SUPPORTING INFORMATION FOR

Efficient Asymmetric Synthesis of [7]Helicenebisquinones

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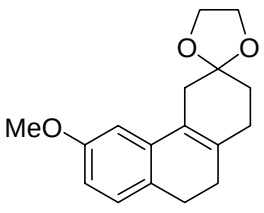
Experimental section

Melting points were obtained in open capillary tubes and are uncorrected. ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. All reactions were monitored by thin-layer chromatography which was performed on precoated sheets of silica gel 60, and flash column chromatography was done with silica gel 60 (230-400 mesh) unless specified. Eluting solvents are indicated in the text. The apparatus for inert atmosphere experiments was dried by flaming in a stream of dry argon. CH_2Cl_2, toluene and THF were dried with 4 A molecular sieves previously activated by calefaction in a microwave oven. All other reagent quality solvents were used without purification. For routine workup, hydrolysis was carried out with water, extractions with CH_2Cl_2, and solvent drying with $MgSO_4$.

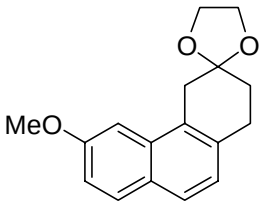
6-Methoxy-3,3(ethylenedioxy)-1,2,3,4,9,10-hexahydrophenanthrene (5)



5

A 2.3 g (10 mmol) sample of 3-keto-6-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene (**4**)[1] was treated with 1.8 mL (32.22 mmol) of ethylene glycol in 20 mL of refluxing toluene containing 12 mg of *p*-toluenesulfonic acid for 2 d until formation of water (Dean-Stark trap) ceased. The toluene layer was washed with water and, after workup, compound **5** was obtained as a red oil (2.9 g, quantitative yield), which was used in the next step without further purification: ^{1}H NMR δ 7.11 (d, *J* = 8.1 Hz, 1H), 6.82 (d, *J* = 2.8 Hz, 1H), 6.75 (dd, *J* = 8.1 and 2.7 Hz, 1H), 4.15-4.05 (m, 4H), 3.87 (s, 3H), 2.82 (t, *J* = 8.1 Hz, 2H), 2.74 (s, 2H), 2.53-2.49 (m, 2H), 2.33-2.27 (m, 2H), 1.97-1.93 (m, 2H); ^{13}C NMR δ 158.2, 136.7, 133.5, 128.0, 127.4, 127.1, 110.2, 108.5, 107.8, 64.2 (2 C), 54.9, 35.4, 30.9, 29.8, 28.6, 27.0; MS (EI): *m/z* (%) 272 (M^+, 79), 257 (16), 227 (8), 211 (18), 199 (5), 186 (100), 171 (33), 165 (8), 155 (20), 141 (13), 128 (21), 115 (16), 99 (5), 86 (16); HRMS (EI) calcd for $C_{17}H_{20}O_3$ (M^+) 272.14059, found 272.14124.

6-Methoxy-3,3(ethylenedioxy)-1,2,3,4-tetrahydrophenanthrene (6)



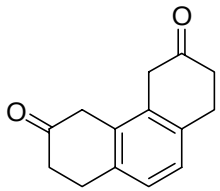
6

DDQ (5.1 g, 22 mmol) in CH_2Cl_2 (100 ml) was added to a solution of **5** (5.1 g, 18 mmol) in CH_2Cl_2 (100 ml). The mixture was stirred at room temperature for 15 min, diluted with CH_2Cl_2, and washed several times with $NaHCO_3$. After several extractions with CH_2Cl_2, elimination of the solvent and flash chromatography (hexane/CH_2Cl_2 1:5), compound **6** (4.1 g, 85% yield) was obtained as a white solid: mp 80–81 ºC; ^{1}H NMR δ 7.76 (d, *J* = 9.3 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.21-7.16 (m, 3H), 4.16-4.04 (m, 4H), 3.95 (s, 3H), 3.35 (s, 2H), 3.20-3.16 (m, 2H), 2.12-

(1) Turner, R. B.; Nettleton, D. E.; Ferelee, R. *J. Am. Chem. Soc.* **1956**, *78*, 5923-5927.

2.07 (m, 2H); ^{13}C NMR δ 157.6, 133.2, 132.9, 129.6, 127.5, 127.1, 125.7, 124.7, 116.7, 108.4, 101.3, 64.2 (2C), 54.9, 36.3, 31.1, 28.6; MS (EI): m/z (%) 270 (M^+, 51), 198 (7), 184 (100), 165 (14), 141 (14), 115 (9); HRMS (EI) calcd for $C_{17}H_{18}O_3$ (M^+) 270.12543, found 270.12559.

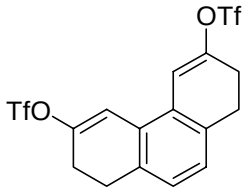
1,2,4,5,7,8-Hexahydrophenanthrene-3,6-dione (7)



7

Sodium was added in small portions, under vigorous stirring, to a solution of **6** (560 mg, 2.1 mmol) in 25 ml of EtOH (HPLC grade) heated at 90 ºC. The addition rate must be adapted to achieve that several pieces of sodium of middle size must be always present in the reaction mixture. The reaction was monitored by TLC until complete extinction of the starting material. After 90 min, EtOH was added and the mixture was stirred until the consumption of all sodium. The mixture was cooled to room temperature and the flask was introduced in a ice bath. HCl was added to bring pH acid and, after 5 min at 0 ºC, the reaction mixture was warmed to room temperature and stirred for 15 min. After several extractions with CH_2Cl_2, the organic phases were neutralized with saturated aqueous $NaHCO_3$. After workup and flash chromatography (CH_2Cl_2/EtOAc 9:1), compound **7** was obtained as a pale-brown solid, in 90% yield: mp 140–141 ºC; ^{1}H NMR δ 7.15 (s, 2H), 3.49 (s, 4H), 3.13-3.04 (m, 4H), 2.64-2.59 (m, 4H); ^{13}C NMR δ 210.2, 135.6, 131.9, 126.9, 41.8, 39.0, 29.4; MS (EI): m/z (%) 214 (M^+, 73), 172 (100), 144 (18), 130 (59), 115 (24), 97 (5), 84 (22), 71 (14); HRMS (EI) calcd for $C_{14}H_{14}O_2$ (M^+) 214.09943, found 214.09938.

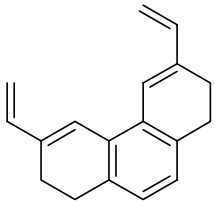
3,6-Bis[(trifluoromethanesulfonyl)oxy]-1,2,7,8-tetrahydrophenanthrene (8)



8

A solution of 0.5M KHMDS in toluene (3.42 mL, 1.71 mmol) was added to a solution of **7** (183 mg, 0.8 mmol) and *N*-phenyl-*bis*-trifluoromethanesulfonymide (611 mg, 1.71 mmol) in dry THF (14 mL) at -78 ºC under argon. The mixture was stirred for 2 h and quenched with H_2O. After workup and flash chromatography (hexane/EtOAc 9:1), compound **8** (249 mg, 65%) was obtained as a white solid: mp 56–57 ºC; ^{1}H NMR δ 7.01 (s, 2H), 6.65 (s, 2H), 3.05-2.97 (m, 4H), 2.70-2.62 (m, 4H); ^{13}C NMR δ 151.3, 132.2, 127.6, 127.2, 114.0, 28.9, 26.3; MS (EI): m/z (%) 478 (M^+, 27), 345 (88), 317 (5), 212 (100), 184 (45), 155 (27), 69 (47); HRMS (EI) calcd for $C_{16}H_{12}O_6F_6S_2$ (M^+) 477.99570, found 477.99795.

3,6-Divinyl-1,2,7,8-tetrahydrophenanthrene (2a)

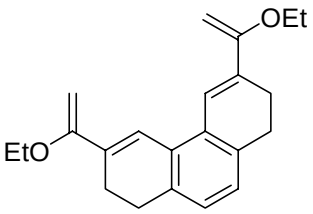


2a

To a stirred solution of compound **8** (339 mg, 0.71 mmol) in dry THF (15 mL), containing LiCl (300 mg, 7.08 mmol) and [$Pd(PPh_3)_4$] (65 mg, 0.05 mmol), vinyltributylstannane (0.41 mL, 1.42 mmol) was added under argon. The mixture was refluxed for 4.5 h, diluted with hexane (50 mL) and washed with 10% aqueous NH_4OH solution, water and brine. After workup and flash chromatography (hexane), compound **2a** was obtained as a white solid, in 86% yield: mp 78–79 ºC; ^{1}H NMR δ 6.97 (s, 2H), 6.89 (s, 2H), 6.72 (dd, *J* = 18 and 10.5 Hz, 2H), 5.43 (d, *J* = 18 Hz, 2H), 5.23 (d, *J* = 10.5 Hz, 2H), 2.89–2.84 (m, 4H), 2.52–2.47 (m, 4H); ^{13}C NMR δ 138.9, 138.6,

134.5, 129.8, 125.7, 123.9, 112.7, 28.3, 22.1; MS (EI): m/z (%) 234 (M^+, 100), 205 (7), 193 (26), 178 (16), 165 (18), 152 (8), 84 (16), 71 (5); HRMS (EI) calcd for $C_{18}H_{18}$ (M^+) 234.13982, found 234.14085.

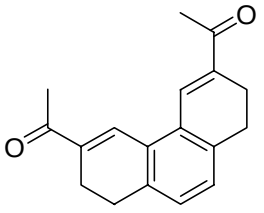
3,6-Bis(1-ethoxyvinyl)-1,2,7,8-tetrahydrophenanthrene (2b)



2b

To a stirred solution of compound **8** (206 mg, 0.43 mmol) in dry THF (9 mL), containing LiCl (233 mg, 5.47 mmol) and [$Pd(PPh_3)_4$] (45 mg, 0.04 mmol), (1-ethoxyvinyl)tributylstannane (0.33 mL, 0.86 mmol) was added under argon. The mixture was refluxed for 5.5 h, diluted with hexane (30 mL) and washed with 10% aqueous NH_4OH solution, water and brine. After workup and flash chromatography (hexane) using alumina deactivated with 10% water as the stationary phase, compound **2b** was obtained as a very unstable white solid, in 35% yield: ^{1}H NMR δ 7.52 (s, 2H), 6.92 (s, 2H), 4.45 (d, *J* = 2.1 Hz, 2H), 4.24 (d, *J* = 2.1 Hz, 2H), 3.89 (q, *J* = 7.0 Hz, 4H), 2.85-2.77 (m, 4H), 2.49-2.41 (m, 4H), 1.45 (t, *J* = 7.0 Hz, 6H).

3,6-Bis(1-oxoethyl)-1,2,7,8-tetrahydrophenanthrene (9)

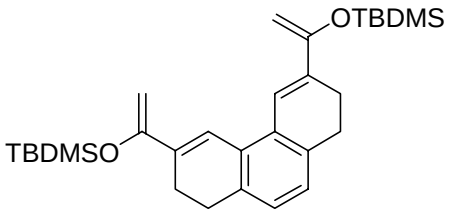


9

To a stirred solution of compound **8** (159 mg, 0.31 mmol) in dry THF (8 mL), containing LiCl (138 mg, 3.15 mmol) and [$Pd(PPh_3)_4$] (31 mg, 0.02 mmol), (1-ethoxyvinyl)tributylstannane (0.20 mL, 0.64 mmol) was added under argon. The mixture was refluxed for 5.5 h. After elimination of the solvent and flash chromatography (CH_2Cl_2, then CH_2Cl_2/EtOAc 1:1), compound **9** (60 mg,

75%) was obtained as a white solid: mp 130-132 ºC; ^{1}H NMR δ 7.94 (s, 2H), 7.40 (s, 2H), 2.97–2.90 (m, 4H), 2.74-2.68 (m, 4H), 2.64 (s, 6H); ^{13}C NMR δ 198.5, 139.9, 136.6, 131.5, 130.13, 129.0, 28.1, 25.7, 21.0; MS (EI): m/z (%) 266 (M^+, 100), 251 (45), 233 (78), 179 (66), 165 (32), 149 (24), 97 (11), 69 (30); HRMS (EI) calcd for $C_{18}H_{18}O_2$ (M^+) 266.13089, found 266.13068.

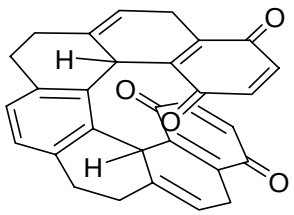
3,6-Bis[1-(*tert*-butyldimethylsililoxy)vinyl]-1,2,7,8-tetrahydrophenanthrene (2c)



2c

To a stirred solution of *bis*-ketone **9** (36 mg, 0.14 mmol) in dry THF (2.4 mL) at -78 ºC was added under argon a solution of 0.5 M KHMDS in toluene (0.58 mL, 0.29 mmol), followed by *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.07 mL, 0.28 mmol). After 1 h, hexane (1.5 mL) was added and the mixture was washed with NaOH 1M. After workup, compound **2c** (71 mg, 93%) was obtained as a yellow solid and used in the next step without further purification: ^{1}H NMR δ 7.28 (s, 2H); 6.92 (s, 2H), 4.67 (s, 2H), 4.41 (s, 2H), 2.82-2.72 (m, 4H), 2.48-2.38 (m, 4H), 1.01 (s, 18H), 0.22 (s, 12H); MS (EI): m/z (%) 494 (M^+, 73), 438 (38), 382 (27), 308 (38), 231 (13), 190 (18), 147 (13); HRMS (EI) calcd for $C_{30}H_{46}O_2Si_2$ (M^+) 494.30380, found 494.303638.

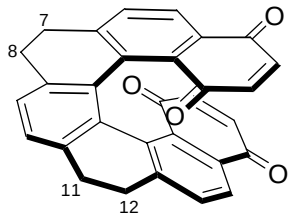
5,6b,7,8,11,12b,14-Octahydro-[7]-helicenebisquinone (10a)



(-)-**10a**

To a solution of *bis*-diene **2a** (110 mg, 0.47 mmol) in CH_2Cl_2 (5 mL), a solution of (S*S*)-**1**[2] (232 mg, 0.94 mmol) in CH_2Cl_2 (5 mL) was added at -20 ºC under argon. After 4 and 8 days, two new portions of (S*S*)-**1** (58 mg, 0.23 mmol) in CH_2Cl_2 (1 mL) were added. The mixture was then stirred for 3 days and the solvent eliminated under reduced pressure. After flash chomatography (CH_2Cl_2), compound **10a** was obtained as an orange solid, in 50% yield: mp > 160 ºC; $[\alpha]^{20}_D$ = -686 (*c* 0.04, $CHCl_3$); ^{1}H NMR δ 7.11-7.05 (m, 2H), 6.67-6.37 (m, 4H), 5.75-5.45 (m, 2H), 4.68-4.46 (m, 2H), 3.67-3.61 (m, 2H), 3.07-2.03 (m, 8H); HRMS (EI) calcd for $C_{30}H_{22}O_4$ (M^+) 446.15240, found 446.15181.

(*M*)-7,8,11,12-Tetrahydro-[7]-helicenebisquinone (3a)



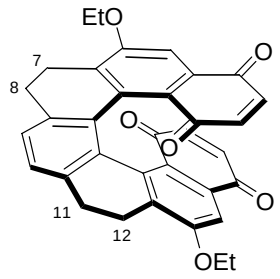
(*M*)-**3a**

A solution of (-)-**10a** (21 mg, 0.05 mmol) and DDQ (42 mg, 0.18 mmol) in CH_2Cl_2 (1.2 mL) was stirred at 5 ºC for 20 h. The mixture was then washed several times with $NaHCO_3$. After workup and flash chromatography (hexane/acetone 2:1), compound (*M*)-**3a** was obtained as an orange solid, in 90% yield: mp > 160 ºC; {$[\alpha]^{20}_D$= -5825 (*c* 0.01, $CHCl_3$), 96% *ee*}; ^{1}H NMR δ 7.82 (d, *J* = 7.7 Hz, 2H), 7.56 (d, *J* = 7.7 Hz, 2H), 7.26 (s, 2H), 6.45 (d, *J* = 10.1 Hz, 2H), 6.04 (d, *J* = 10.1 Hz, 2H), 2.91–2.35 (m, 8H); ^{13}C NMR δ 185.4, 183.9, 150.3, 139.9, 138.7, 135.8, 134.5, 131.9, 131.5, 131.2, 130.6, 127.8, 125.4, 30.7, 30.0; MS (EI): m/z (%) 442 (M^+, 100), 423 (7), 300 (13), 276 (10), 149 (19), 91 (7); HRMS (EI) calcd for $C_{30}H_{18}O_4$ (M^+) 442.12039, found 442.12051.

The *ee* was determined by chiral HPLC (*Chiralcel* OD, hexane/2-propanol 70:30, 0.5 mL/min, R_t = 33.5 min (*M*-enantiomer) and 41.4 min (*P*-enantiomer).

(2) Carreño, M. C.; García Ruano, J. L.; Urbano, A. *Synthesis* **1992**, 651-653.

(*M*)-6,13-Diethoxy-7,8,11,12-tetrahydro[7]helicenebisquinone (3b)



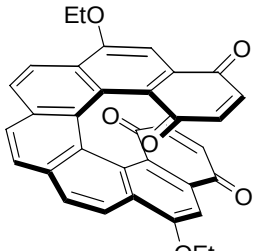
(*M*)-**3b**

From diene 2b. To a stirred solution of **2b** (14 mg, 0.045 mmol) in dry CH_2Cl_2 (0.5 mL) at -20 ºC under argon, a solution of (S*S*)-**1** (22 mg, 0.086 mmol) in CH_2Cl_2 (0.6 mL) was added. After 19 h at -20 ºC, a new portion of (S*S*)-**1** (58 mg, 0.23 mmol) in CH_2Cl_2 (0.6 mL) was added. After 7 d, the solvent was evaporated and the residue purified by flash chromatography (CH_2Cl_2), to give (*M*)-**3b** as a red solid, in 47% yield: {$[\alpha]^{20}_D$= -2938 (*c* 0.06, $CHCl_3$), 96% *ee*}; ^{1}H NMR δ 7.30 (s, 2H), 7.25 (s, 2H), 6.42 (d, *J* = 10.2 Hz, 2H), 6.03 (d, *J* = 10.2 Hz, 2H,), 4.35-4.05 (m, 4H), 3.40-3.30 (m, 2H), 2.88-2.17 (m, 6H), 1.54-1.48 (t, *J* = 7 Hz, 6H); ^{13}C NMR δ 184.4, 184.2, 158.8, 140.2, 139.0, 138.4, 136.7, 135.1, 132.0, 127.4, 106.6, 64.6, 29.7, 22.3, 14.7; MS (EI): m/z (%) 530 (M^+, 100), 501 (15), 473 (7), 287 (6); HRMS (EI) calcd for $C_{34}H_{26}O_6$ (M^+) 530.17194, found 530.17294.

From tetrahydro[7]helicene (*M*)-3c. To a vigorously stirred suspension of CsF (45.6 mg, 0.30 mmol) and EtI (0.23 mL, 3 mmol) in DMF (3 mL), a solution of enantiomerically pure helicene (*M*)-**3c** (21.4 mg, 0.03 mmol) in DMF (3 mL) was added via cannula under argon. The mixture was stirred for 1 h, quenched with water and extracted several times with Et_2O. After workup and flash chromatography (CH_2Cl_2), compound (*M*)-**3b** was obtained in 82% yield: {$[\alpha]^{20}_D$= -3180 (*c* 0.05, $CHCl_3$), >99% *ee*}.

The *ee* for (*M*)-**3b** was determined by chiral HPLC (*Chiralcel* OD, hexane/2-propanol 70:30, 0.5 mL/min, R_t = 27.4 min (*P*-enantiomer) and 76.9 min (*M*-enantiomer).

(*M*)-6,13-Diethoxy[7]helicenebisquinone (11)

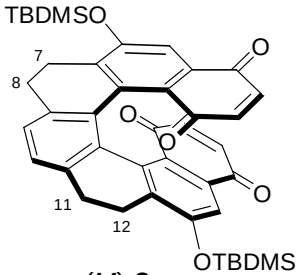


(*M*)-**11**

A solution of enantiopure (*M*)-**3b** (11 mg, 0.02 mmol) and DDQ (56 mg, 0.25 mmol) in toluene (4 mL) was heated at 160-165 ºC in a sealed tube. After 6 days, the residue was purified by flash chromatography (hexane/acetone 4:1) to give compound (*M*)-**11** as a red solid, in 83% yield: mp 136-137 ºC; $\{[\alpha]^{20}_D = -825$ (*c* 0.08, $CHCl_3$), >99% *ee*$\}$; ^{1}H NMR δ 8.42 (d, *J* = 8.9 Hz, 2H), 8.02 (d, *J* = 8.9 Hz, 2H), 7.96 (s, 2H), 7.39 (s, 2H), 6.48 (d, *J* = 10.1 Hz, 2H), 5.95 (d, *J* = 10.1 Hz, 2H), 4.48-4.33 (m, 4H), 1.64 (t, *J* = 7.3 Hz, 6H); MS (EI): m/z (%) 256 (M^+, 100), 501 (15), 473 (7), 287 (6); HRMS (EI) calcd for $C_{34}H_{22}O_6$ (M^+) 526.14240, found 526.14164.

The *ee* for (*M*)-**11** was determined by chiral HPLC (*Chiralcel* OD, hexane/2-propanol 70:30, 0.5 mL/min, R_t = 94.8 min.

(*M*)-6,13-*Bis*[(*tert*-butyldimethylsilyl)oxy]-7,8,11,12-tetrahydro[7]helicenebisquinone (3c)

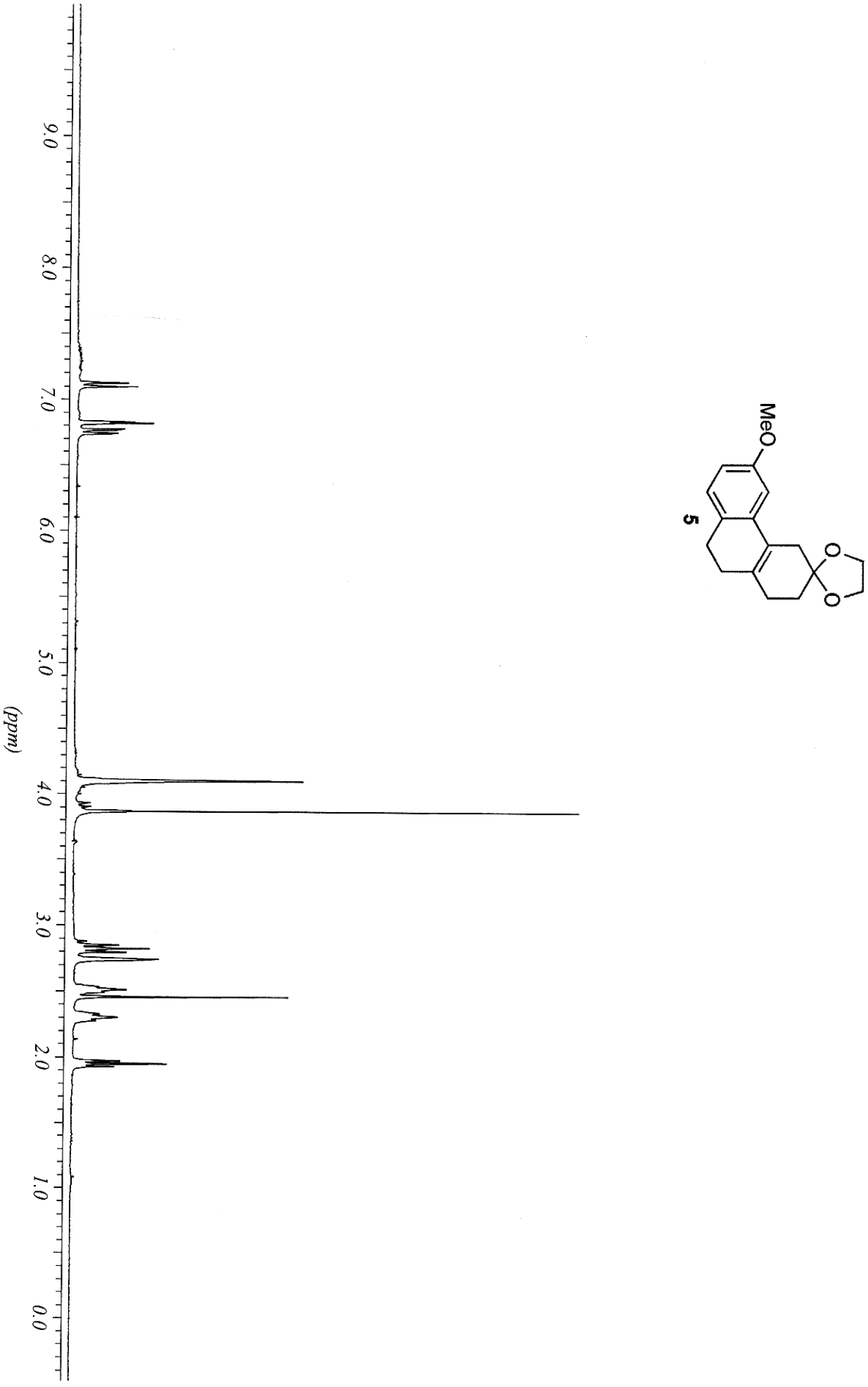


(*M*)-**3c**

To a solution of *bis*-diene **2c** (60 mg, 0.12 mmol) in CH_2Cl_2 (2.5 ml) at -45 ºC, (S*S*)-**1** (59 mg, 0.24 mmol) in CH_2Cl_2 (1.5 mL) was added. After 1 h, DDQ (218 mg, 0.96 mmol) was added and the mixture warmed to -25 ºC. After 2 d, the solvent was evaporated and the residue was purified by flash chromatography (CH_2Cl_2), to give compound (*M*)-**3c** as a red solid, in 25% yield: $\{[\alpha]^{20}_D = -1990$ (*c* 0.02, $CHCl_3$), >99% *ee*$\}$; ^{1}H NMR δ 7.29 (s, 2H), 7.28 (s, 2H), 6.48 (d, *J* =

10.5 Hz, 2H), 6.10 (d, *J* = 10.5 Hz, 2H), 3.34-2.30 (m, 8H), 1.11 (s, 18H), 0.39 (s, 6H), 0.37 (s, 6H); ^{13}C NMR δ 184.1 (2C), 156.1, 141.4, 140.1, 138.4, 137.4, 135.3, 132.2, 131.8, 127.5, 125.2, 114.4, 29.8, 25.7, 23.1, 18.3; MS (EI): m/z (%) 645 (M^+, 100), 125 (5), 97 (16), 73 (70); HRMS (EI) calcd for $C_{42}H_{46}O_6Si_2$ (M^+) 702.28125, found 702.28330.

The *ee* for (*M*)-**3c** was determined by chiral HPLC (*Chiralcel* OD, hexane/2-propanol 95:5, 0.5 mL/min, R_t = 10.0 min (*P*-enantiomer) and 12.5 min (*M*-enantiomer).


MeO
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8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
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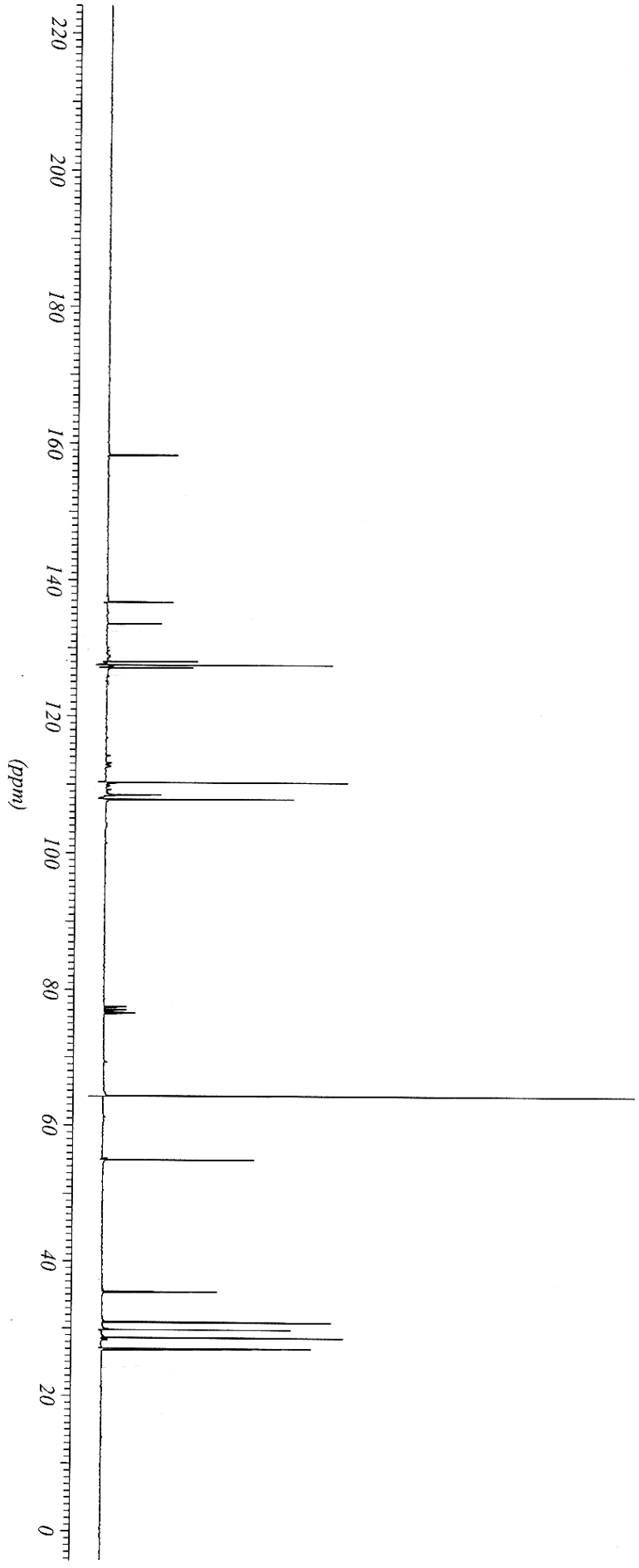

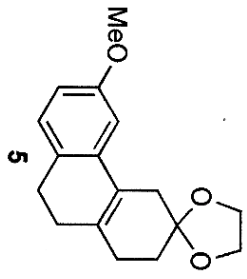

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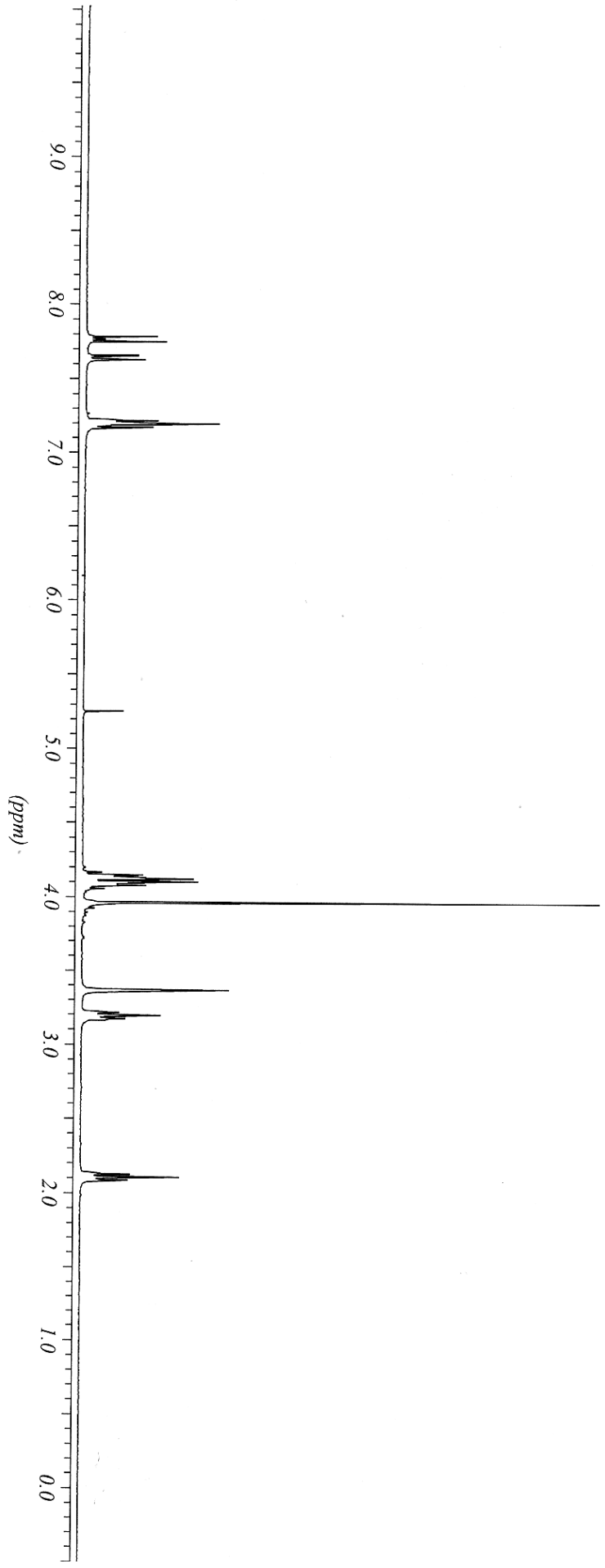

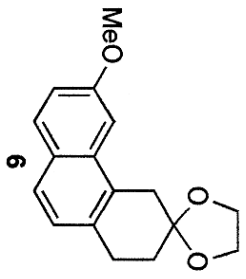

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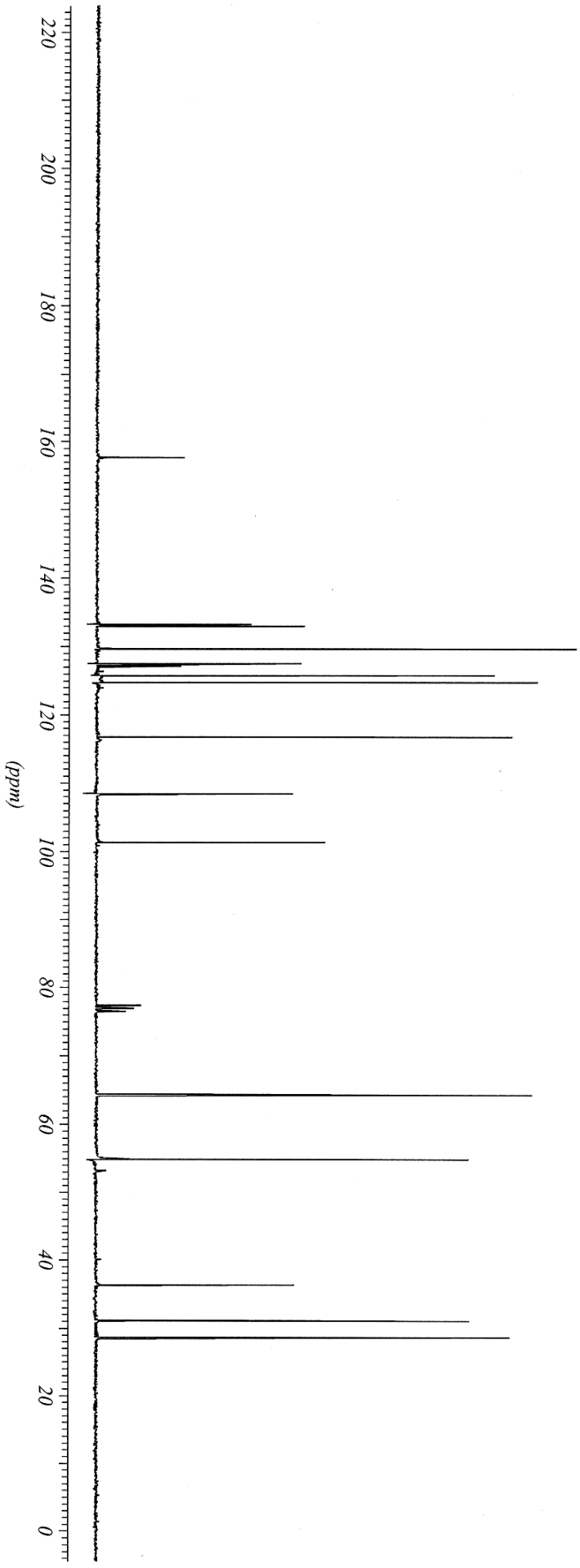

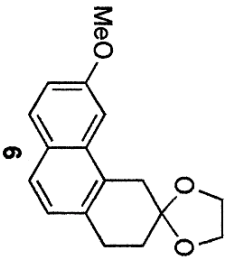

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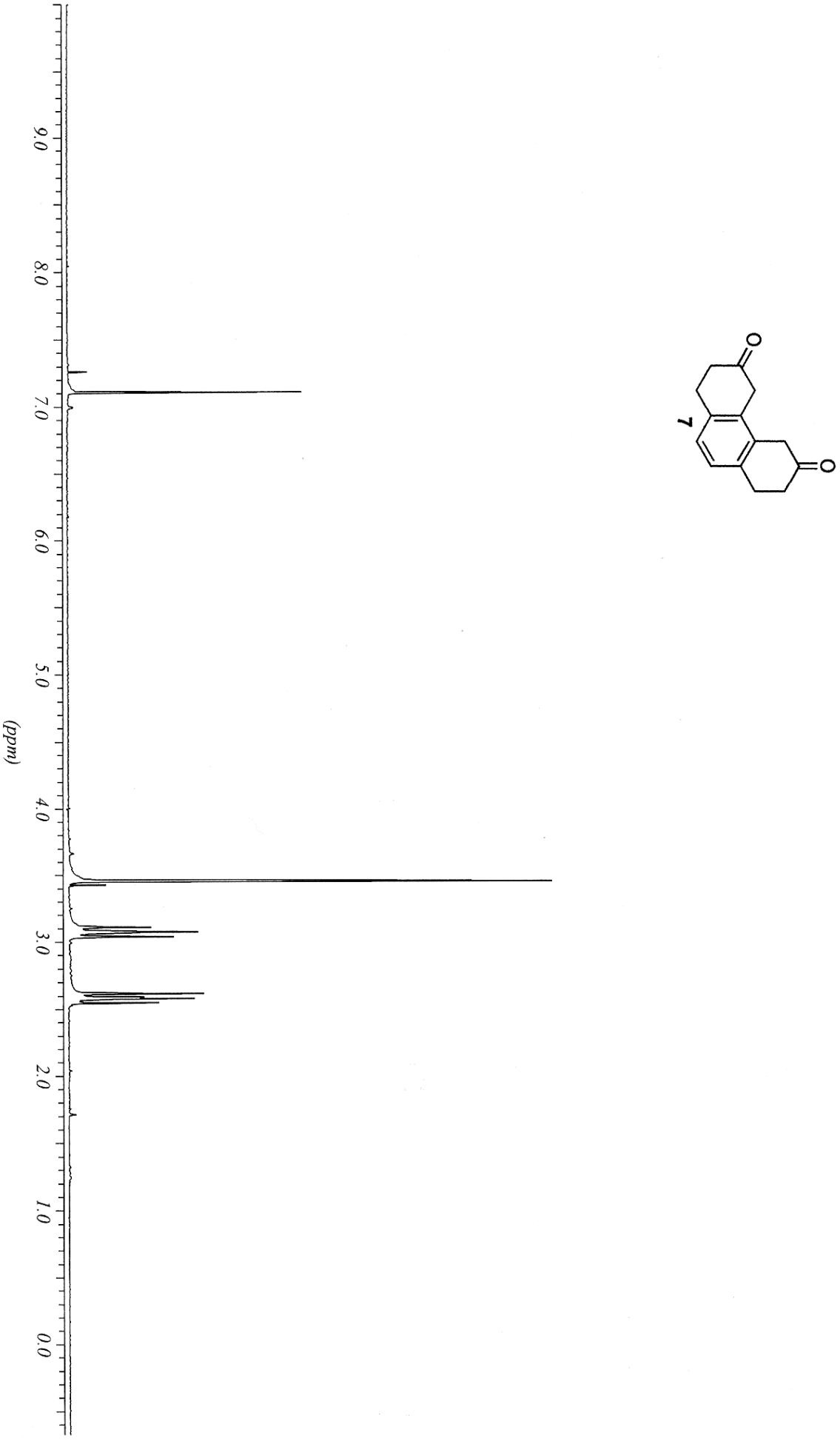
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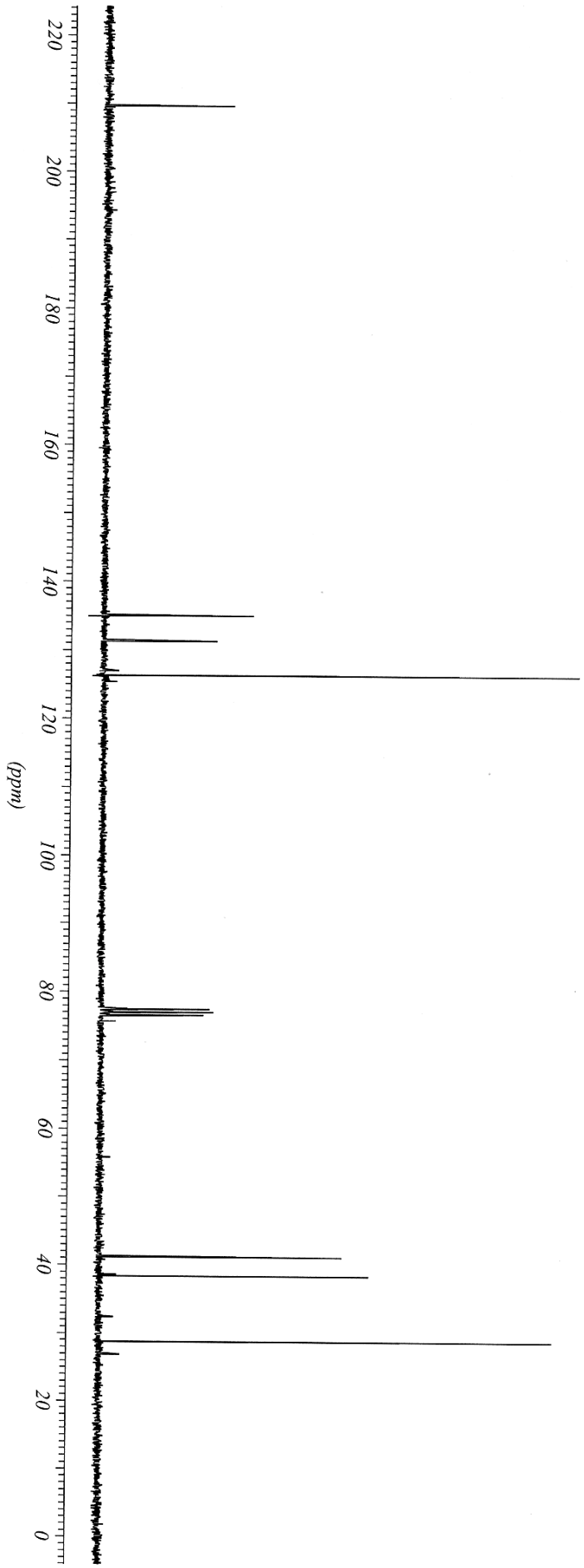

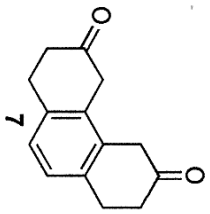

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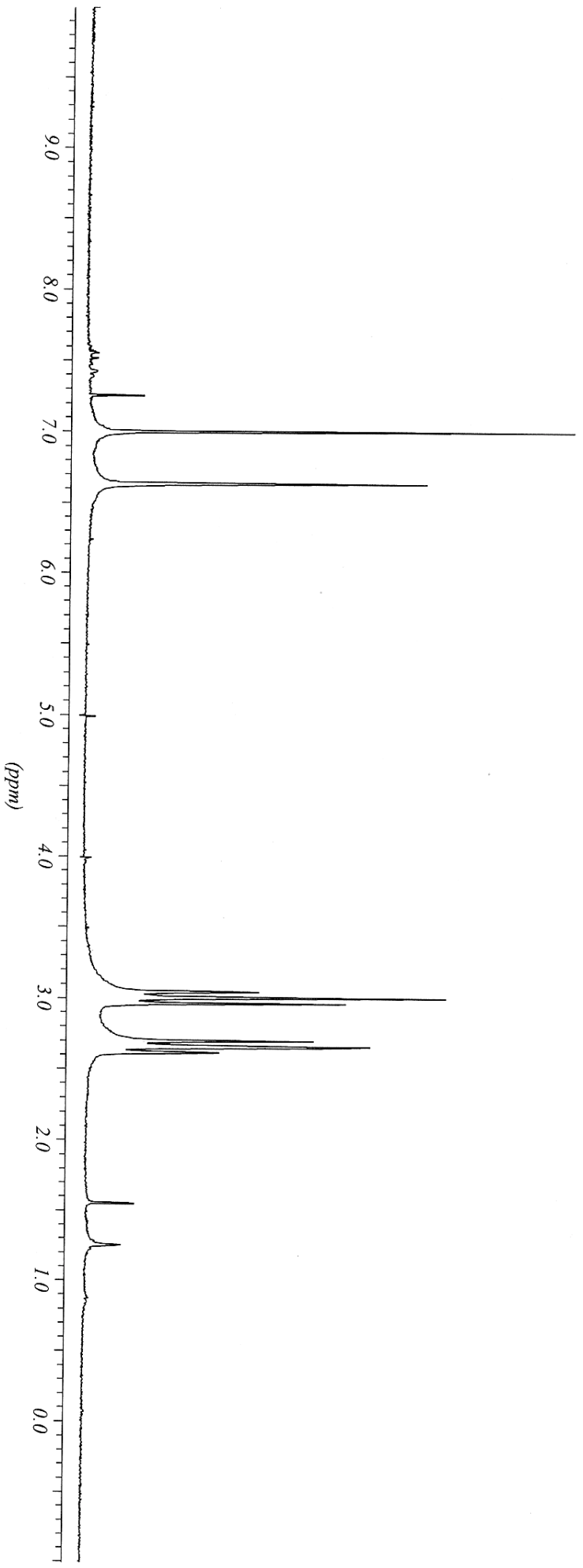
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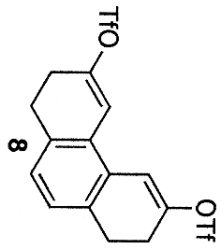
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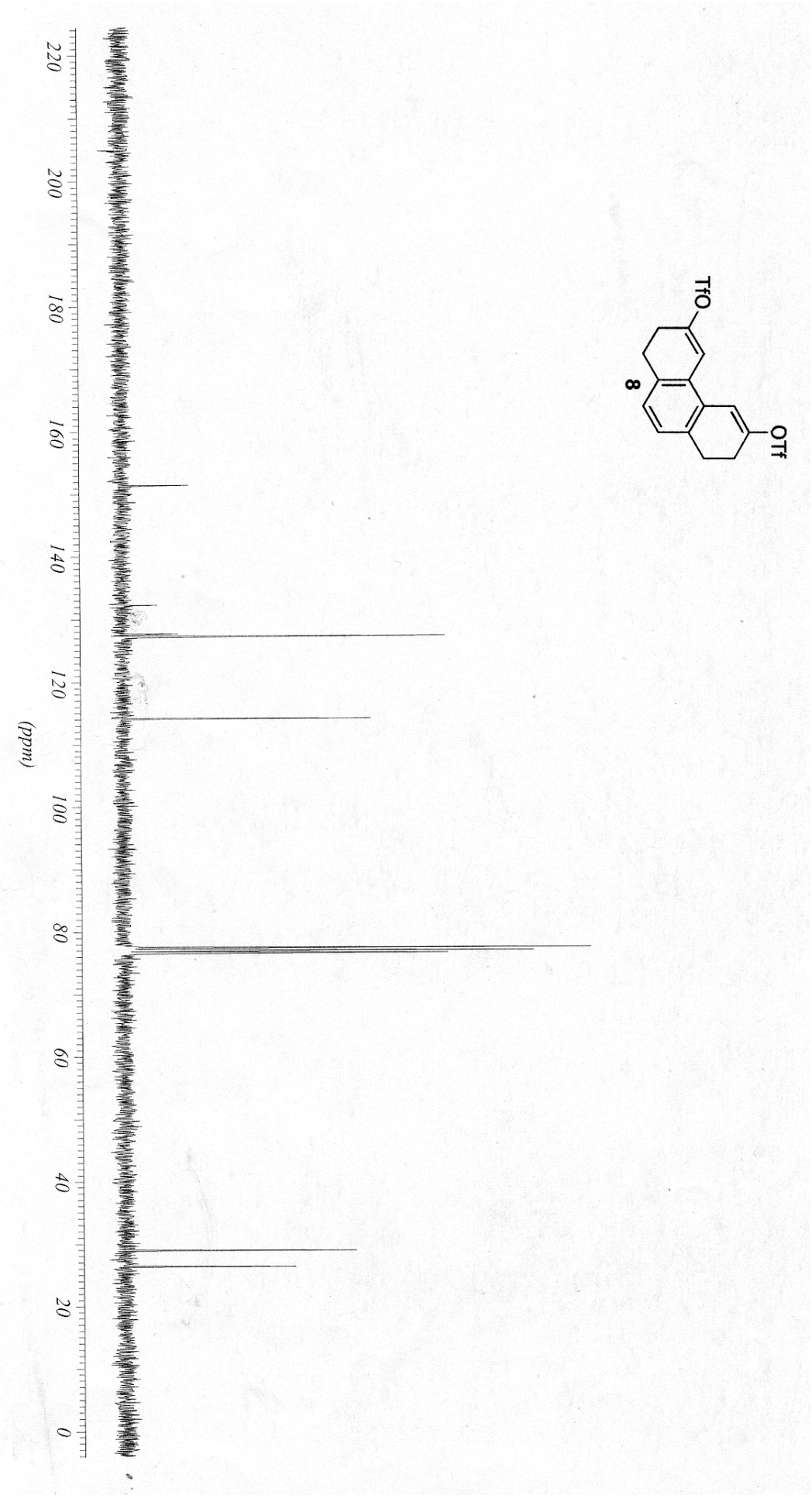
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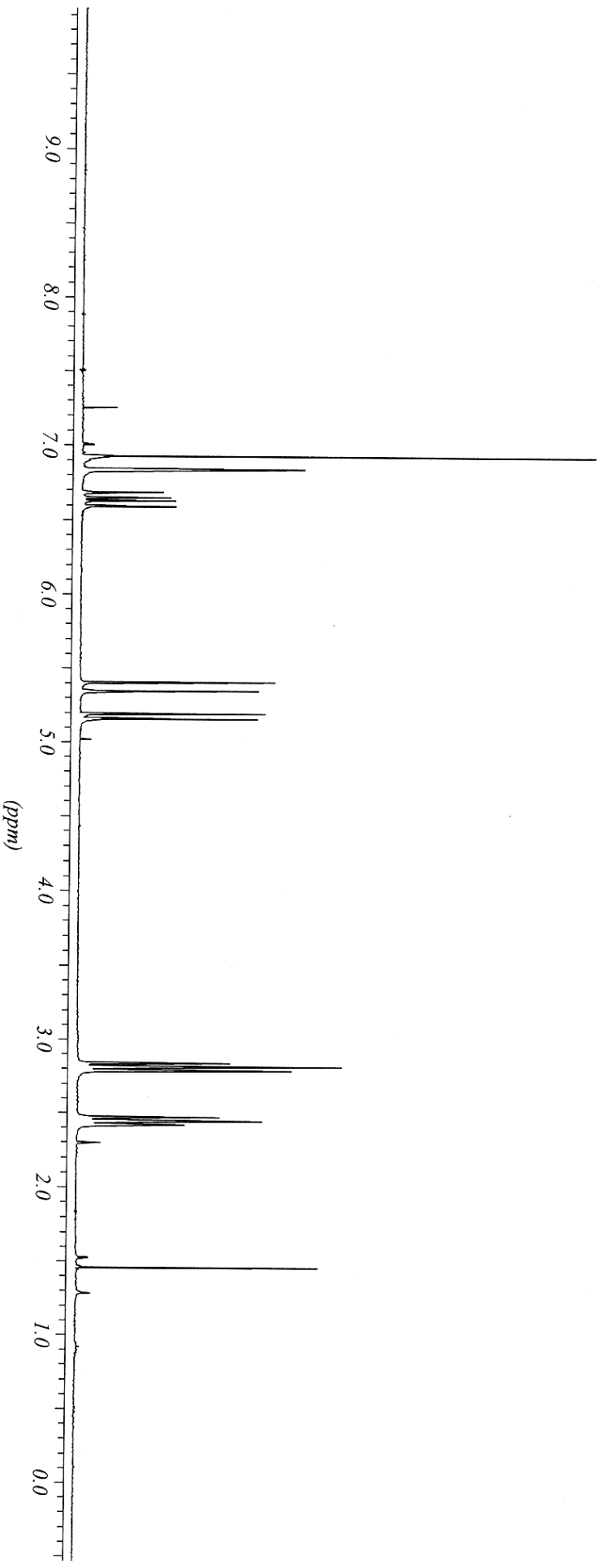

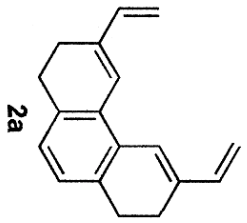

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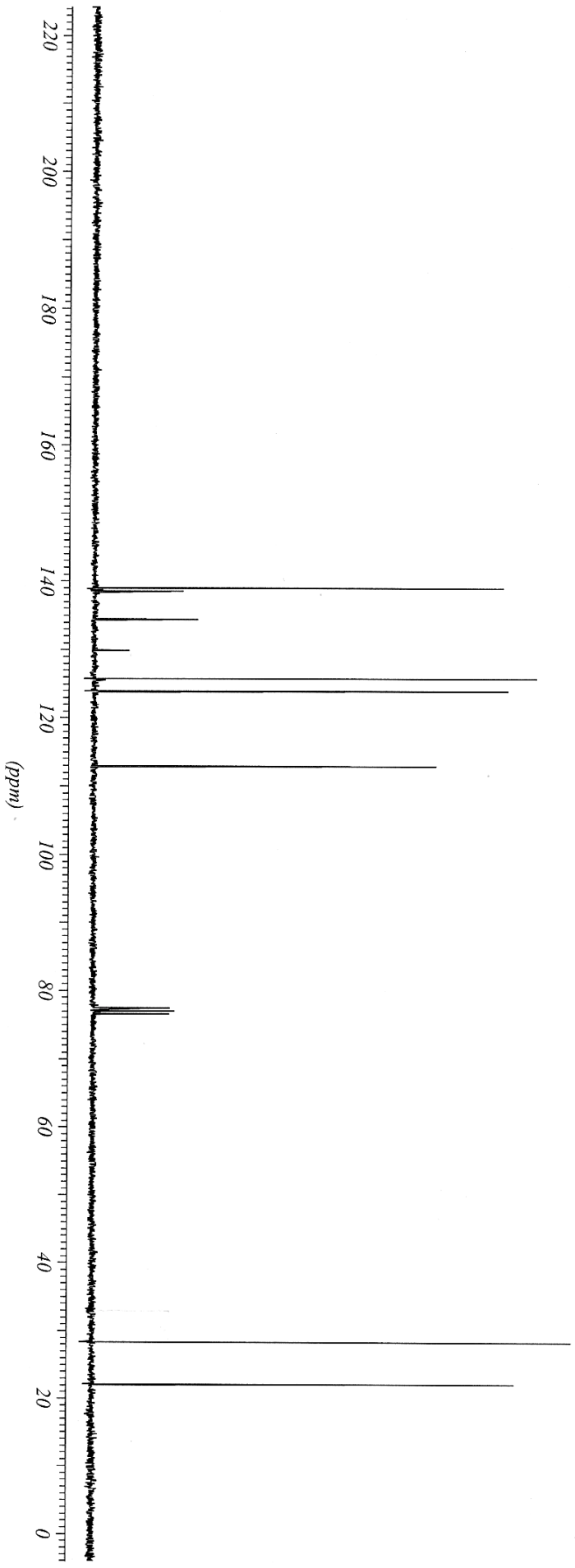

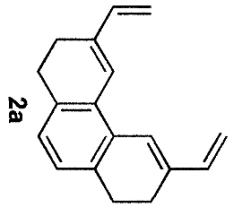

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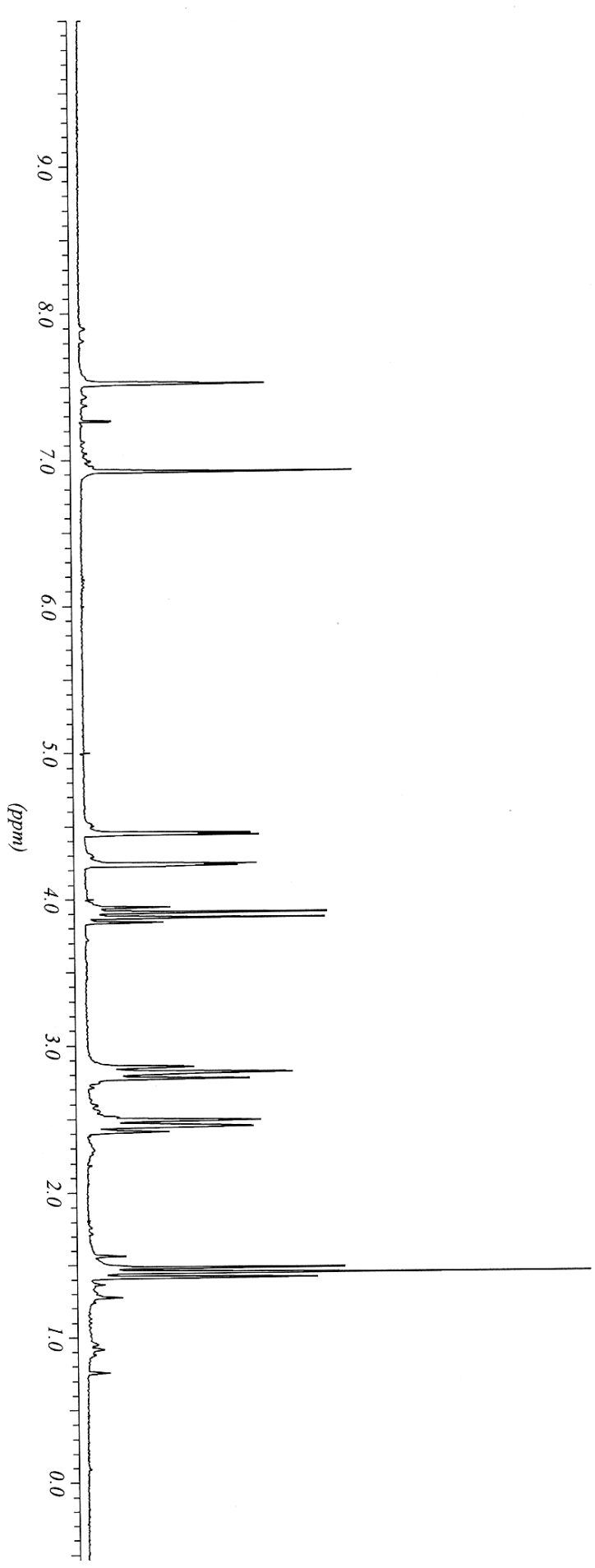

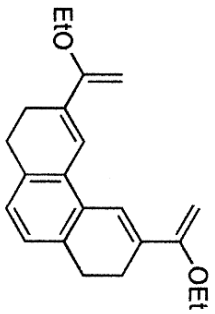

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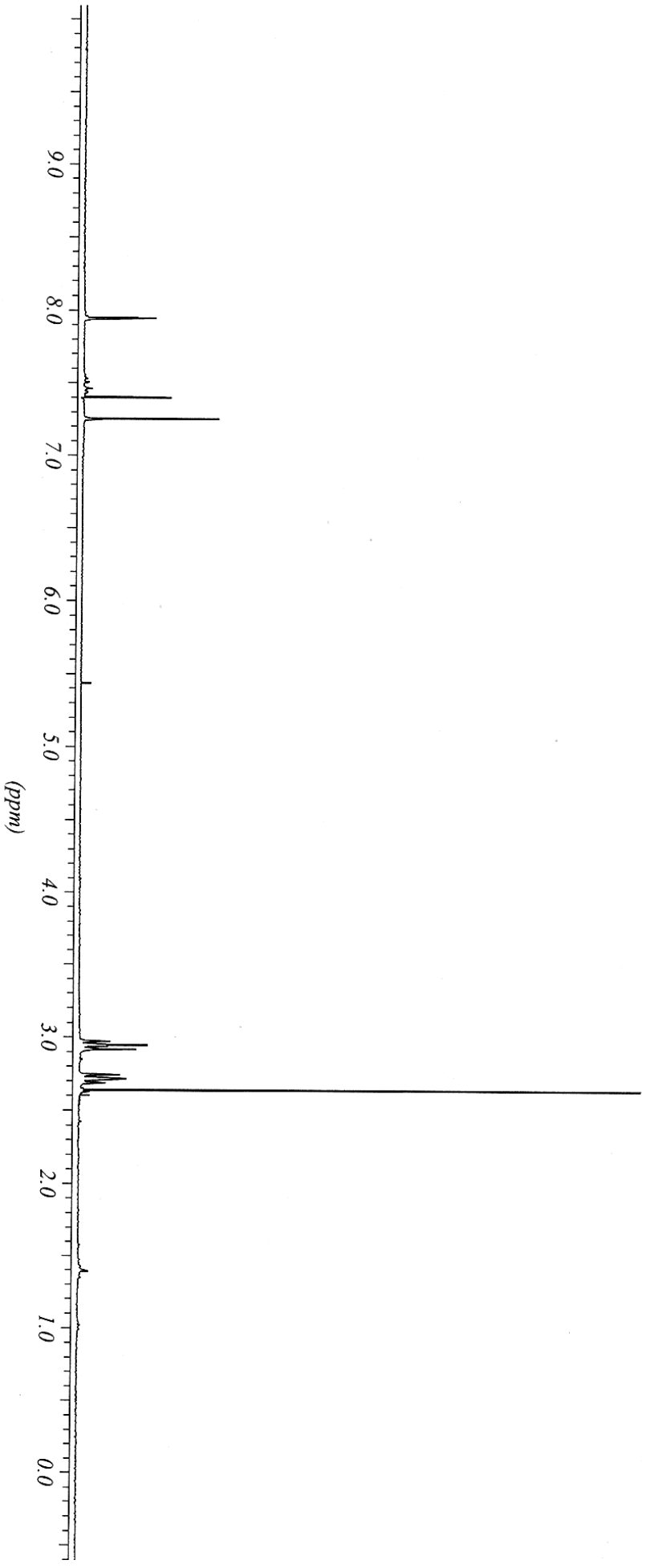

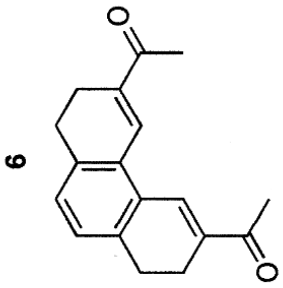

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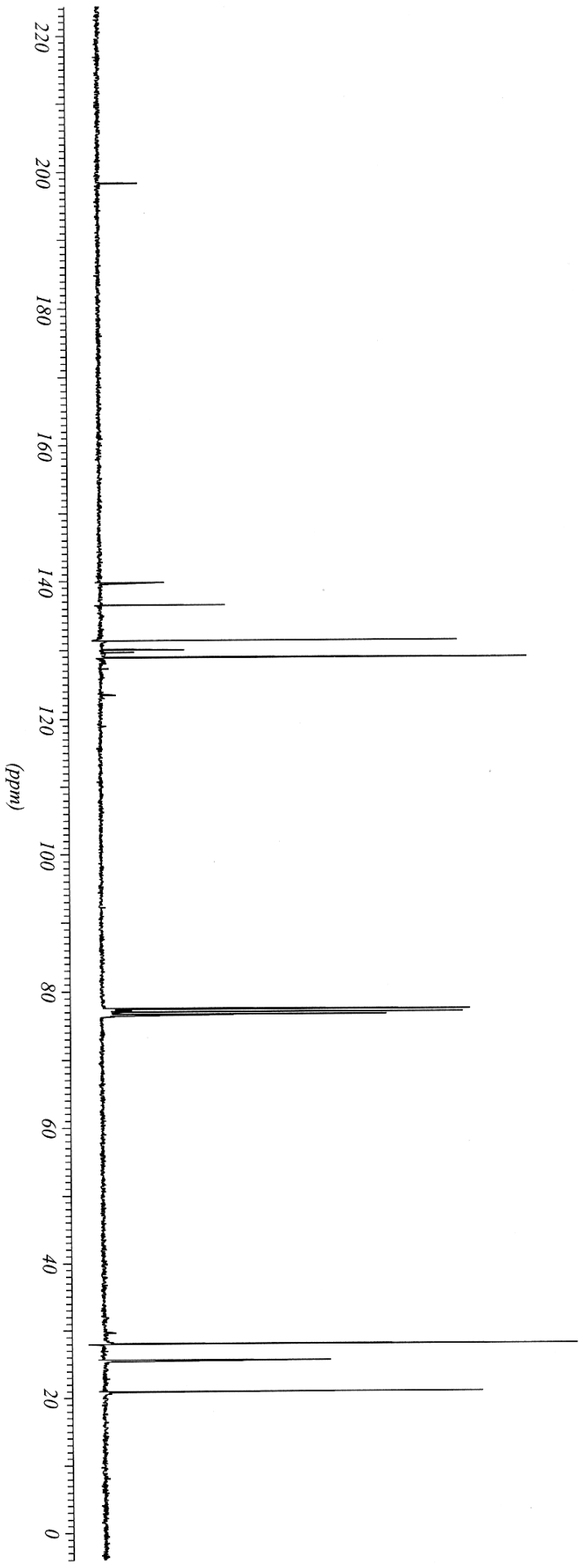

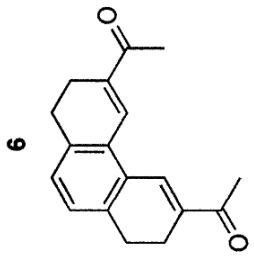

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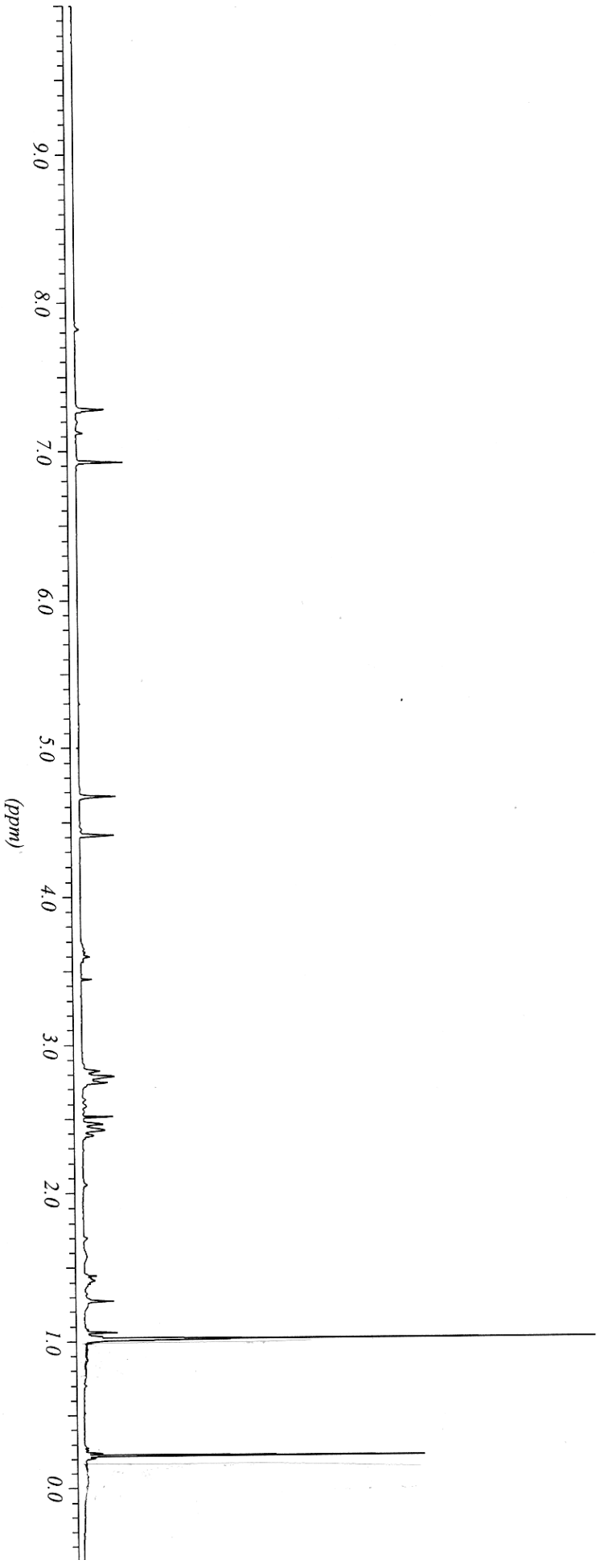

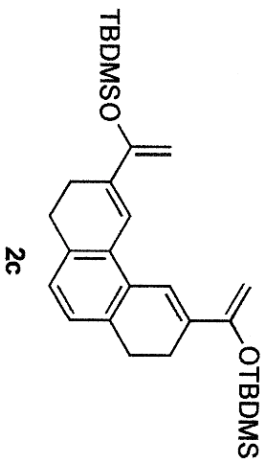

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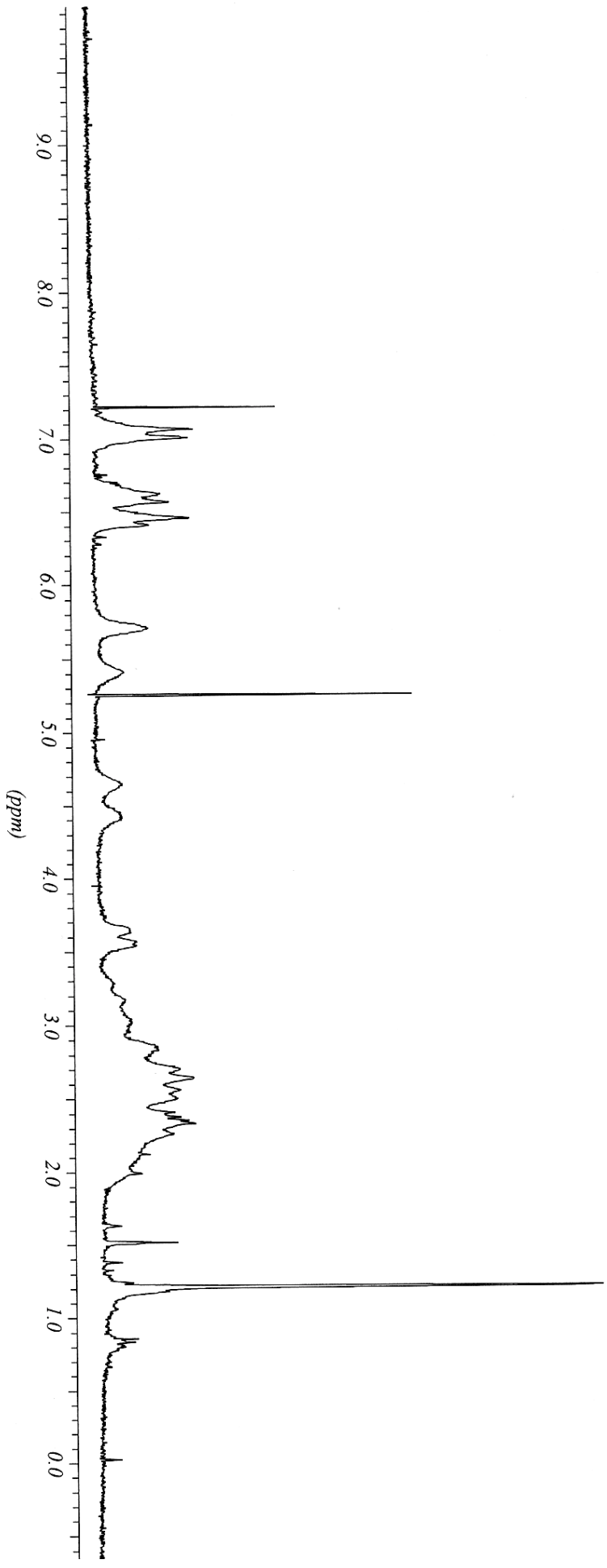

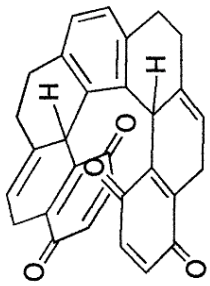

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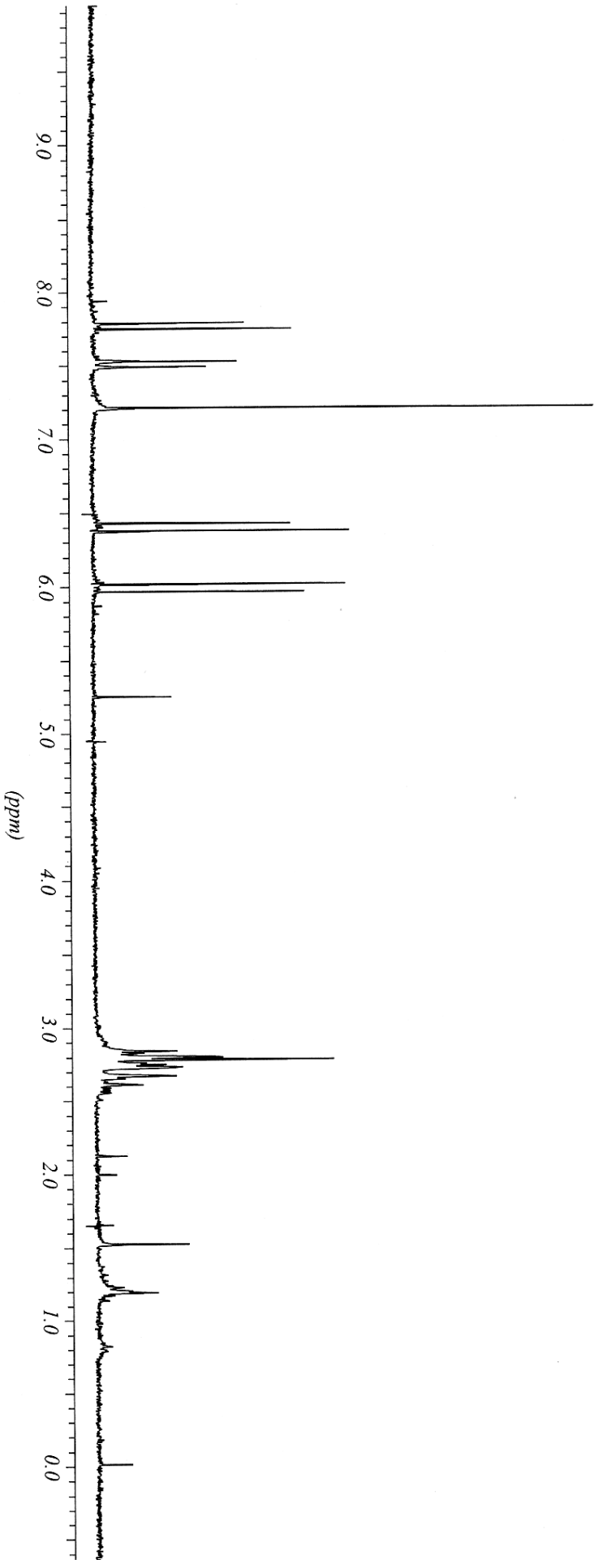

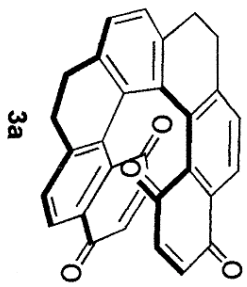

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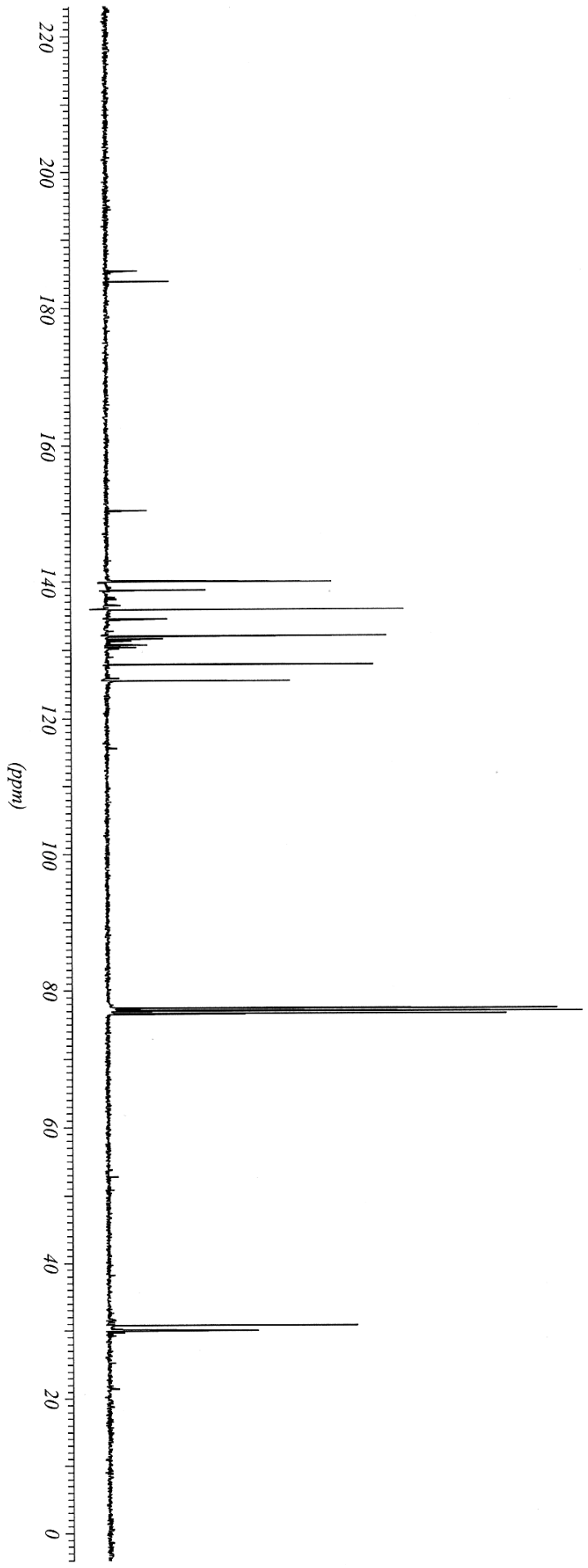

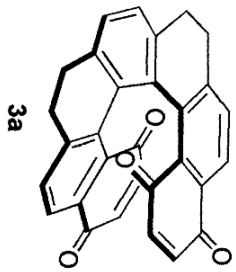

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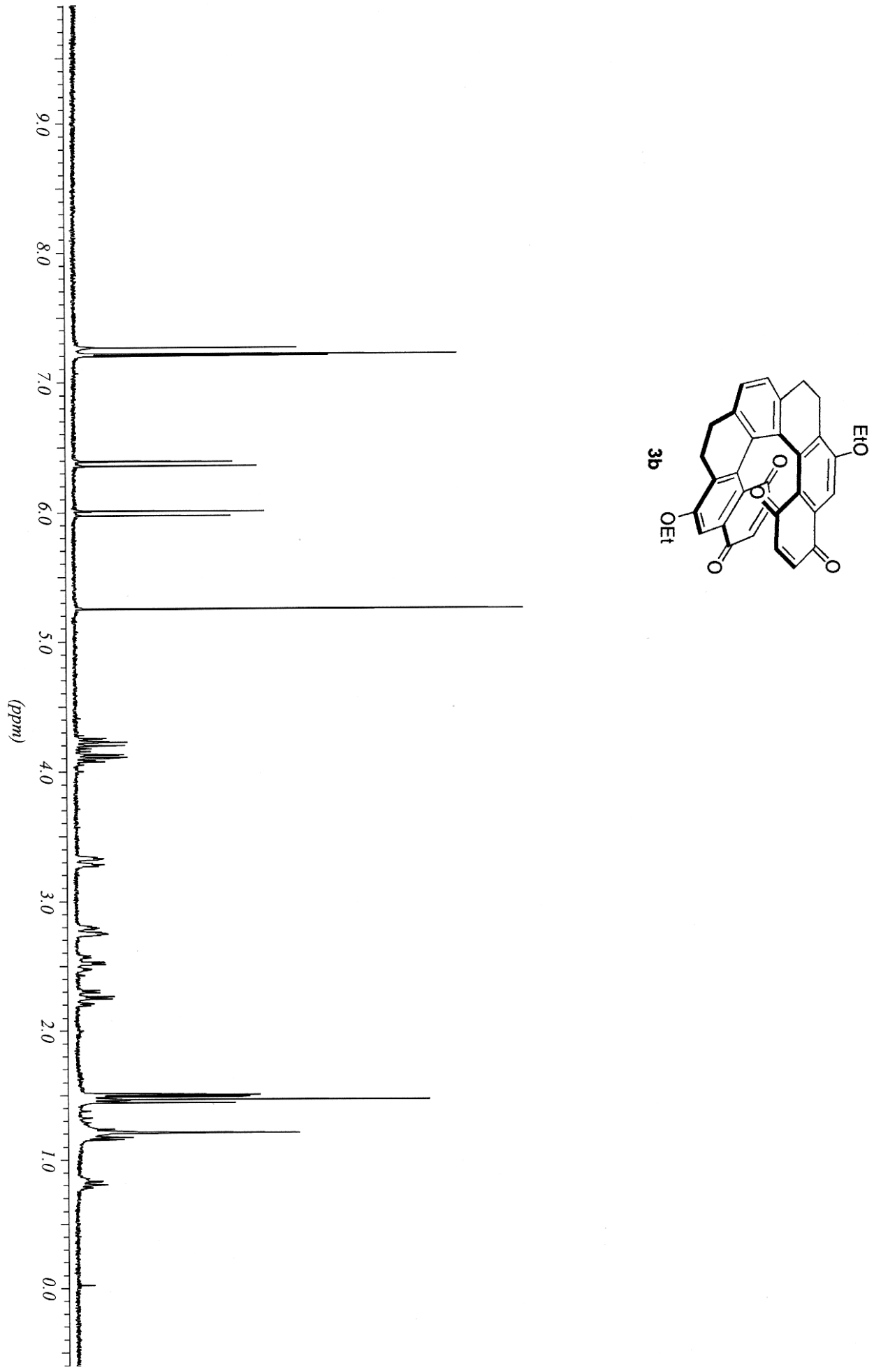
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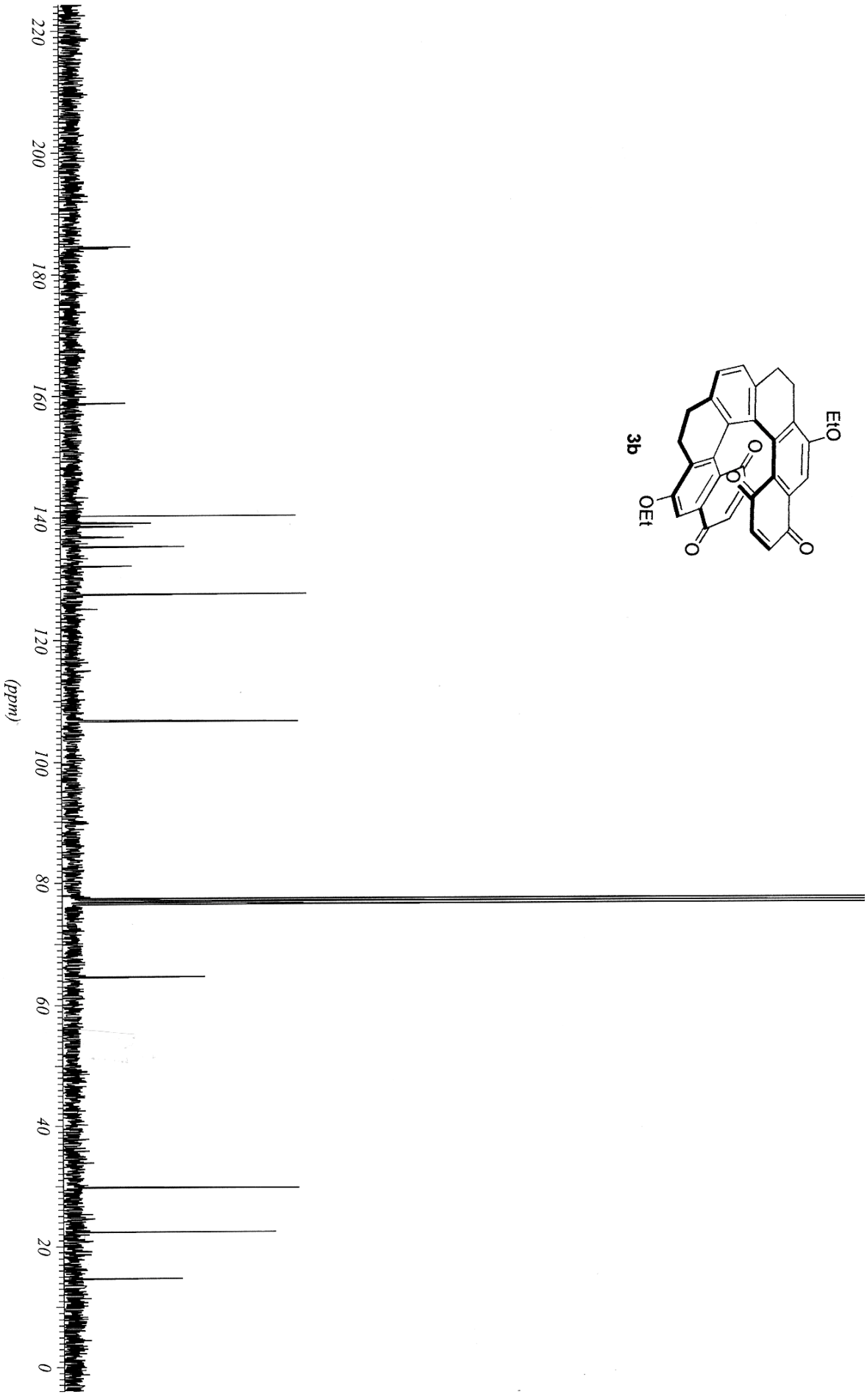
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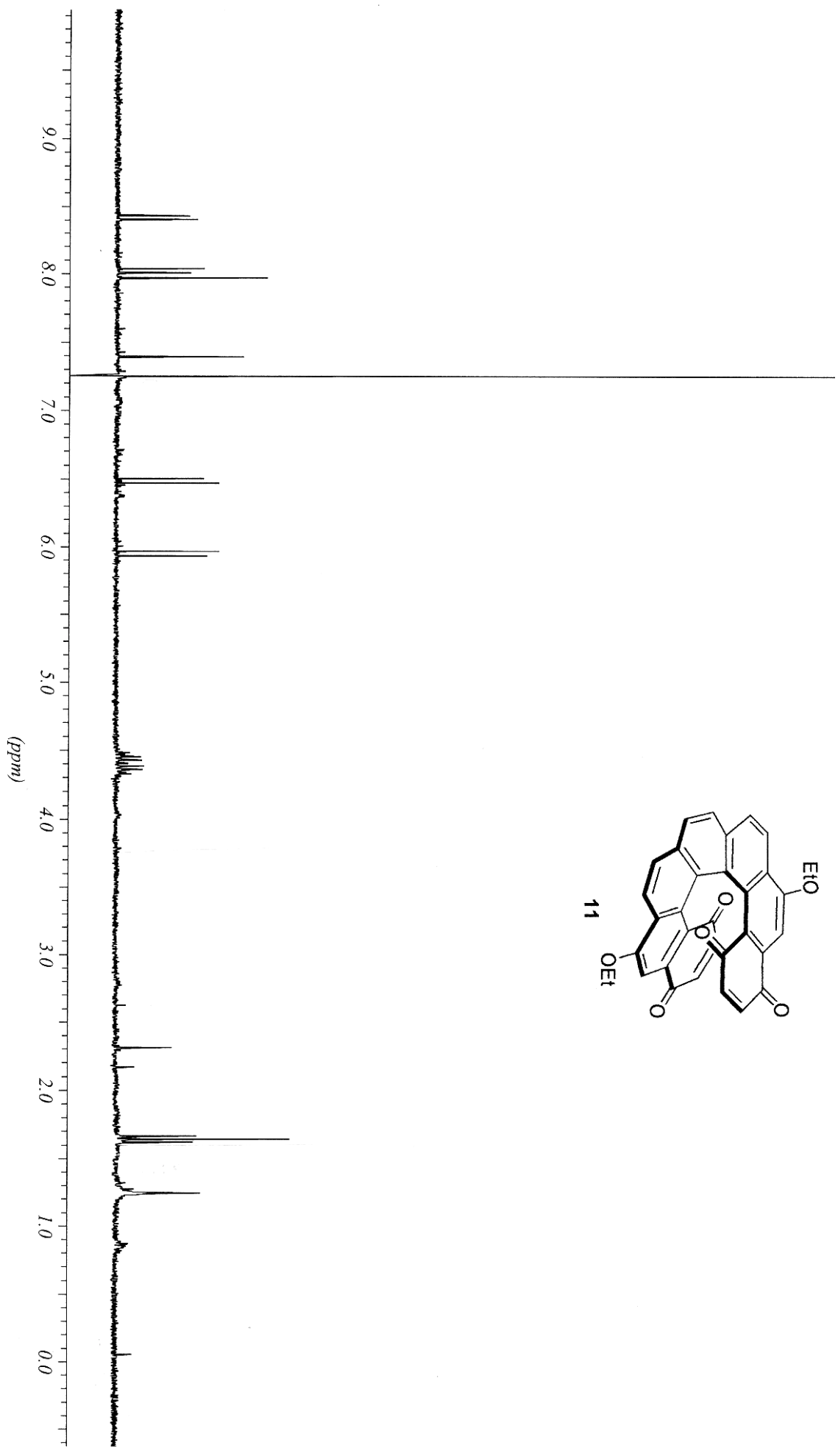

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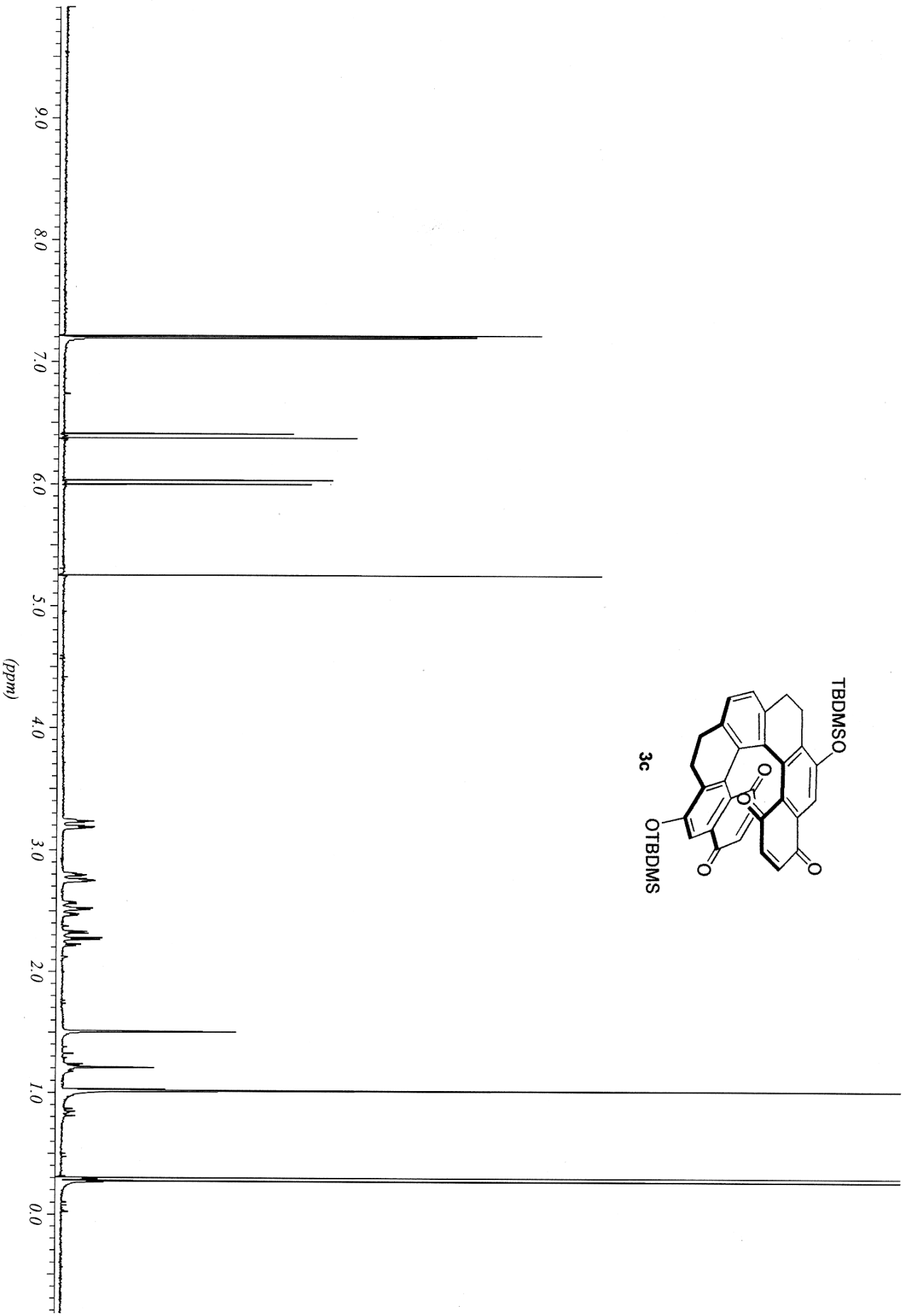
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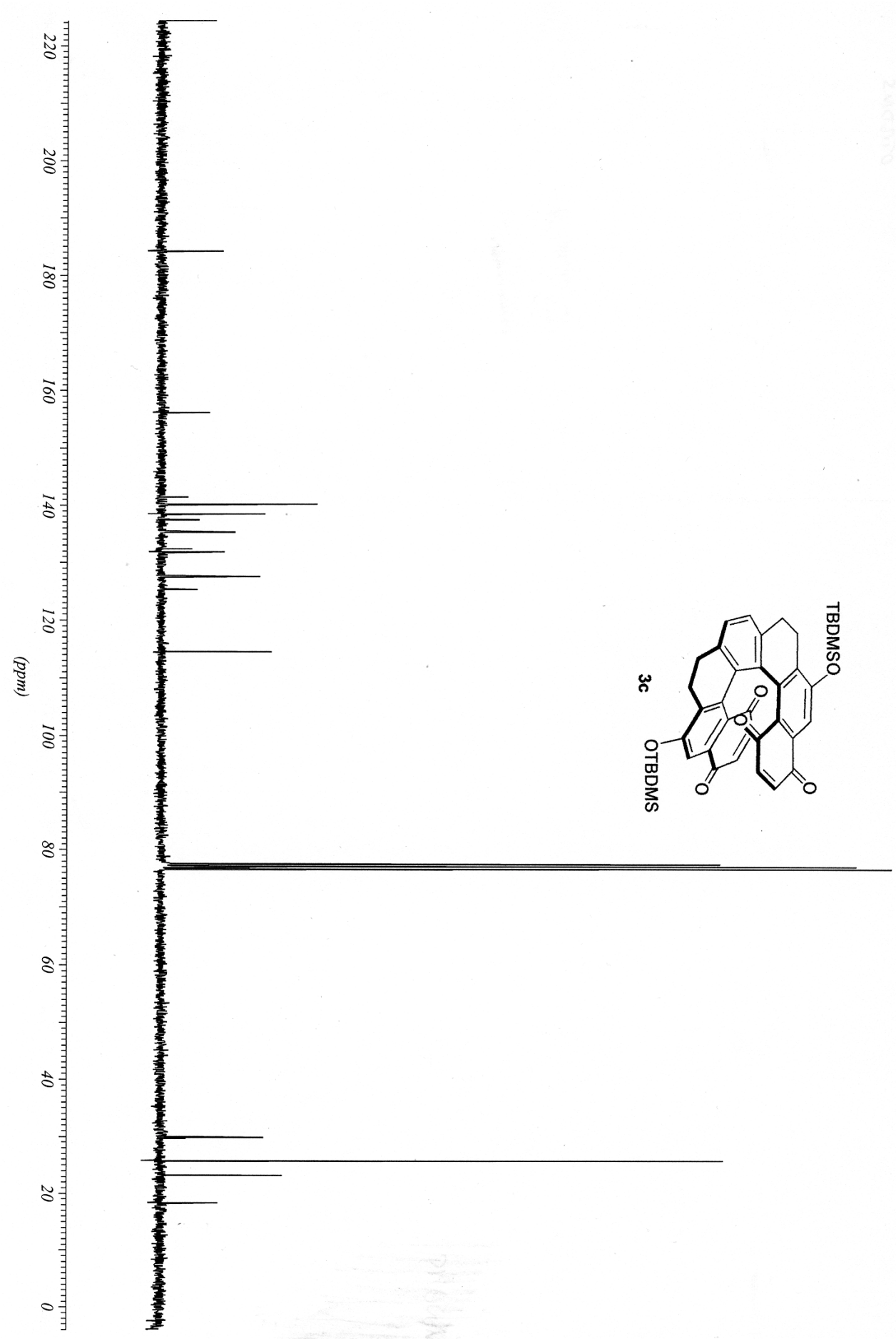
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