SYNLETT

Spotlight 468

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

O-(2,4-Dinitrophenyl)hydroxylamine

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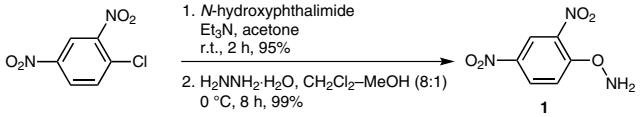
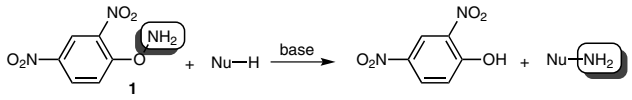
Introduction

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

As an electrophilic amination reagent, **1** is used to donate a free NH_2 group to a variety of C-, N-, and O-nucleophiles to give products of significant importance in both synthetic and medicinal chemistry. The byproduct is 2,4-dinitrophenol (Scheme 2). Amination with **1** features the advantages of mild reaction conditions, simple and safe operations, and wide substrate scope.

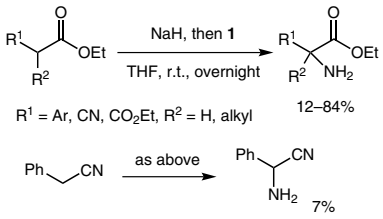


Scheme 2

Abstracts

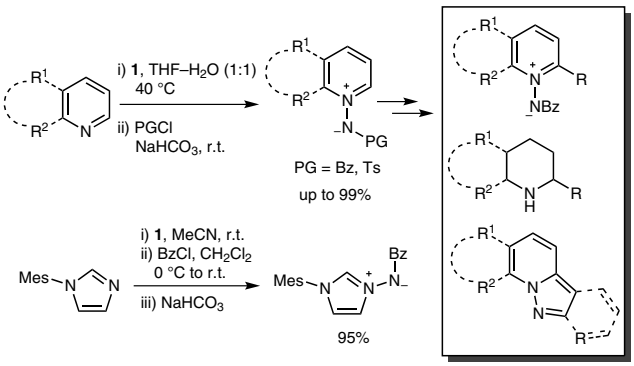
(A) *Amination of C-Nucleophiles*

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 phenylacetonitrile gives the desired product in only 7% yield. In addition, neither Reformatsky reagents nor sily 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 NH_2 group and deprotonation with a base leads to *N*-iminopyridium 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*-iminopyridium ylides are versatile building blocks for the preparation of pyridine derivatives.[3] The amination is also applicable to other heterocycles such as imidazoles.[4]



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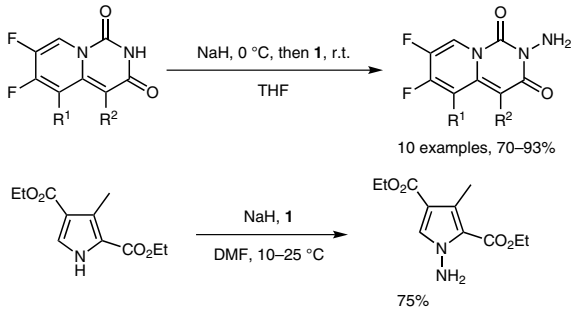
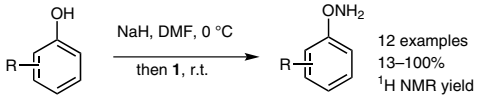
(C) *Amination of N-Nucleophiles with N–H Bonds*

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]



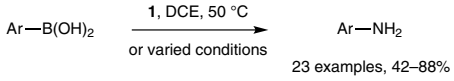
(D) *Amination of O-Nucleophiles*

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.



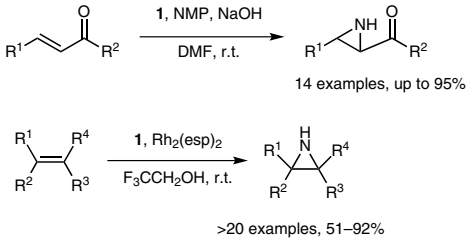
(E) *Amination of Arylboronic Acids*

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.



References

(1) Legault, C.; Charette, A. B. *J. Org. Chem.* **2003**, *68*, 7119.

(2) (a) Sheradsky, T.; Salemnick, G.; Nir, Z. *Tetrahedron* **1972**, *28*, 3833. (b) Radhakrishna, A. S.; Loudon, G. M.; Miller, M. J. *J. Org. Chem.* **1979**, *44*, 4836.

(3) (a) Chatzopoulou, E.; Davies, P. W. *Chem. Comm.* **2013**, *49*, 8617. (b) Xiao, Q.; Ling, L.; Ye, F.; Tan, R.; Tian, L.; Zhang, Y.; Li, Y.; Wang, J. *J. Org. Chem.* **2013**, *78*, 3879. (c) Zhao, J.; Wu, C.; Li, P.; Ai, W.; Chen, H.; Wang, C.; Larock, R. C.; Shi, F. *J. Org. Chem.* **2011**, *76*, 6837. (d) Mousseau, J. J.; Bull, J. A.; Ladd, C. L.; Fortier, A.; Roman, D. S.; Charette, A. B. *J. Org. Chem.* **2011**, *76*, 8243. (e) Mousseau, J. J.; Bull, J. A.; Charette, A. B. *Angew. Chem. Int. Ed.* **2010**, *49*, 1115. (f) Larivee, A.; Mousseau, J. J.; Charette, A. B. *J. Am. Chem. Soc.* **2008**, *130*, 52.

(4) (a) Guernon, H.; Legault, C. Y. *Organometallics* **2013**, *32*, 1988. (b) Katritzky, A. R.; Jishkaiani, D.; Sakhuja, R.; Hall, C. D.; Steel, P. J. *J. Org. Chem.* **2011**, *76*, 4082.

(5) (a) Tran, T. P.; Ellsworth, E. L.; Watson, B. M.; Sanchez, J. P.; Showalter, H. D. H.; Ruin, J. R.; Stier, M. A.; Yip, J.; Nguyen, D. Q.; Bird, P.; Singh, R. *J. Heterocyclic Chem.* **2005**, *42*, 669. (b) Tran, T. P.; Ellsworth, E. L.; Watson, B. M.; Sanchez, J. P.; Watson, B. M.; Showalter, H. D. H.; Domagala, J. M.; Shapiro, M. A.; Joannides, E. T.; Gracheck, S. J.; Nguyen, D. Q.; Bird, P.; Yip, J.; Sharadendu, A.; Ha, C.; Ramezani, S.; Wu, X.; Singh, R. *Bioorg. Med. Chem.* **2007**, *17*, 1312. (c) Chen, Z.; Kim, S.-H.; Barbosa, S. A.; Huynh, R.; Tortolani, D. R.; Leavitt, K. J.; Wei, D. D.; Manne, V.; Ricca, C. S.; Gullo-Brown, J.; Poss, M. A.; Vaccaro, W.; Salvati, M. E. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 628. (d) Hitotsuyanagi, Y.; Lee, J.-E.; Kato, S.; Kim, I.-H.; Kohashi, H.; Fukaya, H.; Takeya, K. *Bioorg. Med. Chem. Lett.* **2011**, *19*, 2458.

(6) Castellino, A. J.; Rapoport, H. *J. Org. Chem.* **1984**, *49*, 1348.

(7) Zhu, C.; Li, G.; Ess, D. H.; Falck, J. R.; Kürti, L. *J. Am. Chem. Soc.* **2012**, *134*, 18253.

(8) Wang, J.-J.; Lao, J.-H.; Li, X.-M.; Lu, R.-J.; Miao, H.; Yan, M. *Synth. Comm.* **2012**, *42*, 1577.

(9) Jat, J. L.; Paudyal, M. P.; Gao, H.; Xu, Q.-L.; Yousufuddin, M.; Devarajan, D.; Ess, D. H.; Kürti, L.; Falck, J. R. *Science* **2014**, *343*, 61.