

[PD1-11] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Synthetic Approach to Natural Antioxidants: Benzastatin E, Benzastatin F and Benzastatin G

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Benzastatins (E, F, G) that contain indoline skeleton are three of seven compounds isolated from culture broth of *Streptomyces nitrosoporeus*. Benzastatins (E, F, G) have been reported as first natural indoline derivatives to show inhibitory activity against glutamate toxicity and strong antioxidant activity (lipid peroxydation inhibition in rat liver microsomes). Aiming at the structure-activity relationship study and development of antioxidants, we tried to synthesize benzastatins (E, F, G) and their analogues. We report here the synthetic method of indole structure via cyclization of ethyl-3-(2-nitrophenyl)-2-propeonate with/without substituent at 5 position and attempts to synthesize alkene side chain of benzastatins (E, F, G).

[PD1-12] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Design and Synthesis of fluorocyclopropanoid Nucleosides

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Novel fluorocyclopropanoid nucleoside analogues with three functionalities were designed and synthesized. First, cyclopropyl group possesses a hybrid character of acyclic chain and carbocyclic moiety and controls the conformation. Second, hydroxymethyl group was introduced for phosphorylation. And finally, fluorine mimics the electronic effect of the oxygen of natural nucleosides and controls the conformation by Gauche effect between fluorine and nitrogen of base.

The key intermediate, (±)-(E/Z)-[2-(tert-butyl-diphenylsilyl-oxymethyl)-1-fluorocyclopropyl] methanol was synthesized by the Lewis acid-catalyzed Furukawa method of Simmon-Smith reaction starting from allyl alcohol. The fluorinated ester with E/Z configuration was synthesized as a major product by Horner-Wadsworth-Emmons olefination.

Mesylate or iodide was coupled with adenine, 2-amino-6-chloropurine, cytosine and thymine under NaH, K₂CO₃, Cs₂CO₃ and DBU conditions and resulted in novel (±)-(E/Z)-(1'-fluoro-2'-hydroxymethyl-cyclopropylmethyl)purine analogues and pyrimidine analogues.

[PD1-13] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Trimeric cinchona alkaloid phase-transfer catalyst: a,a',a''-Tris[O(9)-allyl]cinchonidinium] mesitylene tribromide

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A trimeric Cinchona alkaloid ammonium salt, a,a',a"-tris[O(9) allylcinchonidinium]mesitylene tribromide has been prepared as a novel phase-transfer catalyst. The catalytic enantioselective alkylation of N-(diphenylmethylene)glycine tert-butyl ester using the trimeric catalyst show high enantioselectivity (90 ~ 97% ee).

[PD1-14] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Novel Asymmetric Synthesis of (1R, 2S)-1-Allyl-2-Silanyloxy Carbamates as precursors for the Synthesis of β -Hydroxy- α -Amino Acids using CSI reaction

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β -Hydroxy- α -amino acids are an important class of compounds due to their inherent biological activities and their role as structural components of more complex organic compounds that possess a wide range of biological activities, such as antifungals, antibiotics and immunosuppressants. They are also useful intermediates in the synthesis of other compounds, such as β -lactams, aminosugars, chiral ligands and β -fluoro amino acids. So, a number of elegant approaches have been described for the asymmetric synthesis of various β -hydroxy- α -amino acids in enantiomerically pure form. We have recently described synthetic method for N-protected allylic amines from allyl ethers using chlorosulfonyl isocyanate(CSI) via the stable allylic carbocation.

In this presentation, we will report novel asymmetric synthetic method for (1R, 2S)-1-allyl-2-silanyloxy carbamates as precursors for the synthesis of β -hydroxy- α -amino acids by the simple CSI reaction which we developed with various allyl ethers and discuss mechanism of these reactions.

[PD1-15] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Microbial asymmetric reduction of β -keto ester for the synthesis of 4-acetoxazetidinone

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A chiral compound, 4-acetoxazetidinone is considered as the key intermediate for the preparation of β -lactam antibiotics such as carbapenems or penems. We investigated the microbial asymmetric reduction of ethyl 2-(phthalimidomethyl)acetoacetate as β -keto ester substrate by bacteria and fungi as well as yeasts expecting the production of (2S, 3R)-ethyl 2-(phthalimidomethyl)-3-hydroxybutyrate (syn-1) according to the anti-Prelog rule. We report here the screening results of microbial asymmetric reduction carried out with 465 species of microorganisms according to the conventional screening method. All reaction products were analysed with HPLC and screening results were discussed in detail.

We can expect the production of four stereoisomers, two syn- and two anti-isomers resulted from microbial asymmetric reduction. Therefore, four isomers (syn-1, syn-2, anti-3 and anti-4, respectively) were prepared by NaBH₄ reduction of ethyl 2-(phthalimidomethyl) acetoacetate and identified by HPLC with chiral column. Although most microorganisms produced one syn-isomer (syn-2) and two anti-isomers generally, 10 species showed characteristic product distribution in which main product was (2S, 3S)-ethyl 2-(phthalimidomethyl)-3-hydroxybutyrate (anti-4) corresponding to