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

Hydroxylamine Hydrochloride

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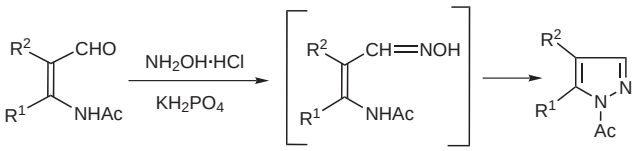
Introduction

Hydroxylamine hydrochloride is a hygroscopic white crystalline powder (mp 151–152 °C). Explosion of the reagent may occur if it is heated above 115 °C. Hydroxylamine hydrochloride is harmful if inhaled or swallowed and it is irritating to eyes, skin, and respiratory tract.[1] The reagent decomposes slowly on contact with moisture and should not be stored above 65 °C. Hydroxylamine as a free base is available in the form of large white flakes or needles; however, due to its instability, commercially available hydroxylamine hydrochloride is used as a stable source of hydroxylamine.[2] This versatile reagent can be prepared by treatment of sulfur dioxide with a cold solution of potassium nitrate and potassium acetate under controlled reaction conditions below 0 °C.

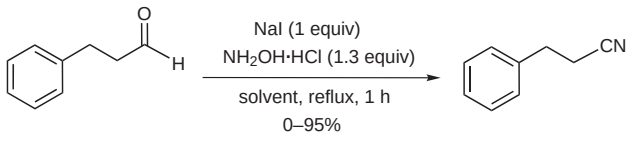
For over a century, hydroxylamine hydrochloride has found wide application in organic synthesis including electrophilic substitution reactions,[1] oximation,[3] the synthesis of pyrazoles,[4] nitriles,[5] isoxazoles,[6] pyridines,[7] nitrones,[8] etc. It is also used as reducing agent[9] and its importance in areas like bioorganic and medicinal chemistry is also vivid. For example, this reagent greatly facilitates the synthesis of a new class of glycosylated β-amino acids, which exhibit good activity against human antimalarial parasite *Plasmodium falciparum*.[10]

Abstracts

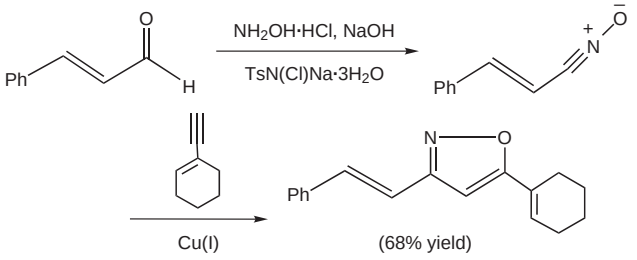
(1) A novel one-pot synthesis of pyrazoles has been accomplished by the reaction of β-formyl enamides with hydroxylamine hydrochloride catalysed by potassium dihydrogenphosphate in acidic medium.[4] The reaction has been successfully extended to steroidal, aliphatic, cyclic, and aromatic β-formyl enamides.



(2) A one-pot transformation of aliphatic and aromatic aldehydes to the corresponding nitriles can be easily performed by the reaction of an aldehyde with a slight excess of hydroxylamine hydrochloride in refluxing acetonitrile and in the presence of 0.5 equivalent of sodium iodide as catalyst.[5]



(3) 3,5-Disubstituted isoxazoles are obtained in good yields by a convenient one-pot, three-step procedure utilizing a regioselective copper(I)-catalysed cycloaddition reaction between in situ generated nitrile oxides and terminal acetylenes.[6a] This corresponding nitrile oxide can be obtained by reacting hydroxylamine hydrochloride in the presence of NaOH and TsN(Cl)Na·3H2O with the unsaturated aldehyde.



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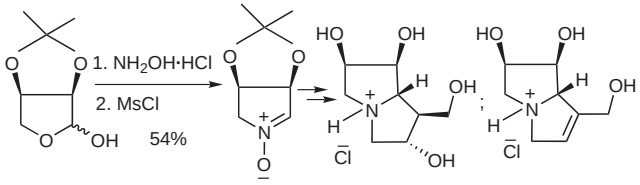
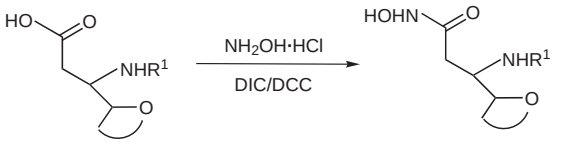
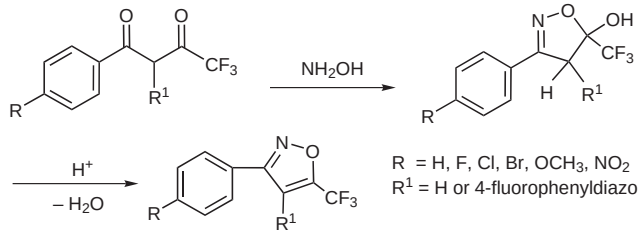
(4) A one-pot synthesis of enantiopure five-membered cyclic nitrones has been accomplished via condensation of hydroxylamine with readily available lactols and subsequent esterification with methanesulfonylchloride. These cyclic nitrones have been employed for the preparation of pyrrolizidines.[8]



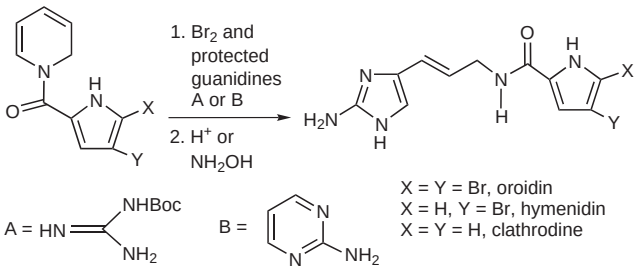
(5) Glycosylated β-amino acids afforded glycosyl β-aminohydroxamates in fair yields on reaction with $NH_2OH{\cdot}HCl$ in the presence of DIC/DCC. These compounds were screened against human malarial parasite.[10]



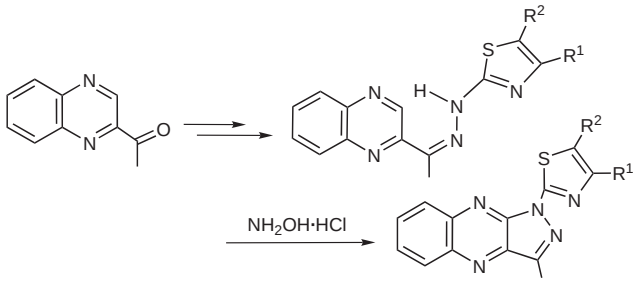
(6) Reaction of hydroxylamine hydrochloride with aryltrifluoromethyl-β-diketones affords 5-hydroxy-5-trifluoromethyl-Δ^2-isoxazoles which, upon dehydration, yield 5-trifluoromethylisoxazoles.[11]



(7) A short synthesis of pyrrolo-2-aminoimidazoles such as oroidin and its derivatives via *N*-acyl-1,2-dihydropyridine intermediate[12] is reported. The key step of the strategy is a one-pot oxidative bromine-mediated addition of protected guanidine to *N*-acyl-1,2-dihydropyridine in the presence of NH_2OH.



(8) Synthesis of 1-(thiazol-2-yl)-1*H*-pyrazolo[3,4-*b*]quinoxalines has been reported starting from 2-acetyl quinoxaline via dehydrogenative cyclisation with hydroxylamine hydrochloride in acidic medium.[13]



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