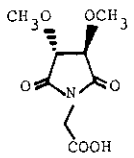
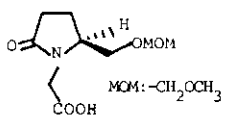
ASYMMETRIC SYNTHESIS OF β-LACTAMS USING CHIRAL FIVE-MEMBERED HETEROCYCLIC COMPOUNDS DERIVED FROM (+)-TARTARIC ACID AND L-AMINO ACIDS

Nobuo Ikota and Akira Hanaki
National Institute of Radiological Sciences,
9-1, Anagawa-4-chome, Chiba-shi 260, Japan

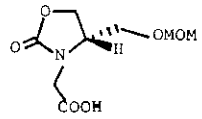
Although a large number of methods for the synthesis of β-lactams have been developed, only a few examples were reported for the asymmetric synthesis. One of the common procedures for preparing β-lactams is the cycloaddition of a ketene and an imine.



I (mp 60°, $[\alpha]_D$+172° ($CHCl_3$))



II ($[\alpha]_D$+6.2° (EtOH))



III ($[\alpha]_D$+23° ($CHCl_3$))

We describe our studies on models for asymmetric [2+2]cycloadditions of chiral ketene derivatives derived from chiral five-membered heterocyclic compounds (I,II, and III) to imine. Compounds I, II, and III were synthesized from (+)-tartaric acid, L-glutamic acid, and L-serine, respectively. They were converted into the corresponding ketenes *in situ*, and were reacted with imine prepared from benzaldehyde and aniline to afford a diastereomeric mixture of *cis* and *trans* β-lactams. The results were summarized in Table I. Only *trans* isomer(68% asymmetric induction) was obtained using I. On the other hand, *cis* isomers were formed as major product using II and III, and very high asymmetric induction (94%) was attained in these cases. Absolute configurations of IV(major diastereomer of *cis* compound) were determined by the correlation with the known phenylalaninol derivative(VI) according to the procedure as shown in Scheme I, and were determined to be 3S, 4R.

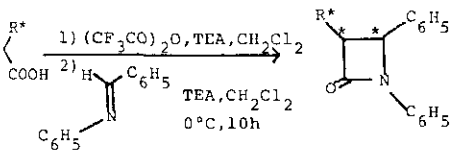


Table I

Reagent	Yield (%)	cis/trans	Ratio of Major Diastereomers	Asymmetric Induction(%)
I	47	0/100	84/16	68
II	63	86/14	97/3	94
III	70	99/1	97/3	94

Scheme I