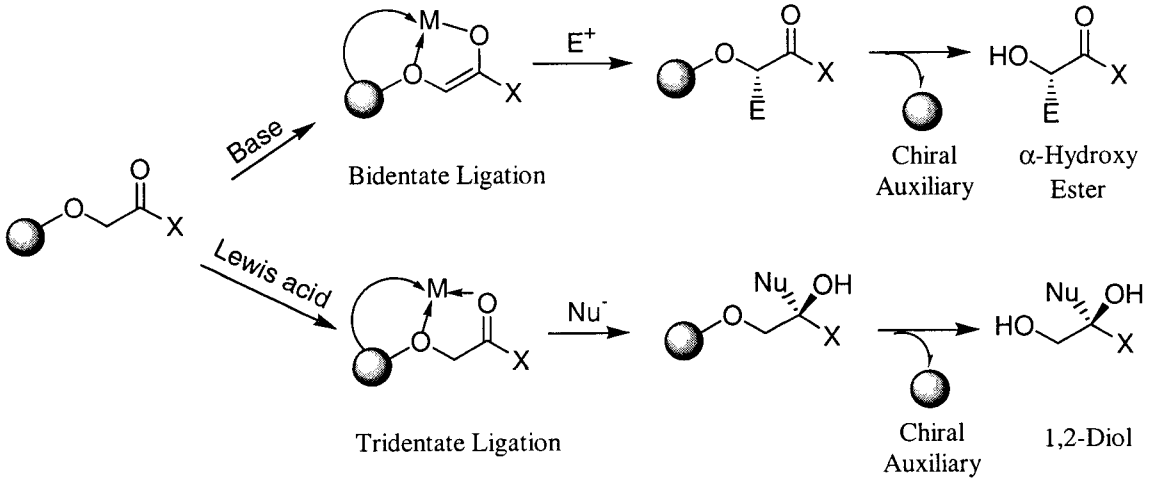
[S1-4] [4/18/2002(Thur) 16:30-17:00/Hall A]

Chelation-controlled Asymmetric Alkylation and it's Application

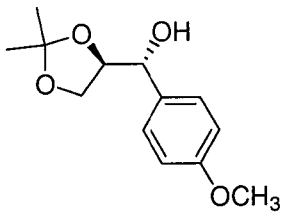
Ju Eun Jung, Hyun Joo Rhee, Young Kyo Kim, Hee-Young Beom and Hee-Doo Kim*

College of pharmacy, Sookmyung Women's University,
Chungpa-dong, Yongsan-ku, Seoul 140-742, Korea

A widespread use of α-hydroxy ester and 1,2-diol as chiral synthons in organic synthesis has grown collaterally with advance in methodology for their asymmetric synthesis. Herein, we present the highly stereoselective method for α-hydroxy esters[1] and 1,2-diol featuring chelation-controlled asymmetric alkylation of chiral glycolate or α-hydroxyketones, in which the chiral auxiliary is attached to the hydroxyl group as ether linkage.

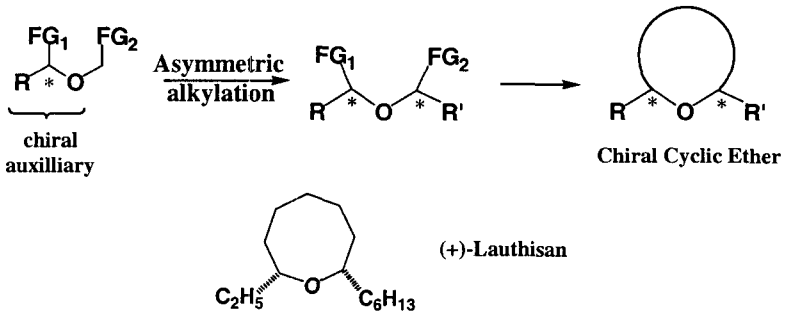


(*S*)-[(*4R*)-2,2-Dimethyl-1,3-dioxolan-4-yl](4-methoxyphenyl)methanol was designed as a novel chiral auxiliary for the construction of highly organized polycyclic ring complexes during chelation. Design, synthesis, and mechanism for this asymmetric induction will be discussed.



As part of our ongoing project to explore the use of our chiral auxiliary in asymmetric synthesis, we have also tried to synthesize the marine natural product (+)-lauthisan as a chiral cyclic ether. Our underlined concept for the synthesis of this chiral cyclic ethers is that chiral auxiliary, usually destined to be removed after chiral induction, is designed to play a dual role as both a chiral inducer and a latent functionality for cyclic ethers.

Scheme 2



The starting D-glyceraldehyde acetonide was converted into(5R)-ethyl-(3S)-hexyl-(6R) -hydroxymethyl-[1,4]dioxan-2-onein7steps*via*bidentatechelationcontrolledasymmetricalkylation Then, the dioxanone was transformed in 5 steps *via* radical allylation and Wittig olefination to the requisite diene for ring closing metathesis. The diene was exposed to Grubbs catalyst to produce 8-membered oxocane possessing the all-carbon framework of the target natural product. Chemical modification of the oxocane ring under conventional conditions completed the total synthesis of (+)-lauthisan..Furtherstudiesontheapplicationoftheseresultstotargetorientedsynthesisarecurrently under investigation.

References

1. Ju Eun Jung, Hyunsoon Ho and Hee-Doo Kim, Bidentate Chelation-controlled Asymmetric Synthesis of alpha-Hydroxy Esters Based on the Glycolate Enolate Alkylations, *Tetrahedron Letters*, 41, 11, 1793-1796 (2000).
2. Hee-Doo; Rhee, HyunJoo; Ryu, Chong Hyon; Nam, Hui-Sun, Asymmetric synthesis of (+)-Lauthisan. Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002 (2002), ORGN-090.