[OD-1] [10/20/2000 (Fri) 10:00 - 10:15 / Hall C]

Facile and Efficient Total Synthesis of (+) -Preussin

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(+)-Preussin (1) possesses significant activity as broad-spectrum antibiotics against yeasts and filamentous fungi. Due to its interesting biological activity and its novel pyrrolidinone structure, a number of its synthetic approaches have been reported.
Recently, we have reported diastereoselective palladium(0)-catalyzed oxazoline formation reaction from the acyclic allylic and homoallylic benzamide (Tetrahedron Lett. 1998, 39, 8129, J. Org. Chem. 1999. 64, 9450).
We envisioned that this method could be utilized to set the vicinal amino alcohol stereochemistry of the (+)-preussin (1). Also, we envisaged that hydrogenolysis of the oxazoline 10 generated amino group, which condensed intramolecularly with the carbonyl group spontaneously to provide pyrroline, which was in situ hydrogenated with hydrogen coming from the least hindered surface to provide the pyrrolidine 11. Interestingly, Hydrogenolysis of oxazoline 10 gave pyrrolidine 11, a known precursor of preussin as a single isomer. This made our application of oxazoline 8 to the synthesis of (+)-preussin facile and efficient.
The key steps in our strategy are diastereoselective oxazoline formation reaction catalyzed by Pd (0) and pyrrolidine formation by hydrogenolysis of oxazoline using Pearlman's catalyst.

[OD-2] [10/20/2000 (Fri) 10:15 - 10:30 / Hall C]

CoMFA analysis of N-acyl-phenylaminoalcohols for cytotoxicity

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Structure of ceramide was studied and N-acyl-phenylaminoalcohol derivatives have been optimized for their cytotoxic activity. The three dimensional quantitative structure-activity relationship (QSAR) was investigated using the comparative molecular field analysis (CoMFA). The result suggested that electrostatic and steric factors of N-acyl-phenylaminoalcohol derivatives were strongly correlated with the cytotoxicity.

[OD-3] [10/20/2000 (Fri) 10:30 - 10:45 / Hall C]

Molecular modeling and asymmetric synthesis of 12 -(S)-HETE as an endogenous vanilloid receptor activator

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Capsaicin, the irritant principle in hot peppers, has a unique effect on the pain sensory system and is a potential candidate for clinical use as an analgesic. A functional vanilloid receptor termed VR1 (vanilloid receptor subtype 1) has recently been cloned. In addition, it has been found that capsaicin serves to open the channel pore of VR1 by lowering the heat threshold of the receptor. However, an endogenous VR activator of the receptor has not yet been found. Recently it has been suggested that an eicosanoids activated the VR1. More recently we performed molecular modeling to show the structural similarity between capsaicin and the eicosanoids in order to