

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

Compiled by Zhanhui Yang

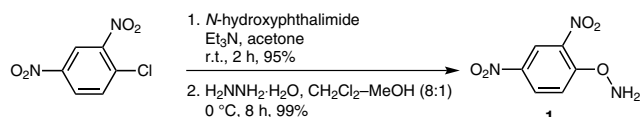
Zhanhui Yang was born in 1987 and raised in Xuchang County, He'nan Province, China. In 2010, he received his B.Sc. degree from Beijing University of Chemical Technology. He is currently pursuing his doctoral studies under the supervision of Professor Jiaxi Xu at the same university. His research focuses on the simple and green synthesis of important sulfonic acid derivatives, the formation mechanism of β -sultams via the reactions of sulfonyl chlorides and imines, and the carbene (carbenoid) reactions of diazosulfonyl compounds.

State Key Laboratory of Chemical Resource Engineering, Department of Organic Chemistry, Faculty of Science, Beijing University of Chemical Technology, Beijing 100029, P. R. of China
E-mail: zhyang_2008a@163.com



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).

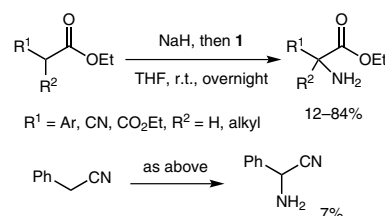


Scheme 1

Abstracts

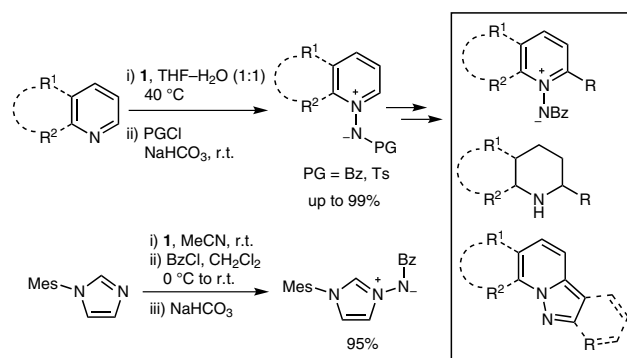
(A) Amination of C-Nucleophiles

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 phenylacetonitrile 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.



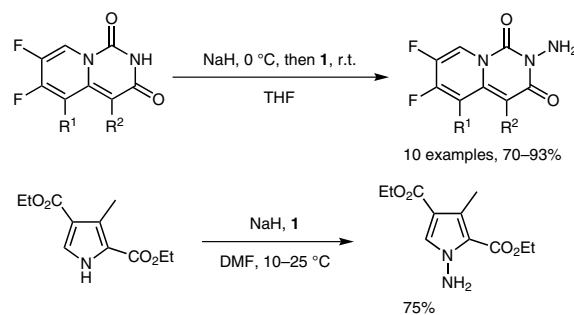
(B) Amination of N-Nucleophiles with C=N Bonds

Amination of pyridines with **1** followed by protection of the resultant free NH₂ group and deprotonation with a base leads to *N*-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



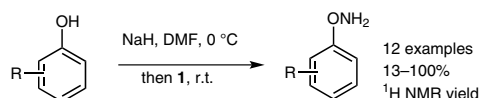
(C) Amination of N-Nucleophiles with N–H Bonds

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}



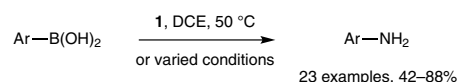
(D) Amination of O-Nucleophiles

Castellino and Rapoport studied the amine exchange reaction of **1** with phenols.⁶ Their results indicated that the process is sensitive to the p*K*_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.



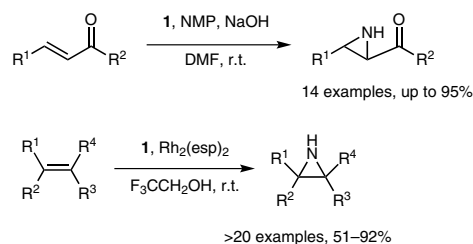
(E) Amination of Arylboronic Acids

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 [Rh₂(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

- Legault, C.; Charette, A. B. *J. Org. Chem.* **2003**, *68*, 7119.
- (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.
- (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.
- (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.
- (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.
- Castellino, A. J.; Rapoport, H. *J. Org. Chem.* **1984**, *49*, 1348.
- Zhu, C.; Li, G.; Ess, D. H.; Falck, J. R.; Kürti, L. *J. Am. Chem. Soc.* **2012**, *134*, 18253.
- Wang, J.-J.; Lao, J.-H.; Li, X.-M.; Lu, R.-J.; Miao, H.; Yan, M. *Synth. Comm.* **2012**, *42*, 1577.
- 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.