TOTAL SYNTHESIS OF FURANOEREMOPHILANES:

(±)-DECOMPOSITIN AND THE RELATED NATURAL PRODUCTS

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Abstract — Total synthesis of furanoeremophilanes, (±)-6β-hydroxy-1,10-dehydrofuranoeremophilan-9-one (1a), (±)-decompositin (1b), (±)-adenostylone (1c), (±)-dihydrodecompositin (16), and (±)-3β,6β-dipropionyloxyeuryopsin-9-one (2), starting from the diene adduct (3) are described. An angular hydroxylation of 10H-furanoeremophilan-9-one derivatives is a key step in these total synthesis.

In the previous papers, we reported the total synthesis of several 10H-furanoeremophilanes starting from the diene adduct (3). Introduction of a hydroxyl group at angular position (C-10) of 10H-furanoeremophilan-9-one derivatives have recently been reported by us using benzeneselenenic anhydride. In this communication, we wish to report the application of the angular hydroxylation to the total synthesis of furanoeremophilanes; (±)-6β-hydroxy-1,10-dehydrofuranoeremophilan-9-one (1a), (±)-decompositin (1b), (±)-adenostylone (1c), (±)-dihydrodecompositin (16), and (±)-3β,6β-dipropionyloxyeuryopsin-9-one (2).

Hydroxylation of 6,9-diketone (4) with benzeneselenenic anhydride gave 10β-hydroxy and 10α-hydroxy compound (5 and 6) in a 57% and 17% yield, respectively. Hydrolysis of 6 with aqueous acetic acid at room temperature for 10 hr gave 10α-hydroxy-4,6,9-trione (7), mp 257-260°, quantitatively [IR cm⁻¹: 3480 (OH), 1715, 1680 (CO); UV λEtOH max 303 nm; M⁺: m/z 276]. Hydroxy-trione (7) was acetylated with Ac₂O-pyridine-4-dimethylaminopyridine (DMAP) to give 10α-acetate (9), mp 178-181°, in a 92% yield [IR cm⁻¹: 1760, 1710 (CO), 1245 (COC)]. The acetate (9) was also prepared from 8, which was derived from 6, by hydrolysis. Treatment of 3,6,9-trione (9) with ethanedithiol in the presence of BF₃-OEt₂ at room temperature for 15
1 min gave the 3,3-dithioketal derivative (10), mp 186-187°, in a 91% yield [IR cm⁻¹: 1750, 1705 (CO), 1250 (COC); NMR δ: 1.94 (3H, s, COCH₃), 3.1-3.5 (4H, m, CH₂); M⁺: m/z 394]. Attempted reductive desulfurization of 10 with Raney nickel (W-2) in refluxing ethanol was examined. However, desulfurization and hydrogenolysis were occurred simultaneously to give 10α-furanoeremophilan-6,9-dione (11), mp 1690 (CO). Treatment of 10 with methanolic-K₂CO₃ at room temperature for 30 min gave a hydroxy compound (12), mp 218-221°, quantitatively [IR cm⁻¹: 3450 (OH), 1700, 1690 (CO)]. Reductive desulfurization of 12 with Raney nickel (W-2) in refluxing dioxane for 2 min afforded 90% yield of a mixture of 13 and dehydro compound (14) in a ratio of 1:1. Catalytic hydrogenation of the above mixture with 10% Pd-charcoal catalyst in AcOEt afforded 10α-hydroxy-6,9-dione (13), mp 189-190.5°, in a 97% yield [IR cm⁻¹: 3450 (OH), 1670 (C=C); UV λ max 314, 248, 226 nm; NMR δ: 6.99 (1H, t, J=4 Hz, 1-H); M⁺: m/z 244]. Reduction of 13 with NaBH₄ in methanol at 0° afforded (±)-6β-hydroxy-1,10-dehydrofuranoeremophilan-9-one (1a), oil, quantitatively [IR cm⁻¹: 3450 (OH), 1670 (C=C); UV λ max 304, 248 nm; NMR δ: 4.96 (1H, d, J=8 Hz, 6-H), 6.92 (1H, t, J=4 Hz, 1-H); M⁺: m/z 288]. The NMR spectrum of (±)-1a was in good agreement with that of (-)-1a, which was isolated from Senecio lanceus by Bohlmann et al.⁵ Acetylation of (±)-1a with Ac₂O-pyridine gave (±)-decompositin (1b), mp 145.5-147°, in a 85% yield [IR cm⁻¹: 1745, 1670 (CO), 1630 (C=C), 1240 (COC); UV λ max 300, 244.5 nm; NMR δ: 6.28 (1H, s, 6-H), 6.96 (1H, t, J=4 Hz, 1-H); M⁺: m/z 288]. The NMR, IR, and UV spectral data of (±)-1b were in good agreement with those of (+)-1b, which was isolated from Cacalia decomposita by Hahn et al.⁶a and Sorm et al.⁶b Treatment of (±)-1a with isobutyric anhydride-pyridine-DMAP at 40° for 4 hr afforded (±)-adenostylone (1c), mp 96-97° [IR cm⁻¹: 1745, 1675 (CO), 1630 (C=C), 1140 (COC); UV λ max 300 nm; NMR δ: 6.32 (1H, s, 6-H), 6.94 (1H, t, J=4 Hz, 1-H); mass: m/z 246 [M-(CH₃)₂C=CO]⁻]. The NMR, IR, and UV spectral data of (±)-1c were in good agreement with those of (-)-1c, which was isolated from Adenostyles alliariae by Sorm et al.⁶b Catalytic hydrogenation of (±)-1a with 10% Pd-charcoal in AcOEt gave (±)-dihydrodecompositin (1d), mp 137-138°, in a 86% yield [IR cm⁻¹: 1750, 1730, 1245 (CO); UV λ max 278.5 nm; NMR δ: 2.17 (3H, s, COCH₃), 6.29 (1H, s, 6-H); M⁺: m/z 290]. The NMR spectrum of (±)-1d was in good agreement with that of natural-1d, which was isolated from Euryops othonnoides by Bohlmann et al.⁷
Treatment of 3β-hydroxyfuranoeremophilane-6,9-dione (17) with propionic anhydride-pyridine at room temperature for 12 hr gave 3β-propionate (18), mp 113-115°, in a 91% yield. Hydroxylation of 18 with benzeneseleninic anhydride in refluxing toluene for 4 hr gave 10β-hydroxy compound (19; 59%, mp 123-125°) [IR cm⁻¹: 3420, 3280 (OH), 1735, 1690 (CO), 1230 (COC); M⁺: m/z 334] and 10α-hydroxy compound (20; 22%, mp 174-176°) [IR cm⁻¹: 3420 (OH), 1745, 1700, 1690, 1680 (CO), 1200 (COC); M⁺: m/z 334]. 10α-Hydroxy compound (20) was treated with thionyl chloride in pyridine at 0° for 10 min to afford 1,10-dehydro derivative (21), mp 152-154°, in a 91% yield. IR cm⁻¹: 1745, 1700, 1680 (CO), 1630, 1595 (C=C), 1190 (COC); UV λ<sub>max</sub> EthOH 313, 227 nm; NMR δ: 5.10 (1H, m, 3-H), 6.76 (1H, t, J=4 Hz, 1-H)]. Reduction of 21 with NaBH₄ in methanol gave 6β-hydroxy derivative (22), oil, stereoselectively in a quantitative yield. Treatment of 22 with propionic anhydride-pyridine in the presence of DMAP afforded (+)-3β,6β-dipropionyloxyeuryopsin-9-one (2), mp 83-85°, quantitatively [IR cm⁻¹: 1750, 1740, 1685 (CO), 1640, 1610 (C≡C), 1195 (COC); NMR δ: 1.04 (3H, d, J=7 Hz, 4-CH₃), 1.26 (3H, s, 5-CH₃), 5.04 (1H, m, 3-H), 6.35 (1H, s, 6-H), 6.71 (1H, t, J=4 Hz, 1-H); M⁺: m/z 374]. The NMR, IR, and mass spectral data of (+)-2 were in good agreement with those of natural-2, which was isolated from Euryops lateriflorus by Bohlmann et al. 8

ACKNOWLEDGMENT We thank Dr. Saito, Tanabe Seiyaku Co. Ltd., for micro analyses, and Miss Sawabe and Mrs. Hasegawa of this laboratory for spectral measurements. This work was supported in part by Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, and also the Foundation for the promotion of Research on Medicinal Research, which are gratefully acknowledged.

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Received, 30th July, 1980