

N-*tert*-Butyl-*N*-chlorocyanamide: a new reagent for the efficient preparation of *gem*-chloronitroso compounds

Vinod Kumar and M. P. Kaushik*

Process Technology Development Division, Defence R&D Establishment, Jhansi Road, Gwalior 474002, MP, India

Received 7 August 2005; revised 14 September 2005; accepted 21 September 2005

Available online 7 October 2005

Abstract—A new reagent for the efficient preparation of *gem*-chloronitroso compounds has been developed. The reaction of ketoximes with *N*-*tert*-butyl-*N*-chlorocyanamide takes place instantaneously in carbon tetrachloride at room temperature with excellent yields under mild conditions.

© 2005 Elsevier Ltd. All rights reserved.

gem-Chloronitroso compounds have proven to be versatile synthons in organic chemistry for the preparation of a variety of compounds¹ and in the cyclization reactions.² The synthesis of these compounds is generally achieved from oximes and is performed with good results by the use of elemental chlorine,³ aqueous hypochlorous acid,³ alkyl hypochlorite⁴ and *N*-halo-compounds,⁵ but often results in the formation of over-oxidized nitro derivatives along with the title compounds. It is always the aim to stop the reaction at the nitroso stage by controlling the reaction temperature and by slow addition of the reagent, but these requirements are often hard to meet and failure results in over-oxidation to nitro compounds. Therefore, there is still considerable interest in the development of selective methods/reagents for this transformation. Although, various methods are known for the synthesis of nitroso compounds, very few are sufficiently selective to terminate the reaction at the nitroso stage. Some of these methods invariably result in contamination of the products, involve pH-dependent reactions requiring stringent precautions, are limited to specific substrates and result in the formation of several by-products, thereby leading to low yields of the desired compounds. Furthermore, these methods are useful only for the synthesis of aliphatic *gem*-chloronitroso compounds and are not suitable for aromatic *gem*-chloronitroso compounds.

Thus a mild, selective and inexpensive reagent is still in demand. During the course of our systematic study and research on the oxidation of organic compounds with *N*-*tert*-butyl-*N*-chlorocyanamide,⁶ we investigated it as a novel, rapid and convenient reagent for selective conversion of oximes to their corresponding *gem*-chloronitroso derivatives.

The reaction of various oximes possessing alkyl, aryl or cyclic moieties with **2** in CCl₄ at room temperature afforded the corresponding products almost immediately with chemoselectivity and without the formation of by-products. The reaction was monitored by TLC and the results are presented in Table 1. The procedure was sufficiently selective to terminate the reaction at the nitroso stage and prevent over-oxidation to the nitro compounds. Even a sterically hindered ketoxime (Table 1, entry 6) was successfully converted into the corresponding *gem*-chloronitroso derivative in excellent yield (Scheme 1). Fenchone oxime was found to react with an equimolar quantity of **2** at the same rate as camphor oxime to give the corresponding *gem*-chloronitroso derivative (Table 1, entry 5) even though it is more hindered (Scheme 1).

All the aliphatic and aromatic *gem*-chloronitroso compounds prepared were stable at low temperature. It has already been reported that aromatic oximes react at a slower rate with chlorinating agents³ as compared to aliphatic oximes. Thus another important feature of this method is that aromatic oximes formed *gem*-chloronitroso compounds immediately on mixing. This indicates that aromaticity did not apparently affect the rate of

Keywords: *N*-*tert*-Butyl-*N*-chlorocyanamide; Ketoximes; *gem*-Chloronitroso compounds.

*Corresponding author. Tel.: +91 751 234 3972; fax: +91 751 234 1148; e-mail: mpkaushik@rediffmail.com

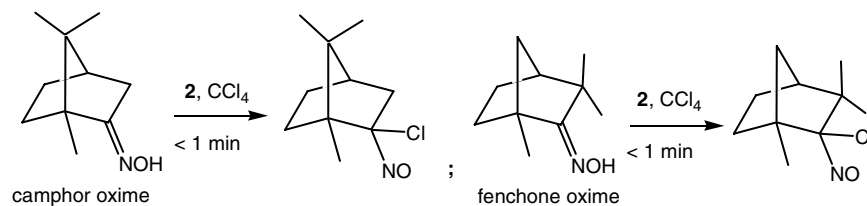
Table 1. Preparation of *gem*-chloronitroso compounds from oximes using **2**

$$\begin{array}{ccccccc}
 \text{R} & & \text{CN} & & \text{R} & & \text{CN} \\
 \diagdown & & | & & \diagdown & & | \\
 \text{C}=\text{NOH} & + & \text{}^t\text{C}_4\text{H}_9\text{--N--Cl} & \xrightarrow{\text{CCl}_4} & \text{C--Cl} & + & \text{}^t\text{C}_4\text{H}_9\text{--N--H} \\
 \diagup & & | & & \diagup & & | \\
 \text{R}' & & \text{Cl} & & \text{R}' & & \text{CN} \\
 \mathbf{1} & & \mathbf{2} & & \mathbf{3} & & \mathbf{4}
 \end{array}$$

Entry	Substrate	Product	Yield ^a
1			94
2			93
3			95
4			92
5			96
6			95
7			90
8			85

All the products were compared with authentic samples and gave satisfactory IR, NMR and MS data.

^a Isolated yields.

**Scheme 1.**

reaction. All the oximes were prepared by standard methods⁷ in which the ketone and hydroxylamine hydrogen chloride reacted at pH 7–8 by adding saturated aque-

ous sodium carbonate. The purity of compounds was checked by TLC. *N-tert*-Butyl-*N*-chlorocyanamide was prepared by the reported method.⁸

In conclusion, we have described an efficient reagent⁹ for the rapid and convenient conversion of oximes to *gem*-chloronitroso compounds under mild conditions. This reagent has advantages over the conventional reagents in terms of high yields, shorter reaction times, easy work up and no side products. In addition to these, the dechlorinated product **4** can be recycled to **2** for further use.

Acknowledgement

We thank Shri K. Sekhar, Director, DRDE, Gwalior, for his keen interest and encouragement.

References and notes

1. (a) Kruglyak, Y. L.; Landau, M. A.; Leibovskaya, G. A.; Martynov, I. V.; Saltykova, L. I. *Zh. Obshch. Khim.* **1971**, *41*, 2338–2339; (b) Cecherelli, P.; Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Tetrahedron Lett.* **1998**, *39*, 4385–4386; (c) Sabuni, M.; Kresz, G.; Braun, H. *Tetrahedron Lett.* **1984**, *25*, 5377–5380; (d) Martynov, I. V.; Chepakova, L. A.; Brel, V. K.; Sokolov, V. B. *Zh. Obshch. Khim.* **1986**, *56*, 2420–2421; (e) Walters, T. R.; Zajac, W., Jr.; Woods, J. M. *J. Org. Chem.* **1991**, *56*, 316–321; (f) Tordeux, M.; Boumizane, K.; Wakselman, C. *J. Org. Chem.* **1993**, *58*, 1939–1940.
2. Wang, Y. C.; Lu, T. M.; Elango, S.; Lin, C. K.; Tsai, C. T.; Van, T. H. *Tetrahedron: Asymmetry* **2002**, *13*, 691–695.
3. Archibald, T. G.; Garver, L. G.; Baur, K.; Cohen, M. C. *J. Org. Chem.* **1989**, *54*, 2869–2873.
4. Corey, E. J.; Estreicher, H. *Tetrahedron Lett.* **1980**, *21*, 1117–1120.
5. Walters, T. R.; Zajac, W. W., Jr.; Woods, J. M. *J. Org. Chem.* **1991**, *56*, 316–321.
6. Kumar, V.; Kaushik, M. P. *Chem. Lett.* **2005**, *34*, 1230–1231.
7. Fournar, P.; Cointet, P.; Laviro, E. *Bull. Soc. Chim. Fr.* **1968**, *6*, 2438–2446.
8. Neale, R. S.; Marcus, N. L. *J. Org. Chem.* **1969**, *34*, 1808–1816.
9. Typical experimental procedure: To a stirred solution of oxime (5 mmol) in dry carbon tetrachloride (10 ml), at room temperature, was slowly added *N*-*tert*-butyl-*N*-chlorocyanamide (1.0 equiv) in dry carbon tetrachloride (5 ml). The reaction took place immediately on mixing, as monitored by TLC and confirmed by the appearance of a blue colour in the reaction mixture (in the case of aliphatic oximes). If the products were liquid, the solution was concentrated and kept in a refrigerator overnight. Compound **4** precipitated (mp 12–13 °C) and was filtered off immediately. The filtrate was evaporated to give the crude product, which on distillation under vacuum, afforded the pure product. If the products were solid, purification was carried out by recrystallization using DCM/petroleum ether (40–60 °C) in a 3:7 ratio.