Oxidized Arenol Intermediates in Intermolecular Carbon-Carbon Bond-Forming Reactions. Naphthoid Cyclohexa-2,4-dienones via Oxidative Nucleophilic Substitution

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Supporting Information

Experimental Section

General. CH_2Cl_2 was distilled from CaH_2 prior to use. Light petroleum refers to the fraction boiling in the 40–60 °C range. All reactions were carried out in flame-dried glassware under Ar. Evaporations were conducted under reduced pressure at temperatures less than 45°C unless otherwise noted. Column chromatography was carried out under positive Ar pressure using 32-63 μm silica gel (Bodman) and the indicated solvents. Preparative thin layer chromatography was performed on silica gel 60 F-254 precoated plates (E. Merck). Melting points are uncorrected. One- and two-dimensional NMR spectra of samples in the indicated solvent were run at 300 MHz (^1H). Carbon multiplicities were determined by DEPT135 experiments.[1] Diagnostic correlation information was obtained with a delayed ^1H-^1H correlative experiment [2] using a fixed delay of 200 ms. Electron impact mass spectra (EIMS) were obtained at 50-70 eV. Chemical ionization low and high resolution mass spectrometric analyses (CIMS, HRMS) were obtained from the mass spectrometry laboratory at the University of Texas at Austin. Combustion analyses were performed by Desert Analytics, Tucson, AZ.

4-(4-Hydroxy-3-methoxyphenyl)-but-2-enal (4a). To a stirred -41°C cooled solution of phenyliodine(III) bis(trifluoroacetoxy) (PIFA, 391 mg, 0.91 mmol) in CH_3CN–CH_2Cl_2 (1:1, 8 mL) was added dropwise pure guaiacol **1a** (100 μL, 0.91 mmol). Stirring was continued for 30 min, after which time the silyl enol ether **3a** (160 μL, 0.91 mmol) was added dropwise. The reaction mixture was then allowed to warm up to room temperature over 2 h, after which time it was poured over ice-cold water, extracted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and evaporated at room temperature. The resulting brownish residue was purified by column chromatography, eluting with hexanes–Et_2O (2:1), to furnish **4a** (18 mg, 10%) as a light brown oil. IR (NaCl) 3420, 1684 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.56 (dd, *J* = 6.7, 1.5 Hz, 2 H), 3.86 (s, 3 H), 5.60 (s, 1 H), 6.09 (ddt, *J* = 15.5, 7.9, 1.5 Hz, 1 H), 6.63 (d, *J* = 1.9 Hz, 1 H), 6.67 (ddt, *J* = 8.0, 2.0, 0.5 Hz, 1 H), 6.86 (d, *J* = 8.0 Hz, 1 H), 6.93 (dt, *J* = 15.5, 6.7 Hz, 1 H), 9.52 (d, *J* = 7.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 193.9, 156.9, 146.8, 144.7, 133.3, 128.8, 121.7, 114.7, 111.3, 56.0, 38.8; CIMS *m/z* (relative intensity) 193 (MH^+, 100), 175 (50), 139 (40), 123 (40); HRMS (CI) calcd for $C_{11}H_{13}O_3$ 193.0865, found 193.0870.

4-(2-Hydroxy-3,4,5-trimethylphenyl)-but-2-enal (4b). To a stirred -78°C cooled solution of 2,3,5-trimethylphenol (100 mg, 0.74 mmol) in CH_2Cl_2 (10 mL) was added dropwise a solution of PIFA (477 mg, 1.11 mmol) in CH_2Cl_2(4 mL). This mixture was maintained at -78°C with stirring for 3h, after which time it was transfered via cannula to a -78°C cooled solution of the silyl enol ether **3a** (360 μL, 2.1 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was maintained at -78°C with stirring for 3 h, after which time it was diluted in CH_2Cl_2 (30 mL), washed twice with 1M H_3PO_4 (2 × 30 ml) and once with brine (30 ml), dried over Na_2SO_4, and evaporated at room temperature. The residue was then submitted to column chromatography, eluting with hexanes–Et_2O (1:1), to furnish a yellow oil (83 mg). This oil was further purified by preparative thin layer chromatography, eluting with hexanes–Et_2O (1:1), to afford **4b** (66 mg, 44%) as a pale yellow oil. IR (NaCl) 3381, 1667 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.138 (s, 3 H), 2.140 (s, 3 H), 2.16 (s, 3 H), 3.61 (dd, *J* = 5.6, 1.8 Hz, 2 H), 5.10 (bs, 1 H), 5.89 (ddt, *J* = 15.5, 8.0, 1.8 Hz, 1 H), 6.50 (s, 1 H), 6.94 (dt, *J* = 15.5, 5.6 Hz, 1 H), 9.50 (d, *J* = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 194.1, 156.9, 152.3, 136.7, 134.5, 132.7, 125.6, 120.7, 114.7, 32.9, 20.0, 16.0, 12.0; EIMS *m/z* (relative intensity) 204 (M^+, 69), 189 (10), 174 (17), 136 (100).

1,2-Dihydro-2-[(*E*)-3-formylprop-2-enyl]-2-methoxy-1-oxo-naphthalene (4c), and 4-[(*E*)-3-formylprop-2-enyl]-2-methoxy-1-naphthol (4d). Protocol A. To a stirred -41°C cooled solution of PIFA (494 mg, 1.15 mmol) in $CH_3CN:CH_2Cl_2$ (1:1, 8 mL) was added dropwise a solution of 2-methoxy-1-naphthol **1c** (200 mg, 1.15 mmol) in CH_2Cl_2 (3 mL). The mixture became bright yellow. Stirring was continued for 30 min, after which time the silyl enol ether **3a** (202 μL, 1.15 mmol) was added dropwise. The orangeish reaction mixture was maintained -41°C for 1 h. The mixture was then allowed to warm up to room temperature over 3 h, after which time it was poured over ice-cold water, extracted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and evaporated at room temperature. The resulting brownish oil (270 mg) was purified by column chromatography, eluting with hexanes–EtOAc (9:1), to furnish **4c** (61 mg, 22%) as a light brown oil, and 30 mg of recovered **1c**.

Protocol B. To a stirred ice-cold solution of **1c** (100 mg, 0.57 mmol) in CH_2Cl_2 (5 mL) was added PIFA (368 mg, 0.86 mmol) as a solid. The mixture was stirred for 10 min, after which time it was added via a cannula to a solution of **3a** (282 μL, 1.61 mmol) in CH_2Cl_2 (7 mL). This reaction mixture turned from purple to a light red colour. It was stirred at room temperature for 35 min, after which time it was diluted with CH_2Cl_2, washed once with saturated aqueous $NaHCO_3$, twice with 1M H_3PO_4, then brine, dried over Na_2SO_4, and evaporated at room temperature. The residue was purified by column chromatography, eluting with hexanes–Et_2O (1:1), to furnish **4c** (76 mg, 55%) and **4d** (37 mg, 27%) as pale yellow oils. Another run was performed by slowly adding dropwise the solution of PIFA-oxidized **1c** to the solution of **3a**, which was then kept stirring at room temperature for 2 h; the cyclohexadienone derivative **4c** was hence obtained in 74% yield (102 mg) and **4d** in 4% yield (5 mg).

4c: IR (NaCl) 1690, 1678 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.62-2.76 (m, 2H), 3.19 (s, 3H), 6.02 (ddt, J = 1.3, 7.9, 15.6 Hz, 1H), 6.11 (d, J = 10.0 Hz, 1H), 6.77 (d, J = 10.0 Hz, 1H), 6.81 (dt, J = 7.7, 15.6 Hz, 1H), 7.23 (d, J = 7.5 Hz, 1H), 7.36 (dt, J = 1.3, 7.5 Hz, 1H), 7.58 (dt, J = 1.3, 7.5 Hz, 1H), 7.98 (d, J = 7.5 Hz, 1H), 9.40 (d, J = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 199.3, 193.5, 150.6, 136.8, 135.8, 135.3, 134.6, 129.8, 129.6, 128.7, 127.8, 127.1, 81.3, 53.8, 42.3; EIMS m/z (relative intensity) 242 (M^+, 10), 174 (21), 173 (100); Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.35; H, 5.83. Found: C, 73.99; H, 5.71.

4d: IR (NaCl) 3418, 1682 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.97 (s, 3H), 4.02 (dd, J = 1.5, 6.2 Hz, 1H), 5.98 (bs, 1H), 6.06 (ddt, J = 1.6, 7.9, 15.6 Hz, 1H), 7.05 (dt, J = 6.2, 15.6 Hz, 1H), 7.10 (s, 1H), 7.35-7.48 (m, 2H), 7.75 (bd, J = 8.0 Hz, 1H), 8.19 (bd, J = 8.0 Hz, 1H), 7.75 (bd, J = 8.0 Hz, 1H), 9.50 (d, J = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 193.6, 156.4, 140.6, 139.3, 133.6, 127.5, 125.4, 124.9, 124.8, 124.6, 123.3, 122.1, 114.7, 57.2, 36.1.

1,2-Dihydro-2-(prop-2-enyl)-2-methoxy-1-oxo-naphthalene (4e). To a stirred solution of 2-methoxy-1-naphthol **1c** (87 mg, 0.50 mmol) and the allylsilane **3b** (80 μL, 0.50 mmol) in CH_2Cl_2 (10 mL) was added at room temperature PIFA (215 mg, 0.50 mmol) as a solid. The reaction mixture turned from bright yellow into deep purple upon adding PIFA. Stirring was continued for 10 min, after which time the mixture was diluted in in CH_2Cl_2 (30 mL), washed twice with 1M H_3PO_4 (2 × 30 mL) and three times with brine (3 × 30 mL), dried over

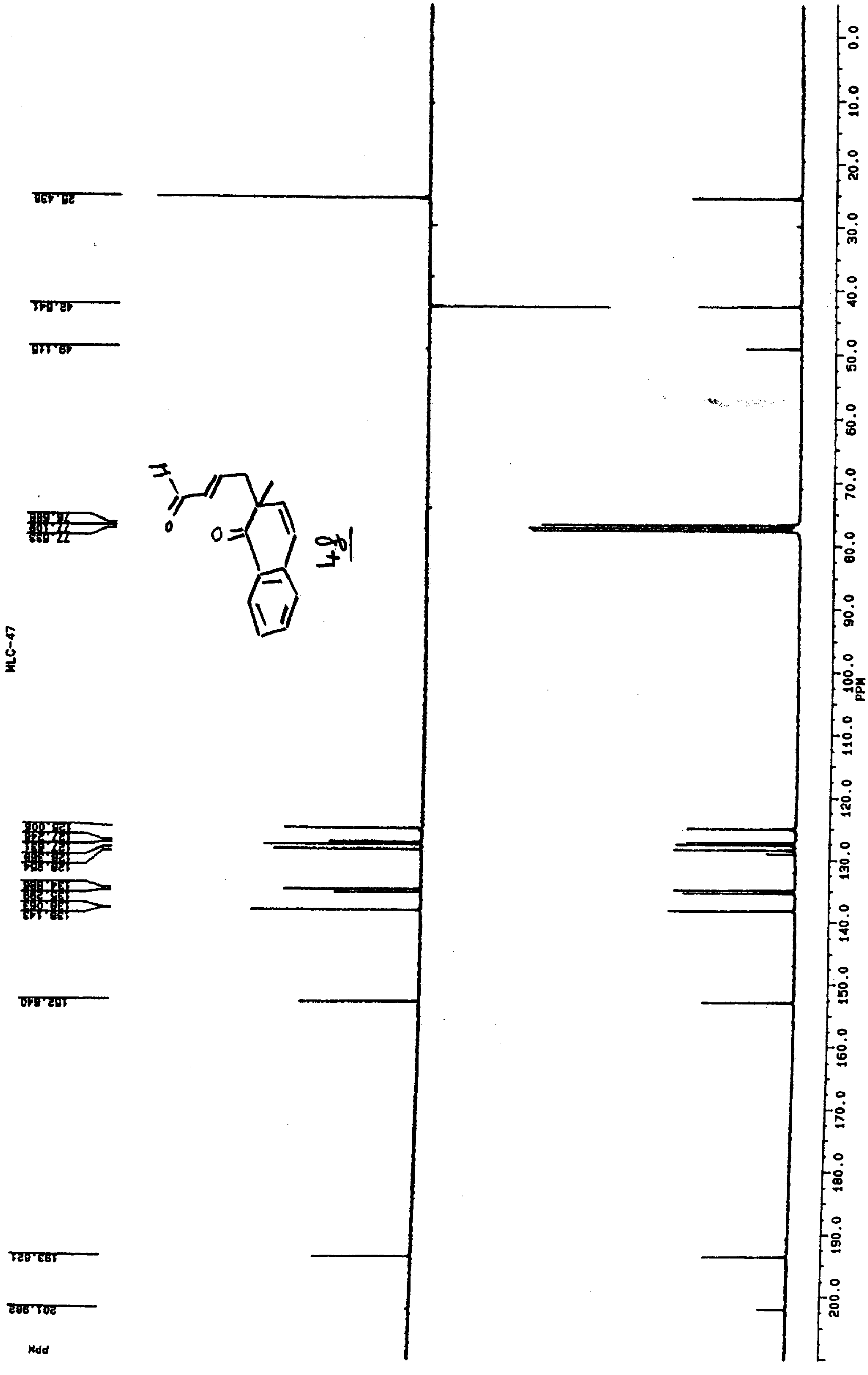
$MgSO_4$, and evaporated at room temperature to give a yellowish purple solid. This residue was then purified by column chromatography, eluting with light petroleum–Et_2O (9:1), to furnish **4e** (74 mg, 69%) as a pale yellow oil. IR (NaCl) 1687 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40-2.56 (m, 2 H), 3.17 (s, 3 H), 4.94-5.02 (m, 2 H), 5.59-5.73 (m, 1 H), 6.12 (d, J = 10.0 Hz, 1 H), 6.74 (d, J = 10.0 Hz, 1 H), 7.22 (dd, J = 7.6, 1.2 Hz, 1 H), 7.33 (td, J = 7.6, 1.2 Hz, 1 H), 7.55 (td, J = 7.6, 1.2 Hz, 1 H), 7.99 (dd, J = 7.6, 1.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 200.4, 137.2, 135.6, 134.9, 130.9, 130.2, 129.0, 128.3, 127.6, 126.8, 119.2, 82.2, 53.7, 44.3; EIMS *m/z* (relative intensity) 214 (M^+, 31), 199 (25), 183 (8), 173 (98); HRMS (CI) calcd for $C_{14}H_{15}O_2$ 215.1072, found 215.1063.

1,2-Dihydro-2-[(*E*)-3-formylprop-2-enyl]-2-methyl-1-oxo-naphthalene (4f). To a stirred -78°C cooled solution of 2-methyl-1-naphthol **1d** (100 mg, 0.63 mmol) in CH_2Cl_2 (10 mL) was added dropwise a solution of PIFA (409 mg, 0.95 mmol) in CH_2Cl_2(4 mL). This mixture was maintained at -78°C with stirring for 1h, after which time it was transfered via cannula to a -78°C cooled solution of the silyl enol ether **3a** (308 μL, 1.76 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was maintained at -78°C with stirring for 3 h, after which time it was diluted in CH_2Cl_2 (30 mL), washed with 1M H_3PO_4 (30 ml) and with brine (30 ml), dried over Na_2SO_4, and evaporated at room temperature. The residue was then submitted to column chromatography, eluting with hexanes–Et_2O (1:1), to furnish partially purified **4f** (96 mg), together with 34 mg of recovered **1d**. The crude **4f** fraction was then further purified by preparative thin layer chromatography, eluting with hexanes–Et_2O (1:1), to afford pure **4f** (67 mg, 47%) as an orange oil. IR (NaCl) 1684 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 3 H), 2.50 (ddd, J = 8.7, 7.6, 1.1 Hz, 1 H), 3.00 (ddd, J = 8.4, 7.3, 1.1 Hz, 1 H), 6.03 (bdd, J = 15.4, 7.9 Hz, 1 H), 6.06 (d, J = 9.7 Hz, 1 H), 6.54 (dt, J = 15.6, 7.3 Hz, 1 H), 6.62 (d, J = 9.8 Hz, 1 H), 7.24 (bd, J = 7.7 Hz, 1 H), 7.36 (td, J = 7.6, 1.1 Hz, 1 H), 7.57 (td, J = 7.4, 1.3 Hz, 1 H), 8.03 (bd, J = 7.8 Hz, 1 H), 9.29 (d, J = 7.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 201.9, 193.6, 152.8, 138.04, 137.97, 135.2, 134.8, 128.8, 128.3, 127.5, 127.2, 124.9, 49.0, 42.5, 25.4; EIMS *m/z* (relative intensity) 226 (M^+, 8), 211 (6), 197 (18), 157 (100); HRMS (CI) calcd for $C_{15}H_{15}O_2$ 227.1072, found 227.1078.

Additional References

(1) Doddrell, D. M.; Pegg, D. T.; Bendall, M. R. *J. Magn. Reson.* **1982**, *48*, 323-327.

(2) Bax, A.; Freeman, R. *J. Magn. Reson.* **1981**, *44*, 542-561.



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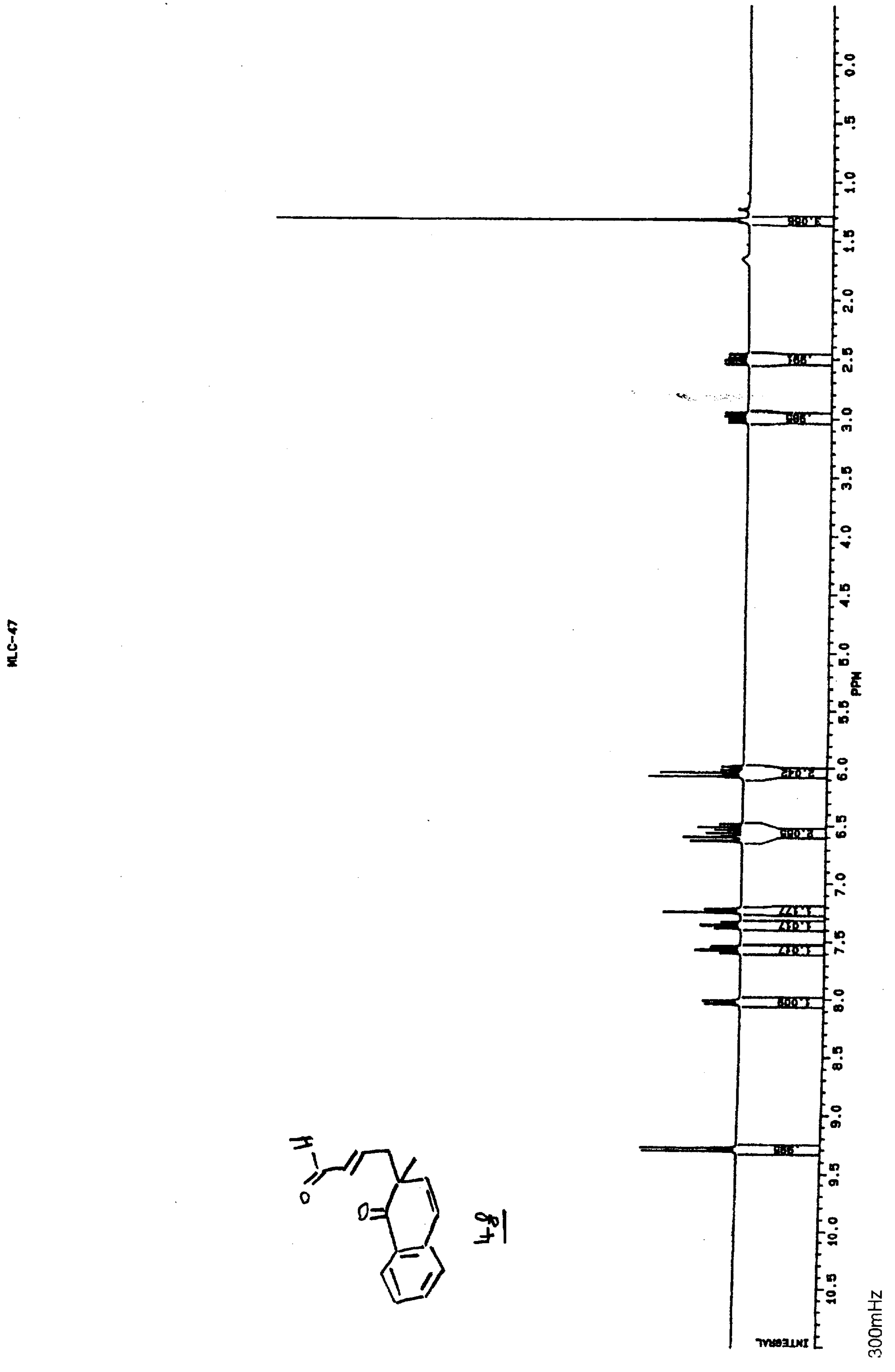
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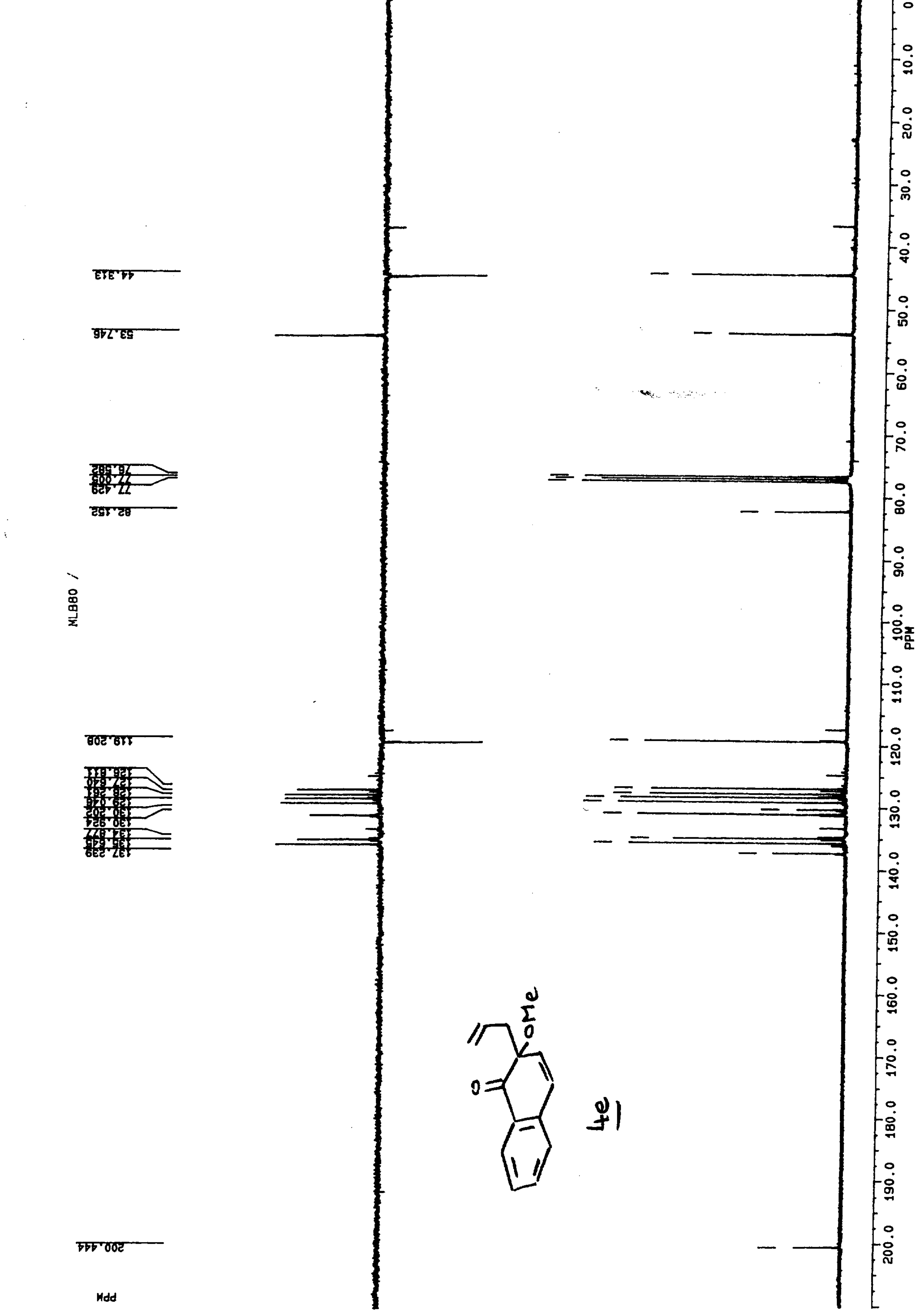
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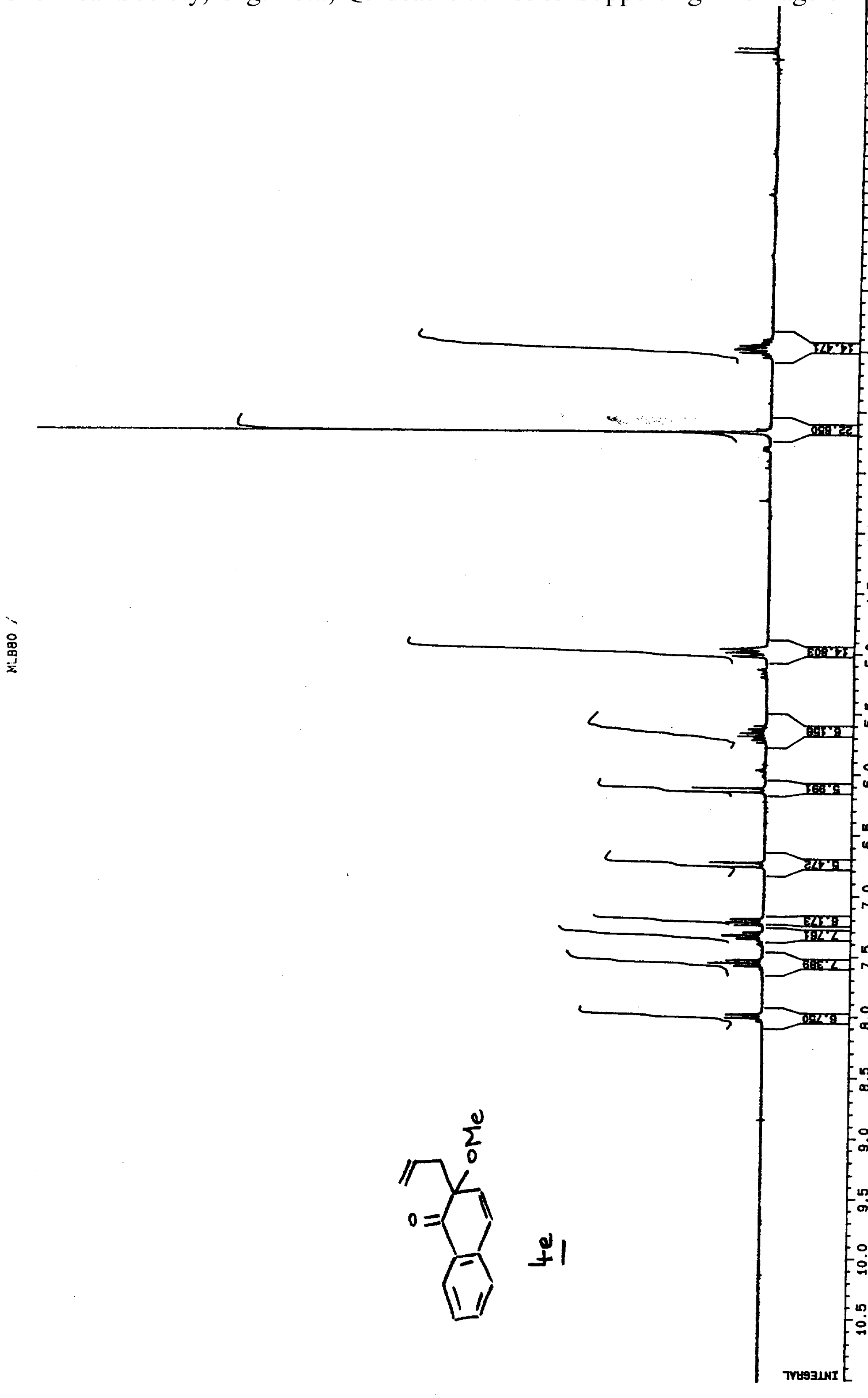
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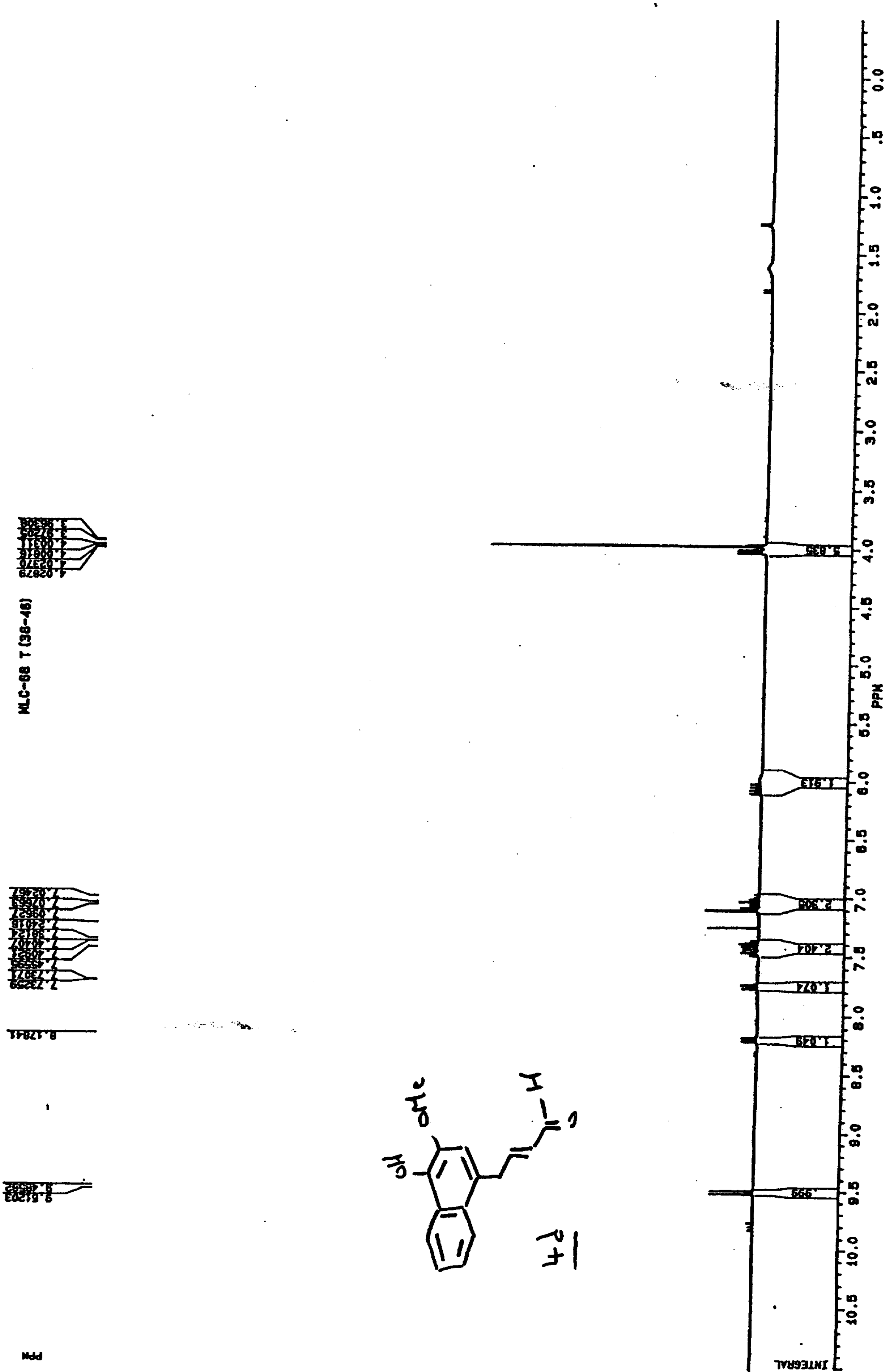
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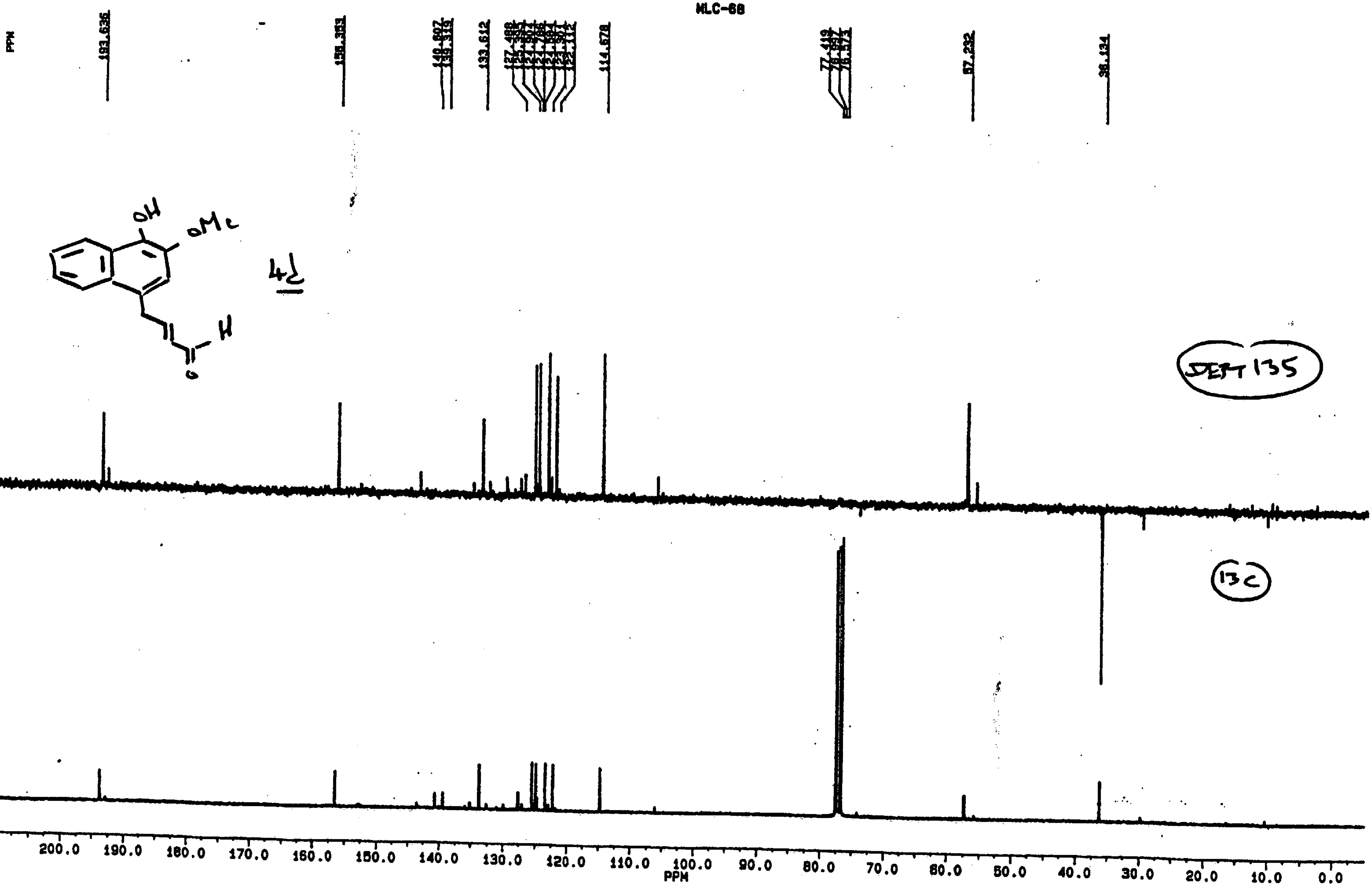
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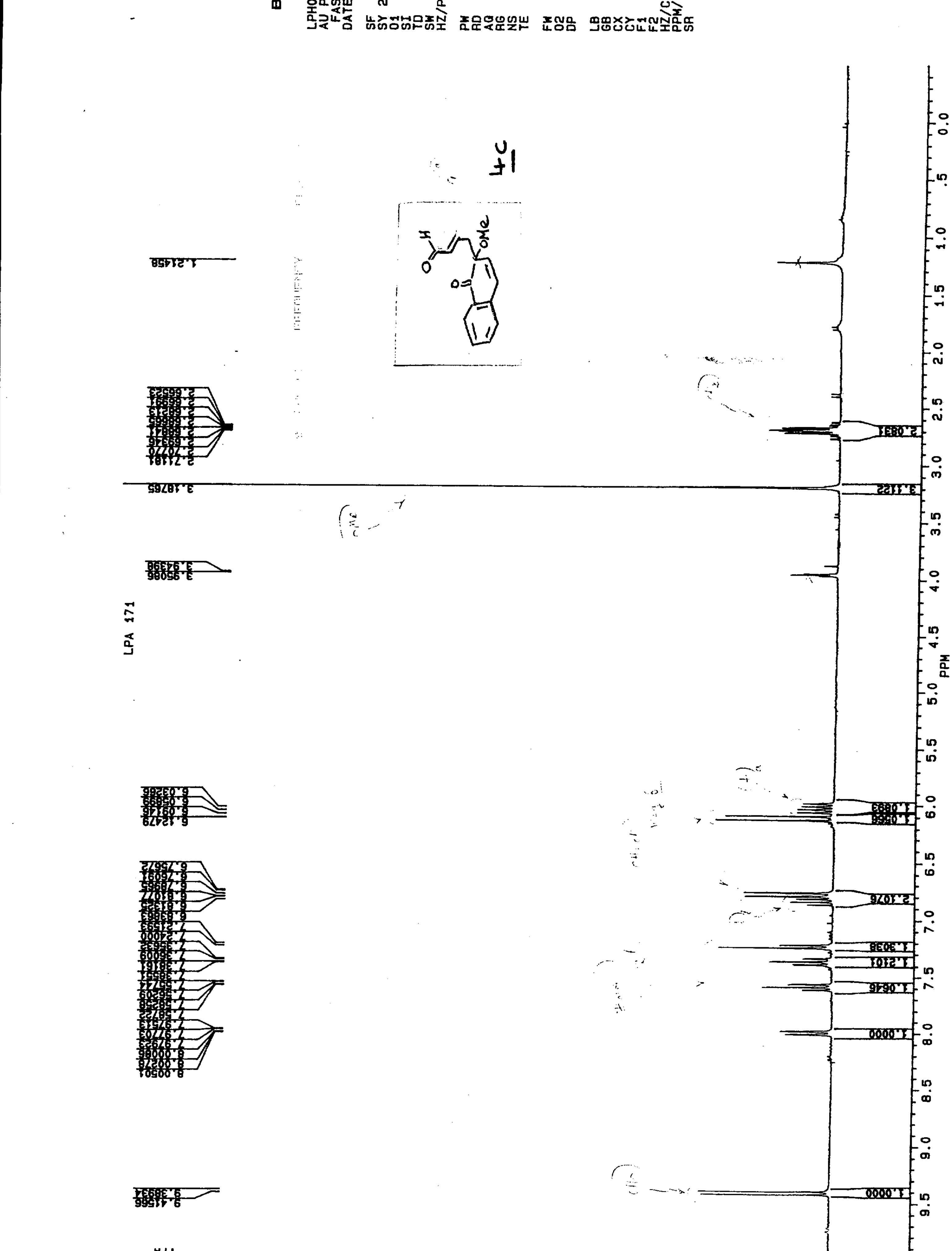
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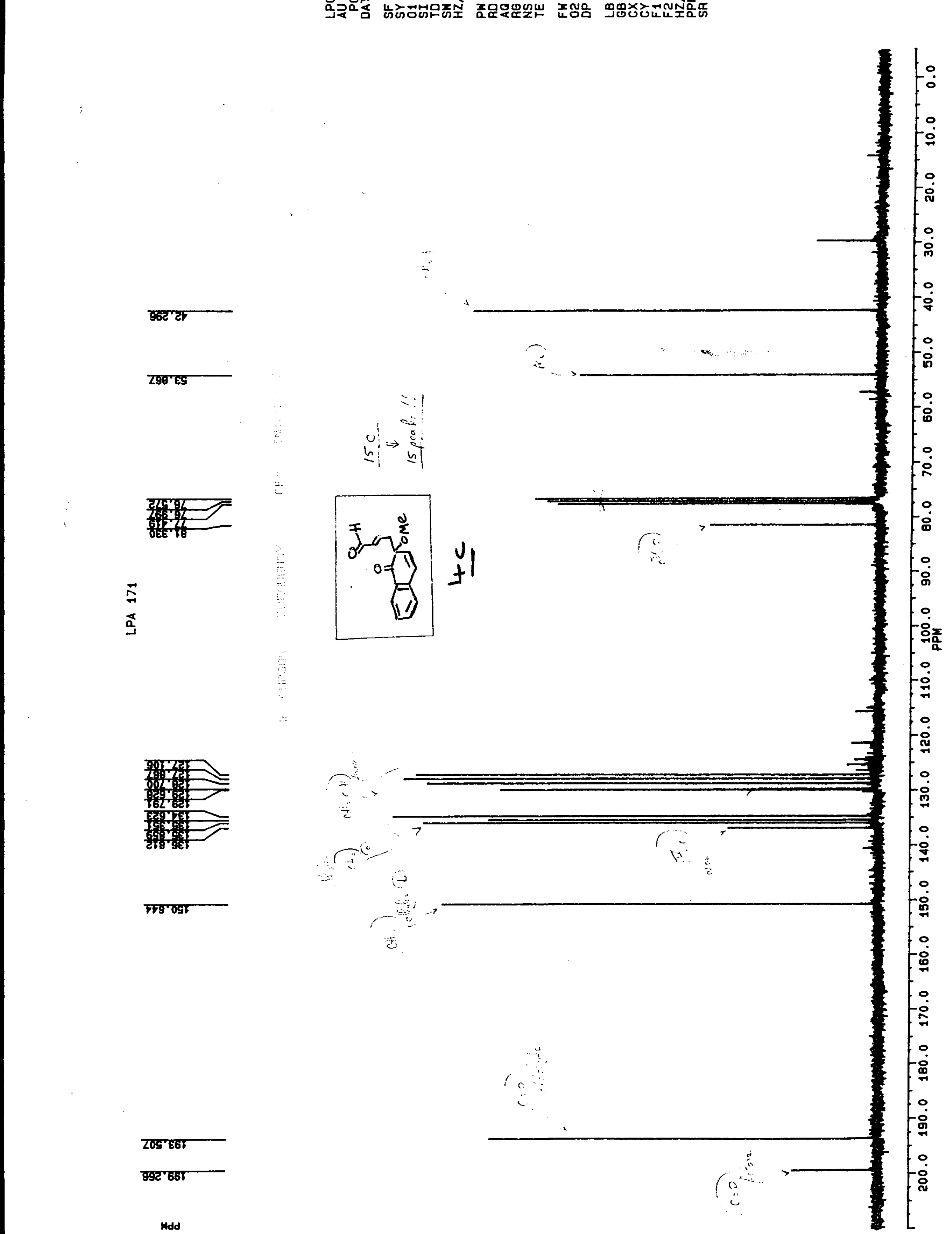
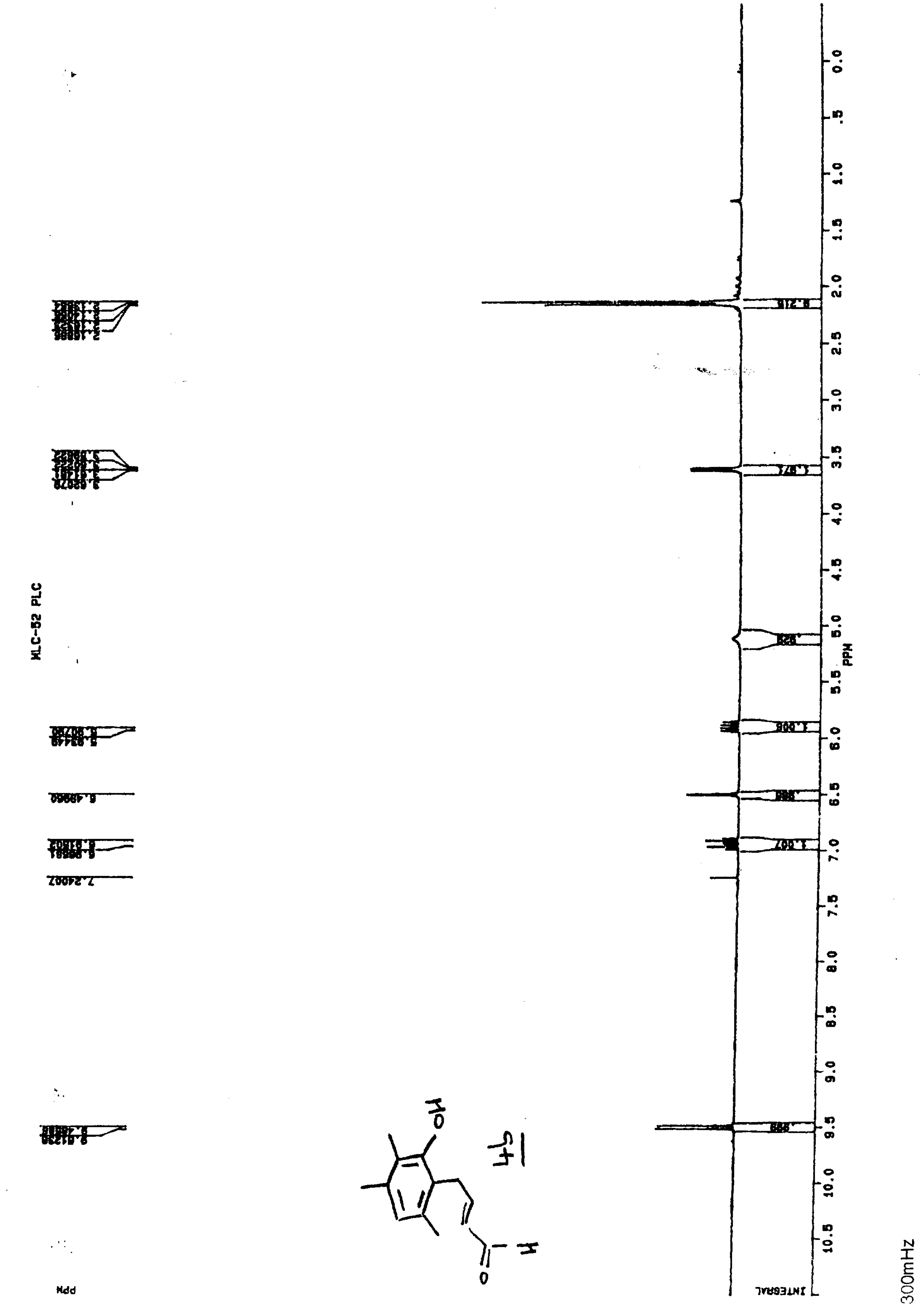


15 C ⇓ 15 peaks !!

4c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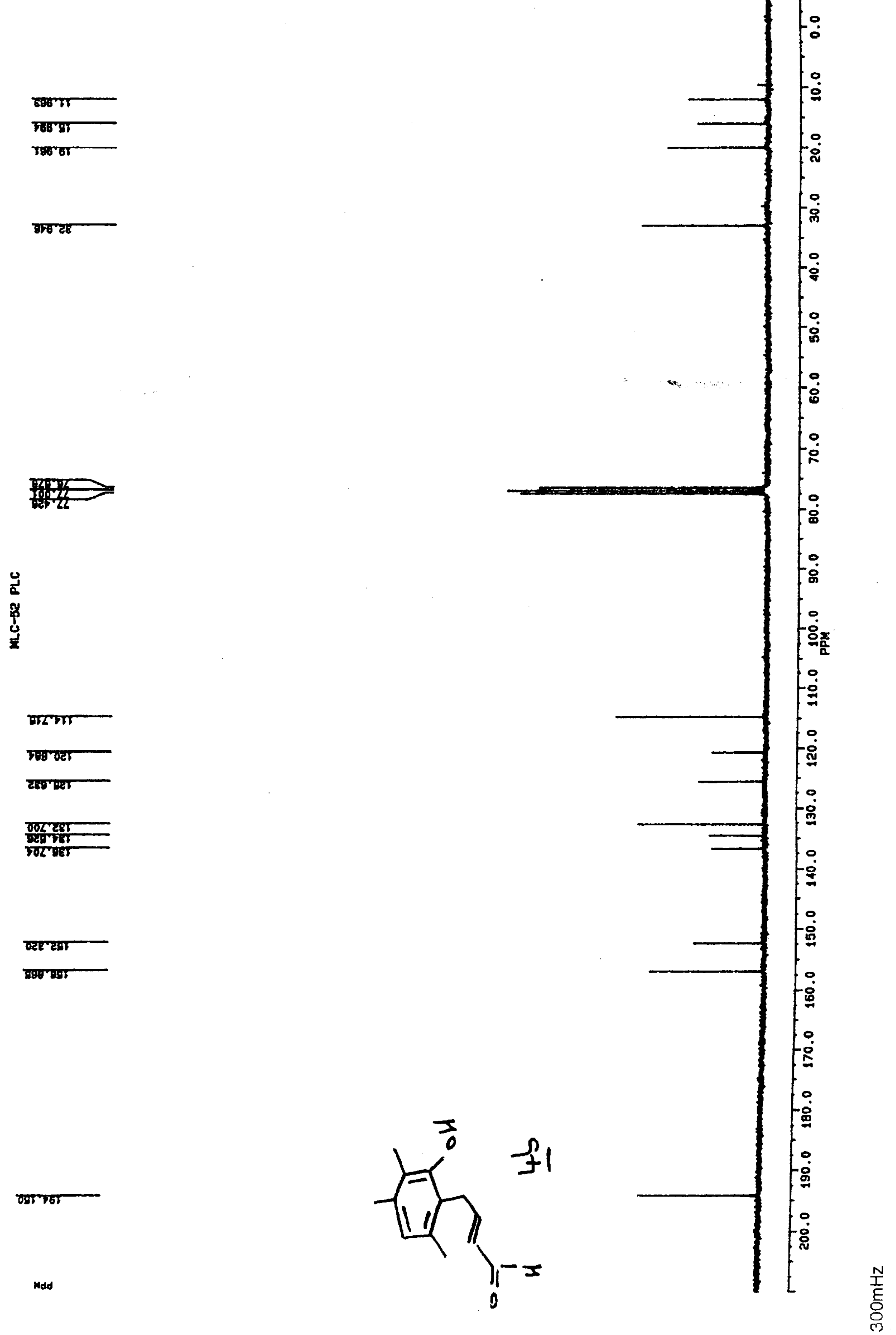
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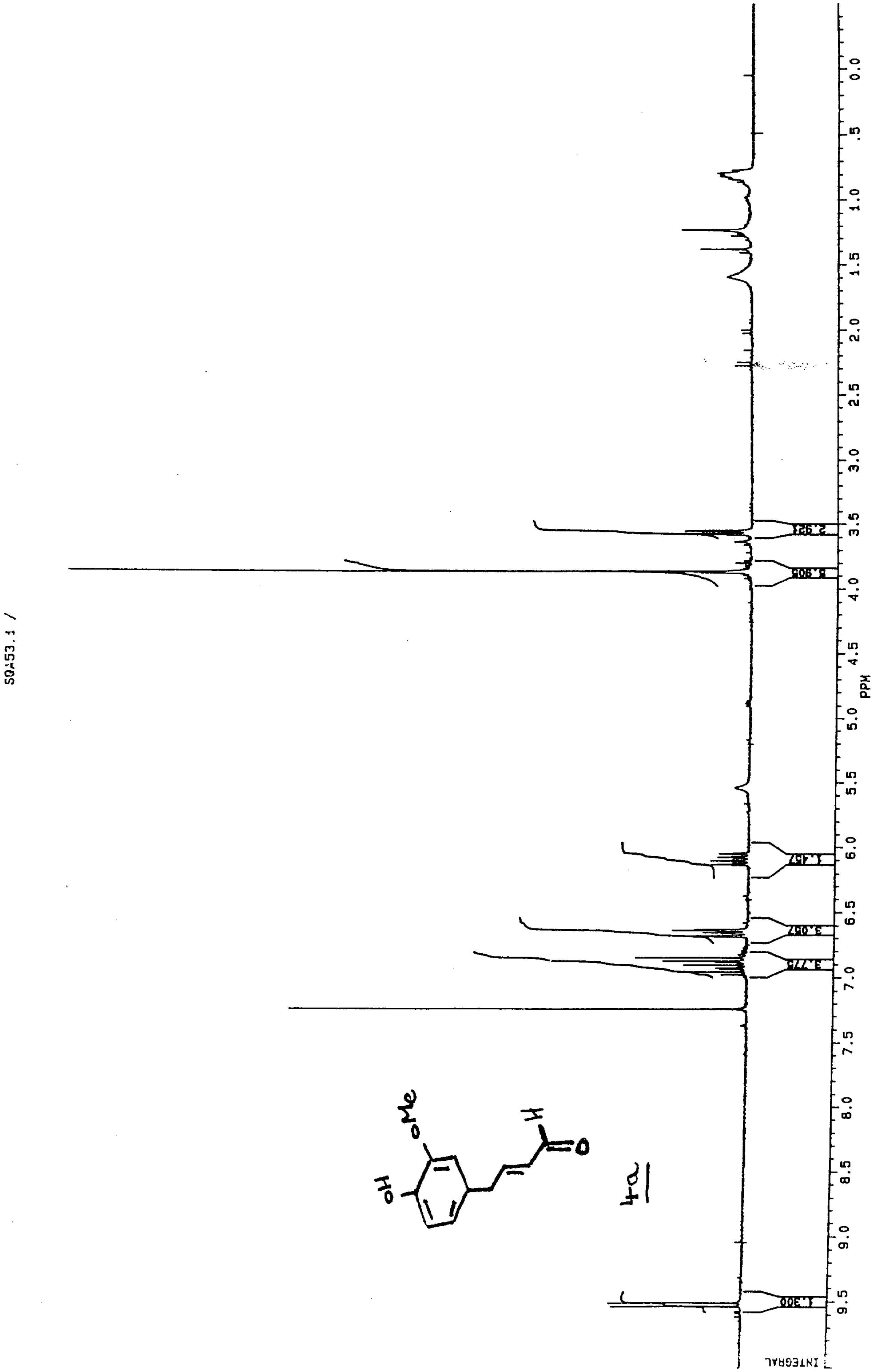
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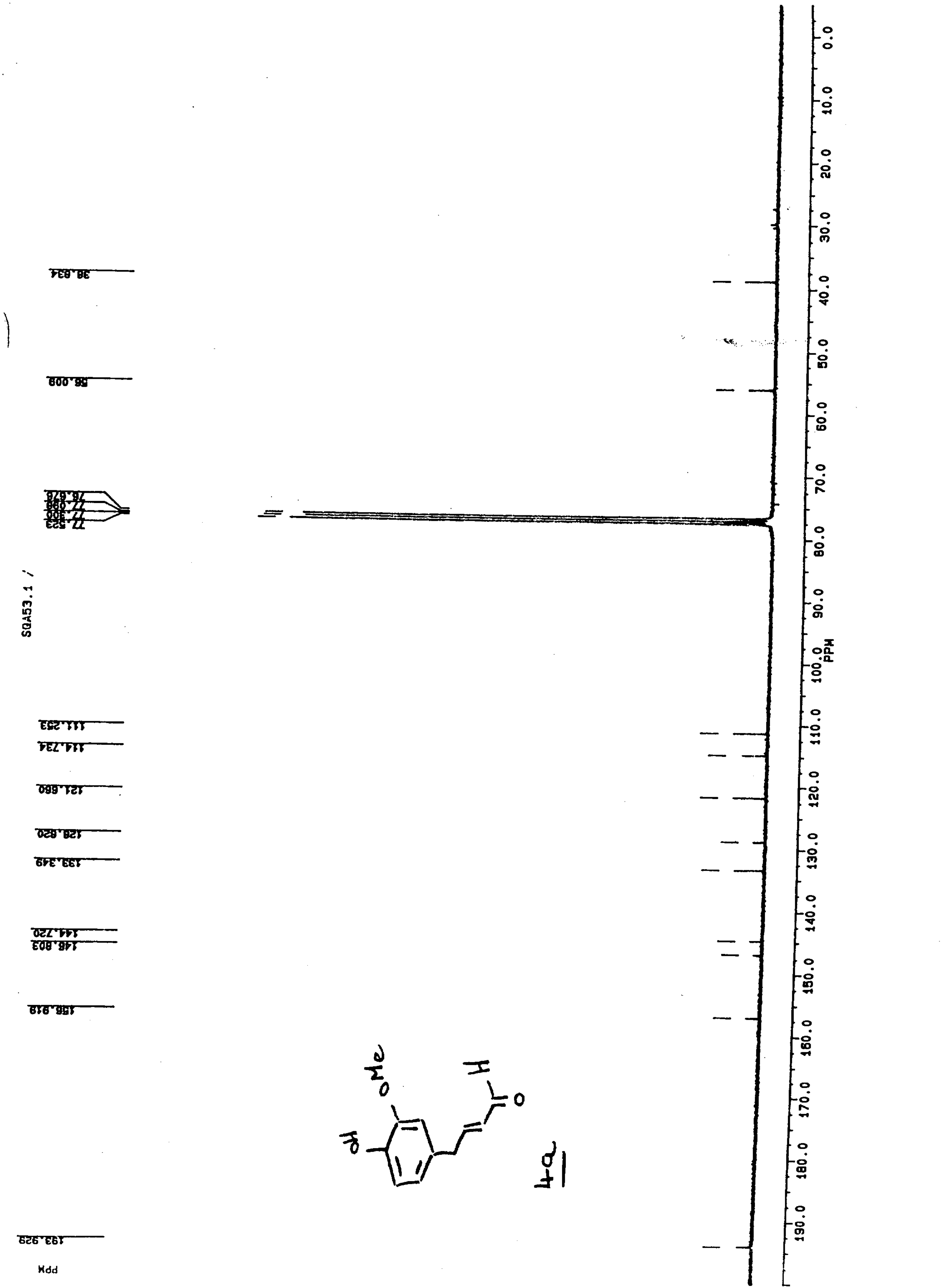
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4a