# Supporting Information

## First Diastereoselective Synthesis of (-)-Methyl Thyrsiflorin A, (-)-Methyl Thyrsiflorin B Acetate and (-)-Thyrsiflorin C

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## Experimental section

**12β-Methoxycarbonyl-12α-Methyl-8(14)-podocarpen-13-one (15).** It was obtained reversing the order of the two steps used for the synthesis of the keto ester **17**. Thus, to a solution of podocarpenone **13** (50 mg, 0.20 mmol) and o-phenanthroline (used as indicator) in THF (5 mL) at –30 °C, a solution of LDA in THF (0.5 M, 447 μL, 0.22 mmol) was slowly added (ca. 1 h). Then, HMPA (36 μL, 0.20 mmol) and $CNCO_2Me$ (81 μL, 1.0 mmol) were successively added via syringe, and the reaction mixture was stirred at the same temperature for 2.5 h, quenched with saturated $NH_4Cl$ (2 mL), poured into water and extracted with diethyl ether. Workup afforded an orange oil which resulted to be a 7:3 (β:α) mixture of epimeric esters at C-12 **14**. $^1H$ NMR of the mixture (300 MHz; $CDCl_3$); for the β–ester: δ 5.85 (1H, br s, H-14), 3.72 (3H, s, OMe), 3.21 (1H, dd, J = 14.0, 5.7, H-12α), 0.88 , 0.84 and 0.78 (3H each, each s, H-18, H-19 and H-20). For the α–ester: δ 5.88 (1H, br s, H-14), 3.64 (3H, s, OMe), 3.34 (1H, dd, J = 5.5, 4.6, H-12β), 0.87, 0.82 and 0.76 (3H each, each s, H-18, H-19 and H-20). This epimeric mixture was submitted to the following step without further purification. Thus, to a solution of the crude ester and a small amount of o-phenanthroline in THF (5 mL) at –78 °C, a solution of LDA in THF (0.5 M, 447 μL, 0.22 mmol) was slowly added (ca. 25 min). Then, HMPA (36 μL, 0.20 mmol) and MeI (63 μL, 1.0 mmol) were added via syringe. The reaction mixture was slowly allowed to warm to –10 °C for 5 h, quenched by

addition of saturated $NH_4Cl$ (2 mL) and poured into aqueous $NH_4Cl$. Extraction with diethyl ether and workup as usual gave a orange residue, which was purified by chromatography, using hexane-ethyl acetate (from 9:1 to 8:2) as eluent, to afford podocarpenone methyl ester **15** as a solid (46 mg, 72%, two steps): mp 108-110 °C (from hexane-EtOAc); $[\alpha]^{27}_D$ +57.6 (c 2.6, $CHCl_3$); IR (KBr) 2943, 1735, 1671, 1626, 1455, 1388, 1264, 1240, 1105, 1003, 881 $cm^{-1}$; $^1H$ NMR (400 MHz; $CDCl_3$) δ 5.81 (1H, dd, J = 2.2, 2.2, H-14), 3.74 (3H, s, OMe), 2.56 (1H, ddd, J = 15.8, 5.0, 1.8, H-7β), 2.33 (1H, dd, J = 13.4, 11.0, H-11β), 2.11 (1H, m, H-9), 1.84 (1H, dd, J = 13.4, 5.0, H-11α), 1.32 (3H, s, H-17), 0.94 (3H, s, H-18), 0.89 (3H, s, H-19), 0.85 (3H, s, H-20); $^{13}C$ NMR (75 MHz; $CDCl_3$) $\delta_C$ 197.98 (s), 173.86 (s), 164.68 (s), 123.32 (d), 53.81 (d), 52.40 (q), 48.35 (d), 41.62 (t), 39.08 (t), 38.70 (s), 35.02 (t), 33.54 (q), 33.39 (s), 30.06 (t), 22.00 (q), 21.70 (t), 19.55 (q), 18.57 (t), 15.14 (q), the signal of a quaternary carbon was hidden by another carbon signal.

**8(14)-Scopadulene-13,15-dione (22).** A solution of ketal **20** (16 mg, 0.047 mmol) in acetone/HCl 12 M (5:1, 3 mL) was stirred at rt for 2.5 h. Workup as usual followed by chromatography, hexane-ethyl acetate (9:1), gave **22** (12.6 mg, 90%) as a white solid: $^1H$ NMR (400 MHz; $CDCl_3$) δ 5.76 (1H, d, J = 2.4, H-14), 2.63 (1H, ddd, J = 17.4, 5.2, 1.5, H-7β), 2.61 (1H, d, J = 17.5, H-16), 2.39 (1H, dddd, J = 17.4, 12.7, 6.5, 2.4, H-7α), 2.30 (1H, dd, J = 11.9, 3.6, H-11β), 2.22 (1H, dd, J = 17.5, 3.6, H-16'), 1.95 (1H, d, J = 11.9, H-11α), 1.20 (3H, s, H-17), 1.00 (3H, s, H-20), 0.92 (3H, s, H-18), 0.91 (3H, s, H-19); $^{13}C$ NMR (100 MHz; $CDCl_3$) $\delta_C$ 211.83 (s), 192.26 (s), 171.42 (s), 125.70 (d), 63.69 (s), 52.57 (s), 47.95 (d), 42.83 (t), 41.64 (t), 41.33 (t), 37.34 (s), 33.71 (q), 33.47 (s), 33.03 (t), 31.03 (t), 22.69 (q), 20.62 (t), 19.10 (q), 18.23 (t), 14.46 (q).

## Spectroscopic and physical data

**Ketone 11.** Representative data: a white solid: mp 91-92 °C (from hexane-EtOAc); $[\alpha]^{26}_{D}$ –2.3 (c 1.8, $CHCl_3$); IR (KBr) 3020, 2966, 2919, 2860, 1715, 1435, 1374, 1228, 1069, 1037, 921 $cm^{-1}$; $^1H$ NMR (300 MHz; $CDCl_3$) δ 2.42 (2H, s, H-14), 1.04 and 0.99 (3H each, each s, H-17 and H-20), 0.80 (6H, s, H-18 and H-19); $^{13}C$ NMR (75 MHz; $CDCl_3$) $\delta_C$ 213.36 (s), 49.79 (s), 48.11 (d), 42.05 (s), 41.86 (t), 41.67 (t), 37.05 (t), 36.92 (t), 36.40 (t), 33.87 (q), 33.56 (s), 33.08 (s), 29.53 (t), 26.49 (d), 21.46 (q), 19.96 (s), 19.86 (q), 18.71 (t), 18.04 (t), 17.32 (q).

**13-Scopadulanone (24).** Representative data: an oil; IR (KBr) 2930, 1710, 1461, 1379, 1261 $cm^{-1}$; $^1H$ NMR (400 MHz; $CDCl_3$) δ 2.21 (1H, dd, J = 14.7, 5.4, H-14), 1.03 (3H, s, H-17), 0.98 (3H, s, H-20), 0.83 (3H, s, H-18), 0.80 (3H, s, H-19); $^{13}C$ NMR (75 MHz; $CDCl_3$) $\delta_C$ 214.64 (s), 53.10 (s), 52.44 (s), 47.98 (d), 45.38 (t), 43.68 (t), 42.12 (t), 40.01 (d), 38.83 (s), 36.88 (t), 33.61 (q), 33.13 (s), 32.55 (t), 30.29 (t), 24.09 (t), 21.96 (q), 21.70 (t), 19.81 (q), 18.70 (t), 17.24 (q).

**13-Acetoxy-7,13-scopaduladiene (25).** Representative data: a solid; $^1H$ NMR (300 MHz; $CDCl_3$) δ 5.59 (1H, s, H-14), 5.24 (1H, dd, J = 5.1, 2.7, H-7), 2.13 (3H, s, COMe), 1.07 , 0.92, 0.91 and 0.84 (3H each, each s, H-17, H-18, H-19 and H-20); $^{13}C$ NMR (75 MHz; $CDCl_3$) $\delta_C$ 169.43 (s), 155.26 (s), 142.45 (s), 118.75 (d), 116.68 (d), 54.56 (s), 44.57 (t), 44.52 (s), 44.47 (d), 42.57 (t), 42.42 (t), 37.05 (s), 33.84 (t), 33.41 (q), 32.83 (s), 32.25 (t), 24.41 (t), 22.31 (q), 20.71 (q), 19.84 (q), 18.67 (t), 17.87 (q).

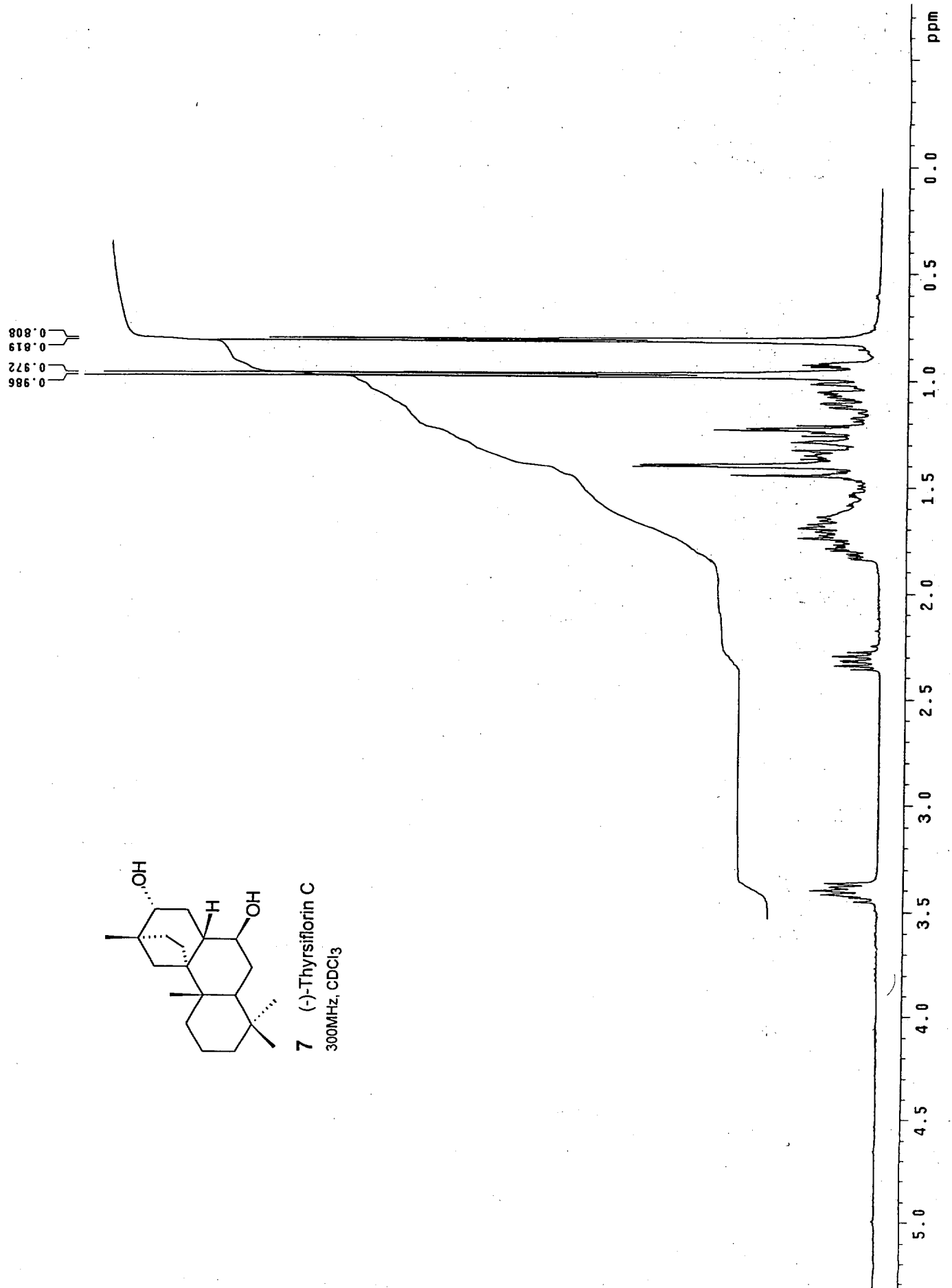
**7α-Hydroxy-8(14)-scopadulen-13-one (26).** Representative data: a solid; $^1H$ NMR (250 MHz; $CDCl_3$) δ 5.96 (1H, s, H-14), 4.50 (1H, dd, J = 3.7, 3.7, H-7), 1.17 (3H, s, H-17), 0.93 and 0.90 (3H and 6H, each s, H-18, H-19 and H-20).

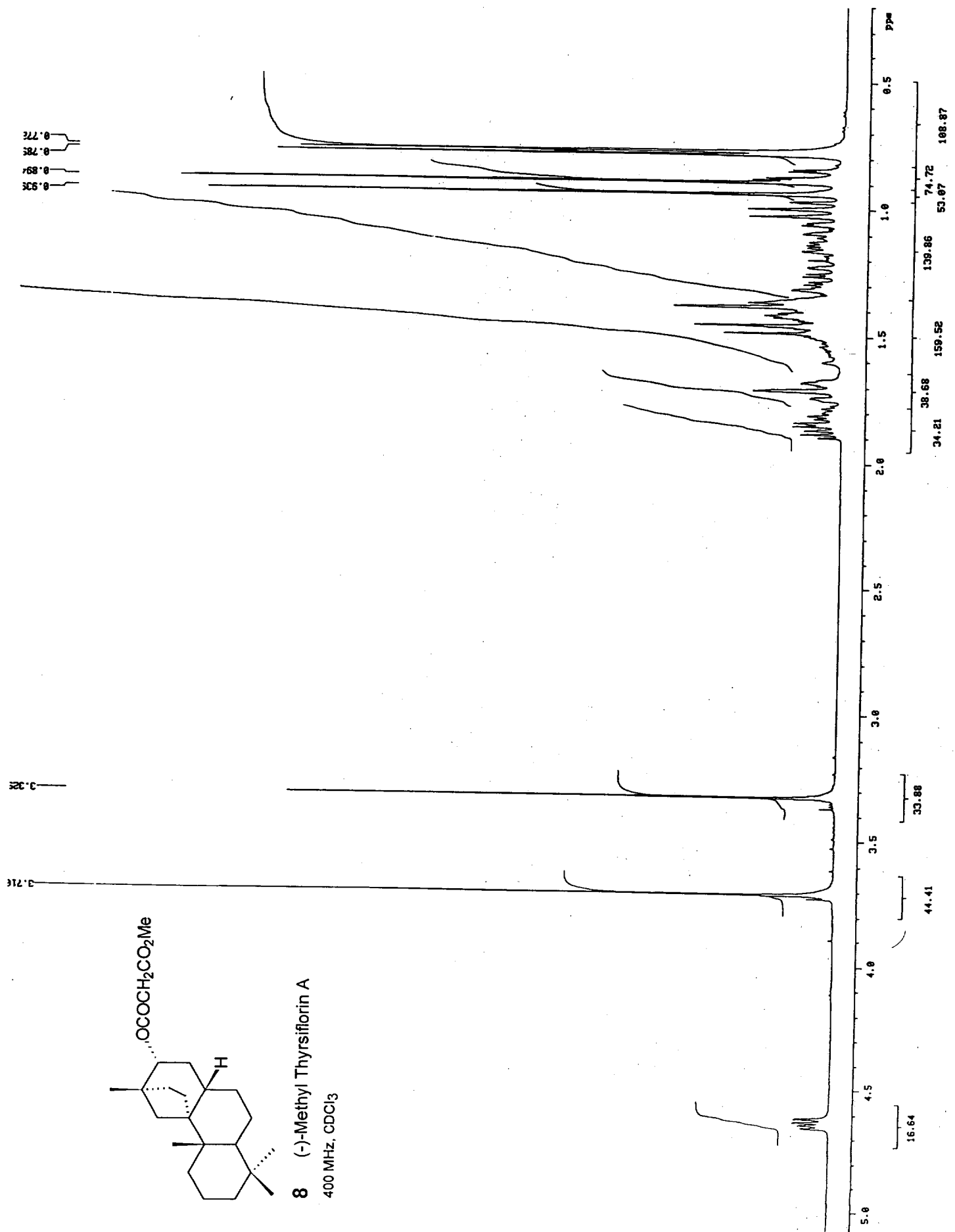
**13,13-Ethylenedioxy-8α-scopadulan-7α-ol (29).** Representative data: a white solid: mp 140-141 °C (from hexane-diethyl ether); $[\alpha]^{27}_D$ –7.6 (c 1.3, $CHCl_3$); IR (KBr) 3402, 2951, 1458, 1367, 1123, 1087, 1041, 1023, 965 $cm^{-1}$; $^1H$ NMR (300 MHz; $CDCl_3$) δ 4.32 (1H, dd, J = 6.6, 6.6, H-7), 4.00-3.73 (4H, m, ketal), 0.94, 0.88, 0.87, and 0.85 (3H each, each s, H-17, H-18, H-19 and H-20); $^{13}C$ NMR (100 MHz; $CDCl_3$) $\delta_C$ 113.19 (s), 68.96 (d), 65.07 (t), 64.82 (t), 50.16 (s), 48.32 (s), 45.09 (d), 44.81 (d), 43.04 (t), 40.87 (t), 38.77 (s), 35.98 (t), 33.87 (q), 33.13 (s), 33.05 (t), 31.90 (t), 31.85 (t), 29.29 (t), 22.53 (q), 20.18 (t), 20.09 (q), 17.94 (q).

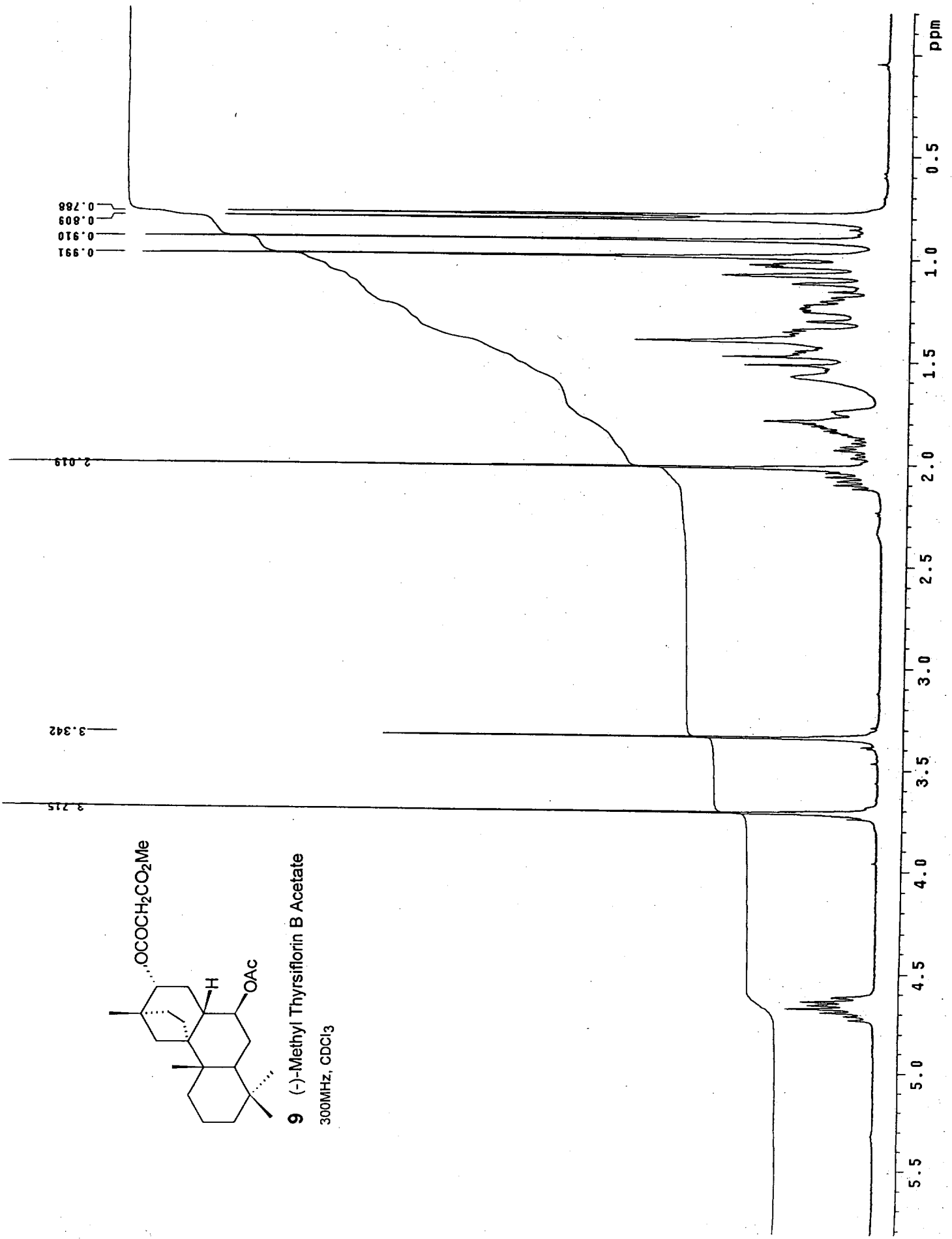
**Rearranged ketone 34.** Representative data: a viscous oil; $[\alpha]^{23}_D$ –92.7 (c 1.7, $CHCl_3$); IR (NaCl) 2924, 2862, 1721, 1455, 1411, 1376, 1185, 1068 $cm^{-1}$; $^1H$ NMR (400 MHz; $CDCl_3$) δ 2.21 (1H, dd, J = 18.3, 3.0, H-14β), 2.0 (1H, d, J = 18.3, H-14α), 1.75 (1H, d, J = 12.9, H-11α), 0.97 and 0.96 (3H each, each s, H-18 and H-19), 0.92 (3H, s, H-17), 0.86 (3H, s, Me-C9); $^{13}C$ NMR (100 MHz; $CDCl_3$) $\delta_C$ 218.65 (s), 133.00 (s), 132.78 (s), 47.29 (t), 46.69 (t), 44.81 (s), 40.11 (t), 39.22 (s), 36.83 (s), 34.09 (s), 30.94 (t), 28.99 (t), 28.93 (q), 27.96 (q), 26.87 (t), 25.95 (t), 24.16 (q), 21.20 (t), 20.25 (q), 19.95 (t); MS (EI) m/z 286 ($M^+$, 27), 272 (25), 271 (100), 244 (9), 229 (13), 173 (4), 159 (4), 147 (4), 105 (5); HRMS $C_{20}H_{30}O$ requires 286.2297, found 286.2300.

**7β-Acetoxy-13β-scopadulanol (38).** Representative data: a colorless oil; $[\alpha]^{25}_D$ +5.3 (c 0.8, $CHCl_3$); $^1H$ NMR (300 MHz; $CDCl_3$) δ 4.67 (1H, ddd, J = 11.0, 11.0, 5.6, H-7), 3.43 (1H, br s, H-13), 2.02 (3H, s, $COCH_3$), 1.03 and 0.98 (3H each, each s, H-17 and H-20), 0.81 and 0.80 (3H each, each s, H-18 and H-19); $^{13}C$ NMR (75 MHz; $CDCl_3$) $\delta_C$ 171.07 (s), 76.58 (d), 74.49 (d), 54.00 (s), 45.92 (d), 43.73 (s), 41.96 (t), 38.55 (s), 38.30 (d), 37.68 (t), 36.27 (t), 33.51 (q), 33.17 (s), 33.10 (t), 32.11 (t), 28.05 (t), 24.24 (t), 23.85 (q), 22.04 (q), 21.35 (q), 18.63 (t), 17.71 (q).

**7β,13β-Scopadulanediol (40).** Representative data: $^1H$ NMR (300 MHz; $CDCl_3$) 3.48 (1H, br s, H-13), 3.36 (1H, ddd, J = 11.0, 10.0, 5.4, H-7), 2.04 (1H, ddd, J = 14.1, 4.8, 1.9), 1.02 and 0.99 (3H each, each s, H-17 and H-20), 0.83 and 0.82 (3H each, each s, H-18 and H-19).

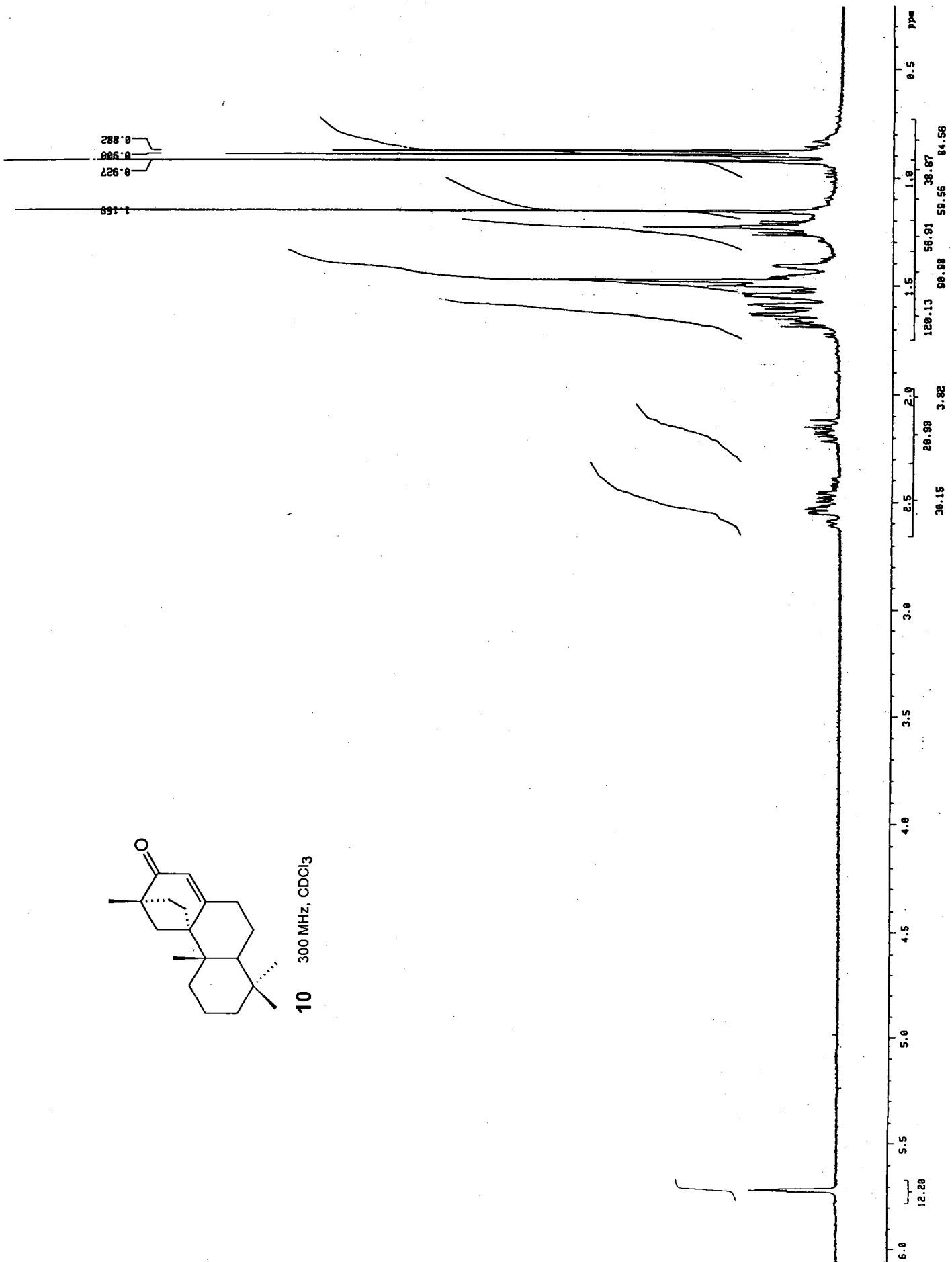







**9** (-)-Methyl Thyrsiflorin B Acetate

300MHz, $CDCl_3$






**10** 300 MHz, $CDCl_3$