

Supporting Information

Convenient Access to Polysubstituted 1-Indanones by Sc(OTf)₃-Catalyzed Intramolecular Friedel-Crafts Acylation of Benzyl Meldrum's Acid Derivatives

Eric Fillion* and Dan Fishlock

*Department of Chemistry, University of Waterloo, Waterloo, Ontario, N2L 3G1,
Canada*

efillion@uwaterloo.ca

General Methods. All reactions were carried out in flame-dried glassware under a dry nitrogen atmosphere. Nitromethane, acetonitrile, dichloromethane, dichloroethane and diisopropylethylamine were distilled from CaH₂. Sc(OTf)₃ was dried under high vacuum for 30 minutes at 180 °C prior to use. Trimethyloxonium tetrafluoroborate (Meerwein's salt) was dried under high vacuum for 30 minutes at room temperature.

¹H NMR spectra were referenced to residual ¹H shift in CDCl₃ (7.24 ppm). CDCl₃ (77.0 ppm) was used as the internal reference for ¹³C NMR. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet.

Reactions were monitored by thin-layer chromatography (TLC) on commercial silica pre-coated plates with a particle size of 60 Å. Developed plates were viewed by UV lamp (254 nm). Flash chromatography was performed using 230-400 mesh silica gel.

Melting points are uncorrected and were performed on solids obtained after concentration of column eluent, unless recrystallized from the solvent system indicated in parentheses.

Experimental.

General Procedure A: Benzyl Meldrum's acid derivative (1.0 mmol) and dry $\text{Sc}(\text{OTf})_3$ (0.12 mmol) were combined in a round bottom flask equipped with a reflux condenser, magnetic stir bar and a rubber septum under a dry nitrogen atmosphere. Solvent (10 mL) was added via syringe and the resulting solution stirred at reflux. The reaction was monitored by TLC, and upon consumption of the starting material the crude reaction mixture was cooled to rt, then concentrated by rotary evaporator. The resultant yellow/brown oil was directly purified by flash chromatography on silica gel and eluted with the appropriate solvent system.

General Procedure B: Benzyl Meldrum's acid derivative (1.0 mmol) and trimethyloxonium tetrafluoroborate (1.35 mmol) were combined in a round bottom flask equipped with a reflux condenser, magnetic stir bar and a rubber septum under a dry nitrogen atmosphere. At 0 °C, CH_2Cl_2 (10 mL) was added via syringe with stirring, followed by diisopropylethylamine (1.4 mmol). The resulting suspension was stirred for 30 minutes at 0 °C then heated at reflux until all starting material was consumed as observed by TLC. The crude reaction mixture was quenched with aqueous 10% HCl then diluted with additional CH_2Cl_2 . The layers were partitioned and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic fractions were dried over MgSO_4 , then filtered and concentrated. The yellow oil was purified by flash chromatography on silica gel to provide the desired β -keto ester.

5,7-Dimethoxy-1-indanone¹ (2a): Prepared using procedure A in CH_3CN . Purified with 2:1 EtOAc:Hex; M.p. 98-99 °C (benzene/petroleum ether). Lit. 98-99 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 6.42 (1H, br s), 6.24 (1H, br s), 3.85 (3H, s), 3.82 (3H, s), 2.94-2.98 (2H, m), 2.56-2.60 (2H, m); ^{13}C NMR (CDCl_3 , 75 MHz) δ 203.3, 166.8, 160.3, 159.2, 119.3, 101.5, 97.3, 55.6, 36.8, 25.8. Anal. calcd. for $\text{C}_{11}\text{H}_{12}\text{O}_3$: C, 68.74; H, 6.29. Found: C, 69.03; H, 6.30.

5,7-Dimethoxy-3-methyl-1-indanone (2b): Prepared using procedure A in CH_3CN . Purified with 2:1 EtOAc:Hex; M.p. 61-62.5 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 6.45 (1H,

br s), 6.27 (1H, br s), 3.87 (3H, s), 3.85 (3H, s), 3.22-3.28 (1H, m), 2.85 (1H, dd, $J = 18.5$ Hz, 7.6 Hz), 2.21 (1H, dd, $J = 18.5$ Hz, 3.5 Hz), 1.32 (3H, d, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 202.4, 167.0, 165.2, 159.0, 118.6, 100.4, 97.2, 55.7, 55.6, 45.9, 32.5, 21.3. Anal. calcd. for $\text{C}_{12}\text{H}_{14}\text{O}_3$: C, 69.88; H, 6.84. Found: C, 69.82; H, 6.73.

5,7-Dimethoxy-3,3-dimethyl-1-indanone² (2c): Prepared using procedure A in CH_3CN . Purified with 2:1 EtOAc:Hex; M.p. 92-94 °C (Et_2O). Lit. 95.5 °C (benzene); ^1H NMR (CDCl_3 , 300 MHz) δ 6.44 (1H, br s), 6.27 (1H, br s), 3.89 (3H, s), 3.87 (3H, s), 2.52 (2H, s), 1.34 (6H, s); ^{13}C NMR (CDCl_3 , 75 MHz) δ 201.6, 165.9, 167.0, 158.8, 117.5, 98.8, 96.9, 55.7, 55.6, 53.4, 37.9, 29.7. Anal. calcd. for $\text{C}_{13}\text{H}_{16}\text{O}_3$: C, 70.89; H, 7.32. Found: C, 70.87; H, 7.49.

5,7-Dimethoxy-(3,3)-pentamethylene-1-indanone (2d): Prepared using procedure A in CH_3CN . Purified with 1:1 EtOAc:Hex; M.p. 132-133 °C (Et_2O); ^1H NMR (CDCl_3 , 300 MHz) δ 6.45 (1H, d, $J = 1.8$), 6.26 (1H, d, $J = 1.8$), 3.88 (3H, s), 3.86 (3H, s), 2.51 (2H, s), 1.19-1.76 (10H, m); ^{13}C NMR (CDCl_3 , 75 MHz) δ 201.9, 169.3, 166.9, 159.0, 117.8, 99.3, 97.2, 55.8, 55.7, 49.1, 42.7, 38.2, 25.4, 23.6. Anal. calcd. for $\text{C}_{16}\text{H}_{20}\text{O}_3$: C, 73.82; H, 7.74. Found: C, 73.93; H, 7.83.

5,7-Dimethyl-1-indanone³ (2e): Prepared using procedure A in CH_3NO_2 . Purified with 8:1 Hex:EtOAc; M.p. 75-76 °C ($\text{MeOH}/\text{H}_2\text{O}$). Lit. 76-77 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.05 (1H, s), 6.89 (1H, s), 2.98-3.02 (2H, m), 2.60-2.64 (2H, m), 2.57 (3H, s), 2.36 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz) δ 207.5, 156.5, 145.0, 138.5, 132.2, 130.3, 124.4, 36.1, 25.2, 21.8, 18.2. Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{O}$: C, 82.46; H, 7.55. Found: C, 82.40; H, 7.36.

5,7-Dimethyl-(3,3)-pentamethylene-1-indanone (2f): Prepared using procedure A in CH_3NO_2 . Purified with 10:1 Hex:EtOAc; M.p. 87.5-88.5 °C (Hex); ^1H NMR (CDCl_3 , 300 MHz) δ 7.08 (1H, s), 6.89 (1H, s), 2.57 (3H, s), 2.52 (2H, s), 2.37 (3H, s), 1.23-1.77 (10H, m); ^{13}C NMR (CDCl_3 , 75 MHz) δ 206.5, 165.6, 145.0, 138.2, 130.5, 121.7, 49.1,

42.1, 38.4, 25.6, 23.8, 22.0, 18.3. Anal. Calcd. for C₁₆H₂₀O: C, 84.16; H, 8.83. Found: C, 84.00; H, 9.12.

5-Methoxy-1-indanone (4a) and **7-Methoxy-1-indanone (5a)**: Prepared using procedure A in CH₃NO₂. The resulting mixture of **4a** and **5a** was separated with 2:1 Hex:EtOAc; **(4a)**: M.p. 108-109 °C (MeOH); ¹H NMR (CDCl₃, 300 MHz) δ 7.65-7.68 (1H, m), 6.87-6.89 (2H, m), 3.86 (3H, s), 3.07 (2H, m), 2.65 (2H, m); ¹³C NMR (CDCl₃, 75 MHz) δ 205.3, 165.2, 158.2, 130.4, 125.3, 115.3, 109.7, 55.6, 36.4, 25.8. Anal. calcd. for C₁₀H₁₀O₂: C, 74.06; H, 6.21. Found: C, 73.90; H, 6.27. **(5a)**: M.p. 96-97.5 °C; ¹H NMR (CDCl₃, 300 MHz) δ 7.50 (1H, t, *J* = 7.9 Hz), 6.99 (1H, d, *J* = 7.5 Hz), 6.76 (1H, d, *J* = 8.0), 3.93 (3H, s), 3.04-3.08 (2H, m), 2.63-2.68 (2H, m); ¹³C NMR (CDCl₃, 75 MHz) δ 204.9, 158.1, 158.0, 136.4, 125.2, 118.4, 108.8, 55.7, 36.8, 25.5. HRMS (EI): *m/z* Calcd. for C₁₀H₁₀O₂ (M⁺) 162.0681. Found 162.0685.

5-Methoxy-(3.3)-pentamethylene-1-indanone (4b) and **7-Methoxy-(3.3)-pentamethylene-1-indanone⁴ (5b)**: Prepared using procedure A in CH₃NO₂. The resulting mixture of **4b** and **5b** was separated with 3:1 Hex:EtOAc; **(4b)**: M.p. 82-82.5 °C (Hex). Lit. 83.5-85 °C; ¹H NMR (CDCl₃, 300 MHz) δ 7.60 (1H, d, *J* = 9.0 Hz), 6.84-6.87 (2H, m), 3.86 (3H, s), 2.53 (2H, s), 1.26-1.77 (10H, m); ¹³C NMR (CDCl₃, 75 MHz) δ 204.2, 167.1, 165.3, 128.8, 125.1, 115.1, 107.4, 55.6, 48.5, 42.9, 38.2, 25.4, 23.7. Anal. calcd. for C₁₅H₁₈O₂: C, 78.23; H, 7.88. Found: C, 78.38; H, 7.84. **(5b)**: M.p. 94-96 °C. Lit. 97.5-99 °C (Et₂O); ¹H NMR (CDCl₃, 300 MHz) δ 7.52 (1H, t, *J* = 7.9 Hz), 7.02 (1H, d, *J* = 7.7), 6.55 (1H, d, *J* = 8.2), 3.92 (3H, s), 2.55 (2H, s), 1.25-1.77 (10H, m); ¹³C NMR (CDCl₃, 75 MHz) δ 203.9, 167.0, 157.6, 136.5, 123.6, 115.6, 108.8, 55.8, 48.9, 42.5, 38.3, 25.5, 23.7. HRMS (EI): *m/z* Calcd. for C₁₅H₁₈O₂ (M⁺): 230.1307. Found: 230.1304.

5-Methyl-1-indanone (4c) and **7-Methyl-1-indanone⁵ (5c)**: Prepared using procedure A in CH₃NO₂. The resulting mixture of **4c** and **5c** was separated with 10:1 Hex:EtOAc; **(4c)**: M.p. 67-68 °C (petroleum ether). Lit. 68-69 °C; ¹H NMR (CDCl₃, 300 MHz) δ 7.62 (1H, d, *J* = 7.8), 7.25 (1H, br s), 7.15 (1H, d, *J* = 7.9 Hz), 3.04-3.08 (2H, m), 2.63-2.67

(2H, m), 2.41 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz) δ 206.6, 155.7, 145.7, 134.8, 128.5, 127.0, 123.5, 36.4, 25.6, 22.0. HRMS (EI): m/z Calcd. for $\text{C}_{10}\text{H}_{10}\text{O}$ (M^+): 146.0732. Found: 146.0732. **(5c)**: M.p. 49-50 °C (petroleum ether). Lit. 52.5-53.5 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.38 (1H, t, $J = 7.5$ Hz), 7.23 (1H, d, $J = 7.4$ Hz), 7.04 (1H, d, $J = 7.4$ Hz), 3.01-3.05 (2H, m), 2.58-2.62 (2H, m), 2.59 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz) δ 207.8, 155.8, 138.6, 134.3, 133.8, 128.9, 123.9, 36.6, 25.2, 18.2. HRMS (EI): m/z Calcd. for $\text{C}_{10}\text{H}_{10}\text{O}$ (M^+): 146.0732. Found: 146.0728.

5-Methyl-(3.3)-pentamethylene-1-indanone (4d) and 7-Methyl-(3.3)-pentamethylene-1-indanone (5d): Prepared using procedure A in CH_3NO_2 . The resulting mixture of **4d** and **5d** was separated with 10:1 Hex:EtOAc; **(4d)**: M.p. 77.5-78.5 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.58 (1H, d, $J = 7.8$ Hz), 7.27 (1H, s), 7.15 (1H, d, $J = 7.8$ Hz), 2.55 (2H, s), 2.43 (3H, s), 1.27-1.79 (10H, m); ^{13}C NMR (CDCl_3 , 75 MHz) δ 205.6, 164.7, 145.9, 133.3, 128.8, 124.3, 123.2, 48.5, 42.9, 38.3, 25.5, 23.8, 22.2. HRMS (EI): m/z Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}$ (M^+) 214.1358. Found 214.1354. **(5d)**: Oil; ^1H NMR (CDCl_3 , 300 MHz) δ 7.42 (1H, t, $J = 7.5$ Hz), 7.29 (1H, d, $J = 7.7$ Hz), 7.07 (1H, d, $J = 7.3$ Hz), 2.61 (3H, s), 2.53 (2H, s), 1.23-1.78 (10H, m); ^{13}C NMR (CDCl_3 , 75 MHz) δ 207.1, 165.1, 138.5, 134.0, 133.0, 129.3, 121.2, 48.9, 42.3, 38.5, 25.5, 23.8, 18.4. Anal. calcd. for $\text{C}_{15}\text{H}_{18}\text{O}$: C, 84.07; H, 8.47. Found: C, 84.19; H, 8.36.

5-Chloro-(3.3)-pentamethylene-1-indanone (4e) and 7-Chloro-(3.3)-pentamethylene-1-indanone (5e): Prepared using procedure A in CH_3NO_2 . The resulting mixture of **4e** and **5e** was separated with 3:1 CH_2Cl_2 :Hex; **(4e)**: M.p. 74-75 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.61 (1H, d, $J = 8.2$ Hz), 7.46 (1H, d, $J = 1.6$ Hz), 7.3 (1H, dd, $J = 8.1$ Hz, 1.6 Hz), 2.57 (3H, s), 1.22-1.80 (10H, m); ^{13}C NMR (CDCl_3 , 75 MHz) δ 204.5, 165.6, 141.2, 134.0, 128.3, 124.7, 124.4, 48.3, 43.2, 38.2, 25.3, 23.7. HRMS (EI): m/z Calcd. for $\text{C}_{14}\text{H}_{15}\text{ClO}$ (M^+) 234.0811. Found 234.0807. **(5e)**: M.p. 159-160 °C (Hex); ^1H NMR (CDCl_3 , 300 MHz) δ 7.48 (1H, t, $J = 7.7$ Hz), 7.38 (1H, d, $J = 7.5$ Hz), 7.27 (1H, d, $J = 7.6$ Hz), 2.60 (2H, s), 1.24-1.80 (10H, m); ^{13}C NMR (CDCl_3 , 75 MHz) δ 202.8, 166.5, 135.1, 131.5, 131.3, 129.1, 122.4, 48.9, 42.3, 38.4, 25.4, 23.7. HRMS (EI): m/z Calcd. for $\text{C}_{14}\text{H}_{15}\text{ClO}$ (M^+) 234.0811. Found 234.0806.

(3.3)-Pentamethylene-1-indanone⁶ (4g): Prepared using procedure **A** in CH₃NO₂. Purified with 7:1 Hex:EtOAc; Oil; Lit. M.p. 58-59 °C (petroleum ether); ¹H NMR (CDCl₃, 300 MHz) δ 7.65 (1H, d, *J* = 7.7 Hz), 7.54 (1H, t, *J* = 7.1 Hz), 7.45 (1H, d, *J* = 7.7 Hz), 7.3 (1H, t, *J* = 7.4 Hz), 2.53 (3H, s), 1.20-1.75 (10H, m); ¹³C NMR (CDCl₃, 75 MHz) δ 205.9, 164.0, 135.4, 134.7, 127.4, 123.8, 123.3, 48.2, 43.0, 38.2, 25.3, 23.7. Anal. calcd. for C₁₄H₁₆O: C, 83.96; H, 8.05. Found: C, 83.60; H, 8.12.

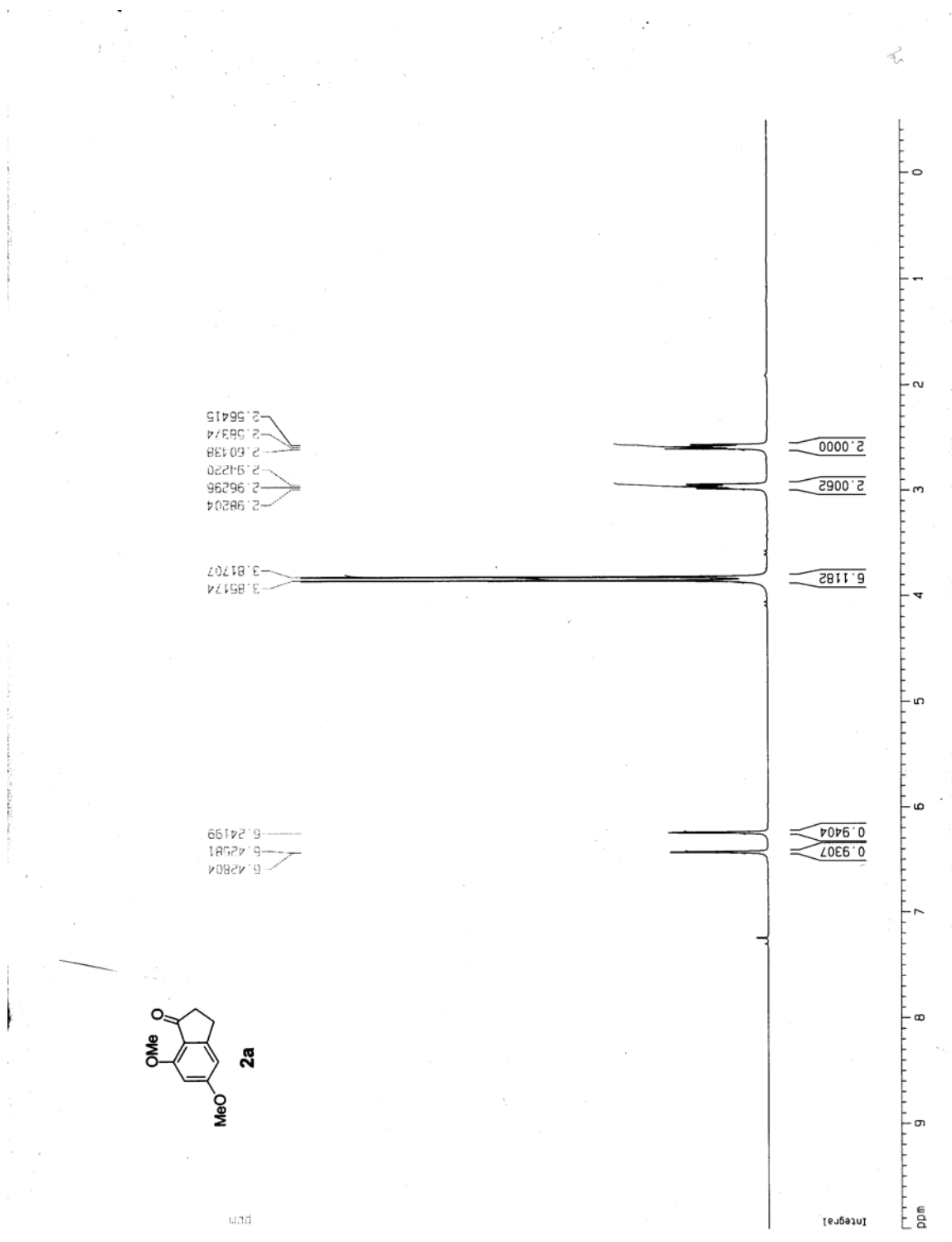
5,7-Dimethoxy-1-indanone-2-carboxylic acid methyl ester⁷ (6a): Prepared using procedure **B**. Purified with 2:1 EtOAc:Hex; M.p. 103-104 °C. Lit. 104-105 °C (EtOAc/Et₂O); ¹H NMR (CDCl₃, 300 MHz) δ 6.48 (1H, br s), 6.28 (1H, br s), 3.88 (3H, s), 3.86 (3H, s), 3.74 (3H, s), 3.66 (1H, dd, *J* = 8.2 Hz, 3.8 Hz), 3.41 (1H, dd, *J* = 17.2 Hz, 3.4 Hz), 3.20 (1H, dd, *J* = 17.3 Hz, 8.3 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 195.1, 170.0, 167.6, 160.0, 158.8, 117.6, 101.6, 97.8, 55.8, 53.7, 52.7, 30.2. HRMS (EI): *m/z* Calcd. for C₁₃H₁₄O₅ (M⁺) 250.0841. Found 250.0839.

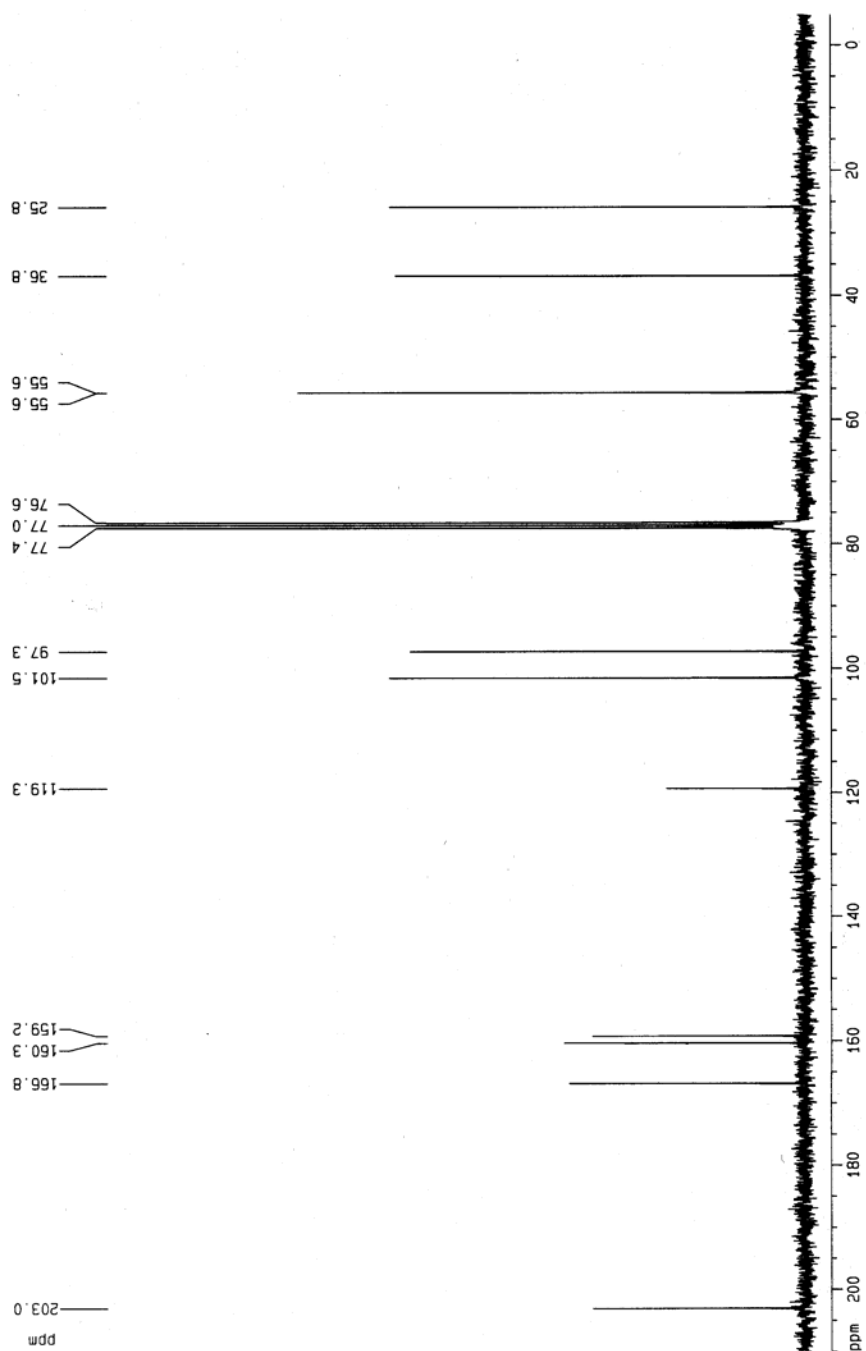
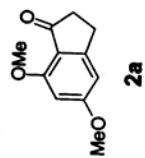
5,7-Dimethoxy-(3.3)-pentamethylene-1-indanone-2-carboxylic acid methyl ester (6b): Prepared using procedure **B**. Purified with 1:1 Hex:EtOAc; M.p. 168-170 °C (Et₂O); ¹H NMR (CDCl₃, 300 MHz) δ 6.46 (1H, d, *J* = 1.7 Hz), 6.28 (1H, d, *J* = 1.6 Hz), 3.88 (6H, s), 3.67 (3H, s), 3.56 (1H, s), 2.04-2.09 (1H, m), 1.16-1.77 (9H, m); ¹³C NMR (CDCl₃, 75 MHz) δ 196.0, 170.0, 168.3, 167.4, 159.6, 116.6, 99.4, 97.4, 64.1, 55.8, 55.7, 52.0, 46.6, 41.8, 31.9, 25.3, 23.6, 22.7. HRMS (EI): *m/z* Calcd. for C₁₈H₂₂O₅ (M⁺): 318.1467. Found: 318.1470.

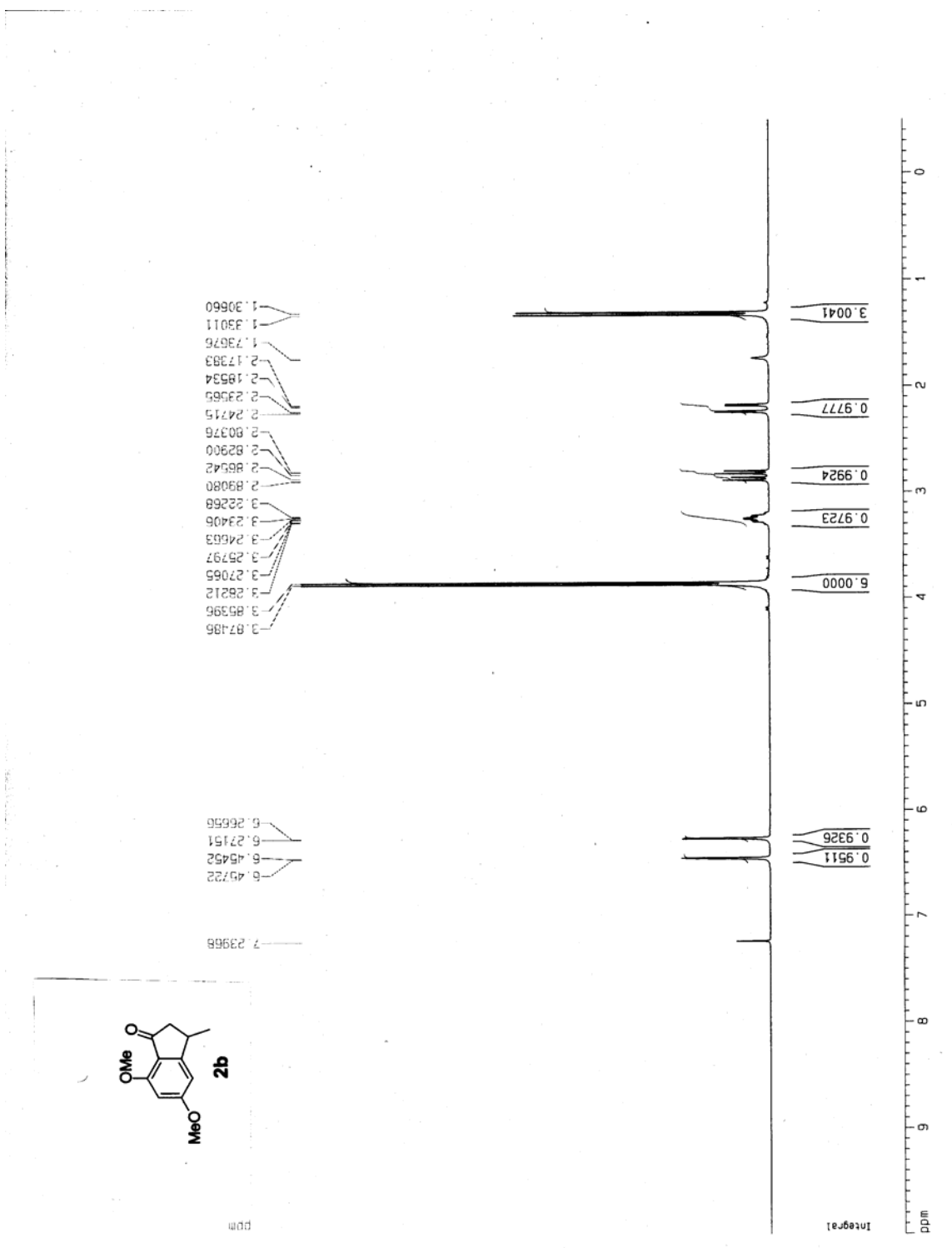
5,7-Dimethoxy-2-methyl-1-indanone^{8,9} (8): Prepared using procedure **A** in CH₃NO₂. Purified with 1:1 Hex:EtOAc; M.p. 71.5-73 °C (Hex). Lit. 76-79 °C; ¹H NMR (CDCl₃, 300 MHz) δ 6.44 (1H, br s), 6.28 (1H, br s), 3.88 (3H, s), 3.85 (3H, s), 3.21-3.29 (1H, m), 2.55-2.69 (2H, m), 1.25 (3H, d, *J* = 7.3 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 205.6, 166.9, 159.5, 158.6, 118.5, 101.5, 97.4, 55.7, 42.3, 35.0, 17.1. Anal. calcd. for C₁₂H₁₄O₃: C, 69.88; H, 6.84. Found: C, 69.58; H, 6.71.

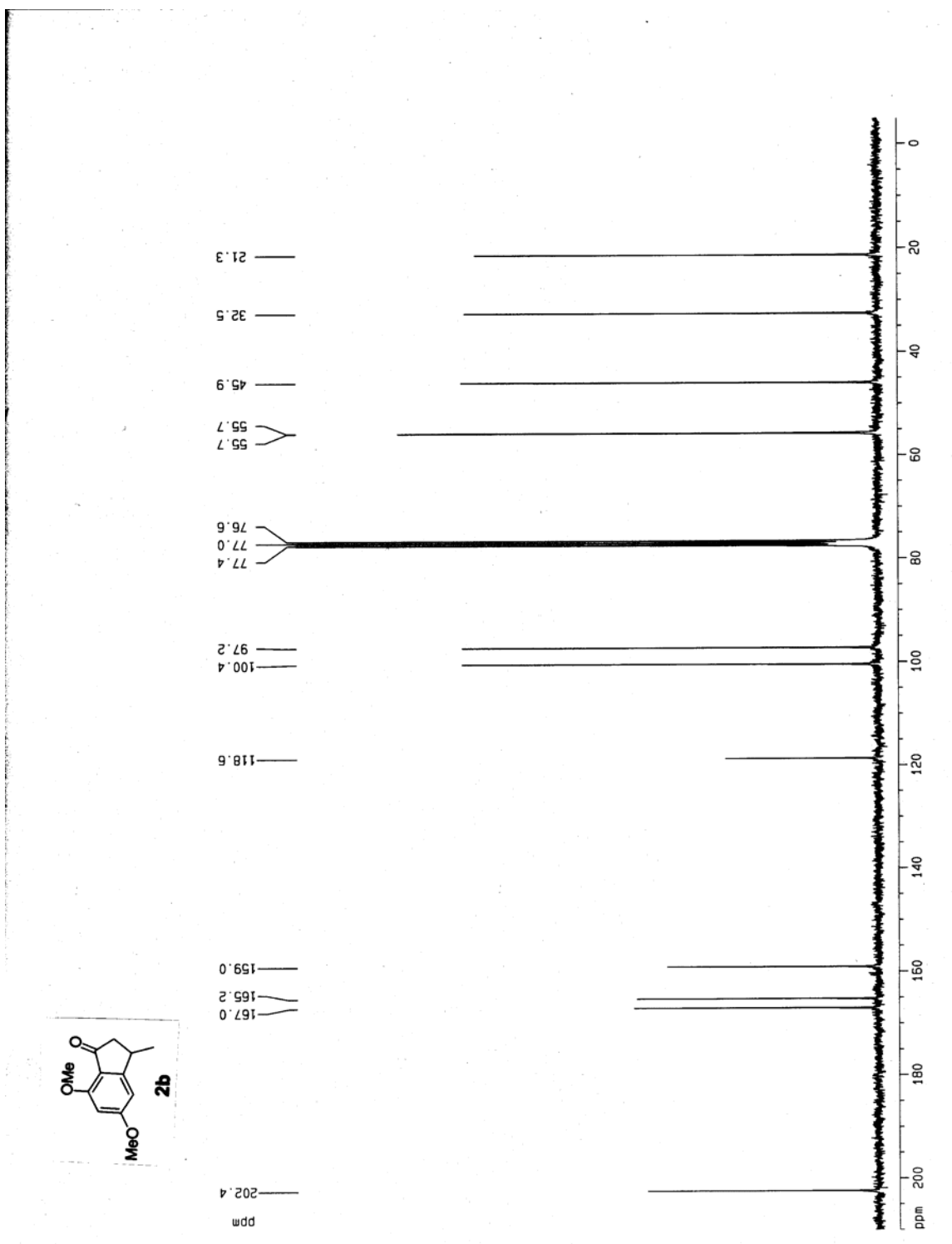
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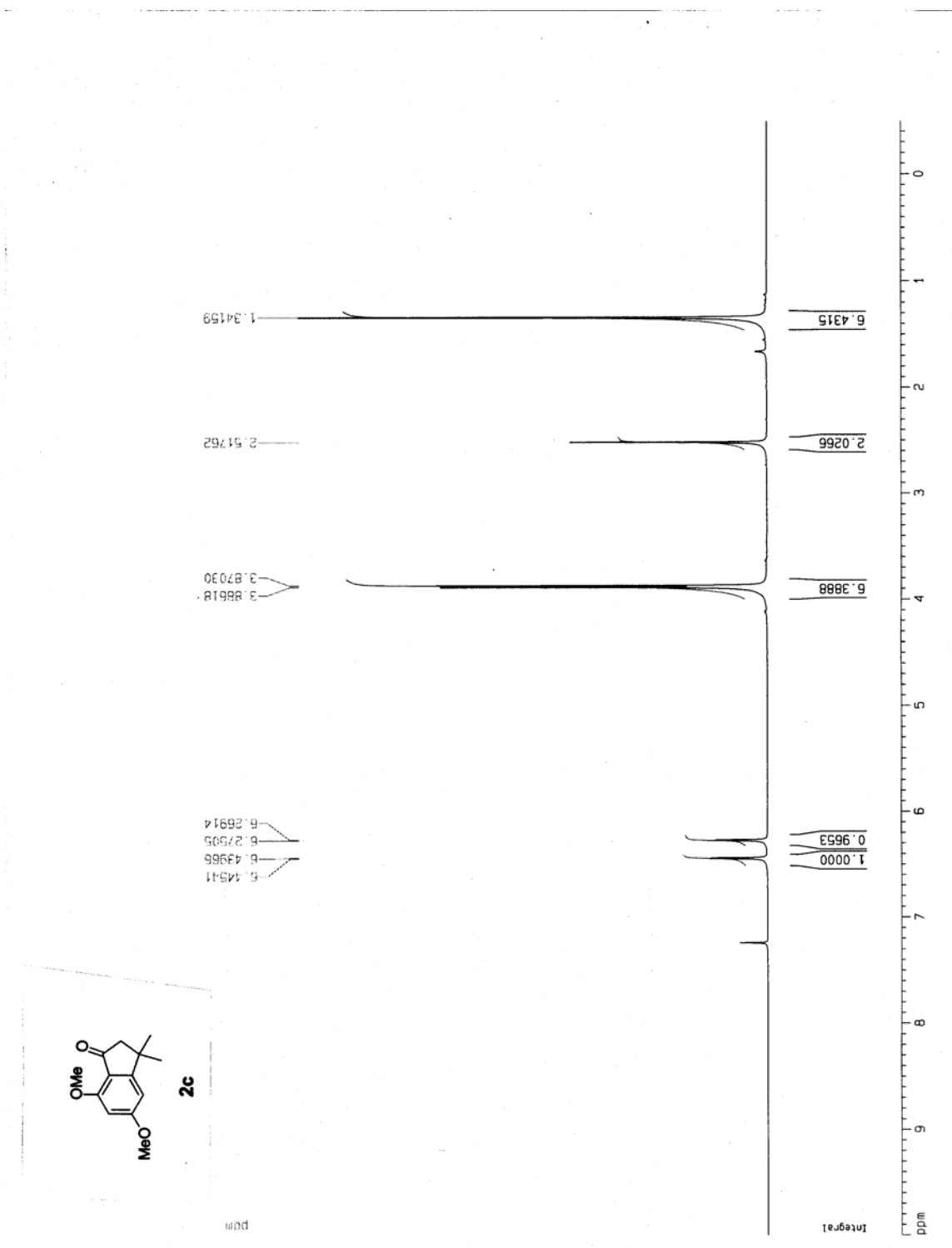
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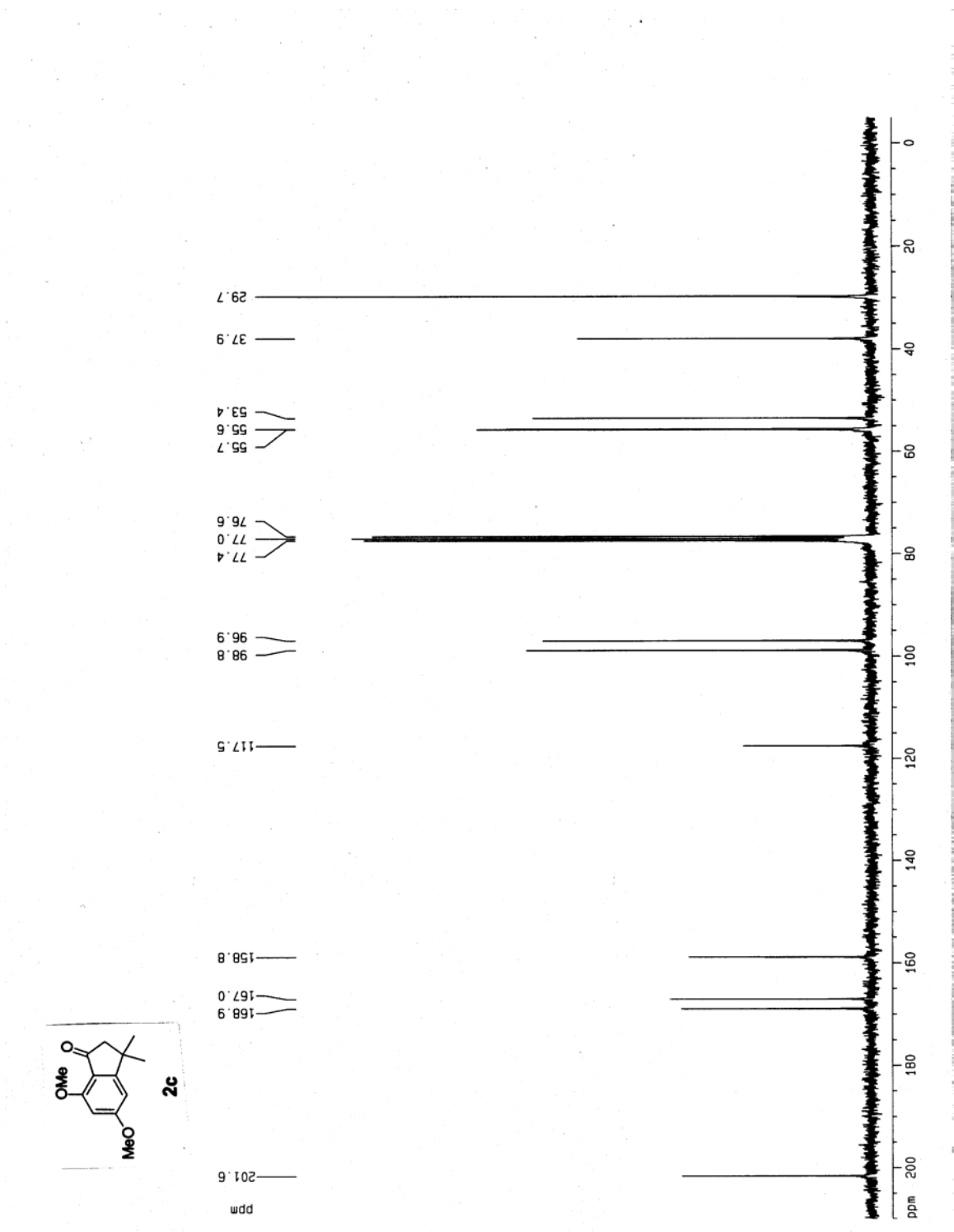


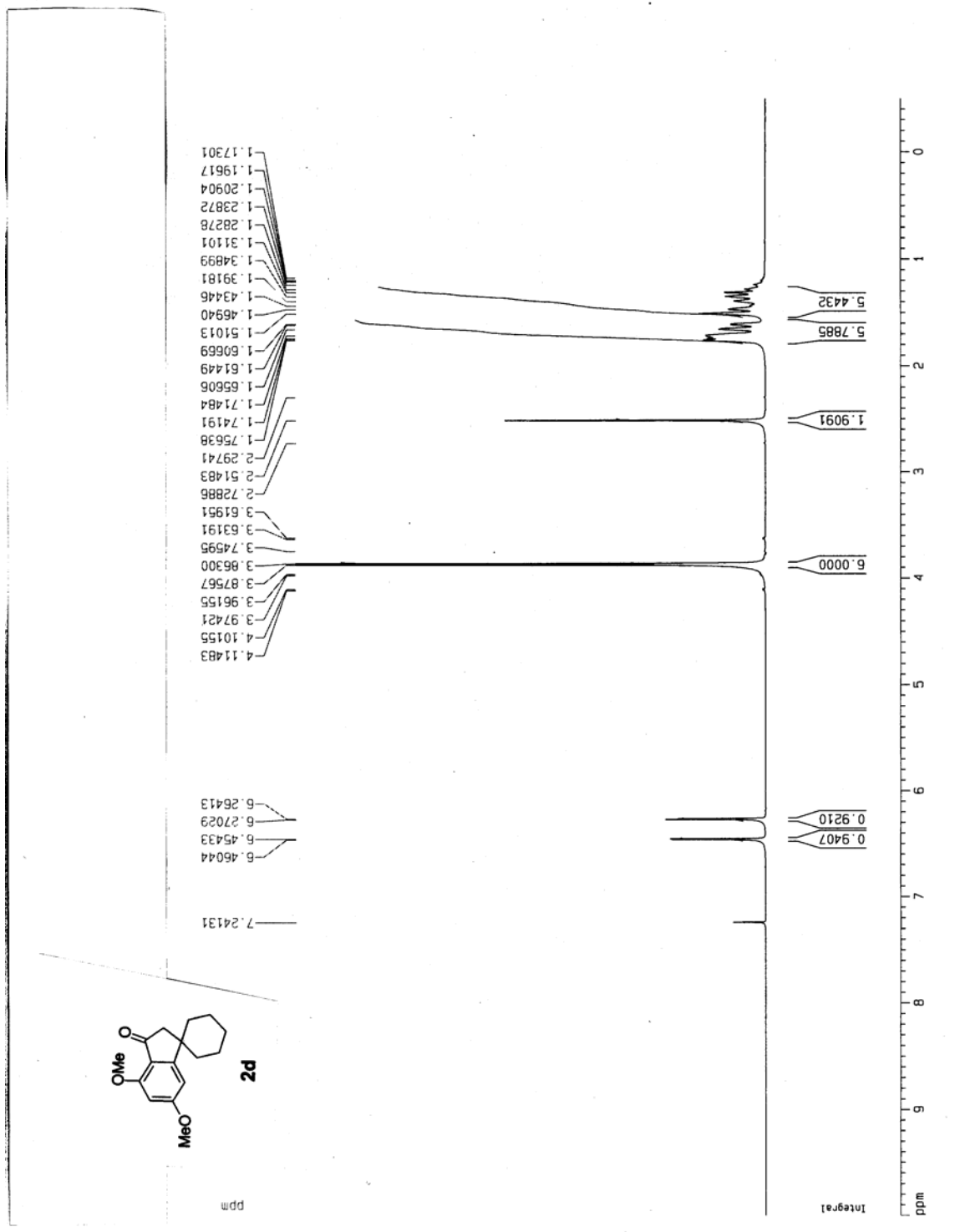


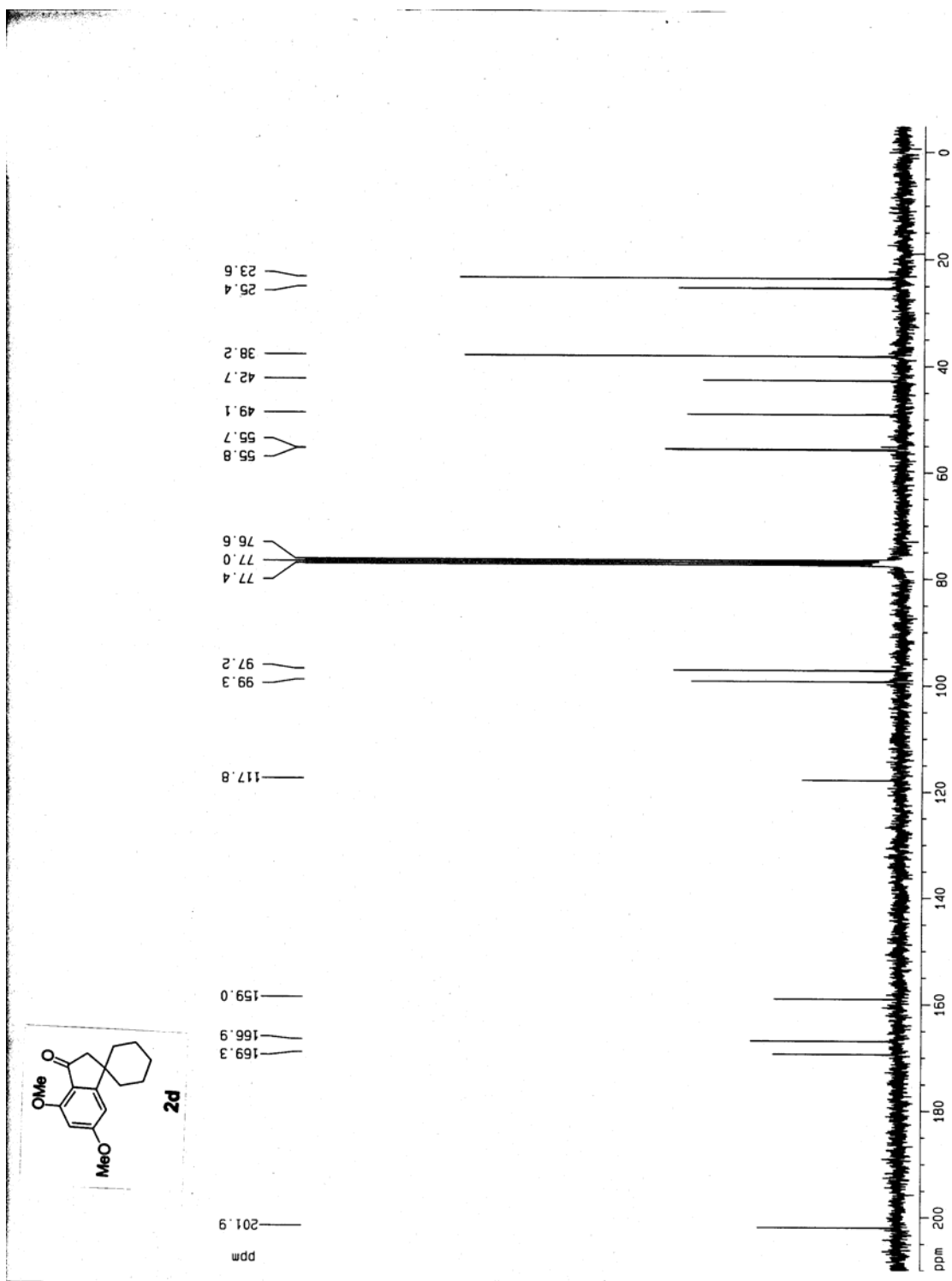


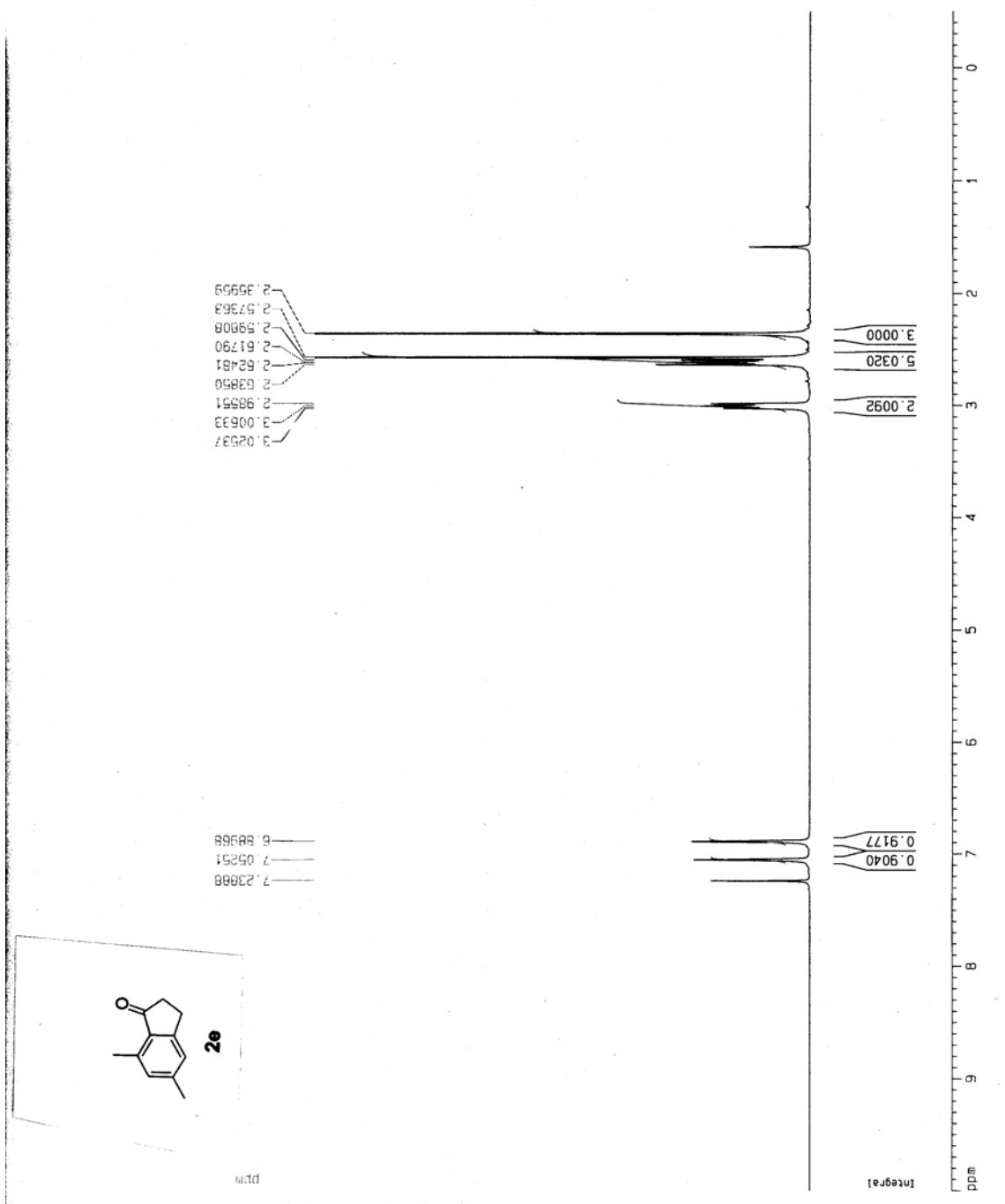


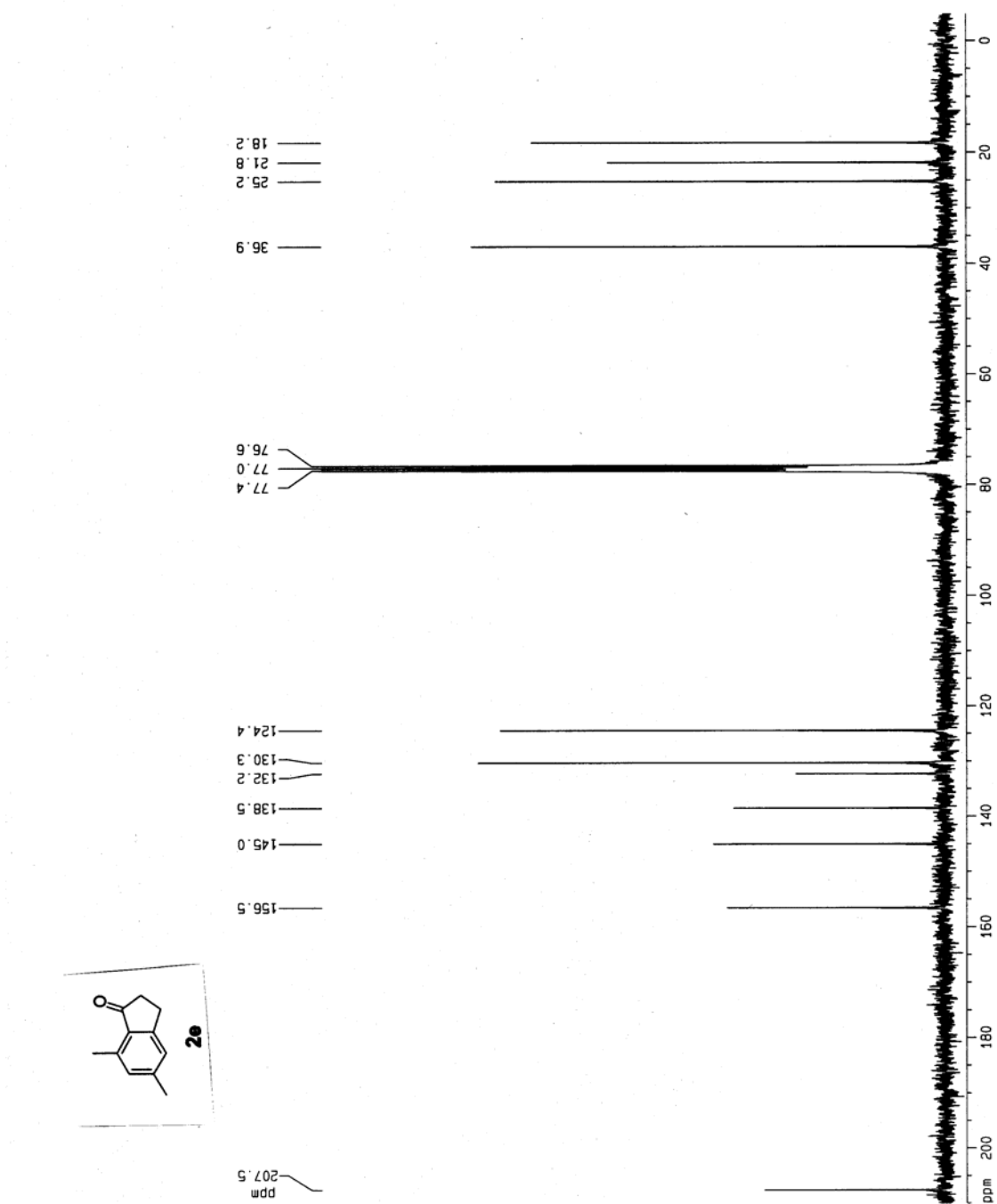


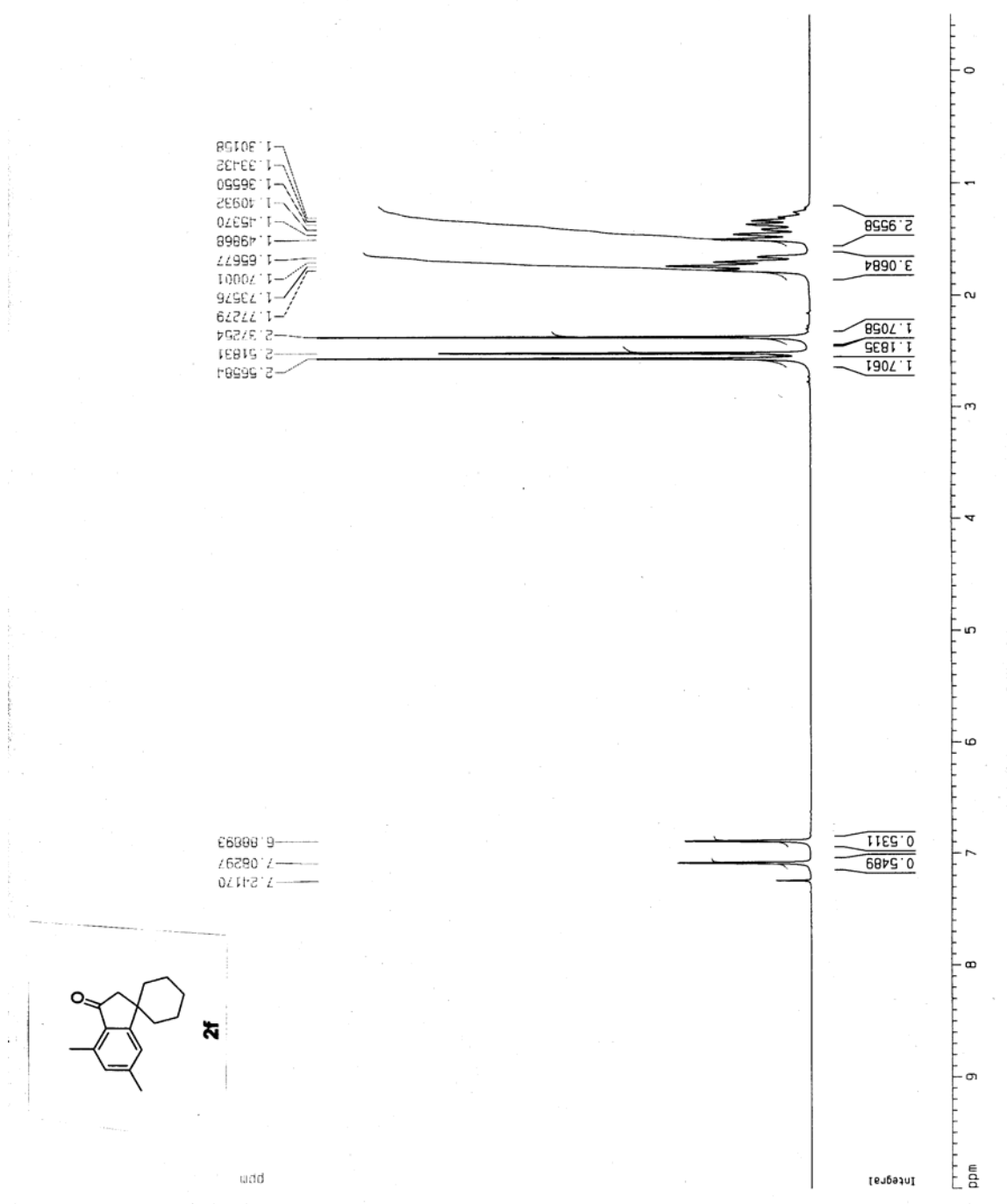


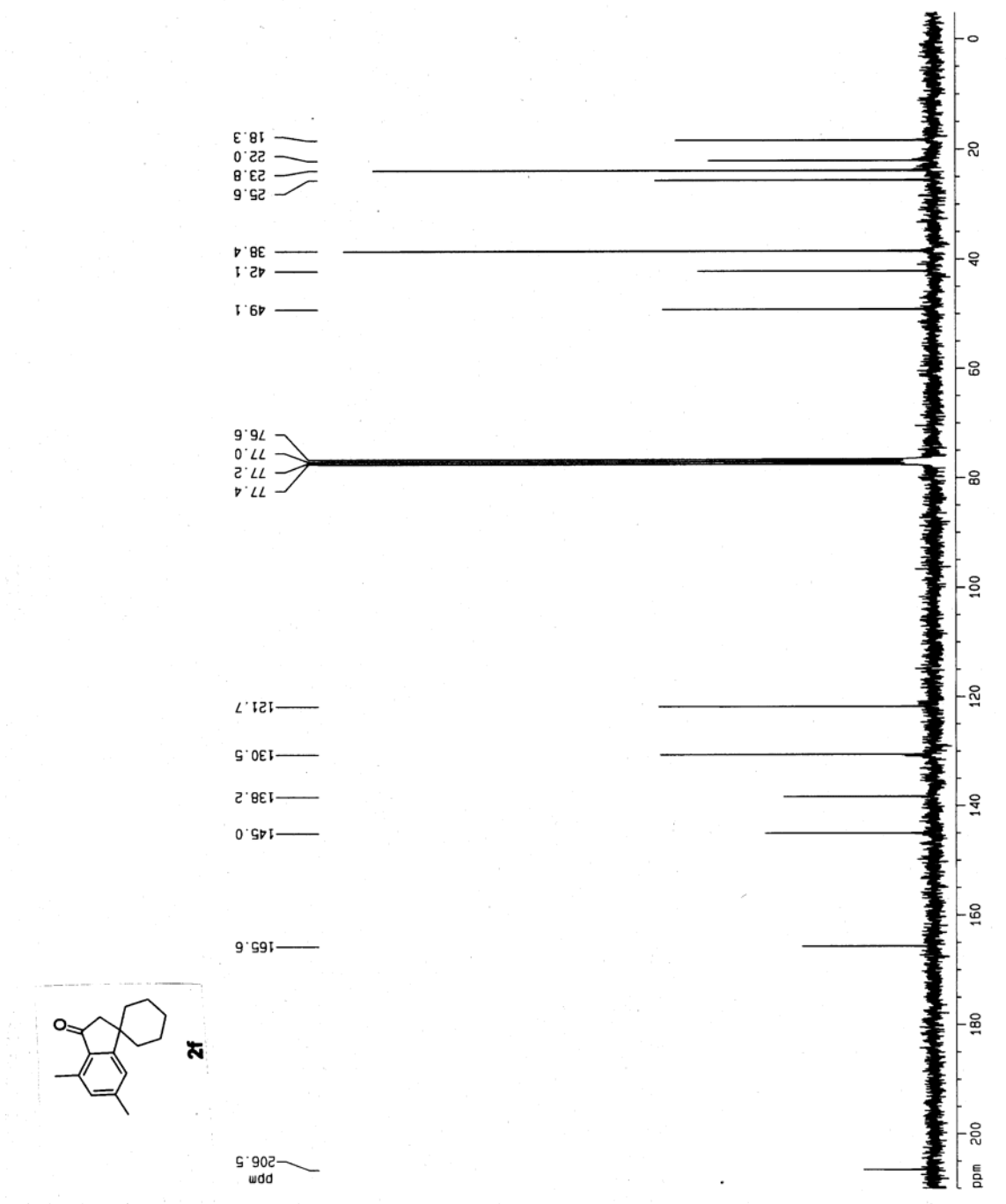


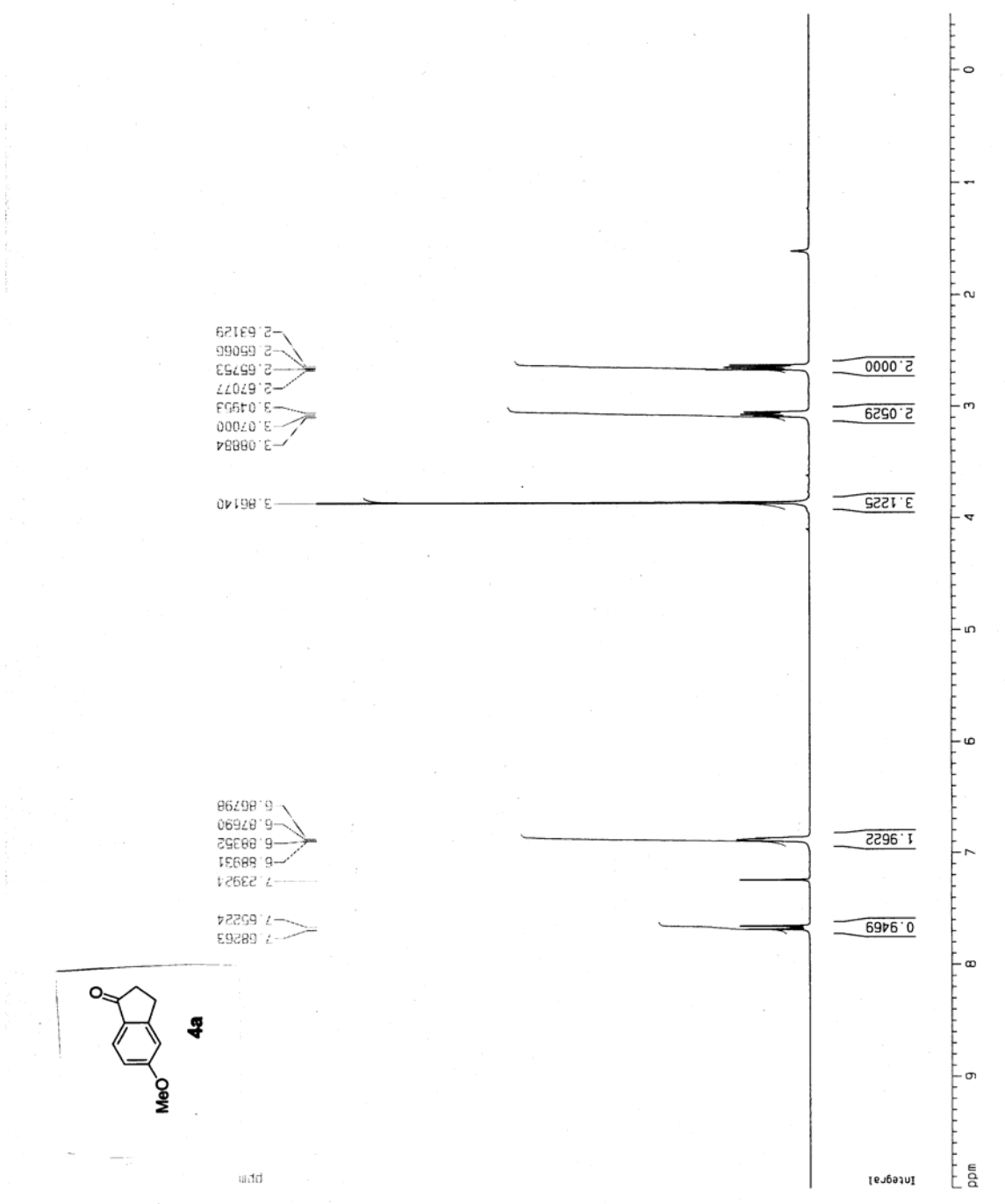


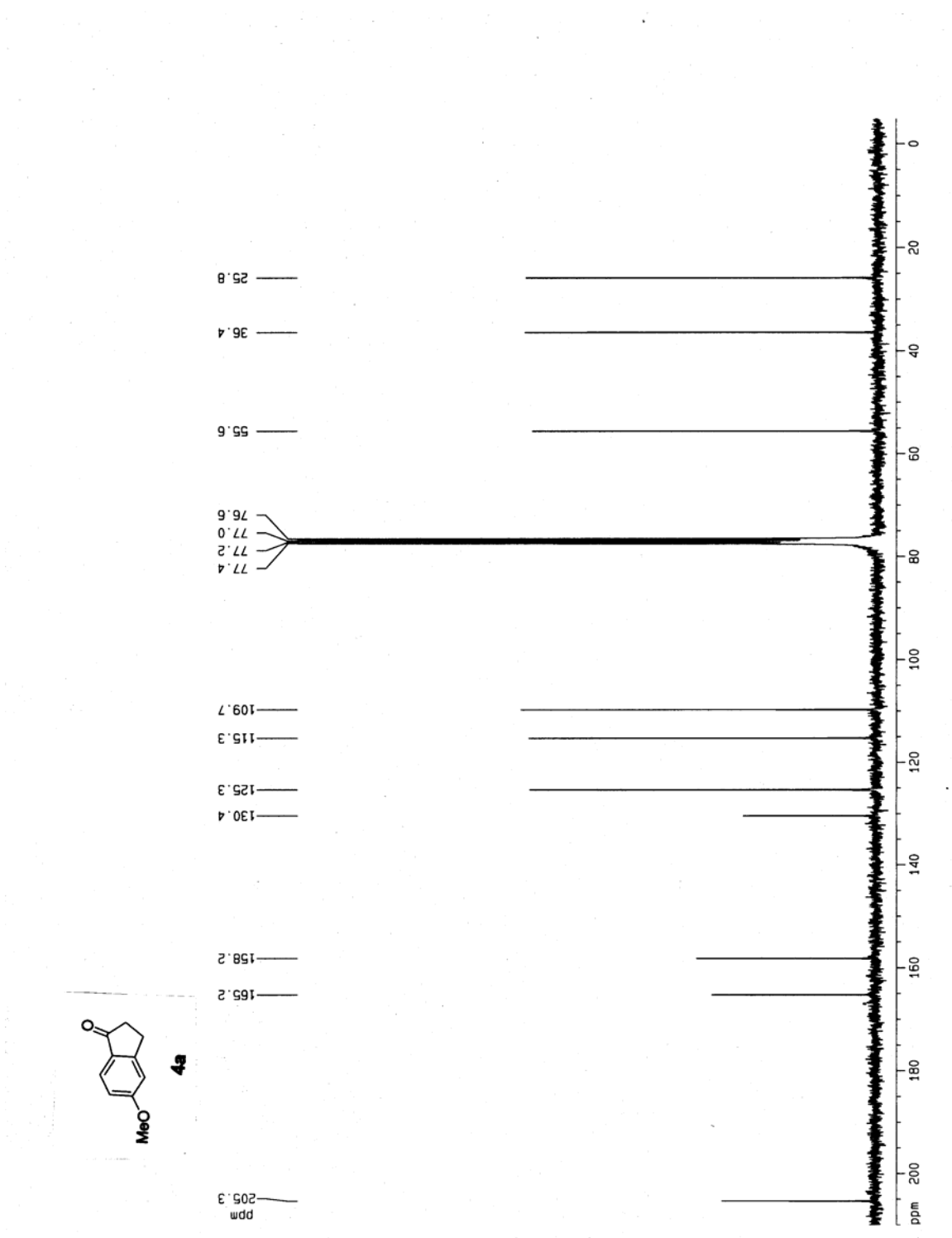


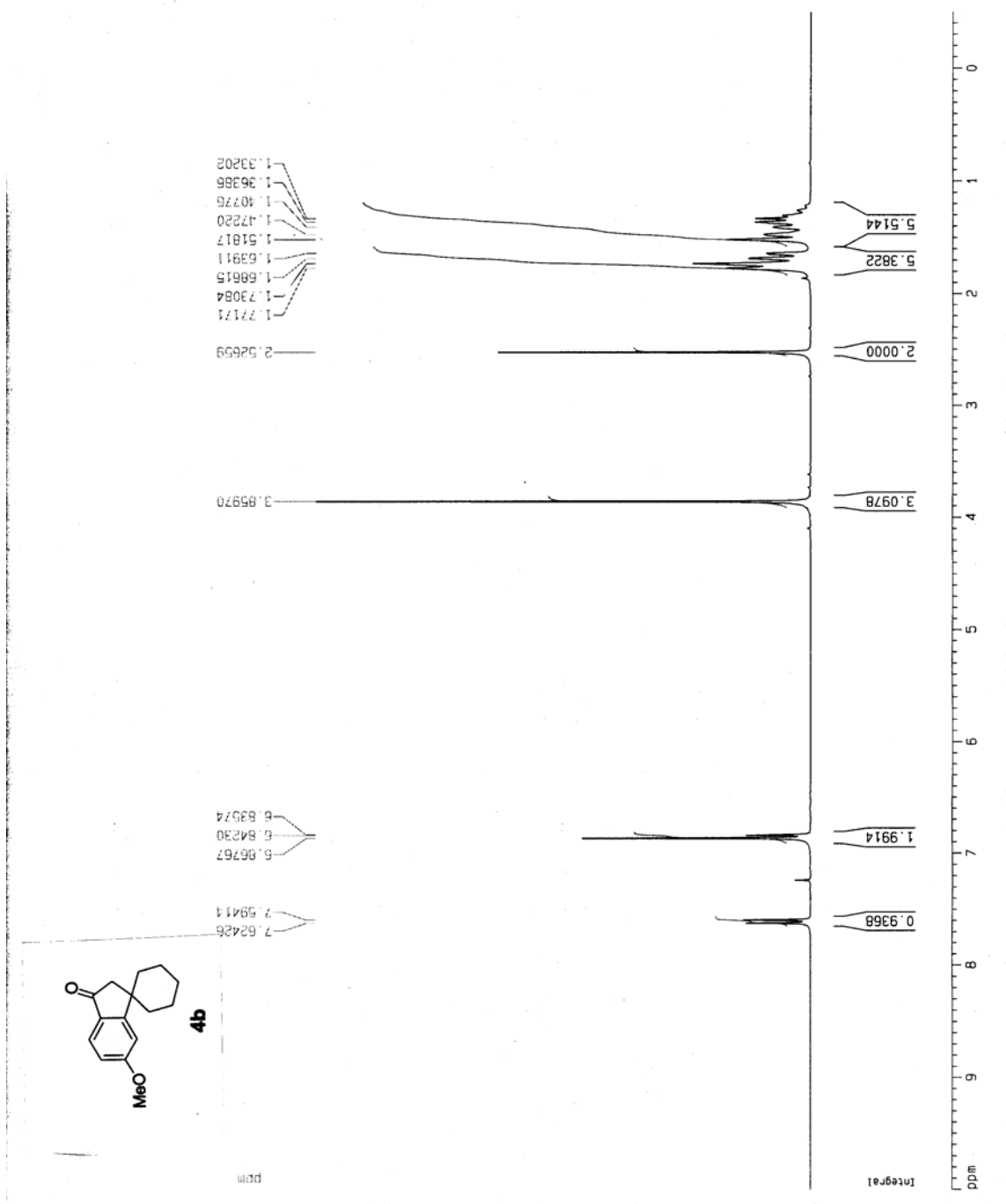


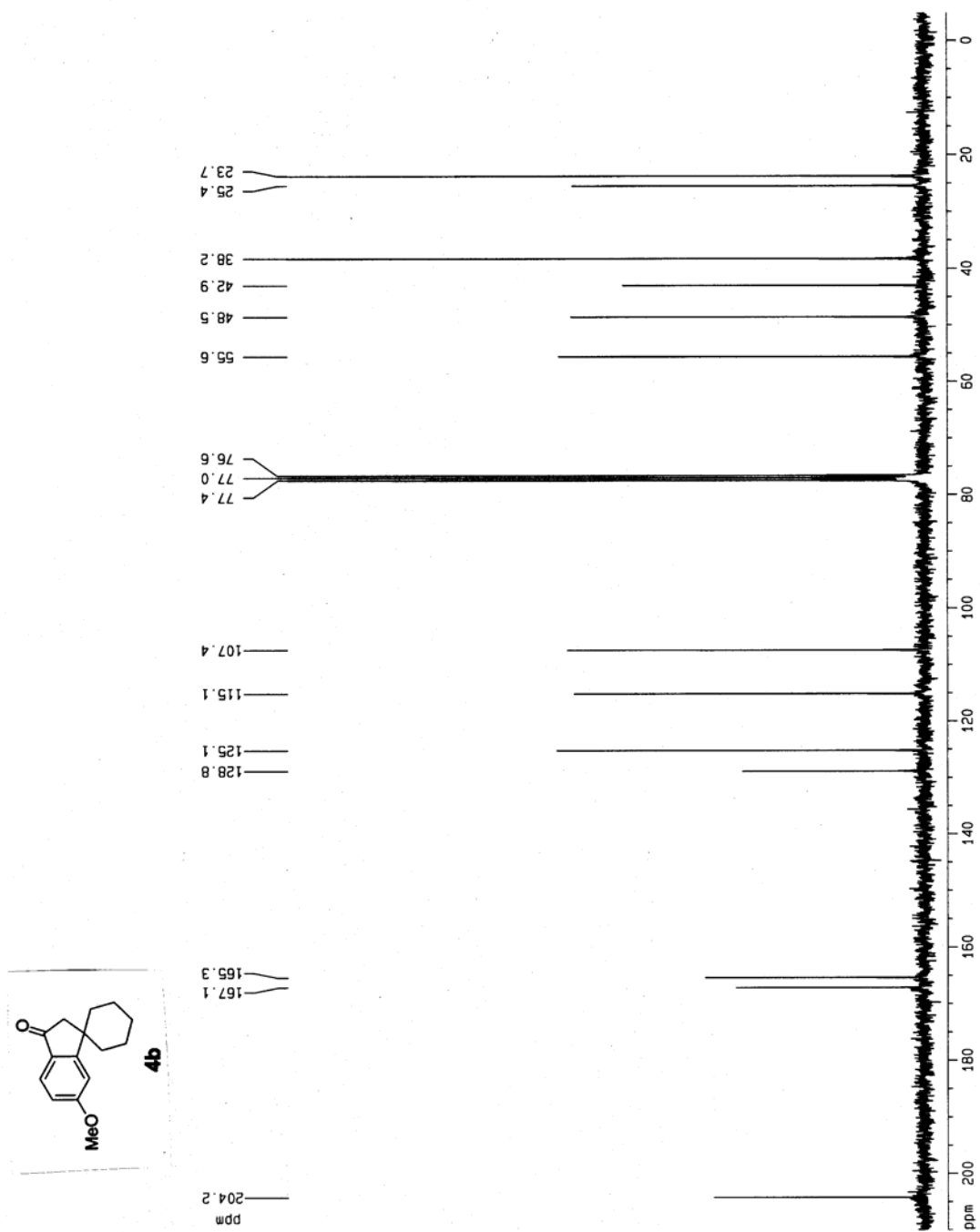


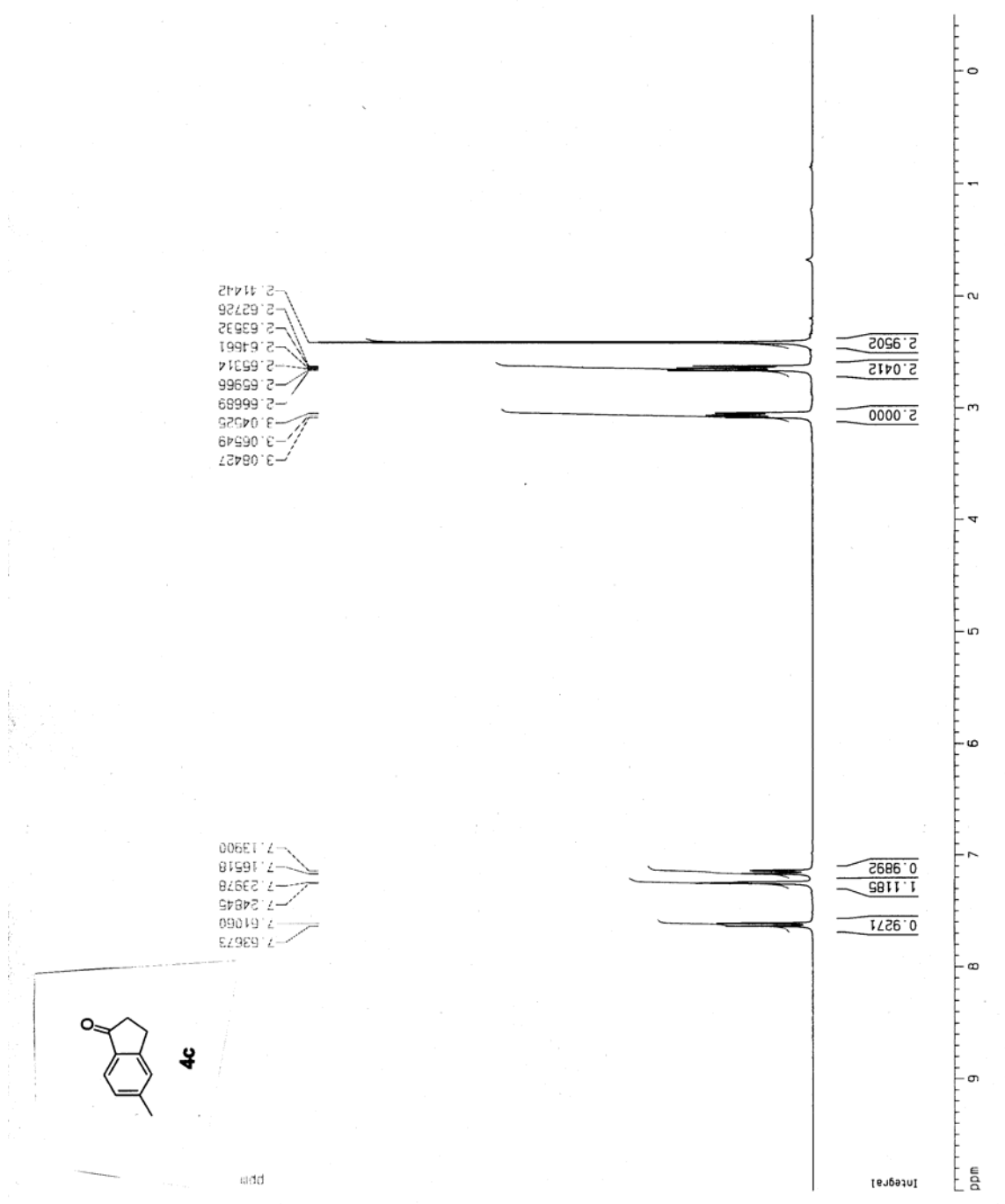


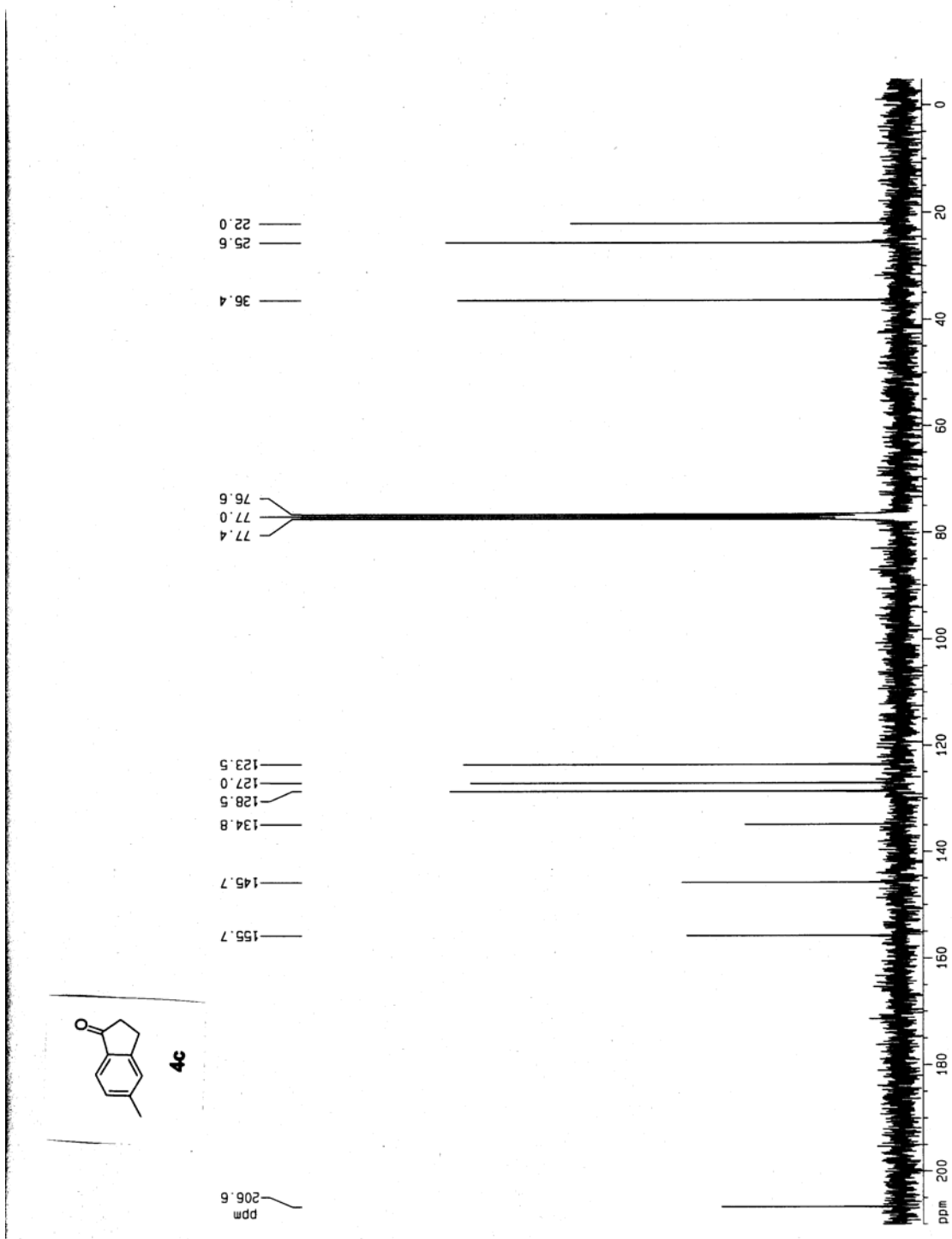


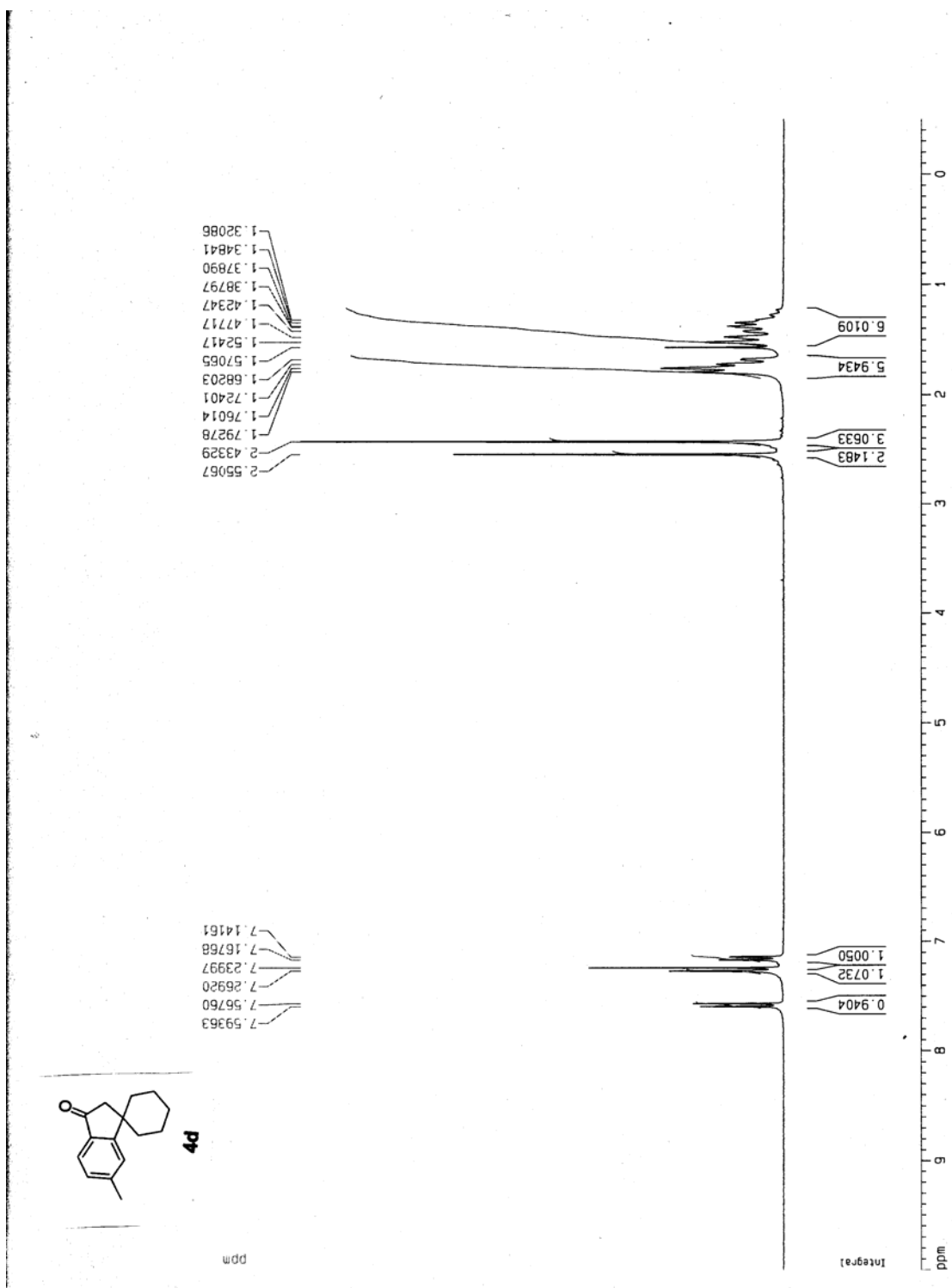


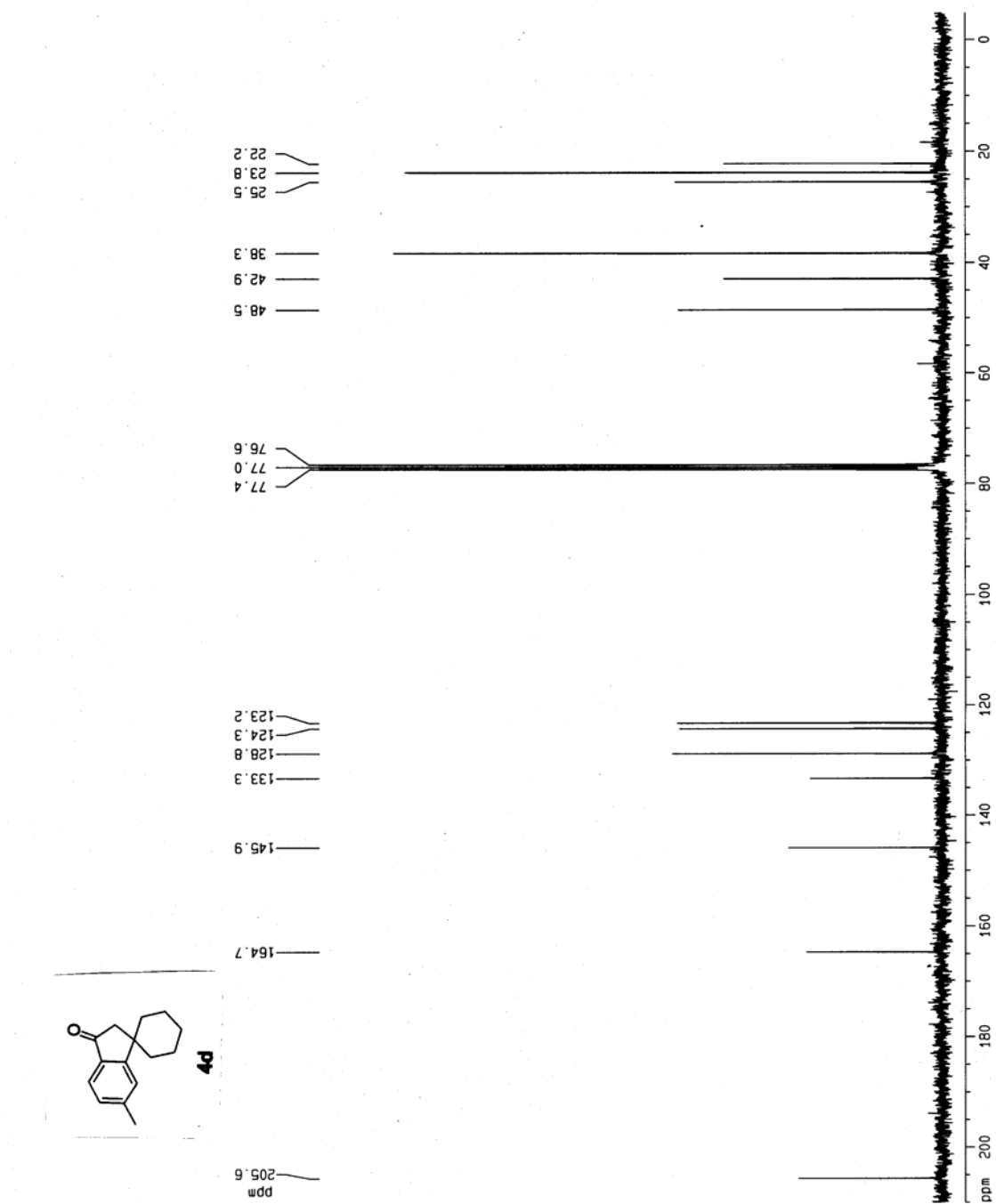


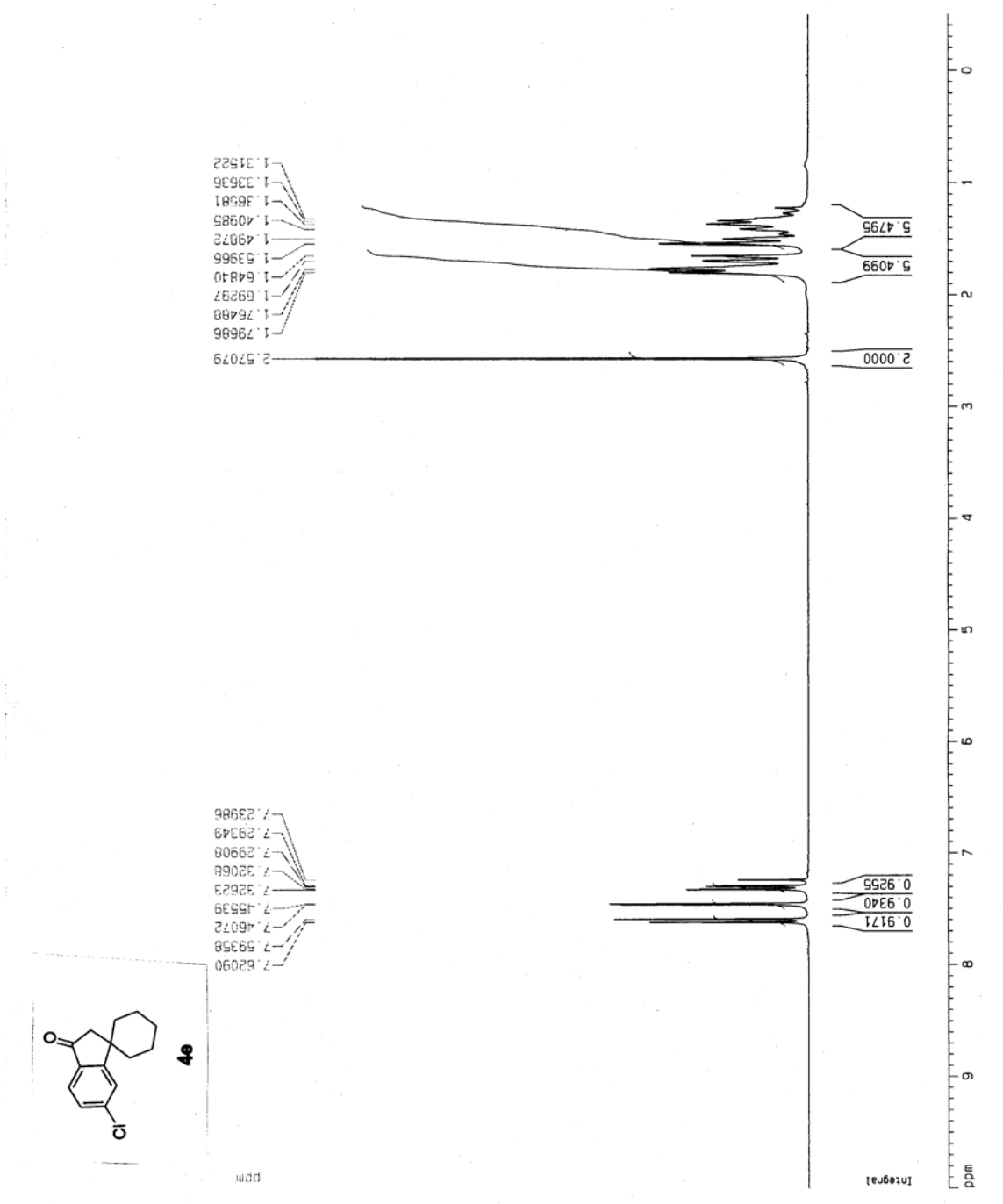


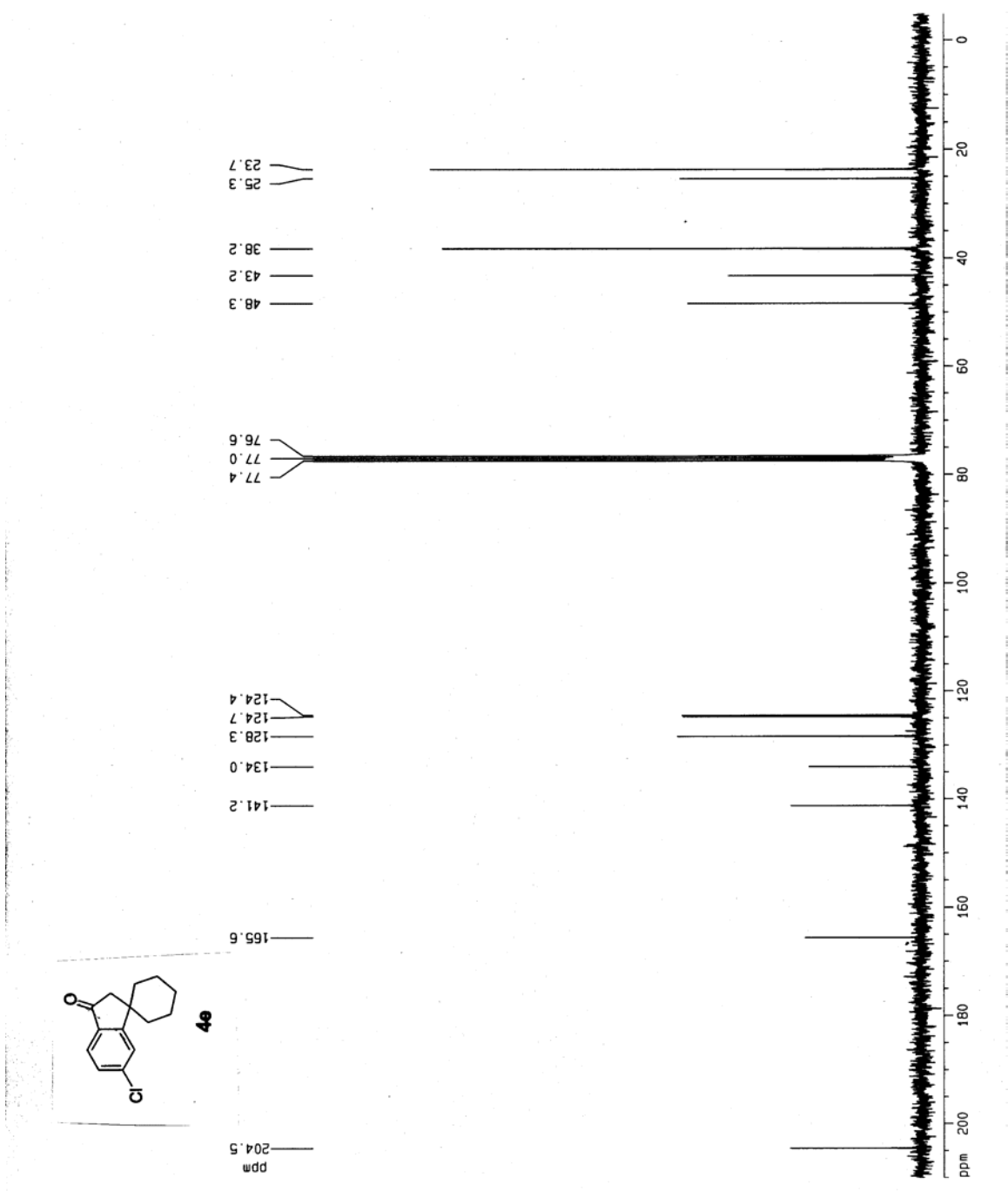


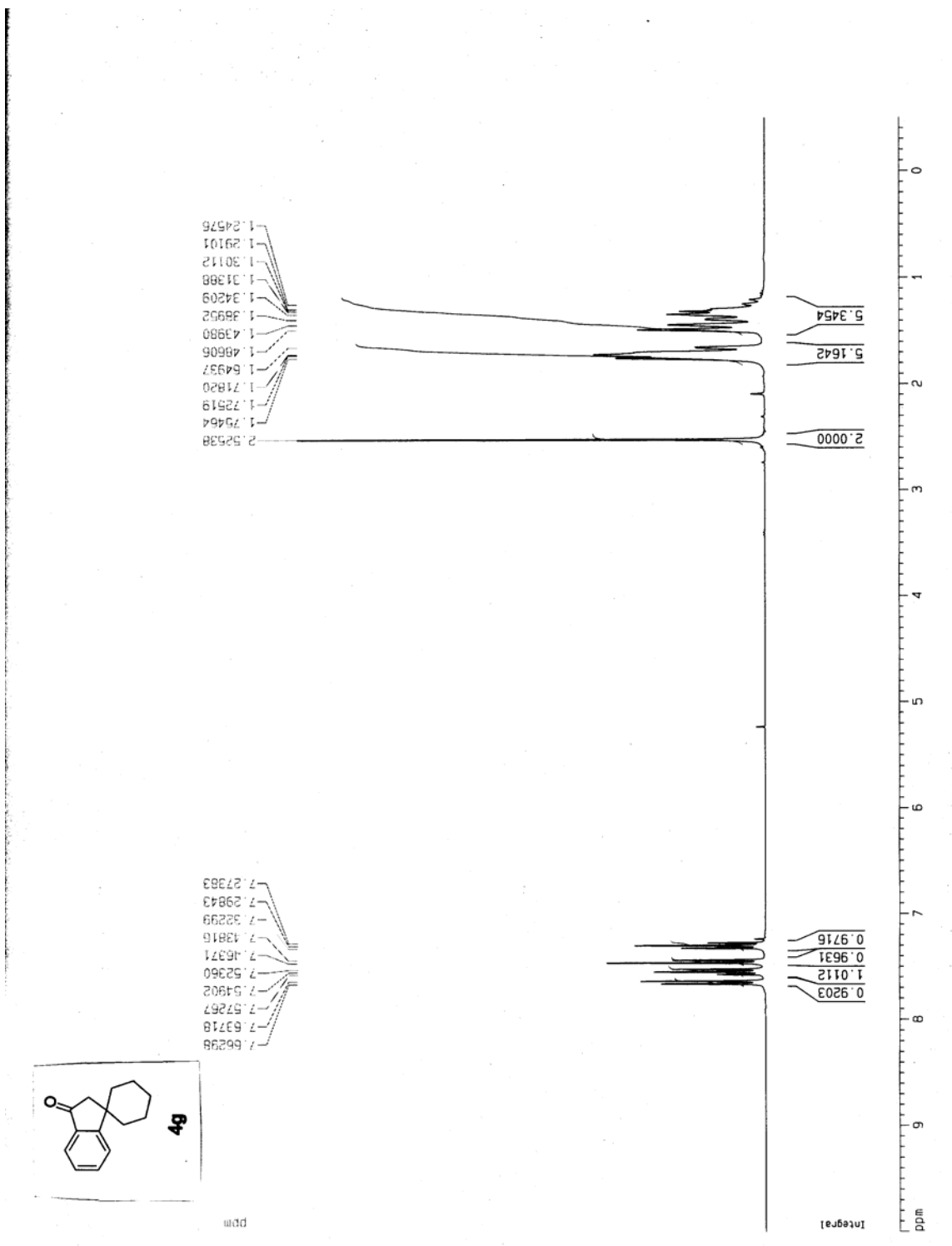


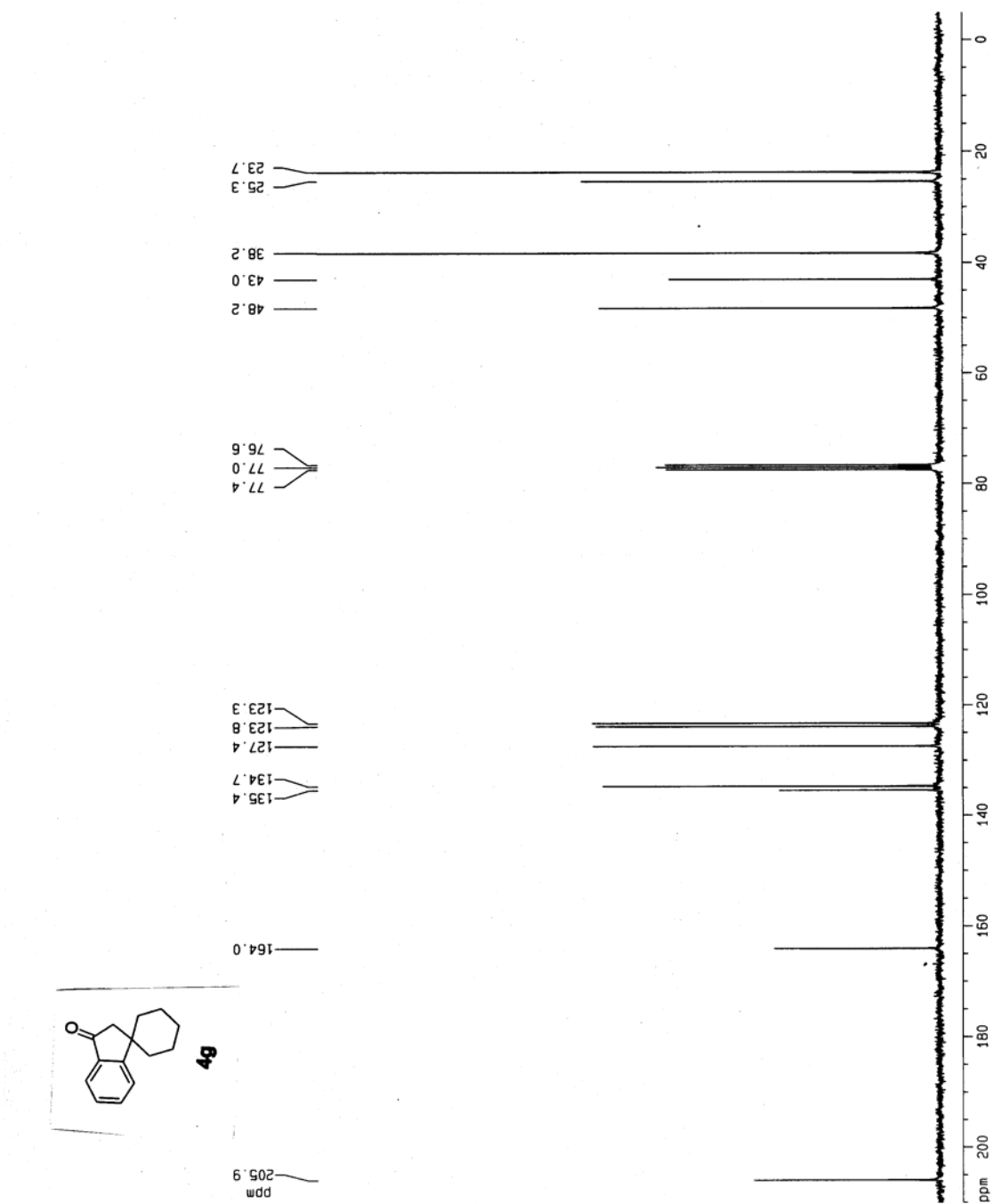


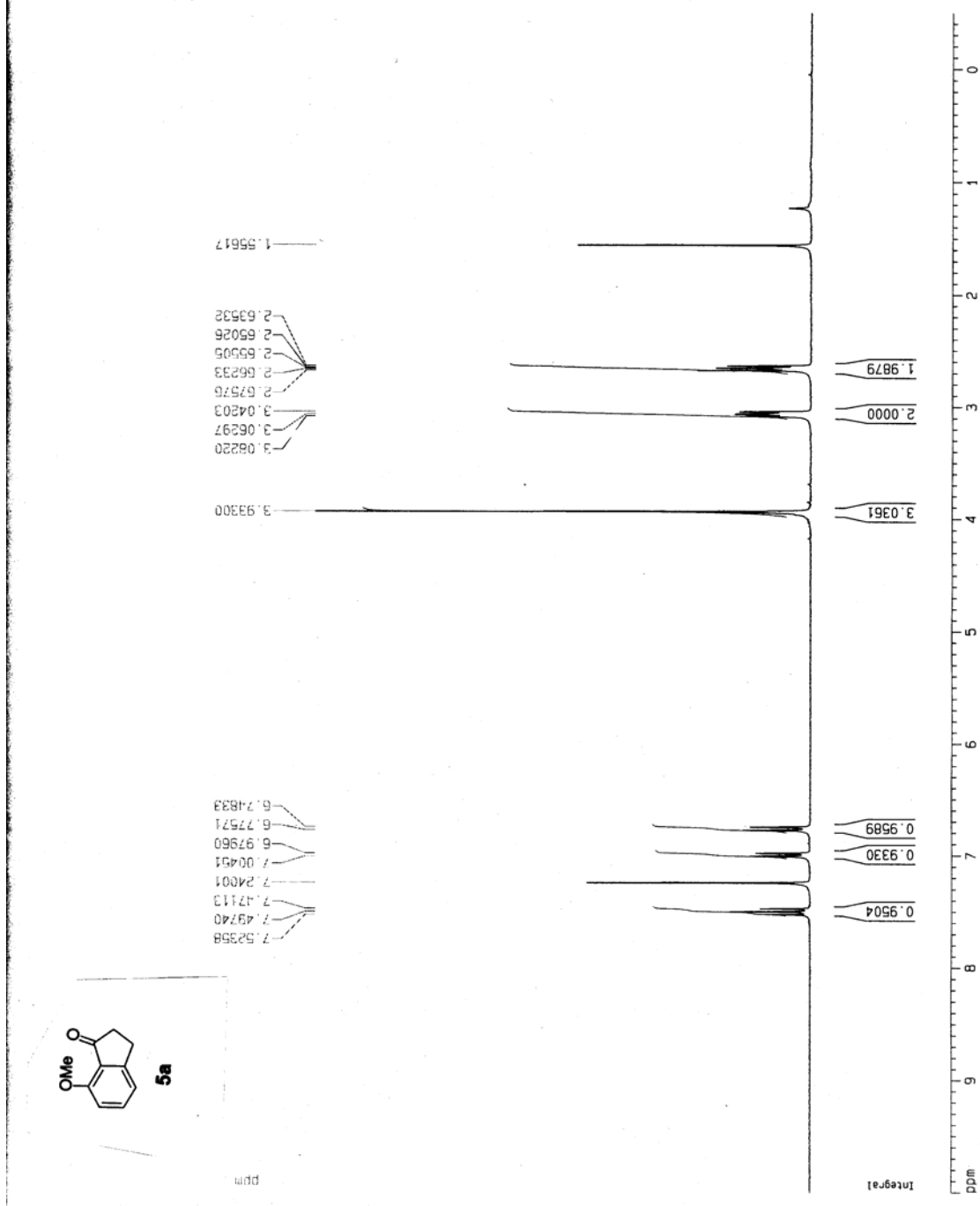


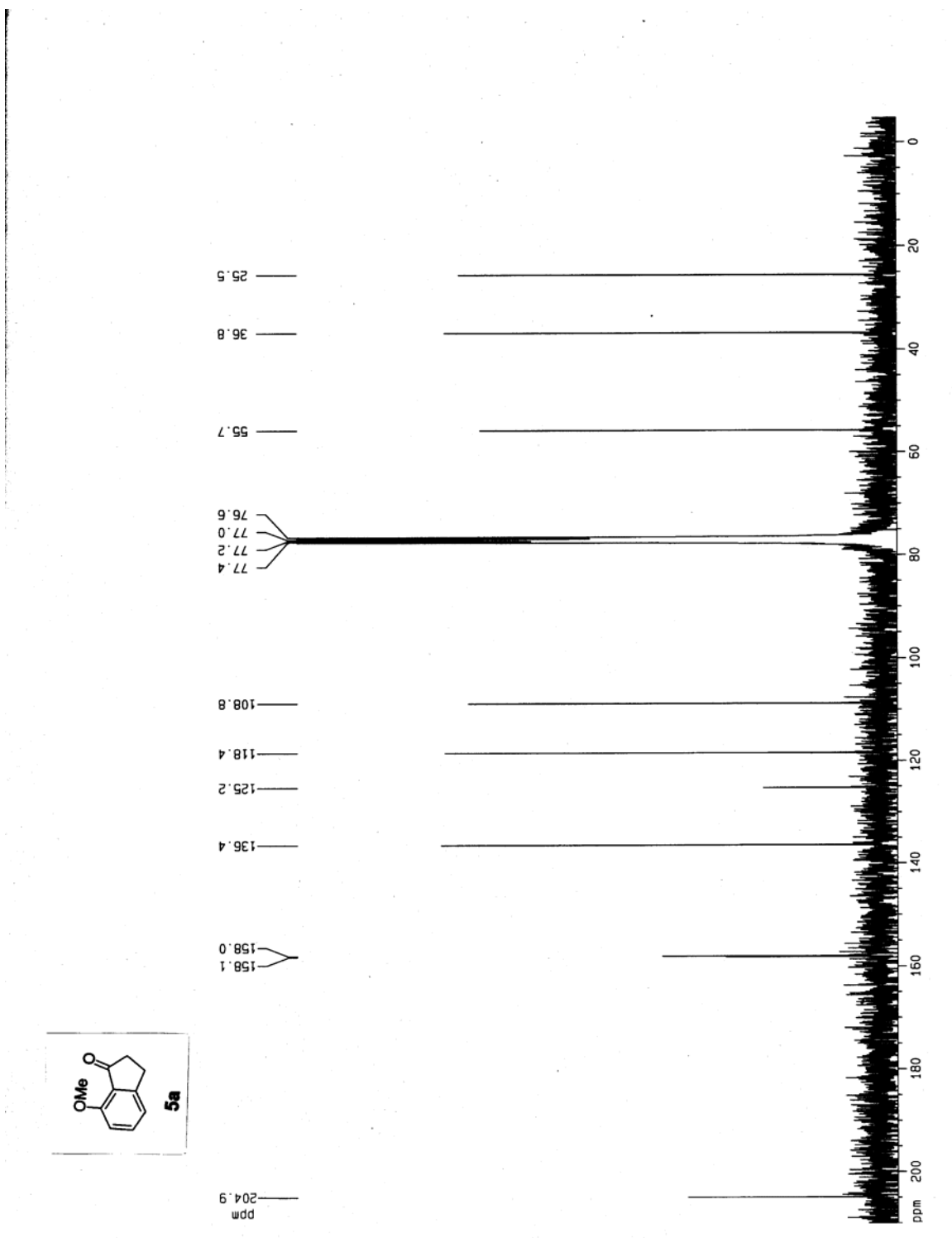


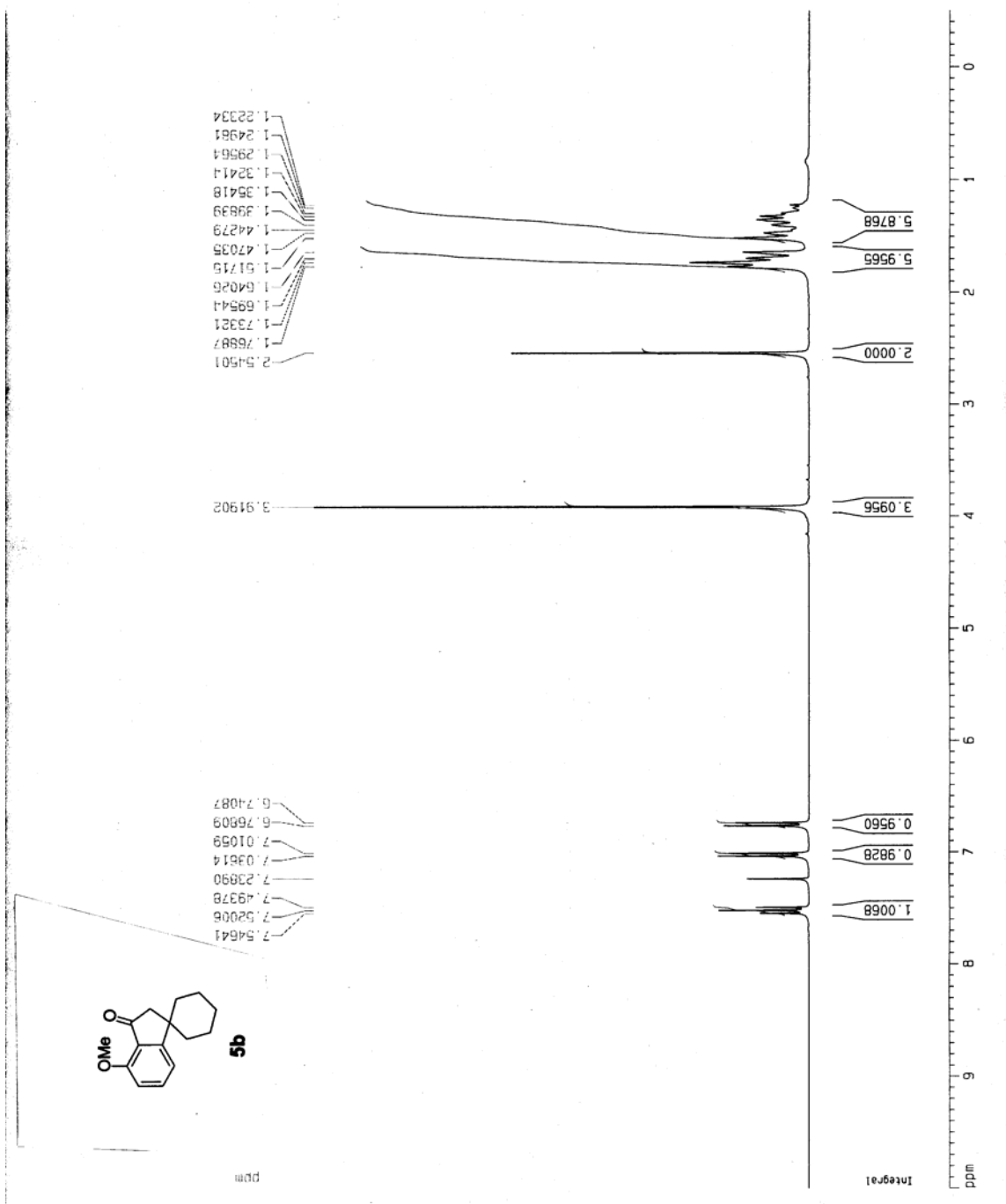


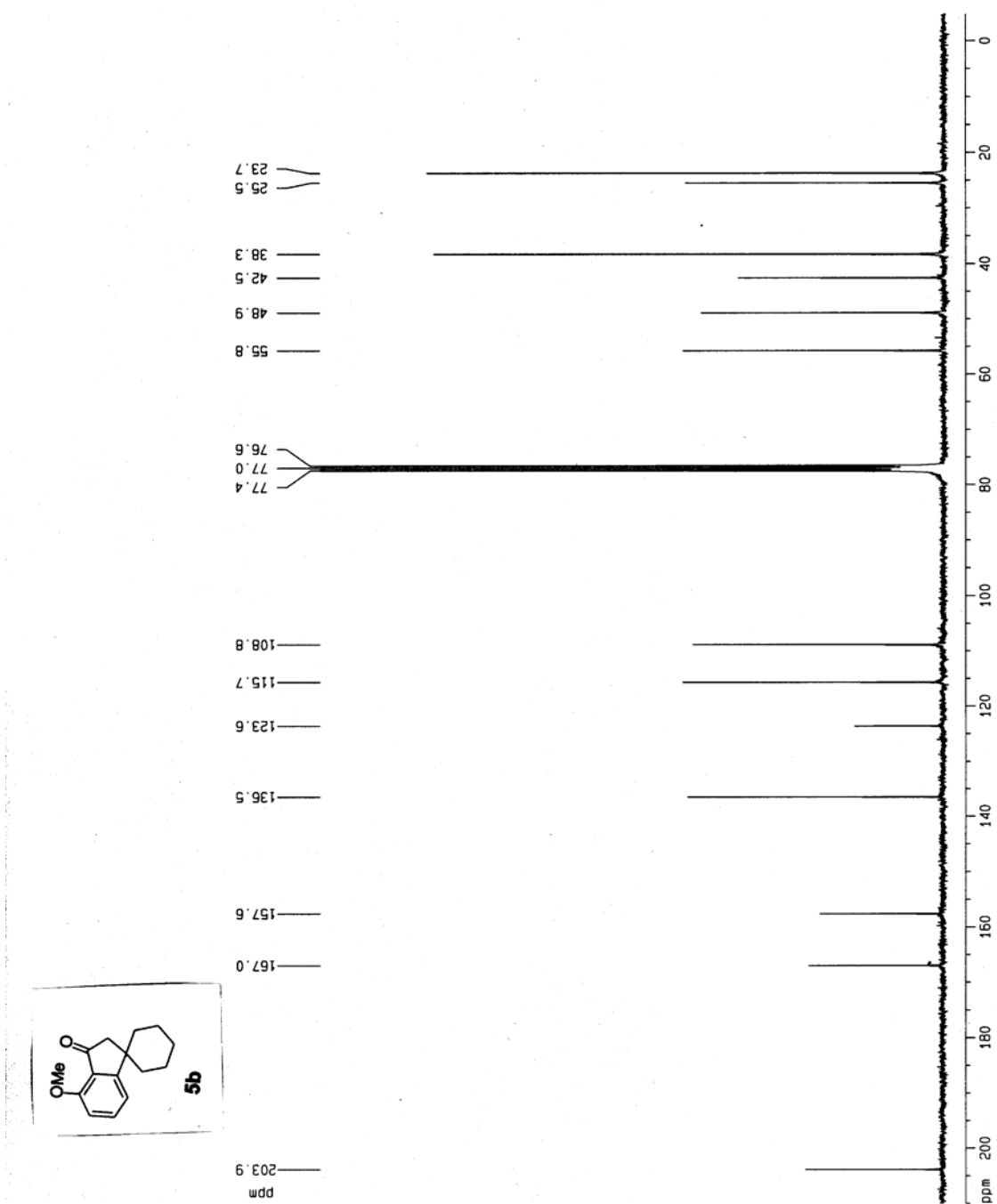


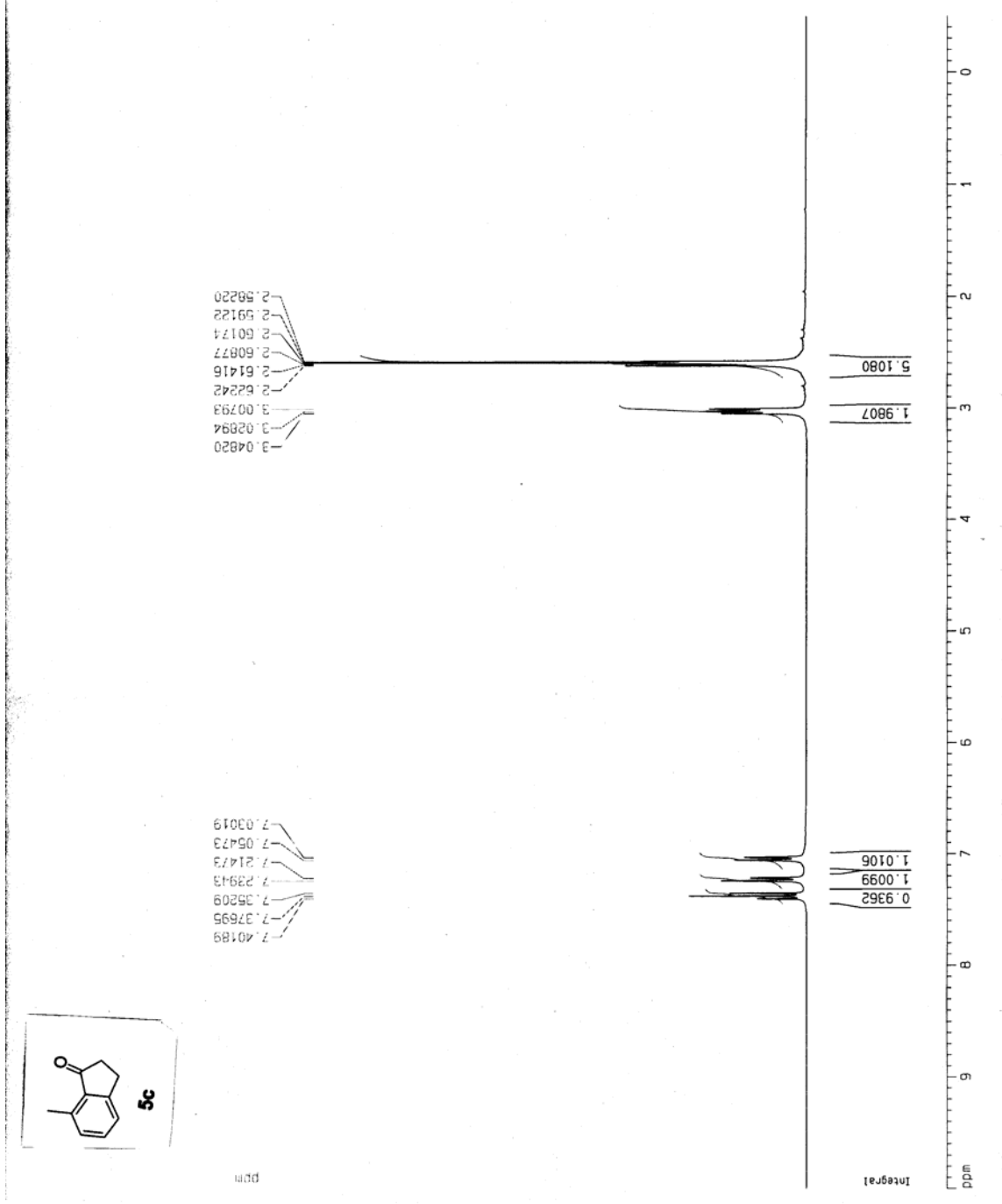


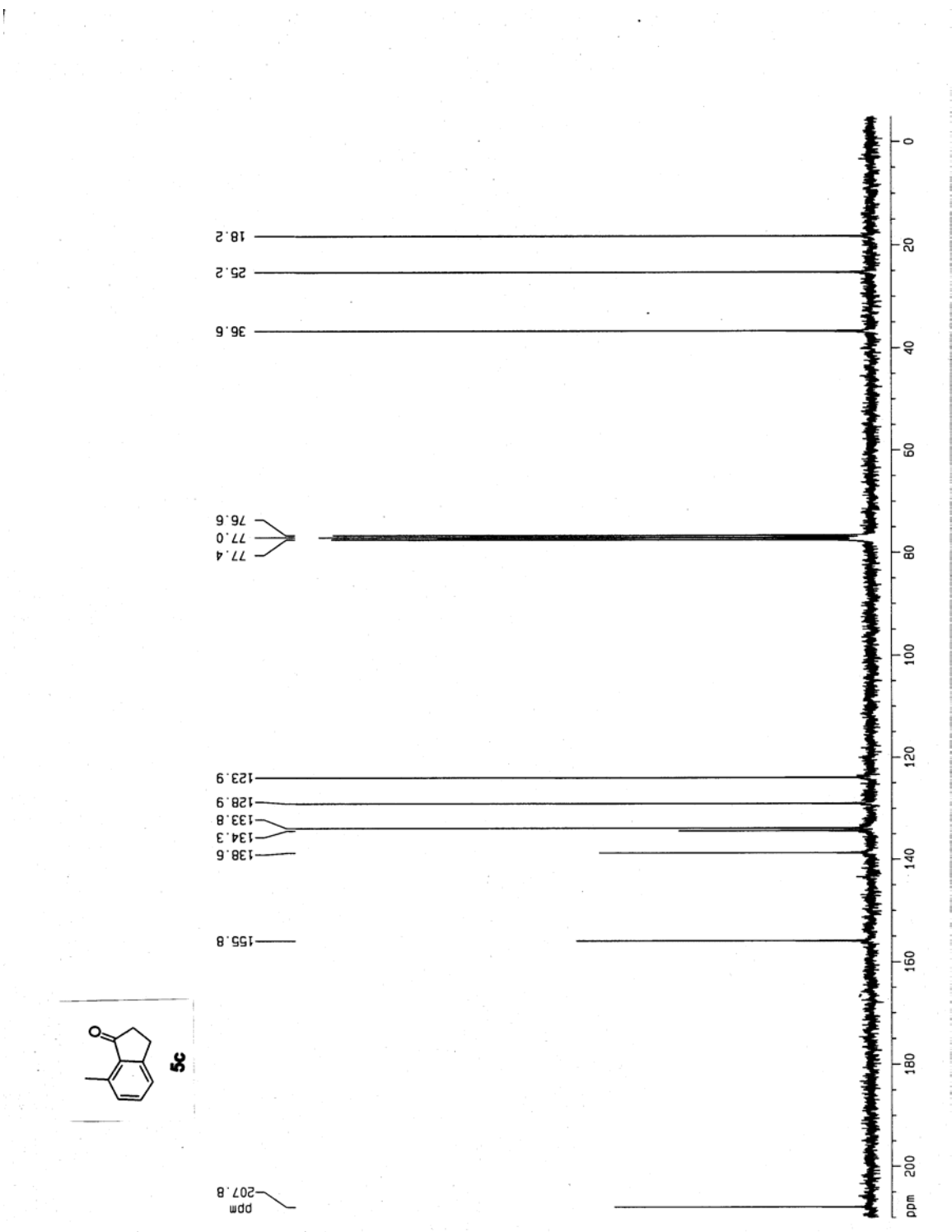


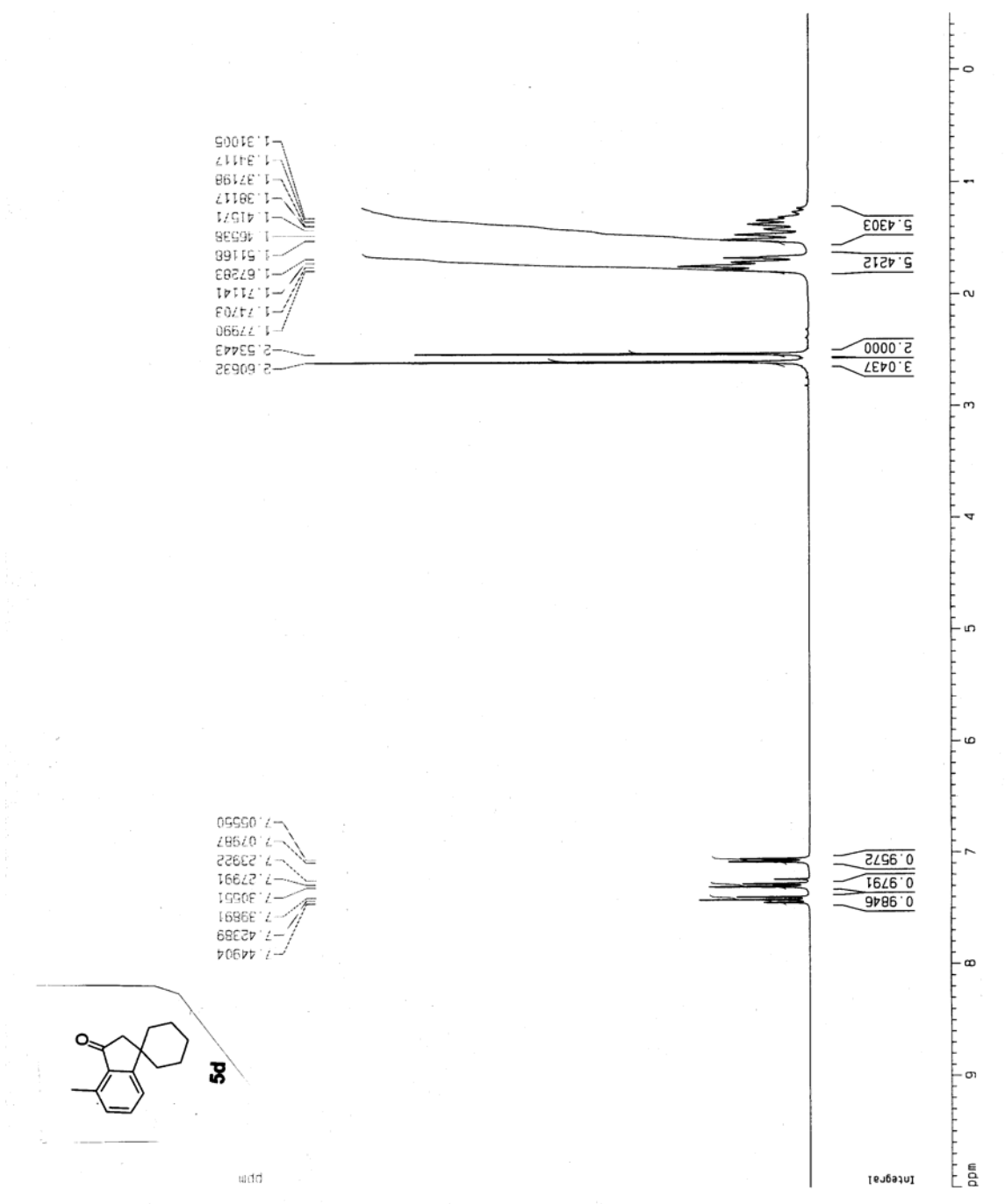


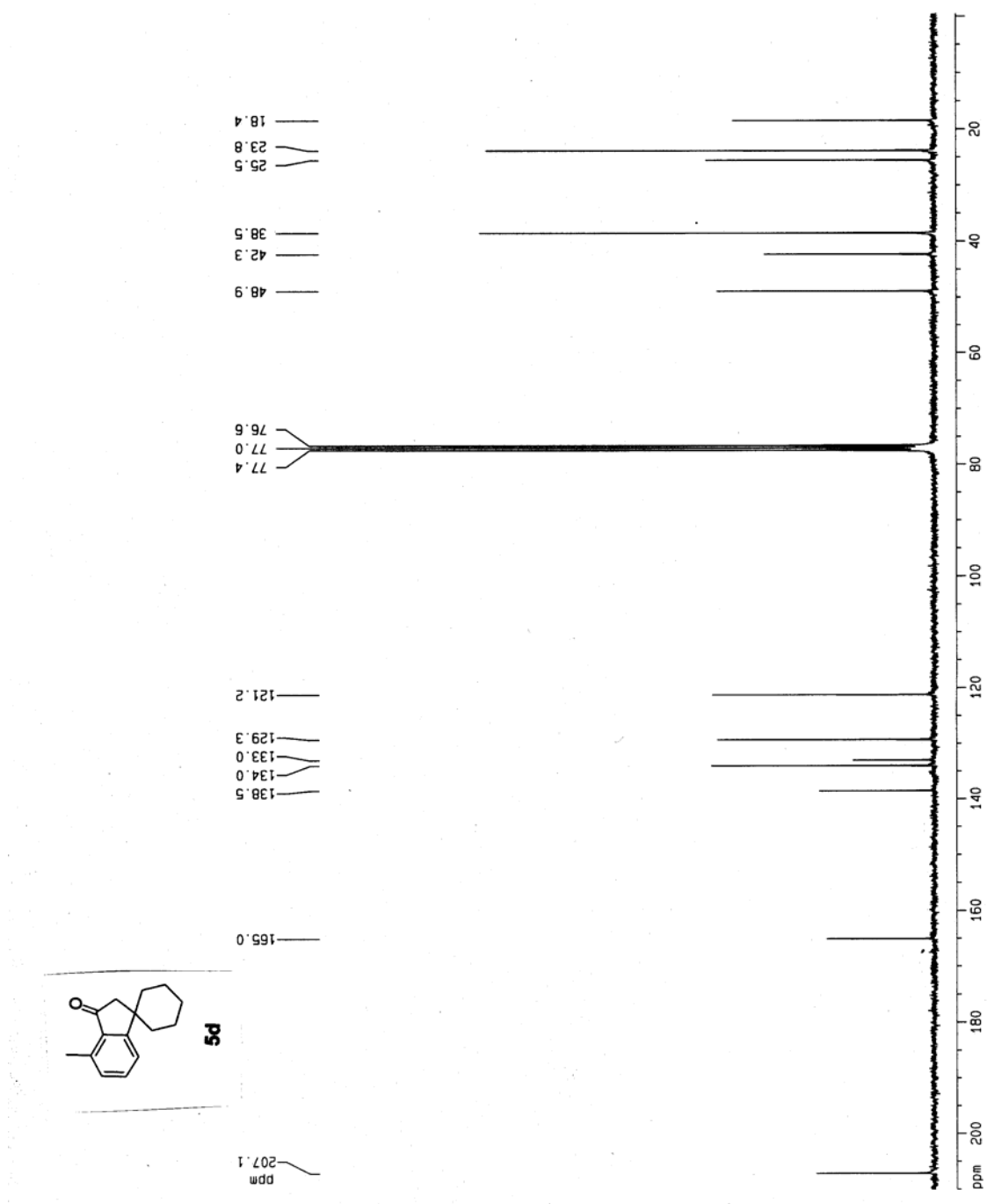












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