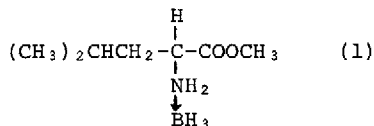


ASYMMETRIC REDUCTION OF KETONES WITH α -AMINO-ESTER BORANES
IN THE PRESENCE OF LEWIS ACIDS

Michael F. Grundon*, David G. McCleery and John W. Wilson
School of Physical Sciences,
The New University of Ulster,
Coleraine, Northern Ireland

In the continuation of our studies of the asymmetric reduction of ketones and related compounds with boron derivatives¹, we decided to investigate the use of amine-boranes. Previous work involving the reduction of ketones with boranes obtained from α -phenylethylamine² or ephedrine³ derivatives resulted in disappointingly low optical yields (1.5-5%). We now report the preparation and reactions of amine-boranes derived from α -amino-acid esters.

Mixing stoichiometric quantities of leucine-methyl ester and diborane in tetrahydrofuran yielded a stable solution, presumably containing the amine-borane(1)



Addition of one equivalent of boron trifluoride etherate, which is known to increase the rates of reduction by amine-boranes,⁴ resulted in complete reaction within 1 h., and led to the quantitative isolation of the α -amino alcohol. This may be the best general method for the preparation of α -amino alcohols from the acids, since other procedures are characterised by long reaction times and only moderate yields.⁵

Reaction of the amine-borane(1) with one equivalent of acetophenone in tetrahydrofuran at ambient temperature resulted in only 48% reduction of the ketone after 5 h. When the reaction mixture at 0°, was treated with boron trifluoride etherate (1 equiv.) immediately after the addition of ketone, reduction was complete in 0.5 h. and work up (treatment with aqueous base, solvent extraction, distillation) furnished 1-phenylethanol only (g.l.c.). Preferential reaction of the Lewis acid with the ketone apparently accounts for reduction of the ketone competing successfully with reduction of the ester group. The reaction was applied to a number of ketones and to a range of α -amino-acid esters, producing in each case the alcohol containing an excess of the enantiomer of S-configuration. The results, which are summarised in the table, indicate that this is a promising method for asymmetric synthesis of alcohols (optical yields 14.7-22.5%).

The Reduction of Ketones by Amino-ester Borane Complexes
in the Presence of $\text{Et}_2\text{O}\cdot\text{BF}_3$ (1.1.1 mole ratio) in THF at 0°

Amino-ester Borane	Ketone ⁶	Derived Alcohol ⁷	
		$[\alpha]_D$	% Optical Purity
L-Leucine methyl ester	acetophenone	-7.29±0.05	17.0±0.1
"	t-butyl methyl ketone	+1.82±0.04	22.5±0.5
"	n-pentyl methyl ketone	+1.53±0.05	14.7±0.5
L-β-Phenylalanine methyl ester	acetophenone	-7.71±0.12	18.0±0.3
L-Valine methyl ester	"	-8.55±0.06	19.9±0.1

The authors thank the Northern Ireland Department of Education for the award of a research studentship (D.G.McC).

References

1. D. R. Boyd, M. F. Grundon and W. R. Jackson, *Tetrahedron Letters*, 1967 (22), 2101; M. F. Grundon, W. A. Khan, D. R. Boyd and W. R. Jackson, *J. Chem. Soc. (C)*, 1971, 2557; J. F. Archer, D. R. Boyd, W. R. Jackson, M. F. Grundon and W. A. Khan, *J. Chem. Soc. (C)*, 1971, 2560.
2. R. F. Borch and S. R. Levitan, *J. Org. Chem.*, 1972, 37, 2347.
3. J. C. Fiaud and H. B. Kagan, *Bull. Soc. Chim. Fr.*, 1969, 2742.
4. W. M. Jones, *J. Amer. Chem. Soc.* 1960, 82, 2528.
5. H. Seki, K. Koga, H. Matsuo, S. Ohki, I. Matsuo and S. Yamada, *Chem. and Pharm. Bull. (Japan)*, 1965, 13, 995; A. K. Saund and N. K. Mathur, *Indian J. Chem.*, 1971, 9, 936; M-L. Anbury, M. Arickx, P. Crooy, R. De Neys and J. Eliaers, *J.C.S. Perkin I.*, 1974, 191.
6. 100% reduction in 0.5 h.
7. Measurements, carried out on the neat liquids at $24\pm 1^\circ$, are the mean of two independent reactions.