SYNLETT Spotlight 468

O-(2,4-Dinitrophenyl)hydroxylamine

Compiled by Zhanhui Yang

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

O-(2,4-Dinitrophenyl)hydroxylamine (**1**) is an orange solid (mp = 112 °C)¹ and fairly stable when exposed to air. It is commercially available and can be readily synthesized by Charette's method on a large scale:¹ Nucleophilic aromatic substitution of 2,4-dinitrochlorobenzene by *N*-hydroxyphthalimide followed by hydrazinolysis gives **1** in 94% yield over two steps (Scheme 1).

Scheme 1

Abstracts

(A) Amination of C-Nucleophiles

Following Sheradsky and co-worker's report,^{2a} the amination of different C-nucleophiles was assessed.^{2b} The results reveal that the enolates derived from deprotonation of variously substituted ethyl acetates smoothly undergo amination with **1**, affording ethyl amino acetates in moderate to good yields in most cases. However, the amination of the carbanion derived from phenylacetone nitrile gives the desired product in only 7% yield. In addition, neither Reformatsky reagents nor silyl enolates are susceptible to this transformation, even under violent reflux conditions.

(B) Amination of N-Nucleophiles with C=N Bonds

Amination of pyridines with **1** followed by protection of the resultant free NH₂ group and deprotonation with a base leads to *N*-iminopyridinium ylides in up to 99% yield.³ The yields are depended on the steric hindrance of the 2- and 6-positions and the electronic densities of the pyridine rings. The product *N*-iminopyridinium ylides are versatile building blocks for the preparation of pyridine derivatives.³ The amination is also applicable to other heterocycles such as imidazoles.⁴

(C) Amination of *N*-Nucleophiles with *N*-H Bonds

Transfer of amino groups to *N*-nucleophiles with *N*-H bonds yields hydrazines which are important intermediates in medicinal chemistry. Amination of the acidic *N*-H bond in 1*H*-quinazoline-2,4-diones was readily achieved by Tran et al. with **1** in the presence of sodium hydride (NaH), delivering the desired products in satisfactory yields.^{5a} Later, the same group extended the methodology to the synthesis of a series of bacterial type 2 topoisomerase inhibitors,^{5b} structures which contain 3-amino-1*H*-quinazoline-2,4-dione motifs. Chen et al. achieved the amination of the less acidic *N*-H bonds of pyrroles with **1** during their synthesis of pyrrolopyridazine MEK inhibitors.^{5c} The synthesis of the complex antitumor structure RA-VII also involves as a key step the amination of an *N*-H bond with **1**.^{5d}

(D) Amination of *O*-Nucleophiles

Castellino and Rapoport studied the amine exchange reaction of **1** with phenols.⁶ Their results indicated that the process is sensitive to the pK_a of the phenol. The reactions of phenols without strong electron-donating groups gave the desired products in moderate to good yields. However, the reaction of 3,5-dimethoxyphenol gave the corresponding product in only 13% NMR yield.

(E) Amination of Arylboronic Acids

Kürti and co-workers reported the first metal-free amination of aromatic boronic acids with **1** under mild reaction conditions, producing diverse primary anilines in moderate to good yields.⁷ One of the key steps involved in the mechanism is an *o*-nitro-facilitated 1,2-aryl migration.

(F) Aziridination of Olefins

Yan and co-workers reported that in the presence of the tertiary amine *N*-methylpyrrolidine (NMP), α,β -unsaturated ketones can be aziridinated with **1** to give *N*-unsubstituted aziridines.⁸ Recent studies by Kürti et al. reveal that electron-rich olefins can be smoothly converted into *N*-unsubstituted aziridines by **1** under the catalysis of Du Bois' catalyst [$Rh_2(esp)_2$], with broad substrate scope and functionality tolerance.⁹ The key intermediate of the former reaction is a hydrazinium salt, while that of the latter is a triplet nitrene.

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