Studies Toward the Total Synthesis of Pancratistatin, Anticancer Natural Product

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The Amaryllidaceae alkaloid pancratistatin was first isolated from the roots of Pancratium littorale in 1984. The promising biological activity as an anticancer agent and low natural abundance have made it an attractive target for total synthesis. The major challenge to synthesis include elaboration of the fused BC ring system and the stereoselective installation of the hydroxyl groups located around C ring. We wish to reporte on the successful synthesis of highly advanced intermediate of pancratistatin from a simple starting material utilizing Claisen rearrangement, Curtius rearrangement and cyclic sulfate chemistry as key steps to construct the fused BC ring system and introduce the hydroxyl groups on C ring.

[PD1-24] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

New approach to the synthesis of (+)-Lauthisan by stereoselective alkylation

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For the enantioselective synthesis of (+)-*cis*-Lauthisan and (-)-*cis*-Lauthisan, we designed and synthesized 2-[1-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-2-trimethylsilanyl-allyloxy]-oct-4-enoic acid tert-butyl ester as a novel chiral auxiliary for optically active(+),(-)-*cis*-Lauthisan. The design of the chiral auxiliary was based on the postulated that a tridentate chelate formed by complexation of basic groups (two oxygens) on the auxiliary and metal cation bonded to ester enolate anion should efficiently shield one of the two diastereotopic faces of the enolate.
In connection with the synthesis of marine products and their analogues as potential antibiotics, we evaluated the chiral auxiliary as a synthetic tool for optically active (+)-*cis*-Lauthisan and (-)-*cis*-Lauthisan as a key step. The chiral auxiliary was alkylated with various kind of electrophiles via corresponding ester enolate generated by lithium hexamethyldisilazane at -78℃. D-Mannitol as achiral synthon was converted to 5-Ethyl-3-hexyl-6-hydroxymethyl-[1,4]dioxan-2-one through 6 steps.
In summary, we developed a novel synthetic method for optically active lactone, a key intermediate for (+),(-)-*cis*-Lauthisan. Taking into account of chiral auxiliary's chemical reactivities and selectivities, our method offer the fascinating possibilities for the development of new strategies for the optically active synthesis of natural marine products having 8-membered oxocane skeletons.

[PD1-25] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Effects of furanocoumarins isolated and semi-synthesized from the root of Angelica duhurica on NO and PGE2 production in murine macrophages

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Six furanocoumarins and related compounds isolated from the roots of Angelica dahurica ("Byak ji" in Korean) and the compound, selectively reduced from the major component, byakangelicin, were evaluated for their effects on NO and PGE_2 production in rat peritoneal macrophages induced by