A Facile Approach to β-Amino Acid Derivatives via Palladium-Catalyzed Hydrocarboxylation of Enimides with Formic Acid

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Supporting Information

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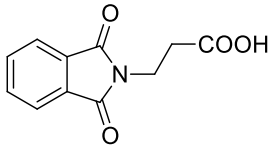
General Methods. All commercially available reagents were used without further purification. All solvents used for the reaction were purified with solvent purification system. Column chromatography was performed on silica gel (200-300 mesh). ^{1}H NMR spectra were recorded on a 400 MHz NMR spectrometer and ^{13}C NMR spectra were recorded on a 100 MHz NMR spectrometer. IR spectra were recorded on a FT-IR spectrometer. Melting points were uncorrected. Compound **1a** was purchased from the commercial supplier and other enimides were synthesized according to the literature procedures.[1,2]

1) V. I. Timokhin, N. R. Anastasi, S. S. Stahl, *J. Am. Chem. Soc.,* 2003, **125**, 12996.
2) J. L. Brice, J. E. Harang, V. I. Timokhin, N. R. Anastasi, S. S. Stahl, *J. Am. Chem. Soc.,* 2005, **127**, 2868.

Representative procedure for hydrocarboxylation (Table 2, 2b). To a mixture of $(\eta^3\text{-}C_3H_5)_2Pd_2Cl_2$ (0.00090 g, 0.0025 mmol), **L3** (0.0054 g, 0.010 mmol), and toluene (0.50 mL) in a vial (5.0 mL) were added enimide **1b** (0.1146 g, 0.50 mmol), HCOOPh (0.0122 g, 0.10 mmol) and HCOOH (0.046 g, 1.00 mmol) successively via syringe. The vial was purged with Ar to remove the air and tightly sealed with a septum cap. The reaction mixture was stirred at 80 ^{o}C for 24 h, cooled to rt, and purified by flash chromatography (silica gel, eluent: petroleum ether/ethyl acetate/HOAc = 10/1/0.11) to give compound **2b** as a light yellow solid (0.1283 g, 93% yield).

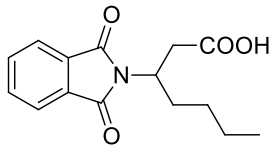
Table 2, 2a



Yellow solid; mp. 161-163^{o}C; IR (film) 3062, 1770, 1709, 1393 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.83 (m, 2H), 7.75-7.70 (m, 2H), 4.01 (t, *J* = 7.3 Hz, 2H), 2.80 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 168.2, 134.3, 132.2, 123.6, 33.6, 32.7; HRMS (ESI) Calcd for $C_{11}H_9NNaO_4$ (M+Na): 242.0424; Found: 242.0422.

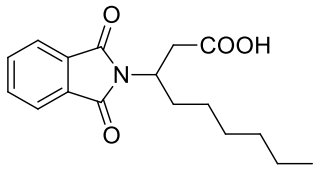
E. Guénin, M. Monteil, N. Bouchemal, T. Prangé, M. Lecouvey, *Eur. J. Org. Chem*., 2007, 3380.

Table 2, 2b



Yellow solid; mp. 118-119 ^{o}C; IR (film) 3225, 1773, 1706, 722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.79 (m, 2H), 7.74-7.68 (m, 2H), 4.66-4.58 (m, 1H), 3.20 (dd, *J* = 16.5, 9.2 Hz, 1H), 2.81 (dd, *J* = 16.5, 5.4 Hz, 1H), 2.11-1.98 (m, 1H), 1.76-1.65 (m, 1H), 1.39-1.10 (m, 4H), 0.83 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 168.5, 134.2, 131.9, 123.5, 47.9, 36.9, 32.3, 28.6, 22.4, 14.1; HRMS (ESI) Calcd for $C_{15}H_{17}NNaO_4$ (M+Na): 298.1050; Found: 298.1043.

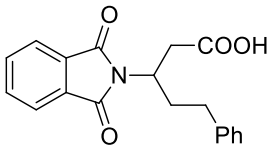
Table 2, 2c



Yellow oil; IR (film) 3222, 1770, 1709, 722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.79 (m, 2H), 7.73-7.68 (m, 2H), 4.67-4.58 (m, 1H), 3.21 (dd, *J* = 16.5, 9.2 Hz, 1H),

2.81 (dd, J = 16.5, 5.5 Hz, 1H), 2.10-1.99 (m, 1H), 1.76-1.65 (m, 1H), 1.34-1.13 (m, 8H), 0.83 (t, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 168.5, 134.2, 131.9, 123.5, 47.9, 36.9, 32.6, 31.8, 28.9, 26.4, 22.7, 14.2; HRMS (ESI) Calcd for $C_{15}H_{17}NNaO_4$ (M+Na): 326.1363; Found: 326.1358.

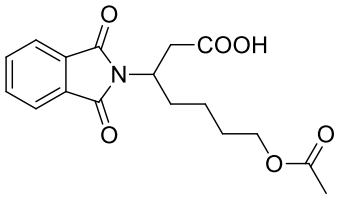
Table 2, 2d



Yellow oil; IR (film) 3225, 1773, 1710, 720 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.74 (m, 2H), 7.71-7.66 (m, 2H), 7.18-7.01 (m, 5H), 4.75-4.66 (m, 1H), 3.20 (dd, J = 16.6, 9.0 Hz, 1H), 2.85 (dd, J = 16.6, 5.7 Hz, 1H), 2.71-2.61 (m, 3H), 2.59-2.43 (m, 2H), 2.08-1.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 168.5, 140.7, 134.1, 131.8, 128.5, 128.4, 126.1, 123.5, 47.8, 37.0, 33.7, 33.0; HRMS (ESI) Calcd for $C_{19}H_{16}NNaO_4$ (M+Na): 346.1050; Found: 346.1048.

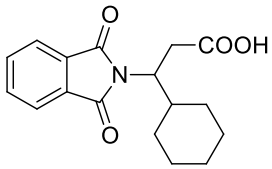
A. Temperini, R. Terlizzi, L. Testaferri, M. Tiecco, *Chem. Eur. J.,* 2009, **15**, 7883.

Table 2, 2e



Yellow oil; IR (film) 3219, 1770, 1733, 1706, 719 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83-7.78 (m, 2H), 7.73-7.67 (m, 2H), 4.66-4.57 (m, 1H), 4.03-3.91 (m, 2H), 3.15 (dd, J = 16.5, 8.9 Hz, 1H), 2.80 (dd, J = 16.5, 5.6 Hz, 1H), 2.14-2.02 (m, 1H), 1.96 (s, 3H), 1.77-1.51 (m, 3H), 1.39-1.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 171.5, 168.5, 134.3, 131.8, 123.5, 64.3, 47.7, 37.0, 32.0, 28.1, 22.9, 21.1; HRMS (ESI) Calcd for $C_{17}H_{19}NNaO_6$ (M+Na): 356.1105; Found: 356.1106.

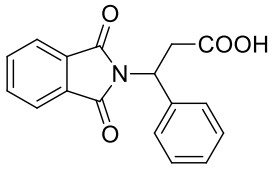
Table 2, 2f



Yellow oil; IR (film) 3224, 1770, 1709, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82-7.77 (m, 2H), 7.73-7.67 (m, 2H), 4.36-4.27 (m, 1H), 3.30-3.20 (m, 1H), 2.84 (dt, *J* = 16.5, 4.2 Hz, 1H), 2.06-1.43 (m, 6H), 1.33-0.80 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 168.6, 134.1, 131.7, 123.5, 52.9, 39.6, 34.2, 30.5, 29.8, 26.1, 25.9, 25.8; HRMS (ESI) Calcd for $C_{17}H_{19}NNaO_4$ (M+Na): 324.1206; Found: 324.1207.

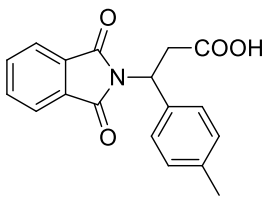
A. Temperini, R. Terlizzi, L. Testaferri, M. Tiecco, *Chem. Eur. J.,* 2009, **15**, 7883.

Table 2, 2g



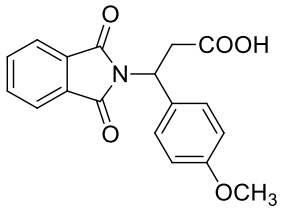
Yellow solid; mp. 177-178 ^oC; IR (film) 3219, 1770, 1711, 719, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82-7.77 (m, 2H), 7.71-7.66 (m, 2H), 7.54-7.49 (m, 2H), 7.35-7.25 (m, 3H), 5.79 (dd, *J* = 9.9, 5.8 Hz, 1H), 3.85 (dd, *J* = 17.1, 9.9 Hz, 1H), 3.28 (dd, *J* = 17.1, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 168.2, 138.5, 134.2, 131.9, 129.0, 128.5, 127.9, 123.6, 50.7, 35.9; HRMS (ESI) Calcd for $C_{17}H_{13}NNaO_4$ (M+Na): 318.0737; Found: 318.0739.

Table 2, 2h



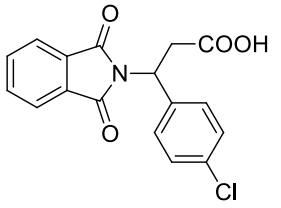
Yellow solid; mp. 175-176 °C; IR (film) 3094, 1770, 1704, 717 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81-7.76 (m, 2H), 7.70-7.65 (m, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 5.76 (dd, *J* = 9.8, 5.9 Hz, 1H), 3.81 (dd, *J* = 17.0, 9.8 Hz, 1H), 3.27 (dd, *J* = 17.0, 5.9 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 168.2, 138.2, 135.5, 134.2, 131.9, 129.6, 127.8, 123.5, 50.4, 35.9, 21.2; HRMS (ESI) Calcd for $C_{18}H_{15}NNaO_4$ (M+Na): 332.0893; Found: 332.0894.

Table 2, 2i



Yellow oil; IR (film) 3213, 1767, 1709, 716 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81-7.76 (m, 2H), 7.70-7.66 (m, 2H), 7.46 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 5.75 (dd, *J* = 9.8, 6.0 Hz, 1H), 3.80 (dd, *J* = 17.0, 9.8 Hz, 1H), 3.76 (s, 3H), 3.28 (dd, *J* = 17.0, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 168.3, 159.6, 134.2, 132.0, 130.7, 129.3, 123.5, 114.2, 55.4, 50.2, 36.0; HRMS (ESI) Calcd for $C_{18}H_{15}NNaO_5$ (M+Na): 348.0842; Found: 348.0846.

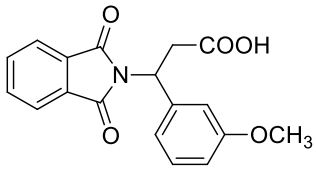
Table 2, 2j



Yellow solid; mp. 149-151 °C; IR (film) 3222, 1771, 1712, 717 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83-7.77 (m, 2H), 7.72-7.67 (m, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 5.76 (dd, *J* = 9.4, 6.2 Hz, 1H), 3.76 (dd, *J* = 17.1, 9.4 Hz, 1H), 3.30 (dd, *J* = 17.1, 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 168.1, 136.9, 134.4, 131.8, 129.5, 129.1,

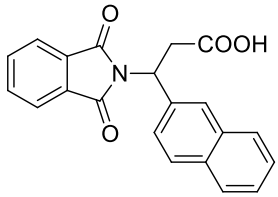
123.7, 50.0, 35.8; HRMS (ESI) Calcd for $C_{17}H_{12}ClNNaO_4$ (M+Na): 352.0347; Found: 352.0350.

Table 2, 2k



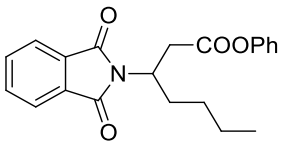
Yellow solid; mp.118-119 ^{o}C; IR (film) 3219, 1770, 1711, 721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.77 (m, 2H), 7.71-7.66 (m, 2H), 7.24 (t, *J* = 8.1 Hz, 1H), 7.12-7.05 (m, 2H), 6.81 (dd, *J* = 8.2, 2.4 Hz, 1H), 5.76 (dd, *J* = 10.0, 5.8 Hz, 1H), 3.84 (dd, *J* = 17.1, 10.0 Hz, 1H), 3.78 (s, 3H), 3.27 (dd, *J* = 17.1, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 168.2, 160.0, 140.0, 134.2, 131.9, 130.0, 123.6, 120.2, 114.0, 113.7, 55.4, 50.8, 35.9; HRMS (ESI) Calcd for $C_{18}H_{15}NNaO_5$ (M+Na): 348.0842; Found: 348.0846.

Table 2, 2l



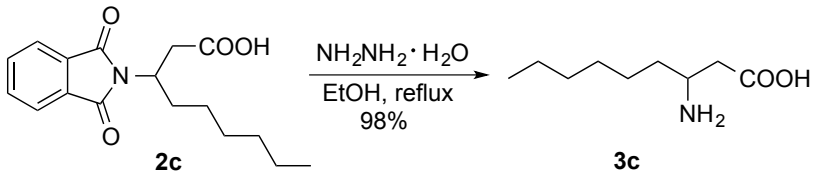
Yellow solid; mp. 173-175 ^{o}C; IR (film) 3463, 1770, 1705 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.86-7.75 (m, 5H), 7.71-7.61 (m, 3H), 7.50-7.42 (m, 2H), 5.97 (dd, *J* = 9.8, 5.9 Hz, 1H), 3.94 (dd, *J* = 17.0, 9.8 Hz, 1H), 3.42 (dd, *J* = 17.0, 5.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 168.3, 135.8, 134.3, 133.3, 133.2, 131.9, 128.9, 128.4, 127.8, 127.1, 126.6, 126.57, 125.7, 123.6, 50.9, 35.8; HRMS (ESI) Calcd for $C_{21}H_{16}NO_4$ (M+H): 346.1074; Found: 346.1076.

Table 1, 3b



Yellow solid; mp. 100-101 ^{o}C; IR (film) 1756, 1708, 1638, 1370 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.80 (m, 2H), 7.73-7.67 (m, 2H), 7.34-7.28 (m, 2H), 7.20-7.14 (m, 1H), 7.01-6.96 (m, 2H), 4.82-4.73 (m, 1H), 3.44 (dd, *J* = 15.9, 9.8 Hz, 1H), 3.02 (dd, *J* = 15.9, 5.0 Hz, 1H), 2.23-2.10 (m, 1H), 1.88-1.77 (m, 1H), 1.44-1.19 (m, 4H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 168.6, 150.6, 134.2, 132.0, 129.6, 126.1, 123.5, 121.6, 48.3, 37.4, 32.4, 28.7, 22.4, 14.1; HRMS (ESI) Calcd for $C_{21}H_{22}NO_4$ (M+H): 352.1543; Found: 352.1545.

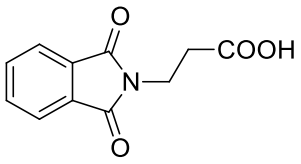
Procedure for the hydrolysis in Scheme 3



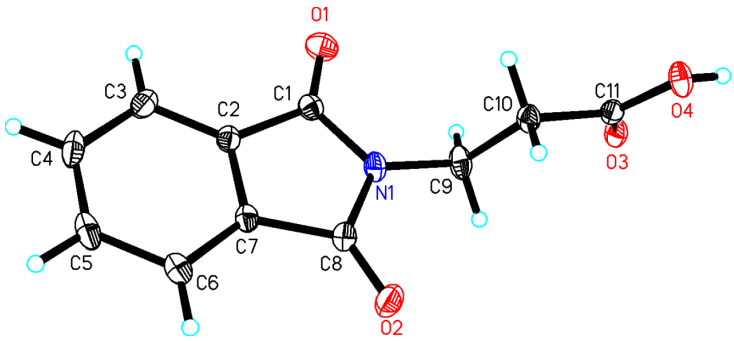
To a solution of compound **2c** (0.1517 g, 0.50 mmol) in EtOH (14 mL) was added hydrazine hydrate (0.41 g, 8.3 mmol) dropwise. The reaction mixture was stirred at reflux for 4 h, cooled to room temperature, filtered, and washed with ether (3x). The filtrate was concentrated to give amino acid **3c** (0.085 g, 98%) as a white solid; mp. 212-213 ^{o}C; IR (film) 3405, 2955, 2926, 2859, 1573, 1396 cm^{-1}; ^{1}H NMR (400 MHz, D_2O) δ 3.54-3.45 (m, 1H), 2.57 (dd, *J* = 16.6, 4.8 Hz, 1H), 2.43 (dd, *J* = 16.6, 8.3 Hz, 1H), 1.66 (m, 2H), 1.45-1.24 (m, 8H), 0.88 (t, *J* = 5.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 49.4, 38.5, 32.1, 30.7, 28.0, 24.3, 21.8, 13.3; HRMS (ESI) Calcd for $C_9H_{20}NO_2$ (M+H): 174.1489; Found: 174.1484.

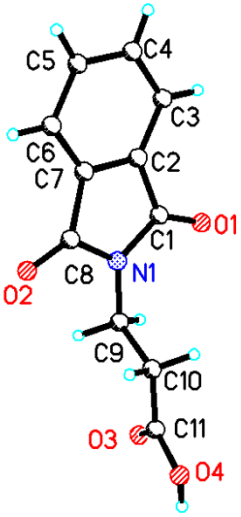
B. Weiner, A. Baeza, T. Jerphagnon, B. L. Feringa, *J. Am. Chem. Soc.*, 2009, **131**, 9473.

The X-ray structure of compound **2a**



2a





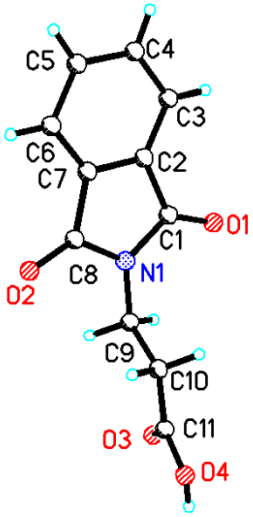


Table 1. Crystal data and structure refinement for **2a**.

Identification code	**2a**	
Empirical formula	C_{11} H_9 N O_4	
Formula weight	219.19	
Temperature	173.1500 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 8.629(2) Å	a= 80.505(11)°.
	b = 10.440(3) Å	b= 76.238(11)°.
	c = 12.379(4) Å	g = 65.983(9)°.
Volume	986.5(5) $Å^3$	
Z	4	
Density (calculated)	1.476 Mg/m^3	
Absorption coefficient	0.114 mm^{-1}	
F(000)	456	
Crystal size	0.43 x 0.32 x 0.24 mm^3	
Theta range for data collection	2.630 to 27.497°.	
Index ranges	-10<=h<=11, -13<=k<=12, -15<=l<=16	
Reflections collected	8415	
Independent reflections	4432 [R(int) = 0.0257]	
Completeness to theta = 26.000°	98.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.8664	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4432 / 0 / 291	
Goodness-of-fit on F^2	1.127	
Final R indices [I>2sigma(I)]	R1 = 0.0492, wR2 = 0.1175	
R indices (all data)	R1 = 0.0553, wR2 = 0.1215	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.248 and -0.252 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **2a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O1	2179(2)	4723(1)	376(1)	39(1)
O2	2132(2)	9137(1)	-688(1)	39(1)
O3	-1203(2)	7294(1)	-2604(1)	29(1)
O4	-3599(2)	8611(1)	-1488(1)	33(1)
N1	1908(2)	6969(1)	-350(1)	27(1)
C1	2480(2)	5757(2)	361(1)	26(1)
C2	3498(2)	6036(2)	1046(1)	25(1)
C3	4341(2)	5203(2)	1882(1)	32(1)
C4	5164(2)	5770(2)	2390(1)	37(1)
C5	5144(2)	7109(2)	2066(1)	36(1)
C6	4310(2)	7944(2)	1211(1)	31(1)
C7	3486(2)	7375(2)	715(1)	24(1)
C8	2458(2)	7994(2)	-185(1)	27(1)
C9	962(2)	7099(2)	-1219(1)	33(1)
C10	-975(2)	7823(2)	-850(1)	27(1)
C11	-1916(2)	7873(2)	-1742(1)	25(1)
O1A	7350(2)	4462(1)	4622(1)	39(1)
O2A	8693(2)	-23(1)	6221(1)	40(1)
O3A	5061(2)	1644(2)	3108(1)	43(1)
O4A	2678(2)	2080(2)	4405(1)	49(1)
N1A	7796(2)	2160(1)	5259(1)	27(1)
C1A	7964(2)	3436(2)	5234(1)	26(1)
C2A	9022(2)	3237(2)	6083(1)	24(1)
C3A	9587(2)	4153(2)	6400(1)	30(1)
C4A	10595(2)	3645(2)	7220(1)	33(1)
C5A	11013(2)	2277(2)	7694(1)	33(1)
C6A	10435(2)	1360(2)	7375(1)	29(1)
C7A	9435(2)	1871(2)	6563(1)	23(1)
C8A	8646(2)	1164(2)	6040(1)	26(1)
C9A	7000(2)	1851(2)	4476(1)	32(1)
C10A	5125(2)	2077(2)	4927(1)	29(1)
C11A	4302(2)	1902(2)	4054(1)	28(1)

Table 3. Bond lengths [Å] and angles [°] for **2a**.

O1-C1	1.205(2)
O2-C8	1.206(2)
O3-C11	1.2161(19)
O4-H4	0.8200
O4-C11	1.3244(19)
N1-C1	1.396(2)
N1-C8	1.394(2)
N1-C9	1.4564(19)
C1-C2	1.490(2)
C2-C3	1.379(2)
C2-C7	1.387(2)
C3-H3	0.9300
C3-C4	1.388(3)
C4-H4A	0.9300
C4-C5	1.384(3)
C5-H5	0.9300
C5-C6	1.395(2)
C6-H6	0.9300
C6-C7	1.381(2)
C7-C8	1.487(2)
C9-H9A	0.9700
C9-H9B	0.9700
C9-C10	1.515(2)
C10-H10A	0.9700
C10-H10B	0.9700
C10-C11	1.502(2)
O1A-C1A	1.2101(19)
O2A-C8A	1.208(2)
O3A-C11A	1.211(2)
O4A-H4AA	0.8200
O4A-C11A	1.308(2)
N1A-C1A	1.392(2)
N1A-C8A	1.393(2)
N1A-C9A	1.4538(19)
C1A-C2A	1.487(2)
C2A-C3A	1.378(2)

C2A-C7A	1.386(2)
C3A-H3A	0.9300
C3A-C4A	1.391(2)
C4A-H4AB	0.9300
C4A-C5A	1.385(3)
C5A-H5A	0.9300
C5A-C6A	1.389(2)
C6A-H6A	0.9300
C6A-C7A	1.379(2)
C7A-C8A	1.485(2)
C9A-H9AA	0.9700
C9A-H9AB	0.9700
C9A-C10A	1.512(2)
C10A-H10C	0.9700
C10A-H10D	0.9700
C10A-C11A	1.498(2)

C11-O4-H4	109.5
C1-N1-C9	123.58(14)
C8-N1-C1	112.17(12)
C8-N1-C9	124.09(14)
O1-C1-N1	124.74(15)
O1-C1-C2	129.49(15)
N1-C1-C2	105.77(13)
C3-C2-C1	130.34(15)
C3-C2-C7	121.70(15)
C7-C2-C1	107.96(13)
C2-C3-H3	121.5
C2-C3-C4	117.08(16)
C4-C3-H3	121.5
C3-C4-H4A	119.4
C5-C4-C3	121.29(16)
C5-C4-H4A	119.4
C4-C5-H5	119.2
C4-C5-C6	121.63(16)
C6-C5-H5	119.2
C5-C6-H6	121.7
C7-C6-C5	116.66(16)

C7-C6-H6	121.7
C2-C7-C8	108.38(13)
C6-C7-C2	121.65(15)
C6-C7-C8	129.96(15)
O2-C8-N1	125.22(15)
O2-C8-C7	129.05(15)
N1-C8-C7	105.73(13)
N1-C9-H9A	109.1
N1-C9-H9B	109.1
N1-C9-C10	112.61(13)
H9A-C9-H9B	107.8
C10-C9-H9A	109.1
C10-C9-H9B	109.1
C9-C10-H10A	109.4
C9-C10-H10B	109.4
H10A-C10-H10B	108.0
C11-C10-C9	111.26(13)
C11-C10-H10A	109.4
C11-C10-H10B	109.4
O3-C11-O4	123.86(14)
O3-C11-C10	123.37(14)
O4-C11-C10	112.77(13)
C11A-O4A-H4AA	109.5
C1A-N1A-C8A	111.99(12)
C1A-N1A-C9A	123.99(13)
C8A-N1A-C9A	123.66(13)
O1A-C1A-N1A	124.52(15)
O1A-C1A-C2A	129.50(15)
N1A-C1A-C2A	105.98(13)
C3A-C2A-C1A	130.58(14)
C3A-C2A-C7A	121.49(14)
C7A-C2A-C1A	107.93(13)
C2A-C3A-H3A	121.4
C2A-C3A-C4A	117.11(15)
C4A-C3A-H3A	121.4
C3A-C4A-H4AB	119.4
C5A-C4A-C3A	121.29(15)
C5A-C4A-H4AB	119.4

C4A-C5A-H5A	119.3
C4A-C5A-C6A	121.38(15)
C6A-C5A-H5A	119.3
C5A-C6A-H6A	121.5
C7A-C6A-C5A	117.01(15)
C7A-C6A-H6A	121.5
C2A-C7A-C8A	108.24(13)
C6A-C7A-C2A	121.72(14)
C6A-C7A-C8A	130.04(15)
O2A-C8A-N1A	124.85(14)
O2A-C8A-C7A	129.29(15)
N1A-C8A-C7A	105.86(13)
N1A-C9A-H9AA	109.0
N1A-C9A-H9AB	109.0
N1A-C9A-C10A	112.87(13)
H9AA-C9A-H9AB	107.8
C10A-C9A-H9AA	109.0
C10A-C9A-H9AB	109.0
C9A-C10A-H10C	109.4
C9A-C10A-H10D	109.4
H10C-C10A-H10D	108.0
C11A-C10A-C9A	111.15(13)
C11A-C10A-H10C	109.4
C11A-C10A-H10D	109.4
O3A-C11A-O4A	123.37(14)
O3A-C11A-C10A	123.10(14)
O4A-C11A-C10A	113.51(14)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **2a**. The anisotropicdisplacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O1	43(1)	35(1)	45(1)	-6(1)	-6(1)	-21(1)
O2	45(1)	30(1)	40(1)	6(1)	-19(1)	-11(1)
O3	33(1)	30(1)	27(1)	-3(1)	-13(1)	-10(1)
O4	29(1)	39(1)	35(1)	-10(1)	-14(1)	-8(1)
N1	28(1)	29(1)	27(1)	-5(1)	-12(1)	-9(1)
C1	24(1)	28(1)	26(1)	-5(1)	-3(1)	-9(1)
C2	21(1)	29(1)	22(1)	-3(1)	-4(1)	-7(1)
C3	27(1)	35(1)	26(1)	4(1)	-4(1)	-6(1)
C4	24(1)	54(1)	23(1)	-1(1)	-9(1)	-4(1)
C5	23(1)	58(1)	31(1)	-13(1)	-6(1)	-13(1)
C6	26(1)	37(1)	33(1)	-7(1)	-6(1)	-13(1)
C7	21(1)	28(1)	24(1)	-3(1)	-6(1)	-7(1)
C8	26(1)	26(1)	26(1)	-3(1)	-8(1)	-7(1)
C9	31(1)	43(1)	28(1)	-10(1)	-13(1)	-9(1)
C10	29(1)	28(1)	26(1)	-4(1)	-12(1)	-11(1)
C11	28(1)	21(1)	28(1)	-1(1)	-10(1)	-11(1)
O1A	39(1)	35(1)	39(1)	9(1)	-18(1)	-11(1)
O2A	49(1)	30(1)	49(1)	0(1)	-17(1)	-20(1)
O3A	29(1)	70(1)	32(1)	-19(1)	-9(1)	-13(1)
O4A	35(1)	91(1)	34(1)	-21(1)	-4(1)	-32(1)
N1A	26(1)	30(1)	27(1)	-4(1)	-11(1)	-9(1)
C1A	22(1)	28(1)	25(1)	-2(1)	-6(1)	-7(1)
C2A	20(1)	27(1)	24(1)	-3(1)	-4(1)	-9(1)
C3A	29(1)	30(1)	34(1)	-5(1)	-3(1)	-14(1)
C4A	28(1)	45(1)	36(1)	-12(1)	-4(1)	-20(1)
C5A	27(1)	51(1)	25(1)	-5(1)	-8(1)	-16(1)
C6A	29(1)	34(1)	26(1)	3(1)	-10(1)	-12(1)
C7A	22(1)	27(1)	23(1)	-3(1)	-4(1)	-10(1)
C8A	26(1)	28(1)	27(1)	-3(1)	-7(1)	-10(1)
C9A	29(1)	44(1)	28(1)	-11(1)	-10(1)	-13(1)
C10A	31(1)	32(1)	26(1)	-5(1)	-11(1)	-12(1)
C11A	28(1)	30(1)	28(1)	-4(1)	-10(1)	-10(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **2a**.

	x	y	z	U(eq)
H4	-4065	8583	-1984	50
H3	4357	4302	2097	39
H4A	5740	5239	2960	44
H5	5700	7461	2426	44
H6	4309	8839	985	37
H9A	1225	6168	-1432	40
H9B	1346	7628	-1870	40
H10A	-1357	7323	-178	32
H10B	-1250	8774	-677	32
H4AA	2247	2109	3874	74
H3A	9306	5070	6080	36
H4AB	10995	4236	7455	40
H5A	11696	1966	8237	40
H6A	10709	443	7695	35
H9AA	7638	881	4295	39
H9AB	7077	2447	3793	39
H10C	5051	1406	5561	34
H10D	4504	3015	5182	34

Table 6. Torsion angles [°] for **2a**.

O1-C1-C2-C3	-1.0(3)
O1-C1-C2-C7	179.53(16)
N1-C1-C2-C3	179.39(16)
N1-C1-C2-C7	-0.06(16)
N1-C9-C10-C11	-177.04(13)
C1-N1-C8-O2	-179.60(15)
C1-N1-C8-C7	0.20(17)
C1-N1-C9-C10	97.04(18)
C1-C2-C3-C4	-178.71(15)
C1-C2-C7-C6	179.23(14)
C1-C2-C7-C8	0.17(16)
C2-C3-C4-C5	-0.3(2)
C2-C7-C8-O2	179.56(16)
C2-C7-C8-N1	-0.23(17)
C3-C2-C7-C6	-0.3(2)
C3-C2-C7-C8	-179.33(14)
C3-C4-C5-C6	-0.5(3)
C4-C5-C6-C7	0.9(2)
C5-C6-C7-C2	-0.5(2)
C5-C6-C7-C8	178.34(15)
C6-C7-C8-O2	0.6(3)
C6-C7-C8-N1	-179.18(16)
C7-C2-C3-C4	0.7(2)
C8-N1-C1-O1	-179.70(15)
C8-N1-C1-C2	-0.09(17)
C8-N1-C9-C10	-87.92(19)
C9-N1-C1-O1	-4.1(2)
C9-N1-C1-C2	175.47(13)
C9-N1-C8-O2	4.9(3)
C9-N1-C8-C7	-175.35(13)
C9-C10-C11-O3	5.8(2)
C9-C10-C11-O4	-174.22(13)
O1A-C1A-C2A-C3A	-0.1(3)
O1A-C1A-C2A-C7A	-179.38(16)
N1A-C1A-C2A-C3A	179.59(15)
N1A-C1A-C2A-C7A	0.28(16)

N1A-C9A-C10A-C11A	173.72(14)
C1A-N1A-C8A-O2A	180.00(15)
C1A-N1A-C8A-C7A	-0.13(17)
C1A-N1A-C9A-C10A	-96.83(18)
C1A-C2A-C3A-C4A	-179.01(15)
C1A-C2A-C7A-C6A	179.10(14)
C1A-C2A-C7A-C8A	-0.36(16)
C2A-C3A-C4A-C5A	0.1(2)
C2A-C7A-C8A-O2A	-179.82(17)
C2A-C7A-C8A-N1A	0.31(16)
C3A-C2A-C7A-C6A	-0.3(2)
C3A-C2A-C7A-C8A	-179.74(14)
C3A-C4A-C5A-C6A	-0.4(3)
C4A-C5A-C6A-C7A	0.4(2)
C5A-C6A-C7A-C2A	0.0(2)
C5A-C6A-C7A-C8A	179.32(15)
C6A-C7A-C8A-O2A	0.8(3)
C6A-C7A-C8A-N1A	-179.09(15)
C7A-C2A-C3A-C4A	0.2(2)
C8A-N1A-C1A-O1A	179.59(15)
C8A-N1A-C1A-C2A	-0.09(17)
C8A-N1A-C9A-C10A	90.54(19)
C9A-N1A-C1A-O1A	6.2(2)
C9A-N1A-C1A-C2A	-173.48(13)
C9A-N1A-C8A-O2A	-6.6(3)
C9A-N1A-C8A-C7A	173.29(13)
C9A-C10A-C11A-O3A	-1.5(2)
C9A-C10A-C11A-O4A	179.63(16)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for **2a** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O4-H4...O3A#1	0.82	1.89	2.7088(17)	175.3
O4A-H4AA...O3#1	0.82	1.89	2.6858(18)	163.8
O4A-H4AA...O2A#2	0.82	2.64	3.1091(19)	117.7

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y+1,-z #2 -x+1,-y,-z+1

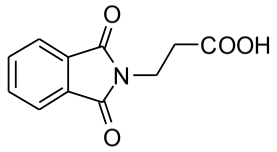
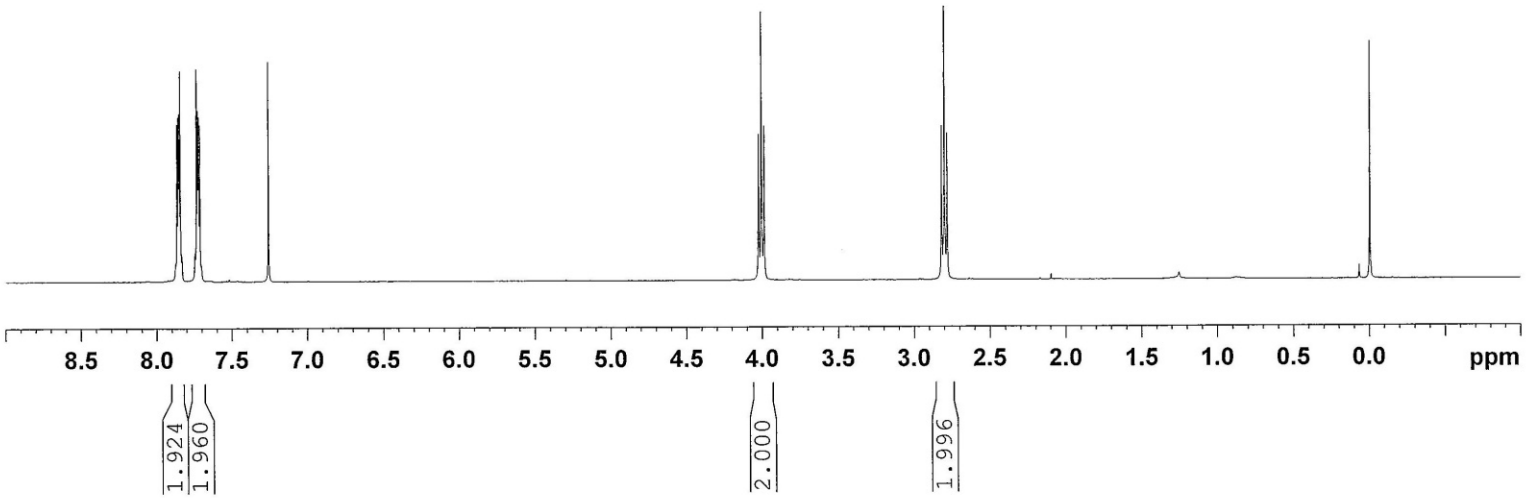

O
COOH
N
O

Table 2, **2a**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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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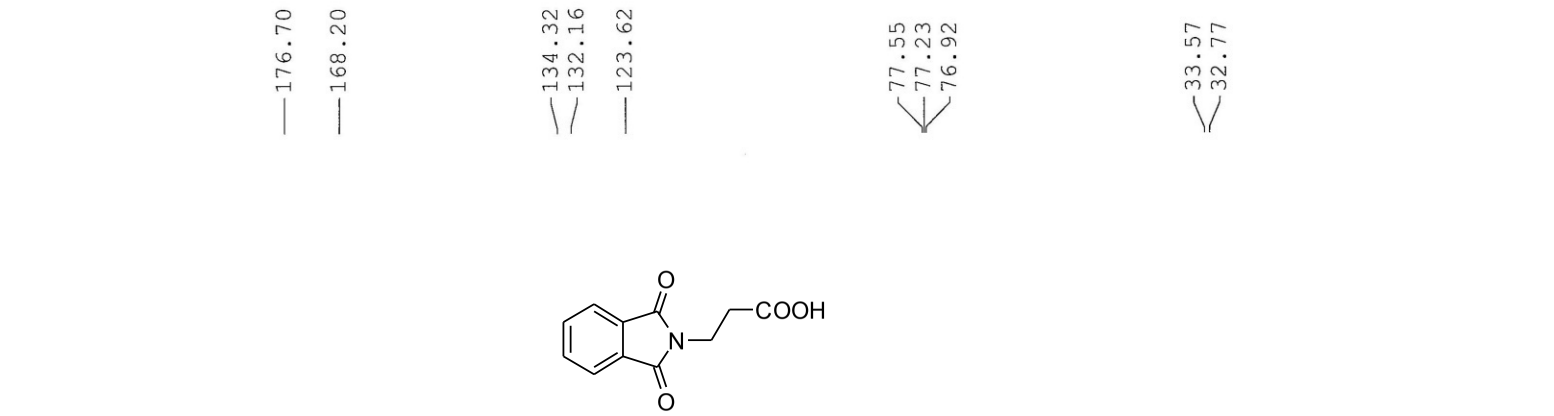
1.960
2.000
1.996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168.20
134.32
132.16
123.62
77.55
77.23
76.92
33.57
32.77
O
N
COOH
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

Table 2, **2a**

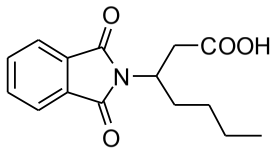
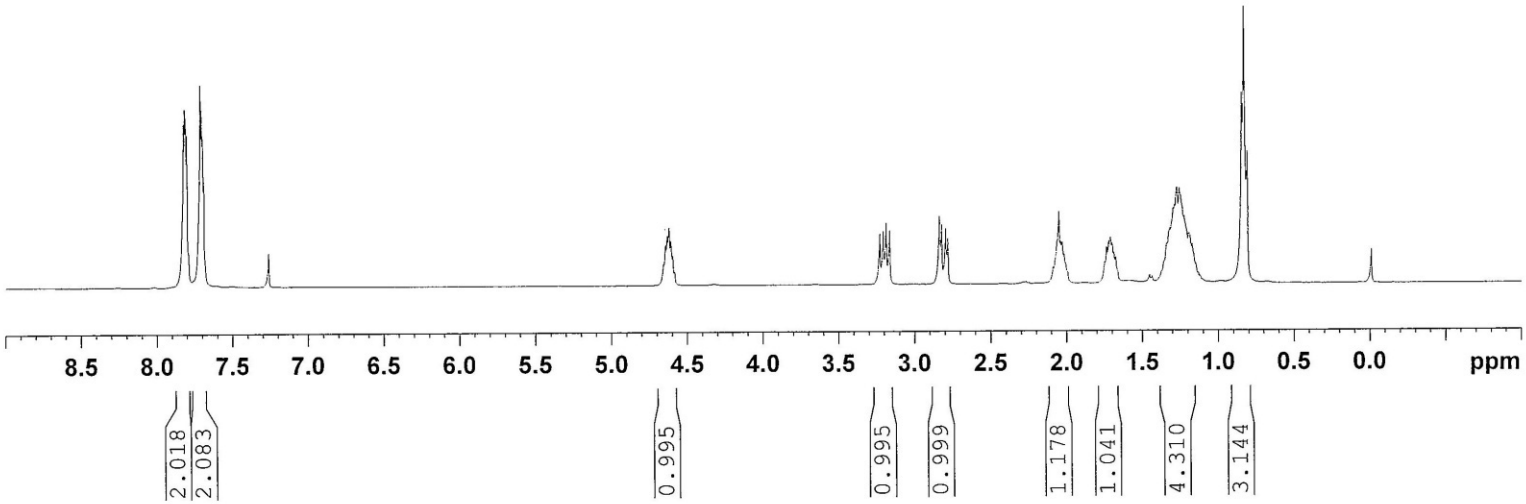

O
COOH
N
O

Table 2, **2b**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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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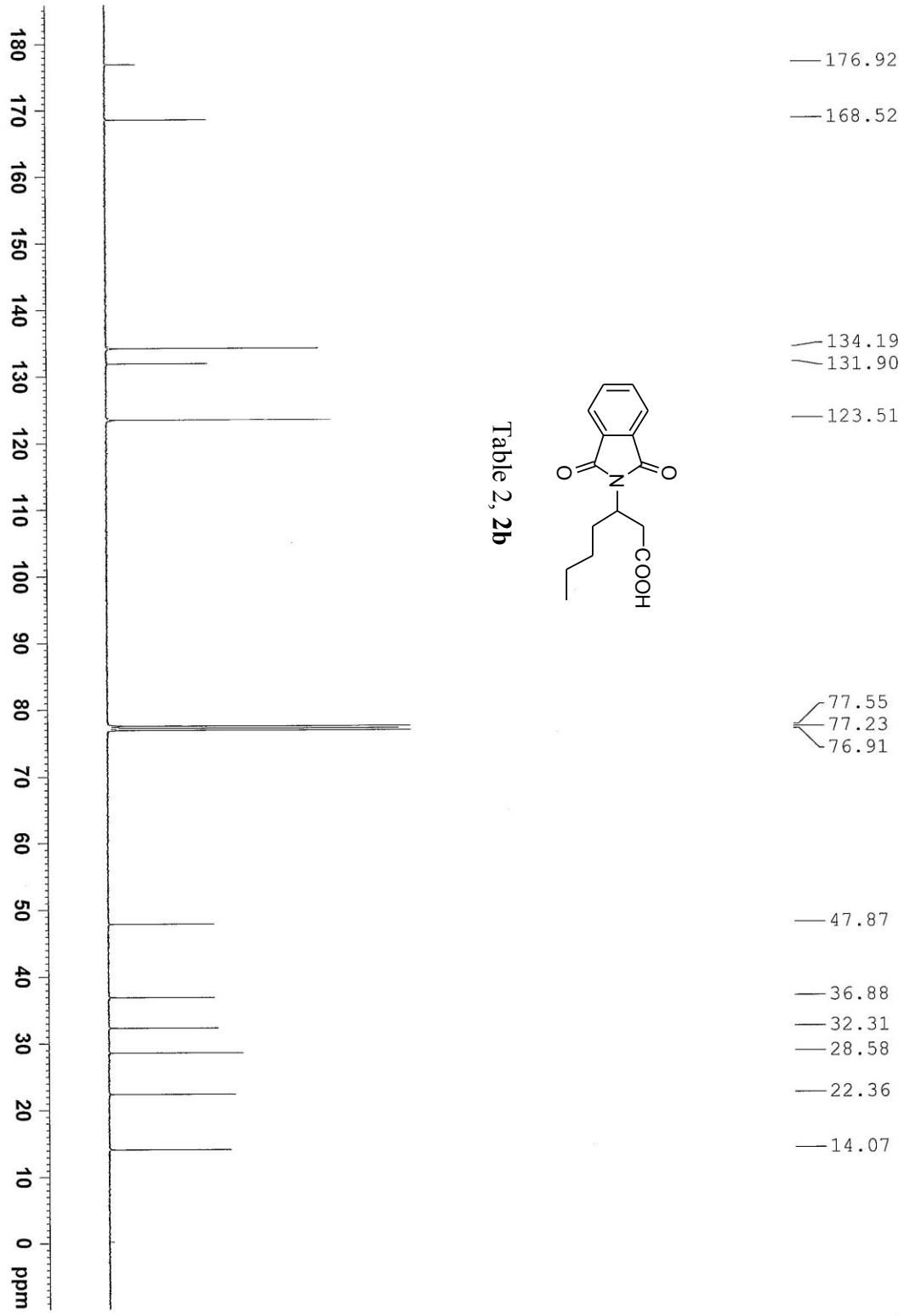
2.083
0.995
0.995
0.999
1.178
1.041
4.310
3.144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168.52
134.19
131.90
123.51
77.55
77.23
76.91
47.87
36.88
32.31
28.58
22.36
14.07
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
O
O
N
COOH

Table 2, **2b**

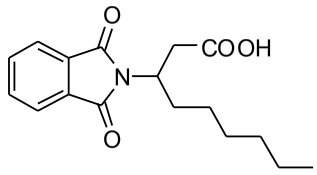
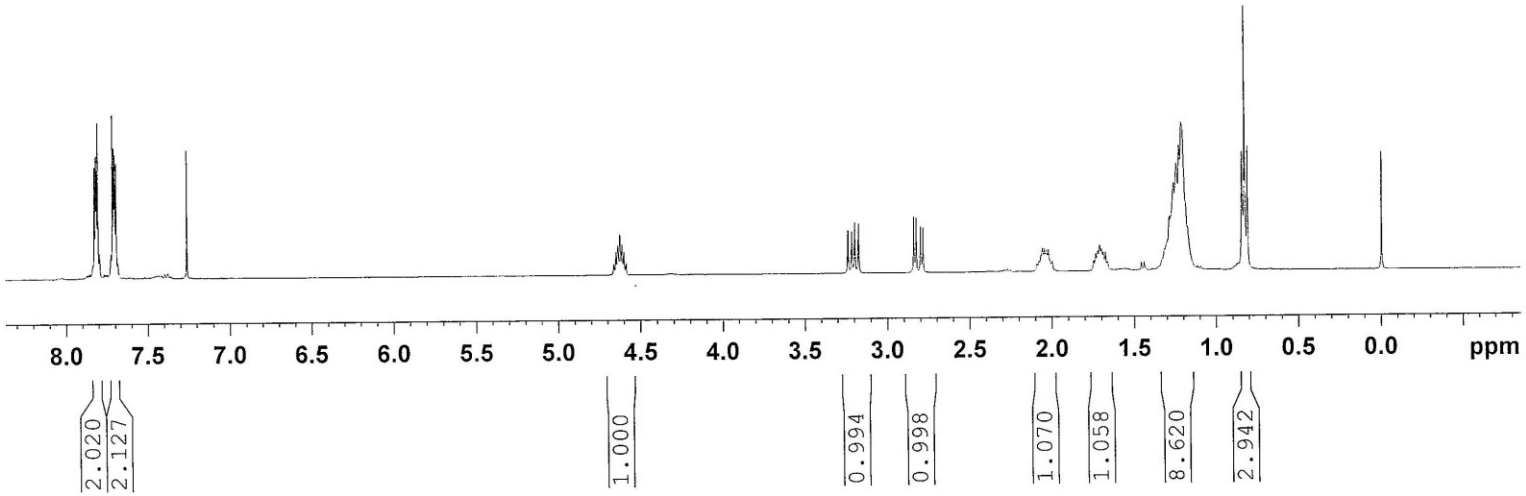

O
COOH
N
O

Table 2, **2c**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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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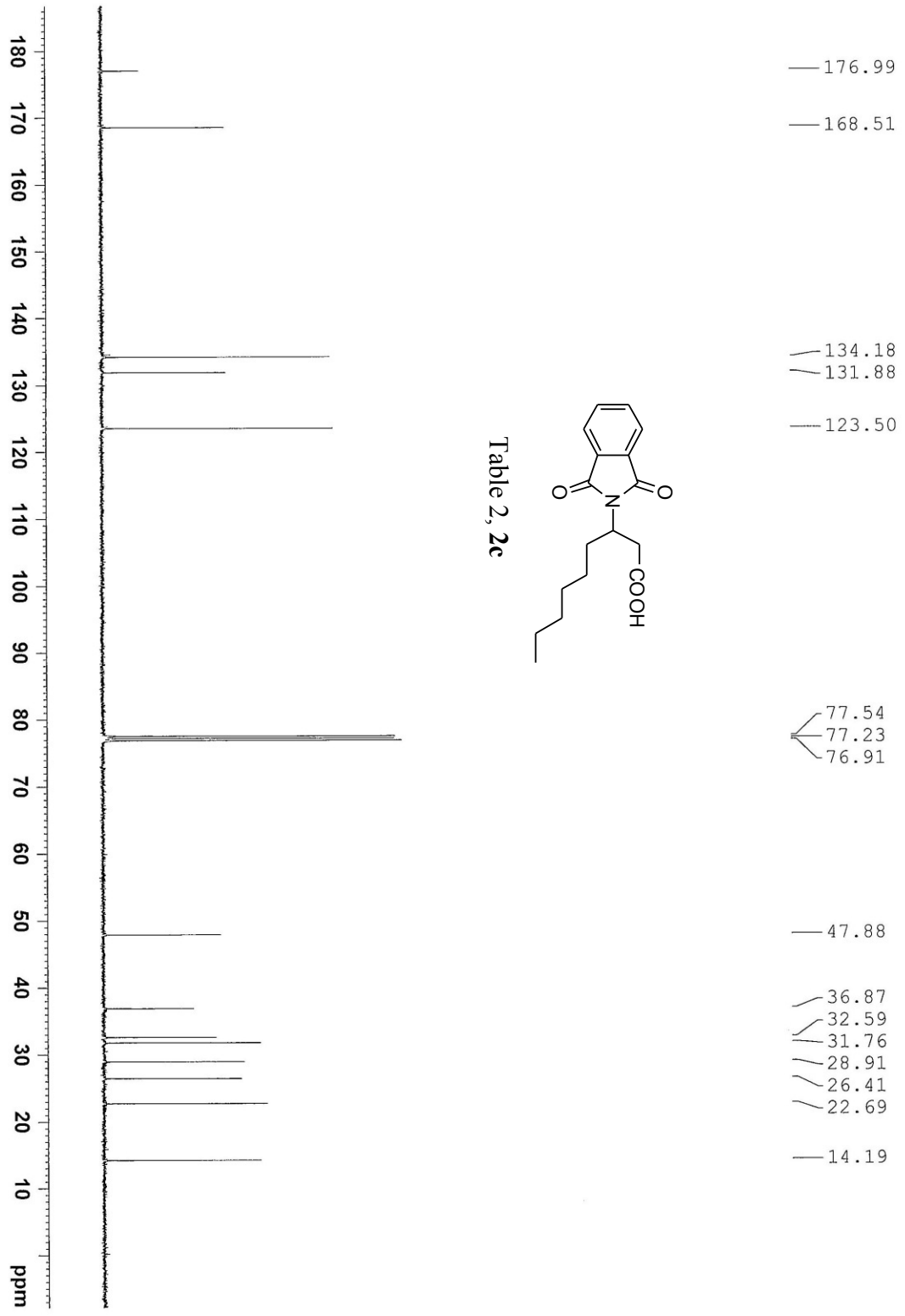
2.127
1.000
0.994
0.998
1.070
1.058
8.620
2.942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131.88
123.50
77.54
77.23
76.91
47.88
36.87
32.59
31.76
28.91
26.41
22.69
14.19
Table 2, 2c
COOH
ppm

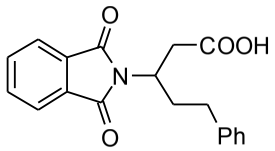
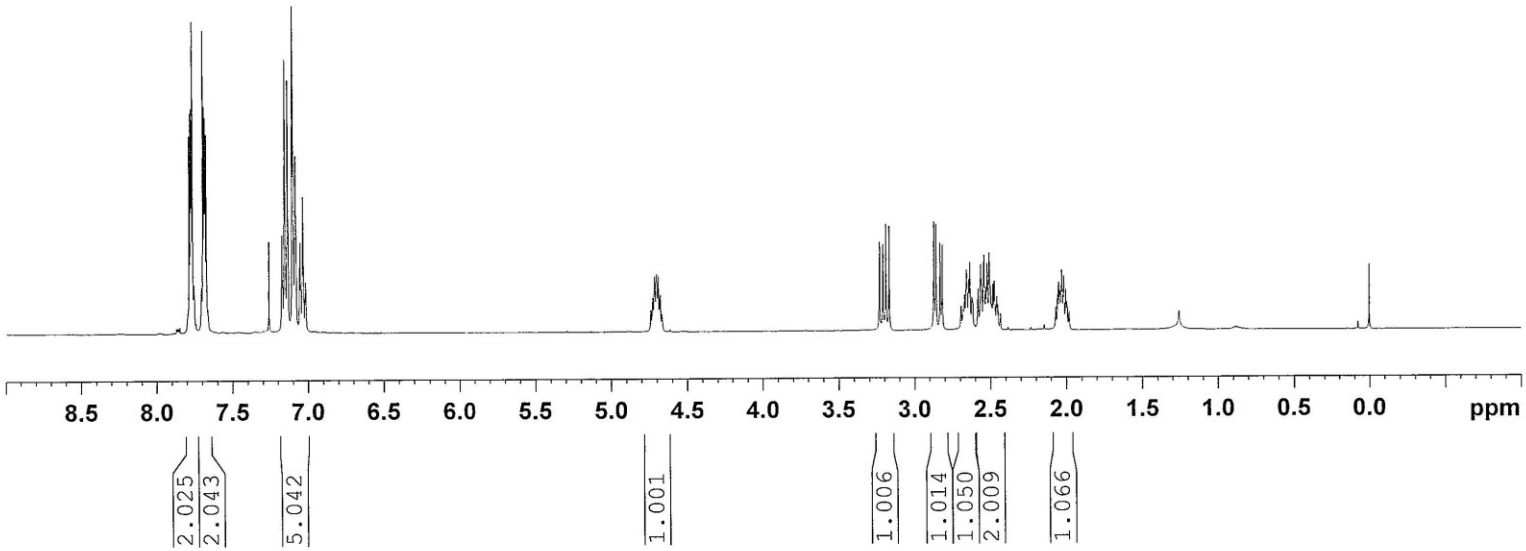

O
COOH
N
O
Ph

Table 2, **2d**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.025
2.043
5.042
1.001
1.006
1.014
1.050
2.009
1.066

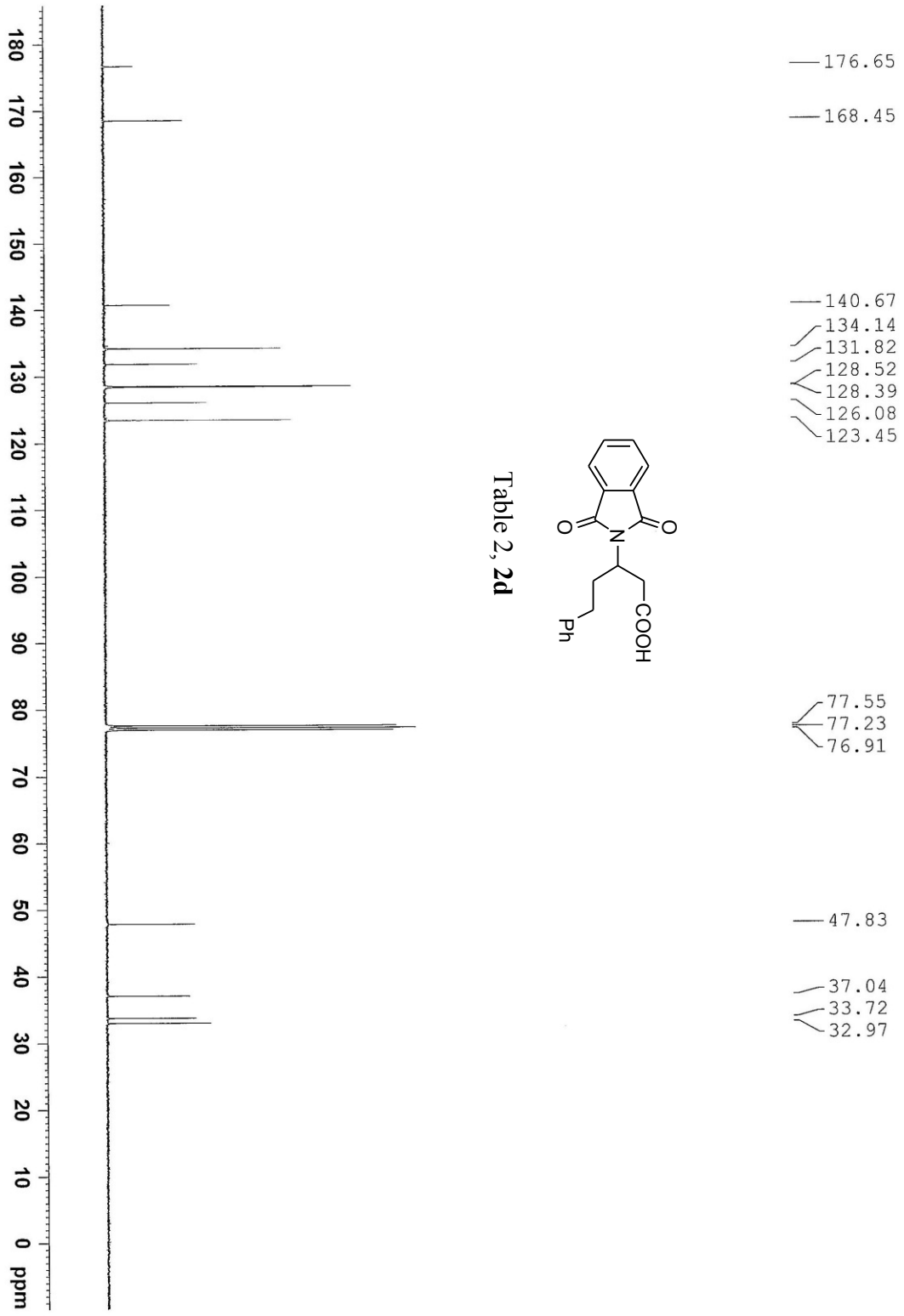
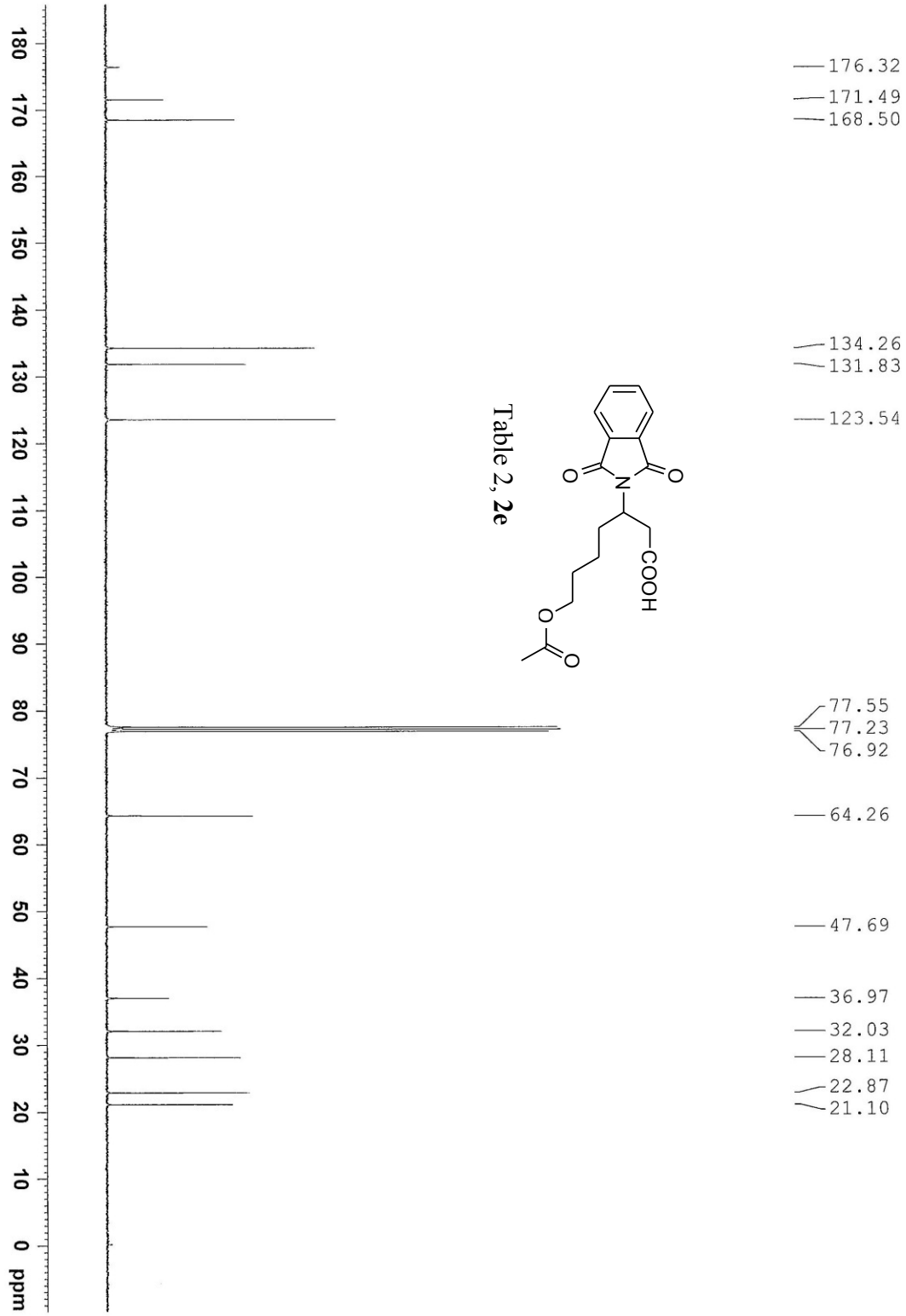

176.65
168.45
140.67
134.14
131.82
128.52
128.39
126.08
123.45
77.55
77.23
76.91
47.83
37.04
33.72
32.97
O
O
N
Ph
COOH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

Table 2, **2d**

2.044
2.032
1.000
2.024
0.968
0.975
1.030
2.984
3.199
1.993
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

Table 2, **2e**

O
O
N
O
COOH
O
O


176.32
171.49
168.50
134.26
131.83
123.54
77.55
77.23
76.92
64.26
47.69
36.97
32.03
28.11
22.87
21.10
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Table 2, 2e
O
O
N
COOH
O
O

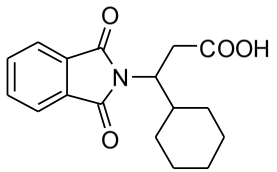
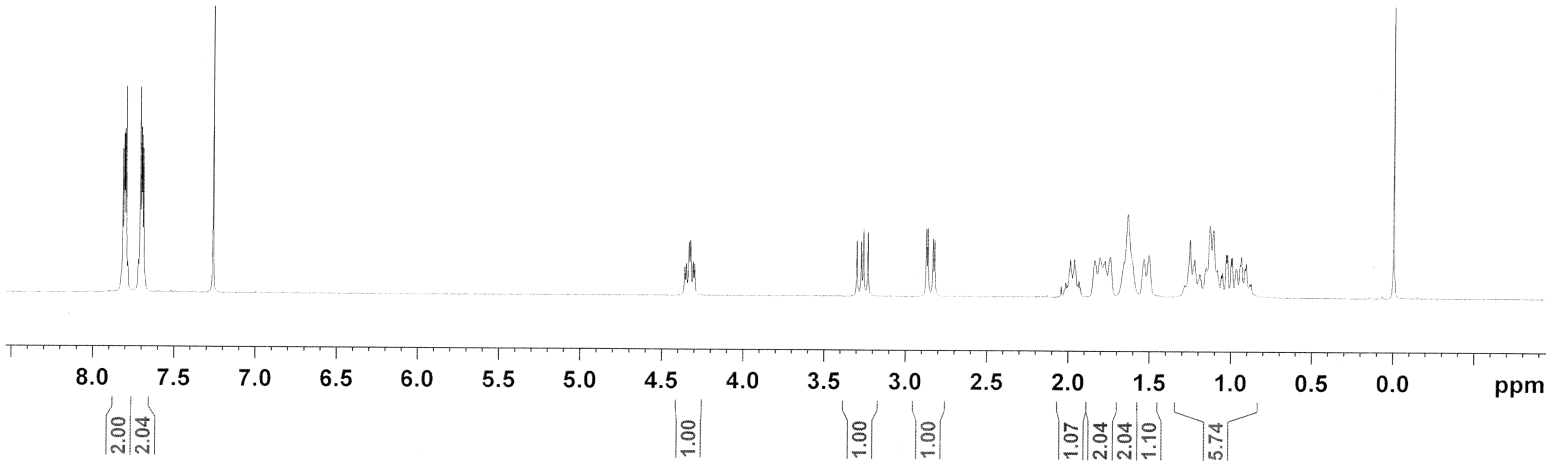

O
COOH
N
O

Table 2, **2f**


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
2.04
1.00
1.00
1.00
1.07
2.04
2.04
1.10
5.74

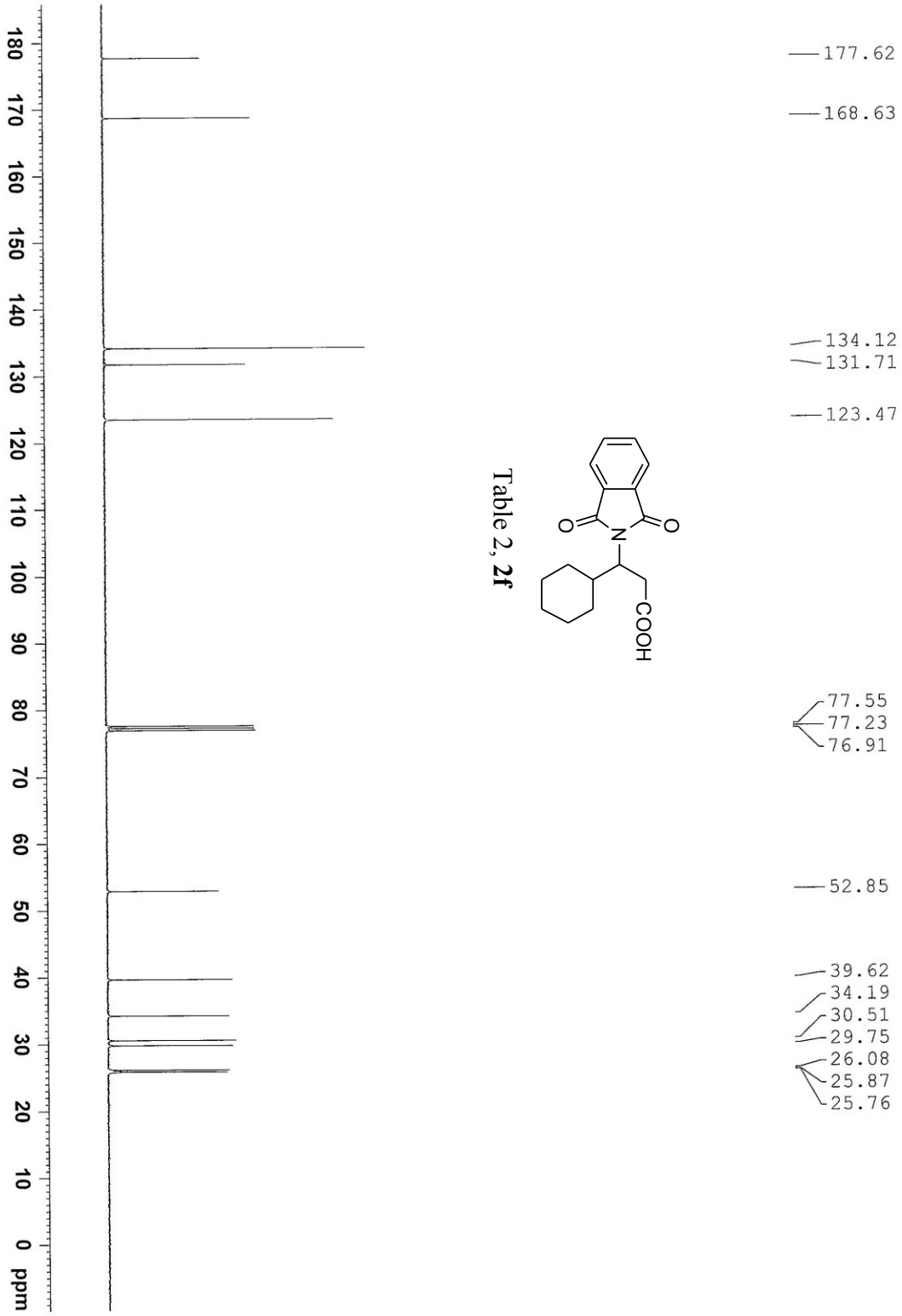

177.62
168.63
134.12
131.71
123.47
77.55
77.23
76.91
52.85
39.62
34.19
30.51
29.75
26.08
25.87
25.76
O
O
N
COOH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

Table 2, **2f**

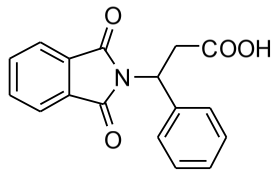
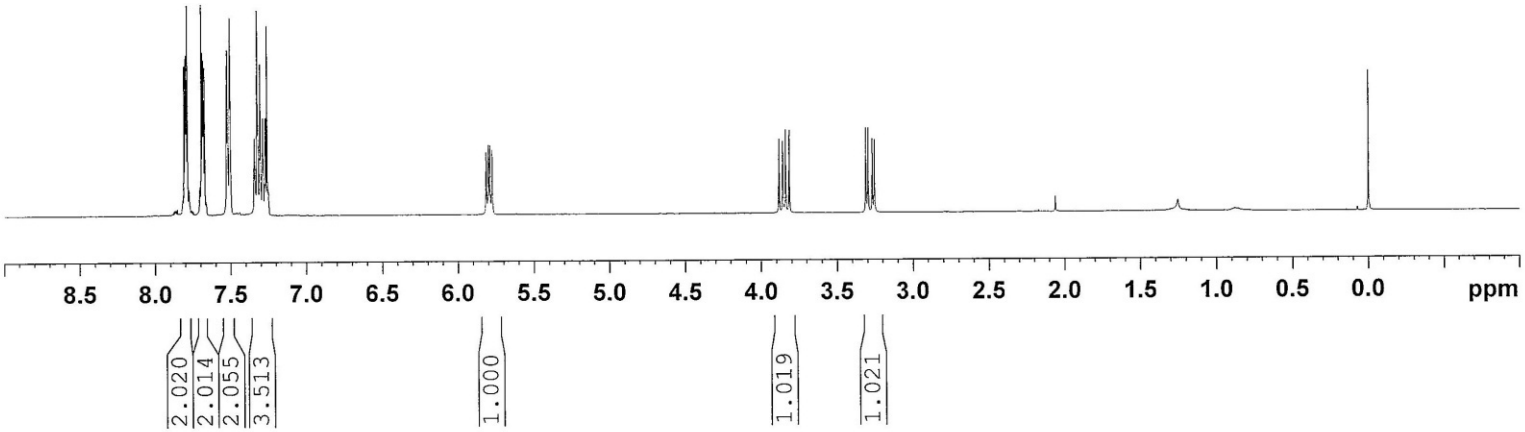

O
COOH
N
O

Table 2, **2g**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.020
2.014
2.055
3.513
1.000
1.019
1.021

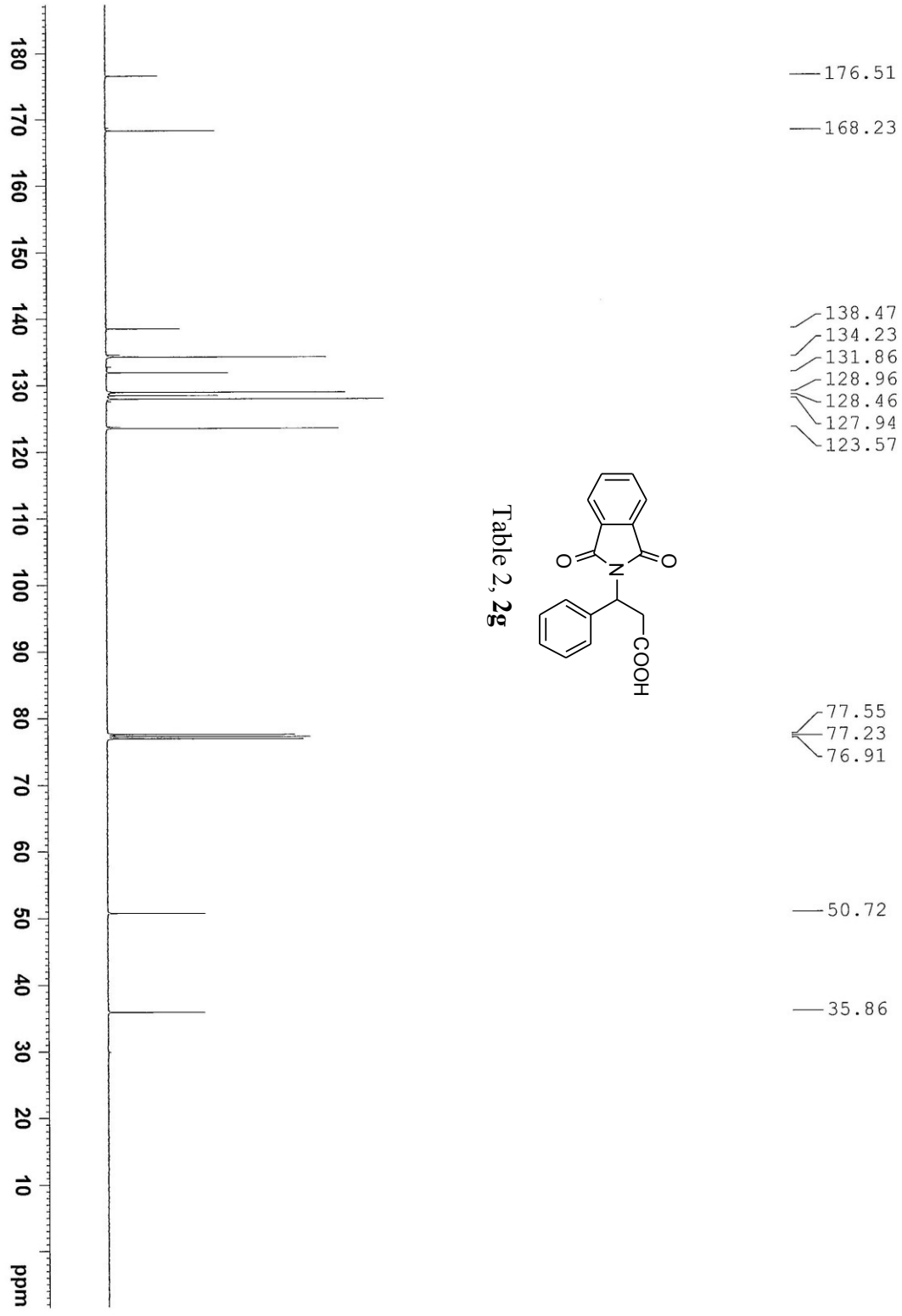

176.51
168.23
138.47
134.23
131.86
128.96
128.46
127.94
123.57
77.55
77.23
76.91
50.72
35.86
O
O
N
O
COOH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Table 2, **2g**

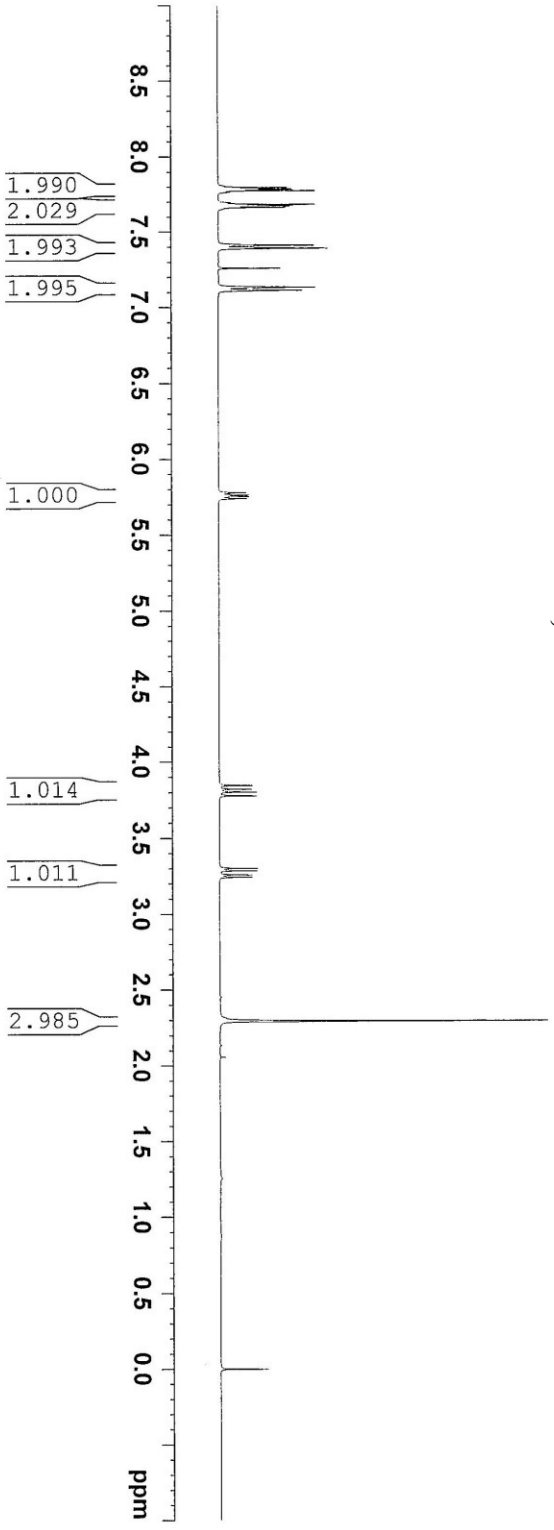
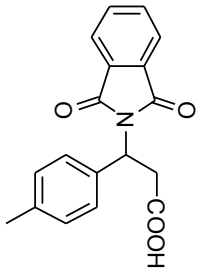

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.990
2.029
1.993
1.995
1.000
1.014
1.011
2.985

Table 2, **2h**


O
N
O
COOH

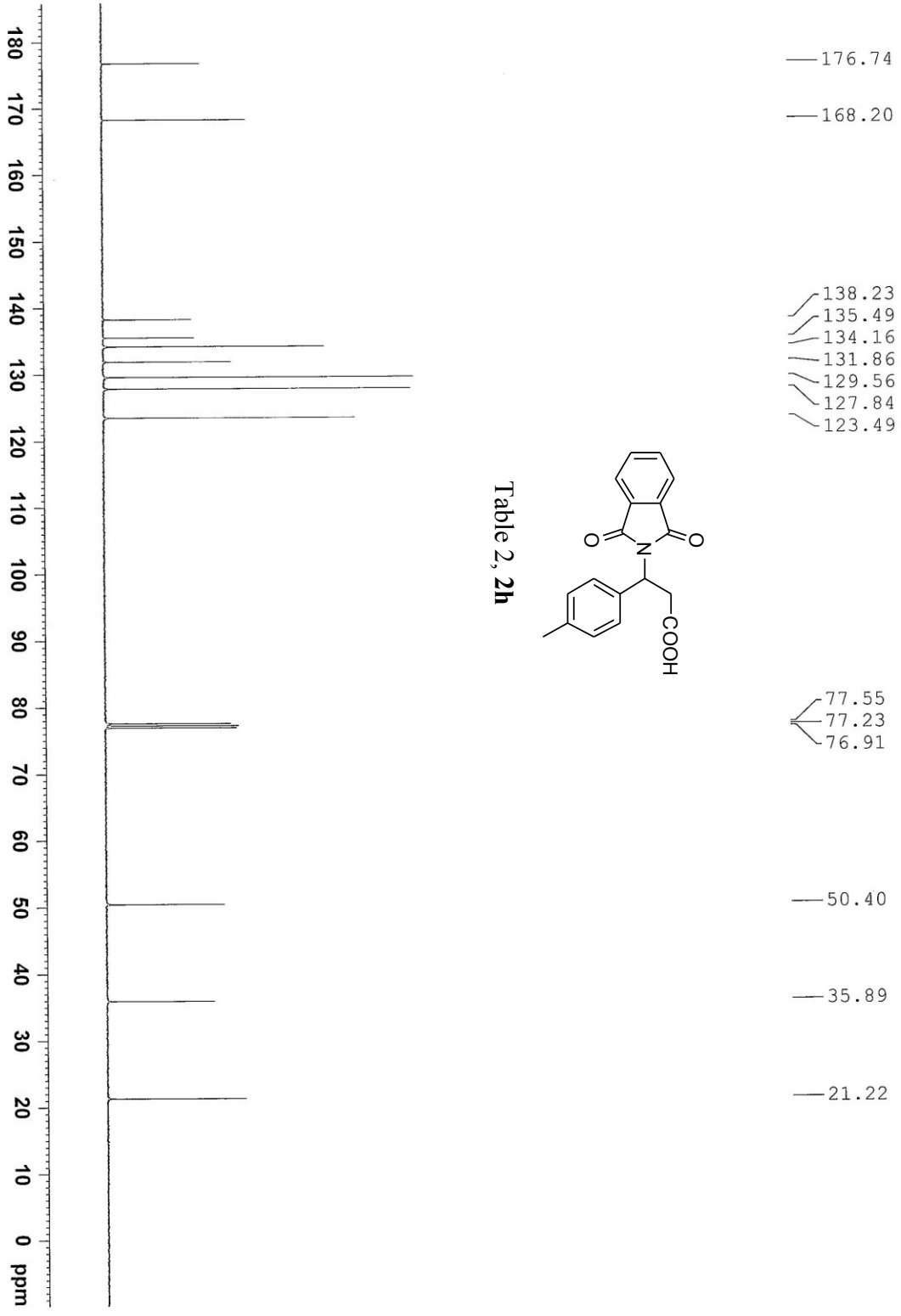

176.74
168.20
138.23
135.49
134.16
131.86
129.56
127.84
123.49
77.55
77.23
76.91
50.40
35.89
21.22
O
O
N
O
COOH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

Table 2, **2h**

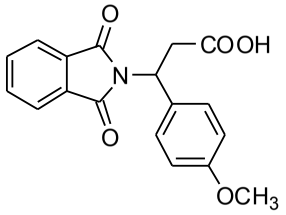
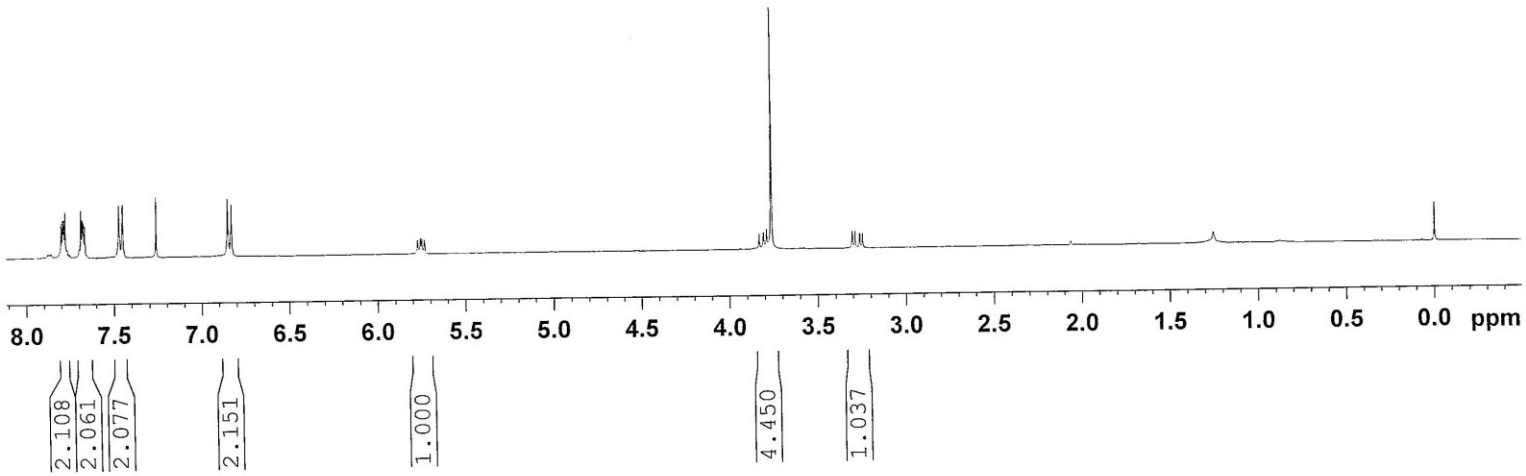

O
N
O
COOH
OCH3

Table 2, **2i**


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.108
2.061
2.077
2.151
1.000
4.450
1.037

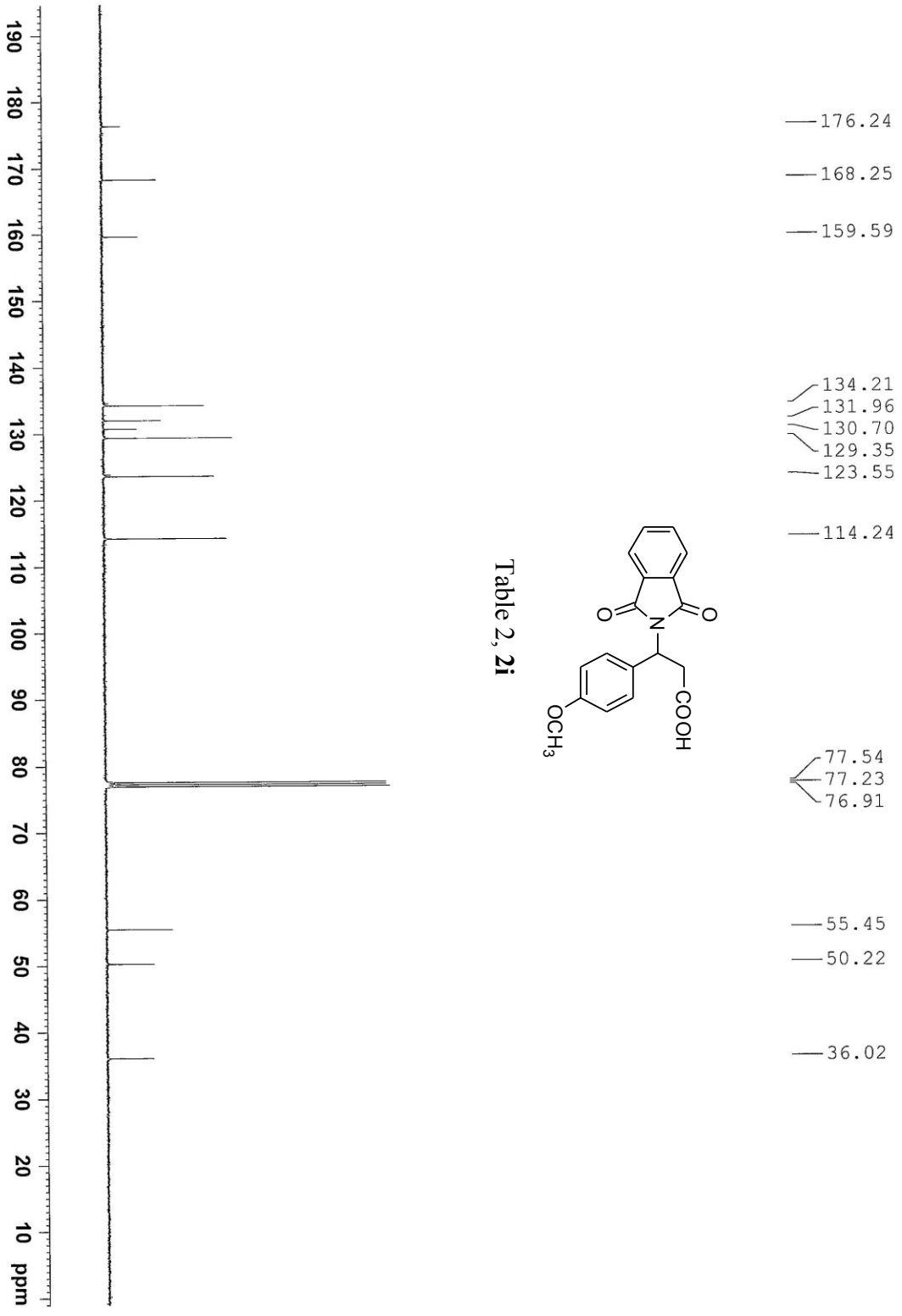

176.24
168.25
159.59
134.21
131.96
130.70
129.35
123.55
114.24
77.54
77.23
76.91
55.45
50.22
36.02
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
O
O
N
COOH
OCH3

Table 2, **2i**

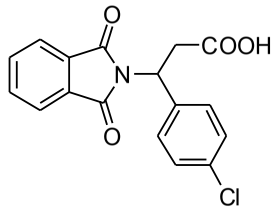
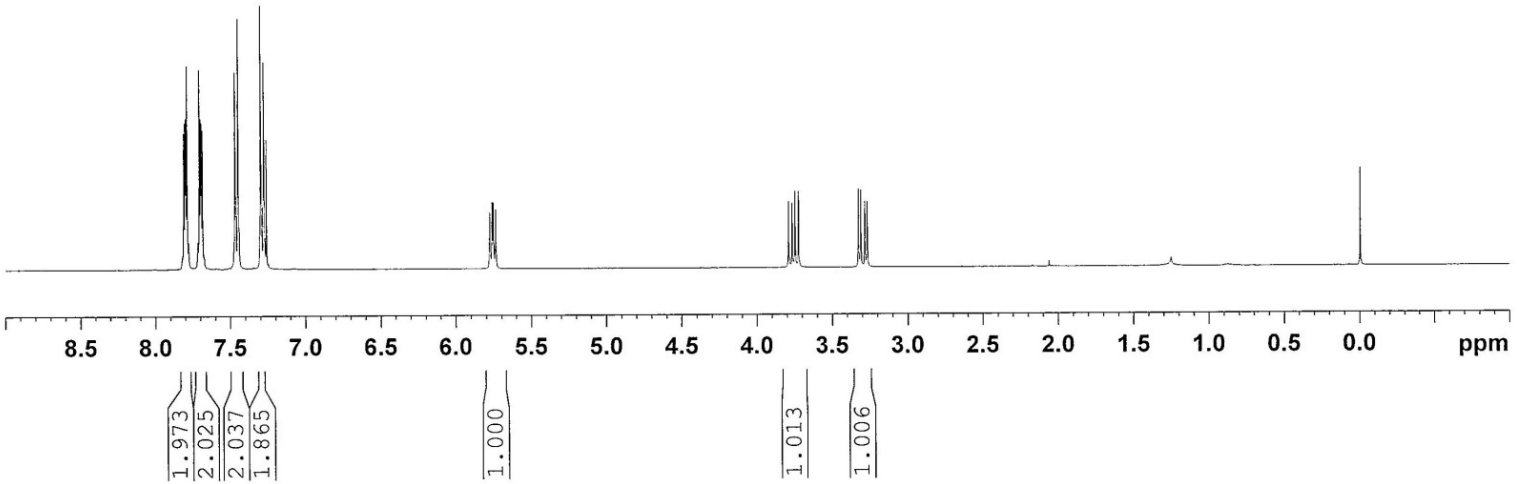

O
COOH
N
O
Cl

Table 2, **2j**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.973
2.025
2.037
1.865
1.000
1.013
1.006

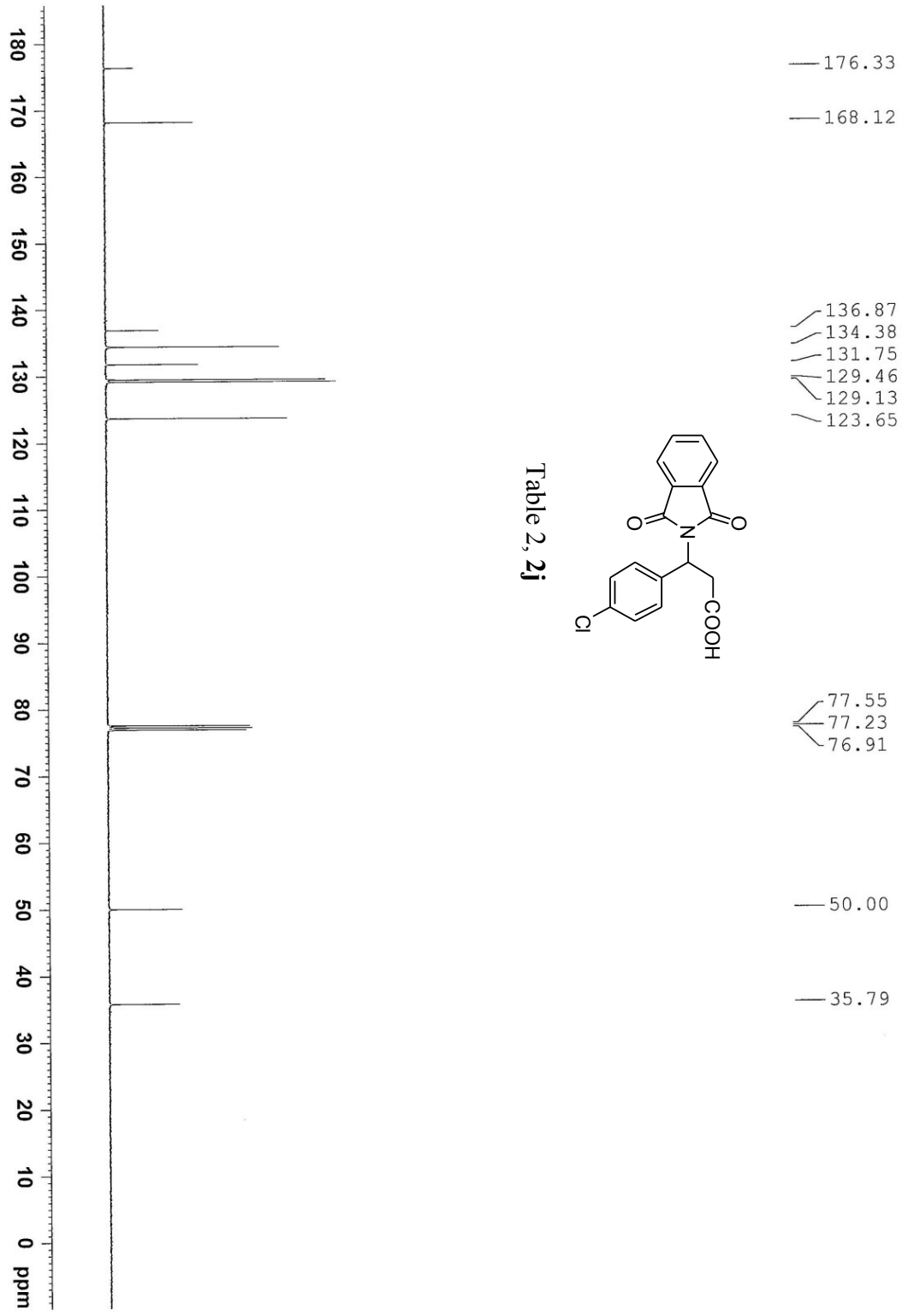

176.33
168.12
136.87
134.38
131.75
129.46
129.13
123.65
77.55
77.23
76.91
50.00
35.79
O
O
N
Cl
COOH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

Table 2, **2j**

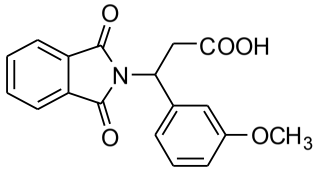
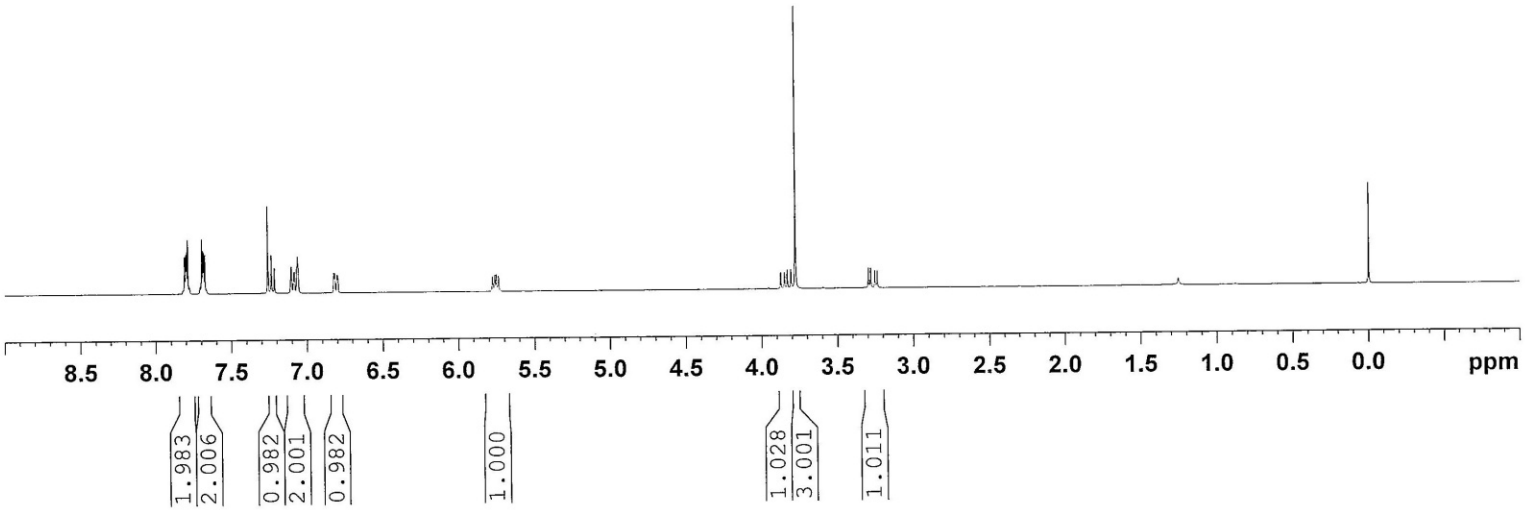

O
COOH
N
O
OCH3

Table 2, **2k**


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.983
2.006
0.982
2.001
0.982
1.000
1.028
3.001
1.011

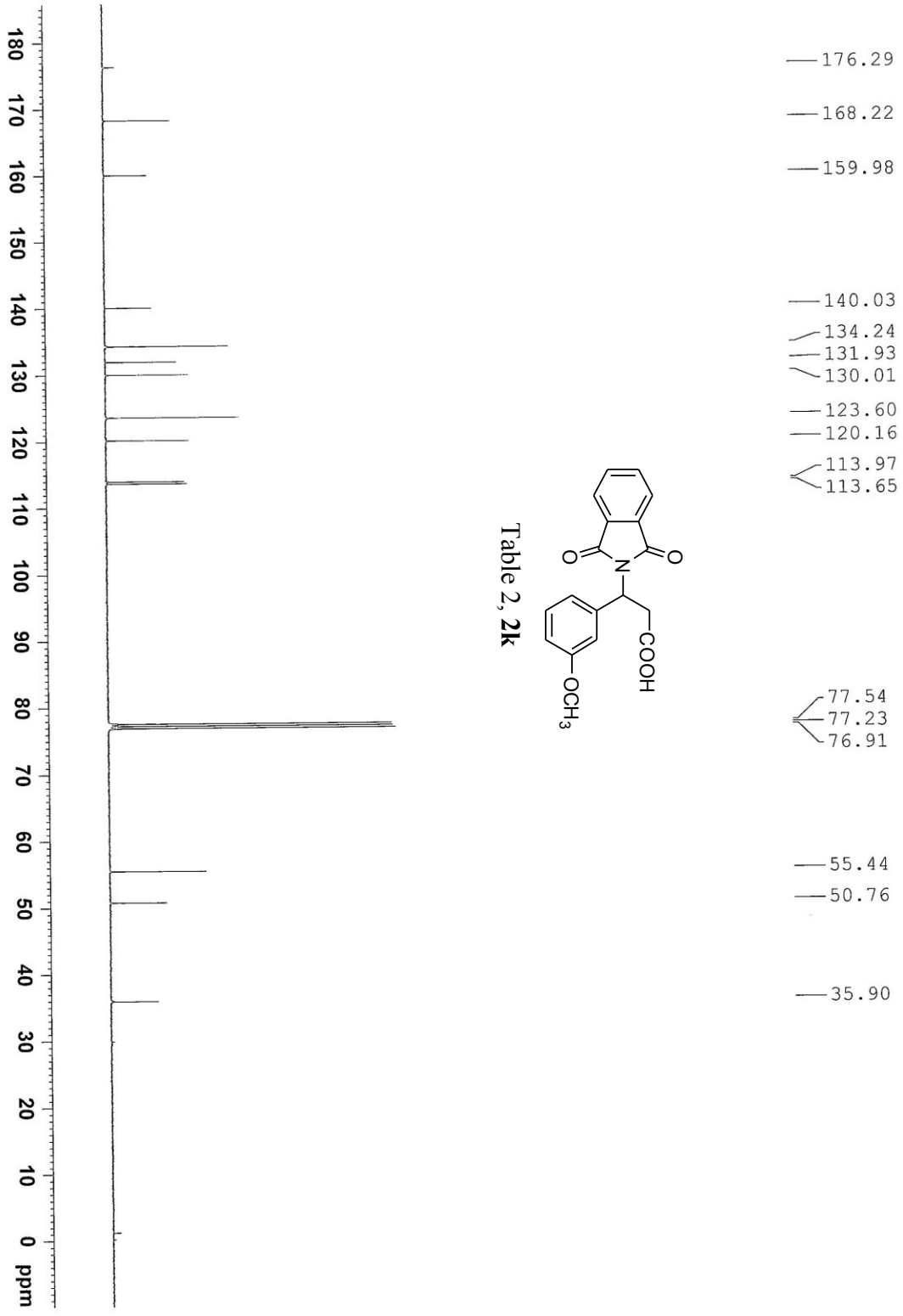

176.29
168.22
159.98
140.03
134.24
131.93
130.01
123.60
120.16
113.97
113.65
77.54
77.23
76.91
55.44
50.76
35.90
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
O
O
N
COOH
OCH3

Table 2, **2k**

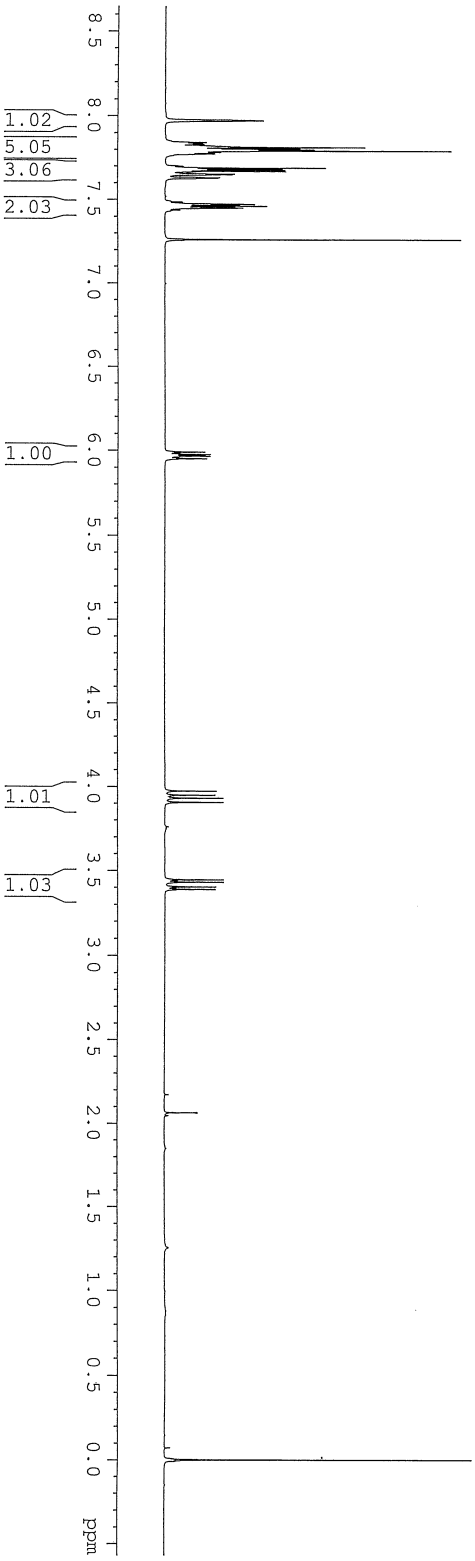
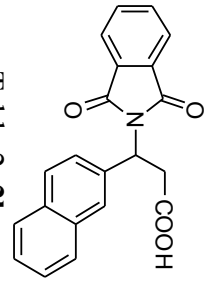
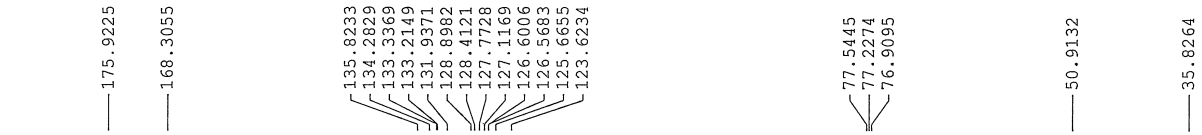

1.02
5.05
3.06
2.03
1.00
1.01
1.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

Table 2, **2l**


O
O
N
COOH


175.9225
168.3055
135.8233
134.2829
133.3369
133.2149
131.9371
128.8982
128.4121
127.7728
127.1169
126.6006
126.5683
125.6655
123.6234
77.5445
77.2274
76.9095
50.9132
35.8264

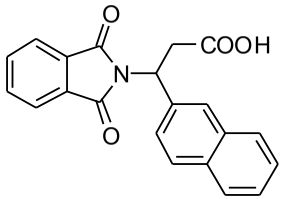
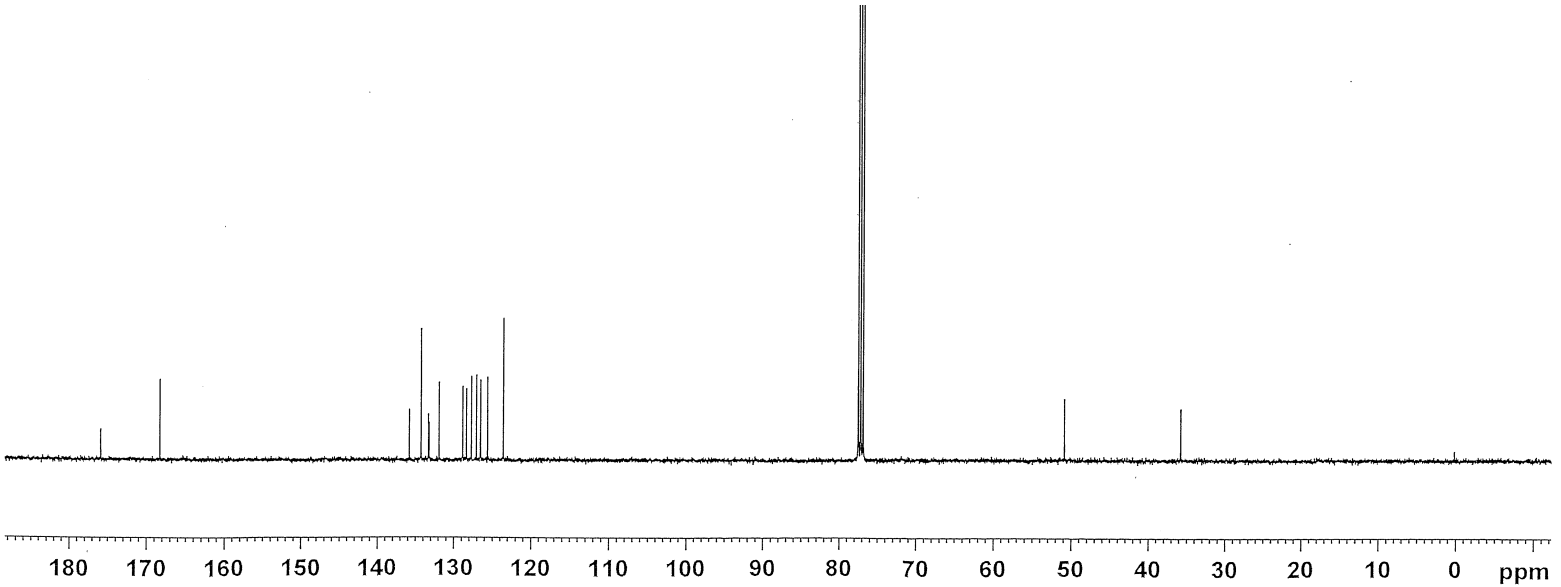

O
N
O
COOH

Table 2, **2l**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

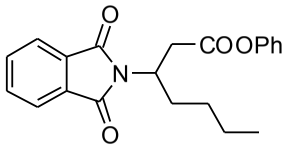
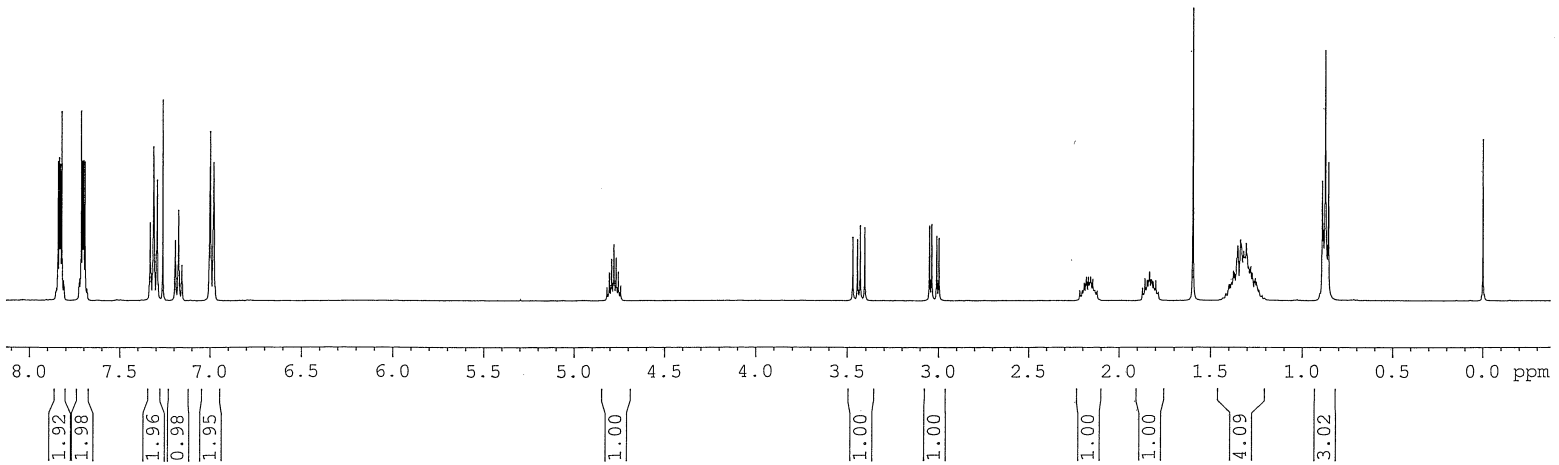


Table 1, Entry 18



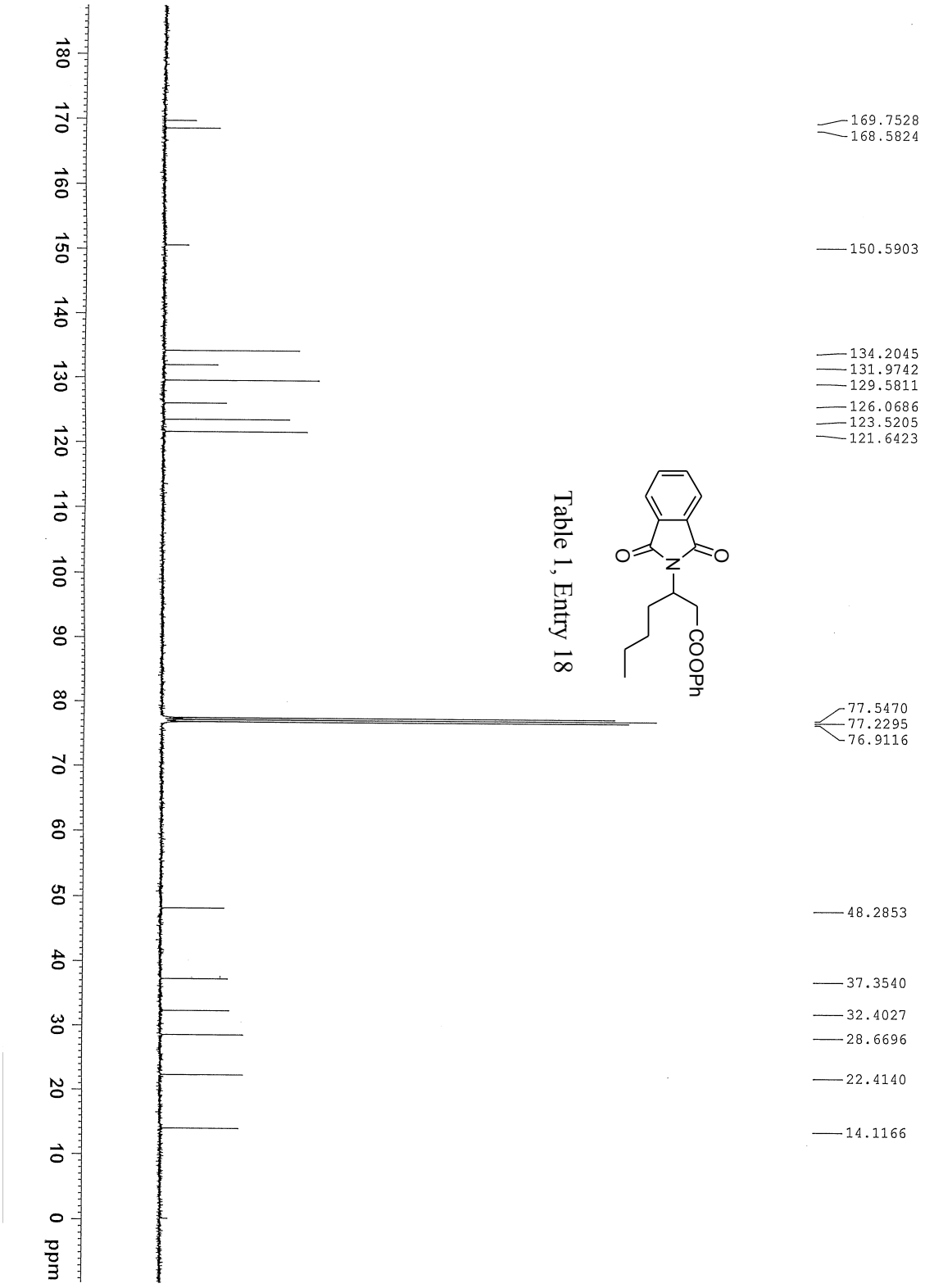
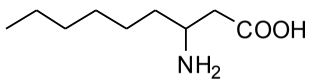
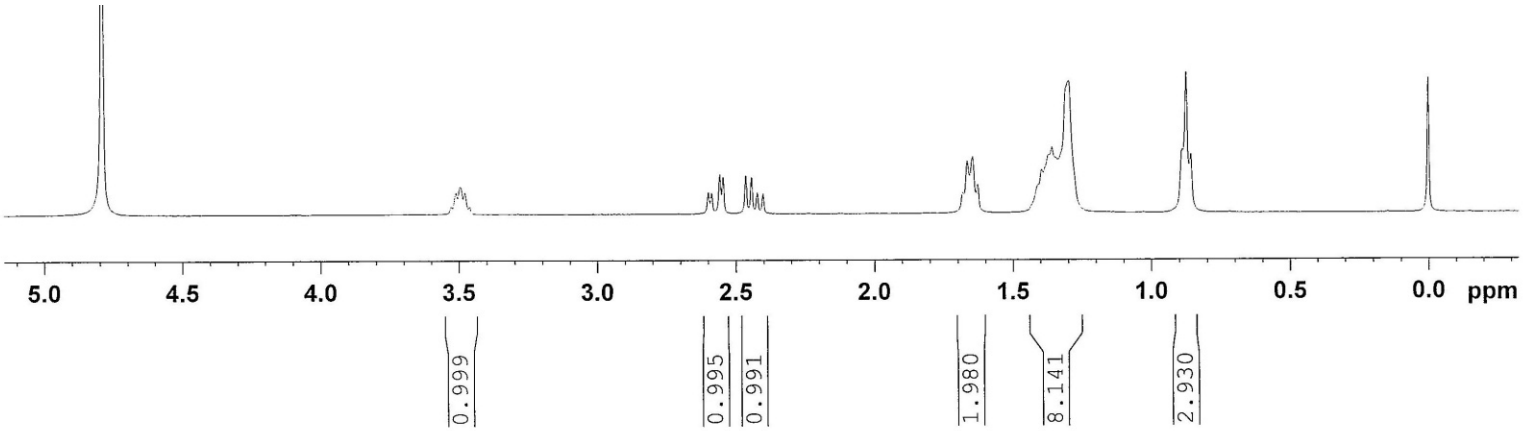
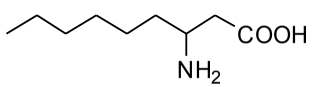


Table 1, Entry 18

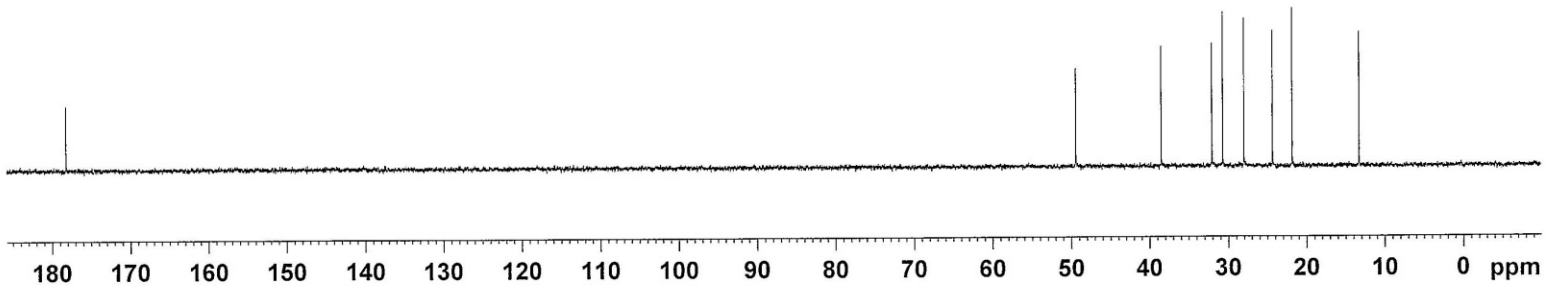

COOH
NH2

Scheme 3, **3c**


5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.999
0.995
0.991
1.980
8.141
2.930


COOH
NH2

Scheme 3, **3c**


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm