

## SUPPLEMENTARY MATERIAL

# Spiroketals via Oxidative Rearrangement of Enol Ethers

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Experimental procedures and spectral data for all new compounds, including copies of  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra. CIF files for **9** and **15**.

**General.** All moisture sensitive reactions were performed under an N<sub>2</sub> atmosphere and all glassware was flame dried under vacuum prior to use. THF and Et<sub>2</sub>O were dried by distillation over Na/benzophenone under a nitrogen atmosphere. Dry CH<sub>2</sub>Cl<sub>2</sub> and Et<sub>3</sub>N were obtained by distillation from CaH<sub>2</sub>. All reactions were monitored by TLC analysis until the starting material had been consumed. Unless otherwise stated, solvents or reagents were used as received without further purification. Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F-254 plates (particle size 0.040-0.055 mm, 230-400 mesh) and visualization was accomplished using UV light or by staining with basic KMnO<sub>4</sub> or anisaldehyde dye. NMR spectra were recorded at 300 MHz/75 MHz (<sup>1</sup>H/<sup>13</sup>C NMR) in CDCl<sub>3</sub> unless otherwise stated on either a Bruker AVANCE 300 MHz or a Bruker QM-300 MHz spectrometer at 23 °C. Chemical shifts (δ) are reported in parts per million and the residual solvent peak was used as an internal standard (CDCl<sub>3</sub>: δ 7.261/77.0, <sup>1</sup>H/<sup>13</sup>C NMR). Data are reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, s = sextet, m = multiplet, b = broad, app = apparent), integration, and coupling constant(s) (Hz). IR spectra were obtained on a Nicolet AVATAR 360 FT-IR E.S.P spectrometer. Mass spectra were obtained on a Micromass Autospec double focusing instrument. Melting points were determined using a Laboratory Devices Mel-Temp II and are uncorrected. Compounds **7**,<sup>1</sup> **10**,<sup>2</sup> and **12**<sup>3</sup> were prepared according to literature procedures. Cyclopentanone (**20**), 2,2-dimethylcyclopentanone, norcamphor and androsterone were purchased from Aldrich Chemical Co.

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<sup>1</sup> K. Matoba, N. Karibe, and T. Yamazaki, *Chem. Pharm. Bull.* 1982, **30**, 3906.

<sup>2</sup> (a) E. Wenkert, N. F. Golob, S. S. Sathe and R. A. J. Smith, *Synth. Commun.*, 1973, **3**, 205 (b) G. F. Hennion and F. P. Kupiecki, *J. Org. Chem.*, 1953, **18**, 1601.

<sup>3</sup> B.-M. Kwon and C. S. Foote, *J. Org. Chem.*, 1989, **54**, 3878.

**(1*R*\*,6*R*\*)-3-Methoxy-5,5-dimethyl-7-oxabicyclo[4.1.0]hept-3-en-2-one (8).** To a 40 °C solution of **7** (0.20 g, 1.3 mmol) in THF (30 mL) was added H<sub>2</sub>O<sub>2</sub> (10 mL, 30% v/v in H<sub>2</sub>O) and K<sub>2</sub>CO<sub>3</sub> (5 mL, 0.4 M in H<sub>2</sub>O). The reaction mixture was stirred for 6 h, diluted with EtOAc, washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. The residue was purified by chromatography on SiO<sub>2</sub> (4:1 hexanes/EtOAc) to afford **8** (0.11 g, 67%) as a colorless oil: IR (neat) 2965, 1694, 1627, 1205, 1158, cm<sup>-1</sup>; <sup>1</sup>H NMR δ 5.23 (d, *J* = 2.5 Hz, 1 H), 3.54 (s, 3 H), 3.50 (d, *J* = 3.8 Hz, 1 H), 3.35 (dd, *J* = 3.8, 2.5 Hz, 1 H), 1.33 (s, 3 H), 1.20 (s, 3 H); <sup>13</sup>C NMR δ 189.4, 146.8, 120.8, 61.2, 55.0, 54.8, 34.6, 28.3, 25.9; MS (EI) *m/z* (intensity) 168 ([M-H<sub>2</sub>O]<sup>+</sup>, 57), 153 (55), 125 (100); HRMS (EI) *m/z* calculated for C<sub>9</sub>H<sub>12</sub>O<sub>3</sub> [M-H<sub>2</sub>O] 168.0786, found 168.0784.

**(1*R*\*,3*S*\*,6*R*\*)-Methyl-2,2-dimethyl-5-oxo-4,7-dioxabicyclo[4.1.0]heptane-3-carboxylate (9).** **General Protocol A.** To a solution of **8** (35 mg, 0.21 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (2.0 mL) was added *m*-CPBA (0.15 g, 0.62 mmol, ~70 wt % *m*-CPBA) and Na<sub>2</sub>HPO<sub>4</sub> (89 mg, 0.62 mmol) and the reaction mixture was stirred for 12 h, treated with 2-methyl-2-butene (0.10 mL of a 2 M solution in THF), stirred for 2 h, diluted with CH<sub>2</sub>Cl<sub>2</sub> and washed with sat. NaHCO<sub>3</sub> (5x). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to afford **9** a colorless solid (42 mg, 80%, contaminated with 10% 3-chlorobenzoic acid). The material was further purified by chromatography on SiO<sub>2</sub> (4:1 hexanes/EtOAc) for analysis: IR (neat) 2966, 1752, 1465, 1250, 1209, 907 cm<sup>-1</sup>; NMR δ 4.81 (s, 1 H), 3.82 (s, 3 H), 3.64 (d, *J* = 4.0 Hz, 1 H), 3.32 (d, *J* = 3.9 Hz, 1 H), 1.37 (s, 3 H), 1.07 (s, 3 H); <sup>13</sup>C NMR δ 167.5, 165.5, 78.6, 61.1, 52.7, 49.8, 34.9, 22.7, 17.8; MS (EI) *m/z* (intensity) 141 ([M-CO<sub>2</sub>Me]<sup>+</sup>, 7), 84 (16); HRMS (EI) *m/z* calculated for C<sub>7</sub>H<sub>9</sub>O<sub>3</sub> [M-CO<sub>2</sub>Me] 141.0552, found 141.0550.

**Methyl tetrahydro-3,3-dimethyl-6-oxo-2H-pyran-2-carboxylate (11).** According to General Protocol A, a solution of **10** (0.14 g, 0.97 mmol), *m*-CPBA (0.67 g, 2.7 mmol, ~70 wt % *m*-CPBA) and Na<sub>2</sub>HPO<sub>4</sub> (0.39 g, 2.7 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) afforded, after 12 h, a light yellow solid (0.13 g, 75%, contaminated with 15% of 3-chlorobenzoic acid; the yield was corrected for this impurity, which could not be removed by base washes or chromatography): IR (neat) 2965, 1751, 1469, 1204, 1159, 1080 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 4.53 (d, *J* = 1.4 Hz, 1 H), 3.79 (s, 3 H), 2.67, 2.60 (AB of ABMX, *J*<sub>AB</sub> = 18.8, *J*<sub>AM</sub> = 7.8 Hz, *J*<sub>AX</sub> = 4.3 Hz, 2 H), 1.89-1.79 (m, 1 H), 1.60 (dddd, *J* = 13.6, 5.7, 4.3, 1.4 Hz, 1 H), 1.20 (s, 3 H), 1.03 (s, 3 H); <sup>13</sup>C NMR δ 169.5 (2C), 85.1, 52.3, 31.4, 31.0, 26.8, 25.3, 24.2; MS (EI) *m/z* (intensity) 171 ([M-CH<sub>3</sub>]<sup>+</sup>, 3), 156 (70), 139 (88), 127(100); HRMS (EI) *m/z* calculated for C<sub>9</sub>H<sub>14</sub>O<sub>4</sub> 186.0892, found 186.0895.

**Methyl tetrahydro-2-methyl-5-oxofuran-2-carboxylate (13).**<sup>4</sup> According to General Protocol A, a solution of **12** (0.11 g, 0.87 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5.0 mL), *m*-CPBA (0.64 g, 2.6 mmol, ~70 wt % *m*-CPBA) and Na<sub>2</sub>HPO<sub>4</sub> (0.37 g, 2.6 mmol) afforded, after 12 h, **13** (48 mg, 35%, corrected for the presence of ~10% of 3-chlorobenzoic acid, which could not be removed by base washes or chromatography) as a colorless solid: IR (neat) 2992, 2957, 1788, 1743, 1457, 1201, 1140 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 3.78 (s, 3 H), 2.73-2.48 (m, 3 H), 2.19-2.08 (m, 1 H), 1.65 (s, 3 H); <sup>13</sup>C NMR δ 175.8, 172.1, 83.7, 52.9, 32.9, 28.3, 23.7; MS (EI) *m/z* (intensity) 99 ([M-CO<sub>2</sub>Me]<sup>+</sup>, 48), 73 (100); HRMS (EI) *m/z* calculated for C<sub>5</sub>H<sub>7</sub>O<sub>2</sub> [M-CO<sub>2</sub>Me] 99.0446, found 99.0447.

**(1*R*\*,2*R*\*,6*R*\*)-3-Methoxy-2,5,5-trimethyl-7-oxabicyclo[4.1.0]hept-3-en-2-ol (14).** To a cooled (-78 °C) solution of **8** (28 mg, 0.17 mmol) in dry THF (4.0 mL) was added MeLi

<sup>4</sup> N. Chatani, M. Tobisu, T. Asaumi, Y. Fukumoto and S. Murai J. Am. Chem. Soc., 1999, **121**, 7160.

(0.19 mL, 0.30 mmol, 1.6 M in Et<sub>2</sub>O). After 30 min, the reaction mixture was quenched with H<sub>2</sub>O (1 mL) and extracted with Et<sub>2</sub>O (3 x 5 mL). The combined organic layers were washed with H<sub>2</sub>O, brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The residue was purified by chromatography on SiO<sub>2</sub> (3:1 hexanes/EtOAc) to afford **14** (28 mg, 91%) as a colorless oil: IR (neat) 3479, 2962, 1667, 1469, 1212, 1162, 1059 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 4.15 (d, *J* = 2.3 Hz, 1 H), 3.51 (s, 3 H), 3.32 (d, *J* = 4.1 Hz, 1 H), 3.06 (dd, *J* = 4.3, 2.1 Hz, 1 H), 1.42 (s, 3 H), 1.20 (s, 3 H), 1.09 (s, 3 H); <sup>13</sup>C NMR δ 152.4, 100.4, 69.2, 61.1, 60.2, 54.5, 33.5, 27.7, 27.1, 25.2; MS (EI) *m/z* (intensity) 184 ([M]<sup>+</sup>, 17), 169 (44), 137 (13); HRMS (EI) *m/z* calculated for C<sub>10</sub>H<sub>16</sub>O<sub>3</sub> 184.1099, found 184.1103.

**(1*R*\*,3*S*\*,5*S*\*,6*R*\*)-Methyl-5-hydroxy-2,2,5-trimethyl-4,7-**

**dioxabicyclo[4.1.0]heptane-3-carboxylate (15).** According to General Protocol A, enol ether **14** (24 mg, 0.13 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1.3 mL), Na<sub>2</sub>HPO<sub>4</sub> (55 mg, 0.39 mmol) and *m*-CPBA (96 mg of ~70% *m*-CPBA) furnished, after 18 h and purification on SiO<sub>2</sub> (1:1 hexanes/EtOAc), ester **15** (5.6 mg, 20%) as a white solid which was a single diastereomer as indicated by <sup>1</sup>H NMR: Mp 114.5-116.3 °C (hexanes/EtOAc); IR (KBr) 3466, 2973, 1737, 1214, 1086, 920 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 4.10 (s, 1 H), 3.75 (s, 3 H), 3.52 (s, 1 H), 3.33 (d, 1 H, *J* = 3.8 Hz), 3.10 (d, 1 H, *J* = 4.0 Hz), 1.64 (s, 3 H), 1.22 (s, 3 H), 1.00 (s, 3 H); <sup>13</sup>C NMR δ 170.0, 92.4, 71.7, 63.4, 57.7, 51.8, 33.7, 26.5, 22.3, 18.5; MS (EI) *m/z* (intensity) 198 ([M-H<sub>2</sub>O]<sup>+</sup>, 49), 156 (32), 139 (76), 114 (77); HRMS (EI) *m/z* calculated for C<sub>10</sub>H<sub>14</sub>O<sub>4</sub> [M-H<sub>2</sub>O] 198.0892, found 198.0891.

**6-Methoxy-1-oxaspiro[4.5]dec-6-ene (22).** **General Protocol B.** A solution of ketone **21**<sup>5</sup> (155 mg, 1.01 mmol) in THF (3 mL) was added dropwise to a solution of KHMDS

<sup>5</sup> L. A. Paquette, J. T. Negri, and R. D. Rogers, *J. Org. Chem.*, 1992, **57**, 3947.

(241 mg, 1.21 mmol) in THF (7 mL) at -78 °C. After 10 min, DMF (2.5 mL) was added. After 10 min, dimethylsulfate (254 mg, 2.01 mmol) was added and the reaction mixture was warmed to ambient temperature over 4 h. Subsequently, sat. aq. NaHCO<sub>3</sub> (5 mL) was added and the aqueous layer was extracted with Et<sub>2</sub>O (4 x 10 mL). The combined organic layers were washed with H<sub>2</sub>O, brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, concentrated and purified on SiO<sub>2</sub> (85:15 pentane/Et<sub>2</sub>O) to furnish enol ether **22** (155 mg, 0.923 mmol, 89%) as a volatile, colorless oil: IR (neat) 2948, 2875, 1717, 1601, 1441, 1367, 1224, 1060, 926 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 4.72 (dd, 1 H, *J* = 3.9, 3.9 Hz), 3.97-3.80 (m, 2 H), 3.51 (s, 3 H), 2.24-1.51 (m, 10 H); <sup>13</sup>C NMR δ 156.9, 96.4, 81.2, 68.6, 54.2, 37.2, 35.1, 26.9, 23.9, 20.5; MS (EI) *m/z* (intensity) 168 ([M]<sup>+</sup>, 43), 140 (40), 137 (37), 123 (52); HRMS (EI) *m/z* calculated for C<sub>10</sub>H<sub>16</sub>O<sub>2</sub> 168.1150, found 168.1151.

**Methyl 1,6-dioxaspiro[4.5]decane-7-carboxylate (23).** According to General Protocol A, enol ether **22** (100 mg, 0.595 mmol), Na<sub>2</sub>HPO<sub>4</sub> (1.79 mmol, 246 mg) and *m*-CPBA (1.79 mmol, 411 mg of ~70% *m*-CPBA) in CH<sub>2</sub>Cl<sub>2</sub> (6 mL) furnished, after 18 h and purification on SiO<sub>2</sub> (4:1 pentane/Et<sub>2</sub>O), spiroketal ester **23** (62 mg, 0.31 mmol, 52%) as a colorless oil and a single diastereomer as indicated by <sup>1</sup>H NMR: IR (neat) 2951, 2882, 1760, 1738, 1456, 1439, 1201, 1011, 857 cm<sup>-1</sup>; <sup>1</sup>H NMR (CD<sub>2</sub>Cl<sub>2</sub>) δ 4.38 (dd, 1 H, *J* = 12.1, 2.4 Hz), 3.89-3.83 (m, 2 H), 3.68 (s, 3 H), 2.08-1.96 (m, 2 H), 1.92-1.60 (m, 8 H); <sup>13</sup>C NMR (CD<sub>2</sub>Cl<sub>2</sub>) δ 172.8, 106.9, 70.6, 67.7, 52.0, 38.1, 33.0, 28.5, 24.1, 20.5; MS (EI) *m/z* (rel intensity) 200 ([M]<sup>+</sup>, 53), 184 (6), 172 (10), 141 (100), 114 (14); HRMS (EI) *m/z* calculated for C<sub>10</sub>H<sub>16</sub>O<sub>4</sub> 200.1049, found 200.1053.

**6-Methoxy-10,10-dimethyl-1-oxaspiro[4.5]dec-6-ene (24).** General Protocol C. A solution of 2,3-dihydrofuran in THF (90 mL) was treated with *t*-BuLi (10.7 mmol, 6.3

mL of a 1.7 M solution in pentane) at -78 °C. After 30 min, the reaction mixture was warmed to 0 °C for 30 min, re-cooled to -78 °C and treated with 2,2-dimethyl cyclopentanone. The reaction mixture was warmed to ambient temperature and quenched after 6 h with aq. NaHCO<sub>3</sub>. The aqueous layer was extracted with Et<sub>2</sub>O (3 x 10 mL) and the combined organic layers washed with H<sub>2</sub>O, brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, concentrated and the crude tertiary alcohol was used directly in the next step. A solution of the crude tertiary alcohol in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was treated with Dowex-50X resin (4.71 g, 0.528 g/mmol) and stirred at ambient temperature for 24 h. The mixture was filtered, concentrated and the residue purified by chromatography on SiO<sub>2</sub> (4:1 hexanes/EtOAc) to furnish the  $\alpha$ -spiroether ketone (1.32 g, 81% over two steps) as a colorless oil: IR (neat) 2965, 2872, 1717, 1462, 1056 cm<sup>-1</sup>; <sup>1</sup>H NMR  $\delta$  3.88-3.79 (m, 1 H), 3.73-3.66 (m, 1 H), 2.82-2.72 (m, 1 H), 2.29-2.19 (m, 2 H), 1.93-1.66 (m, 6 H), 1.43-1.35 (m, 1 H), 0.96 (s, 3 H), 0.83 (s, 3 H); <sup>13</sup>C NMR  $\delta$  212.1, 92.8, 68.7, 40.8, 37.3, 36.0, 26.3, 25.9, 23.1, 22.3, 21.9; MS (EI) *m/z* (intensity) 182 ([M]<sup>+</sup>, 30), 154 (8), 111 (63); HRMS (EI) *m/z* calculated for C<sub>11</sub>H<sub>18</sub>O<sub>2</sub> 182.1307, found 182.1299.

According to General Protocol B, the  $\alpha$ -spiroether ketone (180 mg, 0.988 mmol), KHMDS (236 mg, 1.19 mmol), and Me<sub>2</sub>SO<sub>4</sub> (249 mg, 1.98 mmol) furnished **24** (163 mg, 84%) as a colorless oil: IR (neat) 2926, 1662, 1464, 1215, 1122, 1054 cm<sup>-1</sup>; <sup>1</sup>H NMR  $\delta$  4.56 (dd, 1 H, *J* = 3.8 Hz), 3.99-3.92 (m, 1 H), 3.78-3.71 (m, 1 H), 3.47 (s, 3 H), 2.08-1.63 (m, 10 H), 1.29 (ddd, 1 H, *J* = 12.9, 5.4, 5.4 Hz), 0.94 (s, 3 H), 0.86 (s, 3 H); <sup>13</sup>C NMR  $\delta$  157.6, 93.6, 86.5, 69.8, 54.3, 37.6, 33.6, 30.0, 28.1, 23.1, 22.6, 20.6; MS (EI) *m/z* (intensity) 196 ([M]<sup>+</sup>, 14), 182 (7), 164 (27), 149 (43), 140 (100); HRMS *m/z* calculated for C<sub>12</sub>H<sub>20</sub>O<sub>2</sub> 196.1463, found 196.1458.

**(5S\*,7S\*)-Methyl 10,10-dimethyl-1,6-dioxaspiro[4.5]decane-7-carboxylate (25).**

According to General Protocol A, enol ether **24** (57 mg, 0.29 mmol), *m*-CPBA (200 mg of ~70% *m*-CPBA, 0.871 mmol) and Na<sub>2</sub>HPO<sub>4</sub> (123 mg, 0.871 mmol) furnished, after 18 h and purification by chromatography on SiO<sub>2</sub> (6:1 pentanes/Et<sub>2</sub>O), spiroketal **25** (32 mg, 48%) as a 2:1 mixture of diastereomers as indicated by NMR analysis of the crude reaction product. The diastereomers are partially separable, and after chromatography, the major isomer was enriched to a 9:1 ratio: Major diastereomer: IR (neat) 2954, 2879, 1760, 1740, 1439, 1205, 1064 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 4.40 (dd, 1 H, *J* = 11.1, 3.6 Hz), 3.94-3.86 (m, 2 H), 3.73 (s, 3 H), 2.08-2.00 (m, 1 H), 1.96-1.62 (m, 6 H), 1.38-1.33 (m, 1 H), 1.07 (s, 3 H), 0.90 (s, 3 H); <sup>13</sup>C NMR δ 172.9, 111.6, 69.3, 67.9, 51.9, 34.7, 34.1, 32.1, 25.4, 25.1, 23.9, 23.3; MS (EI) *m/z* (intensity) 228 ([M]<sup>+</sup>, 10), 213 (8), 198 (11), 169 (57), 142 (57); HRMS (EI) *m/z* calculated for C<sub>10</sub>H<sub>17</sub>O<sub>2</sub> [M-CO<sub>2</sub>Me] 169.1229, found 169.1229. Characteristic data for minor diastereomer: <sup>1</sup>H NMR δ 4.17 (dd, 1 H, *J* = 5.1, 2.1 Hz), 3.74 (s, 3 H); <sup>13</sup>C NMR δ 173.4, 112.1, 70.0, 68.7, 51.7, 35.1, 32.2, 31.0, 25.0, 24.8, 23.4, 21.4.

**(1S\*)-3-Methoxy-4',5'-dihydro-3'H-spiro[bicyclo[3.2.1]oct[3]ene-2,2'-furan] (26).**

According to General Protocol B, bicyclic α-spiroether ketone<sup>6</sup> (430 mg, 2.39 mmol), KHMDS (571 mg, 2.86 mmol) and Me<sub>2</sub>SO<sub>4</sub> (451 mg, 3.58 mmol) furnished, after chromatography on SiO<sub>2</sub> (3:1 hexanes/EtOAc), enol ether **26** (308 mg, 67%) as a colorless oil: IR (neat) 2941, 2864, 1647, 1370, 1214, 1053 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 4.80 (d, 1 H, *J* = 7.1 Hz), 3.92 (ddd, 1 H, *J* = 7.8, 7.8, 4.8 Hz), 3.72 (ddd, 1 H, *J* = 7.8, 7.8, 6.6 Hz), 3.41 (s, 3 H), 2.52-2.41 (m, 1 H), 2.22-1.34 (m, 10 H), 1.26-1.19 (m, 1 H); <sup>13</sup>C NMR δ

<sup>6</sup> L. A. Paquette, J. F. P. Andrews, C. Vanucci, D. E. Lawhorn, J. T. Negri and R. D. Rogers, *J. Org. Chem.*, 1992, **57**, 3956.



155.8, 101.9, 86.7, 68.3, 54.1, 44.9, 34.5, 34.0, 32.1, 31.8, 27.4, 23.7; MS (EI)  $m/z$  (intensity) 194 ( $[M]^+$ , 24), 162 (56), 153 (36), 135 (17); HRMS (EI)  $m/z$  calculated for  $C_{12}H_{18}O_2$  194.1307, found 194.1311.

**(1S\*,4S\*)-Methyl dihydro-3'H-3-oxaspiro[bicyclo[3.2.1]octane-2,2'-furan]-4-carboxylate (27).** According to General Protocol A, **26** (303 mg, 1.56 mmol), *m*-CPBA (1.08 g of ~70% *m*-CPBA, 4.68 mmol), and  $Na_2HPO_4$  (664 mg, 4.68 mmol) furnished, after 18 h and purification by chromatography on  $SiO_2$  (3:1 hexanes/EtOAc), spiroketal **27** (187 mg, 53%) as a single diastereomer as indicated by NMR analysis: IR (neat) 2950, 2872, 1759, 1733, 1201, 1043  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  4.37 (s, 1 H), 3.93-3.85 (m, 2 H), 3.72 (s, 3 H), 2.41 (app t, 1 H,  $J = 5.1$  Hz), 2.27 (app d, 1 H,  $J = 11.1$  Hz), 2.16-1.99 (m, 3 H), 1.88-1.77 (m, 1 H), 1.73-1.62 (m, 3 H), 1.59-1.42 (m, 3 H);  $^{13}C$  NMR  $\delta$  171.9, 110.1, 75.6, 67.5, 51.8, 42.8, 37.8, 36.3, 33.1, 26.3, 24.1, 23.4; MS (EI)  $m/z$  (intensity) 226 ( $[M]^+$ , 28), 138 (21), 108 (37); HRMS (EI)  $m/z$  calculated for  $C_{12}H_{18}O_4$  226.1205, found 226.1203.

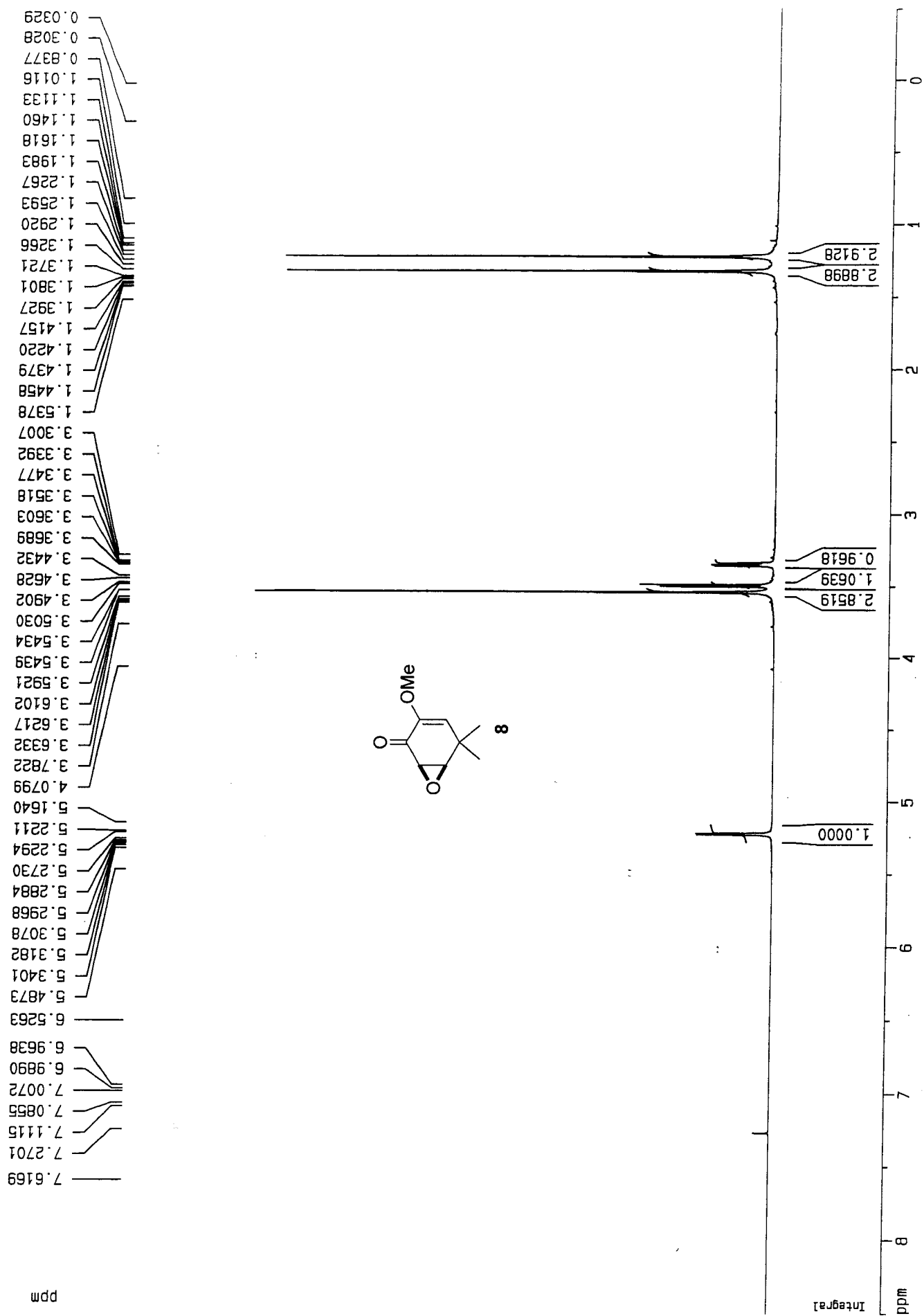
**(1S,4aS,4bR,6aS,8R,10aS,10bS,12aS)-2,8-Dimethoxy-10a,12a-dimethyl-4a,4b,4',5,5',6,6a,7,8,9,10,10a,10b,11,12,12a-hexadecahydro-3'H,4H-spiro[chrysene-1,2'-furan] (28).** According to General Protocol C, androsterone (1.0 g, 3.44 mmol), 2,3-dihydrofuran (507 mg, 7.23 mmol), *t*-BuLi (4.5 mL of a 1.7 M solution in pentanes, 7.57 mmol), and Dowex 50X (1.82 g, 0.528 g/mmol) furnished, after chromatography on  $SiO_2$  (6:1 hexanes/EtOAc), the  $\alpha$ -spiroether ketone (754 mg, 61%) as a white solid and as a single diastereomer as determined by NMR analysis: Mp 196.8-198.5 °C (hexanes/EtOAc); IR (KBr) 3399, 2930, 2865, 1716, 1452, 1052, 732  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  3.99 (br s, 1 H), 3.72 (ddd, 1 H,  $J = 7.7, 7.0, 7.0$  Hz), 3.57 (ddd, 1 H,  $J = 7.9, 6.8, 6.8$  Hz),

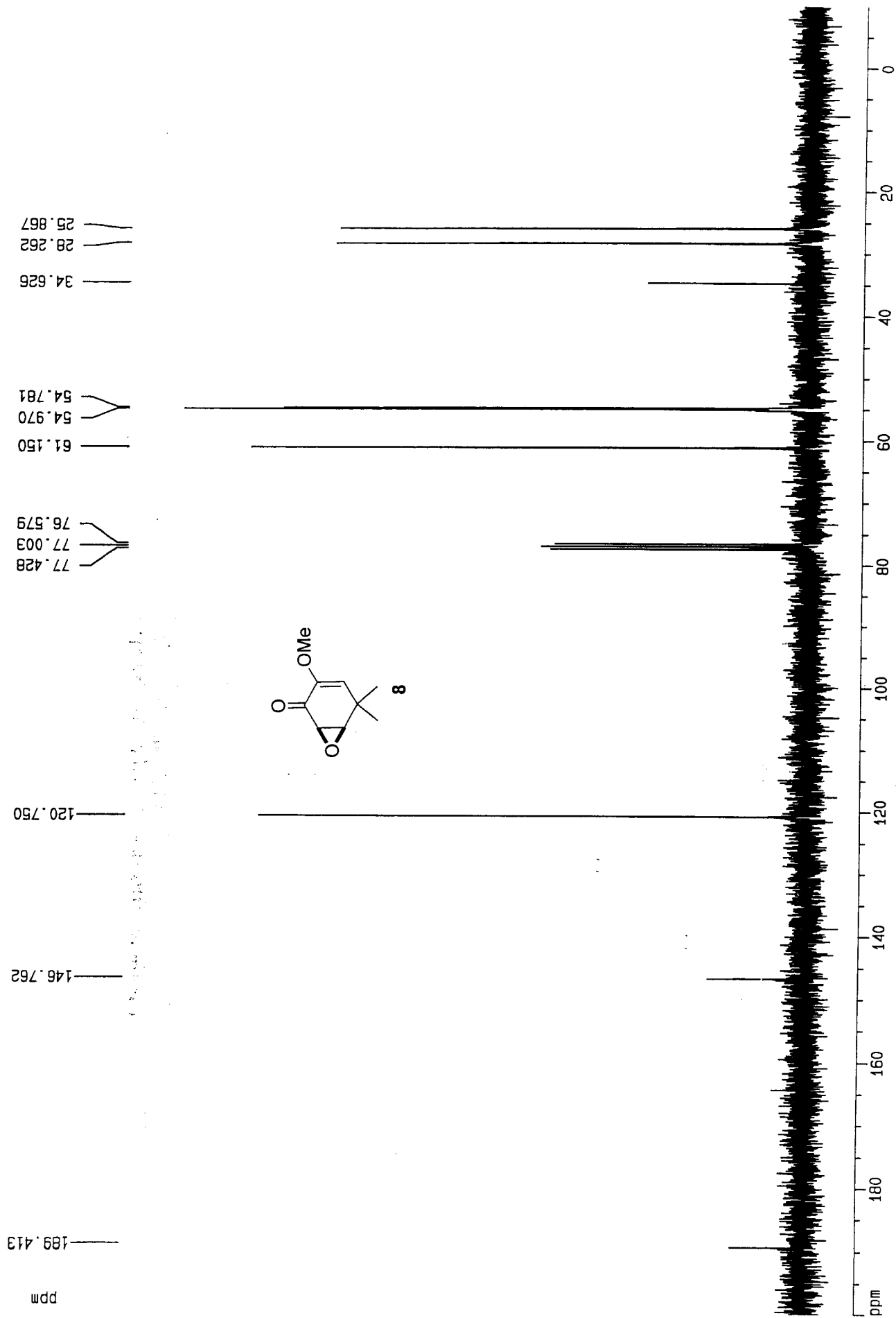
2.86 (ddd, 1 H,  $J = 13.5, 13.5, 7.2$  Hz), 2.38 (ddd, 1 H,  $J = 6.5, 6.1, 6.1$  Hz), 2.17 (dd, 1 H,  $J = 5.6, 2.8$  Hz), 2.04-1.99 (m, 1 H), 1.83-1.69 (m, 5 H), 1.63-1.08 (m, 15 H), 0.94-0.83 (m, 2 H), 0.69 (s, 3 H), 0.61 (s, 3 H);  $^{13}\text{C}$  NMR  $\delta$  211.3, 92.7, 68.5, 66.3, 53.3, 44.2, 43.3, 38.6, 37.0, 36.2, 36.0, 32.0, 31.3, 31.2 (2 C), 29.1, 28.7, 26.3, 25.7, 23.1, 20.1, 14.7, 11.0; MS (ESI)  $m/z$  (intensity) 383 ( $[\text{M}+\text{Na}]^+$ , 38), 361 (86), 272 (15); HRMS (ESI)  $m/z$  calculated for  $\text{C}_{23}\text{H}_{36}\text{O}_3\text{Na}$  ( $\text{M}+\text{Na}$ ) 383.2562, found 383.2545.

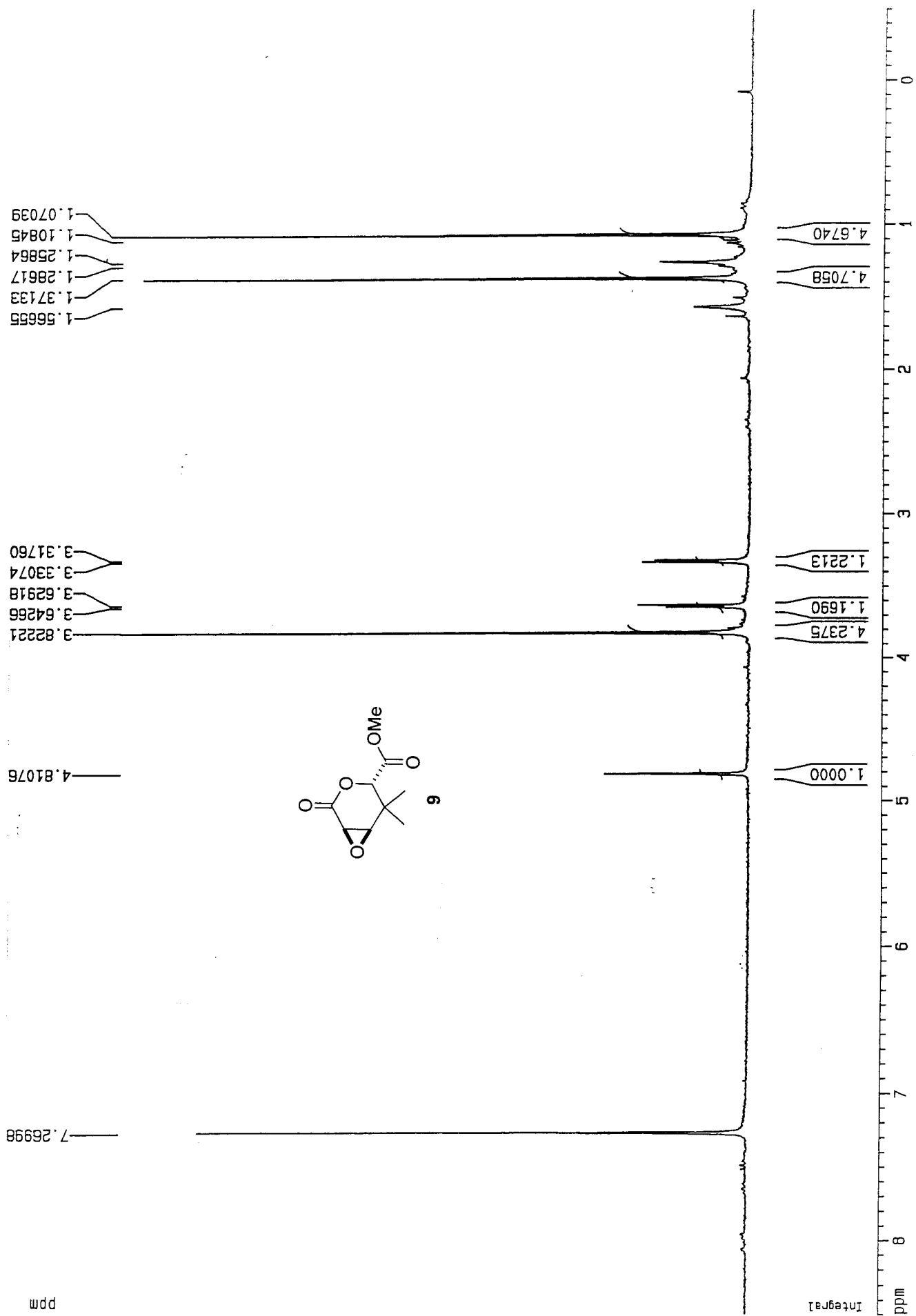
According to General Protocol B, the  $\alpha$ -spiroether ketone (754 mg, 2.09 mmol), KHMDS (918 mg, 4.60 mmol) and  $\text{Me}_2\text{SO}_4$  (1.05 g, 8.37 mmol) furnished, after chromatography on  $\text{SiO}_2$  (6:1 hexanes/EtOAc), enol ether **28** (443 mg, 59%) as a white solid: Mp 157.1-158.5 °C (hexanes/EtOAc); IR (KBr) 2934, 1671, 1447, 1362, 1212, 1092  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  4.60 (dd, 1 H,  $J = 5.0, 1.0$  Hz), 3.96 (ddd, 1 H,  $J = 7.7, 7.7, 2.6$  Hz), 3.64-3.57 (m, 1 H), 3.46 (s, 3 H), 3.41 (br s, 1 H), 3.27 (s, 3 H), 2.31-2.18 (m, 1 H), 2.13-1.93 (m, 2 H), 1.93-1.70 (m, 4 H), 1.66-1.32 (m, 10 H), 1.26-1.03 (m, 5 H), 0.97-0.81 (m, 2 H), 0.77 (s, 3 H), 0.74 (s, 3 H);  $^{13}\text{C}$  NMR  $\delta$  156.4, 94.1, 87.5, 75.4, 69.5, 55.5, 54.1, 52.6, 41.3, 40.8, 38.7, 36.8, 35.8, 32.6, 32.2, 30.7, 30.6, 28.6, 28.3, 27.2, 25.5, 25.0, 20.0, 15.1, 11.2; MS (EI)  $m/z$  (intensity) 389 ( $[\text{M}+\text{H}]^+$ , 12), 388 (50), 374 (11), 357 (10), 154 (66), 141 (100); HRMS (EI)  $m/z$  calculated for  $\text{C}_{24}\text{H}_{37}\text{O}_2$  [ $\text{M}-\text{OCH}_3$ ] 357.2794, found 357.2797.

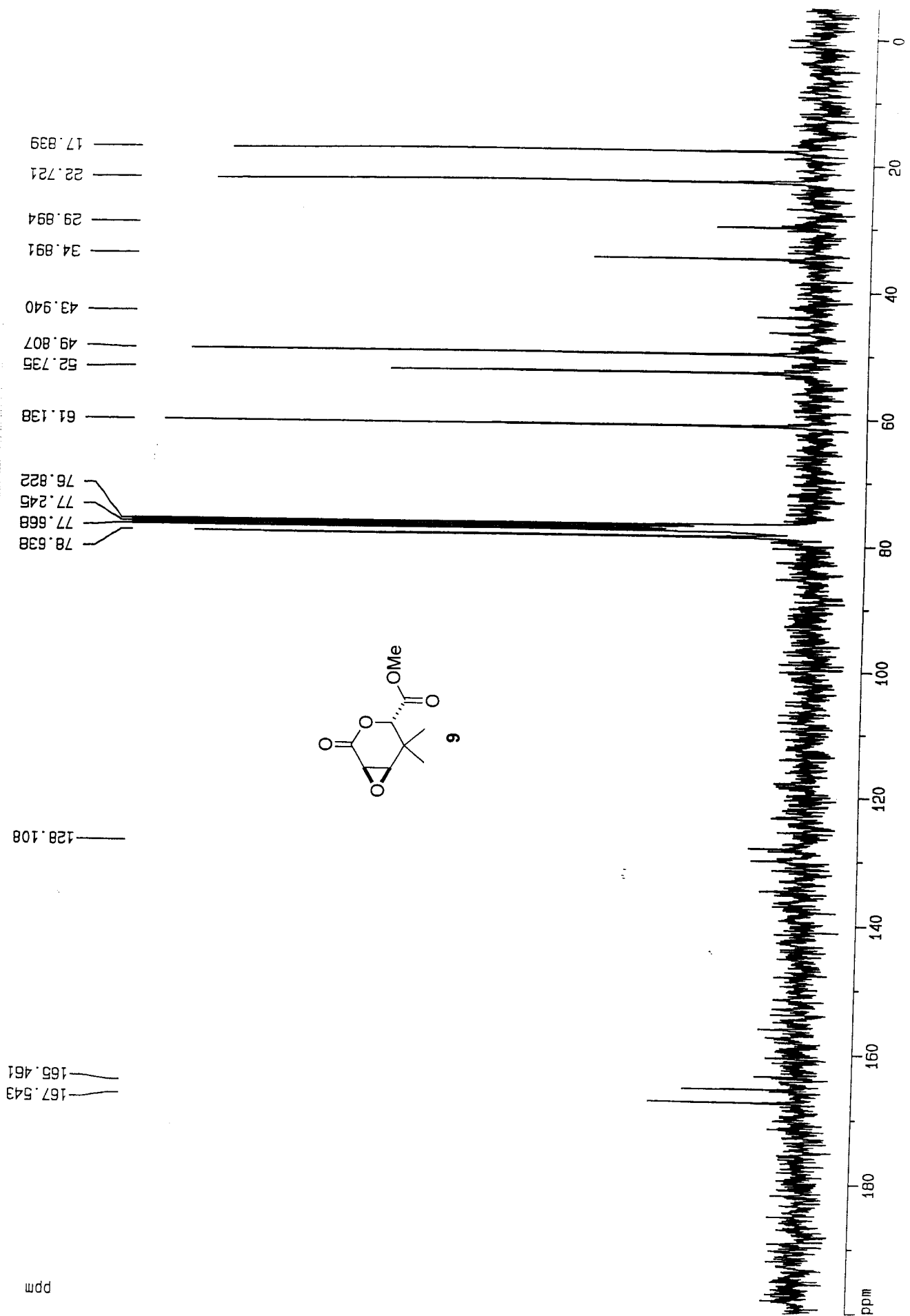
**(1'*R*,3'*S*,4a'*S*,4b'*R*,6a'*S*,8'*R*,10a'*S*,10b'*S*,12a'*S*)-Methyl 8'-methoxy-10a',12a'-dimethyloctadecahydro-3H-spiro[furan-2,1'-naphtho[2,1-f]isochromene]-3'-carboxylate (29).** According to General Protocol A, enol ether **28** (443 mg, 1.24 mmol), *m*-CPBA (855 mg of ~70% *m*-CPBA, 3.72 mmol),  $\text{Na}_2\text{HPO}_4$  (528 mg, 3.72 mmol) furnished, after 18 h and chromatography on  $\text{SiO}_2$  (3:1 hexanes/EtOAc), spiroketal **29** (396 mg, 76%) as a colorless oil and as a single diastereomer by NMR: IR (neat) 2929,

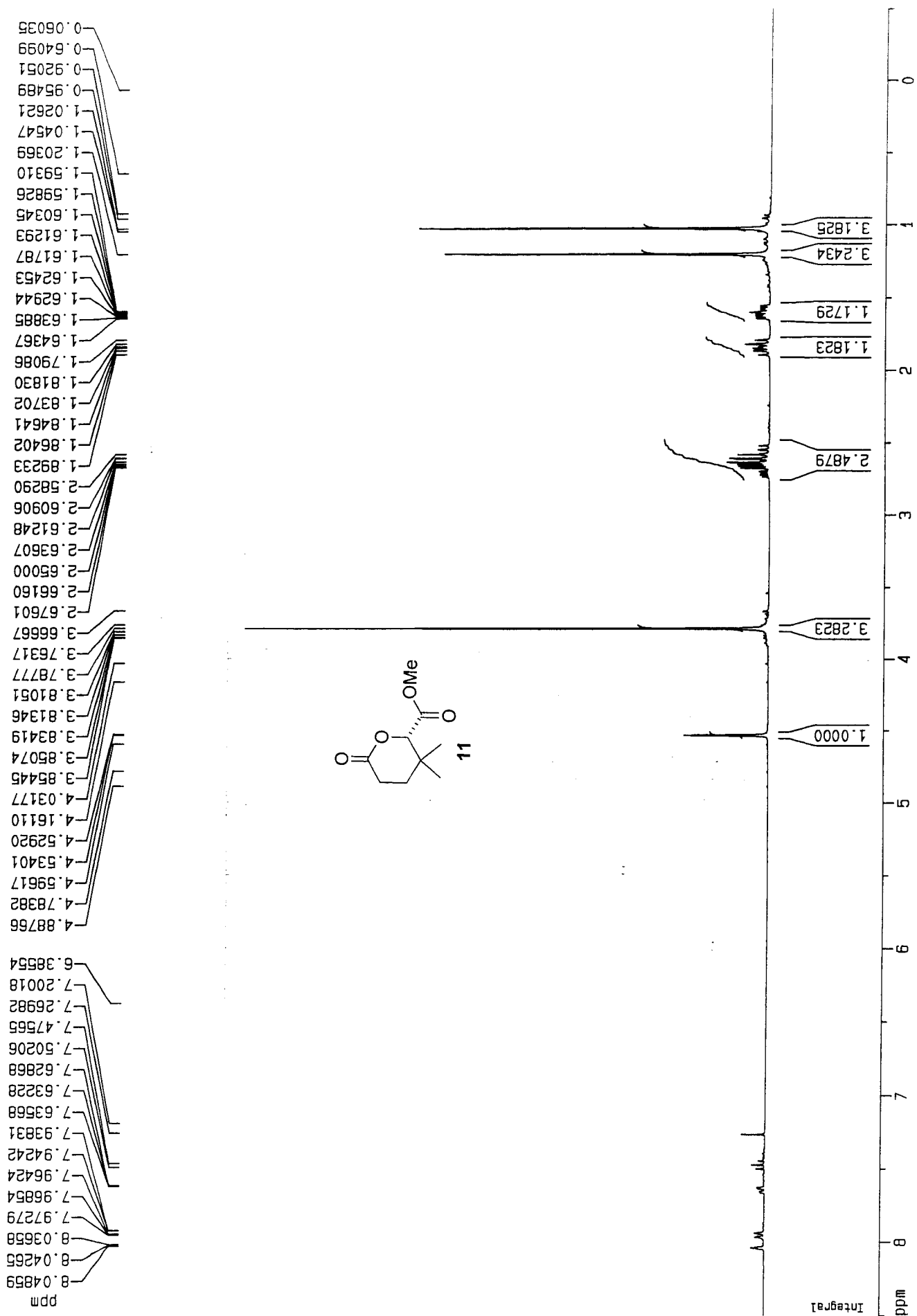
1755, 1446, 1090, 732  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  4.38 (dd, 1 H,  $J = 12.4, 3.2$  Hz), 3.92-3.75 (m, 2 H), 3.70 (s, 3 H), 3.41-3.40 (m, 1 H), 3.27 (s, 3 H), 2.04-1.98 (m, 1 H), 1.88-1.74 (m, 7 H), 1.68-1.09 (m, 14 H), 0.98 (s, 3 H), 0.91-0.81 (m, 2 H), 0.74 (s, 3 H);  $^{13}\text{C}$  NMR  $\delta$  172.9, 111.7, 75.4, 70.0, 67.7, 55.6, 53.1, 51.8, 42.9, 38.9, 38.8, 35.9, 35.0, 32.6, 32.4, 32.2, 31.5, 30.5, 28.5, 27.4, 25.1, 23.8, 19.7, 15.8, 11.3; MS (EI)  $m/z$  (intensity) 421 ( $[\text{M}+\text{H}]^+$ , 27), 361 (51), 334 (80), 248 (100), 216 (95), 190 (87); HRMS (EI)  $m/z$  calculated for  $\text{C}_{25}\text{H}_{41}\text{O}_5$   $[\text{M}+\text{H}]$  421.2954, found 421.2962.



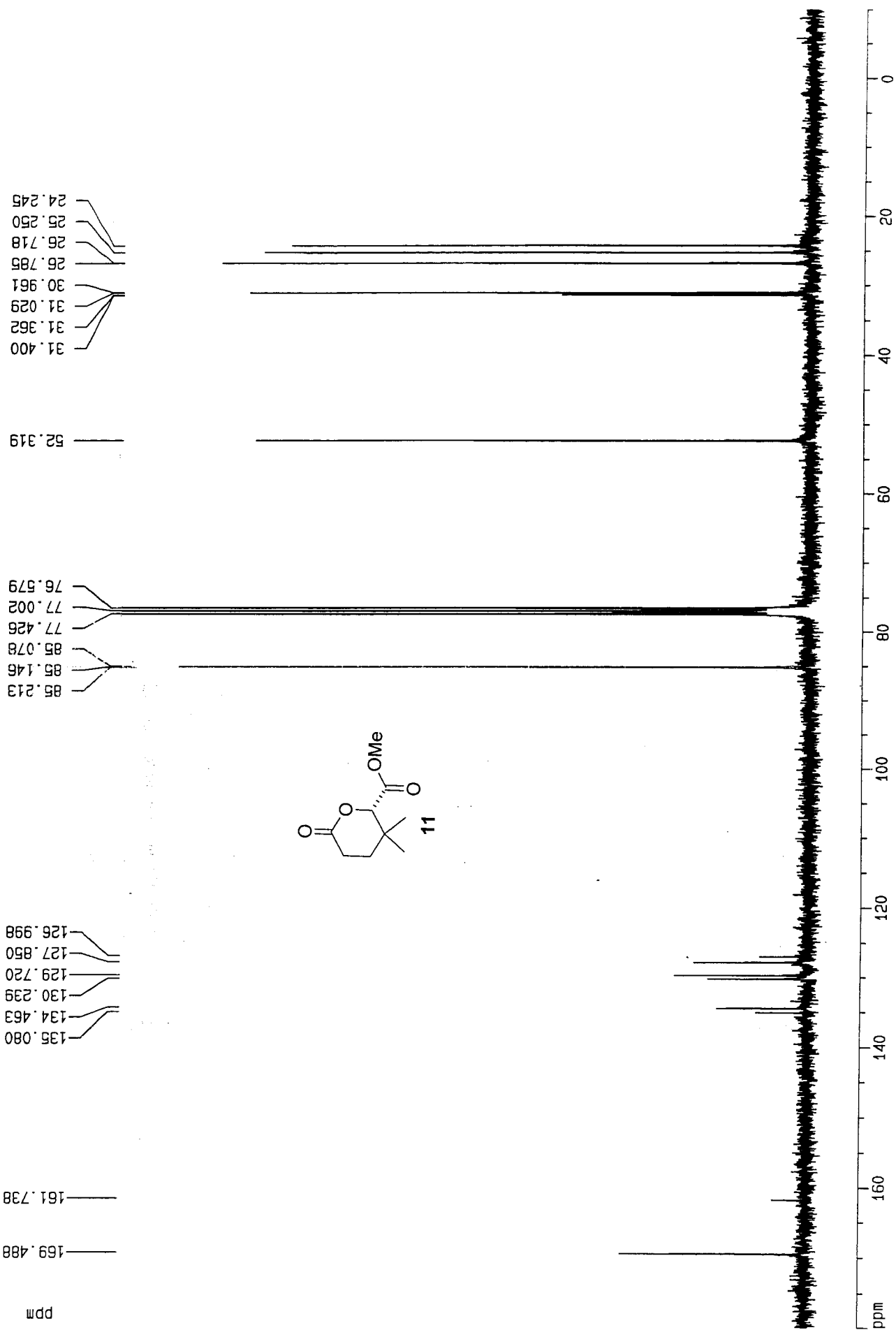


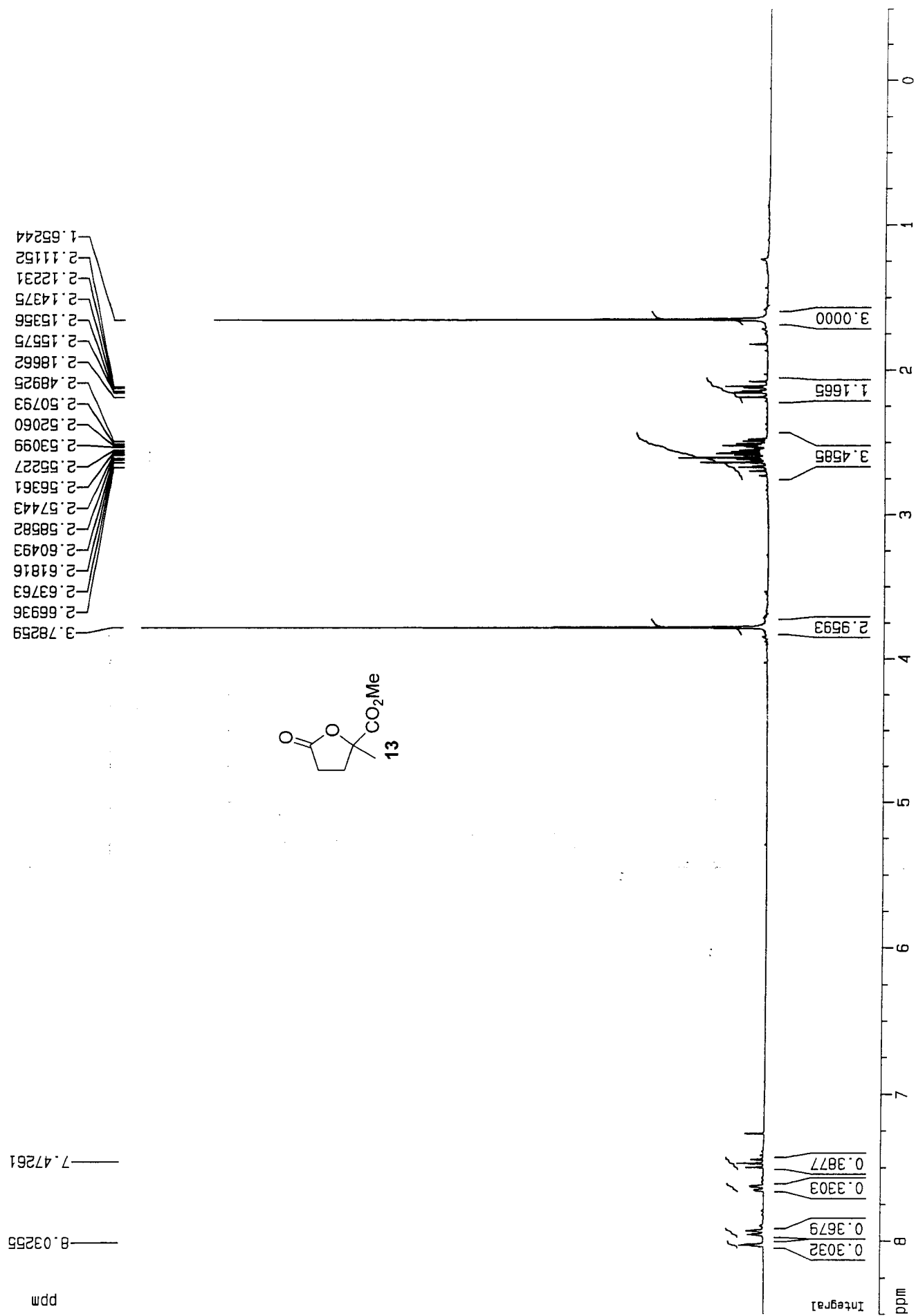


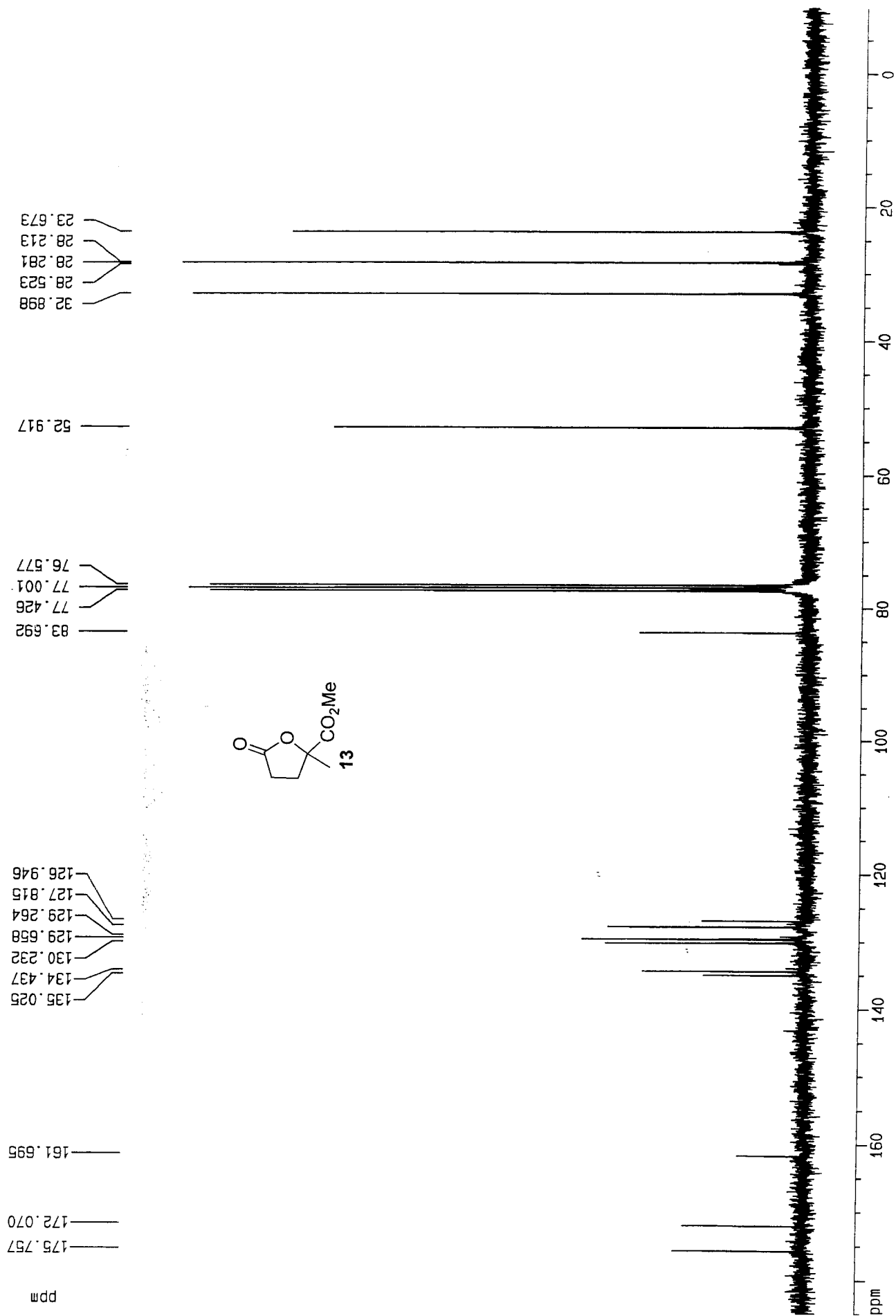


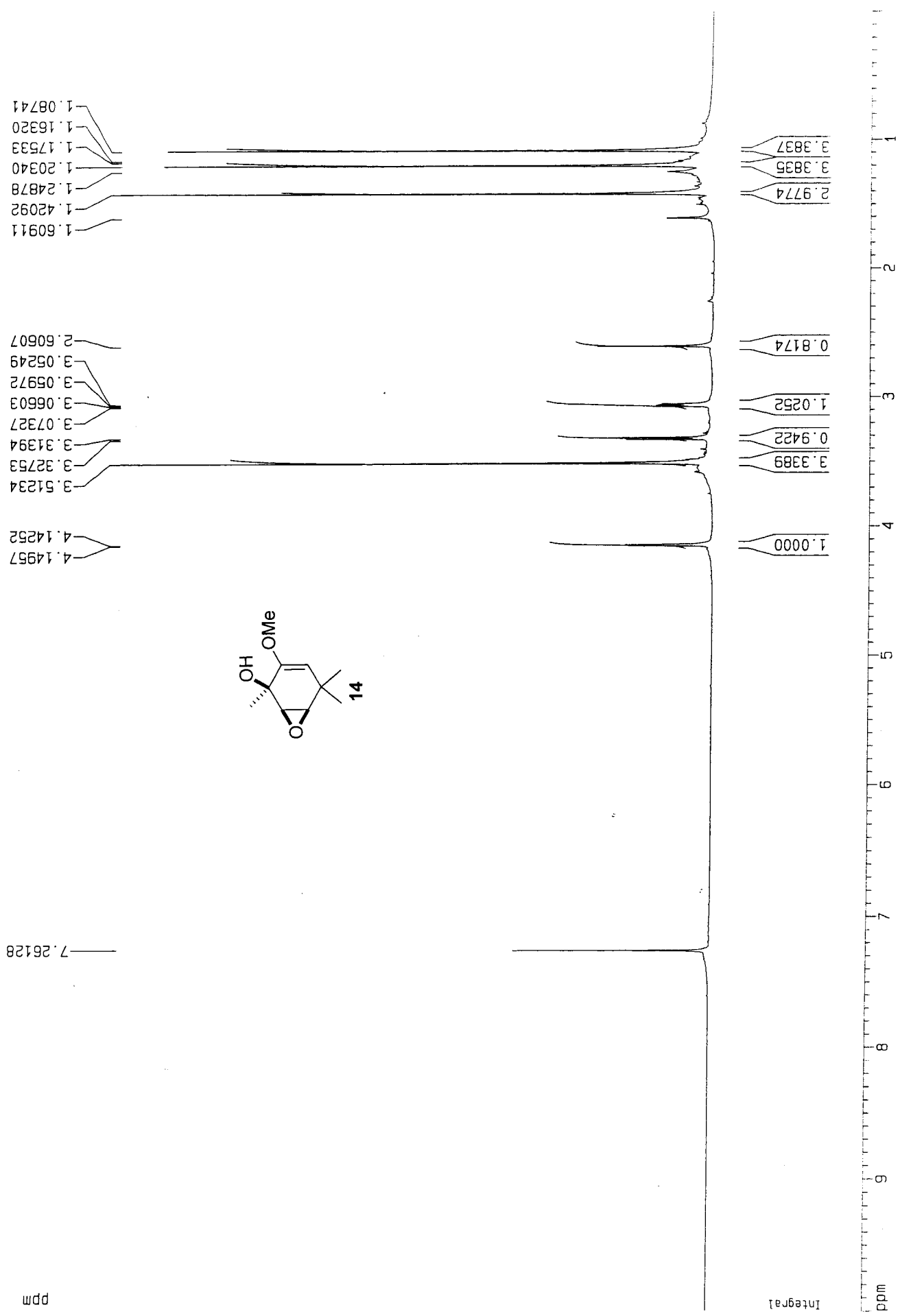












ppm

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76.997

76.574

76.083

69.170

61.094

60.236

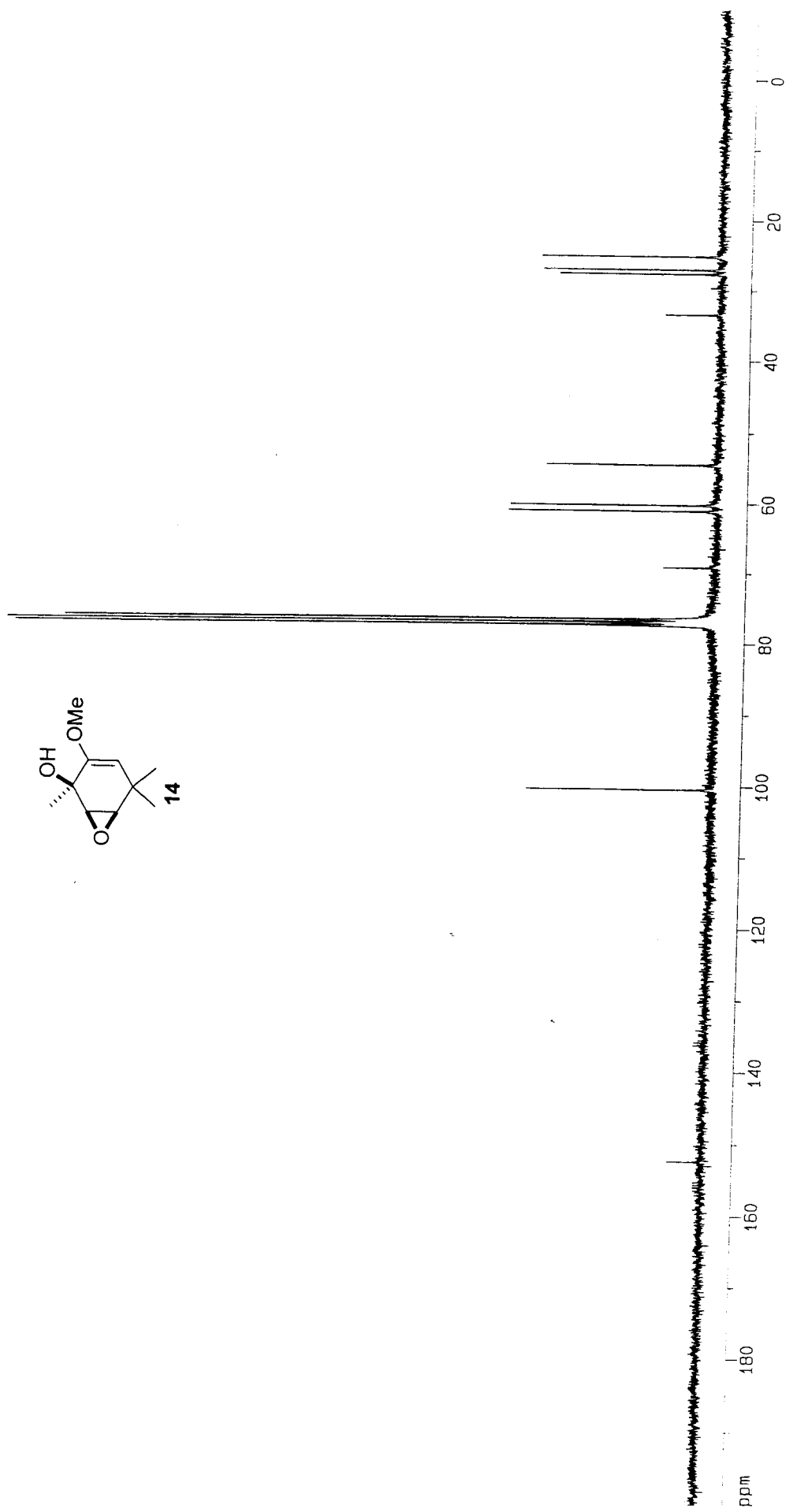
54.516

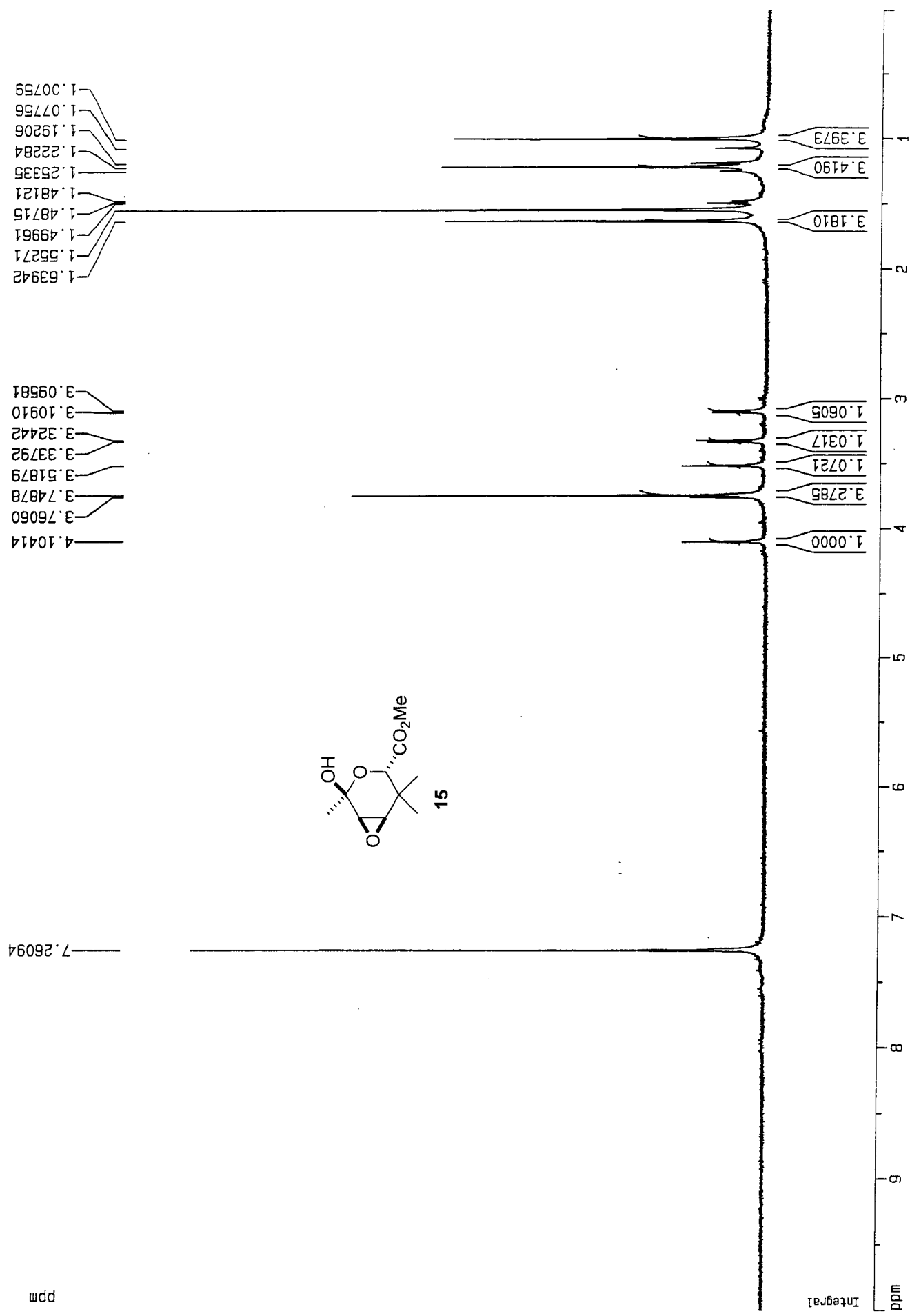
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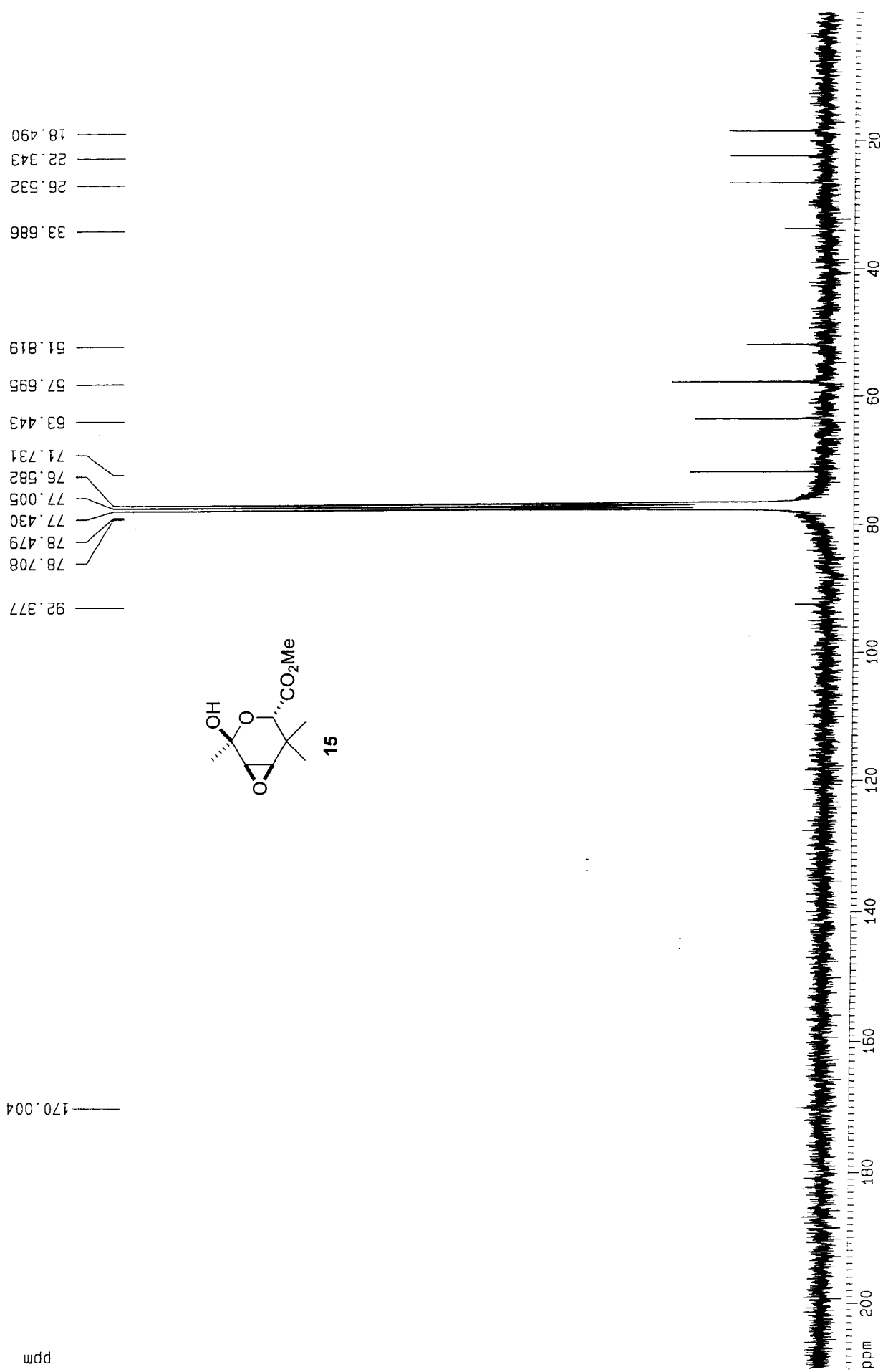
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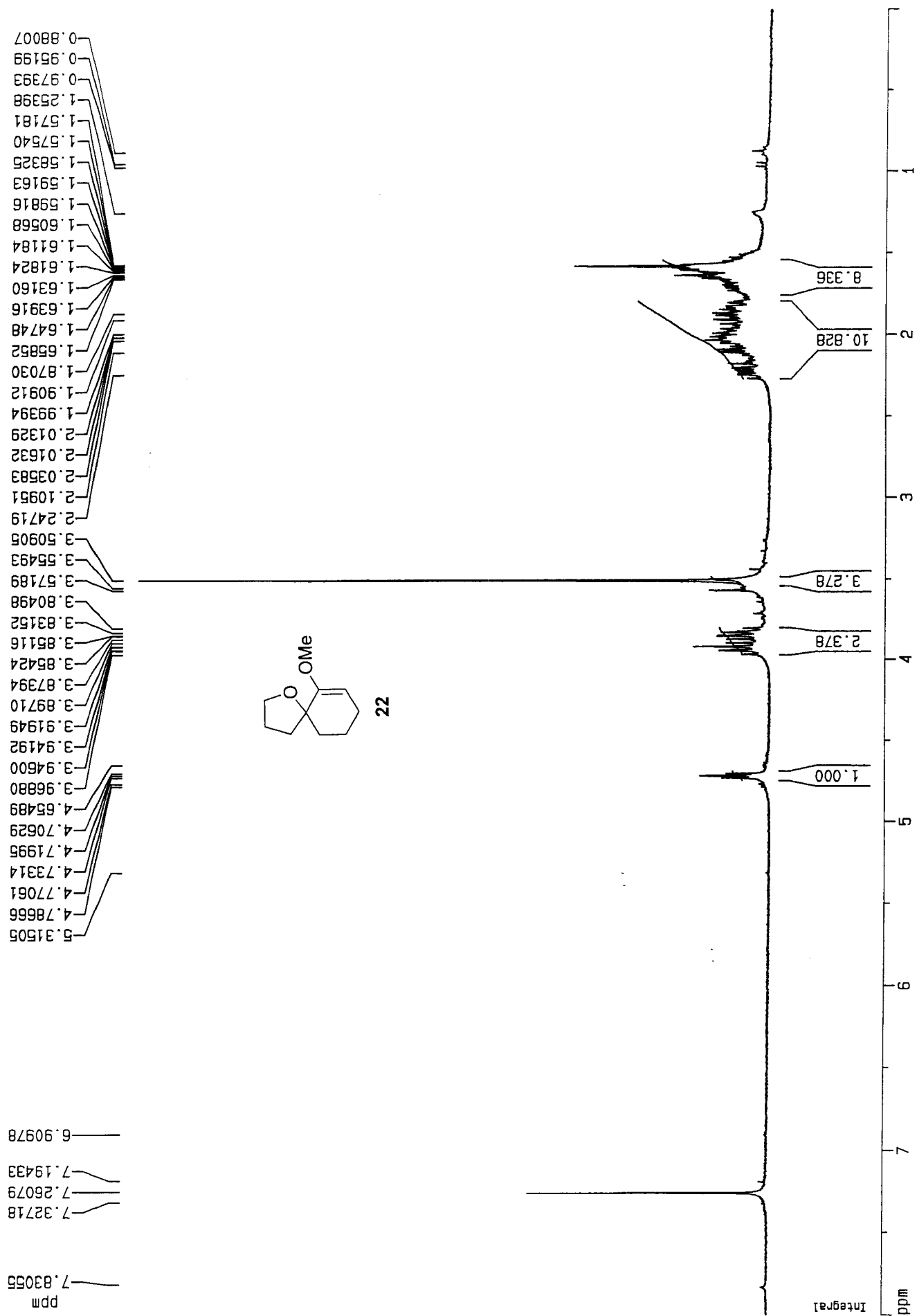
27.098

25.224

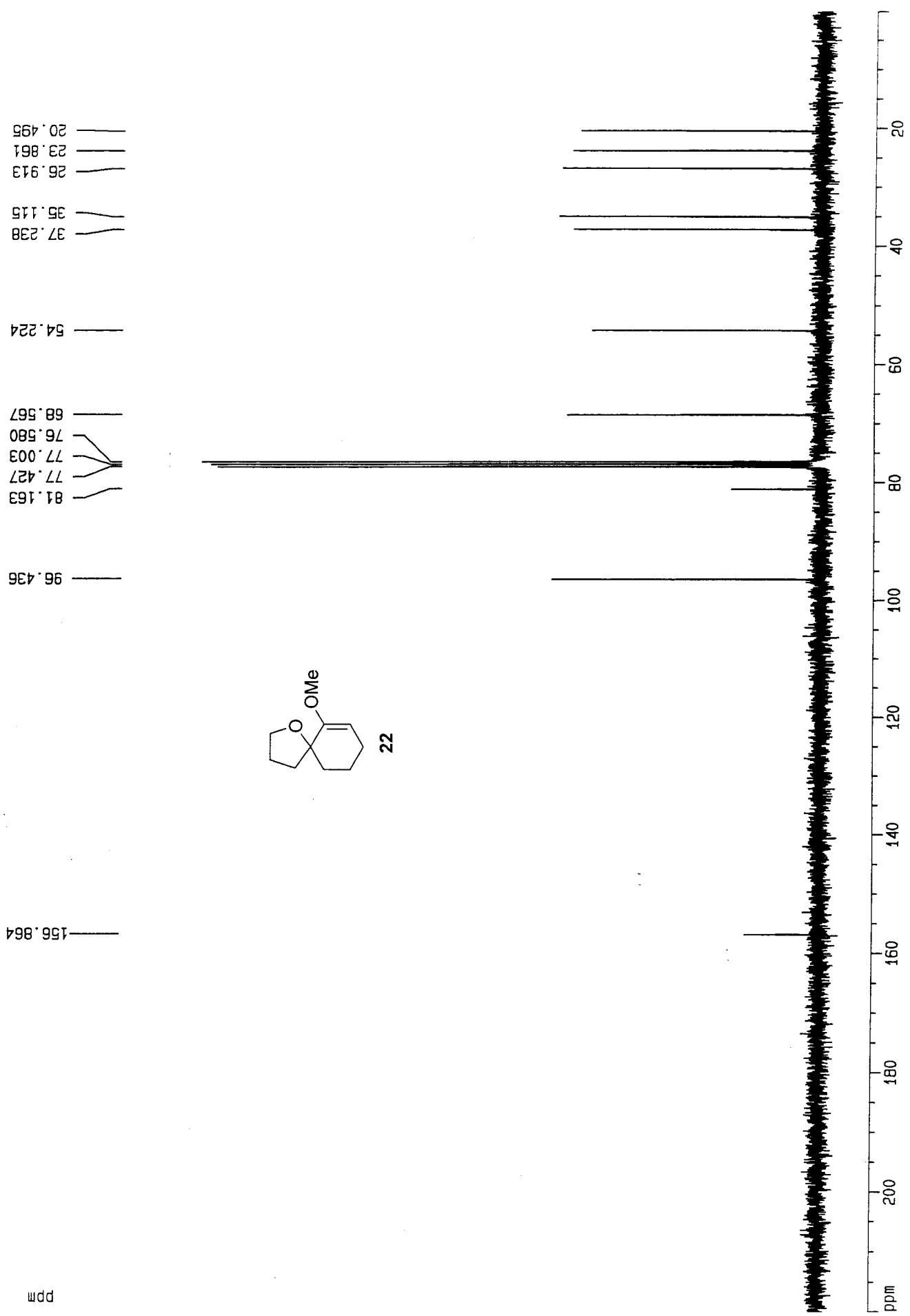




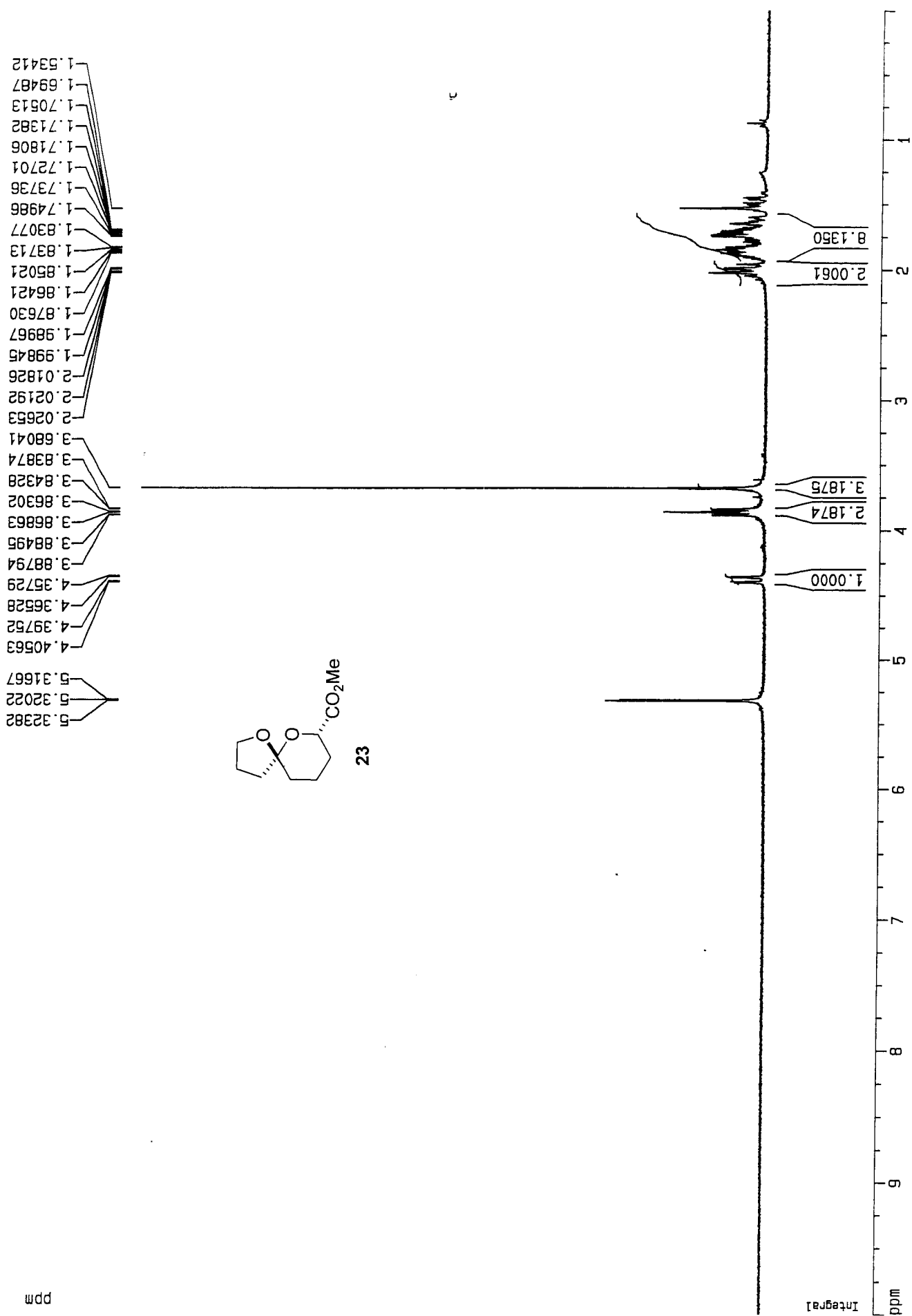


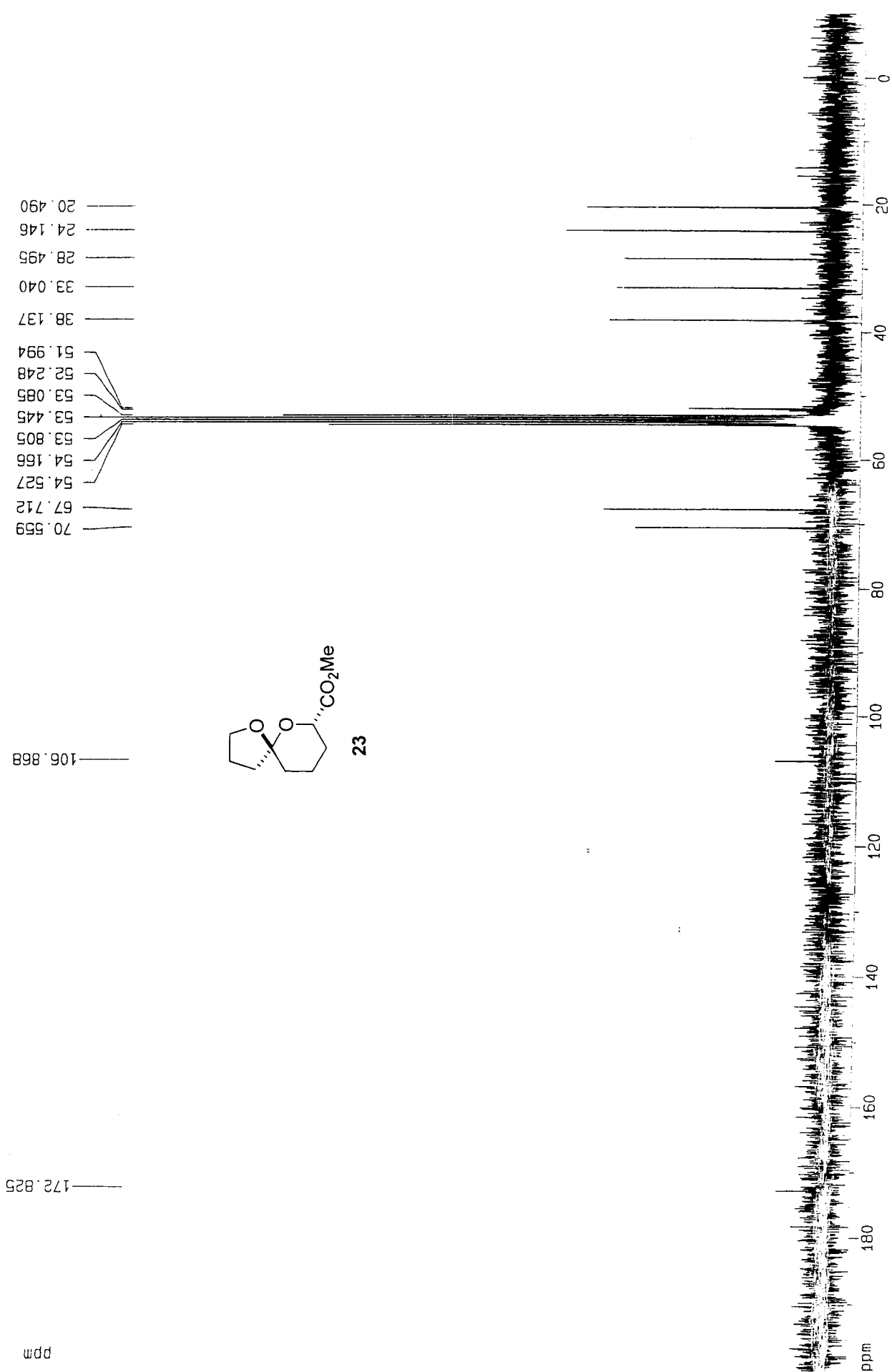


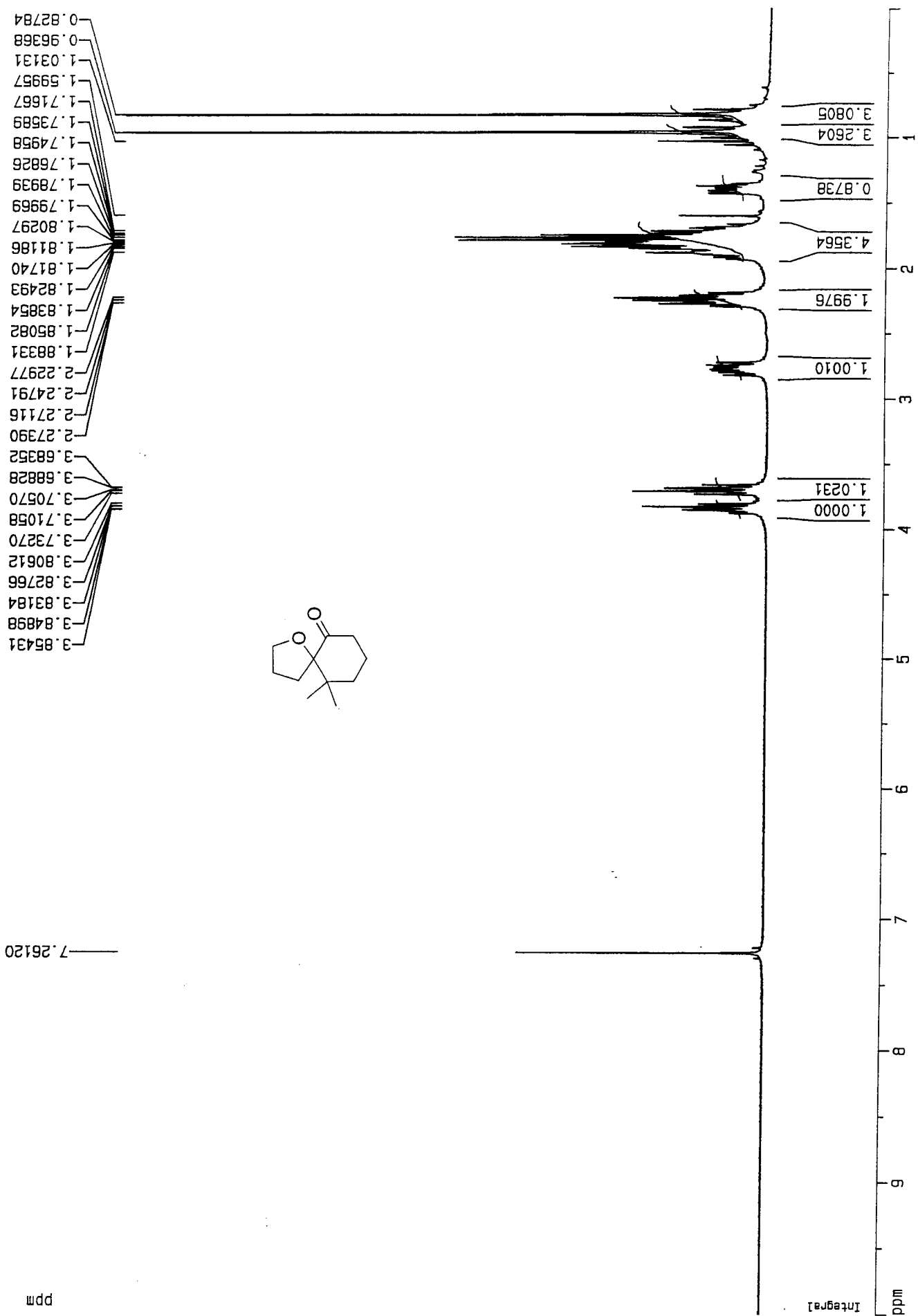


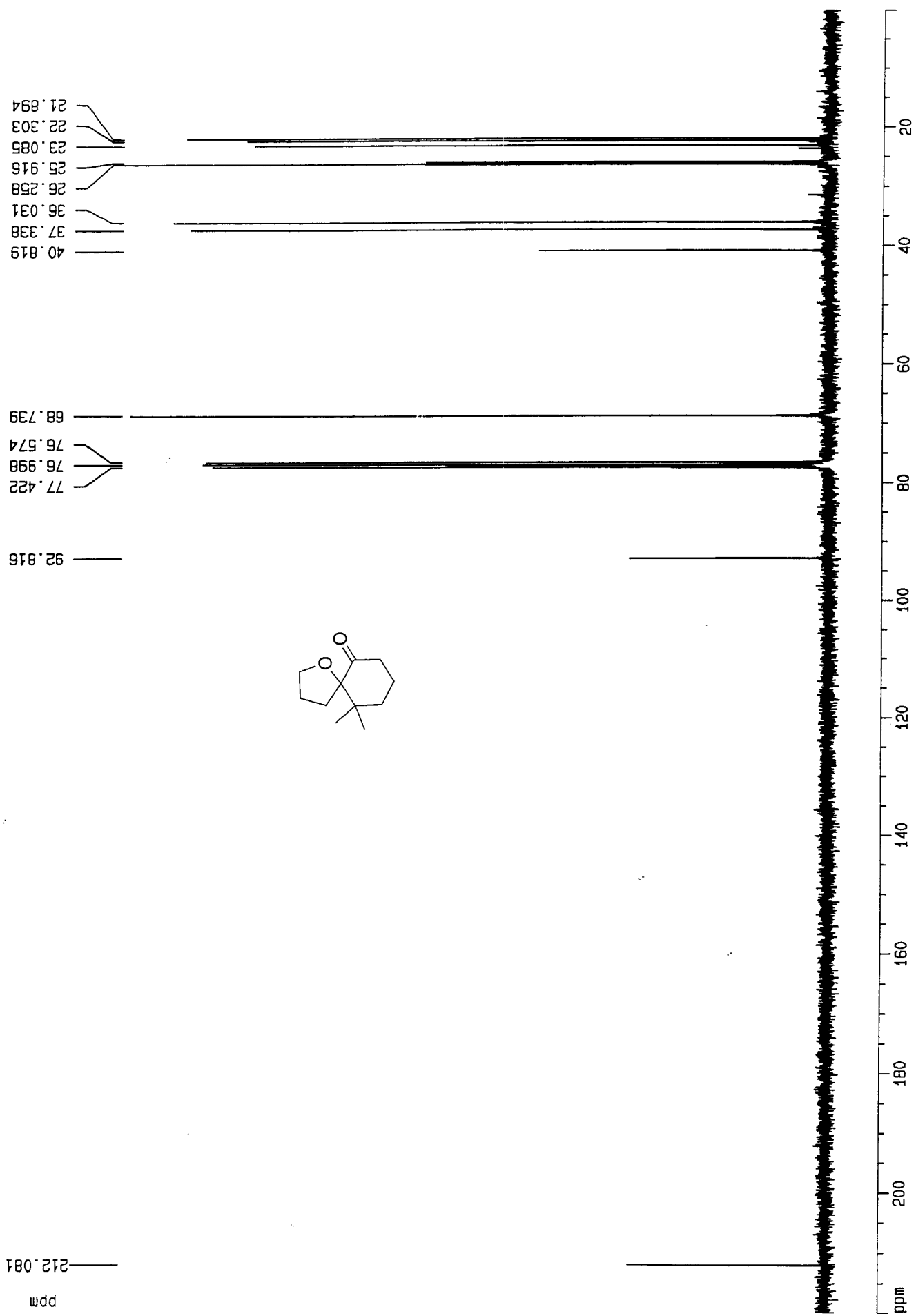


ppm





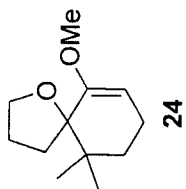




d1w-5-193

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Integral

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ppm

d1w-5-193

