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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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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