[OD1-1] [2003-10-11 09:30 - 09:45 / ASEM Hall Meeting Room 203]

A versatile biomimetic total synthesis of benzo[c]phenanthridine and protobeberine alkaloids using lithiated toluamide-benzonitrile cycloaddition

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Natural benzo[c]phenanthridine and protoberberine alkaloids which have been attractive to synthetic organic chemists and biochemists over the last 2 decades since such compounds have shown interesting biological properties such as antitumor, antiviral and antimicrobacterial activities. For the systematic research on these alkaloids, several total syntheses of these alkaloids have been reported. However, the bulk of reported benzo[c]phenanthridine synthetic studies to date have involved multistep sequences for assembly of the target molecules as well as lack of generality for synthesizing substituted molecules. We have tried to develop a new versatile synthetic method for these compounds using lithiated toluamide-benzonitrile cycloaddition. Retro-synthetic consideration of benzo[c]phenanthridine and protoberberines indicates that the coupling of o-methylbenzonitrile with o-toluamide might afford 3-arylisoquinoline which could be transferred to the aldehyde or primary alcohol. Benzo[c]phenanthridines or protoberberines can be formed by an intramolecular ring cyclization method. Herein, we succeeded in synthesizing natural benzo[c]phenanthridine alkaloids such as oxysanguinarine, oxyavicine, oxychelerythrine, oxynitidine as well as protoberberines such as 8-oxocoptisine, 8-oxoberberine, 8-oxopsedoberberine and 8-oxopsedocoptisine.

[OD1-2] [2003-10-11 09:45 - 10:00 / ASEM Hall Meeting Room 203]

Molecular modeling of COX-2 inhibitors: 3D-QSAR and docking studies

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88 selective COX-2 inhibitors belonging to three chemical classes (triaryl rings, diaryl cycloalkanopyrazoles, and diphenyl hydrazides) were studied using comparative molecular field analysis (CoMFA) and comparative molecular similarity indices analysis (CoMSIA). Partial least squares analysis produced statistically significant models with q^2 values of 0.84 and 0.79 for CoMFA and CoMSIA, respectively. The key spatial properties were detected by careful analysis of the isocontour maps.The binding energies calculated from flexible docking correlated with inhibitory activities by the least-squares fit method. The three chemical classes of inhibitors showed reasonable internal predictability (r^2 = 0.51, 0.49, and 0.54), but the triaryl rings had a much lower binding energy than the others. Differences in binding energies were considered to be due to the electrostatic interaction energy between R513 of the COX-2 active site and the sulfonyl group of the triaryl ring. Comparative binding energy analyses gave q^2 values of 0.64, 0.63, and 0.50 for triaryl rings, diaryl cycloalkanopyrazoles, and diphenyl hydrazides, respectively. In the QSAR models, some protein residues were highlighted as particularly important for inhibitory activity. The combination of ligand-based and structure-based models provided an improved understanding of the three chemical classes of inhibitors and their interactions with COX-2.

[OD1-3] [2003-10-11 10:00 - 10:15 / ASEM Hall Meeting Room 203]

Total Synthesis of Bacillariolide III

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Bacillariolide III was isolated from the culture medium of the marine diatom, Pseudonitzschia multiseries, a causative organism of amnesic shellfish poisoning by Shimizu et al. This extracellular metabolite features bicyclic system of hydroxycyclopentane and (Z)-pentenoic acid-bearing lactone ring. Bacillariolide I is known to possess significant inhibitory activity against phospholipase A_2, but the biological function of bacillariolide III is still under investigation. The unique structural feature as well as the promising biological activity led us to the total synthesis of bacillariolide III.The total synthesis of bacillariolide III has been accomplished via 15 linear steps in a 15% overall yield from the known (R)-a-hydroxybutyrolactone. The key parts of this approach include the stereoselective construction of the cis-disubstituted hydroxycyclopentane skeleton and the convergent and stereocontrolled introduction of the (Z)-pentenoic

acid moiety using the vinyl addition and the ring-closing metathesis (RCM).

[OD2-1] [2003-10-11 10:15 - 10:30 / ASEM Hall Meeting Room 203]

Dereplication and Quantification of Steroidal Saponins in Polygonatum Species Using LC-MS

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Rhizomes of Polygonatum species belong to Liliaceae are important herbal drugs in the traditional medical practice of Asian region. Two representative Chinese drugs derived from this genus are Hwangjeong and Okjuk. Though botanical origins of these drugs are officially listed as P. falcatum, P. sibiricum and P. kingianum for Hwangjeong and P. odoratum var. pluriflorum for Okjuk in the Korean Pharmacopoeia and Korean Herbal Pharmacopoeia, respectively, they are often sold as a mixture of several different species in the market. Therefore, a simple HPLC-MS technique was developed to differentiate these species in this study. This approach was focused on the detection of steroidal saponins that were reported to show hypoglycemic activity. In addition, this method was used to analyze commercial Polygonatum species products and the related tea products. Five spirostanol glycosides (1-5) were isolated from P. sibiricum and used as standard compounds for qualitative and quantitative analysis of Polygonatum species. Among them, compounds 1, 3 and 5 were found to be new spirostanol glycosides through dereplication procedure using MS^n analysis, and other spectroscopic data. These new glycosides have a 6-O-acetyl-β-D-galactopyranose as a common moiety in their structures. The relative distribution of these compounds in each extract of five Polygonatum species was established by HPLC-ESI-MS with SIM mode. Furthermore, eleven Poygonatum species herbal drugs and seven herbal tea products were analyzed. It was found that LC-MS method could be utilized to differentiate these herbal drugs and tea products effectively. In conclusion, the LC-MS technology can improve the accuracy, sensitivity and speed of the analysis when it was compared to the conventional HPLC method.

[OD2-2] [2003-10-11 10:30 - 10:45 / ASEM Hall Meeting Room 203]

Cytotoxic constituents of Zingiber cassumunar

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A new phenylbutenoid dimmer, (±)-trans-3-(3'-methoxy-4'-hydroxyphenyl)-4-[(E)-3''',4'''-dimethoxystyryl] cyclohexene (1), were isolated from the rhizomes of Zingiber cassumunar along with three known phenylbutenoids, (±)-trans-3-(3',4'-dimethoxyphenyl)-4-[(E)-3''',4'''-dimethoxystyryl]cyclohexene (2), 4-(3',4'-dimethoxyphenyl)but-1,3-diene (3) , and 4-(2',4',5'-trimethoxy-phenyl)but-1,3-diene (4), and a known heptanoid, curcumin (7), as cytotoxic constituents against several human cancer cell lines. In addition, two known phenylbutenoids, (E)-3-hydroxy-1-(3',4'-dimethoxy-phenyl)but-3-en-1-yl acetate (5) and (E)-4-(3',4'-dimethoxyphenyl) but-3-en-1-ol (6), were also obtained as inactive constituents in the present study. Structure elucidation of compound 1 will be presented as well as biological activity of the compounds 1-7.

[OD2-3] [2003-10-11 10:45 – 11:00/ ASEM Hall Meeting Room 203]

Antioxidant Activity of Cercis chinensis and Its Protective Effect on Skin Aging

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Reactive oxygen species are capable of damaging biomolecules such as lipids, proteins, and DNA, which can not only lead to various diseases, but also oxidative damage resulting aging. In our previous study, Cercis chinensis (Leguminosae) showed a potent antioxidant activity. Twenty compounds including a new flavonol glycoside were isolated through antioxidant activity-guided fractionation. C. chinensis and some of the