



Mild Oxidation of Alcohols with *o*-Iodoxybenzoic Acid in Liquid Tetrabutylammonium Bromide

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A mild, green and low cost method for *o*-iodoxybenzoic acid mediated oxidation of alcohols to carbonyl compounds has been established. In this protocol, liquid tetrabutylammonium bromide was used as the solvent and the primary alcohols were selectively oxidized to aldehyde and secondary alcohols were easily transformed to ketones.

Keywords: *o*-Iodoxybenzoic acid, Oxidation, Tetrabutylammonium bromide.

INTRODUCTION

The oxidation of alcohols to carbonyl compounds is one of the most fundamental processes^{1,2} in organic chemistry. Traditional methods have required the use of stoichiometric oxidizing reagents, of which toxic transition metals^{3,4} were most commonly used. Serious environmental concerns prompted chemists to develop greener methods. Considerable interest has been paid to using molecular oxygen or air as the terminal oxidant⁵⁻⁷. However, this area is not mature and furthermore, catalytic amount of heavy metals were still used in the systems. Recently, Hu *et al.*⁸ and others⁹⁻¹² have developed a transition metal free oxidation of alcohols utilizing TEMPO-based catalyst systems.

Last few years¹³⁻¹⁷ have seen a great deal of interest in *o*-iodoxybenzoic acid and its oxidation ability of alcohols as well as nitrogen-containing and sulfur-containing organic compounds, which was often achieved in mild conditions, in high yields and with high chemoselectivity. Because of poor solubility of *o*-iodoxybenzoic acid in most organic solvents, the process was often done in DMSO at slightly elevated temperature, which is practically the only solvent that dissolves *o*-iodoxybenzoic acid¹⁸. Recently, several alternative procedures have been introduced in the literature. Vinod and coworkers¹⁹ used a water/acetonitrile biphasic solvent system while Giannis and Schulze²⁰ used a water/ethyl acetate biphasic solvent system with Bu₄NHSO₄ as phase-transfer catalyst. Zheng's group¹⁸ has developed a greener procedure which was achieved in ionic liquid and water. However, the cost was increased by using alkylated imidazoles. Therefore, it is highly desirable to develop an environmentally friendly and economical process for the oxidation of alcohols with *o*-iodoxybenzoic acid.

As an inexpensive common reagent, tetrabutylammonium bromide (TBAB)²¹⁻²³ has been used in many chemical reactions. We²⁴ previously reported that tetrabutylammonium bromide was an efficient media for converting nitriles to 5-substituted 1*H*-tetrazoles. We present here a green and low-cost method for the *o*-iodoxybenzoic acid mediated oxidation of alcohols in liquid tetrabutylammonium bromide (Fig. 1).

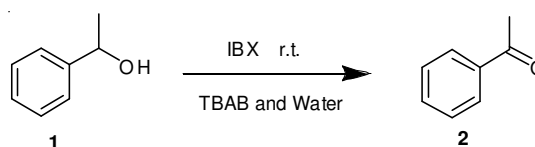


Fig. 1. *o*-Iodoxybenzoic acid (IBX) mediated oxidation of alcohols in liquid tetrabutylammonium bromide (TBAB)

EXPERIMENTAL

All reagents were purchased from commercial suppliers and used without further purification. NMR spectra obtained with tetramethylsilane (TMS, $\delta = 0$ ppm) as internal standard in CDCl₃ using a Bruker Avance 500 spectrometer (500 MHz) or Bruker Avance 300 spectrometer (300 MHz).

General procedure: To a mixture of tetrabutylammonium bromide (2 mmol, 0.64 g) and water (2 mL) was added *o*-iodoxybenzoic acid and the corresponding alcohol **1** (2 mmol). The reaction mixture was stirred at room temperature for 1 h. After the reaction was complete, 10 mL water was added and the liquid phase was extracted with diethyl ether. IBA was recovered by filtration. The organic phase was washed with water, dried over sodium sulfate and concentrated under vacuum to give the pure product **2**. The aqueous phase was evaporated under vacuum and tetrabutylammonium bromide was recovered.

Acetophenone (2a)²⁵, **Table-1, entry 5**: ¹H NMR (300 MHz, CDCl₃) δ 7.97 (m, 2H), 7.57 (m, 1H), 7.46 (m, 2H), 2.61 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 198.13, 136.97, 133.03, 128.47, 128.20, 26.49.

Propiophenone (2b)²⁶, **Table-2, entry 2**: ¹H NMR (300 MHz, CDCl₃) δ 7.96 (m, 2H), 7.54 (d, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 2H), 3.01 (q, *J* = 7.2 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 200.65, 136.79, 132.77, 128.45, 127.85, 31.65, 8.12.

3'-Methoxyacetophenone (2c)²⁷, **Table-2, entry 3**: ¹H NMR (300 MHz, CDCl₃) δ 7.49 (m, 1H), 7.37 (t, 2H), 7.11 (m, 1H), 3.86 (m, 3H), 2.60 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 197.82, 159.68, 138.35, 129.46, 121.00, 119.46, 112.23, 55.28, 26.60.

4'-Methoxyacetophenone (2d)²⁸, **Table-2, entry 4**: ¹H NMR (300 MHz, CDCl₃) δ 7.93 (m, 2H), 6.94 (m, 2H), 3.87 (s, 3H), 2.56 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 196.66, 163.37, 130.47, 130.18, 113.56, 55.34, 26.23.

Benzaldehyde (2e)²⁵, **Table-2, entry 5**: ¹H NMR (500 MHz, CDCl₃) δ 10.05 (s, 1H), 7.90 (m, 2H), 7.66 (m, 1H), 7.56 (t, *J* = 7.6 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 192.26, 134.35, 129.62, 128.90.

2-Methoxybenzaldehyde (2f)²⁵, **Table-2, entry 6**: ¹H NMR (300 MHz, CDCl₃) δ 10.48 (s, 1H), 7.85 (m, 1H), 7.57 (m, 1H), 7.02 (m, 2H), 3.94 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 189.69, 161.74, 135.88, 128.37, 124.71, 120.54, 111.55, 55.52.

3-Methoxybenzaldehyde (2g)²⁵, **Table-2, entry 7**: ¹H NMR (300 MHz, CDCl₃) δ 9.98 (s, 1H), 7.47 (m, 2H), 7.40 (s, 1H), 7.19 (m, 1H), 3.87 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 191.96, 160.00, 137.68, 129.89, 123.24, 121.22, 112.02, 55.23.

4-Methoxybenzaldehyde (2h)²⁵, **Table-2, entry 8**: ¹H NMR (500 MHz, CDCl₃) δ 9.90 (s, 1H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.02 (d, *J* = 8.3 Hz, 2H), 3.90 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 190.77, 164.60, 131.94, 129.93, 114.30, 55.53.

4-Formylbenzotrile (2i)²⁹, **Table-2, entry 9**: ¹H NMR (300 MHz, CDCl₃) δ 10.10 (s, 1H), 8.00 (m, 2H), 7.85 (d, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 190.62, 138.65, 132.82, 129.81, 117.65, 117.47.

4-Nitrobenzaldehyde (2j)²⁵, **Table-2, entry 10**: ¹H NMR (300 MHz, CDCl₃) δ 10.17 (s, 1H), 8.40 (d, *J* = 8.5 Hz, 2H), 8.08 (d, *J* = 8.6 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 190.34, 150.98, 139.97, 130.41, 124.19.

2-Iodobenzaldehyde (2k)³⁰, **Table-2, entry 11**: ¹H NMR (300 MHz, CDCl₃) δ 10.08 (s, 1H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.89 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.31

(dd, *J* = 7.7, 1.7 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 195.75, 140.63, 135.51, 135.05, 130.24, 128.74, 100.81.

4-Phenyl-2-butanone. (2l)³⁰, **Table-2, entry 12**: ¹H NMR (300 MHz, CDCl₃) δ 7.27 (m, 2H), 7.20 (t, *J* = 6.3 Hz, 2H), 2.89 (d, *J* = 7.2 Hz, 2H), 2.78 (d, *J* = 7.3 Hz, 2H), 2.15 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 207.91, 140.93, 128.43, 128.23, 126.04, 45.08, 30.00, 29.65.

2-Octanone (2m)³⁰, **Table-2, entry 13**: ¹H NMR (300 MHz, CDCl₃) δ 2.41 (t, 2H), 2.13 (s, 3H), 1.56 (m, 2H), 1.27 (s, 6H), 0.87 (t, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 209.17, 43.63, 31.45, 29.66, 28.70, 23.67, 22.35, 13.86.

Cyclohexanone (2n)²⁵, **Table-2, entry 14**: ¹H NMR (300 MHz, CDCl₃) δ 2.33 (m, 4H), 1.86 (m, 4H), 1.72 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 212.08, 41.81, 26.87, 24.82.

RESULTS AND DISCUSSION

We initiated our studies with the oxidation of 1-phenylethanol with *o*-iodoxybenzoic acid in water at 80 °C. Only trace acetophenone formed after 10 h (Table-1, entry 1). Then the reaction was carried out in molten tetrabutylammonium bromide at 105 °C (Table-1, entry 2). The mixture soon turned dark and no product was found, probably due to instability of *o*-iodoxybenzoic acid at elevated temperature¹⁴. A small portion of water was then added and the temperature was lowered to 80 °C and acetophenone was formed after 2 h and then isolated in 55 % (Table-1, entry 3). Encouraged by the result, we lowered the temperature again, hopefully the reaction could proceed at room temperature (Table-1, entry 4). Because such attempt was in vain, we next increased the amount of water by 10-fold (Table-1, entry 5). To our delight, the reaction proceeded smoothly and excellent yield was obtained. Further increase of the amount of water was detrimental to the yield (Table-1, entry 6 and 7).

Having optimized the reaction conditions, we next explored the scope of this reaction. The results were shown in Table-2. All primary alcohols were oxidized into aldehyde while no further oxidation was found and secondary alcohols were easily transformed into ketones. It was found that benzyl alcohols generally proceeded well while alkyl alcohols generally were obtained in moderate yield. This phenomenon is in accordance with the literature¹⁴. Electron-donating groups introduced at *o*-, *m*- and *p*-position of the benzyl alcohols all furnished the corresponding product, although slightly better yield was obtained with those introduced at *p*-position (Table-2, entries 3, 4, 6-8). In contrast, only low to moderate yield was obtained with benzyl alcohols bearing strong

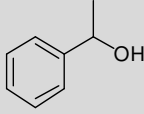
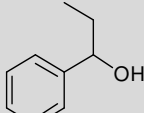
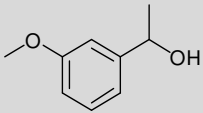
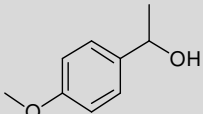
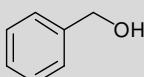
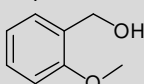
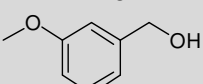
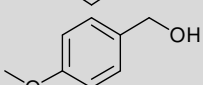
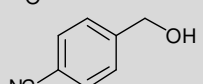
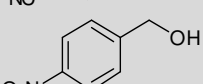
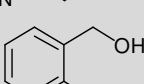
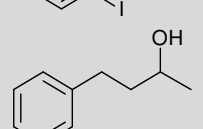
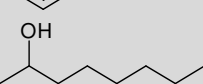
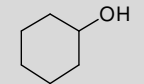
TABLE-1
REACTION OF OPTIMIZATION OF *o*-IODOXYBENZOIC ACID MEDIATED OXIDATION OF 1-PHENYLETHANOL TO 2a^a

Entry	Temperature (°C)	Solvent ^b	Time (h)	Yield (%) ^c
1	80	Water ^d	10	Trace
2	105	TBAB	1	-
3	80	10:1 TBAB-Water (mol/mol)	1	55
4	Room temperature	10:1 TBAB-Water (mol/mol)	1	Trace
5	Room temperature	10:10 TBAB-Water (mol/mol)	1	92
6	Room temperature	10:20 TBAB-Water (mol/mol)	1	87
7	Room temperature	10:40 TBAB-Water (mol/mol)	1	85

^aOxidation of alcohols (2 mmol 1 equiv) was conducted with *o*-iodoxybenzoic acid (2.2 mmol, 1.1 equiv), ^bTBAB(2 mmol) was used,

^cIsolated yield, ^dOnly water was used

TABLE-2
SUBSTRATE SCOPE OF *o*-IODOXYBENZOIC ACID MEDIATED
OXIDATION OF 1-PHENYLETHANOL TO 2a^a

Entry	Substrate	Product	Yield (%) ^b
1		2a	92
2		2b	91
3		2c	93
4		2d	96
5		2e	90
6		2f	91
7		2g	92
8		2h	95
9		2i	61
10		2j	59
11		2k	61
12		2l	79
13		2m	65
14		2n	77

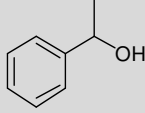
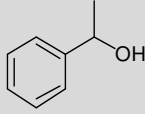
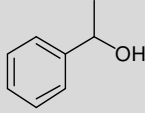
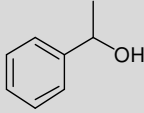
^aOxidation of alcohols (2 mmol 1 equiv.) was conducted with *o*-iodoxybenzoic acid (2.2 mmol, 1.1 equiv.) in TBAB (2 mmol) and water (2 mmol) in 1 h; ^bIsolated yields

electron-withdrawing groups, indicating the limitations of the reaction (Table-2, entries 9,10). Strong steric hindrance of *o*-substituents such as an iodo-group did not deter the desired oxidation from occurring (Table-2, entry 11).

Iodosobenzoylic acid (IBA), the side product of *o*-iodoxybenzoic acid mediated oxidation, could be easily recovered by simple filtration after water was added and then reoxidized

to *o*-iodoxybenzoic acid by oxone. The regenerated *o*-iodoxybenzoic acid was reused and no difference was found from a freshly prepared one (Table-3, entry 4). tetrabutylammonium bromide was also recovered by evaporation under vacuum and reused without obvious decrease of the yields of products (Table-3).

TABLE-3
RESULTS OBTAINED USING RECYCLED
TETRABUTYLAMMONIUM BROMIDE (TBAB)

Entry	Substrate	Cycle	Yield (%) ^a
1		1	92
2		2	92
3		3	91
4		4	91 ^b

^aIsolated yields based on 1-phenylethanol, ^bRecycled *o*-iodoxybenzoic acid was used

Conclusion

We presented here a mild, efficient, low cost and environmentally friendly method for *o*-iodoxybenzoic acid mediated oxidation of alcohols using the inexpensive liquid tetrabutylammonium bromide as solvent. Secondary alcohols were easily oxidized to ketones and primary alcohols were transformed to aldehyde while no further oxidation products were found. The side product emerged and solvent used can be recycled.

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