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First Catalytic and Enantioselective Synthesis of Silyl and Stannyl Substituted Cyclopropylmethanols

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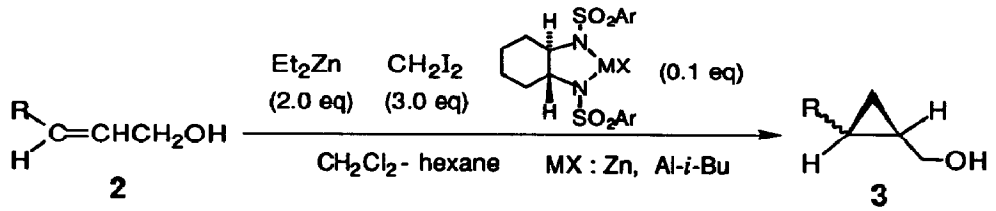
Abstract: *Optically active silyl and stannyl substituted cyclopropylmethanols were effectively obtained by the catalytic and enantioselective cyclopropanation of γ-silyl and γ-stannyl substituted allylic alcohols with Et_2Zn and CH_2I_2 in the presence of chiral N,N'-bis(p-nitrobenzenesulfonyl)-1,2-cyclohexanediamine in good enantioselectivites. The absolute configurations of the resulting metallocyclopropanes were unambiguously established.*

Although silyl and stannyl substituted cyclopropanes have been recognized to exhibit an interesting reactivity,[2] these metallocyclopropanes have not been fully utilized in organic synthesis.[3] Since stereospecific replacement of silyl and stannyl group on cyclopropane skeleton by other functional groups might be possible, the development of practical route to chiral metallocyclopropanes would expand the scope of this class of compounds as valuable synthetic intermediates. However, there have been no precedent for the enantioselective method for the synthesis of metallocyclopropanes. Ukaji and Inomata recently reported the first enantioselective preparation of chiral silyl substituted cyclopropanes with high enantiomeric excesses.[4] This method, however, requires the stoichiometric amount of diethyl tartrate as a chiral auxiliary, and the catalytic version has not yet been developed.

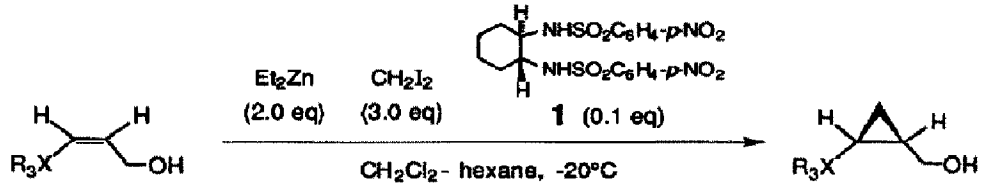
We have recently reported the first catalytic and enantioselective Simmons-Smith reaction of an allylic alcohol in the presence of chiral disulfonamide-modified zinc or aluminum complex[5] (Scheme 1). As one of the applications of the methodology, we examined the cyclopropanation of γ-silyl and γ-stannyl allylic alcohols. Preliminary results are described below.

Scheme 1



Initially, Simmons-Smith reaction of (*Z*)-allylic alcohols (**2a**[3] and **2b**[6]) was examined (Scheme 2). Thus, cyclopropanation of (*Z*)-3-tributylstannyl-2-propen-1-ol (**2a**) with Et_2Zn (2 equiv.) and CH_2I_2 (3 equiv.) was carried out in the presence of a catalytic amount of (1*R*,2*R*)-*N*,*N*'-bis(*p*-nitrobenzenesulfonyl)-1,2-cyclohexanediamine[7] (**1**, 0.1 equiv.) to obtain the corresponding *cis*-stannyl cyclopropane **3a**[8] in 75% yield. The absolute configuration and enantiomeric excess of the resulting **3a** were determined to be 2*S*,3*S* and 66% e.e., respectively, by the comparison of its specific rotation ($[\alpha]_D^{20}$ +6.3° (*c* 0.95, $CHCl_3$)) with that in literature.[9] Similarly, (*Z*)-3-dimethylphenylsilyl-2-propen-1-ol (**2b**) was subjected to cyclopropanation to give the corresponding silyl substituted cyclopropylmethanol **3b**[10] ($[\alpha]_D^{20}$ +4.8° (*c* 1.75, $CHCl_3$)) in 67% yield.

Scheme 2



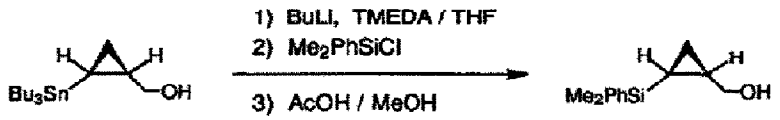
2a: R_3X = Bu_3Sn
2b: R_3X = Me_2PhSi

3a (2*S*,3*S*): R_3X = Bu_3Sn; 75%, 66% e.e. $[\alpha]_D^{20}$ +6.3° (*c* 0.95, $CHCl_3$)

3b (2*S*,3*S*): R_3X = Me_2PhSi; 67%, 59% e.e. $[\alpha]_D^{20}$ +4.8° (*c* 1.75, $CHCl_3$)

The absolute configuration and enantiomeric excess of **3b** were determined as follows: The stannyl cyclopropane (2*S*,3*S*)-**3a** (66% e.e.) was converted to the silyl cyclopropane (2*S*,3*S*)-**3b** in 88% yield by the reaction with BuLi (2 equiv.), *N*,*N*,*N*',*N*'-tetramethylethylenediamine (TMEDA, 2.4 equiv.), and $Me_2PhSiCl$ (2 equiv.) in THF followed by treatment of the silyl ether with AcOH in MeOH (Scheme 3). The resulting (2*S*,3*S*)-**3b** showed the $[\alpha]_D^{20}$ value of +5.4° (*c* 1.45, $CHCl_3$), therefore, the absolute configuration of **3b** obtained by cyclopropanation of **2b** was established as 2*S*,3*S* with 59% e.e.[11]

Scheme 3



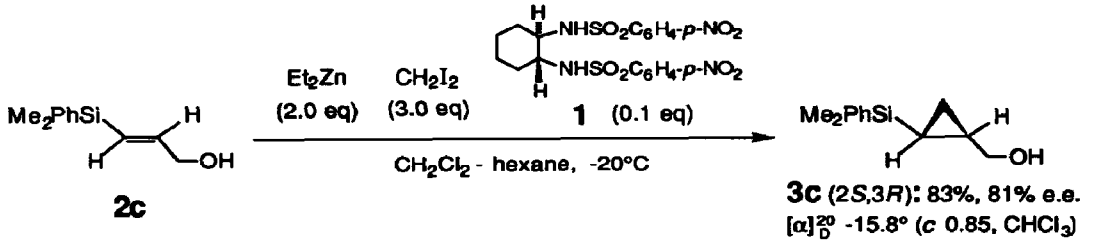
(2*S*,3*S*)-**3a** (66% e.e.)

(2*S*,3*S*)-**3b** (66% e.e.) $[\alpha]_D^{20}$ +5.4° (*c* 1.45, $CHCl_3$)

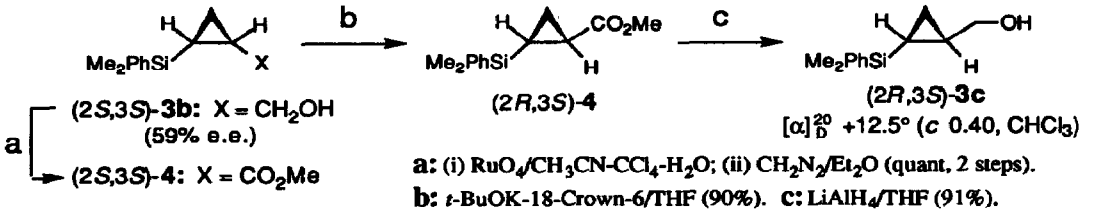
Next, cyclopropanation of (*E*)-allylic alcohols was examined. Cyclopropanation of (*E*)-3-dimethylphenylsilyl-2-propen-1-ol (**2c**) under the same conditions gave **3c**[12] ($[\alpha]_D^{20}$ -15.8° (*c* 0.85, $CHCl_3$)) in 83% yield (Scheme 4). The enantiomeric excess of the product **3c** was determined to be 81% e.e. by HPLC analysis using a Diecel OD column with 5% *i*-PrOH in hexane as an eluent (Rt: 8 min for the major enantiomer and 14 min for the minor one). The absolute configuration of **3c** was unambiguously established to be 2*S*,3*R* by comparison with the authentic 2*R*,3*S*-**3c**, prepared from the stereochemically established *cis*-silyl cyclopropane (2*S*,3*S*)-**3b** as shown in Scheme 5. Thus, (2*S*,3*S*)-**3b** (59% e.e.) was transformed to methyl (2*S*,3*S*)-3-dimethylphenylsilyl-2,3-methanopropionate ((2*S*,3*S*)-**4**, $[\alpha]_D^{20}$ -41.9° (*c* 0.96, $CHCl_3$)) by oxidation

with RuO_4 in MeCN-CCl_4-H_2O and treatment with CH_2N_2 in Et_2O. The (2*S*,3*S*)-**4** was easily isomerized to the thermodynamically more stable *trans*-silyl cyclopropane (2*R*,3*S*)-**4**, and the latter was reduced with $LiAlH_4$ in THF to afford (2*R*,3*S*)-**3c** ($[\alpha]_D^{20}$ +12.5° (*c* 0.40, $CHCl_3$), 62% e.e. from HPLC analysis using Daicel OD column) which was found to be enantiomeric with **3c** produced by the cyclopropanation of **2c** shown in Scheme 4.

Scheme 4

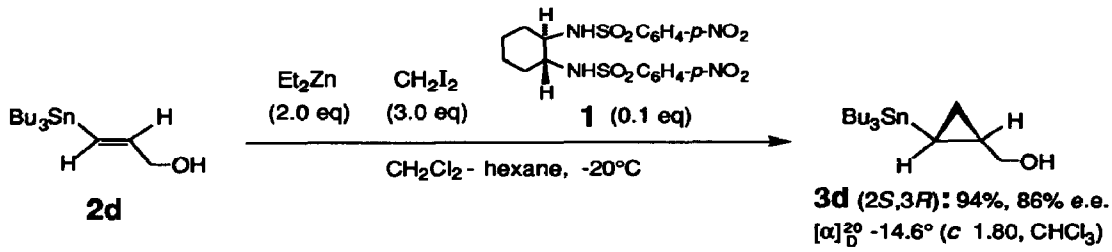


Scheme 5



Finally, cyclopropanation of (*E*)-3-tributylstannyl-2-propen-1-ol (**2d**) was also carried out to give the *trans*-stannyl cyclopropane **3d**[13] in 94% yield (Scheme 6). The enantiomeric excess and the absolute configuration of **3d** were determined to be 86% e.e. and 2*S*,3*R*, respectively, after correlating to the silyl cyclopropane **3c** ($[\alpha]_D^{20}$ -17.4° (*c* 1.49, $CHCl_3$)) by the similar procedure for the conversion of **3a** to **3b** shown in Scheme 3.

Scheme 6



In conclusion, γ-silyl and γ-stannyl substituted allylic alcohols underwent a catalytic and enantioselective Simmons-Smith reaction to obtain the corresponding metallocyclopropylmethanols with good to high enantiomeric excesses.[14] It should also be noted that the sense of enantiofacial selection in the present cyclopropanation utilizing disulfonamide-modified zinc complex is the same as observed in the conventional allylic alcohols reported previously.[5a,b]

A typical procedure of the catalytic and enantioselective cyclopropanation is as follows:

(2*S*,3*R*)-2,3-methano-3-(tributylstannyl)propan-1-ol (3d). To a colorless clear solution of **2d** (1.48g, 4.25mmol, 1 equiv.) and **1** (206mg, 0.43mmol, 0.1 equiv.) in 120mL of anhydrous CH_2Cl_2 were added dropwise at -50°C a solution of Et_2Zn in hexane (1.0M, 8.51mL, 8.51mmol, 2 equiv.) and CH_2I_2 (1.03mL, 12.8mmol, 3 equiv.). The mixture was stirred for 22 h at -20°C, quenched at -20°C with 4mL of Et_3N, diluted with 240mL of Et_2O, washed with 40mL of brine, and dried over $MgSO_4$. After removal of the solvent, the residue was chromatographed on silica gel with a 1:4 mixture of EtOAc and hexane to afford 1.45g (94% yield, $[\alpha]_D^{20}$ -14.6°(*c* 1.80, $CHCl_3$)) of **3d** as a colorless oil.

References and Notes

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6. (*Z*)-3-Dimethylphenylsilyl-2-propen-1-ol (**2b**) was prepared from **2a** in quantitative yield by reaction with BuLi (2 equiv.), TMEDA (2.4 equiv.), and $Me_2PhSiCl$ (2 equiv.) followed by treatment with AcOH in MeOH.
7. Takahashi, H.; Kawakita, T.; Ohno, M.; Yoshioka, M.; Kobayashi, S. *Tetrahedron* **1992**, *48*, 5691.
8. **3a**: ^{1}H-NMR (400MHz, $CDCl_3$): δ= -0.07~-0.04 (1H, m, CHSn), 0.17~0.23 (1H, m, CH_A of cyclopropane), 0.71~0.81 (1H, m, CH_B of cyclopropane), 0.81~0.87 (6H, m, CH_2Sn x 3), 0.89 (9H, t, J= 7.3 Hz, CH_3 x 3), 1.24~1.62 (14H, m, $C\underline{H}_2C\underline{H}_2CH_2Sn$ x 3, $C\underline{H}CH_2O\underline{H}$), 3.21~3.29 (1H, m, $C\underline{H}_AOH$), 3.52~3.60 (1H, m, $C\underline{H}_BOH$).
9. $[\alpha]_D^{19}$ +9.52° ($CHCl_3$) for resolved (2*S*,3*S*)-**3a**. Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1984**, *25*, 2415.
10. **3b**: ^{1}H-NMR (400MHz, $CDCl_3$): δ= 0.01 (1H, dt, J= 7.6, 9.5 Hz, CHSi), 0.28~0.34 (1H, m, CH_A of cyclopropane), 0.32 (6H, s, CH_3 x 2), 0.93~0.98 (1H, m, CH_B of cyclopropane), 1.06 (1H, t, J= 5.8 Hz, OH), 1.37~1.46 (1H, m, $C\underline{H}CH_2OH$), 3.33~3.39 (1H, m, $C\underline{H}_AOH$), 3.41~3.48 (1H, m, $C\underline{H}_BOH$), 7.35~7.39, 7.56~7.60 (3H, 2H, m, m, C_6H_5).
11. Enantiomeric excess of **3b** was determined by the specific rotation value. HPLC analyses (Daicel OD, OJ, AS, or AD column) were unsuccessful because a clean base-line separation was not observed under various conditions.
12. **3c**: ^{1}H-NMR (400MHz, $CDCl_3$): δ= -0.27 (1H, dt, J= 6.6, 10.1 Hz, CHSi), 0.21, 0.22 (3H, 3H, s, s, CH_3 x 2), 0.50~0.59 (2H, m, CH_2 of cyclopropane), 1.04~1.13 (1H, m, $C\underline{H}CH_2OH$), 1.27 (1H, brs, OH), 3.50 (2H, brs, $C\underline{H}_2OH$), 7.34~7.38, 7.52~7.58 (3H, 2H, m, m, C_6H_5).
13. **3d**: ^{1}H-NMR (400MHz, $CDCl_3$): δ= -0.39~-0.28 (1H, m, CHSn), 0.50~0.55 (2H, m, CH_2 of cyclopropane), 0.78~0.84 (6H, m, CH_2Sn x 3), 0.89 (9H, t, J= 7.3 Hz, CH_3 x 3), 1.04~1.13 (1H, m, $C\underline{H}CH_2OH$), 1.25~1.36, 1.44~1.59 (6H, 7H, m, m, $C\underline{H}_2C\underline{H}_2CH_2Sn$ x 3, OH), 3.35~3.44 (1H, m, $C\underline{H}_AOH$), 3.51~3.60 (1H, m, $C\underline{H}_BOH$).
14. Cyclopropanation of **2c** in the presence of chiral aluminum complex[5b] (0.1 equiv.) prepared from (1*R*,2*R*)-*N*,*N*'-bis(benzenesulfonyl)-1,2-cyclohexanediamine and DIBAL also proceeded to obtain (2*S*,3*R*)-**3c** with 60% e.e.

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