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Synthesis of C-7 oxidized abietane diterpenes from racemic ferruginyl methyl ether

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Abstract—A series of naturally occurring C-7 oxidized abietane diterpenes have been synthesized from racemic ferruginyl methyl ether in high yields. 6-Hydroxyl-5,6-dehydrosugiol (**7**) can be converted into stable xanthoperol (**12**) using high temperature. Among the products, the structures of sugiyl methyl ether (**2**) and 6(-hydroxysugiyl methyl ether (**8**) were determined by X-ray analysis. © 2003 Published by Elsevier Science Ltd.

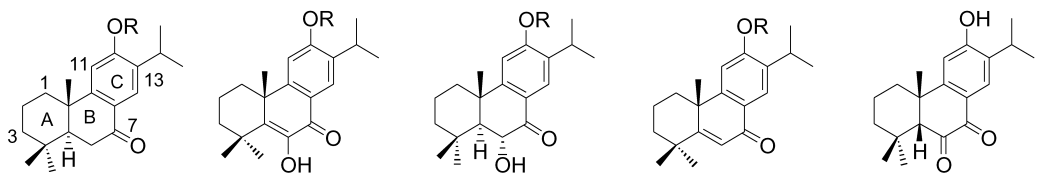
1. Introduction

Abietane diterpenes are widely distributed, naturally occurring products in the plant kingdom. Many of them exhibit significant biological activities, e.g. antibiotic,[1] anti-tumor,[2] anti-virus,[3] antimalarial,[4] anti-oxidant effects.[5] Due to their wide distribution and interesting bioactivities, many synthetic studies have been reported.[6] As part of our continuing efforts to synthesize this kind of biologically active compounds,[7] a series of C-7 oxidized abietane diterpenes were synthesized from racemic ferruginyl methyl ether (**1**), including sugiol (**3**),[8] 6-hydroxy-5,6-dehydro-sugiol (**7**),[9] 6α-hydroxysugiol (**9**),[10] 5,6-dehydrosugiol (**11**)[11] and xanthoperol (**12**).[12] Xanthoperol (**12**) is different from the others in that it has *cis*-fused A/B rings (Fig. 1).[13] Among these compounds, 5,6-dehydrosugiol (**11**) was first isolated from *Taxodium distichum* Rich and showed biological activity against KB tumors.[14] 6α-Hydroxysugiol (**9**) was first isolated from the bark of *Libocedrus formosana Florin*,[15] and recently, Tanaka et al. reported that it showed a strong inhibitory effect on EBV-EA induction.[16] To the best of our knowledge on these naturally occurring molecules and their structure–activity relationships, compounds **7** and **9** were synthesized for the first time.

2. Result and discussion

As shown in Scheme 1, oxidation of ferruginyl methyl ether (**1**) with chromium oxide in acetic acid gave sugiyl methyl ether (**2**). From the X-ray crystallographic analysis, the *trans* conjunction of its A/B rings can be confirmed (Fig. 2). Demethylation of **2** with sodium ethanethiolate in *N*,*N*-dimethylformamide under reflux afforded suginol (**3**). Compound **2** was treated with isopropenyl acetate in the presence of *p*-toluenesulfonic acid monohydrate under reflux to afford acetate **4**.

Oxidation of compound **4** with *m*-chloroperoxybenzoic acid in dichloromethane afforded 6α-acetoxy-12-methoxy-abieta-8, 11, 13-triene-7-one (**5**) in 93% yield. Treatment of **5** with K_2CO_3 in methanol and water (3:1) afforded the



2 R=Me, **3** R=H — **6** R=Me, **7** R=H — **8** R=Me, **9** R=H — **10** R=Me, **11** R=H — **12**

Figure 1.

Keywords: abietane; terpenes and terpenoids; biologically active compounds; X-ray crystal structures.

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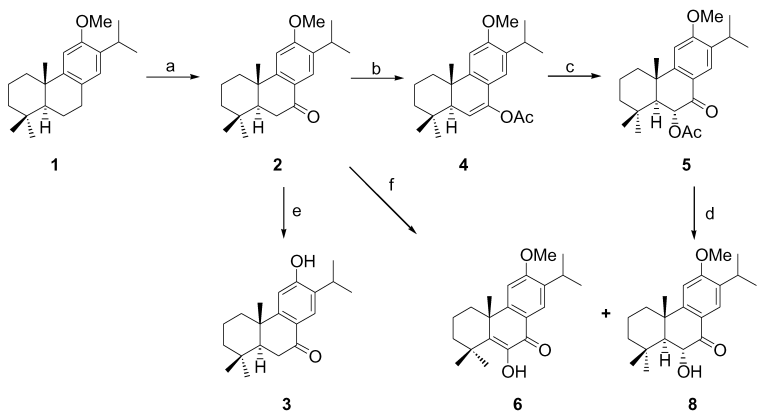
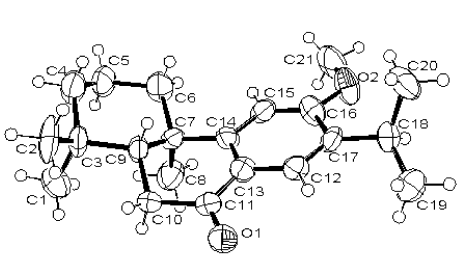


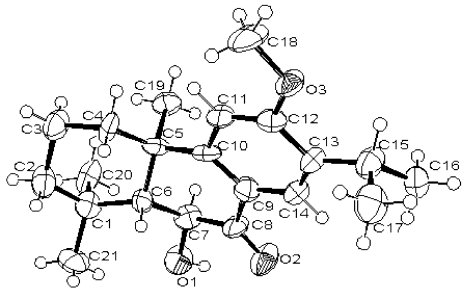
Scheme 1. *Reagents and conditions*: (a) CrO_3/HOAc, 84%; (b) isopropenyl acetate, TsOH, reflux, 3 h, 99%; (c) *m*-CPBA, CH_2Cl_2; KI/H_2O, $Na_2S_2O_3$, 93%, 0°C; (d) K_2CO_3, MeOH/H_2O, 24 h, air, rt, 74%; (e) NaSEt, DMF, reflux, 98%; (f) O_2, *t*-BuOK/*t*-BuOH, 1 h, 0°C; 68%.

desired 6α-hydroxysugiyl methyl ether (**8**) in 74% yield along with an oxidized product **6** in 22% yield. The yield of the over-oxidized product **6** can be decreased to less than 5% by performing the reaction under argon. Compound **6** can also be obtained from sugiyl methyl ether (**2**) through oxidation by oxygen in *t*-BuOK/*t*-BuOH. To further ascertain the configuration of the C-6 hydroxyl group in compound **8**, an X-ray analysis was carried out (Fig. 2), which confirmed the position of the α-hydroxyl group.

To further investigate this family of natural products, compounds **7**, **9**, **11** and **12** and their derivatives were also prepared (Scheme 2). It was shown that demethylation of **8** with sodium ethanethiolate in *N*,*N*-dimethylformamide under argon or air, respectively, produced different products. Under argon the product was the demethylated compound **9**, while in air, the product was the demethylated and oxidized compound **12**. According to the literature,[17] when the A/B rings are *cis*-fused, the δ value of C4-α-methyl group will be about 0.4 ppm; when the A/B rings are *trans*-fused, the δ value of C4-α-methyl group will be about 0.9–1.0 ppm. From the ^{1}H NMR spectrum of **12**, we found

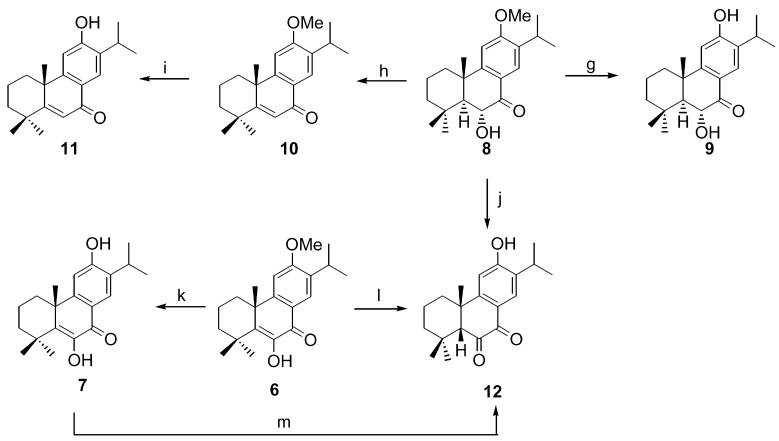


X-ray structure of **2** (CCDC 209202)



X-ray structure of **8** (CCDC 209203)

Figure 2.



Scheme 2. *Reagents and conditions*: (g) NaSEt, DMF, 110°C, 90%, Ar; (h) TsOH, PhH, reflux, Ar, 85%; (i) NaSEt, DMF, reflux, 98%; (j) NaSEt, DMF, reflux, air, 5 h, 92%; (k) BBr_3, CH_2Cl_2, 0°C, 58%; (l) NaSEt, DMF, reflux, 91%; (m) >115°C.

the corresponding methyl signal at 0.3 ppm, thus a *cis* conjunction in the A/B rings was deduced. Dehydration of **8** in benzene in the presence of *p*-toluenesulfonic acid monohydrate under reflux afforded 5,6-dehydrosugiyl methyl ether (**10**), which was subjected to demethylation to afford the desired 5,6-dehydrosugiyl methyl ether (**11**). Treatment of **6** with BBr_3 in dichloromethane at 0°C afforded 6-hydroxy-5,6-dehydrosugiol (**7**), while treatment of **6** with sodium ethanethiolate in *N*,*N*-dimethylformamide under reflux afforded the demethylated isomer **12**. Our studies showed that compound **7** can be converted into **12** above 115°C.

3. Experimental

3.1. General

The ^{1}H NMR spectra were recorded on a Bruker AM-400 MHz spectrometer. ^{13}C NMR spectra were recorded on a Bruker AM-100 MHz spectrometer. The chemical shifts are reported in ppm relative to TMS. IR spectra were recorded on a Nicolet 170 SXFT-IR spectrometer. HRMS spectra were recorded on a Bruker, APEXII spectrometer. Mass spectra were recorded on a ZAB-HS mass spectrometer (EI). Column chromatography was generally performed on silica gel (200–300 mesh) eluting with petroleum ether/ethyl acetate (30:1→8:1, v/v) and TLC inspections were done on silica gel GF_{254} plates with petroleum ether/ethyl acetate (20:1→5:1, v/v) if not noted otherwise.

3.1.1. Sugiyl methyl ether (2). To a solution of **1** (1.5 g, 5 mmol) in acetic acid (20 mL) was added chromium oxide (600 mg, 6 mmol) in acetic acid (5 mL) at room temperature. The mixture was stirred for 0.5 h, then water was added to quench the reaction. After extraction with dichloromethane, the combined organic layers were washed with saturated sodium hydrogen carbonate and brine. The organic solution was evaporated in vacuo, and the crude product was purified by column chromatography to give compound **2** (1.32 g, 84%) as white needle shape crystals, mp 130–132°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (s, 3H), 1.00 (s, 3H), 1.23 (d, 3H, J=7.0 Hz), 1.27 (d, 3H, J=7.0 Hz), 1.28 (s, 3H), 1.29–2.32 (m, 7H), 2.56–2.71 (m, 2H), 3.25 (sept., 1H, J=7.0 Hz), 3.88 (s, 3H), 6.75 (s, 1H), 7.89 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.91, 21.35, 22.37, 22.52, 23.24, 26.51, 32.57, 33.29, 36.02, 37.98, 38.26, 41.37, 49.64, 55.37, 104.41, 124.11, 125.59, 135.20, 156.36, 161.63, 198.46. IR (film)/cm^{-1}: 1677, 1598, 1561, 1495, 1258. HRMS (ESI): found M+H=315.2323, $C_{21}H_{30}O_2$ required M+H=315.2319. *m*/*z* (EI): 314 (72 M^+), 299 (100), 257 (21), 231 (27), 177 (26%).

X-Ray crystal data collection and refinement for **2**: formula, $C_{21}H_{30}O_2$; M_r, 314.45; crystal system, monoclinic; space group, *Pc*; *a*, 11.991(2) Å; *b*, 10.873(2) Å; *c*, 14.778(3) Å; *V*, 1815.7(6) Å^3; *Z*, 4; D_c, 1.150 g cm^{-3}; *F*(000), 688; μ, 0.072 mm^{-1}; *T*, 293 K; independent reflections, 2179; observed data with $I \geq 3\sigma(I)$, 1408; radiation (λ/Å), Mo Kα; scan type, $\omega/2\theta$; $2\theta_{max}$, 50°; *R*, 0.0295; R_w, 0.0555; goodness-of-fit indicator, 1.094.

3.1.2. Sugiol (3). To a solution of **2** (157 mg, 0.5 mmol) in *N*,*N*-dimethylformamide (2 mL) was added ethanethiol (0.4 mL, 5.5 mmol) and sodium hydride (132 mg, 5.5 mmol). The mixture was refluxed for 4 h and cooled to room temperature. The mixture was poured into ice cold 5% hydrochloric acid and extracted with ethyl acetate; the combined organic phases were washed with brine and dried over anhydrous sodium sulfate. The organic solution was evaporated in vacuo and the residue was purified by column chromatography to afford **3** (143 mg, 98%) as colorless crystals, mp 247–248°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.86 (s, 3H), 0.92 (s, 3H), 1.11 (d, J=6.8 Hz, 3H), 1.13 (s, 3H), 1.15 (d, J=6.8 Hz, 3H), 1.20–2.15 (m, 7H), 2.41–2.56 (m, 2H), 3.13 (sept., 1H, J=6.8 Hz), 6.78 (s, 1H), 7.64 (s, 1H), 10.23 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 18.43, 21.08, 22.15, 22.32, 22.98, 26.02, 32.24, 32.81, 35.46, 37.41, 39.92, 40.80, 49.04, 109.26, 122.53, 124.94, 132.44, 155.75, 160.05, 196.40. IR (film)/cm^{-1}: 3118, 2929, 1643, 1600, 1583, 1568, 1310, 1268. HRMS (ESI): found M+H=301.2171, $C_{20}H_{28}O_2$ required M+H=301.2162. *m*/*z* (EI): 300 (71 M^+), 285 (100), 243 (33), 217 (61), 203 (59%).

3.1.3. 7-Acetoxy-12-methoxyabieta-6,8,11,13-tetraene (4). To a solution of **2** (1.22 g, 3.83 mmol) in isopropenyl acetate was added a catalytic mount of *p*-toluenesulfonic acid monohydrate. The mixture was refluxed for 3 h, cooled to room temperature and quenched with saturated sodium hydrogen carbonate. After extraction with diethyl ether, the combined organic layers were washed with saturated sodium hydrogen carbonate and brine, then dried over anhydrous sodium sulfate. After the ether solution was evaporated in vacuo, the residue was purified by column chromatography to afford **4** (1.36 g, 99%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (s, 3H), 1.12 (s, 3H), 1.23 (d, J=7.0 Hz, 3H), 1.26 (s, 3H), 1.28 (d, J=7.0 Hz, 3H), 1.27–2.33 (m, 7H), 2.34 (s, 3H), 3.32 (sept., J=7.0 Hz, 1H), 3.88 (s, 3H), 5.59 (d, J=2.7 Hz, 1H), 6.76 (s, 1H), 7.04 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.85, 20.18, 20.69, 22.26, 22.36, 22.72, 26.54, 32.53, 32.95, 35.90, 38.48, 40.83, 50.60, 55.30, 104.79, 113.52, 119.18, 121.95, 133.63, 145.51, 147.86, 157.19, 169.12. IR (film)/cm^{-1}: 1738, 1637, 1600, 1507, 1468, 1254. HRMS (ESI): found M+H=357.2427, $C_{23}H_{32}O_3$ required M+H=357.2431. *m*/*z* (EI): 356 (15 M^+), 314 (22), 299 (29), 243 (18), 232 (85%).

3.1.4. 6α-Acetoxy-12-methoxyabieta-8,11,13-trien-7-one (5). A mixture of **4** (1.35 g, 3.8 mmol) and *m*-chloroperoxybenzoic acid (785 mg, 4.56 mmol) in dichloromethane (20 mL) was stirred at room temperature for 12 h, then ethyl ether was added. The mixture was washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, saturated sodium hydrogen carbonate and brine. The organic phase was separated and dried over anhydrous sodium sulfate. The ether solution was evaporated in vacuo and the residue was purified by column chromatography to afford **5** (1.32 g, 93%) as a white solid, mp 163–164°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (s, 6H), 1.17 (d, J=7.0 Hz, 3H), 1.22 (d, J=7.0 Hz, 3H), 1.41 (s, 3H), 2.24 (s, 3H), 1.32–2.29 (m, 7H), 3.24 (sept., J=7.0 Hz, 1H), 3.90 (s, 3H), 5.83 (d, J=13 Hz, 1H), 6.76 (s, 1H), 7.90 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.68, 21.36, 21.90, 22.23, 22.43,

25.06, 26.47, 33.68, 35.51, 38.48, 39.78, 42.86, 53.23, 55.40, 75.10, 104.22, 122.39, 126.30, 136.00, 155.28, 162.06, 170.43, 192.86. IR (film)/cm^{-1}: 1744, 1682, 1601, 1496, 1372, 1235. HRMS (ESI): found M+H=373.2373, $C_{23}H_{32}O_4$ required M+H=373.2373. *m/z* (EI): 372 (37 M^+), 357 (10), 330 (35), 297 (22), 245 (37), 217 (100), 149 (50%).

3.1.5. 6-Hydroxy-5,6-dehydrosugiyl methyl ether (6). To a solution of *t*-BuOK (1.2 g) in *t*-BuOH (10 mL) was added **2** (106 mg), then oxygen was slowly bubbled in. After stirring at 0°C for 2 h, 5% dilute hydrochloric acid was added until pH=1. The solution was stirred for another 1 h, then extracted with ether. The ether solution was evaporated and the crude product was purified by column chromatography to afford **6** (76 mg, 68%) as white crystals, mp 144–145°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (d, *J*=6.8 Hz, 3H), 1.26 (d, *J*=6.8 Hz, 3H), 1.45 (s, 6H), 1.55 (s, 3H), 1.47–2.41 (m, 6H), 3.28 (sept., *J*=6.8 Hz, 1H), 3.92 (s, 3H), 6.87 (s, 1H), 7.19 (s, 1H), 8.00 (s, 1H). ^{13}C NMR δ 17.58, 22.33, 22.53, 26.62, 27.58, 28.11, 33.70, 35.04, 35.85, 37.78, 40.59, 55.43, 105.99, 120.44, 124.56, 136.28, 140.61, 143.76, 154.84, 161.14, 179.67. IR (film)/cm^{-1}: 1693, 1624, 1595, 1497, 1463, 1251. HRMS (ESI): found M+H=329.2117, $C_{21}H_{28}O_3$ required M+H=329.2111. *m/z* (EI): 328 (100 M^+), 285 (34), 259 (77), 243 (28), 217 (15%).

3.1.6. 6-Hydroxy-5,6-dehydrosugiol (7). To a solution of **6** (164 mg, 0.5 mmol) in dichloromethane (5 mL) was added boron tribromide (0.2 mL) at −5°C. The mixture was stirred for 1 h at this temperature, then diluted with ether and poured into ice water. The mixture was extracted with ethyl ether. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After evaporation, the residue was purified by flash column chromatography to afford compound **7** (91 mg, 58%) as a white solid, mp>115°C decomposition. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.17 (d, *J*=6.8 Hz, 3H), 1.20 (d, *J*=6.8 Hz, 3H), 1.35 (s, 6H), 1.42 (s, 3H), 1.23–2.28 (m, 6H), 3.18 (sept., *J*=6.8 Hz, 1H), 6.95 (s, 1H), 7.76 (s, 1H), 8.04 (s, 1H), 10.28 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 16.99, 22.11, 22.31, 26.22, 27.38, 27.89, 33.08, 35.26, 35.32, 37.36, 39.57, 110.73, 119.41, 123.93, 133.70, 139.53, 143.87, 153.92, 159.44, 178.66. IR (film)/cm^{-1}: 3376, 2960, 1625, 1582, 1455, 1315, 1260. HRMS (ESI): found M+H=315.1962, $C_{20}H_{26}O_3$ required M+H=315.1955. *m/z* (EI): 314 (7 M^+), 285 (65), 243 (28), 217 (35), 203 (42), 149 (100%).

3.1.7. 6α-Hydroxysugiyl methyl ether (8). To a solution of potassium carbonate (2 g, 145 mmol) in methanol and water (3:1) was added **5** (1.12 g, 3 mmol). The mixture was stirred for 24 h at room temperature, and then evaporated in vacuo. Water and ethyl acetate were added to the residue. The mixture was stirred to form two clear phases. After separation, the aqueous phase was extracted with ethyl acetate; the combined organic layers were washed with brine and then dried over anhydrous sodium sulfate. The crude product was purified by column chromatography to afforded **6** (216 mg, 22%) and **8** (732 mg, 74%) as white crystals. For compound **8**: mp 171–172°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (d, *J*=7.0 Hz, 3H), 1.23 (s, 6H), 1.24 (d, *J*=7.0 Hz, 3H), 1.39 (s, 3H), 1.28–2.31 (m, 7H), 3.25 (sept., *J*=7.0 Hz, 1H), 3.92 (s, 3H), 4.61 (dd, *J*=13, 1.7 Hz, 1H), 6.77 (s, 1H), 7.92 (s, 1H). ^{13}C NMR δ 18.87, 21.84, 22.29, 22.44, 24.69, 26.53, 34.14, 35.79, 38.87, 39.59, 42.92, 55.40, 56.07, 73.82, 104.64, 121.18, 126.07, 135.94, 156.55, 162.35, 199.71. IR (film)/cm^{-1}: 1654, 1600, 1565, 1497, 1462, 1377, 1286. HRMS (ESI): found M+H=331.2275, $C_{21}H_{30}O_3$ required M+H=331.2268. *m/z* (EI): 330 (36 M^+), 315 (39), 301 (74), 245 (74), 217 (100%).

X-Ray crystal data collection and refinement for **8**: formula, $C_{21}H_{30}O_3$; M_r, 330.45; crystal system, triclinic; space group, *P*1; *a*, 8.038 Å; *b*, 10.391 Å; *c*, 12.299 Å; *V*, 909.8 $Å^3$; *Z*, 2; D_c, 1.206 g cm^{-3}; *F*(000), 360; μ, 0.079 mm^{-1}; *T*, 293 K; independent reflections, 1874; observed data with $I \geq 3\sigma(I)$, 1365, radiation (λ/Å), Mo Kα; scan type, $\omega/2\theta$; $2\theta_{max}$, 50°; *R*, 0.0254; R_w, 0.0527; goodness-of-fit indicator, 1.059.

3.1.8. 6α-Hydroxysugiol (9). To a solution of **8** (99 mg, 0.3 mmol) in *N*,*N*-dimethylformamide (2 mL) under Ar was added ethanethiol (0.3 mL, 4 mmol) and sodium hydride (96 mg, 4 mmol). The mixture was heated to 110°C and stirred for 5 h, then cooled to room temperature and poured into ice cold 5% hydrochloric acid. The mixture was extracted with ethyl acetate; the combined organic phases were washed with brine and dried over anhydrous sodium sulfate. The organic solution was evaporated in vacuo and the residue was purified by column chromatography to afford **9** (85 mg, 90%) as a white solid, mp 207–208°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.12 (s, 6H), 1.16 (d, *J*=6.8 Hz, 6H), 1.22 (s, 3H), 1.18–2.13 (m, 7H), 3.15 (sept., *J*=6.8 Hz, 1H), 4.40 (dd, *J*=12.3, 3.4 Hz, 1H), 4.79 (s, 1H), 6.79 (s, 1H), 7.67 (s, 1H), 10.32 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 18.40, 21.65, 22.14, 22.28, 24.69, 26.07, 33.67, 35.91, 38.11, 38.43, 42.72, 54.84, 72.61, 109.21, 120.70, 125.43, 133.06, 155.57, 160.47, 198.47. IR (film)/cm^{-1}: 3421, 1645, 1600, 1500, 1185, 1131. HRMS (ESI): found M+H=317.2114, $C_{20}H_{28}O_3$ required M+H=317.2111. *m/z* (EI): 316 (16 M^+), 301 (18), 287 (48), 231 (43), 203 (51%).

3.1.9. 5,6-Dehydrosugiyl methyl ether (10). To a solution of **8** (99 mg, 0.3 mmol) in benzene (3 mL) was added a catalytic amount of *p*-TsOH. The solution was refluxed for 6 h. After cooling, saturated sodium hydrogen carbonate was added to the solution and the mixture was extracted with ether. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After evaporation, the crude product was purified by column chromatography to give **10** (80 mg, 85%) as a white solid, mp 156–157°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (d, *J*=6.8 Hz, 3H) 1.25 (d, *J*=6.8 Hz, 3H), 1.27 (s, 3H), 1.36 (s, 3H), 1.54 (s, 3H), 1.43–2.46 (m, 6H), 3.25 (sept., *J*=7.5 Hz, 1H), 3.90 (s, 3H), 6.46 (s, 1H), 6.86 (s, 1H), 7.99 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) 16.65, 22.40, 22.50, 26.65, 29.16, 32.50, 32.63, 37.44, 37.80, 40.30, 41.33, 55.39, 105.55, 123.56, 124.08, 124.61, 135.99, 153.80, 160.78, 172.62, 185.12. IR (film)/cm^{-1}: 1646, 1598, 1497, 1464, 1253. HRMS (ESI): found M+H=313.2164, $C_{21}H_{28}O_2$ required M+H=313.2162. *m/z* (EI): 312 (32 M^+), 297 (77), 282 (43), 269 (26), 243 (25), 201 (17%).

3.1.10. 5,6-Dehydrosugiol (11). To a solution of **10** (78 mg, 0.25 mmol) in *N*,*N*-dimethylformamide (2 mL) was added ethanethiol (0.2 mL, 2.6 mmol) and sodium hydride (62 mg, 2.6 mmol). The mixture was refluxed for 3 h and cooled to room temperature. The mixture was poured into ice cold 5% hydrochloric acid and extracted with ethyl acetate. The combined organic phases were washed with brine and dried over anhydrous sodium sulfate. The organic solution was evaporated in vacuo and the residue was purified by column chromatography to afford **11** (73 mg, 98%) as white crystals, mp 281–282°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.16 (d, J=6.8 Hz, 3H), 1.18 (d, J=6.8 Hz, 3H), 1.19 (s, 3H), 1.29 (s, 3H), 1.42 (s, 3H), 1.31–2.30 (m, 6H), 3.16 (sept., J=6.8 Hz, 1H), 6.23 (s, 1H), 6.94 (s, 1H), 7.71 (s, 1H), 10.20 (s, 1H). ^{13}C NMR δ 18.00, 22.17, 22.35, 26.15, 28.85, 32.24, 32.51, 36.92, 37.29, 39.78, 40.44, 110.51, 121.62, 123.76, 123.59, 133.43, 153.44, 159.18, 172.21, 183.25. IR (film)/cm^{-1}: 3113, 2965, 1637, 1614, 1583, 1563, 1505, 1468, 1314. HRMS (ESI): found M+H=299.1998, $C_{20}H_{26}O_2$ required M+H=299.2006. *m*/*z* (EI): 298 (21 M$^+$), 283 (11), 229 (33), 213 (50%).

3.1.11. Xanthoperol (12). (a) To a solution of **6** (99 mg, 0.3 mmol) in *N*,*N*-dimethylformamide (2 mL) was added ethanethiol (0.3 mL, 4 mmol) and sodium hydride (96 mg, 4 mmol). The mixture was refluxed for 4 h and then cooled to room temperature. The mixture was poured into ice cold 5% hydrochloric acid and extracted with ethyl acetate. The combined organic phases were washed with brine and dried over anhydrous sodium sulfate. The organic solution was evaporated in vacuo and the residue was purified by column chromatography to afford **12** (86 mg, 91%) as yellow crystals, mp 257–258°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.31 (s, 3H), 0.82 (s, 3H), 1.11 (s, 3H), 1.16 (s, 6H), 1.32–2.37 (m, 6H), 2.60 (s, 1H), 3.16 (sept., J=6.4 Hz, 1H), 6.91 (s, 1H), 7.77 (s, 1H), 10.88 (s, 1H). ^{13}C NMR δ 18.40, 21.94, 22.09, 23.61, 26.32, 30.96, 34.71, 35.22, 37.94, 38.98, 40.98, 68.07, 110.59, 125.42, 127.95, 134.44, 150.18, 162.25, 179.04, 199.70. IR (film)/cm^{-1}: 3267, 2960, 1656, 1583, 1507, 1368, 1276. HRMS (ESI): found M+H=315.1961, $C_{20}H_{26}O_3$ required M+H=315.1955. *m*/*z* (EI): 314 (16 M$^+$), 300 (13), 271 (29), 217 (26), 204 (100%).

(b) To a solution of **8** (99 mg, 0.3 mmol) in *N*,*N*-dimethylformamide (2 mL) under air was added ethanethiol (0.3 mL, 4 mmol) and sodium hydride (96 mg, 4 mmol). The mixture was refluxed for 5 h, then cooled to room temperature. The reaction mixture was poured into ice-cold 5% hydrochloric acid and extracted with ethyl acetate. The combined organic phases were washed with brine and dried over anhydrous sodium sulfate. The organic solution was evaporated in vacuo and purified by column chromatography to afford **12** (91 mg, 92%) as yellow crystals. The physical and spectroscopic data of **12** were identical to these of a sample prepared previously.

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