

In this presentation, we will report novel regio- and stereocontrolled synthetic method for the precursors of polyhydroxyamines using CSI.

[PD1-10] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Regioselective Substitution of 6,7-Dichloroquinoline-5,8-dione: Synthesis, Cytotoxicity, and X-ray crystal structure of 4a,10,11-Triazabenz[3,2-a]fluorene-5,6-diones

Lee Hyun-Jung^o, Park So-Young, Lee Chong-Ock, Suh Myung-Eun

College of Pharmacy, Ewha Womans University, Seoul 120-750, Korea

6,7-Dichloroquinoline-5,8-dione reacted with 2-aminopyridine derivatives. Out of the four possible products which could be achieved in this reaction, condensation and rearrangement product, 4a,10,11-triazabenz[3,2-a]fluorene-5,6-dione was obtained as major product. The definite structure was identified with X-ray crystallographic study. The preparation of ortho-quinones via nucleophilic substitution at C7 position was an unexpected result when considered the para-quinones via substitution at C6 position which prepared in reaction of 6,7-Dichloroquinoline-5,8-dione with ethyl acetoacetate in our previous work. The antitumor activity of 4a,10,11-triazabenz[3,2-a]fluorene-5,6-dione was superior or similar to doxorubicin and much higher than etoposide. Therefore, nucleophilic substitution at C7 position could provide the effective and simple synthetic rout to prepare biologically active ortho-quinone derivatives.

[PD1-11] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Efficient Solid Phase Library Synthesis of 7-Alkoxy-1,3,4,5-tetrahydro-benzo[e][1,4]diazepin-2-one

Im Isak^o, Kim Yong-Chul

Department of Life Science, Kwangju Institute of Science and Technology, 1 Oryong-dong, Buk-gu, Kwangju 500-712 Republic of Korea

The β -turn has been implicated as an important conformation for biological recognition of peptides or proteins. Benzodiazepine classes have been known as one of the nonpeptide β -turn mimic scaffolds. We have developed an efficient approach for the synthesis and derivatization of a scaffold of hydroxytetrahydrodiazepinone class in order to screen compound library in various protein targets for new lead generations as well as for structure activity relationships of the scaffold. Amino acid esters and aromatic or alkyl halides for the introduction of amino acid side chains were used for building blocks in the library synthesis. Starting from 5-hydroxy-2-nitrobenzaldehyde, the benzodiazepin-2-one scaffold was synthesized in 4 steps in high yields. The validation of the scheme for the next solid phase derivatization of the scaffold has been expedited in a solution phase synthesis using a solid support mimic group, which was 2,4,6-trimethoxybenzaldehyde. After the validation, the scaffold was loaded in PL-FDMP resin through reductive amination and the alkylations of 7-hydroxyl and amide nitrogen were accomplished. TFA cleavages resulted in the initial 48 members of peptidomimetic library in high yields (50-60% purified yield, for the 4 step solid phase synthesis).

[PD1-12] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthesis and hypoglycemic Activity of the Substituted Pyrrolidine Thiazolidinedione Derivatives

Kim BokYoung, Ahn Joong-bok, Lee HongWoo^o, Shin JaeSoo, Moon Kyoung Sik, Kim Joon-Kyum, Lee DoYoung, Ahn SoonKil, Hong ChungIl

New Drug Research Laboratories, CKD Research Institute, Cheonan 330-831, Korea

Non-insulin dependent diabetes mellitus (NIDDM) is characterized by hyperglycemia, hyperinsulinemia, and impaired insulin action. Insulin resistance is considered to be the underlying mechanism in the pathogenesis of