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Oxidation of Alcohols and *vic*-Diols with H_2O_2 by Using Catalytic Amounts of *N*-Methylpyrrolidin-2-one Hydrotribromide

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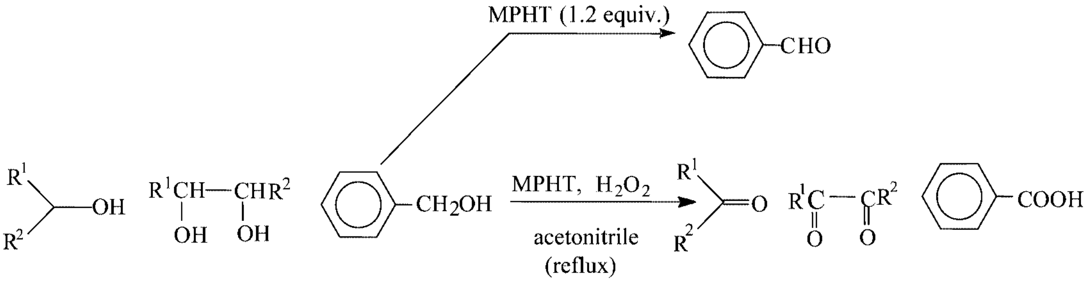
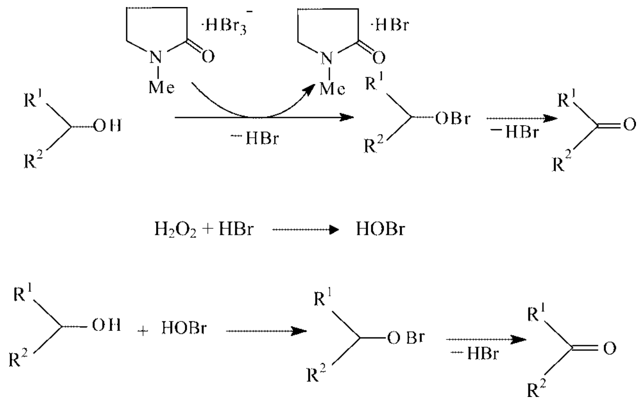
A variety of secondary alcohols, 1,2-diols and primary alcohols were selectively oxidized in excellent yields to their corresponding ketones, 1,2-diketones and aldehydes with aqueous 30 % hydrogen peroxide in refluxing acetonitrile in the presence of catalytic amounts of *N*-methylpyrrolidin-2-one hydrotribromide (MPHT).

The oxidation of alcohols to carbonyl compounds is an important synthetic transformation,[1] and in the recent years emphasis is being given towards the use of environmentally benign oxidants such as molecular oxygen, hydrogen peroxide with a view of developing green methodologies.[2] In this context oxidation of alcohols to ketones with molecular oxygen by using cobalt-,[3] palladium-,[4] ruthenium-based catalysts[5] and cobalt complexes with 2-methylpropanal[6] as the sacrificial aldehyde have been reported in the literature. However, most of the existing methods are associated with one or more drawbacks such as the use of expensive and toxic metals like ruthenium and palladium, oxidation of only activated alcohols such as benzylic and allylic alcohols, the need for a sacrificial aldehyde, and severe reaction conditions like high pressure.

Solid organic ammonium tribromides (OATB) such as pyridine hydrobromide perbromide ($PyHBr_3$),[7] tetramethylammonium tribromide (TMATB),[8] phenyltrimethylammonium tribromide (PTATB),[9] cetyltrimethylammonium tribromide (CetTMATB),[10] and tetrabutylammonium tribromide (TBATB),[11] due to their ease of handling and ability to maintain the desired stoichiometry, find increasing applications as substitutes for molecular bromine for a variety of organic reactions in the recent years.[12] However, to the best of our knowledge there is no literature report on organic ammonium tribromide mediated oxidation of alcohols to carbonyl compounds with hydrogen peroxide. A recent report by Provot et al. on the use of *N*-methylpyrrolidin-2-one hydrotribromide (MPHT)[13] as an efficient and green brominating agent for carbonyl compounds inspired us to explore its potential for the oxidation of alcohols to carbonyl compounds. In this letter we wish to report for the



Scheme 1.



Scheme 2.

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first time a new transition-metal-free, simple, convenient and efficient method for the oxidation of secondary alcohols to ketones, 1,2-diols to 1,2-diketones and primary alcohols to aldehydes with hydrogen peroxide in the presence of catalytic amounts of MPHT (Scheme 1).

The protocol developed for the oxidation of various alcohols and 1,2-diols consist of refluxing substrate (1 mmol), catalytic amounts of MPHT (10 mol-%) and 30 wt.-% aqueous hydrogen peroxide (2 mmol) in acetonitrile (Scheme 2).[14] We first carried out the reaction of benzhydrol (1 mmol) with MPHT (1.2 mmol) in acetonitrile at ambient temperature and observed the reaction to be very slow with poor yield of the benzophenone (Table 1, Entry 1). Subsequently it was observed that reaction rate increases

Table 1. Oxidation of alcohols and diols by using *N*-methylpyrrolidin-2-one hydrotribromide (MPHT) as catalyst and hydrogen peroxide as oxidant.[a]

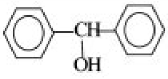
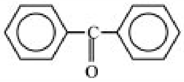
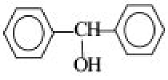
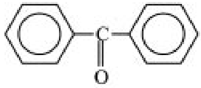
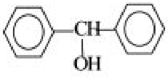
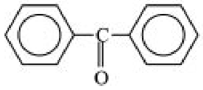
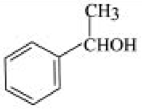
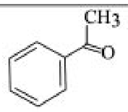
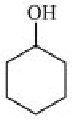
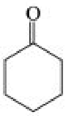
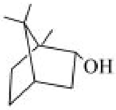
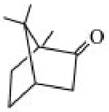
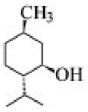
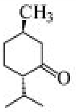
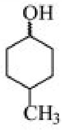
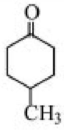
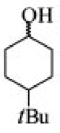
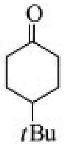
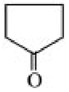
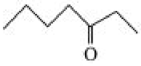
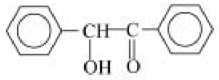
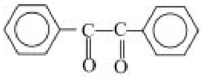
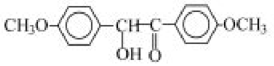
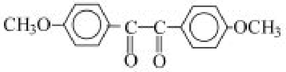
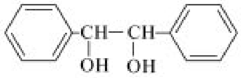
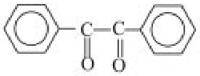
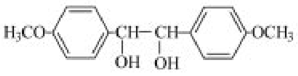
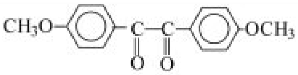
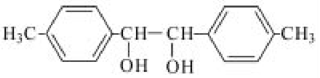
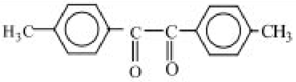
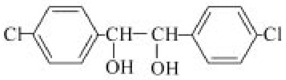
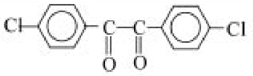
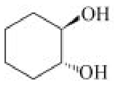
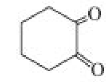
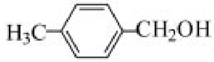
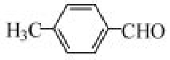
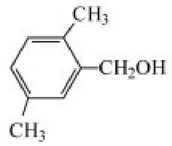
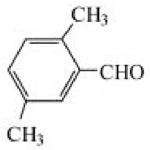
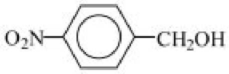
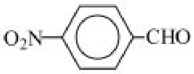
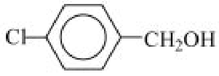
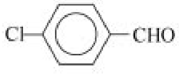
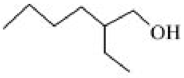
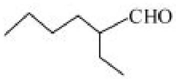
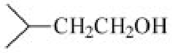
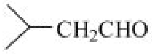
Entry	Substrate	Product	Reaction time (h)	Yield (%)[b]
1			4.5	60[c]
2			2.5	85[d]
3			0.5	94
4			0.70	92
5			1.5	92
6			0.75	90
7			0.85	89
8			0.75	90
9			1.0	91
10			0.42	94
11			1.75	86

Table 1. *(Continued)*

Entry	Substrate	Product	Reaction time (h)	Yield (%)[b]
12			0.15	96
13			0.10	97
14			1.25	95
15			1.0	96
16			1.15	95
17			2.5	85
18			0.5	91
19			2.0	93[e]
20			3.5	95[e]
21			4.0	87[e]
22			10	65
23			12	68
22			3.5	70
23			5.0	78

[a] Reaction conditions: Substrate (1 mmol), MPHT (10 mol-%), aq. hydrogen peroxide (2 mmol, 30 wt.-%), acetonitrile (5 mL) at refluxing temperature. [b] Isolated yields. [c] Experiment carried out using stoichiometric amount of MPHT alone in absence of H_2O_2 at room temperature. [d] Experiment carried out using stoichiometric amount of MPHT at refluxing conditions in absence of H_2O_2. [e] Oxidation carried out with equimolar amounts of MPHT in refluxing acetonitrile in absence of H_2O_2.

with increasing temperature, and oxidation of benzhydrol to benzophenone could be completed within 2.5 h in refluxing acetonitrile (Table 1, Entry 2). In the course of this study it was found that MPHT alone could not oxidize the non-activated alcohols such as borneol and L-menthol. In our further studies we observed that borneol and L-menthol could be easily oxidized to the corresponding ketones in almost quantitative yields by using catalytic amounts of

MPHT and hydrogen peroxide as oxidant in refluxing acetonitrile. This protocol was generalized by performing oxidation of a variety of secondary alcohols to carbonyl compounds, and the results are presented in Table 1 (Entries 3–13). Among the various alcohols studied, benzoins were found to be the most reactive and required shorter reaction times for their oxidation. Furthermore, aromatic-substituted alcohols were found to be more reactive as compared to the aliphatic/alicyclic alcohols. It was also interesting to note that while oxidation of benzhydrol with 2 equiv. of hydrogen peroxide, added in one portion, gave a mixture of benzophenone and unconverted benzhydrol, whereas its dropwise addition afforded benzophenone in excellent yield within 30 min,. The completion of the reaction was indicated by discoloration of the reaction mixture. A variety of 1,2-diols were smoothly oxidized to their corresponding 1,2-diketones using this protocol. The results obtained are shown in Table 1 (Entries 14–18). The results clearly indicate that 1,2-diols substituted with electron-donating groups are more reactive under these reaction conditions.

The selective oxidation of primary alcohols to aldehydes is also an important and desirable synthetic transformation as susceptibility of aldehydes for further oxidation to carboxylic acids narrows the choice of reagent. We therefore also studied the oxidation of various primary alcohols using both catalytic amounts of MPHT along with aqueous 30% H_2O_2 and stoichiometric amounts of MPHT without H_2O_2 as oxidation systems. These results are presented in Table 1 (Entries 19–25). While the benzylic alcohols (Table 1, Entries 19–23) yielded the corresponding acids in refluxing acetonitrile using catalytic amount of MPHT and 30 wt.-% aqueous hydrogen peroxide as oxidant, the aliphatic primary alcohols were selectively converted into the corresponding aldehydes under these reaction conditions (Table 1, Entries 24–25). When oxidation of benzyl alcohols was carried out with stoichiometric amounts of MPHT (without using H_2O_2), the corresponding aldehydes were obtained selectively (Table 1, Entries 19–23). Among the various benzyl alcohols studied, the unsubstituted benzyl alcohol was found to be most reactive and those substituted with electron-donating groups (Table 1, Entries 20–21) were found to be more reactive than those bearing electron-withdrawing groups (Table 1, Entries 22–23). To evaluate the effect of various solvents the oxidation of benzhydrol was carried out in different solvents using catalytic amounts of MPHT and aq. hydrogen peroxide as oxidant under refluxing conditions. Among the various solvents studied – such as acetonitrile, 1,2-dichloroethane, THF and chloroform/acetonitrile was found to be the best suited solvent.

The exact mechanism of this reaction is not clear at this stage; the reaction probably involves the in-situ formation of bromine from MPHT, which, on reaction with alcohol, is reduced to HBr. The reaction of HBr and H_2O_2[15] might generate hypobromous acid, which then reacts with the alcoholic group to afford the hypobromite species followed by the abstraction of hydrogen to yield the corresponding carbonyl compound.

In summary, we have developed a new and highly efficient methodology for the oxidation of various 1,2-diols, as well as secondary and primary alcohols to the corresponding 1,2-diketones, ketones and aldehydes, respectively, using catalytic amounts of MPHT and hydrogen peroxide as oxidant. The easy synthesis, crystalline nature and catalytic use of MPHT, the versatility of the developed protocol towards various substrates, and the capability of the method to selectively oxidize primary alcohols to aldehydes make this an attractive and facile method for the oxidation of alcohols.

Acknowledgments

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[14] General Experimental Procedure: To a stirred solution of substrate (1 mmol) and MPHT (10 mol-%) in acetonitrile (5 mL)

was added dropwise aq. hydrogen peroxide (2 mmol, 30 wt.-%), and the reaction mixture was refluxed for the time given in Table 1. The progress of reaction was monitored by TLC (SiO_2). At the end of reaction, the excess hydrogen peroxide was deactivated by the addition of aq. bisulfite followed by filtration through a small Büchner funnel. After filtration, the reaction mixture was purified by solvent extraction with dichloromethane (3×), and the solvent was evaporated under vacuum. The residue thus obtained was purified by column chromatography on silica gel using ethyl acetate/hexane (1:4) as eluent. Evaporation of the solvent yielded the corresponding carbonyl compound. The reaction times and yields of the products are presented in Table 1. The products were identified by comparing their physical and spectroscopic data with those of authentic compounds reported in the literature. In case of benzylic alcohols the corresponding aldehydes were obtained when the substrate (1 mmol) was treated with MPHT (1.2 mmol) in refluxing acetonitrile without using hydrogen peroxide as oxidant.

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