



Zinc(II)-catalyzed oxidation of alcohols to carbonyl compounds with chloramine-T

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ABSTRACT

Efficient oxidation of primary and secondary alcohols to the corresponding carbonyl compounds can be carried out in acetonitrile, using chloramine-T in the presence of catalytic zinc(II) salts. Primary alcohols are selectively oxidized to aldehydes without carboxylic acid byproduct.

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Oxidation of primary and secondary alcohols to the corresponding carbonyl compounds is a frequently used transformation in organic synthesis.¹ A variety of methods have been documented in the literature,² such as Dess–Martin oxidation,³ Swern oxidation,⁴ and various transition metal reagents. However, the use of a stoichiometric amount of transition metal oxidants and a large quantity of toxic byproducts was still the disadvantage of conventional methods. Therefore, there has been a continuous demand to develop environmentally friendly synthetic methods for this conversion.

Zinc salts have been widely used in organic synthesis especially taking the place of expensive and toxic metals in some reactions, because of their inexpensiveness, abundance, and low toxicity.⁵ At the same time, chloramine-T which was used usually as biocide and mild disinfectant is an inexpensive, commercially available reagent. When used as the oxidant, chloramine-T has an advantageous point that the catalytic oxidation could be performed by a simple operation without adding any bases and dehydrating agents.⁶ Inspired by recent findings,⁷ herein we report that a simple method to oxidized primary and secondary alcohols to corresponding carbonyl compounds under mild conditions by using chloramine-T as an oxidizing agent and zinc(II) salt as a catalyst.

In the preliminary study, we chose the oxidation of diphenylcarbinol **1** as our model system, and several commercial zinc(II) salts as potential catalysts were used to screen the most efficient catalyst and the best reaction conditions. The results were shown in Table 1. It was found that high conversion and good yield of

oxidation product **2** were obtained employing 20 mol % of ZnBr₂ as the catalyst in acetonitrile (Table 1). Modest yields were observed with ZnCl₂, ZnSO₄, and Zn(OAc)₂. ZnBr₂ showed a remarkably high activity even at room temperature, while the transformation cannot proceed in the absence of ZnBr₂ at room temperature.

In order to elucidate the efficiency of the catalyst, several amounts of ZnBr₂ were then examined for the oxidation of diphenylcarbinol using chloramine-T in acetonitrile. As indicated in Table 2, it is clear that 20 mol % ZnBr₂ shows exceedingly high catalytic efficiency compared to 5 mol % ZnBr₂ and there is no significant increase in the yield at a mole rate of 50 mol %. Hence, the required catalyst to ZnBr₂ is 20 mol %, beyond which no appreciable effect on the yield has been observed.

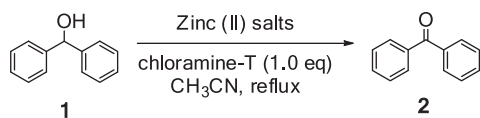
Encouraged by these results, we screened several different solvents for the oxidation of **1** using ZnBr₂ and chloramine-T at room temperature. Excellent yields of benzophenone were observed after 12 h in dichloromethane and acetonitrile (Table 3, entries 1 and 2) among the solvents examined. However, tetrahydrofuran (THF), dimethyl sulfoxide (DMSO), toluene, and diethylether were not suitable for this transformation.

The substrate scope of this method was investigated under standard reaction conditions, and the results are shown in Table 4.⁸ A variety of alcohols were efficiently oxidized to their corresponding carbonyl compounds. The *para*- and *meta*-substituted benzyl alcohols were oxidized to the corresponding substituted benzaldehydes in good to excellent yields (Table 4, entries 2–9). It seems that the reaction rates of benzyl alcohols with electron-donating groups are higher than electron-withdrawing groups. Dimethylamino, thiomethyl, ester, and cyano groups were tolerated under standard

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Table 1
Screening of the zinc(II) salts used as the catalyst



Entry	Catalyst (0.2 equiv)	Time (h)	Yield ^a (%)
1	—	5	46
2 ^b	—	12	N.R.
3	ZnCl ₂	3	80
4	ZnSO ₄	3	85
5	Zn(OAc) ₂	3	88
6	ZnBr ₂	1.5	95
7 ^b	ZnBr ₂	12	87

^a Isolated yield by column chromatography.

^b At room temperature.

Table 2
The amounts of catalyst optimization for the oxidation of diphenylcarbinol

Entry	ZnBr ₂ (equiv)	Time (h)	Yield (%)
1	1	1	95
2	0.5	1.5	95
3	0.2	1.5	95
4	0.1	3	90
5	0.05	5	82

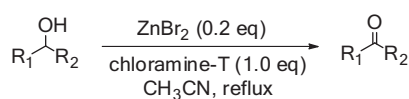
Table 3
Optimization of solvents for the oxidation of diphenylcarbinol

Entry	Solvent	Time (h)	Yield (%)
1	CH ₂ Cl ₂	12	82
2	CH ₃ CN	12	87
3	THF	24	60
4	DMSO	24	65
5	Toluene	24	70
6	Et ₂ O	24	30

conditions (Table 4, entries 3, 5, 7, and 8). Moreover, the generality of the methodology was further confirmed by applying the same reaction conditions to heterocyclic alcohols. The transformation of 2-hydroxymethylpyridine and 3-hydroxymethylpyridine to the corresponding aldehydes proceeded smoothly in good yields (Table 4, entries 10 and 11). Piperonyl aldehyde was achieved from piperonyl alcohol in moderate yield (Table 4, entry 12). Under the present reaction conditions, simple aliphatic alcohols, such as 1-butanol, were also oxidized to aliphatic aldehydes in high yields. With the increase of the carbon chain the reactivity decreased slightly. For example, the oxidation of 1-hexanol needs 2 h with 90% yield, consuming more time than the transformation of 1-butanol. In these reactions, the produced aldehydes were not oxidized further to carboxylic acids, indicating the potential utility of ZnBr₂/chloramine-T system as a selective oxidant.

This method also can be applied to the oxidation of secondary carbinols under the same reaction conditions. Aliphatic and benzylic secondary alcohols were effectively oxidized to corresponding ketones (Table 4, entries 15–23), but the reaction rate is slower than primary alcohols. For example, the oxidation of cyclohexanol afforded cyclohexanone taking 4 h in 96% yield. Similarly, substituted 1-phenylethanols like 1-(2,6-dichloro-3-fluorophenyl) ethanol were converted into the corresponding acetophenones slower than 1-phenylethanol, but still in good yields. Both electron donating and electron withdrawing groups were tolerated in this transformation, such as methoxy- and halogen-substituted

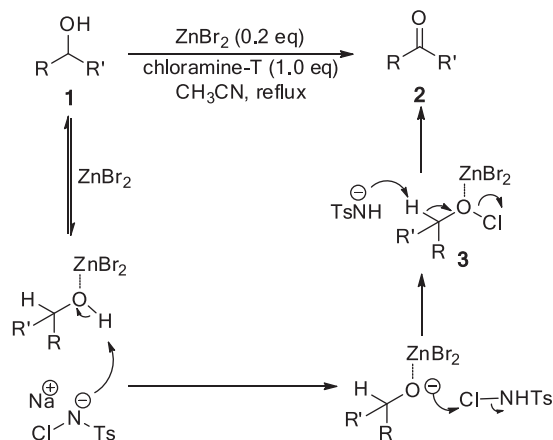
Table 4
Scope of ZnBr₂-catalyzed the oxidation of alcohols to corresponding carbonyls^a



Entry	Alcohols	Time (h)	Yield (%)
1		1.5	95
2		1.5	96 ^b
3		3	85
4		1.5	94
5		2	90
6		2	91
7		3	83
8		4	80
9		2	88
10		2	90
11		2	89
12		4	78
13		1.5	95 ^b
14		2	90 ^b
15		3	91 ^b
16		4	96 ^b
17		5	95
18		5	92
19		5	90
20		5	93
21		4.5	86
22		1.5	94
23		2	89

^a Unless otherwise stated, reaction was run using alcohol (1 mmol), 20 mol % ZnBr₂, and 1 equiv chloramine-T in CH₃CN at reflux.

^b Determined by GC analysis.



Scheme 1. Proposed reaction mechanism of alcohol oxidation by chloramine-T with ZnBr₂ as catalyst.

1-phenylethanols. We also tested some substituted diphenylcarbinols (Table 4, entries 22 and 23). In the case of 4-methylbenzhydrol, its corresponding ketone was obtained in high yield.

On the basis of the above results and mechanism reported in the literature,⁹ a plausible reaction mechanism is shown in Scheme 1. Initially, coordination of alcohols to zinc bromide results in facilitating the cleavage of the hydroxyl bond. Then chloramine-T successively reacts with alcohols to afford the intermediate **3**. Finally, the decomposition of the intermediate **3** into carbonyl compounds proceeds in a concerted manner. Therefore, complexation of the oxygen atom of the alcohols with zinc should accelerate the cleavage of the O–H bond and the hydrogen transfer in the presence of zinc bromide.

In conclusion, an efficient procedure for the conversion of alcohols into the corresponding carbonyl compounds using ZnBr₂/chloramine-T system has been developed. Primary and secondary alcohols are rapidly oxidized without overoxidation to carboxylic acids. This novel method makes use of very easily available and cheaper reagents under mild conditions. It seems to be as conve-

nient for oxidizing both primary and secondary alcohols as other methods reported in the literature. Additional investigations will focus on the extension of this catalytic system.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tetlet.2012.11.076>.

References and notes

- Smith, M. B.; March, J. *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th ed.; Wiley-Interscience: New York, 2001.
- (a) Brink, G.-J. T.; Arends, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636–1639; (b) Mallat, T.; Baiker, A. *Chem. Rev.* **2004**, *104*, 3037–3058; (c) Zhan, B.-Z.; Thompson, A. *Tetrahedron* **2004**, *60*, 2917–2935.
- (a) Dess, D. B.; Martin, J. C. J. *Org. Chem.* **1983**, *48*, 4155–4156; (b) Li, P.; Majireck, M. M.; Korboukh, I.; Weinreb, S. M. *Tetrahedron Lett.* **2008**, *49*, 3162–3164.
- (a) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660; (b) McConnell, J. R.; Hitt, J. E.; Daus, E. D.; Rey, T. A. *Org. Process Res. Dev.* **2008**, *12*, 940–945.
- Wu, X.-F. *Tetrahedron Lett.* **2012**, *53*, 3397–3399.
- Campbell, M. M.; Johnson, G. *Chem. Rev.* **1978**, *78*, 65–79.
- (a) Kitagawa, H.; Mukaiyama, T. *Chem. Pharm. Bull.* **2002**, *50*, 1276–1279; (b) Cao, H. T.; Grée, R. *Tetrahedron Lett.* **2009**, *50*, 1493–1494; (c) Li, S.-J.; Wang, Y.-G. *Tetrahedron Lett.* **2005**, *46*, 8013–8015.
- General procedure for oxidation of alcohols*: A CH₃CN solution of diphenylcarbinol **1** (1 mmol), ZnBr₂ (45 mg, 0.2 mmol), and chloramine-T (282 mg, 1 mmol) was placed in a three necked flask with a reflux condenser. After the mixture was stirred under reflux for 1.5 h, it was quenched by adding water and the resulting mixture was extracted with AcOEt. Removal of the solvent under reduced pressure gave the crude product, which was purified by column chromatography on silica gel (*n*-hexane/AcOEt = 8/1) to give benzophenone **2** (173 mg, 95% yield). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.46–7.51 (m, 4H), 7.57–7.62 (m, 2H), 7.80–7.82 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 128.1, 129.9, 132.3, 137.4, 196.5. ESI-MS: calcd [M+Na]⁺ for C₁₃H₁₀ONa: 205.0624, found: 205.0628. All other carbonyl derivatives have spectral data in agreement with authentic samples and/or with literature data.
- Hassan, Y. I.; Saeed, N. H. M. *E-J. Chem.* **2012**, *9*, 642–649.