Supporting Information

A novel approach to indoloditerpenes by Nazarov photocyclization. Synthesis and biological investigations of terpendole E analogues.

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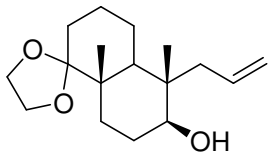
General

All reactions were run under an atmosphere of argon unless otherwise indicated. Room temperature refers to 22°C, ambient pressure to 1013 hPa. All chemicals were purchased from ABCR, Acros, Aldrich, Alfa Aesar, Fluorochem, Fluka, Merck and TCI Europe at highest commercially available purity and used as such. Chromatographic purification was performed as flash chromatography on Acros silica gel 35-70, 60 Å, using a forced flow of eluent (method of Still). Concentration under reduced pressure was performed by rotary evaporation at 40°C at the appropriate pressure. Yields refer to chromatographically purified and spectroscopically pure compounds. NMR spectra were recorded on a Varian Mercury plus 400 (operating at 400 MHz for ^{1}H, 100 MHz for ^{13}C acquisitions), a Varian Mercury plus 300 (operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C acquisitions) and a Varian Gemini 2000 (operating at 200 MHz for ^{1}H and 50 MHz for ^{13}C acquisitions) spectrometer. Chemical shifts δ are reported in ppm with the solvent resonance as the internal standard (d_1-chloroform: 7.260 (^{1}H-NMR), 77.16 (^{13}C-NMR). Coupling constants *J* are given in Hertz (Hz). Multiplicities are classified by the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = quintet and combinations thereof, or m = multiplet or br = broad signal. High resolution mass spectra were obtained on a Bruker Daltonics ESI-FT-ICR-MS APEX II. IR spectra were obtained on an ATI/MATTSON Genesis FT-IR as thin film (in CCl_4) or KBr-disk. Absorbance frequencies are reported in reciprocal centimetres (cm^{-1}). Melting points were measured on a Boetius-micro hot stage and are uncorrected. Optical rotation data was obtained with a Schmidt+Haensch Polartronic MHZ-8 at the sodium-D line (589 nm) using a 50 mm path-length cell in the solvent and concentration indicated.

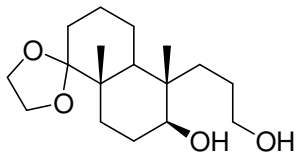
Experimental procedures

Alcohol (**14**)



To a solution of **2**[1] (10.52 g, 37.8 mmol) in ether (390 mL) at -78 ˚C was added LAH (1.0 M solution in ether, 38 mL, 38 mmol). The solution was warmed to room temperature and stirred for 16 h. To the reaction mixture was added saturated aqueous Rochelle salt and the mixture was diluted with ether. The organic phase was separated and the aqueous phase was extracted with ether (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10→20% EtOAc in hexane) to give **14** (10.64 g, quant) as a colorless oil: $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = -13 (c = 0.022 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 3439, 2945 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ5.91-5.84 (m, 1H), 5.10-5.06 (m, 2H), 3.94-3.88 (m, 3H), 3.85-3.79 (m, 1H), 3.50-3.46 (m, 1H), 2.27 (dd, 1H, *J* = 14, 7.2 Hz), 1.99 (dd, 1H, *J* = 14, 7 Hz), 1.67-1.30 (m, 12H), 1.07 (s, 3H), 0.84 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 135.4, 117.7, 113.4, 74.2, 65.5, 64.9, 43.7, 43.2, 42.8, 42.3, 30.6, 28.7, 27.0, 23.0, 20.5, 17.1, 16.0; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{28}O_3Na$: 303.1931, found: 303.1932.

Diol (**15**)

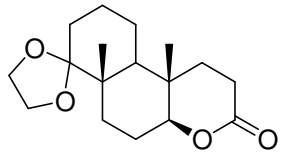


To a solution of **14** (10.16 g, 36.2 mmol) in THF (250 mL) at 0 ˚C was added BH_3•THF (1.0 M solution in THF, 145 mL, 145 mmol). After being stirring at the same temperature for 2.5 h, to the reaction mixture were added water (48 mL), 3 M aqueous NaOH (98 mL) and aqueous 30% H_2O_2 (113 mL). The mixture was allow to warm to room temperature and after being stirred for an additional 1 h, brine was added, and the mixture was diluted with EtOAc. The organic phase was separated and the aqueous phase was extracted

[1] Mewshaw, R.; Taylor, M.A.; Smith, A.B., III *J. Org. Chem.* **1989**, *54*, 3449-3462.

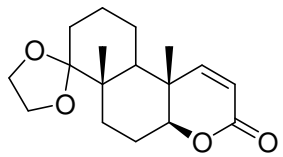
with EtOAc (3×). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (50→100% % EtOAc in hexane) to give **15** (8.46 g, 78%) as a colorless solid: mp 144-145 ˚C (diethyl ether); $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = -6 (c = 0.020 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 3375, 2942 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ3.94-3.89 (m, 3H), 3.83-3.81 (m, 1H), 3.65-3.58 (m, 2H), 3.46 (dd, 1H, *J* = 11, 4.5 Hz), 1.69-1.51 (m, 10H), 1.46-1.31 (m, 7H), 1.07 (s, 3H), 0.81 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 113.5, 73.2, 65.4, 64.9, 63.7, 43.1, 42.6, 41.0, 33.4, 30.6, 28.8, 27.1, 26.1, 23.1, 20.4, 17.2, 17.1; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{30}O_4Na$: 321.2036, found: 321.2039.

Lactone (3)



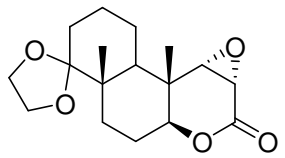
To a solution of **15** (7.0 g, 23.5 mmol) in CH_2Cl_2 (190 mL) were added bisacetoxyiodobenzene (22,6 g, 70.3 mmol) and TEMPO (0.72 g, 4.6 mmol) at room temperature. The reaction mixture was stirred for 6 h, and added saturated aqueous $Na_2S_2O_3$ and ether. The organic phase was separated and the aqueous phase was extracted with ether (2×). The combined organic extracts were washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (20→35% EtOAc in hexane) to give **3** (6.6 g, 95%) as a colorless oil: $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = -86.9 (c = 0.029 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2947, 1740, 1460 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.97-3.82 (m, 5H), 2.60-2.55 (m, 2H), 2.07-1.39 (m, 13H), 1.09 (s, 3H), 0.87 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.6, 112.9, 84.7, 65.4, 64.9, 48.8, 43.3, 36.7, 34.6, 30.4, 28.4, 27.2, 23.5, 23.0, 20.5, 17.0, 13.7; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{26}O_4Na$: 317.1723, found: 317.1722.

Unsaturated lactone (16)



To a solution of *N*,*N*-diisopropyl amine (3.1 mL, 21.7 mmol) in THF (130 mL) at 0 ˚C was added *n*-BuLi (2.30 M solution in hexane, 9.3 mL, 21.4 mmol). After 45 min, the solution was cooled to -78 ˚C, and a solution of **3** (4.41 g, 15 mmol) in THF (45 mL) and a solution of *N-tert*-butylbenzenesulfinimidoyl chloride[2] (5.35 g, 25 mmol) in THF (45 mL) were added. After being stirred for 1 h, the reaction was quenched by saturated aqueous $NaHCO_3$. The resultant was diluted with EtOAc and the organic phase was separated. The aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10→20% EtOAc in hexane) to give 1**6** (3.07 g, 70%) as colorless needles: mp 144-145 ˚C (hexane-EtOAc); $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = +5.1 (c = 0.018 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2958, 1708, 1628, 1129, 1089, 1036 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.00 (d, 1H, *J* = 10 Hz), 5.80 (d, 1H, *J* = 10 Hz), 4.03 (dd, 1H, *J* = 9, 7 Hz), 3.95-3.81 (m, 4H), 1.89-1.43 (m, 11H), 1.14 (s, 3H), 1.02 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 165.0, 157.1, 118.9, 112.8, 85.4, 65.4, 65.0, 43.9, 43.5, 39.3, 30.4, 28.8, 22.9, 22.8, 20.1, 17.9, 14.3; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{24}O_4Na$: 315.1567, found: 315.1570.

Epoxide (**4**)

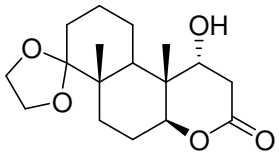


To a solution of 1**6** (4.84 g, 16.57 mmol) in MeOH-THF (3:1, 400 mL) were added aqueous 35% H_2O_2 (20.2 mL) and 6M aqueous NaOH (3.5 mL) at 0 ˚C. After being stirred at the same temperature for 2 h, to the reaction mixture were added H_2O, ether and 2M aqueous HCl. The organic phase was separated and the aqueous phase was extracted with ether (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10→30% EtOAc in hexane) to give **4** (4.64 g, 91%) as colorless plates: mp 182-183 ˚C (hexane-EtOAc); $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = -99 (c = 0.022 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2950, 1730 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.42 (dd, 1H, *J* = 11, 4.7 Hz), 3.96-3.91 (m, 3H), 3.86-3.80 (m, 1H), 3.53 (d, 1H, *J* = 3.7 Hz), 3.49 (d, 1H, *J* = 3.7 Hz), 1.93-1.89 (m, 1H),

[2] Barrett, A.G.M.; Gray, A.A.; Hill, M.S.; Hitchcock, P.B.; Procopiou, P.A.; White, A.J.P. *Inorg. Chem.* **2006**, *45*, 3352-3358.

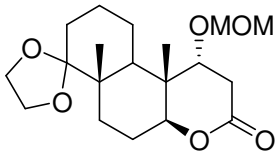
1.81-1.48 (m, 10H), 1,12 (s, 3H), 0.98 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ167.6, 112.6, 78.1, 65.5, 65.1, 59.1, 50.7, 43.7, 43.3, 39.2, 30.3, 28.6, 22.7, 22.4, 20.9, 17.8, 12.1; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{25}O_5$: 309.1697, found: 309.1699.

Alcohol (**17**)



To a mixture of $(PhSe)_2$ (20 g, 63.6 mmol) in EtOH (240 mL), $NaBH_4$ (4.88 g, 127.2 mmol) was added in batches at 0 ˚C. After being stirred at room temperature for 15 min, the solution was cooled down to 0 ˚C and AcOH (9.5 mL, 162.5 mmol) was added. After 10 min, a solution of **4** (4.76 g, 15.4 mmol) in THF-EtOH (1:1, 80 mL) was added at 0 ˚C and the solution was warmed to room temperature and stirred for 6 h. The reaction mixture was diluted with EtOAc into which oxygen was passed for 5 min and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography (20→66% EtOAc in hexane) to give **17** (4.29 g, 90%) as colorless needles: mp 197-199 ˚C (hexane-EtOAc); $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = -93 (c = 0.020 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 3380, 2934, 1715 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ4.43 (dd, 1H, *J* = 12, 4.2 Hz), 3.95-3.82 (m, 5H), 2.94 (dd, 1H, *J* = 19, 6 Hz), 2.52 (d, 1H, *J* = 19 Hz), 2.01-1.96 (m, 2H), 1.90-1.84 (m, 1H), 1.80-1.38 (m, 10H), 1,13 (s, 3H), 0.85 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ170.9, 112.9, 78.6, 68.8, 65.5, 65.0, 43.3, 40.7, 39.9, 37.7, 30.5, 28.0, 23.3, 22.8, 20.1, 17.2, 12.5; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{26}O_5Na$: 333.1672, found: 333.1674.

MOM ether (**5**)

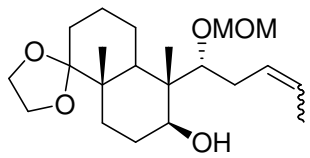


To a freshly prepared solution of MOMCl (3.5 mL, 46.65 mmol) in toluene (12.5 mL),[3] a solution of **17** (4.29 g, 13.83 mmol) in $(CH_2Cl)_2$ (125 mL) and *N,N*-diisopropylethylamine (15.4 mL, 85 mmol) were added at 0 °C. The reaction mixture was

[3] Berliner, M.; Belecki, K.; Paquette, W.D.; Wipf, P. *Org. Synth.* **2007**, *84*, 102-110.

stirred for 24 h at 60˚C, and added ice and EtOAc. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (33% EtOAc in hexane) to give **5** (4.46 g, 91%) as a colorless oil: $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = -95 (c = 0.013 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2947, 1736 1439 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ4.72 (d, 1H, *J* = 7.2 Hz), 4.59 (d, 1H, *J* = 7.2 Hz), 4.46 (dd, 1H, *J* = 12, 4.8 Hz), 3.95-3.90 (m, 3H), 3.83-3.82 (m, 1H), 3.70 (d, 1H, *J* = 8 Hz), 3.40 (s, 3H), 2.82 (dd, 1H, *J* = 19, 6 Hz), 2.65 (dd, 1H, *J* = 19, 1.6 Hz), 2.12 (dd, 1H, *J* = 11, 4 Hz), 1.85-1.84 (m, 1H), 1.73-1.59 (m, 4H), 1.52-1.39 (m, 5H), 1,14 (s, 3H), 0.88 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.6, 113.0, 95.7, 79.6, 74.2, 65.5, 65.0, 56.6, 43.3, 40.5, 39.6, 34.9, 30.5, 28.1, 23.4, 22.7, 20.0, 17.4, 12.5; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{30}O_6Na$: 377.1935, found: 377.1935.

Olefin (6)

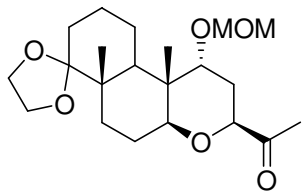


To a solution of **5** (0.59 g, 1.66 mmol) in toluene (6 mL) at -78 ˚C was added a solution of DIBAH (1.2M solution in toluene, 1.89 mL, 2.27 mmol) in toluene (6 mL) over 3 h. After 1 h at the same temperature to the reaction mixture was added saturated aqueous Rochelle salt and ether and the mixture was allowed to warm to room temperature. The organic phase was separated and the aqueous phase was extracted with ether (3×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give the corresponding lactol as white solid (0.59 g) which was used in the next step without further purification.

To a solution of ethyltriphenylphosphonium bromide (2.45 g, 6.63 mmol) in THF (75 mL) was added *n*-BuLi (2.50 M solution in hexane, 2.6 mL, 6.2 mmol) at 0 ˚C. After being stirred at the same temperature for 20 min, to the reaction mixture was added dropwise a solution of lactol (0.59 g, 1.66 mmol) in THF (23 mL). The reaction mixture was stirred at 40 °C for 3 h and to the reaction mixture were added water and ether. The organic phase was separated and the aqueous phase was extracted with ether (3×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10→20% EtOAc in hexane)

to give **6** (0.50 g, 81%) as a colorless oil; $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = -13 (c = 0.016 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 3472, 2947 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.53-5.48 (m, 2H), 4.65 (d, 1H, *J* = 6.8 Hz), 4.57 (d, 1H, *J* = 6.8 Hz), 3.94-3.88 (m, 3H), 3.83-3.78 (m, 1H), 3.66 (dd, 1H, *J* = 8, 6.8 Hz), 3.60-3.56 (m, 1H), 3.37 (s, 3H), 2.46-2.43 (m, 1H), 2.35-2.28 (m, 1H), 1.82-1.78 (m, 2H), 1.70-1.68 (m, 1H), 1.64 (d, 3H, *J* = 4.8 Hz), 1.61-1.46 (m, 6H), 1.39-1.36 (m, 2H), 1.08 (s, 3H), 0.93 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 128.9, 125.2, 113.4, 98.6, 85.3, 73.2, 65.4, 64.9, 56.4, 46.6, 43.4, 42.2, 30.6, 29.6, 28.6, 27.8, 22.9, 22.1, 17.1, 13.1, 12.7; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{21}H_{36}O_5Na$: 391.2455, found: 391.2459.

Ketone (**7**)



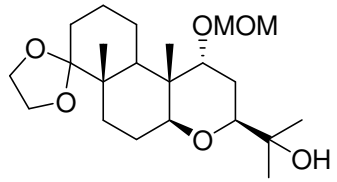
To a solution of **6** (1.04 g, 2.83 mmol) in CH_2Cl_2 (33 mL) was added mCPBA (1.73 g, 10.03 mmol) at 0°C. The reaction mixture was stirred for 1 h at room temperature, and to the solution was added $Sc(OTf)_3$ (0.07 g, 0.14 mmol). After 2 h, to the reaction mixture were added saturated aqueous $Na_2S_2O_3$ and ether. The organic phase was separated and the aqueous phase was extracted with ether (3×). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (35→50% EtOAc in hexane) to give a colorless oil.

The oil was dissolved with CH_2Cl_2 (17 mL), and added to a suspension of $NaHCO_3$ (3.72 g, 44.28 mmol) and Dess-Martin periodinane (2.68 g, 6.32 mmol) in CH_2Cl_2 (20 mL) at 0°C. The reaction mixture was stirred for 13 h at room temperature, and added saturated aqueous $Na_2S_2O_3$ and ether. The organic phase was separated and the aqueous phase was extracted with ether (2×). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*.

The residue was dissolved with MeOH-THF (3:1, 35 mL) and K_2CO_3 (1.2 g, 8.7 mmol) was added at room temperature. After being stirred for 3 h, to the reaction mixture was added water and ether. The organic phase was separated and the aqueous phase was extracted with ether (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column

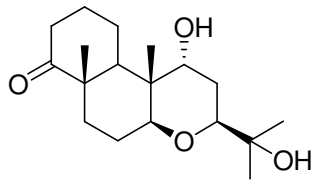
chromatography (25% EtOAc in hexane) to give **7** (0.91 g, 84%) as colorless needles: mp 155-156 °C (hexane-EtOAc); $[\alpha]_D^{23}$ (deg cm^3 g^{-1} dm^{-1}) = -101 (c = 0.028 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2955, 1716 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.73 (d, 1H, *J* = 7 Hz), 4.60 (d, 1H, *J* = 7 Hz), 4.16 (dd, 1H, *J* = 11.6, 3.4 Hz), 3.95-3.78 (m, 4H), 3.61-3.54 (m, 2H), 3.41 (s, 3H), 2.20 (s, 3H), 2.07 (dd, 1H, *J* = 13, 3 Hz), 1.90-1.77 (m, 2H), 1.67-1.54 (m, 5H), 1.52-1.39 (m, 4H), 1.32-1.20 (m, 1H), 1.11 (s, 3H), 0.89 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 210.2, 113.4, 95.9, 79.0, 77.9, 75.8, 65.5, 64.9, 56.5, 43.5, 40.6, 39.8, 30.6, 28.7, 28.4, 25.9, 24.0, 22.9, 19.3, 17.8, 13.9; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{21}H_{34}O_6Na$: 405.2248, found: 405.2249.

Alcohol (**18**)



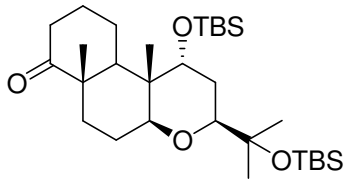
To a solution of **7** (0.75 g, 1.96 mmol) in THF (23 mL) was added MeMgCl (3M solution in THF, 2.0 mL, 6.0 mmol) at 0°C. The reaction mixture was stirred for 20 min at same temperature, and to the solution were added saturated aqueous NH_4Cl and EtOAc. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give **18** (0.78 g, quant.) as a colorless oil: $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = -42 (c = 0.030 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 3432, 2933, 1438 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.73 (d, 1H, *J* = 7 Hz), 4.61 (d, 1H, *J* = 7 Hz), 3.95-3.87 (m, 3H), 3.84-3.78 (m, 1H), 3.57-3.54 (m, 2H), 3.48 (dd, 1H, *J* = 12, 3 Hz), 3.39 (s, 3H), 2.63 (brs, 1H), 2.05 (dd, 1H, *J* = 12, 2 Hz), 1.81-1.74 (m, 1H), 1.70-1.60 (m, 3H), 1.57-1.55 (m, 3H), 1.49-1.37 (m, 4H), 1.31-1.23 (m, 1H), 1.17 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 0.84 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 113.5, 96.3, 79.3, 77.8, 71.8, 65.5, 64.9, 56.2, 43.5, 40.8, 39.8, 30.7, 28.7, 26.7, 26.3, 24.0, 23.8, 23.0, 19.5, 17.8, 13.8; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{22}H_{38}O_6Na$: 421.2561, found: 421.2564.

Keto-diol (**19**)



To a solution of **18** (0.62 g, 1.57 mmol) in MeOH (25 mL) was added conc. HCl (0.5 mL) at room temperature. The reaction mixture was stirred for 22 h at 60˚C, and added water and EtOAc. The organic phase was separated and the aqueous phase was extracted with EtOAc (3×). The combined organic extracts were washed with saturated aqueous $NaHCO_3$, brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (33→66% EtOAc in hexane) to give **19** (0.47 g, 97%) as white crystals: mp 193-194 ˚C (dichloromethane); $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = -41.6 (c = 0.005 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 3425, 2940, 1699 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.81 (m, 1H), 3.47-3.52 (m, 2H), 2.55 (dt, 1H, J = 13.5, 7.3 Hz), 2.20 (d, 1H, J = 13.5 Hz), 1.96-2.22 (m, 3H), 1.57-1.74 (m, 9H), 1.45 (dt, 1H, J = 14.4, 2.8 Hz), 1.18 (s, 6H), 1.12 (s, 3H), 0.93 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 215.0, 78.7, 76.8, 71.8, 69.9, 48.6, 44.5, 41.4, 37.7, 31.2, 30.2, 26.4, 26.1, 23.9, 23.7, 19.7, 19.5, 14.1; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{30}O_4Na$: 333.2024, found: 333.20354.

Ketone (**8**)

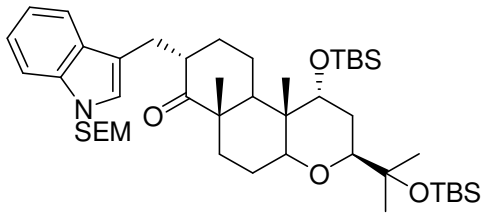


To a solution of **19** (0.45 g, 1.45 mmol) in CH_2Cl_2 (40 mL), 2,6-lutidine (2.5 ml, 21.58 mmol) was added under argon and the mixture was cooled to 0 °C. Subsequently, a solution of TBSOTf (2.1 mL, 9.1 mmol) in CH_2Cl_2 (10 mL) was added dropwise at 0 °C. After being stirred at the same temperature for 2 h, the reaction mixture was treated with saturated aqueous NH_4Cl (60 ml) and extracted with CH_2Cl_2. The aqueous phase was washed with CH_2Cl_2 (×3) and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*.

The crude residue was dissolved in methanol (35 ml) and THF (8 ml), *p*-toluenesulfonic acid monohydrate (276 mg, 1.45 mmol) was added and the reaction mixture was stirred at room temperature for 1 h. A spatula tip of solid sodium bicarbonate was added

to quench the reaction and the solvent was removed *in vacuo*. The oily residue was diluted with dichloromethane and filtered through a path of Celite. The filtrate was concentrated and the crude residue was purified by flash column chromatography (5→30% EtOAc in hexane) to give **8** (0.70 g, 90%) as a white solid: mp 149-151 °C (dichloromethane); $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = -59.2 (c = 0.010 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2954, 2935, 2858, 1700, 1471, 1254, 1094, 836, 773 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.77 (brs, 1H), 3.44 (ddd, 2H, *J* = 20.7, 11.7, 2.9 Hz), 2.55 (dt, 1H, *J* = 13.3, 6.8 Hz), 2.19 (d, 1H, *J* = 13.3 Hz), 2.00-2.04 (m, 1H), 1.78-1.85 (m, 1H), 1.51-1.72 (m, 10H), 1.20 (s, 1H), 1.18 (s, 3H), 1.17 (s, 3H), 0.91 (s, 3H), 0.88 (s, 9H), 0.84 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.00 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 215.2, 79.1, 76.0, 74.7, 71.2, 48.5, 44.1, 41.9, 37.4, 31.1, 29.0, 27.5, 26.0(x3 C), 25.9(x3 C), 25.8, 25.1, 23.7, 19.5, 19.2, 18.1(x2 C), 14.0, -2.1(x2 C), -3.7, -5.0; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{30}H_{58}O_4Si_2Na$: 561.3771, found: 561.3766.

Keto-indole (**10**)



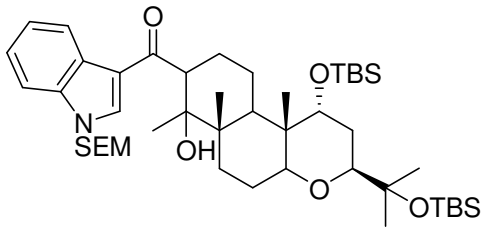
To a solution of **8** (300 mg, 0.56 mmol) and **9**[4] (155 mg, 0.56 mmol) in benzene (3.6 mL) potassium *tert*-butoxyde (65 mg, 0.56 mmol) was added. After being stirred for 10 min at room temperature, the solution was heated at 90°C. After 3.5 h, the mixture was allowed to warm to room temperature and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (5→15% Et_2O in hexane) to give a yellowish oil and recovered **8** (72 mg, 24%).

The oil was dissolved in EtOAc (40 mL) and palladium (82 mg, 10% on carbon) was added. After stirring the suspension under hydrogen atmosphere for 2 h at room temperature it was filtered through a path of Celite and washed with EtOAc (200 mL). The filtrate was concentrated and the crude residue was purified by flash column chromatography (2→10% EtOAc in hexane) to give **10** (291 mg, 68%) as colorless oil: $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = -56.4 (c = 0.010 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2951, 2933, 2857, 1706, 1463, 1250, 1092, 835, 773 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.8 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 1H),

[4] Fresneda, P.M.; Molina, P.; Sanz, M.A. *Synlett* **2000**, 1190-1192.

7.22 (t, J = 7.4 Hz, 1H), 7.12 (t, J = 7.4 Hz, 1H), 6.97 (s, 1H), 5.43 (s, 2H), 3.74 (s, 1H), 3.54–3.37 (m, 3H), 3.27 (dd, J = 14.7, 4.5 Hz, 1H), 2.92 (m, 1H), 2.52 (dd, J = 14.8, 8.2 Hz, 1H), 2.17–2.02 (m, 1H), 1.87–1.43 (m, 11H), 1.20 (s, 3H), 1.17 (s, 6H), 0.88 (m, 14H), 0.84 (s, 12H), 0.08 (s, 3H), 0.06 (s, 6H), -0.03 (s, 3H), -0.06 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 215.5, 136.8, 129.0, 126.5, 122.0, 119.7, 119.0, 114.4, 110.0, 79.3, 76.2, 75.5, 74.9, 71.3, 65.8, 48.7, 46.0, 45.2, 42.1, 33.4, 31.4, 29.1, 27.6, 26.1(x3 C), 26.0(x3 C), 25.3, 25.0, 23.8, 19.9, 19.6(x2 C), 18.3, 17.9, 14.0, -1.3(x3 C), -1.9(x2 C), -3.5, -4.7; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{45}H_{79}NO_5Si_3Na$: 820.5164, found: 820.5158.

Hydroxyketo-indole (**20**)

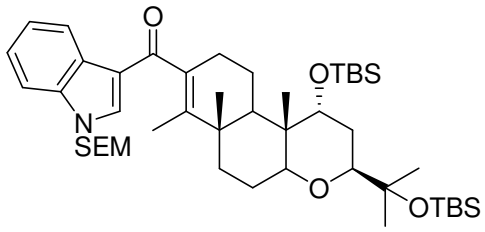


To a solution of **10** (296 mg, 0.37 mmol) in THF (14 mL) was added MeLi (1.6M solution in diethyl ether, 0.5 mL, 0.8 mmol) at -78˚C. The reaction mixture was stirred for 20 min at same temperature and then the cooling bath was removed. After 10 min saturated aqueous NH_4Cl and EtOAc were added to the solution. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give a colorless oil.

The oil was dissolved in THF (10 mL) and pH=7 phosphate buffer (1.8 mL), and then a solution of DDQ (227 mg, 1 mmol) in THF (8 mL) was added at 0°C. The reaction mixture was stirred for 30 min at room temperature, and to the solution were added 3 M aqueous NaOH and EtOAc. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (2×), brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (5→20% EtOAc in hexane) to give **20** (264 mg, 88%) as a colorless oil: $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = -69.6 (c = 0.010 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 3442, 2952, 2932, 2856, 1625, 1529, 1462, 1382, 1249, 1091, 835, 771 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.37–8.40 (m, 1H), 7.84 (s, 1H), 7.54–7.49 (m, 1H), 7.37–7.31 (m, 2H), 5.54 (s, 2H), 4.70 (br, 1H), 3.78 (s, 1H), 3.60 (dd, J = 11.1, 5.1 Hz, 1H),

3.54 (t, J = 8.1 Hz, 2H), 3.48 (dd, J = 11.9, 2.5 Hz, 1H), 3.35 (dd, J = 13.0, 4.0 Hz, 1H), 2.73 (dd, J = 12.5, 2.8 Hz, 1H), 2.07–1.99 (m, 1H), 1.88–1.67 (m, 3H), 1.64–1.45 (m, 4H), 1.44–1.34 (m, 2H), 1.21 (s, 3H), 1.17 (s, 3H), 1.11 (s, 6H), 0.98 (s, 9H), 0.93 (t, J = 8.2 Hz, 2H), 0.85 (s, 12H), 0.09 (s, 3H), 0.07 (s, 3H), 0.06 (s, 6H), -0.04 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 202.9, 137.3, 134.7, 126.6, 124.3, 123.5, 123.0, 118.0, 110.6, 79.2, 76.4, 76.3, 76.1, 75.1, 71.2, 66.8, 49.3, 41.9, 41.0, 35.0, 29.5, 29.1, 27.7, 27.4, 26.2(x3 C), 26.1(x3 C), 25.5, 24.3, 22.0, 19.4, 18.3(x2 C), 17.8, 17.2, 13.8, -1.3(x3 C), -2(x2 C), -3.3, -4.8; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{46}H_{81}NO_6Si_3Na$: 850.6259, found: 850.5264.

Enone (**11**)

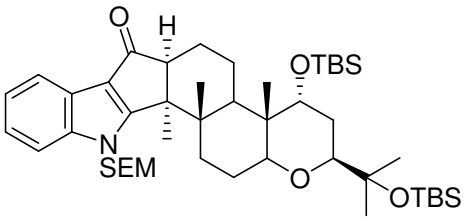


To a solution of **20** (237 mg, 0.28 mmol) in toluene (20 mL), Burgess reagent (300 mg, 1.26 mmol) was added and the resulting mixture was heated at 90°C for 1.5 h. The mixture was allowed to warm to room temperature saturated aqueous NH_4Cl and EtOAc were added to the solution. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give a colorless oil.

The oil was dissolved in *t*-BuOH (20 mL) and potassium *tert*-butoxyde (157 mg, 1.4 mmol) was added. After being stirred at 75°C for 2 h, the resulting mixture was allowed to warm to room temperature and water and EtOAc were added. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (4→10% Et_2O in hexane) to give **11** (119 mg, 51%) as a colorless oil: $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = -19.2 (c = 0.010 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2952, 2855, 1621, 1524, 1461, 1385, 1250, 1091, 834, 772 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, J = 6.3, 2.8 Hz, 1H), 7.58 (s, 1H), 7.54–7.48 (m, 1H), 7.36–7.30 (m, 2H), 5.53 (d, J = 10.9 Hz, 1H), 5.43 (d, J = 10.9 Hz, 1H), 3.87 (s, 1H), 3.68–3.58 (m, 1H), 3.53–3.47 (m, 3H), 2.46 (dd, J = 17.9, 6.3 Hz, 1H), 2.31 (dt, J = 18.1, 8.1 Hz, 1H), 1.99 – 1.89 (m, 1H), 1.88–1.77 (m, 2H), 1.70 – 1.55 (m, 6H), 1.53 (s, 3H), 1.37–1.29 (m,

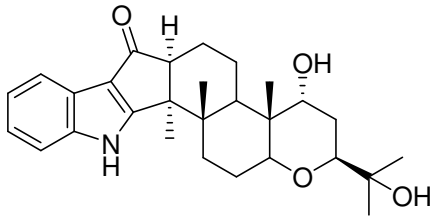
1H), 1.23 (s, 3H), 1.19 (s, 3H), 1.15 (s, 3H), 0.96 (s, 9H), 0.93 (m, 2H), 0.89 (s, 3H), 0.86 (s, 9H), 0.10 (s, 6H), 0.08 (s, 3H), 0.04 (s, 3H), -0.05 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 197.2, 140.6, 137.3, 136.3, 133.2, 126.7, 123.9, 123.1, 122.8, 117.2, 110.5, 79.5, 76.6, 76.5, 75.0, 71.1, 66.5, 41.6, 41.3, 38.0, 34.9, 29.4, 28.2, 27.5, 26.4(x3 C), 26.1(x3 C), 25.4, 24.5, 20.5, 18.5, 18.3, 17.9, 16.7, 15.1, 13.8, -1.3(x3 C), -1.9(x2 C), -3.2, -4.7; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{46}H_{80}NO_5Si_3$: 810.5344, found: 810.5334.

Ketone (**12**)



A solution of **11** (71 mg, 87 μmol) in acetonitrile (20 mL) was degassed by bubbling argon through the solution for 30 min. The solution was then irradiated at 23°C in a Rayonet RPR-100 photochemical reactor at 350 nm for 5.5 h and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (5→15% EtOAc in hexane) to give **12** (57 mg, 80%) as a colorless oil: $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = -14.4 (c = 0.005 g cm^{-3} in $CHCl_3$); IR (film) ν_{max} 2954, 2929, 2856, 1694, 1460, 1387, 1250, 1092, 836, 786 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.96–7.89 (m, 1H), 7.46 (dd, *J* = 6.3, 2.8 Hz, 1H), 7.35–7.21 (m, 2H), 5.58 (d, *J* = 10.2 Hz, 1H), 5.50 (d, *J* = 10.2 Hz, 1H), 3.79 (s, 1H), 3.60–3.54 (m, 3H), 3.46 (dd, *J* = 11.9, 2.7 Hz, 1H), 2.81–2.73 (m, 1H), 2.52 (d, *J* = 14.5 Hz, 1H), 2.12–2.01 (m, 1H), 1.99–1.87 (m, 1H), 1.87–1.75 (m, 1H), 1.71 (s, 3H), 1.67–1.45 (m, 4H), 1.38–1.34 (m, 1H), 1.20 (s, 3H), 1.15 (s, 3H), 0.99 (s, 9H), 0.97–0.87 (m, 4H), 0.84 (s, 9H), 0.80 (s, 3H), 0.44 (s, 3H), 0.12 (s, 6H), 0.07 (s, 3H), 0.06 (s, 3H), -0.04 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 196.2, 168.2, 142.2, 123.6, 122.8, 121.4, 121.3, 121.2, 111.4, 79.3, 76.3, 74.9, 74.8, 71.5, 66.5, 61.5, 51.0, 42.7, 41.6, 36.3, 33.6, 29.4, 27.5, 26.3(x3 C), 26.1(x4 C), 25.2, 24.6, 20.6, 19.8, 19.4, 18.3, 18.1, 14.4, -1.3(x3 C), -1.9(x2 C), -3.7, -4.4; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{46}H_{79}NO_5Si_3$: 810.5344, found: 810.5339.

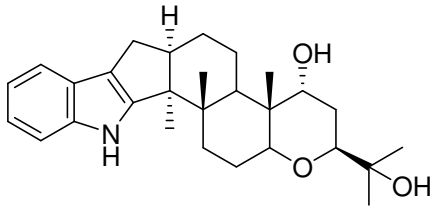
Ketone (**13**)



To a solution of **12** (20 mg, 24 μmol) and ethylenediamine (0.06 mL, 1.11 mmol) in DMF (2 mL) at room temperature, TBAF (1M in THF, 0.12 mL, 0.12 mmol) was added dropwise and the resulting mixture was heated at 80°C for 20 h. The mixture was allowed to warm to room temperature and saturated aqueous NH_4Cl and EtOAc were added to the solution. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with 2M aqueous HCl, brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give a yellowish solid.

The solid was dissolved in ACN (4 mL) and a solution of hydrofluoric acid (50%wt in water, 512 mg) in ACN (4 mL) was added. After being stirred at room temperature for 17 h, the solution was diluted with EtOAc (20 mL) and saturated aqueous $NaHCO_3$ was added. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (33→66% EtOAc in hexane) to give **13** (9.5 mg, 88%) as a white solid: mp 352-354 ˚C (chloroform); $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = +12 (c = 0.002 g cm^{-3} in $CHCl_3$); IR (KBr) ν_{max} 3470, 3427, 2950, 2855, 1693, 1254 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD) δ 7.80 (d, J = 7.2 Hz, 1H), 7.42 (d, J = 7.7 Hz, 1H), 7.26–7.10 (m, 2H), 3.73 (d, J = 12.8 Hz, 1H), 3.56 (dd, J = 9.9, 2.7 Hz, 2H), 2.79 (dd, J = 8.8, 3.0 Hz, 1H), 2.35 (dd, J = 11.5, 5.9 Hz, 1H), 2.19 (dd, J = 12.1, 3.3 Hz, 1H), 2.01 – 1.92 (m, 2H), 1.88–1.83 (m, 1H), 1.83–1.72 (m, 1H), 1.63 (s, 3H), 1.58–1.48 (m, 3H), 1.38–1.24 (m, 3H), 1.16 (s, 6H), 0.86 (s, 3H), 0.44 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 199.9, 172.4, 143.3, 124.4, 123.0, 122.4, 121.5, 119.7, 113.4, 80.4, 78.7, 72.8, 70.7, 62.5, 49.9, 42.4, 41.9, 37.7, 34.3, 30.8, 25.7, 25.3, 25.2, 21.5, 21.4, 20.8, 19.0, 14.7; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{28}H_{37}NO_4Na$: 474.2620, found: 474.2615.

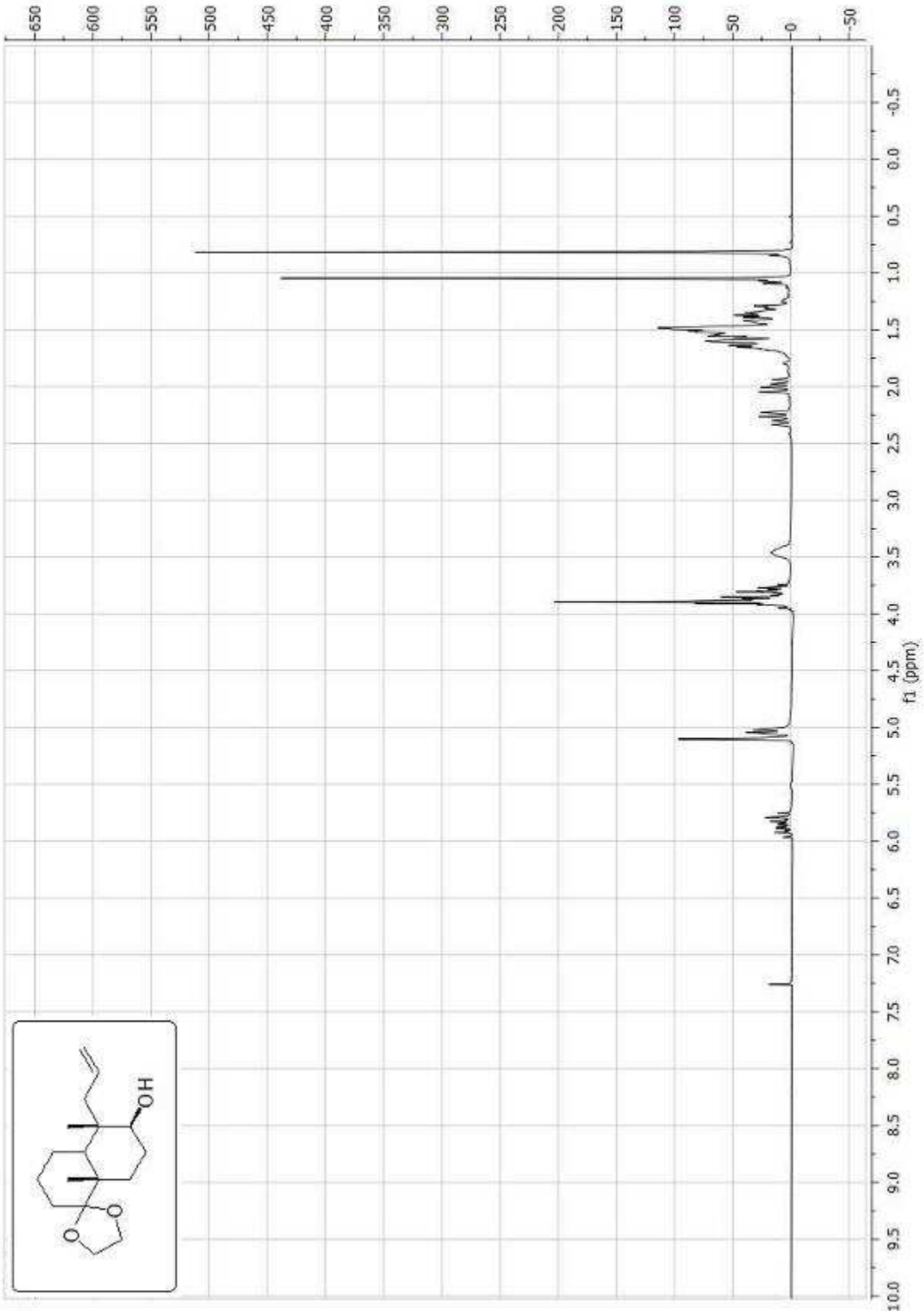
16-*epi*-Terpendole E



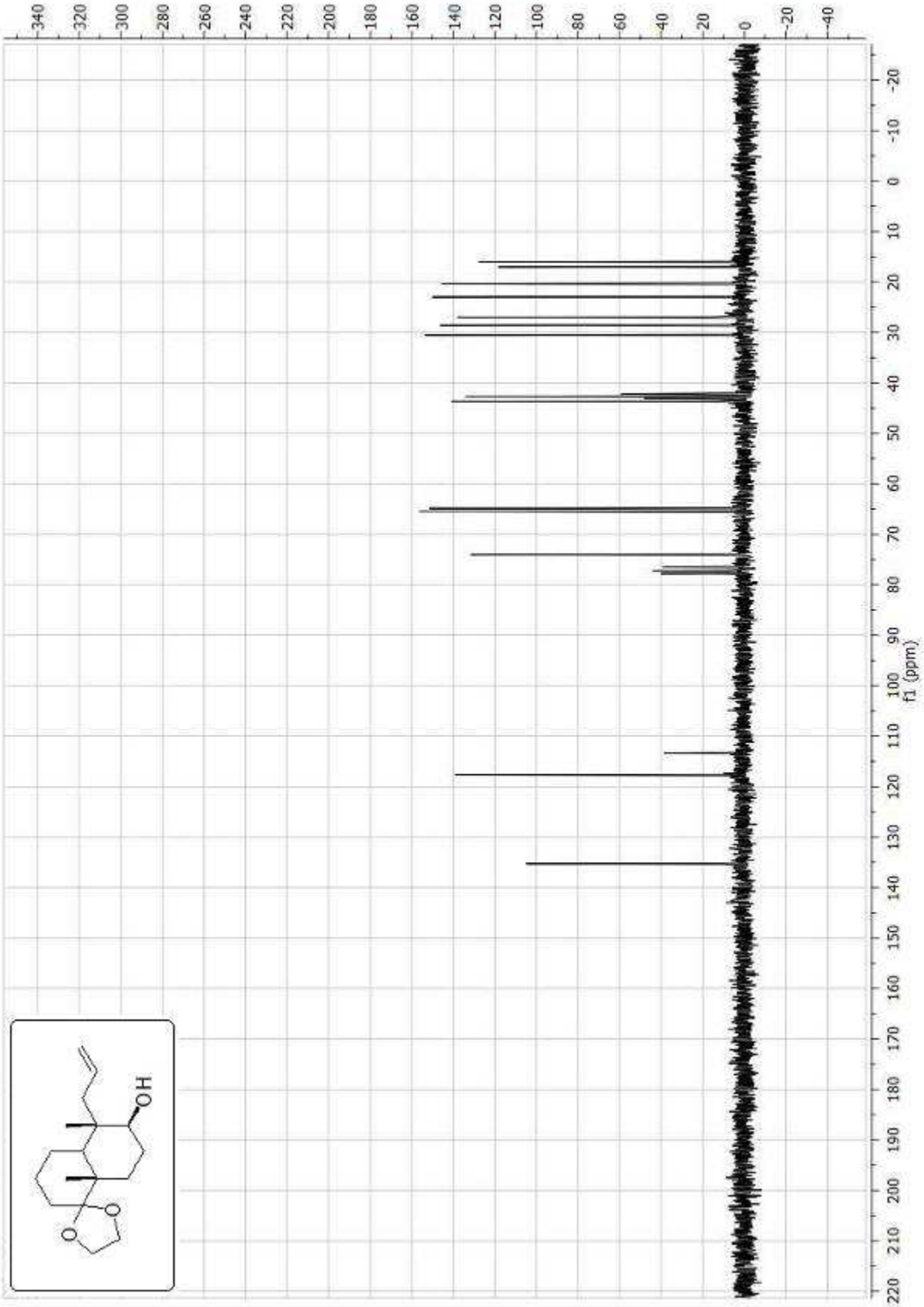
To a solution of **13** (6.3 mg, 14 μmol) in THF (1 mL) at 0°C were added an excess of lithium borohydride and *i*-PrOH (0.01 mL). The solution was warmed to room temperature and stirred for 18 h. To the reaction mixture were added saturated aqueous $NaHCO_3$ and EtOAc, the organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give a colorless solid.

The solid was dissolved in EtOAc (1 mL) and palladium (2 mg, 10% on carbon) was added. After stirring the suspension under hydrogen atmosphere for 2 h at room temperature it was filtered through a path of Celite and washed with EtOAc (20 mL). The filtrate was concentrated and the crude residue was purified by flash column chromatography (33→66% EtOAc in hexane) to give **16-*epi*-terpendole E** (4.5 mg, 74%) as a white solid: mp 257-259 °C (chloroform); $[\alpha]_D^{22}$ (deg cm^3 g^{-1} dm^{-1}) = + 58.8 (c = 0.002 g cm^{-3} in $CHCl_3$); IR (KBr) ν_{max} 3473, 3424, 2953, 2858, 1243 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD) δ 10.16 (s, 1H), 7.32–7.26 (m, 2H), 6.98–6.90 (m, 2H), 3.78 (s, 1H), 3.60–3.46 (m, 2H), 2.78–2.64 (m, 2H), 2.61–2.54 (m, 1H), 2.11–2.02 (m, 1H), 1.98–1.79 (m, 4H), 1.61–1.50 (m, 6H), 1.48 (s, 3H), 1.15 (s, 3H), 0.87 (s, 3H), 0.51 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 149.7, 140.5, 124.7, 119.5, 118.4, 117.9, 116.4, 111.3, 79.2, 77.8, 71.6, 69.8, 54.0, 50.1, 41.7, 40.6, 37.2, 34.1, 31.3, 29.7, 29.6, 26.4, 24.6, 24.1, 23.9, 20.8, 17.9, 13.6; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{28}H_{39}NO_3Na$: 460.2828, found: 460.2819.

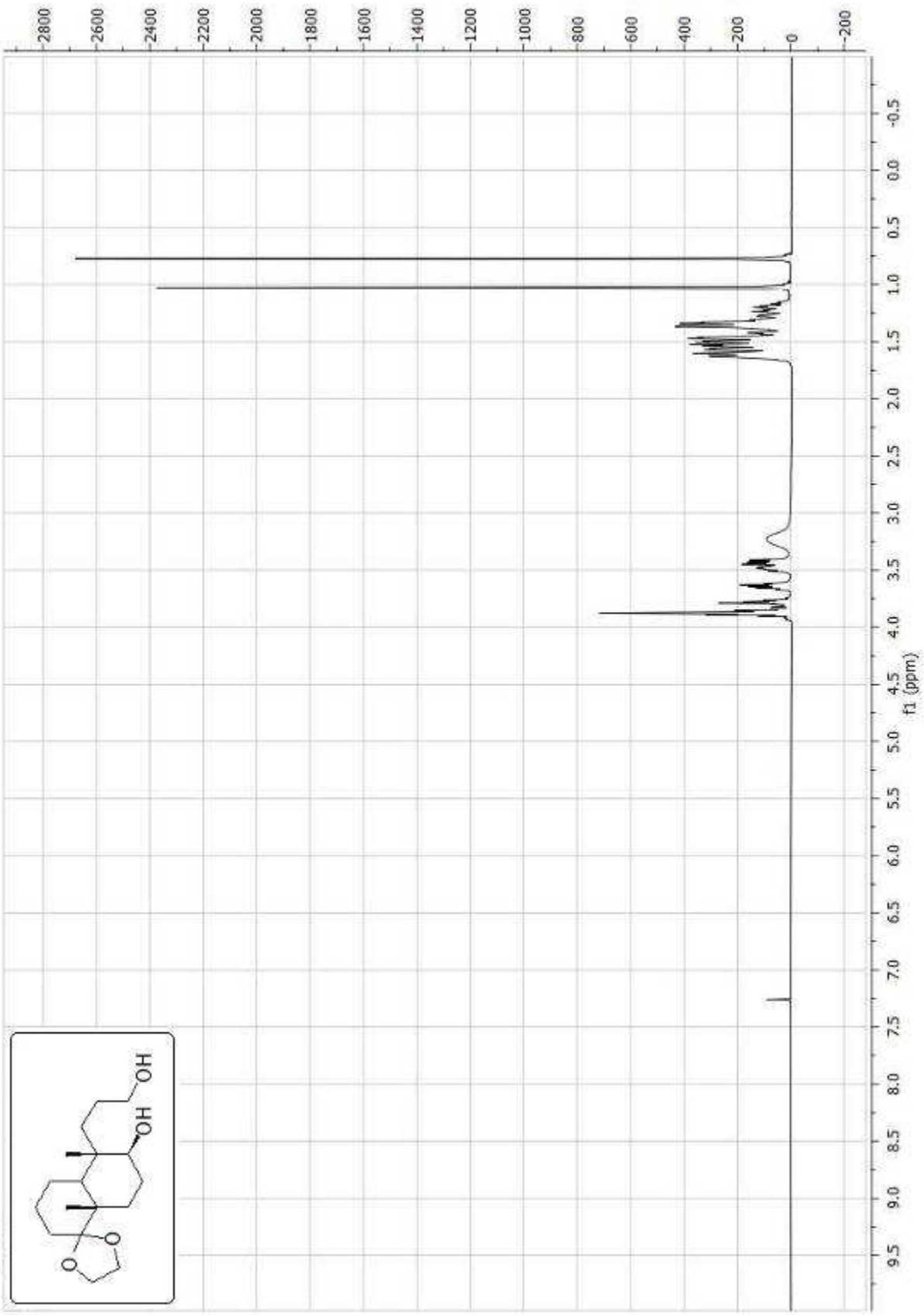
Alcohol (14)



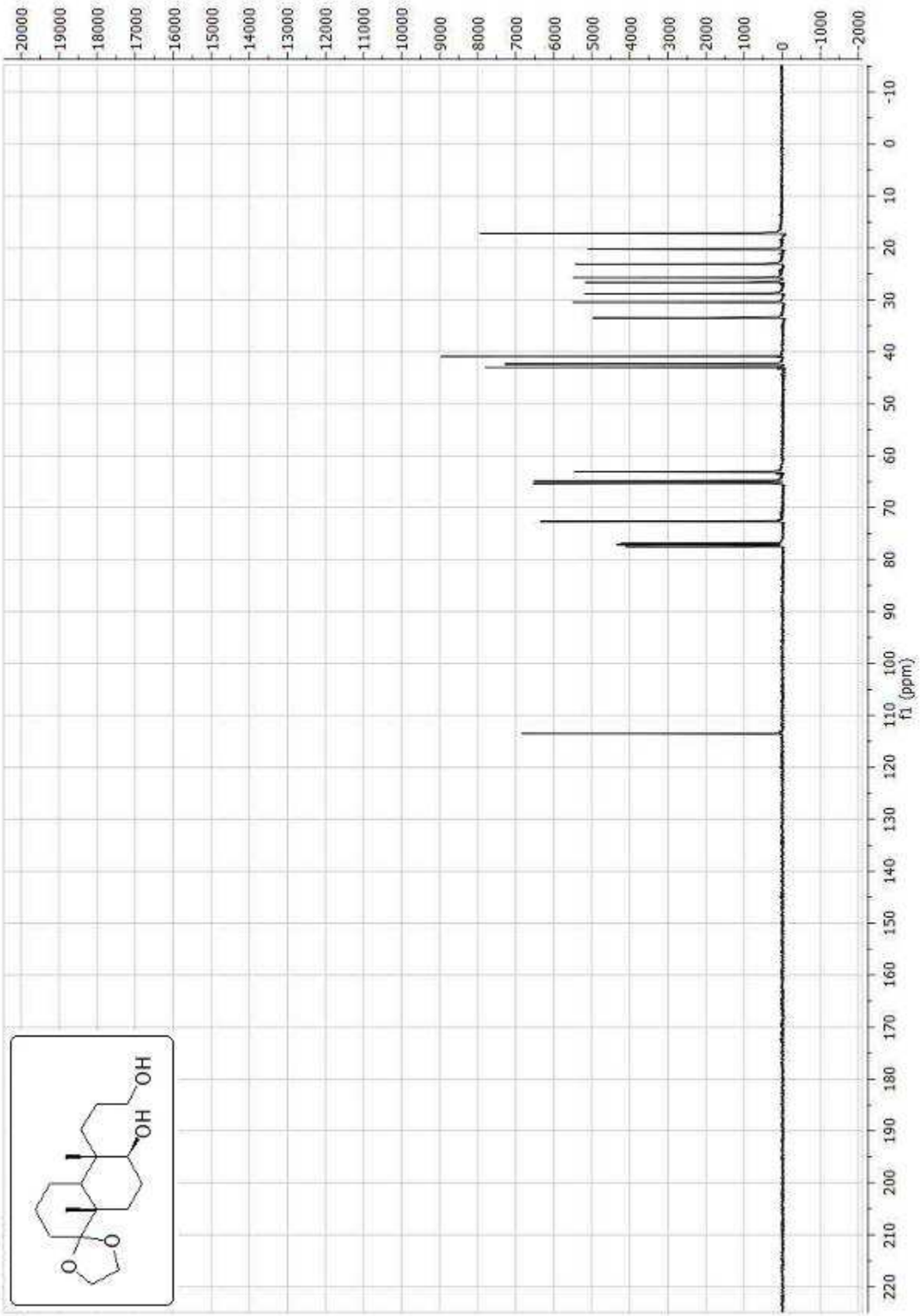
Alcohol (14)



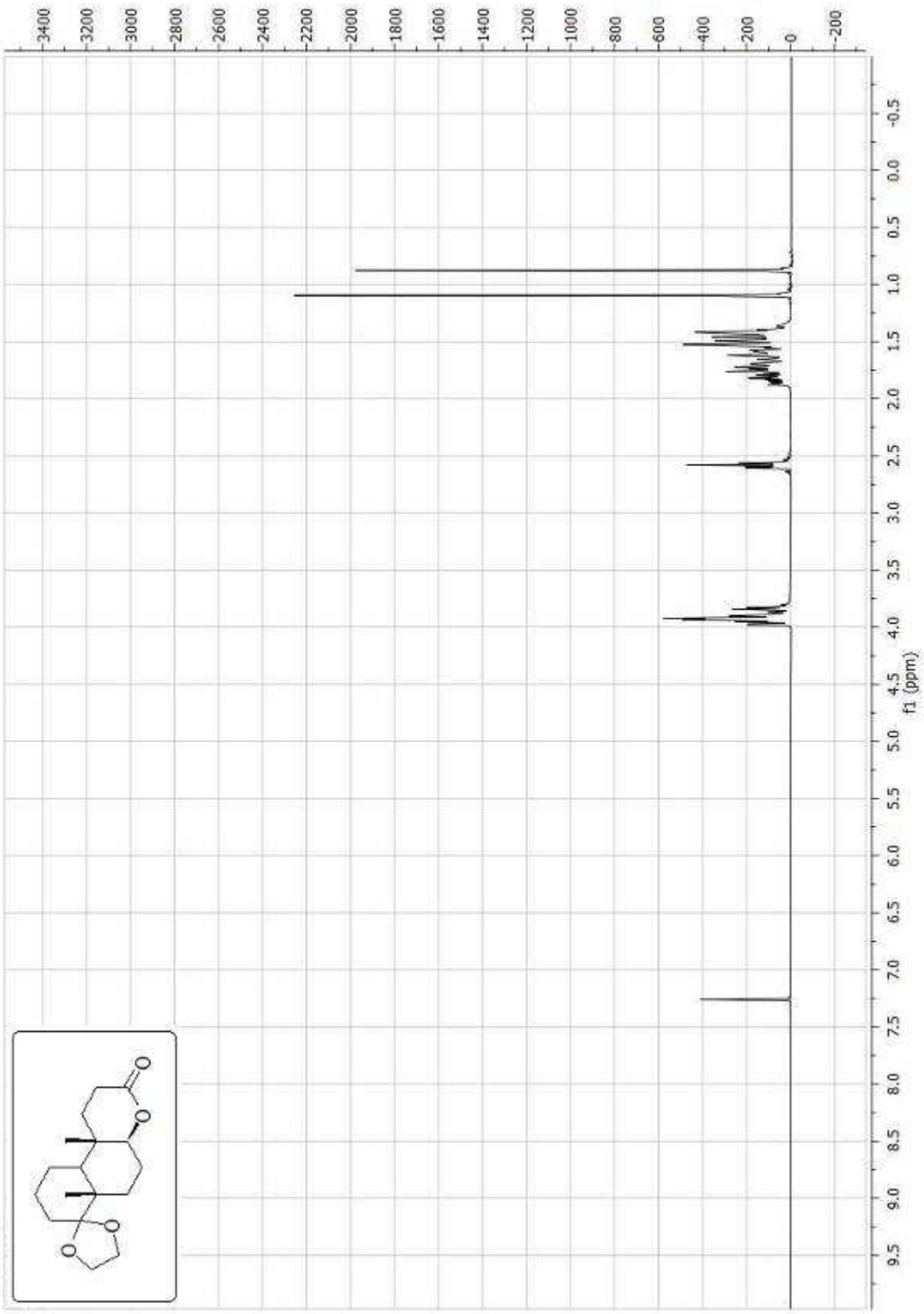
Diol (15)



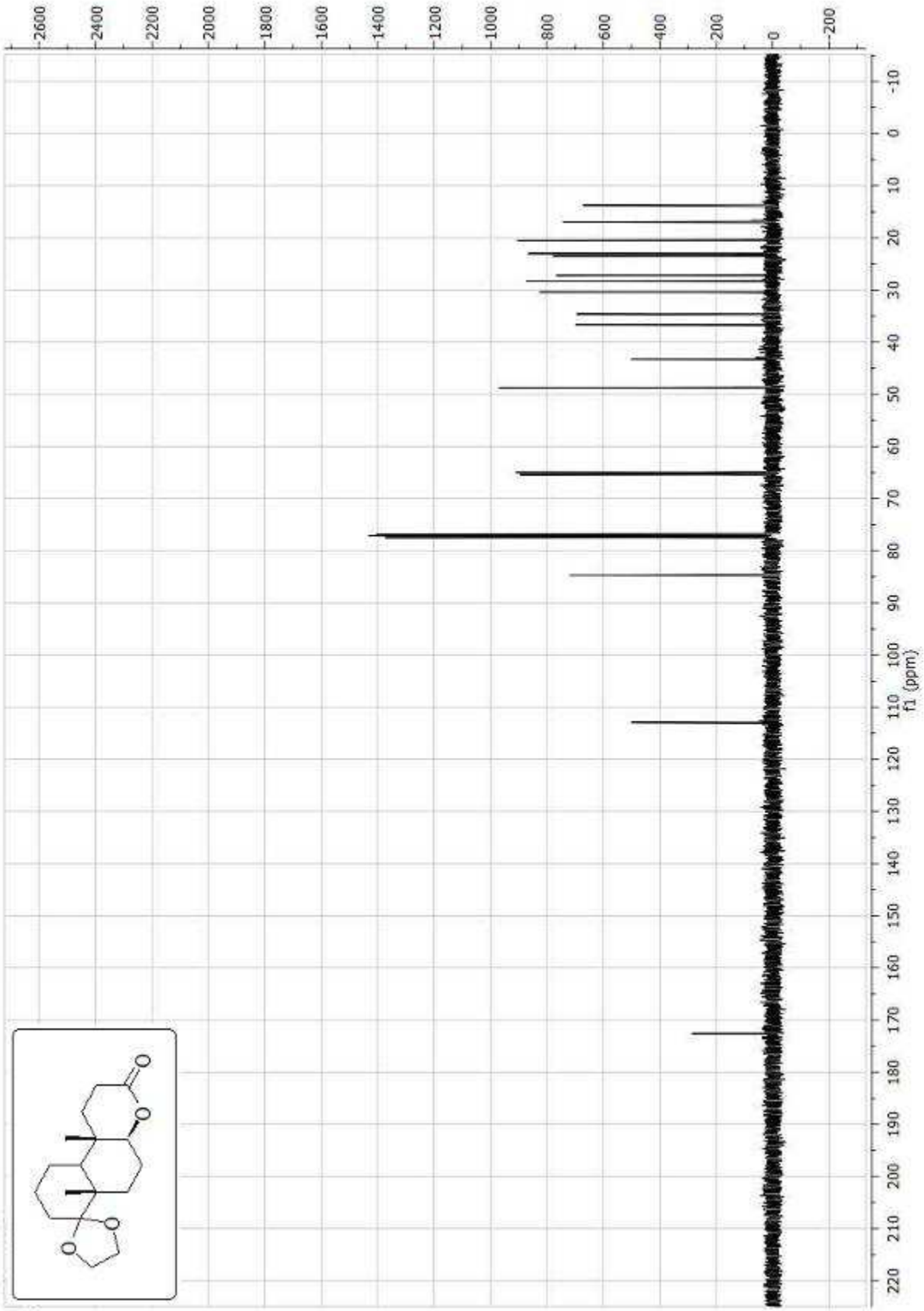
Diol (15)



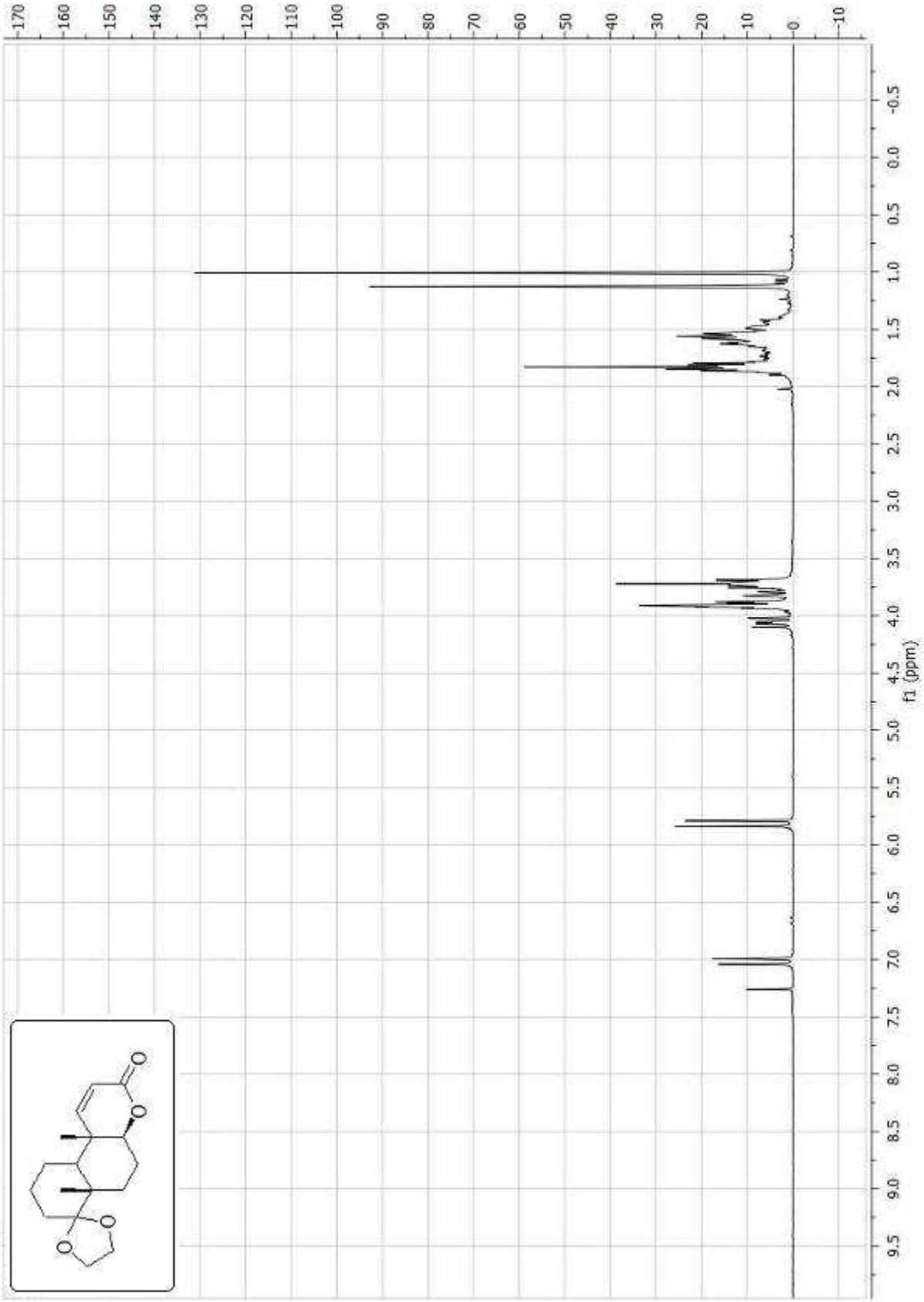
Lactone (3)



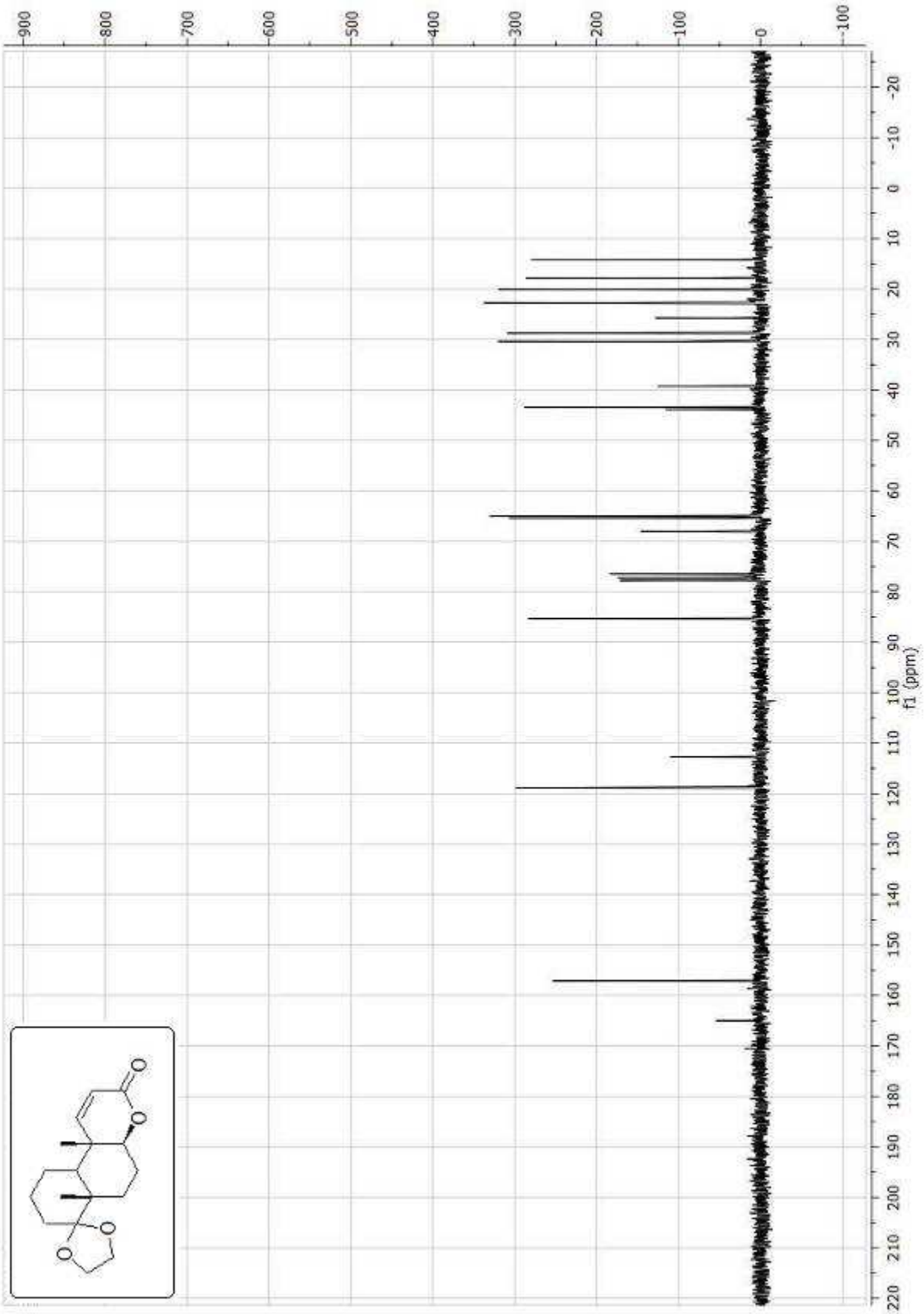
Lactone (3)



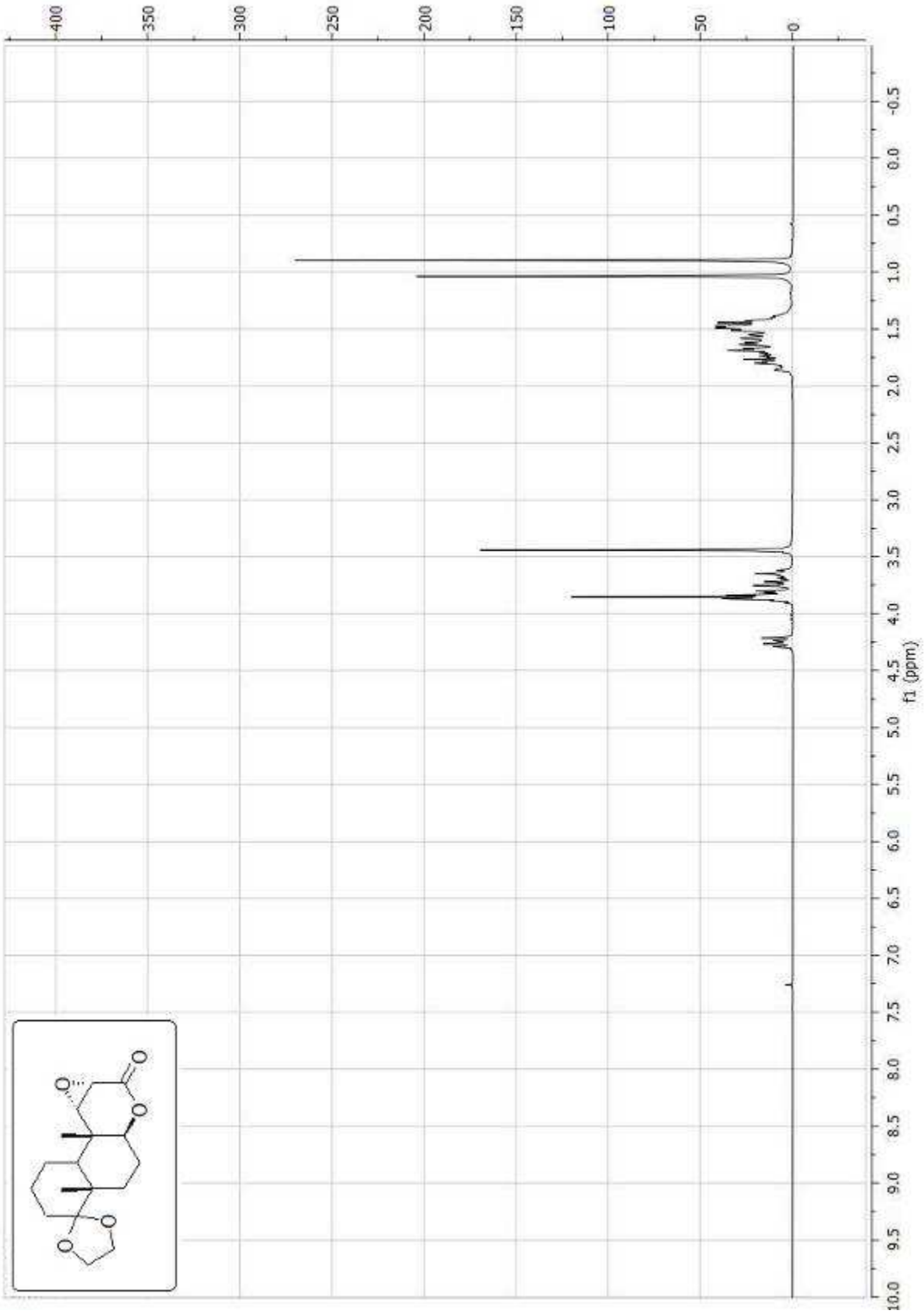
Unsaturated lactone (16)



Unsaturated lactone (16)



Epoxide (4)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3.0
3.5
4.0
4.5
5.0
5.5
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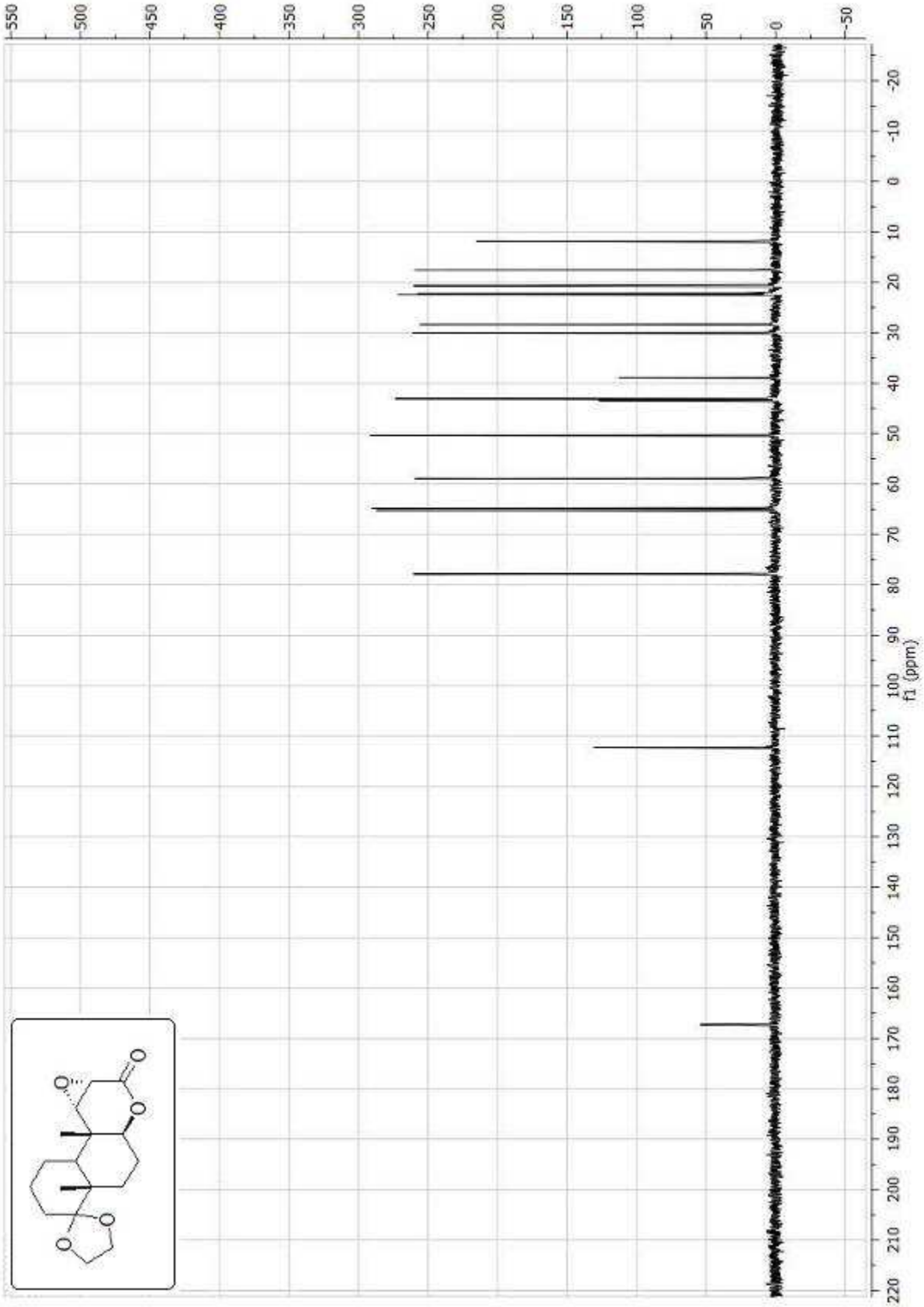
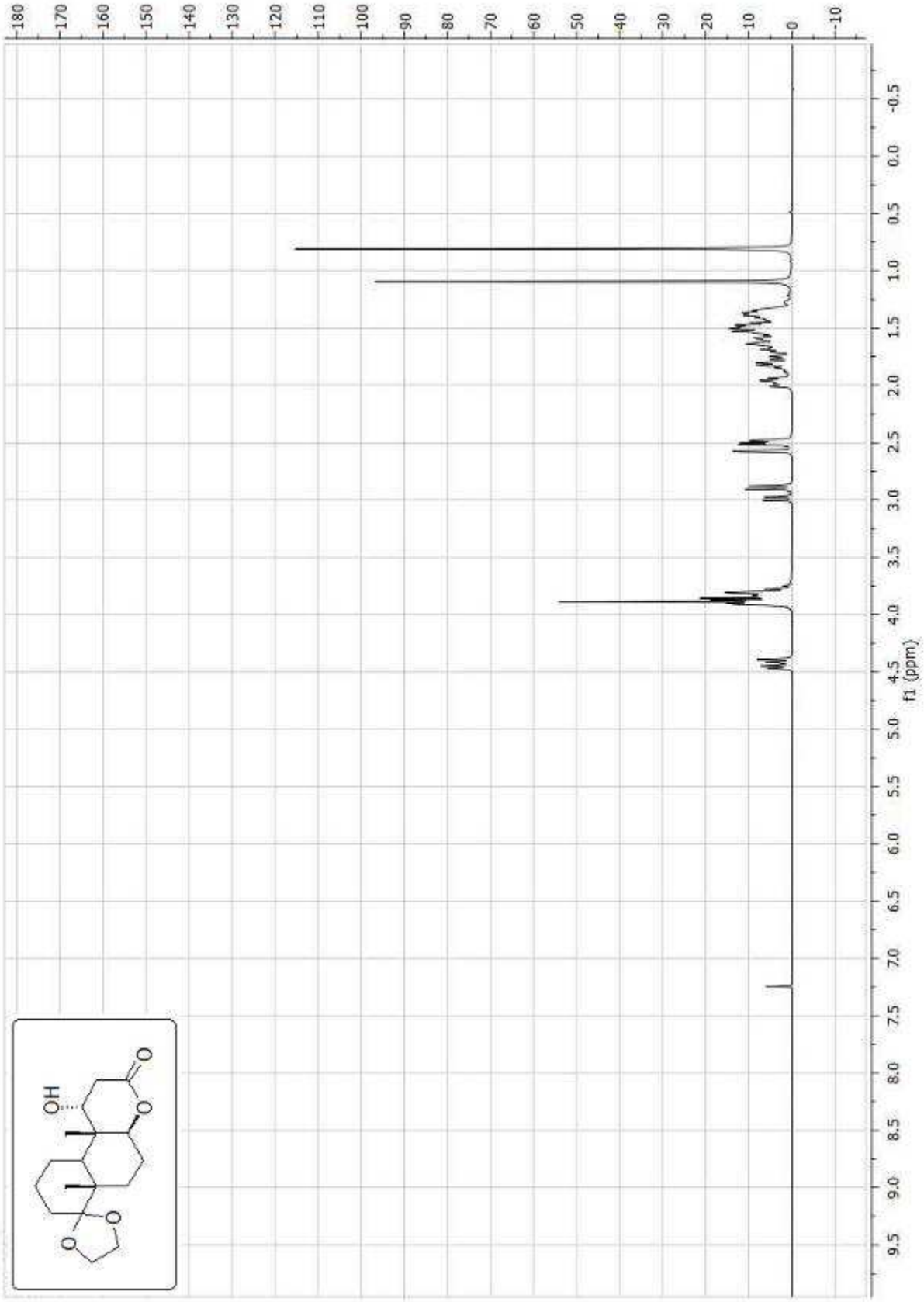
7.0
7.5
8.0
8.5
9.0
9.5
10.0
f1 (ppm)

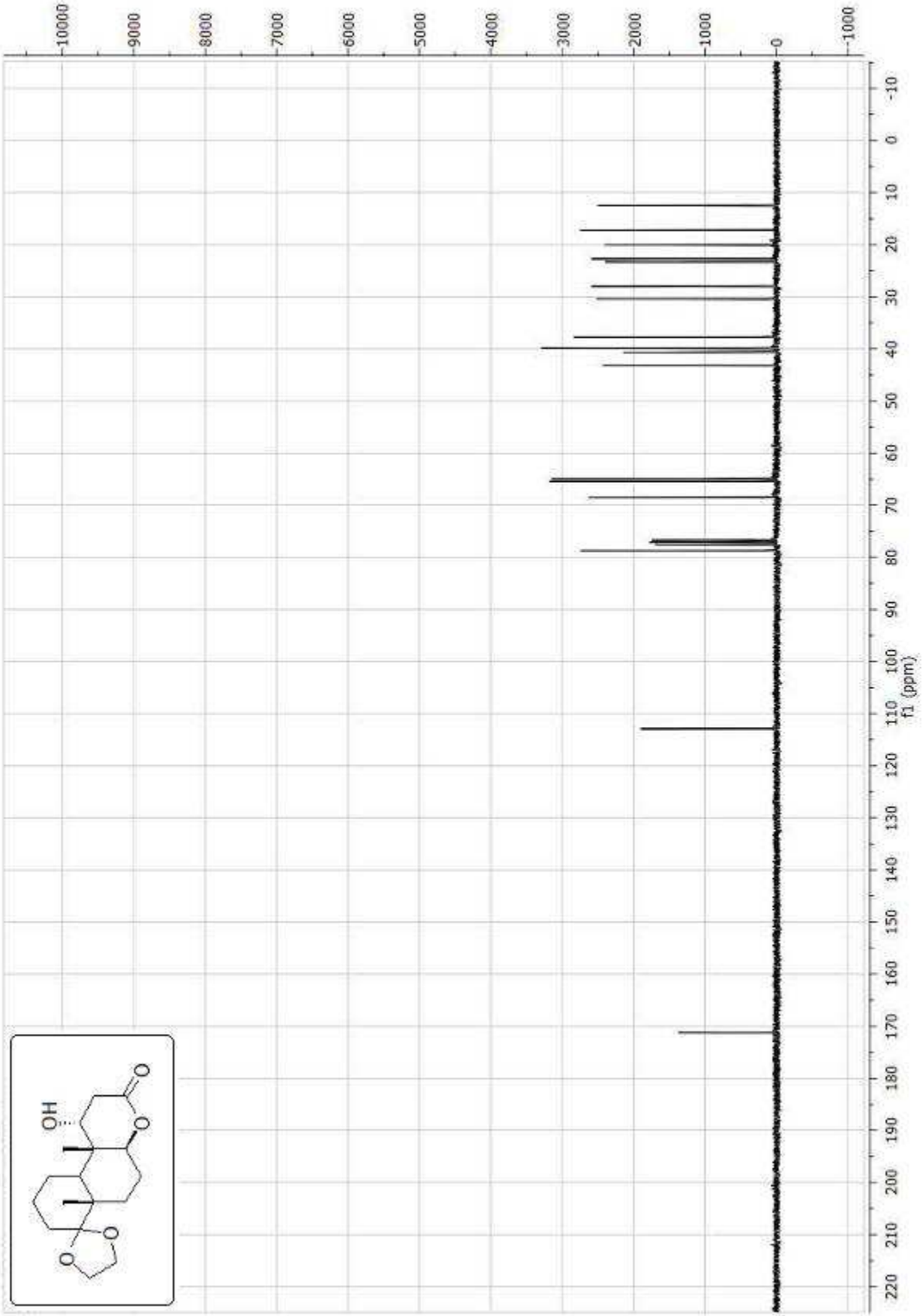
Epoxide (4)



Alcohol (17)



Alcohol (17)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80
90
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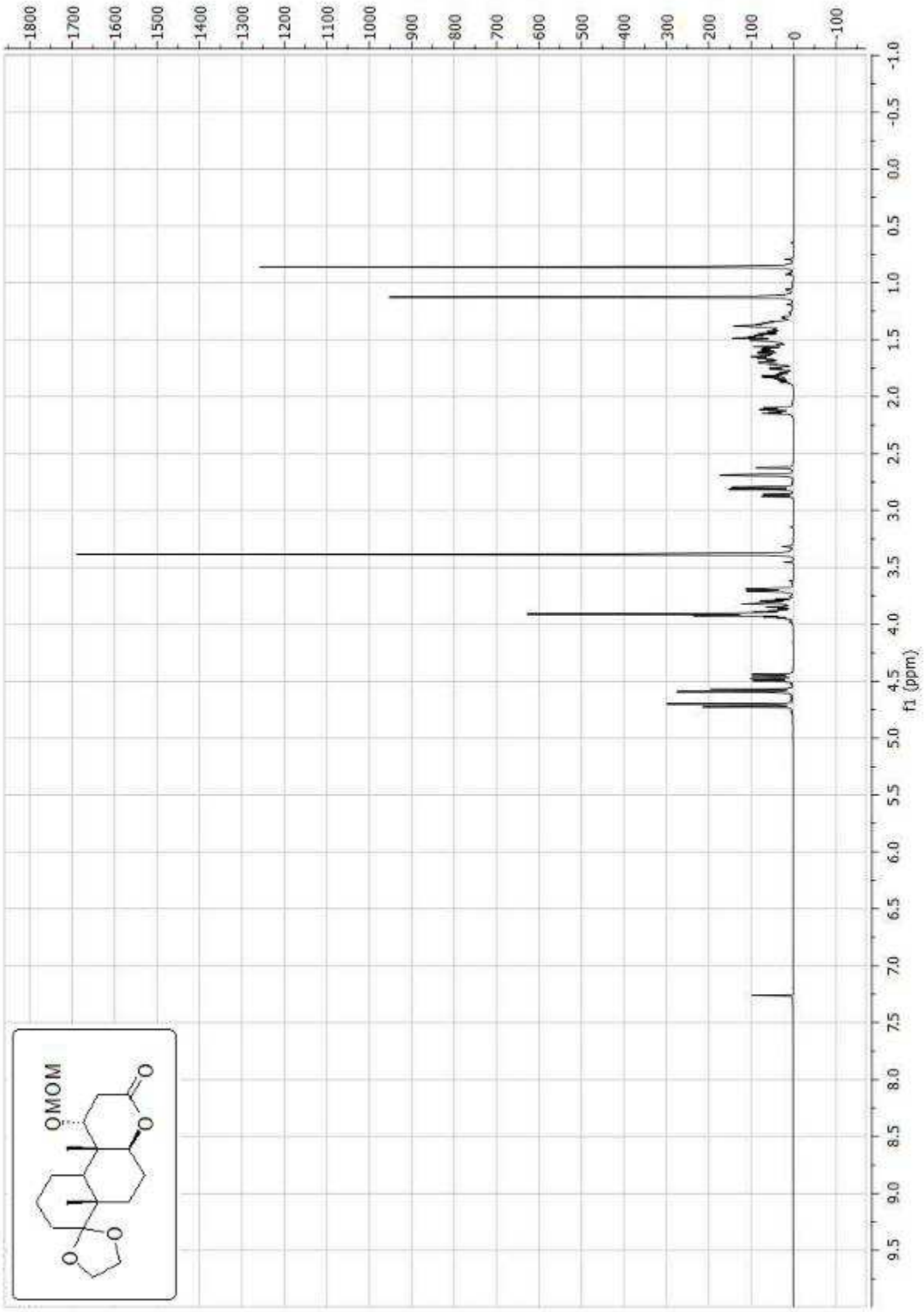
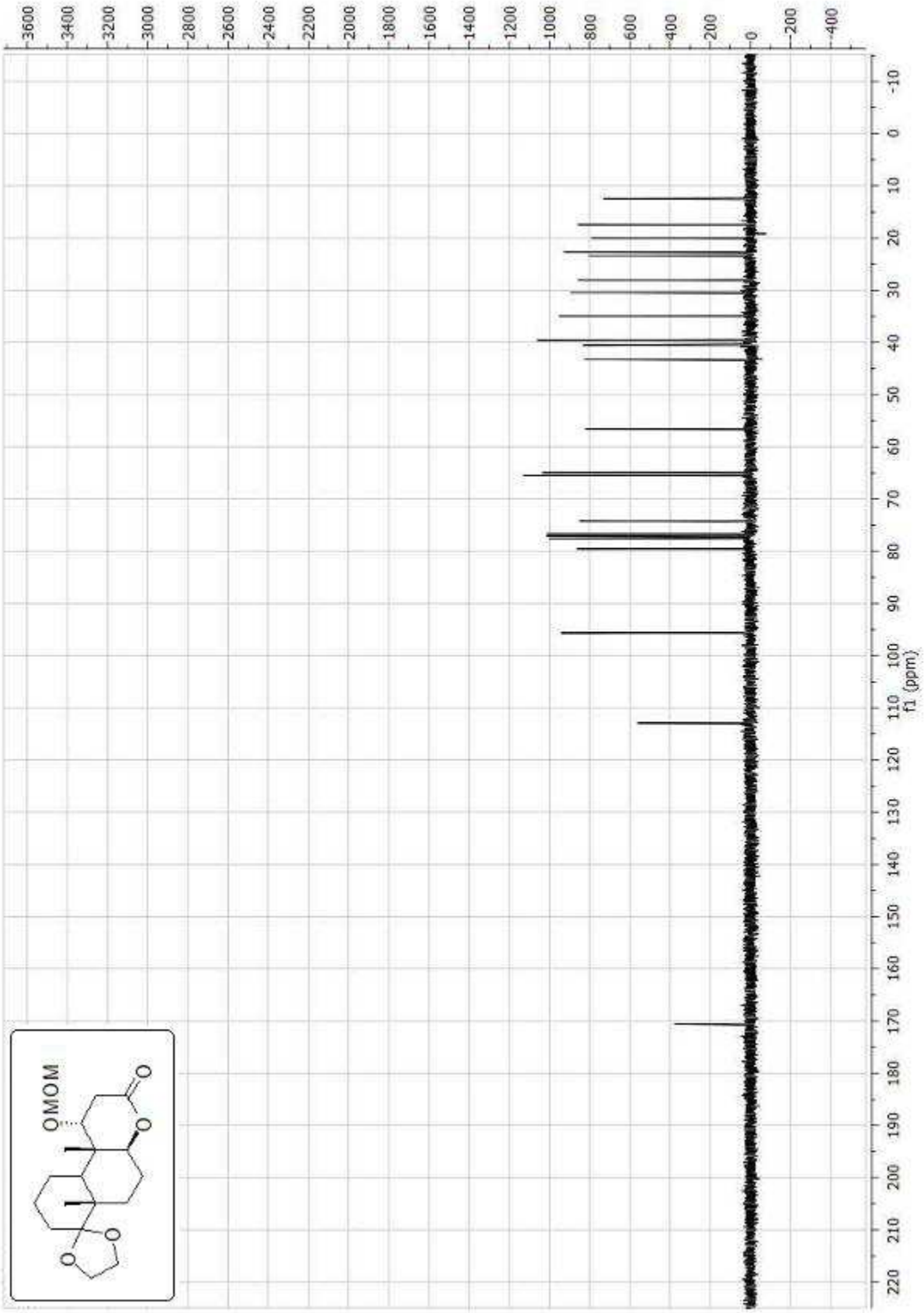
f1 (ppm)
OH
O
O
O
O

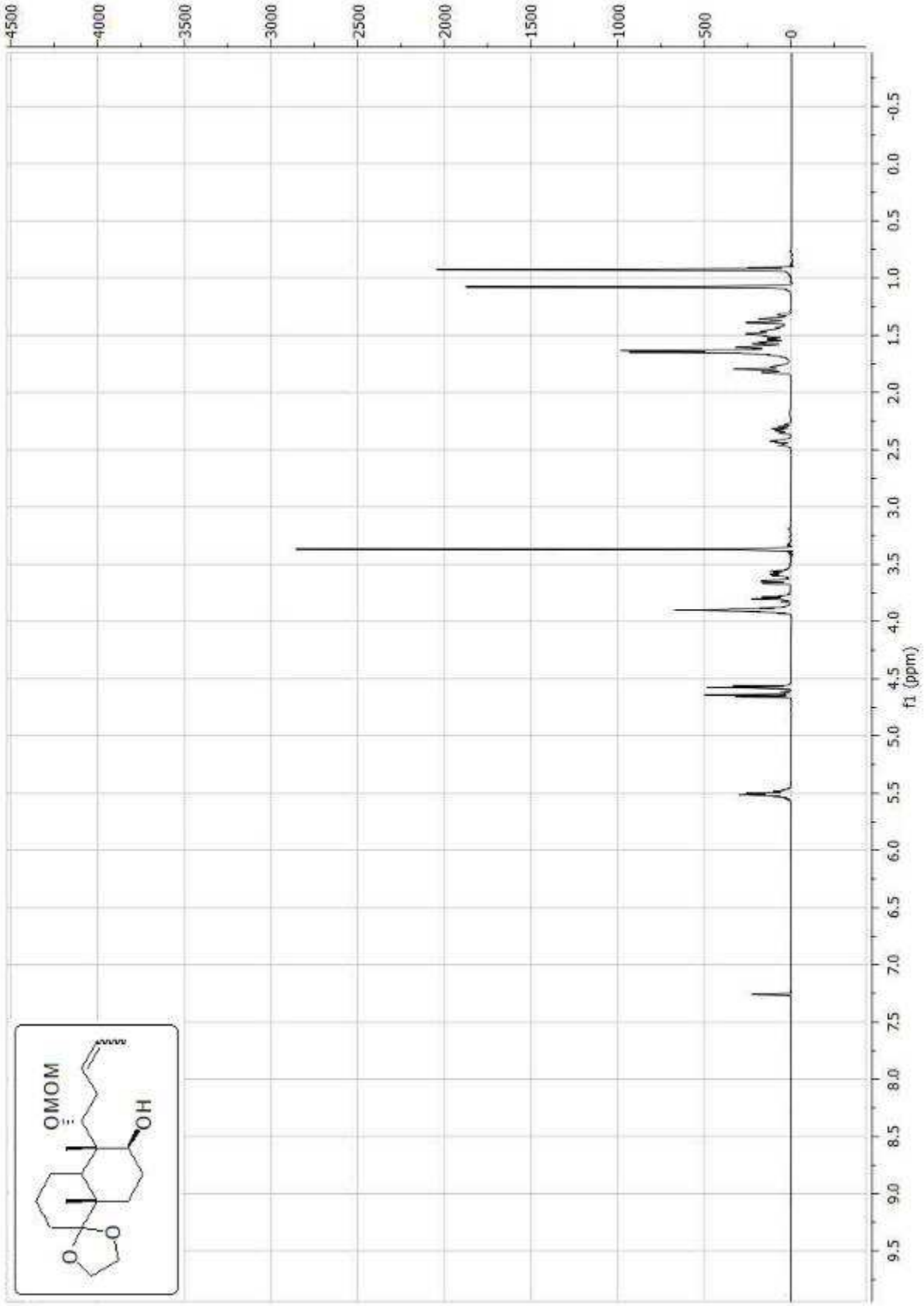
MOM ether (5)



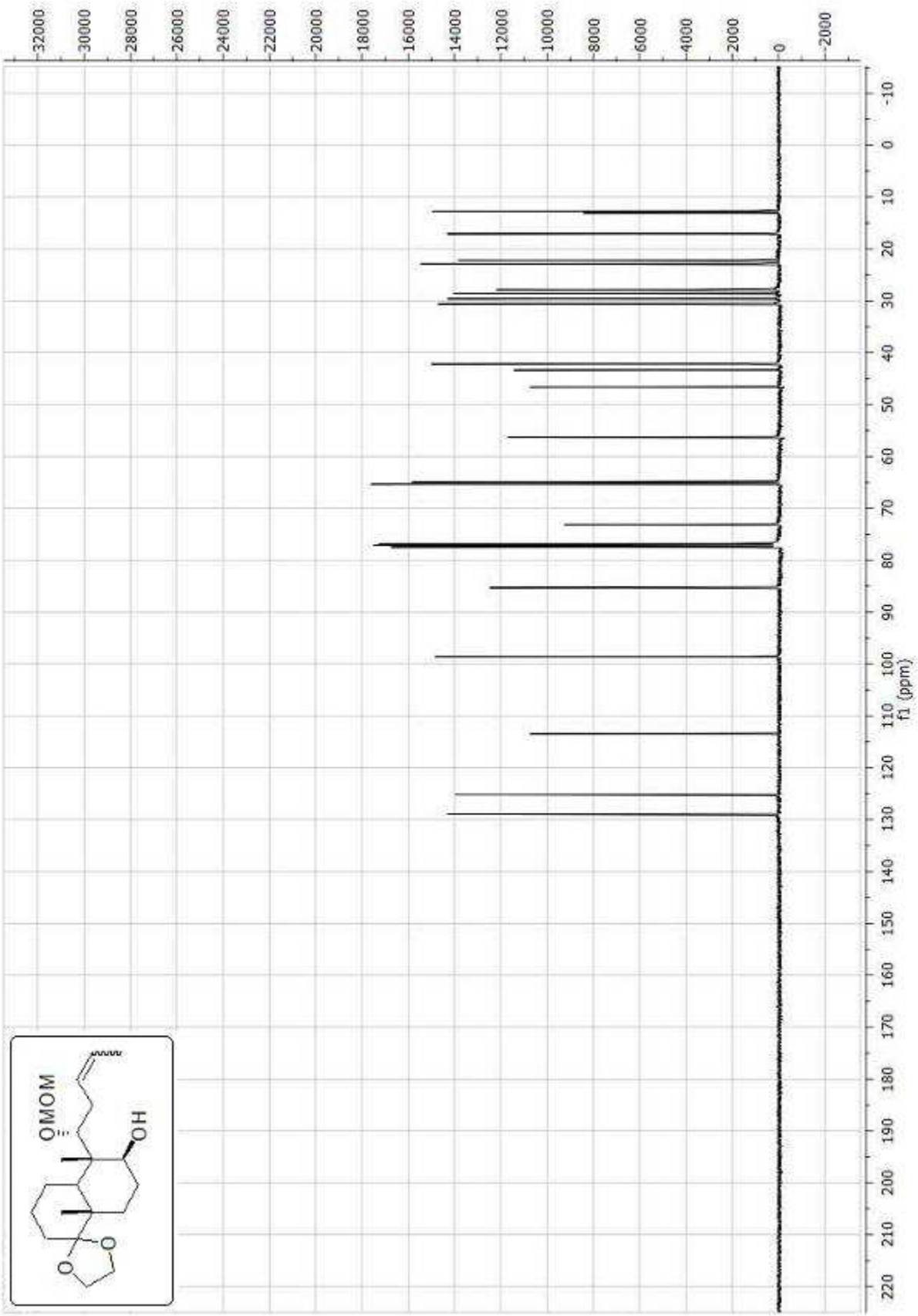
MOM ether (5)



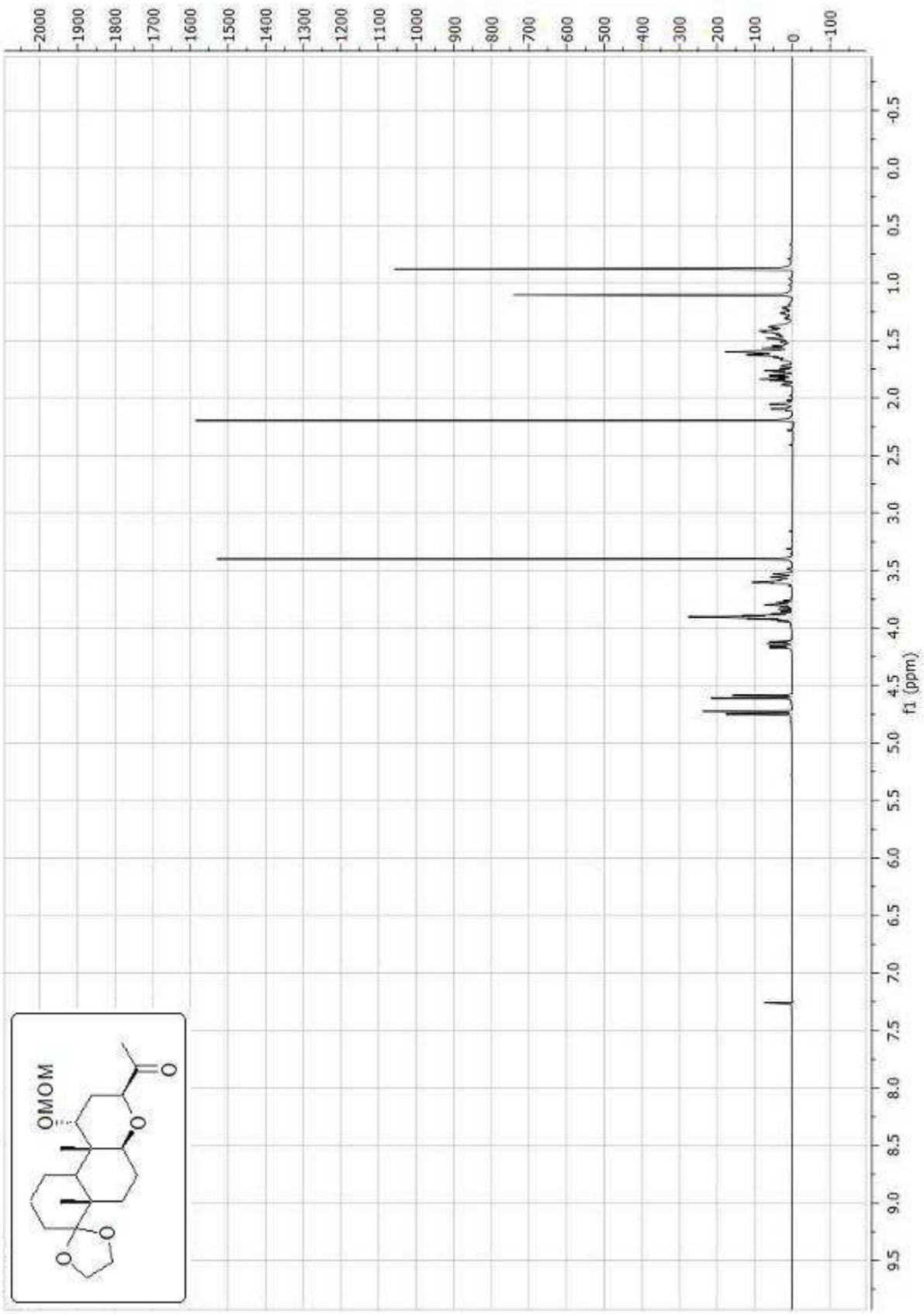
Olefin (6)



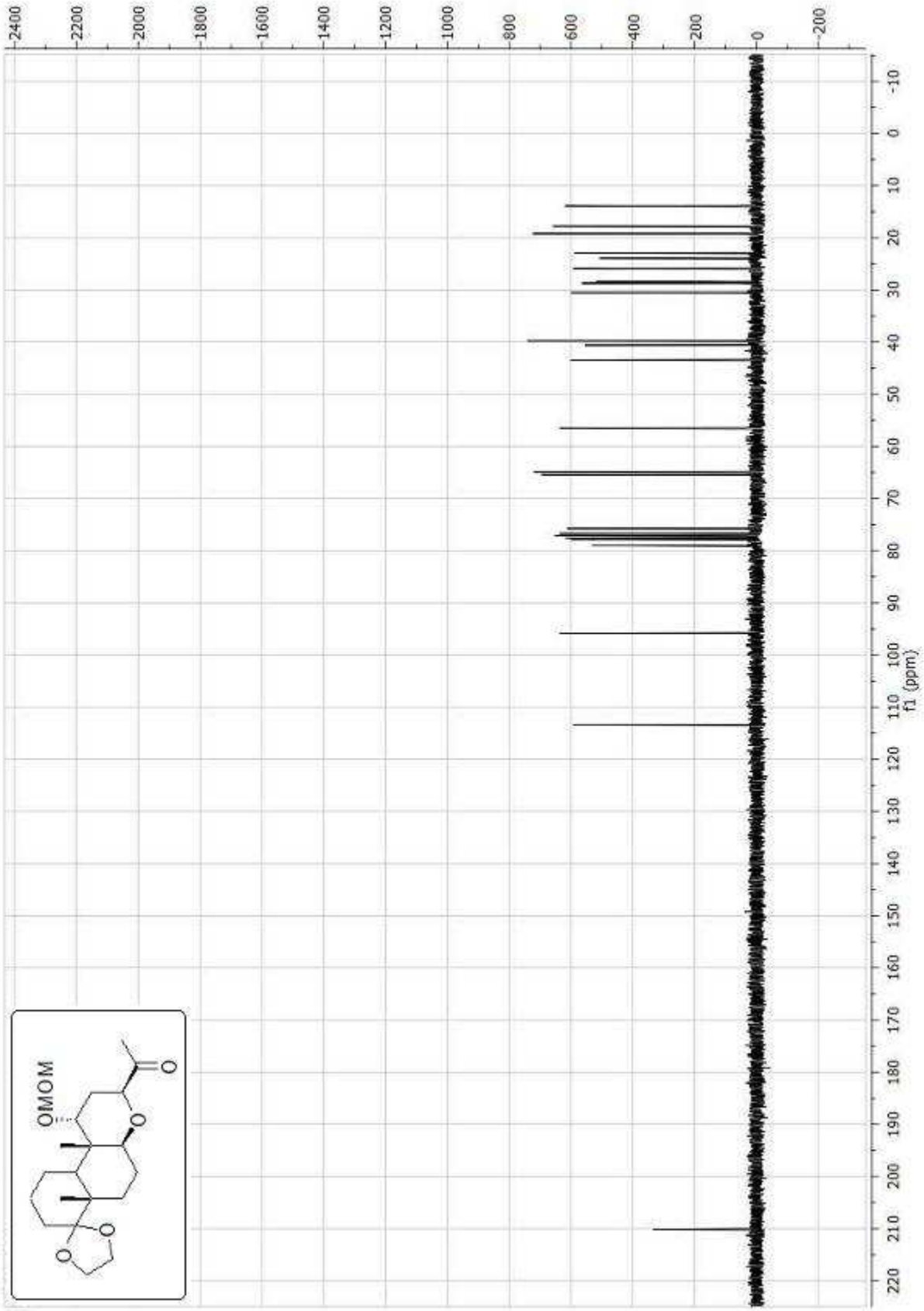
Olefin (6)



Ketone (7)



Ketone (7)



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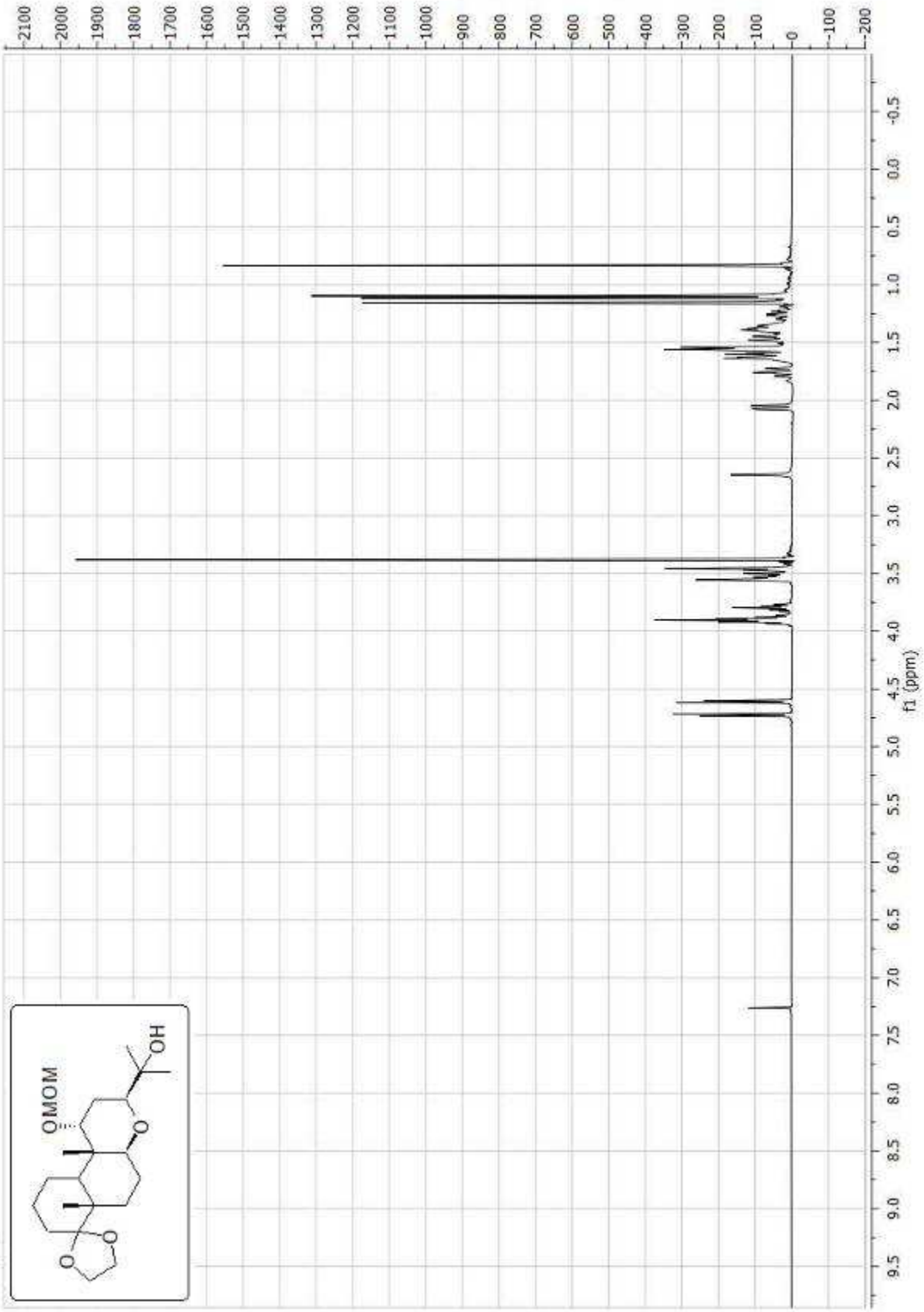
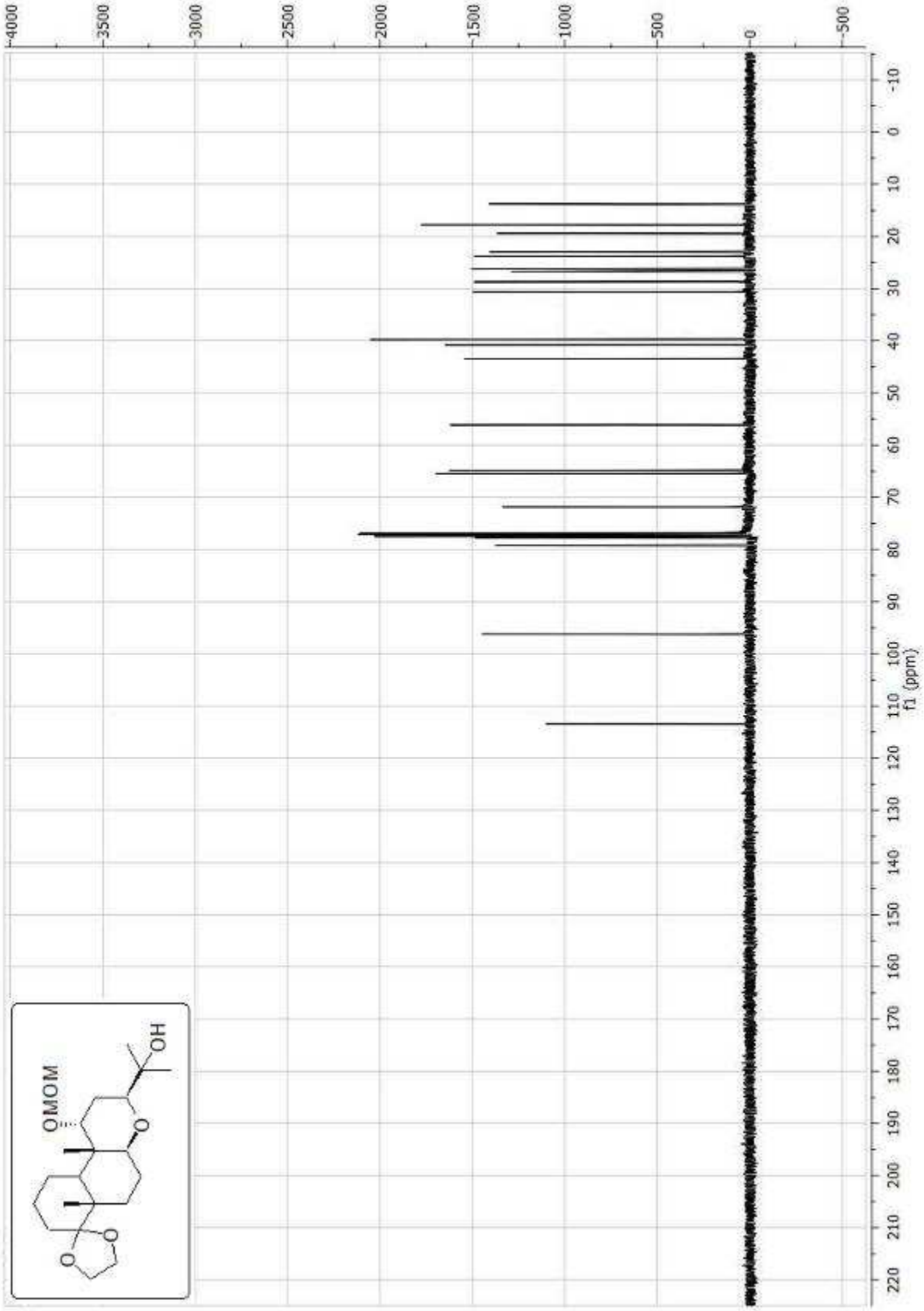
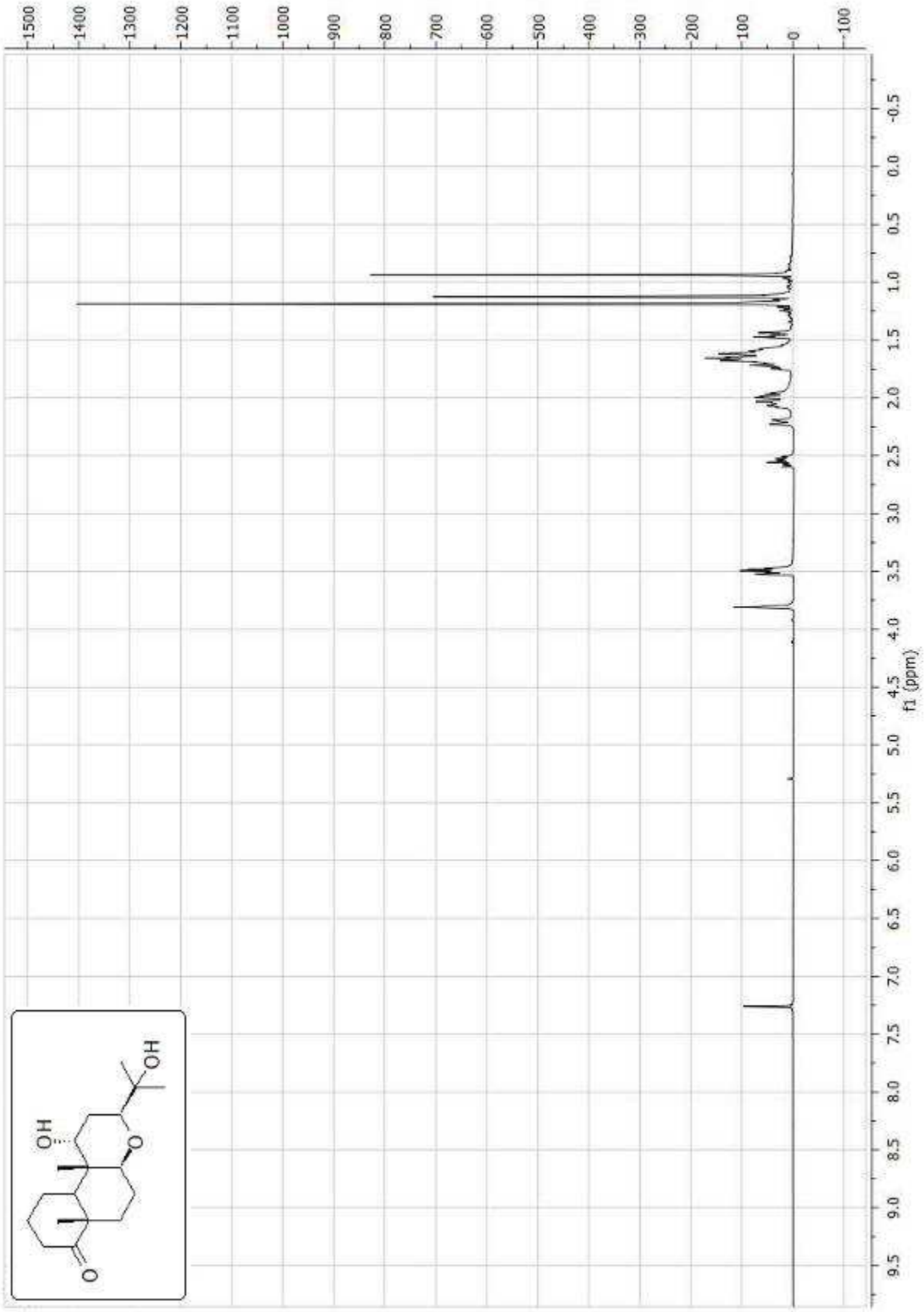


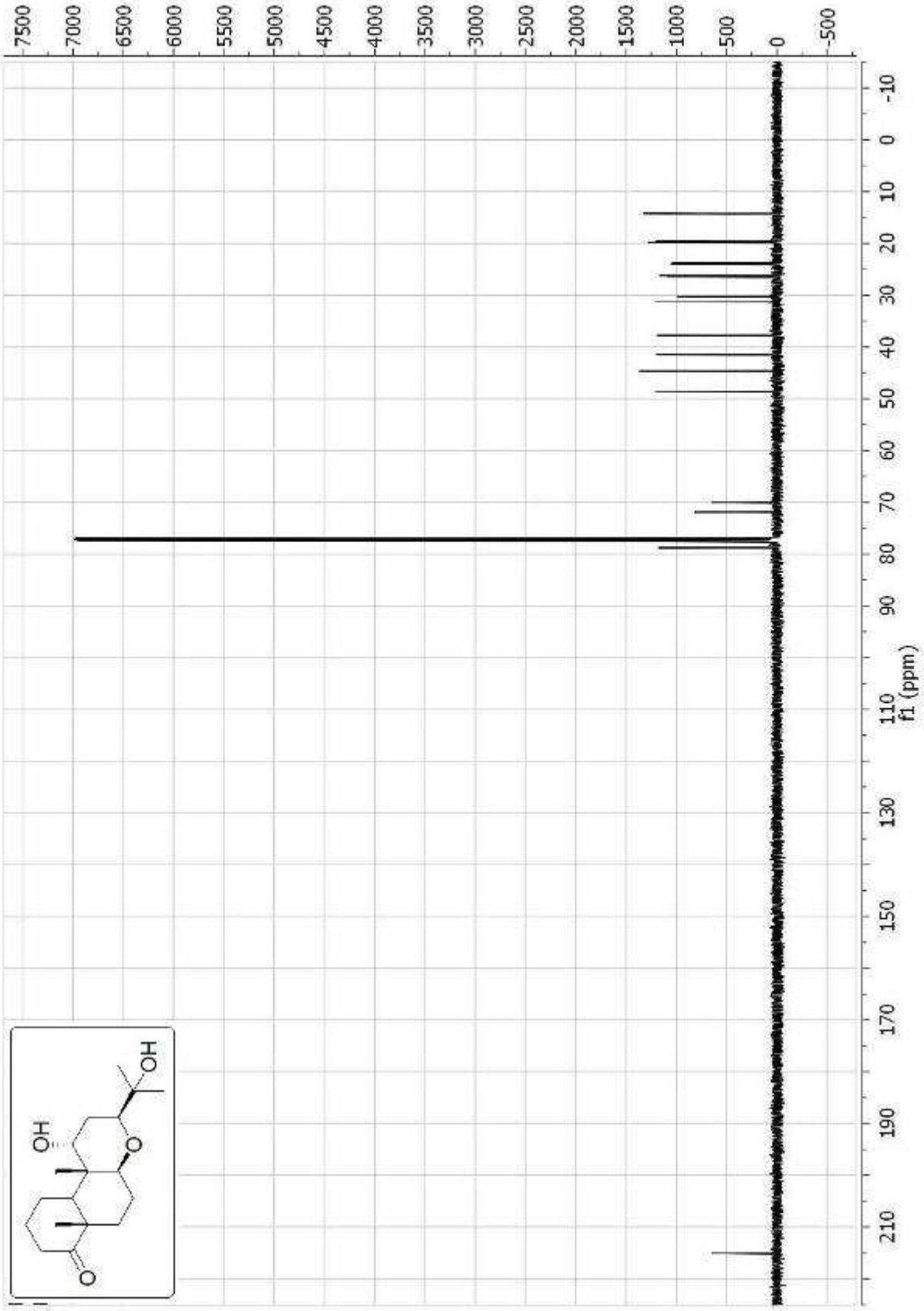
Alcohol (18)



Keto-diol (19)



Keto-diol (19)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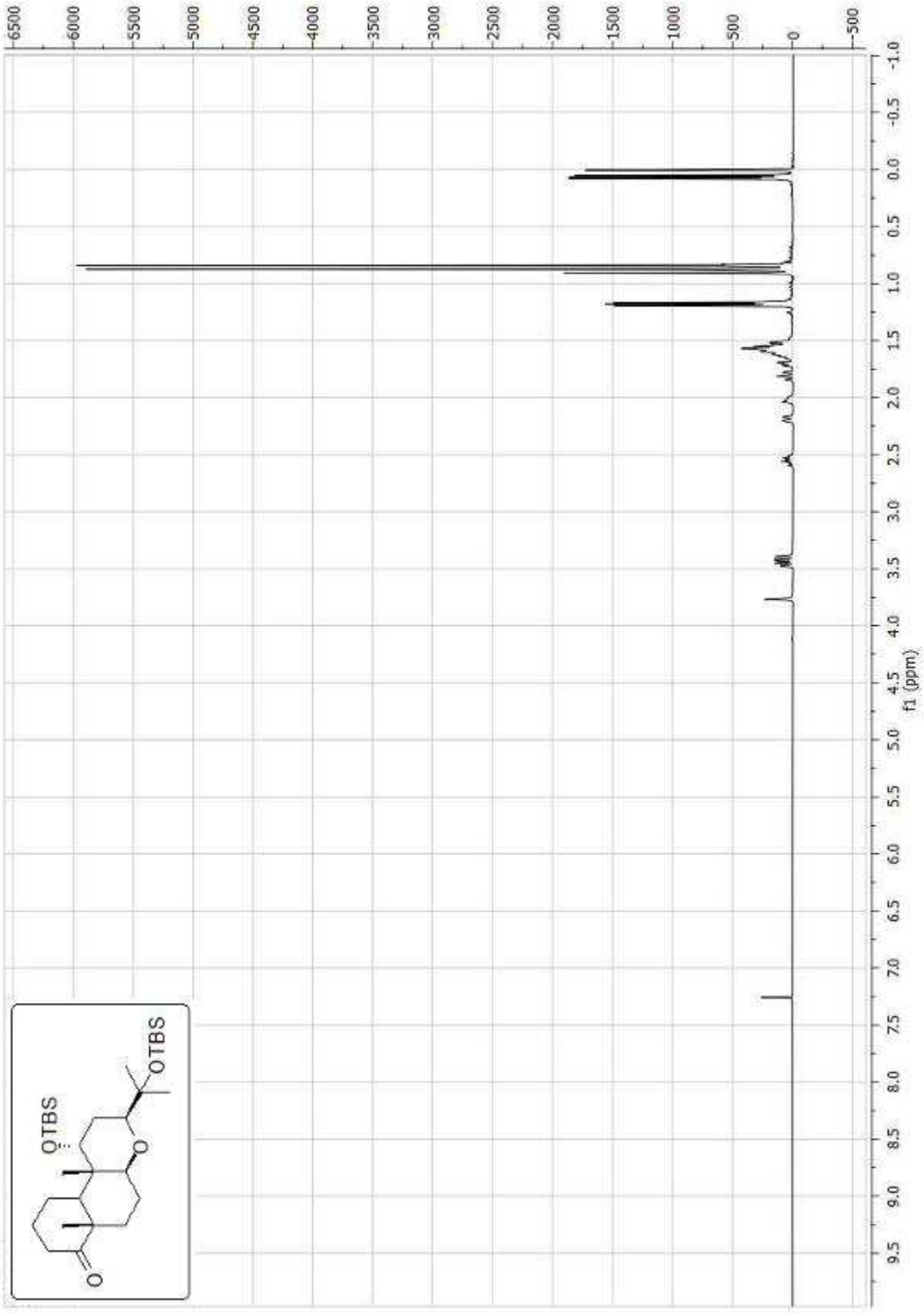
f1 (ppm)
OH
OH
O
O

Ketone (8)



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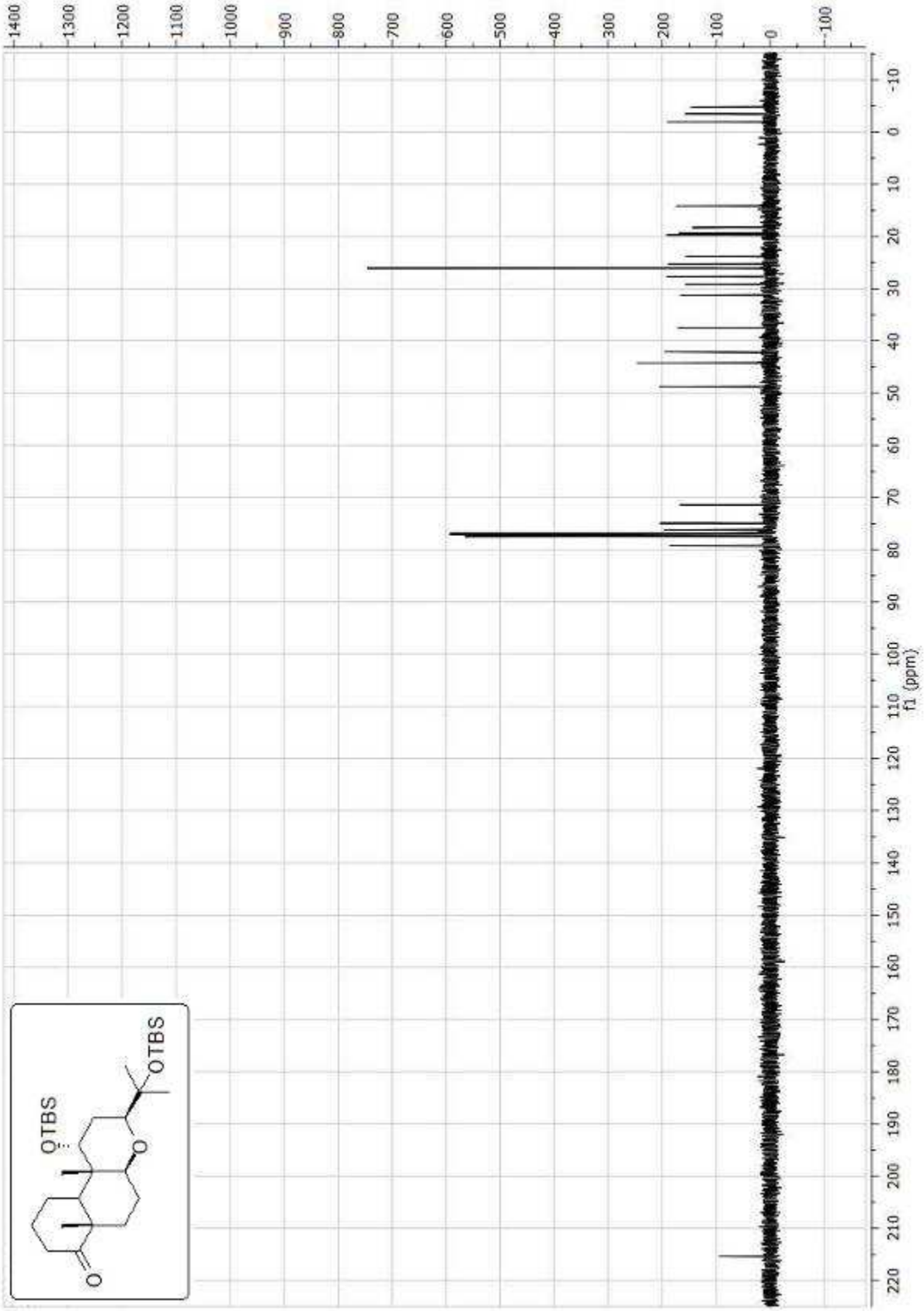

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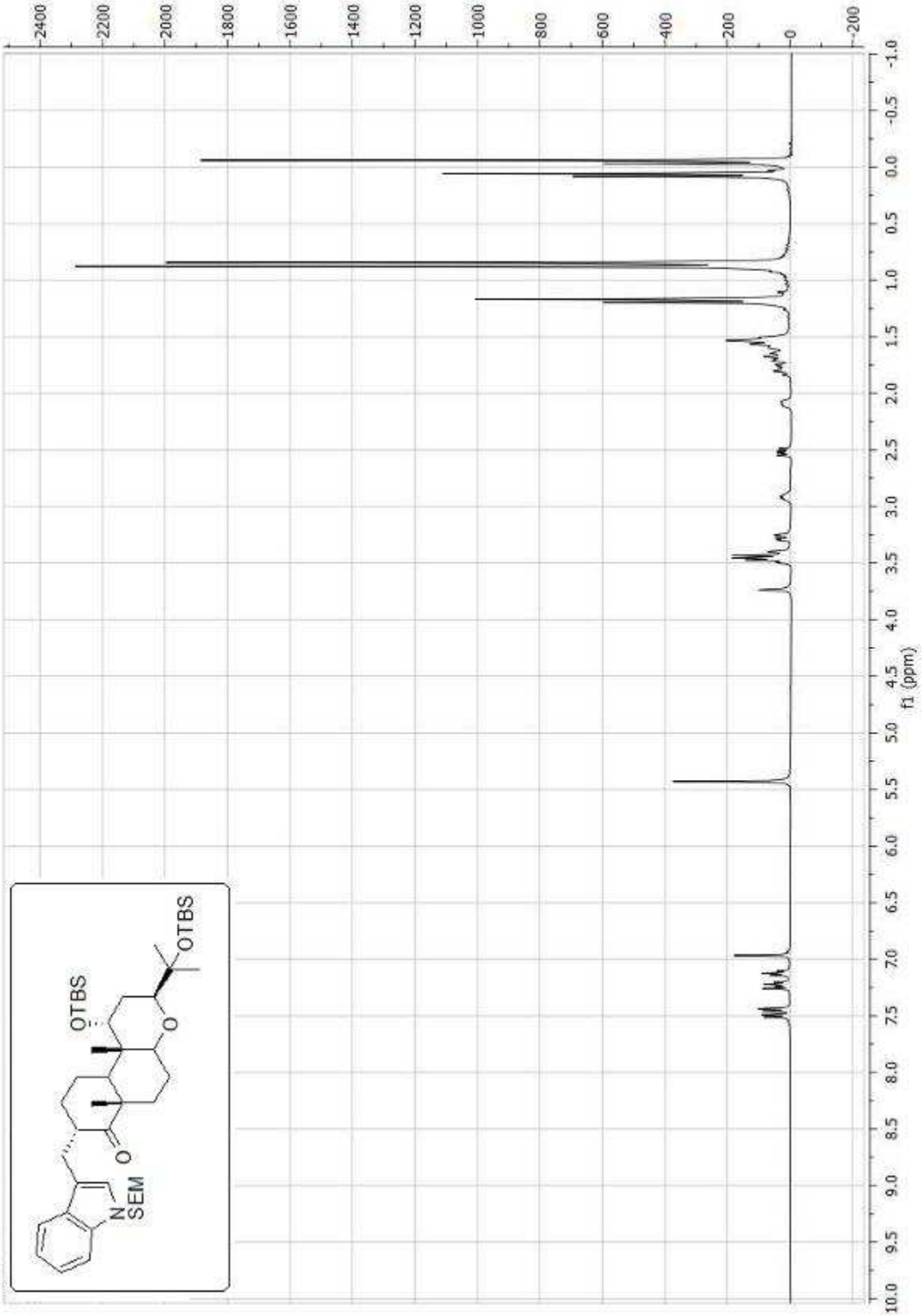

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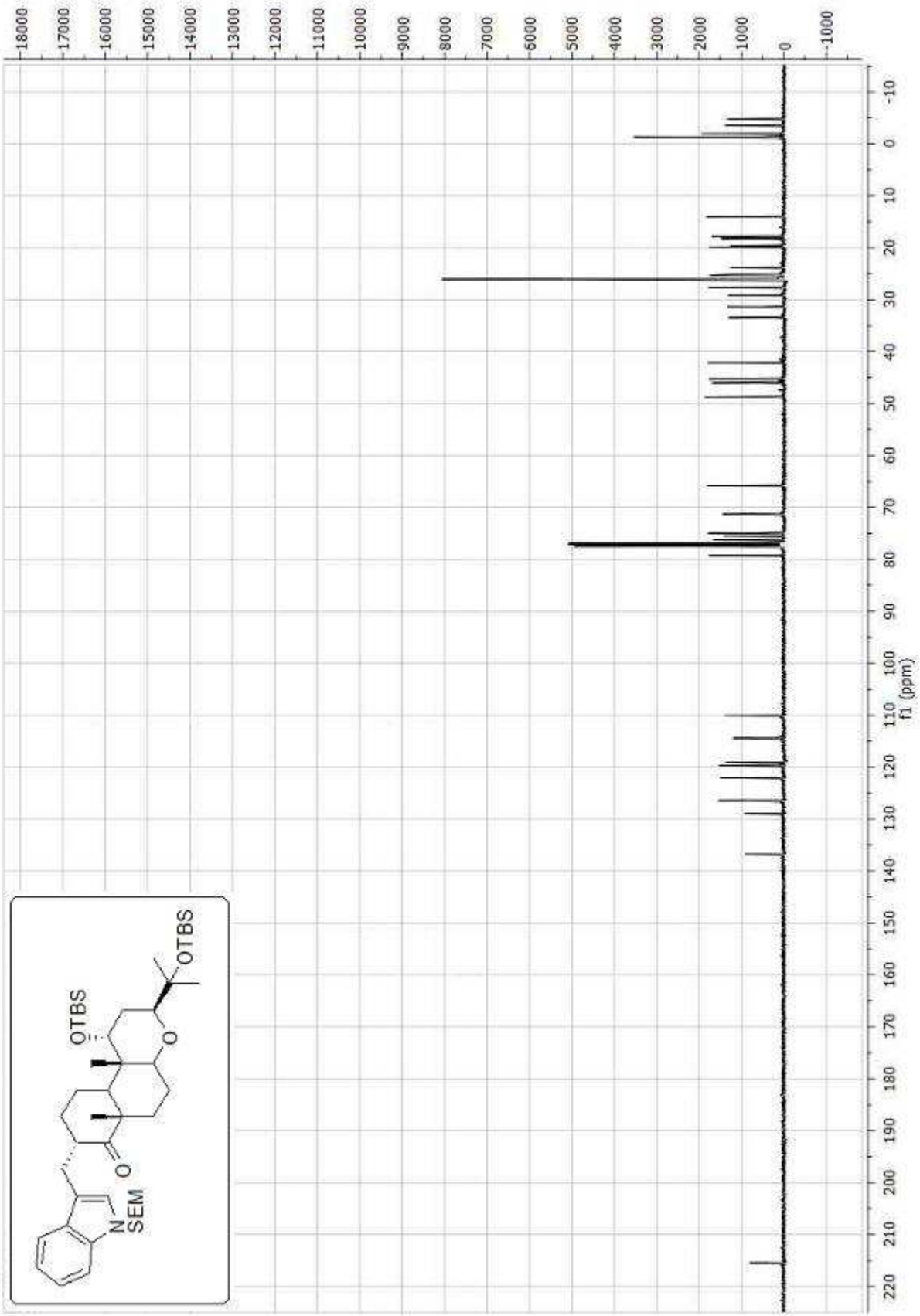
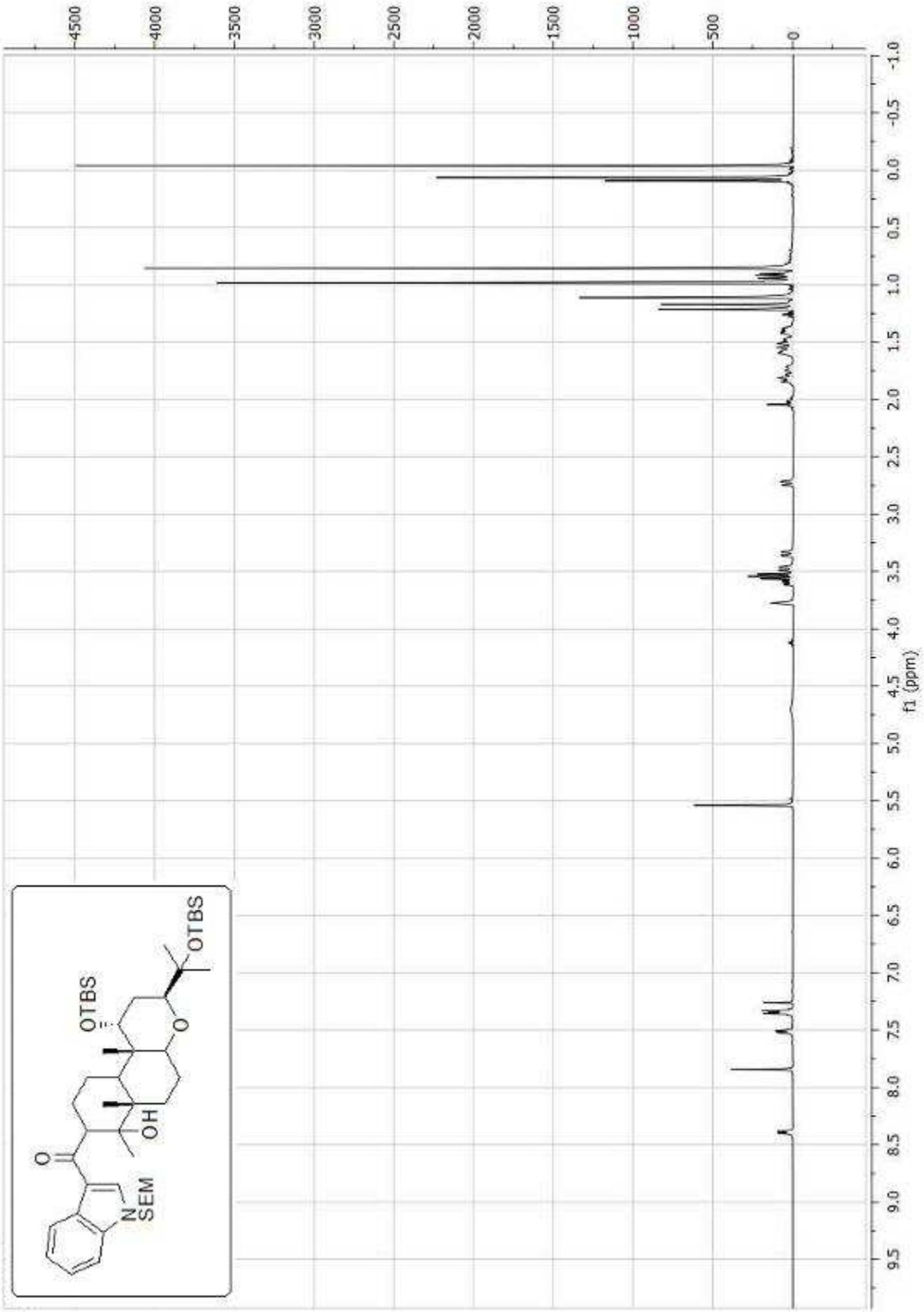
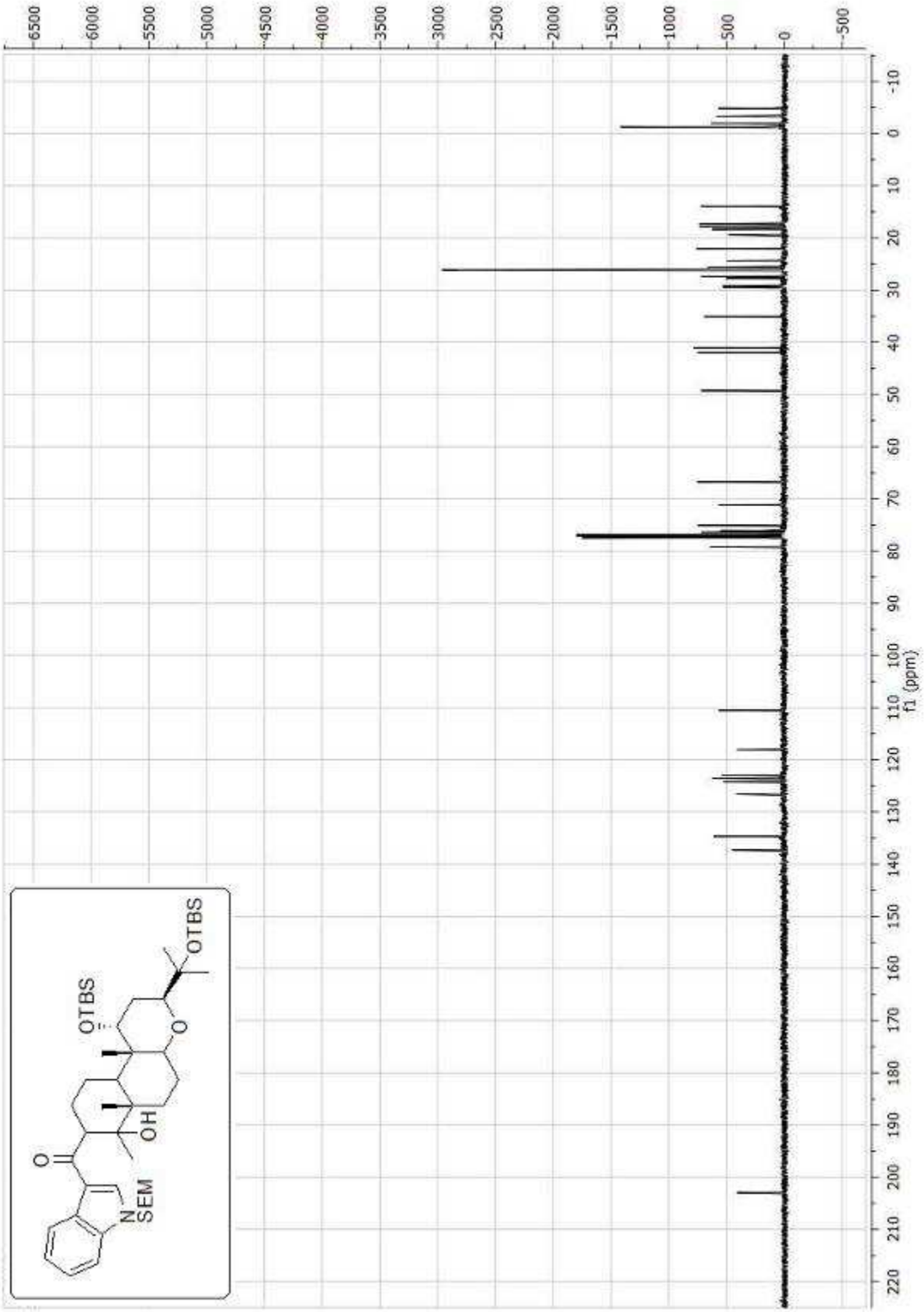


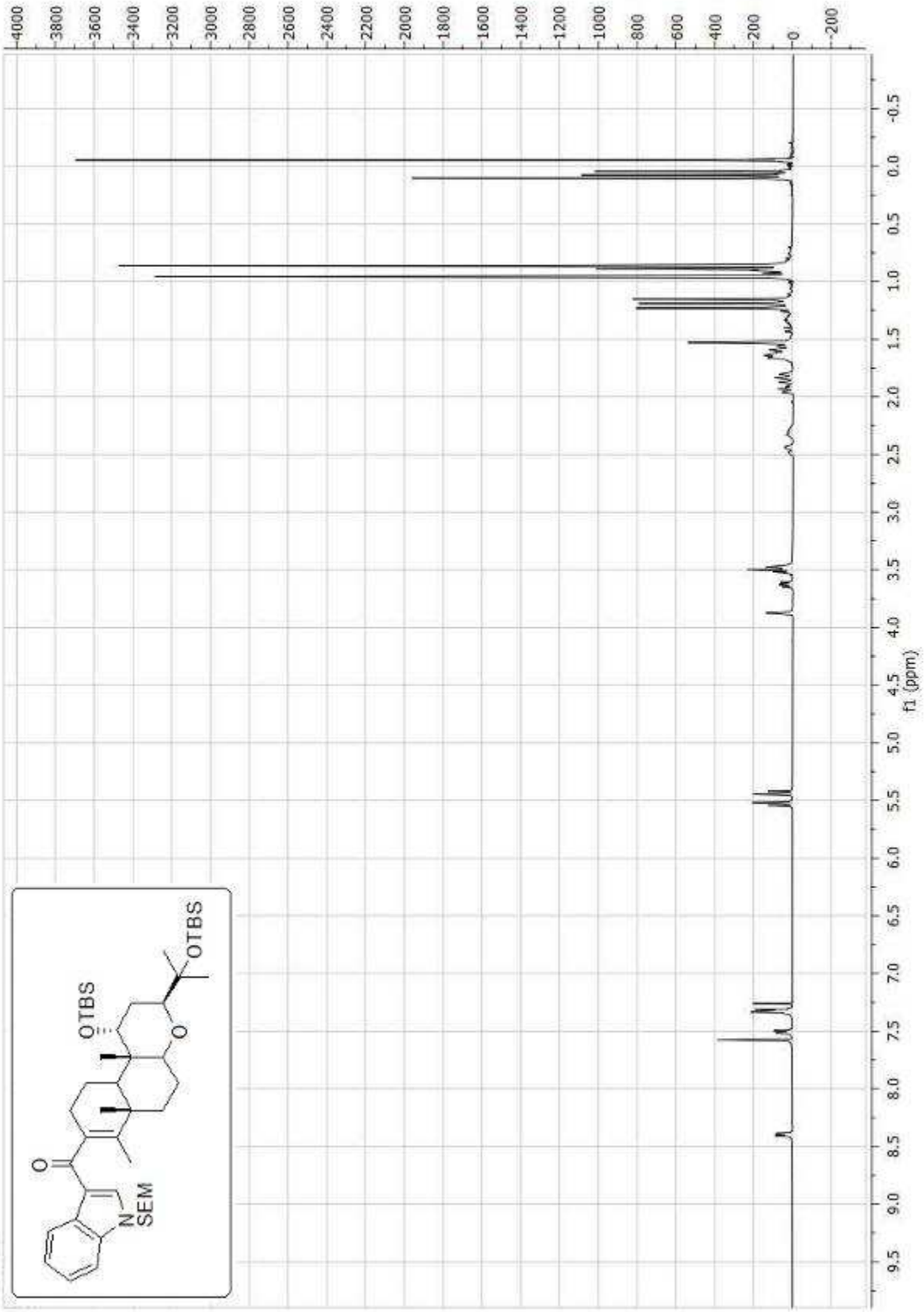
Hydroxyketo-indole (20)



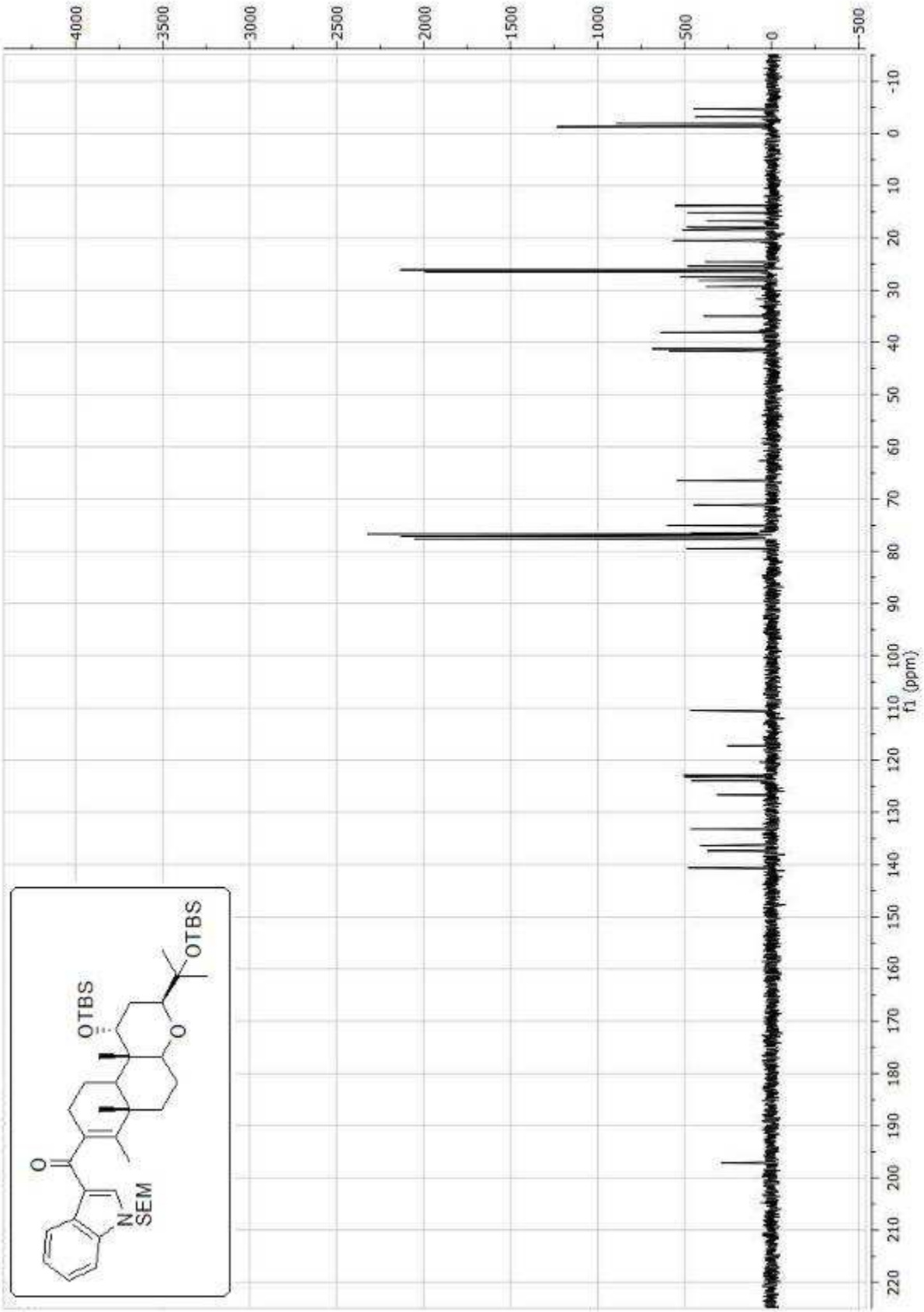
Hydroxyketo-indole (20)



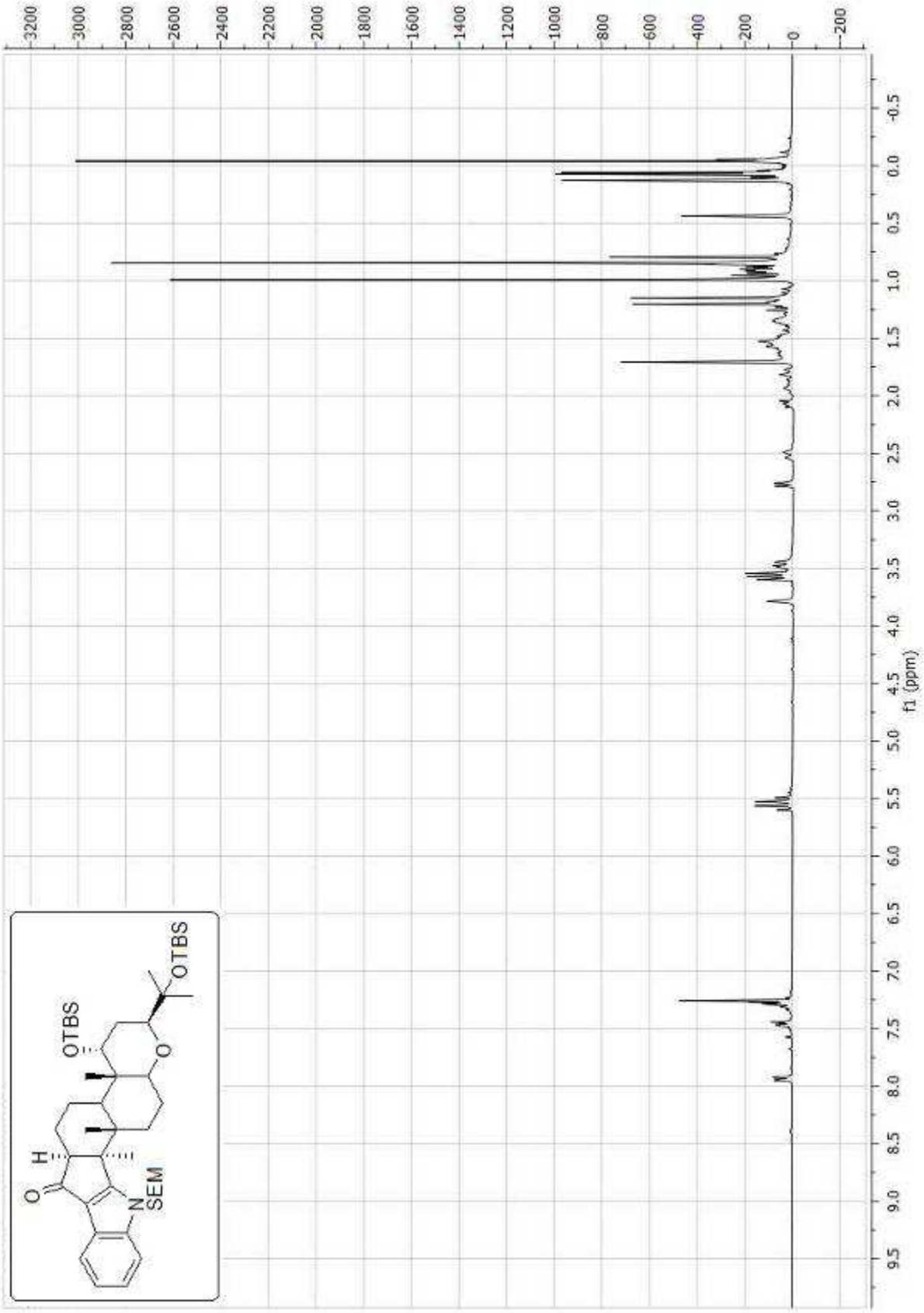
Enone (11)



Enone (11)



Ketone (12)



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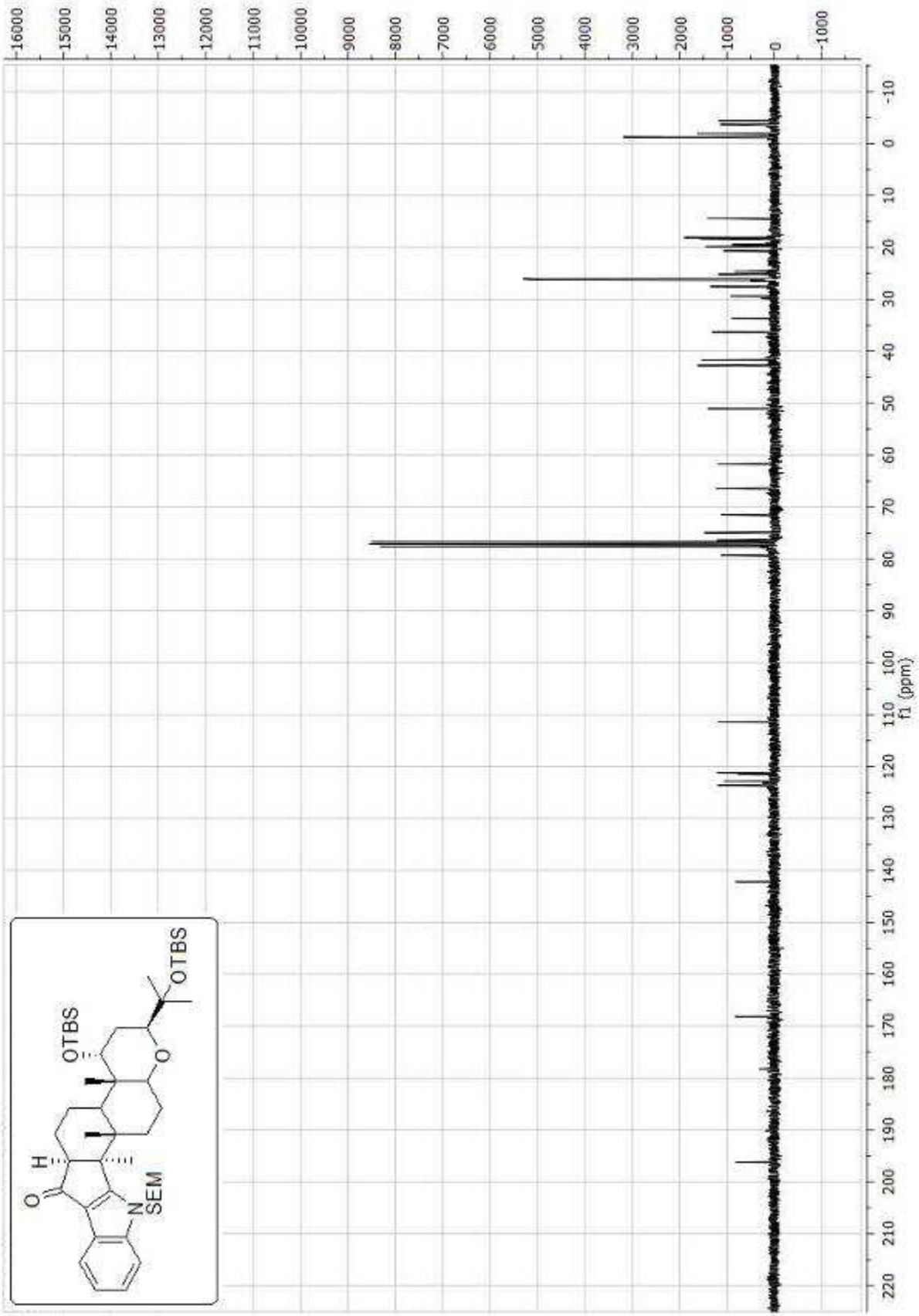
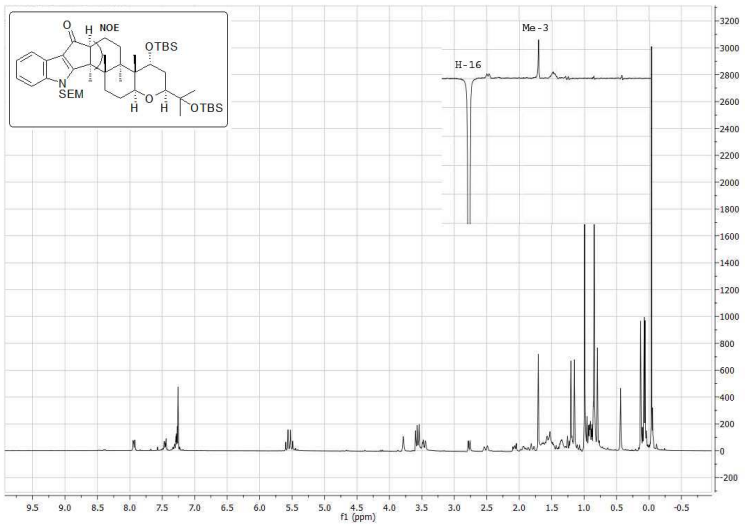
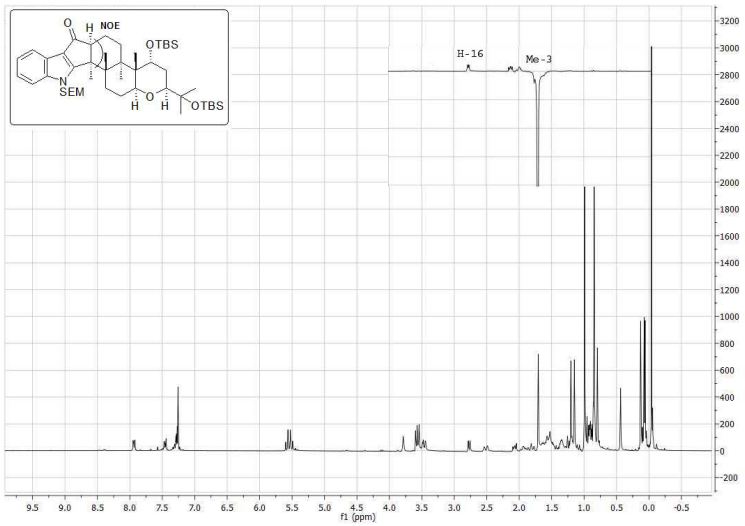
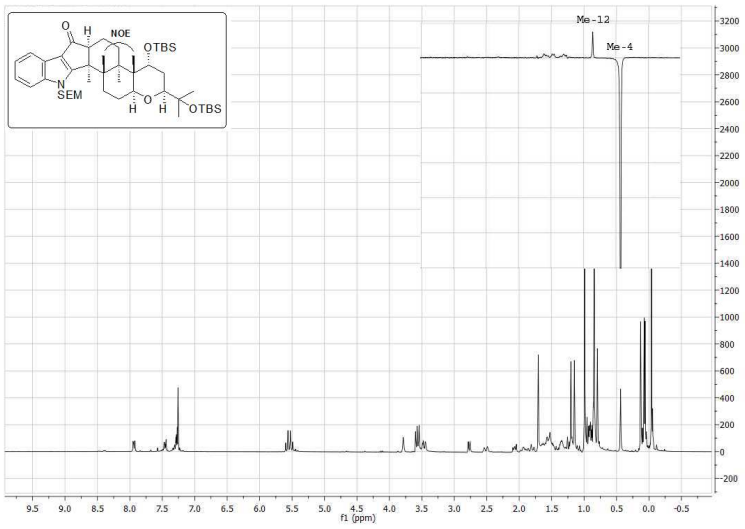


Ketone (12)

NOE difference spectra







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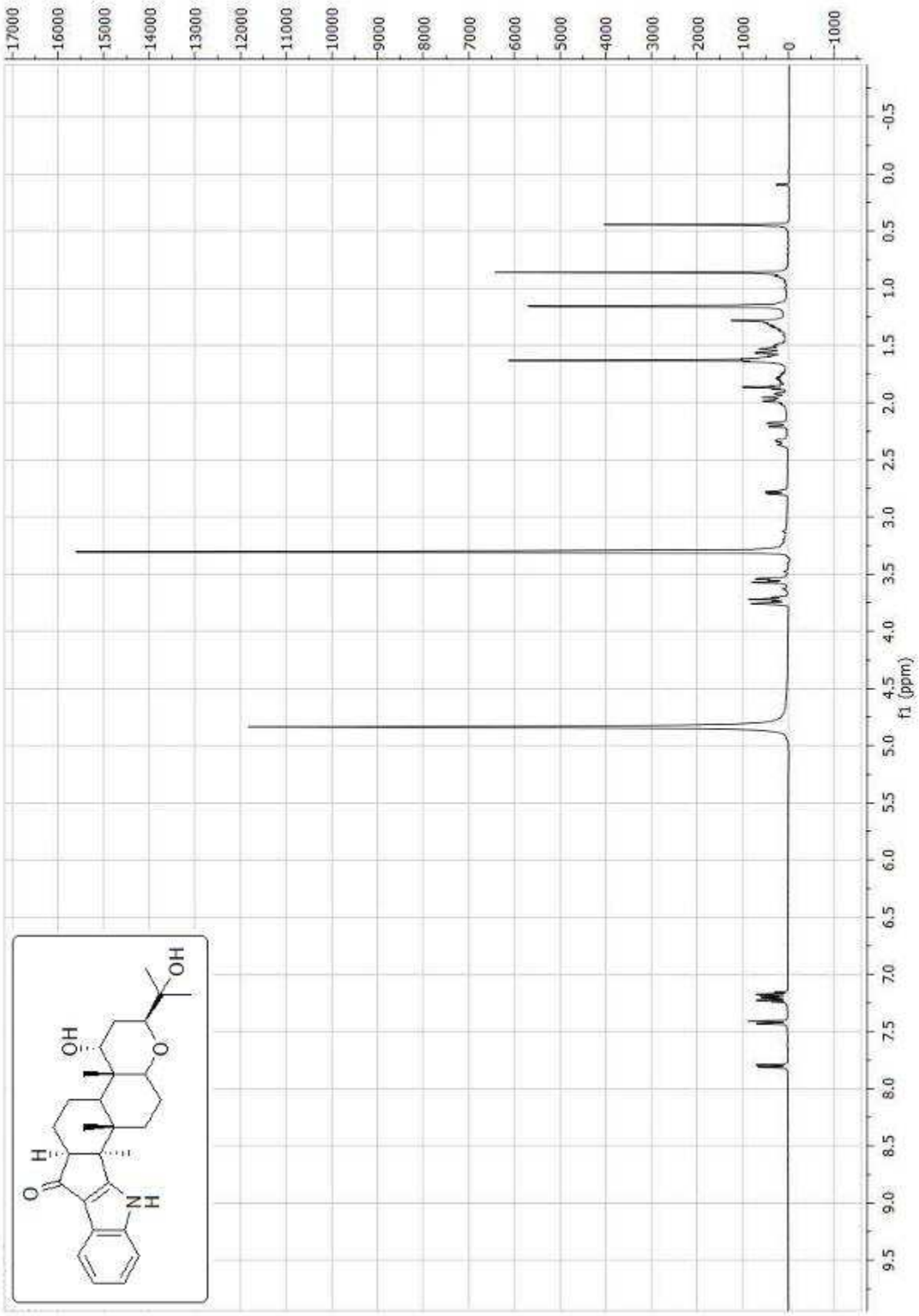
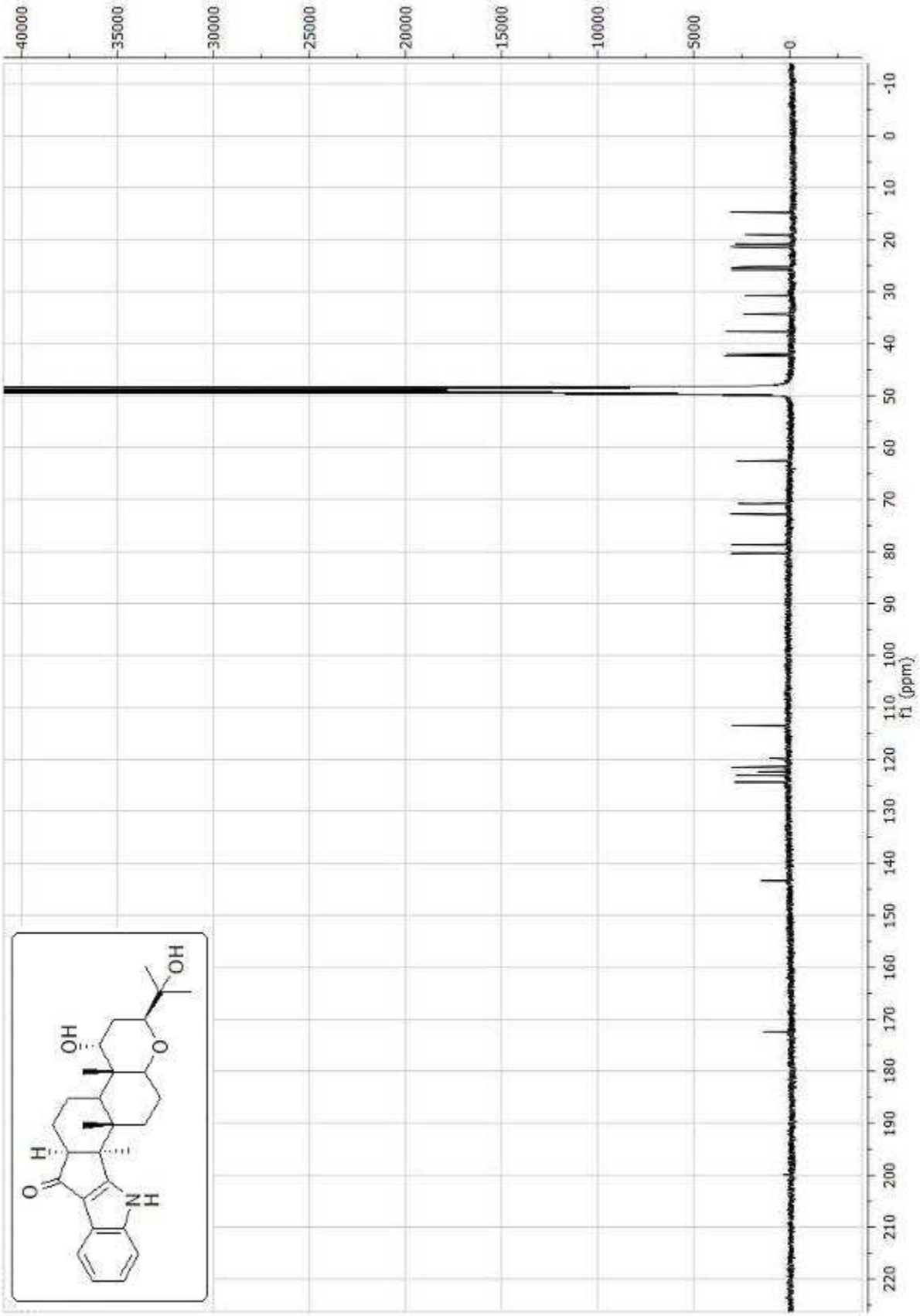


Ketone (13)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110
120
130
140
150
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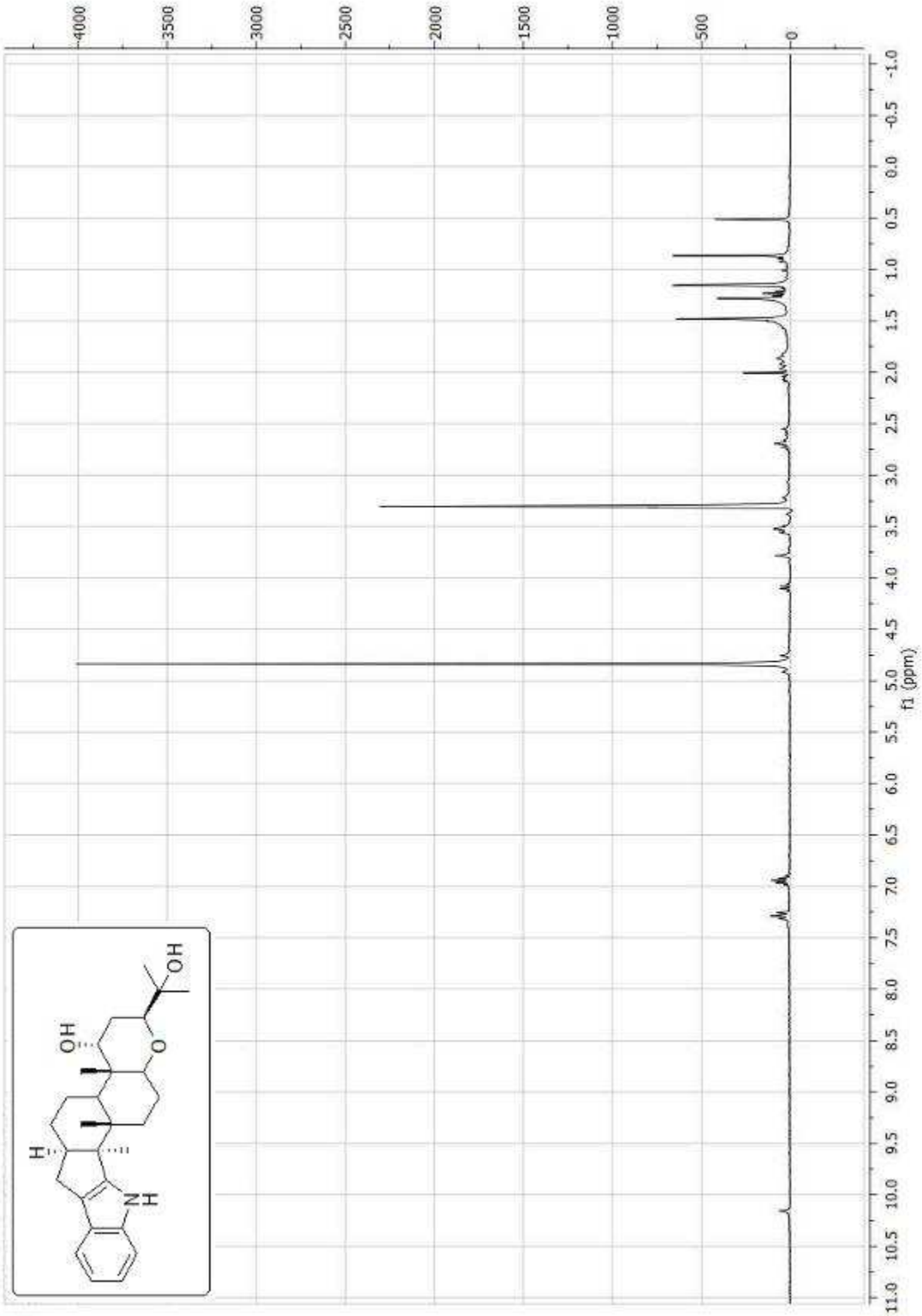
220
f1 (ppm)
O
H
N
H
O
OH
O
OH

16-*epi*-Terpendole E



16-*epi*-Terpendole E