Several studies of terbenzimidazoles and bibenzimidazoles suggested that benzimidazoles, especially 5-nitro-2-(para-methoxyphenyl)benzimidazole, possess topoisomerase I inhibition activities. In order to find out the structure activity relationship of 5-nitro-2-phenyl-benzimidazoles, eight derivatives that are substituted at the para position of 2-phenyl moiety were selected, synthesized & evaluated considering their electronic or lipophilic parameters. Both the topoisomerase I inhibiton activities and the cytotoxicities were related neither to the electronic nor lipophilic parameters. These data suggest that their activities may be related to other parameters including steric bulk or hydrogen-bonding capacities. Further studies are on the way to investigate this relationship.

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

Asymmetric synthesis of (2S, 3R, 4E) 5-Aryl-4-pentene-1,3-diol-2-aminoueras

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(2S 3R, 4E) 5-Aryl-4-pentene-1,3-diol-2-aminoueras had been synthesized for their cytotoxic activity. Pinene was oxidized with KMnO4 to give 2-hydroxy-3-pinanone, which treated with ethyl glycinate to yield iminoglycinate and then reacted with aldehyde derivatives and titanium enolate to afford 3-hydroxy aldol compounds. These aldol compounds was hydrolyzed with HCl and reduced with NaBH4 to give 2-amino-1,3-diols, which was treated with alkyl isocyanates to yield 5-aryl-4-pentene-1,3-diol-2-aminoueras. The aldehyde derivatives was synthesized in three steps from benzelaldehydes.

[PD1-14] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Synthesis of N-methylspiro[1,2,3,4-tetrahydro-naphthalene-1,2'-pyrrolidine]

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A pathway for synthesis of N-methylspiro[1,2,3,4-tetrahydro-naphthalene-1,2'- pyrrolidine] was developed. Formation of the imine compound from α-tetralone and methylamine using titanium tetrachloride followed by ddition of allylmagnesium bromide gave (1-allyl-1,2,3,4-tetrahydro-naphthalen-1-yl)methylamine. Protection of (1-allyl- 1,2,3,4- tetrahydro-naphthalen-1-yl)methylamine followed by substitution reaction with di-tert-butyl carbonate in 10% sodium hydroxide solution gave (1-allyl-1,2,3,4- tetrahydro- thalen-1-yl)methylcarbamic acid tert-butyl ester. Hydroboration-oxidation of (1-allyl-1,2,3,4-tetrahydro-naphthalen-1-yl) methylcarbamic acid tert-butyl ester with borane disulfide complex or borane-THF complex gave [1-(3-hydroxyypropyl-1,2,3,4- tetrahydro-naphthalen-1-yl)methylcarbamic acid tert- butyl ester and deprotection of t-Boc group in 6N hydrochloric acid solution gave 3-(1-methylamino-1,2,3,4-tetrahydro- naphthalen-1-yl)-propan-1-ol. Finally, cyclization of the amino compound in Mitsunobu conditions provided N-methylspiro[1,2,3,4-tetrahydro-naphthalene-1,2'-pyrrolidine].

[PD1-15] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

The Synthesis of Novel Cyclobutyl Nucleoside as Potential Antiviral Agents