J. Chem. Research (S), 1998, 450–451†

First Synthesis of (+)-5α-Hydroxy-β-selinene and (−)-5β-Hydroxy-β-selinene†

Zhaoming Xiong, Gang Zhou, Yonggang Chen and Yulin Li*

National Laboratory of Applied Organic Chemistry and Institute of Organic Chemistry, Lanzhou University, Lanzhou 730000, P.R. China

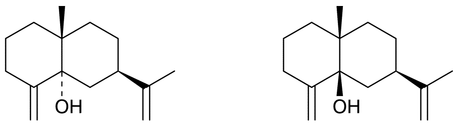
A facile and efficient synthesis of (+)-5α-hydroxy-β-selinene **1** and (−)-5β-hydroxy-β-selinene **2** starting from (+)-dihydrocarvone has been carried out.

Eudesmane derivatives have drawn considerable attention owing to their wide spectrum of biological properties, particularly antifeedant, cell growth inhibitory and plant growth regulating activities.[1–3]

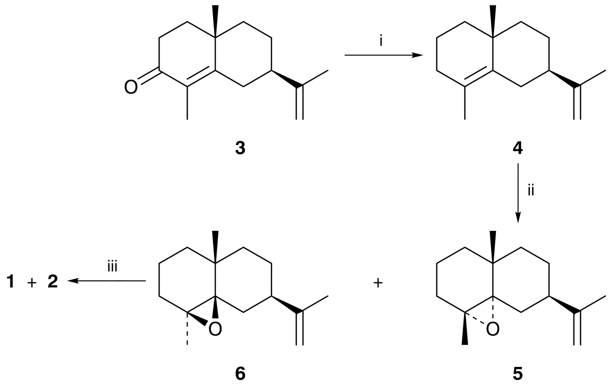
Recently, two epimeric eudesmane derivatives, (+)-5α-hydroxy-β-selinene (**1**) and (−)-5β-hydroxy-β-selinene (**2**), were isolated[4] from the aerial parts of *C. Subtrapica F. Mell.*, and their structures were determined by spectroscopic methods. Herein we report a facile synthesis of both diastereomers, **1** and **2**, from (+)-dihydrocarvone in five steps, using regioselective epoxidation of diene **4** as a key reaction.

Our synthesis began with (+)-dihydrocarvone. By the published method,[5] (+)-α-cyperone **3** was easily prepared from (+)-dihydrocarvone by a two-step procedure, using (*R*)-(+)-α-phenylethylamine as chiral auxiliary (Scheme 1). Deoxygenation[6] of (+)-α-cyperone **3** with $AlCl_2H$[7] gave diene **4** in 85% yield. The purity of **4** was 95% as determined by gas chromatography. Dichloroaluminium hydride was first reported[7] in 1964 for the deoxygenation of α,β-unsaturated carbonyls and allylic alcohols. But its use is seldom reported.[6] We think this may be owing to the undesired side reactions caused by allylic cation intermediates formed in the reduction.[7] Our experimental results suggest that $AlCl_2H$ may be a good reducing reagent for the deoxygenation of particular α,β-unsaturated carbonyls.

Regioselective epoxidation[8] of the electron-rich tetrasubstituted $C^4{=}C^5$ double bond in diene **4** with mCPBA at 0 °C gave a mixture of epimeric epoxides, **5** and **6** (2:1). The ratio of **5** to **6** was estimated by the integration of the 10-methyl protons in the ^1H NMR spectrum of the mixture. On consideration of the steric effect of the 10-methyl group in the epoxidation of **4**, the structures of epoxides **5** and **6** are assigned as 4α,5α-epoxide and 4β,5β-epoxide, respectively. The assignments are also confirmed by the subsequent rearrangements of epoxides to the title compounds. It is a pity that epoxides **5** and **6** cannot be seperated by flash column chromatography on silica gel. The mixture of **5** and **6** was treated with lithium diisopropylamide (LDA) in diethyl ether to afford allylic alcohol **1** in 60% yield and **2** in 32% yield, which can be easily seperated by flash column chromatography. The spectral data of the synthetic products are consistent with **1** and **2**, and also match those of the natural products.[4]



1 **2**



Scheme 1 *Reagents and conditions*: i, $AlCl_2H$, diethyl ether, room temperature, 3 h; ii, mCPBA, CH_2Cl_2, 0 °C, 2 h; iii, LDA, diethyl ether, room temperature, 24 h

Experimental

For column chromatography, 200–300 mesh silica gel and light petroleum (60–90 °C) were used. IR spectra were recorded on a Nicolet FT-170SX as liquid films. ^1H NMR spectra were measured on Bruker AM-400 spectrometers with Me_4Si as an internal standard and $CDCl_3$ as solvent. Mass spectra were determined on a V.G. ZAB-HS spectrometer (EI, 70 eV). Elemental analyses were performed on an Italian 1106 analyser.

7β,10β-Selina-4,11-diene **4**.—To a solution of $AlCl_2H$ (1 M in diethyl ether, 18 mL) was added a solution of (+)-α-cyperone (200 mg) in dry diethyl ether (5 mL) under argon in an ice–salt bath. After stirring at room temperature for 3 h, the reation mixture was poured into crushed ice. The organic layer was separated and the aqueous layer was extracted with diethyl ether (2 × 20 mL). The combined organic fractions were washed with water (2 × 10 mL), sat. aq. $NaHCO_3$ (2 × 10 mL) and brine (2 × 10 mL) and dried ($MgSO_4$). After removal of the solvents, the oily residue was chromatographed on silica gel using light petroleum (30–60 °C) as eluent to afford diene **4** (160 mg, 85%) as a colourless oil; ν_{max}/cm^{-1} 3078, 1642, 1451, 1373, 882; δ_H 1.06 (s, 3 H, 10-Me), 1.62 (s, 3 H, 4-Me), 1.77 (s, 3 H, 11-Me), 2.56 (br d, *J* 11.8 Hz, 1 H), 4.72 (br t, *J* 1.0 Hz, 1 H, 12-H), 4.74 (br s, 1 H, 12-H): *m/z* 204 (M^+, 46%), 189 (100), 161 (20), 147 (31), 133 (74), 119 (24), 105 (52), 91 (60).

Epoxidation of 7β,10β-Selina-4,11-diene **4**.—A mixture of diene **4** (100 mg), $NaHCO_3$ (100 mg) and mCPBA (70%, 120 mg) in CH_2Cl_2 was stirred at 0 °C for 2 h. The reaction mixture was then diluted with ether (20 mL), washed successively with 10% aq. Na_2SO_3 (2 × 10 mL), 5% aq. NaOH (2 × 10 mL), water (2 × 10 mL), and brine (2 × 10 mL) and dried ($MgSO_4$). After removal of the solvents, the oily residue was chromatographed on silica gel, eluting with light petroleum/diethyl ether (15:1) to give a mixture of epoxides **5** and **6** as colourless oils (90 mg, 84%). Spectral data of a mixture of **5** and **6**: ν_{max}/cm^{-1} 3078, 1644, 1456, 1376, 887; δ_H 1.06 (s, 1 H, 10-Me for **6**), 1.07 (s, 2 H, 10-Me for **5**), 1.25 (s, 2 H, 4-Me for **5**), 1.33 (s, 1 H, 4-Me for **6**), 1.74 (s, 3 H, 11-Me for **5** and **6**), 4.71 (br, s, 2 H, 12-H for **5** and **6**); *m/z* 220 (M^+, 7%), 205 (5), 202 (9), 187 (6), 177 (6), 162 (19), 147 (12), 135 (27), 119 (33), 107 (74), 91 (35), 79 (54), 5 (48), 43 (100).

(+)-5α-Hydroxy-β-selinene **1** *and (−)-5β-Hydroxy-β-selinene* **2**.—To a freshly prepared solution of LDA (0.5 M in diethyl ether, 6 mL) was added a solution of epoxides **5** and **6** (40 mg) in dry

---

*To receive any correspondence (*e-mail:* liyl@lzu.edu.cn).

†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

diethyl ether (4 mL) under argon. The reaction mixture was stirred at room temperature for 24 h. Subsequently water was added to the reaction mixture at 0 °C, and stirring was continued for an additional 10 min. The organic layer was separated and the aqueous layer was extracted with diethyl ether (2 × 20 mL). The combined organic fractions were washed with 5% aq. HCl (2 × 10 mL), sat. aq. $NaHCO_3$ (2 × 10 ml) and brine (2 × 10 ml) and dried ($MgSO_4$). After removal of the solvents, the crude products were chromatographed on silica gel, eluting with light petroleum/diethyl ether (8:1) to yield **1** (24 mg, 60%) and **2** (13 mg, 32%) both as colourless oils. **1**: (Found: C, 81.50; H, 10.79. $C_{15}H_{24}O$ requires C, 81.76: H, 10.98%); $[\alpha]^8{}_D$+125.9 (*c* 0.72, $CHCl_3$); ν/cm^{-1} 3446, 3081, 1644, 1446, 1376, 894; δ_H 0.88 (s, 3 H, 10-Me), 1.76 (s, H, 11-Me), 2.52 (m, 1 H), 2.58 (dt, *J* 13.2, 6.4 Hz, 1 H), 4.69 (br s, 1 H), 4.73 (br s, 1 H), 4.75 (br s, 1 H), 4.82 (br s, 1 H); *m/z* 220 (M$^+$, 7%). 205 (23), 202 (29), 187 (67), 137 (20), 109 (31), 107 (30), 95 (57), 43 (100). **2**: (Found: C, 81.63; H, 11.14. $C_{15}H_{24}O$ requires C, 81.76; H, 10.98%) $[\alpha]^8{}_D$ −95.2 (*c* 0.32, $CHCl_3$); ν/cm^{-1} 3438, 3084, 2930, 1447, 887; δ_H 1.05 (s, H, 10-Me), 1.76 (s, 3 H, 11-Me), 4.73 (br s, 1 H), 4.75 (br s, 1 H), 4.95 (br s, 2 H); *m/z* 220 (M$^+$, 13%), 205 (19), 202 (14), 187 (28), 169 (44), 162 (22), 135 (36), 125 (43), 109 (42), 95 (61), 81 (48), 67 (54), 55 (61), 41 (100).

We are grateful for financial support from the National Natural Science Foundation of China (Grant No. 29732060) and the National Laboratory of Elemento-Organic Chemistry at Nankai University (Tianjing, China).

Received, 10th March 1998; Accepted, 8th April 1998
Paper E/8/01951G

References

1 T. A. Van Beek and A. De Grot, *Recl. Trav. Chim. Pays-Bas*, 1986, **105**, 513.
2 V. J. Paul, J. M. Crown and J. H. Cardellina II, *J. Chem. Ecol.*, 1993, **19**, 1847.
3 M. Ando, K. Isogai, H. Azami, N. Hirata and Y. Yanagi, *J. Nat. Prod.*, 1991, **54**, 1017.
4 J. Jakupovic, L. Lehmann, F. Bohlmann, R. M. King and H. Robinson, *Phytochemistry*, 1988, **27**, 3831.
5 Z. M. Xiong, J. Yang and Y. L. Li, *Tetrahedron Asymmetry*, 1996, **7**, 2607.
6 For reviews of the deoxygenation of carbonyl compounds, see (*a*) S. Yamamura and S. Nishiyama, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, New York, 1991, vol. 8, p. 307; (*b*) R. O. Hutchins and M. K. Hutchins, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, New York, vol. 8, p. 327.
7 J. H. Brewster and H. O. Bayer, *J. Org. Chem.*, 1964, **29**, 105; 116.
8 For a review of the epoxidation of alkenes, see A. S. Rao, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, New York, 1991, vol. 7, p. 357.