[PD1-32] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Polyoxygenated Flavone Analogs as Inhibitors of PGE2 Production

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As part of our research to discover novel synthetic flavonoids which can be applied to chronic inflammation diseases, many structurally modified flavone analogs have been synthesized to obtain information concerning the relationships between structures and the anti-inflammatory activities. We previously reported that 7-methoxyflavone analogs generally exhibited strong inhibitory activities against cyclooxygenase-2 catalyzed prostaglandin production. 7-Methxoyflavone analogs with the polyoxygenated B ring were synthesized and evaluated the inhibitory activity of cyclooxygenase-2 catalyzed prostaglandin production. Polyoxygenated flavone analogs were prepared from 2,4-dihydroxyacetophenone in 3 steps. The inhibitory activity of the synthesized flavone analogs against prostaglandin production from lipopolysaccharide-treated RAW 264.7 cells were measured. 2,4,7-Trimethoxyflavone showed best results.

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Synthesis of Brefeldin A Lactam Analogue

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(+)-Brefeldin A (1) has been, since its isolation1 and structural elucidation2 many years ago, one of the most attractive targets for synthetic chemists due to its wide range of biological activities and well-functionalized macrolide structure. Its biological mode of action has been disclosed by a number of important discoveries. Especially the ability of brefeldin A to induce DNA fragmentation associated with apoptosis in cancer cells has stimulated a great deal of recent interest in its preclinical development as an anticancer agent. Since Corey's first total synthesis of 1 in 1976, a number of synthetic routes to this macrolide antibiotic have been explored. In particular, the exciting biological activities of brefeldin A, combined with the impracticality of the previously developed syntheses led us to take on the challenge of the total synthesis of brefeldin A. In planning our approach, we hoped to develop a versatile, practical, and stereocontrolled route that would minimize protecting group manipulations and adapt a platform that leads to a variety of analogues of Brefeldin A. This paper fully describes our synthetic studies9 toward (+)-brefeldin A Lactam Analogue

[PD1-34] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Structure-activity Relationship Study of Fluoro-Neplanocin A as Potential Antiviral and Antitumor Agents

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