

hydroxyl moiety but also the stability of carbocation intermediate affect the diastereoselectivity and established that our CSI reaction is a competitive reaction of  $S_N1$  and  $S_N2$  reaction according to the stability of carbocation intermediate. Namely, the less stable the carbocation intermediate, the greater is the proportion of  $S_N2$  reaction (retention of configuration). And, the more stable the carbocation intermediate, the proportion of the  $S_N1$  reaction (racemisation) increases.

[PD1-28] [ 04/18/2003 (Fri) 13:30 – 16:30 / Hall P ]

**A new synthesis route to nucleoside: Two-directional synthesis of carbocyclic nucleoside using double [3,3]-sigmatropic rearrangement and double RCM**

Jihee Kim<sup>o</sup>, Zhe Fang, Kwan Woo Kim, Joon Hee Hong

College of Pharmacy, Chosun University, Kwangju 501-759, Korea

Extensive efforts in the search of therapeutically useful carbocyclic nucleosides have resulted in a wealth of their synthetic methodologies in racemic and optically active forms. The classical one-directional methods such as linear synthesis and convergent synthesis are the approaches most frequently seen in the literature for the preparation of carbocyclic nucleosides, and their advantages and limitations are well known. The other strategy, two-directional synthesis by simultaneously homologation, has received considerable attention over the last few years. When applied to appropriate target molecules, namely those with a significant element of symmetry, this strategy offers a highly efficient synthetic route to stereochemically pure products in relatively few steps, compared with the one-directional strategy. Although several efficient synthetic procedures for nucleosides have been developed on the basis of one-directional strategy, no attempt has been made for the preparation of nucleosides using more efficient two-directional strategy thus far. In this conference, we would like to disclose the pioneering synthetic example of carbocyclic nucleoside with use of the two-directional synthetic strategy by simultaneous homologation starting from C2-symmetric chiral template.

[PD1-29] [ 04/18/2003 (Fri) 13:30 – 16:30 / Hall P ]

**The Structure-Activity Relationship of Mansonone F, a Potent Anti-MRSA Sesquiterpenoid Quinone: Insights into Minimum Structural Requirements and SAR of C3 position**

Jung JongWha<sup>o</sup>, Shin DongYun, Chae JungHyun, Hyun SoonSil, Suh YoungGer

College of Pharmacy, Seoul National University, San 56-1, Shinrim-Dong, Kwanak-Gu, Seoul 151-742

The resistances to multiple antibiotics of strains of Gram-positive Staphylococci, methicillin-resistant Staphylococcus aureus (MRSA), are now significant clinical problem. One of the major efforts of our laboratory has been the search and design and synthesis of novel lead compound for the purpose of obtaining highly potent anti-MRSA drug. Towards this end, we have recently reported the isolation of a potent anti-MRSA sesquiterpenoid ortho-quinone, mansonone F, from the Korean medicinal plant which has traditionally been used to treat infectious diseases. It has been shown to have antibacterial activities against Gram-positive bacteria and, in particular, MRSA (with an MIC<sub>90</sub> of 2 mg/ml in vitro), comparable to vancomycin. For the identification of pharmacophore and our systemic investigation into the relationship between the structures of quinoid compounds based on the natural product mansonone F and

their anti-MRSA activities, we have synthesized 20 derivatives and screened their anti-MRSA activities.

We herein present the syntheses and anti-MRSA activities of the mansonone F derivatives, prepared to probe the minimal structural requirements for anti-MRSA activities, and SAR at C-3 substituents (mansonone numbering)

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

### Design, Synthesis and Biological Activities of Novel Vanilloid Receptor Antagonists

Suh YoungGer, Lee BoYoung<sup>o</sup>, Lee YongSil, Min KyungHoon, Kim JinKwan, Seung HoSun, Park YoungHo

College of Pharmacy, Seoul National University, Shinlim-Dong, san 56-1, Kwanak-Gu, Seoul, Korea; Pacific R&D Center, 314-1, Bora-Ri, Kiheung-Eup, Yongin-Si, Kyonggi-Do 449-900, Korea.

Advances in understanding of pain and analgesia have been made. Over the past few years, we have designed and synthesized a series of VR agonists, based on the structures of 12-HPETE and capsaicin, the natural VR agonist. But for the development of analgesic drugs, these synthetic VR agonists had problems like burning sensation, hypothermia, etc. So our recent studies have focused on designs and syntheses of VR antagonists based on the structure of capsaicin (natural VR agonist), and capsazepine (synthetic VR antagonist).

In particular, we focused on the lipophilic region. The derivatives which have benzene rings in lipophilic regions showed better activities than alkyl chain derivatives. So, we here present the designs and syntheses of the VR antagonists, which have benzene ring moieties in lipophilic regions.

[PD1-31] [ 04/18/2003 (Fri) 13:30 - 16:30 / Hall P ]

### Synthesis of Novel Alkyl $\alpha$ -Anilinophenylacetate Derivatives Using Hydrolysis of Hydantoin Ring and Its O-Alkylation

Park HaeSun<sup>o</sup>, Park MyungSook, Choi HeeJeon, Kwon SoonKyoung

College of Pharmacy, DukSung Women's University

For the development of new synthetic method for unnatural amino acid esters, alkyl  $\alpha$ -anilinophenylacetates were synthesized through base-catalyzed hydrolysis of 1,5-diphenylhydantoins in methanol and O-alkylation of sodium  $\alpha$ -anilinophenylacetate with alkyl halides in DMF. Even though hydrolysis of hydantoin ring was undertaken under about 30-40°C in methanol, the hydantoic acid sodium salt was continuously converted to the sodium  $\alpha$ -anilinophenylacetate. We used sodium hydroxide as base for the clear one-pot reaction, because various intermediate such as hydantoic acid and ureas were isolated by using triethylamine.

Hydantoin compounds with diaryl substituted moiety at 1- and 5-position decreased resistance toward hydrolysis even though opposite results reported in the literature.

All synthetic process from hydantoin to alkyl  $\alpha$ -anilinophenylacetates could be carried out in one-pot without isolation of intermediates. Hydrolysis with concentrated aqueous and alcoholic alkali is an important synthetic method, gives unnatural  $\alpha$ -amino acids.