SYNLETT Spotlight 147

Sodium Nitrite (NaNO₂)

Compiled by Dan Bernardi

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

The well-known NaNO₂ (mp 271 °C, d = 2.17) has multiple applications in organic synthesis but also in medicine as a vasodilator, bronchodilator and antidote against cyanide and H₂S poisoning. It is produced in the human body from saliva and sodium nitrate to control bacteria in the stomach.

The synthetic utilities of NaNO₂ have been extensively investigated in organic chemistry. Nitrosation of primary amines with nitrous acid (generated in situ from sodium nitrite and a strong acid) leads to diazonium salts. These salts are useful synthetic intermediates used in named reactions like Sandmeyer, Balz-Schiemann,¹ Pschorr,² and Heck³ or in the manufacture of diazo dyes.⁴ NaNO₂ is

also used in the synthesis of alkyl nitrites,⁵ reagents used for the synthesis of diazonium salts in non-aqueous media⁶ or for the diazotization of primary aliphatic amines⁷ in DMF.

NaNO₂ reacts with SO₂ and potassium hydrogen carbonate to afford potassium hydroxylaminedisulfonate salt, which gives after oxidation nitrosodisulfonic acid dipotassium salt. This Fremy's salt is a useful reagent for the selective oxidation of phenols and aromatic amines to quinones (the Teuber reaction).⁸

Hydroxylamine hydrochloride is synthesized from NaNO₂ in a three-step procedure.⁹

Abstracts

(A) *tert*-Butylcarbazate reacts with NaNO₂ in an aqueous media to afford *tert*-butyl azidoformate¹⁰ which is a convenient reagent for the acylation of amine, hydrazine and similar compounds.¹¹

(B) *N*-Nitroso derivatives¹² of secondary amines are prepared by the action of NaNO₂ in aqueous acetic acid. The latter can be reduced by LiAlH₄ to give the corresponding hydrazine derivatives.

(C) Oximes¹³ can also be easily obtained from malonates or malononitrile and NaNO₂ under very mild conditions. Reduction of the oxime allows the formation of the amino derivative.

(D) The benzotriazole ring system¹⁴ is built from monoacyl-*o*-phenylene diamine and NaNO₂ in aqueous acetic acid.

(E) NaNO_2 is a very useful reagent for the production of simple aliphatic nitro compounds.¹⁵ An example from α,β -enones is shown here.

(F) Lindén et al.¹⁶ have used NaNO_2 in the formation of a tricyclic alloxazines. Nitrite was the key reagent for this ring-closure step.

(G) Liu et al.¹⁷ have shown the utility of NaNO_2 as a cocatalyst for the oxidation by TEMPO of alcohols to ketones in water.

(H) Abidi¹⁸ converted the isopropylidene group in geraniol chain into an alkyne group by the action of an excess of NaNO_2 in acetic acid.

(I) Panzella et al.¹⁹ showed that NaNO_2 in acetate buffer (0.05) M mediated the decarboxylative conjugation of caffeic acid with glutathione under mildly acidic conditions.

References

- (1) Laali, K. K.; Gettwert, V. J. *J. Fluorine Chem.* **2001**, 107, 31.
- (2) Wassmundt, F. W.; Kiesman, W. F. *J. Org. Chem.* **1995**, 60, 96.
- (3) (a) Sengupta, S.; Sadhukhan, S. *Org. Synth.* **2002**, 79, 52.
(b) Garcia, A. L. L.; Carpes, M. J. S.; de Oca, A. C. B. M.; dos Santos, M. A. G.; Santana, C. C.; Correia, C. R. D. *J. Org. Chem.* **2005**, 70, 1050.
- (4) Wang, M.; Funabiki, K.; Matsui, M. *Dyes Pigments* **2003**, 7, 77.
- (5) Noyes, W. A. *Org. Synth.* **1936**, 16, 7.
- (6) Doyle, M. P.; Siegfried, B. *J. Org. Chem.* **1977**, 42, 2426.
- (7) Doyle, M. P.; Bosch, R. J.; Seites, P. G. *J. Org. Chem.* **1978**, 3, 4120.
- (8) (a) Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1971**, 71, 229. (b) Teuber, H. J.; Jellinek, G. *Chem. Ber.* **1952**, 85, 95.
- (9) Semon, W. L. *Org. Synth.* **1923**, 3, 61.
- (10) Carpino, L. A.; Carpino, B. A.; Crowley, P. J.; Giza, C. A.; Terry, P. H. *Org. Synth.* **1964**, 44, 15.
- (11) Carpino, L. A. *J. Am. Chem. Soc.* **1957**, 79, 4427.
- (12) Touré, B. B.; Hall, D. G. *J. Org. Chem.* **2004**, 69, 8429.
- (13) (a) Zambito, A. J.; Howe, E. E. *Org. Synth. Coll. Vol. V*; Wiley: New York, **1973**, 373. (b) Ferris, J. P.; Sanchez, R. A.; Mancuso, R. W. *Org. Synth. Coll. Vol. V*; Wiley: New York, **1973**, 32.
- (14) Muir, J. C.; Pattenden, G.; Ye, T. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2243.
- (15) (a) Miyakoshi, T.; Saito, S.; Kumanotani, J. *Chem. Lett.* **1982**, 83. (b) Hong, W. P.; Lee, K. *Synthesis* **2005**, 33.
- (16) Lindén, A. A.; Hermanns, N.; Ott, S.; Krüger, L.; Bäckvall, J. *Chem. Eur. J.* **2005**, 11, 112.
- (17) Liu, R.; Dong, C.; Liang, X.; Wang, X.; Hu, X. *J. Org. Chem.* **2005**, 70, 729.
- (18) Abidi, S. L. *J. Chem. Soc., Chem. Commun.* **1985**, 1222.
- (19) Panzella, L.; Napolitano, A.; d'Ischia, M. *Bioorg. Med. Chem. Lett.* **2002**, 12, 3547.