Pergamon

Tetrahedron Letters, Vol. 38, No. 35, pp. 6259-6262, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01402-0

Reductive diallylation of natural amino acids with triallylborane. The first synthesis of chiral 1,1-diallyl-2-amino alcohols and their cyclization into optically active pyrrolidines.

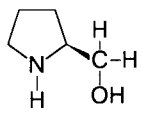
Yuri N. Bubnov,* Mikhail A. Misharin, and Anatoly V. Ignatenko

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
Leninsky Prospect 47, Moscow B-334, Russia

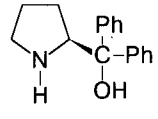
Dedicated to Professor Walter Siebert (Heidelberg) on the occasion of his 60-th birthday.

Abstract: The titled amino alcohols are obtained by treatment of chiral amino acids with triallylborane. Electrophylic iodocyclization of the alcohols leads to pyrrolidine derivatives. © 1997 Elsevier Science Ltd.

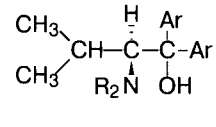
Optically active 2-amino alcohols are widely used in organic synthesis as chiral inductors,[1-3] building blocks,[4] chiral reagents for the resolution of racemic acids and lactones,[5] bases,[6] and for the preparation of optically active organoboranes.[7] (*S*)-Pyrrolidylmethanol (**A**), (*S*)-1,1-diphenyl-1-pyrrolidylmethanol (**B**) and a number of chiral β-amino alcohols derived from (*S*)-valine (**C**) are used as catalysts for asymmetric reduction and alkylation of carbonyl compounds.[1, 8]



A



B



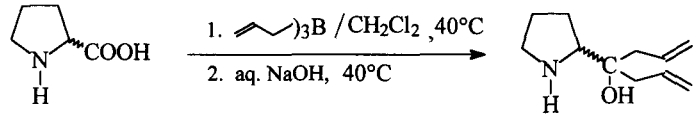
C

However, the syntheses of the majority of optically active 2-amino alcohols from α-amino acids usually involve several steps[1a,8,9]: a) the protection of amino and carboxyl groups; b) the reaction of the resulting compound with RLi (RMgX) or reduction with $LiAlH_4$; c) hydrolysis and removal of the protective groups. The total yield of the product, as a rule, does not exceed 50 % and step b) sometimes proceeds with partial racemisation. Recently, Abiko and Masamune reported an efficient procedure for the reduction of α-amino acids to the corresponding alcohols with in situ generated borane.[9c]

In this paper, a convenient method for the syntheses of hitherto unknown (*R*)- and (*S*)-1,1-diallyl-1-pyrrolidylmethanol and a number of optically active 1,1-diallyl-2-amino alcohols by the reaction of natural α-amino acids with triallylborane is described.

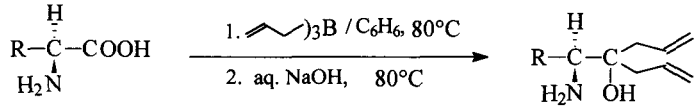
It has been previously shown that carboxylic acids and their esters undergo reductive diallylation upon the action of triallylborane to give the corresponding 1,1-diallylcarbinols.[10] Now we have found that (*R*)- and (*S*)-proline, (S)-leucine, (*S*)-valine, (*S*)-alanine and other α-amino acids react with triallylborane on heating in

benzene or CH_2Cl_2 to give (after deboronation) the corresponding 2-amino alcohols **1–6** in 80—85 % yields.[12]



1: (*S*)-1,1-diallyl-1-pyrrolidylmethanol

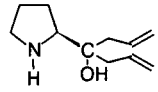
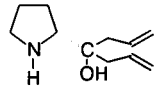
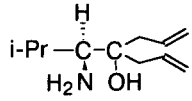
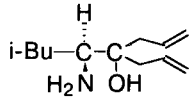
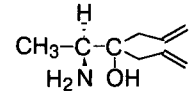
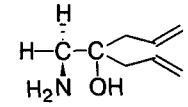
2: (*R*)-1,1-diallyl-1-pyrrolidylmethanol



3: R=$(CH_3)_2CH$ **5:** R=CH_3

4: R=$(CH_3)_2CHCH_2$ **6:** R=H

Table

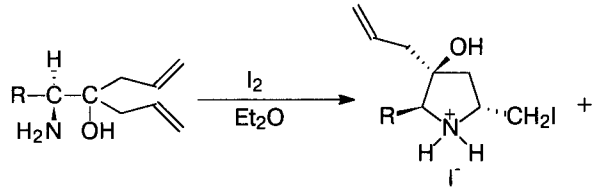
Aminoacid	Product	Yield (%)	B.p., °C (2 Torr)	$[\alpha]_D^{25}$ (CH_2Cl_2, c=1)	**1–6·HCl** m.p.(°C)
(*S*)-Proline	 **1**	80	92	–34.9°	162
(*R*)-Proline	 **2**	80	92	+34.9°	162
(*S*)-Valine	 **3**	85	90	+42.2°	148.5
(*S*)-Leucine	 **4**	85	102	+25.9°	133
(*S*)-Alanine	 **5**	80	70.5	+41.7°	135
Glycine	 **6**	85	102	—	—

The syntheses were carried out as a one-pot procedure, and products **1–6** were isolated and purified by distillation. The corresponding hydrochlorides were also obtained by treating **1–6** with ethereal hydrogen chloride (Table). The structure of amino alcohols **1–6** and their hydrochlorides was confirmed by ^{13}C and ^{1}H NMR spectra. Satisfactory elemental analyses were also obtained for **1–6·HCl**.

Reductive diallylation of α-amino acids with triallylborane proceeds with the retention of configuration of the asymmetric centre of the original amino acid. This was confirmed by comparison of ^{13}C NMR spectra of salts of **1** and **2** with (–)-mandelic acid.

Due to the presence of several functional groups (NH or NH_2,, OH, double bonds), compounds **1–6** can be considered as appropriate starting materials for the synthesis of chiral pyrrolidines, aziridines, piperidines, and a number of other compounds with two or three asymmetric centres.

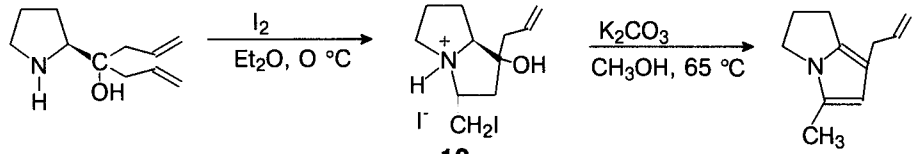
We have found that **3**,**4**, and **5** undergo cyclization under the action of iodine[11] in Et_2O to give substituted pyrrolidines **7**,**8**, and **9**, respectively.



3: R=$(CH_3)_2CH$	**7a**	95%	**7b**	5%	d.e.>90%
4: R=$(CH_3)_2CHCH_2$	**8a**	75%	**8b**	25%	d.e.>50%
5: R=CH_3	**9a**	75%	**9b**	25%	d.e.>50%

The pyrrolidinium salts **7**,**8**, and **9** thus obtained were found to be a mixture of two diastereomers in ratios 95:5, 75:25 and 75:25, respectively (^{13}C NMR). The fact that only two of the four possible isomers are formed implies the complete (>99 %) asymmetric induction at one of the two newly formed chiral centres (presumably on C-3). On the other chiral centre (C-5), the induction is 95 % for **7** and 75 % for **8** and **9**. The predominant diastereomers **7a** and **8a** were isolated by crystallization (CH_3CN:Et_2O = 9:1) and their structures and configurations of asymmetric carbons (2*S*, 3*S*, 5*R*) were established by X-ray analysis.

Under the same conditions, **1** yields a bicyclic product **10**. Unfortunately, in this case the asymmetric induction was low and the reaction gave a mixture of four diastereomers in the ratio of 40:30:25:5 (^{13}C NMR). Treatment of **10** with K_2CO_3 in MeOH gave the achiral aromatic product **11** in 50 % yield.



1 **10** **11**, 50%

Acknowledgment. This work was supported by the Russian Foundation for Basic Research (Grant 96-03-32555)

REFERENCES AND NOTES

1. (a) Corey, E. J.; Saizo Sh.; Bakshi, R. K. *J. Org. Chem.* **1988**, 2861; (b) Corey, E. G.; Bakshi, R.K.; Shibata, S. *J. Am. Chem. Soc.* **1987,** *109*, 5551; (c) Corey, E. J.; Azimioara, M.; Sarshar, S. *Tetrahedron Lett.* **1992**, *33*, 3429; (d) Delair, P.; Einhorn, J.; Luche, J. L. *Tetrahedron* **1995**, *51*, 165.
2. Mathre, D. J.; Thompson, A. S.; Douglas, A. W.; Hoogsteen, K.; Caroll, J. D.; Corey, E. J.; Grabowski, E. J. *J. Org. Chem.* **1993**, *58*, 2880.
3. O. Riant, H. B. Kagan, L. Ricard, *Tetrahedron*, 1994, **50**, 4543; A. H. M. deVries, J. F. G. Jansen, B. L. Feringa, *Tetrahedron*, 1994, **50**, 4479.
4. Evans, D. A.; Takaes, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233.
5. (a) Faustini, F.; DeMunari, S.; Panzeri, A.; Villa, V.; Gandolfi, C. A. *Tetrahedron Lett.* **1981**, *22*, 4533; (b) Saigo, K.; Ogawa, S.; Kikuchi, S.; Kasahara, A.; Mohira, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1568.
6. (a) Larson, E. R.; Raphael, R. A. *J. Chem. Soc., Perkin Trans I* **1982**, 521; (b) Grieko, R. A.; Zelle, R. E.; Liss, R.; Finn, I. *J. Am. Chem. Soc.* **1983**, *105*, 1403.
7. Masamune, S.; Kim, B.; Peterson, J. S.; Sato, T.; Veenstra, S. J. *J. Am. Chem. Soc.* **1985**, *107*, 4549.
8. Mathre, D. J.; Jones, T. K.; Xavier, L. C.; Blacklock, T. J.; Reamer, R. A.; Mohan, J. J.; Jones, E. T. T.; Hoogesteen, K.; Baum, M. W.; Grabowski, E. J. J. *J. Org. Chem.* **1991**, *56*, 751.
9. (a) Feetz, M. T.; Drewes, M. W.; Shmitz, *A. Angew. Chem.* **1987**, 99, 1186; (b) Kano, S.; Yokomatsu, T.; Iwasawa, H.; Shibuya, S. H. *Chem. Lett.* **1987**, 1531; (c) Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1992**, *33*, 5517.
10. (a) Mikhailov, B. M.; Bubnov, Yu. N.; Tsyban, A. V. *Izvestia Acad. Nauk. SSSR, Ser. Chim.* **1978**, 1892; (b) Mikhailov, B. M.; Bubnov, Yu. N.; Tsyban, A. V.; Grigoryan, M. Sh. *J. Organometal. Chem.* **1978**, *154*, 131.
11. (a) Williams, D. R.; Osterhout, M. H.; McGill, J. M. *Tetrahedron Lett.* **1989**, *30*, 1327; (b) Williams, D. R.; Osterhout, M. H.; McGill, J. M. *Tetrahedron Lett.* **1989**, *30*, 1331; (c) Biloski, A. J.; Wood, R. D.; Ganem, B. *J. Am. Chem. Soc.* **1982**, *104*, 3233.
12. Procedure for the synthesis of **3**. Triallylborane (7.8 g, 58.9 mmol) and (*S*)-Valine (3 g, 25.6 mmol) were stirred in dry benzene (15 ml) under reflux for 2 h in Ar atmosphere, than methanol (2 ml) was added dropwise at 0 °C, and the solution was stirred for 10 min. 5.6 N NaOH (20 ml) and mannitol (14.2 g) were added and the mixture was stirred under reflux for 2 h. The solution was extracted with benzene (4 × 15 ml), the organic layers were combined, dried (Na_2SO_4) and evaporated. Distillation of the residue (yellow oil) gave **3** (3.9 g, 85 %, 90 °C/2 Torr) as a colorless oil, $[a]_D^{25}$ +42.2° (c=1, CH_2Cl_2).
^1H NMR:(200 MHz, $CDCl_3$): d 0.90, 0.98 (dd, 6H, CH_3), 1.71 (m, 1H, $CHMe_2$), 1.90—2.58 (m, 5H), 5.04, 5.11 (m, 4H, CH_2=), 5.90 (m, 2H, CH=). ^{13}C NMR (50 MHz, $CDCl_3$): d 20.88, 24.26, 25.08, 40.27, 42.30, 60.01, 73.34, 117.40, 117.51, 134.40, 134.64.

(*Received in UK* 25 *April* 1997; *revised* 4 *July* 1997; *accepted* 11 *July* 1997)