SUPPORTING INFORMATION FOR:

A Formal Total Synthesis of the Marine Diterpenoid Diisocyanoadociane

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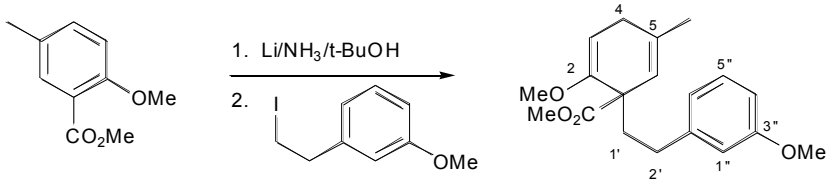
Contents **Page**

General Experimental Directions

Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on a Varian Mercury 300 spectrometer operating at 300 MHz for proton and 75 MHz for carbon nuclei. In addition, selected experiments were run on Varian Inova 500 and 600 spectrometers, and a Bruker Avance 800. Chemical shifts were recorded as δ values in parts per million (ppm). Most spectra were acquired at 300 MHz, in deuterochloroform ($CDCl_3$), at 20 ^{0}C unless otherwise stated. Infrared (IR) spectra (ν_{max}) were recorded on a Perkin–Elmer Spectrum One spectrometer. Low and high resolution mass spectra were recorded on a VG Fisons AutoSpec three sector (E/B/E) double focusing mass spectrometer, using positive ion electron impact techniques. Melting points were recorded on a Gallenkamp Melting Point Apparatus and are uncorrected. Elemental analyses were performed by the Australian National University Microanalytical Services Unit based in the Research School of Chemistry, The Australian National University, Canberra, Australia. Analytical thin layer chromatography (TLC) was conducted on aluminum backed 0.2 mm thick silica gel 60 F_{254} plates (Merck), visualized under a 254 nm UV lamp and/or by treatment with a polymolybdic acid (PMA) dip, followed by heating. Flash chromatography was conducted according to the method of Still and co-workers using silica gel 60 (mesh size 0.040–0.063) or alumina oxide 60 (mesh size 0.063–0.200) as the stationary phase and the analytic (AR) grade solvent indicated. THF, Et_2O, benzene, and toluene were dried using sodium metal and then distilled, as required, from sodium benzophenone ketyl. DCM was distilled from calcium hydride. Ammonia was dried with sodium metal and $FeNO_3$ and then distilled under an inert atmosphere as required. HMPA was dried over 4Å molecular sieves.

(1*RS*) Methyl 2-Methoxy-1-(2′-(3″-methoxyphenyl)ethyl)-5-methylcyclohexa-2,5-diene-1-carboxylate

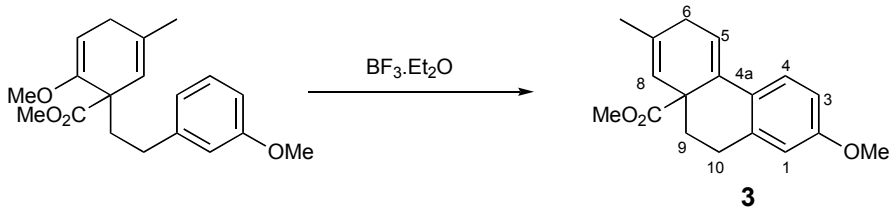


Preparation based on procedure described by S.R. Crabtree, Ph.D. thesis, ANU 1990.

A flame dried 3-necked flask, fitted with a dry ice condenser was charged with 2-methoxy-5-methylbenzoate (2.0 g, 11.1 mmol), THF (20 mL) and *t*-butyl alcohol (2.1 mL, 22.2 mmol) under nitrogen. Dry ammonia (100 mL) was then distilled into the flask cooled to –78 ºC, and small pieces of freshly cleaned lithium wire (0.19 g, 27.8 mg/atom) were added. The resulting blue solution was warmed to –33ºC and stirred for 15 min, before adding isoprene until the blue color dispersed. The ammonia was then boiled off under a stream of nitrogen and the residue cooled to –78 ºC. 2-(3″-Methoxyphenyl)-ethyl iodide (3.2 g, 12.2 mmol) in THF (8.5 mL) was then added dropwise over 10 min and the resulting reaction mixture was stirred at –78 ºC for 30 min, before warming to room temp. and stirring for an additional 16 h. Water (25 mL) was then added and the reaction mixture extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with water (20 mL), brine (20 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give a yellow oil. Purification by flash column chromatography on silica gel using EtOAc : hexane (1 : 9) as eluant gave the title compound (2.0 g, 57%) as a yellow oil. **IR** (thin film) cm^{-1}: 2937s (C-H), 1731s (C=O), 1695s, 1665s, 1601s, 1584s, 1491s (C=C), 1384s, 1365s, 1230br, 1168s, 1045s (C-O). **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 1.77 (s, 3H, 5-CH_3), 2.00 (m, 1H, H-1′), 2.31 – 2.44 (m, 3H, H-1′, H-2′), 2.78 (m, 2H, H-4), 3.56 (s, 3H, -CO_2CH_3), 3.67 (s, 3H, 2-OCH_3), 3.78 (s, 3H, 3″-OCH_3), 4.88 (t, J = 3.6 Hz, 1H, H-3), 5.16 (s (br), 1H, H-6), 6.68–6.76 (m, 3H, H-2″, H-4″, H-6″), 7.16 (dd, J = 8.4, J = 7.5 Hz, 1H, H-5″). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 22.6 (5-CH_3), 30.8 (CH_2, C-1′), 31.3 (CH_2, C-4), 36.1 (CH_2, C-2′), 52.3 (1-CO_2CH_3), 52.5 (C, C-1), 54.4 (2-OCH_3), 55.1 (3″-OCH_3), 93.8 (CH, C-3), 110.8 (CH, C-4″), 113.9 (CH, C-2″), 120.7 (CH, C-6″), 121.6 (CH, C-6), 128.9 (CH, C-5″), 134.7 (C, C-5), 144.1 (C, C-1″), 152.3 (C, C-2),

159.3 (C, C-3″), 174.1 (1-CO). **LRMS (m/z):** 316 (M^+, 31%), 257 (29), 195 (18), 181 (46), 149 (70), 135 (100), 121 (43), 105 (40), 91 (43), 77 (32). **HRMS:** $C_{19}H_{24}O_4$ (M^+) requires 316.1675, found 316.1677.

(8a*RS*) Methyl 9,10-Dihydro-2-methoxy-7-methylphenanthrene-8a(6*H*)-carboxylate (3)



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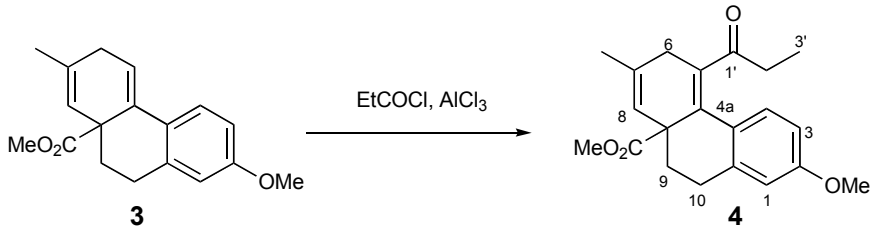
Preparation based on procedure described by S.R. Crabtree, Ph.D. thesis, ANU 1990.

Boron trifluoride diethyl etherate (5.6 mL, 43.9 mmol) was added dropwise to a solution of (1*RS*) Methyl 2-Methoxy-1-(2′-(3″-methoxyphenyl)ethyl)-5-methylcyclohexa-2,5-diene-1-carboxylate (12.6 g, 39.9 mmol) in DCM (250 mL) at –24 ºC under nitrogen. The reaction mixture was warmed to room temp. and stirred for 1 h. Water (60 mL) was then added and the resulting mixture stirred vigorously for 10 min. The organic phase was separated and the aqueous phase further extracted with DCM (2 x 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give a yellow solid. Trituration with hexane gave the title compound **3** (9.64 g, 85%) as a cream powder. A sample was crystallized from methanol to give white needle-like crystals; m.p.: 135–138ºC. **IR** (thin film) cm^{-1}: 2948s (C-H), 1720s (C=O), 1606s, 1572s, 1497s, 1444, 1230s, 1167, 1072. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 1.78 (s, 3H, 7-CH_3), 1.80 (m, 1H, H-9), 2.45 (ddd, J_{gem} = 13.0, $J_{9,10}$ = 5.7, $J_{9,10}$ = 1.6 Hz, 1H, H′-9), 2.73–3.00 (m, 4H, H-6, H-10), 3.57 (s, 3H, 8a-CO_2CH_3), 3.78 (s, 3H, 2-OCH_3), 5.40 (s (br), 1H, H-8), 6.21 (dd, J = 4.4, J = 3.2 Hz, 1H, H-5), 6.56 (d, $J_{1,3}$ = 2.6 Hz, 1H, H-1), 6.74 (dd, $J_{3,4}$ = 8.8, $J_{3,1}$ = 2.6 Hz, 1H, H-3), 7.53 (d, $J_{4,3}$ = 8.8, 1H, H-4). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 23.2 (7-CH_3), 27.7 (CH_2, C-10), 32.6 (CH_2, C-9), 34.2 (CH_2, C-6), 48.9 (C, C-8a), 52.6 (8a-CO_2CH_3), 55.5 (2-OCH_3), 113.1 (CH, C-3), 113.2 (CH, C-1), 118.3 (CH, C-5), 123.6 (CH, C-4), 125.7 (C, C-4a), 128.1 (CH, C-8), 133.3 (C, C-7), 133.8 (C, C-10a), 136.4 (C, C-4b), 158.7 (C, C-2), 174.5 (8a-CO). **LRMS (m/z):** 284 (M^+, 58%), 226 (36), 225

(100), 224 (45), 210 (37), 209 (23), 193 (20), 179 (23), 178 (26), 166 (23), 165 (34), 152 (19). **HRMS:** $C_{18}H_{20}O_3$ (M^+) requires 284.1412, found 284.1415. **Microanalysis:** Calcd. for $C_{18}H_{20}O_3$: C, 76.03%; H, 7.09%. Found: C, 75.92%; H, 6.82%.

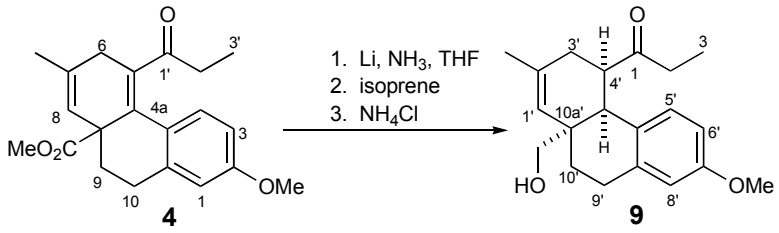
(8a*RS*) Methyl 9,10-Dihydro-5-(1′-oxopropanyl)-2-methoxy-7-methylphenanthrene-8a(6*H*)-carboxylate (4)



$AlCl_3$ (9.4 g, 70.4 mmol) was added to a solution of olefin **3** (5.0 g, 17.6 mmol) and propionyl chloride (4.6 mL, 53.8 mmol) in DCM (150 mL) at –78 °C under nitrogen. The resulting reaction mixture was stirred for 20 min then quenched by pouring over iced water with vigorous stirring. The organic phase was separated and the aqueous phase extracted with DCM (2 x 30 mL). The combined organic extracts were washed with water, aqueous KH_2PO_4 dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give a cream solid. Trituration with hexane gave the title compound **4** (4.5 g, 75%) as a cream powder. A sample was crystallized from EtOAc and hexane to give white crystals, **m.p. :** 139–144 ºC. **IR** (thin film) cm^{-1}: 2936s (C-H), 1729s (C=O), 1679s (C=O), 1605s, 1498s, 1445, 1264, 1239, 1166, 1070. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.94 (t, $J_{3',2'}$ = 7.2 Hz, H-3′), 1.75 (s, 3H, 7-CH_3), 1.90 (ddd, J_{gem} = 13.5 Hz, $J_{9,10}$ = 10.8 Hz, $J_{9,10}$ = 7.0 Hz, 1H, H-9), 2.23 (dq, J = 17.7 Hz, J = 7.2 Hz, 2H, H-2′), 2.57 (m, 1H, H′-9), 2.56 (d, J_{gem} = 21.9 Hz, 1H, H-6), 2.87 (ABdd, J_{gem} = 17.9 Hz, $J_{10,9}$ = 6.0 Hz, 1H, H-10), 3.01 (ddd, J_{gem} = 17.9 Hz, $J_{10,9}$ = 10.8 Hz, $J_{10,9}$ = 7.0 Hz, 1H, H′-10), 3.24 (d, J_{gem} = 21.9 Hz, 1H, H′-6), 3.44 (3H, s, 8a-CO_2CH_3), 3.76 (3H, s, 2-OCH_3), 5.33 (s (br), 1H, H-8), 6.60-6.63 (m, 2H, H-1, H-3), 6.97 (d, $J_{4,3}$ = 8.7 Hz, 1H, H-4). **^{13}C NMR (75 MHz, $CDCl_3$) δ:** 8.7 (CH_3, C-3′), 22.6 (7-CH_3), 26.7 (CH_2, C-9), 34.3 (CH_2), 34.3 (CH_2), 35.6 (CH_2) 50.7 (C, C-8a), 52.2 (8a-CO_2CH_3), 55.1 (2-OCH_3), 111.7 (CH, C-3), 113.2 (CH, C-1), 122.3 (CH, C-4), 126.9 (C, C-4a), 130.4 (C, C-8), 131.0 (C, C-5), 132.7 (C, C-7), 135.2 (CH, C-4b), 137.8 (C, C-10a), 159.5 (C, C-2), 173.5 (8a-CO), 211.8 (1′-CO). **LRMS (m/z):** 340 (M^+, 40%),

311 (10), 281 (62), 263 (26), 251 (30), 223 (39), 209 (19), 178 (14), 165 (26), 57 (100). **HRMS:** $C_{21}H_{24}O_4$ (M^+) requires 340.1675, found 340.1670. **Microanalysis:** Calcd. for $C_{21}H_{24}O_4$: C, 74.09%; H, 7.11%. Found: C, 73.97%; H, 6.97%.

(4′*RS*, 4a′*SR*, 10a′*RS*) 1-(10a′-Hydroxymethyl-7′-methoxy-2′-methyl-3′,4′,4a′,9′,10′,10a′-hexahydrophenanthren-4′-yl)-propan-1-one (9)

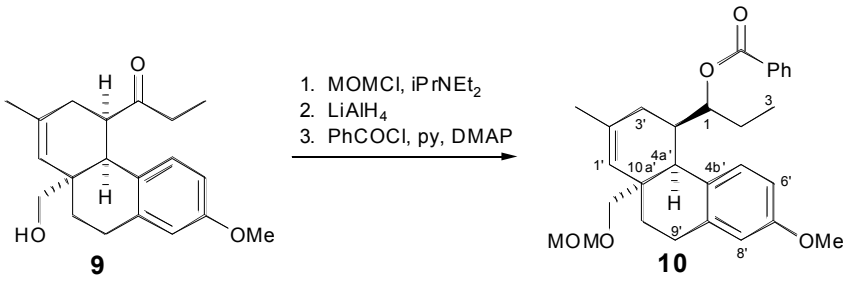


4 **9**

Dry ammonia (480 mL) was distilled into a 3-necked flask fitted with a dry ice condenser, under nitrogen. Small pieces of freshly cleaned lithium wire (1.0 g, 152.7 mmol) were added and the resulting blue solution was stirred at –78 °C for 15 min. A solution of ketone **4** (4.0 g, 11.7 mmol) in THF (200 mL) was then added dropwise over 5 min and the resulting reaction mixture was stirred for 15 min before adding isoprene dropwise until the blue color dispersed. The ammonia was allowed to boil off under a stream of nitrogen and a saturated solution of aqueous NH_4Cl (80 mL) was added. After 15 min, water (50 mL) was added and the aqueous phase extracted with EtOAc (3 x 100 mL). The combined organic extracts were washed with water (50 mL), brine (50 mL) and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave a yellow oil which was purified by flash column chromatography on silica gel using EtOAc : hexane (2 : 3) as eluant to give the title compound **9** (2.7 g, 74%) as a white solid, **m.p.:** 106–109ºC. **IR** (thin film) cm^{-1}: 3436br (C-OH), 2914s (C-H), 1701s (C=O), 1611s, 1502s, 1461, 1278, 1236, 1075, 1038. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 1.04 (t, $J_{3,2}$ = 7.2 Hz, 3H, H-3), 1.54 (dt, J_{gem} = 13.2 Hz, $J_{10',9'}$ = 5.1 Hz, 1H, H-10′), 1.65 (s, 3H, 2′-CH_3), 1.75 (ddd, J_{gem} = 13.2 Hz, $J_{10',9'}$ = 10.5 Hz, $J_{10',9'}$ = 5.1 Hz, 1H, H′-10′), 1.94 (d, J = 6.9 Hz, 2H, H-3′), 2.35-2.56 (m, 3H, H-2, H-9′), 2.74 (ddd, J_{gem} = 16.2, $J_{9',10'}$ = 10.5 Hz, $J_{9',10'}$ = 5.1 Hz, H′-9′), 2.91 (s (br), 1H, -OH), 3.09 (ddd, J = 10.2 Hz, J = 6.9 Hz, J = 3.3

Hz, 1H, H-4′), 3.46, 3.60 (2 x ABd, J = 11.1 Hz, 2H, 10a′-CH_2), 3.71 (d, $J_{4a',4'}$ = 3.3 Hz, 1H, H-4a′), 3.71 (s, 3H, 7′-OCH_3), 4.98 (s (br), 1H, H-1′), 6.54 (d, $J_{8',6'}$ = 2.7 Hz, 1H, H-8′), 6.60 (dd, $J_{6',5'}$ = 8.6 Hz, $J_{6',8'}$ = 2.7 Hz, 1H, H-6′), 6.72 (d, $J_{5',6'}$ = 8.6 Hz, 1H, H-5′). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 8.0 (CH_3, C-3), 23.6 (2′-CH_3), 26.5 (CH_2, C-10′), 28.5 (CH_2), 29.6 (CH_2), 34.3 (CH_2), 39.2 (C, C-10a′), 42.0 (CH, C-4a′), 50.0 (CH, C-4′), 54.9 (7′-OCH_3), 69.3 (C10a′-CH_2OH), 111.7 (CH, C-6′), 113.3 (CH, C-8′), 125.3 (CH, C-1′), 127.9 (CH, C-5′), 128.7 (C, C-4b′), 136.9 (C, C-2′), 139.1 (C, C-8a′), 157.0 (C, C-7′), 215.1 (1-CO). **LRMS (m/z):** 314 (M^+, 60%), 283 (74), 265 (26), 239 (24), 225 (84), 211 (63), 199 (16), 190 (63), 171 (44), 147 (19), 57 (100). **HRMS:** $C_{20}H_{26}O_3$ (M^+) requires 314.1882, found 314.1884. **Microanalysis:** Calcd. for $C_{20}H_{26}O_3$: C, 76.40%; H, 8.33%. Found: C, 76.30%; H, 8.40%.

(4′*RS*, 4a′*SR*, 10a′*RS*, 1*SR* or 1*RS*) 1-[10a′-Methoxmethoxy-7′-methoxy-2′-methyl-4a′,9′,10′,10a′-tetrahydrophenanthren-4′(3′*H*)-yl]-propan-1-yl benzoate (10)



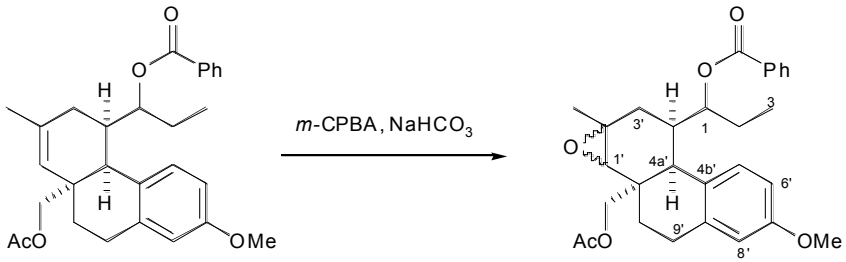
Hünig's base (5.6 mL, 32.1 mmol) was added to alcohol **9** (3.36 g, 10.7 mmol) in DCM (100 mL) at 0 °C under nitrogen. Chloromethyl methyl ether (2.4 mL, 32.1 mmol) was added dropwise and the reaction mixture warmed to room temperature. DMAP (50 mg) was then added and the reaction was stirred for 24 h. The reaction mixture was cooled to 0 °C, saturated sodium bicarbonate (50 mL) was added, and stirring continued for 10 min. The organic phase was then separated and the aqueous phase was extracted with DCM (3 x 50 mL). The combined organic extracts were washed with water (50 mL), 2 *M* HCl (50 mL), saturated sodium bicarbonate (50 mL), brine (50 mL) and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave the MOM ether (3.8 g) as a yellow gum, which was used directly in the next step without further purification.

A solution of the ketone (3.8 g, 10.7 mmol) in diethyl ether (40 mL) was added to a suspension of lithium aluminum hydride (0.8 g, 21.4 mmol) in diethyl ether (40 mL) at 0 ºC under nitrogen. The resulting reaction mixture was warmed to room temperature and stirred for 1 h. Water (0.8 mL) was added, followed by 1 *M* NaOH (0.8 mL) and a further portion of water (0.16 mL). When a white precipitate formed, anhydrous $MgSO_4$ was added and the reaction mixture was filtered through a plug of Celite®. Concentration of the organic phase *in vacuo* gave the alcohol (3.6 g, 93%) as a white foam, which was used directly in the next step without further purification.

Benzoyl chloride (3.5 mL, 29.9 mmol) was added to a solution of the alcohol (3.6 g, 9.96 mmol) in pyridine (100 mL) at room temperature under nitrogen. A catalytic amount of DMAP (5 mol %) was added and the resulting reaction mixture was stirred for 24 h. Water (50 mL) was then added, and the resulting mixture stirred for 10 min before extracting with ethyl acetate (4 x 50 mL). The combined organic extracts were washed with a saturated aqueous solution of copper sulfate (4 x 50 mL), water (50 mL), 1 *M* HCl (50 mL), water (50 mL), and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave a cream solid, which was purified by flash column chromatography on silica gel using EtOAc : hexane (1 : 9) as eluant to give the title compound **10** (4.2 g, 84% over three steps) as a white wax. **IR** (thin film) **cm^{-1}:** 2931s (C-H), 1711s (C=O), 1609s, 1501s, 1451, 1314, 1272, 1237, 1150, 1110, 1045. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.91 (t, $J_{3,2}$ = 7.3 Hz, 3H, H-3), 1.64 (m, 1H, H-10′), 1.74-1.94 (m, 4H, H′-10′, H-3′, H-2), 2.06 (m, 1H, H′-3′), 1.73 (s, 3H, 2′-CH_3), 2.45-2.76 (m, 3H, H-4′, H-9′), 3.17 (d, $J_{4'a,4'}$ = 3.0 Hz, 1H, H-4a′), 3.34 (s, 3H, 10a′-$OCH_2OC\mathit{H_3}$), 3.35, 3.51 (2 x ABd, *J* = 6.6 Hz, 2H, 10a′-CH_2), 3.58 (s, 3H, 7′-OCH_3), 4.60, 4.64 (2 x ABd, *J* = 9.3 Hz, 2H, 10a′-$OC\mathit{H_2}OCH_3$), 5.26 (s (br), 1H, H-1′), 5.53 (ddd, *J* = 9.9 Hz, *J* = 5.4 Hz, *J* = 3.9 Hz, 1H, H-1), 6.26 (d, $J_{8',6'}$ = 2.7 Hz, 1H, H-8′), 6.68 (dd, $J_{6',5'}$ = 8.7 Hz, $J_{6',8'}$ = 2.7 Hz, 1H, H-6′), 7.20 (d, $J_{5',6'}$ = 8.7 Hz, 1H, H-5′), 7.30-7.51 (m, 3H, H-3″, H-4″), 7.74 (d, *J* = 8.4 Hz, 2H, H-2″). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 8.2 (CH_3, C-3), 24.0 (2′-CH_3), 26.0 (CH_2, C-10′), 26.4 (CH_2), 29.1 (CH_2), 31.3 (CH_2), 39.1(C, C-10a′), 40.0 (CH, C-4a′), 40.4 (CH, C-4′), 54.7 (10a′-$OCH_2OC\mathit{H_3}$), 55.0 (7′-OCH_3), 74.2 (CH, C-1), 75.4 (C10a′-CH_2), 96.6 (10a′-$OC\mathit{H_2}OCH_3$), 111.9 (CH, C-6′), 112.8 (CH, C-8′), 127.3 (CH, C-1′), 127.6 (CH, C-5′), 129.3 (Ar), 129.4 (Ar), 130.1 (Ar), 130.2 (Ar), 132.3 (C, C-4b′), 133.6 (C, C-2′),

138.3 (C, C-8a′), 156.6 (C, C-7′), 165.7 (1-O*C*(O)Ph). **LRMS (m/z):** 464 (M^+, 37%), 432 (5), 388 (8), 342 (8), 310 (15), 297 (16), 280 (32), 267 (100), 225 (25), 211 (17), 105(50). **HRMS:** $C_{29}H_{36}O_5$ (M^+) requires 464.2563, found 464.2567.

(4′*RS*, 4a′*SR*, 10a′*RS*) 1-(10a′-Acetoxymethyl-7′-methoxy-2′-methyl-1′,2′-epoxy-4a′,9′,10′,10a′-tetrahydrophenanthren-4-yl)-propan-1-yl Benzoate (11)

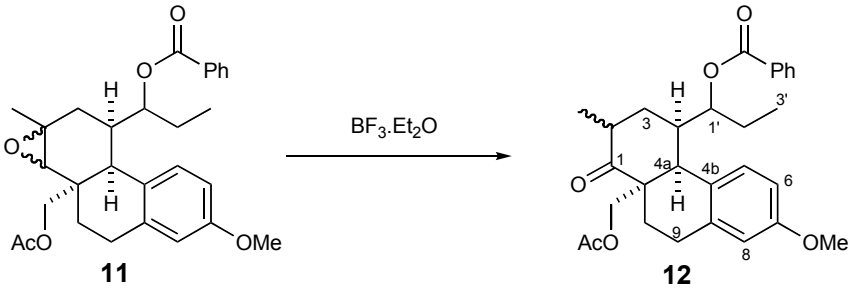


11

m-CPBA (0.81 g, 4.70 mmol) was added to a mixture of the olefin (1.08 g, 2.30 mmol) and $NaHCO_3$ (1.70 g) in DCM (20 mL) at 0 °C under nitrogen. The resulting reaction mixture was warmed to room temp. and stirred for 2 h before 10% Na_2SO_3 (10 mL) was added. After 5 min, the organic phase was separated and the aqueous residue further extracted with DCM (2 x 15 mL). The combined organic extracts were washed with 1*M* NaOH and brine then dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave a white foam which was purified by flash column chromatography on silica gel using EtOAc : hexane (1 : 4) as eluant to give the title compound **11** (0.98 g, 89%) as a white foam. **IR** (thin film) cm^{-1}: 2938s (C-H), 1743s (C=O), 1713s (C=O), 1610s, 1583, 1501s, 1451, 1381, 1364, 1271, 1176, 1070, 1039. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.93 (t, $J_{3,2}$ = 7.5 Hz, 3H, H-3), 1.21 (m, 1H, H-10′), 1.57–1.69 (m, 3H), 1.86–2.11 (m, 2H), 1.30 (s, 3H, 2′-CH_3), 2.03 (s, 3H, 10a′-OC(O)CH_3), 2.50–2.92 (m, 3H), 2.81 (s, 1H), 2.97 (s, 1H), 3.74 (s, 3H, 7′-OCH_3), 4.25 (s, 2H, 10a′-CH_2), 5.38 (m, 1H, H-1), 6.57 (d, $J_{8',6'}$ = 2.4 Hz, 1H, H-8′), 6.73 (dd, $J_{6',5'}$ = 8.4 Hz, $J_{6',8'}$ = 2.4 Hz, 1H, H-6′), 7.10 (d, $J_{5',6'}$ = 8.4 Hz, 1H, H-5′), 7.41–7.64 (m, 3H, H-3″, H-4″), 8.00 (d, J = 7.2 Hz, 2H, H-2″). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 8.2 (CH_3, C-3), 20.9 (-OC(O)*C*H_3), 22.3 (2′-CH_3), 25.0 (CH_2, C-10′), 26.5 (CH_2), 28.6 (CH_2), 31.3 (CH_2), 35.4, 36.2, 37.3, 55.0 (7′-OCH_3), 58.3 (C, C-2′), 64.3 (CH, C-1′), 68.0 (C10a′-CH_2), 75.4 (CH, C-1), 111.7 (CH, C-6′), 113.5 (CH, C-8′), 127.1 (CH, C-5′), 128.2 (Ar), 129.3 (Ar), 130.1 (Ar), 130.4 (Ar), 132.8 (C, C-4b′), 139.5

(C, C-8a′), 157.0 (C, C-7′), 165.7 (1-O*C*(O)Ph), 170.7 (-O*C*(O)CH_3). **LRMS (m/z):** 478 (M^+, 5%), 418 (12), 356 (15), 296 (34), 267 (45), 226 (47), 173 (29), 105 (100). **HRMS:** $C_{29}H_{34}O_6$ (M^+) requires 478.2355, found 478.2359.

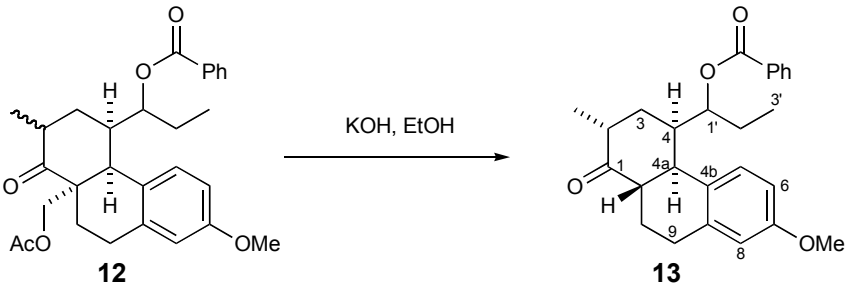
4*RS*, 4b*SR*, 10a*SR*) 10a-acetoxymethyl-4-(1′-Benzoyloxypropyl)-7-methoxy-2-methyl-3, 4, 4a, 9,10, 10a-hexahydrophenanthren-1(2*H*)-one (12)



Boron trifluoride diethyl etherate (0.52 mL, 4.10 mmol) was added dropwise to a solution of epoxide **11** (0.98 g, 2.05 mmol) in DCM (35 mL) at 0 ºC under nitrogen. The reaction mixture was stirred at 0 ºC for 40 min before adding water (15 mL) and stirring vigorously for 10 min. The organic phase was separated, and the aqueous phase extracted with DCM (2 x 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give a white foam. Purification by flash column chromatography on silica gel using EtOAc : hexane (1 : 4) as eluant gave the title compound **12** (0.72 g, 74%) as a white solid. A sample was crystallized from hexane to give white needle-like crystals, **m.p.:** 121–123 ºC. **IR** (thin film) cm^{-1}: 2967s (C-H), 1739s (C=O), 1709s (C=O), 1611s, 1584, 1502s, 1452, 1378, 1337, 1314, 1271, 1174, 1108, 1038. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.89 (t, $J_{3',2'}$ = 7.2 Hz, 3H, H-3′), 1.12 (d, J = 6.3 Hz, 3H, 2-CH_3), 1.55–2.25 (m, 6H), 1.93 (s, 3H, 10a-OC(O)CH_3), 2.45–2.76 (m, 4H), 3.42 (s, 3H, 7-OCH_3), 3.46 (d, $J_{4a,4}$ = 4.2 Hz, 1H, H-4a), 3.94, 4.36 (2 x ABd, J = 10.8 Hz, 2H, 10a-CH_2OH), 5.75 (ddd, J = 10.5 Hz, J = 6.9 Hz, J = 3.6 Hz, 1H, H-1′), 6.18 (d, $J_{8,6}$= 2.7 Hz, 1H, H-8), 6.55 (dd, $J_{6,5}$= 8.6 Hz, $J_{6,8}$= 2.7 Hz, 1H, H-6), 7.17 (d, $J_{5,6}$ = 8.6 Hz, 1H, H-5), 7.26–7.50 (m, 3H, H-3″, H-4″), 7.66 (d, J = 8.4 Hz, 2H, H-2″). **^{13}C NMR (75 MHz, $CDCl_3$) δ:** 8.1 (CH_3, C-3′), 15.8 (2-CH_3), 20.6 (-OC(O)*C*H_3), 25.4 (CH_2, C-10), 25.9 (CH_2), 28.0 (CH_2), 33.2 (CH_2), 38.2, 40.7, 41.6, 50.8, 54.3 (7-OCH_3), 67.2 (C10a-CH_2OH), 74.0 (CH, C-1′), 112.4 (CH, C-6), 112.7 (CH, C-8′), 127.4 (CH, C-5′),

127.6 (Ar), 129.0 (Ar), 129.3 (Ar), 130.0 (Ar), 132.2 (C, C-4b), 135.3 (C, C-8a), 156.9 (C, C-7), 165.1 (1′-O*C*(O)Ph), 170.0 (-O*C*(O)CH_3), 214.2 (1-CO). **LRMS (m/z):** 478 (M^+, 11%), 418 (50), 356 (53), 328 (22), 296 (50), 268 (35), 226 (47), 173 (65), 105(100). **HRMS:** $C_{29}H_{34}O_6$ (M^+) requires 478.2355, found 478.2362. **Microanalysis:** Calcd. for $C_{29}H_{34}O_6$: C, 72.78%; H, 7.16%. Found: C, 72.99%; H, 7.25%.

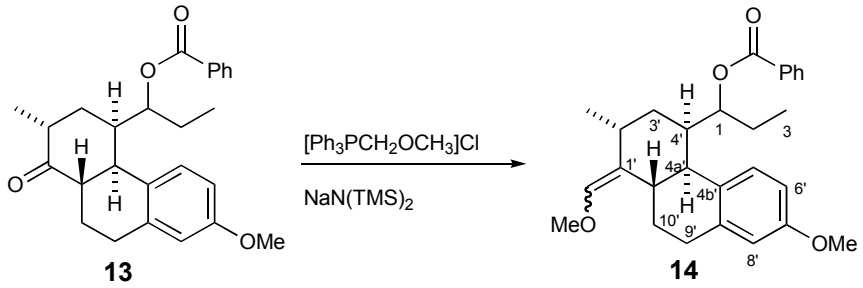
(2*RS*, 4*RS*, 4b*SR*, 10a*SR*) 4-(1′-Benzoyloxypropyl)-7-methoxy-2-methyl-3, 4, 4a, 9,10, 10a-hexahydrophenanthren-1(2*H*)-one (13)



Acetate **12** (0.21 g, 0.44 mmol) was dissolved in ethanolic KOH (0.6 g per 20 mL), and monitored by TLC until all the starting material had been consumed (ca. 1 h). The reaction mixture was neutralised with 1*M* HCl, the ethanol removed *in vacuo* and the residue extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with water (20 mL), brine (20 mL) and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave a brown oil which was purified by flash column chromatography on silica gel using EtOAc : hexane (1 : 4) as eluant to give the title compound **13** (0.12 g, 70%) as a cream solid. A sample was crystallized from hexane to give white crystals, **m.p:** 94–95 ºC. **IR** (thin film) cm^{-1}: 2967s (C-H), 1709s (C=O), 1611s, 1584s, 1503s, 1452s, 1316, 1275s, 1111, 1026. **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 0.95 (t, $J_{3',2'}$ = 7.3 Hz, 3H, H-3′), 1.11 (d, J = 6.3 Hz, 3H, 2-CH_3), 1.48 (m, 1H, H-10), 1.70 (dd, J_{gem} = 14.1 Hz, J = 4.5 Hz, 1H, H-3), 1.81 (m, 1H, H-2′), 1.95 (m, 1H, H′-2′), 2.17 (m, 1H, H′-10), 2.24 (ddd, J_{gem} = 14.1 Hz, J = 6.0, J = 2.1 Hz, 1H, H′-3) 2.45–2.53 (m, 2H, H-9), 2.73 (m, 1H, H-2), 2.99–3.05 (m, 3H, H-4, H-4a, H-10a), 3.46 (s, 3H, 7-OCH_3), 5.88 (ddd, J = 10.8 Hz, J = 8.4 Hz, J = 3.3 Hz, 1H, H-1′), 6.02 (d, $J_{8,6}$ = 2.7 Hz, 1H, H-8), 6.52 (dd, $J_{6,5}$ = 8.7 Hz, $J_{6,8}$ = 2.7 Hz, 1H, H-6), 7.16-7.44 (m, 6H, H-5, H-2″, H-

3″, H-4″). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 9.2 (CH_3, C-3′), 14.7 (2-CH_3), 22.3 (CH_2, C-10), 27.2 (CH_2, C-2′), 29.2 (CH_2, C-9), 38.4 (CH_2, C-3), 40.1 (CH, C-2), 40.4 (CH, C-10a), 46.8 (CH, C-4a), 47.3 (CH, C-4), 54.6 (7-OCH_3), 72.7 (CH, C-1′), 112.4 (CH, C-6), 112.6 (CH, C-8), 127.2 (CH, C-5), 127.9 (Ar), 129.0 (Ar), 129.2 (Ar), 132.1 (C, C-4b), 137.1 (C, C-8a), 156.4 (C, C-7), 165.8 (1′-O*C*(O)Ph), 211.8 (1-CO). **LRMS (m/z):** 406 (M^+, 90%), 284 (51), 242 (56), 216 (30), 187 (87), 160 (76), 128 (13), 105 (100). **HRMS:** $C_{26}H_{30}O_4$ (M^+) requires 406.2144, found 406.2148. **Microanalysis:** Calcd. for $C_{26}H_{30}O_4$: C, 76.82%, H, 7.44%. Found: C, 76.47%, H, 7.37%.

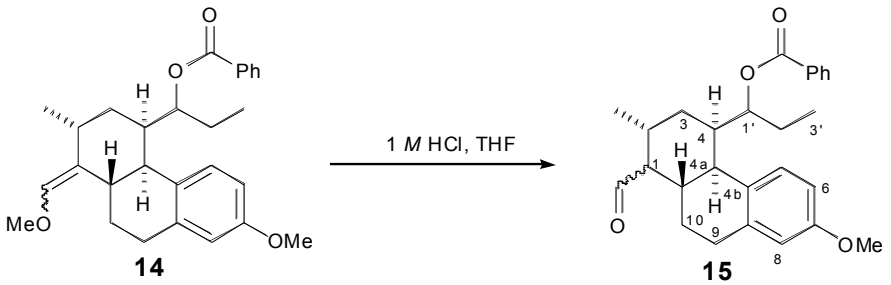
(2′*RS*, 4′*RS*, 4a′*SR*, 10a′*SR*) 1-[7′-Methoxy-1′-methoxymethylene-2′-methyl-1′,1′,2′, 3′,4′,4a′,9′,10′,10a′-octahydrophenanthrene-4′-yl]-propan-1-yl Benzoate (14)



Sodium bis(trimethylsilyl)amide (40.5 mL of a 1*M* solution in THF, 40.5 mmol) was added dropwise to a stirred solution of (methoxymethyl)triphenyl phosphonium chloride (13.9 g, 40.5 mmol) in dry THF (50 mL) at 0 ºC under nitrogen. After 15 min, a solution of ketone **13** (3.29 g, 8.09 mmol) in THF (50 mL) was added dropwise to the red solution and the reaction mixture was stirred at room temp.. After 4 h, the reaction was quenched with water (20 mL) and extracted with EtOAc (4 x 50 mL). The combined organic extracts were washed with water (20 mL), brine (20 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give a yellow oil. Purification by flash column chromatography using ether : hexane (5 : 95) as eluant gave the title compound **14** (2.96 g, 87%) as a colorless oil, a mixture of *E* and *Z* isomers. **IR** (thin film) cm^{-1}: 2931s (C-H), 1709s (C=O), 1672s, 1610s, 1584, 1502s, 1452s, 1315, 1274s, 1224, 1146, 1112, 1045, 1026. **^{1}H NMR** (300 MHz, $CDCl_3$; * indicates peaks belonging to minor isomer) **δ:** 0.84 (t, $J_{3,2}$ = 7.5 Hz, 3H, H-3), 0.87* (t, $J_{3,2}$ = 7.5 Hz, 3H, H-3), 1.04 (d, J = 6.6 Hz, 3H,

2′-CH_3), 1.34* (d, J = 6.6 Hz, 3H, 2′-CH_3), 1.45 (m, 1H, H-10′), 1.59–2.03 (m, 4H), 2.31–2.67 (m, 5H), 2.80–2.96 (m, 2H, H-4a′, H-4′), 3.45 (s, 3H, 1′-CHOCH_3), 3.46 (s, 3H, 7′-OCH_3), 3.50* (s, 3H, 1′-CHOCH_3), 3.51* (s, 3H, 7′-OCH_3), 5.63 (s, 1H, 1′-C$H$$OCH_3$), 5.70* (s, 1H, 1′-C$H$$OCH_3$), 5.71 (m, 1H, H-1), 6.01 (d, $J_{8',6'}$ = 2.7 Hz, 1H, H-8′), 6.10* (d, $J_{8',6'}$ = 2.7 Hz, 1H, H-8′), 6.50 (dd, $J_{6',5'}$ = 8.4 Hz, $J_{6',8'}$ = 2.7 Hz, 1H, H-6′), 6.55* (dd, $J_{6',5'}$ = 8.4 Hz, $J_{6',8'}$ = 2.7 Hz, 1H, H-6′), 7.12 (d, $J_{5',6'}$ = 8.4 Hz, 1H, H-5′), 7.18* (d, $J_{5',6'}$ = 8.4 Hz, 1H, H-5′), 7.18–7.52 (m, 5H, H-2″, H-3″, H-4″). **^{13}C NMR** (75 MHz, $CDCl_3$; * indicates peaks belonging to minor isomer) **δ:** 9.2 (CH_3, C-3), 9.4* (CH_3, C-3), 19.0 (2′-CH_3), 21.0* (2′-CH_3), 26.2 (CH_2), 26.3* (CH_2), 26.9 (CH_2), 27.8* (CH_2), 30.5 (CH_2), 31.3* (CH_2), 31.6 (CH_2), 32.2* (CH_2), 37.9 (CH), 38.8* (CH), 40.2 (CH), 40.4* (CH), 41.0 (CH), 41.4* (CH), 47.3 (CH), 47.6* (CH), 54.6 (7′-OCH_3), 54.7* (7′-OCH_3), 59.6 (1′-CHO$C$$H_3$), 73.6 (CH, C-1), 74.3* (CH, C-1), 112.0 (CH, C-6′), 112.5 (CH, C-8′), 112.6* (CH, C-8′), 123.8 (CH, 1′-$C$$HOCH_3$), 123.9* (CH, 1′-$C$$HOCH_3$), 127.2 (CH, C-5′), 127.3* (CH, C-5′), 127.9 (Ar), 128.0* (Ar), 129.3 (Ar), 129.6* (Ar), 129.7 (Ar), 130.8 (Ar), 131.2* (Ar), 131.9 (C, C-4b′), 132.0* (C, C-4b′), 137.6 (C, C-8a′), 138.2* (C, C-8a′), 139.4 (C, C-1′), 139.6* (C, C-1′), 156.0 (C, C-7′), 156.1* (C, C-7′), 165.6 (1-OC(O)Ph), 165.7* (1-OC(O)Ph). **LRMS (m/z):** 434 (M^+, 9%), 312 (100), 297 (2), 280 (7), 267 (10), 243 (53), 225 (4), 211 (9), 185 (4), 158 (9). **HRMS:** $C_{28}H_{35}O_4$ (MH^+) requires 435.2535, found 435.2541.

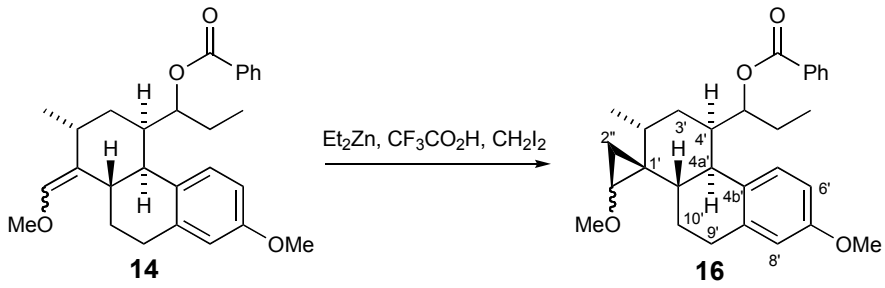
(1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*, 1′*SR*) 4-(1′-Benzoyloxypropyl)-7-methoxy-2-methyl-3,4,4a,9,10,10a-hexahydrophenanthrene-1(2H)-carbaldehyde (15).



1 *M* HCl (~2 mL) was added to a solution of enol ether **14** (0.12g, 0.052 mmol) in THF (20 mL) and the resulting reaction mixture was stirred overnight. The solvent was removed *in vacuo*, and the residue was partitioned between EtOAc and water (1 : 1, 20

mL). After separation of the organic phase, the aqueous phase was extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with water (10 mL), brine (10 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give a colourless oil. Purification by flash column chromatography using EtOAc : hexane (1 : 9) as eluant gave the title compound (0.05 g, 44%) as a colourless oil, a mixture of two isomeric aldehydes. **IR (thin film) cm^{-1}:** 2925s (C-H),1711s (C=O), 1610s, 1503, 1452s, 1315, 1274s, 1111, 1045. **^{1}H NMR** (300MHz, $CDCl_3$; * indicates peaks belonging to minor isomer) **δ:** 0.90 (t, $J_{3',2'}$ = 7.3 Hz, 3H, H-3′), 0.92* (t, $J_{3',2'}$ = 7.3 Hz, 3H, H-3′), 0.94* (d, J = 6.6 Hz, 3H, 2-CH_3), 1.07 (d, J = 6.9 Hz, 3H, 2-CH_3), 1.45-1.55 (m, 1H, H-10′), 1.63-1.93 (m, 4H, H-2′, H-3), 1.98-2.08 (m, 1H, H′-10), 2.12-2.30 (m, 1H, H-2), 2.55-2.67 (m, 3H, H-9, H-10a), 2.71-2.78* (m, 1H, H-4a), 2.70-3.12 (m, 2H, H-1, H-4), 3.24-3.32 (m, 1H, H-4a), 3.45 (s, 3H, 7-OCH_3), 3.47* (s, 3H, 7-OCH_3), 5.64-5.74 (m, 1H, H-1′), 6.00 (d, $J_{8,6}$ = 2.7 Hz, 1H, H-8), 6.04* (d, $J_{8,6}$ = 2.7 Hz, 1H, H-8), 6.51 (dd, $J_{6,5}$ = 8.4 Hz, $J_{6,8}$ = 2.7 Hz, 1H, H-6), 6.52* (dd, $J_{6,5}$ = 8.4 Hz, $J_{6,8}$ = 2.7 Hz, 1H, H-6), 7.17-7.42 (m, 6H, H-5, H-2″, H-3″, H-4″), 9.59* (d, J = 5.4 Hz, 1H, 1-CHO), 10.00 (d, J = 4.5 Hz, 1H, 1-CHO). **^{13}C NMR** (75MHz, $CDCl_3$; * indicates peaks belonging to minor isomer) **δ:** 9.1* (CH_3, C3′), 9.2 (CH_3, C3′), 19.7 (2-CH_3), 20.6* (2-CH_3), 26.5 (CH_2, C10), 26.8* (CH_2, C10′), 27.0 (CH_2, C2), 28.1* (CH_2, C2), 29.5 (CH_2, C9), 29.9* (CH_2, C9), 30.7 (CH_2, C3), 33.3* (CH, C2′), 35.2 (CH, C2′), 37.0 (CH, C10a), 37.8* (CH, C10a), 39.7* (CH, C4), 40.7 (CH, C4), 41.2 (CH, C4a), 44.9* (CH, C4a), 54.6 (7-OCH_3), 57.4* (7-OCH_3), 64.4 (CH, C1), 72.8 (CH, C1′), 73.4* (CH, C1′), 112.2 (CH, C6), 112.5* (CH, C6), 112.6 (CH, C8), 127.2 (CH, C5), 127.4* (CH, C5), 127.8 (C, Ar), 129.2 (C, Ar), 130.0* (C, C4b), 132.0 (C, C4b), 137.1* (C, C8a), 137.3 (C, C8a), 156.2 (C, C7), 165.7 (C, C1), 206.9* (1-CHO), 206.3 (1-CHO). **LRMS (m/z):** 420 (M^+, 5%), 336 (21), 298 (55), 269 (24), 231 (59), 215 (52), 199 (17), 105 (100).

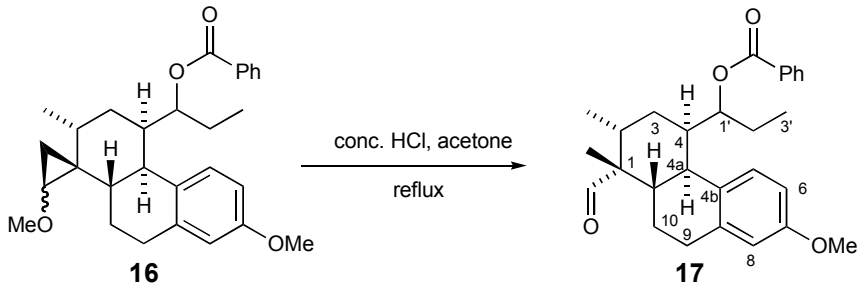
(1′*RS*, 2′*RS*, 4′*RS*, 4a′*SR*, 10a′*SR*) 1-[7′-Methoxy-1″-methoxy-spiro[cyclopropane-1′,1′]-2′-methyl-1′,2′,3′,4′,4a′,9′,10′,10a′-octahydrophenanthrene-4′-yl]-propan-1-yl Benzoate (16).



Diethyl zinc (24.5 mL of a 1 *M* solution in hexanes, 24.5 mmol) was added to DCM (20 mL) at 0 °C under nitrogen. Trifluroacetic acid (1.89 mL, 24.5 mmol) in DCM (10 mL) was then added dropwise and the resulting reaction mixture stirred for 20 min. Diiodomethane (1.98 mL, 24.5 mmol) in DCM (10 mL) was then added and after 20 min enol ether **14** (2.96 g, 7.01 mmol) was added. The reaction mixture was warmed to room temp. and stirred for a further 20 min. The reaction was quenched with a saturated solution of NH_4Cl and extracted with DCM (3 x 50 mL). The combined organic extracts were washed with water, dried over $MgSO_4$ and concentrated *in vacuo* to give the title compound **16** (ca. 3 g) as a yellow oil. The crude product was used directly in the next step without any further purification. A sample was purified by flash column chromatography using ether : petroleum spirit (0.5 : 9.5) for characterization purposes. **IR** (thin film) cm^{-1}: 2929s (C-H),1709s (C=O), 1503s, 1455, 1273s, 1112, 1067, 1042, 1020. **^{1}H NMR** (300 MHz, $CDCl_3$; * indicates peaks belonging to minor isomer) **δ:** 0.59 (d, J = 7.1 Hz, 3H, 2′-CH_3), 0.64 (m, 1H, H-2″), 0.86 (t, $J_{3,2}$ = 7.2 Hz, 3H, H-3), 0.88* (t, $J_{3,2}$ = 7.2 Hz, 3H, H-3), 0.81 (m, 1H, H′-2″), 0.97* (d, J = 7.1 Hz, 3H, 2′-CH_3), 1.57 (m, 1H, H-10′), 1.62–1.89 (m, 4H), 2.11–2.54 (m, 5H), 2.89 (m, 1H, H-4′), 3.10–3.23 (m, 2H, H-4a′, H-1″), 3.22 (s, 3H, 1′-CHOCH_3), 3.30* (s, 3H, 1′-CHOCH_3), 3.43 (s, 3H, 7′-OCH_3), 3.45* (s, 3H, 7′-OCH_3), 5.75 (ddd, J = 11.1 Hz, J = 7.8 Hz, J = 3.3 Hz, 1H, H-1), 5.97 (d, $J_{8',6'}$ = 2.9 Hz, 1H, H-8′), 6.49 (dd, $J_{6',5'}$ = 8.4 Hz, $J_{6',8'}$ = 2.9 Hz, 1H, H-6′), 6.52* (dd, $J_{6',5'}$ = 8.4 Hz, $J_{6',8'}$ = 2.9 Hz, 1H, H-6′), 7.14 (d, $J_{5',6'}$ = 8.4 Hz, 1H, H-5′), 7.17–7.45

(m, 5H). **^{13}C NMR** (75 MHz, $CDCl_3$; * indicates peaks belonging to minor isomer) **δ:** 9.2 (CH_3, C-3), 9.8* (CH_3, C-3), 10.8 (CH_2, 1′-CH_2), 16.6 (2′-CH_3), 18.4* (2′-CH_3), 25.3 (CH_2), 27.0 (CH_2), 29.8 (CH_2), 30.5 (CH_2), 31.3 (CH_2), 32.1* (CH_2), 32.9 (C, C-1′), 33.1* (C, C-1′), 38.6 (CH), 38.9* (CH), 38.4 (CH), 41.8 (CH), 42.0* (CH), 45.7 (CH), 46.0* (CH), 54.6 (7′-OCH_3), 54.7* (7′-OCH_3), 57.8 (1′-CHO*C*H_3), 58.1* (1′-CHO*C*H_3), 59.7 (1′-*C*HOCH$_3$), 60.0* (1′-*C*HOCH$_3$), 73.7 (CH, C-1), 74.0* (CH, C-1), 112.0 (CH, C-6′), 112.2 (CH, C-8′), 112.4* (CH, C-8′), 127.2 (CH, C-5′), 127.4* (CH, C-5′), 127.9 (Ar), 128.1* (Ar), 129.3 (Ar), 129.7* (Ar), 131.6 (C, C-4b′), 131.9* (C, C-4b′), 137.5 (C, C-8a′), 138.2* (C, C-8a′), 155.9 (C, C-7′), 156.0* (C, C-7′), 165.7 (1-O*C*(O)Ph). **LRMS (m/z):** 448 (M^+, 15%), 326 (68), 294 (11), 284 (65), 268 (85), 251 (21), 239 (34) 225 (100), 211 (23), 197 (20), 185 (14). **HRMS:** $C_{29}H_{36}O_4$ (M^+) requires 448.2614, found 448.2615.

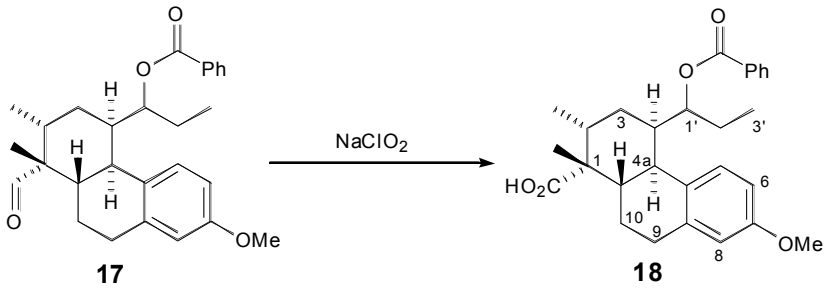
(1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) 4-(1′-Benzoyloxypropyl)-1,2-dimethyl-7-methoxy-3,4,4a,9,10,10a-hexahydrophenanthrene-1(2*H*)-carbaldehyde (17)



Concentrated HCl (4 mL) was added to cyclopropane **16** (3 g, 7 mmol) in acetone (80 mL) and heated at reflux for 10 h. Water (10 mL) was then added and the acetone removed *in vacuo*. The mixture was extracted with EtOAc (4 x 10 mL) and the combined organic extracts washed with brine (10 mL), saturated $NaHCO_3$ (10 mL) then water (10 mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give the title compound **17** (3 g) as a yellow oil which was used in the next step without further purification. A sample was purified by flash column chromatography for characterization purposes, on silica gel using ether : hexane (5 : 95) as eluant to give the

title compound as a white solid. A sample was crystallized from EtOAc : hexane to give white crystals, **m.p:** 150–152 ºC. **IR** (thin film) cm^{-1}: 2917s (C-H),1709s (C=O), 1610s, 1503s, 1453, 1273s, 1108. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.90 (t, $J_{3',2'}$ = 7.3 Hz, 3H, H-3′), 1.01 (d, J = 6.7 Hz, 3H, 2-CH_3), 1.35 (s, 3H, 1-CH_3), 1.26 (m, 1H, H-10), 1.65 (m, 1H, H-2′), 1.77–1.93 (m, 3H, H′-2′, H-3, H-2), 2.07–2.20 (m, 3H, H′-3, H′-10, H-10a), 2.47–2.50 (m, 2H, H-9), 2.98 (m, 1H, H-4), 3.40 (m, 1H, H-4a), 3.44 (s, 3H, 7-OCH_3), 5.72 (ddd, J = 10.8 Hz, J = 7.8 Hz, J = 2.7 Hz, 1H, H-1′), 5.99 (d, $J_{8,6}$ = 2.7 Hz, 1H, H-8), 6.50 (dd, $J_{6,5}$ = 8.4 Hz, $J_{6,8}$ = 2.7 Hz, 1H, H-6), 7.17–7.42 (m, 6H, H-5, H-2″, H-3″, H-4″), 9.93 (s, 1H, 1-CHO). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 9.1 (CH_3, C-3′), 17.2 (2-CH_3), 19.9 (1-CH_3), 24.0 (CH_2, C-10), 26.8 (CH_2, C-2′), 31.1 (CH_2, C-9), 35.5 (CH_2, C-3), 35.6 (CH, C-2), 40.6 (CH, C-4), 41.7 (CH, C-4a), 43.3 (CH, C-10a), 51.9 (C, C-1), 54.7 (7-OCH_3), 72.8 (CH, C-1′), 112.3 (CH, C-6), 112.4 (CH, C-8), 127.3 (CH, C-5), 127.9 (Ar), 129.3 (Ar), 129.4 (Ar), 132.0 (C, C-4b), 137.3 (C, C-8a), 156.3 (C, C-7), 165.7 (1′-O*C*(O)Ph), 207.7 (1-CHO). **LRMS (m/z):** 434 (M^+, 10%), 336 (68), 312 (12), 283 (11), 231 (74), 215 (100), 199 (24), 185 (23). **HRMS:** $C_{28}H_{34}O_4$ (M^+) requires 434.2457, found 434.2452.

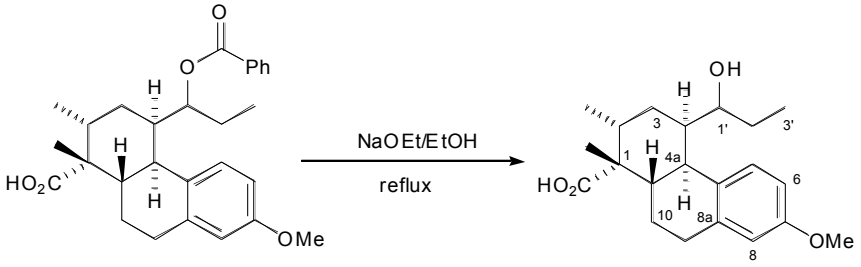
(1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) 4-(1′-Benzoyloxypropyl)-1,2-dimethyl-7-methoxy-3,4,4a,9,10,10a-hexahydrophenanthrene-1(2*H*)-carboxylic acid (18).



Aldehyde **17** (3.25 g, 7.02 mmol) was dissolved in a mixture of acetonitrile (200 mL), hydrogen peroxide (24 mL of a 30% w/v solution) and NaH_2PO_4 buffer (24 mL, pH 2). The solution was cooled to 0 °C and $NaClO_2$ (1.27 g, 14.0 mmol) was added. The resulting reaction mixture was stirred for 5 h then diluted with EtOAc (150 mL) and washed with water (100 mL). The organic phase was separated and the aqueous layer

extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with water (50 mL), brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo* to give a yellow solid. Purification by flash column chromatography using EtOAc : petroleum spirit (1 : 4) with 1% HOAc as eluant gave acid **18** (2.52 g, 80% over three steps) as a white solid. A sample was crystallized from ether : hexane to give white crystals, **m.p:** 203–205 ºC. **IR** (thin film) cm^{-1}: 3289br (C-OH), 2938s (C-H), 1709s (C=O), 1689s (C=O), 1606, 1503, 1450, 1275s, 1109. **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 0.87 (t, $J_{3',2'}$ = 7.5 Hz, 3H, H-3′), 1.00 (d, J = 6.6 Hz, 3H, 2-CH_3), 1.39 (s, 3H, 1-CH_3), 1.09–2.34 (m, 8H, H-2′, H-3, H-2, H-10, H-10a), 2.37–2.58 (m, 2H, H-9), 2.86 (m, 1H, H-4), 3.44 (s, 3H, 7-OCH_3), 3.55 (m, 1H, H-4a), 5.64 (ddd, J = 10.5 Hz, J = 7.5 Hz, J = 2.7 Hz, 1H, H-1′), 5.99 (d, $J_{8,6}$ = 2.7 Hz, 1H, H-8), 6.51 (dd, $J_{6,5}$ = 8.4 Hz, $J_{6,8}$ = 2.7 Hz, 1H, H-6), 7.15–7.41 (m, 6H, H-5, H-2″, H-3″, H-4″). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 9.0 (CH_3, C-3′), 17.4 (2-CH_3), 23.2 (1-CH_3), 24.6 (CH_2, C10), 26.6 (CH_2, C-2′), 30.9 (CH_2, C-9), 34.5 (CH_2, C-3), 35.4 (CH, C-2), 39.8 (CH, C-4), 39.9 (CH, C-4a), 42.5 (CH, C-10a), 49.9 (C, C-1), 54.6 (7-OCH_3), 73.2 (CH, C-1′), 112.2 (CH, C-6), 112.4 (CH, C-8), 127.3 (CH, C-5), 127.9 (Ar), 129.3 (Ar), 129.5 (Ar), 131.4 (Ar), 132.0 (C, C-4b), 137.2 (C, C-8a), 156.1 (C, C-7), 165.9 (1′-O*C*(O)Ph), 181.1 (1-CO_2H). **LRMS (m/z):** 450 (M^+, 90%), 328 (68), 283 (30), 240 (46), 231 (42), 213 (31), 159 (26), 105 (100). **HRMS:** $C_{28}H_{34}O_5$ (M^+) requires 450.2406, found 450.2406. **Microanalysis:** Calcd. For $C_{28}H_{34}O_5$: C, 74.64%, H, 7.61%. Found: C, 74.43%, H, 7.67%.

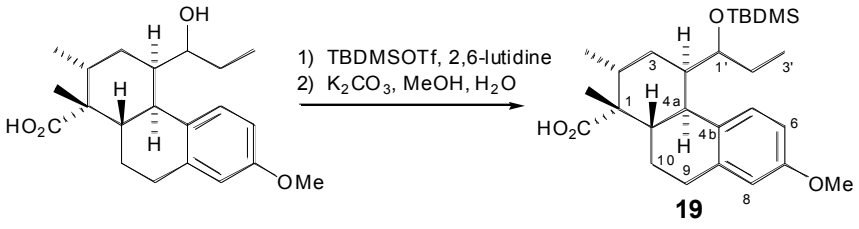
(1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*, 1′*SR*) 4-(1′-hydroxypropyl)-7-methoxy-1,2-methyl-3,4,4a,9,10,10a-hexahydrophenanthrene-1(2*H*)-carbaboxylic acid



Sodium (2 g) was slowly added to the benzoate (2.52 g, 5.62 mmol) in ethanol (120 mL) at room temperature under nitrogen. The reaction mixture was heated at reflux for 2 d,

then water (50 mL) was added and the ethanol removed *in vacuo*. The residue was treated with 1 *M* HCl until pH 5 and extracted with EtOAc (3 x 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product as a yellow solid. Purification by flash column chromatography using EtOAc : petroleum spirit (1 : 9) with 1% acetic acid as eluant gave the title compound (1.24 g, 65%) as a white foam and recovered starting material (0.97 g, 35%) which was re-submitted to the reaction conditions and purified as above to give more of the title compound (1.38 g total, 73%). **IR (thin film) cm^{-1}:** 3546br (C-OH), 2934s (C-H), 1694s (C=O), 1610s, 1500s, 1464, 1256s, 1157. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.92 (t, $J_{3',2'}$ = 7.5 Hz, 3H, H-3′), 0.96 (d, J = 6.6 Hz, 3H, 2-CH_3), 1.26-1.67 (m, 6H), 1.34 (s, 3H, 1-CH_3), 1.97 (td, J = 12.0 Hz, J = 1.5 Hz, 1H), 2.08 (m, 1H), 2.57 (m, 1H, H-4), 2.68-2.89 (m, 2H, H-9), 3.59 (m, 1H, H-4a), 3.74 (s, 3H, 7-OCH_3), 3.94 (m, 1H, H-1′), 6.58 (d, $J_{8,6}$ = 2.7 Hz, 1H, H-8), 6.73 (dd, $J_{6,5}$ = 8.7 Hz, $J_{6,8}$ = 2.7 Hz, 1H, H-6), 7.29 (d, $J_{5,6}$ = 8.7 Hz, 1H, H-5). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 9.5 (CH_3, C-3′), 17.3 (2-CH_3), 23.2 (1-CH_3), 24.5 (CH_2), 29.0 (CH_2), 31.3 (CH_2), 34.4 (CH_2), 35.4 (CH), 39.8 (CH), 42.0 (CH), 43.1 (CH), 49.7 (C, C-1), 55.0 (7-OCH_3), 72.8 (CH, C-1′), 112.3 (CH, C-6), 114.1 (CH, C-8), 128.0 (CH, C-5), 130.9 (C, C-4b), 138.5 (C, C-8a), 157.2 (C, C-7), 180.7 (1-CO_2H). **LRMS (m/z):** 346 (M^+, 75%), 328 (15), 283 (11), 241 (25), 199 (26), 187 (66), 174 (100), 161 (37). **HRMS:** $C_{21}H_{30}O_4$ (M^+) requires 346.2144, found 346.2143.

(1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*, 1′*SR*) 4-(1′-*t*.-butyldimethylsilyloxyproyl)-7-methoxy-1,2-methyl-3,4,4a,9,10,10a-hexahydrophenanthrene-1(2*H*)-carbaboxylic acid (19)



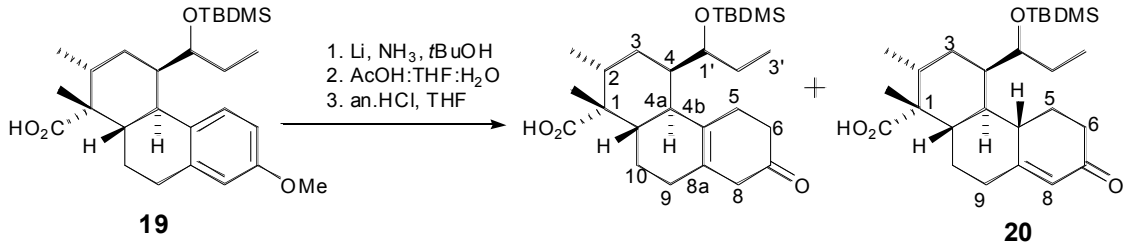
19

t-Butyldimethylsilyl trifluoromethanesulfonate (1.43 mL, 6.23 mmol) was added dropwise to the alcohol (0.72 g, 2.08 mmol) and 2,6-lutidine (0.97 mL, 8.32 mmol) in DCM (20 mL) at room temperature under nitrogen. After 15 min water (20 mL) was

added and the organic phase was separated then the aqueous layer extracted with DCM (2 x 20 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give the crude *bis*-protected product as a yellow gum.

Potassium carbonate (10% in water 10 mL) was added to a solution of the TBDMS ester in THF : MeOH (1 : 3, 40 mL) and stirred at room temperature for 1 h 45 min. The methanol was removed *in vacuo*, the residue treated with 1 *M* HCl until pH 5 and then extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo* to give a yellow oil. Purification by flash column chromatography on silica gel using EtOAc : hexane (1 : 9) with 1% acetic acid as eluant gave the title compound **19** (0.78 g, 81%) as a white solid. A sample was crystallised from hexane to give white crystals, **m.p:** 172-173 ºC. **IR** (thin film) **cm^{-1}:** 3500br (C-OH), 2929s (C-H), 1692s (C=O), 1611, 1502s, 1472, 1255s, 1079. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** -0.11 (s, 3H, -$SiCH_3$), -0.07 (s, 3H, -$SiCH_3$), 0.80 (s, 9H, -Si^{t}Bu), 0.75-0.84 (m, 3H, H-3′), 0.98 (d, J = 6.6 Hz, 3H, 2-CH_3), 1.87-2.16 (m, 8H), 1.33 (s, 3H, 1-CH_3), 2.68-2.84 (m, 3H), 3.53 (dd, $J_{4a,10a}$ = 12.0 Hz, $J_{4a,4}$ = 4.5 Hz, 1H, H-4a), 3.77 (s, 3H, 7-OCH_3), 3.87 (m, 1H, H-1′), 6.54 (d, $J_{8,6}$ = 2.7 Hz, 1H, H-8), 6.70 (dd, $J_{6,5}$ = 8.7 Hz, $J_{6,8}$ = 2.7 Hz, 1H, H-6), 7.23 (d, $J_{5,6}$ = 8.7 Hz, 1H, H-5). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** -4.5 ($SiCH_3$), -3.9 ($SiCH_3$), 9.8 (CH_3, C-3), 17.7 (2-CH_3), 18.2 (SiC), 23.5 (1-CH_3), 25.2 (CH_2), 26.1 (Si^{t}Bu), 28.7 (CH_2), 31.4 (CH_2), 31.9 (CH_2), 36.8 (CH), 39.2 (CH), 39.4 (CH), 43.6 (CH), 49.6 (C, C-1), 55.2 (7-OCH_3), 72.7 (CH, C-1′), 111.8 (CH, C-6), 113.2 (CH, C-8), 128.4 (CH, C-5), 131.1 (C, C-4b), 137.4 (C, C-8a), 156.7 (C, C-7), 181.4 (1-CO_2H). **LRMS (m/z):** 460 (M^+, 15%), 437 (17), 405 (50), 403 (98), 283 (23), 241 (23), 173 (100), 117 (70). **HRMS:** $C_{27}H_{44}O_4Si$ (M^+) requires 460.3009, found 460.3007. **Microanalysis:** Calcd. for $C_{27}H_{44}O_4Si$: C, 70.39%, H, 9.63%. Found: C, 70.06%, H, 9.49%.

(1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) 4-(1′-*t*.-Butyldimethylsilyloxypropyl)-1,2-dimethyl-7-oxo-3,4,4a,4b,5,6,7,9,10,10a-decahydrophenanthrene-1(2*H*)-carboxylic Acid (20)

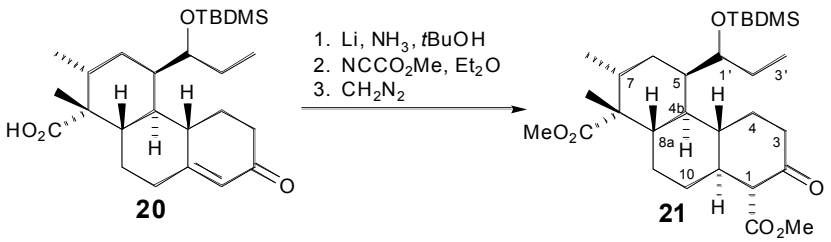


Dry ammonia (200 mL) was distilled into a 3-necked flask fitted with a dry ice condenser under nitrogen. Small pieces of freshly cleaned lithium wire (1.65 g, 245.3 mmol) were added at –78ºC and the resulting blue solution was stirred for 15 min. Silyl ether **19** (2.26 g, 4.91 mmol) in THF (50 mL) was added over 10 min, stirred for 15 min, then *t*-butanol (50mL) was added. The blue reaction mixture was warmed to –40ºC and stirred for 3 h. The reaction was then quenched with methanol and the ammonia allowed to boil off under a stream of nitrogen before a saturated aqueous solution of NH_4Cl (80 mL) was added. After 15 min water (50 mL) was added and the aqueous phase adjusted to pH 5 with 1*M* HCl then extracted with EtOAc (3 x 100 mL). The combined organic extracts were washed with water (50 mL), brine (50 mL) and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave a colorless oil, which was taken up in a solution of AcOH: THF : water (4 : 2 : 1, 50 mL) and stirred for 2 h under nitrogen. The solvent was removed *in vacuo* and the aqueous residue was extracted with ethylacetate (3 x 50 mL) then dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave the crude βγ-enone as a colorless oil, which was used directly in the next reaction without further purification. Concentrated H_2SO_4 was added dropwise to NaCl. The resulting hydrogen chloride gas was passed through concentrated H_2SO_4 and then bubbled through THF (35 mL) for 1 min. The crude βγ-enone in THF (35 mL) was then added to the acidic THF then the reaction was monitored by TLC until half of the starting material had been consumed, and a new UV active spot was observed. Concentration of the organic phase *in vacuo* gave a yellow gum, which was purified by flash column chromatography on silica gel using EtOAc : hexane (1 : 9 – 1 : 4) as eluant to give the βγ-enone (1.31 g, 39%) as a colorless oil, and the αβ-enone **20** (1.20 g, 35%) as a white foam (74% combined yield).

βγ-enone: IR (thin film) cm^{-1}: 2931s (C-H), 1721s (C=O), 1694 (C=O), 1472, 1463, 1254s, 1075s. **^{1}H NMR** (300 MHz, $CDCl_3$) δ: –0.10 (s, 3H, -$SiCH_3$), -0.01 (s, 3H, -$SiCH_3$), 0.82 (s, 9H, -Si^{t}Bu), 0.87 (t, $J_{3',2'}$ = 7.5 Hz, 3H, H-3′), 0.91 (d, J = 6.6 Hz, 3H, 2-CH_3), 1.28 (s, 3H, 1-CH_3), 1.44-2.20 (m, 11H), 2.26–2.38 (m, 2H), 2.41–2.46 (m, 2H), 2.67 (s(br), 2H, H-8), 2.70–2.90 (m, 2H), 4.05 (dt, J = 9.9 Hz, J = 3.3 Hz, 1H, H-1′). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: –4.6 ($SiCH_3$), –3.4 ($SiCH_3$), 6.6 (CH_3, C-3′), 17.5 (2-CH_3), 18.2 (SiC), 23.6 (1-CH_3), 24.6 (CH_2), 26.2 (Si^{t}Bu), 27.5 (CH_2), 28.2 (CH_2), 30.5 (CH_2), 34.3 (CH_2), 35.3 (CH), 36.0 (CH), 39.1 (CH_2), 41.7 (CH), 42.2 (CH), 44.7 (CH_2, C-8), 49.8 (C), 70.7 (CH, C-1′), 122.8 (C, C-8a), 133.0 (C, C-4b), 181.2 (1-CO_2H), 212.2 (7-CO). **LRMS (m/z):** 391 ((M-^{t}Bu)$^+$, 50%), 316 (70), 277 (22), 224 (21), 173 (100), 147 (43), 73 (79). **HRMS:** $C_{22}H_{35}O_4Si$ ((M-^{t}Bu)$^+$) requires 391.2305, found 391.2304.

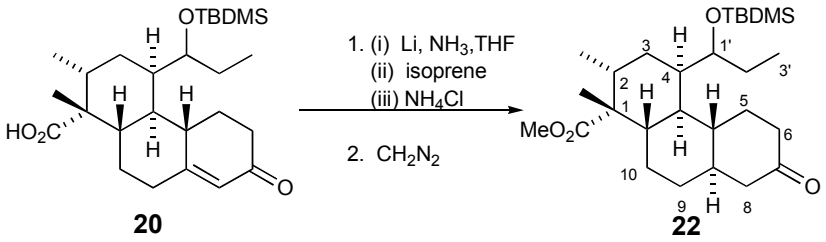
αβ-enone (20): IR (thin film) cm^{-1}: 2932s (C-H), 1694s (C=O), 1671 (C=O), 1472, 1462, 1256s, 1208. **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 0.07 (s, 3H, -$SiCH_3$), 0.08 (s, 3H, -$SiCH_3$), 0.89 (s, 9H, -Si^{t}Bu), 0.91 (t, $J_{3',2'}$ = 7.5 Hz, 3H, H-3′), 0.86–0.94 (m, 3H, 2-CH_3), 1.26 (s, 3H, 1-CH_3), 1.05–2.31 (m, 14H), 2.34–2.45 (m, 2H, H-6), 2.91 (m, 1H, H-4b), 4.16 (dt, J = 8.4 Hz, J = 3.9 Hz, 1H, H-1′), 5.79 (s, 1H, H-8).**^{13}C NMR** (75MHz, $CDCl_3$) δ: –3.8 ($SiCH_3$), –3.3 ($SiCH_3$), 7.4 (CH_3, C3′), 17.6 (2-CH_3), 18.2 (SiC), 23.9 (1-CH_3), 26.1 (Si^{t}Bu), 27.0 (CH_2), 28.0 (CH_2), 28.4 (CH_2), 33.1 (CH_2), 35.2 (CH), 35.3 (CH), 35.7 (CH_2), 36.2 (CH_2), 39.0 (CH), 43.5 (CH), 46.3 (CH), 50.1 (C, C-1), 72.3 (CH, C-1′), 123.7 (CH, C-8), 167.8 (C, C-8a), 180.2 (1-CO_2H), 200.9 (7-CO). **LRMS (m/z):** 448 (M^+, 1%), 319 (80), 345 (15), 316 (100), 273 (21), 224 (48), 173 (91). **HRMS:** $C_{26}H_{44}O_4Si$ (M^+) requires 448.3009, found 448.3010.

(1*RS*, 4a*RS*, 4b*SR*, 5*RS*, 7*RS*, 8*SR*, 8a*SR*, 10a*SR*, 1'*SR*) Dimethyl 5-(1′-*t*.-Butyldimethylsilyloxypropyl)-7,8-dimethyl-2-oxo-3,4,4a,4b,5,6,7,8, 8a,9,10,10a-Dodecahydrophenanthrene-1,8(2*H*, 8a*H*)-dicarboxylate (21)



Dry ammonia (10 mL) was distilled into a 3-necked flask fitted with a dry ice condenser under nitrogen. Small pieces of freshly cleaned lithium wire (0.002 g, 0.29 mmol) were added at -78 ºC and the resulting blue solution stirred for 10 min. A solution of enone **20** (0.030 g, 0.067 mmol) in *t*-butyl alcohol (6.4 µL, 0.067 mmol) and ether (2 mL) was added dropwise, and the resulting reaction mixture stirred for 15 min. The reaction was quenched with isoprene until the blue colour dispersed, and the ammonia allowed to boil off under a stream of nitrogen. The residue was dried under high vacuum for 5 min then nitrogen was reintroduced. Ether (3 mL) was added and the reaction mixture was cooled to -78 ºC. Methyl cyanoformate (11 µL, 0.13 mmol) was added and the reaction mixture was stirred for 15 min before quenching with lithium hydroxide (2 mL, 2 *M*). The reaction mixture was warmed to room temperature and monitored by TLC until only one product was observed. The reaction mixture was extracted with ether (3 x 15 mL) and the combined organic extracts were washed with water (5 mL), brine (5 mL) and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave a colourless oil which was purified by flash column chromatography on silica gel using EtOAc : hexane (5 : 95 - 20 : 80) as eluant to give the keto ester (7.3 mg, 21%) as a colourless oil. Futher elution gave starting material **20** (0.016 g, 53%). The crude keto ester (7.3 mg) was dissolved in ether (1 mL) and diazomethane (1 mL) was added. The reaction mixture was stirred for 15 minutes then excess diazomethane and ether were allowed to blow off under nitrogen to obtain the title compound **21** as a colourless oil (7.3 mg, 100%). **IR (thin film) cm^{-1}:** 2918s (C-H), 1775s (C=O), 1725 (C=O), 1489, 1261, 1189, 1096, 1025. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 0.09 (s, 3H, -$SiCH_3$), 0.10 (s, 3H, -$SiCH_3$), 0.91 (s, 9H, -Si^{t}Bu), 0.77 (d, J = 6.3 Hz, 3H, 7-CH_3), 0.85-0.95 (m, 3H, H-3′), 0.98-2.54 (m, 21H), 3.09 (d, $J_{1,10a}$ = 12.0 Hz, 1H, H-1), 3.62 (s, 3H, 8-CO_2CH_3), 3.74 (s, 3H, 1-CO_2CH_3), 4.08 (m, 1H, H-1′). **LRMS (m/z):** 465 ((M-^{t}Bu)$^+$, 50%), 407 (15), 345 (5), 215 (8), 173 (100), 115 (20), 73 (60). **HRMS:** $C_{25}H_{41}O_6Si$ (M-^{t}Bu$^+$) requires 465.2672, found 465.2675.

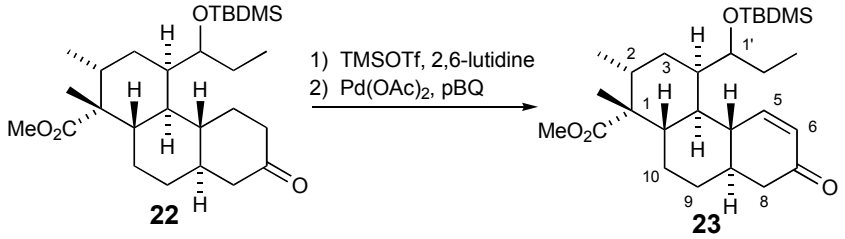
(1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) Methyl 4-(1′-*t*.-Butyldimethylsilyloxypropyl)-1,2-dimethyl-7-oxo-3,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-1(2*H*)-carboxylate (22)



Dry ammonia (70 mL) was distilled into a 3-necked flask fitted with a dry ice condenser under nitrogen. Small pieces of freshly cleaned lithium wire (0.056 g, 8.22 mmol) were added at –78 ºC and the resulting blue solution was stirred for 10 min. A solution of enone **20** (1.23 g, 2.74 mmol) in *t*-butanol (0.26 mL, 2.74 mmol) and THF (40 mL) was added dropwise, and the resulting reaction mixture was stirred for 30 min at –33 ºC . The reaction was quenched with isoprene until the blue color dispersed, and the ammonia was allowed to boil off under a stream of nitrogen. A saturated solution of aqueous NH_4Cl (40 mL) was then added and stirring continued for a further 15 min. Water (10 mL) was added and the aqueous phase adjusted to pH 5 with 1*M* HCl then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with water (20 mL), brine (20 mL) and dried over anhydrous $MgSO_4$. Concentration of the organic phase in *vacuo* gave a crude yellow oil which was used directly in the next step without further purification. A freshly prepared solution of diazomethane in ether (120 mL) was added to the crude carboxylic acid (2 g) in ether (50 mL) at 0 °C. The yellow reaction mixture was stirred for 30 min, and the excess diazomethane and ether blown off with a stream of nitrogen. Purification by flash column chromatography using EtOAc : petroleum spirit (1 : 9) as eluant gave the title compound **22** (1.2 g, 55% over two steps) as a colorless oil, and an alcohol (7-OH, 0.45 g, 21% over the two steps) which was subsequently converted to **22** by oxidation with DMP (a total of 76% yield over two steps). **IR** (thin film) cm^{-1}: 2952s (C-H), 1721s (C=O), 1472, 1462, 1255, 1145. **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 0.08 (s, 3H, -$SiCH_3$), 0.09 (s, 3H, -$SiCH_3$), 0.78 (d, J = 7.2 Hz, 3H, 2-CH_3), 0.92 (s, 9H, -Si^{t}Bu), 0.93 (t, $J_{3',2'}$ = 7.2 Hz, 3H, H-3′), 0.79 (m, 1H, H-10), 1.09 (m, 1H, H-9), 1.24 (s, 3H, 1-CH_3), 1.26–1.35 (m, 2H, H-8a, H-5), 1.48–1.75 (m, 8H, H-2′, H-4b, H-3, H-2, H-10a, H′-

9), 1.85 (m, 1H, H-4a), 1.95 (m, 1H, H′-10), 2.06 (m, 1H, H-8), 2.18 (m, 1H, H-4), 2.27 (m, 1H, H′-8), 2.30–2.34 (m, 2H, H-6), 2.44 (m, 1H, H′-5), 3.62 (s, 3H, 1-CO_2CH_3), 4.03 (dt, J = 7.2 Hz, J = 4.2 Hz, 1H, H-1′). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: –4.2 ($SiCH_3$), –3.0 ($SiCH_3$), 8.7 (CH_3, C-3′), 17.8 (2-CH_3), 18.2 (SiC), 23.9 (2-CH_3), 26.2 (Si^{t}Bu), 28.1 (CH_2, C-10), 28.6 (CH_2, C-2′), 30.9 (CH_2, C-5), 32.4 (CH_2, C-3), 33.7 (CH_2, C-9), 35.7 (CH), 36.1 (CH, C-4), 40.9 (CH_2, C-6), 42.0 (CH, C-4b), 43.5 (CH, C-8a), 44.0 (CH, C-4a), 44.3 (CH), 48.5 (CH_2, C-8), 50.3 (C, C-1), 50.6 (1-CO_2CH_3), 72.9 (CH, C-1′), 175.0 (1-CO_2CH_3), 211.8 (7-CO). **LRMS (m/z):** 407 ((M-^{t}Bu)$^+$, 91%), 255 (28), 215 (18), 173 (100), 145 (13), 115 (27). **HRMS:** $C_{23}H_{39}O_4Si$ ((M-^{t}Bu)$^+$) requires 407.2618, found 407.2621.

Methyl (1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) Methyl 4-(1′-*t*.-Butyldimethylsilyloxypropyl)-1,2-dimethyl-7-oxo-3,4,4a,4b,7,8,8a,9,10,10a-decahydrophenanthrene-1(2*H*)-carboxylate (23)



Trimethylsilyl trifluoromethanesulfonate (1.52 mL, 8.39 mmol) was added dropwise to ketone **22** (1.30 g, 2.80 mmol) and 2,6-lutidine (1.30 mL, 11.19 mmol) in DCM (30 mL) at 0 °C under nitrogen. Water (15 mL) was added and the organic phase was separated before further extraction of the aqueous layer with DCM (2 x 15 mL). The combined organic extracts were then washed with brine and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave a mixture of two silyl enol ethers (20 : 1, 6,7-enol ether : 7,8-enol ether). The crude silyl enol ethers in acetonitrile (30 mL) were added to palladium acetate (0.63 g, 2.80 mmol) and *p*-benzoquinone (0.15 g, 1.40 mmol) in acetonitrile (30 mL) at room temp. under nitrogen. The resulting reaction mixture was stirred for 30 h, then filtered through a plug of Celite® and washed with ether (60 mL). Concentration *in vacuo* gave a black gum, which was purified by flash column chromatography on silica gel using EtOAc : petroleum spirit (1 : 9) as eluant to give the title αβ-enone **23** (1.03 g, 79%) as a white solid. A sample was crystallized from hexane

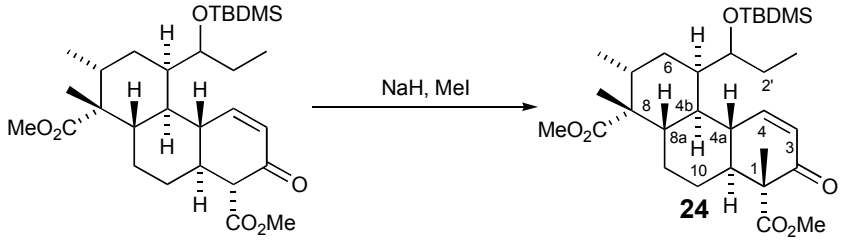
to give white crystals, **m.p:** 99–101 ºC. **IR** (thin film) cm^{-1}: 2933s (C-H), 1722s (C=O), 1684s (C=O), 1472s, 1463, 1253s, 1195. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.05 (s, 3H, -$SiCH_3$), 0.08 (s, 3H, -$SiCH_3$), 0.79 (d, J = 6.6 Hz, 3H, 2-CH_3), 0.87 (s, 9H, -Si^{t}Bu), 0.93 (t, $J_{3',2'}$ = 7.2 Hz, 3H, H-3′), 0.87 (m, 1H, H-10), 1.25 (s, 3H, 1-CH_3), 1.18 (m, 1H, H-9), 1.46–1.69 (m, 8H), 1.80 (m, 1H), 1.96–2.14 (m, 2H, H-8, H-10), 2.35–2.41 (m, 2H, H-8, H-4), 2.55 (m, 1H, H-4b), 3.62 (s, 3H, 1-CO_2CH_3), 4.17 (dt, J = 8.7 Hz, J = 3.9 Hz, 1H, H-1′), 5.97 (m, 1H, H-6), 7.27 (dd, J = 9.0 Hz, J = 1.8 Hz, 1H, H-5). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ**: –3.7 ($SiCH_3$), –3.3 ($SiCH_3$), 6.9 (CH_3, C-3′), 17.7 (2-CH_3), 18.3 (SiC), 23.9 (1-CH_3), 26.2 (Si^{t}Bu), 27.4 (CH_2), 27.7 (CH_2), 32.4 (CH_2), 33.1 (CH_2), 35.1 (CH), 35.4 (CH), 41.6 (CH), 42.3 (CH), 43.7 (CH), 44.7 (CH), 45.3 (CH_2, C-8), 50.5 (C, C-1), 50.7 (1-CO_2CH_3), 71.6 (CH, C-1′), 128.7 (CH, C-6), 154.1 (CH, C-5), 175.0 (1-CO_2CH_3), 200.2 (7-CO). **LRMS (m/z):** 405 ((M-^{t}Bu)$^+$, 93%), 330 (22), 270 (25), 213 (14), 173 (100), 115 (33). **HRMS:** $C_{23}H_{37}O_4Si$ ((M-^{t}Bu)$^+$) requires 405.2461, found 405.2459.

Dimethyl (1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) 5-(1′-*t.*-Butyldimethylsilyloxypropyl)-7,8-dimethyl-2-oxo-4a,4b,5,6,7,9,10,10a-octahydrophenanthrene-1,8(2*H*, 8a*H*)-dicarboxylate

n-Butyllithium (1.0 mL of a 1.6*M* solution in hexanes, 1.60 mmol) was added to diisopropylamine (0.22 mL, 1.60 mmol) in THF (10 mL) at –20 °C under nitrogen. The reaction mixture was stirred for 20 min, warmed to 0 °C and stirred for a further 30 min. The solution was cooled to –78 °C, ketone **23** (0.37 g, 0.80 mmol) in THF (10 mL) was added, and then `stirred for 1 h at 0 °C. The reaction mixture was then cooled to –78 °C, HMPA (0.14 mL, 0.80 mmol) was added followed by methyl cyanoformate (0.12 mL, 1.60 mmol). After 20 min the mixture was poured into water and extracted with ether (3 x

15 mL). The combined organic extracts were washed with water (10 mL), brine (10mL) and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave a yellow oil, which was purified by flash column chromatography on silica gel using EtOAc : hexane (1 : 9) as eluant to give the title compound (0.35 g, 83%) as a colorless oil. **IR** (thin film) cm^{-1}: 2952s (C-H), 1746s (C=O), 1722s (C=O), 1681s (C=O), 1472s, 1462s, 1254s, 1149. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ**: 0.05 (s, 3H, -$SiCH_3$), 0.07 (s, 3H, -$SiCH_3$), 0.79 (d, J = 6.6 Hz, 3H, 7-CH_3), 0.86 (s, 9H, -Si^{t}Bu), 0.93 (t, $J_{3',2'}$ = 7.2 Hz, 3H, H-3′), 1.26 (s, 3H, 8-CH_3), 0.90 (m, 1H, H-9), 1.17 (m, 1H, H-10), 1.47–1.72 (m, 6H), 1.82 (m, 1H), 1.95–2.14 (m, 3H, H-4b, H-9, H-10), 2.38 (m, 1H, H-5), 2.69 (m, 1H, H-4a), 3.10 (d, $J_{1,10a}$ = 12.9 Hz, 1H, H-1), 3.62 (s, 3H, 8-CO_2CH_3), 3.76 (s, 3H, 1-CO_2CH_3), 4.22 (dt, J = 9.3 Hz, J = 3.6 Hz, 1H, H-1′), 6.03 (dd, J = 10.2 Hz, J = 2.7 Hz, 1H, H-3), 7.33 (dd, J = 10.2 Hz, J = 1.8 Hz, 1H, H-4). **^{13}C NMR** (75MHz, $CDCl_3$) **δ**: –3.6 ($SiCH_3$), –3.2 ($SiCH_3$), 6.4 (CH_3, C-3′), 17.7 (7-CH_3), 18.3 (SiC), 23.9 (8-CH_3), 26.2 (Si^{t}Bu), 27.1 (CH_2, C-9), 27.4 (CH_2), 30.4 (CH_2), 33.3 (CH_2), 34.8 (CH), 35.2 (CH), 42.6 (CH), 42.7 (CH), 43.6 (CH), 44.4 (CH), 50.5 (C, C-8), 50.8 (8-CO_2CH_3), 52.0 (1-CO_2CH_3), 60.9 (CH, C-1), 71.4 (CH, C-1′), 127.5 (CH, C-3), 154.3 (CH, C-4), 170.5 (1-CO_2CH_3), 174.7 (8-CO_2CH_3), 194.6 (2-CO). **LRMS (m/z):** 463 ((M-^{t}Bu)$^+$, 93%), 405 (49), 388 (50), 329 (67), 269 (47), 213 (40), 173 (100). **HRMS:** $C_{25}H_{39}O_6Si$ ((M-^{t}Bu)$^+$) requires 463.2516, found 463.2514.

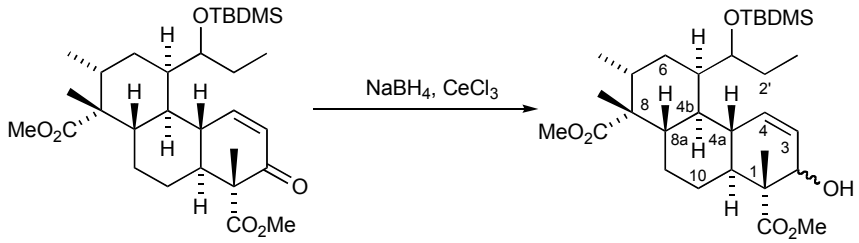
(1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) Dimethyl 5-(1′-*t.*-Butyldimethylsilyloxypropyl)-2-oxo-1,7,8-trimethyl-4a,4b,5,6,7,9,10,10a-octahydrophenanthrene-1,8(2*H*, 8a*H*)-dicarboxylate (24)



NaH (0.018 g, 0.76 mmol) was added to the β-ketoester (0.33 g, 0.64 mmol) in THF (10 mL) at room temp. under nitrogen. After 5 min iodomethane (0.048 mL, 0.76 mmol) was

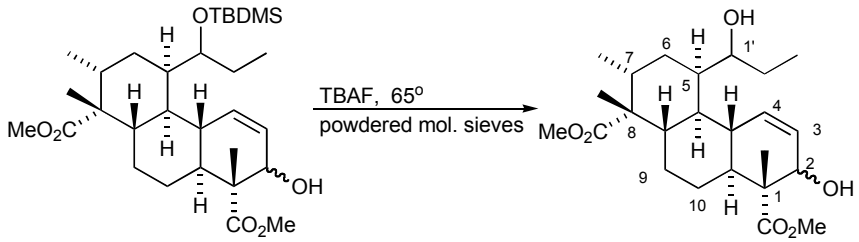
added and the reaction mixture stirred for 18 h. The reaction was quenched with water and extracted with EtOAc (4 x 10 mL). The combined organic extracts were washed with water (5 mL), brine (5 mL) and dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave a yellow oil which was purified by flash column chromatography on silica gel using EtOAc : petroleum spirit (1 : 9) as eluant to give the title compound **24** (0.29 g, 88%) as a white solid. A sample was crystallized from hexane to give white crystals, **m.p:** 47–50 ºC. **IR** (thin film) cm^{-1}: 2950s (C-H), 1741s (C=O), 1721s (C=O), 1679s (C=O), 1461, 1258s, 1212. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.04 (s, 3H, -$SiCH_3$), 0.09 (s, 3H, -$SiCH_3$), 0.79 (d, J = 6.6 Hz, 3H, 7-CH_3), 0.89 (s, 9H, -Si^{t}Bu), 0.93 (t, $J_{3',2'}$ = 7.2 Hz, 3H, H-3′), 1.26 (s, 6H, 1-CH_3, 8-CH_3), 0.91 (m, 1H, H-9), 1.25 (m, 1H, H-10), 1.47–1.68 (m, 6H), 1.81 (m, 1H), 2.01 (m, 1H, H-9), 2.08–2.26 (m, 2H, H-10, H-4b), 2.38 (m, 1H, H-5), 2.56 (m, 1H, H-4a), 3.64 (s, 3H, 8-CO_2CH_3), 3.72 (s, 3H, 1-CO_2CH_3), 4.19 (dt, J = 8.7 Hz, J = 3.9 Hz, 1H, H-1′), 5.96 (dd, J = 10.4 Hz, J = 2.7 Hz, 1H, H-3), 7.28 (dd, J = 10.4 Hz, J = 1.5 Hz, 1H, H-4). **^{13}C** NMR (75 MHz, $CDCl_3$) **δ:** –3.6 ($SiCH_3$), –2.9 ($SiCH_3$), 6.9 (CH_3, C-3′), 14.1 (1-CH_3), 17.6 (7-CH_3), 18.4 (SiC), 23.8 (8-CH_3), 26.3 (Si^{t}Bu), 26.7 (CH_2, C-9), 27.4 (CH_2), 27.9 (CH_2), 33.3 (CH_2), 35.1 (CH), 35.2 (CH), 39.3 (CH), 43.5 (CH), 44.5 (CH), 46.2 (CH), 50.6 (C, C-8), 50.8 (8-CO_2CH_3), 52.2 (1-CO_2CH_3), 58.6 (C, C-1), 72.0 (CH, C-1′), 126.3 (CH, C-3), 152.8 (CH, C-4), 173.2 (1-CO_2CH_3), 174.8 (8-CO_2CH_3), 199.1 (2-CO). **LRMS (m/z):** 477 ((M-^{t}Bu)$^+$, 84%), 459 (22), 419 (37), 357 (38), 343 (53), 283 (22), 173 (100). **HRMS:** $C_{26}H_{41}O_6Si$ (M-^{t}Bu)$^+$ requires 477.2672, found 477.2669.

Dimethyl (1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) 5-(1′-*t*.-Butyldimethylsilyloxypropyl)-2-hydroxy-1,7,8-trimethyl-4a,4b,5,6,7,9,10,10a-octahydrophenanthrene-1,8(2*H*, 8a*H*)-dicarboxylate



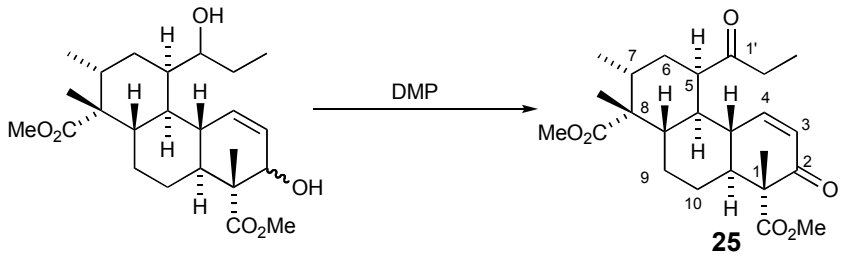
Ketone **24** (0.36 g, 0.67 mmol) in MeOH (10 mL) was added to $CeCl_3$ heptahydrate (0.28 g, 0.74 mmol) under nitrogen. The solution was cooled to –78 °C, $NaBH_4$ (0.03 g, 0.74 mmol) was added and the mixture gradually warmed to 0 °C over 50 min. The reaction was quenched with water and the methanol was removed *in vacuo*. The aqueous residue was extracted with EtOAc (4 x 30 mL), then the combined organic extracts were washed with brine (10 mL), back-extracted with EtOAc (2 x 10 mL) and dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave two epimeric products, which were purified by flash column chromatography on silica gel using EtOAc : petroleum spirit (1.5 : 8.5) as eluant to give the major alcohol (0.27 g, 75%) as a white solid and the minor alcohol (0.02 g, 5%) as a white solid. A sample of the major alcohol was crystallized with ether to give white crystals, **m.p:** 133–136 ºC. **IR** (thin film) cm^{-1}: 3497br (C-OH), 2951s (C-H), 1723s (C=O), 1468s, 1387, 1255s, 1212. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ**: 0.05 (s, 3H, -$SiCH_3$), 0.08 (s, 3H, -$SiCH_3$), 0.76 (d, J = 6.6 Hz, 3H, 7-CH_3), 0.88 (s, 9H, -Si^{t}Bu), 0.91 (t, $J_{3',2'}$ = 7.2 Hz, 3H, H-3′), 0.85 (m, 1H, H-9), 1.06 (s, 3H, 1-CH_3), 1.22 (s, 3H, 8-CH_3), 1.18 (m, 1H, H-10), 1.46–1.77 (m, 8H), 1.89–2.10 (m, 3H), 2.31 (m, 1H, H-5), 3.63 (s, 3H, 8-CO_2CH_3), 3.70 (s, 3H, 1-CO_2CH_3), 4.09 (m, 1H, H-1′), 4.73 (m, 1H, H-2), 5.51 (m, 1H, H-3), 6.05 (m, 1H, H-4). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** –3.9 ($SiCH_3$), –3.0 ($SiCH_3$), 7.9 (CH_3, C-3′), 9.1 (1-CH_3), 17.7 (7-CH_3), 18.4 (SiC), 23.9 (8-CH_3), 26.3 (Si^{t}Bu), 26.9 (CH_2), 28.0 (CH_2), 28.4 (CH_2), 32.8 (CH_2), 35.4 (CH), 36.0 (CH), 39.5 (CH), 44.0 (CH), 44.5 (CH), 46.2 (CH), 50.6 (2 x C, C-8 and C-1), 50.8 (8-CO_2CH_3), 51.9 (1-CO_2CH_3), 72.2 (CH, C-1′), 73.2 (CH, C-2), 128.8 (CH, C-3), 130.6 (CH, C-4), 175.2 (1-CO_2CH_3), 177.1 (8-CO_2CH_3). **LRMS (m/z):** 479 ((M-^{t}Bu)$^+$, 53%), 419 (82), 404 (79), 387 (80), 361 (41), 355 (33), 345 (100). **HRMS:** $C_{26}H_{43}O_6Si$ ((M-^{t}Bu)$^+$) requires 479.2829, found 479.2830. **Microanalysis:** Calcd. For $C_{30}H_{52}O_6Si$: C, 67.12%, H, 9.76%. Found: C, 67.43%, H, 10.00%.

Dimethyl (1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) 5-(1′-hydroxypropyl)-2-hydroxy-1,7,8-trimethyl-2-hydroxy-4a,4b,5,6,7,9,10,10a-octahydrophenanthrene-1,8(2*H*, 8a*H*)-dicarboxylate



Tetrabutyl ammonium fluoride (1.51 mL of a 1*M* solution in THF, 1.51 mmol) was added to the TBDMS ether (0.27 g, 0.50 mmol) in THF (20 mL) containing powdered 4Å molecular sieves at room temp. under nitrogen, then heated to 65 °C for 36 h. The reaction mixture was cooled to room temp., water (5 mL) was added and the mixture extracted with EtOAc (4 x 20 mL). The combined organic extracts were washed with water (10 mL), brine (10 mL) and dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave a yellow oil, which was purified by flash column chromatography on silica gel using EtOAc : hexane (2 : 3 – 4 : 1) as eluant to give the title compound (0.15 g, 84% based on recovered starting material) as a white solid, **m.p:** 164–165 ºC. **IR** (thin film) cm^{-1}: 3497br (C-OH), 2948s (C-H), 1718s (C=O), 1459, 1387, 1256, 1211. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ**: 0.75 (d, J = 6.9 Hz, 3H, 7-CH_3), 0.84 (m, 1H, H-9), 0.98 (t, $J_{3',2'}$ = 7.5 Hz, 3H, H-3′), 1.05 (s, 3H, 1-CH_3), 1.21 (s, 3H, 8-CH_3), 1.20 (m, 1H, H-10), 1.31–1.99 (m, 10H), 2.14 (m, 1H, H-5), 2.26 (m, 1H, H-4a), 3.63 (s, 3H, 8-CO_2CH_3), 3.69 (s, 3H, 1-CO_2CH_3), 3.91 (td, J = 8.7 Hz, J = 2.7 Hz, 1H, H-1′), 4.72 (m, 1H, H-2), 5.49 (m, 1H, H-3), 6.10 (m, 1H, H-4). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 9.2 (1-CH_3), 9.5 (CH_3, C-3′), 17.9 (7-CH_3), 24.1 (8-CH_3), 27.2 (CH_2), 28.3 (CH_2), 28.6 (CH_2), 33.6 (CH_2), 35.4 (CH), 38.6 (CH), 40.1 (CH), 44.4 (CH), 44.8 (CH), 46.2 (CH), 50.7 (C), 51.1 (8-CO_2CH_3), 52.1 (C), 52.2 (1-CO_2CH_3), 71.9 (CH, C-1′), 73.5 (CH, C-2), 128.7 (CH, C-3), 131.4 (CH, C-4), 175.4 (1-CO_2CH_3), 177.5 (8-CO_2CH_3). **LRMS (m/z):** 404 ($(M-H_2O)^+$, 20%), 386 (20), 345 (41), 327 (44), 285 (51), 278 (56), 221 (70), 189 (67), 161 (100). **HRMS:** $C_{24}H_{36}O_5$ $(M-H_2O)^+$ requires 404.2563, found 404.2562.

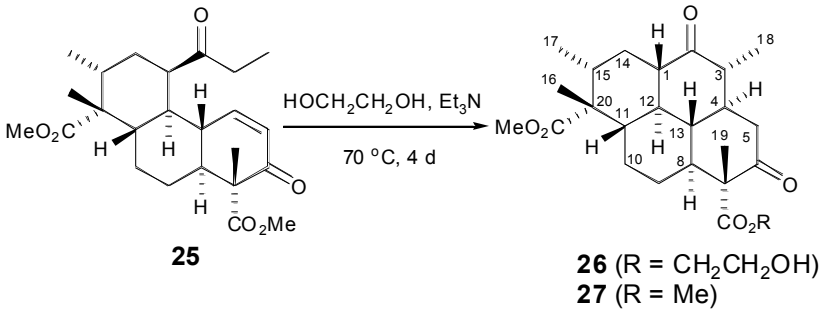
Dimethyl (1*RS*, 2*RS*, 4*RS*, 4a*SR*, 10a*SR*) 5-(1′-oxopropyl)-2-oxo-1,7,8-trimethyl-4a,4b,5,6,7,9,10,10a-octahydrophenanthrene-1,8(2*H*, 8a*H*)-dicarboxylate (25)



25

Dess–Martin periodinane (0.45 g, 1.07 mmol) was added to the diol (0.15 g, 0.36 mmol) in DCM (10 mL) at 0 °C under nitrogen. After 1.5 h, the reaction mixture was stirred with 1*M* sodium thiosulfate (5 mL) and a saturated aqueous solution of $NaHCO_3$ (5 mL) until the cloudiness disappeared. The organic phase was separated and the aqueous phase further extracted with DCM (3 x 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give a white solid. Purification by flash column chromatography on silica gel using EtOAc : hexane (1 : 9) as eluant gave the title compound **25** (0.12 g, 81%) as a white solid. A sample was crystallized from ether/hexane to give white crystals, **m.p:** 143–145 ºC. **IR** (thin film) cm^{-1}: 2947s (C-H), 1736s (C=O), 1720s (C=O), 1678s (C=O), 1458, 1377, 1263. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.82 (d, J = 6.9 Hz, 3H, 7-CH_3), 0.78 (m, 1H, H-9), 1.04 (t, $J_{3',2'}$ = 7.2 Hz, 3H, H-3′), 1.23 (s, 6H, 1-CH_3, 8-CH_3), 1.17–1.51 (m, 2H), 1.68–1.75 (m, 2H), 1.93–2.44 (m, 7H), 2.69 (m, 1H, H-2′), 3.35 (m, 1H, H-5), 3.63 (s, 3H, 8-CO_2CH_3), 3.71 (s, 3H, 1-CO_2CH_3), 5.96 (dd, J = 10.5 Hz, J = 2.7 Hz, 1H, H-3), 6.88 (dd, J = 10.5 Hz, J = 1.5 Hz, 1H, H-4). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 7.9 (CH_3, C-3′), 13.5 (1-CH_3), 17.2 (7-CH_3), 22.9 (8-CH_3), 26.7 (CH_2, C-9), 27.5 (CH_2, C-10), 32.2 (CH_2, C-6), 35.4 (CH), 35.5 (CH_2, C-2′), 38.9 (CH), 41.5 (CH), 44.6 (CH), 46.0 (CH), 46.1 (CH, C-5), 49.9 (C, C-8), 50.9 (8-CO_2CH_3), 52.3 (1-CO_2CH_3), 58.7 (C, C-1), 127.6 (CH, C-3), 149.5 (CH, C-4), 172.9 (1-CO_2CH_3), 174.8 (8-CO_2CH_3), 198.8 (2-CO), 213.9 (1′-CO). **LRMS (m/z):** 418 (M^+, 94%), 358 (58), 299 (59), 241 (61), 213 (20), 159 (22), 121 (21), 57 (100). **HRMS:** $C_{24}H_{34}O_6$ (M^+) requires 418.2355, found 418.2354. **Microanalysis:** Calcd. for $C_{24}H_{34}O_6$: C, 68.88%, H, 8.19%. Found: C, 68.89%, H, 8.12%.

(±)-Dimethyl 2,6-Dioxo-isocycloamphilectane-7,20-dicarboxylate (27)



25

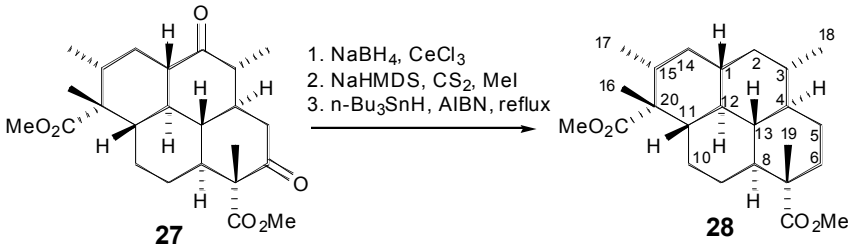
26 (R = CH_2CH_2OH)
27 (R = Me)

Enone **25** (0.058 g, 0.14 mmol) in ethylene glycol (3 mL) and triethylamine (0.3 mL) was heated to 70 °C under nitrogen for 4 d. Water was then added and the resulting mixture extracted with a pentane : DCM mixture (2 : 1, 3 x 10 mL). The aqueous phase was then saturated with NaCl and further extracted with pentane : DCM (2 : 1, 3 x 10 mL). The combined organic extracts were washed with water (5 mL), brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product mixture as a yellow oil. Purification by flash column chromatography on silica gel using EtOAc : petroleum spirit (1.5 : 8.5) as eluant gave the title compound **27** (R = Me, 0.013 g, 30% based on recovered starting material) as a white solid and the trans-esterified product **26** (R = CH_2CH_2OH, 0.018 g, 41% based on recovered starting material) as a colorless oil. A sample of **27** (R = Me) was crystallized from methanol to give white needle like crystals, **m.p:** 174–175 ºC. **IR** (thin film) cm^{-1}: 2950s (C-H), 1732s (C=O), 1712s (C=O), 1456, 1434, 1380, 1235, 1091. **^{1}H NMR** (800 MHz, $CDCl_3$) **δ:** 0.92 (d, *J* = 6.4 Hz, 3H, 17-CH_3), 0.91 (m, 1H, H-10), 1.02 (d, *J* = 7.2 Hz, 3H, 18-CH_3), 1.17 (m, 1H, H-11), 1.24 (m, 1H, H-14), 1.25 (s, 3H, 16-CH_3), 1.33 (m, 1H, H-9), 1.39 (s, 3H, 19-CH_3), 1.39–1.44 (m, 2H, H'-9, H-15), 1.59 (m, 1H, H-13), 1.66 (m, 1H, H-4), 1.74 (m, 1H, H'-14), 1.84 (m, 1H, H-12), 1.95 (dq, *J* = 13.6 Hz, *J* = 2.4 Hz, 1H, H'-10), 2.15-2.19 (m, 2H, H-8, H-1), 2.28 (m, 1H, H-3), 2.35 (m, 1H, H-5), 2.56 (dd, *J* = 14.4 Hz *J* = 4.0 Hz, 1H, H'-5), 3.63 (s, 3H, 20-CO_2CH_3), 3.75 (s, 3H, 7-CO_2CH_3). **^{13}C NMR** (150 MHz, $CDCl_3$) **δ:** 11.1 (18-CH_3), 15.5 (19-CH_3), 17.4 (17-CH_3), 23.3 (16-CH_3), 26.4 (CH_2, C-10), 27.4 (CH_2, C-9), 29.5 (CH_2, C-14), 39.6 (CH, C-15), 42.3 (CH_2, C-5), 44.6 (CH, C-13), 45.1 (CH, C-8), 46.3 (CH, C-12), 48.4 (CH, C-4), 49.5 (C, C-20), 49.6 (CH, C-3), 51.0 (CH, C-11), 51.1 (20-CO_2CH_3), 52.4 (7-CO_2CH_3), 52.4 (CH, C-1), 61.4 (C, C-7), 172.7 (7-CO_2CH_3), 174.4

(20-*C*O_2CH_3), 207.9 (6-CO), 209.9 (2-CO). **LRMS (m/z):** 418 (M^+, 40%), 400 (78), 358 (51), 341 (100), 281 (60), 229 (50), 211 (54). **HRMS:** $C_{24}H_{34}O_6$ (M^+) requires 418.2355, found 418.2354. **Microanalysis:** Calcd. For $C_{24}H_{34}O_6$: C, 68.88%, H, 8.19%. Found: C, 68.65%, H, 7.91%.

A sample of **26** (R = CH_2CH_2OH) was characterized as its MOM ether: **IR** (thin film) cm^{-1}: 2931s (C-H), 1736s (C=O), 1712s (C=O), 1459, 1380, 1254, 1091. **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 0.91 (d, *J* = 6.9 Hz, 3H, 17-CH_3), 0.87 (m, 1H, H-10), 1.01 (d, *J* = 6.6 Hz, 3H, 18-CH_3), 1.12–2.04 (m, 10H), 1.24 (s, 3H, 16-CH_3), 1.38 (s, 3H, 19-CH_3), 2.11–2.40 (m, 4H), 2.57 (dd, *J* = 14.4 Hz *J* = 3.9 Hz, 1H, H-5), 3.35 (s, 3H, 3′-$OCH_2OC\mathit{H}_3$), 3.61 (s, 3H, 20-$CO_2C\mathit{H}_3$), 3.72–3.75 (m, 2H, 3′-H), 4.33–4.36 (m, 2H, 2′-H), 4.62 (s, 2H, 3′-$OC\mathit{H}_2OCH_3$). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 11.1 (CH_3), 15.4 (CH_3), 17.4 (CH_3), 23.3 (CH_3), 26.3 (CH_2), 27.4 (CH_2), 29.5 (CH_2), 39.6 (CH), 42.2 (CH_2), 44.5 (CH), 45.0 (CH), 46.3 (CH), 48.3 (CH), 49.5 (C), 49.6 (CH), 50.9 (CH), 51.0 (20-$CO_2\mathit{C}H_3$), 52.4 (CH), 55.2 (3′-$OCH_2O\mathit{C}H_3$), 61.4 (C), 64.2 (CH_2, C-2′), 65.5 (CH_2, C-3′), 96.4 (3′-$O\mathit{C}H_2OCH_3$), 172.1 (3-$\mathit{C}O_2$R), 174.4 (20-$\mathit{C}O_2CH_3$), 207.8 (6-CO), 209.9 (2-CO). **LRMS (m/z):** 492 (M^+, 4%), 460 (19), 386 (20), 358 (41), 299 (37), 281 (38), 229 (30), 45 (100). **HRMS:** $C_{27}H_{40}O_8$ (M^+) requires 492.2723, found 492.2726.

(±)-Dimethyl Isocycloamphilectane-7,20-dicarboxylate (28)



The dione (0.028 g, 0.067 mmol) in MeOH (2 mL) was added to cerium (III) chloride heptahydrate (0.056 g, 0.15 mmol) under nitrogen. The solution was cooled to 0 °C, and $NaBH_4$ (0.01 g, 0.26 mmol) was added in four batches over 2 h, until TLC revealed the consumption of all starting material. The reaction was quenched with water and the methanol was removed *in vacuo*. The aqueous residue was extracted with EtOAc (3 x 10 mL), then the aqueous phase saturated with NaCl, and extracted with EtOAc (2 x 10 mL).

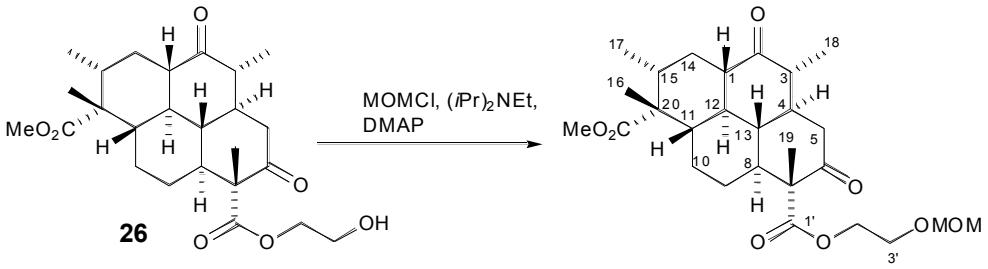
The combined organic extracts were washed with brine (10 mL) and dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave the desired product as a mixture of four epimeric alcohols (0.028g), which was used directly in the next step without further purification.

The crude diols (0.028 g, 0.066 mmol) were dissolved in THF (3 mL) and Sodium bis(trimethylsilyl)amide (0.26 mL of a 1*M* solution in THF, 0.26 mmol) was added at room temp. under nitrogen. The resulting reaction mixture was stirred for 2 h then carbon disulfide (0.016 mL, 0.26 mmol) was added. The reaction mixture was stirred for 2 h and then iodomethane (0.016 mL, 0.26 mmol) was added. After a further 2 h, the reaction was quenched with AcOH (0.5 mL) and diluted with a saturated aqueous NH_4Cl solution, before extracting with EtOAc (4 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product as a mixture of four epimeric xanthates (~0.40 g), which was used directly in the next step without further purification.

The crude xanthate esters (~0.40 g, 0.066 mmol) were dissolved in toluene (3 mL) and tributyl tin hydride (0.071 mL, 0.26 mmol) was added under nitrogen. A catalytic amount of AIBN was added and the reaction mixture heated to 80 °C for 2.5 h, after which time starting material remained so excess tribuyl tin hydride (0.03 mL, 0.11 mmol) and AIBN (catalytic) were added. After 1 h at 80 °C TLC revealed the consumption of all starting material. The toluene was removed *in vacuo* and the residue purified by flash column chromatography on silica gel using EtOAc : petroleum spirit (5 : 95) as eluant to give the title compound **27** (7.1 mg, 27% over 3 steps) as a white oil, and a mono-deoxygenated product (11 mg, 40% over 3 steps), which was recycled to give the title compound **27** (5.1 mg), (12.2 mg, 47% total yield of the title compound over three steps). **IR** (thin film) cm^{-1}: 2925s (C-H), 1726s (C=O), 1456, 1260, 1160, 1097. **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 0.68 (q, *J* = 10.8 Hz, 1H), 0.83 (d, *J* = 6.6 Hz, 3H, 17-CH_3), 0.86 (d, *J* = 6.6 Hz, 3H, 18-CH_3), 0.74–0.91 (m, 4H), 1.08 (s, 3H, 16-CH_3), 1.19 (s, 3H, 19-CH_3), 0.96–1.21 (m, 4H), 1.23–1.45 (m, 5H), 1.53–1.63 (m, 3H), 1.72–1.85 (m, 3H), 3.62 (s, 3H, 20-CO_2CH_3), 3.64 (s, 3H, 7-CO_2CH_3). **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 15.1 (16-CH_3), 17.4 (17-CH_3), 19.9 (18-CH_3), 23.4 (19-CH_3), 25.2 (CH_2), 27.2 (CH_2), 28.5 (CH_2), 36.7 (CH_2 and CH), 38.4 (CH_2), 40.5 (CH), 41.0 (CH), 42.7 (CH_2, C6), 45.0 (CH), 45.4 (CH), 46.2

(CH), 46.6 (C), 48.2 (CH), 50.2 (C), 50.3 (CH), 50.7 (CO_2CH_3), 51.7 (CO_2CH_3), 175.3 (20-CO_2CH_3), 179.1 (7-CO_2CH_3). **LRMS (m/z):** 390 (M^+, 25%), 330 (100), 271 (92), 217 (24), 201 (20), 149 (34), 81 (53), 69 (98). **HRMS:** $C_{24}H_{38}O_4$ (M^+) requires 390.2770, found 390.2763.

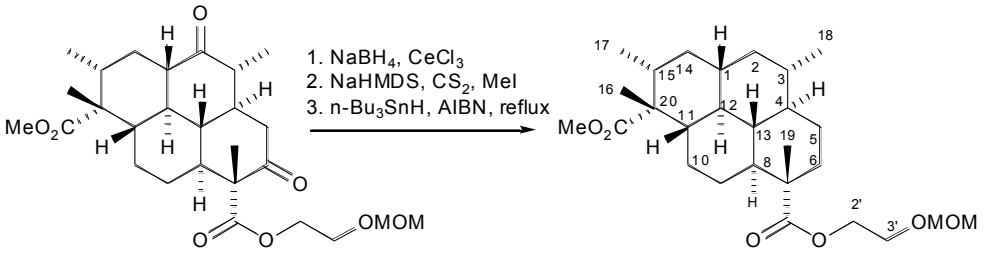
(±)-7-(2'-Methoxmethoxyethyl)-20-Methyl-2,6-Dioxo-isocycloamphilectane-7,20-dicarboxylate



Hünig's base (0.15 mL, 0.86 mmol) was added to alcohol **26** (0.077 g, 0.17 mmol) in DCM (5 mL) at 0 °C under nitrogen. Chloromethyl methyl ether (0.065 mL, 0.86 mmol) was added dropwise and the reaction mixture was warmed to room temperature. A catalytic amount of DMAP was then added and the reaction mixture stirred for 24 h. The reaction mixture was cooled to 0 °C, saturated aqueous sodium bicarbonate (5 mL) was added, and the resulting mixture stirred for 10 min. The organic phase was separated and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic extracts were washed with water (5 mL), 1 *M* HCl (5 mL), saturated aqueous sodium bicarbonate (5 mL), brine (5 mL) and dried over anhydrous $MgSO_4$. Concentration of the organic phase *in vacuo* gave a yellow gum which was purified by flash column chromatography on silica gel using EtOAc : hexane (1 : 4) as eluant to give the title compound (0.036 g, 43%) as a colourless oil. **IR** (thin film) cm^{-1}: 2931s (C-H), 1736s (C=O), 1712s (C=O), 1459, 1380, 1254, 1091. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.91 (d, *J* = 6.9 Hz, 3H, 17-CH_3), 0.87 (m, 1H, H-10), 1.01 (d, *J* = 6.6 Hz, 3H, 18-CH_3), 1.12-2.04 (m, 10H), 1.24 (s, 3H, 16-CH_3), 1.38 (s, 3H, 19-CH_3), 2.11-2.40 (m, 4H), 2.57 (dd, *J* = 14.4 Hz *J* = 3.9 Hz, 1H, H-5), 3.35 (s, 3H, 3′-OCH_2OCH_3), 3.61 (s, 3H, 20-CO_2CH_3), 3.72-3.75 (m, 2H, 3′-H), 4.33-4.36 (m, 2H, 2′-H), 4.62 (s, 2H, 3′-OCH_2OCH_3). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 11.1 (CH_3), 15.4 (CH_3), 17.4 (CH_3), 23.3 (CH_3), 26.3 (CH_2), 27.4 (CH_2), 29.5 (CH_2),

39.6 (CH), 42.2 (CH_2), 44.5 (CH), 45.0 (CH), 46.3 (CH), 48.3 (CH), 49.5 (C), 49.6 (CH), 50.9 (CH), 51.0 (20-CO_2CH_3), 52.4 (CH), 55.2 (3′-OCH_2OCH_3), 61.4 (C), 64.2 (CH_2, C-2′), 65.5 (CH_2, C-3′), 96.4 (3′-OCH_2OCH_3), 172.1 (3-CO_2R), 174.4 (20-CO_2CH_3), 207.8 (6-CO), 209.9 (2-CO). **LRMS (m/z):** 492 (M^+, 4%), 460 (19), 386 (20), 358 (41), 299 (37), 281 (38), 229 (30), 45 (100). **HRMS:** $C_{27}H_{40}O_8$ (M^+) requires 492.2723, found 492.2726.

(±)-7-(2'-Methoxmethoxyethyl)-20-Methyl-isocycloamphilectane-7,20-dicarboxylate



The dione (0.019 g, 0.039 mmol) in MeOH (2 mL) was added to cerium (III) chloride heptahydrate (0.032 g, 0.085 mmol) under nitrogen. The solution was cooled to 0 °C, and sodium borohydride (0.006 g, 0.16 mmol) was added in four batches over 2 h, until TLC revealed the consumption of all starting material. The reaction was quenched with water and the methanol was removed *in vacuo*. The aqueous residue was extracted with EtOAc (3 x 10 mL), then the aqueous phase saturated with NaCl, and extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine (10 mL) and dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave the desired product as a mixture of four epimeric alcohols (0.019 g), which was used directly in the next step without further purification.

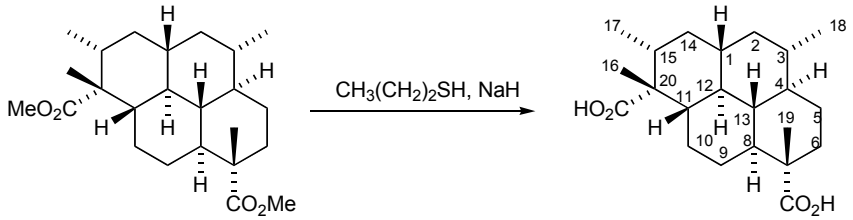
The crude diols (0.019 g, 0.038 mmol) were dissolved in THF (3 mL) and Sodium bis(trimethylsilyl)amide (0.23 mL of a 1 *M* solution in THF, 0.23 mmol) was added at room temperature under nitrogen. The resulting reaction mixture was stirred for 2 h then carbon disulfide (0.017 mL, 0.23 mmol) was added. The reaction mixture was stirred for 2 h and then iodomethane (0.014 mL, 0.23 mmol) was added. After a further 2 h, the reaction was quenched with acetic acid (0.5 mL) and diluted with a saturated aqueous ammonium chloride solution, before extracting with EtOAc (4 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to give the crude

product as a mixture of four epimeric xanthates (~0.03 g), which was used directly in the next step without further purification.

The crude xanthate esters (~0.03 g) were dissolved in toluene (3 mL) and tributyl tin hydride (0.049 mL, 0.18 mmol) was added under nitrogen. A catalytic amount of AIBN was added and the reaction mixture heated to 80 °C for 2.5 h, after which time starting material remained so excess tribuyl tin hydride (0.025 mL, 0.09 mmol) and AIBN (catalytic) were added. After 1 h at 80 °C TLC revealed the consumption of all starting material. The toluene was removed *in vacuo* and the residue purified by flash column chromatography on silica gel using EtOAc : petroleum spirit (1 : 9) as eluant to give the title compound (7 mg, 39% over 3 steps) as a white oil. **IR** (thin film) cm^{-1}: 2926s (C-H), 1725s (C=O), 1459, 1382, 1255, 1230, 1157, 1042. **^{1}H NMR** (300 MHz, $CDCl_3$) **δ:** 0.68 (q, *J* = 9.9 Hz, 1H), 0.83 (d, *J* = 6.0 Hz, 3H, 17-CH_3), 0.86 (d, *J* = 6.3 Hz, 3H, 18-CH_3), 1.09 (s, 3H, 16-CH_3), 1.19 (s, 3H, 19-CH_3), 0.73-1.43 (m, 12H), 1.51-1.67 (m, 4H), 1.72-1.84 (m, 3H), 3.36 (s, 3H, 3′-$OCH_2OC\mathit{H}_3$), 3.61 (s, 3H, 20-$CO_2C\mathit{H}_3$), 3.69-3.73 (m, 2H, 3′-H), 4.22-4.25 (m, 2H, 2′-H), 4.62 (s, 2H, 3′-$OC\mathit{H}_2OCH_3$). **^{13}C NMR** (75 MHz, $CDCl_3$) **δ:** 15.1 (16-CH_3), 17.4 (17-CH_3), 19.9 (18-CH_3), 23.4 (19-CH_3), 25.2 (CH_2), 27.2 (CH_2), 28.5 (CH_2), 36.7 (CH_2 and CH), 38.4 (CH_2), 40.5 (CH), 41.0 (CH), 42.7 (CH_2, C-6), 44.9 (CH), 45.4 (CH), 46.2 (CH), 46.6 (C), 48.2 (CH), 50.2 (C), 50.3 (CH), 50.7 (20-$CO_2\mathit{C}H_3$), 55.2 (3′-OCH_2OCH_3), 63.4 (CH_2, C-2′), 65.6 (CH_2, C-3′), 96.4 (3′-$O\mathit{C}H_2OCH_3$), 175.3 (20-$\mathit{C}O_2CH_3$), 178.5 (1'-CO). **LRMS (m/z):** 464 (M^+, 5%), 419 (15), 372 (10), 359 (12), 331 (31), 271 (100), 215 (15), 201 (15). **HRMS:** $C_{27}H_{44}O_6$ (M^+) requires 464.3138, found 464.3142.

(±)-Isocycloamphilectane-7,20-dicarboxylic Acid

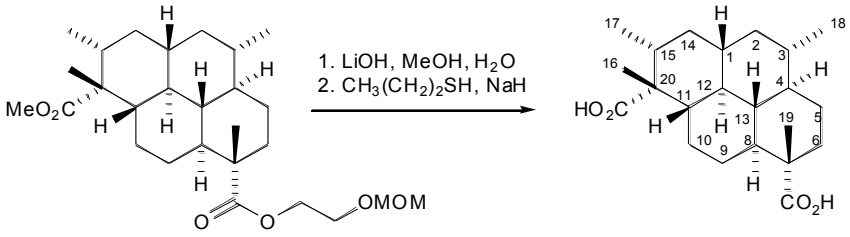
Method A:



Freshly distilled propane thiol (0.35 mL, 3.87 mmol) was added to a degassed suspension of NaH (0.12 g, 5.0 mmol) in HMPA (2.5 mL) under nitrogen. The reaction mixture was

stirred for 2 h then left to stand for 1h at room temp. An aliquot of the thiolate solution prepared above (0.19 mL, 0.30 mmol) was added to a solution of diester **27** (0.015 g, 0.038 mmol) in HMPA (0.3 mL) at room temp. under nitrogen. The reaction mixture was stirred for 1.5 d, after which time EtOAc (5 mL) was added and the crude carboxylic acid was extracted with a water : saturated $NaHCO_3$ solution (2 : 1, 3 x 10 mL). The combined aqueous washings were treated with 1 *M* HCl until pH 2, then the resulting mixture was extracted with EtOAc (4 x 5 mL). The combined organic extracts were washed with saturated copper (II) chloride solution (2 x 5 mL), brine and dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave a yellow gum, which was purified by flash column chromatography on silica gel using EtOAc : petroleum spirit (1 : 4) as eluant to give the title compound (0.012 g, 87%) as a white solid.

Method B:

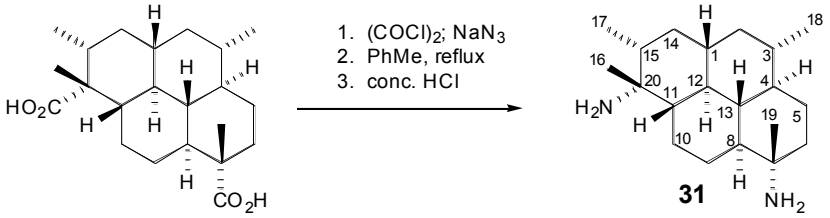


Lithium hydroxide (13 mg, 0.30 mmol) was added to the ester (7 mg, 0.015 mmol) in methanol : water (3 : 1, 4 mL) and the reaction mixture was heated to reflux for 24 h. The reaction mixture was cooled to room temperature and the methanol removed *in vacuo*. The aqueous residue was then extracted with EtOAc (3 x 5 mL) and the combined organic extracts dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave the crude ester (~6 mg) as a colourless oil.

An aliquot of the thiolate solution prepared in method A (0.10 mL, 0.15 mmol) was added to a solution of crude ester (~6 mg, 0.015 mmol) in HMPA (0.3 mL) at room temperature under nitrogen. The reaction mixture was stirred for 1.5 d, after which time EtOAc (5 mL) was added and the crude carboxylic acid was extracted with water : saturated sodium bicarbonate solution (2 : 1, 3 x 10 mL). The combined aqueous washings were treated with 1 *M* HCl until pH 2 then the residue was extracted with EtOAc (4 x 5 mL). The combined organic extracts were washed with a saturated copper

(II) chloride solution (2 x 5 mL), brine and dried over $MgSO_4$. Concentration of the organic phase *in vacuo* gave a yellow gum, which was purified by flash column chromatography on silica gel using EtOAc : petroleum spirit (1 : 4) as eluant to give the title compound (~1 mg, ~20% over two steps) as a white solid, **m.p:** decomposed at 280 ºC. **IR** (thin film) cm^{-1}: 3200br (C-OH), 2924s (C-H), 1693s (C=O), 1456, 1379, 1261. **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 0.83 (d, J = 6.3 Hz, 3H, 17-CH_3), 0.88 (d, J = 6.6 Hz, 3H, 18-CH_3), 1.05 (s, 3H, 16-CH_3), 1.16 (s, 3H, 19-CH_3). See *bis*-methyl ester derivative **27** for full ^{1}H NMR characterization. **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 14.9 (16-CH_3), 17.3 (17-CH_3), 19.8 (18-CH_3), 23.4 (19-CH_3), 25.1 (CH_2), 27.0 (CH_2), 28.4 (CH_2), 36.6 (CH_2), 36.7 (CH), 38.2 (CH_2), 40.2 (CH), 40.9 (CH), 42.7 (CH_2, C-6), 44.9 (CH), 45.4 (CH), 46.0 (CH), 46.2 (C), 48.2 (CH), 49.8 (C or CH), 50.1 (C or CH), 178.4 (20-*C*O_2H), 182.1 (7-*C*O_2H). **LRMS (m/z):** 362 (M^+, 18%), 316 (100), 298 (12), 271 (75), 262 (50), 217 (43), 201 (25), 161 (20), 149 (20). **HRMS:** $C_{22}H_{34}O_4$ (M^+) requires 362.2457, found 362.2465.

(±)-Isocycloamphilectane-7,20-diamine (31)

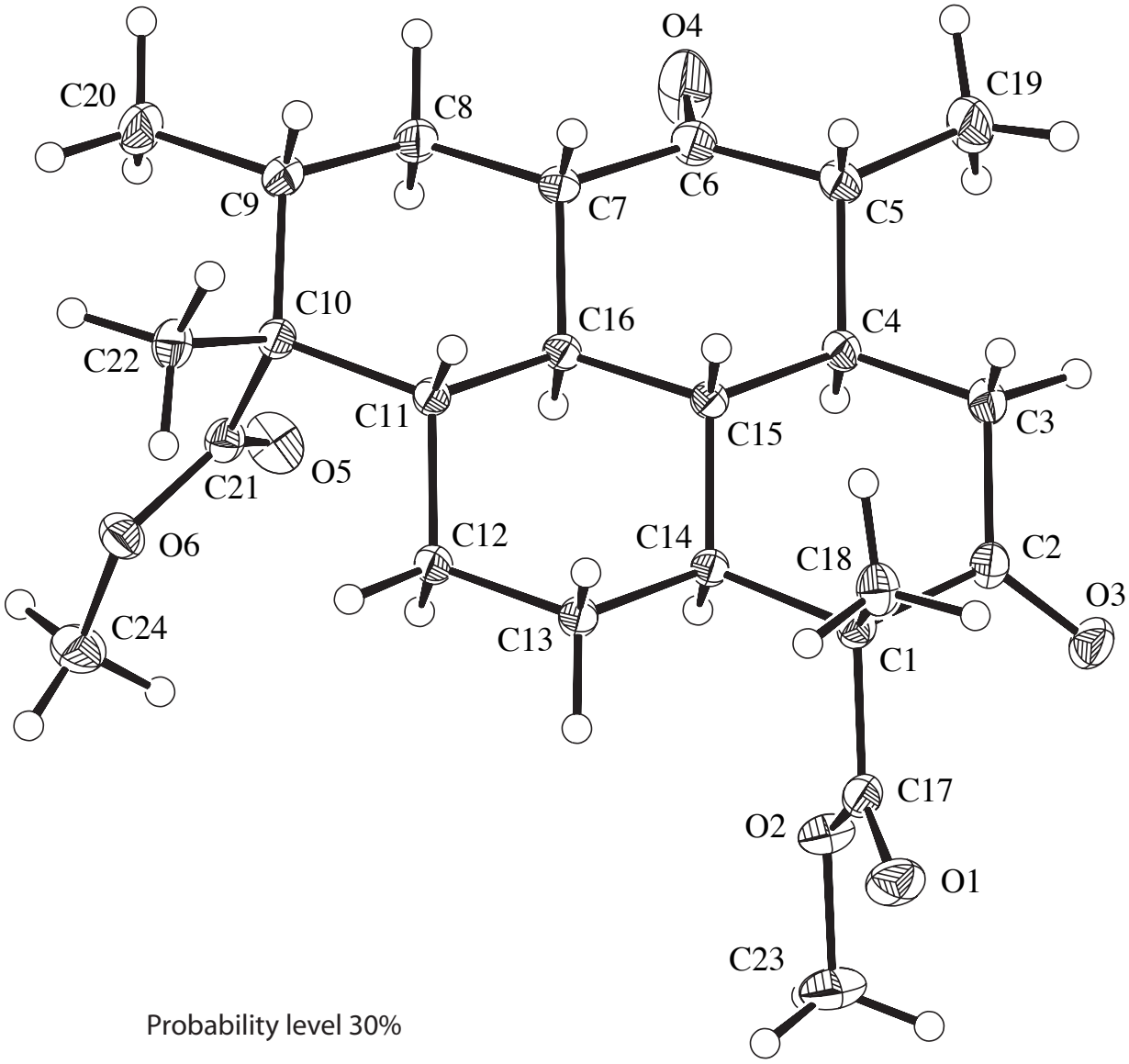


Oxalyl chloride (0.072 mL, 0.83 mmol) was added to the dicarboxylic acid (0.015 g, 0.041 mmol) in DCM (3 mL) at room temp. under nitrogen. After 3 h, analysis by IR spectroscopy revealed a peak at 1781 cm^{-1}, due to the formation of an acid chloride. The reaction mixture was concentrated *in vacuo* and dried under high vacuum for 5 min.

The crude acid chloride was taken up in THF (3 mL) and NaN_3 (0.054 g 0.083 mmol) was added. The resulting reaction mixture was stirred for 18 h, after which time analysis by IR spectroscopy revealed the disappearance of the peak at 1781 cm^{-1}, and the formation of a peak at 2131 cm^{-1}, due to the formation of an acyl azide. The reaction mixture was then diluted with water (5 mL) and extracted with EtOAc (5 x 5 mL). The combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo* to give the crude acyl azide **29** as a yellow oil.

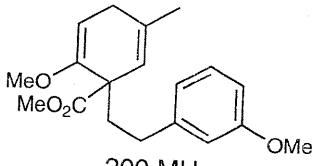
Toluene (3 mL) was added to the crude acyl azide and the resulting solution was heated to reflux for 15 min then cooled to room temp.. Analysis by IR spectoscopy revealed a new peak at 2260 cm^{-1}, and the disappearance of the peak at 2131 cm^{-1}, indicating that the desired isocyanate **30** had formed. Concentrated HCl (2 mL) was then added to the isocyanate in toluene and the mixture heated to 100 °C for 18 h. After cooling the solution to room temp., the mixture was extracted with water (2 x 10 mL). The combined aqueous layers were treated with 10% aqueous NaOH until pH 10, then extracted with chloroform (5 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to give the title compound **31** (4.70 mg, 39% over three steps) as a white solid, which was further purified by reverse-phase HPLC on C-18 stationary phase heated to 40 °C (5–100% acetonitrile and 100–5% water gradient containing 0.1% TFA), **IR** (thin film) cm^{-1}: 3368br (N-H), 2920s (C-H), 1729, 1642, 1544, 1455, 1378, 1261, 1101. **^{1}H NMR** (TFA salt, 600 MHz, CD_3OD) δ: 0.78 (m, 1H), 0.86 (ddd, 3x*J* = 10.2 Hz, 1H), 0.86–0.91 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.95 (ddd, 3x*J* = 10.2 Hz, 1H), 1.03 (d, *J* = 7.2 Hz, 3H), 1.03 (m, 1H), 1.09–1.15 (m, 2H), 1.20–1.28 (m, 2H), 1.25 (s, 3H), 1.30–1.35 (m, 3H), 1.35 (s, 3H), 1.53–1.63 (m, 3H), 1.75 (m, 1H), 1.86–1.91 (m, 2H), 1.99 (m, 1H), 2.10 (m, 1H). **^{13}C NMR** (200 MHz, $CDCl_3$) δ: 15.6, 18.0, 20.0, 22.2, 25.8, 26.1, 26.8, 37.6, 37.8, 38.6, 40.4, 41.9, 43.1, 46.8, 47.2, 48.2, 58.0 , 60.4. Two peaks obscured by CD_3OD. **LRMS (m/z):** 304 (M^+, 32%), 289 (37), 256 (9), 221 (12), 204 (25), 105 (20), 84 (100). **HRMS:** $C_{20}H_{36}N_2$ (M^+) requires 304.2878, found 304.2876.

Compound **27**

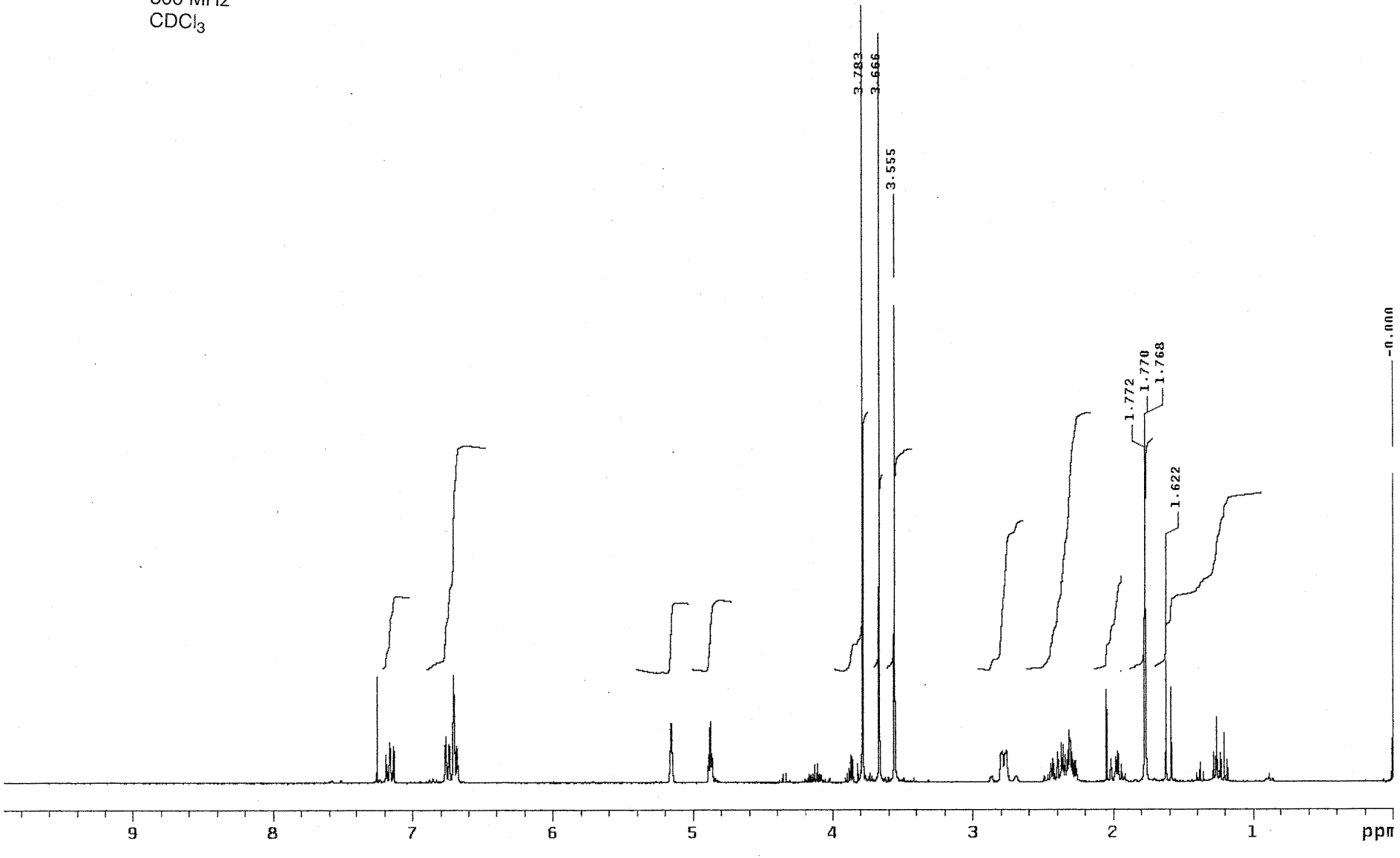


Probability level 30%

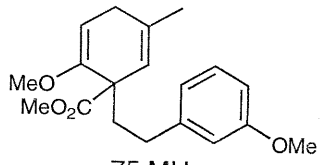
^{1}H NMR



300 MHz
$CDCl_3$

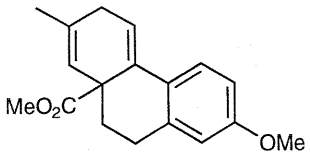


^{13}C NMR



75 MHz
$CDCl_3$

^{1}H NMR

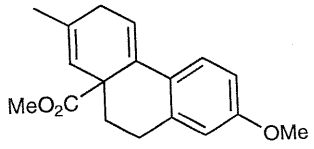


3

300 MHz

$CDCl_3$

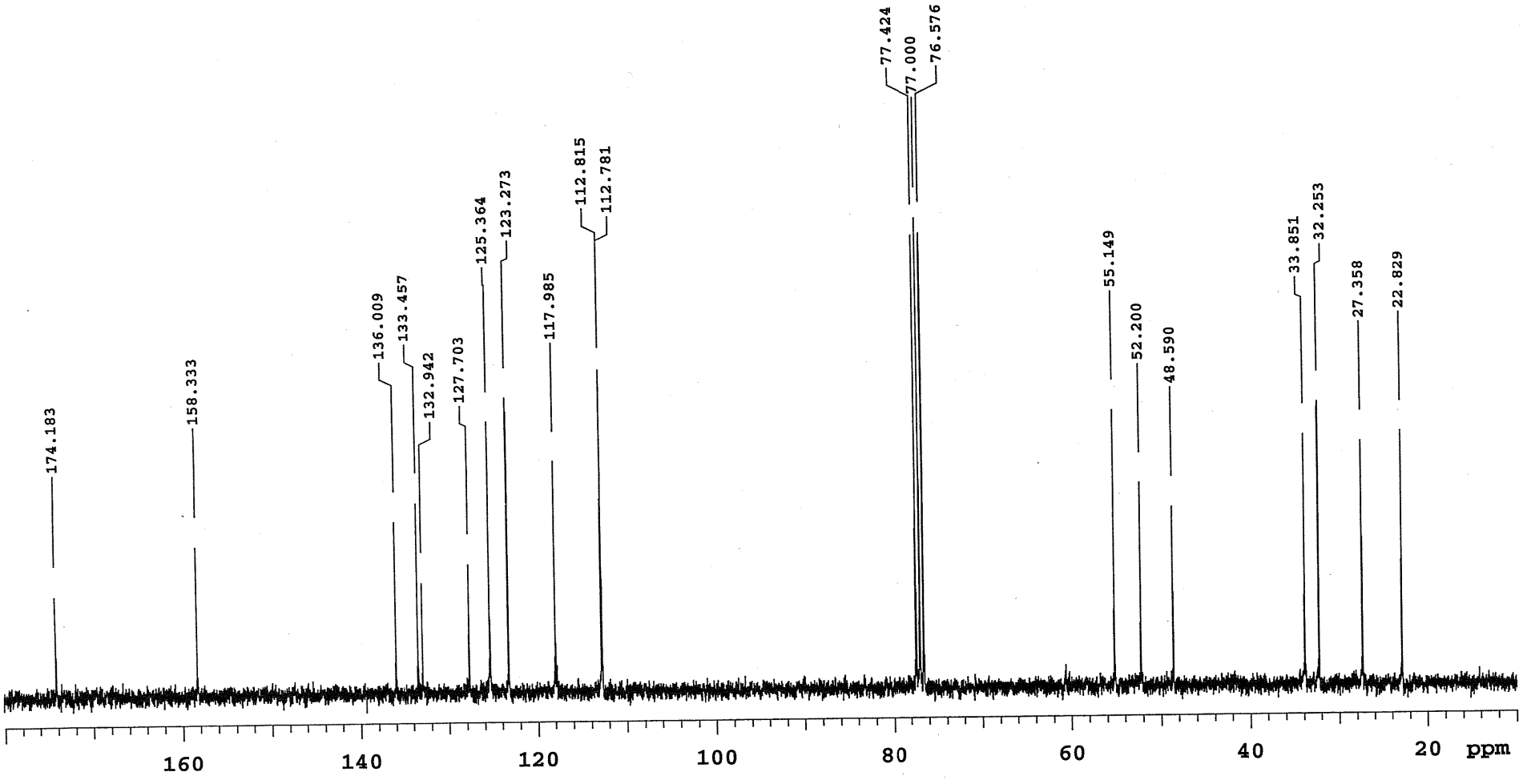
^{13}C NMR



3

75 MHz

$CDCl_3$



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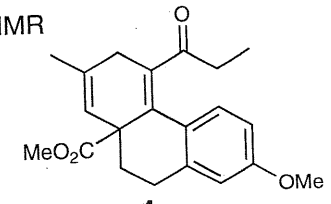
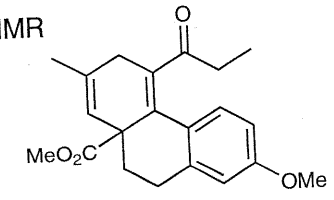


4

300 MHz

$CDCl_3$

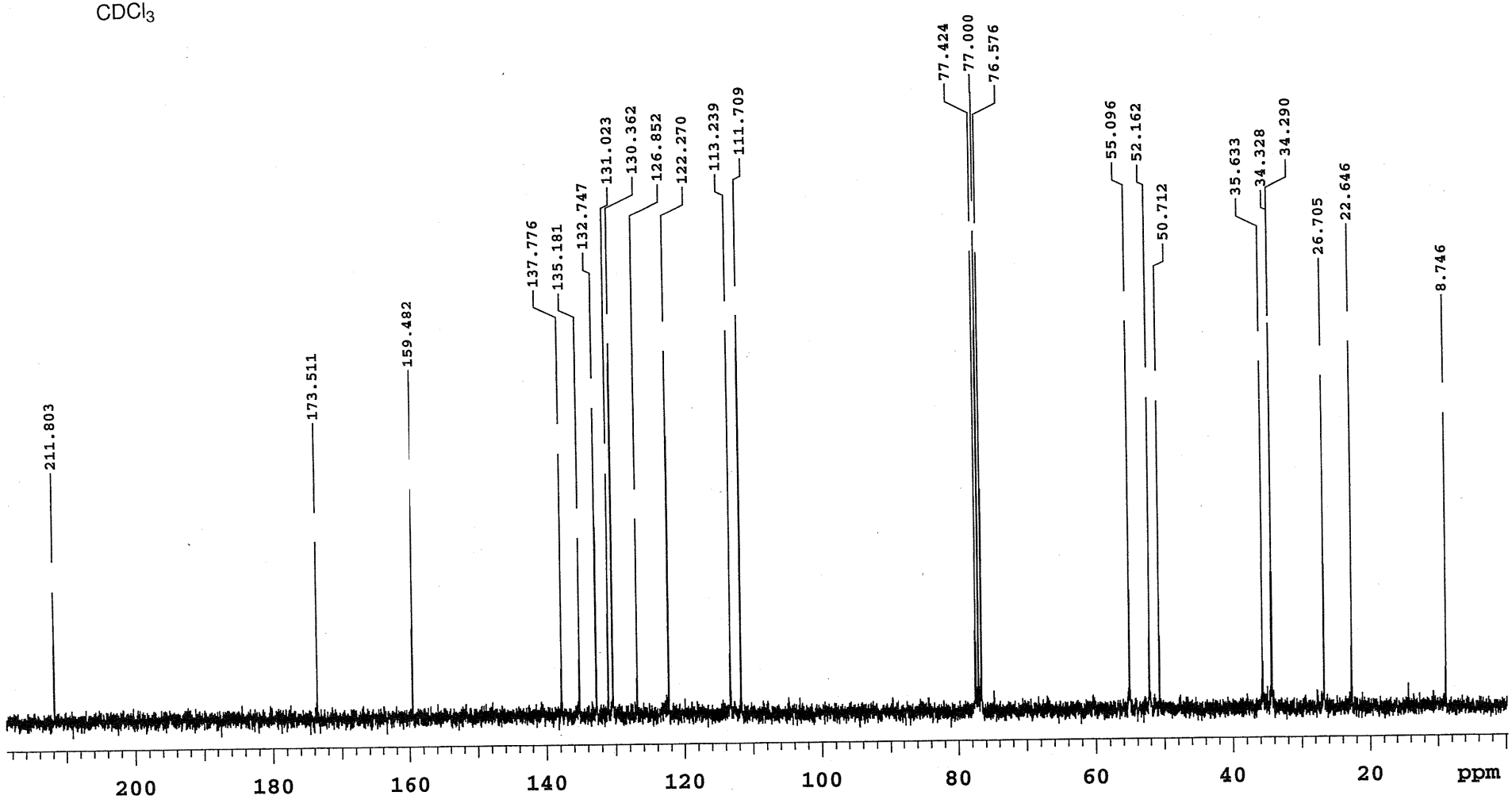
^{13}C NMR



4

75 MHz

$CDCl_3$



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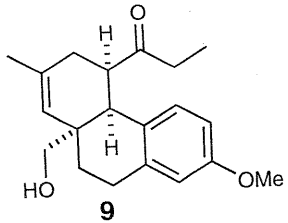
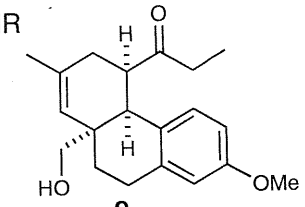


9

300 MHz

$CDCl_3$

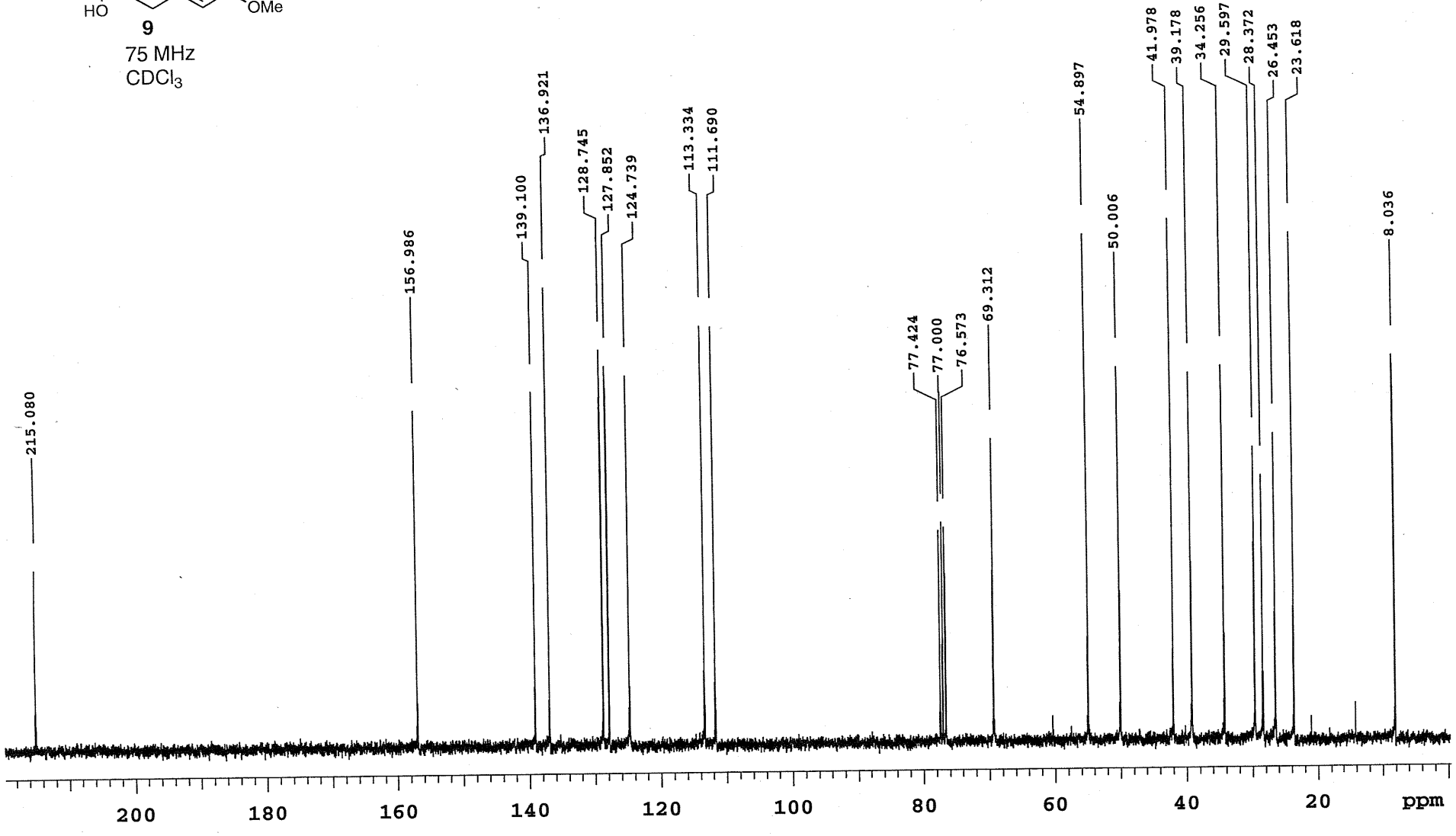
^{13}C NMR



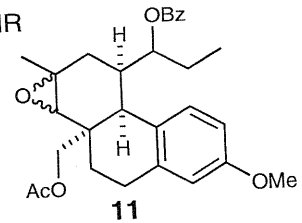
9

75 MHz

$CDCl_3$



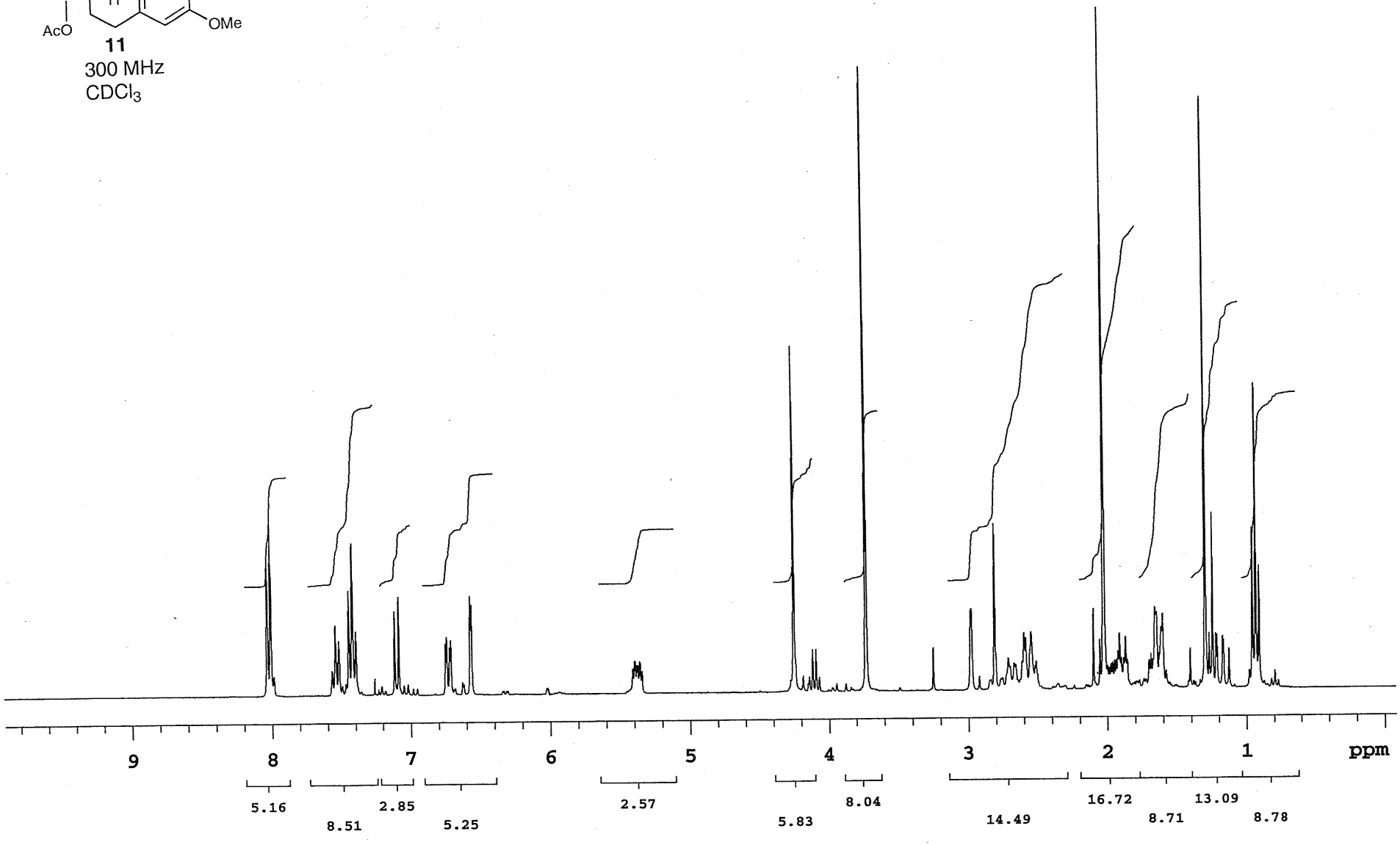
^{1}H NMR



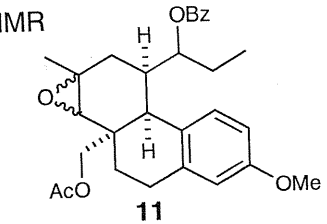
11

300 MHz

$CDCl_3$



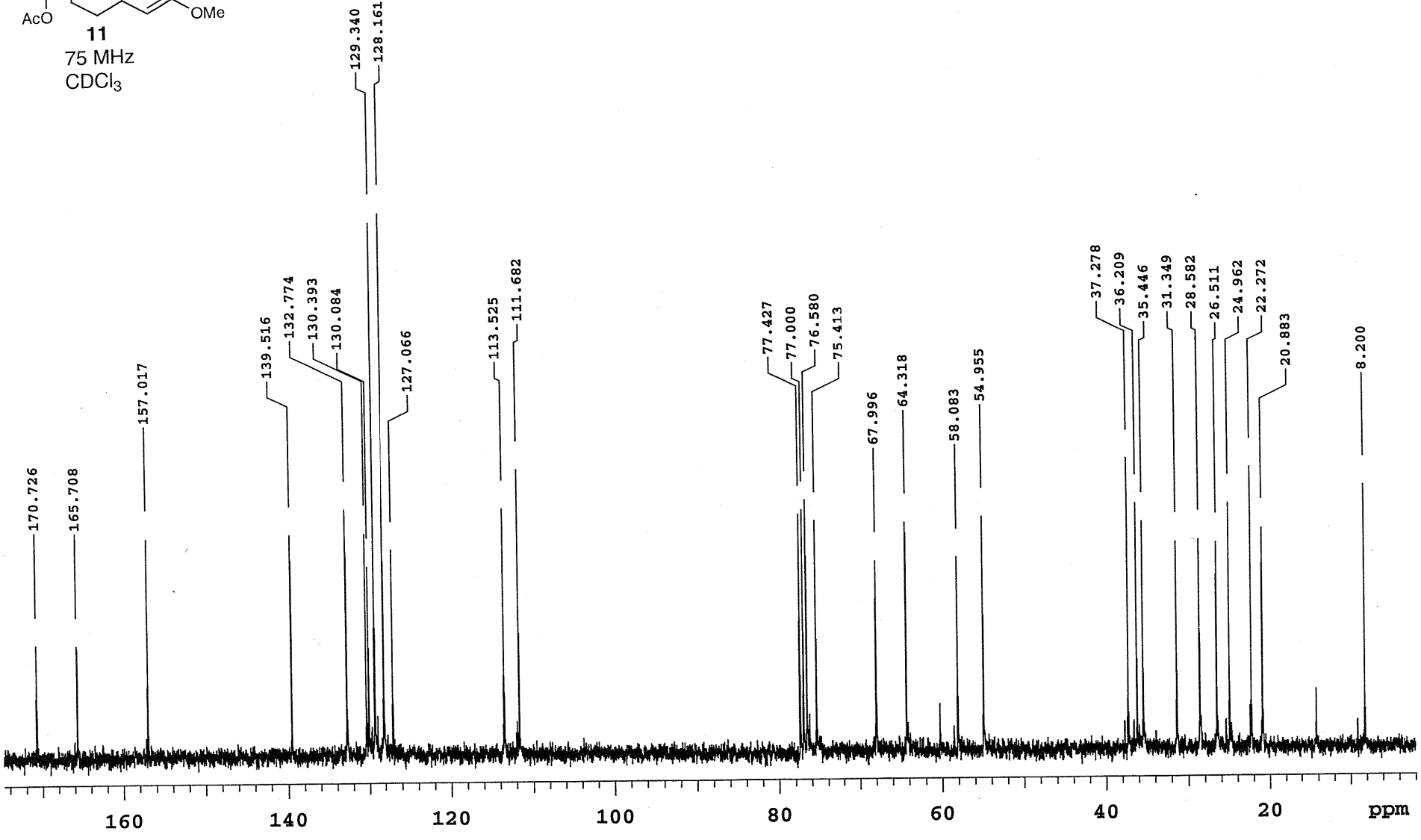
^{13}C NMR



11

75 MHz

$CDCl_3$



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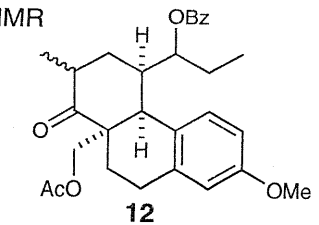

12

300 MHz

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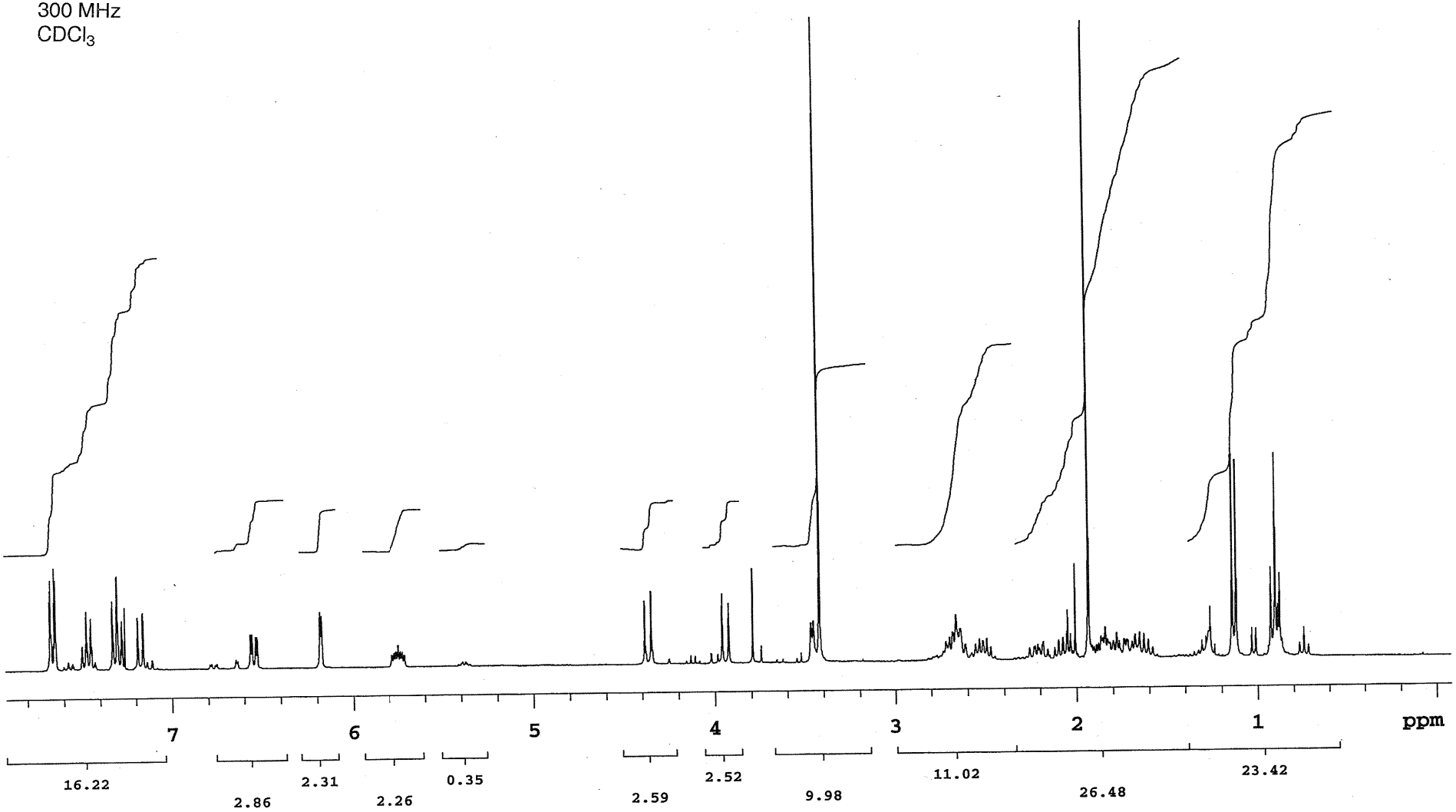
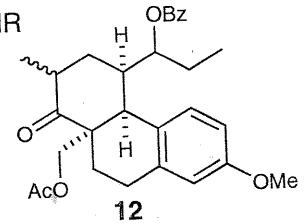


^{13}C NMR



12

75 MHz

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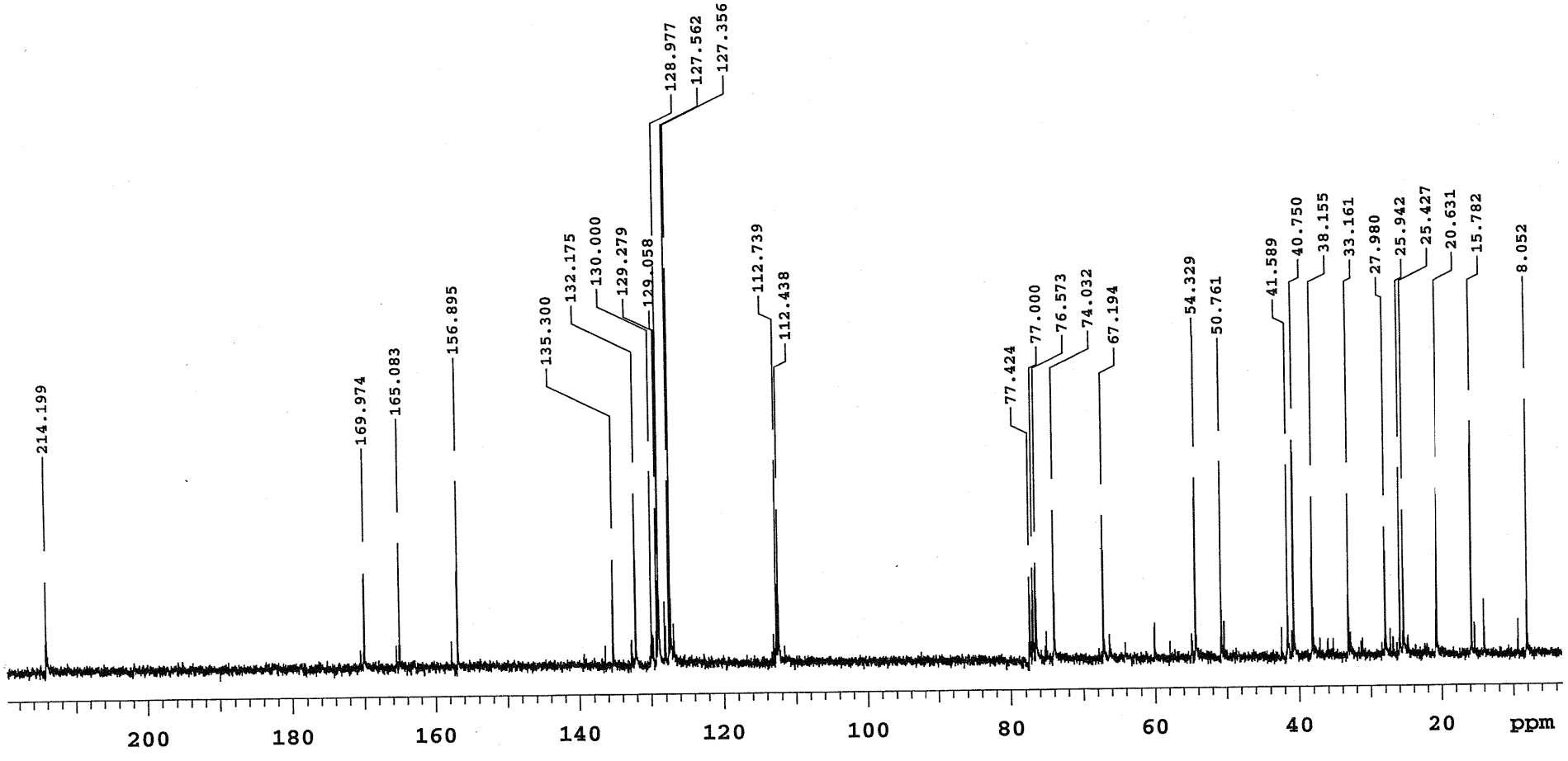
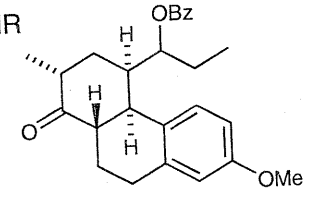


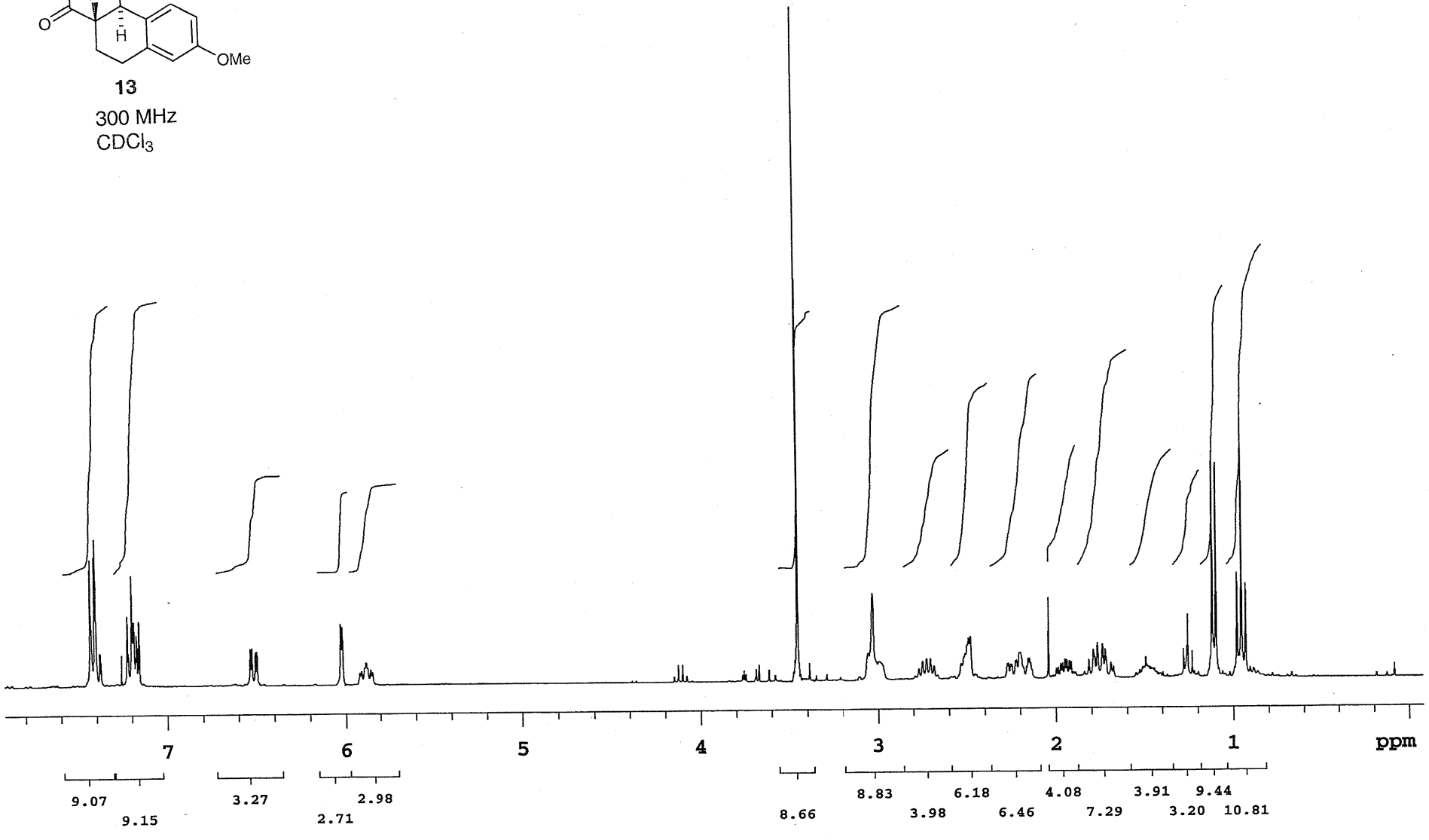
^{1}H NMR



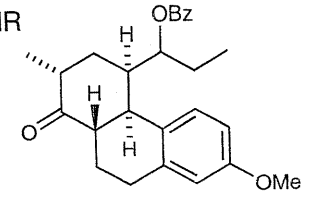
13

300 MHz

$CDCl_3$



^{13}C NMR

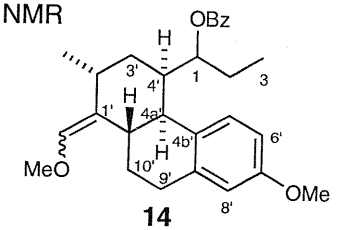


13

75 MHz

$CDCl_3$

^{1}H NMR

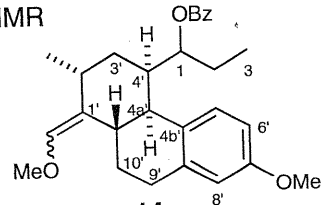


14

300 MHz

$CDCl_3$

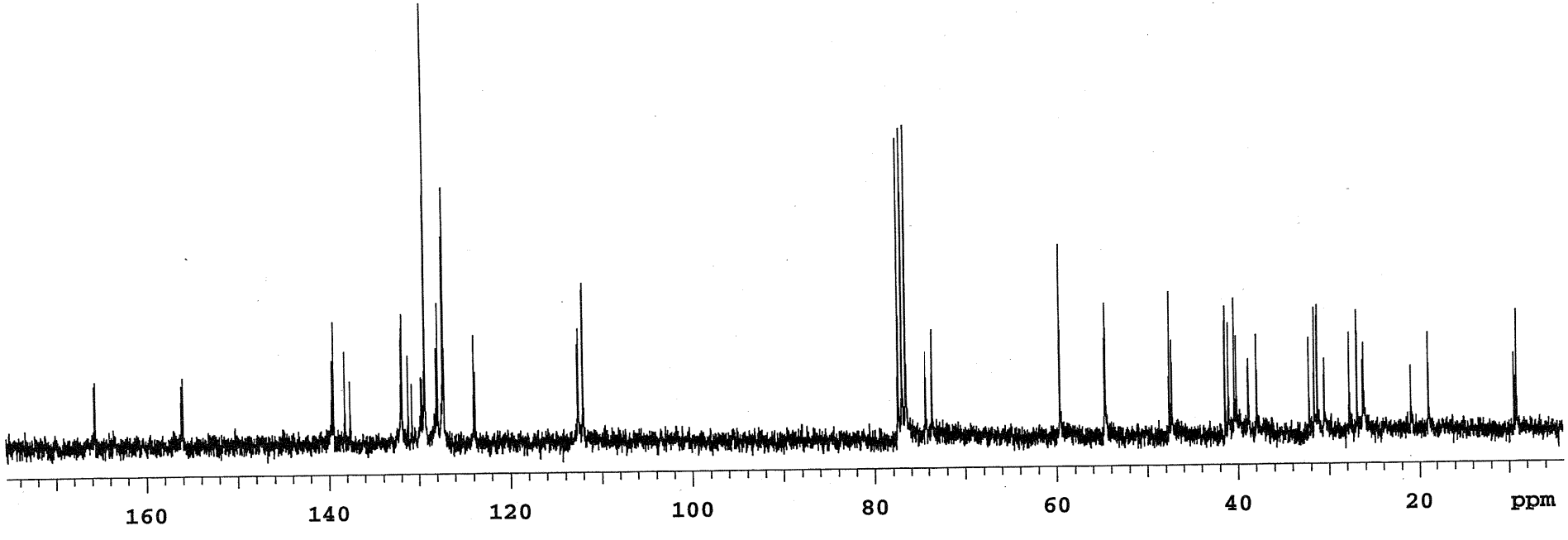
^{13}C NMR



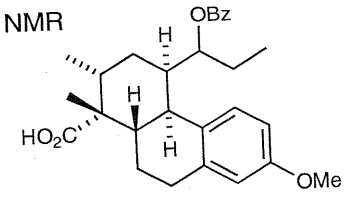
14

75 MHz

$CDCl_3$

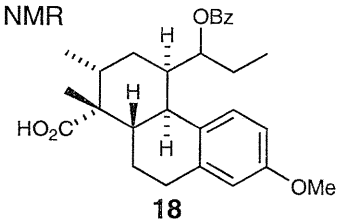


^{1}H NMR



18
300 MHz
$CDCl_3$

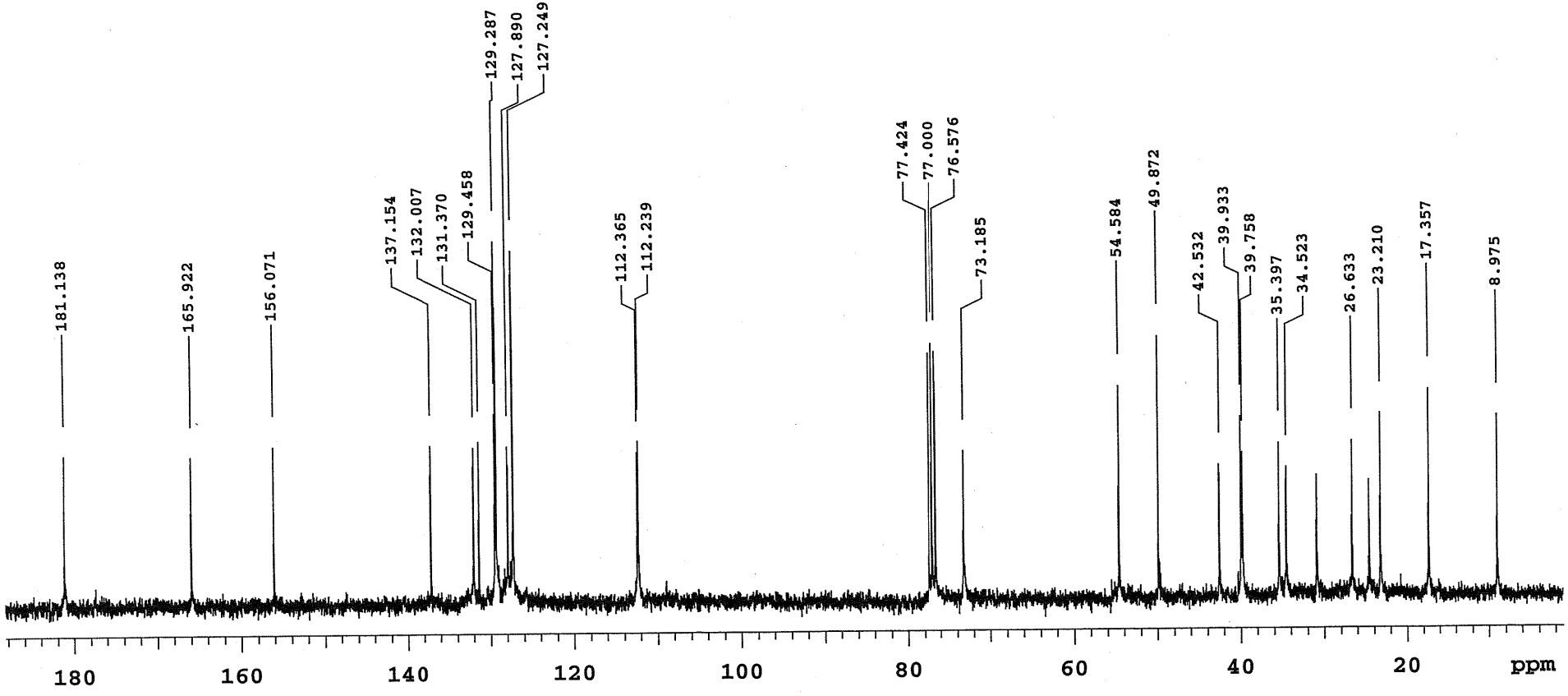
^{13}C NMR



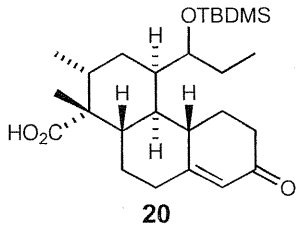
18

75 MHz

$CDCl_3$



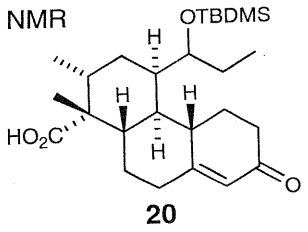
^{1}H NMR



20

300 MHz
$CDCl_3$

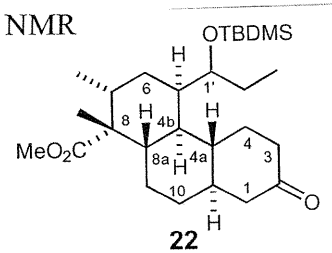
^{13}C NMR



20

75 MHz
$CDCl_3$

^{1}H NMR

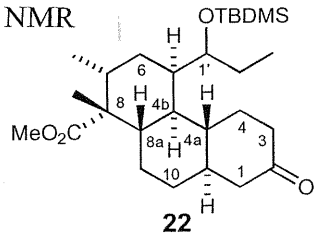


22

600 MHz

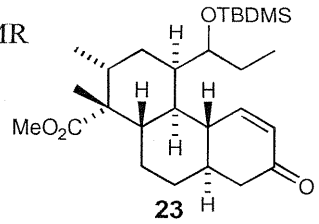
$CDCl_3$

^{13}C NMR



22
75 MHz
$CDCl_3$

^{1}H NMR

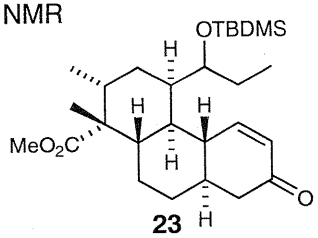


23

300 MHz

$CDCl_3$

^{13}C NMR

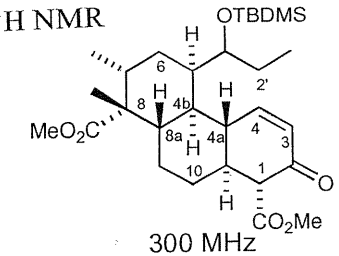


23

75 MHz

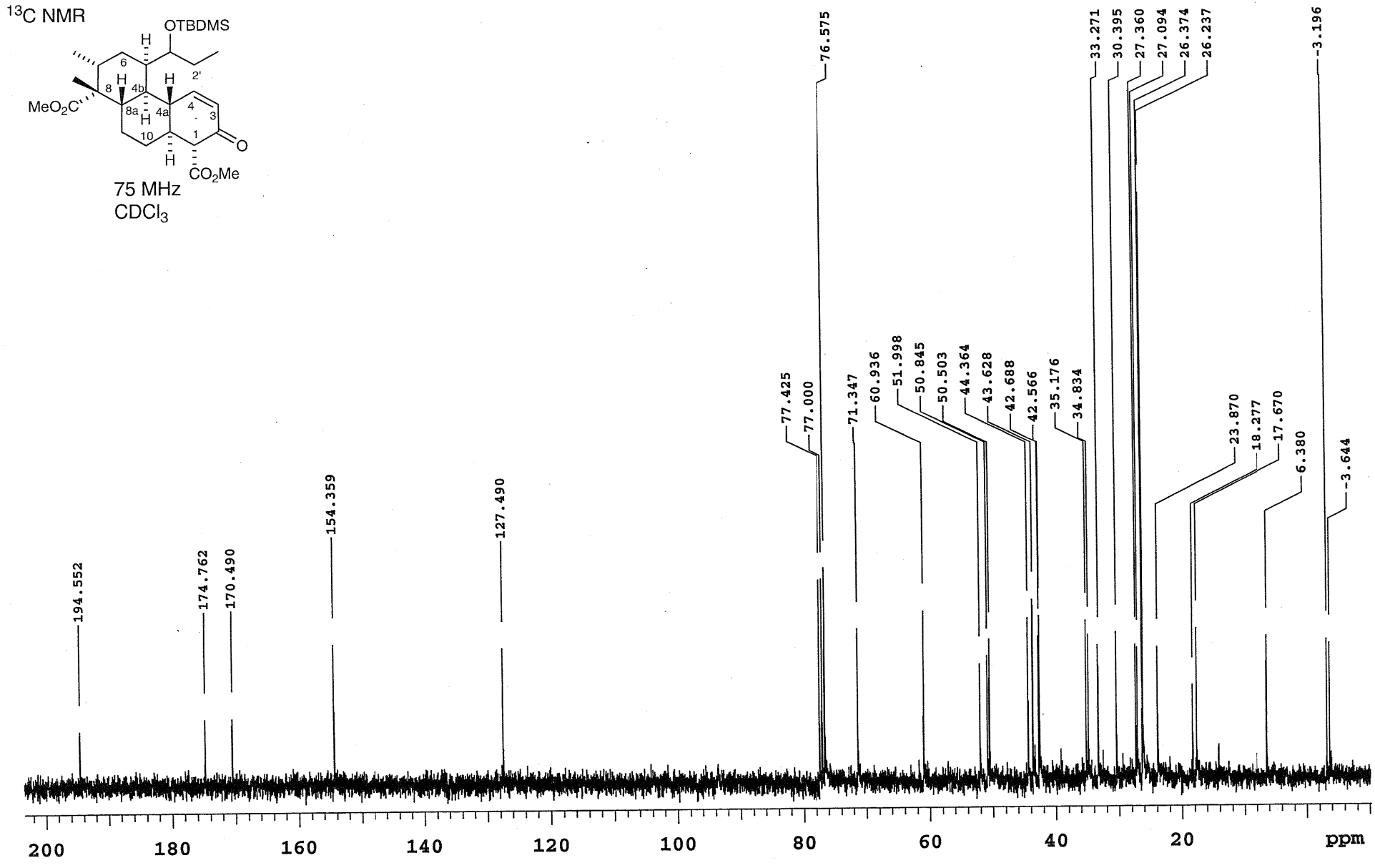
$CDCl_3$

^{1}H NMR

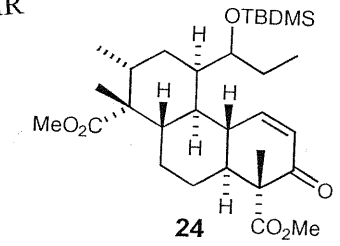


300 MHz

$CDCl_3$


^{13}C NMR
OTBDMS
MeO$_2$C
CO$_2$Me
75 MHz
CDCl$_3$
194.552
174.762
170.490
154.359
127.490
77.425
77.000
76.575
71.347
60.936
51.998
50.845
50.503
44.364
43.628
42.688
42.566
35.176
34.834
33.271
30.395
27.360
27.094
26.374
26.237
23.870
18.277
17.670
6.380
-3.196
-3.644
200
180
160
140
120
100
80
60
40
20
ppm

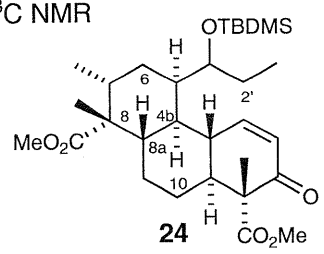
^{1}H NMR



24

300 MHz
$CDCl_3$

^{13}C NMR

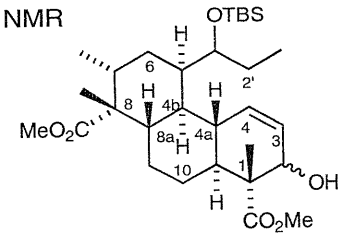


24

75 MHz

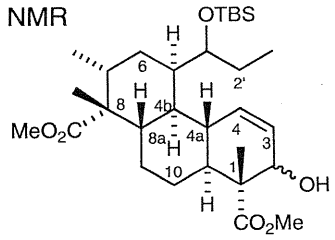
$CDCl_3$

^{1}H NMR

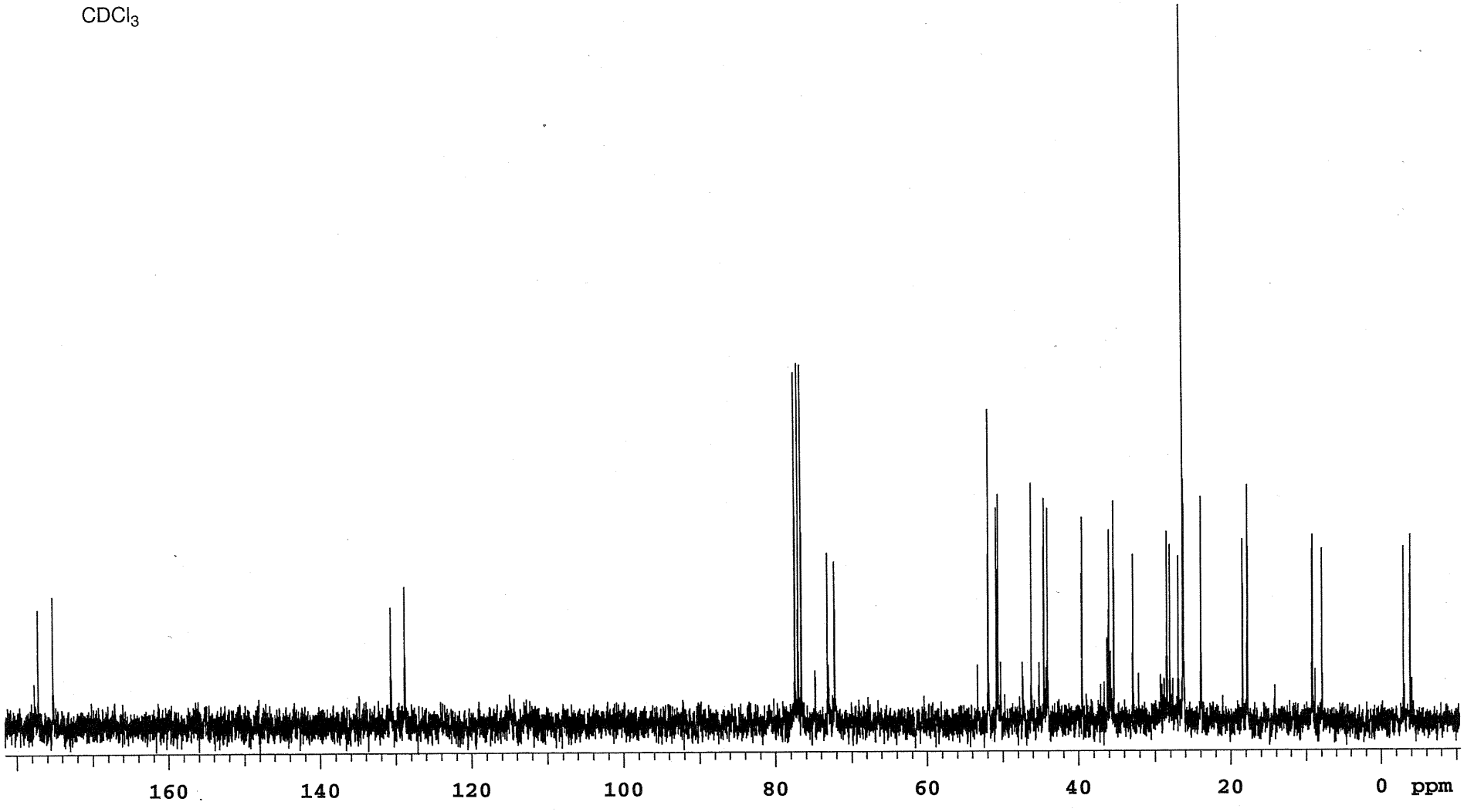


300 MHz
$CDCl_3$

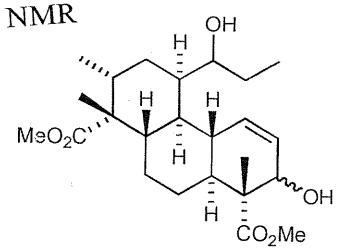
^{13}C NMR



75 MHz
$CDCl_3$

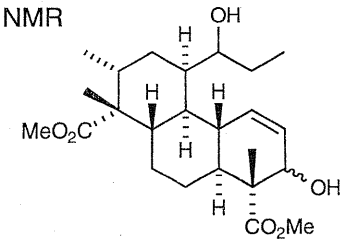


^{1}H NMR

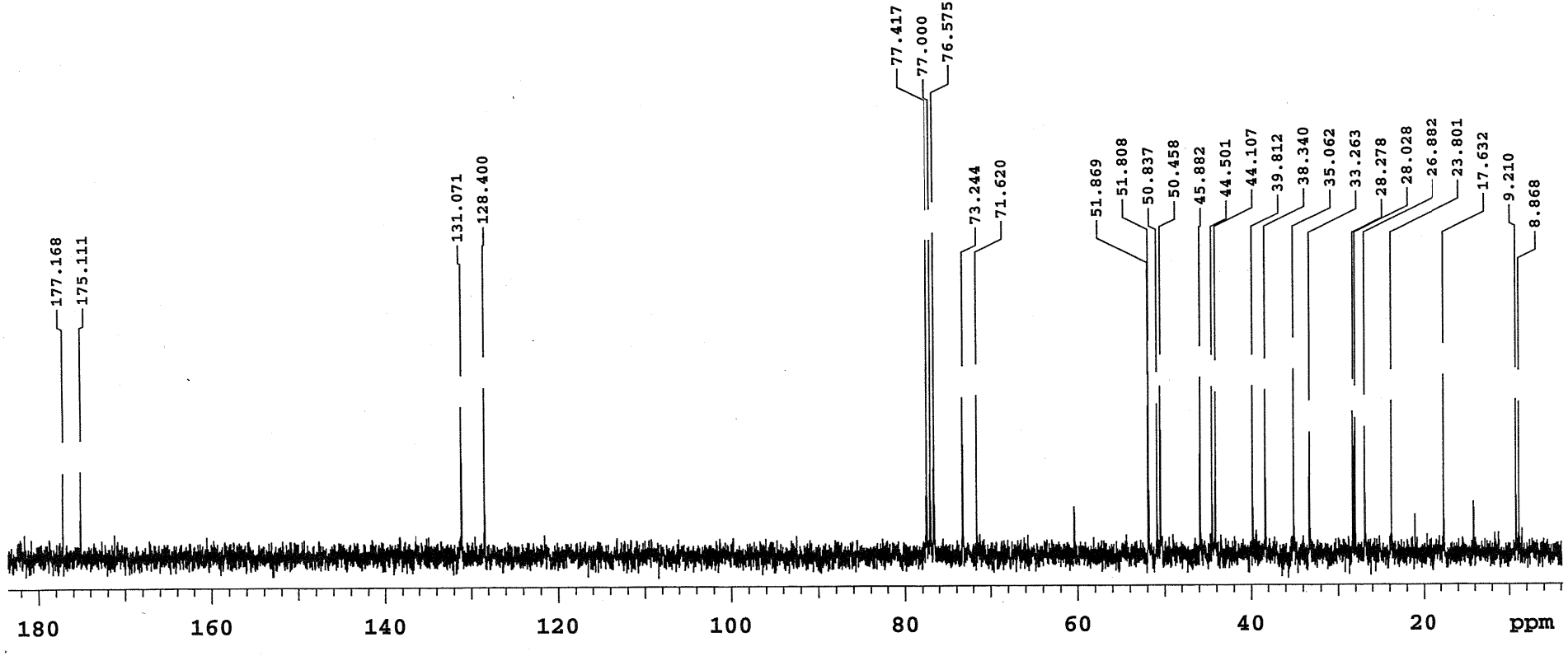


300 MHz
$CDCl_3$

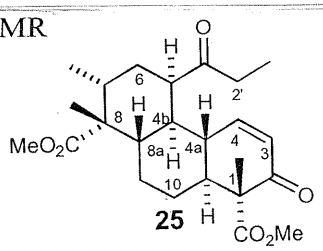
^{13}C NMR



75 MHz
$CDCl_3$



^{1}H NMR

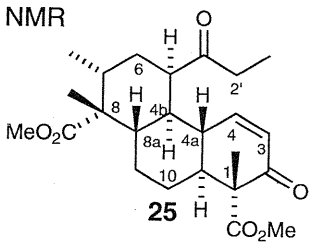


25

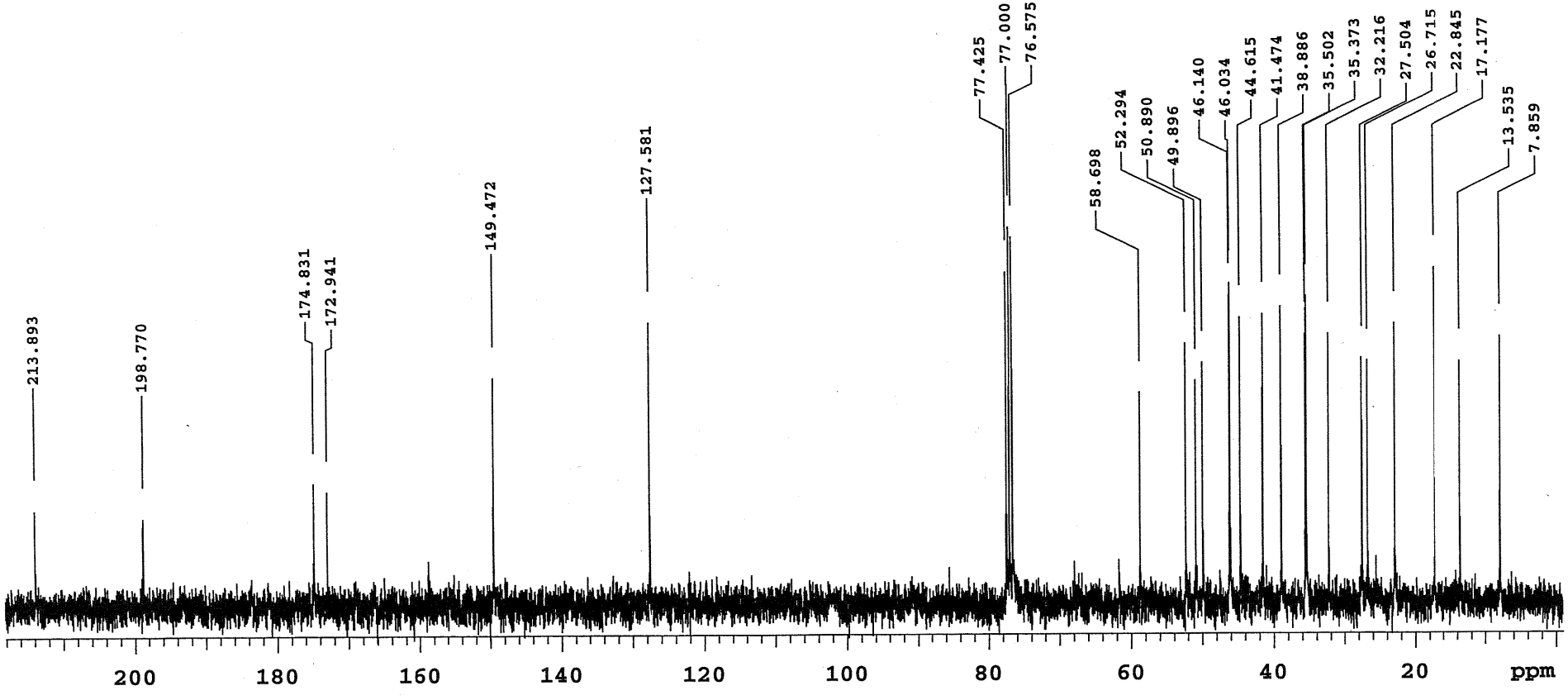
300 MHz

$CDCl_3$

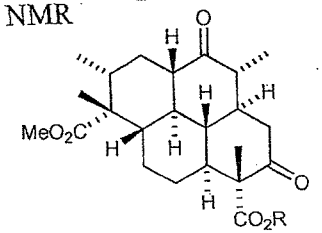
^{13}C NMR



75 MHz
$CDCl_3$

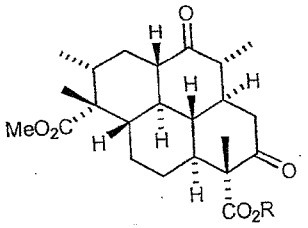


^{1}H NMR

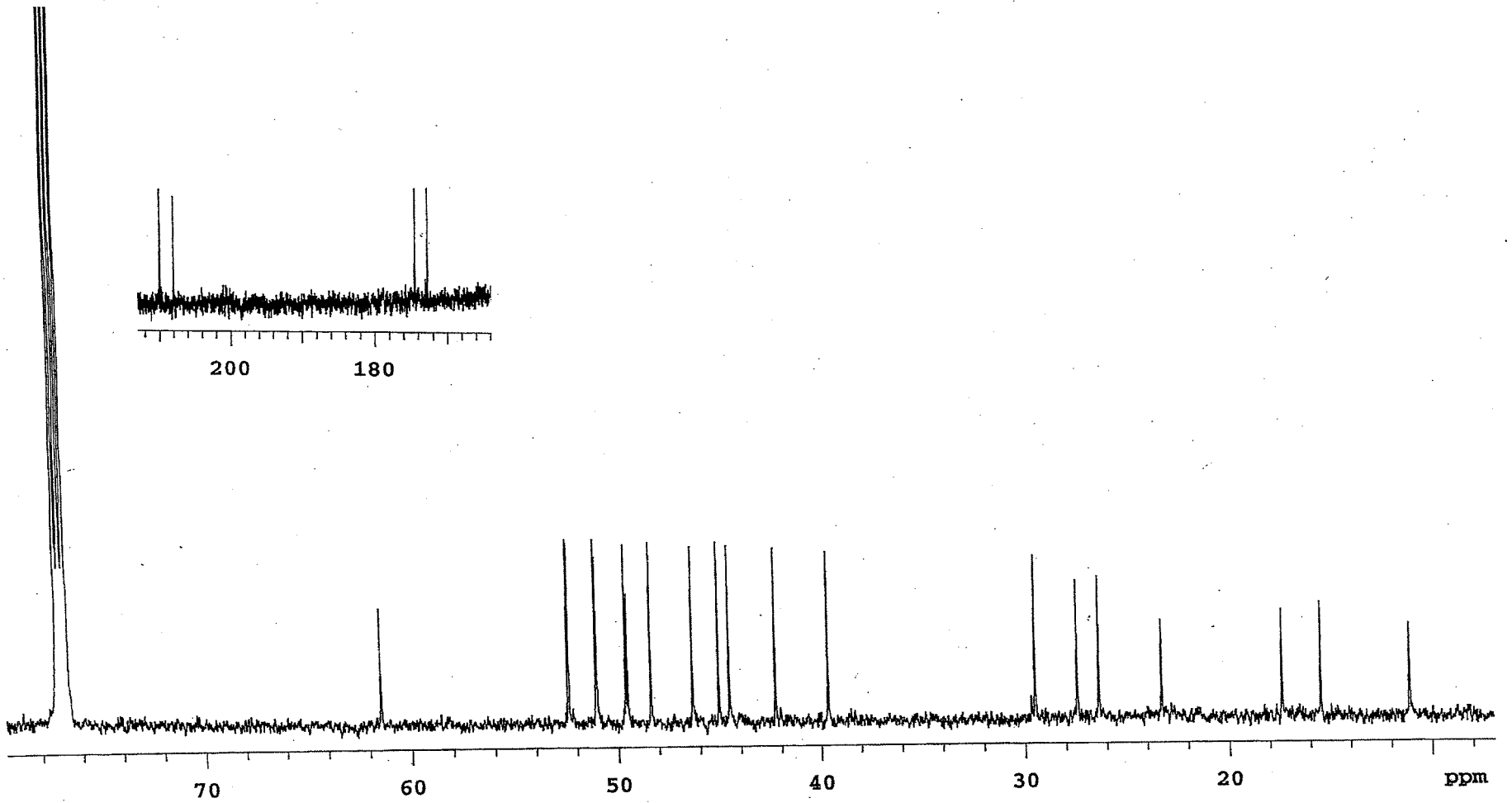


27 R = Me
800 MHz
$CDCl_3$

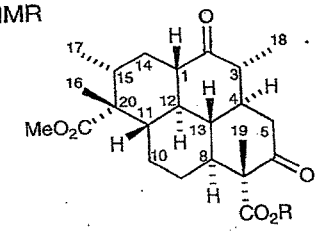
^{13}C NMR



27 R = Me



^{1}H NMR

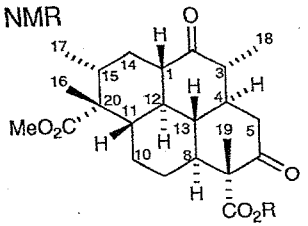


$R = CH_2CH_2OMOM$

300 MHz

$CDCl_3$

^{13}C NMR

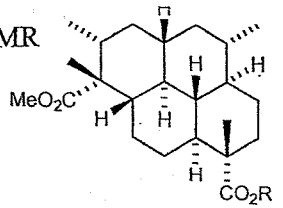


R = CH_2CH_2OMOM

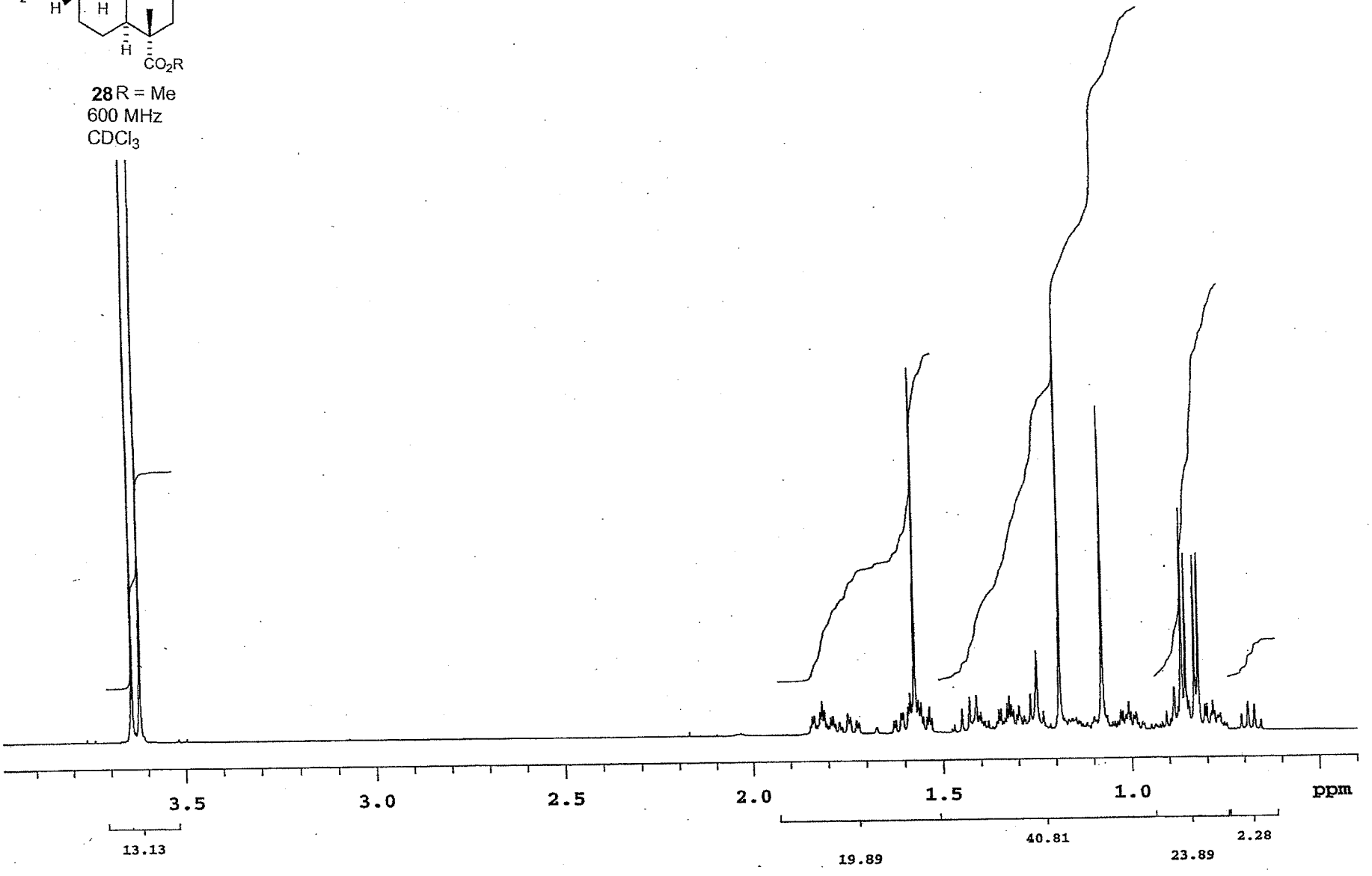
75 MHz

$CDCl_3$

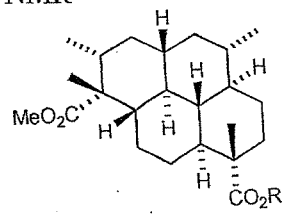
^{1}H NMR



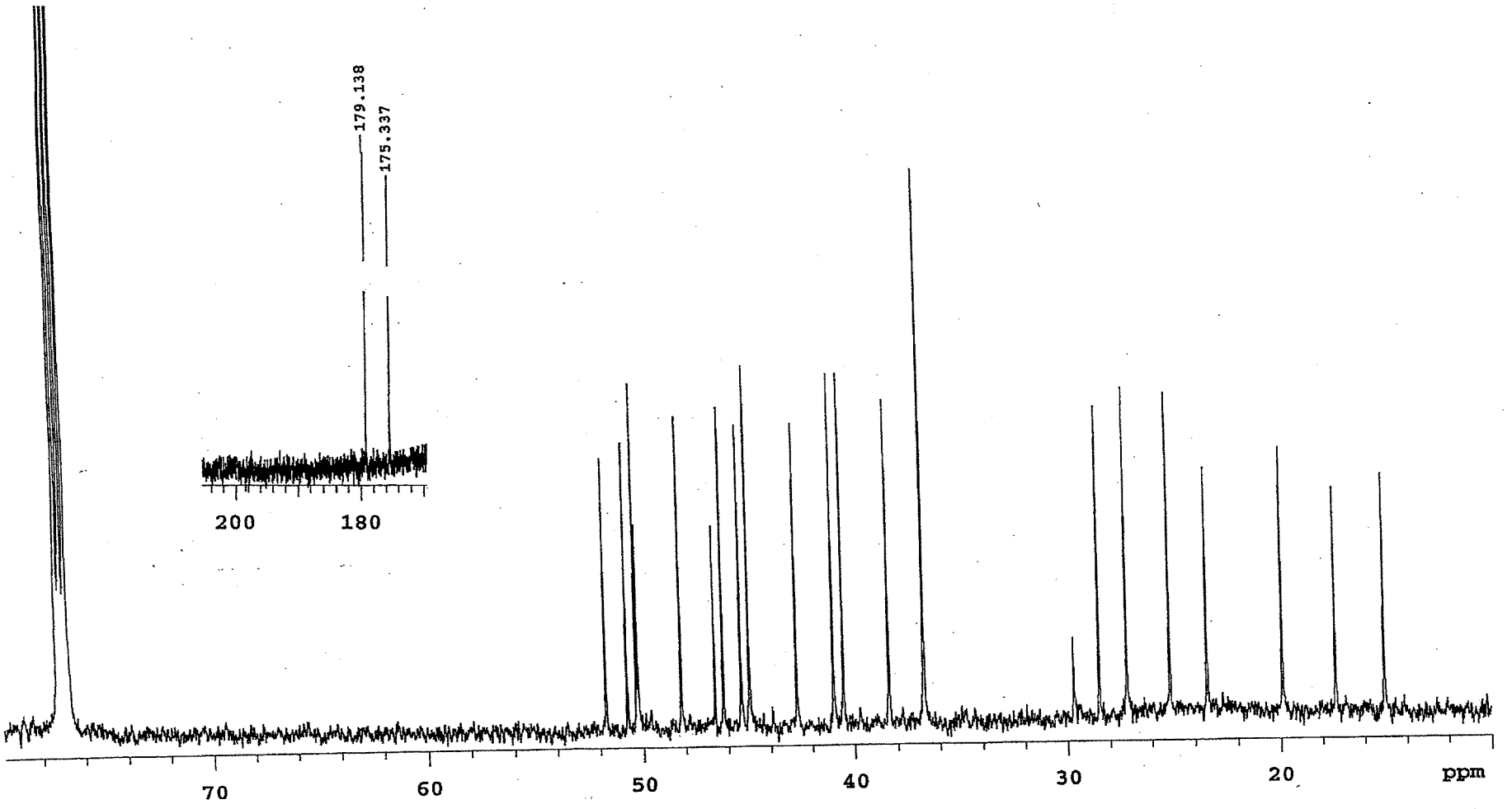
28 R = Me
600 MHz
$CDCl_3$



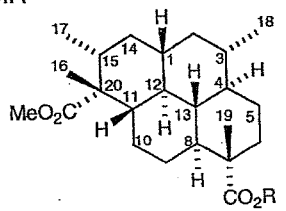
^{13}C NMR



28 R = Me



^{1}H NMR

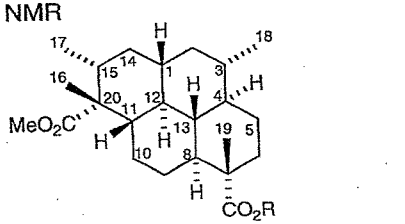


$R = CH_2CH_2OMOM$

300 MHz

$CDCl_3$

^{13}C NMR

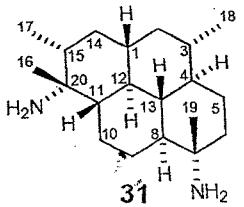


R = CH_2CH_2OMOM

75 MHz

$CDCl_3$

^{1}H NMR of the TFA salt of **31** (synthetic sample)

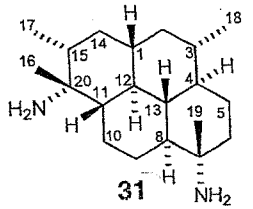


31

600 MHz

CD_3OD

^{1}H NMR of the TFA salt of **31** (authentic sample)

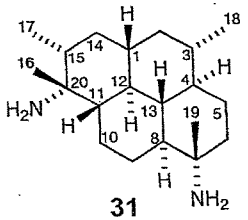


31

600 MHz

CD_3OD

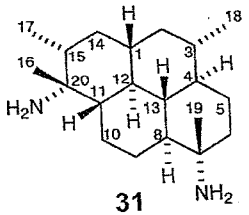
^{13}C NMR of the TFA salt of **31** (synthetic sample)



31

CD_3OD

^{13}C NMR of the TFA salt of **31** (authentic sample)



31

CD_3OD