# Reversal of Regioselection in the Sharpless Asymmetric Aminohydroxylation of Aryl Ester Substrates

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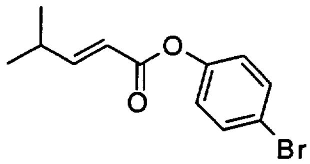
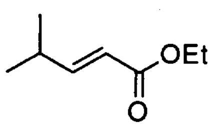
## Supporting Information

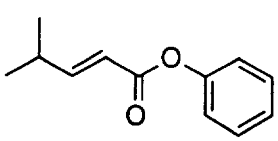
$^1$H NMR spectra were recorded on a 400 MHz spectrometer at ambient temperature. $^{13}$C NMR were recorded on a 75.5 Hz spectrometer at ambient temperature. Chemical shifts are reported in parts per million relative to chloroform ($^1$H, δ 7.24; $^{13}$C, δ 77.0), deuterium oxide ($^1$H, δ 4.76), methanol ($^1$H, δ 3.31; $^{13}$C, δ 49.15). All $^{13}$C NMR were recorded with complete proton decoupling. Infrared spectra were recorded on a FT-spectrophotometer. Optical rotations were recorded on a digital polarimeter at 589 nm. High resolution mass spectra were obtained in the Boston University Mass Spectrometry Laboratory. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F plates. Flash chromatography was performed as previously described.[1] When specified as "anhydrous", solvents were distilled and / or stored over 4 Å sieves prior to use. Yields refer to chromtographically pure materials, unless otherwise stated. Tetrahydrofuran was freshly distilled under argon from sodium / benzophenone ketyl. Dichloromethane ($CH_2Cl_2$) was distilled from calcium hydride prior to use. Isobutyraldehyde was freshly distilled from $CaSO_4$ prior to use. Benzyl carbamate was recrystallized from water, phenol was recrystallized from pet ether. All other reagents were purchased from Aldrich and used as received.



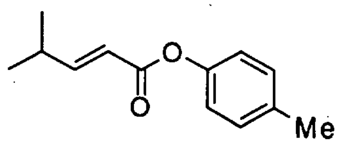
**General Procedure for Olefination Using (para-Bromophenyl)-diethyl-phosphonoacetate illustrated for: (para-Bromophenyl)-4-methyl-2-(*E*)-pentenoate (2d).** To a suspension of NaH (0.31 g, 7.62 mmol, 1.1 equiv) in THF (30 mL, 0.25 **M**) at 0 °C was added dropwise a solution of *p*-(bromophenyl)-diethylphosphonoacetate[2] (2.8 g, 7.62 mmol, 1.1 equiv) in dry THF (8 mL, 1**M**). The mixture was stirred for 10 minutes at 0 °C then warmed to ambient temperature for 10 minutes. To this yellow solution was added isobutyraldehyde (0.63 mL, 6.93 mmol) and the solution stirred for 1 hour at ambient temperature. The reaction mixture was subsequently diluted with $NH_4Cl$ (30 mL), extracted with EtOAc (3 x 20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification on $SiO_2$ (5% EtOAc/PE) afforded **2d** as a white solid (1.3 g, 70%): $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.47 (d, 2H, J = 9.2 Hz), 7.14 (dd, 1H, $J_1$ = 22.4 Hz, $J_2$ = 6.8 Hz), 6.99 (d, 2H, J = 9.2 Hz), 5.93 (dd, 1H, $J_1$ = 17.2 Hz, $J_2$ = 1.2 Hz), 2.53-2.51 (m, 1H), 1.10 (d, 6H, J = 6.4 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 165.0, 158.3, 149.8, 132.4, 123.4, 118.7, 117.6, 31.2, 21.1; IR (neat) $\nu_{max}$ 3449, 2967, 2119, 1740, 1653; CIHRMS M+H$^+$ (calculated for $C_{12}H_{14}BrO_2$): 269.0178, found: 269.0162.



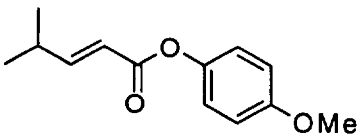
**Ethyl-4-methyl-2-(*E*)-pentenoate (1):** $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.92 (dd, 1H, $J_1$ = 6.4 Hz, $J_2$ = 6.8 Hz); 5.74 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 15.6 Hz); 4.16 (q, 2H, J = 6.8 Hz); 2.45-2.43 (m, 1H); 1.27 (t, 3H, J = 6.8 Hz); 1.04 (d, 6H, J = 6.8 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 166.9, 155.2, 118.7, 60.0, 30.9, 21.2, 14.2.



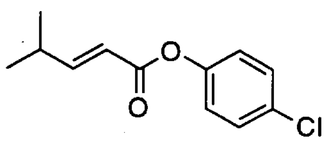
**(Phenyl)-4-methyl-2-(*E*)-pentenoate (2a):** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.37 (t, 2H, J = 7.6 Hz); 7.23-7.16 (m, 1H); 7.11 (t, 2H, J = 8 Hz); 5.96 (dd, 1H, $J_1$ = 1.2 Hz, $J_2$ = 15.6 Hz); 2.54-2.52 (m, 1H); 1.11 (d, 6H, J = 7.2 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 165.2, 157.5, 129.3, 125.6, 121.6, 118.1, 35.0, 31.2, 21.2.



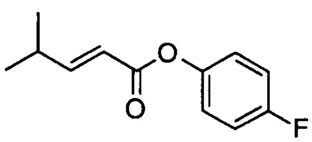
**(para-Cresol)-4-methyl-2-(*E*)-pentenoate (2b):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, 2H, J = 8.4 Hz); 7.12 (dd, 1H, $J_1$ = 6.4 Hz, $J_2$ = 6.8 Hz); 6.97 (d, 2H, J = 8.8 Hz); 5.95 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 15.6 Hz); 2.55-2.50 (m, 1H); 2.33 (s, 3H); 1.10 (d, 6H, J = 6.8 Hz); $^{13}$C (75.5 MHz, $CDCl_3$) δ 165.5, 157.4, 135.2, 129.9, 121.3, 118.2, 55.8, 35.0, 31.2, 21.2.



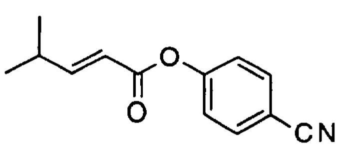
**(para-Methoxyphenyl)-4-methyl-2-(*E*)-pentenoate (2c):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.12 (dd, 1H, $J_1$ = 6.8 Hz, $J_2$ = 6.4 Hz); 7.01 (d, 2H, J = 9.2 Hz); 6.87 (d, 2H, J = 9.2 Hz); 5.94 (dd, 1H, $J_1$ = 1.2 Hz, $J_2$ = 15.6 Hz); 3.78 (s, 3H); 254-2.49 (m, 1H); 1.10 (d, 6H, J = 6.8 Hz); $^{13}$C (75.5 MHz, $CDCl_3$) δ 165.6, 157.4, 144.2, 122.4, 118.2, 114.5, 55.6, 35.0, 31.2, 24.7.



**(para-Chlorophenyl)-4-methyl-2-(*E*)-pentenoate (2e):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, 2H, J = 8.8 Hz); 7.14 (dd, 1H, $J_1$ = 6.4 Hz, $J_2$ = 6.4 Hz); 7.05 (d, 2H, J = 8.8 Hz); 5.94 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 16 Hz); 2.56-2.50 (m, 1H); 1.10 (d, 6H, J = 6.4 Hz); $^{13}$C (75.5 MHz, $CDCl_3$) δ 165.0, 158.2, 149.4, 131.0, 129.4, 123.0, 117.8, 31.2, 29.7, 21.2.

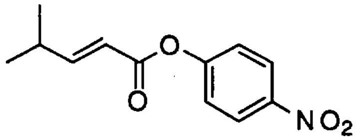


**(para-Fluorophenyl)-4-methyl-2-(*E*)-pentenoate (2f):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, 1H, $J_1$ = 6.8 Hz, $J_2$ = 6.4 Hz); 7.22 (d, 4H, J = 2 Hz); 6.12 (dd, 1H, $J_1$ = 1.2 Hz, $J_2$ = 17.2 Hz); 2.72-2.70 (m, 1H); 1.29 (d, 6H, J = 6.8 Hz); $^{13}$C (75.5 MHz, $CDCl_3$) δ 158.1, 123.0, 117.7, 116.2, 115.8, 34.9, 31.2, 24.7, 21.1.

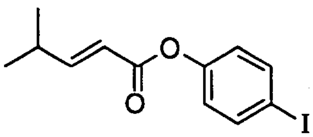


**(para-Cyanophenyl)-4-methyl-2-(*E*)-pentenoate (2g):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, 2H, J = 8.4 Hz); 7.15 (dd, 1H, $J_1$ = 7.2 Hz, $J_2$ = 16 Hz); 5.93 (dd, 1H, $J_1$ = 2 Hz, $J_2$ = 16 Hz);

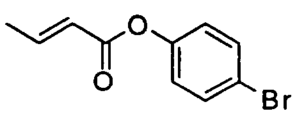
2.54-2.52 (m, 1H); 1.10 (d, 6H, J = 6.8 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 164.2, 159.1, 154.3, 133.6, 122.7, 117.4, 109.6, 31.3, 21.1.



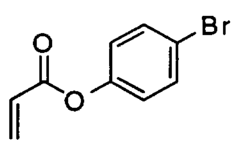

**(para-Nitrophenyl)-4-methyl-2-(*E*)-pentenoate (2h):** $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.25 (d, 2H, J = 8.8 Hz); 7.29 (d, 2H, J = 9.2 Hz); 7.19 (dd, 1H, $J_1$ = 6.4 Hz, $J_2$ = 6.4 Hz); 5.95 (dd, 1H, $J_1$ = 1.2 Hz, $J_2$ = 15.6 Hz); 2.58-2.52 (m, 1H); 1.11 (d, 6H, J = 6.8 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 164.1, 159.3, 155.7, 145.3, 125.1, 122.4, 117.3, 31.3, 21.1.



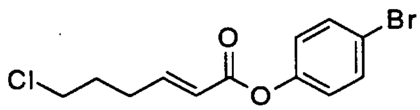

**(para-Iodophenyl)-4-methyl-2-(*E*)-pentenoate (2i):** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2H, J = 8.8 Hz); 7.13 (dd, 1H, $J_1$ = 6.8 Hz, $J_2$ = 6.0 Hz); 6.87 (d, 2H, J = 8.8 Hz); 5.93 (dd, 1H, $J_1$ = 1.2 Hz, $J_2$ = 15.6 Hz); 2.55-2.50 (m, 1H); 1.11 (d, 6H, J = 6.8 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 164.8, 158.2, 138.4, 123.8, 117.8, 35.0, 31.2, 24.7, 21.1.



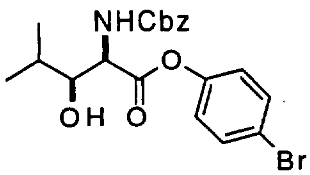

**(para-Bromophenyl)-2-(*E*)-butenoate (4a):** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.47 (d, 2H, J = 8.4 Hz); 7.20-7.14 (m, 1H); 6.99 (d, 2H, J = 8.8 Hz); 6.01 (dd, 1H, $J_1$ = 1.2 Hz, $J_2$ = 15.2 Hz); 1.95 (dd, 3H, $J_1$ = 1.2 Hz, $J_2$ = 7.2 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 164.5, 149.7, 147.5, 132.4, 123.4, 121.7, 118.7, 18.3.



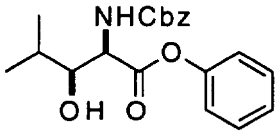

**(para-Bromophenyl)-2-propenoate (4b):** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.49 (d, 2H, J = 8.4 Hz); 7.01 (d, 2H, J = 8.8 Hz); 6.59 (dd, 1H, $J_1$ = 1.2 Hz, $J_2$ = 17.6 Hz); 6.29 (dd, 1H, $J_1$ = 10.4 Hz, $J_2$ = 10.4 Hz); 6.02 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 130.4 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 164.1, 149.7, 132.8, 132.5, 127.7, 123.3, 119.0.



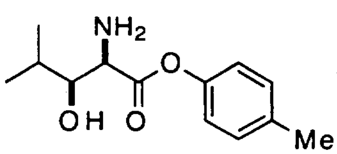
**(para-Bromophenyl)-6-chloro-2-(*E*)-hexenoate (4c):** $^1$H NMR (400 MHz, CDCl3) δ 7.48 (d, 2H, J = 8.8 Hz); 7.16-7.01 (m, 1H); 6.99 (d, 2H, J = 9.6 Hz); 6.05 (d, 1H, J = 15.6 Hz); 3.57 (t, 2H); 2.49-2.43 (m, 2H); 2.03-1.95 (m, 2H); $^{13}$C (75.5 MHz, CDCl3) δ 164.2, 149.8, 132.5, 123.4, 121.6, 118.8, 43.8, 30.7, 29.7, 29.5.



**General Procedure for the Asymmetric Aminohydroxylation of the Olefinic Substrates illustrated for: (2*R*,3*S*)-(para-Bromophenyl)-2-benzylcarbamate-3-hydroxy-4-methylpentanoate (3d).** A solution of 0.4 **N** sodium hydroxide (280 mL, 3.05 equiv) was stirred in an ambient temperature water bath in a dimly lit hood. A small amount of this solution (*ca.* 20 mL) was used to dissolve potassium osmate dihydrate (0.54 g, 1.49 mmol, 0.04 equiv) in a separate vial. To the remaining sodium hydroxide solution was added n-propanol (150 mL) followed by benzyl carbamate (17.4 g, 0.115 mole, 3.1 equiv). Freshly prepared t-butyl hypochlorite[3] (13.0 mL, 0.113 mole, 3.05 equiv) was added to the reaction mixture and the mixture stirred for five minutes. To this homogeneous solution was added a solution of $(DHQ)_2$-AQN ligand (1.6 g, 1.86 mmol, 0.05 equiv) in n-propanol (160 mL, 0.011 **M**) followed by (*p*-bromophenyl)-4-methyl-2-(*E*)-pentenoate (**2d**) (10.0 g, 37.2 mmol, 1.0 equiv) in n-propanol (50 mL, 0.75 **M**) and the potassium osmate dihydrate solution. The reaction mixture was stirred at ambient temperature for 4 hours at which time sodium bisulfite (18.6 g) was added and the reaction subsequently diluted with EtOAc (100 mL). The reaction mixture was extracted with EtOAc (3 x 50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification on $SiO_2$ (30% EtOAc/PE) afforded **3d** as a white solid (9.7 g, 60%, 87% ee). Subsequent recrystallization from EtOH/$H_2O$ (1:1) afforded **3d** (8.3 g, 51 %) as a single enantiomer (ee > 99%) as determined by HPLC analysis. $^1$H NMR (400 MHz, CDCl3) 7.47 (d, 2H, J = 8.8 Hz), 7.35-7.30 (m, 5H), 6.97 (d, 2H, J = 8.0 Hz), 5.60 (d, 1H, J = 9.2 Hz), 5.14 (d, 2H, J = 2.4 Hz), 4.76 (d, 1H, J = 9.6 Hz), 4.10 (s, 1H), 3.88 (d, 1H, J = 9.2 Hz), 1.85-1.79 (m, 1H), 1.04 (d, 3H, J = 6.4 Hz), 1.0 (d, 3H, 2.4 Hz); $^{13}$C NMR (75.5 MHz, $CDCl_3$) 170.3, 156.6, 149.5, 136.1, 132.5, 128.6, 128.3, 128.0, 123.2, 119.3, 77.6, 77.2, 67.3, 56.3, 30.9, 18.9; FTIR (neat) $\nu_{max}$ 3417, 2089, 1653; CIHRMS M+H$^+$ (calculated for $C_{20}H_{23}BrNO_5$): 436.0761, found 436.0739; $[\alpha]_{23}{}^{D}$ = +5.00 (c = 0.75, $CHCl_3$); HPLC: Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^i$PrOH 85/15, 0.6 mL/min, wavelength = 230 nm, 12.89 min (2*S*, 3*R*), 16.50 min (2*R*, 3*S*). The regioselectivity of the Sharpless aminohydroxylation was determined by measuring the relative peak heights of the corresponding $^1$H NMR spectral lines of the two regioisomers using the resonances at *ca.* 1.0 ppm corresponding to the methyl doublets of the isopropyl functionality.

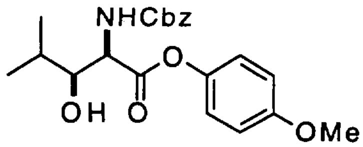



**(2*R*,3*S*)-(Phenyl)-2-amino-3-hydroxy-4-methylpentanoate (3a):** $^1$H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 10H); 5.50 (br d, 1H); 5.12 (d, 2H, J = 2.5 Hz); 4.51 (d, 1H, J = 9.2 Hz); 3.65 (br.s, 1H); 2.01 (d, 1H, J = 4.9 Hz); 1.78 (m, 1H); 1.05 (d, 3H, J = 6.8 Hz); 1.00 (d, 3H, J = 6.8 Hz); $^{13}$C (75.5 MHz, $CDCl_3$) δ 172.5, 162.1, 157.0, 151.3, 141.2, 136.3, 129.1, 128.3, 119.1, 116.8, 67.0, 61.8, 31.0, 18.9, 14.1; FTIR (neat) $\nu_{max}$ 3500, 2980, 2830, 1760, 1510; CIHRMS M+H$^+$ (calculated for $C_{20}H_{24}NO_5$): 358.1654, found 358.1701; $[\alpha]_{23}{}^{D}$ = +3.60 (c = 0.25, $CHCl_3$); HPLC:: Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^i$PrOH 85/15, 0.6 mL/min, wavelength = 210 nm, 13.40 min (2*S*, 3*R*), 14.10 min (2*R*, 3*S*).

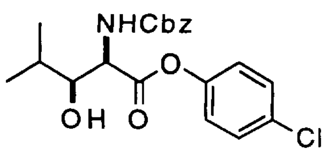



**(2*R*,3*S*)-(para-Cresol)-2-amino-3-hydroxy-4-methylpentanoate (3b):** $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.31 (m, 5H); 7.15 (d, 2H, J = 8.4 Hz); 6.95 (d, 2H, J = 8 Hz); 5.59 (d, 1H, J = 9.2 Hz); 5.14 (s, 2H); 4.76 (d, 1H, J = 10 Hz); 3.88 (br. t, 1H); 1.85-1.81 (m, 1H); 1.04 (d, 3H, J = 6.8 Hz); 1.00 (d, 3H, J = 6.8 Hz); $^{13}$C (75.5 MHz, $CDCl_3$) δ 173.2, 148.1, 136.1, 130.1, 120.9, 78.0, 76.1, 71.3, 31.2, 20.9, 19.0; FTIR (neat) $\nu_{max}$ 3400, 2925, 2854, 1745, 1507; CIHRMS M+H$^+$ (calculated for $C_{13}H_{20}NO_3$): 372.1811, found 372.1852;

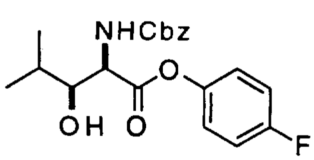
$[\alpha]_{23}{}^{D}$ = +3.90 (c = 0.51, $CHCl_3$); HPLC: Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^{i}$PrOH 85/15, 0.6 mL/min, wavelength = 210nm, 13.18 min (2*S*, 3*R*), 14.31 min (2*R*, 3*S*).




**(2*R*,3*S*)-(para-Methoxyphenyl)-2-benzylcarbamate-3-hydroxy-4-methylpentanoate (3c):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 5H); 6.98 (d, 2H, J = 8.8 Hz); 6.82 (d, 2H, J = 9.2 Hz); 5.53 (br d, 1H); 5.17-5.13 (m, 2H); 4.50 (d, 1H, J = 8.8 Hz); 3.90 (s, 3H); 3.88 (br. t, 1H); 2.09 (d, 1H, J = 4.8 Hz); 1.85-1.80 (m, 1H); 0.99 (d, 3H, J = 6.4 Hz); 0.95 (d, 3H, J = 6.4 Hz); $^{13}$C (75.5 MHz, $CDCl_3$) δ 171.9, 157.0, 153.4, 150.0, 148.4, 128.5, 128.1, 116.0, 114.7, 106.6, 67.2, 55.7, 34.9, 25.4, 24.7, 21.9; FTIR (neat) $\nu_{max}$ 3500, 2980, 2840, 1760, 1450; CIHRMS M+H$^{+}$ (calculated for $C_{21}H_{26}NO_6$): 388.1760, found 388.2720; $[\alpha]_{23}{}^{D}$ = +4.0 (c = 0.50, $CHCl_3$); HPLC: Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^{i}$PrOH 85/15, 0.6 mL/min, wavelength = 210nm, 13.40 min (2*S*, 3*R*), 14.10 min (2*R*, 3*S*).

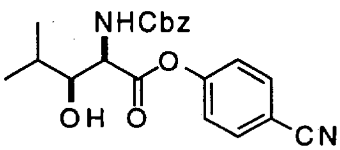



**(2*R*,3*S*)-(para-Chlorophenyl)-2-benzylcarbamate-3-hydroxy-4-methylpentanoate (3e):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.33-7.27 (m, 7H); 7.02 (d, 2H, J = 8.4 Hz); 5.59 (d, 1H, J = 9.6 Hz); 5.18-5.13 (m, 2H); 4.76 (d, 1H, J = 9.2 Hz); 3.88 (br. d, 1H); 2.09 (d, 1H, J = 4.8 Hz); 1.85-1.79 (m, 1H); 1.04 (d, 3H, J = 6.4 Hz); 1.00 (d, 3H, J = 6.4 Hz); $^{13}$C (75.5 MHz, $CDCl_3$) δ 170.1, 162.0, 158.6, 156.4, 145.9, 136.0, 128.3, 123.0, 116.1, 116.0, 67.1, 56.4, 31.2, 22.3, 19.0; FTIR (neat) $\nu_{max}$ 3450, 2920, 2840, 1755, 1500; CIHRMS M+H$^{+}$ (calculated for $C_{20}H_{23}ClNO_5$): 392.1264, found 392.1300; $[\alpha]_{23}{}^{D}$ = +5.6 (c = 0.30, $CHCl_3$); HPLC: Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^{i}$PrOH 85/15, 0.6 mL/min, wavelength = 250 nm, 12.76 min (2*S*, 3*R*), 16.46 min (2*R*, 3*S*).

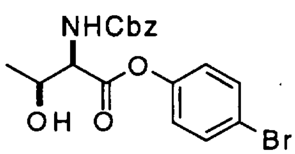



**(2*R*,3*S*)-(para-Fluorophenyl)-2-benzylcarbamate-3-hydroxy-4-methylpentanoate (3f):** $^{1}$H NMR (400 MHz,

$CDCl_3$) δ 7.34-7.30 (m, 7H); 7.04 (d, 2H, J = 6 Hz); 5.60 (br. d, 1H); 5.18-5.11 (m, 2H); 3.88 (br. t, 1H); 2.10 (br. s, 1H); 1.85-1.79 (m, 1H); 1.04 (d, 3H, J = 6.8 Hz); 1.00 (d, 3H, J = 6.4 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 170.5, 162.1,158.8, 156.6,146.5, 136.3, 128.5, 128.0, 122.8, 116.3, 115.9, 67.3, 56.5, 31.0, 22.0, 18.9; FTIR (neat) $\nu_{max}$ 3420, 2091, 1648; CIHRMS M+H$^+$ (calculated for $C_{20}H_{23}FNO_5$): 376.1560, found 376.1599; $[\alpha]_{23}{}^{D}$ = +3.4 (c = 0.32, $CHCl_3$); HPLC: Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^{i}$PrOH 85/15, 0.6 mL/min, wavelength = 209 nm, 15.88 min (2*S*, 3*R*), 16.46 min (2*R*, 3*S*).

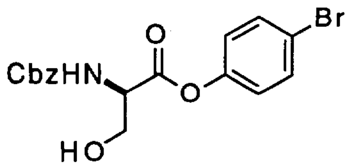



**(2*R*,3*S*)-(para-Cyanophenyl)-2-benzylcarbamate-3-hydroxy-4-methylpentanoate (3g):** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.53 (d, 2H, J = 8.8 Hz); 7.34-7.30 (m, 5H); 6.88 (d, 2H, J = 8.4 Hz); 5.51 (d, 1H, J = 7.6 Hz); 5.11 (d, 2H, J = 2.4 Hz); 4.51 (d, 1H, J = 9.2 Hz); 3.70 (d, 1H, J = 8 Hz); 1.00 (d, 3H, J = 6.8 Hz); 0.95 (d, 3H, J = 6.8 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 174.2, 163.2, 159.8, 158.2, 152.4, 132.2, 128.4, 128.1, 122.9, 118.0, 116.3, 114.0, 67.9, 57.0, 32.3, 31.2, 20.0; FTIR (neat) $\nu_{max}$ 3430, 2045, 1645; CIHRMS M+H$^+$ (calculated for $C_{21}H_{23}N_2O_5$): 383.1607, found 383.2600; $[\alpha]_{23}{}^{D}$ = +2.0 (c = 0.50, $CHCl_3$); HPLC: Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^{i}$PrOH 85/15, 0.6 mL/min, wavelength = 213 nm, 12.57 min (2*S*, 3*R*), 13.82 min (2*R*, 3*S*).

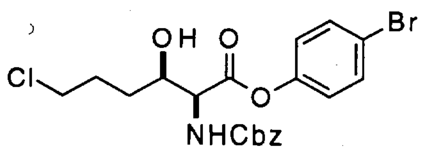



**(2*R*, 3*S*)-(para-Bromophenyl)-2-benzylcarbmate-3-hydroxy-butanoate (5a):** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.45 (d, 2H, J = 8.8Hz); 7.36-7.25 (m, 5H); 6.94 (d, 2H, J = 8.4 Hz); 5.66 (br. t, 1H); 5.12-5.05 (m, 2H); 4.30-4.25 (m, 1H); 2.76 (d, 1H, J = 6 Hz); 1.79-1.53 (m, 1H); 1.24 (d, 3H, J = 6.8 Hz); $^{13}C$ (75.5 MHz, $CDCl_3$) δ 173.1, 164.0, 132.5, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 123.3, 106.7, 73.0, 67.2, 28.0; FTIR (neat) $\nu_{max}$ 3445, 2390, 2355, 2100, 1660, 1545; CIHRMS M+H$^+$ (calculated for $C_{18}H_{19}BrNO_5$): 408.0446, found 408.0520; HPLC:

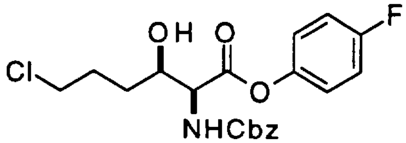
Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^{i}$PrOH 85/15, 0.6 mL/min, wavelength = 230 nm, 20.42 min (2*S*, 3*R*), 28.47 min (2*R*, 3*S*).



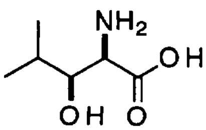

**(2*R*)-(para-Bromophenyl)-2benzylcarbamate-3-hydroxy-propionoate (5b):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, 2H, J = 8.8 Hz); 7.34-7.30 (m, 5H); 6.95 (d, 2H, J = 8.8Hz); 5.61 (br. t, 1H); 5.13-5.07 (m, 2H); 4.42 (br. t, 1H); 3.63-3.54 (m, 3H); $^{13}$C (75.5 MHz, $CDCl_3$) δ 173.0, 163.8, 132.0, 128.8, 128.5, 128.3, 128.1, 128.0, 127.8, 123.0, 106.5, 72.8, 66.8 ; FTIR (neat) $\nu_{max}$ 3415, 2390, 2349, 2087, 1653, 1539; CIHRMS M+H$^+$ (calculated for $C_{17}H_{17}BrNO_5$): 394.0289, found 394.0574; $[\alpha]_{23}{}^{D}$ = +3.8 (c = 0.71, $CHCl_3$); HPLC: Chiralcel OD-H 0.46 cm x 25 cm, hexane / $^{i}$PrOH 85/15, 0.6 mL/min, wavelength = 208 nm, 41.32 min (2*S*), 44.81 min (2*R*).




**(2*S*,3*R*)-(para-Bromophenyl)-2-benzylcarbamate-3-hydroxy-6-chlorohexanoate (5c):** $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, 2H, J = 8.8 Hz); 7.35-7.30 (m, 5H); 6.93 (d, 2H, J = 8.8 Hz); 5.66 (br. t, 1H); 5.12-5.08 (m, 2H); 4.33 (d, 1H, J = 2.8 Hz); 4.16-4.11 (br. m, 1H); 3.56 (br. d, 1H); 2.77 (dq, 2H, J = 12.8Hz); 1.87-1.71 (m, 4H); $^{13}$C (75.5 MHz, $CDCl_3$) δ 132.5, 129.8, 129.0, 123.1, 106.2, 67.9, 66.7, 66.5, 51.4, 47.8, 43.2, 39.3, 31.4, 29.0, 28.2, 7.2; FTIR (neat) $\nu_{max}$ 3450, 2400, 2350, 2080, 1663, 1540; CIHRMS M+H$^+$ (calculated for $C_{20}H_{22}BrClNO_5$): 470.0369, found 470.0402; $[\alpha]_{23}{}^{D}$ = +30.0 (c = 0.10, $CHCl_3$); 82% ee (The optical purity (*ee*) of this sample was determined by a Mosher analysis of the derived *R*-(O)-acetylmandelate ester. The mandelate ester was prepared by the coupling of **5c** (1.0 equiv) and *R*-(O)-acetyl-D-mandelic acid (1.2 equiv) with DCC (1.2 equiv.) and catalytic DMAP (0.05 equiv) in $CH_2Cl_2$ (0.1M) at 0 °C. The diastereomeric resonances of the crude ester were used to determine the optical purity of the sample).

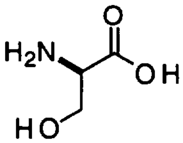


**(2*S*,3*R*)-(para-Fluorophenyl)-2-benzylcarbamate-3-hydroxy-6-chlorohexanoate (5d):** $^1$H NMR (400 MHz, $CDCl_3$) δ 7.40-7.30 (m, 9H); 5.74 (t, 1H); 5.18 (s, 2H); 5.16-5.12 (m, 1H); 4.32 (d, 1H, J = 3.6 Hz); 4.26 (dd, 1H, J = 1.2 Hz, 1.2 Hz); 3.60-3.55 (m, 2H); 1.89-1.76 (m, 4H); $^{13}$C (75.5 MHz, $CDCl_3$) δ 207.2, 169.8, 136.0, 128.5, 128.1, 126.9, 122.7, 116.2, 116.0, 71.3, 66.9, 60.4, 58.3, 44.6, 30.9, 28.7; FTIR (neat) $\nu_{max}$ 3500, 2410, 2400, 2120, 1670, 1540; CIHRMS M+H$^+$ (calculated for $C_{20}H_{22}ClFNO_5$): , found ; $[\alpha]_{23}{}^D$ = (c = , $CHCl_3$); 90% ee (The optical purity (*ee*) of this sample was determined by a Mosher analysis of the derived *R*-(O)-acetylmandelate ester. The mandelate ester was prepared by the coupling of **5d** (1.0 equiv) and *R*-(O)-acetyl-D-mandelic acid (1.2 equiv) with DCC (1.2 equiv.) and catalytic DMAP (0.05 equiv) in $CH_2Cl_2$ (0.1**M**) at 0 °C. The diastereomeric resonances of the crude ester were used to determine the optical purity of the sample).



**Proof of Absolute Stereochemistry: (2*R*, 3*S*)-3-Hydroxyleucine.** A dilute solution of **3d** (0.1 g, 0.23 mmol) in anhydrous MeOH (9.2 mL, 0.025 **M**) was treated with 10% Pd-C (0.020 g, 20 wt%). The suspension was stirred under 1 atmosphere of hydrogen for 12 hours. The resulting suspension was filtered through Celite, washed with MeOH, and concentrated *in vacuo*. The crude amino alcohol was immediately dissolved in THF/$H_2O$ (1:1, 1.0 mL, 0.25 **M**) and the solution cooled to 0 °C. To this solution was added LiOH (20 mg, 0.46 mmol, 2.0 equiv) and the solution warmed to room temperature with vigorous stirring over a period of 10 hours. The reaction mixture was subsequently acidified dropwise with concentrated HCl to a pH of ~2. The biphasic mixture was then concentrated *in vacuo* to remove the THF. The reaction mixture was extracted with EtOAc (3 x 20 mL), dried ($MgSO_4$), and concentrated *in vacuo* to afford (2*R*, 3*S*)-3-hydroxyleucine as a white solid (0.033 g, 98%, 2 steps). $^1$H NMR (400 MHz, $D_2O$) 3.93 (d, 1H, J = 3.6 Hz), 3.76 (dd, 1H, J = 3.6 Hz, 8.4 Hz), 1.71 (m, 1H), 0.97 (d, 3H, J = 6.8 Hz), 0.92 (d, 3H, 6.8 Hz); $^{13}$C NMR (75.5 MHz, $D_2O/CD_3OD$) 173.7, 76.0, 57.5, 31.3, 19.4, 18.7; IR (KBr) $\nu_{max}$ 3320, 1636, 1507;

CIHRMS M+H+ (calculated for $C_{16}H_{14}NO_3$): 148.0974, found 148.0982; $[\alpha]_{23}{}^{D}$ = +3.33 (c = 0.75, $H_2O$), $[\alpha]_{23}{}^{D}$ (lit.[4]) = +3.5 (c = 1.0, $H_2O$).



**Proof of Absolute Stereochemistry: D-Serine.** Using the same procedure as above with **5b**, D-Serine was obtained. $^1$H NMR (400 MHz, $D_2O$) δ 4.00-3.91 (m, 2H); 3.84-3.82 (m, 1H); $^{13}$C (75.5 MHz, $D_2O/CD_3OD$) δ 172.9, 61.5, 57.7; CIHRMS M+H+ (calculated for $C_3H_8NO_3$): 106.0504, found 106.0475; $[\alpha]_{23}{}^{D}$ = -14.0 (c = 0.74, 1**N** HCl), $[\alpha]_{23}{}^{D}$ (Aldrich) = -14.7 (c = 10, 1**N** HCl).

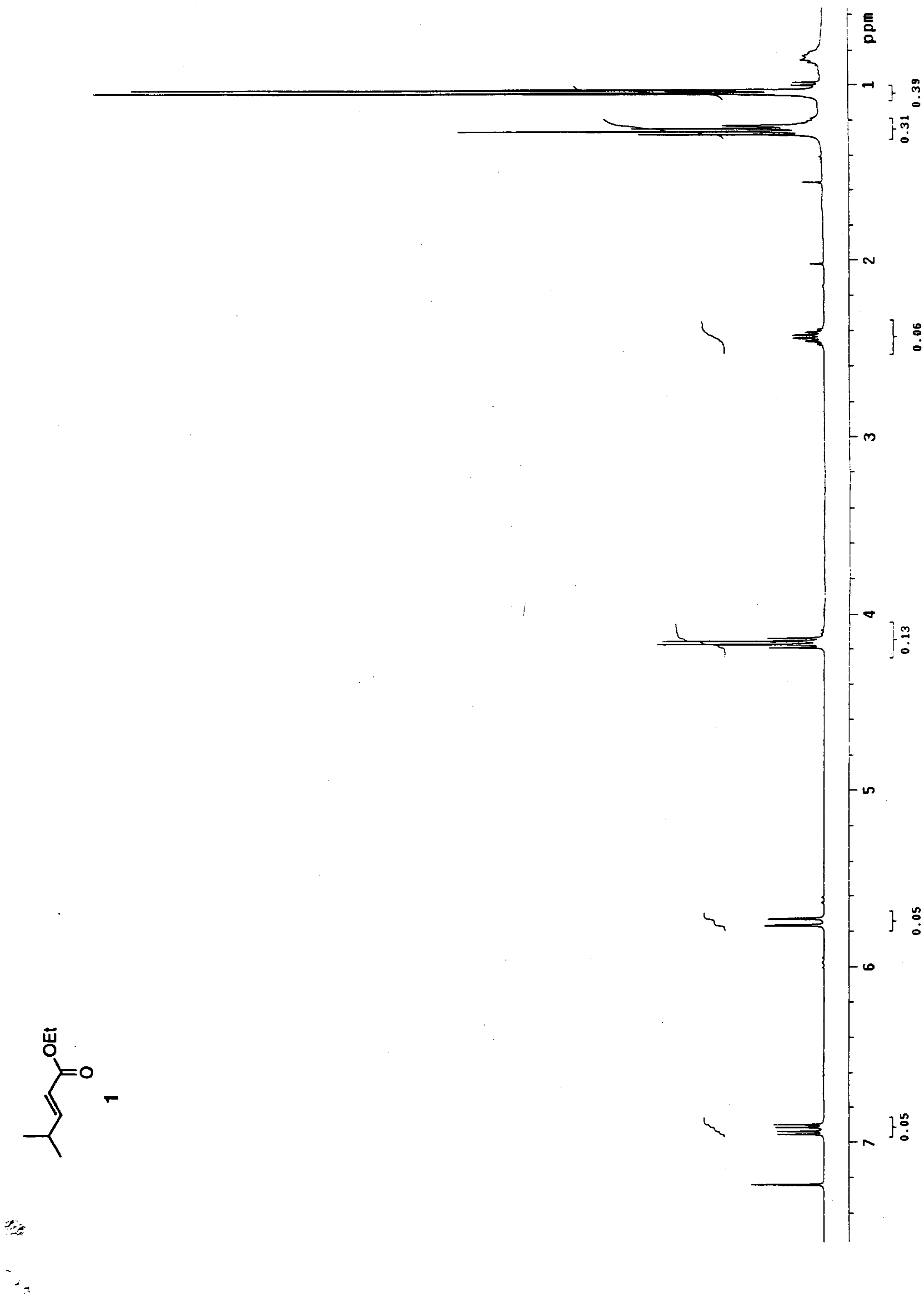
**Additional Notes and References**

(1) Still, W. C.; Kahn, M; Mitra, A.*J. Org. Chem.* **1978**, 43, 2923-2925.

(2) *p*-(Bromophenyl)-diethylphosphonoacetate was prepared by the coupling of diethylphosphonoacetic acid and *p*-bromophenol with DCC (1.1 equiv.) and catalytic DMAP (0.1 equiv) in $CH_2Cl_2$ (0.5M) at 0 °C. The crude material was used without further purification.

(3) Mintz, M. J; Walling, C. *Org. Synth.* **1973**, *Col. Vol 5*, 184-187.

(4) Nagamitsu, T.; Sunazuka, T.; Tanaka, H.; Omura, S.; Sprengler, P. A.; Smith, A. B. III, *J. Am. Chem. Soc.* **1996**, *118*, 3584-3590.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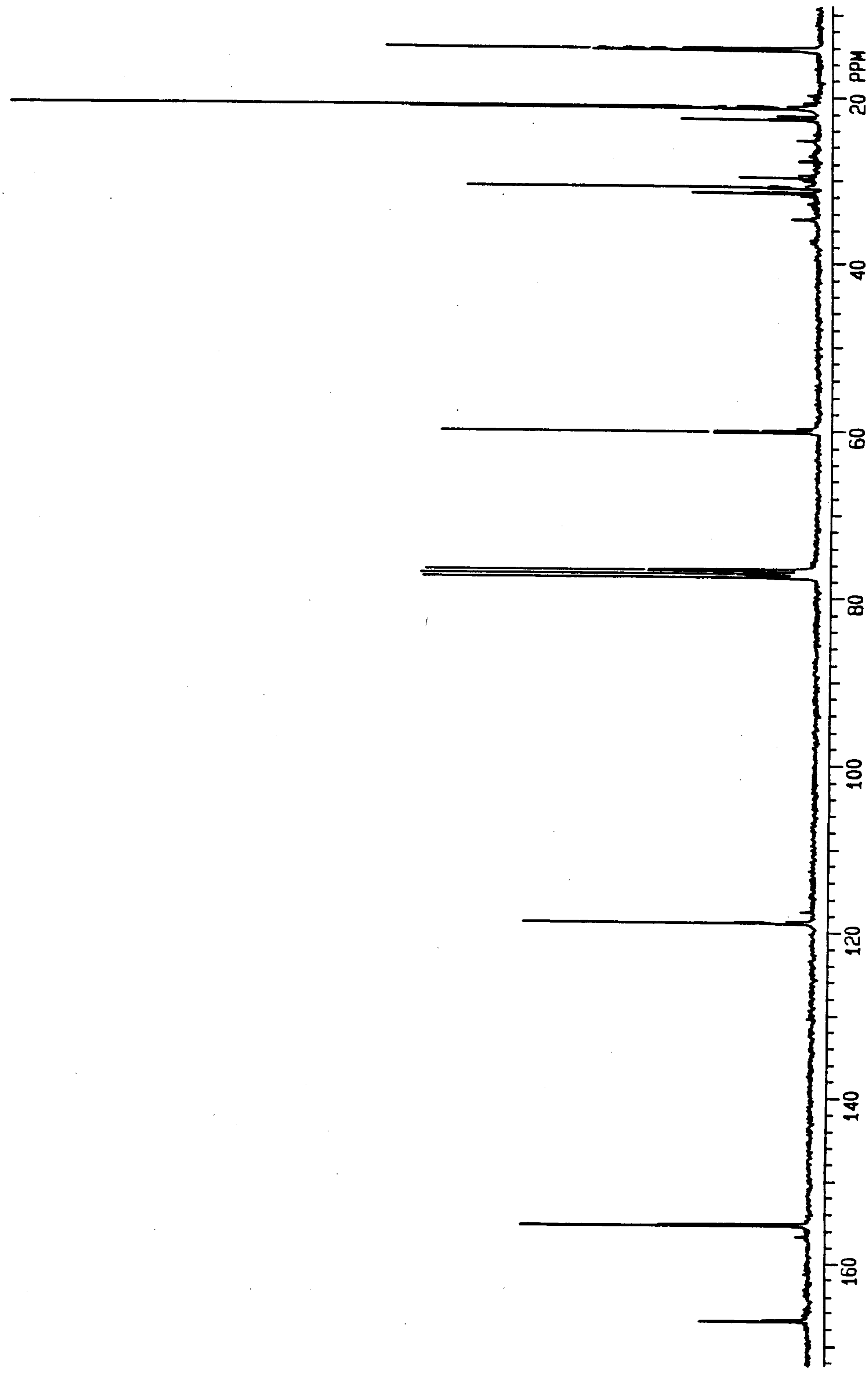


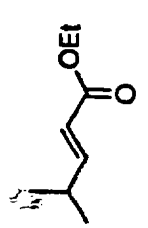


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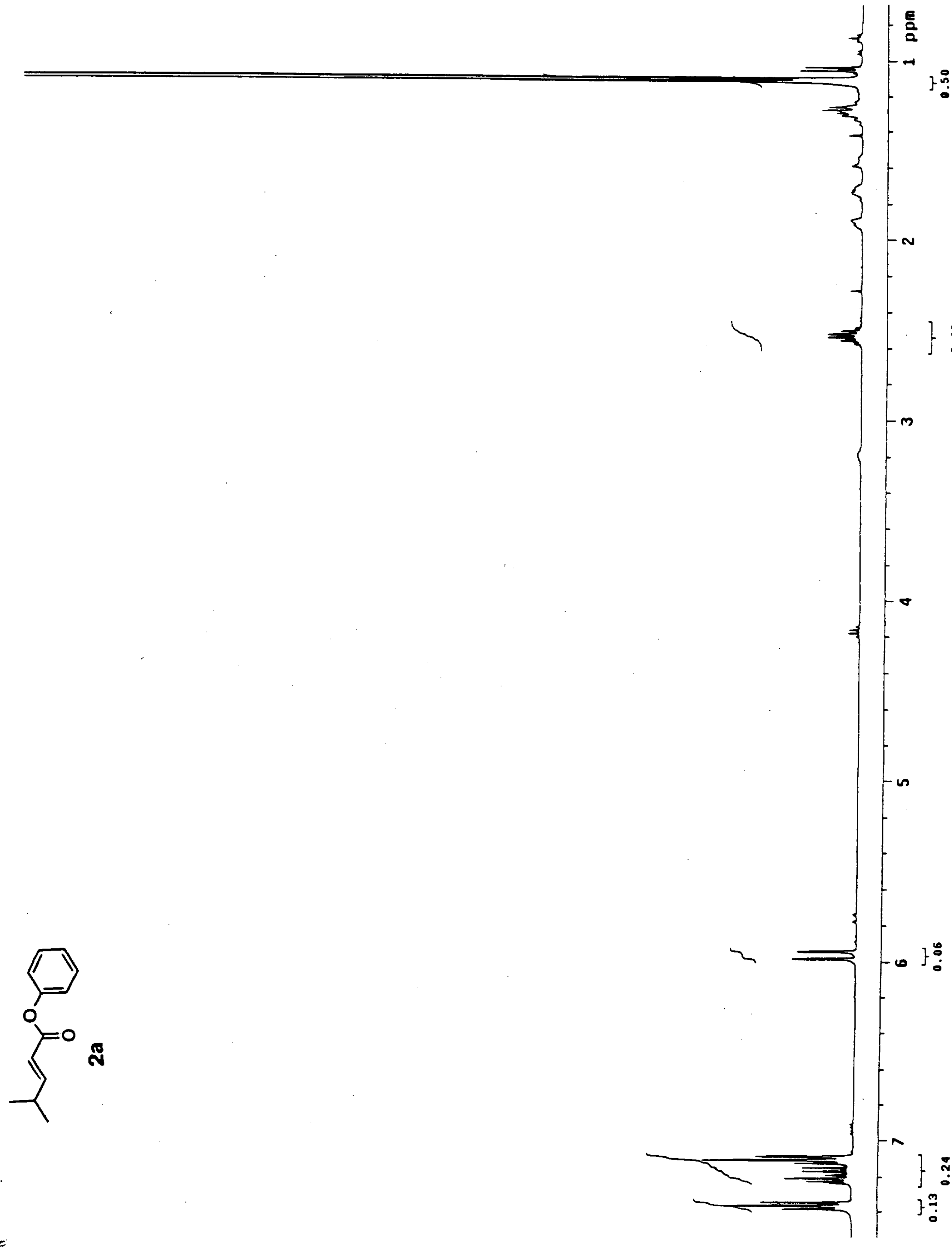
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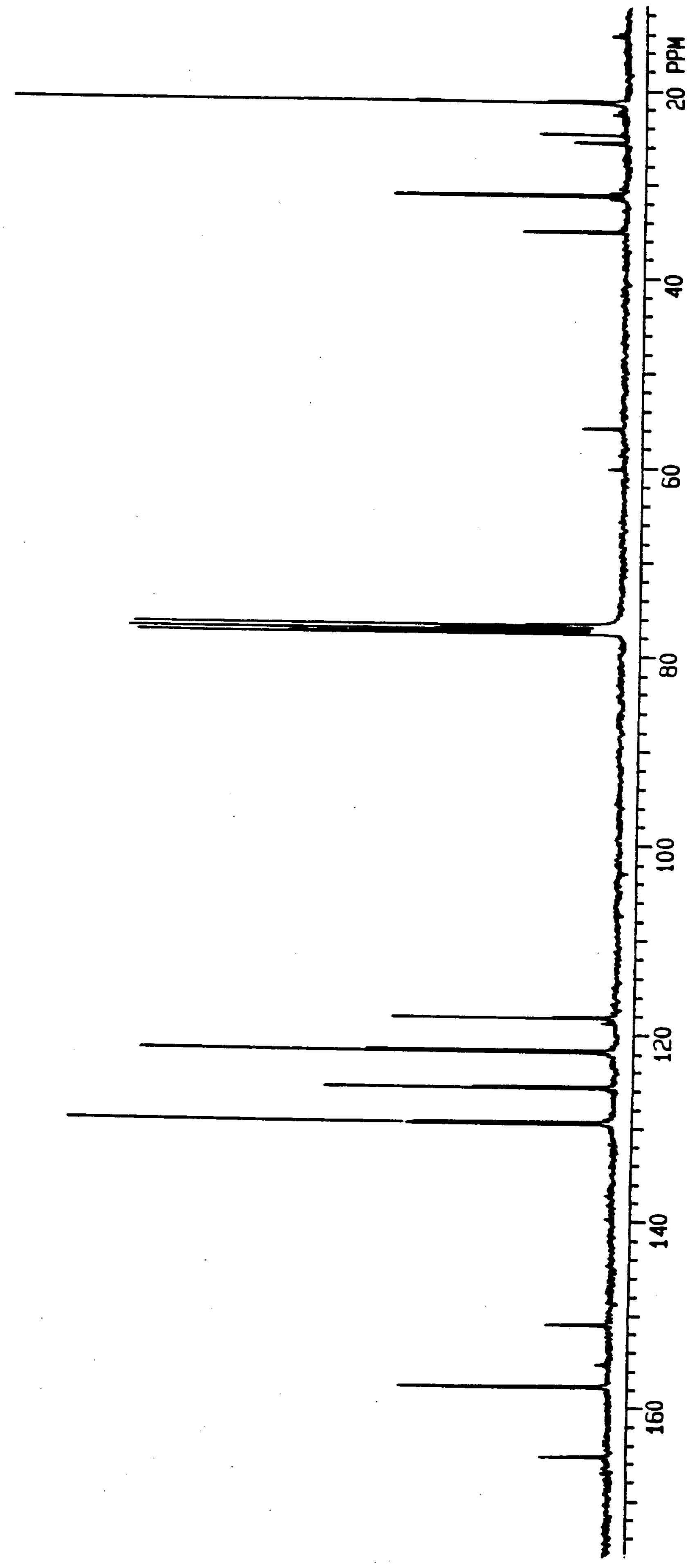


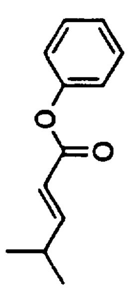

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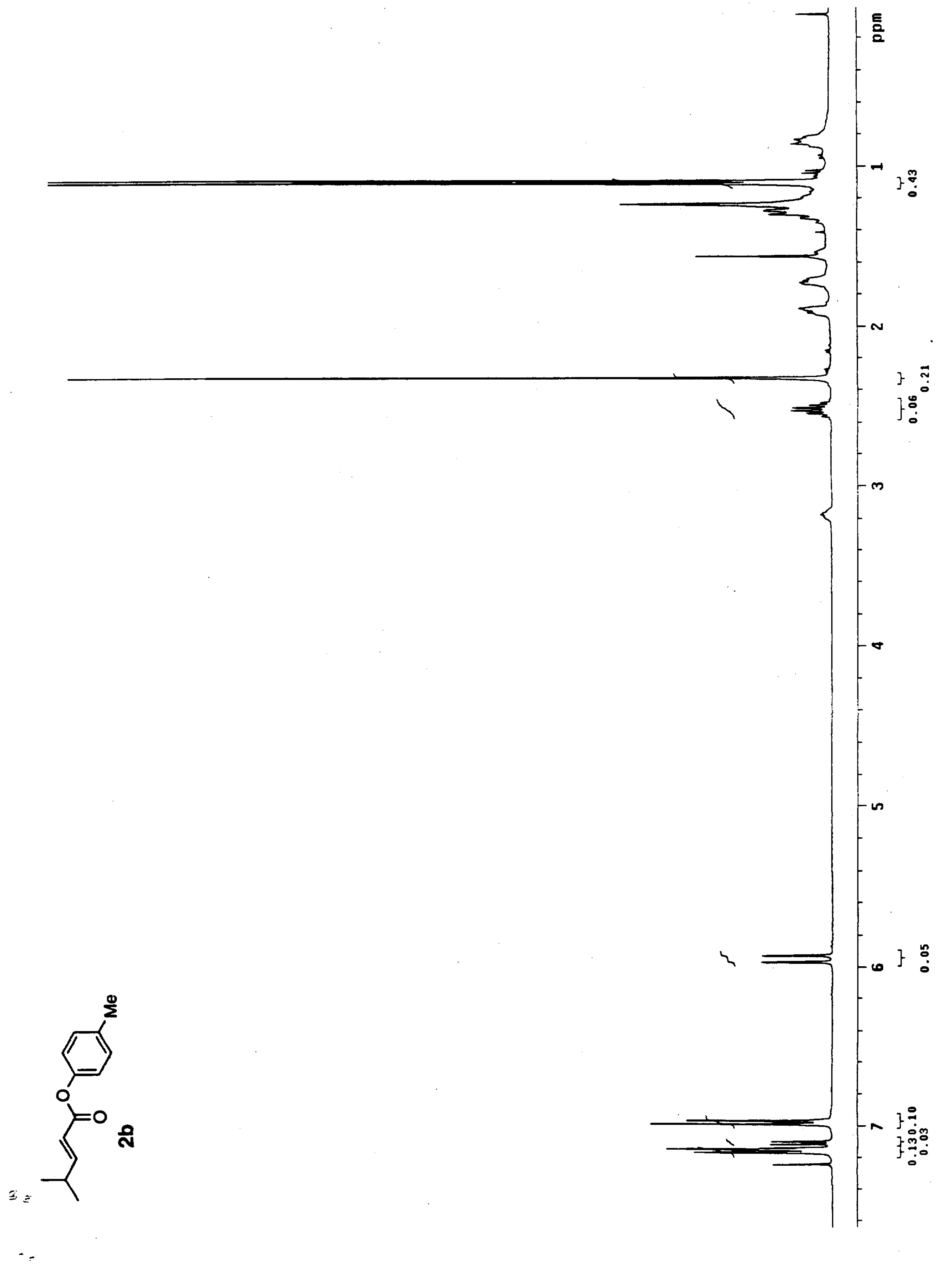

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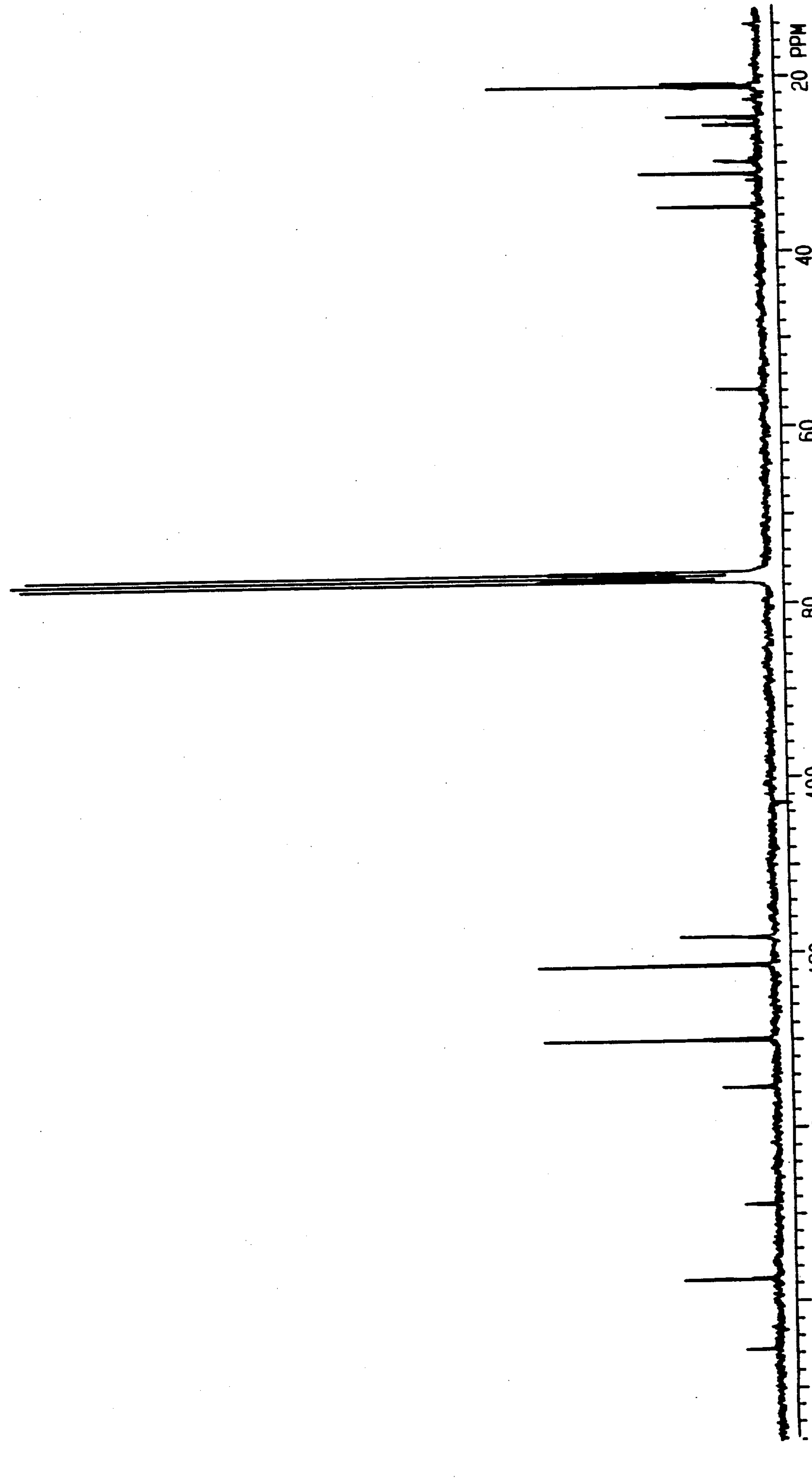


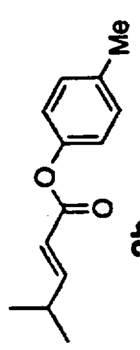


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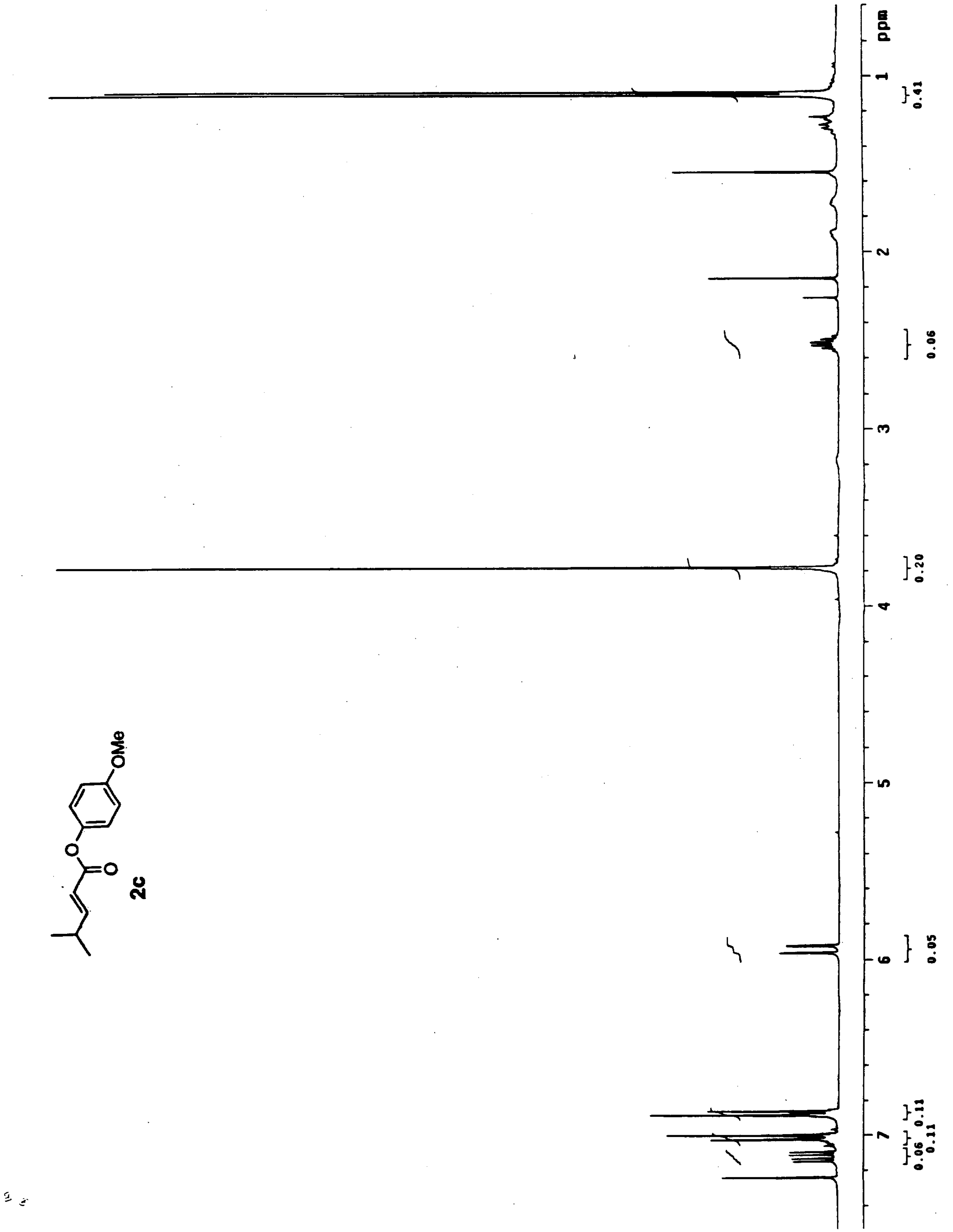


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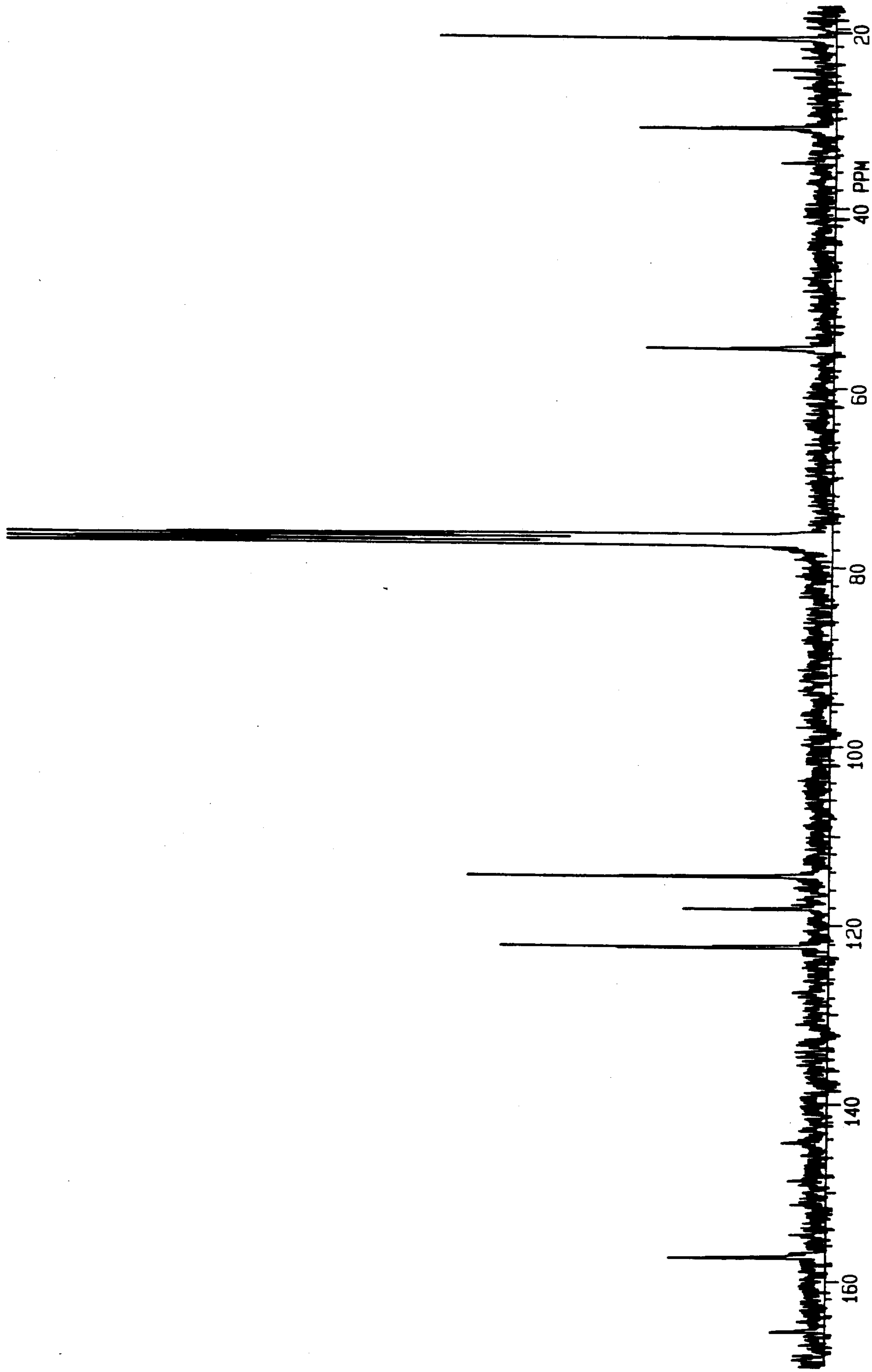


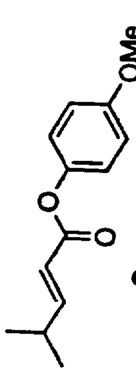


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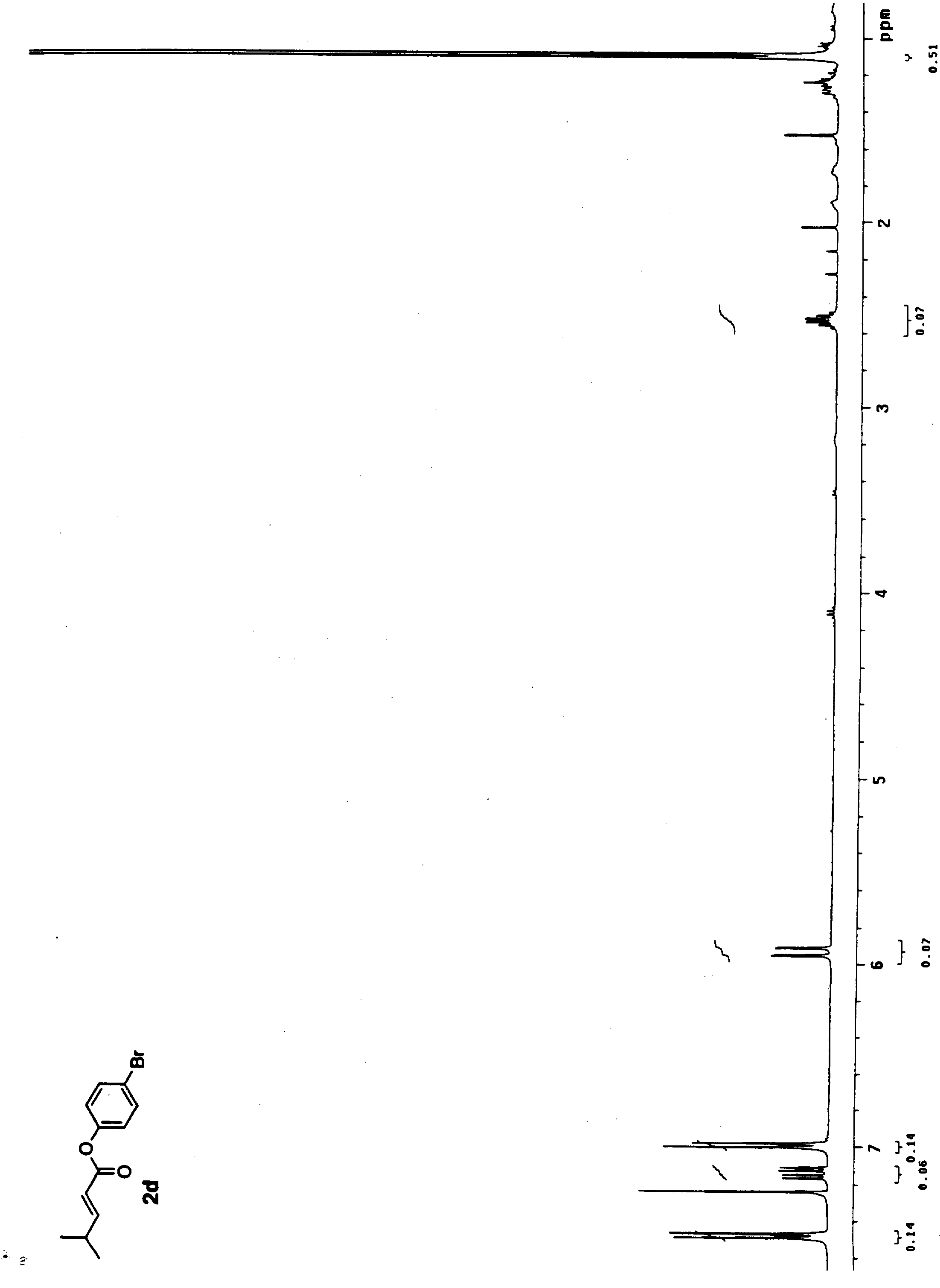

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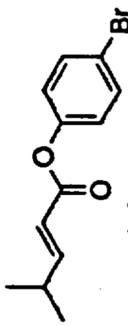


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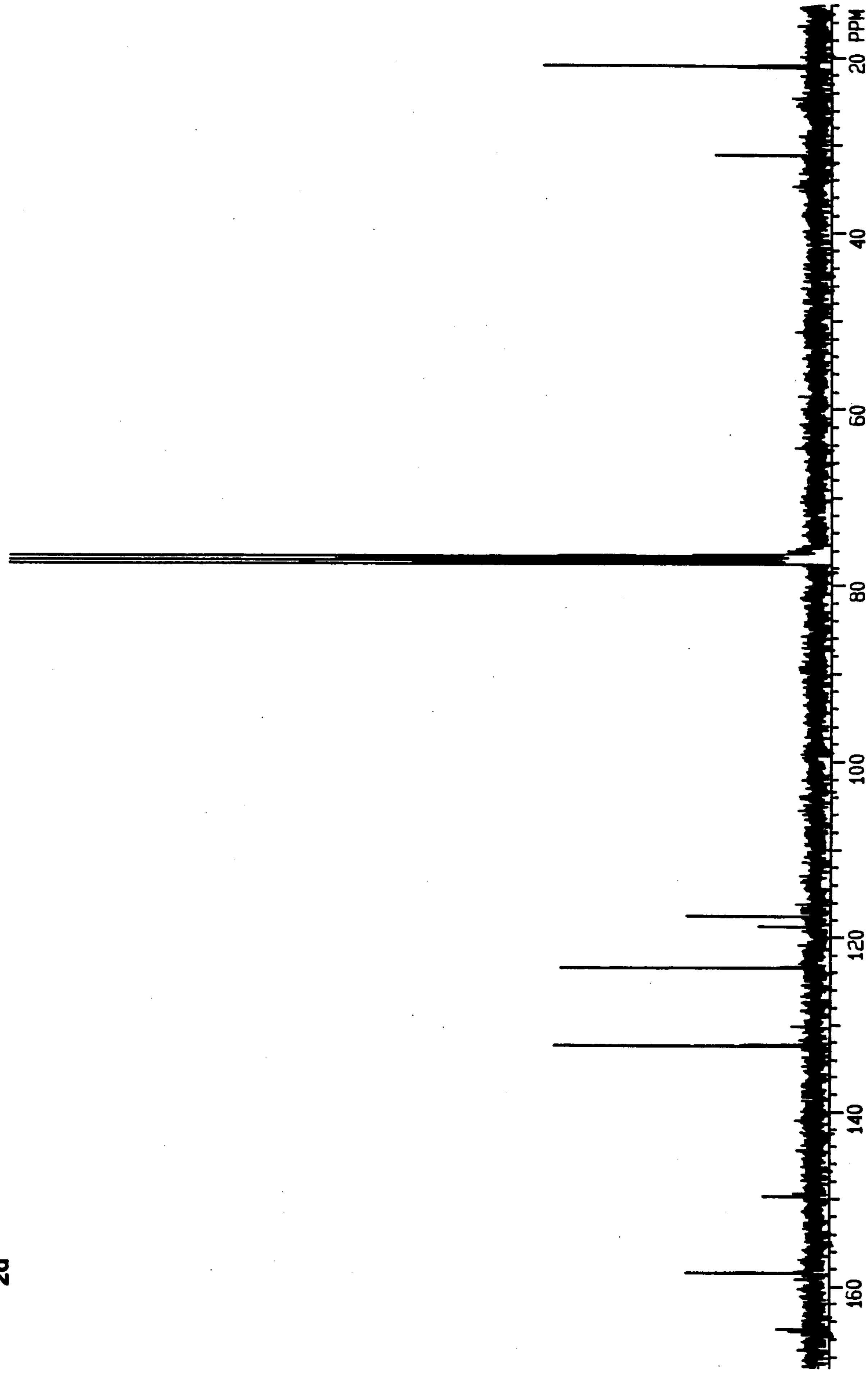

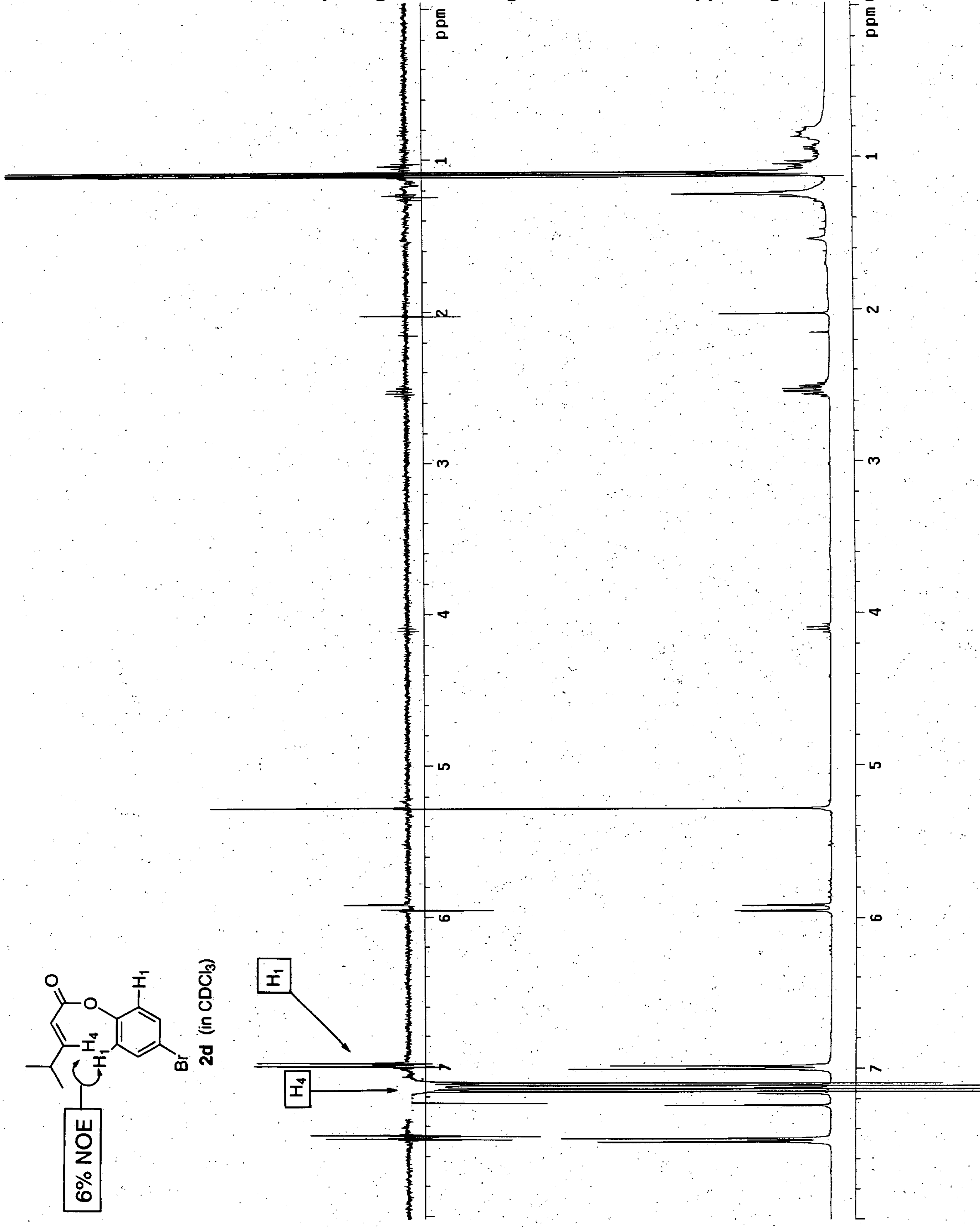
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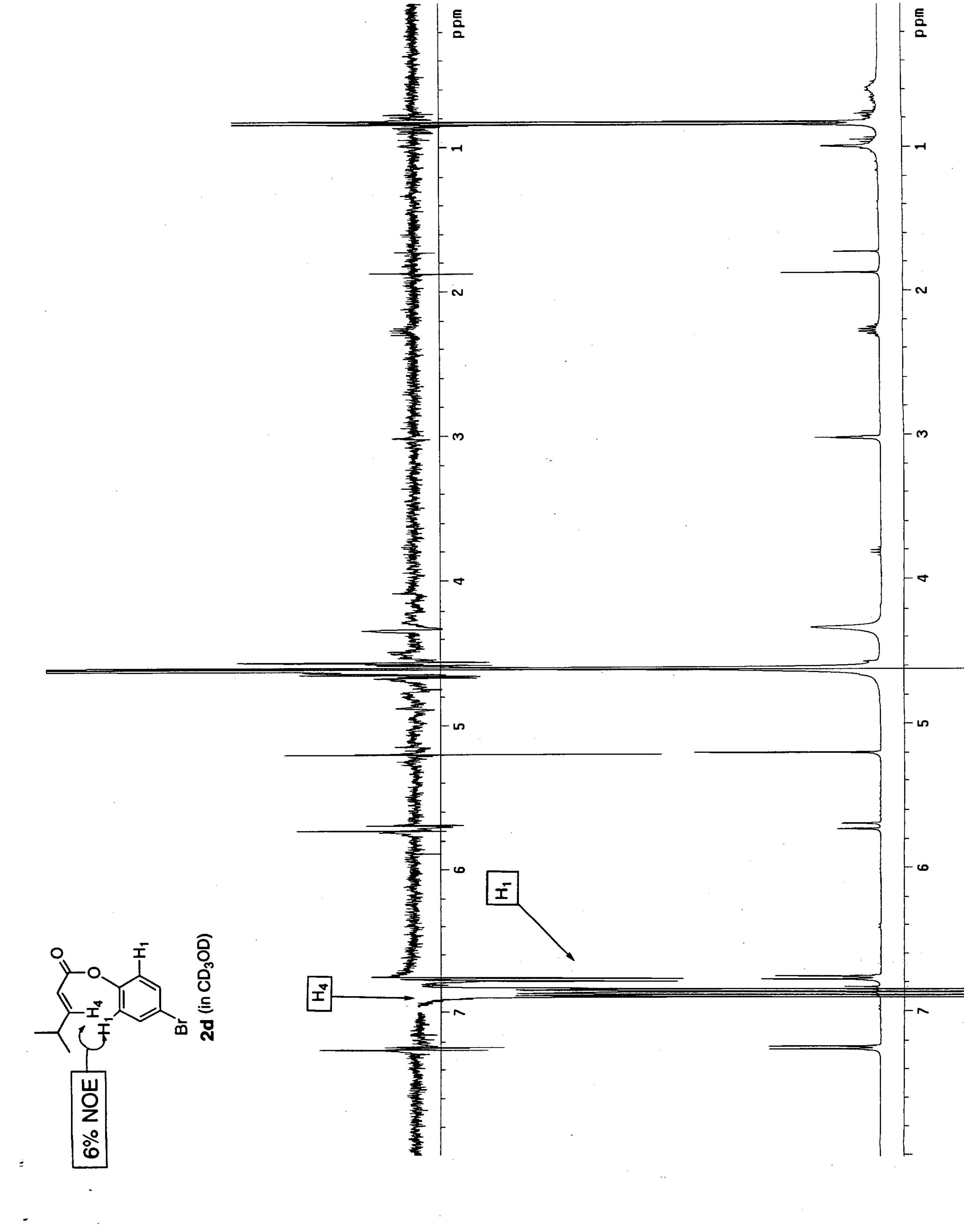

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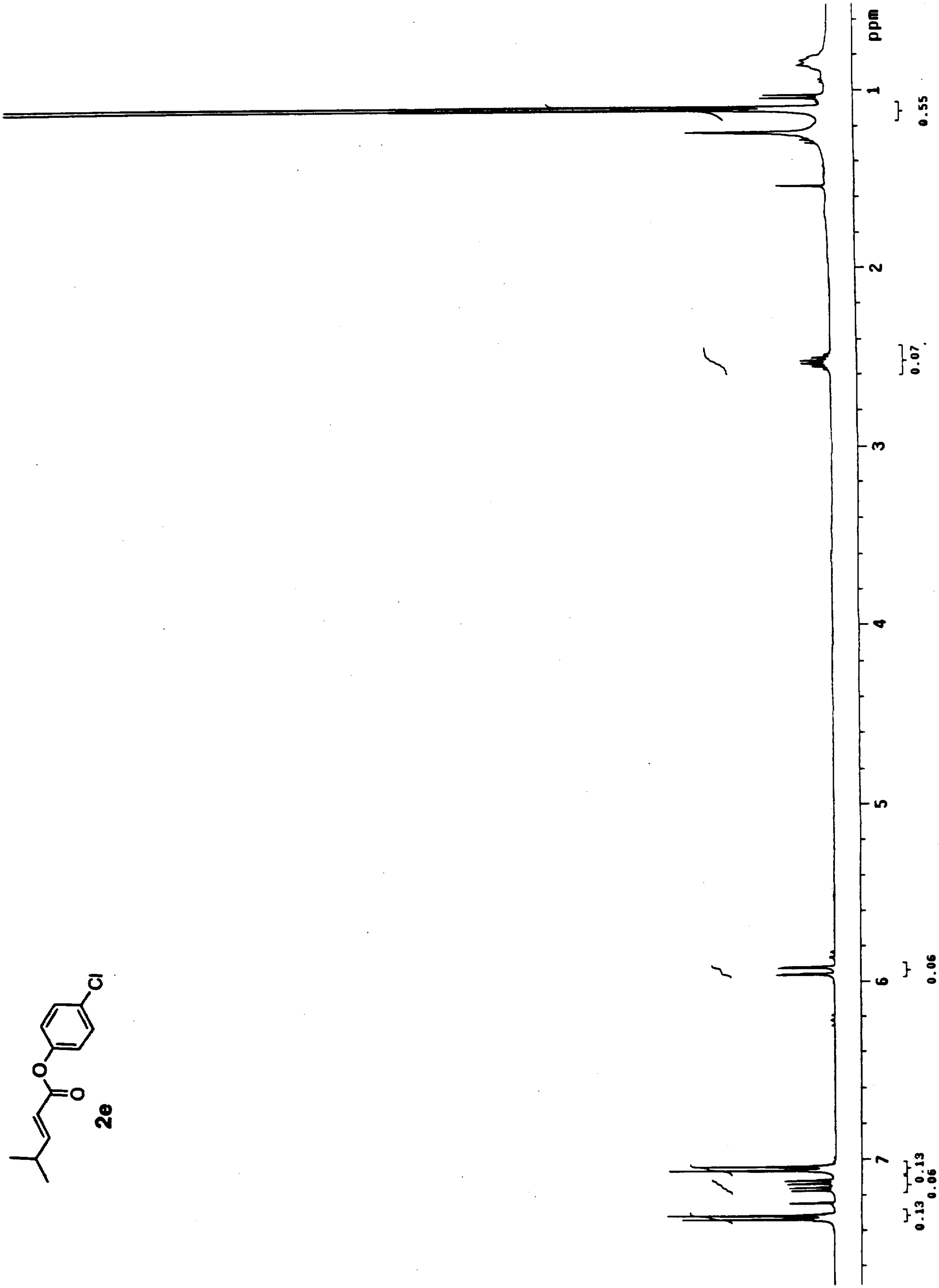
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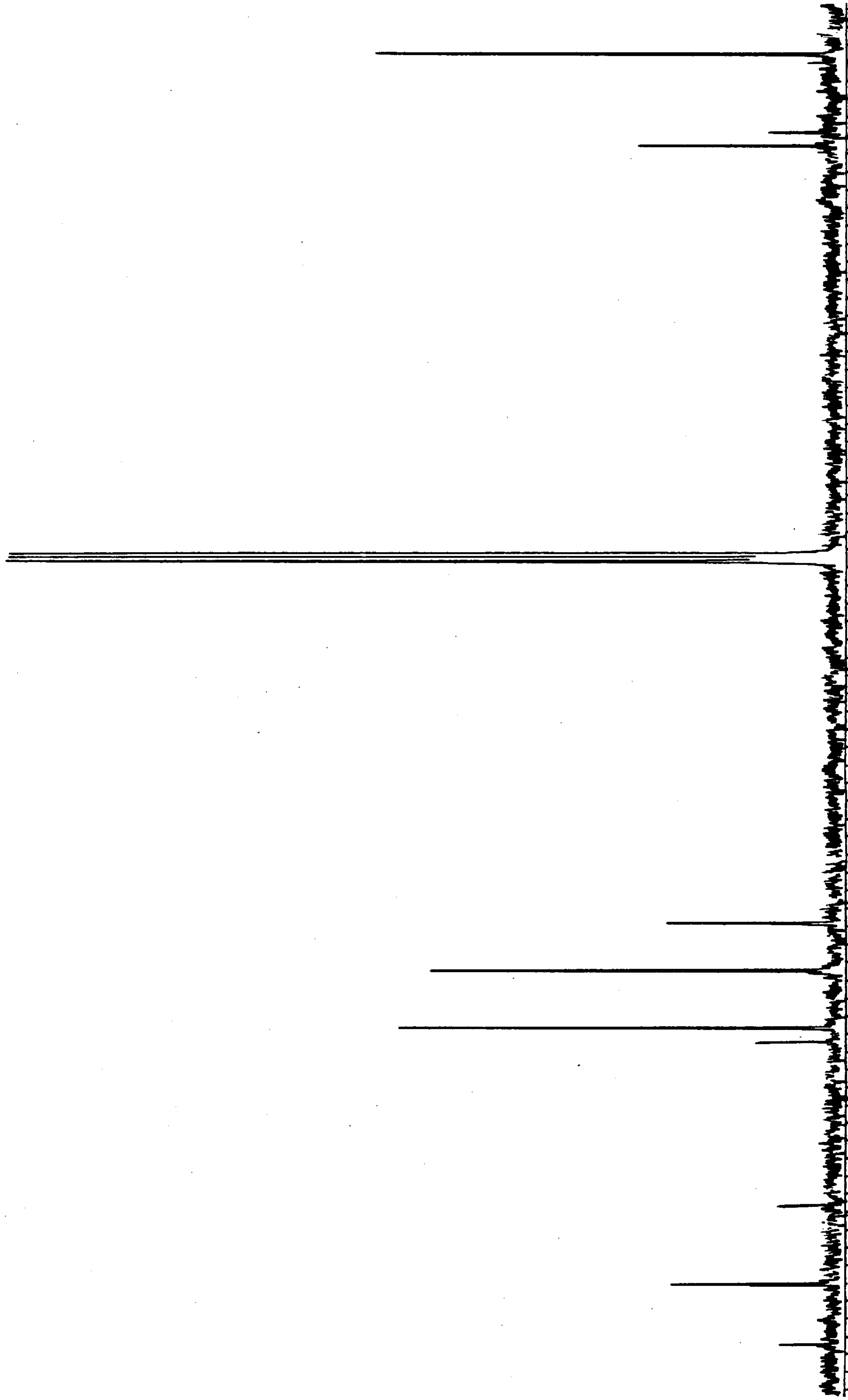


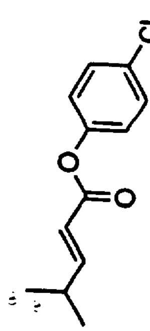


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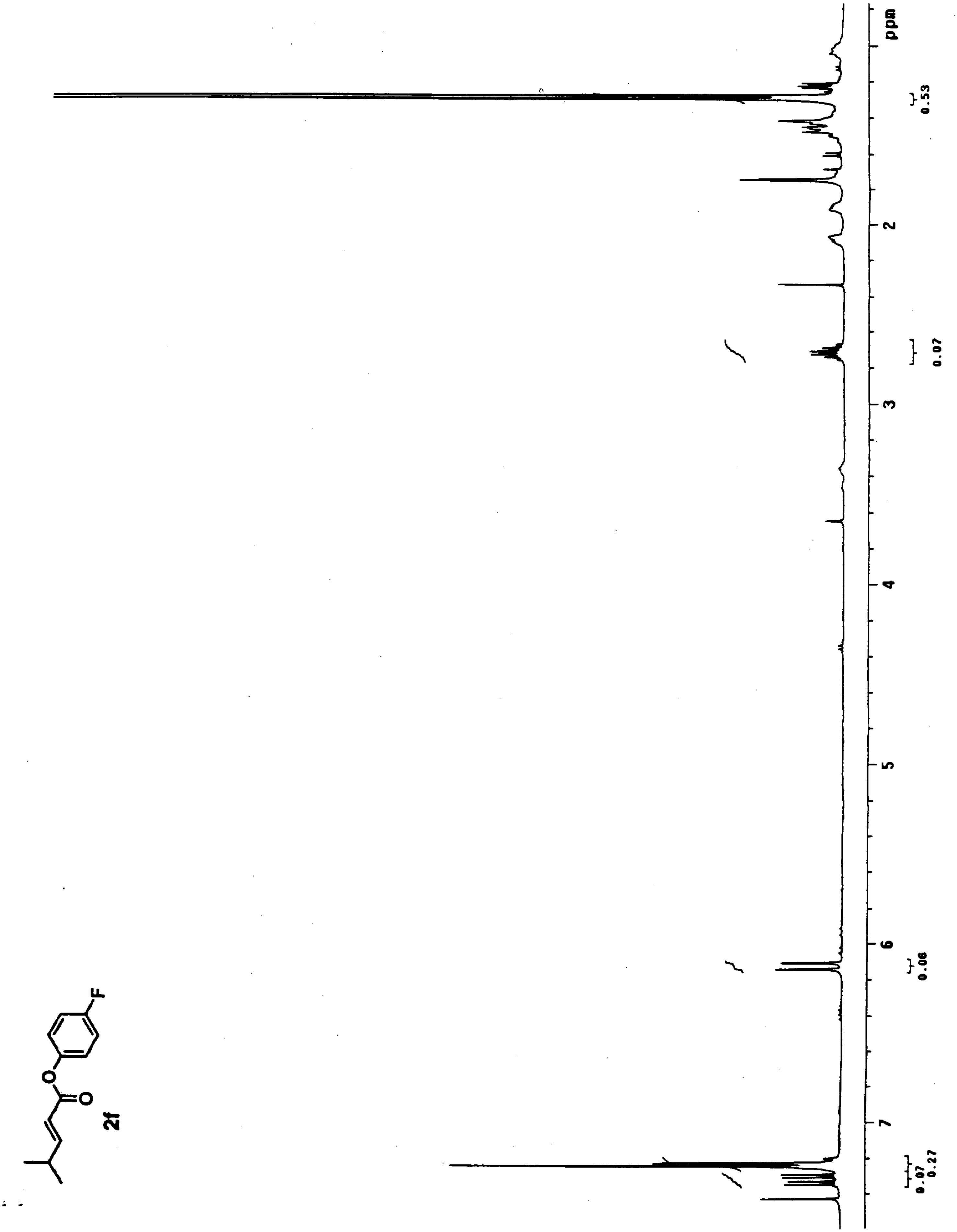

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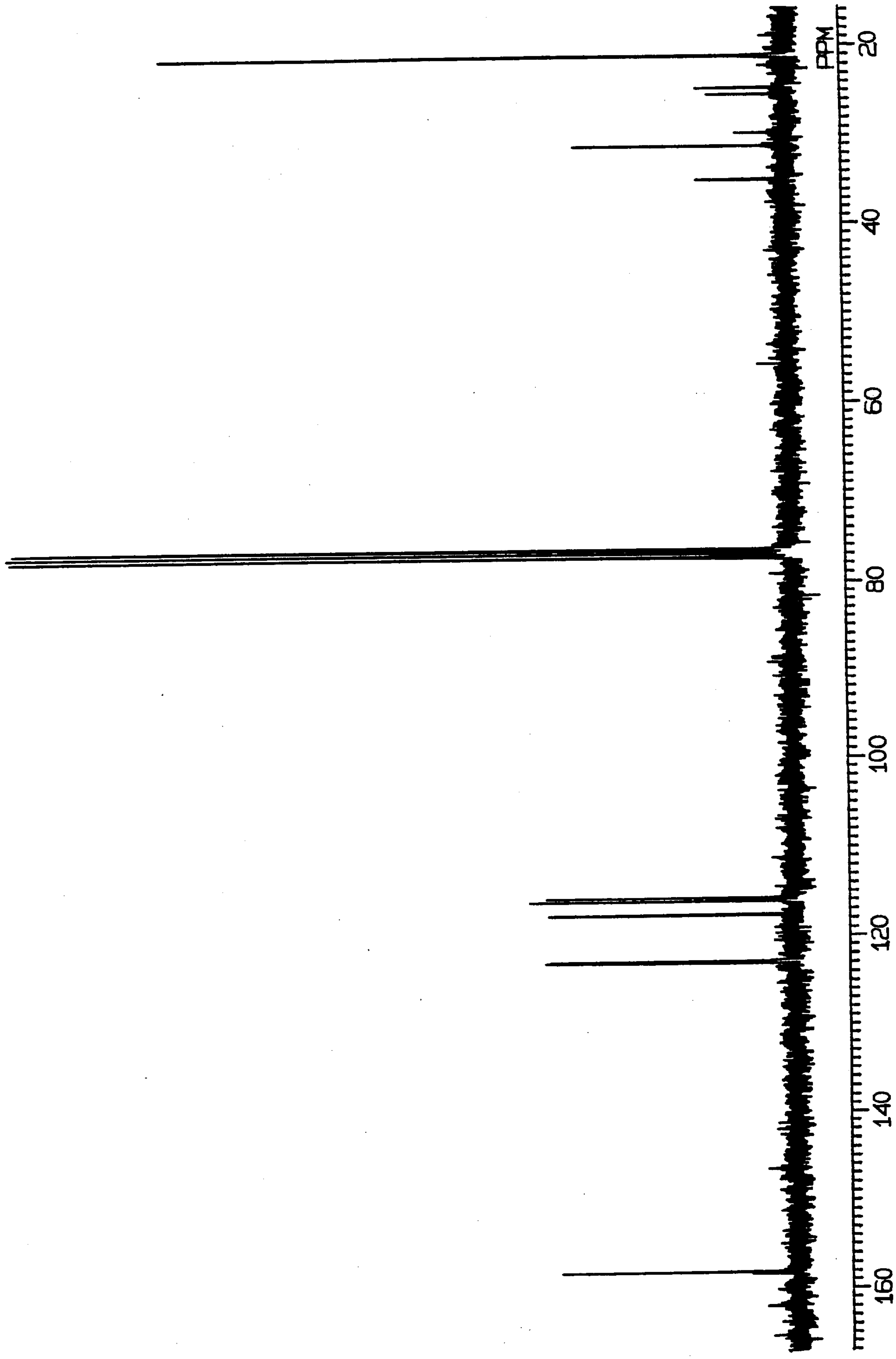


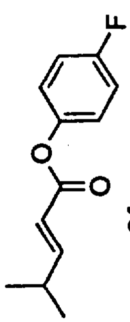


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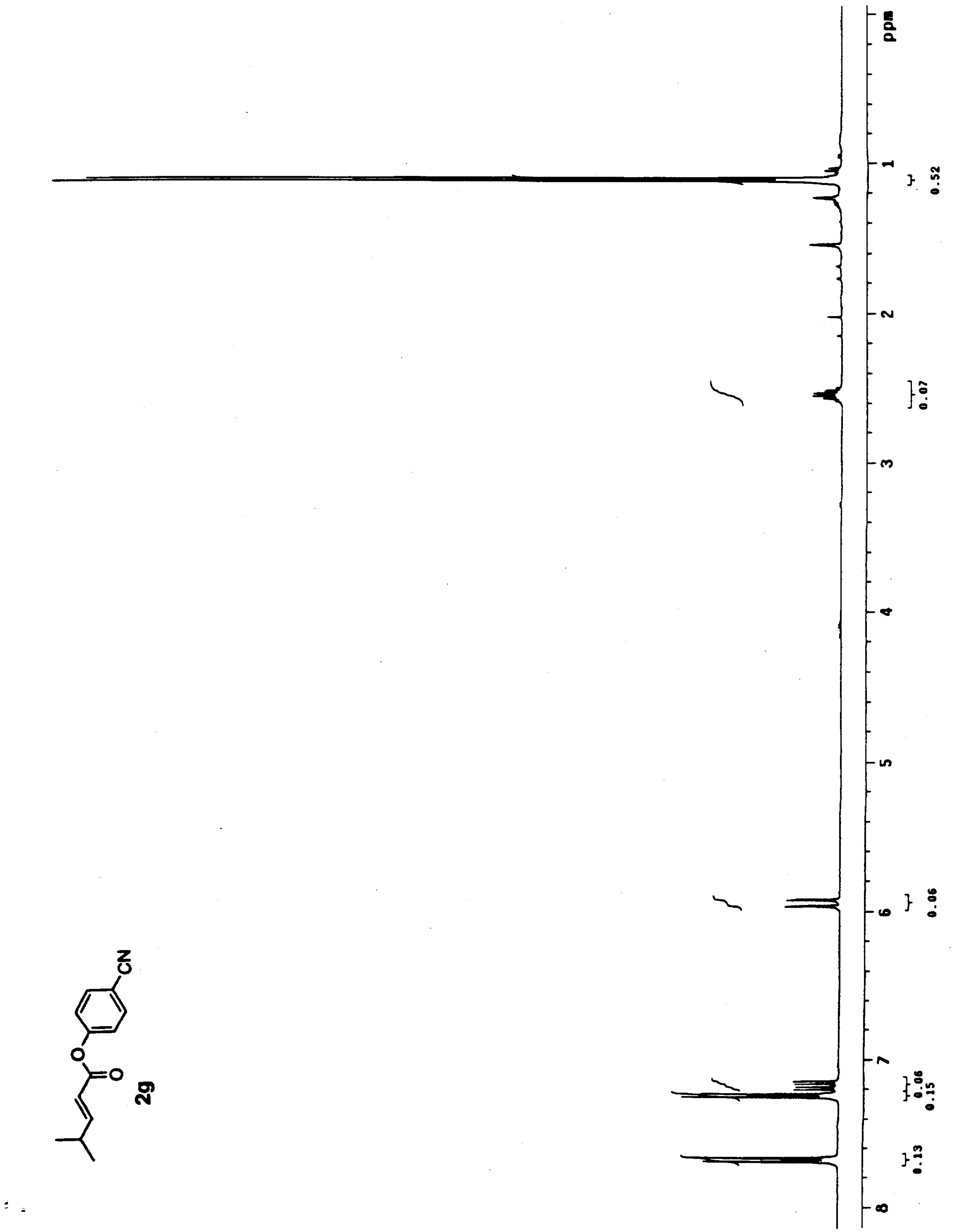
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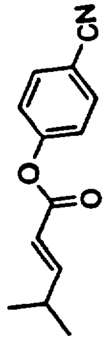


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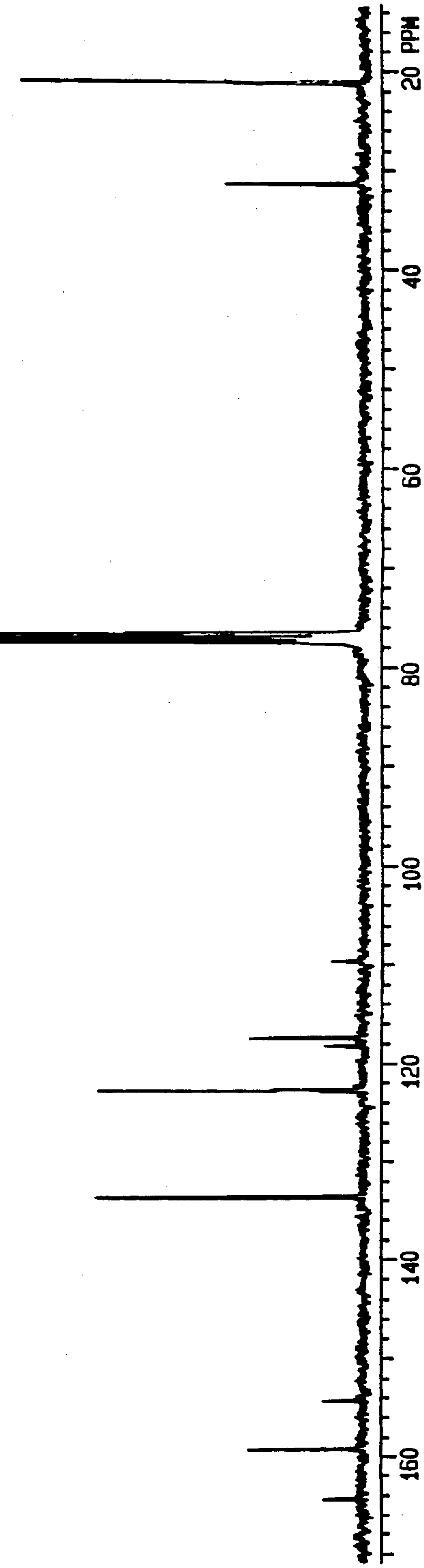

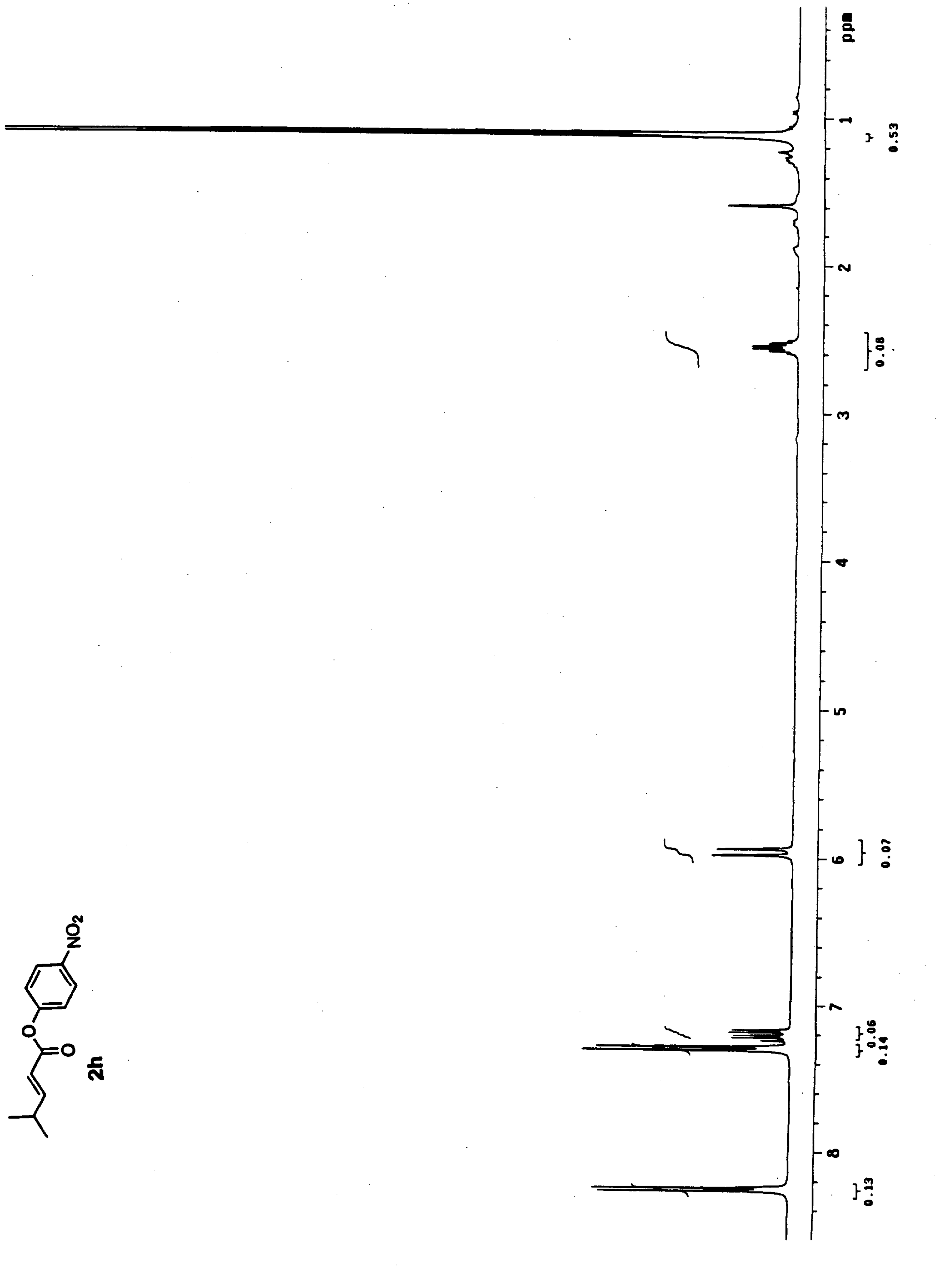
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3
4
5
6
7
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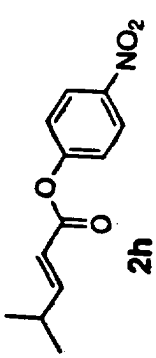
0.08
0.07
0.06
0.14
0.13

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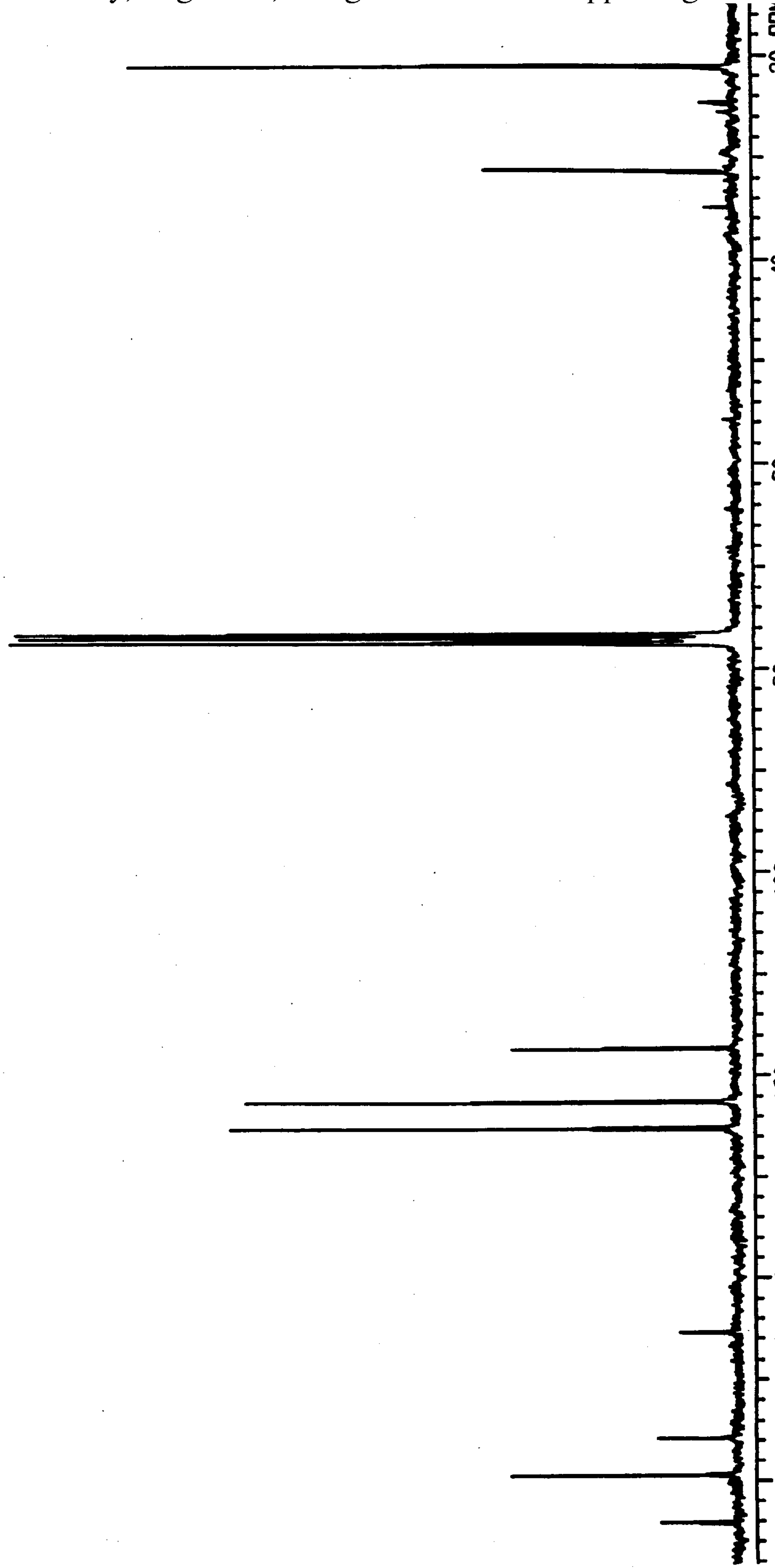

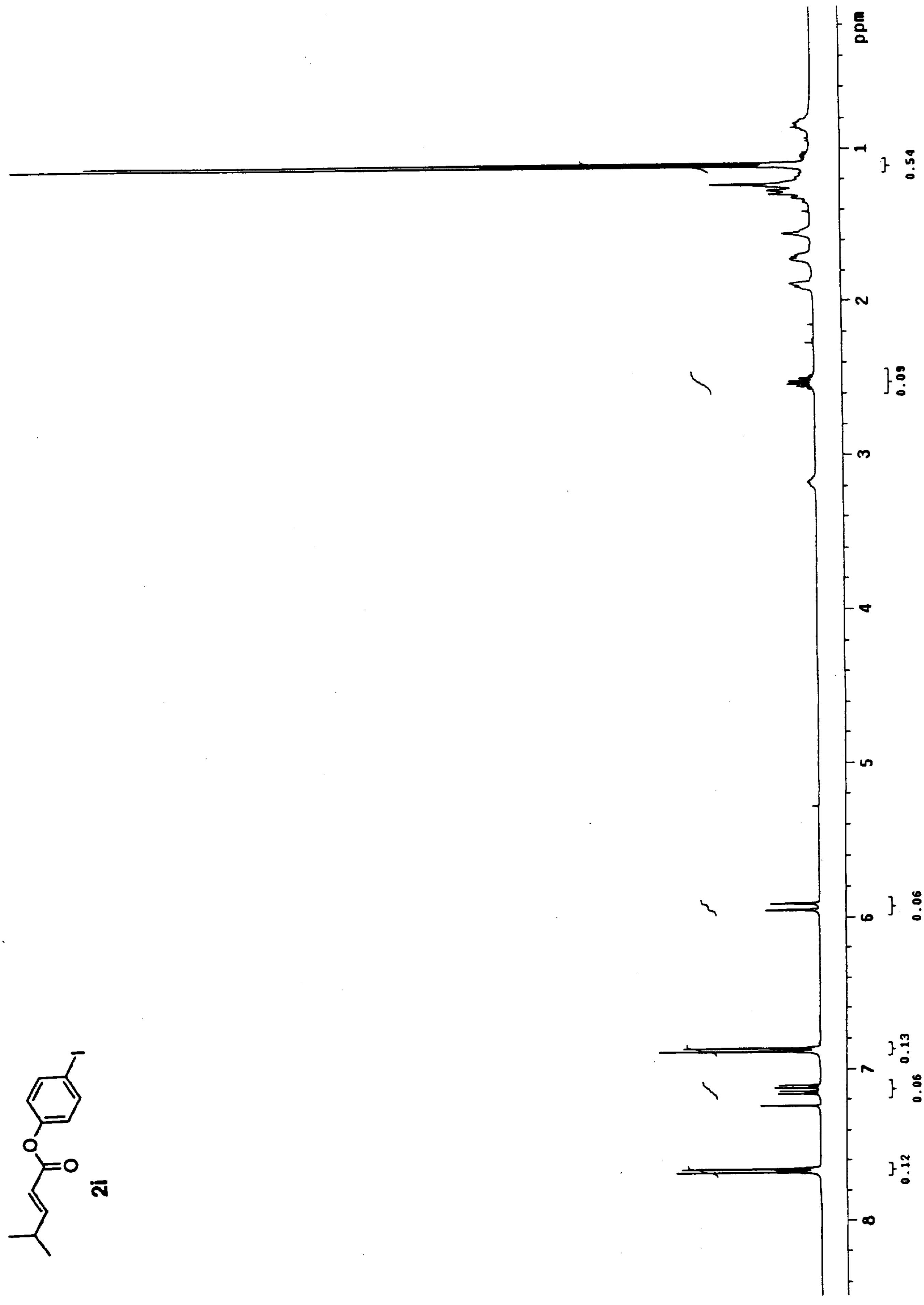
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0.06
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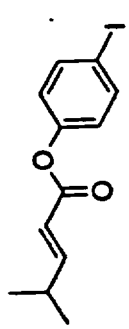
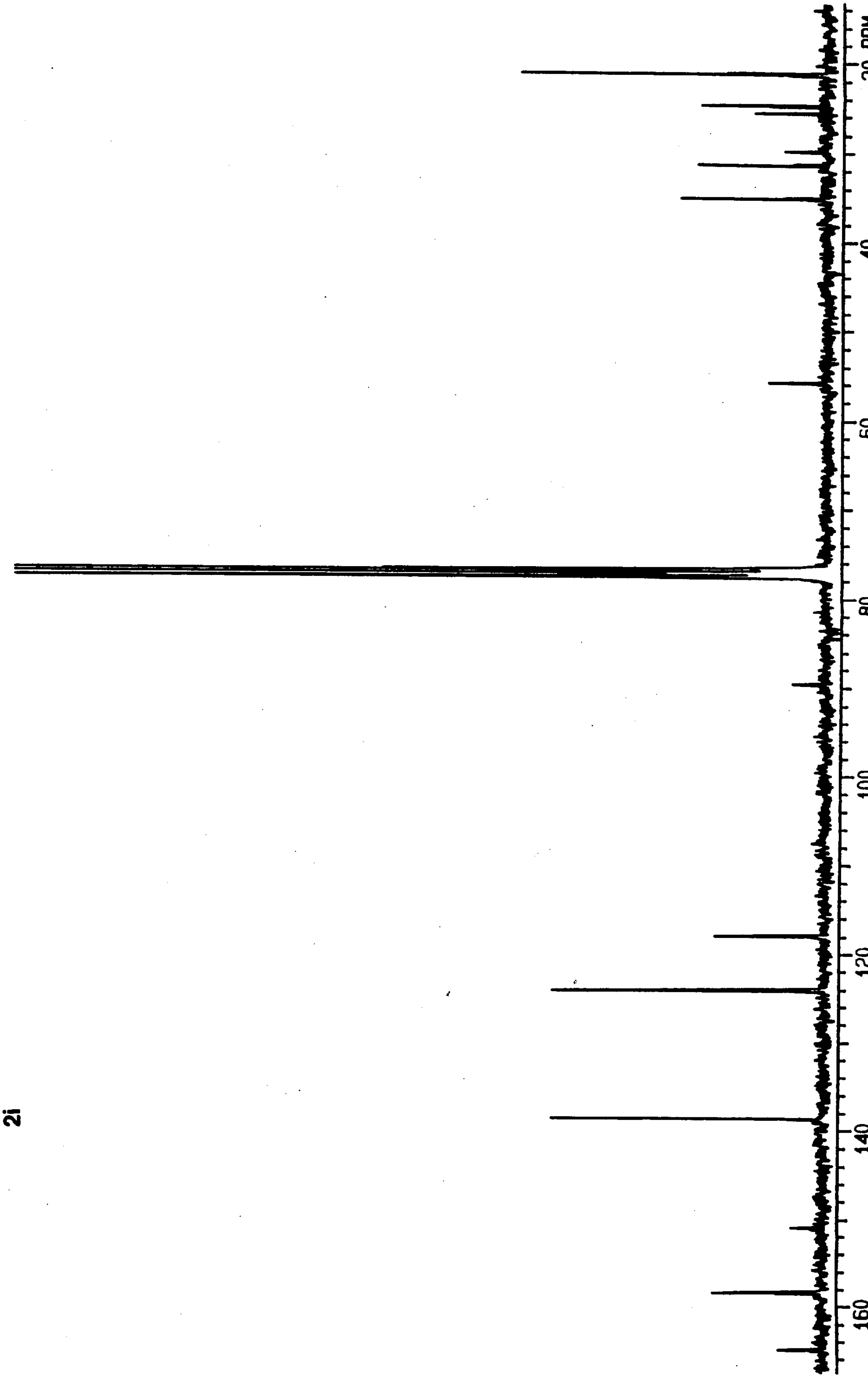
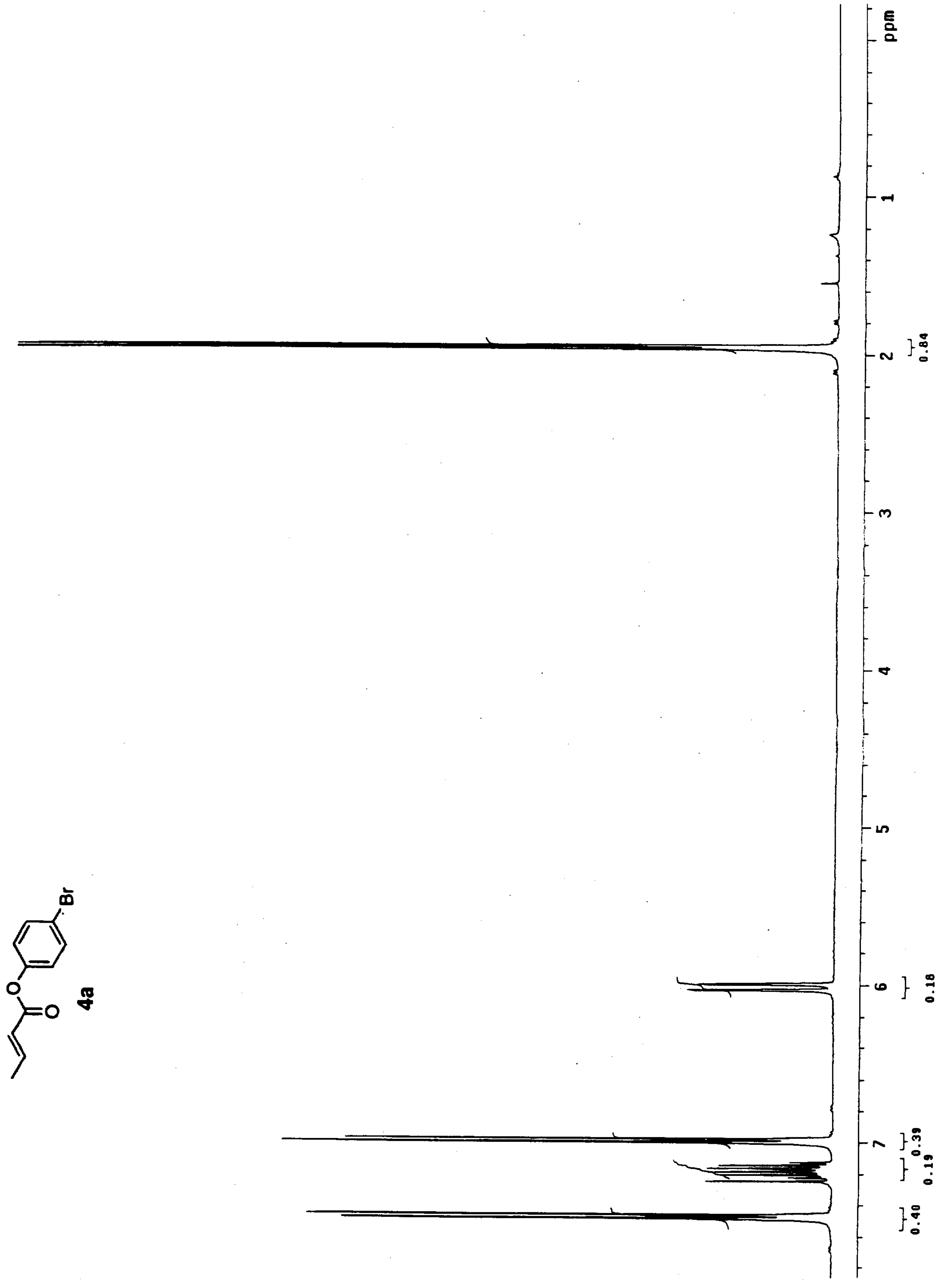


**2i**





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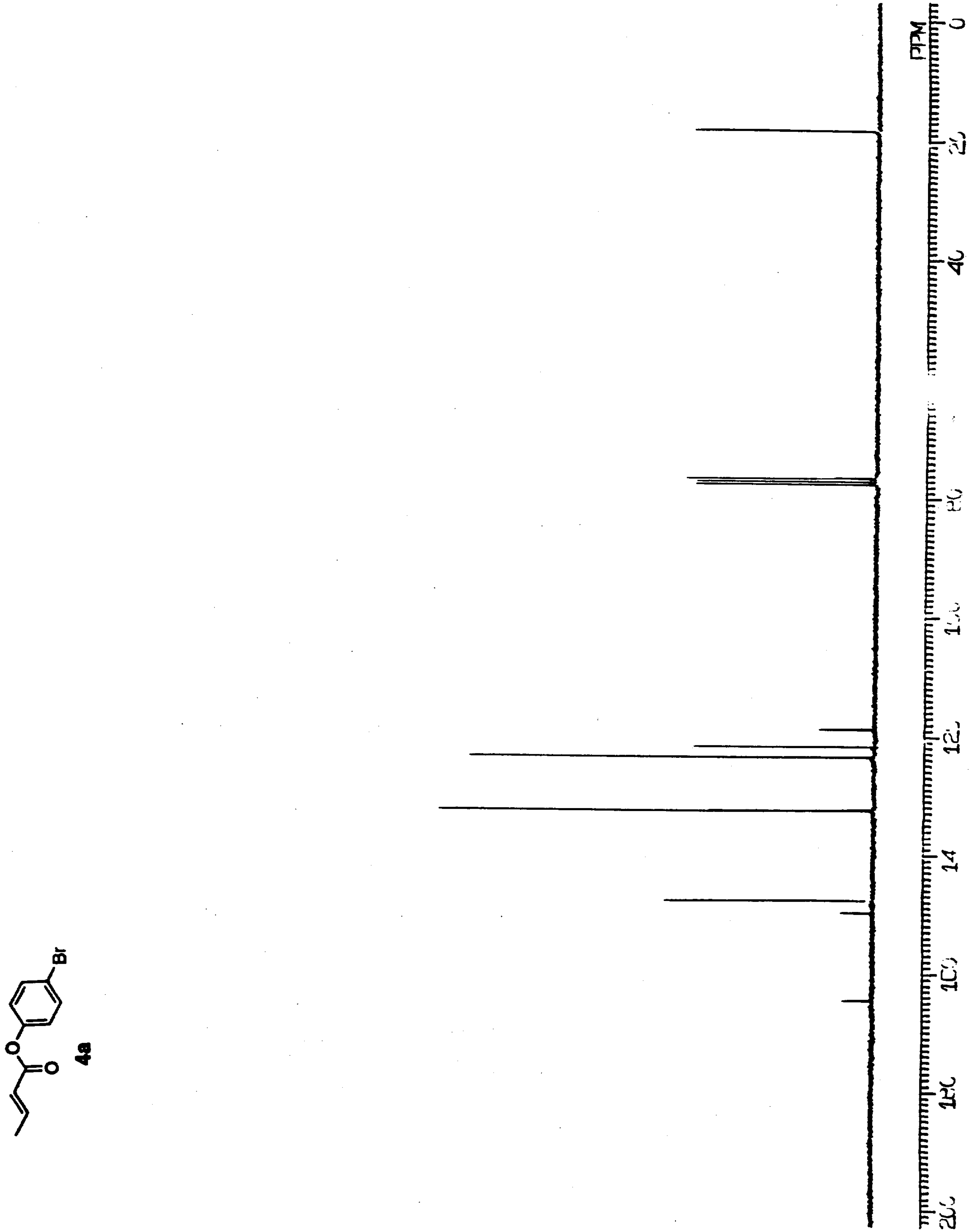
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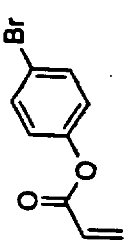
O
4a
PPM
0
40

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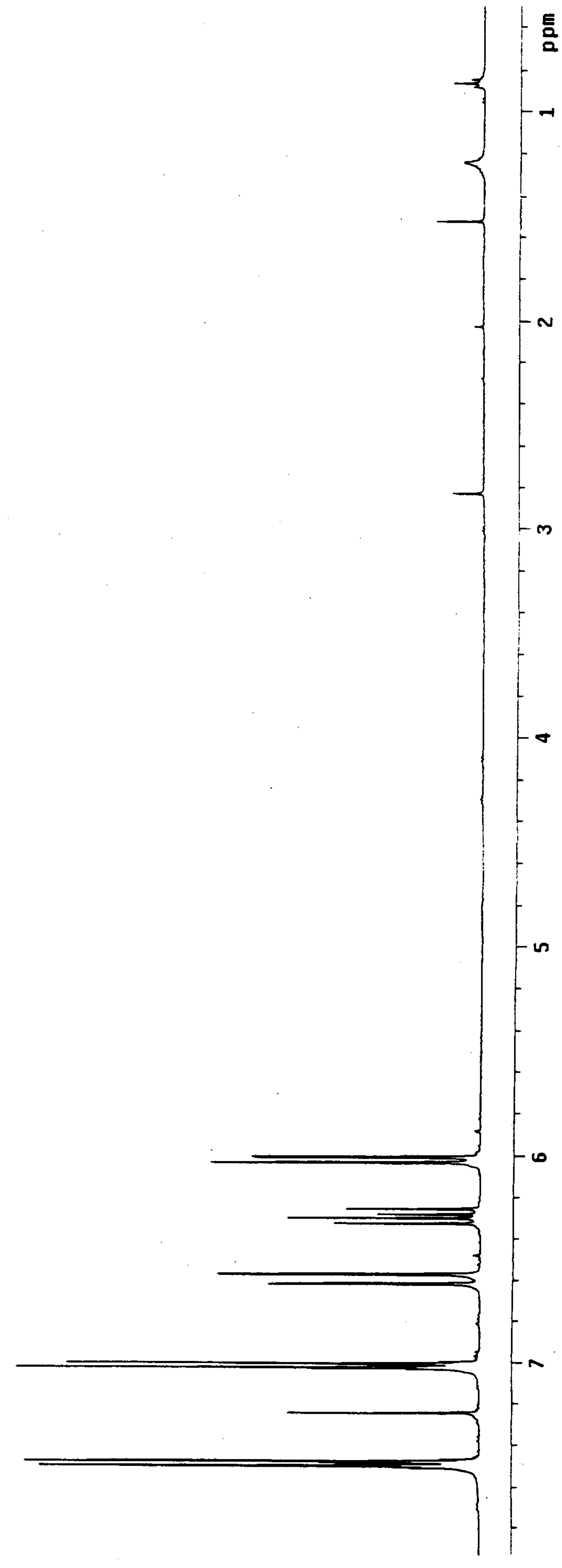
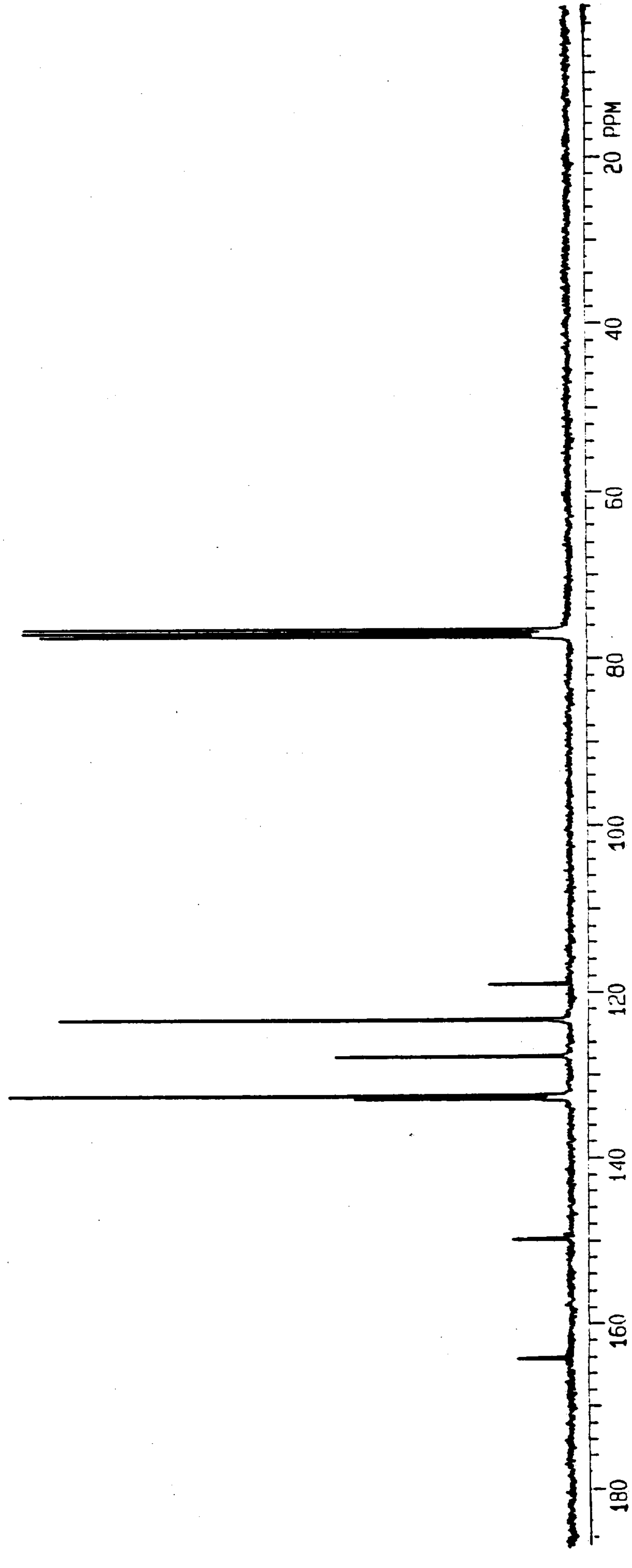
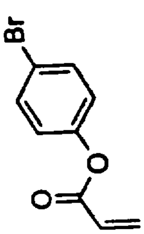
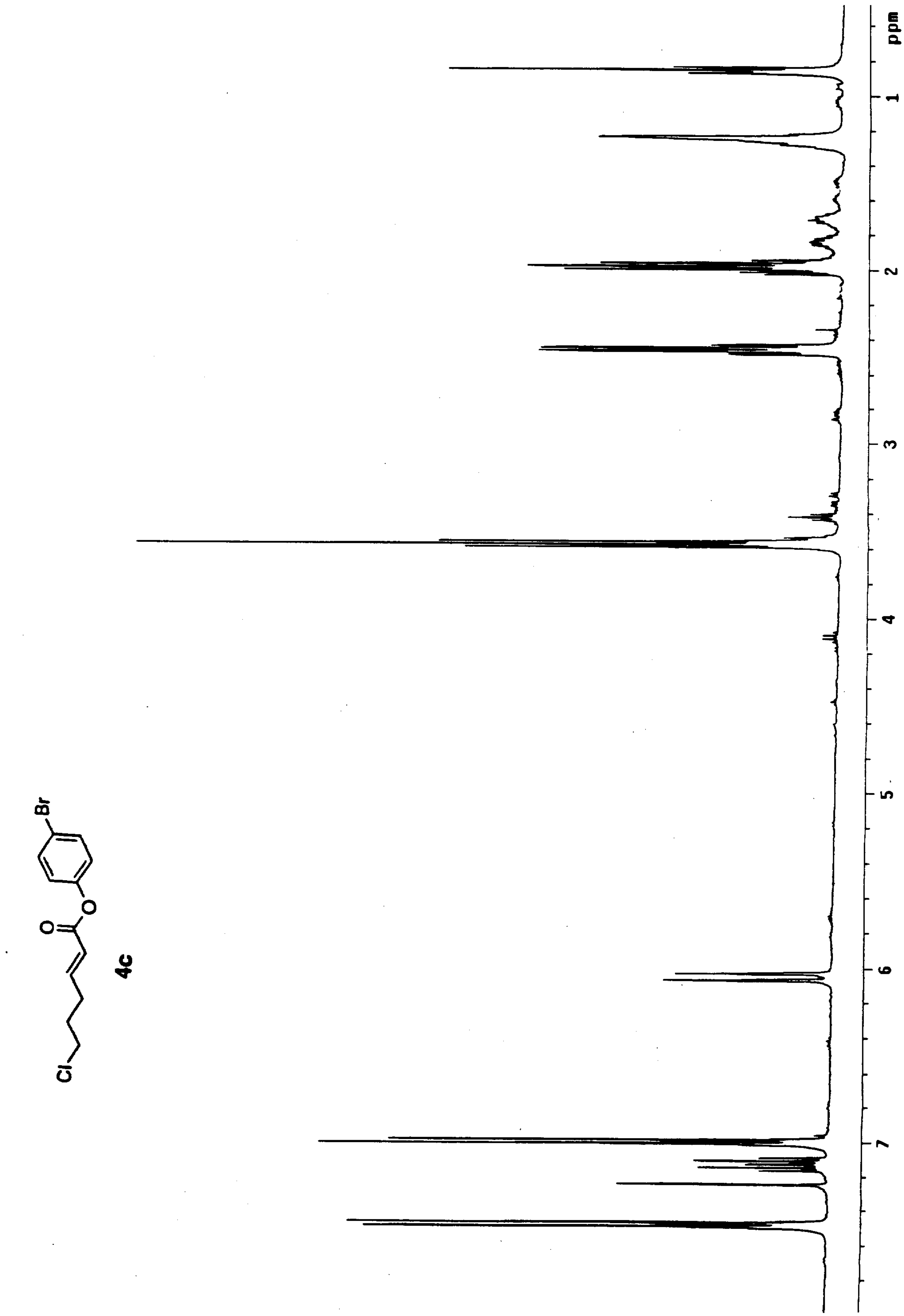





**4b**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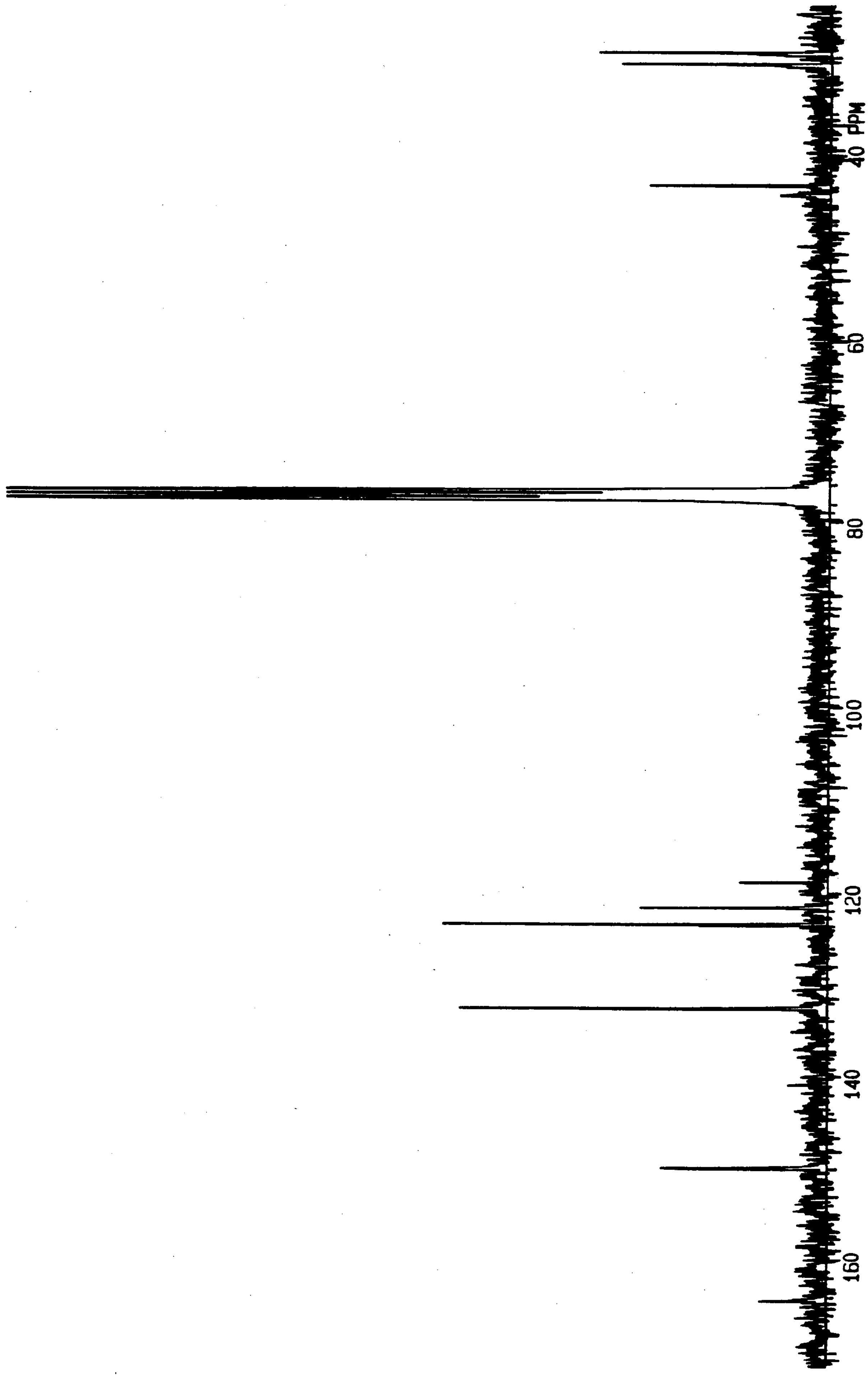
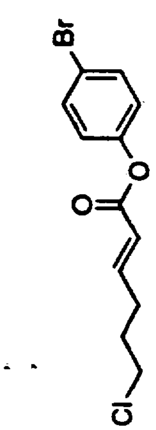
5
6
7
Br
O
O
Cl
4c

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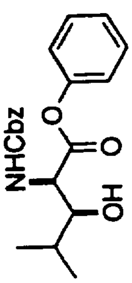
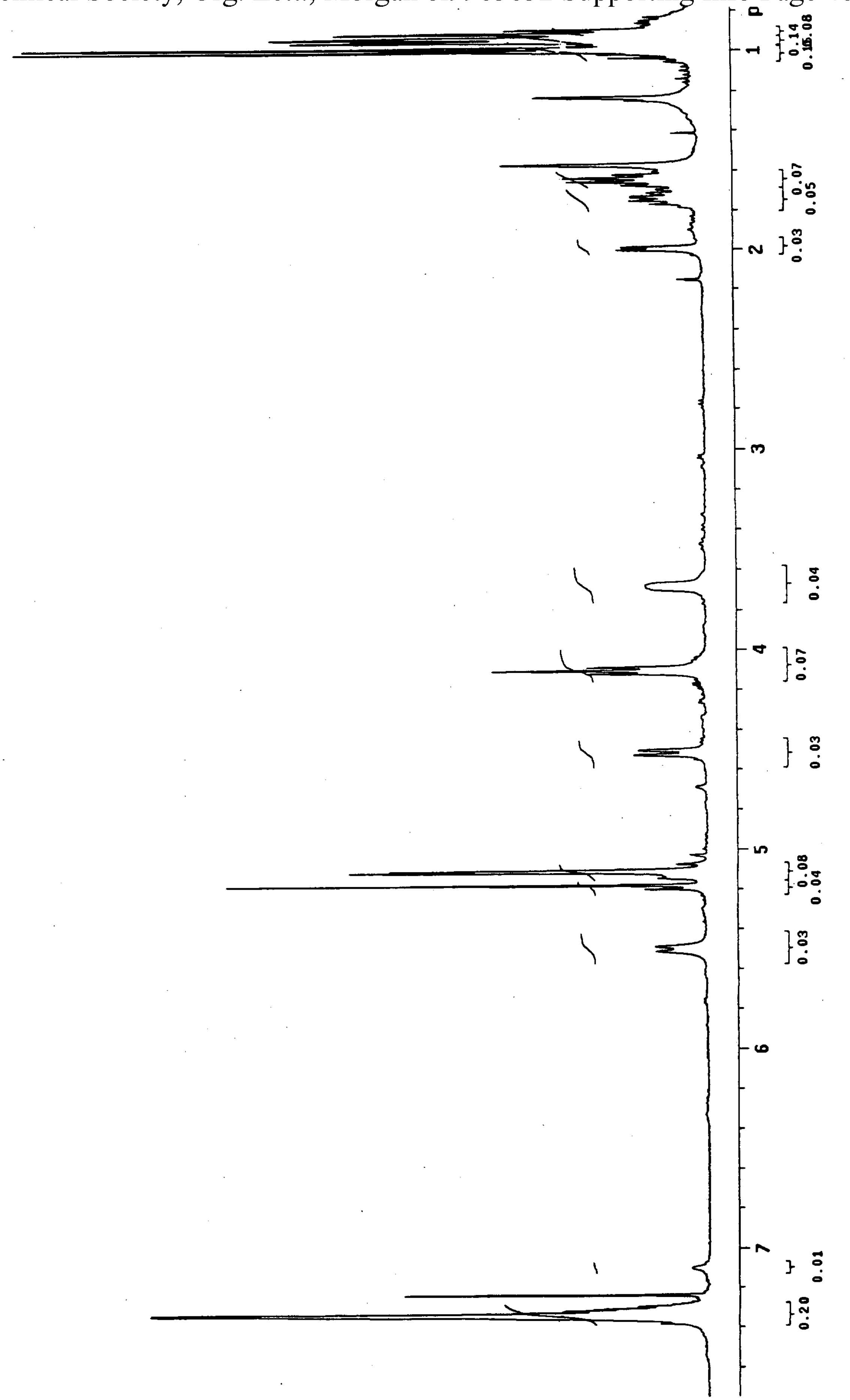


3a



p
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5
6
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0.08
0.07
0.05
0.03
0.04
0.07
0.03
0.08
0.04
0.03
0.01
0.20