like OBn, *O*-allyl, OMe and ethylenic as well as acetylenic functions are stable under the reaction conditions.

Cupric chloride dihydrate in methanol is a useful combination for the cleavage of THP ethers to the corresponding alcohols.[46] Other functional groups such as methoxy, methoxyethoxymethyl (MEM), methylenedioxy, benzyl ethers, esters are unaffected and also do not result in addition-elimination reactions with the multiple bonds present in the system. However, TBS and TBDPS ether functions are also cleaved under these conditions.

Treatment of tetrahydropyranyl ethers with cerium(III) chloride heptahydrate in methanol provides a simple, convenient and selective method for detetrahydropyranylation.[47] Isopropylidine, *N*-Boc, OBn groups are unaffected during the reaction. Salehi and co-workers have recently reported a method for the unmasking of THP ethers using $ZrCl_4$ in methanol.[48] Very recently, potassium dodecatangestocobaltate trihydrate ($K_5CoW_{12}O_{40}.3H_2O$) has been used for the detetrahydropyranylation of various THP ethers to the corresponding alcohols.[49]

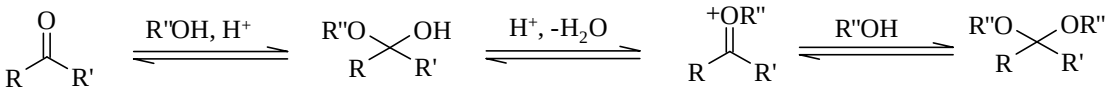
IIA.1.2 Carbonyl Protecting Groups

Due to electrophilicity of the carbonyl group it has to be protected during a multistep synthesis against the attack by various reagents such as strong bases, Grignard reagents, hydrides, redox reagents, alkylating, acylating agents and catalytic hydrogenation. The protection of aldehydes and ketones has been served by a relatively small repertoire of protecting groups and of these, acetals and thioacetals have proven most useful. One of the reasons why there are comparatively few protecting groups for carbonyls is because they reveal a useful range of reactivity in both the protection and deprotection steps, which allows a modicum of selectivity.

IIA.1.2.1 Acetals and Ketals

Aldehydes and ketones react with alcohols under acidic conditions to form acetals or ketals and water in an equilibrium process, which proceeds *via* an oxonium ion, a common

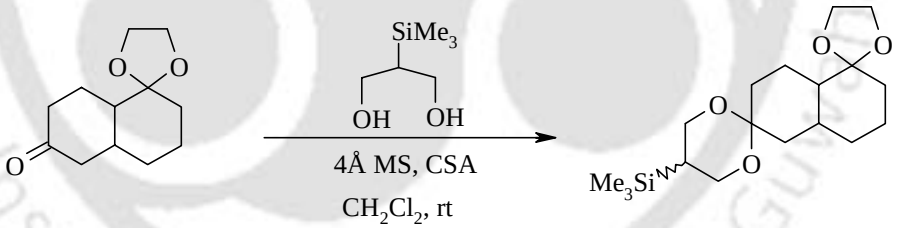
intermediate in many acid catalysed acetal synthesis as shown below, Scheme 2.28.



Scheme 2.28

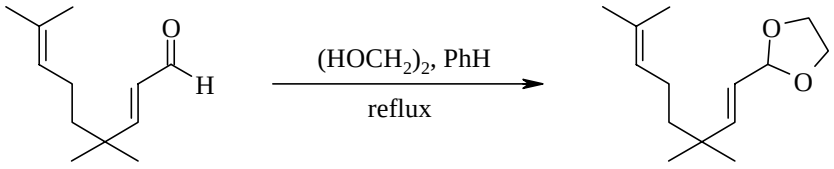
A large number of methods are known for the protection of carbonyl groups as cyclic or acyclic acetals. Greene and Wuts[4] have compiled a list of reagents for protection of carbonyl groups as acetals and have been reviewed by Kocienski[1f] and Meskens.[50] The following section is about some of the recent developments on protection of carbonyl groups as acetals or ketals.

Lipshutz and co-workers devised a new carbonyl protecting group involving the formation of 'cyclo-SEM' derivative in the reaction with 2-trimethylsilylpropane-1,3-diol.[51] The reaction is performed using 5.4 equiv of 2-trimethylsilyl-propane-1,3-diol and catalytic quantity of CSA (0.25 equiv) in dichloromethane, Scheme 2.29.



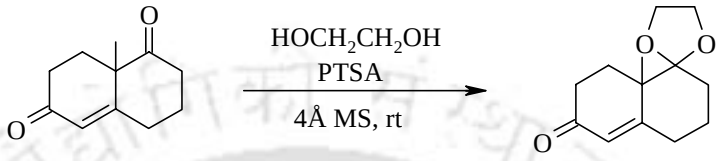
Scheme 2.29

Acetalisation of α,β-unsaturated carbonyl compounds is often difficult with conventional acid catalysts. Malaeria and co-workers[52] applied the method of Otera group[53] using distannoxanes for the acetalisation of the following sensitive substrate, Scheme 2.30.



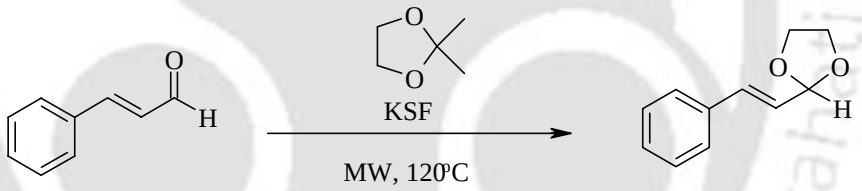
Scheme 2.30

Selective acetalisation of ketones in the presence of α,β-unsaturated ketones can be achieved in high yields using ethylene glycol as a solvent and a stoichiometric amount of *p*-toluenesulphonic acid (PTSA), Scheme 2.31.[54]



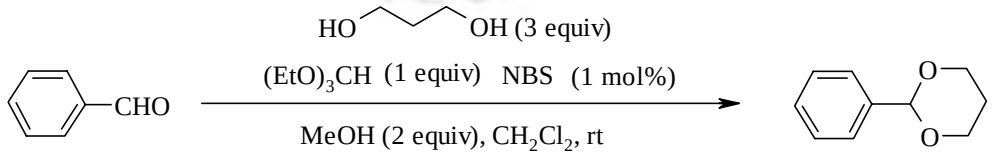
Scheme 2.31

Solvent free acetalisation of aldehydes and ketones under microwave irradiation has been described by Hamelin *et al.*[55] Methyl or ethyl orthoformate, ethylene glycol or 2,2'-dimethyl-1-dioxalane can be used as reagents and PTSA or montmorillonite clay KSF as a catalyst, Scheme 2.32.



Scheme 2.32

Varieties of aldehydes are converted to their 1,3-dioxane derivatives on reaction with a catalytic amount of NBS in the presence of propane-1,3-diol (3 equiv) and triethyl orthoformate (1 equiv) at room temperature, Scheme 2.33.[56]



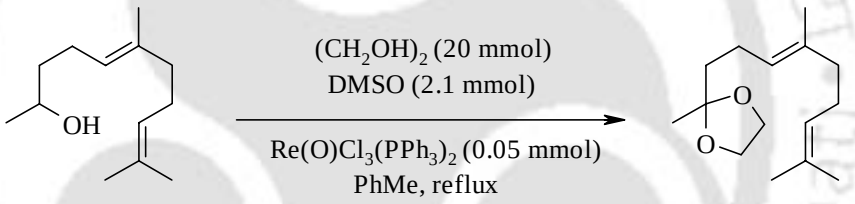
Scheme 2.33

By replacing dimethyl tartarate instead of propane-1,3-diol corresponding 1,3-dioxalane derivatives can also be prepared. Acid-sensitive groups such as THP and TBS groups are unaffected and ketones react much slower to yield corresponding ketal

derivatives. It is assumed that HBr is generated from NBS that catalyses the reaction. Absolute ethanol has been replaced for propane-1,3-diol for the preparation of the corresponding diethylacetals of various carbonyl compounds.[57]

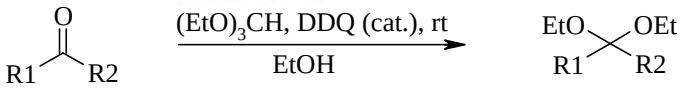
Zirconium tetrachloride catalyses the transacetalisation of carbonyl compounds under mild conditions.[58] A mixture of the carbonyl compound, propane-1,3-diol, and triethyl orthoformate in dichloromethane is stirred at room temperature until the reaction is complete. The reaction is selective for aldehydes in the presence of ketones but the selectivity diminishes when the ketone is cyclic.

The *in situ* generated ketone from secondary alcohol by DMSO and a catalytic amount of $Re(O)Cl_3(PPh_3)_2$ in the presence of ethylene glycol gave directly the ketals of the corresponding ketones, Scheme 2.34.[59]



Scheme 2.34

Various types of structurally different carbonyl compounds in the presence of ethyl orthoformate could be efficiently converted to their diethyl acetals by using a catalytic amount of DDQ under mild conditions, Scheme 2.35.[60] Aldehydes can be chemoselectively acetylated in the presence of ketones and acid-sensitive protecting groups such as THP ethers remained unaffected during the reaction.



Scheme 2.35

Prajapati *et al.* [61] have achieved a new selective method of acetalisation of aldehydes and ketalisation of ketones with 1,2-diols, 1,3-diols or alcohols mediated by cadmium iodide under microwave irradiation.

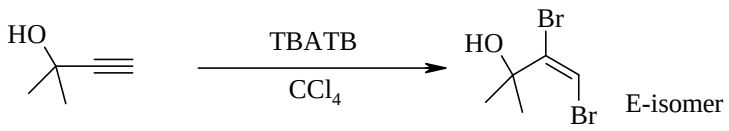
Silica gel supported metallic sulfates are efficient catalysts for the protection of both aromatic and aliphatic aldehydes as 1,3-dioxolanes under microwave in solvent-free conditions. Aldehydes has been chemoselectively acetylated in the presence of ketones.[62] OBn, OPh, OMe, methylenedioxy, phenacyl and cyano groups resists hydrolysis allowing selective protection of carbonyl compounds.

Curini group[63] have recently reported a convenient method for the preparation of cyclic ketals and thioketals using zirconium sulfophenyl phosphonate [$Zr(O_3PCH_3)_{1.2}(O_3PC_6H_4SO_3H)_{0.8}$] as catalyst.

IIA.2 Tetrabutylammonium Tribromide in Organic Synthesis

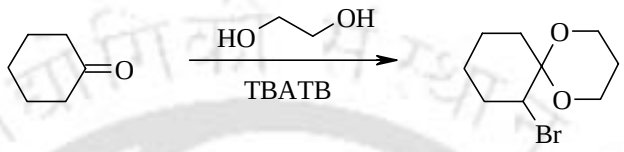
Tetrabutylammonium tribromide, $(C_4H_9)_4NBr_3$ ($^nBu_4NBr_3$, TBATB) is an orange crystalline compound and has been known in literature for quite some time.[64] It is useful as a brominating agent as well as an oxidising agent. The main advantages of organic ammonium tribromides (OATB) are that they are crystalline, easy to handle and maintain the desired stiochiometry. Several tribromides have been reported in the literature such as: tetramethylammonium tribromide (TMATB),[65] phenyltrimethylammonium tribromide (PTATB),[66] cetyltrimethylammonium tribromide (CetTMATB),[67] tetrabutylammonium tribromide (TBATB),[64,68] 1,8-diazabicyclo [5,4,0]-tetrabutylammonium tribromide ($DBUHBr_3$),[69] and pyridine hydrobromide perbromide ($PyHBr_3$).[70]

Organic ammonium tribromides are mild and efficient brominating reagents for a large number of organic substrates. Tetra-*n*-butylammonium tribromide (TBATB) allows easy double bond bromination under mild conditions with very good yields in chloroform.[71] The bromination of alkynes is usually difficult and gives mixture of products. The use of TBATB in CCl_4, at room temperature leads to the (*E*) isomer of 1,2-dibromo alkenes in high yields,[72] Scheme 2.36.



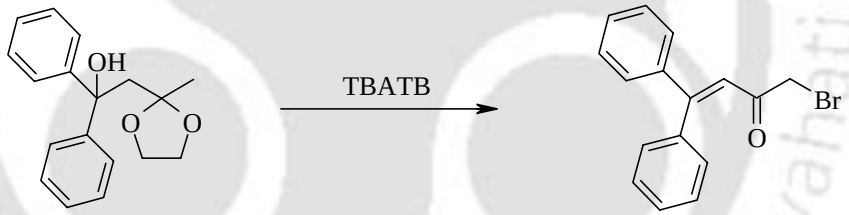
Scheme 2.36

α-Bromoacetals are useful reagents of the synthesis of α,β-unsaturated ketones. These derivatives are usually prepared in two steps: first bromination followed by an acetalisation. TBATB is a convenient reagent, which gives α-bromoketals from ketones when used with ethylene glycol, Scheme 2.37.[71]



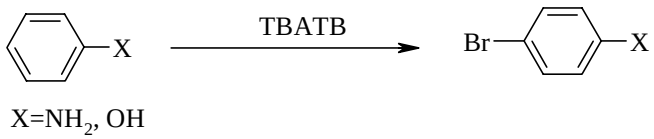
Scheme 2.37

The reagent TBATB is also an excellent oxidative-brominating reagent as demonstrated during the conversion of 1,1-diphenyl-3-ethylenedioxy-1-butanol to 4-bromo-1,1-diphenylbuten-3-one,[73] Scheme 2.38**.**



Scheme 2.38

Reactions of several aromatic amines, aminopyridines and phenols in an aprotic and no basic solvent gave exclusively the *p*-brominated compounds in high yields, Scheme 2.39.[74] Phenols were brominated in the para position using TBATB in chloroform. If the para position is not available ortho position was brominated.[74b, 75]



Scheme 2.39

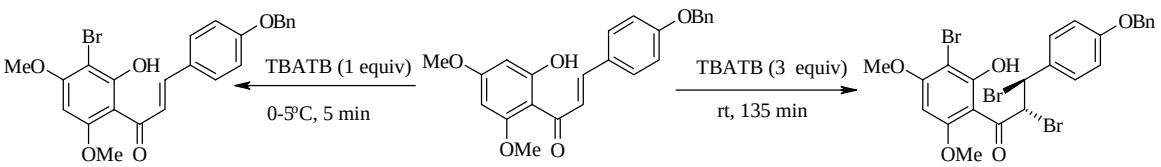
Berthelot and co-workers for the determination of the unsaturation number in organic compounds have developed a method. Their method is based on bromination with TBATB in

polar medium followed by electrochemical monitoring of Br_3^-.[76] They have also described bromination of double bond of para substituted chalcones under mild conditions in aprotic solvents using TBATB. In methanol, the main reaction is (α–β) bromoethoxylation.[77]

Berthelot group[78] have achieved bromination of substituted alkenes using TBATB under mild conditions with ultrasonic irradiation. This process gives quantitatively the corresponding vicinal bromide in high yields. The reaction of TBATB with mono and disubstituted alkynes in methanol at 20°C leads to the formation of mainly the corresponding α,α-dibromo-β,β-dimethoxyalkane and E-(α,β)-dibromoalkene.[79]

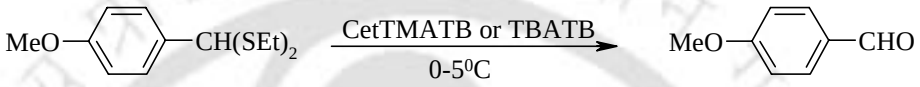
Both (R) and (S)-2,3-dibromo-1-propanol with enantiomeric excess (*ee)* up to 60% have been obtained by diastereoselective addition of Br_2 to allyl glucosides and galactosides having only one unprotected hydroxyl group at C-2 or C-6 using tetrabutylammonium tribromide, followed by hydrolysis. The absolute configuration is shown to depend on the position of the free hydroxyl and at the anomeric center.[80]

Preparation of organicammonium tribromides invariably involves the use of elemental bromine and in some cases HBr as well. This again causes an environmental concern. To overcome this problem Chaudhuri *et al.* have developed an environmentally benign method for the preparation of TBATB. Tetrabutylammonium bromide (TBAB) was oxidised in presence of catalyst (V_2O_5) and hydrogen peroxide (H_2O_2) and alkali metal bromides in an acidic medium.[81] Peroxovanadium(V) species so generated was responsible for bringing about the oxidation of bromide (Br^-) to tribromide (Br_3^-).[82] The product was isolated in high yields and it can be crystallised from acetonitrile to an orange crystalline compound. The efficacy of the reagent thus synthesised was tested with a variety of organic substrates. This reagent brominates a range of substrates rather easily under mild conditions. An activated ring is selectively brominated in the presence of olefinic double bonds, Scheme 2.40.



Scheme 2.40

Khan and co-workers have reported a method for the preparation of various cyclic and acyclic α-bromoenones in a one-pot procedure employing organicammonium tribromides such as cetyltrimethylammonium tribromide (CetTMATB) and TBATB in the presence of K_2CO_3 in dichloromethane in good yields.[83] Further this was used as a brominating agent during the synthesis of natural products such as aurones and flavones.[84] They have also utilised this reagent for the cleavage of dithioacetal,[85] Scheme 2.41.



Scheme 2.41

Thus, most of organicammonium tribromides are either used as a brominating agents and some time as oxidising agents.[73,86] Thus, organicammonium tribromides are useful reagents and its synthetic potential has not been fully exploited. It has been shown that benzyltrimethylammonium tribromide generates HBr and MeOBr in methanol.[87] It is expected that tetrabutylammonium tribromide should generate HBr in alcohol.

With this objective it was decided to

- Use this reagent in combination with an alcohol for the deprotection of acid-sensitive protecting groups such as TBS, THP and DMT ethers. The objective being chemoselective deprotection and compatibility with other protecting groups.
- To develop a method for acetalisation of carbonyl compounds with an aim of chemoselective acetalisation and to study the stereo-electronic factors on the rate of acetalization.

The results obtained from the above problems comprise Chapter II of the Ph.D dissertation.

IIA.3 References

1. (a) Reese, C. B. "*Protection of Alcoholic Hydroxyl Groups and Glycol Systems*," in *Protective Groups in Organic Chemistry*, J. F. W. McOmie, Ed.; Plenum: New York and London, 1973, p.95. (b) Flowers, H. M. "*Protection of Hydroxyl Group*," in *The Chemistry of the Hydroxyl Group*, S. Patai, Ed., Wiley-

Interscience: New York, 1971, Vol. 10/2, p.1001–1044. (c) Reese, C. B. *Tetrahedron* **1978**, *34*, 3143. (d) Amarnath, V.; Broom, A. D. *Chem. Rev*. **1977**, *77*, 183. (e) Lalonde M.; Chan, T. H. *Synthesis* **1985**, 817. (f) Kocienski, P. *Protecting Groups*, Thieme Medical Publishers: New York, 1994, p.21.

2. (a) Kunx, H.; Waldman, H. *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming, I.; Eds.; Pergamon: Oxford, 1991, Vol. 6, p.631. (b) Peishoff, C. E.; Jorgenson, W. L. *J. Org. Chem.* **1983**, *48*, 1970. (c) Sommer, L. H. *Stereochemistry, Mechanism and Silicon*, McGraw Hill: New York, 1965. (d) Shirai, N.; Moriya, K.; Kawazoe, Y. *Tetrahedron* **1986**, *42*, 2211.
3. Stork, G.; Hudrlic, P. F. *J. Am. Chem. Soc*. **1968**, *90*, 4462.
4. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed., John Wiley and Sons, Inc.: New York, 1999.
5. Nelson, T.D.; Crouch, R.D. *Synthesis* **1996**, 1031.
6. Maiti, G.; Roy, S. C. *Tetrahedron Lett.* **1997**, *38*, 495.
7. Debenham, J. S.; Rodebaugh, R.; Fraser-Reid, B. *J. Org. Chem.* **1997**, *62*, 4591.
8. Boger, D. L.; Borzilleri, R. M.; Nukui, S.; Beresis, R. T. *J. Org. Chem.* **1997**, *62*, 4721.
9. Bartoli, G.; Bosco, M.; Marcantoni, E.; Sambri, L.; Torregiani, E. *Synlett* **1998**, 209.
10. Corey, E. J.; Yi, K. Y. *Tetrahedron Lett.* **1992**, *33*, 2289.
11. Kadota, I.; Yamamoto, Y. *J. Org. Chem.* **1998**, *63*, 6597.
12. Westman, E.; Stromberg, R. *Nucleic Acids Res.* **1994**, *22*, 2430.
13. Tius, M. A.; Hu, H. P.; Kawakami, J. K.; Petersen, J. B. *J. Org. Chem.* **1998**, *63*, 5971.
14. Oriyama, T.; Kobayashi, Y.; Noda, K. *Synlett* **1998**, 1047.
15. Lipshutz, B. H.; Keith, J. *Tetrahedron Lett.* **1998**, *39*, 2495.
16. Farras, J.; Serra, C.; Vilarrasa, J. *Tetrahedron Lett.* **1998**, *39*, 327.
17. Lee, A. S. Y.; Yeh, H. C.; Shie, J. J. *Tetrahedron Lett.* **1998**, *39*, 5249.
18. Paterson, I.; Woodrow, M. D.; Cowden, C. J. *Tetrahedron Lett.* **1998**, *39*, 6041.

19. Kakarla, R.; Ghosh, M.; Anderson, J. A.; Dulina, R. G.; Sofia, M. J. *Tetrahedron Lett.* **1999**, *40*, 5.
20. Crouch, R. D.; Stieff, M.; Frie, J. L.; Cadwallader, A. B.; Bevis, D. C. *Tetrahedron Lett.* **1999**, *40*, 3133.
21. Kartha, K. P. R.; Field, R. A. *Synlett* **1999**, 311.
22. Ranu, B. C.; Jana, U.; Majee, A. *Tetrahedron Lett*. **1999**, *40*, 1985.
23. Sabita, G.; Syamala, M.; Yadav, J. S. *Org. Lett.* **1999**, *1*, 1701.
24. Grieco, P. A.; Markworth, C. J. *Tetrahedron Lett.* **1999**, *40*, 665.
25. Yu, Z. K.; Verkade, J. G. *J. Org. Chem.* **2000**, *65*, 2065.
26. Seki, M.; Yamanaka, T.; Kondo, K. *J. Org. Chem.* **2000**, *65*, 517.
27. Yang, Y. -Y.; Yang, W. -B.; Teo, C. -F.; Lin, C. -H. *Synlett* **2000**, 1634.
28. Bajwa, J. S.; Vivelo, J.; Slade, J.; Repic, O.; Blacklock, T. *Tetrahedron Lett.* **2000**, *41*, 6021.
29. DeGroot, A. H.; Dommisse, R. A.; Lemiere, G. L. *Tetrahedron* **2000**, *56*, 1541.
30. Yadav, J. S.; Reddy, B. V. S.; Madan, C. *New J. Chem.* **2000**, *24*, 853.
31. Parham, W. E.; Anderson, E. L. *J. Am. Chem. Soc.* **1948**, *70*, 4187.
32. Hon, Y. -S.; Lee, C. -F. *Tetrahedron Lett.* **1999**, *40*, 2389.
33. Kim, S.; Park, J. H. *Tetrahedron Lett.* **1987**, *28*, 439.
34. Ramasamy, K. S.; Bandaru, R.; Averett, D. *Synth. Commun.* **1999**, *29*, 2881.
35. Lee, A. S. -Y.; Cheng, C. -L. *Tetrahedron* **1997**, *53*, 14255.
36. Lee, A. S. -Y.; Su, F. -Y.; Liao,Y. -C. *Tetrahedron Lett*. **1999**, *40*, 1323.
37. Marko, I. E.; Ates, A.; Augustyns, B.; Gautier, A.; Quesnel, Y.; Turet, L.; Wiaux, M. *Tetrahedron Lett*. **1999**, *40*, 5613.
38. Taniguchi, T.; Kadota, K.; ElAzab, A. S.; Ogasawara, K. *Synlett* **1999**, 1247.
39. Ramasamy, K. S.; Averett, D. *Synlett* **1999**, 709.
40. Raina, S.; Singh, V. K. *Synth. Commun.* **1995**, *25*, 2395.
41. Yadav, J. S.; Srinivas, D.; Reddy, G. S. *Synth. Commun.* **1998**, *28*, 1399.
42. Heravi, M. M.; Ajami, D.; Mojtahedi, M. M.; Ghassemzadeh, M. *Tetrahedron Lett.* **1999**, *40*, 562.

43. Kumar, H. M. S.; Reddy, B. V. S.; Reddy, E. J.; Yadav, J. S. *Chem. Lett*. **1999**, 857.
44. Deka, N.; Sarma, J. C. *Synth. Commun.* **2000**, *30*, 4435.
45. Reddy, M. A.; Reddy, L. R.; Bhanumathi, N.; Rao, K. R. *Synth. Commun.* **2000**, *30*, 4323.
46. Davis, K. J.; Bhalerao, U. T.; Rao, B. V. *Synth. Commun.* **2000**, *30*, 2301.
47. Reddy, G. S.; Neelakantan, P.; Iyenger, D. S. *Synth. Commun.* **2000**, *30*, 4107.
48. Rezai, N.; Meybodi, F. A.; Salehi, P. *Synth. Commun.* **2000**, *30*, 1799.
49. Habibi, M. H.; Tangestaninejad, S.; Baltork, I. M.; Mirkhani, V.; Yadollahi, B. *Tetrahedron Lett.* **2001,** *42*, 2851.
50. Meskens, A. J. *Synlett* **1981**, 501.
51. Lipshutz, B. H.; Mollard, P.; Lindsley, C.; Chang, V. *Tetrahedron Lett.* **1997**, *38*, 1873.
52. Elliott, M. R.; Dhimane, A. L.; Malacria, M. *J. Am. Chem. Soc.* **1997**, *119*, 3427.
53. Otera, J.; Dan-oh, N.; Nozaki, H. *Tetrahedron* **1992**, *48*, 1449.
54. Ciceri, P.; Demnitz, F. W. J. *Tetrahedron Lett.* **1997**, *38*, 389.
55. Perio, B.; Dozias, M. J.; Jacquault, P.; Hamelin, J. *Tetrahedron Lett.* **1997**, *38*, 7867.
56. Karimi, B.; Ebrahimian, G. R.; Seradj, H. *Org. Lett*. **1999**, *1*, 1737.
57. Karimi, B.; Seradj, H.; Ebrahimian, G. R. *Synlett* **1999**, 1456.
58. Firouzabadi, H.; Iranpoor, N.; Karimi, B. *Synlett* **1999**, 321.
59. Arterburn, J. B.; Perry, M. C. *Org. Lett.* **1999**, *1*, 769.
60. Karimi, B.; Ashtiani, A. M. *Chem. Lett*. **1999**, 1199.
61. Laskar, D. D.; Prajapati, D.; Sandhu, J. S. *Chem. Lett*. **1999**, 1283.
62. Yadav, J. S.; Subba Reddy, B. V.; Srinivas, R.; Ramalingam, T. *Synlett* **2000**, 701.
63. Curini, M.; Epifano, F.; Marcotulio, M. C.; Rosati, O. *Synlett* **2001**, 1182.
64. Buckles, R. E.; Popov, A. I.; Zeleny, W. F.; Smith, R. J. *J. Am. Chem. Soc*. **1951**, *73*, 4525.

65. (a) Cattaway, F. D.; Hoyle, G. *J. Chem. Soc.* **1923**, 654. (b) Avramoff, M.; Weiss, J.; Schaechter, O. *J. Org. Chem.* **1963**, *28*, 3256.

66. Kajigneshi, S.; Kakinami, T.; Tokiyama, H.; Hirakawa, T.; Okamoto, T. *Chem. Lett.* **1987**, 627.

67. Saburo, K.; Isao, I.; Yoshinobu, H. (Nippon Soda Co. Ltd.) Japan, Kokai 7414, 411 (Cl. 16B314); 07 Feb 1974, Appl. 7258, 343, 12 June 1972; 5 PP. *Chem. Abstr.* **1974**, *81*, 13401, 13393c.

68. Paquette, L. A. Ed. *Encyclopedia of Reagents for Organic Synthesis*, John Wiley & Sons: New York, 1995, Vol. 7, p.4738.

69. Muathen, H. A. *J. Org. Chem.* **1992**, *57*, 2740.

70. (a) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*, Wiley: New York, 1967, 967. (b) Paquette, L. A. Ed. *Encyclopedia of Reagents for Organic Synthesis*, John Wiley & Sons, New York, 1995, Vol. 6, p.4370.

71. Fournier, M.; Fournier, F.; Berthelot, J. *Bull. Soc. Chim. Belg.* **1984**, *93*, 157.

72. Berthelot, J.; Fournier, M. *Can. J. Chem.* **1986**, *64*, 603.

73. Berthelot, J.; Fournier, F.; Fournier, M. *Synth. Commun*. **1985**, *15*, 213.

74. (a) Berthelot, J.; Guette, C.; Desbene, P. -L.; Basselier, J. -J.; Chaquin, P.; Masure, D. *Can. J. Chem.* **1989**, *67*, 2061. (b) Berthelot, J.; Guette, C.; Essayegh, M.; Desbene, P. L.; Basselier, J. J. *Synth. Commun.* **1986**, *16*, 1641.

75. (a) Berthelot, J.; Guette, C.; Desbene, P. -L.; Basselier, J. -J.; Chaquin, P.; Masure, D. *Can. J. Chem.* **1989**, *67*, 2061. (b) Berthelot, J.; Guette, C.; Ouchefoune, M.; Desbene, P. L.; Basselier, J. J. *J. Chem. Res. (S)* **1986**, 381.

76. (a) Berthelot, J.; Basselier, J. J.; Desbene, P. L.; Desbene-Monvernay, A. *Analusis* **1987**, *15*, 22. (b) Desbene-M. A.; Karazoun, O.; Berthelot, J.; Desbene, P. -L. *Can. J. Chem.* **1992**, *70*, 870.

77. Berthelot, J.; Benammar, Y.; Desmazieres, B. *Can. J. Chem.* **1995**, *73*, 1526.

78. Berthelot, J.; Benammar, Y.; Lange, C. *Tetrahedron Lett.* **1991**, *32*, 4135.

79. Berthelot, J.; Benammar, Y.; Desmazieres, B. *Synt. Commun.* **1997**, *27*, 2865.

80. Bellucci, G.; Chiappe, C.; D'Andrea, F. *Tetrahedron: Asymmetry* **1995**, *6*, 221.

81. Bora, U.; Chaudhuri, M. K.; Khan, A. T.; Patel B. K. *Patent Applied. Application No.28/CAL/2000, 19th Jan, 2000.*

82. Chaudhuri, M. K.; Khan, A. T.; Patel, B. K.; Dey, D.; Kharmawophlang, W.; Lakshmiprabha, T. R.; Mandal, G. C. *Tetrahedron Lett.* **1998**, *39*, 8163.

83. Bose, G.; Barua, P. M. B.; Chaudhuri, M. K. Kalita, D.; Khan, A. T. *Chem. Lett.* **2001**, 290.

84. Bose, G.; Mondal, E.; Khan, A. T.; Bordoloi, M. J. *Tetrahedron Lett.* **2001**, *42*, 8907.

85. Mondal, E.; Bose, G.; Khan, A. T. *Synlett* **2001**, 785.

86. Baghmar, M.; Sharma, P. K. *Int. J. Chem. Kinet.* **2001**, *33*, 390.

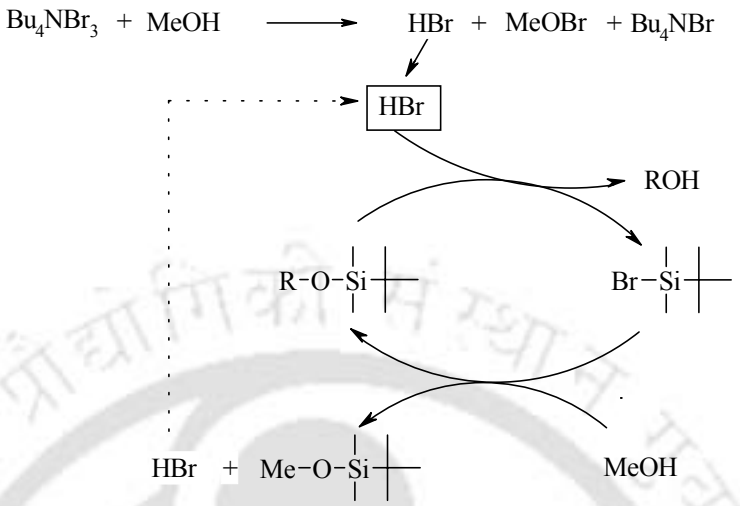
87. Kajigaeshi, S.; Kakinami, T.; Hirakawa, T. *Chem. Lett.* **1987**, 627.

IIB Present Work

IIB.1 Tetrabutylammonium Tribromide (TBATB) -Methanol as an Efficient Reagent for the Deprotection of Acid-Sensitive Groups

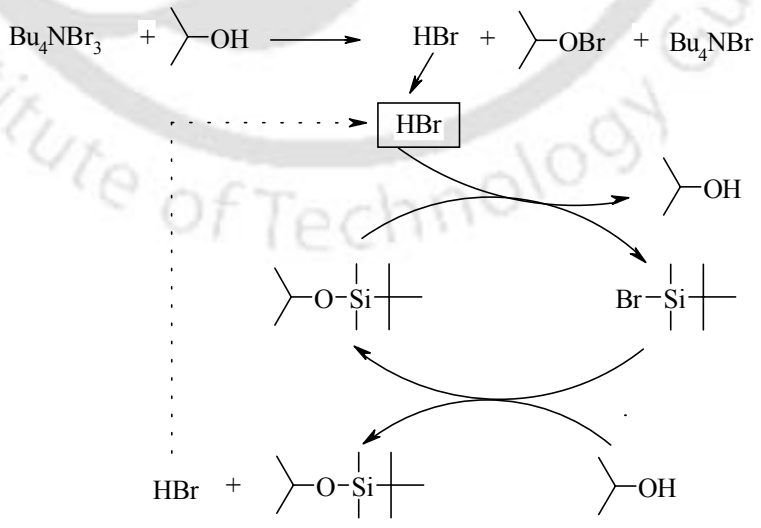
The protection-deprotection of alcohol functionalities is important in synthetic organic chemistry, and a plethora of reagents and methods have been devised to this end. The importance of protecting the hydroxyl group frequently appears in synthesis of biologically active molecules. Of all the hydroxyl-protecting groups,[1] the *tert*-butyldimethylsilyl (TBS) ether still occupies a prominent position because of its easy preparation[2] and stability to a wide range of reaction conditions. A variety of reagents exist for the removal of TBS ethers[1] and very recently several methods for the deprotection of silyl ethers under various reaction conditions have been reported in the literature.[3] Unfortunately, many of these procedures require longer reaction times, drastic reaction conditions, large excess of phase transfer reagents, moisture-sensitive and expensive reagents causing serious problem for large-scale reaction. Moreover most of these reagents are either strongly acidic, basic, oxidising or reducing in nature, a property that is not always desirable.

Tetrabutylammonium tribromide (TBATB) is known as an efficient brominating agent for a number of substrates in various solvents.[4–6] However, when we used this reagent in methanol for the bromination of TBS protected cinnamyl alcohol **32**, we discovered that TBS ether was removed quantitatively within 10 min. This result was not surprising since the other halogen (I_2),[7] I_2/MeOH,[3a] interhalogen compounds I-Cl and I-Br[3g] and $BiBr_3$/ MeCN[3m] have been used for the deprotection of TBS ethers. It is believed that the haloacids generated *in situ* from the above reagents might be the species responsible for the hydrolysis of TBS ethers. It has been shown that benzyltrimethylammonium tribromide generates HBr and MeOBr in methanol.[8] In the present case the hydrolysis may be catalysed by HBr that is generated *in situ* from the reaction of TBATB with MeOH as shown in Scheme 2.42.



Scheme 2.42. Proposed Mechanism of Deprotection of TBS Ether

In a control experiment, treatment of silyl ether of 1-decanol **34m** with 0.01 equiv of 48% HBr in MeOH at room temperature in <5 min leads to a deprotected alcohol in a quantitative yield. When TBS ether of isopropanol was treated with TBATB in isopropanol as the solvent, no deprotection was observed even after 48 h. This is because the deprotected isopropanol reacts with *tert*-butyldimethylsilyl bromide to yield the starting TBS ether, rendering its effective concentration practically unaltered (Scheme 2.43). However, addition

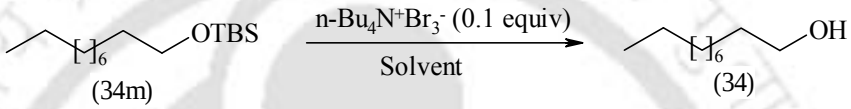


Scheme 2.43. Proposed Mechanism of Deprotection of TBS Ether of i*so*-Propanol in *iso*-Propanol

of methanol shifted the equilibrium to the right leading to a 90% deprotection after 5 h, as observed. We therefore explored the possibility of utilising tetrabutylammonium tribromide (TBATB) as an effective reagent for the cleavage of TBS ethers.

The results of solvent dependent cleavage of primary TBS ether **34m** with TBATB (0.1 mol%) as shown in Table 2.1, suggests that polar organic solvents are relatively more suitable for deprotection and methanol turns out to be the best protic medium for desilylation.

Table 2.1. Solvent Dependent Cleavage of C_{10}-TBS Ether



Solvent(s)	Time/h	Yield %[a]
MeOH	0.40	99
MeOH:H_2O (9:1)	1.80	99
EtOH	1.80	93
^{i}PrOH	10.0	98
CH_3CN	3.00	95
Toluene	24.0	Nil
CH_2Cl_2	24.0	Nil

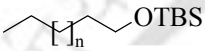
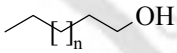
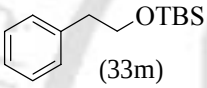
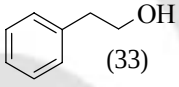
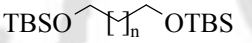
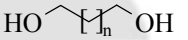
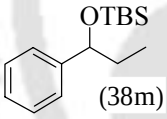
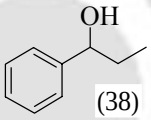
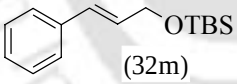
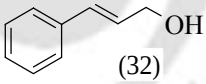
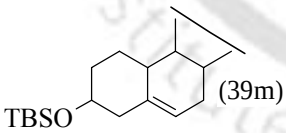
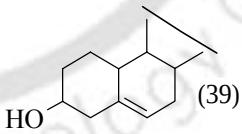
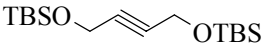
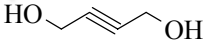
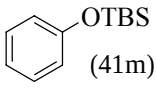
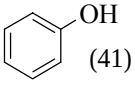
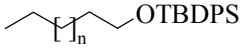
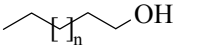
[a] GC determined

In a typical reaction, to a solution of TBS ether (1 mmol) in methanol (5 mL) was added TBATB (0.1 mmol). The reaction times are as shown for each substrate in Table 2.2. It is important to note that a lower quantity of TBATB (*i.e.,* 0.01 mol%) also gave satisfactory results at longer reaction times. For instance, substrate **34m** containing a primary TBS group was deprotected at room temperature in a quantitative yield within 2.5 h, but a TBS protected secondary alcohol **38m** could be deprotected to the extent of 93% in 4 days at room temperature. However, refluxing the reaction mixture can accelerate the reaction rate (90%, 6 h). For the present investigation, 0.1 mol% of the reagent has been used for each substrate.

A wide spectrum of structurally varied TBS ethers was subjected to deprotection by this procedure, and the result is summarised in Table 2.2. Aliphatic TBS protected primary

alcohols **34m**, **35m**, **33m**, **36m** and **37m** were deprotected quantitatively in nearly 1 h. TBS protected secondary alcohols **38m** and **39m** produced the corresponding alcohols in excellent yields but the reaction rates were relatively slow. The slow rate of deprotection of TBS protected cholesterol **39m** could be in part due to a different solvent system (MeOH : CH_2Cl_2, 1:1) used for this substrate.

Table 2.2. Deprotection[a] of TBS Ethers with TBATB (0.1 equiv) in Methanol

Substrate	Time/h	Product [b]	Yield (%)[c]
 n=6, 14 (34m, 35m)	0.41	 n=6, 14	97
 (33m)	0.66	 (33)	97
 n=1, 3 (36m, 37m)	1.15	 n=1, 3 (36, 37)	99[d]
 (38m)	7.00	 (38)	98
 (32m)	0.08	 (32)	97
 (39m)	8.00[e]	 (39)	96
 (40m)	0.50	 (40)	94
 (41m)	6.00[g]	 (41)	92
 n=6, 8 (34p, 42p)	6.00[f,g]	 n=6, 8 (34, 42)	50

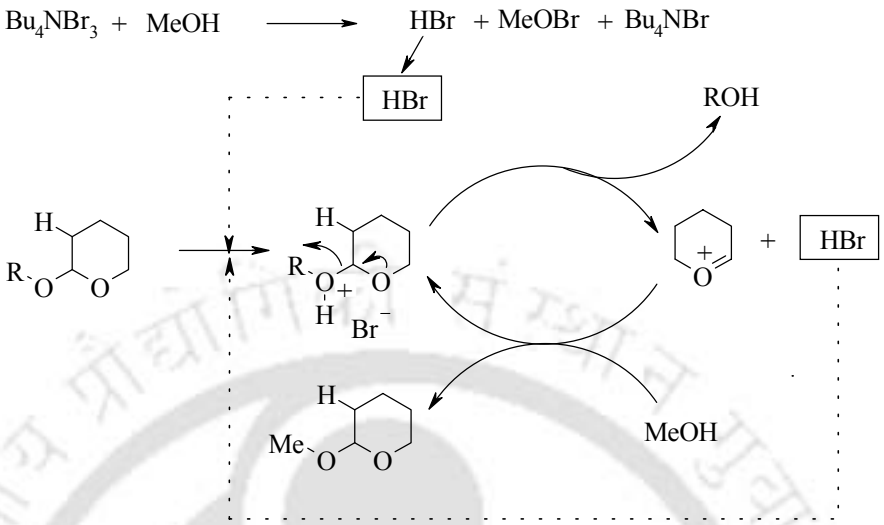
[a]Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Isolated yield. [d]GC yield. [e]The reaction was performed in MeOH:CH_2Cl_2 (1:1) and [f]MeOH:CH_2Cl_2 (5:2). [g]The reaction was performed at reflux temperature.

The compatibility of the reagent was further illustrated by selective deprotection of TBS protected alcohols containing ethylenic **32m** and acetylenic **40m** systems. Importantly, no other side product *viz.* bromination was observed, although this reagent is an efficient brominating agent for ethylenic and acetylenic substrates.[5] TBDPS ethers of primary alcohol and phenolic TBS ethers are reluctant to hydrolysis and hydrolysed slowly. The selectivity of this methodology was further tested with other substrates containing *tert*-butyldiphenylsilyl (TBDPS) ethers **34p** and **42p**, and phenolic TBS ethers **41m**.

THP ethers are one of the most widely used protecting groups employed during a multistep organic synthesis because of low cost and stability towards various reaction conditions such as strong bases, Grignard reagents, hydrides, redox reagents, alkylating, acylating agents and catalytic hydrogenation and easy removal under mild acidic conditions. Numerous methods have been reported for tetrahydropyranylation and detetrahydropyranylation.[1,9] Protection is normally achieved with a mild acidic reagent in an aprotic solvent such as CH_2Cl_2, THF, acetone etc., and deprotection also with an acidic reagent but in a polar or protic solvents such as methanol, ethanol, isopropanol, acetonitrile etc. Commonly used catalysts are potassium dodecatangestocobaltate trihydrate ($K_5CoW_{12}O_{40}.3H_2O$),[10] $ZrCl_4$,[11] I_2-microwave irradiation,[12] LiBr,[13] acetonyltriphenylphosphonium bromide,[14] I_2,[15] NH_4Cl,[16] heteropoly acids,[17] which catalyse both these transformations effectively by merely changing the solvent system. However, some of these procedures suffer due to the use of expensive and toxic reagents, high temperature, longer reaction times and incompatibility with other acid-sensitive functional groups.

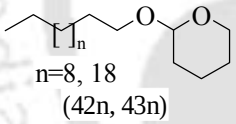
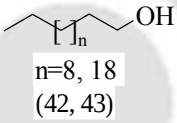
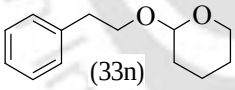
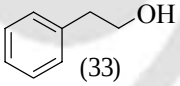
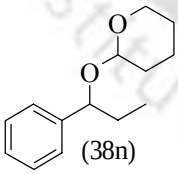
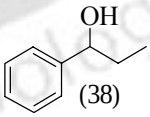
HBr generated by the action of TBATB and methanol also smoothly deprotects acid-sensitive protecting groups like THP ethers. The proposed mechanism for the cleavage of THP ether is shown in the following Scheme 2.44. Gas chromatographic co-injection analysis unequivocally established the formation of 2-methoxytetrahydropyran as a transacetalisation product and in turn the mechanism.

In a typical reaction, to a solution of THP ether (1 mmol) in methanol (5 mL) was added TBATB (0.1 mmol). Primary THP ethers **33n** and **43n** were cleaved faster compared to secondary secondary THP ether **38n** as shown in Table 2.3.



Scheme 2.44. Proposed Mechanism of Deprotection of THP Ether

Table 2.3. Deprotection[a] of THP Ethers with TBATB (0.1 equiv) in Methanol

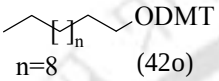
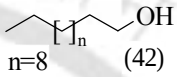
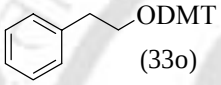
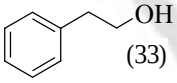
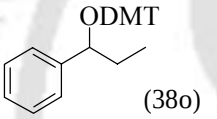
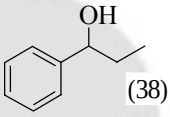
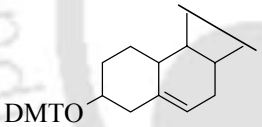
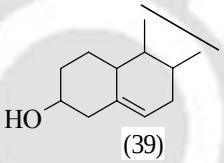
Substrate	Time/h	Product [b]	Yield (%)[c]
 n=8, 18 (42n, 43n)	0.08	 n=8, 18 (42, 43)	95
 (33n)	0.83	 (33)	96
 (38n)	1.20	 (38)	97

[a]Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Isolated yield.

4,4'-Dimethoxytrityl (DMT) group has been used widely for the protection of 5'-hydroxyl groups of nucleosides during oligonucleotide synthesis, which is removed with acetic acid or trifluoro acetic acid. Cleavage of dimethoxytrityl ether was investigated with different primary and secondary ethers as shown in Table 2.4. Deprotection of DMT group was performed by treating a solution of DMT ether (1 mmol) in methanol (3 mL) and

TBATB (0.1 mmol). Facile deprotection of acid-sensitive DMT ethers of both primary and secondary DMT ethers, Table 2.4 further supports the formation of HBr, proposed in Scheme 2.42 and 2.44.

Table 2.4. Deprotection[a] of DMT Ethers with TBATB (0.1 equiv) in Methanol

Substrate	Time/h	Product[b]	Yield (%)[c]
 n=8 (42o)	0.25	 n=8 (42)	98
 (33o)	0.25	 (33)	97
 (38o)	0.25	 (38)	97
 (39o)	0.30	 (39)	95

[a]Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Isolated yield.

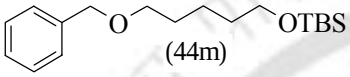
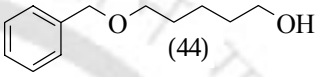
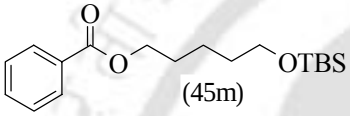
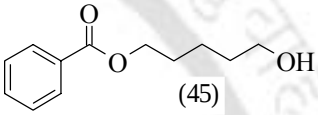
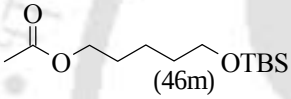
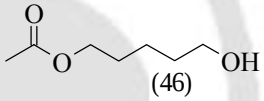
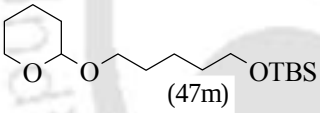
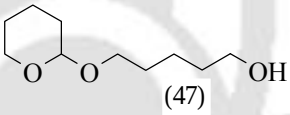
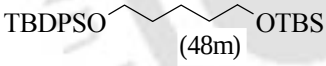
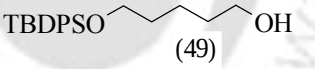
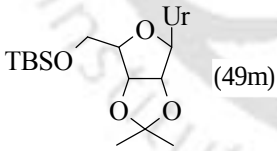
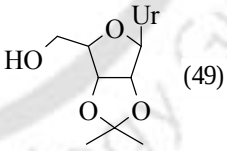
We also examined the intramolecular chemoselective deprotection of TBS ethers in the presence of Bn **44m**, Bz **45m**, Ac **46m**, THP **47m** TBDPS **48m** and isopropylidene **49m**, protecting groups and the result is very encouraging. As could be seen from Table 2.5, primary TBS group can be selectively deprotected in the presence of Bn, Bz, Ac, THP and isopropylidine groups.

Intermolecular chemoselectivity was determined by treating equimolar mixture of two different substrates **X** and **Y** with 0.1 mol % of the reagent in an appropriate solvent and reaction was monitored by GC. An internal standard was used when both the deprotected products were same.

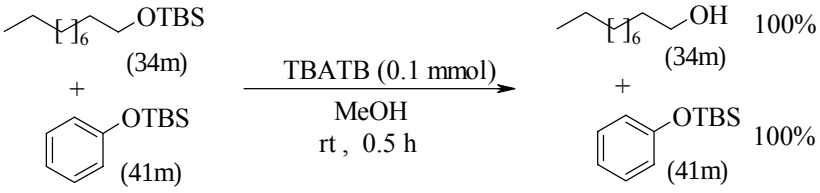
Selectivity = %Y deprotected - % X deprotected at time[18]

Intermolecular chemoselectivity for aliphatic TBS ether **34n** in the presence of phenolic TBS ether **41n** gave 100% selective deprotection of aliphatic TBS ether over phenolic TBS ether, Scheme 2.45.

Table 2.5. Intramolecular Deprotection[a] of TBS Ethers With TBATB (0.1 equiv) in Methanol

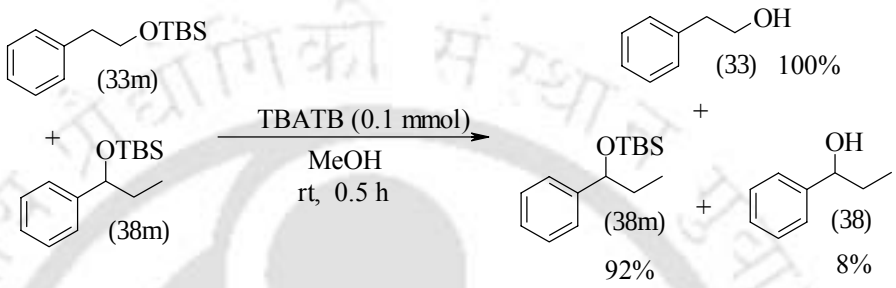
Substrate	Time/h	Product [b]	Yield (%)[c]
 (44m)	0.41	 (44)	96
 (45m)	0.41	 (45)	98
 (46m)	0.41	 (46)	96
 (47m)	0.30	 (47)	95
 (48m)	0.35	 (49)	98
 (49m)	9.50	 (49)	95

[a]Reactions were monitored by TLC, GC. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Isolated yield.



Scheme 2.45

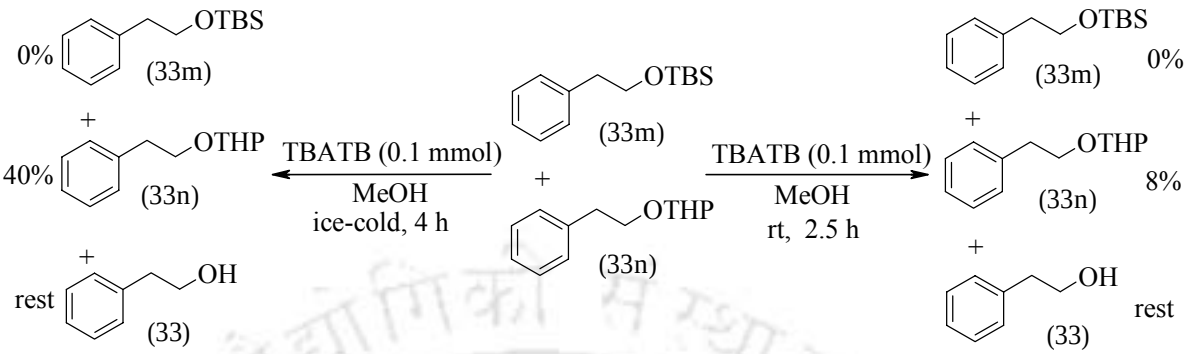
Primary TBS ether **33m** was selectively deprotected compared to the secondary TBS ether **38m** and the selectivity was 92% at room temperature (Scheme 2.46). Similarly primary DMT ether **33o** was selectively cleaved in the presence of primary TBS ether **33m** with 95% selectivity with in 5 min at room temperature.



Scheme 2.46

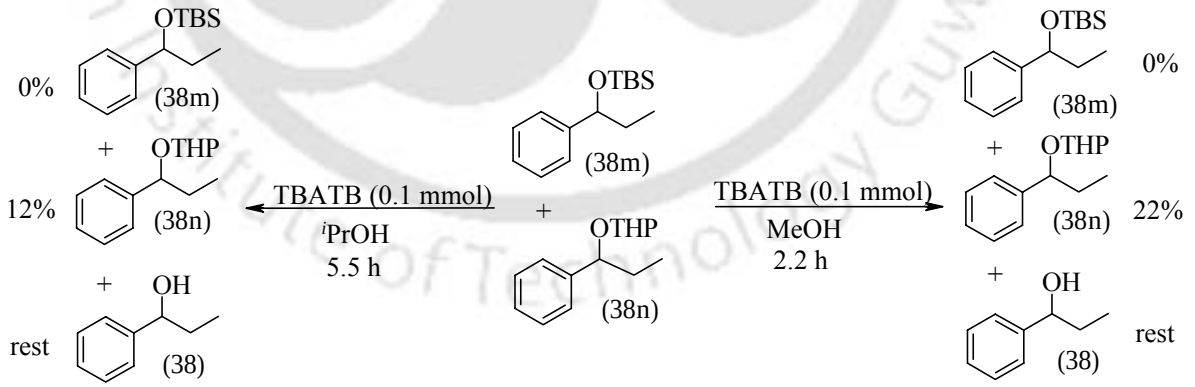
The reagent *o*-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluranium tetrafluoroborate (TBTU)[3h] selectively deprotected primary THP ether in the presence of TBS ether. Exactly opposite selectivity was observed with TBATB for both, with intermolecular as well as intramolecular deprotection. The former reagent is a fluoride-based reagent and has higher affinity towards silicon. The Si-F bond strength is 30 kcal/mol greater than the Si-O bond strength. But the later reagent the cleavage is by a hydrolytic path involving HBr.

In a competitive intermolecular deprotection between a primary TBS ether **33m** and a primary THP ether **33n** in methanol at room temperature, it was observed that both were deprotected with nearly equal rates (only 8% selectivity, 0.5 h). Notably, a better intermolecular chemoselectivity (60%) was obtained for **33m** by performing the reaction under an ice-cold condition, although longer reaction time (4 h) was required for the process. However, a quantitative intramolecular selectivity (100%) was observed as demonstrated for substrate **47m** (Table 2.5). 1-Decanol **34** was used as the internal standard for this investigation and percentages were calculated with respect to 1-decanol.



Scheme 2.47

In contrast to the preferential deprotection of primary TBS over primary THP ether a completely opposite selectivity was observed for the corresponding secondary ethers. Thus, in a competitive deprotection study between secondary TBS ether **38m** and secondary THP ether **38n**, the use of methanol at room temperature gave 78% selectivity after 2.2 h for **38n** (Scheme 2.48). It is interesting to note that the desilylation becomes much slower when methanol is replaced with more sterically hindered alcohol. The use of isopropanol as a solvent, however, enhances the selectivity (88%, 5.6 h) for **38n** over **38m** although longer reaction times were required. Thus, we have found a better intramolecular selectivity as compared to the intermolecular selectivity in our investigation.



Scheme 2.48

In conclusion, these results indicate that TBATB can readily differentiate not only THP ethers over TBS ethers but also TBS over TBDPS ethers. The apparent order of stability as obtained from our present study is phenolic TBS > 1^{o}OTBDPS > 2^{o}OTBS > 2^{o}OTHP > 1^{o}OTHP > 1^{o}OTBS > 1^{o}ODMT. TBS ether has been cleaved selectively in the

presence of isopropylidine, Bn, Ac, Bz, THP and TBDPS groups. This method is high yielding, chemoselective, safe, operationally simple under mild reaction conditions, fast, cost effective, clean and no precaution is needed to exclude moisture or oxygen from the reaction system. Moreover, no strongly acidic or basic conditions are used; therefore it is most suitable for practical organic synthesis.

IIB.1.1 References

1. (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed., John Wiley & Sons: New York, 1999. (b) Kocieński, P. J. *Protecting Groups*; Georg Thieme Verlag: New York,1994.
2. Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
3. (a) Lipshutz, B. H.; Keith, J. *Tetrahedron Lett.* **1998**, *39*, 2495. (b) Bartoli, G.; Bosco. M.; Marcantoni, E.; Sambri, L.; Torregiani, E. *Synlett* **1998**, 209. (c) Paterson, I.; Cowden, C. J.; Rahn, V. S.; Woodrow, M. D. *Synlett* **1998**, 915. (d) Oriyama, T.; Kobayashi, Y.; Noda, K. *Synlett* **1998**, 1047. (e) Grieco, P. A.; Markworth, C. J. *Tetrahedron Lett.* **1999**, *40*, 665. (f) Jarowicki, K.; Kocieński, P. *J. Chem. Soc., Perkin Trans. I* **1999**, p.1590 and the refs. cited therein. (g) Kartha, K. P. R.; Field, R. A. *Synlett* **1999**, 311. (h) Ramasamy, K. S.; Averett, D. *Synlett* **1999**, 709. (i) Ranu, B. C.; Jana, U.; Majee, A. *Tetrahedron Lett.* **1999**, *40*, 1985. (j) Crouch, R. D.; Stieff, M.; Frie, J. L.; Cadwallader, A. B.; Bevis, D. C. *Tetrahedron Lett.* **1999**, *40*, 3133. (k) Hunter, R.; Hinz, W.; Richards, P. *Tetrahedron Lett.* **1999**, *40*, 3643. (l) Sabitha, G.; Syamala, M.; Yadav, J. S. *Org. Lett.* **1999**, *1*, 1701. (m) Bajwa, J. S.; Vivelo, J.; Slade, J.; Repič, O.; Blacklock, T. *Tetrahedron Lett*. **2000**, *41*, 6021.
4. Bora, U.; Bose, G.; Chaudhuri, M. K.; Dhar, S. S.; Gopinath, R.; Khan, A. T.; Patel, B. K. *Org. Lett*. **2000**, *2*, 247.
5. Chaudhuri, M. K.; Khan, A. T.; Patel, B. K.; Dey, D.; Kharmawophlang, W.; Lakshmiprabha, T. R.; Mandal, G. C. *Tetrahedron Lett*. **1998**, *39*, 8163.
6. Paquette, L. A. ed. *Encyclopedia of Reagents for Organic Synthesis*, John Wiley & Sons: New York, 1995, Vol. 7, p.4738.

7. Vaino, A. R.; Szarek, W. A. *J. Chem. Soc., Chem. Commun*. **1996**, 2351.
8. Kajigaeshi, S.; Kakinami, T.; Hirakawa, T. *Chem. Lett*. **1987**, 627.
9. (a) Deka, N.; Sarma, J. C. *J. Org. Chem.* **2001**, *66*, 1947. (b) Branco, L. C. *Tetrahedron* **2001**, *57*, 4405. (c) Babu, B. S.; Balasubramanian, K. K. *Synlett* **1999**, 1261. (d) Nishiguchi, T.; Hayakawa, S.; Hirasaka, Y.; Saitoh, M. *Tetrahedron Lett.* **2000**, *41*, 9843. (e) Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O.; Costantino, U. *Tetrahedron Lett*. **1998**, *28*, 8159. (f) Babu, B. S.; Balasubramanian, K. K. *Tetrahedron Lett.* **1998**, *39*, 9287.
10. Habibi, M. H.; Tangestaninejad, S.; Baltork, I, M.; Mirkhani, V.; Yadollahi, B. *Tetrahedron Lett.* **2001**, *42*, 2851.
11. Rezai, N.; Meybodi, F. A.; Salahi, P. *Synth. Commun.* **2000**, *30*, 1799.
12. Deka, N.; Sarma, J. C. *Synth. Commun.* **2000**, *30*, 4435.
13. Reddy, M. A.; Reddy, L. R.; Bhanumathi, N.; Rao, K. R. *Synth. Commun.* **2000**, *30*, 4323.
14. Hon, Y. -S.; Lee, C. -F. *Tetrahedron Lett.* **1999**, *40*, 2389.
15. Kumar, H. M. S.; Reddy, B. V. S.; Reddy, E. J.; Yadav, J. S. *Chem. Lett.* **1999**, 857.
16. Yadav, J. S.; Srinivas, D.; Reddy, G. S. *Synth. Commun.* **1998**, *28*, 1399.
17. Molnar, A.; Beregszaszi, T. *Tetrahedron Lett.* **1996**, *37*, 8597.
18. Pilcher, A. S.; DeShong, P. *J. Org. Chem.* **1993**, *58*, 5130.

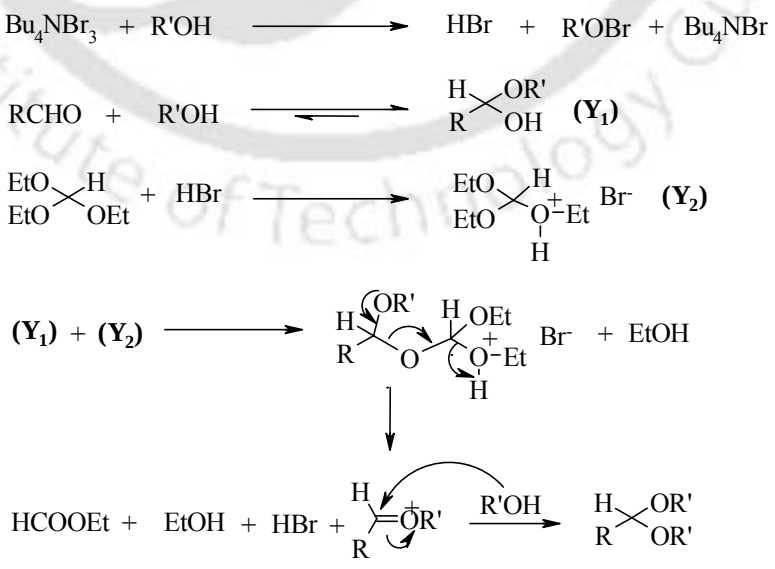
IIB.2 Tetrabutylammonium Tribromide (TBATB) as an Efficient Reagent for Acetalisation of Carbonyl Compounds

During a multistep synthesis, a carbonyl group may have to be protected against an attack by various reagents such as nucleophiles, oxidants, basic, catalytic, or hydride reducing agents, including organometallic reagents.[1] Acetals are generally formed under acidic conditions, and water formed during a reaction is removed either by physical or chemical methods.[1c] Orthoesters such as triethyl orthoformate are used as one of the chemical methods for the removal of water, which reacts with the water formed by the reaction of aldehyde and ketone with an alcohol to form ethanol and ethylformate, resulting in the equilibrium shifting to the right.[1c] Methods are available for the conversion of carbonyl groups in aldehydes and ketones to their corresponding acetals using trialkyl orthoformates in the presence of acid catalysts such as HCl,[2] $FeCl_3$,[3] Amberlyst-15,[4] $ZrCl_4$,[5] DDQ,[6] NBS,[7] and $Sc(NTf_2)_3$.[8] Unfortunately, many of these procedures often require a large excess of reagents, longer reaction times, drastic reaction conditions, and moisture-sensitive and expensive reagents. Also, some of these reagents do not always prove to be satisfactory for the acetalisation of cyclic and aromatic ketones.

Previously, tetrabutylammonium tribromide (TBATB) has been used as a brominating agent,[9,10,11] for the cleavage of acid-sensitive protecting groups like, TBS, THP, DMT ethers (previous section) and dithioacetals,[12] and the pyranylation-depyranylation of alcohols.[13] The identification of tetrabutylammonium tribromide as a catalytic, mild, and chemoselective reagent for the acetalisation of carbonyl compound is the basis of this investigation.

In this chapter, we have described a mild, efficient, and environmentally benign method for the acetalisation of carbonyl compounds, using tetrabutylammonium tribromide (0.01 equiv) as a promoter in the presence of triethyl orthoformate (1.1 equiv) in absolute alcohol at room temperature. Acetals of corresponding carbonyl compounds can also be

obtained, using trimethyl orthoformate instead of triethyl orthoformate. Open chain acetals have frequently been subjected to special attention, adding to their liability as compared with cyclic *O*,*O*-acetals.[1] Under the experimental conditions, various carbonyl compounds can be acetalised to the corresponding *O*,*O*-acetals in excellent yields and the result is summarised in Table 2.6. The homogeneous reaction mixture was left at room temperature for a specified period of time as shown for each substrate in Table 2.6. HBr generated *in situ* from the reaction of TBATB with alcohol, as shown in Scheme 2.49, may catalyse the reaction. The solvent also plays a very important role in this reaction. When benzaldehyde (1 equiv) was reacted with triethyl orthoformate (1.1 equiv) and TBATB (0.01 equiv) in CH_2Cl_2, instead of absolute alcohol, after 24 h, only a small amount (<5%) of the corresponding diethyl acetal was formed. This may be due to the fact that alcohol accelerates the formation of hemiacetal **Y_1** as shown in Scheme 2.49, which is further facilitated by the HBr generated in the medium. On the other hand, HBr also protonates triethyl orthoformate to produce an oxonium species **Y_2** which in turn reacts with intermediate hemiacetal to give the desired acetal as shown in Scheme 2.49. In a control experiment, treatment of the reaction mixture with a catalytic amount of a saturated HBr solution in absolute ethanol, instead of TBATB, led to a quantitative conversion of benzaldehyde diethyl acetal within 10 min when benzaldehyde **1** was used as the substrate.



Scheme 2.49. Proposed Mechanism of Acetalisation

Table 2.6. Acetalisation[a] of Carbonyl Compounds

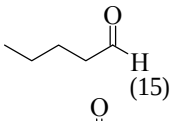
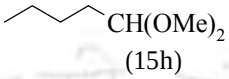
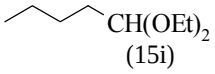
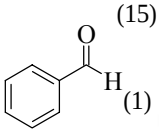
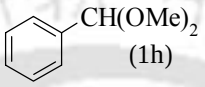
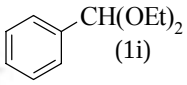
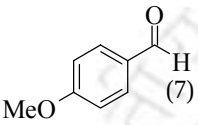
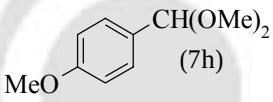
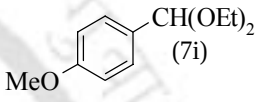
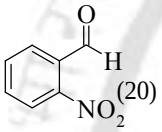
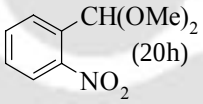
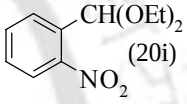
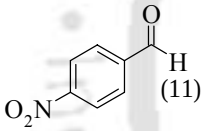
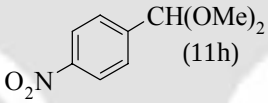
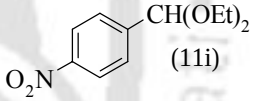
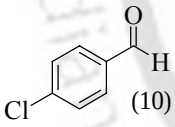
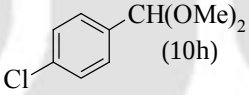
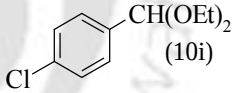
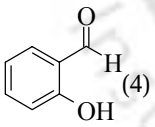
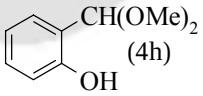
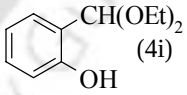
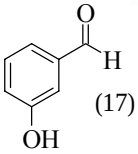
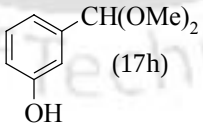
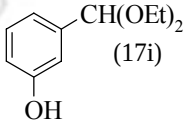
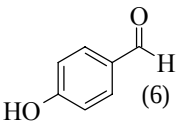
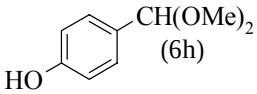
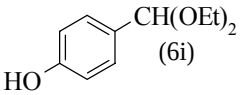
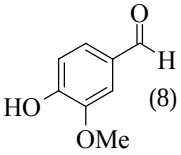
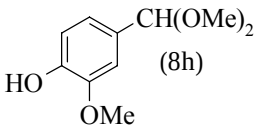
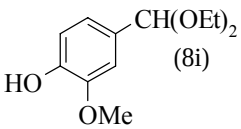
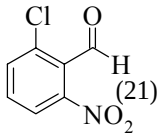
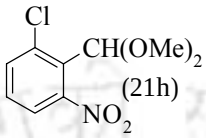
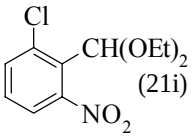
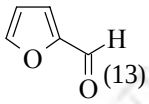
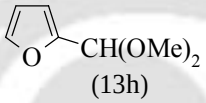
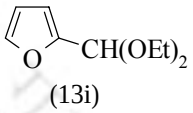
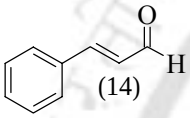
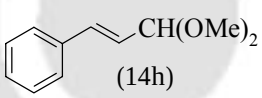
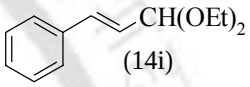
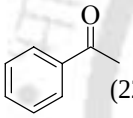
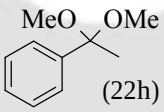
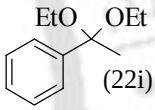
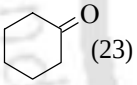
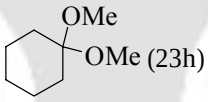
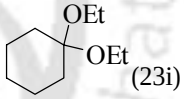
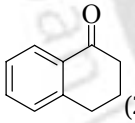
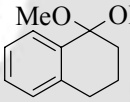
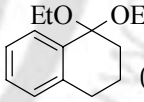
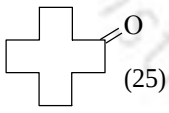
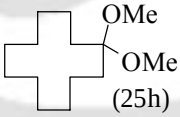
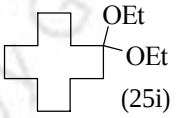
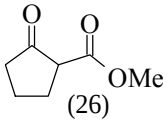
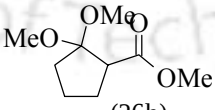
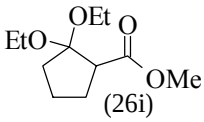
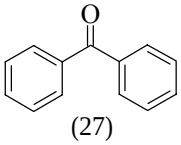
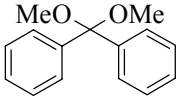
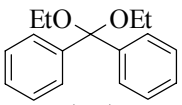
Substrate	Time/ h	X_1[b]	Yield[c] (%)	X_2[b]	Yield[c] (%)
 (15)	0.16	 (15h)	95	 (15i)	97
 (1)	0.16	 (1h)	97	 (1i)	95
 (7)	0.33	 (7h)	80	 (7i)	80
 (20)	2.50	 (20h)	95	 (20i)	90
 (11)	0.50	 (11h)	95	 (11i)	92
 (10)	0.16	 (10h)	94	 (10i)	95
 (4)	24	 (4h)	00	 (4i)	00
 (17)	2.0	 (17h)	62	 (17i)	70
 (6)	2.0	 (6h)	25	 (6i)	35
 (8)	0.5	 (8h)	60	 (8i)	60

Table 2.6. Acetalisation[a] of Carbonyl Compounds

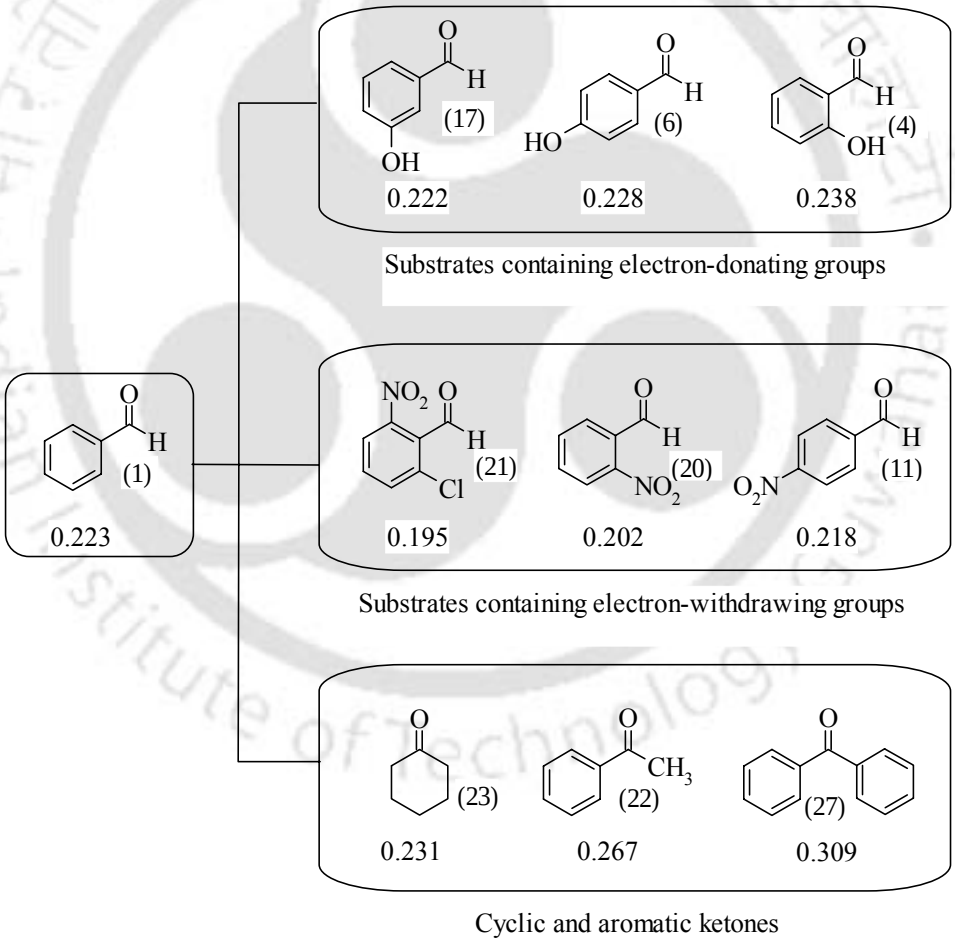
Substrate	Time/ h	X_1[b]	Yield[c] (%)	X_2[b]	Yield[c] (%)
 (21)	3.5	 (21h)	85	 (21i)	60
 (13)	0.16	 (13h)	96	 (13i)	92
 (14)	0.33	 (14h)	90[d]	 (14i)	93[d]
 (22)	0.33	 (22h)	97	 (22i)	89
 (23)	0.33	 (23h)	99	 (23i)	90
 (24)	0.41	 (24h)	95	 (24i)	87
 (25)	0.33	 (25h)	97	 (25i)	97
 (26)	2.00	 (26h)	98	 (26i)	89
 (27)	24	 (27h)	00	 (27i)	08

[a]Reactions were monitored by TLC/GC. X_1=dimethyl acetals; X_2= diethyl acetals. [b]Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c]Isolated yields. [d] 2.2 equiv of trialkyl orthoformate and 0.02 equiv of TBATB were used.

By the present methodology, aromatic aldehyde, benzaldehyde **1** and substituted aldehydes, with both electron-donating and -withdrawing groups at the ortho and para positions such as *p*-methoxybenzaldehyde **7**, *p*-chlorobenzaldehyde **10**, *p*-nitrobenzaldehyde **11** and *o*-nitrobenzaldehyde **20**, produced the corresponding dialkyl acetals in excellent yields. It may be mentioned here that the ortho substituted substrate reacts more slowly than the para substituted one, which could be due to steric factors. It is interesting to note that the hydroxyl group substituted at different positions in an aromatic ring greatly influences the reaction rates. For instance, the hydroxyl group substituted at the meta and para positions, as in the case of *m*-hydroxybenzaldehyde **17** and *p*-hydroxybenzaldehyde **6**, in 2 h gave about 70 and 30% of the corresponding dialkyl acetals, respectively. However, when the same group is present at the ortho position as in the case of *o*-hydroxy benzaldehyde **4**, no product could be detected even after 24 h, which could be both due to the steric and electronic factors. It is seen from Table 2.6, that the electron donating groups disfavour product formation as demonstrated for *o*-hydroxybenzaldehyde **4** and *p*-hydroxybenzaldehyde **6**, and the electron-withdrawing group favours the formation of product as shown for *o*-nitrobenzaldehyde **20** and *p*-nitrobenzaldehyde **11**, respectively. In contrast, the electron withdrawing groups favour the formation of products is further supported with a sterically hindered substrate containing electron-withdrawing groups 2-chloro-6-nitrobenzaldehyde **21**. Thus, under the reaction conditions, 2-chloro-6-nitrobenzaldehyde **21** gave dialkyl acetal in 60% yield.

To further support our explanation, the electron density at the carbonyl carbon was calculated using semi-empirical molecular orbital calculations, the AM1 method as implemented in the Hyperchem package (Hyperchem, Inc.; Gainsville, FL.), and the result is shown in Scheme 2.50. The calculated electron density is in excellent agreement with our explanation. Thus, due to both unfavourable steric and electronic factors, *o*-hydroxybenzaldehyde **4** did not form any trace of dialkyl acetal. For *o*-hydroxybenzaldehyde **4** due to a higher electron density around the carbonyl carbon it is less susceptible to nucleophilic attack by alcohols. Moreover, a higher activation energy is required due to steric crowding by the *o*-hydroxyl group. Substrate *p*-hydroxybenzaldehyde **6**, where steric crowding is absent due to a relatively higher electron density around the carbonyl carbon, it

is less susceptible to nucleophilic attack by alcohols for the acetal formation. However, due to a relatively favourable electronic factor and absence of steric crowding *m*-hydroxybenzaldehyde **17** gave a better yield than ortho and para hydroxybenzaldehydes. Thus, for acetalisation, electronic factors predominate over the steric factors, which is clearly demonstrated in case of 2-chloro-6-nitrobenzaldehyde **21**. This methodology can also be extended to the heterocyclic aldehyde 2-furaldehyde **13** and unsaturated aldehydes such as cinnamaldehyde **14**.



Scheme 2.50. Electron Density at the Carbonyl Carbon

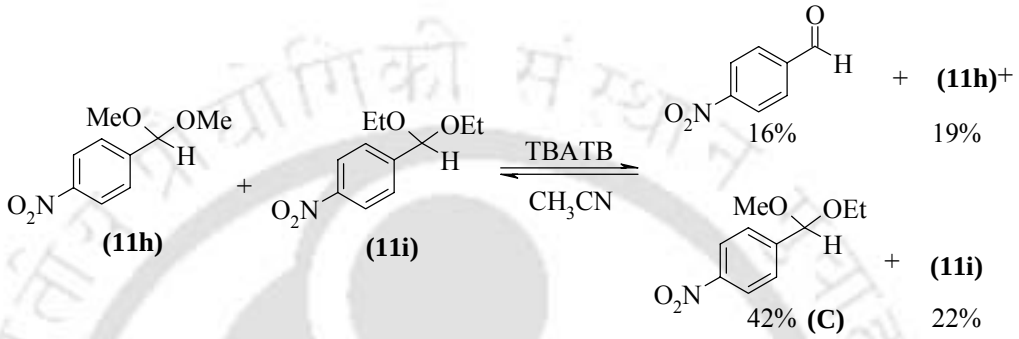
The formations of dialkyl ketals from the corresponding cyclic and aromatic ketones using conventional acid catalysis were not generally satisfactory due to stereo-electronic factors. It is well known that aldehydes (RCHO) are more reactive than ketones (RCOR) for two reasons. First, ketones are more stable in the ground state than aldehydes; this is primarily due to the appended alkyl groups providing electron density through the sigma bond framework to stabilise the carbonyl dipole. Second, the transition state for an aldehyde addition reaction is lower in energy than that of the ketone. This is due to steric crowding of the transition state by the ketonic R groups. Since the ketone starts at a lower energy in the ground state, it has lower reactivity than an aldehyde. However, by the present method, dialkyl ketals were also obtained in high yields when acetophenone **22** and cyclohexanone **23** were used as the models for acyclic and cyclic saturated ketones. The efficacy of the methodology was successfully applied to other ketones such as tetralone **24** and cyclopentanone-2-methylcarboxylate **26**. However, the dialkyl ketalisation of hindered ketones such as benzophenone **27** was not successful, probably due to higher electron density at the carbonyl carbon (Scheme 2.50), thereby making it less susceptible to attack by hydroxyl nucleophiles for ketalisation.

Formation of mixed acetal was not observed in the above cases since the presence of absolute alcohol was in excess. However, significant amounts of mixed acetal, ethyl–methyl acetal, could be obtained when alcohol was not used in excess. When benzaldehyde was reacted with triethyl orthoformate (1.1 equiv) in absolute MeOH (0.1 mL), after 1 h the ratio of dimethyl, ethyl-methyl, and diethyl acetals formed was 70:23:1.3.

When the same reaction was performed with trimethyl orthoformate (1.1 equiv) in absolute ethanol (0.1 mL), the product distribution after 1 h was the opposite: as the ratio of dimethyl, ethyl–methyl, and diethyl acetals formed was 4:32:60. Unsymmetrical acetals are normally formed from the symmetric diacetals *via* transacetalisation.[14]

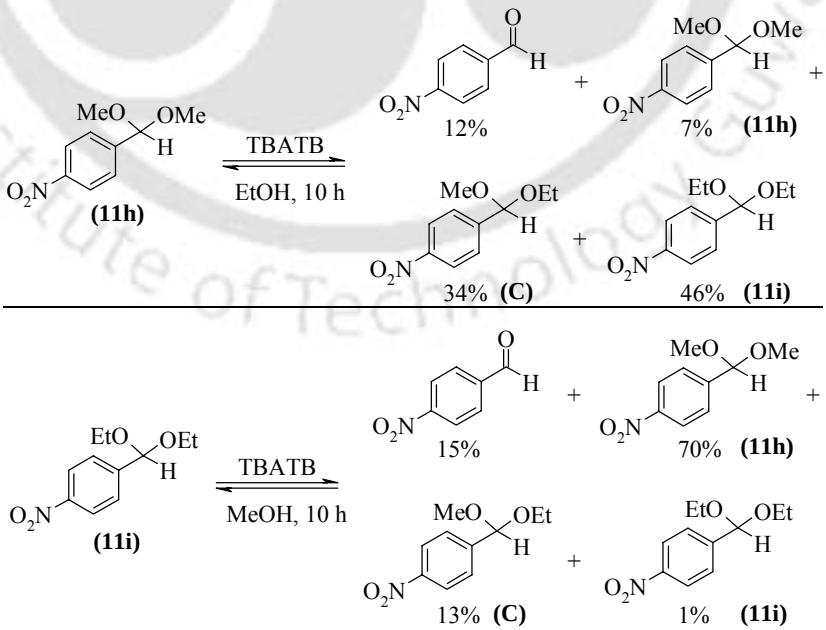
Treatment of an equimolar mixture of dimethyl acetal **11h** and diethyl acetal **11i** of *p*-nitrobenzaldehyde with TBATB (0.01 equiv) in acetonitrile after 1 h gave 42% of unsymmetrical acetal, *p*-nitrobenzaldehyde ethyl–methyl acetal **C**, along with 19% **11h**, 22% **11i** and 15% *p*-nitrobenzaldehyde as shown in Scheme 2.51.

Similar acetal exchange has been observed with other acid-catalysed reactions.[14] The formation of a small amount of *p*-nitrobenzaldehyde could be due to the generation of HBr by the reaction of TBATB with acetonitrile containing a trace amount of water. Thus, our method will be useful for the preparation of unsymmetrical acetals if desired.



Scheme 2.51. Transacetalisation Reaction

Alkoxy exchange also occurs between an acetal and an alcohol through the formation of a mixed acetal. The equilibrium can be shifted to the right by using a large excess of alcohol. Thus, when dimethy acetal **11h** (1 equiv) was treated with ethanol (0.1 mL) and TBATB (0.01 equiv), significant amounts of ethyl-methyl **C** and diethyl acetals **11i** were obtained as shown in Scheme 2.52.



Scheme 2.52. Acetal Exchange Reaction with an Alcohol

In another experiment, when diethyl acetal **11i** was treated with absolute methanol (0.1 mL) in TBATB, dimethyl acetal **11h**, along with a small amount of mixed acetal **C**, was obtained as shown in Scheme 2.52. Thus, mixed acetals and other acetals can be prepared by this methodology using appropriate quantities of alcohol.

Cyclic Acetal Formation. Cyclic acetals such as 1,3-dioxolanes and 1,3-dioxanes are also important protecting groups for carbonyl compounds. They are generally prepared by the reaction of aldehydes and ketones with 1,2-ethanediol or 1,3-propanediol in presence of acid catalysts[1] under homogeneous conditions. They are also prepared under heterogeneous media using inorganic solids such as $[Zr(O_3PCH_3)_{1.2}(O_3PC_6H_4SO_3H)_{0.8}]$,[15] supported silica gel,[16] Al_2O_3,[17] clay,[18] zeolites,[19] and kaoline.[20] Cyclic acetals are generally more easily formed than open chain acetals.[1c] Various aldehydes and ketones gave corresponding 1,3-dioxolanes and 1,3-dioxanes in excellent yields upon treatment with $(EtO)_3CH$ (1.1 equiv), 1,2-ethanediol, or 1,3-propanediol (4 equiv), and a catalytic amount of TBATB (0.01 equiv) as shown in Table 2.7. Carbonyl compounds such as **1**, **4**, **7**, **6** and **11** gave the corresponding cyclic acetals in good to excellent yields. It may be mentioned here that acetalisation of electron-rich aromatic aldehydes *o*-hydroxybenzaldehyde **4** and *p*-hydroxybenzaldehyde **6** are generally unsuccessful by conventional methods.[1,7b] Nevertheless, this acetal has been prepared using an expensive ruthenium catalyst and longer reaction times.[21]

As shown in Table 2.7, electron-withdrawing groups favoured acetal formation as demonstrated with *p*-nitrobenzaldehyde **11**. Sterically hindered aldehyde 2-chloro-6-nitrobenzaldehyde **21**, did not yield any trace of 1,3-dioxolanes but gave 21% of 1,3-dioxanes. This shows the preferential formation of 1,3-dioxanes over 1,3-dioxolanes for hindered aldehyde. Acid-sensitive substrate, 2-furaldehyde **13** and the conjugated carbonyl compound cinnamaldehyde **14** were converted to the corresponding cyclic acetals in good yields. Aromatic ketones also formed respective cyclic ketals under these conditions. Substrates such as acetophenone **22**, tetralone **24** and cyclopentanone-2-methylcarboxylate **26** could be converted to the corresponding cyclic ketals in satisfactory yields. Hindered ketone, benzophenone **27** gave very a poor yield of 1,3-dioxolanes even after 24 h, but gave moderate yield of 1,3-dioxanes. Thus, from Table 2.8 it is evident that unhindered ketone

prefers 1,3-dioxolane, while a hindered ketone and aldehyde prefer 1,3-dioxanes, as demonstrated for substrates **21** and **27**. It is also worthy to note that aldehyde containing acid-sensitive groups such as phenolic TBS ether **28** gave excellent yield of cyclic acetals without affecting the phenolic TBS group.

Table 2.7. Acetalisation[a] of Carbonyl Compounds

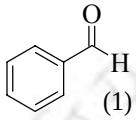
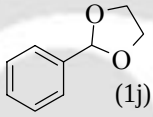
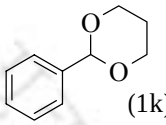
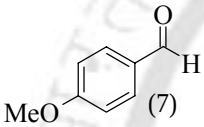
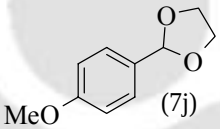
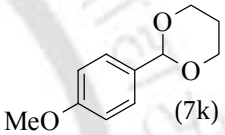
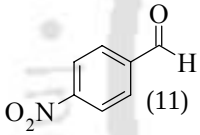
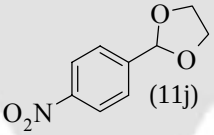
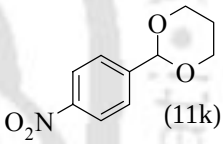
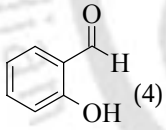
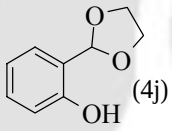
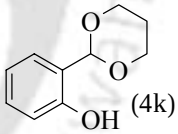
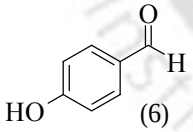
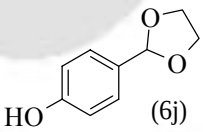
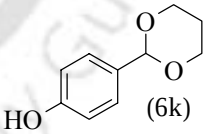
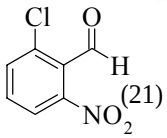
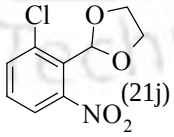
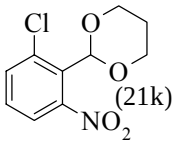
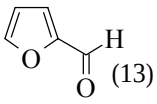
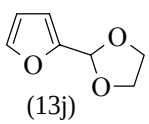
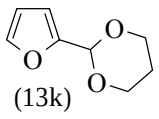
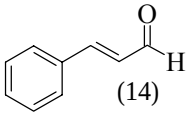
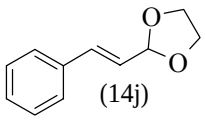
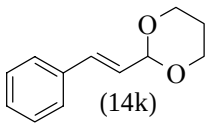
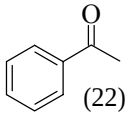
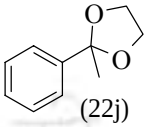
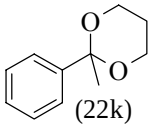
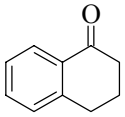
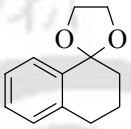
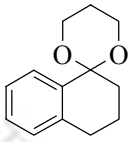
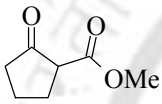
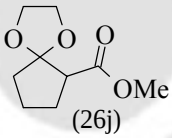
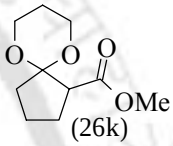
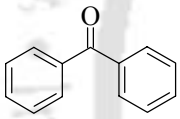
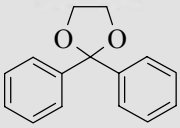
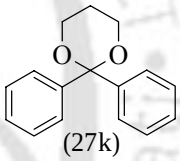
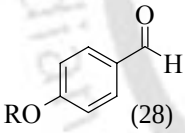
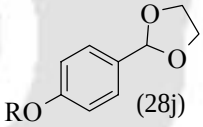
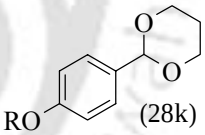
Substrate	Time/ h	X_3[b]	Yield[c] (%)	X_4[b]	Yield[c] (%)
 (1)	0.08	 (1j)	92	 (1k)	93
 (7)	0.08	 (7j)	75	 (7k)	85
 (11)	0.5	 (11j)	97	 (11k)	97
 (4)	1.5	 (4j)	88[d]	 (4k)	95
 (6)	0.08	 (6j)	93[d]	 (6k)	93
 (21)	24	 (21j)	00	 (21k)	21
 (13)	0.08	 (13j)	80	 (13k)	85
 (14)	0.16	 (14j)	65	 (14k)	49

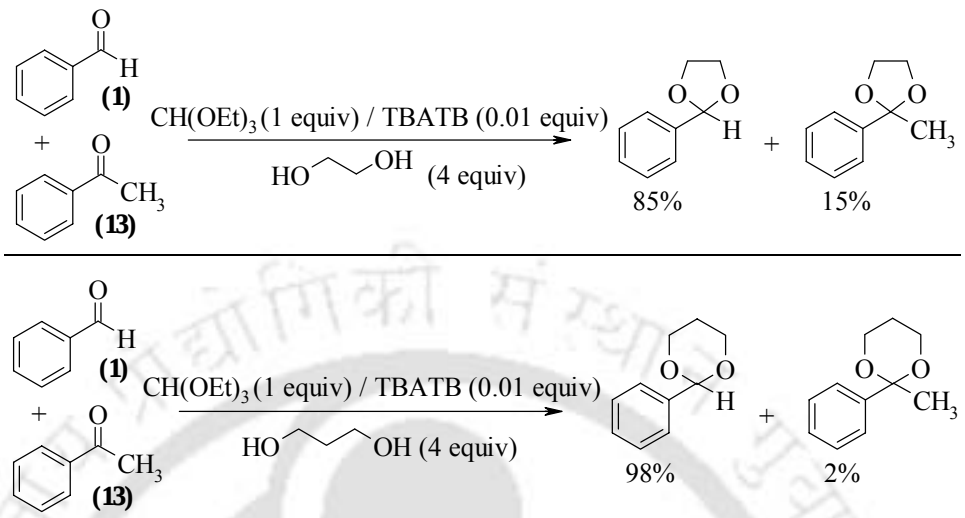
Table contd.....

Table 2.7. Acetalisation[a] of Carbonyl Compounds

Substrate	Time/ h	X_3[b]	Yield[c] (%)	X_4[b]	Yield[c] (%)
 (22)	0.08	 (22j)	90[d]	 (22k)	80
 (24)	0.08	 (24j)	94	 (24k)	94
 (26)	0.08	 (26j)	97	 (26k)	97
 (27)	24	 (27j)	00	 (27k)	64
 (28) R=TBS	0.08	 (28j) R=TBS	92	 (28k) R=TBS	93

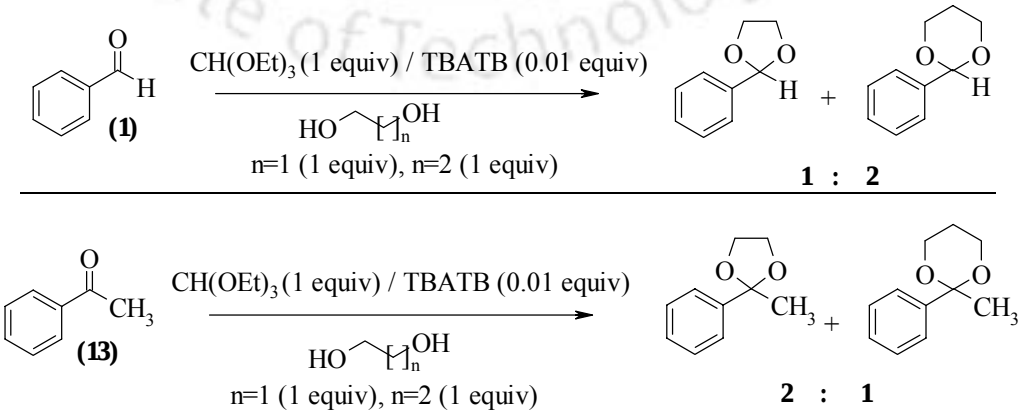
[a] Reactions were monitored by TLC / GC. X_3=1,3-dioxolanes; X_4= 1,3-dioxanes. [b] Confirmed by comparison with IR and ^{1}H NMR of the authentic sample. [c] Isolated yields. [d] 2.2 equiv of trialkyl orthoformate and 0.02 equiv of TBATB was used.

It is well known that aldehydes react faster than the ketones, which is also the case with our methodology. When an equimolar mixture of benzaldehyde **1** and acetophenone **22** was allowed to react with 1,2-ethanediol, benzaldehyde was chemoselectively acetalysed over acetophenone. A better degree of selectivity was found when 1,3-propanediol was used as shown in Scheme 2.53. Thus, this methodology will be useful for chemoselective acetalisation of aldehydes in the presence of ketones.



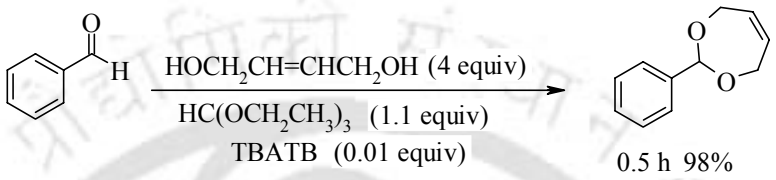
Scheme 2.53. Chemoselective Acetalisation of Aldehyde

The preferential formation of 1,3-dioxanes over 1,3-dioxolanes for aldehydes was also supported by the following experiment. When benzaldehyde **1** was reacted both in the presence of 1,2-ethanediol and 1,3-propanediol in equimolar amounts, the ratio of 1,3-dioxolane and 1,3-dioxane was found to be 1:2. It is interesting to note that, when a similar competitive reaction was done with acetophenone **22**, exactly opposite selectivity was observed as shown in Scheme 2.54, supporting a preferential formation of 1,3-dioxolanes for ketones. From the present study, the apparent order of acetal formation for different carbonyl groups is aldehyde-1,3-dioxanes > aldehyde-1,3-dioxolanes > ketone-1,3-dioxolanes > ketone-1,3-dioxanes.



Scheme 2.54. Chemoselective Acetalisation of Aldehyde

The present methodology was extended towards seven membered cyclic acetals. 2-Alkyl-4,7-dihydro-1,3-dioxepin was prepared easily by the present method. 1,3-Dioxepins are useful in pharmaceutical drugs like pyridoxine and intermediates for polyether antibiotics**.**



Scheme 2.55. Preparation of 2-Alkyl-4,7-dihydro-1,3-dioxepin

In conclusion, we have shown that acetalisation of various carbonyl compounds can be achieved by this methodology. Chemoselective acetalisation of aldehydes in the presence of ketones can be accomplished by this method. Electronic factors predominate over the steric factors during the acetal formation. Cyclic acetals of activated substrates can be achieved in high yields. Acid-sensitive groups such as the phenolic TBS ether are stable under the reaction condition. Unhindered ketones prefers 1,3-dioxolanes, while hindered ketones and aldehydes prefer 1,3-dioxanes. This method is high yielding, safe, operationally simple under mild reaction conditions, and cost effective. The catalytic nature of this methodology makes it more suitable for practical organic synthesis.

IIB.2.1 References

1. (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed., John Wiley & Sons: New York, 1999. (b) Kocieński, P. J. *Protecting Groups*; Georg Thieme Verlag: New York: 1994. (c) Meskens, F. A. J. *Synthesis* **1980**, 501. (d) Schelhaas, M.; Waldmann, H. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 2056.
2. Fife, T. H.; Jao, L. K. *J. Org. Chem*. **1965**, *30*, 1492.
3. Bornstein, J.; Bedell, S. F.; Drummond, P. E.; Kosloski, C. L. *J. Am. Chem. Soc*. **1956**, *78*, 83.
4. Patwardhan, S. A.; Dev, S. *Synthesis* **1974**, 348.

5. Firouzabadi, H.; Iranpoor, N.; Karimi, B. *Synlett* **1999**, 321.
6. Karimi, B.; Ashtiani, A. M. *Chem. Lett.* **1999**, 1199.
7. (a) Karimi, B.; Seradj, H.; Ebrahimian, G. R. *Synlett* **1999**, 1456. (b) Karimi, B.; Ebrahimian, G. R.; Seradj, H. *Org. Lett*. **1999**, *1*, 1737.
8. Ishihara, K.; Karumi, Y.; Kubota, M.; Yamamoto, H. *Synlett* **1996**, 839.
9. Bora, U.; Bose, G.; Chaudhuri, M. K.; Dhar, S. S.; Gopinath, R.; Khan, A. T.; Patel, B. K. *Org. Lett*. **2000**, *2*, 247.
10. Chaudhuri, M. K.; Khan, A. T.; Patel, B. K.; Dey, D.; Kharmawophlang, W.; Lakshmiprabha, T. R.; Mandal, G. C. *Tetrahedron Lett*. **1998**, *39*, 8163.
11. (a) Bose, G.; Bhujarbarua, P. M.; Chaudhuri, M. K.; Kalita, D.; Khan, A. T. *Chem. Lett.* **2001**, 290. (b) Bose, G.; Mondal, E.; Khan, A. T.; Bordoloi, M. J. *Tetrahedron Lett*. **2001**, *42*, 8907.
12. Mondal, E.; Bose, G.; Khan, A. T. *Synlett* **2001**, 785.
13. Naik, S.; Gopinath, R.; Patel, B. K. *Tetrahedron Lett*. **2001**, *42*, 7679.
14. (a) Moedritzer, K.; van Wazer, J. R. *J. Org. Chem.* **1965**, *30*, 3925. (b) Fujiwara, J.; Fukutani, Y.; Hasegawa, M.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc*. **1984**, *106*, 5004.
15. Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Synlett* **2001**, 1182.
16. Yadav, J. S.; Reddy, B. V. S.; Srinivas, R.; Ramalingam, T. *Synlett* **2000**, 701.
17. Kamitori, Y.; Hojo, M.; Masuda, R.; Yoshida, T. *Tetrahedron Lett.* **1985**, *26*, 4767.
18. (a) Tateiwa. J.; Horiuchi, H.; Uemura, S. *J. Org. Chem.* **1995**, 60, 4039. (b) Perio, B.; Dozias, M. -J.; Jacquault, P.; Hamelin, J. *Tetrahedron Lett.* **1997**, *38*, 7867.
19. (a) Tanaka, Y.; Sawamura, N.; Iwamoto, M. *Tetrahedron Lett.* **1998**, *39*, 9457. (b) Climent, M. J.; Corma, A.; Velty, A.; Susarte, M. *J. Catal.* **2000**, *196*, 345.
20. Ponde, D.; Borate, H. B.; Sudalai, A.; Ravindranathan, T.; Deshpande, V. H. *Tetrahedron Lett.* **1996**, *26*, 4605.
21. Ma, S.; Venanzi, L. M. *Synlett* **1993**, 751.

IIC Experimental

IIC.1 Preparation of Dry Solvents[1]

Methanol.

A dry 2 litre round-bottomed flask was fitted with a double surface condenser and a calcium chloride guard-tube. To this was added 5 g of clean dry magnesium turnings and 0.5 g of iodine, followed by 50-75 mL of methanol. Warmed the mixture until all the magnesium was converted into methanolate, to this was then added 900 mL of methanol and refluxed the mixture for 30 minutes. Distilled the methanol directly and stored over a Type 4Å molecular sieve.

Ethanol.

Ethanol was treated with active calcium oxide, refluxed, then distilled and treated again with iodine and magnesium similar to methanol to obtain dry ethanol.

Dimethylformamide.

Distilled a mixture of 1 litre of DMF and 100 mL of benzene at atmospheric pressure and collected the water-benzene azeotrope which distils between 70 and 75^{o}C. The residual solvent was shaked with powdered barium oxide, filtered and distilled under nitrogen at reduced pressure. Collected the fraction having b.p.76^{o}C/39 mm Hg. The distillate was stored over a Type 4Å molecular sieve.

Pyridine.

The analytical grade of pyridine was refluxed over potassium hydroxide pellets and then distilled with careful exclusion of moisture and stored over solid potassium hydroxide pellets.

Dichloromethane.

Commercial grade of dichloromethane was stored over calcium chloride for 24 h and then distilled under nitrogen atmosphere.

Diethyl ether.

Peroxides were removed by passing through a column of activated basic alumina. Sodium wire was inserted into the solution along with a catalytic amount of benzophenone and refluxed the mixture until the solution becomes blue in colour. Distilled the ether under nitrogen atmosphere and stored over sodium wire.

Tetrahydrofuran.

Similar to diethyl ether.

Benzene.

Similar to diethyl ether.

Hexane.

Decant the solvent, previously treated with conc. sulphuric acid, directly on to a basic alumina (Grade I) column using about 50 g of adsorbent for each 100 mL of solvent; the first 5 percent of eluate was discarded. The column receiver should be suitably protected from the ingress of moisture by the attachment of a calcium chloride tube.

IIC.2 Experimental Procedures

IIC.2.1. General Procedure for Monobenzylation of Symmetrical 1,n-Diols. [2]

Silver oxide (7.5 mmol) was suspended in dry CH_2Cl_2 (5 mL) after being washed with dry hexane. The diol (5 mmol) was added to this mixture and stirred for 45 min. The benzyl bromide (5.5 mmol) was then added, and vigorous stirring was continued for 6 h. The mixture was poured into ether (20 mL), washed with 10% aqueous K_2CO_3 (5 mL) followed by brine (5 mL) and finally dried over anhyd. Na_2SO_4, and concentrated *in vacuo*. The resulting oil was purified by column chromatography (silica gel, hexane : ethyl acetate) to afford the product.

IIC.2.2. General Procedure for Monobenzoylation of Symmetrical 1,n-Diols.[3]

To a solution of diol (5 mmol), pyridine (15 mmol) in dry CH_2Cl_2 (5 mL) was added benzoyl chloride (BzCl), (5.5 mmol), and the reaction mixture was allowed to stir at room temperature. After completion of the reaction, the reaction mixture was treated with dilute

HCl (2N, 1 × 5 mL) and extracted the product using ethyl acetate (2 × 15 mL). The solvent was evaporated *in vacuo* and chromatographed to obtain the pure monobenzoylated product.

IIC.2.3. General Procedure for Acylation.[4]

To a solution of alcohol (5 mmol), pyridine (15 mmol) in dry CH_2Cl_2 was added acetic anhydride (Ac_2O), (5.5 mmol), and the reaction mixture was allowed to stir at room temperature. After completion of the reaction, the reaction mixture was treated with dilute HCl (2N, 1 × 5 mL) and extracted the product using ethyl acetate (2 × 15 mL). The solvent was evaporated *in vacuo* and chromatographed to obtain the pure acetylated product.

IIC.2.4. General Procedure for Protection of 1,2-Diols as Acetonide.[5]

To a solution of 1,2-diol (5 mmol) in dry acetone (10 mL) was added *p*-tolune-sulfonic acid (0.005 mmol) and the reaction mixture was refluxed on a water bath. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was concentrated *in vacuo* and treated with saturated sodium bicarbonate solution (5 mL). The product was extracted with ethyl acetate (20 mL), next washed with brine (5 mL) and dried over anhyd. Na_2SO_4. The solvent was evaporated *in vacuo* and the product was purified using column chromatography (silica gel, ethyl acetate : methanol) to afford the product.

IIC.2.5. General Procedure for the Preparation of *tert*-Butyldimethyl Silyl Ethers.[6]

To a stirred solution of alcohol (5 mmol) and imidazole (15 mmol) in dry CH_2Cl_2 (10 mL) was added *tert*-butyldimethylsilyl chloride (TBSCl), (5.5 mmol) at room temperature. The progress of the reaction was monitored by TLC and GC. After completion of the reaction, the reaction mixture was concentrated *in vacuo* and redissolved in ethyl acetate. The organic layer was first treated with dilute HCl (2N, 1 × 5 mL) and later washed with saturated $NaHCO_3$ solution (1 × 5 mL). The organic layer was separated and dried over anhyd. Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, hexane : ethyl acetate) to afford the product silyl ether.

IIC.2.6. General Procedure for the Monosilylation of Symmetrical 1,n-Diols.[7]

Sodium hydride (50% in oil) (10 mmol) was suspended in dry THF (10 mL) after being washed with dry hexane. The diol (5 mmol) was added and stirred vigorously for 45 min. The *tert*-butyldimethylsilyl chloride (TBDMSCl), (5 mmol), was then added, and vigorous stirring was continued for 45 min. The mixture was poured into ether (100 mL), washed with 10% aqueous K_2CO_3 (30 mL) and brine (30 mL), dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. The resulting oil was purified by column chromatography (silica gel, hexane:ethyl acetate) to afford the product.

IIC.2.7. General Procedure for the Prepration of Tetrahydropyranyl Ethers.[8]

To a solution of alcohol (5 mmol) in dry dichloromethane (10 mL) was added 3,4-dihydro-2*H*-pyran (5.5 mmol) and iodine (0.125 mmol). The progress of the reaction was monitored by TLC and GC. On completion, 10% hypo solution (10 mL) was added and the product was extracted with CH_2Cl_2 (2 × 25 mL). The organic layer was separated, washed with water, and dried over anhy. Na_2SO_4. The solvent was removed *in vacuo* and purified by using column chromatography (silica gel, hexane : ethyl acetate) to afford the product.

IIC.2.8. General Procedure for the Preparation of Dimethoxytrityl Ethers.[9]

To a stirred solution of alcohol (5 mmol) in dry pyridine (5 mL) was added 4,4'-dimethoxytrityl chloride (5.5 mmol). The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was trated with 5% $NaHCO_3$ solution (10 mL) and extracted the product using CH_2Cl_2 (2 × 20 mL). The CH_2Cl_2 layer was washed once with water (5 mL), then dried over anhy. Na_2SO_4 and concentrated *in vacuo* and the residue was purified by using column chromatography (silica gel; column was saturated with 1% triethyl amine, hexane:ethyl acetate) to afford the product.

IIC.2.9. General Procedure for the Cleavage of *tert*-Butyldimethylsilyl Ether Using Tetrabutylammonium Tribromide (TBATB)–MeOH.

To a solution of silyl ether (5 mmol) in methanol (5 mL) was added tetrabutylammonium tribromide (TBATB), 241 mg (0.5 mmol). The progress of the reaction was monitored by TLC and GC. On completion of the reaction, the methanol was removed

under reduced pressure and the residue was redissolved in ethyl acetate (20 mL). The organic layer was washed with 5% sodium metabisulfite solution (1 x 5 mL) followed by water (1 x 5 mL) and finally dried over anhy. Na_2SO_4. The solvent was removed *in vaccuo* and the residue was purified by column chromatography (silica gel, hexane : ethyl acetate) to afford the product.

IIC.2.10. General Procedure for the Cleavage of Tetrahydropyranyl Ethers Using Tetrabutylammonium Tribromide (TBATB)–MeOH.

Similar to General Procedure 9 (p.157); tetrahydropyranyl ether was used instead of *tert*-butyldimethylsilyl ether.

IIC.2.11. General Procedure for the Cleavage of Dimethoxytrity Ethers Using Tetrabutylammonium Tribromide (TBATB)–MeOH.

Similar to General Procedure 9 (p.157); dimethoxytrityl ether was used instead of *tert*-butyldimethylsilyl ether.

IIC.2.12. Intermolecular Chemoselective Deprotection of Acid-sensitive Groups Using Tetrabutylammonium Tribromide (TBATB)–MeOH.[10]

Intermolecular chemoselectivity was determined by treating an equimolar mixutre of two different substrates having different protecting groups (X) and (Y), (X or Y = aliphatic or aromatic TBS, THP, TBDPS, DMT ethers) with 0.1 mol% of the reagent, tetrabutyl-ammonium tribromide, (TBATB) in an appropriate solvent (methanol or propanol) at room temperature or under an ice cold condition, and the percentage deprotection was monitored by GC. An internal standard (1-decanol), which does not involve in the reaction was used when both the deprotected products were same. Percentage selectivity was determined using following formula

Selectivity = % Y deprotected - % X deprotected at time *t*.

IIC.2.13. General Procedure for Preparation of Dimethyl Acetals / Ketals Using Trimethylorthoformate–TBATB.

To a solution of carbonyl compound (5 mmol) and trimethyl orthoformate (5.5 mmol) in dry methanol (5 mL) was added tetrabutylammonium tribromide (0.05 mmol). The

homogeneous reaction was left at room temperature, and the progress of the reaction was monitored by TLC and GC. After completion of the reaction, the reaction mixture was poured into saturated $NaHCO_3$ solution (10 mL) (except in the case of hydroxy aldehydes, which were washed with water) and the product extracted with ethyl acetate (2 × 25 mL). The organic layer was separated, dried over anhyd. Na_2SO_4, and concentrated. Further purification was achieved by vacuum distillation or by passing through a short column of silica gel.

IIC.2.14. General Procedure for Preparation of Diethyl Acetals/Ketals Using Triethylorthoformate–TBATB.

Similar to General Procedure 13 (p.158); triethyl orthoformate and ethanol was used instead of trimethyl orthoformate and methanol, respectively.

IIC.2.15. General Procedure for Acetalisation of Aldehydes.[11]

To a 100 mL two-necked, round-bottomed flask, equipped with a Dean-Stark apparatus and a reflux condenser, containing the aldehyde (5 mmol), *p*-tolunesulfonic acid (0.025 mmol), and anhydrous magnesium sulphate ($MgSO_4$), (5 mmol) in dry benzene (25 mL) was added a solution of ethylene glycol (10 mmol) in dry benzene (2 mL) over a period of 20 min. The reaction mixture was heated to reflux and the progress of the reaction was monitored by TLC and GC until no starting aldehyde was detected. After the completion of the reaction, the mixture was cooled, solid sodium hydrogen carbonate ($NaHCO_3$), (2.5 mmol) was added to neutralise the acid, and the mixture was stirred for 30 min. The reaction mixture was then filtered through a pad of anhy. $NaHCO_3$, and the filter cake was washed with CH_2Cl_2 (3 × 10 mL). Concentration of the filtrate gave the acetal in high purity. This material was further purified by using column chromatography (silica gel, hexane:ethyl acetate) to afford the product.

IIC.2.16. General Procedure for Preparation of 1,3-Dioxolanes of Aldehydes/Ketones Using Triethylorthoformate–TBATB.

To the mixture of carbonyl compound (5 mmol), triethyl orthoformate (5.5 mmol), and 1,2-ethanediol (20 mmol) was added tetrabutylammonium tribromide (0.05 mmol). The

homogeneous reaction was left at room temperature, and the progress of the reaction was monitored by TLC and GC. After completion of the reaction, the reaction mixture was poured into saturated $NaHCO_3$ solution (10 mL) (except in the case of hydroxy aldehydes, which were washed with water) and the product extracted with ethyl acetate (2 × 25 mL). The organic layer was separated, dried over anhy. Na_2SO_4, and concentrated. Further purification was achieved by vacuum distillation or by passing through a short column of silica gel.

IIC.2.17. General Procedure for Preparation of 1,3-Dioxanes of Aldehydes / Ketones Using Triethylorthoformate–TBATB.

Similar to General Procedure 16 (p.159); 1,3-propanediol was used instead of 1,2-ethanediol.

IIC.2.18. General Procedure for Preparation of 2-Phenyl-4,7-dihydro-[1,3]dioxepin Using Triethylorthoformate, TBATB.

Similar to General Procedure 16 (p.159); 1,4-but-2-ene-diol was used instead of 1,2-ethanediol.

IIC.2.19. Chemoselective Acetalisation of Aldehydes in the Presence of Ketones.

To the mixture of benzaldehyde (1 mmol), acetophenone (1 mmol), triethyl orthoformate (1.1 mmol), and 1,2-ethanediol or 1,3-propanediol (4 mmol) was added tetrabutylammonium tribromide (0.01 mmol). The homogeneous reaction was left at room temperature. The percentage of products formed at different times was determined by gas chromatography.

IIC.2.20. Quantum Mechanical Calculations on Model Systems.[12]

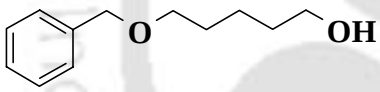
The electron density at the carbonyl carbon was calculated using semi-empirical molecular orbital calculations, the AM1 method as implemented in the Hyperchem package. The steps followed are as follows:

1. By the help of the molecular builder, the molecule was drawn on workspace and added hydrogen atoms to that to build the molecular model.

2. The atom charges were displayed by the help of display labels. As default, initial stage the charges of all atoms were zero.
3. The semi-emperical method, the AM1 was chosen by keeping the default options.
4. The electron density of the atoms were obtained by computing the geometry optimisation.

IIC.3 Spectral Data

IIC.3.1 Benzyl derivatives

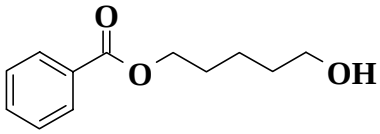


5-Benzyloxy-pentan-1-ol (44)

IR (Neat): 3436, 2939, 2868, 1721, 1659, 1460, 1398, 1367, 1321, 1280, 1209, 1178, 1101, 912, 743, 702 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.40-1.71 (m, 6H, Ar-CH_2-O-CH_2-(C<u>H_2</u>)$_3$-CH_2-OH), 2.16 (br, 1H, -O<u>H</u>), 3.47 (t, 2H, Ar-CH_2-O-CH_2-$(CH_2)_3$-C<u>H_2</u>-OH), 3.62 (t, 2H, Ar-CH_2-O-C<u>H_2</u>-$(CH_2)_3$-CH_2-OH), 4.49 (s, 2H, Ar-C<u>H_2</u>-O-), 7.32 (m, 5H, Ar<u>H</u>)

IIC.3.2 Benzoyl derivatives

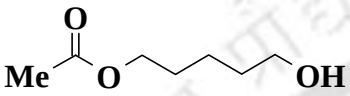


Benzoic acid 5-hydroxy-pentyl ester (45)

IR (Neat): 2842, 1695, 1608, 1582, 1460, 1429, 1337, 1291, 1188, 1132, 1081, 1029, 942, 814, 717 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.6 (m, 6H, Ar-COO-CH_2-($C\underline{H_2}$)$_3$-CH_2-OH), 3.6 (t, 2H, Ar-COO-CH_2-$(CH_2)_3$-$C\underline{H_2}$-OH), 4.3 (t, 2H, Ar-COO-$C\underline{H_2}$-$(CH_2)_3$-CH_2-OH), 7.5 (m, 3H, Ar$\underline{H}$), 8.3 (m, 2H, Ar$\underline{H}$)

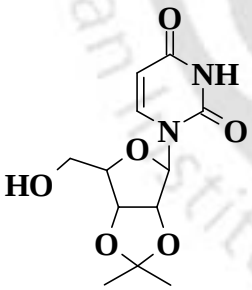
IIC.3.3 Acetyl derivatives



Acetic acid 5-hydroxy-pentyl ester (46)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.5 (m, 6H, CH_3-COO-CH_2-($C\underline{H_2}$)$_3$-CH_2-OH), 2.0 (s, 3H, -OCO-$C\underline{H_3}$), 3.6 (t, 2H, CH_3-COO-CH_2-$(CH_2)_3$-$C\underline{H_2}$-OH), 4.0 (t, 2H, CH_3-COO-$C\underline{H_2}$-$(CH_2)_3$-CH_2-OH)

IIC.3.4 Acetonide

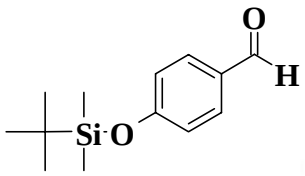


2',3'-Isopropylidene uridine (49)

IR (KBr): 3313, 3236, 1705, 1675, 1475, 1398, 1275, 1244, 1219, 1163, 1127, 1081, 860, 804, 768, 722 cm^{-1}

^{1}H NMR (400 MHz, DMSO-*d6*): δ 1.38 (s, 3H, -$C\underline{H_3}$), 1.60 (s, 3H, -$C\underline{H_3}$), 3.83 (m, 1H, -$C\underline{H}$(H)OH), 3.95 (m, 1H, -CH($\underline{H}$)OH), 4.31 (m, 1H, 4'-$C\underline{H}$-), 4.99 (m, 1H, 3'-$C\underline{H}$-), 5.07 (m, 1H, 2'-$C\underline{H}$-), 5.58 (d, 1H, C5-$C\underline{H}$-), 5.75 (d, 1H, 1'-$C\underline{H}$-), 7.39 (d, C6-$C\underline{H}$-)

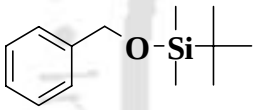
IIC.3.5 *tert*-Butyldimethyl silyl ethers



4-*tert*-Butyldimethylsilanyloxy-benzaldehyde (28)

IR (Neat): 2962, 2936, 860, 1620, 1519, 1478, 1377, 1266, 1154, 1114, 1018, 992, 916, 840, 785 cm^{-1}

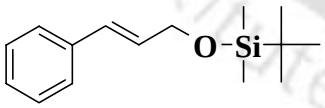
^1H NMR (400 MHz, $CDCl_3$): δ 0.17 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.91 (s, 9H, -Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 6.87 (d, 2H, Ar$\underline{H}$), 7.71 (d, 2H, Ar.$\underline{H}$), 9.81 (s, 1H, -C$\underline{H}$O)



Benzyloxy-*tert*-butyl-dimethyl-silane (29m)

IR (Neat): 2962, 2936, 2860, 1483, 1377, 1256, 1210, 1099, 1073, 845, 780, 729 cm^{-1}

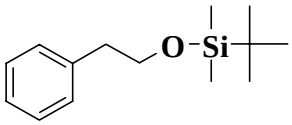
^1H NMR (400 MHz, $CDCl_3$): δ 0.08 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.88 (s, 9H, -Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 4.43 (d, 1H, Ar-C$\underline{H}$(H)-), 4.82 (d, 1H, Ar-CH($\underline{H}$)-), 7.25 (m, 5H, Ar$\underline{H}$)



***tert*-Butyl-dimethyl-(3-phenyl-allyloxy)-silane (32m)**

IR (Neat): 2962, 2941, 2960, 1473, 1392, 1362, 1256, 1073, 835, 775, 704 cm^{-1}

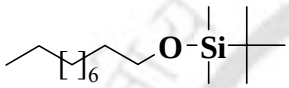
^1H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.81 (s, 9H, -Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 4.10 (m, 2H, Ar-CH=CH-C$\underline{H}_2$-O-), 6.33 (m 1H, Ar-CH=C$\underline{H}$-CH_2-O-), 6.63 (d,1H, Ar-C$\underline{H}$=CH-CH_2-O-), 7.42 (m, 5H, Ar$\underline{H}$)



tert-**Butyl-dimethyl-phenethyloxy-silane (33m)**

IR (Neat): 2955, 2929, 2858, 1475, 1255, 1101, 835, 778, 748, 702 cm^{-1}

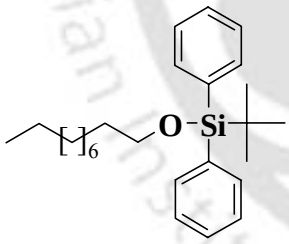
^1H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.88 (s, 9H, -Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 2.83 (t, 2H, Ar-$C\underline{H}_2$-CH_2-), 3.82 (t, 2H, Ar-CH_2-$C\underline{H}_2$-O-), 7.27 (m, 5H, Ar$\underline{H}$)



tert-**Butyl-decyloxy-dimethyl-silane (34m)**

IR (Neat): 2926, 2855, 1471, 1387, 1361, 1254, 1102, 835, 774 cm^{-1}

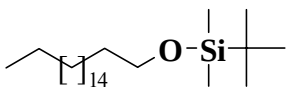
^1H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.84 (brs, 12H, $C\underline{H}_3$-(CH_2)$_7$-CH_2-CH_2-O-Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 1.21 (brm, 14H, -($C\underline{H}_2$)$_7$-CH_3), 1.47 (m, 2H, -$C\underline{H}_2$-CH_2-O-), 3.54 (t, 2H, -CH_2-$C\underline{H}_2$-O-)



tert-**Butyl-decyloxy-diphenyl-silane (34p)**

IR (Neat): 2956, 2928, 2855, 1471, 1427, 1389, 1111, 823, 738, 701 cm^{-1}

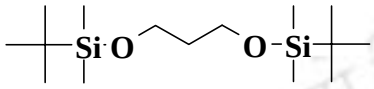
^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, -$CH_2C\underline{H}_3$), 1.04 (s, 9H, -Si(Ar)$_2$-C($C\underline{H}_3$)$_3$), 1.24 (brm, 10H, -($C\underline{H}_2$)$_5$-), 1.54 (m, 2H, -$C\underline{H}_2$-CH_2-O-), 3.64 (t, 2H, -CH_2-$C\underline{H}_2$-O-), 7.38 (m, 6H, Ar$\underline{H}$), 7.66 (m, 4H, Ar$\underline{H}$)



tert-**Butyl-octadecyloxy-dimethyl-silane (35m)**

IR (Neat): 2926, 2855, 1471, 1387, 1361, 1254, 1102, 835, 774 cm^{-1}

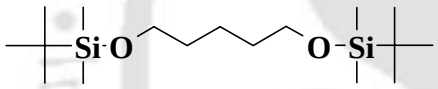
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.84 (s, 12H, C$\underline{H}_3$-$(CH_2)_{15}$-CH_2-CH_2-O-Si$(CH_3)_2$-C(C$\underline{H}_3$)$_3$), 1.20 (brm, 30H, -(C$\underline{H}_2$)$_{15}$- CH_3), 1.50 (m, 2H, -C$\underline{H}_2$-CH_2-O-), 3.54 (t, 2H, - CH_2-C$\underline{H}_2$-O-)



1,3-Bis-(*tert*-butyl-methyl-silanyloxy)-propane (36m)

IR (Neat): 2965, 2929, 2858, 1475, 1393, 1362, 1260, 1096, 1050, 988, 937, 835 cm^{-1}

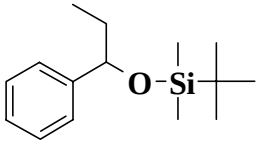
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.04 (s, 12H, 2 × -Si(C$\underline{H}_3$)$_2$-), 0.89 (s, 18H, 2 × -Si$(CH_3)_2$-C(C$\underline{H}_3$)$_3$), 1.71 (m, 2H, -O-CH_2-C$\underline{H}_2$-CH_2-O-), 3.69 (t, 4H, -O- C$\underline{H}_2$-CH_2-C$\underline{H}_2$-O-)



1,3-Bis-(*tert*-butyl-methyl-silanyloxy)-pentane (37m)

IR (Neat): 2945 2929, 1741, 1644, 1454, 1352, 1260, 1198, 1122, 1075, 1035, 912, 870, 840, 814, 737 cm^{-1}

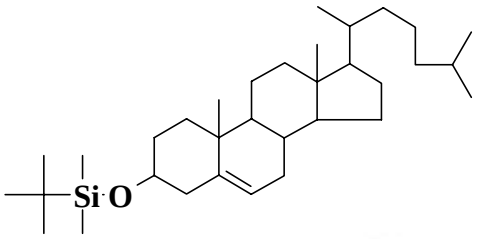
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.04 (s, 12H, 2 × -Si(C$\underline{H}_3$)$_2$-), 0.89 (s, 18H, 2 × -Si$(CH_3)_2$-C(C$\underline{H}_3$)$_3$), 1.35 (m, 2H, -O-$(CH_2)_2$-C$\underline{H}_2$-$(CH_2)_2$-O-), 1.52 (m, 4H, 2 × -O-CH_2-C$\underline{H}_2$-), 3.61 (t, 4H, 2 × -O-C$\underline{H}_2$-CH_2-)



***tert*-Butyl-dimethyl-(1-phenyl-propoxy)-silane (38m)**

IR (Neat): 2967, 2936, 2860, 1661, 1478, 1266, 1094, 1033, 800, 704 cm^{-1}

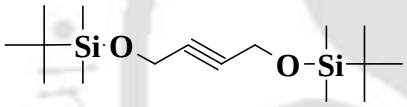
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.03 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.084 (brs, 12H, C$\underline{H}_3$-CH_2-CH(Ar)-O-Si$(CH_3)_2$-C(C$\underline{H}_3$)$_3$), 1.67 (m, 2H, -C$\underline{H}_2$-CH_3), 4.55 (m, 1H, Ar-C$\underline{H}$-) , 7.23 (m, 2H, Ar$\underline{H}$), 7.32 (m, 3H, Ar$\underline{H}$)



***tert*-Butyldimethylsilyl ether of cholesterol (39m)**

IR (Neat): 2939, 2858, 1475, 1327, 1255, 1101, 891, 871, 840, 773 cm^{-1}

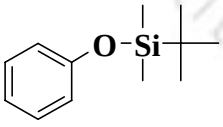
^1H NMR (400 MHz, $CDCl_3$): δ 0.01 (s, 6H), 0.61 (s, 3H), 0.80 (d, 6H), 0.82 (s, 9H), 0.85 (d, 3H), 0.94 (s, 3H), 1.10 (m, 2H), 1.28 (m, 6H), 1.46 (m, 5H), 1.64 (m, 8H), 1.74 (m, 2H), 1.93 (m, 1H), 2.12 (m, 2H), 2.21 (m, 2H), 3.42 (m, 1H), 5.25 (m, 1H)



1,4-Bis-(*tert*-butyl-dimethyl-silanyloxy)-but-2-yne (40m)

IR (Neat): 2936, 2971, 1706, 1475, 1362, 1261, 1139, 1083, 1007, 845, 780, 729 cm^{-1}

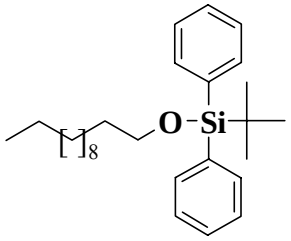
^1H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 12H, 2 × -Si($C\underline{H}_3$)$_2$-), 0.79 (s, 18H, 2 x -Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 4.22 (s, 4H, 2 x -C-$C\underline{H}_2$-O-)



***tert*-Butyl-dimethyl-phenoxy-silane (41m)**

IR (Neat): 2960, 2934, 2893, 2863, 1669, 1598, 1495, 1475, 1393, 1362, 1260, 1070, 1004, 917, 845, 784, 763, 697, 666 cm^{-1}

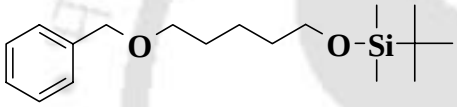
^1H NMR (400 MHz, $CDCl_3$): δ 0.43 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 1.20 (s, 9H, -Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 6.90 (m, 2H, Ar$\underline{H}$), 7.25 (m, 3H, Ar$\underline{H}$)



***tert*-Butyl-dodecyloxy-diphenyl-silane (42p)**

IR (Neat): 2934, 2858, 1475, 1429, 1393, 1362, 1111, 830, 743, 702, 615, 507 cm^{-1}

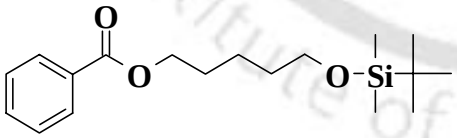
^1H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, 3H, -$CH_2C\underline{H}_3$), 1.05 (s, 9H, -$Si(Ar)_2$-$C(C\underline{H}_3)_3$), 1.30 (brm, 18H, -$(C\underline{H}_2)_9$-CH_3), 1.55 (m, 2H, -$C\underline{H}_2$-CH_2-O-), 3.65 (t, 2H, -CH_2-$C\underline{H}_2$-O-), 7.35 (m, 6H, Ar$\underline{H}$), 7.65 (m, 4H, Ar$\underline{H}$)



(5-Benzyloxy-pentyloxy)-*tert*-butyl-dimethyl-silane (44m)

IR (Neat): 2929, 2857, 1471, 1397, 1361, 1255, 1097, 836, 775, 734, 697 cm^{-1}

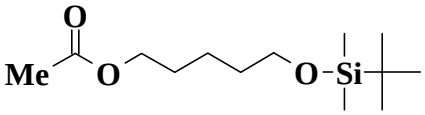
^1H NMR (400 MHz, $CDCl_3$): δ 0.06 (s, 6H, -$Si(C\underline{H}_3)_2$-), 0.90 (s, 9H, -$Si(CH_3)_2$-$C(C\underline{H}_3)_3$), 1.56 (m, 6H, -O-CH_2-$(C\underline{H}_2)_3$-CH_2-O-), 3.48 (t, 2H, -$Si(CH_3)_2$-O-$C\underline{H}_2$-), 3.64 (t, 2H, Ar-CH_2-O-$C\underline{H}_2$-), 4.51 (s, 2H, Ar-$C\underline{H}_2$-O-), 7.37 (m, 5H, Ar$\underline{H}$)



Benzoic acid 5-(*tert*-butyl-dimethyl-silanyloxy)-pentyl ester (45m)

IR (Neat): 2953, 2929, 2857, 1721, 1452, 1315, 1274, 1108, 1026, 936, 836, 770 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, -$Si(C\underline{H}_3)_2$-), 0.84 (s, 9H, -$Si(CH_3)_2$-$C(C\underline{H}_3)_3$), 1.53 (m, 2H, -O-$(CH_2)_2$-$C\underline{H}_2$-$(CH_2)_2$-O-), 1.74 (m, 4H, 2 × -O-CH_2-$C\underline{H}_2$-), 3.59 (t, 2H, -$Si(CH_3)_2$-O-$C\underline{H}_2$-), 4.27 (t, 2H, -$C\underline{H}_2$-O-CO-Ar), 7.48 (m, 3H, Ar$\underline{H}$), 8.04 (m, 2H, Ar$\underline{H}$)

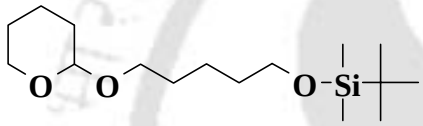


Acetic acid 5-(*tert*-butyl-dimethyl-silanyloxy)-pentyl ester (46m)

IR (Neat): 2954, 2857, 1743, 1636, 1472, 1399, 1363, 1241, 1097, 1042, 836 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.07 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.88 (s, 9H, -Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 1.39 (m, 2H, -O-(CH_2)$_2$-$C\underline{H}_2$-(CH_2)$_2$-O-), 1.59 (m, 4H, 2 × -O-CH_2-$C\underline{H}_2$-), 2.04 (s, 3H, -O-CO-$C\underline{H}_3$), 3.61 (t, 2H, -Si(CH_3)$_2$-O$C\underline{H}_2$-), 4.06 (t, 2H, -$C\underline{H}_2$-O-CO-CH_3)

MS (FAB): m/z 261 $(M+H)^+$

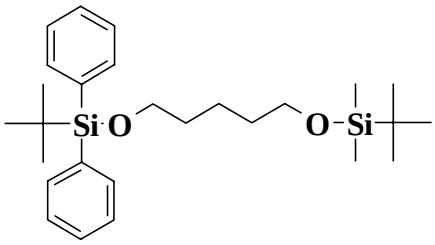


***tert*-Butyl-dimethyl-[5-(tetrahydro-pyran-2-yloxy)-pentyloxy]-silane (47m)**

IR (Neat): 2945, 2863, 1741, 1644, 1454, 1352, 1260, 1198, 1122, 1075, 1035, 912, 876, 840, 814, 737 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.04 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.89 (s, 9H, -Si(CH_3)$_2$-C($C\underline{H}_3$)$_3$), 1.37-1.71 (brm, 12H, (-O-CH_2-($C\underline{H}_2$)$_3$-CH-)-O-CH_2-($C\underline{H}_2$)$_3$-CH_2-O-Si(CH_3)$_2$-), 3.39 (m, 1H, (-O-CH_2-(CH_2)$_3$-CH-)-OC$\underline{H}$(H)-), 3.50 (m, 1H, (-O-CH_2-(CH_2)$_3$-CH-)-O-CH($\underline{H}$)-), 3.61 (t, 2H, -$C\underline{H}_2$O-Si(CH_3)$_2$-), 3.73 (m, 1H, (-O-C$\underline{H}$(H)-(CH_2)$_3$-CH-)-O-), 3.86 (m, 1H, (-O-CH($\underline{H}$)-(CH_2)$_3$-CH-)-O-), 4.58 (m, 1H, (-O-CH_2-(CH_2)$_3$-C$\underline{H}$-)-O-)

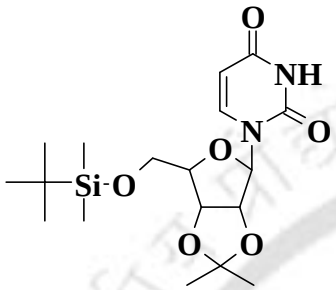
MS (FAB): m/z 303 $(M+H)^+$



1-(*tert*-butyl-dimethyl-silanyloxy)-5-(*tert*-butyl-diphenyl-silanyloxy)-pentane (48m)

IR (Neat): 2936, 2865, 1473, 1428, 1392, 1362, 1256, 1114, 835, 775, 739, 704 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.03 (s, 6H, -Si(C<u>*H*</u>$_3$)$_2$-), 0.08 (s, 9H, -Si(CH$_3$)$_2$-C(C<u>*H*</u>$_3$)$_3$), 1.05 (s, 9H, -Si(Ar)$_2$-C(C<u>*H*</u>$_3$)$_3$), 1.54 (brm, 6H, -O-CH$_2$-(C<u>*H*</u>$_2$)$_3$-CH$_2$-O-), 3.66 (m, 4H, 2 × -O-C<u>*H*</u>$_2$-), 7.38 (m, 6H, Ar<u>*H*</u>), 7.67 (m, 4H, Ar<u>*H*</u>)

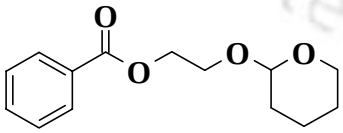


2',3'-Isopropylidene-5'-*O*-*tert*-butyldimethylsilyl uridine (49m)

IR (KBr): 2939, 2863, 1700, 1465, 1403, 1270, 1132, 1091, 1065, 973, 840, 778 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.00 (s, 6H, -Si(C<u>*H*</u>$_3$)$_2$-), 0.80 (s, 9H, -Si(CH$_3$)$_2$-C(C<u>*H*</u>$_3$)$_3$), 1.26 (s, 3H, -O-C(C<u>*H*</u>$_3$)CH$_3$-O-), 1.49 (s, 3H, -O-C(CH$_3$)C<u>*H*</u>$_3$-O-), 3.71 (m, 1H, -C<u>*H*</u>(H)-Si-), 3.84 (m, 1H, -CH(<u>*H*</u>)-Si-), 4.22 (m, 1H, 4'-C<u>*H*</u>-), 4.57 (m, 1H, 3'-C<u>*H*</u>-), 4.66 (m, 1H, 2'-C<u>*H*</u>), 5.58 (d, 1H, C5-C<u>*H*</u>-), 5.88 (d, 1H, 1'-C<u>*H*</u>-), 7.60 (d, 1H, C6-C<u>*H*</u>-)

IIC.3.6 Tetrahydropyranyl ethers



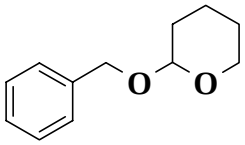
Benzoic acid 2-(tetrahydro-pyran-2-yloxy)-ethyl ester (1cn)

IR (Neat): 2942, 2872, 1718, 1602, 1452, 1385, 1314, 1275, 1201, 1176, 1124, 1071, 1035, 986, 712 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50-1.90 (brm, 6H, (-O-CH$_2$-(C<u>*H*</u>$_2$)$_3$-CH-)-O-), 3.51 (m, 1H, (-O-C<u>*H*</u>(H)-(CH$_2$)$_3$-CH-)-O-), 3.90 (m, 1H, (-O-CH(<u>*H*</u>)-(CH$_2$)$_3$-CH-)-O-), 4.03 (m, 2H, (-O-CH$_2$-(CH$_2$)$_3$-CH-)-O-C<u>*H*</u>$_2$-), 4.51 (m, 2H, -CO-O-C<u>*H*</u>$_2$-), 4.71 (m,

1H, (-O-CH_2-$(CH_2)_3$-C*H*-)-O-), 7.44 (m, 2H, Ar*H*), 7.55 (m, 1H, Ar*H*), 8.06 (m, 2H, Ar*H*)

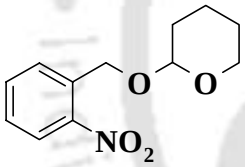
MS(FAB): m/z 251 $(M+H)^+$



2-Benzyloxy-tetrahydro-pyran (29n)

IR (Neat): 2945, 2868, 1460, 1352, 1265, 1203, 1122, 1081, 978, 906, 876, 814 cm^{-1}

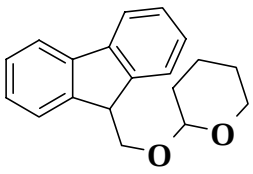
^1H NMR (400 MHz, $CDCl_3$): δ 1.49-1.89 (brm, 6H, (-O-CH_2-(CH_2)$_3$-CH-)-O-), 3.52 (m, 1H, (-O-C*H*(H)-$(CH_2)_3$-CH-)-O-), 3.89 (m, 1H, (-O-CH(*H*)-$(CH_2)_3$-CH-)-O-), 4.42 (d, 1H, Ar-C*H*(H)-O-), 4.82 (d, 1H, Ar-CH(*H*)-O-), 4.69 (m, 1H, (-O-CH_2-$(CH_2)_3$-C*H*-)-O-), 7.25 (m, 5H, Ar*H*)



2-(2-Nitro-benzyloxy)-tetrahydro-pyran (30n)

IR (Neat): 2955, 2868, 1531, 1444, 1347, 1203, 1122, 1065, 1034, 978, 860, 794 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.35-2.00 (brm, 6H, -(-O-CH_2-(CH_2)$_3$-CH-)-O-), 3.56 (m, 1H, -(-O-C*H*(H)-$(CH_2)_3$-CH-)-O-), 3.89 (m, 1H, -(-O-CH(*H*)-$(CH_2)_3$-CH-)-O-), 4.48 (d, 1H, Ar-C*H*(H)-O-), 4.75 (d, 1H, Ar-CH(*H*)-O-), 4.82 (d, 1H, Ar-C*H*(H)-O-), 7.22-7.53 (m, 4H, Ar*H*)

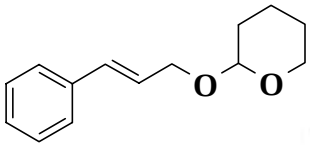


2-(9H-Fluoren-9-ylmethoxy)-tetrahydro-pyran (31n)

IR (Neat): 2945, 2878, 1639, 1603, 1449, 1352, 1203, 1122, 1035, 973, 912, 871 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.35-2.06 (brm, 6H, (-O-CH_2-(CH_2)$_3$-CH-)-O-), 3.52 (m, 2H, (-O-C*H*$_2$-$(CH_2)_3$-CH-)-O-), 3.86 (m, 1H, Ar-C*H*(Ar)-CH_2-O-), 4.09 (t, 1H,

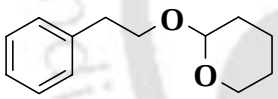
Ar-CH(Ar)-C*H*(H)-O-), 4.24 (t, 1H, Ar-CH(Ar)-CH(*H*)-O-), 4.71 (m, 1H, (-O-CH_2-$(CH_2)_3$-C*H*-)-O-), 7.31 (m, 5H, Ar*H*), 7.72 (m, 3H, Ar*H*)



2-(3-Phenyl-allyloxy)-tetrahydro-pyran (32n)

IR (Neat): 2950, 2878, 1639, 1603, 1454, 1398, 1275, 1203, 1178, 1116, 1075 cm^{-1}

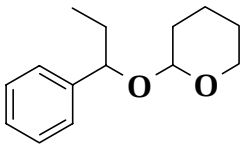
^1H NMR (400 MHz, $CDCl_3$): δ 1.51 (brm, 6H, (-O-CH_2-(CH_2)$_3$-CH-)-O-), 3.52 (m, 1H, (-O-C*H*(H)-$(CH_2)_3$-CH-)-O-), 3.81 (m, 1H, (-O-CH(*H*)-$(CH_2)_3$-CH-)-O-), 4.14 (m, 1H, Ar-CH=CH-C*H*(H)-O-), 4.36 (m, 1H, Ar-CH=CH-CH(*H*)-O-), 4.71 (m, 1H, (-O-CH_2-$(CH_2)_3$-C*H*-)-O-), 6.30 (m, 1H, Ar-CH=C*H*-CH_2-O-), 6.61 (d, 1H, Ar-C*H*=CH-CH_2-O-), 7.39 (m, 5H, Ar*H*)



2-Phenethyloxy-tetrahydro-pyran (33n)

IR (Neat): 2938, 2869, 1728, 1605, 1498, 1450, 1354, 1269, 1200, 1141, 1120, 1066, 1034, 970, 906, 869, 816, 752, 698 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.35-2.00 (brm, 6H, (-O-CH_2-(CH_2)$_3$-CH-)-O-), 2.91 (m, 2H, Ar-C*H*$_2$-), 3.45 (m, 1H, -O-C*H*(H)-CH_2-Ar), 3.61 (m, 1H, -O-CH(*H*)-CH_2-Ar), 3.64 (m, 1H, (-O-C*H*(H)-$(CH_2)_3$-CH-)-O-), 3.96 (m, 1H, (-O-CH(*H*)-$(CH_2)_3$-CH-)-O-), 4.59 (m, 1H, (-O-CH_2-$(CH_2)_3$-C*H*-)-O-), 7.25 (m, 5H, Ar*H*)

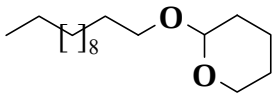


2-(1-Phenyl-propoxy)-tetrahydro-pyran (38n)

IR (Neat): 2938, 2874, 1456, 1381, 1205, 1114, 1077, 1018, 997, 906, 864, 757 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, 3H, -C*H*$_3$), 1.48-2.01 (m, 8H, (-O-CH_2-(C*H*$_2$)$_3$-CH-)-

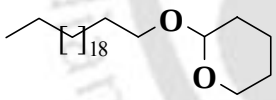
O-CH(Ar)-C<u>*H*</u>$_2$-CH$_3$), 3.48 (m, 1H, (-O-C<u>*H*</u>(H)-(CH$_2$)$_3$-CH-)-O-), 3.95 (m, 1H, (-O-CH(<u>*H*</u>)-(CH$_2$)$_3$-CH-)-O-), 4.41 (m, 1H, (-O-CH$_2$-(CH$_2$)$_3$-CH-)-O-C<u>*H*</u>(Ar)-), 4.60 (m, 1H, (-O-CH$_2$-(CH$_2$)$_3$-C<u>*H*</u>-)-O- 7.40 (m, 5H, Ar<u>*H*</u>)



2-Dodecyloxy-tetrahydro-pyran (42n)

IR (Neat): 2925, 2854, 1376, 1644, 1465, 1440, 1364, 1200, 1126, 1082, 1034, 906, 864, 810 cm^{-1}

^{1}H NMR (400 MHz, CDCl$_3$): δ 0.88 (t, 3H, -CH$_3$), 1.26 (brm, 26H, (-O-CH$_2$-(C<u>*H*</u>$_2$)$_3$-CH-)-O-CH$_2$-(C<u>*H*</u>$_2$)$_{10}$-CH$_3$), 3.37 (m, 1H, (-O-CH$_2$-(CH$_2$)$_3$-CH-)-O-C<u>*H*</u>(H)-), 3.50 (m, 1H, (-O-CH$_2$-(CH$_2$)$_3$-CH-)-O-CH(<u>*H*</u>)-), 3.72 (m, 1H, (-O-C<u>*H*</u>(H)-(CH$_2$)$_3$-CH-)-O-), 3.86 (m, 1H, (m, 1H, (-O-CH(<u>*H*</u>)-(CH$_2$)$_3$-CH-)-O-), 4.56 (m, 1H, (-O-CH$_2$-(CH$_2$)$_3$-C<u>*H*</u>-)-O-)

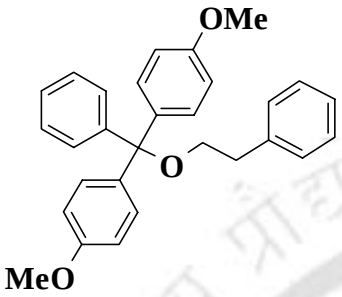


2-Docosyloxy-tetrahydro-pyran (43n)

IR (Neat): 2924, 2852, 1659, 1475, 1388, 1265, 1203, 1127, 1086, 1034, 912, 876, 819, 763, 722, 702 cm^{-1}

^{1}H NMR (400 MHz, CDCl$_3$): δ 0.88 (t, 3H, -C<u>*H*</u>$_3$), 1.25 (brm, 46H, (-O-CH$_2$-(C<u>*H*</u>$_2$)$_3$-CH-)-O-CH$_2$-(C<u>*H*</u>$_2$)$_{20}$-CH$_3$), 3.39 (m, 1H, (-O-CH$_2$-(CH$_2$)$_3$-CH-)-O-C<u>*H*</u>(H)-),3.51 (m, 1H, (-O-CH$_2$-(CH$_2$)$_3$-CH-)-O-CH(<u>*H*</u>)-), 3.73 (m, 1H, (m, 1H, (-O-C<u>*H*</u>(H)-(CH$_2$)$_3$-CH-)-O-), 3.86 (m, 1H, (-O-CH(<u>*H*</u>)-(CH$_2$)$_3$-CH-)-O-), 4.57 (m, 1H, (-O-CH$_2$-(CH$_2$)$_3$-C<u>*H*</u>-)-O-)

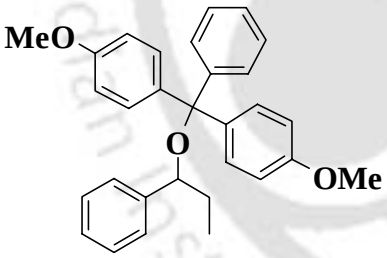
IIC.3.7 4,4'-Dimethoxytrityl ethers



2-Phenethyl-4,4'-dimethoxytrityl ether (33o)

IR (Neat): 3024, 2928, 2816, 2064, 1955, 1897, 1654, 1600, 1574, 1504, 1443, 1379, 1292, 1225, 1180, 1156, 1100, 1078, 1027, 905, 819, 755, 697 cm^{-1}

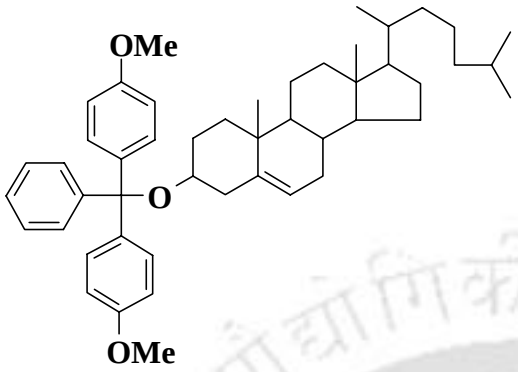
^1H NMR (400 MHz, $CDCl_3$): δ 2.86 (t, 2H, Ar-CH_2-C$\underline{H}_2$-O-), 3.25 (t, 2H, Ar-C$\underline{H}_2$-CH_2-O-), 3.78 (s, 6H, 2 × Ar-OC$\underline{H}_3$), 6.78 (m, 5H, Ar$\underline{H}$), 7.26 (m, 13H, Ar$\underline{H}$)



1-Phenyl-propyl-4,4'-dimethoxytrityl ether (38o)

IR (Neat): 2976, 2864, 2048, 1600, 1574, 1500, 1446, 1292, 1244, 1161, 1052, 822 cm^{-1}

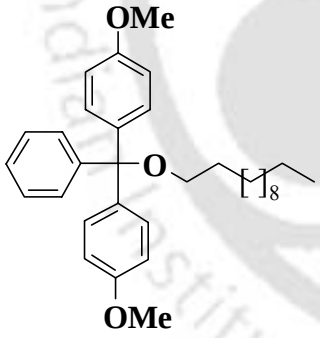
^1H NMR (400 MHz, $CDCl_3$): δ 0.53 (t, 3H, Ar-CH(OC(Ar)$_3$)-CH_2-C$\underline{H}_3$), 1.42 (m, 2H, Ar-CH(OC(Ar)$_3$)-C$\underline{H}_2$-CH_3), 3.71 (s, 6H, 2 × Ar-OC$\underline{H}_3$), 4.36 (m, 1H, Ar-C$\underline{H}$(OC(Ar)$_3$)-CH_2-CH_3), 6.73 (m, 5H, Ar$\underline{H}$), 7.31 (m, 13H, Ar$\underline{H}$)



Cholesterol-4,4'-dimethoxytrityl ether (39o)

IR (Neat): 3420, 2940, 2866, 1637, 1605, 1465, 1382, 1265, 1107, 1061, 1023, 805 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.67 (s, 3H), 0.88 (d, 6H), 0.92 (d, 3H), 1.00 (s, 3H), 1.11 (m, 8H), 1.49 (m, 13H), 1.82 (m, 3H), 2.17 (m, 2H), 2.27 (m, 2H), 3.51 (m, 1H), 3.80 (s, 3H), 3.89 (s, 3H), 5.34 (m, 1H), 6.82 (m, 3H), 6.99 (m, 1H), 7.16 (m, 3H), 7.27 (m, 5H), 7.84 (m, 1H)

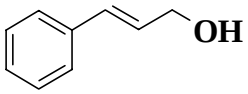


1-Dodecyl-4,4'-dimethoxytrityl ether (42o)

IR (Neat): 499, 2931, 2861, 1610, 1582, 1512, 1470, 1447, 1307, 1256, 1177, 1116, 074, 1037, 912, 833, 758 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, 3H, -C$\underline{H}_3$), 1.25 (brm, 18H, -(C$\underline{H}_2$)$_9$-CH_3), 1.65 (m, 2H, -O-CH_2-C$\underline{H}_2$-), 3.02 (t, 2H, -O-C$\underline{H}_2$-CH_2-), 3.78 (s, 6H, 2 × Ar-OC$\underline{H}_3$), 6.83 (m, 5H, Ar$\underline{H}$), 7.32 (m, 8H, Ar$\underline{H}$)

IIC.3.8 Alcohols

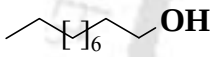


Cinnamyl alcohol (32)

IR (Neat): 3360, 3029, 2862, 1659, 1599, 1579, 1497, 1450, 1200, 1095, 1070, 1009, 968, 749, 737, 695 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 2.29 (brs, 1H, -O*H*), 4.2 (d, 2H, Ar-CH=CH-C*H*$_2$-OH), 6.34 (m, 1H, Ar-CH=C*H*-CH_2-OH), 6.57 (d, 2H, Ar-C*H*=CH-CH_2-OH), 7.18-7.41 (m, 5H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 63.50, 126.38, 127.57, 128.43, 128.50, 130.91, 136.58

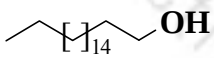


1-Decanol (34)

IR (Neat): 3332, 2928, 2857, 1468, 1380, 1123, 1060, 724 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, -CH_2-C*H*$_3$), 1.27 (brm, 14H, -(C*H*$_2$)$_7$-CH_3), 1.56 (m, 2H, -C*H*$_2$-CH_2-OH), 1.97 (brs, 1H, -O*H*), 3.62 (t, 2H, -C*H*$_2$-OH)

^{13}C NMR (100 MHz, $CDCl_3$): δ 32.80, 14.12, 22.70, 25.75, 29.35, 29.48, 29.59, 29.66, 31.92, 62.95



Octadecan-1-ol (35)

IR (Neat): 3330, 2920, 2849, 1462, 1380, 1065, 722 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, -CH_2-C*H*$_3$), 1.26 (br, 30H, -(C*H*$_2$)$_{15}$-CH_2-OH), 1.56 (m, 2H, -C*H*$_2$-CH_2-OH), 1.69 (br, 1H, -O*H*), 3.62 (t, 2H, -CH_2-C*H*$_2$-OH)

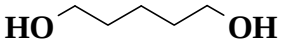
Propane-1,3-diol (36)

IR (Neat): 3340, 2948, 2882, 1662, 1420, 1180, 1063, 980, 942, 923 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.57 (m, 2H, -C*H*$_2$-CH_2-OH), 3.46 (m, 4H, 2 × -C*H*$_2$-OH),

4.35 (brm, 2H, 2 × -O<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 35.69, 57.98

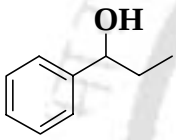


Pentane-1,5-diol (37)

IR (Neat): 3340, 2928, 2862, 1462, 1378, 1171, 1060, 972, 920, 891 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (m, 2H, -C<u>*H*</u>$_2$- CH_2-CH_2-OH), 1.56 (m, 4H, 2 × -C<u>*H*</u>$_2$-CH_2-OH), 3.60 (m, 4H, 2 × -C<u>*H*</u>$_2$-OH), 4.82 (brs, 2H, 2 × -O<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 24.18, 33.79, 64.34

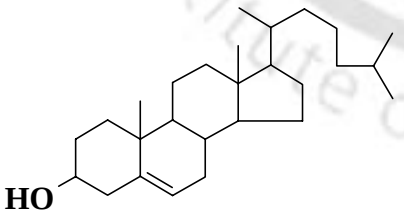


1-Phenyl-1-propanol (38)

IR (Neat): 3360, 2960, 2938, 2880, 1496, 1458, 1204, 1100, 1050, 1018, 976, 920, 900, 836, 765, 747, 703 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (t, 3H, -C<u>*H*</u>$_3$), 1.74 (m, 2H, -C<u>*H*</u>$_2$-CH_3), 2.30 (brs, 1H, -O<u>*H*</u>), 4.52 (t, 1H, Ar-C<u>*H*</u>(OH)-), 7.25 (m, 5H, Ar<u>*H*</u>)

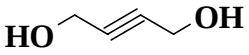
^{13}C NMR (100 MHz, $CDCl_3$): δ 10.10, 31.83, 75.90, 125.93, 127.36, 128.28, 144.57



Cholesterol (39)

IR (Neat): 3372, 2931, 1468, 1379, 1367, 1058, 1024, 960, 956, 842, 802 cm^{-1}

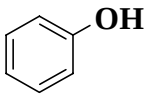
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.68 (s, 3H), 0.87 (d, 6H), 0.91 (d, 3H), 1.00 (s, 3H), 1.02 (m, 2H), 1.11 (m, 6H), 1.32 (m, 5H), 1.47 (m, 8H), 1.72 (m, 2H), 1.83 (m, 1H), 1.98 (m, 2H), 2.27 (m, 2H), 3.52 (m, 1H), 5.34 (m, 1H)



2-Butyne-1,4-diol (40)

IR (Neat): 3310, 2925, 2870, 1420, 1220, 1135, 1000 cm^{-1}

^1H NMR (400 MHz, Acetone-*d6*): δ 4.23 (brs, 4H, 2 × -C<u>*H*</u>$_2$-OH), 4.39 (brs, 2H, 2 × -O<u>*H*</u>)

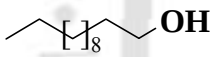


Phenol (41)

IR (Neat): 3380, 1597, 1500, 1472, 1362, 1220, 1071, 1029, 1000, 890, 812, 757 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 5.69 (brs, 1H, -O<u>*H*</u>), 6.86 (m, 3H, Ar<u>H</u>), 7.22 (m, 2H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 115.35, 120.91, 129.68, 155.17

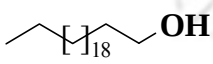


1-Dodecanol (42)

IR (Neat): 3330, 2929, 2858, 1469, 1380, 1123, 1059, 723 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, -CH_2-C<u>*H*</u>$_3$), 1.27 (brm, 18H, -(C<u>*H*</u>$_2$)$_9$-CH_3), 1.57 (m, 2H, -C<u>*H*</u>$_2$-CH_2-OH), 1.77 (brs, 1H, -O<u>*H*</u>), 3.62 (t, 2H, -C<u>*H*</u>$_2$-OH)

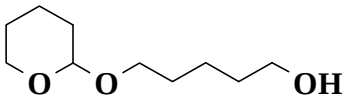
^{13}C NMR (100 MHz,$CDCl_3$): δ 14.11, 22.71, 25.79, 29.38, 29.48, 29.64, 31.94, 32.82, 62.99



1-Docosanol (43)

IR (Neat): 3331, 2928, 2857, 1470, 1382, 1125, 1060, 721 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, -C<u>*H*</u>$_3$), 1.27 (brm, 38H, -(C<u>*H*</u>$_2$)$_{19}$-CH_3), 1.57 (m, 2H, -C<u>*H*</u>$_2$-CH_2-OH), 1.77 (brs, 1H, -O<u>*H*</u>), 3.62 (t, 2H, -C<u>*H*</u>$_2$-OH)

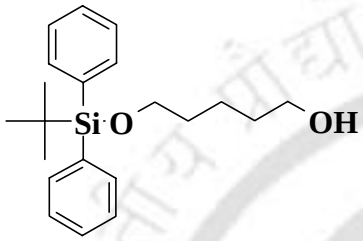


5-(Tetrahydro-pyran-2-yloxy)-pentan-1-ol (47)

^1H NMR (400 MHz, $CDCl_3$): δ 1.48-1.82 (brm, 12H, (-O-CH_2-(C<u>*H*</u>$_2$)$_3$-CH-)-O-CH_2-(C<u>*H*</u>$_2$)$_3$-

CH_2-OH), 3.40 (m, 1H, (-O-C<u>*H*</u>(H)-$(CH_2)_3$-CH-)-O-), 3.50 (m, 1H, (-O-CH_2-$(CH_2)_3$-CH-)-O-C<u>*H*</u>(H)-), 3.66 (t, 2H, -C<u>*H*</u>$_2$-OH), 3.76 (m, 1H, (-O-CH_2-(C<u>*H*</u>$_2$)$_3$-CH-)-O-CH(<u>*H*</u>)-), 3.85 (m, 1H, (-O-CH(<u>*H*</u>)-$(CH_2)_3$-CH-)-O-), 4.58 (m, 1H, (-O-CH_2-CH_2-CH_2-CH_2-C<u>*H*</u>-)-O-)

MS FAB: m/z 189 $(M+H)^+$

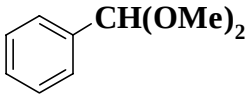


5-(2,2-Dimethyl-1,1-diphenyl-propylsilyl)-pentan-1-ol (48)

IR (Neat): 3392, 2936, 2860, 1483, 1377, 1256, 1210, 1099, 1073, 845, 780, 729 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (s, 9H, -Si-C(C<u>*H*</u>$_3$)$_3$), 1.41 (m, 2H, -OCH_2-CH_2-C<u>*H*</u>$_2$-CH_2-CH_2-OH), 1.56 (m, 4H, -OCH_2-C<u>*H*</u>$_2$-CH_2-C<u>*H*</u>$_2$-CH_2O-), 2.17 (s, 1H, -O<u>*H*</u>), 3.64 (m, 4H, -OC<u>*H*</u>$_2$-CH_2-CH_2-CH_2-C<u>*H*</u>$_2$O-), 7.38 (m, 6H, Ar<u>*H*</u>), 7.66 (m, 4H, Ar<u>*H*</u>)

IIC.3.9 Dimethyl acetals

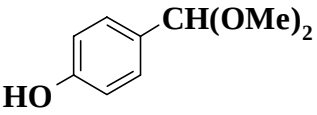


Benzaldehyde dimethyl acetal (1h)

IR (Neat): 2941, 2832, 1496, 1454, 1357, 1314, 1209, 1108, 1080, 1056, 983, 932, 916, 876, 747, 703 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.33 (s, 6H, Ar-CH(OC<u>*H*</u>$_3$)$_2$), 5.38 (s, 1H, Ar-C<u>*H*</u>$(OCH_3)_2$), 7.34 (m, 3H, Ar<u>*H*</u>), 7.45 (m, 2H, Ar<u>*H*</u>)

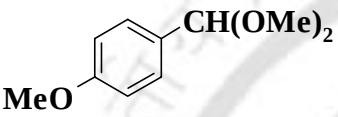
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.61, 103.08, 126.63, 128.12, 128.37, 138.00



4-Hydroxybenzaldehyde dimethyl acetal (6h)

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.32 (s, 6H, Ar-CH(OC<u>*H*</u>$_3$)$_2$), 5.34 (s, 1H, Ar-C<u>*H*</u>(OCH$_3$)$_2$), 6.82 (d, 2H, Ar<u>*H*</u>), 7.28 (d, 2H, Ar<u>*H*</u>)

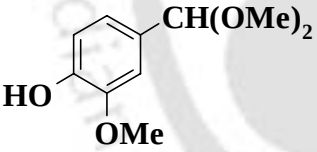
^{13}C NMR (100 MHz, $CDCl_3$): δ 53.29, 104.01, 115.61, 128.51, 133.18, 156.92



4-Methoxybenzaldehyde dimethyl acetal (7h)

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.31 (s, 6H, Ar-CH(OC<u>*H*</u>$_3$)$_2$), 3.81 (s, 3H, Ar-OC<u>*H*</u>$_3$), 5.34 (s, 1H, Ar-C<u>*H*</u>(OCH$_3$)$_2$), 6.89 (d, 2H, Ar<u>*H*</u>), 7.36 (d, 2H, Ar<u>*H*</u>)

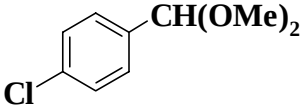
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.57, 55.21, 103.04, 113.49, 127.88, 130.33, 159.64



4-Hydroxy-3-methoxybenzaldehyde dimethyl acetal (8h)

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.66 (s, 6H, Ar-CH(OC<u>*H*</u>$_3$)$_2$), 3.74 (s, 3H, Ar-OC<u>*H*</u>$_3$), 5.08 (s, 1H, Ar-C<u>*H*</u>(OCH$_3$)$_2$), 6.60 (d, 1H, Ar<u>*H*</u>), 7.18 (m, 2H, Ar<u>*H*</u>)

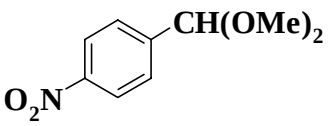
^{13}C NMR (100 MHz, $CDCl_3$): δ 56.34, 56.55, 103.39, 110.67, 113.49, 114.56, 118.08, 125.00, 145.86



4-Chlorobenzaldehyde dimethyl acetal (10h)

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.31 (s, 6H, Ar-CH(OC<u>*H*</u>$_3$)$_2$), 5.37 (s, 1H, Ar-C<u>*H*</u>(OCH$_3$)$_2$), 7.39 (m, 4H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 52.56, 102.29, 128.14, 128.37, 130.96, 136.58

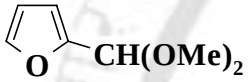


4-Nitrobenzaldehyde dimethyl acetal (11h)

IR (Neat): 2938, 2832, 1608, 1524, 1447, 1344, 1315, 1206, 1102, 1058, 1015, 854, 831, 746, 712 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.34 (s, 6H, Ar-CH(OCH_3)$_2$), 5.47 (s, 1H, Ar-C*H*(OCH_3)$_2$), 7.63 (d, 2H, Ar*H*), 8.22 (d, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 52.70, 101.55, 123.42, 127.81, 145.00, 148.00

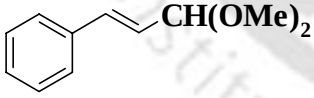


2-Furfural dimethyl acetal (13h)

IR (Neat): 2944, 2832, 1504, 1450, 1408, 1354, 1194, 1157, 1109, 1061, 1008, 981, 906, 885, 810, 741, 608 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.35 (s, 6H, Ar-CH(OCH_3)$_2$), 5.43 (s, 1H, Ar-C*H*(OCH_3)$_2$), 6.36 (dd, 1H, Ar*H*), 6.41 (d, 1H, Ar*H*),7.41 (m, 1H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 52.83, 97.98, 108.42, 110.04, 142.48



***trans*-Cinnamaldehyde dimethyl acetal (14h)**

IR (Neat): 2939, 2832, 1495, 1449, 1352, 1198, 1137, 1050, 973, 912, 845, 753 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.35 (s, 6H, Ar-CH=CH-CH(OCH_3)$_2$), 4.96 (d, 1H, Ar-CH=CH-C*H*(OCH_3)$_2$), 6.15 (dd, 1H, Ar-CH=C*H*-CH-), 6.73 (d, 1H, Ar-C*H*=CH-), 7.37 (m, 5H, Ar*H*)

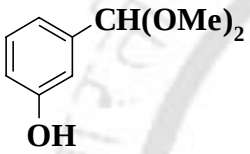
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.73, 102.93, 125.68, 126.72, 128.09, 128.57, 129.10, 133.58, 136.09

Pentanal dimethyl acetal (15h)

IR (Neat): 2970, 2933, 2858, 1472, 1365, 1248, 1210, 1157, 1114, 1061, 933, 730 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, -CH_2-C$\underline{H}_3$), 1.35 (m, 4H, -C$\underline{H}_2$-C$\underline{H}_2$-CH_3), 1.64 (m, 2H, -C$\underline{H}_2$-$CH(OCH_3)_2$), 3.39 (t, 1H, -CH_2-C$\underline{H}(OCH_3)_2$), 4.83 (s, 6H, -CH_2-$CH(OC\underline{H}_3)_2$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 13.93, 22.46, 23.19, 31.51, 34.33, 101.69

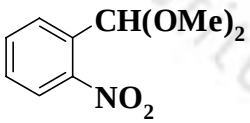


3-Hydroxybenzaldehyde dimethyl acetal (17h)

IR (Neat): 3367, 2940, 2832, 1605, 1456, 1352, 1273, 1196, 1155, 1102, 1055, 1000, 865, 821, 779 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.33 (s, 3H, Ar-$CH(OC\underline{H}_3)OCH_3$), 3.50 (s. 3H, Ar-$CH(OCH_3)OC\underline{H}_3$), 5.34 (s, 1H, Ar-C$\underline{H}(OCH_3)_2$), 6.82-7.42 (m, 4H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 52.83, 103.11, 114.76, 122.17, 123.18, 130.31, 139.80, 157.64

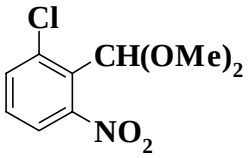


2-Nitrobenzaldehyde dimethyl acetal (20h)

IR (Neat): 2954, 2832, 1616, 1525, 1445, 1344, 1205, 1104, 1061, 858, 837, 752 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 3.40 (s, 6H, Ar-$CH(OC\underline{H}_3)_2$), 5.92 (s, 1H, Ar-C$\underline{H}(OCH_3)_2$), 7.47 (m, 1H, Ar$\underline{H}$), 7.60 (m, 1H, Ar$\underline{H}$), 7.80 (m, 2H, Ar$\underline{H}$)

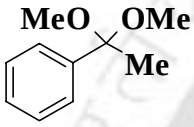
^{13}C NMR (100 MHz, $CDCl_3$): δ 54.55, 99.84, 124.16, 128.07, 129.31, 132.42, 132.62, 148.92



2-Chloro-6-nitrobenzaldehyde dimethyl acetal (21h)

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.44 (m, 6H, Ar-CH(OC<u>*H*</u>$_3$)$_2$), 5.22 (s, 1H, Ar-C<u>*H*</u>(OCH$_3$)$_2$), 7.60 (d, 1H, Ar<u>*H*</u>), 8.32 (dd, 1H, Ar<u>*H*</u>), 8.68 (d, 1H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 54.21, 100.11, 124.92, 129.23, 132.41

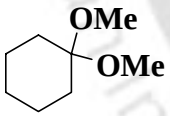


Acetophenone dimethyl ketal (22h)

IR (Neat): 2996, 2945, 2832, 1454, 1378, 1280, 1198, 1152, 1096, 1045, 881, 768 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (s, 3H, Ar-C(OCH$_3$)$_2$-C<u>*H*</u>$_3$), 3.19 (s, 6H, Ar-C(OC<u>*H*</u>$_3$)$_2$-CH$_3$), 7.27 (m, 1H, Ar<u>*H*</u>), 7.34 (m, 2H, Ar<u>*H*</u>), 7.48 (m, 2H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.05, 48.92, 101.60, 126.17, 127.46, 128.00, 142.82

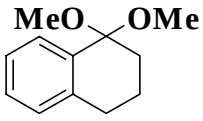


Cyclohexanone dimethyl ketal (23h)

IR (Neat): 2949, 2862, 1454, 1372, 1285, 1259, 1162, 1111, 1059, 931, 849, 824 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (brm, 10H, -(C<u>*H*</u>$_2$)$_5$-), 3.49 (s, 6H, 2 × -OC<u>*H*</u>$_3$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 24.0, 25.3, 35.3, 64.1, 109.0

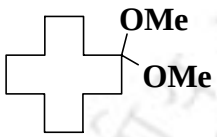


α-Tetralone dimethyl ketal (24h)

IR (Neat): 2949, 1689, 1612, 1464, 1443, 1403, 1331, 1290, 1198, 1136, 1100, 1034, 998, 942, 803, 762 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.07 (m, 2H, Ar-CH_2-C$\underline{H}_2$-CH_2-), 2.59 (t, 2H, Ar-C$\underline{H}_2$-CH_2-CH_2-), 2.89 (t, 2H, Ar-C$(OCH_3)_2$-C$\underline{H}_2$-), 3.41 (s, 6H, 2 × -OC$\underline{H}_3$), 7.17-7.47 (m, 3H, Ar$\underline{H}$), 7.96 (m, 1H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.26, 29.70, 39.14, 73.84, 126.61, 127.16, 128.75, 132.59, 133.38, 144.47

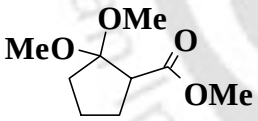


Cyclododecanone dimethyl ketal (25h)

IR (Neat): 2941, 2855, 1721, 1478, 1453, 1372, 1326, 1291, 1230, 1185, 1129, 1088, 1053, 967, 866, 749, 729 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (brm, 18H, -(C$\underline{H}_2$)$_9$-), 1.61 (brm, 4H, -C$\underline{H}_2$-C$(OCH_3)_2$-C$\underline{H}_2$-), 3.17 (s, 6H, 2 × -OC$\underline{H}_3$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.29, 21.87, 22.37, 26.16, 29.37, 40.30, 47.77, 104.21



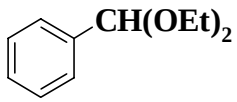
Cyclopentanone-2-methyl-carboxylate dimethyl ketal (26h)

IR (Neat): 2956, 2837, 1738, 1440, 1354, 1338, 1269, 1210, 1162, 1114, 1050, 970, 874, 853, 752 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63 (m, 1H, -C$(OCH_3)_2$-C$\underline{H}$(H)-), 1.87 (m, 4H, -C$(OCH_3)_2$-CH_2-C$\underline{H}_2$-C$\underline{H}_2$-), 2.04 (m, 1H, -C$(OCH_3)_2$-CH($\underline{H}$)-CH_2-CH_2-), 3.00 (m, 1H, -C$\underline{H}$($COOCH_3$)C$(OCH_3)_2$), 3.22 (s, 3H, -C(OC$\underline{H}_3$)(OCH_3)-CH(H)-), 3.25 (s, 3H, -C(OCH_3)(OC$\underline{H}_3$)-CH(H)-), 3.69 (s, 3H, -COOC$\underline{H}_3$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.92, 27.53, 34.29, 48.71, 50.02, 50.52, 51.67, 112.34, 173.65

IIC.3.10 Diethyl acetals

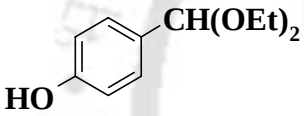


Benzaldehyde diethyl acetal (1i)

IR (Neat): 2980, 2888, 1454, 1377, 1341, 1213, 1121, 1059, 942, 911, 839, 757 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.23 (t, 6H, Ar-CH(-$OCH_2C\underline{H}_3)_2$), 3.49 (q, 4H, Ar-CH($OC\underline{H}_2CH_3)_2$), 5.48 (s, 1H, Ar-C$\underline{H}$($OCH_2CH_3)_2$), 7.29(m, 3H, Ar$\underline{H}$), 7.42 (m, 2H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.24, 60.28, 100.95, 126.66, 127.91, 128.01, 138.99

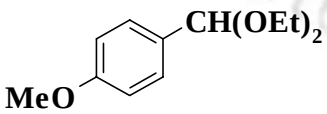


4-Hydroxybenzaldehyde diethyl acetal (6i)

IR (Neat): 3387, 2934, 2941, 2901, 1620, 1524, 1448, 1377, 1342, 1276, 1215, 1169, 1099, 1058, 840, 805 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.25 (t, 6H, 2 × -$OCH_2C\underline{H}_3$), 3.64 (m, 4H, 2 × -$OC\underline{H}_2CH_3$), 5.44 (s, 1H, Ar-C$\underline{H}$($OCH_2CH_3)_2$), 6.82 (d, 2H, Ar$\underline{H}$), 7.31 (d, 2H, Ar$\underline{H}$)

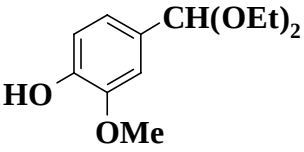
^{13}C NMR (100 MHz, $CDCl_3$): δ 15.07, 60.78, 104.21, 115.80, 128.81, 133.20, 156.97



4-Methoxybenzaldehyde diethyl acetal (7i)

IR (Neat): 2842, 1689, 1602, 1515, 1469, 1428, 1326, 1264, 1223, 1167, 1029, 839 cm^{-1}

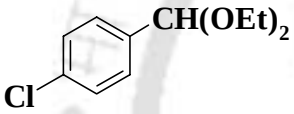
^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, 6H, 2 × -$OCH_2C\underline{H}_3$), 3.72 (q, 4H, 2 × -$OC\underline{H}_2CH_3$), 3.88 (s, 3H, Ar-$OC\underline{H}_3$), 5.30 (s, 1H, Ar-C$\underline{H}$($OCH_2CH_3)_2$), 6.95 (d, 2H, Ar$\underline{H}$), 8.05 (d, 2H, Ar$\underline{H}$)



4-Hydroxy-3-methoxybenzaldehyde diethyl acetal (8i)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, 6H, 2 × -$OCH_2C\underline{H}_3$), 3.71 (m, 4H, 2 × -$OC\underline{H}_2CH_3$), 3.97 (s, 3H, $ArOC\underline{H}_3$), 5.29 (s, 1H, Ar- $C\underline{H}(OCH_2CH_3)_2$), 6.96 (d, 1H, Ar$\underline{H}$), 7.41 (m, 2H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.70, 56.37, 56.58, 101.61, 110.59, 113.40, 114.50, 118.71, 124.97, 146.58

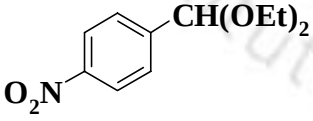


4-Chlorobenzaldehyde diethyl acetal (10i)

IR (Neat): 2976, 2929, 2881, 1598, 1490, 1443, 1397, 1371, 1337, 1204, 1171, 1113, 1089, 1056, 1016, 921, 846, 803 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (t, 6H, 2 × -$OCH_2C\underline{H}_3$), 3.60 (q, 4H, 2 × -$OC\underline{H}_2CH_3$), 5.45 (s, 1H, Ar-$C\underline{H}(OCH_2CH_3)_2$), 7.32 (m, 4H, Ar$\underline{H}$)

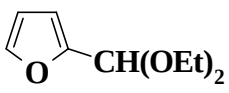
^{13}C NMR (100 MHz, $CDCl_3$): δ 15.06, 60.84, 100.63, 128.01, 128.21, 133.95, 137.59



4-Nitrobenzaldehyde diethyl acetal (11i)

IR (Neat): 2980, 2888, 1607, 1525, 1351, 1208, 1111, 1059, 865, 752, 726 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (t, 6H, 2 × -$OCH_2C\underline{H}_3$), 3.57 (q, 4H, 2 × -$OC\underline{H}_2CH_3$), 5.56 (s, 1H, Ar-$C\underline{H}(OCH_2CH_3)_2$), 7.65 (d, 2H, Ar$\underline{H}$), 8.18 (d, 2H, Ar$\underline{H}$)

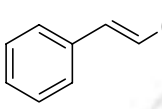


2-Furfural diethyl acetal (13i)

IR (Neat): 2980, 2893, 1705, 1684, 1474, 1397, 1336, 1234, 1157, 1121, 1059, 752 cm^{-1}

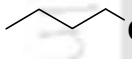
^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, 6H, 2 × -$OCH_2C\underline{H}_3$), 3.74 (m, 4H, 2 × -$OC\underline{H}_2CH_3$), 5.50 (s, 1H, Ar-$C\underline{H}(OCH_2CH_3)_2$), 6.40 (dd, 1H, Ar$\underline{H}$), 6.47 (d, 1H, Ar$\underline{H}$), 7.40 (m, 1H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0, 67.0, 95.7, 106.9, 110.0, 142.1



***trans*-Cinnamaldehyde diethyl acetal (14i)**

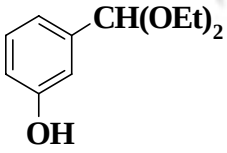
^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, 6H, 2 × –$OCH_2C\underline{H}_3$), 3.76 (m, 4H, 2 × -$OC\underline{H}_2CH_3$), 5.17 (d, 1H, Ar-CH=CH-$C\underline{H}(OCH_2CH_3)_2$), 6.20 (t, 1H, Ar-CH=C$\underline{H}$-), 6.74 (d, 1H, Ar-C$\underline{H}$=CH-), 7.30 (m, 5H, Ar$\underline{H}$)



Pentanal diethyl acetal (15i)

^1H NMR (400 MHz, $CDCl_3$): δ 0.87 (m, 9H, $C\underline{H}_3$-$(CH_2)_3$-$CH(OCH_2C\underline{H}_3)_2$) 1.31 (m, 4H, -$CH_3$-$(C\underline{H}_2)_2$-$CH_3$), 1.63 (m, 2H, -$C\underline{H}_2$-$CH(OCH_2CH_3)_2$), 2.39 (m, 4H, 2 × -$OC\underline{H}_2CH_3$), 4.79 (t, 1H, -$CH_2$-$C\underline{H}(OCH_2CH_3)_2$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.34, 22.13, 22.89, 22.96, 23.61, 34.76, 102.06



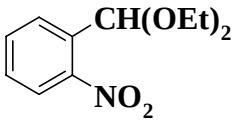
3-Hydroxybenzaldehyde diethyl acetal (17i)

IR (Neat): 3363, 2976, 2884, 1593, 1455, 1373, 1332, 1265, 1228, 1171, 1100, 1053, 882, 775 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.69 (m, 6H, 2 × -$OCH_2C\underline{H}_3$), 3.66 (m, 4H, 2 × -$OC\underline{H}_2CH_3$), 5.37 (s, 1H, Ar-$C\underline{H}(OCH_2CH_3)_2$), 6.92-7.33 (m, 4H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 18.56, 58.85, 101.87, 115.21, 122.70, 123.24, 130.63,

138.10, 157.63

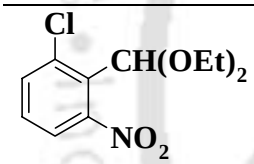


2-Nitrobenzaldehyde diethyl acetal (20i)

IR (Neat): 2976, 2933, 2885, 1536, 1445, 1365, 1200, 1125, 1056, 842, 794, 736 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, 6H, 2 × -OCH_2CH_3), 3.60 (m, 2H, -OCH_2CH_3), 3.71 (m, 2H, -OCH_2CH_3), 6.03 (s, 1H, Ar-$CH(OCH_2CH_3)_2$), 7.45 (m, 1H, Ar-H), 7.60 (m, 1H, Ar-H), 7.82 (m, 2H, Ar-H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.04, 63.40, 98.31, 124.08, 127.97, 129.13, 132.43, 133.65, 148.99

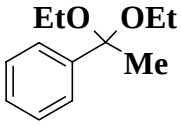


2-Chloro-6-nitrobenzaldehyde diethyl acetal (21i)

IR (Neat): 3106, 2978, 2929, 2882, 1610, 1578, 1826, 1462, 1347, 1294, 1248, 1195, 1114, 1056, 953, 919, 826, 742 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, 6H, 2 × -OCH_2CH_3), 3.64 (m, 4H, 2 × -OCH_2CH_3), 5.73 (s, 1H, Ar-$CH(OCH_2CH_3)_2$), 7.53 (d, 1H, Ar-H), 8.13 (dd, 1H, Ar-H), 8.55 (d, 1H, Ar-H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.08, 62.56, 98.14, 123.54, 124.25, 130.51



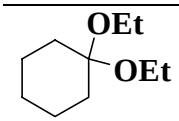
Acetophenone diethyl ketal (22i)

IR (Neat): 2975, 2929, 2884, 1493, 1446, 1390, 1371, 1267, 1171, 1125, 1101, 1069, 1050, 1028, 951, 861, 764, 701 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, 6H, 2 × -OCH_2CH_3), 1.59 (s, 3H, Ar-$C(OCH_2CH_3)_2$-CH_3), 3.47 (m, 4H, 2 × -OCH_2CH_3), 7.25-7.57 (m, 3H, Ar-H), 7.60 (m, 2H,

Ar*H*)

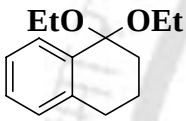
^{13}C NMR (100 MHz, $CDCl_3$): δ 15.31, 27.11, 56.61, 101.19, 126.10, 127.31, 127.93, 143.84



Cyclohexanone diethyl ketal (23i)

IR (Neat): 2939, 2867, 1454, 1367, 1280, 1259, 1172, 1095, 1064, 967, 829 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17 (t, 6H, 2 × -OCH_2CH_3), 1.50-1.80 (brm, 6H, -$(CH_2)_3$-), 2.27 (t, 4H, -CH_2-$C(OCH_2CH_3)_2$-CH_2-), 3.65 (m, 4H, 2 × -OCH_2CH_3)

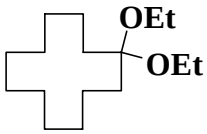


α-Tetralone diethyl ketal(24i)

IR (Neat): 2954, 2883, 1689, 1607, 1464, 1356, 1336, 1295, 1234, 1193, 1146, 1121, 1075, 1044, 936, 911, 803, 773, 742 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, 6H, 2 × -OCH_2CH_3), 2.13 (m, 2H, Ar-CH_2-CH_2-CH_2-), 2.69 (t, 2H, Ar-CH_2-CH_2-CH_2-), 2.96 (t, 2H, Ar-$C(OCH_2CH_3)_2$-CH_2-), 3.71 (q, 4H, 2 × -OCH_2CH_3), 7.28 (m, 2H, Ar*H*), 7.46 (m, 1H, Ar*H*), 8.04 (m, 1H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 18.39, 23.26, 29.67, 39.13, 58.40, 126.10, 127.15, 128.74, 132.60, 133.37, 144.47

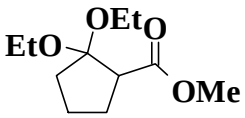


Cyclododecanone diethyl ketal (25i)

IR (Neat): 2941, 2855, 1721, 1478, 1453, 1372, 1326, 1291, 1230, 1185, 1129, 1088, 1053, 967, 866, 749, 729 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (brm, 18H, -$(CH_2)_9$- and 2 × -OCH_2CH_3), 1.66 (brm, 4H, -CH_2-$C(OCH_2CH_3)_2$-CH_2-), 2.39 (m, 4H, 2 × -OCH_2CH_3)

^{13}C NMR (100 MHz, $CDCl_3$): δ 18.80, 22.72, 22.93, 24.60, 24.98, 25.12, 40.75, 58.76

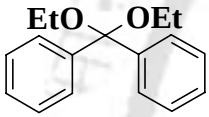


Cyclopentanone-2-methyl-carboxylate diethyl ketal (26i)

IR (Neat): 2959, 2893, 1751, 1730, 1438, 1351, 1305, 1269, 1213, 1126, 1024, 962 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04-1.35 (m, 7H), 1.50-2.43 (brm, 5H), 3.00 (m, 1H), 3.38-3.72 (m, 7H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.55, 22.34, 27.70, 35.02, 51.07, 51.85, 56.76, 58.64, 112.18, 174.28



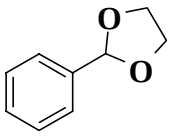
Benzophenone diethyl ketal (27i)

IR (KBr): 2936, 2827, 1488, 1450, 1214, 1172, 1082, 1061, 1030, 993, 771, 746 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, 6H, 2 × -$OCH_2C\underline{H}_3$), 3.32 (q, 4H, 2 × -$OC\underline{H}_2CH_3$), 7.24 (m, 6H, Ar$\underline{H}$), 7.53 (m, 4H, Ar$\underline{H}$)

Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 78.03; H, 8.02

IIC.3.11 1,3-Dioxolanes



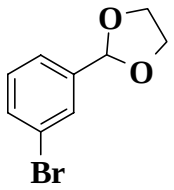
Benzaldehyde 1,3-dioxolane (1j)

IR (Neat): 2958, 2889, 1461, 1440, 1317, 1295, 1222, 1100, 1072, 1030, 968, 943, 917, 850, 760, 700 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.99 (m, 2H, -OC$\underline{H}$(H)-C$\underline{H}$(H)O-), 4.07 (m, 2H, -OCH($\underline{H}$)-CH($\underline{H}$)O-), 5.79 (s, 1H, Ar-C$\underline{H}$(-OCH_2CH_2O-)), 7.35 (m, 3H, Ar$\underline{H}$), 7.48 (m,

2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 65.22, 103.65, 126.35, 128.26, 129.10, 137.80



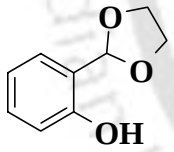
Br

***m*-Bromobenzaldehyde 1,3-dioxolane (2j)**

IR (Neat): 2957, 2889, 1722, 1574, 1479, 1438, 1381, 1280, 1260, 1217, 1100, 1082, 1030, 971, 945, 884, 786 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.05 (m, 4H, 2 × -OC*H*$_2$-), 5.78 (s, 1H, Ar-C*H*(-O(CH_2CH_2O-)), 7.23 (t, 1H, Ar*H*), 7.38 (d, 1H, Ar*H*), 7.49 (d, 1H, Ar*H*), 7.62 (s, 1H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 65.25, 102.62, 122.36, 125.08, 129.42, 129.86, 132.07, 140.23

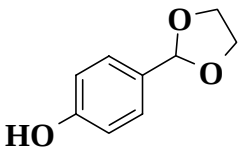


OH

2-Hydroxybenzaldehyde 1,3-dioxolane (4j)

IR (Neat): 3416, 2955, 2888, 1649, 1465, 1408, 1280, 1203, 1091, 1045, 891 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.05 (m, 4H, 2 × -OC*H*$_2$-), 5.91 (s, 1H, Ar-C*H*(-O(CH_2)$_2$O-), 6.75-7.40 (m, 4H, Ar*H*)



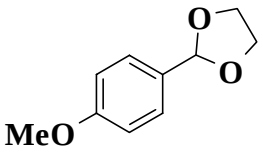
HO

4-Hydroxybenzaldehyde 1,3-dioxolane (6j)

IR (Neat): 3211, 1680, 1608, 1526, 1465, 1393, 1321, 1291, 1244, 1224, 1168, 1091, 1050, 866, 835, 799, 712 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.11 (m, 4H, 2 × -OC*H*$_2$-), 5.24 (s, 1H, Ar-C*H*(-O(CH_2)$_2$O-)),

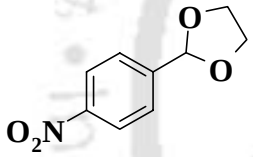
6.73 (d, 2H, Ar*H*), 7.36 (d, 2H, Ar*H*)



4-Methoxybenzaldehyde 1,3-dioxolane (7j)

IR (Neat): 2959, 2888, 2839, 1626, 1520, 1475, 1439, 1399, 1308, 1253, 1182, 1086, 1041, 975, 950, 844 cm^{-1}

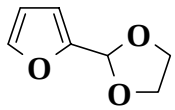
^1H NMR (400 MHz, $CDCl_3$): δ 3.74 (m, 4H, 2 × -OC*H*$_2$-), 3.81 (s, 3H, Ar-OC*H*$_3$), 5.76 (s, 1H, Ar-C*H*(-OCH_2CH_2O-)), 6.91 (d, 2H, Ar*H*), 7.40 (d, 2H, Ar*H*)



4-Nitrobenzaldehyde 1,3-dioxolane (11j)

IR (KBr): 2968, 2898, 1610, 1526, 1433, 1358, 1316, 1293, 1265, 12223, 1084, 1023, 981, 944, 851, 758 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 4.10 (m, 4H, 2 × -OC*H*$_2$-), 5.90 (s, 1H, Ar-C*H*(-$O(CH_2)_2O$-), 7.66 (d, 2H, Ar*H*), 8.24 (d, 2H, Ar*H*)

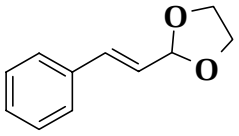


2-Furfural 1,3-dioxolane (13j)

IR (Neat): 3125, 2960, 2894, 1604, 1505, 1357, 1227, 1157, 1075, 937, 890, 750 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 4.06 (m, 4H, 2 × -OC*H*$_2$-), 5.54 (s, 1H, Ar-C*H*(-$O(CH_2)_2O$-), 6.39 (m, 2H, Ar*H*), 7.41 (m, 1H, Ar*H*)

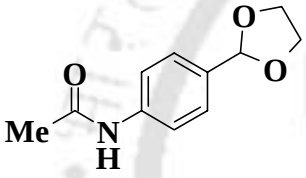
^{13}C NMR (100 MHz, $CDCl_3$): δ 65.0, 97.6, 108.6, 110.0, 143.0



***trans*-Cinnamaldehyde 1,3-dioxolane (14j)**

IR (Neat): 2959, 2888, 1682, 1494, 1453, 1398, 1149, 1068, 967, 830, 749, 693 cm^{-1}

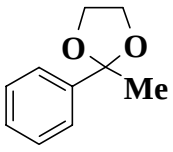
^1H NMR (400 MHz, $CDCl_3$): δ 3.72 (brm, 4H, 2 × -OC<u>*H*</u>$_2$-), 6.47 (d, 1H, Ar-CH=CH-C<u>*H*</u>-), 7.41 (m, 5H, Ar<u>*H*</u>), 7.50-7.60 (q, 1H, Ar-CH=C<u>*H*</u>-), 7.76-7.81 (d, 1H, Ar-C<u>*H*</u>=CHC<u>*H*</u>-)



4-N-Acetamidobenzaldehyde 1,3-dioxolane (19j)

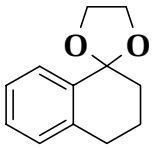
IR (KBr): 3308, 3267, 1680, 1603, 1541, 1429, 1378, 1321, 1270, 1219, 1168, 1086, 1024, 840 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 2.22 (s, 3H, -NHCOC<u>*H*</u>$_3$), 4.05 (m, 2H, -OC<u>*H*</u>(H)C<u>*H*</u>(H)O-), 4.13 (m, 2H, -OCH(<u>*H*</u>)CH(<u>*H*</u>)O-), 5.77 (s, 1H, Ar-C<u>*H*</u>(-OCH$_2$CH$_2$O-)), 7.52 (d, 2H, Ar<u>*H*</u>), 7.85 (d, 2H, Ar<u>*H*</u>)



Acetophenone 1,3-dioxolane (22j)

^1H NMR (400 MHz, $CDCl_3$): δ 2.14 (s, 1H, -C<u>*H*</u>$_3$), 3.40 (m, 4H, 2 × -OC<u>*H*</u>$_2$-), 7.21 (m, 1H, Ar<u>*H*</u>), 7.30 (m, 2H, Ar<u>*H*</u>), 7.75 (m, 2H, Ar<u>*H*</u>)

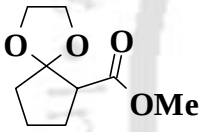


α-Tetralone 1,3-dioxolane (24j)

IR (Neat): 2944, 2888, 1689, 1607, 1459, 1336, 1295, 1234, 1193, 1141, 1121, 1070, 1039, 942, 911, 767, 742 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 2.14 (m, 2H, Ar-CH_2-C$\underline{H}_2$-CH_2-), 2.65 (t, 2H, Ar-C$\underline{H}_2$-CH_2-CH_2-), 2.96 (t, 2H, Ar-C(-OCH_2CH_2O-)-C$\underline{H}_2$-), 3.73 (m, 4H, 2 × -OC$\underline{H}_2$-), 7.27 (m, 2H, Ar$\underline{H}$), 7.48 (m, 1H, Ar$\underline{H}$), 8.02 (m, 1H, Ar$\underline{H}$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.25, 29.67, 39.13, 63.69, 65.09, 126.60, 127.10, 128.70, 132.60, 133.40, 144.50

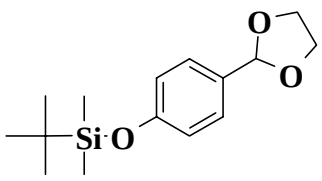


Cyclopentanone-2-methyl-carboxylate 1,3-dioxolane (26j)

IR (Neat): 2960, 1741, 1690, 1654, 1562, 1511, 1342, 1265, 1209, 1163, 1045, 912 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.82-1.95 (m, 4H, -C(OCH_2CH_2O)$_2$-CH_2-C$\underline{H}_2$-C$\underline{H}_2$-), 2.12 (m, 1H, -C$\underline{H}$(H)C(-OCH_2CH_2O-)), 2.31 (m, 1H, -CH($\underline{H}$)C(-OCH_2CH_2O-), 3.17 (m, 1H, -C$\underline{H}$($COOCH_3$)C(-OCH_2CH_2O-), 3.75 (s, 3H, -COOC$\underline{H}_3$), 3.86-4.03 (m, 4H, -O-C$\underline{H}_2$-CH_2-O-)

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.99, 26.91, 36.70, 51.65, 52.19, 64.5, 65.1, 118.3, 172.8



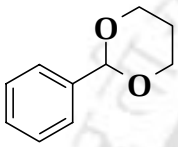
4-*tert*-Butyldimethylsilanyloxy-benzaldehyde 1,3-dioxolane (28j)

^1H NMR (400 MHz, $CDCl_3$): δ 0.16 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.92 (s, 9H, -Si(CH_3)$_2$-C(C$\underline{H}_3$)$_3$), 3.84 (m, 4H, 2 × -OC$\underline{H}_2$-), 5.36 (s, 1H, Ar-C$\underline{H}$(-OCH_2CH_2O-)), 6.82 (d, 2H,

Ar*H*), 7.31 (d, 2H, Ar*H*)

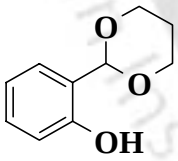
^{13}C NMR (100 MHz, $CDCl_3$): δ -3.97, 18.63, 25.93, 55.03, 101.40, 120.86, 130.79, 132.29, 161.89

IIC.3.12 1,3-Dioxanes



Benzaldehyde 1,3-dioxane (1k)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (m, 1H, -O-CH_2-C*H*(H)-CH_2-O-), 2.14 (m, 1H, -O-CH_2-CH(*H*)-CH_2-O-), 3.83 (m, 2H, 2 × -O-C*H*(H)-), 4.14 (m, 2H, 2 × -O-CH(*H*)-), 5.32 (s, 1H, Ar-C*H*(-$OCH_2CH_2CH_2O$-)), 7.34 (m, 3H, Ar*H*), 7.45 (m, 2H, Ar*H*)

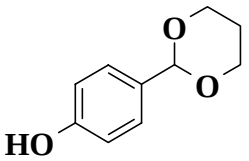


2-Hydroxybenzaldehyde 1,3-dioxane (4k)

IR (Neat): 3380, 2965, 2868, 1669, 1623, 1593, 1495, 1460, 1388, 1285, 1239, 1157, 1091, 988, 953, 922, 758 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.51 (m, 1H, -O-CH_2-C*H*(H)-CH_2-O-), 2.27 (m, 1H, -OCH_2-CH(*H*)-CH_2O-), 2.29 (brs, 1H, -O*H*), 3.91 (m, 2H, -O-C*H*$_2$-CH_2-CH_2-O-), 4.04 (m, 1H, -OCH_2-CH_2-C*H*(H)-O-), 4.31 (m, 1H, -O-CH_2-CH_2-CH(*H*)-O-), 5.66 (s, 1H, Ar-C*H*(-O-CH_2-CH_2-CH_2-O-)), 7.01 (m, 2H, Ar*H*), 7.23 (m, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.6, 64.4, 110.0, 117.1, 120.0, 126.2, 126.5, 129.9, 154.4

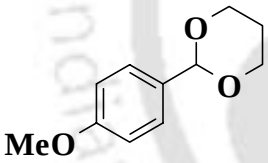


4-Hydroxybenzaldehyde 1,3-dioxane (6k)

IR (Neat): 3334, 3272, 2980, 2955, 2929, 2878, 1623, 1598, 1526, 1454, 1403, 1383, 1352, 1280, 1244, 1229, 1168, 1147, 1096, 10047, 973, 953, 922, 896, 830, 816, 737 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.44 (m, 1H, -O-CH_2-C*H*(H)-CH_2-O-), 1.85 (m, 1H, -O-CH_2-CH(*H*)-CH_2-O-), 3.87 (m, 2H, -O-C*H*(H)-CH_2-C*H*(H)-O-), 4.25 (m, 2H, -OH(*H*)-CH_2-CH(*H*)-), 5.46 (s, 1H, Ar-C*H*(-$OCH_2CH_2CH_2O$-)), 6.76 (d, 2H, Ar*H*), 7.34 (d, 2H, Ar*H*)

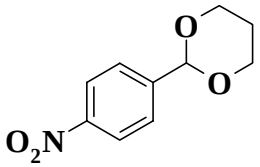
^{13}C NMR (100 MHz, $CDCl_3$): δ 33.6, 61.9, 116.0, 129.1, 132.6, 162.7, 191.6



4-Methoxybenzaldehyde 1,3-dioxane (7k)

IR (Neat): 2965, 2842, 1690, 1603, 1521, 1465, 1429, 1393, 1321. 1250, 1163, 1106, 1035, 988, 835 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.81 (m, 1H, -O-CH_2-C*H*(H)-CH_2-O-), 2.21 (m, 1H, -OCH_2-CH(*H*)-CH_2-O-), 3.59 (s, 3H, Ar-OCH_3), 3.80 (m, 4H, 2 × -OCH_2-), 5.20 (s, 1H, Ar-C*H*(-$OCH_2CH_2CH_2O$-)), 6.84 (d, 2H, Ar*H*), 7.41 (d, 2H, Ar*H*)

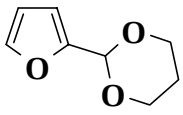


4-Nitrobenzaldehyde 1,3-dioxane (11k)

IR (KBr): 2994, 2959, 2929, 2858, 1616, 1525, 1475, 1444, 1394, 1364, 1288, 1248, 1217, 1157, 1106, 1030, 965, 869, 753, 722 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52 (m, 1H, -OCH_2-C*H*(H)-CH_2-O-), 2.25 (m, 1H, -OCH_2-CH(*H*)-CH_2-O-), 4.02 (m, 2H, 2 × -OC*H*(H)-), 4.30 (m, 2H, 2 × -OCH(*H*)-), 5.74 (s, 1H, Ar-C*H*(-$OCH_2CH_2CH_2$O-), 7.66 (d, 2H, Ar*H*), 8.21 (d, 2H, Ar*H*)

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 67.4, 99.9, 127.1

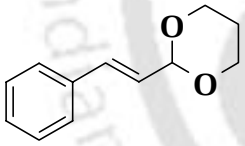


2-Furfural 1,3-dioxane (13k)

IR (Neat): 2970, 2863, 1516, 1475, 1383, 1280, 1239, 1157, 1111, 932, 860, 748 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (m, 1H, -O-CH_2-C*H*(H)-CH_2-O-), 2.21(m, 1H, -O-CH_2-CH(*H*)-CH_2-O-), 3.94 (m, 2H, 2 × -OC*H*(H)-), 4.24 (m, 2H, 2 × -OCH(*H*)-), 5.57 (s, 1H, Ar-C*H*(-$OCH_2CH_2CH_2$O-), 6.35 (dd, 1H, Ar*H*), 6.43 (d, 1H, Ar*H*), 7.39 (m, 1H, Ar*H*)

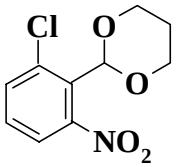
^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5, 67.2, 96.0, 107.2, 110.1, 142.4



***trans*-Cinnamaldehyde 1,3-dioxane (14k)**

IR (Neat): 2965, 2847, 1685, 1500, 1454, 1378, 1280, 1239, 1142, 1091, 968, 830 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (m, 1H, -O-CH_2-C*H*(H)-CH_2-O-), 2.18 (m, 1H, -O-CH_2-CH(*H*)-CH_2-O-), 3.79 (m, 2H, 2 × -OC*H*(H)-), 4.28 (m, 2H, 2 × -OCH(*H*)-), 5.15 (d, 1H, Ar-CH=CH-C*H*-), 6.21 (t, 1H, Ar-CH=C*H*-CH-), 6.78 (d, 1H, Ar-C*H*=CH-CH-), 7.25-7.57 (m, 5H, Ar*H*)

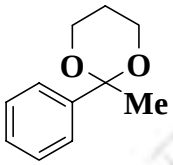


2-Chloro-6-nitrobenzaldehyde 1,3-dioxane (21k)

IR (Neat): 2986, 2929, 2883, 1618, 1577, 1526, 1465, 1347, 1250, 1198, 1116, 1060, 922, 830, 743 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (m, 2H, -O-CH_2-C<u>*H*</u>$_2$-CH_2-O-), 3.66 (m, 4H, 2 × -OC<u>*H*</u>$_2$-), 5.74 (s, 1H, Ar-C<u>*H*</u>(-$OCH_2CH_2CH_2$O-)), 7.53 (d, 1H, Ar<u>*H*</u>), 8.13 (dd, 1H, Ar<u>*H*</u>), 8.54 (d, 1H, Ar<u>*H*</u>)

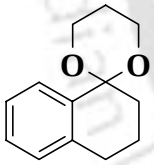
^{13}C NMR (100 MHz, $CDCl_3$): δ 15.1, 62.6, 98.2, 123.6, 124.3, 130.6



Acetophenone 1,3-dioxane (22k)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (m, 1H, -O-CH_2-C<u>*H*</u>(H)-CH_2-O-), 1.51 (s, 3H, -C<u>*H*</u>$_3$), 2.12 (m, 1H, -O-CH_2-CH(<u>*H*</u>)-CH_2-O-), 3.83 (m, 4H, 2 × -OC<u>*H*</u>$_2$-), 7.30-7.95 (m, 5H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.4, 32.3, 61.2, 100.5, 126.8, 127.5, 128.6, 141.2

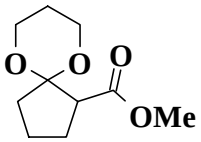


α-Tetralone 1,3-dioxane (24k)

IR (Neat): 2949, 1694, 1612, 1464, 1336, 1295, 1228, 1126, 1095, 1029, 773, 742 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17 (m, 1H, -O-CH_2-C<u>*H*</u>(H)-CH_2-O-), 1.31 (m, 1H, -O-CH_2-CH(<u>*H*</u>)-CH_2-O-), 2.06 (m, 2H, Ar-CH_2-C<u>*H*</u>$_2$-CH_2-), 2.61 (t, 2H, Ar-C<u>*H*</u>$_2$-CH_2-), 2.89 (t, 2H, Ar-CH_2-CH_2-C<u>*H*</u>$_2$-), 3.63 (m, 2H, 2 × -OC<u>*H*</u>(H)-), 4.27 (m, 2H, 2 × -OCH(<u>*H*</u>)-), 7.22 (m, 2H, Ar<u>*H*</u>), 7.40 (m, 1H, Ar<u>*H*</u>), 7.97 (m, 1H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 18.81, 23.68, 30.10, 39.56, 58.82, 127.03, 127.17, 131.33, 133.80, 144.80

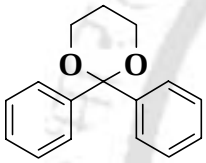


Cyclopentanone-2-methyl-carboxylate 1,3-dioxane (26k)

IR (Neat): 2955, 2873, 1731, 1439, 1357, 1255, 1209, 1157, 1106, 1060, 1040, 983, 932, 860 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.25-2.48 (brm, 8H), 3.02 (m, 1H), 3.68-4.00 (brm, 7H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.61, 25.35, 26.29, 32.26, 51.67, 52.88, 61.68, 109.70, 172.90

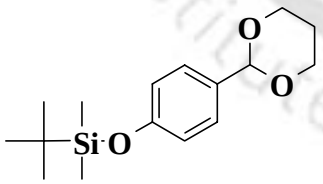


Benzophenone 1,3-dioxane (27k)

IR (Neat): 3071, 2965, 2929, 2873, 1661, 1601, 1494, 1453, 1322, 1281, 1251, 1205, 1104, 1017, 972, 931, 860, 779, 759, 718, 647, 566 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 1.80 (m, 2H, -O-CH_2-C<u>*H*</u>$_2$-CH_2-O-), 4.03 (m, 4H, 2 × -OC<u>*H*</u>$_2$-), 7.23 (m, 2H, Ar<u>*H*</u>), 7.32 (m, 4H, ArH). 7.54 (m, 4H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 61.6, 126.4, 127.7, 128.4, 130.0, 142.4



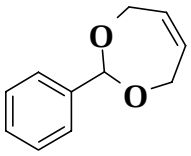
4-*tert*-Butyldimethylsilanyloxy-benzaldehyde 1,3-dioxane (28k)

IR (Neat): 2962, 2936, 2860, 1620, 1519, 1478, 1377, 1266, 1154, 1114, 1018, 992 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 0.16 (s, 6H, -Si(C<u>*H*</u>$_3$)$_2$-), 0.97 (s, 9H, -Si(CH_3)$_2$-C(C<u>*H*</u>$_3$)$_3$), 1.42 (m, 1H, -O-CH_2-C<u>*H*</u>(H)-CH_2-O-), 2.21 (m, 1H, -O-CH_2-CH(<u>*H*</u>)-CH_2-O-), 3.97 (m, 2H, 2 × -OC<u>*H*</u>(H)-), 4.25 (m, 2H, 2 × -OCH(<u>*H*</u>)-), 5.45 (s, 1H, Ar-C<u>*H*</u>(-$OCH_2CH_2CH_2$O-)), 6.82 (d, 2H, Ar<u>*H*</u>), 7.34 (d, 2H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ -4.5, 18.2, 25.7, 67.4, 101.6, 119.9, 127.2, 131.9, 156.1

IIC.3.13 1,3-Dioxepin



2-Phenyl-4,7-dihydro-[1,3]dioxepin (1l)

IR (Neat): 3038, 2941, 2858, 1495, 1467, 1357, 1260, 1120, 1077, 1018, 1008, 927, 786, 743, 703 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 4.31 (dd, 4H, 2 × -O-C<u>*H*</u>$_2$-), 5.74 (m, 2H, 2 × -O-CH_2-C<u>*H*</u>-), 5.83 (s, 1H, Ar-C<u>*H*</u>(-O-CH_2-CH=CH-CH_2-O-), 7.35 (m, 3H, Ar<u>*H*</u>), 7.52 (m, 2H, Ar<u>*H*</u>)

^{13}C NMR (100 MHz, $CDCl_3$): δ 64.51, 102.08, 126.35, 128.30, 129.85, 138.82

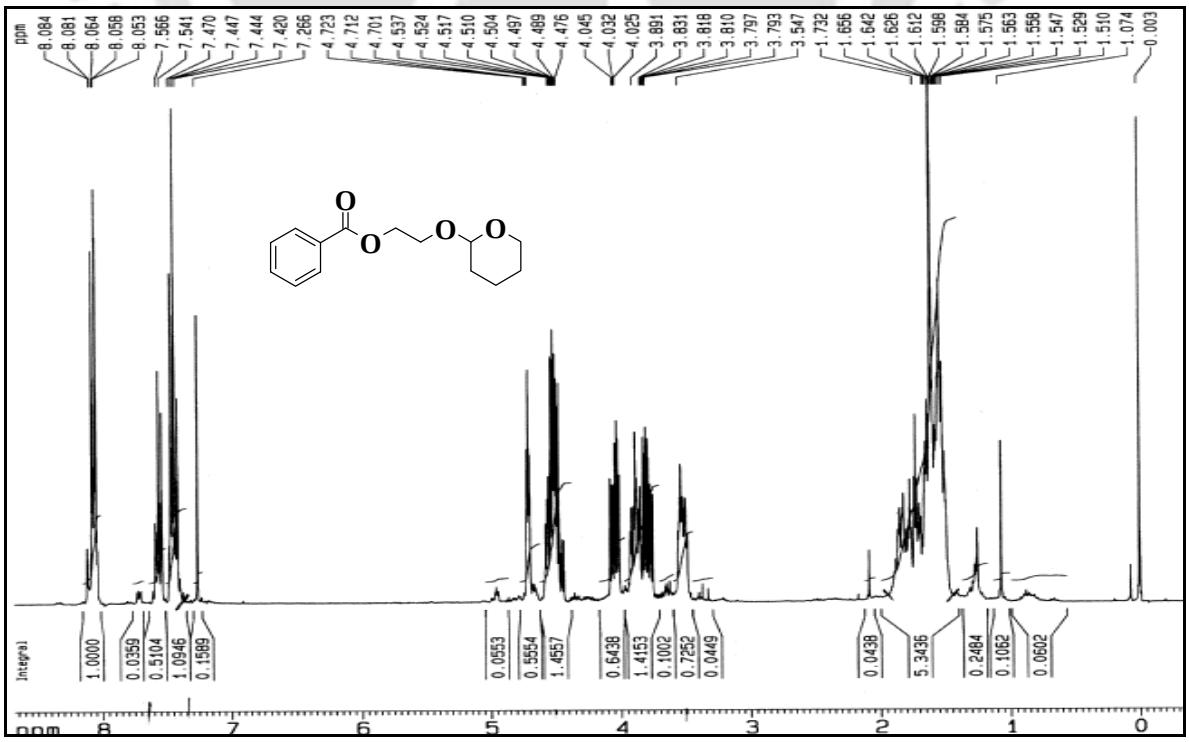
IIC.4 References

1. Furniss, B. S.; Hannaford, A. J.; Rogers, V.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Text Book of Practical Organic Chemistry*, 4th ed., ELBS publication: London, 1984.
2. Bouzide, A.; Sauve, G. *Tetrahedron Lett.* **1997**, *38*, 5945.
3. Schlessinger, R. H.; Lopes, A. *J. Org. Chem.* **1981**, *46*, 5252.
4. Zhdanov, R.I.; Zhenodarova, S.M. *Synthesis* **1975**, 222.
5. Nishiyama, S.; Ikeda, Y.; Yoshida, S.; Yamamura, S. *Tetrahedron Lett.* **1989**, *30*, 105.
6. Hansen, Jr., D. W.; Pilipauskas, D. *J. Org. Chem.* **1985**, *5*0, 945.
7. McDougal, P. G.; Rico, J. G.; Oh, Y.; Condon, B. D. *J. Org. Chem.* **1986**, *51*, 3388.
8. Kumar, H. M. S.; Reddy, B. V. S.; Reddy, E. J.; Yadav, J. S. *Chem. Lett*. **1999**, 857.

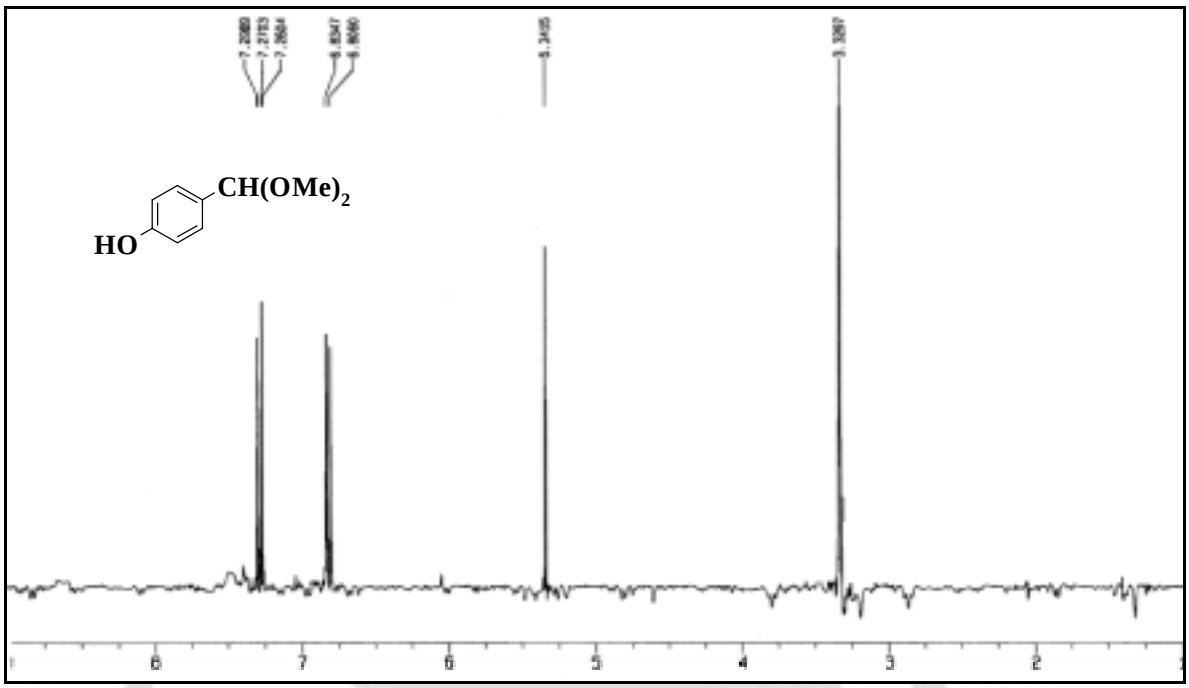
9. Hakimelahi, G. H.; Proba, Z. A.; Ogilvie, K. K. *Can. J. Chem.* **1982**, *60*, 1106.
10. Pilcher, A. S.; DeShong, P. *J. Org. Chem.* **1993**, *58*, 5130.
11. Lu, T.; Yang, J.; Sheu, L. *J. Org. Chem.* **1995**, *60*, 2931.
12. Hyperchem, Inc.; Gainsville, FL.

IID Spectra

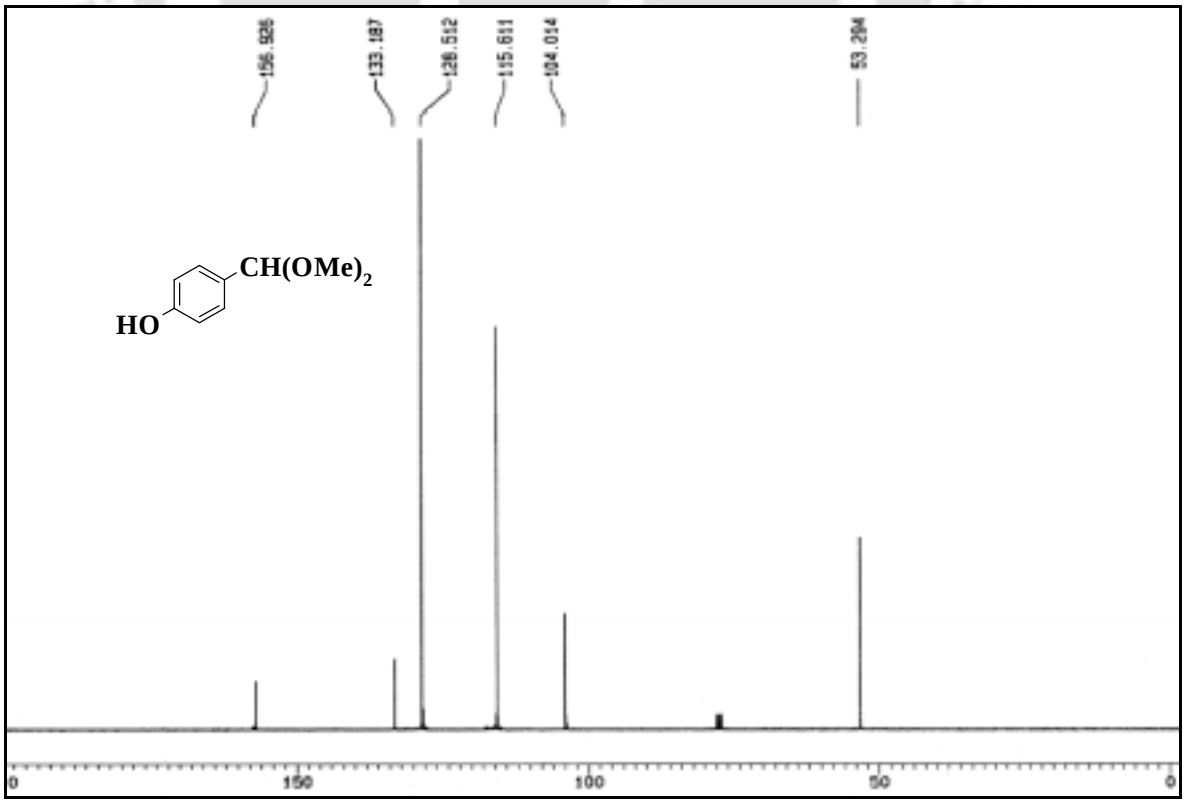
^{1}H NMR (400 MHz, $CDCl_3$): Benzoic acid 2-(tetrahydro-pyran-2-yloxy)-ethyl ester (1cn)



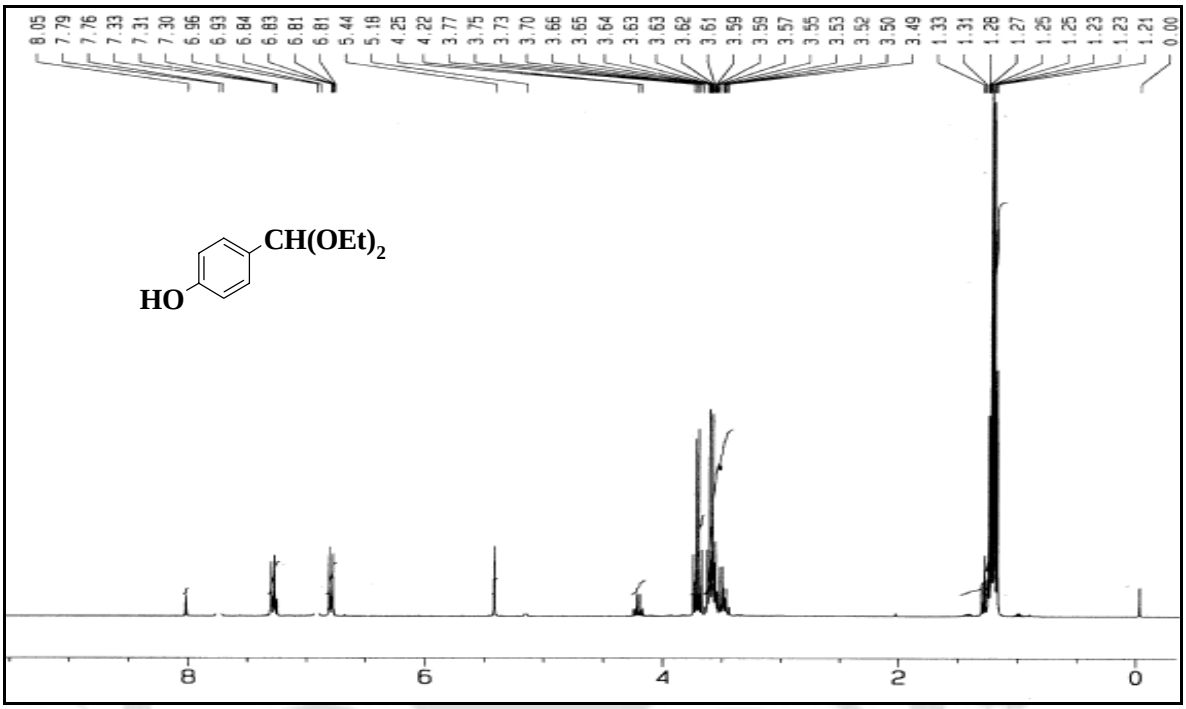
^{1}H NMR (400 MHz, $CDCl_3$): 4-Hydroxybenzaldehyde dimethyl acetal (6h)



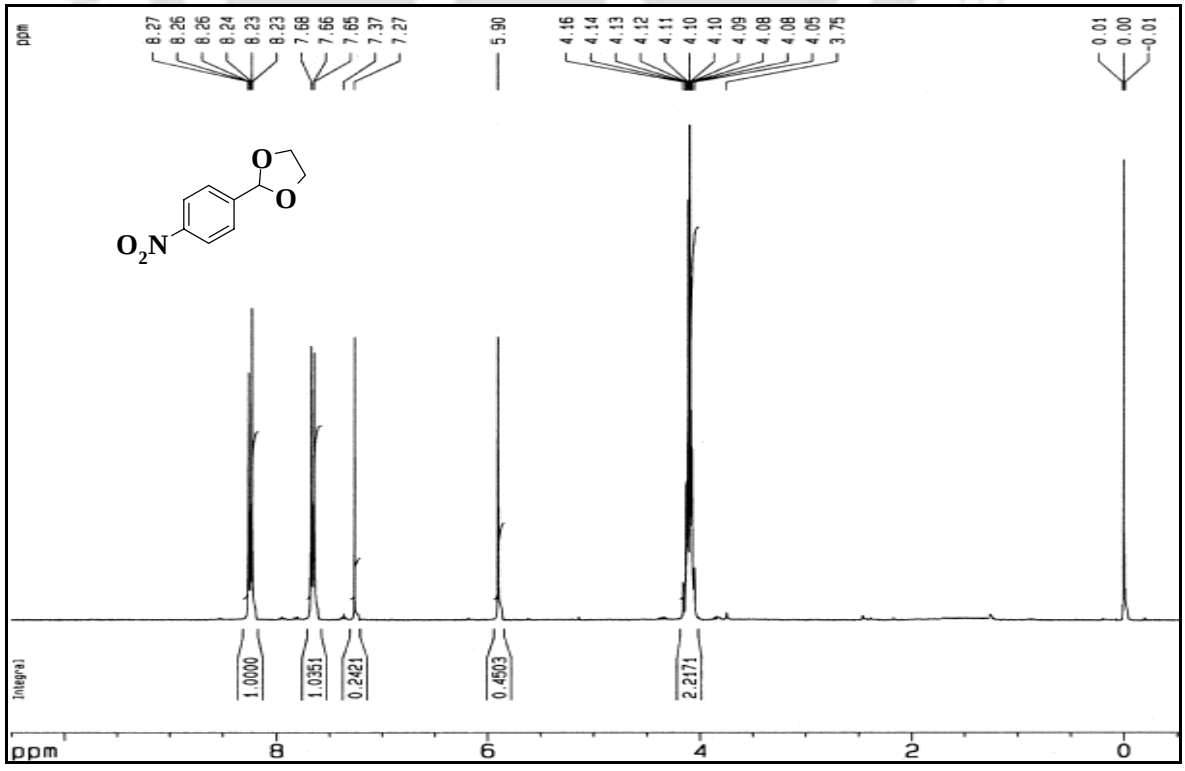
^{13}C NMR (100 MHz, $CDCl_3$): 4-Hydroxybenzaldehyde dimethyl acetal (6h)



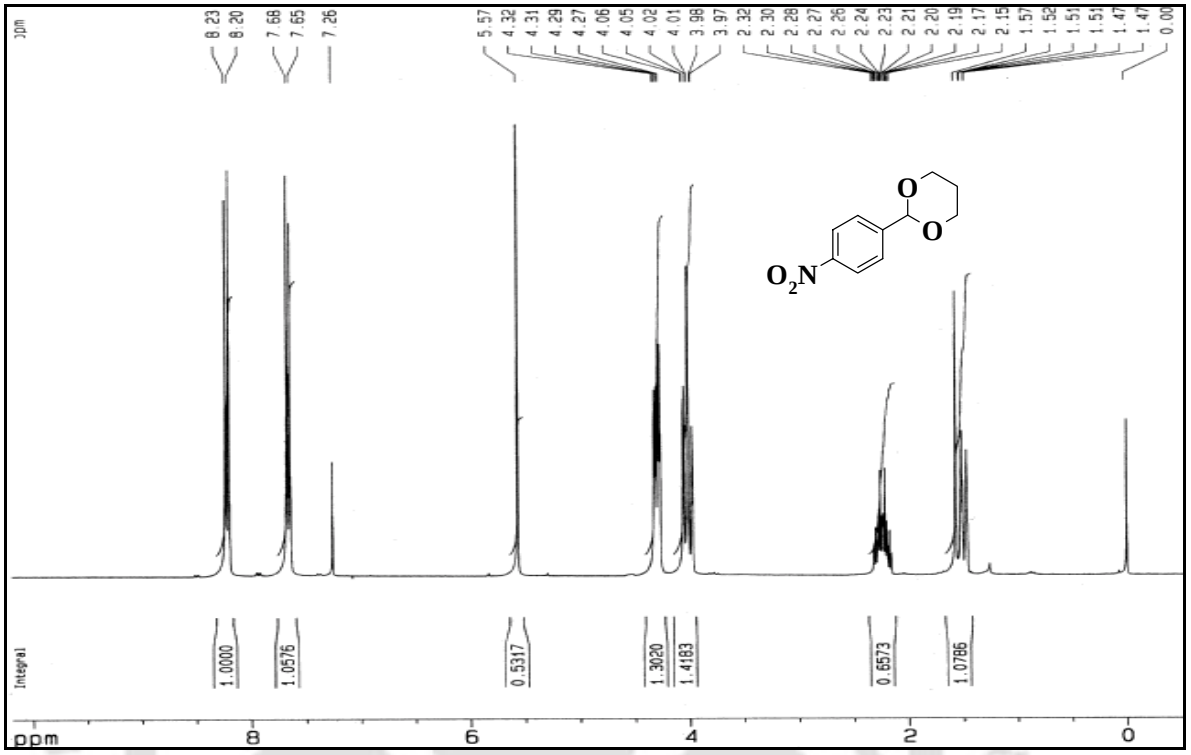
^{1}H NMR (400 MHz, $CDCl_3$): 4-Hydroxybenzaldehyde diethyl acetal (6i)



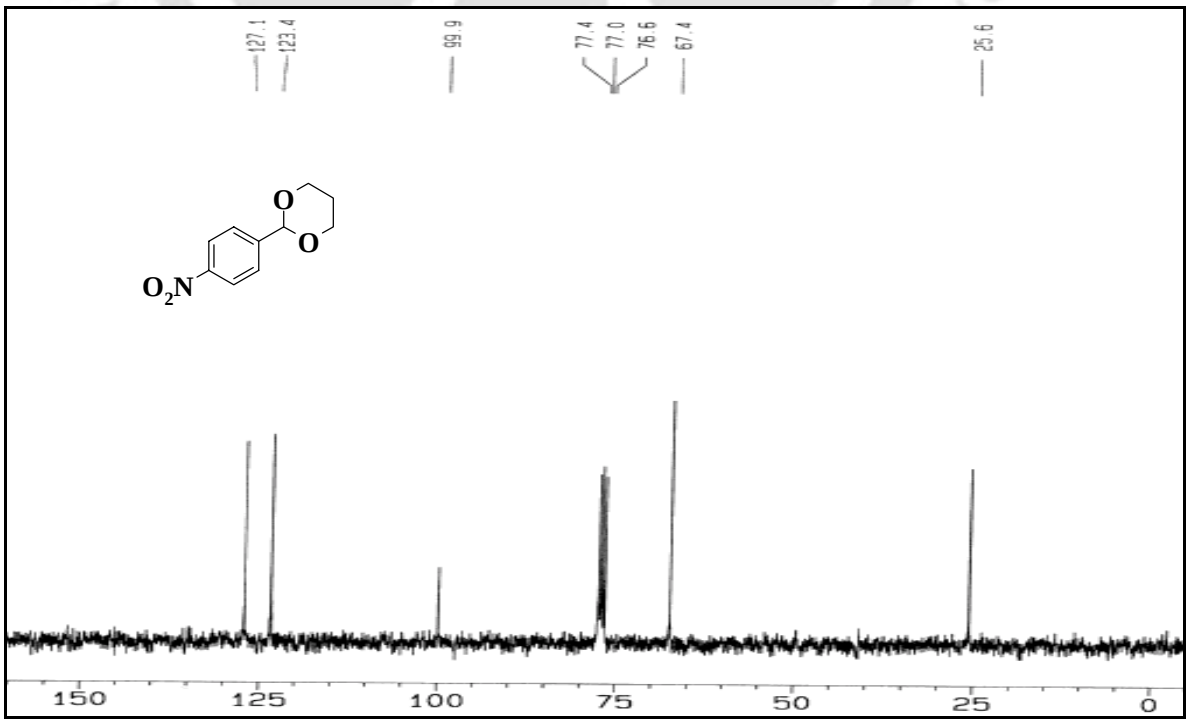
^{1}H NMR (400 MHz, $CDCl_3$): 4-Nitrobenzaldehyde 1,3-dioxolane (11j)



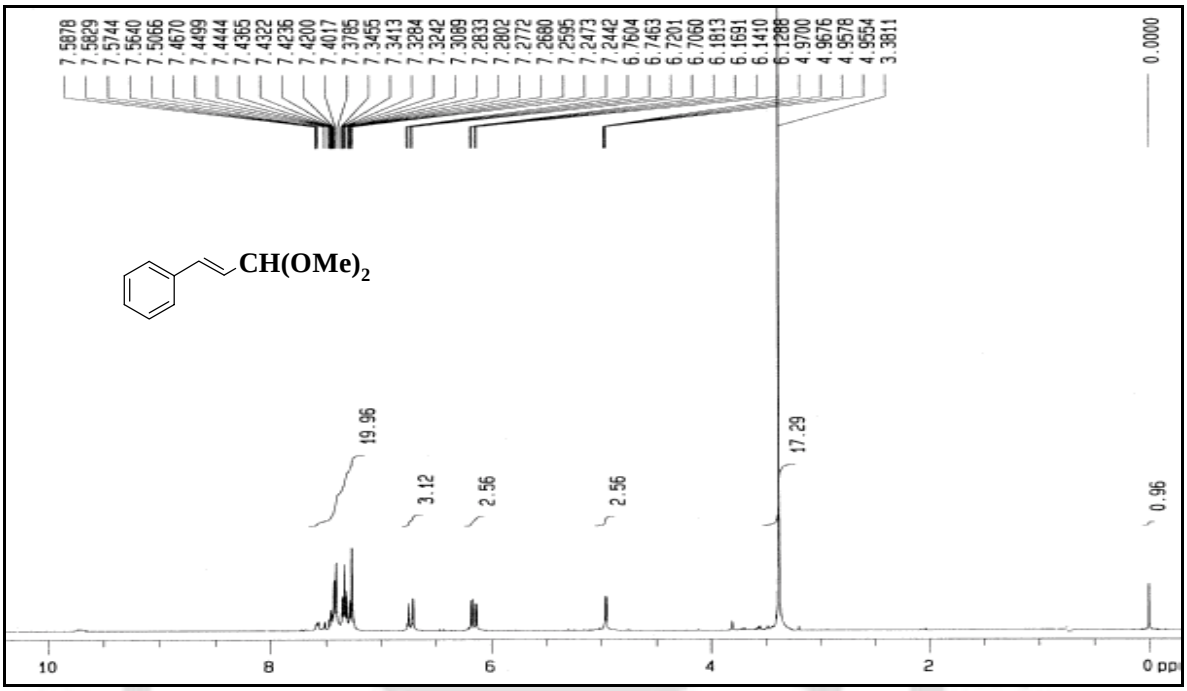
^{1}H NMR (400 MHz, $CDCl_3$): 4-Nitrobenzaldehyde 1,3-dioxane (11k)



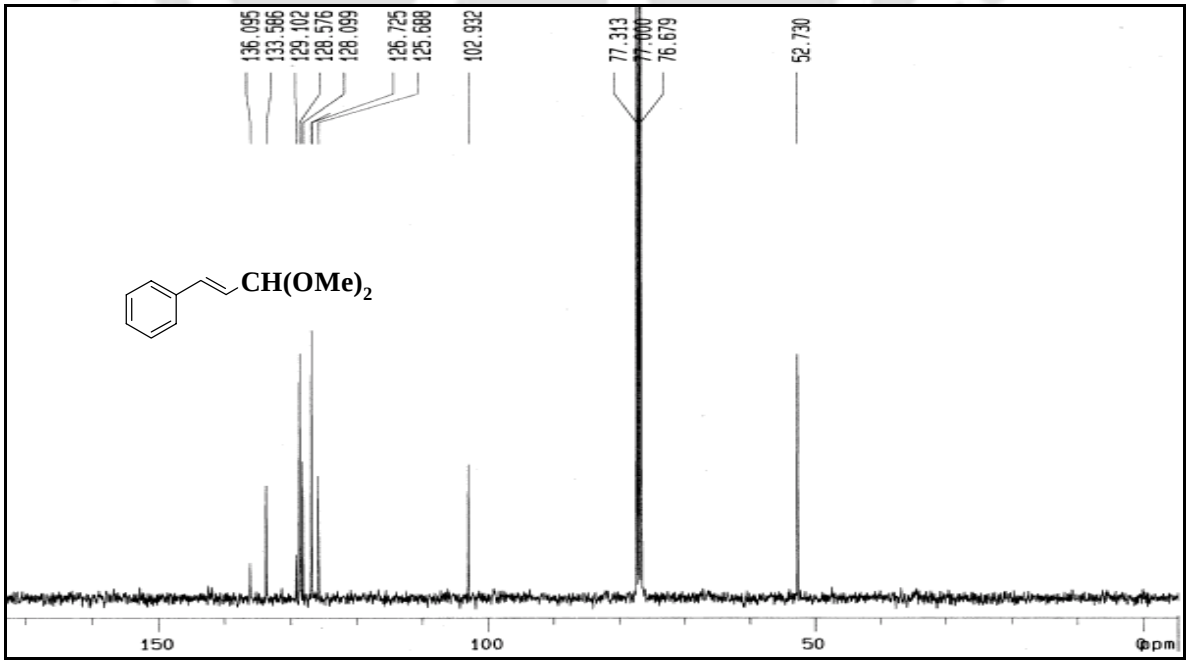
^{13}C NMR (100 MHz, $CDCl_3$): 4-Nitrobenzaldehyde 1,3-dioxane (11k)



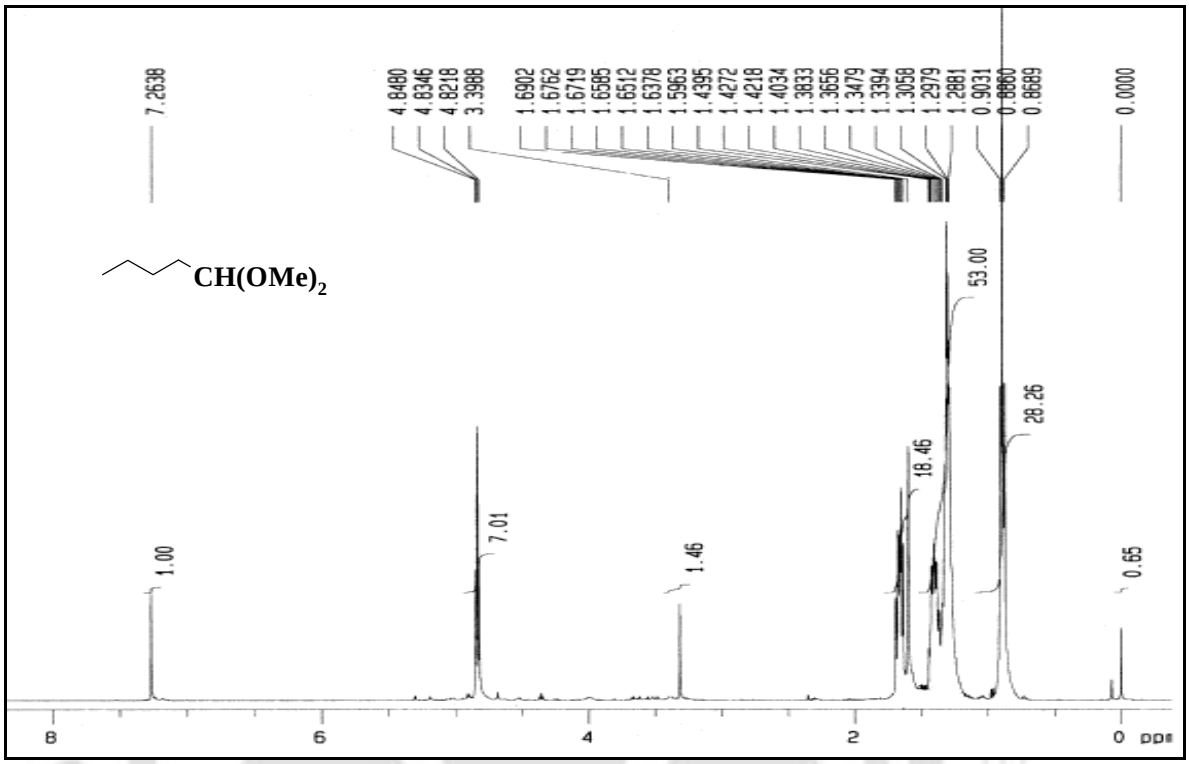
^{1}H NMR (400 MHz, $CDCl_3$): *trans*-Cinnamaldehyde dimethyl acetal (14h)



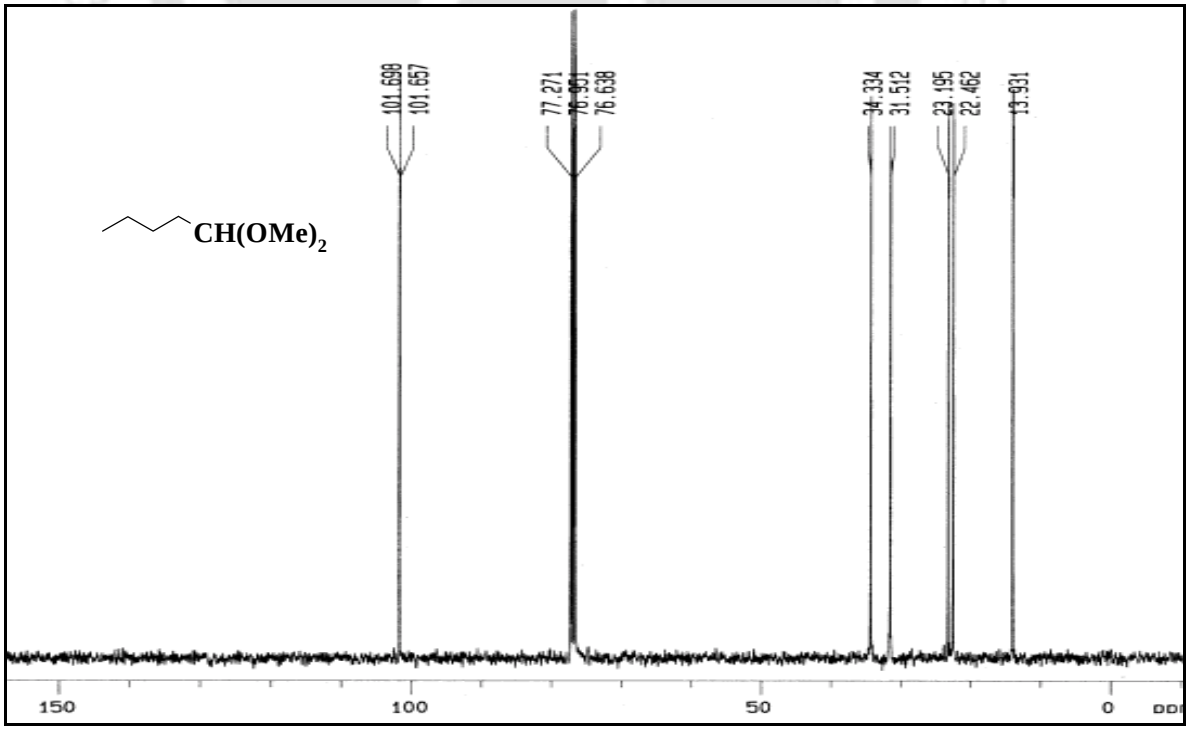
^{13}C NMR (100 MHz, $CDCl_3$): *trans*-Cinnamaldehyde-dimethyl acetal (14h)



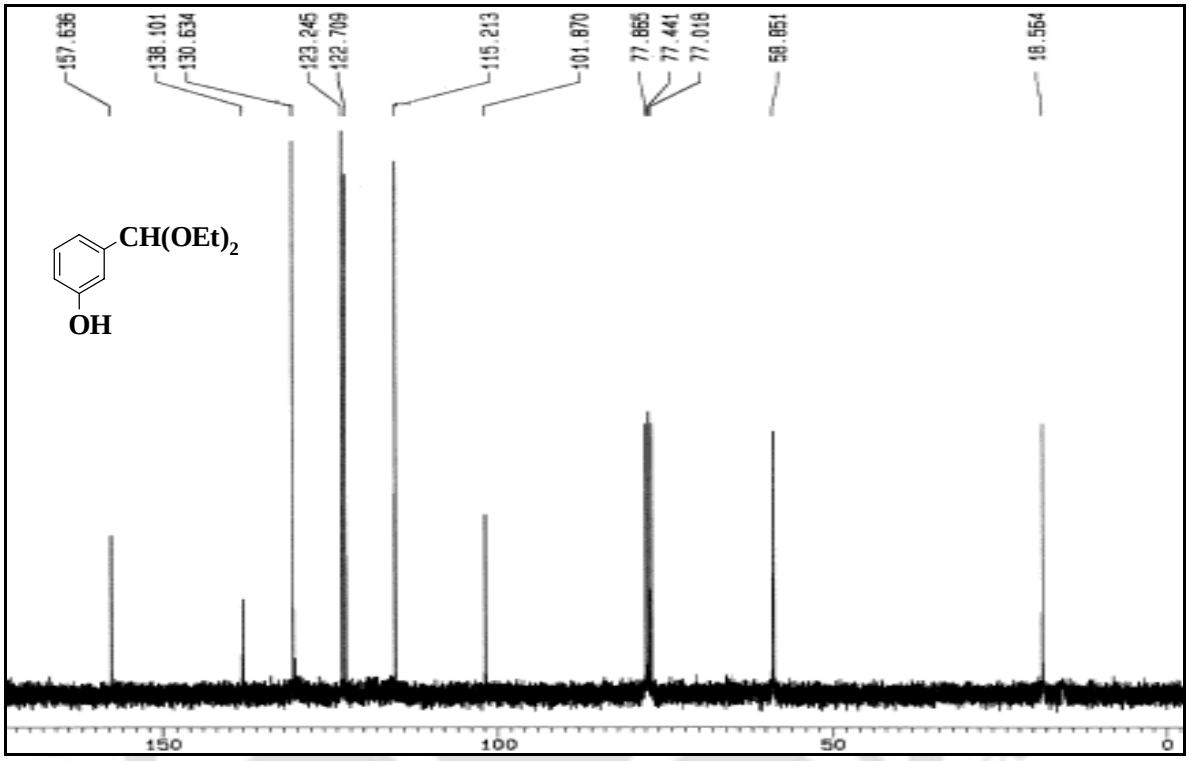
^{1}H NMR (400 MHz, $CDCl_3$): Pentanal dimethyl acetal (15h)



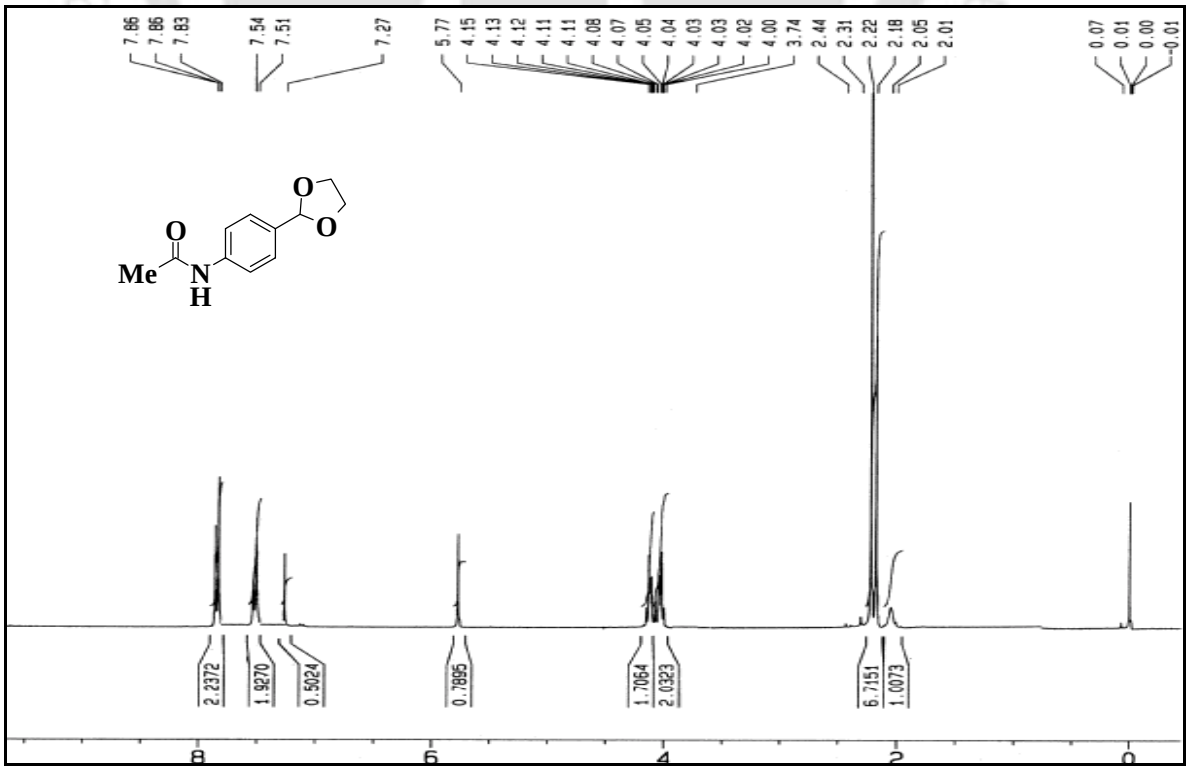
^{13}C NMR (100 MHz, $CDCl_3$): Pentanal dimethyl acetal (15h)



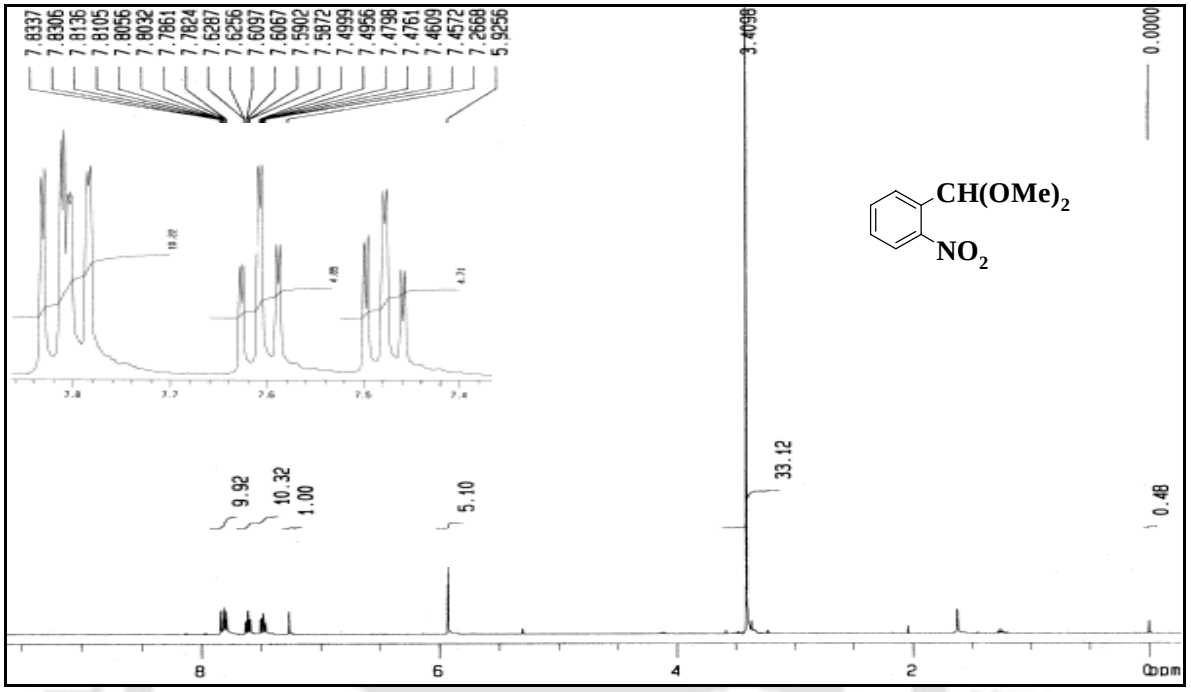
^{13}C NMR (100 MHz, $CDCl_3$): 3-Hydroxybenzaldehyde diethyl acetal (17i)



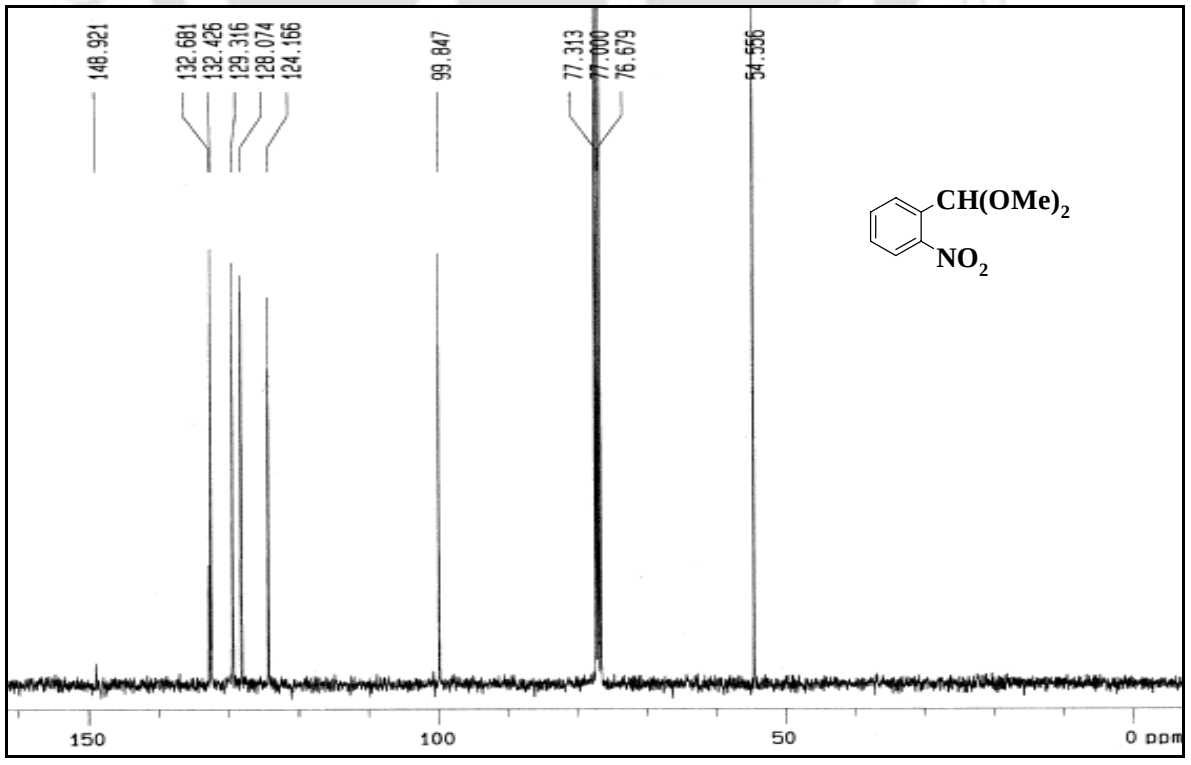
^{1}H NMR (400 MHz, $CDCl_3$): 4-N-Acetamidobenzaldehyde 1,3-dioxolane (19j)



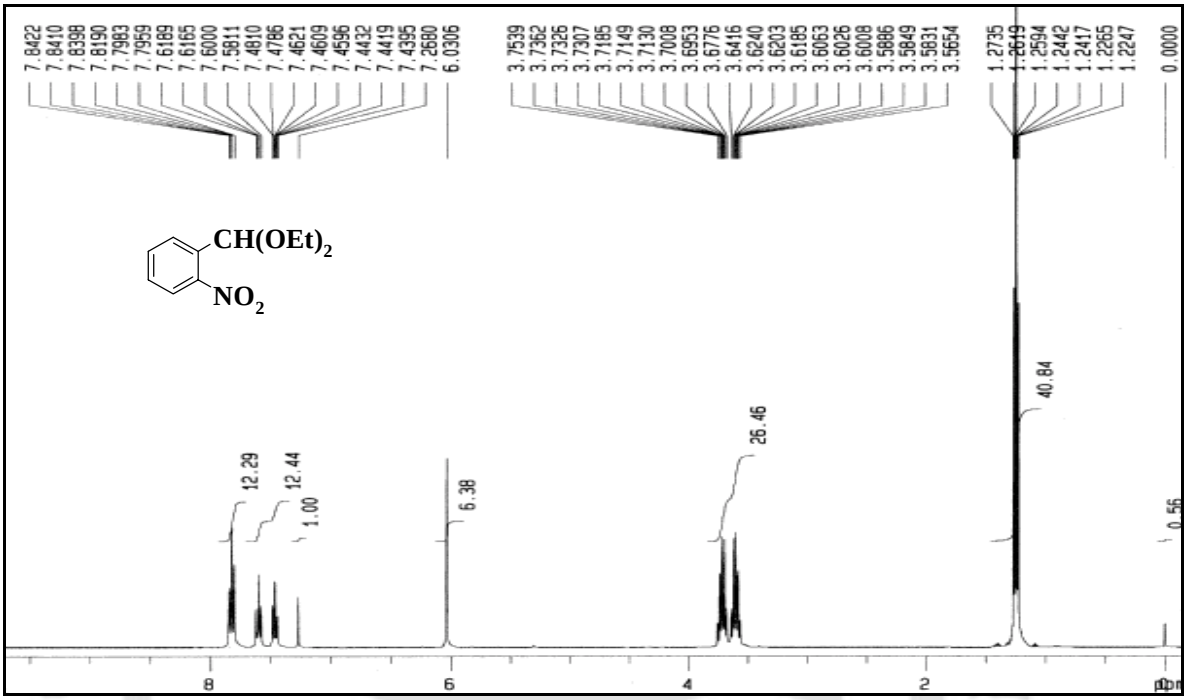
^{1}H NMR (400 MHz, $CDCl_3$): 2-Nitrobenzaldehyde dimethyl acetal (20h)



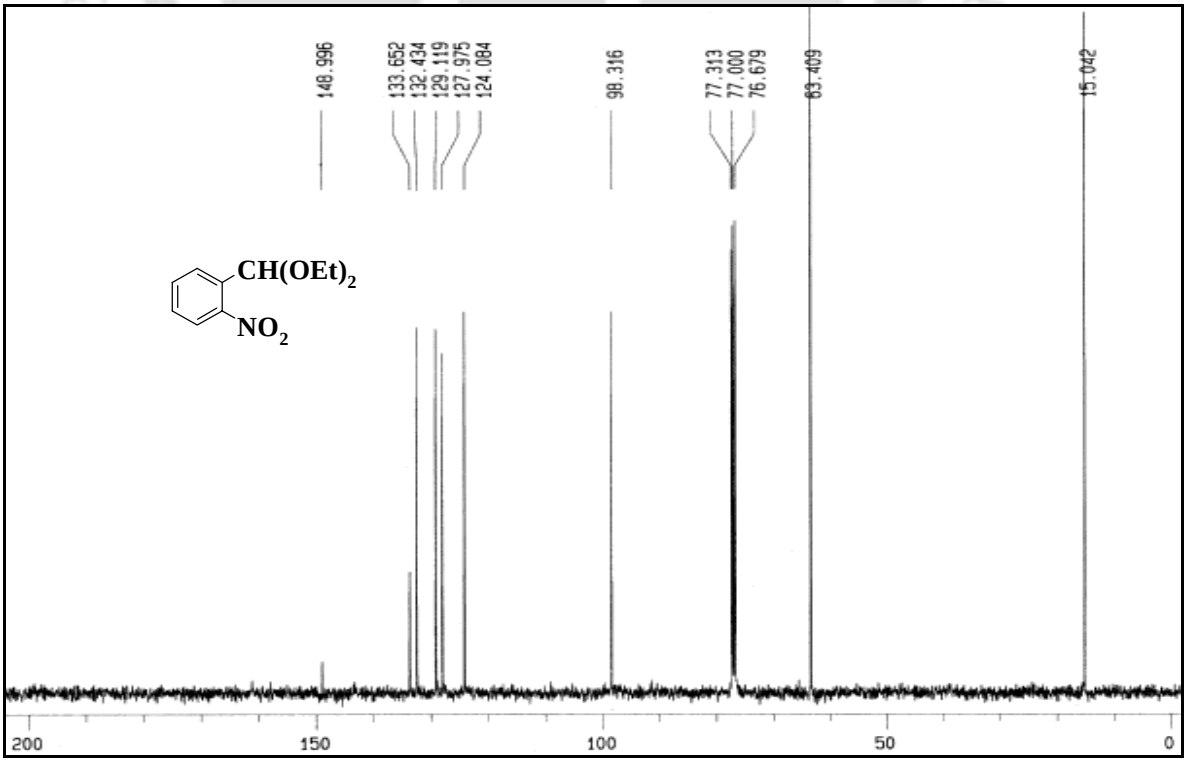
^{13}C NMR (100 MHz, $CDCl_3$): 2-Nitrobenzaldehyde dimethyl acetal (20h)



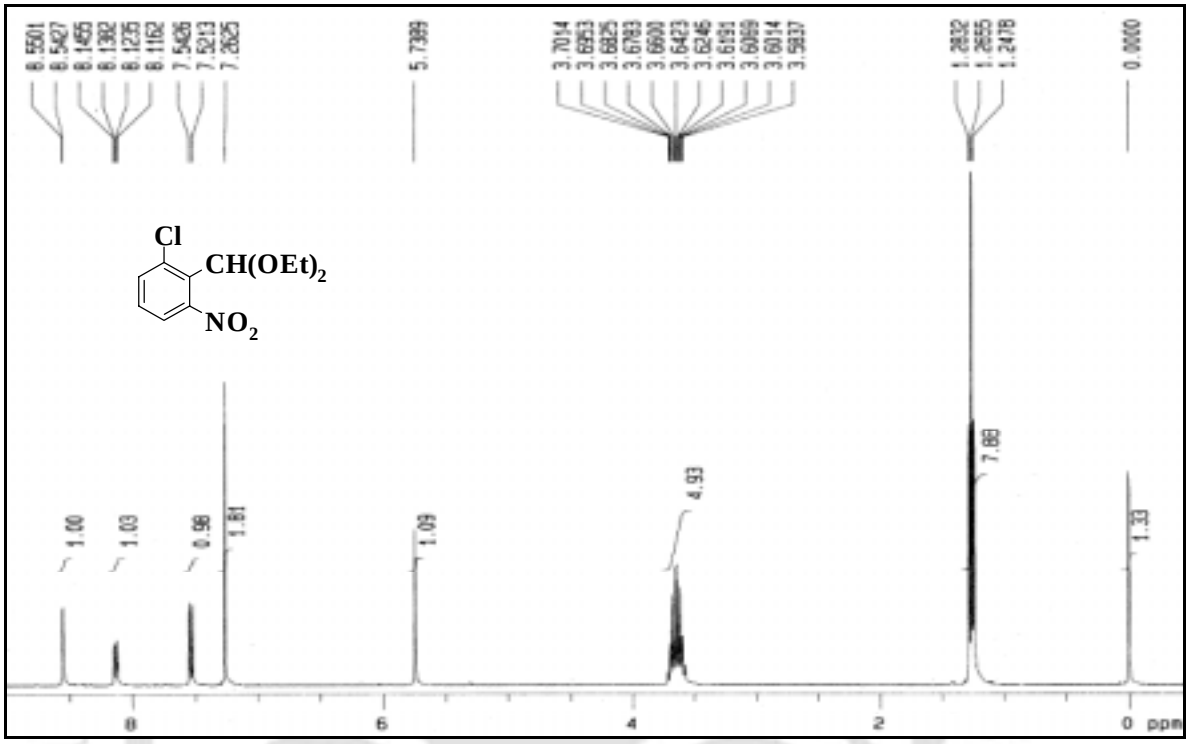
^{1}H NMR (400 MHz, $CDCl_3$): 2-Nitrobenzaldehyde diethyl acetal (20i)



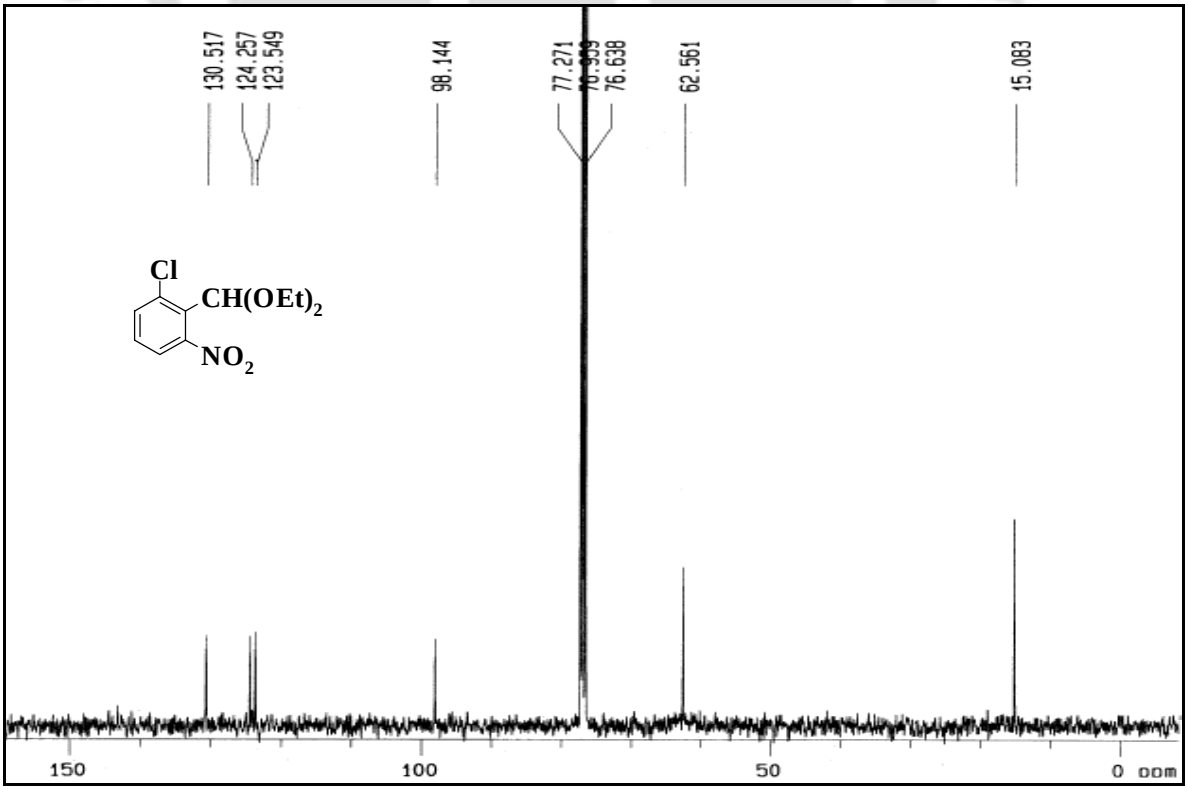
^{13}C NMR (100 MHz, $CDCl_3$): 2-Nitrobenzaldehyde diethyl acetal (20i)



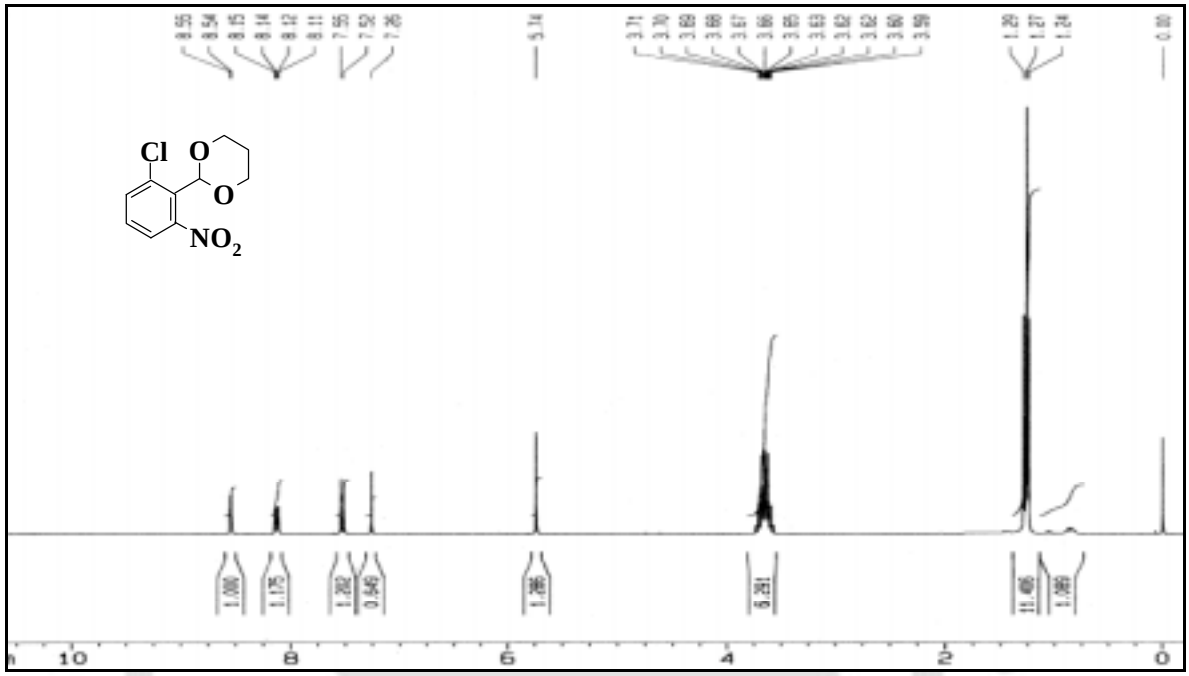
^{1}H NMR (400 MHz, $CDCl_3$): 2-Chloro-6-nitrobenzaldehyde diethyl acetal (21i)



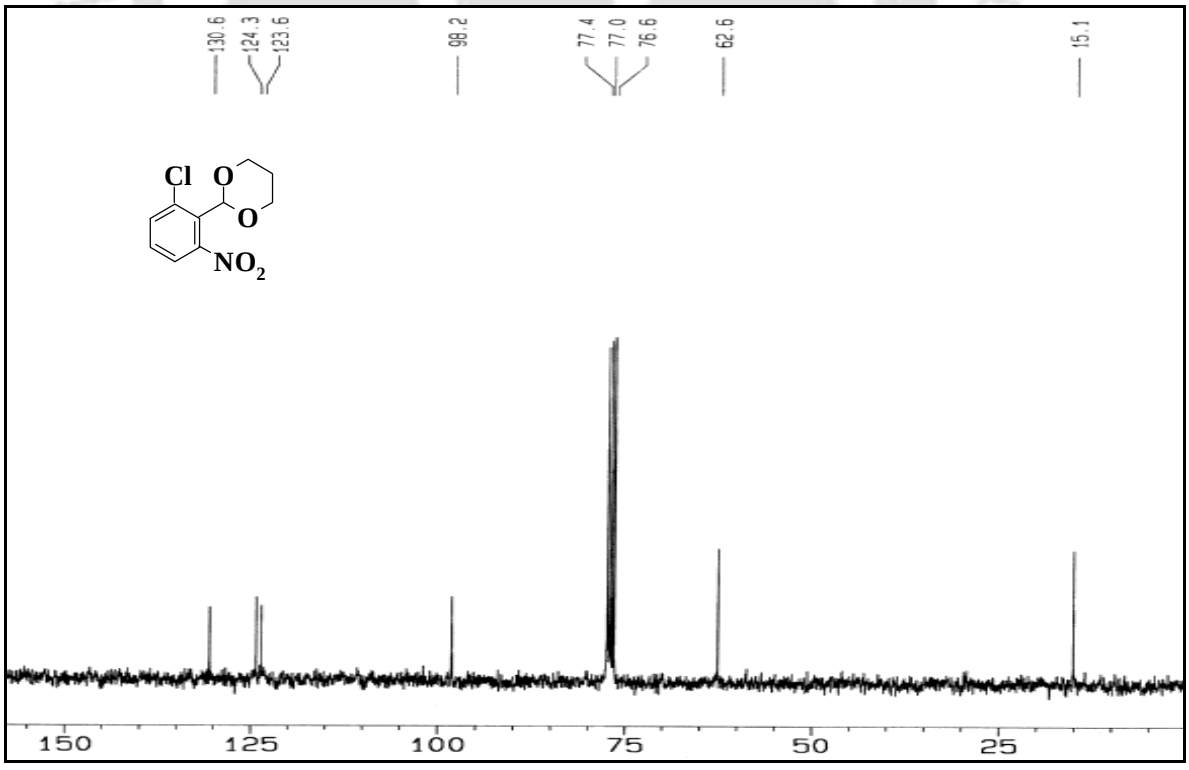
^{13}C NMR (100 MHz, $CDCl_3$): 2-Chloro-6-nitrobenzaldehyde diethyl acetal (21i)



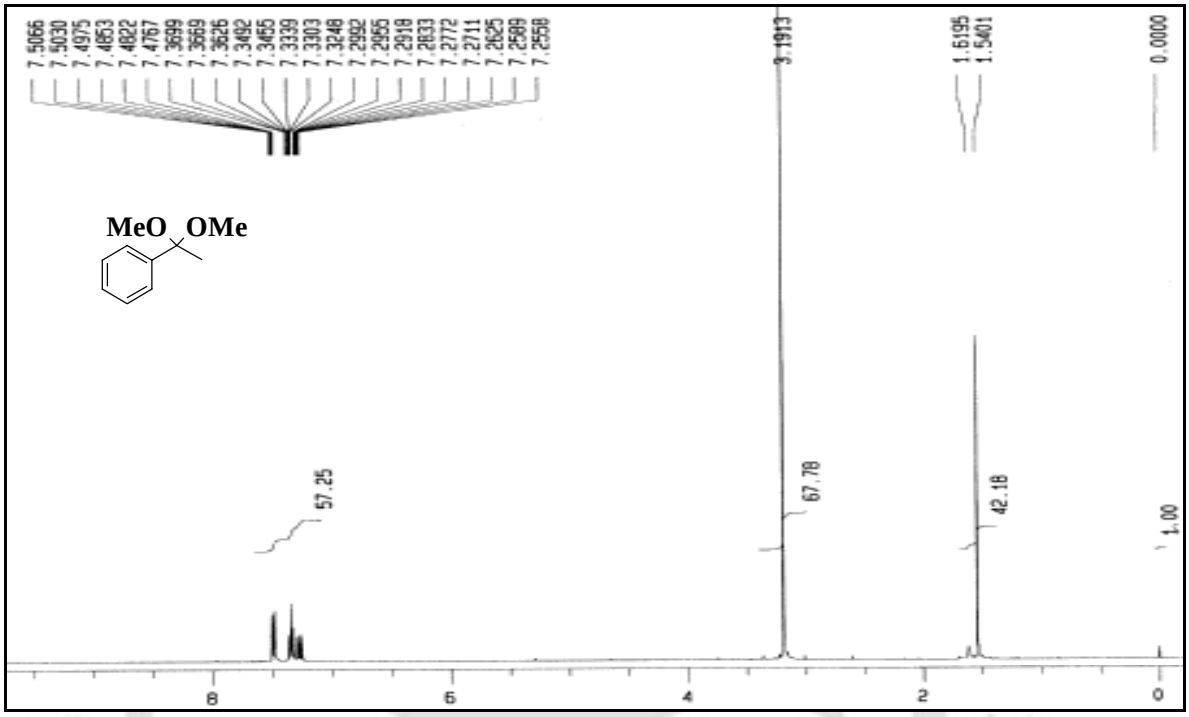
^{1}H NMR (400 MHz, $CDCl_3$): 2-Chloro-6-nitrobenzaldehyde 1,3-dioxane (21k)



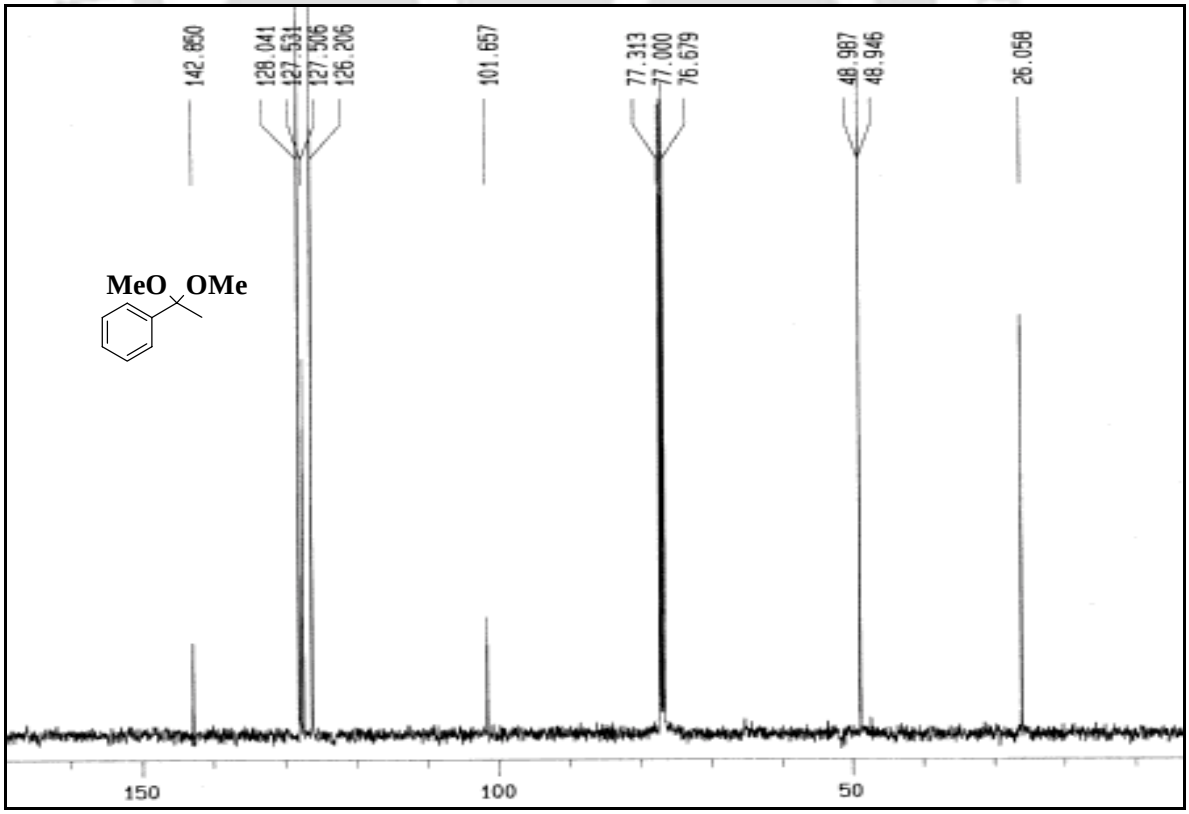
^{13}C NMR (100 MHz, $CDCl_3$): 2-Chloro-6-nitrobenzaldehyde 1,3-dioxane (21k)



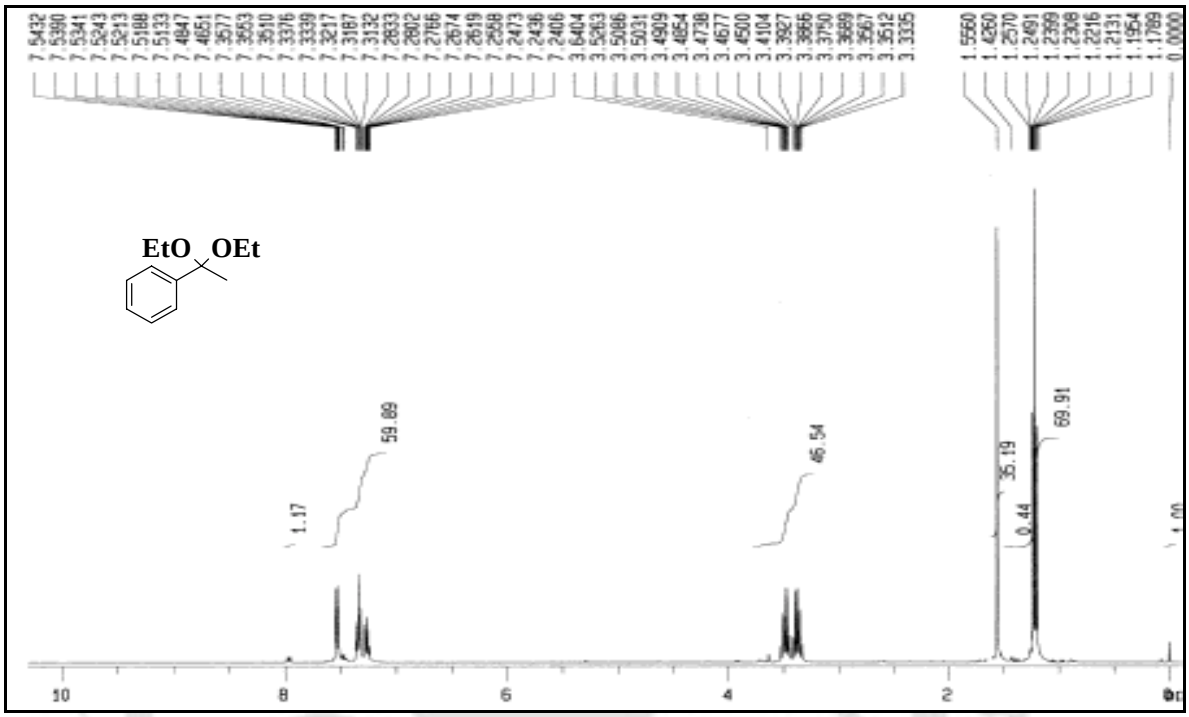
^{1}H NMR (400 MHz, $CDCl_3$): Acetophenone dimethyl ketal (22h)



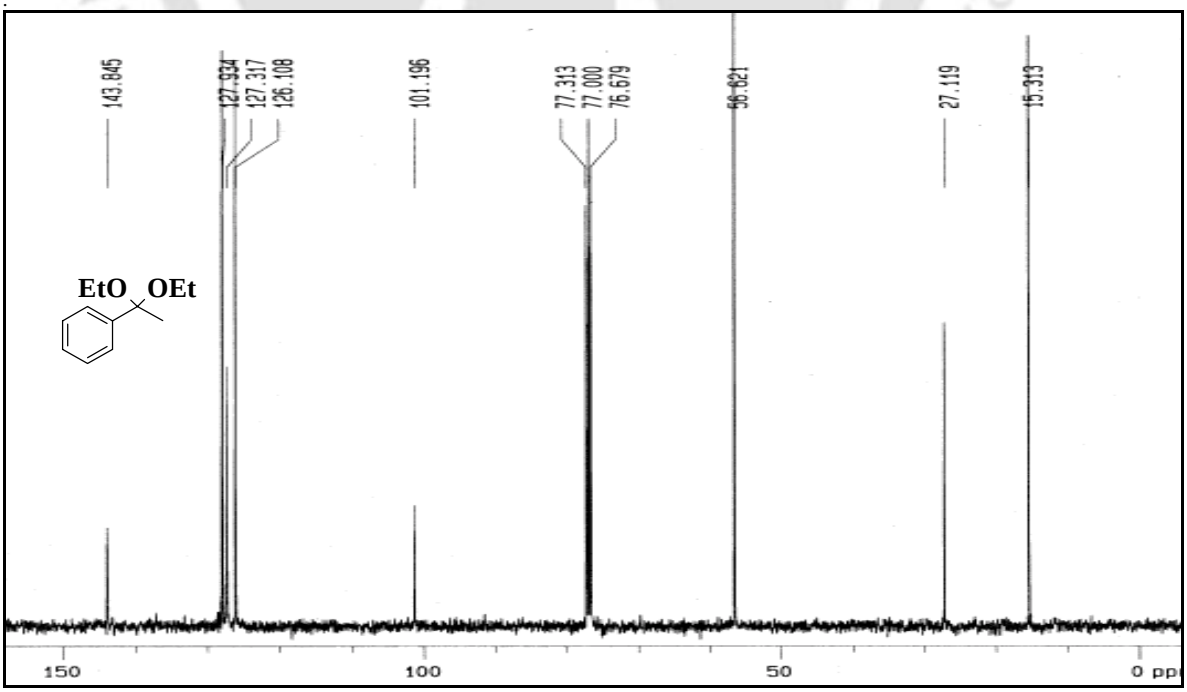
^{13}C NMR (100 MHz, $CDCl_3$): Acetophenone dimethyl ketal (22h)



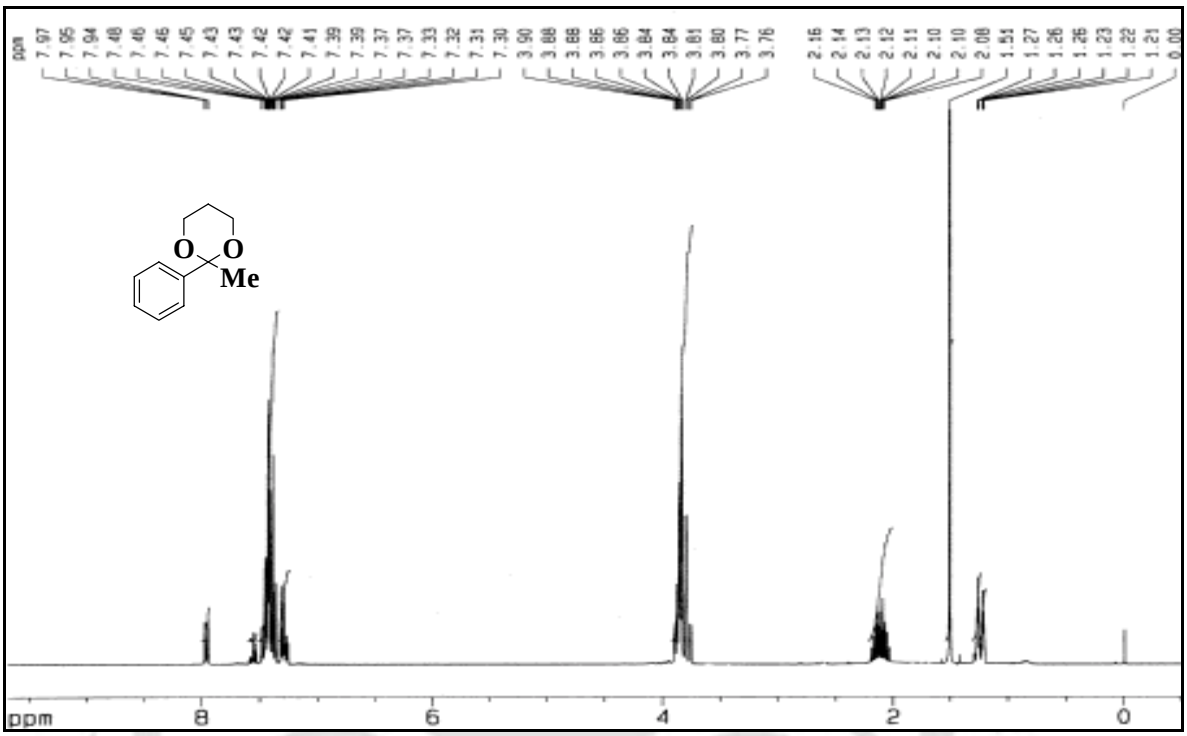
^{1}H NMR (400 MHz, $CDCl_3$): Acetophenone diethyl ketal (22i)



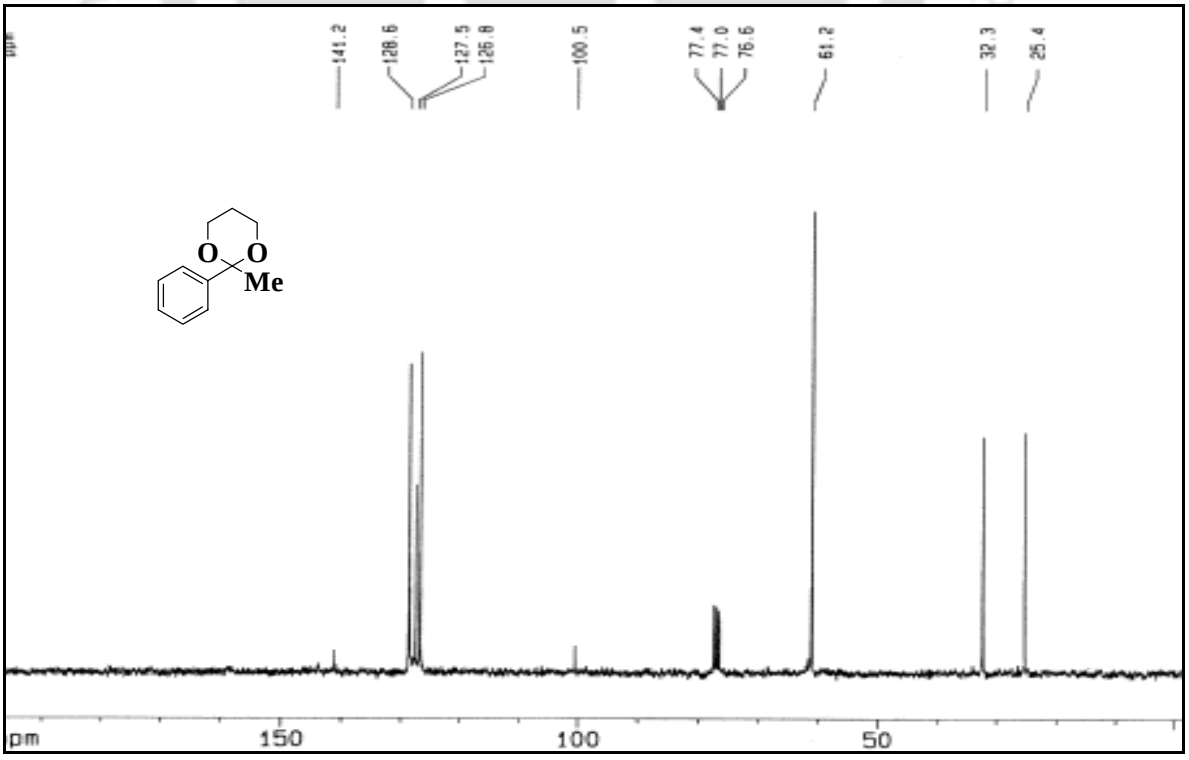
^{13}C NMR (100 MHz, $CDCl_3$): Acetophenone diethyl ketal (22i)



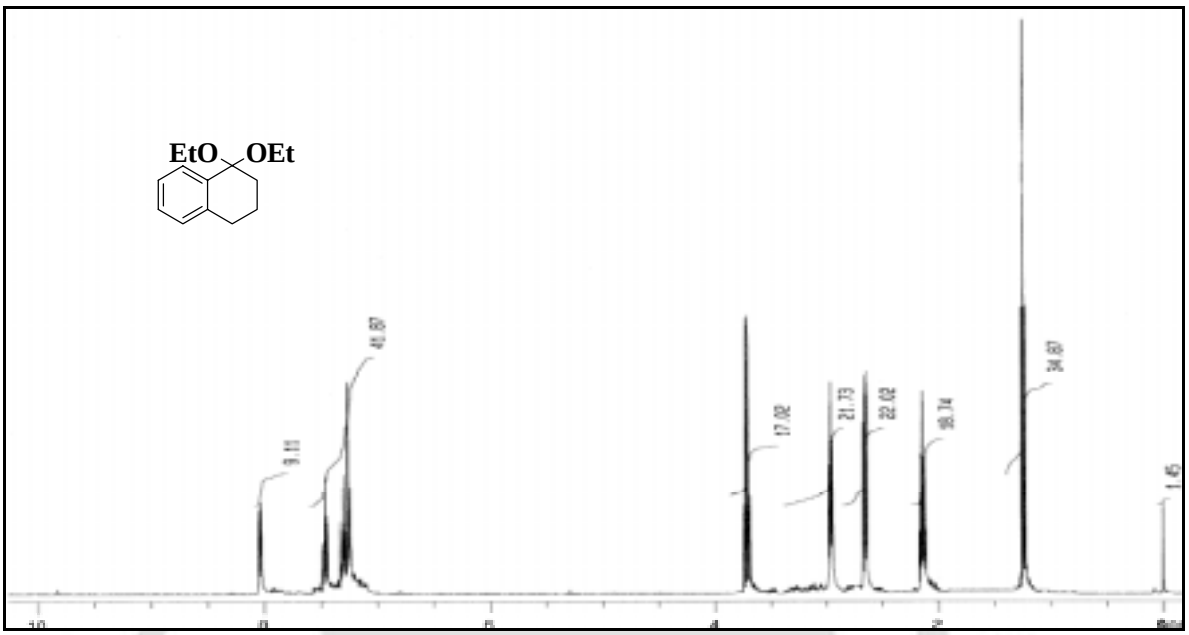
^{1}H NMR (400 MHz, $CDCl_3$): Acetophenone 1,3-dioxane (22k)



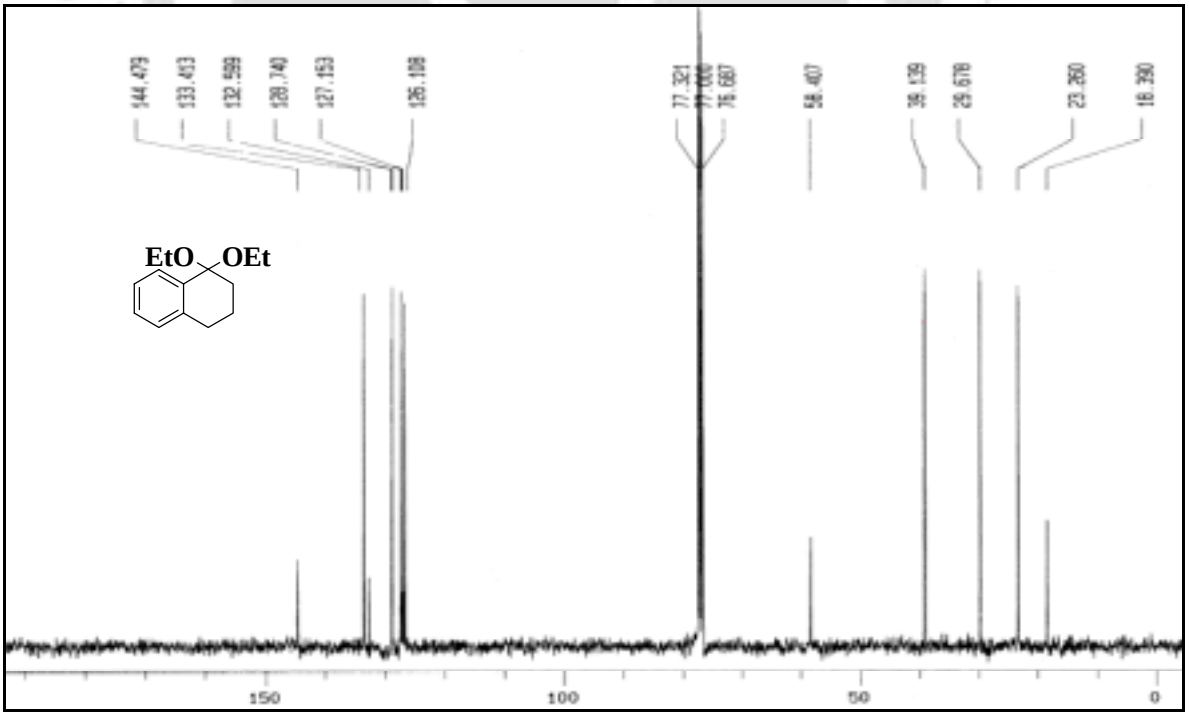
^{13}C NMR (100 MHz, $CDCl_3$): Acetophenone 1,3-dioxane (22k)



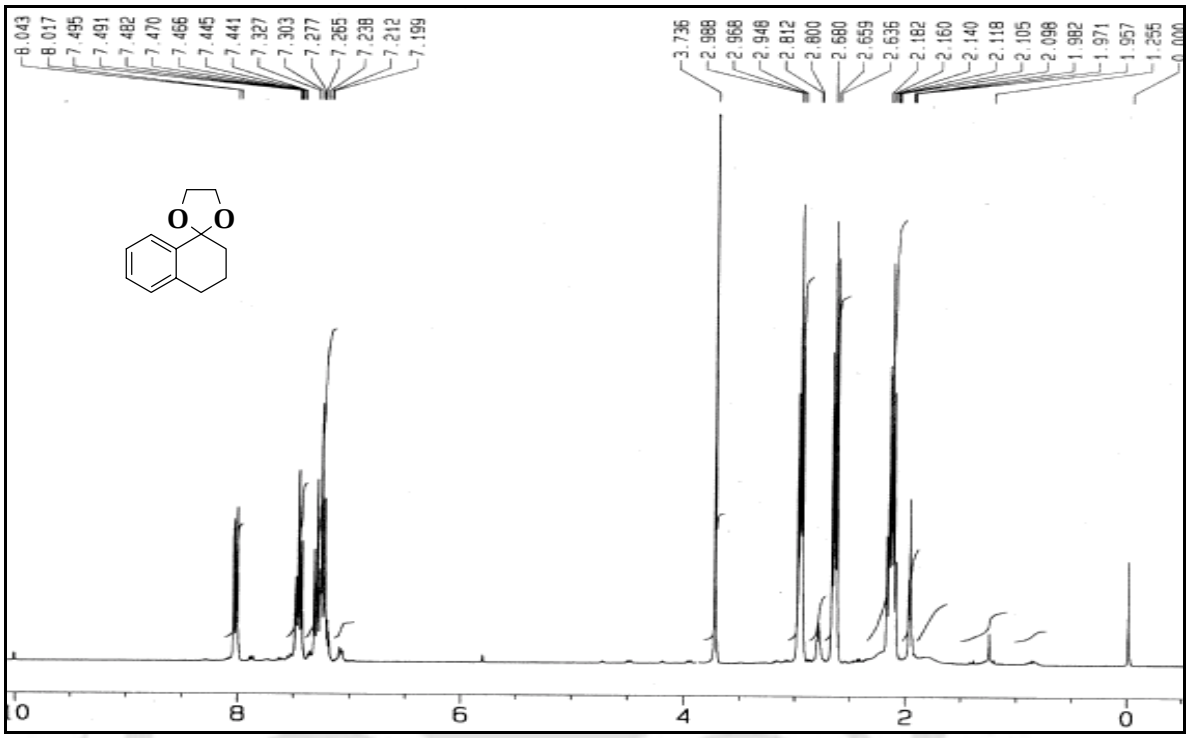
^{1}H NMR (400 MHz, $CDCl_3$): α-Tetralone diethyl ketal(24i)



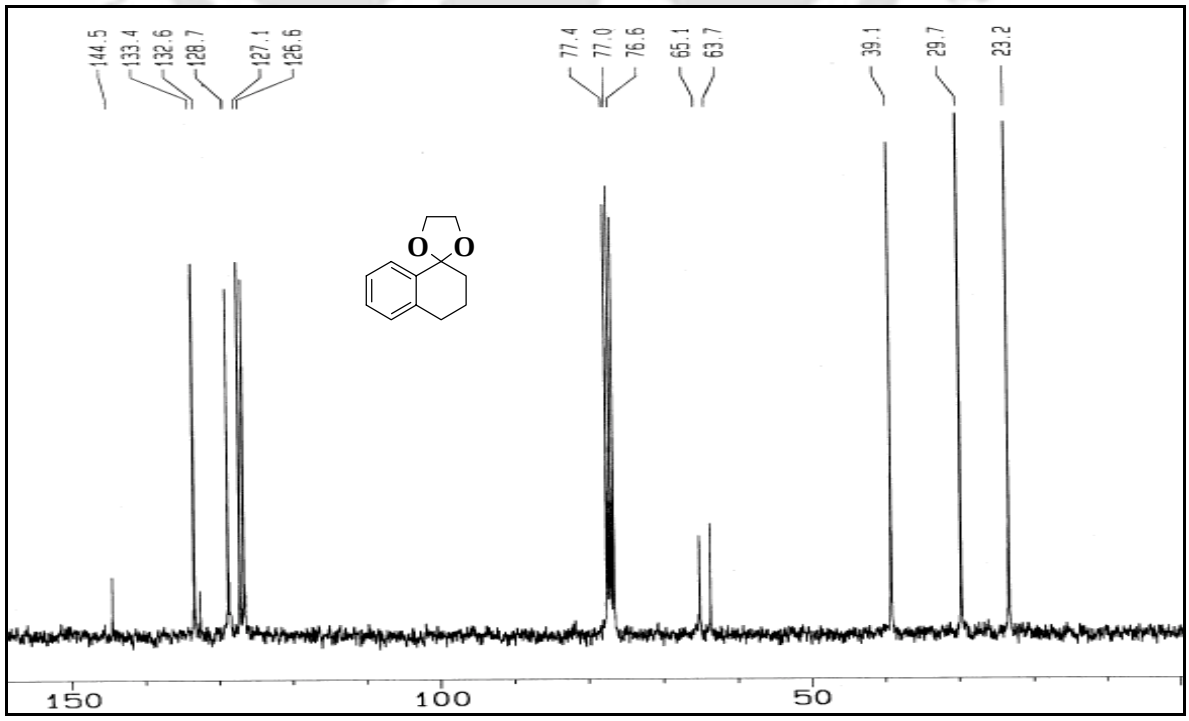
^{13}C NMR (100 MHz, $CDCl_3$): α-Tetralone diethyl ketal(24i)



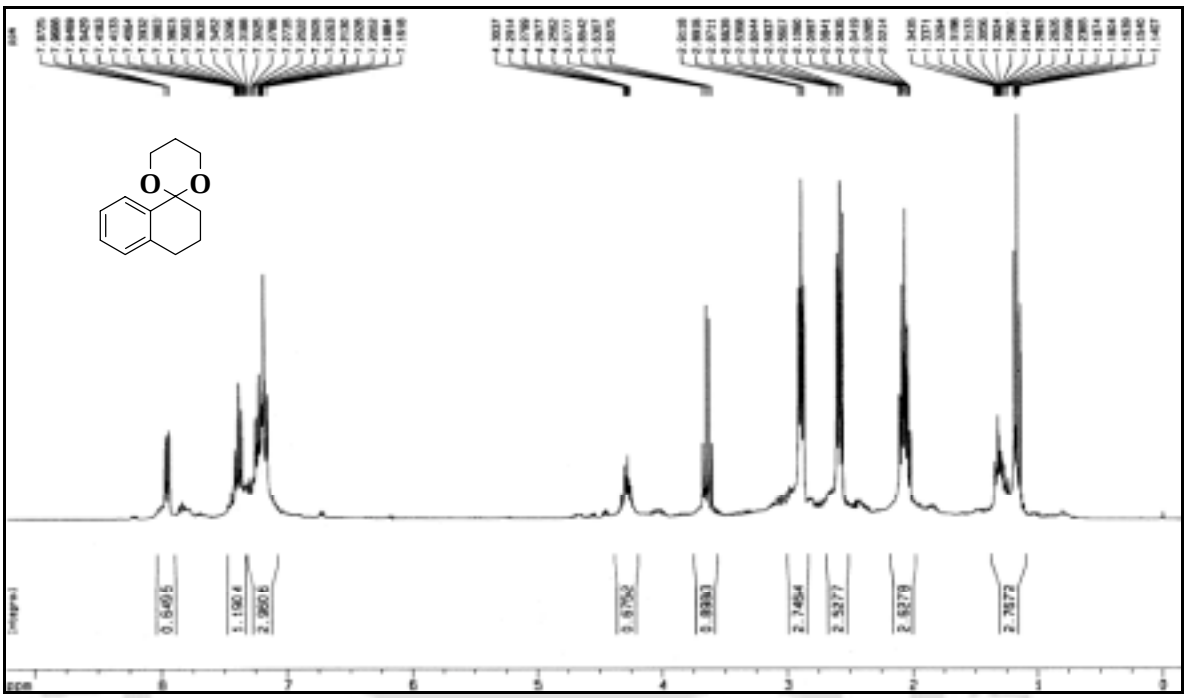
^{1}H NMR (400 MHz, $CDCl_3$): α-Tetralone 1,3-dioxolane (24j)



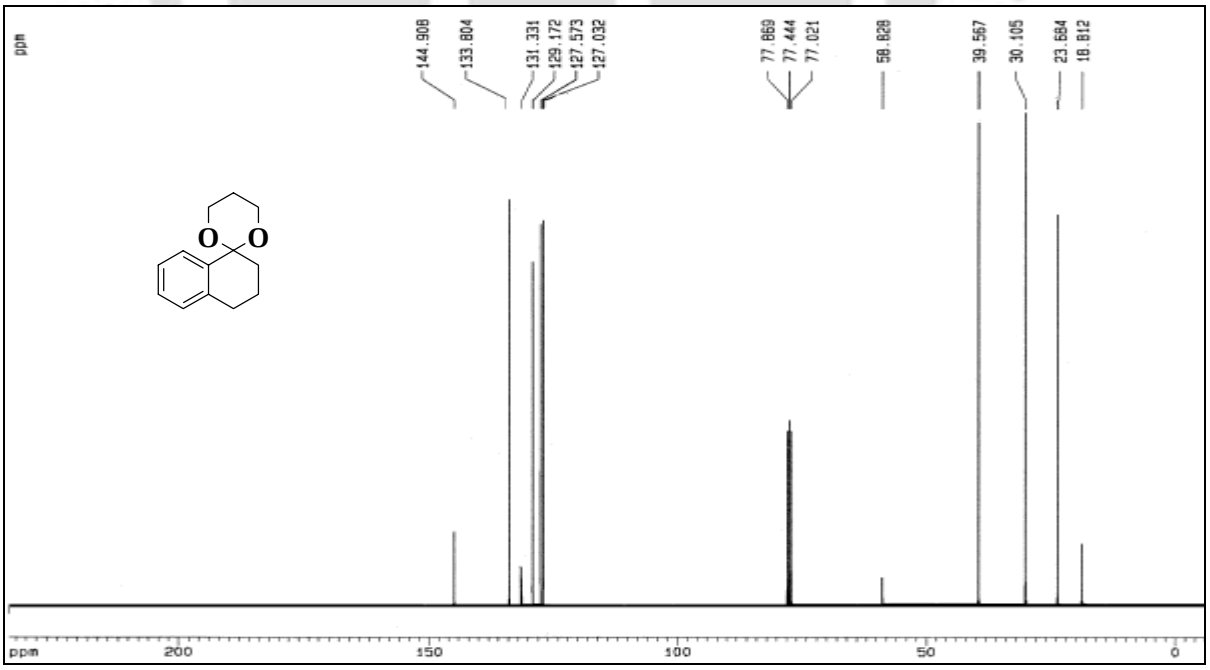
^{13}C NMR (100 MHz, $CDCl_3$): α-Tetralone 1,3-dioxolane (24j)



^{1}H NMR (400 MHz, $CDCl_3$): α-Tetralone 1,3-dioxane (24k)

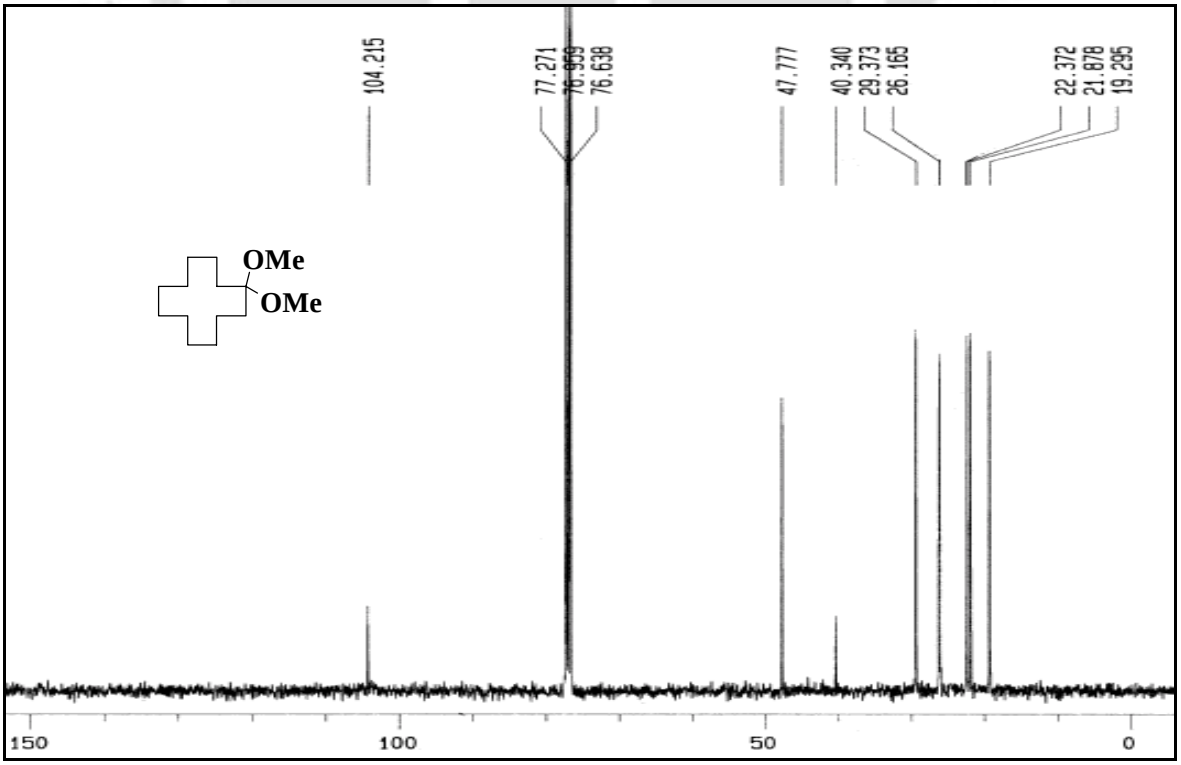


^{13}C NMR (100 MHz, $CDCl_3$): α-Tetralone 1,3-dioxane (24k)

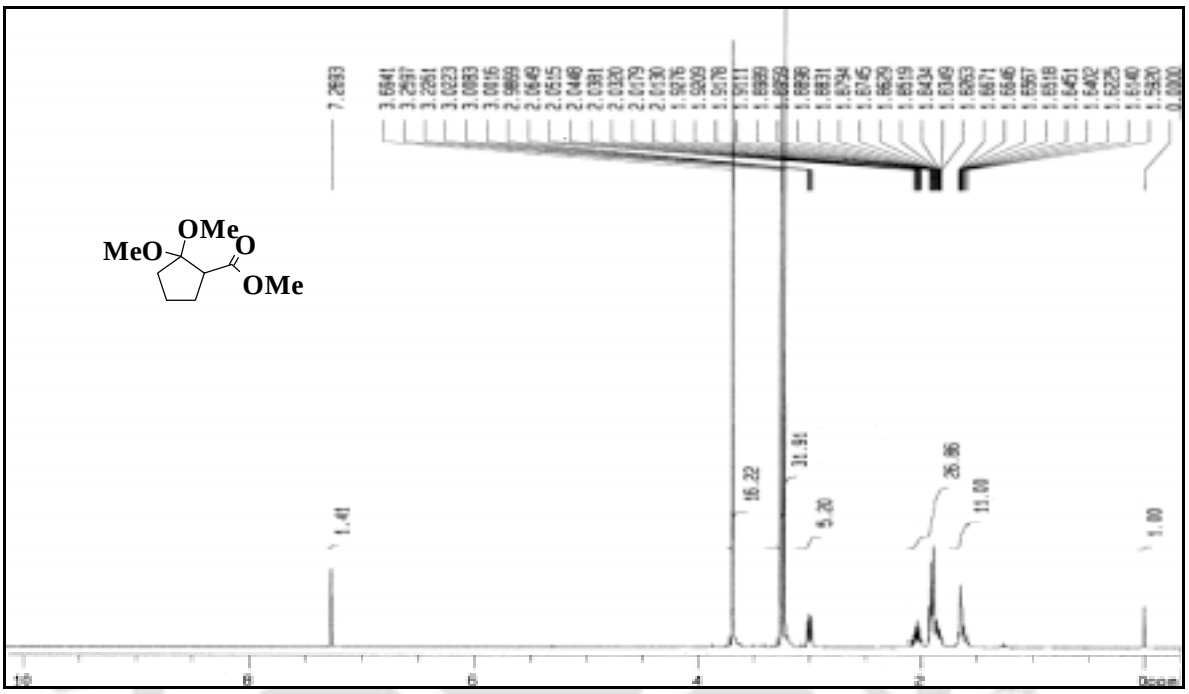


^{1}H NMR (400 MHz, $CDCl_3$): Cyclododecanone dimethyl ketal (25h)

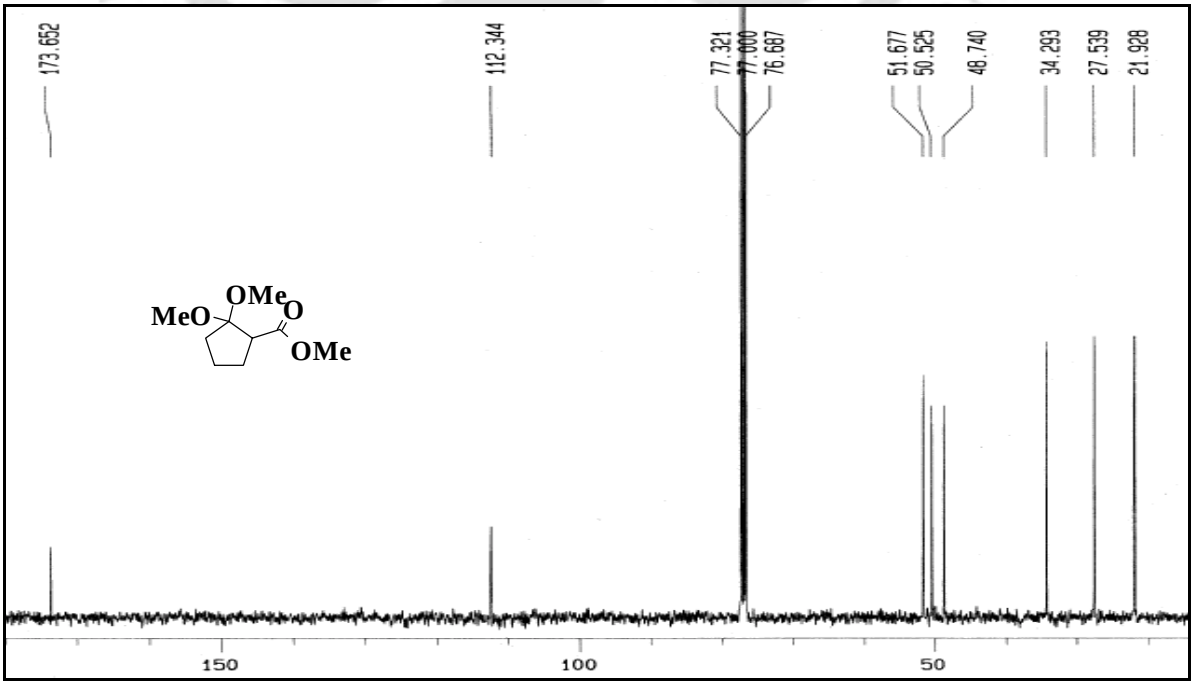
^{13}C NMR (100 MHz, $CDCl_3$): Cyclododecanone dimethyl ketal (25h)



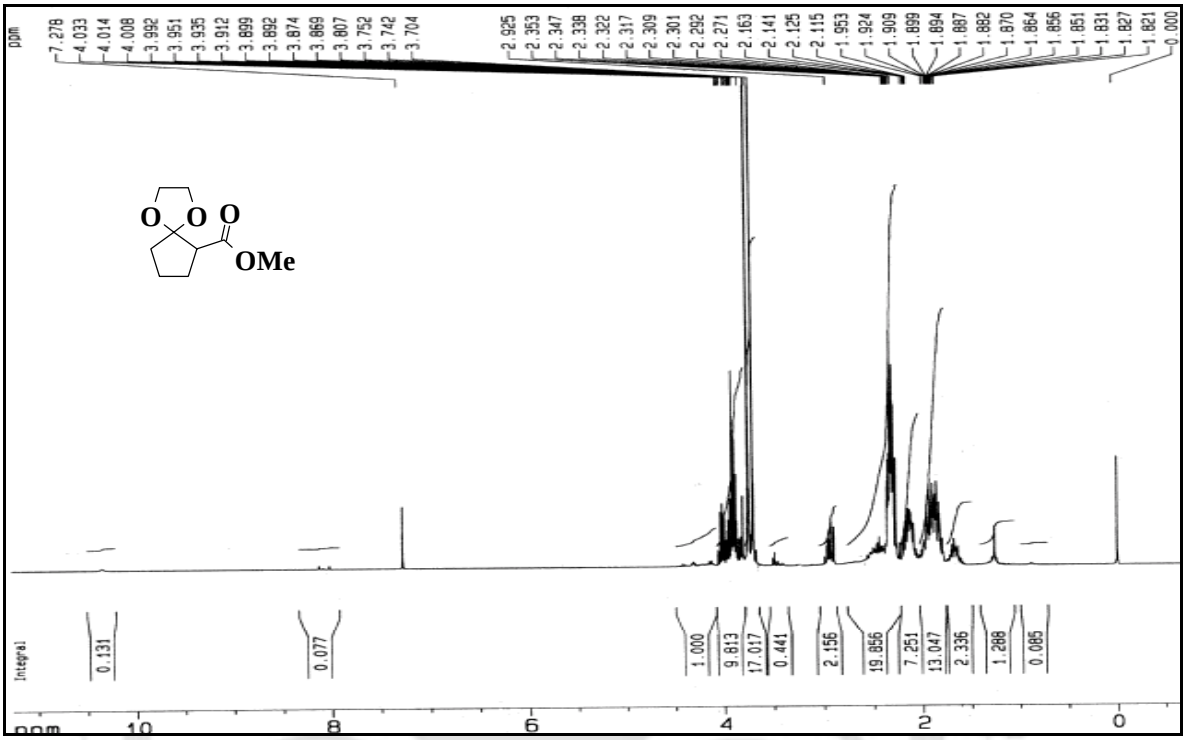
^{1}H NMR (400 MHz, $CDCl_3$): Cyclopentanone-2-methyl-carboxylate dimethyl ketal (26h)



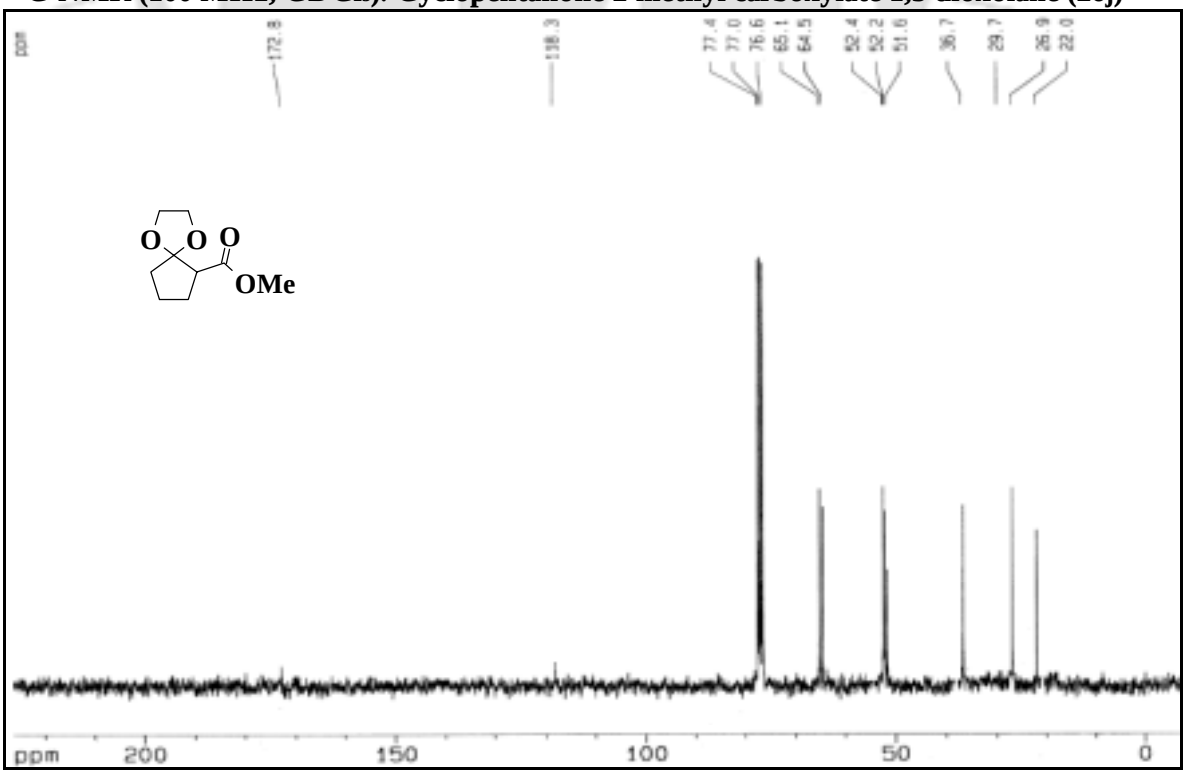
^{13}C NMR (100 MHz, $CDCl_3$): Cyclopentanone-2-methyl-carboxylate dimethyl ketal (26h)



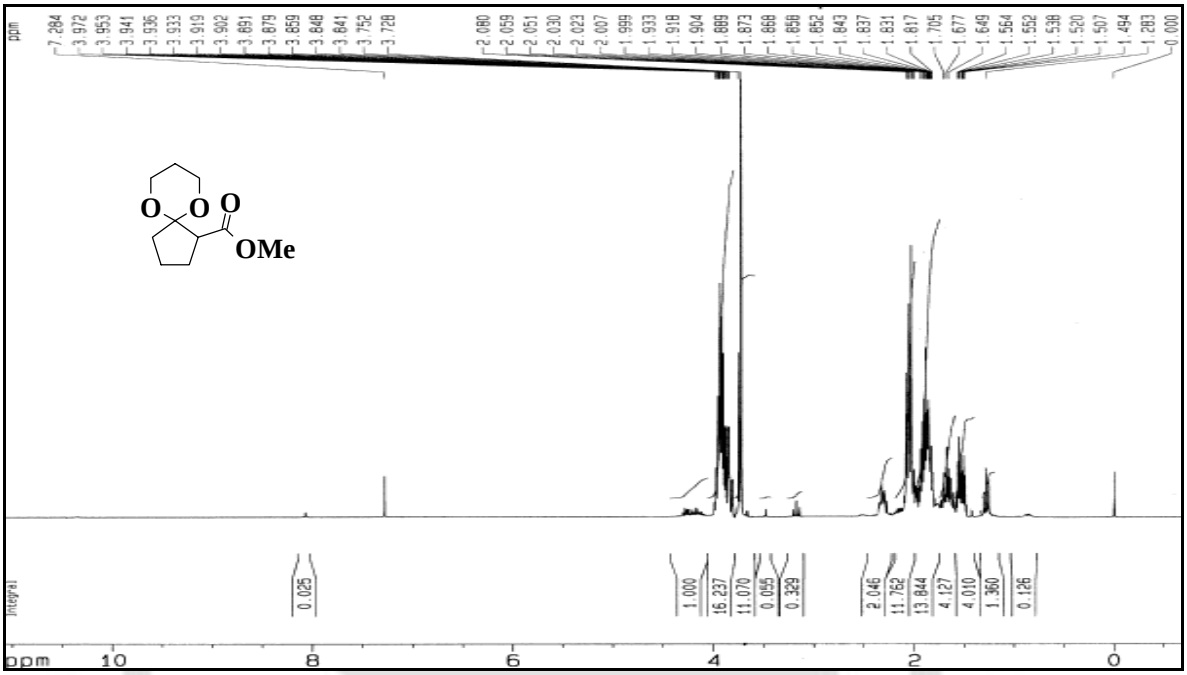
^{1}H NMR (400 MHz, $CDCl_3$): Cyclopentanone-2-methyl-carboxylate 1,3-dioxolane (26j)



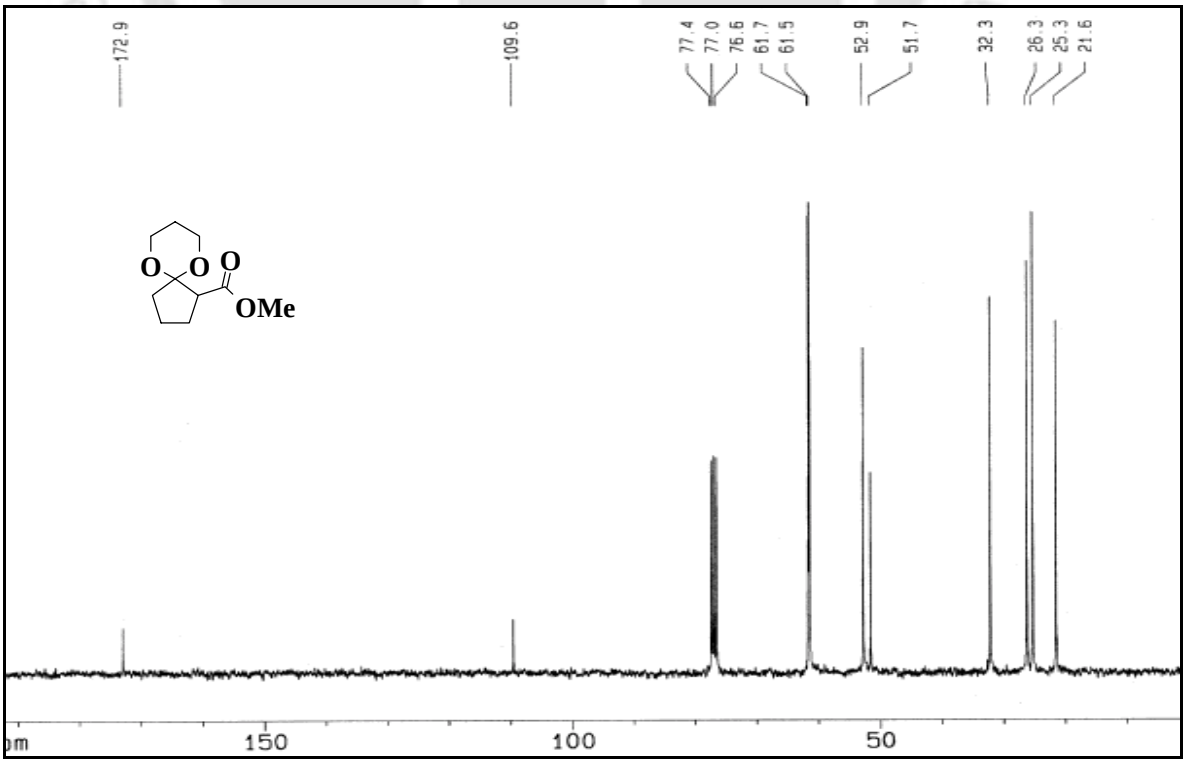
^{13}C NMR (100 MHz, $CDCl_3$): Cyclopentanone-2-methyl-carboxylate 1,3-dioxolane (26j)



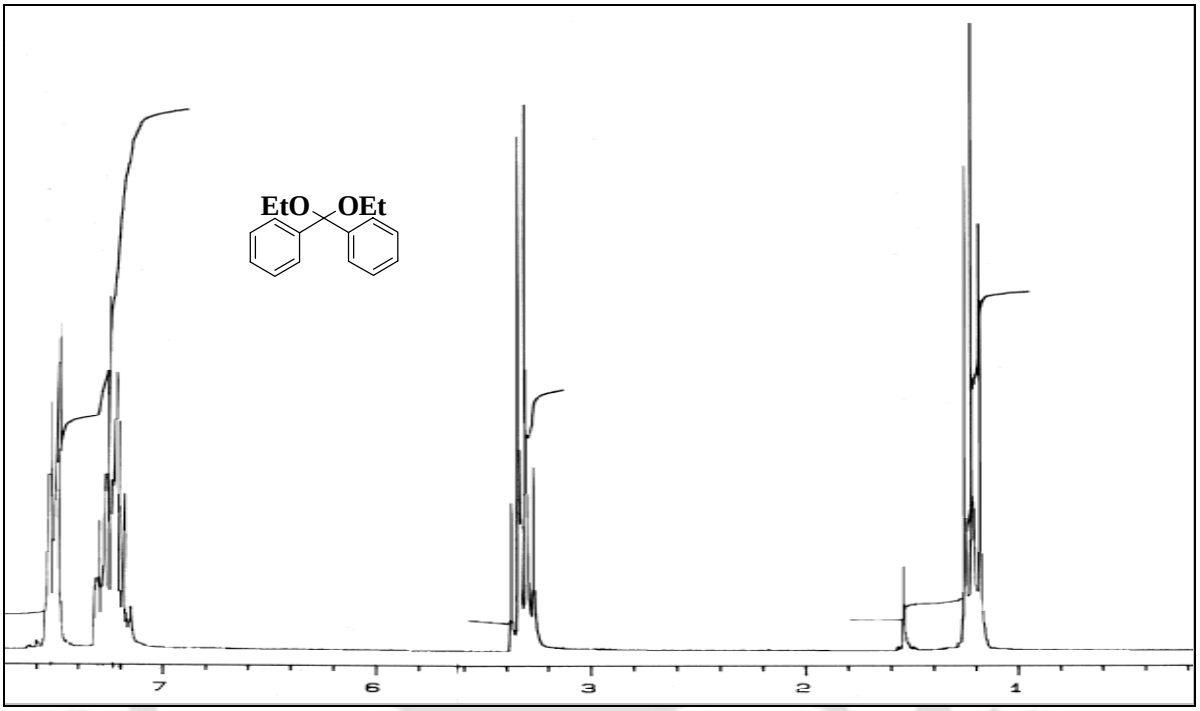
^{1}H NMR (400 MHz, $CDCl_3$): Cyclopentanone-2-methyl-carboxylate 1,3-dioxane (26k)



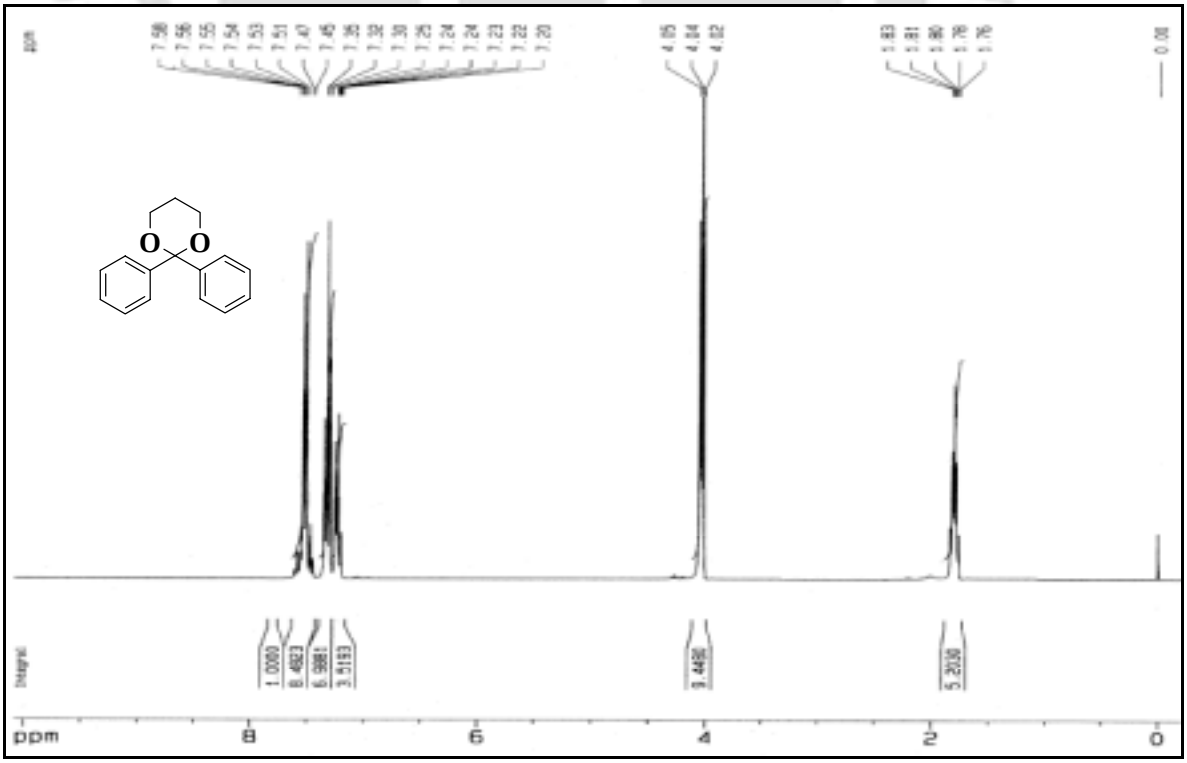
^{13}C NMR (100 MHz, $CDCl_3$): Cyclopentanone-2-methyl-carboxylate 1,3-dioxane (26k)



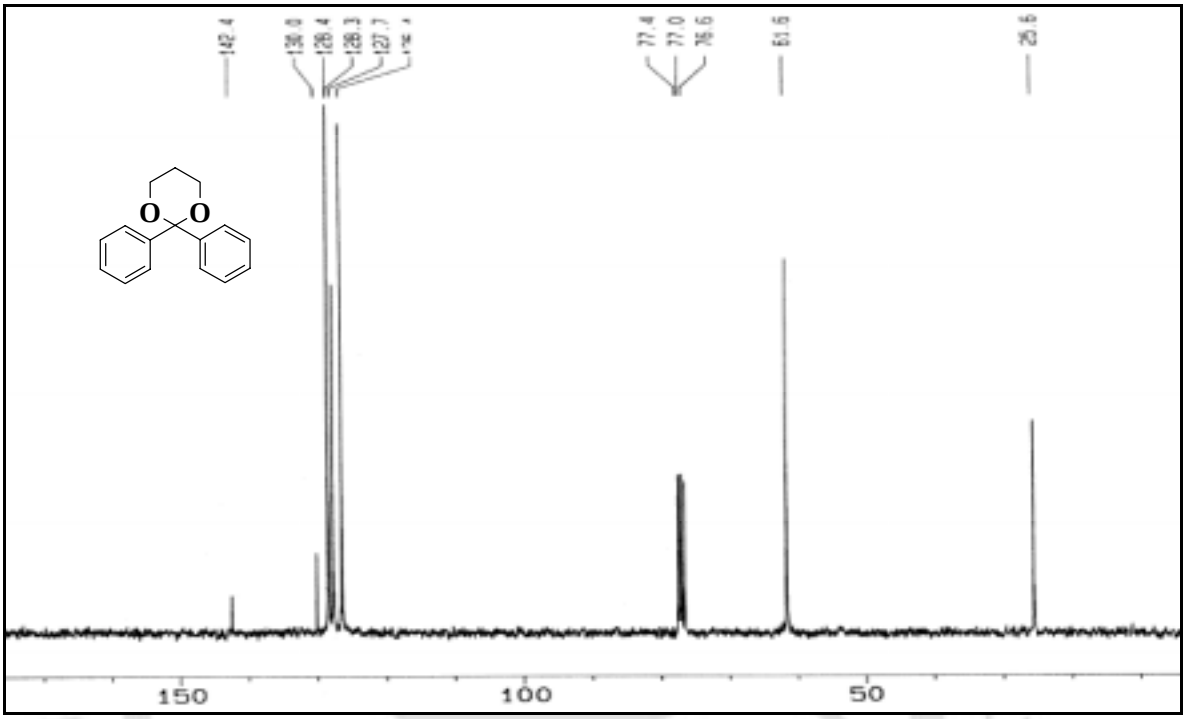
^{1}H NMR (200 MHz, $CDCl_3$): Benzophenone diethyl ketal (27i)



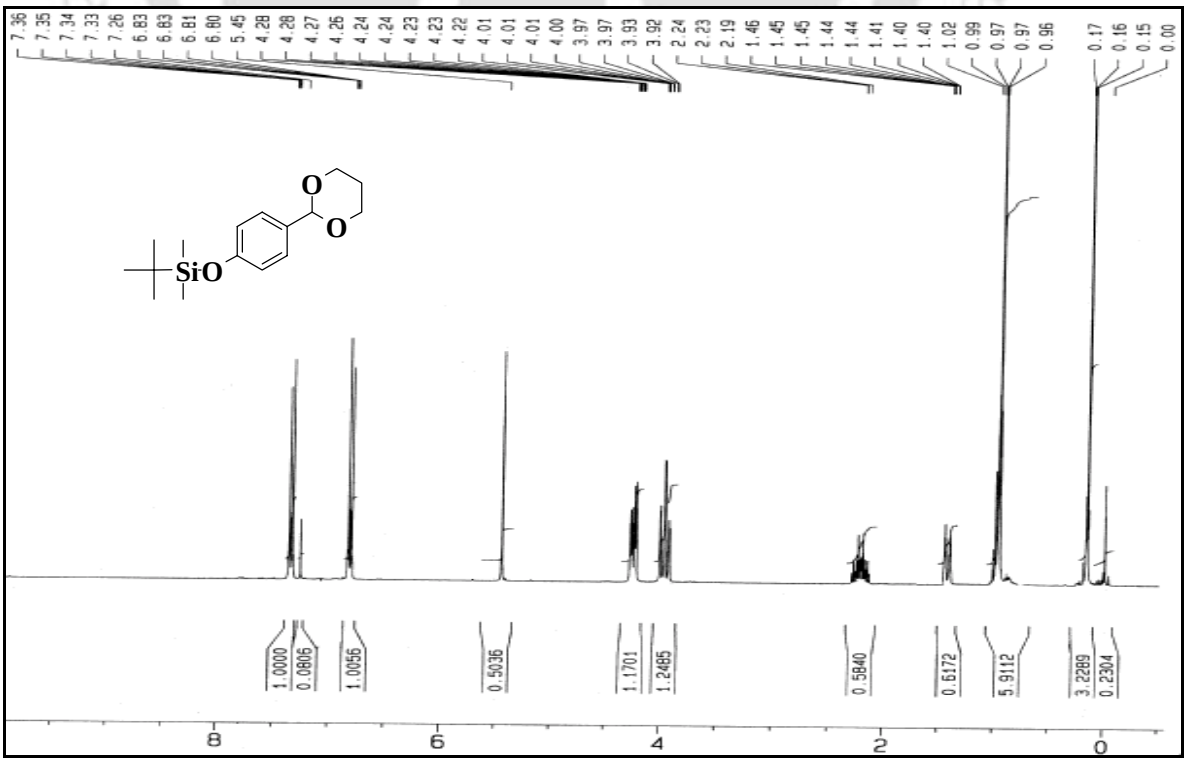
^{1}H NMR (400 MHz, $CDCl_3$): Benzophenone 1,3-dioxane (27k)



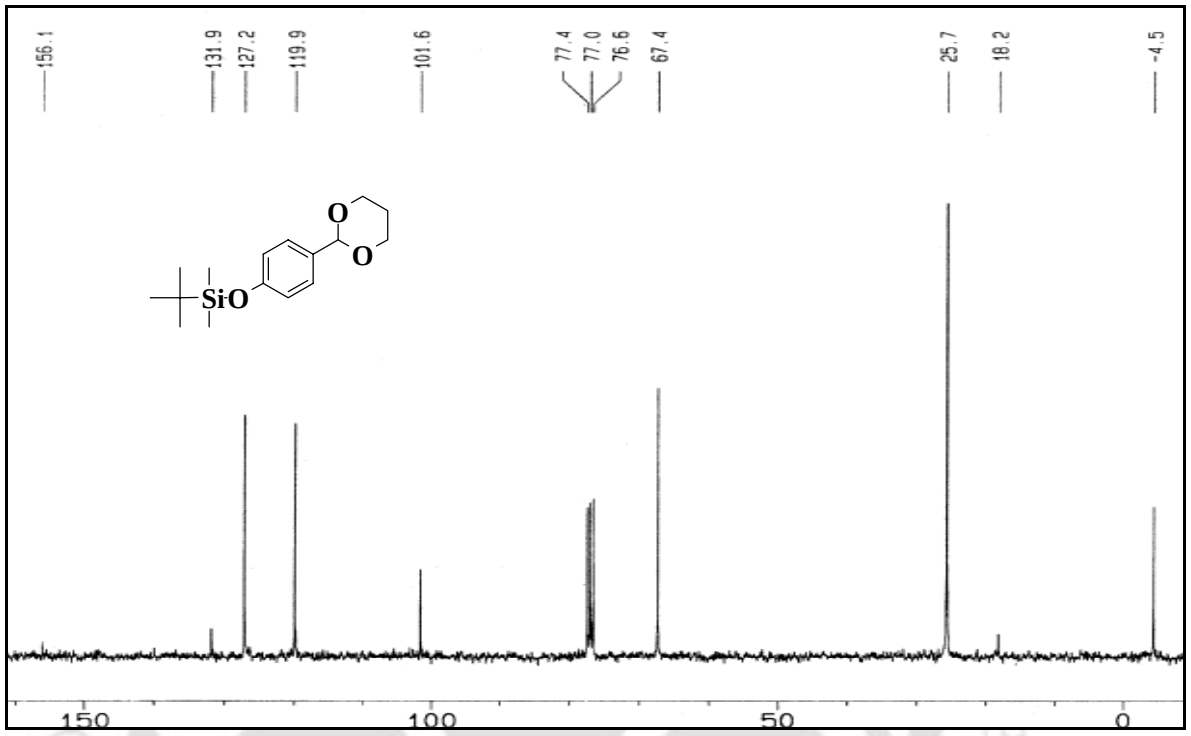
^{13}C NMR (100 MHz, $CDCl_3$): Benzophenone 1,3-dioxane (27k)



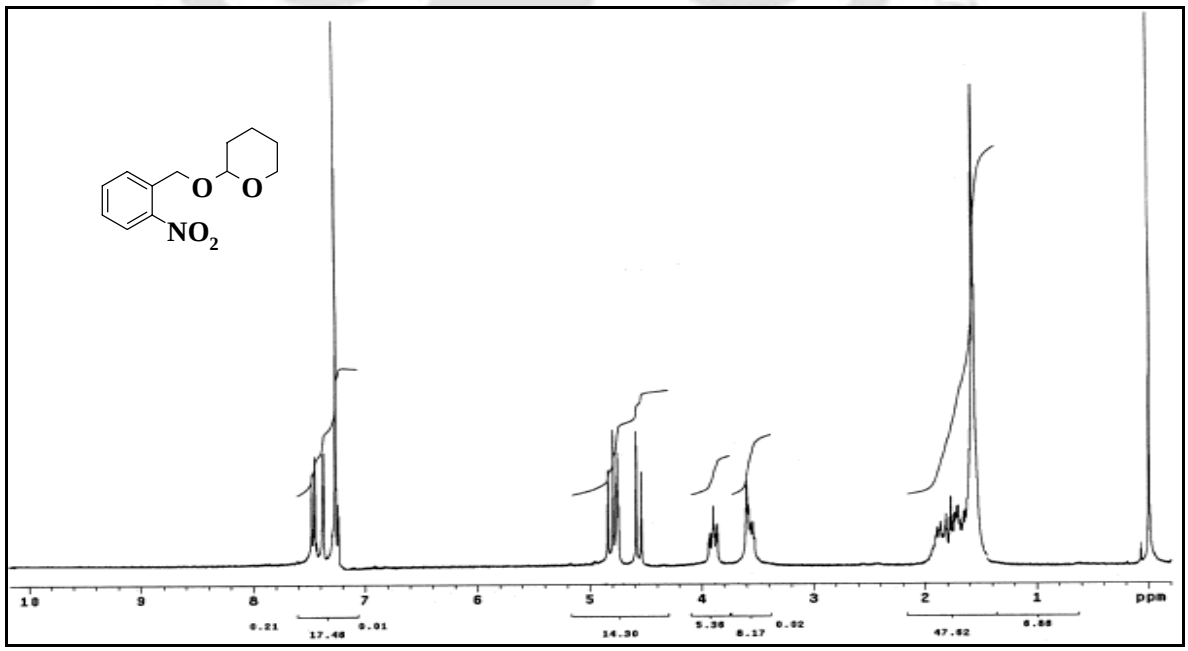
^{1}H NMR (400 MHz, $CDCl_3$): 4-*tert*-Butyldimethylsilanyloxy-benzaldehyde 1,3-dioxane (28k)



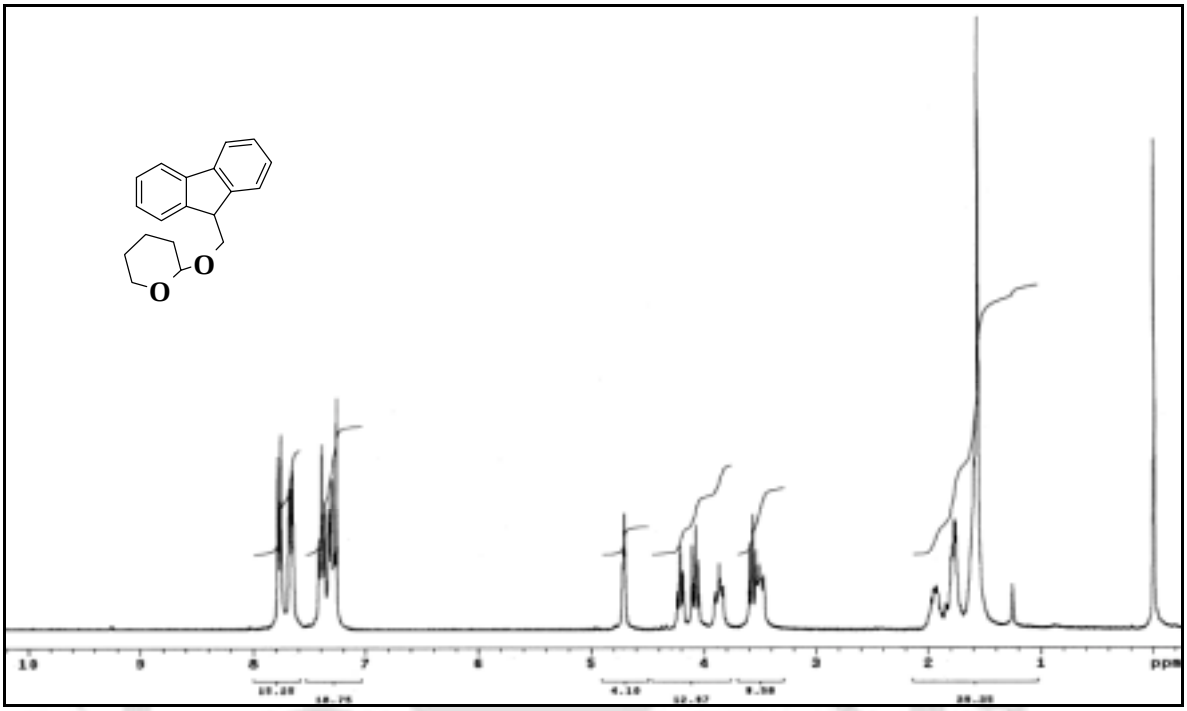
^{13}C NMR (100 MHz, $CDCl_3$): 4-*tert*-Butyldimethylsilanyloxy-benzaldehyde 1,3-dioxane (28k)



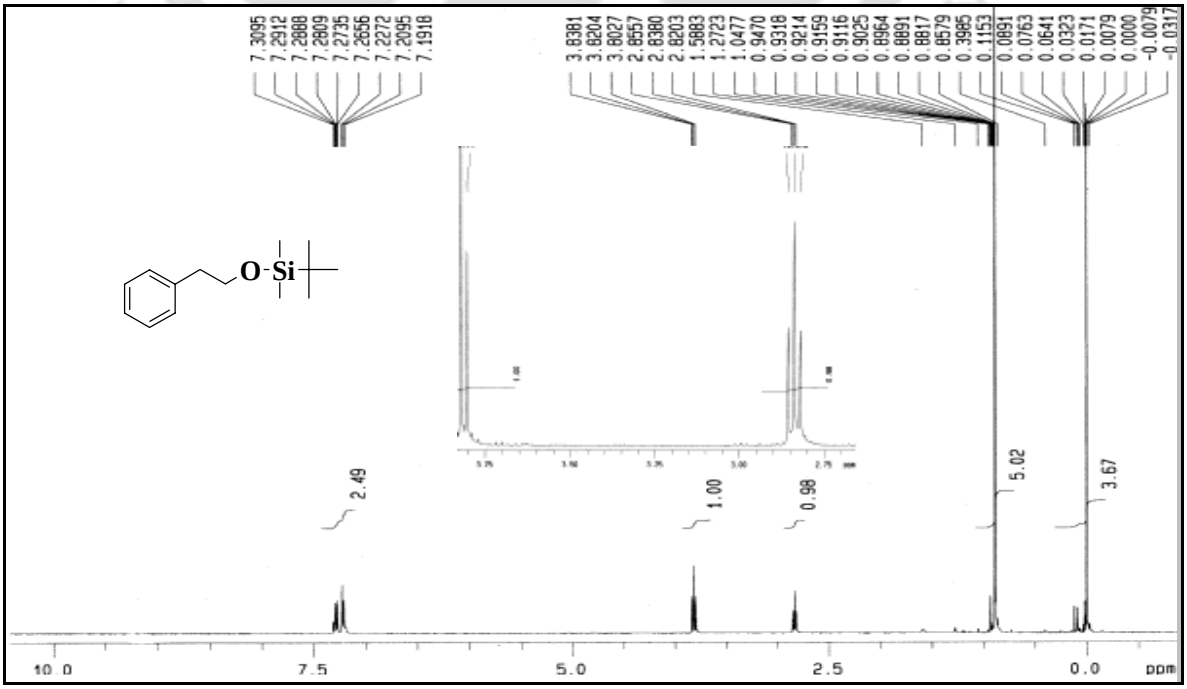
^{1}H NMR (400 MHz, $CDCl_3$): 2-(2-Nitro-benzyloxy)-tetrahydro-pyran (30n)



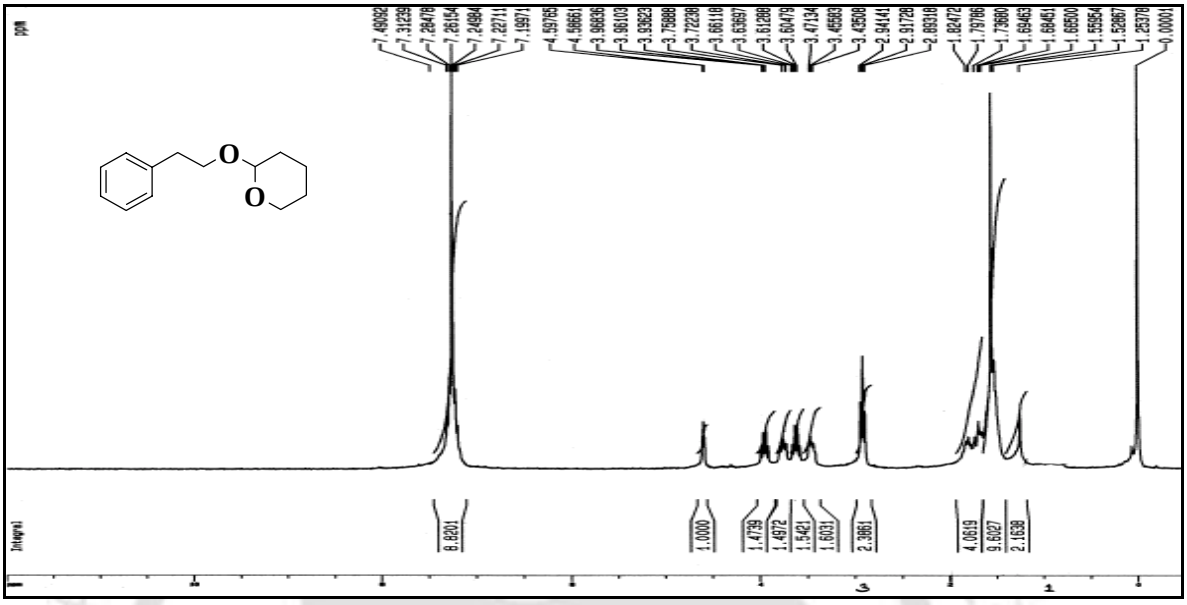
^{1}H NMR (400 MHz, $CDCl_3$): 2-(9H-Fluoren-9-ylmethoxy)-tetrahydro-pyran (31n)



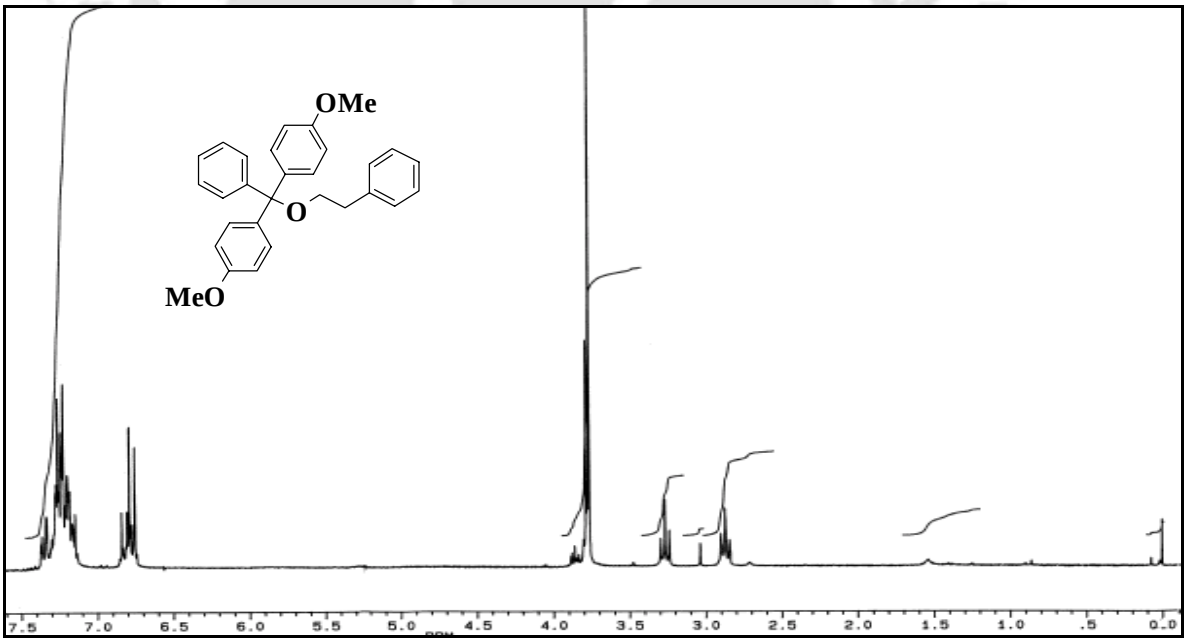
^{1}H NMR (400 MHz, $CDCl_3$): *tert*-Butyl-dimethyl-phenethyloxy-silane (33m)



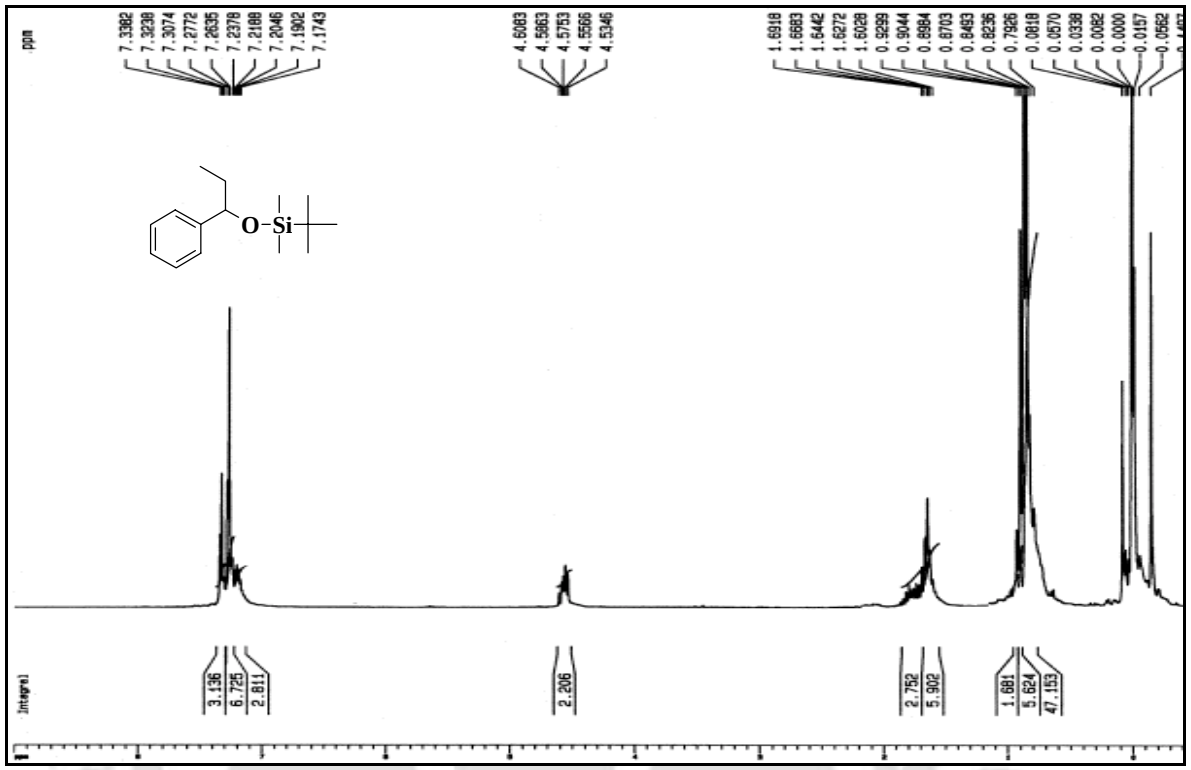
^{1}H NMR (400 MHz, $CDCl_3$): 2-Phenethyloxy-tetrahydro-pyran (33n)



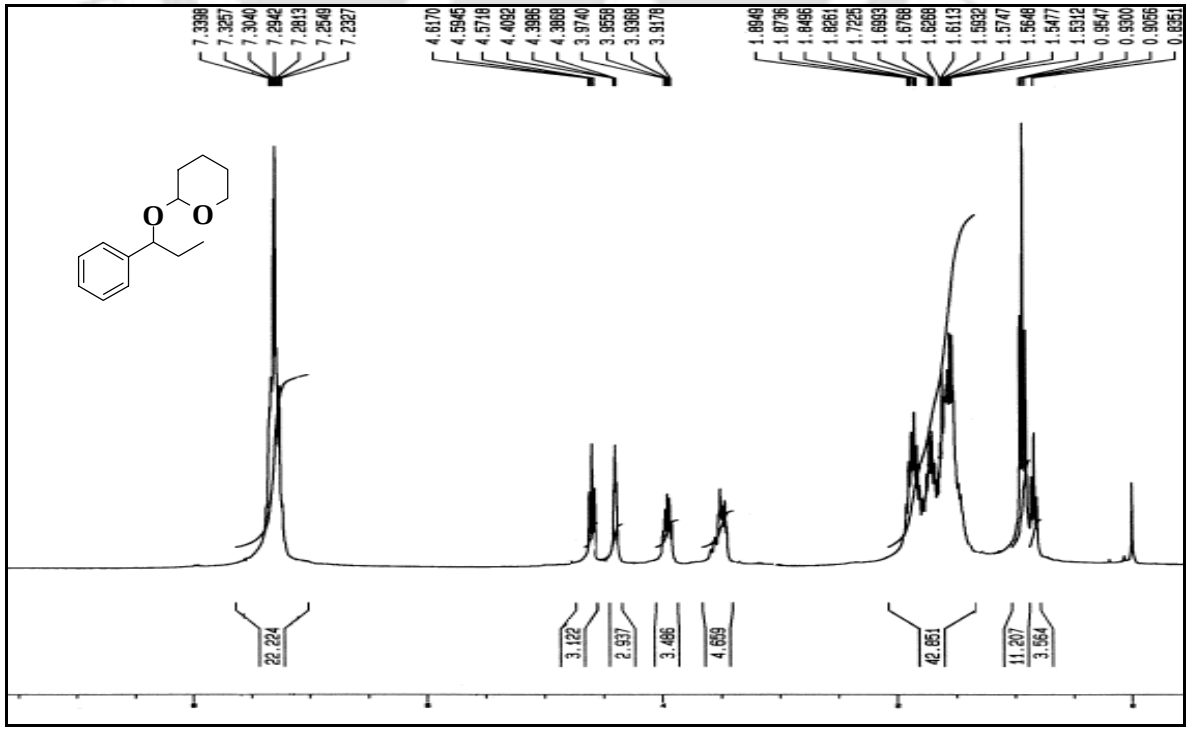
^{1}H NMR (400 MHz, $CDCl_3$): 2-Phenethyl-4,4'-dimethoxytrityl ether (33o)



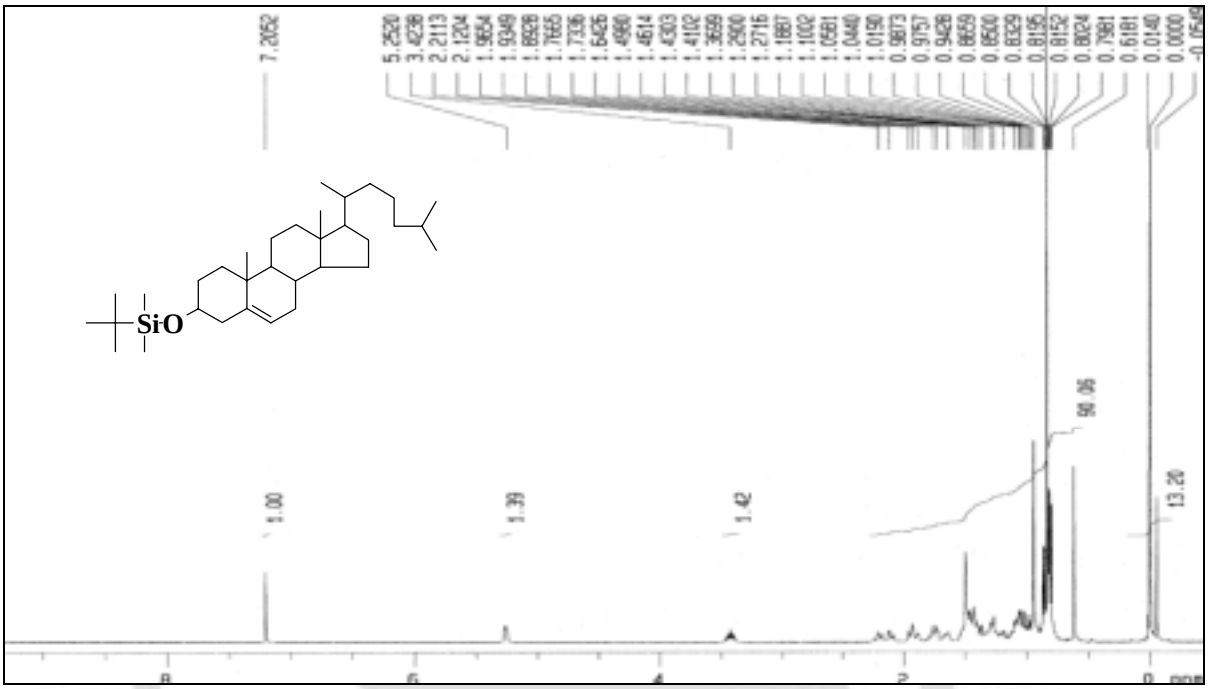
^{1}H NMR (400 MHz, $CDCl_3$): *tert*-Butyl-dimethyl-(1-phenyl-propoxy)-silane (38m)



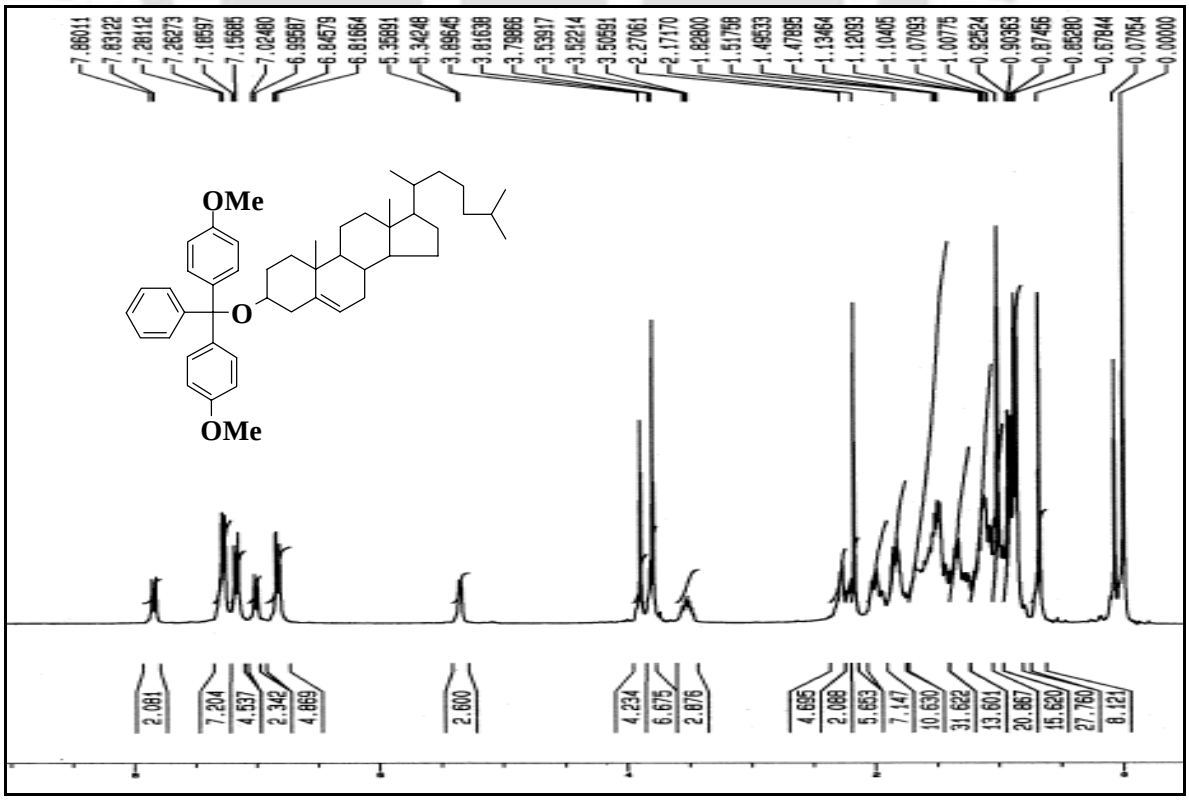
^{1}H NMR (400 MHz, $CDCl_3$): 2-(1-Phenyl-propoxy)-tetrahydro-pyran (38n)



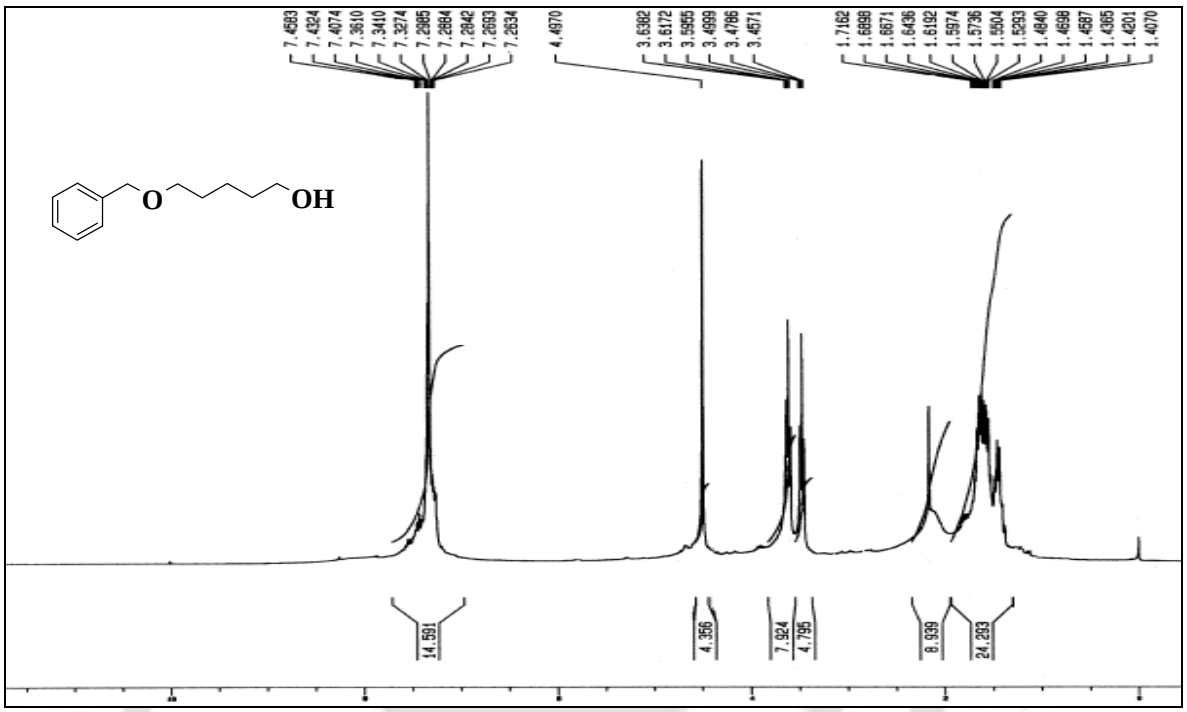
^{1}H NMR (400 MHz, $CDCl_3$): *tert*-Butyldimethylsilyl ether of cholesterol (39m)



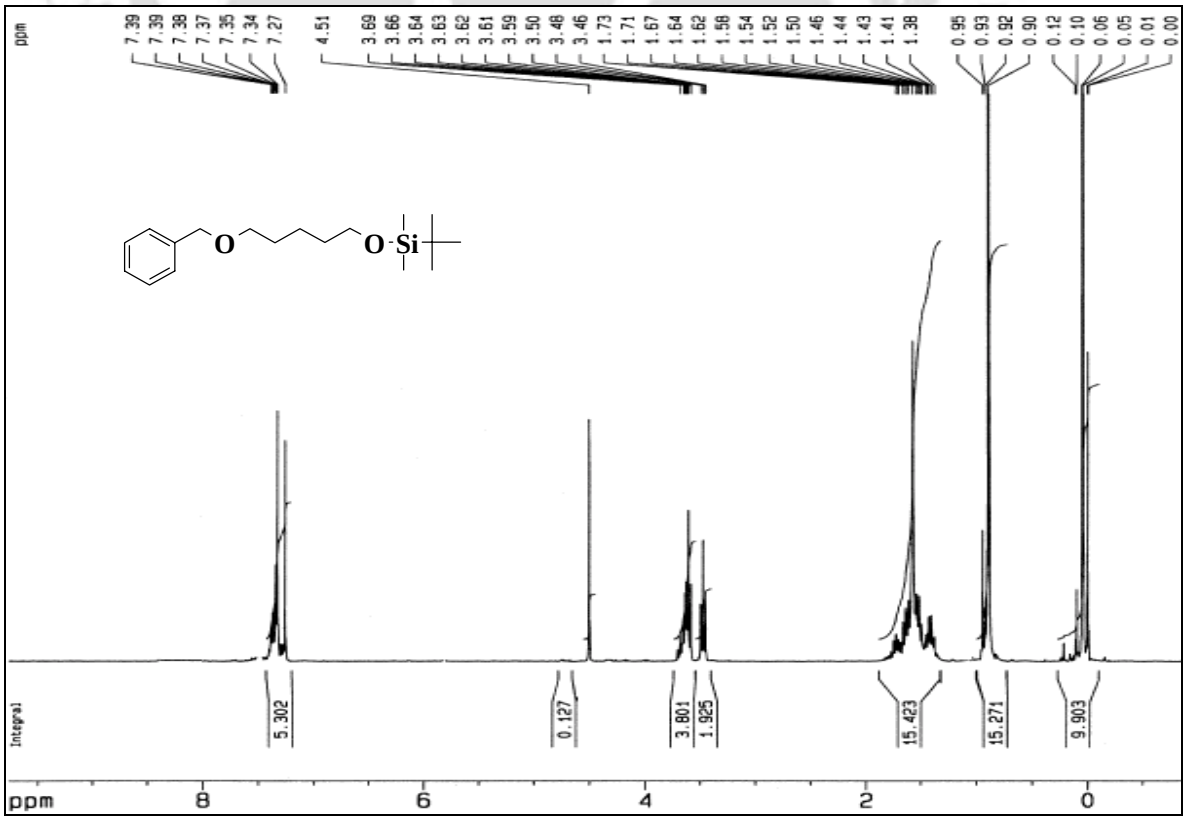
^{1}H NMR (400 MHz, $CDCl_3$): Cholesterol-4,4'-dimethoxytrityl ether (39o)



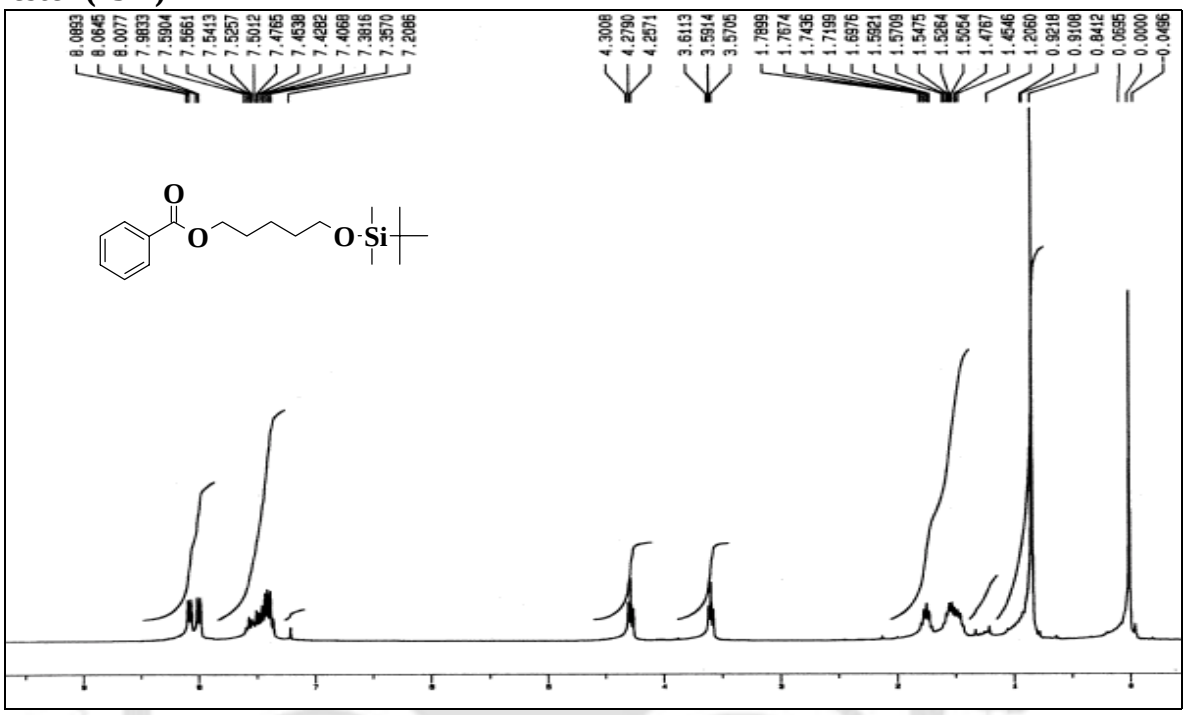
^{1}H NMR (400 MHz, $CDCl_3$): 5-Benzyloxy-pentan-1-ol (44)



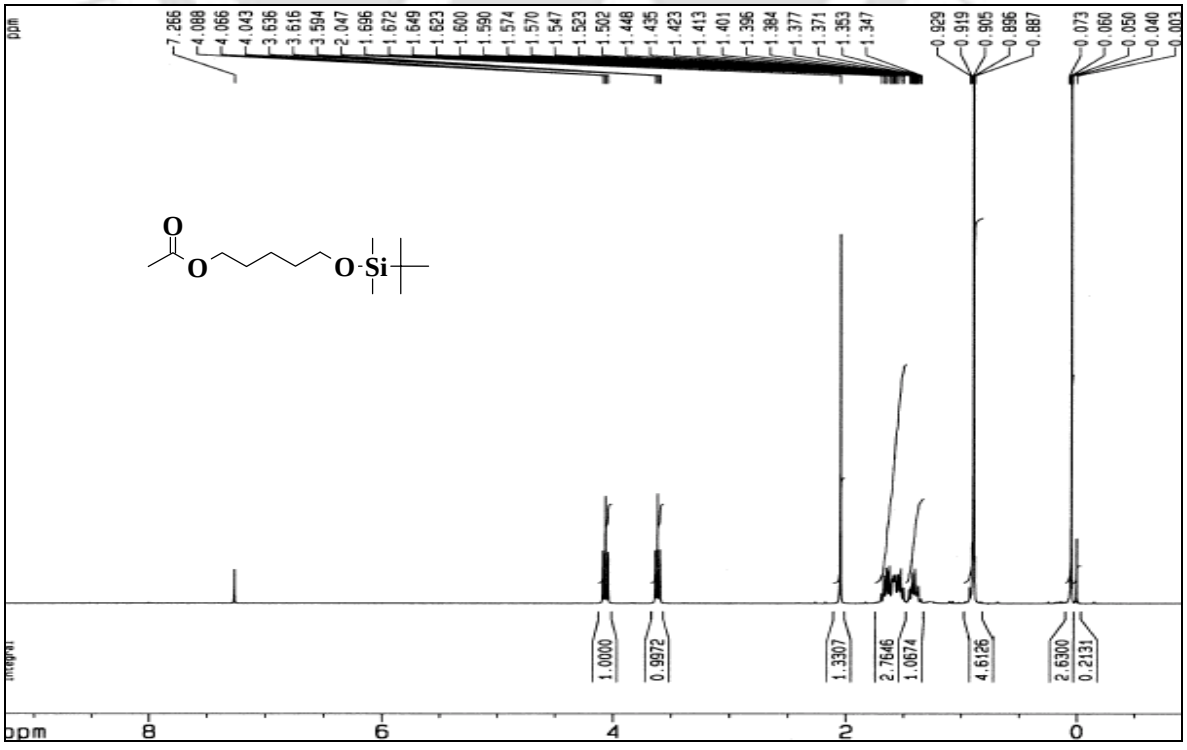
^{1}H NMR (400 MHz, $CDCl_3$): (5-Benzyloxy-pentyloxy)-*tert*-butyl-dimethyl-silane (44m)



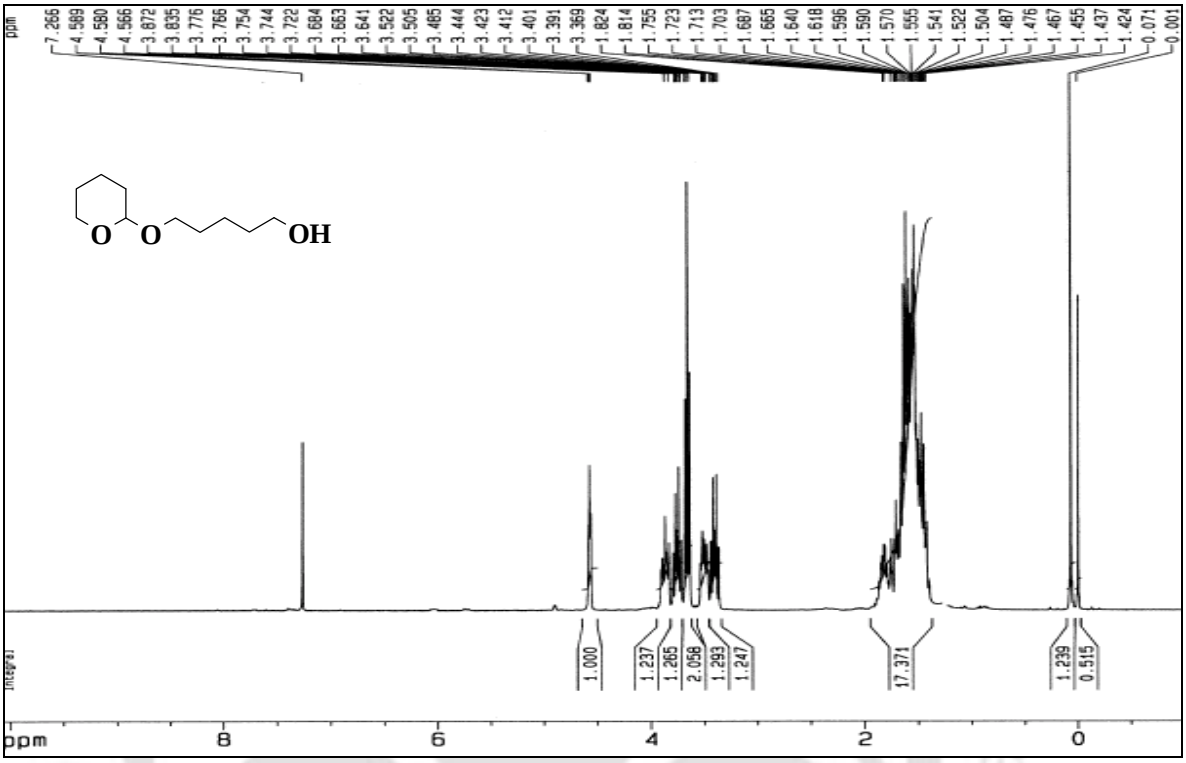
^{1}H NMR (400 MHz, $CDCl_3$): Benzoic acid 5-(*tert*-butyl-dimethyl-silanyloxy)-pentyl ester (45m)



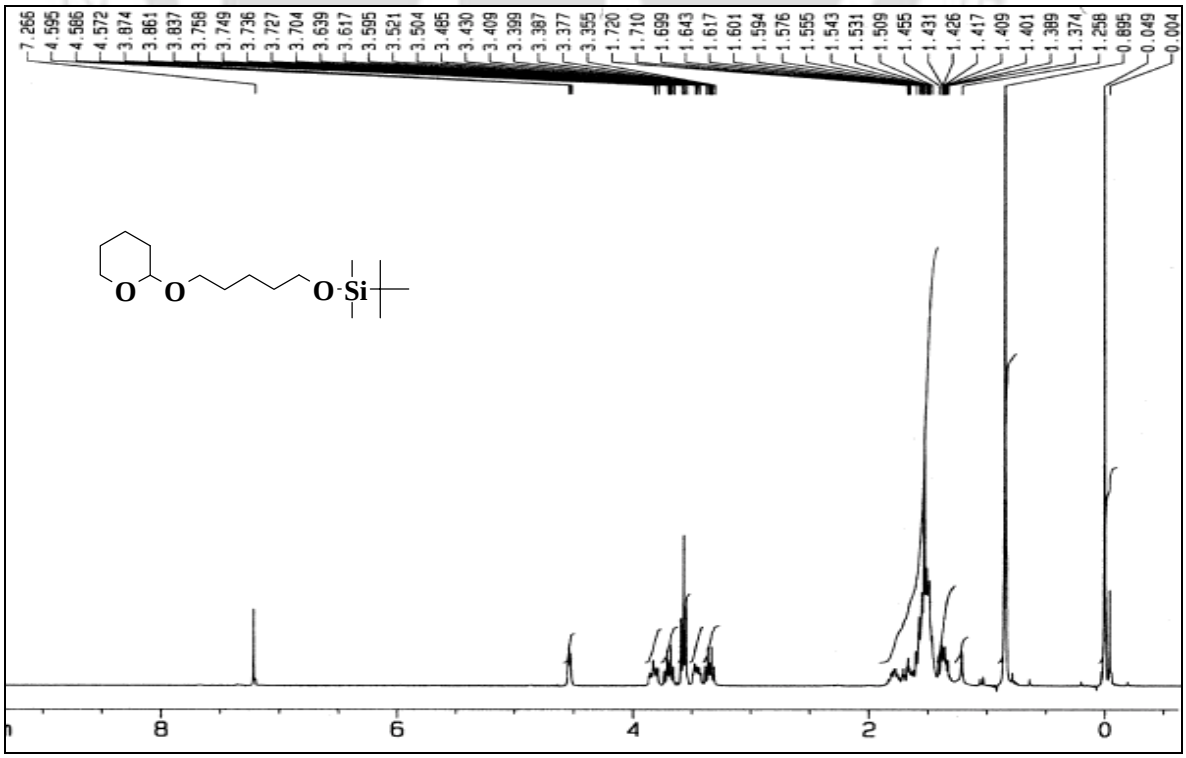
^{1}H NMR (400 MHz, $CDCl_3$): Acetic acid 5-(*tert*-butyl-dimethyl-silanyloxy)-pentyl ester (46m)



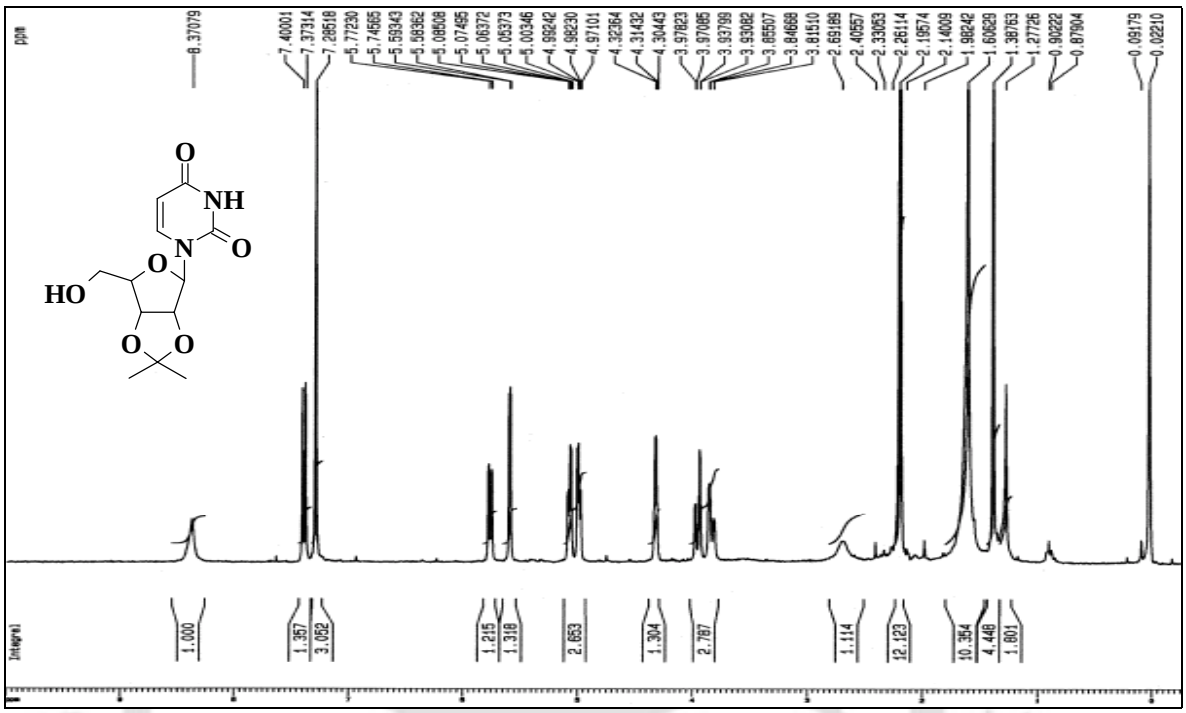
^{1}H NMR (400 MHz, $CDCl_3$): 5-(Tetrahydro-pyran-2-yloxy)-pentan-1-ol (47)



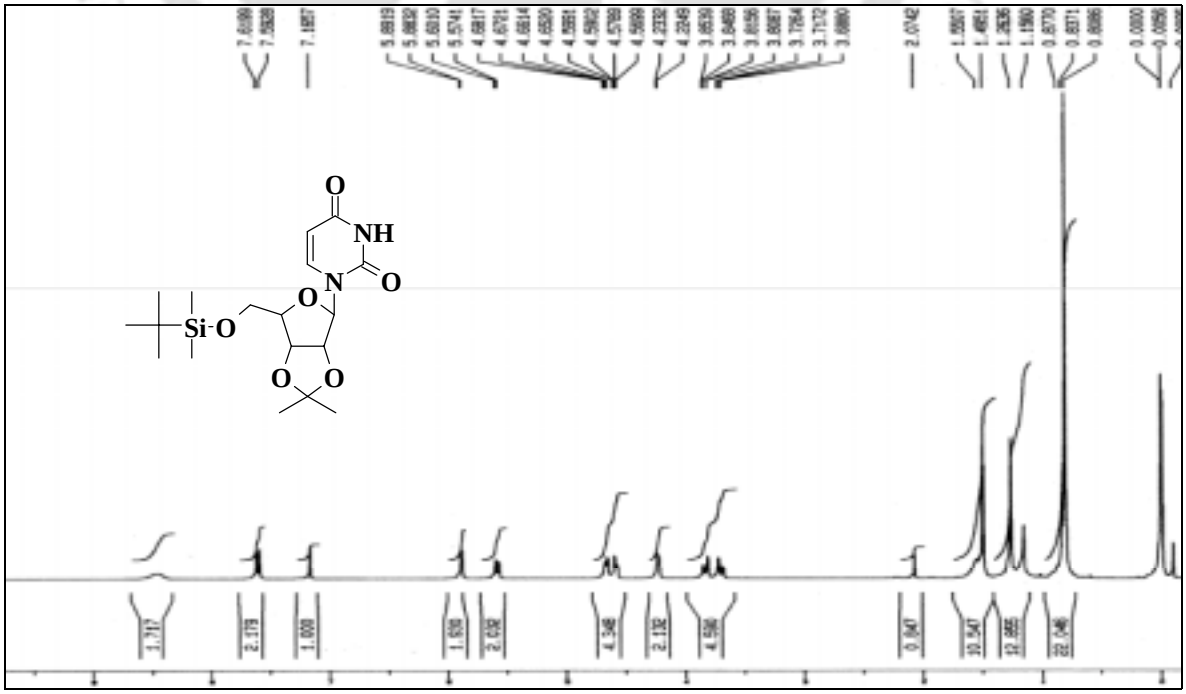
^{1}H NMR (400 MHz, $CDCl_3$): *tert*-Butyl-dimethyl-[5-(tetrahydro-pyran-2-yloxy)-pentyloxy]-silane (47m)



^{1}H NMR (400 MHz, DMSO-*d6*): 2',3'-Isopropylidene uridine (49)



^{1}H NMR (400 MHz, $CDCl_3$): 2',3'-Isopropylidene-5'-*O*-*tert*-butyldimethylsilyl uridine (49m)



List of Publications

1. Regioselective Bromination of Organic Substrates by Tetrabutylammonium Bromide Promoted by V_2O_5-H_2O_2: An Environmentally Favourable Synthetic Protocol
   Bora, U.; Bose, G.; Chaudhuri, M. K.; Dhar, S. S.; **Gopinath, R.**; Khan, A. T.; Patel, B. K. *Org. Lett.* **2000**, *2*, 247.
2. A Catalytic Oxidative Esterification of Aldehydes Using V_2O_5-H_2O_2
   Gopinath, R.; Patel, B. K. *Org. Lett.* **2000**, *2*, 577.
3. Tetrabutylammonium Tribromide (TBATB)-MeOH: An Efficient Chemoselective Reagent for the Cleavage of tert-Butyldimethylsilyl (TBDMS) Ethers
   Gopinath, R.; Patel, B. K. *Org. Lett.* **2000**, *2*, 4177.
4. Tetrabutylammonium Tribromide (TBATB) Promoted Tetrahydropyranylation / Depyranylation of Alcohols
   Naik, S.; **Gopinath, R.**; Patel, B. K. *Tetrahedron Lett.* **2001**, *42*, 7679.
5. Direct Oxidation of Acetals to Esters Using V_2O_5-H_2O_2
   Gopinath, R.; Paital, A. R.; Patel, B. K. *Tetrahedron Lett.* **2002**, *43*, 5123.
6. Tetrabutylammonium Tribromide (TBATB) as an Efficient Generator of HBr for an Efficient Chemoselective Reagent for Acetalisation of Carbonyl Compounds
   Gopinath, R.; Haque, Sk. J.; Patel, B. K. *J. Org. Chem.* **2002**, *67*, 5842.
7. Peroxovanadium Catalysed Oxidative Esterification of Aldehydes
   Gopinath, R.; Barkakaty, B.; Talukdar, B.; Patel, B. K. *J. Org. Chem.* **2003** (*in press*)