# Hexamethylenetetramine–Bromine: A Novel Reagent for Selective Regeneration of Carbonyl Compounds from Oximes and Tosylhydrazones†‡

*J. Chem. Research (S)*, 1998, 154–155†

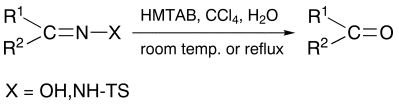
**Babasaheb P. Bandgar,*[a] Shivaji B. Admane[b] and Sandip S. Jare[b]**

[a]*Organic Chemistry Research Laboratory, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Dnyanteerth, Vishnupuri, Nanded-431 602, PO Box 87, Maharashtra, India*

[b]*Department of Chemistry R.B.N.B. College, Shrirampur-413709, Dist. Ahmadnagar, India*

Hexamethylenetetramine–bromine (HMTAB) has been found to be an efficient and selective reagent for the mild oxidative cleavage of the C=N of oximes and tosylhydrazones to yield their corresponding carbonyl compounds in good to excellent yields under mild conditions.

There has been considerable growth in interest in the development of mild methods for the regeneration of carbonyl compounds from stable and readily prepared oximes and tosylhydrazones.[1] This is because such derivatives of carbonyl compounds serve as effective protecting groups for aldehydes and ketones in organic synthesis.[2] Oximes are also extensively used for the purification and characterization of carbonyl compounds. Since oximes can be prepared from non-carbonyl compounds,[3] the regeneration of carbonyl compounds from oximes provides an alternative method for the preparation of aldehydes and ketones. Most of the known methods of regenerating carbonyl compounds from their nitrogen derivatives have several limitations.[4–11] It is most important to note that most of the reported methods are suitable for the regeneration of ketones but not for aldehydes from their oximes and tosylhydrazones, and that yields are low owing to the over oxidation of regenerated aldehydes to acids. Therefore it is desirable that a method which leads to high recoveries of a wide range aldehydes and ketones should be available. We now report an efficient and general method for the effective and selective cleavage of the C=N of oximes and tosylhydrazones with HMTAB under neutral and mild conditions (Scheme 1).




**Scheme 1**

Hexamethylenetetramine–bromine complex could be readily prepared by adding bromine to a chloroform solution of hexamethylenetetramine and it has been used successfully for the oxidation of primary and secondary alcohols to aldehydes and ketones, respectively.[12] This yellow–orange, non-hygroscopic, homogenous solid is very stable at room temperature and is not affected by ordinary exposure to light, air or water and has no offensive odour of bromine or amine. Ease of work-up and the stability of the reagent make it a safe and convenient source of active bromine.[13] The reagent is transformed during reaction into easily removable products and presents a convenient alternative to other *N*-halogenoamines.[14–17]

Table 1 summarizes the results of various oximes which underwent oxidative cleavage with HMTAB to form corresponding carbonyl compounds in good yields under mild conditions. The rate of oxidative cleavage of benzophenone oximes (entries 12–14) was fast. Even the sterically hindered ketone oximes (entries 15, 16) successfully underwent oxidative deoximation with HMTAB to give ketones in good yields.

**Table 1** Oxidative cleavage of oximes with HMTAB in $CCl_4$

| Entry | Substrate | Reaction conditions | | Product[a] | Yield[b] (%) |
|---|---|---|---|---|---|
| | | Temp. ($T$/°C) | Time ($t$/h) | | |
| 1 | 4-Chlorobenzaldoxime | 60 | 7 | 4-Chlorobenzandehyde | 76 |
| 2 | 4-*N*,*N*-Dimethylaminobenzaldoxime | 25 | 3 | 4-*N*,*N*-Dimethylaminobenzaldehyde | 77 |
| 3 | 2-Nitrobenzaldoxime | 60 | 5.3 | 2-Nitrobenzaldehyde | 98 |
| 4 | 3-Nitrobenzaldoximes | 60 | 7 | 3-Nitrobenzaldehyde | 87 |
| 5 | 4-Nitrobenzaldoximes | 60 | 6 | 4-Nitrobenzaldehyde | 69 |
| 6 | Salicylaldehyde oxime | 25 | 4 | Salicylaldehyde | 40 |
| 7 | Cyclopentanone oxime | 25 | 4 | Cyclopentanone | 86 |
| 8 | Cyclohexanone oxime | 25 | 4 | Cyclohexanone | 85 |
| 9 | Acetophenone oxime | 25 | 3 | Acetophenone | 88 |
| 10 | 4-Chloracetophenone oxime | 60 | 4 | 4-Chloracetophenone | 84 |
| 11 | 4-Methylacetophenone oxime | 25 | 2.5 | 4-Methylacetophenone | 77 |
| 12 | Benzophenone oxime | 25 | 1.5 | Benzophenone | 78 |
| 13 | 4-Bromobenzophenone oxime | 25 | 2 | 4-Bromobenzophenone | 90 |
| 14 | 4-Chlorobenzophenone oxime | 25 | 2 | 4-Chlorobenzophenone | 76 |
| 15 | Camphor oxime | 25 | 2 | Camphor | 80 |
| 16 | Menthone oxime | 25 | 2 | Menthone | 87 |

[a]Characterized by IR, $^1$H NMR and comparison with authentic samples. [b]Isolated yields.

The most remarkable advantage of this methodology is that it is a general method for oxidative cleavage of a variety of aldoximes and ketone oximes with HMTAB to give the corresponding carbonyl compounds in good yields under neutral, and mild conditions, and no trace of

*To receive any correspondence.

†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

‡Dedicated to Professor M. S. Wadia on the occasion of his 60th birthday.

**Table 2** Oxidative cleavage of tosylhydrazones with HMTAB in $CCl_4$ at 25 °C

| Entry | Substrate | Reaction time ($t$/h) | Product[a] | Yield[b] (%) |
|---|---|---|---|---|
| 1 | Butanone tosylhydrazone | 0.5 | α-Bromobutanone | 74 |
| 2 | 4-Chlorobenzaldehyde tosylhydrazone | 2 | 4-Chlorobenzandehyde | 69 |
| 3 | 2,4-Dichlorobenzaldehyde tosylhydrazone | 1.5 | 2,4-Dichlorobenzaldehyde | 87 |
| 4 | Furfuraldehyde tosylhydrazone | 2 | Furfuraldehyde | 60 |
| 5 | 2-Nitrobenzaldehyde tosylhydrazone | 1.5 | 2-Nitrobenzaldehyde | 88 |
| 6 | 3-Nitrobenzaldehyde tosylhydrazone | 5 | 3-Nitrobenzaldehyde | 89 |
| 7 | 4-Nitrobenzaldehyde tosylhydrazone | 6 | 4-Nitrobenzaldehyde | 98 |
| 8 | Salicylaldehyde tosylhydrazone | 2 | Salicyladehyde | 40 |
| 9 | Cyclopentanone tosylhydrazone | 2 | Cyclopentanone | 50 |
| 10 | Cyclohexanone tosylhydrazone | 2.5 | Cyclohexanone | 81 |
| 11 | 4-Chloroacetophenone tosylhydrazone | 0.5 | 4-Chloroacetophenone | 69 |
| 12 | Benzophenone tosylhydrazone | 0.5 | Benzophenone | 90 |

[a]Characterized by IR, $^1$H NMR and comparision with authentic samples. [b]Isolated product.

acid was formed owing to over oxidation of regenerated aldehyde. This procedure is also useful for chemoselective oxidative deoximation of ketone oximes in preference to aldoximes.

When a mixture of 2,4-dichlorobenzaldoxime and cyclopentanone oxime or 4-nitrobenzaldoxime and acetophenone oxime or 4-chlorobenzaldoxime and 4-bromobenzophenone oxime in $CCl_4$ was allowed to react with HMTAB at room temperature (25 °C) for a period of 4, 3 and 2 h, respectively, the ketoximes cyclopentanone oxime, acetophenone oxime and 4-bromobenzophenone oxime underwent chemoselectively oxidative deoximation giving cyclopentanone (80%), acetophenone (86%) and bromobenzophenone (89%) whereas the aldoximes 2,4-dichlorobenzaldoxime, 4-nitrobenzaldoxime and 4-chlorobenzaldoxime were recovered unchanged.

Table 2 shows the oxidative cleavage of tosylhydrazones with HMTAB in $CCl_4$ to give the corresponding carbonyl compounds in good yields. The aliphatic ketone tosylhydrazone shown in entry 1 underwent oxidative cleavage with HMTAB to give the α-bromoketone due to subsequent bromination of the regenerated ketone. The present procedure is general for the oxidative cleavage of aliphatic, aromatic, heteroaromatic and cyclic tosylhydrazones and no trace of acid was formed owing to over oxidation of regenerated aldehyde. In contrast recently reported methodology, involving the use of 70% TBHP, is suitable only for the deprotection of ketone tosylhydrazones and failed for aliphatic and heteroaromatic tosylhydrazones. In this connection, the present methodology is important and noteworthy.

In conclusion, we hope that the present deprotection methodology of oximes and tosylhydrazones finds wide application in organic systhesis because of the simplicity of work-up and use of readily prepared oxidant (HMTAB) under neutral and mild conditions.

## Experimental

*Preparation of the Hexamethylenetetramine–Bromine Complex.*—A solution of bromine (20.0 g, 125 mmol) in $CHCl_3$ (100 ml) was added dropwise with stirring to a solution of hexamethylenetetramine (8.5 g, 60 mmol) in chloroform (100 ml). A yellow solid separated out as the bromine was taken up. The mixture was stirred for an additional 30 min, then the yellow solid was collected by vacuum filtration. Yield: 25.5 g (92%), mp = 170–175 °C (dec.); $\nu_{max}$/cm$^{-1}$ (KBr) 1460, 1360, 1325, 1045, 840 and 782 (Found: C, 15.9; H, 2.7; N, 12.8. $C_6H_{12}Br_4N_4$ requires C, 15.87; H, 2.63; N, 12.68%). The active bromine content of this complex is 1.5 mol $Br_2$ per mol of the complex, as determined by thiosulfate titrations.

Oximes or tosylhydrazones in $CCl_4$, when stirred at room temperature (25 °C) or boiled under reflux with HMTAB, gave the corresponding carbonyl compounds in good yields.

*A Typical Procedure.*—A mixture of 4-bromobenzophenone oxime (3 mmol) and HMTAB (3.1 mmol) in $CCl_4$ (10 ml) and 1 ml water was stirred at room temperature (25 °C) for 2 h. After the reaction was complete (TLC), insoluble hexamethylenetetramine was removed by filtration and washed with $CCl_4$ ($2 \times 10$ ml); the $CCl_4$ layer was dried over anhdrous $Na_2SO_4$. Removal of the solvent under reduced pressure gave the product in good yield and in almost pure form.

*Received, 23rd September 1997; Accepted, 14th November 1997*
*Paper E/7/06884K*

## References

1 Y. H. Kim, J. C. Jung and K. S. Kim, *Chem. Ind.*, 1992, 31 and references cited therein.
2 S. R. Sandler and W. Karo, *Organic Functional Group Preparations*, Academic Press, London, 1989, p. 430; T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, Wiley, New York, 1991.
3 G. W. Kabalka, R. D. Pace and P. P. Wadgaonkar, *Synth. Commun.*, 1990, **20**, 2453 and references cited therein.
4 R. E. Donaldson, J. C. Saddler, S. Byrn, A. T. Mckenzie and P. L. Fuch, *J. Org. Chem.*, 1983, **48**, 2167 and references cited therein.
5 J. C. Lee, K. H. Kwak, J. P. Hwang, *Tetrahedron Lett.*, 1990, **31**, 6677; B. Tamani, and N. Goudarizian, *Eur. Polym. J.*, 1992, **28**, 1035.
6 D. P. Curran, J. F. Brill and D. M. Rakiewicz, *J. Org. Chem.*, 1984, **49**, 1654; J. Drabowicz, *Synthesis*, 1990, 125; E. J. Corey, P. B. Hopkines, S. Kim, S. Yoo, K. P. Nambiar and J. R. Falk, *J. Am. Chem. Soc.*, 1979, **101**, 7131.
7 P. Laszlo and E. Polla, *Synthesis*, 1985, 439.
8 G. A. Olah, Q. Liao, C. S. Lee and G. K. Suryaprakash, *Synlett*, 1993, **427**.
9 R. Joseph, A. Sudalai and T. Ravindranthan, *Tetrahedron Lett.*, 1994, **35**, 5493; P. Kumar, V. R. Hegde, B. Pandey and T. Ravindranathan, *J. Chem. Soc., Chem. Commun.*, 1993, 1553.
10 N. B. Barhate, A. S. Gajare, R. D. Wakharkar and A. Sudalai, *Tetrahedron Lett.*, 1997, **38**, 635.
11 D. H. R. Barton, D. J. Lester and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1212.
12 I. Yavari and A. Shaabani, *J. Chem. Res. (S)*, 1994, 274.
13 For a review of positive halogens, see A. Foucaud, *Chem. Halides, Pseudo-halides, Azides*, 1983, **1**, 441.
14 S. Kondo, M. Ohira, S. Kawasoe, H. Kunisada and Y. Yuki, *J. Org. Chem.*, 1993, **58**, 5003.
15 F. Minisci, E. Vismara, F. Fontana, E. Platone and J. Faraci, *J. Chem. Soc., Perkin Trans. 2*, 1989, 123.
16 L. K. Blair, S. Hobbs, N. Bagnoli, L. Husband and N. Badika, *J. Org. Chem.*, 1992, **57**, 1600.
17 R. E. Banks, S. N. Mohialdin-Khaffaf, G. S. Lal, I. Sharif and R. G. Syvert, *J. Chem. Soc., Chem. Commun.*, 1992, 595.