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

Stereospecfic Synthesis of Trans-1-benzyl-2-ethoxycarbonyl-3-phenyl Aziridine

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Published online: 23 Sep 2006.

To cite this article: S. Wattanasin & F. G. Kathawala (1992) Stereospecfic Synthesis of Trans-1-benzyl-2-ethoxycarbonyl-3-phenyl Aziridine, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 22:10, 1487-1490, DOI: 10.1080/00397919208021617

To link to this article: http://dx.doi.org/10.1080/00397919208021617

SYNTHETIC COMMUNICATIONS, 22(10), 1487-1490 (1992)

STEREOSPECIFIC SYNTHESIS OF TRANS-1-BENZYL-2-ETHOXYCARBONYL-3-PHENYL AZIRIDINE

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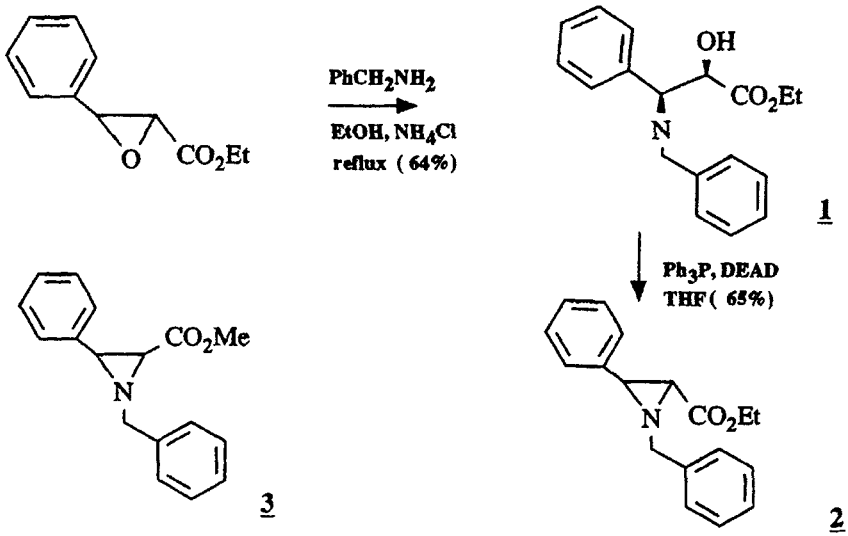
Abstract: Treatment of trans- ethyl-3-phenyl glycidate with benzylamine gave α-hydroxy β-amino ester 1, which was converted stereospecifically into trans-1-benzyl-2-ethoxycarbonyl-3-phenyl aziridine (2) via Mitsunobu reaction.

Aziridine-2-carboxylates are useful intermediates in organic synthesis.[1] Several pathways[1-5] exist for the synthesis of aziridine carboxylates but most of these methods are not stereospecific. A sterically controlled synthesis of cis-1-benzyl-2-methoxycarbonyl-3-phenyl aziridine (3) is available from the reaction between methyl 2,3-dibromo-3-phenylpropionate and benzylamine.[6] The method, however, is not applicable to the stereospecific synthesis of the corresponding trans-isomer.[7]

In this communication, we report a simple and stereospecific pathway for the synthesis of trans-1-benzyl-2-ethoxycarbonyl-3-phenyl aziridine (2).



Reaction[8] of trans-ethyl 3-phenyl glycidate[9] with benzylamine in ethanol and aqueous NH_4Cl at 80°C for 5h gave the hydroxy ester 1 as the only regioisomer. None of the α-opened product was detected.[10,11]

Treatment[12] of the hydroxy amino ester 1 with triphenyl phosphine and diethyl azodicarboxylate (Mitsunobu reaction) in THF furnished only the trans-aziridine carboxylate 2.[13] Its trans stereochemistry was readily determined by NMR analysis and a direct comparison with the corresponding cis-isomer.[6,14]

In conclusion, the present route provides a simple stereospecific synthesis of N-substituted trans- aziridine carboxylate 2 from the readily available trans-epoxide in two steps.[15]

References

1. For a review on the chemistry of 2-aziridine-carboxylic acids, see: Okawa, K.; Nakajima, K.; Tanaka, T., J. Synth. Org. Chem., 1984, 390.

2. Nakamura, I.; Harada, K., Chem. Lett., 1979, 313.

3. Nakagawa, Y.; Tsuno, T.; Nakajima, K.; Iwai, M.; Kawai, H.; Okawa, O., Bull. Chem. Soc. Jap., 1972, 45, 1162.

4. McDaniel, R. S.; Oehlschlager, A. C., Tetrahedron, 1969, 25, 1381.

5. Alkinson, R. S.; Tughan, G., J. Chem. Soc. Perkin Trans I, 1987, 2787.

6. Nakamura, I.; Harada, K., Heterocycles, 1978, 9, 473.

7. In general, the formation of the aziridine carboxylate from α,β-dibromo compounds is not stereospecific; see for example, Ploux, O.; Caruso, M.; Chassaig, G.; Marquet, A., J. Org. Chem., 1988, 53, 3154.

8. A mixture of trans ethyl glycidate (5 g, 0.026 mol), benzylamine(7ml), saturated NH_4Cl (4 ml) in ethanol (30 ml) was heated at 80°C for 5 h. After cooling, the reaction mixture was diluted with Et_20 and sat. $NaHCO_3$ was added. The solution was filtered through a pad of Celite (EtOAc rinse), dried, and concentrated. The crude product was purified by column chromatography (20% EtOAc - petrol, SiO_2) to give 1 as a colorless oil (5.0 g, 64%) which solidified on standing, mp 52-54°C. IR (neat) 1731 cm-1; ^1H NMR ($CDCl_3$) 1.1 (t, 3H), 2.2 (broad S, 1H), 3.2 (d, 1H), 3.7 (q, 2H), 4.1 (m, 2H), 4.5 (t, 1H), 7.3 (m, 10H). Anal. Calcd. for $C_{18}H_{21}O_3N$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.27; H, 7.23; N, 4.67.

9. Koua, K. O.; Borredon, M. E.; Delmas, M.; Gaset, A., Synthetic Communications, 1987, 17, 1593.

10.For a leading example of nucleophilic opening of 2,3-epoxy acids, see: Chong, J. M.; Sharpless, K. B., J. Org. Chem., 1985, 50, 1560.

11. a. The regiochemistry of the product was confirmed by a comparison with its corresponding regioisomer prepared from phenylserine and benzaldehyde via a reductive amination reaction with $NaCNBH_3$in methanol.
b. About 10% yield of the corresponding benzylamide of 1 was also isolated.

12. To a solution of 1 (0.47 mg,0.00158 mmol) and Ph_3P (0.62 g, 0.00237 mol) in THF (3 ml) at 0°C was added a solution of diethyl azodicarboxylate (0.37 ml, 0.00237 mol) in THF (2 ml) dropwise. The solution was stirred at 0°C for 1 h and then stirred at r.t. for 10 h. Concentration and purification of the crude product by column chromatography (20% EtOAc-petrol, $Si0_2$) gave the trans aziridine 2 (0.29 g, 65%) as a colorless oil. IR (film) 1727 cm^{-1}; ^1H NMR ($CDCl_3$) 1.1 (t, 3H), 2.8 (broad d, J= 2Hz, 1H), 3.1 (broad d, J= 2Hz, 1H), 4.1 (m, 4H), 7.1 (m, 10H); HRMS: ($C_{18}H_{19}NO_2$) calcd: 281.1416. Found: 281.1426.

13. For a previous application of Mitsunobu reaction to the synthesis of simple aziridines, see: Pfister, J. R., Synthesis, 1984, 969.

14.a. Batterham, T. J. "NMR spectra of Simple Heterocycles," pp 137-140, John Wiley & Sons, New York (1973), trans aziridine ring protons: J = 2.0-2.7 Hz, cis aziridine ring protons: J = 5.0-6.0 Hz.
b. The cis-aziridine 3 was prepared according to the reported procedure[6].

15.For a recent synthesis of N-unsubstituted aziridines from epoxides, see: Legters, J.; Thijs, L.; Zwanenburg, B., Tett. Lett. 1989, 36, 4881.

(Received in USA 13 January, 1992)