

Oxidation of Benzylic and Secondary Alcohols to Carbonyl Compounds by NaBrO₃–NH₄Cl Reagent in Aqueous Acetonitrile†

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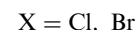
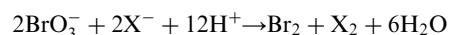
NaBrO₃ combined with NH₄Cl is found to be an efficient reagent for the conversion, in aqueous acetonitrile and under mild conditions, of benzylic and secondary alcohols into aldehydes and ketones, respectively.

The oxidation of alcohols to carbonyl compounds is a fundamental transformation of organic chemistry which is attracting much current interest.^{1–4} A great number of oxidizing agents can effect the conversion of alcohols into carbonyl compounds, and synthetic chemists are faced with an wide choice of methods for this reaction. However, the susceptibility of aldehydes to further oxidation narrows the choice of reagents for the oxidation of primary alcohols to aldehydes in good yield, and if the alcohol group is part of a complex molecule that is sensitive to acidic or basic reagents then the choice of effective oxidants is narrowed still further. The discovery of new oxidants for the transformation of alcohols to carbonyl compounds under mild conditions with a variety of alcohols is of prime importance in synthetic organic chemistry. Oxidations of alcohols by NaBrO₃ in the presence of cerium(IV) ammonium nitrate (CAN),⁵ bromine,⁶ NaHSO₃,⁷ HBr,⁸ H₂SO₄,⁹ HClO₄¹⁰ and HOAc,¹¹ have been reported, most of the reactions having occurred in relatively strong acidic solutions. We report here the oxidation of benzylic and secondary alcohols with NaBrO₃–NH₄Cl into the corresponding aldehydes and ketones.

We have found that this method of oxidation is very convenient for the conversion of alcohols into carbonyl compounds because of its simplicity and use of mild reaction conditions. Furthermore, NH₄Cl and NaBrO₃ are both cheap and easily available compared to most other oxidizing agents that have so far been employed. As shown in Table 1, a wide variety of secondary alcohols and some benzylic alcohols could be easily oxidized to the corresponding carbonyl compounds. However, other primary alcohols (Table 1, entries 3–5) were recovered practically unchanged.

In order to obtain some information about the reaction pathway, cyclohexanol was allowed to react with (a) NaBrO₃–NH₄OAc [5 mmol NaBrO₃ and 7 mmol NH₄OAc in 10 ml solvent mixture (acetonitrile–water 7:3)] and (b) NaBrO₃ (5 mmol NaBrO₃ in 10 ml same solvent mixture) in the absence of NH₄Cl. Neither NaBrO₃–NH₄OAc nor bromate ion alone was capable of oxidizing cyclohexanol. This fact excludes the possibility of the alcohols being oxidized with just BrO₃[–] ion and also when bromate ion exists in the presence of NH₄⁺ ion in a solution which does not have any acidic property (the pH of 5 mmol NaBrO₃ and 7 mmol NH₄OAc in 3 ml of H₂O is 7.20). However, in a solution in which both bromate and NH₄⁺ ions co-exist, NH₄⁺ ion hydrolysis gives an acidic solution (the pH of 5 mmol NaBrO₃ and 7 mmol NH₄Cl in 3 ml of H₂O is 4.00) while the BrO₃[–] ions are capable of oxidizing the alcohols. In order to illustrate the role of NH₄Cl in providing an acidic solution, we performed experiments in various buffer

solutions in the absence of chloride ion. Thus we repeated the oxidation of cyclohexanol in HOAc–NaOAc (7 ml CH₃CN + 3 ml buffer solution with pH = 4.62), potassium hydrogen phthalate (7 ml CH₃CN + 3 ml buffer solution with pH = 3.99) and NaH₂PO₄ (7 ml CH₃CN + 3 ml buffer solution with pH = 3.86). No reaction occurred in any of these experiments after 3 h at 80 °C. These experiments showed that the reaction is not only pH-dependent, but also requires the definite presence of Cl[–] from NH₄Cl in order to proceed. The chloride ion mentioned above is suggested to generate bromine and chlorine *via* the following reaction:¹²



and can in turn oxidize alcohols.¹³

We have found that Br₂ is generated after *ca.* 2.5 h when NaBrO₃ (5 mmol) is added to a solution of NH₄Cl (7 mmol, in 7 ml CH₃CN + 3 ml H₂O) at room temperature.

Also, a of NH₄Br–NaBrO₃ mixture was observed to release bromine and we suggest that this system could be a good candidate for the oxidation of alcohols or as a brominating agent of alkenes.

In conclusion, NaBrO₃–NH₄Cl is an excellent oxidizing agent which promises to be economical with high yields, employs simple and mild reaction conditions, and is thus a convenient reagent for selective oxidation of secondary and benzylic alcohols.

Experimental

All products are known compounds and were identified by comparison of their physical and spectral data with those of authentic samples. Melting points were determined in open capillaries using an oil-bath and are uncorrected. IR spectra were recorded as neat films or as KBr pellets on a Shimadzu 470 spectrometer. ¹H NMR spectra were recorded at 90 MHz on a JEOL EX-90 instrument with CDCl₃ as solvent and Me₄Si as an internal standard. pH Measurements were carried out with a Schott CG model 825 pH meter equipped with a combined glass–calomel electrode; all the pH measurements were performed in aqueous solution. All alcohols are commercial materials and were purchased from Fluka, Aldrich or Merck. Reagent-quality solvents were used without further purification. Yields reported refer to isolated products or 2,4-dinitrophenylhydrazone derivatives (2,4-DNP)^{14,15} of the carbonyl compounds.

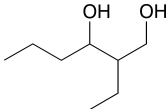
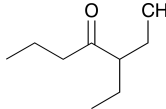
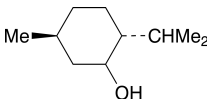
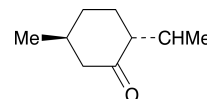
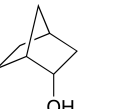
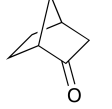
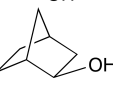
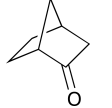
General Procedure.—Alcohol (5 mmol) was added to a mixture of NaBrO₃ (0.755 g, 5 mmol) and NH₄Cl (0.4 g, 7.5 mmol) in aqueous acetonitrile (CH₃CN–H₂O = 7/3 v/v; 10 ml). The mixture was stirred at 80 °C for 1–3 h. When the reaction was complete, the resulting solution was extracted with methylene dichloride (20 ml × 2). The combined organic layers were washed with a saturated aqueous solution of NaHCO₃ and dried over MgSO₄. After filtration, the solution was concentrated to afford the crude carbonyl compound, which was frequently of good purity without further treatment, although, if necessary, it could be purified by distillation, crystallization or chromatography, as appropriate.

Financial support by the Research Council of Shahid Beheshti University is gratefully acknowledged.

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Oxidation of alcohols to carbonyl compounds by NaBrO₃-NH₄Cl in acetonitrile-water (7:3 v/v) at 80 °C

Entry	Reactant	Product	Reaction time (t/h)	Yield (%)		Bp of carbonyl product at 760 Torr (T/°C)	Mp of carbonyl product (T/°C)	Mp of 2,4-DNP (T/°C)
				2,4-DNP	Isolated			
1	CH ₃ CH ₂ CH ₂ CH(OH)CH ₃	CH ₃ CH ₂ CH ₂ COCH ₃	3.0	75	80	102 (100–101 ^a)	—	142 (144 ^b)
2	(CH ₃) ₂ CHCH(OH)CH ₃	(CH ₃) ₂ CHCOCH ₃	3.30	90	88	94 (94–95 ^a)	—	120 (117 ^b)
3			2.30	50	49	—	—	118 (118.5–119.5 ^c)
4	Octan-1-ol	No reaction	6.0					
5	Hexan-1-ol	No reaction	6.0					
6	Cyclopentanol	Cyclopentanone	1.0	90	85	127–139 (131 ^a)	—	144 (142 ^b)
7	Cyclooctanol	Cyclooctanone	3.0	90	83	185–193 (195 ^a)	—	162 (163 ^b)
8	Cyclohexanol	Cyclohexanone	2.0	90	91	150–155 (155 ^a)	—	160–161 (162 ^b)
9 ^d	4- <i>tert</i> -Butylcyclohexanol	4- <i>tert</i> -Butylcyclohexanone	3.0	70	72	—	48–49 (47–50 ^c)	
10 ^d	2- <i>tert</i> -Butylcyclohexanol	2- <i>tert</i> -Butylcyclohexanone	3.0	50	53	62 ^f		
11 ^g			4.0	80	81	202–203 (207 ^a)	—	146 (146 ^b)
12	PhCH ₂ OH	PhCHO	2.0	86	80	175 (179 ^a)	—	230 (237 ^b)
13	PhCH(OH)Me	PhCOMe	2.0	95	88	199–201 (202 ^a)	—	240 (250 ^b)
14	4-O ₂ NC ₆ H ₄ CH ₂ OH	4-O ₂ NC ₆ H ₄ CHO	2.0	80	78	—	104–105 (106 ^b)	315 dec (320 dec ^b)
15 ^h			1.0	60	62	—	93–95 (94–96 ^e)	125 (125–126 ^f)
16 ⁱ			1.0	60	61	—	93–95 (94–96 ^e)	—
17	Me ₃ COH	No reaction						
19 ^k	Cyclohexanol	No reaction						

^aFrom ref. 16 at 760 Torr (≈101080 Pa). ^bFrom ref. 16. ^cFrom ref. 17. ^d*cis* and *trans* isomers. ^eFrom ref. 18. ^fAt 5 Torr (≈665 Pa) (lit.,¹⁵ 62.5, 4 Torr ≈532 Pa). ^g(-)-Menthol. ^h(+)-*endo*-Norborneol. ⁱFrom ref. 4. ^j(+)-*exo*-Norborneol. ^kIn the absence of NH₄Cl.

Received, 10th March 1997; Accepted, 28th October 1997
Paper E/7/01647F

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