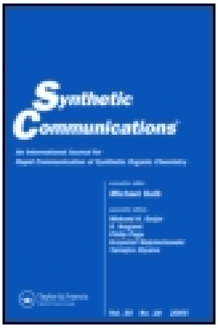

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Unusual Reactivity of Zinc Borohydride - Conversion of Amino Acids to Amino Alcohols

S. Narasimhan [a] , S. Madhavan [a] & K. Ganeshwar Prasad [a]

[a] Centre for Agrochemical Research, SPIC Science Foundation, 110, Mount Road, Guindy, Madras, 600 032, INDIA

Version of record first published: 21 Nov 2007.

To cite this article: S. Narasimhan , S. Madhavan & K. Ganeshwar Prasad (1996): Unusual Reactivity of Zinc Borohydride - Conversion of Amino Acids to Amino Alcohols, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 26:4, 703-706

To link to this article: http://dx.doi.org/10.1080/00397919608086744

SYNTHETIC COMMUNICATIONS, 26(4), 703-706 (1996)

Unusual Reactivity of Zinc Borohydride - Conversion of Amino Acids to Amino Alcohols

S. Narasimhan*, S. Madhavan and K. Ganeshwar Prasad

Centre for Agrochemical Research, SPIC Science Foundation.
110, Mount Road, Guindy Madras 600 032. INDIA.

Abstract: Zinc borohydride reduces amino acids with only stoichiometric amounts of hydride to the corresponding chiral alcohols in excellent yields in the absence of any Lewis acid.

Chiral amino alcohols are important intermediates in the synthesis of several insecticidal compounds[1], in asymmetric synthesis[2] and in other applications. The conversion of amino acids to amino alcohols has been reported using borane-dimethyl sulphide[3], lithium aluminum hydride[4] or sodium borohydride in the presence of reagents such as trimethylchlorosilane[5a], sulfuric acid[5b] or iodine[5c]. Though borane reagents reduce acids readily, two equivalents are needed due to the formation of amine-borane complexes. Reduction using $LiAlH_4$ utilizes large excess of the reagent, resulting in laborious work up procedures and high cost. On the other hand, reduction with sodium borohydride always requires excess reagent and addition of Lewis acids.

In the course of our study on tandem reduction - hydroboration using metal borohydrides we found that zinc borohydride exhibited hydroboration characteristics similar to boranes[6]. This prompted us to study its utility in the reduction of carboxylic acids[7]. The results indicate that zinc borohydride reduces carboxylic acids to the corresponding alcohols in excellent yields without the need for the addition of any Lewis acids. The simple procedure utilizing only stoichiometric quantities of hydride prompted us to employ this reagent for the reduction of amino acids which would overcome the difficulties encountered in the earlier procedures.

A solution of zinc borohydride in THF was prepared by the metathesis reaction of sodium borohydride and zinc chloride as reported earlier[8]. After the completion of the reaction, the solution was allowed to settle and the clear supernatant liquid (0.28M in borohydride) was used as such.

Initially, we reduced the amino acids with two equivalents of borohydride and quenched the reaction after 5 hours. The hydrolysis of the excess reagent was very fast, unlike in the case of borane reductions, which require drastic conditions indicating that the excess reagent may not form a strong complex similar to amine boranes which are well known to be quite unreactive. Therefore, we inferred that just one equivalent of borohydride would be sufficient for the conversion of amino acids to alcohols. Indeed, we found that under stoichiometric conditions phenyl alanine was reduced to phenylalanol in 87% yield.

In a typical procedure, phenyl alanine (5 mmol) was added to zinc borohydride (18 mL, 0.28M of borohydride in THF, 20 mmol of hydride). The reaction mixture was refluxed for 5h and then quenched with MeOH. The residue was dissolved in water (10 mL) and NaOH (2g) was added and was stirred at room temperature for 0.5 hours. The solution was then saturated with potassium carbonate and the layers were separated. The aqueous layer was extracted with THF and the combined organic extracts were dried over anhydrous potassium carbonate. The solvent was removed under vacuum to yield 0.7g (87%) of phenylalanol melting at 89 °C (90-91).

Table 1. Reduction of Amino Acids by Zinc Borohydride

Substrate	Time (h)	Product	Yield (%)	Rotation
Glycine	7	2-Aminoethanol	70	-
L-Phenylalanine	5	L-Phenylalanol	87	-21.7 (1.7 EtOH)
L-Leucine	4	L-Leucinol	90	+4.2 (0.9 EtOH)
L-Isoleucine	3	L-Isoleucinol	85	+6.7 (1.0 EtOH)
L-Valine	4	L-Valinol	85	+8.7 (1.1 EtOH)
L-Proline	3	L-Prolinol	85	+37.0 (1.0 C_6H_6)

Although, the formation of acyloxyborohydride is common to metal borohydrides, the reduction proceeds only in the case of zinc borohydride which is suggested to exist as a contact ion pair[9]. The reason could be attributed to the better coordinating ability of Zn coupled with its moderate acidic character in comparison to Li or Ca, which are hard acids. Though the mechanism of the reduction is unclear, it is viewed that an oxazaborolidine type intermediate may be formed. It should be noted that a second borane molecule would only weakly bind to the nitrogen atom and hence would be hydrolyzed faster.

In conclusion, zinc borohydride offers a simple and convenient method for the conversion of amino acids to the corresponding alcohols utilizing only stoichiometric quantities of hydride without the need for any Lewis acids .

Acknowledgments

The authors thank Prof. N. S. Narasimhan and Prof. T. R. Govindachari for their encouragement. K.G.P. and S.M. thank CSIR Govt. of India for financial assistance.

References

1. Wu, S.; Takeya; R., Eto, M. and. Tonizawa, C. *J. Pest. Sci.*, **1987**, *12*, 221.
2. Coppola, G. M. and Schuster, H. F., *Asymmetric Synthesis*; John Wiley & Sons. New York, **1987**.
3. Lane, C. F., U.S. Patent 3 935 280, 1976; *Chem Abstr.*, **1976**, *84*, 135101p; Smith, G. A; Gawley, R. E., *Org. Synth.*, **1985**, *63*, 136; Gage, J. R.; Evans, D. A. *Org. Synth.*, **1989**, *68*, 77; Meyers, A. I.; Dickmann, D. A.; Bailey, T. R. *J. Amer. Chem. Soc.*, **1985**, *107*, 7974; Brown; H.C. Choi, Y. M; Narasimhan, S. *J. Org. Chem.*, **1982**, *47*, 3153.
4. Enders, D.; Eichenauer, H., Chem Ber., **1979**, *112*, 2933; Dickman, D. A.; Meyers, A. I.; Smith, G. A; Gawley, R. E., *Org Synth. Collective vol VIII.*, **1990**, 530.
5. (a) Dharanipragada, R.; Alarcon, A.; Hruby, V. J., *Org Prep Proc Int.*, **1991**, *23*, 390. (b) Abiko, A.; Masumune, S., *Tett. Lett.*, **1992**, *33*, 5517. (c) McKennon, M. J.; Meyers, A. I.; Drauz, K.; Schwarm, M., *J. Org. Chem.*, **1993**, *58*, 3568.
6. Narasimhan. S; Madhavan. S., *Communicated, J. Org. Chem.*
7. Narasimhan. S.; Madhavan. S.; Ganeshwar Prasad. K. *J. Org Chem., in press.*
8. Narasimhan S.; Prem Palmer; Ganeshwar Prasad K., *Ind. J. Chem.*, **1991**, *30B*, 1150.
9. Ranu, B. C., *Synlett.*, **1993**, 885.

(Received in the UK 28 June 1995)