Monatshefte für Chemie 136, 2035–2039 (2005)
DOI 10.1007/s00706-005-0364-1

Monatshefte für Chemie
Chemical Monthly
Printed in Austria

Efficient Chemoselective Oxidation of Phenylmethanols to Aldehydes with Iodosobenzene

Patrina Paraskevopoulou[1,*], **Eleftheria Petalidou**[1],
Nikos Psaroudakis[1], **Pericles Stavropoulos**[2], and **Konstantinos Mertis**[1,*]

[1] Department of Inorganic Chemistry, Faculty of Chemistry, University of Athens,
Panepistimioupoli Zographou 15771, Athens, Greece
[2] Department of Chemistry, University of Missouri-Rolla, Rolla, MO 65409, USA

Received January 24, 2005; accepted (revised) March 1, 2005

Summary. Primary phenylmethanols are selectively and efficiently oxidized to the corresponding aldehydes by the system $C_6H_5IO/(C_6H_5)_4PBr/CH_2Cl_2$, $T = 298\,K$ under aerobic conditions. The use of the relatively stable iodosobenzene, an iodine(III) compound, in place of the usually employed and potentially explosive iodine(V) reagents, the easy work-up procedure, and the facile recycling of solvent and oxidant provides a convenient and environmentally benign oxidation method.

Keywords. Alcohols; Chemoselectivity; Hypervalent compounds; Iodine; Oxidations.

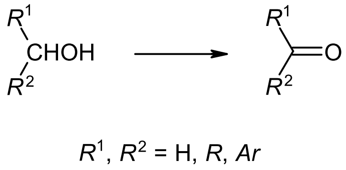
Introduction

The selective oxidation of alcohols to the corresponding carbonyl compounds (Scheme 1) plays a central role in organic chemistry, hence a variety of stoichiometric and catalytic reactions involving both metals and non-metals have been developed [1]. In particular, the conversion of primary alcohols to aldehydes is crucial for the synthesis of fine chemicals, such as fragrances or food additives. However, despite the spectacular progress in the oxidation of alcohols and the use of environmentally friendly systems [2], there are still severe limitations with respect to the chemo-, regio-, and stereoselectivity of the reaction.

Hypervalent iodine(V) reagents, such as *Dess-Martin* periodinane [3] and *o*-iodoxybenzoic acid [4] oxidize alcohols mildly and efficiently to carbonyl compounds in high yields in organic solvents (CH_2Cl_2, *DMSO*, acetone), but despite their utility, they are potentially explosive and require often an excess amount of

---

* Corresponding author. E-mail: cmertis@cc.uoa.gr



Scheme 1

reagent. Therefore, replacement with relatively stable iodine(III) reagents is highly desirable.

Oxo(phenyl)-λ^3-iodane (iodosobenzene, $C_6H_5I=O$, **1**) is capable of oxidizing activated alcohols [5], *e.g.* phenylmethanol, to carbonyl compounds under drastic conditions (dry dioxane, reflux, 12 h). Activation of **1** with ruthenium catalysts, such as $RuCl_2(P(C_6H_5)_3)_2$, $Ru_3(CO)_{12}$, $RuCl_3 \cdot H_2O$, or ruthenocene [6] results in the oxidation of a variety of alcohols to carbonyl compounds and carboxylic acids, whereas in the presence of ytterbium(III) salts [7] aldehydes or ketones are selectively produced at 80°C in 1,2-dichloroethane solutions. The combination of **1** and potassium bromide (KBr) in water induces the oxidation of primary alcohols exclusively to their carboxylic acids, and of secondary alcohols to the corresponding ketones [8, 9].

Herein, as an extension of our studies on the catalytic oxidation of alcohols with rhenium complexes [10], we report that by replacing the system **1**/KBr/H_2O with **1**/$(C_6H_5)_4PBr/CH_2Cl_2$, overoxidation to the acids can be avoided and the corresponding aldehydes can be obtained instead.

Results and Discussion

Reagent **1** oxidizes $C_6H_5CH_2OH$ to C_6H_5CHO in CH_2Cl_2 in a non-catalytic reaction, in poor yields (Table 1, Entry 1). In contrast, upon addition of tetraphenylphosphonium bromide, the reaction becomes catalytic and the yield is dramatically improved. Specifically, for a ratio of **1**:$(C_6H_5)_4PBr = 1{:}0.1$ the reaction becomes quantitative at 24 h (Table 1, Entry 5). Use of $(C_6H_5)_4PI$ was proved to be less effective (Table 1, Entries 14–17) and employment of $(C_6H_5)_4PCl$ is ineffective (Table 1, Entry 18). Under anaerobic conditions the yield is decreased (Table 1, Entries 6–9). Excess moisture poisons the reaction (Table 1, Entry 11).

Thus, the typical system, which was used for the oxidation of a range of alcohols consists of **1** (1 eq), $(C_6H_5)_4PBr$ (0.1 eq), and alcohol (1 eq). The reaction was performed aerobically at $T = 298$ K and some representative results are shown in Table 2.

Substituted phenylmethanols in general are efficiently oxidized (Table 2, Entries 3–9, 13). Lower yields (*e.g.* Entries 2, 10) can be significantly improved by changing the molar ratio **1**:$(C_6H_5)_4$PBr:alcohol (*e.g.* 1:0.2:1 gives 80% yield for *o*-$CH_3OC_6H_4CH_2OH$ and 67% for *o*-$O_2NC_6H_4CH_2OH$). *Para-* or *ortho*-substituents with electron releasing or withdrawing properties do not induce any change in the selectivity of the reaction except in the cases of *p*-$CH_3OC_6H_4CH_2OH$ (Table 2, Entry 3) and *p*-$CF_3C_6H_4CH_2OH$ (Table 2, Entry 13), where the esters (*ca.* 0.2% and 10%) were formed. In the first case, traces of the chloride (<1%) were detected at the end of the reaction. Introduction of $-NO_2$ groups lowers the yield (Table 2, Entries 10–12). Primary aliphatic alcohols were not oxidized. Secondary alcohols

Table 1. Oxidation of $C_6H_5CH_2OH$ with **1**/$(C_6H_5)_4PX$ (X = Cl, Br, I)[a]

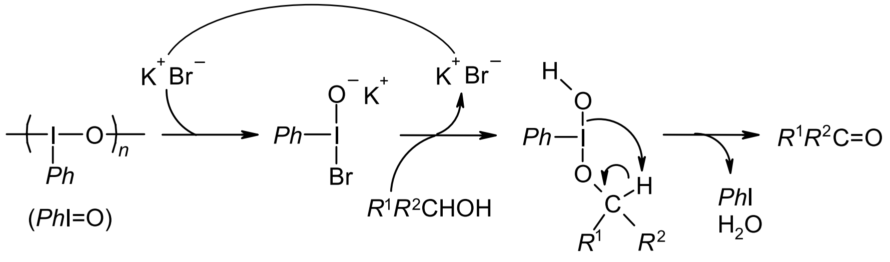
Entry	X	Molar ratio **1**:$(C_6H_5)_4PX$:$C_6H_5CH_2OH$	C_6H_5CHO/%
1	–	1:0:1	10[b]
2	Br	1:1:1	31[b]
3	Br	1:0.5:1	48[b]
4	Br	1:0.2:1	70[b]
5	Br	1:0.1:1	>99[b]
6	Br	1:1:1	13[c]
7	Br	1:0.5:1	45[c]
8	Br	1:0.2:1	68[c]
9	Br	1:0.1:1	80[c]
10	Br	1:0.1:1	46[c,d]
11	Br	1:0.1:1	1[c,e]
12	Br	1:0.1:1	24[c,f]
13	Br	1:0.1:1	60[f,g]
14	I	1:1:1	14[b]
15	I	1:0.5:1	32[b]
16	I	1:0.2:1	35[b]
17	I	1:0.1:1	22[b]
18	Cl	1:0.5:1	18[c]

[a] Reaction conditions: CH_2Cl_2 (15.0 cm^3), $T = 298$ K, $t = 24$ h; [b] aerobically; [c] anaerobically; [d] CH_2Cl_2 not dried over CaH_2; [e] CH_2Cl_2 saturated in H_2O; [f] molecular sieves (type 3Å) were used; [g] strictly in the absence of H_2O, in an atmosphere of dry O_2

Table 2. Oxidation of alcohols by **1**/$(C_6H_5)_4PBr$[a]

Entry	Alcohol	Carbonyl compound	Yield/%(blanc)[b]
1	*Ph*–CH_2–OH	*Ph*–CHO	>99 (10)
2	2-CH_3O–*Ph*–CH_2OH	2-CH_3O–*Ph*–CHO	61 (26)
3	4-CH_3O–*Ph*–CH_2OH	4-CH_3O–*Ph*–CHO	96 (44)
4	2-CH_3–*Ph*–CH_2OH	2-CH_3–*Ph*–CHO	74 (15)
5	3-CH_3–*Ph*–CH_2OH	3-CH_3–*Ph*–CHO	80 (36)
6	4-CH_3–*Ph*–CH_2OH	4-CH_3–*Ph*–CHO	92 (26)
7	2-Cl–*Ph*–CH_2OH	2-Cl–*Ph*–CHO	92 (12)
8	3-Cl–*Ph*–CH_2OH	3-Cl–*Ph*–CHO	91 (28)
9	4-Cl–*Ph*–CH_2OH	4-Cl–*Ph*–CHO	>99 (29)
10	2-O_2N–*Ph*–CH_2OH	2-O_2N–*Ph*–CHO	45 (3)
11	3-O_2N–*Ph*–CH_2OH	3-O_2N–*Ph*–CHO	72 (29)
12	4-O_2N–*Ph*–CH_2OH	4-O_2N–*Ph*–CHO	55 (20)
13	4-F_3C–*Ph*–CH_2OH	4-F_3C–*Ph*–CHO	89 (32)
14	*Ph*$CHOHCH_3$	*Ph*$COCH_3$	53 (3)
15	cyclohexanol	cyclohexanone	50 (0)
16	2-propanol	2-propanone	10 (0)
17	2-octanol	2-octanone	28 (0)

[a] Reaction conditions: **1** (1 mmol), $(C_6H_5)_4PBr$ (0.1 mmol), alcohol (1 mmol), CH_2Cl_2 (15.0 cm^3), $T = 298$ K, $P = 1$ atm, $t = 24$ h; [b] in the absence of $(C_6H_5)_4PBr$



Scheme 2

were oxidized in lower yields (Table 2, Entries 14–17). Allylic and homoallylic alcohols (2-propen-1-ol, 3-buten-1-ol) were unreactive.

Electrospray ionization mass spectrometric (ESI-MS) studies for the aqueous system suggested [9] that the reaction proceeds through the formation of a highly reactive iodine species $C_6H_5I(Br)O^-K^+$ (Scheme 2). This type of activation is very different from the mechanism involving transition metals or 2,2,6,6-tetramethyl-1-piperidinyloxy free radical, where metal-oxo or *N*-oxoammonium salt moieties function as reactive species.

However, it is noteworthy that in the present system water and/or dioxygen seem to be essential components for successful oxidation (Table 1, Entries 12, 13), which implies that more subtle aspects may be involved in the mechanism of the reaction with the **1**/KBr/H_2O system.

In summary, the system **1**/$(C_6H_5)_4PBr/CH_2Cl_2$ oxidizes efficiently, aerobically, and selectively primary phenylmethanols to aldehydes. In addition, the use of the relatively stable iodosobenzene, the easy work-up procedure, and the facile recycling of solvent and oxidant provides a convenient and environmentally benign oxidation method. Further studies to improve the rate of the reaction and obtain mechanistic insight are in progress.

Experimental

CH_2Cl_2 and *n*-hexane were distilled over CaH_2 by fractional distillation (*Vigreux* column). Diethyl ether was distilled over Na/*Ph*$_2$CO in an inert atmosphere. Anaerobic reactions were performed under Ar or N_2 atmosphere, using *Schlenk* and syringe techniques on an inert gas/vacuum manifold. The solvent was degassed by three freeze-pump-thaw cycles. $C_6H_5CH_2OH$ and Na_2SO_4 were purified and dried according to Ref. [11]. O_2 was dried by passing through a tube of anhydrous P_2O_5. All chemicals and solvents were purchased from Aldrich, except for decahydronaphthalene ($C_{10}H_{18}$, *cis* and *trans* mixture of isomers, Riedel-de-Haën). Reagent **1** was prepared according to Ref. [12]. ^1H and ^{13}C NMR spectra were obtained on a Varian 300 Unity Plus spectrometer. GC-MS experiments were performed on a Varian Star 3400CX GC coupled with a Varian Saturn 2000 MS. Column: 30 m×0.25 mm ID, 0.25 μm, CP-Sil 8 CB; LB/MS column with 2 m fused Silica precolumn; injection: 1 mm^3, 50:1 split; flow: 1 cm^3/min He, constant flow; oven: 50°C/hold 3.00 min, 7°C/min to 150°C, 50°C/min to 280°C, 280°C/hold 2.12 min, 5°C/min to 300°C, 300°C/hold 4.00 min; injector: 280°C; transfer line: 280°C; MSD scan range: 10–600 amu.

Typical Procedure

To 8.1 mg $(C_6H_5)_4PBr$ (19 μmol) dissolved in 15.0 cm^3 CH_2Cl_2 42.5 mg **1** (193 μmol) and 20×10^{-3} cm^3 $C_6H_5CH_2OH$ (21 mg, 193 μmol) were added. The mixture was stirred for 24 h at

$T = 298$ K. The same procedure was also followed in the anaerobic reactions. The analysis of the samples by GC-MS was performed as follows: $C_{10}H_{18}$ (internal standard for quantification) was added to the mixture at the end of the reaction and the solvent was removed under vacuum. The organic compounds were extracted with *n*-hexane or diethyl ether, depending on their solubility, and were dried (Na_2SO_4). The organic products were also analyzed by ^1H and ^{13}C NMR in $CDCl_3$.

Acknowledgements

We thank the Research Account of the University of Athens (70/4/3342) for financial assistance.

References

[1] a) Hudlicky M (1990) Oxidations in Organic Chemistry. ACS Monograph Ser, Am Chem Soc. Washington, DC; b) Adam W, Saha-Möller CR, Ganeshpure PA (2001) Chem Rev **101**: 3499; c) Sheldon RA, Kochi JK (1981) Metal-Catalyzed Oxidations of Organic Compounds. Academic Press, New York; d) Sheldon RA (1991) In: Simandi LL (ed) Dioxygen Activation and Homogeneous Catalytic Oxidations. Elsevier, Amsterdam, p 573; e) James BR (1991) In: Simandi LL (ed) Dioxygen Activation and Homogeneous Catalytic Oxidations. Elsevier, Amsterdam, p 195

[2] a) ten Brink G, Arends IWCE, Sheldon RA (2000) Science **287**: 1636; b) Seddon KR, Stark A (2002) Green Chem **4**: 119

[3] a) Dess DB, Martin JC (1983) J Org Chem **48**: 4155; b) Meyer SD, Schreiber SL (1994) J Org Chem **59**: 7549

[4] Surendra K, Srilakshmi Krishnaveni N, Arjun Reddy M, Nageswar YVD, Rama Rao K (2003) J Org Chem **68**: 2058

[5] Takaya T, Enyo H, Imoto E (1968) Bull Chem Soc Jpn **41**: 1032

[6] Müller P, Godoy J (1981) Tetrahedron Lett **22**: 2361

[7] Yokoo T, Matsumoto K, Oshima K, Utimoto K (1993) Chem Lett 571

[8] Tohma H, Takizawa S, Maegawa T, Kita Y (2000) Angew Chem Int Ed Engl **39**: 1306

[9] Tohma H, Maegawa T, Takizawa S, Kita Y (2002) Synth Catal **344**: 328

[10] a) Neumann D, Paraskevopoulou P, Psaroudakis N, Mertis K, Staples RJ, Stavropoulos P (2000) Inorg Chem **39**: 5530; b) Paraskevopoulou P, Psaroudakis N, Koinis S, Stavropoulos P, Mertis K (2005) J Mat Catal A Chem (in press)

[11] Perrin DD, Armarego WLF (1989) Purification of Laboratory Chemicals, 3rd ed. Pergamon Press, UK

[12] Saltzman H, Sharefkin JG (1973) Organic Syntheses. CV 5, 658, vol 43, p 60