Indian Institute of Technology Guwahati
Guwahati 781 039
India

Newer Catalytic Methodologies for C-N, C-S Bonds Formation and Oxidation of Sulfides, Bromide and Alcohols with H_2O_2

Submitted by
Sahid Hussain
Supervisor: **Mihir K. Chaudhuri**
Department of Chemistry
June 2007

Newer Catalytic Methodologies for C-N, C-S Bonds Formation and Oxidation of Sulfides, Bromide and Alcohols with H_2O_2

A Dissertation Submitted to the

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As Partial Fulfillment for the Degree of

Doctor of Philosophy

Submitted by

Sahid Hussain
Department of Chemistry

to the

Indian Institute of Technology Guwahati

Guwahati-781 039

June 2007

Dedicated to

My Parents
and
Brother

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
Guwahati 781 039, India
Department of Chemistry

STATEMENT

I do hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology Guwahati, India under the guidance of Professor Mihir K, Chaudhuri, FASc., FNA.

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

June, 2007.
IIT Guwahati

Sahid Hussain

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
Guwahati 781 039, India

Dr. Mihir K. Chaudhuri, FASc., FNA
Professor, Department of Chemistry
Phone: +91-361-2582302
Fax: +91-361-2582349
E-mail: mkc@iitg.ernet.in

CERTIFICATE

It is certified that the work contained in the thesis entitled "**Newer Catalytic Methodologies for C-N, C-S Bonds Formation and Oxidation of Sulfides, Bromide and Alcohols with H_2O_2**" by Sahid Hussain, a student in the Department of Chemistry, Indian Institute of Technology, Guwahati for the award of degree of Doctor of Philosophy has been carried out under my supervision and that this work has not been submitted elsewhere for a degree.

June 2007.
IIT Guwahati

Mihir K. Chaudhuri
Supervisor

Vice Chancellor,
Tezpur University,
Tezpur 784 028, India
Phone: +91-3712-267003
Fax: +91-3712-267006
E-mail: mkc@tezu.ernet.in

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
Guwahati 781 039, India
Department of Chemistry

CERTIFICATE OF COURSE WORK

This is to certify that Sahid Hussain has satisfactorily completed all the courses required for the Ph.D degree program. These courses include

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

Sahid Hussain has successfully completed his Ph.D qualifying examination in April 2004.

Professor A. T. Khan
Head
Department of Chemistry
IIT Guwahati

Dr. Anil K. Saikia
Secretary
Departmental Post Graduate Committee
IIT Guwahati

INDIAN INSTITUTE OF TECHNOLOGY
GUWAHATI
Guwahati 781 039, India

Ph.D. GRADE CARD

Roll No.: 03612207 Department: Chemistry

Name: Sahid Hussain Semester: July 2003-April 2004

Course	Course Name	Credit	Grade
CH 603	Supra Molecules: Concept and Applications	6	BB
CH 611	Bioinorganic Chemistry	6	BB
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CH 630	A Molecular Approach to Physical Chemistry	6	BB

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

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Assistant Registrar
(Academic)

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And, I thank God for being there for me in a way no one else can.

(Sahid Hussain)

Abstract

Catalysis plays an important part in rendering chemical transformations very effective, highly selective and environmentally safer. Catalysis is indeed not only one of the principal tenets of 'Green Chemistry' but also is an integral part of it. The timely publication of a compendium on 'Green Chemistry and Catalysis' by Sheldon puts this point affirm beyond any scope of imagination. The invention of a new, clean and appropriate catalyst for a chosen transformation is extremely important. And for this, a clear understanding of the chemistry of a prospective catalyst or a catalytic system and the transformation on which the catalyst is to be applied upon is an essential prerequisite. The domain of catalysis thus expands by crossing boundaries of several sub-disciplines including bio and abio chemistry and material science, for instance. The world market of catalysts is *ca* 12 billion US dollars, and the chemical transformation leading to specific products through catalysis is estimated to be 1.2-6.0 trillion US dollars. This in itself underscores the need to develop practical catalytic processes involving homogeneous, heterogeneous and bio-catalysts. In fact, catalysis in one form or the other dominates the contemporary chemical literature. In consonance with the current trend and appreciating the need for clean chemistry practices, the present thesis has been framed mainly on the development of newer catalysts. The chosen organic transformations include aza- and thia-Michael condensations, selective oxidation of organic sulfides to the corresponding sulfoxides and the peroxo form of vanadium bromoperoxidase cofactor mimicking radical bromination of toluenes and electrophillic oxidation of benzylic alcohols to the corresponding aldehydes. The catalysts have been drawn from $Cu(acac)_2$[acac = acetylacetonate, $C_5H_7O_2^-$], $B(OH)_3$, $Na_2B_4O_7.10H_2O$, $(NH_4)_2HPO_4$ and two newly synthesized and fully characterized compounds, $[VO_2F(dmpz)_2]$ and $K[V(O_2)_3].3H_2O$. Water has been used as solvent as far as practicable and H_2O_2 has been our oxidant of choice. H_2O_2 is an innocuous reagent that produces water as the only by product thereby rendering it be an ecobenevolent chemical species. It can be highly cost effective if used in a controlled fashion.

The text of the thesis has been distributed over a total of six chapters. While **Chapter 1** is based on introduction and scope of the work, **Chapter 2** provides the details of materials and methods, and equipments that were used to characterize the products and do their physico-chemical studies. **Chapter 3** gives a full account of our endeavour on aza- and thia-Michael reactions involving $Cu(acac)_2$ immobilized in ionic liquids (IL), boric acid in water and borax in water as the catalysts. While investigating the thia-Michael reactions using $B(OH)_3$ or $Na_2B_4O_7.10H_2O$ as the catalysts, some of the condensed products attracted our attention as prospective candidates for studying their self-assembled H-bonding interactions in the crystal lattice. Accordingly, X-ray crystallography of

three β-sulfidocarbonyls was carried out and some interesting observations were made. These results constitute, in part, the subject matter of this chapter.

In pursuance of a sustained activity of our laboratories on oxidation chemistry, catalytic oxidation of organic sulfide selectively to sulfoxide was chosen as a part of the present Ph. D. research project. The targeted selective oxidation has been achieved with H_2O_2 as the terminal oxidant and each of the following, i.e., Borax, $(NH_4)_2HPO_4$ and $VO_2F(dmpz)_2$ as the catalyst. The reactions have been conducted in water. Synthesis and complete characterization of the catalyst, $[VO_2F(dmpz)_2]$, have been disclosed. The results of these studies constitute, in large part, the text of **Chapter 4.** As a logical extension of this work, oxidative desulfurization of diesel using $[VO_2F(dmpz)_2]$–H_2O_2 has been achieved with reasonable success. The result of this endeavour has been incorporated in this chapter. Radical bromination of toluenes to the corresponding benzyl bromide in water without the direct use of Br_2, but by Br^-, H_2O_2 and $K[V(O_2)_3].3H_2O$ as the precatalyst has been successful. The same precatalyst also enabled electrophillic oxidation of benzylic alcohols by H_2O_2 selectively to the corresponding aldehydes in very good yields. The active catalyst has been identified to be a μ-hydroxo(dioxo)tetraperoxodivanadate(V) species, $[(O_2)_2OV–(OH)–VO(O_2)_2]^{3-}$, as ascertained from the results of physico-chemical studies including X-ray crystallography. This catalysis has been modeled on the oxidized form of vanadium bromoperoxidase (VBrPO) reactivity. In addition, $[VO_2F(dmpz)_2]$ has been shown to be a good VBrPO–mimicking catalysts that is capable of efficiently catalyzing the oxidative extraction of bromide (Br^-) from "bittern" (slightly concentrated sea water) with H_2O_2 in presence of an acid. The oxidized bromide has been identified as tribromide Br_3^-, that was thwarted out of the solution with the help of tetrabutylammonium cation. The final product i.e. tetrabutylammonium tribromide (TBATB) has been characterized and its structure determined by X-ray studies. A nearly quantitative extraction was possible in this way. A comprehensive account of this work has been presented in **Chapter 5**. The thesis concludes with a small presentation of a piece of work that addresses the microwave assisted synthesis of quinolines[10] from *o*–notrobenzaldehyde and enolizable ketones in the presence of $SnCl_2.2H_2O$ as the reductant. **Chapter 6** contains an interpretative account of this work. Each chapter has been made self-contained with sections on introduction, experimental and results and discussion followed by the relevant bibliography.

A brief content of each chapter is set out below.

Chapter 1. Introduction and Scope of Work in the Area

This chapter presents a brief account of prior arts of reactions in water and ionic liquids, as well as the peroxo-based oxidation chemistry. Importance of C-N, C-S bonds formation and oxidations of sulfides, bromide and alcohols with H_2O_2 in the field of organic synthesis are highlighted. It also emphasizes the need for development of safe and cost effective biomimetic catalysts and catalytic systems for various industrially important reactions. Apart from this importance of microwave in organic reactions are discussed.

Contemporary importance of the chosen aspects of chemistry selected for the present Ph. D. research provides a distinct scope of the work and much more beyond.

Chapter 2. Details of Materials, Methods and Equipment

The sources of chemicals and solvents, methods for quantitative chemical estimations, determination of elements and details of all the equipment used for physico-chemical studies are provided in this chapter. The characterization was done using appropriate physico-chemical techniques.

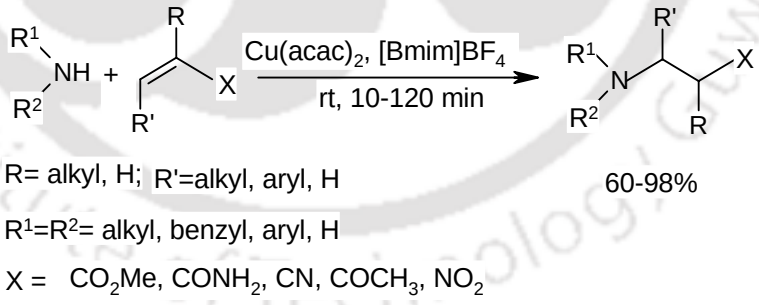
Chapter 3. Catalytic Hetero-Michael Reactions

The Michael reaction since its discovery in 1889 has been one of the most frequently studied reactions in organic synthesis for C-C, C-N, C-O and C-S bonds formation. The conjugate addition of a nitrogen or sulfur nucleophile to an electron rich or electron deficient electrophile, known as aza- or thia-Michael reaction to form a C-N or C-S bond, respectively, constitutes a key reaction in biosynthesis as well as organic synthesis. β-Aminocarbonyl and β-thiocarbonyl compounds are the adducts of aza- and thia-Michael reactions, respectively, usually encountered in naturally occurring biologically active compounds such as alkaloids and polyketides and are widely used throughout the chemical industry as a basic intermediate to prepare pharmaceutically or agrochemically useful chemicals. Owing to their wide ranging biological properties, they are much sought after as chemotherapeutic agents for the treatment of various diseases. They serve as essential intermediates in the synthesis of γ-amino alcohols, diamines, β-amino acid derivatives, β-lactam antibiotics, β-acylvinyl cation, homoenolate anion equivalents, β-calcium antagonist diltiazem and natural products. The thia-Michael reaction also provides an elegant strategy for the

chemoselective protection of the olefinic double bond of conjugated enones due to ease of generation of the double bond through removal of the sulfur moiety by copper(I) induced oxidative elimination. Some thia-adducts of amides are known to have topical relevance to the investigation of host-guest interactions and are also useful as photographic development accelerators. Consequently, the development of newer and practical synthetic routes to these important compounds has stimulated constant interest of many research groups over the years. **Chapter 3** reports a few newer methods for aza-, thia-Michael reactions and X-ray structure of three β-sulfidocarbonyls. In order to make the presentation expressive, **Chaper 3** has been divided into four sections.

3.1 $Cu(acac)_2$ Immobilized in Ionic Liquids: A Recoverable and Reusable Catalytic System for Aza-Michael Reactions

Copper(II) acetylacetonate immobilized in ionic liquids has been shown to efficiently catalyze the aza-Michael reaction of amines with α,β-unsaturated carbonyl compounds to produce the corresponding β-amino carbonyl compounds with great alacrity in excellent yields (**Scheme 3.1**). The reactions are far more facile than those reported earlier. The methodology works very well using a low catalyst loading with easy catalyst and solvent recycling. This method is capable of being scaled up, if desired.

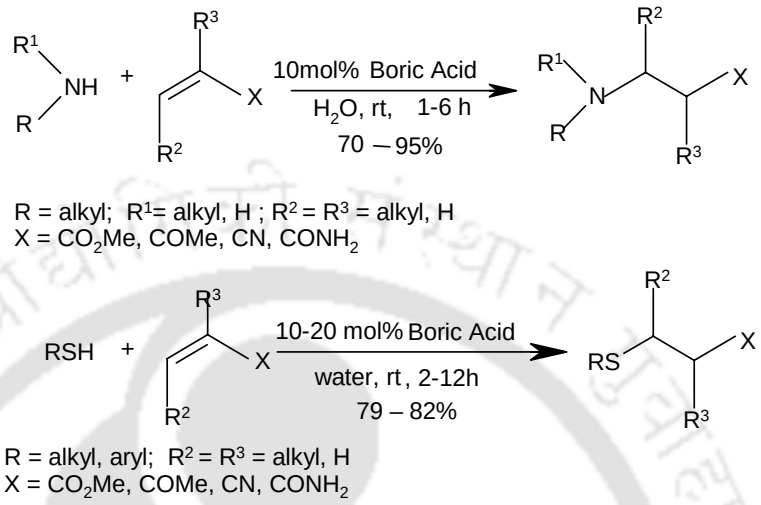


Scheme 3.1

3.2 Boric Acid: A Novel and Safe Metal-Free Catalyst for Aza- and Thia-Michael Reactions

Boric acid efficiently catalyzes the conjugate addition of amines or thiols to α,β-unsaturated compounds to produce β-amino and thia-compounds, with great alacrity and excellent yields, in water under mild conditions (**Scheme 3.2**). Aromatic amines do not participate effectively in the reaction. The use of boric acid, being a safe chemical, as the catalyst and water as the reaction medium are important attributes in the present protocol. The reaction is capable of being performed

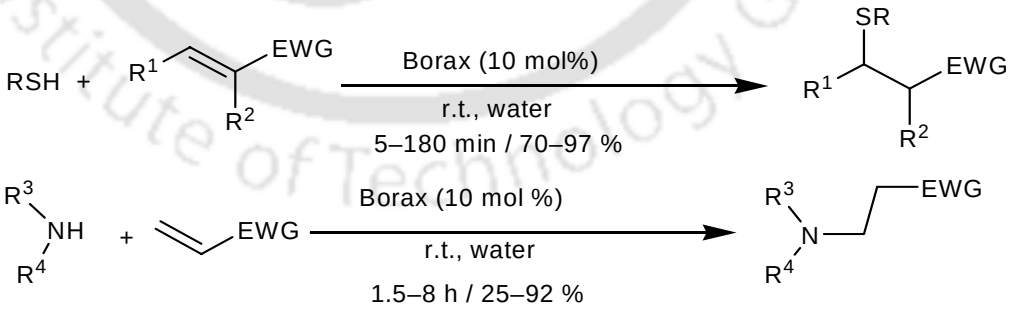
neatly in the chosen solvent at ambient temperature without catalyst poisoning. The thia-Michael reactions can be performed in ethanol or methanol, as reported in this section.



Scheme 3.2

3.3 Borax as an Efficient Metal-Free Catalyst for Hetero-Michael Reactions

Borax, a naturally occurring material, very efficiently catalyzes the conjugate addition of thiols, dithiols and amines to α,β-unsaturated ketones, nitriles, amides, aldehydes and esters in aqueous medium to afford the corresponding Michael adducts in good yields at room temperature (**Scheme 3.3**). Recycling of the catalyst and scaling up of reactions are important attributes in this catalysis. The reactions of thiols and dithiols were relatively more facile than the corresponding amines.



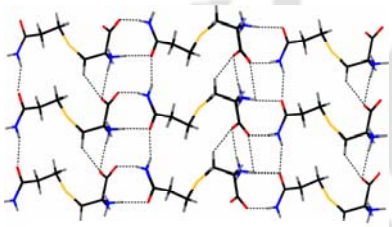
Scheme 3.3

An internal comparison of the results of thiol additions with those of amine additions, under similar experimental conditions, shows that the former are more facile than the latter. Indeed, this

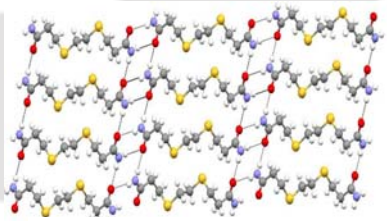
observation is in agreement with the result of some earlier kinetic studies. Based on kinetic data it was predicted that –SH groups were many times more reactive than amines in aqueous alkaline solution. A comparison of the present results with those of the corresponding boric acid catalyzed aza-Michael reactions suggests that under similar experimental conditions borax appears to be either as good as or somewhat better than boric acid in catalyzing the chosen reactions.

3.4 X-Ray Studies on β-Sulfidocarbonyls Evidencing Intermolecular Hydrogen Bonded Self-Assembled β-Pleated Sheet Structures

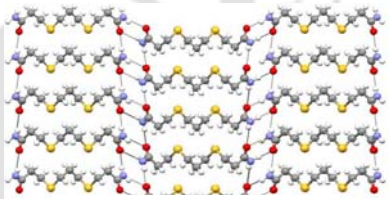
In the course of our research endeavor in this area, three crystalline compounds were obtained by the conjugate addition of cysteine, 1,2 and 1, 3 dithiols each to acrylamide catalyzed by borax in water at room temperature. The compounds have been characterized well by chemical analyses, IR and NMR spectroscopic studies. The hitherto unprecedented crystal structures of the chosen compounds not only support their molecular structures but also provide evidence for strong intermolecular hydrogen bonding with β-sheet type of molecular rearrangement in addition to the occurrence of rather unconventional C–H---O and C–H---S type of H-bonding in the crystal lattice.



*Crystal packing in adduct **1***



*Crystal packing in adduct **2***



*Crystal packing in adduct **3***

It is expected that the chosen compounds might serve as suitable probes to study hydrogen-bonding interactions in (*c.f.* protein structure) and obtain insights into the realm of sulfidoamide chemistry.

Chapter 4. Development of New Catalysts for Selective Oxidation of Sulfides with H_2O_2

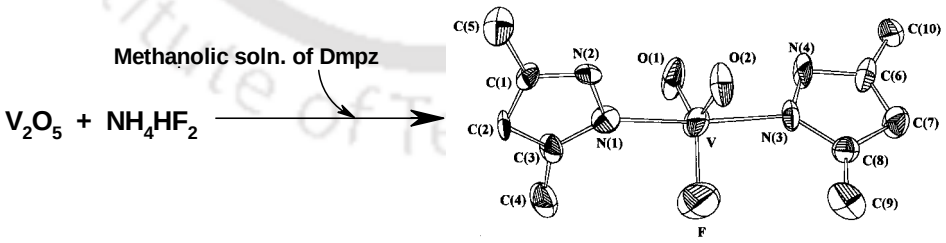
Apart from the transformations highlighted above, oxidation is a widely used multifarious chemical process having application in almost all of the important fine and specialty chemical industries manufacturing pharmaceuticals, agrochemicals etc. A wide variety of reagents, catalysts and catalystic systems were developed and well documented. Endeavor has been made to overcome the problems associated with oxidation such as overoxidation and less selectivity. Some

success has been achieved but search is still on to get an ideal process. In the current scenario, the bio-inspired, or metal-free, catalysis seems to be the safest option since the nature allows the bioorganic reactions utilizing enzyme vanadium bromoperoxidase (VBrPO) as the catalyst for bromination and oxidation (*c.f.* organic sulfides) of the required organic molecules. The knowledge obtained from our studies on peroxo vanadium chemistry and the literature information on VBrPO reactivity encouraged us to develop new and cleaner protocols for oxidations.

In this chapter, we have described the oxidation of sulfides with a newly synthesized vanadium complex $[VO_2F(dmpz)_2]$, borax or phosphate as the catalyst and H_2O_2 as the oxidant. As a logical extension, oxidative desulfurization of diesel was attempted with $[VO_2F(dmpz)_2]$–H_2O_2 and a reasonable success has been achieved. A brief account of this experiment has also been included in this chapter.

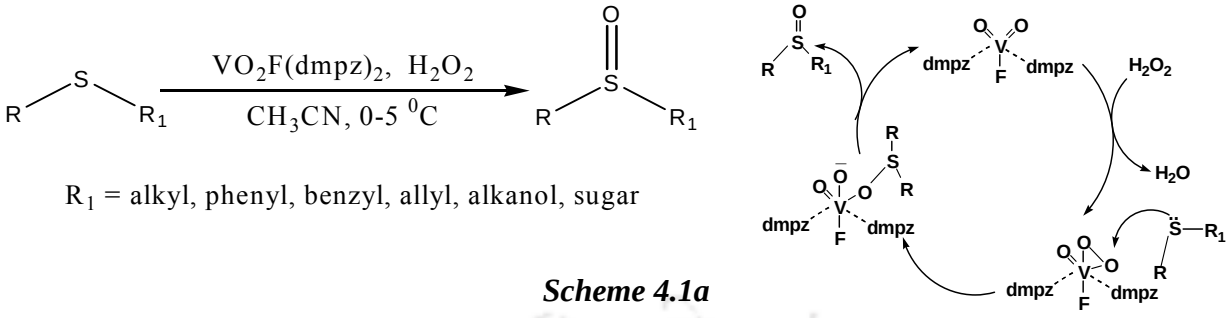
4.1 Development of a New Catalyst $[VO_2F(dmpz)_2]$ for Oxidation of Organic Sulfides

The synthesis $VO_2F(dmpz)_2$ has been achieved by conducting the reaction of V_2O_5 with NH_4HF_2 and 3,5-dimethyl pyrazole under the specified conditions. It has been ascertained from repeated reactions that pH=4.2 of the reaction is crucial for its successful synthesis. The lemon yellow compound is stable for a long period. The single crystal X-ray analysis shows that the compound is a penta coordinated vanadium (V) mononuclear species.



ORTEP view of $VO_2F(dmpz)_2$

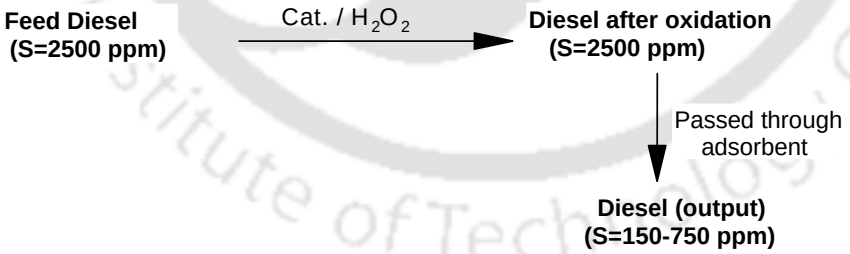
Coordinative unsaturation of vanadium(V) in $[VO_2F(dmpz)_2]$ provides an additional site for H_2O_2 coordination and the resemblance of pyrazole with imidazole set some arguments in favor of VBrPO mimic. And with the so designed mimic, we carried out oxidation reactions of sulfides (**Scheme 4.1a**) with H_2O_2.



Scheme 4.1a

Various aliphatic and aromatic groups attached to sulfur atom and refractory sulfur (e.g. dibenzothiophene (DBT), 4-methyl-DBT and 4,6-dimethyl DBT) compounds were subjected to oxidation with H_2O_2 catalyzed by $VO_2F(dmpz)_2$. The oxidations were selective affording sulfoxides. In case of allylic sulfides oxidation, sulfoxides were formed without the cleavage of carbon-carbon bond.

As a sequel to our research and in view of the pressing need for reducing the sulfur content of diesel to an ultra low level, it was thought worthwhile to try out the efficacy of the newly developed catalyst for the purpose. Accordingly, the $[VO_2F(dmpz)_2]$–H_2O_2 system was applied to diesel containing >2200 ppm of sulfur (**Scheme 4.1b)**. The fuel containing oxidized organic sulfurs was purified by passing through an adsorption column packed with Al_2O_3 and activated charcoal (90:10). The output was found to contain 150-700 ppm of sulfur. This process has been scaled up to 2 L.

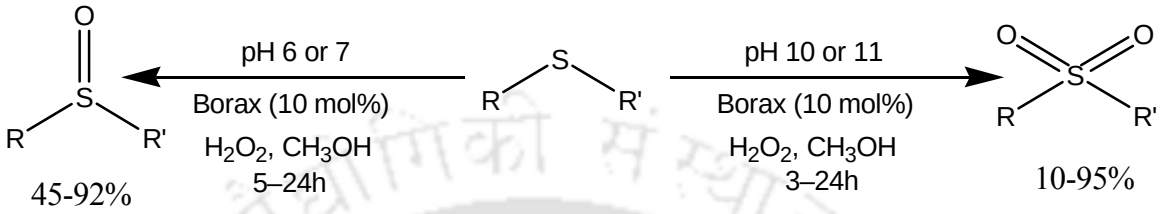


Scheme 4.1b

4.2 Borax and Phosphate Catalyzed Selective Oxidation of Organic Sulfides

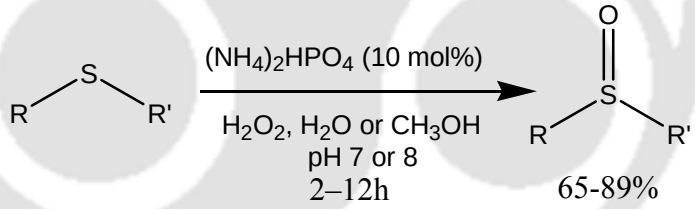
The selective oxidation of sulfides to sulfoxides and sulfones has been achieved in high yields at room temperature with borax as a recyclable catalyst and H_2O_2 as the terminal oxidant by varying pH of the reaction medium (**Scheme 4.2**). The borax–H_2O_2 system can chemoselectively oxidize alkyl as well as aryl sulfides in presence of oxidation prone functional groups such as C=C, –CN, –OH. Some refractory sulfides, *viz*, dibenzothiophene (DBT) and 4-methyl-DBT are also

capable of being oxidized quite effectively though with less selectivity. The oxidations of DBTs are especially important in the context of transportation fuel chemistry research targeting desulfurization of diesel and gasoline, for instance.



Scheme 4.2

Selective oxidation of organic sulfides to the corresponding sulfoxides seems to be possible with $(NH_4)_2HPO_4$, as well. Thus, $(NH_4)_2HPO_4$–H_2O_2 oxidized a variety of organic sulfides at pH 7 or 8 (**Scheme 4.3**). The reaction worked well in the chemoselective oxidation of sulfides in presence of C=C, –CN –OH groups. Unfortunately, the catalytic system could not bring about the oxidation of refractory sulfurs. A comparison of the results of borax catalyzed reaction with those of $(NH_4)_2HPO_4$, clearly suggests that the former is a better catalyst.



Scheme 4.3

Chapter 5. VBrPO-Mimicking Catalysis in Water for Radical Bromination as well as Electrophillic Oxidation, and Oxidative Extraction of Bromide from Sea Water

Environmentally cleaner access to benzyl bromides, which serve as precursors of benzyl alcohols, appears to be quite a synthetic challenge, while the global requirement for benzaldehydes that are obtained from the corresponding alcohols is very high (> 20,000 tons per year). Benzyl halides including benzyl bromides are synthesized from the corresponding toluenes. Benzylic bromination of toluenes is accomplished by radical bromination. The bromination of organic molecules with molecular bromine is fraught with the problems of handling transportation and use owing to its high toxicity and corrosive nature. To ease out the problems several methods were developed, but the brominating agents used therein are not ecobenevolent, not easy to handle and

are highly toxic. In the given situation, bio-inspired catalysis seems to be the promising option since the nature allows such reactions utilizing vanadium bromoperoxidase (VBrPO) enzyme as the catalyst for bromination of the required organic molecules.

Besides the radical bromination, oxidation of alcohols to aldehydes or ketones is a fundamental transformation in chemical industries. However, green catalytic oxidation of benzyl alcohols as opposed to the spate of stoichiometric oxidations is a relatively grey area that needs attention because most of the several green procedures have been based on costly metals thereby rendering the process economically non viable, in many instances.

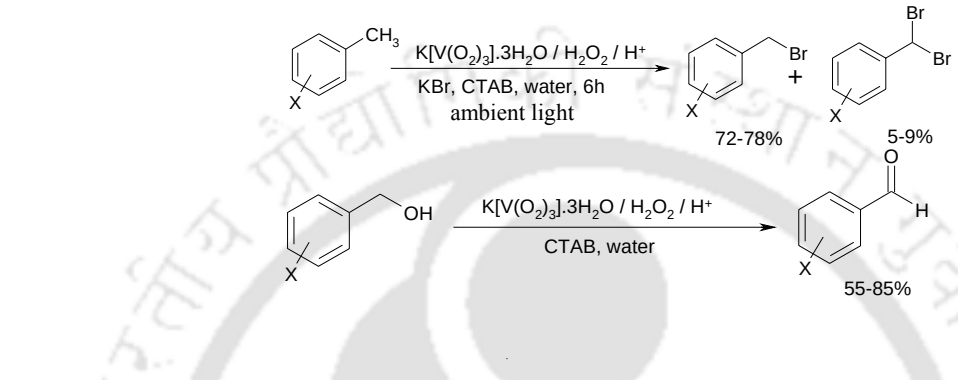
In view of this and also because of the availability of a highly peroxygenated vanadium(V) species, $[V(O_2)_3]^-$, at our disposal, it was considered quite apt to use this as a precatalyst for oxidative brominations, and selective oxidation of alcohols with H_2O_2. While we were engaged in the triperoxovanadate(V) catalyzed reactions, it was observed that our $[VO_2F(dmpz)_2]$ catalyst very efficiently catalyzed the oxidation of bromide to tribromide, Br_3^-, by H_2O_2. This encouraged us to try out the oxidative extraction of bromide from sea water using this catalyst.

5.1 An Improved Synthesis of $[K(V(O_2)_3].3H_2O$ and its Use as a Precatalyst for Radical Bromination and Oxidation

The synthesis of $[K(V(O_2)_3].3H_2O$ has been achieved from the reaction of V_2O_5 with H_2O_2 in the presence of relatively large concentration of alkaline medium with the molar ratio of V_2O_5 : H_2O_2 : KOH being maintained at 1: 42 : 9. The complex was obtained by the addition of ethanol, which facilated precipitation. The temperature, time and order of addition of the reagents play crucial role in successful synthesis of the catalyst. A minor change in the reaction conditions leads to the formation of mixed peroxo complexes.

We have investigated benzylic bromination of toluene and selective oxidation of benzyl alcohols with H_2O_2 as the terminal oxidant and the optimal reaction conditions have been worked out. Under the optimized reaction conditions, a wide variety of toluene and benzylic alcohols were converted to their corresponding benzyl bromide and benzaldehyde selectively and efficiently in good yields (**Scheme 5.1)**. The catalyst can be recycled five times without the loss of activity. The procedures are scaled up upto 10 g and 5 g for toluene and benzyl alcohol, respectively. The peroxovanadium complex isolated from the aqueous solution at pH 4 or 5 before the reactions as well as after extracting the oxidized product from the reaction mixture was identified as

$K_3[(O_2)_2OV\text{-}(\mu\text{-}OH)\text{-}VO(O_2)_2].H_2O$. This is indeed the active catalyst. Based on the present studies and the knowledge gathered from the studies of peroxovanadium chemistry, we proposed the reaction mechanisms as given in Figs. 1 and 2. The yield of the targeted product in each case has been good to very good.



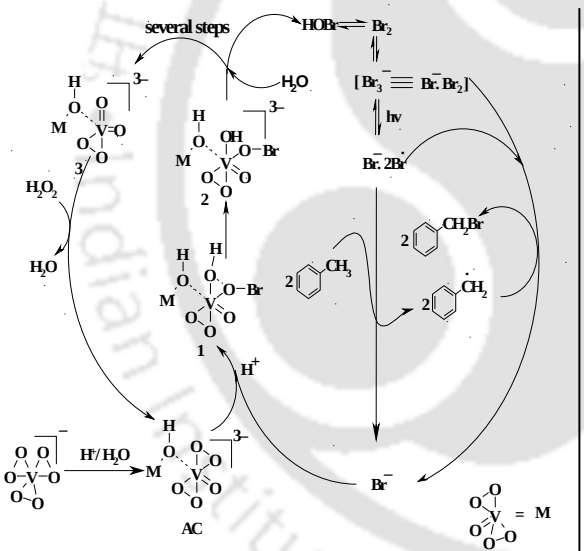


Fig. 1. Plausible mechanism for free radical bromination

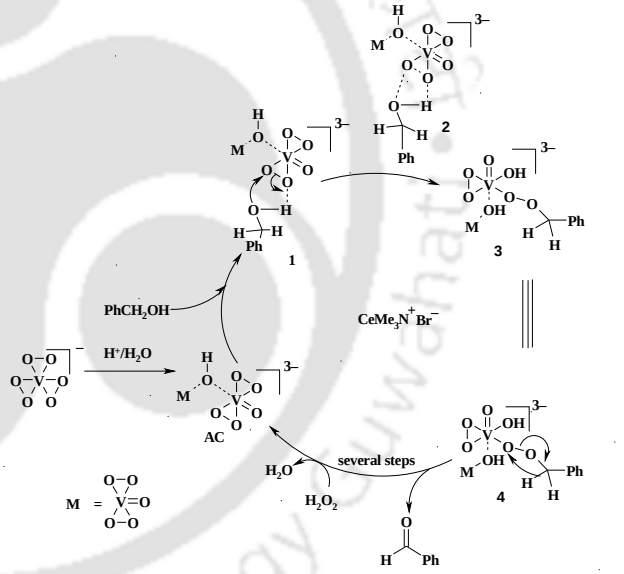


Fig. 2. Plausible mechanism for benzyl alcohol oxidation

5.2 $[VO_2F(dmpz)_2]$ Catalyzed Oxidative Extraction of Bromide from Sea Water

The fact that the peroxo form of the enzyme vanadium bromoperoxidase (VBrPO) catalyzes the oxidative bromination of organic molecules in the marine environment, and that VBrPO mimicking catalysts catalyze the *in situ* oxidation of Br^- to Br_3^- by H_2O_2 in the presence of catalytic amount of acid is highly significant in the realm of peroxovanadium(V) chemistry. By analyzing the bio and abiotic events, it was anticipated that a suitable VBrPO mimicking catalyst

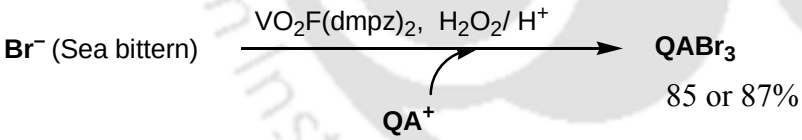
might enable extraction of bromide from sea water in a very soft way. Accordingly, several catalysts have been developed in our laboratories and the performance of $[VO_2F(dmpz)_2]$ as a representative example has been reported in this section. A slightly concentarted pre-analysed sea water generally known as 'bittern' was obtained from a bromine producing industry (Tata Chemicals Ltd., India). The bromide content of the bittern was 2 g/L.

In the present study, $[VO_2F(dmpz)_2]$ has been shown to efficiently and selectively catalyze the oxidation of Br – in bittern by H_2O_2 in the presence of a small amount of acid. The oxidized bromide has been isolated from the water solution using either tetrabutyl ammonium or benzyltriethyl ammonium ion as the corresponding tribromide. The extraction of the Br^- has beeen found to be very high (85%).

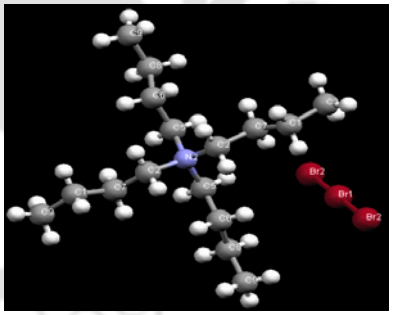
QA^+= Tetrabutylammonium or Benzyl triethyl ammonium

Scheme 5.2a

The identity of the compound has been ascertained from the results of IR, UV and X-ray crystallography.



QA^+= Tetrabutyl ammonium or Benzyltriethyl ammonium

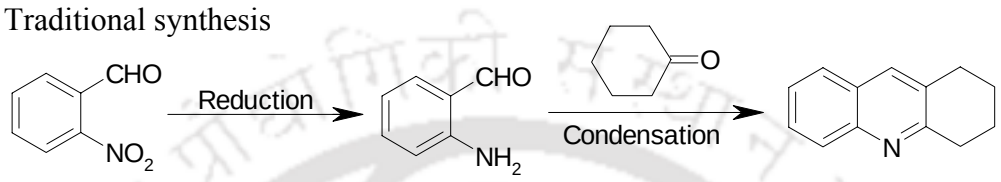


Scheme 5.2b

Chapter 6. Microwave Assisted Synthesis of Quinolines

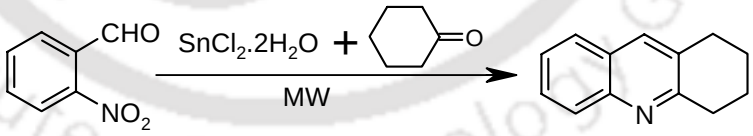
The Friedlaender synthesis of quinolines is a classic method, that involves two steps, wherein reduction of *o*-nitro aryl aldehyde is first achieved followed by the condensation of enolizable carbonyl compound in presence of a Brønsted acid or a Lewis acid catalyst. The relative instability of the intermediate, *o*-amino aldehyde, with its strong tendency to undergo self-condensation rendered such reactions rather complicated. Subsequently, the synthesis has undergone several modifications over the years. Considering the development, it was quite

imperative that quinolines synthesis required further attention to obviate the need to maintain stringent experimental conditions, use of expensive catalysts, and prepare and isolate the *o*-amino carbonyls as synthetic precursors.



Scheme 6.1

In view of the above, a relatively more versatile yet simplified procedure was perceived based on the reasoning that the substrates like *o*-nitrobenzaldehyde and enolizable ketones could be made to interact in the presence of $SnCl_2$ under microwave irradiation without using any solvent. Our arguments have been that under microwave irradiation, the reduction of *o*-nitrobenzaldehyde by $SnCl_2$ to the corresponding amino derivatives, *in situ* enolization of the chosen ketones, and enhanced dipole-dipole interactions between the activated reaction intermediates would lead to an instantaneous condensation to afford quinolines without the use of any solvent or catalyst. The strategy worked well affording the desired products in respectable yields (Scheme 6.2).



Scheme 6.2

This protocol is applicable to a wide range of enolizable ketones (cycloalkyl, *n*-alkyl, alkyl aryl). It is evident from the results that alkyl and cycloalkyl enolizable ketones readily cyclized with the *in situ* generated *o*-amino benzaldehyde to afford the corresponding quinolines in good to very good yields. **Chapter 6** is based on a relatively small piece of work entailing this study.

Introduction and Scope of Work

1A. Introduction

It is widely acknowledged that there is a growing need for more environmentally acceptable processes in the chemical industry. This trend towards what has become known as 'Green Chemistry' or 'Sustainable Technology'[1-9] necessitates a paradigm shift from traditional concepts of process efficiency, that focuses largely on chemical yield, to one that assigns economic value to eliminating waste at source and avoiding the use of toxic and/or hazardous substances. As a part of an on going programme of the laboratory where the present Ph. D. research was carried out, development of newer catalysts or catalytic formulations takes an important share. As well documented, catalysts or catalytic formulations, which are characterized by a much lower production volume and much higher added value, find wide applications in the domain of fine and bulk chemicals, agro chemicals and pharmaceuticals.

Noncatalytic stoichiometric organic transformations using conventional reagents are still being used in the production of a wide variety of pharmaceuticals, fragrances and agrochemicals, etc. Despite the important role still played by stoichiometric reagents, the general trend is the development of catalytic processes to replace traditional stoichiometric reagents. An obvious reason for this has been the global concern for making chemical processes more catalytic rather than stoichiometric thereby rendering the protocols more cost-effective, efficient and selective also reducing the burden on the environment.

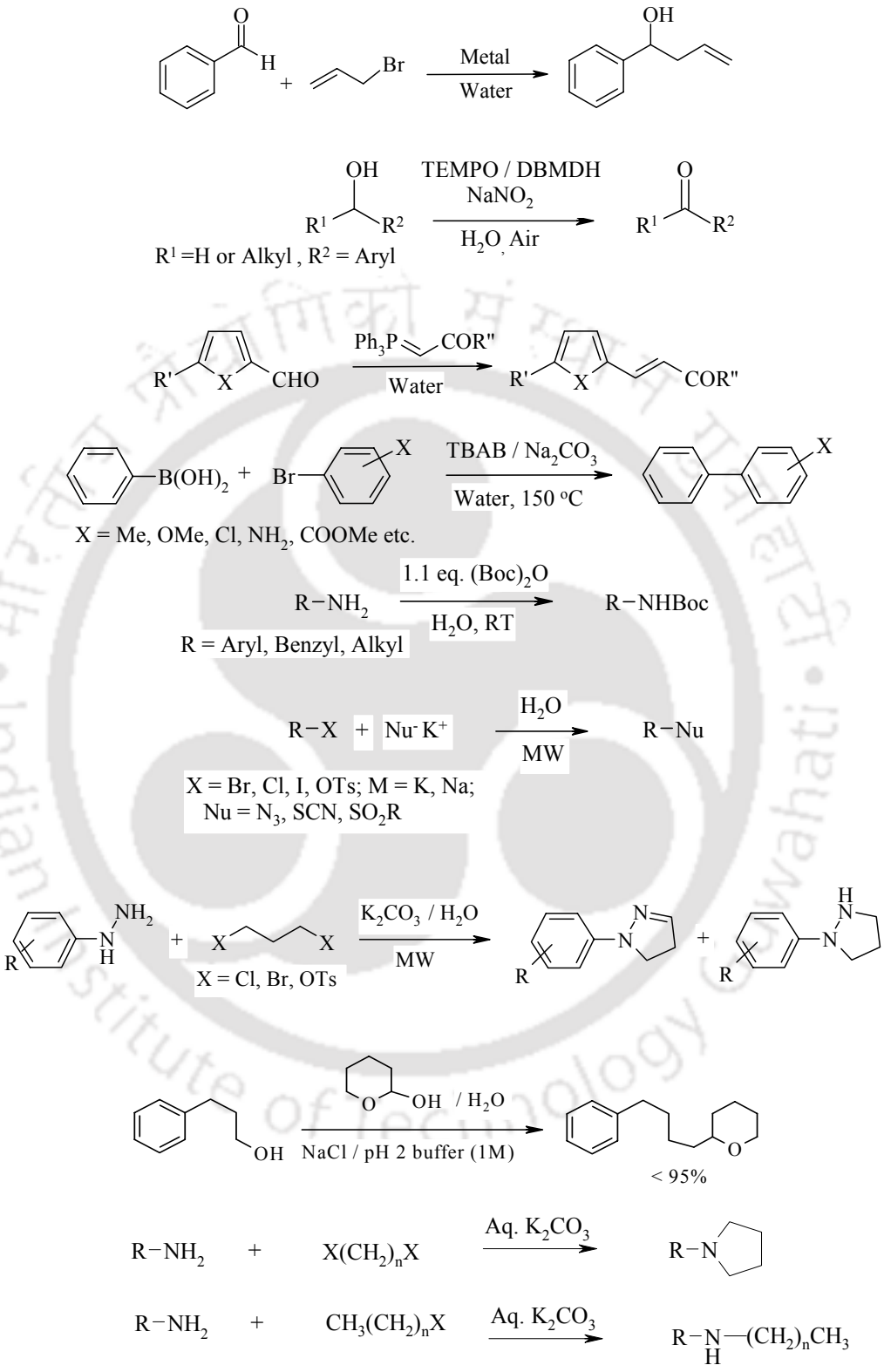
Catalysis plays an important part in rendering chemical transformations very effective, highly selective and environmentally safer. Catalysis is indeed not only one of the principal tenets of 'Green Chemistry' but also is an integral part of it. The invention of a newer, clean and appropriate catalyst for a chosen transformation is extremely important. And for this, a clear understanding of the chemistry of a prospective catalyst or a catalytic system as well as the transformation on which the catalyst is to be applied upon is an essential prerequisite. The domain of catalysis thus expands by crossing boundaries of several sub-disciplines including bio and abio chemistry and material science, for instance. The world market of catalysts is *ca* 12 billion US dollars, and the chemical transformations leading to specific products through catalysis is estimated to be 1.2-6.0 trillion US dollars.[2] This in itself underscores the need for developing practical catalytic processes involving homogeneous, heterogeneous and bio-catalysts.

Catalyses were performed in a chosen organic solvent, which provided a homogeneous reaction medium for distribution of the reactant over a wide range of concentration. Though

homogeneous catalysis in organic solvent is characterized by superior activity and selectivity but it usually involves a cumbersome process of separation of catalyst from reaction products and lowers activity of the recovered catalyst, in many instances. Taking these shortcomings into account, one would like to opt for either or both the following alternatives: (i) *use of water as the solvent of choice in case of water soluble catalysts* and (ii) *heterogenization of the homogeneous catalysts by immobilization.* In fact the potential advantages[10,11] of replacing organic solvents with water are the following: (i) use of 'water as solvent' provides homogeneous medium for high catalytic efficiency, activity and selectivity, (ii) it allows for isolation of organic products and quantitative recovery and recycling of the water soluble catalyst through simple phase separation, and (iii) 'use of water' is cost-effective, safe and preferred in view of the global environmental norms.

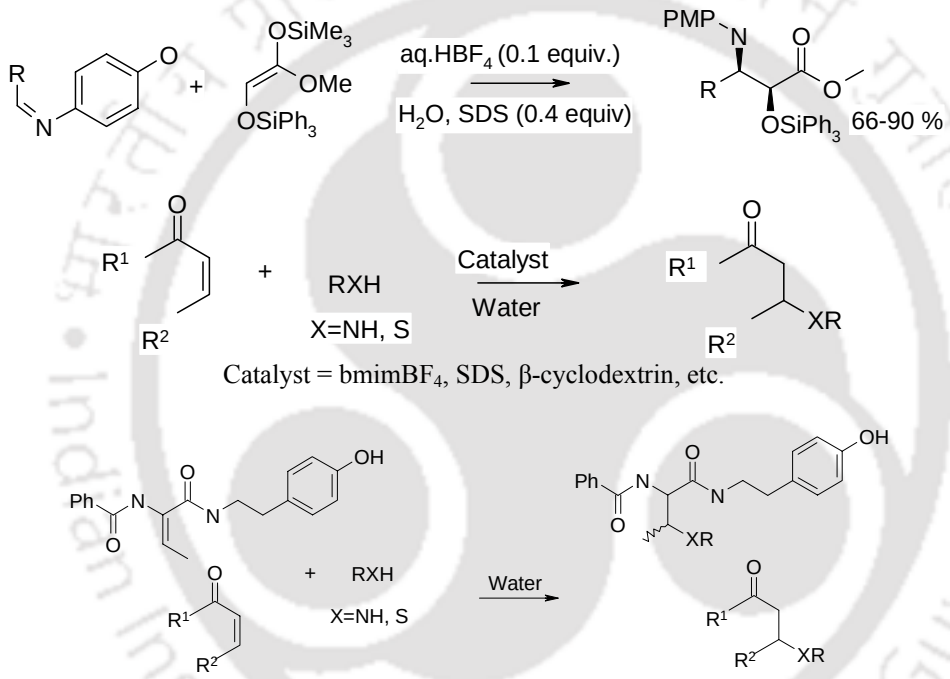
Accordingly, considerable interest has been generated in the use of water in organic synthesis either at normal temperature (3-150 ^{o}C, 1-5 atm), at elevated temperature (250 -500 ^{o}C, 40-170 atm) or under super critical conditions (400 ^{o}C, 250-500 atm).[12-14] At elevated temperature and pressure the spatial structures of water changes significantly and consequently the physiochemical properties such as dielectric constant, density, solubility parameter and dissociation constant[15] also alter. It may be mentioned in passing that under supercritical conditions water can act either as a reagent or as an acid or a base. Many non-polar organic substrates and gases are soluble in aqueous phase facilitating or making organic reactions possible that were previously thought to occur only in the presence of strong acids, bases or organic solvents.

Without overlooking some earlier contributions, the discoveries made in the laboratories of Breslow[16-18] and Grieco[19,20] in the early 1980s on the positive affect of water on rates and selectivities of Diels-Alder reactions triggered a more widespread interest in the field. Since then, significant progress has been made in the field of **organic chemistry in water/ aqueous media**, and new additions are continuously being made to the list of organic transformations that can be performed efficiently in water. Besides Diels-Alder reaction, other examples include Claisen-rearrangement,[21,22] aldol reactions,[23,24] and oxidations[25-27] and hydrogenations of alkenes,[28,29] Barbier coupling,[30] Wittig reactions,[31] Suzuki reaction,[32] pyranylation,[33] N-alkylation of primary amines or secondary amines,[34] N-*tert*-butyloxycarbonylation,[35] synthesis of various azides, thiocyanates, sulfones, 4,5-dihydro-pyrazole, pyrazolidine and 1,2-dihydro-phthalazine[36,37] (**Scheme 1.1**) to mention a few.



Scheme 1.1. *Some examples of organic reactions in water*

In addition, the development of Mannich type and hetero-Michael reactions in aqueous media has provided the incentive of finding a milder and more convenient approach towards the construction of β-amino and β-thio ketone or esters. Towards this end, several research groups have recently reported Mannich type, aza- and thia-Michael reactions in water to give β-amino, β-thio carbonyl compounds using various Lewis (**Scheme 1.2**) or Brønsted acids catalysts.[38-46] Some more discussions on this will be made at the appropriate place where our results on hetero-Michael reactions will be reported.



Scheme 1.2. *Some examples of organic reactions in water*

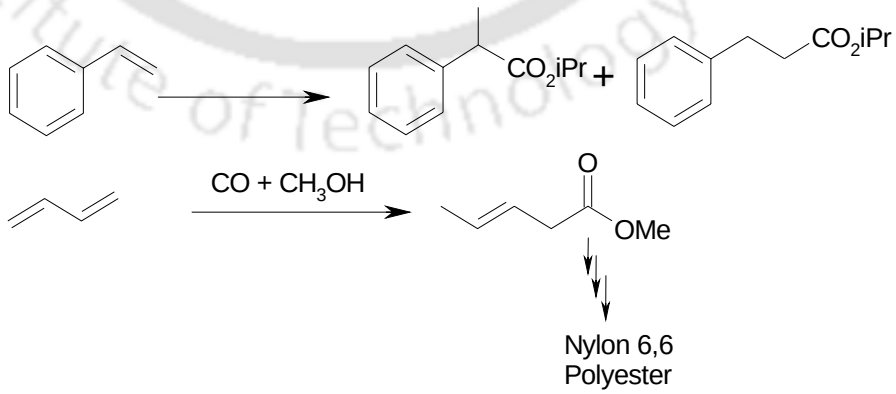
Some examples of using water as an alternative solvent for chemical reactions with wide-ranging possibilities that include direct use of water soluble renewable materials, C-C bond forming reactions using organometallic reagents, and exploiting the use of alternate energy sources such as solar, microwave and ultrasound in accelerating chemical syntheses has been highlighted in some of the recent reviews, text books and monographs.[47-53]

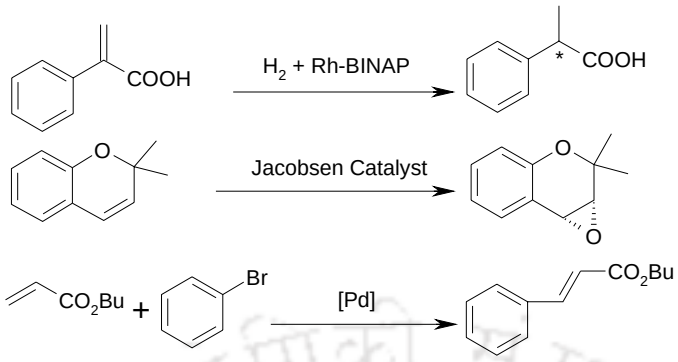
In so far as heterogeneization of catalysts[54-61] is concerned, there has been a metamorphosis from the simplest strategy i.e., supporting the active sites on large surface area solids, to the more elaborate ones in which the active sites are part of the solid structure. Eventually, the massive increase in the use and the broadening range of applications for polymeric supports in chemistry illustrate the immense significance of the techniques to the chemists. The concept of performing

traditional solution-phase reactions under "pseudo homogeneous" conditions has rapidly expanded into the domain of the medicinal, organic, organometallic, inorganic and polymer chemists, each exploiting the benefits, first realized by the peptide chemists, for their own advantages.[62]

While immobilization of catalysts into polymer being regarded as one of the most effective way of heterogeneization, yet another potential technique e.g., use of ionic liquid[63-65] has emerged out with a bang. Ionic liquids are fused salts containing only ions,[64,66] nonetheless those which are liquids at or below room temperatures draw attention of synthetic organic chemists. Ionic liquids with weakly coordinated anion and suitable cation are highly justified as alternative "Green Solvent".[67] It provides an innocuous solvent system for biphasic catalysis, heterogeneizing the catalyst and product into two separate and immiscible phases without loosing the selectivity and efficiency inherent in homogeneous catalysis. It has been well established that reactions can be accelerated in ionic liquids with improved selectivity. In fact an increased stability of catalyst is observed in the ionic liquid. Finally, its nonvolatile nature enables significant advantage for distillative product separation, and the catalyst solution is available for immediate reuse.[68]

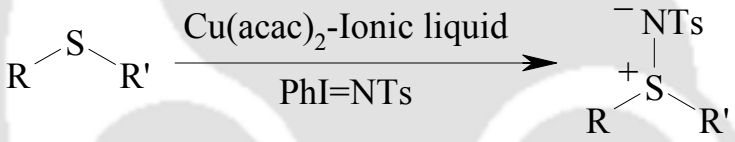
De souza *et al.*[69] addressed the Rh-catalyzed hydrogenation of cyclohexene in butylmethylimidazolium tretrafluoroborate. Chauvin *et al.*[70] dissolved the cationic Osborn complex $[Rh(nbd)(PPh_3)]PF_6$ in ionic liquids for biphasic hydrogenation of 1-pentene. Moreover, several groups have been investigating transition metal catalysis, such as oxidation[71] hydroformylation,[72] alkoxycarbonylation,[73] Heck reactions,[74] and hydrodimerisation[75] by immobilizing catalyst in suitable ionic liquids (**Scheme 1.3)**.





Scheme 1.3. *Transition metal catalyzed reactions in ionic liquid*

Incidentally, the group with which the present Ph.D research was carried out has been involved in the synthesis of inorganic complexes followed by exploring their use as catalyst for organic transformations. In line with this, many reactions have been investigated using Cu-catalyst immobilized in ionic liquids in our laboratories (**Scheme 1.4**).[76]



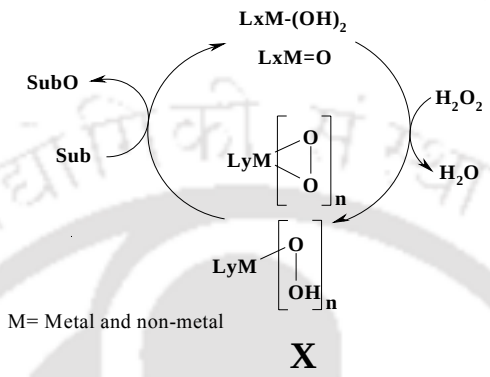
Scheme 1.4. *Transition metal catalyzed reactions in ionic liquid*

The use of ionic liquid as alternative solvent and pseudo-homogeneous medium is very promising and is currently receiving a lot of attention, as already discussed. More discussion on this aspect will find place later in **Chapter 3**.

With transition-metal-catalyzed oxidation reactions being some of the most fundamental reactions in both inorganic and organic chemistry, there has been for many years now, an intrinsic chemical interest in the synthesis, characterization, and reactivity studies of systems amenable to such activity. As far as partial oxidations are concerned,[77-79] oxo- or peroxo-metallates of transition metals (e.g. Ti, V, Mo, W) in presence of ecofriendly terminal oxidant, such as O_2 and H_2O_2, occupy the center-stage and they are of immense interest for their use as catalysts.[80] Pertinently, metal-catalyzed oxidations are generally modeled on certain enzymes which perform the oxidation of organic substrates in natural systems.[81,82]

Simple peroxometallates (*c.f.* binary peroxides and peroxo-metals) are often unstable, suitably ligated peroxometal complexes can be isolated and stored in many instances for prolonged periods.[83-85] Apart form this, some non-metals (B, C, P, etc.)[86-89] also form peroxo-complexes

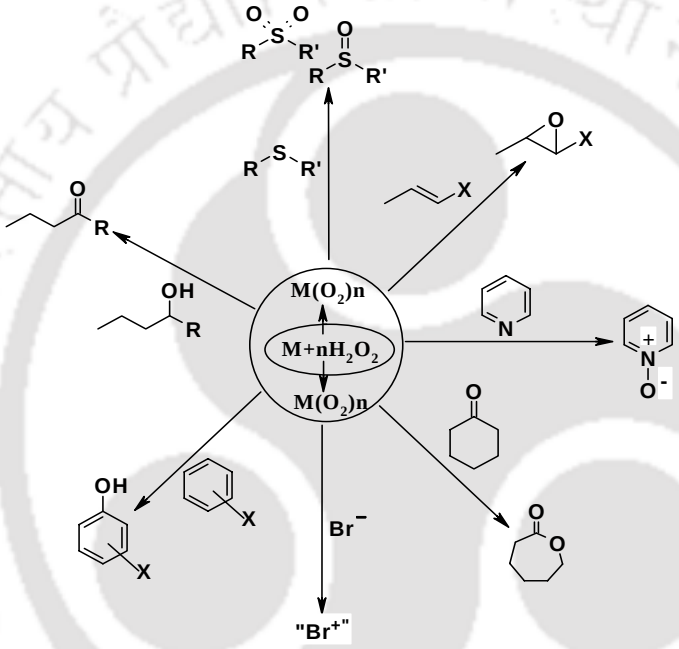
similar to transition metal. By nature of reactivity they can be classified either as stoichiometric reagents or as catalytic agents. The general mechanism of catalysis, if the catalyst is not isolated, has been described graphically in **Scheme 1.5**, in which **'X'** is the real oxidant in solution. Its reduced form adds hydrogen peroxide again thus accounting for the catalysis.[90]



Scheme 1.5. *A general mechanism for catalytic oxidation by peroxo-complexes*

One of the main reasons for the commercial importance of peroxo-complexes lies in the fact that the peroxide (O_2^{2-}) is activated by a higher-valent transition metal and some non-metals rendering it suitable for effective oxidations. Notable is that hydrogen peroxide, H_2O_2, is a very attractive oxidant for liquid-phase reactions.[91] It can oxidize organic compounds with atom efficiency of 47% generating water as the only co-product. It is relatively cheap, <0.7 US dollar Kg^{-1} (100%, H_2O_2), and about 2.4 million metric tons are produced for use, mainly as bleach.[92] The H_2O_2 oxidation is particularly useful for the synthesis of high-value fine chemicals, pharmaceuticals, agrochemicals and electronic materials which require high chemical purity. It may also be used for improving the environment by oxidative removal of very small amounts of toxic compounds. However, despite a sustained effort in industry, the current cost of H_2O_2 still does not allow for the economical production of inexpensive compounds in large quantities. There will be significant changes depending on the development of low cost H_2O_2 production, demand for high product quality, stringent environmental regulations, and changes in public opinion, legislation, and taxation policy regarding environment protection. In fact, there is a trend to use H_2O_2 as an oxidant for large volume processes such as caprolactam synthesis and propylene oxidation. H_2O_2 oxidation methods may switch to *in situ* or on-site technology using H_2 and O_2. One of the major advantages of the H_2O_2 oxidation is the high tenability of the reaction parameters. It should be noted that H_2O_2 can be ideal, waste-avoiding oxidant only when it is used in a controlled manner. It is an oxidant which is also not environmentally demanding.[93]

Unfortunately, it alone is a very weak oxidant in many instances. Thus, in order that the reactions become synthetically significant and commercially viable, the oxidations by hydrogen peroxide need to be catalyzed.[94] Among the oldest but very efficient catalysts that have been discovered are the derivatives of some transition metal ions like Ti, V, Mo and W in their highest oxidation states. Needless to mention that the peroxo-metal complexes referred to above are much stronger oxidants than H_2O_2 with their reactivity being many orders of magnitude larger than that of hydrogen peroxide.[95-98] A few examples in **Scheme 1.6** show the versatility of peroxometal oxidants.[90]



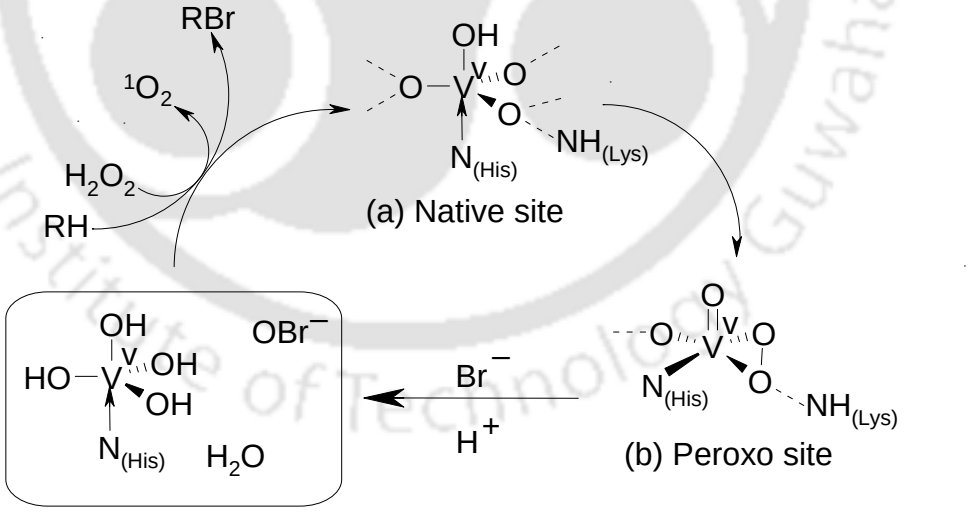
Scheme 1.6. *Selected oxidations of organic compounds by peroxo-metal complexes (M = Ti, V, Mo, W)*

In the domain of peroxometal chemistry, studies involving vanadium have drawn considerable attention of contemporary researchers in recent years. The synthesis, structural delineation, catalysis and biomodelling have become the center of interest.[99,100] In so far as the vanadium chemistry is concerned, the interest in biomodelling was largely triggered by the discovery[101] of a class of marine enzymes (vanadium bromoperoxidase) requiring vanadium(V) and hydrogen peroxide for their activity, which are responsible for the production of a large variety of halogenated organic molecules.[102] Yet another manifestation of peroxovanadium chemistry is the potential of complex peroxovanadium species as a clinical alternative of insulin for the treatment of diabetes.[103-105]

Peroxo-element chemistry is one area that has received continued attention of our research group and the elements have so far been drawn mainly from Ti,[106-109] V,[110-118] Mo, W, Zr,[119] Th,[120] UO_2^{2+},[112,121-127] B[86] and P.[89] Among these, it is vanadium that seems to have claimed the largest share and a good number of peroxo and heteroligand peroxovanadates(V) were synthesized in our laboratories. Subsequently, the reaction chemistry of peroxovanadates(V) became one of the thrust areas of our investigations.[128-138] Indeed it is at these manifestations of vanadium (plus H_2O_2) chemistry where a part of the present Ph.D. research found its root.

The involvement of peroxovanadates as catalysts in living systems was realized in 1983-84 when Vilter *et al.* reported the discovery of the vanadium bromoperoxidase (VBrPO)[101] enzyme from the marine algae *Ascophyllum nosodum*. The haloperoxidases (of which VBrPO is a member) are a group of enzymes which usually contain the FeHeme moiety or vanadium as an essential constituent at their active site, though a few haloperoxidases which lack a metal cofactor are also known.

Vanadium haloperoxidases (VHPO) are found in marine algae, lichens and certain terrestrial fungi and are known to catalyze the halogenations–chlorination, bromination and iodination–of organic substrates or the halide-assisted disproportionation of hydrogen peroxide (**Scheme1.7**).



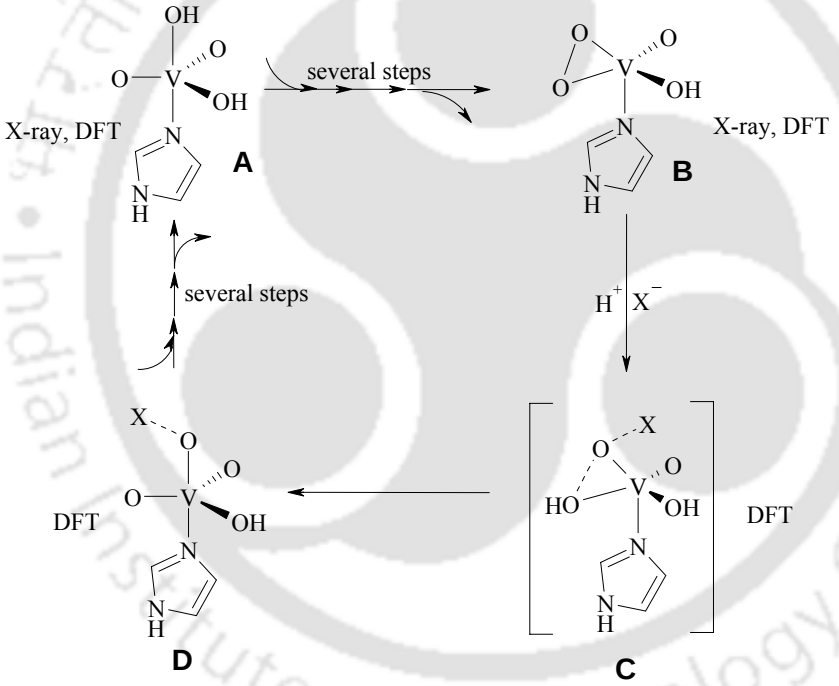
Scheme 1.7. *Proposed catalytic cycle for VHPO*

The X-ray structures of vanadium haloperoxidases (VHPOs) are expected to serve as 'blueprints' not only to provide cues for the construction of low molecular weight analogous and mimics but also to give information about the active site composition and geometry. The present status, in so far as VHPO is concerned, is the following.[139] The X-ray structures of VClPO from

Curvularia inaequalis and the vanadium bromoperoxidases (VBrPO) from *Corallina officinalis* and *Ascophyllum nosodum* reveal that the active site resembles vanadate (HVO_4^{2-}) which is coordinated to the protein by one histidine residue in a trigonal bipyramidal geometry (**Scheme 1.7**). The histidine that directly binds vanadium(V) and the amino acids involved in H-bonding to the vanadate oxygen atoms are conserved. Further, structural characterization of VClPO from *C. inaequalis* in the presence of H_2O_2 shows that the metal [V(V)] is coordinated axially by a terminal oxo group, and equatorially by peroxide, histidine, and the oxide ligand, in strongly distorted bipyramidal geometry (**Scheme 1.7**). Clearly in the enzyme the peroxo ligand is coordinated to the vanadium(V) centre in an η^2-fashion, in a manner similar to many mononuclear vanadium monoperoxo complexes.[140] It is relevant to note that H-bonding seems to be very important in the regulation of metal ion reactivity[141] in biology. Especially important is its effect on the heterolytic cleavage of O-O bonds in heme enzymes *viz.*, peroxidase and catalase.[141] In view of this, a striking feature at the active site of VClPO is the apparent H-bonding (2.76 Å) between Lys_{353} and the bound peroxide. Albeit peroxo derivatives of VBrPO have not yet been structurally characterized, the conserved amino acid residues found in the active sites of VBrPOs (*C. officinalis and A. nosodum*) suggest that the redundant Lys residues (Lys_{398} and Lys_{349}, respectively) are also appropriately positioned to H-bond to a vanadium(V)–peroxo moiety in VBrPOs. Moreover, a very important implication of the H-bonding issue discussed above is the outcome of the mechanistic studies of VHPO and its model complexes. Indeed, the results of mechanistic studies of VHPO and VHPO model complexes suggest that peroxide activation may be best achieved by protonation of the V(V)–bound peroxo group to generate a side-on bound hydroperoxide complex.[142] It is believed that an increase in positive charge on a peroxo-oxygen (O_{peroxo}), by protonation, makes attack by halide more favourable to the other.[143,144] As a matter of fact it has been observed in several independent experiments conducted in our laboratories that peroxo-metal mediated bromide oxidation to tribromide (Br_3^-) can be only possible in an appropriately acidic medium.[136-138,145] Recently, with DFT studies[146] it has been shown that protonation is crucial in the activation of peroxovandium cofactor[147,148] where Lys_{353} serves the purpose of protonation through H-bonding and possibly being a crucial factor in tuning the reactivity of the enzyme towards Br^- and Cl^- ions. The experimental and computational results are in good agreement with each other[149-156] and converge on the following scenario in which (i) protonation is a key step in the activation of cofactor, (ii) reaction between the resting state of vanadium cofactor takes place according to dissociative mechanism and spontaneously lead to

side-on peroxo species, (iii) an acid–base catalysts strongly accelerates the conversion of the initial H_2O_2 adduct to the side-on peroxo form which further leads to facile attack of nucleophile [X^- and neutral nucleophile (dimethyl sulfide)]. This has been illustrated in **Scheme 1.8**. The intermediate steps from **A** to **B** and **C** to **D** are still not fully understood, but it is believed to proceed via dissociative mechanism.[146]

Importantly in peroxovanadium catalyzed bromide oxidation, vanadium remains in its pentavalent state throughout just as it happens in the enzyme.[99] With this understanding being the basis, a number of oxo-peroxo complexes of vanadium(V) have been subsequently synthesized in quest of functional models for vanadium-haloperoxidases.[99,139]



Scheme 1.8. *Reaction scheme showing substrate binding to VBrPO.*

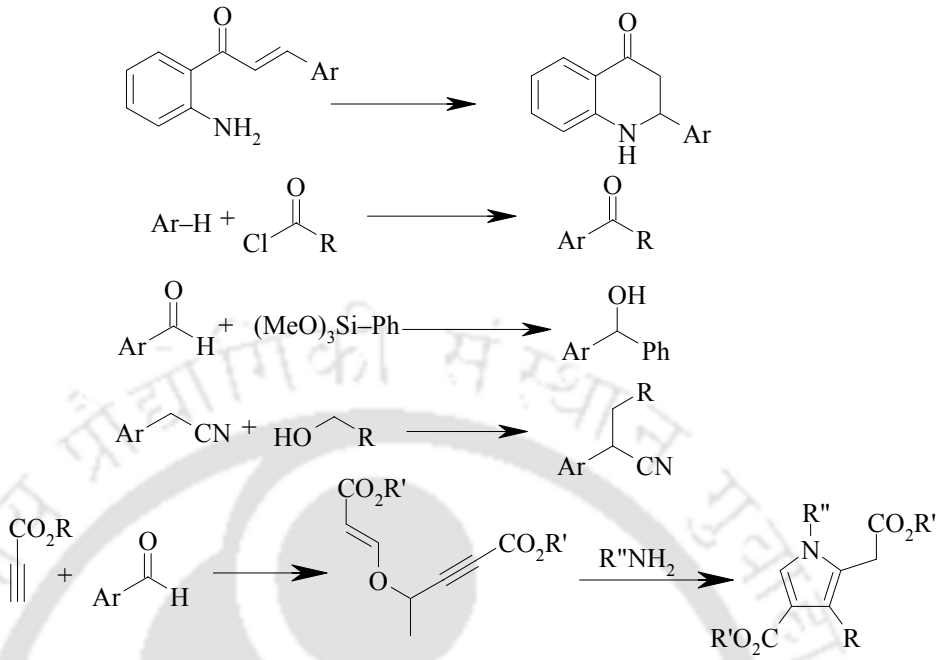
VO_2^+ is regarded as a functional mimic of VBrPO although, unlike VBrPO, it functions in acid and at much lower turnover rates.[157] *Cis*-dioxovanadium(V) in acidic solution (pH value 1.1) coordinates 1 equiv of hydrogen peroxide forming the sole monoperoxo,$VO(O_2)^+$, at concentration ratio V(V) : H_2O_2 of 1:2. As the pH is increased (≥3) the almost exclusive formation of diperoxo, $VO(O_2)_2^-$, species is obtained with strong decrease in reaction rates.[154] This results point to the involvement of monoperoxo species in the formation of 'bromine eqivalent', the diperoxo species is believed to act just as a reservoir of the actual oxidant, opposing the involvement of

dioxotriperoxodivanadium(V), $(VO)_2(O_2)_3$ as suggested by Butler *et al.*[140] This observation was further supported by ESI-MS analysis and theoretical calculations.[154]

Therefore, the discussions made above are convincing enough to believe that the synthesis of mimics of the naturally occurring vanadium peroxidase enzymes is a very important area of research in itself. Importantly, understanding of their reactivity profiles provide important cues in the development of bromoperoxidase mimics as greener alternatives to the oxidative bromination, extraction of bromide from sea-water as well as to the oxidation of sulfides, alcohols, etc. The development of newer catalysts modeled on some bio-catalysts will certainly enjoy a special status in the domain of catalysis. It would be relevant to entertain additional discussion in **Chapters 4** and **5**.

Quite apart from what have been overviewed so far, microwave has emerged as a good tool in the area of synthetic organic chemistry.[158] Over the past two decades, it gained interest surprisingly and established its root in the field of chemistry due to intensified research. In the future, microwave chemistry is likely to become a preferred method for conducting analytical and synthetic reactions in laboratories.[159-161] This is validated by the increasing number of publications in the field, from about 500 in 1997, to over 2500 up to 2007. At present, about 25,000-30,000 chemists use microwave technology to conduct chemical reactions worldwide.[158]

Reactions conducted through microwaves are cleaner and more environmentally friendly than conventional heating methods.[162] Microwaves heat the compounds directly, therefore, usage of solvents in the chemical reaction can be reduced or eliminated, as for example, Hamelin developed an approach to carry out a solvent- free chemical reaction on a sponge-like material with the help of microwave heating. The reaction is conducted by heating a spongy material such as alumina. The chemical reactants are adsorbed to alumina, and on exposure to microwaves, react at a faster rate than conventional heating.[163] Since then, chemists have successfully conducted a large range of organic reactions. These include the following: The Diels-Alder reaction, racemisation of large organic molecules through Diels-Alder cyclo-reversion, the ene reaction, Heck reaction, Suzuki reaction, Mannich reaction, hydrogenation of β-lactams, hydrolysis, dehydration, esterification, cycloaddition reaction, epoxidation, reductions, condensations, protection and deprotection, cyclisation reactions, etc.[164-172] Some examples of microwave reactions are presented in **Scheme 1.9.**



Scheme1.9. *Microwave assisted organic reactions*

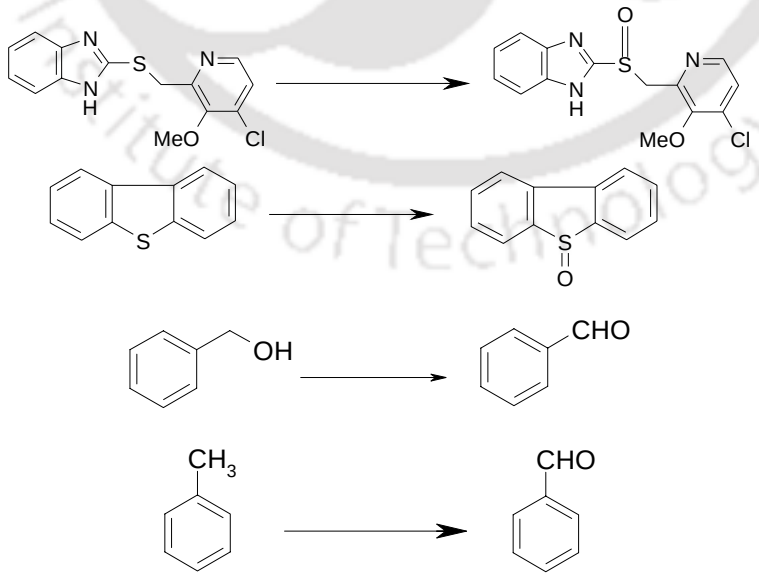
The use of microwaves has also reduced the amount of purification required for the end products of chemical reactions involving toxic reagents.[158] A little more discussion will be presented in the **Chapter 6**.

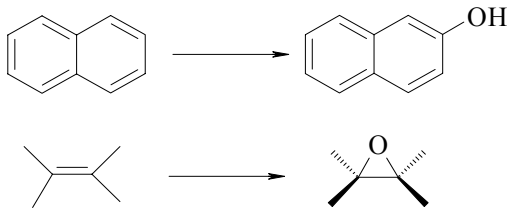
1B. Scope of Work

Being a part of the environment, we do not have right to harm it if we cannot save. Due to our deeds in the past we deserve humiliation and were humiliated. Having been rightly instigated by the hostility of chemical wastes and reckless disposal of unsafe chemical agents causing the environment to be unsafe for the human habitat and ecology, it became incumbent upon experimental **chemists to address the need of Clean Chemistry and its application.** This area of chemistry is attracting increasing attention involving quite a challenging problem that chemists and some chemical industries are now encountered with. Philosophically, the implied issue falls in the regime of triple bottom line concept. Recently, the clean chemistry's bandwagon started and chemists started looking into the possibility where they can contribute. Catalysis is not only one of the important tenets but also an integral part of it. The invention of a clean and appropriate catalyst or catalytic system for a chosen transformation is extremely important which have already been highlighted.

It is known that Michael reactions serve as synthetic routes to essential intermediates of γ-amino alcohols, diamines, β-amino acid derivatives, β-lactam antibiotics, β-acylvinyl cation, homoenolate anion equivalents, β-calcium antagonist diltiazem and natural products. Consequently, the development of novel protocols for the Michael reactions has attracted a great deal of attention in synthetic organic chemistry. Notably the success of conjugate addition reactions lie in the use of either acidic or basic conditions which, if not selected judiciously, can be detrimental to the desired synthesis allowing unwanted side reactions to contaminate the product. Moreover, the possibility of poisoning of metal-based catalyst by thiols, alkyl or aryl amines cannot be completely ruled out. In order to alleviate some of these problems the Michael reaction has undergone metamorphosis over the years involving a number of reagents and catalysts and alternative procedures. One of the rational alternatives would be to use an appropriate catalyst soluble in either ionic liquid or water as the solvent of choice. Importantly, both the solvents provide pseudo homogeneous medium for the reaction and provide easy recycling of the catalysts.

In the realm of oxidation chemistry, the partial oxidation of organic molecules (typically sulfides and alcohols) is a diverse and widely used area of chemistry with applications in almost all of the fine and speciality chemicals industries including those manufacturing pharmaceuticals, agrochemicals and monomers, for example (**Scheme 1.10**):





Scheme 1.10. *Some important partial oxidation reactions*

Significantly, chromium(VI) and manganese(VII) are perhaps the best known oxidizing agents in chemistry commonly used in both bench scale as well as on large scale partial oxidation reactions. Endeavor is on to replace them by O_2 or H_2O_2 and catalyst derived from Ti, V, Mo, W, etc. An important point to be made here is that the use of Cr (VI) and Mn(VII) oxidant on a large scale leads to a rather large volume of toxic metal waste. Thus, interests on the efficacious catalytic systems are certainly going to be in demand and are likely to draw special attention. Research addressing the problems highlighted above is not only of topical importance but also rewarding.

Oxidative brominations and the other investigations related to the understanding of VBrPO and its activity is unquestionably very important which have already been highlighted. Equally important is to develop a VBrPO mimetic catalyst. For this reasons vanadium(V) compounds containing appropriate heteroligands are considered suitable candidates for VBrPO mimetic studies. $[V(O)_2(OH)(H_2O)(imz)]$, (Imz = imidazole), which has been considered as the resting form of VHPO cofactor, was recently studied by DFT calculation to derive information on catalytic reactivity. Similar vanadium(V) species containing 3,5-dimethyl pyrazole (dmpz) as the heteroligand deserves the attention of vanadium chemists since such complexes are in all probability likely to be as VHPO mimic as the analogous imidazole containing vanadium(V) cofactor is. This might be all the more rational because of the structural similarity betwen dmpz and imidazole. In addition, studies involving dmpz as a ligand may not be very trivial because dmpz complexes of vanadium(IV) or (V) seems to have been very little worked on. Thus, the coordination chemistry of V(V)–dmpz deserves attention.

As a sustained scientific curiosity in reaction chemistries under microwave irradiation, our attention was drawn to Friedlaender synthesis of quinolines. This reaction is an important chemical process especially when it is used to generate highly useful intermediates for natural products and drugs, copolymers for electronic and optoelectronics. General method is a two-step process where isolation of *o*-aminobenzaldehyde suffers from the problem of polymerization and condensation

with enolizable ketone is achieved by the use of Lewis acids. Thus, development of improved process for the synthesis of quinolines is desirable.

The present overview, including a critical assessment of the state-of-art of the problems addressed therein, provide reasons that are persuasive enough to undertake studies addressing the identified problems. In resonance with this, the present Ph.D research was initiated in 2003 in order to investigate some of the above-mentioned problems. The nature of the problems is such that there have been significant developments in nearly every couple of months thereby rendering it rather difficult to keep pace with. The outcome of our endeavor has finally led to the following end results:

(i) The development of clean aza- and thia-Michael reactions involving $Cu(acac)_2$ immobilized in ionic liquids (IL), boric acid in water and borax in water as the catalysts. While investigating the thia-Michael reactions using $B(OH)_3$ or $Na_2B_4O_7.10H_2O$ as the catalysts, some of the condensed products attracted our attention as prospective candidates for studying their self-assembled H-bonding interactions in the crystal lattice. Accordingly, X-ray crystallography of three β-sulfidocarbonyls was carried out and some interesting observations were made. These results constitute the subject matter of **Chapter 3**.

(ii) The selective oxidation of sulfides has been achieved with a newly synthesized vanadium complex, $[VO_2F(dmpz)_2]$, borax or phosphate as the catalyst and H_2O_2 as the oxidant. As a logical extension, oxidative desulfurization of diesel was attempted with $[VO_2F(dmpz)_2]$–H_2O_2 and reasonable success has been achieved. The results obtained from this exercise constitute the subject matter of **Chapter 4**.

(iii) An improved synthesis of highly peroxygenated vanadium(V) species, $[V(O_2)_3]^-$ has been achieved and it was considered quite apt to use this as a precatalyst for oxidative brominations, and selective oxidation of alcohols with H_2O_2. While we were engaged in the triperoxovanadate(V) catalyzed reactions, it was observed that our $[VO_2F(dmpz)_2]$ catalyst very efficiently catalyzed the oxidation of bromide to tribromide, (Br_3^-), by H_2O_2. This encouraged us to try out the oxidative extraction of bromide from seawater using this catalyst. A comprehensive account of this work has been presented in **Chapter 5**.

(iv) **Chapter 6**, the concluding chapter of the thesis, gives an account of efficient solvent-free one-pot synthesis of quinolines achieved from *o*-nitrobenzaldehyde and enolizable ketones using $SnCl_2.2H_2O$ and subjecting them to microwaves.

In addition to this Chapter (i.e., **Chapter 1**) which introduces the identified problems for the Ph.D. research, provides an overview of the status of the problem, and also pin points the scope of work, **Chapter 2** describes the sources of chemicals and solvents that were used in the work, methods of preparation of a few starting materials, details of the methods of chemical analyses, and particulars of various instruments and equipment used for physico-chemical studies and characterization of the reported compounds. Each chapter from **3** through **6** has been deliberately designed to be self-contained having a brief introduction and sections on results and discussion, and experimental followed by bibliography. While some of the results have been published, manuscripts based on the rest are either under communication or under preparation.

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Details of Materials, and Methods and Equipment

Detailed procedures adopted for the preparation of different starting materials are described in this chapter. Also described herein are the details of the methods used for quantitative determination of various constituents and relevant particulars of the instruments/equipment used for characterization and structural assessment of the newly synthesized compounds.

The chemicals and solvents used for the present work were of analytical grade quality. Following are the sources of chemicals and solvents: s.d.fine-chem ltd, Qualigens Fine Chemicals, E. Merck (India) Limited, Sisco Research Laboratories Pvt. Ltd, Central Drug House (P) Ltd, Bengal Chemicals and Pharmaceuticals Ltd, Loba Chemie Industries, and Spectrochem (India), Sigma- Aldrich (India), Lancaster (India).

2A. Preparation of starting materials

1-Butyl-3-methyl imidazolium chloride, BMIC [1]

A mixture of n-butyl chloride (0.40 mol, 37.04 g) and 1-methylimidazole (0.40 mol, 31.9 g) was stirred at 70-80 ^{0}C for 1 or 2 days under nitrogen. The mixture was cooled to room temperature and ethyl acetate (70 mL) was added causing precipitation of 1-butyl-3-methyl imidazolium chloride as a white solid which was recovered by filtration and washed with ethyl acetate followed by ethyl ether. Yield: 43.52 g (63%).

1-Butyl-3-methyl imidazolium tetrafluoroborate, BMIM.BF_4 [1]

The 1-butyl-3-methyl imidazolium chloride salt was added to a suspension of $NaBF_4$ (1.2 equiv, 52.7 g 0.48 mol) in acetone (150 mL). After the mixture was stirred for 48 h at room temperature, the sodium chloride precipitate was removed by filtration and the filtrate concentrated to an oil (~100 mL) by rotary evaporation. This oil still contained some 1-butyl-3-methyl imidazolium chloride because it gave a precipitate when mixed with aqueous silver nitrate. The oil was (~100 mL) was dissolved in methanol (100 mL) and an aqueous solution of $AgBF_4$ (generated from the reaction of Ag_2O with HBF_4) was added drop wise until no more precipitate was formed. The mixture was filtered through Celite (no. 545), concentrated by rotary evaporation, dissolved in dichloromethane (100 mL), and filtered again to remove insoluble material. The product was purified by column chromatography in three portions on silica gel (~400 g) and then eluted with dichloromethane/methanol (9:1). The solvent removal under vacuum yielded pale yellow oil. Yield: 78.10 g (72%).

1-Butyl-3-methyl imidazolium hexafluorophosphate, BMIM.PF_6 [2]

To a solution of BMIC (9.3 g, 53.1 mmol) in acetone (50 mL) at room temperature was added sodium hexafluorophosphate (5.83 g, 53.1 mmol). After 24 h of stirring, the reaction mixture was filtered through a plug of celite (length = 3 cm) and the volatiles were removed under reduced pressure to obtain the title compound. Yield: 10.8 g (90%).

Copper(II) Acetylacetonate, Cu $(acac)_2$ [3]

Copper(II) acetate monohydrate (10 g, 50.09 mmol) was dissolved in 300 mL of water in a 500 mL beaker by warming at 60 °C for 15 min. To the cooled solution, 20% aqueous solution of KOH was slowly added with constant stirring to precipitate the metal as its hydrated oxide. The addition of alkali was continued till pH of the solution was raised to *ca.* 8. The hydrated metal oxide was washed free of alkali by repeated washing with water by decantation, finally followed by filtration through Whatman No. 42 filter paper and again washing twice with cold water. Then the precipitate was quantitatively transferred into a 100 mL beaker. Distilled acetylacetone (11.06 mL, 110 mmol) was added to the precipitate and mixed thoroughly with a glass rod. An exothermic reaction set in leading to the formation of blue shiny crystals of $Cu(acac)_2$. It was allowed to stand at room temperature for 30 min and then placed in an ice-water bath for 15 min. The compound was filtered through Whatman No. 42 filter paper and dried *in vacuo* over fused $CaCl_2$. Yield: 12.49 g (95.3%)

3,5-Dimethylpyrazole (dmpz) [4]

A methanolic solution of 25 mL of hydrazine hydrate, $N_2H_4.H_2O$, (25.0 g, 499.4 mmol) was added slowly with stirring to a methanolic solution of 25 mL of acetylacetone (25.0 g, 249.7 mmol) in an ice-cold condition. A light yellow solution was obtained. The solution was concentrated to *ca.* 20 mL on a steam bath and left overnight in a refrigerator. A white crystalline compound was obtained and this was isolated by filtration, washed 4 or 5 times with water and dried in air. The yield of pure 3,5-dimethylpyrazole (dmpz) was 23.5 g (98 %). Mp 106-108 °C.

General procedure for the preparation of sulfides [5]

To a stirred solution of thiol (6 mmol) in ethanol (15 ml), KOH (6 mmol) was added at ambient temperature. Alkyl or aryl halide (6 mmol) was then added drop wise to the reaction mixture. The progress of the reaction was monitored by TLC. After completion, ethanol was removed on a rotary evaporator under reduced pressure and the residue was treated with ethyl

acetate and water (3:1). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to yield a residue which was passed trough a short pad of silica gel using ethyl acetate and hexane as eluent to provide analytically pure sulfides.

2B. Elemental analyses

Vanadium [6]

Vanadium was estimated iodometrically.

An accurately weighed amount (*ca.* 0.1 g) of vanadium compound was dissolved in 100 mL of water. To the solution was added 5 mL of 5M H_2SO_4. The solution was boiled for 10 min to remove peroxide. To this solution was added 5 g of potassium persulfate followed by the addition of one drop of silver nitrate solution. The resultant mixture was boiled for 1 h. After this, 15 mL of 5M H_2SO_4 was added and the solution boiled for a further period of 30 min. The solution was allowed to cool to room temperature and *ca.* 2 g of KI was added with stirring. This was then kept in the dark for 15 min. The liberated iodine was titrated with standard $Na_2S_2O_3$ solution using starch as an indicator. The end point was detected by the appearance of a light-blue colour.

1 mL of 0.1 M $Na_2S_2O_3$ = 0.00519 g of vanadium

Fluoride [7]

An accurately weighed amount (*ca.* 0.1 g) of the fluoride containing compound of vanadium was dissolved in 150 mL of water. The solution containing fluorovanadate(V) compound was boiled with 20–25 mL of 0.1 M NaOH for *ca.* 30 min. The mixture was digested on a steam bath for *ca.* 30 min. and filtered to separate the hydrated oxide. The residue was washed thoroughly with water. To the combined filtrate and washings, two or three drops of bromophenol blue indicator and 3 mL of a 10% sodium chloride solution were added and diluted to *ca.* 250 mL. 6 M nitric acid was added to it until the color just changed to yellow followed by the addition of 0.1 M NaOH solution until the color changed to blue. The mixture was then treated with 1 mL of conc. HCl and 5 g of $Pb(NO_3)_2$ and heated on a steam-bath. After the entire lead nitrate had dissolved, 5 g of crystallized sodium acetate was added to the solution and the whole was digested on a steam bath for *ca.*30 min. with occasional stirring. A white precipitate of PbClF formed which was then allowed to stand overnight.

The precipitate was filtered through a Whatman 542 filter paper, washed five or six times with water to make it free from chloride. The precipitate was dissolved in 1% HNO_3 by slight warming. A known excess of standard $AgNO_3$ (0.1 M) solution was added and the suspension of

AgCl heated almost to boiling under vigorous stirring. The beaker and its contents were kept in the dark for 1 h, the precipitated AgCl was filtered out and washed with water. The unreacted $AgNO_3$ was finally titrated with standard KSCN solution using $Fe(NO_3)_3$ as indicator. The end point was marked with the appearance of a faint-red brown colour. The volume of $AgNO_3$ in the filtrate thus found was subtracted from the amount that was originally added. The fluoride content was calculated from the volume of $AgNO_3$ solution consumed.

1 mL of 1 M $AgNO_3$ = 0.019 g of fluoride

Bromide [8]

Bromide was estimated volumetrically following Volhard's method.

An accurately weighed amount (*ca.* 0.1 g) of organicammonium tribromide was dissolved in 20 mL of acetonitrile. The solution was treated with 20 mL of a 20% NaOH solution, followed by the addition of 100 mL of water. The solution was boiled for 1 h and acidified with dilute (1:1) HNO_3. The acidified bromide solution was then treated with an excess of 0.1 M silver nitrate solution. The suspension was heated almost to boiling under vigorous stirring. The beaker along with the suspension was kept in the dark for 30 min. The precipitated AgBr was separated out by filtration and washed several times with water. The filtrate and the washings were collected and the unreacted $AgNO_3$ was titrated with standard KSCN solution using $Fe(NO_3)_3$ as the indicator. The end point was marked by the appearance of a faint red–brown color. From the equivalence of standard $AgNO_3$ and standard KSCN solutions, the volume of excess $AgNO_3$ was calculated and this was subtracted from the volume of $AgNO_3$ that was initially added. The difference is the volume of $AgNO_3$ solution consumed.

1 mL of 1 M $AgNO_3$ = 0.0799 g of bromide

Peroxide

(a) Permanganometry [9]

Nearly 1 g of boric acid was dissolved in 100 mL of water taken in a conical flask. To this was added an accurately weighed amount (*ca.* 0.1 g) of peroxo compound followed by the addition of 7 mL of 5M H_2SO_4. The solution was shaken well to dissolve the compound. The peroxide was then estimated by redox titration with standard $KMnO_4$ solution. The end point was marked by the appearance of a permanent faint pink colour.

1 mL of 0.2 M $KMnO_4$ = 0.01701 g of peroxide (O_2^{2-})

(b) Iodometry [9]

To a freshly prepared 2 M sulphuric acid solution, containing an appropriate amount of potassium iodide (~2 g in 100 mL) was added an accurately weighed amount (*ca.* 0.1 g) of a peroxo compound with stirring. The mixture was allowed to stand for *ca.* 15 min in carbon dioxide atmosphere in the dark. The amount of iodine liberated was then titrated with a standard sodium thiosulphate solution, adding 2 mL of freshly prepared starch solution when the colour of the iodine was nearly discharged.

$$1 \text{ mL of } 1M\ Na_2S_2O_3 = 0.01701 \text{ g of peroxide } (O_2^{2-})$$

[In case of a peroxovanadate(V) complex, this method gives the total amount of peroxide plus vanadium present in the compound. On deduction of the contribution of vanadium (V) from the total amount of iodine liberated, the net peroxide content of the compound is evaluated.]

2C. Particulars of Instruments/Equipment used for the following Physico-Chemical Studies

All reactions were monitored by TLC on silica gel 60 F_{254} (0.25mm), visualization was effected with UV and/or by developing in iodine. Chromatography refers to open column chromatography on silica gel (60-120 mesh).

Carbon, Hydrogen, Nitrogen and Sulfur (Micro Analysis)

The carbon, hydrogen, nitrogen and sulfur contents were estimated by micro-analytical methods. The results of the analyses were obtained using a 2400 Perkin Elmer Series II CHNS/O Analyzer. The analysis was carried out by the Micro-analysis Lab., IIT Guwahati, Guwahati 781039.

pH Measurement

pH values of the reaction solutions were recorded with a Systronics Type 335 digital pH meter and also by using Merck pH indicator paper.

Recording of Melting Point

Melting points of the compounds were recorded using a Type B-540 Buchi melting point apparatus. The heating rate was maintained at 2°C per min.

Microwave Oven

Microwave reactions were carried out in a Samsung microwave oven (model# CE118KF, Tunable 100-1500W) at 1050W.

Infrared Spectroscopy

Infrared spectra of the compounds were recorded as KBr pellets, nujol mulls or as thin films using a Nicolet Impact–410 Fourier Transform Infra Red Spectrophotometer or on a and Perkin Elmer 983 Fourier Transform Infra Red Spectrophotometer.

Electronic Absorption Spectroscopy

UV-visible spectra were recorded, by dissolving a calculated amount of the sample in an appropriate solvent, on a Hitachi UV–visible U–2001 Spectrophotometer or on a Perkin Elmer Lambda 25 UV–visible Spectrophotometer.

^{1}H and ^{13}C Nuclear Resonance Spectroscopy

^{1}H and ^{13}C NMR spectra were recorded on a Varian 400MHz, Varian Gemini 200 MHz and BRUKER 300 MHz NMR spectrometers using tetramethylsilane (TMS) as internal standard.

Thermal Analysis

Thermogravimetry (TG) and Differential Scanning Calorimetry (DSC) experiments were conducted on a Mettler-Toledo TGA/SDTA 851^{e} and DSC 821^{e} instruments. Experiments were done using either aluminium or platinum crucibles. Pure N_2 gas was used as the flow gas.

Gas Chromatography-Mass Spectrometry

GC-MS was recorded on a Perkin-Elmer Precisely Clarus 500 instrument using a capillary column (30×0.25×0.25 mμ) in EI mode.

X-ray Crystallography

The X-ray data were collected at 293 K with MoK_α radiation (λ= 0.71073Å) on a Bruker Nonious SMART CCD difractometer equipped with graphite monochromater. The SMART software was used for data collection, indexing the reflection and determination of the unit cell parameters. Integration of the collected data was made using SAINT XPREP software.[10] Multi-scan empirical absorption corrections were applied to the data using the program SADABS.[11] The

structures were solved by direct methods and refined by full-matrix least-square calculations by using SHELXTL software.[12] All non-hydrogen atoms were refined in the anisotropic approximation against F^2 of all reflections. The hydrogen atoms attached were located in difference Fourier maps and refined with isotropic displacement coefficients. The hydrogen atoms were placed in their geometrically generated positions. Crystal parameters for the compounds are presented in the experimental section of the respective chapters.

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Newer Catalytic Hetero-Michael Reactions*

* The work described in this chapter has been published

1. *Adv. Synth. Catal.* **2005**, 347, 763-766
2. *Tetrahedron Lett.* **2005**, 46, 8329-8331
3. *Eur. J. Org. Chem.* **2007** 361-365
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5. *J. Mol. Structure* **2007**, *837*, 190-196

The conjugate addition of a nitrogen or a sulfur nucleophile to an electron rich or electron deficient electrophile, known as the aza- or thia-Michael reaction to form a C-N or C-S bond, constitutes a key reaction in biosynthesis as well as organic synthesis.[1-3] β-Aminocarbonyl and β-thiocarbonyl compounds which are the adducts of the aza- and thia-Michael reactions, respectively, are usually encountered in naturally occurring biologically active compounds such as alkaloids and polyketides[4,5] and are widely used throughout the chemical industry as a basic intermediate to prepare pharmaceutically or agrochemically useful products.[6,7] They serve as essential intermediates in the synthesis of γ-amino alcohols, diamines, β-amino acid derivatives,[8-10] β-lactam antibiotics,[11-13] β-acylvinyl cation,[14] homoenolate anion equivalents,[15] β-calcium antagonist diltiazem[2] and natural products.[16-18] The thia-Michael reaction also provides an elegant strategy for the chemoselective protection of olefinic double bond of conjugated enones[19] due to the ease of generation of the double bond through removal of the sulfur moiety by copper(I) induced[20] and oxidative[14] eliminations. Some thia-adducts of amides are known to have topical relevance to the investigation of host-guest interactions[21] and are also useful as photographic development accelerators.[22,23] Consequently, the development of novel protocols for the conjugate addition of thiols and amines to electron deficient olefins leading to the formation of C–S and C–N bonds, respectively, have attracted a great deal of attention in contemporary organic chemistry research. Notably, the success of conjugate addition reactions lie in the use of either acidic or basic conditions which, if not selected judiciously, can be detrimental to the desired synthesis allowing unwanted side reactions to contaminate the product. Moreover, the possibility of poisoning of metal-based catalysts by thiols, alkyl or aryl amines[24] cannot be completely ruled out. In order to alleviate some of these problems the Michael reaction has undergone metamorphosis over the years involving a number of reagents or catalysts and alternative procedures, for instance, a variety of inorganic salts,[25-41] quaternary ammonium salts,[42] ionic liquids (IL),[43] a combination of IL and water,[44] palladium,[24] supported $CeCl_3.7H_2O$-NaI,[45] Clay,[46] silica-gel,[47] SiO_2-$HClO_4$,[48] solid acid,[49] KF/alumina,[50,51] polyethylene glycol (PEG),[52] cyclodextrin in water,[53] and even miceller solution of SDS.[54] In no denial of fact, each method has some advantages over the other, however, the search still continues for improved versions of the Michael reaction. In order to overcome many of these limitations, if not all, endeavor has been made by us to develop catalysts and catalytic systems, which is indeed the main theme of **Chapter 3.** For convenience, the subject matter of this chapter is divided into four sections. The use of water [55-57] or ionic liquids[58-60] as a prospective alternative to organic solvents seems to be a current trend in synthetic organic chemistry. Room

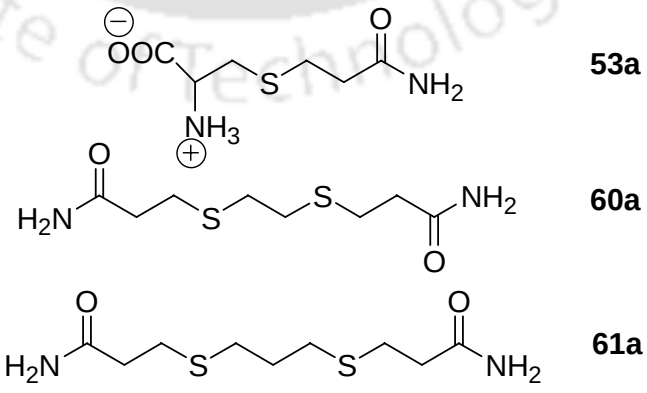
temperature ionic liquids (ILs) are considered to be ecobenevolent substitues to volatile organic solvents and have other useful properties like very low vapor pressure, wide liquid range, high thermal stability and possessing highly conductive solvation ability for a variety of organic substrates and catalysts including Lewis acids and enzymes. Considering all these, it was thought that a combination of a suitable Lewis acid catalyst, *viz*, $Cu(acac)_2$, immobilized in an ionic liquid would enable facile conjugate additions. To our knowledge, the aza-Michael reactions involving a combination of the chosen catalyst and an ionic liquid were unprecedented while this work was carried out. **Section 3.1** contains the details of the aza-Michael reactions of amines with α,β-unsaturated carbonyl compounds and nitriles to produce the corresponding β-amino ketones and nitriles in very high yields under mild reaction conditions using $Cu(acac)_2$ immobilized in ionic liquids.

In view of our sustained interest in the development of suitably designed and environmentally cleaner protocols for a variety of organic transformations and guided by the knowledge gathered especially from the seminal contributions of Spancer *et al.*,[61] we were quite convinced that it is the Brønsted acid which is important in bringing about the aza- and thia-Michael condensations irrespective of whether the reaction was a catalytic one or not. Relevantly, the Michael additions in water are relatively scarce but not unprecedented.[62-64] The use of water as a reaction solvent has received considerable attention[55-57] because reaction in such medium has several advantages including the fact that the solvent and substrates can be directly used without drying. Also, it is believed that more and more reactions in water will contribute to the progress of green chemistry and pseudo natural catalysis chemistry. Considering all these and in persuance of our interest in developing reactions that use catalytic amount of either a nontoxic or minimally toxic, readily available and ecologically favourable agent, we opted for boric acid as the catalyst of choice and water as the solvent. Demonstrated here in S**ection 3.2** is the boric acid catalyzed reaction of amines and thiols, respectively, with α,β-unsaturated carbonyls and nitriles in water at room temperature.

Interestingly, most of the methods recently developed have involved metal-based acidic catalysts, presumably because the Michael reactions in basic media are rather sluggish without providing satisfactory yields even with long reaction times. However, there is intrinsic interest in the Michael addition of thiols to enones in basic aqueous media under mild conditions and such reactions are highly relevant to "Dynamic Combinatorial Chemistry" which offers a conceptually new approach to the investigation of host-guest interactions. Taking cognizance of these and being

intrigued by the fact that pH of an aqueous solution of borax is 9.5, it was perceived that a mild Brønsted base could also bring about the hetero-Michael reactions. The result of this endeavor is discussed in the **Section 3.3**.

In the course of our research in this area, three very interesting compounds *viz*., 2-Amino-3-(2-carbamoyl-ethylsulfanyl)-proionic acid (**53a**), 3-[2-(2-carbamoyl-ethylsulfanyl)-ethylsulfanyl]-propionamide (**60a**) and 3-[2-(2-carbamoyl-ethylsulfanyl)-propylsulfanyl]-propionamide (**61a**) were obtained from the borax catalyzed thia-Michael reaction discussed in **Section 3.3**. They attracted our attention especially because of the following reasons: (i) while the compound **53a** has topical relevance to the investigation of host-guest interactions,[21] compounds **60a** and **61a** appear to be highly useful as photographic development accelerator[22,23] and they serve also as color photographic developer and are used in the lithographic plate processing solutions, (ii) all the three compounds afforded x-ray diffraction quality crystals, and (iii) the terminal groups of the molecules of each of them are amenable to the formation of supramolecular connectivites through N–H**…**O hydrogen bonding. In addition, the possibility of formation of sheet like structures through N–H**…**O, C–H**…**O and C–H**…**S cross-linking cannot be ruled out. Pertinently, the β-sheet assembly is biochemically relevant to the understanding of the chemistry of natural and synthetic peptide analogs. In addition, self-assembly of molecules through noncovalent interactions is believed to be one of the fundamental processes in biology[66-71] wherein a peptide bond can adopt different confirmations through such a process.[72,73] Accordingly, the self-assembly and supramolecular organization of each of **53a**, **60a** and **61a** in the respective crystals was determined by X-ray crystallography and the results of these studies are described in **Section 3.4**.



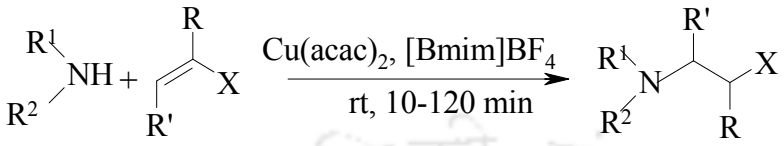
53a

60a

61a

3A. Results and Discussions

3.1 $Cu(acac)_2$ Immobilized in Ionic Liquids: A Recoverable and Reusable Catalytic System for Aza-Michael Reactions



Scheme 3.1.1

$BmimBF_4$ and $bmimPF_6$ were synthesized by the procedures as given in **Chapter 2** and used for this work. First, the catalytic effect of $Cu(acac)_2$ for the conjugate addition of piperidine to methyl acrylate was studied, and the results are summarized in **Table 3.1.1**. In order to investigate if $CuCl_2$ would catalyze similar aza-Michael reactions, an independent experiment was carried out using $CuCl_2$ in lieu of $Cu(acac)_2$. The result was quite interesting showing that $CuCl_2$ is equally effective as an aza-Michael catalyst in ionic liquids. Furthermore, in recognition of the fact that an ionic liquid alone is capable of catalyzing both the Michael[74] as well as the aza-Michael reactions,[63,75] an experiment was conducted without any metal catalyst but using only either $bmimBF_4$ or $bmimPF_6$ with other conditions being similar to those maintained in the $Cu(acac)_2$-catalyzed reactions. It was observed that the reactions occur readily, however, with far lower yield.

Table 3.1.1. *Aza-Michael reaction between piperidine and methyl acrylate under different reaction conditions*[a]

Entry	Catalyst	Solvent	Isolated Yield(%)
1	$Cu(acac)_2$	IL	98[b]
2	$CuCl_2$	IL	95[b]
3	–	IL	60[b]
4	$Cu(acac)_2$	CH_3CN	30
5	$Cu(acac)_2$	H_2O	46
6	$CuCl_2$	H_2O	40
7	$Cu(acac)_2$	H_2O+IL	54[c]
8	–	H_2O+IL	32[c]

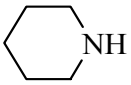
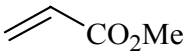
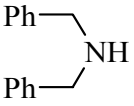
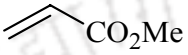
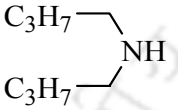
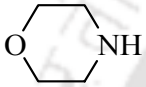
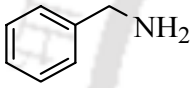
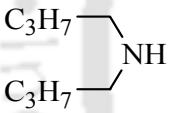
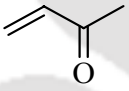
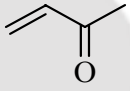
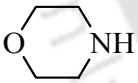
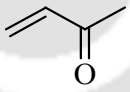
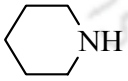
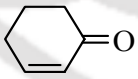
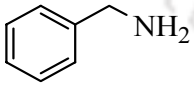
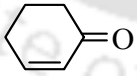
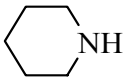
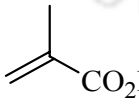
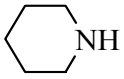
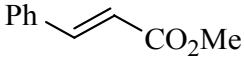
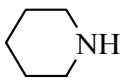
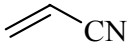
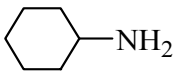
[a] *Reaction conditions: piperidine (1 mmol), methyl acrylate (1.2 mmol), Cu catalyst (2 mol %) at room temperature for 10 min.*
[b] *Using 1 mL of the ionic liquid (IL).*
[c] *Using 1 mL of H_2O and 10 mol% of ionic liquid.*

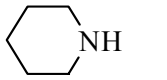
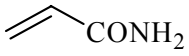
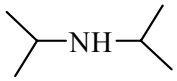
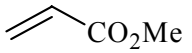
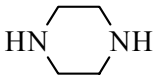
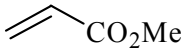
Thus, the importance of the catalysts in the present methodology is quite clear. To ascertain the superior performance of ionic liquids over other solvents, several experiments were conducted using $Cu(acac)_2$ or $CuCl_2$ as the catalyst separately in acetonitrile, water, and a mixture of water and ionic liquid, with and without a metal catalyst. The conjugate addition took place in each case albeit with low yields.

A variety of α,β-unsaturated carbonyl compounds or nitriles such as methyl acrylate, acrylonitrile, methyl vinyl ketone, and cyclohexenone underwent 1,4-addition with a wide range of aliphatic amines in the presence of 2 mol % of $Cu(acac)_2$ in 1 mL ionic liquid at room temperature to give the corresponding β-amino compounds or nitriles in high yields in a very short time. The results are summarized in **Table 3.1.2**. Cyclic α,β-unsaturated ketone such as cyclohexenone reacted readily with benzylamine and piperidine to give the corresponding 1,4-adducts in high yields (entries **9** and **10,** Table 3.1.2). In the case of primary amines, 8–15% of the bis-adducts was also formed (entries **5** and **14,** Table 3.1.2). Sterically hindered amines were found to be less active and gave the corresponding 1,4-adducts in moderate yields after 2 h (entries **2** and **16,** Table 3.1.2).

Both $bmimBF_4$ and $bmimPF_6$ showed almost similar activities in the aza-Michael reaction of amines with α,β-unsaturated carbonyl compounds (entry **1,** Table 3.1.2). When benzylamine and cyclohexylamine were reacted with an excess of methyl acrylate, bis-addition products were observed. In order to extend the scope of this methodology, α,β-substituted Michael acceptors like methyl methacrylate and methyl trans-cinnamate were tested under the same reaction conditions (**Table 3.1.2**). It was found that methyl methacrylate reacted readily with piperidine to give the corresponding 1,4-adduct in a very high yield (entry **11,** Table 3.1.2) whereas methyl trans-cinnamate reacted rather sluggishly to give the 1,4-adduct in a relatively low yield (entry **12,** Table 3.1.2). Some other electron-deficient olefins like ω-nitrostyrene and cinnamaldehyde, for instance, failed to react with piperidine, although acrylamide afforded the corresponding 1,4-adduct in good yield (entry **15,** Table 3.1.2). Furthermore, with a view to demonstrate the scope of practical applicability of this methodology, the aza-Michael reaction was carried out on a larger scale (20 mmol) using $Cu(acac)_2$-IL. The reaction was complete in 15 min affording the 1,4-adduct in 96% yield (entry **1,** Table 3.1.2) lending credence to the contention that the method can be scaled up. Finally, upon completion of the reaction, the ionic liquid phase containing $bmimBF_4$ and $Cu(acac)_2$ was almost quantitatively recovered by simple extraction of the product with diethyl ether. The recovered ionic liquid phase containing the catalyst was reused for several cycles with consistent activity (entry **1,** Table 3.1.2).

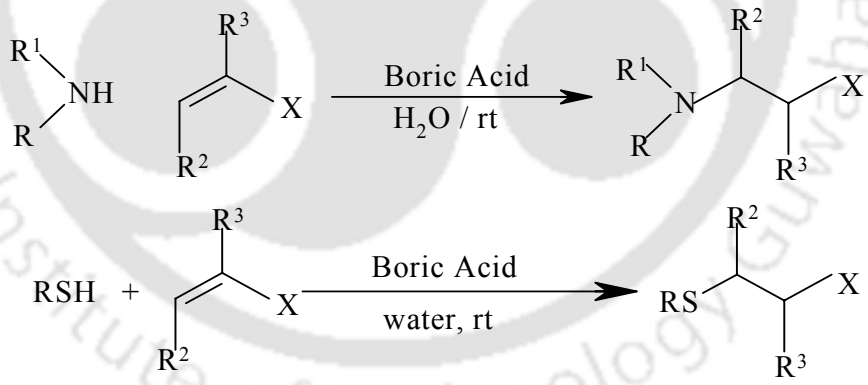
Table 3.1.2. *$Cu(acac)_2$-catalyzed aza-Michael reaction of amines with α,β-unsaturated carbonyl compounds and nitriles in $[bmim]BF_4$*

Entry	Amines	Olefins	Time(min)	Product	Yield (%)[a]
1			10	1a	98, 98[b], 96[c], 97[d]
2			120	2a	60
3			15	3a	90
4			10	4a	86
5			15	5a	85
6			10	6a	92
7			10	7a	96
8			15	8a	90
9			25	9a	85
10			25	10a	80
11			30	11a	85
12			60	12a	62
13			10	13a	98
14			25	14a	85[e]

15			30	15a	80
16			90	16a	70
17			20	17a	88[f]

[a] *Yield of isolated product*
[b] *With Bmim[PF_6]*
[c] *Reaction on 20 mmol scale*
[d] *Yield after fifth cycle*
[e] *With 2 mmol of α,β-unsaturated compound*
[f] *8-15% of the bis adduct were formed*

3.2 Boric Acid: A Novel and Safe Metal-Free Catalyst for Aza- and Thia-Michael Reactions



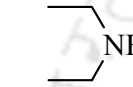
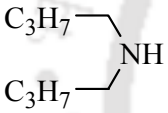
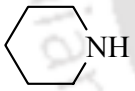
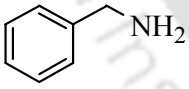
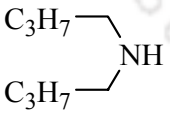
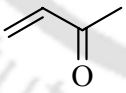
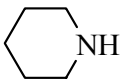
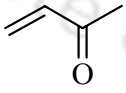
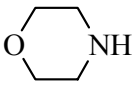
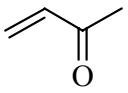
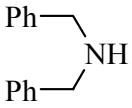
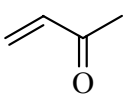
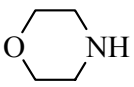
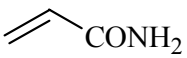
Scheme 3.2.1

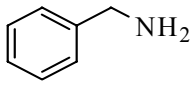
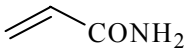
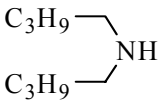
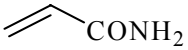
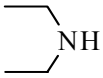
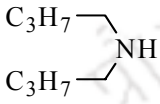
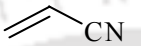
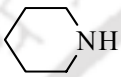
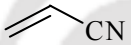
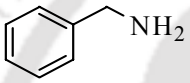
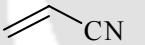
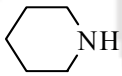
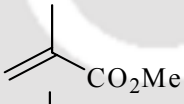
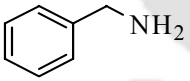
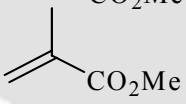
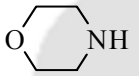
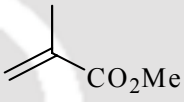
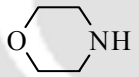
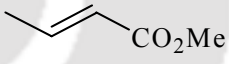
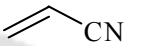
The selection of boric acid as the catalyst was instigated by one of its most fundamental properties that enables it produce Brønsted acid from its reaction with water or alcohol, $B(OH)_3 + H_2O \rightarrow B(OH)_4^- + H^+$ or $B(OH)_3 + ROH \rightarrow B(OH)_3(OR)^- + H^+$. Thus, boric acid in water or alcohol is expected to make an ideal combination for the Michael type additions. Accoridingly, this combination was used first for the aza-Michael reaction.

A variety of α,β-unsaturated compounds such as methylacrylate, acrylonitrile, methylvinyl ketone, acryl amide, methyl methacrylate underwent 1,4 addition with a wide range of aliphatic

amines in the presence of 10 mol% of boric acid at room temperature to give the corresponding β-amino compounds in high yields. The results are summarized in **Table 3.2.1.** In general secondary amines gave higher yields than the primary amines. Pertinent is to mention that benzyl amines gave only mono adducts (entries **5, 11, 16** and **18,** Table 3.2.1) whereas with primary amines, mostly bis-adducts (entries **21** and **22,** Table 3.2.1) were formed. A sterically hindered amine also gave the corresponding 1,4-adducts in good yield (entry **9,** Table 3.2.1).

Table 3.2.1. *Boric acid catalyzed conjugate addition of amines to α,β–unsaturated compounds in water*

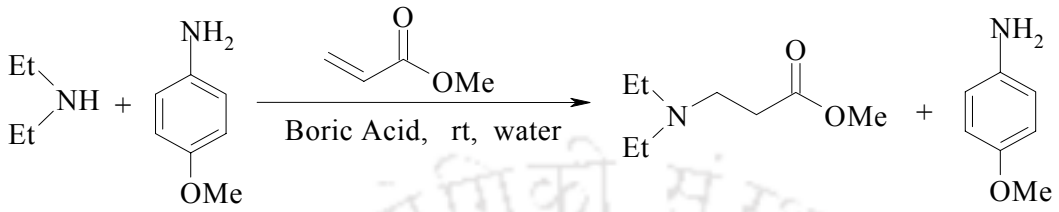
Entry	Amines	Olefins	Time(h)	Product	Yield (%)[a]
1			3.5	18a	90
2			4	3a	88
3			1.5	4a	85
4			1.5	1a	90, 93[b]
5			2.5	5a	90
6			5	6a	80
7			2.5	7a	80
8			3	8a	85
9			5.5	19a	85
10			4	20a	87

11			4	21a	85
12			5	22a	85
13			6	23a	78
14			2	24a	90
15			1.5	13a	95
16			2.5	25a	92
17			2	11a	90
18			3.5	26a	90
19			2	27a	88
20			5	28a	80
21	*n*-Bu—NH_2		1	29a	85[c]
22	*n*-Bu—NH_2		1	30a	30+35[c] (89[c])

[a] *Isolated Yield*
[b] *Yield on 5g scale*
[c] *Bis adduct*

In order to investigate the fate of the aza-Michael condesation involving aromatic amines such as aniline, *p*-methoxyaniline, *p*-nitroaniline with methyl acrylate as the Michael acceptor, the $B(OH)_3$—water protocol was applied to such reactions. Not to our surprise, only *p*-methoxyaniline reacted to afford a maximum of 15% of the addition product. This renders us to state that the $B(OH)_3$—water protocol is more selective for aliphatic amines. In order to lend support to our inference a separate reaction was conducted between methyl acrylate and equimolar mixture of *p*-methoxyaniline and diethylamine. The result is depicted in **Scheme 3.2.2** augmenting our

assertion regarding the selectivity of the present protocol. This selectivity may find usefulness in organic synthesis.



Scheme 3.2.2

Finally, upon completion of the reaction, catalyst recyclability was examined through a series of reactions with piperidine and methyl acrylate using the aqueous phase containing boric acid **Table 3.2.2**. The reactions went on well giving good yields, however, at relatively longer reaction times. This is explained by leaching of the catalyst. It is also important to note that the reaction can be performed at a relatively larger scale (5g) giving good yield (entry **4,** Table 3.2.1) showing its potential for industrial applicability.

Table 3.2.2. *Recycling of the catalyst using piperidine and methyl acrylate in water*

Entry	Yields (%)	Time (h)
1	92	1.5
2	90	2.5
3	90	5

To extend scope of the $B(OH)_3$─water protocol, α and β-substituted Michael acceptors were tested under the present conditions. It was found that with Me being either at α or β position, the protocol gave good yields (entries **17-20,** Table 3.2.1), whereas with Ph at β-position, it failed. This selectivity may be due to the steric and polar effects in olefins.

Having successfully applied the $B(OH)_3$─water protocol for amines, it was thought worthwhile to investigate if it would catalyze the thia-Michael reactions. The reaction strategies worked well and a variety of structurally diverse α,β–unsaturated compounds underwent 1,4 addition with a wide range of thiols in the presence of 10-20 mol% of boric acid at room temperature to give the corresponding β-sulfido compounds in good yields The same reactions are capable of being conducted in MeOH or EtOH.

A comparison of the results (**Table 3.2.3**) of catalysis using HCl, H_2SO_4, TsOH and CH_3COOH each in water, with all other conditions being maintained the same as that of $B(OH)_3$–H_2O, shows that $B(OH)_3$ is much more effective. With these acids, the yields were not only low but also some side reactions seemed to have occurred. The one property that is common to all these acids is their higher acidity compared to that of $B(OH)_3$. This may be the reason for their less effectiveness. Thus, because of the ease in handling and operation, its weak acidity leading to the desired reactions, no side reactions and efficacy, $B(OH)_3$ appears to be superior to the other acids studied herein. To ascertain the efficacy of the catalyst in water, the conjugate additions of thiophenol to methyl acrylate were separately conducted in water and four different organic solvents. The results are summarized in **Table 3.2.4**. Accordingly, water, MeOH or EtOH became the solvent of choice with 10–20% of the chosen catalyst.

Table 3.2.3. *Reaction of thiophenol with cyclohexenone using various catalysts and solvents*

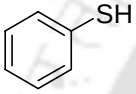
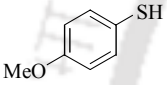
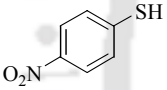
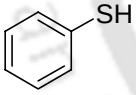
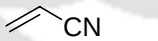
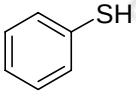
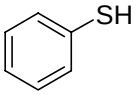
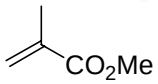
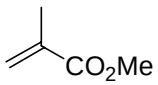
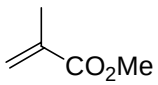
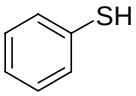
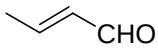
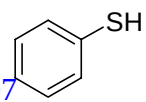
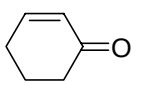
Entry	Catalyst	Solvent	Time (h)	Yield (%)
1	$B(OH)_3$	H_2O	4	88
		CH_3OH	3	92
		C_2H_5OH	4	89
2	HCl	H_2O	3	23
3	H_2SO_4	H_2O	3	15
4	TsOH	H_2O	3	22
5	CH_3COOH	H_2O	3	11

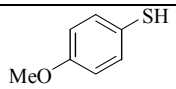
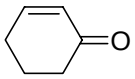
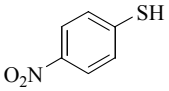
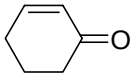
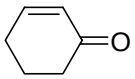
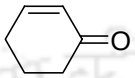
Table 3.2.4. *Reaction of thiophenol with methyl acrylate in different solvents with varying mol% of $B(OH)_3$*

Entry	$B(OH)_3$ (mol%)	Solvent	Time(h)	Yield(%)
1	1	MeOH	8	55
2	20	MeOH	2	92
3	10	MeOH	3	90
4	10	H_2O	4	89
5	20	H_2O	3	90
6	10	EtOH	4	85
7	20	EtOH	3	85
8	10	CH_3CN	8	64

A variety of structurally diverse α,β–unsaturated compounds such as methyl acrylate, acrylonitrile, crotonaldehyde, acrylamide, cyclohexenone and methyl methacrylate underwent 1,4 addition with a wide range of thiols in the presence of 10-20 mol% of boric acid at room temperature to give the corresponding β-sulfido compounds in good to very good yields (**Table 3.2.5**). It is notable that the reaction can be performed on a relatively larger scale (5 g) giving good yields (entry **1,** Table 3.2.5) showing its potential for large-scale preparations.

Table 3.2.5. *$B(OH)_3$ (10mol%) catalyzed conjugate addition of thiols to α,β–unsaturated compounds in MeOH at room temperature*

Entry	Thiol	Olefin	Product	Time min(h)	Yield (%)[a]
1			31a	4, 3[c]	89, 92,[b] 90,[c] 85[d]
2			32a	4	82
3			33a	5	79[e]
4	C_2H_5SH		34a	3	87, 91[d]
5	$C_{12}H_{25}SH$		35a	12	90
6			36a	3.5, 3[c]	92, 91[c]
7	C_4H_9SH		37a	3	87
8	$C_{12}H_{25}SH$		38a	12, 8[d]	78, 82[d]
9			39a	5	78[e]
10	C_4H_9SH		40a	6	70[e]
11			41a	5	85
12	C_4H_9SH		42a	5	79
13	C_2H_5SH		43a	4, 3[c]	82, 81[d]
14			44a	4	(80, 83[d])[e]
15			45a	4, 3[c]	88, 92,[c] 89[d]

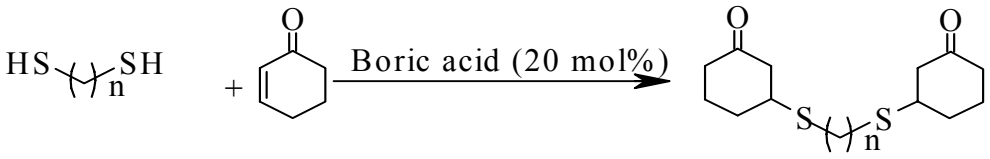
16			46a	3, 2[d]	90, 85[d]
17			47a	4	88
18	C_2H_5SH		48a	3, 2[c]	90,78,[c] 85[d]
19	$C_{12}H_{25}SH$		49a	12	90

[a] *Isolated Yields,*
[b] *Yield on a 5g scale,*
[c] *Reaction in MeOH,*
[d] *Reaction in EtOH,*
[e] *20 mol% catalyst used*

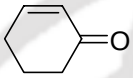
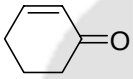
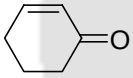
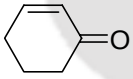
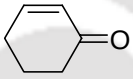
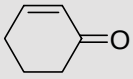
To extend scope of this protocol, α- and β-substituted Michael acceptors were tested under the present conditions. It was found that with Me groups at either the α- or β-positions, the procedure gave good yields (entries **11-14,** Table 3.2.5), whereas with a Ph group at the β-position it failed. In view of synthetic importance of the present results, it may be mentioned that prolonging the reaction time can increase yields further. The reaction works well in MeOH or EtOH. The reactions in alcohols appear to be somewhat faster than in water. However, considering the cost factor and need for avoidance of organic solvents, one might prefer water as the reaction medium. Finally, upon completion of the reaction, recyclability of the catalyst was examined through a series of reactions with thiophenol and cyclohexenone using aqueous phase containing boric acid. The reaction continued giving good results from second through the fourth cycles with the yields being 89, 86 and 85%, respectively. However, the yield dropped to 80% at the fifth cycle. This is explained by attrition and leaching of the catalyst.

Under similar experimental conditions, dithiols underwent the Michael addition giving bis-adducts in good yields (**Scheme 3.2.3, Table 3.2.6**). These reactions were nearly as facile as the monothiols. Incidentally, the Michael reactions involving dithiols appear to be quite scarce.[49] Such reactions may be highly useful in the designed synthesis of organosulfur polymers, supramolecular architectures and macromolecules.

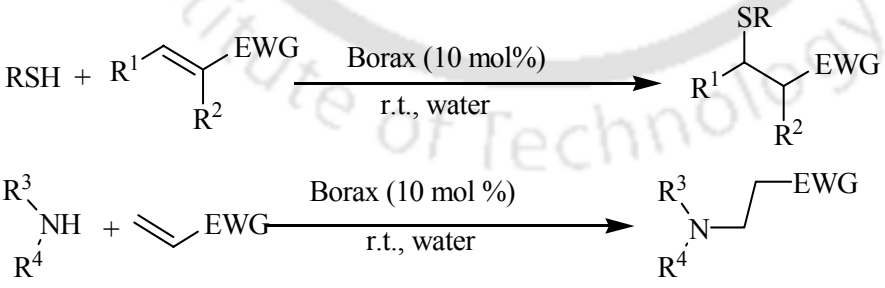
Table 3.2.6. *$B(OH)_3$ (20mol%) catalyzed conjugate addition of thiols to α,β–unsaturated compounds in MeOH at room temperature*



Scheme 3.2.3

Entry	HS SH (n)	Olefins	Solvent	Product	Time (min)	Yield (%)
1	n=2		H_2O	50a	5	75
2	n=3		H_2O	51a	5	85
3	n=2		MeOH	50a	4	75
4	n=3		MeOH	51a	4	78
5	n=2		EtOH	50a	4	71
6	n=3		EtOH	51a	4	76

3.3 Borax as an Efficient Metal-Free Catalyst for Hetero-Michael Reactions



Scheme 3.3.1

In order to ascertain efficacy of the chosen catalyst in water, the conjugate additions of thiophenol to methyl acrylate were separately conducted in water and four different organic solvents. The results are summarized in **Table 3.3.1**. It is evident that the reaction takes place in

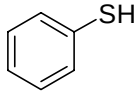
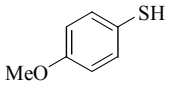
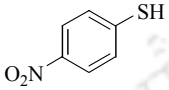
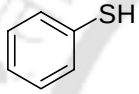
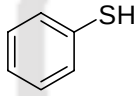
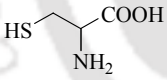
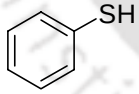
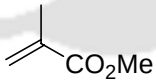
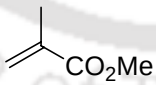
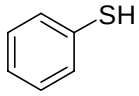
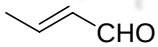
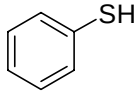
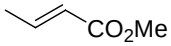
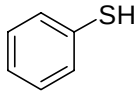
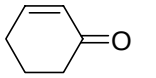
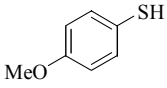
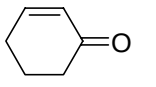
each case with the best performance being in water containing 10 mol% of the catalyst. Accordingly, all the reactions discussed herein after were conducted with this combination.

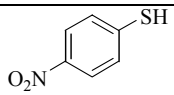
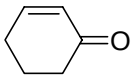
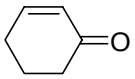
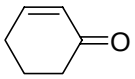
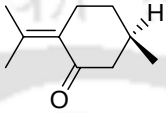
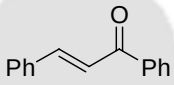
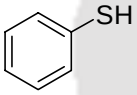
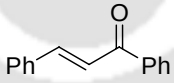
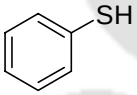
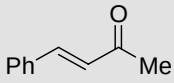
Table 3.3.1. *The Michael addition of thiophenol with methyl acrylate under different reaction conditions*

Entry	Borax(mol%)	Solvent	Time (min)	Yield (%)
1	0	H_2O	5	5
2	20	H_2O	5	95
3	10	H_2O	5	95
4	1	H_2O	5	40
5	10	MeOH	5	30
6	10	CH_3CN	5	64
7	10	$(CH_3)_2CO$	5	70
8	10	AcOEt	5	70

A variety of electron deficient olefins such as methylacrylate, acrylonitile, acrylamide, cyclohexanone and methyl methacrylate underwent facile 1,4 addition with a wide range of thiols catalyzed by borax (10 mol%) in water at room temperature to afford the corresponding β-adducts in high to very high yields (**Table 3.3.2**). Unsaturated ketones, nitriles, amides, aldehydes and esters reacted readily with both aliphatic and aromatic thiols to provide the corresponding Michael adducts (entries **1-20,** Table 3.3.2). The reactions were clean. The borax-water system worked also very well for α- and β-substituted Michael acceptors at ambient temperatures. It was found that with methyl being either at α- or β-position, the protocol gave good yields (entries **12-15,** Table 3.3.2) in 5-10 min, while with phenyl at β-position took longer reaction times (1.5-3 h, entries **23-25,** Table 3.3.2). Acceptors like carvone and pulegone reacted readily with aliphatic thiols (entries **21** and **22,** Table 3.3.2). Notably, the present protocol worked well for the conjugate addition of cysteine to acrylamide (entry **11,** Table 3.3.2) giving 88% isolated yield of the adduct. This reaction is relevant in the context of alkylation of cysteine in proteins with acrylamide under mildly aqueous alkaline conditions and is considered to be useful for cysteine identification during protein sequencing.[76,77]

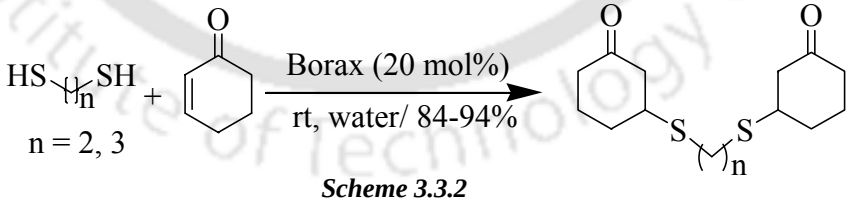
Table 3.3.2. *Borax catalysed Michael addition of thiols to olefins in water at room temperature*

Entry	Thiol	Olefin	Product	Time min(h)	Yield (%)[a]
1			31a	5	95, 97[b]
2			32a	5	92
3			33a	5	92
4	C_2H_5SH		34a	5	89
5	$C_{12}H_{25}SH$		35a	(3)	75
6			36a	5	94
7	C_2H_5SH		52a	5	87
8	$C_{12}H_{25}SH$		38a	(2.5)	72
9			39a	5	93, 96[b]
10	C_4H_9SH		40a	5	87
11			53a	30	88
12			41a	5	88
13	C_4H_9SH		42a	5	82
14			44a	10	85
15			54a	10	86
16			45a	5	92
17			46a	5	90

18			47a	5	88
19	C_2H_5SH		48a	5	90
20	$C_{12}H_{25}SH$		49a	(2.5)	70
21	C_2H_5SH		55a	(3)	85
22	C_2H_5SH		56a	(3)	82
23	C_2H_5SH		57a	(1.5)	89
24			58a	(3)	75
25			59a	(2)	80

[a] *Isolated Yield,*
[b] *Yield on 7 g scale*

The borax catalyzed Michael addition in water is applicable also to dithiols without any difficulty, as shown in **Scheme 3.3.2.**

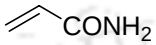
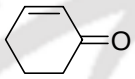
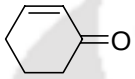


Scheme 3.3.2

The reactions proceeded with alacrity giving bis-adducts in very good yields (**Table 3.3.3**). Such reactions are expected to be useful in the designed synthesis of organo-sulfur polymers, supramolecular architectures and macromolecules. Incidentally, H_2N-CO-CH_2-CH_2-S-CH_2-CH_2-S-CH_2-CH_2-CO-NH_2 obtained from the reaction of 1,3 propanedithiol and two equivalents of acrylamide (entry **2,** Table 3.3.3) is an interesting compound,[22,23] the preparation of which does not seem to be available in open literature. Two Japanese patents[22,23] reported the use of the compound as a photographic development accelerator

and a constituent of color photographic developer. This was used also in lithographic plate processing solution.

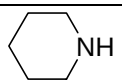
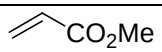
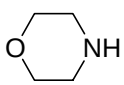
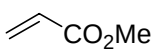
Table 3.3.3 *Borax catalysed Michael addition of dithiols to olefins in water at room temperature*

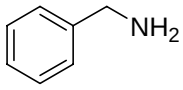
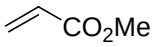
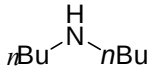
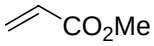
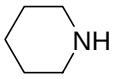
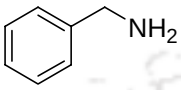
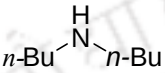
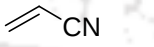
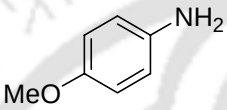
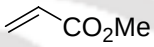
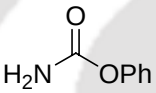
Entry	HS(CH$_2$)$_n$SH	Olefins	Product	Time (min)	Yield (%)[a]
1	n=2		**60a**	15	92
2	n=3		**61a**	15	94
3	n=2		**50a**	15	84
4	n=3		**51a**	20	87
5	n=2		**62a**	15	86
6	n=2		**63a**	20	85

[a] *Isolated Yields*

The borax-water protocol is applicable to aza-Michael reactions as well. A variety of α,β-unsaturated compounds underwent 1,4 addition with a wide range of aliphatic amines in the presence of 10 mol% of borax at ambient temperatures to afford the corresponding β-amino compounds in high yields. Some representative examples are set out in **Table 3.3.4**. An internal comparison of the results of thiol additions with those of amine additions under similar experimental conditions shows that the former are more facile than the latter. Indeed, this observation is in agreement with the result of an earlier kinetic studies.[78] Based on kinetic data it was predicted that –SH groups are many times more reactive than amines in aqueous alkaline solution.

Table 3.3.4. *Borax catalyzed Michael addition of amines to olefins in water at room temperature*

Entry	Amine	Olefin	Product	Time(h)/ Yield(%)[a]
1			1a	3/86
2			4a	3/92

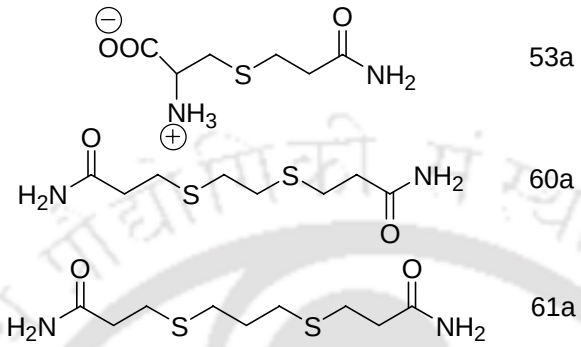
3			5a	2/89
4			3a	2/92
5			13a	2/90
6			25a	1.5/86
7			24a	2/92
8			64a	8/25
9			65a	8/0

[a] *Isolated Yields*

Finally, recyclability of the catalyst was examined through a series of reactions with thiophenol and methyl acrylate using aqueous phase containing borax. The reaction continued giving good results from second through the fifth cycles with the yields being 95, 94, 92 and 90%, respectively. However, the yield was reduced to 80% at the sixth cycle. This is explained by attrition and leaching of the catalyst. Important is also to note that the borax-water protocol can be applied to a relatively larger scale (7 g) of operation giving very good yields (Table 3.3.4, **entries 1** and **9**).

A comparison of the present results with those of the corresponding boric acid catalyzed aza- and thia-Michael reactions, as presented under **Section 3.2**, suggests that under similar experimental conditions borax appear to be either as good as or slightly better than boric acid in catalyzing the chosen reactions.

3.4 X-Ray Studies on β-Sulfidocarbonyls Evidencing Intermolecular Hydrogen Bonded Self-Assembled β-Pleated Sheet Structures



Some of our main concerns in this section have been to ascertain the occurrence and relative strength of hydrogen bonding, the consequences of hydrogen bonding in the intermolecular networking, and to rule out the possibility of polymerization of the compounds especially for **60a** and **61a**. It is hoped that the results might help in providing insight into the nature of hydrogen bonding in protein structures. Accordingly, X-ray diffraction analyses of the three compounds were done and supramolecular organization in the crystals determined. The resultant ORTEP depictions with atom numbering schemes are presented in **Figs. 3.4.1, 3.4.4** and **3.4.9** and pertinent structural data are provided in experimental section of this chapter.

The compound **53a** crystallizes in the monoclinic space group $P2_1$ with one molecule in the asymmetric unit. It appears that conformational freedom of molecule in the crystal lattice is not so restricted thereby allowing different packing options (**Fig. 3.4.2**). Thus, there is a significant

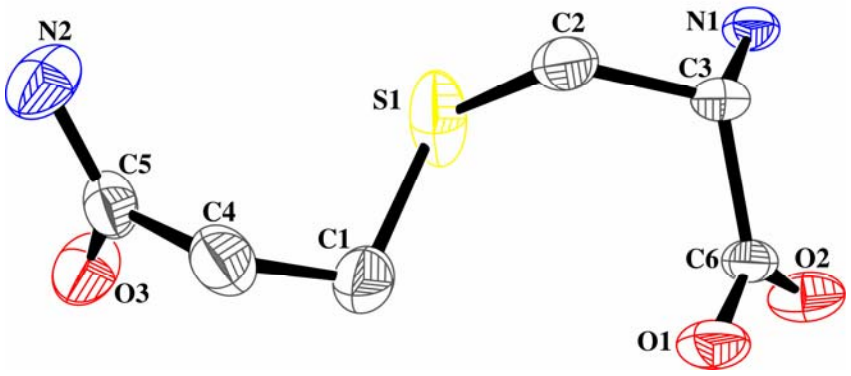


***Fig. 3.4.1**. ORTEP plot of **53a**. Hydrogen atoms are omitted for clarity*

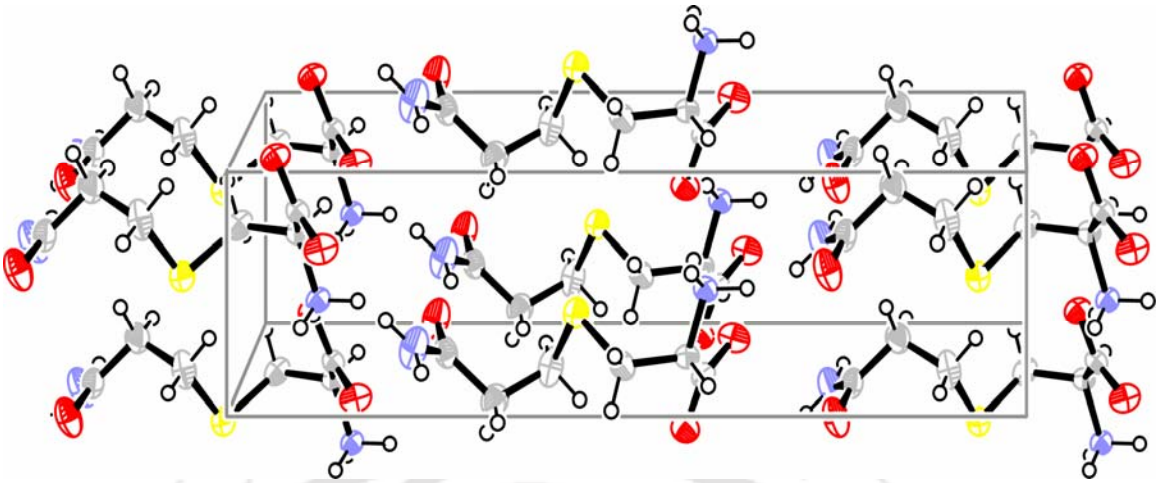


Fig. 3.4.2. *Packing diagram of* ***53a.***

degree of reciprocal intermolecular hydrogen bonding between two neighboring molecules along the crystallographic *b* axis involving a carboxylate oxygen of one and an amide hydrogen of the other (N2–H2**…**O2 = 2.927 Å), and an ammonium hydrogen of one and the carbonyl oxygen of amide of the other (N1–H1**…**O3 = 2.833 Å). The hydrogen bond distances fall in the normal range and the results compare very well with those reported in literature.[79-82] The contiguous molecules of **53a** being intermolecularly H-bonded form an undulated chain through tail-to-head interactions (**Fig. 3.4.3**). Interestingly, due to the favorably positioned donor and acceptor atoms in the hydrogen bonded chained molecules, the chains associate to produce β-sheet type of structural arrangement (**Fig 3.4.3**). The stacking of undulated chains takes place along the crystallographic *c* axis with the interlayer connectivities being favored by hydrogen bonding (**Table 3.4.1**). The interchain N–H**…**O hydrogen bonds arise from amide-amide interactions between the N–H proton of amide moiety of one molecule and the carbonyl oxygen atom of amide moiety of a neighboring molecule (N2–H1**…**O3=2.878 Å). It is thus quite evident that the crystal growth along the crystallographic *c* axis entails head-to-head and tail-to-tail hydrogen bonding. Another notable feature of the crystal structure of **53a** is the formation of six membered intermolecular hydrogen bonding C–H**…**O network involving H2A and the neighboring carboxylate O1 atom (C2–H2A**…**O1 = 3.370 Å) (**Fig. 3.4.3**). Although C–H**…**O hydrogen bonding is a rather weak binding force (< 4 Kcal/mol), it is recognized to be of importance in providing support, by playing a secondary role, to the relatively stronger hydrogen bonds[79,80] thereby reinforcing β-sheet like structures. The structural motif may have some relevance to the chemistry of glutathione (GSH).

Table 3.4.1. *Hydrogen bond distances (Å) and angles (°) in* ***53a, 60a*** *and* ***61a***

Compound	D–H…A	D–H (Å)	H…A(Å)	D…A(Å)	∠D–H…A (°)
53a	N1–H2…O1	0.911	1.954	2.816	157.13
	N1–H3…O1	0.852	2.129	2.962	165.68
	N1–H1…O3	0.951	1.893	2.833	169.24
	N2–H1…O3	0.860	2.075	2.878	155.11
	N2–H2…O2	0.861	2.072	2.927	172.11
	C2–H2A…O2	0.970	2.637	3.370	132.66
	C1–H1A…O1	0.980	2.213	3.106	132.66
60a	N1–H2…O1	0.827	2.144	2.966	172.85
	N1–H1…O1	0.827	2.154	2.973	170.50
	C2–H2A…O1	0.930	2.590	3.507	168.93
	C3–H3B…S1	0.948	2.952	3.790	148.10
61a	N1–H1…O1	1.040	1.911	2.948	174.26
	N1–H2…O1	0.709	2.327	3.021	166.51
	N1–H3…O2	0.906	2.103	3.008	174.87
	N1–H4…O2	0.808	2.189	2.959	159.37
	C2–H2B…O1	0.970	2.633	3.588	168.04
	C8–H8B…O2	0.969	2.642	3.597	168.30
	C4–H4A…S1	0.970	2.896	3.786	153.01
	C3–H3A…S1	0.971	2.884	3.785	154.71
	C6–H6A…S2	0.970	2.899	3.792	153.53
	C7–H7A…S2	0.970	2.884	3.780	154.09

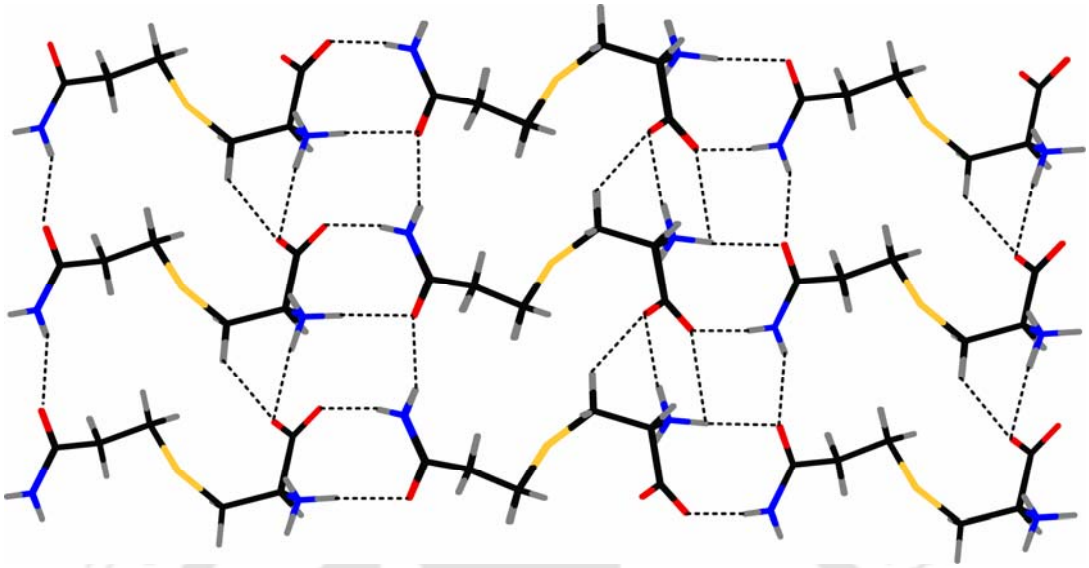


Fig. 3.4.3. *N–H…O and C–H…O type hydrogen bonding in* ***53a.***

The compound **60a** crystallizes in the monoclinic space group $P2_{1/C}$ (**Fig. 3.4.4**). The molecule is symmetrical with one half of it, as shown in **Fig. 3.4.4**, being just the mirror image of the other half. It is possibly because of symmetrical nature of the compound that it enables a very regular packing of molecules in the crystal lattice as reflected in the packing diagram (**Fig. 3.4.5**) as well as the hydrogen bond distances. The crystal grows along both the crystallographic *b* as well as *c* axis. Along the crystallographic *b* axis, the molecules communicates with each other through crystallographic inequivalent N–H**…**O hydrogen bonding involving N–H hydrogen of one amide moiety and carbonyl oxygen of another amide moiety (N1–H2**…**O1 = 2.966 Å, N1–H1**…**O1 = 2.973 Å). These interactions are propagated and the molecules are self-organized into the infinite 1D kinked chain. These chains in turn self-assemble along the crystallographic *c* axis by interlayer

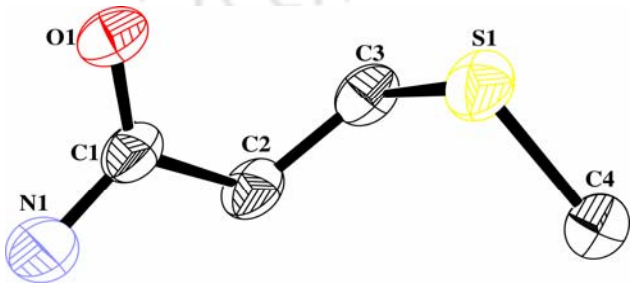


Fig. 3.4.4. *ORTEP plot of* ***53a****. Hydrogen atoms are omitted for clarity.*

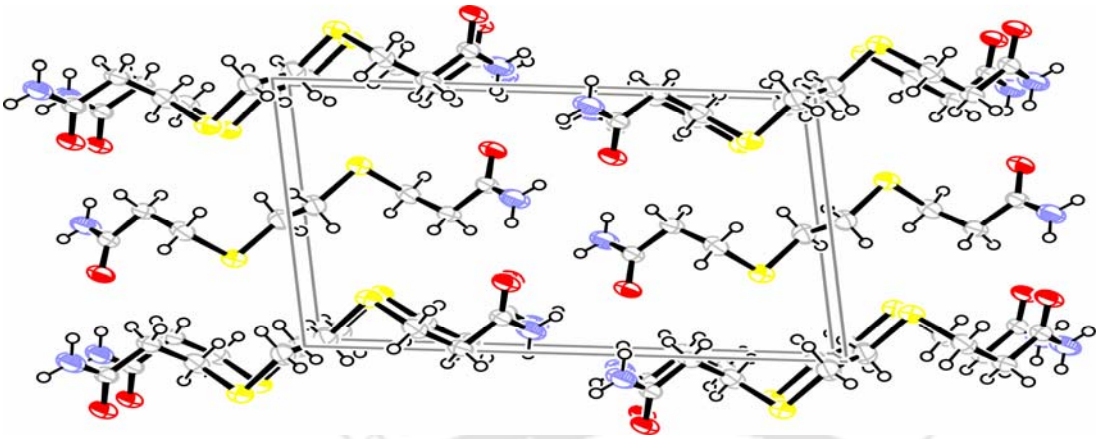


Fig. 3.4.5. *Packing diagram of* ***53a.***

head-to-head and tail-to-tail interactions through N–H…O hydrogen bonding leading to a well organized parallel β-sheet like structure (N1–H2**…**O1 = 2.966 Å and N1–H1**…**O1 = 2.973 Å). The later interactions gave rise to the formation of 8-membered hydrogen bonded cyclic networks as shown in **Fig. 3.4.6**. The hydrogen bond strength is normal.[79-82] Another notable feature of crystal structure of the compound **60a** is the occurrence of weak intermolecular and interchain C–H**…**O (C2–H2**…**O1 = 3.507 Å) hydrogen bonding and relatively weaker hydrogen bonding[83,84] originating from C–H…S interaction (C3–H3**…**S1 = 3.790 Å) as shown in **Fig. 3.4.7**. These interchains hydrogen bonding provides additional support to the promotion of a regular array of parallel β-sheet like structure.[85] Finally, as the crystal grows on, it leads to the formation of zig-zag hydrogen bonding network along the crystallographic *c* axis (**Fig. 3.4.8**).

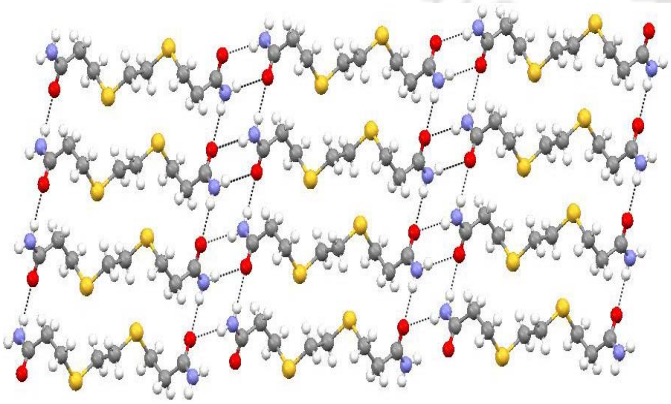


Fig. 3.4.6*. Packing diagram of* ***60a*** *viewed along crystallographic b axis*

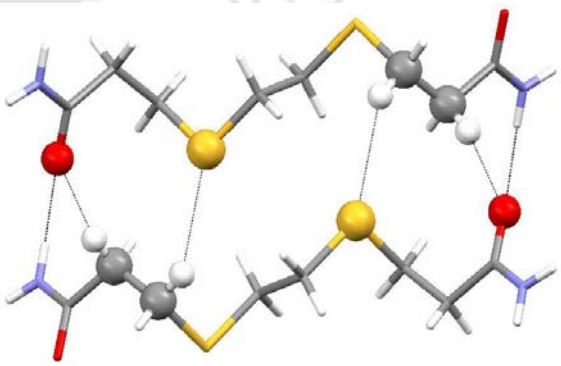


Fig. 3.4.7*. C–H…O and C–H…S type hydrogen bonding in* ***60a****.*

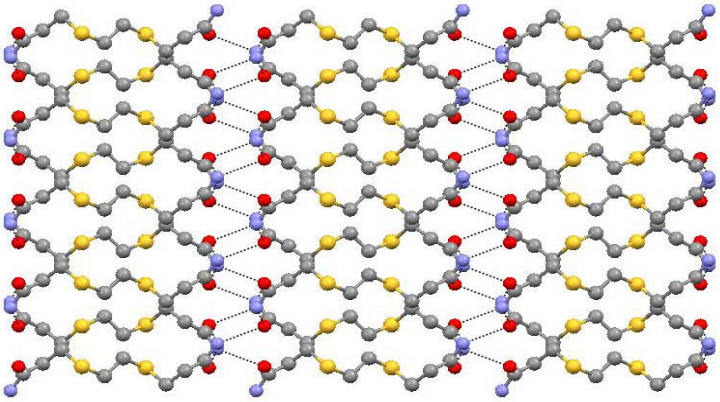


***Fig.3.4.8**. Zigzag hydrogen bonding network of **60a** viewed along crystallographic c axis.*

The compound **61a** is relatively less symmetrical compared to **60a** and crystallizes in monoclinic space group $P2_{1/c}$. The main difference between the two molecules is the presence of an additional methylene group (C_5) in **61a** causing it to be rather less symmetrical. The crystal grows along both *a* and *b* axis. The intermolecular connectivities along the crystallographic *a* axis are established through the crstallographically inequivalent reciprocal N–H**…**O hydrogen bonding (N1–H1**…**O1 = 2.948 **Å**, N1–H4**…**O2 = 2.959 Å**)** (**Table 3.4.1**) of normal strength**.** This self-association continues leading to an infinite 1D kinked chain. The chains so formed self-organize along the crystallographic *b* axis through head-to-head and tail-to-tail hydrogen bonding interaction involving N–H**…**O (N1–H2**…**O1 = 3.021 Å, N1–H3**…**O2 = 3.008 Å) of amides of the neighboring molecules. An internal comparison of the results of X-ray crystallographic analysis shows that unlike in **60a**, the reciprocal N–H**…**O bond distances in **61a** seem to vary rather considerably presumably because of the unsymmetrical disposition of **61a**. The amide hydrogen bond distances of this compound along the crystallographic *b* axis are normal[79-82]: H2N**…**O1 = 2.33Å and H2N**…**O2 = 2.10Å, whereas along the crystallographic *a* axis are: H1N**…**O1 = 1.91Å and H2N**…**O2 = 2.19 Å. The C–H**…**O hydrogen bondings in **61a** are (H8B**…**O2 = 2.64 Å and H2B = 2.63 Å), however, weaker than those in **60a**. Notably, this compound appears to be comparatively more amenable to the formation of C–H**…**S type hydrogen bonding than **60a**. Thus, it forms C–H**…**S hydrogen bonds not only more in number but also comparable in strength (H3A**…**S1 = 2.88 Å, H4A**…**S2 = 2.89 Å, H6A**…**S2 = 2.89 Å and H7A**…**S2 = 2.88 Å) to those of **60a**.

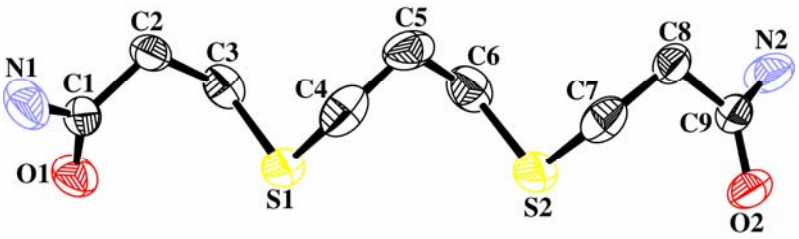


***Fig. 3.4.9**. ORTEP plot of **61a**. Hydrogen atoms are omitted for clarity.*

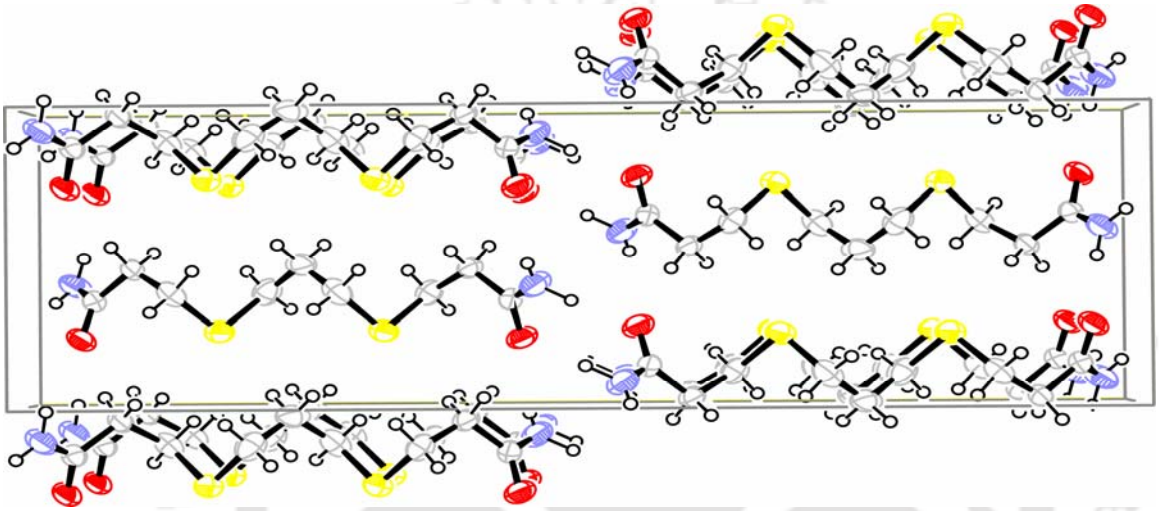


***Fig. 3.4.10**. Packing diagram of **61a**.*

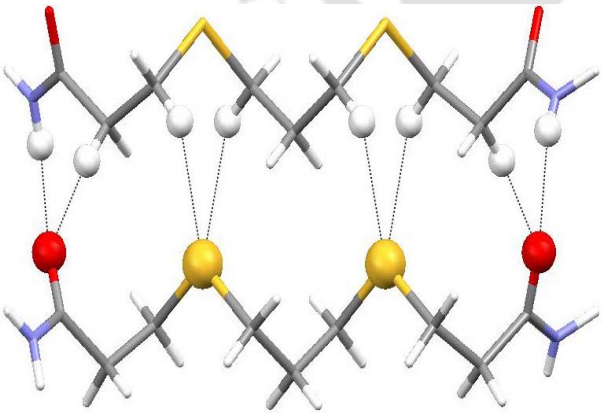


***Fig. 3.4.11**. C–H···O and C–H···S type hydrogen bonding in **61a**.*

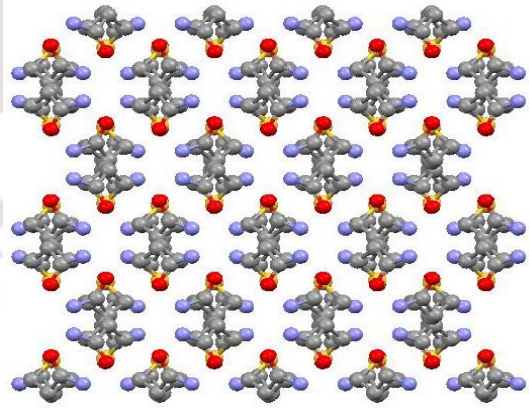


***Fig. 3.4.12**. Packing diagram of **61a** viewed along crystallographic a axis.*

Owing to favorable positioning of the donor and acceptor atoms, the crystal structure also shows the presence of, not so commonly encountered, bifurcated C–H**…**S type hydrogen bonding (**Fig. 3.4.11**). Here again C–H**…**S hydrogen bonding support the N–H**…**O hydrogen bonding in

augmenting the sheet structure formation, as observed. Like in **60a**, the molecules in the crystals of **61a** organize in such a manner that leads to the formation of zig-zag hydrogen bonding network. Finally, the molecules arrange themselves along *bc* plane forming a 3D mosaic like network (**Fig. 3.4.12**).

3B. Conclusion

The Michael reaction being one of the most fundamental and versatile reaction of C-C, C-N, C-O and C-S bonds formation in organic chemistry has received a continued attention of chemists over many years in their attempts to render the reaction protocols for more and more environment friendly, facile, soft practical and cost-effective. Our participation in this endeavor led to the development of three new protocols enabling to conduct the aza- and thia-Michael reactions quite efficiently. While one of the protocols is based on the use of bis-acetylacetonatocopper(II), $Cu(acac)_2$, as the catalyst in ionic liquid, the the other two are based on the use of metal-free catalyst *viz.*,boric acid and borax, in water or alcohol. The later two catalysts are to the best of our knowledge perhaps the soft catalysts to be used for the purpose. The other attributes in these methodologies are their efficacy in water as the solvent and cost effectiveness thereby rendering them to adhere to some of the "Green Chemistry" tenets and triple bottom line mandates. The results also demonstrate the task specific performance of boric acid as a very weak acid, and borax as a rather weak base, for chosen aza- and thia-Michael reactions thereby widening the scope for further studies.

As an additional incentive to this investigation, the X-ray structure analysis of the three β-sulfidocarbonyls **53a**, **60a** and **61a**, revealed self-organization of molecules in the crystals through N–H**…**O and C–H**…**O in all, in addition to C–H…S in **60a** and **61a,** hydrogen-bonding network. The self-assembly gives rise to β-sheet type of structural arrangement of intermolecularly hydrogen-bonded molecules in the crystal lattice. Among the three varieties of hydrogen bonds encountered in the compounds, the N–H**…**O interaction appear to be strongest followed by C–H**…**O and C–H**…**S interactions. The S atom in **61a** is bifurcated *via* two C–H**…**S bonds. It is anticipated that the chosen compounds might serve as suitable probes to study hydrogen-bonding interactions in and obtain insights into the realm of sulfidoamide chemistry and the structural type that they might represent (*c.f.* protein structure).

3C. Experimental

The sources of chemicals and solvents, the methods for quantitative determination of elements and the details of all the equipment used for physico-chemical studies have been described in **Chapter 2**.

General experimental procedure for $Cu(acac)_2$-imobilized in ionic liquid catalyzed aza-Michael reaction

A mixture of $Cu(acac)_2$ (0.005 g, 2 mol%), amine (2 mmol) and α,β-unsaturated compound (2.2 mmol) in ionic liquid ($bmimBF_4$ or $bmimPF_6$) (1 mL) was stirred at room temperature for the appropriate time as given in **Table 3.1.2**. After completion of the reaction, as indicated by TLC, the product was extracted with diethyl ether (3x10 mL). The combined ether extracts was concentrated under vacuum and the resulting product was purified by column chromatography on silica gel (mesh size 60-120) with ethyl acetate and n-hexane (2 : 8) as eluent to afford the pure β-amino adduct. The ionic liquid containing $Cu(acac)_2$ was dried under vacuum for the next run. The results are summarized in **Table 3.1.2.**

General procedure for boric acid catalyzed aza-Michael reaction

Boric acid (0.3mmol, 0.018g) was dissolved in water (3mL), followed by the addition of amine (3 mmol) and α,β–unsaturated compounds (3.3mmol) and the whole was stirred at room temperature. Progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3×10 mL). The combined organic extracts (dried over Na_2SO_4) were concentrated in vacuo and the resulting product was purified by column chromatography on silica gel (mesh size 60-120) with ethyl acetate and n-hexane [Ratio varied with product. For amides, ethyl acetate and methanol (9:1) was used] as eluent to afford pure β-amino adduct. The aqueous layer containing boric acid was reused for the next run. The results are set out in **Table 3.2.1.**

General procedure for boric acid catalyzed thia-Michael reaction

Boric acid (0.2 mmol, 0.012 g) was dissolved in water or MeOH or EtOH (1 mL) followed by the addition of the thiol (2 mmol) or dithiol (1 mmol) and α,β–unsaturated compounds (2.2 mmol) and the whole was stirred at room temperature. Progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3×5 mL),

dried over Na_2SO_4 and the resulting product was purified (in case of MeOH or EtOH the reaction mixture was concentrated, adsorbed on silica gel and directly loaded) on silica gel (mesh size 60-120) and eluted with ethyl acetate and n-hexene (1: 9) as eluent to efford pure β–sulfido adduct. A precipitate occurred for the reactions of amide with thiols. The precipitate was fitered and washed with water followed by recrystalization from MeOH. **Tables 3.2.5** and **3.2.6** contain the outcome of the reactions.

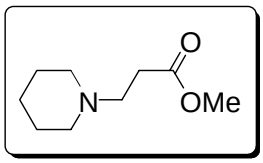
General experimental procedure for borax catalyzed aza- and thia-Michael reaction

Borax (0.2 mmol, 0.076 g) was dissolved in water (2 mL) followed by the addition of a thiol or an amine (2 mmol) or a dithiol (1 mmol) and α,β–unsaturated compound (2.2 mmol) and the whole was stirred at room temperature. Progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3×5 mL). The combined extracts (dried over Na_2SO_4) was dried *in vacuo* and the resulting product was purified on silica gel (mesh size 60-120) with ethyl acetate and *n*-hexene (1:9 for thia and 3:7 for aza-adduct) as eluent to efford the pure adduct. The aqueous layer containing borax can be reused for the next run. A 25% methanol in water was used as reaction medium for entries **23-25** (Table 3.3.2). Precipitate occurred in the reactions of amide with thiols (entries **9-11**, Table 3.3.2 and **1** and **2,** Table 3.3.3). The precipitate was fitered and washed with water followed by recrystalization from MeOH or hot water. The results are summerized in **Tables 3.3.2, 3.3.3 and 3.3.4**.

3D. Characterization of the products

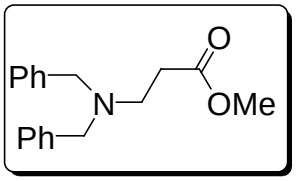
The compounds were characterized by mp, elemental analysis, IR, ^1H and ^{13}C NMR, Mass spectrometry and X-ray crystallography and data for the products are summarized as follows.

Methyl 3-Piperidin-1-yl-propionate (1a)



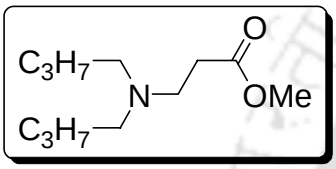
IR (KBr) : 2937, 2854, 2808, 2954, 2854, 2812, 1739(s), 1438, 1373, 1045, 861, 751 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : δ 1.38-1.47(m, 2H), 1.52-1.62(m, 4H), 2.34-2.42 (m, 4H), 2.44-2.50(m, 2H), 2.58-2.66(m, 2H), 3.67(s, 3H); MS (EI): m/z 171 (M^+), 98 (100%).

Methyl 3-Dibenzylamino-propionate (2a)



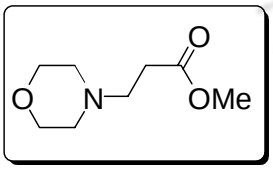
IR (KBr) : 2966, 2930, 2832, 1742(s), 1614, 1501, 1319, 1132, 753 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz): 1.98(s, 3H), 2.57(t, *J* = 7.2Hz, 2H), 2.78(t, *J* = 7.2Hz, 2H), 3.55(s, 4H); 7.16-7.30 (m, 10H).

Methyl 3-(*N*,*N*-Dibutylamino)-propionate (3a)



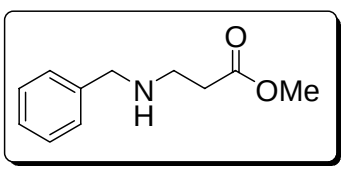
IR (KBr) : 2956, 2872, 2805, 1743(s), 1481, 1481, 1436, 1202, 1100, 743 cm^{-1} ; ^1H NMR: ($CDCl_3$, 400MHz) : 0.90(t, *J* = 6.8Hz, 6H), 1.26-1.44(m, 8H), 2.39(t, *J* = 7.2Hz, 2H), 2.60(t, *J* = 7.2Hz, 2H), 2.77(t, *J* = 7.6Hz, 2H), 3.66(s, 3H); ^{13}C NMR($CDCl_3$, 100MHz) : δ 14.50, 21.04, 29.70, 32.68, 47.18, 49.70, 50.17, 51.82, 54.00, 173.42; MS (EI): m/z 215 (M^+), 172 (100%).

Methyl 3-morpholin-4-yl-propionate (4a)



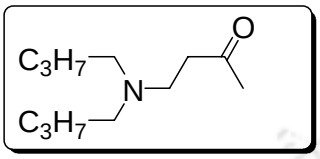
IR (KBr) : 2954, 2854, 2812, 1739(s), 1438, 1373, 1298, 1118, 1012, 871 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 2.46(t, *J* = 4.4Hz, 4H), 2.51(t, *J* = 7.6Hz, 2H), 2.68(t, *J* = 7.6Hz, 2H), 3.68-3.70(m, 7H); ^{13}C NMR ($CDCl_3$, 100MHz) : δ 32.26, 52.98, 53.72, 54.26, 67.18, 172.8; MS (EI): m/z 173(M^+), 100(100%).

Methyl 3-Benzylamino-propionate (5a)



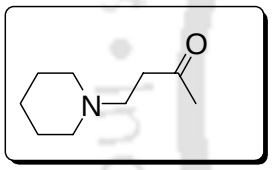
IR (KBr) : 3467, 3032, 2955, 2832, 1742(s), 1614, 1501, 1445, 1173, 1127 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 1.87(s, 1NH), 2.52(t, *J* = 6.8Hz, 2H), 2.88(t, *J* = 6Hz, 2H), 3.66(s, 3H), 3.79(s, 2H), 7.20-7.30(m, 5H).

4-(*N*,*N*-Dibutylamino)-butan-2-one (6a)



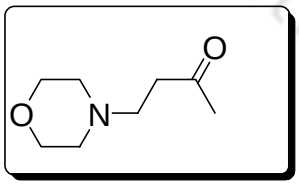
IR (KBr) : 2956, 2872, 2805, 1703(s), 1481, 1481, 1436, 1202, 1100, 743 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 0.91(t, *J* = 4.4Hz, 6H), 1.25-1.42(m, 8H), 2.14(s, 3H), 2.36(t, *J* = 4.4Hz, 4H), 2.51(t, *J* = 4.4Hz, 2H), 2.69(t, *J* = 5.2Hz, 2H); MS (EI): m/z 199 (M^+), 172 (100%)

4-Piperidin-1-yl-butan-2-one (7a)



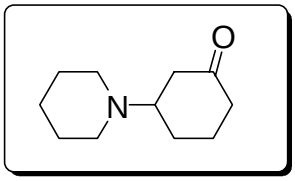
IR (KBr) : 2937, 2854, 2808, 2259, 1710, 1455, 1259, 1158, 1117, 1045, 861, 751, 416 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : δ 1.36-1.48(m, 2H), 1.54-1.63(m, 4H), 1.94(s, 3H), 2.36-2.49(m, 6H), 2.60-2.67(m, 2H); MS (EI): m/z 155 (M^+), 98 (100%).

4-Morpholin-4-yl-butan-2-one (8a)



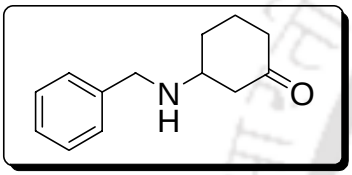
IR (KBr) : 2954, 2854, 2812, 1708(s), 1438, 1373, 1298, 1118, 1012, 871 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 2.15(s, 3H), 2.40(t, *J* = 4.4Hz, 4H), 2.56-2.61(m, 4H), 3.63(t, *J* = 4.8Hz, 3H); MS (EI): m/z 157(M^+), 100(100%)

3-Piperidin-1-yl-cyclohexanone (9a)



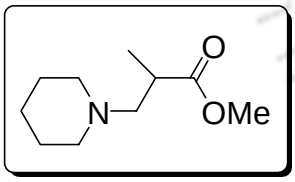
IR (KBr) : 2954, 2854, 2812, 1716, 1455, 1259, 1158, 1117, 861, 751, 416 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 1.64-1.76(m, 6H), 1.81-1.89(m, 2H), 2.15-2.26(m, 2H), 2.39-2.49(m, 4H), 2.73-2.77(m, 4H), 3.04-3.11(m, 1H); MS (EI): m/z 181 (M^+), 98 (100%).

3-Benzylamino-cyclohexanone (10a)



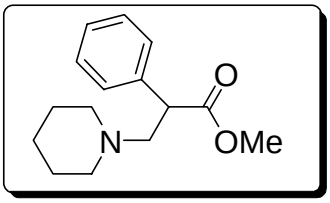
IR (KBr) : 3334, 3037, 2945, 2843, 1710, 1490, 1435, 1230, 1132, 779, 707 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 1.57(s, 1NH), 1.66-1.77(m, 2H), 2.09-2.16(m, 2H), 2.24-2.39(m, 3H), 2.64-2.69(m, 1H), 3.27-3.33(m, 1H), 3.81(s, 2H), 7.24-7.28(m, 5H); MS (EI): m/z 203(M^+), 91(100%).

Methyl 2-Methyl-3-piperidin-1-yl-propionate (11a)



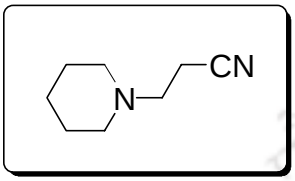
IR (KBr) : 2936, 2853, 2761, 2377, 1741, 1455, 1271, 1219, 1171, 871, 771 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 1.14(d, J = 4.6Hz, 3H), 1.39-1.55(m, 6H), 2.22-2.35(m, 5H), 2.50-2.60(m, 2H), 3.66(s, 3H); MS (EI): m/z 185(M^+), 98(100%).

Methyl 2-Phenyl-3-piperidin-1-yl-propionate (12a)



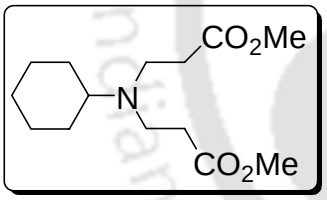
IR (KBr) : 2853, 2761, 2377, 1741, 1455, 1271, 1219, 1171, 871, 771 cm^{-1}; 1.40-1.49(m, 2H), 1.56-1.63(m, 4H), 2.38-2.44 (m, 4H), 2.92-2.98(m, 2H), 3.67(s, 3H), 3.84-3.90(m, 1H) 7.08-7.18(m, 3H), 7.24-7.29(m, 2H).

3-Piperidin-1-yl-propionitrile (13a)



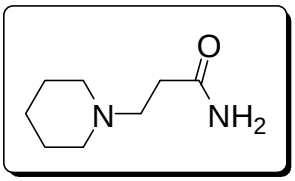
IR (KBr) : 2937, 2854, 2808, 2259, 1455, 1353, 1259, 1158, 1117, 1045, 861, 751, 416 cm^{-1}; ^1H NMR ($CDCl_3$, 200MHz) : δ 1.44-1.49(m, 2H), 1.57-1.65(m, 4H), 2.40-2.50 (m, 6H), 2.62-2.69(m, 2H); MS (EI): m/z 138(M^+), 98 (100%).

Methyl-3-[Cyclohexyl-(2-methoxycarbonyl-ethyl)-amino]-propionate (14a)



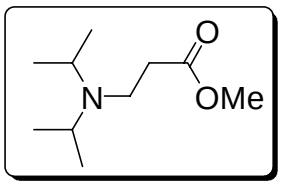
IR (KBr) : 2937, 2854, 2808, 1744, 1145, 879 cm^{-1}; ^1H NMR ($CDCl_3$, 200MHz) : δ 1.10-1.30(m, 2H), 1.60-1.90(m, 8H), 2.40-2.60(m, 5H), 2.90(t, *J* = 6.8Hz, 4H), 3.68(s, 6H); MS (EI): m/z 271(M^+), 128 (100%).

3-Piperidin-1-yl-propionamide (15a)



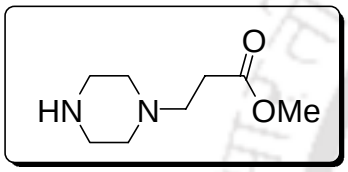
IR (KBr) : 3335, 3221, 2954, 2807, 1677, 1424, 1286, 1122, 876, 637 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 1.38-1.47(m, 2H), 1.52-1.62(m, 4H), 2.34-2.42 (m, 4H), 2.62(t, *J* = 5.4Hz, 2H), 3.62(t, *J* = 4.6Hz, 4H), 5.75(bs, 1NH), 7.53(bs, 1NH); MS (EI): m/z 156(M^+), 98(100%).

Methyl 3-Diisopropylamino propionate (16a)



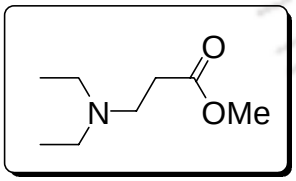
IR (KBr) : 2966, 2930, 2868, 2254, 1742, 1634, 1470, 1429, 1319, 1132, 753 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz): δ 0.98(d, *J* = 6.8 Hz, 12H), 2.38(t, *J* = 7.2Hz, 2H), 2.75 (t, *J* = 7.2 Hz, 2H), 3.68(s, 3H)

Methyl 3-Piperazin-1-yl-propionate (17a)



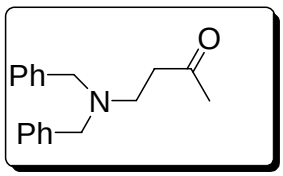
IR (KBr) : 3472, 3037, 2955, 2854, 2808, 2954, 2854, 2812, 1739(s), 1438, 1373, 1045, 751 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : δ 2.34-2.42 (m, 4H), 2.44-2.50(m, 2H), 2.58-2.66(m, 2H), 3.67(s, 3H); MS (EI): m/z 171 (M^+), 98 (100%).

Methyl 3-Diethylamino-propionate (18a)



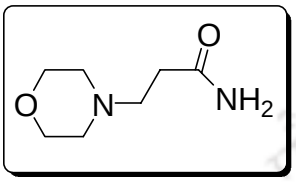
IR (KBr) : 2954, 2873, 2812, 1739(s), 1434, 1197, 1091, 743 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 1.03(t, *J* = 6.8Hz, 6H), 2.46(t, *J* = 7.2Hz, 2H), 2.52(q, *J* = 8Hz, 4H), 2.80(t, *J* = 7.2Hz, 2H), 3.68(s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) : δ 12.24, 32.46, 47.18, 48.36, 51.90, 173.34; MS (EI): m/z 159(M^+), 86(100%).

Methyl 3-Dibenzylamino-propionate (19a)



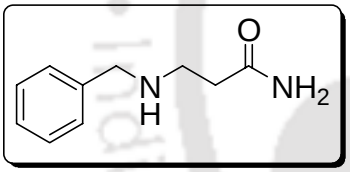
IR (KBr) : 2966, 2930, 2868, 2254, 1709, 1634, 1470, 1429, 1319, 1132, 753 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz): 1.98(s, 3H), 2.57(t, *J* = 7.2Hz, 2H), 2.78(t, *J* = 7.2Hz, 2H), 3.55(s, 4H), 7.16-7.30 (m, 10H).

3-Morpholin-4-yl-propionamide (20a)



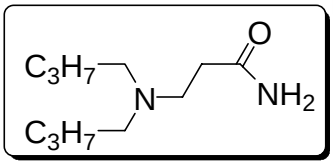
IR (KBr) : 3401, 3212, 2960, 2807, 1675, 1424, 1286, 1122, 1009, 876, 636 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 2.36(t, *J* = 6.6Hz, 2H), 2.48(t, *J* = 4.8Hz, 4H), 2.62(t, *J* = 5.4Hz, 2H), 3.68(t, *J* = 4.6Hz, 4H), 5.89(bs, 1NH), 7.73(bs, 1NH); MS (EI): m/z 158(M^+), 100(100%).

3-Benzylamino-propionamide (21a)



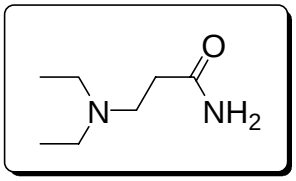
IR (KBr) : 3192, 2919, 2853, 1665, 1494, 1452, 1408, 1114, 1035, 740, 699 cm^{-1}; ^1H NMR: ($CDCl_3$, 300MHz) : 1.50(s, 1NH), 2.37(t, *J* = 6Hz, 2H), 2.90(t, *J* = 5.10Hz, 2H), 3.79(s, 2H), 5.40(bs, 1NH), 7.23-7.30(m, 6H).

3-(*N,N*-Dibutylamino)-propionamide (22a)



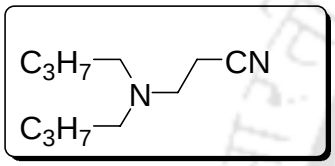
IR (KBr) : 3339, 3193, 2957, 2932, 2871, 2282, 1672, 1465, 1377, 1102 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 0.93(t, *J* = 7.4Hz, 6H), 1.22-1.52(m, 8H), 2.37(t, *J* = 4.4Hz, 2H), 2.44(t, *J* = 6.8Hz, 4H), 2.66(t, *J* = 6Hz, 2H), 5.60(bs, 1NH); MS (EI): m/z 200(M^+), 157(90%), 86(90%), 44(100%).

3-Diethylamino-propionamide (23a)



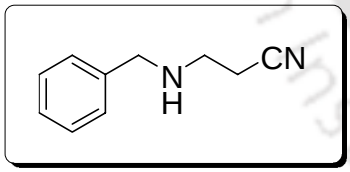
IR (KBr) : 3350, 3186, 2976, 2945, 2817, 1685, 1624, 1419, 1204, 1071, 994, 779, 661 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 1.04(t, *J* = 7.2Hz, 6H), 2.39(t, *J* = 5.6Hz, 2H), 2.56(q, *J* = 7.2Hz, 4H), 2.67(t, *J* = 6Hz, 2H), 5.53(bs, 1NH), 8.46(bs, 1NH); MS (EI): m/z 144(M^+), 86(100%).

3-Dibutylamino-propionitrile (24a)



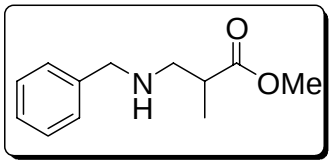
IR (KBr) : 2958, 2925, 2871, 2812, 2259, 1466, 1377, 1219, 1086, 771 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 0.92(t, *J* = 4.8Hz, 6H), 1.25-1.45(m, 8H), 2.35-2.44(m, 6H), 2.76(t, *J* = 7.6Hz, 2H); MS (EI): m/z 182 (M^+), 139 (100%).

3-Benzylamino-propionitrile (25a)



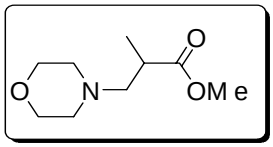
IR (KBr) : 3334, 3037, 2945, 2843, 2254, 1500, 1460, 1230, 1132, 779, 707 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 1.50(s, 1NH), 2.47(t, *J* = 4.4Hz, 2H), 2.90(t, *J* = 4.6Hz, 2H), 3.81(s, 2H), 7.24-7.28(m, 5H); MS (EI): m/z 160(M^+), 91(100%).

Methyl 3-Benzylamino-2-methyl-propionate (26a)



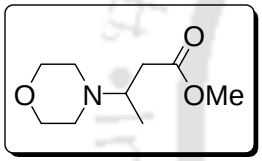
IR (KBr) : 3350, 3032, 2930, 1742, 1578, 1455, 1281, 1194, 764, 712 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 1.16(d, *J* = 4.6Hz, 3H), 1.71(bs, 1NH), 2.63(m, 2H), 2.83(m, 1H), 3.67(s, 3H), 3.76(s, 2H), 3.81(s, 2H), 7.18-7.27(m, 5H); MS (EI): m/z 207(M^+), 91(100%).

Methyl 2-Methyl-3-morpholin-4-yl-propionate (27a)



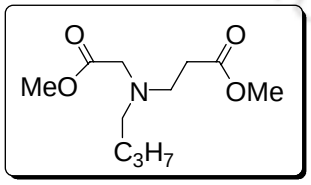
IR (KBr) : 2954, 2853, 2809, 1739, 1388, 1275, 1200, 1118, 1013, 865, 750 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 1.14(d, *J* = 4.6Hz, 3H), 2.6-2.38(m, 5H), 2.44-2.48(m, 2H), 3.63(t, *J* = 3.2Hz, 4H), 3.67(s, 3H); MS (EI): m/z 187(M^+), 100(100%).

Methyl 3-Morpholin-4-yl-butyrate (28a)



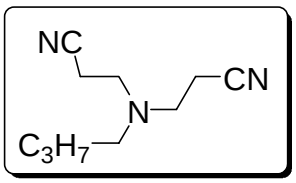
IR (KBr) : 2868, 2812, 1752, 1445, 1363, 1117, 1076, 974, 779 cm^{-1}; ^1H NMR: ($CDCl_3$, 200MHz) : 1.12(d, *J* = 4.6Hz, 3H), 2.28(dd, J^1 = 7.6Hz, J^2 = 14.4Hz, 1H), 2.55(q, *J* = 4.2Hz, 4H), 2.63(d, *J* = 7.0Hz, 1H), 3.14(sext, *J* = 7.4Hz, 1H), 3.69(t, *J* = 4Hz, 4H) 3.72(s, 3H); MS (EI): m/z 187(M^+), 114(100%).

Methyl 3-[Butyl-(2-methoxycarbonyl-ethyl)-amino]-propionate (29a)



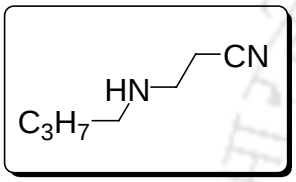
IR (KBr) : 2960, 2872, 1752(s), 1481, 1461, 1446, 1199, 1055, 743 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 0.90(t, *J* = 7.6Hz, 3H), 1.28(sext, *J* = 6.8Hz, 2H), 1.40(q, *J* = 7.6Hz, 2H), 2.40(t, *J* = 7.6Hz, 2H), 2.44(t, *J* = 7.2Hz, 4H), 2.76(t, *J* = 6.8Hz, 4H), 3.66(s, 3H).

3-[Butyl-(2-cyano-ethyl)-amino]-propionitrile (30a bis adduct)



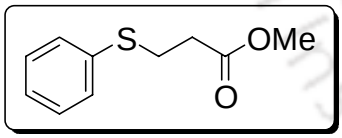
IR (KBr) : 2976, 2926, 2868, 2264, 1436, 1431, 1324, 1129, 758 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 0.93(t, *J* = 7.2Hz, 3H), 1.35(sext, *J* = 8Hz, 3H), 1.43(q, *J* = 7.2Hz, 2H), 2.46(t, *J* = 7.2Hz, 4H), 2.53(t, *J* = 7.2Hz, 2H), 2.85(t, *J* = 6.8Hz, 4H).

3-Butylamino-propionitrile (30a mono adduct)



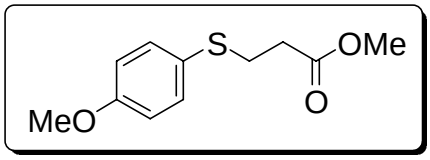
IR (KBr) : 3324, 2966, 2930, 2868, 2254, 1470, 1429, 1319, 1132, 753 cm^{-1}; ^1H NMR: ($CDCl_3$, 400MHz) : 0.92(t, *J* = 7.2Hz, 3H), 1.35(sext, *J* = 8Hz, 3H), 1.48(q, *J* = 7.2Hz, 2H), 1.60(bs, 1NH), 2.53(t, *J* = 6.4Hz, 2H), 2.63(t, *J* = 7.2Hz, 2H), 2.93(t, *J* = 6.4Hz, 2H).

Methyl 3-Phenylsulfanyl-propionate (31a)



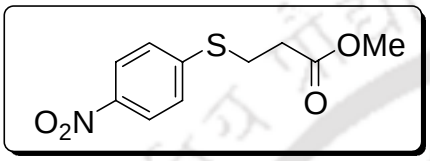
IR (KBr) : 1740 cm^{-1} ; ^1H NMR ($CDCl_3$, 400MHz) : δ 2.62(t, *J* = 7.6Hz, 2H), 3.15(t, *J* = 7.6Hz, 2H), 3.66(s, 3H), 7.15-7.19(m, 1H), 7.24-7.28(m, 2H), 7.32-7.35(m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 29.13, 34.28, 51.81, 126.42, 128.85(2C), 129.95 (2C), 135.00, 171.90.

Methyl 3-(4-Methoxy-phenylsulfanyl)-propionate (32a)



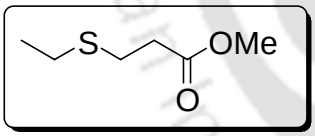
IR (KBr) : 1738 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 2.53(t, *J* = 7.6Hz, 2H), 3.01(t, *J* = 7.2Hz, 2H), 3.62(s, 3H), 3.75(s, 3H), 6.80(d, *J* = 8.4Hz, 2H), 7.32(d *J* = 8.4Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 29.13, 34.28, 51.81, 55.53, 126.42, 128.85(2C), 129.95 (2C), 135.00, 171.90.

Methyl 3-(4-Nitro-phenylsulfanyl)-propionate (33a)



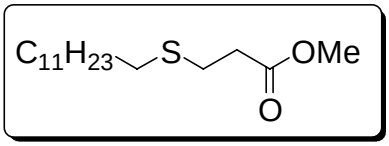
IR (KBr) : 1340 and 1511 (NO_2), 1733 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 2.71(t, *J* = 7.6Hz, 2H), 3.30(t, *J* = 7.2Hz, 2H), 3.71(s, 3H), 7.34(d, *J* = 8.8Hz, 2H), 8.12(d, *J* = 8.8Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 27.39, 33.73, 52.37, 124.20(2C), 126.76(2C), 145.21, 146.27, 171.89.

Methyl 3-Ethylsulfanyl-propionate (34a)



IR (neat) : 1744 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 1.24(t, *J* = 7.2Hz, 3H), 2.54(q, *J* = 7.2Hz, 2H), 2.59(t, *J* = 7.6Hz, 2H), 2.77(t, *J* = 7.6Hz, 2H), 3.67(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 14.87, 26.11, 26.67, 34.83, 51.84, 172.24.

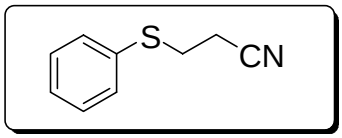
Methyl 3-Dodecylsulfanyl-propionate (35a)



IR (neat) : 747 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 0.87(t, *J* = 6.4Hz, 3H), 1.25-1.59(m, 20H), 2.51(t, *J* = 7.6Hz, 2H), 2.60(t, *J* = 7.2Hz, 2H), 2.77(t, *J* = 7.2Hz, 2H), 3.69(s, 3H); ^{13}C NMR

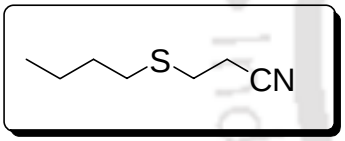
(100MHz, $CDCl_3$) : δ 14.80, 23.36, 27.66, 29.53, 29.88, 29.99(2C), 30.18(2C), 30.25(2C), 32.56, 32.86, 35.40, 52.37, 172.38.

3-Phenylsulfnyl-propionitrile (36a)



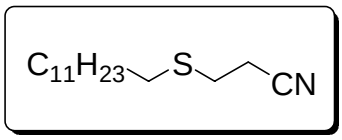
IR (neat) : 2254 (C≡N) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 2.57(t, *J* = 7.2Hz, 2H), 3.10(t, *J* = 7.2Hz, 2H), 7.25-7.32(m, 3H), 7.38-7.40(m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 18.19, 30.13, 117.74, 127.37, 129.06(2C), 131.02(2C), 132.92.

3-Butylsulfanyl-propionitrile (37a)



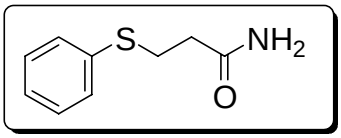
IR (neat) : 2250 (C≡N) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 0.93(t, *J* = 7.2Hz, 3H), 1.36-1.48(m, 2H), 1.54-1.63(m, 2H), 2.57-2.66(m, 4H), 2.79(t, *J* = 7.2Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 14.0, 19.3, 22.3, 28.1, 31.9, 32.4, 118.8.

3-Dodecylsulfanyl-propionitrile (38a)



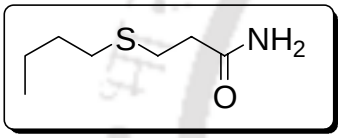
IR (neat) : 2340 (C≡N) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 0.87(t, *J* = 6.8Hz,3H), 1.25-1.60(m, 20H), 2.58(t, *J* = 8Hz, 2H), 2.62(t, *J* = 7.2Hz, 2H), 2.77(t, *J* = 7.2,Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 14.24, 19.05, 22.79, 27.76, 28.87, 29.28, 29.43, 29.57(2C), 29.72(3C), 32.00, 32.44, 118.25.

3-Phenylsulfnyl-propionamide (39a)



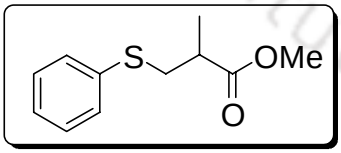
IR (neat) : 1657 (C=O), 3186 and 3384 (NH_2) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 2.51(t, *J* = 7.2Hz, 2H), 3.19(t, *J* = 7.6Hz, 2H), 5.65(bs, 2H), 7.16-7.20(m,1H), 7.25-7.29(m, 2H), 7.33-7.35(m, 2H) ^{13}C NMR (100MHz, $CDCl_3$) : δ 29.22, 35.4, 126.34, 128.88(2C), 129.62(2C), 135.13, 173.24.

3-Butylsulfnyl-propionamide (40a)



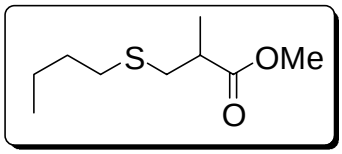
IR (neat) : 1657 (C=O), 3197 and 3374 (NH_2) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 0.91(t, *J* = 7.6Hz, 3H), 1.41(sext, *J* = 7.6Hz, 2H), 1.57(quin, *J* = 7.6Hz, 2H), 2.48-2.56(m, 4H), 2.79(t, *J* = 7.2Hz, 2H), 6.02(bs, NH), 6.02(bs, NH); ^{13}C NMR (100MHz, $CDCl_3$) : δ 13.95, 22.21, 27.71, 31.85, 32.24, 36.23, 174.14.

Methyl 2-Methyl-3-phenylsulfanyl-propanate (41a)



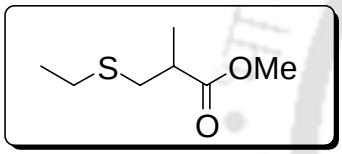
IR (neat) : 1745 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 1.26(d, *J* = 6.8Hz, 3H), 2.65-2.73(m, 1H), 2.91(dd, J^1 = 6.8, J^2 = 13.2Hz, 1H), 3.25(dd, J^1 = 6.8, J^2 = 13.2Hz, 1H), 3.64(s, 3H), 7.14-7.18(m, 1H), 7.23-7.27(m, 2H), 7.33-7.35(m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 16.82, 37.41, 39.75, 51.93, 126.32, 128.83(2C), 129.83(2C), 135.51, 175.14.

Methyl 3-Butylsulfanyl-2-methyl-propanate (42a)



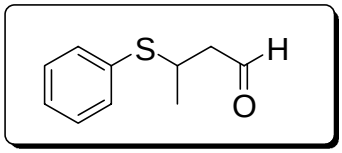
IR (neat) : 1739(C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400MHz) : δ 0.85(t, *J* = 7.2Hz, 3H), 1.18(d, *J* = 6.8Hz, 3H), 1.33(sext, *J* = 7.6Hz, 2H), 1.49(quin, *J* = 7.6Hz, 2H), 2.44(t, *J* = 7.6Hz, 2H), 2.47-2.52(m, 1H), 2.58-2.63(m, 1H), 2.73-2.78(m, 1H), 3.62(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 13.86, 17.01, 22.13, 31.86, 32.49, 35.67, 40.34, 51.85, 175.46.

Methyl 3-ethylsulfanyl-2-methyl-propanate (43a)



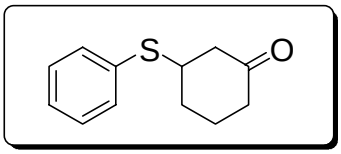
IR (neat) : 1739(C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400MHz) : δ 1.18(t, *J* = 7.2Hz, 3H), 1.21(d, *J* = 6.8Hz, 3H), 2.53(q, *J* = 7.2Hz, 2H), 2.58-2.63(m, 1H), 2.73-2.78(m, 2H), 3.62(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 13.86, 17.01, 32.49, 35.67, 40.34, 51.85, 175.46.

3-Phenylsulfanyl-butyraldehyde (44a)



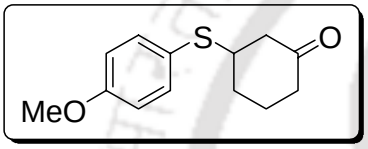
IR (neat) : 1739(C=O) cm^{-1}; 1H NMR ($CDCl_3$, 400MHz) : δ 1.34(d, *J* = 6.8Hz, 3H), 2.5 (dd, J^1 = 7.6, J^2 = 17.2Hz, 1H), 2.69 (dd, J^1 = 5.6, J^2 = 16.8Hz, 1H), 3.65-3.70(m, 1H), 7.25-7.31(m, 3H), 7.39-7.42(m, 2H), 9.71 (s, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 21.20, 37.63, 50.10, 127.46, 128.85,(2C), 132.75(2C), 139.21.

3-Phenylsulfanyl-cyclohexanone (45a)



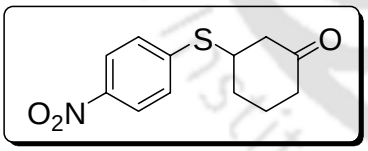
IR (neat) : 1716(C=O) cm^{-1}; 1H NMR ($CDCl_3$, 400MHz) : δ 1.66-1.77(m, 2H), 2.09-2.16(m, 2H), 2.24-2.39(m, 3H), 2.64-2.69(m, 1H), 3.37-3.43(m, 1H), 7.24-7.30(m, 3H), 7.38-7.40(m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 24.03, 31.24, 40.83, 46.7, 47.71, 127.53, 128.82 (2C), 132.82(2C), 132.94, 208.92.

3-(4-Methoxy phenylsulfanyl)-cyclohexanone (46a)



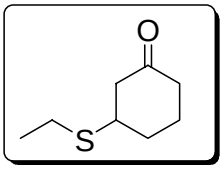
IR (neat) : 1719(C=O) cm^{-1}; 1H NMR ($CDCl_3$, 400MHz) : δ 1.64-1.70(m, 2H), 2.07-2.14(m, 2H), 2.26-2.35(m. 3H), 2.60-2.65(m, 1H), 3.19-3.25(m, 1H), 3.79(s, 3H), 6.83(d, J = 6.8Hz, 2H), 7.37(d, J = 6.8Hz, 2H).

3-(4-Nitro-phenylsulfanyl)-cyclohexanone (47a)



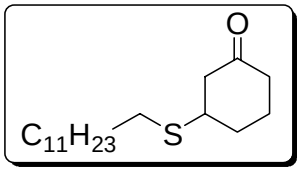
IR (KBr) : 1340 and 1508 (NO_2), 1717 (C=O) cm^{-1}; 1H NMR ($CDCl_3$, 400MHz) : δ 1.81-1.89(m, 2H), 2.15-2.26(m, 2H), 2.39-2.49(m, 3H), 2.76-2.80(dd, J^1 = 4.4Hz, J^2 = 14Hz, 1H), 3.68-3.75(m, 1H), 7.399(d, J = 8.4Hz, 2H), 8.12(d, J = 8.4Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 24.25, 31.22, 41.09, 44.73, 47.50, 124.22(2C), 129.21(2C), 144.28, 146.04, 207.27.

3-Ethylsulfanyl-cyclohexanone (48a)



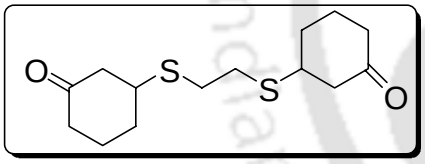
IR (KBr) : 1717 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) **:** δ 1.25(t, *J* = 7.2Hz, 3H), 1.66-1.75(m, 2H), 2.08-2.15(m, 2H), 2.30-2.40(m, 3H), 2.57(q, *J* = 7.2Hz, 2H), 2.68-2.74(m, 1H), 3.04-3.11(m, 1H).

3-Dodecylsulfanyl-cyclohexanone (49a)



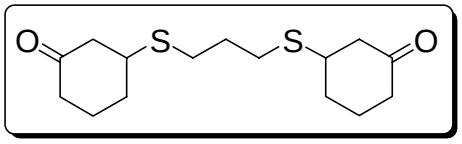
IR (neat) : 1717 (C=O) cm^{-1}; ^1H NMR (CDCl3, 400MHz) : 0.87(t, *J* = 6.4Hz, 3H), 1.25-1.59(m, 20H), 1.67-1.73(m, 2H), 2.10-2.15(m, 2H), 2.32-2.39(m, 3H), 2.53(t, *J* = 7.6Hz, 2H), 2.67-2.72(m, 1H) 3.10-3.11(m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : 14.80, 23.35, 24.96, 29.61, 29.86, 29.99, 30.15, 30.27(2C), 30.39(2C), 31.24, 32.36, 32.55, 41.59, 43.41, 48.89, 209.22.

3-[2-(3-Oxocyclohexylsulfanyl)-ethylsulfanyl]-cyclohexane-1-one (50a)



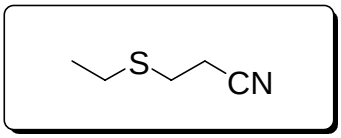
IR (neat) : 1700(C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 1.70-1.74(m, 4H), 2.13-2.16(m, 4H), 2.31-2.40(m, 6H), 2.67-2.75(m, 6H), 3.08-3.14(m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) : 24.25, 30.91, 31.74, 41.09, 42.68, 48.27, 208.53.

3-[3-(3-Oxocyclohexylsulfanyl)-proylsulfanyl]-cyclohexane-1-one (51a)



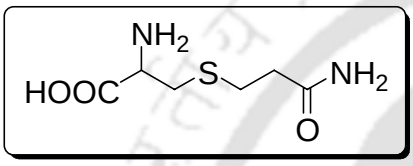
IR (neat) : 1700(C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 1.68-1.76(m, 4H), 1.84(quin, *J* = 7.2Hz, 2H), 2.09-2.17(m, 4H), 2.29-2.40(m, 6H), 2.62-2.72(m, 6H), 3.02-3.07(m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) : 24.51, 29.72, 29.74, 31.93, 41.28, 43.24, 48.47, 209.10.

3-Ethylsulfanyl-propionitrile (52a)



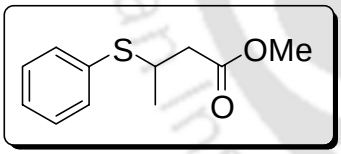
IR (neat) : 2254 (C≡N) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 1.28(t, *J* = 7.6Hz, 3H), 2.59-2.65(m, 4H), 2.79(t, *J* = 6.8Hz, 2H).

2-Amino-3-(2-carbamoyl-ethylsulfanyl)-propionic acid (53a)



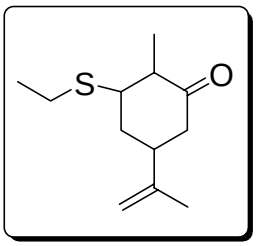
IR (KBr) : 3196, 3380, 2628, 2116, 1634, 1455, 1363, 1317, 1186, 1071, 856, 666, 549 cm^{-1}; ^1H NMR (D_2O 400MHz) : δ 2.63(t, *J* = 6.8Hz, 2H), 2.87(t, *J* = 6.8Hz, 2H), 3.04-3.19(m, 2H), 3.92-3.95(m, 1H).

Methyl 3-Phenylsulfanyl-butyrate (54a)



IR (neat) : 1739(C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : δ 1.33(d, *J* = 6.8Hz, 3H), 2.54-2.66 (m, 2H), 3.64-3.68(m, 4H), 7.15-7.19(m, 1H), 7.24-7.28(m, 2H), 7.32-7.35(m, 2H).

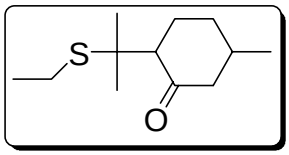
3-Ethylsulfanyl-5-isopropenyl-2-methyl-cyclohexanone (55a)



IR (neat) : 1711 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 1.15(d, *J* = 7.2Hz, 3H), 1.24(t, *J* = 7.6Hz, 3H), 1.76(s, 3H), 1.95-2.02(m, 1H), 2.15-2.25(m, 2H), 2.40-2.60(m, 3H), 2.76-2.84(m, 1H),

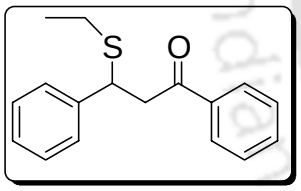
2.87-3.15(m, 1H), 3.42(dd, J^1 = 3.2Hz, J^2 = 8.4Hz, 1H), 4.73(d, J = 20.00 Hz, 1H), 4.81(d, J = 7.6Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : 14.82, 20.92, 26.14, 35.91, 40.72, 46.00, 48.83, 49.21, 110.03, 146.90, 209.49.

2-(1-Ethylsulfanyl-1-methyl-ethyl)-5-methyl-cyclohexanone (56a)



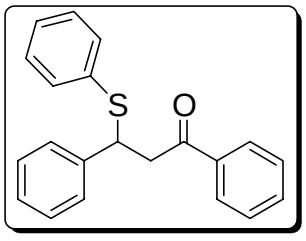
IR (neat) : 1718 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400MHz) : 1.00(d, J = 6.0Hz, 3H), 1.21(t, J = 7.6Hz, 3H), 1.36(s, 3H), 1.40-1.60(m, 2H), 1.52(s, 3H), 1.82-2.20(m, 3H), 2.27-2.30(m, 1H), 2.42(dd, J^1 = 3.6, J^2 = 11.6Hz, 1H), 2.48-2.57(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) : 14.52, 21.71, 22.34, 24.09, 28.01, 29.71, 34.82, 36.72, 46.91, 52.41, 58.13, 210.32.

3-Ethylsulfanyl-1,3-diphenyl-propan-1-one (57a)



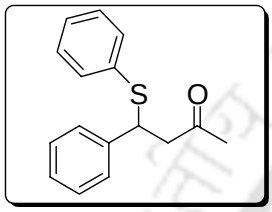
IR (neat) : 1693 C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400MHz) : 1.16(t, J = 7.2Hz, 3H), 2.30-2.39(m, 2H), 3.52(d, J = 7.6Hz, 2H), 4.57(t, J = 7.2Hz, 1H), 7.18(t, J = 7.2Hz, 1H), 7.28(t, J = 8.0Hz, 2H), 7.38-7.43(m, 4H), 7.52(t, J = 7.2Hz, 1H), 7.89(d, J = 7.6Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : 14.81, 25.91, 44.43, 45.82, 127.42, 128.02(2C), 128.34(2C), 128.71(2C), 133.42, 137.01, 142.42, 196.89.

1,3-Diphenyl-3-phenylsulfanyl-propan-1-one (58a)



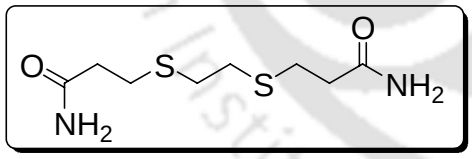
IR (neat) : 1685 C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 3.56(dd, J^1 = 6.0, J^2 = 17.2Hz, 1H), 3.64(dd, J^1 = 8.4, J^2 = 17.2Hz, 1H), 4.93(dd, J^1 = 6.0, J^2 = 8.4Hz, 1H), 7.14-7.23(m, 6H), 7.28-7.31(m, 4H), 7.40(t, J = 7.6Hz, 2H), 7.51(t, J = 7.6Hz, 1H), 7.85(d, J = 8.0Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) : 44.8, 48.34, 127.21, 127.62(2C), 127.9(2C), 128.31(2C), 128.42(2C), 128.71(2C), 132.62(2C), 133.14, 134.13, 136.61, 141.03, 196.71.

4-Phenyl-4-phenylsulfanyl-butan-2-one (59a)



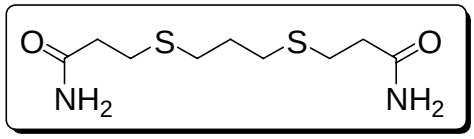
IR (neat) : 1710 C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 2.05(s, 3H), 3.03(dd, J^1 = 5.2, J^2 = 7.6Hz, 2H), 4.69(dd, J^1 = 6.8, J^2 = 8.0Hz, 1H), 7.17-7.21(m, 4H), 7.22-7.27(m, 6H); ^{13}C NMR (75MHz, $CDCl_3$) : 30.73, 48.45, 49.85, 128.06, 128.18, 129.05, 129.22, 129.44, 133.28, 137.43, 141.51, 205.88.

3-(2-Carbamoylmethylsulfanyl-ethylsulfanyl)-propionamide (60a)



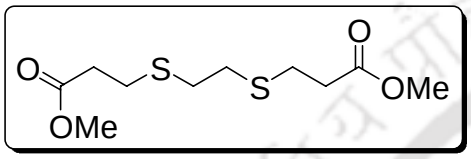
IR (neat) : 1646(C=O), 3200 and 3395 (-NH_2) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 2.62(t, J = 7.2Hz, 4H), 2.74(s, 4H), 2.82(t, J = 7.2Hz 4H), 3.69(s, 6H); ^{13}C NMR (100MHz, $CDCl_3$) **:** 27.33, 32.39, 34.96, 52.12, 171.22.

3-[3-(2-Carbamoyl-ethylsulfanyl)-propylsulfanyl]-propionamide (61a)



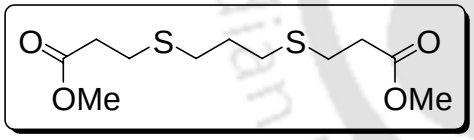
IR (neat) : 1648(C=O), 3200 and 3397 (-NH_2) cm^{-1}; ^1H NMR (DMSO-d_6, 400MHz) :) 1.74(quin, *J* = 7.2Hz, 2H), 2.30(t, *J* = 7.2Hz, 4H), 2.55(t, *J* = 7.2Hz, 4H), 2.64(t, *J* = 7.6Hz, 4H), 6.81(bs, NH), 7.31(bs, NH); ^{13}C NMR (100MHz, DMSO-d_6) : 26.88(2C), 29.03, 29.89(2C), 35.54(2C), 172.21(2C).

Methyl 3-[2-(2-Methoxycarbonyl-ethylsulfanyl)-ethylsulfanyl]-propionate (62a)



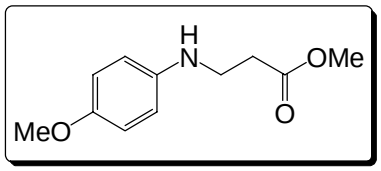
IR (neat) : 1732 C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 2.62(t, *J* = 7.2Hz, 4H), 2.74(s, 4H), 2.82(t, *J* = 7.2Hz, 4H), 3.69(s, 6H); ^{13}C NMR (100MHz, $CDCl_3$) : 27.33(2C), 32.39(2C), 34.96(2C), 52.12(2C), 171.22(2C).

Methyl 3-[3-(2-Methoxycarbonyl-ethylsulfanyl)-propylsulfanyl]-propionate (63a)



IR (neat) : 1735 C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 1.85(quin, *J* = 7.2Hz, 2H), 2.60(t, *J* = 7.6 Hz, 4H), 2.62(t, *J* = 7.6Hz, 4H), 2.76(t, *J* = 7.2Hz, 4H), 3.68(s, 6H); ^{13}C NMR (100MHz, $CDCl_3$) : 27.26(2C), 29.32, 31.14(2C), 34.93(2C), 52.04(2C), 172.28(2C).

Methyl 3-[3-(2-Methoxycarbonyl-ethylsulfanyl)-propylsulfanyl]-propionate (64a)



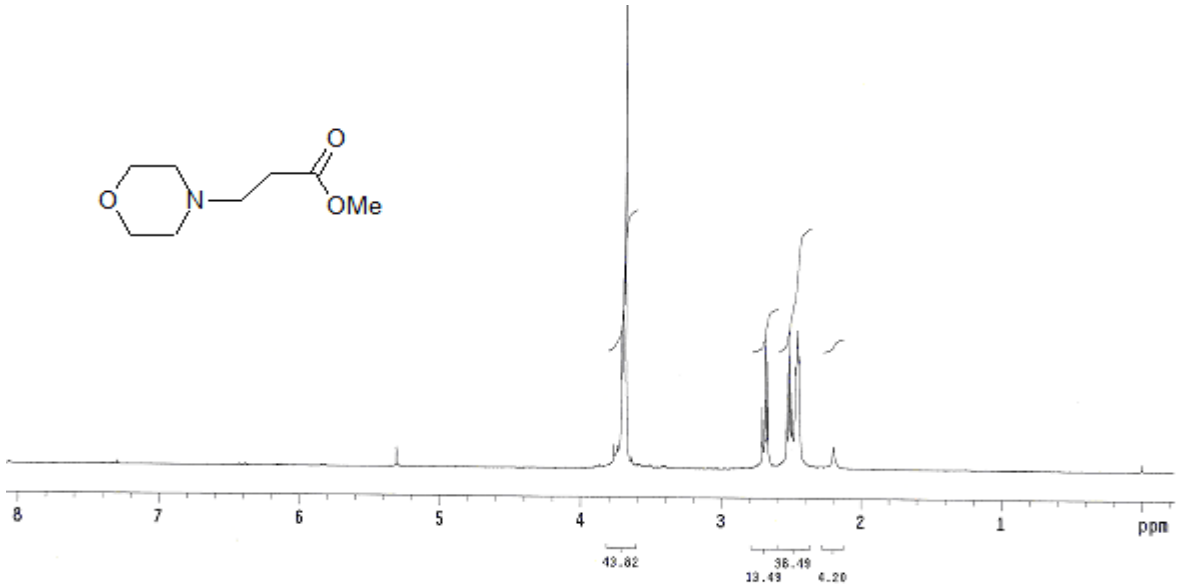
IR (neat) : 1735 C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz) : 2.60(t, *J* = 6.8Hz, 2H), 3.46(t, *J* = 6.8Hz, 2H), 3.75(s, 3H), 6.60(d, *J* = 8.8Hz, 2H), 6.80(d, *J* = 8.8Hz, 2H); ^{13}C NMR (100MHz**,** $CDCl_3$) : 18.1, 40.8, 55.7, 114.8, 115.0, 118.2, 140.0, 153.9.

Table 3D.1. Crystallographic data table for 53a, 60a and 61a

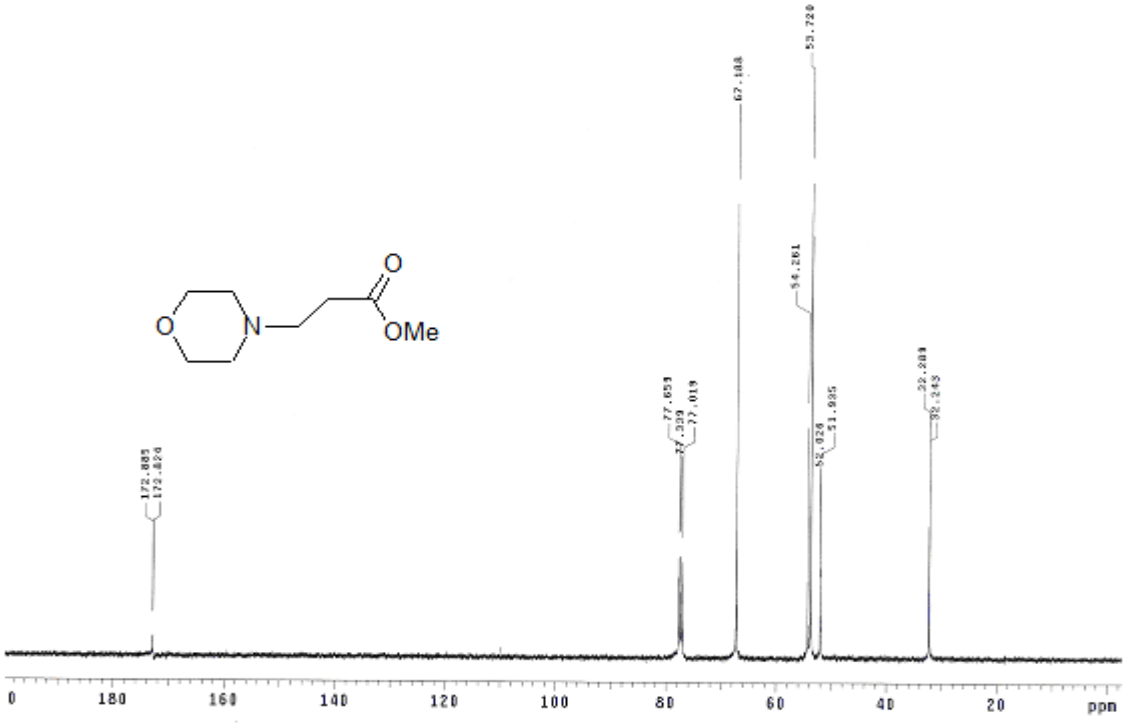
		53a	**60a**	**61a**
Chemical formula		$C_6H_{12}N_2O_3S$	$C_8H_{16}N_2O_2S_2$	$C_9H_{18}N_2O_2S_2$
Fw		192.25	236.37	250.37
Crystal system		Monoclinic	Monoclinic	Monoclinic
Crystal size (mm)		0.22x0.18x0.16	0.26x0.20x0.15	0.29x0.22x0.18
Space group		P 2_1	P 2_1/C	P 2_1/C
a, Å		5.0311(2)	13.3687(4)	27.3690(17)
b, Å		18.6542(10)	4.9624(2)	5.2523(4)
c, Å		5.0643(2)	8.7502(2)	8.6275(5)
α /°		90	90	90
β/°		110.992(3)	97.366(2)	89.995(4)
γ /°		90	90	90
V, A^3		443.75(3)	575.71(3)	1240.16(14)
Z		2	4	4
D(cald.) Mg/m^3		1.451	1.363	1.341
T (K)		273(2)	273(2)	273(2)
μ (mm^{-1})		0.339	0.441	0.414
F(000)		218	252	536
Final R indices[I>2σ]	R1	0.0399	0.0316	0.0536
	wR2	0.0980	0.0764	0.1585
R indices (all data)	R1	0.0435	0.0441	0.1212
	wR2	0.1001	0.0820	0.1866
Goodness of fit		1.475	1.076	0.947

Spectra of some selected compounds

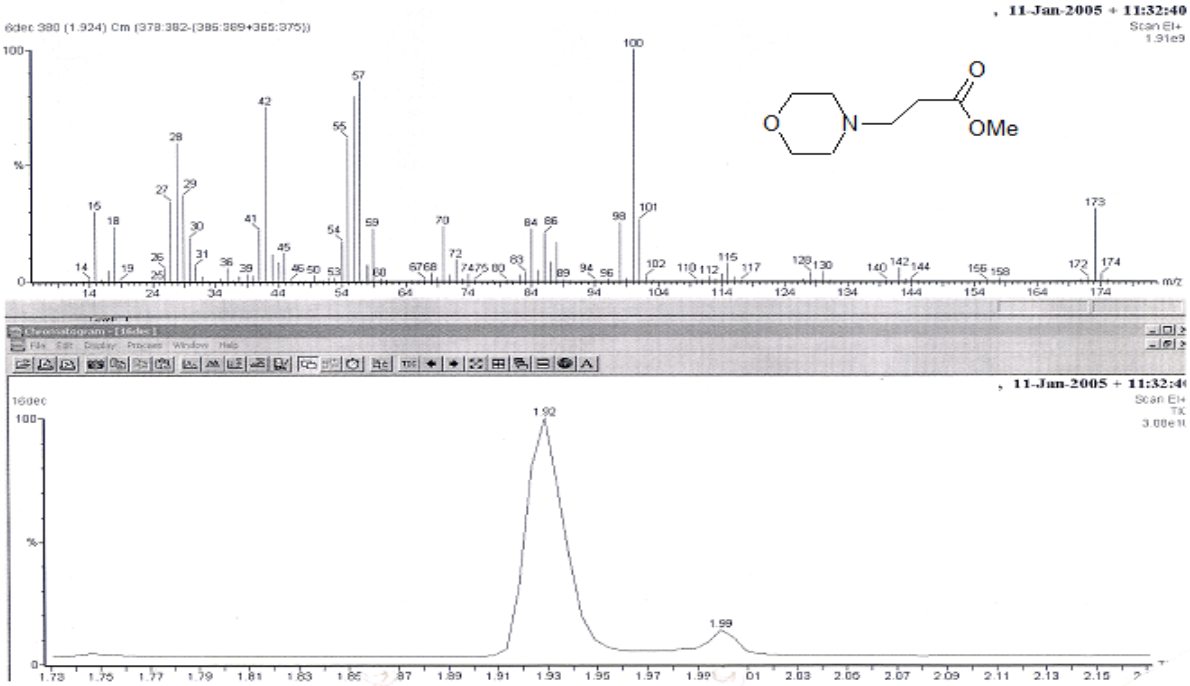
^{1}H NMR Spectrum of Methyl 3-morpholin-4-yl-propionate (4a):



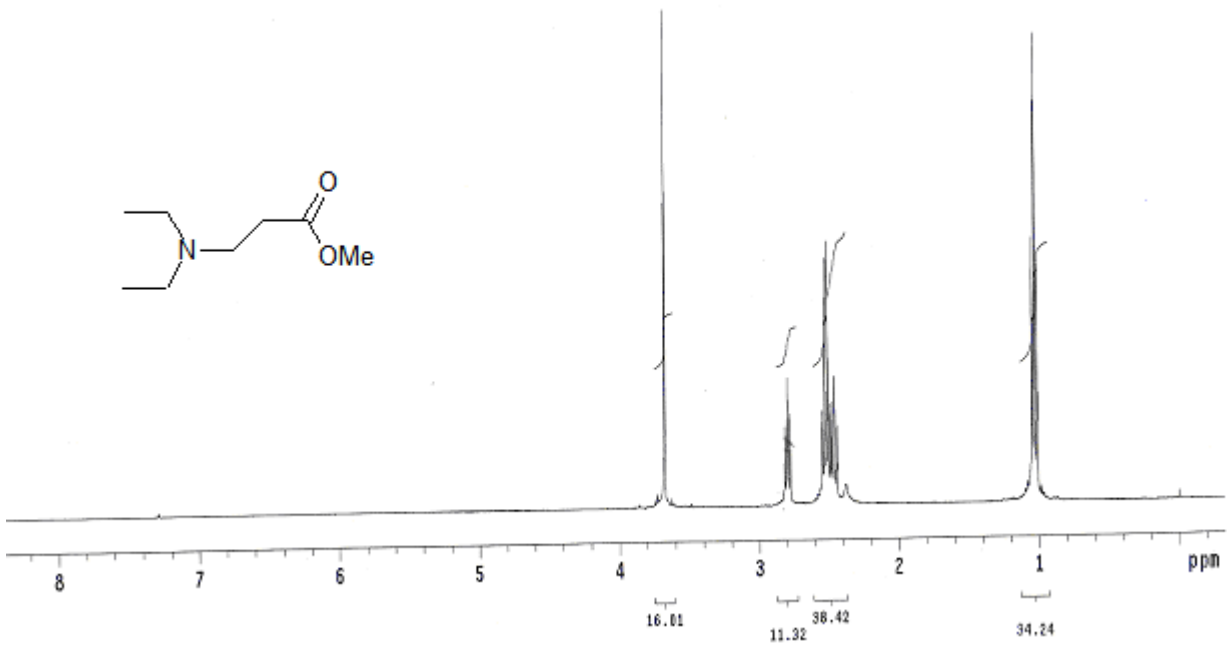
^{13}C NMR Spectrum of Methyl 3-morpholin-4-yl-propionate (4a):



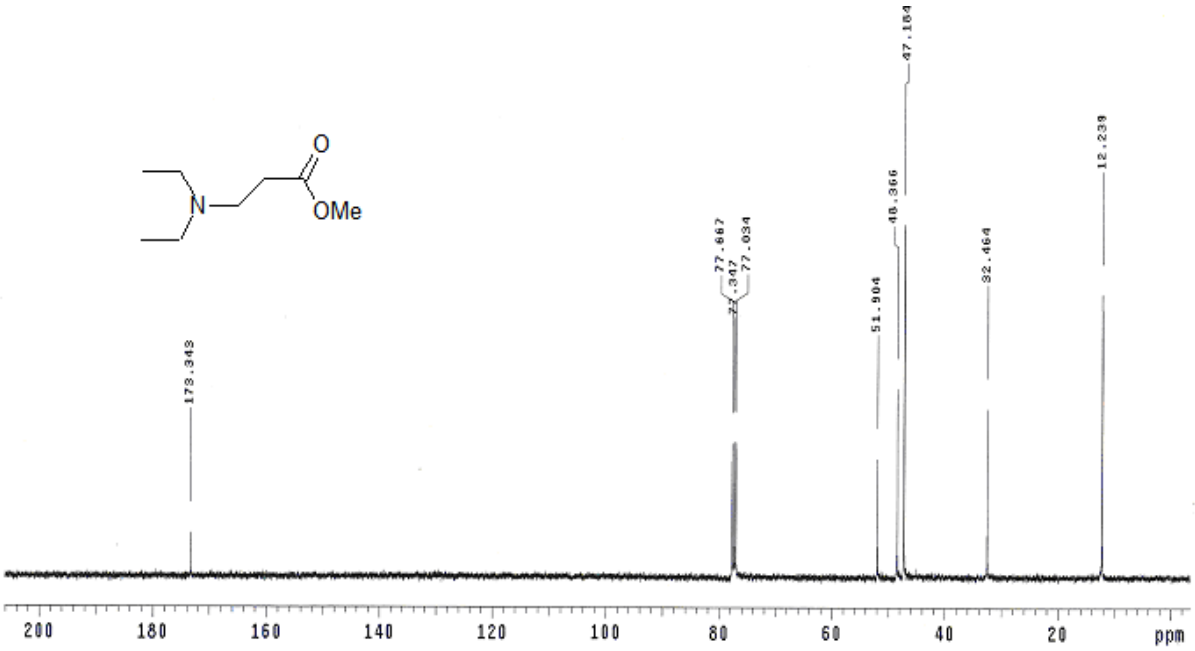
GC MS Spectrum of Methyl 3-morpholin-4-yl-propionate (4a):



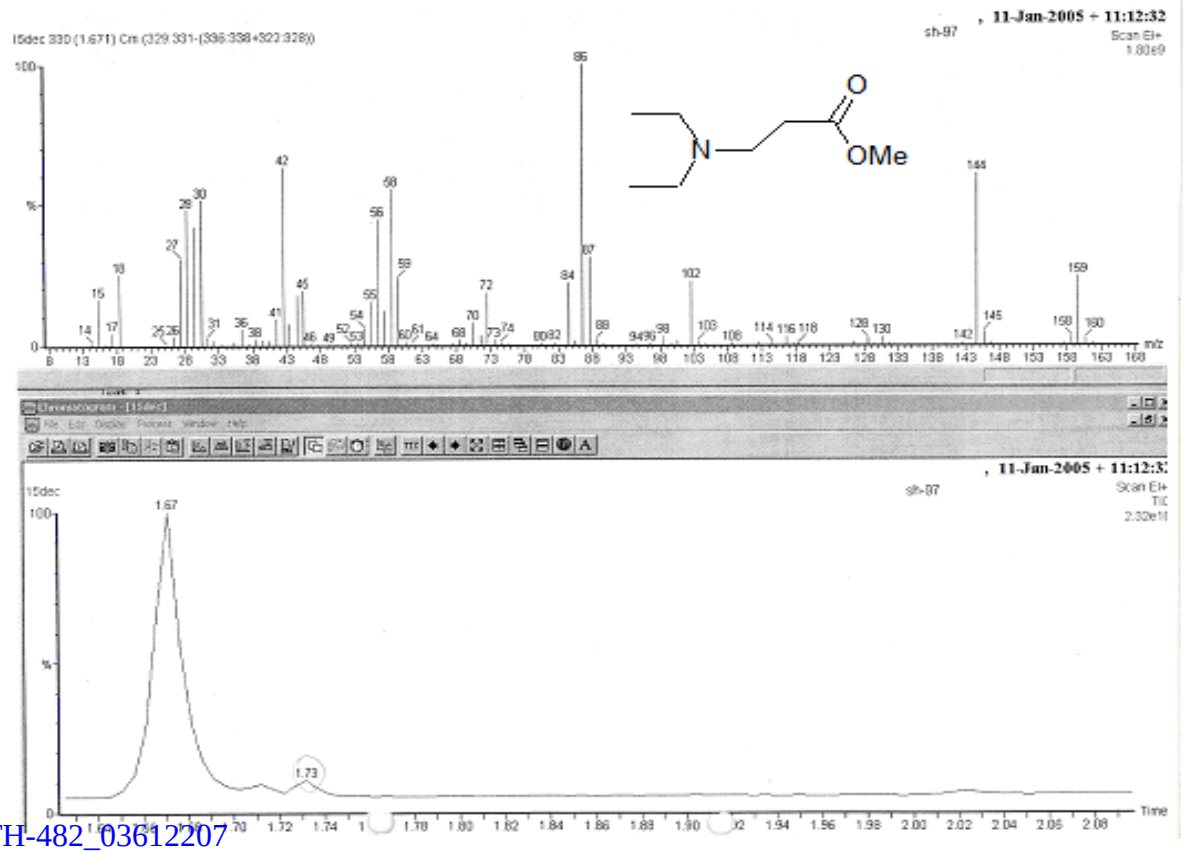
^{1}H NMR Spectrum of Methyl 3-Diethylamino-propionate (18a):



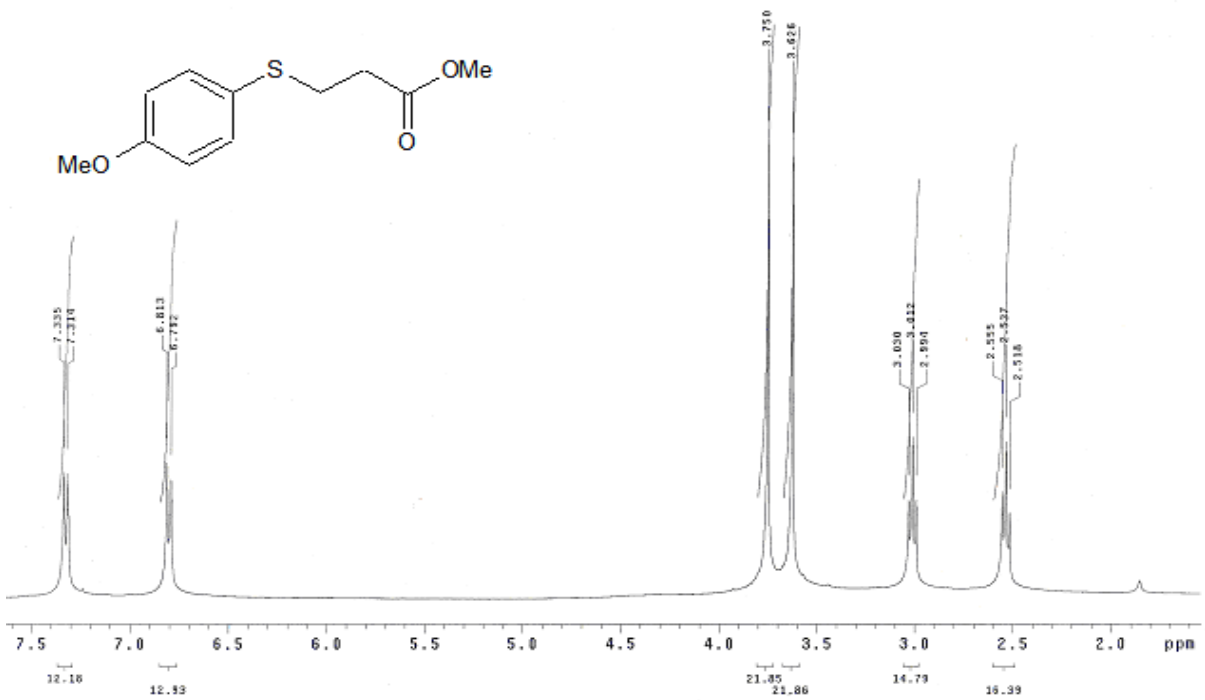
^{13}C NMR Spectrum of Methyl 3-Diethylamino-propionate (18a):



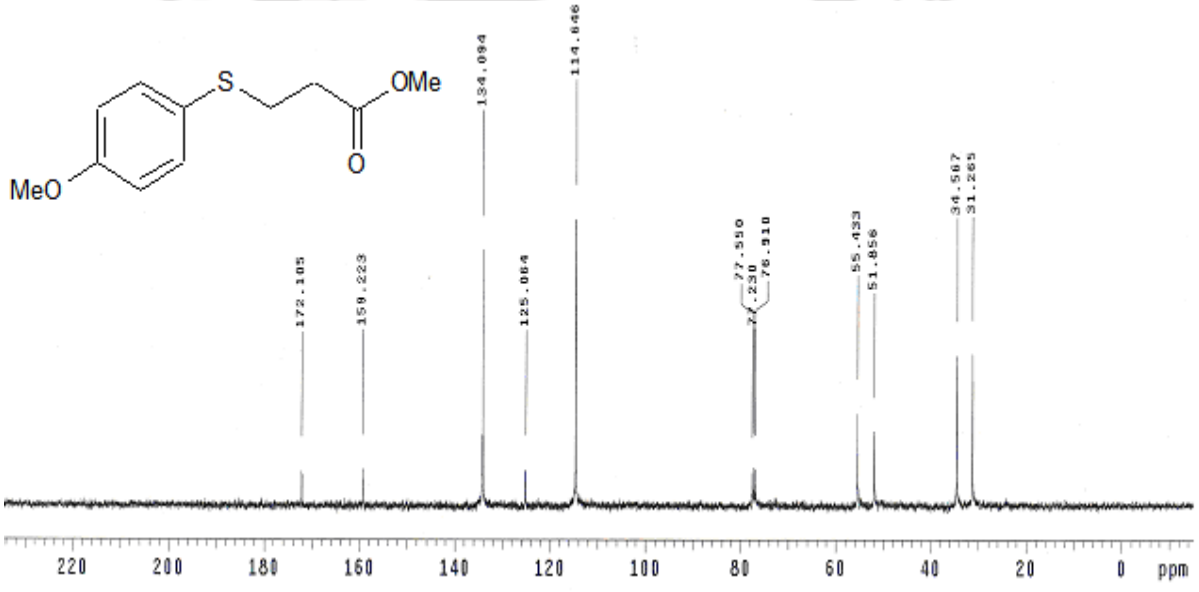
GC MS Spectrum of Methyl 3-Diethylamino-propionate (18a):



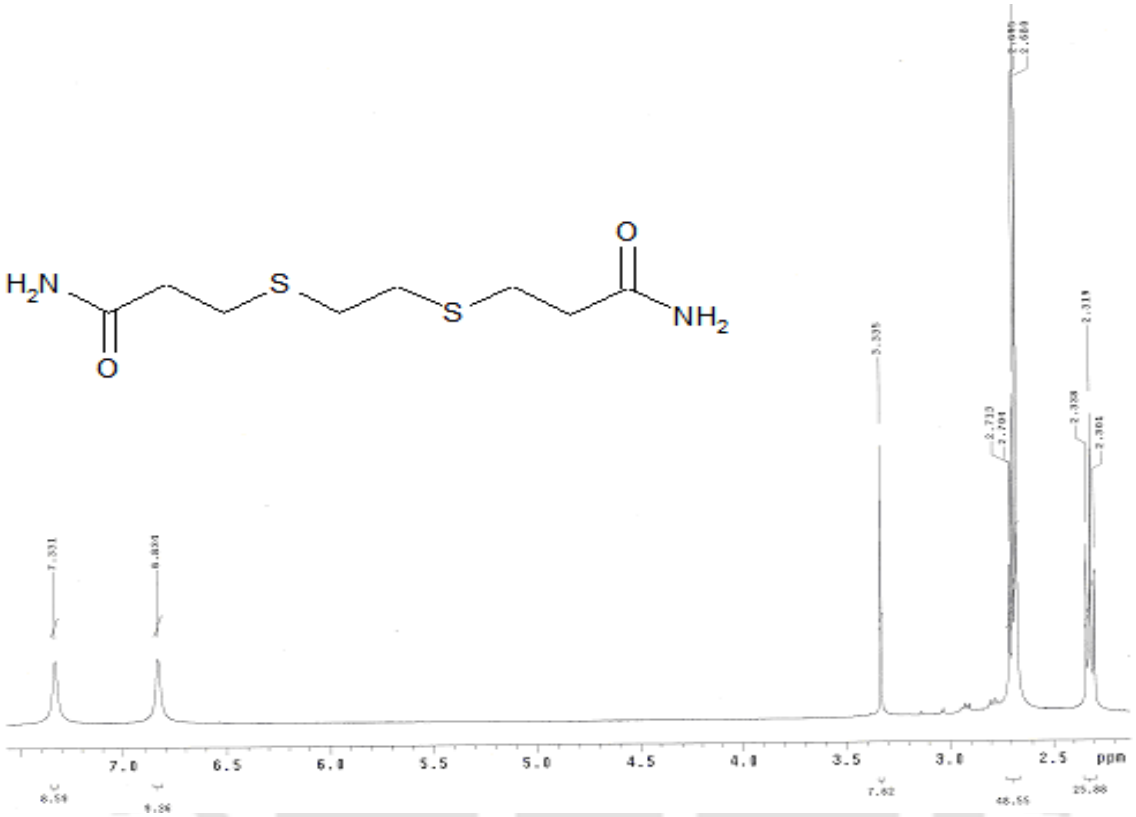
^{1}H NMR Spectrum of Methyl 3-(4-Methoxy-phenylsulfanyl)-propionate (32a):



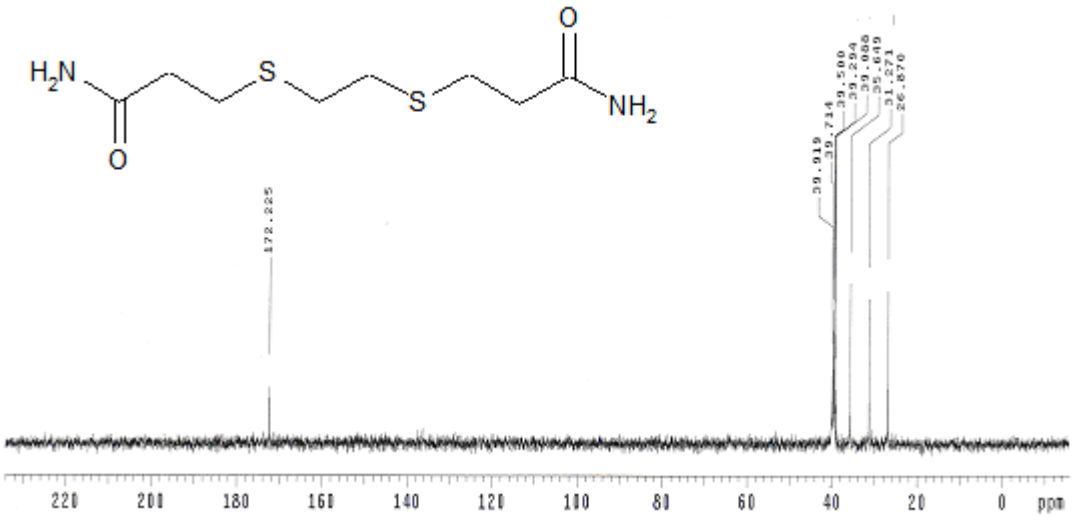
^{13}C NMR Spectrum of Methyl 3-(4-Methoxy-phenylsulfanyl)-propionate (32a):



^{1}H NMR Spectrum of 3-[3-(2-Carbamoyl-ethylsulfanyl)-propylsulfanyl]-propionamide (61a):



^{13}C NMR Spectrum of 3-[3-(2-Carbamoyl-ethylsulfanyl)-propylsulfanyl]-propionamide (61a):



3E. Reference

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Development of Newer Catalysts for Selective Oxidation of Sulfides with H_2O_2

There is a general interest related to binding, interaction and reactivity of coordination compounds of vanadium (V) center starting from synthetic inorganic chemistry through biochemistry,[1-3] theoretical chemistry[4,5] and catalysis.[6-10] The reason for this can be the potential of these complexes to act as oxidizing agent as well as catalyst for the oxidation of both inorganic[6] and organic substrates,[7-10] besides being models for understanding biologically important molecules. Furthermore, the chemistry of vanadium gained momentum due to the discovery of vanadium haloperoxidases (VHPO),[11] a class of enzyme in marine organisms, and its insulin mimic activity.[12] It has been confirmed that bromoperoxidase involves vanadium in oxidation state V,[11] and are found to catalyze halogenations, such as chlorination, bromination and iodination, of organic substrates in presence of hydrogen peroxide. VO_2^+ is regarded as a functional mimic of vanadium bromoperoxidases (VBrPO) although, unlike VBrPO, it functions in acid and at much lower turnover rates.[13] *Cis*-dioxovanadium(V) in acidic solution coordinates 1 or 2 equiv of hydrogen peroxide forming the red monoperoxo, $VO(O_2)^+$, or the yellow diperoxo, $VO(O_2)_2^-$ species, as described in the literature.[14]

Thus, the aforementioned informations are convincing enough to believe that the synthesis of mimics of the naturally occurring vanadium peroxidase enzyme is a very important area of research in itself. Importantly, understanding of their reactivity profiles provides important cues to the development of bromoperoxidase mimics. Accordingly, we started maneuvering synthetic vanadium chemistry to eventually produce a viable VBrPO mimic, which could be used as an active and selective catalyst.

The discovery of new catalysts leading to applications in synthetic organic chemistry is of much current interest in catalysis, in view of the following advantages, for example, easy work-up, reusability, atom economy, and reduction of waste. This assumes a greater importance and acceptability all the more when a bio-inspired catalyst is invented. For the present, our interest was to develop a catalyst, for the selective oxidation of organic sulfides to the corresponding sulfoxides by H_2O_2, modeled on VBrPO.

The vast chemistry of sulfoxides and sulfones makes them very useful reagents in organic synthesis in general and useful synthetic intermediates for the construction of various chemically and biologically significant molecules in particular.[15,16] For this reason the oxidation of sulfides to sulfoxides or sulfones has been the subject of extensive studies and a number of synthetic procedures are now available.[17-52] There are several reagents available for this purpose including nitric acid,[17] $KMnO_4$,[18] MnO_2,[19] $NaClO_4$,[20] $NaBO_3$,[21] NaOCl,[22] $Ca(ClO)_2$,[23]

H_5IO_6/[Mn^{IV}-Mn^{IV}-(μ-O)$_3L_2$]$(PF_6)_2$,[24] $KHSO_5$,[25,26] $(NH_4)_2Ce(NO_3)_6$,[27] $NaIO_4$,[28,29] CF_3CO_3H,[30] dimethyldioxirane,[31,32] *t*-$C_4H_9O_2H$,[33] RuO_4,[34] 4-methylmorpholine oxide with OsO_4,[35] 3-$ClC_6H_4CO_3H$,[36] [(n-C_4H_9)$_4$N]HSO_5,[37,38] bromine,[39] nitrogen tetraoxide,[40] benzeneseleninic peracid,[41] sulfinyl peroxy compounds,[42] iodosobenzene diacetate[43] Cetyltrimethylammonium tribromide[44] and NBS.[45] Incidentally, most of these reagents are not satisfactory for medium to large-scale synthesis for one or the other reasons like low content of effective oxygen, the formation of environmentally unfavorable by-products, and cost effectiveness. Singlet oxygen or molecular oxygen combined with 2-methylpropanal and Co (II) complexes[46,47] as well as H_2O_2 with various metal (Zr, Ti, Cu, Mo, W)[48-52] catalyst have also been used. Generally, it is important to stop the oxidation at the sulfoxide stage by controlling the electrophilic character of the oxidant, but this requirement is often hard to meet and failure results in over oxidation to sulfones. The reported methods rarely offer the ideal combination of simplicity of method, selective reactions and high yields of products and often suffer from a lack of generality and economic viability, and hence the search for newer methods for the selective oxidation of sulfides to sulfoxides has continued.

Over the past few years, the importance of hydrogen peroxide and its derivatives as oxidizing agents has grown considerably. In contrast to other oxidizing agents, hydrogen peroxide is an ideal waste-avoiding oxidant, cheap and the most attractive from the environmental viewpoint. Although it is a powerful oxidant, the reactions of hydrogen peroxide are generally rather slow, and the challenge is to overcome this kinetic barrier in more cost-effective and "green chemical" ways. Therefore, the development of catalysts for tuning the oxidation potentiality of H_2O_2 will be quite valuable for the oxidations. And this indeed is the subject matter of Chapter 4. Accordingly, we have synthesized [$VO_2F(dmpz)_2$] as VBrPO mimic and investigated its reactivity towards the oxidation of sulfides including refractory sulfurs. **Section 4.1** discusses the synthesis of [$VO_2F(dmpz)_2$] and its use as a catalyst for the oxidation of sulfides with H_2O_2.

In consonance with the current trend of research and the need for clean chemistry practices, we turned our attention to metal-free catalysis for the oxidation of organic sulfides as the next task. While working on sulfide oxidation we became aware of the discovery of hydrogen carbonate catalyzed oxidation of organic sulfides[53,54] through peroxocarbonate, HCO_4^-, and the subsequent relevant contributions of Davies and coworkers[55] showing that borate is a better catalyst than HCO_4^- with rapidly formed peroxoborates, $HOOB(OH)_3^-$ and $(HOO)_2B(OH)_2^-$,

being more reactive than HCO_4^-, and extending the pH functional range to the 8-12 region. These appeared to be very important developments in the realm of oxidation chemistry of organic sulfur.

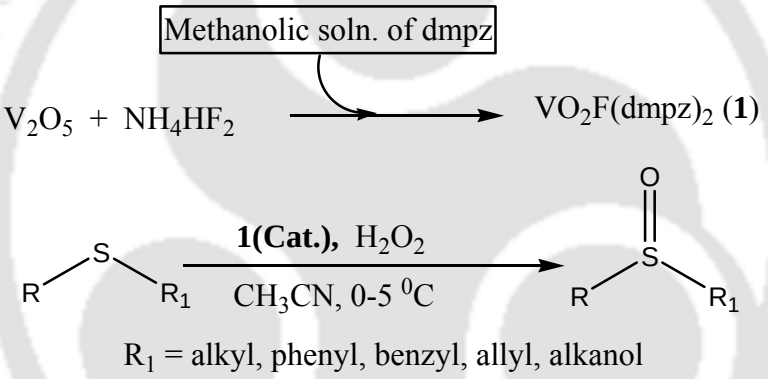
Sulfide oxidations by H_2O_2 or peroxides are believed to proceed by nucleophilic attack of the sulfide on an electrophillic peroxy oxygen and the mechanism is generally well understood.[56] The examples to support this contention include the oxidants like H_2O_2,[52,57] periodate,[58] peracids,[59,60] permonosulfate[61] and peroxymonocarbonate.[62,63] It was suggested that a protic solvent facilitated the nucleophilic displacement of the carbonate in the case of HCO_4^- oxidations. Also, it was shown from a rather recent *ab initio* calculations on the oxidation of $(CH_3)_2S$ by H_2O_2 in aqueous solutions[64] that the transition state involved O–O bond breaking concurrent with S–O bond formation, and that hydrogen transfer occurred after the system had passed the transition state. Solvent molecules or H_2O_2 in the case of higher concentrations of H_2O_2 can efficiently lower the activation barrier for the oxidative transformations. In so far as the oxidation of organic sulfides by peroxoborate is concerned, the reactions though generally proceed in the manner similar to other peroxo based oxidants, for instance, development of positive charge on the sulfur atom in the transition state with the sulfide behaving as a nucleophile, yet there is a succinct difference. The difference lies in mono and diperoxborates having the transition state earlier along the reaction coordinate[55] with relatively less positive charge being developed on the sulfur atom. This in turn emphasizes that proton transfer would play a significant role in the peroxoborate oxidation of organic sulfides. Indeed it was proposed[55] that the lower extent of positive charge development on the sulfur atom for the reaction of the peroxoborates was due to the greater importance of the proton transfer in stabilizing the transition state by peroxoborates. These results and those of Pizer and Tihal[65] on the effect of pH on the formation of different peroxoborates and the elegant reviews by McKillop and Sanderson[63] on SPB oxidations in addition to our earlier experience in the synthetic peroxo-boron[66] and phosphate chemistry[67] caused us to perceive the possibility of borax activated H_2O_2 and pH controlled selective oxidation of organic sulfides in protic medium like MeOH or MeOH-H_2O.

Given the environmental acceptability, cost effectiveness and easy to handle, borax-H_2O_2 system offers an ideal combination for the chosen oxidations. Our main concern for this work has been the selective oxidation of organic sulfide in an environmentally cleaner and catalytic manner with H_2O_2 being the terminal oxidant. We illustrate herein under **Section 4.2** the results of our endeavor in borax catalysed oxidation of organic sulphides to sulfoxides and sulfones by H_2O_2 in methanol at pH 6 or 7 and 10 or 11, respectively.

Being encouraged by the success with selective oxidation of organic sulfides by borax–H_2O_2 system, we tried similar experiments with $(NH_4)_2HPO_4$–H_2O_2 because phophate is known to activate H_2O_2 and is environmentally safe as well. Thus, $(NH_4)_2HPO_4$–H_2O_2 has been shown to be an effective oxidizing system capable of selective oxidation of a variety of organic sulfides to the corresponding sulfoxides. The results of these experiments have been discussed in **Section 4.2**.

4A. Results and Discussions

4.1. $[VO_2F(dmpz)_2]$ (dmpz = 3,5-dimethylpyrazole) as a new catalyst for oxidation of organic sulfides



Scheme 4.1.1

The compound, $[VO_2F(dmpz)_2]$ was synthesized from the reaction of V_2O_5, NH_4HF_2 and 3,5-dimethylpyrazole. The strategy of the synthesis was that V_2O_5 would react with NH_4HF_2, a mildly acid fluoridating agent, to produce oxofluorovanadates(V) in solution which would then react with 3,5-diethylpyrazole(dmpz) to afford $[VO_2F(dmpz)_2]$ (**1**), as targeted. Owing to the insolubility of dmpz in water, an ethanolic solution of it was used for the reaction. Ethanol might have also helped in precipitation of the complex out of the reaction solution. Strategically important was also the selection of NH_4HF_2 as an important reagent. The role of NH_4HF_2 was not only to afford fluoridation but also to provide mild acidity (pH~ 4) of the reaction medium. This has facilitated coordination of dmpz through its non-protonated N-donor atom. A higher acidity is not conducive to the synthesis. The compound is obtained in very high yield and found to be highly crystalline lemon yellow solid, stable in air, soluble in nearly all polar organic solvents and water.

The compound has a sharp decomposition point at 156˚C. The IR spectrum of it showed characteristic absorption bands due to coordinated dmpz , fluoride and oxo ligands. A strong band at 446 cm^{-1} is due to ν(V-N) stretching. This is very important in support of the dmpz coordination. The strong bands appearing at 953, 922 are due to ν (V=O). Splitting of this band is a clear indication of the occurrence of a cis-dioxovanadyl center. The UV-Vis spectrum showed one intense broad band at 245 nm which might be due to ligand (dmpz) to metal charge transfer (LMCT) transition. Single crystals suitable for X-ray diffraction were isolated from CH_3CN solution at room temperature. The ORTEP diagram with atomic numbering scheme is shown in **Fig. 4.1.1**. It is a penta coordinated vanadium(V) species of molecular formula $[VO_2F(dmpz)_2]$. The complex crystallizes in Cc space group. It is similar to serendipitously obtained $[(t\text{-}Bupz)_2VO_2F]$[68] showing distorted trigonal bipyramidal geometry (TBP) (∠O1-V1-N1 is 86.15º and ∠O1-V1-N3 is 91.27º). The distortion of the coordination of polyhedron from the square pyramid to the trigonal-bipyramidal has been calculated by the Addition parameters (τ)[69] as an index of the degree of trigonality; τ is defined by (β-α)/60 where β and α are the two trans-basal angles. For a perfectly square pyramidal geometry τ is equal to zero, while it becomes unity for perfectly trigonal-bipyramidal geometry. For complex **1,** τ value is 0.078. The two cis-dioxo and fluoride (O1, O2 and F1) atoms forming the basal plane and the elongated apical position is occupied by the nitrogen atoms of the strong σ-donor ligand 3,5-dimethyl pyrazole (mean V–N distance is 2.093Å and mean V–O distance is 1.724Å). It is notable that the V–F bond length (1.60 Å) is considerably shorter than what was found in a similar complex $[(t\text{-}Bupz)_2VO_2F]$ and others (1.66Å).[70] Vanadium lies exactly on the equatorial plane i.e. plane formed by F1, O1 and O2. The data (**Table 4.1.1**) shows that the V=O bond distances (mean V=O is 1.724Å) and O=V=O bond angles (122.33º) are slightly greater than the generally observed value in pervanadyl complexes.[68] The packing of the molecules along the *a* axis shows the presence of layer of V-shaped monomer in alternate direction (**Fig. 4.1.2**).

Presence of different types of strong (N–H···O) as well as weak (C–H···O, C–H···N, C–H···F, C–H···π) hydrogen bonding network results of the formation of 3D 'zig-zag' coordination polymer comprise of V-shaped monomer (**Fig. 4.1.3**). The presence of two oxo groups (O1 and O2) and two 2° amino hydrogen (H2N and H4N) in dmpz provide both hydrogen bond acceptor and donors respectively in the same molecule which facilitates the formation of inter-molecularly

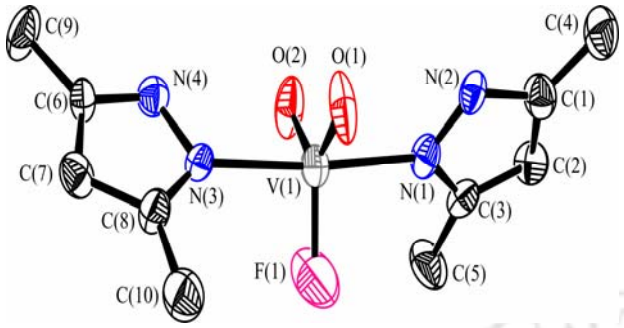


Fig. 4.1.1. *ORTEP plot of* ***1****. Hydrogen atoms are omitted for clarity.*

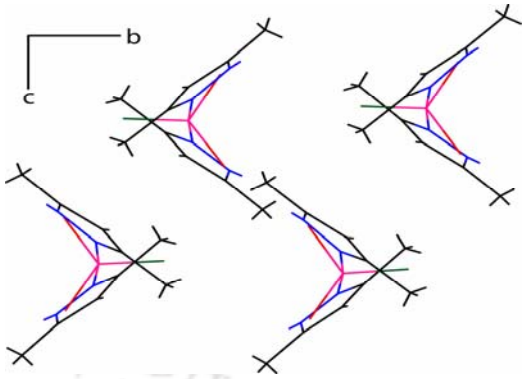


Fig. 4.1.2*. Packing diagram of* ***1*** *along crystallographic a axis.*

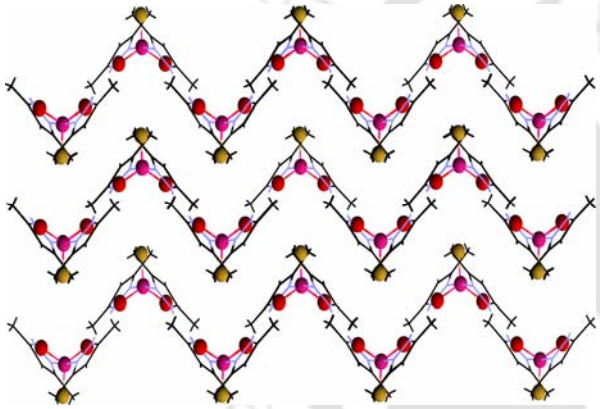


Fig. 4.1.3. *3D zig-zag network of complex* ***1*** *along crystallographic a axis.*

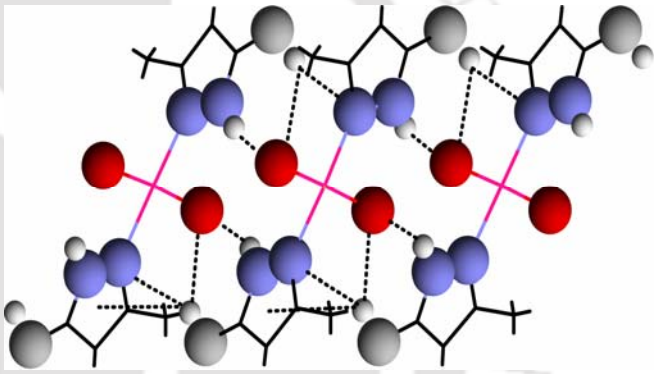


Fig. 4.1.4. *Inter-molecular hydrogen bonding responsible for the formation of zig-zag chain.*

hydrogen bonded 3D coordination polymer. The two nitrogen atoms, N2 and N4 form strong inter-molecularly N–H···O type hydrogen bonding with the oxo groups of the neighboring complex (**Fig 4.1.4**). Each monomeric unit is capable of forming complementary H-bonding network with the neighboring monomeric unit due to simultaneous presence of H-bond donor and acceptor in the same molecule in an almost orthogonal orientation. Each zig-zag chain is further stabilized by the formation of several other types of weak inter-molecular hydrogen bonding (*viz.* C–H···O, C–H···N, C–H···π) interactions (**Table 4.1.2**). This hydrogen bonded zig-zag network grows along crystallographic *c* axis. In the crystal lattice each zig-zag chain is held together by strong π···π interactions (3.571 Å) and intermolecular C–H···F type hydrogen bonding (**Fig. 4.1.5**).

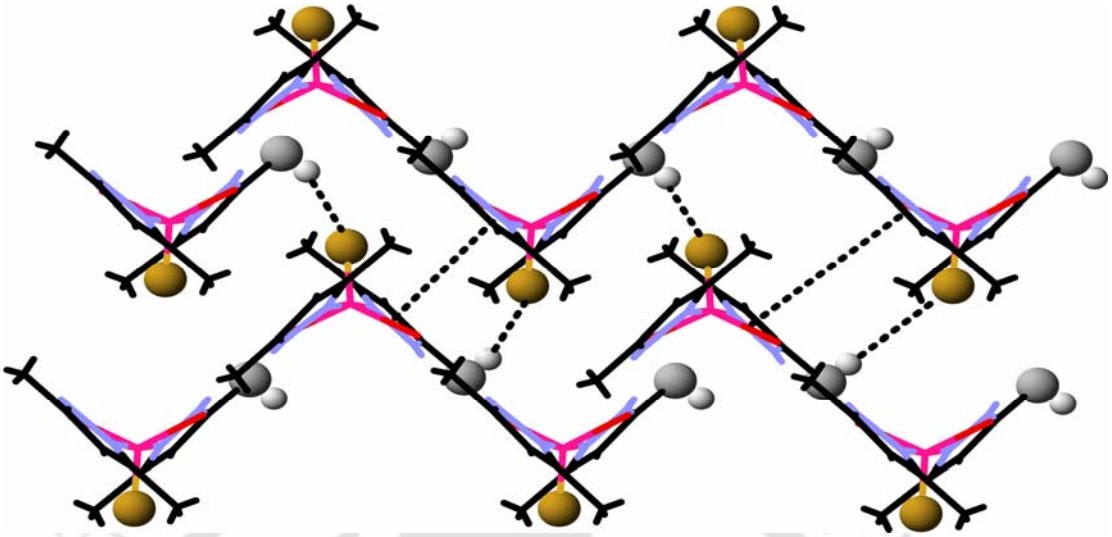


Fig. 4.1.5. *π-stacking and C–H···F hydrogen bonding between the zig-zag chains.*

Table 4.1.1*. Selected bond distances and bond angles of* $VO_2F(dmpz)_2$

Bond distances	(Å)	Bond angles	(˚)
V-F	1.607(6)	F-V-O1	126 (2)
V-O1	1.70(3)	F-V-O2	112 (2)
V-O2	1.75 (3)	F-V-N1	92 (1)
V-N1	2.07 (3)	F-V-N3	93 (1)
V-N3	2.15 (3)	O1-V-O2	122.1(7)
		O1-V-N1	92 (1)
		O1-V-N3	86 (1)
		O2-V-N1	87 (1)
		O2-V-N3	90(1)
		N1-V-N3	174.7(5)

***Table 4.1.2**. Selected bond lengths and bond angles*

D–H•••A[a]	D–H (Å)	H•••A (Å)	D•••A (Å)	D–H•••A (°)
N2–H2N…O2	0.860	2.143	2.951	156.40
N4–H4N…O1	0.860	2.078	2.901	160.25
C4–H4C…O2	0.960	2.592	3.419	144.52
C4–H4C…N1	0.960	2.745	3.633	154.00
C9–H9C…N3	0.960	2.721	3.611	154.40
C9–H9C…π[b]	0.960	2.857	3.550	129.85
C9–H9C…π[c]	0.960	2.775	3.547	138.02
C4–H4B…F1	0.960	2.617	3.638	160.84

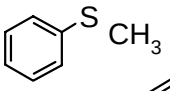
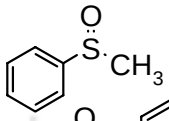
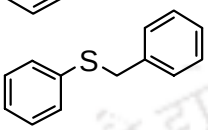
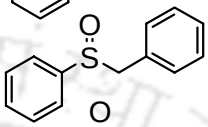
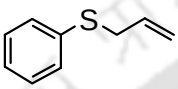
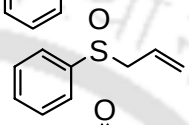
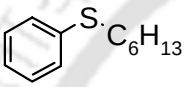
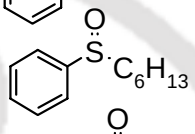
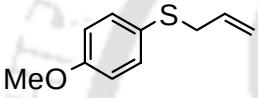
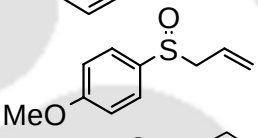
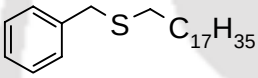
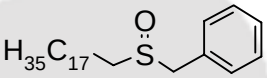
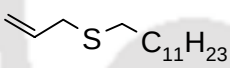
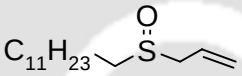
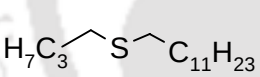
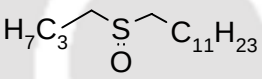
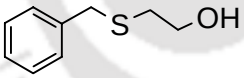
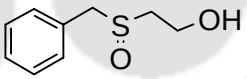
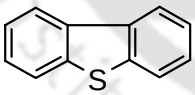
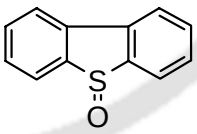
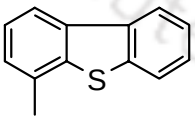
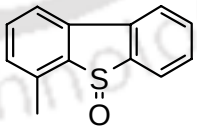
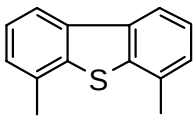
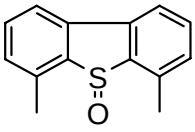
[a] *D = donor, A = acceptor*
[b] *centroid of C1-N2 ring;*
[c] *centroid of C6-N4 ring.*

The complex thus prepared was first screened for the oxidation of sulfides in the presence of aqueous 30% H_2O_2. To optimize the reaction condition, we carried out oxidation of methyl phenyl sulfide in acetonitrile at room temperature (**Table 4.1.3**). It was found that methyl phenyl sulfide was oxidized to a 3:1 mixture of methyl phenyl sulfoxide and sulfone in the presence of 5 mol% of the catalyst and 2 equiv. of H_2O_2. Encouraged by the result, we performed the oxidation in different solvents (**Table 4.1.3**) maintaining the same conditions to get

***Table 4.1.3.** Optimization of reaction conditions for the oxidation of methyl phenyl sulfide with 30% H_2O_2*

Entry	Catalyst mol%	Time (h)	Temp (^{0}C)	H_2O_2 equiv.	Solvent	Sulfoxide (%)	Sulfone (%)
1	5	2.5	27	2	CH_3CN	75	25
2	5	2.5	27	2	C_2H_5OH	70	30
3	5	5	27	2	H_2O	55	20
4	5	3	27	1.1	CH_3CN	65	20
5	5	3.5	0-5	1.1	CH_3CN	95	--
6	3	4.0	0-5	1.1	CH_3CN	95	--
7	1	5	0-5	1.1	CH_3CN	95	--
8	1	12	0-5	0	CH_3CN	0	--
9	0	12	0-5	1.1	CH_3CN	35	--
10	5	5.5	0-5	1.1	C_2H_5OH	92	--

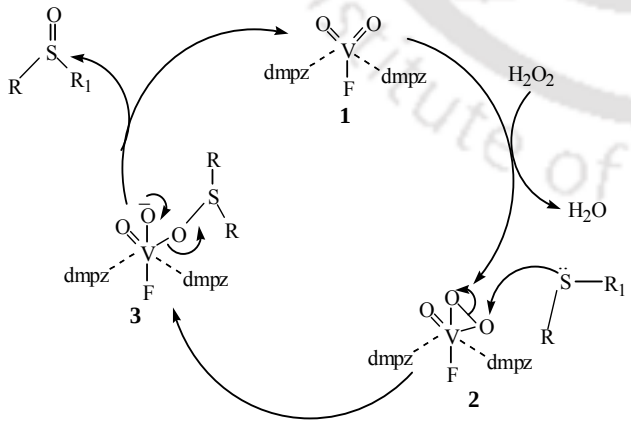
Table 4.1.4. *$VO_2F(dmpz)_2$ (catalyst **1**) catalyzed oxidation of organic sulfides with 30% H_2O_2 in CH_3CN*

Entry	Substrate	Time (h)	Sulfoxide		Yield(%)[a]
1		5		**1a**	95, 86[b]
2		5		**2a**	93
3		2		**3a**	97
4		5.5		**4a**	87
5		4.5		**5a**	85
6		6.5		**6a**	95
7		6.5		**7a**	86
8		6		**8a**	87
9		4.5		**9a**	82
10		5		**10a**	88
11		8		**11a**	80[c]
12		12		**12a**	75[c]

[a] *Yield refers to isolated yield,*
[b] *Yield after fifth cyle,*
[c] *Reaction at room temperature.*

sulfoxide selectively. Unfortunately, over oxidation could not be averted. The problem of over oxidation could not be overcome even by lowering the amount of H_2O_2 to 1.1 equiv. The attention was then turned on to the temperature of the reaction. Sulfoxide as the sole product was found when the reaction was carried out at ice temperature. To ascertain efficacy of the catalyst several reactions were carried out with or without catalyst. The reactions took place in each case with the best performance being in acetonitrile with 1 mol% of catalyst. Accordingly, all the reactions discussed herein after were conducted with this combination. Various aliphatic and aromatic groups attached to sulfur atom and refractory sulfur (e.g. dibenzothiophene (DBT), 4-methyl-DBT and 4,6-dimethyl DBT) compounds were subjected to oxidation with H_2O_2 catalyzed by $VO_2F(dmpz)_2$. The oxidations were selective affording sulfoxides. In case of allylic sulfides oxidation, sulfoxides were formed without the cleavage of carbon-carbon bond. The catalyst recycleability was examined through a series of reaction with methyl phenyl sulfide using the aqueous phase containing the catalyst. The reaction went on well giving good yields for five times without significant loss of activity and selectivity as presented in **Fig. 4.1.6.**

The plausible catalytic cycle in the oxidation of sulfides to sulfoxides may be presented as depicted in Scheme 4.1.2. The mechanism suggested herein is in line with the VBrPO oxidation mechanism. It is believed that the catalyst **1** interacts with H_2O_2 to form a peroxometal intermediate of the type **2** thereby activating the bound peroxide. The sulfide oxidation is then likely to proceed via **3** as shown below.



Scheme 4.1.2. *Plausible mechanism of oxidation of sulfide with* ***1*** *and* H_2O_2

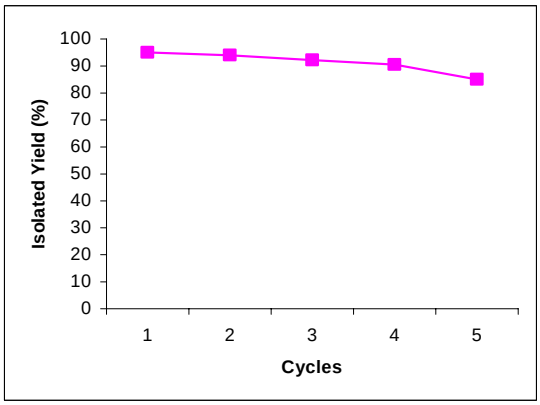


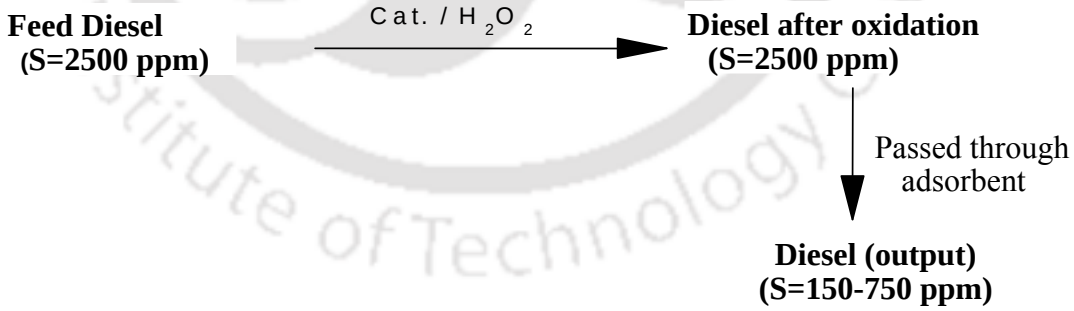
Fig. 4.1.6. *Isolated yield obtained with multiple cycles of* ***1*** *in the oxidation of methyl phenyl sulfide using* H_2O_2

As a sequel to our research and also in view of the pressing need for reducing the sulfur content of diesel to an ultra low level, it was thought worthwhile to explore efficacy of the newly developed catalyst for the purpose. Accordingly, the $[VO_2F(dmpz)_2]$–H_2O_2 system was applied to diesel containing >2200 ppm of sulfur (**Scheme 4.1.3)**. In a typical process, 1L of diesel containing 2500 ppm of sulfur was taken in 2L beaker and to it was added 20 mol% of the catalyst and 20 equiv. of H_2O_2 (with respect to sulfur). The mixture was stirred for 5 h. To begin with there was froth formation simaltanious with the rise in temperature by ~7 ºC from the ambient temperature. The reaction mixture was kept standing for half an hour for layers seperation. The upper layer was decanted and passed through an adsorption column packed with Al_2O_3 and activated charcoal (90:10). The column was connected to a two-necked round bottomed flask with one neck being connected to a suction pump. The diameter of the column was 3.5 cm and was packed upto a height of 11 cm. The collection of the out put was made in three fractions. The first fraction (**F1**-100 mL) was practically colorless, whereas the second (**F2**-300 mL) and third (**F3**- 500mL) fractions were light and dark yellow in color, respectively. The collected fractions were found to contain the following amounts of total sulfur:

F1-100 mL : 150-175 ppm

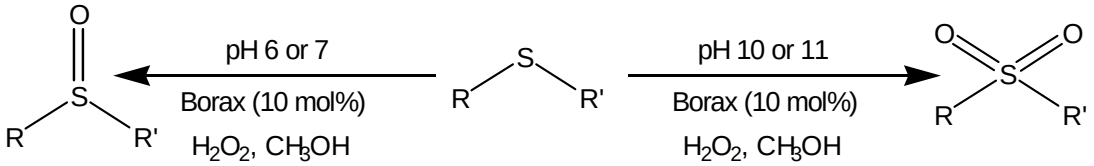
F2-300 mL : 300-350 ppm

F3- 500mL : 600-700 ppm



Scheme 4.1.3

4.2 Borax and phosphate catalyzed selective oxidation of organic sulfides



Scheme 4.2.1

The selection of borax as catalyst was originated from its reaction with H_2O_2, enabling H_2O_2 to be more reactive. Thus, borax bocomes the catalyst of choice for sulfide oxidation. In order to ascertain the optimum conditions, several reaction runs were carried out at the out set on methyl phenyl sulfide as the model substrate each time with 2 mmol of the substrate, 6 mmol of H_2O_2 (45% aqueous solution), 10 mol% of borax in 2 mL of MeOH at different pH, as shown in **Table 4.2.1.** pH of the reaction solution was adjusted by careful addition of 0.1M NaOH solution. The solution pH of 6 or 7 appeared suitable for sulfoxidation. Use of four or five molar equivalents of H_2O_2, instead of three molar equivalents, at pH 6 or 7 reduces the reaction time by *ca* 1 h, however, 15-20% of sulfone was formed along with the sulfoxide thereby reducing the selectivity. The selective oxidation to sulfone, if desired, can be best done at pH 10 or 11 (**Table 4.2.1**).

Table 4.2.1. *Optimization of pH and solvent for selective oxidation of methyl phenyl sulfide with borax–H_2O_2*

Entry	Catalyst mol%	pH	Time (h)	H_2O_2 equiv.	Sulfoxide (%)	Sulfone (%)
1	10	6	5	3	80	--
2	10	6	6	3	90	--
3	10	7	6	3	92	--
4	10	7	7	3	85	10
5	10	8	6	3	75	25
6	10	9	6	3	35	65
7	10	10	2.5	3	--	93
8	10	11	2.5	3	--	93
9	5	7	12	3	55	--
10	0	7	12	3	45	--
11	10	7	5	5	75	20
12	10	7	5	6	62	35

A perusal of the distribution diagram of peroxo-borate system presented by Pizer and Tihal,[65] makes it evident that at pH 6 or 7 mono and diperoxoborates, $(HO)_3BOOH^-$ and

$(HO)_2B(OOH)_2^-$, respectively, occur in equal but relatively lower concentrations along with a very minute amount of inactive peroxoboric acid, $(HO)_2BOOH$. With the increase in pH to 10 or 11, peroxoboric acid disappears while both the peroxoborates occur in relatively higher concentrations, with the concentration of $(HO)_2B(OOH)_2^-$ being much higher. This may be indicative of the fact that a higher concentration of diperoxoborates favours sulfone formation over the corresponding sulfoxide.

In order to generalize the reactions, a series of structurally diverse sulfides were subjected to oxidation under the optimized reaction conditions and the results are presented in **Table 4.2.2**. The reactions went on well affording the products in high yields. It is notable that sulfides were

Table 4.2.2. *Borax catalyzed sulfide oxidation in MeOH by H_2O_2 at room temperature*

Run	Substrate	pH=6 or 7		pH=10 or 11	
		Time (h)	Sulfoxide (%)a	Time (h)	Sulfone (%)[a]
1	$PhSCH_3$	6	92, 83[b] (1a)	2.5	93, 85,[b] 95[c] (1b)
2	$PhSC_4H_9$	8	82 (13a)	4	90 (13b)
3	$PhSC_6H_{13}$	24	65 (4a)	24	87 (4b)
4	$C_{12}H_{25}SC_4H_9$	5	82 (8a)	3	84 (8b)
5	$C_4H_9SC_4H_9$	8	78 (14a)	3.5	78 (14b)
6	$PhSCH_2CH{=}CH_2$	8	85 (3a)	6	90 (3b)
7	$PhSCH_2CH_2CN$	7	85 (15a)	6	88 (15b)
8	$PhCH_2SCH_2CH_2OH$	5	90 (9a)	--	--
9	$PhCH_2SPh$	8	90 (2a)	3	94 (2b)
10	$p\text{-}NO_2PhCH_2SPh$	6	88 (16a)	2.5	95 (16b)
11	Dibezothiophene (DBT)	10	55 + 42[d] (10a)	6	75 (10b)
12	4-Methyl -DBT	24	45+ 58[d] (11a)	24	75 (11b)
13	4,6-Dimethyl-DBT	--	--	24	10 (12b)

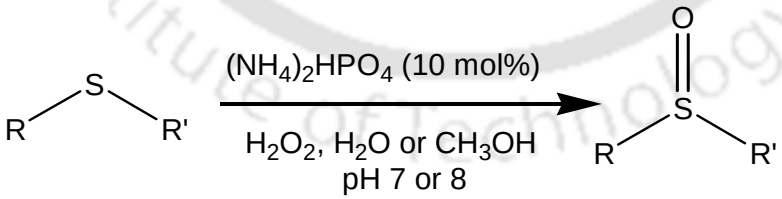
[a]*Isolated yields,*
[b]*Yield after 7th cycle,*
[c]*Yield at 5 g scale,*
[d] *% of sulfone*

chemoselectively oxidized in presence of some oxidation prone functional groups such as C=C, –CN, –OH (entries **6-8,** Table 4.2.2). Dibenzothiophene (DBT) and substituted DBT oxidations are rather difficult with the generally practiced oxidation procedures. However, upon treatment with

borax-H_2O_2 system some of these were converted to the corresponding sulfoxides and sulfones (entries **11** and **12,** Table 4.2.2). Although we succeeded in oxidizing DBT and 4-methyl-DBT, our protocol did not work well for 4,6-dimethyl-DBT. Only 10% oxidation has been achieved in 24 h. The result is not too surprising because this is the most difficult among the refractory sulfides to oxidize. Owing to steric crowding by the methyl groups on DBT, it is rather difficult to approach the sulfur by the oxidant thereby causing the problem, as encountered (entry **13,** Table 4.2.2). It may be mentioned that with the increase in alkyl chain length of the sulfides, the rate of reaction becomes slower. This may probably be due to the orientation of hydrophobic alkyl chain around the sulfur atom.

Recyclability of the catalyst was examined through a series of reactions with methyl phenyl sulfide by using the aqueous phase containing borax, obtained after extraction of the reaction mixture with EtOAc. This was charged with a fresh substrate and 3 equivalents of H_2O_2 and pH was adjusted at either 6 or 7 or at 10 or 11. Interestingly, the catalyst could be reused for at least seven reaction cycles with consistent activity. It is also important to note that the reaction can be performed on a relatively larger scale (5 g) giving good yields (entry **1,** Table 4.2.2) showing its potential for scaled-up applications.

While working on borax catalyzed sulfide oxidations and the knowledge gathered from the present experience, we anticipated that phosphate can also bring about this types of reactions. Accordingly, $[(NH_4)_2HPO_4]$ was used as catalyst with H_2O_2 being the oxidant for sulfide oxidations (Scheme 4.2.2). The goal was to achieve sulfoxidation.



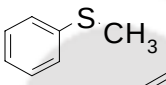
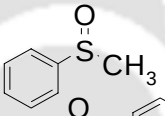
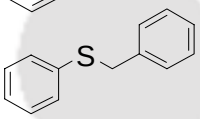
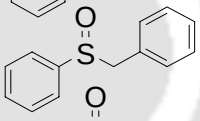
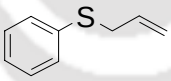
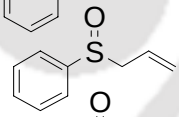
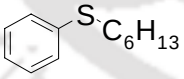
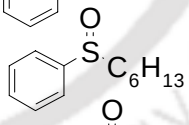
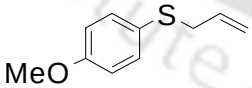
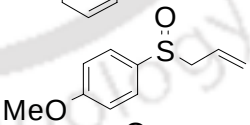
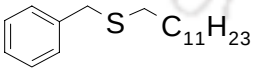
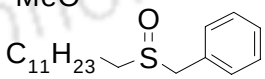
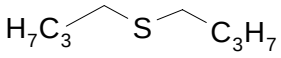
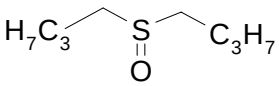
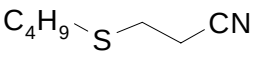
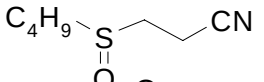
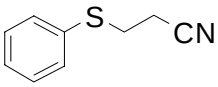
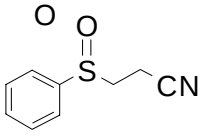
Scheme 4.2.2

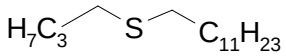
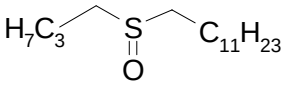
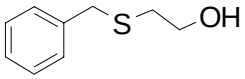
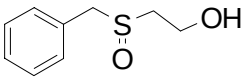
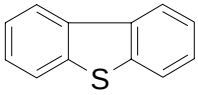
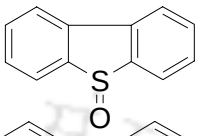
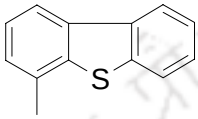
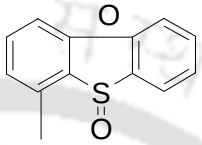
Here again the work began with optimization of reaction conditions. The results of this exercise are summarized in **Table 4.2.3.** It is evident that the reaction takes place in each case with the best performance being with 3 equiv. H_2O_2 containing 10 mol% of the catalyst at pH 7 or 8. Accordingly, all the subsequent reactions were conducted with this combination.

Table 4.2.3. *Optimization of pH for selective oxidation of methyl phenyl sulfide to the corresponding sulfoxide with $[(NH_4)_2HPO_4]$–H_2O_2 in MeOH at room temperature*

Entry	Catalyst mol%	pH	Time (h)	H_2O_2 equiv.	Sulfoxide (%)	Sulfone (%)
1	20	9	2.5	5	60	25
2	10	9	3	3	72	12
3	10	8	4	3	85	--
4	10	8	5	1.5	55	--
5	10	7	5	3	82	--
6	5	7	12	3	80	--
7	2	7	12	3	55	--
8	0	7	12	3	45	--

Table 4.2.4. *$(NH_4)_2HPO_4$ catalyzed sulfide oxidation in MeOH by H_2O_2 at room temperature using 0.1 equivalent of catalyst*

Entry	Substrate	Time (h)	Sulfoxide		Yield(%)[a]
1		4		**1a**	85
2		8		**2a**	89
3		8		**3a**	88
4		9		**4a**	65
5		12		**5a**	85
6		8		**6a**	89
7		3		**14a**	85
8		3		**17a**	79
9		6		**15a**	82

10		4.5		**8a**	88
11		4		**9a**	84
12		12		**10a**	00
13		12		**11a**	00

[a]*Isolated yields*

A variety of sulfides such as alkyl, aryl and allyl sulfides were subjected to oxidation by $(NH_4)_2HPO_4$ (10 mol%) in MeOH at room temperature to afford the corresponding sulfoxides in high to very high yields (**Table 4.2.4**). The facility of the reaction was dependent on the nature of the substituents. Thus, alkyl sufides were more reactive in comparison to aryl and allyl sulfides. Under these conditions, allylic double bonds, –CN and –OH did not undergo any oxidation. Though we were successful in oxidizing a variety of organic sulfides, this protocol did not work well for dibenzothiophenes (DBTs). Finally, upon completion of the reaction, the aqueous phase containing phosphate was reused for several cycles with consistent activity (5 cycles).

A comparison of the results of sulfide oxidations with borax-H_2O_2 and $[(NH_4)_2HPO_4]$-H_2O shows that the former performs relatively better under the given experimental conditions.

4B. Conclusion

The bis-(3,5-dimethyl pyrazole)fluorodioxovanadium(V), $[VO_2F(dmpz)_2]$ has been synthesized in an interesting manner. Equally interesting is that the pentavalent vanadium center maintains penta coordination, as evident from the X-ray structure analysis. This could be one of the reasons for its efficient catalytic activity of the three catalytic systems reported in this chapter. $[VO_2F(dmpz)_2]$–H_2O_2 seems to be the best in terms of performance followed by borax–H_2O_2 and then $(NH_4)_2HPO_4$–H_2O_2. There are, however, some special attributes in borax and $(NH_4)_2HPO_4$ as catalysts in that they are of a relatively lesser represented class, i.e., metal-free catalysts, softer in nature, and relatively more eco compatible than a vanadium based catalyst. Borax is also a natural material. All of them act as efficient and selective catalysts and work well in relatively safer

solvents. Chemoselectivety, i.e. sulfoxidation over C=C, C–N and –OH, being simultaneously present, is yet another important attributes in the newly developed protocols. The biomimicity of $[VO_2F(dmpz)_2]$ requires a special mention. These catalytic systems seem to provide clear scope for further studies in the realm of oxidation chemistry.

4C. Experimental

The sources of chemicals and solvents, the methods for quantitative determination of elements and the details of all the equipment used for physico-chemical studies have been described in **Chapter 2.**

Synthesis of bis(3,5-dimethylpyrazole) dioxofluorovanadium(V), $[VO_2F(dmpz)_2]$

An aqueous suspension (15-20 mL) of 0.5g (2.75 mmol) V_2O_5 was treated with 0.55g (9.64mmol) NH_4HF_2 followed by heating on a steam bath to get a clear solution. An ethanolic solution (15-20 mL) of 1.33g (13.73mmol) of 3,5-dimethyl pyrazole was then added to it and the solution was allowed to concentrate *(ca.*10-12 mL) by heating on a steam bath. The concentrated solution was kept in a freezer until shiny lemon yellow crystals of $[VO_2F(dmpz)_2]$ were obtained. The compound was separated by decantation and dried *in vacuo* over conc. H_2SO_4. The yield was 1.3g (81 %).

General procedure for sulfide oxidation with $[VO_2F(dmpz)_2]$

Organic sulfide (2 mmol) in acetonitrile (5 mL) solvent was reacted with $[VO_2F(dmpz)_2]$ (0.02 mmol) and H_2O_2 (2.2 mmol) under stirring at ice bath temperature for the time as presented in **Table 4.1.4**. The reaction was monitored by TLC (eluent: n-hexane/ethyl acetate: 7/3). On completion of the reaction, acetonitrile was removed under reduced pressure and 5 mL of water was added. The product was extracted with ethyl acetate, dried over $MgSO_4$ and evaporated to dryness, while the aqueous layer was retained for recovery of the catalyst. In order to remove any traces of $[VO_2F(dmpz)_2]$, the product was transferred to silica gel (60-120 mesh) column and eluted with ethyl acetate : hexane (3 : 7). Methyl phenyl sulfoxide was isolated as a liquid in 89.88% yield. The aqueous layer was concentrated and reused.

General procedure for oxidative desulfurization

To 1L of diesel (S=2500 ppm of S) in 2L beaker, $[VO_2F(dmpz)_2]$ (20 mol%) was added and stirred followed by addition of 30% H_2O_2 (20 equiv.). The whole was stirred for 5 h at room temperature and allowed to stand for half an hour in order to allow formation of layers. The upper layer was passed through adsorption column packed with Al_2O_3 and activated charcoal (100 g, 90:10). The column was connected to a two-necked round bottomed flask with one neck being connected to a suction pump. The output was collected in fractions: first (F1-100 mL), second (F2-300 mL) and third (F3- 500mL).

Analysis of sulfur content

The total sulfur content of the samples was determined by microcoulometry (detection limit, 0.1ng/µl). The original diesel and the diesel after oxidation and desulfurization were analyzed by GC-FPD (GC: Agilent 6890N equipped with a capillary column [PONA, 50 m × 0.2 mm i.d. × 0.5 µm]; FPD: Agilent H9261). Analysis conditions were as follows: injection port temperature, 280 °C; detector temperature, 250 °C; oven temperature program, 100 °C, held for 1 min, 100–150 °C at a 10 °C/min gradient, held for 1 min, 150–280 °C at a 5 °C/min gradient, held for 12 min; split ratio, 1/100; carrier gas, ultrapurity nitrogen; column flow, 0.9 ml/min; reagent gases, air flow of 100 ml/min, hydrogen flow of 75 ml/min; injection volume of sample, 1 µl. Analysis of the sample was done by Research and Development Division, Indian Oil Corporation Limited, Faridabad, India.

General procedure for sulfide oxidation with borax as the catalyst

In a 25 mL flask equipped with a magnetic stirrer, 6.0 molar equivalents of H_2O_2 was taken, then 0.2 molar equivalent of borax and 2 mL of MeOH as a solvent were added followed by 2 molar equivalent of thioanisole. To the resulting solution 0.1 M NaOH was added to maintain the pH of the solution at either 6 or 7 or at 10 or 11 and the mixture was stirred at room temperature for the time indicated in **Table 4.2.2.** The reaction was monitored by TLC (eluent : n-hexane/ethyl acetate: 7/3). After complete disappearance of the reactant, the product was extracted with EtOAc. To the EtOAc extract, Na_2SO_3 was added to destroy any excess of H_2O_2, if present, and then filtered and dried over anhydrous Na_2SO_4 .The solvent of the pure fraction was evaporated, the product was fully dried and the isolated yield was recorded. The aqueous layer containing borax can be reused

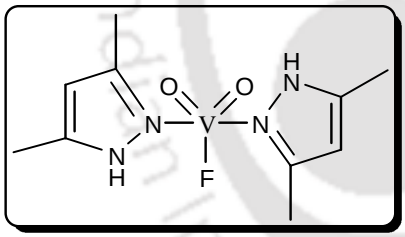
General procedure for sulfide oxidation with phosphate as the catalyst

In a 25 mL flask equipped with a magnetic stirrer, 6.0 molar equivalents of H_2O_2 was taken, then 0.2 molar equivalent of $(NH_4)2HPO_4$ and 2 mL of MeOH as a solvent were added followed by 2 molar equivalent of thioanisole. The reaction mixture acquires a pH of 7 or 8 automatically and the mixture was stirred at room temperature for the time indicated in **Table 4.2.4**. The reaction was monitored by TLC (eluent : n-hexane/ethyl acetate: 7/3). After complete disappearance of the reactant, the product was extracted with EtOAc. To the EtOAc extract, Na_2SO_3 was added to destroy any excess of H_2O_2, if present, and then filtered and dried over anhydrous Na_2SO_4 .The solvent of the pure fraction was evaporated, the product was fully dried and the isolated yield was recorded. The aqueous layer containing phosphate can be reused.

4D. Characterization of the products

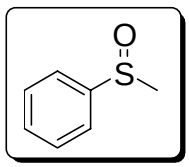
The compounds were characterized by mp, IR and ^{1}H NMR spectroscopy and data for the products are summarized as follows:

Dioxofluoro(bis-dimethylpyrazole) vanadium(V), $[VO_2F(dmpz)_2]$ (1)



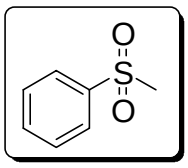
IR(KBr): 3257, 1577, 1285, 953, 922 cm^{-1} ; ^{1}HNMR (400MHz, $CDCl_3$) : δ 2.13 (s, 3H), 2.47 (s, 3H), 5.85 (s, 1H), 11.62 (bs, 1H, N-H); ^{19}FNMR (400MHz, $CDCl_3$): δ -146.32 (br, 1F).

Methyl phenyl sulfoxide(1a)



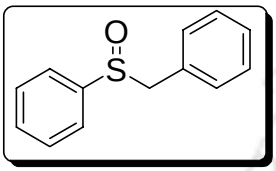
IR(neat): 1032 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.74 (s, 3H), 7.51-7.53(m, 3H), 7.64-7.66 (m, 2H) ppm; MS : m/z 157 (M^+).

Methyl phenyl sulfone (1b)



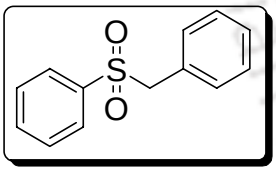
IR (neat): 1148, 1286 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.06 (s, 3H), 7.58(t, *J* = 7.2Hz, , 2H), 7.66(t, *J* = 8Hz, 1H), 7.95(d, *J* = 7.6Hz, 2H).

Benzyl phenyl sulfoxide (2a)



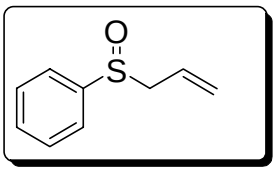
IR (neat): 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.99(d, *J* = 12.8Hz, 1H), 4.16(d, *J* = 12.4Hz, 1H), 6.95(m, 2H), 7.19-7.28(m, 3H), 7.34-7.44(m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 63.8, 124.5(2C), 128.3, 128.5(2C), 128.9(2C), 129.2, 130.4(2C), 131.2, 142.7.

Benzyl phenyl sulfone (2b)



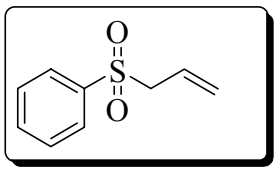
IR (KBr): 1153, 1373 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.30(s, 2H), 7.03-7.06 (m, 2H), 7.21-7.29(m, 3H), 7.40-7.44(m, 2H), 7.56-7.61(m, 3H).

Allyl phenyl sulfoxide (3a)



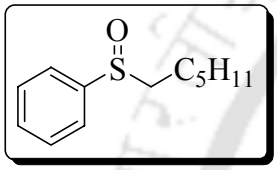
IR (neat): 1044 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.48-3.60 (m, 2H), 5.18 (d, *J* = 16.8Hz, lH), 5.33 (d, 1H, *J* = 10.8Hz, 1H), 5.58-5.68 (m, lH), 7.48-7.53 (m, 3H), 7.55-7.58(m, 2H).

Allyl phenyl sulfone (3b)



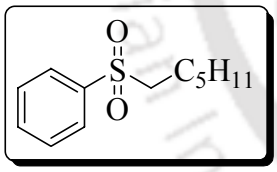
IR (neat): 1158, 1327 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.81(d, *J* = 6.8 Hz, 2H), 5.14 (d, *J* = 17.2 Hz, lH), 5.31 (d, *J* = 10 Hz,1H), 5.70-5.80(m, lH), 7.54(t, *J* = 8Hz, 2H), 7.64(t, *J* = 6.4Hz, 1H), 7.85(d, *J* = 8.4Hz, 2H).

Hexyl phenyl sulfoxide (4a)



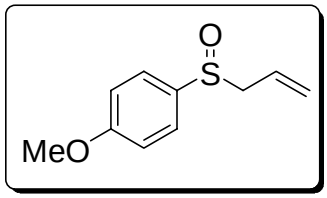
IR (KBr): 1041 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.86(t, *J* = 6.4Hz, 3H), 1.25-1.47(m, 6H), 1.56-1.77(m, 2H), 2.74-2.87(m, 2H), 7.47-7.52(m, 3H), 7.60-7.62(m, 2H).

Hexyl phenyl sulfone (4b)



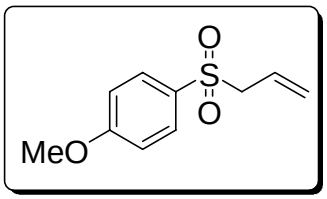
IR (KBr): 1146, 1306 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ 0.83 (t, *J* = 6.4Hz, 3H), 1.21-1.36 (m, 6H), 1.64-1.72(m, 2H), 3.05(t, *J* = 8.0Hz, 2H), 7.53 (t, *J* = 7.6Hz, 2H), 7.62(t, *J* = 6.8Hz, 1H), 7.87(d, *J* = 7.2Hz, 2H).

Allyl 4-methoxyphenyl sulfoxide (5a)



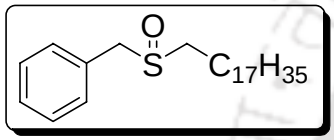
IR (neat): 1044 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ 3.45-3.57(m, 2H), 3.78(s, 3H), 5.18(d, *J* = 16.8Hz, 1H), 5.31(d, *J* = 10.8Hz, 1H), 5.58-5.68(m, 1H), 7.47-7.51(m, 3H), 7.54-7.57(m, 2H).

Allyl 4-methoxyphenyl sulfone (5b)



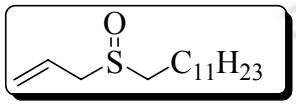
IR (neat): 1158, 1329cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ 3.78(d, *J* = 7.2Hz, 2H), 3.81(s, 3H), 5.14(d, *J* = 17.2Hz, 1H), 5.31(d, *J* = 10.4Hz, 1H), 5.74-5.83(m, 1H), 6.99(d, *J* = 8.4Hz, 2H), 7.77(d, *J* = 8.8Hz, 2H).

Benzyl octadecyl sulfoxide (6a)



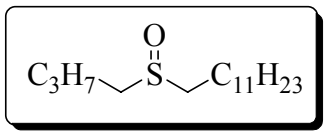
IR (neat): 1015 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ 3.45-3.57(m, 2H), 3.78(s, 3H), 5.18(d, *J* = 16.8Hz, 1H), 5.31(d, *J* = 10.8Hz, 1H), 5.58-5.68(m, 1H), 7.47-7.51(m, 3H), 7.54-7.57(m, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ 14.3, 22.6, 22.8, 29.0, 29.3, 29.5, 29.6, 29.7, 29.8(3C), 30.0(5C), 32.1, 51.1, 58.5, 128.5, 129.1(C), 130.2(3C).

Allyl dodecyl sulfoxide (7a)



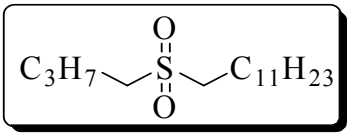
IR (KBr): 1035 cm^{-1}; ^{1}H NMR(400MHz, $CDCl_3$): δ 0.9(t, *J* =6.4Hz, 3H), 1.31-1.46(m, 16H), 1.78-1.88(m, 2H), 2.93(t, *J* = 8.4Hz,2H), 3.69(d, *J* = 8.4Hz, 2H), 5.42(d, *J* = 16.4Hz, 1H), 5.49(d, *J* = 10.8Hz, 1H), 5.85-6.0(m, 1H).

Butyl dodecyl sulfoxide (8a)



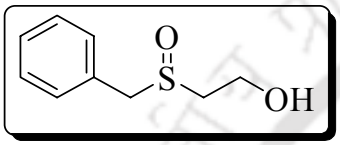
IR (KBr): 1025 cm^{-1}; ^{1}H NMR(400MHz, $CDCl_3$): δ 0.89(t, *J* = 6.8Hz, 3H), 0.98(t, *J* = 6.8Hz, 3H), 1.22-1.56(m, 20H), 1.72-1.8(m, 4H), 2.57-2.74(m, 4H).

Butyl dodecyl sulfone (8a)



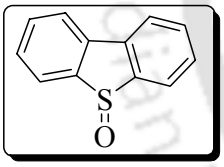
IR (KBr): 1145, 1325 cm^{-1}; ^1H NMR(400MHz, $CDCl_3$): δ 0.89(t, *J* = 6.8Hz, 3H), 0.98(t, *J* = 6.8Hz, 3H), 1.22-1.56(m, 20H), 1.76-1.86(m, 4H), 2.88-2.92(m, 4H).

2-Phenylmethanesulfinyl-ethanol (9a)



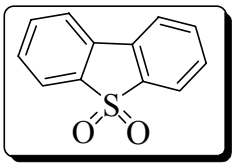
IR (KBr): 1025 cm^{-1}; ^1H NMR(400MHz, $CDCl_3$): δ 2.72-2.77(m, 1H), 2.81-2.87(m, 1H), 4.05-4.13(m, 4H), 7.29-7.31(m, 2H), 7.34-7.38(m, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 53.34, 55.29, 58.04, 128.60(2C), 129.11(2C), 130.04, 130.52.

Dibenzothiophene sulfoxide (10a)



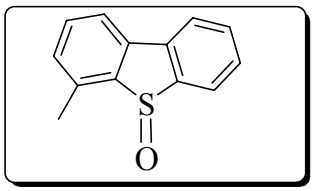
IR (KBr): 1025cm^{-1}; ^1H NMR(400MHz, $CDCl_3$): δ 7.48 (t, *J* = 7.6 Hz, 2H) , 7.58 (t, *J* = 7.6 Hz, 2H), 7.79 (d, *J* = 7.6 Hz , 2H) , 7.97 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR(100MHz, $CDCl_3$): δ 121.8(2C), 127.4 (2C) , 129.4 (2C) , 132.4 (2C), 136.9 (2C), 144.9 (2C).

Dibenzothiophene sulfone (10b)



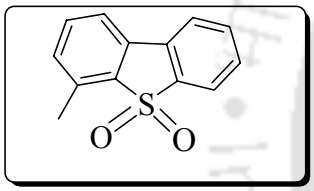
IR (KBr): 1162,1287 cm^{-1}; ^1H NMR(400MHz, $CDCl_3$): δ 7.52 (t, *J* = 7.6 Hz, 2H), 7.63 (t , *J* = 8.8Hz, 2H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.81 (d, *J* = 7.6 Hz, 2H).

4-Methyldibenzothiophene sulfoxide (11a)



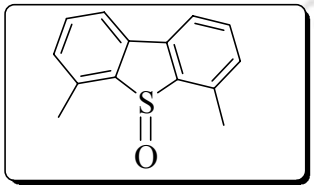
IR (KBr): 1028 cm^{-1}; ^1H NMR(400MHz, $CDCl_3$): δ 4.32 (d, *J* = 12.8 Hz, 1.5H) , 4.50 (d, *J* = 13.2 Hz, 1.5H), 7.14-7.27 (m, 3H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H).

4-Methylbenzothiophene sulfone (11b)



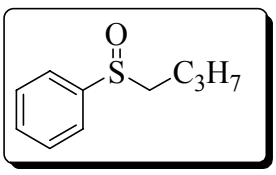
IR (KBr): 1168,1283 cm^{-1}; ^1H NMR(400MHz, $CDCl_3$): δ 4.43(s, 3H), 7.14-7.29 (m, 3H), 7.46-7.56 (m, 2H) , 7.92-8.08 (m, 2H).

4, 6-Dimethyldibenzothiophene sulfoxide (12a)



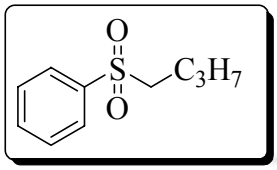
IR (KBr): 1028 cm^{-1} ; ^1H NMR(400MHz, $CDCl_3$): δ 2.52 (s, 6H), 7.14-7.27 (m, 3H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.4Hz, 1H).

Butyl phenyl sulfoxide (13a)



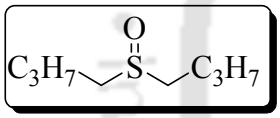
IR (KBr): 1041 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ 0.88 (t, *J* = 7.2 Hz,3H) , 1.38 (sext, *J* = 7.6Hz, 2H), 1.64-1.733 (m, 2H), 2.78-2.91 (m, 2H) , 7.50-7.57 (m, 2H) , 7.60-7.66 (m, 1H), 7.87-7.90 (m, 2H).

Butyl phenyl sulfone (13b)



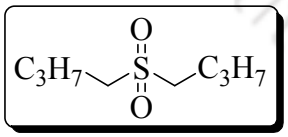
IR (KBr): 1148, 1306 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ 0.87 (t, *J* = 7.6 Hz,3H), 1.36(sext, *J* = 7.6 Hz, 2H), 1.62-1.70 (m, 2H) , 3.04-3.08 (m, 2H), 7.51-7.55 (m, 2H), 7.59-7.63 (m, 1H) , 7.85-7.88 (m, 2H).

Dibutyl sulfoxide (15a)



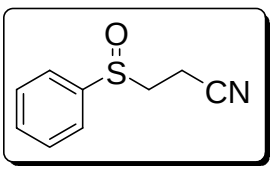
IR (KBr): 1021 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.92(t, *J* = 7.2 Hz ,6H), 1.39-1.49 (m, 4H), 1.66-1.80 (m, 4H), 2.55-2.67 (m, 4H).

Dibutyl sulfone (15b)



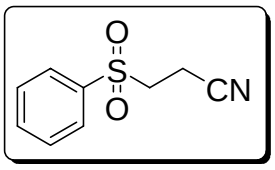
IR (KBr): 1127, 1260 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.91(t, *J* = 7.2Hz, 6H), 1.39-1.49 (m, 4H), 1.64-1.80 (m, 4H), 2.87-2.92 (m, 4H).

3-Benzenesulfinyl-propionitrile (16a)



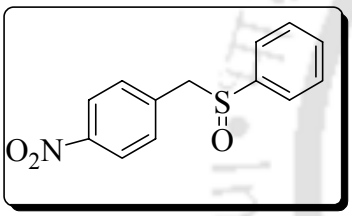
IR (neat): 1044, 2362 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.81(t, *J* = 7.6 Hz, 2H) , 3.17-3.26 (m, 2H), 7.53-7.73 (m, 5H).

3-Benzenesulfonyl-propionitrile (16b)



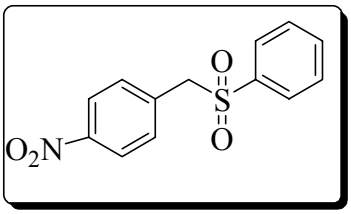
IR (neat): 1146, 1306, 2258 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.76 (t, *J* = 7.6 Hz, 2H), 3.40 (t, *J* = 7.2 Hz, 2H), 7.54-7.71 (m, 3H), 7.87-7.91 (m, 2H).

4-Nitrobenzyl phenyl sulfoxide (17a)



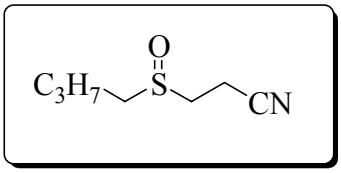
IR (KBr): 1026 1347, 1515 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.98 (d, *J* = 12.8 Hz, 1H), 4.18 (d, *J* = 12.4Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 2H), 7.31-7.33 (m, 2H), 7.40-7.47(m, 3H), 8.06(d, *J* = 6.8Hz, 2H); ^{13}CNMR : 62.04, 123.3 (2C), 124.2 (2C), 129.2 (2C), 131.3 (2C), 131.6, 136.2, 141.7, 147.7.

4-Nitrobenzyl phenyl sulfone (17b)



IR (KBr): 1148, 1306, 1350, 1525 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.39(s, 2H), 7.24-7.28(m, 2H), 7.45-7.49(m, 2H), 7.61-7.65(m, 3H), 8.1(d, *J* = 8.4Hz, 2H).

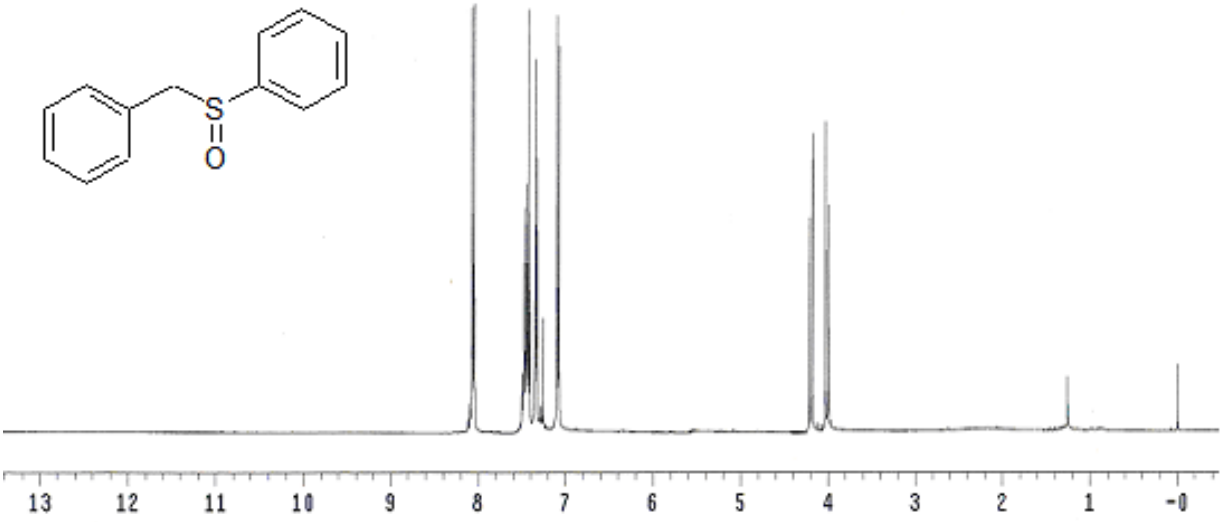
3-(Butane-1-sulfinyl)-propionitrile (18a)



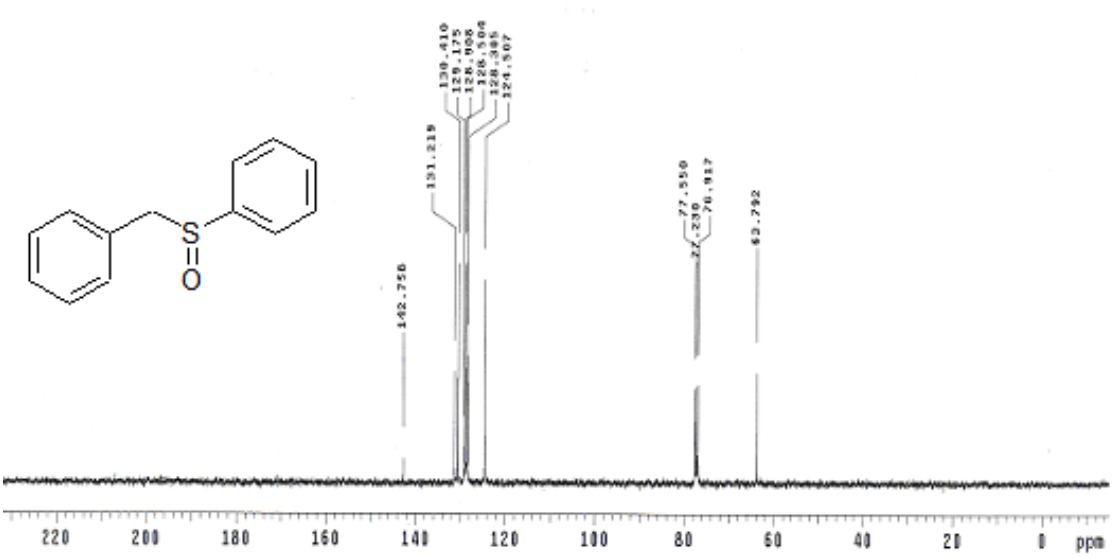
IR (KBr): 1054, 2356 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ ^{1}HNMR : 0.98 (t, *J* = 7.2 Hz, 3H), 1.50 (sext, *J* =7.2 Hz, 2H), 1.81-1.88 (m,2H), 2.92 (t, *J* = 7.6 Hz, 2H), 3.06-3.10 (m,2H), 3.26 (t, *J* = 7.6 Hz, 2H).

Spectra of some selected compounds

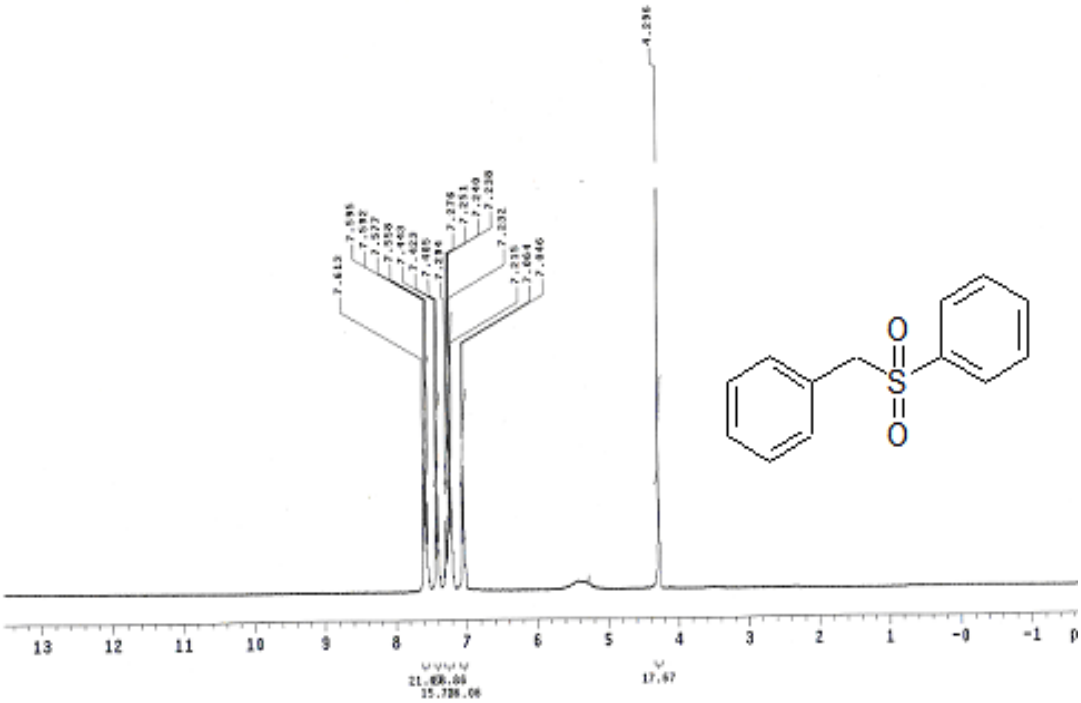
^{1}H NMR Spectrum of Benzyl phenyl sulfoxide (2a):



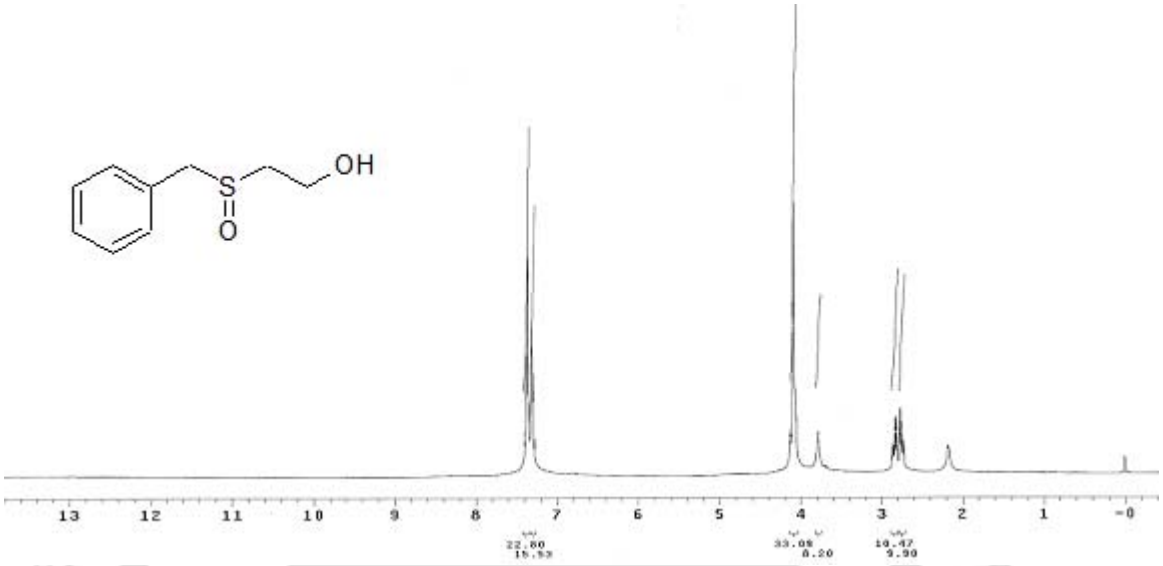
^{13}C NMR Spectrum of Benzyl phenyl sulfoxide (2a):



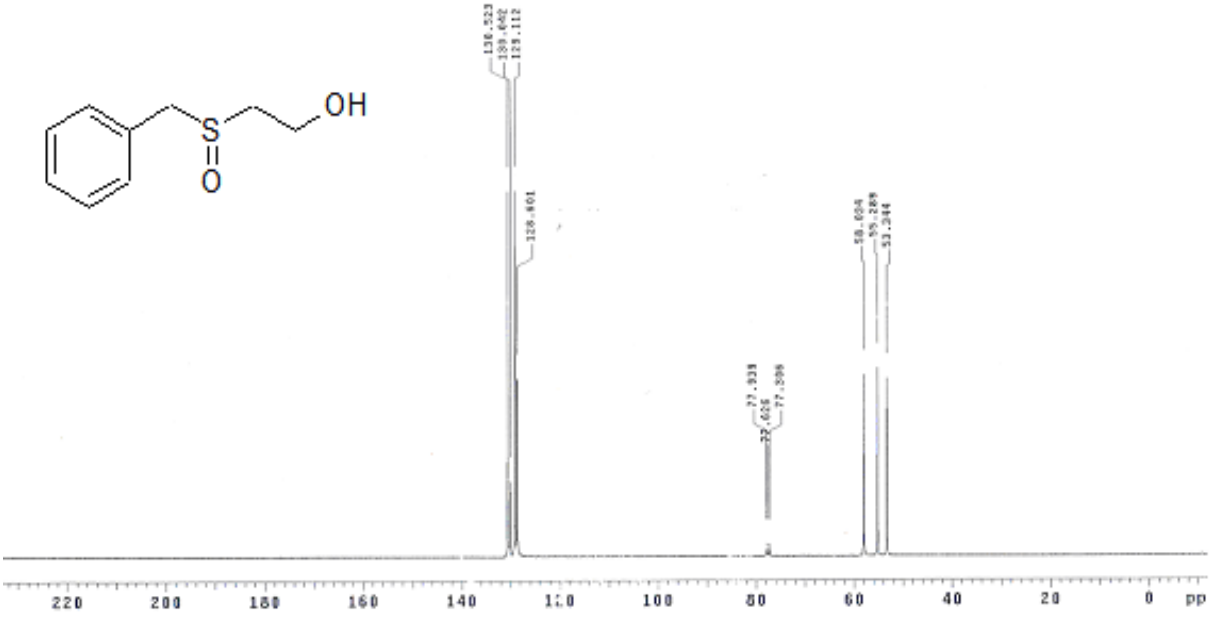
^{1}H NMR Spectrum of Benzyl phenyl sulfone (2b):



^{1}H NMR Spectrum of 2-Phenylmethanesulfinyl-ethanol (9a):



^{13}C NMR Spectrum of 2-Phenylmethanesulfinyl-ethanol (9a):



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VBrPO-Mimicking Catalysis in Water for Radical Bromination, Electrophillic Oxidation and Oxidative Extraction of Bromide from Sea Water

Environmentally cleaner access to benzyl bromides that serve as precursors of benzyl alcohols appears to be a synthetic challenge,[1,2] while the global requirement for benzaldehydes that are generally obtained from the corresponding alcohols is very high (> 20,000 tons per year).[3] Benzyl halides are synthesized from the corresponding toluenes. The radical bromination of toluenes with molecular bromine is fraught with the problems of handling, transportation and use owing to its high toxicity and corrosive nature. The bromination with molecular bromine may thus be classified as an environmentally unsafe process[4] because of only 50% atom-economy and formation of hazardous HBr. The Wohl-Zigler bromination involving NBS in boiling CCl_4 and a radical initiator[5] and several modifications there to[6-10] have been used as alternatives to molecular bromine, however, they are generally accompanied by dibromination and electrophillic brominations as well. In order to render the free-radical bromination more effective, reduction of $NaBrO_3$ with $NaHSO_3$[11] and oxidation of bromide with H_2O_2[1,2] were developed while for the former $NaBrO_3$ preparation is based on the use molecular bromine, the latter requires an excess of sulfuric acid and a halo organic solvent.[1] A very recent report[2] on free-radical bromination involved the oxidation of HBr by H_2O_2 under incandescent light. The brominating agent used therein is not ecobenevolent, highly toxic and not easy to handle. In the present scenario, bio-inspired catalysis seems to be the safest option since the nature operates biogenic reactions utilizing vanadium bromoperoxidase (VBrPO) enzyme as the catalyst for bromination of the required organic molecules.[12] To the best of our knowledge, VBrPO-activity based bio-mimicking catalytic radical bromination is not precedented in the literature. Considering the information providing an insight into the peroxo-forms of vanadium haolperoxidase cofactor reactivity,[13,14] there is finite possibility of developing a VBrPO mimicking free-radical bromination of benzylic systems (*c.f.* toluenes). Once this is achieved, an easy access to benzyl alcohols can be gained simply by alkaline hydrolysis. Besides the radical bromination, oxidation of alcohols to aldehydes or ketones is a fundamental transformation in chemical industries. However, green catalytic oxidation of benzyl alcohols,[15] as opposed to the spate of stoichiometric oxidations,[16-24] is a relatively grey area that needs attention because most of the reported green procedures[25] have been based on costly metals[26-33] thereby rendering the process economically less attractive. Notwithstanding this, in majority of the studies the reagents or the catalysts act as electrophiles. This is also true in the cases of alcohol oxidations by H_2O_2 with some excellent catalysts[25] like Na_2MoO_4 or Na_2WO_4. Although the discovery of vanadium bromoperoxidase in marine organisms has provided great fillip to the research activity on peroxovandium chemistry, VBrPO related

alcohol oxidations involving vanadium as the central metal *per se* are not many to be reckoned. Drawing an analogy with DMSO, Li *et al.*[15] have reported very recently the dual roles of oxoperoxovanadate(V) both as nucleophile and oxidant for benzyl alcohols and benzyl halides. While peroxovanadate(V) acting as an oxidant has precedence,[34] its role as nucleophile is rather unusual. Also, a solution of V_2O_5 in H_2O_2 at pH 4, as used in the study, will contain more than one peroxovanadate(V) species[35] and all of them may not be equally active. In addition, the presence of benzyltriethylammonium bromide (BTEAB) in such a solution would enable oxidation of bromide,[36,37] as well, which in turn would participate in oxidation of substrate. Taking cues from the results of investigation on the peroxo form of vanadium haloperoxidase cofactor reactivity,[14] including the very recent DFT studies,[13,14] and our experience in *in vitro* experiments on peroxovanadate catalyzed oxidation of bromide (Br^-) leading to the isolation of tribromide (Br_3^-) guided us to chose a triperoxovanadate(V) complex, $K[V(O_2)_3].3H_2O$, as the precursor catalyst.[38-40]

Accordingly, we have developed an improved method for the synthesis of $K[V(O_2)_3].3H_2O$ and subsequently investigated benzylic bromination of toluene and selective oxidation of benzyl alcohols with H_2O_2 as the terminal oxidant. Under the optimized reaction conditions, a few toluenes and benzylic alcohols were converted to their corresponding benzyl bromide and benzaldehyde selectively and efficiently in good yields. These results have been discussed in **Section 5.1**.

The fact that the peroxo form of the enzyme vanadium bromoperoxidase (VBrPO) catalyzes the oxidative bromination of organic molecules in the marine environment[41] and that VBrPO mimicking catalysts catalyzes the *in situ* oxidation of Br^- to Br^{3-} by H_2O_2 in the presence of small amount of acid is highly significant in the realm of peroxovanadium(V) chemistry.[36,37,42-44] By conjuring the bio and abiotic events, it was anticipated that a suitable VBrPO mimicking catalyst might enable extraction of bromide from sea water in a very soft way. Accordingly, several catalysts have been developed in our laboratories and the performance of $[VO_2F(dmpz)_2]$ as a representative example has also been reported in this Chapter. A slightly concentarted pre-analysed sea water generally known as 'bittern' was obtained from a bromine producing industry (Tata Chemicals Ltd., India). The bromide content of the bittern was 2 g/L. The compound, $[VO_2F(dmpz)_2]$ has been shown to efficiently and selectively catalyze the oxidation of Br^- in bittern by H_2O_2 in the presence of a small amount of acid. The oxidised bromide has been

isolated from the water solution using either tetrabutylammonium or benzyltriethyl ammonium ion as the corresponding tribromide. This work forms the subject matter of **Section 5.2.**

5A. Results and Discussions

5.1. An Improved Synthesis of $[K(V(O_2)_3].3H_2O$ and its Use as a Precatalyst for Radical Bromination and Oxidation

The first task was to standardize the method of preparation of $[K(V(O_2)_3].3H_2O$ that has been achieved from the reaction of V_2O_5 with H_2O_2 in the presence of a relatively large concentration of alkaline medium. The detailed of the procedure is described in experimental section. Vanadium(V) undergoes fast and favourable addition reactions with hydrogen peroxide producing peroxo complexes whose nature depends upon the concentration of the reagent and on the pH of the solution. The synthesis of blue potassium triperoxovanadate(V) trihydrate, $K[V(O_2)_3].3H_2O$, has been achieved from the reaction of V_2O_5 with H_2O_2 in the presence of relatively large concentration of alkaline medium with the molar ratio of V_2O_5 : H_2O_2 : KOH being maintained at 1: 42 : 9. The complex was obtained by the addition of ethanol, which fascilated precipitation. The temperature, time and order of addition of the reagents play crucial role in the successful synthesis of the catalyst. A minor change in the reaction conditions may lead to the formation of mixed peroxo complexes. The characterization of the catalyst was accomplished by elemental analysis, UV-Vis and IR spectroscopy.[38-40] Elemental analyses show three peroxide groups being present per V(V) center. The UV-Vis spectrum of the complex showed absorption at 240 nm and 561 nm with molar extinction coefficient being 10412 and 1523, respectively. These peaks are assigned to the ligand to metal charge transfer (LMCT) transitions. The vibrational spectrum of $K[V(O_2)_3].3H_2O$ shows bands due to the presence of coordinated peroxide (O_2^{2-}).[45] Appearance of a strong band at 850 cm^{-1} has been assigned to $\upsilon(O_2)$ stretching. The strong band at 550 cm^{-1} and a medium band at 600 cm^{-1} are due to $\upsilon_s(V\text{-}O_2^-)$, $\upsilon_a(V\text{-}O_2^-)$, respectively.[45] The IR spectrum shows no peaks corresponding to υ(V-O) (oxo) group at *ca*. 950 cm^{-1} that generally appears as a strong band indicating that the complex does not contain V=O group. The typical pattern of the spectrum suggest that the peroxo ligand is coordinated to the metal center in a triangular bidanted manner.[38] After complete characterization of the complex, one of our major concern was to explore the reactivity of $K[V(O_2)_3].3H_2O$, especially for the radical bromination and electrophillic oxidation of benzylic systems. Some of the reasons for the selection

of its reactivity are that an aqueous solution of the complex salt is alkaline, unstable and with lowering pH to 5 or 4 by careful addition of very dilute sulfuric acid or perchloric acid generates $[(O_2)_2OV\text{-}(\mu\text{-}OH)\text{-}VO(O_2)_2]^{3-}$ *in situ* which has been isolated as $K_3[V_2O_2(O_2)_4(OH)].H_2O$ and crystallographically characterized (**Fig. 5.1.1**). The structure compares very well with that of $NH_4[V_2O_2(O_2)_4(OH)].H_2O$ reported in literature.[46] Ensuring existence of the dimeric μ-hydroxo diperoxvanadate(V) species under the above mentioned condition, it was decided to use such a solution for the subsequent reactivity studies. The active intermediate, $[(O_2)_2OV\text{-}(\mu\text{-}OH)\text{-}VO(O_2)_2]^{3-}$, will be abbreviated as **AC** and for the sake of clarity, only one coordinated peroxide will be involved in delineating the mechanism (**Schemes 5.1.1 and 5.1.2**). The analytical and X-ray data are tabulated in experimental section.

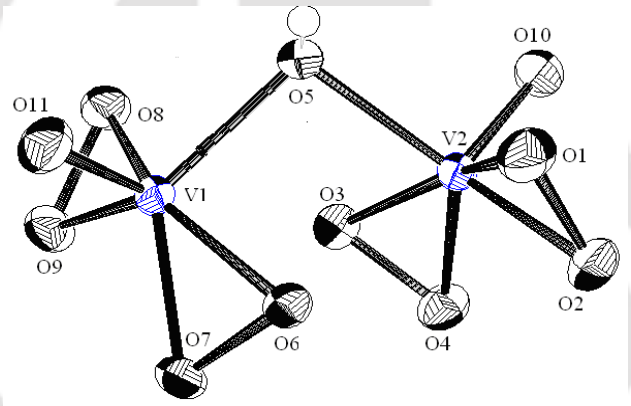


Fig. 5.1.1. *The ORTEP view of $K_3[(O_2)_2OV\text{-}(\mu\text{-}OH)\text{-}VO(O_2)_2].H_2O$. K and H_2O are removed for clarity*

In so far as the radical bromination is concerned, the reaction is expected to proceed in the following way. The addition of acid would lead to protonation that would play an important role in the activation of peroxo-vanadium (V) complex (**AC**) (*c.f.* the hydrogen bonding interaction of lysine residue (K353) with the equatorial peroxo oxygen atom in the activation of peroxo form of the cofactor)[13] and the oxo-transfer to Br^- would involve the unprotonated peroxo oxygen atom as shown in **Scheme 5.1.1** (**1** and **2**)**.** Interaction of **2** with water would give **3** liberating HOBr. The hypobromous acid would equilibrate as HOBr $\rightleftharpoons$ Br_2 $\rightleftharpoons$ Br_3^-, and it is Br_3^- that would act as the brominating agent.[43,47] Br_3^- ($\equiv Br^- + Br_2$) being the store house of bromine is expected to produce bromine radicals(Br·) thus formed would lead to bromination of toluene in the usual way (**Fig. 5.1.2**).

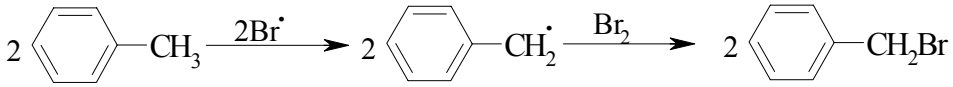


Fig. 5.1.2

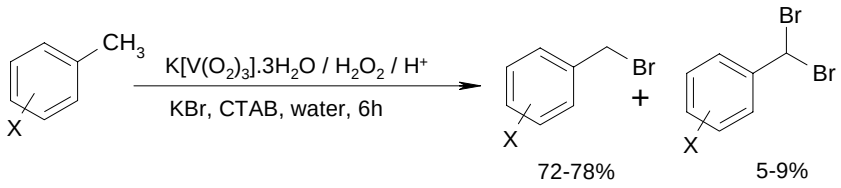
Table 5.1.1. *$K[V(O_2)_3].3H_2O$ catalyzed radical bromination of toluene using various amounts of H_2O_2*

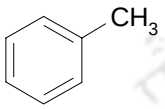
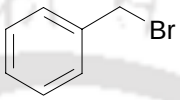
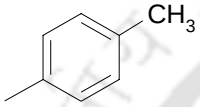
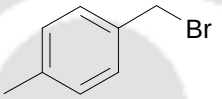
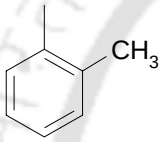
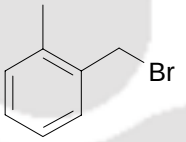
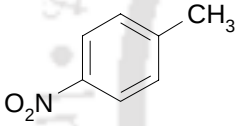
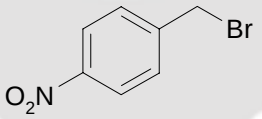
Entry	$K[V(O_2)_3]$(mmol)	H_2O_2 (mmol)	Time (h)	Yield (%)
1	0.1	1.0	6	65
2	0.1	1.5	6	75
3	0.1	2.0	6	75

The hypothesis worked well with toluene and the reaction was optimized by varying the amount of the H_2O_2 and the catalyst, $K[V(O_2)_3].3H_2O$. Toluene was chosen as a model substrate to ascertain the optimal condition. First we screened various amounts of H_2O_2 for this oxidation reaction employing 1.0 mol equivalent of toluene, 0.1mol equivalent of the catalyst, 1.2 equiv. of KBr, 0.001 mol equivalent of CTAB and maintaining the pH at 5 or 4. On lowering the amount of catalyst, the yield was decreased and required long reaction time whereas on increasing the amount of catalyst there was no significant change in the reaction time and yield. The best result was obtained when the concentration of the H_2O_2 was 1.5 mol equivalents (**Table 5.1.1**).

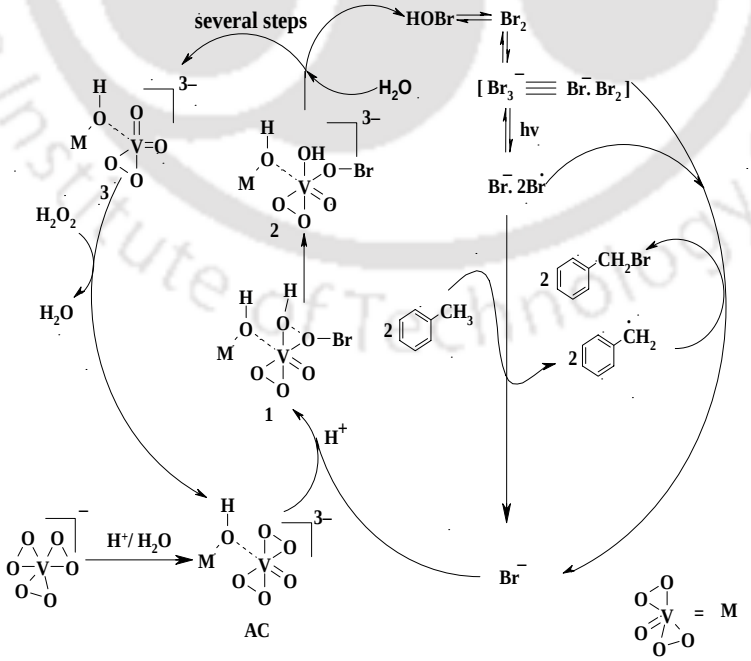
Under the optimized reaction condition, reactions were carried out with substituted tolune (entries **2-4,** Table 5.1.2**)**. The deactivating substituent does not seem to have any pronounced effect on the yield. The active catalyst **AC**, once generated in solution, remained active for five cycles thereafter the yield started falling. We believe that attrition of AC in the work up step must be responsible for the decrease in the yields. The reaction is capable of being scaled up (10 g) without any apparent difficulty (entry **1,** Table 5.1.2).

Table 5.1.2. *Free radical bromination of benzylic substrates using $K[V(O_2)_3].3H_2O$ as the precursor catalyst and H_2O_2 as the oxidant*



Entry	Substrate	Time(h)	Product		Yield(%)[a]
1		6		**1a**	75,78[b],71[c]
2		6		**2a**	70
3		6		**3a**	78
4		6		**4a**	72

[a] *Isolated yield,*
[b] *Yield on 10 g scale,*
[c] *Yield after fifth cycle*



Scheme 5.1.1. *Plausible mechanism for free radical bromination of toluene*

Our next concern was to achieve efficient oxidation of benzyl alcohols using hydrogen peroxide as the terminal oxidant. Pertinently, metal-catalyzed oxidations are often modelled on certain enzymes which perform the oxidation of organic substrates in natural systems.[48,49] Our strategy was to model on the peroxo form of VBrPO cofactor reactivity and to try out the chosen oxidations. Here again the active intermediate **AC** was first generated at pH 5 or 4 that interacted with benzyl alcohols in an electrophillic manner (**Scheme 5.1.2**).

The reaction was optimized with *p*-chlorobenzyl alcohol as a model substrate by varying the amount of the H_2O_2 and the catalyst, $K[V(O_2)_3].3H_2O$. First we screened various amount of H_2O_2 for this oxidation reaction employing 1.0 mol equivqlent of *p*-chlorobenzyl alcohol, 0.1mol equivalent of the catalyst, 0.001 mol equivalent of CTAB and maintaining the pH at 5 or 4. The reaction runs were carried out at 60ºC. The best result was obtained when the concentration of H_2O_2 was taken as 1.2 mol equivalents. Though the yield was slightly high when the concentration of H_2O_2 was taken 1.5 mol equivalents, but a small amount of carboxylic acid was formed along with aldehyde (**Table 5.1.3**). Hence, to get the aldehyde selectively, subsequent reactions were carried out with 1.2 mol equivalents of H_2O_2. In order to achieve catalyst optimization, we then changed the amount of catalyst, $K[V(O_2)_3].3H_2O$, for the same reaction employing 1.0 mol equivalent of *p*-chlorobenzyl alcohol, 1.2 mol equivalents of H_2O_2, 0.001 mol equivalent of CTAB at pH at 5 or 4 with the temperature being maintained at 60ºC . When 0.1 mol equivalent of the catalyst was used, more than 75% of *p*-chlorobenzyl alcohol was transformed to *p*-chlorobenzaldehyde (**Table 5.1.4**). To see the effect of temperature on the reaction, the reaction was carried out at room temperature for 45 minutes but the yield was very low (15%). Thus, for the oxidation of substrate: H_2O_2: catalyst: CTAB ratio was maintained at 1.0: 1.2: 0.1: 0.001 at pH at 5 or 4. The reactions were all conducted at 60ºC.

Table 5.1.3. *$K[V(O_2)_3].3H_2O$ catalyzed oxidation of p-chlorobenzyl alcohol using various amounts of H_2O_2*

Entry	$K[V(O_2)_3]$(mmol)	H_2O_2 (mmol)	Time (min)	Yield(%)
1	0.1	1.0	35	65
2	0.1	1.2	30	80
3	0.1	1.5	30	76

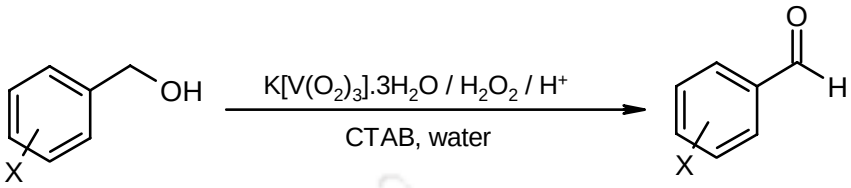
Table 5.1.4. *$K[V(O_2)_3].3H_2O$ catalyzed oxidation of p-chlorobenzyl alcohol with H_2O_2 using various amounts of the catalyst*

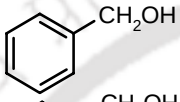
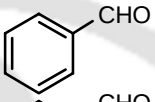
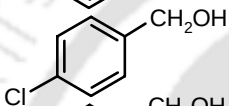
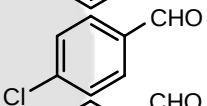
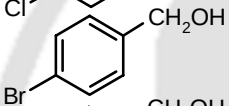
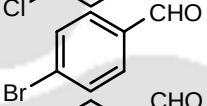
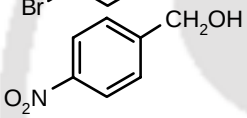
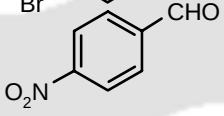
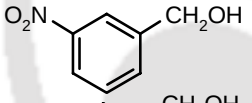
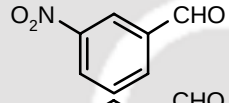
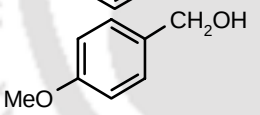
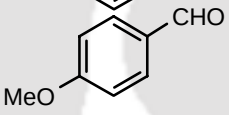
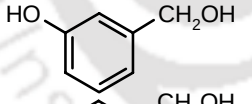
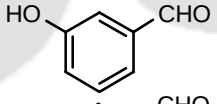
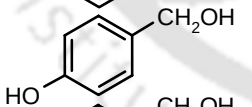
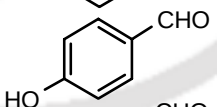
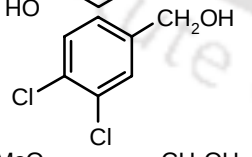
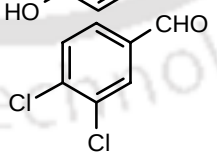
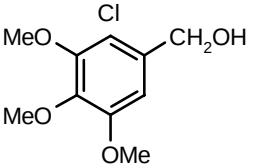
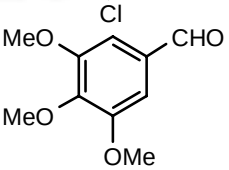
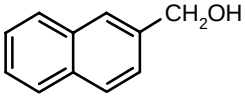
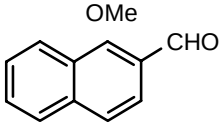
Entry	$K[V(O_2)_3].3H_2O$/ Substrate (Molar ratio)	H_2O_2 (mmol)	Time (min)	Yield (%)
1	0	2.0	120	35
2	0.01	1.2	55	60
3	0.02	1.2	45	70
4	0.05	1.2	45	70
5	0.07	1.2	40	73
6	0.1	1.2	40	80

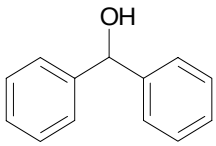
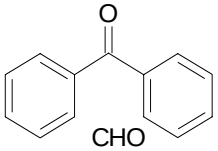
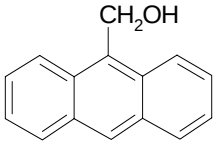
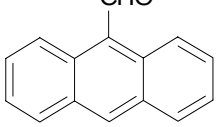
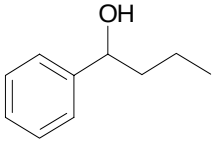
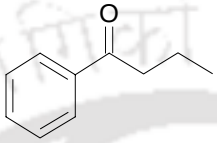
Under the optimized condition a wide variety of primary and secondary alcohols were subjected to oxidation as shown in the **Table 5.1.5**. Benzyl alcohol and substituted benzyl alcohols were converted to their corresponding aldehydes selectively and efficiently. Benzaldehyde was obtained selectively with 78% yield after 20 minutes. But, when the reaction was prolonged further, the obtained products were benzaldehyde and benzoic acid. These results show that the substituents have no significant effect on the oxidation of benzylic alcohols. 2-naphthyl alcohol and 9-anthranyl alcohol furnished products with low yield. The main reason for low yields is the low solubility of the above substrates in aqueous medium. In order to ensure the role of CTAB, a few reactions were carried out without CTAB under similar reaction conditions, and the results are presented in **Table 5.1.5**. The results reveal that CTAB not only acts as a phase transfer catalyst but also takes a key role in the oxidation step.

The recyclability of the active catalyst **AC** was ascertained in the following way. After the first cycle (entry **2**) the product was extracted with ethyl acetate and the aqueous layer used for the second and subsequent cycles with added hydrogen peroxide. The pH was maintained at 5 or 4. The consistent activity was observed for five cycles. Thereafter the yield started falling due to attrition of **AC**. An experiment was conducted on 5g scale with either 4-chlorobenzaldehyde or 1-phenyl butan-1-ol using the same protocol for two reasons, first to explore the possibility of scaling up and second to isolate the active intermediate and ascertain its identity. The experiment was successful in each case giving very good yield. The peroxovanadium complex isolated from the aqueous solution after extracting the oxidized product was identified as $K_3[(O_2)_2OV\text{-}(\mu\text{-}OH)\text{-}VO(O_2)_2].H_2O$ from the results of FT IR spectroscopy and the X-ray unit cell determinations carried out on single crystal. The results thus far obtained show *inter alia* that the metal centre does not undergo redox cycling (*c.f.* VBrPO reactivity).

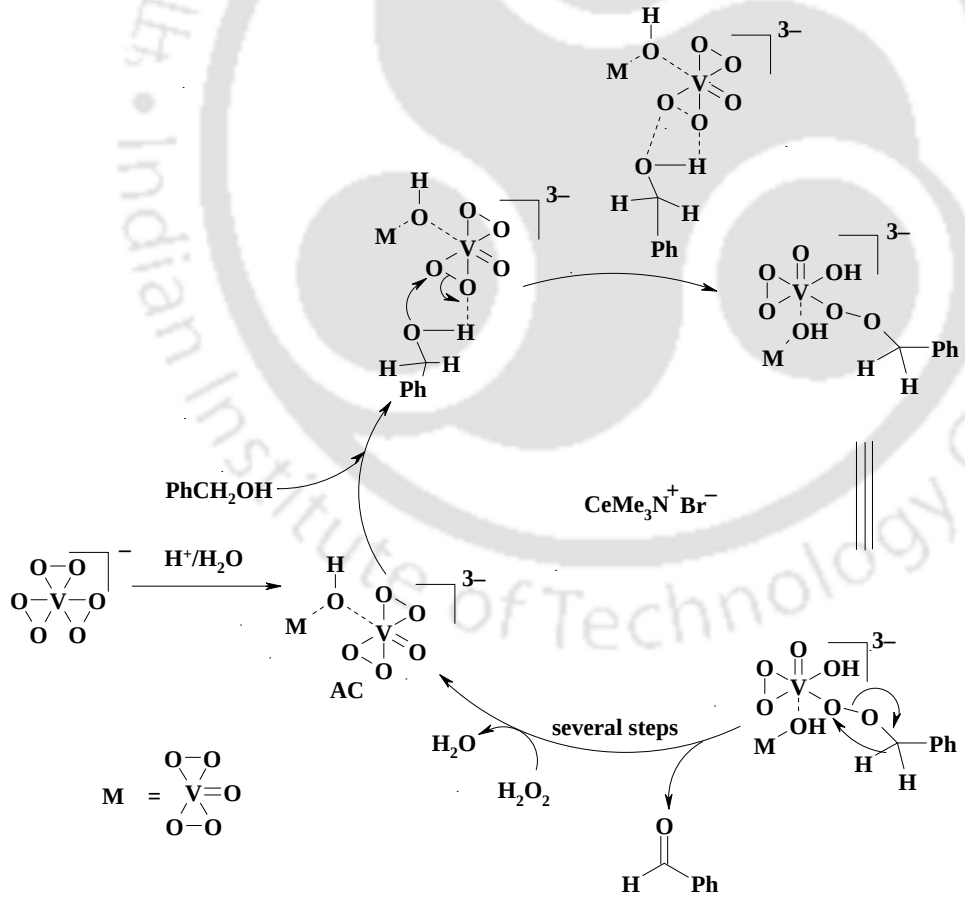
***Table 5.1.5**. Selective oxidation of benzyl alcohols using $K[V(O_2)_3].3H_2O$ as precursor catalyst and H_2O_2 as the oxidant*



Entry	Substrate	Time (min)	Product		Yield(%)[a]	Li *et al*.[15] time(h)/ Yield(%)
1		20,50[b]		**5a**	78, 66[b]	6/84
2		30		**6a**	80, 72[c] 83[d]	7/84
3		30		**7a**	82	
4		60		**8a**	79	
5		60		**9a**	80	
6		20,60[b]		**10a**	77, 64[b]	8/83
7		30		**11a**	82	
8		20		**12a**	80	
9		30		**13a**	81	
10		60		**14a**	75	
11		70		**15a**	70	

12		90 140[b]		**16a**	75, 55[b]	2.5/88
13		80		**17a**	55	
14		40 130[b]		**18a**	82, 64[b], 85[d]	

[a] *Yield referred to those of pure and isolated products,*
[b] *Reaction without CTAB,*
[c] *Yield after fifth cycle,*
[d] *Yield on 5g scale*

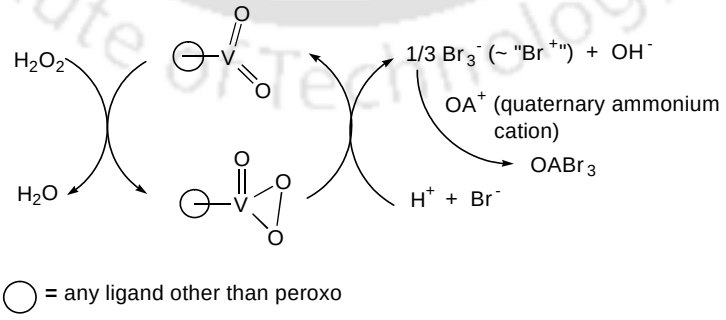


Scheme 5.1.2. Plausible mechanism for benzyl alcohol oxidation

5.2 $[VO_2F(dmpz)_2]$ catalyzed oxidative extraction of bromide from sea water

Incidently, we have $[VO_2F(dmpz)_2]$ at our disposal as a biomimic of VBrPO. This was already used for the oxidation of sulfide in **Chapter 4**. The copmlex was synthesized anticipating its use as a model species mimicking VBrPO, as isolated earlier vide (**Chapter 4**). Herein, this complex has been used for the oxidative extraction of bromide from bittern (slightly concentrated sea water).

Referring back to the *in vitro* laboratory experiments on Br^- oxidation, what was observed was that 2 equiv. of KBr and 1 equiv. of tetrabutylammonium bromide, Bu_4NBr, on being reacted with peroxovanadium(V) complexes, afforded orange-yellow crystalline product in very high yield which was finally identified to be tetrabutylammonium tribromide, TBATB, Bu_4NBr_3.[36] Significantly, the existence of Br_3^- in solution can be monitored by its characteristic absorption spectrum showing a strong absorption at *ca.* 268 nm (ε greater than 50,000 [usually 52,000] $M^{-1}cm^{-1}$) with a shoulder at 400 nm (ε ≈ 145 $M^{-1}cm^{-1}$).[50,51] In vanadium(V) catalyzed reactions, the involvement of peroxovanadium(V) intermediate as an active oxidant can be ascertained from the observance of the peroxo-vanadium charge transfer (CT) band at 430 nm (ε ≈ 300 $M^{-1}cm^{-1}$) in aqueous vanadium(V)–H_2O_2 solution.[36] Indeed this provided a lead to further our studies in this direction with a hope that there might be an emergence of some parallelism between such laboratory experiments and VBrPO enzyme catalyzed natural processes. The laboratory experiments producing Br_3^- in solution and ultimately affording solid quaternary ammonium tribromides, QATBs, may be depicted as shown in **Scheme 5.1.3.**



Scheme 5.1.3. *Mechanistic pathway for QATB synthesis*

Mechanistically, for instance, VO_2^+ serves as a functional mimic of VBrPO although, unlike the enzyme, it functions in acidic conditions and at much lower turnover rates.[41] What

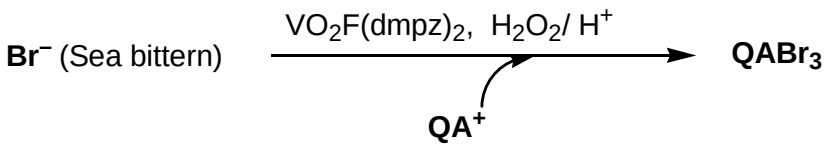
happens in a weakly acidic condition, therefore, is that cis- VO_2^+ coordinates with one or two equivalent of H_2O_2 in solution forming $VO(O_2)^+$ and/or $VO(O_2)_2^-$ species both of which being capable of oxidizing bromide to HOBr ⇆ Br_2 ⇆ Br_3^-.[41] It was shown by our group that Br_3^- can be isolated quantitatively in solid state using appropriate counter cations.[36]

Taking cues from the sucessful synthesis of QATBs and in order to fortify our assumption we carried out oxidation of bromide by $VO_2F(dmpz)_2$, using KBr as the source, with H_2O_2 in water at room temperature. The oxidation was monitored by its characteristic absorption spectrum[36,50,51] showing a strong absorption at *ca.* 268 nm with a shoulder at *ca.* 385 nm along with the band at *ca.* 445 nm for peroxovanadium intermediate. The oxidized bromide was then isolated using either tetrabutylammonium chloride or benzyltriethylammonium chloride (Scheme 5.2.1). The optmized reaction condition is summerized as the general procedure in the experimental section. The isolated compunds are characterized by melting point, IR and UV-vis spectroscopy and results match well with the literature values.[36]

QA^+= Tetrabutylammonium or Benzyl triethyl ammonium

Scheme 5.2.1

Our concern at this juncture was to achieve extraction of bromide from 'bittern' through oxidation with this model catalyst in a similar manner as VBrPO does in nature and isolate them as solid tribromides using different organicammonium cations. The 'bittern' is a slightly concentarted sea water that contains $MgBr_2$–2.26, $MgCl_2$–125.23, NaCl–163.36, $MgSO_4$–8.59 grams per litre (obtained from TATA Chemisals Ltd., India).



QA^+= Tetrabutylammonium or Benzyltriethylammonium

Scheme 5.2.2

A reaction was carried out in bittern at room temperature in a similar way as discussed in KBr system. Unfortunately, a very low yield was obtained**.** In order to optimize the reaction, various conditions were sampled but a 1: 125 : 100 : 10 ratio of catalyst to H_2O_2 to acid to tetrabutylammonium chloride gave the best result. In a typical reaction, $[VO_2F(dmpz)_2]$ (1 mmol) was dissolve in IL of bittern. To this was added H_2O_2 (125 mmol) followed by H_2SO_4 (100 mmol) and tetrabutylammonium chloride (10 mmol). The reaction mixture stirred magnetically at room temperature for 3h whereupon yellow coloured compound was formed throughout the volume. The product was filtered and recrystallized from acetonitrile to yield the pure product in nearly quantitative yield.

Table 5.2.1*. Oxidative extraction of bromide from 1L of bittern (24.5 mmol of* Br^-*) using* $VO_2F(dmpz)_2$ *as catalyst*

S. No.	$VO_2F(dmpz)_2$ (mmol)	H_2O_2 (mmol)	H_2SO_4 (mmol)	TBAC (mmol)	Yield (%)[a]
1	1.0	25	25	10	0
2	1.0	50	25	10	15
3	1.0	75	50	10	32
4	1.0	150	100	15	87
5	1.0	125	100	10	85
6	1.0	125	75	10	82
7	1.0	125	50	10	62
8	0.75	125	75	10	78
9	1.5	125	75	10	85

[a] *Yield after recrystallization*

When a reaction was carried out with benzyltriethylammonium chloride as the counter cation 87% of yield was obtained under the optimized reaction condition. The identity of the compounds[36,52] has been ascertained from the results of IR, UV and X-ray crystallography.

Solution electronic spectroscopy seems to be an extremely important technique for characterization of tribromides as Br_3^- in solution bears characteristic signatures at *ca.* 265 nm with a shoulder at *ca.* 385 nm due to the transitions σ - σ^* and π - π^*, respectively.[36,51] The σ - σ^* and

π - π^* transitions for the tribromides under discussion were observed in the range 267–269 nm and 390–400 nm, respectively, (**Table 5.2.2**) thereby conforming to the identity of the compounds as tribromides.

Table 5.2.2. *IR and electronic spectral bands of* ***TBATB and BTEATB***

Compound (QATB)	IR ν (cm^{-1})	Uv-vis	
		λ (nm) (ε, $M^{-1}cm^{-1}$)	Assignment
TBATB ($C_{16}H_{36}NBr_3$)	171(s) 191(s)	267 (52000) 400 (150)	σ - σ^* π - π^*
BTEATB ($C_{13}H_{22}$ N Br_3)	162(s) 195(s)	269 (50500) 390 (151)	σ - σ^* π - π^*

Most significant in the context of structural evaluation is the X-ray crystal structure of tetrabutylammonium tribromide (**TBATB**) and benzyltriethylammonium tribromide **(BTEATB)** (**Figure 5.2.1**)**.** The X-ray data are presented in the experimental section.

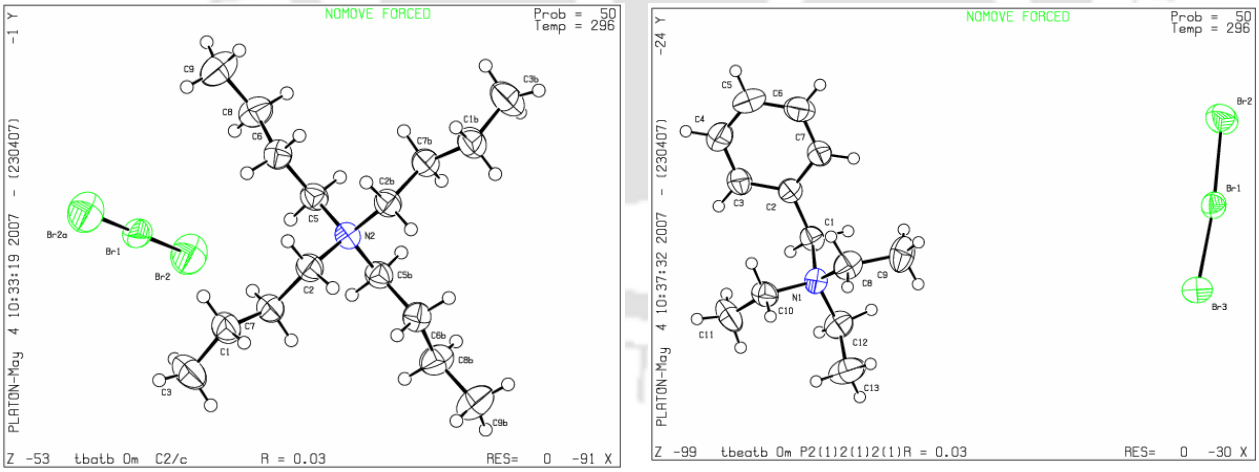


Figure 5.2.1. *Ortep plot of TBATB and BTEATB*

Thus, the synthesis of the tribromides described herein not only provides an easy access to such compounds but also evidences the formation of Br_3^- in solution being catalyzed by peroxo-vanadium intermediates. However, although it is certain that Br_3^- is an oxidized product of Br^-

under VBrPO mimicking condition, formation of other oxidized bromide transient species like OBr^- or Br_2 are not ruled out.

5B. Conclusion

An improved synthesis of potassium triperoxvandate(V) trihydrate, $K[V(O_2)_3].3H_2O$ has been achieved. The complex so synthesized is used as precursor for $[(O_2)_2OV\text{-}(\mu\text{-}OH)\text{-}VO(O_2)_2]^{3-}$ *in situ* at pH 5 or 4. The μ-OH complex (AC) acts as the active catalyst mimicking peroxo form of VBrPO cofactor reactivity in water and catalyze the H_2O_2 oxidation of Br^- to Br_3^- and benzyl alcohols in an acidic medium in presence of CTAB as a phase transfer catalyst. Br_3^- being a storehouse of Br_2, enables radical bromination of toluenes to the corresponding benzyl bromides in the presence of ambient light. Recycleability of the catalyst and scalability of the process are some of the important attributes in the protocols. Interestingly, the new manifestation of $[VO_2F(dmpz)_2]$, in the **Section 5.2**, reaction chemistry in the oxidation of bromide (Br^-) to a tribromide (Br_3^-) in bittern is a paradigmatic example for the assertion to establish connections between biochemically significant natural processes and laboratory-designed experimentations. This reaction has not only provided a general route leading to an extraction of bromide from sea water as tribromides, but also satisfying some "Green Chemistry" norms and triple bottom line mandates. The results are expected to add value to the rich and diverse chemistry of perox-vanadium (V) systems.

5C. Experimental

The sources of chemicals and solvents, the methods for quantitative determination of elements and the details of all the equipment and instruments used for physico-chemical studies have been repoted in **Chapter 2.**

Synthesis of potassium triperoxvanadate(V) trihydrate $K[V(O_2)_3].3H_2O$

To finely powdered V_2O_5, an excess of 30% hydrogen peroxide was added with slow stirring in the molar ratio of V_2O_5 : H_2O_2 as 1 : 42. Solid KOH was slowly added to the above mixture under continuous stirring until a dark blue color developed (molar ratio of V_2O_5 : H_2O_2 : KOH as 1 : 42 : 9). The blue solution was then cooled in an ice water bath for *ca.* 30 min followed by the addition of an excess of precooled ethyl alcohol until the blue shiny microcrystalline $K[V(O_2)_3].3H_2O$ ceased to appear. The blue compound was separated by

centrifugation, washed four or five times with cold ethanol and finally dried in a vacuum desiccator over $CaCl_2$. Yield of $K[V(O_2)_3].3H_2O$ was 86%.

General procedure for benzylic bromination

To 10 mL of water, were added the triperoxovanadate complex (0.1 mmol), H_2O_2 (3 mmol), toluene (2 mmol), KBr (2 mmol), and CTAB (0.002 mmol). The pH of the reaction mixture was adjusted at 5 or 4 using dilute H_2SO_4 and stirred in the ambient light at room temperature for the time given in **Table 5.1.2**. The reaction was monitored by GC MS and TLC and on completion of the reaction the product was extracted with hexane (2 x 5 mL). The combined organic layers was dried (Na_2SO_4), concentrated and purified by column (silica) chromatography (hexane) to afford the pure compound. The aqueous layer after extraction can be reused, if desired.

General procedure for oxidation of benzylic alcohols

In a 25 mL round-bottomed flask equipped with a magnetic stirrer 0.1 mmol of triperoxovanadate complex, 2.2 mmol of H_2O_2 (50%), 2 mmol of alcohol, and 0.002 mmol of CTAB were added and mixed with 10 mL of water. A dilute H_2SO_4 solution was added to adjust the pH of the solution at 5 or 4. The mixture was then heated to 60°C under stirring for the time specifed in **Table 5.1.5**. The reactions were monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3x5 mL). The combined extracts was dried over Na_2SO_4, concentrated and purified by column (silica) chromatography (hexane/ethyl acetate: 90/10) and then the isolated yield was calculated. Here again the aqueous layer after extraction can be reused, if desired.

General procedure for the $[VO_2F(dmpz)_2]$ catalyzed synthesis of TBATB

An amount of 0.03 g (0.1 mmol) $[VO_2F(dmpz)_2]$ was added to 3.6 mL (32 mmol) of 30 % hydrogen peroxide (H_2O_2), taken in a pre-cooled 250 mL beaker. The solution was stirred magnetically at 0-5°C. To the solution was added an acidic solution of 2.78 g (10 mmol) of tetrabutylammomium chloride (TBAC) and 3.88 g (32 mmol) of potassium bromide (KBr) in 12 mL of 1M sulphuric acid (H_2SO_4). The reaction mixture was stirred when orange yellow compound started precipitating out. When precipitation was complete, the compound was filtered by suction filtration and dried in a vacuum desiccator over anhydrous calcium chloride ($CaCl_2$) as the desiccant. Yield was 85% (4.1 g).

General procedure for the extraction of Br^- from bittern as QATB

To 1L of bittern was added 0.06 g (0.2 mmol) $[VO_2F(dmpz)_2]$, 8 mL (125 mmol) of 55% hydrogen peroxide (H_2O_2). The solution was stirred magnetically at room temperature. To the solution was added 2.8 g (10.62 mmol) of tetrabutylammomium chloride (TBAC) or benzyltriethylammonium chloride (BTEAC) and 16 mL of 5M sulphuric acid (H_2SO_4). The reaction mixture was stirred for 3h whereupon orange yellow colored compound was formed throughout the volume. This was allowed to settle and then the compound was filtered by suction filtration and dried in a vacuum desiccator using anhydrous calcium chloride ($CaCl_2$) as the desiccant. Yield of TBATB was 4.1g (85%) and BTEATB was 3.79 g (87%).

5D. Characterization of the products

The compounds were characterized by mp, elemental analysis, IR, ^1H and ^{13}C NMR and X-ray crystallography and data for the products are summarized as follows

Analytical data of **$K_3[V_2O_2(O_2)_4(OH)]H_2O$ (AC)**

$K_3[V_2O_2(O_2)_4(OH)]H_2O$	Calculated	Found
% age of V	24.3	25
% age of O_2^{2-}	30.9	30.77
UV λ_{max}=327 nm (10^{-3}M solution in water)		
IR (KBr)= 3190, 1052, 970, 946, 868, 617 cm^{-1}.		

Table 5D.1. Crystal data and structure refinement for $K_3[(O_2)_2OV$-(μ-OH)-$VO(O_2)_2]H_2O$

Empirical formula	$H_3\ K_3\ O_{12}\ V_2$
Formula weight	414.00
Temperature (K)	296(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
a (Å)	6.7083(3) Å
b(Å)	9.9553(5) Å
c (Å)	15.8095(6) Å
α(°)	90°.

β(°)	93.719(3)°.
γ(°)	90°
V(Å^3)	1053.58(8) Å^3
Z	4
Density (mg/m^3)	2.118 mg/m^3
μ mm^{-1}	2.218 mm^{-1}
F(000)	656
Crystal size(mm^3)	0.28 x 0.22 x 0.13 mm^3
θ range(^{0})	2.42 to 28.20°.
Index ranges	-8<=h<=8, -13<=k<=11, -20<=l<=20
Reflections collected	9891
Independent reflections	2563 [R(int) = 0.0383]
Completeness to theta = 28.20°	99.2 %
Data / restraints / parameters	2563 / 0 / 166
Goodness-of-fit on F^2	1.095
Final R indices [I>2sigma(I)]	R1 = 0.0427, wR2 = 0.1229
R indices (all data)	R1 = 0.0504, wR2 = 0.1308

[a] $R_1 = \Sigma \, ||F_0| - |F_0|| / \Sigma \, |F_0|$

[b] $wR_2 = \{\Sigma[w(F_0^2 - F_c^2)^2] / \Sigma[wF_0^2)^2]\}^{1/2}$

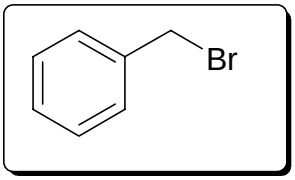
Table 5D.2. Bond lengths [Å] for $K_3[(O_2)_2OV\text{-}(\mu\text{-}OH)\text{-}VO(O_2)_2]H_2O$

V(1)-O(5)	2.006(3)	V(2)-O(1)	1.885(3)
V(1)-O(6)	1.916(2)	V(2)-O(1)	1.885(3)
V(1)-O(7)	1.880(3)	V(2)-O(2)	1.871(2)
V(1)-O(8)	1.903(3)	V(2)-O(4)	1.874(3)
V(1)-O(9)	1.878(3)	V(2)-O(3)	1.908(2)
V(1)-O(11)	1.604(3)	V(2)-O(5)	1.997(2)
V(1)-V(2)	3.0474(8)	V(2)-O(10)	1.617(3)
O(3)-O(4)	1.464(3)	O(2)-O(1)	1.470(4)
O(6)-O(7)	1.466(3)	O(9)-O(8)	1.468(4)

Table 5D.3. Bond angles [°] for $K_3[(O_2)_2OV$-(μ-OH)-$VO(O_2)_2]H_2O$

O(11)-V(1)-O(9)	104.66(14)	O(11)-V(1)-O(7)	106.90(13)
O(9)-V(1)-O(7)	89.00(12)	O(11)-V(1)-O(8)	105.34(13)
O(9)-V(1)-O(8)	45.71(12)	O(7)-V(1)-O(8)	129.73(12)
O(11)-V(1)-O(6)	101.61(13)	O(9)-V(1)-O(6)	132.57(12)
O(7)-V(1)-O(6)	45.43(11)	O(8)-V(1)-O(6)	152.03(12)
O(11)-V(1)-O(5)	99.54(14)	O(9)-V(1)-O(5)	129.52(12)
O(7)-V(1)-O(5)	125.00(11)	O(8)-V(1)-O(5)	85.48(11)
O(6)-V(1)-O(5)	82.82(10)	O(11)-V(1)-V(2)	128.40(11)
O(9)-V(1)-V(2)	125.50(10)	O(7)-V(1)-V(2)	86.97(8)
O(8)-V(1)-V(2)	101.87(9)	O(6)-V(1)-V(2)	54.16(8)
O(5)-V(1)-V(2)	40.31(7)	O(11)-V(1)-K(2)	58.11(10)
O(10)-V(2)-O(2)	103.99(14)	O(10)-V(2)-O(4)	104.97(14)
O(2)-V(2)-O(4)	89.01(12)	O(10)-V(2)-O(1)	105.20(14)
O(2)-V(2)-O(1)	46.06(11)	O(4)-V(2)-O(1)	130.61(12)
O(10)-V(2)-O(3)	103.15(14)	O(2)-V(2)-O(3)	131.78(12)
O(4)-V(2)-O(3)	45.54(11)	O(1)-V(2)-O(3)	150.71(13)
O(10)-V(2)-O(5)	99.61(13)	O(2)-V(2)-O(5)	131.59(12)
O(4)-V(2)-O(5)	124.55(11)	O(1)-V(2)-O(5)	87.23(11)
O(3)-V(2)-O(5)	80.94(11)	O(10)-V(2)-V(1)	132.38(10)
O(5)-V(2)-V(1)	40.52(8)	O(3)-O(4)-V(2)	68.45(14)
O(1)-O(2)-V(2)	67.47(14)	O(2)-O(1)-V(2)	66.47(14)
V(2)-O(5)-V(1)	99.17(11)	O(7)-O(6)-V(1)	66.00(14)
O(6)-O(7)-V(1)	68.57(14)	O(8)-O(9)-V(1)	68.04(14)
O(9)-O(8)-V(1)	66.25(14)	V(1)-O(11)-K(2)	97.05(11)

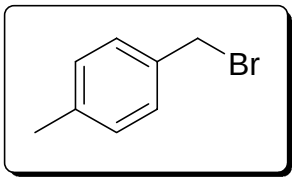
Benzyl bromide (1a)



Nature : Colorless liquid

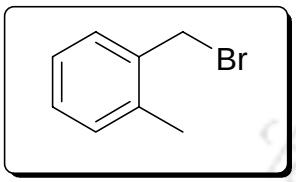
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.49(s, 3H), 7.28-7.37(m, 5H).

4-Methyl Benzyl bromide (2a)



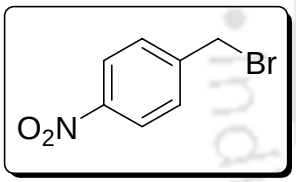
Nature : Colorless liquid
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34(s, 3H), 4.48(s, 2H), 7.14(d, *J* = 7.6Hz, 2H), 7.27(d, *J* = 8.4Hz, 2H).

2-Methyl Benzyl bromide (3a)



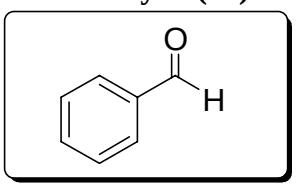
Nature : Colorless liquid
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.44(s, 3H), 4.49(s, 2H), 7.09-7.36(m, 4H).

4-Nitro Benzyl bromide (4a)



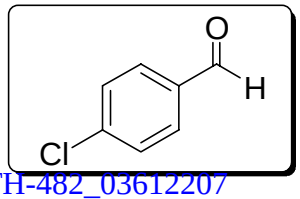
Nature: Light yellow solid
Melting point : 98 °C
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.52(s, 2H), 7.49(d, *J* = 7.6Hz, 2H), 8.11(d, *J* = 8.8Hz, 2H).

Benzaldehyde (5a)



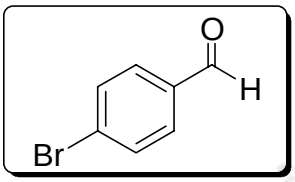
Nature: Colourless liquid
IR(Neat): 1706 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47(t, *J* = 7.6 Hz, 2H), 7.54(t, *J* = 7.8 Hz, 2H), 7.89(d, *J* = 7.6 Hz, 1H), 10.02 (s,1H).

4-Chlorobenzaldehyde (6a)



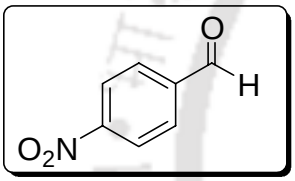
Nature: White Solid
Mp 46-47^{0}C
IR(KBr): 1702 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51(d, *J* = 8.4 Hz, 2H), 7.82(d, *J* = 8.8 Hz, 2H), 9.98 (s,1H).

4-Bromobenzaldehyde (7a)



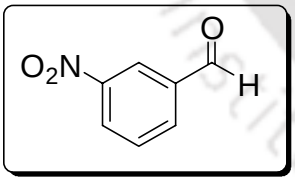
Nature: White Solid
Mp 58 ^{0}C
IR(KBr): 1692 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69(d, *J* = 8.4 Hz, 2H), 7.76(d, *J* = 8.4 Hz, 2H), 9.98 (s,1H).

4-Nitrobenzaldehyde (8a)



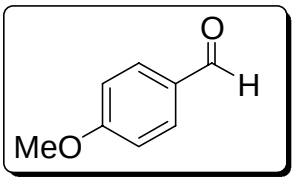
Nature: Yellow Solid
Mp 104 ^{0}C
IR(KBr): 1706, 1541, 1358 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69(d, *J* = 8.4 Hz, 2H), 7.76(d, *J* = 8.4 Hz, 2H), 9.98 (s,1H).

3-Nitrobenzaldehyde (9a)



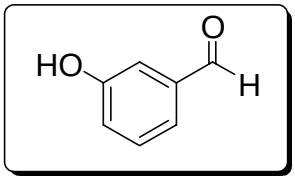
Nature: Yellow Solid
Mp 57-59^{0}C
IR(KBr):1712, 1534, 1349 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77(t, *J* = 7.6 Hz, 1H), 8.23(d, *J* = 7.6 Hz, 1H), 8.49(d, *J* = 8.4 Hz, 1H) 8.72(s, 1H) 10.13(s, 1H).

4-Methoxybenzaldehyde (10a)



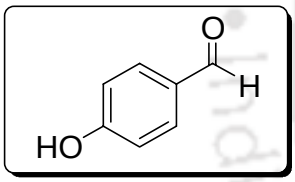
Nature : Colorless viscous liquid
IR(Neat): 1685 cm^{-1}
^1H NMR (400 MHz, $CDCl_3$): δ 3.90(s, 3H) 7.01(d, *J* = 7.6 Hz, 2H), 7.85(d, *J* = 7.6 Hz, 2H), 9.89 (s,1H).

3-Hydroxybenzaldehyde (11a)



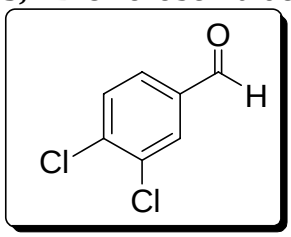
Nature : Off white solid
Mp : 102-104 ^0C
IR(Neat): 1685 cm^{-1}
^1H NMR (400 MHz, $CDCl_3$): δ 5.66(s,1H), 7.15(d, *J* = 8.4Hz, 1H), 7.37(s, 1H), 7.44(m, 2H) 9.96(s, 1H).

4-Hydroxybenzaldehyde (12a)



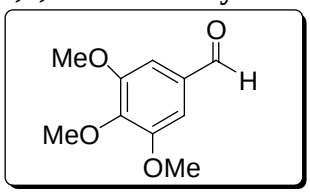
Nature : Off white solid
Mp : 117-119 ^0C
IR(Neat): 1695 cm^{-1}
^1H NMR (400 MHz, $CDCl_3$): δ 6.63(s, 1H), 6.97(d, *J* = 8.4Hz, 2H), 7.81(d, *J* = 7.6 Hz, 2H), 9.86(s,1H).

3,4-Dichlorobenzaldehyde (13a)



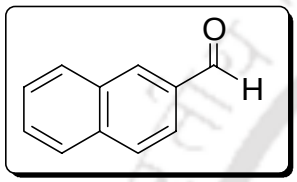
Nature : White solid
Mp : 41-43^0C
IR(KBr): 1690 cm^{-1}
^1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.40(m, 1H), 7.51(d, *J* = 2.0Hz, 1H), 7.88(d, *J* = 8.4Hz, 1H) 9.89 (s,1H).

3,4,5-Trimethoxybezaldehyde (14a)



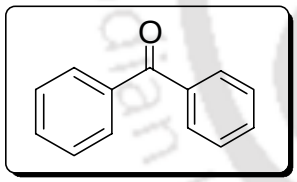
Nature : White solid
Mp : 73-75^{0}C
IR(KBr): 1706 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.92(s, 9H), 7.13(s, 2H), 9.85(s,1H).

2-Napthaldehyde (15a)



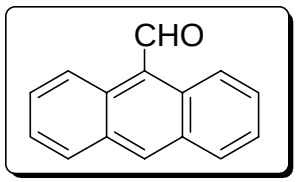
Nature: Light pink solid
Mp : 56-58^{0}C
IR(KBr):1665 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55-7.63(m, 2H), 7.83-7.97(m, 4H), 8.27(s,1H), 10.12(s, 1H).

Benzophenone (16a)



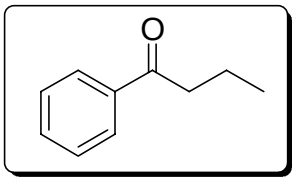
Nature : White solid
Mp : 47^{0}C
IR (KBr): 1665 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47(t, *J* = 8.0 Hz, 4H), 7.57(t, *J* = 8.0 Hz, 2H), 7.78(d, *J* = 7.6 Hz, 4H).

9-Anthranaldehyde (17a)



Nature : Yellowish green solid
Mp : 101-103^{0}C
IR(KBr):1665 cm^{-1}
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (t, *J* =15.2 Hz, 2H), 7.69(t, *J* = 15.6, 2H), 8.07(d, *J* = 8.8Hz, 2H), 8.70(s, 1H), 8.99(d, *J* = 9.2Hz, 2H), 11.53(s,1H).

Butyrophenone (18a)



Nature : Viscous liquid
IR(Neat): 1688 cm^{-1}
^1H NMR (400 MHz, $CDCl_3$): δ 1(t, *J* = 7.2 Hz, 3H), 1.77(sext, *J* = 7.2 Hz, 2H), 2.94(t, *J* = 7.2 Hz, 2H), 7.43 (t, *J* = 8.0 Hz, 2H) 7.52(t, *J* = 7.2Hz, 1H) 7.94(d, *J* = 7.2 Hz, 2H).

Table 5D.4. *Crystal data and structure refinement for TBATB and BTEATB*

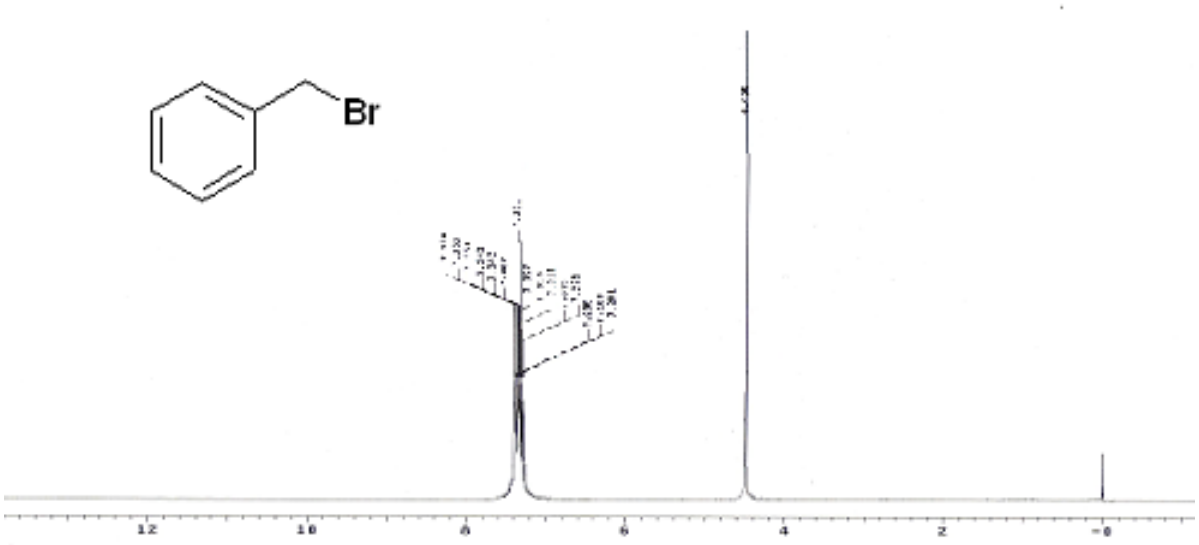
	TBATB	**BTEATB**
Chemical formula	$C_{16}H_{36}Br_3N$	$C_{13}H_{22}Br_3N$
Fw	482.19	432.05
Crystal system	Monoclinic	Orthorhombic
Crystal size (mm^3)	0.44 x 0.23 x 0.08	0.50 x 0.22 x 0.08
Space group	C2/c	P2(1)2(1)2(1)
a, Å	12.9819(7)	8.422(4)
b, Å	10.3823(6)	10.132(4)
c, Å	16.2421(8)	19.475(9)
α /°	90	90
β/°	93.921(3)°.	90
γ /°	90	90
V, A^3	2184.0(2)	1661.9(13)
Z	4	4
D(cald.) Mg/m^3	1.466	1.727
T (K)	296(2)	296(2)
μ (mm^{-1})	5.536	7.264
F(000)	976	848
Final R indices[I>2σ] R1/ wR2	0.0317 / 0.0688	0.0317 / 0.0539
R indices (all data)R1/ wR2	0.0664 / 0.0793	0.0648 / 0.0871
Goodness of fit	1.009	0.924

Table 5D.5. *Tribromide bond distances and bond angles in TBATB and BTEATB*

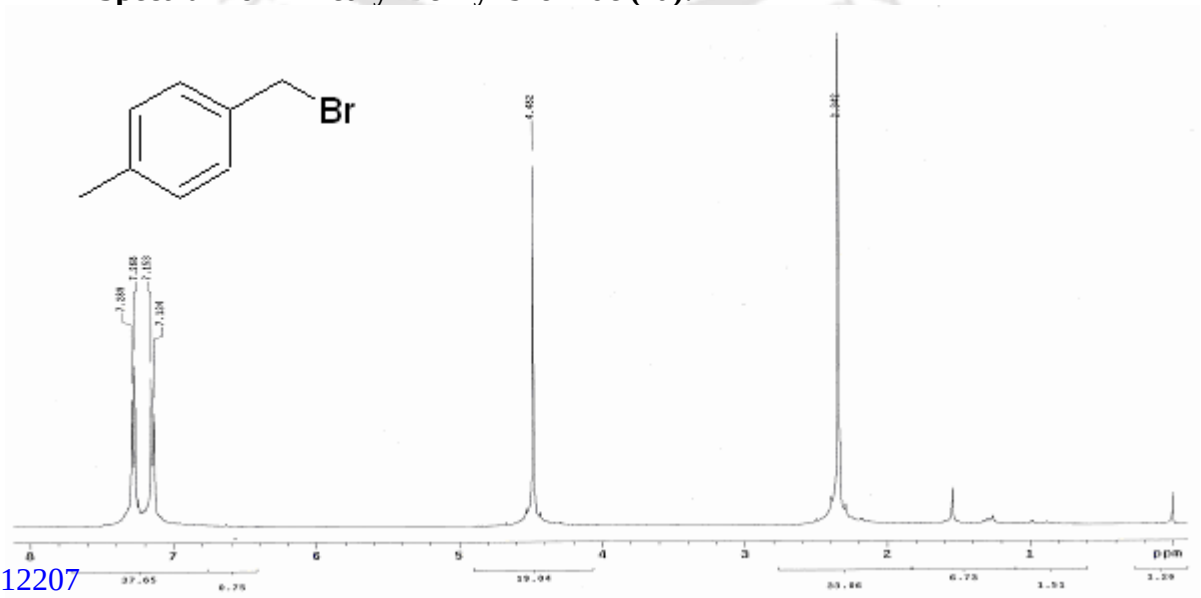
Bond angle in BTEATB		**Bond angle in TBATB**	
Br(2)-Br(1)-Br(3)	174.75(2)	Br(2)-Br(1)-Br(2)#1	180.0
Bond distance in BTEATB		**Bond distance in TBATB**	
Br(1)-Br(2)	2.5314(13)	Br(1)-Br(2)	2.5391(4)
Br(1)-Br(3)	2.5322(13)	Br(1)-Br(2)#1	2.5391(4)

Spectra of some selected compounds

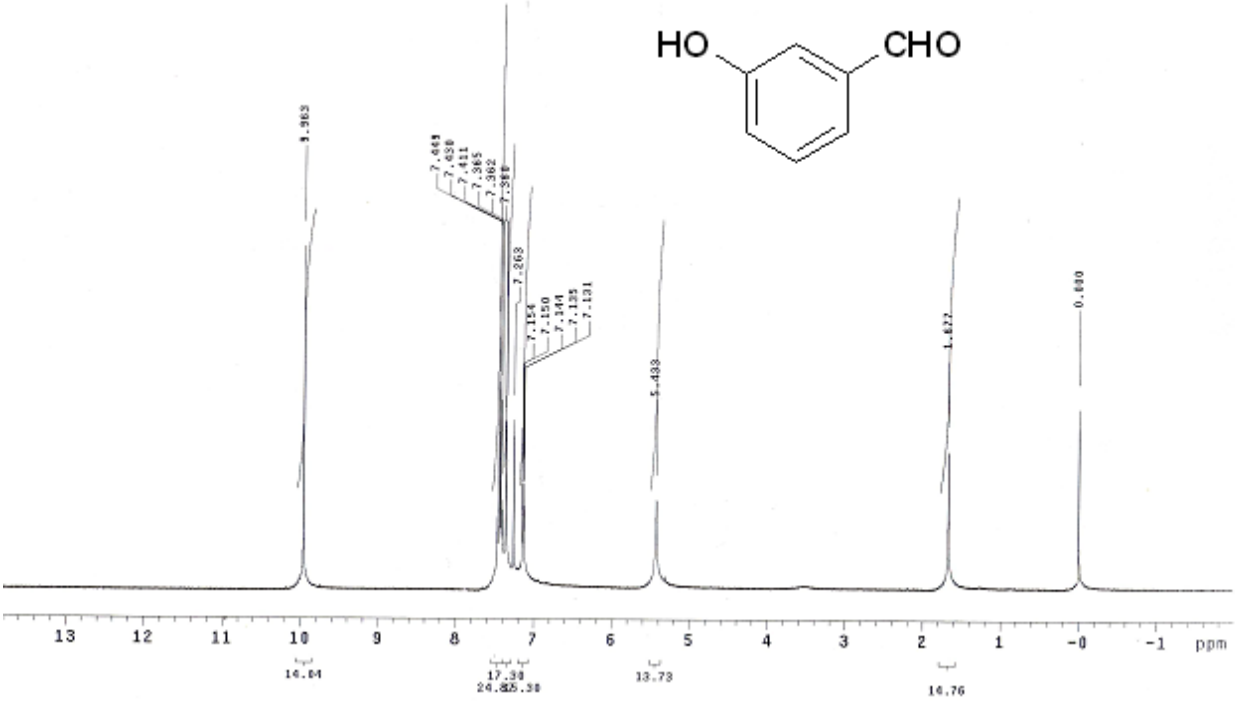
^{1}H NMR Spectrum of Benzyl bromide (1a):



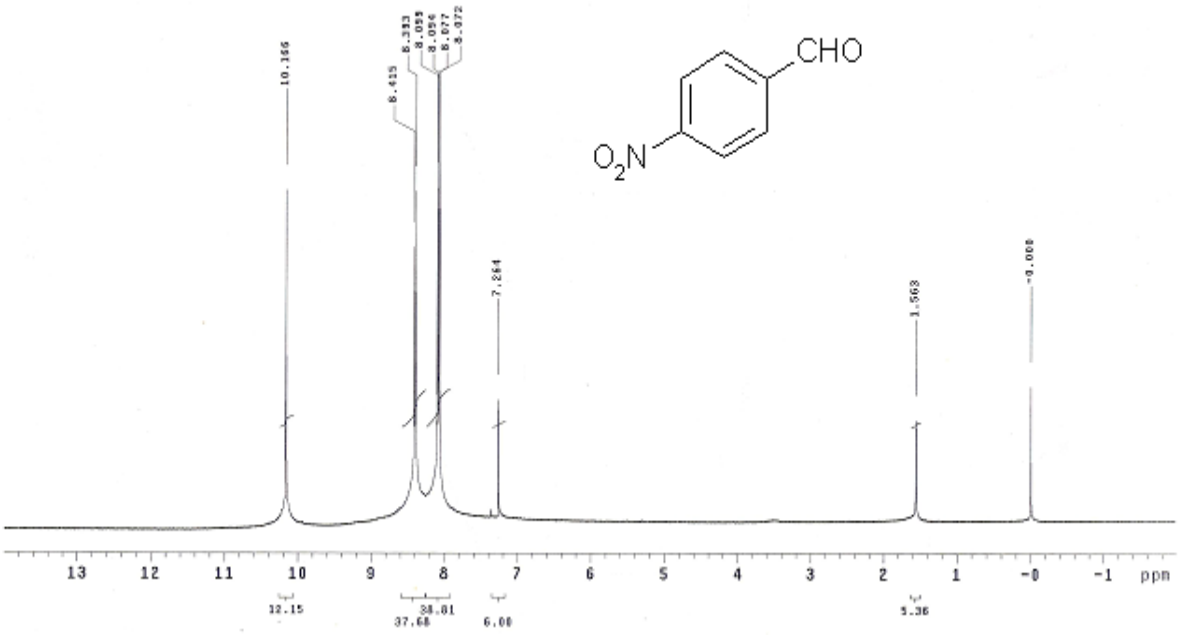
^{1}H NMR Spectrum of 4-Methyl Benzyl bromide (2a):



^{1}H NMR Spectrum of 3-Hydroxybenzaldehyde (11a) :



^{13}C NMR Spectrum of 3-Hydroxybenzaldehyde (11a):



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An Efficient Synthesis of Quinolines under Solvent-free Conditions*

* The work described in this chapter has been published

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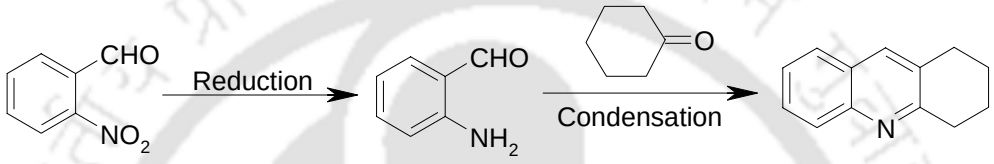
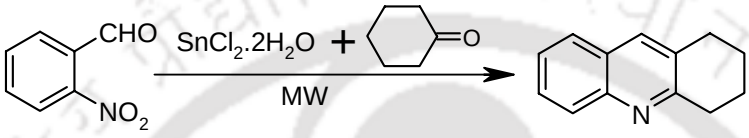
Quinoline derivatives have been well known not only in medicinal chemistry, because of their wide occurrence in natural products[1,2] and drugs,[3,4] but also in polymer chemistry, electronics and optoelectronics for their excellent mechanical properties.[5-7] Diblock and triblock copolymers incorporating polyquinoline blocks have been found to undergo hierarchical self assembly into a variety of nano- and meso-structures with interesting electronic and photonic functions.[8,9] The Friedländer synthesis of quinolines is a classic method,[10] that involves two steps, wherein reduction of *o*-nitro aryl aldehyde is first achieved followed by the condensation of enolizable carbonyl compound in presence of a Brønsted or Lewis acid catalyst (**Scheme 6.1**).



Scheme 6.1

The relative instability of the intermediate (*o*-amino aldehyde), with its strong tendency to undergo self-condensation made such reactions rather complicated. Accordingly, there have been continuous efforts to develop clean and rapid newer protocols[11-41] for the construction of quinoline-based structures. This has resulted in a few improved procedures for the synthesis of quinolines. As a part of our programme on the development of newer processes for organic transformations,[42-44] our attention was drawn to two protocols,[28,30] in one of which the *o*-aminobenzaldehyde was generated *in situ* and reacted immediately with an enolizable ketone to produce a quinoline.[28] This reaction was conducted in anhydrous ethanol under an atmosphere of nitrogen using $SnCl_2$ as the reductant (e.g. $–NO_2$ to NH_2) and $ZnCl_2$ as the facilitator of enolate formation from the enolizable ketones leading to the concomitant coupling condensation with the amine affording quinolines in rather low yields. The yields of products were remarkably increased by the addition of a significant amount of 4 Å molecular sieves to the reaction solution. Evidently, the success of this methodology appears to depend on the avoidance of both water and air as well as the use of $ZnCl_2$ as a Lewis acid catalyst. The other protocol[30] was based on microwave-assisted coupling condensation reactions between acetophenones and 2-amino-acetophenones or benzophenones in the presence of diphenylphosphate (DPP) as the acid catalyst, which was essential to enhance cyclization, without the use of any solvent. In addition, there is a very recent report by Perumal *et al.*[45] on the synthesis of polysubstituted quinolines under solvent-free conditions having some advantages over many other protocols. However, here again the authors

have used *o*-aminoarenes, rather than the corresponding *o*-nitroarenes, thereby entailing similar problems as emphasized above. Thus, it is quite imperative that quinolines synthesis requires further attention to obviate the need to maintain stringent experimental conditions, use of expensive catalysts, and prepare and isolate the *o*-amino cabonyls as synthetic precursors. This chapter demonstrates an efficient solvent-free one-pot synthesis of quinolines achieved from *o*-nitrobenzaldehyde and enolizable ketones using $SnCl_2.2H_2O$ and subjecting them to microwaves (**Scheme 6.2**).

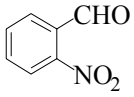
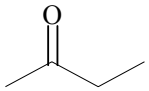
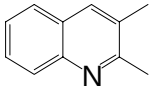
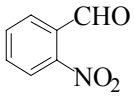
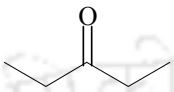
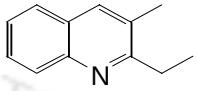
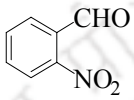
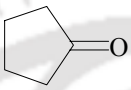
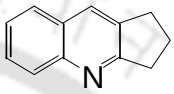
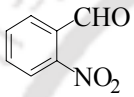
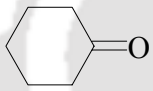
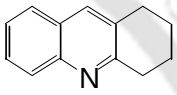
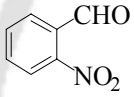
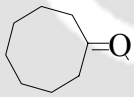
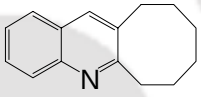
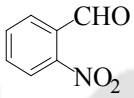
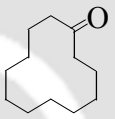
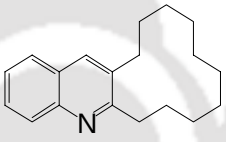
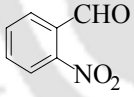
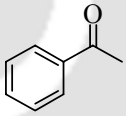
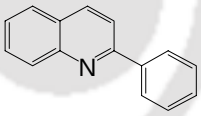
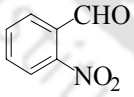
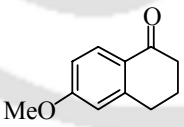
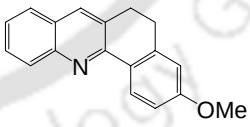
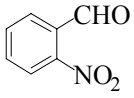
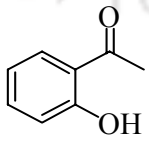
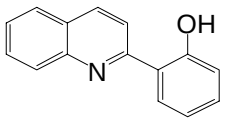


Scheme 6.2

6A. Results and Discussions

In view of the problems encountered in quinoline synthesis, a relatively more versatile yet simplified procedure was perceived based on the reasoning that the substrates like *o*-nitrobenzaldehyde and enolizable ketones could be made to interact in the presence of $SnCl_2$ under microwave irradiation without using any solvent. Microwave synthesis has received attention as a relatively new strategy for organic synthesis due to the fact that many reactions seem to proceed with much alacrity under such conditions as opposed to the corresponding thermal-assisted reactions.[46-49] Our arguments have been that under microwave irradiation, the reduction of *o*-nitrobenzaldehyde by $SnCl_2$ to the corresponding amino derivatives, *in situ* enolization of the chosen ketones, and enhanced dipole–dipole interactions between the activated reaction intermediates would lead to an instantaneous condensation to afford quinolines without the use of any solvent or catalyst. The strategy worked well affording the desired products in respectable yields (**Scheme 6.2**). Notably, the present reactions have been relatively faster, as anticipated, compared to those of Perumal *et al*.[45] It is necessary to mention that in all cases the conversion was less than 100%. Small amounts of starting materials were recovered after each reaction. Temperature of the reaction mixture recorded immediately after microwave irradiation for the given period of time was found to be *ca* 105ºC. To ensure the contribution of microwave effects, the reactions in entries **1** and **7** were examined by simply heating in a same duration as mentioned in the typical procedure with microwave irradiation.

Table 6.1. *Microwave-assisted synthesis of quinolines under solvent-free conditions*

Entry	Aryl aldehyde	Enolizable ketone	Products	Yields (%)[a]
1			 **1a**	80
2			 **2a**	77
3			 **3a**	69
4			 **4a**	75
5			 **5a**	72
6			 **6a**	73
7			 **7a**	55
8			 **8a**	58
9			 **9a**	0

[a] *Isolated Yield*

A very small amount (1–3%) of quinoline derivative was isolated in each case leading us to state that, under the given experimental conditions, microwave irradiation is responsible for bringing about the reaction. A wide range of enolizable ketones (cycloalkyl, *n*-alkyl, alkyl aryl)

was screened in order to ascertain the scope of the present reaction protocol and the results are summarized in **Table 6.1**. It is evident from the results that alkyl and cycloalkyl enolizable ketones readily cyclized with the *in situ* generated *o*-amino benzaldehyde to afford the corresponding quinolines in good to very good yields. However, lower yields were observed with alkyl aryl ketones (entries **7** and **8**) and no quinoline formation was observed with a hydroxy-substituted aromatic ring of an alkyl aryl ketone (entry **9**).

6B. Conclusion

A solvent-free, microwave-assisted and very facile protocol has been developed for the synthesis of quinolines without the intervention of any acid catalyst and molecular sieves. Another important advantage is the redundancy of extra preparation and isolation of *o*-amino benzaldehyde. This protocol offers scope for further work involving a variety of substrates with varied substituents. The microwave-facilitated version of quinoline synthesis is expected to be a viable alternative to the classic Friedlaender synthesis, owing to several advantages summarized herein.

6C. Experimental

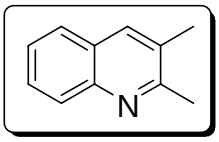
General procedure for the Friedländer reaction

Typically, 2-nitro aryl aldehyde (2 mmol) and an enolizable ketone (2 mmol) were uniformly mixed with $SnCl_2.2H_2O$ (6mmol). The resulting mixture was then irradiated with microwaves in a microwave oven (Samsung model# CE118KF) at 1050W (70% of total power) for 5 minutes (3 + 2 with an intermission of 5 minutes). The reaction mixture was cooled at room temperature and rendered basic (pH 8) with 10% $NaHCO_3$, and then extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated to leave behind the crude product, which was further purified by column chromatography over silica gel (hexane : ethyl acetate :: 4 : 1).

6D. Characterization of the products

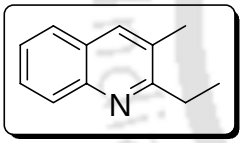
The compounds were characterized by ^{1}H and ^{13}C NMR and Mass spectrometry and the data for the products are summerised as follows.

2,3 Dimethyl-quinoline (1a)



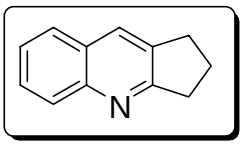
^{1}H NMR ($CDCl_3$, 400MHz) : δ 2.42 (s, 3H), 2.67 (s, 3H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.80 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 19.7, 23.6, 125.5, 126.5, 127.1, 128.0, 128.20, 129.6, 135.0, 146.3, 159.7; MS : m/z 157 (M^+).

2-Ethyl-3-methyl-quinoline (2a)



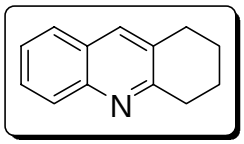
^{1}H NMR ($CDCl_3$, 400MHz) : δ 1.28 (s, 3H), 2.40 (s, 3H), 2.77 (q, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.82 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 19.6, 22.5, 25.2, 125.5, 126.5, 127.0, 128.0, 128.1,129.6, 135.0, 146.5, 159.2; MS : m/z 171 (M^+).

2,3-Dihydro-1H-cyclopenta[b]quinoline (3a)



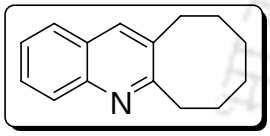
^{1}H NMR ($CDCl_3$, 400MHz) : δ 2.20 (quin, *J* = 7.2 Hz, 2H), 3.08(t, *J* = 7.2 Hz, 2H), 3.16(t, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 6.8 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.87 (s, 1H), 8.1 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 23.7, 30.5, 34.7, 125.3, 127.3(2C), 128.2, 128.4, 130.2, 135.4, 147.3, 167.6; MS : m/z 169 (M^+).

1,2,3,4-Tetrahydro-acridine (4a)



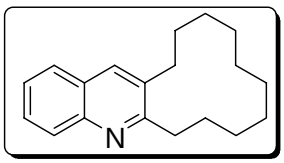
^{1}H NMR ($CDCl_3$, 400MHz) : δ 1.86–1.91 (m, 2H), 1.96–2.00 (m, 2H), 2.96 (t, *J* = 6.4 Hz, 2H), 3.12 (t, *J* = 6.8 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.59 (t, *J* = 9.6 Hz, 1H), 7.68 (dd, *J* = 1.2 Hz, *J* = 8.0 Hz, 1H), 7.78 (*s*, 1H), 7.97 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 23.0, 23.3, 29.3, 33.6, 125.4, 126.7, 127.0, 128.0, 128.3, 130.8, 134.8, 146.4, 159.0; MS : m/z 183(M^+).

6,7,8,9,10,11-Hexahydro-cycloocta[b]quinoline (5a)



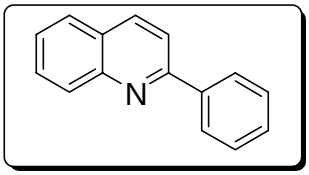
^{1}H NMR ($CDCl_3$, 400MHz) : δ 1.37–1.91 (m, 8H), 2.94 (t, *J* = 6.4 Hz, 2H), 3.21 (t, *J* = 6.0 Hz, 2H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 8.8 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.80 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 27.1, 28.9, 29.8, 32.3, 35.5, 40.1, 125.6, 126.6, 127.2, 128.2 (2C), 134.3 (2C), 146.0, 164.4; MS : m/z 211(M^+).

6,7,8,9,10,11,12,13,14,15-Decahydro-5-aza-cyclododeca[b]naphthalene (6a)



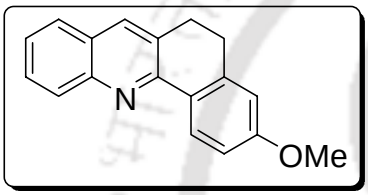
^{1}H NMR ($CDCl_3$, 400MHz) : δ 1.42–1.56 (m, 12H), 1.78–1.82 (m, 2H), 1.94–1.98 (m, 2H), 2.83 (t, *J* = 8.0 Hz, 2H), 3.03 (t, *J* = 8.0 Hz, 2H), 7.42 (t, *J* = 6.4 Hz, 1H), 7.60 (t, *J* = 6.8 Hz, 1H), 7.70 (dd, *J* = 1.2 Hz, *J* = 8.4 Hz, 1H), 7.89 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 23.1, 23.2, 25.6, 26.1, 26.6, 26.8, 28.5, 29.7, 29.8, 32.8, 125.4, 126.6, 127.0, 128.1, 128.2, 134.7, 135.6, 146.3, 162.4; MS : m/z 267 (M^+).

2-Phenyl-quinoline (7a)



^{1}H NMR ($CDCl_3$, 400MHz) : δ 7.41-7.52 (m, 4H), 7.61-7.71(m, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.80(d, *J* = 8.5 Hz, 1H), 8.12-8.18 (m, 4H); **^{13}C NMR (100MHz, $CDCl_3$) :** δ 118.9, 126.2, 127.1, 127.4, 127.5, 128.7, 129.2, 136.7, 139.6, 148.2, 157.2; **MS : m/z** 205 (M^+).

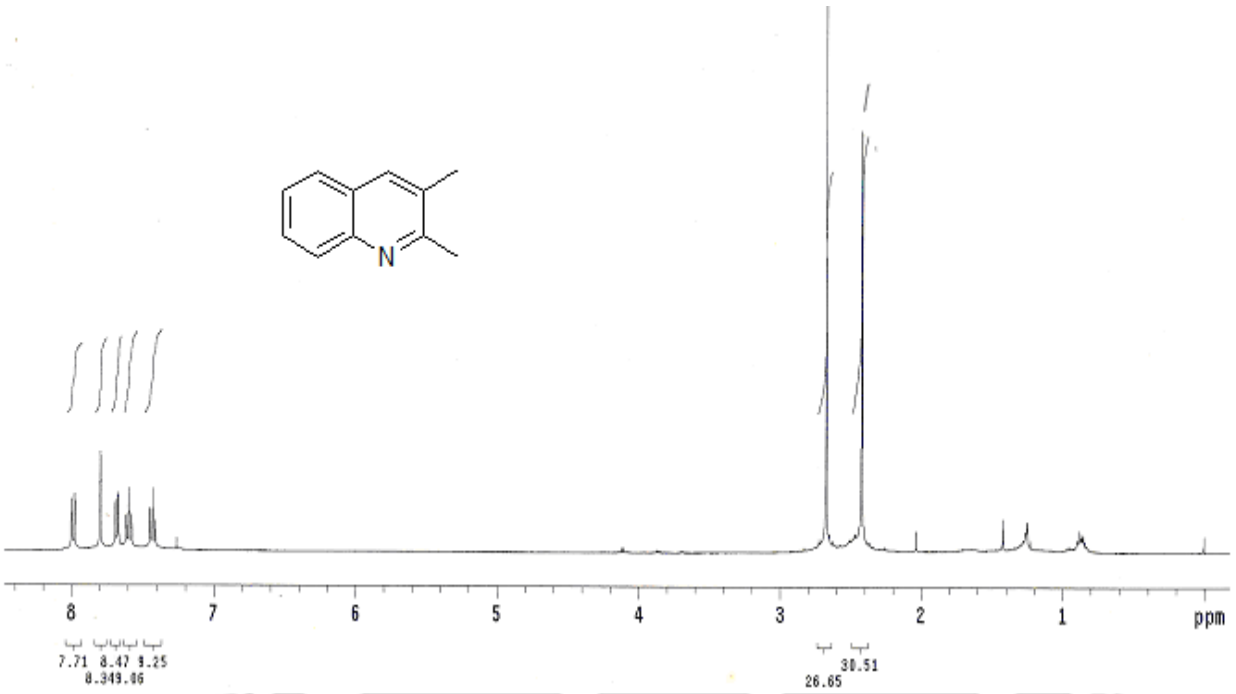
3-Methoxy-5,6-dihydro-benzo[c]acridine (8a)



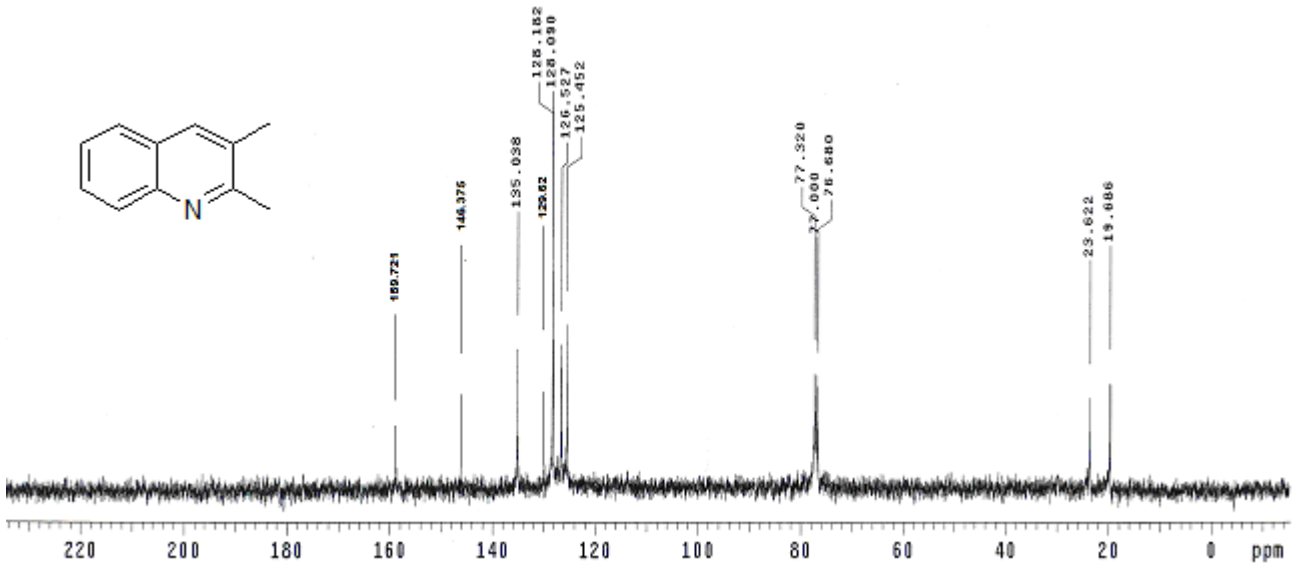
^{1}H NMR ($CDCl_3$, 400MHz) : δ 2.97 (t, *J* = 6.4 Hz, 2H), 3.10 (t, *J* = 7.6 Hz, 2H), 3.87 (s, 3H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.62 (t, *J* = 6.8 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.87 (s, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 8.50 (d, *J* = 8.8 Hz, 1H); **MS : m/z** 261 (M^+).

Spectra of some selected compounds

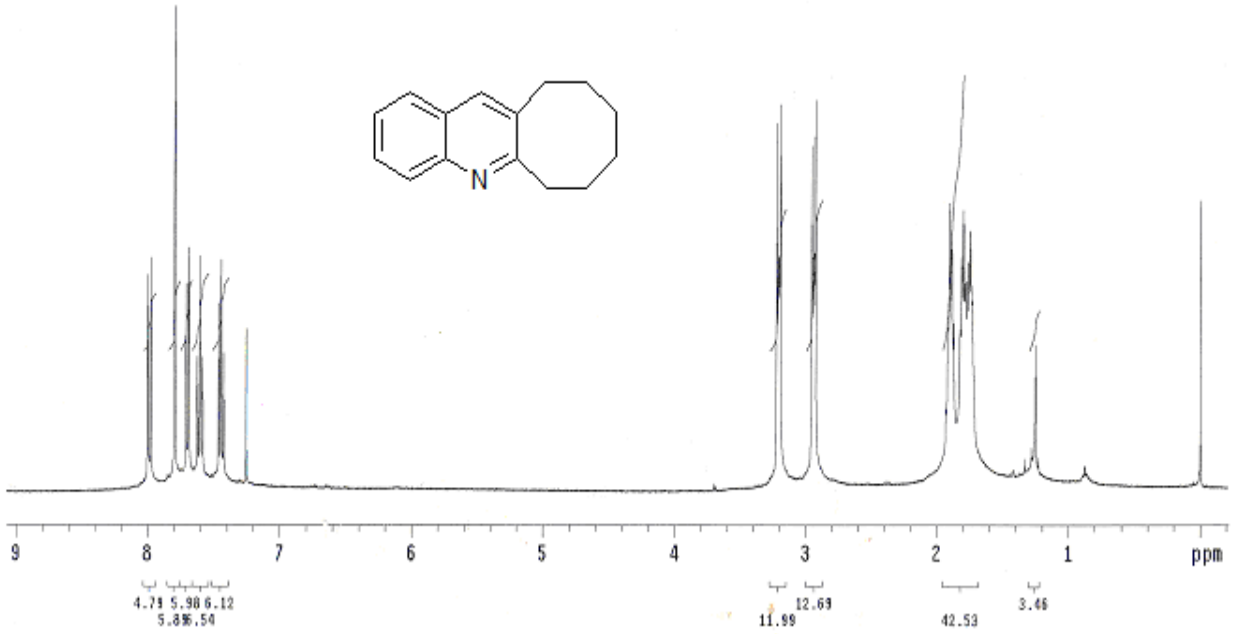
^{1}H NMR Spectrum of 2,3 Dimethyl-quinoline (1a):



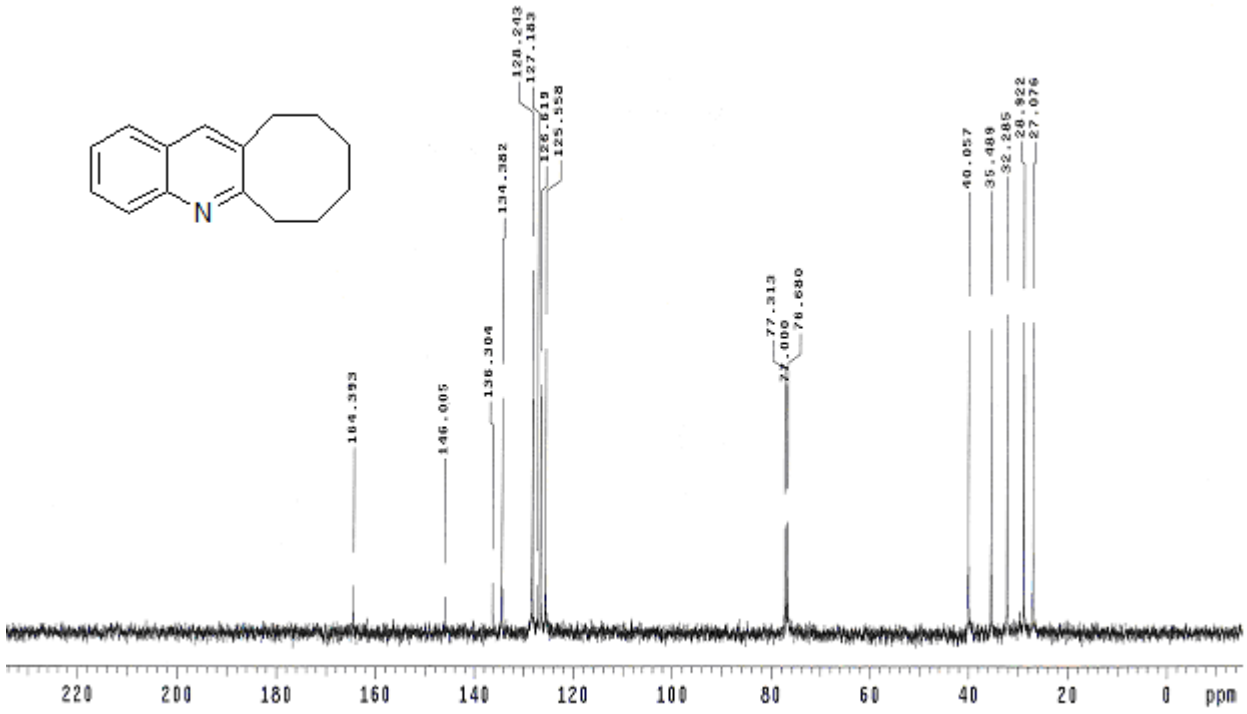
^{13}C NMR Spectrum of 2,3 Dimethyl-quinoline (1a):



^{1}H NMR Spectrum of 6,7,8,9,10,11-Hexahydro-cycloocta[b]quinoline (5a):



^{13}C NMR Spectrum of 6,7,8,9,10,11-Hexahydro-cycloocta[b]quinoline (5a):



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List of Publications

1. $Cu(acac)_2$ immobilized in ionic liquids: A recoverable and reusable catalytic system for aza-Michael Reactions

   Adv. Synth. Catal. **2005**, *347*, 763 -766

   M. Lakshmi Kantam, V. Neeraja, B. Kavita, B. Neelima, Mihir K. Chaudhuri and **Sahid Hussain**

2. Barbier coupling in water: $SnCl_2$-mediated and $Co(acac)_2$-catalyzed allylation of carbonyls

   Tetrahedron Lett. **2005**, *46*, 6247-6251

   Mihir K. Chaudhuri, Sanjay K. Dehury and **Sahid Hussain**

3. 3,5-Dimethylpyrazolium fluorochromate(VI)-catalysed oxidation of organic substrates by hydrogen peroxide under solvent-free conditions,

   Adv. Synth. Catal. **2005**, *347*, 1349-1352

   Mihir K. Chaudhuri, Sanjay K. Dehury, **Sahid Hussain**, Ankur Duarah, Nayanmoni Gogoi and M. Lakshmi Kantam.

4. Boric acid: A novel and safer catalyst for aza-Michael reaction in water.

   Tetrahedron Lett. **2005,** *46*, 8329-8331

   Mihir K. Chaudhuri, **Sahid Hussain**, M. Lakshmi Kantam and B. Neelima

5. An efficient synthesis of quinolines under solvent-free conditions.

   J. Chem Sci. **2006,** *118*, 199-202

   Mihir K. Chaudhuri and **Sahid Hussain**

6. The selective solid-phase oxidation of alcohols and other organic substrates by 3,5-dimethylpyrazolium fluorochromate.

   Org. Prep. Proc. Int. **2006**, *38*, 331-336.

   Mihir K. Chaudhuri, Sanjay K. Dehury, **Sahid Hussain**, Ankur Duarah and Nayanmoni Gogoi

7. Borax as an efficient metal-free catalyst for hetero-Michael reactions in aqueous medium,

   Eur. J. Org. Chem. **2007,** 374-378

   Sahid Hussain, Saitanya K. Bharadwaj, Mihir K. Chaudhuri and Harjyoti Kalita

8. Boric acid catalysed thia-Michael reactions in water or alcohol,

   J. Mol.Catal. A: Chemical **2007**, *269*, 214-217.

   Mihir K. Chaudhuri and **Sahid Hussain**

9. Intermolecular hydrogen bonded andself-assembled β-pleated sheet structures of β-sulfidocarbonyls

   J. Mol. Structure, **2007,** *837*, 190-196

   Sahid Hussain, Mihir K. Chaudhuri and Gopal Das

10. Borax catalyzed and pH controlled selective oxidation of organic sulfides by H_2O_2: An environmentally clean and efficient protocol

    Manuscript under communication

    Sahid Hussain, Ravindra Pandey, Saitanya K. Bharadwaj, Mihir K. Chaudhuri

11. VBrPO-mimiking catalysis in water for radical bromination and electrophillic oxidation using Triperoxovanadate (V) as a precatalyst

    Manuscript under communication

    Sahid Hussain, Saitanya K. Bharadwaj, N. Gogoi H. Kalita and Mihir K. Chaudhuri

12. A new vanadium catalyst $VO_2F(dmpz)_2$ for selective oxidation of organic sulfides to sulfoxides with H_2O_2.

    Manuscript under preperation

    Sahid Hussain, Mihir K. Chaudhuri, Gopal Das and M. Lakshmi Kantam

13. Phosphate catalyzed selective oxidation of organic sulufides with H_2O_2

    Manuscript under preparation

    Sahid Hussain, Mihir K. Chaudhuri

14. Bio mimetic oxidative extraction of bromide from sea water

    Manuscript under preperation

    Saitanya K. Bhardwaj, **Sahid Hussain**, Neeraj Chandrol, Mihir K. Chaudhuri