[PD1-1] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Liquid phase combinatorial synthesis of non-peptide bradykinin antagonists and evaluation of their activity on guinea-pig ileum

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Bradykinin is an autocoid related to acute and chronic pain and inflammation. The non-peptide bradykinin antagonists are of interest as novel anti-inflammatory therapeutics and some active compounds such as FR 173657, LF 16-0687, and bradyzide were reported very recently.
In our search for the new bradykinin antagonists, we designed to synthesize the analogues of FR173657 with two to three amide bonds and lipophilic ring system in each molecule.
To produce large numbers of diverse compounds rapidly and efficiently, combinatorial synthesis using the iminodiacetic acid template was employed. The template contains three positions which can be sequentially functionalized enabling the synthesis of libraries with up to three variable units. Also in each step, for both the isolation and purification of each intermediate and final product from the starting material, reactants, reagents and their reaction byproducts by simple liquid/liquid extraction may be used.
The libraries are consist of 50 individual compounds prepared on a 10-50 mg scale in addition to 10 mixture libraries of 5 compounds.
Most of the compounds synthesized showed the bradykinin inhibition activity at 0.1 uM concentration in the guinea-pig ileum.

[PD1-2] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Design and Synthesis of 7-Hydroxy-2-Alkyl-Chromen-4-one and -Chroman Derivatives as Potential Antioxidants

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Many neurodegenerative disorders such as stroke, Alzheimer's disease, and Parkinson's disease have been known to be associated with an excessive generation of reactive oxygen species (ROS) and oxidative stress. Therefore, the antioxidants have recently received much attention as therapeutic agent for the treatment of neurodegenerative disease.
In this study, we describe the synthesis of a series of 7-hydroxy-2-alkyl-chromenone and -chroman derivatives which were prepared from 2,4-dihydroxyacetophenone. The target compounds were designed to include the structural feature of caffeic acid, flavonoid, and tocopherol known as antioxidants.
7-hydroxy-2-alkyl-chromenone and -chroman derivatives were evaluated for the effects on lipid peroxidation in rat brain homogenate. The chroman derivatives were more potent then the chromenone derivatives. These compounds were also 2-4 times more potent then caffeic acid and trolox which were used as positive control.