rearrangement, Grubbs' ring closing metathesis, and Trost's allylic alkylation. The reiterative three-step sequence (i.e. sigmatropic rearrangement, ring closing methathesis, and allylic alkylation) can also provide acess to further synthesis of structually complicated novel carbocyclic nucleosides.

[PD1-20] [ 04/19/2002 (Fri) 10:00 - 13:00 / Hall E ]

## Synthesis of Novel 1,5-diarylhydantoins as Selective COX-2 Inhibitors

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The most common side-effects of NSAIDs are generally gastro-intestinal disturbances such as discomfort, nausea, peptic ulcer and severe bleeding. It has been proposed that NSAIDs act through inhibition of cyclooxygenase-1(COX-1) and cyclooxygenase-2(COX-2) and that inhibition of COX-1 is associated with adverse gastro-intestinal effects while inhibition of COX-2 is associated with anti-inflammatory activity. On the basis of this fact, specific COX-2 inhibitors such as celecoxib and rofecoxib are introduced in the drug market. The distinguished feature of these drugs is that the 5-membered heterocycle ring is substituted with two aryl groups. This study reports on synthesis of novel 1,5-diarylhydantoin derivatives, candidates for selective COX-2 inhibitors. These compounds were synthesized through esterification, bromination, α-substitution and cyclization from commercially available phenylacetic aicd.

[PD1-21] [ 04/19/2002 (Fri) 10:00 - 13:00 / Hall E ]

## Novel Dimeric Cinchona Alkaloid Ammonium Salts with 2,7-Naphthalene Ligand: Highly Enantioselective and Practical Phase-Transfer Catalysts for the Synthesis of alpha-Amino acids

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Phase-transfer catalysis (PTC) is one of the most useful methodologies for the practical syntheses because of the operational simplicity and mild reaction conditions, which enable this method to be applied to the industrial process. Recently, PTC has been extensively applied for the asymmetric synthesis by using chiral quaternary ammonium salts. Chiral phase-tranfer catalysts derived from the cinchona alkaloids have been developed and successfully applied to various useful organic reactions. Based on the fact that the introduction of a bulky subunit at the N(1)-position of cinchona alkaloids leads to enhance the enantioselectivity, we recently reported the efficient dimeric and trimeric catalyst by using benzene as a ligand. The enhancement of stereoselectivity is due to the screening effect of each two Cinchona unit, which can make the substrate approach to only one direction. As part of our program to develop practical catalyst which can be used in industrial process, we further investigate the more optimal dimeric catalyst by modifying ligand instead of benzene ligand. In this poster, we report the preparation of new symmetrical dimeric cinchona alkaloid-derived catalysts having naphthalene moiety as a new optimal ligand and their application to the catalytic enantioselective phase-transfer alkylation of N-(diphenylmethylene)glycine tert-butyl ester.

[PD1-22] [ 04/19/2002 (Fri) 10:00 - 13:00 / Hall E ]

## The Cyclobutyl Intermediate for Synthesis of Novel Carbocyclic Nucleosides , Potential Antiviral Agents

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Carbonucleosides has extensively been studied as a promising antiviral agents having chemical and metabolical stability. As yet there are no rules relating the structures of carbocyclic nucleosides to their therapeutic activity, although trends among certain kinds of structure have been tentatively put forward. Some vinyl cyclobutyl nucleosides can be considered to be analogue of exomethylene cyclopentyl nucleosides, BMS-200475. In our research program for discovery of anti-viral drugs, the key intermediate containing vinyl group has been synthesized from D-glucose, via several steps involving ring contraction reaction by zirconium complex.

[PD1-23] [ 04/19/2002 (Fri) 10:00 - 13:00 / Hall E ]

## Structure-transport relationship of drugs in Caco-2 monolayer system: through sildenafil derivatives and dopamine receptor antagonists

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Bioanalysis and Biotransformation Research Center, Korea Institute of Science and Technology

To investigate about prediction of intestinal absorption is very important process in drug discovery, development of lead drug candidates derived by combinatorial synthesis and combinatorial screening paradigms. Researches for predictable factor of intestinal absorption already accomplished and tried means every possible in several places. Polar surface area (PSA) and Log P, well-known factors of chemical structure, are compared with apparent permeability coefficient (Papp), a single factor of transport assay of in vitro system. However, those studies are tended to diminish why the flaw, have no connection with structure and absorption of in vivo. The aim of this study is to make clear of complicated relationship between predictable factors and absorption in vivo. 24 compounds, derivatives of sildenafil and dopamine receptor antagonist, examined and calculated apparent permeability coefficient (Papp). Polar surface area (PSA) and Log P of these compounds obtained by Sybyl 6.7 (software).

[PD1-24] [ 04/19/2002 (Fri) 10:00 - 13:00 / Hall E ]

## Oxidation of Methyl Substituted Benzo- or Pyridoquinoxalinediones

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The high temperature and pressure oxidative reaction using 18% nitric acid is known to oxidize benzylic methyl group of a quinone containing aromatic ring system to a carboxylic acid. We have previously reported the oxidation of 3-methylazaanthraquinone and 7,8-dimethylazaanthraquinone to give the azaanthraquinone carboxylic acids.
However, an interesting result was obtained in the same reaction of 7,8-dimethylbenzo quinoxalinedione, 7-methylpyridoquinoxalinedione, 8-methylbenzoquinoxalinedione.
Both benzylic methyl group and 2- and 3-carbon of quinoxalinediones were oxidized.
Oxidation of quinoxaline that is not to go by way of quinoxaline oxide intermediate is rare. The only reported example of the direct method is to reflux a mixture of quinoxaline and ammonium peroxosulfate in water (42%).

[PD1-25] [ 04/19/2002 (Fri) 10:00 - 13:00 / Hall E ]

## CoMFA Analysis of 2-Alkylureido-1-phenyl propanols for N-SMase inhibitory activity

Im ChaeUK, Kwon OhHyeok° Jun SangChul, Choi SeKyungi, Yim ChulBu