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LETTERS

PHASE TRANSFER CATALYZED OXIDATION OF ALCOHOLS WITH SODIUM HYPOCHLORITE

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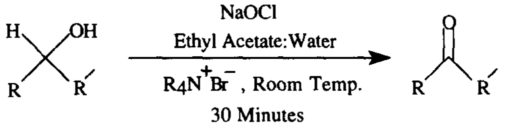
ABSTRACT: Phase transfer catalyzed oxidation of alcohols with sodium hypochlorite in ethyl acetate media resulted in good to excellent yield of oxidized products. These reactions are mild, efficient, and safe. The experimental procedures and work-ups are very convenient. © 1998 Elsevier Science Ltd. All rights reserved.

Oxidation is an important type of reaction in organic synthesis and as such is used in most research laboratories. Commonly used oxidants include nitric acid which is dangerous and very corrosive, and salts of manganese or chromium which are highly toxic, mutagenic, cancer suspect agents, environmentally harmful and often messy.[1]

In this paper, we report a safer sodium hypochlorite procedure for the oxidation of alcohols. In addition our experimental procedures and work-ups are easy, the yields of oxidation products are good to excellent, and the reaction time is short. Thus our method is even more attractive than the previously described methods for oxidation of alcohols.[1-2] It is hoped that this method will have an immediate application in the way oxidation chemistry reactions, in particular, the oxidation of alcohols are performed.[3]

Various alcohols (primary, secondary, and benzylic) were subject to sodium hypochlorite oxidation under the mild experimental conditions specified below. In all cases, good to excellent yield of oxidized products were obtained.



R = Alkyl Group, R' = H
R = R' = Alkyl Groups
R = Aryl Group, R' = H
R = R' = Aryl Groups

The products were analyzed by IR, and GC-MS techniques. The absence of the alcohol OH stretch , and the appearance of new carbonyl (C=O) stretching for the oxidized products were an indication of the products' identity and the GC-MS analysis provided the molar mass and confirmed the purity of the products. Reactions were all done in ethyl acetate as the organic phase with tetrabutylammonium bromide as the phase transfer catalyst.[4] The oxidation reaction is essentially complete in 30 minutes, and the yields ranged from 72% for the oxidation of cholesterol to 93% for the oxidation of benzyl alcohol. It is essential that fresh bleach be used in

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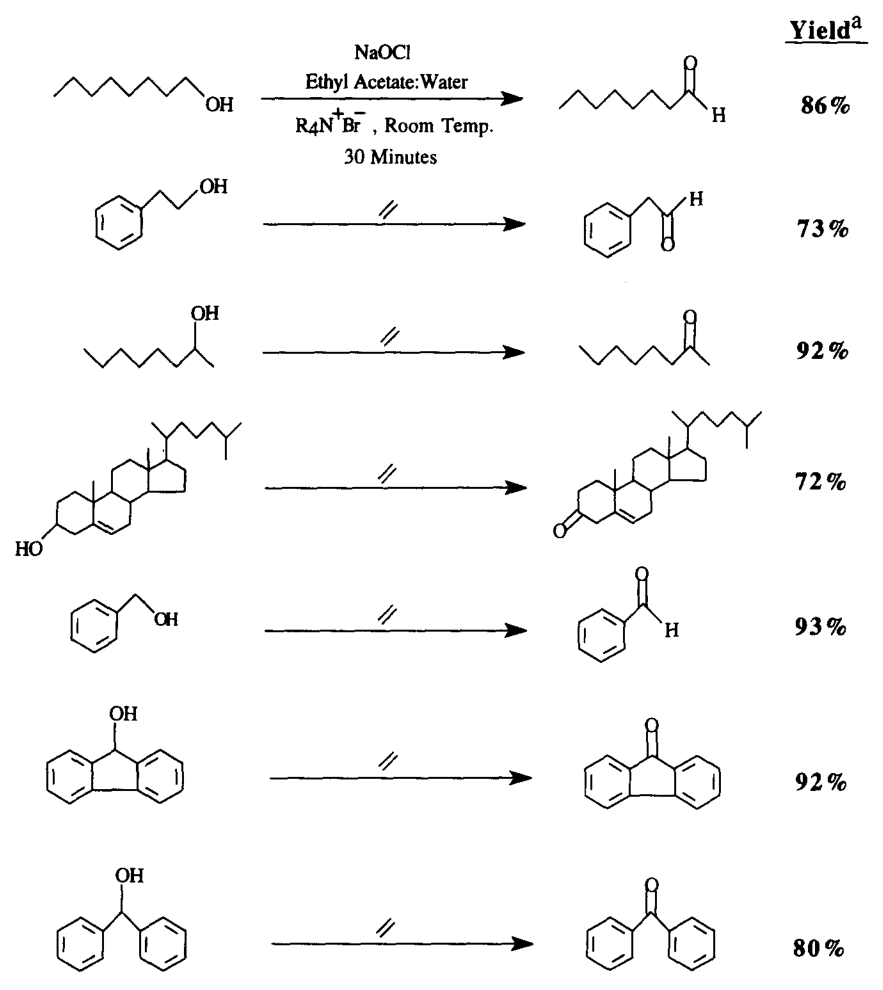
order to minimize the amounts of impurities, and maximize yields of the oxidized products.[5] Table 1 summarizes our results for the oxidation of primary, secondary, and benzylic alcohols.[6-7]

Table 1. Phase Transfer Catalyzed Oxidation of Alcohols With NaOCl (Bleach)



[a] Yields are after final purification.

We have shown that phase transfer catalyzed oxidation of primary, secondary, and benzylic alcohols with sodium hypochlorite results in good to excellent yields of the desired oxidized products. This method of oxidation is mild, efficient, and safe. The experimental procedures and work-ups are very convenient.[7] In addition, the low cost and availability of sodium hypochlorite as commercial household bleach makes this method of oxidation of alcohols very attractive.

ACKNOWLEDGMENT:

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2. Stevens, R.V.; Chapman, K.T.; Stubbs, C. A.; Tam, W. W.; Albizatie, K. F. *Tetrahedron Lett.* **1982**, *23*, 4647. This article reported successful oxidation of secondary alcohols using sodium hypochlorite in acetic acid. However, the method is not effective for oxidation of primary alcohols and alcohols containing double bonds. It is reported that oxidation of primary alcohols leads to dimeric esters under the acidic condition described. For instance, oxidation of 1-decanol leads to decyl decanoate as the major product. Also oxidation of alcohols containing double bonds is reported to produce chlorine-containing products. Reactions times are long, they typically require 2-4 hours for completion. In addition, reagents used are potentially dangerous. Glacial acetic acid is corrosive and causes burns; the vapor is extremely irritating to mucous membranes and the upper respiratory tract, and a sodium hypochlorite solution in glacial acetic acid emits chlorine gas, which is a respiratory and eye irritant. We believe our method of phase transfer catalyzed oxidation of alcohol in ethyl acetate is superior over this both in terms of its application and safety consideration.
3. This paper was presented in the Division of Chemical Education at the 213th ACS National Meeting in San Francisco, California, April 13-17, 1997 (Abstract # 100).
4. In the absence of phase transfer catalyst, little or no reaction is evident and the alcohol is recovered unchanged.
5. Other commercial bleaches work as effectively when used fresh. For precise work, samples may be titrated according to the procedure of Kolthoff, I. M.; Belcher, R. Volumetric Analysis, Interscience: New York, 1957, P. 262.
6. Materials and Methods: 1-Octanol, 2-phenylethanol, 2-octanol, cholesterol, benzyl alcohol, 9-fluorenol, benzhydrol, tetrabutylammonium bromide, ethyl acetate, dichloromethane were all purchased from Aldrich Chemical Company and were used as such without further purification. Thin layer chromatography (TLC) was performed on Eastman Kodak TLC plates (coated film, #13179) with a fluorescence indicator. Commercial Clorox Fresh Scent Bleach (5.25% Sodium hypochlorite) was used. Fourier-transform infrared (FT-IR) were performed neat or as solutions in dichloromethane on a Nicolet 510P Spectrometer. The low resolution mass spectra (LRMS) were obtained on a Hewlett-Packard 5970 GC-MS spectrometer equipped with an HP-1 Cross-linked Methyl Silicone Gum (12 m x 0.2 mm x 0.33 mm film thickness)

capillary column. The initial column temperature of 60°C (1 min) then 10°/min increments up to 250° (5min) were used for all the analysis except cholesterol where the initial column temperature of 150°C (1 min) then 10°/min increments up to 250°C (15 min) were used.

7. General Procedure: In a 50.00-mL round bottom flask equipped with a magnetic stir bar, 5.56 mmol of the appropriate alcohol, and 15.00 mL of ethyl acetate were mixed. The solution was vigorously stirred at room temperature, and while stirring, 15.00 ml of commercially available Clorox Fresh Scent Bleach (5.25% Sodium hypochlorite), and 0.300 g (0.93 mmole) of phase transfer reagent tetrabutylammonium bromide were added. The progress of reactions was monitored by TLC using hexane:ethylacetate (8:2 v/v) as the mobile phase. Oxidation reactions were essentially complete in 30 minutes, but in some cases the reactions were allowed to stir for a period of one hour to insure the complete oxidation process. The organic phase was removed and the aqueous layer was extracted with 20 mL of ethyl acetate or diethyl ether. The combined organic layer was then washed once with 20 mL of water, and then dried over anhydrous magnesium sulfate. After removal of the drying agent by filtration, and removal of the volatile materials under reduced pressure, the percent yield were calculated. The GC-MS and IR analysis of the products were conducted in dichloromethane solvent. Both confirmed that the products were pure and contained no starting materials.

Benzaldehyde: isolated yield, 93%; LRMS m/e 106, 105, 77 (base), 51; FT-IR (CH_2Cl_2) υ max: 3065, 2965, 2822, 2739, 1701 (C=O), 1588, 1204, 828, 714 cm^{-1}.

Octanal: isolated yield, 86%; LRMS m/e 128, 84, 69, 57, 43 (base), 29; FT-IR (CH_2Cl_2) υ max: 2986, 2961, 2932, 2859, 1732 (C=O), 1375, 1264, 1047, 746 cm^{-1}.

2-Octanone: isolated yield, 92%; LRMS m/e 128, 113, 58, 43 (base), 27; FT-IR (CH_2Cl_2) υ max: 2961, 2932, 2860, 1715 (C=O), 1265, 737 cm^{-1}.

9-Fluorenone: isolated yield, 93%; mp 82-84° (recrystallized from hexane); LRMS m/e 180 (base), 152, 126, 87, 76; FT-IR (CH_2Cl_2) υ max: 3056, 2988, 1717 (C=O), 1422, 1264, 897, 747 cm^{-1}.

Δ^5-Cholesten-3-one: isolated yield, 72%; mp 125-127°, LRMS m/e 384 (base), 229, 156, 124; FT-IR (CH_2Cl_2) υ max: 3058, 2986, 2943, 2909, 2876, 1736 (C=O), 1447, 1375, 1246, 1047, 740 cm^{-1}.

Benzophenone: isolate yield, 80%; mp 47-48°C (recrystallized from hexane); LRMS m/e 182, 105 (base), 77, 51; FT-IR (CH_2Cl_2) υ max: 3056, 2984, 1736 (C=O), 1662, 1449, 1373, 1277, 1244, 1047, 704 cm^{-1}.

Phenylethanal: isolated yield, 73%; LRMS m/e 120, 91 (base), 65; FT-IR (CH_2Cl_2) υ max: 3056, 2986, 2938, 2868, 2807, 1740 (C=O), 1375, 1242, 1047, 739 cm^{-1}.

Microscale oxidation reactions using 0.556 mmol of the appropriate alcohol, 1.5 mL of ethyl acetate, 1.5 mL of bleach, and 0.030 g (0.093 mmol) of tetrabutylammonium bromide produced a similar yield of products but in a shorter period of time, about 20 minutes.