

# SYNLETT Spotlight 370

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

## Zinc Ammonium Chloride

Compiled by Bishwajit Saikia

Bishwajit Saikia was born in Jorhat, Assam (India) in 1981. He obtained his B.Sc. (2003) and M.Sc. (2005) degree with specialization in Organic Chemistry from the Dibrugarh University, Assam (India). At present, he is working towards his Ph.D. degree at the Natural Products Chemistry Division, North-East Institute of Science & Technology (CSIR), Jorhat, Assam (India) under the guidance of Dr. Nabin C. Barua. His area of research interest is partial and total synthesis of natural products of biological significance and the development of new synthetic methodologies for target-oriented synthesis.

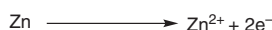
Natural Products Chemistry Division, North-East Institute of Science & Technology, Jorhat 785006, Assam, India  
E-mail: bishwajitsaikia@rediffmail.com

Dedicated to my honorable mentor Dr. Nabin C. Barua



### Introduction

Zinc belongs to the group IIB of the periodic table. The  $d^{10}s^2$  configuration of this family is not conducive to redox chemistry. The overwhelming tendency is to lose the  $s$ -electrons to become a stable +2 cation; indeed, this essentially describes the entire redox chemistry of zinc and other family members. It has a negative electrode potential  $E^0 (M^{2+}/M) V = -0.7619$ .

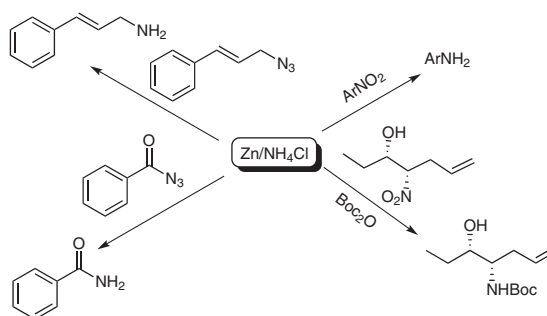


### Scheme 1

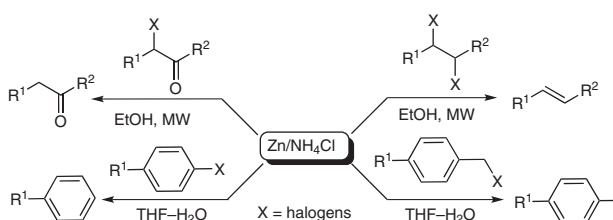
Non-oxidizing acids dissolve zinc under evolution of hydrogen. This property of zinc can be used to reduce various functional groups in organic chemistry.

### Abstracts

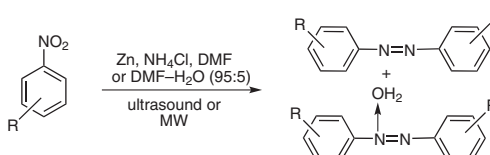
(A) The zinc ammonium chloride reagents are capable to reduce a wide range of functional groups as summarized in the Scheme. The reduction of azides to amines is of considerable importance for the introduction of primary amino groups in organic synthesis because of the easy preparation of azide by regio- and stereocontrolled procedure. Zinc and ammonium chloride reduces a broad spectrum of alkyl or acyl azides to amines or amides under mild conditions.<sup>1</sup> Zinc ammonium chloride has affected the conversion of nitrophenols into amino phenols and not to the respective hydroxylamine.<sup>1</sup> A variety of nitroalcohols can be reduced in a chemoselective manner with aqueous zinc ammonium chloride and  $(Boc)_2O$  to the corresponding  $\beta$ -hydroxycarbamates. Other functional groups, such as carbonyl, halide and also double bonds remain unaffected under this reaction conditions.<sup>1</sup>



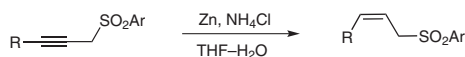
(B) The process of reductive elimination of halogens from aromatic rings as well as aliphatic chains is a quite difficult task. The low-cost and highly effective reagent, zinc ammonium chloride, has been used for the dehalogenation of arylhalides and alkylhalides in different solvent systems.<sup>2</sup>



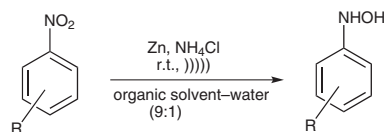
(C) The chemoselective reduction of nitroarenes to azo or azoxy compounds can be easily achieved by means of zinc powder and ammonium chloride.<sup>3</sup>



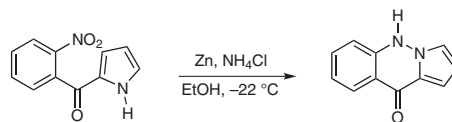
(D) Sheldrake et al.<sup>4</sup> have revealed that propargylic sulfones can be *cis*-hydrogenated using commercial zinc powder and ammonium chloride with good chemoselectivity. Other reducible groups, such as alkene and benzyloxy, are not affected.



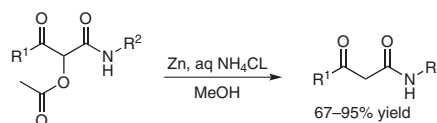
(E) Reduction by zinc in the presence of ammonium chloride in aqueous solution is one of the methods available for the preparation of hydroxylamines from the corresponding nitro compounds.<sup>5</sup>



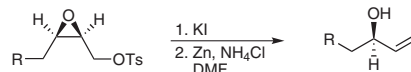
(F) The reduction of 2- and 3-acetylpyrroles can be carried out with zinc and ammonium chloride in ethanol at low temperature to produce the corresponding fused heteroaromatic system.<sup>6</sup>



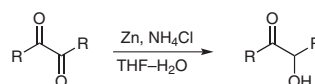
(G)  $\beta$ -Keto acyloxyamides are readily transformed into the corresponding  $\beta$ -keto amides by reductive deacetoxylation in extraordinarily mild conditions, using activated zinc metal in a mixture of saturated aqueous ammonium chloride and methanol.<sup>7</sup>



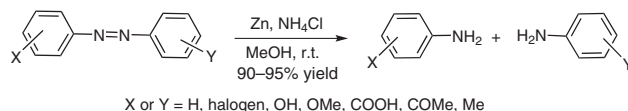
(H) Habashita et al.<sup>8</sup> described a convenient and efficient method for the synthesis of synthetically useful non-racemic allylic alcohols from 4-methylbenzenesulfonates of non-racemic 2,3-epoxy alcohols by reaction with potassium iodide followed by zinc powder and ammonium chloride in a one-pot manner.



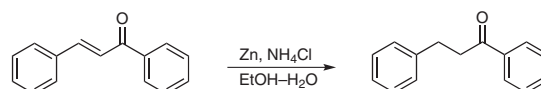
(I) Problems arise from overreduction of diketones to diols or monoketones. Hekmatshoar et al.<sup>9</sup> successfully employed zinc in a THF-saturated aqueous ammonium chloride reduction system for the conversion of 1, 2-diketones into  $\alpha$ -hydroxy ketones.



(J) Azo compounds can be productively reduced to the corresponding anilines with zinc dust in the presence of ammonium chloride.<sup>10</sup>



(K) The chemoselective reduction of conjugated carbonyl compounds is a useful functional group transformation in organic synthesis. Zinc ammonium chloride was applied for the selective 1,4-reduction of chalcones under mild conditions with high selectivity.<sup>11</sup>



## References

- (1) (a) Lin, W.; Zhang, X.; He, Z.; Jin, Y.; Gong, L.; Mi, A. *Synth. Commun.* **2002**, 32, 3279. (b) Khan, F. A.; Dash, J.; Sudheer, C.; Gupta, R. K. *Tetrahedron Lett.* **2003**, 44, 7783. (c) Saikia, P. P.; Baishya, G.; Goswami, A.; Barua, N. C. *Tetrahedron Lett.* **2008**, 49, 6508. (d) Gubler, D. A.; Williams, R. M. *Tetrahedron Lett.* **2009**, 50, 4265. (e) Sridharan, V.; Karpagavalli, M.; Muthusubramanian, S.; Sivasubramanian, S. *Ind. J. Chem.* **2004**, 43, 2243.
- (2) (a) Li, J.; Ye, D.; Liu, H.; Luo, X.; Jiang, H. *Synth. Commun.* **2008**, 38, 567. (b) Hekmatshoar, R.; Sajadi, S.; Heravi, M. M. *J. Chin. Chem. Soc.* **2008**, 55, 616.
- (3) Cravotto, G.; Boffa, L.; Bia, M.; Bonrath, W.; Curini, M.; Heropoulos, G. A. *Synlett* **2006**, 2605.
- (4) Sheldrake, H. M.; Wallace, T. W. *Tetrahedron Lett.* **2007**, 48, 4407.
- (5) Ung, S.; Falguieres, A.; Guy, A.; Ferroud, C. *Tetrahedron Lett.* **2005**, 46, 5913.
- (6) Kimbaris, A.; Varvounis, G. *Tetrahedron* **2000**, 56, 9675.
- (7) Neo, A. G.; Delgado, J.; Polo, C.; Marcaccini, S.; Marcos, C. F. *Tetrahedron Lett.* **2005**, 46, 23.
- (8) Habashita, H.; Kawasaki, T.; Akaji, M.; Tamamura, H.; Kimachi, T.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1997**, 38, 8307.
- (9) Hekmatshoar, R.; Heravi, M. M.; Beheshtiha, Y. S.; Faridbod, F. *Monatsh. Chem.* **2002**, 133, 195.
- (10) Sridhara, M. B.; Srinivasa, G. R.; Gowda, D. C. *Synth. Commun.* **2004**, 34, 1441.
- (11) Li, J.-P.; Zhang, Y.-X.; Ji, Y. *J. Chin. Chem. Soc.* **2008**, 55, 390.