Synergism of ionic liquid and microwave towards metal-free activation of H₂O₂ for oxidation of benzyl alcohols

2.1 Introduction:
Oxidation reactions belong to the repertoire of organic chemistry [Lenoir (2006); Memeo et al. (2011)]. In conventional terms, it is defined as either the addition of oxygen atom or the removal of hydrogen atom. In electronic terms, it is the removal of electrons from an organic/inorganic system. Among various types of oxidation reactions, oxidation of alcohols (Figure 1) is a fundamental organic transformation widely used in synthetic organic chemistry [Hudlicky (1990); Larock (1999); Smith and March (2001); Sharma (2010)] because of the utility of ensuing carbonyl compounds in pharmaceuticals, dyes, fragrances, industrially important chemicals and natural products [Singh et al. (1979); Pybus and Sell (1999)].

2.2 Traditional oxidants for oxidation of alcohols:
Traditional methods for the oxidation of alcohols involve use of expensive stoichiometric/super-stoichiometric amounts of metallic oxidants notably chromium based reagents (such as PCC, PDC etc) [Lee and Spitzer (1970); Cainelli and Cardillo (1984); Muzart (1992)], permanganates [Regen and Koteel (1977); Menger and Lee (1981)], ruthenium (VIII) oxide [Berkowitz and Rylander (1958); Griffith (1992)] etc. These reagents are often toxic, have poor atom efficiency and produce undesirable amount of noxious heavy metal waste.

2.3 Green chemistry context: Use of green oxidants, ionic liquids and metal-free protocols:
From economical and environmental viewpoints, the development of various catalytic oxidation protocols that use clean, inexpensive terminal oxidants, such as molecular oxygen (O₂) or hydrogen peroxide (H₂O₂) remains an important pursuit. In this context, significant
progress has been made in the field of transition metal catalyzed oxidations [Gamez et al. (2003); Zhu et al. (2008)] particularly utilizing H₂O₂ as green oxidant. Further, in milieu of green chemistry use of ionic liquids (ILs), microwave (MW) besides metal-free approaches for oxidation reactions are being increasingly explored which are discussed in details as below:

2.3.1 Transition metal catalyzed oxidation with H₂O₂:

H₂O₂ is an ecologically sustainable green oxidant [Martin et al. (2006)] with high oxidation potential and water as the only by-product. However, oxidation with H₂O₂ requires prior catalysis due to poor leaving tendency of the hydroxide ion. Consequently, a number of transition metal based catalysts, notably complexes of Mo and W have been studied for the activation of H₂O₂.

For instance, Na₂WO₄ in conjunction with a phase-transfer catalyst (PTC) bearing HSO₄ group has been utilized as an efficient catalytic system for H₂O₂ assisted oxidation of alcohols into ketones under organic/aqueous biphasic conditions (Scheme 1) [Sato et al. (1997)].

![Scheme 1](image)

Similarly, number of reports on the use of sandwich type-polyoxometalates complexes of Mo and W (such as [PV₂Mo₁₀O₄₀]⁵⁻, [ZnWZn₂(H₂O)₂(ZnW₉O₃₄)]¹²⁻, Na₁₂[WZn₃(H₂O)₂][(ZnW₉O₃₄)] etc) for H₂O₂ assisted oxidation of a wide range of alcohols have been furnished in literature [Daniel and Neumann (2003); Rozner et al. (2004); Vasylyev and Neumann (2004)]. However, most of these homogeneous catalysts were used along with halogenated solvents. Ingle et al. reported a [SbW₉O₃₃]-based polyoxometalate complex for selective oxidation of a variety of alcohols with aqueous H₂O₂ in the absence of any organic solvent [Ingle et al. (2007)]. The method has provided the selective oxidation of allylic alcohols over epoxidation reaction.

In another instance, H₂O₂ assisted oxidation of alcohols in the presence of quaternary ammonium decatungstate catalyst (hexadecyl trimethyl ammonium decatungstate) has been reported (Scheme 2) [Guo (2004)].
Lin et al. achieved the activation of \( \text{H}_2\text{O}_2 \) over tetra-alkylpyridinium octamolybdate catalysts (Scheme 3) [Lin and Zhen (2007)].

Likewise, Hida et al. reported almost a neutral system (pH = 6.5) for the oxidation of alcohols to corresponding carbonyls. The reaction was carried out in \( N,N \)-dimethylacetamide (DMA) using \( \text{H}_2\text{O}_2 \) and a catalytic amount of \( \text{Na}_2\text{WO}_4 \) along with \( \text{Na}_2\text{HPO}_4 \) (Scheme 5) [Hida and Nogusa (2009)].
The above developed neutral reagent system was further applied for the oxidation of hydroxyl group of oleanolic acid (Scheme 6) [Hida et al. (2010)]. It was observed that use of various other oxidizing agents such as Ca(OCl)₂/acetic acid or Swern oxidation etc proved futile for this oxidation.

![Scheme 6](image)

In a recent report, H₂O₂-assisted oxidation of alcohols to carbonyls has been carried out by using a polymeric phosphotungstate catalysts bearing a poly(ethylene oxide-pyridinium) matrix [Yamada et al. (2010)]. This method provided the chemoselective oxidation of secondary alcohols in the presence of primary alcohols (Scheme 7).

![Scheme 7](image)

2.3.2 Transition metal catalysed oxidation with H₂O₂ under microwave:

MW assisted synthesis of organic compounds is beneficial in terms of shortening the reaction time besides improvement in the yield and selectivity as mentioned earlier in the introduction section 1.4.5.1.2 (page 21). Bogdal et al. described an efficient MW induced method for oxidation of alcohols [Bogdal and Lukasiewicz (2000)] using 30% aqueous H₂O₂ and Na₂WO₄ as a catalyst (Scheme 8).

![Scheme 8](image)
Similarly, Varma et al. [Varma and Dahiya (1998)] reported the oxidation of alcohols under MW irradiation using claycop [copper (II) nitrate on clay]-H₂O₂ as catalytic system. In another instance, combination of MW and H₂O₂ has also been explored for the oxidation of some arenes using tungstoboric acid as catalyst (Scheme 9) [Lukasiewicz et al. (2006)].

![Scheme 9]

One of the common drawbacks encountered with H₂O₂ mediated oxidation in aqueous medium is catalyst/product separation besides the need of organic co-solvent or phase transfer catalyst [Ingle et al. (2007)]. In this context, various oxidation methodologies using ILs as reaction media (without use of organic solvent) have been developed as described below:

### 2.3.3 Transition metal catalysed oxidation with H₂O₂ in ionic liquids:

The strong interest in ILs for catalyzed reaction is because of efficient immobilization of the catalysts in the IL resulting in recycling of the catalyst/solvent [Muzart (2006)]. Furthermore, ILs have a rate acceleration effect on some catalytic reactions, and they are often considered as green alternatives to volatile organic solvents although their toxicity and biodegradability are yet to be fully determined [Aggarwal et al. (2002); Wilkes (2004)]. However, it has been realized so far that most ILs in use are stable to oxidation and thus provide ideal solvents for oxidation processes. Consequently, various catalytic methodologies utilizing ILs have been developed [Muzart (2006)] for the oxidation of alcohols and various other substrates (such as benzaldehydes and phenols) as mentioned below:

#### 2.3.3.1 Oxidation of alcohols with H₂O₂ in ionic liquids:

Chhikara et al. [Chhikara et al. (2005a)] disclosed the H₂O₂ assisted oxidation of aliphatic and benzylic alcohols in ionic liquid [C₄mim]BF₄ using a novel catalyst [C₄mim]₄[W₁₀O₃₃]. The catalyst was prepared by the reaction of [C₄mim]Br with sodium tungstate in aqueous HCl (Scheme 10). Primary aliphatic alcohols were not oxidized under developed conditions therefore allowing the selective oxidation of 1-phenyl-1,2-diethanol. The developed catalytic system has been successfully reused for five consecutive cycles.
Further, \([\text{C}_4\text{mim}]_3[\text{PO}_4(W(O)(O_2)_2)_4]\) metal catalysts was prepared by the reaction of \([\text{C}_4\text{mim}]\text{Br}\) with tungstate ion [Chhikara et al. (2005b)]. The oxidation of secondary alcohols (aliphatic and benzylic) to ketone was conducted with this catalyst and \(\text{H}_2\text{O}_2\) in \([\text{C}_4\text{mim}]\text{BF}_4\) ionic liquid (Scheme 11).

In another report, \(\text{H}_2\text{O}_2\) has been used for the oxidation of benzhydrol and 1-phenylethanol using methyltrioxorhenium \(\text{CH}_3\text{ReO}_3\) (MTO) based complexes in \([\text{bmim}]\text{PF}_6\) [Bianchini et al. (2005)]. Out of various complexes of MTO screened for above oxidation, the best results have been achieved using microencapsulated catalyst i.e. 2PS-Re (Scheme 12).
In a similar approach, Jain et al. reported the H$_2$O$_2$ assisted oxidation of secondary alcohols to the corresponding ketones in [bmim]BF$_4$ using MTO along with NaBr (Scheme 13) as catalytic system [Jain et al. (2006a)].

![Scheme 13](image)

Kumar et al. investigated the biomimetic oxidation of veratryl alcohol using H$_2$O$_2$ as oxidant. An iron (III) porphyrin complex (Scheme 14) was used as a catalyst and the reaction was carried out in [bmim]PF$_6$ [Kumar et al. (2007)]. The above complex showed better catalytic activity when compared with the enzyme horseradish peroxidase (HRP).

![Scheme 14](image)

Moreover, combination of IL and MW for the oxidation of alcohols using KIO$_4$ as oxidant has been utilized [Hajipour et al. (2006)].

### 2.3.3.2 Oxidation of benzaldehydes and phenols with H$_2$O$_2$ in ionic liquids:

Aromatic aldehydes have been oxidised using MTO/H$_2$O$_2$ in [bmim]BF$_4$ [Bernini et al. (2005)]. Thus, it was observed that benzaldehydes possessing electron-releasing group at meta position mainly led to the formation of corresponding acids, whereas, in case of ortho or para substituted benzaldehyde (particularly in case of hydroxy substitution) Dakin product i.e. phenol rather than acid was isolated as the major compound (Scheme 15).
Further, the above catalytic system (MTO/H₂O₂) in [bmim]BF₄ was used for the oxidation of alkylated phenol derivatives into corresponding 1,4-benzoquinones in good yield (Scheme 16). Various synthesized quinone derivatives were also tested in vitro for their antifungal activity against soil fungi and some of them were found to be potent inhibitors of Fusarium sp. [Bernini et al. (2006)].

Though, many of these methods appear to have broad synthetic utility yet from the green chemistry perspective there is a still room for improvement. Limitations such as use of toxic and expensive metals, halogenated solvents, laborious work-up procedures and generation of huge amount of metal waste add to the constraints of such processes. Moreover, the need to develop metal-free transformation is strongly felt in the pharmaceutical industry [Caron et al. (2006)]. In this direction, significant attempts have been made towards the development of transition metal-free oxidation protocols.

2.3.4 Transition metal-free oxidation approaches:
Increasing emphasis on the use of transition metal-free catalysts has led to the development of several metal independent oxidation protocols which include β-CD/NaOCl [Ji et al. (2005)], KI/I₂/K₂CO₃ [Gogoi and Konwar (2005)], TBA-OX [Lei et al. (2006)], HBr/H₂O₂ [Jain et al. (2006b)], I₂/hv [Farhadi et al. (2006)], NBS/NH₄Cl [Jain and Sain (2006)], HIO₄/KBr [Zolfigol et al. (2007)] etc. Of particular interest in metal-free oxidations are catalytic systems involving hypervalent iodine [Uyanik et al. (2009); Uyanik and Ishihara (2009)] and TEMPO (2,2,6,6-tetramethylpiperidine N-oxyl) [Sheldon and Arends (2004);
Karimi *et al.* (2007)] based systems. Recently, TEMPO in combination with non-metallic oxidants or H$_2$O$_2$ and O$_2$ [Liu *et al.* (2004; 2005); Herrerías *et al.* (2006); Karimi *et al.* (2007); He *et al.* (2009)] is gaining lot of attention for oxidation of alcohols. Furthermore, to address the recyclability and environmental issues related to expensive TEMPO, various methodologies using supported-TEMPO catalysis [Jiang and Ragauskas (2005); Karimi *et al.* (2007)] have been devised. For instance, Jiang *et al.* reported the catalytic oxidation of benzylic alcohols with H$_2$O$_2$ and hydrobromic acid (HBr) in [bmim]PF$_6$ using acetamido-TEMPO as a recyclable metal-free catalytic system (Scheme 17) [Jiang and Ragauskas (2005)].

![Scheme 17](image)

Recently, Karimi *et al.* disclosed ionic liquid ([bmim]Br) supported TEMPO as a recyclable catalytic system for the transition-metal-free aerobic oxidation of alcohols to aldehydes and ketones [Karimi and Badreh (2011)].

Similarly, hypervalent iodine based reagents such as Dess-Martin periodinane (DMP) or o-iodoxybenzoic acids (IBX) have been extensively studied for the oxidation reactions [Uyanik and Ishihara (2009)]. Yadav *et al.* reported a process for the oxidation of alcohols in hydrophilic [bmim]BF$_4$ and hydrophobic [bmim]PF$_6$ ionic liquids at room temperature with IBX or with DMP. It was observed that oxidations occurred at faster rate in these ILs as compared to conventional solvents like DMSO, DMF, EtOAc and H$_2$O. Moreover, the ILs could be recycled in subsequent reactions with consistent activity [Yadav *et al.* (2004)]. Qian *et al.* disclosed an ionic liquid supported hypervalent iodine reagent system (1-(4-diaceatoxyiodobenzyl)-3-methylimidazolium tetrafluoroborate) for effective oxidation of alcohols to carbonyl compounds (Scheme 18) [Qian *et al.* (2005)]. The above oxidation was performed using ionic liquid [emim]BF$_4$ as reaction media.
In view of the above literature precedents, it would be apparent that a majority of the prevalent oxidation approaches employ harsh oxidants/conditions besides transition metal catalysts. Although there have been noteworthy efforts to devise more benign oxidation conditions with various improvements using green oxidant H$_2$O$_2$ and ILs, however, these have also been found to be constrained by an indispensable usage of either transition metal catalysts or use of complicated ligands which are sometimes not commercially available or require multiple steps for their synthesis. On the other hand, various metal-free approaches mainly employ oxidants such as TEMPO or hypervalent iodine based reagents. However, the utility of TEMPO mediated systems is compromised due to constraints like expensive nature [Jiang and Ragauskas (2005); Mannam et al. (2007); He et al. (2009)], functional group tolerance and lengthy work up procedures especially when the reactions are run on large scale. On the other side, hypervalent iodine based reagents may be potentially explosive. In this context, it would be highly desirable if a mild and metal-free methodology for the oxidation of alcohols using green oxidant H$_2$O$_2$ and ILs could be devised in short reaction time.

2.4 Results and Discussion:
We were intrigued by the possibility of exploring room temperature ILs and green oxidant H$_2$O$_2$ for the oxidation of benzylic alcohols to carbonyls without any metal catalyst. Consequently, 4-methoxyphenyl-1-propanol (1a) was irradiated under MW (optimized condition; 120°C and 150W) with [hmim]Br (Table 1, entry 1) in the presence of 30% aqueous H$_2$O$_2$ for 10 min. We observed the metal-free oxidation and 4-methoxyphenyl propanone (1b) was obtained in 72% isolated yield along with starting 1a. In our efforts to further increase the yield, the effect of various ILs on the oxidation of 1a was studied (Table 1). Thus, we found that, apart from [hmim]Br, [bmim]Br (Table 1, entry 2) was able to provide 1b in a 70% isolated yield. On the contrary, [bmim]Cl (entry 3) gave 1b in 42% yield along with over oxidation leading to 4-methoxybenzaldehyde (12%), 4-
methoxybenzoic acid (12%) and other side products. Similar result was obtained with [bmim]BF₄ (entry 4) as 1b was obtained in 46% yield along with 4-methoxybenzaldehyde (17%) and 4-methoxybenzoic acid (13%). Surprisingly, no product formation was noticed with [bmim]PF₆ (entry 5) whereas in acidic ionic liquid [Hmim]pTSA (entry 6), 1b was obtained in low yield (6%) due to some complex formation (poor recovery after work up) with 1a and formation of unexpected 4-methoxyphenol (27% yield). On the other hand, moderate conversion (1b in 25% yield) was achieved with basic ionic liquid [bmim]OH (entry 7).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ionic liquid</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[hmim]Br</td>
<td>10</td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td>[hmim]Br</td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>[bmim]Cl</td>
<td>10</td>
<td>42</td>
</tr>
<tr>
<td>4</td>
<td>[bmim]BF₄</td>
<td>10</td>
<td>46</td>
</tr>
<tr>
<td>5</td>
<td>[bmim]PF₆</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>[Hmim]pTSA</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>[bmim]OH</td>
<td>15</td>
<td>25</td>
</tr>
<tr>
<td>8</td>
<td>[hmim]Brᵤ</td>
<td>8</td>
<td>83 (89)</td>
</tr>
<tr>
<td>9</td>
<td>MImᵥ</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>10</td>
<td>DMSOᵤ</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>[hmim]Brᵤ</td>
<td>2 h</td>
<td>68</td>
</tr>
</tbody>
</table>

*CEM monomode microwave; General conditions: 0.6 mmol of 1a, 0.5 g ionic liquid, 30% H₂O₂ (1ml), 150W, 120°C; Isolated yield; Yield based on GC-MS; Amount of ionic liquid increased from 0.5 g to 1 g; 1 ml of 1-methylimidazole was used in place of ionic liquid; 1 ml of DMSO was used in place of ionic liquid; Conventional heating oil bath (120°C) using [hmim]Br (1 g).

Encouraged by the above result with [hmim]Br and our quest to further increase the yield of 1b, we explored various other options. However, further optimization using different combinations of temperature, time, power and percentage of H₂O₂ (15, 20 and 30%) proved futile to improve the reaction performance. Subsequently, a combination of IL cocktailed...
with organic solvents such as PEG, DMSO, THF, DMG etc were tried but none of them was found suitable to enhance the yield of 1b. Till this stage we were hesitant to increase the amount of IL as it might divert the reaction path towards arylalkene formation via dehydration with IL [Kumar et al. (2008)] instead of oxidation. However, our presumption proved wrong when treatment of 1a with increased amount of [hmim]Br (1 g in place of 0.5 g) in H2O2 not only provided the desired 1b in isolated 83% yield (89% yield on GC-MS basis, Table 1, entry 8) but also reduced the reaction time to 8 min under same reaction conditions (150W, 120°C). These optimized conditions were found critical as any further increase either in the amount of IL or reaction temperature led to the formation of some dehydrated product. Curiously, replacement of the IL with 1-methylimidazole (Table 1, entry 9) as solvent gave only 17% yield of 1b, whereas the reaction using DMSO (Table 1, entry 10) did not proceed at all even after prolonged MW irradiation.

In order to ascertain the synergism of [hmim]Br and MW for H2O2 activation, 1a was stirred in the presence of [hmim]Br-H2O2 at room temperature (without MW) for five days whereby 1b was obtained only in 3% yield (GC-MS basis). Similarly, reaction in H2O2 under MW without using [hmim]Br did not show any conversion into 1b (Scheme 19).

Moreover, conventional refluxing for 2 h (oil bath, 120°C) using [hmim]Br-H2O2 provided the desired product in lower yield (68%, Table 1, entry 11) along with some side products.

![Scheme 19. Synergism of [hmim]Br and microwave for oxidation of 1a](image)

After successful oxidation of 1a into 1b with 30% H2O2, we explored the effectiveness of other oxidants in [hmim]Br for the above conversion. It was observed that with oxidants such as oxone, urea-hydrogen peroxide (UHP) etc mainly dehydrated product i.e. anethole was formed along with minor 1b. On addition of water (to avoid competitive dehydration) yield of 1b increased, however, it was still significantly lower than that obtained in case of H2O2 (Table 2, entry 1). In addition, a number of side products were formed with m-CPBA.
(entry 4) and oxone (entry 5) while incompatibility of DDQ with [hmim]Br was observed (Table 2, entry 7). These results once again emphasized the benefit of using H₂O₂ in [hmim]Br.

**Table 2. Effect of various oxidants on the oxidation of 1a using [hmim]Br under microwave<sup>a</sup>**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxidants</th>
<th>Time (min)</th>
<th>Conv. (%)</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H₂O₂</td>
<td>8</td>
<td>95</td>
<td>89 (83)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>THHP</td>
<td>10</td>
<td>56</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>UHP</td>
<td>10</td>
<td>70</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>m-CPBA</td>
<td>24 h&lt;sup&gt;d&lt;/sup&gt;</td>
<td>100</td>
<td>21</td>
</tr>
<tr>
<td>5</td>
<td>Oxone</td>
<td>8</td>
<td>100</td>
<td>23</td>
</tr>
<tr>
<td>6</td>
<td>NaClO₂</td>
<td>10</td>
<td>54</td>
<td>37</td>
</tr>
<tr>
<td>7</td>
<td>DDQ&lt;sup&gt;e&lt;/sup&gt;</td>
<td>8</td>
<td>98</td>
<td>nd&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>CEM monomode microwave; General conditions: 1a (0.6 mmol), [hmim]Br (1 g), 150 W, 120 °C; <sup>b</sup>Yield of 1b based on GC-MS analysis; <sup>c</sup>Isolated yield; <sup>d</sup>Addition of m-CPBA to [hmim]Br led to exothermic reaction, therefore stirred at room temperature; <sup>e</sup>DDQ and [hmim]Br gave black mass due to some complexation leading to formation of side products; <sup>f</sup>Not detected.

In order to check the versatility of developed protocol, a wide range of substituted alcohols (Table 3) were subjected to oxidation and corresponding aldehydes or ketones were obtained in good to moderate yields, wherein, the yield of reaction was found to markedly depend upon electronic factors and nature of alcohol. The electron-donating substituents on aromatic ring, in general, increased the yield of product whereas electron-withdrawing substituent (Table 3, entry 10) gave low yield of product along with unreacted starting material even after prolonged MW heating. Further, biphenyl and naphthalene alcohols (Table 3, entries 2 & 11) were also oxidized to the corresponding ketones in good yield. However primary benzyl alcohols were found to be highly reactive as compared to secondary benzyl alcohols and competitive oxidation of the resulting aldehyde with hydrogen peroxide to corresponding acid became prominent (Table 3, entries 13-14) under the same reaction conditions. On the other side, primary β-alcohol (Table 3, entry 15) did not undergo any conversion which clearly indicates discrimination between benzylic alcohols (Table 3, entries 1-14) over aliphatic analogue (entry 15).
Table 3. Oxidation of benzyl alcohols (a) into carbonyls (b) with [hmim]Br and 30% H₂O₂ under microwave\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (a)</th>
<th>Time (min)</th>
<th>Product (b)</th>
<th>Yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>8</td>
<td></td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>8</td>
<td></td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>15</td>
<td></td>
<td>51</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>8</td>
<td></td>
<td>72</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>15</td>
<td></td>
<td>60(^c)</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>8</td>
<td></td>
<td>94</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>8</td>
<td></td>
<td>61</td>
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<td>8</td>
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<td>8</td>
<td></td>
<td>87</td>
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<tr>
<td>12</td>
<td></td>
<td>8</td>
<td></td>
<td>57</td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>8</td>
<td></td>
<td>(54, 32)(^c)</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>8</td>
<td></td>
<td>(53, 28)(^c)</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>15</td>
<td></td>
<td>nd(^c,d)</td>
</tr>
</tbody>
</table>

\(^a\)CEM monomode microwave; General conditions: substrate 1a-15a (0.6 mmol), [hmim]Br (1 g), 30% H₂O₂ (1 ml), 150W, 120°C; \(^b\)Isolated yield; \(^c\)Based on GC-MS analysis; \(^d\)Not detected.

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To further ascertain the chemoselective oxidation of benzylic alcohols over aliphatic/cyclic alcohols, a mixture of 4-methoxyphenyl-1-propanol (1a) and secondary β-alcohol (Table 4, entry 16) was treated under developed condition where 1b was obtained in 80% yield without any conversion of secondary β-alcohol. Similarly, oxidation of 1a in presence of aromatic γ-alcohol (Table 4, entry 17), cyclic alcohol (Table 4, entry 18) and aliphatic alcohol (Table 4, entry 19) led to the facile oxidation of only benzyl alcohol (1a) without any conversion or interference by other alcoholic substrates. Thus, the developed chemoselective approach is evidently useful for the manipulation of substrates with multifunctional groups.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alcohols</th>
<th>Time (min)</th>
<th>Products</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>1a</td>
<td>8</td>
<td>1b</td>
<td>(80, 0)</td>
</tr>
<tr>
<td>17</td>
<td>1a</td>
<td>8</td>
<td>1b</td>
<td>(81, 0)</td>
</tr>
<tr>
<td>18</td>
<td>1a</td>
<td>8</td>
<td>1b</td>
<td>(82, 0)</td>
</tr>
<tr>
<td>19</td>
<td>1a</td>
<td>8</td>
<td>1b</td>
<td>(80, 0)</td>
</tr>
</tbody>
</table>

\(^{a}\)CEM monomode microwave; 150W, 120°C; \(^{b}\)Equimolar (0.6 mmol) mixture of each alcohol, [hmin]Br (1 g), \(\text{H}_2\text{O}_2\) (1 ml); \(^{c}\)Yields are on the basis of GC-MS analysis.

Thereafter, the developed method was extended for the oxidation of acetylated/benzoylated derivatives of alcohols (Table 5, entries 20-23) which underwent one pot tandem hydrolysis-oxidation to provide the corresponding ketones in 46-72% yield.
It may be mentioned here that during the oxidation of polyaromatic benzyl alcohols such as 9-anthracenyl propanol (24a, Scheme 20), instead of expected 24b, an unexpected product (yellow solid; m.p. 284-286°C) was obtained. The $^1$H NMR spectra of this compound did not show any triplet or quartet for the propyl side chain as expected in the case of 24b, but only two signals at $\delta$ 8.32 ppm and 7.80 ppm were observed for aromatic protons. Moreover, a $^{13}$C NMR peak at $\delta$ 183.3 indicated the presence of C=O group in the molecule. Subsequently, the above product was subjected to detail NMR (DEPT, HMBC, HMQC) and HRMS investigations and it was confirmed to be 9,10-anthraquinone (24c, Scheme 20). Later on, literature survey also revealed a report wherein cleavage of carbinol side chain and subsequent formation of quinone moiety has been observed with DDQ as an oxidant [Becker et al. (1980)].
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Because of this surprising behaviour, we tried to explore the possible pathways for the formation of unexpected product 24c. Consequently, we hypothesized that instead of oxidation of 24a into 24b, the highly conjugated 9-anthracenyl propanol (24a) preferentially provided the dehydration product (9-anthracenyl propene, 25a) which subsequently was cleaved to 9-anthraldehyde (26a) with H2O2 (Figure 2) [Alvarez et al. (2007); Xiao et al. (2008)] followed by its transformation into corresponding phenol [Roy et al. (1999); Bernini et al. (2005)]. In the next step, phenol interacts with imadazolium cation of [hmim]Br in the presence of water and MW to provide 9,10-anthraquinone (24c).

![Figure 2. Plausible pathway of anthraquinone formation](image)

To prove this hypothesis, 9-anthracenyl propene (Table 6, entry 25) was subjected to oxidation and 24c was indeed obtained in 94% yield. On the other hand, use of 9-anthraldehyde (Table 6, entry 26) under similar reaction conditions also gave 24c in 90% yield. To our surprise, quinone (24c) was obtained even by the oxidation of anthracene (Table 6, entry 28) without use of any metal catalyst albeit in moderate yield (51% based upon HPLC) along with unreacted starting and some side products. Further MW irradiation led to the degradation of starting anthracene. Thus the above method may provide an attractive alternative for the synthesis of quinone derivatives, many of which are important intermediates for drugs, vitamins as well as pigments and dyes [Suzuki et al. (2005); Hossein et al. (2009)].

After above metal-free oxidation of polyaromatic substrates (Table 6, entries 24-28), we thought to trap the in situ generated active oxygen for oxidation of various other substituted arylalkenes and arylaldehydes leading to the formation of quinone derivatives.
Table 6. Oxidation of arylalkenes, arylaldehydes, phenols with 30% H_2O_2 and [hmim]Br under microwave^a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (a)</th>
<th>Time (min)</th>
<th>Product</th>
<th>Yield (%)^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td></td>
<td>15</td>
<td>(24b)</td>
<td>(0, 92)</td>
</tr>
<tr>
<td>25</td>
<td></td>
<td>15</td>
<td>(24c)</td>
<td>94</td>
</tr>
<tr>
<td>26</td>
<td></td>
<td>15</td>
<td>(24c)</td>
<td>90</td>
</tr>
<tr>
<td>27</td>
<td></td>
<td>15</td>
<td>(24c)</td>
<td>86</td>
</tr>
<tr>
<td>28</td>
<td></td>
<td>25</td>
<td>(24c)</td>
<td>51^c</td>
</tr>
<tr>
<td>29</td>
<td></td>
<td>48 h^d</td>
<td>(0, 36, 32)^g</td>
<td>(0, 36, 32)^e</td>
</tr>
<tr>
<td>30</td>
<td></td>
<td>48 h^d</td>
<td>(0, 92)</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td></td>
<td>30 h^d</td>
<td>(0, 53, 7)^a</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td></td>
<td>8</td>
<td>(nd, nd)^c,f</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td></td>
<td>8</td>
<td>(nd)^e,f</td>
<td></td>
</tr>
</tbody>
</table>

^aCEM monomode microwave, General conditions: substrate 24a-33a (0.6 mmol), [hmim]Br (1 g), H_2O_2 (1 ml), M.W: (150W, 120°C); ^bIsolated yield; ^cBased on HPLC with comparison to standard; ^dStirring at room temperature; ^eBased on GC-MS analysis; ^fNot detected.

Consequently, anethole (Table 6, entry 29) was stirred at room temperature with [hmim]Br and H_2O_2 (as it proceed smoothly in comparison to MW heating), providing a mixture of anisaldehyde (36%), 4-methoxybenzoic acid (32%) and other side products without formation of expected quinone. On the other hand, oxidation of 3,4-dimethoxybenzaldehyde (Table 6, entry 30) gave the corresponding acid in 92% yield, while the 2,4,5-
trimethoxybenzaldehyde (Table 6, entry 31) afforded the unexpected 1-bromo-2,4,5-trimethoxybenzene (53% yield) along with some amount of 2,4,5-trimethoxybenzoic acid. Further, our attempts to synthesize quinone derivatives from syringaldehyde (Table 6, entry 32) or 1-naphthol (Table 6, entry 33) proved futile as both substrates were found highly reactive and resulted in a number of side products.

2.5 Conclusion:
A synergistic combination of ionic liquid [hmim]Br and microwave is reported for activation of H₂O₂ as an alternative for transition metal-free oxidation reactions. The remarkable chemoselectivity and operational simplicity of the developed method for the oxidation of benzyl alcohols and their derivatives over aromatic (β, γ) and aliphatic/cyclic alcohols is useful in multistep complex natural product synthesis. In addition a new metal-free methodology for the synthesis of anthraquinone has been successfully explored.

2.6 Experimental Section:
2.6.1 General Procedure:
All the reagents were either obtained from commercial sources (Merck or Acros) or synthesized from the corresponding benzaldehydes/Grignard reagents [Sharma et al. (2004)] or reduction with sodium borohydride of the corresponding acetophenones/propiophenones [Botteghi et al. (2003)]. H₂O₂ was 30% aqueous solution purchased from Merck. The ILs used in this study were obtained either commercially (Merck & Alfa Aesar) or synthesized ([bmim]Br, [hmim]Br, [Hmim]pTSA, [bmim]OH) according to reported methods [Zhao et al. (2004); Nockemann et al. (2005); Ranu and Banerjee (2005)]. The purity of the synthesized ILs was checked by NMR spectra before use. The solvents used for isolation/purification of compounds were obtained from commercial sources (Merck) and used without further purification. ¹H (300 MHz) and ¹³C (75.4 MHz) NMR spectra were recorded on a Bruker Avance-300 spectrometer. HRMS-ESI spectra were determined using micromass Q-TOF ultima spectrometer. The melting points were determined on a digital Barnsted Electrothermal 9100 apparatus. GC-MS analysis was undertaken using a Shimadzu-2010 spectrometer. CEM Discover© focused microwave (2450 MHz, 300W) was used wherever mentioned. The temperature of reactions in MW experiments was measured by an inbuilt infrared temperature probe that determined the temperature on the surface of reaction flask. The sensor is attached in a feedback loop with an on-board microprocessor to control the temperature rise rate. In the case of conventional
heating in an oil bath, the temperature of reaction mixture was monitored by an inner thermometer. HPLC analysis was performed using a Shimadzu HPLC (Model LC-20AT pump, DGU-20A5 degasser) equipped with auto sampler (SIL-20AC), photo diode array detector (CBM-20A; Shimadzu, Kyoto, Japan) and interfaced with IBM Pentium 4 personal computer.

2.6.2 Optimization of reaction conditions:
2.6.2.1 Oxidation of 4-methoxyphenyl-1-propanol (1a) using [hmim]Br (0.5 g) under microwave (Table 1, entry 1):

4-Methoxyphenyl-1-propanol (1a, 0.1 g, 0.6 mmol) was dissolved in [hmim]Br (0.5 g). Then 1 ml of 30% aqueous H₂O₂ was added and the reaction mixture was irradiated under focused MW system (150W, 120°C) fitted with reflux condenser for 10 min. After the completion of reaction (on TLC basis), the reaction mixture was cooled and extracted with diethyl ether (3 x 8 ml). The combined organic layer was washed with water (5 ml), brine (5 ml), dried (anhyd. Na₂SO₄) and vacuum evaporated. The crude product was purified by column chromatography on silica gel (60-120 mesh size) with a mixture of n-hexane-ethyl acetate (19:1) to give 1b (0.071, 72% yield) as a colorless liquid which was confirmed by ¹H and ¹³C NMR spectra.

4-Methoxyphenyl-1-propanone (1b) [Choudhary et al. (2002)]

![Chemical structure of 4-Methoxyphenyl-1-propanone](image)

Colorless viscous liquid, ¹H NMR (300 MHz, CDCl₃); δ (ppm) 8.29 (2H, d, J = 9.2 Hz), 7.27 (2H, d, J = 9.2 Hz), 4.19 (3H, s), 3.31 (2H, q, J = 7.7 Hz), 1.57 (3H, t, J = 7.7 Hz); ¹³C NMR (75.4 MHz, CDCl₃); δ (ppm) 199.8, 163.7, 130.5, 114.0, 55.8, 31.7 and 8.8.

2.6.2.2 Oxidation of 1a using various other ionic liquids [bmim]Br, [bmim]Cl, [bmim]BF₄, [bmim]PF₆, [Hmim]pTSA and [bmim]OH (Table 1, entries 2-7):

A mixture of 4-methoxyphenyl-1-propanol (1a, 0.1 g, 0.6 mmol) and 30% aqueous H₂O₂ (1 ml) was treated separately with the following ionic liquids (0.5 g each); [bmim]Br or [bmim]Cl or [bmim]BF₄ or [bmim]PF₆ or [Hmim]pTSA or [bmim]OH under MW conditions (for 10 min or more) as mentioned in section 2.6.2.1. After the completion of reaction, each of the reaction mixture was worked up as mentioned in the preceding section. The column purification (as in section 2.6.2.1) of crude mixture in case of [bmim]Br (Table
1, entry 2) provided the desired $1b$ in 70% yield. The spectral data ($^1H$ and $^{13}C$ NMR) of above $1b$ matched well with that obtained in section 2.6.2.1.

In cases of [bmim]Cl, [bmim]BF$_4$, [bmim]PF$_6$, [Hmim]-pTSA and [bmim]OH the crude mixture were analyzed with the help of GC-MS analysis providing conversion yields of $1b$ in the range of 0 to 46% (Table 1, entries 3-7).

2.6.2.3 Oxidation of $1a$ with $H_2O_2$ using $1g$ of [hmim]Br in place of $0.5g$ of [hmim]Br under microwave (Table 1, entry 8):

4-Methoxyphenyl-1-propanol ($1a$, 0.1 g, 0.6 mmol) was dissolved in [hmim]Br (1 g). Then 1 ml of 30% aqueous $H_2O_2$ was added and the mixture was shaken to make it homogeneous. The flask was irradiated under focused MW system (150W, 120°C) for 8 min. After the completion of reaction, the reaction mixture was worked up as mentioned in section 2.6.2.1. The crude product was analyzed by GC-MS providing 89% conversion yield of $1b$. Further, the crude product was purified by column chromatography (as in section 2.6.2.1) providing the desired $1b$ in 83% isolated yield. The spectral data ($^1H$ and $^{13}C$ NMR) of above $1b$ matched well with that obtained in section 2.6.2.1.

Further increase in the amount of [hmim]Br (more than 1 g) provided $1b$ in lower yield due to formation of 4-methoxyphenylpropene (due to competitive dehydration) along with desired $1b$.

2.6.2.4 Control experiments (Table 1, entries 9-11 & Scheme 19):

Control experiments with 1-methylimidazole (Table 1, entry 9) or DMSO (Table 1, entry 10) in place of IL were also carried out. GC-MS analysis showed lower conversion yield (17%) of $1b$ in case of 1-methylimidazole, whereas, no product formation occurred with DMSO as a solvent.

Similarly, $1a$ was refluxed with 30% $H_2O_2$ in [hmim]Br (1g) in an oil bath (120°C) for 2 h (Table 1, entry 11). After the completion of reaction, the work up and column purification (as mentioned in section 2.6.2.1) provided $1b$ in 68% yield. On the other hand, oxidation of $1a$ using $H_2O_2$-MW (without [hmim]Br) or $H_2O_2$-[hmim]Br (without MW) provided the product ($1b$) in negligible amount as analyzed with GC-MS (Scheme 19).

2.6.2.5 Effect of various oxidants (TBHP, UHP, m-CPBA, Oxone, NaClO$_2$, DDQ) on oxidation of $1a$ in [hmim]Br under microwave (Table 2, entry 1-7):

A mixture of 4-methoxyphenyl-1-propanol ($1a$, 0.1 g, 0.6 mmol), oxidant ($H_2O_2$ or TBHP or UHP or oxone or NaClO$_2$ or DDQ) and water (0.2 ml, except in case of $H_2O_2$) was irradiated under MW (150W, 120°C) for 8 min or more. In case of m-CPBA (Table 2, entry...
4) the reaction mixture was stirred at room temperature for 48 h instead of MW irradiation. After the completion of reaction, the reaction mixture was worked up as described in section 2.6.2.1. The crude mixtures in each case were analyzed by GC-MS which showed conversion yields of 1b from 0% to 89%.

2.6.2.6 Optimized procedure for the oxidation of 1a with H₂O₂ using [hmim]Br under microwave (Table 3, entry 1):

4-Methoxyphenyl-1-propanol (1a, 0.1 g, 0.6 mmol) was dissolved in [hmim]Br (1 g). Then 1 ml of 30% aqueous H₂O₂ was added and the mixture was shaken to make it homogeneous. The flask was irradiated under focused MW system (150W, 120°C) for 8 min. After the completion of reaction, the reaction mixture was worked up and purified by column chromatography (as in section 2.6.2.1) providing the desired 1b in 83% yield (0.082 g). The spectral data (¹H and ¹³C NMR) of above 1b matched well with that obtained in section 2.6.2.1.

The above procedure was also followed for the oxidation of various other alcohols (Table 3, entries 2-15)

1-(Biphenyl-4-yl)propan-1-one (2b) [Sharma et al. (2010)]

![Biphenyl-4-yl]propan-1-one (2b)

White solid (84%), m.p. 84-86°C, ¹H NMR (300 MHz, CDCl₃); δ (ppm) 8.07 (2H, d, J = 8.1 Hz), 7.71 (2H, d, J = 7.9 Hz), 7.66 (2H, d, J = 7.9 Hz), 7.51-7.39 (3H, m), 3.08 (2H, q, J = 7.3 Hz), 1.3 (3H, t, J = 6.8 Hz), ¹³C NMR (75.4 MHz, CDCl₃); δ (ppm) 200.7, 145.9, 140.3, 136.0, 129.3, 128.9, 128.5, 127.6, 127.5, 32.2 and 8.7.

1-Phenylpropan-1-one (3b) [Kuhakarn et al. (2005)]

![Phenyl]propan-1-one (3b)

Colorless liquid (51%), ¹H NMR (300 MHz, CDCl₃); δ (ppm) 7.79 (2H, d, J = 8.8 Hz), 7.39-7.24 (3H, m), 2.85 (2H, q, J = 7.3 Hz), 1.07 (3H, t, J = 7.1 Hz); ¹³C NMR (75.4 MHz, CDCl₃); δ (ppm) 201.1, 137.3, 133.2, 128.9, 128.3, 32.1 and 8.6.

1-(4-Methoxyphenyl)butanone (4b) [Choudhary et al. (2002)]

![4-Methoxyphenyl]butanone (4b)

Viscous liquid (72%), ¹H NMR (300 MHz, CDCl₃); δ (ppm) 7.88 (2H, d, J = 8.8 Hz), 6.86 (2H, d, J = 8.8 Hz), 3.78 (3H, s), 2.83 (2H, t, J = 7.1 Hz), 1.78 (2H, m),
1.01 (3H, t, J = 7.5 Hz); $^{13}$C NMR (75.4 MHz, CDCl$_3$); δ (ppm) 199.1, 163.5, 130.4, 113.9, 55.6, 40.4, 18.2 and 14.1.

3,4-Dihydronaphthalen-1(2H)-one (5b)

Compound 5b was confirmed by GC-MS analysis with reference standard.

1-(3,4-Dimethoxyphenyl)ethanone (6b) [Sharma et al. (2010)]

![Chemical Structure](image1)

White solid (94%), m.p. 48-51°C, $^1$H NMR (300 MHz, CDCl$_3$); δ (ppm) 7.56 (1H, d, J = 8.6 Hz), 7.49 (1H, s), 6.87 (1H, d, J = 8.6 Hz), 3.92 (6H, s), 2.54 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); δ (ppm) 197.2, 153.8, 149.6, 131.1, 123.7, 110.7, 56.5 and 26.6.

1-(3,4,5-Trimethoxyphenyl)ethanone (7b)

![Chemical Structure](image2)

White solid (61%), m.p. 78-81°C, $^1$H NMR (300 MHz, CDCl$_3$); δ (ppm) 7.27 (2H, s), 3.97 (9H, s), 2.6 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); δ (ppm) 197.1, 153.5, 143.1, 132.9, 106.4, 61.3, 56.7 and 26.7.

Diphenylmethanone (8b) [Chhikara et al. (2005b)]

![Chemical Structure](image3)

White solid (55%), m.p. 47-49°C, $^1$H NMR (300 MHz, CDCl$_3$); δ (ppm) 7.83 (4H, d, J = 8.1 Hz), 7.61-7.56 (2H, m), 7.50-7.45 (4H, m); $^{13}$C NMR (75.4 MHz, CDCl$_3$); δ (ppm) 197.0, 138.0, 132.8, 130.7 and 128.6.

1-(1,3-Benzodioxol-5-yl)ethanone (9b) [Sharma et al. (2010)]

![Chemical Structure](image4)

White solid (80%), m.p. 85-88°C, $^1$H NMR (300 MHz, CDCl$_3$); δ (ppm) 7.40 (1H, d, J = 7.7 Hz), 7.26 (1H, s), 6.70 (1H, d, J = 8.4 Hz), 5.88 (2H, s), 2.38 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); δ (ppm) 196.1, 151.8, 148.2, 132.2, 124.8, 108.0, 107.8, 101.9, and 26.4.
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1-(4-Nitrophenyl)ethanone (10b) [Mannam et al. (2007)]

\[
\text{White solid (58%), m.p. 77-80°C, } ^1\text{H NMR (300 MHz, CDCl}_3\text{); } \delta (\text{ppm}) \\
7.43 (2H, d, J = 8.9 Hz), 7.27 (2H, d, J = 8.8 Hz), 1.83 (3H, s); ^13\text{C NMR (75.4 MHz, CDCl}_3\text{); } \delta (\text{ppm}) 196.6, 150.7, 141.8, 129.6, 124.1, \text{ and 27.2.}
\]

1-(Naphthalen-2-yl)ethanone (11b) [Chhikara et al. (2005b)]

\[
\text{White solid (87%), m.p. 52-56°C, } ^1\text{H NMR (300 MHz, CDCl}_3\text{); } \delta (\text{ppm}) \\
8.13 (1H, s), 7.74 (1H, d, J = 8.8 Hz), 7.65 (1H, d, J = 7.5 Hz), 7.56 (2H, d, J = 8.4 Hz), \\
7.31-7.21 (2H, m), 2.40 (3H, s); ^13\text{C NMR (75.4 MHz, CDCl}_3\text{); } \delta (\text{ppm}) 198.3, 136.3, 134.9, \\
132.9, 130.5, 129.9, 128.8, 128.7, 128.1, 127.1, 124.2 \text{ and 27.0.}
\]

(2\text{E})-1-(1,3-Benzodioxol-5-yl)-3-(4-chlorophenyl)prop-2-en-1-one (12b)

\[
\text{White solid (57%), m.p. 164-167°C, } ^1\text{H NMR (300 MHz, CDCl}_3\text{); } \delta (\text{ppm}) \\
7.68 (1H, d, J = 15.7 Hz), 7.57 (1H, d, J = 8.1 Hz), 7.49-7.44 (3H, m), \\
7.40 (1H, d, J = 15.7 Hz), 7.31 (2H, d, J = 8.5 Hz), 6.82 (1H, d, J = 8.1 Hz), 5.98 (2H, s); \\
^13\text{C NMR (75.4 MHz, CDCl}_3\text{); } \delta (\text{ppm}) 187.9, 151.8, 148.3, 142.7, 136.2, 133.5, 132.8, \\
129.5, 129.2, 124.7, 122.1, 108.4, 107.9 \text{ and 101.9. HRMS-ESI: } m/z [\text{M+H}]^+ \text{ for} \\
\text{C}_{16}\text{H}_{11}\text{ClO}_3, \text{ calculated 287.0470; observed 287.0469.}
\]

Thus, oxidation of 2° benzylic alcohols (Table 3, entries 1-12) provided the corresponding carbonyl derivatives (1-12b) as mentioned above, however, oxidation of 1° benzylic alcohols (Table 3, entries 13-14) led to the mixture of benzaldehyde and corresponding acids as analyzed with GC-MS. On the other side, aromatic β-alcohol (aliphatic analogue) did not undergo oxidation and starting remained unreacted (Table 3, entry15).

2.6.2.7 Procedure for chemoselective oxidation of benzylic alcohol 1a in presence of aliphatic analogues using H\textsubscript{2}O\textsubscript{2} in [hmim]Br under microwave (Table 4, entries 16-19):

To the mixture of 4-methoxyphenyl-1-propanol (1a, 0.6 mmol) and 1-(4-methoxyphenyl)propan-2-ol (0.6 mmol) in [hmim]Br (1 g), 1 ml of 30% aqueous H\textsubscript{2}O\textsubscript{2} was added and the mixture irradiated under focused MW system (150W, 120°C) for 8 min. The reaction mixture was worked up as mentioned in section 2.6.2.1. The crude mixture was
analyzed with GC-MS, showing selective oxidation of 1a (80% conversion yield of 1b) without any oxidation of 1-(4-methoxyphenyl)propan-2-ol.

Using the same procedure as mentioned above, oxidation of 1a in the presence of aromatic γ-alcohol (Table 4, entry 17), cyclic alcohol (Table 4, entry 18) and aliphatic alcohol (Table 4, entry 19) were also carried out. GC-MS analysis showed the chemoselective oxidation of only benzyl alcohol (1a) in each case without any conversion of other alcoholic substrates.

2.6.2.8 Procedure for tandem hydrolysis-oxidation of acetylated/benzoylated alcohol derivatives using H$_2$O$_2$ in [hmim]Br under microwave (Table 5, entries 20-23):

1-(4-Methoxyphenyl)propyl acetate (20a, 0.125 g, 0.6 mmol) was dissolved in [hmim]Br (1 g). Then 1.5 ml of 30% aqueous H$_2$O$_2$ was added and the mixture was shaken to make it homogeneous. The flask was irradiated under focused MW system (150W, 120°C) for 25 min. The reaction mixture was worked up and purified as mentioned in section 2.6.2.1. The oxidised product was obtained in an optimum 63% yield (0.062 g). The spectral data (1H and 13C NMR) of above 1b matched well with that obtained in section 2.6.2.1.

The same procedure was also applied for the tandem hydrolysis-oxidation of other acetylated and benzoylated derivative of alcohols (Table 5, entries 21-23). The spectral data (1H and 13C NMR) of corresponding products matched well with that obtained in section 2.6.2.1 and 2.6.2.6 (i.e. 6b, 11b, 1b).

2.6.2.9 Procedure for synthesis of 9,10-anthraquinone (24c) from oxidation of 9-substituted anthracene derivatives using H$_2$O$_2$ in [hmim]Br under microwave (Table 6, entry 24-28):

A mixture of 9-anthracenyl propanol (0.142 g, 0.6 mmol) (Table 6, entry 24) and 30% aqueous H$_2$O$_2$ (1 ml) in [hmim]Br (1 g) was irradiated under MW (150W, 120°C) for 15 min. After the completion of reaction, the reaction mixture was cooled and extracted with ethyl acetate (3x15 ml). The combined organic layer was washed with water (2x5 ml), brine (5 ml), dried over Na$_2$SO$_4$ and passed through a small bed of silica gel (60-120 mesh size) to give 9,10-anthraquinone (24c) in 92% yield (0.115 g) as a yellow solid. The above product (24c) was confirmed by NMR (1H, 13C, DEPT 135°, HMBC, HMQC) and HRMS spectroscopy.
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9,10-anthraquinone (24c) [Lukasiewicz et al. (2006)]

Yellow solid, m.p. 284-286°C, \(^1\)H NMR (300 MHz, CDCl\(_3\)); \(\delta\) (ppm) 8.32 (4H, s), 7.80 (4H, s); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)); \(\delta\) (ppm) 183.3, 134.3, 133.7 and 127.4. HRMS-ESI: \(m/z\) [M+H]\(^+\) for C\(_{14}\)H\(_8\)O\(_2\), calculated 209.0597; observed 209.0592.

The same procedure was also applied for the oxidation of 9-anthracenyl propene (Table 6, entry 25), 9-anthraldehyde (Table 6, entry 26) and 9-anthracenyl ethanol (Table 6, entry 27). In each case 24c was obtained as the sole product in 94%, 90% and 86% isolated yields respectively. In case of oxidation of anthracene (Table 6, entry 28), the reaction was performed and worked up in the same manner as given in section 2.6.2.9. The crude product was analysed with the help of HPLC analysis by comparison with reference standard providing 24c with a conversion yield of 51%.

2.6.2.10 Procedure for oxidation of 4-methoxyphenylpropene using H\(_2\)O\(_2\) in [hmim]Br (Table 6, entry 29)

A mixture of 4-methoxyphenylpropene (29a, 0.089 g, 0.6 mmol) and 30% aqueous H\(_2\)O\(_2\) (1 ml) in [hmim]Br (1 g) was stirred at room temperature for 48 h. The reactions upon completion followed by work up (same as in section 2.6.2.9) and GC-MS analysis provided a mixture of 4-methoxybenzaldehyde and 4-methoxybenzoic acid with conversion yields of 36% and 32% respectively.

2.6.2.11 Procedure for oxidation of 3,4-dimethoxybenzaldehyde using H\(_2\)O\(_2\) in [hmim]Br (Table 6, entry 30)

A mixture of 3,4-dimethoxybenzaldehyde (30a, 0.1 g, 0.6 mmol) and 30% aqueous H\(_2\)O\(_2\) (1 ml) in [hmim]Br (1 g) was stirred at room temperature for 48 h. The reactions upon completion followed by work up (same as in section 2.6.2.9) and column purification on silica gel (60-120 mesh size) using hexane-ethylacetate (1:1) provided 3,4-dimethoxybenzoic acid in 92% yield (0.1 g) whose NMR spectra (\(^1\)H and \(^{13}\)C NMR) is given below:

3,4-Dimethoxybenzoic acid (Table 6, entry 30) [Buffin et al. (2005)]

White solid, m.p. 178-181°C, \(^1\)H NMR (300 MHz, CDCl\(_3\)); \(\delta\) (ppm) 7.79 (1H, d, \(J = 8.2\) Hz), 7.60 (1H, s), 6.93 (1H, d, \(J = 8.2\) Hz), 3.96 (6H, s); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)); \(\delta\) (ppm) 171.7, 153.9, 148.9, 124.7, 122.0, 112.6, 110.5 and 56.2.
2.6.2.12 Procedure for oxidation of 2,4,5-trimethoxybenzaldehyde, syringaldehyde and 1-naphthol using H$_2$O$_2$ in [hmim]Br (Table 6, entries 31-33)

A mixture of 2,4,5-trimethoxybenzaldehyde (31a, 0.117 g, 0.6 mmol) and 30% aqueous H$_2$O$_2$ (1 ml) in [hmim]Br (1 g) was stirred at room temperature for 30 h. The reactions upon completion followed by work up (same as in section 2.6.2.9) and upon GC-MS analysis showed the formation of 1-bromo-2,4,5-trimethoxybenzene and 2,4,5-trimethoxybenzoic acid with conversion yields of 53% and 7% respectively.

Oxidation of syringaldehyde (Table 6, entry 32) and 1-naphthol (Table 6, entry 33) were performed in the same manner as given in section 2.6.2.3. However, in both cases number of side products were observed as analysed with GC-MS.

2.7 References:


Bianchini, G., Crucianelli, M., Angelis, F. D., Neri, V. and Saladino, R. (2005). Highly efficient CH insertion reactions of hydrogen peroxide catalyzed by homogeneous and


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oxidation of alcohols with H₂O₂, and spectroscopic investigation. *Journal of Molecular Catalysis A: Chemical* **262**: 52–58.


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NMR spectra of some compounds

\[ \text{H NMR (in CDCl}_3\text{) spectrum of 1-(Biphenyl-4-yl)propan-1-one (2b, Table 3)} \]

\[ \text{C NMR (in CDCl}_3\text{) spectrum of 1-(Biphenyl-4-yl)propan-1-one (2b, Table 3)} \]
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$\text{H NMR (in CDCl}_3\text{) spectrum of 1-(4-Methoxyphenyl)butanone (4b, Table 3)}$

$\text{\textsuperscript{13}C NMR (in CDCl}_3\text{) spectrum of 1-(4-Methoxyphenyl)butanone (4b, Table 3)}$
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$\text{1H NMR (in CDCl}_3\text{) spectrum of 9,10-anthraquinone (24c, Table 6)}$

$\text{13C NMR (in CDCl}_3\text{) spectrum of 9,10-anthraquinone (24c, Table 6)}$
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DEPT 135° NMR (in CDCl₃) spectrum of 9,10-anthraquinone (24c, Table 6)

HRMS spectrum of 9,10-anthraquinone (24c, Table 6)