SYNLETT
Spotlight 147

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

Sodium Nitrite ($NaNO_2$)

Compiled by Dan Bernardi

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Introduction

The well-known $NaNO_2$ (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 H_2S poisoning. It is produced in the human body from saliva and sodium nitrate to control bacteria in the stomach.

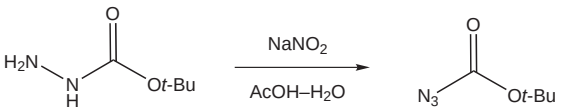
The synthetic utilities of $NaNO_2$ have been extensively investigated in organic chemistry. Nitrosation of primary amines with nitrous acid (generated in situ from sodium nitrite and a strong acid) leads to diazonium salts. These salts are useful synthetic intermediates used in named reactions like Sandmeyer, Balz-Schiemann,[1] Pschorr,[2] and Heck[3] or in the manufacture of diazo dyes.[4] $NaNO_2$ is also used in the synthesis of alkyl nitrites,[5] reagents used for the synthesis of diazonium salts in non-aqueous media[6] or for the diazotization of primary aliphatic amines[7] in DMF.

$NaNO_2$ reacts with SO_2 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]

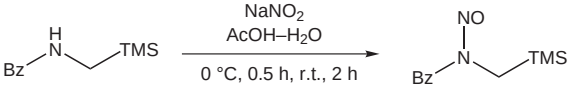
Hydroxylamine hydrochloride is synthesized from $NaNO_2$ in a three-step procedure.[9]

Abstracts

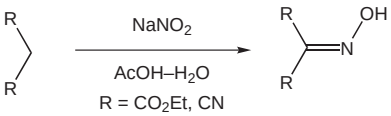
(A) *tert*-Butylcarbazate reacts with $NaNO_2$ in an aqueous media to afford *tert*-butyl azidoformate[10] which is a convenient reagent for the acylation of amine, hydrazine and similar compounds.[11]



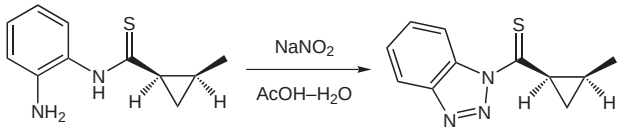
(B) *N*-Nitroso derivatives[12] of secondary amines are prepared by the action of $NaNO_2$ in aqueous acetic acid. The latter can be reduced by $LiAlH_4$ to give the corresponding hydrazine derivatives.



(C) Oximes[13] can also be easily obtained from malonates or malononitrile and $NaNO_2$ under very mild conditions. Reduction of the oxime allows the formation of the amino derivative.



(D) The benzotriazole ring system[14] is built from monoacyl-*o*-phenylene diamine and $NaNO_2$ in aqueous acetic acid.



SYNLETT 2006, No. 1, pp 0153–0154
Advanced online publication: 16.12.2005
DOI: 10.1055/s-2005-922781; Art ID: V14905ST
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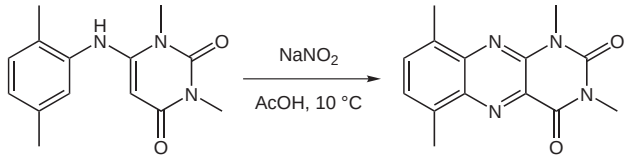
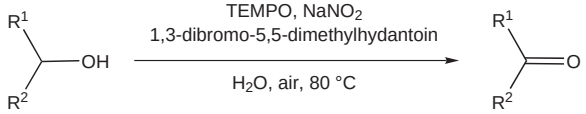
(E) $NaNO_2$ is a very useful reagent for the production of simple aliphatic nitro compounds.[15] An example from α,β-enones is shown here.

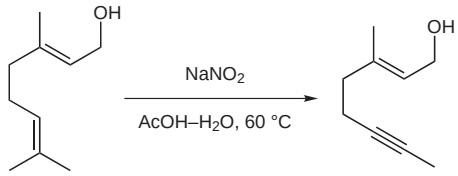
(F) Lindén et al.[16] have used $NaNO_2$ in the formation of a tricyclic alloxazines. Nitrite was the key reagent for this ring-closure step.



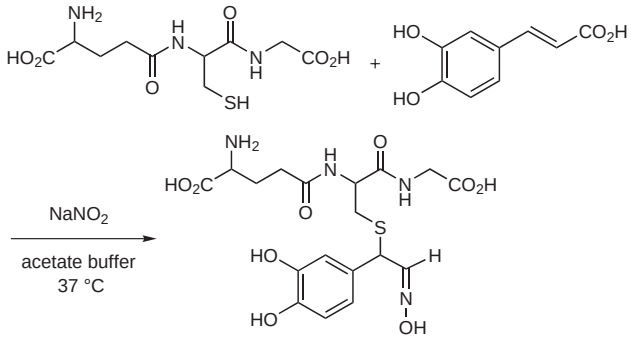
(G) Liu et al.[17] have shown the utility of $NaNO_2$ as a cocatalyst for the oxidation by TEMPO of alcohols to ketones in water.



(H) Abidi[18] 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.

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