

This article was downloaded by: [Michigan State University]

On: 30 January 2015, At: 05:48

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954

Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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/lcyc20>

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

S. Wattanasin^a & F. G. Kathawala^a

^a Sandoz Research Institute East Hanover, NJ, 07936

Published online: 23 Sep 2006.

To cite this article: S. Wattanasin & F. G. Kathawala (1992) Stereospecific 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](https://doi.org/10.1080/00397919208021617)

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

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages,

and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

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

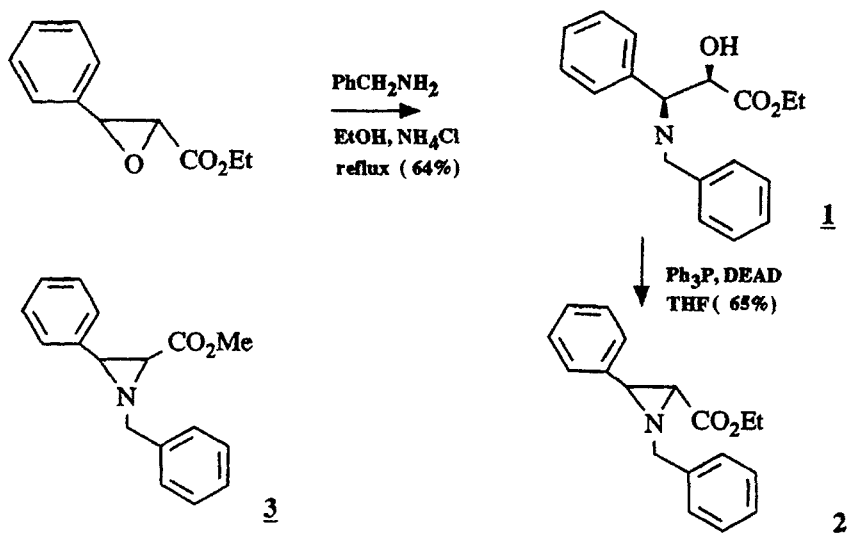
S. Wattanasin and F. G. Kathawala

Sandoz Research Institute
East Hanover, NJ 07936

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 pathways¹⁻⁵ 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).



Reaction⁸ of trans-ethyl 3-phenyl glycidate⁹ 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}

Treatment¹² 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 (7 ml), 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_2O 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 $52\text{--}54^\circ\text{C}$. 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 $\text{C}_{18}\text{H}_{21}\text{O}_3\text{N}$: 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, SiO_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, $J = 2\text{ Hz}$, 1H), 3.1 (broad d, $J = 2\text{ Hz}$, 1H), 4.1 (m, 4H), 7.1 (m, 10H); HRMS: ($\text{C}_{18}\text{H}_{19}\text{NO}_2$) 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 procedure⁶.

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)