Ethylenebis(*N*-methylimidazolium) Chlorochromate (EBMICC): A New Selective and Mild Reagent for Oxidation of Alcohols, Hydroquinones and Trimethylsilyl Ethers

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The ethylenebis(*N*-methylimidazolium) chlorochromate was prepared by addition of *N*-methylimidazole to 1,2-dibromoethane to form the corresponding dibromide salt and subsequent treatment of this salt with CrO_3 in 6N HCl solution. It is a stable yellow-orange solid which selectively oxidized benzylic and allylic alcohols, hydroquinones and trimethylsilyl ethers in refluxing acetonitrile. Oxidation of alcohols was also examined under solvent-free conditions and showed much better yields of the corresponding carbonyls in a very short reaction time when compared with the conventional method.

Keywords: Ethylenebis(*N*-methylimidazolium) chlorochromate; Oxidation; Alcohols; Trimethylsilyl ethers; Solvent free; Microwave.

INTRODUCTION

Since the appearance of Collins reagent in 1968,[1] the development of new chromium(VI) oxidizing agents for the effective and selective oxidation of organic substrates, in particular alcohols, has attracted a great deal of continued interest in organic synthesis. Up to now several efficient chromium(VI) reagents such as pyridinium chlorochromate,[2] pyridinium dichromate,[3] 2,2-bipyridinium chlorochromate,[4] 2,6-dicarboxypyridinium chlorochromate,[5] 2,6-dicarboxypyridinium fluorochromate,[6] tetrabutylphosphonium dichromate,[7] 1-methylimidazolium chlorochromate[8] and 1-(benzoylamino)-3-methylimidazolium chlorochromate[9] have been introduced to improve the selectivity, the mildness and the effectiveness of the oxidant species, especially in the oxidation of complex and highly sensitive compounds. Although many chromium(VI) reagents are available for the oxidation of organic substrates, they have certain limitations such as instability, the need of an excess amount of the reagent, and poor selectivity to substrates. Therefore there still exists a need for highly efficient and mild oxidizing agents.

Recently an area of intense synthetic endeavor has emphasized the use and design of reagents without any solvent.[10] Avoiding organic solvents during the reactions in organic synthesis leads to clean, efficient, and economical technology. In solid state reactions, work-up is considerably simplified, cost is reduced, increased amounts of reagents can be used in the same equipment, and reactivities and sometimes selectivities are enhanced without dilution. Organic solid state reactions are usually carried out by keeping a mixture of finely powdered reactant and reagent at room temperature. In some cases, these reactions are accelerated by heating, shaking, and grinding of the reaction mixture using a mortar and pestle and irradiation with ultrasound or microwave.[11] The microwave enhanced organic reactions have gained popularity over the usual homogeneous and heterogeneous reactions, as they can be conducted rapidly and produce pure products in quantitative yields without the use of solvents.[12,13]

RESULTS AND DISCUSSION

As a part of our continuous efforts to develop new efficient oxidizing agents,[5,6] we have synthesized ethylenebis(*N*-methylimidazolium) chlorochromate (EBMICC) and studied its oxidizing properties for alcohols, hydroquinones and trimethylsilyl ethers under different reaction conditions.

This compound is easily and cheaply prepared from *N*-methylimidazole and 1,2-dibromoethane followed by treatment with CrO_3 in the presence of HCl in high yield. It

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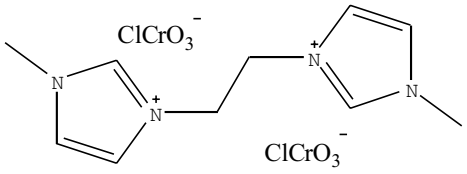


EBMICC

is soluble in DMF, acetone and acetonitrile, and insoluble in methylenechloride, *n*-hexane and diethyl ether. It shows a pH value of 2.6 (0.01 N aqueous solution) that attests to its less acidic character in comparison to PCC and *N*-methyl piperidinium chlorochromate (The pH of 0.01 N solutions of PCC and *N*-methyl piperidinium chlorochromate were found to be 1.75 and 1.85, respectively).[14] One more advantage of EBMICC is that it is much less hygroscopic and can be used after one year of its preparation without any decomposition which is not the case with PCC and similar Cr(VI) reagents. The chromium content of the reagent was determined by atomic absorption and the experimental and calculated results are in very good agreement.

A wide variety of alcohols such as benzylic, allylic and aliphatic were treated with one equivalent of EBMICC in refluxing CH_3CN. As shown in Table 1, benzylic alcohols were oxidized to the corresponding aldehydes or ketones in 3-6 h (Table 1, entries 1-13). The oxidation of allylic alcohols were somewhat slower. Thus cinnamyl alcohol required 10 h for completion of the reaction (Table 1, entry 14). It is evident from Table 1 that with the exception of 2-nitro benzyl alcohol (Table 1, entry 9), the reaction for all benzylic and allylic alcohols gave good yields of the products. Furthermore, hydroquinones in acetonitrile at room temperature were oxidized very fast and gave excellent yields of the corresponding benzoquinones (Table 1, entries 15 and 16). Triphenylphosphine was also oxidized under the same reaction conditions and gave excellent yield of triphenylphosphine oxide in 4 minutes (Table 1, entry 17). The selectivity of this reagent was indicated by the oxidation of benzylic and allylic alcohols and hydroquinones in the presence of aliphatic primary and secondary alcohols. For example, treatment of 1-heptanol or cyclohexanol in refluxing CH_3CN with EBMICC for 15 h led to recovery of unchanged alcohols (Table 1, entries 18 and 19).

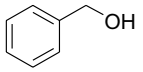
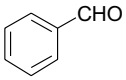
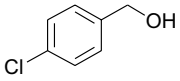
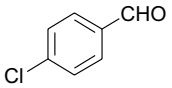
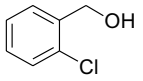
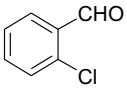
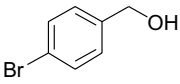
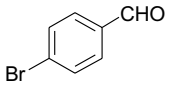
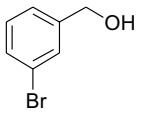
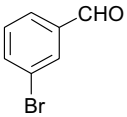
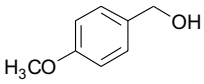
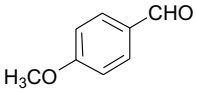
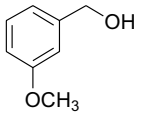
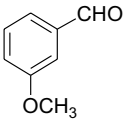
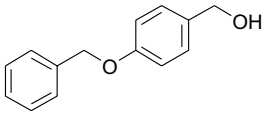
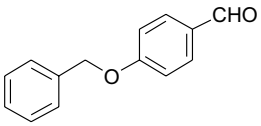
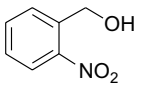
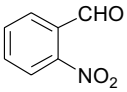
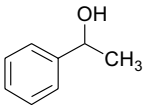
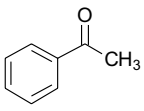
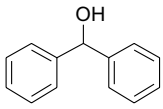
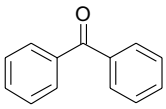
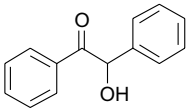
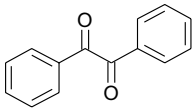
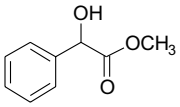
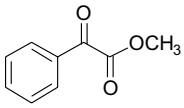
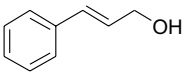
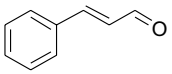
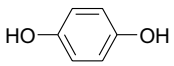
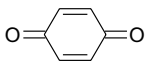
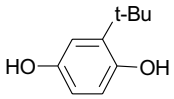
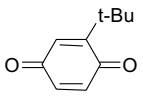
It is noteworthy that acid-labile groups such as tetrahydropyranyl ethers and oximes and also phenolic groups survive under reaction conditions. Thus treatment of 1-heptyl tetrahydropyranyl ether, propiophenone oxime or phenol with this reagent in refluxing acetonitrile for 20 h led to recovery of unchanged starting material (Table 1, entries 20-22).

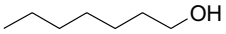
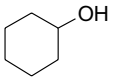
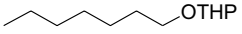
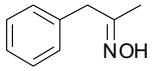
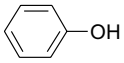
We have also conducted these oxidation reactions under solvent-free conditions and microwave irradiation. We have found that by keeping a mixture of finely powdered reactant and reagent at 80 °C, the reaction was completed in 10-45 min. The results in Table 1 indicate that under solvent-free conditions, all reactions gave better yields in comparison to conventional conditions. Also, that aliphatic alcohols remained unchanged attests to the selectivity of this reagent under solvent-free conditions (Table 1, entries 18 and 19). When we carried out the oxidation reaction under microwave irradiation, oxidation of allylic and benzylic alcohols occurred in an even much shorter time (4-7 min) in excellent yields (Table 1).

Conversion of the hydroxyl function to trimethylsilyl ether is one of the most useful and convenient methods for the protection of this functional group and oxidation of trimethylsilyl ethers to the corresponding carbonyl compounds has received considerable attention during recent years.[15-18] We have studied the treatment of a variety of trimethylsilyl ethers such as benzylic, allylic and aliphatic, with one equivalent of EBMICC in refluxing acetonitrile. The results presented in the Table 2 show that under reaction conditions benzylic and allylic trimethylsilyl ethers converted to the corresponding aldehydes or ketones in high yields (Table 2, entries 1-6), but in the case of aliphatic saturated trimethylsilyl ethers only deprotection was observed and corresponding alcohols remained unchanged even after 15 h (Table 2, entries 7 and 8).

In conclusion, we have shown that EBMICC is an efficient and inexpensive reagent for selective oxidation of benzylic and allylic alcohols, hydroquinones and trimethylsilyl ethers. Tetrahydropyranyl ether, oxime and phenolic groups survive in the procedure of oxidation in refluxing acetonitrile. Allylic and benzylic alcohols under solvent-free conditions are oxidized in a much shorter reaction time than in refluxing acetonitrile. Under microwave irradiation alcohols are oxidized in 4-7 min in excellent yields. Over-oxidation of products to the corresponding carboxylic acids was not observed at all. Interestingly, the α,β-unsaturated alcohols and trimethylsillyl ethers underwent oxidation very efficiently without affecting the olefinic bond and the reaction is essentially chemoselective. Furthermore, functional groups such as chloro, methoxy and nitro were also inert to this reagent and no byproduct formation was

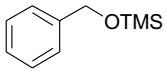
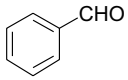
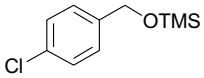
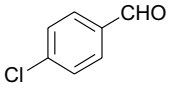
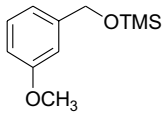
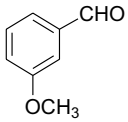
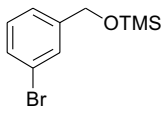
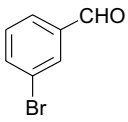
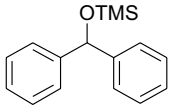
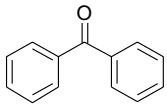
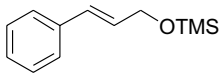
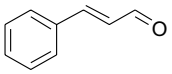
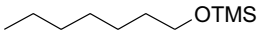
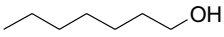
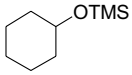
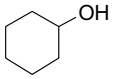
Table 1. Oxidation of alcohols and hydroquinones with EBMICC

Entry	Substrate	Product	Yield/%[a] (Time)		
			Solution	Solvent free	MW[b]
1			85 (3.5 h)	88 (10 min)	93 (4 min)
2			87 (3 h)	90 (10 min)	94 (4 min)
3			82 (6 h)	91 (25 min)	93 (6 min)
4			90 (3.5 h)	92 (10 min)	95 (5 min)
5			85 (4 h)	87 (15 min)	94 (5.5 min)
6			89 (3.5 h)	91 (20 min)	96 (5 min)
7			80 (6 h)	85 (25 min)	94 (7 min)
8			87 (4.5 h)	92 (20 min)	94 (5 min)
9			27 (6 h)	72 (45 min)	92 (6 min)
10			89 (4.5 h)	91 (20 min)	93 (5 min)
11			83 (5 h)	89 (25 min)	94 (5 min)
12			90 (6 h)	93 (25 min)	93 (7 min)
13			91 (4 h)	94 (15 min)	95 (4.5 min)
14			90 (10 h)	91 (35 min)	93 (7 min)
15			95 (4 min)	—	—
16			94 (4 min)	—	—

17	Ph_3P	$Ph_3P=O$	94 (4 min)	—	—
18		—	N.R (15 h)	N.R (60 min)	—
19		—	N.R (15 h)	N.R (60 min)	—
20		—	N.R (20 h)	—	—
21		—	N.R (20 h)	—	—
22		—	N.R (20 h)	—	—

[a] Yield refers to isolated products; all products were identified by comparing IR, NMR, and TLC with those of authentic samples. [b] Activation by domestic microwave oven (operating at 2.45 GHz, 900 W). The final temperature of the reactions after irradiation depending on the reaction time varies between 120-160 °C.

Table 2. Deprotection of trimethylsilyl ethers with EBMICC

Entry	Substrate	Product	Time (h)	Yield% [a]
1			4.5	87
2			4	91
3			5	89
4			5.5	85
5			7	83
6			11	88
7			1	92
8			1	90

[a] Yield refers to isolated products; all products were identified by comparing IR, NMR, and TLC with those of authentic samples.

observed.

EXPERIMENTAL SECTION

Preparation of ethylenebis(*N*-methylimidazolium) chlorochromate (EBMICC)

A mixture of *N*-methylimidazole (4.0 g, 48.7 mmol) and 1,2-dibromoethane (1.9 mL, 22 mmol) was stirred in DMF (40 mL) at 120 °C for 2 h. After cooling the mixture, the white solid formed was filtered, washed with diethyl ether and dried under vacuum. Then it was dissolved in 40 mL of 6N HCl and slowly was added to a stirred solution of CrO_3 (4.4 g, 44 mmol) in 6N HCl (40 mL). The reaction mixture was cooled to 0 °C and the yellow-orange solid

formed was collected by filtration, washed with cold water and dried under vacuum to give EBMICC (7.0 g, 69%). m.p. 99-101 °C. ^{1}H NMR (300.13 MHz, DMSO-d_6): δ 3.75 (s, 6H, CH_3), 4.60 (s, 4H, CH_2), 7.43 (s, 2H, imi-*H*), 7.49 (s, 2H, imi-*H*), 8.78 (s, 2H, NC*H*N). ^{13}C NMR (75.48 MHz, DMSO-d_6): δ 36.4 (*C*H$_3$), 48.9 (*C*H$_2$), 122.8 (imi-*C*), 124.4 (imi-*C*), 137.6 (N*C*HN). IR (KBr) 945, 897, 740 cm^{-1}. Anal. Calcd. for $C_{10}H_{16}Cl_2Cr_2N_4O_6$: C, 25.93; H, 3.48; Cr, 22.45. Found: C, 25.97; H, 3.54; Cr, 22.12.

General procedure for oxidation of alcohols, hydroquinones, triphenylphosphine and trimethylsilyl ethers in acetonitrile

To a solution of an alcohol or trimethylsilyl ether (10 mmol) in acetonitrile (150 mL) was added EBMICC (10 mmol) and the reaction mixture was refluxed for the time specified in Tables 1 and 2. The solvent was evaporated and diethyl ether was added to the residue. The supernatant was decanted and the insoluble residue was washed three times with diethyl ether. The combined ether extracts were concentrated under reduced pressure and the crude product was purified by distillation or by passing through a short column of silica gel. For oxidation of hydroquinones and triphenylphosphine: to a solution of a hydroquinone or triphenylphosphine (10 mmol) in acetonitrile (150 mL) was added EBMICC (10 mmol). The reaction mixture was stirred at room temperature for 4 min and worked up as above.

General procedure for oxidation of alcohols under solvent-free conditions

A mixture of an alcohol (5 mmol) and EBMICC (5 mmol) was kept at 80 °C for the time specified in Table 1. The mixture is then washed with a minimum amount of diethyl ether. The solvent was evaporated and the resulting crude material was purified on a silica gel column. When a microwave digester was used, a mixture of an alcohol (1 mmol) and EBMICC (1 mmol) was irradiated in a closed-vessel in an microwave oven (operating at 900 W) for the time given in Table 1 and worked up as above to get the corresponding aldehyde or ketone.

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