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 ($NaNO_2$)

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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.

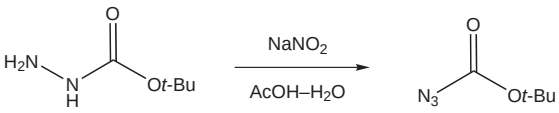
The synthetic utilities of $NaNO_2$ have been extensively investigated in organic chemistry. Nitrosation of primary amines with nitrous acid (generated in situ from sodium nitrite and a strong acid) leads to diazonium salts. These salts are useful synthetic intermediates used in named reactions like 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]

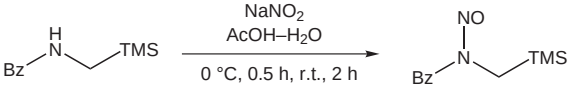
Hydroxylamine hydrochloride is synthesized from $NaNO_2$ in a three-step procedure.[9]

Abstracts

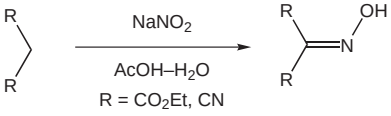
(A) *tert*-Butylcarbazate reacts with $NaNO_2$ in an aqueous media to afford *tert*-butyl azidoformate[10] which is a convenient reagent for the acylation of amine, hydrazine and similar compounds.[11]



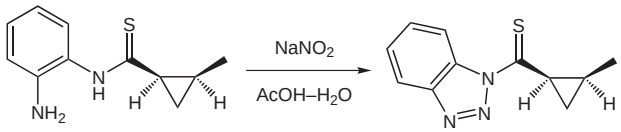
(B) *N*-Nitroso derivatives[12] of secondary amines are prepared by the action of $NaNO_2$ in aqueous acetic acid. The latter can be reduced by $LiAlH_4$ to give the corresponding hydrazine derivatives.



(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.



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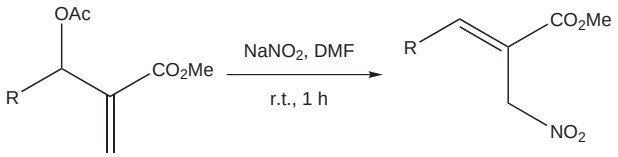
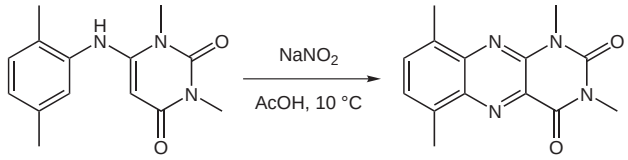
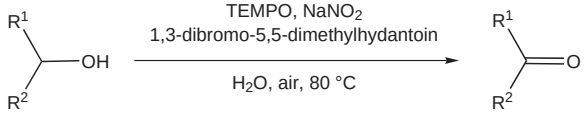
(E) $NaNO_2$ is a very useful reagent for the production of simple aliphatic nitro compounds.[15] An example from α,β-enones is shown here.



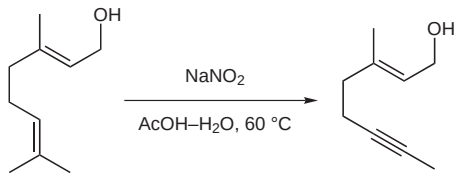
(F) Lindén et al.[16] have used $NaNO_2$ in the formation of a tricyclic alloxazines. Nitrite was the key reagent for this ring-closure step.



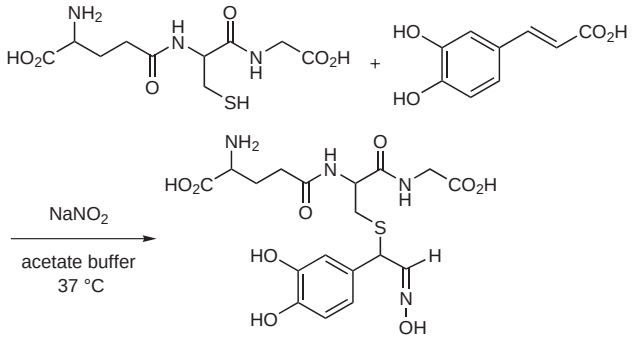
(G) Liu et al.[17] have shown the utility of $NaNO_2$ as a cocatalyst for the oxidation by TEMPO of alcohols to ketones in water.



(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.



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