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Expedient Method for Oxidation of Alcohol by Hydrogen Peroxide in the Presence of Amberlite IRA 400 Resin (Basic) as Phase-Transfer Catalyst

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Abstract: Amberlite IRA 400 (strongly basic), a classical polymer imparts phase-transfer catalysis in the oxidation of primary and secondary alcohols by hydrogen peroxide to give excellent yields of the corresponding carbonyl compounds or carboxylic acids in acetonitrile solvent at reflux temperature in 4–6 h. The catalytic system is inert to other susceptible oxidation sites such as carbon–carbon double bonds

Keywords: Amberlite resin, oxidation, progesterone, sodium tungstate

Catalytic oxidation of alcohols to the corresponding carbonyl compounds and carboxylic acids is a highly desirable functional group transformation both in industrial chemistry as well as in organic synthesis because of the wide-ranging utility of these products as important precursors and intermediates for many drugs, vitamins, and fragrances.^[1,2] Historically such oxidations were carried out with toxic oxo chromium(V) reagents,^[3] pyridinium chlorochromate,^[4] hypochlorites,^[5] permanganate,^[6] oxidants, etc. Subsequent developments involved the use of other oxidizing agents activated by different transition metals,^[7,8] heavy metals,^[9] halides,^[10] dimethyl sulphoxide (DMSO),^[11] hypervalent iodines such as Des-Martin-Periodate,^[12] etc. However, these reagents are either toxic, hazardous to handle, cannot be stored because of their explosive nature, or

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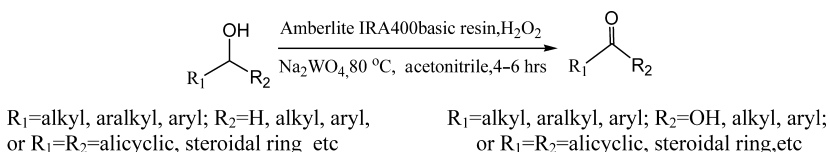
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sensitive to other susceptible sites apart from the target, and in some cases it is cumbersome to recover the catalyst from the products. Quite a few reports^[13–16] have appeared using oxygen or hydrogen peroxide under different catalytic conditions for such purposes, but these are not devoid of many problems. Keeping in mind the different problems associated with the reported methods and taking the mandatory environmental considerations into account, it was deemed desirable to have a recyclable catalytic system for oxidation of primary and secondary alcohols using hydrogen peroxide as the oxidant because it is convenient and cheap and produces water as the only by-product.

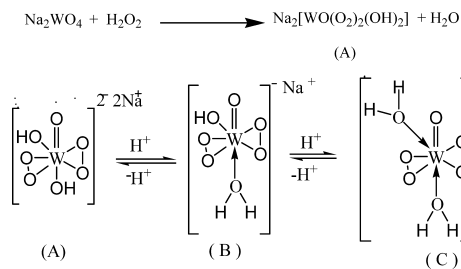
RESULTS AND DISCUSSIONS

Because hydrogen peroxide is the desired green oxidant of choice^[17] and also because of our success^[18] in the oxidative transformation of functional group, we wanted to study the much-sought-after oxidation of primary and secondary alcohols with hydrogen peroxide under the influence of a suitable catalytic system that is recyclable and hence economical, mild and efficient. Among the polyoxometallic compounds, sodium tungstate is considered as ecologically benign^[19] and suitable to activate hydrogen peroxide (Scheme 1).

Therefore, we studied the oxidation of several primary and secondary aliphatic and aromatic alcohols with hydrogen peroxide (30%) using sodium tungstate in the presence of strongly basic amberlite IRA-400 resin in chloride form. The use of basic amberlite IRA-400 resin has two advantages. First, it acts as a phase-transfer catalyst (PTC), and second, it can very easily be separated out from the reaction mixture as it remains in the solid form. The molar ratio of the substrate–hydrogen peroxide–sodium tungstate was 10:40–60:1. Sodium tungstate needs activation prior to its participation in the oxidation reaction. Reaction was therefore performed by first stirring together sodium tungstate and hydrogen peroxide (30%) in the presence of a little dilute sulfuric acid for about 30 min at room temperature at pH 1.5 followed by addition of the substrate, amberlite resin, and more of hydrogen peroxide in acetonitrile. It was refluxed for 4–6 h to give a good yield of the carbonyl products. The catalyst Na_2WO_4 was first oxidized by hydrogen peroxide to bis-peroxotungstate complex (A), which is feebly active towards alcohols (Scheme 2). However, at pH 1.5, this peroxo complex was converted to the



Scheme 1.



Scheme 2.

monoprotonated active form (B), which remains in equilibrium with the diprotonated form (C). The diprotonated bisperoxo complex (C) present as minor component is reactive in the homogenous phase but unable to move into the organic phase. The dominant active monoprotonated complex (B) formed at pH 1.5 moves into the organic phase by the exchange of its anionic part with the chloride anion of the basic resin (Q^+Cl^- , Q^+ = ammonium cation on styrene divinylbenzene matrix) and oxidized the substrate alcohol to the corresponding carbonyl compound. The requirement of acidic pH is therefore advocated for the formation of the active monoprotonated bisperoxotungstate complex (B), and the basic resin has no role to play at this stage but is essential at the later stage to bring it to the organic phase through exchange and carry forward the oxidation.

When this reaction was carried out^[20] in the presence of a strongly acidic resin (amberlite IR 120 resin, sulphonic acid group on styrene divinylbenzene matrix), the entire reaction followed a different course to form phenolic compounds from the benzylic alcohols, which is under further investigation.

The reaction was studied in a series of solvents to check the efficiency in terms of product yield, time duration, and temperature (Table 1) with three

Table 1. Oxidation of alcohols to carbonyls in different solvent systems using Na_2WO_4 , H_2O_2 (30%) and amberlite IRA-400 resin (strongly basic)

Entry	Solvent	Time (h)	Temperature ($^{\circ}\text{C}$)	Yield (%) ^b		
				7	10	14
1	Dichloromethane ^a	120	42	—	—	—
2	Dichloroethane	8–16	80	81	87	90
3	Acetonitrile	4–6	80	86	93	96
4	Ionic liquid	7–10	50	75	80	83
5	Water	12–16	90	73	79	81

^aProducts were not isolated.

^bIsolated yield.

Table 2. Oxidation of primary and secondary alcohols to carbonyls and carboxylic acids

Entry	Substrate	Product ^a	Reaction condition		
			Alcohol–H ₂ O ₂ – Na ₂ WO ₄	Time (h)	Yield (%) ^b
1	Benzyl alcohol	Benzaldehyde	10:50:1	4	83
2	4-Methoxybenzyl alcohol	4-Methoxy benzaldehyde	10:50:1	4	79
3	4-Nitrobenzyl alcohol	4-Nitro benzaldehyde	10:50:1	4	81
4	4-Chlorobenzyl alcohol	4-Chloro benzaldehyde	10:50:1	4	80
5	Cinnamyl alcohol	Cinnamaldehyde	10:50:1	4	73
6	Cyclopentanol	Cyclopentanone	10:40:1	5	84
7	Cyclohexanol	Cyclohexanone	10:40:1	5	86
8	2,6-Dimethyl cyclohexanol	2,6-Dimethyl cyclohexanone	10:40:1	6	78
9	4- <i>tert</i> -Butyl cyclohexanol	4- <i>tert</i> -Butyl cyclohexanone	10:40:1	6	63
10	1-Phenyl ethanol	Acetophenone	10:60:1	5	93
11	1-(4- <i>iso</i> -Butyl)-phenyl ethanol	4-Isobutyl acetophenone	10:60:1	6	87
12	Benzoin	Benzil	10:40:1	6	87
13	Cholesterol	5-Cholesten-3-one	10:60:1	6	73
14	Benzhydrol	Benzophenone	10:60:1	4	96
15	Octanol	Octanoic acid	10:60:1	6	85 ^c
16	Hexanol	Hexanoic acid	10:60:1	6	90 ^c
17	Borneol	(±)-Camphor	10:60:1	6	61
18	2-Methyl-1-butanol	2-Methylbutyric acid	10:60:1	6	81
19	4-Hydroxy-3-methoxybenzyl alcohol	Vanillin	10:60:1	4	75
20	Pregnenelone	Pregn-5-ene-3,20-dione	10:60:1	5	73

^aThe products were identified by comparison of physical and spectroscopic data with the authentic samples.^[8b,10d,21,22]

^bIsolated yield.

^cRemaining ester.

representative substrates, viz cyclohexanol, 1-phenylethanol, and benzhydrol (7, 10, and 14, Table 2). Although the reaction does not take place at all in dichloromethane, it gives the best yield in acetonitrile at reflux temperature in half the time (4–6 h) as water and dichloroethane (8–16 h). On the other hand, the reaction in ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate

was completed within 7–10 h at 50 °C with 75–83% yield. It is clear from Table 2 that most substrates underwent direct oxidation to give the corresponding aldehydes, ketones, acids, and esters in excellent yields. The oxidation of aliphatic as well as aromatic secondary alcohols (**6–12**, **14**, Table 2) proceeded with high efficiency to give ketones, and the primary aromatic alcohols proceeded with moderate efficiency to give aldehydes (**1–5**, **17**, **19**, Table 2). The primary aliphatic alcohols (**15**, **16**, **18**, Table 2) underwent oxidation to provide synthetically and commercially useful acids or esters. The resin that functions as the PTC does not require any regeneration and hence can be used along with the aqueous layer containing the metal catalyst for more than five runs without any appreciable loss of activity, as no structural change was observed. This is confirmed from the observation of superimposable IR spectra of fresh IRA amberlite 400 resin, and the resin was isolated after use more than five times (Fig. 1). The polymeric basic amberlite resin PTC with sodium tungstate as the activator for hydrogen peroxides has the advantage that C=C double bond present in any alcohol substrates is left untouched (**5** and **20**, Table 2). The untouchability of the C=C bond by this oxidizing system is further observed when the synthesis of an important pregnan series steroidal hormone progesterone (**20d**) was undertaken as a part of our continued effort^[23] for preparation of different corticosteroid drug intermediates. Thus, during the oxidation of the secondary hydroxyl group in the 3-position of pregnenolone (**20b**) by the Oppenauer reaction (Scheme 3), the 5,6 double bond is shifted to the 4,5 position (appeared at δ_{H} 5.70 ppm) to give progesterone^[24] with the stable α,β conjugated enone form. However, when pregnenolone (**20b**) was oxidized with hydrogen peroxide and sodium

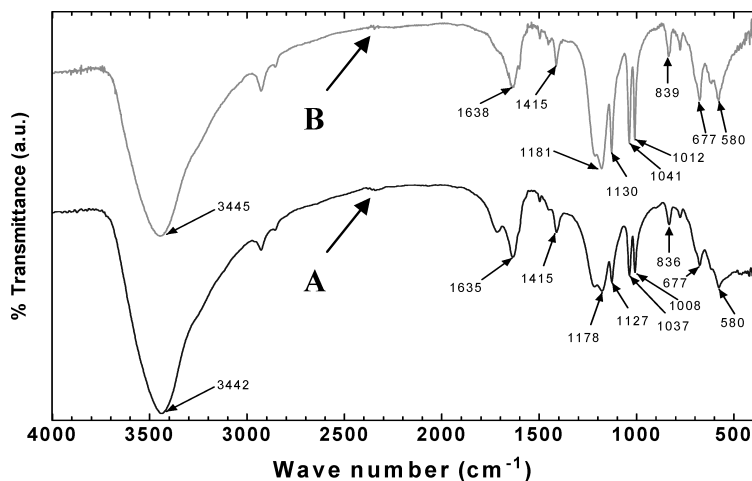
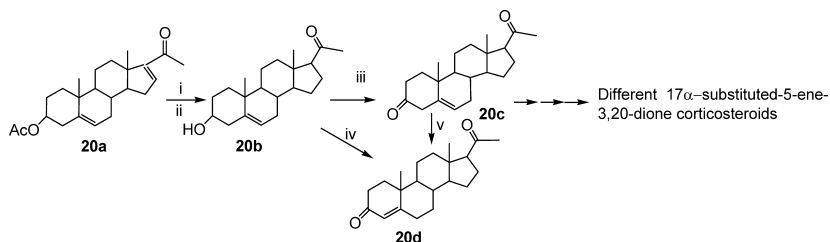


Figure 1. Superimposable IR spectra of fresh amberlite IRA 400 resin (basic) (**A**) and the resin isolated after use (**B**).



Scheme 3. Synthesis of progesterone and pregn-5-ene-3,20-dione: (i) Pd-C/H₂, rt, 8 h; (ii) KHSO₄-SiO₂-MeOH, 64 °C, 4 h.^[26]; (iii) H₂O₂-Na₂WO₄-amberlite IRA-400 (resin), 80 °C 6 h; (iv) Oppenauer oxidation; (v) (COOH)₂-EtOH, 3 h.^[25a]

tungstate with amberlite basic resin, no shift of this double bond at the 5,6 position (appeared at δ_{H} 5.23 ppm) was observed in the product pregn-5-ene-3,20-dione (**20c**). Preg-5-ene-3,20-dione is a very important intermediate for preparation of different 17 α -substituted 5-ene-3,20-dione corticosteroid^[25] drugs.

In summary, we have described an expedient method for oxidation of primary and secondary alcohols by hydrogen peroxide using amberlite IRA 400 resin in chloride form (strongly basic) and sodium tungstate as catalyst. This method is high yielding, clean, safe, operationally simple, and cost-effective and can be exploited successfully for large-scale industrial production of carbonyl compounds by recycling the catalytic system.

REPRESENTATIVE EXPERIMENTAL PROCEDURE

Sodium tungstate (0.329 g, 1 mmol) was stirred with dil. H₂SO₄ (0.5 mL, pH 1.5) and H₂O₂ (30%, 6.8 mL, 0.06 mol) in a 50-mL flask for 30 min. Then resin (0.1 g, <1% of the total reaction volume) and diphenylmethanol (1.84 g, 10 mmol) in acetonitrile (15 mL) were added to the reaction mixture. The resultant was then heated to 80 °C. The aliquots of the reaction mixture were taken at different time intervals and monitored by gas and thin-layer chromatography (TLC). After about 4 h the reaction mixture was cooled to room temperature. The solid resin was filtered, and the solvent removed under reduced pressure. The residual aqueous layer was extracted in ethyl acetate (50 mL) and then washed with water (3 × 10 mL), at which time no residual peroxide was detected in the organic phase. It was dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residual crude reaction mixture was purified by silica-gel column chromatography using 20% ethyl acetate in pet. ether (40–60 °C) as eluent to give the pure ketone benzophenone (1.75 g, 95%). The catalyst (amberlite resin) was washed thoroughly with ethyl acetate and dried at 100 °C for 2 h. The same catalyst and aqueous layer were then used

for other different substrates. The reaction carried out under triphase catalysis in other organic ionic solvents and water was worked up in an analogous manner to isolate the products from the organic phase. Similarly the other substrate alcohols were oxidized to the corresponding carbonyl derivatives (Table 2).

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