A simple biomimetic protocol for the oxidation of alcohols with sodium hypochlorite in the presence of β -cyclodextrin in water

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Abstract: A simple and efficient protocol, which is inexpensive, convenient, clean, and facile, for oxidation of alcohols to carbonyl compounds has been developed using sodium hypochlorite in the presence of β -cyclodextrin with water as solvent. A series of alcohols were oxidized at room temperature in excellent yields.

Key words: oxidation, alcohols, sodium hypochlorite, KBr, β -cyclodextrin, biomimetic, water.

Résumé : On a mis au point un protocole simple et efficace d'oxydation des alcools en composés carbonylés qui est peu coûteux, pratique, propre, et facile et qui fait appel à l'utilisation d'hypochlorite de sodium en présence de β -cyclodextrine dans l'eau comme solvant. On a oxydé une série d'alcools, à la température ambiante, avec d'excellents rendements.

Mots clés : oxydation, alcools, hypochlorite de sodium, KBr, β -cyclodextrine, biomimétique, eau.

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Introduction

Green chemistry is becoming a central issue in both academic and industrial research in the 21st century (1). Industrial chemistry is not sustainable without this approach. Hence, the goal of present-day industrial research is to develop environmentally benign and clean synthetic technologies, thereby minimizing the cost of waste disposal.

Among various reactions of industrial significance, oxidation of alcohols to carbonyl compounds is a pivotal reaction and is essential for the preparation of organic intermediates, fragrances, and food additives (2). Numerous methods have been developed for these oxidations (3-17). All these traditional methods involve the use of stoichiometric amounts of inorganic oxidants, e.g., Cr(VI), which generate copious amounts of waste heavy metals. Moreover, these methods involve the use of hazardous reagents and solvents, and sometimes expensive reagents and transition metal catalysts, which interfere and make the recovery of catalyst cumbersome. In some cases, overoxidation products have also been detected. The use of molecular O₂ for oxidation is often difficult to control and sometimes results in combustion, and the reaction is performed with low conversion to avoid overoxidation.

Among various oxidizing agents, sodium hypochlorite seems to be the most inexpensive with the highest potential for industrial application. The earliest application of NaOCI as a practical synthetic reagent for alcohol oxidation involved its use in a two-phase system with a phase-transfer catalyst (18). More recently, two improved methods for bleach oxidation of alcohols have been developed. One method employs acetic acid as a solvent in a monophasic system (19) while the other uses catalytic amounts of TEMPO in a buffered biphasic medium (20). All these methods involve the use of biphasic systems employing dichloromethane or toluene as the organic phase, a phase-transfer catalyst, and subsequent formation of overoxidation products. It is difficult to find a procedure that is selective, cheap, efficient, and easy to work up.

In a continuation of our work on supramolecular chemistry involving cyclodextrins (21), we have attempted the oxidation of alcohols with sodium hypochlorite in the presence of β-cyclodextrin in water to develop an environmentally viable process. Cyclodextrins, which are cyclic oligosaccharides, exert microenvironmental effects leading to selective reactions. They catalyze reactions by supramolecular catalysis through non-covalent bonding as seen in enzymes. Complexation depends on the size, shape, and hydrophobicity of the guest molecule. Thus, mimicking biochemical selectivity, where orientation of the substrate by complex formation positioning presents only certain regions for favorable attack, will be superior to chemical selectivity, which involves random attack at different regions due to the intrinsic reactivity of the substrate. These attractive features of cyclodextrins in the biomimetic modeling of chemical reactions prompted us to investigate a variety of oxidations us-

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Table 1. Oxidation of alcohols with NaOCl–KBr in the presence of β -CD in water.

Entry	Substrate	Product ^a	Time (h)	Yield (%) ^b
1	ОН	СНО	8	94
2	МеО	CICHO	8	94
3	ОН	CHO Me	8	91
4	ОН	СНО	10	89
5		CHO	12	88
6	HO OH	HO CHO	12	89
7	тврихо	тврмо	8	90
8	ОН	СНО	8	92
9	(CH ₂) ₈ OH OH	(CH ₂) ₈ CHO	12	84
10	ОН		12	88
11	F OH	F O	12	86
12	Me	Me	12	86
13	ОН		12	84
14			14	82

^a All products were characterized by ¹ H NMR, IR, and MS, and all

physical characteristic comparisons were done with authentic samples.

^b Isolated and unoptimized yields.

ing the substrate β -cyclodextrin complexes with sodium hypochlorite in water. The complexes were formed with β -cyclodextrin since it is easily accessible and the least expensive among the cyclodextrins.

There are reports of utilizing sodium hypochlorite in conjunction with cyclodextrins for certain oxidations such as for the chlorination of anisole at the para position (22), for asymmetric catalytic epoxidation (23), and sulfoxidation (24). To date, no alcohol oxidations to important carbonyl compounds have been carried out with sodium hypochlorite under supramolecular catalysis involving cyclodextrins.

Experimental

Materials

All reactions were carried out in an air atmosphere without any special precautions. Chemicals and solvents were purchased from Fluka and S. D. Fine Chemicals and used as received. ¹H NMR spectra were obtained on a Gemini-200 or 300 MHz spectrometer. IR spectra were recorded on a Nicolet Nexus 670 FT-IR spectrometer. Mass spectra were observed on a Micromass VG AutoSpec M spectrometer.

Typical procedure for oxidation

 $\hat{\beta}$ -Cyclodextrin (1 mmol) was dissolved in water (15 mL) at 60 °C, then substrate (1 mmol) previously dissolved in methanol/acetone (1 mL) was added slowly with stirring and cooled to room temperature. Later, the reaction was cooled in an ice bath and sodium hypochlorite (5 mmol) was added slowly, followed by addition of KBr (1 mmol) and subsequent stirring at room temperature was continued until the reaction had gone to completion (Table 1). It was extracted with ethyl acetate and filtered. The organic layer was dried over anhydrous Na₂SO₄ and the solvent was removed in vacuum to obtain the crude product, which was purified by column chromatography using *n*-hexane : ethyl acetate (95:5) on silica gel.

Results and discussion

The reaction was carried out by the in situ formation of the β -cyclodextrin complex of the alcohol in water followed by addition of sodium hypochlorite and KBr at 0-5 °C and later stirring at room temperature until the reaction went to completion. A variety of alcohols have been oxidized to their corresponding carbonyl compounds in impressive yields using NaOCl-KBr under supramolecular catalysis in water (Scheme 1). This methodology is also compatible in the presence of other functionalities such as methoxy, methylenedioxy, nitro, hydroxy, and alkene double bonds. The yields of oxidation products of primary alcohols are comparatively better than secondary alcohols. Though inclusion complexation takes place in situ during the reaction, the complexes have been isolated and characterized by powder X-ray (25) and ¹H NMR studies (26). All the compounds were characterized by MS, ¹H NMR, and IR techniques followed by comparison of the collected data to known compounds (27).

The reaction has also been studied in detail for various ratios of β -cyclodextrin and KBr by taking 4-methoxybenzyl alcohol as an example (Table 2). It was observed that optiScheme 1.



Table 2. Oxidation of 4-methoxybenzyl alcohol using NaOCl–KBr system.

Entry	β-CD ^{<i>a</i>} (mmol/L)	Hypo ^b (mmol/L)	KBr (mmol/L)	Alcohol (mmol/L)	Yield (%)
1	0.1	5.0	0.1	1.0	30
2	0.1	5.0	1.0	1.0	45
3	1.0	5.0	0.1	1.0	68
4	1.0	5.0	1.0	1.0	94

^aβ-Cyclodextrin.

^bSodium hypochlorite.

mum yields were obtained when β -cyclodextrin and KBr were taken in equimolar ratios of 1 equiv. each. However, the yields were comparatively less with lower ratios of β -cyclodextrin and KBr. Another point of interest is that the yields were drastically reduced with lower equivalents of KBr in spite of higher ratios of β -cyclodextrin. Thus, it could be seen that KBr plays a major role in these oxidations and its function can be explained as follows.

The oxidation of alcohols in the presence of β -cyclodextrin using sodium hypochlorite and KBr can take place through the initial formation of β -cyclodextrin-hypochlorite as observed by Breslow and co-workers (22) followed by the in situ generation of the more active β -cyclodextrin-hypobromite, which further increases the oxidation yields. This is substantiated by the fact that no oxidation was observed when the alcohol was reacted in the presence of β -cyclodextrin using hydrogen peroxide and KBr.

In conclusion, we have developed an inexpensive, ecoconscious chemical process for the oxidation of alcohols to carbonyl compounds in aqueous medium. This methodology is simple, inexpensive, and can be applied to a variety of substrates with high potential for industrial applications.

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