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Palladium-Catalyzed Intramolecular Nucleophilic Substitution at the Alkoxycarbonyl Group

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General Methods. ^{1}H- and ^{13}C NMR spectra were recorded in $CDCl_3$ solution, using Me_4Si as internal standard. ^{31}P NMR spectra were recorded in $CDCl_3$ with external H_3PO_4 as reference. Chemical shifts are reported in ppm downfield (δ) from Me_4Si. TLC was carried out on SiO_2 (silica gel 60 F_{254}, Merck), and the spots were located with UV light, iodoplatinate reagent or 1% aqueous $KMnO_4$. Flash chromatography was carried out on SiO_2 (silica gel 60, SDS, 230-400 mesh ASTM). Drying of organic extracts during workup of reactions was performed over anhydrous $MgSO_4$. Evaporation of solvents was accomplished with a rotatory evaporator. Microanalyses were performed by the Centro de Investigación y Desarrollo (CSIC), Barcelona.

Experimental procedures and characterization data for the starting materials:

Methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]propionate (1a)

A solution of *p*-toluidine (0.5 g, 4.67 mmol) and methyl acrylate (0.34 mL, 3.73 mmol) in acetic acid (0.25 mL) was stirred at 90°C in a sealed tube for 24 h.[1] The reaction mixture was poured into cooled (ice) water, basified with Na_2CO_3, and extracted with Et_2O. The organic extracts were washed with saturated aqueous Na_2CO_3 solution, dried, and concentrated. The residue was dissolved in a CH_2Cl_2 (18 mL)-MeOH (9 mL) mixture, and $CaCO_3$ (0.53 g, 5.30 mmol) and $BTMAICl_2$[2] (1.57 g, 4.48 mmol) were added. The mixture was stirred at room temperature for 6 h and then filtered. The solution was concentrated and the residue was partitioned between water and EtOAc. The organic layer was washed with brine, dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to 4:1 hexanes-EtOAc) to give methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]propionate (892 mg, 75%).

A mixture of methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]propionate (892 mg, 2.80 mmol), K_2CO_3 (774 mg, 5.60 mmol), and iodomethane (1.42 mL, 22.4 mmol) in acetonitrile (5 mL) was stirred at 50°C in a sealed tube for 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]propionate[3] (**1a**, 694 mg, 74%).

Methyl 3-[*N*-(2-bromo-4-methylphenyl)-*N*-methylamino]propionate (1b)

A solution of 2-bromo-4-methylaniline (0.33 mL, 2.6 mmol) and methyl acrylate (0.7 mL, 7.8 mmol) in acetic acid (0.25 mL) was stirred at 90°C in a sealed tube for 24 h. The reaction mixture was poured into cooled (ice) water, basified with Na_2CO_3, and extracted with Et_2O.

[1] Johnson, W. S.; Woroch, E. L.; Buell, B. G. *J. Am. Chem. Soc.* **1949**, *71*, 1901-1905.
[2] Kajigaeshi, S.; Kakinami, T.; Yamasaki, H.; Fujisaki, S.; Okamoto, T. *Bull. Chem. Soc. Jpn* **1988**, *61*, 600-602.
[3] Solé, D.; Díaz, S.; Solans, X.; Font-Bardia, M. *Organometallics* **2006**, *25*, 1995-2001.

The organic extracts were washed with saturated aqueous Na_2CO_3 solution, dried, and concentrated. The residue was dissolved in acetonitrile (6 mL) and K_2CO_3 (0.72 g, 5.2 mmol) and iodomethane (0.6 mL, 9.6 mmol) were added. The mixture was stirred at 50°C in a sealed tube for 5 days. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 4%) to give methyl 3-[*N*-(2-bromo-4-methylphenyl)-*N*-methylamino]propionate (**1b**, 0.3 g, 40%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.27 (s, 3H), 2.54 (t, *J* = 7.5 Hz, 2H), 2.73 (s, 3H), 3.32 (t, *J* = 7.5 Hz, 2H), 3.64 (s, 3H), 6.99 (d, *J* = 8.1 Hz, 1H), 7.05 (dd, *J* = 8.1 and 1.8 Hz, 1H), 7.38 (d, *J* = 1.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.3 (CH_3), 32.5 (CH_2), 41.7 (CH_3), 51.5 (CH_3), 51.6 (CH_2), 120.5 (C), 122.0 (CH), 128.6 (CH), 134.1 (CH), 134.6 (C), 147.7 (C), 172.6 (C).

Methyl 3-[*N*-(2-iodo-4-methoxyphenyl)-*N*-methylamino]propionate (4a)

A solution of 2-iodo-4-methoxyaniline (0.5 g, 2 mmol) and methyl acrylate (0.54 mL, 6 mmol) in acetic acid (0.25 mL) was stirred at 90°C in a sealed tube for 24 h. The reaction mixture was poured into cooled (ice) water, basified with Na_2CO_3, and extracted with Et_2O. The organic extracts were washed with saturated aqueous Na_2CO_3 solution, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to CH_2Cl_2) to give methyl 3-[*N*-(2-iodo-4-methoxyphenyl)amino]propionate (417 mg, 62%).

A mixture of methyl 3-[*N*-(2-iodo-4-methoxyphenyl)amino]propionate (417 mg, 1.24 mmol), K_2CO_3 (344 mg, 2.49 mmol), and iodomethane (0.62 mL, 9.95 mmol) in acetonitrile (6 mL) was stirred at 50°C in a sealed tube for 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to 1:1 hexanes-EtOAc)) to give methyl 3-[*N*-(2-iodo-4-methoxyphenyl)-*N*-methylamino]propionate (**4a**, 435 mg, quantitative).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.49 (t, *J* = 7.5 Hz, 2H), 2.64 (s, 3H), 3.22 (t, *J* = 7.5 Hz, 2H), 3.66 (s, 3H), 3.76 (s, 3H), 6.88 (dd, *J* = 8.7 and 3 Hz, 1H), 7.04 (d, *J* = 8.7 Hz, 1H), 7.38 (d, *J* = 3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 32.9 (CH_2), 43.4 (CH_3), 51.7 (CH_3), 52.5 (CH_2), 55.6 (CH_3), 100.8 (C), 115.0 (CH), 122.5 (CH), 124.4 (CH), 146.4 (C), 156.8 (C), 172.7 (C). HRMS (ESI-TOF) calcd for $C_{12}H_{17}INO_3$: 350.0248 $[M+H]^+$; found: 350.0233.

Methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)amino]propionate

A solution of methyl *p*-aminobenzoate (1 g, 6.62 mmol) and methyl acrylate (0.66 mL, 7.28 mmol) in acetic acid (0.5 mL) was stirred at 90°C in a sealed tube for 24 h. The reaction mixture was poured into cooled (ice) water, basified with Na_2CO_3, and extracted with Et_2O. The organic extracts were washed with saturated aqueous Na_2CO_3 solution, dried, and

concentrated. The residue was dissolved in a CH_2Cl_2 (12 mL)-MeOH (6 mL) mixture, and $CaCO_3$ (793 mg, 7.92 mmol) and $BTMAICl_2$ (2.55 g, 7.31 mmol) were added. The mixture was stirred at room temperature for 24 h and then filtered. The solution was concentrated and the residue was partitioned between water and EtOAc. The organic layer was washed with brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to 3:1 hexanes-EtOAc) to give methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)amino]propionate (984 mg, 41%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.68 (t, *J* = 6.6 Hz, 2H), 3.57 (broad t, *J* = 6.6 Hz, 2H), 3.74 (s, 3H), 3.86 (s, 3H), 5.04 (broad, 1H), 6.53 (d, *J* = 8.7 Hz, 1H), 7.90 (dd, *J* = 8.7 and 2.1 Hz, 1H), 8.35 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 33.3 (CH_2), 39.2 (CH_2), 51.3 (CH_3), 51.9 (CH_3), 83.9 (C), 108.5 (CH), 120.0 (C), 131.4 (CH), 140.8 (CH), 149.9 (C), 165.7 (C), 172.0 (C).

Methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)-*N*-methylamino]propionate (4b)

A mixture of methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)amino]propionate (984 mg, 2.71 mmol), K_2CO_3 (750 mg, 5.42 mmol), and iodomethane (1.7 mL, 27.1 mmol) in acetonitrile (6 mL) was stirred at 90°C in a sealed tube for 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)-*N*-methylamino]propionate (**4b**, 645 mg, 63%) and methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)amino]propionate (266 mg, 27%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.61 (t, *J* = 7.5 Hz, 2H), 2.79 (s, 3H), 3.41 (t, *J* = 7.5 Hz, 2H), 3.66 (s, 3H), 3.89 (s, 3H), 7.05 (d, *J* = 8.4 Hz, 1H), 7.97 (dd, *J* = 8.4 and 2.1 Hz, 1H), 8.50 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 32.7 (CH_2), 41.8 (CH_3), 51.5 (CH_2), 51.8 (CH_3), 52.1 (CH_3), 96.1 (C), 120.9 (CH), 126.4 (C), 130.4 (CH), 141.8 (CH), 157.7 (C), 165.4 (C), 172.3 (C). HRMS (ESI-TOF) calcd for $C_{13}H_{17}INO_4$: 378.0196 $[M+H]^+$; found: 378.0198.

Benzyl 3-[*N*-(4-methylphenyl)amino]propionate

A solution of *p*-toluidine (0.5 g, 4.67 mmol) and benzyl acrylate (758 mg, 4.67 mmol) in acetic acid (0.25 mL) was stirred at 90°C in a sealed tube for 24 h. The reaction mixture was poured into cooled (ice) water, basified with Na_2CO_3, and extracted with Et_2O. The organic extracts were washed with saturated aqueous Na_2CO_3 solution, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 6%) to give benzyl 3-[*N*-(4-methylphenyl)amino]propionate (635 mg, 51%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.23 (s, 3H), 2.64 (t, *J* = 6.3 Hz, 2H), 3.44 (t, *J* = 6.3 Hz, 2H), 3.84 (broad, 1H), 5.13 (s, 2H), 6.52 (d, *J* = 8.7 Hz, 2H), 6.98 (d, *J* = 8.7 Hz, 2H), 7.30-7.42 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.3 (CH_3), 33.9 (CH_2), 39.8 (CH_2), 66.3 (CH_2), 113.2

(CH), 126.9 (C), 128.1 (CH), 128.2 (CH), 128.5 (CH), 129.7 (CH), 135.7 (C), 145.1 (C), 172.1 (C).

Benzyl 3-[*N*-(2-iodo-4-methylphenyl)amino]propionate

To a solution of benzyl 3-[*N*-(4-methylphenyl)amino]propionate (635 mg, 2.36 mmol) in a CH_2Cl_2 (12 mL)-MeOH (6 mL) mixture were added $CaCO_3$ (307 mg, 3.07 mmol) and $BTMAICl_2$ (904 mg, 2.60 mmol). The mixture was stirred at room temperature for 6 h and then filtered. The solution was concentrated and the residue was partitioned between water and EtOAc. The organic layer was washed with brine, dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to 85:15 hexanes-EtOAc) to give benzyl 3-[*N*-(2-iodo-4-methylphenyl)amino]propionate (870 mg, 93%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.20 (s, 3H), 2.69 (t, *J* = 6.6 Hz, 2H), 3.49 (q, *J* = 6.6 Hz, 2H), 4.33 (broad t, *J* = 6.6 Hz, 1H), 5.16 (s, 2H), 6.50 (d, *J* = 8.1 Hz, 1H), 7.01 (dd, *J* = 8.1 and 1.5 Hz, 1H), 7.30-7.40 (m, 5H), 7.50 (d, *J* = 1.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 19.8 (CH_3), 34.0 (CH_2), 40.0 (CH_2), 66.6 (CH_2), 85.8 (C), 110.6 (CH), 128.3 (2 CH), 128.5 (C), 128.6 (CH), 130.0 (CH), 135.7 (C), 139.4 (CH), 144.5 (C), 171.8 (C).

Benzyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]propionate (4c)

A mixture of benzyl 3-[*N*-(2-iodo-4-methylphenyl)amino]propionate (870 mg, 2.2 mmol), K_2CO_3 (608 mg, 4.4 mmol), and iodomethane (1.1 mL, 17.6 mmol) in acetonitrile (7 mL) was stirred at 50°C in a sealed tube for 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give benzyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]propionate (**4c**, 825 mg, 92%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.26 (s, 3H), 2.56 (t, *J* = 7.5 Hz, 2H), 2.67 (s, 3H), 3.29 (t, *J* = 7.5 Hz, 2H), 5.10 (s, 2H), 6.98 (d, *J* = 8.1 Hz, 1H), 7.10 (dd, *J* = 8.1 and 1.5 Hz, 1H), 7.30-7.38 (m, 5H), 7.67 (d, *J* = 1.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.2 (CH_3), 33.1 (CH_2), 43.0 (CH_3), 52.1 (CH_2), 66.3 (CH_2), 99.8 (C), 121.9 (CH), 128.1 (CH), 128.2 (CH), 128.5 (CH), 129.7 (CH), 135.8 (C), 135.9 (C), 140.2 (CH), 150.8 (C), 172.0 (C). HRMS (ESI-TOF) calcd for $C_{18}H_{21}INO_2$: 410.0612 $[M+H]^+$; found: 410.0600.

Methyl 2-methyl-3-[*N*-(4-methylphenyl)amino]propionate

A solution of *p*-toluidine (1 g, 9.34 mmol) and methyl methacrylate (1.1 mL, 10.3 mmol) in acetic acid (0.5 mL) was stirred at 90°C in a sealed tube for 24 h. The reaction mixture was poured into cooled (ice) water, basified with Na_2CO_3, and extracted with Et_2O. The organic extracts were washed with saturated aqueous Na_2CO_3 solution, dried, and concentrated. The

residue was purified by flash chromatography (SiO_2, from hexanes to 1:1 hexanes-EtOAc) to give methyl 2-methyl-3-[*N*-(4-methylphenyl)amino]propionate (332 mg, 17%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.22 (d, *J* = 6.9 Hz, 3H), 2.23 (s, 3H), 2.80 (m, 1H), 3.19 (dd, *J* = 13.2 and 5.4 Hz, 1H), 3.39 (dd, *J* = 13.2 and 7.8 Hz, 1H), 3.69 (s, 3H), 3.82 (broad, 1H), 6.53 (d, *J* = 8.1 Hz, 2H), 6.98 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 15.0 (CH_3), 20.3 (CH_3), 39.2 (CH), 47.3 (CH_2), 51.7 (CH_3), 113.1 (CH), 126.7 (C), 129.7 (CH), 145.4 (C), 175.8 (C).

Methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]-2-methylpropionate

To a solution of methyl 2-methyl-3-[*N*-(4-methylphenyl)amino]propionate (332 mg, 1.60 mmol) in a CH_2Cl_2 (10 mL)-MeOH (5 mL) mixture were added $CaCO_3$ (208 mg, 2.08 mmol) and $BTMAICl_2$ (613 mg, 1.76 mmol). The mixture was stirred at room temperature for 6 h and then filtered. The solution was concentrated and the residue was partitioned between water and EtOAc. The organic layer was washed with brine, dried and concentrated. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]-2-methylpropionate (410 mg, 77%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.24 (d, *J* = 7.2 Hz, 3H), 2.20 (s, 3H), 2.83 (m, 1H), 3.24 (dd, *J* = 13.2 and 6 Hz, 1H), 3.43 (dd, *J* = 13.2 and 7.8 Hz, 1H), 3.72 (s, 3H), 4.40 (broad, 1H), 6.49 (d, *J* = 8.1 Hz, 1H), 7.01 (dd, *J* = 8.1 and 2.1 Hz, 1H), 7.49 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 15.0 (CH_3), 19.8 (CH_3), 38.9 (CH), 47.4 (CH_2), 51.9 (CH_3), 85.7 (C), 110.6 (CH), 128.4 (C), 130.0 (CH), 139.4 (CH), 144.5 (C), 175.4 (C).

Methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]-2-methylpropionate (7)

A mixture of methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]-2-methylpropionate (410 mg, 1.23 mmol), K_2CO_3 (340 mg, 2.46 mmol), and iodomethane (0.6 mL, 9.84 mmol) in acetonitrile (5 mL) was stirred at 50°C in a sealed tube for 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]-2-methylpropionate (**7**, 400 mg, 94%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (d, *J* = 6.9 Hz, 3H), 2.26 (s, 3H), 2.64 (s, 3H), 2.65 (m, 1H), 2.97 (dd, *J* = 12.6 and 6.6 Hz, 1H), 3.28 (dd, *J* = 12.6 and 8.1 Hz, 1H), 3.67 (s, 3H), 6.99 (d, *J* = 8.1 Hz, 1H), 7.11 (dd, *J* = 8.1 and 1.8 Hz, 1H), 7.67 (d, *J* = 1.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 15.5 (CH_3), 20.2 (CH_3), 38.5 (CH), 44.3 (CH_3), 51.8 (CH_3), 59.0 (CH_2), 99.8 (C), 122.0 (CH), 129.8 (CH), 135.8 (C), 140.2 (CH), 151.2 (C), 176.1 (C). HRMS (ESI-TOF) calcd for $C_{13}H_{19}INO_2$: 348.0455 $[M+H]^+$; found: 348.0453.

Methyl 2,2-dimethyl-3-[*N*-(4-methylphenyl)amino]propionate

Following the previously described protocol for the preparation of closely related products,[4] to a solution of SDS (625 mg, 2.16 mmol) in water (29 mL) were successfully added *p*-toluidine (580 mg, 5.41 mmol), formaldehyde (37 wt. % in water, 0.45 mL), 1-methoxy-1-trimethylsiloxy-2-methylpropene (3.3 mL, 14.3 mmol), and 48% aqueous HBF_4 solution (0.1 mL, 0.55 mmol) at 0°C. After being stirred at the same temperature for 30 min, Dowex 1-X8 (100-200 mesh, Cl^- form) and water were added to quench the reaction, and the reaction mixture was further stirred for 10 min. The mixture was extracted with CH_2Cl_2 and the combined organic extracts were washed with brine, dried, and concentrated to give methyl 2,2-dimethyl-3-[*N*-(4-methylphenyl)amino]propionate (1.20 g, quantitative), which was used in the next step without purification.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26 (s, 6H), 2.22 (s, 3H), 3.21 (s, 2H), 3.67 (s, 3H), 3.80 (broad, 1H), 6.55 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.3 (CH_3), 23.5 (CH_3), 43.7 (C), 52.0 (CH_3), 53.2 (CH_2), 113.1 (CH), 126.5 (C), 129.6 (CH), 146.2 (C), 177.5 (C).

Methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]-2,2-dimethylpropionate (10a)

To a solution of methyl 2,2-dimethyl-3-[*N*-(4-methylphenyl)amino]propionate (1.20 g, 5.41 mmol) in a CH_2Cl_2 (23 mL)-MeOH (10 mL) mixture were added $CaCO_3$ (720 mg, 7.2 mmol) and $BTMAICl_2$ (1.88 g, 5.41 mmol). The mixture was stirred at room temperature for 6 h and then filtered. The solution was concentrated and the residue was partitioned between water and EtOAc. The organic layer was washed with brine, dried, and concentrated to give methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]-2,2-dimethylpropionate (1.64 g, 87%), which was used in the next step without purification.

A mixture of methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]-2,2-dimethylpropionate (1.53 g, 4.40 mmol), K_2CO_3 (1.22 g, 8.80 mmol), and iodomethane (2.2 mL, 35.3 mmol) in acetonitrile (15 mL) was stirred at 50°C in a sealed tube for 72 h. Iodomethane (2.2 mL, 35.3 mmol) was added and the mixture was stirred at 50°C in a sealed tube for an additional 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to 8:2 hexanes-EtOAc) to give methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]-2,2-dimethylpropionate (**10a**, 1.10 g, 69%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 6H), 2.25 (s, 3H), 2.64 (s, 3H), 3.24 (s, 2H), 3.56 (s, 3H), 7.05-7.13 (m, 2H), 7.66 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.2 (CH_3), 23.9 (CH_3), 44.6 (C), 46.8 (CH_3), 51.6 (CH_3), 65.1 (CH_2), 100.5 (C), 123.7 (CH), 129.9 (CH), 135.6 (C),

[4] Akiyama, T.; Takaya, J.; Kagoshima, H. *Adv. Synth. Catal.* **2002**, *344*, 338-347.

140.0 (CH), 153.1 (C), 177.7 (C). HRMS (ESI-TOF) calcd for $C_{14}H_{21}INO_2$: 362.0612 $[M+H]^+$; found: 362.0604.

Methyl 3-[*N*-(2-iodo-4-methoxyphenyl)amino]-2,2-dimethylpropionate

To a solution of SDS (115 mg, 0.40 mmol) in water (5 mL) were successfully added 2-iodo-4-methoxyaniline (250 mg, 1 mmol), formaldehyde (37 wt. % in water, 80 µL), 1-methoxy-1-trimethylsiloxy-2-methylpropene (0.6 mL, 3 mmol), and 48% aqueous HBF_4 solution (18 µL, 0.1 mmol) at 0°C. After being stirred overnight at room temperature, Dowex 1-X8 (100-200 mesh, Cl^- form) and water were added to quench the reaction, and the reaction mixture was further stirred for 10 min. The mixture was extracted with CH_2Cl_2 and the combined organic extracts were washed with brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give methyl 3-[*N*-(2-iodo-4-methoxyphenyl)amino]-2,2-dimethylpropionate (192 mg, 53%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.30 (s, 6H), 3.20 (s, 2H), 3.70 (s, 3H), 3.72 (s, 3H), 4.13 (broad, 1H), 6.55 (d, *J* = 8.7 Hz, 1H), 6.82 (dd, *J* = 8.7 and 3 Hz, 1H), 7.26 (d, *J* = 3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 23.6 (CH_3), 43.5 (C), 52.1 (CH_3), 53.9 (CH_2), 56.0 (CH_3), 85.8 (C), 111.6 (CH), 115.6 (CH), 124.4 (CH), 142.2 (C), 151.8 (C), 177.1 (C).

Methyl 3-[*N*-(2-iodo-4-methoxyphenyl)-*N*-methylamino]-2,2-dimethylpropionate (10b)

A mixture of methyl 3-[*N*-(2-iodo-4-methoxyphenyl)amino]-2,2-dimethylpropionate (192 mg, 0.53 mmol), K_2CO_3 (146 mg, 1.1 mmol), and iodomethane (0.26 mL, 4.2 mmol) in acetonitrile (5 mL) was stirred at 50°C in a sealed tube for 72 h. Iodomethane (0.26 mL, 4.2 mmol) was added and the mixture was stirred at 50°C in a sealed tube for an additional 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 2%) to give methyl 3-[*N*-(2-iodo-4-methoxyphenyl)-*N*-methylamino]-2,2-dimethylpropionate (**10b**, 140 mg, 70%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 6H), 2.61 (s, 3H), 3.20 (s, 2H), 3.55 (s, 3H), 3.75 (s, 3H), 6.87 (dd, *J* = 8.7 and 3 Hz, 1H), 7.11 (d, *J* = 8.7 Hz, 1H), 7.36 (d, *J* = 3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 24.0 (CH_3), 44.5 (C), 47.0 (CH_3), 51.7 (CH_3), 55.6 (CH_3), 65.6 (CH_2), 101.2 (C), 115.2 (CH), 124.1 (CH), 124.4 (CH), 148.8 (C), 156.5 (C), 177.7 (C). HRMS (ESI-TOF) calcd for $C_{14}H_{21}INO_3$: 378.0561 $[M+H]^+$; found: 378.0553.

Methyl 3-[*N*-(4-methoxycarbonylphenyl)amino]-2,2-dimethylpropionate

To a solution of SDS (575 mg, 2 mmol) in water (25 mL) were successfully added methyl 4-aminobenzoate (750 mg, 4.96 mmol), formaldehyde (37 wt. % in water, 0.4 mL), 1-methoxy-1-trimethylsiloxy-2-methylpropene (3 mL, 15 mmol), and 48% aqueous HBF_4 solution (90 µL,

0.5 mmol) at 0°C. After being stirred at room temperature for 4 h, Dowex 1-X8 (100-200 mesh, Cl^- form) and water were added to quench the reaction, and the reaction mixture was further stirred for 10 min. The mixture was extracted with CH_2Cl_2 and the combined organic extracts were washed with brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 7:3) to give methyl 3-[*N*-(4-methoxycarbonylphenyl)amino]-2,2-dimethylpropionate (507 mg, 39%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26 (s, 6H), 3.29 (s, 2H), 3.67 (s, 3H), 3.83 (s, 3H), 4.53 (broad, 1H), 6.57 (d, *J* = 8.7 Hz, 2H), 7.83 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 23.4 (CH_3), 43.7 (C), 51.4 (CH_3), 51.5 (CH_2), 52.0 (CH_3), 111.4 (CH), 118.2 (C), 131.4 (CH), 152.1 (C), 167.1 (C), 177.1 (C).

Methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)amino]-2,2-dimethylpropionate

To a solution of methyl 3-[*N*-(4-methoxycarbonylphenyl)amino]-2,2-dimethylpropionate (507 mg, 1.9 mmol) in a CH_2Cl_2 (12 mL)-MeOH (5 mL) mixture were added $CaCO_3$ (250 mg, 2.5 mmol) and $BTMAICl_2$ (0.8 g, 2.3 mmol). After stirring at room temperature for 24 h, $CaCO_3$ (250 mg, 2.5 mmol) and $BTMAICl_2$ (0.4 g, 1.15 mmol) were added. The mixture was stirred at room temperature for 6 h and then filtered. The solution was concentrated and the residue was partitioned between water and EtOAc. The organic layer was washed with brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)amino]-2,2-dimethylpropionate (582 mg, 78%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31 (s, 6H), 3.32 (s, 2H), 3.72 (s, 3H), 3.85 (s, 3H), 5.15 (broad, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 7.87 (dd, *J* = 8.4 and 1.8 Hz, 1H), 8.33 (d, *J* = 1.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 23.5 (CH_3), 43.5 (C), 51.7 (CH_3), 52.1 (CH_2), 52.3 (CH_3), 84.0 (C), 108.8 (CH), 119.7 (C), 131.4 (CH), 140.8 (CH), 150.6 (C), 165.9 (C), 176.8 (C).

Methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)-*N*-methylamino]-2,2-dimethylpropionate (10c)

A mixture of methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)amino]-2,2-dimethylpropionate (563 mg, 1.44 mmol), K_2CO_3 (400 mg, 2.89 mmol), and iodomethane (0.9 mL, 14.5 mmol) in acetonitrile (10 mL) was stirred at 80°C in a sealed tube for 72 h. Iodomethane (0.9 mL, 14.5 mmol) was added and the mixture was stirred at 80°C in a sealed tube for an additional 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 8%) to give methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)-*N*-methylamino]-2,2-dimethylpropionate (**10c**, 345 mg, 59%) and

methyl 3-[*N*-(2-iodo-4-methoxycarbonylphenyl)amino]-2,2-dimethylpropionate (225 mg, 40%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 6H), 2.78 (s, 3H), 3.38 (s, 2H), 3.55 (s, 3H), 3.88 (s, 3H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.95 (dd, *J* = 8.4 and 2.1 Hz, 1H), 8.49 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 23.8 (CH_3), 44.7 (C), 46.1 (CH_3), 51.7 (CH_3), 52.8 (CH_3), 64.0 (CH_2), 97.5 (C), 122.8 (CH), 126.4 (C), 130.4 (CH), 141.7 (CH), 159.6 (C), 165.4 (C), 177.3 (C). HRMS (ESI-TOF) calcd for $C_{15}H_{21}INO_4$: 406.0510 $[M+H]^+$; found: 406.0496.

Methyl 2-methyl-3-[*N*-(4-methylphenyl)amino]-2-phenylpropionate

To a solution of SDS (185 mg, 0.64 mmol) in water (8 mL) were successfully added *p*-toluidine (170 mg, 1.59 mmol), formaldehyde (37 wt. % in water, 0.13 mL), 1-methoxy-1-trimethylsiloxy-2-phenylpropene (1.5 g, 6.35 mmol), and 48% aqueous HBF_4 solution (30 μL, 0.17 mmol) at 0°C. After being stirred at the same temperature for 5 h, Dowex 1-X8 (100-200 mesh, Cl^- form) and water were added to quench the reaction, and the reaction mixture was further stirred for 10 min. The mixture was extracted with CH_2Cl_2 and the combined organic extracts were washed with brine and concentrated. The residue was dissolved in Et_2O and extracted with 2N HCl. The aqueous layer was alkalinized with Na_2CO_3 and extracted with CH_2Cl_2. The organic extracts were dried and concentrated to give methyl 2-methyl-3-[*N*-(4-methylphenyl)amino]-2-phenylpropionate (250 mg, 55%), which was used in the next step without purification.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.68 (s, 3H), 2.21 (s, 3H), 3.45 (d, *J* = 12.6 Hz, 1H), 3.68 (s, 3H), 3.72 (d, *J* = 12.6 Hz, 1H), 6.50 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 7.24-7.40 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.3 (CH_3), 21.5 (CH_3), 51.9 (C), 52.3 (CH_3), 52.6 (CH_2), 113.1 (CH), 126.1 (CH), 126.6 (C), 127.2 (CH), 128.6 (CH), 129.6 (CH), 141.3 (C), 146.1 (C), 179.9 (C).

Methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]-2-methyl-2-phenylpropionate

To a solution of methyl 2-methyl-3-[*N*-(4-methylphenyl)amino]-2-phenylpropionate (250 mg, 0.88 mmol) in a CH_2Cl_2 (12 mL)-MeOH (5 mL) mixture were added $CaCO_3$ (114 mg, 1.14 mmol) and $BTMAICl_2$ (334 mg, 0.96 mmol). The mixture was stirred at room temperature for 6 h and then filtered. The solution was concentrated and the residue was partitioned between water and EtOAc. The organic layer was washed with brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 8%) to give methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]-2-methyl-2-phenylpropionate (257 mg, 71%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.70 (s, 3H), 2.17 (s, 3H), 3.50 (dd, *J* = 12.6 and 5.1 Hz, 1H), 3.71 (m, 1H), 3.72 (s, 3H), 4.18 (broad t, *J* = 6 Hz, 1H), 6.47 (d, *J* = 8.4 Hz, 1H), 6.96 (dd, *J* =

8.4 and 1.8 Hz, 1H), 7.24-7.40 (m, 5H), 7.45 (d, *J* = 1.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 19.7 (CH_3), 21.4 (CH_3), 51.7 (C), 52.4 (CH_3), 52.6 (CH_2), 85.9 (C), 110.8 (CH), 126.2 (CH), 127.4 (CH), 128.1 (C), 128.7 (CH), 129.8 (CH), 139.2 (CH), 140.9 (C), 145.2 (C), 175.7 (C).

Methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]-2-methyl-2-phenylpropionate (10d)

A mixture of methyl 3-[*N*-(2-iodo-4-methylphenyl)amino]-2-methyl-2-phenylpropionate (257 mg, 0.63 mmol), K_2CO_3 (174 mg, 1.26 mmol), and iodomethane (0.4 mL, 6.3 mmol) in acetonitrile (5 mL) was stirred at 90°C in a sealed tube for 72 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2-MeOH 2%) to give methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]-2-methyl-2-phenylpropionate (**10d**, 268 mg, quantitative).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.66 (s, 3H), 2.25 (s, 3H), 2.52 (s, 3H), 3.42 (d, *J* = 13.8 Hz, 1H), 3.60 (s, 3H), 3.88 (d, *J* = 13.8 Hz, 1H), 7.08 (m, 2H), 7.20-7.38 (m, 5H), 7.65 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.2 (CH_3), 21.6 (CH_3), 47.2 (CH_3), 52.0 (CH_3), 52.6 (C), 65.1 (CH_2), 100.7 (C), 124.1 (CH), 126.2 (CH), 126.9 (CH), 128.3 (CH), 130.0 (CH), 136.6 (C), 140.0 (CH), 142.2 (C), 153.6 (C), 175.7 (C). HRMS (ESI-TOF) calcd for $C_{19}H_{23}INO_2$: 424.0768 $[M+H]^+$; found: 424.0752.

Methyl 3-[*N*-(2-iodo-5-methylphenyl)amino]-2,2-dimethylpropionate

To a solution of SDS (390 mg, 1.36 mmol) in water (18 mL) were successfully added 2-iodo-5-methylaniline (790 mg, 3.39 mmol), formaldehyde (37 wt. % in water, 0.28 mL), 1-methoxy-1-trimethylsiloxy-2-methylpropene (2 mL, 10 mmol), and 48% aqueous HBF_4 solution (62 μL, 0.34 mmol) at 0°C. After being stirred at room temperature for 24 h, Dowex 1-X8 (100-200 mesh, Cl^- form) and water were added to quench the reaction, and the reaction mixture was further stirred for 10 min. The mixture was extracted with CH_2Cl_2 and the combined organic extracts were washed with brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 4%) to give methyl 3-[*N*-(2-iodo-5-methylphenyl)amino]-2,2-dimethylpropionate (198 mg, 17%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31 (s, 6H), 2.26 (s, 3H), 3.25 (s, 2H), 3.71 (s, 3H), 6.28 (dd, *J* = 7.8 and 2.1 Hz, 1H), 6.41 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100.5 MHz) δ 21.4 (CH_3), 23.6 (CH_3), 43.4 (C), 52.1 (CH_3), 52.8 (CH_2), 81.9 (C), 111.6 (CH), 119.8 (CH), 138.6 (CH), 139.4 (C), 147.1 (C), 177.1 (C).

Methyl 3-[*N*-(2-iodo-5-methylphenyl)-*N*-methylamino]-2,2-dimethylpropionate (12a)

A mixture of methyl 3-[*N*-(2-iodo-5-methylphenyl)amino]-2,2-dimethylpropionate (198 mg, 0.57 mmol), K_2CO_3 (158 mg, 1.14 mmol), and iodomethane (0.7 mL, 11.3 mmol) in acetonitrile (5 mL) was stirred at 90°C in a sealed tube for 68 h. The solvent was removed *in vacuo*, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 2%) to give methyl 3-[*N*-(2-iodo-5-methylphenyl)-*N*-methylamino]-2,2-dimethylpropionate (**12a**, 140 mg, 68%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.19 (s, 6H), 2.28 (s, 3H), 2.66 (s, 3H), 3.26 (s, 2H), 3.56 (s, 3H), 6.61 (dd, *J* = 8 and 1.6 Hz, 1H), 7.00 (d, *J* = 1.6 Hz, 1H), 7.67 (d, *J* = 8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100.5 MHz) δ 21.0 (CH_3), 23.9 (CH_3), 44.6 (C), 46.6 (CH_3), 51.6 (CH_3), 64.9 (CH_2), 96.2 (C), 125.1 (CH), 126.8 (CH), 139.2 (C), 139.4 (CH), 155.5 (C), 177.8 (C). HRMS (ESI-TOF) calcd for $C_{14}H_{21}INO_2$: 362.0611 $[M+H]^+$; found: 362.0612.

Methyl 3-[*N*-(5-chloro-2-iodophenyl)-*N*-methylamino]-2,2-dimethylpropionate (12b)

Sodium (235 mg, 10.2 mmol) was slowly added to MeOH (10 mL). Once the evolution of hydrogen had ceased, 5-chloro-2-iodoaniline (515 mg, 2.03 mmol) was added and the resulting solution was poured onto a suspension of paraformaldehyde (85 mg, 2.83 mmol) in MeOH (5 mL). The resulting mixture was stirred at room temperature for 5 h and then hydrolyzed with cool water and extracted with Et_2O. The organic extracts were washed with water, dried, and concentrated in vacuo, taking care that the temperature remained below 25 °C. A 1:1 mixture of 5-chloro-2-iodoaniline and *N*-(methoxymethyl)-5-chloro-2-iodoaniline[5,6] was obtained. This mixture was dissolved in dichloromethane (5 mL) and the solution was cooled to -78°C. A solution of $BF_3{\cdot}Et_2O$ (0.3 mL, 2.4 mmol) in dichloromethane (3 mL) was added dropwise, the resulting mixture was stirred at -78°C for 5 min and then a solution of 1-methoxy-1-trimethylsiloxy-2-methylpropene (0.25 mL, 1.25 mmol) in dichloromethane (3 mL) was added. After 4 h at -78°C, the reaction mixture was allowed to reach room temperature, poured into brine, and extracted with dichloromethane. The organic extracts were dried and concentrated to give a 1:5 mixture of 5-chloro-2-iodoaniline and methyl 3-[*N*-(5-chloro-2-iodophenyl)amino]-2,2-dimethylpropionate. The mixture was dissolved in CH_3CN (5 mL) and K_2CO_3 (0.25 g, 1.8 mmol) and iodomethane (0.56 mL, 9 mmol) were added. After 72 h at 90 °C in a sealed tube, iodomethane (1.5 mL, 24 mmol) was added, and heating was maintained for 24 h. The solvent was removed in vacuo and the residue was partitioned

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between dichloromethane and water. The organic extracts were dried and concentrated. Chromatography (from hexanes to hexanes-EtOAc 1%) yielded **12b** (107 mg, 14%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.19 (s, 6H), 2.68 (s, 3H), 3.26 (s, 2H), 3.57 (s, 3H), 6.79 (dd, *J* = 8.4 and 2 Hz, 1H), 7.15 (d, *J* = 2 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100.5 MHz) δ 23.9 (CH_3), 44.6 (C), 46.5 (CH_3), 51.7 (CH_3), 64.6 (CH_2), 97.2 (C), 124.7 (CH), 125.8 (CH), 134.8 (C), 140.5 (CH), 156.8 (C), 177.5 (C).

Methyl 3-[*N*-(2-iodophenyl)-*N*-(methoxycarbonyl)amino]propionate (14a)

A solution of 2-iodoaniline (1 g, 4.56 mmol) and methyl acrylate (1.24 mL, 13.7 mmol) in acetic acid (0.5 mL) was stirred at 90°C in a sealed tube for 24 h. The reaction mixture was poured into cooled (ice) water, basified with Na_2CO_3, and extracted with Et_2O. The organic extracts were washed with saturated aqueous Na_2CO_3 solution, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to 3:7 hexanes-CH_2Cl_2) to give methyl 3-[*N*-(2-iodophenyl)amino]propionate (245 mg, 18%).

A mixture of methyl 3-[*N*-(2-iodophenyl)amino]propionate (245 mg, 0.80 mmol) and K_2CO_3 (221 mg, 1.60 mmol) in methyl chloroformate (5 mL) was stirred at 60°C for 12 h. The mixture was poured into water and extracted with CH_2Cl_2. The organic extracts were dried and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to 7:3 hexanes-EtOAc) to give methyl 3-[*N*-(2-iodophenyl)-*N*-(methoxycarbonyl)amino]propionate (**14a**, 269 mg, 93%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.69 (t, *J* = 7.5 Hz, 2H), 3.63 (s, 3H), 3.65 (s, 3H), 3.66 (m, 1H), 4.13 (dt, *J* = 13.8 and 7.5 Hz, 1H), 7.03 (ddd, *J* = 7.8, 7.2, and 1.5 Hz, 1H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.37 (ddd, *J* = 7.8, 7.5, and 1.5 Hz, 1H), 7.89 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 33.0 (CH_2), 46.1 (CH_2), 51.6 (CH_3), 53.1 (CH_3), 100.2 (C), 129.2 (CH), 129.5 (CH), 139.7 (CH), 143.6 (C), 155.2 (C), 171.7 (C). HRMS (ESI-TOF) calcd for $C_{12}H_{15}INO_4$: 364.0040 $[M+H]^+$; found: 364.0031.

Methyl 3-[*N*-(2-iodophenyl)-*N*-(*p*-toluenesulfonyl)amino]propionate (14b)

A solution of methyl 3-[*N*-(2-iodophenyl)amino]propionate (348 mg, 1.14 mmol) and *p*-toluenesulfonyl chloride (2.17 g, 11.4 mmol) in pyridine (12 mL) was stirred at reflux for 24 h. The mixture was poured into water and extracted with Et_2O. The organic extracts were washed with 1N hydrochloric acid and 10% aqueous KOH solution, dried and concentrated. The residue was purified by flash chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2-MeOH 5%) to give methyl 3-[*N*-(2-iodophenyl)-*N*-(*p*-toluenesulfonyl)amino]propionate (**14b**, 407 mg, 78%).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.45 (s, 3H), 2.66 (m, 2H), 3.59 (s, 3H), 3.70 (ddd, *J* = 14.1, 9.3, and 6 Hz, 1H), 3.98 (ddd, *J* = 14.1, 9.6, and 6.3 Hz, 1H), 6.96 (dd, *J* = 7.8 and 1.5 Hz,

1H), 7.04 (ddd, *J* = 7.8, 7.5, and 1.5 Hz, 1H), 7.26-7.32 (m, 3H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.92 (dd, *J* = 7.8 and 1.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 21.5 (CH_3), 33.4 (CH_2), 47.4 (CH_2), 51.6 (CH_3), 102.9 (C), 128.0 (CH), 128.8 (CH), 129.5 (CH), 130.0 (CH), 130.2 (CH), 135.6 (C), 140.4 (CH), 141.2 (C), 143.8 (C), 171.1 (C). HRMS (ESI-TOF) calcd for $C_{17}H_{19}INO_4S$: 460.0074 $[M+H]^+$; found: 460.0056.

Representative procedure for the Pd-catalyzed nucleophilic attack at the alkoxycarbonyl group:

A mixture of methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]propionate (**1a**, 75 mg, 0.23 mmol), K_3PO_4 (143 mg, 0.68 mmol), Et_3N (0.32 mL, 2.25 mmol), and $Pd(PPh_3)_4$ (52 mg, 0.045 mmol) in toluene (6 mL) was stirred at 110°C in a sealed tube for 72 h. The reaction mixture was poured into water and extracted with Et_2O. The organic extracts were washed with brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from hexanes to hexanes-EtOAc 8%) to give 1,6-dimethyl-2,3-dihydro-1*H*-quinolin-4-one (**2**, 27 mg, 65%) and methyl 3-[*N*-methyl-*N*-(4-methylphenyl)amino]propionate (**3**, 14 mg, 30%).

1,6-Dimethyl-2,3-dihydro-1*H*-quinolin-4-one (2)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.25 (s, 3H), 2.72 (t, *J* = 6.9 Hz, 2H), 2.96 (s, 3H), 3.42 (t, *J* = 6.9 Hz, 2H), 6.65 (d, *J* = 8.7 Hz, 1H), 7.23 (dd, *J* = 8.7 and 2.1 Hz, 1H), 7.72 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.1 (CH_3), 38.5 (CH_2), 39.5 (CH_3), 51.7 (CH_2), 113.4 (CH), 119.8 (C), 126.4 (C), 127.7 (CH), 136.5 (CH), 151.0 (C), 193.9 (C). Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.70; H, 7.53; N, 8.01. HRMS (ESI-TOF) calcd for $C_{11}H_{14}NO$: 176.1069 $[M+H]^+$; found: 176.1069.

Methyl 3-[*N*-methyl-*N*-(4-methylphenyl)amino]propionate (3)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.25 (s, 3H), 2.56 (t, *J* = 7.5 Hz, 2H), 2.90 (s, 3H), 3.64 (t, *J* = 7.5 Hz, 2H), 3.67 (s, 3H), 6.67 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.2 (CH_3), 31.4 (CH_2), 38.4 (CH_3), 49.0 (CH_2), 51.7 (CH_3), 113.0 (CH), 126.2 (C), 129.7 (CH), 146.6 (C), 172.8 (C).

6-Methoxy-1-methyl-2,3-dihydro-1*H*-quinolin-4-one (5a)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.73 (t, *J* = 7.2 Hz, 2H), 2.94 (s, 3H), 3.39 (t, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 6.71 (d, *J* = 9 Hz, 1H), 7.07 (dd, *J* = 9 and 3 Hz, 1H), 7.41 (d, *J* = 3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 38.5 (CH_2), 39.7 (CH_3), 51.9 (CH_2), 55.7 (CH_3), 108.9 (CH), 115.0 (CH), 120.0 (C), 124.9 (CH), 148.3 (C), 151.6 (C), 193.6 (C). Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.83; H, 6.93; N, 7.13.

Methyl 3-[*N*-(4-methoxyphenyl)-*N*-methylamino]propionate (6a)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.54 (t, *J* = 7.2 Hz, 2H), 2.86 (s, 3H), 3.59 (t, *J* = 7.2 Hz, 2H), 3.66 (s, 3H), 3.76 (s, 3H), 6.72-6.86 (m, 4H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 31.4 (CH_2), 38.9 (CH_3), 49.9 (CH_2), 51.7 (CH_3), 55.7 (CH_3), 114.8 (CH), 115.1 (CH), 143.4 (C), 152.1 (C), 172.8 (C). HRMS (ESI-TOF) calcd for $C_{12}H_{18}NO_3$: 224.1281 $[M+H]^+$; found: 224.1283.

Methyl 1-methyl-4-oxo-1,2,3,4-tetrahydroquinoline-6-carboxylate (5b)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.77 (t, *J* = 7.2 Hz, 2H), 3.09 (s, 3H), 3.58 (t, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 6.71 (d, *J* = 9 Hz, 1H), 8.04 (dd, *J* = 9 and 2.4 Hz, 1H), 8.57 (d, *J* = 2.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 37.7 (CH_2), 39.3 (CH_3), 50.9 (CH_2), 51.8 (CH_3), 112.8 (CH), 118.4 (C), 118.7 (C), 130.5 (CH), 136.1 (CH), 154.7 (C), 166.7 (C), 192.6 (C). Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.97; H, 6.10; N, 5.85.

Methyl 3-[*N*-(4-methoxycarbonylphenyl)-*N*-methylamino]propionate (6b)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.61 (t, *J* = 7.2 Hz, 2H), 3.03 (s, 3H), 3.68 (s, 3H), 3.74 (t, *J* = 7.2 Hz, 2H), 3.86 (s, 3H), 6.66 (d, *J* = 9 Hz, 2H), 7.90 (d, *J* = 9 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 31.6 (CH_2), 38.3 (CH_3), 48.0 (CH_2), 51.5 (CH_3), 51.8 (CH_3), 110.7 (CH), 117.4 (C), 131.3 (CH), 151.6 (C), 167.2 (C), 172.1 (C). HRMS (ESI-TOF) calcd for $C_{13}H_{18}NO_4$: 252.1230 $[M+H]^+$; found: 252.1226.

Benzyl 3-[*N*-methyl-*N*-(4-methylphenyl)amino]propionate (6c)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.24 (s, 3H), 2.60 (t, *J* = 7.2 Hz, 2H), 2.87 (s, 3H), 3.65 (t, *J* = 7.2 Hz, 2H), 5.10 (s, 2H), 6.66 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 7.30-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.2 (CH_3), 31.7 (CH_2), 38.4 (CH_3), 49.0 (CH_2), 66.4 (CH_2), 113.1 (CH), 126.2 (C), 128.2 (CH), 128.5 (CH), 129.7 (CH), 135.8 (C), 146.6 (C), 172.2 (C). HRMS (ESI-TOF) calcd for $C_{18}H_{22}NO_2$: 284.1645 $[M+H]^+$; found: 284.1639.

1,3,6-Trimethyl-2,3-dihydro-1*H*-quinolin-4-one (8)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21 (d, *J* = 7.2 Hz, 3H), 2.26 (s, 3H), 2.72 (m, 1H), 2.97 (s, 3H), 3.15 (t, *J* = 11.7 Hz, 1H), 3.39 (dd, *J* = 11.7 and 5.4 Hz, 1H), 6.64 (d, *J* = 8.7 Hz, 1H), 7.23 (ddd, *J* = 8.7, 2.4, and 0.6 Hz, 1H), 7.73 (dd, *J* = 2.4 and 0.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 12.6 (CH_3), 20.1 (CH_3), 39.4 (CH_3), 41.4 (CH), 58.3 (CH_2), 113.2 (CH), 119.1 (C), 126.3 (C), 127.9 (CH), 136.2 (CH), 150.7 (C), 196.6 (C). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.30; H, 8.15; N, 7.22.

Methyl 2-methyl-3-[*N*-methyl-*N*-(4-methylphenyl)amino]propionate (9)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (d, *J* = 7.2 Hz, 3H), 2.24 (s, 3H), 2.90 (m, 1H), 2.91 (s, 3H), 3.27 (dd, *J* = 14.7 and 6.6 Hz, 1H), 3.62 (s, 3H), 3.64 (dd, *J* = 14.7 and 7.8 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 15.1 (CH_3), 20.2 (CH_3), 38.3 (CH), 39.2 (CH_3), 51.7 (CH_3), 56.7 (CH_2), 112.5 (CH), 125.8 (C), 129.6 (CH), 146.9 (C), 176.1 (C).

1,3,3,6-Tetramethyl-2,3-dihydro-1*H*-quinolin-4-one (11a)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 6H), 2.26 (s, 3H), 2.99 (s, 3H), 3.13 (s, 2H), 6.64 (d, *J* = 8.7 Hz, 1H), 7.23 (dd, *J* = 8.7 and 2.4 Hz, 1H), 7.73 (dd, *J* = 2.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.1 (CH_3), 22.0 (CH_3), 39.3 (CH_3), 41.8 (C), 63.5 (CH_2), 112.9 (CH), 117.9 (C), 126.1 (C), 128.3 (CH), 136.1 (CH), 149.9 (C), 198.8 (C). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.63; H, 8.48; N, 6.81.

6-Methoxy-1,3,3-trimethyl-2,3-dihydro-1*H*-quinolin-4-one (11b)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.17 (s, 6H), 2.98 (s, 3H), 3.11 (s, 2H), 3.79 (s, 3H), 6.70 (d, *J* = 9 Hz, 1H), 7.07 (dd, *J* = 9 and 2.7 Hz, 1H), 7.43 (d, *J* = 2.7 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 22.0 (CH_3), 39.6 (CH_3), 41.9 (C), 55.7 (CH_3), 63.8 (CH_2), 109.5 (CH), 114.6 (CH), 118.1 (C), 124.5 (CH), 147.2 (C), 151.5 (C), 198.6 (C). Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 70.75; H, 7.96; N, 6.17.

Methyl 1,3,3-trimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-6-carboxylate (11c)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15 (s, 6H), 3.10 (s, 3H), 3.26 (s, 2H), 3.85 (s, 3H), 6.69 (d, *J* = 9 Hz, 1H), 8.00 (dd, *J* = 9 and 2.1 Hz, 1H), 8.57 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 21.9 (CH_3), 39.2 (CH_3), 41.4 (C), 51.7 (CH_3), 62.7 (CH_2), 112.3 (CH), 117.0 (C), 118.4 (C), 131.2 (CH), 135.6 (CH), 153.6 (C), 166.7 (C), 197.5 (C). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.88; H, 6.86; N, 5.48.

1,3,6-Trimethyl-3-phenyl-2,3-dihydro-1*H*-quinolin-4-one (11d)

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.46 (s, 3H), 2.23 (s, 3H), 2.99 (s, 3H), 3.44 (d, *J* = 12.8 Hz, 1H), 3.73 (d, *J* = 12.8 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 7.15-7.31 (m, 6H), 7.79 (s, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.1 (CH_3), 23.2 (CH_3), 39.1 (CH_3), 49.7 (C), 61.9 (CH_2), 113.0 (CH), 118.9 (C), 126.2 (C), 126.3 (CH), 126.9 (CH), 128.3 (CH), 128.5 (CH), 136.3 (CH), 140.9 (C), 149.7 (C), 196.5 (C). Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28. Found: C, 79.86; H, 7.20; N, 5.13.

1,3,3,7-Tetramethyl-2,3-dihydro-1*H*-quinolin-4-one (13a)

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (s, 6H), 2.33 (s, 3H), 3.01 (s, 3H), 3.15 (s, 2H), 6.50 (s, 1H), 6.57 (d, *J* = 8 Hz, 1H), 7.82 (d, *J* = 8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 22.0 (CH_3), 23.3 (CH_3), 39.2 (CH_3), 41.6 (C), 63.5 (CH_2), 112.9 (CH), 116.0 (C), 118.5 (CH), 128.8 (CH), 145.9 (C), 151.7 (C), 198.4 (C). Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.63; H, 8.48; N, 6.81.

7-Chloro-1,3,3-trimethyl-2,3-dihydro-1*H*-quinolin-4-one (13b)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 6H), 3.02 (s, 3H), 3.19 (s, 2H), 6.69 (s, 1H), 6.70 (dd, *J* = 7.8 and 1.8 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 21.9 (CH_3), 39.2 (CH_3), 41.6 (C), 63.2 (CH_2), 112.5 (CH), 116.5 (C), 117.5 (CH), 130.3 (CH), 141.4 (C), 152.0 (C), 197.7 (C). Calcd for $C_{12}H_{14}ClNO$: C, 64.43; H, 6.31; N, 6.26. Found: C, 64.59; H, 6.20; N, 6.71.

Methyl 3-[*N*-(methoxycarbonyl)-*N*-phenylamino]propionate (15a)

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.61 (t, *J* = 7.5 Hz, 2H), 3.60 (s, 3H), 3.68 (s, 3H), 3.98 (t, *J* = 7.5 Hz, 2H), 7.15-7.40 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 33.2 (CH_2), 46.5 (CH_2), 51.6 (CH_3), 52.9 (CH_3), 126.9 (CH), 127.3 (CH), 129.1 (CH), 141.3 (C), 155.8 (C), 171.7 (C). HRMS (ESI-TOF) calcd for $C_{12}H_{15}NO_4Na$: 260.0893 $[M+Na]^+$; found: 260.0885.

Methyl 3-[*N*-phenyl-*N*-(*p*-toluenesulfonyl)amino]propionate (15b)

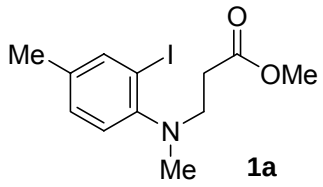
^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (s, 3H), 2.56 (t, *J* = 7.5 Hz, 2H), 3.60 (s, 3H), 3.84 (t, *J* = 7.5 Hz, 2H), 7.04 (m, 2H), 7.23-7.33 (m, 5H), 7.47 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 21.6 (CH_3), 34.0 (CH_2), 46.8 (CH_2), 51.7 (CH_3), 127.7 (CH), 128.1 (CH), 128.9 (CH), 129.1 (CH), 129.4 (CH), 135.1 (C), 139.0 (C), 143.5 (C), 171.3 (C). HRMS (ESI-TOF) calcd for $C_{17}H_{20}NO_4S$: 334.1108 $[M+H]^+$; found: 334.1110.

Palladium complex 16

To a solution of methyl 3-[*N*-(2-iodo-4-methylphenyl)-*N*-methylamino]propionate (**1a**, 40 mg, 0.12 mmol) in benzene (10 mL) were added $Pd_2(dba)_3$ (77 mg, 0.084 mmol) and PPh_3 (44 mg, 0.168 mmol).[7] The reddish reaction mixture was stirred at room temperature for 24 h. The solvent was evaporated, and the residue was purified by "flash" chromatography (SiO_2). Elution with hexane/EtOAc (75:25) afforded pure azapalladacycle **16** as an orange foam (115 mg, 73%).

[7] Solé, D.; Vallverdú, L.; Solans, X.; Font-Bardia, M.; Bonjoch, J. *Organometallics*, **2004**, *23*, 1438-1447.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.88 (s, 3H), 2.84 (m, 1H), 3.16 (d, *J* = 3 Hz, 3H), 3.28-3.68 (m, 3H), 3.55 (s, 3H), 5.54 (s, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 7.30-7.50 (m, 9H), 7.65-7.75 (m, 6H). ^{13}C NMR ($CDCl_3$, 100.5 MHz) δ 21.8 (CH_3), 34.0 (CH_2), 51.3 (CH_3), 51.6 (CH_3), 54.9 (CH_2), 118.9 (CH), 125.8 (d, *J* = 10.1 Hz, C), 126.1 (CH), 128.2 (d, *J* = 11.6 Hz, CH), 129.0 (d, *J* = 7.7 Hz, CH), 130.8 (d, *J* = 2.3 Hz, CH), 131.6 (d, *J* = 52.7 Hz, C), 135.0 (d, *J* = 12.4 Hz, CH), 158.6 (d, *J* = 3.9 Hz, C), 171.5 (C). One C was no observed. ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ 40.6. HRMS (ESI-TOF) calcd for $C_{30}H_{32}INO_2PPd$: 702.0245 $[M+H]^+$; found: 702.0234.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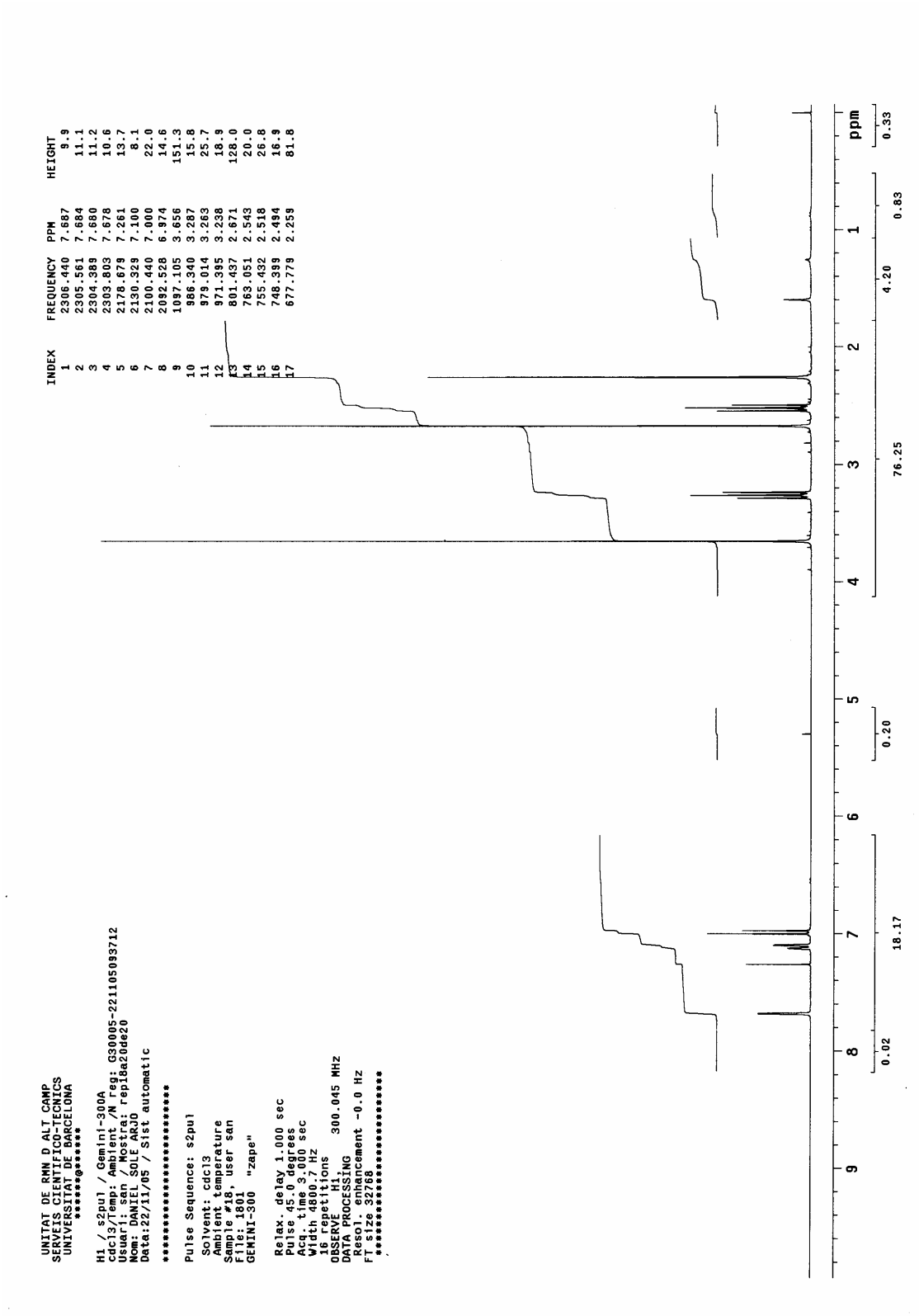
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UNIVERSITAT DE BARCELONA
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Solvent: cdcl3
Ambient temperature
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7 2100.440 7.000 22.0
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9 1097.105 3.656 151.3
10 986.340 3.287 15.8
11 979.014 3.263 25.7
12 971.395 3.238 18.9
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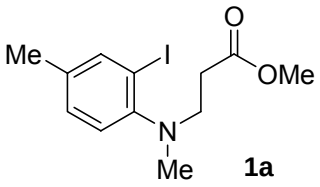
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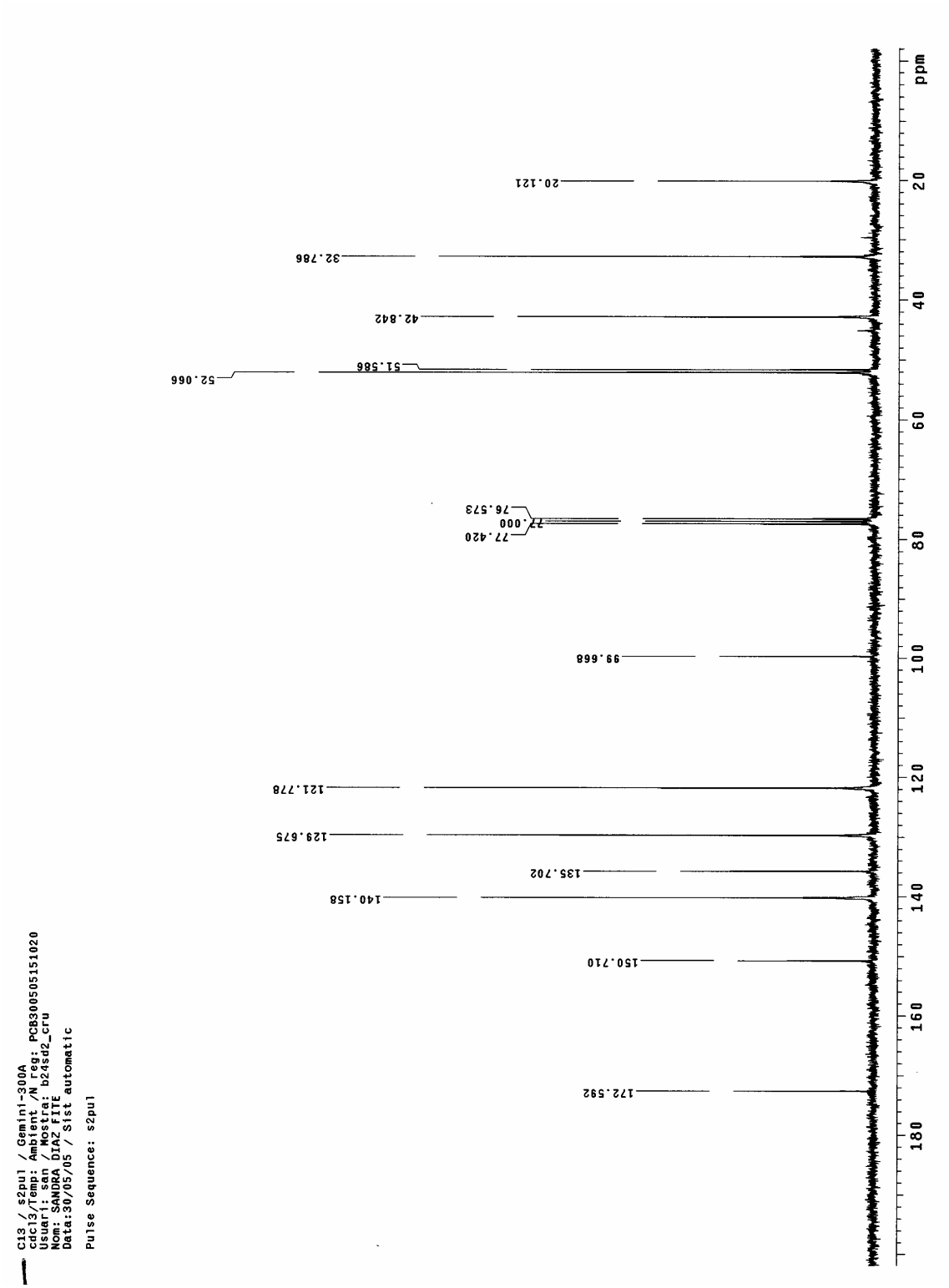
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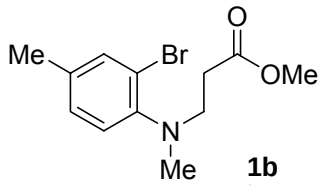

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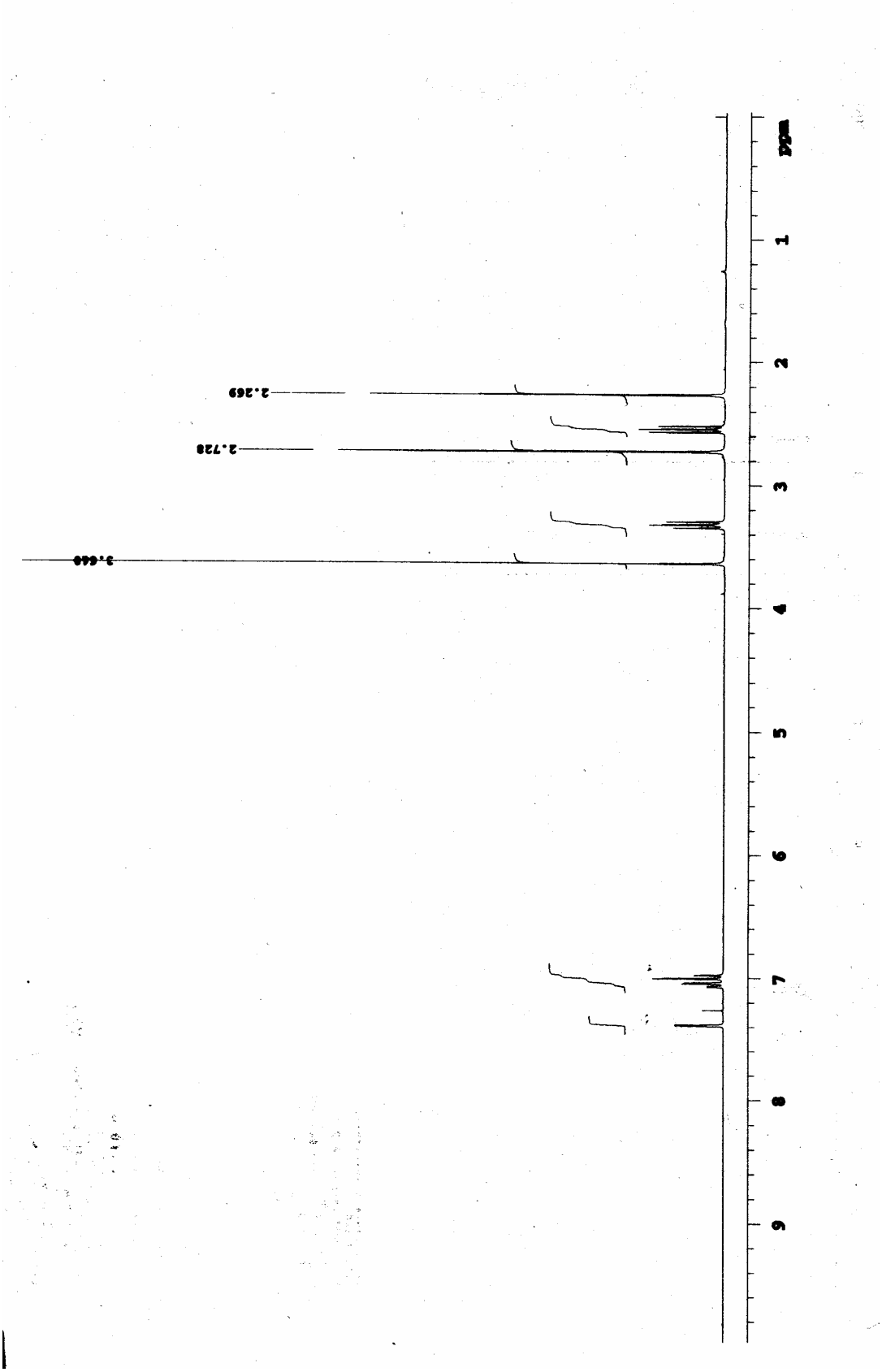

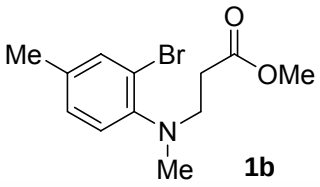
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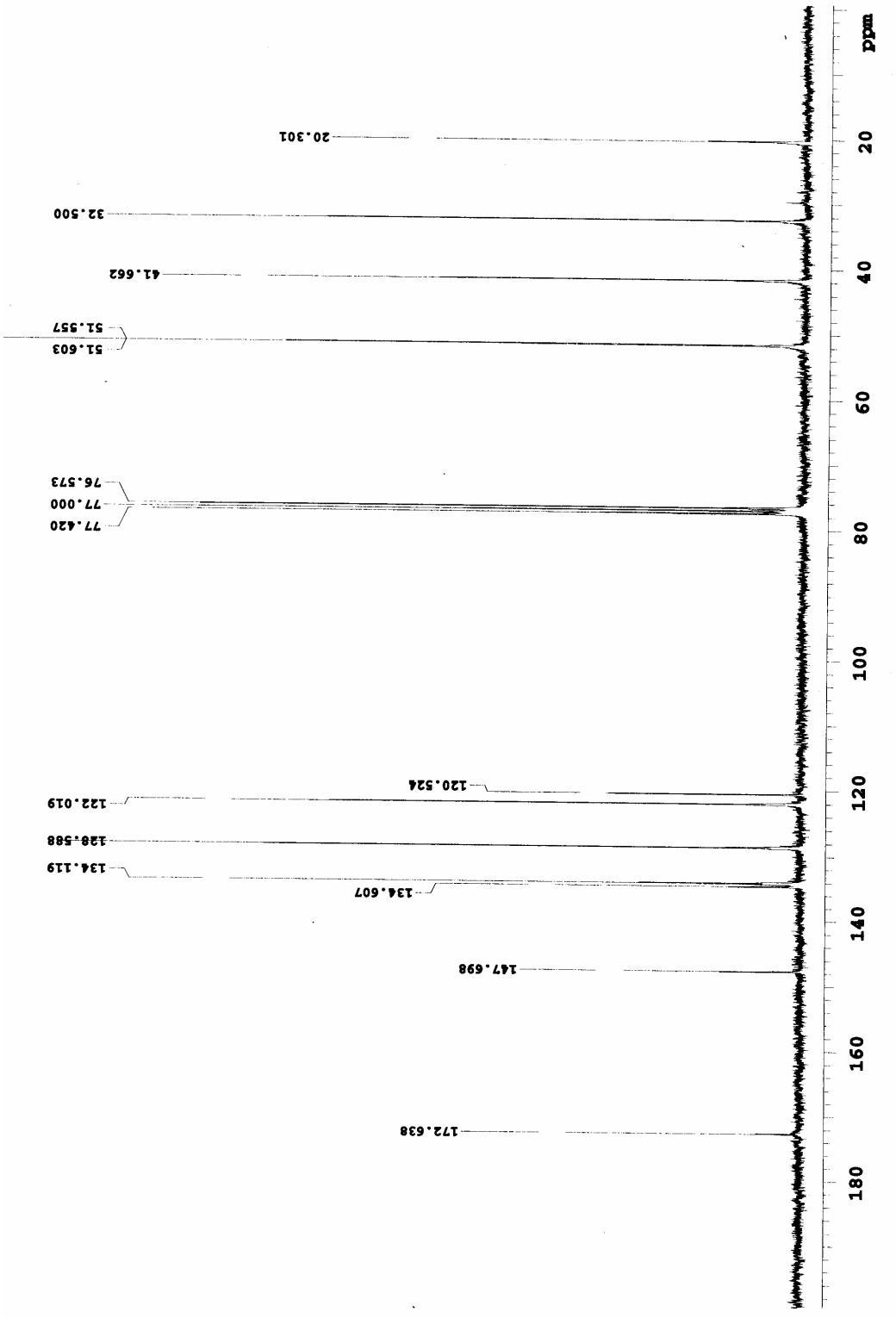
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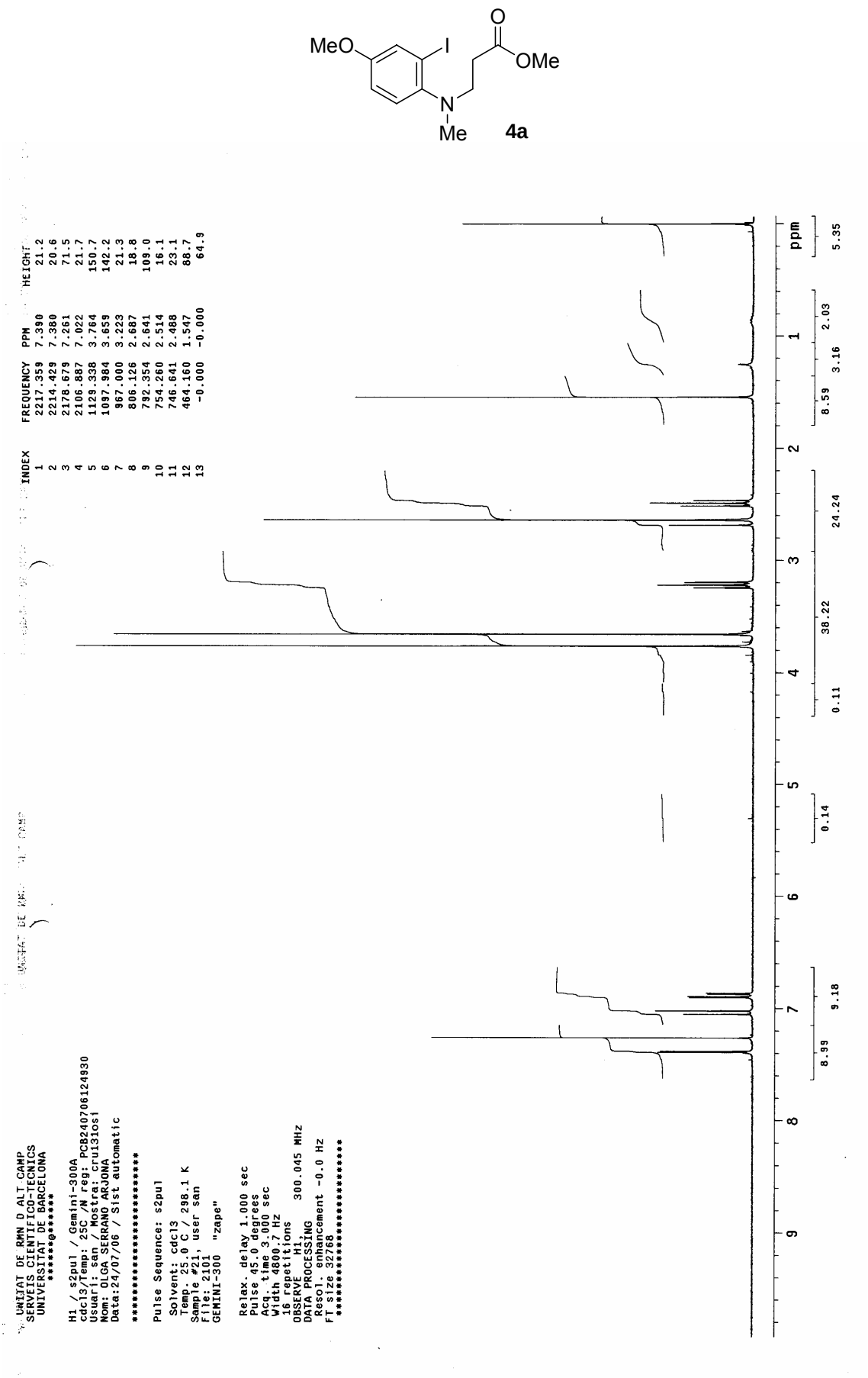
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UNIVERSITAT DE BARCELONA
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7 967.000 3.223 21.3
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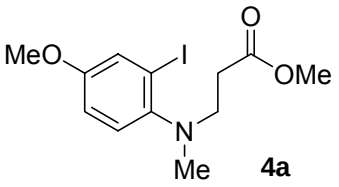
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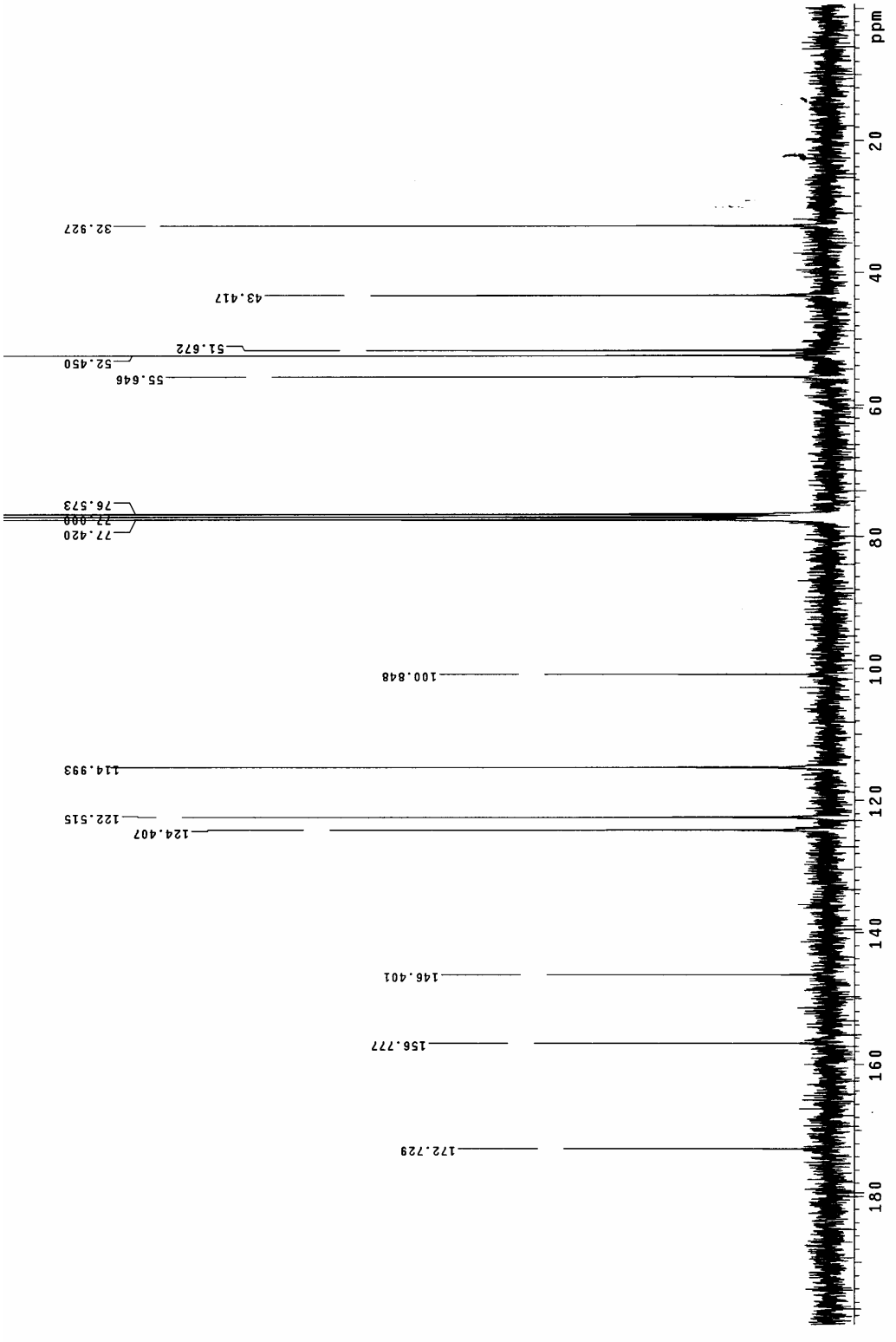
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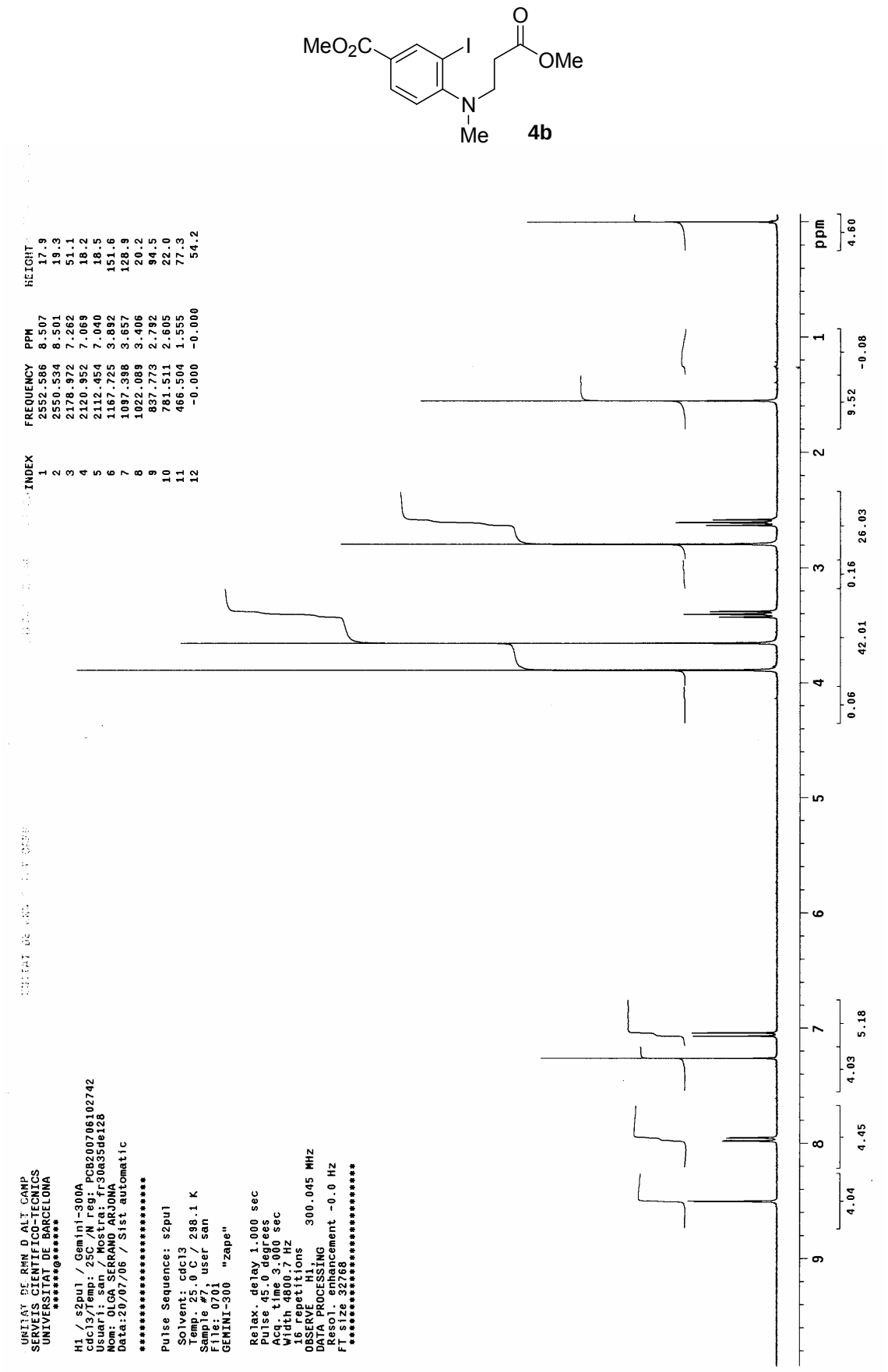
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6 1167.725 3.892 151.6
7 1097.398 3.657 128.9
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10 781.511 2.605 22.0
11 466.504 1.555 77.3
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UNITAT DE RMN D'ALT CAMP
SERVEIS CIENTIFICO-TECNICS
UNIVERSITAT DE BARCELONA
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Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Sample #7, user san
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Pulse 45.0 degrees
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Width 4800.7 Hz
16 repetitions
OBSERVE H1, 300.045 MHz
DATA PROCESSING
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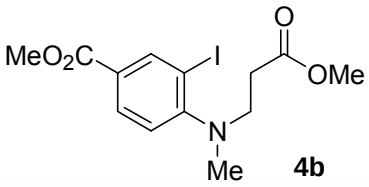
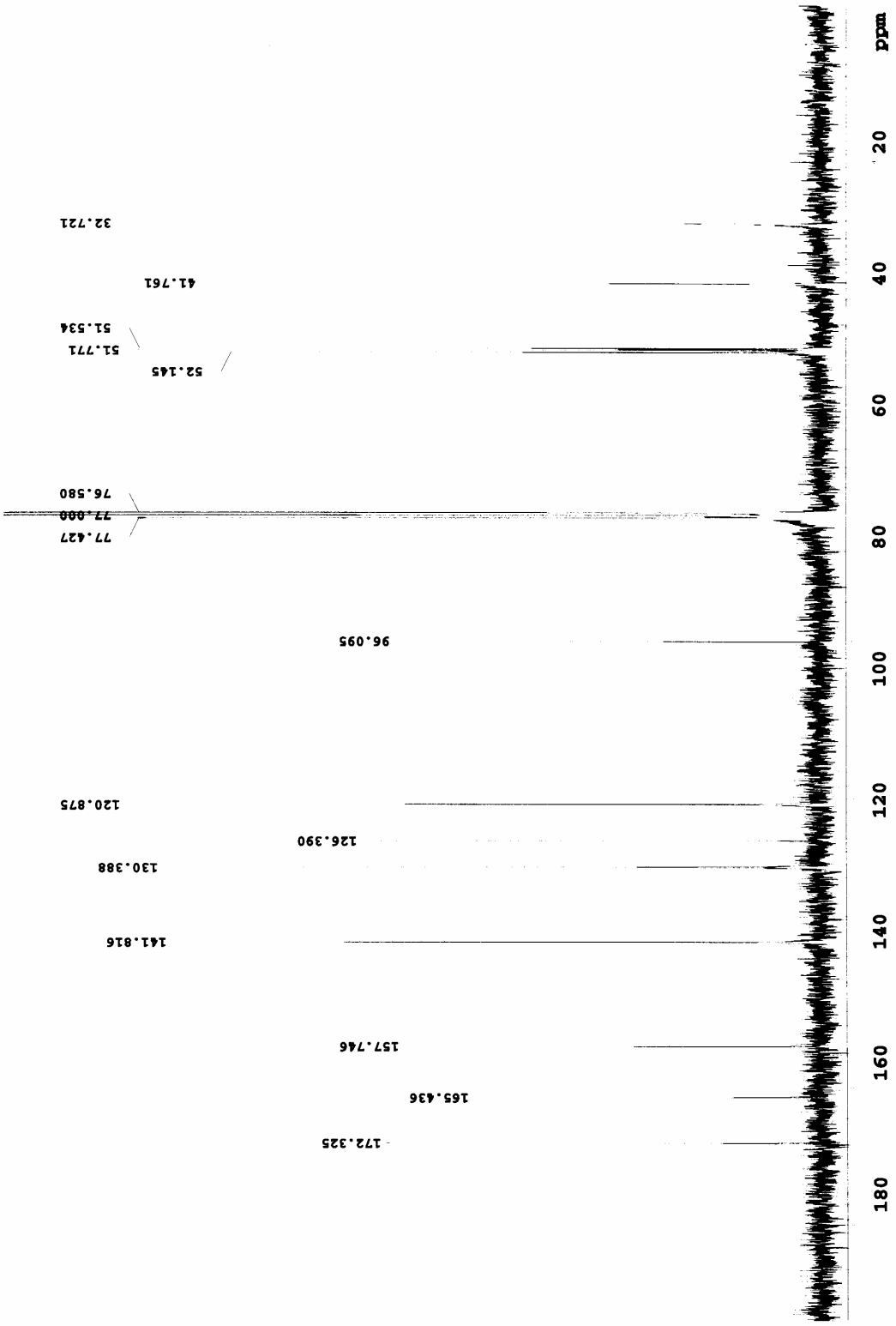
FT size 32768
ppm
4.04 4.45 4.03 5.18
0.06 42.01 0.16 26.03
9.52 -0.08 4.60


MeO2C
I
O
OMe
N
Me

4b


ppm
20
40
60
80
100
120
140
160
180
32.721
41.761
51.534
51.771
52.145
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77.000
77.427
96.095
120.875
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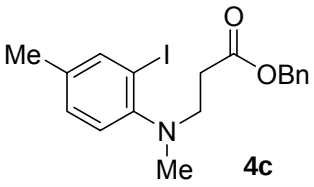
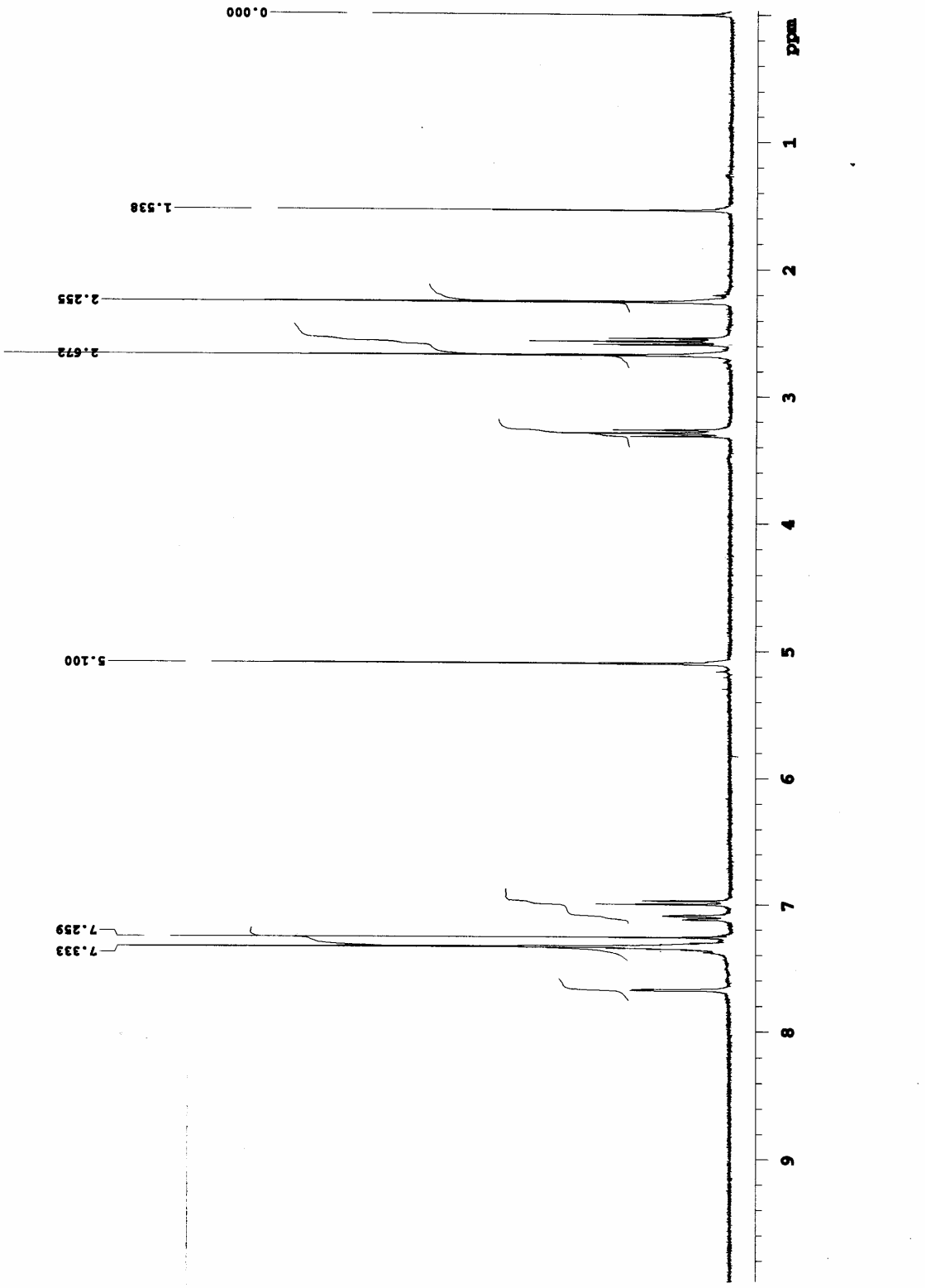
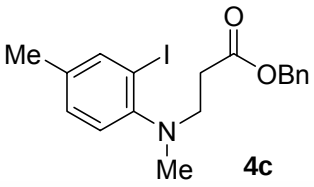
130.388
141.816
157.746
165.436
172.325

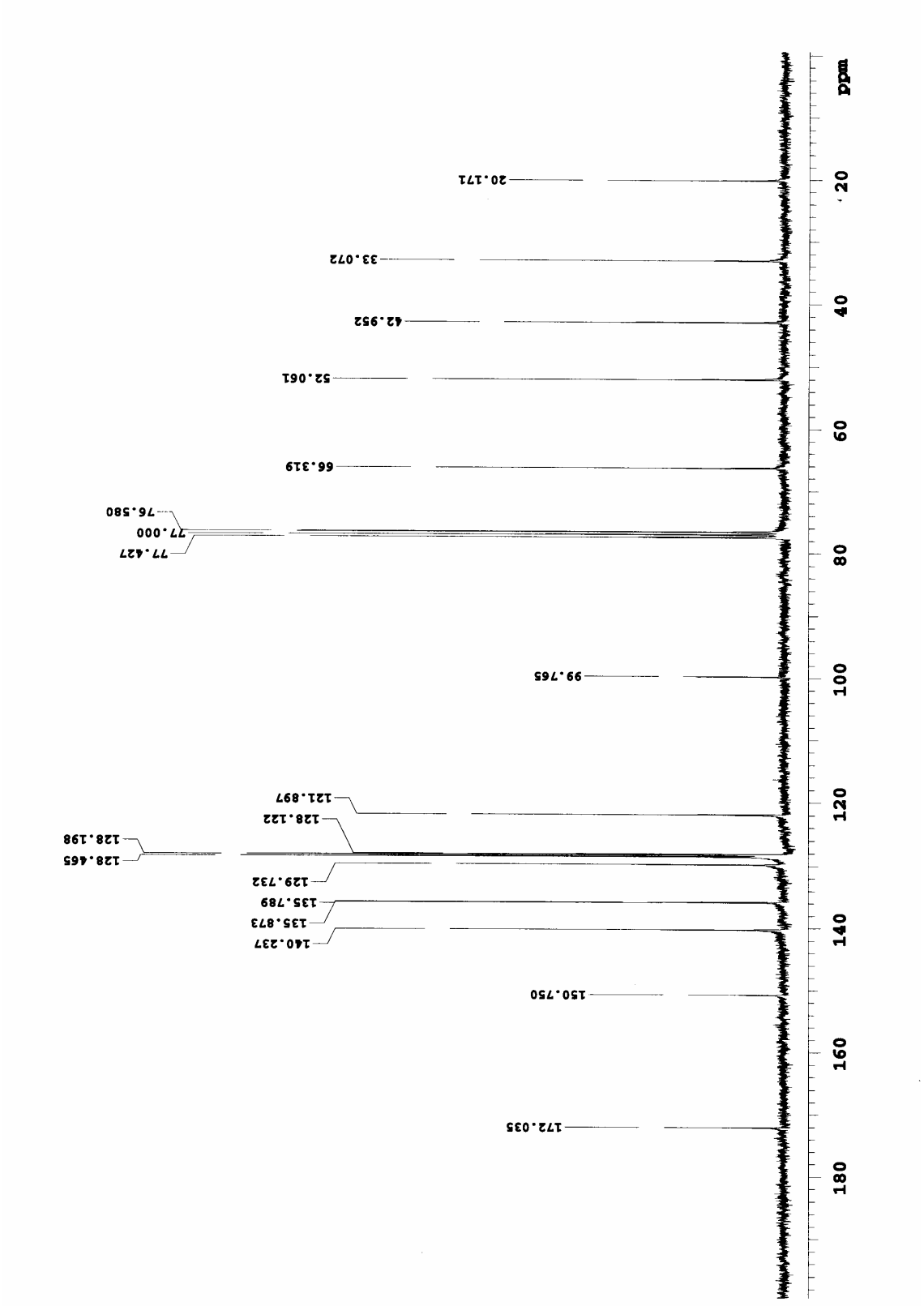

Me
I
O
OBn
N
Me

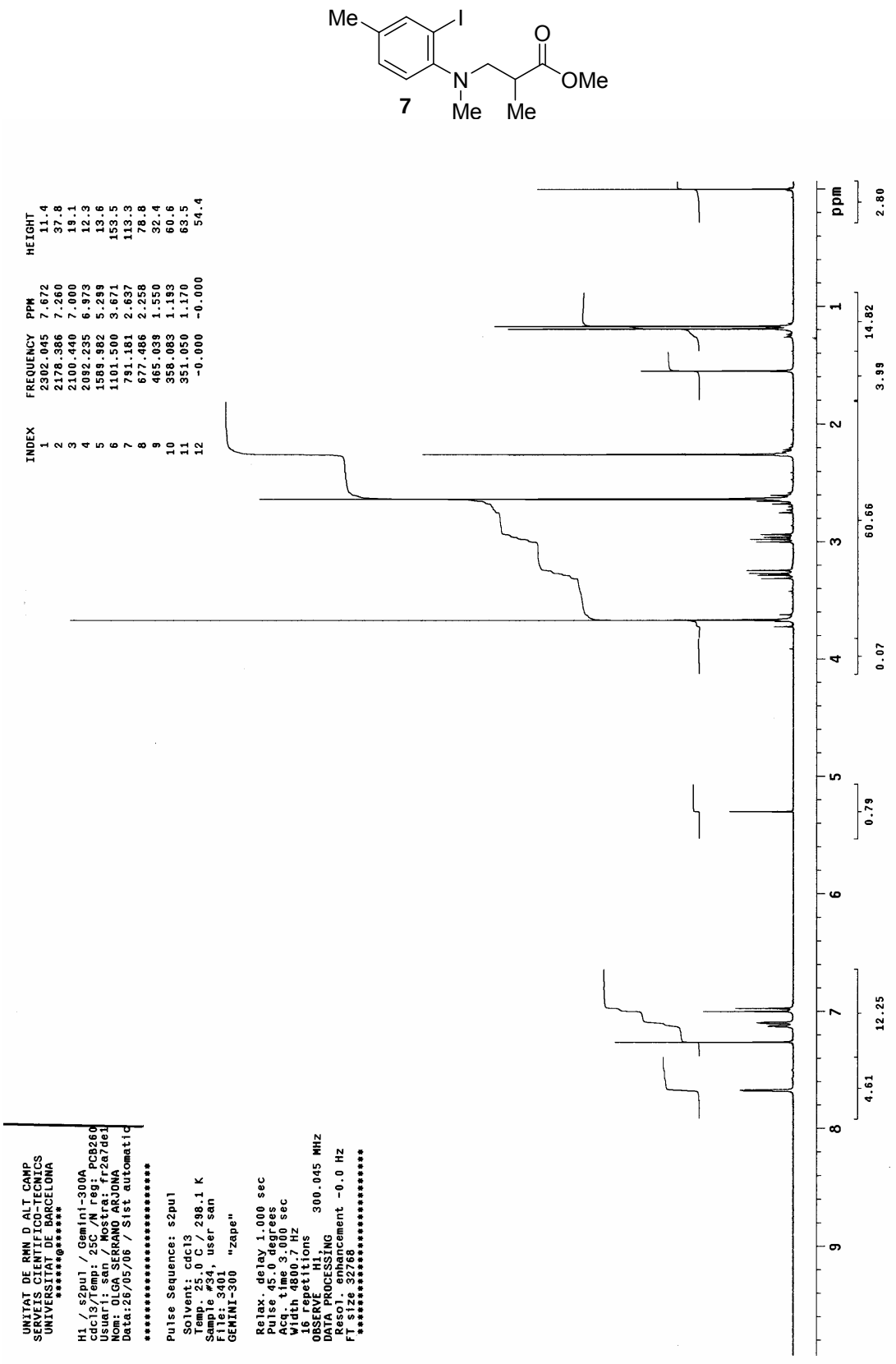
4c

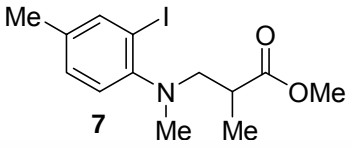

0.000
1.538
2.255
2.672
5.100
7.259
7.333
ppm
1
2
3
4
5
6
7
8
9


Me
I
O
OBn
N
Me

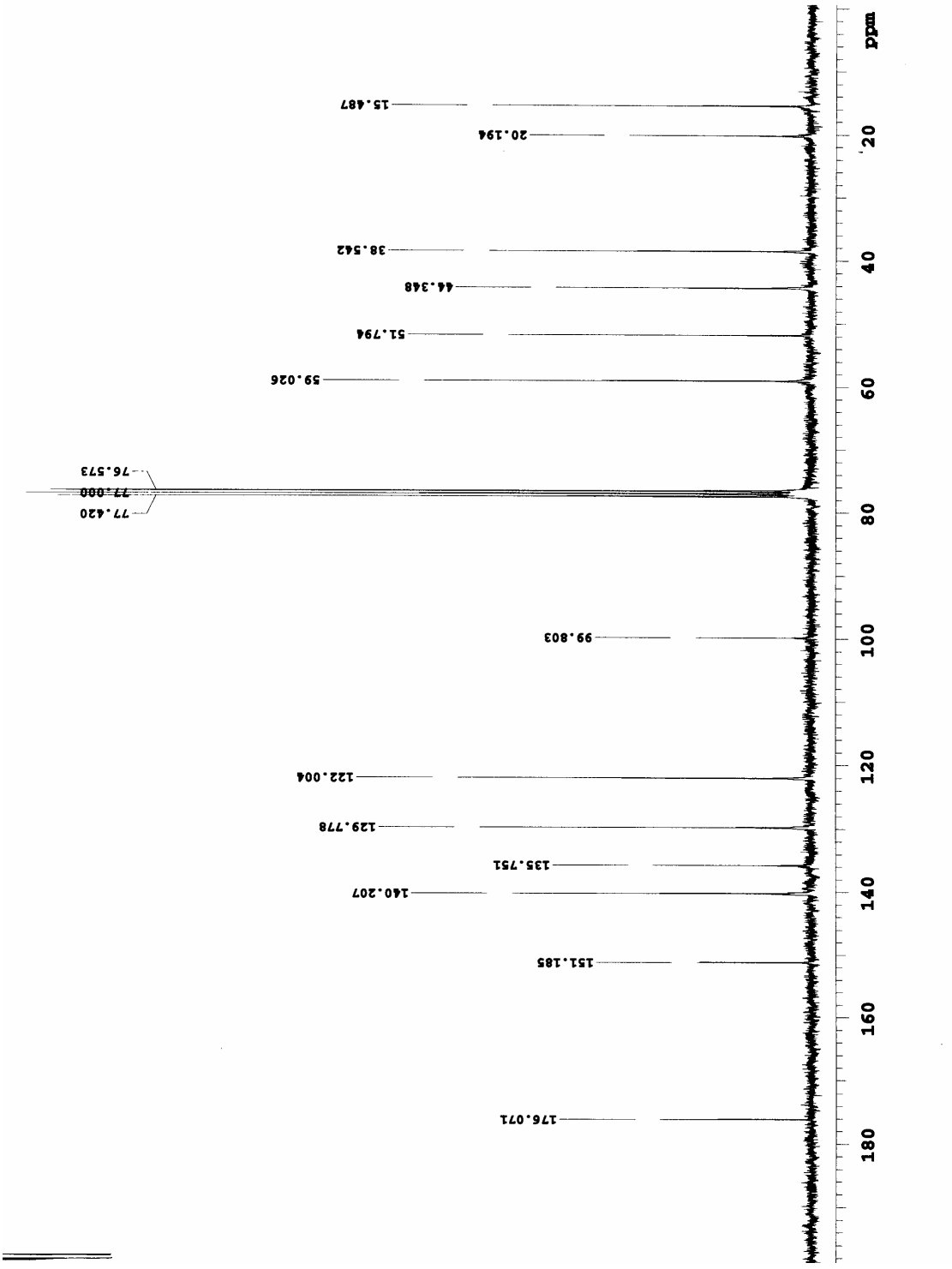
4c

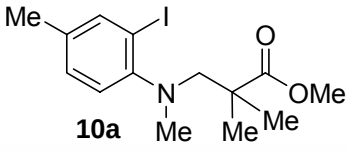

20.171
33.072
42.952
52.061
66.319
76.580
77.000
77.427
99.765
121.897
128.122
128.198
128.465
129.732
135.789
135.873
140.237
150.750
172.035
ppm
20
40
60
80
100
120
140
160
180


Me
I
O
N
OMe
Me
Me
7
UNITAT DE RMN D ALT CAMP
SERVEIS CIENTIFICO-TECNICS
UNIVERSITAT DE BARCELONA
H1 / s2pul / Gemini-300A
cdcl3/Temp: 25C /N reg: PCB260
Usuari: san / Mostra: fr2a7de1
Nom: DJA SERRANO ARJONA
Data:26/05/06 / Sist automatic
Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Sample #34, user san
File: 3401 "zape"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 4800.7 Hz
16 repetitions
OBSERVE H1, 300.045 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 32768
INDEX FREQUENCY PPM HEIGHT
1 2302.045 7.672 11.4
2 2178.386 7.260 37.8
3 2100.440 7.000 19.1
4 2092.235 6.973 12.3
5 1589.982 5.299 13.6
6 1101.500 3.671 153.5
7 791.181 2.637 113.3
8 677.486 2.258 78.8
9 465.039 1.550 32.4
10 358.083 1.193 60.6
11 351.050 1.170 63.5
12 -0.000 -0.000 54.4
ppm
4.61
12.25
0.79
0.07
60.66
3.99
14.82
2.80

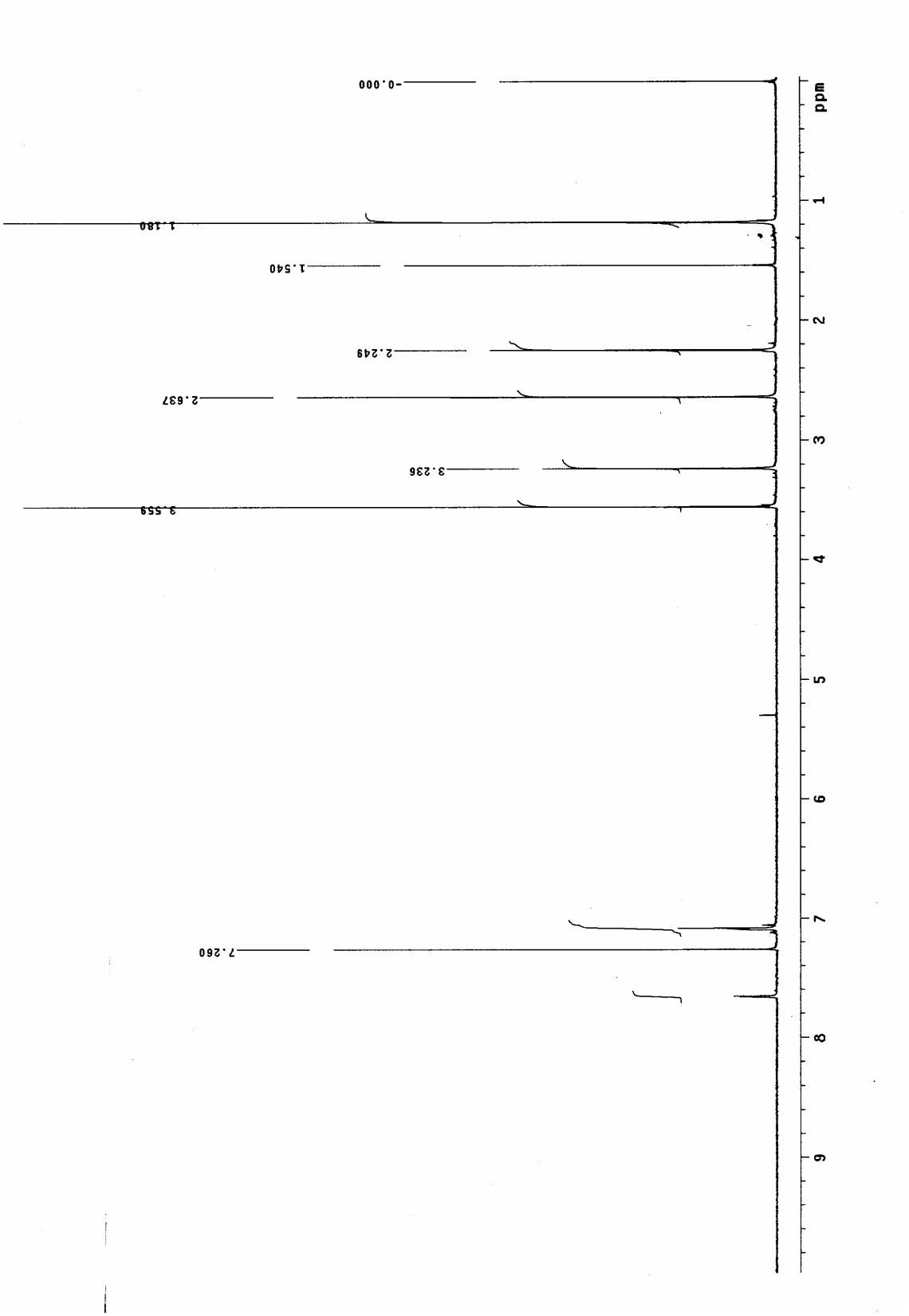

Me
I
O
N
OMe
Me
Me

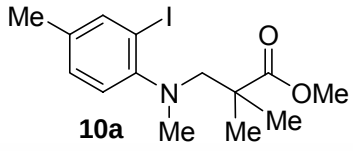
7


15.487
20.194
38.542
44.348
51.794
59.026
76.573
77.000
77.420
99.803
122.004
129.778
135.751
140.207
151.185
176.071
ppm
20
40
60
80
100
120
140
160
180

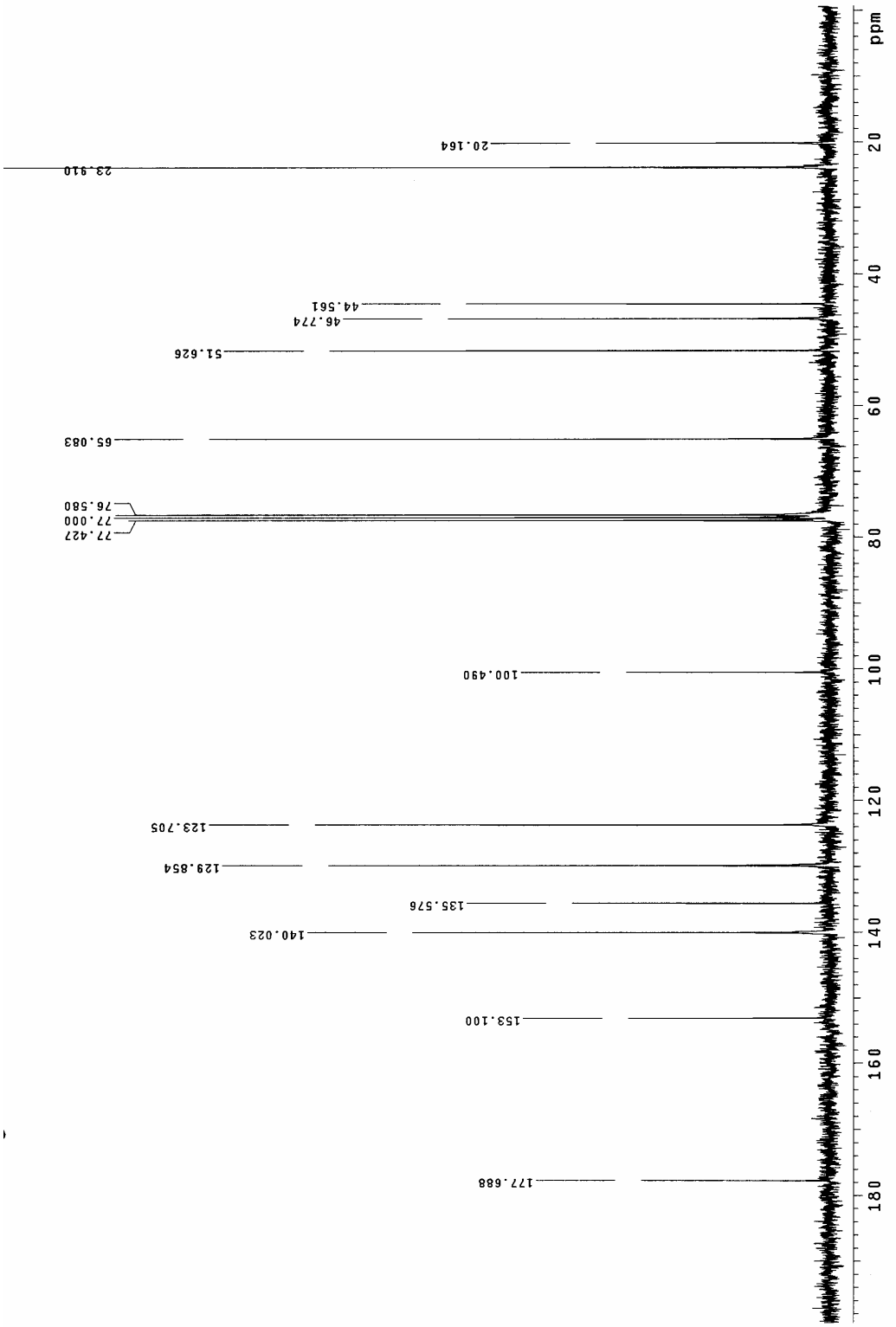

Me
I
O
N
OMe
Me
Me
Me

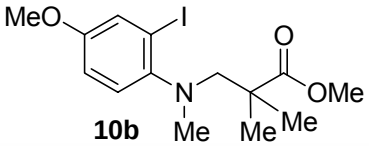
10a


0.000
1.180
1.540
2.249
2.637
3.236
3.559
7.260
ppm
1
2
3
4
5
6
7
8
9

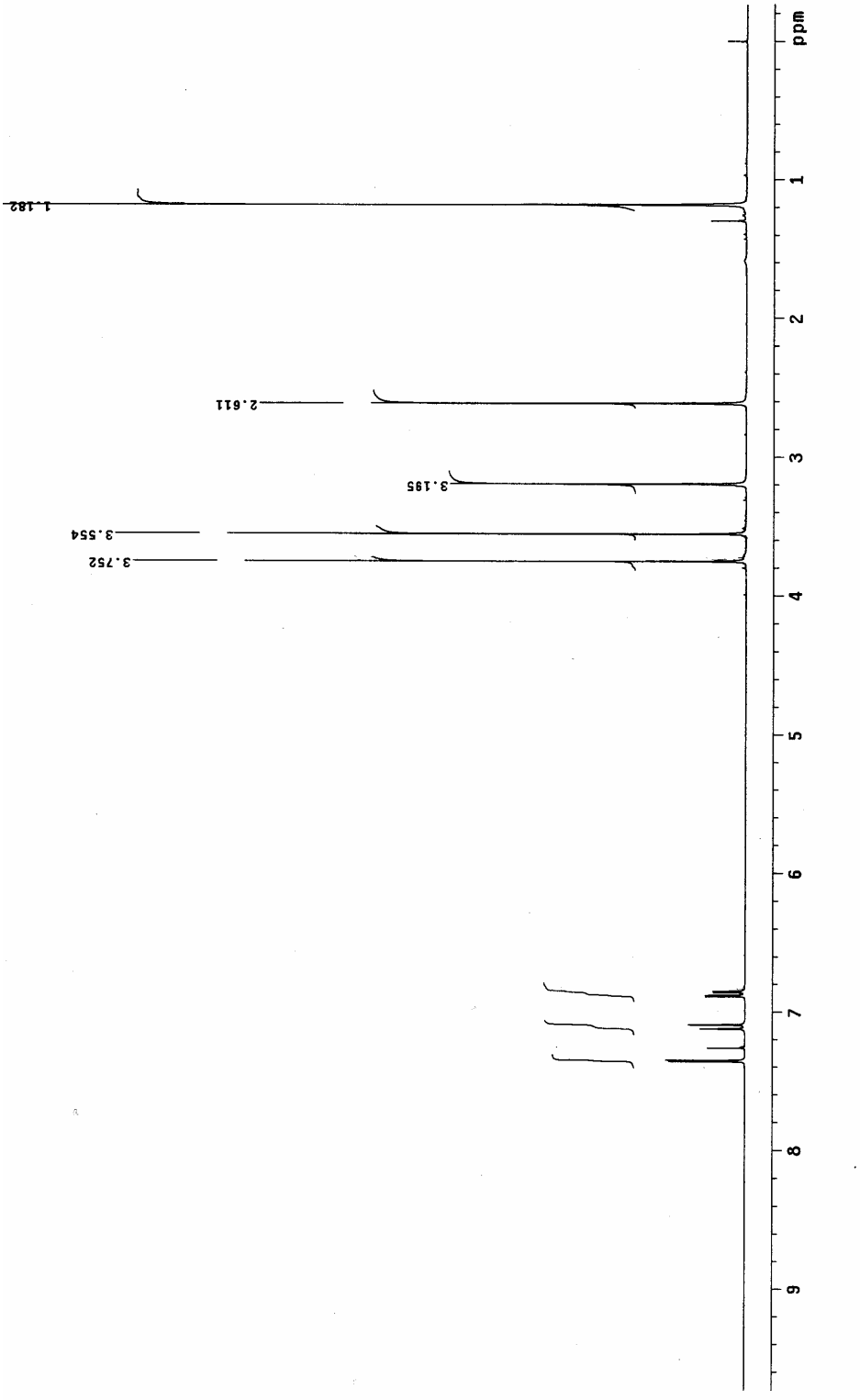

Me
I
O
N
OMe
Me
Me
Me

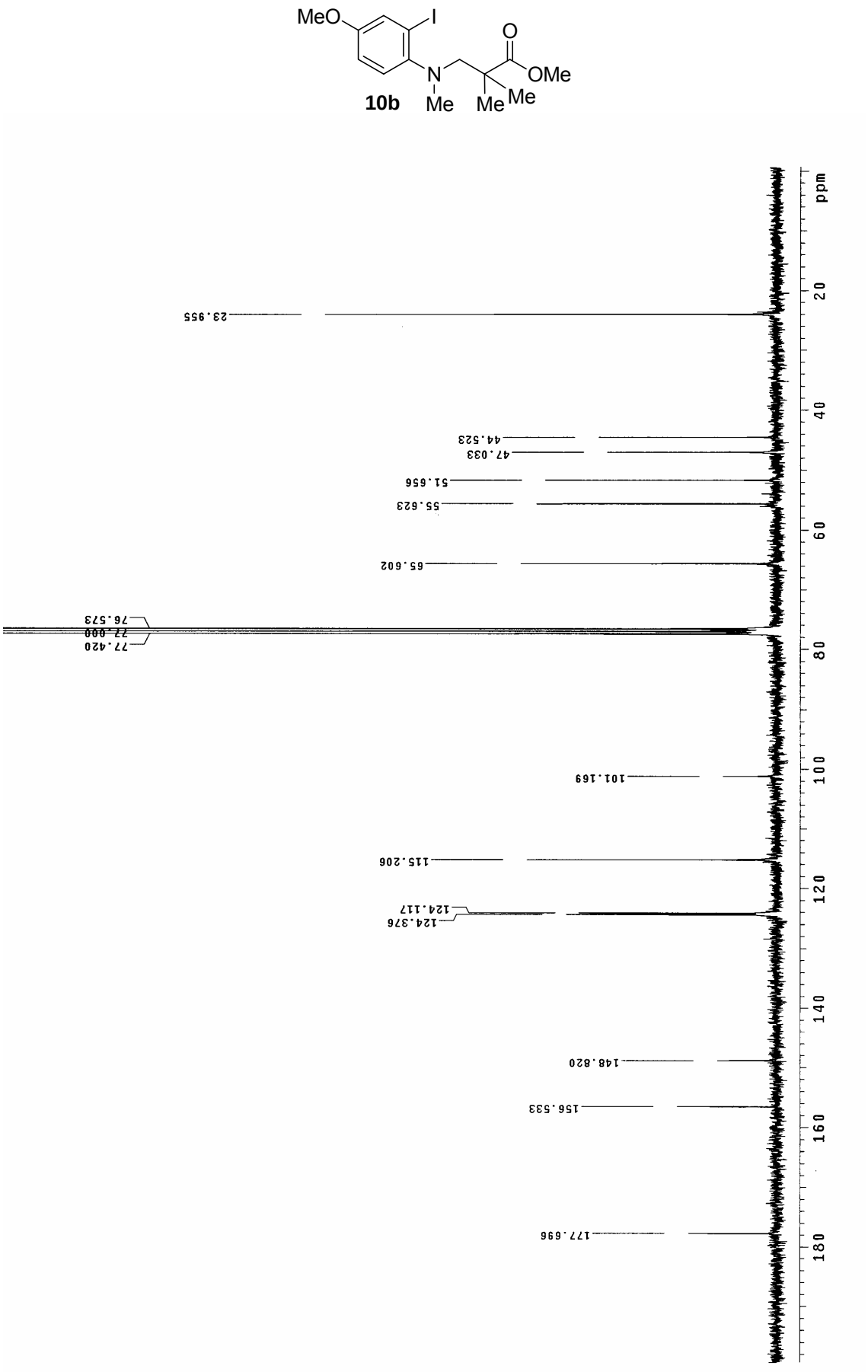
10a

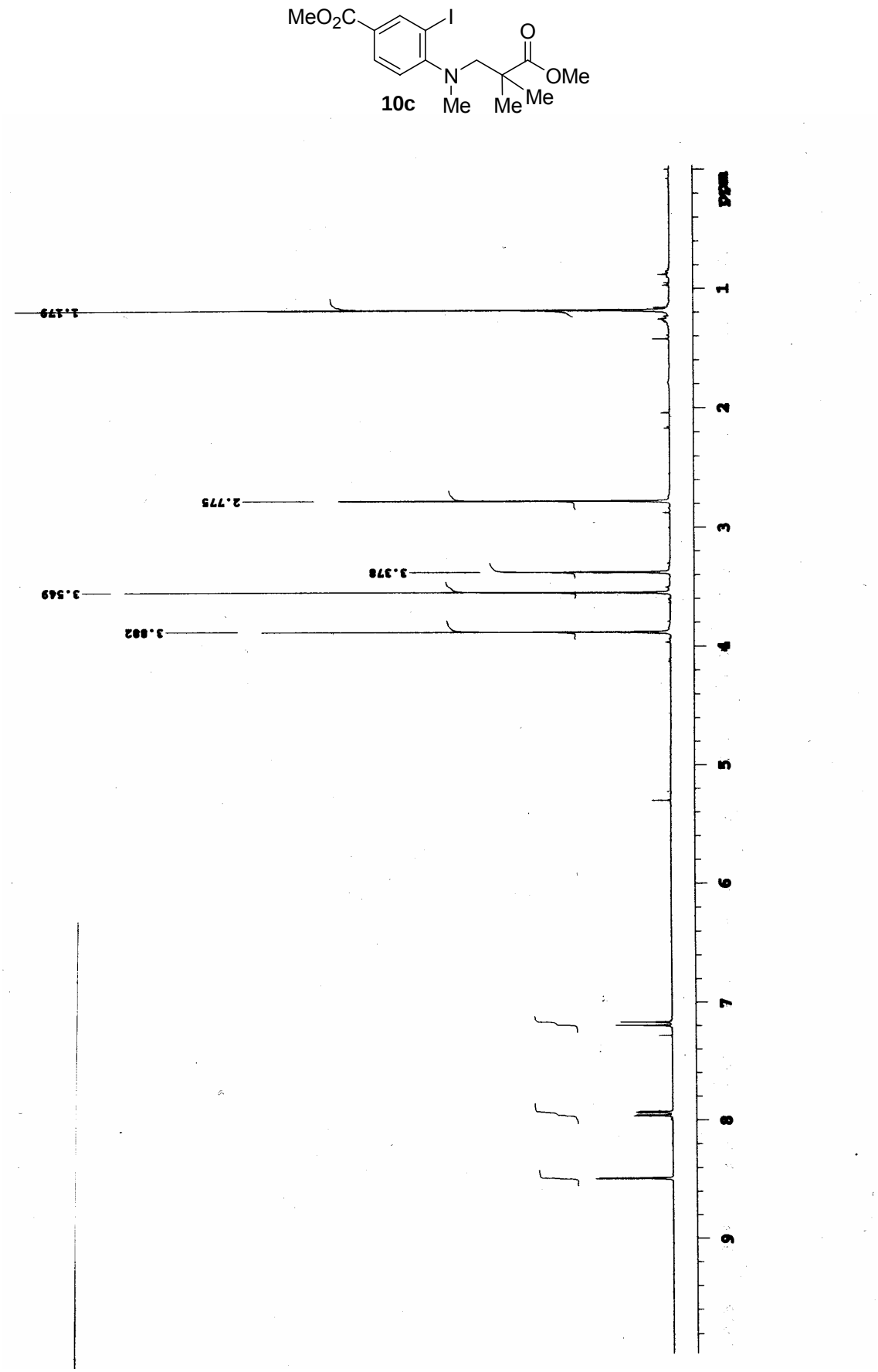

ppm
20
40
60
80
100
120
140
160
180
20.164
23.910
44.561
46.774
51.626
65.083
76.580
77.000
77.427
100.490
123.705
129.854
135.576
140.023
153.100
177.688

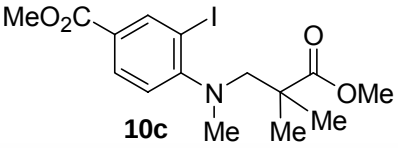


10b

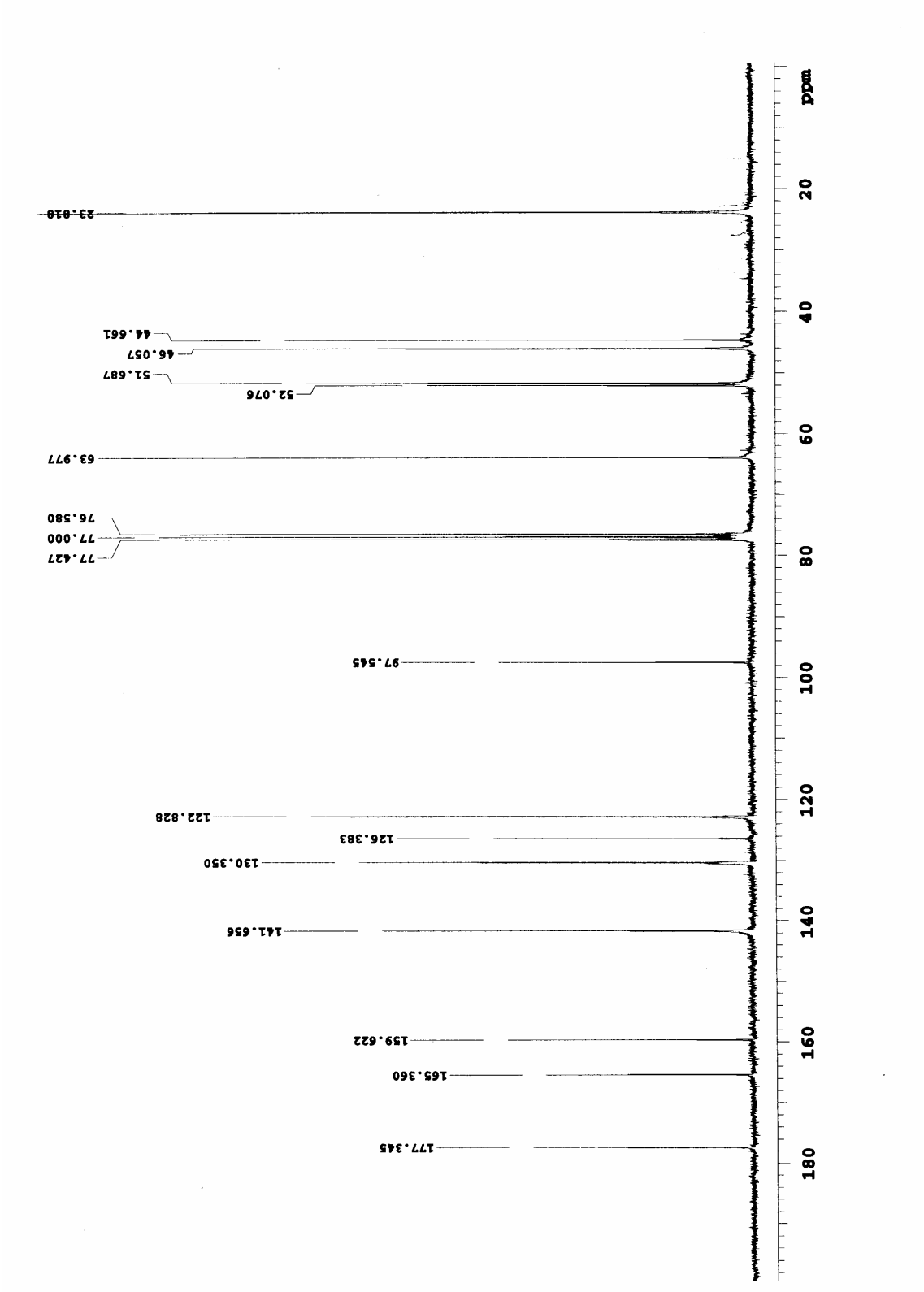


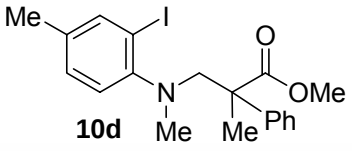

MeO
I
O
N
OMe
Me
Me
Me
10b
ppm
20
40
60
80
100
120
140
160
180
23.955
44.523
47.033
51.656
55.623
65.602
76.573
77.000
77.420
101.169
115.206
124.117
124.376
148.820
156.533
177.696


MeO2C
I
O
N
OMe
Me
Me
Me
10c
2.179
2.775
3.378
3.549
3.882

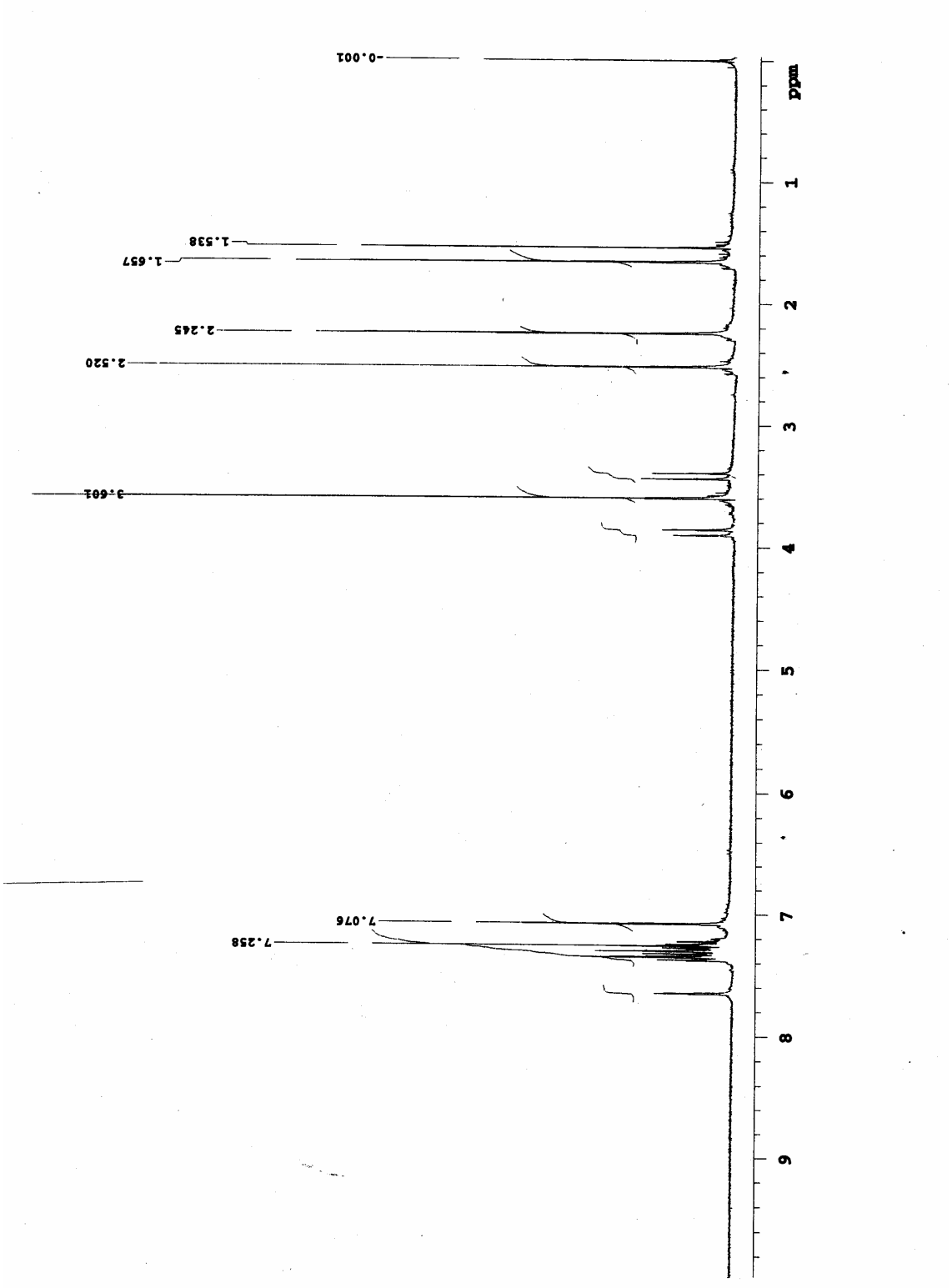

MeO2C
I
O
N
OMe
Me
Me
Me

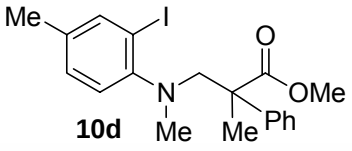
10c


23.818
44.661
46.057
51.687
52.076
63.977
76.580
77.000
77.427
97.545
122.828
126.383
130.350
141.656
159.622
163.360
177.345
ppm
20
40
60
80
100
120
140
160
180

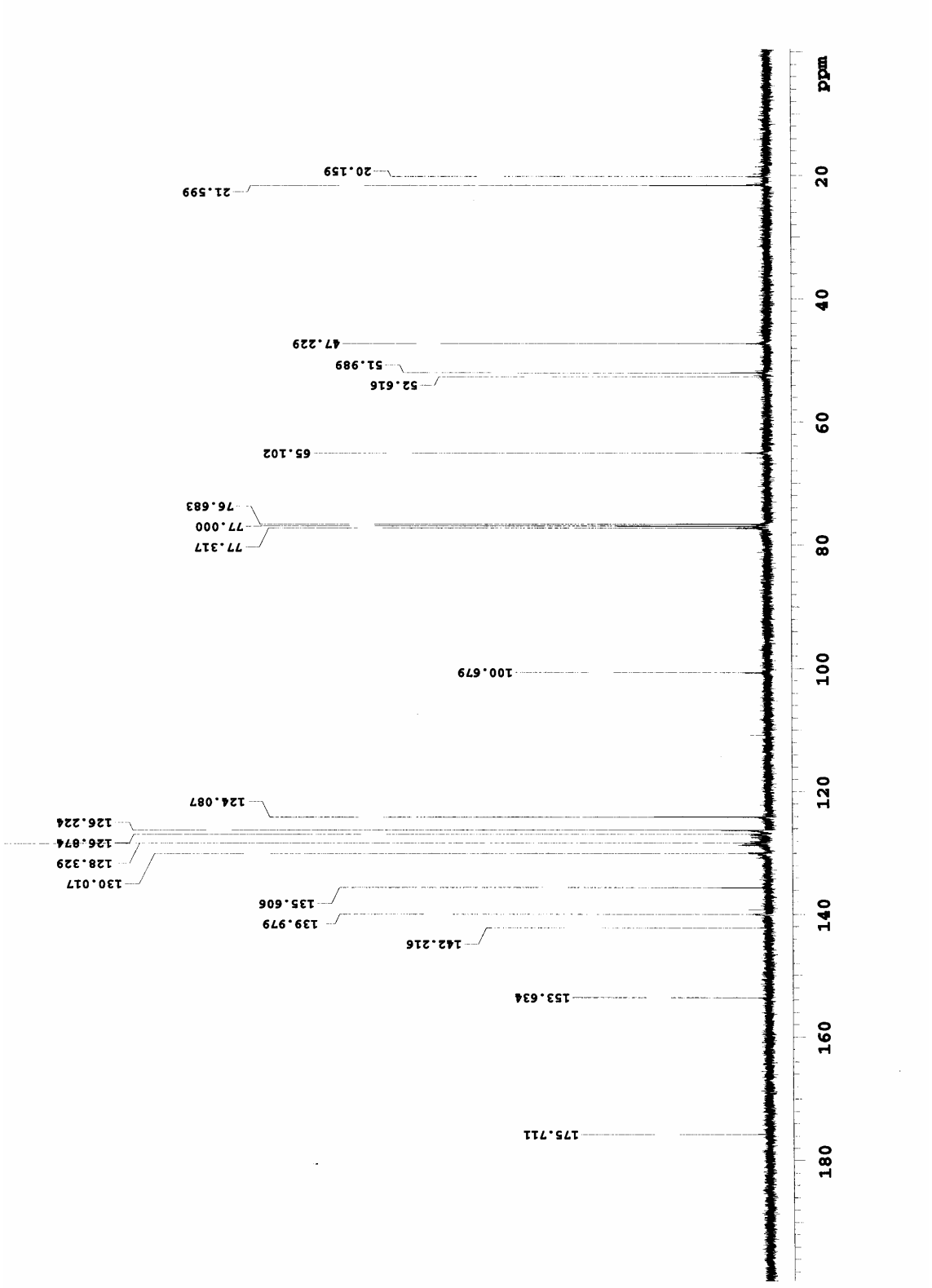


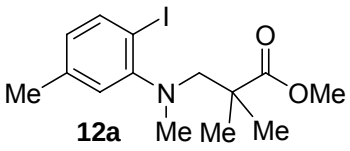
10d



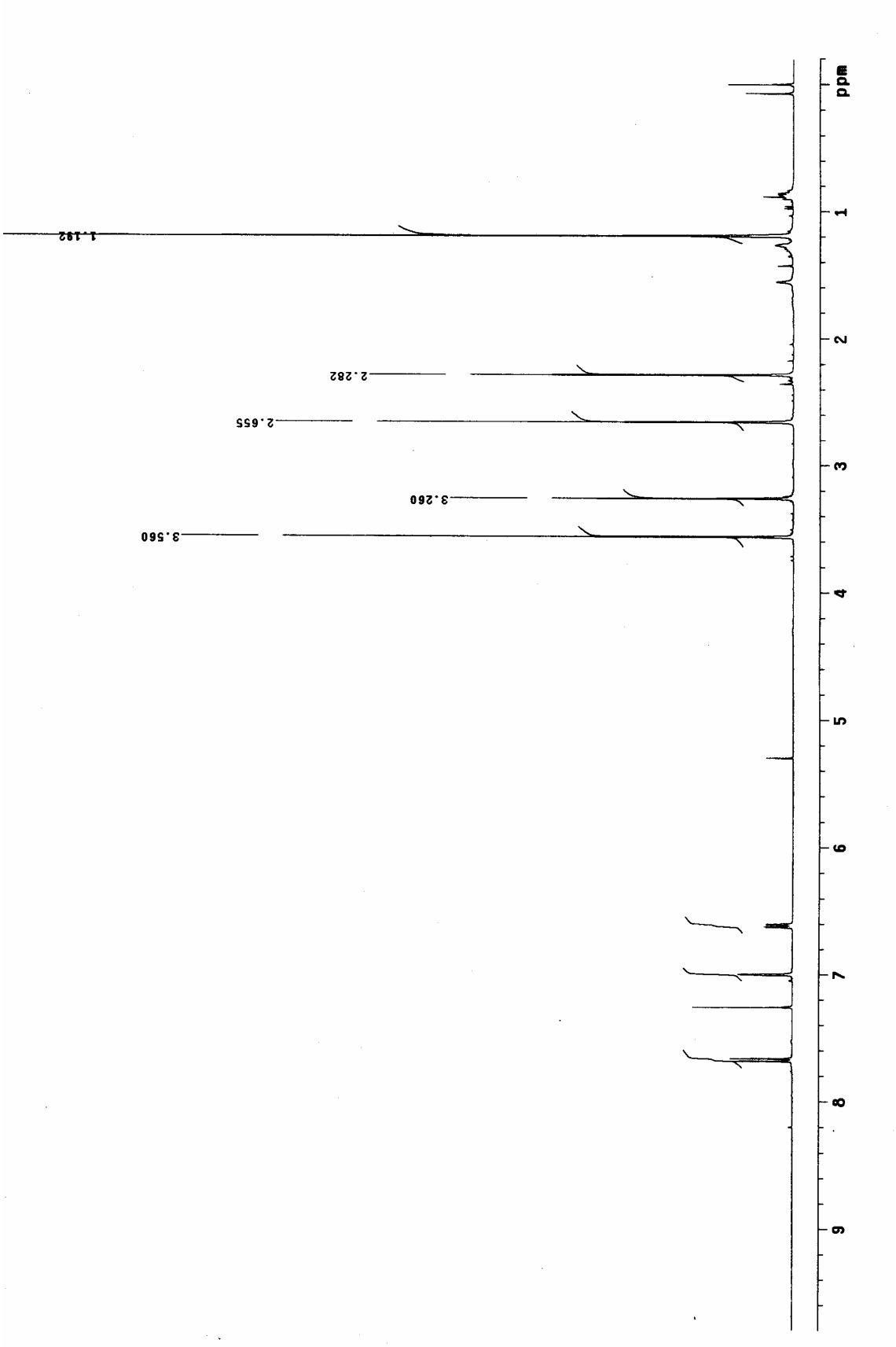

Me
I
O
N
OMe
Me
Me
Ph

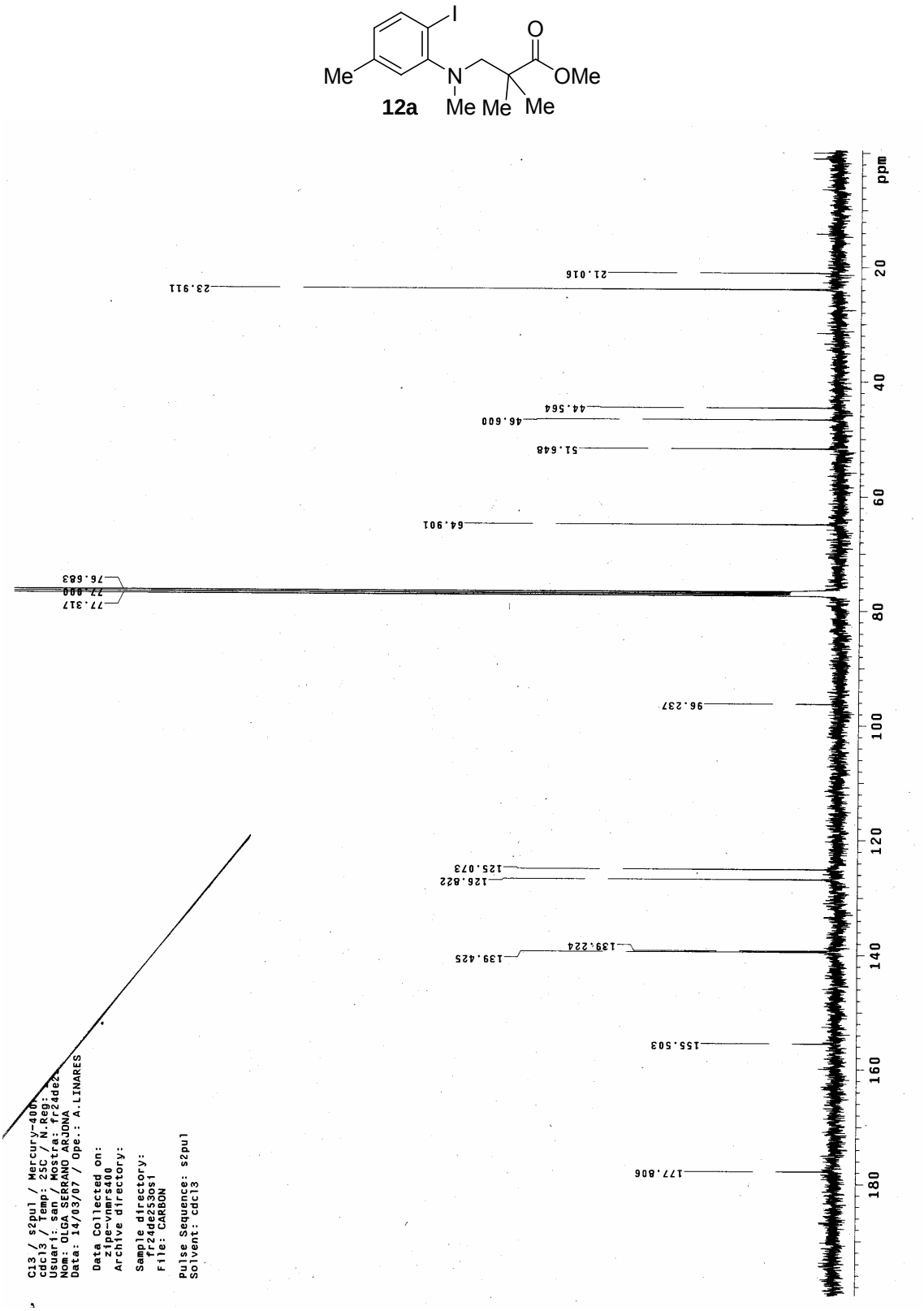
10d

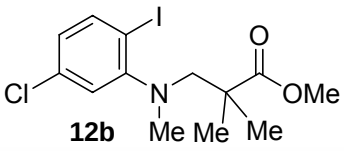

ppm
20
40
60
80
100
120
140
160
180
20.159
21.599
47.229
51.989
52.616
65.102
76.683
77.000
77.317
100.679
124.087
126.224
126.874
128.329
130.017
135.606
139.979
142.216
153.634
175.711



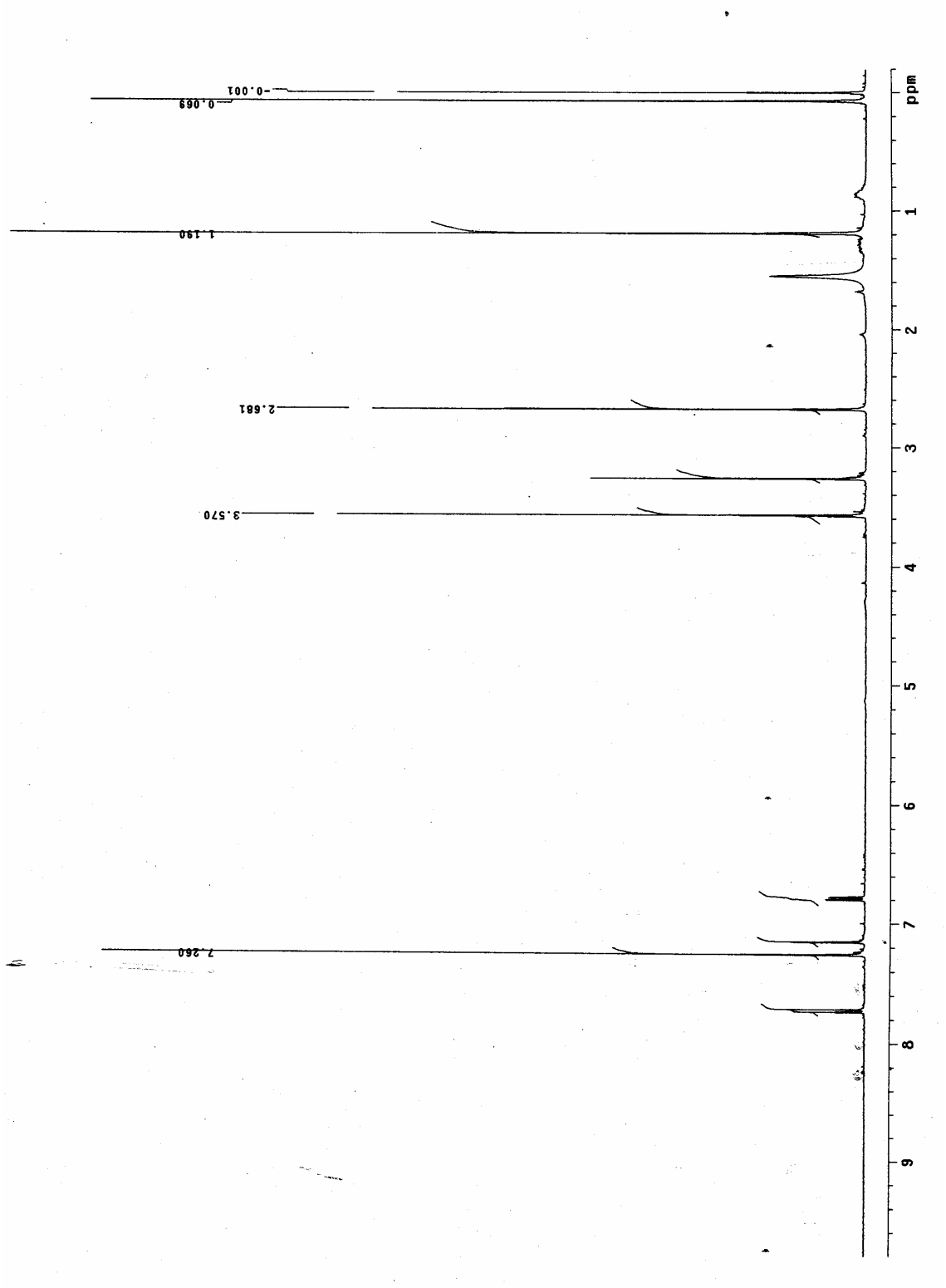
12a

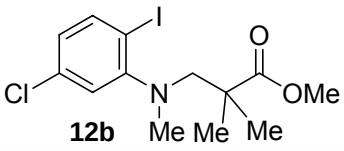



I
O
Me
N
OMe
Me Me Me
12a
ppm
20
40
60
80
100
120
140
160
180
21.016
23.911
44.564
46.600
51.648
64.901
76.683
77.000
77.317
96.237
125.073
126.822
139.224
139.425
155.503
177.806
C13 / s2pul / Mercury-400
cdcl3 / Temp: 25C / N.Reg:
Usuari: san / Mostra: fr24de2
Nom: OLGA SERRANO ARJONA
Data: 14/03/07 / Ope.: A.LINARES
Data Collected on:
zipe-vnmrs400
Archive directory:
Sample directory:
fr24de253os1
File: CARBON
Pulse Sequence: s2pul
Solvent: cdcl3

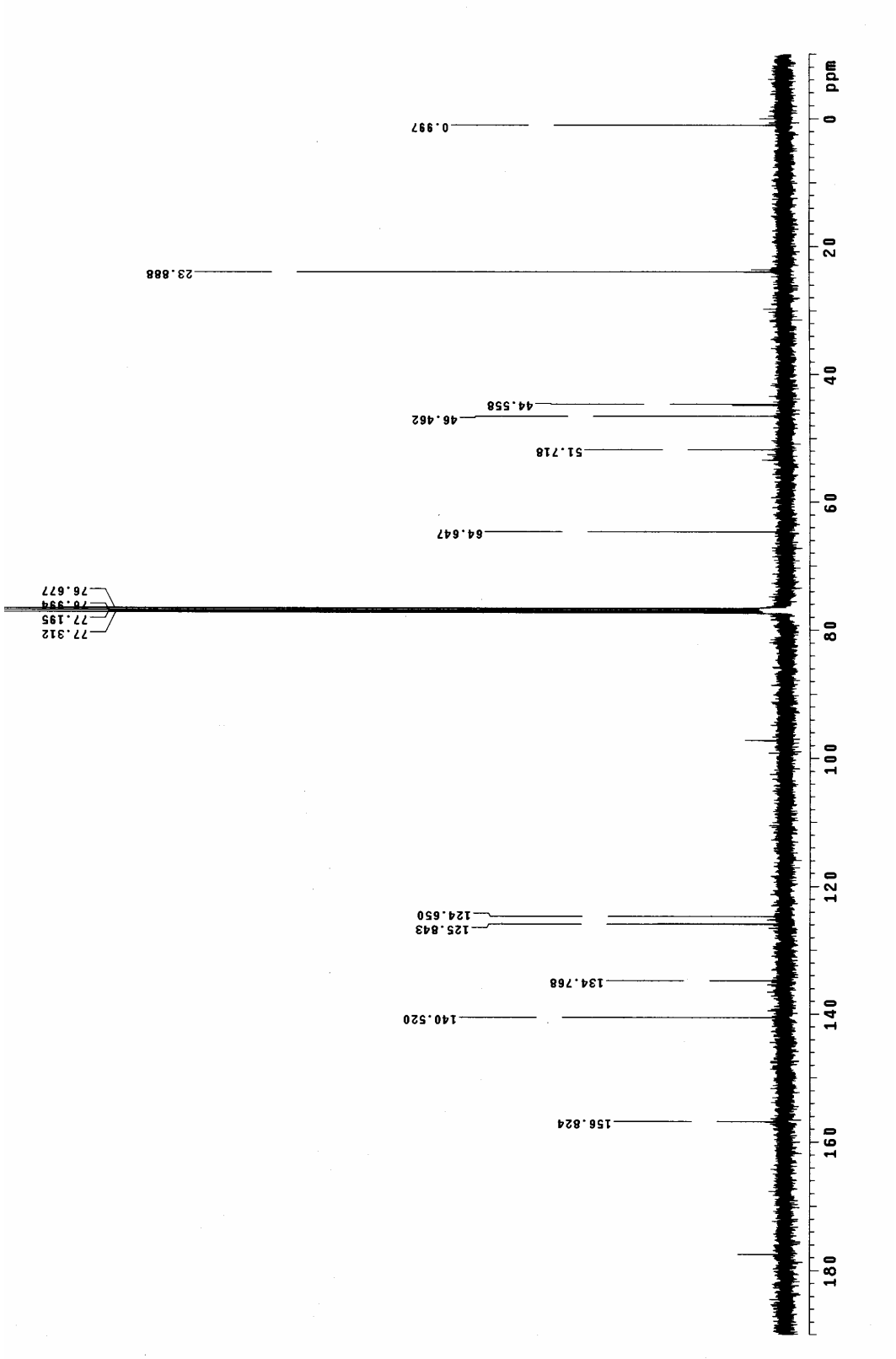

I
Cl
N
O
OMe
Me
Me
Me

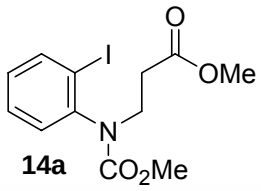
12b


-0.001
0.069
1.190
2.681
3.570
7.260
ppm
1
2
3
4
5
6
7
8
9

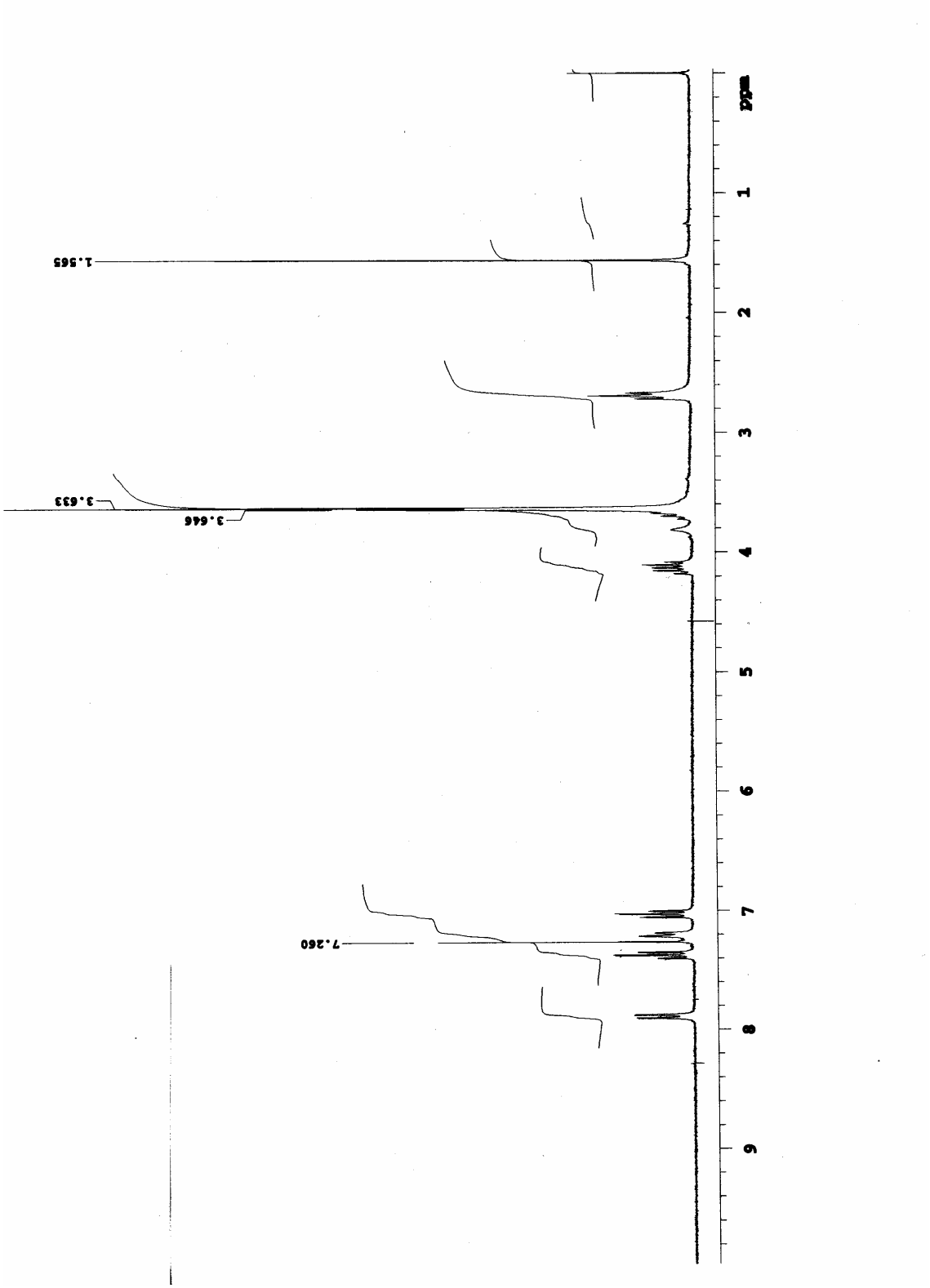

I
Cl
N
O
OMe
Me
Me
Me

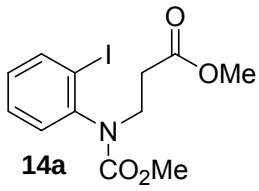
12b


0.997
23.888
44.558
46.462
51.718
64.647
76.677
76.994
77.195
77.312
124.650
125.843
134.768
140.520
156.824
ppm
0
20
40
60
80
100
120
140
160
180

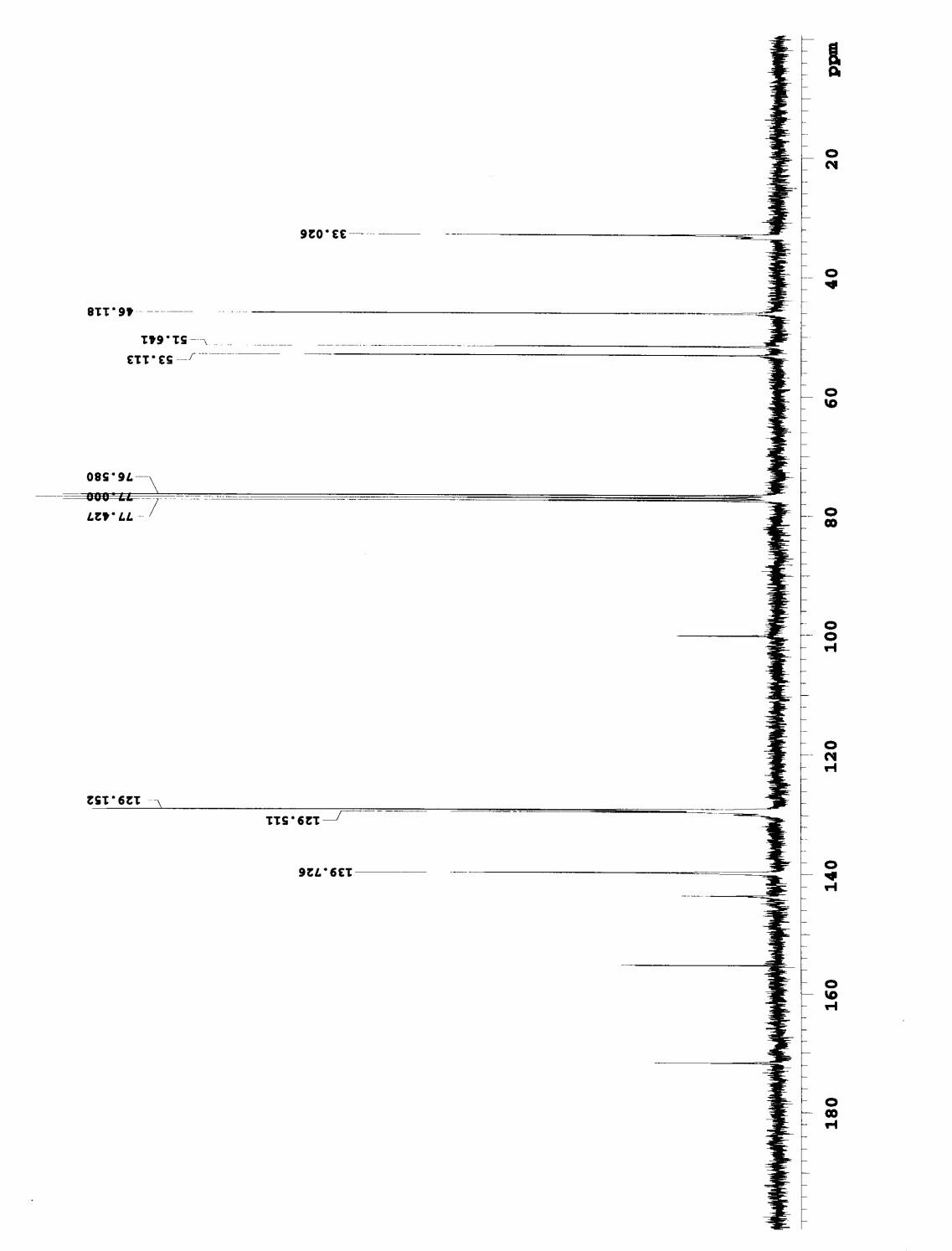


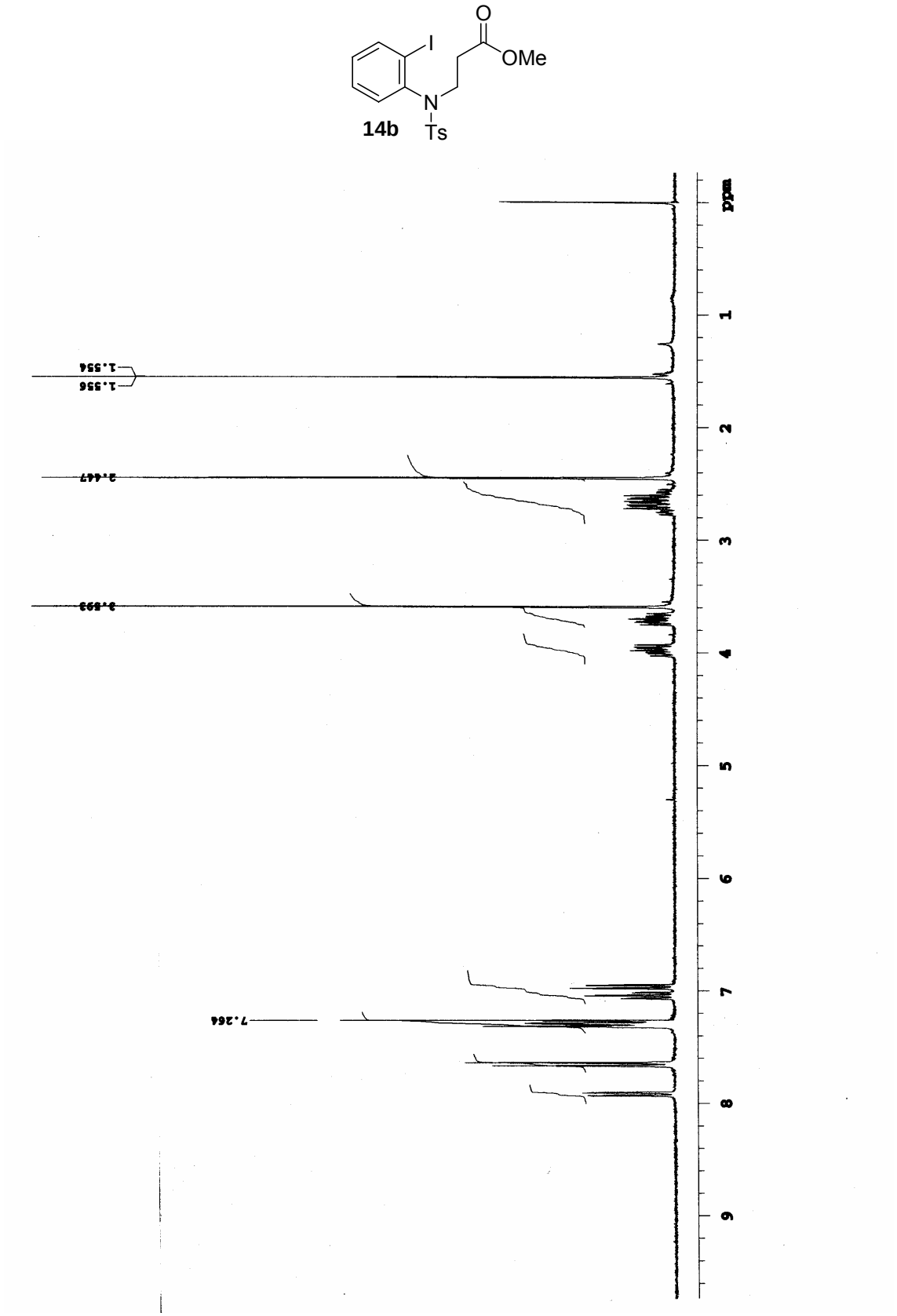
14a

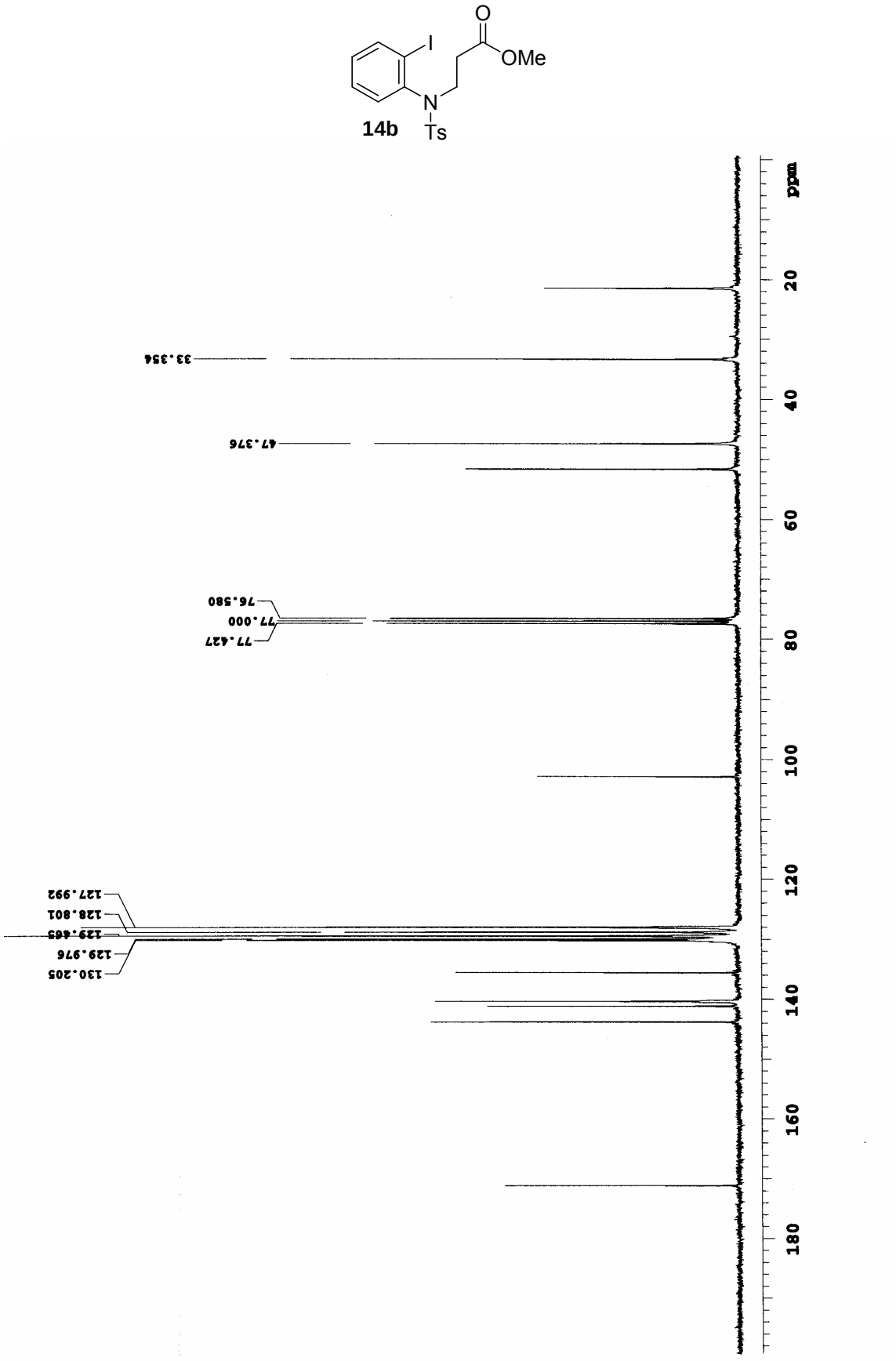


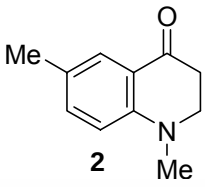

O
I
OMe
N
CO2Me

14a

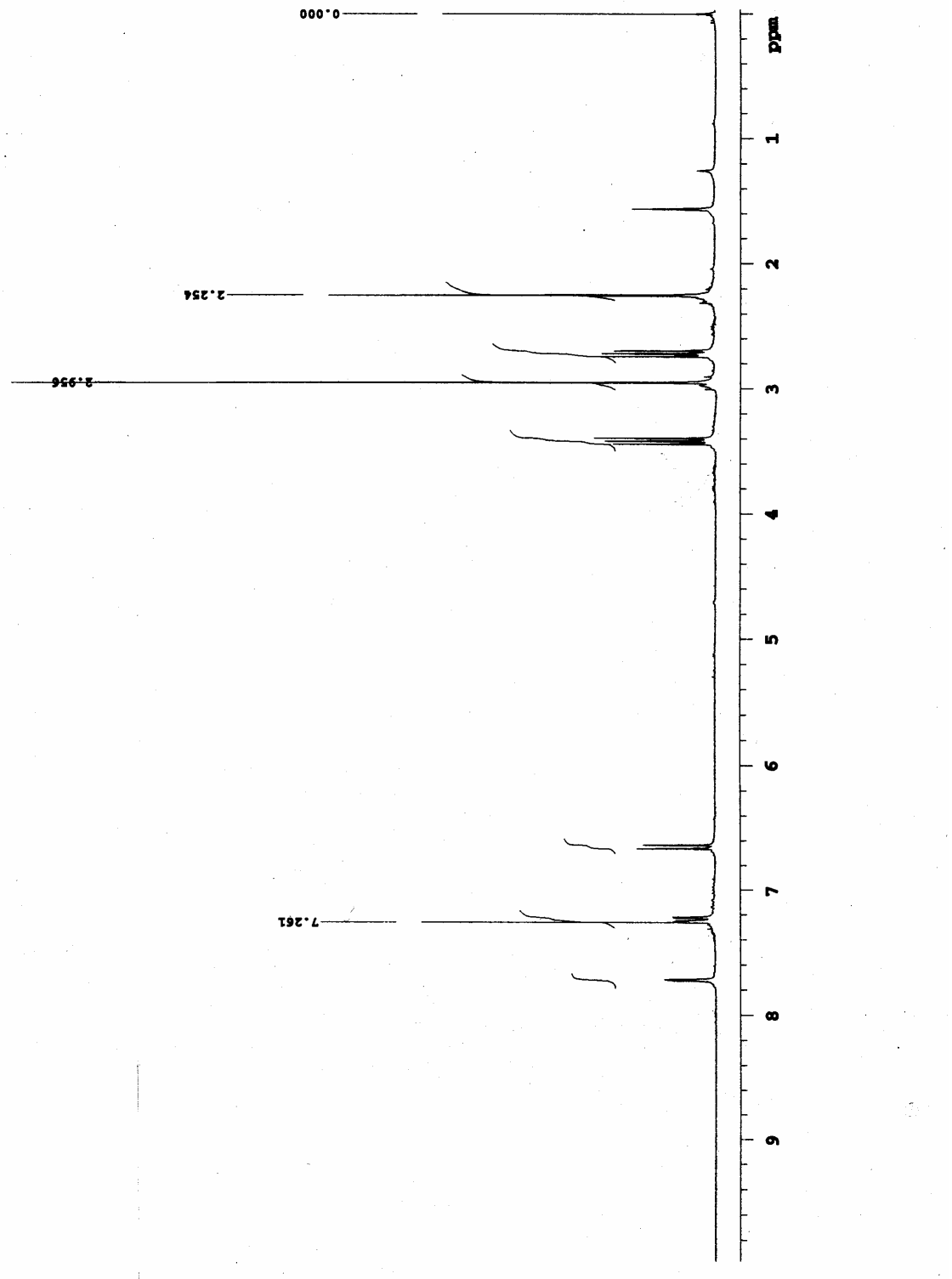

ppm
20
40
60
80
100
120
140
160
180
33.026
46.118
51.641
53.113
76.580
77.000
77.427
129.152
129.511
139.726

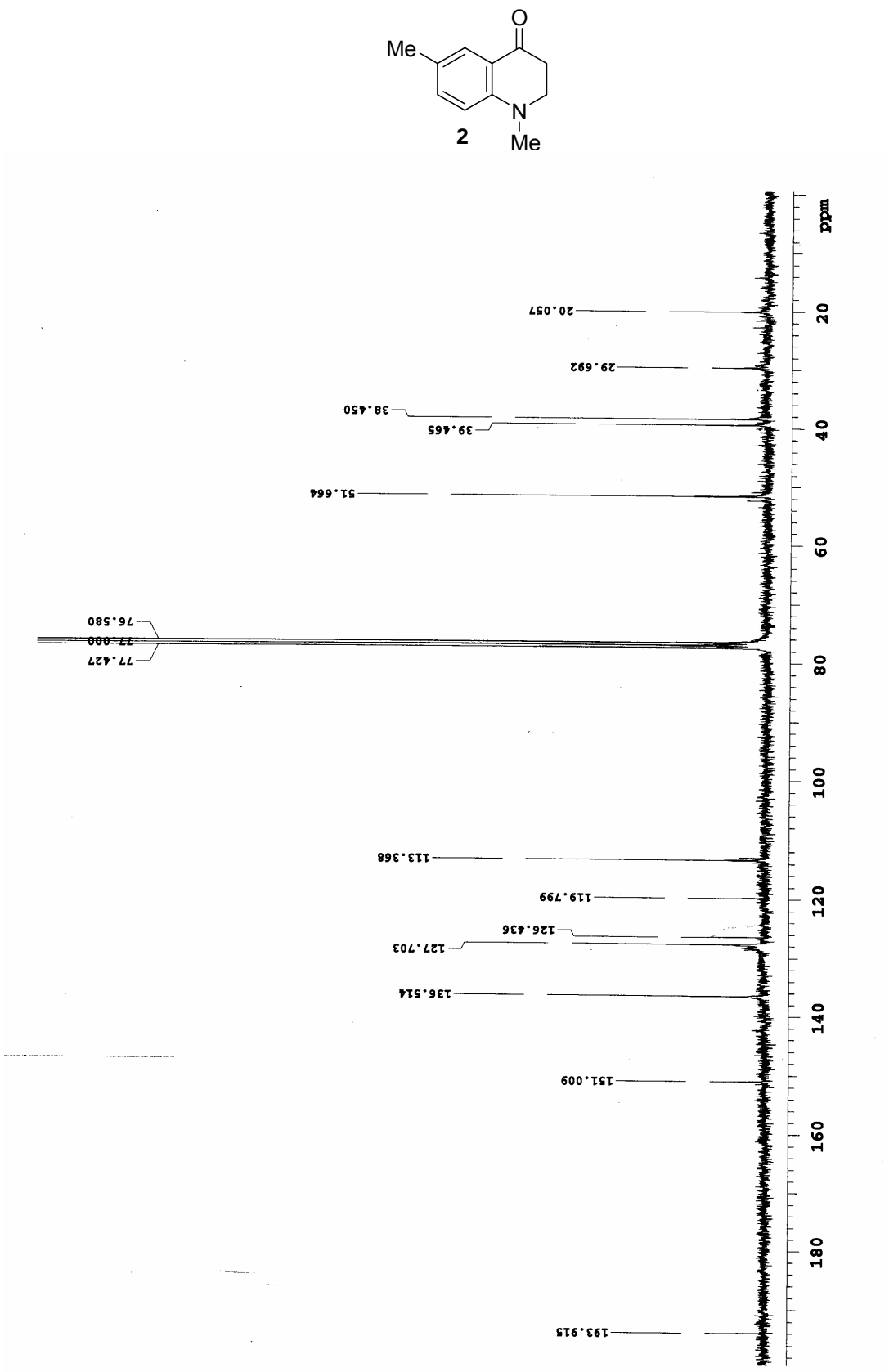

O
I
OMe
N
Ts
14b
1.554
1.556
2.447
3.893
7.264
ppm
1
2
3
4
5
6
7
8
9

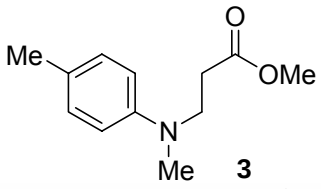

O
I
OMe
N
Ts
14b
33.354
47.376
76.580
77.000
77.427
127.992
128.801
129.465
129.976
130.205
ppm
20
40
60
80
100
120
140
160
180



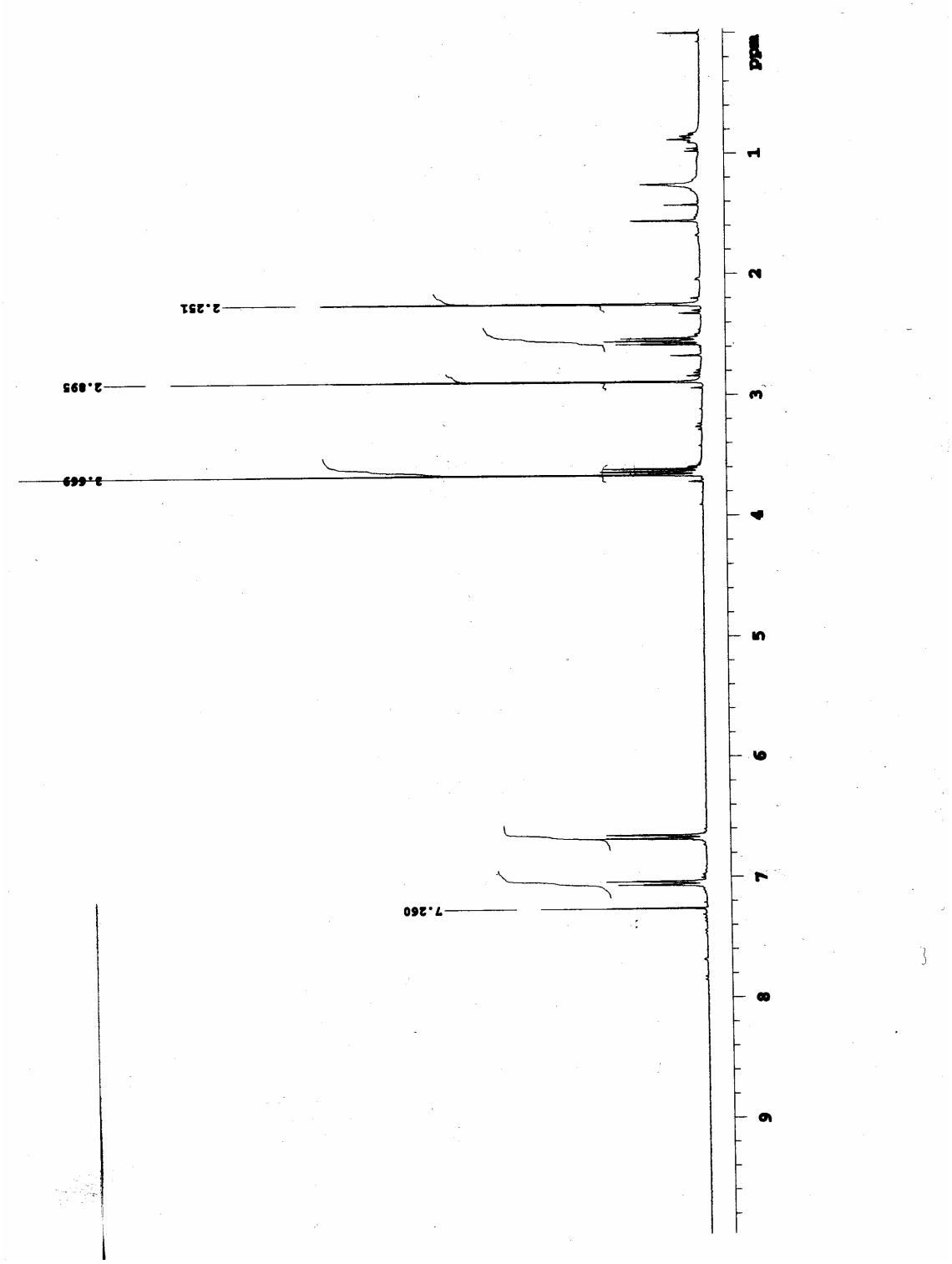
2

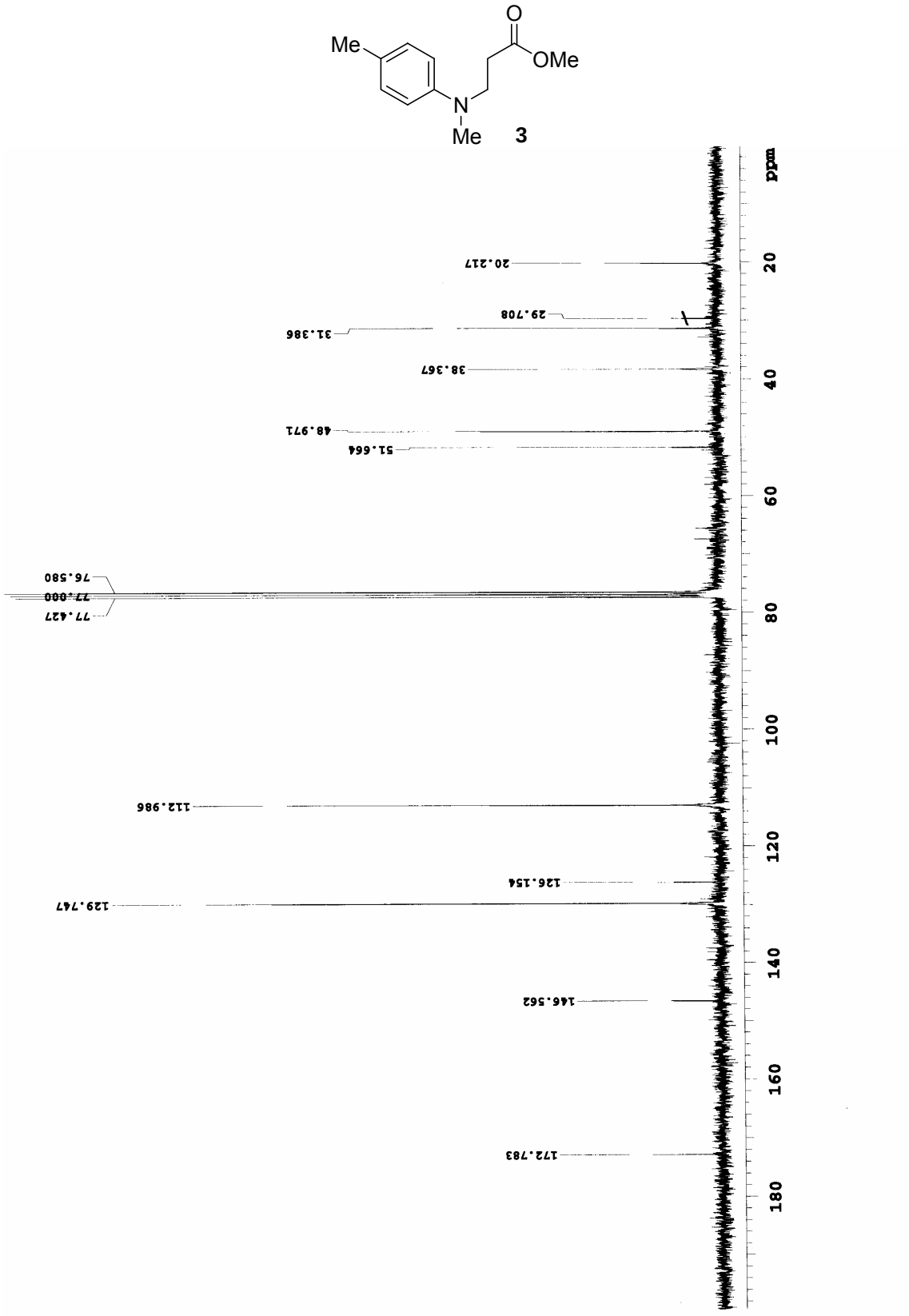


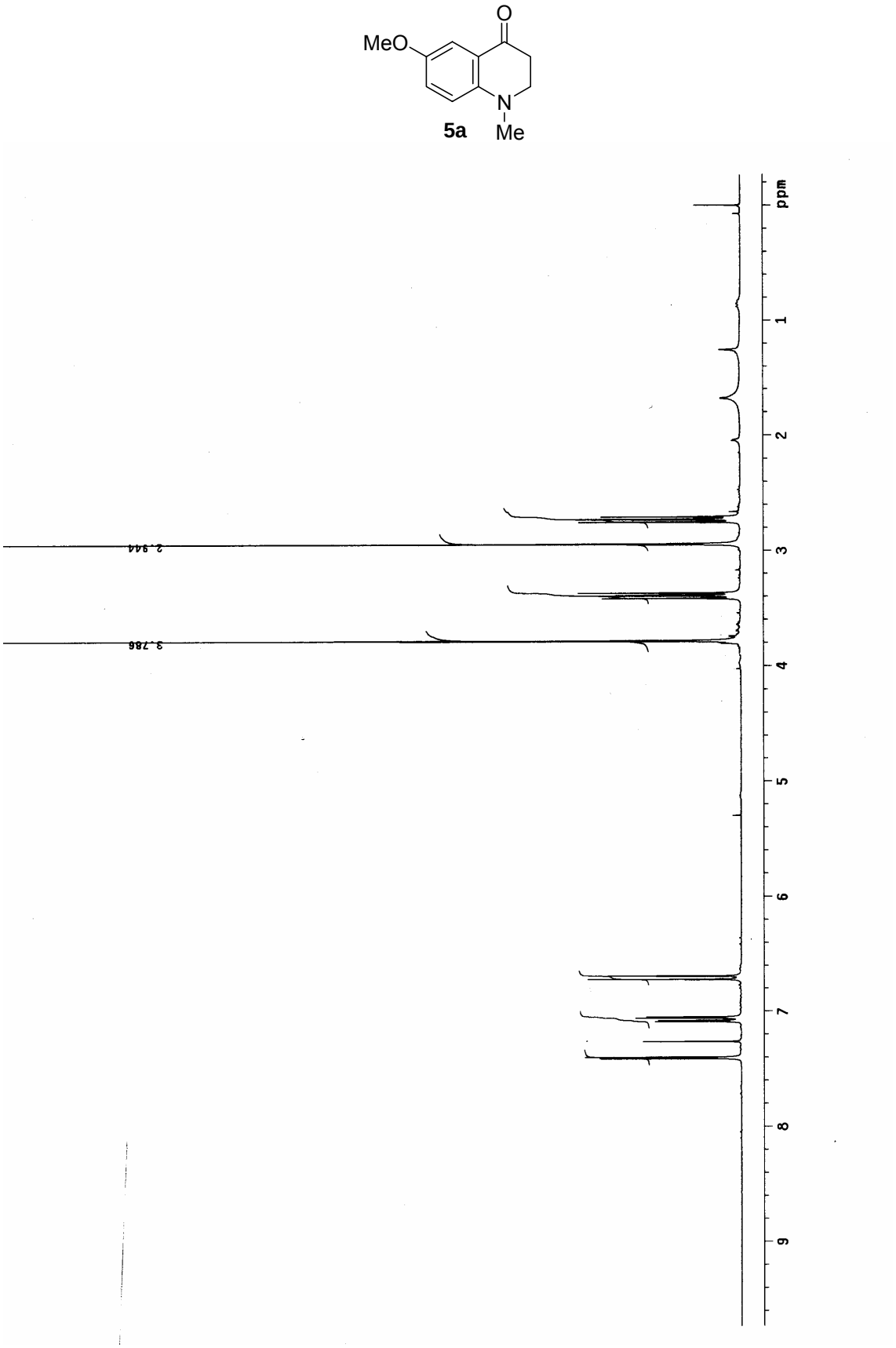

O
Me
N
Me
2
193.915
151.009
136.514
127.703
126.436
119.799
113.368
77.427
77.000
76.580
51.664
39.465
38.450
29.692
20.057
ppm
20
40
60
80
100
120
140
160
180

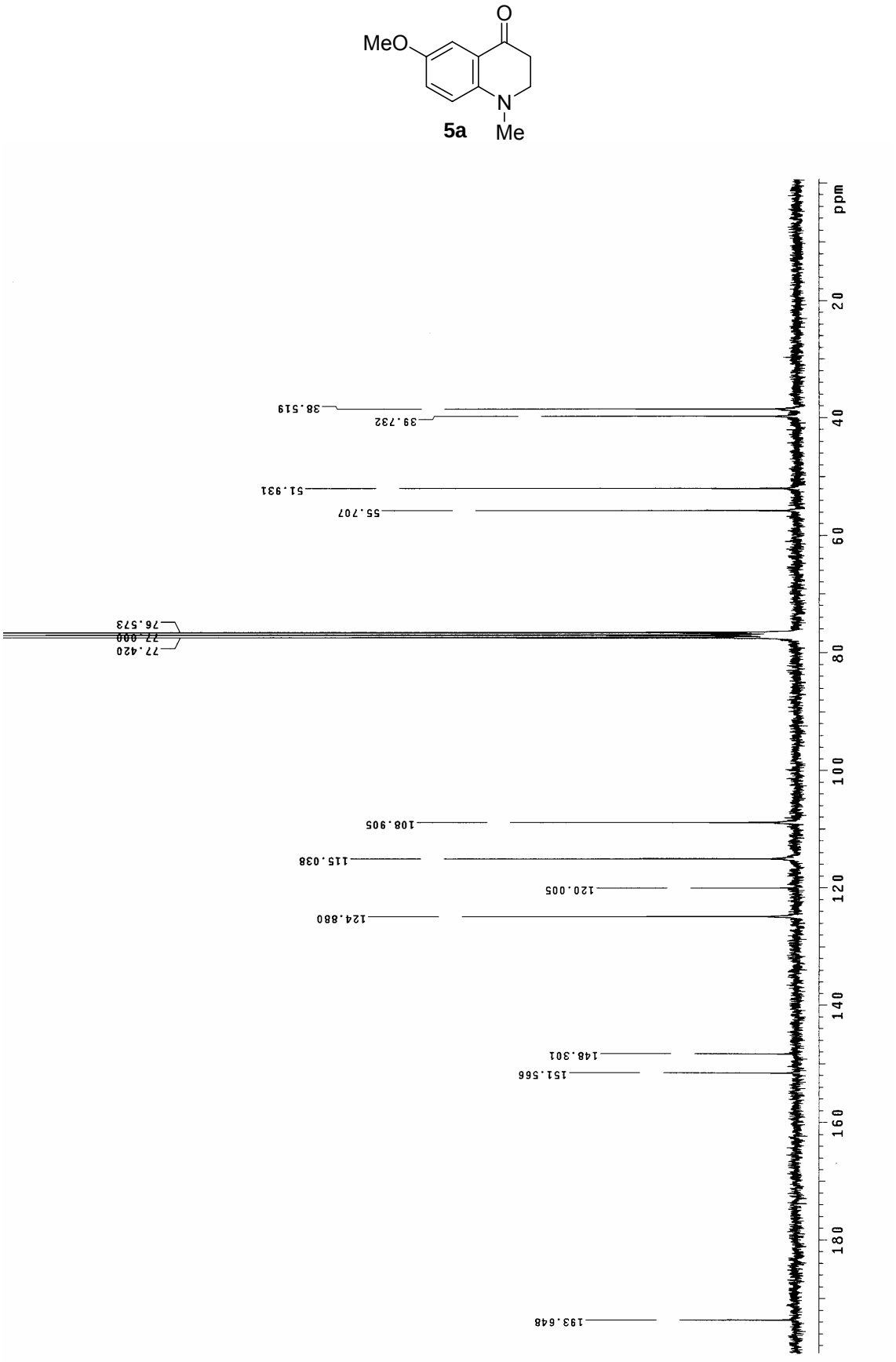


3




Me
O
OMe
N
Me
3
ppm
20.217
29.708
31.386
38.367
48.971
51.664
76.580
77.000
77.427
112.986
126.154
129.747
146.562
172.783


MeO
O
N
Me
5a
2.944
3.786
ppm
1
2
3
4
5
6
7
8
9


MeO
O
N
Me
5a
193.648
151.566
148.301
124.880
120.005
115.038
108.905
77.420
77.089
76.573
55.707
51.931
39.732
38.519
ppm
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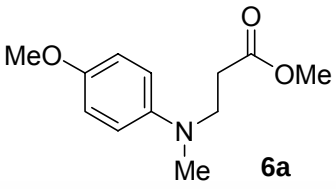
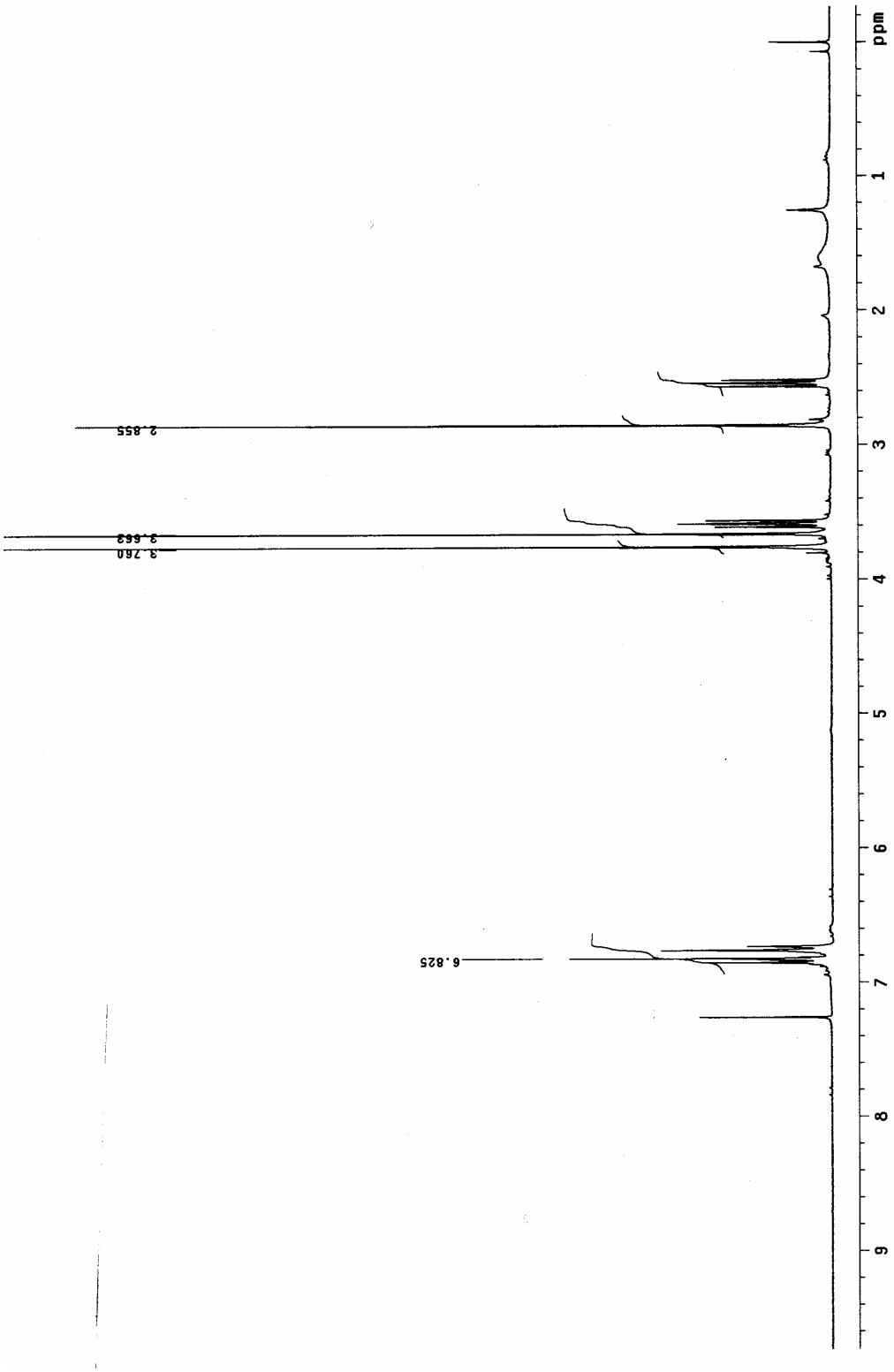
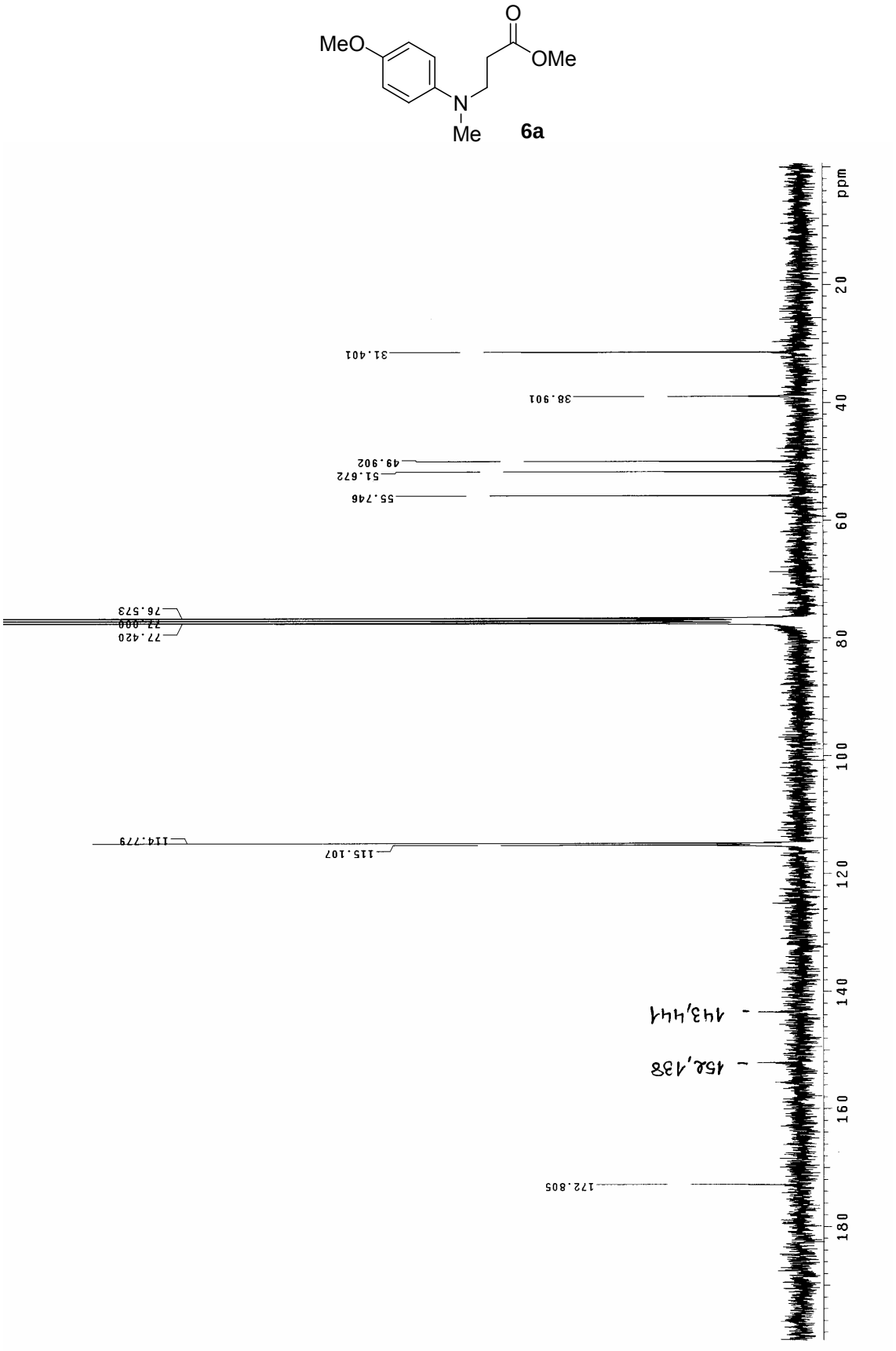
40
60
80
100
120
140
160
180



6a




MeO
O
OMe
N
Me
6a
ppm
20
40
60
80
100
120
140
160
180
31.401
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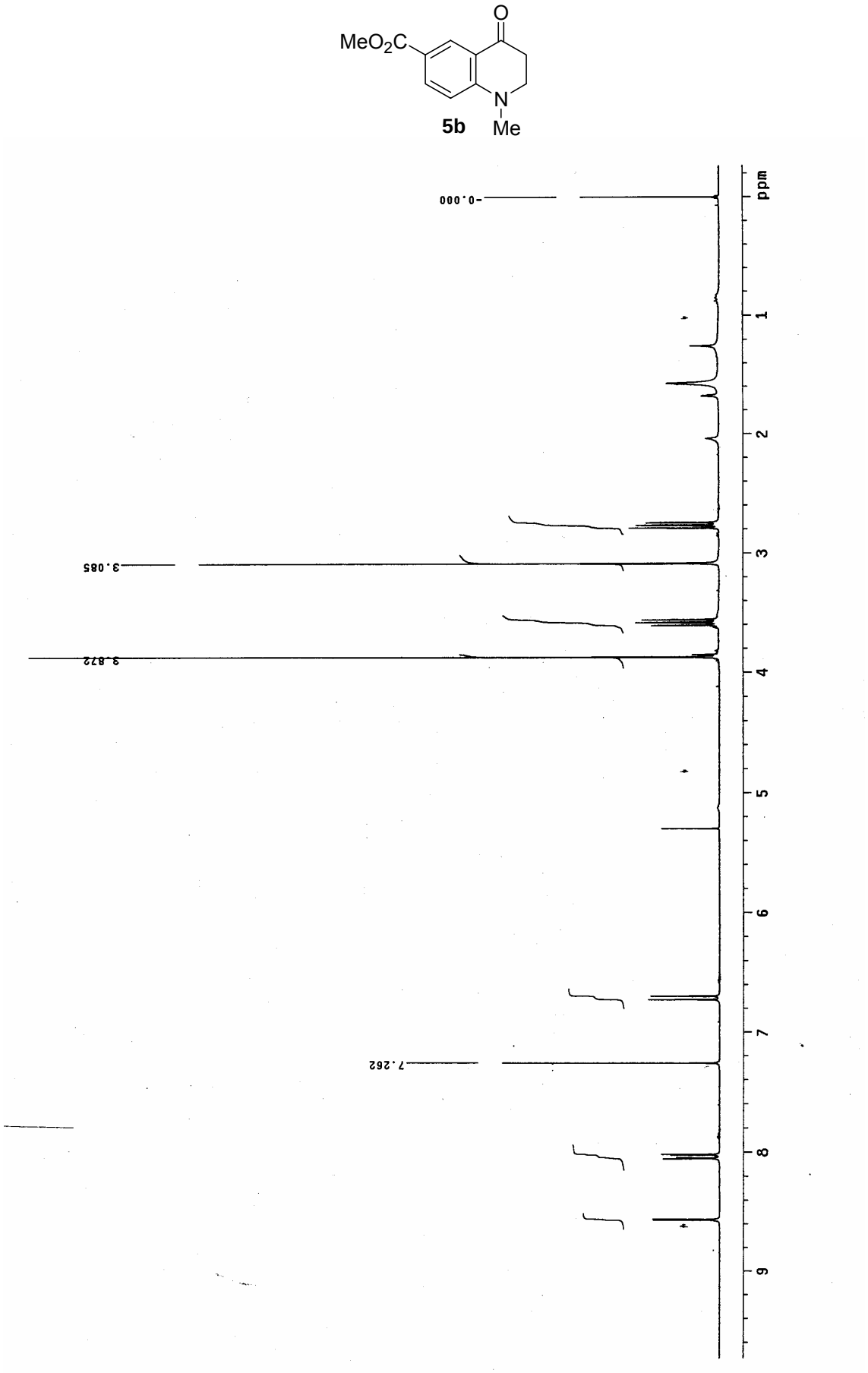
77.420
114.779
115.107
143.144
152.438
172.805


MeO2C
O
N
Me
5b
0.000
3.085
3.822
7.262
ppm
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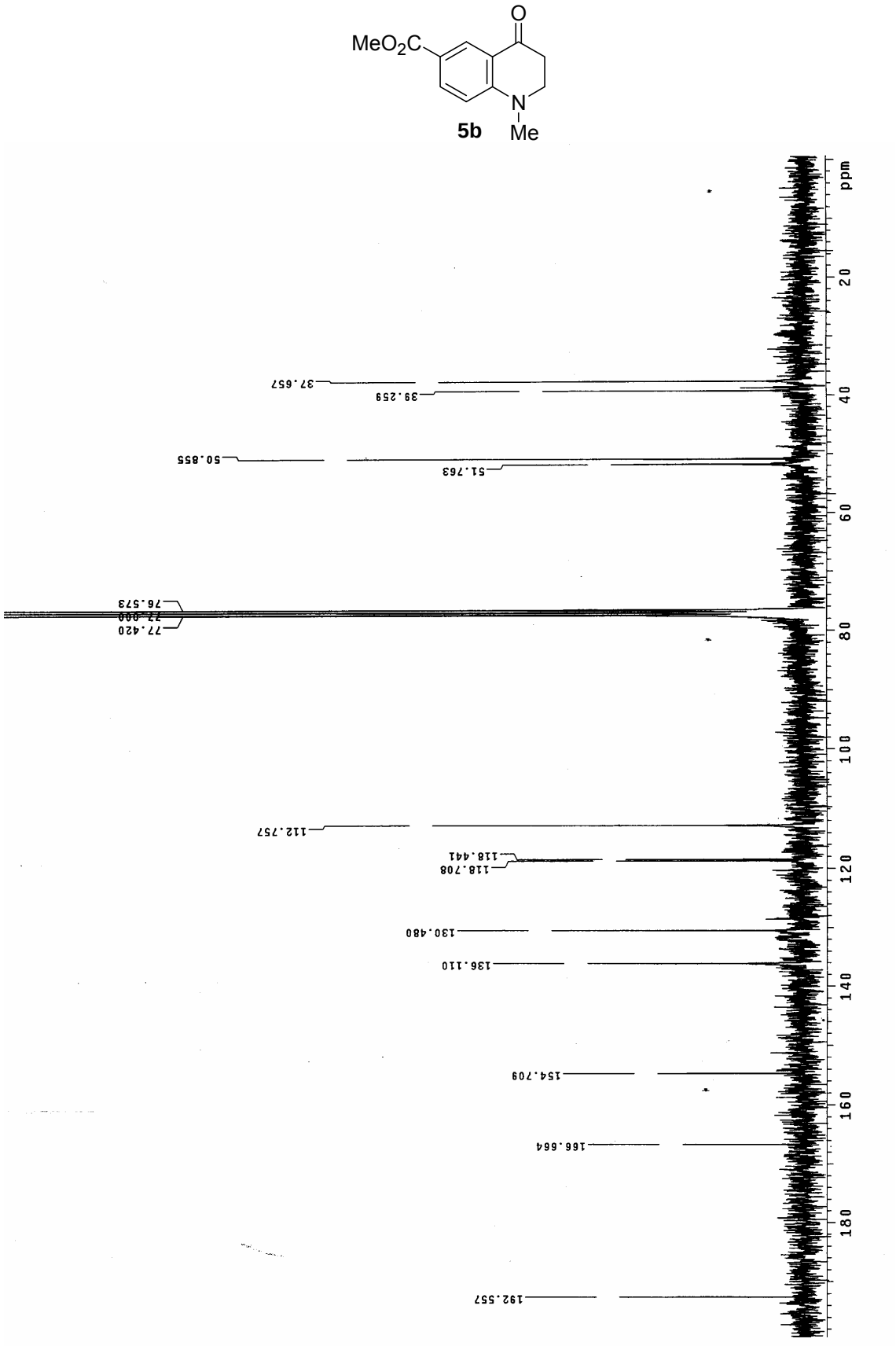
2
3
4
5
6
7
8
9


MeO2C
O
N
Me
5b
ppm
20
40
60
80
100
120
140
160
180
192.557
166.664
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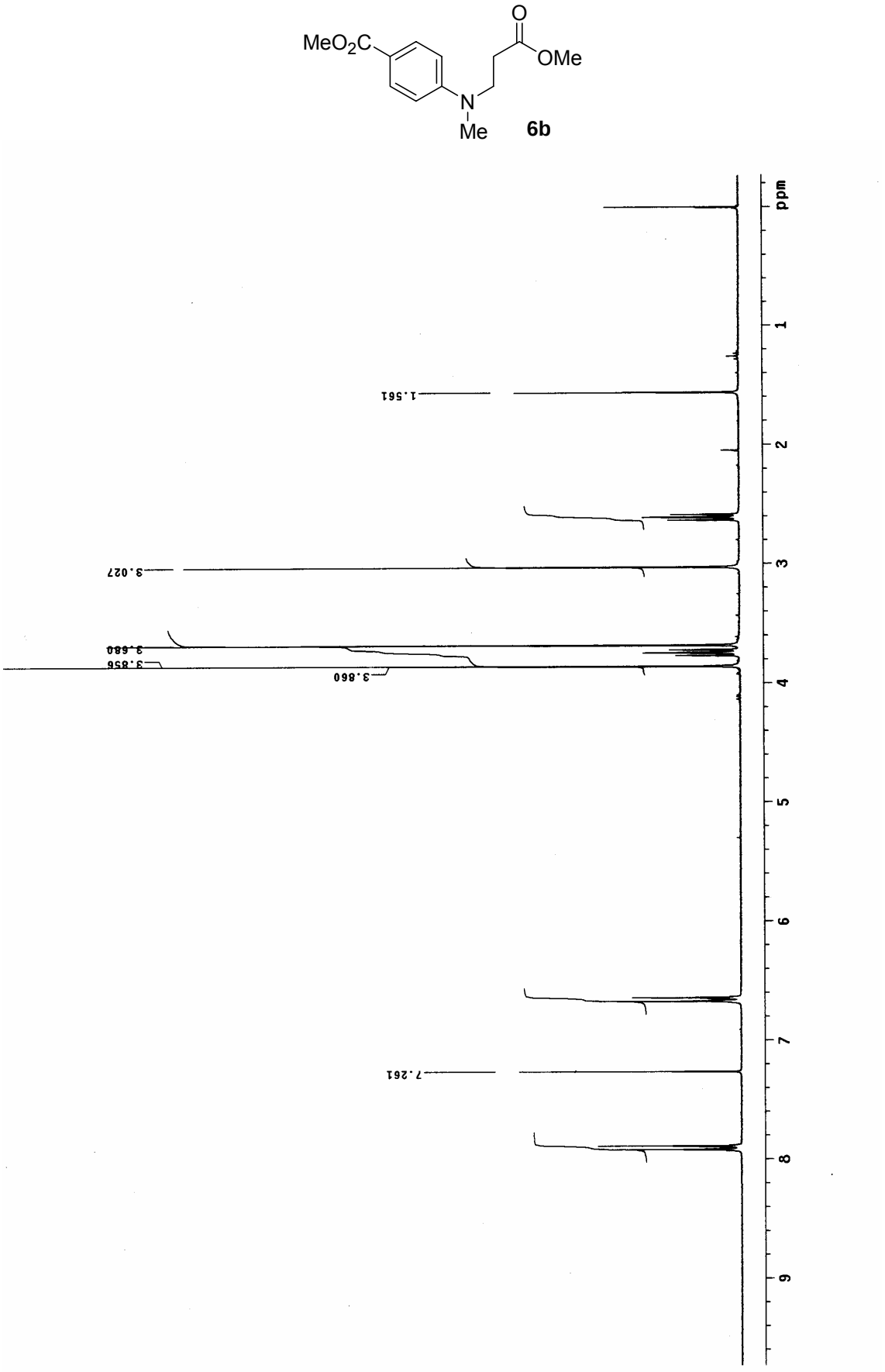
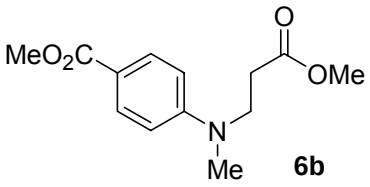
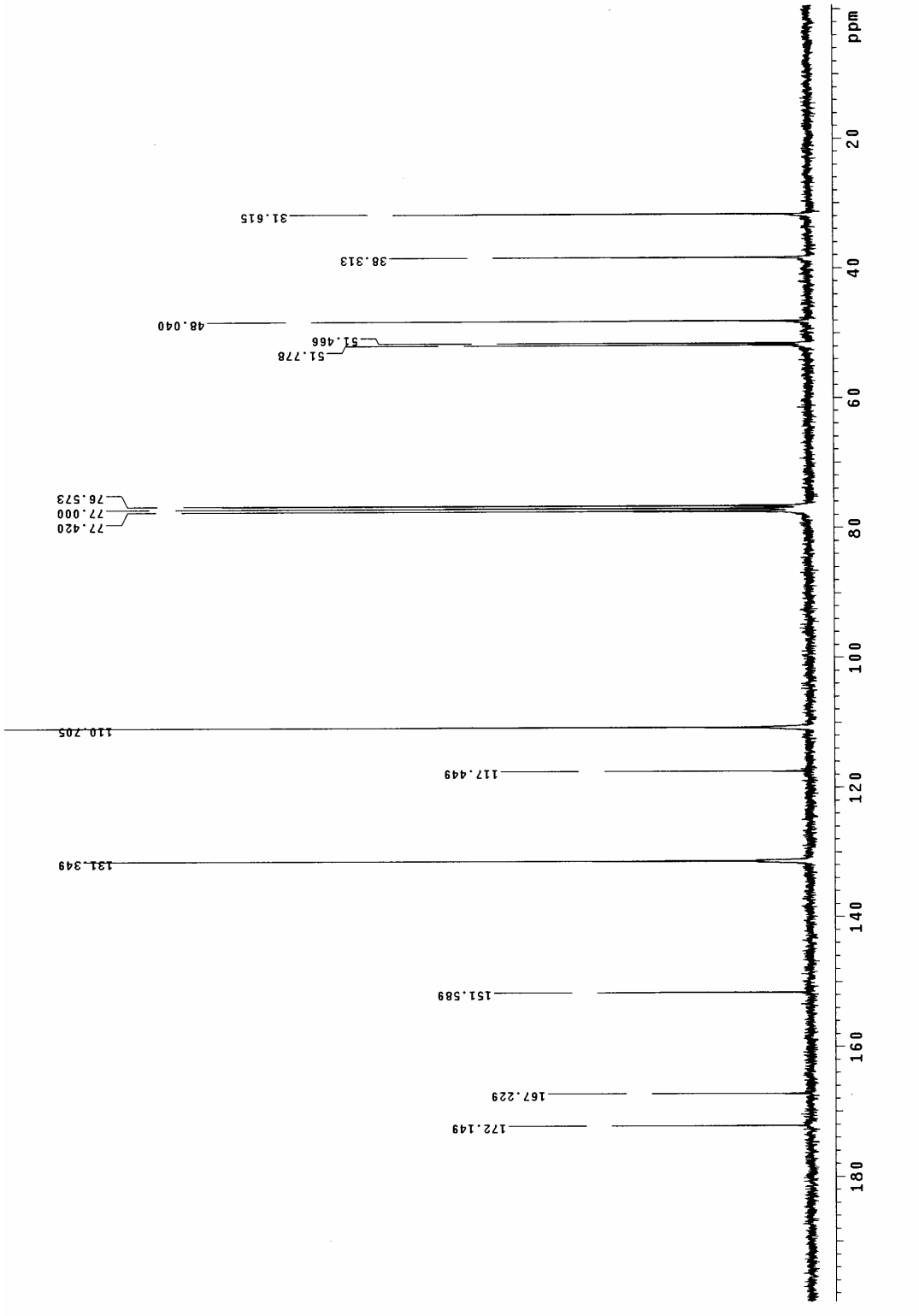
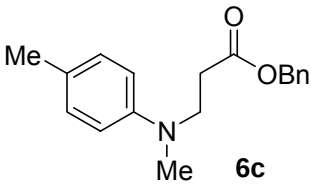
77.420
76.573
50.855
51.763
39.259
37.657


MeO2C
O
OMe
N
Me
6b
1.561
3.027
3.680
3.856
3.860
7.261
ppm
1
2
3
4
5
6
7
8
9

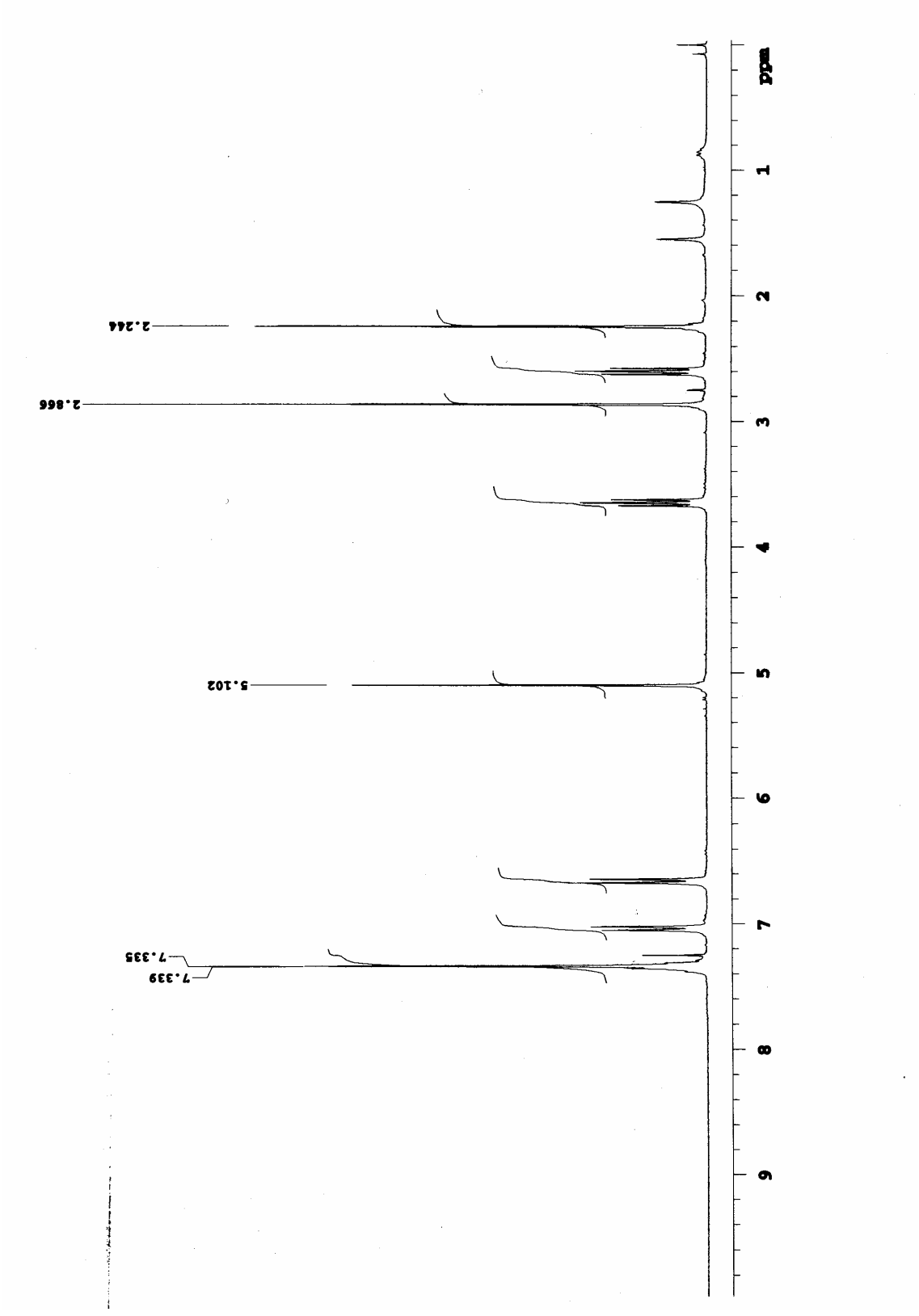

MeO2C
O
OMe
N
Me

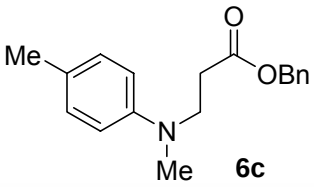
6b


ppm
20
40
60
80
100
120
140
160
180
31.615
38.313
48.040
51.466
51.778
76.573
77.000
77.420
110.205
117.449
131.349
151.589
167.229
172.149

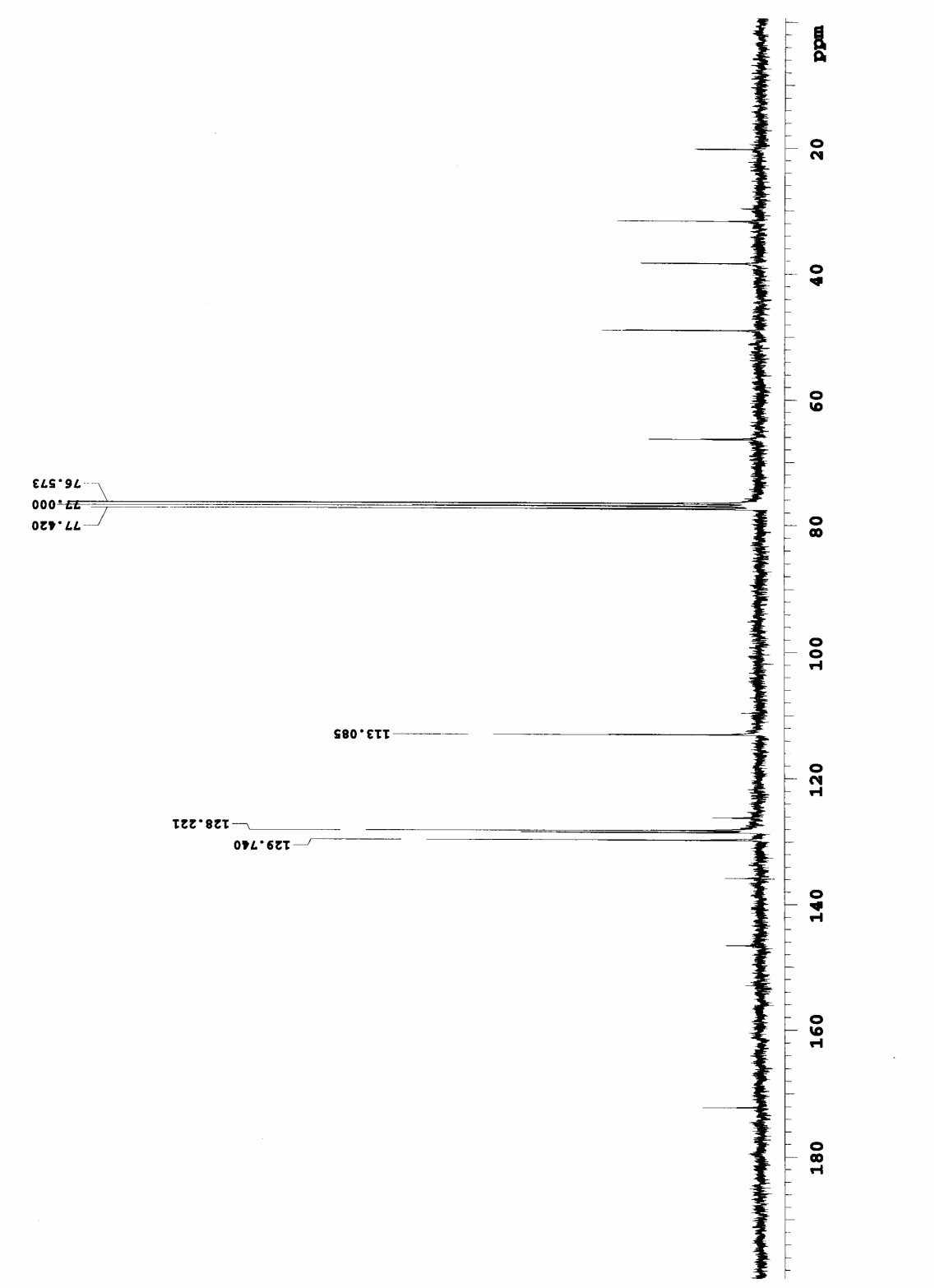


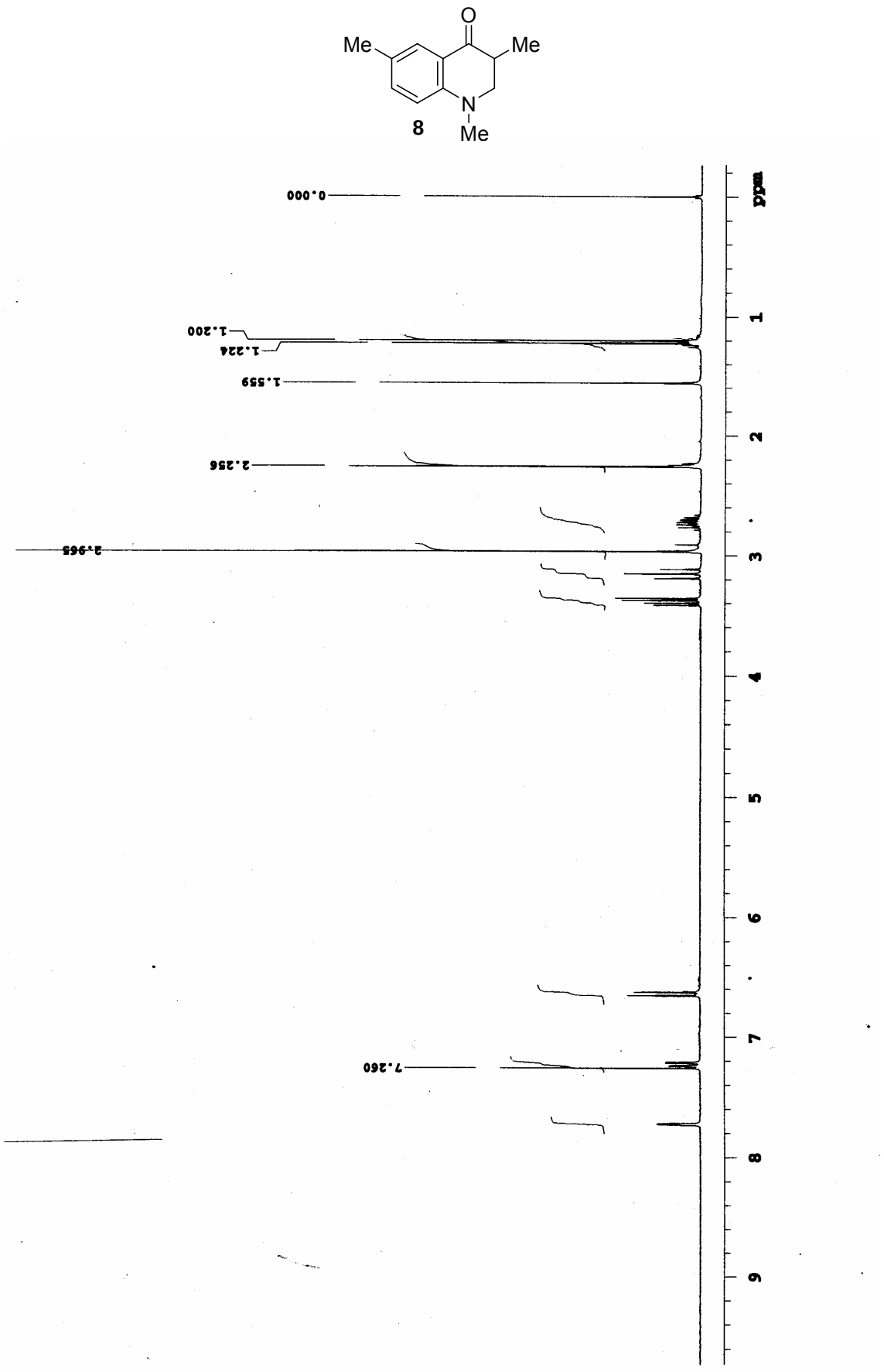
6c

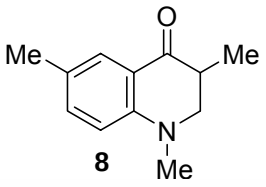



Me
O
OBn
N
Me

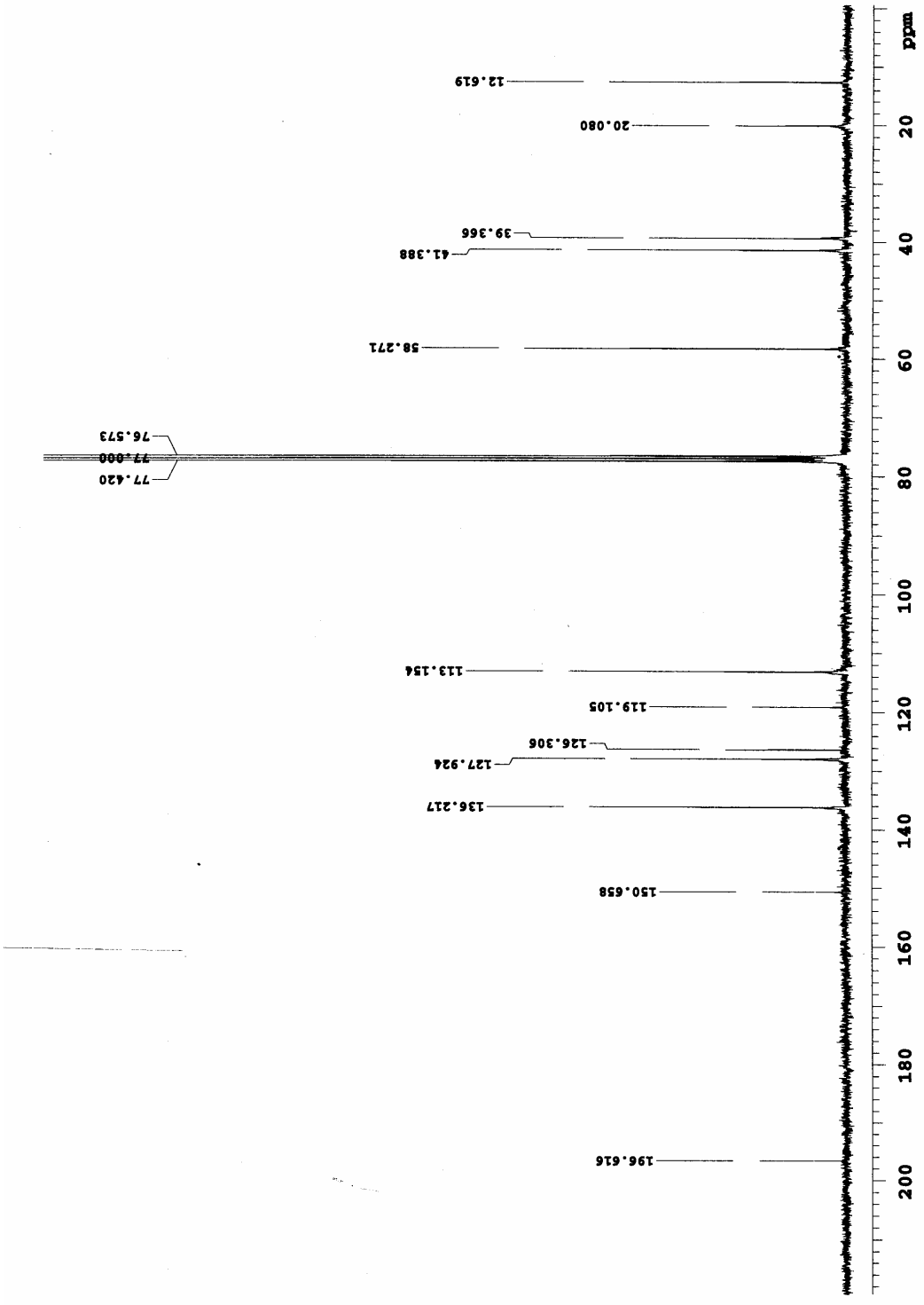
6c

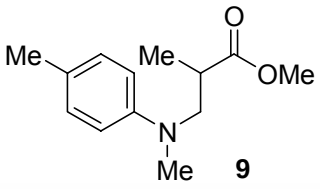

ppm
20
40
60
80
100
120
140
160
180
76.573
77.000
77.420
113.085
128.221
129.740


O
Me
Me
N
Me
8
0.000
1.200
1.224
1.559
2.256
2.965
7.260
ppm
1
2
3
4
5
6
7
8
9

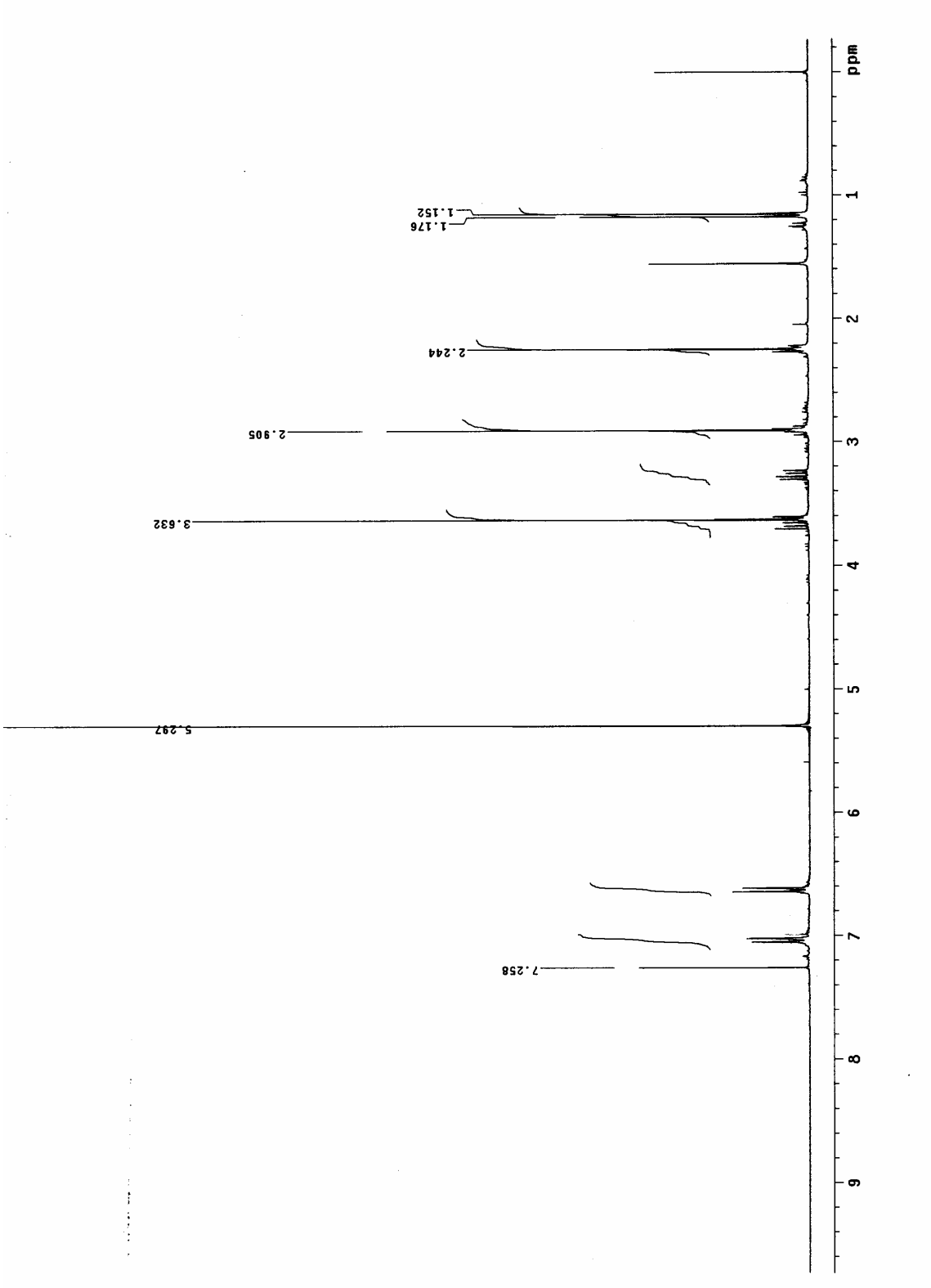

O
Me
Me
N
Me

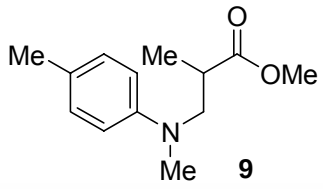
8


12.619
20.080
39.366
41.388
58.271
76.573
77.000
77.420
113.154
119.105
126.306
127.924
136.217
150.658
196.616
ppm
20
40
60
80
100
120
140
160
180
200

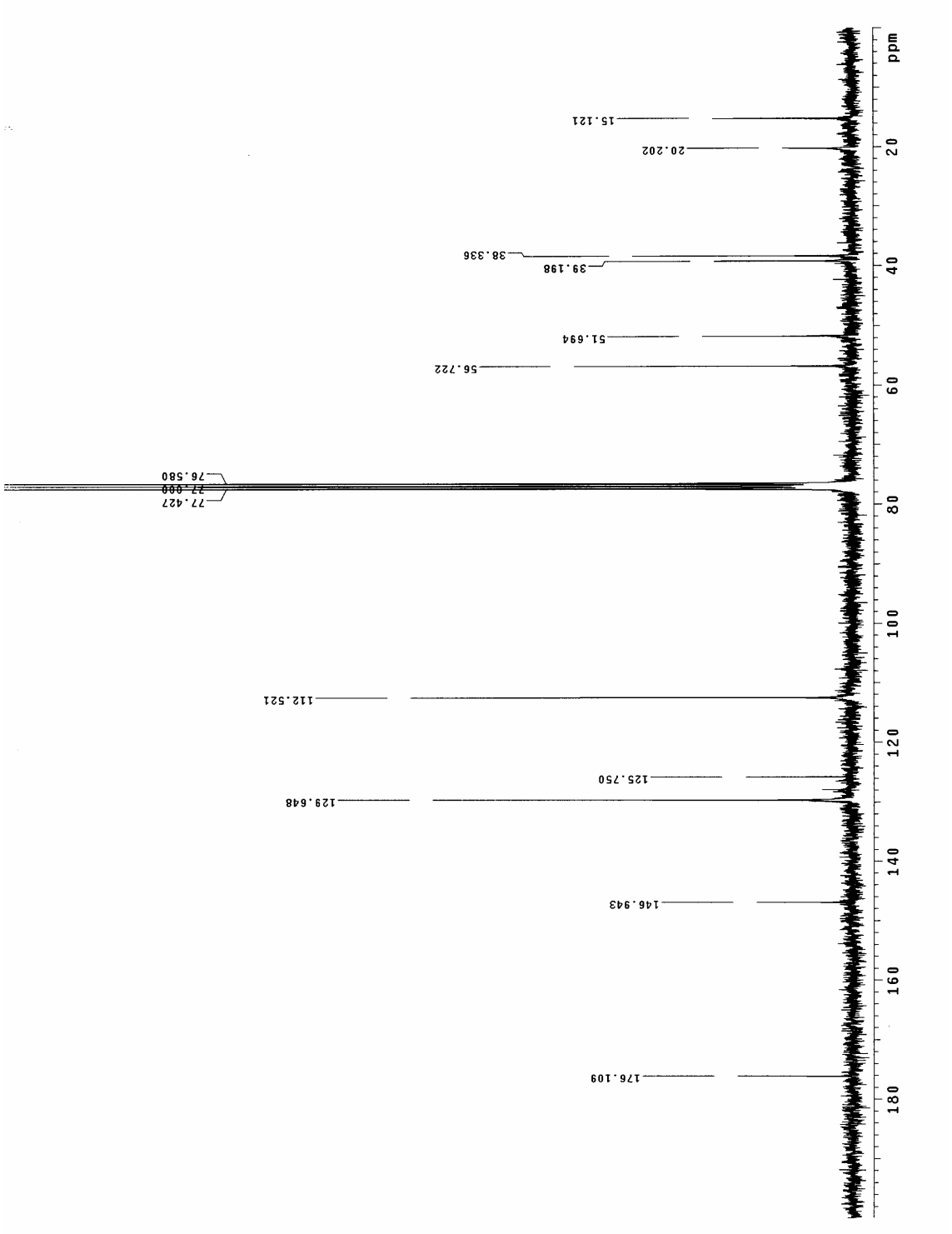


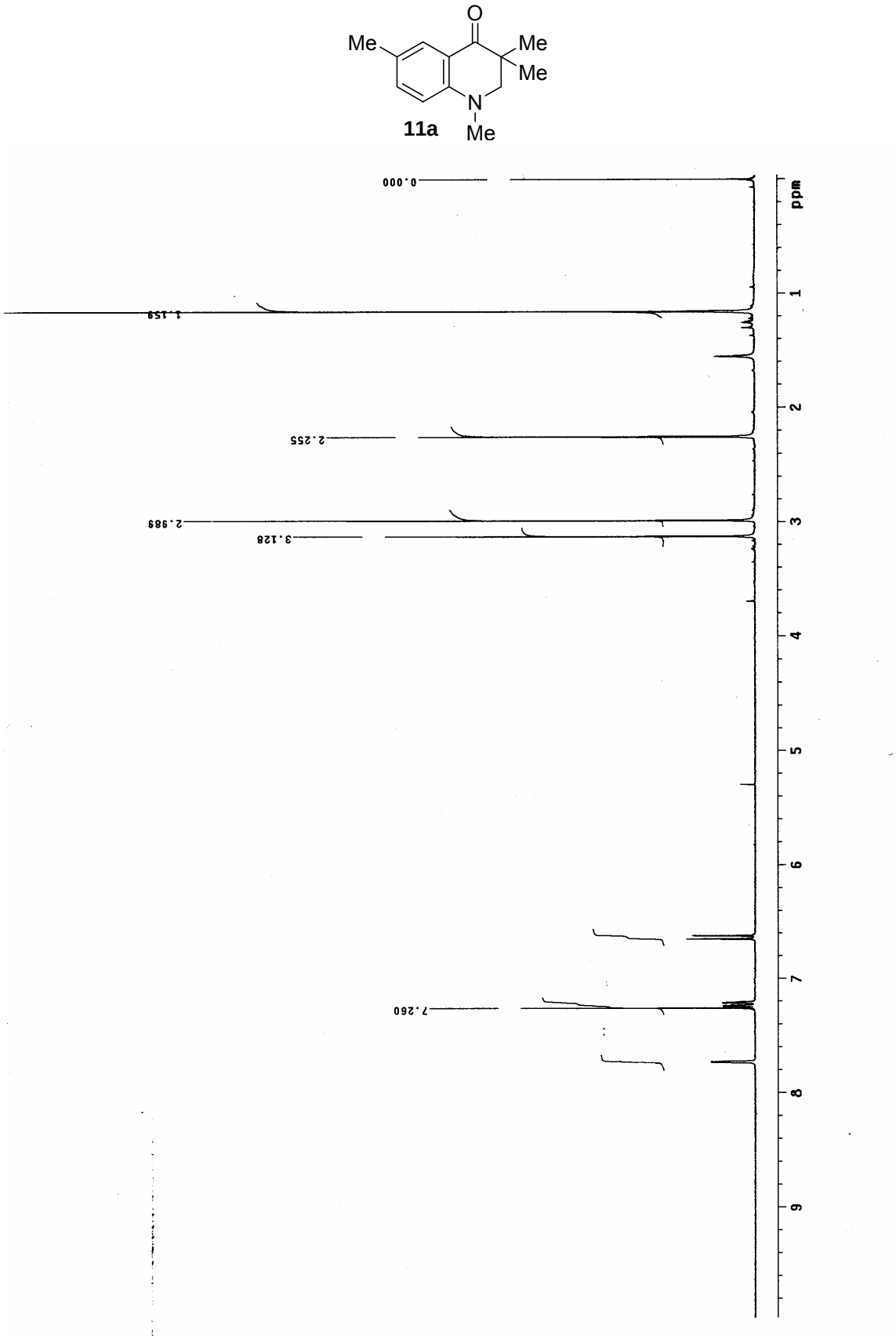
9

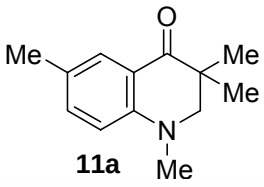



Me
Me
O
OMe
N
Me

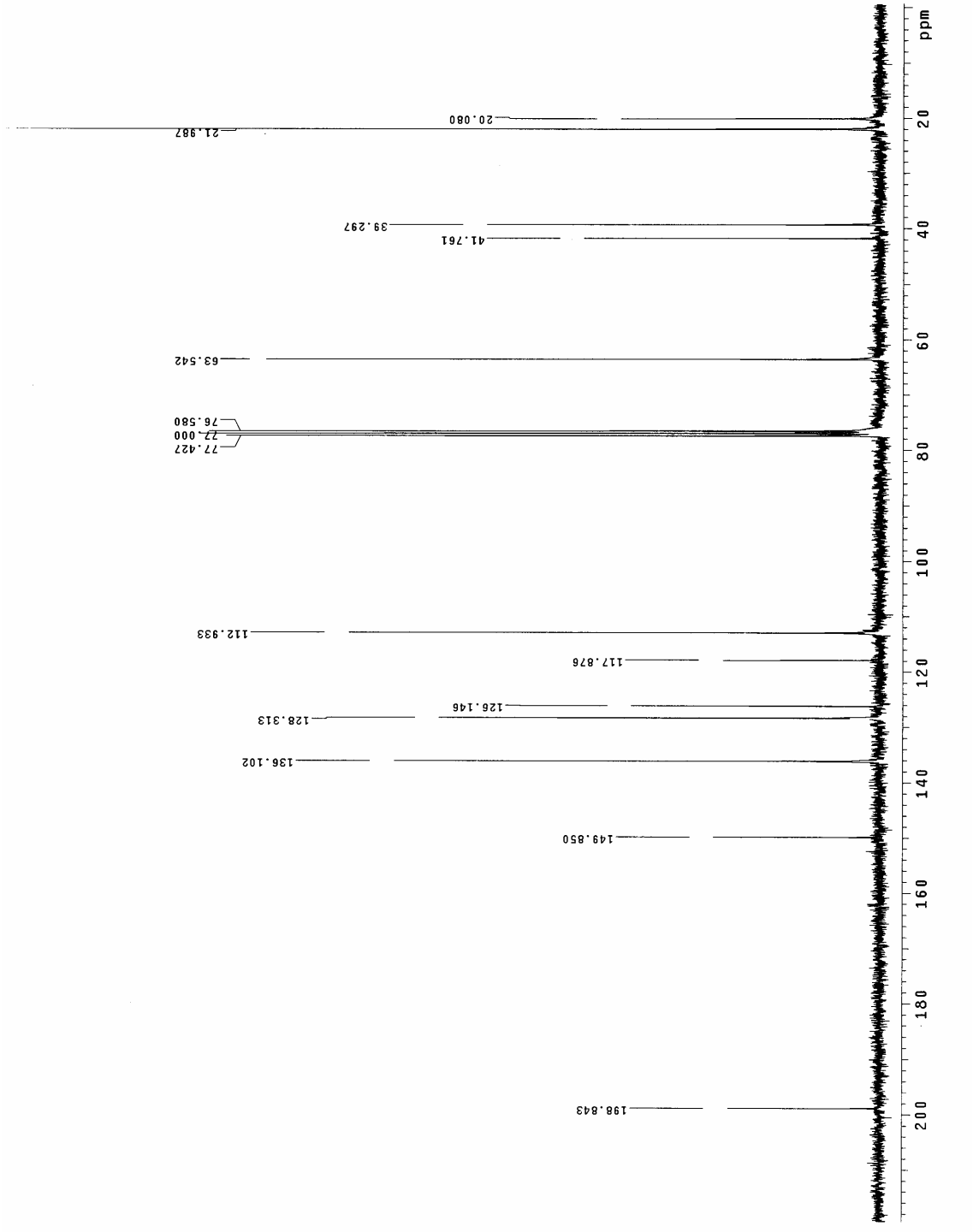
9

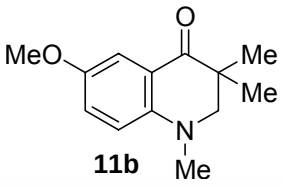

15.121
20.202
38.336
39.198
51.694
56.722
76.580
77.000
77.427
112.521
125.750
129.648
146.943
176.109
ppm
20
40
60
80
100
120
140
160
180


O
Me
Me
Me
N
Me
11a
0.000
1.159
2.255
2.989
3.128
7.260
ppm
1
2
3
4
5
6
7
8
9

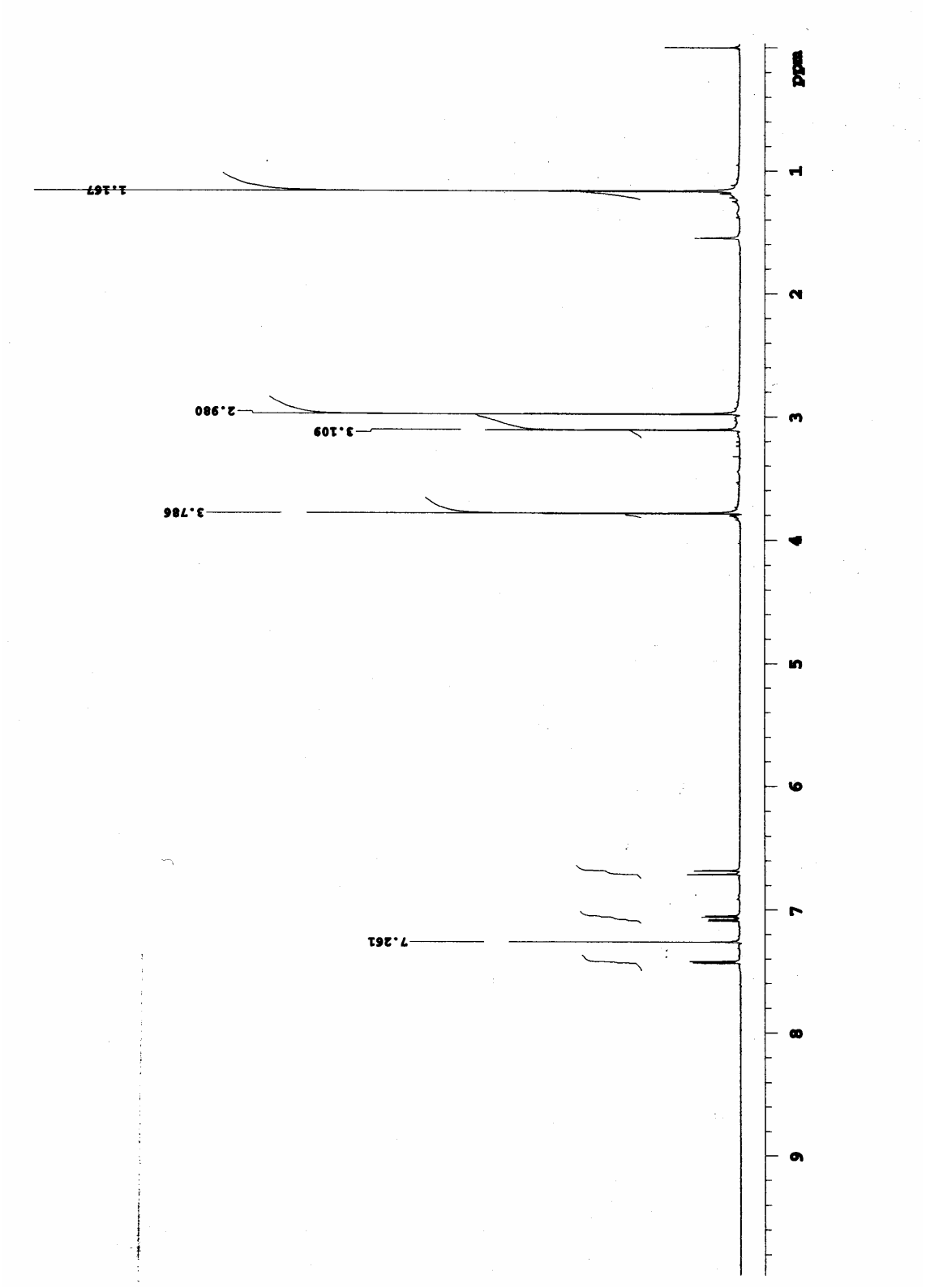

O
Me
Me
Me
N
Me

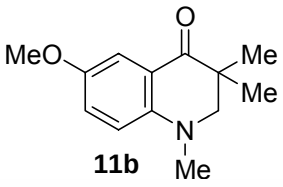
11a


198.843
149.850
136.102
128.313
126.146
117.876
112.933
77.427
77.000
76.580
63.542
41.761
39.297
21.987
20.080
ppm
20
40
60
80
100
120
140
160
180
200

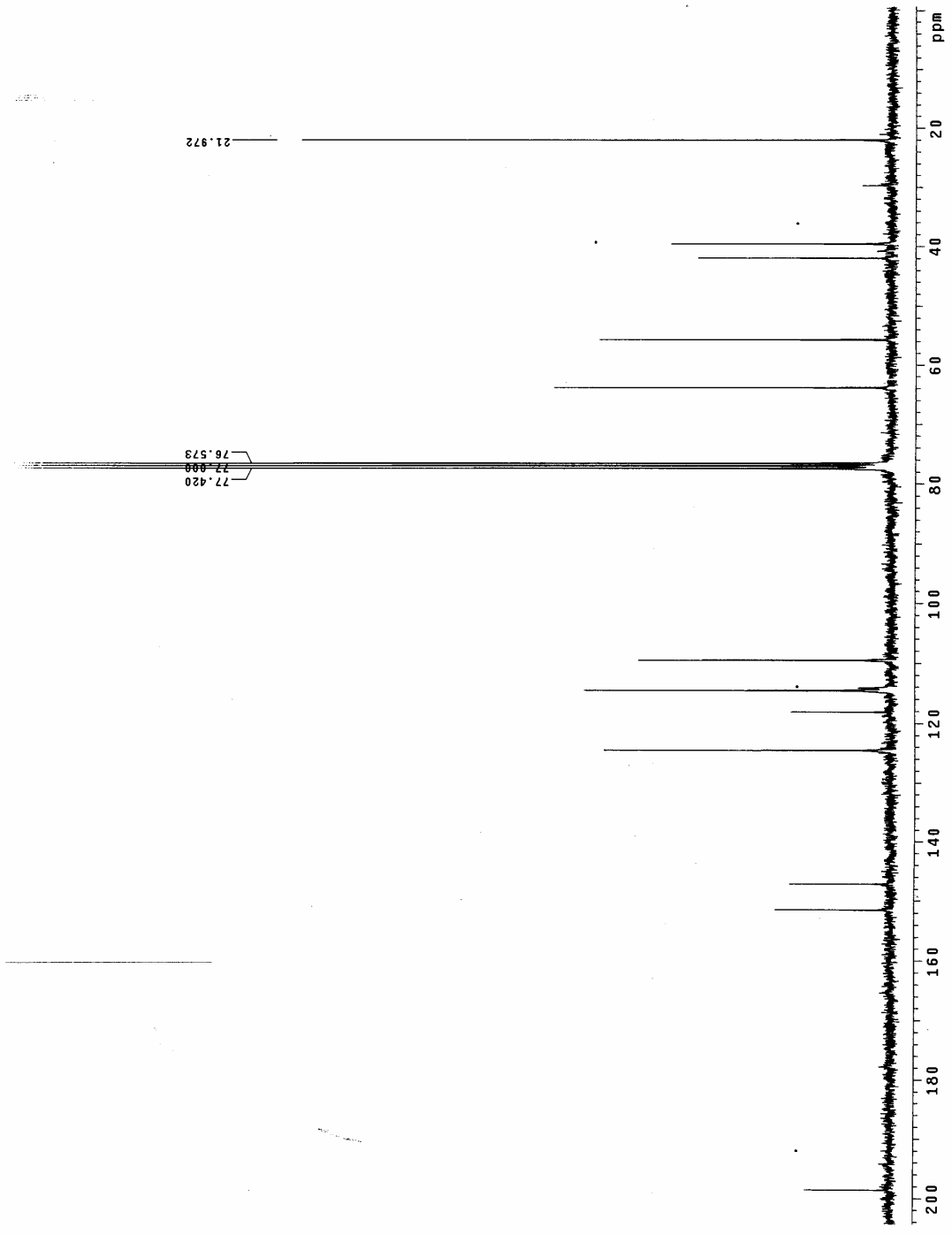


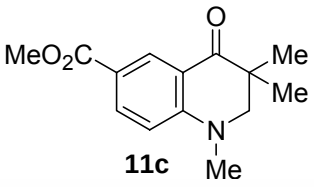
11b



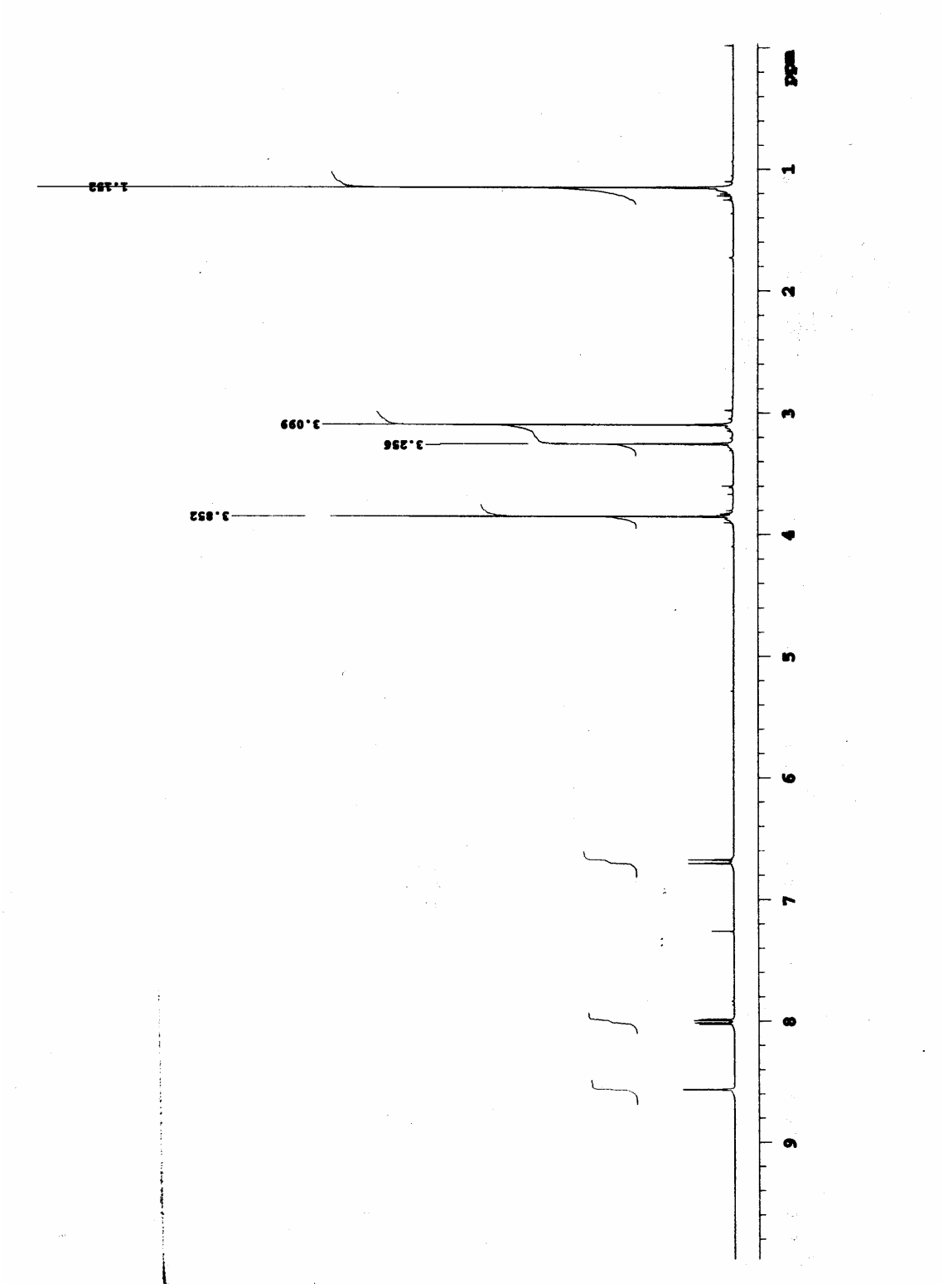

O
MeO
Me
Me
N
Me

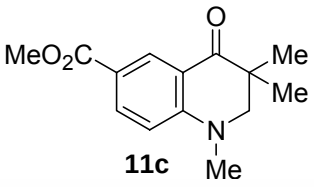
11b


21.972
76.573
77.000
77.420
ppm
20
40
60
80
100
120
140
160
180
200

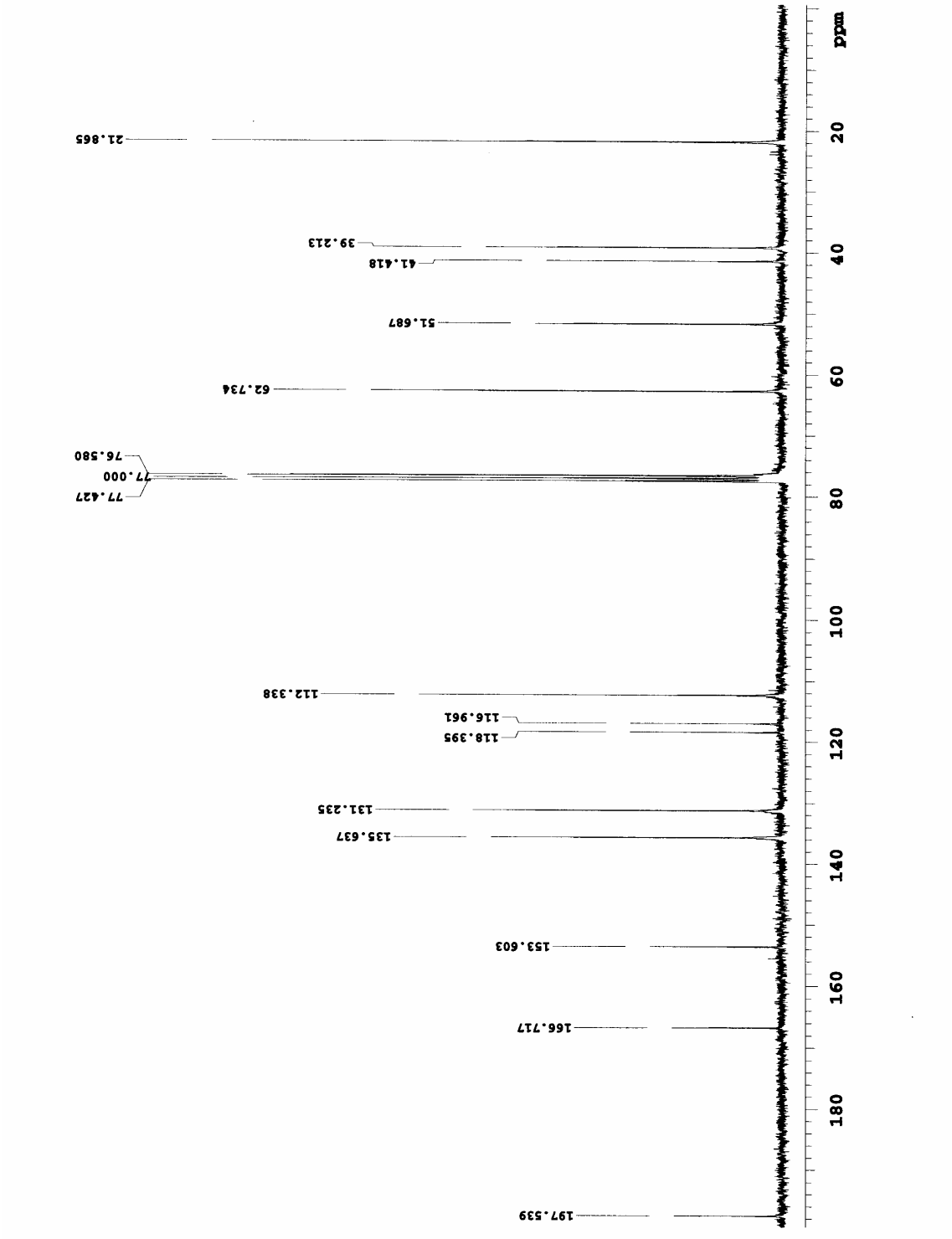


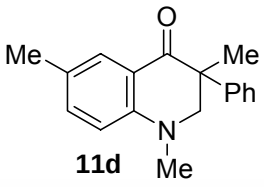
11c



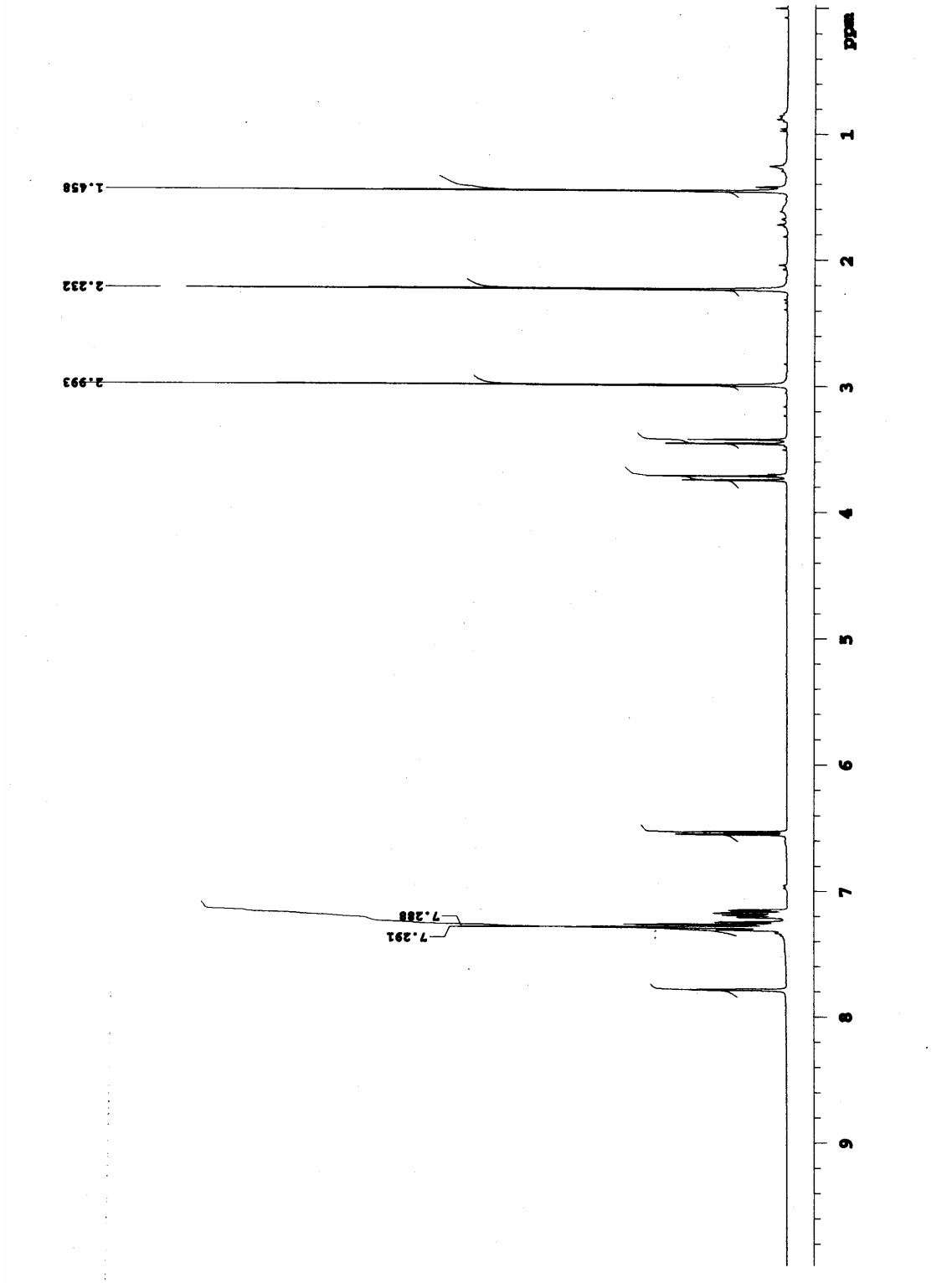

O
MeO2C
Me
Me
N
Me

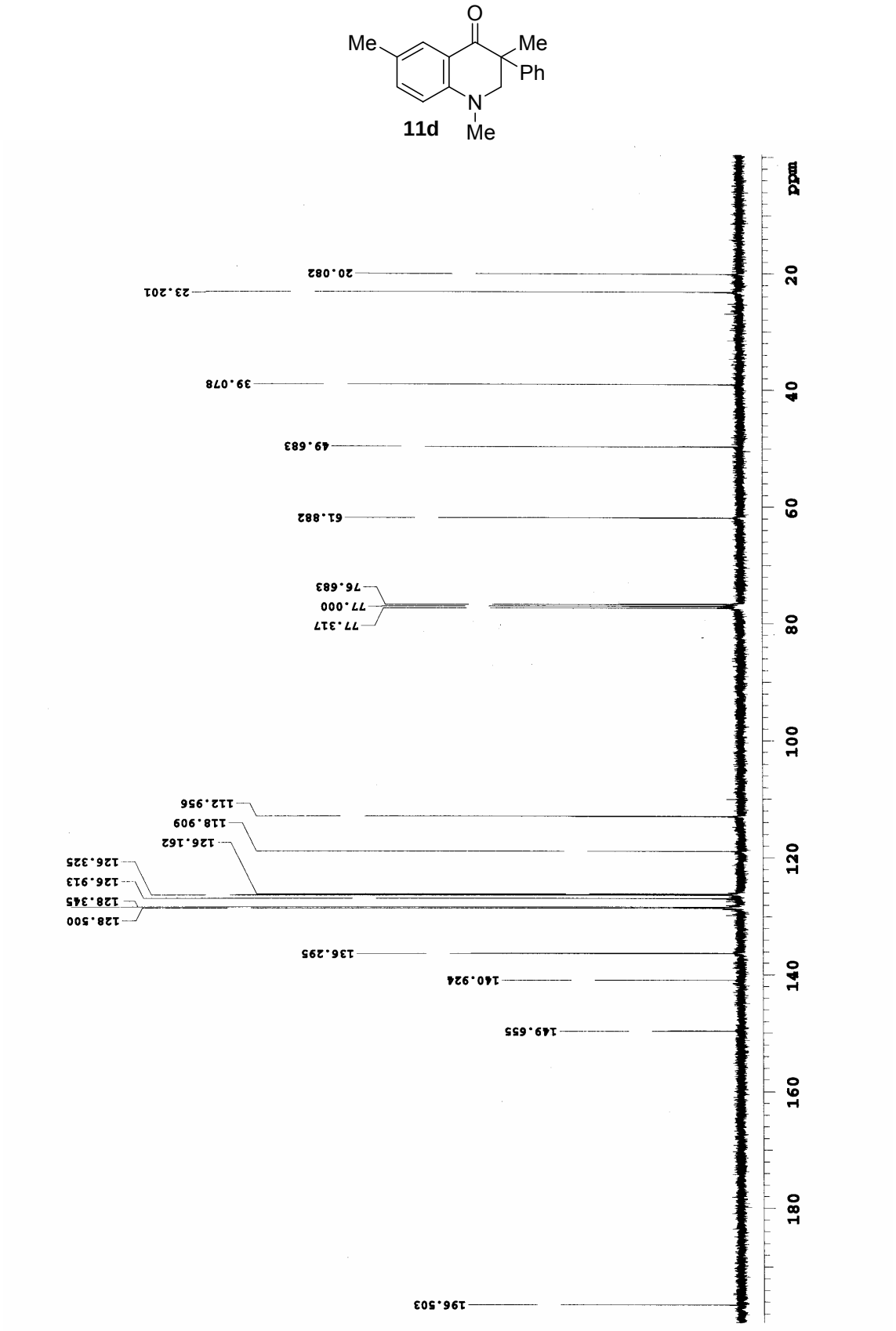
11c

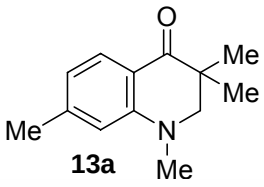

21.865
39.213
41.418
51.687
62.734
76.580
77.000
77.427
112.338
116.961
118.395
131.235
135.637
153.603
166.717
197.539
ppm
20
40
60
80
100
120
140
160
180



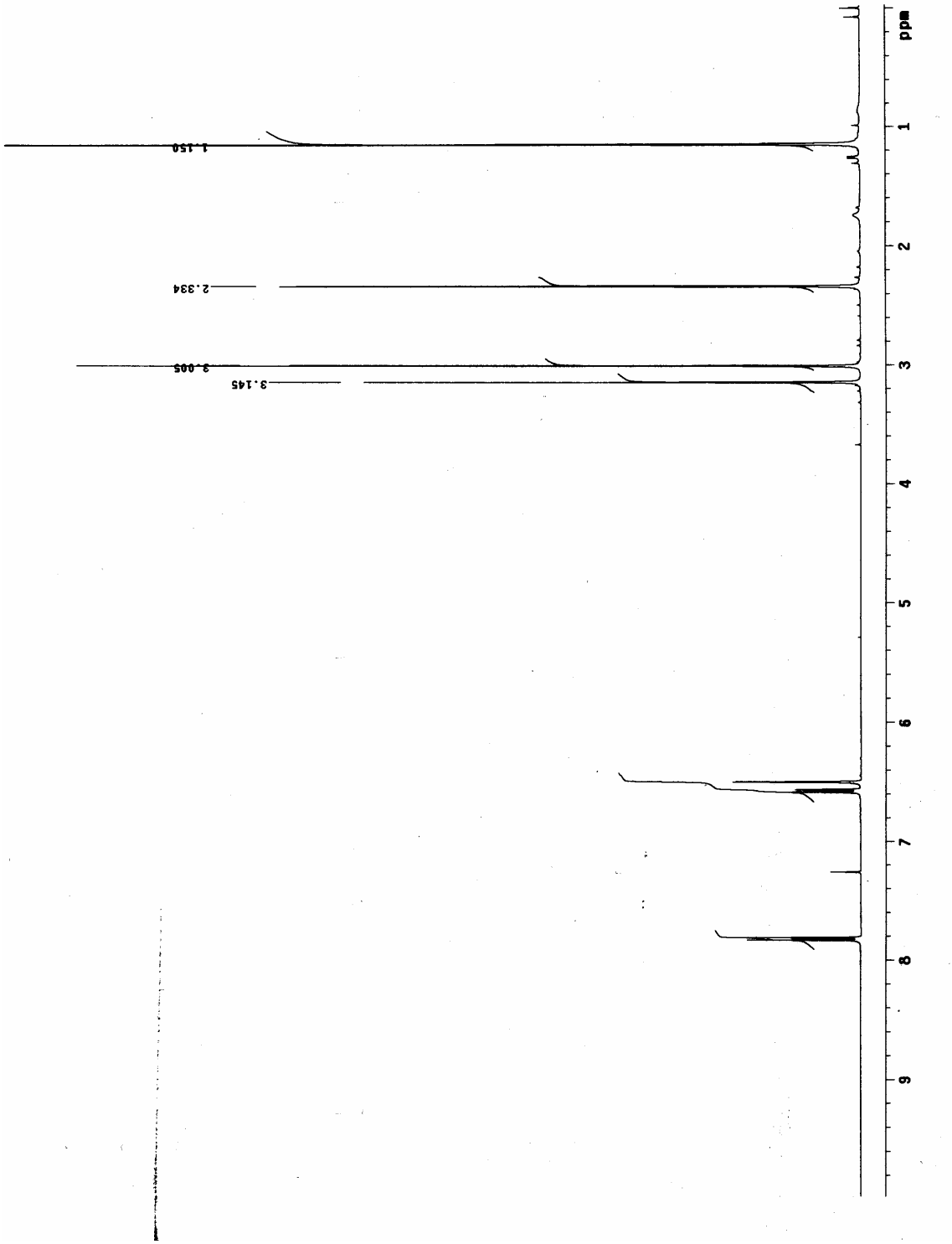
11d

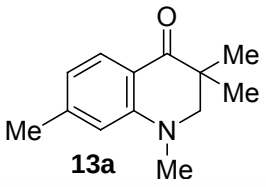



O
Me
Me
Ph
N
Me
11d
ppm
20
40
60
80
100
120
140
160
180
20.082
23.201
39.078
49.683
61.882
76.683
77.000
77.317
112.956
118.909
126.162
126.325
126.913
128.345
128.500
136.295
140.924
149.655
196.503

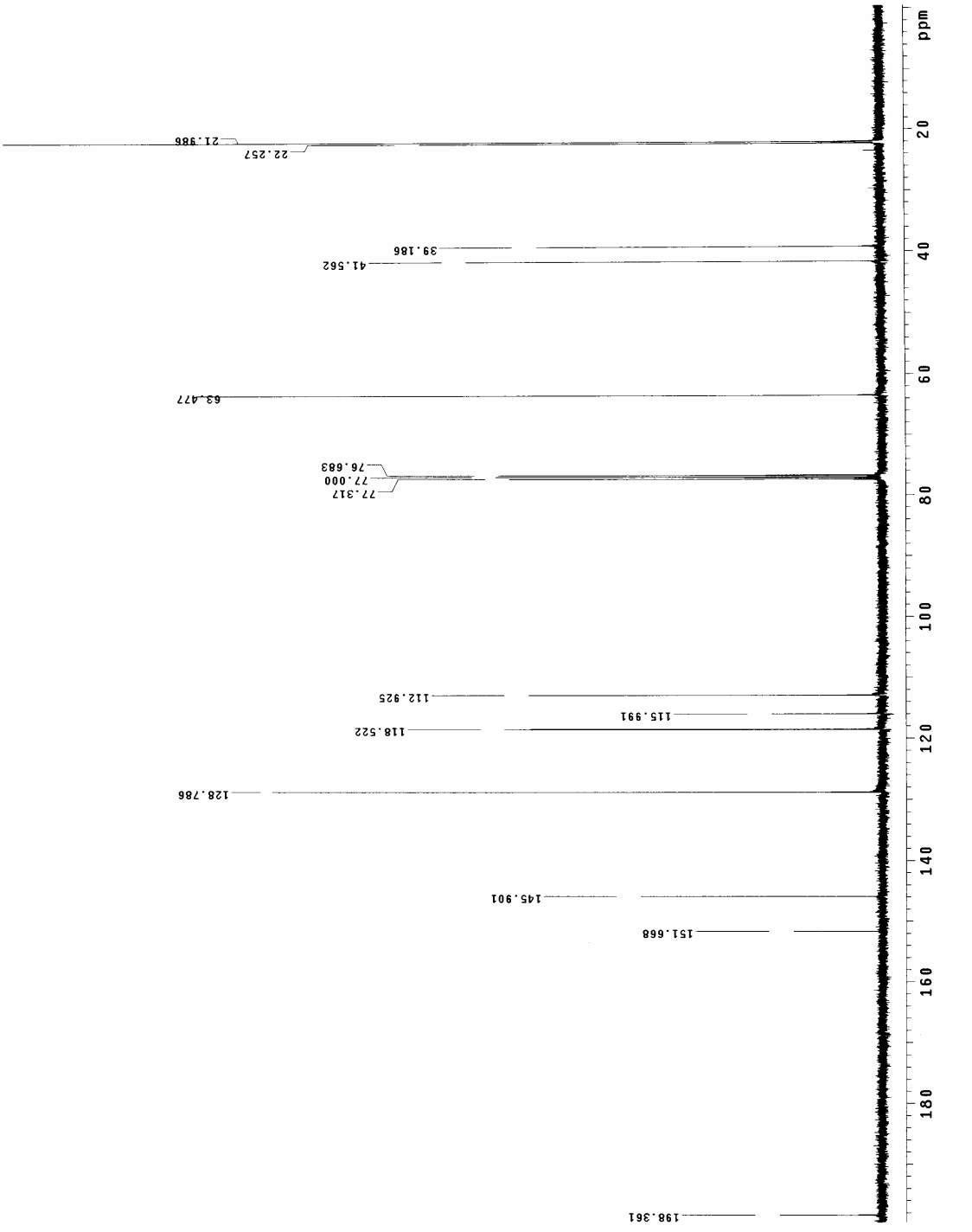


13a




O
Me
Me
Me
N
Me

13a


ppm
20
40
60
80
100
120
140
160
180
21.986
22.257
39.186
41.562
63.477
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77.000
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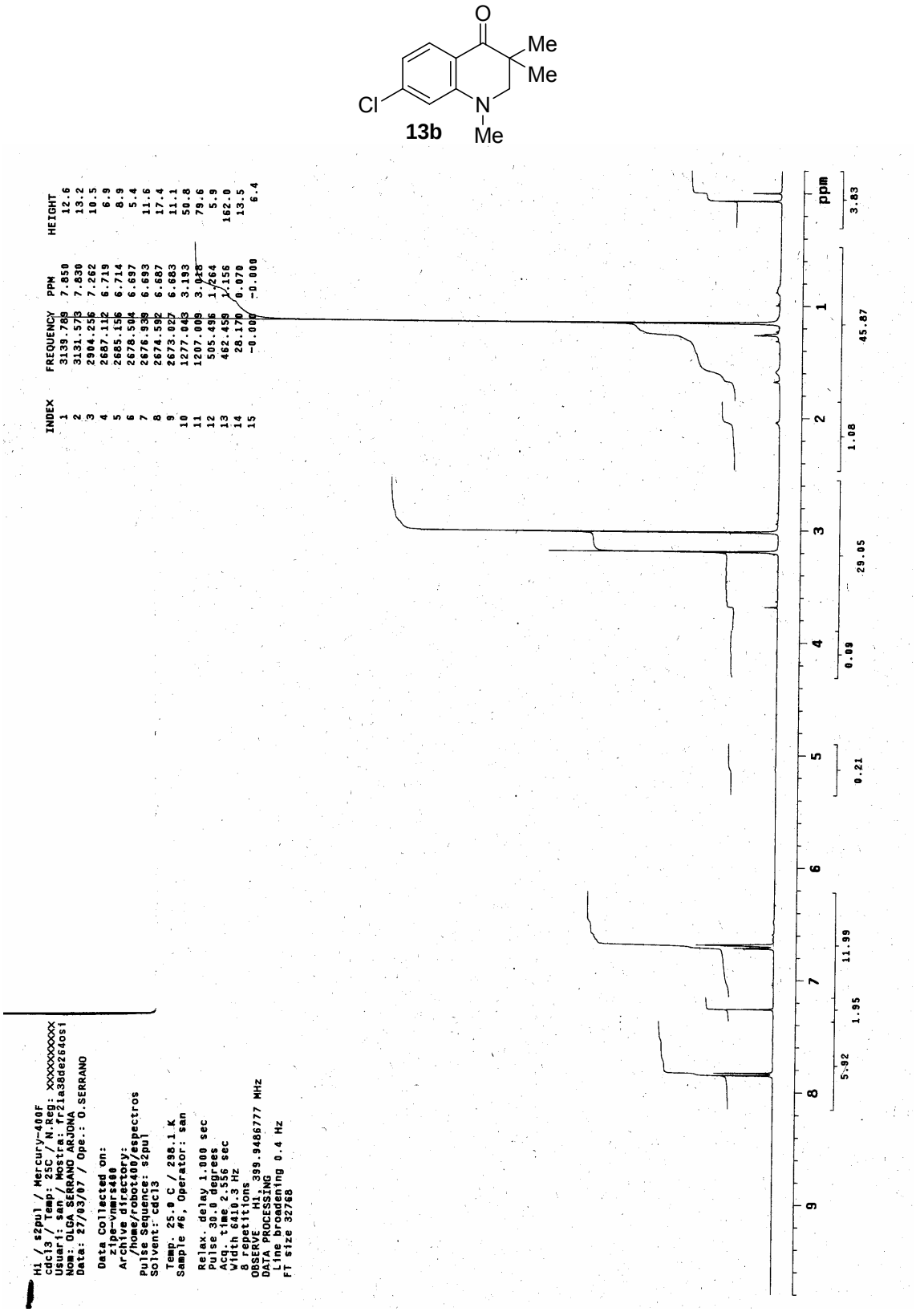
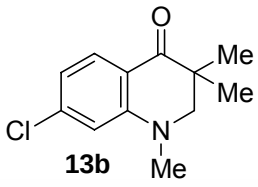
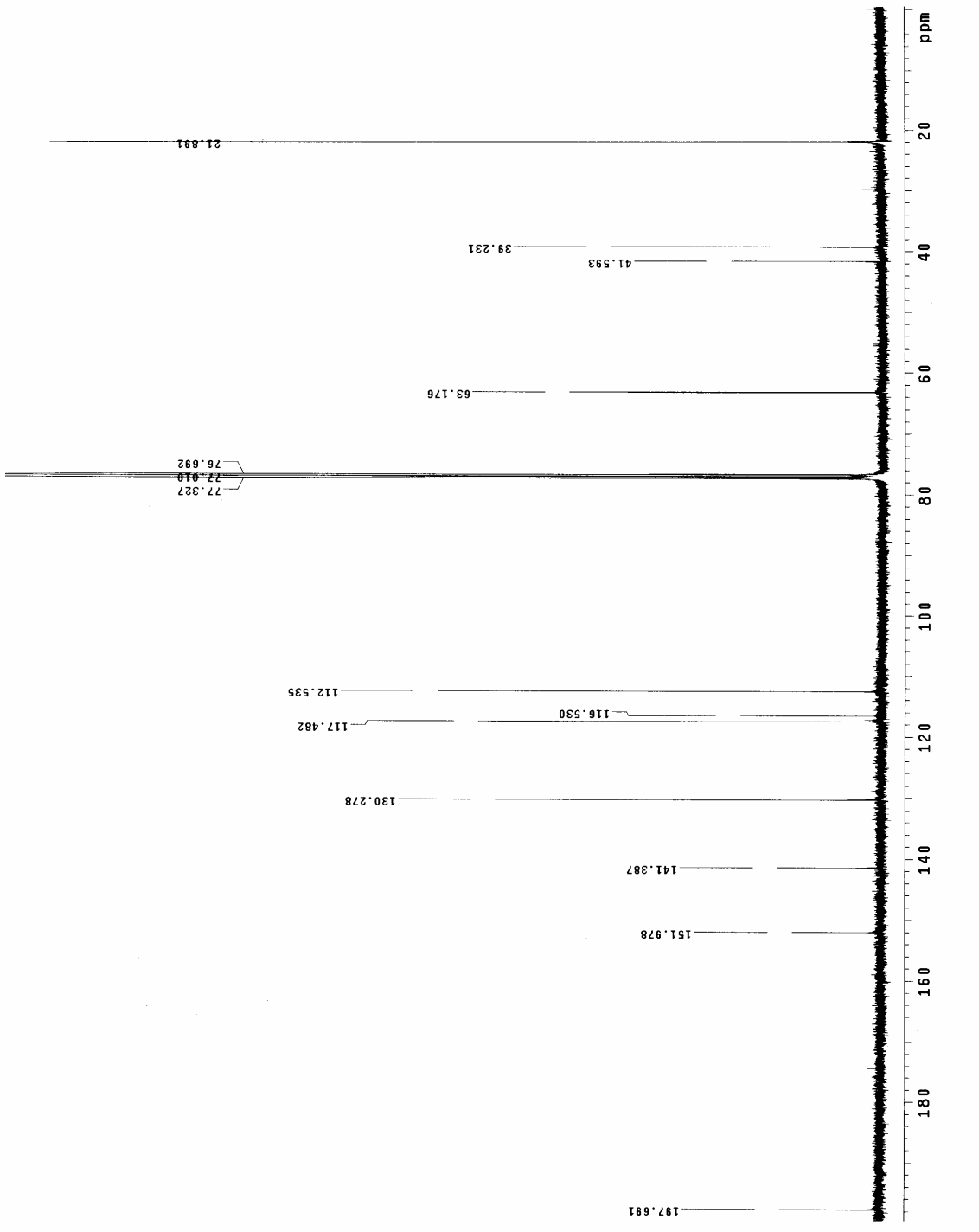
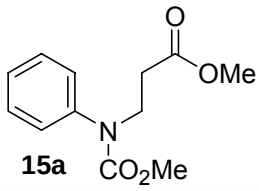
118.522
128.786
145.901
151.668
198.361


O
Me
Me
Cl
N
Me
13b
H1 / s2pul / Mercury-400F
cdcl3 / Temp: 25C / N.Reg: XXXXXXXXX
Usuari: san / Mostra: fr21a38de264os1
Nom: OLGA SERRANO ARJONA
Data: 27/03/07 / Ope.: O.SERRANO
Data Collected on:
zipdevmercu40
Archive directory:
/home/robot400/espectros
Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Sample #6, Operator: san
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.9486777 MHz
DATA PROCESSING
Line broadening 0.4 Hz
FT size 32768
INDEX FREQUENCY PPM HEIGHT
1 3139.788 7.850 12.6
2 3131.573 7.830 13.2
3 2904.256 7.262 10.5
4 2687.112 6.719 6.9
5 2685.156 6.714 8.9
6 2678.504 6.697 5.4
7 2676.930 6.693 11.6
8 2674.592 6.687 17.4
9 2673.027 6.683 11.1
10 1277.043 3.193 50.8
11 1207.009 3.018 79.6
12 505.496 1.264 5.9
13 462.458 1.156 162.0
14 28.170 0.070 13.5
15 -0.000 -0.000 6.4
ppm
5.92
1.95
11.99
0.21
0.89
29.05
1.08
45.87
3.83

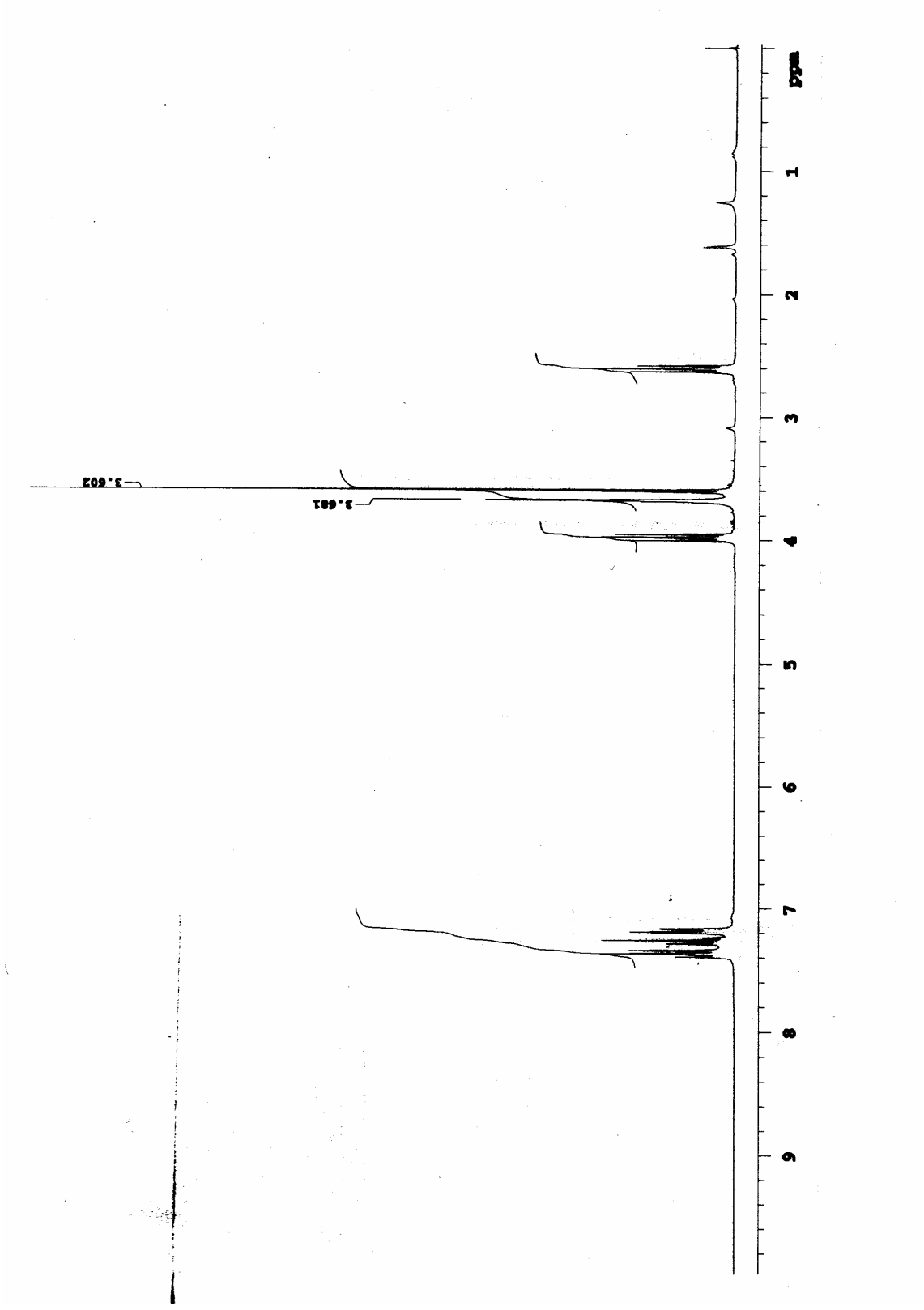

O
Me
Me
Cl
N
Me

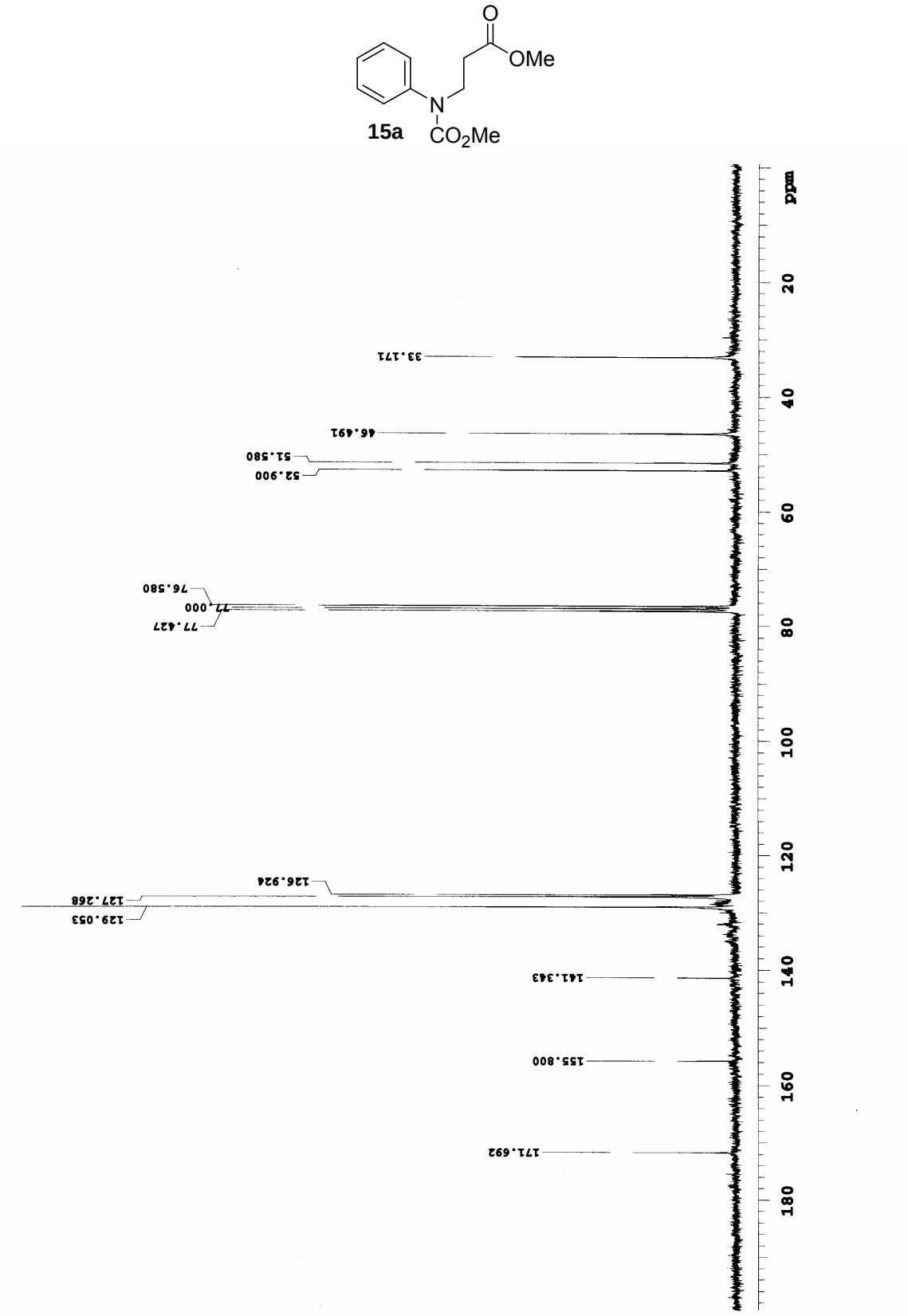
13b

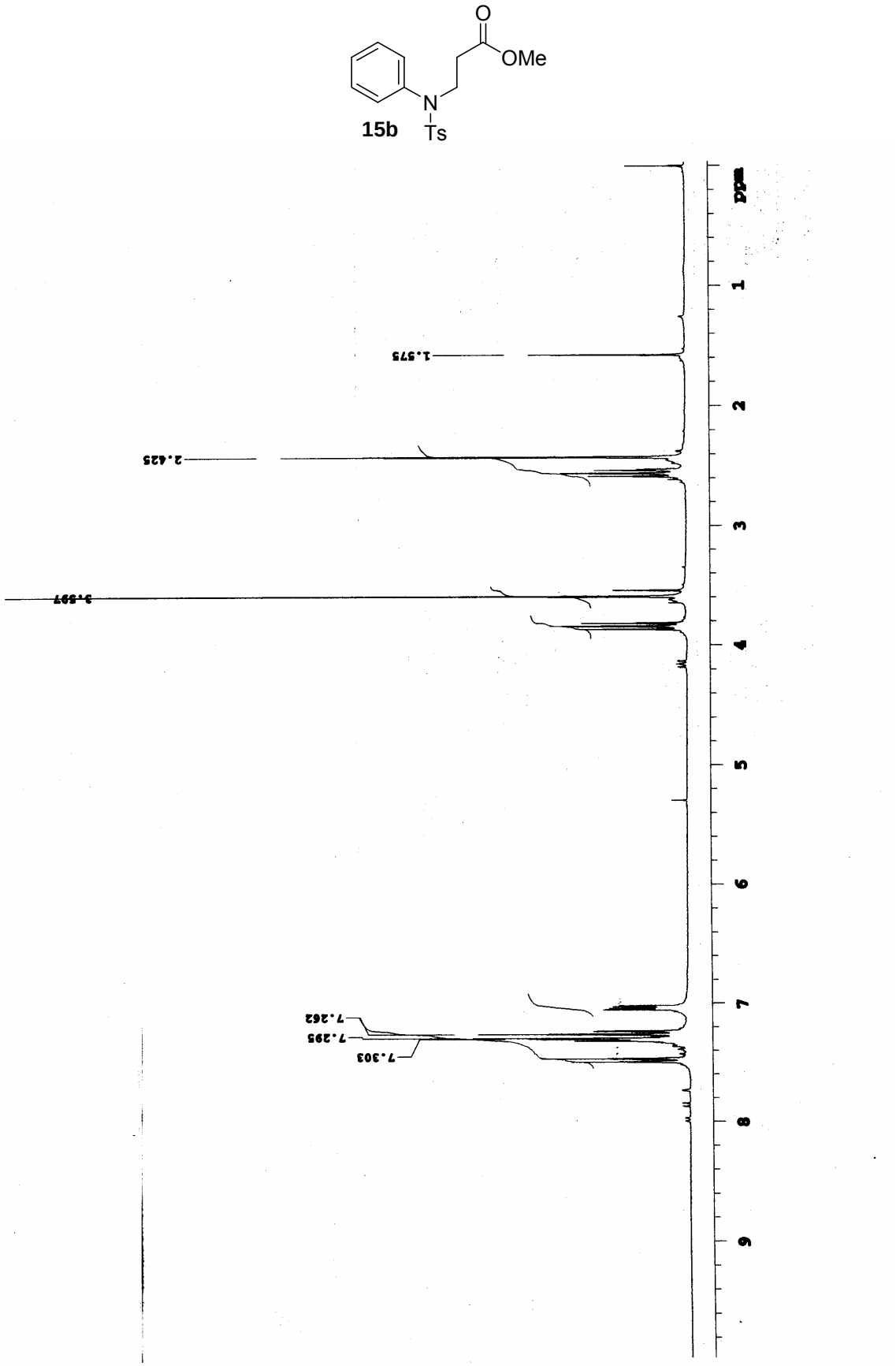

21.891
39.231
41.593
63.176
76.692
77.019
77.327
112.535
116.530
117.482
130.278
141.387
151.978
197.691
ppm
20
40
60
80
100
120
140
160
180

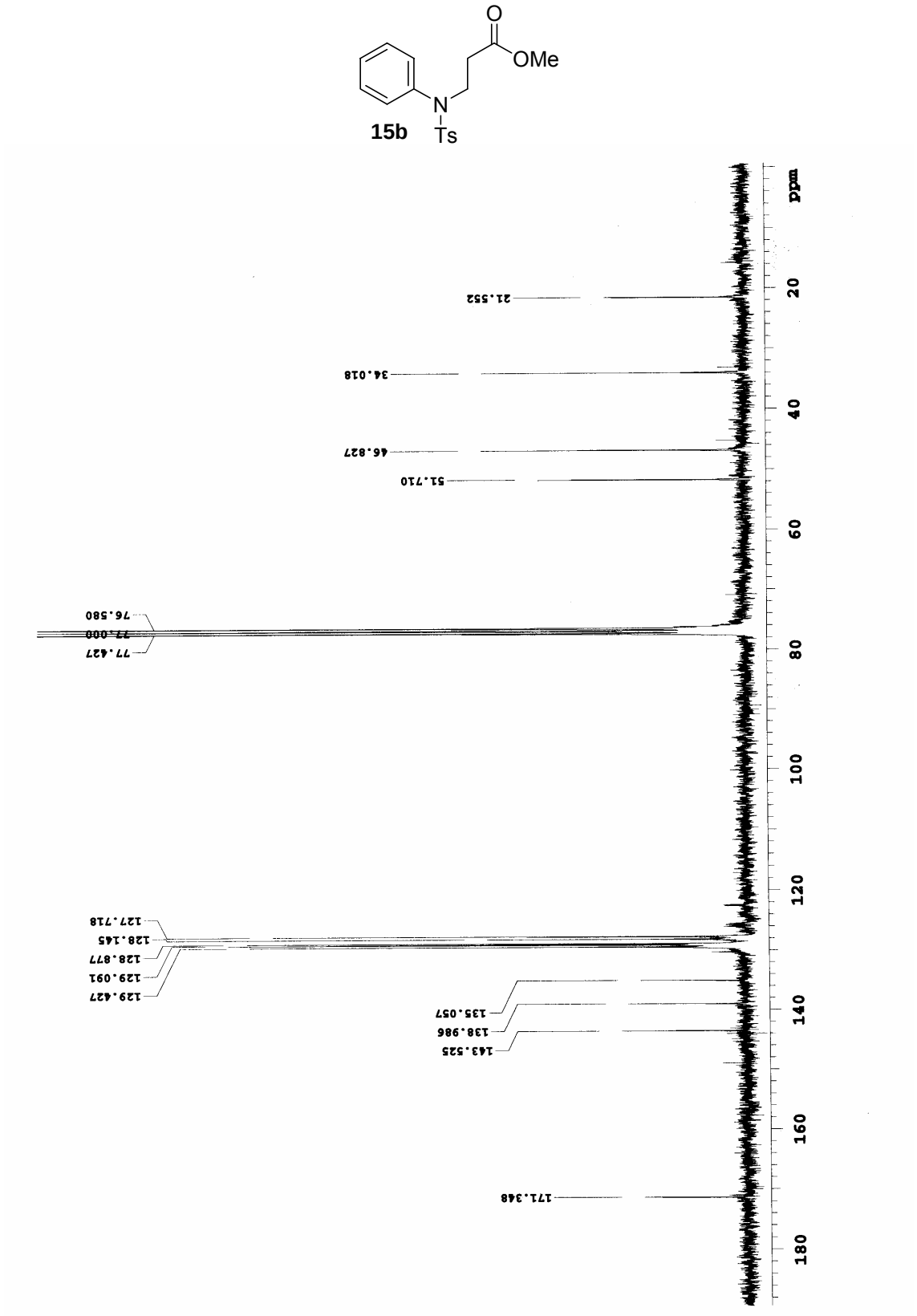


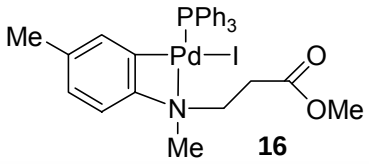
15a



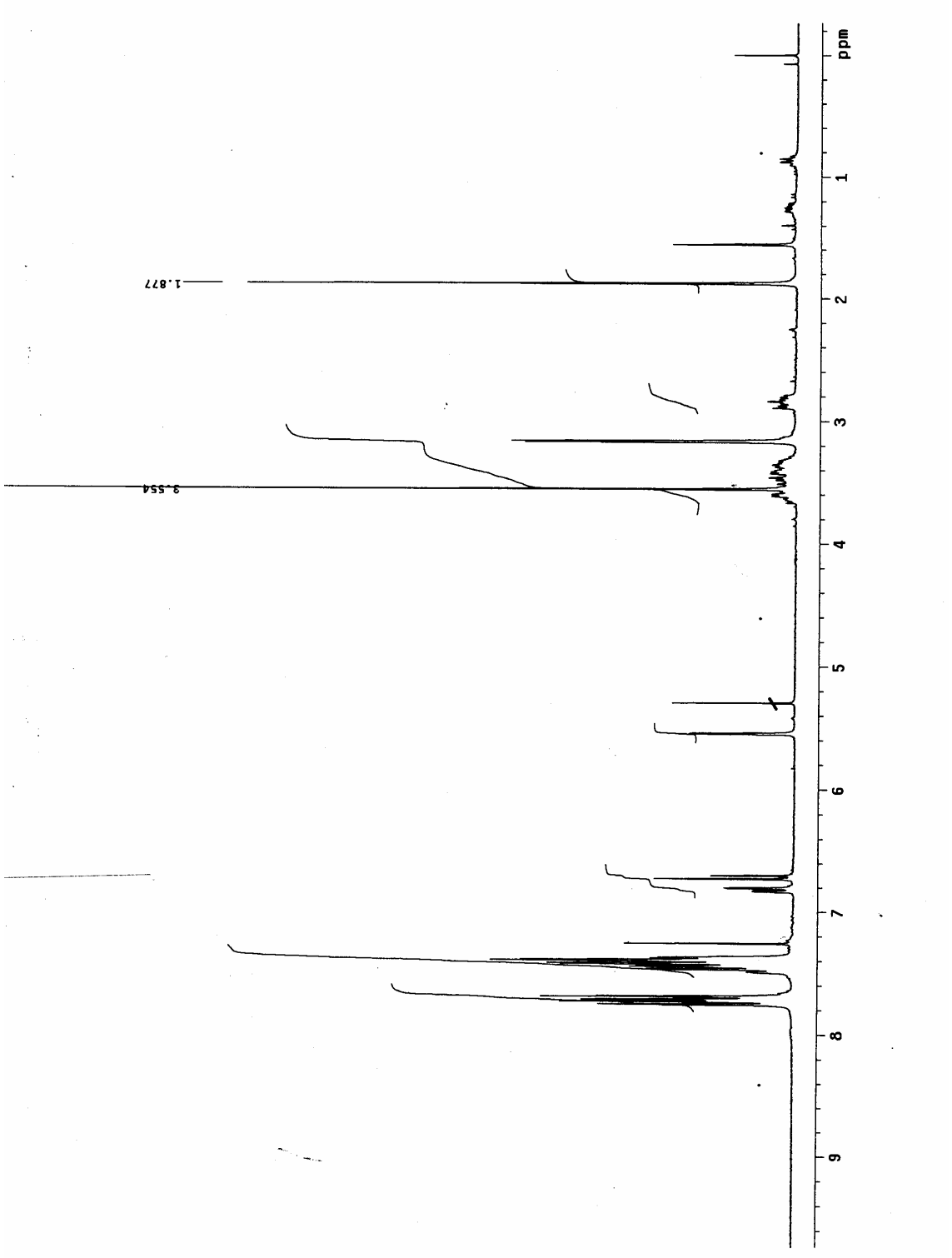

O
OMe
N
CO2Me
15a
ppm
20
40
60
80
100
120
140
160
180
33.171
46.491
51.580
52.900
76.580
77.000
77.427
126.924
127.268
129.053
141.343
155.800
171.692

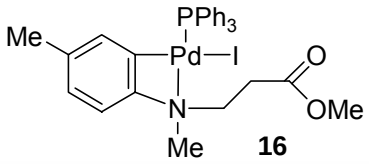

O
OMe
N
Ts
15b
1.573
2.425
3.997
7.262
7.295
7.303
ppm


O
OMe
N
Ts
15b
ppm
20
40
60
80
100
120
140
160
180
21.552
34.018
46.827
51.710
76.580
77.000
77.427
127.718
128.145
128.877
129.091
129.427
135.057
138.986
143.525
171.348

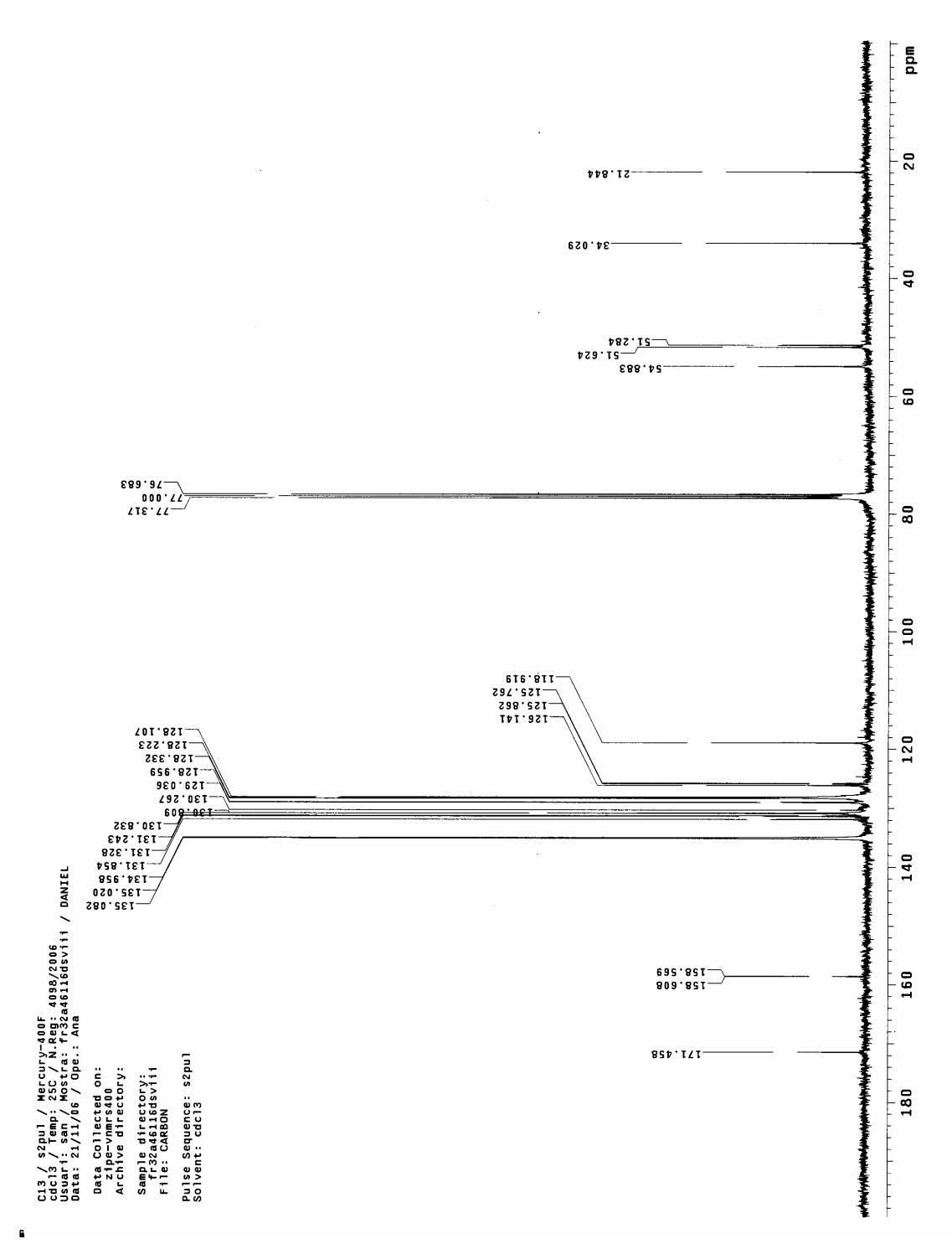


16




PPh3
Me
Pd
I
O
N
OMe
Me

16


C13 / s2pul / Mercury-400F
cdcl3 / Temp: 25C / N.Reg: 4098/2006
Usuari: san / Mostra: fr32a46116dsviii / DANIEL
Data: 21/11/06 / Ope.: Ana
Data Collected on:
z1pe-vnmrs400
Archive directory:
Sample directory:
fr32a46116dsviii
File: CARBON
Pulse Sequence: s2pul
Solvent: cdcl3
21.844
34.029
51.284
51.624
54.883
76.683
77.000
77.317
118.919
125.762
125.862
126.141
128.107
128.223
128.332
128.959
129.036
130.267
130.809
130.832
131.243
131.328
131.854
134.958
135.020
135.082
158.569
158.608
171.458
ppm