Development of Newer Catalysts for Selective Oxidation of Sulfides, Aldehydes and Bromide with $\text{H}_2\text{O}_2$

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Section 5A

**VO$_2$F(dmpz)$_2$: a new catalyst for selective oxidation of organic sulfides to sulfoxides with H$_2$O$_2$**

There is an increasing interest related to binding interaction and reactivity of heteroligand vanadium(V) compounds starting from synthetic inorganic chemistry through biochemistry, theoretical chemistry and catalysis [1-6]. Participation of vanadium(V) as an intermediate electron carrier in the oxidation of NADH [7] in stimulating nitrogen fixation [8] and active involvement in oxidizing organics [9-15] are very exciting contributions to the current knowledge of biochemical and catalytic involvement of the metal. Dioxovanadium(V) complexes are also studied as biomimetic synthetic models [16-20] and information obtained thereof is valuable in the context of biomodeling and developing practically useful catalytic systems. Penta coordinated complexes of 3,5-dimethylpyrazole (dmpz) vanadium(V) are scanty and incidentally no rational synthesis [21] for the mixed fluorodioxovanadium(V) was known. In view of the above reasons and resemblance of pyrazole with imidazole our attention was drawn towards this synthesis. Yet, another reason was to gain an access to a penta coordinated vanadium complex so as to enable *in situ* generation of an active peroxo complex through its reaction with H$_2$O$_2$ and then used for organic sulfur oxidations.

Selective oxidation of organic sulphides to the corresponding sulfoxide and sulfones are of immense interest because of their extensive applications as reagents in organic chemistry as well as synthetic intermediates for the construction of various biologically active molecules [22,23]. For this reason the oxidation of sulphides to sulfoxide or sulfones has been the subject of extensive studies. There are many reagents available for the oxidation of sulphides such as halogen compounds [24-26], nitrates[27], transition metal oxides[28], oxygen and hydrogen peroxide [29-31]. Incidentally, most of these reagents are not satisfactory for the medium to large-scale synthesis for one or the other reasons like low content of effective oxygen, over oxidation, the formation of environmentally unfavourable by-products and cost effectiveness. 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 over oxidation to sulfones. This chapter describes a
rational synthesis of VO$_2$F(dmpz)$_2$, complete characterization and its catalytic efficacy for selective oxidation of organic sulphides at sub ambient temperature.

5A. 1 Experimental Section

Reagent grade chemicals such as V$_2$O$_5$ (E. Merck, India), H$_2$O$_2$ (Merck, India) were used as purchased. The strength of H$_2$O$_2$ was ascertained by permanganometry before use. Dibenzothiophene (DBT), 4-methyl DBT, 4,6-dimethyl DBT were purchased from Sigma Aldrich, India. Other organic sulfides were prepared by literature procedures.

a) Synthesis of Dioxofluoro(bis-dimethylpyrazole)vanadium(V), VO$_2$F(dmpz)$_2$

An aqueous suspension (15-20 mL) of 0.5 g (2.75 mmol) V$_2$O$_5$ was treated with 0.55 g (9.64 mmol) NH$_4$HF$_2$ followed by heating on a steam bath to get a clear solution. An ethanolic solution (15-20 mL) of 1.33 g (13.73 mmol) 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$_2$F(dmpz)$_2$ were obtained. The compound was separated by decantation and dried in vacuo over conc. H$_2$SO$_4$. The yield was 1.3 g (81%).

b) Typical procedure for the oxidation of organic sulfide

Alkyl, aryl or allyl sulfide (2 mmol) in acetonitrile (2 mL) solvent was reacted with VO$_2$F(dmpz)$_2$ (0.006 g, 0.02 mmol) and H$_2$O$_2$ (30% aqueous solution, 25 μL, 2.2 mmol) under stirring at ice bath temperature for 5 h. TLC was used to monitor the reaction.

\[ \text{R}_1 = \text{alkyl, phenyl, benzyl, allyl, alkanol etc.} \]

Scheme 5.1: Oxidation of sulfide to sulfoxides

On completion of the reaction, acetonitrile was removed under reduced pressure and 1 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. The catalyst can be recovered from the aqueous layer during
work up procedure and can be reused. In order to remove any traces of VO$_2$F(dmpz)$_2$, the product was transferred to silica gel (60-120 mesh) column and eluted with ethyl acetate : hexane (1 :7).

**5A. 2 Results and Discussion**

The strategy of the synthesis was that V$_2$O$_5$ would react with NH$_4$HF$_2$, a mildly acid fluoridating agent, to produce oxofluorovanadates (V) in solution which would then react with dmpz to afford VO$_2$F(dmpz)$_2$, as targeted, in a very high yield (scheme-5.2). 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$_4$HF$_2$ as an important reagent. The role of NH$_4$HF$_2$ 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 targeted product is found to be highly crystalline lemon yellow solid, stable in air, soluble in nearly all-polar solvents and having sharp decomposition point at 156 °C. Its solution electrical conductance value of 26 mho cm$^2$ mol$^{-1}$ in acetonitrile attests its neutral character [32].

\[
\text{V}_2\text{O}_5 + \text{NH}_4\text{HF}_2 \rightarrow \text{RT} \rightarrow \text{VO}_2\text{F(dmpz)}_2
\]

**Scheme 5.2: Synthesis of the VO$_2$F(dmpz)$_2$**

Magnetic susceptibility measurement shows that the compound is diamagnetic with Gram susceptibility being -0.369X10$^{-6}$ cgs [33]. The IR spectrum of VO$_2$F(dmpz)$_2$ showed characteristic absorption bands due to coordinated dmpz [34], fluoride [35], and oxo ligands [36]. A strong band at 446 cm$^{-1}$ is due to $\nu$(V-N) stretching. This is very important in support of the dmpz coordination. The strong bands appearing at 948, 930 cm$^{-1}$ are due to $\nu$(V=O). Splitting of this band is a clear indication of the occurrence of a cis-dioxovanadyl center [36]. The Laser Raman (LR) spectrum showed complimentary signals at 547 cm$^{-1}$ due to $\nu_{V-F}$, and at 947 and 930 cm$^{-1}$.
assigned to $v_{\nu=O}$ originating from the cis-VO$_2$ core. The UV-Vis spectrum showed one intense broad band at 245 nm which might be for ligand to metal charge transfer [37]. The X-ray analysis of the compound [38] indicates that it is a penta coordinated mononuclear vanadium (V) species [VO$_2$F(dmpz)$_2$] with space group Cc (table 5.1). The ORTEP diagram of the compound with the atom-numbering scheme is shown in the figure 5.1. This complex is similar to serendipitously obtained [(t-Bupz)$_2$VO$_2$F] [21] showing same trigonal bipyramidal (TBP) geometry with dmpz ligands, as purely strong $\sigma$-donor, occupying the apical positions and the oxo and fluoride groups in the equatorial site. The X-ray data shows that the V=O bonds and O=V=O angle are slightly greater (mean V=O bond = 1.722 Å and O=V=O angle =122.2˚) than the normal (V=O bond 1.604 Å to 1.649 Å and O=V=O angle 108.2 to 110.7˚) which might be due to the formation of intramolecular hydrogen bonding between N-H hydrogens and cis-disposed dioxo groups (table 5.2). The mean O…H is found to be 2.108 Å which is unlike with the reported [(t-Bupz)$_2$VO$_2$F] [21].

**Table 5.1:** Crystal data and structure refinement for compound VO$_2$F(dmpz)$_2$

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Empirical formula</strong></td>
<td>C$<em>{10}$H$</em>{16}$FN$_4$O$_2$V</td>
</tr>
<tr>
<td><strong>Formula weight (amu)</strong></td>
<td>294.21</td>
</tr>
<tr>
<td><strong>Temperature (K)</strong></td>
<td>298</td>
</tr>
<tr>
<td><strong>Wavelength (nm)</strong></td>
<td>0.71073</td>
</tr>
<tr>
<td><strong>Crystal system</strong></td>
<td>Monoclinic</td>
</tr>
<tr>
<td><strong>Space group</strong></td>
<td>Cc</td>
</tr>
<tr>
<td><strong>Unit cell dimensions, Å and $^\circ$</strong></td>
<td>a = 11.2074(4) $\alpha$= 90</td>
</tr>
<tr>
<td></td>
<td>b = 11.9492(5) $\beta$= 94.380</td>
</tr>
<tr>
<td></td>
<td>c = 9.7556(6) $\gamma$= 90</td>
</tr>
<tr>
<td><strong>V(Å$^3$)</strong></td>
<td>1302.64</td>
</tr>
<tr>
<td><strong>Z</strong></td>
<td>4</td>
</tr>
<tr>
<td><strong>Density (mg/m$^3$) Mg/m$^3$</strong></td>
<td>1.5</td>
</tr>
<tr>
<td><strong>Absorption coeff., $\mu$ mm$^{-1}$</strong></td>
<td>0.77</td>
</tr>
<tr>
<td><strong>F(000)</strong></td>
<td>608</td>
</tr>
<tr>
<td><strong>Goodness-of-fit on F$^2$</strong></td>
<td>1.324</td>
</tr>
<tr>
<td><strong>R indices (all data) R1, wR2</strong></td>
<td>0.0449, 0.053</td>
</tr>
</tbody>
</table>
Table 5.2: Selected bond distances and bond angles of VO₂F(dmpz)₂

<table>
<thead>
<tr>
<th>Bond distances</th>
<th>Bond angles</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1-F3</td>
<td>1.601(2) F3-V1-O3</td>
</tr>
<tr>
<td>V1-O2</td>
<td>1.721(5) F3-V1-O2</td>
</tr>
<tr>
<td>V1-O3</td>
<td>1.723 (5) F3-V1-N2</td>
</tr>
<tr>
<td>V1-N2</td>
<td>2.056 (5) F3-V1-N3</td>
</tr>
<tr>
<td>V1-N3</td>
<td>2.151 (5) O2-V1-O3</td>
</tr>
<tr>
<td></td>
<td>O2-V1-N2</td>
</tr>
<tr>
<td></td>
<td>O2-V1-N3</td>
</tr>
<tr>
<td></td>
<td>O2-V1-N2</td>
</tr>
<tr>
<td></td>
<td>O3-V1-N2</td>
</tr>
<tr>
<td></td>
<td>N2-V1-N3</td>
</tr>
</tbody>
</table>

It is also interesting to note that the V-F bond is short which might possess more than single bond character to nullify the charge density drawn from vanadium for intramolecular hydrogen bond. The present investigation clearly demonstrates that dmpz complex of vanadium (V) can be synthesized from an aqueous solution in presence of fluoride.

Figure 5.1: ORTEP plot of VO₂F(dmpz)₂

From the prior knowledge in the peroxovanadium chemistry [39-43], it is believed that the complex interacts with H₂O₂ to form peroxovanadium intermediate thereby activating the bound peroxide. Sometimes it was found that peroxovanadium species in presence of electron donating ligands (EDL) could not oxidize bromide but even after having EDL it worked well, which might be due to the presence of fluoride.
Our interest in peroxovanadium catalyzed oxidation inspired us to use this complex as catalyst for sulfide oxidation.

**Table 5.3**: Optimization of reaction condition for the oxidation of methyl phenyl sulphone

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst mol%</th>
<th>Time (h)</th>
<th>Temp (°C)</th>
<th>H$_2$O$_2$ equiv.</th>
<th>Solvent</th>
<th>Sulfoxide (%)</th>
<th>Sulfone (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>2.5</td>
<td>27</td>
<td>2</td>
<td>CH$_3$CN</td>
<td>75</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>2.5</td>
<td>27</td>
<td>2</td>
<td>C$_2$H$_5$OH</td>
<td>70</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>5</td>
<td>27</td>
<td>2</td>
<td>H$_2$O</td>
<td>55</td>
<td>20</td>
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<td>4</td>
<td>5</td>
<td>3</td>
<td>27</td>
<td>1.1</td>
<td>CH$_3$CN</td>
<td>65</td>
<td>20</td>
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<tr>
<td>5</td>
<td>5</td>
<td>3.5</td>
<td>0-5</td>
<td>1.1</td>
<td>CH$_3$CN</td>
<td>95</td>
<td>&lt;1</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>4.0</td>
<td>0-5</td>
<td>1.1</td>
<td>CH$_3$CN</td>
<td>95</td>
<td>&lt;1</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>5</td>
<td>0-5</td>
<td>1.1</td>
<td>CH$_3$CN</td>
<td>95</td>
<td>&lt;1</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>12</td>
<td>0-5</td>
<td>0</td>
<td>CH$_3$CN</td>
<td>0</td>
<td>--</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>12</td>
<td>0-5</td>
<td>1.1</td>
<td>CH$_3$CN</td>
<td>35</td>
<td>--</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>5.5</td>
<td>0-5</td>
<td>1.1</td>
<td>C$_2$H$_5$OH</td>
<td>92</td>
<td>5</td>
</tr>
</tbody>
</table>

The complex was screened for oxidation of sulides with aqueous 30% H$_2$O$_2$. To optimize the reaction condition, we carried out oxidation of methyl phenyl sulhide in acetonitrile at room temperature (table 5.3). It was found that methyl phenyl sulhide 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$_2$O$_2$. We also performed the oxidation in different solvents (table 5.3) maintaining the same conditions. Unfortunately, over oxidation could not be averted. The over oxidation could not be overcome even by lowering the amount of H$_2$O$_2$ 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-bath temperature. To ascertain the 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 the catalyst. Accordingly, all the reactions discussed herein after were conducted with this combination. In order to generalize the scope, a series of structurally diverse sulides were subjected to oxidation under the optimized reaction conditions and the results are presented in table 5.4. The reactions went well affording the products in high yields. It is notable that sulides were chemoselectively oxidized in presence of some oxidation prone functional groups such as C=C, –CN, –OH (entries 7-11, table 5.4).
Table 5.4: VO$_2$F(dmpz)$_2$ catalyzed oxidation of organic sulfide with H$_2$O$_2$ in CH$_3$CN

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Time (h)</th>
<th>Sulfoxide$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(Me)$_2$S</td>
<td>30 min</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td><img src="image1.png" alt="Chemical structure" /></td>
<td>5</td>
<td>95,90$^b$,86$^c$,97$^d$</td>
</tr>
<tr>
<td>3</td>
<td><img src="image2.png" alt="Chemical structure" /></td>
<td>5</td>
<td>93</td>
</tr>
<tr>
<td>4</td>
<td><img src="image3.png" alt="Chemical structure" /></td>
<td>5.5</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td><img src="image4.png" alt="Chemical structure" /></td>
<td>6.5</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td><img src="image5.png" alt="Chemical structure" /></td>
<td>6</td>
<td>87</td>
</tr>
<tr>
<td>7</td>
<td><img src="image6.png" alt="Chemical structure" /></td>
<td>3</td>
<td>97</td>
</tr>
<tr>
<td>8</td>
<td><img src="image7.png" alt="Chemical structure" /></td>
<td>6.5</td>
<td>86</td>
</tr>
<tr>
<td>9</td>
<td><img src="image8.png" alt="Chemical structure" /></td>
<td>4.5</td>
<td>85</td>
</tr>
<tr>
<td>10</td>
<td><img src="image9.png" alt="Chemical structure" /></td>
<td>4.5</td>
<td>82</td>
</tr>
<tr>
<td>11</td>
<td><img src="image10.png" alt="Chemical structure" /></td>
<td>2</td>
<td>85</td>
</tr>
</tbody>
</table>
Dibenzothiophene (DBT) and substituted DBT oxidations are rather difficult with the standard oxidation procedures \[44\]. However, upon the treatment with \(\text{VO}_2\text{F(dmpz)}_2\cdot\text{H}_2\text{O}_2\) system these were converted to the corresponding sulfoxides (entries 12-14, table 5.4) in good yields. It is noteworthy to mention that the catalytic conversion of foul smelling toxic gas, i.e. dimethyl sulfide (DMS) generated in many medicinal industries (e.g. during Renitidine HCl synthesis) to the corresponding sulfoxide is important to stop the release of such toxic gas into the environment.

DMS is found in many industrial waste gas streams and has very low odorous threshold value and toxic for both the environment and the human health. The low vapour density of the gas facilitates its easy diffusion into and rapid mixing of atmospheric air thereby rendering the air stinky. Moreover, methylmercaptans are health hazard because they cause dizziness, headache, nausea, respiratory arrest and even coma and unconsciousness. A little longer exposure to high concentration of the gas can be fatal. The sustained contact with the liquid and the gas may cause frostbite as well.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Structure</th>
<th>Isolated Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>![Structure 12]</td>
<td>5</td>
</tr>
<tr>
<td>13</td>
<td>![Structure 13]</td>
<td>8</td>
</tr>
<tr>
<td>14</td>
<td>![Structure 14]</td>
<td>12</td>
</tr>
<tr>
<td>15</td>
<td>![Structure 15]</td>
<td>5</td>
</tr>
<tr>
<td>16</td>
<td>![Structure 16]</td>
<td>5</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated Yield, <sup>b</sup> Reaction in ethanol, <sup>c</sup> Yield after fifth cycle, <sup>d</sup> Yield at 5g scale, <sup>e</sup> Reaction at room temperature
It may be mentioned that with the increase in alkyl chain length of the sulfides, the rate of reaction becomes slower (entries 4, 5 & 6, table 5.4). This may 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 VO$_2$(dmpz)$_2$, obtained after extraction of the reaction mixture with ethylacetate. This was charged with fresh substrate and 1.1 equivalents of H$_2$O$_2$. The catalyst could be reused for at least five reaction cycles with consistent activity. Importantly, the reaction can be performed on a relatively larger scale (5 g) to give good yields (entry 2, table 5.4) showing its potential for scaled-up applications. Chu and Trout’s report said that the major reaction coordinates of the reaction were the breaking of the O-O of the intermediate and the formation of the S-O bond in the sulfide oxidation to sulfoxide by H$_2$O$_2$ [45].

![Scheme 5.3: Plausible mechanism of the reaction](image)

The oxidation is expected to progress via metal-oxygen shift mechanism in the present reaction as depicted in scheme 5.3. The ease of the formation of sulfoxide is likely to happen through the nucleophilic attack by the sulfide to the electrophillic O-O bond of peroxometal species thus facilitating the regeneration of the catalyst. It is found that the presence of electron withdrawing group in the substrates hinder the reaction which is expected according to the proposed mechanism of the reaction.
5A. 3 Conclusions

In conclusion, a new penta-coordinated VO$_2$F(dmpz)$_2$ catalyst has been developed and fully characterized. Its throughput as catalyst for the oxidation of alkyl as well as aryl sulfides in presence of oxidation prone functional groups such as C=C, –CN, –OH and its reusability offers a potentially competitive practicable process. The selective oxidation of DMS to DMSO is industrially important in the context of ranitidine hydrochloride. Refractory sulfides are also capable of being oxidized quite effectively. The oxidations of DBTs are especially important in the context of transportation fuel chemistry research targetting desulfurization of diesel and gasolene, for instance.
5A. 4 Spectral Data

**VO$_2$F(dmpz)$_2$**

FT-IR(KBr): 3257, 1577, 948, 930 cm$^{-1}$; $^1$HNMR (400MHz, CDCl$_3$): $\delta$ 2.13 (s, 3H), 2.47 (s, 3H), 5.85 (s, 1H), 11.62 (brs, 1H, N-H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 11.74, 105.04, 145.76.

**Demethyl sulfoxide (entry 1, table 5.4)**

FT-IR(KBr): 950, 1018, 3419 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.17 (s, 6H)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 31

**Methyl phenyl sulfoxide (entry 2, table-5.4)**

FT-IR(KBr): 1032 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.74 (s, 3H), 7.51-7.53 (m, 3H), 7.64-7.66 (m, 2H); MS : m/z 157 (M$^+$).
Benzyl phenyl sulfoxide (entry 3, table-5.4)

\[
\begin{align*}
\text{FT-IR (KBr): } & 1035 \text{ cm}^{-1}; \ \ ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 3.99 (d, J = 12.8\text{Hz}, 1\text{H}), \\
& 4.16 (d, J = 12.4\text{Hz}, 1\text{H}), 6.95 (m, 2\text{H}), 7.19-7.28 (m, 3\text{H}), 7.34-7.44 (m, 5\text{H}); \ ^{13}\text{C NMR (100 MHz, CDCl}_3\text{): } \delta 63.8, 124.5, 128.3, 128.5, 128.9, 129.2, 130.4, 131.2, 142.7.
\end{align*}
\]

Allyl phenyl sulfoxide (entry 7, table -5.4)

\[
\begin{align*}
\text{FT-IR (KBr): } & 1044 \text{ cm}^{-1}; \ ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 3.48-3.60 (m, 2\text{H}), 5.18 (d, J = 16.8\text{Hz}, 1\text{H}), 5.33 (d, 1\text{H}, J = 10.8\text{Hz}, 1\text{H}), 5.58-5.68 (m, 1\text{H}), 7.48-7.53 (m, 3\text{H}), 7.55-7.58 (m, 2\text{H}).
\end{align*}
\]

Allyl 4-methoxyphenyl sulfoxide (entry 9, table-5.4)

\[
\begin{align*}
\text{FT-IR (KBr): } & 1044 \text{ cm}^{-1}; \ ^1\text{H NMR (400MHz, CDCl}_3\text{): } \delta 3.45-3.57 (m, 2\text{H}), 3.78 (s, 3\text{H}), 5.18 (d, J = 16.8\text{Hz}, 1\text{H}), 5.31 (d, J = 10.8\text{Hz}, 1\text{H}), 5.58-5.68 (m, 1\text{H}), 7.47-7.51 (m, 3\text{H}), 7.54-7.57 (m, 2\text{H}).
\end{align*}
\]
Allyl dodecyl sulfoxide (entry 8, table-5.4)

\[
\text{SO} \quad \text{C}_{11}\text{H}_{23}
\]

FT-IR (KBr): 1035 cm\(^{-1}\); \(^1\)H NMR (400MHz, CDCl\(_3\)): \(\delta\) 0.9 (t, \(J = 6.4\) Hz, 3H), 1.31-1.46 (m, 16H), 1.78-1.88 (m, 2H), 2.93 (t, \(J = 8.4\) Hz, 2H), 3.69 (d, \(J = 8.4\) Hz, 2H), 5.42 (d, \(J = 16.4\) Hz, 1H), 5.49 (d, \(J = 10.8\) Hz, 1H), 5.85-6.0 (m, 1H)

---

2-Phenylmethanesulfinyl-ethanol (entry 10, table-5.4)

\[
\text{Ph} \quad \text{SO} \quad \text{OH}
\]

FT-IR (KBr): 1025 cm\(^{-1}\); \(^1\)H NMR (400MHz, CDCl\(_3\)): \(\delta\) 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\(_3\)): \(\delta\) 53.34, 55.29, 58.04, 128.60, 129.11, 130.04, 130.52.

---

4, 6-Dimethyldibenzothiophene sulfoxide (entry 14, table-5.4)

\[
\text{O} \quad \text{S} \quad \text{O}
\]

FT-IR (KBr): 1028 cm\(^{-1}\); \(^1\)H NMR (400MHz, CDCl\(_3\)): \(\delta\) 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, \(J = 8.4\) Hz, 1H).
4-nitrophenyl methyl sulfoxide (entry 15, table-5.4)

\[
\text{O}_2\text{N} \quad \text{S} \quad \text{CH}_3
\]

FT-IR (KBr): 3578, 1509, 1338, 1078, 1037, 835, 664; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 8.37-8.39\) (d, \(J=8\) Hz, 2H), 7.81-7.83 (d, \(J=8\) Hz, 2H), 2.78 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 153.34, 149.61, 149.45, 124.74, 43.97\).

4-nitrophenyl phenyl sulfoxide (entry 16, table-5.4)

\[
\text{O}_2\text{N} \quad \text{S} \quad \text{O}
\]

FT-IR (KBr): 3449, 3091, 1516, 1338, 1086, 1037, 843, 730, 680, 526 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 8.28-8.30\) (d, \(J=8\) Hz, 2H), 7.80-7.83 (d, \(J=8\) Hz, 2H), 2.78 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 153.34, 149.61, 149.45, 124.74, 43.97\).
**Image 22:** FT-IR spectrum of 4-nitrophenyl phenyl sulfoxide

**Image 23:** $^1$H NMR spectrum of 4-nitrophenyl phenyl sulfoxide
Image 24: $^{13}$C NMR spectrum of 4-nitrophenyl phenyl sulfoxide

Image 25: FT-IR spectrum of 4-nitrophenyl methyl sulfoxide
Image 26: $^1$H NMR spectrum of 4-nitrophenyl methyl sulfoxide

Image 27: $^{13}$C spectrum of 4-nitrophenyl methyl sulfoxide
Image 28: FT-IR spectrum of VO₂F(dmpz)₂

Image 29: FT-IR spectrum of VO₂F(dmpz)₂ showing the split peak due to cis-dioxovanadyl species
Image 30: $^{13}$C NMR spectrum of $\text{VO}_2\text{F(dmpz)}_2$

Image 31: $^{13}$C NMR spectrum of DMPZ
5A. 5 References
Chapter 5

Section 5B

**VO(acac)₂: an efficient catalyst for the oxidation of aldehydes to the corresponding acids in presence of aqueous H₂O₂**

In the plethora of oxidation processes, aldehyde oxidation occupies an important position owing to their diversified importance in the industrial manufacturing, and in synthetic chemistry [1-3]. The classical methods for the oxidation of aldehyde involve the use of oxidising reagents like Jones reagent [4,5], KMnO₄[6,7], bromine [8,9], HNO₃ [10] Ag₂O [11] which are not desirable because of the current industrial and environmental demand. In recent times, various catalysts and catalyst systems have been reported for the catalytic oxidation of aldehyde, e.g. CuCl [12], AgNO₃ [13], Bi₂O₃ [14] supported metal acetyl acetonate [15] etc. In the domain of green oxidation processes, hydrogen peroxide is considered as the ultimate green oxidizing (active oxygen 47.1%) reagent because the by-product is water. The first report of oxidation of aldehydes using H₂O₂ is almost seven decades old [16]. Noyori *et al.* exploited the ability of H₂O₂ for the oxidation of aldehyde to the corresponding acid [17]. In recent years, H₂O₂ has been extensively used in synthetically important processes like epoxidation [18,19], oxidation of sulphides [20,21], oxidation of alcohols [22,23], Baeyer-Villiger oxidation [24] etc. The oxidizing ability of H₂O₂ can be enhanced by adding a little vanadium compound to the reaction mixture [25]. Such activation of H₂O₂ by vanadium compound leads to the generation of various reactive peroxovanadium species with various co-ordination modes [26–28]. V₂O₅/H₂O₂ has been used to oxidize aldehyde to the corresponding esters [29,30].

**Scheme 5.4:** VO(acac)₂ catalyzed oxidation of aldehyde

The five co-ordinate VO(acac)₂ has been proved to be a good oxidation catalyst [31]. It is found that VO(acac)₂ along with H₂O₂ can oxidize aldehydes to the corresponding acids or the esters depending on the solvents used (scheme 5.4) *viz.* methyl ester is formed in the presence of methanol and acid is the product in the
presence of acetonitrile. Activity of various vanadium sources-H$_2$O$_2$ systems have been studied for the oxidation of aldehydes to the corresponding acids

**5B. 1 Experimental:**

a) *Procedure for the oxidation of 4-ClC$_6$H$_4$CHO with VO(acac)$_2$*

In a typical procedure, 0.007 g of VO(acac)$_2$ (4 mol%) was dissolved in 0.34 mL (3 mmol) of 30% H$_2$O$_2$; the color of the mixture changed to reddish brown. To this mixture, 0.14 g (1 mmol) of 4-chlorobenzaldehyde dissolved in minimum amount of acetonitrile was added and allowed to stir. Progress of the reaction was monitored by thin layer chromatography (TLC). On completion of the reaction, acetonitrile was removed under reduced pressure and 3 mL of water was added. The product was extracted with ethyl acetate (3×10 mL) and the organic layer was dried over anhydrous Na$_2$SO$_4$. Finally, the product was purified by column chromatographic technique.

b) *Typical procedure for the preparation of VO(acac)$_2$ catalyst*

To an aqueous suspension of vanadium pentoxide (5 g, 27.49 mmol) in 20 mL of water taken in a 500 mL beaker, 30% hydrogen peroxide (37.37 mL, 329.88 mmol) was added dropwise in an ice-cold condition and stirred till a clear dark solution was formed. To the dark brown colored solution, distilled acetylacetone (19.84 mL, 192.5 mmol) was added dropwise very carefully with continuous stirring. Vigorous effervescence took place after 15 min., stirring for a period of 30 min led to a precipitation of a brown colored microcrystalline compound. The reaction mixture was heated at 70 °C for 15 min under stirring. The precipitate turned olive green with shiny crystalline appearance with the solution also turning green. The solution was concentrated by heating on a steam bath for 30 min and then placed in an ice-water bath for 15 min. The compound was filtered through Whatman No. 42 filter paper, washed with acetone and dried in vacuo over fused CaCl$_2$. Yield: 11.7 g (80%).

c) *Preparation of VO(acac)$_2$ supported on titania (VO(acac)$_2$–TiO$_2$) [32]*

To a solution of VO(acac)$_2$ (265 mg) in anhydrous THF (50 mL), TiO$_2$ (1.0 g) was added and stirred at 293 K for 12 h under nitrogen atmosphere. The solid catalyst was filtered, washed several times with anhydrous THF, and finally dried in vacuo.
Measurement of the mass increase of the resultant VO(acac)$_2$–TiO$_2$ indicates that 170 mg of VO(acac)$_2$ is supported, and the vanadium content is 0.64 mmol/g.

d) **Procedure for the oxidation of 4-NO$_2$C$_6$H$_4$CHO with TiO$_2$-VO(acac)$_2$**

In a typical procedure, 0.0075 g of TiO$_2$-VO(acac)$_2$ (5 wt%) was taken in 0.34 mL (3 mmol) of 30% H$_2$O$_2$. To this mixture, 0.15 g (1 mmol) of 4-nitrobenzaldehyde dissolved in minimum amount of acetonitrile was added and allowed to stir. Progress of the reaction was monitored by thin layer chromatography (TLC). On completion of the reaction, the mixture was filtered to recover the catalyst, acetonitrile was removed under reduced pressure. The product was extracted with ethyl acetate (3×10) and dried over anhydrous Na$_2$SO$_4$. The recovered catalyst was washed with chilled ethanol and dried at 120 °C for 1 h and then used it for further reaction. Finally, the product was purified by column chromatographic technique.

**5B. 2 Results and Discussion**

The results of our initial attempts to optimize the reaction condition using 4-chlorobenzaldehyde as the model substrate in the presence of H$_2$O$_2$ as the oxidant and VO(acac)$_2$ as the catalyst are elaborated in table 5.5.

Table 5.5: Optimization of the reaction condition$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>H$_2$O$_2$ (mmol)</th>
<th>Solvent</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>MeCN</td>
<td>-</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>MeCN</td>
<td>VO(acac)$_2$, MeCN</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>MeCN</td>
<td>VO(acac)$_2$, (1 mol%)</td>
<td>8</td>
<td>48</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>MeCN</td>
<td>VO(acac)$_2$, (1 mol%)</td>
<td>8</td>
<td>55</td>
</tr>
<tr>
<td>No.</td>
<td>2</td>
<td>Solvent</td>
<td>Catalyst</td>
<td>%</td>
<td>Yield</td>
</tr>
<tr>
<td>-----</td>
<td>---</td>
<td>---------</td>
<td>----------</td>
<td>---</td>
<td>-------</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>MeCN</td>
<td>VO(acac)$_2$ (1 mol%)</td>
<td>8</td>
<td>56</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>MeCN</td>
<td>VO(acac)$_2$ (2 mol%)</td>
<td>7</td>
<td>65</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>MeCN</td>
<td>VO(acac)$_2$ (3 mol%)</td>
<td>6</td>
<td>78</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>MeCN</td>
<td>VO(acac)$_2$ (4 mol%)</td>
<td>5</td>
<td>82</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>MeCN</td>
<td>VO(acac)$_2$ (4 mol%)</td>
<td>4</td>
<td>97</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>Toluene</td>
<td>VO(acac)$_2$ (4 mol%)</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>CH$_2$Cl$_2$</td>
<td>VO(acac)$_2$ (4 mol%)</td>
<td>8</td>
<td>45</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>MeOH</td>
<td>VO(acac)$_2$ (4 mol%)</td>
<td>3</td>
<td>90$^d$</td>
</tr>
<tr>
<td>13</td>
<td>3</td>
<td>EtOH</td>
<td>VO(acac)$_2$ (4 mol%)</td>
<td>4</td>
<td>45</td>
</tr>
<tr>
<td>14</td>
<td>3</td>
<td>CH$_3$CN</td>
<td>V$_2$O$_5$ (4 mol%)</td>
<td>4</td>
<td>45</td>
</tr>
<tr>
<td>15</td>
<td>3</td>
<td>CH$_3$CN</td>
<td>NH$_4$VO$_3$ (4 mol%)</td>
<td>4</td>
<td>62</td>
</tr>
</tbody>
</table>

$^a$p-chlorobenzaldehyde (1 mmol), stirred at room temperature.
$^b$30% H$_2$O$_2$.
$^c$Yields are referred to as isolated yields.
$^d$Ester is the product.

To ascertain the presence and efficacy of the catalyst several reactions were carried out with and without catalyst (entries 1-15, table 5.5). From our study it is found that, in the absence of H$_2$O$_2$, only VO(acac)$_2$ cannot catalyze the oxidation of the aldehyde (entry 2). The oxidizing ability of H$_2$O$_2$ in the absence of VO(acac)$_2$ was found to be negligible (<5% yield was isolated) (entry 1). 4 mol% of the catalyst and three fold amount of H$_2$O$_2$ provided the best result (entry 9). Effect of various solvents and vanadium catalysts on the above model reaction are also studied (entries 1-15, table 5.5). The study revealed that VO(acac)$_2$ and acetonitrile were the best catalyst and solvent respectively for the oxidation of aldehyde to the corresponding acid (entry 9). Interestingly, under the reaction condition, in ethanol corresponding acid was obtained (entry 13) in moderate yield while in methanol corresponding methyl ester was obtained in excellent yield (entry 12). Gas
chromatogram of the reaction mixture does not show any decomposition product; only acid or ester and unreacted aldehyde are present in the reaction mixture.

To demonstrate the generality and scope of the reaction, a series of structurally diverse aldehydes were subjected to oxidation under the optimized condition and the outcome is summarized in table 5.6 (entries 1-12). The reaction went well affording moderate to excellent yields of the product. As can be seen from the table 5.6, the method was equally effective for the oxidation of both aromatic and heterocyclic aldehydes (entries 1-9). However, aliphatic aldehydes (entries 10 and 11) except unsaturated aldehyde (entry 12) reacted slowly to afford moderate yield of product. This might be due to the low electrophilicity of aliphatic carbonyl carbon than the aromatic one. Notably, oxidation prone functional groups such as -OH (entry 3), -OMe (entry 5) and -C=C (entry 6) in aldehydes remain unaffected during the reaction that showed the chemoselectivity of the protocol. Similarly, heterocyclic aldehydes are also prone to oxidation at the hetero atom. Notably, in our protocol oxidation occurs only at the aldehydic group without affecting the hetero atom (entries 7 and 8).

Table 5.6: Oxidation of aldehyde catalyzed by VO(acac)₂

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>Acid</th>
<th>Ester</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-ClC₆H₄CHO</td>
<td>VO(acac)₂</td>
<td>4</td>
<td>97</td>
<td>97</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>4</td>
<td>96</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>2-ClC₆H₄CHO</td>
<td>VO(acac)₂</td>
<td>5.30</td>
<td>94</td>
<td>89</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>5.30</td>
<td>93</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>4-OHC₆H₄CHO</td>
<td>VO(acac)₂</td>
<td>5.30</td>
<td>96</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>5.30</td>
<td>91</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>4-NO₂C₆H₄CHO</td>
<td>VO(acac)₂</td>
<td>6</td>
<td>98</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>6</td>
<td>97</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>4-MeOC₆H₄ CHO</td>
<td>VO(acac)₂</td>
<td>4</td>
<td>96</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>4</td>
<td>94</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>trans-cinnamaldehyde</td>
<td>VO(acac)₂</td>
<td>7</td>
<td>90</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>7</td>
<td>87</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Thiophene-2-carbaldehyde</td>
<td>VO(acac)$_2$</td>
<td>6.30</td>
<td>92</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>--------------------------</td>
<td>-------------</td>
<td>------</td>
<td>----</td>
<td>----</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>6.30</td>
<td>90</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Pyridine-2-carbaldehyde</td>
<td>VO(acac)$_2$</td>
<td>5.30</td>
<td>91</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>5.30</td>
<td>87</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2-Furaldehyde</td>
<td>VO(acac)$_2$</td>
<td>6</td>
<td>89</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>6</td>
<td>86</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Pentanal$^d$</td>
<td>VO(acac)$_2$</td>
<td>7</td>
<td>65</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>7</td>
<td>62</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Gluteraldehyde$^d$</td>
<td>VO(acac)$_2$</td>
<td>8</td>
<td>42</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>7</td>
<td>42</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Acrylaldehyde</td>
<td>VO(acac)$_2$</td>
<td>6</td>
<td>76</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSV</td>
<td>6</td>
<td>76</td>
<td>74</td>
<td></td>
</tr>
</tbody>
</table>

*Yields are referred to as isolated yields. All the reactions are carried out with 4 mol% of VO(acac)$_2$, and 3 mmol of 30% H$_2$O$_2$ in MeCN at room temperature under stirring. $^d$ MeOH was used as solvent. $^d$ Reactions were carried out at 60 °C. $^d$ TSV= TiO$_2$ supported VO(acac)$_2$.

Mechanistically, peroxovanadium species is involved in the reaction. The intermediacy of the peroxovanadium species in the catalytic process can be observed from the UV-Visible spectrum of H$_2$O$_2$, VO(acac)$_2$ and solvent mixture. The peak at around 414 nm is due to the ligand to metal charge transfer transition, which is a characteristic of peroxovanadium compounds. Accordingly, a plausible mechanism involving peroxovanadium species is described in figure 5.2. VO(acac)$_2$ and H$_2$O$_2$ form a reactive peroxovanadium species (II). In the absence of methanol, the metal peroxo oxygen atom in (II) attacks the electrophilic carbonyl carbon of aldehyde affording the corresponding acid (path b). The alcoholic proton in methanol is more acidic than ethanol, therefore it is easily abstracted by (II) resulting the methoxide ion which further attacks the carbonyl carbon of aldehyde resulting the ester as the product (path a). Interestingly, when the reaction was carried out at elevated temperature, i.e. 50-60 °C in presence of ethanol the product was the corresponding ethyl ester (table 5.7) along with the corresponding acid as the side product and some amount of unreacted starting aldehyde. This observation is supported by the suggested mechanism (path a, figure 5.2). Higher temperature facilitates the abstraction of comparatively less acidic alcoholic proton of ethanol.
Homogeneous catalytic processes produce unwanted waste and hence heterogenization of the homogeneous process is important. TiO$_2$ supported VO(acac)$_2$ (TSV) has been reported for the oxidation of the organic sulfides to the corresponding sulfoxides [32]. This impregnated catalyst also showed good results as summarized in table 5.8 (entries 1-5).

**Figure 5.2:** Plausible mechanism for the oxidation of aldehyde

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Time (h)</th>
<th>Yield (%)$^{a,b}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pentanal</td>
<td>4</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>$p$-chlorobenzaldehyde</td>
<td>2.5</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>$p$-nitrobenzaldehyde</td>
<td>3</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>2-furaldehyde</td>
<td>4</td>
<td>57</td>
</tr>
</tbody>
</table>

$^a$Yields are referred to as isolated yields. $^b$Trace amount of acid is formed as the corresponding side product.

With a change in the catalyst loading, variation in the yield of the product was also observed, which are shown in the table 5.8. Best result was obtained when the
catalyst loading was 5 wt% (entry 5). Vanadium content in the catalyst was found to be approx 0.64 mmol/g. Further increasing the catalyst loading and reaction time did not improve the yield of the reaction.

In catalysis, recyclability is one of the important attributes. For this, we have conducted a series of reactions with the recycled TSV catalyst. The catalyst can be effectively recycled for at least five cycles with reasonably consistent activity.

Table 5.8: Effect of catalyst (TSV) loading on the product yield

<table>
<thead>
<tr>
<th>Entry</th>
<th>TSV (wt%)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>6</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>6</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>6</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>6</td>
<td>97</td>
</tr>
</tbody>
</table>

The reactions have been carried out considering p-nitrobenzaldehyde as the substrate in acetonitrile under stirring at room temperature.

Yields are referred to as isolated yields.

The recycled TSV catalyst shows slow deactivation, which may be due to the slow leaching out of vanadium from the surface of the support. The activity of the catalyst can be easily regained simply by treating the recycled catalyst with a solution of VO(acac)₂ in THF [33]. The regenerated catalyst has the same activity as the fresh catalyst (table 5.9).

Table 5.9: Yield of product without and after regeneration of the catalyst

<table>
<thead>
<tr>
<th>Run</th>
<th>Time (h)</th>
<th>Yield without regeneration (%)</th>
<th>Yield after regeneration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh</td>
<td>6</td>
<td>97</td>
<td>-</td>
</tr>
<tr>
<td>1st</td>
<td>6.5</td>
<td>94</td>
<td>94</td>
</tr>
<tr>
<td>2nd</td>
<td>6.5</td>
<td>92</td>
<td>93</td>
</tr>
<tr>
<td>3rd</td>
<td>7</td>
<td>89</td>
<td>93</td>
</tr>
<tr>
<td>4th</td>
<td>7</td>
<td>87</td>
<td>92</td>
</tr>
<tr>
<td>5th</td>
<td>7.5</td>
<td>87</td>
<td>90</td>
</tr>
</tbody>
</table>

Isolated yield of product.

Reactions were carried out using p-nitrobenzaldehyde (1 mmol) as the substrate at room temperature in MeCN and H₂O₂ (3 mmol) as the oxidant using 5 wt% of the TSV.
However, calcination (at 450 °C) of the catalyst helps in decreasing the leaching of the vanadium from the surface of the catalyst but the activity of the catalyst for the oxidation of the aldehyde decreases. Gas chromatographic analysis of the product mixture of the oxidation of p-nitrobenzaldehyde showed 30% of ester and 7% of acid after 6 hours when calcined catalyst was used.

5B. 3 Conclusions
In summary, we have developed an efficient catalytic process for the oxidation of aldehyde. We anticipate that the simplicity and the catalytic nature of the protocol will make it appealing to the synthetic chemist, particularly those who are practicing the green oxidation process.
5B. 4 Spectral Data

4-Hydroxybenzoic acid (entry 3, table-5.6)

FT-IR (KBr): 3375, 1682, 1592, 1422, 933 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 10.24, 7.76-7.79 (d, \(J=12\) Hz, 2H), 6.80-6.82 (d, \(J=8\)Hz, 2H); \(^13\)C NMR (100 MHz, DMSO-\(d_6\)): \(\delta\) 115.64, 121.05, 132.05, 162.09, 167.70.

Furan-2-carboxylic acid (entry 9, table-5.6)

FT-IR (KBr): 1718, 3025; \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 6.50-7.61(m, 2H), 7.62(2H), 7.92-7.94(d, \(J=8\)Hz, 2H); \(^13\)C NMR (100 MHz, DMSO-\(d_6\)): 113.7, 120.4, 145.8, 147.6, 162.14.

4-Methoxybezoic acid (entry 5, table-5.6)

FT-IR (KBr): 1710, 2980; \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 3.67 (s, 3H), 6.87-6.89 (d, \(J=8\)Hz, 2H), 7.92-7.94(d, \(J=8\)Hz, 2H); \(^13\)C NMR (100 MHz, DMSO-\(d_6\)): 54.5, 114.3, 132.3, 164.2, 167.4.

Acrylic acid (entry 12, table-5.6)

FT-IR (KBr): 3507, 1732, 1406, 1289, 1185, 811 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 10.40 (s, 1H), 6.48-6.53 (m, 1H), 6.13-6.14 (m, 1H), 5.87-5.97 (m,1H); \(^1\)H (100 MHz, CDCl\(_3\)): \(\delta\) 33.58,133.10, 166.14.
4-Chloro-benzoic acid methyl ester (entry 1, table-5.6)

\[ \text{Cl}\begin{array}{c} \text{COOMe} \\
\end{array} \]

\(^1\text{H NMR (400 MHz, CDCl}_3\text{): 3.92 (s, 3H), 7.44-7.46 (d, } J=8\text{Hz, 2H), 8.02-8.04 (d, } J=8\text{Hz, 2H).} \quad \text{\(^{13}\text{C NMR (100 MHz, CDCl}_3\text{): 52.13, 129, 131.75, 140.4, 169.4.}\)\]

4-Methoxy-benzoic acid methyl ester (entry 5, table-5.6)

\[ \text{MeO}\begin{array}{c} \text{COOMe} \\
\end{array} \]

\(^1\text{H NMR (400 MHz, CDCl}_3\text{): 3.94 (s, 3H), 8.11-8.17 (dd, 4H);} \quad \text{\(^{13}\text{C NMR (400 MHz, CDCl}_3\text{): 55.68, 113.8, 121.74, 132.42, 164.11, 171.61.}\)\]

4-Hydroxy-benzoic acid methyl ester (entry 3, table-5.6)

\[ \text{HO}\begin{array}{c} \text{COOMe} \\
\end{array} \]

\(\text{FT-IR (KBr): 3300, 2910, 1680, 775 cm}^{-1}; \quad \text{\(^1\text{H NMR (400MHz, CDCl}_3\text{): } \delta 7.89-7.91 \) (d, } J=8\text{Hz, 2H), 6.87-6.89 (d, } J=8\text{Hz, 2H), 5.44 (brs, 1H), 3.92 (s, 3H);} \quad \text{\(^{13}\text{C NMR(100 MHz, CDCl}_3\text{): } \delta 51.2, 115.3, 121.5, 132.1, 162.4, 165.7.}\)\]

4-Nitro-benzoic acid methyl ester (entry 4, table-5.6)

\[ \text{O}_2\text{N}\begin{array}{c} \text{COOMe} \\
\end{array} \]

\(\text{FT-IR (KBr): 3100, 2875, 1720, 1512, 1387, 722cm}^{-1}; \quad \text{\(^1\text{H NMR (400 MHz, CDCl}_3\text{): 8.17 (dd, 4H), 3.89 (s, 3H);} \quad \text{\(^{13}\text{C NMR (100 MHz, CDCl}_3\text{): 52.7, 124.2, 131.7, 134.5, 153.4, 166.4.}\)\]
5B. 5 Reference and Note


33. Regeneration of the catalyst: To a solution of VO(acac)$_2$ (265 mg) in anhydrous THF (50 mL), the recovered catalyst (1 g) was added stirred at room temperature under nitrogen atmosphere. The solid catalyst was filtered and dried in the vacuum.
A green route to tribromides: an experimental and theoretical insight into reactivity of organic ammonium tribromides (OATBs)

Bromoorganics occupy a cardinal position in the domain of organic chemistry [1,2]. They find wide applications in the synthesis of a large number of natural products as well as the manufacture of pharmaceuticals, agrochemicals and numerous industrially valuable chemicals including fire retardants. It is noteworthy that of the various bromoorganics, arylbromides find extensive applications for carbon-carbon and carbon-heteroatom bond forming reactions [3-5]. Electrophilic substitution is the most common method for bromination of organics wherein, the regioselectivity is controlled by the electronic properties of the substituents [6]. For over a century, molecular bromine has been the most commonly and widely used brominating reagent because of being inexpensive and easily available. However, bromine is found to be a very toxic chemical and it is difficult to manipulate it as a brominating reagent [7-10]. Furthermore, substitution reactions involving elemental bromine (Br₂) gives only 50% atom economy and leads to generation of toxic HBr waste [11]. Due to such toxicity associated with elemental bromine, researchers have been searching for alternative brominating reagents and methods for bromination of organics. Apart from such toxicity issues it is very difficult to maintain the stoichiometry of the reagent when elemental bromine is used as a brominating reagent. The concerns expressed above led to the development of a number of new brominating reagents over the years.

Developing greener protocols for the synthesis of commercially important compounds is a major challenge in chemical research. Therefore, revisiting the traditional methods for organic and inorganic synthesis by introducing greener reagents or mild and efficient catalysts are much sought after in academia and industrial research.

To overcome the problems associated with the use of molecular bromine, a number of alternative strategies have been devised. One of such strategies is to generate bromine in situ by oxidation of bromide. The oxidizing agents and the bromide sources used for the purpose include HBr tert-butyldihydroperoxide (TBHP) [12], HBr/DMSO [13], BuOBr/Zeolite [14], NaBr/dimethyldioxirane [15], LiBr-(NH₄)₂S₂O₈ [16] and LDH-WO₄/H₂O₂/Br₂ [17] etc. In spite of such vast literature reports, the industrial applicability of such processes is restricted by the use of toxic
and expensive reagents/catalysts, volatile organic solvents, low yield, lack of regioselectivity and discharge of HBr waste [18-29].

Apart from such in situ generation of bromine, there are latent brominating reagents like N-bromosuccinimide for allylic bromination, 2,4,4,6-tetrabromo-2,5-hexadiene-1-one (TBCD) for the monobromination with para selectivity, but their preparation still needs use of elemental bromine [30-33].

Since early eighties, our group has been working on peroxo metal and non-metal chemistry where H\textsubscript{2}O\textsubscript{2} activated by various metals like V(\textsubscript{V}), Mo(\textsubscript{VI}), W(\textsubscript{VI}), Ti(\textsubscript{IV}) and non-metals like B, P, etc. are used. While trying to ligate bromide with peroxovanadates, we ended up with the isolation of tribromides (Br\textsubscript{3}) using organic ammonium cation. Subsequently, environmentally benign synthesis of new solid brominating agents by the reaction of V\textsubscript{2}O\textsubscript{5}, aqueous H\textsubscript{2}O\textsubscript{2} and KBr was reported [34]. In continuation of this work, subsequently we extended the use of this philosophy to the extraction of bromide from sea-water [35]. The versatility of the protocol is demonstrated with different organic counter cations [36] that modulate the properties of the tribromides. Until then, tribromide did not receive much attention, even though it is a greener alternative for hazardous bromine. However, thereafter, scientific workers realized their potentiality and now they find a respectable position in terms of their applicability as reagents as well as catalysts in various organic reactions [37-41].

Following the aforementioned strategy a series of (second generation) brominating reagents has been developed by our group which includes tetramethyl ammonium tribromide (TMATB), tetrabutyl ammonium tribromide (TBATB), tetraethyl ammonium tribromide (TEATB), cetyltrimethyl ammonium tribromide (CTMATB), pyridine hydrobromide perbromide (PHPB) and benzyltriethyl ammonium tribromide (BTEATB) [42]. A variety of brominations have also been carried out by us and others by using these reagents. Significantly, it was observed that less usual bromination, e.g. bromination of imidazoles has not been very successful with many of these tribromides. It was then considered worthwhile to develop newer organic ammonium tribromides with varying counter cations and study their reaction profiles focusing on such less usual bromainations.

Here in this thesis, two new tribromides, namely, terapropyl ammonium tribromide (C\textsubscript{12}H\textsubscript{28}NBr\textsubscript{3}, TPATB) and tetradecyldecyltrimethyl ammonium tribromide (C\textsubscript{17}H\textsubscript{39}NBr\textsubscript{3}, TDTMATB) have been introduced. These two tribromides have been characterized by a variety of physico-chemical analysis. Studies have been done on
the relative reactivity of the different tribromides that have been synthesized by us. Some less usual brominations have been observed with tetrapropylammonium tribromide (TPATB). The observed unusual reactivity of TPATB has been rationalized on the basis of density functional theory (DFT).

5C. 1 Experimental

a. General: All the reactions were conducted in oven-dried glassware. Reagents and solvents were used as purchased. All the products were recrystallized from acetonitrile. Melting points were recorded in a Büchi B-545 melting point apparatus and were uncorrected. $^1$H NMR and $^{13}$C NMR spectra were recorded on JEOL 400 MHz and Varian 400 MHz spectrophotometers. Chemical shifts are reported in (ppm) relative to TMS ($^1$H and $^{13}$C) internal standards. IR spectra were recorded in KBr with a Nicolet Impact 410 spectrophotometer. Elemental analyses were carried out on a Perkin-Elmer 2400 automatic carbon, hydrogen, nitrogen and sulfur analyzer. The X-ray data were collected at 293 K with Mo K$_\alpha$ radiation ($\lambda$= 0.71073Å) on a Bruker Nonius SMART CCD diffractometer equipped with graphite monochromater.

b. Computational details: All calculations were performed with the DMol3 program using BLYP functional and DNP basis set. The size of the DNP basis sets is comparable to that of the Gaussian 6-31G** basis sets, but this numerical basis set is more accurate than a Gaussian basis set of the same size. The Fukui functions were evaluated using Hirshfeld population analysis (HPA) and Mulliken population analysis (MPA) schemes. The integration grid referred to as FINE in the software program has been used for optimization of the complexes.

5C. 2 Synthesis of Tetrapropylammonium Tribromide (TPATB), (C$_3$H$_7$)$_4$NBr$_3$

Two different methods have been developed for the synthesis of TPATB

a. Method-I

In a typical synthesis, 0.03 g (0.16 mmol) of vanadium pentoxide, V$_2$O$_5$ was added to 3 mL (26.50 mmol) of 30% hydrogen peroxide, H$_2$O$_2$, taken in a pre-cooled 250 mL beaker (Care should be taken to maintain ice-cold condition as the reaction between V$_2$O$_5$ and H$_2$O$_2$ is exothermic). The reaction mixture was stirred
magnetically at 0-5 °C temperature in an ice-water bath till all the V$_2$O$_5$ dissolved and the solution became reddish-brown. A solution of 2.38 g (20 mmol) of potassium bromide, KBr and 2.66 g (10 mmol) of tetrapropylammonium bromide (TPAB) dissolved in 35 mL of water was added. To this, 40 mL of 1M sulphuric acid (H$_2$SO$_4$) was added in small portions. Magnetic stirring was continued for a further period of 2h at ice-water temperature. The product thus formed was isolated by suction filtration using Whatman No. 42 filter paper. The compound was then dried in a vacuum desiccator using anhydrous calcium chloride, CaCl$_2$, as desiccant. The product was obtained as bright yellow micro-crystals. The yield of the product was 4.5 g (88.3%). m.p. 120 °C.

b. Method-II

In a typical example molybdic acid monohydrate, H$_2$MoO$_4$·H$_2$O (0.16 mmol, 0.03g), potassium bromide, KBr, (20 mmol, 2.38 g) and tetrapropylammonium bromide (TPAB) (10 mmol, 2.66 g) were powdered separately, mixed together smoothly and thoroughly. The whole content was transferred to a boat kept on an ice-water bath and 30% hydrogen peroxide, H$_2$O$_2$ (26.50 mmol, 3 mL) was added drop wise with continuous grinding for 15 min, followed by drop wise addition of H$_2$SO$_4$ (1.55 mL, 10M). The whole was stirred smoothly with a glass rod for 10 min and then at room temperature for 30 min. An exothermic reaction set in to form orange-yellow crystalline tetrapropylammonium bromide (TPATB). The compound was dried over fused CaCl$_2$ and extracted with ethyl acetate by dissolving in a minimum amount of solvent followed by filtration through Whatman No. 42 filter paper. Aqueous phase, if present, could be removed using anhydrous sodium sulphate. The organic layer was concentrated to get yellow-orange TPATB, which was recrystallized from acetonitrile. Yield: 4.3 g (85.3%).

5C.3 Synthesis of Tetradecyltrimethylammonium tribromide (TDTMATB), C$_{17}$H$_{39}$NBr$_3$

a. Method-I

In a typical synthesis, 0.03 g (0.16 mmol) of vanadium pentoxide, V$_2$O$_5$ was added to 3 mL (26.50 mmol) of 30% hydrogen peroxide, H$_2$O$_2$, taken in a pre-cooled 250 mL beaker (Care should be taken to maintain ice-cold condition as the reaction between V$_2$O$_5$ and H$_2$O$_2$ is exothermic). The reaction mixture was stirred
magnetically at 0-5 °C temperature in an ice-water bath till all the \( V_2O_5 \) dissolved and the solution became reddish-brown. A solution of 1.85 g (15.5 mmol) of potassium bromide, KBr and 2.10 g (7.5 mmol) of tetradecyltrimethyl bromide (TDTMATB), dissolved in 35 mL of water was added. To this, 40 mL of 1M sulphuric acid (\( H_2SO_4 \)) was added in small portions. Magnetic stirring was continued for a further period of 2h at ice-water temperature. The product thus formed was isolated by suction filtration using Whatman No. 42 filter paper. The compound was then dried in a vacuum desiccator using anhydrous calcium chloride, CaCl\(_2\), as desiccant. The product was obtained as bright yellow micro-crystals. Yield 3.8 g (96.2 %). m.p. 67 °C

**b. Method-II**

In a typical example molybdic acid monohydrate, \( H_2MoO_4 \cdot H_2O \) (0.16 mmol, 0.03g), potassium bromide, KBr, (20 mmol, 2.38 g) and tetradecyltrimethylammonium tribromide (10 mmol, 2.80 g) were powdered separately, mixed together smoothly and thoroughly. The whole content was transferred to a boat kept on an ice-water bath and 30% hydrogen peroxide, \( H_2O_2 \), (26.5 mmol, 3 mL) was added drop wise with continuous grinding for 15 min, followed by drop wise addition of \( H_2SO_4 \) (15.5 mL, 1M). The whole was stirred smoothly with a glass rod for 10 min and then at room temperature for 30 min. An exothermic reaction set in to form orange-yellow crystalline tetradecyltrimethylammonium tribromide (TDTMATB). The compound was dried over fused CaCl\(_2\) and extracted with ethyl acetate by dissolving in a minimum amount of solvent followed by filtration through Whatman No.42 filter paper. Aqueous phase, if present, could be removed using anhydrous sodium sulphate. The organic layer was concentrated to get yellow-orange TDTMATB, which was recrystallized from acetonitrile. Yield: 3.3 g (64%).

### 5C.4 Typical Procedure for Bromination of Organic Substrates using TPATB

**a. Bromination of Styrene**

An amount of 0.10 g (1 mmol) styrene was taken in a rotary bottle, added 6 mL dichloromethane (DCM) and allowed to stir using magnetic stirrer and a magnetic needle. Then 0.46 g (2 mmol) of TPATB was added to the stirring solution. The reaction was allowed to stir at room temperature and the progress of the reaction was monitored by TLC. The reaction was allowed to stir for about 45 min. The product
was extracted with ethyl acetate. The extract was dried using anhydrous Na$_2$SO$_4$. Ethyl acetate was removed with the help of rotary evaporator and the residue was purified by column chromatography. The residue was run on silica gel of mesh 60-120 with 1% ethyl acetate-hexane to get the corresponding pure brominated product, 1-(1,2-dibromo)ethyl benzene in solution with the solvent mixture. Then solvent was removed using rotary evaporator to get solid product. The isolated yield of the product was \( \sim 100\% \) for this reaction (scheme-5.5).

![Scheme 5.5: Bromination of styrene by TPATB](image)

**Scheme 5.5:** Bromination of styrene by TPATB

![Scheme 5.6: Bromination of imidazole with TPATB](image)

**Scheme 5.6:** Bromination of imidazole with TPATB

### 5C. 5 Results and Discussion

Peroxometal based (V, Mo, W) oxidation of bromide to tribromide with H$_2$O$_2$ has lead to isolation of several tribromides, e.g. TMATB, TEATB, TPATB, TBATB, BTEATB, TDTMATB, and CTMATB [42]. Unlike traditional methods the use of bromine and HBr is completely avoided in their synthesis. Both solid and liquid phase syntheses of tribromides were developed to provide easy access to the commercially important organicammonium tribromides (OATB). The proposed mechanism of the reaction leading to OATB is depicted in scheme 5.7(a).

![Scheme 5.7: (a) Peroxo-metal catalyzed synthesis of OATBs (b) Crystals of TPATB](image)

**Scheme 5.7:** (a) Peroxo-metal catalyzed synthesis of OATBs (b) Crystals of TPATB
According to the proposed mechanism, VO$_2^+$, for example, serves as a functional mimic of VBrPO (vanadium bromoperoxidase) which coordinates with one or two equivalents of H$_2$O$_2$ in solution forming VO(O$_2$)$_2^+$ and/or VO(O$_2$)$_2^-$ species and both of them are capable of oxidizing bromide to HOBr $\rightleftharpoons$ Br$_2$ $\rightleftharpoons$ Br$_3^-$. The Br$_3^-$ thus formed can be isolated as organic ammonium tribromide. Alternatively, in presence of an appropriate organic substrate in the reaction the corresponding brominated product is formed.

The tribromides TBATB, BTEATB, CMTATB, TEATB, TMATB, TPATB and TDTMATB are all bright yellow or orange in color. Recrystallization from acetonitrile gives deep orange crystals (scheme-5.7 (b)). All of them have moderate to high solubility in the common organic solvents. The tribromides have a very long shelf life too. They remain stable for months. Organic ammonium tribromides are thus known as the store house of bromine. However, TEATB and TMATB are less stable than other tribromides. Their stability can be monitored by the determination of bromine contents periodically and recording melting points from time to time.

Solution electronic spectra of the tribromides show characteristic signature at ca. 265 nm with a shoulder at ca. 385 nm due to the transitions $\sigma-\sigma^*$ and $\pi-\pi^*$, respectively. The tribromides give values in the range 267–269 nm and 380–400 nm, (figures 5.3)[43,44].

**Figures 5.3:** UV-visible absorbtion of QATBs at around 267 nm and 380 nm
For a linear tribromide (Br$_3^-$), three vibrational modes, $\nu_{\text{sym}}$ ($\nu_1$), $\nu_{\text{asym}}$ ($\nu_3$) and bending ($\nu_2$) are expected in the far-IR region [45]. Of the three modes $\nu_1$ and $\nu_3$ occur at ca. 165 cm$^{-1}$ and ca. 195 cm$^{-1}$, respectively, while the bending mode $\nu_2$ generally appears at a far low value of ca. 50 cm$^{-1}$. In the present vibrational spectroscopic experiments $\nu_1$ and $\nu_3$ have been observed in the range 145–172 cm$^{-1}$ and 185–192 cm$^{-1}$ in complete agreement with those expected for a linear Br$_3^-$ species (figure 5.4, table 5.10). Unfortunately, owing to the instrumental limitations the region of the peak corresponding to $\nu_2$ mode (at ca. 50 cm$^{-1}$) could not be covered.

**Table 5.10:** Structurally significant IR and electronic spectral bands of tribromides

<table>
<thead>
<tr>
<th>Compounds (QATBs)</th>
<th>IR bands (cm$^{-1}$)</th>
<th>UV-visible ($\lambda$, nm) ($\varepsilon$, M$^{-1}$cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBATB (C$<em>{16}$H$</em>{36}$NBr$_3$)</td>
<td>171(s), 191(s)</td>
<td>267 (49000), 400 (150)</td>
</tr>
<tr>
<td>BTEATB (C$<em>9$H$</em>{16}$NBr$_3$)</td>
<td>156(s), 195(s)</td>
<td>268 (51000), 385 (152)</td>
</tr>
<tr>
<td>CTMATB (C$<em>{19}$H$</em>{42}$NBr$_3$)</td>
<td>152(s), 203(s)</td>
<td>269 (51500), 385 (155)</td>
</tr>
<tr>
<td>TEATB (C$<em>8$H$</em>{20}$NBr$_3$)</td>
<td>162(s), 192(s)</td>
<td>269 (52000), 390 (150)</td>
</tr>
<tr>
<td>TMATB (C$<em>4$H$</em>{12}$NBr$_3$)</td>
<td>146(s), 188(s)</td>
<td>269 (50500), 380 (149)</td>
</tr>
<tr>
<td>TPATB (C$<em>{12}$H$</em>{28}$NBr$_3$)</td>
<td>170(s), 191(s)</td>
<td>269 (51000), 385 (155)</td>
</tr>
<tr>
<td>TDTMATB (C$<em>{17}$H$</em>{39}$NBr$_3$)</td>
<td>153(s), 195(s)</td>
<td>268 (51500), 386 (150)</td>
</tr>
</tbody>
</table>

**Figure 5.4:** Representative far-IR spectra of TBATB, CTMATB and TMATB
Single crystal X-ray structures of TBATB, TPATB, BTEATB, TDTMATB, and CTMATB have been determined. The ORTEP diagrams of these tribromides are shown in figure 5.5. The crystal data and structure refinement results are incorporated in table 5.11. TBATB, TDTMATB and CTMATB crystallize in monoclinic system, whereas TPATB and BTEATB crystallize in triclinic and orthorhombic systems, respectively.

**Figure 5.5**: ORTEP diagrams of (a) TBATB (b) TPATB (c) TDTMATB (d) CTMATB and (e) BTEATB
Table 5.11: Crystallographic details of TPATB, TBATB, TDTMATB, CTMATB and BTEATB

<table>
<thead>
<tr>
<th>Crystal data</th>
<th>TBATB(1)</th>
<th>TPATB(2)</th>
<th>TDTMATB(3)</th>
<th>CTMATB(4)</th>
<th>BTEATB(5)</th>
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<td><strong>Formula</strong></td>
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<td>C₁₂H₂ₘNBr₃</td>
<td>C₁₇H₃₉NBr₃</td>
<td>C₁₉H₴₂NBr₃</td>
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<tr>
<td><strong>Formula weight</strong></td>
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<td>Monoclinic</td>
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<td>Orthorhombic</td>
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<td><strong>Space group</strong></td>
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<td>P2(1)/m</td>
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<td>7.495(4)</td>
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<tr>
<td><strong>R</strong></td>
<td>0.032</td>
<td>0.079</td>
<td>0.033</td>
<td>0.039</td>
<td>0.031</td>
</tr>
<tr>
<td><strong>wR2</strong></td>
<td>0.069</td>
<td>0.207</td>
<td>0.077</td>
<td>0.102</td>
<td>0.053</td>
</tr>
<tr>
<td><strong>GoF</strong></td>
<td>1.009</td>
<td>0.871</td>
<td>0.981</td>
<td>1.071</td>
<td>0.924</td>
</tr>
</tbody>
</table>

Tri bromides are known to be capable of bromination of organic substrates and do most of the job what molecular bromine does. It is expected that the counter cation of tribromide anion might change its reactivity, due to which number of tribromides have been synthesized with different cations (organic as well as inorganic). The variation in reactivity might have some relation with the bond angle (تحركات Br-Br-Br) and bond length (Br-Br). Moreover, cation like cetylammonium acts as a phase transfer agent in the reaction medium. The bond angles and Br-Br distances of these tribromides are summarized in table 5.12. Notably, TBATB shows equal bond lengths of two Br-Br bonds and a linear structure with ∠Br-Br-Br = 180°. Although the two
Br-Br bond distances are almost similar, the bond angle of BTEATB is 174.75°. In case of TPATB, TDTMATB, and CTMATB the bond angles are found to be 179.38°, 179.07° and 179.03°, respectively, which are close to linearity. The two Br-Br bond distances in TPATB, TDTMATB and CTMATB are not equal.

Table 5.12: Selected bond angles and bond lengths of tribromides

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TBATB</th>
<th>TPATB</th>
<th>TDTMATB</th>
<th>CTMATB</th>
<th>BTEATB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br1-Br2 (Å)</td>
<td>2.539</td>
<td>2.517</td>
<td>2.625</td>
<td>2.623</td>
<td>2.531</td>
</tr>
<tr>
<td>Br1-Br3 (Å)</td>
<td>2.539</td>
<td>2.530</td>
<td>2.467</td>
<td>2.462</td>
<td>2.539</td>
</tr>
<tr>
<td>Br2-Br1-Br3 (°)</td>
<td>180.000</td>
<td>179.380</td>
<td>179.030</td>
<td>179.070</td>
<td>174.750</td>
</tr>
</tbody>
</table>

![Figure 5.6](image)

**Figure 5.6:** Different weak interactions between H and Br in (a) TBATB (b) BTMATB and (c) CTMATB. Numbers of weak interactions and distances are depicted in the figure.

Apart from the differences in bond angles (\( \angle \text{Br-Br-Br} \)) and bond distances (Br-Br), several weak H-Br hydrogen bonding are observed from the single crystal structure (figure 5.6). The H-Br distance varies from 2.816Å to 3.017Å. This interaction
decreases the electron density on the bromine atom. The number of weak interactions in BTEATB is five while TDTMATB and CTMATB have three such weak interactions but TBATB and TPATB possess only two. The H-Br distances are comparatively shorter in BTEATB. Shorter H-Br distance implies a stronger hydrogen bonding interactions in case of BTEATB. From these observations we predict BTEATB to be the most reactive tribromide in the group.

5C. 6 Some representative examples of bromination with organic ammonium tribromide

Tribromide has already been exploited as an alternative to elemental bromine. These reagents have been gaining remarkable popularity in organic transformations not only as reagent but also as catalyst [46-50]. Several reactions other than bromination have also been reported in literature.

As we mentioned earlier that reactivity of tribromides might be tailored by changing the counter cation. Hence, a comparative study of different tribromides has been done in terms of yield towards bromination of organic substrates. The results that we have obtained are shown in table 5.13.

Table 5.13: Comparative study of various tribromides towards bromination of organic substrates

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Reagent</th>
<th>Sub: TB</th>
<th>Time</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
</table>
| ![](N\H) | TMATB | 1:1 | 3 h | ![Monobrominated imidazole is obtained when TPATB used as brominating reagent](Br Br)
<p>| TEATB | 1:1 | 3 h |
| TBATB | 1:1 | 4 h |
| CTMATB | 1:1 | 3 h |
| BTEATB | 1:1 | 1 h |
| TPATB | 1:1 | 1.5 h |
| TDTMATB | 1:1 | 1 h |
| <img src="N%5CH" alt="" /> | TMATB* | 1:1 | 15 min |
| TEATB* | 1:1 | 45 min |
| TBATB | 1:1 | 2 h |
| CTMATB | 1:1 | 4.5 h |
| BTEATB | 1:1 | 30 min |
| TPATB | 1:1 | 1.5 h |
| TDTMATB | 1:1 | 45 min |</p>
<table>
<thead>
<tr>
<th>Substrate</th>
<th>TMATB</th>
<th>TEATB*</th>
<th>TBATB</th>
<th>CTMATB</th>
<th>BTEATB</th>
<th>TPATB</th>
<th>TDTMATB</th>
<th>Time (h)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenol</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>5 h</td>
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<td>94</td>
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<tr>
<td>Aniline</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
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<td>1:1</td>
<td>1:1</td>
<td>20 min</td>
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<tr>
<td>Imidazole</td>
<td>1:1</td>
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<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>4.5h</td>
<td>67</td>
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</tbody>
</table>

*M.Examples are drawn from U. Borah, PhD thesis, IITG, Sub= Substrate, TB= Tribromide

From the table 5.13 it is interesting to note that unlike other tribromides, TPATB shows some regioselectivity towards the bromination of organics. The most striking result is the monobromination of imidazole.

Monobromination of imidazole is a very important and difficult task to achieve because bromination of imidazole by Br₂ gives 2,4,5-tribromo imidazole in presence of chloroform, dichloroethane, etc. as solvent [51]. Monobromination and dibromination of imidazole are very difficult. It has been reported that reaction of imidazole and 4(5)-substituted imidazole with Br₂ or NBS did not give brominated
product and undergo oxidative degradation of heterocyclic ring. The products formed are ammonia, glyoxal (or the corresponding substituted dioxal) (scheme 5.8). The ring degradation of imidazole with bromine is shown below [52].

Scheme 5.8: Ring degradation of imidazole in presence of elemental bromine

Mono and dibromoimidazole are generally obtained by debromination of tribromo imidazole by tetramethylammonium fluoride (TMAF) in aprotic solvent [53] (scheme 5.9). However, this process is an indirect one and rather lengthy, and the yield is less. Hence direct mono- and dibromination is desirable.

Scheme 5.9: Debromination of tribromo imidazole

Scheme 5.10: Bromination of phenol by various tribromides
Apart from imidazole, regioselectivity is also observed in the bromination of activated aromatics like phenol and aniline (table 5.13).

While trying to brominate activated aromatics like aniline or phenol with organic ammonium tribromides we observed the formation of a mixture of mono-, di- and tri- brominated products (schemes 5.10 and 5.11). However, maintaining the substrate:tribromide stoichiometry at 1:1 regioselectivity could be achieved to some extent (table-5.13). Interestingly, when TPATB was used as the brominating reagent high degree of $p$-selectivity was observed. The high regioselectivity observed in case of TPATB renders it as important brominating reagent in the organic synthesis. It may be noted, direct $p$-selectivity could not be achieved for the activated aromatics like aniline and phenol by simple brominating reagents. Traditional method involves the derivatization of such activated aromatics e.g. acetylation of aniline to the corresponding acetonilide to achieve para selectivity. Such derivatization is not desirable from the “green chemistry” point of view.

To expand the scope of TPATB as brominating reagent a number of reactions were conducted. The specific molar ratios of substrates, reagents, solvent used along with the reaction conditions and percentage yield of the corresponding products are given in table 5.14.
Table 5.14: Application of TPATB as a brominating reagent for the bromination of various organic substrates

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Substrate: TPATB</th>
<th>Reaction condition</th>
<th>Time</th>
<th>Product</th>
<th>% yield&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>OH</td>
<td>1:1</td>
<td>RT, CH$_3$CN</td>
<td>45 min</td>
<td><a href=""><img src="" alt="Bromo-substituted benzene" /></a></td>
<td>85%</td>
</tr>
<tr>
<td>OH</td>
<td>1:1</td>
<td>RT, CH$_3$CN</td>
<td>40 min</td>
<td><a href=""><img src="" alt="Bromo-substituted naphthalene" /></a></td>
<td>87%</td>
</tr>
<tr>
<td>NH$_2$</td>
<td>1:1</td>
<td>RT, CH$_3$CN</td>
<td>2.5h</td>
<td><a href=""><img src="" alt="Bromo-substituted aniline" /></a></td>
<td>89%</td>
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</tbody>
</table>

<sup>a</sup> Yields are given on the basis of the starting material (TPATB) and not the isolated product.
Since all the tribromides that we have synthesized so far are similar from the structural point of view, hence there must be an electronic factor that might be responsible for the reactivity difference, as observed. To rationalize the reactivity of the different tribromides we took help of the density functional theory (DFT) method, which is elaborated in the next section.

5C. 7 Theoretical investigations

DFT has played an important role in determining structure and reactivity of chemical compounds [54-57]. The global reactivity descriptors namely, global hardness ($\eta$), global softness ($S$), electronegativity ($\chi$), chemical potential ($\mu$) and electrophilicity index ($\omega$) introduced within the context of conceptual DFT represent properties of a molecule as a whole [58- 60]. Other type of descriptors are local reactivity descriptors such as local softness ($s(\gamma)$), Fukui functions ($f(\gamma)$) etc., which have attracted considerable interests to describe the relative reactivity and site
selectivity in chemical reactions [60, 61]. Fukui functions, \( f^+_k \) and \( f^-_k \), are evaluated to locate the electrophilic and nucleophilic sites, respectively. In most cases these are found to be successful in explaining experimentally observed trends of reactivity. However, in some systems, atom with high electrophilicity i.e. having higher value of \( f^+_k \) may also show high nucleophilicity i.e. having higher value of \( f^-_k \). Then their ratios ‘relative electrophilicity’\(( f^+_k / f^-_k \)\), and ‘relative nucleophilicity’\(( f^-_k / f^+_k \)\), expresses the reactivity of atoms in molecules in a better way. We have calculated local reactivity descriptors namely, Fukui functions \( f^+_k \) and \( f^-_k \) and their ratio, the relative nucleophilicity \(( f^-_k / f^+_k \)\) of the bromine atoms of the tribromide molecules to derive their reactivity sequence [62].

The calculated global reactivity descriptors of the tribromide molecules are given in table 5.15. It is seen that the global softness value for BTEATB is maximum indicating the highest reactivity of this reagents among the tribromides. The global softness value represents how soft is a molecule towards and incoming electrophile or a nucleophile. However, the global parameters cannot provide the sites (atoms) which take part in chemical reaction. In order to determine the active sites of the complexes we calculated the Fukui functions \(( f^+, f^- \)\) and relative nucleophilicity of each atom of the tribromides. The Fukui function value of ‘electrophilic attack on the system’ of the compounds is shown in figure 5.7. In table 5.16 we present the average Fukui function and relative nucleophilicity values of Br atoms. The relative nucleophilicity values confirm that the BTEATB is the most reactive and TPATB is the least reactive tribromide in the series.

**Table 5.15:** Energy values of HOMO, LUMO, HOMO-LUMO gap and global reactivity descriptors, chemical hardness and softness of tribromides

<table>
<thead>
<tr>
<th>MOLECULE</th>
<th>( E_{\text{HOMO}} ) au</th>
<th>( E_{\text{LUMO}} ) au</th>
<th>( E_{\text{HOMO-LUMO}} ) au</th>
<th>HARDNESS au</th>
<th>SOFTNESS au</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBATB</td>
<td>-0.145</td>
<td>-0.049</td>
<td>0.096</td>
<td>0.048</td>
<td>10.422</td>
</tr>
<tr>
<td>BTEATB</td>
<td>-0.151</td>
<td>-0.071</td>
<td>0.080</td>
<td>0.040</td>
<td>12.493</td>
</tr>
<tr>
<td>CTMATB</td>
<td>-0.151</td>
<td>-0.055</td>
<td>0.096</td>
<td>0.048</td>
<td>10.432</td>
</tr>
<tr>
<td>TDTMATB</td>
<td>-0.139</td>
<td>-0.054</td>
<td>0.084</td>
<td>0.042</td>
<td>11.870</td>
</tr>
<tr>
<td>TPATB</td>
<td>-0.162</td>
<td>-0.067</td>
<td>0.095</td>
<td>0.048</td>
<td>10.516</td>
</tr>
</tbody>
</table>
Table 5.16: The average Fukui function and relative nucleophilicity values of Br atoms of the complexes

<table>
<thead>
<tr>
<th>Molecule</th>
<th>$f^-$</th>
<th>$f^+$</th>
<th>$f^+/f^-$</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBATB</td>
<td>0.39</td>
<td>0.33</td>
<td>0.86</td>
</tr>
<tr>
<td>BTEATB</td>
<td>0.32</td>
<td>0.15</td>
<td>0.46</td>
</tr>
<tr>
<td>CTMATB</td>
<td>0.35</td>
<td>0.33</td>
<td>0.95</td>
</tr>
<tr>
<td>TDTMATB</td>
<td>0.10</td>
<td>0.10</td>
<td>1.02</td>
</tr>
<tr>
<td>TPATB</td>
<td>0.32</td>
<td>0.03</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Figure 5.7: Graphical representation of the Fukui function value for ‘nucleophilic attack on the system’ derived from DFT/GGA/BLYP calculations

5C. 8 Conclusions
In summary, we have reported the synthesis, structure and properties of structurally diverse OATBs. Two synthetic methods for organic ammonium tribromide are described in this chapter. For small scale synthesis, both the methods are effective to get organic ammonium tribromides. However first (Method-I) is preferable for large
scale synthesis of OATBs. The reactivities of TBATB, TPATB, TMATB, CTMATB and BTEATB have been compared. The experimental results are well supported by DFT calculations. BTEATB is found to be more reactive than others OATBs in the series. Both structural and the electronic parameters conforms the high reactivity of the BTEATB. Remarkably, selective p-bromination of activated aromatics e.g. phenol, aniline are achieved by using TPATB as the brominating reagent. Unlike the other tribromides that we have synthesized so far TPATB shows some unusual reactivity towards the bromination of activated aromatics. The most exciting result that was observed using TPATB is the selective monobromination of imidazole. Density functional theory (DFT) implies TPATB to be the least reactive tribromide in the series. Less reactivity of TPATB might be the region behind the selectivity that we observe during bromination of organics. Most interesting aspect of our study is that the important role played by the intermolecular hydrogen bond in determining reactivity of tribromides. Stronger intermolecular hydrogen bonding interaction possible in case of BTEATB decreases electron density over the corresponding Br$_3^-$, makes it facile to release Br$^+$. 
5C. 9 Physical and Spectral data

4-Bromo-phenol

Oily liquid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 5.03 (brs, 1H), 6.70 (d, $J$=8.8 Hz, 2H), 7.30 (d, $J$=7.6 Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 113, 117.4, 133.2, 154.4

4-Bromo-aniline

Greenish solid. m.p: 58-62 °C

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 3.65 (brs, 2H), 6.56 (d, $J$=8 Hz, 2H), 7.24 (d, $J$=6.4 Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 110.3, 116.8, 132.1, 145.5.

(1,2-Dibromo-ethyl)-benzene

White solid. m.p. 71-73 °C

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 4.02-4.07 (m, 2H), 5.12-5.15 (t, 2H), 7.36-7.40 (m, 5H)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 35.09, 50.94, 127.7, 128.9, 129.28, 138.69
9-Bromo-anthracene

Yellow solid: m.p. 96-100 °C
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.50-7.53 (t, 2H), 7.58-7.62 (t, 2H), 7.98-8.0 (d, $J$=8, 2H), 8.44(s, 1H), 8.507-8.509 (d, $J$=13.2, 2H)
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 122, 125.72, 127.18,127.26,127.71,128.68,130, 132

1-Bromo-naphthalen-2-ol

Black Solid. m.p.: 79-80 °C
$^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 7.23-7.25 (d, $J$=8, 1H), 7.26-7.28(t, 1H), 7.45-7.47(t, 1H),7.75-7.79 (m, 2H), 7.95-7.98 (d, $J$=12,1H ), 10.49 (brs, OH)
$^{13}$C NMR (100 MHz, DMSO-d$_6$):$\delta$ 104.79, 118.82, 123.96, 125.26, 128.27, 128.75, 129.17, 129.42, 152.92, 206.99

4,5-Dibromo-1-methyl-1H-imidazole

White solid. m.p: 74-78 °C
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.57 (s. 1H), 3.65 (s, 3H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 137.85,116.36,104.75,34.18
2-Bromo-1H-imidazole

White solid. m.p: 197-202 °C

$^1$H NMR (400MHz, CDCl$_3$): $\delta$ 7.25 (s, 1H), 7.6 (s, 1H), 12.35 (bs, 1H)

$^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ 116.18, 114.00, 136.43

(2-Bromo-imidazol-1-yl)-(4,5-dibromo-imidazol-1-yl)-methanone

White solid. m.p: 120-124

$^1$H NMR (400 MHz, DMSO-d6): $\delta$ 8.26 (s, 1H), 7.28 (s, 2H)

$^{13}$C NMR (100 MHz, DMSO-d6): $\delta$ 109.21,121.16,135.33
**Image 32:** $^1$H NMR spectrum of (1,2-Dibromo-ethyl)-benzene

**Image 33:** $^{13}$C NMR spectrum of (1,2-Dibromo-ethyl)-benzene
**Image 34:** $^1$H NMR spectrum of 9-bromoanthracene

**Image 35:** $^{13}$C NMR spectrum of 9-bromoanthracene
Image 36: $^1$H NMR spectrum of 2-Bromo-1H-imidazole

Image 37: $^{13}$C NMR spectrum of 2-Bromo-1H-imidazole
Image 38: $^1$H NMR spectrum of (2-Bromo-imidazol-1-yl)-(4,5-dibromo-imidazol-1-yl)-methanone

Image 39: $^{13}$C NMR spectrum of (2-Bromo-imidazol-1-yl)-(4,5-dibromo-imidazol-1-yl)-methanone
Image 40: $^1$H NMR spectrum of TPATB

Image 41: $^{13}$C NMR spectrum of TPATB
Image 42: $^1$H NMR spectrum of TDTMATB

Image 43: $^{13}$C NMR spectrum of TDTMATB
5C. 10 References


