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

Ma Eunsook, Kim HakSoon, Kim EunJung, Jung WonYoung°, Choi TaeYoung

Department of Pharmacy, Catholic University of Daegu, Hayang, 712-702

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

Yoon UngChan, Kwon HyukChul, Cho YongJin°

Pusan National University, Department of Chemistry

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.