

Stereocontrolled asymmetric synthesis of pancratistatin

Park Je Eun^O, Kim Sanghee, Ko Hyojin

Natural Products Research Institute, College of Pharmacy, Seoul National University, 28 Yungun, Jongro, Seoul 110-460, Korea

Pancratistatin is a highly oxygenated phenanthridone alkaloid, exhibits a high level of in vitro and in vivo cancer cell growth inhibitory activity, and antiviral activity. The asymmetric synthesis of this alkaloid has been accomplished from the commercially available (R)-(+)-3-Butyn-2-ol. We utilized the Claisen rearrangement and metathesis to install stereogenic centers in the cyclohexene ring that has absolute chemistry. Further functionalization of cyclohexene ring as described, previously by us led to the asymmetric total synthesis of (+)-Pancratistatin.

[PD1-60] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Total synthesis of Antofine by using Intramolecular 1,3-dipolar cycloaddition of Azidealkene

Lee Jaekwang^O, Lee Taeho, Song Soyoun

서울대학교 천연물과학연구소

Antofine belongs to the Phenanthroindolizidine group of alkaloids. This natural products exhibit interesting biological properties such as antitumour activity, and anti-inflammatory. Wittig reaction of phenathrenealdehyde with the phosphonium salt provided the phenathreneazidealkene in good yield. Intramolecular 1,3-dipolar cycloaddition of the resulting azidealkene in refluxing benzene proceeded the imine. It was reduced with cyanoborohydride or Noyori's Asymmetric Hydrogenation. Then, completion of the total synthesis was achieved by using Pictet-Spengler cyclization.

[PD1-61] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

An Asymmetric Synthesis of (+)-Polyoxamic acid

Lee KiHan^O, Oh ChangYoung, Lee Keeyoung, Kim YongHyun, Lee Yiusuk, Joo JaeEun, Ham WonHun

College of Pharmacy, Sungkyunkwan University

The Polyoxin complex is an antifungal antibiotics produced by *Streptomyces cacaoi* var. *asoensis* that exhibit marked and selective activity against phytopathogenic fungi. They incorporate carbamoylated dipeptides attached to the sugar moiety. Controlled alkaline hydrolysis of polyoxins result in several products, one of which has been identified as (+)-(2*S*, 3*S*, 4*S*)-2-amino-3, 4, 5-trihydroxypentonic acid (polyoxamic acid). A variety of chemical syntheses of polyoxamic acid have been developed over several years. However, development of new method for synthesizing this polyhydroxy amino acid still remains challenging and worthwhile.

Recently, we have developed a new Pd(0)-catalyzed procedure for the stereoselective formation of an oxazoline ring from an acyclic allylic and homoallylic amide having a benzoyl substituent as an N-protecting group. We would like to report here the stereoselective synthesis of oxazine ring from *trans*-oxazoline. The most significant point of this synthesis is that it is based on the oxazine ring formation in palladium(0) catalyzed condition.

After a few unsuccessful trial, we could find the right combination of reaction sequence and achieved (+)-polyoxamic acid from oxazine.

[PD1-62] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthetic study of costunolide

Jeong JinHyun, Shin MinHwan^o

Department of Pharmaceutical Science Graduate School Kyung Hee University Seoul, Korea

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

Sumaila Abu^o, Jeong JinHyun, Shin DongHyok

College of Pharmacy, Kyung Hee Univ.

Costunolide, a sesquiterpene lactone is isolated from *Magnolia Sieboldii*. It is known to possess antitumour 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

Kim Myongjung^o, Chung SoonYong, Liang ChengWu, Chun MoonWoo

College of Pharmacy, Seoul National University, Seoul 151-742, Korea

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

Kim MyongJung^o, Lee JiYoung, Shin JiHye, Chun MoonWoo