Transition metal-free oxidation of activated alcohols to aldehydes and ketones in 1,1,1,3,3,3-hexafluoro-2-propanol

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ABSTRACT

A simple and convenient procedure for the oxidation of various benzylic, allylic and some aliphatic alcohols to their corresponding carbonyl compounds is described using sodium hypochlorite as the oxidant in 1,1,1,3,3,3-hexafluoro-2-propanol without use of a catalyst or any other additive. The solvent can be readily recovered from reaction products in excellent purity for direct reuse.

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1. Introduction

Oxidation reactions play an important role in organic synthesis, and there is currently a demand for more selective and efficient oxidation methods [1,2]. Oxidation of primary and secondary alcohols into the corresponding aldehydes and ketones without forming over-oxidized product is one of the pivotal transformations in the contemporary organic, still many oxidation processes use non-environmentally friendly oxidants [3–5]. The oxidation of alcohols is traditionally carried out with stoichiometric amounts of oxidants such as chromium reagents [6–10], permanganates [11,12], ruthenium (VIII) oxide [13,14], TPAP/NMO (tetra-N-propylammonium perruthenate/N-methyl-morpholine-N-oxide) [15,16], activated dimethyl sulfoxide (DMSO) reagents [17], or Dess–Martin periodinane reagent [18]. Recently some methods for aerobic oxidation of alcohol by using gold cluster are reported [19–22]. Unfortunately, the vast majority of common oxidants are required in at least stoichiometric amounts. Moreover, they are usually hazardous or toxic and generate large quantities of noxious by-products [23]. Many industrial organic oxidations can be accomplished with oxygen or hydrogen peroxide using heterogeneous catalysts, but the reaction conditions can often lead to over-oxidation of the product to give carbon dioxide and water [24]. Nevertheless, heterogeneous systems are industrially useful for

synthesizing commodity chemicals from abundant feedstocks because modest selectivity is often compensated by the low cost of the oxidant, usually oxygen gas. However, with complex and expensive alcohols (fine chemical synthesis), a more selective route is desirable [25]. Sodium hypochlorite is an effective, inexpensive and non-toxic oxidant, which has been reported to be transferred into the organic phase in the presence of a quaternary ammonium salt and is capable of oxidizing alcohols, including benzyl alcohol, although it can be difficult to control selectivity [26–31]. However, organic solvents used in this phase transfer catalytic reaction are environmentally undesirable, and catalyst separation and recovery are significant challenges. Although several modern methods are devised recently [32–34] oxidation with sodium hypochlorite is still the most reliable and controllable method in organic synthesis for the conversion of benzylic and allylic alcohols into the corresponding aldehydes. The use of fluorinated solvent, as chemical reaction media in place of conventional volatile organic solvents, has grown dramatically in recent years [35–37]. Highly fluorinated alcohols exhibit high hydrogen bonding donor ability, low nucleophilicity, high ionizing power and the ability to solvate water. Therefore, today they have marched far beyond this border, showing their significant role in controlling the reaction as powerful reaction media. These alcohols display interesting properties, such as solvent, co-solvent, or additives in various catalytic processes and consequently they are often used in studies of peptide and protein structure [38], solvolysis [39–42], their effect on various organic transformations [43–50], and notably the activation of hydrogen peroxide for oxidation, epoxidation and the Baeyer–Villiger rearrangement [51–56].

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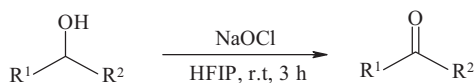
Scheme 1. Conversion of alcohols to carbonyl compounds.

Due to the current challenges for developing environmentally benign synthetic processes and in continuation of our interest in the application of fluorinated solvents for various organic transformations [57–61], we report a simple and convenient procedure for the high yielding direct oxidation of substituted benzyl alcohols using sodium hypochlorite as an oxidant in hexafluoroisopropanol (HFIP) (Scheme 1).

2. Results and discussion

Preliminary experiments were carried out on benzyl alcohol with NaOCl, as a model reaction in different reaction conditions including the amount of NaOCl, the amount of HFIP and reaction temperature to find the optimum reaction conditions. As a result, 1 mL of HFIP, 5 mL of NaOCl (13%) and 25–30 °C were chosen as a suitable reaction condition for oxidation of alcohols. In view of the efficient oxidation of benzyl alcohol, the oxidation for various other alcohols was investigated and the results are shown in Table 1.

It was found that when benzyl alcohol was treated with 5 mL of NaOCl in HFIP (1 mL) at 25–30 °C, complete conversion from benzyl alcohol to benzaldehyde was obtained within 3 h without the formation of by-products such as benzoic acid (Table 1, entry 1). To evaluate the scope and limitations of the current procedure, oxidation reactions with a wide array of electronically diverse benzylic alcohols were investigated and the results are shown in Table 1. It has been seen from Table 1 that in general, various hydroxyl compounds such as p-nitrobenzyl alcohol, p-chloroben-zyl alcohol, benzhydrol, 1-phenylethanol and cinnamyl alcohol underwent oxidation reactions in nearly quantitative yields. The present method could equally work with electron rich and very electron deficient benzylic alcohols (entries 2–7). All the reactions occurred with complete selectivity for ketones or aldehydes and no other products were detected in the reaction mixture. Application of present method for the oxidation of primary and secondary aliphatic alcohols gave very low conversion. Moreover, there is no reaction between HFIP and NaOCl in the absence of any alcohol at room or higher temperature. We examined the reaction of benzyl alcohol and NaOCl in different solvents. The results are summarized in Scheme 2, and show that, high conversions were obtained with HFIP.

Although there is no solid evidence to support the catalytic mechanism of HFIP in the reaction, it may be assumed that this unprecedented activity pattern of HFIP is primarily a result of its well-documented capacity to the stabilizing ability of HFIP for cationic intermediates [62,63]. Moreover, Legros and co-workers demonstrated recently that HFIP act as Brønsted acid [64] and play a significant role in increasing the electrophilic character of the electrophiles. It is reasonable to assume that the latter assists the leaving of the hydroxyl moiety, leading to the benzylic carbocation [46], the widely accepted intermediate of the reaction. After the reaction, HFIP can be easily separated (by distillation) and reused without decrease in its activity. For example, benzyl alcohol was converted to the corresponding aldehydes in 95%, 95% and 93% isolated yield over three cycles. The notable advantages of this method are the operational simplicity, direct use of alcohols and inexpensive, reusable and non-toxic HFIP medium which render this method an important alternative to previously reported methods.

Table 1
Oxidation of various alcohols in HFIP.

Entry	Alcohol	Product	Yield (%)
1			90
2			92
3			90
4			95
5			85
6			95
7			92
8			95
9			95
10			95
11			92
12			80
13			50
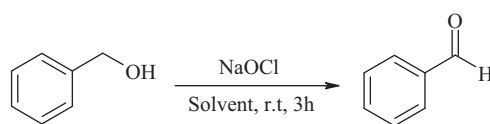
Solvent	Yield (%)
CH$_2$Cl$_2$	N.R[a]
CH$_3$CN	N.R
CHCl$_3$	N.R
Toluene	N.R
Ethanol	N.R
t-BuOH	N.R
TFE	N.R
HFIP	90

[a] N.R= No reaction

Scheme 2. The reaction of benzyl alcohol and NaOCl in different solvents.

3. Conclusion

In conclusion, we have developed an efficient procedure for the oxidation of various benzylic, allylic and some aliphatic alcohols to their corresponding carbonyl compounds using sodium hypochlorite as the oxidant in 1,1,1,3,3,3-hexafluoro-2-propanol without use of a catalyst or any other additive. In contrast to the existing methods using potentially hazardous catalysts/additives, this new method offers the following competitive advantages: (i) avoiding the use of any base, metal or Lewis acid catalyst (ii) short reaction time, (iii) ease of product isolation/purification (iv) high chemoselectivity, (v) no side reaction, and (vi) low costs and simplicity in process and handling. The recovered HFIP can be reusable.

4. Experimental

General procedure: Alcohol (1 mmol) and NaOCl (ca. 13%, 5 mL) were dissolved in HFIP (1 mL) and was stirred at 25–30 °C in a vial for 3 h. After completion of the reaction as indicated by TLC, the HFIP was separated by distillation and then the mixture was extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with H_2O and dried over $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by chromatography. All the products were characterized by comparison of their physical and spectral data with those of authentic samples. Spectroscopic data for selected examples are shown below.

Benzaldehyde (Table 1, **entry 1**): Oil, IR (KBr): 3064, 2819, 1701, 1311 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.52 (t, J = 7.54 Hz, 2H), 7.62 (t, J = 7.43 Hz, 1H), 7.87 (d, J = 7.69 Hz, 2H) 10.0 (s, 1H). ^{13}C NMR: (CDCl$_3$, 100 MHz): δ = 128.8, 129.6, 134.4, 136.4, 192.3.

4-Chlorobenzaldehyde (Table 1, **entry 3**): White solid, mp 48–49 °C; IR (KBr): 2727, 1710, 1311 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 7.52 (d, J = 8.6 Hz, 2H), 7.83 (d, J = 8.6 Hz, 2H), 9.99 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 129.4, 130.8, 134.6, 140.9, 190.8.

4-Methoxybenzaldehyde (Table 1, **entry 6**): Oil; IR (KBr): 2840, 2739, 1683 cm^{-1}; ^{1}H NMR CDCl$_3$, 400 MHz): δ = 3.90 (s, 3H), 7.01 (d, J = 8.7 Hz, 2H), 7.85 (d, J = 8.7 Hz, 2H), 9.89 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 55.5, 114.2, 129.8, 131.9, 164.5, 190.7.

Acetophenone (Table 1, **entry 8**): Oil; IR (KBr): 3654, 3062, 1685, 1265 cm^{-1}, ^{1}H NMR: (400 MHz, CDCl$_3$): δ = 2.60 (s, 3H), 7.45 (t, J = 7.675 Hz, 2H), 7.55 (t, J = 7.30 Hz, 1H), 7.95 (d, J = 7.78 Hz, 2H). ^{13}C NMR: (CDCl$_3$, 100 MHz): δ = 26.5, 128.2, 128.5, 133.1, 137.2, 198.1.

Benzophenone (Table 1, **entry 10**): White solid, mp 47–48 °C; IR (KBr): 3643, 3055, 1982, 1650, 1276 cm^{-1}; ^{1}H NMR: (400 MHz, CDCl$_3$): δ = 7.48 (t, J = 7.37 Hz, 4H,), 7.58 (t, J = 7.22 Hz, 2H), 7.80 (d, J = 7.75 Hz, 4H). ^{13}C NMR: (CDCl$_3$, 100 MHz): δ = 128.2, 130.1, 132.4, 137.5, 196.7.

Cinnamaldehyde (Table 1, **entry 11**): Oil; IR (KBr): 2816, 2743, 1676 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 6.73 (dd, J = 16.1 Hz, 7.8 Hz, 1H), 7.43–7.47 (m, 3H), 7.49 (d, J = 16.0 Hz, 1H), 7.57–7.59 (m, 2H), 9.72 (d, J = 7.8 Hz, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 128.4, 128.5, 129.1, 131.2, 133.9, 152.8, 193.7.

Acknowledgment

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