TOTAL SYNTHESIS OF FURANOEREMOPHILANES: (±)-DECOMPOSITIN AND THE RELATED NATURAL PRODUCTS[1]

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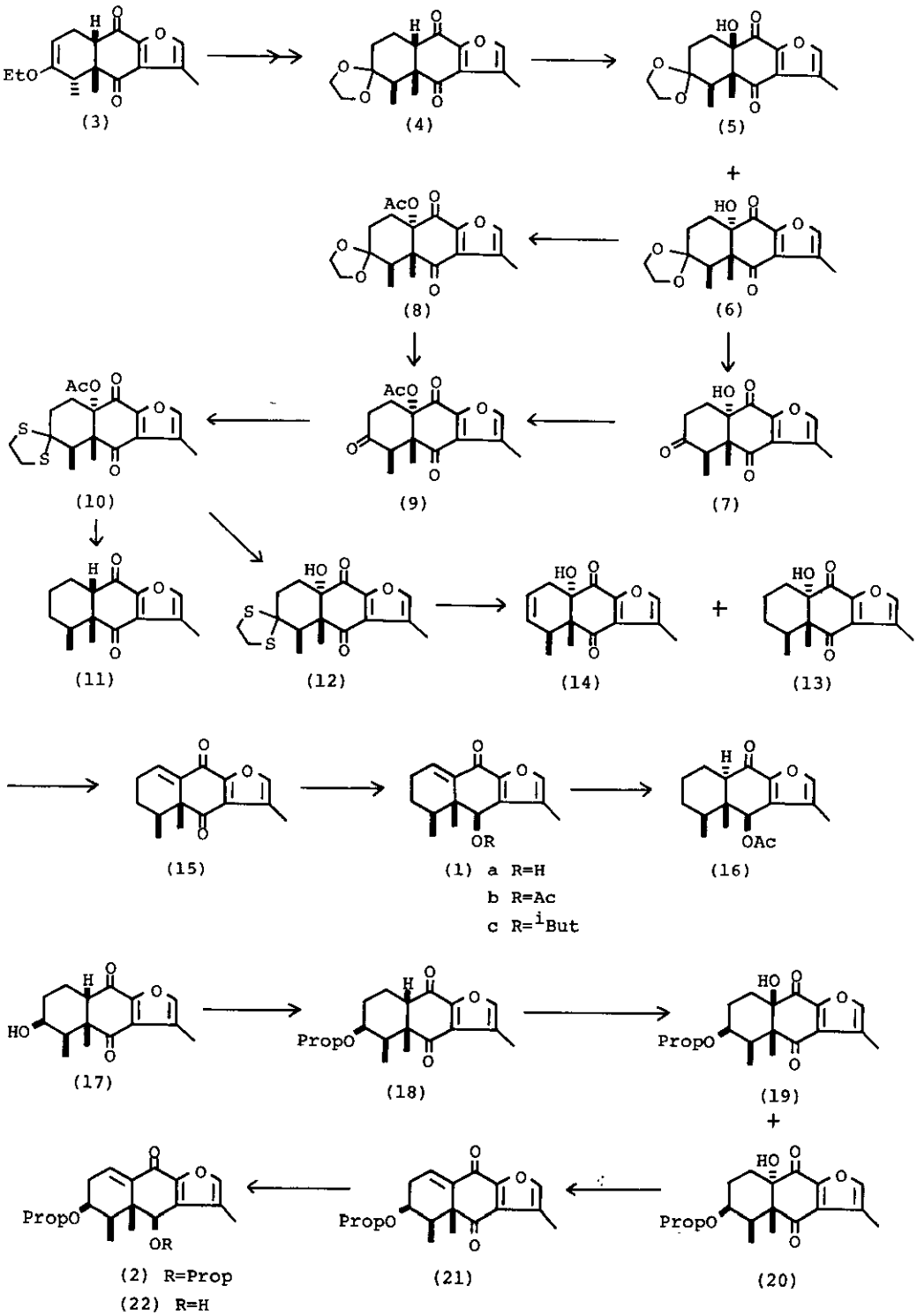
Abstract —— Total synthesis of furanoeremophilanes, (±)-6β-hydroxy-1,10-dehydrofuranoeremophilan-9-one (1a), (±)-decompositin (1b), (±)-adenostylone (1c), (±)-dihydrodecompositin (16), and (±)-3β,6β-dipropionyloxyeuryopsin-9-one (2), starting from the diene adduct (3) are described. An angular hydroxylation 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).[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; (±)-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 benzeneseleninic anhydride gave 10β-hydroxy and 10α-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 10α-hydroxy-3,6,9-trione (7), mp 257-260°, quantitatively [IR cm^{-1}: 3480 (OH), 1715, 1680 (CO); UV λ_{max}^{EtOH} 303 nm; M^+: m/z 276]. Hydroxy-trione (7) was acetylated with Ac_2O-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 BF_3-OEt_2 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, $\begin{matrix}CH_2S\\CH_2S\end{matrix}$>); M^+: m/z 394]. Attempted reductive desulfurization of 10 with Raney nickel (W-2) in refluxing ethanol was examined. However, desulfurization and hydrogenolysis were occured simultaneously to give 10βH-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 10α-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 λ_{max}^{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 (±)-6β-hydroxy-1,10-dehydrofuranoeremophilan-9-one (1a), oil, quantitatively [IR cm^{-1}: 3450 (OH), 1670 (CO), 1630 (C=C); UV λ_{max}^{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 (±)-1a was in good agreement with that of (-)-1a, which was isolated from Senecio lanceus by Bohlmann et al.[5] Acetylation of (±)-1a with Ac_2O-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}^{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 (±)-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}^{EtOH} 300 nm; NMR δ: 6.32 (1H, s, 6-H), 6.94 (1H, t, J=4 Hz, 1-H); mass: m/z 246 $[M-(CH_3)_2C{=}CO]^+$]. 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 (16), mp 137-138°, in a 86% yield [IR cm^{-1}: 1750, 1730, 1680 (CO), 1245 (COC); UV λ_{max}^{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 (±)-16 was in good agreement with that of natural-16, which was isolated from Euryops othonnoides by Bohlmann et al.[7]


(3)
(4)
(5)
(6)
(8)
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(12)
(14)
(13)
(15)
(1) a R=H
b R=Ac
c R=iBut
(16)
(17)
(18)
(19)
(20)
(21)
(2) R=Prop
(22) R=H

Treatment of 3β-hydroxyfuranoeremophilan-6,9-dione[4] (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_{max}^{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 $NaBH_4$ 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-CH_3), 1.26 (3H, s, 5-CH_3), 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]

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