

Synthesis of (–) Ilimaquinone via a Radical Decarboxylation and Quinone Addition Reaction

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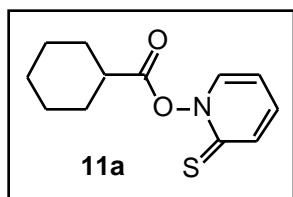
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Supporting Information

General techniques. All reagents were commercially obtained (Aldrich, Acros) at highest commercial quality and used without further purification except where noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation below 45 °C at about 20 mmHg. All nonaqueous reactions were carried out using flame-dried glassware, under an argon atmosphere in dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. THF and Et₂O were distilled from sodium/benzophenone; CH₂Cl₂ and toluene from calcium hydride; and benzene from potassium. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and *p*-anisaldehyde solution and heat as developing agents. E. Merck silica gel (60, particle size 0.040-0.063 mm) was used for flash chromatography. Preparative thin-layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Varian Mercury 300, 400 and/or Unity 500 MHz instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet; d = doublet, t = triplet,

q = quartet, m = multiplet, b = broad. IR spectra were recorded on a Nicolet 320 Avatar FT-IR spectrometer and values are reported in cm^{-1} units. Optical rotations were recorded on a Jasco P-1010 polarimeter. High resolution mass spectra (HRMS) were recorded on a VG 7070 HS mass spectrometer under chemical ionization (CI) conditions or on a VG ZAB-ZSE mass spectrometer under fast atom bombardment (FAB) conditions.

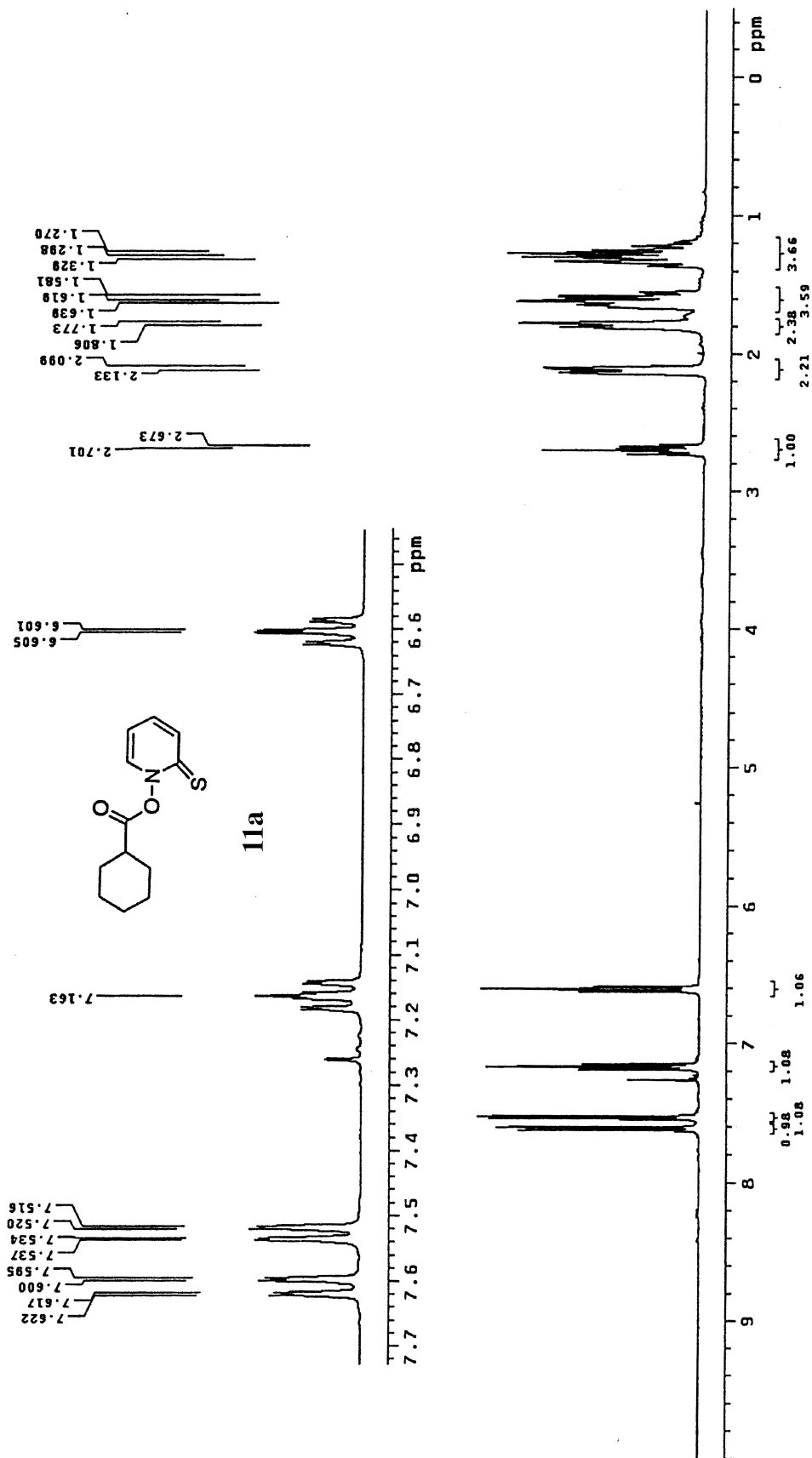
General procedure for the preparation of thiohydroxamic acid derivatives: In a flask protected from the light with aluminum foil at $0\text{ }^{\circ}\text{C}$ was added the corresponding carboxylic acid (6.66 mmol) and 2-mercaptopyridine N-oxide (846 mg, 6.66 mmol) in 5 ml of dry CH_2Cl_2 . DCC (1.37 g, 6.66 mmol) was then added and the mixture was stirred for 12 h at $25\text{ }^{\circ}\text{C}$. After completion of the reaction the solid DCU was removed with gravity filtration and the organic layer was washed with aqueous saturated NaHCO_3 (2 x 10 ml) and then with Brine (1 x 10 ml). While minimizing exposure to light, the combined aqueous layers were extracted with CH_2Cl_2 (2 x 10 ml) and the organic layers were dried (MgSO_4), filtered and concentrated under reduced pressure at $25\text{ }^{\circ}\text{C}$. The residue was filtered through a short pad of silica gel (CH_2Cl_2 : Et_2O :hexanes= 1:2:7), concentrated under vacuum at $25\text{ }^{\circ}\text{C}$ and crystallized from CH_2Cl_2 /hexane.

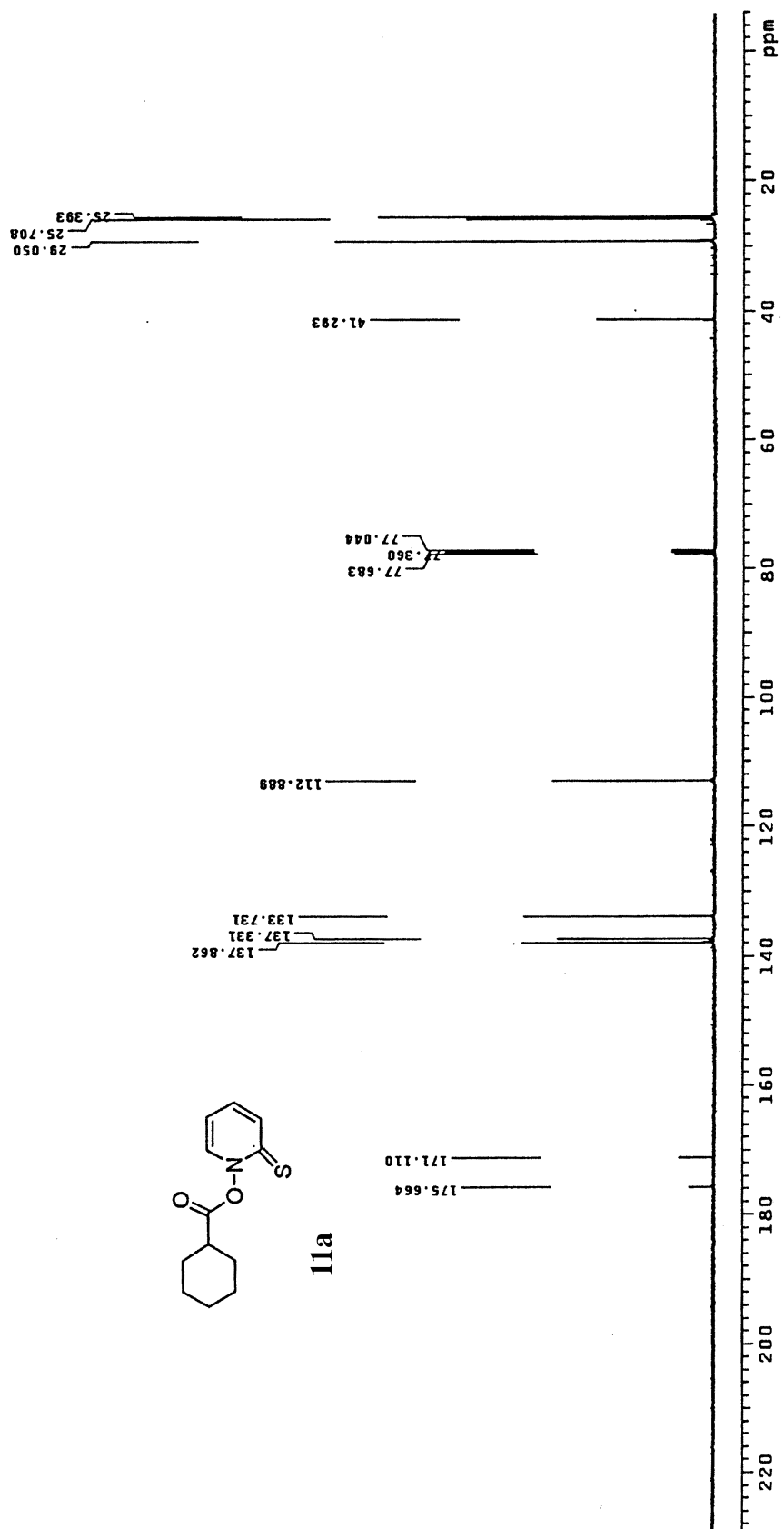


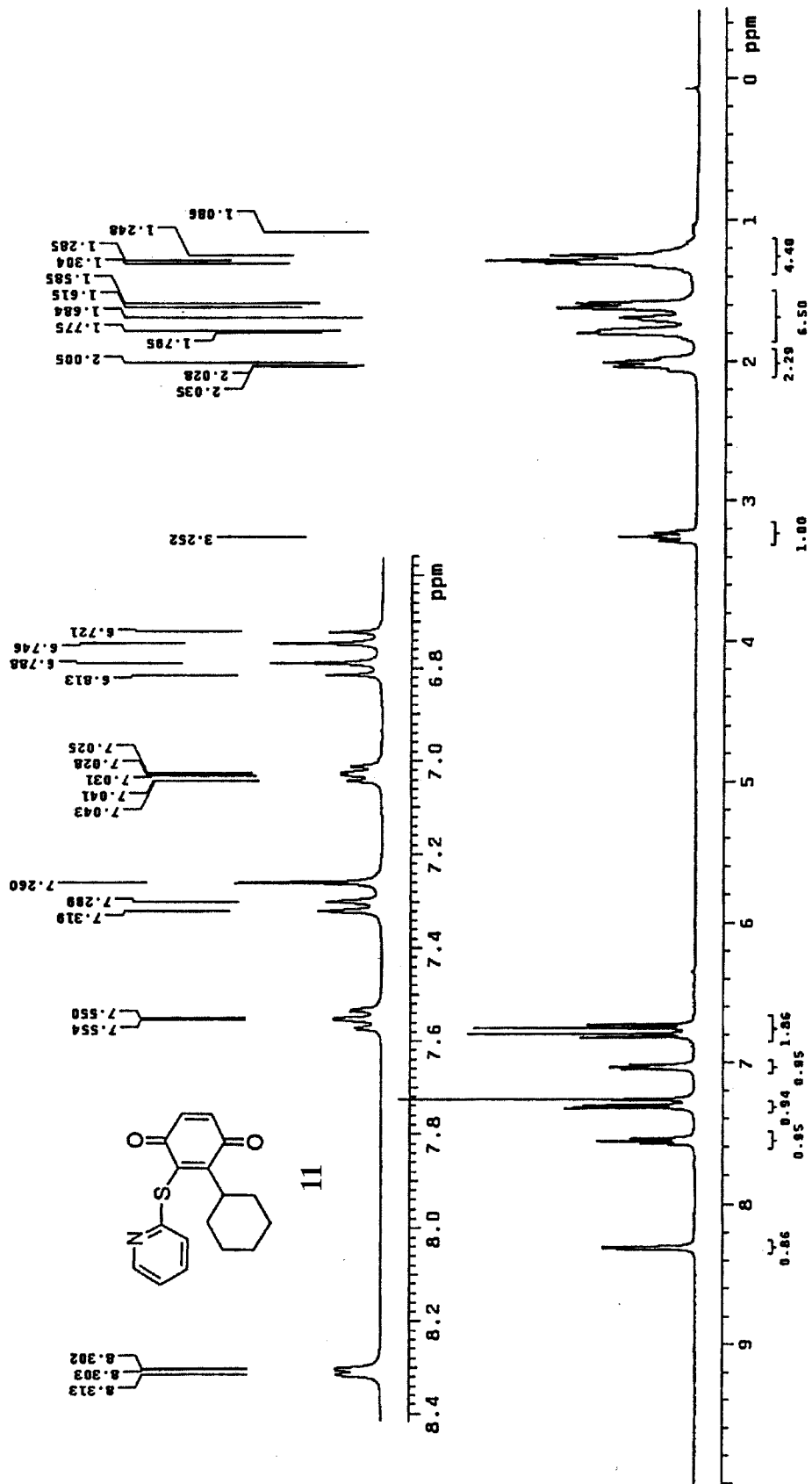
Compound 11a: (0.712g, 3.00 mmol, 80%); Pale green solid; $R_f = 0.8$ (75% ether in hexanes); IR (film) ν_{max} 2991, 2927, 2857, 1780, 1527; ^1H NMR (400MHz, CDCl_3) 7.61 (dd, 1H, $J = 2\text{Hz}, 8\text{Hz}$), 7.53 (dd, 1H, $J = 2\text{Hz}, 8\text{Hz}$), 7.16 (dt, 1H, $J = 2\text{Hz}, 8\text{Hz}$), 6.61 (dt, 1H, $J = 2\text{Hz}, 8\text{Hz}$), 2.70 (t, 1H, $J = 7\text{Hz}$), 1.2-2.2 (Cpx, 10H); ^{13}C NMR (400MHz, CDCl_3) 175.7, 171.1, 137.9, 137.3, 133.7, 112.9, 41.3, 29.1, 25.7, 25.4; HRMS calc for $\text{C}_{17}\text{H}_{15}\text{NO}_2\text{S}$ ($\text{M}+\text{Cs}^+$) 369.9874, found 369.9851.

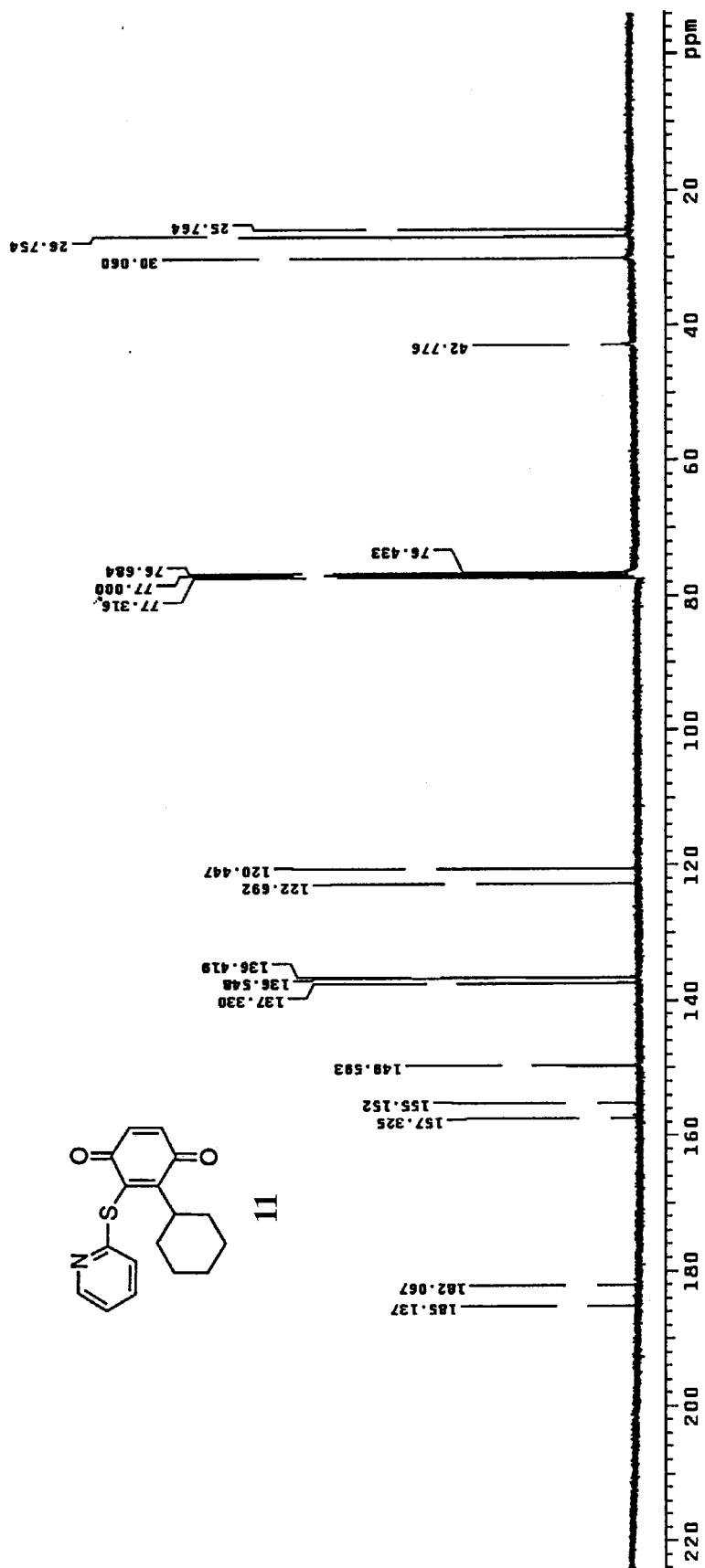
Compound 8: (94%); yellow solid; $R_f = 0.25$ (silica, 50 % ether in hexanes); ^1H NMR (500 MHz, CDCl_3) 7.62 d, 1H, $J = 8\text{Hz}$), 7.44 d, 1H, $J = 8\text{Hz}$), 7.16 (t, 1H, $J = 8\text{Hz}$), 6.59 (t, 1H, $J = 8\text{Hz}$), 4.48 (s, 2H), 2.79 (d, 1H, $J = 16.0\text{Hz}$), 2.66 (d, 1H, $J = 16.0\text{Hz}$), 1.052.40 (m, 12H), 1.03 (s, 3H), 0.92 (d, 3H, $J = 6.0\text{Hz}$), 0.84 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3) 175.4, 166.6, 159.4, 137.7, 137.3, 133.4, 112.5, 103.1, 49.4, 41.6, 40.0, 39.6, 37.8, 36.6, 32.7, 28.2, 27.1, 22.4, 20.4, 16.9, 16.2.

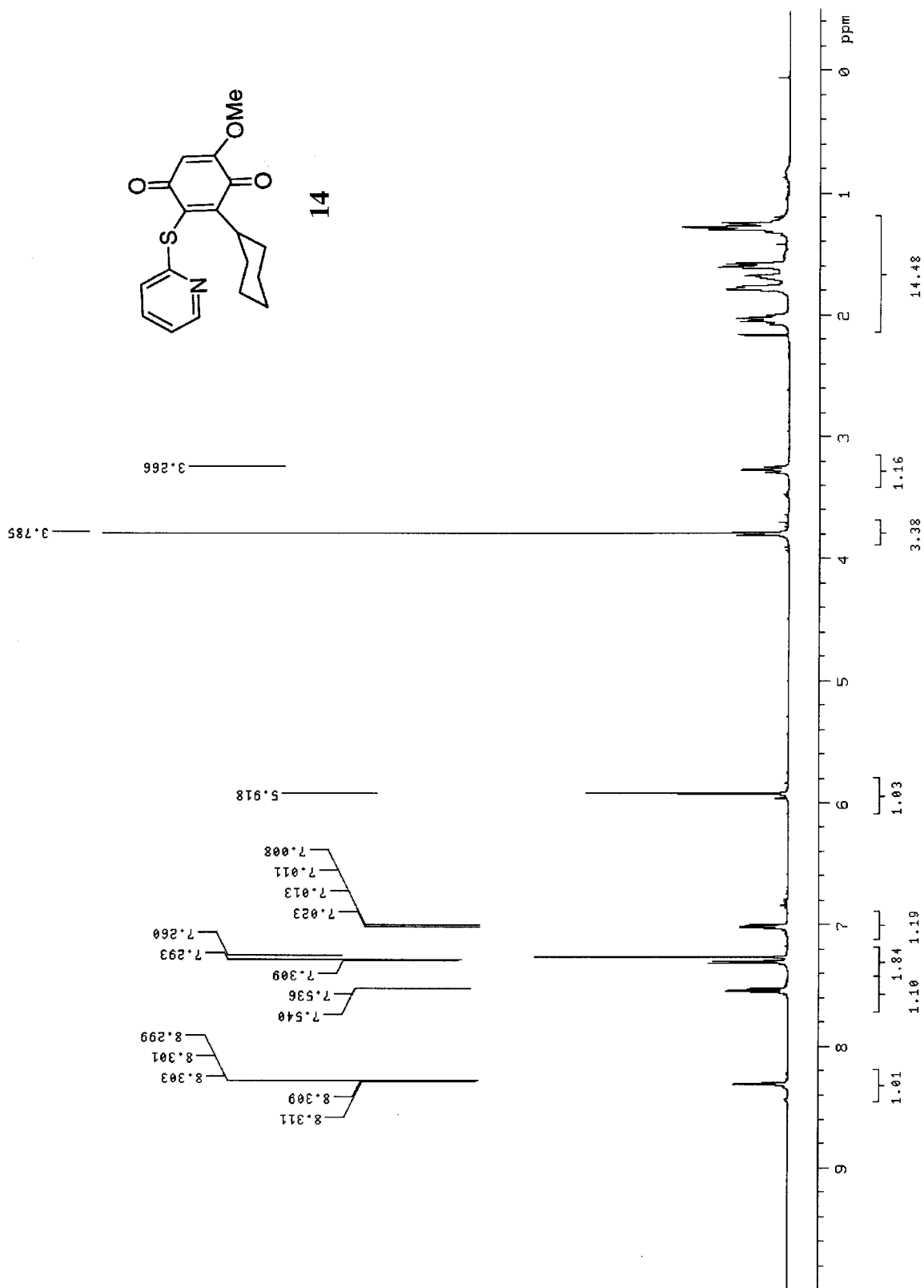
Quinone 11: In a flask protected from the light with aluminum foil under argon atmosphere was added ester **11a** (3.10 g, 13.2 mmol) and 1,4-benzoquinone (**9**) (4.28 g, 39.6 mmol) in 40 ml of dry CH_2Cl_2 at 0 °C. The reaction mixture was subsequently exposed to light using two 500 W halogen lamps from a distance of 30 cm, while maintaining the temperature at 0-5 °C. After the end of the reaction (approximately 3h), the crude reaction mixture was concentrated and the residue purified with flash chromatography (silica, 10% CH_2Cl_2 , 5-30 % Et_2O in hexanes) to afford quinone adduct **11** (3.44 g, 11.5 mmol, 87 % yield). **11:** Orange solid; $R_f = 0.5$ (50% ether in hexanes); IR (film) ν_{max} 3050, 2927, 1655; ^1H NMR (400MHz, CDCl_3) 8.31 (d, 1H, $J = 4.4$ Hz), 7.55 (t, 1H, $J = 8$ Hz), 7.30 (d, 1H, $J = 8$ Hz), 7.01 (m, 1H), 6.80 (d, 1H, $J = 10$ Hz), 6.72 (d, 1H, $J = 10$ Hz), 3.25 (m, 1H), 2.1-1.95 (m, 2H), 1.8-1.6 (m, 4H), 1.4-1.2 (m, 4H); ^{13}C NMR (400MHz, CDCl_3) 185.1, 182.1, 157.3, 155.2, 149.6, 137.3, 136.6, 136.4, 122.7, 120.4, 42.8, 30.1, 26.8, 25.8; HRMS calc for $\text{C}_{17}\text{H}_{17}\text{NO}_2\text{S}$ ($\text{M}+\text{Cs}^+$) 432.0031, found 432.0043.

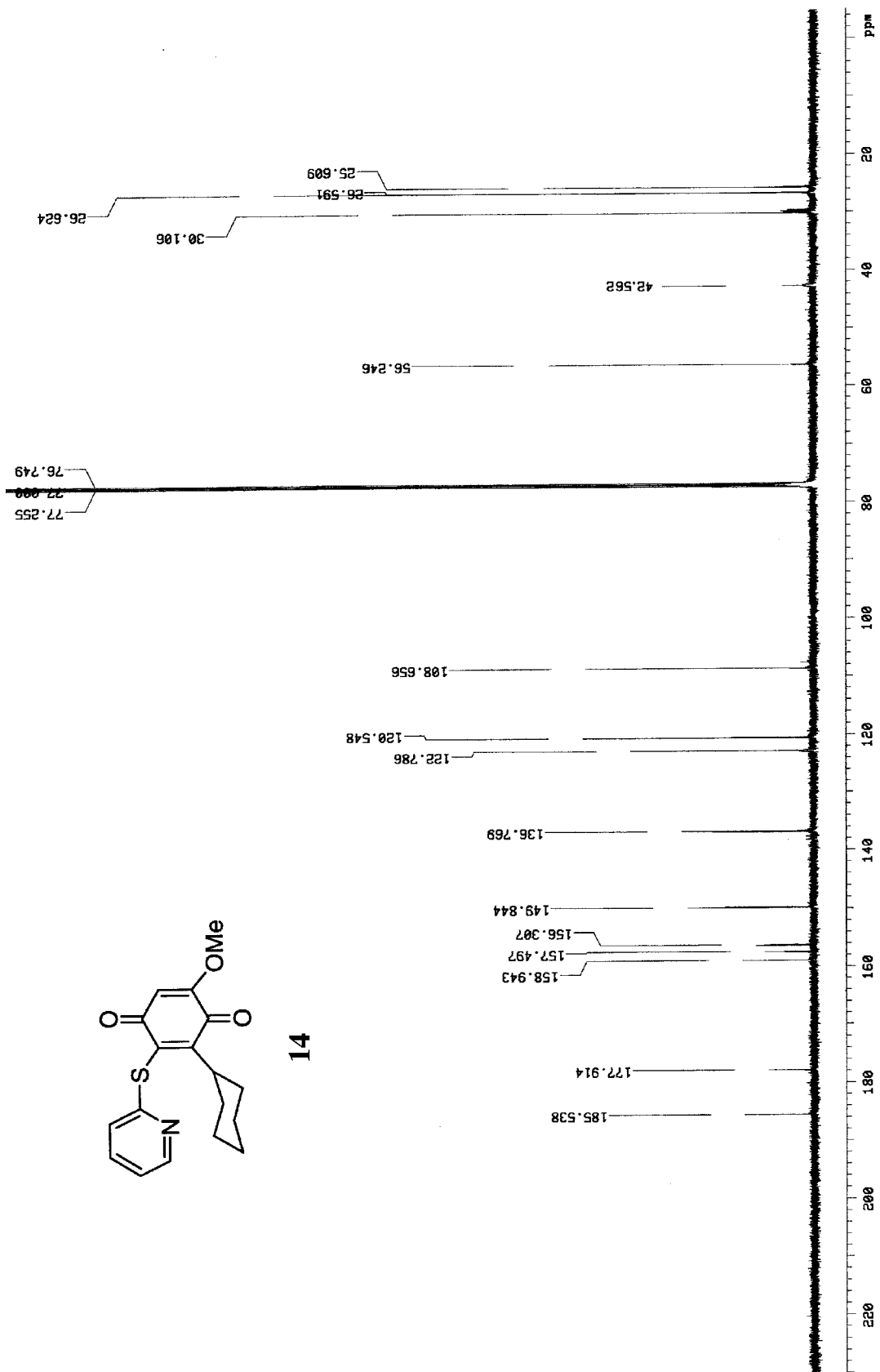


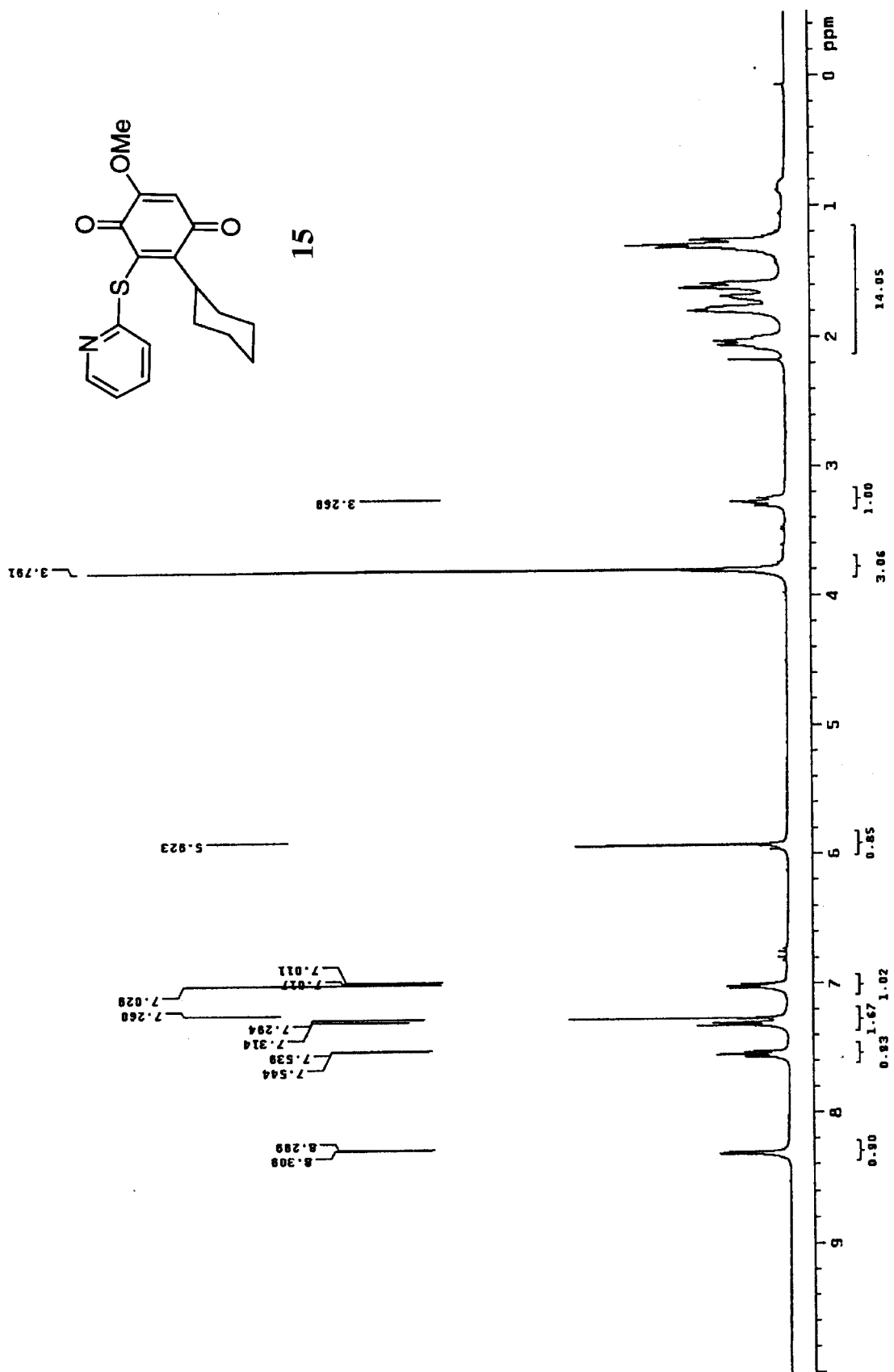


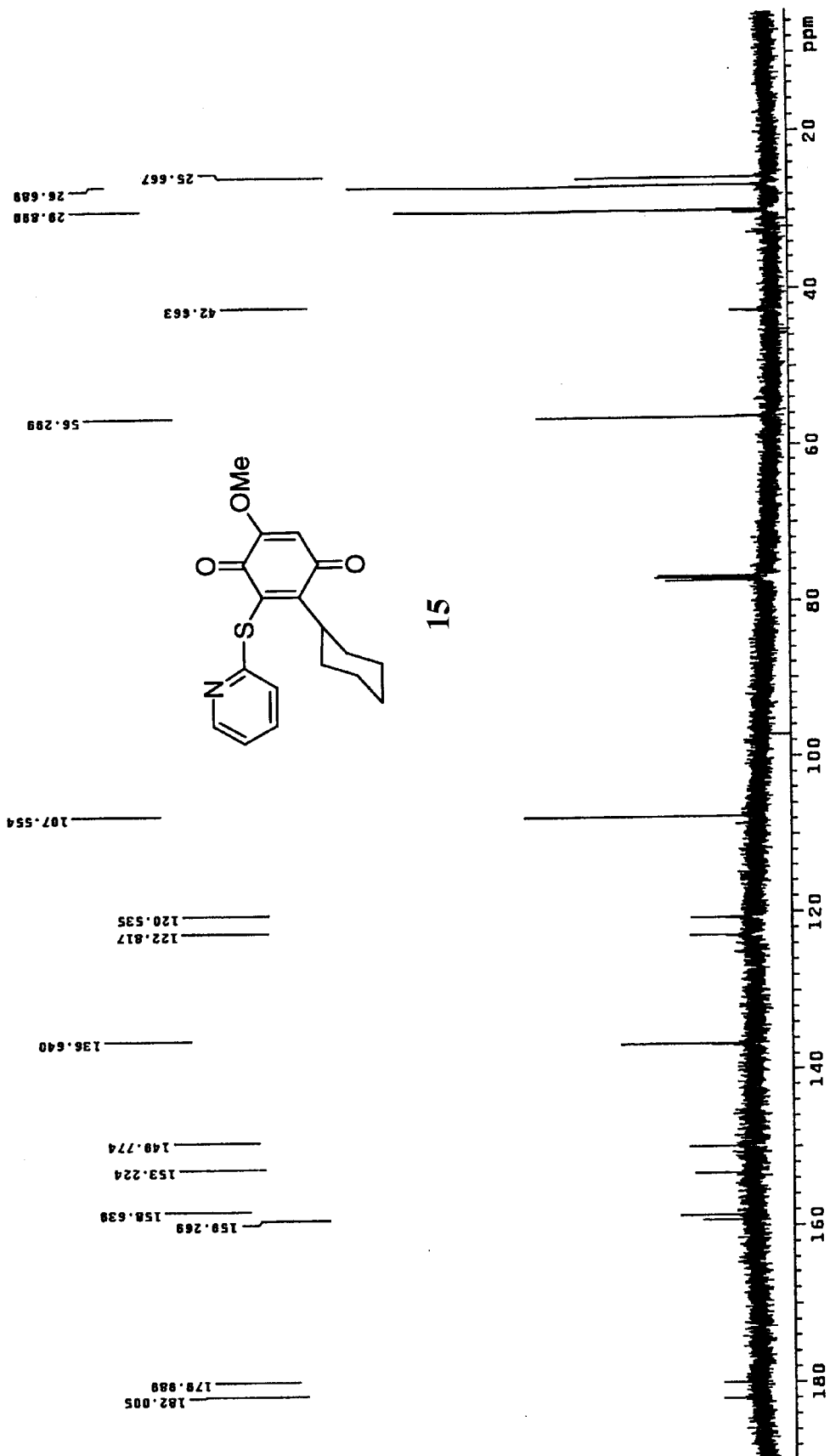


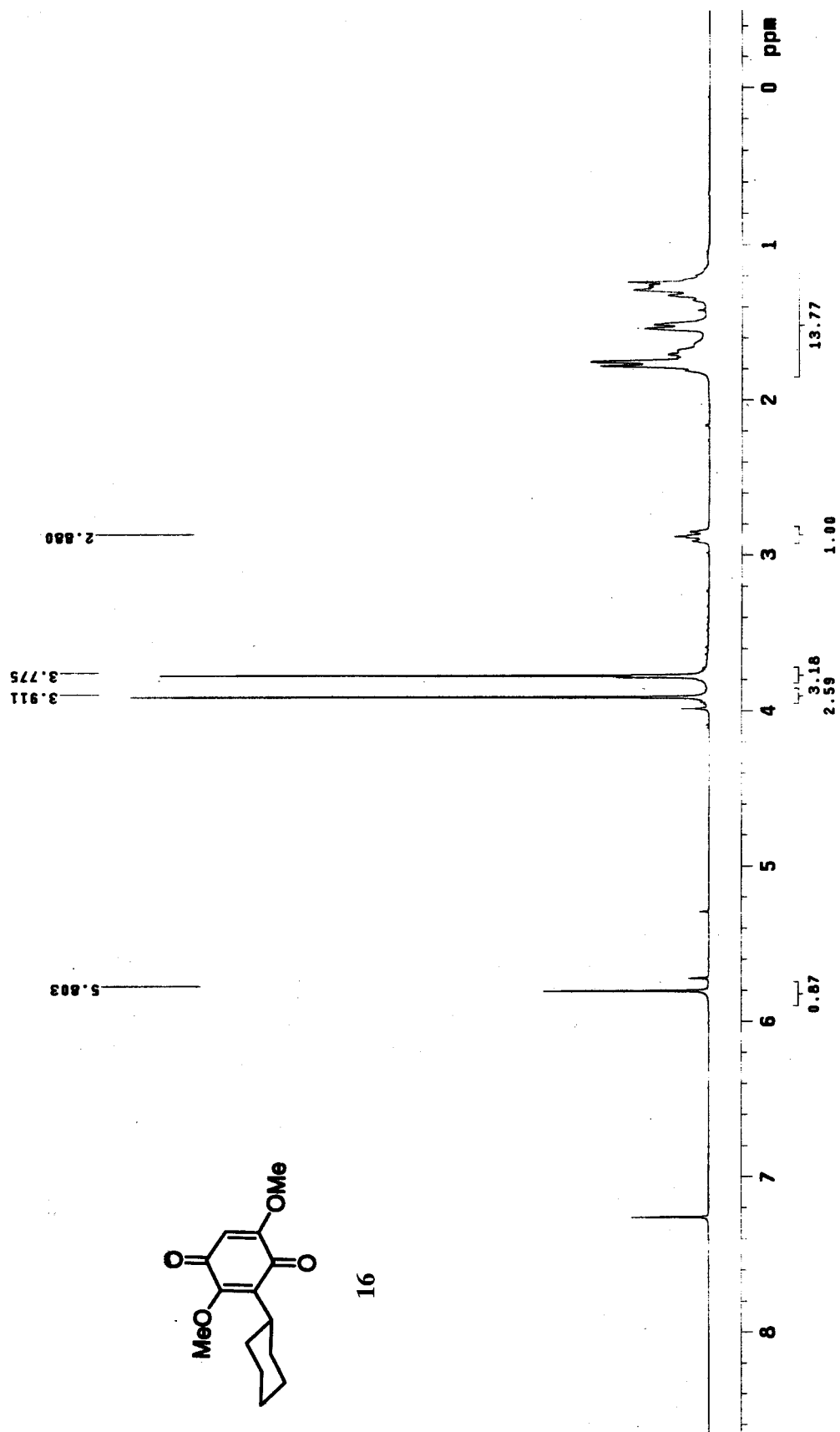


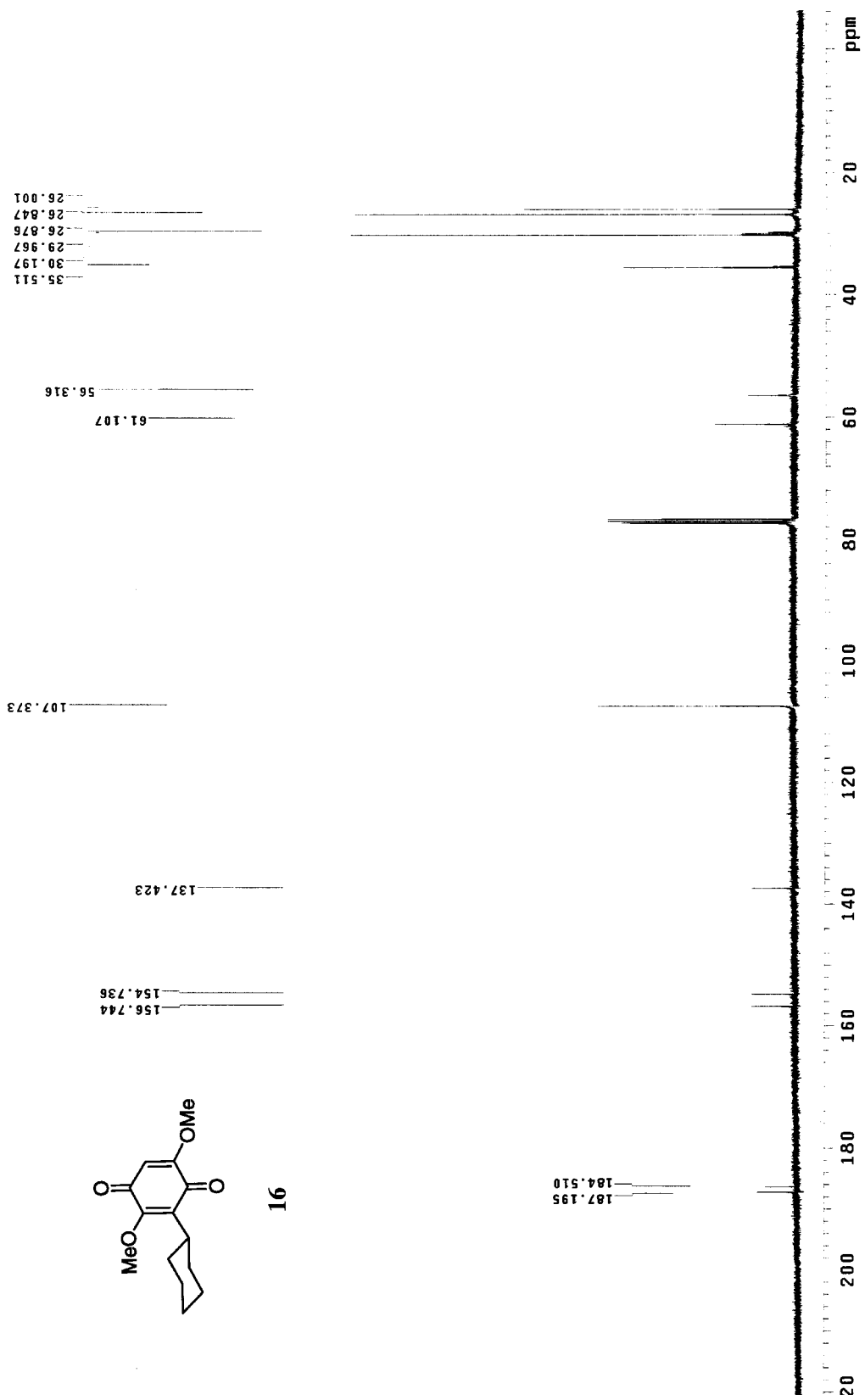


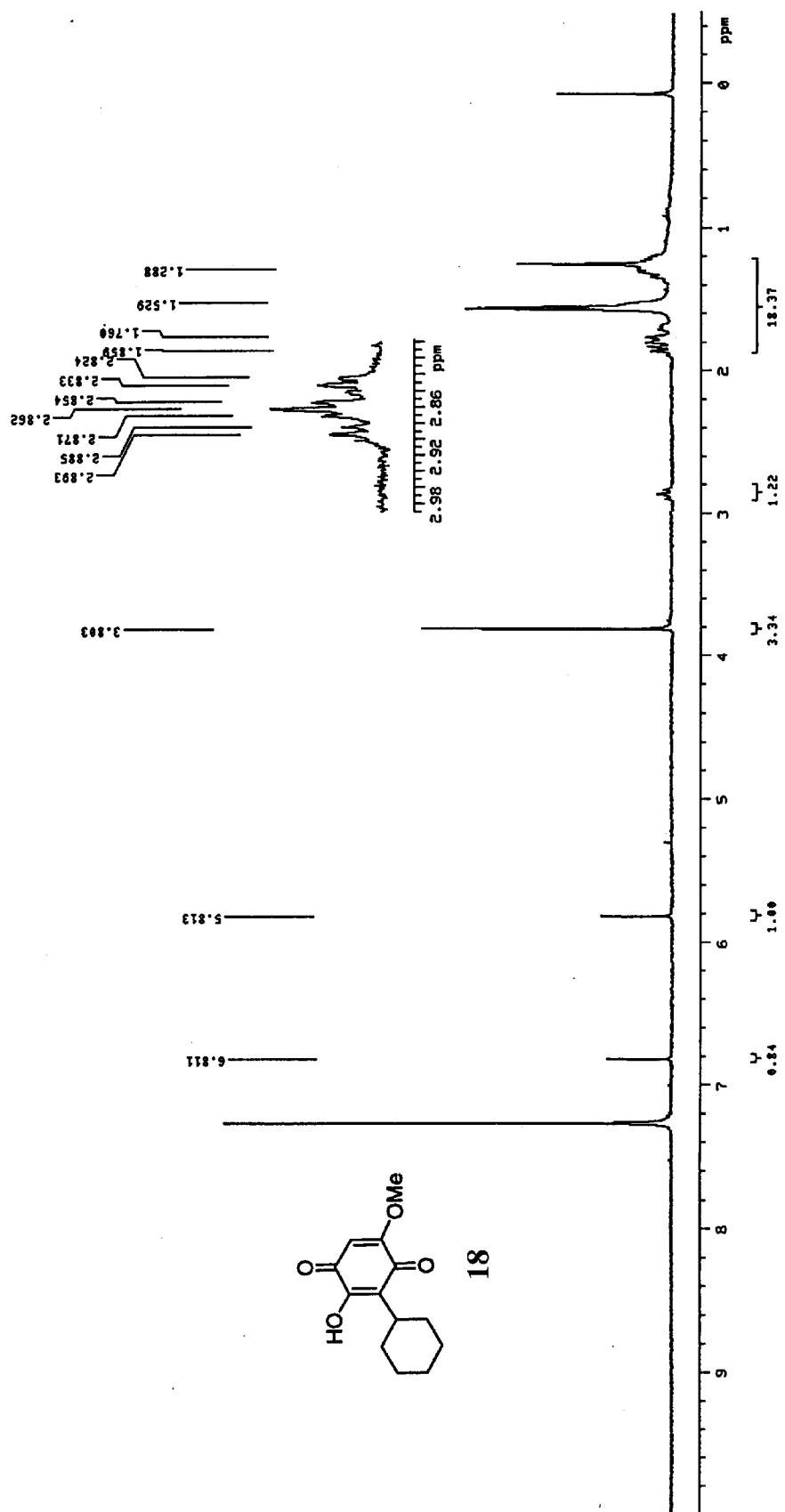


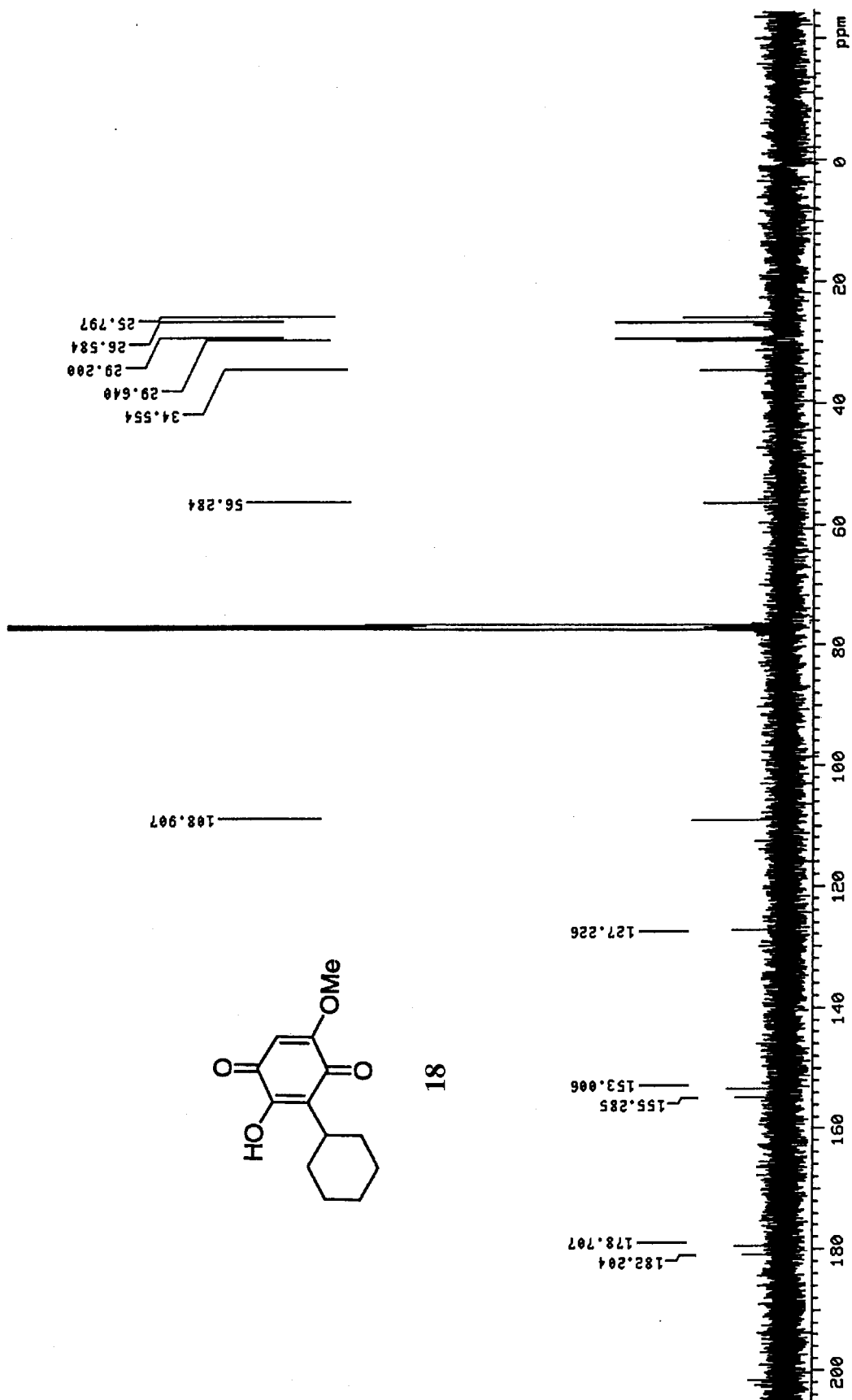


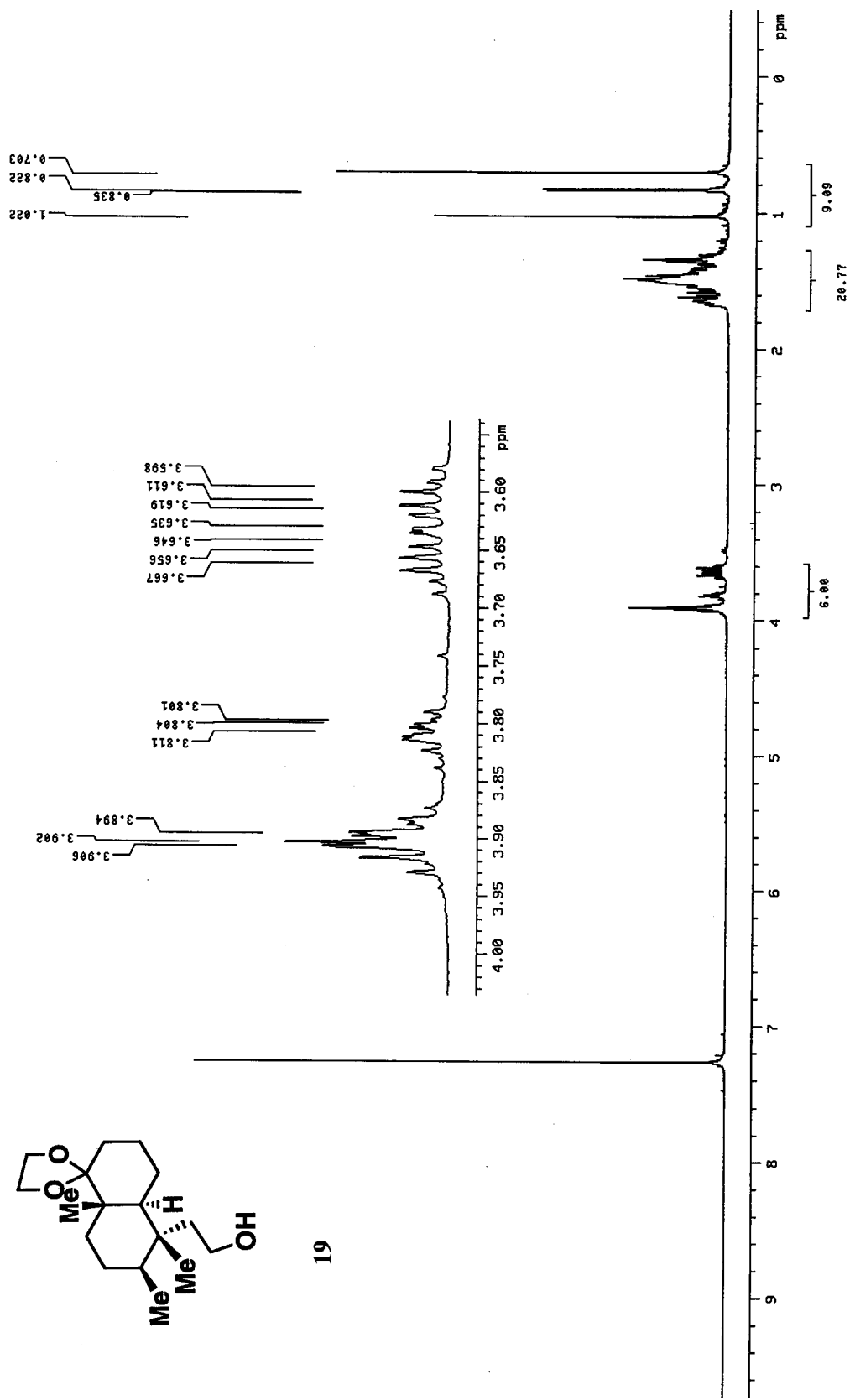


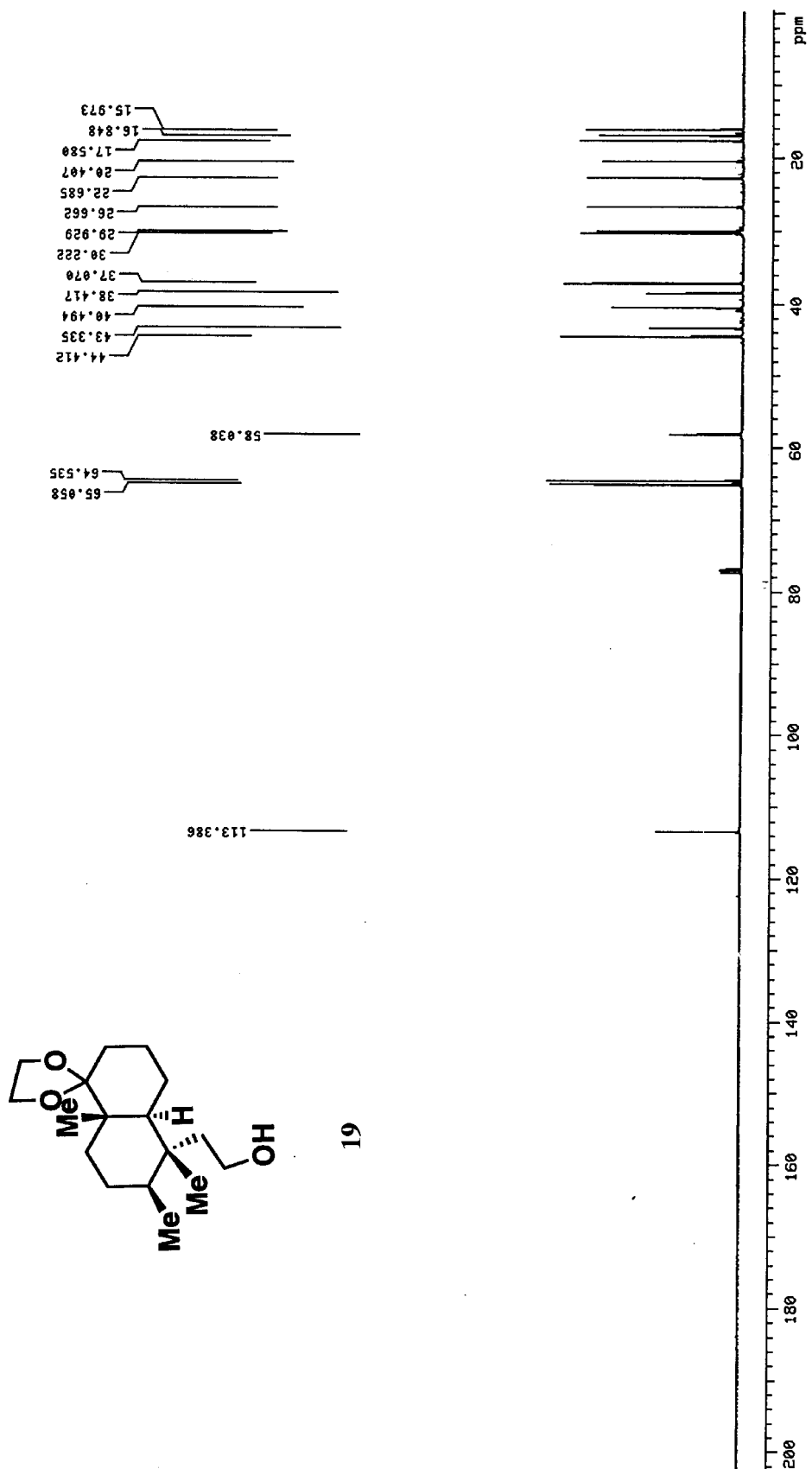


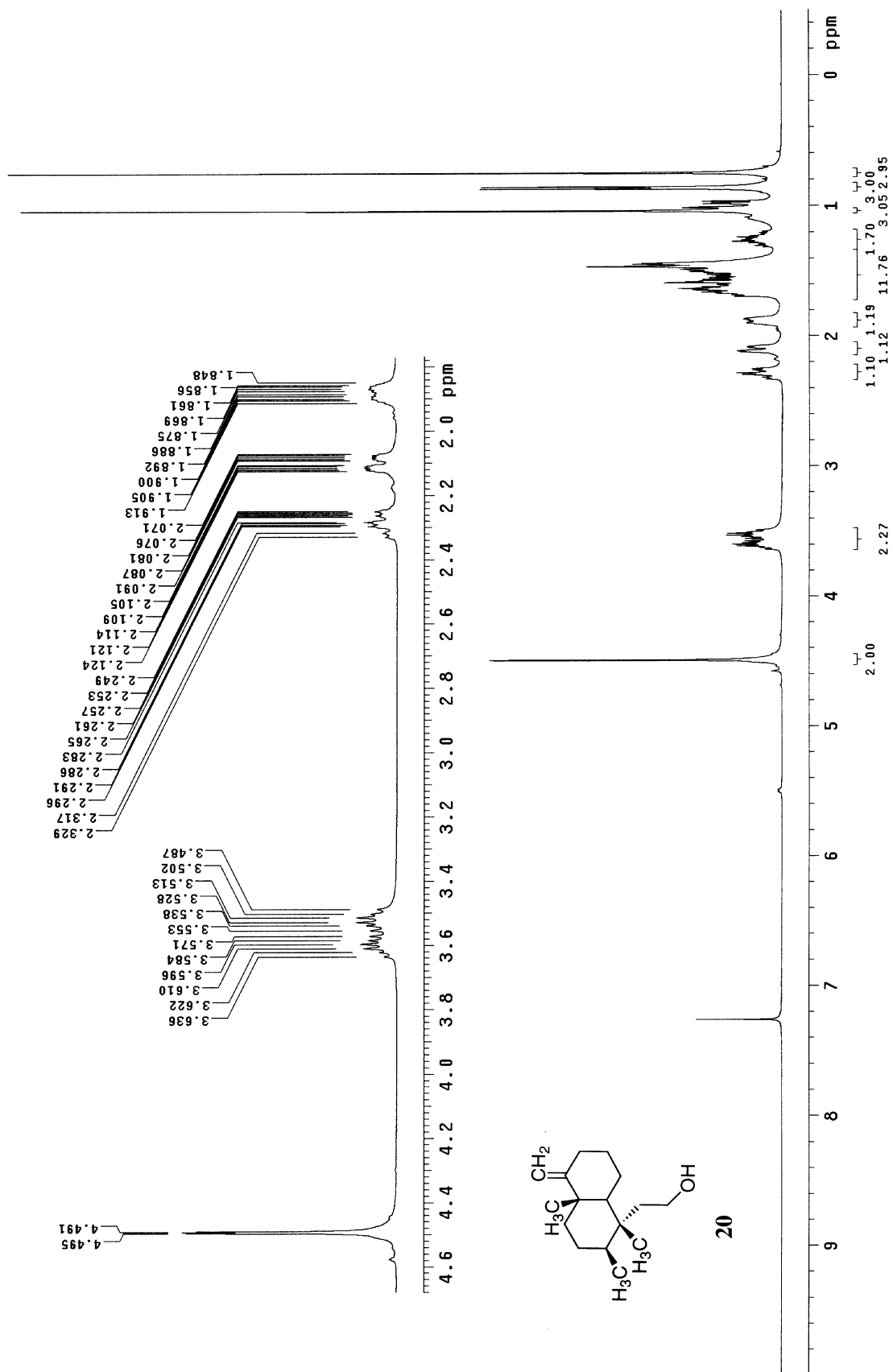


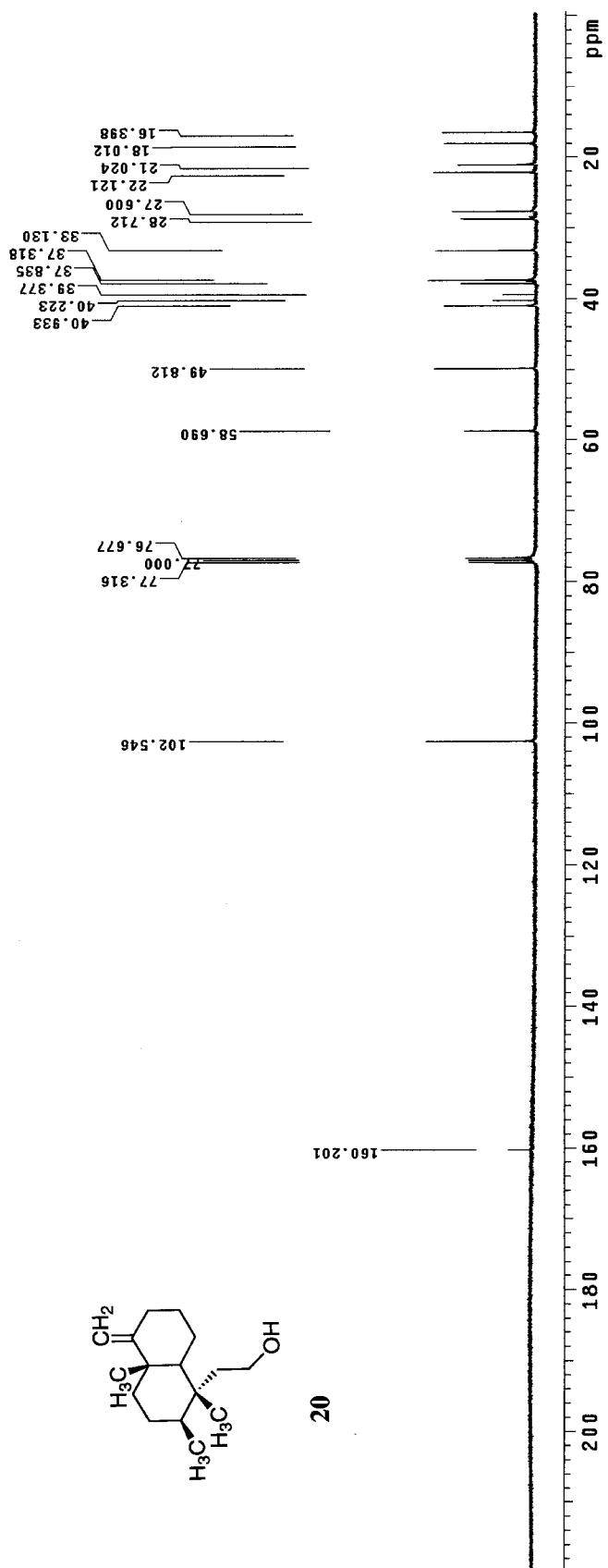


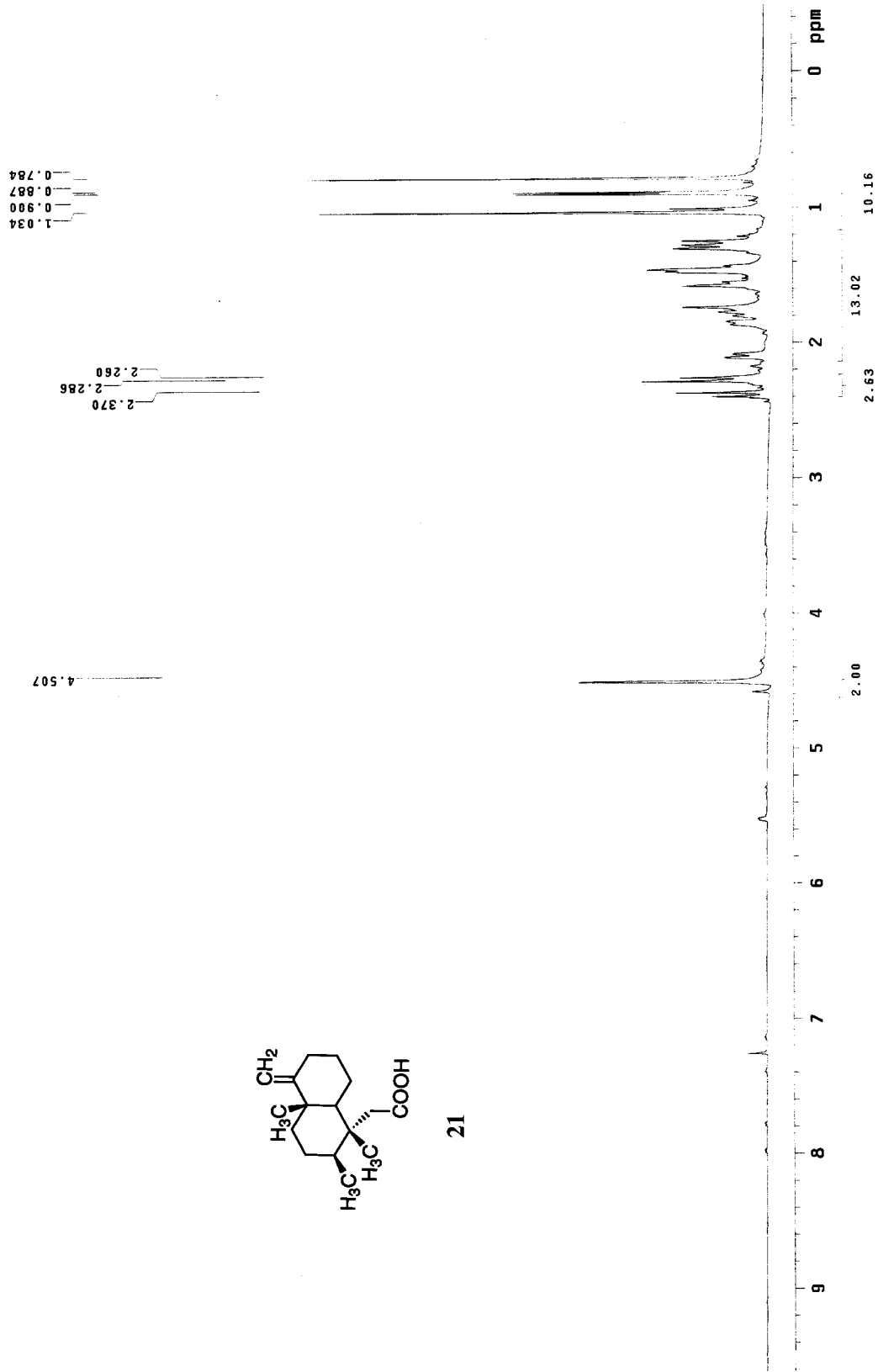




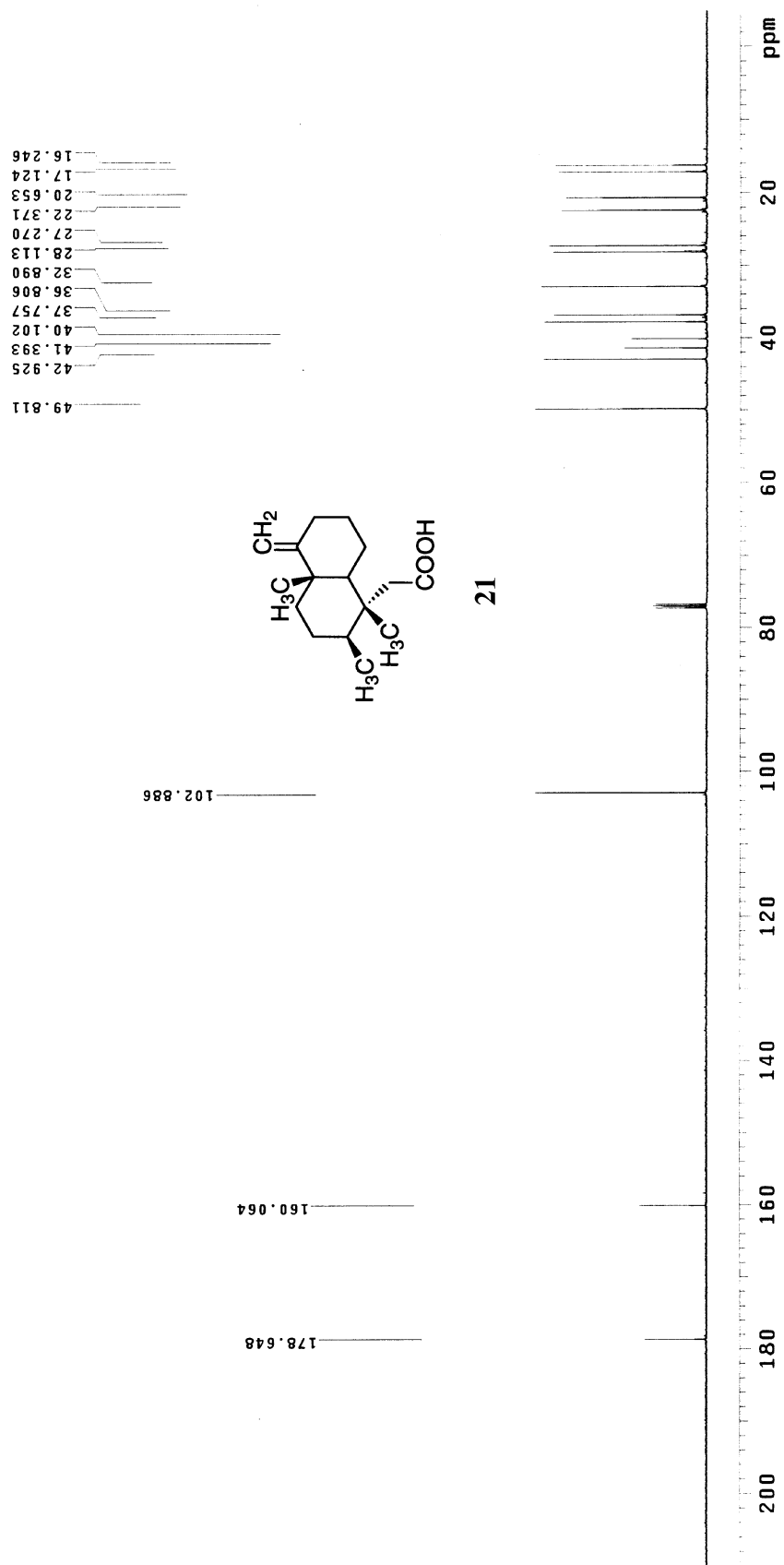


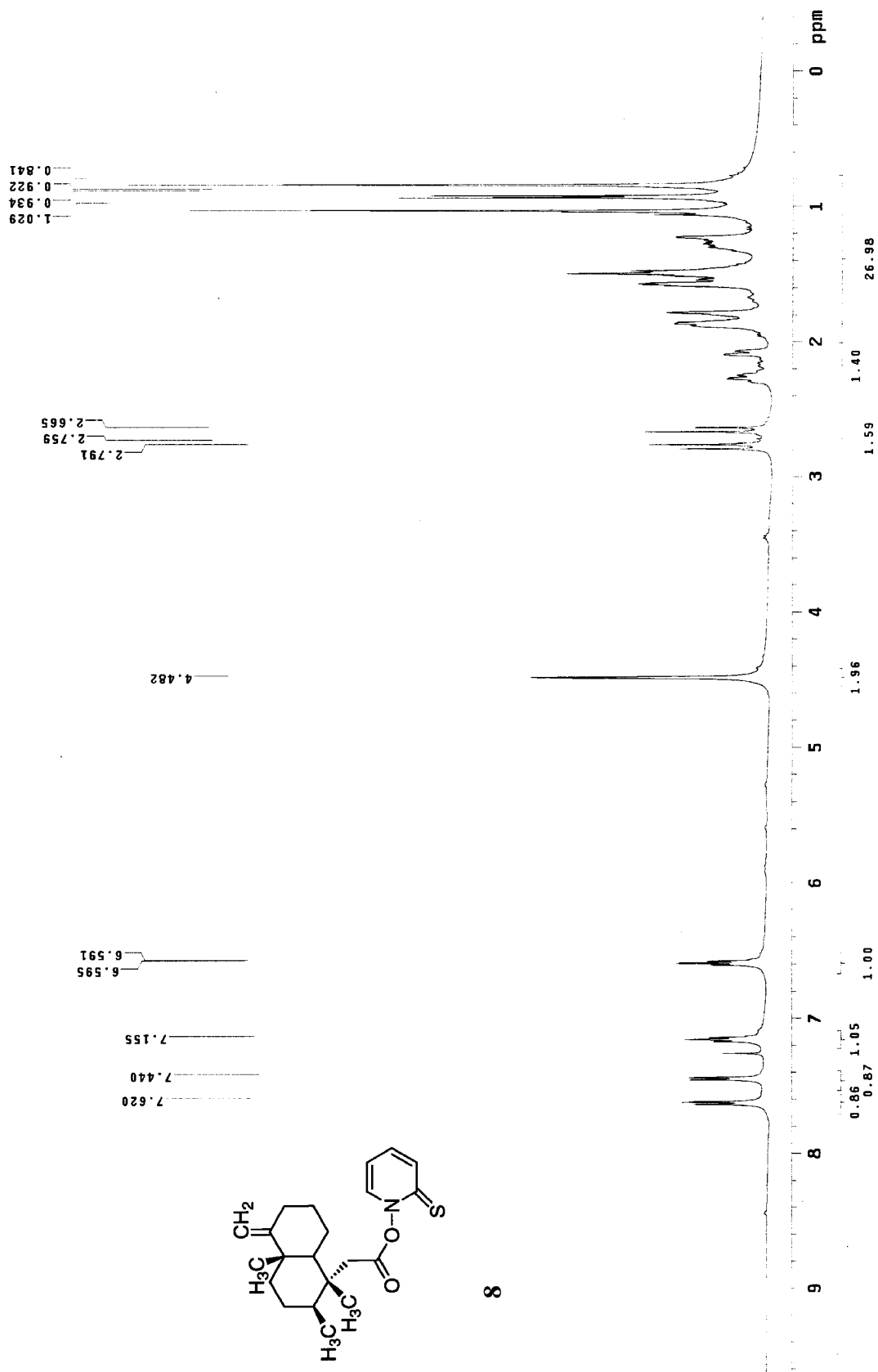




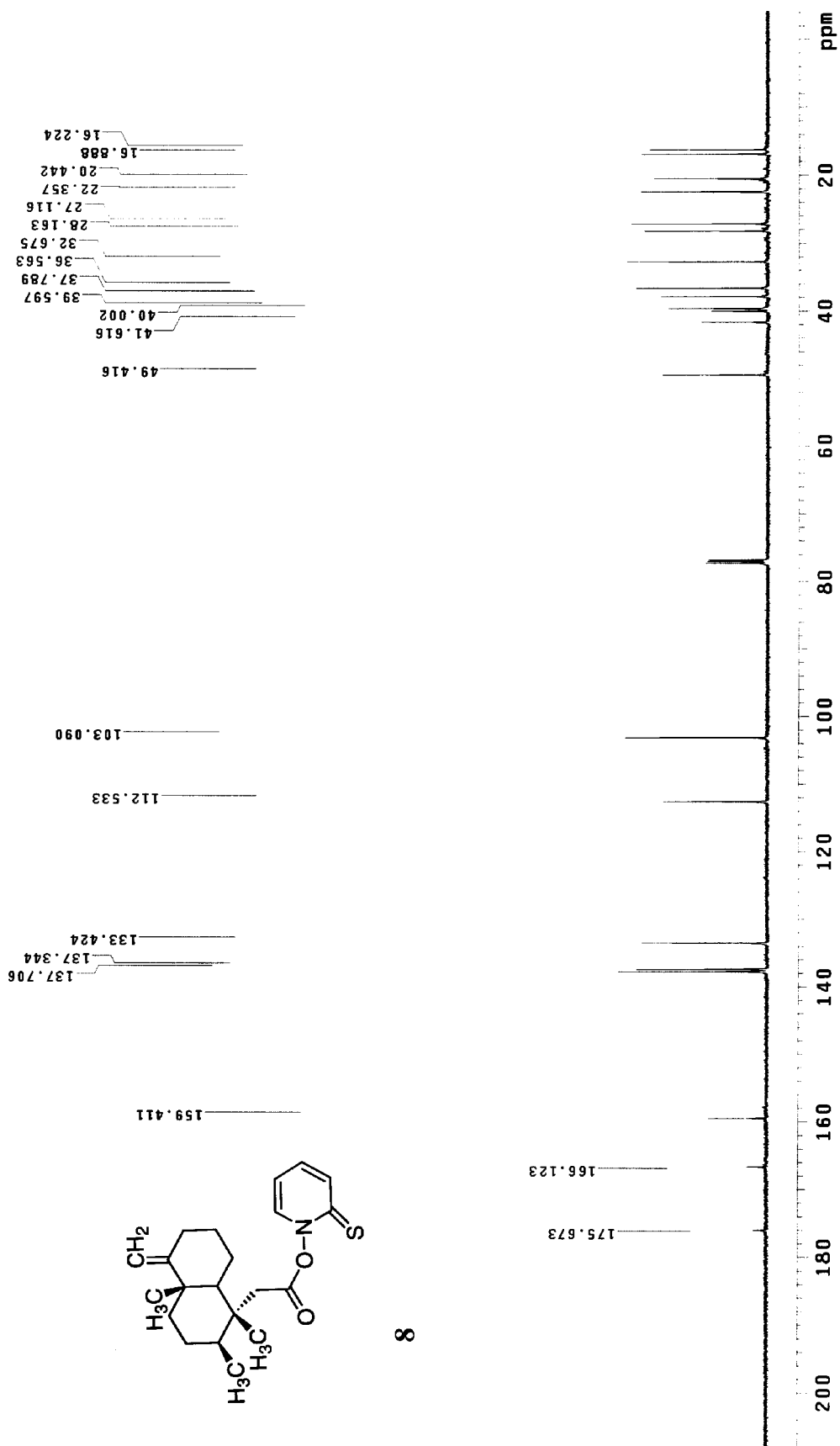


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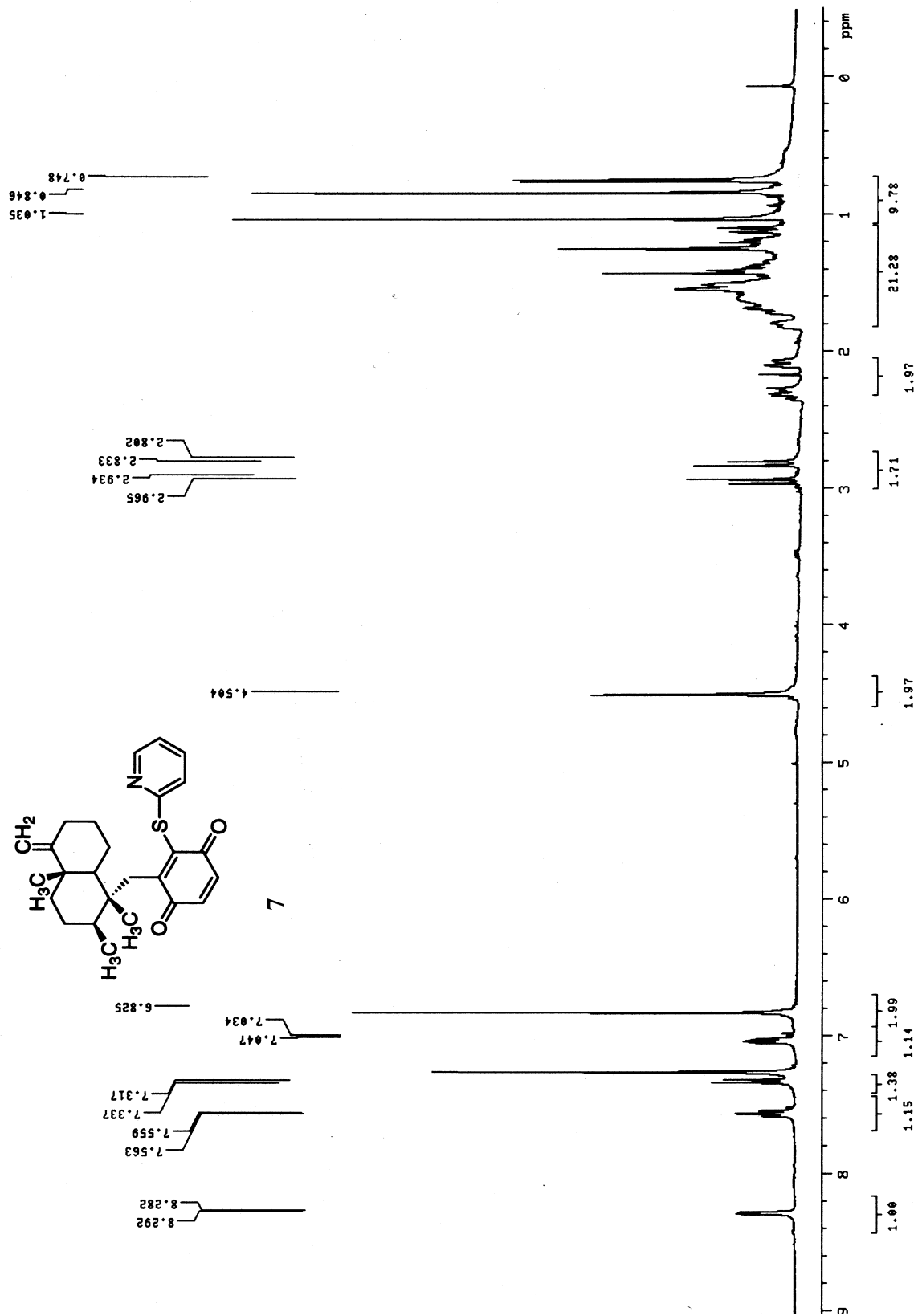


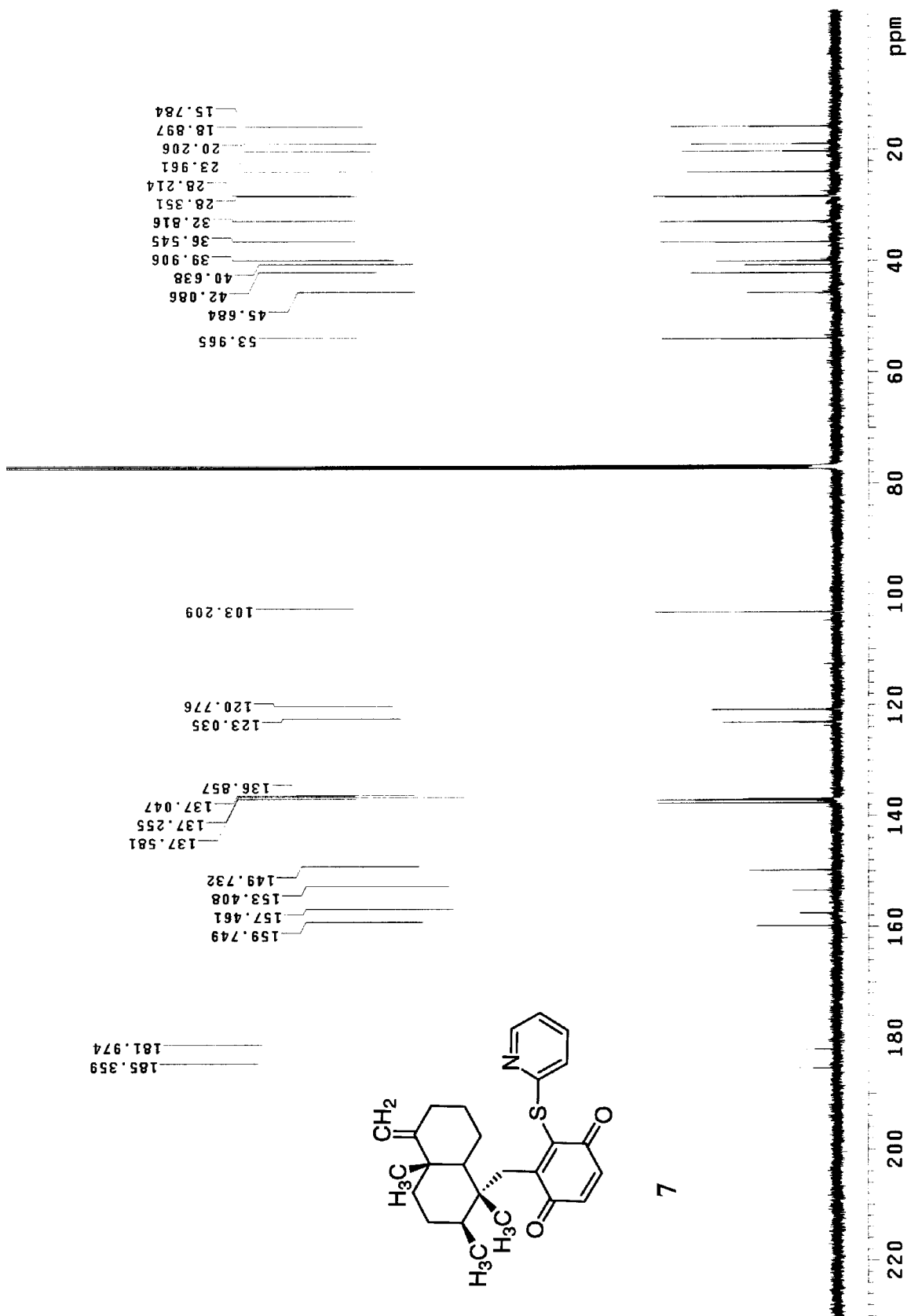


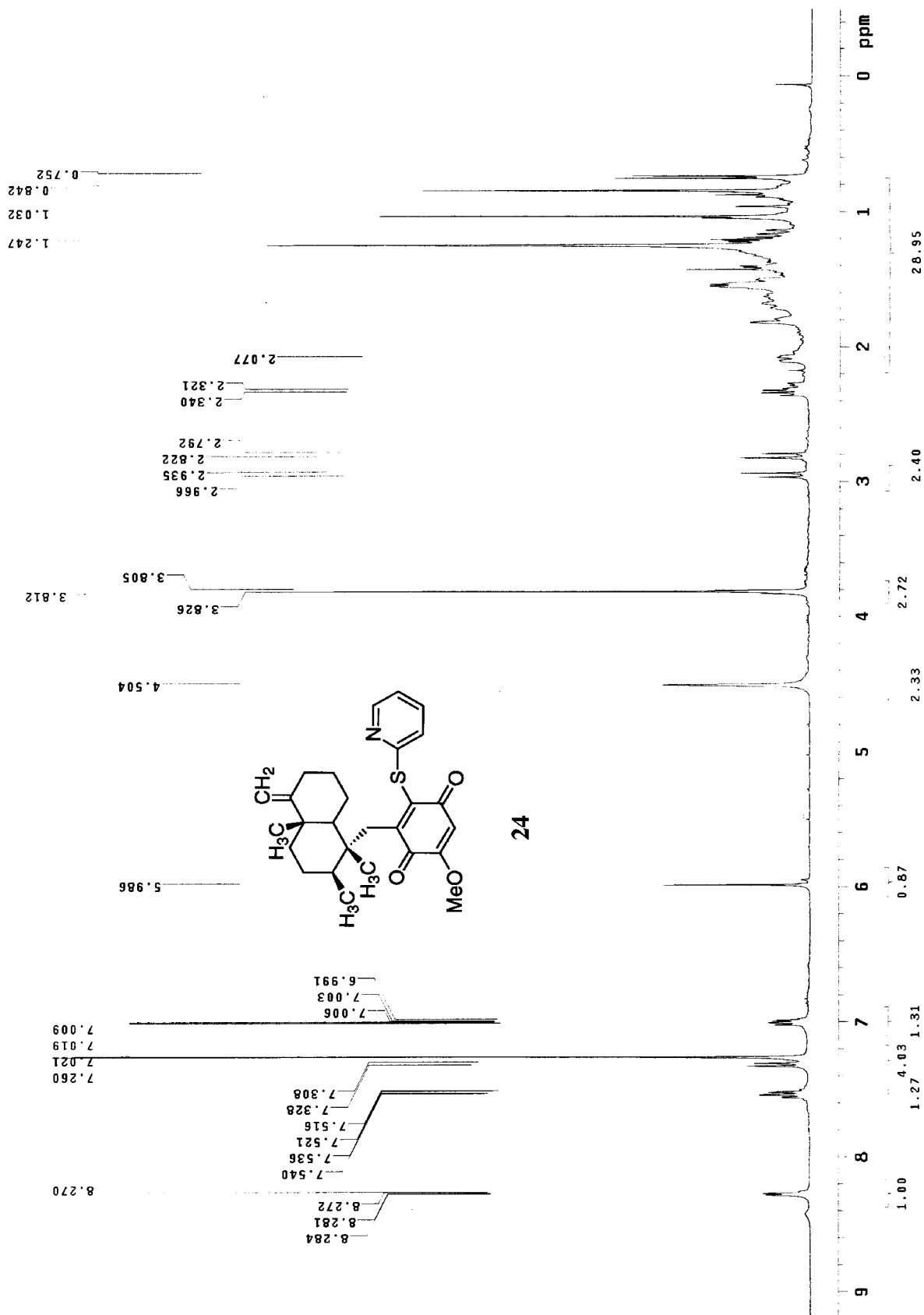
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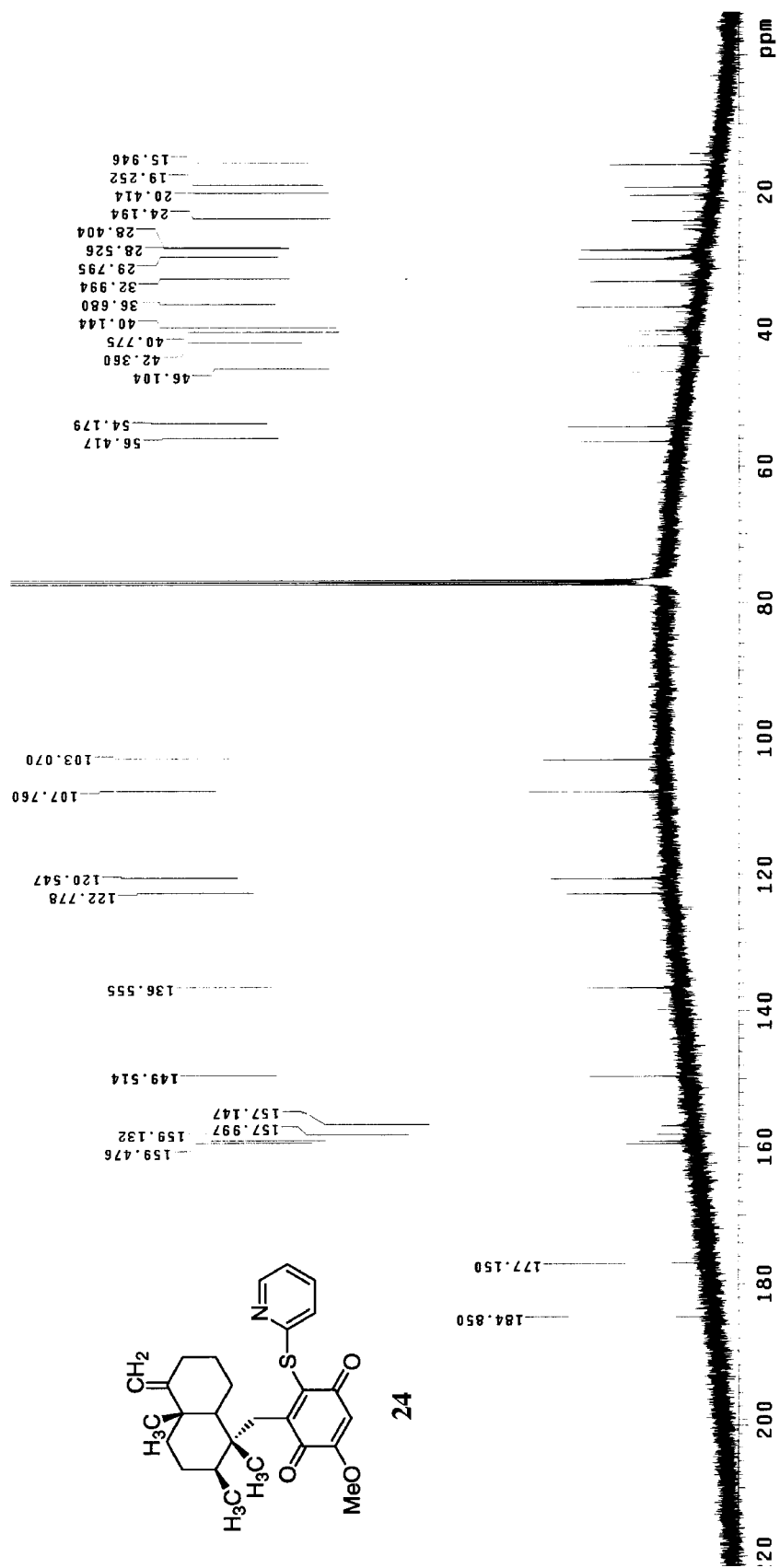


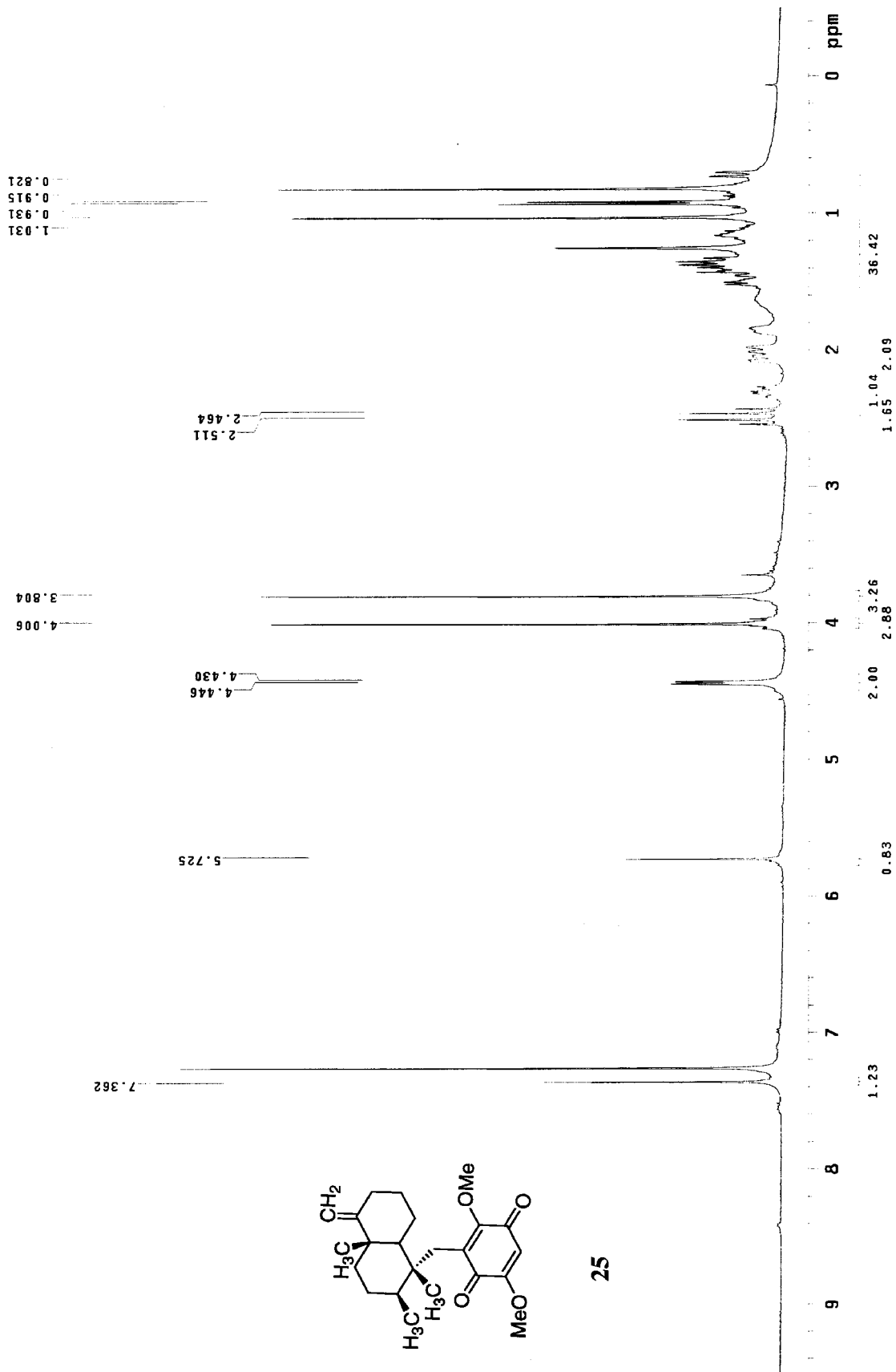
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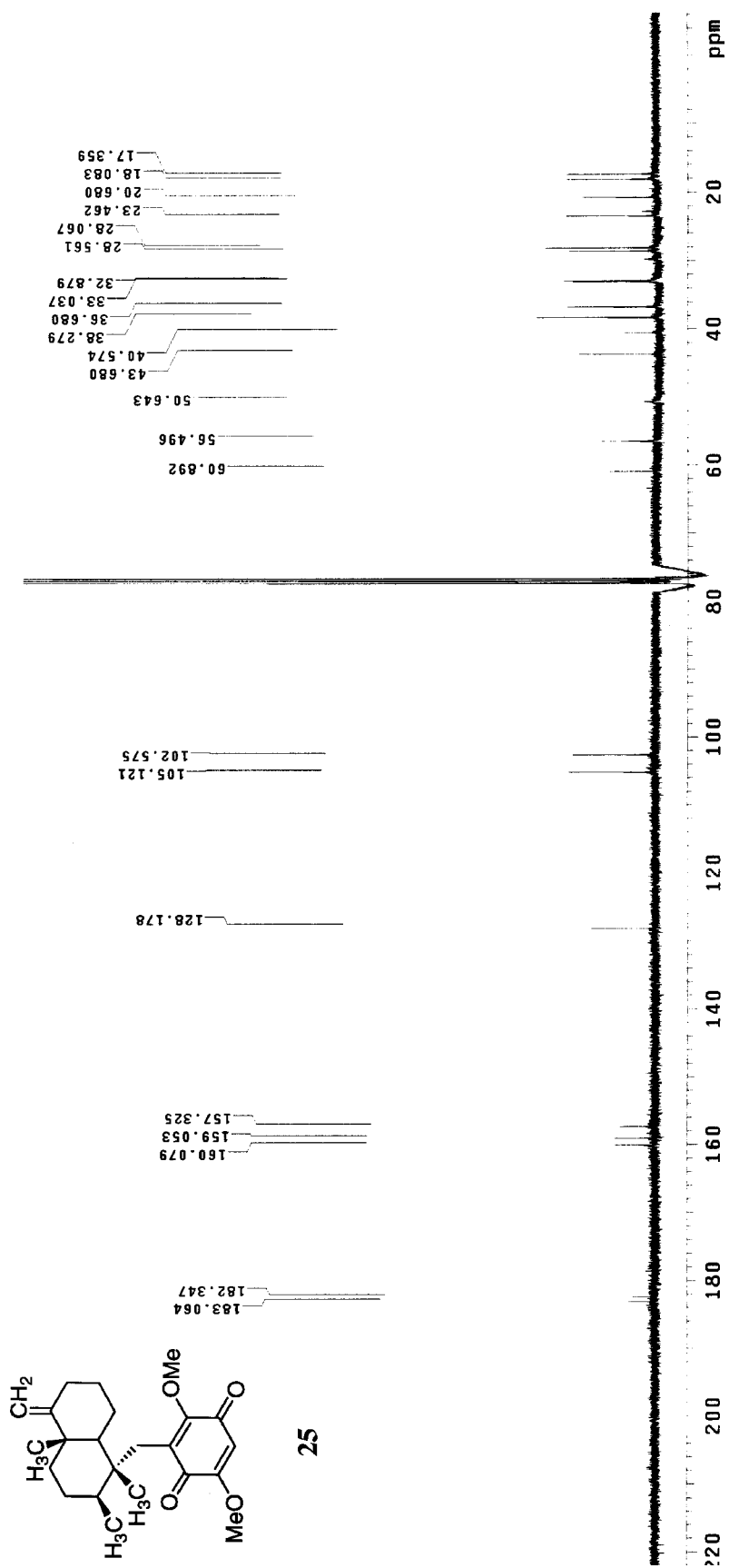


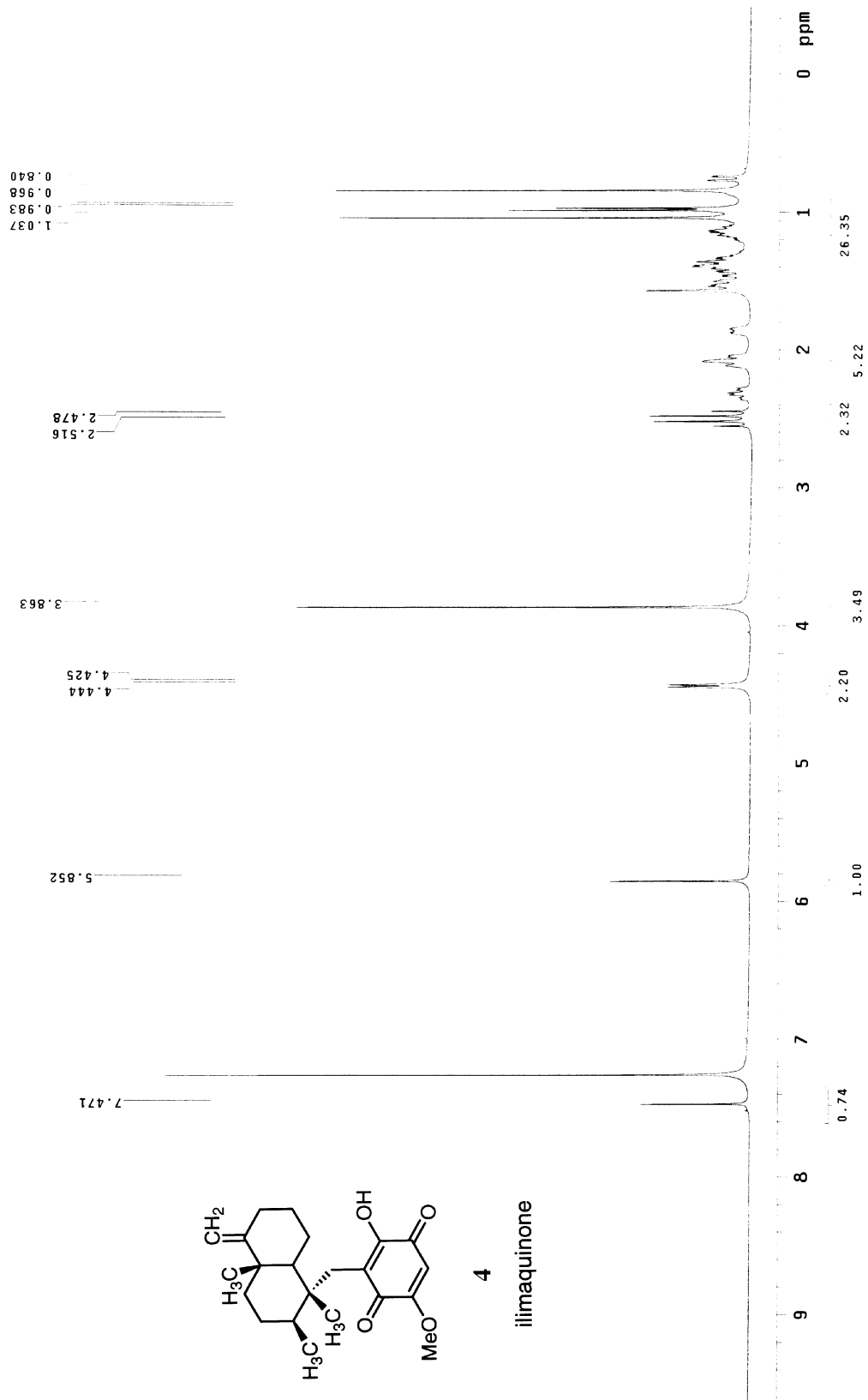


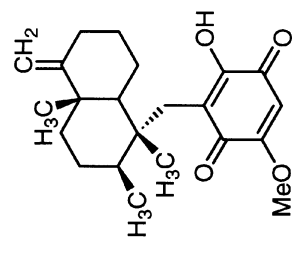
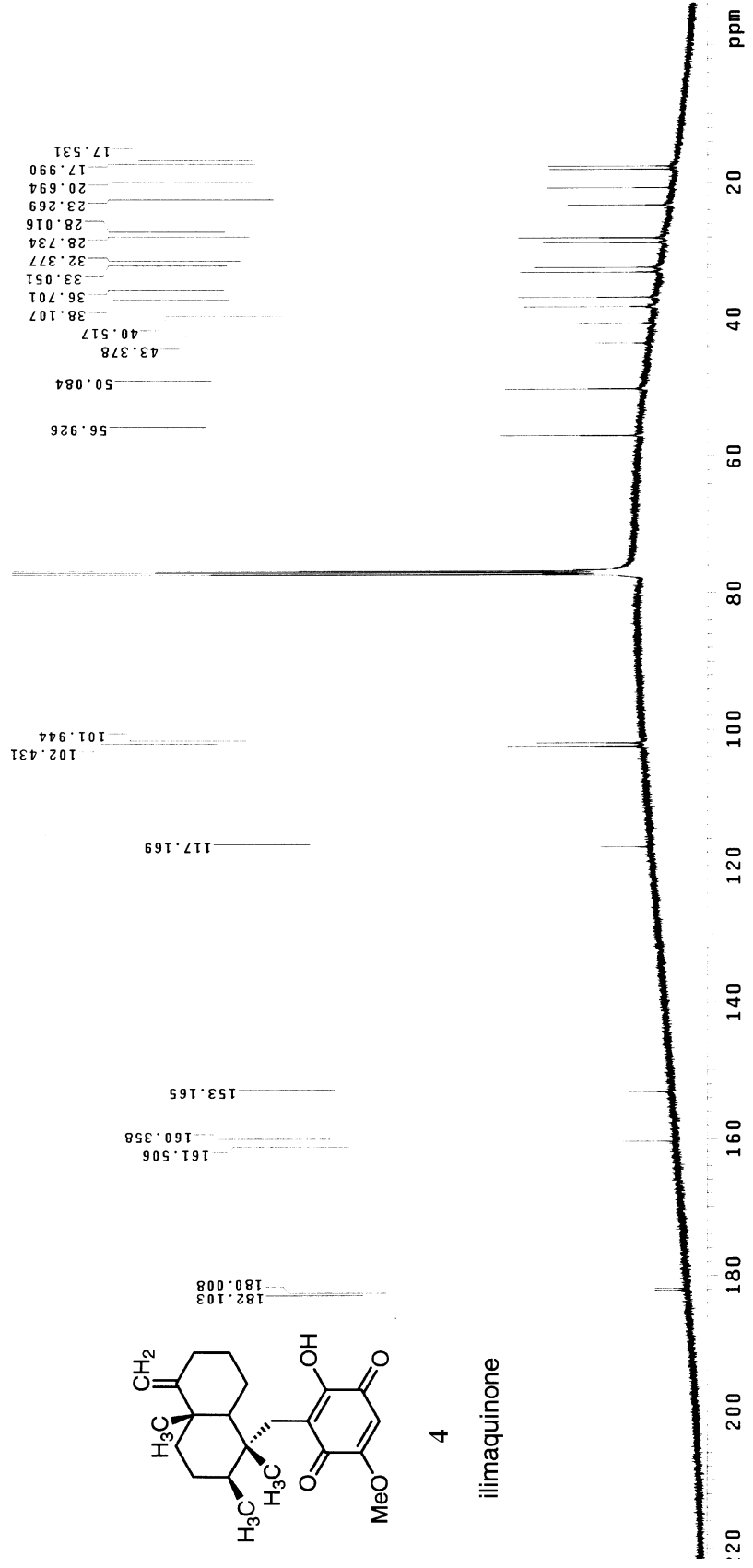












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