[PD1-3] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Structural Requirement of New Chalcones for the Inhibitory Activity of Interleukin-5

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Interleukin (IL)-5 appears to be one of the main proinflammatory mediators among a growing number of cytokines and chemokines that induce eosinophilic inflammation. Sophoricoside and their analogs isolated from Sophora japonica show relatively potent inhibitory activity of interleukin (IL)-5 as a small molecule. Initial attempt to identify the structural requirement of this isoflavonone led to find new chalcones to exhibit the inhibitory activity of IL-5. Among them, 4-[3-(2-benzyl-6-hydroxyphenyl)-3-oxopropen]benzoic acid show the compatible activity with that of sophoricoside. The structure activity relationship of these chalcones will be discussed.

[PD1-4] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Reagentselective and positionselective epoxidation of 25(R)-1,4,6-spirostatrien-3-one and 25(R)-4,6-spirostadien-3β-ol

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Diosgenin(25(R)-spirost-5-en-3β-ol) is the steroid saponin, was isolated from Mexican yam (Dioscorea).Estrogenic, progesterogenic and anti-inflammatory effects of diosgenin has been hypothesized due to its structural similarity to estrogen, progesterone precursors. And diosgenin had been reported to lower serum cholesterol in chicken and rabbits fed cholesterol and to decrease liver cholesterol in cholesterol-fed rats. Diosgenin was used commercially to produce steroid hormones such as cortisone, estrogen, and progesterone by in vitro chemical modification.
In order to synthesize the various diosgenin derivatives, 25(R)-spirost-5-en-3β-ol was oxidized with 2,3-dichloro-5,6-dicyanobenzoquinone to form 25(R)-1,4,6-spirostatrien-3-one(1). And compound(1) was reduced with NaBH4 to give 25(R)-4,6-spirostadien-3β-ol(2). Compound 1 and 2 was epoxidized with hydroren peroxide, m-chloroperoxybenzoic acid, (R,R) and (S,S)-Jacobsen's catalyst with NaOCl, D-(-)-diisopropyltartrate and L-(+)-diisopropyltartrate, titanium tetriospropoxide with TBHP, respectively.

[PD1-5] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Novel Heteroaromatic Arylsulfonylimidazolones as Anticancer Agent

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Novel arylsulfonylimidazolidinones were previously demonstrated to have broad and highly potent cytotoxicities against a wide range of cancer cell line. Among them 4-phenyl-1N-(p-

aminobenzoyl)indoline-5-sulfonyl imidazolidinone (PA) was proved to have good pharmacological profile. Recently modification of indoline moiety of PA led us to find new analogs which show better pharmacological profiles compared to PA. Especially 4-acylamino-3alky (or halogeno)benzenesulfonyl-4-phenyl
imidazolidinones show outstanding cytotoxicity against human solid cancer cell lines. Although the roles of phenyl motif at 4-position of imidazolidinone for their activity was proved, in order to investigate the role of heteroaromatic motif at this position 4-acylamino-3-methylbenzensulfonyl-4-furyl(thienyl)imidazolones were synthesized and tested against various human solid cancer cell lines. Interestingly, some analogs of this series have also been found to have a strong cytotoxicity.

[PD1-6] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Reagentselective reduction of 25(R)-1,4,6-spirostatrien-3-one

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Spicatoside A and spicatoside B were isolated from Liriopis tuber. Spicatoside A has anticancer activity and it is composed of 1β-hydroxy
diosgenin and trisaccharides. Spicatoside B has the preventive effect of diabetes mellitus and also has 1β-hydroxy derivatives, which is clevaged the ether linkage of F ring of diosgenin. Therefore, selective synthesis of 1β-hydroxydiosgenin is required.
25(R)-5-spirosten-3β-ol(diosgenin) was oxidized with DDQ to synthesize 25(R)-1,4,6-spirostatrien-3-one. This trienone was reduced with sodium borohydride to give 25(R)-4,6-spirostadien-3β-ol. But this compound isn't able to epoxidize at the 1,2 position and then can not convert the 1β-hydroxy derivatives by metal dissolving reduction.
In order to search the reagent to reduce carboyl group of 25(R)-1,4,6-spirostatrien-3-one stereoselectively, we used sodium borohydride, lithium
aluminium hydride, L-selectride, 9-BBN, Red-Al, borane-dimethysulfide complex.

[PD1-7] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Cyclic Aminoalcohols with C-18 Alkenyl Substituents and Their Nanomolar Level-Activities as Tissue Factor Inhibitors

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Development of new tissue factor (TF) inhibitor is still needed for improved compositions having anticoagulant activity and which can be administed orally or non-intravenously at low doses. Our studies for the development of new TF inhibitors uncovered that aminoalcohols with C-18 alkenyl group, 9-octadecenyl- or 9,12-octadecadienyl groups exhibits in vitro nanomolar level activities.

In continuing studies, cyclic aminoalcohols (1-(3-piperidinol)-, 1-(4-piperidinol)-, 1-(3-pyrrolidinol)-) tethered with C-18 alkenyl (9-octadecenyl- or 9,12-octadecadienyl-) substitents were synthesized and their in vitro TF inhibitory activity were examined. They showed very potent nanomolar level-inhibitory activities. Details of the studies will be discussed.