

OXIDATION OF ALCOHOLS WITH PYRIDINIUM BROMOCHROMATE

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ABSTRACT

Pyridinium bromochromate (PBC) is a versatile and inexpensive oxidizing agent. It converts different classes of alcohols to the corresponding carbonyl compounds. Primary and secondary benzylic alcohols are oxidized in moderate to high yields. Synthetic utility of the reagent has been shown to increase in the presence of glacial acetic acid for the oxidation of alcohols.

INTRODUCTION

Oxidation of organic substrates in aprotic solvents, under mild and neutral conditions is important in modern organic synthesis. Chromium (VI) reagents are highly valuable oxidizing agents in organic chemistry (Cainelli and Cardillo, 1984; March, 1992). Chromium trioxide, potassium and sodium dichromate have long been used for the oxidation of organic substrates. These two reagents are not suitable oxidizing agents for the complex and acid sensitive compounds. To surmount these difficulties, chromium trioxide-pyridine complex (Collins, Hess and Frank, 1968) was prepared and has found widespread application for the oxidation of primary and secondary alcohols to their carbonyl compounds. Recently, pyridinium chlorochromate -Corey's reagent (Corey and Suggs, 1975; Agarwal, Tiwari and Sharma, 1990) and pyridinium dichromate (Corey and Schmidt, 1979) were introduced and have rapidly become the reagents most widely used for oxidation of alcohols. A variety of related heterocyclic bases also form salts with chromic acid or chlorochromic acid, many of which are selective reagents for oxidation of alcohols to carbonyl compounds (Luzzio and Guziec, 1988). Typical reagents are 4-(N,N-dimethylamino)- pyridinium chlorochromate (Guziec and Luzzio, 1982),

tetrabutylammonium chlorochromate (Santaniello, Milani and Casati, 1983), nicotinium dichromate (Lopez, Gonzolez, Casio and Palomo, 1985), 2,2'-bipyridinium chlorochromate (Guziec and Luzzio, 1980) triethylammonium chlorochromate (Rao, Radhakrishna, Bali Singh and Bhatnagar, 1983), benzyltriethyl-ammonium dichromate (Huang and Chan, 1982), pyridinium silver dichromate (Firouzabadi, Sardarian and Gharibi, 1984), pyridinium chlorochromate on polymer support (Frechet, Darling and Farrell, 1981), or on alumina (Cheng, Liu and Chen, 1980), and other halochromates such as pyridinium and quinolinium fluorochromate (Bhattacharjee, Chaudhuri, Dasgupta and Roy, 1982; Murugesan and Pandurangan, 1992), quinolinium bromochromate (Özgün and Değirmenbaşı, 1996). However most of these reagents suffer from some disadvantages such as instability, difficulty of preparation, requirement of large excess of reagent, hygroscopicity, low selectivity or cost of use.

This paper describes an investigation of the reactivity and scope of a new chromium (VI) agent, pyridinium bromochromate ($C_5H_5NHCrO_3Br$). The use of this compound, particularly for the bromination of aromatic compounds has previously been described (Narayanan and Balasubramanian, 1986). To our knowledge, no key synthetic applications of this reagent for oxidation of a wide variety of alcohols have appeared in the literature.

EXPERIMENTAL

Melting points were determined in open capillaries on an Electrothermal 9200 apparatus and are uncorrected. All the alcohols were commercially available in the highest purity and used without further purification. The column was packed with silica gel 60 (70-230 mesh ASTM).

Pyridinium bromochromate was prepared from CrO_3 , pyridine and HBr according to the method described by Narayanan and Balasubramanian.

Typical procedure for the oxidation of alcohols:

To a suspension of PBC (3.12 g, 0.012 mole) in purified chloroform (20 ml) was added the substrate (0.010 mole) dissolved in a small amount of chloroform (1-2 ml). The reaction mixture was heated under reflux

with stirring magnetically. All reactions were carried out in flasks blackened from the outside to prevent any photochemical reactions. The progress of the reaction was followed by TLC on silica gel using benzene-ethyl acetate (9:1, v/v). The completion of the reaction was also evidenced from change in the colour of the contents to green. Then the reaction mixture was diluted with 20 ml of ether and stirred for 5 minutes. The powdery brown reduction products were removed by filtration through a sintered glass funnel. The resulting solution was concentrated and passed through a previously prepared short column (2x15 cm; ca 45 g) of silica gel using diethyl ether as eluent. The eluent was concentrated to oily residue and was treated with an excess (20 ml) of a solution of 2,4-dinitrophenylhydrazine (2,4-DNP; 0.75 g) and 1.5 ml concd. H_2SO_4 in methanol to afford hydrazone, which was recrystallized from glacial acetic acid prior to measurement of its melting point.

In the case of catalyzed oxidation reactions, 100 μ l of glacial acetic acid were added to the well stirred suspension of PBC (3.12 g, 0.012 mole) in 20 ml of chloroform. After stirring for at least 5 minutes, alcohol was added to the oxidant catalyst solution. Rest of the procedure is the same as with the uncatalyzed oxidation reaction.

RESULTS AND DISCUSSION

The oxidation of some structurally different hydroxyl compounds such as primary, secondary; allylic and benzylic alcohols by PBC have been carried out. In order to establish the optimum molar ratio of substrate: reagent in the oxidation of alcohols to carbonyl compounds, the method was tested with a representative alcohol such as benzyl alcohol in chloroform at room temperature. A 1:1.5, 1:2 or 1:3 molar ratio of substrate to reagent was used to ensure ready and complete conversion to the product. The results were given in Table 1 (entries 2,3 and 4). As expected the reaction rate increased when the molar ratio of PBC to alcohol was increased and the fastest reaction could be obtained by using a molar ratio of alcohol: PBC 1:3. However a 1:1.5 molar ratio gave roughly the same yield for a longer reaction time.

The reaction time for a total oxidation of alcohols was also investigated by using various solvents. PBC is fairly insoluble in chloroform; it has low solubility in acetone and is completely soluble in DMSO. When benzyl alcohol was treated with PBC both in chloroform

and in acetone, the respective yields and reaction times were similar (entries 1 and 2). However, the reaction time required for the oxidation of cyclohexanol is very different depending on the solvents used. PBC oxidizes cyclohexanol in 24 h when the reaction is carried out in chloroform, but the reaction rate decreases notably when DMSO is used as solvent (entries 5 and 6). Thus, the reaction time increases with the solubility of PBC in the solvent employed.

Table 1. Oxidation of alcohols by PBC under different molar ratios.^a

Entry	Substrate (solvent) ^b (10 mmole)	Molar ^c ratio	Time (h)	Product (%)	Yield ^d
1	Benzyl alcohol (acetone)	1:1.5	24	Benzaldehyde	76
2	Benzyl alcohol	1:1.5	24	Benzaldehyde	73
3	Benzyl alcohol	1:2	6	Benzaldehyde	66
4	Benzyl alcohol	1:3	3	Benzaldehyde	69
5	Cyclohexanol	1:1.5	24	Cyclohexanone	39
6	Cyclohexanol (DMSO)	1:1.5	72	Cyclohexanone	47

^a All reactions were run at room temperature

^b Unless otherwise indicated the solvent is chloroform

^c Alcohol: PBC

^d The % yield was determined on the basis of 2,4-DNP derivative

Examining the synthetic utility of PBC reagent, we have found that the addition of glacial acetic acid is effective in the conversion of alcohols into the corresponding carbonyl compounds. Both catalyzed and uncatalyzed oxidation reactions for five alcohols have been performed in chloroform at reflux temperature (Table 2). The results clearly demonstrate the catalytic effect of glacial acetic acid on the reactions. The reaction in all the cases, except in the cases of *p*-nitrobenzyl alcohol and cinnamyl alcohol markedly accelerated and the reaction time is reduced to half. Although colour changes were observed, low yields of cinnamaldehyde and *p*-nitrobenzaldehyde were obtained for acid catalyzed reactions and the work up was complicated in each case.

As revealed from Table 2, the oxidation reaction examined between some primary benzylic alcohols and PBC is dependent of the substituent attached in the aromatic ring. Thus while oxidation of *p*-anisyl alcohol and *p*-methylbenzyl alcohol gives *p*-anisaldehyde and *p*-tolualdehyde in

86% and 81% conversions respectively after 3 h at reflux temperature, oxidation of p-nitrobenzyl alcohol results in 46% conversion under the same conditions. Whereas PBC with 1-octanol, 2-octanol and cyclohexanol failed to achieve 50% conversion, a moderate yield was obtained with 4-t-butylcyclohexanol. That PBC is a relatively mild oxidation agent was illustrated by the reaction with benzoin forming benzil in 81% yield. In addition, decarboxylation did not take place upon oxidation of mandelic acid, and α -oxophenylacetic acid was obtained in 66% yield.

Table 2. Oxidation of selected alcohols with pyridinium bromochromate.^a

Substrate	Product	Time ^b (h)	Yield ^c (%)
1-Octanol	Octanal	3	43
2-Octanol	2-Octanone	3	37
Cyclohexanol	Cyclohexanone	3(1.5)	45(47)
4-t-Butylcyclohexanol	4-t-Butylcyclohexanone	3	62
p-Methyl benzyl alcohol	p-Tolualdehyde	3(1.5)	81(83)
		1.5(40 min)	68(67)
p-Methoxybenzyl alcohol	p-Anisaldehyde	3(1.5)	86(86)
Benzyl alcohol	Benzaldehyde	3	75
p-Nitrobenzyl alcohol	p-Nitrobenzaldehyde	3(1.5)	46(24)
Benzoin	Benzil	3	81
Diphenylcarbinol	Benzophenone	3	83
Cinnamyl alcohol	Cinnamaldehyde	1.5	42
		3(1.5)	61(34)
Mandelic acid	α -Oxophenylacetic acid	3	66

^a Reactions were conducted in refluxing chloroform using 1.2 molar equiv. of PBC

^{b,c} Values in parantheses refer to the reaction times and yields % respectively for catalyzed reactions. Glacial acetic acid was used as catalyst.

CONCLUSION

PBC is a selective, inexpensive and readily available reagent and of great efficiency for the oxidation of primary and secondary benzylic alcohols to corresponding carbonyl compounds. The reactions can be carried out in acetone or chloroform with only a modest excess of the oxidant both in neutral and slightly acidic conditions. The results obtained for the oxidation of saturated primary, secondary and allylic alcohols show that PBC is reasonably useful reagent for the transformation of these compounds.

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