[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

explain why capsaicin mimics 12-(S)-HPETE in activating the channel. Our modeling studies show 12-(S)-HPETE is the most structurally similar to capsaicin among them. As a part of our program directed toward development of the VR1 agonist and antagonist, we initially investigated possible synthetic strategies for eicosanoids. Particularly, the asymmetric synthesis of 12-(R) and (S)-HETE has been accomplished in our laboratory. Our synthesis illustrates a general and efficient synthetic scheme to HETE and analogues thereof.

[OD-4] [10/20/2000 (Fri) 10:45 - 11:00 / Hall C]

Antioxidative triterpenoidal saponins from the fruits of Ternstroemia japonica Thunberg

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Ternstroemia japonica THUNBERG has been used for heartache in Koean folk medicine. In our chemical study of this plant, an antioxidant activity was detected in the saponin fraction of the fruits. Five new triterpenoidal saponins were isolated, and their structures were elucidated by chemical and spectral evidences as follows: 1, Primulagenin A 3-[β-D-glucopyranosyl(1→2)][α-L-rhamnopyranosyl(1→2)-β-D-galactopyranosyl(1→3)]-β-D-glucopyranosiduronic acid, 2, Camelliagenin A 3-[β-D-glucopyranosyl(1→2)][α-L-rhamnopyranosyl(1→2)-β-D-galactopyranosyl(1→3)]-β-D-glucopyranosiduronic acid, 3, A_1-barringenol 3-[β-D-glucopyranosyl(1→2)][α-L-rhamnopyranosyl(1→2)-β-D-galactopyranosyl(1→3)]-β-D-glucopyranosiduronic acid, 4, 16-Acetyl camelliagenin A 3-[β-D-glucopyranosyl(1→2)][α-L-rhamnopyranosyl(1→2)-β-D-galactopyranosyl(1→3)]-β-D-glucopyranosiduronic acid, and 5, 3β, 16α, 22α, 28-Tetrahydroxy-olean-12-ene 3-[β-D-glucopyranosyl(1→2)][α-L-rhamnopyranosyl (1→2)-β-D-galactopyranosyl(1→3)]-β-D-glucopyranosiduronic acid.

[OD-5] [10/20/2000 (Fri) 11:00 - 11:15 / Hall C]

Novel Resveratrol Tetramers from Vatica diospyroides

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A novel reveratrol tetramer, vatdiospyroidol, was isolated as a cytotoxic constituent by bioassay-guided chromatographic fractionation, monitored by the KB (human oral epidermoid carcinoma, EC50 1.0 μg/mL) cell line from the ethyl acetate extract of the stems of Vatica diospyroides Sym. (subfamily, Dipterocarpoideae; family, Dipterocarpaceae). The compound also showed cytotoxic activities against the Col2 (human colon, EC50 1.9 μg/mL) and BC1 (human breast, EC50 3.8 μg/mL) cancer cell lines. Another novel resveratrol teramer, vaticaphenol A, was found to be an inactive constituent, although it was derived from a cytotoxic fraction. In addition, the knwon compounds bergenin, betulin, betulinic acid, mangiferonic acid, and (E)-resveratrol 3-O-β-glucoside were obtained. They were found to be non-cytotoxic substances when evaluated against a small panel of human cancer cells. (E)-Resveratrol 3-O-β-glucoside is the first resveratrol monomer to have been isolated from a plant in the family Dipterocarpaceae. Structures of resveratrol teramers were elucidated by spectral analysis, including 1D and 2D NMR experiments.

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