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Costunolide which is known as a chemopreventive drug is a sesquiterpene compound isolated from *Magnolia Sieboldii*. and has antitumor and antiinflammatory activities. it is very hard to collect enough amount of natural extracts of costunolide for the activity studies. therefore, synthesis of costunolide derivatives is honestly needed. the aim of this research is to develop new methods for costunolide synthesis and to test biological activities. two different macrocyclization methods were applied : application of a low-valent chromium reagent for the construction of the germacrane-skeleton from the linear precursor. this application already was carried out and we got a small amount of costunolide : application of selenium reagent for the construction of the same moiety

[PD1-63] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Chiral Synthesis of Costunolide

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Costunolide, a sesquiterpene lactone is isolated from *Magnolia Sieboldii*. It is known to possess antitumor and anti-inflammatory activities. This compound is synthesized from the easily available decalin dione using the ring cleavage approach to construct the ten-membered ring system. The two key points in this work are the chiral induction on the allyl alcohol moiety using Sharpless epoxidation reaction, and opening of the epoxide with an organocuprate reagent which leads to a α -exomethylene lactone.

[PD1-64] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthesis and Biological Evaluation of Pyrimidine Nucleosides Fused with 3',4'-Tetrahydrofuran Ring

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A number of 2',3'-deoxynucleosides have been discovered to possess significant antiviral activity against HIV-1 and other viruses. Since it has been suggested that proper conformation of the dideoxynucleosides in terms of ring puckering of the five-membered sugar moiety is required for them to exhibit antiviral activity, a number of nucleoside analogues to fix sugar-ring puckering have been synthesized and evaluated for antiviral activity. Among them, bicyclic nucleoside analogues like the 3',4'-oxetane-ring or 2',3'-methylene fused nucleosides have been reported to inhibit HIV replication, but 3',4'-cyclopentane fused pyrimidine nucleosides did not show antiviral activity. Therefore, based on these findings, novel 3',4'-tetrahydrofuran fused pyrimidine nucleosides were designed and synthesized to obtain further information regarding the correlation between sugar ring conformation and antiviral activity. The desired pyrimidine nucleosides and their 2'-deoxy analogues were straightforwardly synthesized, starting from D-glucose. 3',4'-Tetrahydrofuran ring was introduced by the intramolecular cyclization reaction of 3-C-hydroxymethyl-4-bis-mesyl sugar derivative with sodium hydride. The final nucleosides were assayed for antiviral activities against HIV-1, VSV and HCMV, among which thymidine analogue and its corresponding 2'-deoxy analogue exhibited high cytotoxicity instead of antiviral activities. It is concluded that this class of conformationally rigid nucleosides can be a lead for antitumor agents, not antiviral agents. Synthesis biological activity will be presented in the meeting.

[PD1-65] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthesis of 5-Azacytidine Nucleosides With Rigid Sugar Moiety As Potential Antitumor Agents

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