Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Nonenzymic Polycyclisation of Analogues of Oxidosqualene with a Preformed C-ring.

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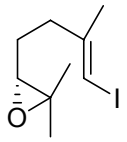
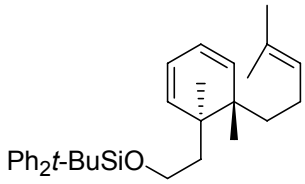
Electronic Supplementary Information

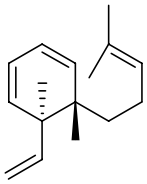
General details. All reactions were conducted under an inert atmosphere of argon gas in oven or flame dried glassware. Reagents were added through septa using dried syringes or *via cannula*, under the positive pressure of argon. The reactions were monitored by thin layer chromatography (TLC) using SIL G-25 UV254 pre-coated silica gel plates (0.25 mm thickness). The TLC plates were visualized using an anisaldehyde (5% anisaldehyde in ethanol with 1% sulfuric acid) or a PMA (5% phosphomolybdic acid in ethanol) solution. Flash column chromatography was performed using BIOSOLVE silica gel (0.063-0.200 mm particle size). High Performance Liquid Chromatography (HPLC) was performed on a Bio-Sil D 90-10 silica gel column (250 mm length, 10 mm diameter) using a Kontron 420 pump and a Valco CV-6-UHPa-N60 injector. NMR spectra were recorded at 500 MHz or 300 MHz for proton and at 125 MHz or 75 MHz for carbon nuclei in chloroform-d or benzene-d6. Carbon spectra were recorded as APT experiments to establish assignment. Chemical shifts are reported in units of parts per million (ppm), referenced relative to the residual 1H or 13C peaks of the used solvent as internal standards (chloroform-d: δH 7.26 and δC 77.16; benzene-d6: δH 7.16, δC 128.06). Infrared spectra (IR) were recorded on a PERKIN-ELMER 1600 series FTIR spectrometer and reported in wave numbers (cm-1). Samples were prepared as a thin film (neat) on KBr plate. Optical rotations were measured using a 1 ml cell with a 10 cm path length on a PERKIN-ELMER 241 polarimeter and are reported in the standard format for $[\alpha]$ in 10^{-1} deg cm^2 g^{-1}. Electron impact mass spectrometry (EI-MS) was performed on a Hewlett-Packard 5859A mass spectrometer at 70 eV ionisation potential, via a particle beam. All chemicals and solvents were purchased and used without any further purification, except tetrahydrofuran (THF), which was distilled from Na/benzophenone prior to use and dichloromethane, which was distilled from CaH_2.



(3*R*)-(4-Iodo-3-methyl-but-3-enyl)-2,2-dimethyl-oxirane. The title compound was prepared according to the procedure for the synthesis of its (*S*)-enantiomer, as reported in reference 11 of the title communication. All data were in accordance with those previously reported for its (S)-enantiomer, except: $[\alpha]^{20}_{D}$ +12 (*c* 1.23 $CHCl_3$)).

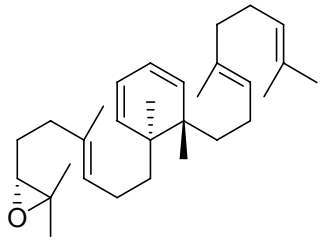


***tert*-Butyl-{2-[1,6-dimethyl-6-(4-methylpent-3-enyl)-cyclohexa-2,4-dienyl]-ethoxy}-diphenylsilane (11').** Silyloxypolyene **10** (1.45 g, 3.48 mmol) was cross-coupled with 1-bromo-2-methylpropene (0.447 + 0.107 g, 3.31 + 0.80 mmol) according to the general procedure for cross-coupling (*E*)-1-iodo-2,6-dimethyl-1,5-heptadiene, as reported in reference 11 of the title communication. Flash chromatography (silica gel, 0.25 to 0.75% ethyl acetate in iso-octane) afforded **11'** (1.37 g, 83%) as a clear colourless oil, R_f 0.46 (iso-octane/ethyl acetate 99/1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.81-7.77 (4H, band), 7.23-7.19 (6H, band), 5.66-5.56 (2H, band), 5.27 (1H, d(br), *J* = 9.3 Hz), 5.19 (1H, d(br), J= 9.1 Hz), 5.12 (1H, t(br), *J* = 7.1 Hz), 3.84 (2H, dd, *J* = 2 × ±7.6 Hz), 2.21 (1H, ddd, *J* = 13.1, 2 × ±7.5 Hz), 2.00-1.92 (2H, band), 1.77 (1H, ddd, *J* = 12.7, 10.4, 6.7 Hz), 1.17 (9H, s), 1.16 (1H, ddd, *J* = 13.0, 10.8, 5.9), 0.84 (6H, s(br)); ^{13}C NMR (75 MHz, C_6D_6) δ 136.3 (CH), 135.9 (4CH), 135.8 (CH), 134.5 (C), 134.4 (C), 130.5 (C), 129.7 (2CH), 127.9 (4CH), 125.9 (CH), 122.4 (CH), 122.1 (CH), 62.0 (CH_2), 39.7 (C), 39.5 (C), 38.1 (CH_2), 34.7 (CH_2), 27.0 ($3CH_3$), 25.6 (CH_3), 23.9 (CH_2), 19.4 (CH_3), 19.3 (C), 18.6 (CH_3), 17.5 (CH_3); IR (neat) ν_{max} 3071 (w), 3045 (w), 3028 (w), 2962 (s), 2931 (s), 2857 (m), 1960 (vw), 1890 (vw), 1825 (vw), 1661 (vw), 1590 (w), 1472 (m), 1428 (m), 1381 (m), 1302 (w), 1255 (w), 1190 (w), 1112 (s), 1081 (s), 1039 (w), 998 (w), 824 (m), 738 (m), 701 (s), 614 (m), 506 (s) cm^{-1}; EI-MS m/z (%): 472 ($M^{\circ+}$, 0.5), 457 (0.2), 443 (0.4), 437 (0.6), 429 (1), 415 ($M^{\circ+}$ - *t*-Bu, 25), 359 (2), 337 (6), 333 (4), 291 (6), 239 (5), 225 (27), 199 (Ph_2SiOH^+, 92), 133 (55), 108 (100), 83 (30), 55 (77), 41 (78); $[\alpha]^{20}_{D}$ +172 (*c* 1.28 $CHCl_3$).

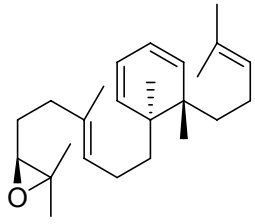


5,6-Dimethyl-5-(4-methylpent-3-enyl)-6-vinylcyclohexa-1,3-diene (12'). Polyene **12'** (0.345 g, 57% over 3 steps) was prepared as a clear colourless oil from silyloxypolyene **11'** (1.37 g, 2.90 mmol), according to the general procedures for desilylation and Grieco-Sharpless elimination described in reference 11 of the title communication. Flash chromatographic purification of **12'** was performed on silica gel with 0.5% ether in pentane and the solvent was very carefully removed under reduced pressure (relatively volatile compound!), R_f 0.77 (iso-octane); ^{1}H NMR (500 MHz, C_6D_6) δ 6.11 (1H, dd, *J* = 17.4, 10.8 Hz), 5.76-5.71 (2H, band(AB)), 5.41

(1H, m), 5.30 (1H, m), 5.18 (1H, t(br), *J* = 7.1 Hz), 5.035 (1H, dd, *J* = 17.4, 1.5 Hz), 4.98 (1H, dd, *J* = 10.8, 1.5 Hz), 2.10-1.99 (2H, band), 1.85 (1H, ddd, *J* = 13.1, 11.3, 5.5 Hz), 1.67 (3H, s(br)), 1.56 (3H, s(br)),1.19 (1H, ddd, *J* = 13.1, 11.7, 5.0 Hz), 1.02 (3H, s), 0.97 (3H, s); ^{13}C NMR (125 MHz, C_6D_6) δ 142.2 (CH), 136.1 (CH), 135.9 (CH), 130.8 (C), 125.9 (CH), 122.5 (CH), 122.1 (CH), 112.4 (CH_2), 44.7 (C), 39.4 (C), 35.2 (CH_2), 25.8 (CH_3), 23.7 (CH_2), 20.0 (CH_3), 17.6 (CH_3), 17.5 (CH_3); IR (neat) ν_{max} 3082 (w), 3030 (m), 2967 (vs), 2927 (vs), 2855 (s), 1630 (m), 1451 (m), 1377 (m), 1102 (m), 1001 (m), 908 (s), 835 (w), 780 (w), 716 (s), 648 (m) cm^{-1}; EI-MS m/z (%): 216 ($M^{\circ+}$, 12), 201 (2), 173 (8), 159 (2), 145 (15), 134 (100), 119 (35), 117 (20), 105 (34), 91 (35), 79 (20), 69 (56), 55(20), 41 (76).

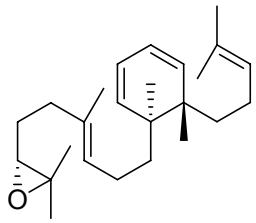


(3*R*)-{6-[6-(4,8-Dimethyl-nona-3,7-dienyl)-(1*S*,6*S*)-dimethyl-cyclohexa-2,4-dienyl]-3-methyl-hex-3-enyl}-2,2-dimethyl-oxirane (*ent*-4). Polyene **12** (0.182 g, 0.64 mmol) was cross-coupled with the above described (3*R*)-(4-Iodo-3-methyl-but-3-enyl)-2,2-dimethyl-oxirane (0.165 g, 0.62 mmol) according to the general procedure reported in reference 11 of the title communication. Flash chromatography (silica gel, 2% ethyl acetate in *iso*-octane) afforded ***ent*-4** (0.098 g, 37%) as a clear colourless oil, R_f 0.56 (*iso*-octane/ethyl acetate 95/5); ^{1}H NMR (500 MHz, C_6D_6) δ 5.77-5.75 (2H, band), 5.39-5.37 (2H, band), 5.22-5.18 (2H, 2 overl. t(br), 2 × *J* = 6.9 Hz), 2.56 (1H, t, *J* = 6.2 Hz), 2.13 (1H, ddd, *J* = 13.9, 9.0, 6.2 Hz), 2.09-2.00 (5H, band), 1.94-1.88 (2H, band), 1.67 (3H, s(br)), 1.64-1.48 (2H, band), 1.58 (3H, s(br)), 1.56 (3H, s(br)), 1.19-1.12 (2H, band), 1.14 (3H, s(br)), 1.09 (3H, s(br)), 0.92 (6H, s(br)); ^{13}C NMR (125 MHz, C_6D_6) δ 136.53 (CH), 136.42 (CH), 134.0 (C), 130.7 (C), 126.3 (CH), 126.1 (CH), 122.34 (CH), 122.29 (CH), 63.5 (CH), 57.2 (C), 40.1 (2C), 36.8 (CH_2), 35.24 (CH_2), 35.16 (CH_2), 28.0 (CH_2), 25.8 (CH_3), 25.0 (CH_3), 24.1 (CH_3), 24.0 (CH_3), 18.9 (CH_3), 18.8 ($2CH_3$), 17.6 (CH_3), 16.0 (CH_3).; IR (neat) ν_{max} 3052 (w), 3026 (m), 2963 (vs), 2925 (s), 2866 (m), 1450 (s), 1377 (s), 1118 (m), 774 (m), 721 (m) cm^{-1}; EI-MS m/z (%): 356 ($M^{\circ+}$, 0.6), 341 (1), 323 (0.7), 313 (1.5), 306 (0.4), 295 (1), 287 (1), 274 (4), 270 (4.5), 255 (4), 229 (5), 213 (3), 203 (6), 187 (6), 177 (7), 175 (6), 159 (8), 133 (15), 119 (80), 91 (40), 69 (70), 55 (90), 41 (100); $[\alpha]^{20}_D$ +168 (*c* 0.52 $CHCl_3$).

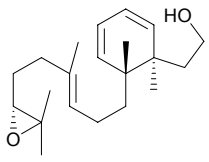


(3*S*)-{6-[(1*S*,6*S*)-Dimethyl-6-(4-methylpent-3-enyl)-cyclohexa-2,4-dienyl]-3-methylhex-(3*E*)-enyl}-2,2-dimethyloxirane (5'). Polyene **12'** (0.175 g, 0.809 mmol) was cross-coupled with (3*S*)-(4-Iodo-3-methyl-but-3-enyl)-2,2-dimethyl-oxirane (0.205 g, 0.77 mmol) according to the general procedure reported in reference 11 of the title communication. Flash chromatography (silica gel, 2% ethyl acetate in *iso*-octane) afforded epoxy polyene **5'** (0.134 g, 47%) as a clear colourless oil, R_f 0.43 (*iso*-octane/ethyl acetate 95/5); ^{1}H NMR (500 MHz, C_6D_6) δ 5.77-5.75 (2H, band), 5.39-5.37 (2H, band), 5.22-5.18 (2H, 2 overl. t(br), 2 × *J* = 6.9 Hz), 2.55 (1H, t, *J*

= 6.1 Hz), 2.13 (1H, ddd, *J* = 13.9, 9.0, 6.2 Hz), 2.09-2.00 (5H, band), 1.94-1.87 (2H, band), 1.67 (3H, s(br)), 1.63-1.48 (2H, band), 1.57 (3H, s(br)), 1.56 (3H, s(br)), 1.19-1.12 (2H, band), 1.14 (3H, s(br)), 1.09 (3H, s(br)), 0.92 (6H, s(br)); ^{13}C NMR (125 MHz, C_6D_6) δ 136.53 (CH), 136.46 (CH), 133.9 (C), 130.7 (C), 126.3 (CH), 126.1 (CH), 122.33 (CH), 122.28 (CH), 63.6 (CH), 57.3 (C), 40.1 (2C), 36.8 (CH_2), 35.24 (CH_2), 35.16 (CH_2), 28.0 (CH_2), 25.8 (CH_3), 25.0 (CH_3), 24.1 (CH_3), 24.0 (CH_3), 18.9 (CH_3), 18.8 ($2CH_3$), 17.6 (CH_3), 16.0 (CH_3).; IR (neat) ν_{max} 3052 (w), 3027 (m), 2964 (vs), 2927 (s), 2878 (m), 2855 (m), 1455 (s), 1378 (s), 1248 (w), 1170 (m), 984 (w), 899 (w), 875 (w), 834 (m), 762 (m), 721 (m) cm^{-1}; EI-MS m/z (%): 356 ($M^{\circ+}$, 0.8), 341 (0.8), 323 (0.3), 313 (1), 306 (0.4), 295 (0.5), 287 (1), 274 (2), 270 (2.5), 255 (2.5), 241 (0.9), 229 (3), 213 (2.5), 203 (3), 187 (4.5), 175 (5.5), 159 (4.5), 133 (18), 119 (28), 91 (29), 69 (32), 55 (59), 41 (100); $[\alpha]^{20}_D$ +261 (*c* 0.91 $CHCl_3$).

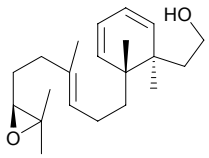


(3*R*)-{6-[(1*S*,6*S*)-Dimethyl-6-(4-methylpent-3-enyl)-cyclohexa-2,4-dienyl]-3-methylhex-(3*E*)-enyl}-2,2-dimethyloxirane (*ent*-4'). Polyene **12'** (0.124 g, 0.573 mmol) was cross-coupled with the above described (3*R*)-(4-Iodo-3-methyl-but-3-enyl)-2,2-dimethyl-oxirane (0.145 g, 0.55 mmol) according to the general procedure reported in reference 11 of the title communication. Flash chromatography (silica gel, 2% ethyl acetate in *iso*-octane) afforded ***ent*-4'** (0.087 g, 43%) as a clear colourless oil, R_f 0.43 (*iso*-octane/ethyl acetate 95/5); ^{1}H NMR (500 MHz, C_6D_6) δ 5.77-5.75 (2H, band), 5.39-5.37 (2H, band), 5.22-5.18 (2H, 2 overl. t(br), 2 × *J* = 6.9 Hz), 2.56 (1H, t, *J* = 6.2 Hz), 2.13 (1H, ddd, *J* = 13.9, 9.0, 6.2 Hz), 2.09-2.00 (5H, band), 1.94-1.88 (2H, band), 1.67 (3H, s(br)), 1.64-1.48 (2H, band), 1.58 (3H, s(br)), 1.56 (3H, s(br)), 1.19-1.12 (2H, band), 1.14 (3H, s(br)), 1.09 (3H, s(br)), 0.92 (6H, s(br)); ^{13}C NMR (125 MHz, C_6D_6) δ 136.53 (CH), 136.42 (CH), 134.0 (C), 130.7 (C), 126.3 (CH), 126.1 (CH), 122.34 (CH), 122.29 (CH), 63.5 (CH), 57.2 (C), 40.1 (2C), 36.8 (CH_2), 35.24 (CH_2), 35.16 (CH_2), 28.0 (CH_2), 25.8 (CH_3), 25.0 (CH_3), 24.1 (CH_3), 24.0 (CH_3), 18.9 (CH_3), 18.8 ($2CH_3$), 17.6 (CH_3), 16.0 (CH_3).; IR (neat) ν_{max} 3052 (w), 3026 (m), 2963 (vs), 2925 (s), 2866 (m), 1450 (s), 1377 (s), 1118 (m), 774 (m), 721 (m) cm^{-1}; EI-MS m/z (%): 356 ($M^{\circ+}$, 0.6), 341 (1), 323 (0.7), 313 (1.5), 306 (0.4), 295 (1), 287 (1), 274 (4), 270 (4.5), 255 (4), 229 (5), 213 (3), 203 (6), 187 (6), 177 (7), 175 (6), 159 (8), 133 (15), 119 (80), 91 (40), 69 (70), 55 (90), 41 (100); $[\alpha]^{20}_D$ +168 (*c* 0.52 $CHCl_3$).



2-{6-[6-((1R)-3,3-Dimethyloxiranyl)-4-methylhex-3-enyl]-(1S,6S)-dimethylcyclohexa-2,4-dienyl}-ethanol (14). The epoxy silyl ether **13** (0.460 g, 0.826 mmol) was desilylated using the general procedure as previously described.[11] The crude product was purified by flash chromatography, eluting with *iso*-octane-ethyl acetate (17/3), to give the title alcohol (0.171 g, 65%) as a colourless oil. R_f 0.29 (*iso*-octane/acetone 7/3); $[\alpha]_D^{20}$ +226 (*c* 0.93 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3394 (O-H), 2964vs, 2927, 2875, 1456, 1380, 1250, 1114, 1049, 1016; ^{1}H

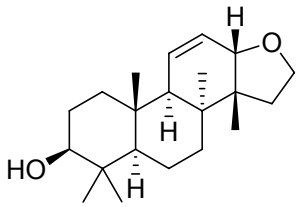
NMR (500 MHz, C_6D_6) δ 5.71-5.65 (2H, band)), 5.33 (1H, d(br), *J* = 9.1 Hz), 5.27 (1H, d(br), *J* = 9.1 Hz), 5.18 (1H, t(br), *J* = 7.0 Hz), 3.51-3.45 (2H, band), 2.55 (1H, dd, *J* = 2 × ±6.2 Hz), 2.125 (1H, ddd(br), *J* = 13.8, 8.9, 6.1 Hz), 2.05-1.95 (4H, band), 1.86-1.80 (1H, m), 1.64-1.48 (2H, band), 1.55 (3H, s(br)), 1.23 (1H, ddd, *J* = 13.3, 8.5, 6.1 Hz), 1.14 (3H, s), 1.11-1.05 (1H, m), 1.09 (3H, s), 0.87 (3H, s), 0.85 (3H, s), 0.64 (1H, s(br,OH)); ^{13}C NMR (125 MHz, C_6D_6) δ 136.6 (CH), 136.1 (CH), 134.0 (C), 126.2 (CH), 122.6 (CH), 122.3 (CH), 63.5 (CH), 60.1 (CH_2), 57.4 (C), 39.8 (C), 39.5 (C), 38.4 (CH_2), 36.8 (CH_2), 34.8 (CH_2), 27.9 (CH_2), 25.0 (CH_3), 23.9 (CH_2), 19.6 (CH_3), 18.9 (CH_3), 18.8 (CH_3), 16.0 (CH_3).



2-{6-[6-((1*S*)-3,3-Dimethyloxiranyl)-4-methylhex-3-enyl]-(1*S*,6*S*)-dimethylcyclohexa-2,4-dienyl}-ethanol (16). The epoxy silyl ether **15** (0.311 g, 0.558 mmol) was desilylated using the procedure as previously described.[11] The crude product was purified by flash chromatography, eluting with *iso*-octane-ethyl acetate (4/1), to give the alcohol (0.113 g, 64%) as a colourless oil. R_f 0.29 (*iso*-octane/acetone 7/3); $[\alpha]_D^{20}$ +175 (*c* 0.94 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3402 (O-H), 2963vs, 2914, 1456, 1379, 1250, 1114, 1049, 1011; ^{1}H NMR (500 MHz, C_6D_6) δ 5.71-5.65 (2H, band)), 5.325 (1H, d(br), *J* = 9.0 Hz), 5.265 (1H, d(br), *J* = 9.0 Hz), 5.18 (1H, t(br), *J* = 7.0 Hz), 3.51-3.45 (2H, band), 2.55 (1H, dd, *J* = 2 × ±6.1 Hz), 2.125 (1H, ddd(br), *J* = 13.7, 9.1, 5.8 Hz), 2.05-1.95 (4H, band), 1.825 (1H, ddd(br), *J* = 12.8, 10, 7 Hz), 1.64-1.58 (1H, m), 1.55 (3H, s(br)), 1.54-1.49 (1H, m), 1.22 (1H, ddd, *J* = 13.4, 8.6, 6.1 Hz), 1.14 (3H, s), 1.11-1.05 (1H, m), 1.09 (3H, s), 0.87 (3H, s), 0.84 (3H, s), 0.62 (1H, s(br,OH)); ^{13}C NMR (125 MHz, C_6D_6) δ 136.6 (CH), 136.1 (CH), 134.0 (C), 126.2 (CH), 122.6 (CH), 122.3 (CH), 63.6 (CH), 60.1 (CH_2), 57.4 (C), 39.8 (C), 39.5 (C), 38.3 (CH_2), 36.8 (CH_2), 34.8 (CH_2), 27.9 (CH_2), 25.0 (CH_3), 23.9 (CH_2), 19.6 (CH_3), 18.9 (CH_3), 18.8 (CH_3), 16.0 (CH_3); EI-MS *m/z*: 300 (M^+ - H_2O, 1%), 285 (1), 274 (2), 255 (1), 245 (1), 242 (1), 232 (5), 219 (2), 213 (2), 201 (2.5), 199 (5), 191 (7), 173 (6), 159 (7), 147 (18), 133 (100), 119 (65), 105 (60), 91 (61), 79 (30), 59 (65), 41 (87).

Cyclisation of the Epoxy Polyenol 16 – The Tetracyclic Alcohol (20). A solution of epoxy polyenol **16** (55 mg, 0.173 mmol) in dichloromethane (43 ml) was stirred at 10°C and a 1.0 M solution of tin(IV)chloride in dichloromethane (0.043 ml, 0.043 mmol, 0.25 equiv) was added. The resulting mixture was stirred at 10°C for five minutes. The reaction was quenched by adding a saturated potassium bicarbonate solution (8.0 ml). After separation of the organic layer, the aqueous phase was further extracted with *tert*-butyl methyl ether. The combined organic extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was filtered over a small pad of silica gel with ether and the concentrated filtrate was carefully fractionated by HPLC, eluting with *iso*-octane-acetone (4/1). The fastest eluting fraction gave tetracyclic alcohol **20** (5.0 mg, 9%) as a white solid. R_f 0.37 (*iso*-octane/acetone 7/3); IR (neat) ν_{max}/cm^{-1} 3432 (O-H), 2972, 2940, 2872, 1456, 1386, 1325, 1170, 1121, 1049; ^{1}H NMR (500 MHz, $CDCl_3$) 5.59 (1H, ddd, J = 10.5, 1.4, 1.4), 5.54 (1H, ddd, J = 10.5, 3.5, 1.3), 3.91 (1H, s(br)), 3.82 (1H, ddd, J= 8.4, 8.3, 8.2), 3.77 (1H, ddd, J = 10.3, 8.3, 3.5), 3.28 (1H, ddd, J = 11.2, 5.8, 4.6), 1.93 (1H, ddd, J = 11.6, 10.3, 8.2), 1.87 (1H, ddd, J = 13.2, 3.5, 3.5), 1.76 (1H, s(br)); 1.70 (1H, m),

1.66 (1H, m), 1.62 (2H, band), 1.53 (2H, band), 1.44 (1H, ddd, J = 11.6, 8.4, 3.5), 1.41 (1H, m), 1.35 (1H, d, J = 5.8, OH), 1.25 (1H, m), 1.15 (3H, s), 1.03 (3H, s), 0.98 (3H, s), 0.89 (3H, s), 0.78 (3H, s); ^{13}C NMR (APT, 125 MHz, $CDCl_3$) δ 130.1 (CH), 127.8 (CH), 79.2 (CH), 78.9 (CH), 64.3 (CH_2), 55.0 (CH), 48.9 (C), 45.4 (CH), 40.8 (CH_2), 39.4 (C), 38.4 (C), 36.4 (C), 34.9 (CH_2), 27.6 (CH_3), 27.4 (CH_2), 26.7 (CH_2), 26.3 (CH_3), 20.7 (CH_3), 17.7 (CH_2), 17.6 (CH_3), 15.1 (CH_3); ES-MS: 336 (MNH_4^+); EI-MS *m/z* 318 (M^+, 4%), 300 (M^+ - H_2O, 4), 285 (0.5), 273 (0.5), 250 (0.5), 231 (0.5), 210 (0.5), 203 (1), 189 (1), 177 (2), 175 (2), 164 (5), 149 (15), 135 (20), 119 (23), 105 (35), 91 (60), 79 (56), 57 (80), 43 (100), 41 (95). Full configurational and conformational assignments were made via 2D-NMR experiments, as described in the supplementary data.† Later eluting fractions contained the cyclic ether **17a** (8.0 mg, 15%), R_f 0.31 (*iso*-octane/acetone 7/3); IR (film) ν_{max}/cm^{-1} 3414 (O-H), 3027, 2962, 2919, 2869, 1464, 1382, 1193, 1108, 1049, 1005; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (1H, ddd, J = 9.4, 4.8(AB), 0.9), 5.78 (1H, ddd, J = 9.4, 4.8(AB), 0.9), 5.44 (1H, d(br), J = 9.4), 5.40 (1H, d(br), J = 9.4), 3.71-3.62 (3H, band), 2.07 (1H, ddd, J = 13.3, 8.6, 6.5), 1.88 (1H, ddd, J = 12.6, 9.0, 4.8), 1.76 (1H, ddd, J = 12.9, 12.9, 4.0), 1.69-1.61 (3H, band), 1.50-1.25 (6H, band), 1.29 (3H, s), 1.16 (1H, m), 1.05-1.00 (2H, band), 1.00 (3H, s), 0.97 (3H, s), 0.96 (3H, s), 0.92 (3H, s); ^{13}C NMR (125 MHz, $CDCl^3$) δ 136.5 (CH=*C*H), 135.4 (CH=*C*H), 122.7 (CH=*C*H), 121.9 (CH=*C*H), 86.6 (C-OR), 86.0 (CH-OR), 60.3 (CH2-OH), 56.8 (CH), 45.2 (C), 38.9 (CH2), 37.9 (CH2), 33.6 (CH2), 26.1 (CH3), 25.5 (CH2), 23.1 (CH3), 22.7 (CH2), 19.6 (CH3), 18.8 (CH3), 18.4 (CH3).EI-MS *m/z* 318 (M^+, 2%), 300 (M^+-H_2O, 0.5), 285 (0.5), 274 (2), 255 (3), 245 (0.5), 213 (1), 199 (2), 185 (2), 178 (4), 167 (4), 166 (6), 159 (11), 149 (9), 133 (60), 119 (23), 105 (21), 91 (20), 67 (23), 55 (50), 43 (100), 41 (56); and an impure fraction mainly containing the rearranged ketonic structure **18a** (9.5 mg, 17%) whose shown structural assignment was based on similarity in R_f and proton NMR data (R_f 0.25 (*iso*-octane/acetone 7/3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.86 (2H, band), 5.45-5.39 (2H, band), 3.72-3.63 (2H, band), 2.42-2.29 (3H, band), 2.17-2.06 (1H, m), 1.97-1.79 (2H, band), 1.75-1.55 (3H, band), 1.42-1.25 (3H, band), 1.25-1.10 (2H, band), 1.08-0.95 (1H, m), 1.01 (3H, s(br)), 0.99 (3H, s(br)), 0.84 (3H, d, J = 6.7 Hz), 0.80 (3H, d, J = 6.7 Hz), 0.54 (3H, s(br))) to pure ketonic material obtained in experiments using the related models ***ent*-4'** and **5'**, *vide infra*. Furthermore, some minor and more complex fractions containing structures like diol **19a** (1.8 mg, 3%) were isolated, R_f 0.19 (iso-octane:acetone 7/3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87-5.83 (2H,band), 5.49 (1H, d(br), J = 9.3 Hz), 5.39 (1H, d(br), J = 9.3 Hz), 3.72-3.62 (2H, band), 3.49-3.41 (1H, m), 2.15-1.75 (7H, band), 1.70-1.55 (2H, band), 1.53 (3H, s), 1.45-1.25 (4H, band), 1.02 (3H, s), 0.99 (3H, s), 0.97 (3H, s), 0.96 (3H, s); EI-MS m/z 318 (M^+, 0.2%), 255 (1), 159 (3), 149 (6), 133 (35), 105 (50), 91(55), 79 (35), 67 (23), 43 (100), 41 (56). Except for that of **20**, all fractions showed the characteristic resonances for an intact conjugated diene (NMR).



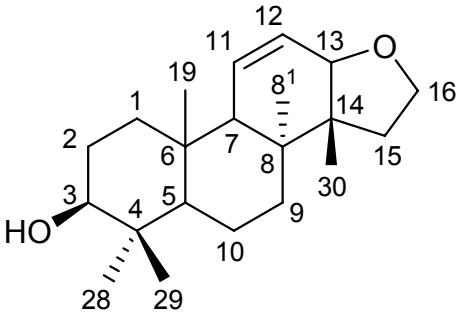
Characterisation via analysis of 2D-NMR data for the tetracyclic alcohol (20)

^{1}H NMR + HSQC + COSY + NOESY (500 MHz, $CDCl_3$):

δ	int.	mult.	*J* (Hz)	HSQC	COSY	NOESY
5.59	1H	ddd	10.5, 1.4, 1.4	127.8	5.54, 3.91, 1.76	
5.54	1H	ddd	10.5, 3.5, 1.3	130.1	5.59, 3.91, 1.76	1.87, 1.76, 0.78
3.91	1H	s(br)		78.9	5.59, 5.54, 1.76	1.41, 1.03
3.82	1H	ddd	8.4, 8.3, 8.2	64.3	3.77, 1.93, 1.44	
3.77	1H	ddd	10.3, 8.3, 3.5	64.3	3.82, 1.93, 1.44	
3.28	1H	ddd	11.2, 5.8, 4.6	79.2	1.62, 1.35	1.53, 1.25, 0.98
1.93	1H	ddd	11.6, 10.3, 8.2	34.9	3.82, 3.77, 1.44	1.76
1.87	1H	ddd	13.2, 3.5, 3.5	40.8	1.62, 1.25	5.54
1.76	1H	s(br)		55.0	5.59, 5.54, 3.91	5.54, 1.93, 1.53, 1.25, 1.15
1.70	1H	m		17.7	1.66, 1.53, 1.41	1.15, 0.98
1.66	1H	m		26.7	1.70, 1.53, 1.41	1.03
1.62	2H	band		27.4	3.28, 1.87, 1.25	
1.53	2H	band		17.7+45.4	1.70, 1.66, 1.41	3.28, 1.15, 0.98, 0.89
1.44	1H	ddd	11.6, 8.4, 3.5	34.9	3.82, 3.77, 1.93	
1.41	1H	m		26.7	1.70, 1.66, 1.53	3.91
1.35	1H	d	5.8 (OH)	-	3.28	
1.25	1H	m		40.8	1.87, 1.62	3.28, 1.76
1.15	3H	s(br)		26.3	-	1.76, 1.70, 1.66, 1.53, 1.03
1.03	3H	s(br)		20.7	-	3.91, 1.66, 1.15
0.98	3H	s(br)		27.6	-	3.28, 1.70, 1.53
0.89	3H	s(br)		15.1	-	1.53, 0.78
0.78	3H	s(br)		17.6	-	5.54, 0.89

APT + HSQC + HMBC (500 MHz, $CDCl_3$):

assignment	δ	type	HSQC	HMBC
C-11	130.1	CH	5.54	3.91, 1.76
C-12	127.8	CH	5.59	1.76
C-3	79.2	CH	3.28	1.87, 1.87, 0.98, 0.89
C-13	78.9	CH	3.91	5.54, 3.82, 1.03
C-16	64.3	CH_2	3.82, 3.77	3.91, 1.93
C-7	55.0	CH	1.76	5.59, 1.66, 1.62, 1.53, 1.25, 1.15, 0.78
C-14	48.9	C	-	5.59, 1.93, 1.44, 1.15, 1.03
C-5	45.4	CH	1.53	1.87, 1.70, 1.66, 1.62, 1.53, 1.41, 0.98, 0.89, 0.78
C-1	40.8	CH_2	1.87, 1.25	1.76, 0.78,
C-4	39.4	C	-	1.70, 1.53, 0.98, 0.89
C-6	38.4	C	-	1.87, 1.76, 1.70, 1.53, 1.25, 0.78
C-8	36.4	C	-	5.54, 1.93, 1.76, 1.66, 1.62, 1.53, 1.15, 1.03
C-15	34.9	CH_2	1.93, 1.44	3.91, 3.82, 1.03,
C-28	27.6	CH_3	0.98	0.89
C-2	27.4	CH_2	1.62	1.87
C-9	26.7	CH_2	1.66, 1.41	1.53, 1.15,
C-8^1	26.3	CH_3	1.15	1.76, 1.03
C-30	20.7	CH_3	1.03	3.91, 1.93, 1.44, 1.15
C-10	17.7	CH_2	1.70, 1.53	-
C-19	17.6	CH_3	0.78	1.76, 1.66, 1.53, 1.41
C-29	15.1	CH_3	0.89	1.53, 0.98



From the 1D proton and carbon (APT) NMR spectra, together with the HSQC 2D spectrum, 4 carbon atoms can be assigned unequivocally by their distinctive chemical shift values and ^{1}H-splitting patterns: C-3, C-7, C-13 and C-16. Furthermore, the resonance at 1.35 ppm clearly corresponds to the O-H proton as it has no carbon partner. The resonances at 5.54 and 5.59 ppm ofcourse correspond to the C-11 and C-12 protons.

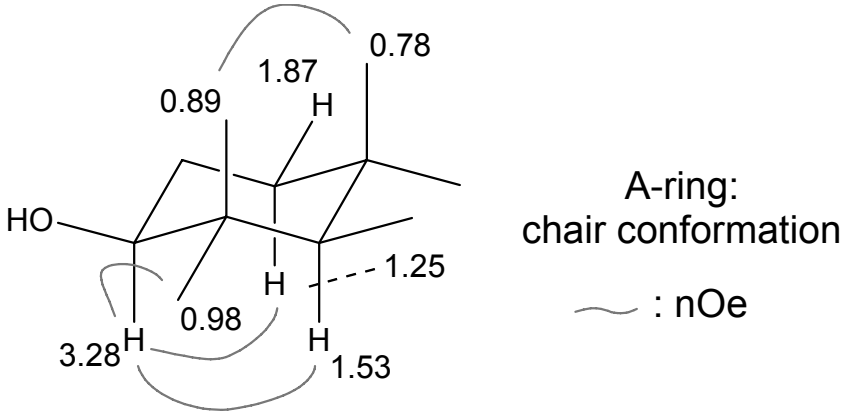
Starting from C-16: C-15 is defined by COSY-correlation of the attached protons and the C-30 methyl group is defined by HMBC relations to C-13 and C-15.

Starting from C-3: C-2 and C-1 are readily determined by proton COSY-correlations and the geminal methyl groups C-28 and C-29 are revealed (but not distinguished from each other) by the HMBC-correlations, as

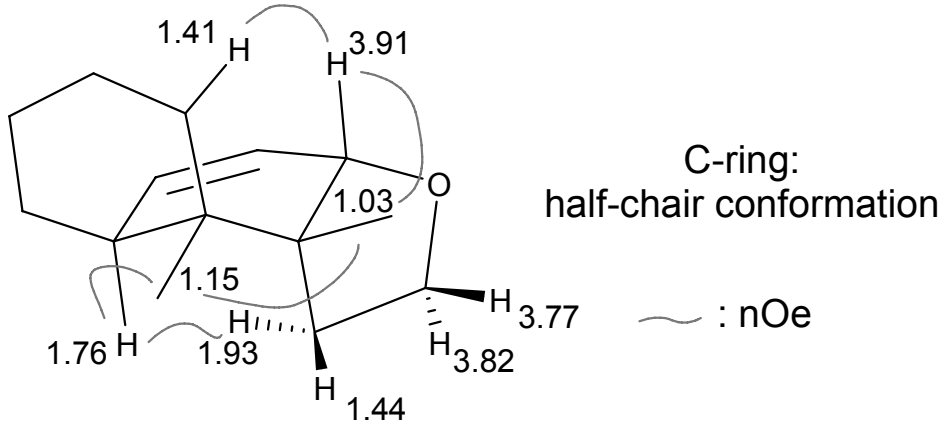
is the quaternary C-4 carbon. Also the C-5 tertiary carbon, the C-6 quaternary carbon and its C-19 methyl group can be distinguished in this manner. By COSY- and HMBC-relations from C-5, the assignment of the C-10 and C-9 methylene groups follows.

The assignment of the last C-8[1] methyl group is now evident by the exclusion principle. Of the two remaining quaternary carbon centers (C-8 and C-14), C-8 can be identified by HMBC-relation with the C-10 protons (C-14 then follows as the last unassigned quaternary carbon).

The adjacent olefinic carbons C-11 and C-12 cannot be distinguished from each other by COSY or HMBC relations. The overall connectivity of the basic structure is, however, completely supported by all observed COSY- and HMBC-relations.

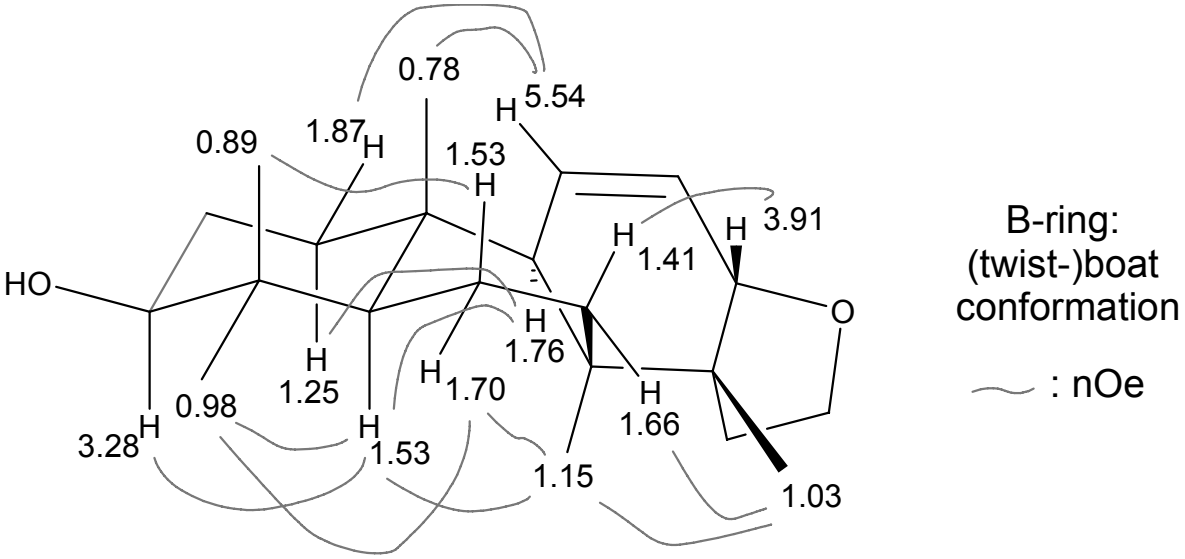


From the splitting pattern of the C-3 proton (indicating axial dispostion), an equatorial hydroxylgroup is assured. Similarly, the C-1 proton at 1.87 ppm clearly adopts an equatorial position, so its geminal partner at 1.25 ppm has an axial position. This is further supported by nOe-correlation of the 1,3-diaxial protons at C-3 and C-1. Two furher diagnostic nOe-relations of the C-3 proton show the axial position of the C-5 proton and the equatorial position of the 0.98 ppm methyl group (C-28). The now distinguished 0.89 ppm axial methyl group (C-29) shows a clear nOe-relation with the C-19 methyl group, indicating 1,3-syn-diaxial disposition.



The splitting pattern of the olefinic and allylic protons on the C-ring imply near perpendicular torsion angles for the corresponding C-H bonds. The olefinic protons can be unambiguously assigned by various nOe-relations. The nOe-relation between the C-7 proton and the C-8[1] methyl group can only be explained by a *cis*-fusion to the B-ring. Similarly, the C-13 proton and C-30 methyl nOe-relation reveals the *cis*-fusion to the D-ring. The clear nOe-relation of the vicinal methyl groups C-8[1] and C-30 shows the specific half-chair conformation of the C-ring, with the methyl susbstituents in a (pseudo-)equatorial position. This conformation is

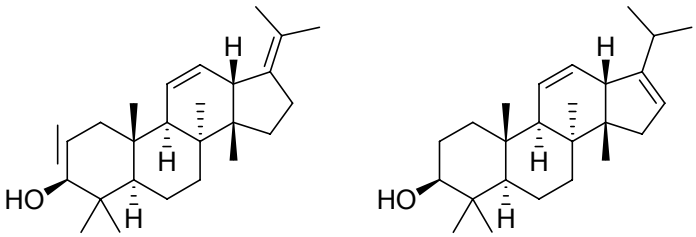
further supported by all observed nOe-relations, for instance between (pseudo-)axial methylene ring residues and the (pseudo-)axial allylic protons.



The *anti*-configuration of the C-7 proton and C-19 methyl on the B-ring is indicated by the absence of a nOe-relation between these nicely resolved signals. It is unambiguously determined by the nOe-relations between the olefinic C-11 proton and both the C-19 methyl group and the 1.87 ppm C-1 equatorial (β) proton. Also the nOe-relation between the C-1 axial (α) proton and the C-7 proton clearly supports this configuration. A relaxed chair configuration of the B-ring is clearly incompatible with the unambiguously determined chair and half-chair conformations of the A- and C-ring. Alternatively, a (twist-)boat like conformation can be postulated, which is in strong agreement with all observed nOe-relations. Although the C-5 proton and the C-10 β-proton are not resolved (1.53 ppm), the nOe-relations of the 1.53 ppm resonance can be unambiguously attributed to one or the other candidate: the nOe-relation of the 1.70 ppm C-10 α-proton with the C-8^1 methyl group, excludes the possibility of a nOe-relation of its geminal partner to the C-8^1 methyl group. In this way, the very diagnostic nOe-relation between the C-5 proton and the C-8^1 methyl group is confirmed (such a close proximity is only possible in a boat or twist-boat conformation). All other nOe-relations further support the derived configuration and conformation.

Cyclisation of the Epoxy Polyene 5' – The (9α,13β)-Δ17,20-Protolanostane Alcohols (21a and 21b). The epoxy polyene **5'** (121.5 mg, 0.341 mmol) was cyclised using the same procedure as described for the cyclisation of epoxy polyenol **16** to tetracyclic alcohol **20**. Purification using HPLC, eluting with 6% acetone in *iso*-octane, gave three major fractions: the first containing monocyclised bridged A-ring ether **17b** (36 mg, 30%), R_f 0.75 (*iso*-octane/acetone 9/1); IR (film) ν_{max}/cm^{-1} 3027, 2964, 2916, 2871, 1470, 1464, 1435, 1380, 1364, 1191, 1109, 1005; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80-5.74 (2H, band), 5.402 (1H, d(br), *J* = 9.2 Hz) , 5.395 (1H, d(br), *J* = 9.1 Hz), 5.06 (1H, t(br), *J* = 7.1 Hz), 3.68 (1H, d, *J* = 5.3 Hz), 1.94-1.85 (3H, band), 1.78-1.60 (4H, band), 1.66 (3H, s(br)), 1.57 (3H, s(br)), 1.50-1.38 (2H, band), 1.35-1.28 (1H, m), 1.29 (3H, s), 1.20 (1H, dddd, *J* = 12.5, 12.5, 9.5, 4.2 Hz), 1.08-1.03 (2H, band), 1.01 (3H, s), 0.934 (3H, s), 0.928 (3H, s), 0.924 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.1 (2CH), 130.8 (C), 125.4 (CH), 121.74 (CH), 121.71 (CH), 86.7 (C), 86.0 (CH), 56.8 (CH), 45.2 (C), 39.9 (C), 39.7 (C), 38.9 (CH_2), 34.4 (CH_2), 33.9 (CH_2), 26.1 (CH_3), 25.6 (CH_2), 25.5 (CH_3), 23.4 (CH_2), 23.2 (CH_3), 22.7 (CH_2), 18.8 (CH_3), 18.5 (CH_3), 18.3 (CH_3), 17.5 (CH_3); EI-MS *m/z* 356 (M^+, 11%), 341 (2), 339 (2), 327 (1), 313 (19), 287 (2), 274 (14), 259 (2), 255 (3), 229 (4), 216 (5), 201 (6), 189 (11), 187 (11), 173 (11), 159 (18), 148 (27), 133 (22), 119 (95), 107 (33), 105 (33), 91 (35), 83 (75), 69 (44), 55 (100), 43 (77), 41 (80); second, a rearranged A-ring ketonic compound **18b** (29 mg, 24%), R_f 0.63 (*iso*-octane/acetone 9/1); IR (film) ν_{max}/cm^{-1} 3053, 3027, 2966, 2919, 2876, 1714 (C=O), 1455, 1379, 1296, 1192, 1114, 1069, 1015; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80-5.77 (2H, band), 5.41-5.37 (2H, band), 5.05 (1H, t(br), *J* = 7.1 Hz), 2.40 (1H, q(br), *J* = 6.7 Hz), 2.33-2.29 (2H, band), 1.98-1.87 (3H, band), 1.84-1.74 (2H, band), 1.72-1.64 (2H, band), 1.66 (3H, s(br)), 1.62-1.55 (1H, m), 1.57 (3H, s(br)), 1.31 (1H, ddd, *J* = 2 × ±13.7, 4.3 Hz), 1.19 (1H, ddd, *J* = 2 × ±13.8, 3.7 Hz), 1.08-1.00 (1H, band), 0.97 (3H, s), 0.95 (3H, s), 0.845 (3H, d, *J* = 6.8 Hz), 0.81 (3H, d, *J* = 6.7 Hz), 0.54 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.2 (C=O), 136.3 (CH), 136.2 (CH), 130.9 (C), 125.4 (CH), 122.0 (CH), 121.9 (CH), 50.4 (CH), 43.4 (C), 41.4 (CH_2), 40.1 (C), 39.3 (C), 35.8 (CH), 34.4 (CH_2), 31.6 (CH_2), 30.9 (CH_2), 25.7 (CH_2), 25.5 (CH_3), 23.6 (CH_2), 18.7 (CH_3), 18.4 (CH_3), 17.5 (CH_3), 15.5 (CH_3), 14.8 (CH_3), 7.2 (CH_3); EI-MS *m/z* 356 (M^+, 8%), 313 (20), 274 (13), 255 (6), 227 (1), 217 (2), 189 (8), 187 (8), 173 (6), 159 (13), 148 (23), 139 (95), 119 (93), 105 (28), 91 (32), 83 (65), 69 (40), 55 (100), 43 (28), 41 (65); and third, a fraction with the inseparable tetracyclic compounds **21a** and **b** as a white solid (25 mg, 21%), R_f 0.24 (*iso*-octane/acetone 9/1); IR (neat) ν_{max}/cm^{-1} 3260 (O-H), 3027, 2946, 2875, 1466, 1447, 1386, 1365, 1091, 1039; ^{1}H NMR (**21a**, 500 MHz, $CDCl_3$) δ 5.43 (1H, ddd, J = 10.2, 3.6, 2.7 Hz), 5.26 (1H, ddd, J = 10.2, 1.6, 1.6 Hz), 3.27 (1H, dd(br), J = 10.8, 4.9 Hz, C*H*-OH), 2.69 (1H, s(br)), 2.18 (1H, m), 2.12 (1H, m), 1.85 (1H, ddd, J = 13.1, 3.4, 3.4 Hz), 1.80 (1H, d(br), J = 12.1 Hz), 1.69 (3H, s), 1.69 (1H, s), 1.66 (1H, m), 1.61-1.46 (6H, band), 1.58 (3H, s), 1.31 (1H, dd, J = 12.1, 8.5 Hz), 1.22 (1H, ddd, J = 12.5, 12.5, 4.3 Hz), 1.07 (3H, s), 0.98 (3H, s), 0.90 (3H, s), 0.81 (3H, s), 0.77 (3H, s); ^{13}C NMR (**21a**, 125 MHz, $CDCl_3$) δ 139.6 (C), 128.9 (CH), 128.5 (CH), 121.0 (C), 79.5 (CH-OH), 55.2 (CH), 48.3 (C), 46.9 (CH), 45.2 (CH), 41.1 (CH_2), 39.6 (C), 38.5 (C), 36.6 (C), 32.4 (CH_2), 27.8 (CH_3), 27.6 (CH_2), 26.14 (CH_2), 26.13 (CH_2), 25.7 (CH_3), 20.9 (CH_3), 20.72 (CH_3), 20.65 (CH_2), 17.9 (CH_3), 17.8 (CH_2), 15.4 (CH_3); ^{1}H NMR (resolved signals for **21b**, integrating for 15%, 500 MHz, $CDCl_3$) δ 5.41 (2H, m), 5.12 (1H, ddd, J = 3.0, 1.5, 1.5 Hz), 2.46 (1H, s), 2.36 (1H, d, J = 15 Hz), 2.32 (1H, m), 1.80 (1H, m), 1.77 (1H, m), 1.11 (1H, d, J = 5.4 Hz), 1.07 (3H, d, J = 6.8 Hz), 1.06 (3H, s), 1.02 (3H, d, J = 6.8 Hz), 0.97 (3H, s), 0.91 (3H, s), 0.88 (3H, s), 0.80 (3H, s); ^{13}C NMR (resolved signals for **21b**, APT, 125 MHz, $CDCl_3$) δ 126.2 (CH), 124.3 (CH), 118.8 (CH), 55.5 (CH), 53.1 (CH_2), 49.7 (CH), 47.3 (CH_2), 41.3 (CH_2), 41.0 (CH_2), 39.5

(CH_2), 30.1 (CH_3), 28.1 (CH), 27.9 (CH_3), 25.5 (CH_3), 21.4 (CH_3), 21.0 (CH_3), 17.7 (CH_3), 15.4 (CH_3); EI-MS *m/z* 356 (M^+, 41%), 341 (3), 338 (3), 323 (3), 313 (20), 295 (6), 255 (1), 233 (2), 219 (6), 203 (15), 189 (44), 173 (57), 159 (30), 145 (37), 133 (45), 131 (44), 119 (51), 107 (35), 105 (45), 91 (54), 79 (41), 67 (52), 57 (30), 55 (56), 43 (100), 41 (84). Besides, minor fractions of mixtures of structures of the cyclohexenolic type (**19b**) (10 mg, 8% and 4.5 mg, 4%) were isolated. Furthermore, a very small but relatively pure fraction was shown to contain the unexpected spirocyclic compound **22**, R_f 0.43 (*iso*-octane/acetone 9/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 (1H, ddd, J = 10.0, 4.7, 2.8 Hz), 5.17 (1H, ddd, J = 10.0, 2.0, 2.0 Hz, 3.41 (1H, s), 2.69 (1H, s), 2.27 (1H, s), 2.18 (1H, m(AB)), 2.12 (1H, m(AB)), 1.96-1.89 (2H, band), 1.86 (1H, ddd, J = 13.0, 5.0, 2.0 Hz), 1.75 (1H, dd, J = 11.0, 11.0 Hz), 1.71 (1H, dd, J = 13.0, 6.6 Hz), 1.67 (3H, s), 1.65 (1H, m), 1.59 (3H, s), 1.58 (1H, m), 1.51 (1H, m), 1.38 (1H, dd, J = 12.0, 8.5 Hz), 1.33 (1H, m), 1.29 (1H, dd, J = 12.0, 6.5 Hz), 1.14 (3H, s), 1.01 (3H, s), 0.99 (3H, s), 0.86 (3H, d, J = 6.6 Hz), 0.83 (3H, s); ^{13}C NMR (APT, 125 MHz, $CDCl_3$) δ 139.4 (C), 130.7 (CH), 128.7 (CH), 121.4 (C), 78.8 (CH), 55.0 (C), 50.7 (CH), 46.7 (CH), 44.1 (C), 41.9 (C), 39.3 (CH_2), 33.4 (CH_2), 32.5 (CH), 28.6 (CH_2), 27.7 (CH_2), 26.8 (CH_2), 26.6 (CH_2), 25.4 (CH_3), 24.3 (CH_3), 24.2 (CH_3), 20.9 (CH_3), 20.81 (CH_3), 20.79 (CH_3), 20.7 (CH_3). EI-MS *m/z* 356 (M^+, 28%), 338 (M^+ - H_2O, 3), 313 (10), 189 (55), 173 (50), 149 (33), 119 (50), 105 (45), 91 (55), 67 (40), 55 (60), 43 (100), 41 (80). Finally, a small - very apolar - complex fraction contained dehydrated products (6%) and some very small complex fractions (2.5% total) remained uncharacterised.



Characterisation via analysis of 2D-NMR data for the tetracyclic alcohols (26a and 26b)

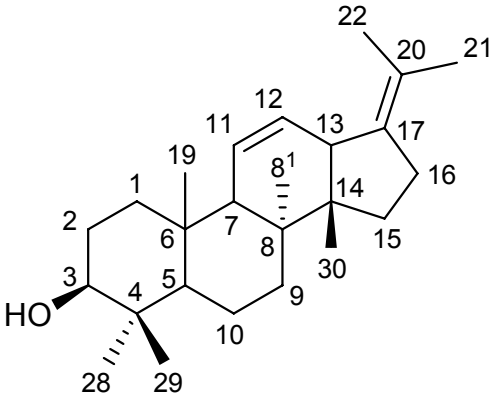
^{1}H-NMR + HSQC + COSY + NOESY (500 MHz, $CDCl_3$):

δ	int.	mult.	*J* (Hz)	HSQC	COSY	NOESY
5.43	1H	ddd	10.2, 3.6, 2.7	128.9	5.26, 2.69, 1.69	1.85, 1.69, 0.805
5.26	1H	ddd	10.2, 2 × ±1.6	128.5	5.43, 2.69, 1.69	2.69, 1.69
3.27	1H	dd(br)	10.8, 4.9	79.5	1.59(band)	1.59, 1.22, 0.975
2.69	1H	s(br)		46.9	5.43, 5.26, 2.12, 1.69, 1.58(s), 1.31	5.26, 1.69, 1.48, 0.77
2.18	1H	m(AB)		26.13	2.12, 1.80, 1.69, 1.58(s), 1.31	1.31, 0.77
2.12	1H	m(AB)		26.13	2.69, 2.18, 1.80, 1.69, 1.58(s), 1.31	1.80
1.85	1H	ddd	13.1, 2 × ±3.4	41.1	1.60-1.53, 1.31, 1.22	5.43, 1.58, 1.22, 0.805
1.80	1H	d(br)	12.1	32.4	2.18, 2.12, 1.31, 0.77	1.69, 1.31, 1.07
1.69	3H	s(br)		20.9	? ↓ 5.43, 5.26, 2.69, 2.18, 2.12, 1.85, 1.60-1.53, 1.48	? ↓ 1.80, 1.07
1.69	1H	s(br)		55.2	? ↑	? ↑
1.66	1H	m		17.8	1.60-1.53	0.975
1.59	2H	band		27.6	3.27	
1.58	1H	band		45.2	? ↓ 2.69, 2.18, 2.12	? ↓ 1.85
1.58	3H	s(br)		20.65	? ↑	? ↑
1.57	1H	band		26.14		
1.55	1H	band		17.8		0.895
1.48	1H	band		26.14	1.69, 1.60-1.53	2.69
1.31	1H	dd(br)	12.1, 8.5	32.4	2.69, 2.18, 2.12, 1.80	2.12, 1.80, 0.77
1.22	1H	ddd	2 × ±12.5, 4.3	41.1	1.85, 1.60-1.53, 0.805	3.27, 1.69, 1.85
1.07	3H	s		25.7	1.48	
0.975	3H	s		27.8		
0.895	3H	s		15.4		1.55
0.805	3H	s		17.9	1.22, 1.60-1.53	5.43, 1.85

0.770	3H	s		20.7	1.80	2.69, 2.18, 1.31

APT + HSQC + HMBC (500 MHz, $CDCl_3$):

assignment	δ	type	HSQC	HMBC
C-17	139.6	C	-	5.26, 2.69, 2.18, 2.12, 1.69, 1.58, 1.31
C-11	128.9	CH	5.43	5.26, 1.07
C-12	128.5	CH	5.26	5.43, 2.69, 1.69, 0.77
C-20	121.0	C	-	2.18, 1.69, 1.58
C-3	79.5	CH	3.27	1.85, 1.60-1.53, 1.22, 0.975, 0.895
C-7	55.2	CH	1.69	5.43, 5.26, 1.60-1.53, 1.22, 1.07, 0.805
C-14	48.3	C	-	1.80, 1.07
C-13	46.9	CH	2.69	5.43, 5.26, 1.31
C-5	45.2	CH	1.58	1.85, 1.69, 1.60-1.53, 1.48, 0.975, 0.895, 0.805
C-1	41.1	CH_2	1.85, 1.22	0.805
C-4	39.6	C	-	3.27, 1.66, 1.60-1.53, 0.975, 0.895
C-8	38.5	C	-	1.85, 1.66, 1.55, 1.22, 0.805
C-6	36.6	C	-	1.80, 1.66, 1.55, 1.07, 0.77
C-15	32.4	CH_2	1.80, 1.31	2.69, 2.18, 0.77
C-28	27.8	CH_2	0.975	3.27, 0.895
C-2	27.6	CH_2	1.59	1.85, 1.22
C-9	26.14	CH_2	1.57, 1.48	? ↓
				2.69, 1.80, 1.69, 1.31, 1.07
C-16	26.13	CH_2	2.18, 2.12	? ↑
C-8[1]	25.7	CH_3	1.07	1.60-1.55, 1.48
C-22	20.9	CH_3	1.69	1.58
C-30	20.72	CH_3	0.770	? ↓
				2.69, 1.69, 1.31
C-21	20.65	CH_3	1.58	? ↑
C-19	17.9	CH_3	0.805	? ↓
				1.85, 1.60-1.53, 1.22
C-10	17.8	CH_2	1.66, 1.55	? ↑
C-29	15.4	CH_3	0.895	3.27, 1.60-1.53, 0.975



From the 1D proton and carbon (APT) NMR spectra, together with the HSQC 2D spectrum, 4 carbon atoms can be assigned unequivocally by their distinctive chemical shift values and ^{1}H-splitting patterns: C-3, C-7, C-13 and C-16. By exclusion, the remaining 1.58 ppm CH-type proton can then be assigned to C-5. Furthermore, the resonances at 5.43 and 5.26 ppm clearly correspond to the C-11 and C-12 protons. The two methyl groups at relatively high chemical shift values (1.69 and 1.58 ppm) correspond to the geminal pair on the tetrasubstitited olefin (C-21 and C-22).

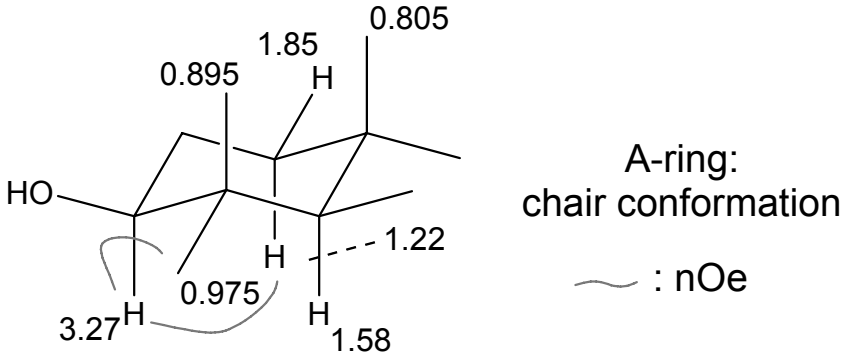
The analyses are somewhat complicated by two overlaps in the proton spectrum: at 1.69 ppm the signal of a methyl group overlaps that of the C-7 proton, and at 1.58 ppm the C-5 proton is overlapped by the other methyl group. In the HMBC-spectrum, some ^{13}C resonances are too close to be discerned.

Starting from C-3: C-2 is readily determined by proton COSY-correlations and the next methylene group C-1 (41.1 ppm) follows from HMBC-correlations, as do the geminal methyl groups C-28 and C-29 (no relative assignment at this stage). Also the C-4 and C-6 quaternary carbons and the C-19 methyl group can be distinguished in this manner. By COSY-and HMBC-relations from C-5, the assignment of the C-10 and C-9 methylene groups follows and that of C-7 is reassured.

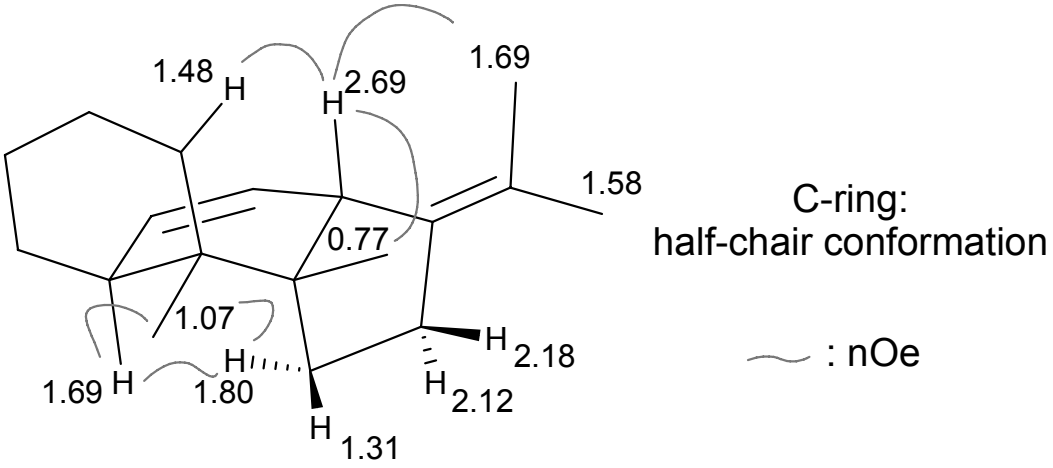
Starting from C-16: C-15 (32.4 ppm) is defined by COSY-correlation of the attached protons. The C-22, C-21 and C-13 protons show long range scalar coupling over the C-17,C-20 olefinic bond. The C-17 and C-20 quaternary carbons are clearly defined by HMBC relations to the protons of C-13 and C-15. The C-30 methyl group is recognized by its HMBC relation to C-15 and by a long-range W-type scalar coupling to a C-15 proton (1.80 ppm).

The assignment of the last C-8^{1} methyl group is now evident by the exclusion principle. The quaternary carbon C-8 is determined by HMBC-relation with the C-10 protons, which leaves C-14 as the last unassigned quaternary carbon (48.3 ppm).

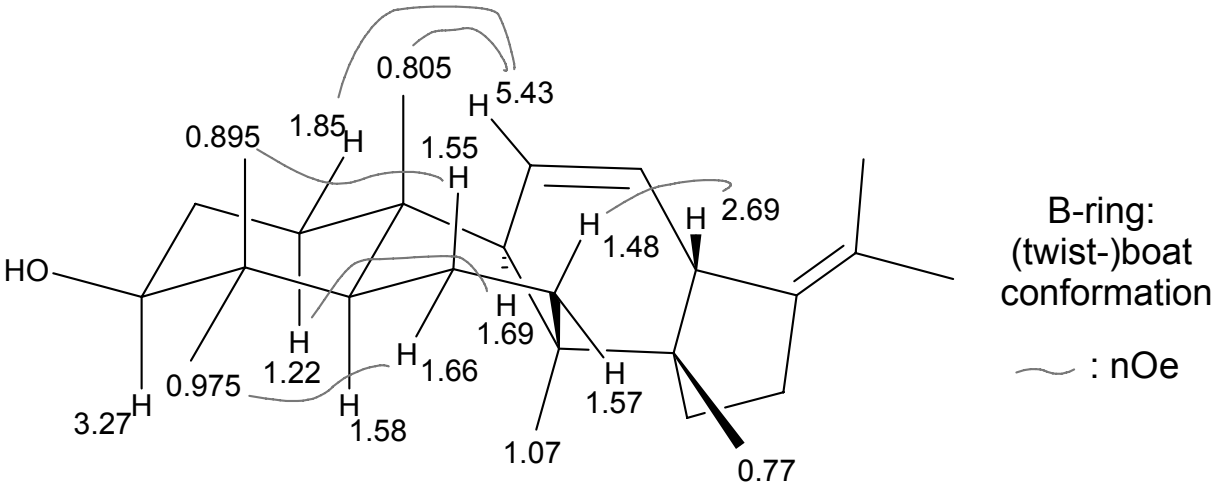
The adjacent olefinic carbons C-11 and C-12 cannot be distinguished from each other by COSY or HMBC relations, as is the case for the geminal C-21,C-22 and C-28,C-29 methyl groups. The overall connectivity of the basic structure is, however, completely supported by all observed COSY- and HMBC-relations.



From the splitting pattern of the C-3 proton (indicating axial dispostion), an equatorial hydroxylgroup is assured. Similarly, the C-1 proton at 1.85 ppm clearly adopts an equatorial position (just one large scalar coupling) and its geminal partner at 1.22 ppm has an axial position (two large scalar couplings). This is further supported by nOe-correlation of the 1,3-diaxial protons at C-3 and C-1. The similarities of the ^{1}H and ^{13}C chemical shift values with those determined for the A-ring of compound **20** is striking. This observation compensates for the lack of clear nOe-correlations (obtained NOESY spectrum quality is poor).



The olefinic C-11 and C-12 protons can be unambiguously assigned by various nOe-relations. The nOe-relation between the C-7 proton and the C-8^{1} methyl group can only be explained by a *cis*-fusion to the B-ring. Similarly, the C-13 proton and C-30 methyl nOe-relation reveals the *cis*-fusion to the D-ring. The expected nOe-relation of the vicinal methyl groups C-8^{1} and C-30 cannot be discerned in the 2D NOESY data, but the half-chair conformation of the C-ring is clearly supported by all observed nOe-relations, for instance between (pseudo-)axial methylene ring residues and the (pseudo-)axial allylic protons.



The *anti*-configuration of the C-7 proton and C-19 methyl group is assured by various nOe-relations. The overall (twist-)boat conformation of the B-ring is supported by all nOe-relations that can be discerned.

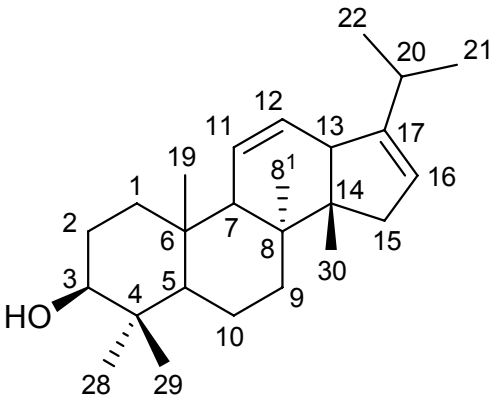
Due to the presence of the isomer **21b**, the observed HMBC, COSY or NOESY relations could in some cases be arising from underlying signals of this compound. Any ambiguity concerning the overall conformation of the tetracyclic structure **21a** is, however, compensated by virtue of similarity of the chemical shift values to those of the very unambiguously conformationally determined compound **20**.

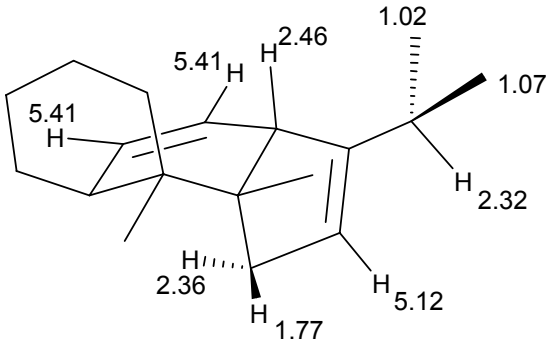
Next to these major signals, the following minor signals (integrating for 15%) are discerned in the NMR spectra, corresponding to the isomer **21b**. Any other signals are probably overlapped by those of the major isomer:
^{13}C NMR (APT, 125 MHz, $CDCl_3$) δ 126.2 (CH), 124.3 (CH), 118.8 (CH), 55.5 (CH), 53.1 (CH_2), 49.7 (CH), 47.3 (CH_2), 41.3 (CH_2), 41.0 (CH_2), 39.5 (CH_2), 30.1 (CH_3), 28.1 (CH), 27.9 (CH_3), 25.5 (CH_3), 21.4 (CH_3), 21.0 (CH_3), 17.7 (CH_3), 15.4 (CH_3).

^{1}H NMR + HSQC + COSY + NOESY (500 MHz, $CDCl_3$):

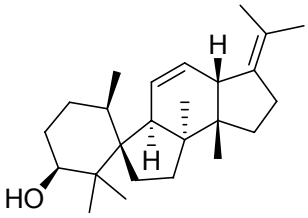
δ	int.	mult.	*J* (Hz)	HSQC	COSY	NOESY	assignment
5.41	2H	m(AB)		126.2, 124.3	2.46	2.46	C-11, C-12
5.12	1H	ddd	3.0, 2 × ±1.5	118.8	2.36, 1.77	2.32, 1.07, 1.02	C-16
2.46	1H	s(br)		49.7	5.41, 1.77	5.41, 1.02	C-13
2.36	1H	d(br)	15	41.3	5.12, 1.77		C-15
2.32	1H	m		28.1	1.07, 1.02	5.12	C-20
1.80	1H	m		55.5			C-7
1.77	1H	m		41.3	5.12, 2.36	5.12	C-15
1.11	1H	d	5.4	53.1			
1.07	3H	d	6.8	21.0	2.32	5.12	C-21

1.06	3H	s		?			
1.02	3H	d	6.8	21.4	2.32	5.12, 2.46	C-22
0.965	3H	s		30.1			
0.910	3H	s		?			
0.880	3H	s		?			
0.795	3H	s		?			





All discernible signals can be assigned to the differing D-ring part of the proposed structure. Assignment and connectivity of C-11, C-12, C-13, C-15, C-16, C-20, C-21 and C-22 is based on COSY-relations of the attached protons. Assignment of the complete structure is solely based on its likelihood by similarity with the major isomer.



Characterisation via analysis of 2D-NMR data for the spirocyclic tetracycle (22)

^{1}H-NMR + HSQC + COSY + NOESY (500 MHz, $CDCl_3$):

δ	int.	mult.	*J* (Hz)	HSQC	COSY	NOESY
5.68	1H	ddd	10, 4.7, 2.8	130.7	5.17, 2.69, 2.27	1.94
5.17	1H	ddd	10, 2 × ±2	128.7	5.68, 2.69, 2.27	
3.41	1H	s(br)		78.8	1.86, 1.51, 1.33	0.99
2.69	1H	s(br)		46.7	5.68, 5.17, 2.27, 2.12, 1.59, 1.38	0.86
2.27	1H	s(br)		50.7	5.68, 5.17, 2.69	1.14, 1.01
2.18	1H	m(AB)		26.6	1.73, 1.67, 1.38	
2.12	1H	m(AB)		26.6	2.69, 1.75, 1.67, 1.38	
1.94	1H	band		32.5	1.58, 0.86	5.68
1.91	1H	band		26.8	1.65, 1.29	
1.86	1H	ddd	13(AB), 5, 2	28.6	3.41, 1.51	
1.75	1H	dd(br)	2 × ±11	33.4	2.18, 2.12, 1.38, 0.83	

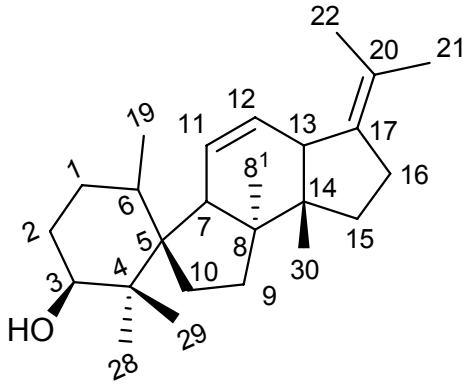
1.71	1H	dd(br)	13, 6.6	39.3	1.29	
1.67	3H	s(br)		20.8	2.18, 2.12, 1.29	
1.65	1H	m		26.8	1.91	
1.59	3H	s(br)		20.7	2.69	
1.58	1H	band		27.7	1.94, 1.33	
1.51	1H	band		28.6	1.86, 1.58(?)	
1.38	1H	dd(br)	12, 8.5	33.4	2.18, 2.12, 1.75, 1.51(?)	
1.33	1H	band		27.7	1.58	
1.29	1H	dd	12, 6.5	39.3	1.91, 1.71	
1.14	3H	s		24.2		2.27
1.01	3H	s		25.4		2.27
0.99	3H	s		24.3		3.41
0.86	3H	d	6.6	20.8	1.94	2.69
0.83	3H	s		20.9	1.75	

APT + HSQC + HMBC (500 MHz, $CDCl_3$):

Assignment	δ	type	HSQC	HMBC
C-17	139.4	C	-	1.67, 1.59
C-11	130.7	CH	5.68	1.01
C-12	128.7	CH	5.17	0.83
C-20	121.4	C	-	1.67, 1.59
C-3	78.8	CH	3.41	1.14, 0.99
C-5	55.0	C	-	1.91, 1.29, 1.14, 0.99, 0.86
C-7	50.7	CH	2.27	1.65, 1.01
C-13	46.7	CH	2.69	5.68, 0.83
C-8 or C-14	44.1	C	-	5.68, 1.01, 0.83
C-4	41.9	C	-	1.14, 0.99
C-9	39.3	CH_2	1.71, 1.29	1.91, 1.01
C-15	33.4	CH_2	1.75, 1.38	0.83
C-6	32.5	CH	1.94	1.91, 1.65, 0.86
C-2	28.6	CH_2	1.86, 1.51	
C-1	27.7	CH_2	1.58, 1.33	
C-10	26.8	CH_2	1.91, 1.65	
C-16	26.6	CH_2	2.18, 2.12	

C-8[1]	25.4	CH_3	1.01	
C-29	24.3	CH_3	0.99	1.14
C-28	24.2	CH_3	1.14	0.99
C-30	20.9	CH_3	0.83	
C-22, C-19	20.8	$2CH_3$	1.67, 0.86	1.59
C-21	20.7	CH_3	1.59	1.67

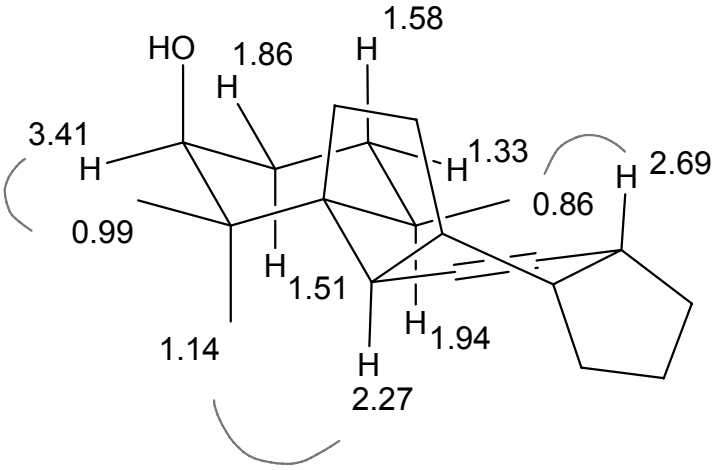
Although the spectra do show some impurities, the main connectivity and even the configuration of the main constituent can be determined from the analysis of the different spectra.



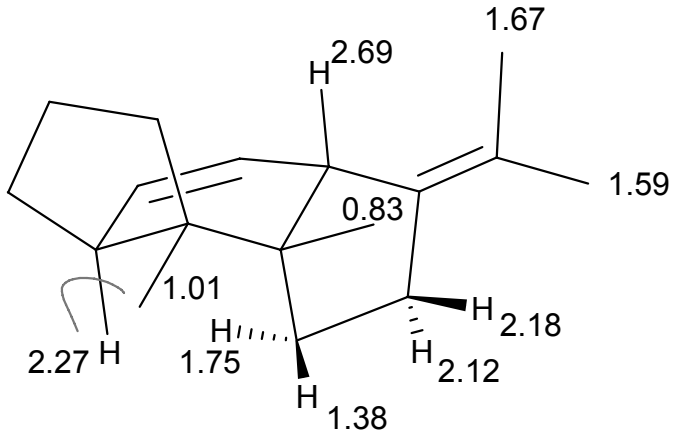
Starting from the readily assignable C-3 (78.8 ppm), the rest of the A-ring can be assembled through COSY and HMBC relations. Its COSY-partners at C-2 (1.86 and 1.51 ppm) and C-1 (1.33 ppm, via a W-type long range coupling) lead the way to C-6 as a methyl (C-19) bearing CH group. From this isolated spin system, various HMBC relations let us determine the quaternary carbons C-4 and C-5 and the geminal methyl groups C-28 and C-29 (however, these last two cannot be unambiguously distinguished from each other).

Starting from the also readily assignable C-13 proton (2.69 ppm), COSY relations indicate the C-11,C-12-pair, as well as the C-7 proton and the C-16 methylene group. From C-16 and C-13: C-15, C-21 and C-22 are quickly identified via COSY correlations. The olefinic qauternary carbons C-17 and C-20 are revealed by their HMBC relations. Only one of the C-ring quaternary centers is discernible in the ^{13}C NMR spectrum. The C-8[1] and C-30 methyl group are identified by exclusion (1.01 and 0.83 ppm), from which C-30 is discernible via W-type long range coupling to a C-15 proton (COSY) ánd via HMBC-relation to C-13. The remaining methylene groups C-9 and C-10 show COSY relations only to each other. C-9 can be distinguished via HMBC-relation to the C-8[1] methyl protons, and C-10 is identified by HMBC-relations of its protons to C-6.

The crucial identification of C-5 as a spirocyclic point of fusion is in accord with its HMBC relations to the protons of C-28, C-29, C-19, C-10 and C-9.



For the configuration and conformation of the A-ring, the C-3 proton (3.41 ppm) clearly shows an equatorial position, as no large scalar coupling is present. Also the 1.86 ppm proton is equatorial, as it has only one large coupling. The 1.33 ppm proton is also equatorial, as indicated by the long range coupling to C-3. The equatorial position of the C-19 methyl group is supported by the very diagnostic nOe-relation to the C-13 proton, which also strongly supports the spiro-configuration, as does the nOe-relation between the C-28 methyl protons and the C-7 proton.

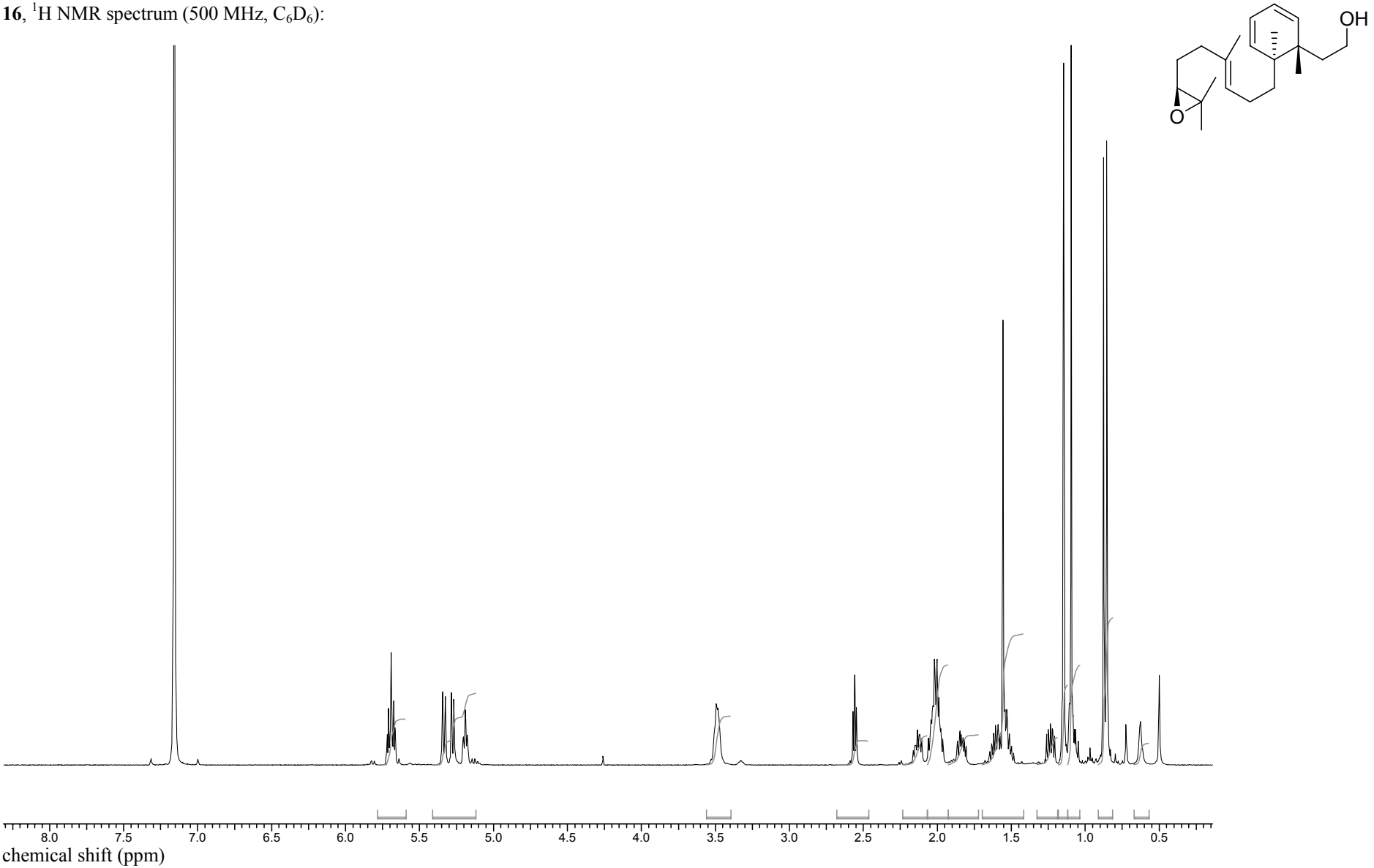


For the C-ring area, the B-C *cis*-fusion is indicated by a nOe relation. Other expected nOe-relations are not observed in the NOESY spectrum, but the overall configuration and conformation is strongly supported by similarity to data obtained for the tetracyclic compound **21a**.

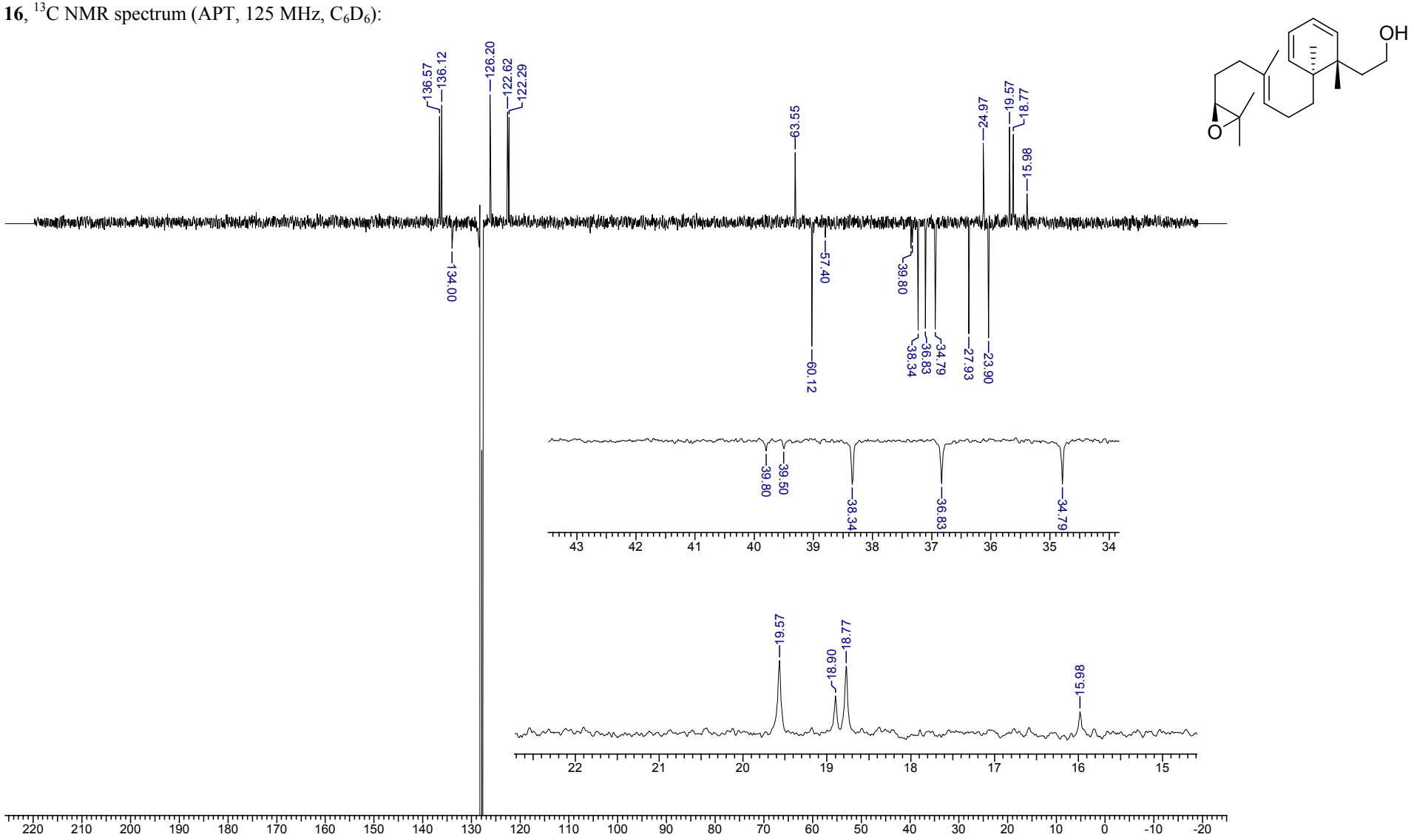
Cyclisation of the Epoxy Polyene *ent*-4'. Epoxy polyene ***ent*-4'** (81 mg, 0.227 mmol) was subjected to the same procedure as epoxy polyene **5'** (*vide supra*). Upon purification by HPLC, eluting with 6% acetone in *iso*-octane, two major fractions were collected which showed compounds of the previously obtained monocyclised type: the bridged A-ring ether (32.5 mg, 40%), R_f 0.75 (*iso*-octane/acetone 9/1); IR (film) ν_{max}/cm^{-1} 3026, 2963, 2920, 2871, 1462, 1380, 1363, 1193, 1109, 1004; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80-5.75 (2H, band), 5.42-5.39 (2H, band), 5.06 (1H, t(br), *J* = 7.1 Hz), 3.69 (1H, d, *J* = 5.3 Hz), 1.95-1.86 (3H, band), 1.76-1.60 (4H, band), 1.66 (3H, s(br)), 1.57 (3H, s(br)), 1.47 (1H, ddd, *J* = 11.5(AB), 9.1, 4.6 Hz), 1.40 (1H, ddd, *J* = 12.0, 11.5(AB), 4.5 Hz), 1.28-1.23 (1H, m), 1.27 (3H, s), 1.08-1.00 (3H, band), 1.02 (3H, s), 0.98 (3H, s), 0.935 (3H, s(br)), 0.931 (3H, s(br)); ^{13}C NMR (APT, 125 MHz, $CDCl_3$) δ 136.2 (CH), 136.1 (CH), 130.8 (C), 125.4 (CH), 121.7 (2CH),

86.8 (C), 85.9 (CH), 56.6 (CH), 45.2 (C), 40.0 (C), 39.7 (C), 38.9 (CH_2), 34.5 (CH_2), 34.0 (CH_2), 26.1 (CH_3), 25.6 (CH_2), 25.5 (CH_3), 23.5 (CH_2), 23.3 (CH_3), 22.6 (CH_2), 18.8 (CH_3), 18.5 (CH_3), 18.3 (CH_3), 17.5 (CH_3). EI-MS *m/z* 356 (M^+, 11%), 341 (2), 313 (18), 287 (2), 274 (11), 255 (4), 229 (4), 216 (5), 203 (6), 201 (6), 189 (11), 187 (11), 173 (10), 159 (17), 148 (30), 133 (21), 119 (95), 107 (32), 105 (32), 91 (35), 83 (66), 69 (41), 67 (33), 55 (100), 43 (78), 41 (80); and the rearranged A-ring ketone (25.5 mg, 32%), R_f 0.61 (*iso*-octane/acetone 9/1); IR (film) ν_{max}/cm^{-1} 3027, 2966, 2916, 2872, 1713 (C=O), 1449, 1378, 1193, 1115, 1015; ^1H NMR (500 MHz, $CDCl_3$) δ 5.83-5.78 (2H, band), 5.43-5.37 (2H, band), 5.06 (1H, t(br), *J* = 7.1 Hz), 2.42 (1H, q(br), *J* = 6.7 Hz), 2.33-2.30 (2H, band), 1.96-1.85 (4H, band), 1.85-1.74 (2H, band), 1.66 (3H, s(br)), 1.63-1.55 (2H, band), 1.57 (3H, s(br)), 1.27-1.23 (2H, band), 1.05 (1H, ddd, *J* = 12.8, 11.3, 5.3 Hz), 3.08 (3H, s), 0.94 (3H, s), 0.88 (3H, d, *J* = 6.7 Hz), 0.79 (3H, d, *J* = 6.8 Hz), 0.55 (3H, s); ^{13}C NMR (APT, 125 MHz, $CDCl_3$) δ 214.2 (C), 136.4 (CH), 136.2 (CH), 130.9 (C), 125.4 (CH), 122.0 (CH), 121.9 (CH), 50.2 (CH), 43.4 (C), 41.4 (CH_2), 40.1 (C), 39.4 (C), 35.9 (CH), 34.5 (CH_2), 31.6 (CH_2), 30.8 (CH_2), 25.8 (CH_2), 25.5 (CH_3), 23.6 (CH_2), 18.7 (CH_3), 18.4 (CH_3), 17.5 (CH_3), 15.5 (CH_3), 14.7 (CH_3), 7.35 (CH_3); EI-MS *m/z* 356 (M^+, 8%), 339 (1), 313 (17), 274 (6), 255 (5), 227 (2), 189 (7), 159 (10), 148 (18), 139 (79), 119 (79), 107 (20), 105 (21), 83 (50), 69 (44), 55 (100), 43 (25), 41 (70). Next to a small apolar fraction (5%) and some minor complex fractions (total of 6%), three small fractions of low purity are collected: a possibly polycyclic fraction (3.4 mg, 4%), as judged by the absence of the characteristic resonances for the conjugated diene system in the proton NMR spectrum, which also shows many impurities. Another polycyclic fraction (1.7 mg, 2%) was less impure but its structure could not be determined due to insufficient amounts of material. A final fraction contained A-ring cyclohexenolic structures (cf. **19b**) **(**1.3 mg, 2%).

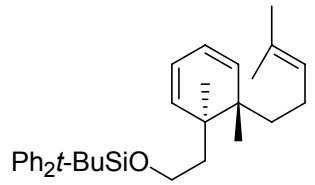
16, ^{1}H NMR spectrum (500 MHz, C_6D_6):

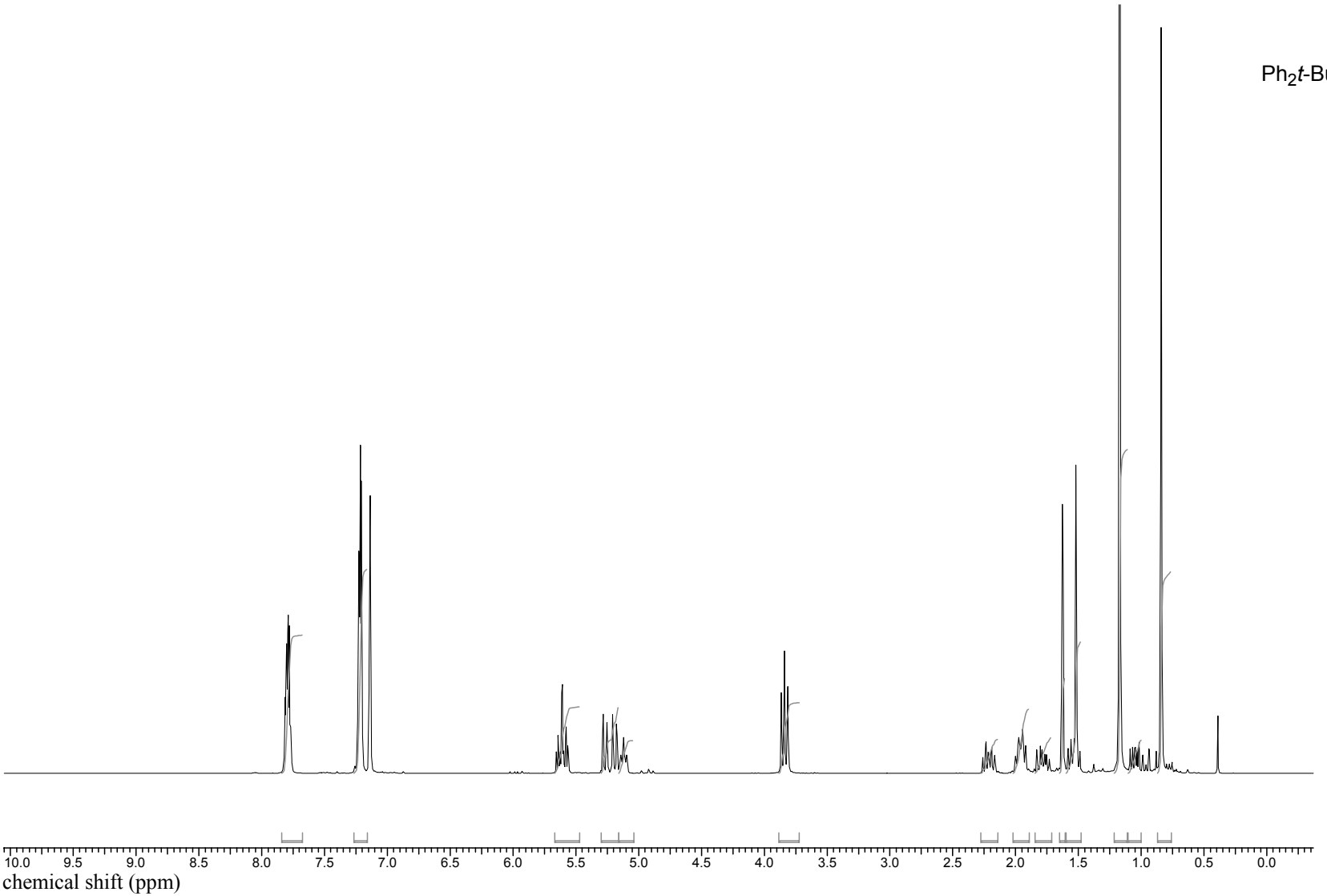


16, ^{13}C NMR spectrum (APT, 125 MHz, C_6D_6):

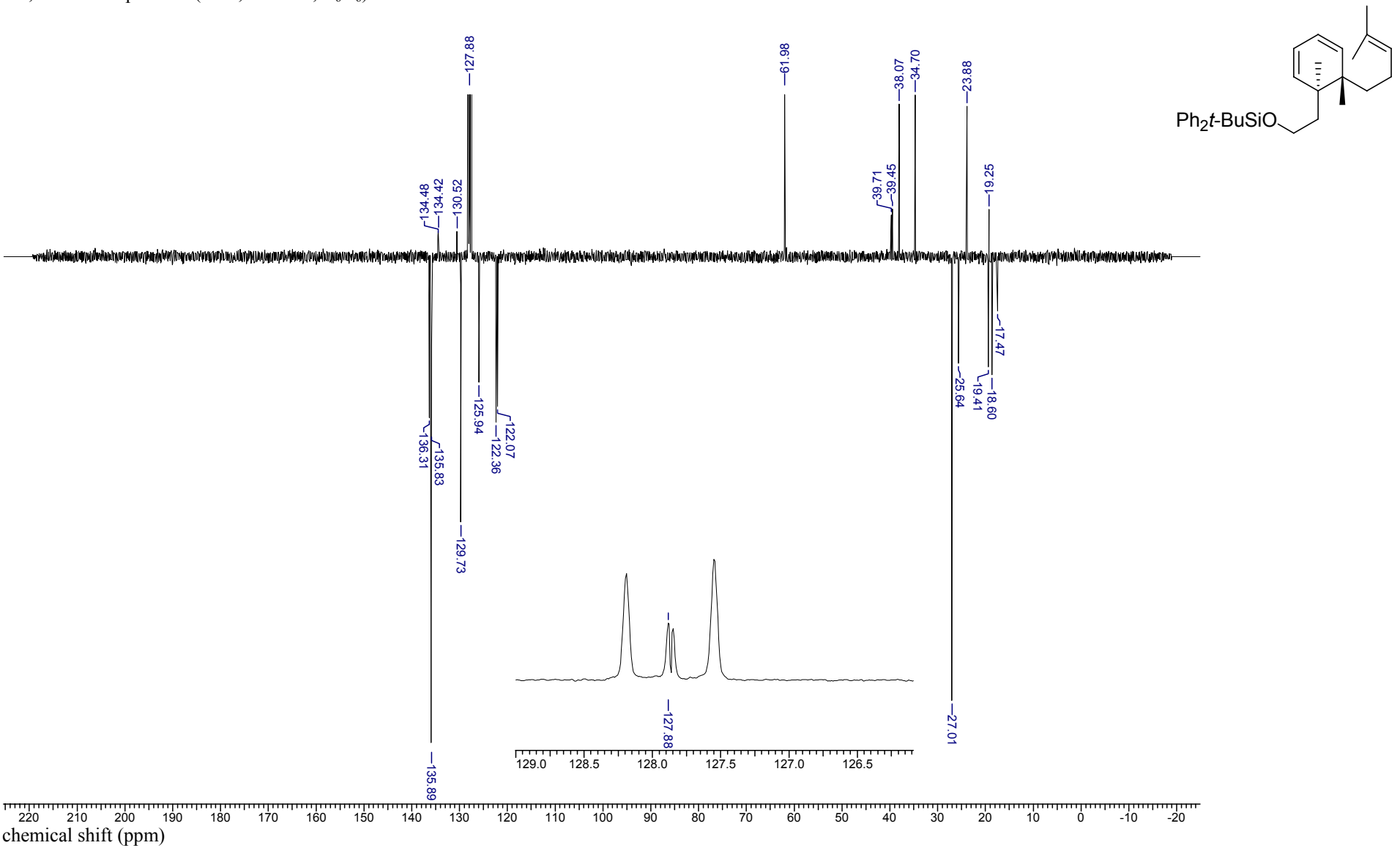


11', ^{1}H NMR spectrum (300 MHz, C_6D_6):

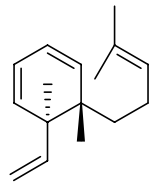


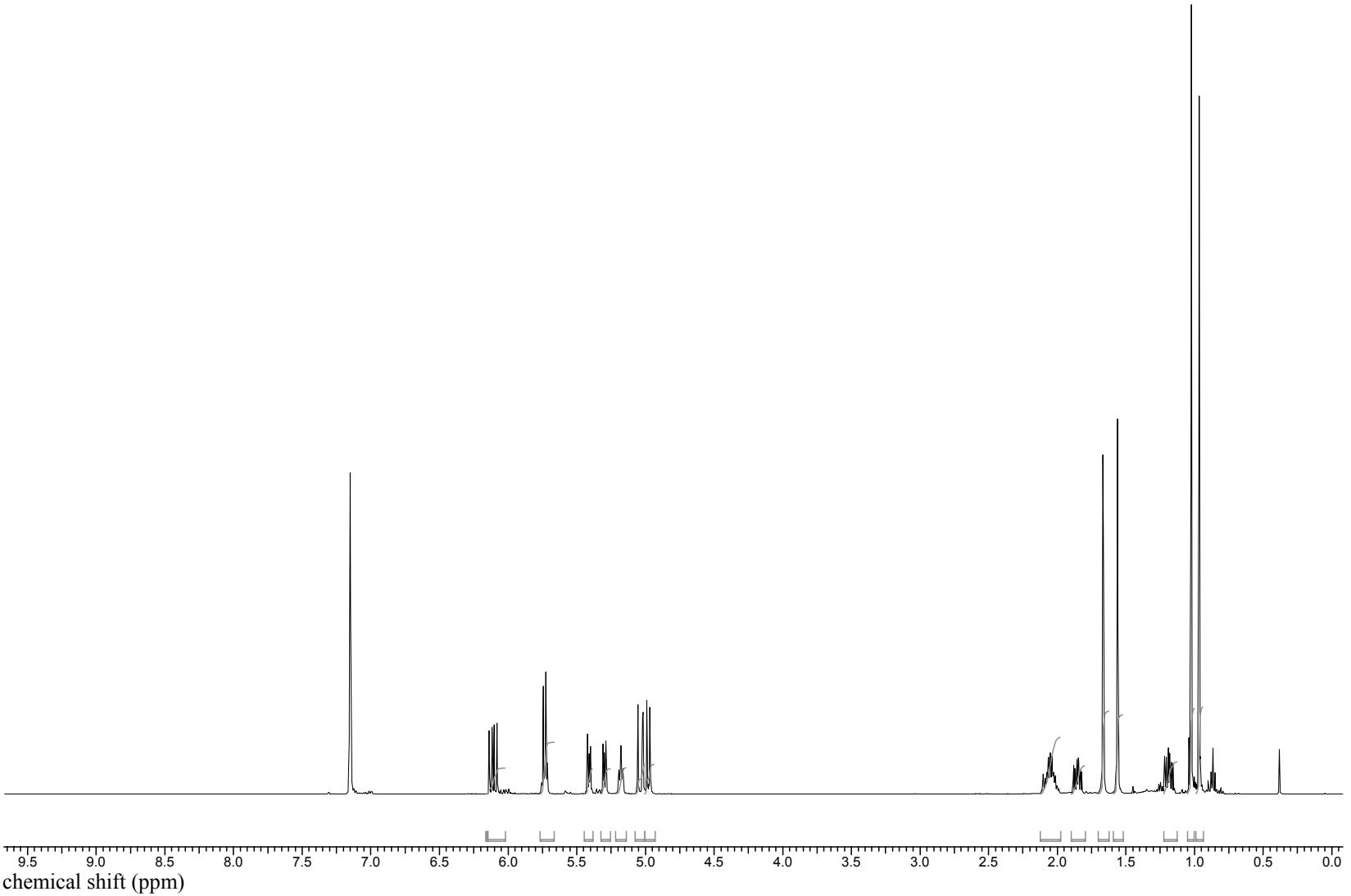


11', ^{13}C NMR spectrum (APT, 75 MHz, C_6D_6):

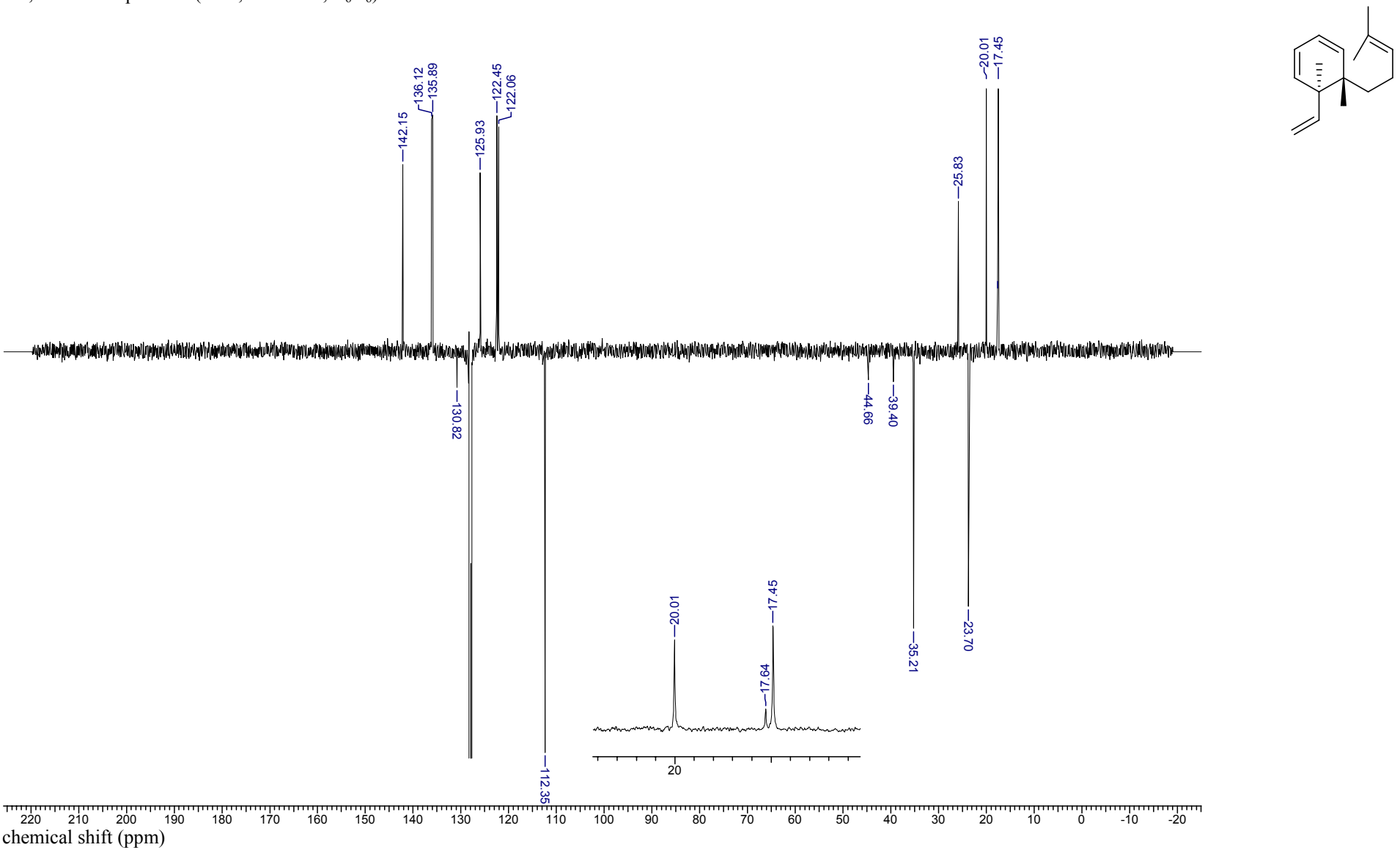


12', ^{1}H NMR spectrum (500 MHz, C_6D_6):

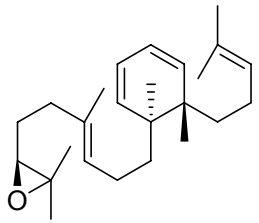


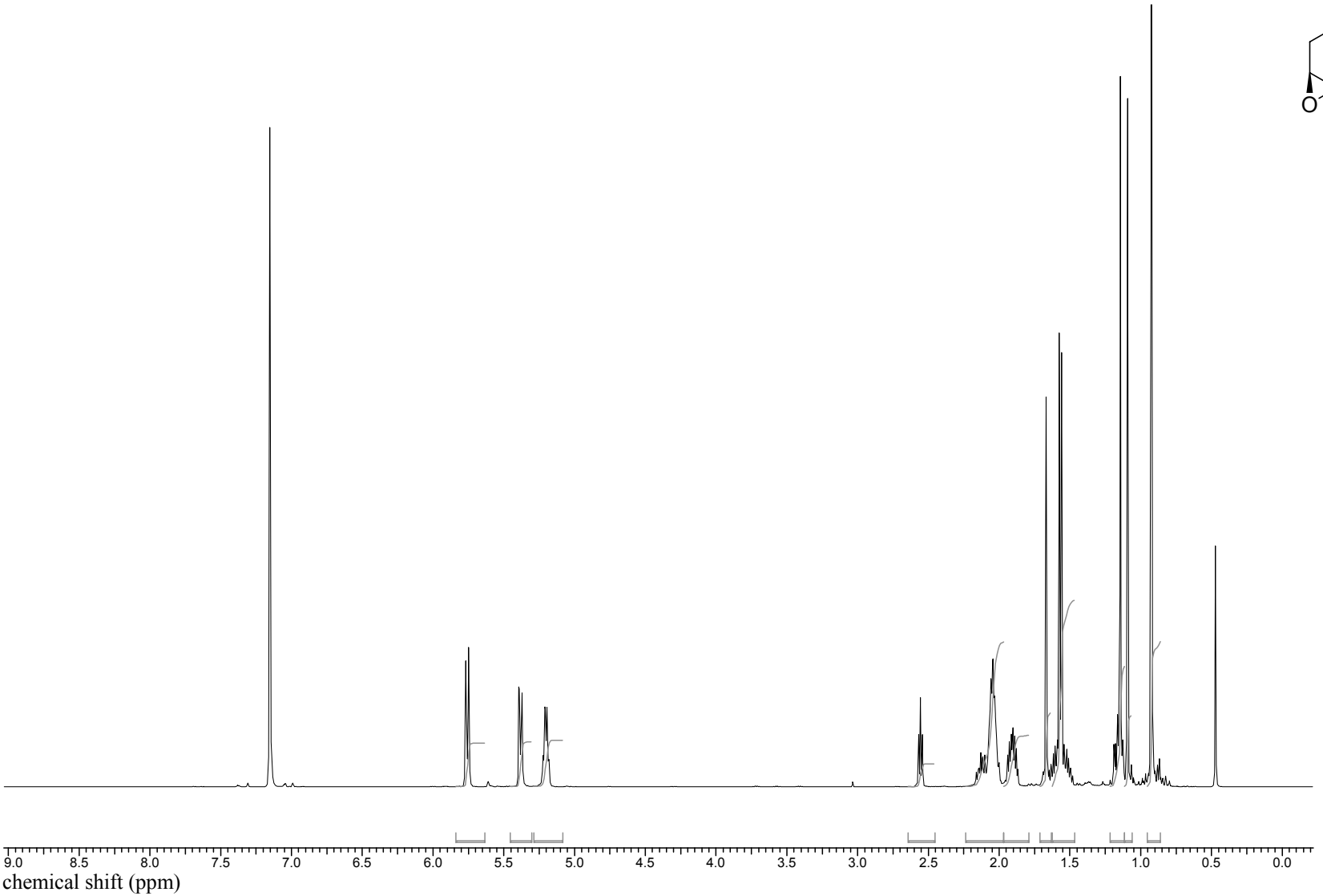


12', ^{13}C NMR spectrum (APT, 125 MHz, C_6D_6):

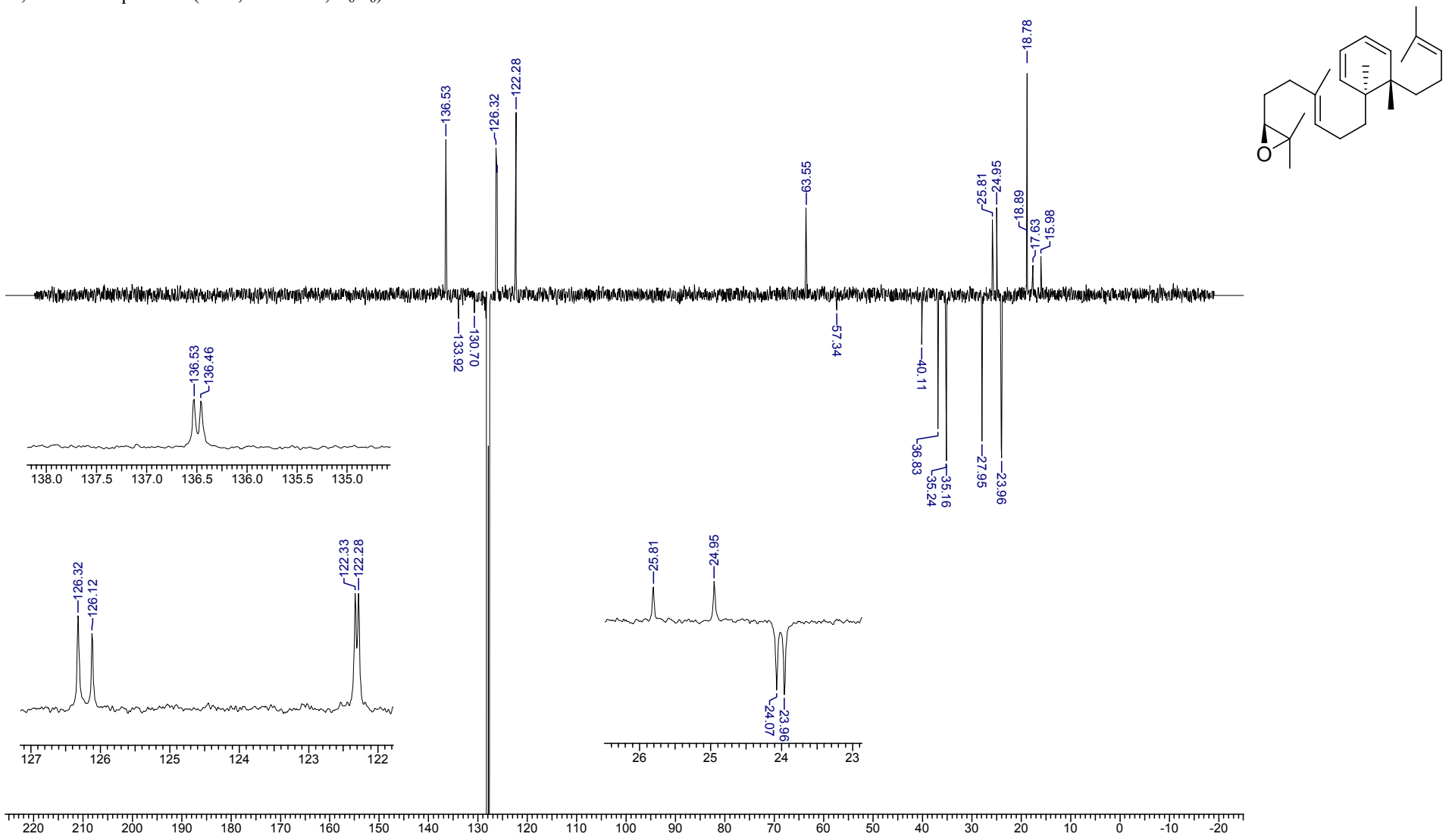


5', ^{1}H NMR spectrum (500 MHz, C_6D_6):

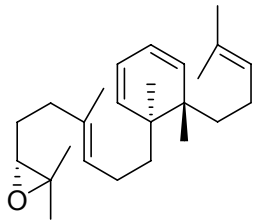


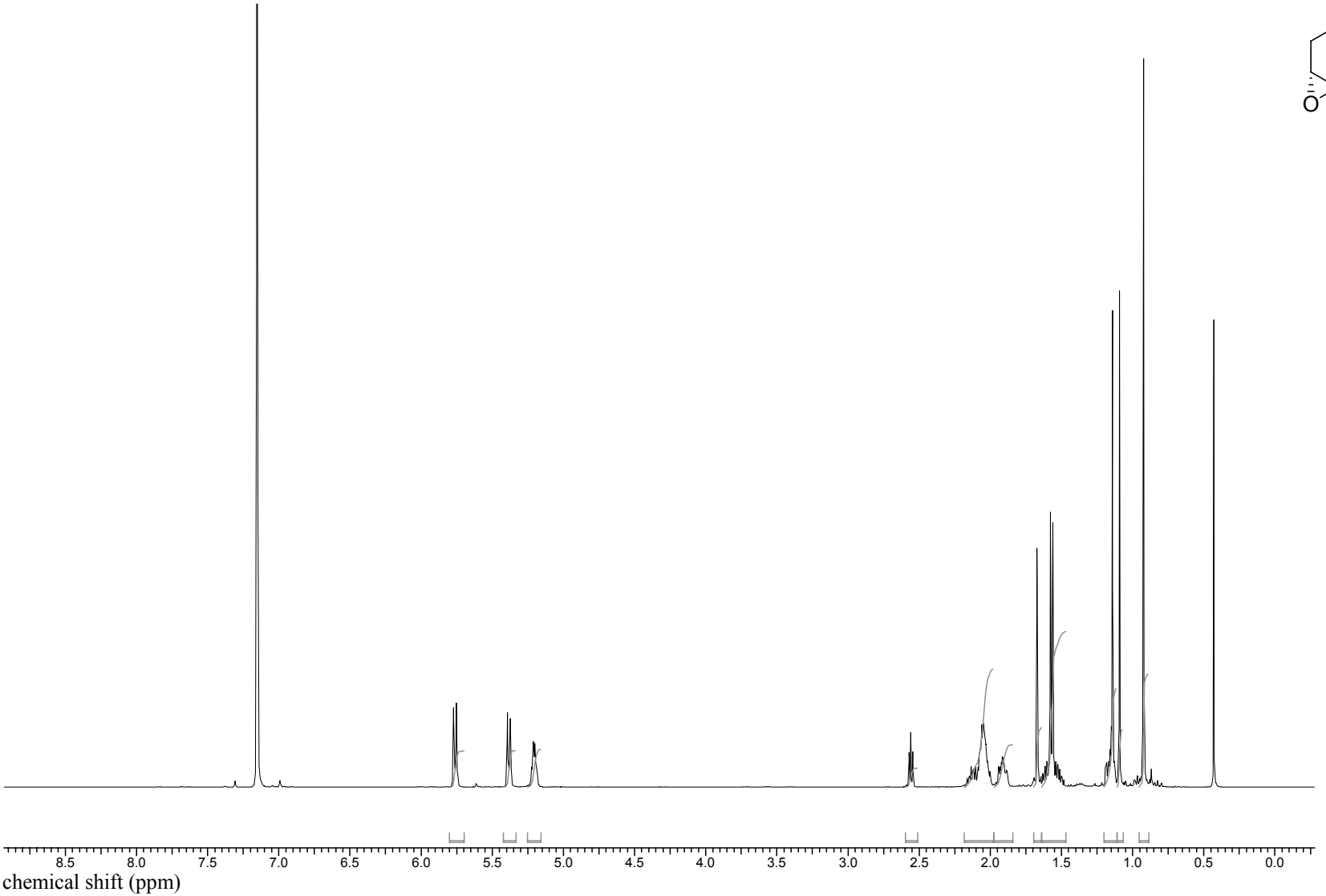


5', ^{13}C NMR spectrum (APT, 125 MHz, C_6D_6):

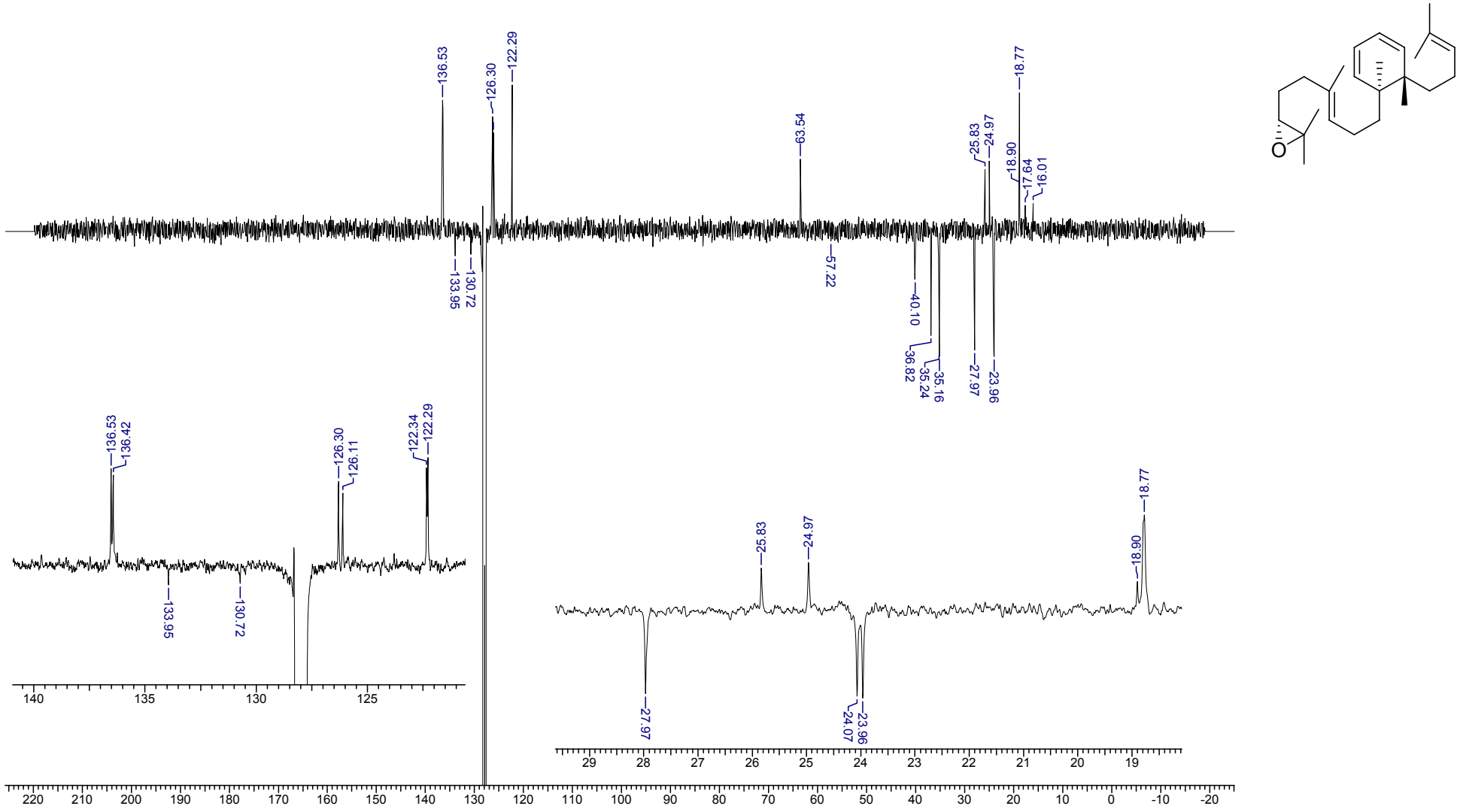


***ent*-4'**, ^{1}H NMR spectrum (500 MHz, C_6D_6):

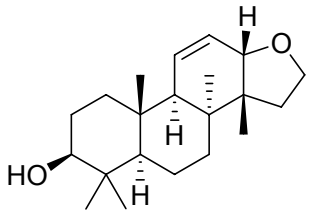


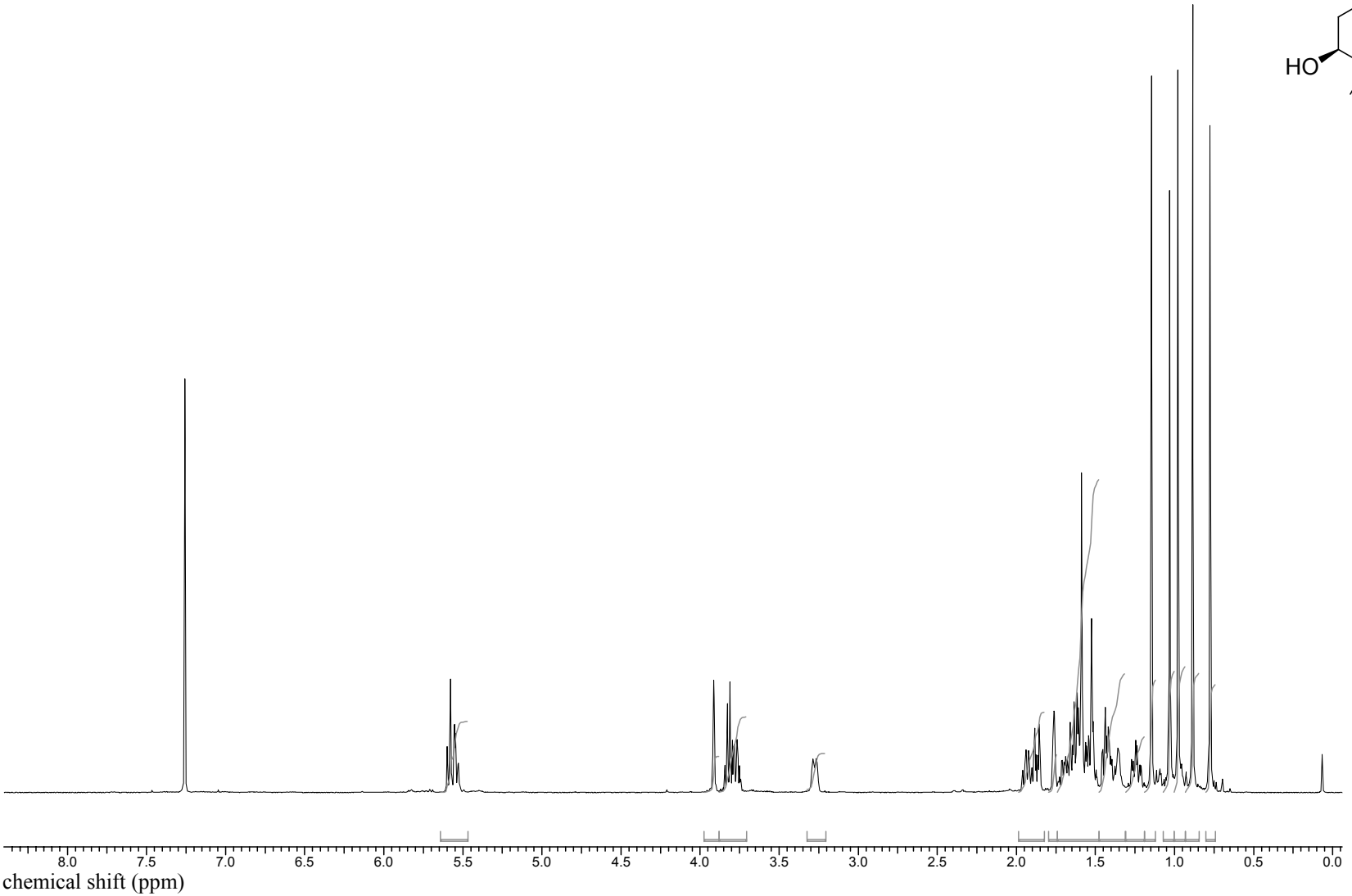


***ent*-4'**, ^{13}C NMR spectrum (APT, 125 MHz, C_6D_6):

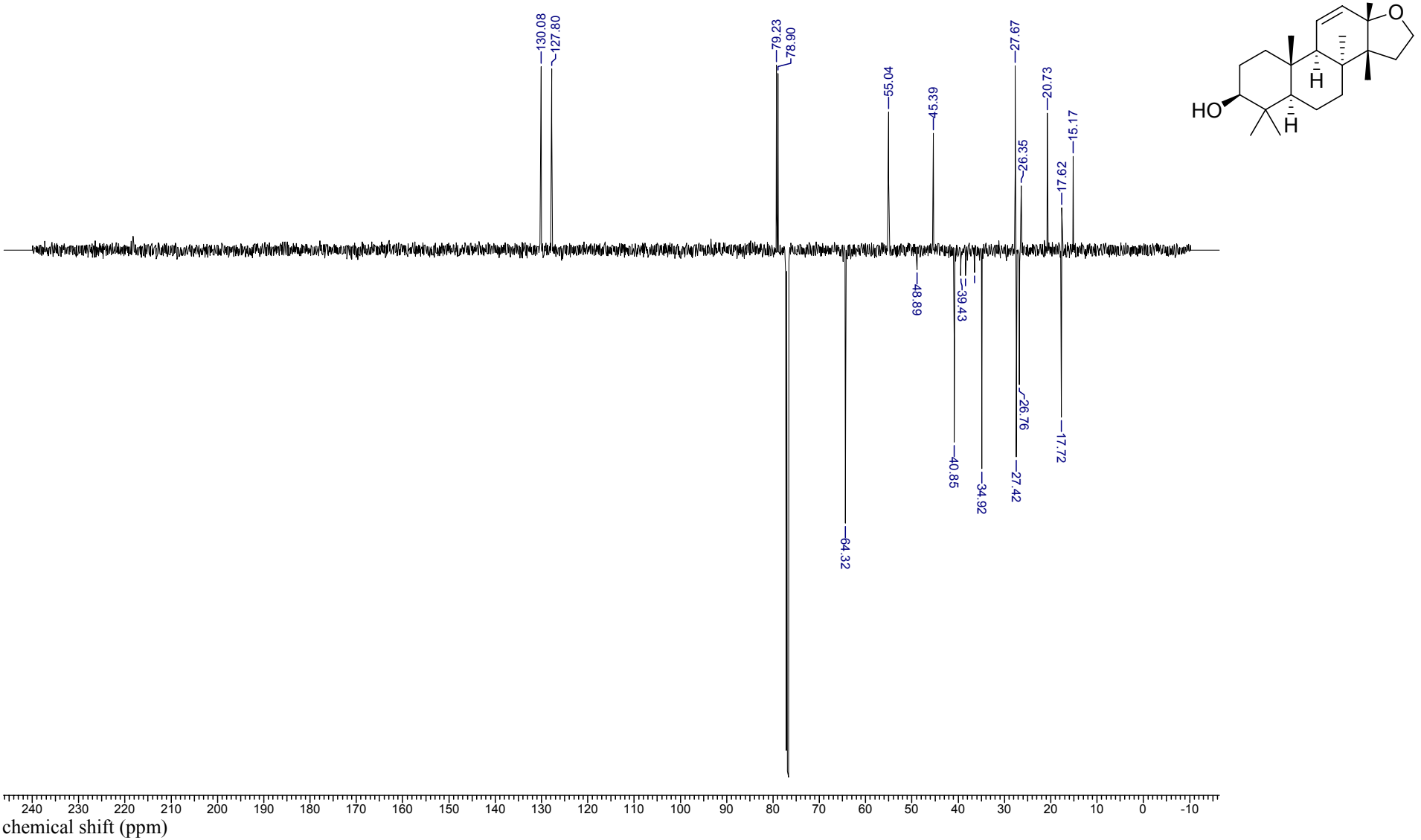


20, ^{1}H NMR spectrum (500 MHz, $CDCl_3$):

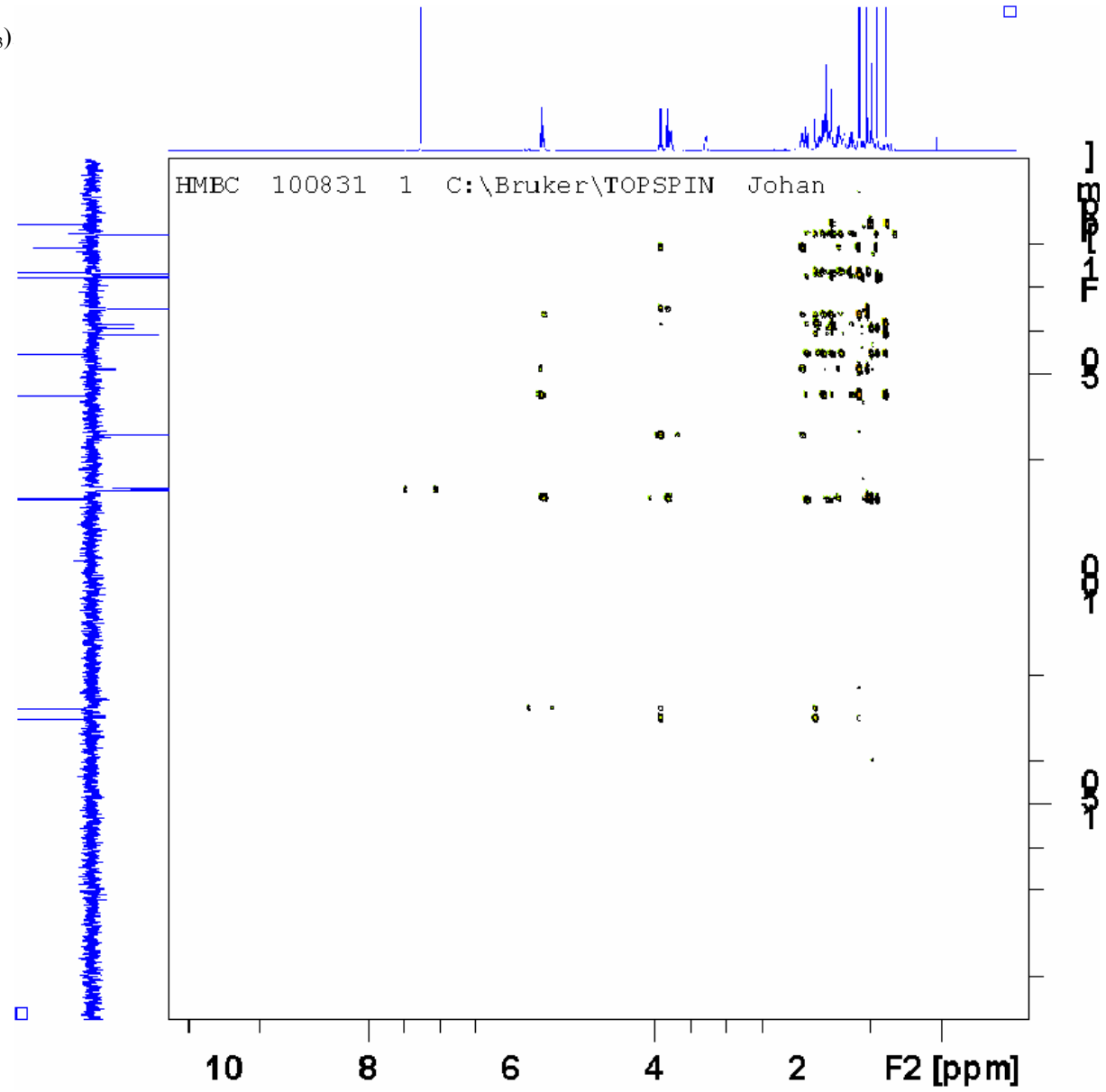


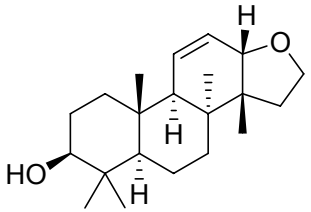


20, ^{13}C NMR spectrum (APT, 125 MHz, $CDCl_3$):

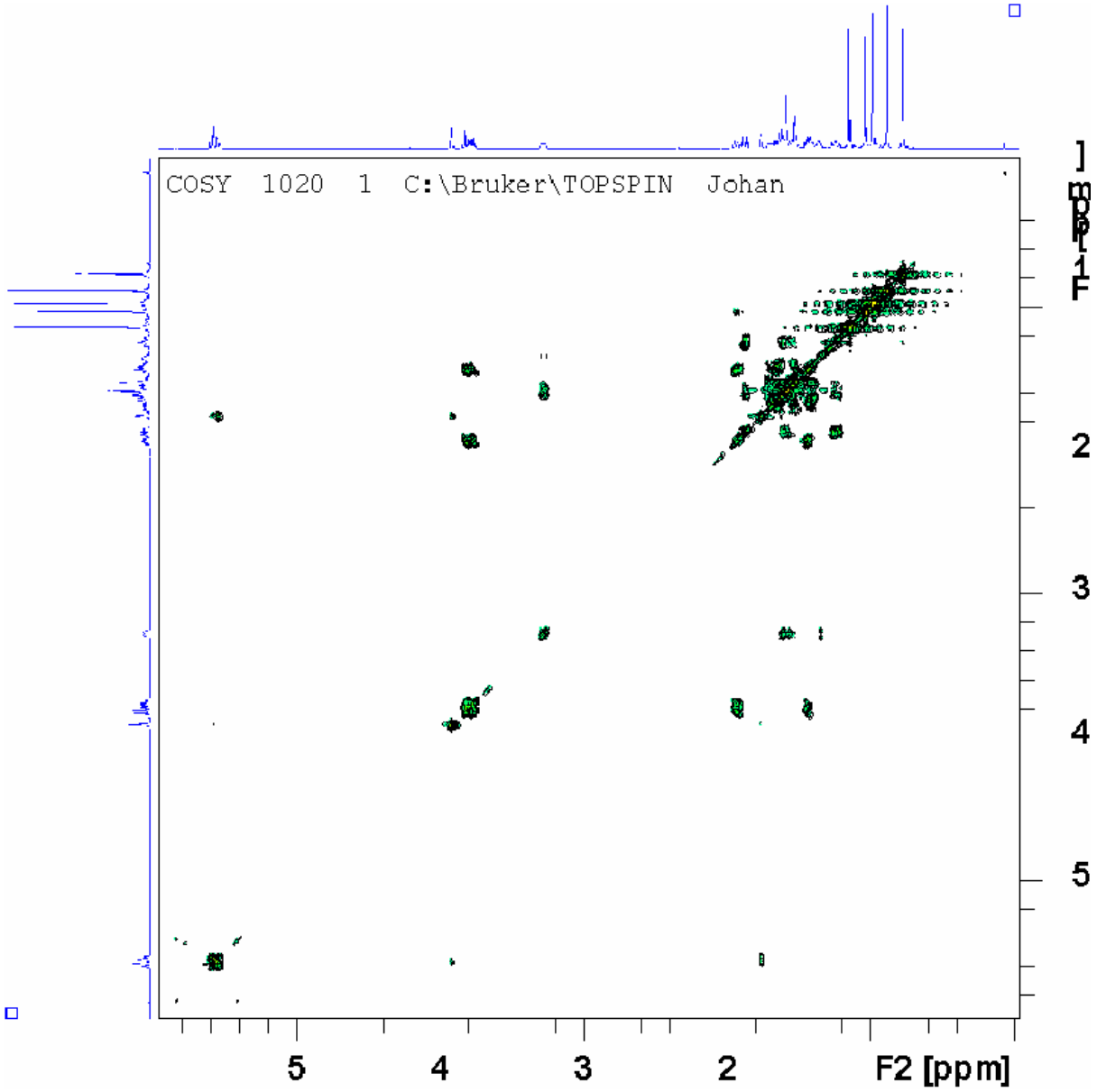


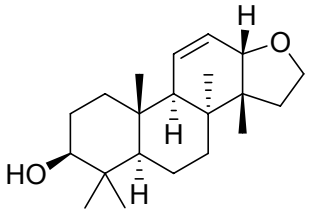
20, HMBC (500 MHz, $CDCl_3$)



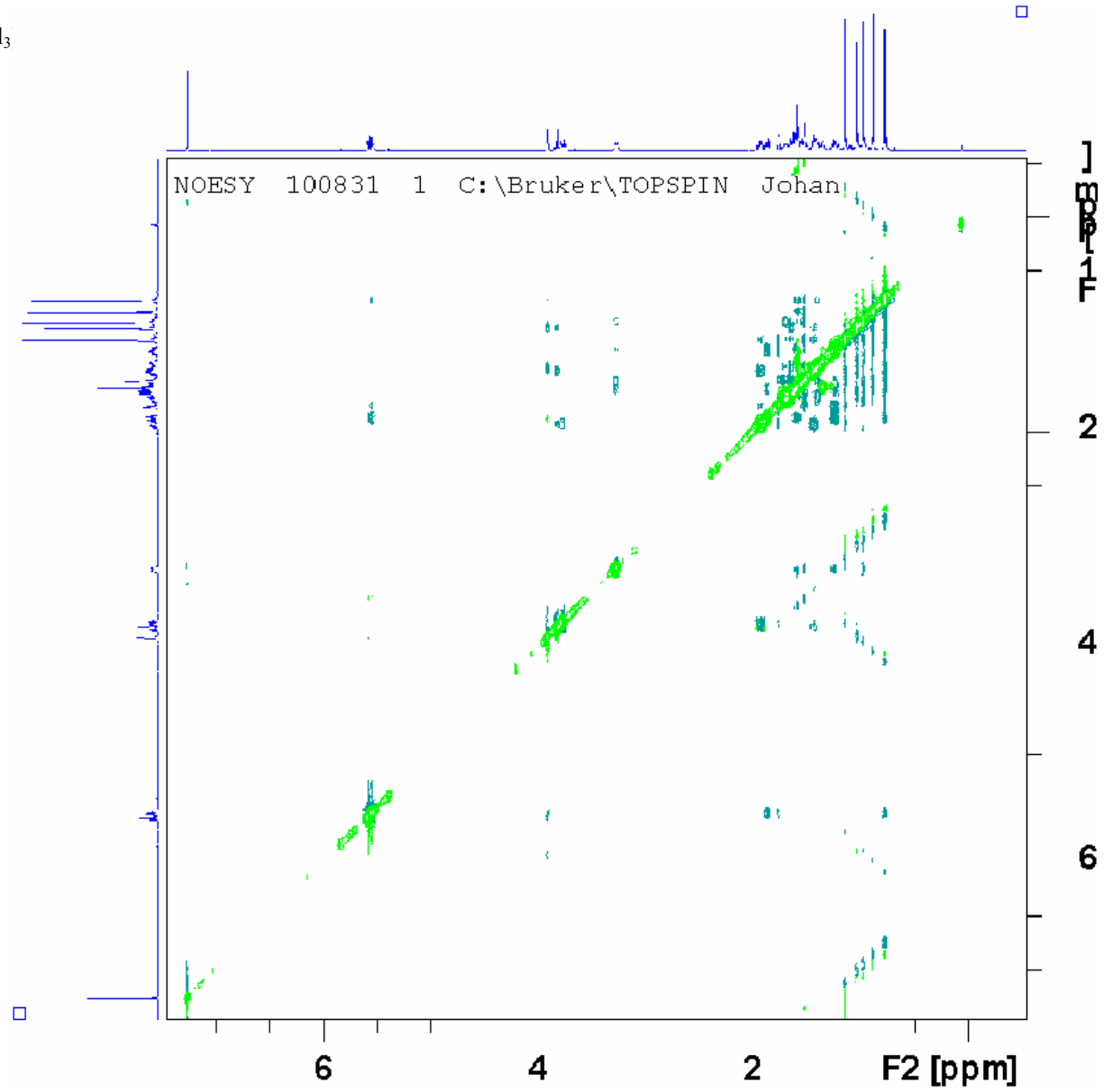


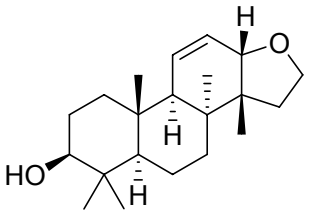
20, COSY (500 MHz, $CDCl_3$):



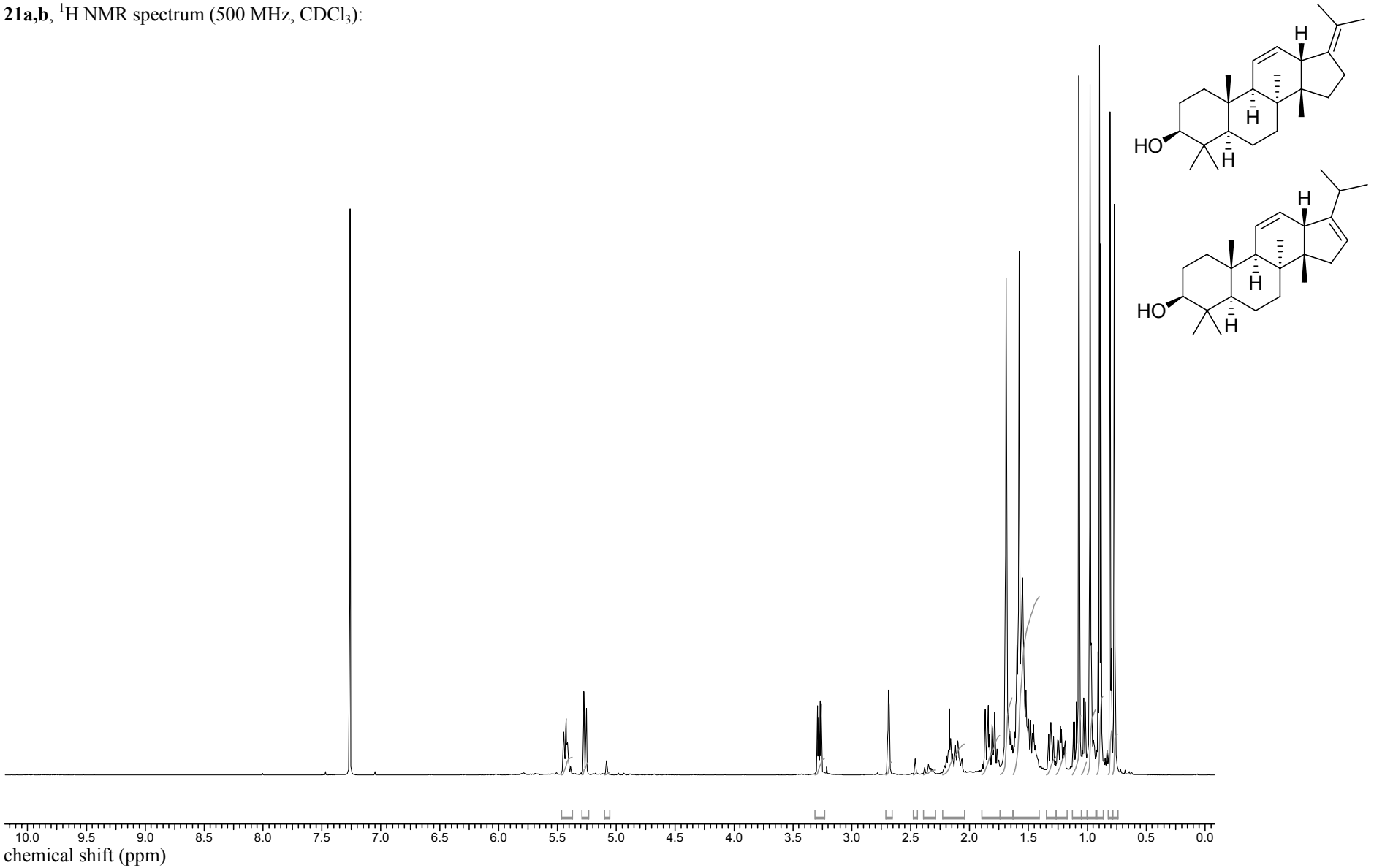


20, NOESY (500 MHz, $CDCl_3$

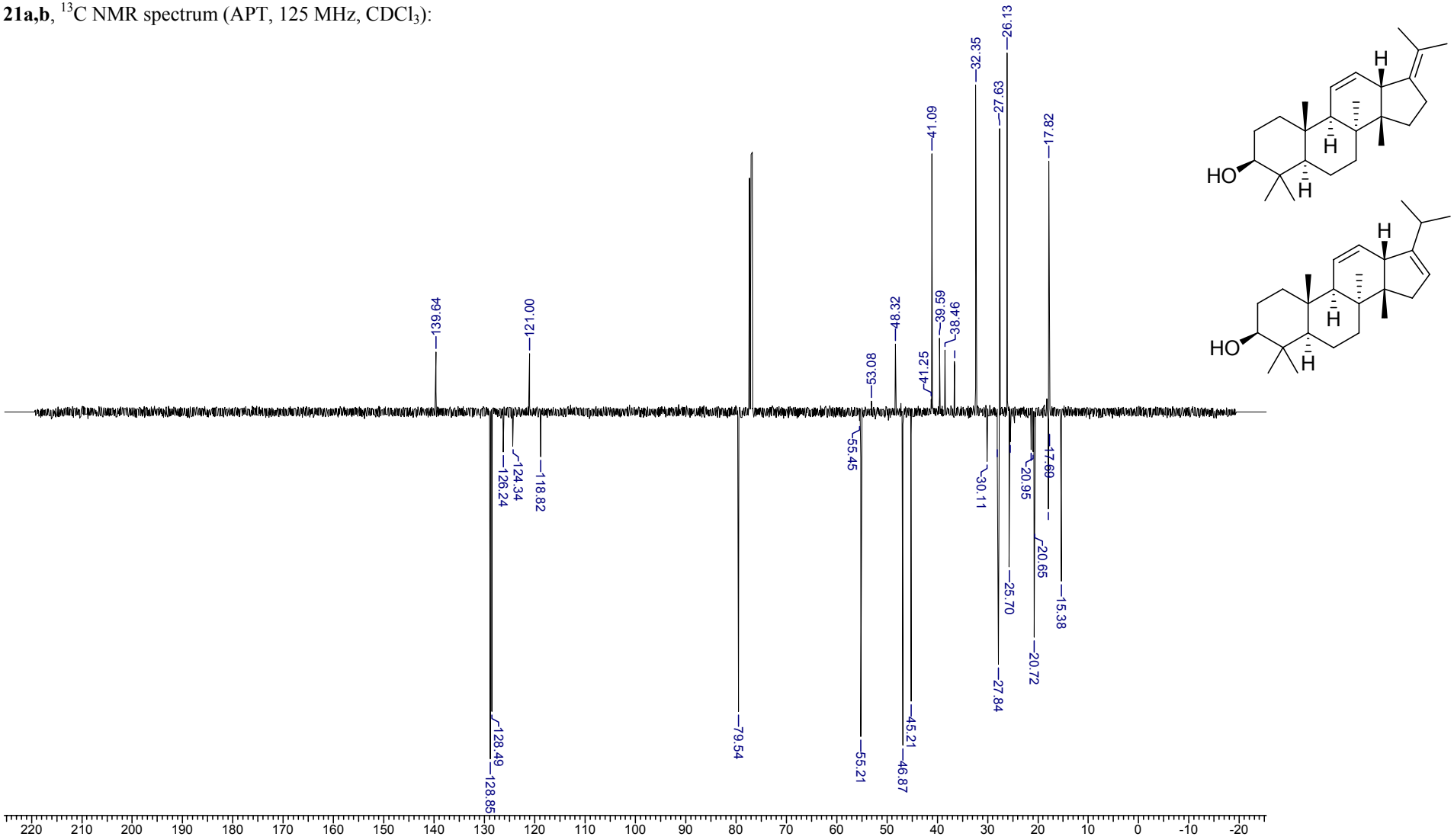




21a,b, ^{1}H NMR spectrum (500 MHz, $CDCl_3$):

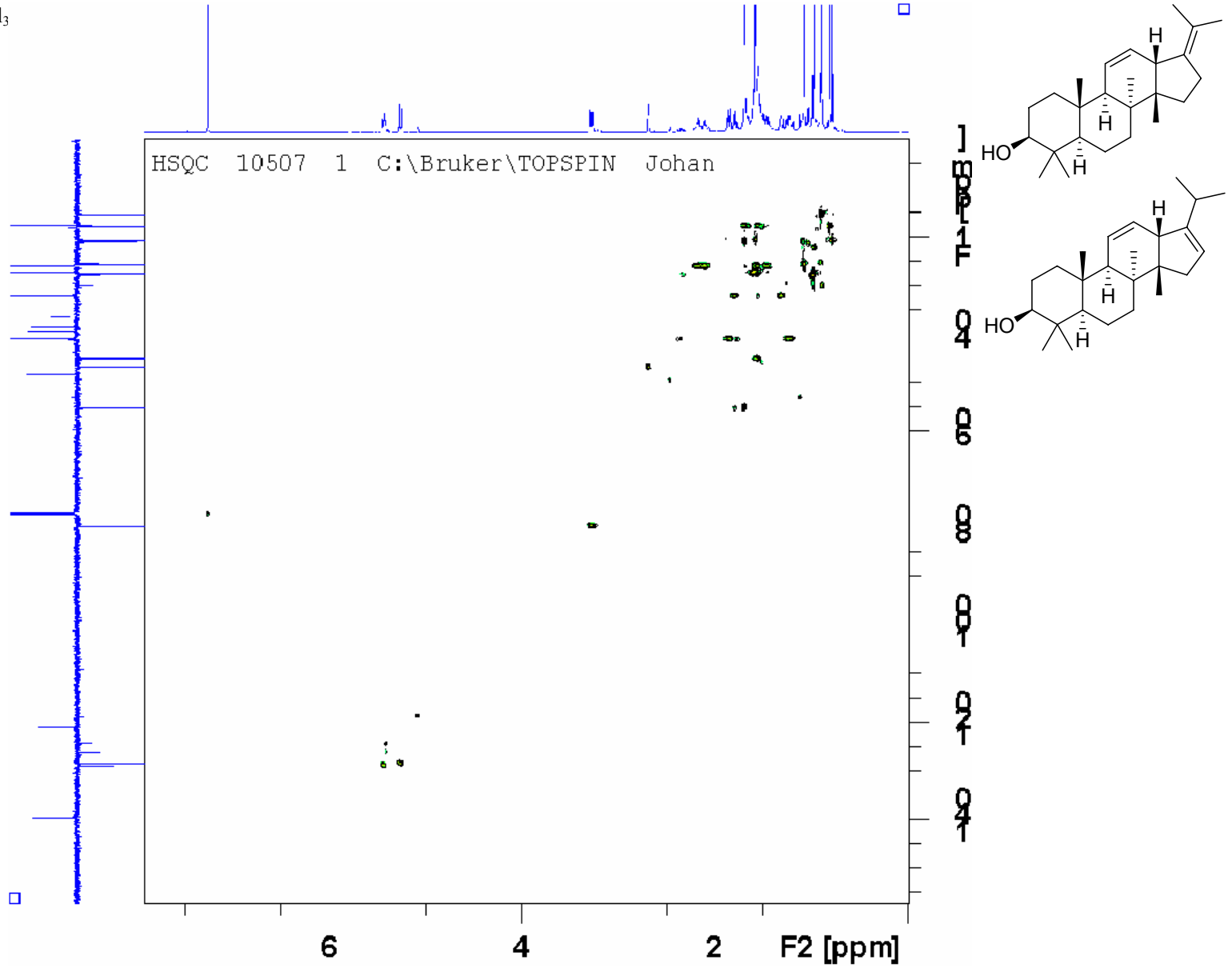


21a,b, ^{13}C NMR spectrum (APT, 125 MHz, $CDCl_3$):

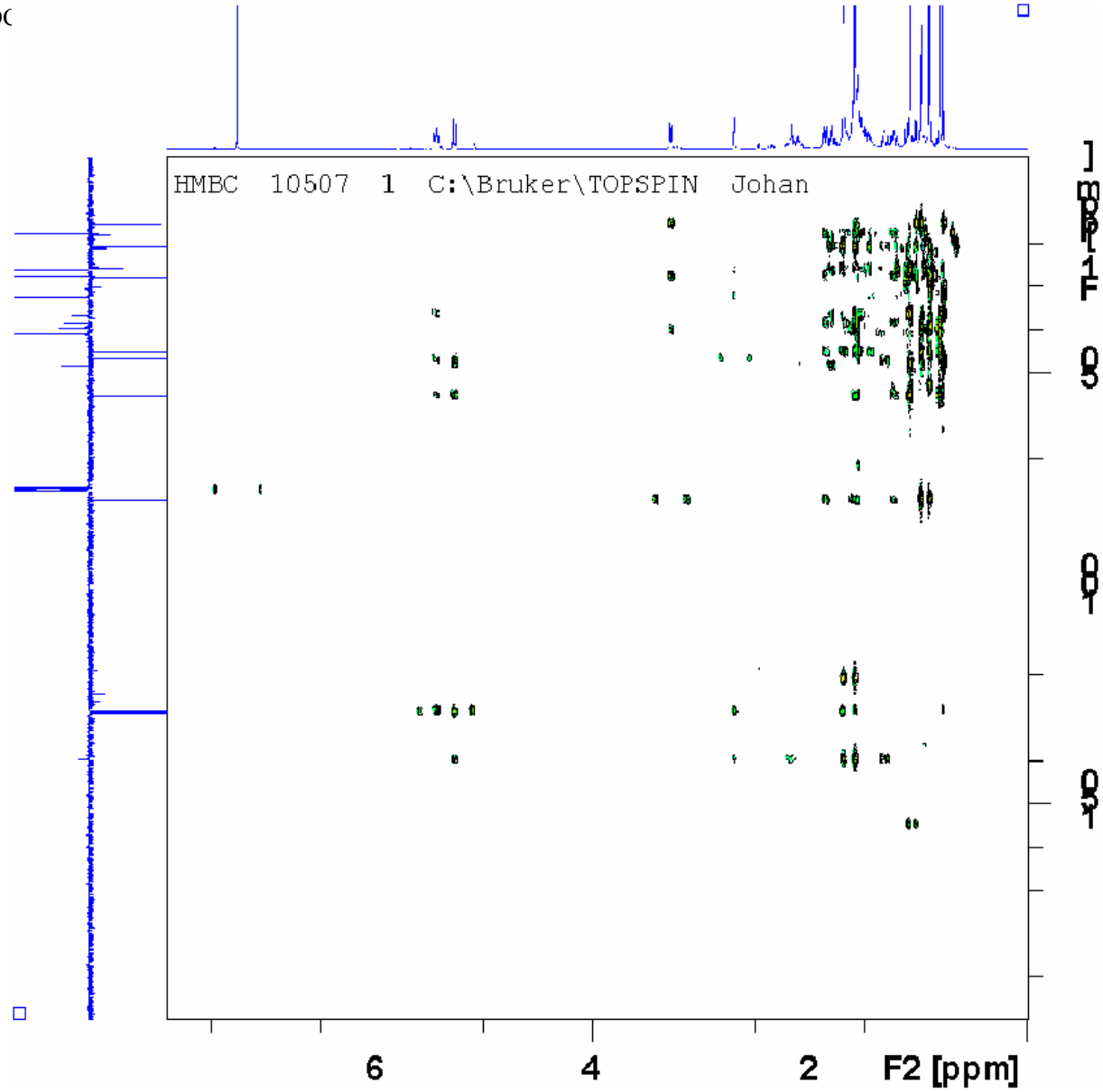


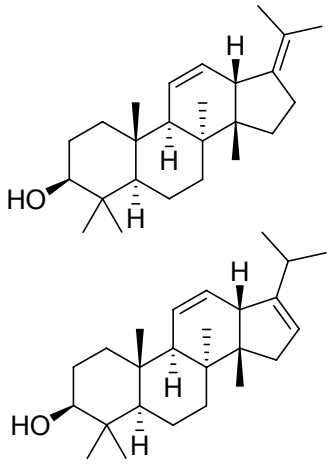
chemical shift (ppm)

21a,b, HSQC (500 MHz, $CDCl_3$

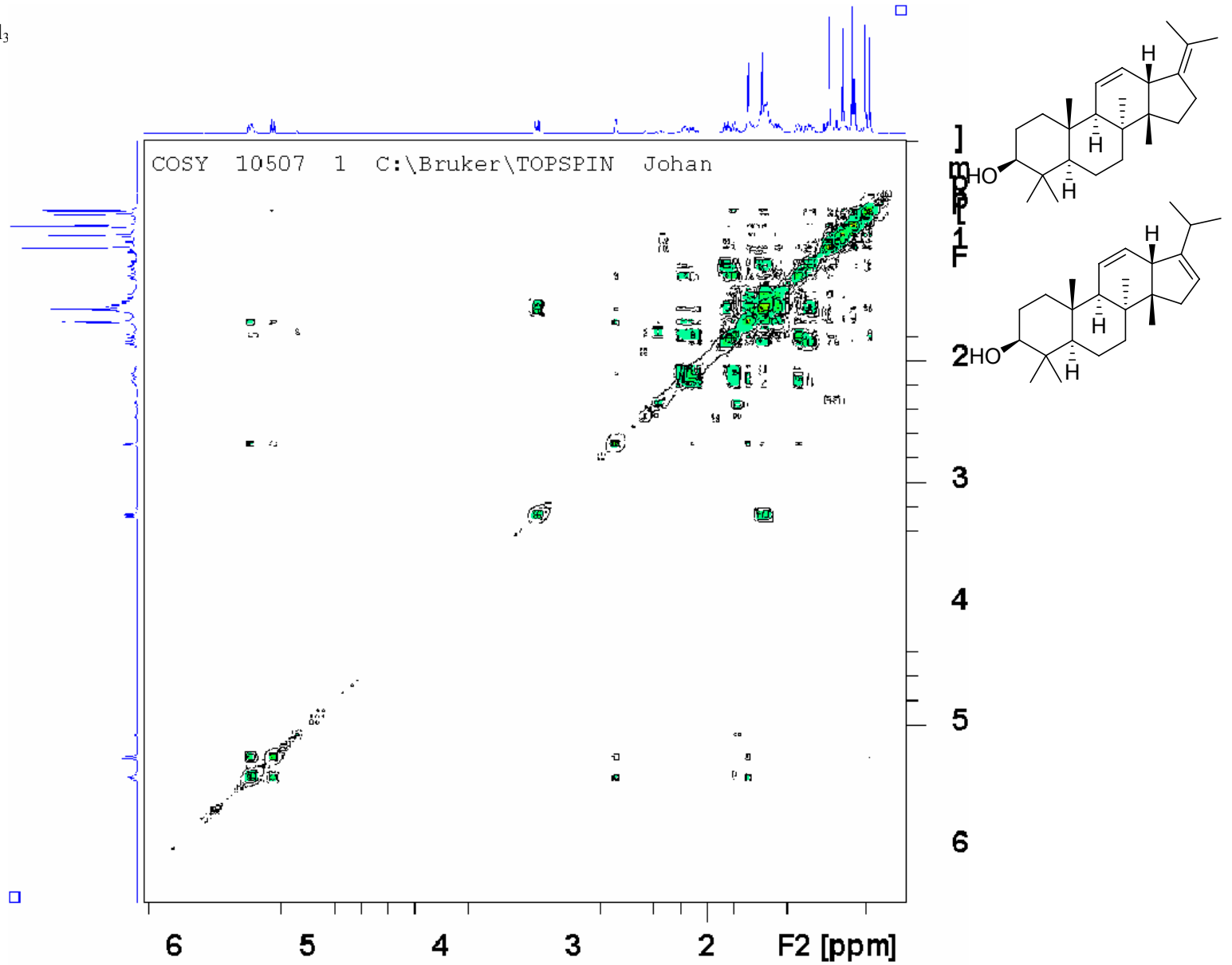


21a,b, HMBC (500 MHz, CDC

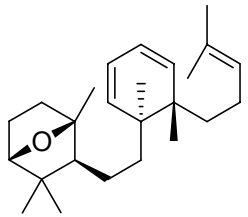


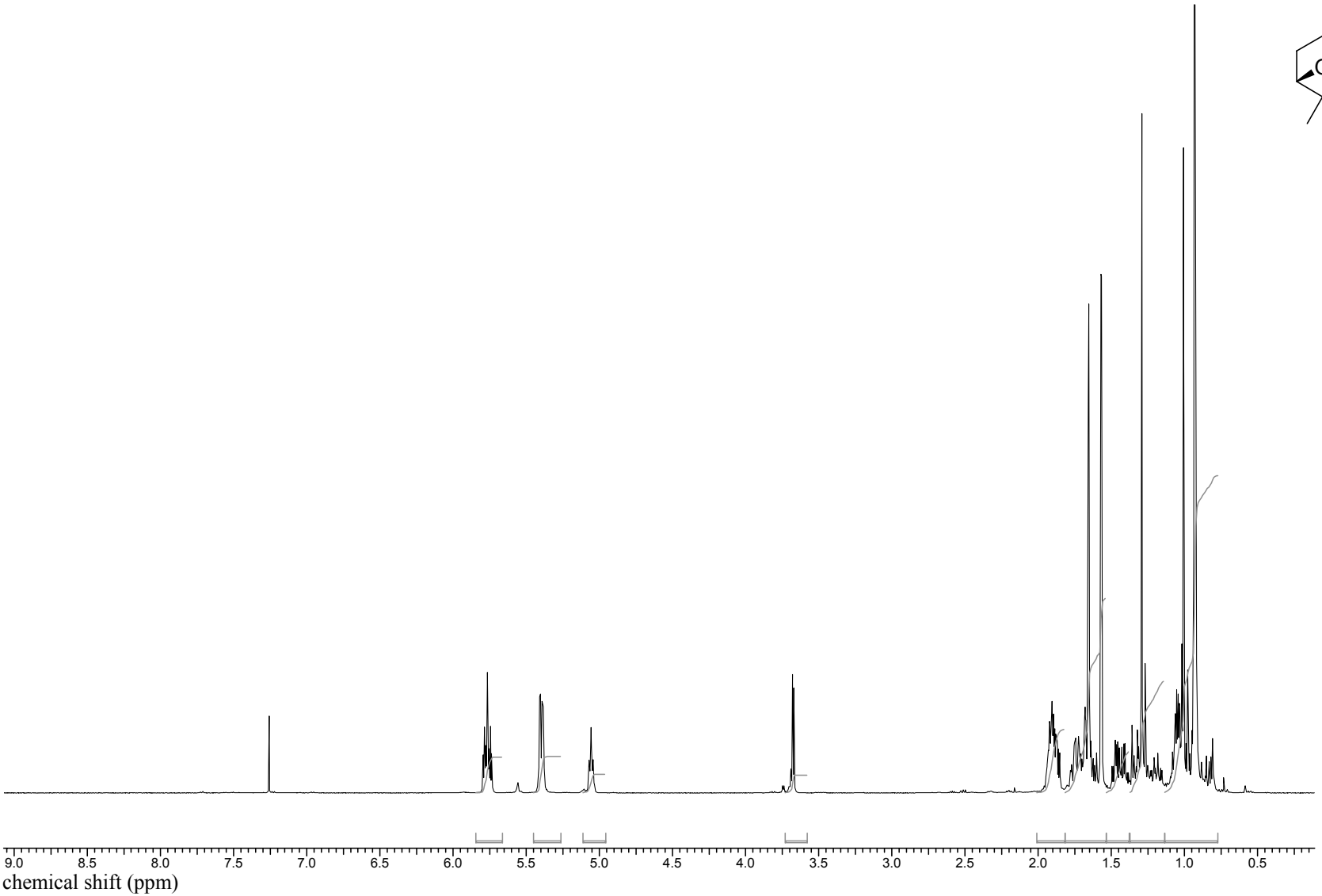


21a,b, COSY (500 MHz, $CDCl_3$

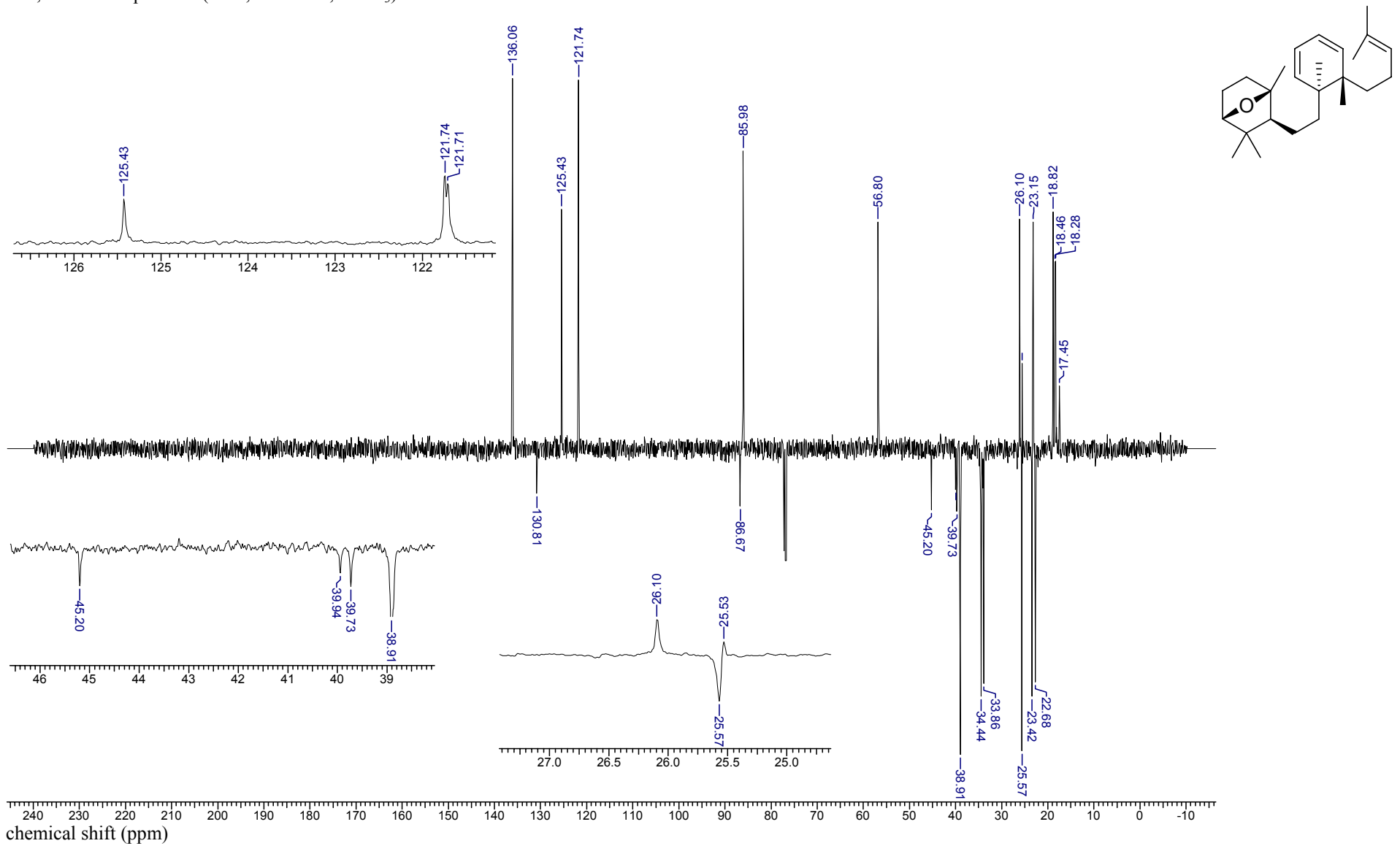


17b, ^{1}H NMR spectrum (500 MHz, $CDCl_3$):

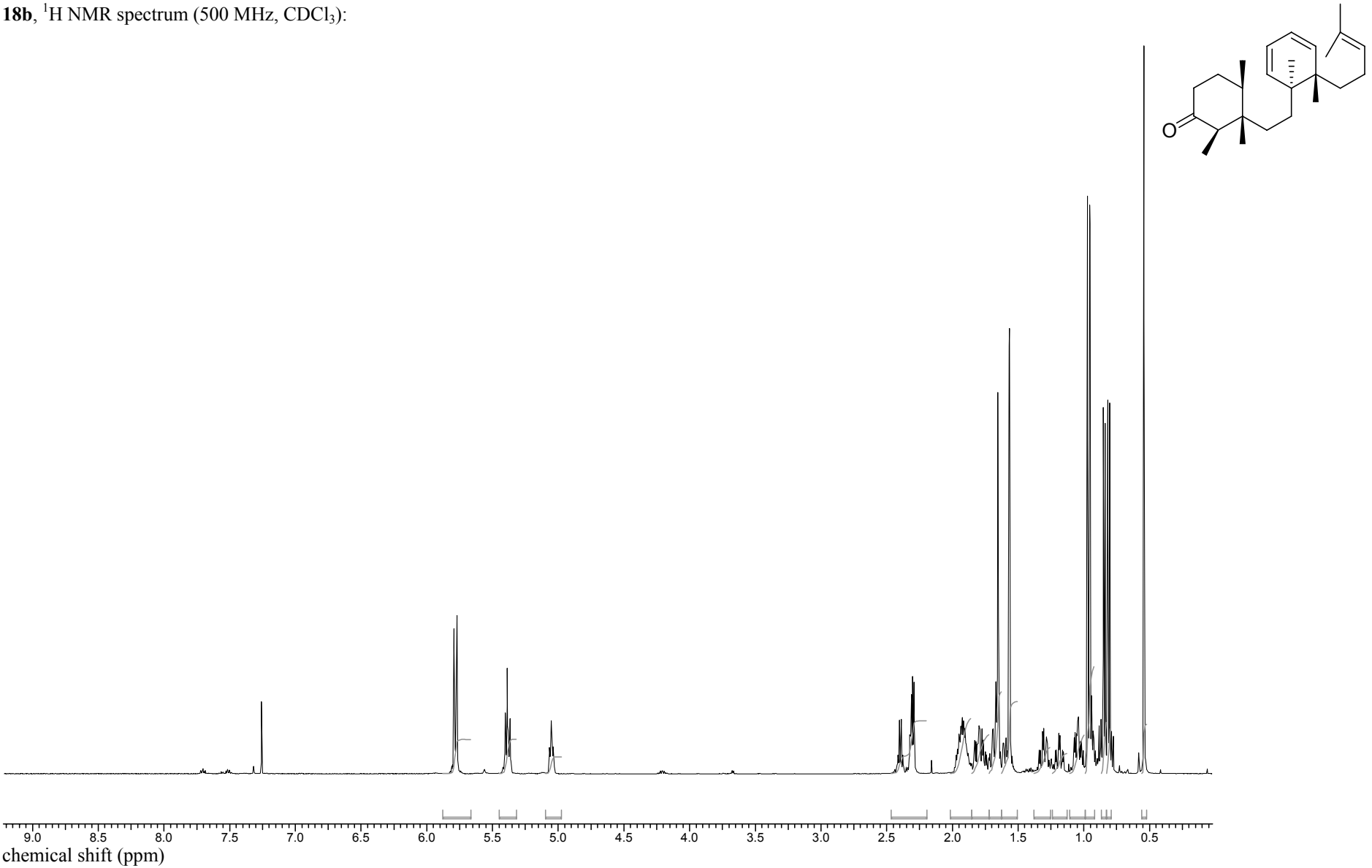




17b, ^{13}C NMR spectrum (APT, 125 MHz, $CDCl_3$):



18b, ^{1}H NMR spectrum (500 MHz, $CDCl_3$):



18b, ^{13}C NMR spectrum (APT, 125 MHz, $CDCl_3$):

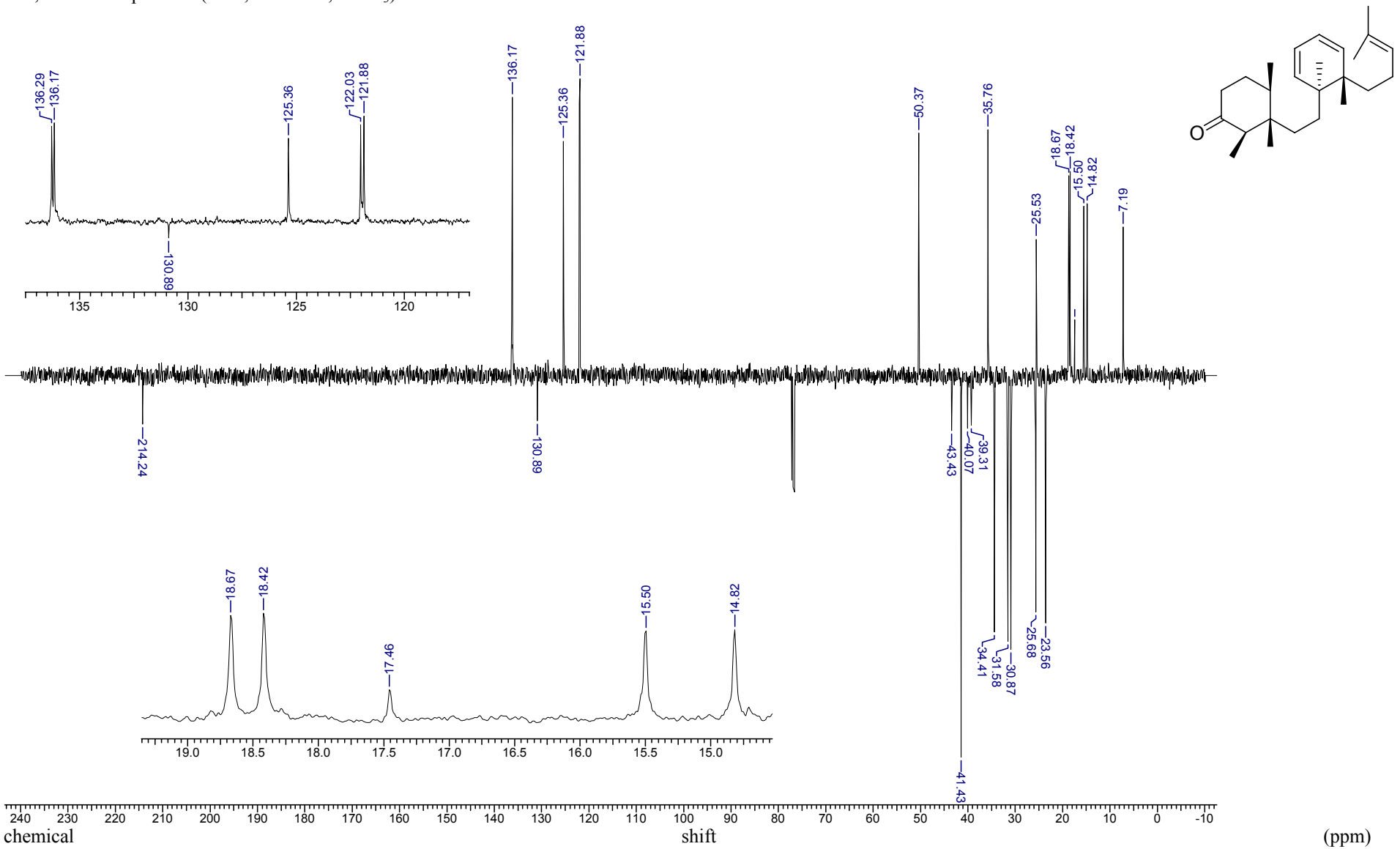


Table SM1: Crystal structure data for compound 21a

Empirical formula (Unit Cell)	C51 H84 O3
Formula weight	745.18
Temperature	100(2) K
Wavelength	0.7114(1) Å
Crystal system	Orthorombic
Space group	P 21 21 21
Unit cell dimensions	a = 6.429(1) Å
	b = 13.631(2) Å
	c = 50.896(6) Å
Volume	4460.2 $Å^3$
Z	4
Density (calculated)	1.104 Mg/m^3
Absorption coefficient	0.066 mm^{-1}
F(000)	1656
Crystal size	0.120 x 0.040 x 0.005 mm^3
Theta range for data collection	1.55 to 17.23°.
Index ranges	-5<=h<=5, -11<=k<=11, -24<=l<=40
Reflections collected	3482
Independent reflections	1637 [R(int) = 0.0381]
Completeness to theta = 17.23°	98.97 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1637 / 10 / 213
Goodness-of-fit on F^2	1.057
Final R indices [I>2sigma(I)]	R1 = 0.2009, wR2 = 0.5235
R indices (all data)	R1 = 0.2217, wR2 = 0.5641
Largest diff. peak and hole	0.597 and -0.483 $e.Å^{-3}$

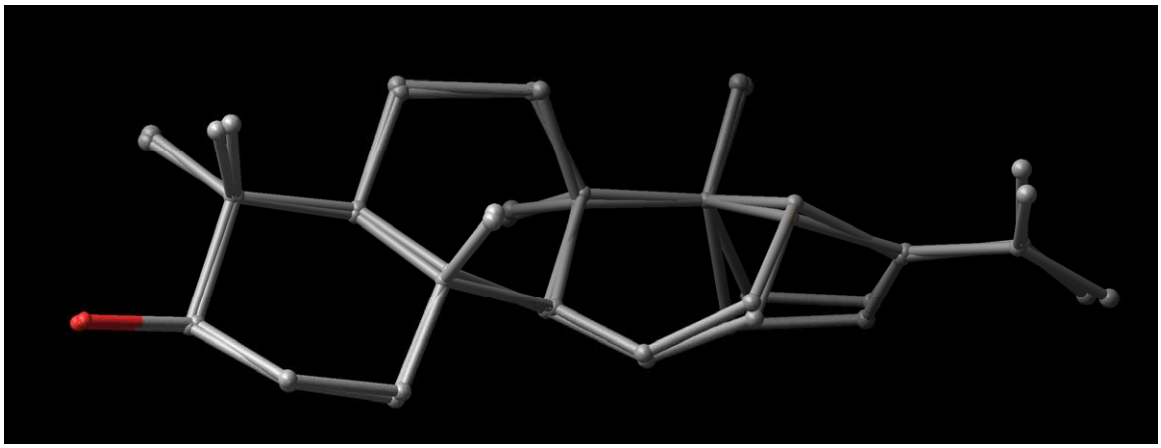


Figure SM1: Superposition of the two conformations in the asymmetric unit of **21a** crystal structures

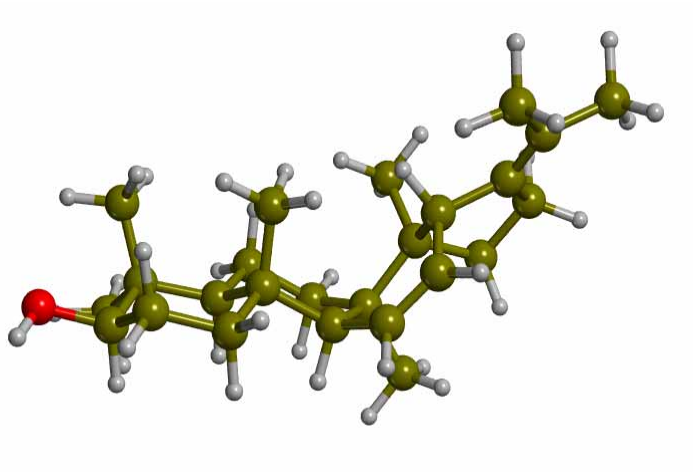


Figure SM2: Compound **21a** with B-ring assuming the chair conformation after B3LYP/6-31G(d,p) geometry optmization.

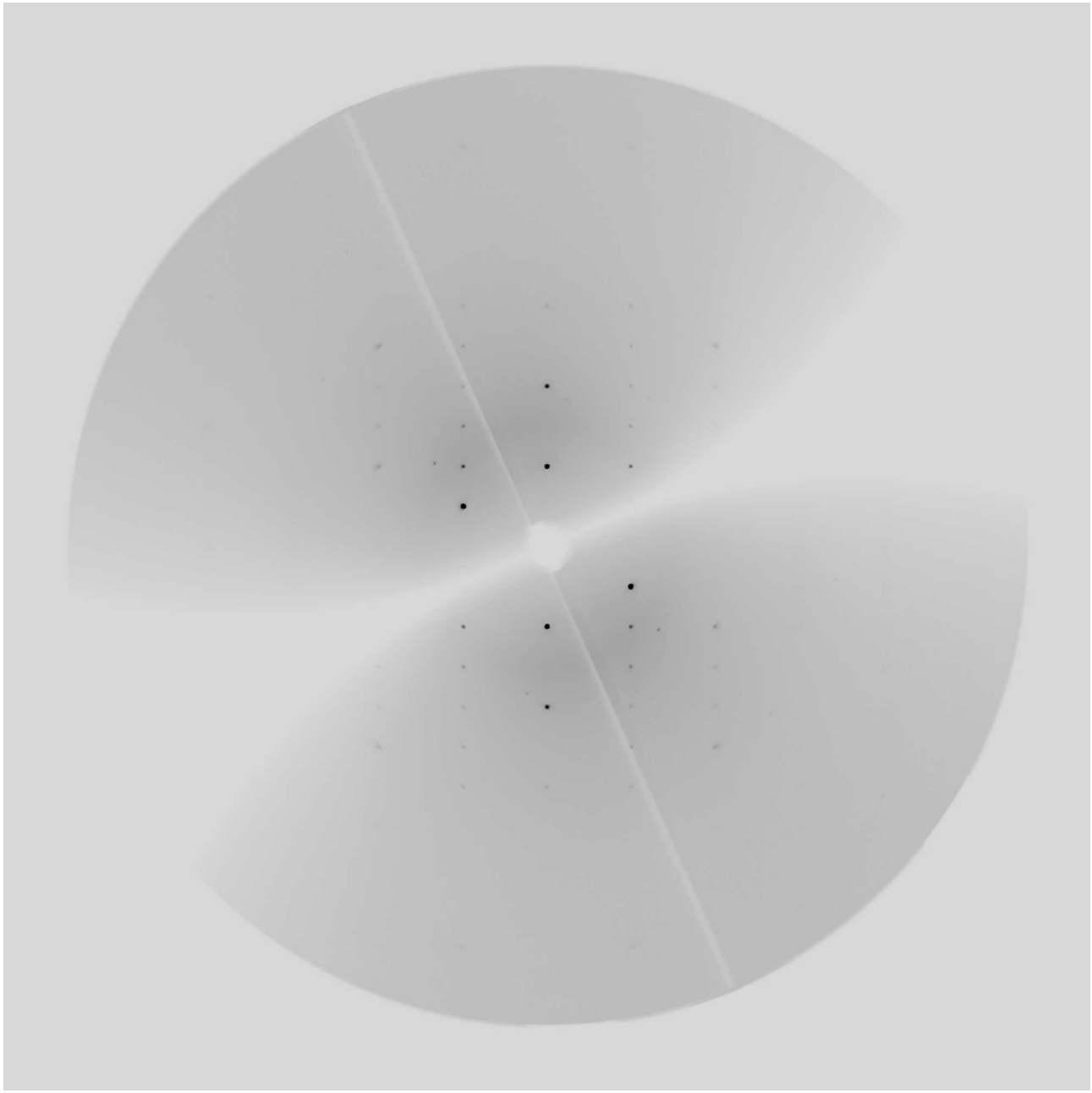


Figure SM3: Reconstrucrion of the reciprocal lattice of **21a** from experimental X-ray diffraction data along hk0 direction.

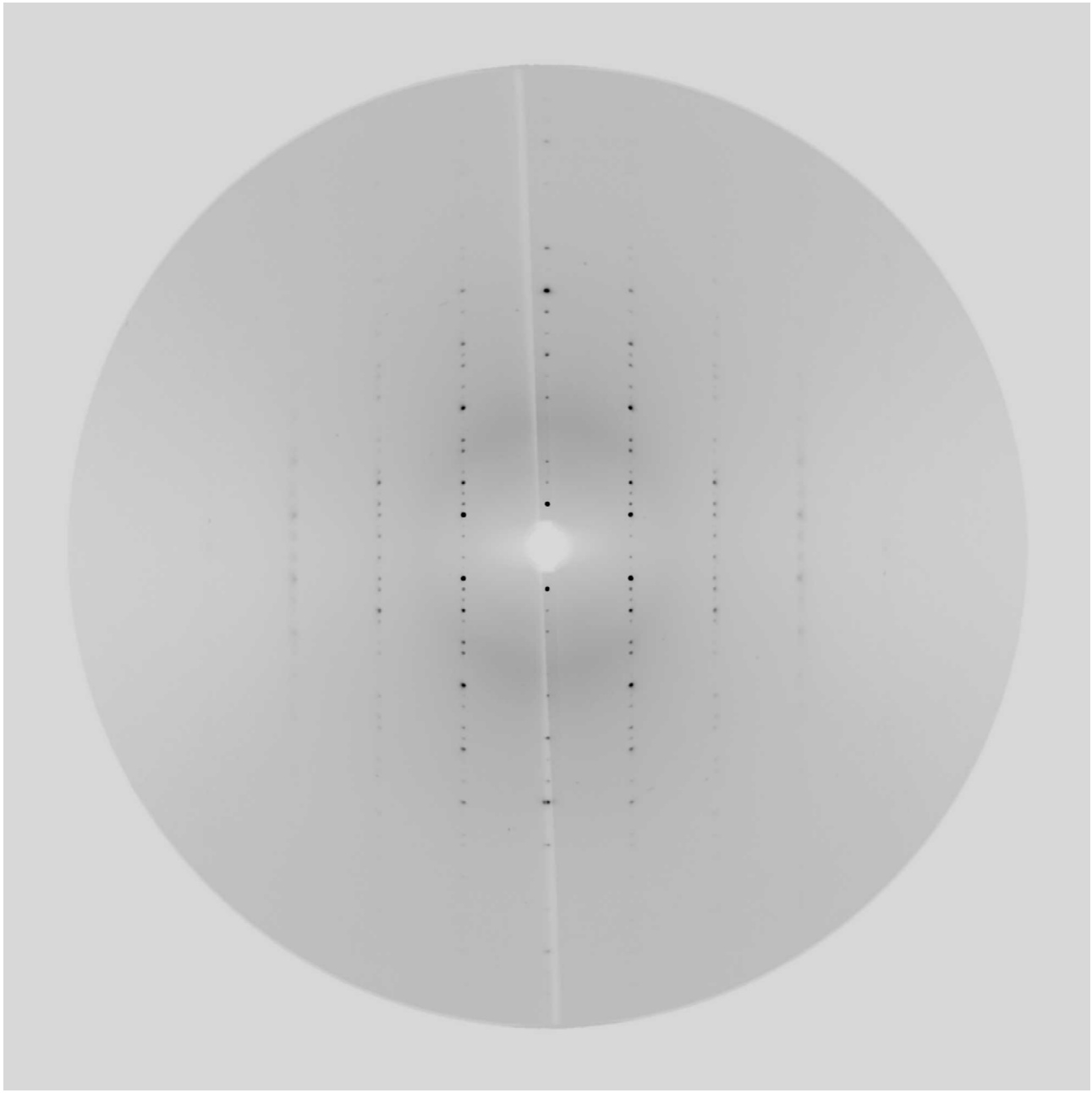


Figure SM4: Reconstrucrion of the reciprocal lattice of **21a** from experimental X-ray diffraction data along h0l direction.

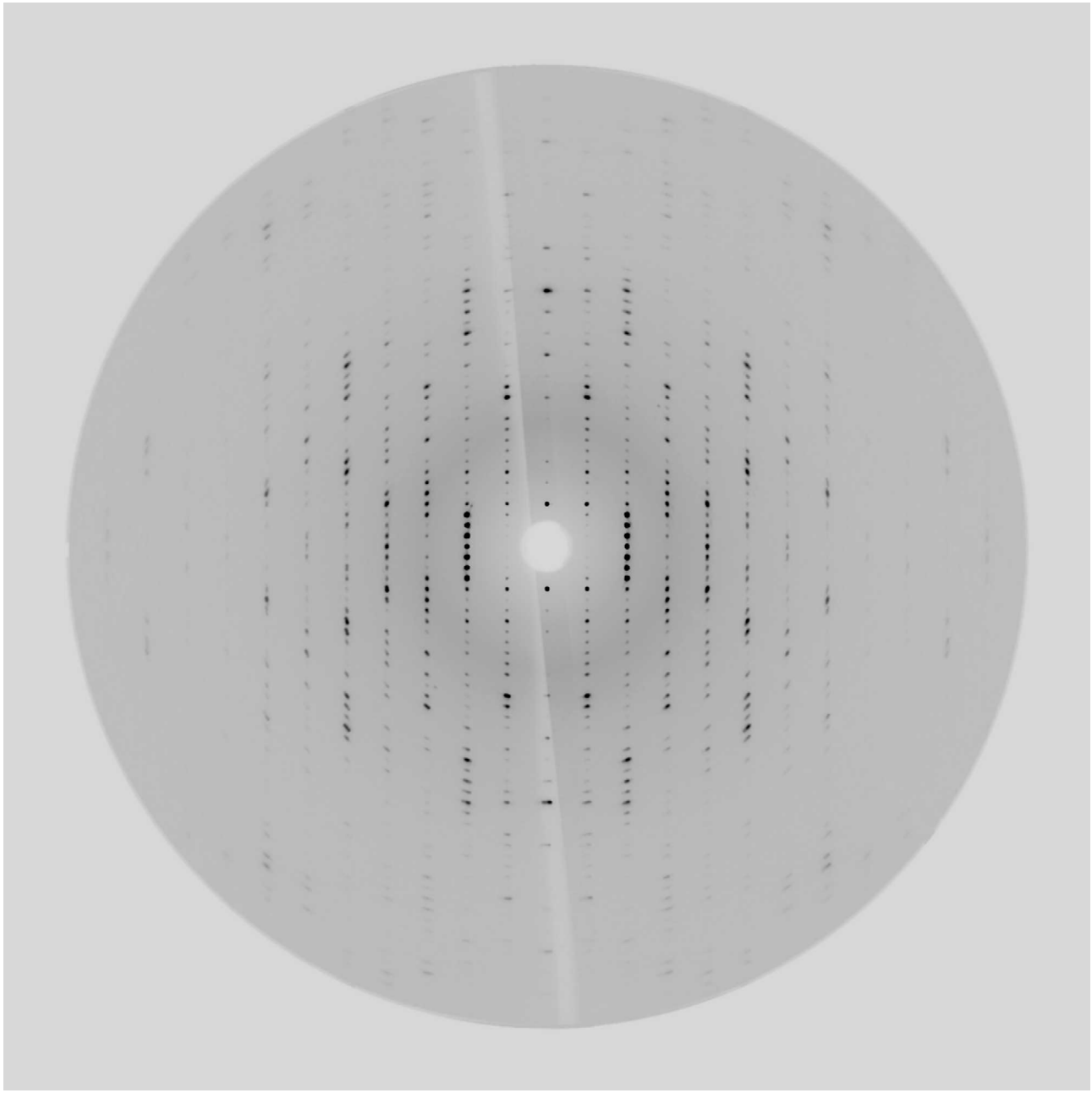


Figure SM5: Reconstrucrion of the reciprocal lattice of **21a** from experimental X-ray diffraction data along 0kl direction.