SUPPORTING INFORMATION

Novel and Flexible Entries into Prostaglandins and Analogues Based on Ring Closing Alkyne Metathesis or Alkyne Cross Metathesis

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General. All reactions were carried out under Ar in pre-dried glassware using Schlenk techniques. The solvents were dried by distillation over the drying agents indicated and were stored and transferred under Ar: CH_2Cl_2 (P_4O_{10}), toluene (Na/K), Et_2O, THF (magnesium/anthracene), MeOH (Mg), HMPA (CaH_2), pyridine, Et_3N (KOH). Flash chromatography: Merck silica gel (230-400 mesh). Mp: Gallenkamp apparatus (uncorrected). NMR: Spectra were recorded on a Bruker AC 200, DPX 300, AMX 400 or DMX 600 spectrometer in the solvent indicated. Chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. IR: Nicolet FT-7199, wavenumbers in cm^{-1}. MS: Finnigan MAT 8200 (70 eV) or Finnigan MAT SSQ 7000 (70 eV). HRMS: MAT 95 (70 eV). Elemental analyses: Dornis & Kolbe, Mülheim. Commercially available reagents (Aldrich, Fluka) were used as received.

SUBSTRATES

Enone **9**,[23] 5-heptynoic acid **14**,[24b] 6-bromo-2-hexyne[39] and 9-undecynoic acid[12] were obtained according to literature procedures, other substrates were prepared as described below.

1-Iodo-2-butyne (11). Iodide **11** was prepared as a pale yellow liquid (73%) by treatment of commercially available 2-butyn-l-ol with PPh_3, I_2 and imidazole according to a literature procedure[24a]; bp 68-69°C/32 mm Hg [Lit.[40] bp. 51-52°C/16 mm Hg]. ^1H NMR (300 MHz, $CDCl_3$) δ 3.68 (2H, q, J = 2.6 Hz), 1.82 (3H, t, J = 2.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 82.1, 76.0, 4.0,

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[39] Flahaut, J., Miginiac, P. *Helv. Chim. Acta* **1978**, *61*, 2275.

[40] Ashworth, P. J.; Whitham, G. H.; Whiting, M. C. *J. Chem. Soc.* **1957**, 4633.

–16.9; MS (EI) *m/z* (rel intensity) 180 ([M]$^{+\cdot}$, 68), 127 (31), 53 (100); IR (neat) 2998, 2915, 2848, 2234, 1437, 1419, 1178, 1145, 1027, 557 cm^{-1}.

(1*S*,2*E*)-1-Pentyl-3-(1,1,1-tributylstannyl)-2-propenyl (1,1,1-triethylsilyl) ether ((–)-8). Compound **8** was prepared from commercially available propargyl alcohol **7** (Aldrich, *ee* = 98%) as described in ref.[22] for the racemic compound. Colorless liquid: $[\alpha]_D^{20} = -14.3$ (*c* = 1.1, $CHCl_3$); bp 125-130°C/0.025 mm Hg [lit.[22] bp 165°C/0.05 mm Hg]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.06-5.84 (2H, m), 4.00 (1H, q, *J* = 6.0 Hz), 1.70-0.8 (47H, m), 0.60 (6H, q, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 126.6, 76.9, 38.0, 31.8, 29.1, 27.3, 25.1, 22.7, 14.0, 13.7, 9.4, 6.9, 4.9; MS (EI) *m/z* (rel intensity) 475 ([M–C_4H_9]$^+$, 100), 491 (3), 365 (13), 363 (11), 309 (8), 263 (40), 241 (22), 223 (20), 221 (12), 207 (38), 195 (18), 179 (10).

2-(4-Hexynyloxy)benzoic acid (28). A solution of methyl salicylate (0.784 g, 5.0 mmol) in DMF (5 mL) was slowly added to a suspenion of NaH (60% in mineral oil, 0.217 g, 5.0 mmol) in DMF (5 mL) at 0°. After 15 min at that temperature, the reaction mixture was warmed to r.t. over a period of 45 min. A solution of 6-bromo-2-hexyne (0.855 g, 5 mmol) in DMF (3 mL) was then added to the clear solution formed and the resulting mixture was stirred for 24 h at 50°. For work-up, the reaction mixture was slowly poured into TBME (200 mL). The unreacted methyl salicylate was removed by washing with aq. NaOH (1 M). Saponification was achieved as follows: A mixture of crude methyl 2-(4-hexynyloxy)benzoate (1.099 g; ca. 95% according to GC-MS), KOH (1.42 g, 15 mmol) and water (10 mL) was stirred for 16h at r.t. The aqueous solution was extracted with TBME (25 mL), acidified with aq. HCl (18%) and extracted again with TBME (4x20 mL). The organic phase was washed with water, dried, concentrated in vacuo, and the crude product was purified by passing through a short column with silica gel to yield acid **28** as a pale yellow syrup (0.768 g, 70%). R_f 0.10 (hexanes/ethyl acetate 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.90 (1H, br. s), 8.18 (1H, dd, *J* = 1.8, 7.8 Hz), 7.56 (1H, ddd, *J* = 1.8, 8.3, 7.8 Hz), 7.17-7.05 (2H, m), 4.37 (2H, t, *J* = 6.3 Hz), 2.37 (2H, m), 2.07 (2H, quint, *J* = 6.3 Hz), 1.77 (3H, t, *J* = 2.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 157.4, 135.0, 133.8, 122.2, 117.7, 112.6, 77.3, 76.8, 69.0, 28.0, 15.5, 3.4; MS (EI) *m/z* (rel intensity) 218 ([M]$^{+\cdot}$, 11), 200 (4), 185 (5), 174 (3), 138 (92), 120 (94), 92 (25), 79 (100), 65 (28), 53 (71); IR (neat) 3275, 2920, 1738, 1695, 1603, 1458, 1251, 1164, 1043, 756 cm^{-1}; HRMS (EI) *calcd.* for $C_{13}H_{14}O_3$: 218.0943, *found* 218.0941.

TOTAL SYNTHESES OF (–)-PGE$_2$-1,15-LACTONE, 15-*epi*-PGE$_2$-1,15-LACTONE AND ANALOGUES

Three-component-coupling: (2*R*,3*R*,4*R*)-4-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-2-(2-butynyl)-3-{(*E*,3*S*)-3-[(1,1,1-triethylsilyl)oxy]-1-octenyl}cyclopentan-1-one ((–)-12).[25] *n*-BuLi (1.1 mL, 1.6 M in hexanes) was added to a solution of vinylstannane **8** (1.090 g, 2.0 mmol) in THF (10 mL) at –78° and the resulting yellow mixture was stirred at that temperature for 60 min. Me_2Zn (1.0 mL, 2M in toluene) was then introduced. The mixture was warmed to 0°, stirred at that temperature for 15 min and cooled back to –78°. A solution of enone **9** (94% *ee*, 0.176 g, 1.8 mmol) in THF (5 mL)

was then added over a period of 60 min via syringe pump and stirring was continued at –78° for 15 min prior to the addition of HMPA (18.5 mmol, 3.5 mL). After another 10 min, a solution of iodide **11** (1.71 g, 9.25 mmol) in THF (3 mL) was added dropwise and the resulting mixture was stirred for 18 h at –40°. For work-up, the reaction was quenced with sat. aq. NH_4Cl (3 mL), the resulting mixture was extracted with EtOAc (5x10 mL), the combined organic layers were dried over $MgSO_4$, evaporated and the crude product was subjected to column chromatography (toluene/ether ether, 1.5:1.0) to yield semi-purified product **12** as a colorless oil (0.834 g), which was used directly in next step: $[\alpha]_D^{20}$ = –24.0 (*c* = 0.33, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.66 (1H, dd, *J* = 5.3, 15.5 Hz), 5.54 (1H, dd, *J* = 7.6, 15.5 Hz), 4.15-4.03 (2H, m), 2.85-1.95 (6H, m), 1.75 (3H, t, *J* = 2.4 Hz), 1.60-1.20 (11H, m), 0.97 (9H, t, *J* = 8.1 Hz), 0.89 (9H, s), 0.59 (6H, q, *J* = 8.1 Hz), 0.08 (3H, s), 0.06 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 136.6, 128.1, 75.2, 73.1, 72.7, 72.3, 52.9, 51.7, 47.7, 38.6, 31.9, 28.8, 25.8, 25.7, 25.1, 22.6, 18.1, 16.8, 14.0, 6.9, 6.8, 5.0, 3.5, –4.6, –4.7; MS (EI) *m/z* (rel intensity) 506 ($[M]^{+\cdot}$, 13), 477 (14), 449 (51), 435 (100), 319 (48), 303 (51), 249 (61), 215 (30), 189 (81), 75 (87); IR (neat) 2955, 2858, 1750, 1412, 1251, 1115, 1006, 972, 838, 777 cm^{-1}; HRMS (EI) *calcd.* for $C_{29}H_{54}O_3Si_2$: 506.3611, *found* 506.3613.

Representative procedure for a TES Group Deprotection: (2*R*,3*R*,4*R*)-4-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-2-(2-butynyl)-3-[(*E*,3*S*)-3-hydroxy-1-octenyl]cyclopentan-1-one ((–)-13). A solution of product **12** (0.3819 g) in a mixture of AcOH/H_2O/THF (55:25:15, 9 mL) was stirred at r.t. for 9h. The reaction mixture was then poured into aqueous $NaHCO_3$ (3.5 g in 20 mL of water), the aqueous phase was extracted with EtOAc (5x10mL), the combined organic phases were dried and evaporated, and the crude product was chromatographed (hexanes/ethyl acetate, 9:1 → 5:1) to yield alcohol **13** as a colorless syrup (0.2368g, 74% over two steps). $[\alpha]_D^{20}$ = –33.4 (*c* = 0.211, $CHCl_3$); Chiral HPLC: ~100% *ee* (Chiracel OD-H, *n*-heptane/2-propanol); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.71 (1H, dd, *J* = 6.0, 15.4 Hz), 5.58 (1H, ddd, *J* = 0.5, 7.8, 15.4 Hz), 4.16-4.04 (2H, m), 2.82-1.98 (6H, m), 1.75 (3H, t, *J* = 2.6 Hz), 1.70-1.25 (12H, m), 0.89 (9H, s), 0.07 (3H, s), 0.06 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.6, 136.5, 129.8, 110.2, 77.5, 75.2, 72.9, 72.6, 52.9, 52.3, 47.5, 37.4, 31.7, 25.7, 25.2, 22.6, 18.1, 16.7, 14.0, 3.5, –4.5, –4.6; MS (EI) *m/z* (rel intensity) 392 ($[M]^{+\cdot}$, 0.5), 335 ($[M–C_4H_9]^+$, 22), 215 (13), 189 (100), 147 (9), 133 (25), 119 (35), 105 (57), 91 (35), 75 (54); IR (neat) 3467, 2929, 2858, 1747, 1471, 1252, 1117, 972, 883, 838 cm^{-1}; Anal. *calcd.* for $C_{23}H_{40}O_3Si$ (392.66): C, 70.36; H, 10.27; *found* C, 70.43; H, 10.22.

Preparation of (±)-13 and of (2*R,3*R**,4*R**)-4-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-2-(2-butynyl)-3-[(*E*,3*R**)-3-hydroxy-1-octenyl]cyclopentan-1-one (*epi*-(±)-13).** The three component coupling and TES-deprotection steps were carried out as described above using racemic starting materials. The crude product (1.6788 g) was chromatographed on a Lobar® column (Lichoprep Si60, 40-63 μm, E. Merck) using hexanes/ethyl acetate 5:1 as the eluent. The first fraction contained (±)-**13** (0.4497 g, 30% over two steps), the analytical data of which are identical to those described above for (–)-**13**. A second, more polar product delivered (±)-*epi*-**13** (0.4610 g, 31% over two steps) which shows the following analytical and spectroscopic properties: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (1H, dd, *J* = 6.3, 15.3 Hz), 5.57 (1H, ddd, *J* = 0.6, 8.0, 15.3 Hz), 4.16-4.03 (2H, m),

2.80-1.99 (6H, m), 1.75 (3H, t, J = 2.5 Hz), 1.70-1.20 (12H, m), 0.90 (9H, s), 0.06 (3H, s), 0.05 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.6, 136.7, 130.2, 77.5, 75.3, 72.8, 72.7, 53.0, 52.4, 47.5, 37.3, 31.8, 25.7, 25.0, 22.6, 18.1, 16.8, 14.0, 3.5, –4.6, –4.7; MS (EI) *m/z* (rel intensity) 392 ($[M]^{+\cdot}$, 0.5), 335 ($[M-C_4H_9]^+$, 18), 215 (13), 189 (100), 147 (9), 133 (25), 119 (35), 105 (59), 91 (36), 75 (60); IR (neat) 3445, 2926, 2857, 1736, 1471, 1255, 1116, 974, 887, 839 cm^{-1}; Anal. *calcd.* for $C_{23}H_{40}O_3Si$ (392.66): C, 70.36; H, 10.27; *found* C, 70.44; H, 10.22.

Representative procedure for Esterification: (1*S*,2*E*)-3-[(1*R*,2*R*,5*R*)-5-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-2-(2-butynyl)-3-oxocyclopentyl]-1-pentyl-2-propenyl 5-heptynoate ((–)-15). To a stirred solution of alcohol **13** (41.8 mg, 0.106 mmol) in CH_2Cl_2 (5 mL) was added a solution of diisopropyl carbodiimide (27.2 mg, 0.212 mmol), DMAP cat. and acid **14** (27.9 mg, 0.212 mmol) in CH_2Cl_2 (5 mL). The resulting mixture was stirred at r.t. until TLC showed complete conversion (3h). The clear colorless solution was diluted with EtOAc (20 mL) and quenched with water (1 mL). A standard extractive work-up followed by column chromatography (hexanes/ethyl acetate, 9:1) gave product **15** (51.2 mg, 96%) as a colorless syrup. $[\alpha]_D^{20}$ = –55.6 (c = 0.22, $CHCl_3$); Chiral HPLC: ~ 100% *ee* (Chiracel OD-H, *n*-heptane/2-propanol); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.63-5.58 (2H, m), 5.29 (1H, m), 4.07 (1H, dt, J = 7.1, 8.8 Hz), 2.80-1.20 (29H, m), 0.87 (9H, s), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.3, 172.4, 132.3, 132.1, 77.9, 77.2, 76.3, 75.1, 74.1, 72.7, 52.9, 52.5, 47.5, 34.6, 33.5, 31.5, 25.7, 24.9, 24.3, 22.5, 18.2, 18.0, 16.7, 14.0, 3.5, 3.4, –4.7, MS (EI) *m/z* (rel intensity) 500 ($[M]^{+\cdot}$, 0.3), 443 ($[M-C_4H_9]^+$, 8), 317 (33), 243 (98), 215 (37), 183 (82), 133 (25), 109 (71), 91 (41), 75 (100); IR (neat) 2929, 2858, 1748, 1735, 1471, 1250, 1162, 1116, 973, 838 cm^{-1}; Anal. *calcd.* for $C_{30}H_{48}O_4Si$ (500.80): C, 71.95; H, 9.66; *found* C, 71.87; H, 9.73.

The following compounds have been prepared analogously:

(1*R,2*E*)-3-[(1*R**,2*R**,5*R**)-5-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-2-(2-butynyl)-3-oxocyclopentyl]-1-pentyl-2-propenyl 5-heptynoate ((±)-19).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.63-5.56 (2H, m), 5.28 (1H, m), 4.07 (1H, dt, J = 7.0, 8.9 Hz), 2.80-1.22 (29H, m), 0.89 (9H, s), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.4, 172.5, 132.4, 132.1, 77.9, 76.4, 75.1, 74.1, 72.7, 52.9, 52.2, 47.5, 34.4, 33.5, 31.6, 25.7, 24.8, 24.3, 22.5, 18.2, 18.0, 16.5, 14.0, 3.5, 3.4, 1.0, –4.6, –4.8; MS (EI) *m/z* (rel intensity) 500 ($[M]^{+\cdot}$, 1), 443 ($[M-C_4H_9]^+$, 10), 317 (35), 243 (85), 215 (37), 201 (17), 189 (47), 183 (100), 133 (29), 75 (84), IR (neat) 2929, 2858, 1745, 1471, 1252, 1159, 1079, 972, 837 cm^{-1}; Anal. *calcd.* for $C_{30}H_{48}O_4Si$ (500.80): C, 71.95; H, 9.66; *found* C, 72.06; H, 9.58.

(1*S*,2*E*)-3-[(2*R*,5*R*)-5-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-2-(2-butynyl)-3-oxocyclopentyl]-1-pentyl-2-propenyl 9-undecynoate ((–)-24). $[\alpha]_D^{20}$ = –49.2 (c = 1.02, $CHCl_3$); Chiral HPLC: ~100% *ee* (Chiracel OD-H, *n*-heptane:2-propanol); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (2H, m), 5.28 (1H, m), 4.07 (1H, dt, J = 7.0, 8.8 Hz), 2.80-2.52 (3H, m), 2.30-1.96 (7H, m), 1.80-1.25 (27H, m), 0.87 (9H, m), 0.048 (3H, s), 0.046 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.4, 172.9, 132.2, 132.2, 79.2, 75.4, 75.1, 73.9, 72.7, 52.9, 52.4, 47.5, 34.6, 34.6, 31.5, 29.1, 29.0, 28.8, 28.7, 25.7, 25.0, 24.9, 22.5, 18.7, 18.0, 16.6, 14.0, 3.6, 3.5, –4.7, –4.7; MS (EI) *m/z* (rel intensity) 556 ($[M]^{+\cdot}$,

1), 499 (12), 317 (40), 243 (100), 239 (29), 215 (35), 189 (42), 119 (30), 105 (52), 75 (53); IR (neat) 2952, 2930, 2858, 1749, 1736, 1468, 1377, 1250, 1117, 838 cm^{-1}; Anal. *calcd.* for $C_{34}H_{56}O_4Si$ (556.91): C, 73.33; H, 10.14; *found* C, 73.36; H, 10.08.

(1*S*,2*E*)-3-[(2*R*,5*R*)-5-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-2-(2-butynyl)-3-oxocyclopentyl]-1-pentyl-2-propenyl 2-(4-hexynyloxy)benzoate ((–)-29). $[\alpha]_D^{20}$ = –16.0 (*c* = 1.00, $CHCl_3$); Chiral HPLC: ~100% *ee* (Chiracel OD-H, *n*-heptane:2-propanol); ^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (1H, dd, *J* = 1.8, 7.9 Hz), 7.43 (1H, ddd, *J* = 1.8, 7.9, 8.5 Hz), 7.00-6.92 (2H, m), 5.71 (2H, m), 5.43 (1H, m), 4.10 (2H, m), 2.80-0.85 (28H, m), 0.82 (9H, s), 5.94 (3H, s), –0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.5, 165.5, 158.4, 133.2, 132.1, 131.9, 131.6, 120.8, 119.9, 112.9, 78.1, 77.5, 76.1, 75.2, 74.4, 72.7, 67.1, 52.8, 52.3, 47.5, 34.8, 31.6, 28.7, 25.7, 25.0, 22.5, 18.0, 16.7, 15.5, 14.0, 3.5, 3.4, –4.7, –4.8; MS (EI) *m/z* (rel intensity) 592 ($[M]^{+\cdot}$, 0.5), 535 (5), 317 (15), 293 (48), 275 (100), 243 (21), 201 (68), 195 (51), 145 (36), 121 (25); IR (neat) 2955, 2929, 2857, 1749, 1727, 1701, 1601, 1452, 1251, 838 cm^{-1}; Anal. *calcd.* for $C_{36}H_{52}O_5Si$ (592.90): C, 72.93; H, 8.84; *found* C, 72.76; H, 8.89.

Representative Procedure for a Diyne Metathesis: (3*S*,11a*R*,14*R*,14a*R*)-14-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-3-pentyl-9,10-didehydro-6,7,8,11,11a,13,14,14a-octahydro-3*H*-cyclopenta [*e*]oxacyclotridecine-5,12-dione ((–)-16). The orange-brown solution of the molybdenum complex **5** or **6** (7.5 mol%) in dry toluene (10 mL) and CH_2Cl_2 (2 mL) was stirred at r.t. for 5 min. A solution of diyne **15** (52.8 mg, 0.105 mmol) in toluene (4 mL) was then added and the resulting solution was quickly warmed to 80° and stirred for 16h at that temperature. The resulting mixture was cooled to r.t., the solvent was evaporated and the residue was purified by flash chromatography (hexanes/ethyl acetate, 9:1) to yield product **16** as a pale yellow syrup (32.8 mg, 70%). $[\alpha]_D^{20}$ = –189.7 (*c* = 0.23, $CHC1_3$); ^1H NMR (300 MHz, $CDC1_3$) δ 5.88 (2H, m), 5.10 (1H, dt, *J* = 8.0, 5.2 Hz), 4.0 (1H, m) , 2.98 (1H, d, *J* = 15.4 Hz), 2.69 (1H, dd, *J* = 18.4, 7.8 Hz), 2.50-1.20 (21H, m), 0.87 (9H, s), 0. 04 (3H, s), 0.03 (3H, s); ^{13}C NMR (75 MHz, $CDC1_3$) δ 211.8, 172.4, 132.3, 130.4, 79.6, 79.3, 73.0, 72.2, 56.1, 54.8, 34.9, 46.6, 34.1, 31.6, 25.7, 25.7, 22.6, 22.5, 19.0, 18.0, 17.5, 14.0, –4.6, –4.8; MS (EI) 446 ($[M]^{+\cdot}$, 1), 431 (1), 389 (33), 317 (18), 297 (8), 225 (5), 155 (5), 129 (10), 91 (12), 75 (100), 55 (21); IR (neat) 2955, 2930, 2857, 1746, 1252, 1154, 1115, 964, 839, 778 cm^{-1}; HRMS (EI) *calcd.* for $C_{26}H_{42}O_4Si$: 446.2852, *found* 446.2850. Anal. *calcd.* for $C_{26}H_{42}O_4Si$ (446.71): C, 69.91; H, 9.48; *found* C, 70.08; H, 9.42.

The following compounds were prepared analogously:

(3*R,11a*R**,14*R**,14a*R**)-14-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-3-pentyl-9,10-didehydro-6,7,8,11,11a,13,14,14a-octahydro-3*H*-cyclopenta[*e*]oxacyclotridecine-5,12-dione ((±)-20).** ^1H NMR (300 MHz, $CDCl_3$) δ 5.92 (1H, dd, *J* = 9.2, 14.9 Hz), 5.49 (1H, dd, *J* = 8.9, 15.9 Hz), 5.30 (1H, m), 4.10 (1H, m), 3.02 (1H, dm, *J* = 17.0 Hz), 2.67 (1H, ddd, *J* = 0.9, 7.7, 18.8 Hz), 2.45-1.22 (21H, m), 0.87 (9H, s), 0.04 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.5, 172.7, 137.6, 130.8, 80.1, 78.8, 74.4, 71.8, 57.5, 54.2, 46.4, 34.8, 33.7, 31.6, 25.7, 25.0, 23.1, 22.5, 18.9, 18.6, 18.0, 14.0, –4.6, –4.7; MS (EI) *m/z* (rel intensity) 446 ($[M]^{+\cdot}$, 1.4), 431 (2), 389 ($[M–C_4H_9]^+$, 100), 371 (39), 297 (22), 225 (14), 185 (13), 129 (26), 117 (24), 75 (81); IR (neat) 2955, 2930, 2858, 1746,

1471, 1374, 1249, 1151, 896, 838 cm^{-1}; Anal. *calcd.* for $C_{26}H_{42}O_4Si$ (446.71): C, 69.91; H, 9.48; *found* C, 69.73; H, 9.56.

(3*S*,15a*R*,18*R*,18a*R*)-18-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-3-pentyl-13,14-didehydro-6,7,8,9,10,11,12,15,15a,17,18,18a-dodecahydro-3*H*-cyclopenta[*e*]oxacycloheptadecine-5,16-dione ((–)-25). Colorless oil. $[\alpha]_D^{20}$ = –64.8 (*c* = 1.20, $CHCl_3$); Chiral HPLC: ~100% *ee* (Chiralpak AD, *n*-heptane:2-propanol); ^1H NMR (300 MHz, $CDCl_3$) δ 5.76 (1H, dd, *J* = 6.1, 15.9 Hz), 5.59 (1H, ddd, *J* = 1.1, 6.1, 15.9 Hz), 5.32 (1H, dt, *J* = 6.3, 6.6 Hz), 4.20 (1H, dt, *J* = 5.8, 5.7 Hz), 2.91 (1H, dd, *J* = 7.0, 6.3 Hz), 2.62-1.20 (30H, m), 0.88 (9H, s), 0.08 (3H, s), 0.06 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.1, 173.3, 132.3, 131.3, 82.1, 77.4, 73.3, 73.2, 52.2, 51.3, 46.9, 34.5, 33.6, 31.5, 28.2, 27.9, 27.8, 27.7, 25.7, 25.1, 25.0, 22.5, 18.7, 18.4, 18.0, 14.0, –4.8; MS (EI) *m/z* (rel intensity) 502 ($[M]^{+\cdot}$, 0.5), 487 (1), 445 (61), 427 (100), 417 (27), 373 (33), 353 (52), 227 (8), 185 (15), 117 (26), 75 (98); IR (neat) 2952, 2931, 2858, 1747, 1734, 1471, 1377, 1250, 1120, 838 cm^{-1}; Anal. *calcd.* for $C_{30}H_{50}O_4Si$ (502.82): C, 71.66; H, 10.02; *found* C, 71.51; H, 10.11.

(11a*R*,14*R*,14a*R*,17*S*)-14-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-17-pentyl-9,10-didehydro-7,8,11,11a,13,14,14a,17-octahydro-19*H*-cyclopenta[*h*][1,13]benzodioxacyclohexadecine-12,19(6*H*)-dione ((–)-30). Colorless oil. $[\alpha]_D^{20}$ = –121.3 (*c* = 0.52, $CHCl_3$); Chiral HPLC: ~99% *ee* (Chiracel OD-H, *n*-heptane:2-propanol); ^1H NMR (300 MHz, $CDCl_3$) δ 7.72 (1H, dd, *J* = 1.8, 7.6 Hz), 7.42 (1H, ddd, *J* = 1.8, 7.6, 8.2 Hz), 7.00 (2H, m), 5.85 (2H, m), 5.64 (1H, m), 4.30-4.00 (2H, m), 2.87-2.55 (2H, m), 2.40-1.25 (20H, m), 0.90 (9H, s), 0.07 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.8, 166.9, 157.3, 132.7, 131.4, 131.2, 130.4, 123.1, 121.0, 115.4, 81.2, 78.4, 73.9, 72.7, 67.5, 55.0, 53.0, 46.8, 33.5, 31.6, 29.9, 27.6, 25.7, 25.1, 22.5, 19.1, 18.0, 14.8, 14.0, –4.6, –4.7, MS (EI) *m/z* (rel intensity) 538 ($[M]^{+\cdot}$, 2), 481 (58), 463 (34), 389 (100), 361 (16), 269 (27), 215 (44), 195 (30), 121 (56), 75 (61); IR (neat) 2954, 2928, 2857, 1742, 1702, 1600, 1453, 1293, 1249, 840 cm^{-1}; Anal. *calcd.* for $C_{32}H_{46}O_5Si$ (538.81): C, 71.33; H, 8.61; *found* C, 71.29 H, 8.54.

Representative procedure for a Lindlar Reduction: (3*S*,11a*R*,14*R*,14a*R*)-14-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-3-pentyl-6,7,8,11,11a,13,14,14a-octahydro-3*H*-cyclopenta[*e*]oxacyclotridecine-5,12-dione ((–)-17). A solution of quinoline in *n*-hexane (0.05 mL of a stock solution of 0.05 mL of quinoline in 10 mL of hexane) was added to a solution of cycloalkyne **16** (30.6 mg, 0.0685 mmol) in *n*-hexane (5 mL). Lindlar catalyst (14.2 mg) was added and the resulting suspension was stirred under an atmosphere of H_2 (1 atm) until TLC indicated complete conversion (ca. 2h). For work up, the catalyst was filtered off, the solvent was evaporated and the residue was purified by column chromatography (hexanes/ethyl acetate, 18:1 → 9:1) to give product **17** as a colorless syrup (26.5 mg, 86% yield). $[\alpha]^{20}_D$ = –148.7 (*c* = 0.16, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.01 (1H, dd, *J* = 6.4, 15.8 Hz), 5.77 (1H, dd, *J* = 8.6, 15.8 Hz), 5.61 (1H, m), 5.35 (1H, m), 5.21 (1H, dt, *J* = 6.1, 8.1 Hz), 4.06 (1H, dt, *J* = 8.6, 7.7 Hz), 2.71 (1H, ddd, *J* = 1.3, 7.7, 18.8 Hz), 2.42-1.20 (22H, m), 0.87 (9H, s), 0.03 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 173.1, 133.8, 132.8, 129.5, 128.7, 72.4, 71.9, 57.4, 55.1, 46.8, 34.5, 34.2, 31.6, 25.6, 25.5, 25.3, 23.9, 22.5, 18.0, 14.0, 1.0, –4.6, –4.8; MS (EI) *m/z* (rel intensity) 448 ($[M]^{+\cdot}$, 1), 391 ($[M–C_4H_9]^+$, 98), 373

(100), 319 (49), 299 (35), 245 (16), 185 (26), 161 (7), 105 (20), 93 (20), 75 (77); IR (neat) 3011, 2956, 2858, 1745, 1471, 1377, 1248, 1116, 970, 837, 778 cm^{-1}; HRMS (EI) *calcd.* for $C_{26}H_{44}O_4Si$: 448.3009, *found* 448.2997; Anal. *calcd.* for $C_{26}H_{44}O_4Si$ (448.72): C, 69.60; H, 9.88; *found* C, 69.48, H, 9.79.

The following compounds were prepared analogously:

(3*R,11a*R**,14*R**,14a*R**)-14-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-3-pentyl-6,7,8,11,11a,13,14,14a-octahydro-3*H*-cyclopenta[*e*]oxacyclotridecine-5,12-dione ((±)-21).** ^1H NMR (300 MHz, $CDCl_3$) δ 5.70 (1H, dd, *J* = 8.8, 15.1 Hz), 5.60-5.31 (4H, m), 4.10 (1H, dt, *J* = 7.8, 8.9 Hz), 2.67 (1H, ddd, *J* = 1.1, 7.6, 18.8 Hz), 2.42-1.23 (22H, m), 0.86 (9H, s), 0.03 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.0, 173.5, 135.8, 134.0, 130.0, 127.2, 74.5, 72.1, 55.9, 54.7, 46.8, 35.0, 33.7, 31.5, 25.7, 25.6, 25.4, 24.9, 23.4, 22.5, 18.0, 14.0, –4.6, –4.8; MS (EI) *m/z* (rel intensity) 448 ($[M]^{+\cdot}$, 1), 433 (2), 391 ($[M-C_4H_9]^+$, 100), 373 (89), 319 (34), 299 (36), 185 (16), 161 (6), 105 (16), 93 (12), 75 (55), IR (neat) 3027, 2930, 2858, 1745, 1715, 1463, 1360, 1244, 1153, 971, 837, 777 cm^{-1}; Anal. *calcd.* for $C_{26}H_{44}O_4Si$ (448.72): C, 69.60; H, 9.88; *found* C, 69.73; H, 9.78.

(3*S*,15a*R*,18*R*,18a*R*)-18-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-3-pentyl-6,7,8,9,10,11,12,15,15a,17,18,18a-dodecahydro-3*H*-cyclopenta[*e*]oxacycloheptadecine-5,16-dione ((–)-26). Colorless syrup. $[\alpha]_D^{20}$ = –110.7 (*c* = 0.665, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.84 (1H, dd, *J* = 6.2, 15.8 Hz), 5.58 (1H, dd, *J* = 6.5, 15.8 Hz), 5.49-5.16 (3H, m), 3.96 (1H, dt, *J* = 7.2, 8.8 Hz), 2.63 (1H, dd, *J* = 17.9, 6.9 Hz), 2.58-1.20 (30H, m), 0.87 (9H, s), 0.05 (3H, s), 0.03 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.4, 173.1, 133.0, 132.5, 129.6, 125.0, 73.8, 73.7, 52.4, 50.8, 48.0, 34.3, 33.8, 31.5, 28.1, 28.1, 27.9, 27.1, 26.6, 25.7, 25.1, 24.6, 24.5, 22.5, 18.0, 14.0, –4.6, –4.8; MS (EI) *m/z* (rel intensity) 504 ($[M]^{+\cdot}$, 1), 447 (52), 429 (100), 419 (40), 401 (19), 375 (72), 355 (63), 239 (11), 105 (16), 75 (66); IR (neat) 2930, 2857, 1744, 1463, 1375, 1250, 1155, 1116, 838, 777 cm^{-1}; Anal. *calcd.* for $C_{30}H_{52}O_4Si$ (504.83): C, 71.38; H, 10.38; *found* C, 71.58; H, 10.46.

(11a*R*,14*R*,14a*R*,17*S*)-14-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-17-pentyl-7,8,11,11a,13,14,14a,17-octahydro-19*H*-cyclopenta[*h*][1,13]benzodioxacyclohexadecine-12,19(6*H*)-dione ((–)-31). Colorless syrup. $[\alpha]_D^{20}$ = –105.2 (*c* = 0.93, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (1H, dd, *J* = 1.8, 7.6 Hz), 7.40 (1H, ddd, *J* = 1.8, 7.6, 8.4 Hz), 6.98 (1H, dd, *J* = 1.0, 7.6 Hz), 6.92 (1H, d, *J* = 8.4 Hz), 5.88 (1H, dd, *J* = 6.5, 15.8 Hz), 5.71 (1H, ddd, *J* = 0.8, 6.5, 15.8 Hz), 5.57-5.41 (3H, m), 4.02 (2H, m), 2.66 (1H, ddd, *J* = 0.9, 7.6, 18.5 Hz), 2.55-1.21 (20H, m), 0.90 (9H, s), 0.06 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.8, 167.2, 157.3, 132.5, 132.1, 131.4, 130.5, 130.4, 126.3, 122.2, 120.1, 112.5, 74.9, 73.3, 68.4, 53.3, 51.9, 47.6, 33.6, 31.6, 29.6, 25.7, 25.2, 24.7, 24.4, 22.5, 18.0, 14.0, –4.6, –4.8; MS (EI) *m/z* (rel intensity) 540 ($[M]^{+\cdot}$, 3), 483 (23), 465 (40), 411 (16), 391 (100), 322 (11), 271 (14), 195 (28), 121 (36), 81 (44); IR (neat) 2951, 2927, 2855, 1726, 1598, 1447, 1246, 1057, 837, 757 cm^{-1}; Anal. *calcd.* for $C_{32}H_{48}O_5Si$ (540.82): C, 71.07; H, 8.95; *found* C, 70.96; H, 9.06.

Representative procedure for a TBS Group Deprotection: (3*S*,11a*R*,14*R*,14a*R*)-14-hydroxy-3-pentyl-6,7,8,11,11a,13,14,14a-octahydro-3*H*-cyclopenta[*e*]oxacyclotridecine-5,12-dione; Prostaglandin E_2-1,15-Lactone ((–)-1). The reaction was carried out in a polyethylene bottle. A solution of compound **17** (21.8 mg, 0.0486 mmol) in MeCN (6 mL) was added to HF (48% in water; 1 mL) in MeCN (3 mL)[28]. After 1 h the resulting clear mixture was slowly poured into aq. $NaHCO_3$ (2.34 g, 32 mmol, in water (10 mL)) (CAUTION!). After extraction of the aqueous phase with EtOAc (5x10 mL), the combined organic layers were dried over $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 3:2) affording prostaglandin lactone **1** (14.3 mg, 88%) as colorless needles; mp 76.5-77.5°C (Et_2O/pentane) [Lit.[4a,2b] mp 73-76°C (Et_2O/hexane)]; $[\alpha]_D^{20}$ = –185.0 (c = 0.15, $CHCl_3$); ^1H MR (600 MHz, $CDCl_3$) δ 6.11 (1H, dd, *J* = 15.8, 6.6 Hz), 5.81 (1H, dd, *J* = 15.9, 8.7 Hz), 5.60 (1H, dt, *J* = 10.5, 5.9 Hz), 5.35 (1H, ddd, *J* = 10.4, 9.6, 5.5 Hz), 5.20 (1H, dt, *J* = 8.5, 6.0 Hz), 4.14 (1H, dt, *J* = 7.9, 9.2 Hz), 2.80 (1H, ddd, *J* = 18.8, 7.8, 1.2 Hz), 2.40 (1H, ddd, *J* = 13.3, 8.7, 3.2 Hz) 2.29 (1H, dt, *J* = 13.2, 8.8 Hz), 2.21 (1H, dd, *J* = 18.9, 9.3 Hz), 2.20 (1H, ddd, *J* = 13.2, 9.4, 3.3 Hz), 2.18-1.20 (16H, m), 0.89 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.1, 173.2, 134.7, 131.9, 129.3, 128.9, 71.8, 71.7, 57.9, 55.0, 45.5, 34.2, 34.0, 31.5, 25.6, 25.5, 25.3, 23.9, 22.5, 14.0; IR (KBr) 3431, 3002, 2938, 2857, 1726, 1377, 1243, 1160, 1041, 728 cm^{-1}. MS (EI) 334 ($[M]^{+\cdot}$, 24), 316 (38), 298 (13), 262 (39), 208 (63), 163 (64), 151 (22), 145 (15),133 (25), 121 (28), 107 (42) , 91 (78) , 79 (100) , 67 (83), 55 (93).

The following compounds have been prepared analogously using a mixture of aq. HF/THF (1:6):

(3*R,11a*R**,14*R**,14a*R**)-14-hydroxy-3-pentyl-6,7,8,11,11a,13,14,14a-octahydro-3*H*-cyclo penta[*e*]oxacyclotridecine-5,12-dione ((±)-22).** Colorless crystals; mp 71-72°C (Et_2O/hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.76 (1H, dd, *J* = 8.8, 15.2 Hz), 5.59 (1H, dd, *J* = 8.8, 15.2 Hz), 5.55-5.33 (3H, m), 4.17 (1H, dt, *J* = 7.8, 9.2 Hz), 2.77 (1H, ddd, *J* = 1.3, 7.8, 18.8 Hz), 2.44-1.20 (20H, m), 0.89 (3H, t, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.2, 173.5, 134.8, 130.2, 126.9, 74.4, 71.6, 56.3, 54.5, 45.7, 35.0, 33.6, 31.5, 25.6, 25.4, 25.0, 23.3, 22.5, 14.0; MS (EI) *m/z* (rel intensity) 334 ($[M]^{+\cdot}$, 22), 316 (39), 263 (43), 208 (96), 182 (20), 163 (93), 147 (18), 95 (91), 55 (100); IR (KBr) 3453, 2954, 2861, 1730, 1457, 1330, 1242, 1154, 1088, 970 cm^{-1}; HRMS (EI) *calcd.* for $C_{20}H_{30}O_4$ 334.2144; *found* 334.2145.

(3*S*,11a*R*,14*R*,14a*R*)-14-hydroxy-3-pentyl-9,10-didehydro-6,7,8,11,11a,13,14,14a-octahydro-3*H*-cyclopenta[*e*]oxacyclotridecine-5,12-dione ((–)-18). Colorless oil. $[\alpha]_D^{20}$ = –268.6 (c = 0.54, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.35 (1H, dd, *J* = 5.4, 15.8 Hz), 5.80 (1H, dd, *J* = 7.2, 15.8 Hz), 5.09 (1H, dt, *J* = 5.6, 7.9 Hz), 4.05 (1H, dt, *J* = 8.7, 9.5 Hz), 2.97 (1H, dm, *J* = 17.2 Hz), 2.79 (1H, dd, *J* = 7.9, 18.9 Hz), 2.50-1.20 (19H, m), 0.90 (3H, t, *J* = 4.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0, 172.5, 133.2, 129.9, 79.9, 79.0, 72.6, 71.4, 56.1, 55.4, 45.2, 34.9, 34.1, 31.5, 25.4, 22.5, 22.5, 18.9, 17.5, 14.0; MS (EI) *m/z* (rel intensity) 332 ($[M]^{+\cdot}$, 24), 314 (12), 276 (10), 261 (52), 205 (29), 163 (50), 117 (34), 91 (56), 79 (52), 55 (100); IR (neat) 3468, 2932, 2859, 1734, 1431, 1374, 1218, 1153, 1086, 965 cm^{-1}.

(3*R,11a*R**,14*R**,14a*R**)-14-hydroxy-3-pentyl-9,10-didehydro-6,7,8,11,11a,13,14,14a-octahydro-3*H*-cyclopenta[*e*]oxacyclotridecine-5,12-dione ((±)-23).** Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.98 (1H, dd, *J* = 8.6, 15.1 Hz), 5.57 (1H, dd, *J* = 8.6, 15.1 Hz), 5.30 (1H, m), 4.17 (1H, dt, *J* = 8.5, 8.8 Hz), 3.03 (1H, dm, *J* = 17.0 Hz), 2.79 (1H, dd, *J* = 7.8, 18.8 Hz), 2.50-1.20 (19H, m), 0.89 (3H, t, *J* = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.7, 172.7, 136.2, 131.5, 80.4, 78.5, 74.1, 71.1, 57.2, 54.7, 45.2, 34.8, 33.7, 31.5, 25.0, 23.0, 22.5, 18.9, 18.6, 14.0; MS (EI) *m/z* (rel intensity) 332 ([M]$^{+\cdot}$, 59), 314 (10), 276 (13), 261 (63), 205 (49), 163 (60), 117 (42), 91 (61), 79 (58), 55 (100); IR (neat) 3462, 2955, 2932, 2861, 1741, 1432, 1236, 1152, 1088, 968 cm^{-1}.

(3*S*,15a*R*,18*R*,18a*R*)-18-hydroxy-3-pentyl-6,7,8,9,10,11,12,15,15a,17,18,18a-dodecahydro-3*H*-cyclopenta[*e*]oxacycloheptadecine-5,16-dione ((–)-27). Colorless oil. $[\alpha]_D^{20}$ = −131.5 (*c* = 0.44, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (1H, dd, *J* = 6.5, 15.9 Hz), 5.65 (1H, dd, *J* = 5.0, 15.9 Hz), 5.53-5.14 (3H, m), 4.09 (1H, dt, *J* = 7.3, 9.2 Hz), 2.76 (1H, ddd, *J* = 0.9, 7.5, 18.5 Hz), 2.60-1.20 (28H, m), 0.88 (3H, t, *J* = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.7, 173.4, 133.2, 131.1, 131.0, 124.7, 73.2, 72.5, 53.8, 51.0, 47.0, 34.4, 33.5, 31.5, 28.4, 28.2, 27.9, 27.3, 26.7, 25.9, 24.9, 24.8, 24.7, 24.5, 22.5, 14.0; MS (EI) *m/z* (rel intensity) 390 ([M]$^{+\cdot}$, 24), 372 (28), 354 (11), 319 (22), 247 (23), 238 (32), 208 (64), 164 (48), 151 (38), 95 (100); IR (KBr) 3454, 2930, 2858, 1732, 1461, 1371, 1247, 1157, 1079, 973 cm^{-1}; HRMS (EI) *calcd.* for $C_{24}H_{38}O_4$: 390.2770; *found* 390.2775.

(11a*R*,14*R*,14a*R*,17*S*)-14-hydroxy-17-pentyl-7,8,11,11a,13,14,14a,17-octahydro-19*H*-cyclo penta[*h*][1,13]benzodioxacyclohexadecine-12,19(6*H*)-dione ((–)-32). Colorless crystals. mp 103-104°C (Et_2O/hexanes); $[\alpha]_D^{20}$ = −139.9 (*c* = 0.765, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (1H, dd, *J* = 1.8, 7.6 Hz), 7.41 (1H, ddd, *J* = 1.8, 7.6, 8.2 Hz), 6.99 (1H, dd, *J* = 1.0, 7.6 Hz), 6.93 (1H, d, *J* = 8.2 Hz), 5.86-5.83 (2H, m), 5.58 (1H, m), 5.52-5.40 (2H, m), 4.15-4.00 (2H, m), 2.78 (1H, dd, *J* = 7.6, 18.6 Hz), 2.50-1.20 (19H, m), 0.89 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 167.3, 157.3, 132.6, 131.9, 131.8, 130.7, 130.3, 126.0, 122.2, 120.2, 112.6, 74.2, 72.4, 68.5, 54.5, 52.1, 46.6, 33.3, 31.6, 29.7, 25.1, 24.8, 24.4, 22.5, 14.0; MS (EI) *m/z* (rel intensity) 426 ([M]$^{+\cdot}$, 8), 408 (21), 390 (13), 288 (7), 270 (8), 208 (87), 164 (40), 151 (18), 121 (80), 81 (100); IR (neat) 3459, 2947, 2858, 1736, 1678, 1601, 1453, 1305, 1248, 756 cm^{-1}; HRMS (EI) *calcd.* for $C_{26}H_{34}O_5$: 426.2406; *found* 426.2407.

ALKYNE CROSS METATHESIS (ACM). SYNTHESIS OF (–)-PGE$_2$ AND FURTHER PROSTAGLANDIN ANALOGUES

Alkyne Cross Metathesis. Preparation of 7-[3-(*tert*-Butyl-dimethyl-silanyloxy)-5-oxo-2-(3-triethylsilanyloxy-oct-2-enyl)-cyclopentyl]-hept-5-ynoic acid methyl ester ((–)-34). To a solution of complex **5** (12 mg, 0.019 mmol) in toluene (4 mL) and CH_2Cl_2 (200 μL) is added compound **12** (97 mg, 0.19 mmol) and 5-decyn-dioic acid dimethyl ester **33** (86 mg, 0.38 mmol) and the resulting solution is stirred at 80°C for 9 h. After evaporation of the solvent, the residue is purified by flash chromatography (hexanes/ethyl acetate, 15:1) affording product **34** as a colorless

syrup (58 mg, 51 %). $[\alpha]_D^{20}$ = −14.6 (c = 0.78, $CHCl_3$). IR 2956, 2929, 2858, 1748, 1607, 1464, 1252, 1110, 837, 776; ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 6.37 (m, 1H), 5.73 - 5.55 (m, 2H), 4.20 - 4.08 (m, 1H), 3.66 (s, 3H), 2.90 - 2.55 (m, 2H), 2.41 (t, *J* = 7.4 Hz, 2H), 2.35 - 2.00 (m, 7H), 1.77 (dt, *J* = 14.4, 7.2 Hz, 2H), 1.60 - 1.19 (m, 7H), 1.05 - 0.85 (m, 21H), 0.62 (q, *J* = 8.0 Hz, 6H), 0.08 (d, *J* = 4.0 Hz, 6H); ^{13}C NMR (CD_2Cl_2, 75 MHz): δ 213.9, 173.8, 137.1, 128.6, 120.2, 115.4, 81.2, 77.7, 73.4, 73.2, 53.1, 52.2, 51.7, 48.1, 39.0, 33.1, 32.3, 30.3, 25.9, 25.5, 24.6, 23.0, 18.4, 18.3, 17.1, 14.2, 7.1, 5.4, −4.5, −4.6; MS (EI) *m/z* (rel. intensity) 593 ([M$^+$], 3), 563 (21), 535 (85), 521 (25), 460 (8), 431 (47), 389 (65), 297 (21), 115 (30), 87 (58),75 (100), 59 (23); HRMS ($C_{33}H_{60}O_5Si_2$ - C_4H_9): *calcd.* 535.327506, *found* 535.327411; Anal. *calcd.* for $C_{33}H_{60}O_5Si_2$ (593.00): C, 66.84; H, 10.20; *found* C, 66.52; H, 10.18.

Methyl (*Z*)-7-((1*R*,2*R*,3*R*)-3-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-5-oxo-2-{(*E*,3*S*)-3-[(1,1,1-triethylsilyl)oxy]-1-octenyl}cyclopentyl)-5-heptenoate ((−)-35). The Lindlar reduction was carried out according to the representative procedure described in the previous section. Colorless oil. $[\alpha]_D^{20}$ = −39.1 (*c* = 1.11, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55 (2H, m), 5.37 (2H, m), 4.14-4.00 (2H, m), 3.66 (3H, s), 2.62 (1H, dd, *J* = 6.8, 18.1 Hz), 2.55-1.20 (19H, m), 0.95 (9H, t, *J* = 7.9 Hz), 0.87 (9H, s), 0.58 (6H, q, *J* = 7.9 Hz), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.5, 174.0, 136.3, 130.7, 128.6, 126.7, 77.2, 73.2, 72.7, 53.8, 52.5, 51.4, 47.7, 38.6, 33.5, 31.9, 26.7, 25.8, 25.3, 25.1, 24.7, 22.6, 18.0, 14.0, 6.9, 5.0, −4.6, −4.7; MS (EI) *m/z* (rel intensity) 594 ([M]$^{+\cdot}$, 2), 565 (23), 537 (100), 523 (26), 462 (12), 391 (40), 337 (37), 277 (33), 115 (34), 75 (16); IR (neat): 2955, 2931, 2858, 1745, 1462, 1250, 1157, 1117, 1098, 970, 838 cm^{-1}.

Methyl (*Z*)-7-{(1*R*,2*R*,3*R*)-3-hydroxy-2-[(*E*,3*S*)-3-hydroxy-1-octenyl]-5-oxocyclopentyl}-5-heptenoate; Prostaglandin E_2 Methyl Ester ((−)-36). The final deprotection was performed according to the representative procedure described in the previous section using aq. HF in THF as the reagent. Colorless syrup. $[\alpha]_D^{20}$ = −69.2 (*c* = 0.49, CH_3OH); [Lit.[41] $[\alpha]_D^{20}$ = −71.8 (*c* = 1.31, CH_3OH)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 (1H, dd, *J* = 6.6, 15.3 Hz), 5.56 (1H, dd, *J* = 8.0, 15.3 Hz), 5.36 (2H, m), 4.20-3.96 (2H, m), 3.67 (3H, s), 3.15 (1H, br. s), 2.74 (1H, ddd, *J* = 0.9, 7.4, 18.5 Hz), 2.48-1.20 (20H, m), 0.89 (3H, t, *J* = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 174.2, 137.0, 131.0, 130.9, 126.5, 77.2, 77.0, 72.8, 72.1, 54.5, 53.5, 51.6, 46.1, 37.3, 33.4, 31.7, 26.6, 25.2, 25.0, 24.7, 22.6, 14.0; MS (EI) *m/z* (rel intensity) 366 ([M]$^{+\cdot}$, 0.5), 348 ([M–H_2O]$^{+\cdot}$, 21), 330 (16), 277 (32), 245 (25), 208 (79), 190 (46), 164 (86), 99 (76), 43 (100); IR (neat) 3420, 2954, 2931, 2859, 1742, 1437, 1245, 1159, 1074, 970 cm^{-1}.

3-Butyl-4-(*tert*-butyl-dimethyl-silanyloxy)-2-but-2-ynyl-cyclopentanone ((±)-37). To a cooled solution (−78°C) of *n*-BuLi (1.62 mL, 2.59 mmol, 1.6 M in hexane) in THF (10 mL) is added a solution of $Zn(CH_3)_2$ (1.29 mL, 2.59 mmol, 2M in toluene). The mixture is stirred for 15 min at 0° C (ice bath) and cooled again to −78 °C prior to the slow addition of a solution of ketone (±)-**9** (500 mg, 2.35 mmol) in THF (8 mL) via a syringe pump (addition time ca. 60 min). To the resulting enolate solution is added DMPU (5 mL), followed by iodide **11** (2.11 g, 11.75 mmol). After stirring

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[41] Johnson, C. J., Penning, T. D. *J. Am. Chem. Soc.* **1988**, *110*, 4726.

for 15 h at −40°C, the reaction is quenched with aq. sat. NH_4Cl solution, the aqueous phase is extracted with MTBE (3x50 mL), the combined organic layers are dried over Na_2SO_4, the solvents are evaporated and the residue is purified by flash chromatography (hexane/toluene, 1:1) affording (±)-**37** as a pale yellow syrup (554 mg, 73 %). IR: 2956, 2929, 2858, 1748, 1607, 1464, 1252, 1110, 837, 776; ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 4.08 (dt, *J* = 13.2, 6.8 Hz, 1H), 2.70 - 0.80 (m, 27H), 0.1 (d, *J* = 9.6 Hz, 6H); ^{13}C NMR (CD_2Cl_2, 75 MHz) δ 215.8, 77.3, 73.5, 52.6, 48.9, 48.0, 31.6, 29.2, 25.9, 23.4, 18.9, 18.2, 14.1, 3.5, −4.5, −4.8; MS (EI) *m/z* (rel. intensity) 322 ([M^+], <1), 307 (2), 265 (100), 209 (11), 195 (6), 179 (5), 157 (8), 131 (5), 101 (6), 75 (42), 59 (7), 41 (7); HRMS ($C_{19}H_{34}O_2$ Si+H): *calcd.* 323.240634; *found.* 323.240626; Anal. *calcd.* for $C_{19}H_{34}O_2Si$ (322.56): C, 70.75; H, 10.62; *found* C, 70.59; H, 10.52.

Representative Procedure for Alkyne Cross Metathesis. Preparation of 7-[2-Butyl-3-(*tert*-butyl-dimethyl-silanyloxy)-5-oxo-cyclopentyl]-hept-5-ynoic acid methyl ester ((±)-41). To a solution of complex **5** (19 mg, 0.030 mmol) in toluene (4 mL) and CH_2Cl_2 (200 μL) is added substrate (±)-**37** (93 mg, 0.29 mmol) and 5-decyn-dioic acid dimethyl ester **33** (130 mg, 0.57 mmol) and the resulting solution is stirred at 80°C for 8 h. After evaporation of the solvent, the residue is chromatographed (hexanes/ethyl acetate, 15:1) affording product (±)-**41** as a colorless syrup (51 mg, 43 %). IR 2955, 2929, 2857, 2246, 1745, 1602, 1463, 1251, 1109, 837, 776; ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 4.10 (dt, *J* = 13.2, 6.7 Hz, 1H), 3.66 (s, 3H), 2.70- 0.80 (m, 30H), 0.1 (d, *J* = 10 Hz, 6H); ^{13}C NMR (CD_2Cl_2, 75 MHz): δ 215.8, 173.8, 80.9, 78.4, 73.6, 52.6, 51.7, 49.0, 48.0, 33.1, 31.8, 29.4, 25.9, 24.6, 23.4, 21.6, 19.1, 18.4, 14.2, −4.4, −4.8; MS (EI) *m/z* (rel. intensity) 408 ([M^+], <1), 351 (100), 319 (19), 277 (6), 245 (18), 189 (7), 163 (14), 89 (13), 75 (45), 55 (22), 43 (14); HRMS ($C_{23}H_{40}O_4Si$+H): *calcd* 409.277414, *found* 409.277113. Anal. *calcd.* for $C_{23}H_{40}O_4Si$ (408.65): C, 67.60; H, 9.87; *found* C, 67.71; H, 9.81.

The following compounds were prepared analogously:

3-Butyl-4-(*tert*-butyl-dimethyl-silanyloxy)-2-(6-chloro-hex-2-ynyl)-cyclopentanone ((±)-**38**). IR 2956, 2929, 2857, 2246, 1747, 1603, 1464, 1252, 1110, 837, 776; ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 4.10 (dt, *J* = 13.2, 6.6 Hz, 1H), 3.66 (t, *J* = 6.4 Hz, 2H), 2.70 - 0.80 (m, 28H), 0.1 (d, *J* = 10 Hz, 6H); ^{13}C NMR (CD_2Cl_2, 75 MHz): δ 215.8, 80.1, 78.6, 73.6, 63.9, 52.6, 49.0, 48.0, 44.2, 32.1, 31.9, 29.4, 25.9, 25.6, 23.4, 19.2, 18.2, 16.4, 14.2, −4.4, −4.8; MS (EI) *m/z* (rel. intensity) 384 (<1), 369 (2), 327 (19), 271 (6), 235 (27), 217 (51), 191 (66), 135 (46), 93 (39), 75 (100), 59 (25), 41 (21); Anal. *calcd.* for $C_{21}H_{37}O_2Cl_1Si$ (385.06): C, 65.50; H, 9.69; *found* C, 65.39; H, 9.68.

7-[2-Butyl-3-(*tert*-butyl-dimethyl-silanyloxy)-5-oxo-cyclopentyl]-hept-5-yne nitrile ((±)-**39**). IR 2956, 2929, 2857, 2248, 1746, 1603, 1463, 1252, 1110, 837, 777; ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 4.10 (dt, *J* = 13.2, 6.5 Hz, 1H), 2.70 - 0.80 (m, 30H), 0.10 (d, *J* = 9.9 Hz, 6H); ^{13}C NMR (CD_2Cl_2, 75 MHz): δ 215.7, 119.6, 79.5, 79.3, 73.5, 52.5, 49.1, 48.0, 31.8, 29.4, 25.9, 23.4, 19.2, 18.2, 16.4, 14.2, −4.4, −4.8; MS (EI) *m/z* (rel. intensity) 375 ([M^+], <1), 360 (2), 318 (79), 290 (18), 243 (5), 215 (11), 200 (10), 133 (6), 117 (8), 91 (11), 75 (100), 55 (12), 41 (15); Anal. *calcd.* for $C_{22}H_{37}O_2NSi$ (375.62): C, 70.35; H, 9.93; N, 3.73; *found* C, 70.20; H, 9.88; N, 3.61.

3-Butyl-4-(*tert*-butyl-dimethyl-silanyloxy)-2-[6-(tetrahydro-pyran-2-yloxy)-hept-2-ynyl]-cyclopentanone ((±)-40). IR 2953, 2931, 2858, 1748, 1603, 1464, 1257, 1119, 1035, 837, 776; ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 4.56 (t, *J* = 3.8 Hz, 1H), 4.10 (dt, *J* = 13.2, 6.7 Hz, 1H), 3.80 - 3.65 (m, 2H), 3.55 - 3.30 (m, 2H), 2.70 - 0.8 (m, 36H), 0.10 (d, *J* = 10Hz, 6H); ^{13}C NMR (CD_2Cl_2, 75 MHz): δ 215.9, 99.1, 82.0, 77.6, 73.6, 67.2, 62.4, 52.7, 48.9, 48.1, 31.8, 31.2, 29.4, 29.3, 26.3, 26.0, 25.9, 23.4, 20.0, 19.2, 18.8, 18.2, 14.2, –4.4, –4.8; MS (EI) *m/z* (rel. intensity) 464 ([M^+], <1), 407 (5), 365 (1), 323 (23), 231 (10), 159 (11), 111 (6), 85 (100), 75 (18), 57 (8), 43 (8); Anal. *calcd.* for $C_{27}H_{48}O_4Si$ (464.75): C, 69.78; H, 10.41; *found* C, 69.88; H, 10.37.

X-Ray Structure Analysis of Compound 22

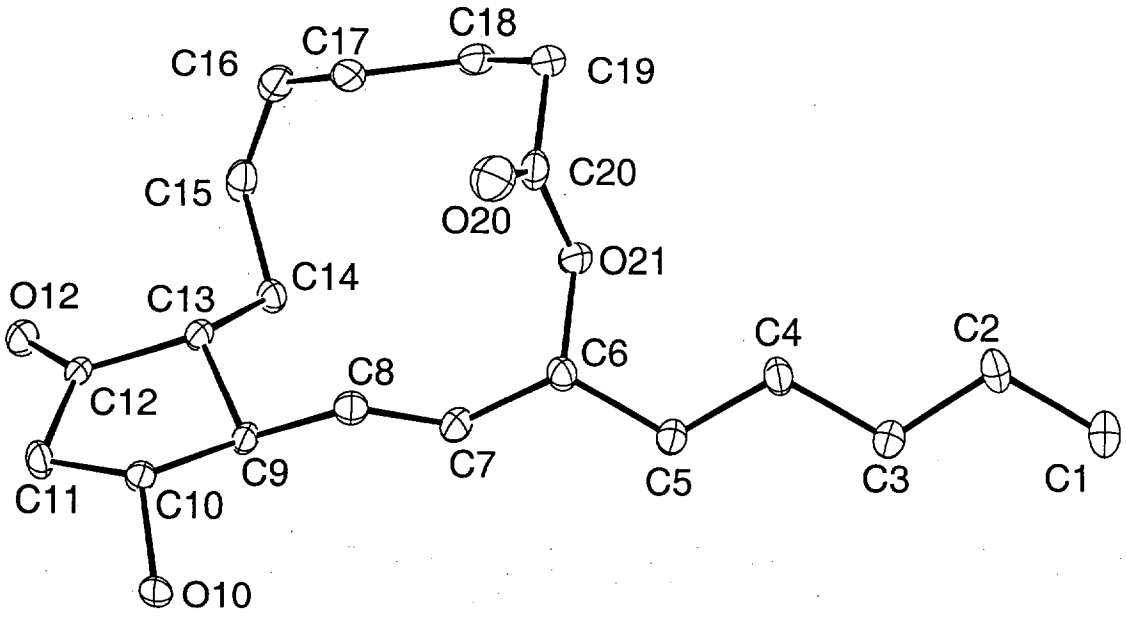


Figure 1. ORTEP diagram of the molecular structure of compound **22**. Anisotropic replacement parameter ellipsoids are drawn at 50% probability, hydrogen atoms are omitted for clarity.

Empirical formula	$C_{20}H_{30}O_4$	
Color	colorless	
Formula weight	334.44 g · mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	**$P2_1/c$, (no. 14)**	
Unit cell dimensions	a = 21.9719(19) Å	α= 90°.
	b = 9.6249(8) Å	β= 97.264(4)°.
	c = 8.9318(8) Å	γ = 90°.
Volume	1873.7(3) Å^3	
Z	4	
Density (calculated)	1.186 Mg · m^{-3}	
Absorption coefficient	0.081 mm^{-1}	
F(000)	728 e	
Crystal size	0.51 x 0.31 x 0.08 mm^3	
θ range for data collection	1.87 to 29.99°.	
Index ranges	$-23 \le h \le 30$, $-13 \le k \le 12$, $-12 \le l \le 12$	
Reflections collected	17986	
Independent reflections	5337 [R_{int} = 0.1124]	
Reflections with I>2σ(I)	2768	
Completeness to θ = 29.99°	97.4 %	
Absorption correction	Empirical	
Max. and min. transmission	1.00 and 0.29	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5337 / 0 / 217	
Goodness-of-fit on F^2	0.962	
Final R indices [I>2σ(I)]	R_1 = 0.0732	wR^2 = 0.1503
R indices (all data)	R_1 = 0.1585	wR^2 = 0.1875
Largest diff. peak and hole	0.478 and -0.372 e · Å^{-3}	

Table 1. Atomic coordinates and equivalent isotropic displacement parameters (Å^2).
U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C(1)	0.0179(1)	-0.6622(3)	-0.8914(3)	0.029(1)
C(2)	-0.0106(1)	-0.6027(3)	-0.7572(3)	0.025(1)
C(3)	-0.0750(1)	-0.6591(2)	-0.7465(3)	0.021(1)
C(4)	-0.1034(1)	-0.6009(2)	-0.6124(3)	0.020(1)
C(5)	-0.1705(1)	-0.6418(2)	-0.6112(3)	0.019(1)
C(6)	-0.1989(1)	-0.5822(2)	-0.4787(3)	0.017(1)
C(7)	-0.2666(1)	-0.6077(2)	-0.4841(3)	0.018(1)
C(8)	-0.2969(1)	-0.6059(2)	-0.3646(3)	0.018(1)
C(9)	-0.3653(1)	-0.6012(2)	-0.3739(2)	0.015(1)
O(10)	-0.3956(1)	-0.8216(2)	-0.2764(2)	0.023(1)
C(10)	-0.3946(1)	-0.6755(2)	-0.2486(2)	0.016(1)
C(11)	-0.4584(1)	-0.6110(2)	-0.2548(3)	0.022(1)
O(12)	-0.4961(1)	-0.3891(2)	-0.3573(2)	0.022(1)
C(12)	-0.4535(1)	-0.4707(2)	-0.3271(2)	0.016(1)
C(13)	-0.3890(1)	-0.4500(2)	-0.3640(2)	0.015(1)
C(14)	-0.3820(1)	-0.3569(2)	-0.4994(2)	0.017(1)
C(15)	-0.3901(1)	-0.2042(2)	-0.4718(3)	0.020(1)
C(16)	-0.3466(1)	-0.1229(2)	-0.4020(3)	0.022(1)
C(17)	-0.2837(1)	-0.1719(2)	-0.3388(3)	0.021(1)
C(18)	-0.2345(1)	-0.1456(2)	-0.4428(3)	0.023(1)
C(19)	-0.1723(1)	-0.2072(3)	-0.3805(3)	0.025(1)
O(20)	-0.1669(1)	-0.4189(2)	-0.2343(2)	0.030(1)
C(20)	-0.1757(1)	-0.3618(3)	-0.3550(3)	0.021(1)
O(21)	-0.1904(1)	-0.4299(2)	-0.4868(2)	0.019(1)

Table 2. Bond lengths [Å] and angles [°].

C(1)-C(2)	1.531(3)	C(1)-H(1A)	0.9600
C(1)-H(1B)	0.9600	C(1)-H(1C)	0.9600
C(2)-C(3)	1.531(3)	C(2)-H(2A)	0.9700
C(2)-H(2B)	0.9700	C(3)-C(4)	1.526(3)
C(3)-H(3A)	0.9700	C(3)-H(3B)	0.9700
C(4)-C(5)	1.527(3)	C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700	C(5)-C(6)	1.519(3)
C(5)-H(5A)	0.9700	C(5)-H(5B)	0.9700
C(6)-O(21)	1.480(3)	C(6)-C(7)	1.501(3)
C(6)-H(6)	0.9800	C(7)-C(8)	1.328(3)
C(7)-H(7)	0.9300	C(8)-C(9)	1.496(3)
C(8)-H(8)	0.9300	C(9)-C(10)	1.537(3)
C(9)-C(13)	1.552(3)	C(9)-H(9)	0.9800
O(10)-C(10)	1.427(3)	O(10)-H(10)	0.8200
C(10)-C(11)	1.527(3)	C(10)-H(10A)	0.9800
C(11)-C(12)	1.506(3)	C(11)-H(11A)	0.9700
C(11)-H(11B)	0.9700	O(12)-C(12)	1.226(3)
C(12)-C(13)	1.507(3)	C(13)-C(14)	1.528(3)
C(13)-H(13)	0.9800	C(14)-C(15)	1.505(3)
C(14)-H(14A)	0.9700	C(14)-H(14B)	0.9700
C(15)-C(16)	1.329(3)	C(15)-H(15)	0.9300
C(16)-C(17)	1.501(3)	C(16)-H(16)	0.9300
C(17)-C(18)	1.533(3)	C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700	C(18)-C(19)	1.529(3)
C(18)-H(18A)	0.9700	C(18)-H(18B)	0.9700
C(19)-C(20)	1.508(3)	C(19)-H(19A)	0.9700
C(19)-H(19B)	0.9700	O(20)-C(20)	1.203(3)
C(20)-O(21)	1.351(3)		
C(2)-C(1)-H(1A)	109.5	C(2)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5	C(2)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5	H(1B)-C(1)-H(1C)	109.5
C(3)-C(2)-C(1)	112.9(2)	C(3)-C(2)-H(2A)	109.0
C(1)-C(2)-H(2A)	109.0	C(3)-C(2)-H(2B)	109.0
C(1)-C(2)-H(2B)	109.0	H(2A)-C(2)-H(2B)	107.8
C(4)-C(3)-C(2)	113.03(19)	C(4)-C(3)-H(3A)	109.0
C(2)-C(3)-H(3A)	109.0	C(4)-C(3)-H(3B)	109.0
C(2)-C(3)-H(3B)	109.0	H(3A)-C(3)-H(3B)	107.8
C(3)-C(4)-C(5)	113.64(19)	C(3)-C(4)-H(4A)	108.8
C(5)-C(4)-H(4A)	108.8	C(3)-C(4)-H(4B)	108.8
C(5)-C(4)-H(4B)	108.8	H(4A)-C(4)-H(4B)	107.7
C(6)-C(5)-C(4)	113.62(19)	C(6)-C(5)-H(5A)	108.8

C(4)-C(5)-H(5A)	108.8	C(6)-C(5)-H(5B)	108.8
C(4)-C(5)-H(5B)	108.8	H(5A)-C(5)-H(5B)	107.7
O(21)-C(6)-C(7)	106.92(17)	O(21)-C(6)-C(5)	105.60(17)
C(7)-C(6)-C(5)	114.60(19)	O(21)-C(6)-H(6)	109.8
C(7)-C(6)-H(6)	109.8	C(5)-C(6)-H(6)	109.8
C(8)-C(7)-C(6)	124.5(2)	C(8)-C(7)-H(7)	117.7
C(6)-C(7)-H(7)	117.7	C(7)-C(8)-C(9)	123.9(2)
C(7)-C(8)-H(8)	118.0	C(9)-C(8)-H(8)	118.0
C(8)-C(9)-C(10)	117.15(18)	C(8)-C(9)-C(13)	111.55(17)
C(10)-C(9)-C(13)	102.72(16)	C(8)-C(9)-H(9)	108.4
C(10)-C(9)-H(9)	108.4	C(13)-C(9)-H(9)	108.4
C(10)-O(10)-H(10)	109.5	O(10)-C(10)-C(11)	113.64(17)
O(10)-C(10)-C(9)	109.27(17)	C(11)-C(10)-C(9)	104.53(17)
O(10)-C(10)-H(10A)	109.8	C(11)-C(10)-H(10A)	109.8
C(9)-C(10)-H(10A)	109.8	C(12)-C(11)-C(10)	105.39(17)
C(12)-C(11)-H(11A)	110.7	C(10)-C(11)-H(11A)	110.7
C(12)-C(11)-H(11B)	110.7	C(10)-C(11)-H(11B)	110.7
H(11A)-C(11)-H(11B)	108.8	O(12)-C(12)-C(11)	125.0(2)
O(12)-C(12)-C(13)	125.5(2)	C(11)-C(12)-C(13)	109.41(18)
C(12)-C(13)-C(14)	116.22(18)	C(12)-C(13)-C(9)	102.74(17)
C(14)-C(13)-C(9)	115.88(17)	C(12)-C(13)-H(13)	107.1
C(14)-C(13)-H(13)	107.1	C(9)-C(13)-H(13)	107.1
C(15)-C(14)-C(13)	114.67(18)	C(15)-C(14)-H(14A)	108.6
C(13)-C(14)-H(14A)	108.6	C(15)-C(14)-H(14B)	108.6
C(13)-C(14)-H(14B)	108.6	H(14A)-C(14)-H(14B)	107.6
C(16)-C(15)-C(14)	124.0(2)	C(16)-C(15)-H(15)	118.0
C(14)-C(15)-H(15)	118.0	C(15)-C(16)-C(17)	124.4(2)
C(15)-C(16)-H(16)	117.8	C(17)-C(16)-H(16)	117.8
C(16)-C(17)-C(18)	113.96(19)	C(16)-C(17)-H(17A)	108.8
C(18)-C(17)-H(17A)	108.8	C(16)-C(17)-H(17B)	108.8
C(18)-C(17)-H(17B)	108.8	H(17A)-C(17)-H(17B)	107.7
C(19)-C(18)-C(17)	112.5(2)	C(19)-C(18)-H(18A)	109.1
C(17)-C(18)-H(18A)	109.1	C(19)-C(18)-H(18B)	109.1
C(17)-C(18)-H(18B)	109.1	H(18A)-C(18)-H(18B)	107.8
C(20)-C(19)-C(18)	112.23(19)	C(20)-C(19)-H(19A)	109.2
C(18)-C(19)-H(19A)	109.2	C(20)-C(19)-H(19B)	109.2
C(18)-C(19)-H(19B)	109.2	H(19A)-C(19)-H(19B)	107.9
O(20)-C(20)-O(21)	123.5(2)	O(20)-C(20)-C(19)	125.5(2)
O(21)-C(20)-C(19)	111.0(2)	C(20)-O(21)-C(6)	117.11(17)

Table 3. Anisotropic displacement parameters (Å²).

The anisotropic displacement factor exponent takes the form:

$-2\pi^2[\, h^2 a^{*2} U_{11} + \ldots + 2\, h\, k\, a^*\, b^*\, U_{12}\,]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.025(1)	0.033(2)	0.033(2)	-0.003(1)	0.016(1)	-0.002(1)
C(2)	0.021(1)	0.031(1)	0.027(1)	0.000(1)	0.013(1)	-0.005(1)
C(3)	0.020(1)	0.020(1)	0.024(1)	-0.002(1)	0.009(1)	0.001(1)
C(4)	0.017(1)	0.020(1)	0.025(1)	0.002(1)	0.010(1)	0.000(1)
C(5)	0.020(1)	0.018(1)	0.020(1)	-0.001(1)	0.009(1)	0.000(1)
C(6)	0.018(1)	0.014(1)	0.021(1)	0.002(1)	0.008(1)	0.000(1)
C(7)	0.019(1)	0.015(1)	0.022(1)	-0.002(1)	0.007(1)	0.002(1)
C(8)	0.020(1)	0.013(1)	0.021(1)	0.002(1)	0.005(1)	0.001(1)
C(9)	0.017(1)	0.013(1)	0.018(1)	-0.001(1)	0.009(1)	0.002(1)
O(10)	0.026(1)	0.007(1)	0.037(1)	0.002(1)	0.017(1)	-0.001(1)
C(10)	0.022(1)	0.009(1)	0.020(1)	0.002(1)	0.010(1)	0.000(1)
C(11)	0.022(1)	0.014(1)	0.034(1)	0.004(1)	0.018(1)	0.001(1)
O(12)	0.020(1)	0.013(1)	0.034(1)	-0.001(1)	0.012(1)	0.003(1)
C(12)	0.019(1)	0.011(1)	0.020(1)	-0.003(1)	0.010(1)	0.000(1)
C(13)	0.018(1)	0.011(1)	0.018(1)	-0.001(1)	0.008(1)	0.000(1)
C(14)	0.018(1)	0.014(1)	0.021(1)	0.002(1)	0.009(1)	0.000(1)
C(15)	0.022(1)	0.018(1)	0.022(1)	0.005(1)	0.011(1)	0.005(1)
C(16)	0.033(1)	0.012(1)	0.023(1)	0.003(1)	0.014(1)	0.002(1)
C(17)	0.026(1)	0.018(1)	0.021(1)	-0.003(1)	0.009(1)	-0.005(1)
C(18)	0.032(1)	0.014(1)	0.027(1)	-0.003(1)	0.013(1)	-0.003(1)
C(19)	0.028(1)	0.021(1)	0.031(1)	-0.009(1)	0.014(1)	-0.007(1)
O(20)	0.036(1)	0.033(1)	0.022(1)	-0.002(1)	0.005(1)	-0.002(1)
C(20)	0.015(1)	0.028(1)	0.022(1)	-0.006(1)	0.008(1)	-0.002(1)
O(21)	0.023(1)	0.014(1)	0.020(1)	-0.002(1)	0.008(1)	-0.002(1)

There are only a few crystal structures of 13-membered lactones known so far. In addition to the one reported here, several brefeldin A analogues have been characterised structurally,[32] which also incorporate a trans disubstituted five-membered ring. While the overall geometry of the macrocycles in **22** and in the brefeldin analogue described in ref.[32b] agree within 1 Å r.m.s., a better fit of the macrocycles is prevented by the different position and conformation of the double bonds and the ester group (Fig. 2).

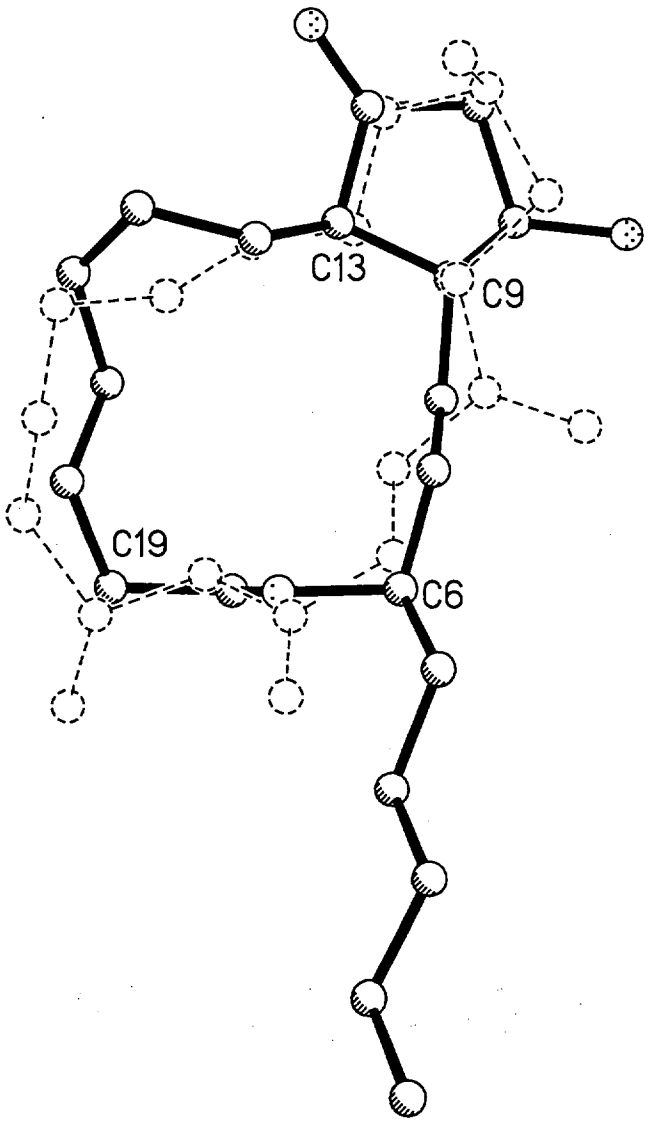


Figure 2. Molecular fit of **22** (solid) and a brefeldin derivative described by Weber et al.[32b] (dashed). Carbon atoms C6 to C14 and C18 to C20 and oxygen O21 were fitted with equal weights to the corresponding atoms in the brefeldin derivative. The r.m.s. deviation is 0.76 Å. The approximately rectangular ring shape is determined by the chain folding at C6, C9, C15 and C19.

X-Ray Structure Analysis of Compound 32

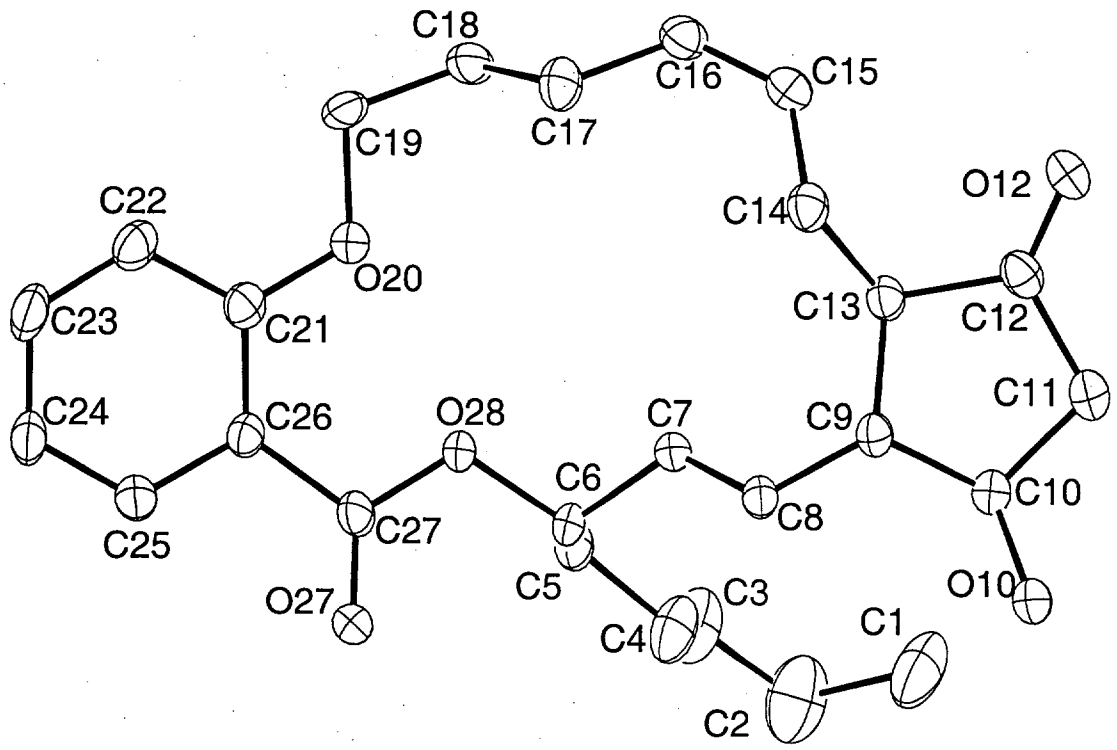


Figure 3. ORTEP diagram of the molecular structure of compound **32**. Anisotropic replacement parameter ellipsoids are drawn at 50% probability, hydrogen atoms are omitted for clarity.

Empirical formula	$C_{26}H_{34}O_5$	
Color	white	
Formula weight	426.53 g · mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	**$P2_1/c$, (no. 14)**	
Unit cell dimensions	a = 9.6241(3) Å	α= 90°.
	b = 25.6146(7) Å	β= 94.8710(10)°.
	c = 9.3871(3) Å	γ = 90°.
Volume	2305.73(12) Å^3	
Z	4	
Density (calculated)	1.229 Mg · m^{-3}	
Absorption coefficient	0.084 mm^{-1}	
F(000)	920 e	
Crystal size	0.43 x 0.05 x 0.08 mm^3	
θ range for data collection	2.12 to 29.46°.	
Index ranges	$-13 \le h \le 13$, $-35 \le k \le 35$, $-12 \le l \le 12$	
Reflections collected	39716	
Independent reflections	5899 [R_{int} = 0.063]	
Reflections with I>2σ(I)	2178	
Completeness to θ = 29.46°	92.0 %	
Absorption correction	Empirical	
Max. and min. transmission	1.00 and 1.00	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5899 / 0 / 281	
Goodness-of-fit on F^2	0.898	
Final R indices [I>2σ(I)]	R_1 = 0.0599	wR^2 = 0.1352
R indices (all data)	R_1 = 0.2094	wR^2 = 0.2183
Largest diff. peak and hole	0.670 and -0.586 e · Å^{-3}	

Table 4. Atomic coordinates and equivalent isotropic displacement parameters (Å²).
U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C(1)	-0.5737(4)	-0.4101(2)	0.0165(4)	0.060(1)
C(2)	-0.4235(4)	-0.4277(2)	0.0298(5)	0.062(1)
C(3)	-0.3442(4)	-0.4139(2)	-0.0928(4)	0.047(1)
C(4)	-0.4036(4)	-0.4327(2)	-0.2378(4)	0.041(1)
C(5)	-0.3208(3)	-0.4138(1)	-0.3556(3)	0.029(1)
C(6)	-0.3936(3)	-0.4214(1)	-0.5040(3)	0.024(1)
C(7)	-0.5183(3)	-0.3874(1)	-0.5323(3)	0.023(1)
C(8)	-0.6475(3)	-0.4043(1)	-0.5435(3)	0.023(1)
C(9)	-0.7772(3)	-0.3721(1)	-0.5543(4)	0.024(1)
O(10)	-0.9434(2)	-0.4226(1)	-0.4179(3)	0.039(1)
C(10)	-0.8621(3)	-0.3771(1)	-0.4218(4)	0.028(1)
C(11)	-0.9587(3)	-0.3300(1)	-0.4299(4)	0.031(1)
O(12)	-0.9413(2)	-0.2492(1)	-0.5600(2)	0.032(1)
C(12)	-0.8926(3)	-0.2911(1)	-0.5232(4)	0.025(1)
C(13)	-0.7584(3)	-0.3135(1)	-0.5694(3)	0.023(1)
C(14)	-0.7184(3)	-0.2935(1)	-0.7135(3)	0.026(1)
C(15)	-0.6523(3)	-0.2411(1)	-0.7021(3)	0.028(1)
C(16)	-0.5287(3)	-0.2284(1)	-0.7441(4)	0.030(1)
C(17)	-0.4284(3)	-0.2627(1)	-0.8118(4)	0.031(1)
C(18)	-0.2782(3)	-0.2521(1)	-0.7579(4)	0.028(1)
C(19)	-0.1763(3)	-0.2865(1)	-0.8247(4)	0.028(1)
O(20)	-0.1905(2)	-0.3381(1)	-0.7688(2)	0.026(1)
C(21)	-0.1044(3)	-0.3756(1)	-0.8123(3)	0.024(1)
C(22)	-0.0113(3)	-0.3663(1)	-0.9159(4)	0.029(1)
C(23)	0.0764(3)	-0.4049(1)	-0.9553(4)	0.035(1)
C(24)	0.0756(4)	-0.4532(1)	-0.8924(4)	0.038(1)
C(25)	-0.0173(3)	-0.4634(1)	-0.7926(4)	0.033(1)
C(26)	-0.1096(3)	-0.4256(1)	-0.7507(4)	0.025(1)
O(27)	-0.2122(2)	-0.4871(1)	-0.6014(3)	0.036(1)
C(27)	-0.2085(3)	-0.4432(1)	-0.6457(4)	0.026(1)
O(28)	-0.2960(2)	-0.4063(1)	-0.6086(2)	0.025(1)

Table 5. Bond lengths [Å] and angles [°].

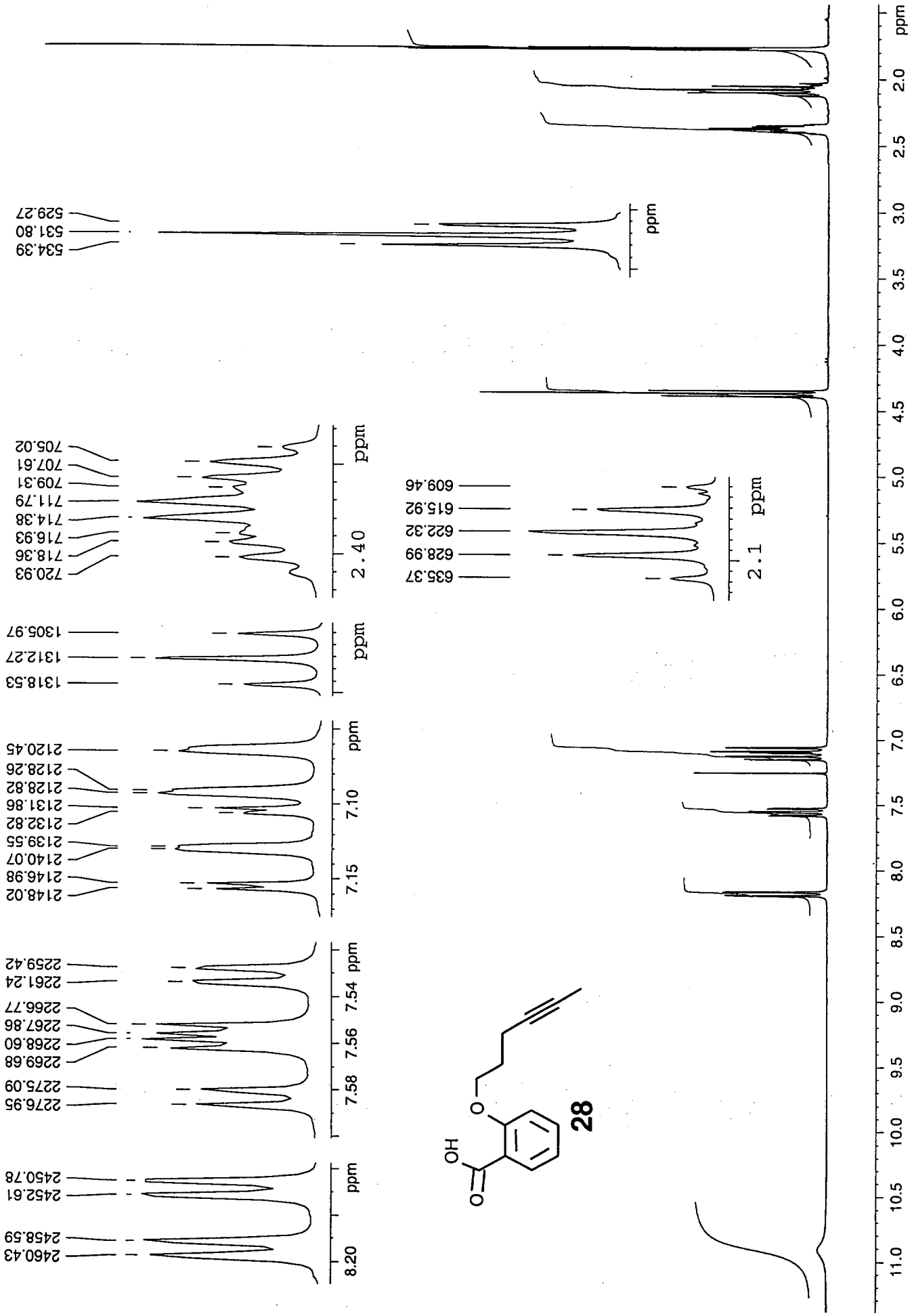
C(1)-C(2)	1.509(5)	C(1)-H(1A)	0.9600
C(1)-H(1B)	0.9600	C(1)-H(1C)	0.9600
C(2)-C(3)	1.477(5)	C(2)-H(2A)	0.9700
C(2)-H(2B)	0.9700	C(3)-C(4)	1.510(5)
C(3)-H(3A)	0.9700	C(3)-H(3B)	0.9700
C(4)-C(5)	1.498(4)	C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700	C(5)-C(6)	1.518(4)
C(5)-H(5A)	0.9700	C(5)-H(5B)	0.9700
C(6)-O(28)	1.468(3)	C(6)-C(7)	1.489(4)
C(6)-H(6A)	0.9800	C(7)-C(8)	1.312(4)
C(7)-H(7A)	0.9300	C(8)-C(9)	1.491(4)
C(8)-H(8A)	0.9300	C(9)-C(13)	1.521(4)
C(9)-C(10)	1.550(4)	C(9)-H(9A)	0.9800
O(10)-C(10)	1.407(4)	O(10)-H(10A)	0.8200
C(10)-C(11)	1.520(4)	C(10)-H(10B)	0.9800
C(11)-C(12)	1.504(4)	C(11)-H(11A)	0.9700
C(11)-H(11B)	0.9700	O(12)-C(12)	1.208(4)
C(12)-C(13)	1.511(4)	C(13)-C(14)	1.526(4)
C(13)-H(13A)	0.9800	C(14)-C(15)	1.484(4)
C(14)-H(14A)	0.9700	C(14)-H(14B)	0.9700
C(15)-C(16)	1.325(4)	C(15)-H(15A)	0.9300
C(16)-C(17)	1.487(4)	C(16)-H(16A)	0.9300
C(17)-C(18)	1.515(4)	C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700	C(18)-C(19)	1.495(4)
C(18)-H(18A)	0.9700	C(18)-H(18B)	0.9700
C(19)-O(20)	1.433(3)	C(19)-H(19A)	0.9700
C(19)-H(19B)	0.9700	O(20)-C(21)	1.355(4)
C(21)-C(22)	1.398(4)	C(21)-C(26)	1.407(4)
C(22)-C(23)	1.369(4)	C(22)-H(22A)	0.9300
C(23)-C(24)	1.373(5)	C(23)-H(23A)	0.9300
C(24)-C(25)	1.374(5)	C(24)-H(24A)	0.9300
C(25)-C(26)	1.394(4)	C(25)-H(25A)	0.9300
C(26)-C(27)	1.497(4)	O(27)-C(27)	1.201(4)
C(27)-O(28)	1.332(4)		
C(2)-C(1)-H(1A)	109.5	C(2)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5	C(2)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5	H(1B)-C(1)-H(1C)	109.5
C(3)-C(2)-C(1)	114.8(4)	C(3)-C(2)-H(2A)	108.6
C(1)-C(2)-H(2A)	108.6	C(3)-C(2)-H(2B)	108.6
C(1)-C(2)-H(2B)	108.6	H(2A)-C(2)-H(2B)	107.6
C(2)-C(3)-C(4)	116.4(3)	C(2)-C(3)-H(3A)	108.2
C(4)-C(3)-H(3A)	108.2	C(2)-C(3)-H(3B)	108.2
C(4)-C(3)-H(3B)	108.2	H(3A)-C(3)-H(3B)	107.3
C(5)-C(4)-C(3)	112.2(3)	C(5)-C(4)-H(4A)	109.2
C(3)-C(4)-H(4A)	109.2	C(5)-C(4)-H(4B)	109.2
C(3)-C(4)-H(4B)	109.2	H(4A)-C(4)-H(4B)	107.9
C(4)-C(5)-C(6)	113.7(3)	C(4)-C(5)-H(5A)	108.8
C(6)-C(5)-H(5A)	108.8	C(4)-C(5)-H(5B)	108.8

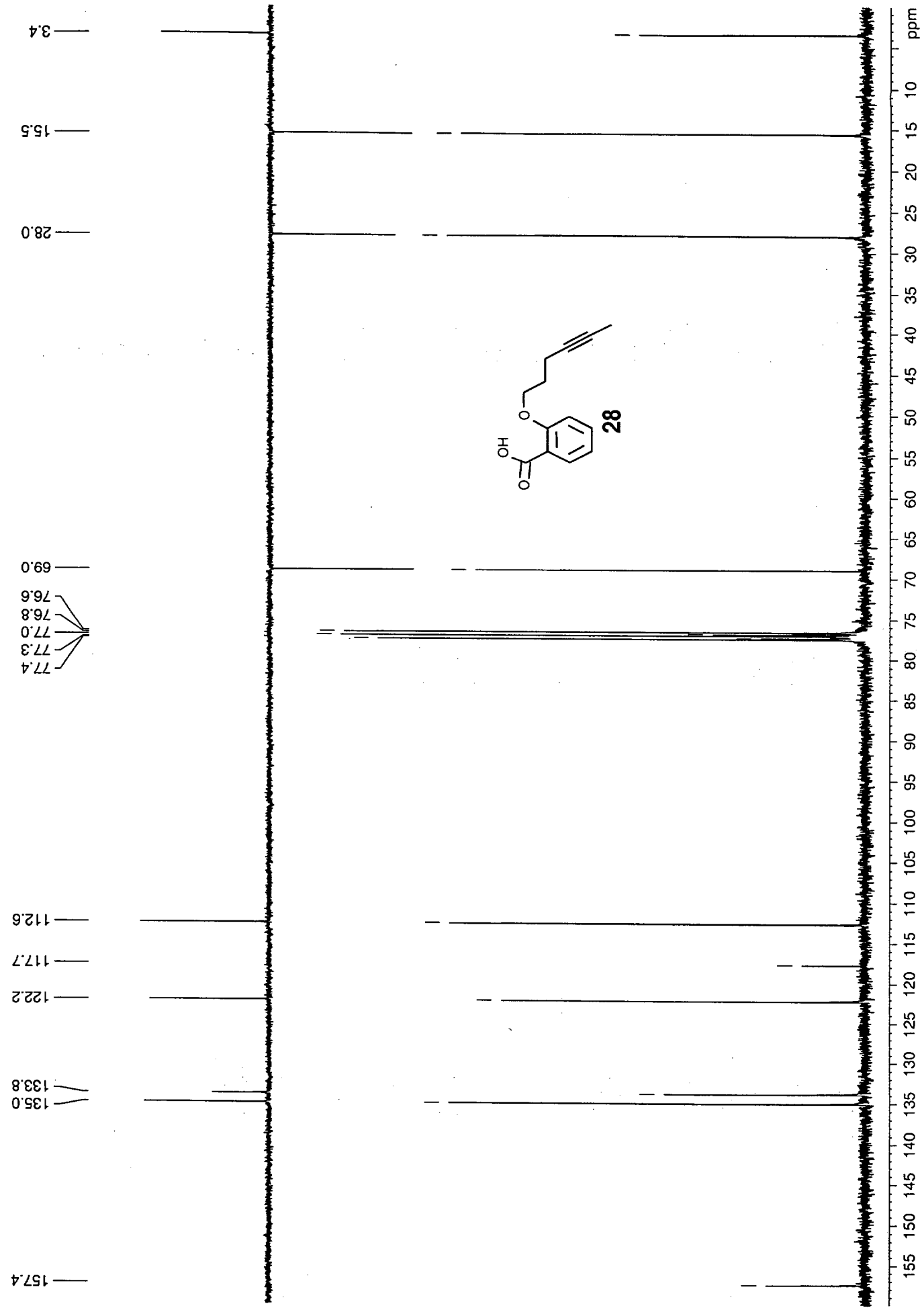
C(6)-C(5)-H(5B)	108.8	H(5A)-C(5)-H(5B)	107.7
O(28)-C(6)-C(7)	106.1(2)	O(28)-C(6)-C(5)	107.9(2)
C(7)-C(6)-C(5)	113.0(3)	O(28)-C(6)-H(6A)	109.9
C(7)-C(6)-H(6A)	109.9	C(5)-C(6)-H(6A)	109.9
C(8)-C(7)-C(6)	124.4(3)	C(8)-C(7)-H(7A)	117.8
C(6)-C(7)-H(7A)	117.8	C(7)-C(8)-C(9)	127.2(3)
C(7)-C(8)-H(8A)	116.4	C(9)-C(8)-H(8A)	116.4
C(8)-C(9)-C(13)	116.5(3)	C(8)-C(9)-C(10)	113.3(3)
C(13)-C(9)-C(10)	103.3(2)	C(8)-C(9)-H(9A)	107.8
C(13)-C(9)-H(9A)	107.8	C(10)-C(9)-H(9A)	107.8
C(10)-O(10)-H(10A)	109.5	O(10)-C(10)-C(11)	108.6(3)
O(10)-C(10)-C(9)	114.9(3)	C(11)-C(10)-C(9)	104.9(3)
O(10)-C(10)-H(10B)	109.4	C(11)-C(10)-H(10B)	109.4
C(9)-C(10)-H(10B)	109.4	C(12)-C(11)-C(10)	105.5(3)
C(12)-C(11)-H(11A)	110.6	C(10)-C(11)-H(11A)	110.6
C(12)-C(11)-H(11B)	110.6	C(10)-C(11)-H(11B)	110.6
H(11A)-C(11)-H(11B)	108.8	O(12)-C(12)-C(11)	125.6(3)
O(12)-C(12)-C(13)	125.2(3)	C(11)-C(12)-C(13)	109.2(3)
C(12)-C(13)-C(9)	103.7(2)	C(12)-C(13)-C(14)	114.4(3)
C(9)-C(13)-C(14)	117.1(3)	C(12)-C(13)-H(13A)	107.0
C(9)-C(13)-H(13A)	107.0	C(14)-C(13)-H(13A)	107.0
C(15)-C(14)-C(13)	112.3(3)	C(15)-C(14)-H(14A)	109.1
C(13)-C(14)-H(14A)	109.1	C(15)-C(14)-H(14B)	109.1
C(13)-C(14)-H(14B)	109.1	H(14A)-C(14)-H(14B)	107.9
C(16)-C(15)-C(14)	126.2(3)	C(16)-C(15)-H(15A)	116.9
C(14)-C(15)-H(15A)	116.9	C(15)-C(16)-C(17)	127.9(3)
C(15)-C(16)-H(16A)	116.1	C(17)-C(16)-H(16A)	116.1
C(16)-C(17)-C(18)	112.8(3)	C(16)-C(17)-H(17A)	109.0
C(18)-C(17)-H(17A)	109.0	C(16)-C(17)-H(17B)	109.0
C(18)-C(17)-H(17B)	109.0	H(17A)-C(17)-H(17B)	107.8
C(19)-C(18)-C(17)	113.3(3)	C(19)-C(18)-H(18A)	108.9
C(17)-C(18)-H(18A)	108.9	C(19)-C(18)-H(18B)	108.9
C(17)-C(18)-H(18B)	108.9	H(18A)-C(18)-H(18B)	107.7
O(20)-C(19)-C(18)	107.7(3)	O(20)-C(19)-H(19A)	110.2
C(18)-C(19)-H(19A)	110.2	O(20)-C(19)-H(19B)	110.2
C(18)-C(19)-H(19B)	110.2	H(19A)-C(19)-H(19B)	108.5
C(21)-O(20)-C(19)	117.7(2)	O(20)-C(21)-C(22)	122.2(3)
O(20)-C(21)-C(26)	118.5(3)	C(22)-C(21)-C(26)	119.2(3)
C(23)-C(22)-C(21)	120.8(3)	C(23)-C(22)-H(22A)	119.6
C(21)-C(22)-H(22A)	119.6	C(22)-C(23)-C(24)	120.5(3)
C(22)-C(23)-H(23A)	119.7	C(24)-C(23)-H(23A)	119.7
C(23)-C(24)-C(25)	119.5(3)	C(23)-C(24)-H(24A)	120.2
C(25)-C(24)-H(24A)	120.2	C(24)-C(25)-C(26)	121.8(3)
C(24)-C(25)-H(25A)	119.1	C(26)-C(25)-H(25A)	119.1
C(25)-C(26)-C(21)	118.1(3)	C(25)-C(26)-C(27)	115.6(3)
C(21)-C(26)-C(27)	126.3(3)	O(27)-C(27)-O(28)	122.5(3)
O(27)-C(27)-C(26)	123.3(3)	O(28)-C(27)-C(26)	114.2(3)
C(27)-O(28)-C(6)	116.2(2)		

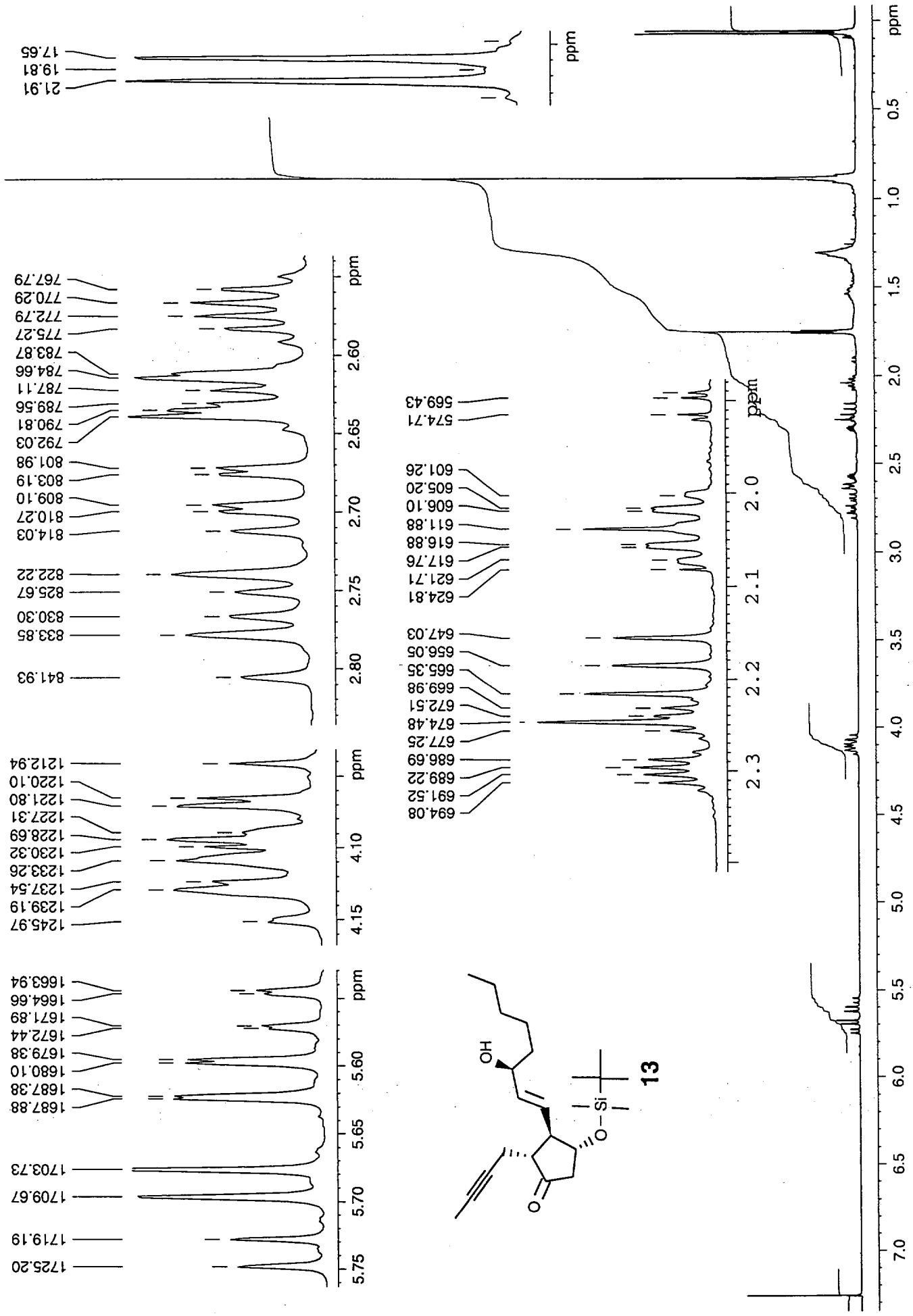
Table 6. Anisotropic displacement parameters (Å²).

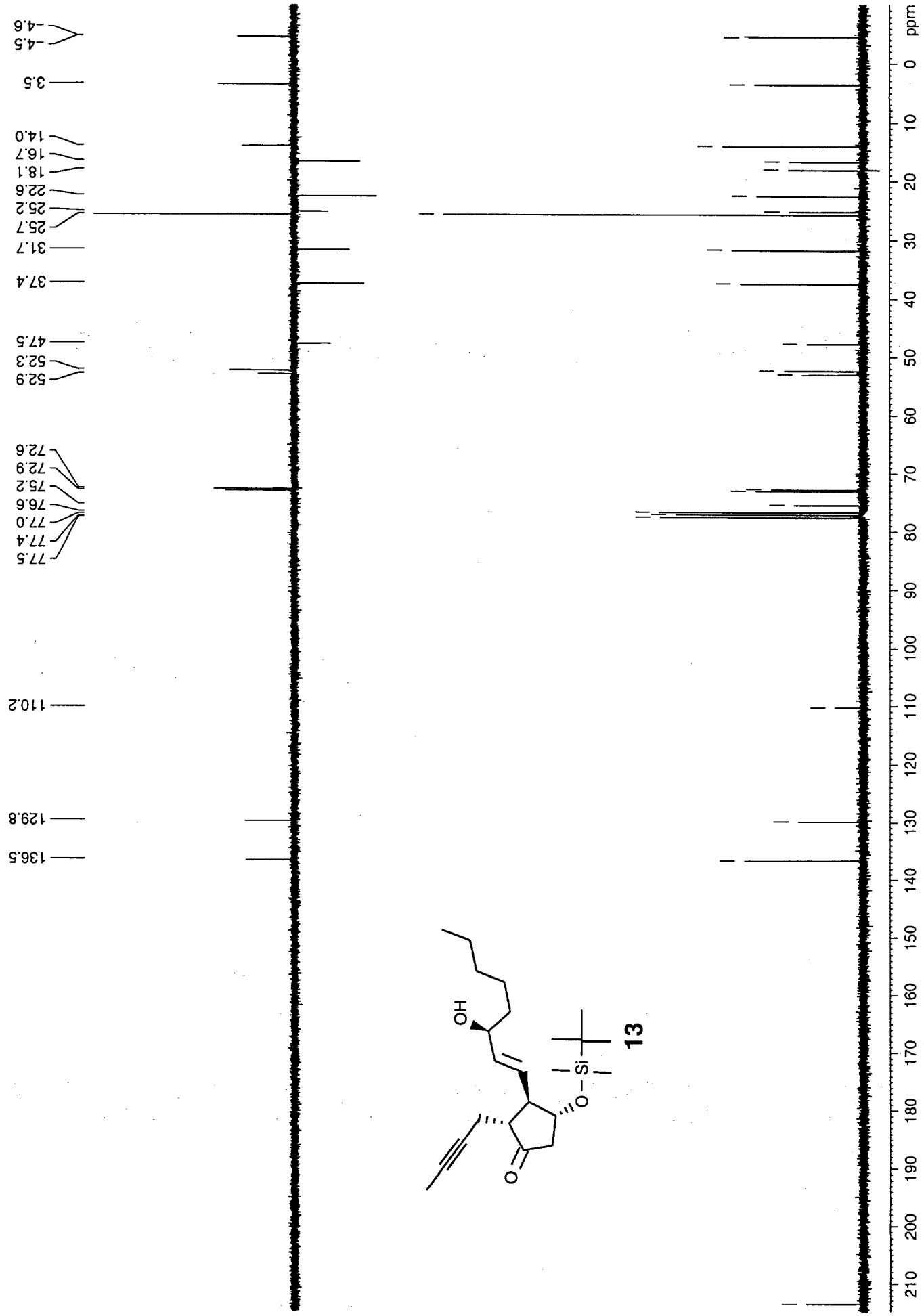
The anisotropic displacement factor exponent takes the form:
$-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$.

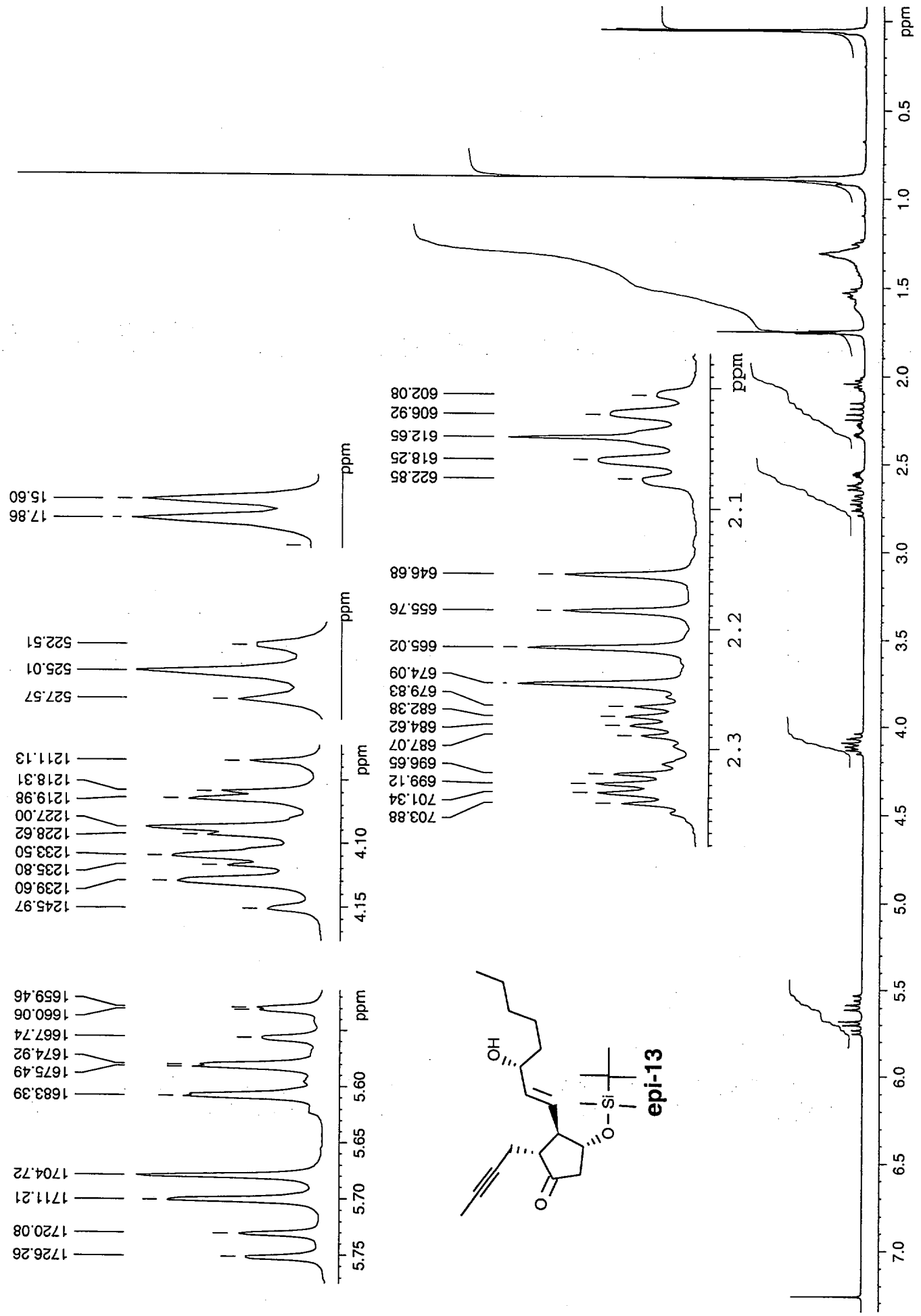
	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.030(2)	0.095(4)	0.055(3)	-0.026(3)	0.008(2)	0.002(2)
C(2)	0.036(2)	0.100(4)	0.049(3)	-0.011(3)	-0.002(2)	-0.010(2)
C(3)	0.030(2)	0.078(3)	0.032(2)	0.001(2)	-0.003(2)	-0.003(2)
C(4)	0.024(2)	0.064(3)	0.036(2)	0.004(2)	0.003(2)	-0.004(2)
C(5)	0.019(2)	0.031(2)	0.036(2)	-0.001(2)	0.005(2)	0.002(2)
C(6)	0.017(2)	0.024(2)	0.032(2)	0.002(2)	0.010(2)	0.000(2)
C(7)	0.020(2)	0.019(2)	0.031(2)	0.002(2)	0.007(2)	0.001(1)
C(8)	0.020(2)	0.022(2)	0.028(2)	-0.002(2)	0.007(2)	0.001(2)
C(9)	0.016(2)	0.028(2)	0.029(2)	0.002(2)	0.004(2)	0.003(2)
O(10)	0.025(1)	0.030(1)	0.065(2)	0.010(1)	0.018(1)	0.007(1)
C(10)	0.023(2)	0.026(2)	0.036(2)	0.003(2)	0.010(2)	0.002(2)
C(11)	0.026(2)	0.031(2)	0.039(2)	0.003(2)	0.009(2)	0.007(2)
O(12)	0.030(1)	0.026(1)	0.041(2)	0.000(1)	0.008(1)	0.008(1)
C(12)	0.022(2)	0.024(2)	0.030(2)	-0.006(2)	-0.001(2)	0.002(2)
C(13)	0.018(2)	0.024(2)	0.027(2)	-0.001(2)	0.003(2)	0.002(1)
C(14)	0.019(2)	0.032(2)	0.028(2)	0.001(2)	0.001(2)	0.003(2)
C(15)	0.027(2)	0.025(2)	0.032(2)	0.004(2)	0.002(2)	0.005(2)
C(16)	0.026(2)	0.025(2)	0.037(2)	0.003(2)	-0.001(2)	0.002(2)
C(17)	0.021(2)	0.037(2)	0.035(2)	0.000(2)	0.002(2)	0.001(2)
C(18)	0.025(2)	0.020(2)	0.040(2)	0.002(2)	0.002(2)	-0.001(2)
C(19)	0.021(2)	0.023(2)	0.040(2)	0.010(2)	0.004(2)	-0.004(2)
O(20)	0.022(1)	0.022(1)	0.035(1)	0.004(1)	0.009(1)	0.002(1)
C(21)	0.017(2)	0.026(2)	0.029(2)	-0.002(2)	0.000(2)	-0.003(2)
C(22)	0.021(2)	0.032(2)	0.035(2)	0.000(2)	0.005(2)	-0.007(2)
C(23)	0.024(2)	0.040(2)	0.042(2)	-0.004(2)	0.016(2)	-0.005(2)
C(24)	0.026(2)	0.033(2)	0.059(3)	-0.006(2)	0.022(2)	0.000(2)
C(25)	0.027(2)	0.023(2)	0.050(2)	-0.001(2)	0.014(2)	0.000(2)
C(26)	0.018(2)	0.025(2)	0.033(2)	-0.002(2)	0.007(2)	-0.002(2)
O(27)	0.030(1)	0.021(1)	0.059(2)	0.008(1)	0.020(1)	0.005(1)
C(27)	0.016(2)	0.024(2)	0.040(2)	-0.001(2)	0.004(2)	0.001(2)
O(28)	0.018(1)	0.022(1)	0.037(1)	0.003(1)	0.011(1)	0.002(1)

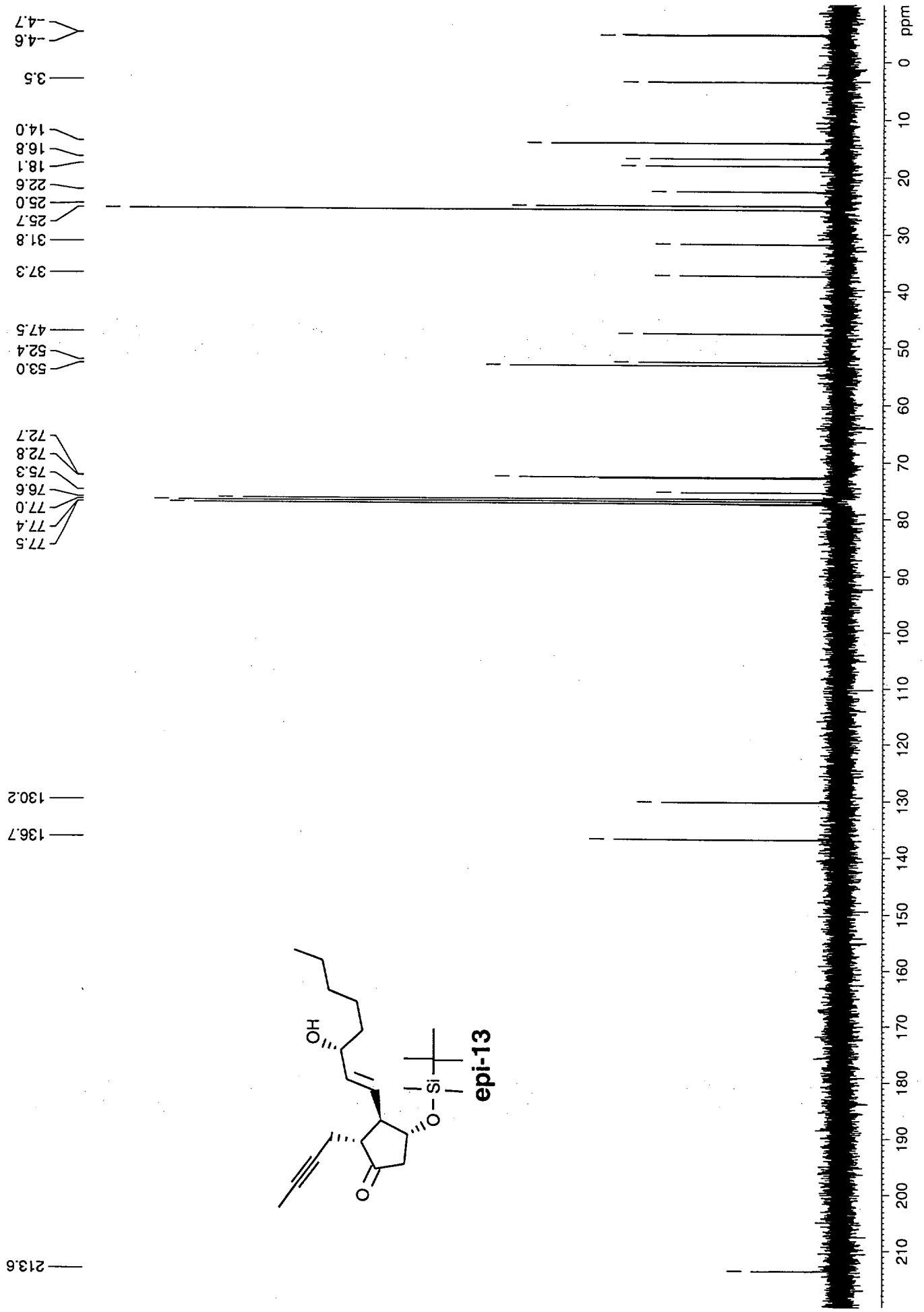


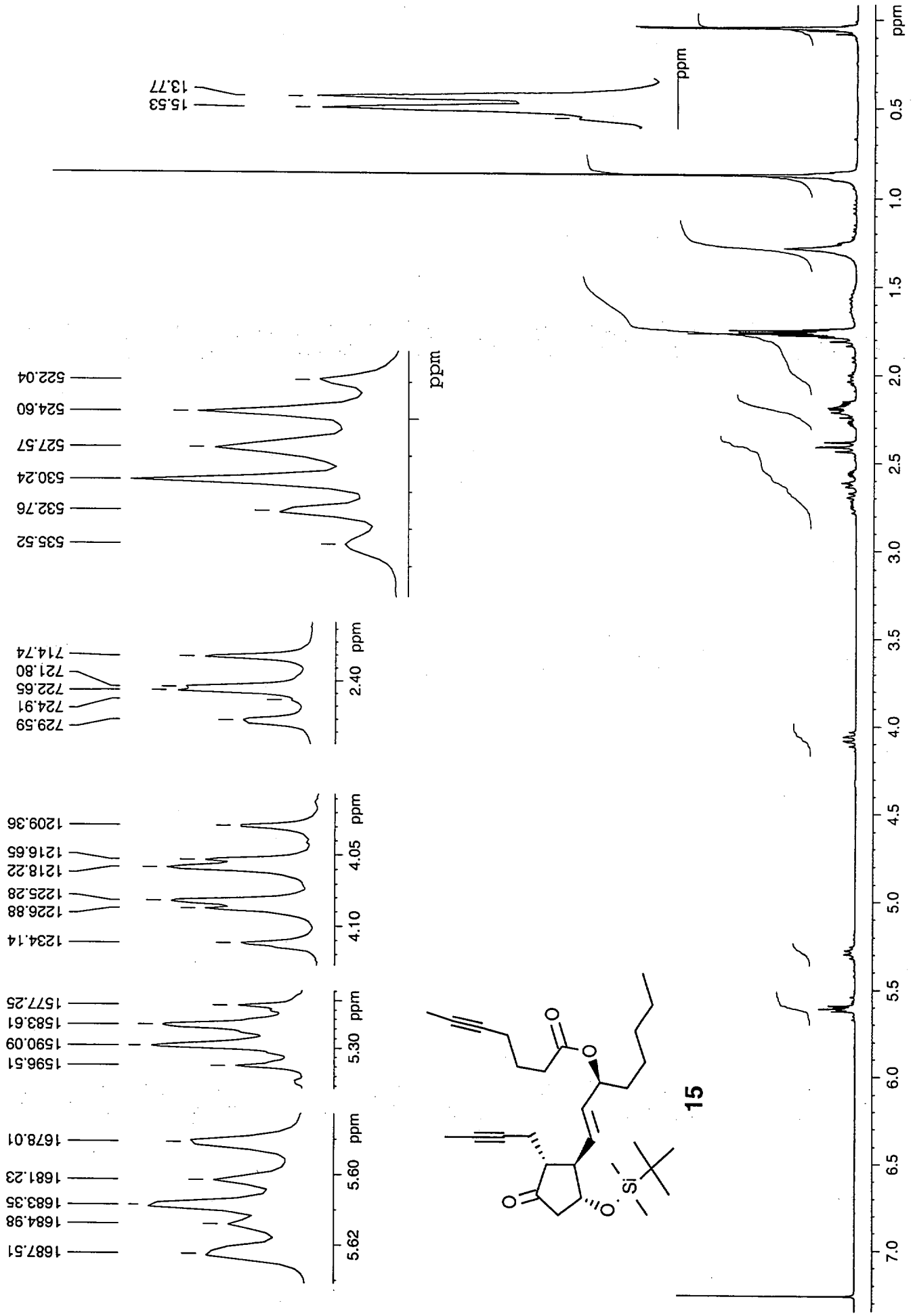


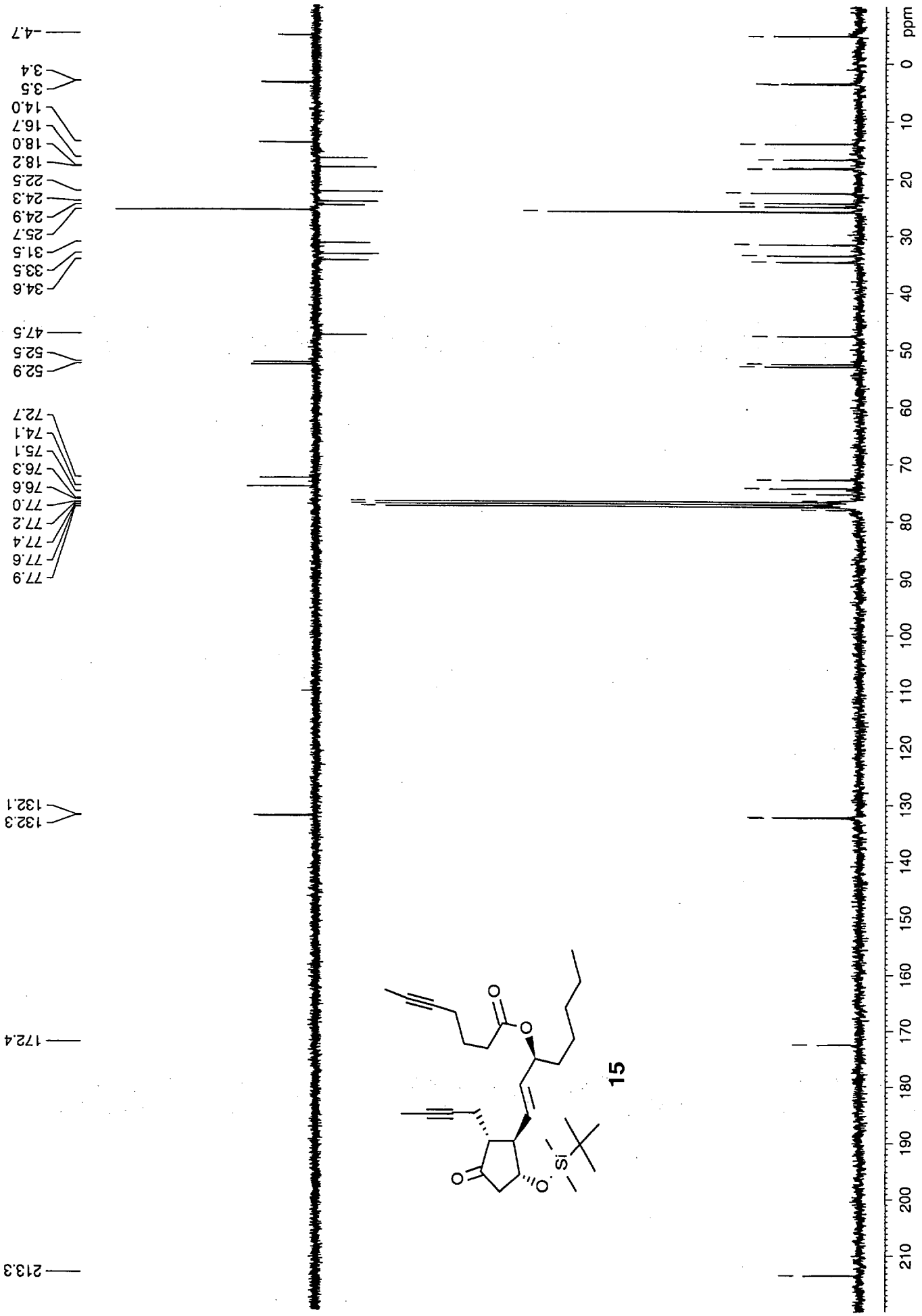


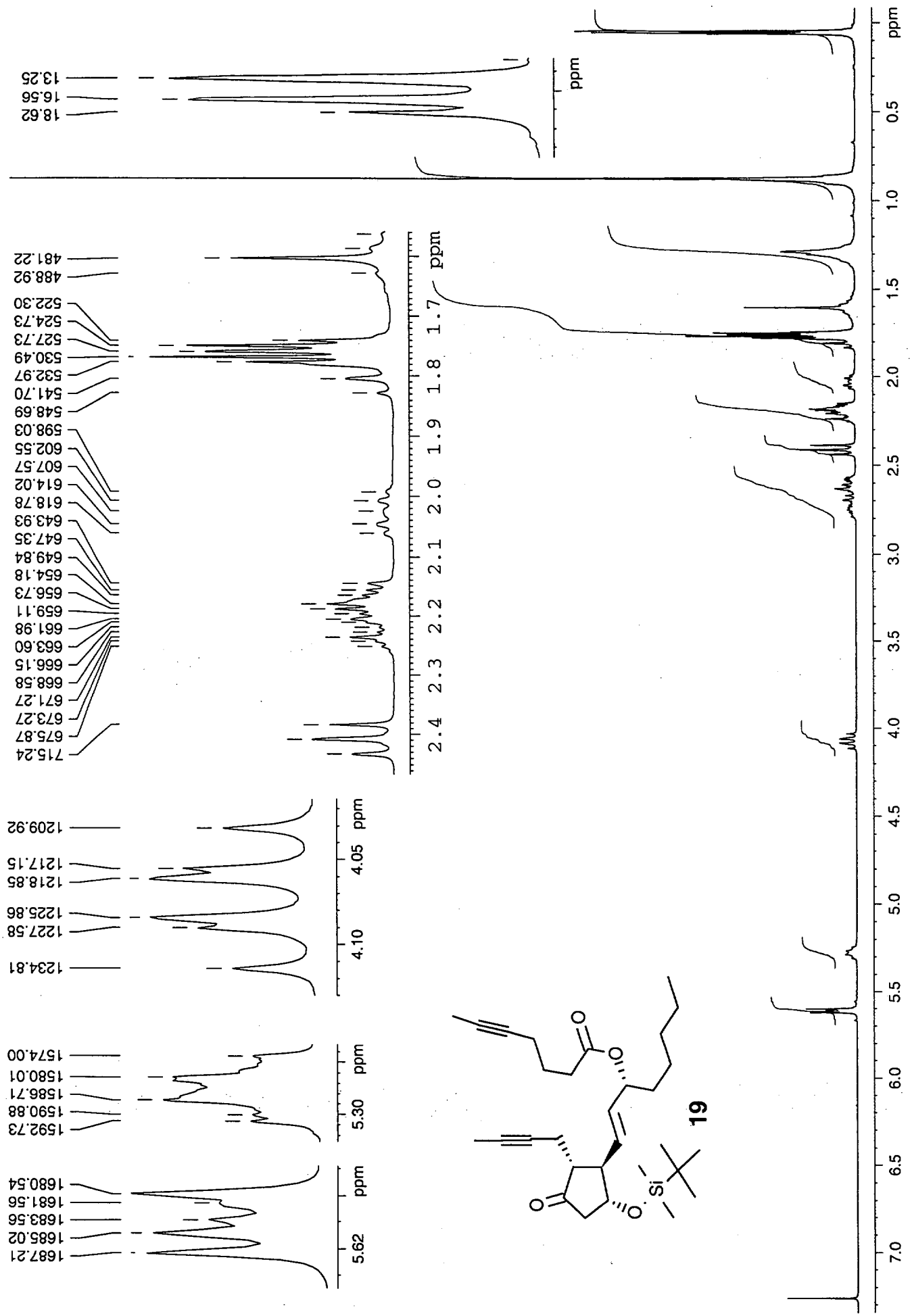


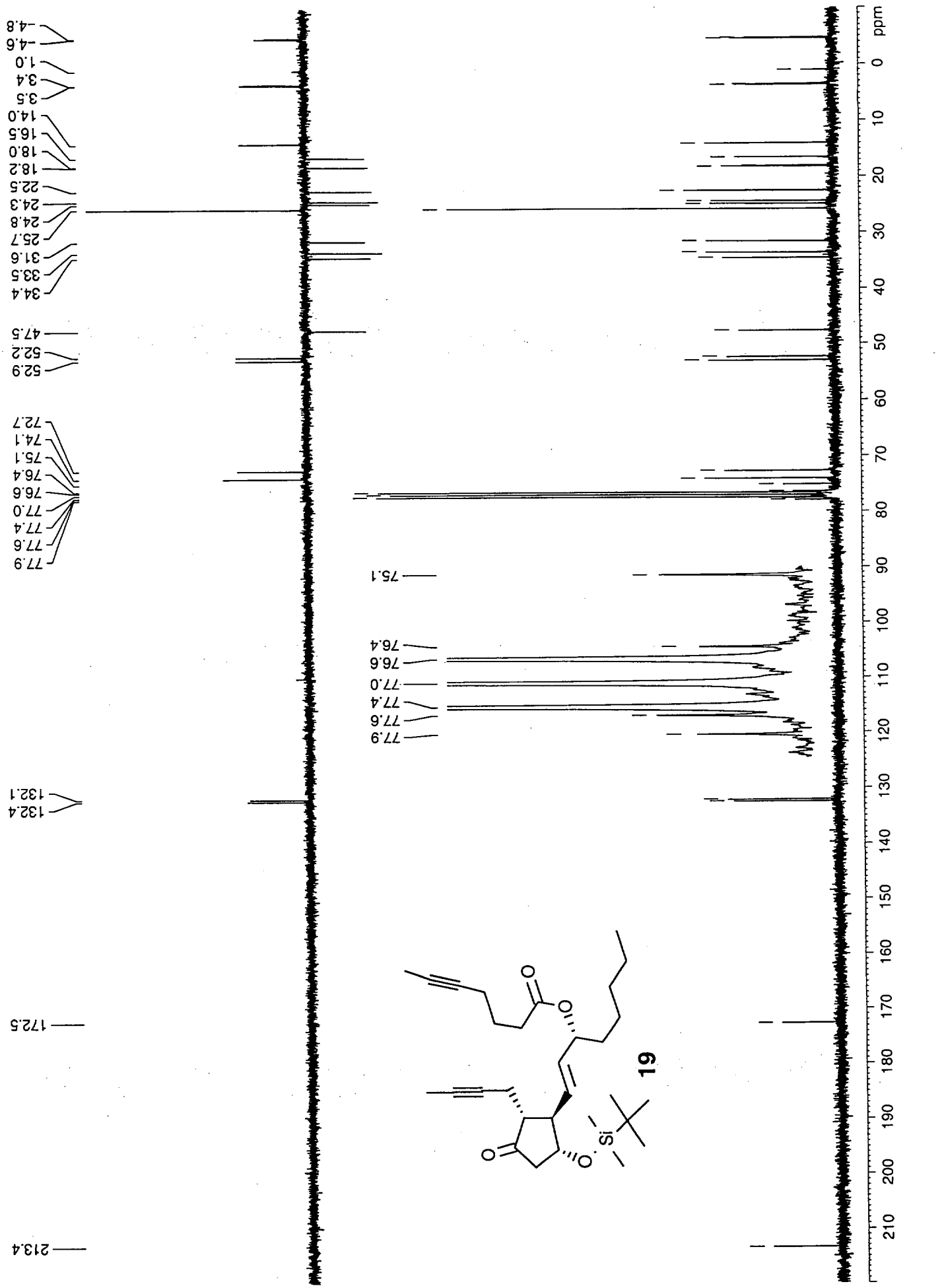


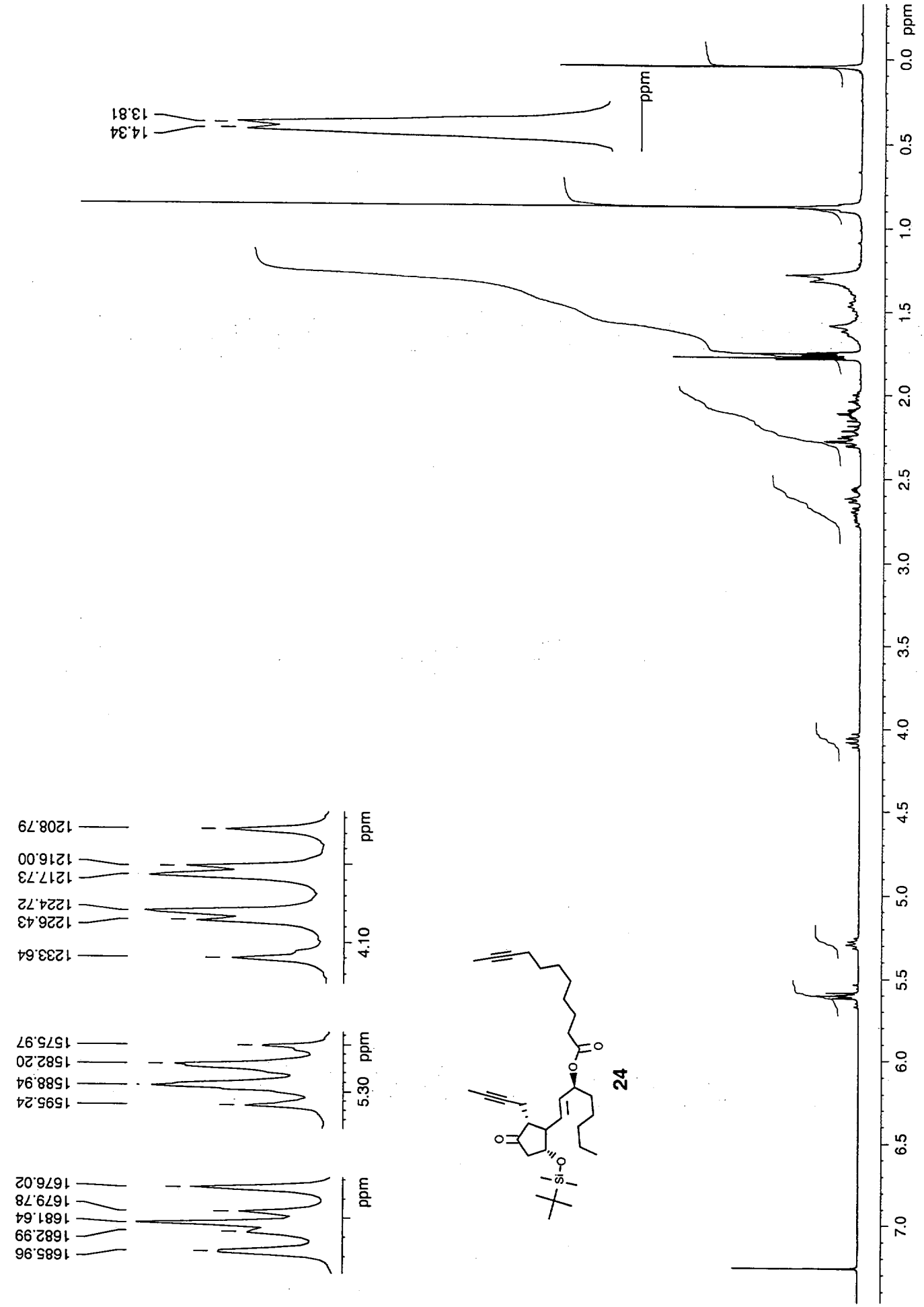


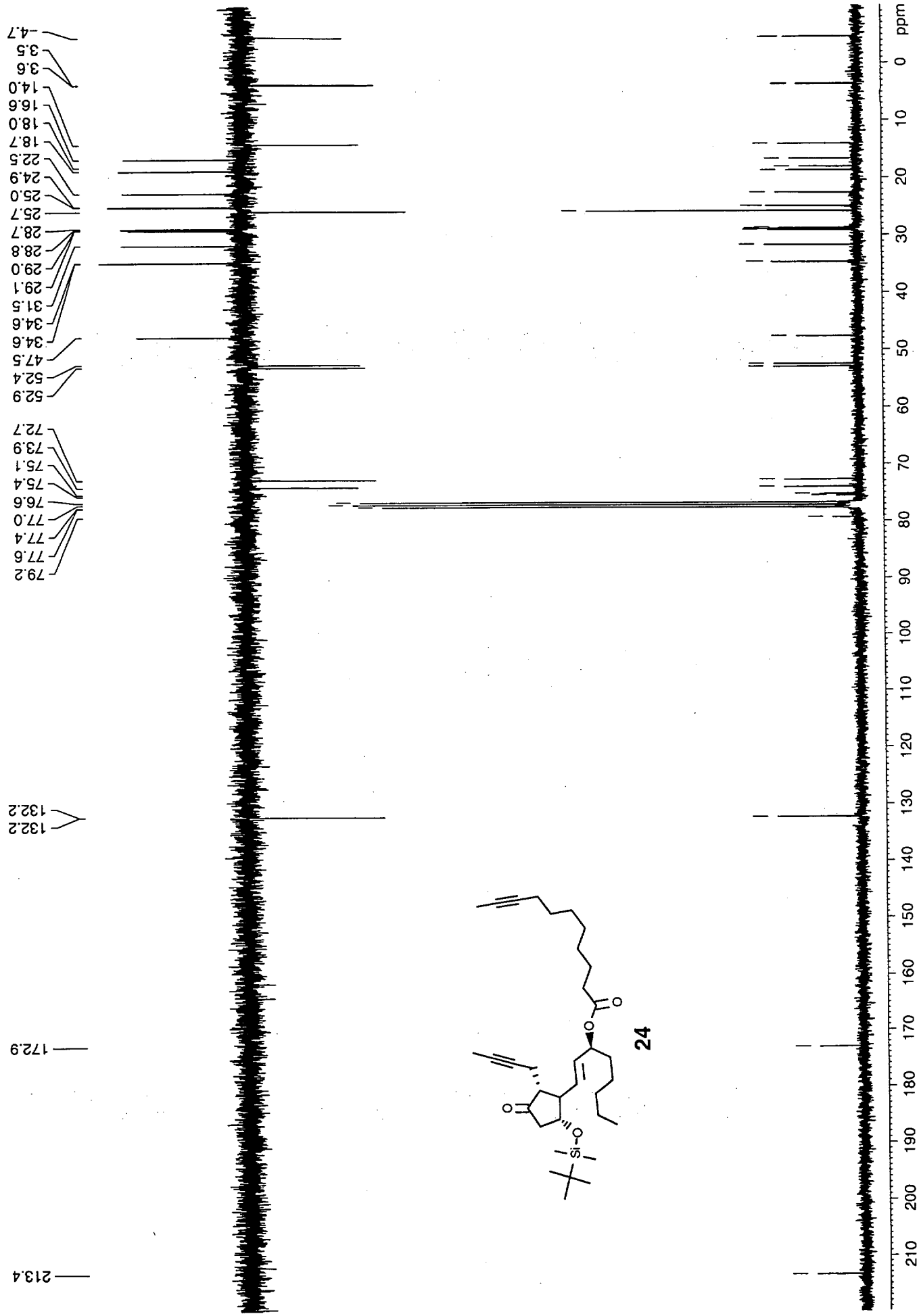


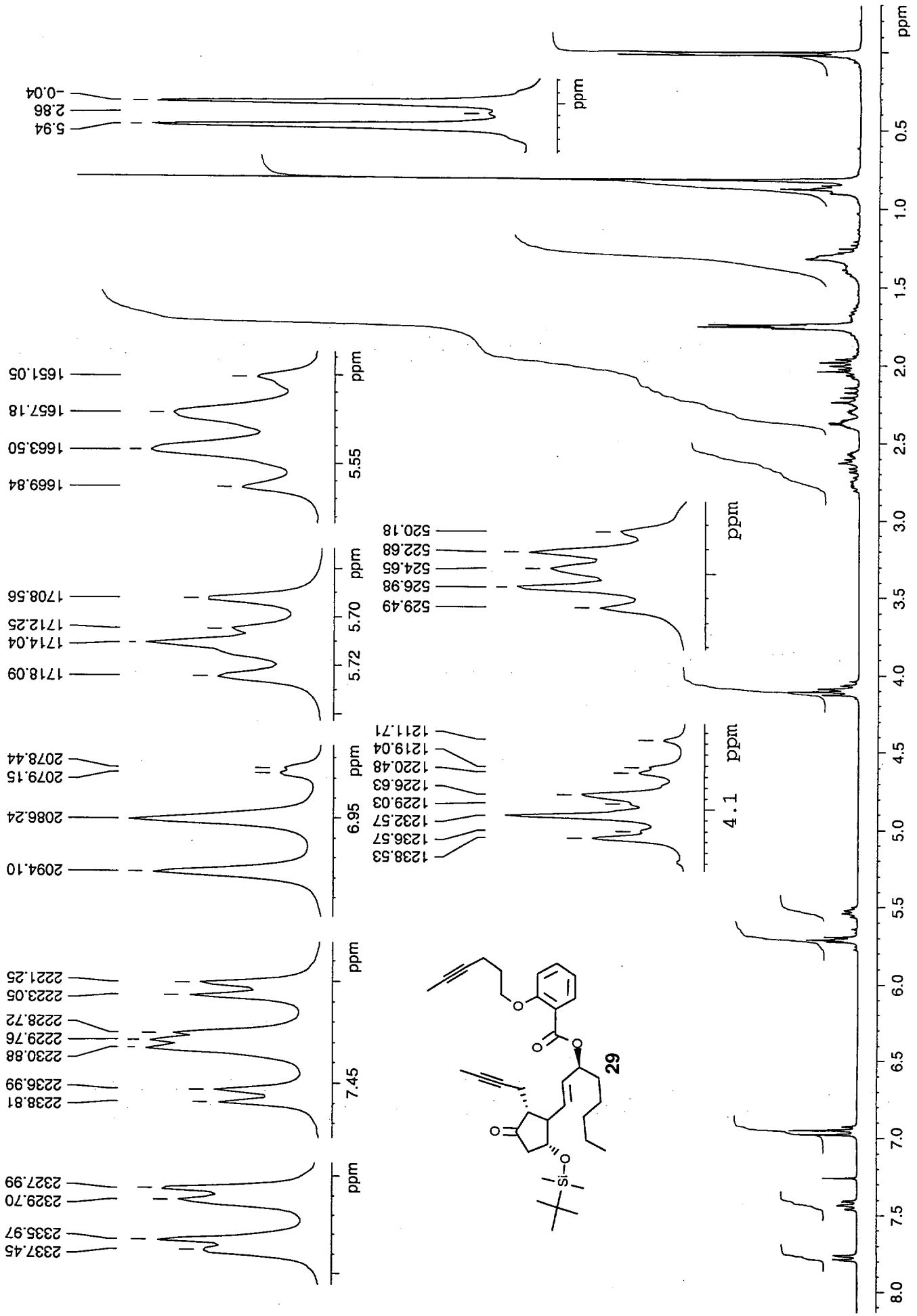


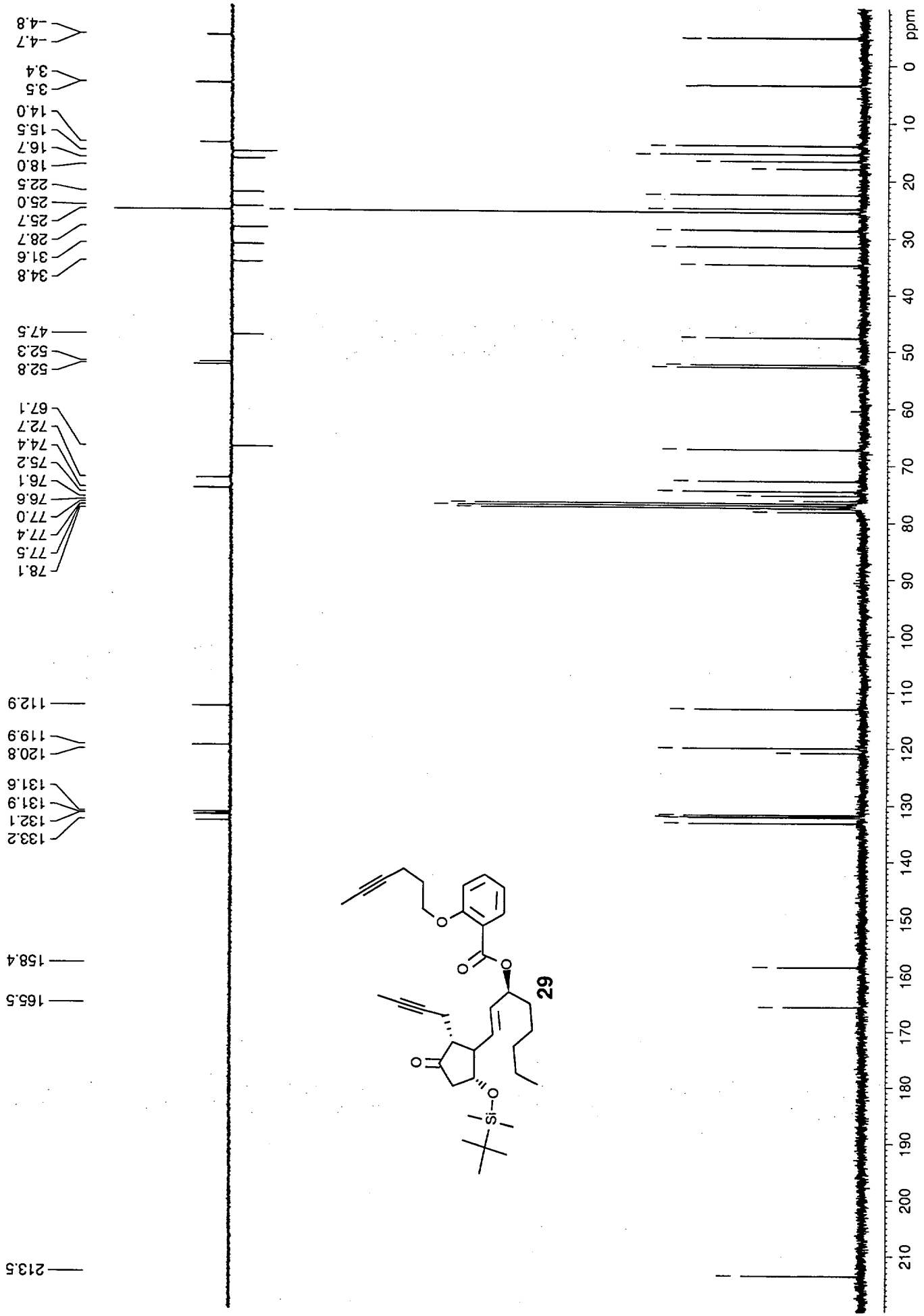


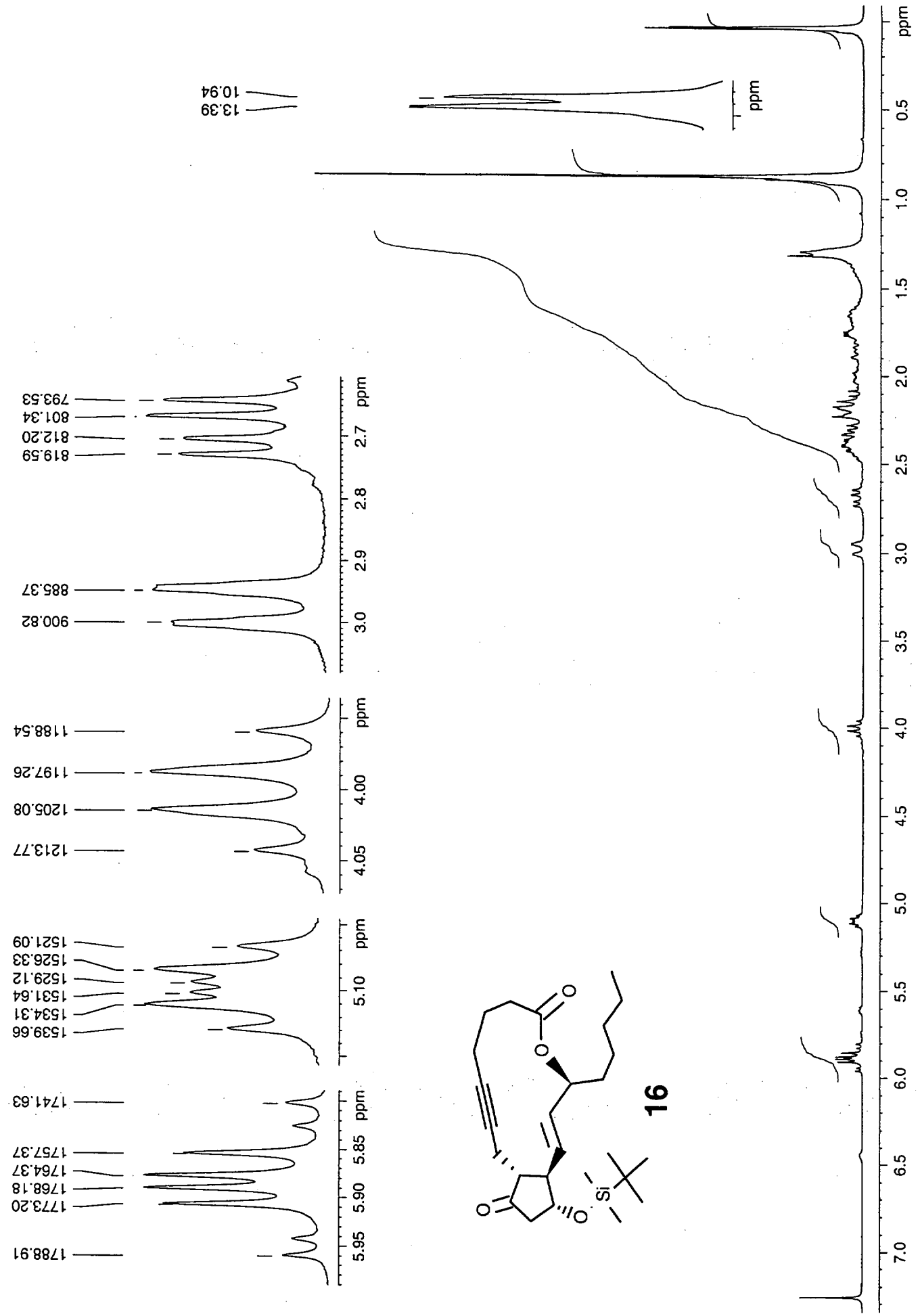


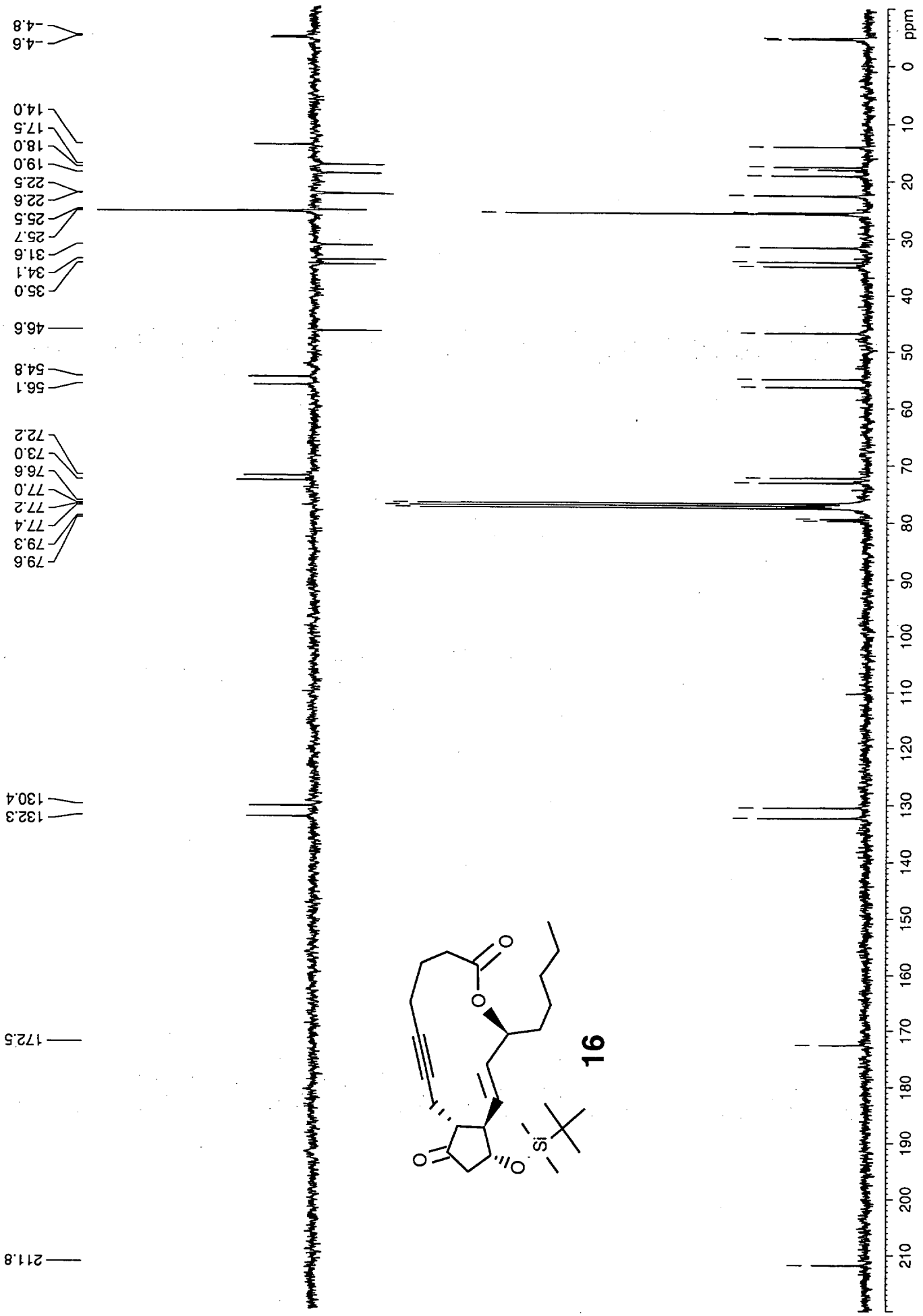












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