A new metal-free protocol for oxidation of alcohols using *N*,*N*-dibromo-*p*-toluenesulfonamide

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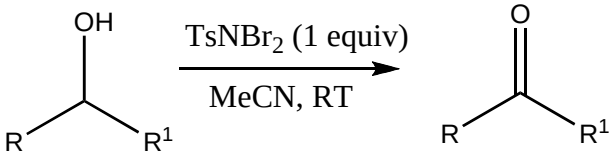
Abstract

N,*N*-Dibromo-*p*-toluenesulfonamide ($TsNBr_2$) is shown to be a reagent for oxidation of alcohols, without a catalyst. The remarkable feature of this reagent is that it oxidizes primary alcohols very efficiently in excellent yields besides other secondary and benzylic alcohols, which undergo oxidation within a short time.

Keywords: Oxidation, $TsNBr_2$, alcohol, carbonyl compound, metal-free oxidant

Introduction

Oxidation of alcohols to their corresponding carbonyl compounds is a fundamental reaction in synthetic organic chemistry.[1] Traditionally, oxidation of alcohols is carried out using stoichiometric amounts of metallic oxidants notably chromium(VI) reagents,[2] permanganates,[3] and ruthenium(VIII) oxide,[4] which produce environmentally unacceptable heavy metal wastes.[5] Both stoichiometric procedures utilizing a variety of oxidants. as well as catalytic methods based on the use of coordination compounds of transition metals. have been reported.[6] Thus developing an efficient system for oxidation of organic substrates is of great importance both economically as well as environmentally. Besides metal-based oxidizing agents, a variety of halogen-based reagents such as bromine,[7] *N*-bromosuccinimide,[8] pyridinium hydrobromide perbromide,[9] [Bmim][Br_3],[10] *N*-bromoacetamide,[11] *N*-chlorosuccinimide,[12] etc. have been developed over the past several decades.[13] Among *N*-halogenated reagents reported in the literature, NBS has been found to be the most versatile reagent for oxidation. But in most cases of NBS assisted oxidation, it is necessary to use a catalyst in order to carry out the reaction.[8] Secondly, oxidation with NBS is restricted to secondary or benzylic alcohols, even in the presence of a catalyst. Oxidation of primary alcohols is not effective using *N*-halogenated reagents. Recently we have developed a new method for the synthesis of bromohydrins, alkoxybromides and bromoazides using $TsNBr_2$.[14] We report herein a rapid and efficient procedure for the oxidation of alcohols to carbonyl compounds using $TsNBr_2$ (Scheme 1) under mild reaction conditions.



R = aryl, alkyl, cycloalkyl
R^1= H, alkyl, cycloalkyl

Scheme 1

Results and Discussion

N,*N*-Dibromo-*p*-toluenesulfonamide has long been known as a reagent for aminobromination. Since the discovery of this reagent by Kharasch,[15] it has been utilized for aminobromination of a variety of olefinic substrates.[16] We found that treatment of $TsNBr_2$ with an olefin in the presence of water or alcohol produces bromohydrins and alkoxybromides respectively.[14a] We were able to synthesize methoxybromides and *tert*-butoxybromides in a very efficient manner using this reagent.[14a] After this success, we sought to extend the procedure for alkoxybromide synthesis by using a variety of alcohols. However, when we employed benzyl alcohol as a substrate, instead of methanol or *tert*-butanol, the reaction produced a mixture of benzaldehyde and benzoic acid in a rapid and exothermic process. So, we have carefully studied the process to develop a new methodology for the oxidation of alcohols. To best of our knowledge, oxidation of alcohol with $TsNBr_2$ is not known in the literature. The brominating agent $TsNBr_2$ employed for this purpose was prepared from chloramine-T, following a literature procedure.[17]

Firstly, 1-phenylethanol was used as a model substrate. The reaction was carried out by adding $TsNBr_2$ (1.0 mmol) to a solution of the alcohol (1 mmol) in acetonitrile (2 ml) at room temperature. Various solvents were examined to find the most suitable. The results are summarized in Table 1. It was found that acetonitrile is the most suitable solvent for oxidation of 1-phenylethanol to acetophenone.

Table 1. Acetophenone synthesis in various solvents[a]

Entry	Solvent	Time (min)	Yield (%)[b]
1	MeCN	30	82
2	$CHCl_3$	35	68
3	CH_2Cl_2	60	39
4	CCl_4	45	55

[a]Reaction conditions: 1-phenylethanol (1 mmol), $TsNBr_2$ (1 mmol), solvent (2 mL), room temperature.
[b]Isolated yield.

Thereafter, the reaction was examined using different amounts of the oxidant (Table 2). We found that, the use of 1 equivalent of the reagent is the best choice in terms of yield and reaction

time.

Table 2. Acetophenone synthesis with varying amount of $TsNBr_2$[a]

Entry	$TsNBr_2$ amount (mmol)	Time (min)	Yield (%)[b]
1	0.5	30	40
2	1.0	30	82
3	1.5	30	72
4	1.8	30	74

[a]Reaction conditions: 1-phenylethanol (1 mmol), MeCN (2mL), room temperature.
[b]Isolated yield

After optimizing the reaction conditions, we extended the process to a variety of alcohols, (Table 3). The method works well for all kind of alcohols such as primary, secondary and benzylic alcohols to produce the corresponding carbonyl compound in excellent yield. In the case of secondary benzylic alcohols, the reaction is very fast and produces the corresponding carbonyl compounds within 30 minutes. However, in case of benzyl alcohol, over-oxidation took place and benzoic acid was also produced. Cyclic secondary alcohols such as cyclohexanol and menthol took about 30 minutes for completion of reaction whereas 2-octanol underwent complete oxidation in 45 minutes, in high yield (Table 3, entries 5-8). Primary alcohols such as 1-octanol took 1 hour for complete oxidation in 80% yield (Table 3, entry 9). However, dodecanol took 2 hours for completion of reaction, but in excellent yield (Table 3, entry 10). Similarly, 2-phenylethanol and 3-phenylpropan-1-ol were oxidized efficiently with high yields in 1 hour (Table 3, entries 11 and 12). Thus, it can be seen that the yields are very high regardless of the structural variations in the alcohol.

Table 3. Oxidation of various alcohols using $TsNBr_2$[a]

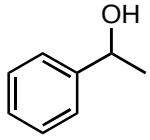
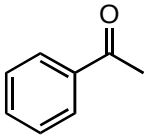
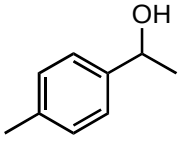
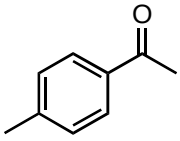
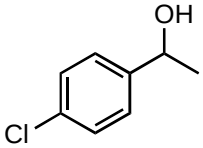
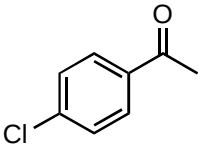
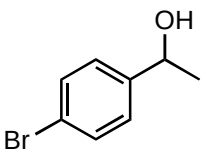
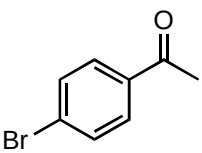
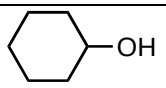
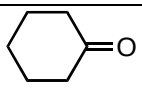
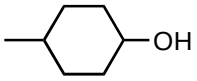
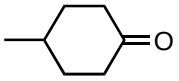
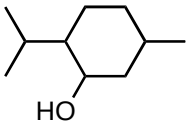
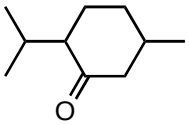
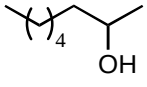
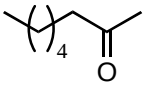
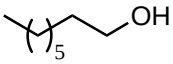
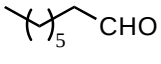
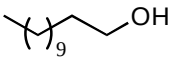
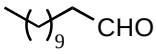
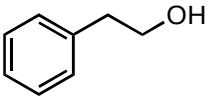
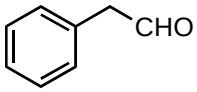
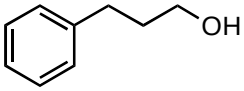
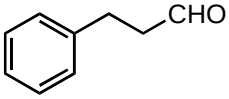
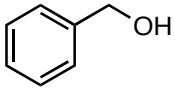
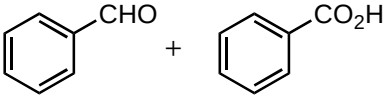
Entry	Substrate	Product[b]	Time (min)	Yield (%)[c]
1			30	82
2			30	81
3			30	80
4			30	82

Table 3. Continued

Entry	Substrate	Productb	Time (min)	Yield (%)c
5			30	79
6			30	83
7			30	85
8			45	82
9			60	80
10			120	90
11			60	82
12			60	85
13			30	40 + 33

[a]Reaction conditions: alcohol (1 mmol), $TsNBr_2$ (1mmol), MeCN (2 mL), rt.
[b]All products were characterized by comparison of their IR and ^1H NMR spectra with those of authentic samples.
[c]Isolated yield.

Conclusion

In conclusion, a new protocol has been developed for oxidation of alcohols to corresponding carbonyl compounds using *N*,*N*-dibromo-*p*-toluenesulfonamide as oxidizing agent. This procedure is rapid, easy to perform at room temperature and applicable to different kinds of primary and secondary alcohols, such as aromatic, aliphatic, cyclic and benzylic alcohols to give the corresponding carbonyl compounds in excellent yields. Benzyl alcohol is converted into both aldehyde and acid whereas aliphatic primary alcohols are converted into aldehyde only. This protocol has wide scope for oxidation of a variety of alcohols in an efficient manner.

Experimental Section

General procedure for oxidation of alcohols

To a solution of alcohol (1 mmol) in MeCN (2 ml) was added $TsNBr_2$ (1 mmol). The color of solution changed slowly from light yellow to orange. After the reaction was complete sodium thiosulfate was added to the reaction mixture with 1 ml of water and the whole stirred for 20 min. The reaction mixture was taken up in ether, washed with brine, dried (Na_2SO_4), and concentrated. Purification of the crude product by flash chromatography on silica gel (230-400 mesh) with petroleum ether-EtOAc (0-5%) as eluent gave the pure product.

In the case of benzyl alcohol, the extraction of the product from the reaction mixture was done with ethyl acetate and the crude product was purified with petroleum ether-EtOAc (5-20%) as eluent to give the pure product.

Acknowledgements

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Reference

1. (a) Larock, R. C. *Comprehensive Organic Transformations*, VCH: New York, 1989, pp 604–834. (b) Hudlicky, M. *Oxidations in Organic Chemistry*, ACS Monograph Ser. 186, American Chemical Society, Washington, DC, 1990, 114. (c) *Comprehensive Organic Functional Group Transformations*, Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W.; Pattenden G.; Moody, C. J., Eds. Elsevier Science: Oxford, 1995, Vols. 3 and 5.
2. (a) Cainelli, G.; Cardillo, G. *Chromium Oxidants in Organic Chemistry*, Springer-Verlag, Berlin, 1984. (b) Patel, S.; Mishra, B. K. *Tetrahedron* **2007**, *63*, 4367.
3. (a) Regen, S. L.; Koteel, C. *J. Am. Chem. Soc.* **1977**, *99*, 3837. (b) Menger, F. M.; Lee, C. *Tetrahedron Lett.* **1981**, *22*, 1655.
4. Griffith, W. P. *Chem. Soc. Rev*. **1992**, *21*, 179.
5. March, J. *Advanced Organic Chemistry*, John Wiley: New York, 1992, p 1167.
6. (a) Schultz, M. J.; Sigman, M. S. *Tetrahedron* **2006**, *62*, 8227. (b) Zhan, B.-Z.; Thompson, A. *Tetrahedron* **2004**, *60*, 2917. (c) Muzart, J. *Tetrahedron*, **2003**, *59*, 5789; (d) Brandt, C.; van Eldic, R. *Chem. Rev*. **1995**, *95*, 119. (d) Punniyamurthy, T.; Velusamy, S.; Iqbal, J. *Chem. Rev*. **2005,** *105*, 2329.
7. (a) Al. Neirabeyeh, M.; Ziegler, J. C.; Gross, B.; Caubere, P. *Synthesis* **1976**, 811. (b) Doyle, M. P.; Bagheri, V. *J. Org. Chem*. **1981**, *46*, 4806. (c) Williams, D. R.; Klingler, F. D.; Allen, E. E.; Lichtenthaler, F. W. *Tetrahedron Lett.*, **1988**, *29*, 5087. (d) Tanaka, T.; Murakami, K.; Okuda, O.; Kuroda, T.; Inoue, T.; Kamei, K.; Murata, T.; Yoshino. H.; Imanishi, T.; Iwata, C. *Chem. Pharm. Bull.* **1994**, *42*, 1756. (e) Miljkovic, C.; Kuhajda, K.; Hranisavljevic, J. *J.*

Chem. Res. (S) **1996**, 106. (f) Matsuo, J.-i.; Kawana, A.; Yamanaka, H.; Mukaiyama, T. *Chem. Lett.* **2003,** *32*, 182.

8. (a) Fieser, L. F.; Rajagopalan, S. *J. Am. Chem. Soc.* **1949**, *71*, 3935. (b) Fieser, L. F.; Rajagopalan, S. *J. Am. Chem. Soc*., **1949**, *71*, 3938. (c) Sharma, J. P.; Singh, R. N. P.; Singh, A. K.; Singh, B. *Tetrahedron*, **1986**, *42*, 2739. (d) Singh, A. K.; Chopra, D.; Rahmani, S.; Singh, B. *Carbohyd. Res*. **1998**, *314*, 157. (e) Kim, D. W.; Choi, H. Y.; Lee, K.-J.; Chi, D. Y. *Org. Lett.*, **2001**, *3*, 445. (f) Sharma, V. B. Jain, S. L.; Sain, B. *J. Mol. Catal. A: Chem*. **2005**, *227*, 47. (g) Lee, J. C.; Lee, J. Y.; Lee, J. M. *Synth. Commun*. **2005**, *35*, 1911. (h) Onomura, O.; Arimoto, H.; Matsumura, Y.; Demizu, Y. *Tetrahedron Lett*. **2007**, *48*, 8668.
9. Sayama, S.; Onami, T. *Synlett* **2004**, 2739.
10. Zhang, Y.; Bao, W. *J. Chem. Res.* **2006**, 263.
11. Mukherjee, J.; Banarji, K. K. *J. Org. Chem*. **1981**, *11*, 46.
12. (a) Mukaiyama, T.; Matsuo, J. -i.; Iida. D.; Kitagawa, H. *Chem. Lett*. **2001**, *30*, 846. (b) Nasim, S.; Crooks, P. A. *Tetrahedron Lett.* **2009**, *50*, 257
13. (a) Filler, R. *Chem. Rev*. **1963**, 21. (b) Arterburn, J. B. *Tetrahedron* **2001**, *57*, 9765.
14. (a) Phukan, P.; Chakraborty, P.; Kataki, D. *J. Org. Chem.* **2006**, *71*,7533. (b) Saikia, I.; Phukan, P. *Tetrahedron Lett.* **2009**, *50*, 5083.
15. Kharasch, M. S.; Priestley, H. N. *J. Am. Chem. Soc*. **1939**, *61*, 3425.
16. (a) Terauchi, H.; Kowata, K.; Minematsu, T.; Takemura, S. *Chem. Pharm. Bull.* **1977**, *25*, 556. (b) Hegedus, L. S.; McKearin, J. M. *J. Am.Chem. Soc*. **1982**, *104*, 2444. (c) Revesz, L.; Blum, E.; Wicki, R. *Tetrahedron Lett*. **2005**, *46*, 5577. (e) Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc*. **1996**, *118*, 9526. (d) Shen, R.; Huang, X. *J. Org. Chem.* **2007**, *72*, 3961. (e) Han, J.; Li, T.; Pan, Y.; Kattuboina, A.; Li, G. *Chem. Biol. Drug. Des*. **2008**, *71*, 71.
17. Nair, C. G. R.; Indrasen, P. *Talanta* **1976**, *23*, 239.