ASYMMETRIC SYNTHESES OF OPTICALLY ACTIVE AZETIDINONES UTILIZING CHIRAL FIVE-MEMBERED HETEROCYCLES

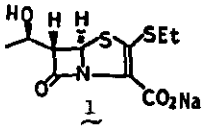
Yoshimitsu Nagao,[1] Toshio Kumagai,[1] Sachiko Takao,[1] Yuichi Hagiwara,[1] Takao Abe,[1] Masahito Ochiai,[1] Eiichi Fujita,[2] Tooru Taga,[3] Sakae Aoyagi,[4] Yunosuke Nagase,[4] and Yoshinori Inoue[4]

[1]Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, [2]Osaka College of Pharmacy, 10-65 Kawai 2-Chome, Matsubara 580, [3]Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606, and [4]Chemical and Formulation Laborotory, Lederle (JAPAN) Ltd., Kashiwacho, Shiki, Saitama 353, Japan

Recently, we are interested very much in the development of a short-steps synthesis of optically active penams and penems, because of fascinating biological activities of a penem-type β-lactam antibiotic 1 and penam-type β-lactamase inhibitors 2 and 3.

C4-Chiral five-membered heterocycles have been proved to be excellent reagents for asymmetric syntheses.[1] We have developed a very simplified synthetic route for chiral penam- and penem-type β-lactams 4, 5, and 6 employing 4(S)-2-MeSe-Δ^2-1,3-thiazoline derivatives (7 and 8). In this asymmetric synthesis, methylseleno-promoted ketene-imine cycloaddition between methoxyacetyl chloride and chiral imines (7 and 8) was effectively utilized as a key reaction.

We have readily prepared a chiral azetidinone 9 from an active amide 10 which can be obtained by a highly diastereo-controlled aldol type reaction.[2]



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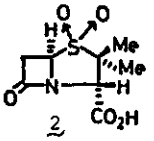

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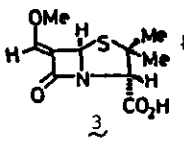

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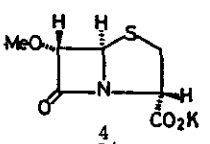

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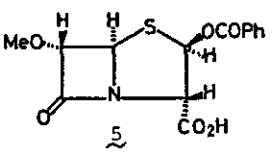

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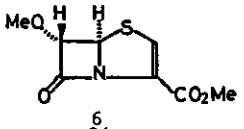

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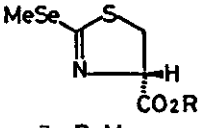
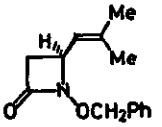


7 R=Me
8 R=CH2Ph



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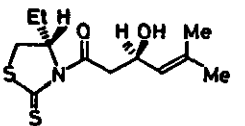

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References:

1. Y. Nagao and E. Fujita, J. Synth. Org. Chem. Jpn., 42, 622 (1984) and references cited therein.
2. Y. Nagao, et al., The abstracts of papers of the 16th Congress of Heterocyclic Chemistry, Osaka, Japan, p.237 (1984).