

Asymmetric Synthesis of a New Monocyclic β -Lactam as a potential biological active compound

A. A. Jarrahpour*, A. R. Jahaniani

Department of Chemistry, College of Sciences, Shiraz University,
Shiraz 71454, Iran

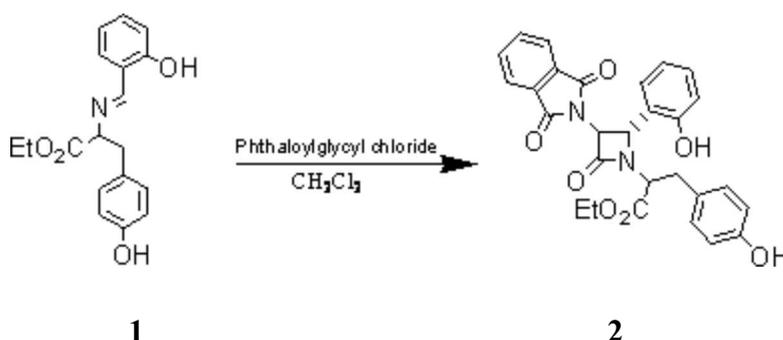
Tel. 0098 711 228 4822, Fax: 0098 711 228 0926, e-mail: aliasghar6683@yahoo.com ,
jarrah@chem.susc.ac.ir

Received: 2 June 2005 / Accepted: 22 September 2005 / Published: 1 October 2005

Keywords: Schiff base, asymmetric Staudinger reaction, [2+2] cycloaddition, monocyclic β -lactam

The asymmetric synthesis of monocyclic β -lactams belong to five categories: a) asymmetric induction from the imine component; b) asymmetric induction from the ketene component; c) double stereodifferentiating cycloadditions; d) carbacephem intermediates and e) 2-oxaisocephems and 2-isocephems. The asymmetric induction in the reaction of achiral ketenes with chiral imines has been effected from imines derived from chiral aldehydes and achiral amines and also from imines derived from chiral amines and achiral aldehydes [1-6]. Hashimoto and his coworkers have used chiral imines derived from erythro 2-methoxy-1,2-diphenylethylamine and aromatic aldehydes to prepare β -lactams in good yields with high diastereoselectivity [7]. Recently high levels of asymmetric induction has also been reported for monocyclic β -lactam formation [8-9]. Thus, we decided to synthesize a diastereoselective monocyclic β -lactam using the asymmetric induction by the chiral imine component and achiral ketene.

Treatment of S- (-)-tyrosine ethyl ester hydrochloride with 2-hydroxybenzaldehyde (salicylaldehyde) in the presence of triethylamine in dry benzene afforded Schiff base **1** as a yellow crystal. This chiral Schiff base was then transformed into the monocyclic β -lactam **2** by treatment with achiral ketene which was prepared *in situ* from phthaloylglycyl chloride and triethylamine in dry methylene chloride.



To the cold solution of mixture of Schiff base **1** (3.13 g, 10.00 mmol) and phthaloylglycyl chloride (2.37 g, 10.00 mmol) in dry methylene chloride (30 ml/g of phthaloyl), was added slowly triethylamine (1.31 g, 13.00 mmol) in methylene chloride (10 ml/g of the base). The reaction mixture was stirred at room temperature for 24 hours. The formation of new product was confirmed by the presence of β -lactam carbonyl group at 1780 cm^{-1} in its IR spectrum. Then it was washed with water ($3 \times 30\text{ ml}$). The organic layer was separated and dried (Na_2SO_4), filtered and the solvent was evaporated under reduced pressure. The crude β -lactam **2** was recrystallized from ether-hexane (3.13 g, 61%).

This [2+2] cycloaddition (Staudinger reaction) afforded the cis stereoisomer. The coupling constant for H_3 and H_4 was 6.19 Hz which is consistent with this kind of geometry. The other stereoisomer was not detected in TLC and NMR. Its biological activities such as antibacterial, antifungal, antiproliferative are

under study.

Melting point: 158-160°C.

IR (KBr, cm^{-1}): 1725; 1775 (Phthalimido CO); 1740 (CO_2Et); 1784 (β -lactam CO); 3180-3300 (OH).

$^1\text{H-NMR}$ (250MHz, CDCl_3): δ = 1.09-1.14 (3H, t, CH_3); 3.11-3.20 (1H, t, CHCO_2Et); 4.10-4.32 (4H, m, PhCH_2 , OCH_2); 4.40-4.54 (1H, d, $J=6.19$ Hz, H_4); 4.61-4.88 (1H, d, $J=6.19$, H_3); 6.99-7.92 (12H, m, ArH).

MS (m/z , %): 500 (M^+ , 3.6%); 499 ($\text{M}^+ -1$, 3.9%); 174 ($\text{PhthCH}_2\text{CH}_2$, 100.00%).

Acknowledgment

The authors thank the Research Council of Shiraz University for financial support (Grant No. 83-GR-SC-31 and 84-GR-SC-23).

References

1. a) Jarrahpour A. A.; Shekarriz M.; Taslimi.A. *Molecules* **2004**, *9*, 29. b) Jarrahpour A. A.; Shekarriz M.; Taslimi.A. *Molecules* **2004**, *9*, 939
2. Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. *Eur. J. Org. Chem.* **1999**, 3223.
3. Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. *Amino Acids* **1999**, *16*, 321.
4. Ojima, I.; Chen, H. J. C.; Qiu, X. *Tetrahedron*, **1988**, *44* (17), 5307.
5. Van der Steen, F. H.; Van Koten, G. *Tetrahedron* **1991**, *47*, 7503.
6. Georg, G. I.; Ravikumar, V. T. in: *The Organic Chemistry of β -Lactams*, (Ed.: G. I.Georg), WCH, New York, **1993**, 295.
7. Hashimoto, Y.; Ogasawara, T.; Hayashi, M.; Saigo, K. *Heterocycles* **2000**, *52*, 1001.
8. Arunkumar, N.; Keyan, W.; Ramamurthy, V.; Scheffer, J. R.; Brain, P. *Org. Lett.* **2002**, *4*, 1443.
9. France, S.; Wack, H.; Hafez, A. M.; Taggi, A. E.; Witsil, D. R.; Lectka T. *Org. Lett.* **2002**, *4*, 1603

Sample Availability: Available from MDPI.

© 2005 [MDPI](http://www.mdpi.org). All rights reserved.