

TOTAL SYNTHESIS OF FURANOEREMOPHILANES:

($\pm$)-DECOMPOSITIN AND THE RELATED NATURAL PRODUCTS¹

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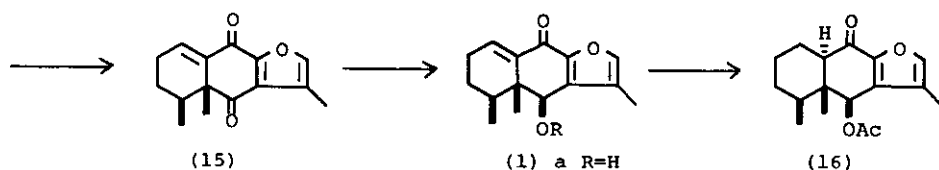
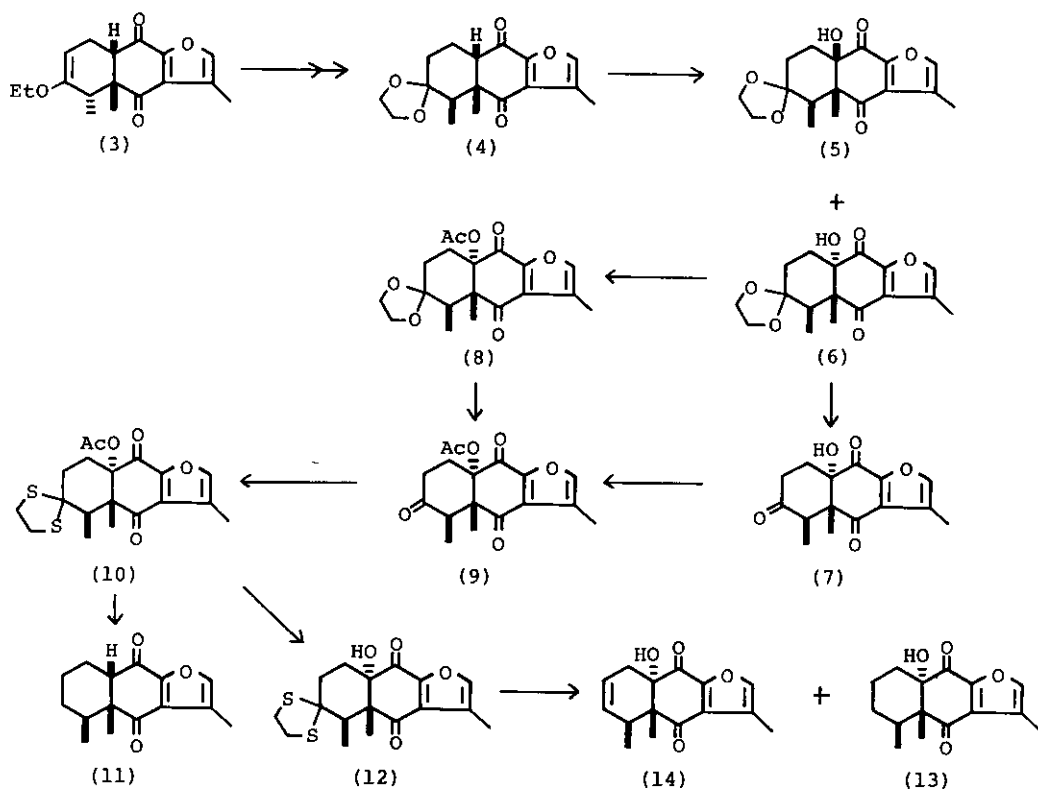
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Abstract — Total synthesis of furanoeremophilanes, ($\pm$)-6 β -hydroxy-1,10-dehydrofuranoeremophilan-9-one (1a), ($\pm$)-decompositin (1b), ($\pm$)-adenostylone (1c), ($\pm$)-dihydrodecompositin (16), and ($\pm$)-3 β ,6 β -dipropionyloxyeuryopsin-9-one (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.

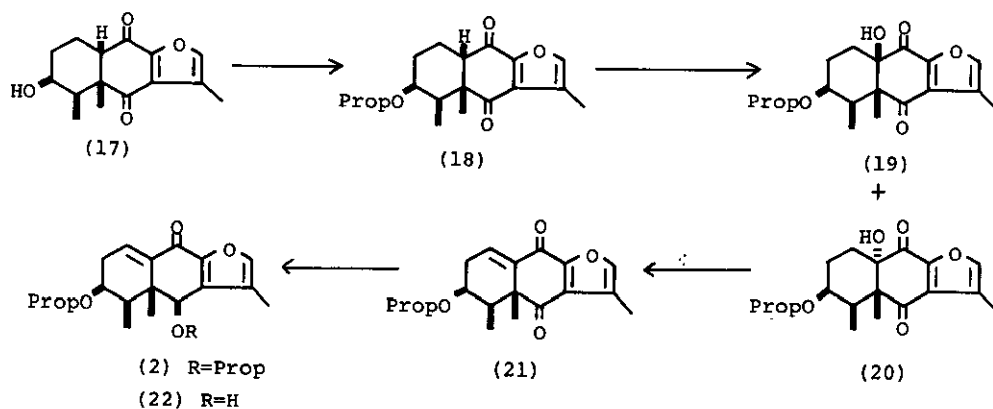
In the previous papers, we reported the total synthesis of several 10H-furanoeremophilanes starting from the diene adduct (3).^{2a-c} Introduction of a hydroxyl group at angular position (C-10) of 10H-furanoeremophilan-9-one derivatives have recently been reported by us using benzeneseleninic anhydride.³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

Hydroxylation of 6,9-diketone (4) with benzeneseleninic anhydride gave 10 β -hydroxy and 10 α -hydroxy compound (5 and 6) in a 57% and 17% yield, respectively.³ Hydrolysis of 6 with aqueous acetic acid at room temperature for 10 hr gave 10 α -hydroxy-3,6,9-trione (7), mp 257-260°, quantitatively [IR cm⁻¹: 3480 (OH), 1715, 1680 (CO); UV $\lambda_{\text{max}}^{\text{EtOH}}$ 303 nm; M⁺: m/z 276]. Hydroxy-trione (7) was acetylated with Ac₂O-pyridine-4-dimethylaminopyridine (DMAP) to give 10 α -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

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, COCH_3), 3.1-3.5 (4H, m, CH_2S); 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 10 β H-furanoeremophilan-6,9-dione (11),⁴ in a 54% yield. Treatment of 10 with methanolic- K_2CO_3 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 10 α -hydroxy-6,9-dione (13), mp 189-190.5°, in a 97% yield [IR cm^{-1} : 3480 (OH), 1690, 1675 (CO); M^+ : m/z 262]. Treatment of 13 with thionyl chloride in pyridine at 0° for 10 min gave 1,10-dehydro compound (15), mp 89-90°, in a 95% yield [IR cm^{-1} : 1700, 1680 (CO), 1630 (C=C); UV $\lambda_{\text{max}}^{\text{EtOH}}$ 314, 247, 226 nm; NMR δ : 6.99 (1H, t, $J=4$ Hz, 1-H); M^+ : m/z 244]. Reduction of 15 with NaBH_4 in methanol at 0° afforded ($\pm$)-6 β -hydroxy-1,10-dehydrofuranoeremophilan-9-one (1a), oil, quantitatively [IR cm^{-1} : 3450 (OH), 1670 (CO), 1630 (C=C); UV $\lambda_{\text{max}}^{\text{EtOH}}$ 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 246]. The NMR spectrum of ($\pm$)-1a was in good agreement with that of (-)-1a, which was isolated from Senecio lanceus by Bohlmann et al.⁵ Acetylation of ($\pm$)-1a with Ac_2O -pyridine gave ($\pm$)-decompositin (1b), mp 145.5-147°, in a 85% yield [IR cm^{-1} : 1745, 1670 (CO), 1630 (C=C), 1240 (COC); UV $\lambda_{\text{max}}^{\text{EtOH}}$ 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 ($\pm$)-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 ($\pm$)-1a with isobutyric anhydride-pyridine-DMAP at 40° for 4 hr afforded ($\pm$)-adenostylone (1c), mp 96-97° [IR cm^{-1} : 1745, 1675 (CO), 1630 (C=C), 1140 (COC); UV $\lambda_{\text{max}}^{\text{EtOH}}$ 300 nm; NMR δ : 6.32 (1H, s, 6-H), 6.94 (1H, t, $J=4$ Hz, 1-H); mass: m/z 246 [$M-(\text{CH}_3)_2\text{C}=\text{CO}$]⁺. The NMR, IR, and UV spectral data of ($\pm$)-1c were in good agreement with those of (-)-1c, which was isolated from Adenostyles alliariae by Sorm et al.^{6b} Catalytic hydrogenation of ($\pm$)-1a with 10% Pd-charcoal in AcOEt gave ($\pm$)-dihydrodecompositin (16), mp 137-138°, in a 86% yield [IR cm^{-1} : 1750, 1730, 1680 (CO), 1245 (COC); UV $\lambda_{\text{max}}^{\text{EtOH}}$ 278.5 nm; NMR δ : 2.17 (3H, s, COCH_3), 6.29 (1H, s, 6-H); M^+ : m/z 290]. The NMR spectrum of ($\pm$)-16 was in good agreement with that of natural-16, which was isolated from Euryops othonnoides by Bohlmann et al.⁷



a R=H
b R=Ac
c R=ⁱBut



(2) R=Prop
(22) R=H

Treatment of 3 β -hydroxyfuranoeremophilan-6,9-dione⁴ (17) with propionic anhydride-pyridine at room temperature for 12 hr gave 3 β -propionate (18), mp 113-115°, in a 91% yield. Hydroxylation of 18 with benzeneseleninic anhydride in refluxing toluene for 4 hr gave 10 β -hydroxy compound (19; 59%, mp 123-125°) [IR cm⁻¹: 3420, 3280 (OH), 1735, 1690 (CO), 1230 (COC); M⁺: m/z 334] and 10 α -hydroxy compound (20; 22%, mp 174-176°) [IR cm⁻¹: 3420 (OH), 1745, 1700, 1690, 1680 (CO), 1200 (COC); M⁺: m/z 334]. 10 α -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 $\lambda_{\text{max}}^{\text{EtOH}}$ 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 6 β -hydroxy derivative (22), oil, stereoselectively in a quantitative yield. Treatment of 22 with propionic anhydride-pyridine in the presence of DMAP afforded ($\pm$)-3 β ,6 β -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 ($\pm$)-2 were in good agreement with those of natural-2, which was isolated from Euryops lateriflorus by Bohlmann et al.⁸

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