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An Atom-Efficient Catalytic Oxidation of Alcohols Using TEMPO/I_2O_5 in Water

Zhong-Quan Liu · Xiaojie Shang · Lingzhi Chai · Qiuju Sheng

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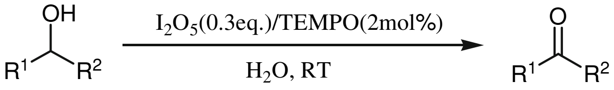
Abstract A metal-free room-temperature oxidation of electron-rich alcohols to the corresponding aldehydes or ketones can be efficiently catalyzed by TEMPO/I_2O_5 in water.

Keywords Oxidation · Alcohols · Aldehydes · Ketones · TEMPO · Hypervalent Iodine

1 Introduction

Oxidation of alcohols to the corresponding aldehydes or ketones is one of the most important functional group transformations in organic synthesis and numerous methods using a variety of reagents and conditions have been developed. Recent demand for greener, more atom efficient methods has encouraged the development of selective alcohol oxidation using safe, economic and environmentally benign agents [1]. In the area of metal-free catalytic alcohol oxidations relatively stable nitroxyl radicals (e.g., 2, 2, 6, 6-tetramethyl-piperidyl-1-oxyl, TEMPO) have emerged as the catalyst of choice [2–6]. However, the high cost and availability of TEMPO on large scale have encouraged the development of the variety of stoichiometric oxidants. Herein we wish to report an efficient selective catalytic oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones in water by using the most simple iodine (δ)-based reagents: HIO_3 (iodic acid, IA) and its anhydride I_2O_5 (iodine pentoxide, IP) as the stoichiometric oxidants. Although the iodine (δ) reagents such as 1-hydroxy-1,2-benziodoxal-3(1H)-one-1-oxide (IBX) and Dess-Martin periodinane (DMP) have been successfully used for the oxidation of alcohols to the corresponding carbonyl compounds [7, 8, 9], most of these procedures were conducted in organic solvents such as DMSO, CH_2Cl_2 and acetone. Despite their extensive use in industry [10–12], IA and IP have rarely been employed in organic synthesis. According to the investigation of Nicolaou et al. [13], alcohols are inert to the unique simple iodine (δ) reagents. Our research was inspired by the results of the TEMPO-Br_2/I_2 system by Miller et al. [14] and the PhIO-KBr system by Kita et al. [15]. Although these two systems are very efficient, both are suffered from overloading of the terminal oxidants and catalysts (Miller's system: 2 eq. I_2/10 mol% TEMPO/Toluene; Kita's system: 2.2 eq. PhIO/ 10 mol% KBr or 1.1 eq. PhIO/ 1.0 eq. KBr). Combining with our former researches [16–18], we began to question that a TEMPO-catalyzed process with more atom-efficient stoichiometric IA and IP could be established. Fortunately, we successfully accomplished an efficient TEMPO-catalyzed alcohols oxidation at room temperature with a number of economic, commercially available, atom efficient, environmental friendly, and safe iodine (δ) agents in water although it seems only electron-rich alcohols could be smoothly oxidized to the corresponding aldehydes and ketones (Scheme 1).



Scheme 1

Z.-Q. Liu (✉) · X. Shang · L. Chai · Q. Sheng
Institute of Organic Chemistry, Gannan Normal University, Ganzhou, Jiangxi 341000, P.R. China
e-mail: liuzhongquan@yahoo.cn

2 Experimental

2.1 General

^{1}H NMR spectra were recorded on a Varian Mercury Plus-300 spectrometer in $CDCl_3$ with TMS as internal standard. GC/MS were determined using an Agilent 6890/5973N GC/MS system. All products were identified by NMR and/or comparison with authentic samples. IA, IP, TEMPO, 4-hydroxy-TEMPO, alcohols and other reagents were all purchased from commercial sources.

2.2 Typical Experimental Procedure for Oxidation of Alcohols Using TEMPO/I_2O_5

An alcohol (10 mmol) was mixed with iodine pentoxide (3 mmol) and TEMPO (0.2 mmol) in water (30 mL). The mixture was stirred at room temperature until the reaction was completed as monitored by TLC. Extraction of the reaction mixture with ether, washed by Na_2SO_3, dried with anhydrous $MgSO_4$, removal of the solvent under reduced pressure and column chromatographic separation gave the pure product which was identified by ^{1}H NMR. The conversion and selectivity were determined by GC-MS.

3 Results and Discussion

Although almost equally efficient, we favored the use of IP and TEMPO in these reactions over respectively the diploid dosage oxidant IA and the more expensive derivatives 4-hydroxy-2, 2, 6, 6-tetramethyl-1-piperidinyloxyl (4-hydroxy-TEMPO). Initial investigation of the room-temperature stoichiometric oxidation of alcohols utilization of IP catalyzed by TEMPO was carried out using 1-phenylethanol as substrate in water. Theoretically, the mole ratio of I_2O_5/alcohol may be about 1/5 as iodine was produced in the system. As a matter of fact, the complete oxidation of 1-phenylethanol can not be achieved unless more than 20 mol% of I_2O_5 or 40 mol% of HIO_3 is present regardless of the dosage of TEMPO. Additionally, the appropriate quantity of the catalyst was investigated in the oxidation of 1-phenylethanol using 30 mol% of I_2O_5 catalyzed by TEMPO with quantity varying from 1 mol% to 5 mol%. It is seen from Fig. 1 that 2 mol% of TEMPO is chosen since it affords complete conversion at sufficient reaction rate comparing with overloading catalyst.

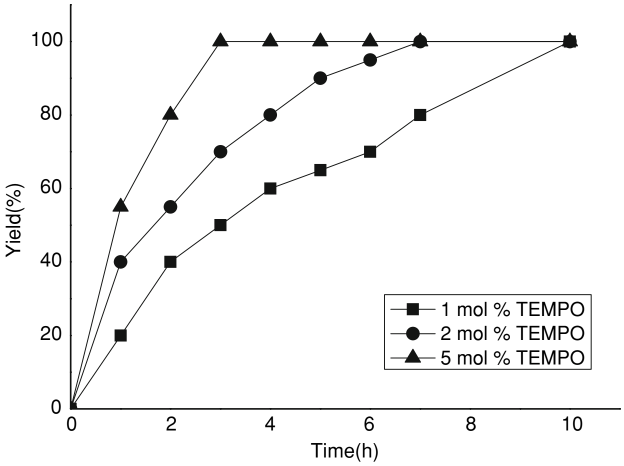
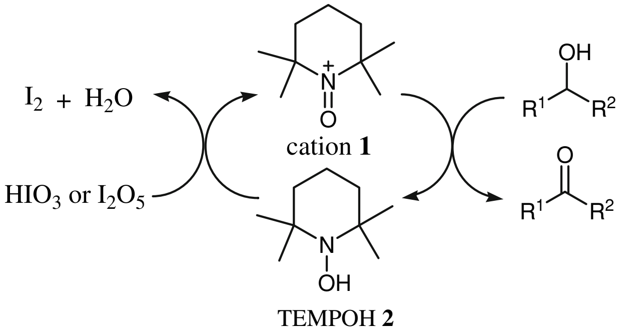


Fig. 1 Oxidation of 1-phenylethanol using I_2O_5 catalyzed by TEMPO with varying quantity

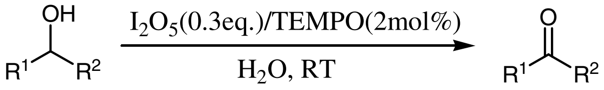
Under the following conditions: 10 mmol of alcohol, 30 mol% of I_2O_5, 2 mol% of TEMPO, H_2O, room temperature, almost all electron-rich alcohols were converted into their corresponding aldehydes and ketones in good to excellent yields without any over oxidation by-products (Table 1). It is seen from Table 1 that substituted benzyl alcohols gave high yields of the corresponding benzaldehydes derivatives (entries 1–5). Aromatic secondary alcohols gave good yields of the corresponding ketones (entries 6–12) except for 1-(4-nitrophenyl)ethanol (entry 8). Due to the presence of double bond, the α, β-unsaturated aldehydes and ketones were not obtained from the corresponding alcohols (entries 13). A mixture was formed in the oxidation of some simple alcohols such as ethanol (entry16). The oxidation of aliphatic alcohols (entries 14, 15) are not achieved in the catalytic process, however, the metal-free, cost-low, atom-efficient and the organic solvent-free features make this system very attractive.

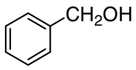
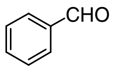
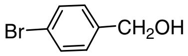
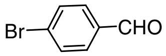
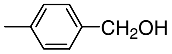
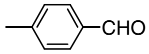
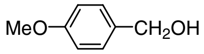
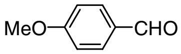
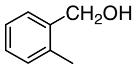
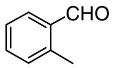
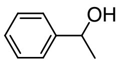
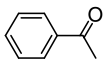
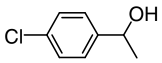
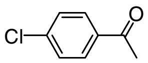
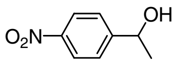
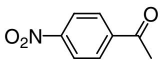
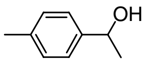
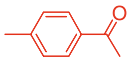
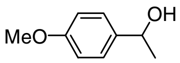
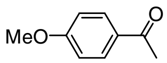
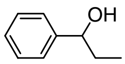
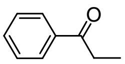
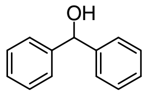
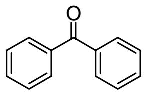
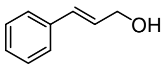
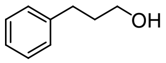
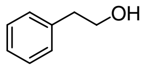
A possible mechanism of this efficient simple inorganic iodine (δ)-mediated catalytic oxidation is depicted in Scheme 2. Oxoammonium cation (**1**), which is initially oxidized from TEMPO, is an active oxidant of alcohols in this system [19, 20, 21]. Cation **1** is continuously provided by oxidizing TEMPOH **2**, the reduced form of TEMPO, with IP, which in turn, is reduced into I_2.



Scheme 2

Table 1 Metal-free oxidation of alcohols using TEMPO/I_2O_5 in water[a]



Entry	Substrate	Product	Method	Time [h]	Conv. [%][b]	Select. [%][b]	Yield [%][c]
1			A	6.5	94.0	100	92
2			B	18	87.1	100	85
3			A	6	100	100	97
4			A	9	92.6	100	90
5			A	8	100	100	96
6			A	7	100	100	98
7			A	16	93.6	100	91
8			B	20	49.2	100	46
9			A	6.5	86.6	98.5	83
10			A	5	85.4	100	82
11			A	16	79.3	100	75
12			C	9	74.1	100	72
13		Mixture	B	24	-	-	-
14		Trace	B	24	-	-	-
15		Trace	B	24	-	-	-
16	EtOH	Mixture	B	24	-	-	-

[a] Reaction conditions: alcohol (10 mmol), water, room temperature. Method A: I_2O_5 (3 mmol), TEMPO (0.2 mmol); Method B: I_2O_5 (5 mmol), TEMPO (0.4 mmol); Method C: I_2O_5 (5 mmol), TEMPO (0.4 mmol), 80 °C

[b] Conversions and selectivities are determined by GC-MS

[c] Yield of isolated chromatographically pure compound

4 Conclusion

In conclusion, we have demonstrated a convenient oxidation of electron-rich alcohols using HIO_3 and I_2O_5 as environmentally benign, commercially available, more atom-efficient, and safer stoichiometric oxidants with catalytic amounts of TEMPO or 4-hydroxy-TEMPO in water. These mild conditions may be helpful for a variety of other substrates that cannot tolerate strong oxidants. Further studies on the chemoselectivity and extension of this process to expanded functional groups are underway in our laboratory.

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