SYNLETT
Spotlight 245

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

O-(Diphenylphosphinyl)hydroxylamine

Compiled by Ewen Bodio

Ewen Bodio was born in Brest, France in 1983. He received his M.Sc. degrees in Organic Chemistry from Toulouse Engineering School of Chemistry, France and in Biomolecular Chemistry from Montpellier University, France. Presently he pursues his Ph.D. studies under the supervision of Dr. David Deniaud and Dr. Karine Julienne at Nantes University, France. His research is focused on the design of new N_2S_2 chelating agents via the synthesis of hydrazines.

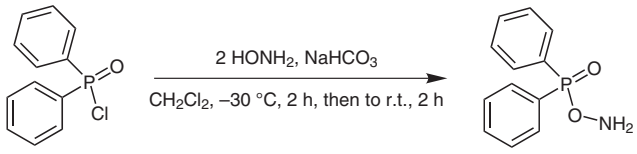
CEISAM, UMR CNRS 6230, Chimie et Interdisciplinarité Synthèse, Analyse, Modélisation, UFR des Sciences et des Techniques, Université de Nantes, 2 rue de la Houssinière, BP 92208, 44322 Nantes Cedex 3, France
E-mail: Ewen.Bodio@univ-nantes.fr

Introduction

Electrophilic amination gains more and more importance with the increasing interest in primary amines. Indeed they are valuable as synthetic intermediates or entries into nitrogen-containing heterocyclic systems. Moreover, electrophilic amination allows a direct metal-free access to hydrazines.

To perform electrophilic amination, activated hydroxylamines are the most common kind of reagents used.[1] Lots of such hydroxylamines exist, but *O*-(diphenylphosphinyl)hydroxylamine (**1**) presents many advantages. In fact, it has the most extensive track record for amination.[2] Compared to other activated hydroxylamines, the diphenylphosphinyl reagent has the best reputation for stability: The solid compound may be stored for long periods at 0 °C and does not show any degradation when employed below 140 °C.[3] It presents only a low tendency toward side reactions and supports strong bases like lithium diisopropylamide or butyllithium.[1]

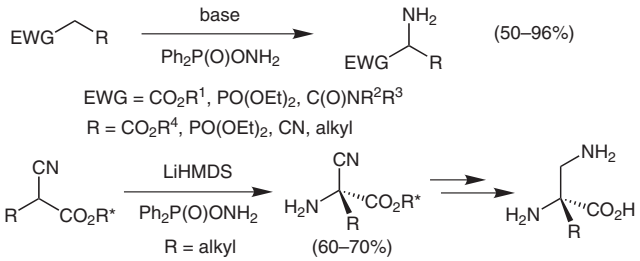
Compound **1** is not commercially available but it can be readily and rapidly prepared in a one-step reaction from diphenylphosphonic chloride and hydroxylamine.[4]



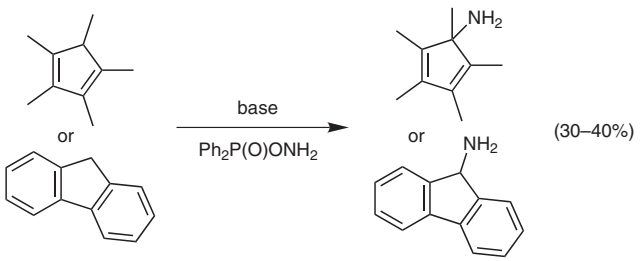
Scheme 1

Abstracts

(A) The direct amination of stabilized enolates or enolate-like compounds can be achieved in good to excellent yields using **1**.[5] The more stabilized the carbanion is, the higher is the achieved yield. Depending on the steric hindrance of substrates, chirality may be introduced.[6] An obvious application is the synthesis of amino acids.[7]

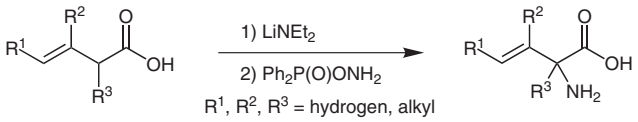


(B) The stabilization of carbanions by conjugate systems as aryls or olefins allows their amination by **1**. The cyclopentadiene derivatives obtained are often used in stereoselective Diels–Alder reactions.[8]

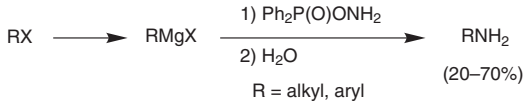


SYNLETT 2008, No. 11, pp 1744–1745
Advanced online publication: 11.06.2008
DOI: 10.1055/s-2008-1077826; Art ID: V25007ST

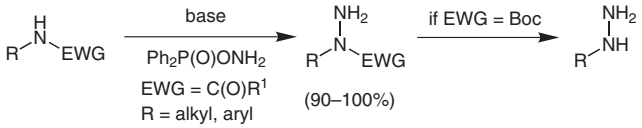
(C) The electrophilic amination of lithium diene- and trienediolate of unsaturated carboxylic acids leads to useful unsaturated amino acids. The amination occurs selectively at the α-carbon. The moderate yields are induced by the difficult isolation of this kind of amino acids due to their well-known instability.[9]



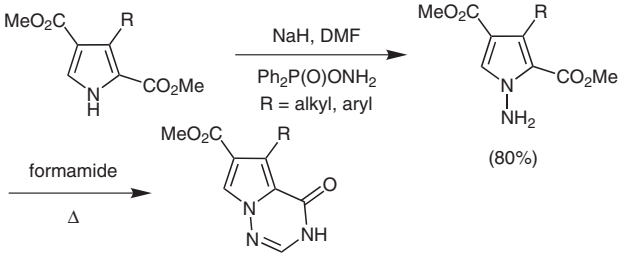
(D) Access to a wide range of primary amines is easily provided starting from the corresponding halogen derivatives by an Umpolung strategy. The amination yield increases in the order RMgBr < RMgCl.[1,4]



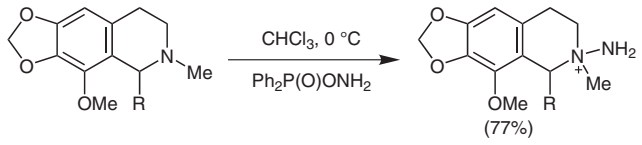
(E) A highly efficient metal-free strategy to synthesize hydrazines from secondary amines bearing an electron-withdrawing group can be carried out using **1**.[10] If the substrate is a primary amine protected by a Boc group, a monosubstituted hydrazine can be synthesized in only two steps.



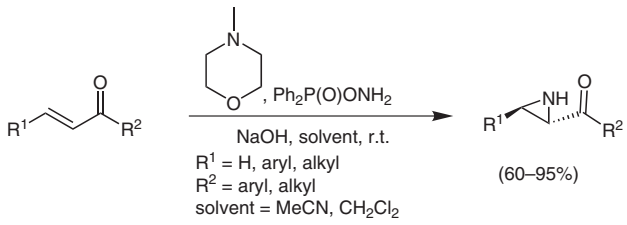
(F) Electrophilic N-amination of aromatic π-electron-rich nitrogen heterocycles occurs in high yields.[3,11] It often represents the key step of the synthesis of variously substituted bicycles. For example, they can be easily obtained by heating the hydrazine derivatives in a sealed tube in the presence of formamide.[12]



(G) Compound **1** may furnish ammonium salts from tertiary amines.[13] Ammonium salts can be very interesting reagents for further reactions (cf. H).



(H) A novel efficient method for the aziridination of a large range of enone systems uses a key reagent prepared in situ by N-amination of a tertiary amine.[14]



References

(1) Erdik, E.; Ay, M. *Chem. Rev.* **1989**, *89*, 1947.
(2) Boche, G.; Bernheim, M.; Schrott, W. *Tetrahedron Lett.* **1982**, *23*, 5399.
(3) Klötzer, W.; Baldinger, H.; Karpitschka, E. M.; Knoflach, J. *Synthesis* **1982**, 592.
(4) Colvin, E. W.; Kirby, G. W.; Wilson, C. *Tetrahedron Lett.* **1982**, *23*, 3835.
(5) (a) Pfefferkorn, J. A.; Nugent, R.; Gross, R. J.; Greene, M.; Mitchell, M. A.; Reding, M. T.; Funk, L. A.; Anderson, R.; Wells, P. A.; Shelly, J. A.; Anstadt, R.; Finzel, B. C.; Harris, M. S.; Kilkuskie, R. E.; Kopta, L. A.; Schwende, F. J. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2812. (b) Smulik, J. A.; Vedejs, E. *Org. Lett.* **2003**, *5*, 4187.
(6) Baldwin, J. E.; Adlington, R. M.; Jones, R. H.; Schofield, C. J.; Zaracostas, C.; Greengrass, C. W. *Tetrahedron* **1986**, *42*, 4879.
(7) (a) Badorrey, R.; Cativiela, C.; Díaz-de-Villegas, M. D.; Gálvez, J. A. *Tetrahedron: Asymmetry* **1995**, *6*, 2787. (b) Cativiela, C.; Díaz-de-Villegas, M. D.; Gálvez, J. A. *Tetrahedron: Asymmetry* **1994**, *5*, 1465.
(8) Macaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 1136.
(9) Aurell, M. J.; Gil, S.; Martinez, P. V.; Parra, M.; Tortajada, A.; Mestres, R. *Synth. Commun.* **1991**, *21*, 1833.
(10) (a) Elliot, E. L.; Bushell, S. M.; Cavero, M.; Tolan, B.; Kelly, T. R. *Org. Lett.* **2005**, *7*, 2449. (b) Cook, G. R.; Kargbo, R.; Maity, B. *Org. Lett.* **2005**, *7*, 2767.
(11) Belley, M.; Schweigetz, J.; Dubé, P.; Dolman, S. *Synlett* **2001**, 222.
(12) (a) Heim-Riether, A.; Healy, J. *J. Org. Chem.* **2005**, *70*, 7331. (b) Borzilleri, R. M.; Cai, Z.; Ellis, C.; Fargnoli, J.; Fura, A.; Gerhart, T.; Goyal, B.; Hunt, J. T.; Mortillo, S.; Qian, L.; Tokarski, J.; Vyas, V.; Wautlet, B.; Zheng, X.; Bhide, R. S. *Bioorg. Med. Chem.* **2005**, *15*, 1429.
(13) Schmidhammer, H.; Obendorf, D.; Pirkner, G.-F.; Sams, T. *J. Org. Chem.* **1991**, *56*, 3457.
(14) Armstrong, A.; Baxter, C. A.; Lamont, S. G.; Pape, A. R.; Wincewicz, R. *Org. Lett.* **2007**, *9*, 351.