Supporting information

Palladium-Catalyzed Decarboxylative Coupling of Quinolinone-3-carboxylic Acids and Related Heterocyclic Carboxylic Acid with (Hetero)aryl Halides

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Contents

General experimental methods

All reactions were conducted under an argon atmosphere. Solvents: cyclohexane, ethyl acetate (EtOAc) and methylene chloride (CH_2Cl_2) for extraction and chromatography were technical grade.

Instrumentation

The compounds were all identified by usual physical methods, i.e. ^{1}H-NMR, ^{13}C-NMR, IR, elemental analysis. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ or DMSO-d_6 on a 300 MHz spectrometer. ^{1}H chemical shifts are reported in ppm from an internal standard TMS or of residual chloroform (7.27 ppm). The following abreviation are used: m (multiplet), s (singlet), br s (broad singlet), d (doublet), t (triplet) dd (doublet of doublet), td (triplet of doublet), q (quadruplet), quint (quintuplet). ^{13}C chemical shifts are reported in ppm from the central peak of deuteriochloroform (77.14). IR spectra were acquired on a FT-IR and are reported in wave numbers (cm^{-1}). Elemental analyses were performed with a Perkin-Elmer 240 analyser. R_f values refer to TLC on 0.25 mm silica gel plates (60-F_{254}). Flash chromatography was performed on silica gel 60 (0.040-0.063 mm). Melting points (m.p.) were determined on a capillary melting point apparatus and were uncorrected. Aryl bromides, iodides and 1,8-naphthyridin-4(1*H*)-one 3-carboxylic acid are commercially available compounds. Quinolone-3-carboxylic acid **1**[1]**,** coumarins 3-carboxylic acid, [2] quinolin-2(1*H*)-ones 3-carboxylic acid [3] as well as chromone 2-carboxylic acid[4] were synthesized as described.

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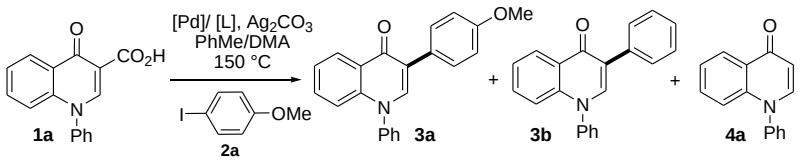
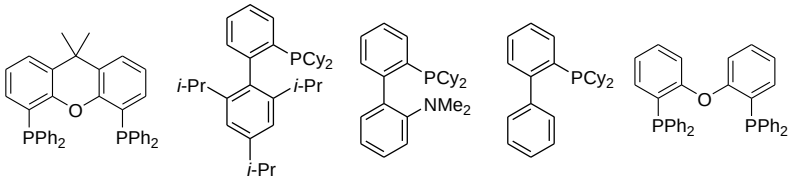
2 Du, J.-L.; Li, L.-J.; Zhang, D.-H. *Eur-J. Chem.*, **2006**, *3,* 1-4; Ma; Y.; Luo; W.; Quinn; P. J.; Liu; Z.; Hider, R. C. *J. Med. Chem.*, **2004**, *47*, 6349-6362.
3 Suzuki, M.; Ohuchi, Y.; Asanuma, H. Kaneko, T.; Yokomori, S.; Ito, C.; Isobe, Y.; Muramatsu, M. *Chem. Pharm. Bull*. **2000**, *48*, 2003-2008.
4. Bratulescu, G. *Acta Chim. Slov.*, **2002**, *49*, 173-180.

Table 1 – Full optimisation of decarboxylative coupling of quinoline-3-carboxylic acid 1a with 4-iodoanisole 2a[a]





Xantphos Xphos Davephos CyJohnphos DPEphos

Entry	[Pd]	L	Solvent	Base	Ratio **1a/3a/3b/4a**[b]	Yield (%)[c]
1	$PdCl_2$	PPh_3	Toluene/DMA	Ag_2CO_3	7/56/29/8	42
2	$PdBr_2$	PPh_3	Toluene/DMA	Ag_2CO_3	0/64/32/5	52
3	PdI_2	PPh_3	Toluene/DMA	Ag_2CO_3	20/47/22/11	39
4	$Pd(OAc)_2$	PPh_3	Toluene/DMA	Ag_2CO_3	40/42/15/2	-
5	$PdBr_2$	P(*o*-tolyl)$_3$	Toluene/DMA	Ag_2CO_3	0/17/0/83	-
6	$PdBr_2$	P(*c*-hexyl)$_3$	Toluene/DMA	Ag_2CO_3	12/20/68	-
7	$PdBr_2$	Xantphos	Toluene/DMA	Ag_2CO_3	2/51/43/4	49
8	$PdBr_2$	Xphos	Toluene/DMA	Ag_2CO_3	0/36/0/64	-
9	$PdBr_2$	Davephos	Toluene/DMA	Ag_2CO_3	1/40/0/59	-
10	$PdBr_2$	CyJohnphos	Toluene/DMA	Ag_2CO_3	1/15/0/84	-
11	$PdBr_2$	DPEphos	Toluene/DMA	Ag_2CO_3	0/82/13/5	77
12[a]	**$PdBr_2$**	**DPEphos**	Toluene/DMA	Ag_2CO_3	**0/85/10/5**	**81**
13	$PdBr_2$	DPEphos	Toluene/DMA	Ag_2CO_3	7/72/16/5	60
14[u]	$PdBr_2$	DPEphos	Toluene	Ag_2CO_3	2/70/12/16	65
15[a]	$PdBr_2$	DPEphos	DMA	Ag_2CO_3	4/75/11/9	61
16[a]	$PdBr_2$	DPEphos	DMF	Ag_2CO_3	20/17/16/48	
17[u]	$PdBr_2$	DPEphos	Mesitylene	Ag_2CO_3	1/61/6/32	60
18[u]	$PdBr_2$	DPEphos	Cyclopentyl methyl ether	Ag_2CO_3	7/50/8/35	37
19[a]	$PdBr_2$	DPEphos	DMSO	Ag_2CO_3	14/71/8/8	-
20[a]	$PdBr_2$	DPEphos	Toluene/DMA	Ag_2CO_3[e]	100/0/0/0	-
21[a]	$PdBr_2$	DPEphos	Toluene/DMA	K_2CO_3	100/0/0/0	-
22[u]	$PdBr_2$	DPEphos	Toluene/DMA	Ag_2CO_3	7/76/12/5	74[f]

[a] **1a** (1 equiv), 4-iodoanisole (2 equiv), [Pd] (5 mol %), [L] (10 mol %), Ag_2CO_3 (1 equiv), Toluene/DMA (3.6/0.4 mL, 0.05M), 8h at 150 °C. [b] Ratio was determined by ^{1}H NMR in the crude reaction mixture based on the chemical shift of the proton signal (ppm) at the 2-position (**1a**: δ = 8.79, **3a**: δ = 7.79, **3b**: δ = 7.83). [c] Isolated yields. [d] The coupling reaction of **1a** with **2a** was performed under microwave irradiation (MWI) for 1h at 150 °C. [e] The coupling reaction of **1a** with **2a** was performed using 10 mol% of Ag_2CO_3. [f] The coupling reaction of **1a** with **2a** was performed under microwave irradiation for 90 min at 135 °C.

General procedure for decarboxylative arylation of quinolone-3-carboxylic acid 1 and related heterocyclic carboxylic acid with (hetero)aryl halides under microwave irradiation

A flame-dried resealable 2–5 mL Pyrex reaction vessel was charged with the solid reactant(s): $PdBr_2$ (5.0 mol %), DPEphos (10 mol %), heterocyclic carboxylic acid (1 equiv), (hetero)aryl halide (2 equiv) and Ag_2CO_3 (1 equiv). The reaction vessel was capped with a rubber septum, evacuated and backfilled with argon; this evacuation/backfill sequence was repeated one additional time. The liquid reactant(s) and toluene/DMA (9:1, 0.05M) were added through the septum. The septum was replaced with a Teflon screwcap. The reaction vessel was sealed, then placed in the Emrys Optimizer and exposed to microwave irradiation according to the following

specifications: temperature: 150 °C; 1 h; fixed hold time: on; high absorption: high; pre-stirring: 60 s. The resulting suspension was cooled to room temperature and filtered through a pad of Celite eluting with ethyl acetate, and the inorganic salts were removed. The filtrate was concentrated and purification of the residue by silica gel column chromatography gave the desired product.

Compound 3a. Yield: 81%; brown solid; mp: 151-153 °C; TLC : R_f 0.5 (*c*-hexane/EtOAc : 7/3); IR (neat): ν(cm^{-1}) 1625, 1554, 1511, 1478, 1391, 1327, 1249, 1174, 1037, 866, 779, 757; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.79 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.61 – 7.56 (m, 3H), 7.52 – 7.41 (m, 3H), 7.40 – 7.35 (m, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 159.0, 141.6, 141.1, 140.8, 131.7, 130.4 (2C), 130.0 (2C), 129.6, 127.8 (2C), 127.4, 126.7, 123.9, 121.9, 117.2, 113.9 (2C), 55.5. HRMS (ESI): calc. for $C_{22}H_{17}NO_2$ (M+H) 328.1338, found: 328.1336.

Compound 3b. Yield: 91%; yellow solid; mp: 201-203 °C; TLC : R_f 0.55 (*c*-hexane/EtOAc : 6/4); IR (neat): ν(cm^{-1}) 1617, 1577, 1549, 1497, 1477, 1326, 1255, 1028, 915, 754, 695; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.84 (s, 1H), 7.75 – 7.71 (m, 2H), 7.65-7.55 (m, 3H), 7.54-7.25 (m, 7H), 7.05 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 141.6, 141.5, 140.8, 135.4, 131.8, 130.5 (2C), 129.6, 129.3, 128.8 (2C), 128.4 (2C), 127.7 (2C), 127.4, 127.3, 126.9, 124.1, 122.2, 117.2. HRMS (ESI): calc. for $C_{21}H_{15}NO$ (M+H) 298.1247, found: 298.1232.

Compound 3c. Yield: 88%; brown solid; mp: 52-64 °C; TLC : R_f 0.2 (*c*-hexane/EtOAc : 6/4); IR (neat): ν(cm^{-1}) 1721, 1622, 1583, 1552, 1419, 1345, 1293, 1241, 1123, 1003, 754, 700, 643; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.1 Hz, 1H), 7.82 (s, 1H), 7.71 – 7.56 (m, 2H), 7.60 – 7.44 (m, 4H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 6.95 (s, 2H), 3.90 (s, 6H), 3.86 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 153.1 (2C), 141.3, 140.6, 137.5, 131.8, 130.8, 130.4 (2C), 129.6, 127.6 (2C), 127.1, 126.6, 124.0, 121.9, 117.1, 106.1, 60.84, 56.3 (2C). HRMS (ESI): calc. for $C_{24}H_{21}NO_4$ (M+H) 388.1563, found: 388.1549.

Compound 3d. Yield: 99%; yellow solid; mp: 170-172 °C; TLC : R_f 0.55 (*c*-hexane/EtOAc : 6/4); IR (neat): ν(cm^{-1}) 1621, 1588, 1554, 1477, 1315, 1235, 1029, 894, 865, 806, 781, 753, 699; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.0 Hz, 1H), 8.21 (s, 1H), 7.95 (s, 1H), 7.87 (s, 4H), 7.60 (s, 3H), 7.55 – 7.32 (m, 6H), 7.05 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 141.9, 141.5, 140.8, 133.6, 132.9, 132.7, 131.9, 130.5 (2C), 129.7, 128.2, 127.8 (3C), 127.6, 127.4, 127.3, 127.1, 126.9, 126.0, 125.8, 124.2, 122.1, 117.3; HRMS (ESI): calc. for $C_{25}H_{17}NO$ (M+H) 348.1388, found: 348.1405.

Compound 3e. Yield: 73%; yellow solid; mp: 127-129 °C; TLC : R_f 0.62 (CH_2Cl_2/EtOAc : 9/1); IR (neat): ν(cm^{-1}) 1627, 1587, 15553, 1493, 1493, 1475, 1392, 1325, 1275, 1022, 766, 694; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.82 (s, 1H), 7.69 – 7.43 (m, 6H), 7.42 – 7.24 (m, 3H), 7.12 – 6.94 (m, 3H), 3.80 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 157.4, 143.0, 141.7, 140.9, 132.1, 131.6, 130.3 (2C), 129.4, 129.0, 127.7 (2C), 127.4, 126.7, 124.2, 123.8, 120.7, 119.4, 117.1, 111.5, 56.0. HRMS (ESI): calc. for $C_{22}H_{17}NO_2$ (M+H) 328.1338, found: 328.1344.

Compound 3f. Yield: 60%; yellow solid; mp: 198-200 °C; TLC : R_f 0.5 (*c*-hexane/EtOAc : 7/3); IR (neat): ν(cm^{-1}) 1631, 1590, 1524, 1356, 1335, 765, 699, 646; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.99 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.84 (s, 1H), 7.70 – 7.31 (m, 10H), 7.04 (d, *J* = 8.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1, 150.2, 141.3, 141.1, 141.0, 132.8, 132.2 (2C), 130.5 (2C), 129.9, 129.8, 128.5 (2C),

127.7, 127.4, 126.0, 124.5, 124.4, 120.4, 117.3. HRMS (ESI): calc. for $C_{21}H_{14}N_2O_3$ (M+H) 343.1083, found: 343.1078.

Compound 3g. Yield: 90%; yellow solid; mp: 124-126 °C; TLC : R_f 0.5 (CH_2Cl_2/EtOAc : 9/1); IR (neat): ν(cm^{-1}) 1626, 1589, 1555, 1490, 1368, 1327, 1248, 753, 706; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.85 (d, *J* = 1.3 Hz, 1H), 7.68 (td, *J* = 7.6, 1.7 Hz, 1H), 7.65 – 7.42 (m, 6H), 7.53 – 7.42 (m, 3H), 7.41 – 7.35 (m, 1H), 7.33 – 7.24 (m, 1H), 7.18 (td, *J* = 7.5, 1.3 Hz, 1H), 7.15 – 7.08 (m, 1H), 7.05 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.6, 160.24 (d, J_{C-F} = 244.5 Hz), 143.1, 143.0, 141.4, 140.9, 132.4 (d, J_{C-F} = 3 Hz), 131.9, 130.4, 129.6, 129.1 (d, J_{C-F} = 8.25 Hz), 127.7, 127.3, 126.7, 124.2, 124.0, 123.9, 122.8 (d, J_{C-F} = 14.25 Hz), 117.3, 116.6, 115.8 (d, J_{C-F} = 23.25 Hz). HRMS (ESI): calc. for $C_{21}H_{14}FNO$ (M+H) 316.1138, found: 316.1122.

Compound 3h. Yield: 40%; yellow solid; mp: 145-147 °C; TLC : R_f 0.33 (*c*-hexane/EtOAc : 7/3); IR (neat): ν(cm^{-1}) 1709, 1625, 1590, 1479, 1365, 1327, 1293, 1259, 1132, 1018, 790, 757, 695; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.85 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.66 (s, 1H), 7.58 – 7.35 (m, 6H), 7.34 – 7.24 (m, 3H), 7.17 – 7.04 (m, 1H), 6.99 – 6.91 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 1.08 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 168.1, 141.6, 141.1, 140.7, 135.4, 132.5, 131.8, 131.6, 131.18, 130.4 (2C), 129.9, 129.5, 129.1, 128.3, 127.8 (2C), 127.6, 127.4, 126.2, 125.4, 123.9, 123.6, 117.1, 60.9, 14.1. HRMS (ESI): calc. for $C_{24}H_{19}NO_3$ (M+H) 370.1443, found: 370.1455.

Compound 3i. Yield: 72%; yellow solid; mp: 125-127 °C; TLC : R_f 0.7 (CH_2Cl_2); IR (neat): ν(cm^{-1}) 1717, 1623, 1584, 1552, 1492, 1274, 1206, 1103, 907, 794, 701, 624; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.24 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.88 (s, 1H), 7.72 – 7.44 (m, 7H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 166.9, 141.7, 141.4, 140.9, 135.7, 133.8, 132.0, 130.7, 130.5 (2C), 129.8, 129.3, 128.4 (2C), 127.8 (2C), 127.3, 126.8, 124.2, 121.2, 117.3, 61.1, 14.5. HRMS (ESI): calc. for $C_{24}H_{19}NO_3$ (M+H) 370.1443, found: 370.1446.

Compound 3j. Yield: 77%; yellow solid; mp: 196-198 °C; TLC : R_f 0.45 (CH_2Cl_2/EtOAc : 9/1); IR (neat): ν(cm^{-1}) 1727, 1624, 1583, 1553, 1493, 1478, 1386, 1329, 1255, 1089, 864, 829, 786, 757, 703, 616; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.0 Hz, 1H), 7.81 (s, 1H), 7.73 – 7.30 (m, 11H), 7.03 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 141.5, 140.8, 133.8, 133.1, 132.0, 130.5 (2C), 130.1 (2C), 129.8, 128.5 2C), 127.7 (2C), 127.3, 126.8, 124.2, 121.0, 117.3. HRMS (ESI): calc. for $C_{21}H_{14}ClNO$ (M+H) 332.0842, found: 332.0846.

Compound 3k. Yield: 90%; yellow solid; mp: 167-169 °C; TLC : R_f 0.55 (*c*-hexane/EtOAc : 6/4); IR (neat): ν(cm^{-1}) 1575, 1553, 1509, 1478, 1327, 1257, 1223, 1160, 869, 836, 779, 755, 694, 655; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.0 Hz, 1H), 7.79 (s, 1H), 7.74 – 7.43 (m, 8H), 7.38 (m, 1H), 7.11-7.01 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 162.2 (d, J_{C-F} = 244.5 Hz), 141.5, 141.4, 140.8, 131.9, 131.3, 130.5 (2C), 130.4, 129.7, 127.7 (2C), 127.3, 126.7, 124.1, 121.3, 117.3, 115.4, 115.1. HRMS (ESI): calc. for $C_{21}H_{14}FNO$ (M+H) 316.1138, found: 316.1147.

Compound 3l. Yield: 40%; yellow solid; mp: 249-251 °C; TLC : R_f 0.44 (*c*-hexane/EtOAc : 7/3); IR (neat): ν(cm^{-1}) 1716, 1619, 1585, 1549, 1478, 1373, 1321, 1280, 1122, 997, 918, 865, 775, 757, 698; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.76 (s, 1H), 8.57 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.72 – 7.46 (m, 8H), 7.42 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 7.36 – 7.27 (m, 2H), 7.14 – 7.03 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 161.3, 153.1,

144.9, 142.3, 141.4, 140.2, 132.1, 131.1 (2C), 130.5, 129.8, 128.4 (2C), 127.7, 127.3, 126.7, 124.6 (2C), 120.1, 117.6, 116.3, 113.4. HRMS (ESI): calc. for $C_{24}H_{15}NO_3$ (M+H) 366.1130, found: 366.1131.

Compound 3m. Yield: 57%; yellow solid; mp: 202-204 °C; TLC : R_f 0.36 (*c*-hexane/EtOAc : 7/3); IR (neat): ν(cm^{-1}) 1622, 1547, 1478, 1452, 1370, 1327, 1281, 1220, 755, 699; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (s, 2H), 8.51 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.62 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.57 – 7.39 (m, 6H), 7.38 – 7.27 (m, 2H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.15 (dd, *J* = 11.0, 4.0 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 161.4, 145.1, 141.7, 140.3, 139.4, 138.1, 131.7, 130.4 (2C), 130.2, 129.6, 129.5, 127.8 (2C), 127.3, 126.9, 124.2, 123.7, 122.1, 121.4, 117.4, 115.1, 113.7, 38.1, 12.9. HRMS (ESI): calc. for $C_{26}H_{20}N_2O_2$ (M+H) 393.1603, found: 393.1604.

Compound 3n. Yield: 61%; yellow solid; mp: 146-148 °C; TLC : R_f 0.26 (*c*-hexane/ CH_2Cl_2/ : 7/3); IR (neat): ν(cm^{-1}) 1623, 1591, 1495, 1260, 1112, 884, 780, 695 ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, *J* = 8.7 Hz, 1H), 7.79 (s, 1H), 7.74 – 7.54 (m, 5H), 7.53 – 7.37 (m, 4H), 7.37 – 7.31 (m, 2H), 7.00 (d, *J* = 1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 141.8, 141.5, 141.1, 138.3, 134.9, 130.7 (2C), 130.0, 129.3, 128.8 (2C), 128.5 (2C), 127.6 (2C), 127.6, 125.3, 124.8, 122.9, 116.8. HRMS (ESI): calc. for $C_{21}H_{14}ClNO$ (M+H) 332.0842, found: 332.0846.

Compound 3o. Yield: 90%; yellow solid; mp: 133-135 °C; TLC : R_f 0.4 (*c*-hexane/ CH_2Cl_2/ : 8/2); IR (neat): ν(cm^{-1}) 1612, 1590, 1562, 1485, 1310, 1212, 1025, 942, 885, 811, 783, 759, 741, 699; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 9.1, 3.0 Hz, 1H), 7.82 (s, 1H), 7.72 – 7.52 (m, 5H), 7.51 – 7.37 (m, 4H), 7.35 – 7.20 (m, 2H), 7.04 (dd, *J* = 9.3, 4.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 158.5 (d, $J_{C\text{-}F}$ = 244.5 Hz), 140.6, 140.4, 136.4, 134.0, 129.6 (2C), 128.8, 127.8 (2C), 127.4 (2C), 126.6 (2C), 126.4, 120.6, 119.5 (d, $J_{C\text{-}F}$ = 25.5 Hz), 118.6, 118.5, 110.8 (d, $J_{C\text{-}F}$ = 22.5 Hz). HRMS (ESI): calc. for $C_{21}H_{14}FNO$ (M+H) 316.1138, found: 316.1131.

Compound 3p. Yield: 70%; brown solid; mp: 136-138 °C; TLC : R_f 0.6 (*c*-hexane/EtOAc : 6/4); IR (neat): ν(cm^{-1}) 1611, 1589, 1509, 1489, 1345, 1296, 1249, 1163, 1029, 862, 834, 817, 748; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.01 (d, *J* = 2.9 Hz, 1H), 7.92 – 7.75 (m, 5H), 7.51 – 7.43 (m, 2H), 7.37 (d, *J* = 8.8 Hz, 2H), 7.14 (dd, *J* = 9.3, 2.9 Hz, 1H), 7.08 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 9.2 Hz, 1H), 3.95 (s, 3H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 160.2, 156.6, 141.5, 135.9, 134.3, 133.7, 133.3, 132.7, 128.8 (2C), 128.2, 128.1, 127.7, 127.6, 127.4, 127.1, 125.9, 125.7, 122.6, 120.8, 119.1, 115.4 (2C), 106.1, 55.9, 55.8. HRMS (ESI): calc. for $C_{27}H_{21}NO_3$ (M+H) 408.1600, found: 408.1599.

Compound 3q. Yield: 83%; brown solid; mp: 144-146 °C; TLC : R_f 0.5 (*c*-hexane/EtOAc : 5/5); IR (neat): ν(cm^{-1}) 1611, 1573, 1552, 1510, 1489, 1372, 1328, 1297, 1247, 1225, 1163, 1028, 884, 843, 828, 693, 627; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 3.0 Hz, 1H), 7.74 (s, 1H), 7.70 (d, *J* = 5.5 Hz, 1H), 7.67 (d, *J* = 5.5 Hz, 1H), 7.34 (d, *J* = 8.9 Hz, 2H), 7.18 – 7.04 (m, 5H), 6.97 (d, *J* = 9.3 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3, 162.2 (d, $J_{C\text{-}F}$ = 243.75 Hz), 160.3, 156.6, 141.0, 135.9, 134.2, 131.6 (d, $J_{C\text{-}F}$ = 8.25 Hz), 130.5, 130.4, 128.8 (2C), 127.9, 122.7, 120.1, 119.1, 115.4 (2C), 115.1 (2C, d, $J_{C\text{-}F}$ = 21.0 Hz), 106.0, 55.9, 55.8. HRMS (ESI): calc. for $C_{23}H_{18}FNO_3$ (M+H) 376.1349, found: 376.1353.

Compound 3r. Yield: 60%; brown solid; mp: 102-104 °C; TLC : R_f 0.7 (CH_2Cl_2); IR (neat): ν(cm^{-1}) 1625, 1581, 1551, 1492, 1364, 1261, 1013, 864, 798, 750, 698, 637; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, *J* = 8.4 Hz, 1H), 7.77 – 7.56 (m, 4H), 7.53 – 7.36 (m, 4H), 7.31 (d, *J* = 7.4 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (75 MHz,

$CDCl_3$) δ 175.0, 141.7, 139.1, 134.6, 131.1, 127.8 (2C), 127.4 (2C), 126.8, 126.4, 126.2, 122.92, 121.2, 114.2, 39.8. HRMS (ESI): calc. for $C_{16}H_{13}NO$ (M+H) 236.1075, found: 236.1067.

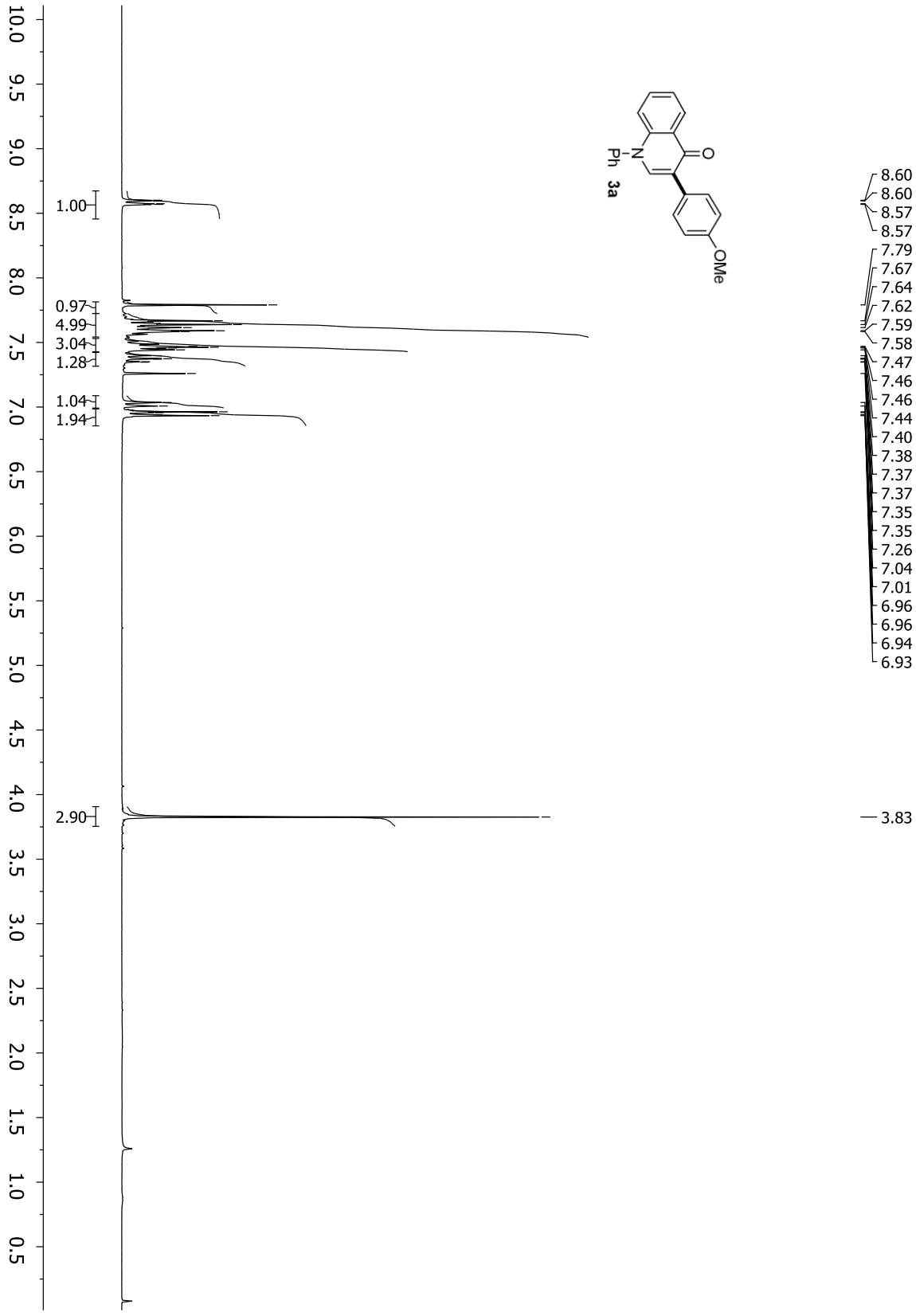
Compound 5. Yield: 45%; brown solid; mp: 118-120 °C; TLC : R_f 0.5 (*c*-hexane/EtOAc : 5/5); IR (neat): ν(cm^{-1}) 1622, 1584, 1513, 1494, 1442, 1337, 1258, 1242, 1177, 1010, 793, 630; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (d, *J* = 8.1 Hz, 1H), 7.80 (s, 1H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 4.48 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 2.66 (s, 3H), 1.48 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5, 162.2, 159.1, 148.6, 140.6, 136.8, 129.9 (2C), 127.8, 122.9, 119.9, 119.7, 114.0 (2C), 55.50, 45.8, 25.3, 15.4. HRMS (ESI): calc. for $C_{18}H_{18}N_2O_2$ (M+H) 295.1447, found: 295.1440.

Compound 6a. Yield: 72%; yellow solid; mp: 150-152 °C; TLC : R_f 0.5 (*c*-hexane/EtOAc : 6/4); IR (neat): ν(cm^{-1}) 1758, 1718, 1628, 1592, 1513, 1457, 1291, 1258, 1203, 953, 810, 614; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.67 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 6.44 (d, *J* = 2.1 Hz, 1H), 6.29 (d, *J* = 2.2 Hz, 1H), 3.90 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 159.7, 157.1, 156.00, 134.2, 129.74 (2C), 127.9, 122.5, 113.9 (2C), 111.9, 105.0, 94.96, 92.5, 56.1, 55.9, 55.5. HRMS (ESI): calc. for $C_{18}H_{16}O_5$ (M+H) 313.1076, found: 313.1082.

Compound 6b. Yield: 69%; yellow solid; mp: 104-106 °C; TLC : R_f 0.4 (*c*-hexane/EtOAc : 6/4); IR (neat): ν(cm^{-1}) 1714, 1626, 1606, 1506, 1368, 1271, 1200, 1160, 1124, 1026, 984, 829, 783, 694, 628; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.74 – 7.65 (m, 2H), 7.52 – 7.34 (m, 4H), 6.95 – 6.81 (m, 2H), 3.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 161.0, 155.5, 140.1, 135.2, 128.9, 128.6 (5C), 125.0, 113.5, 112.9, 100.6, 55.9. HRMS (ESI): calc. for $C_{16}H_{12}O_3$ (M+H) 253.0865, found: 253.0864.

Compound 7. Yield: 44%; yellow solid; mp: 124-126 °C; TLC : R_f 0.5 (*c*-hexane/EtOAc : 6/4); IR (neat): ν(cm^{-1}) 1730, 1644, 1592, 1454, 1232, 1119, 786, 750, 719, 693, 636; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.76 – 7.68 (m, 2H), 7.67 – 7.59 (m, 1H), 7.59 – 7.51 (m, 1H), 7.49 – 7.35 (m, 4H), 7.31 – 7.22 (m, 1H), 3.81 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 139.8, 136.9, 132.7, 130.4, 129.1, 130.0, 128.3, 128.2, 122.3 (2C), 120.9 (2C), 114.1, 30.1. HRMS (ESI): calc. for $C_{16}H_{13}NO$ (M+H) 236.1075, found: 236.1065.

Compound 8. Yield: 52%; yellow solid; mp: 91-93 °C; TLC : R_f 0.25 (CH_2Cl_2); IR (neat): ν(cm^{-1}) 1642, 1569, 1495, 1464, 1448, 1374, 1261, 1225, 1129, 1044, 905, 850, 768, 753, 688, 672; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 – 8.20 (m, 1H), 8.02 – 7.87 (m, 2H), 7.70 (ddd, *J* = 8.7, 7.1, 1.7 Hz, 1H), 7.63 – 7.49 (m, 4H), 7.43 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 6.83 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.6, 163.6, 156.43, 133.9, 131.9, 131.7, 129.2 (2C), 126.4 (2C), 125.9, 125.4, 124.1, 118.2, 107.8. HRMS (ESI): calc. for $C_{15}H_{10}O_2$ (M+H) 223.0759, found: 223.0765.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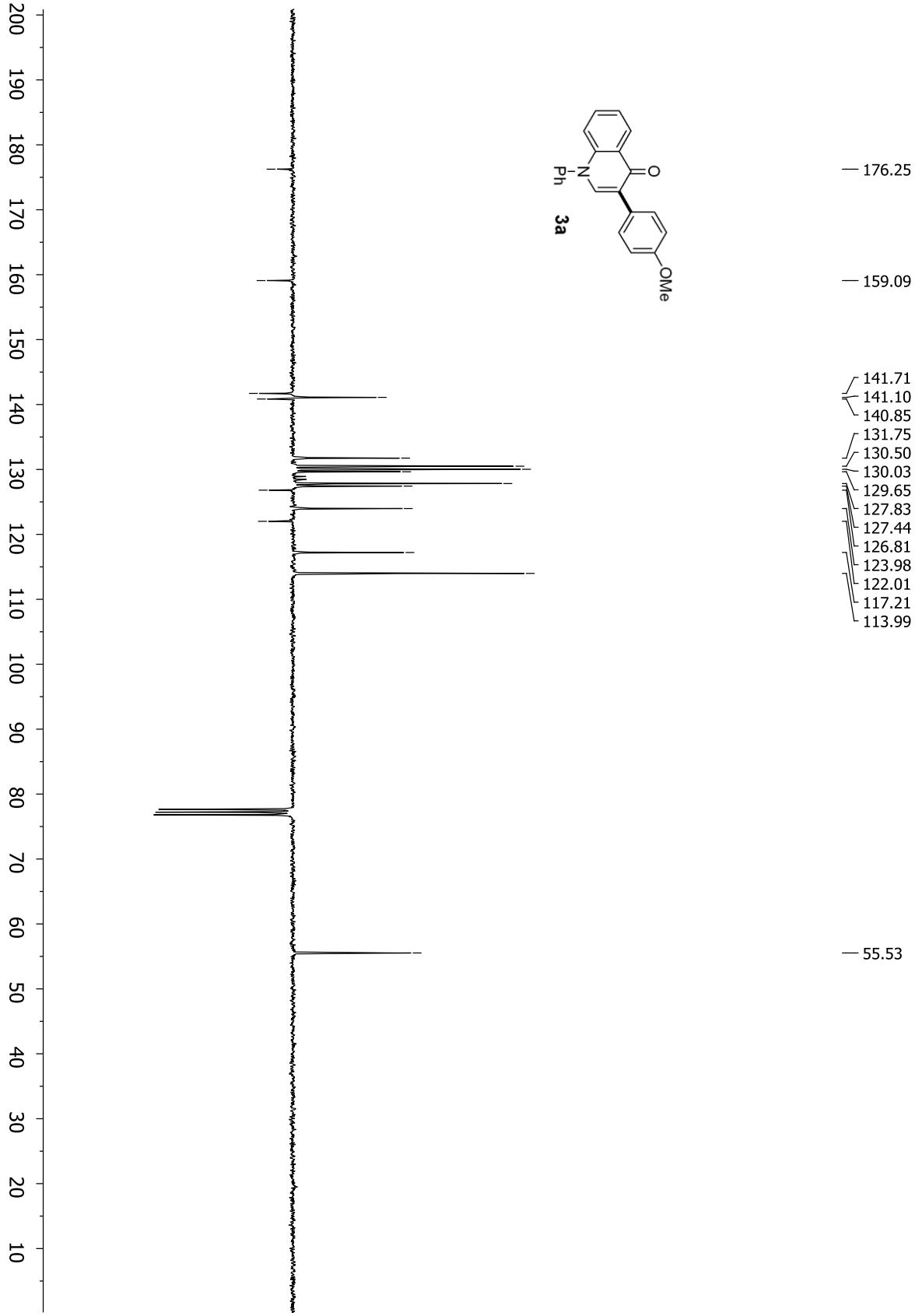
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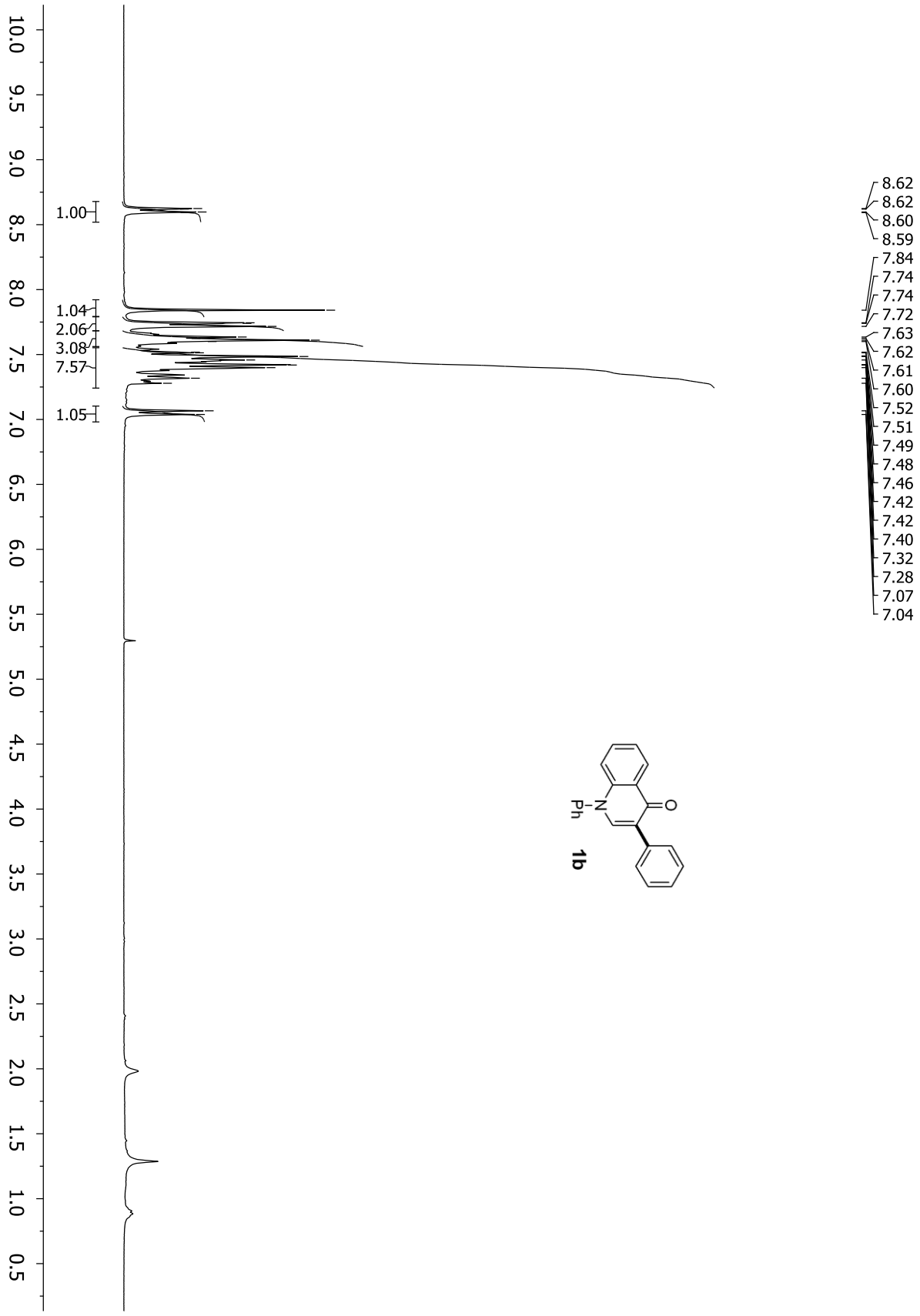
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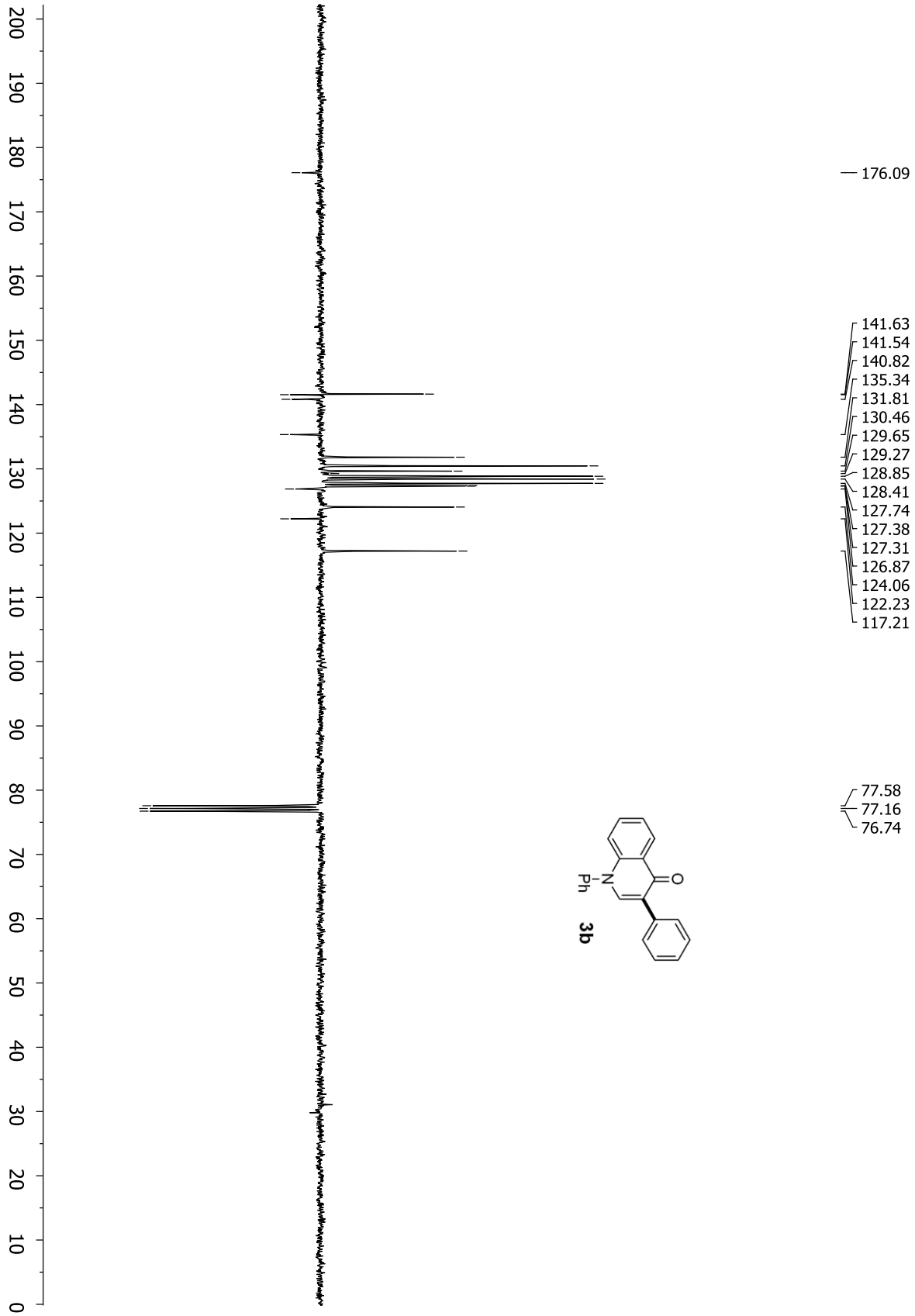
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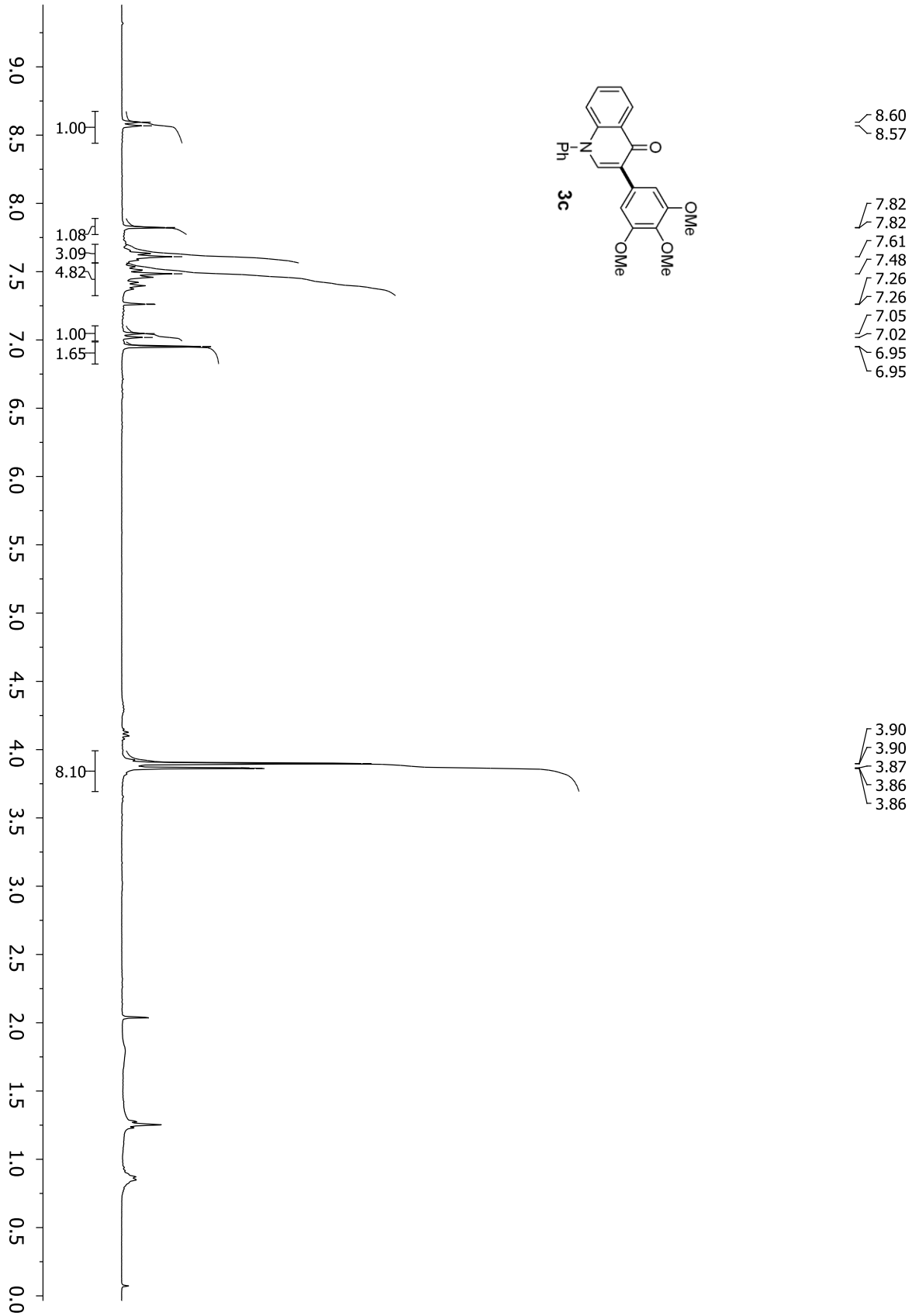
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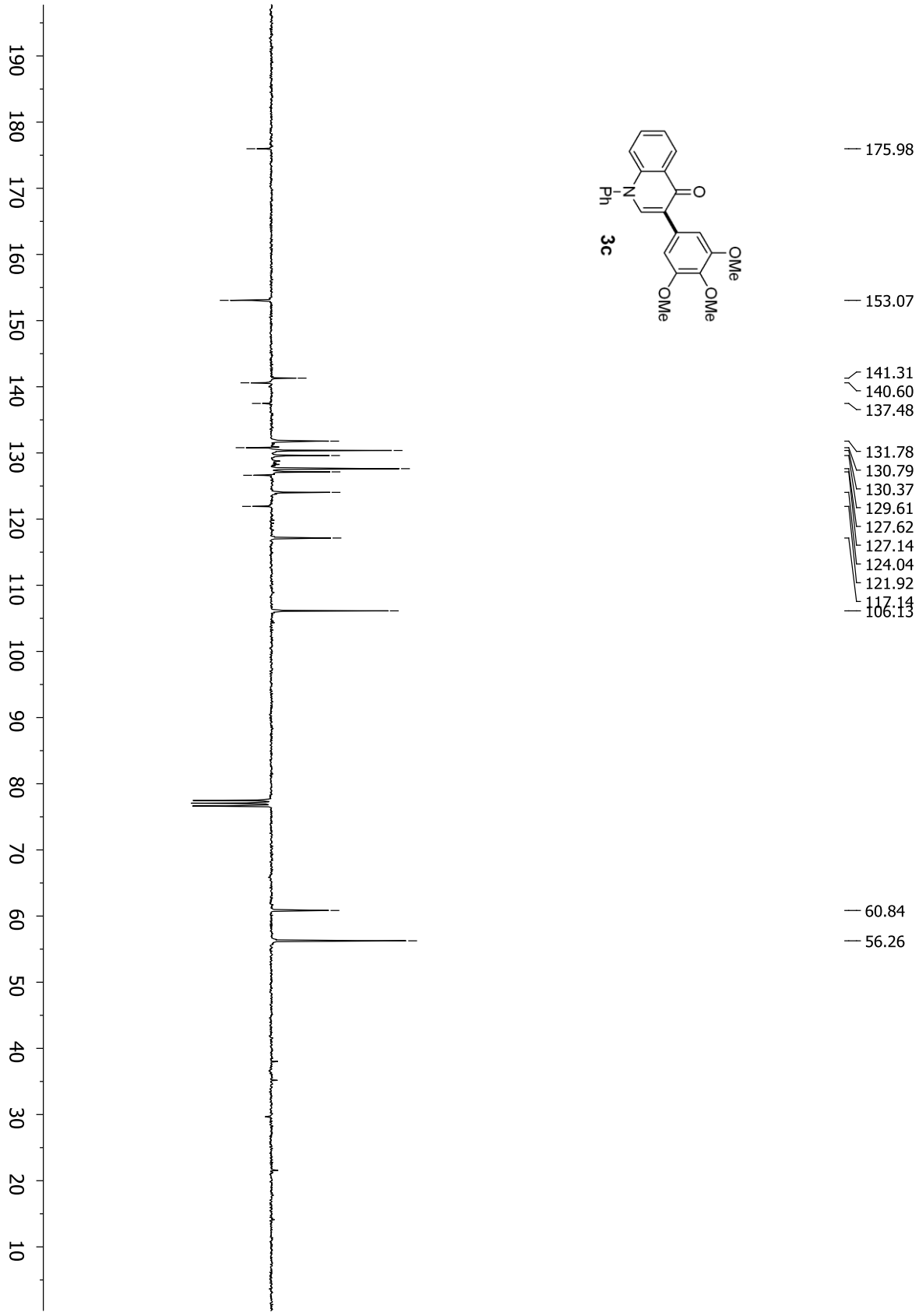
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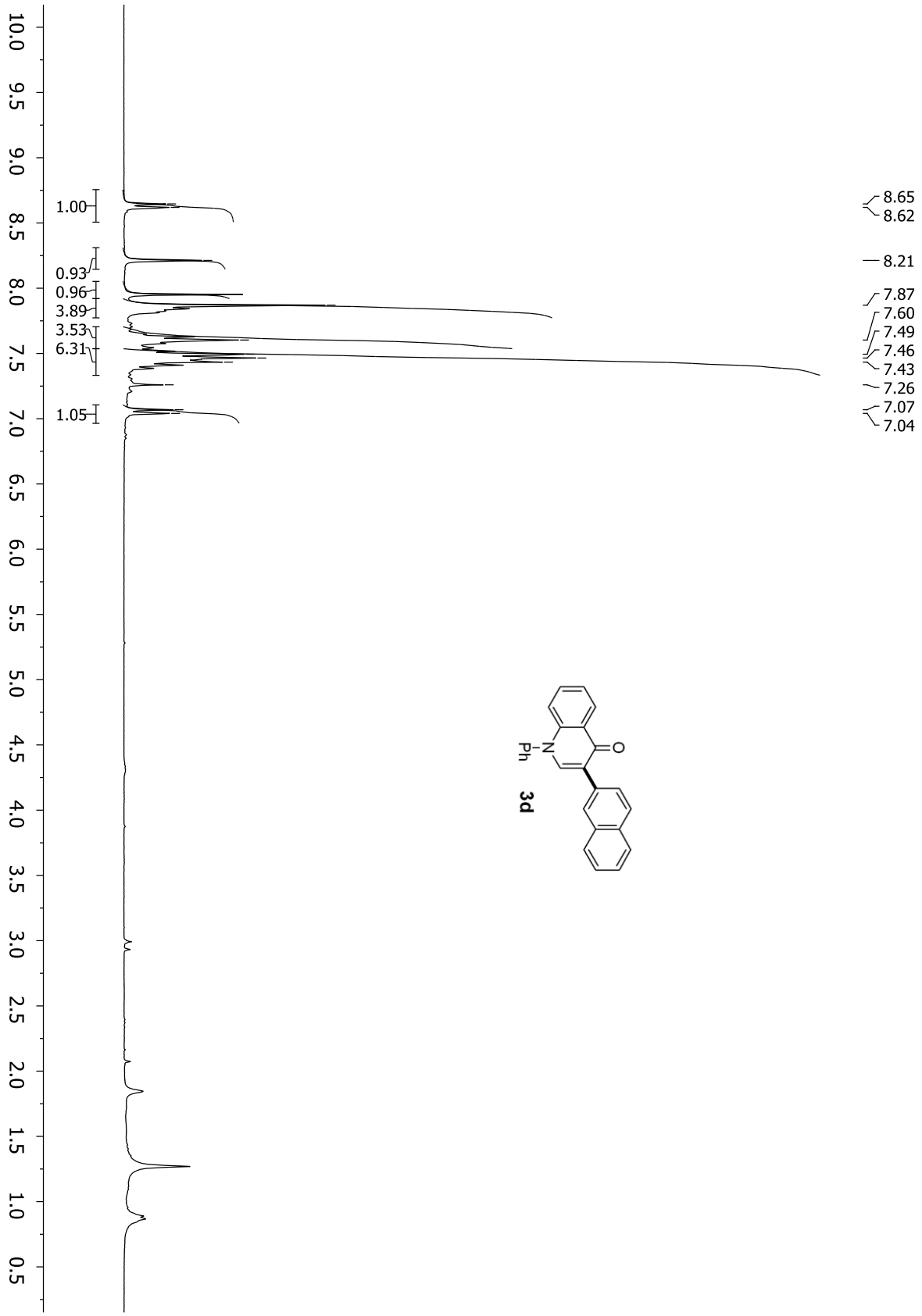
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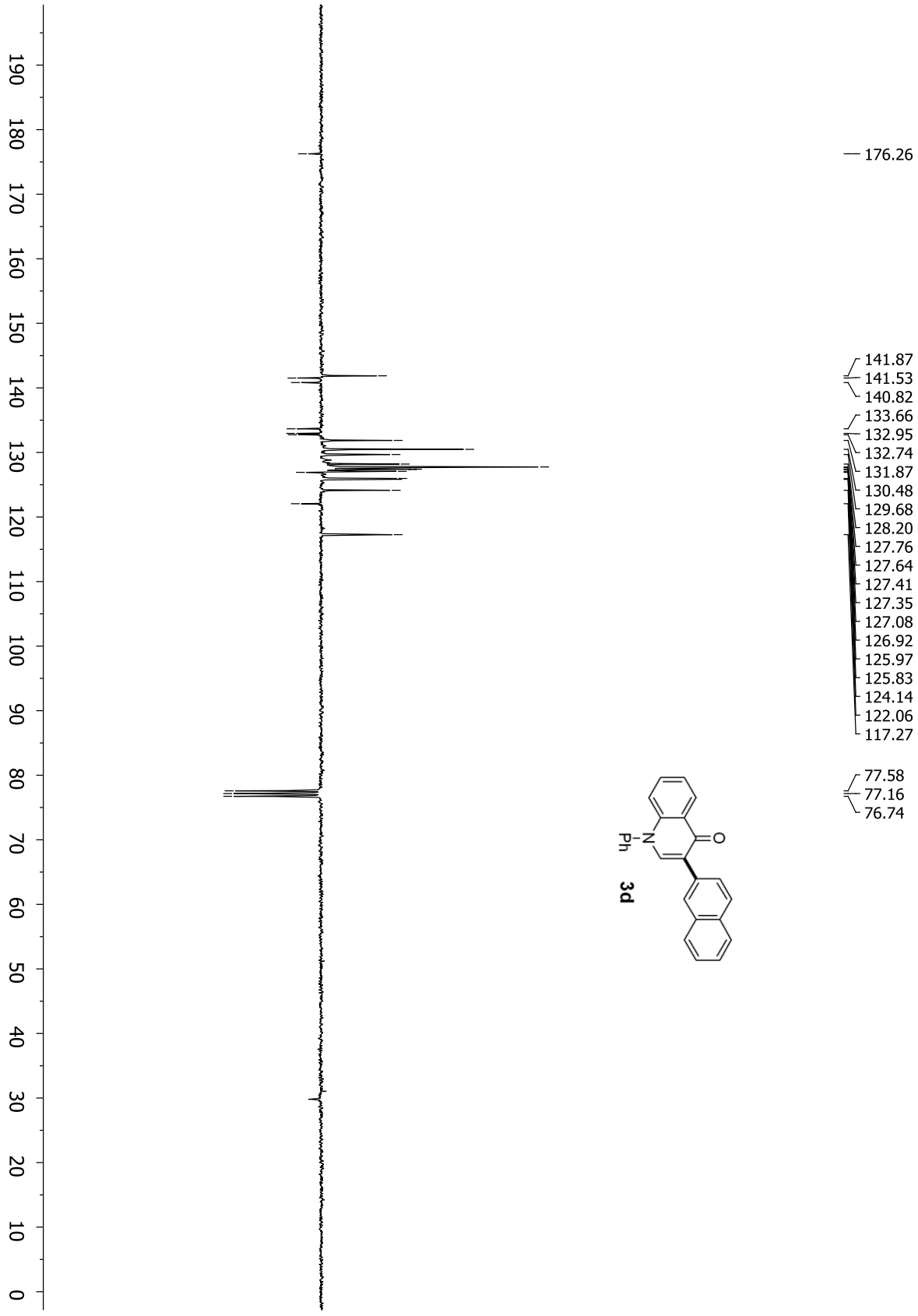
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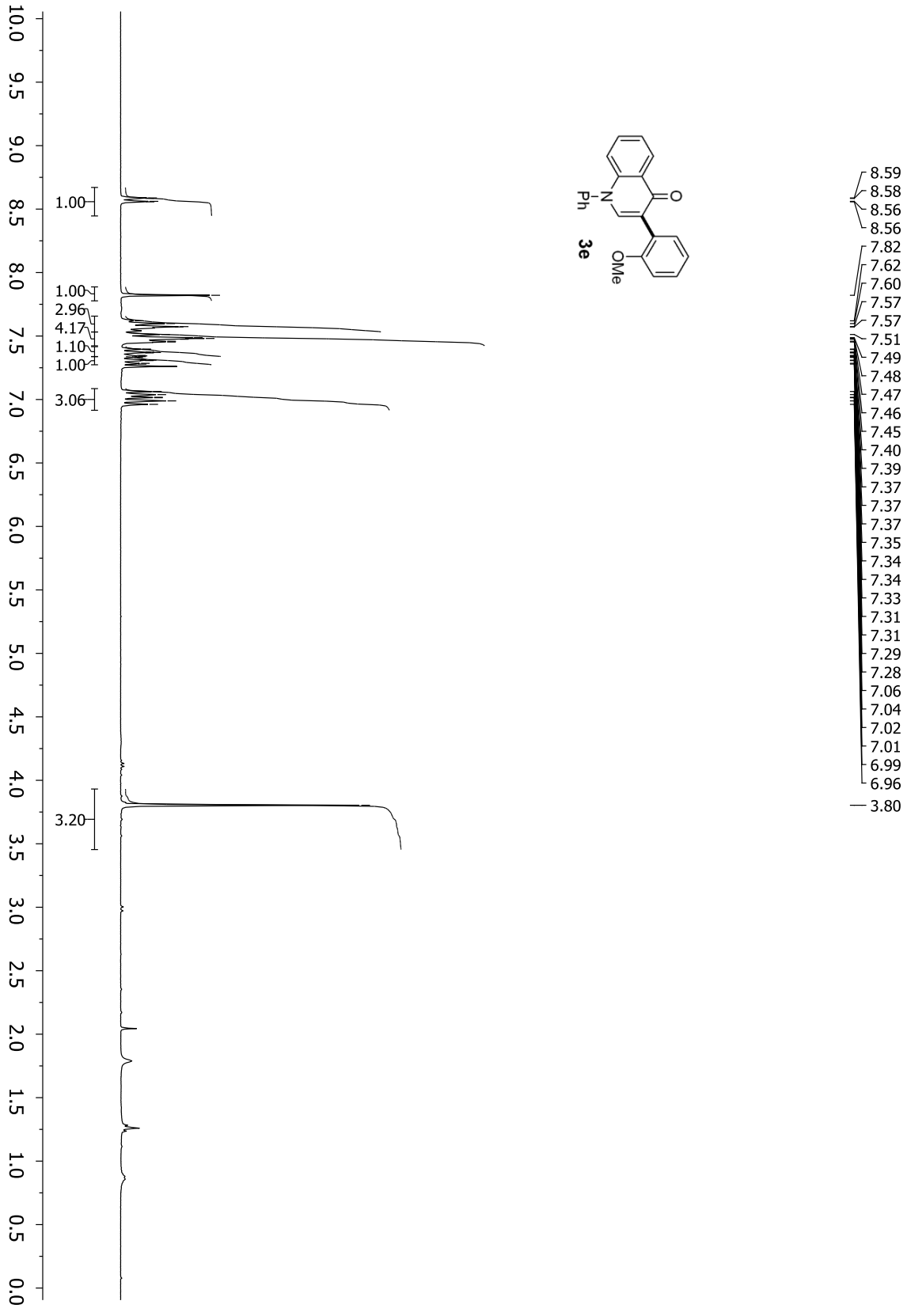
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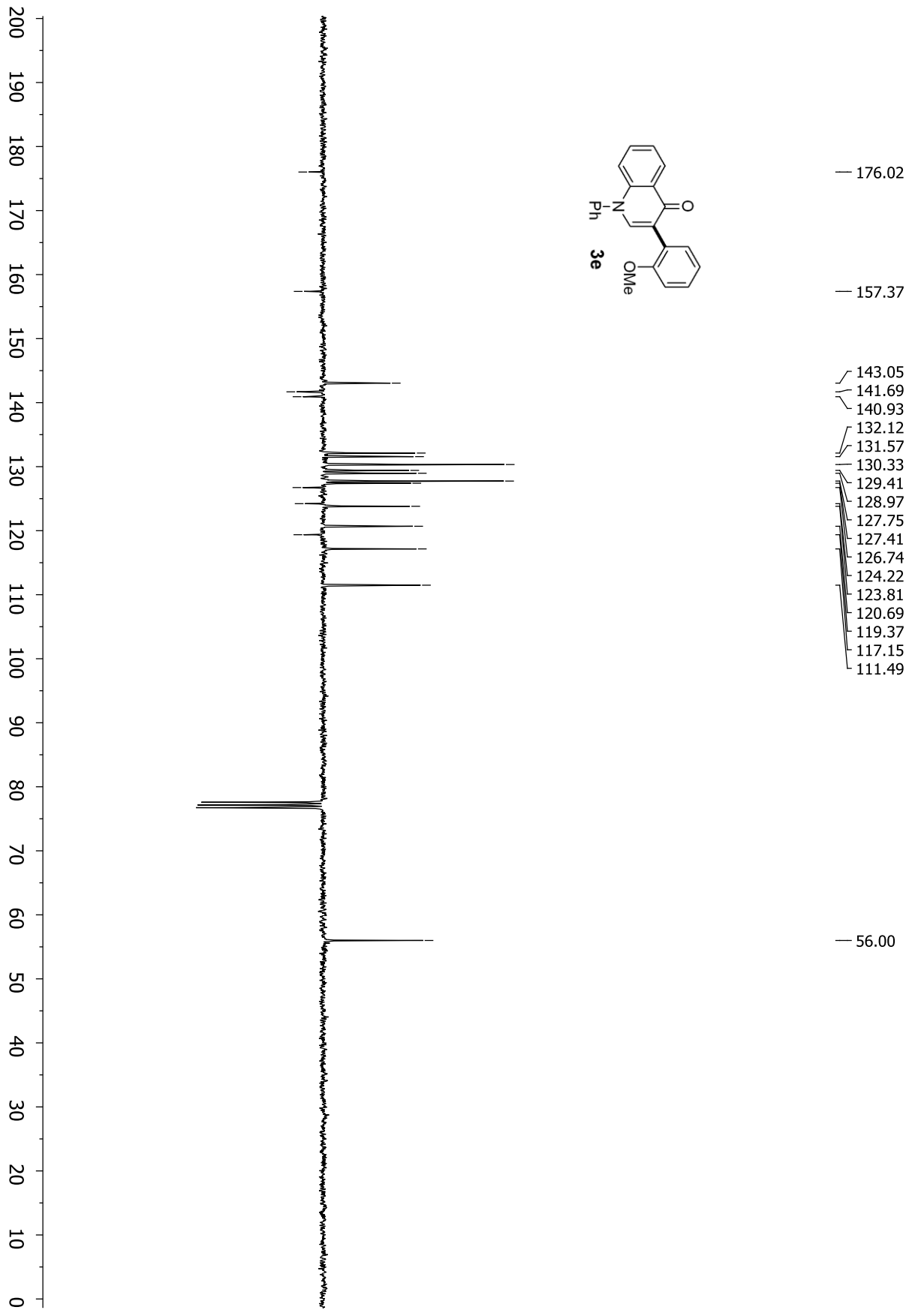
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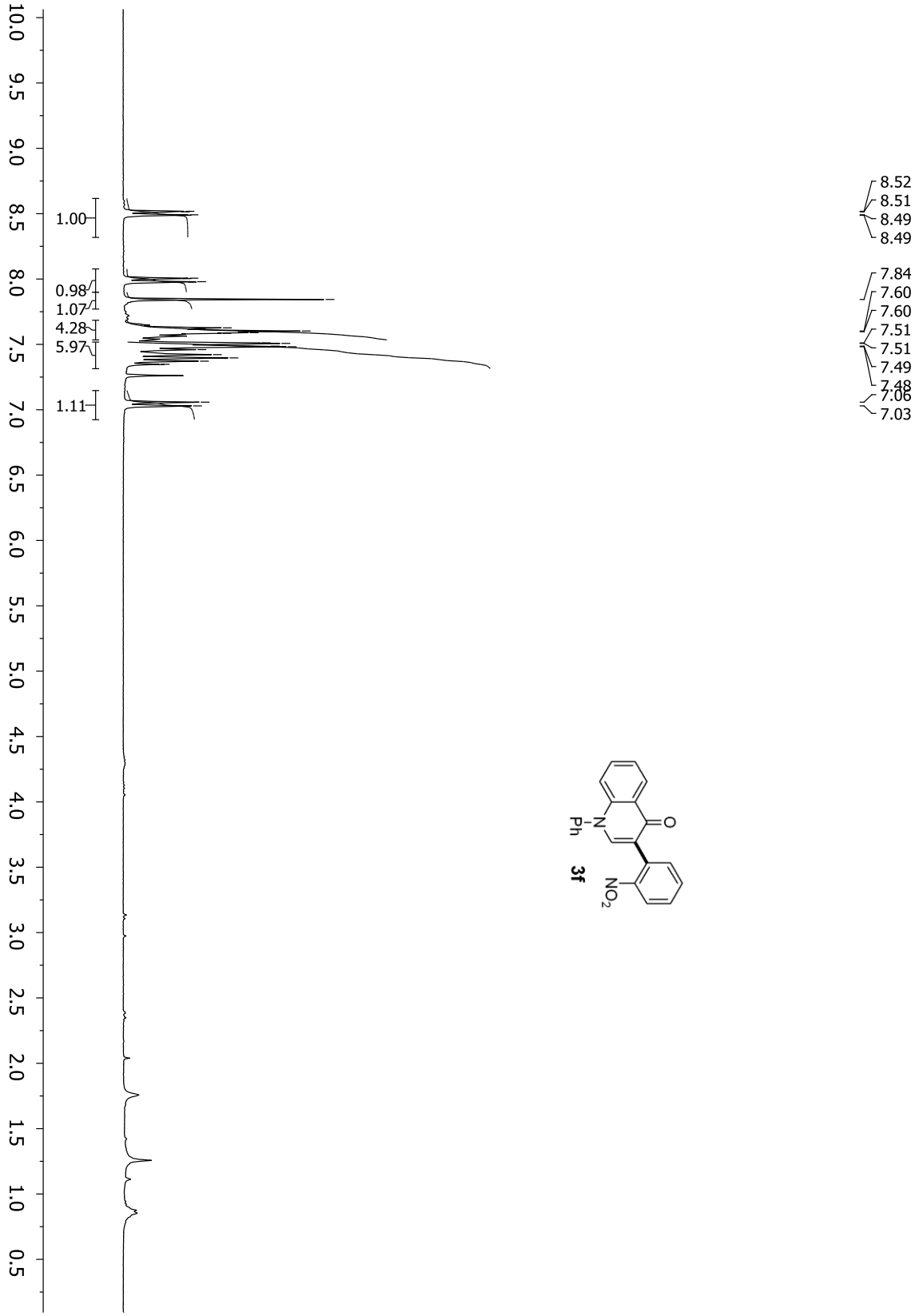
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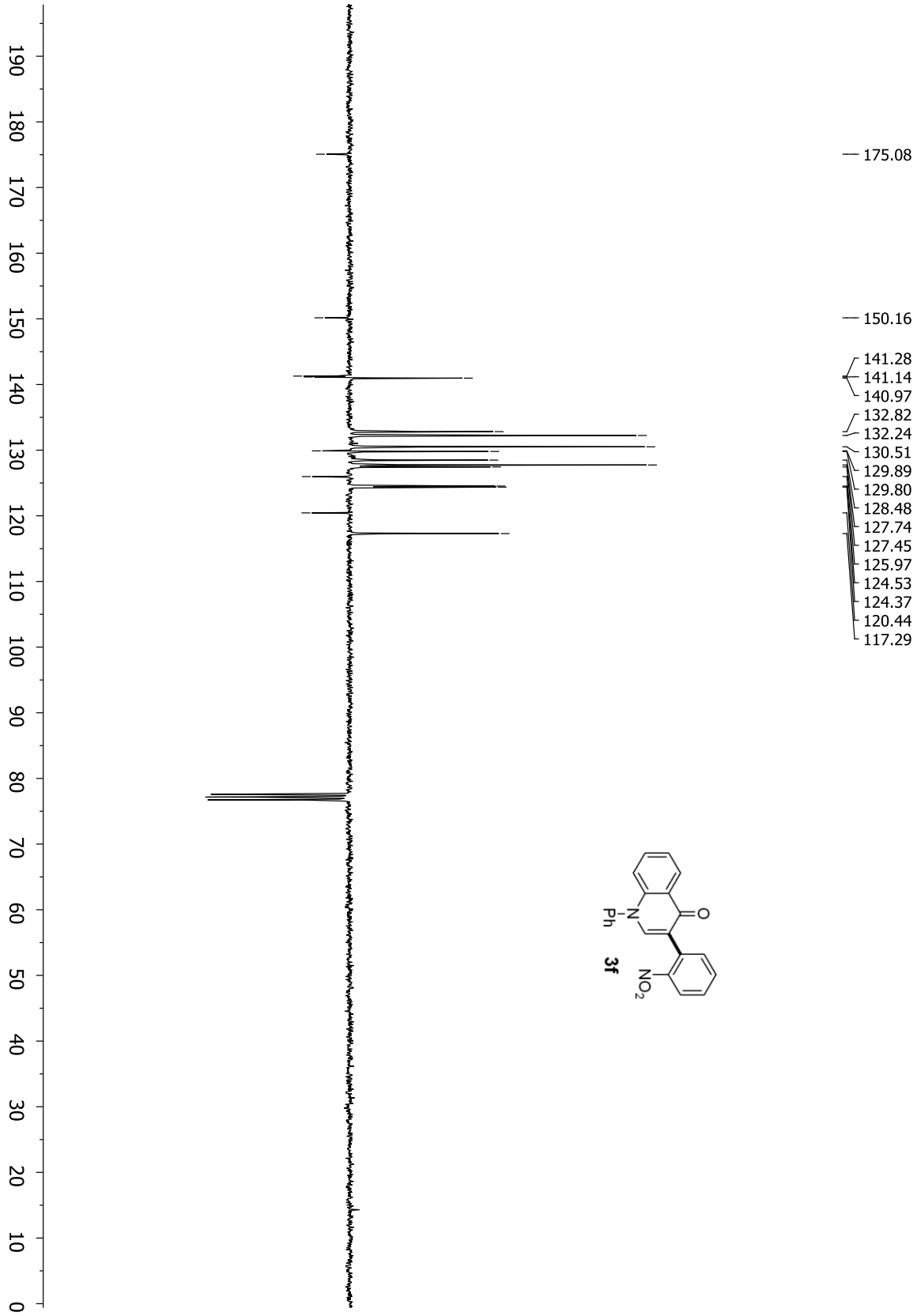
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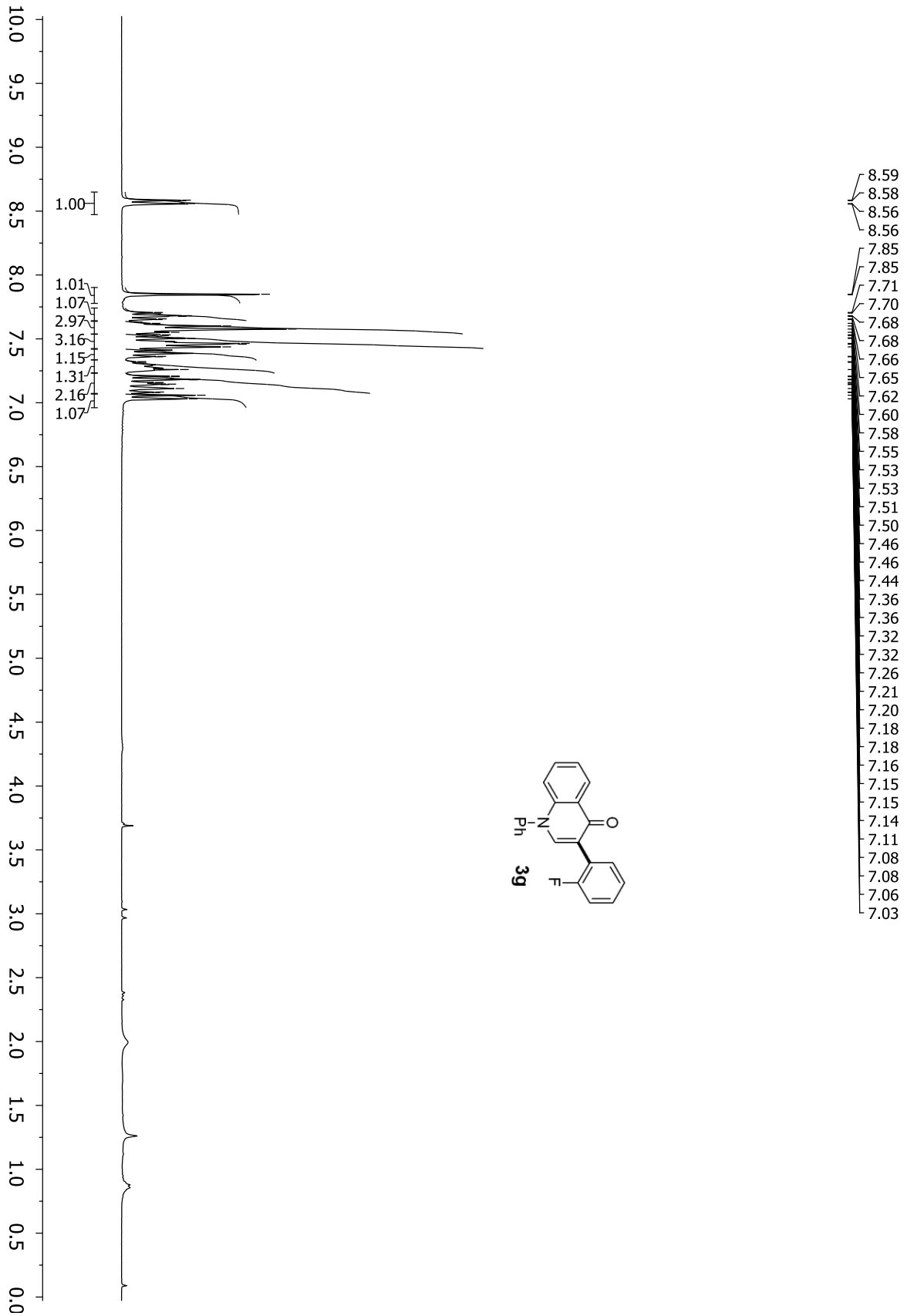
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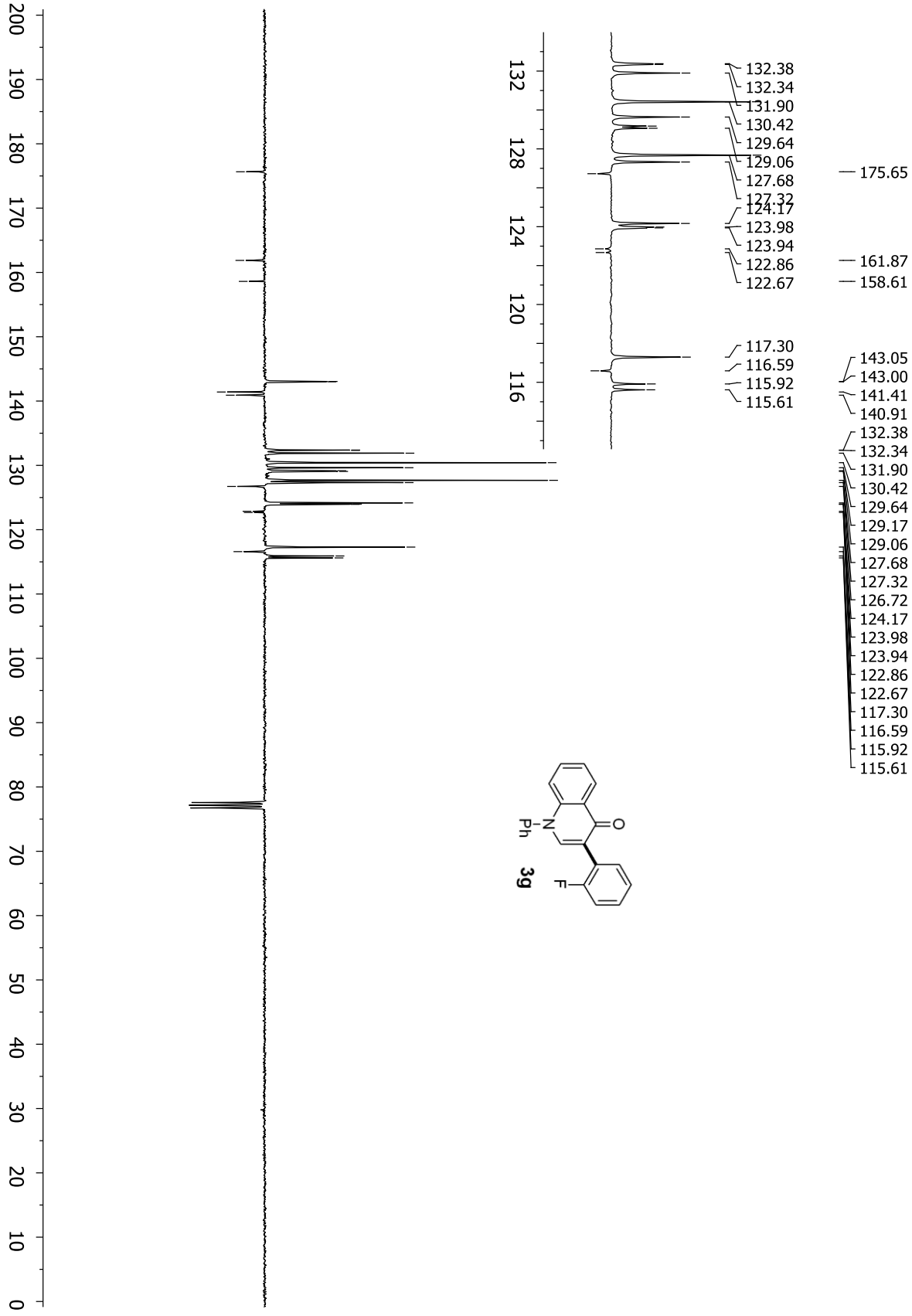
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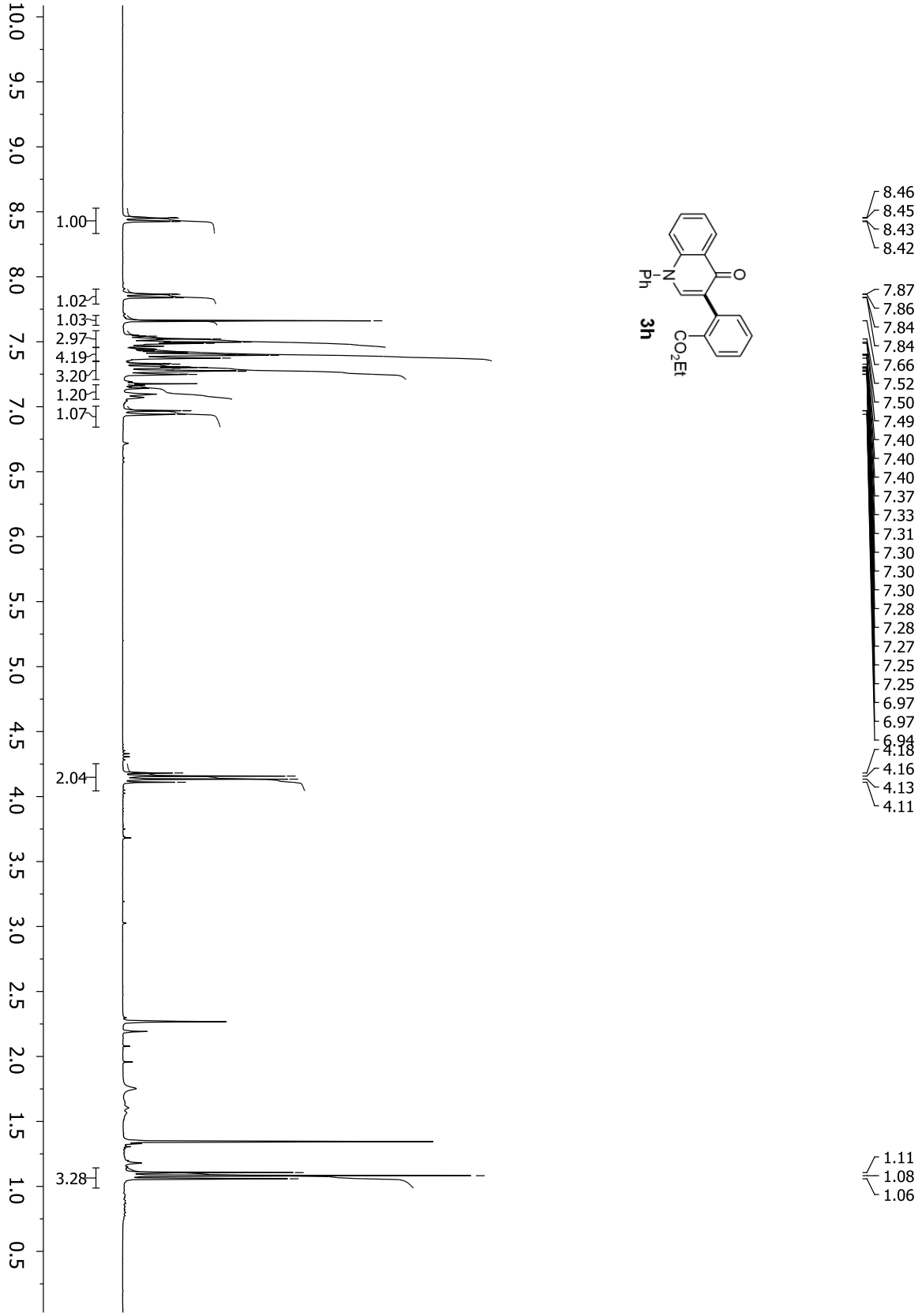
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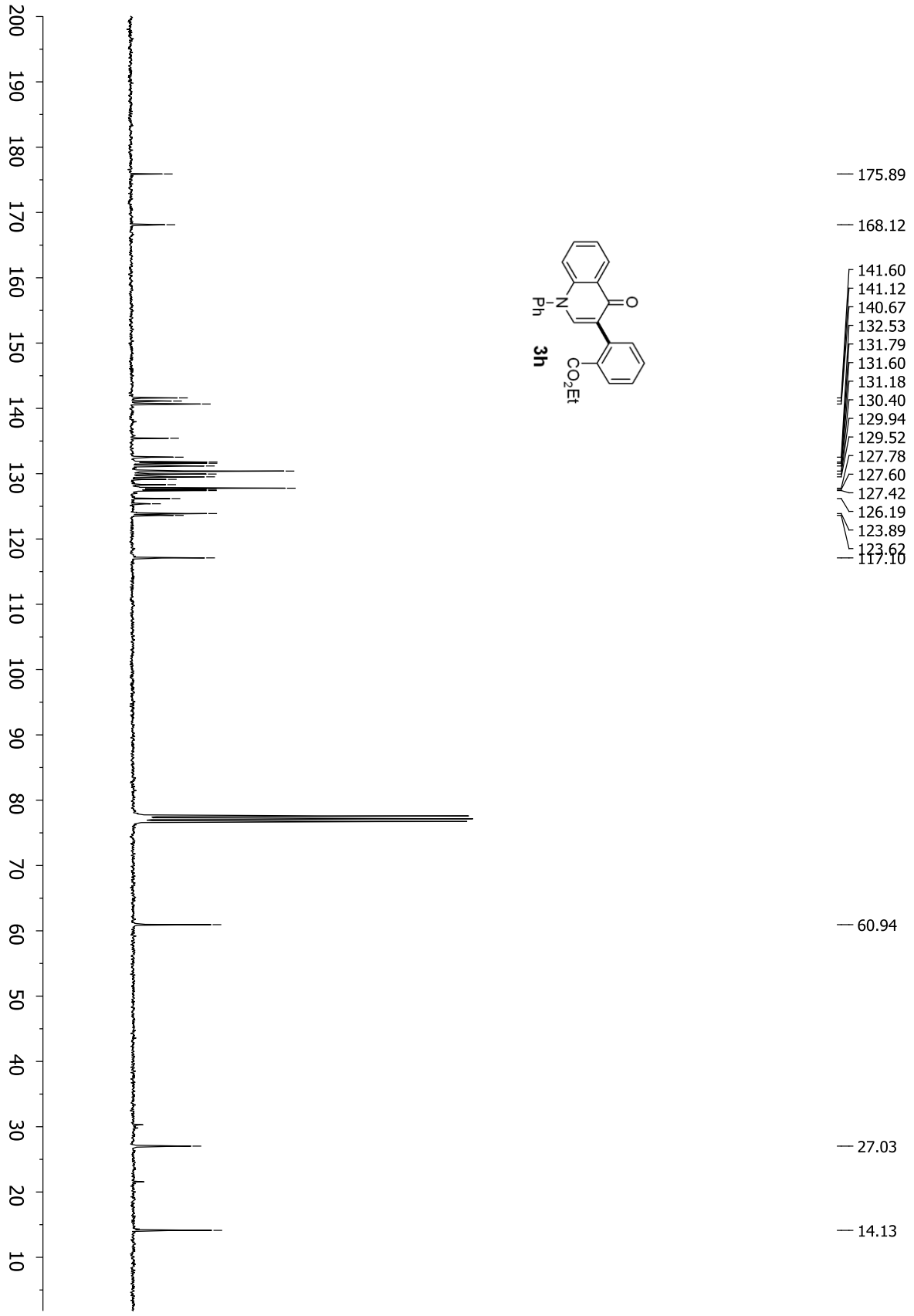
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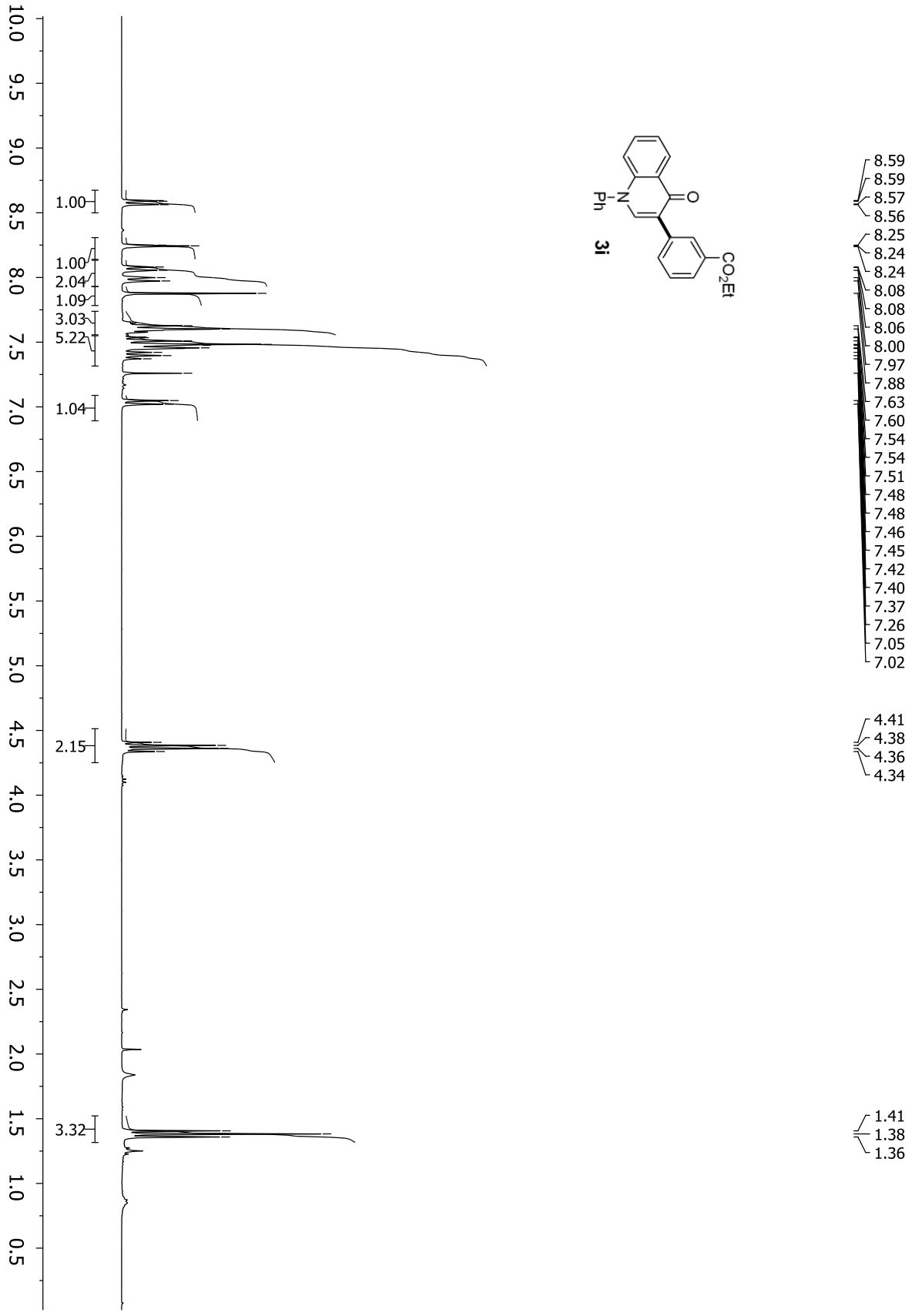
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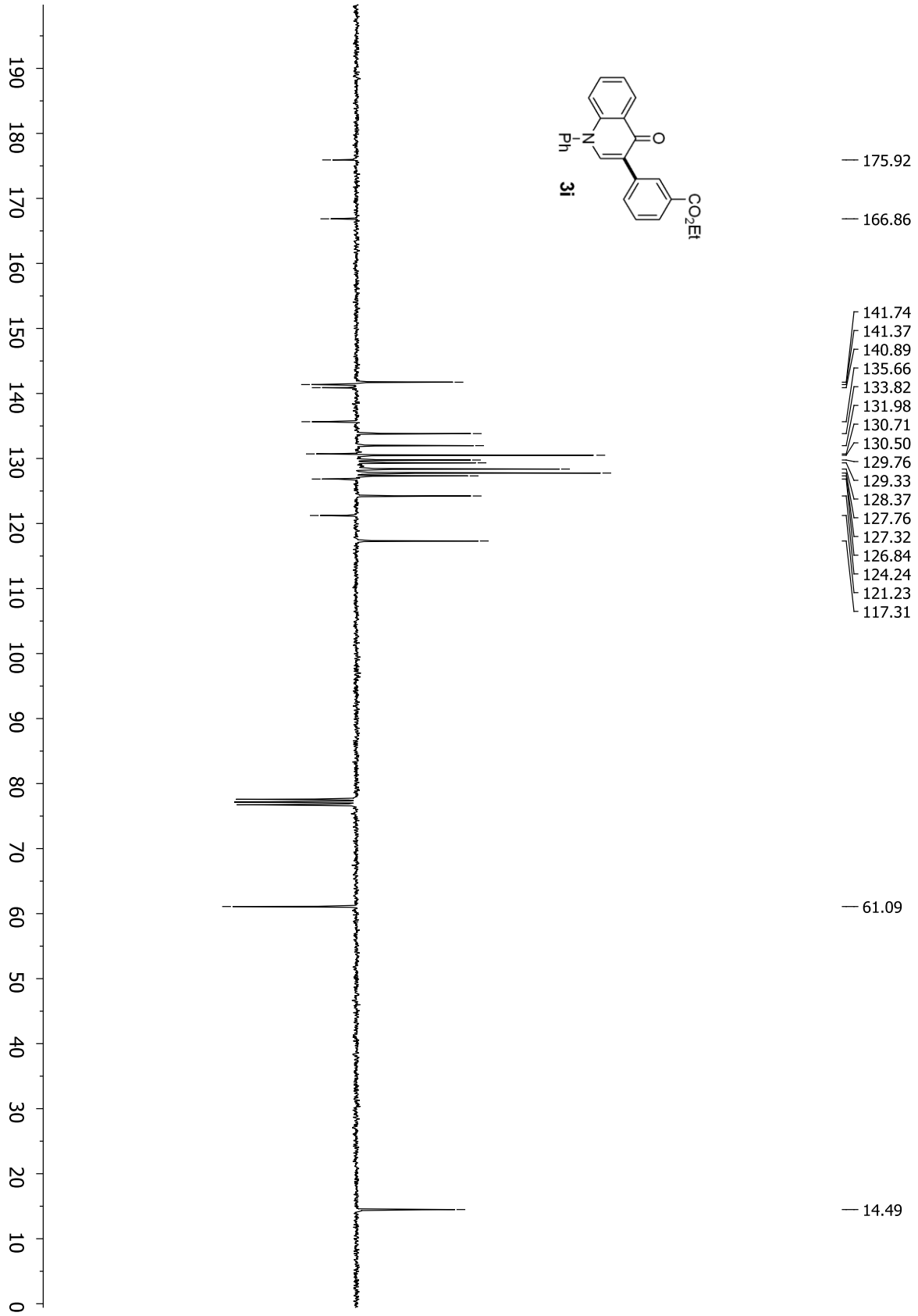
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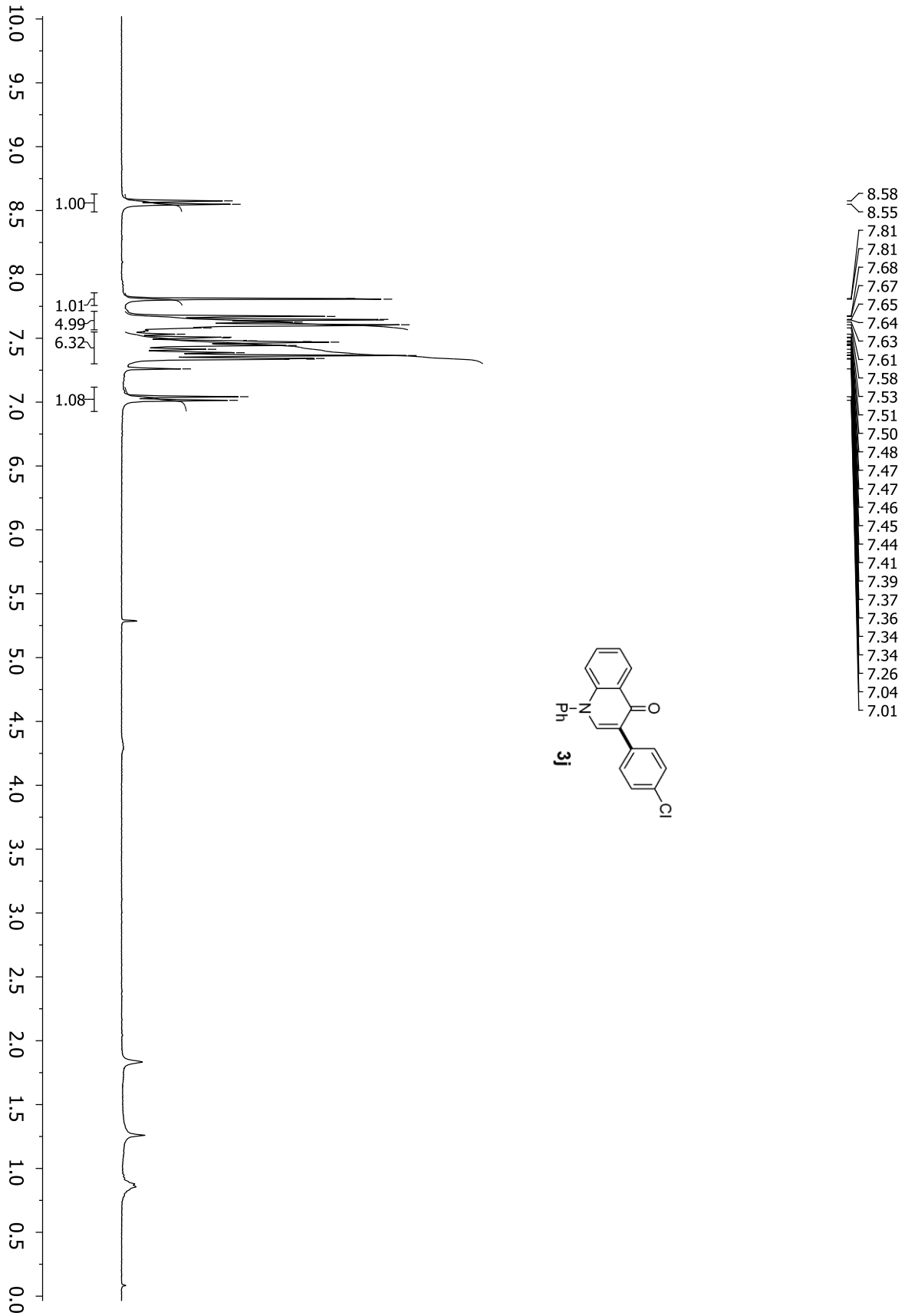
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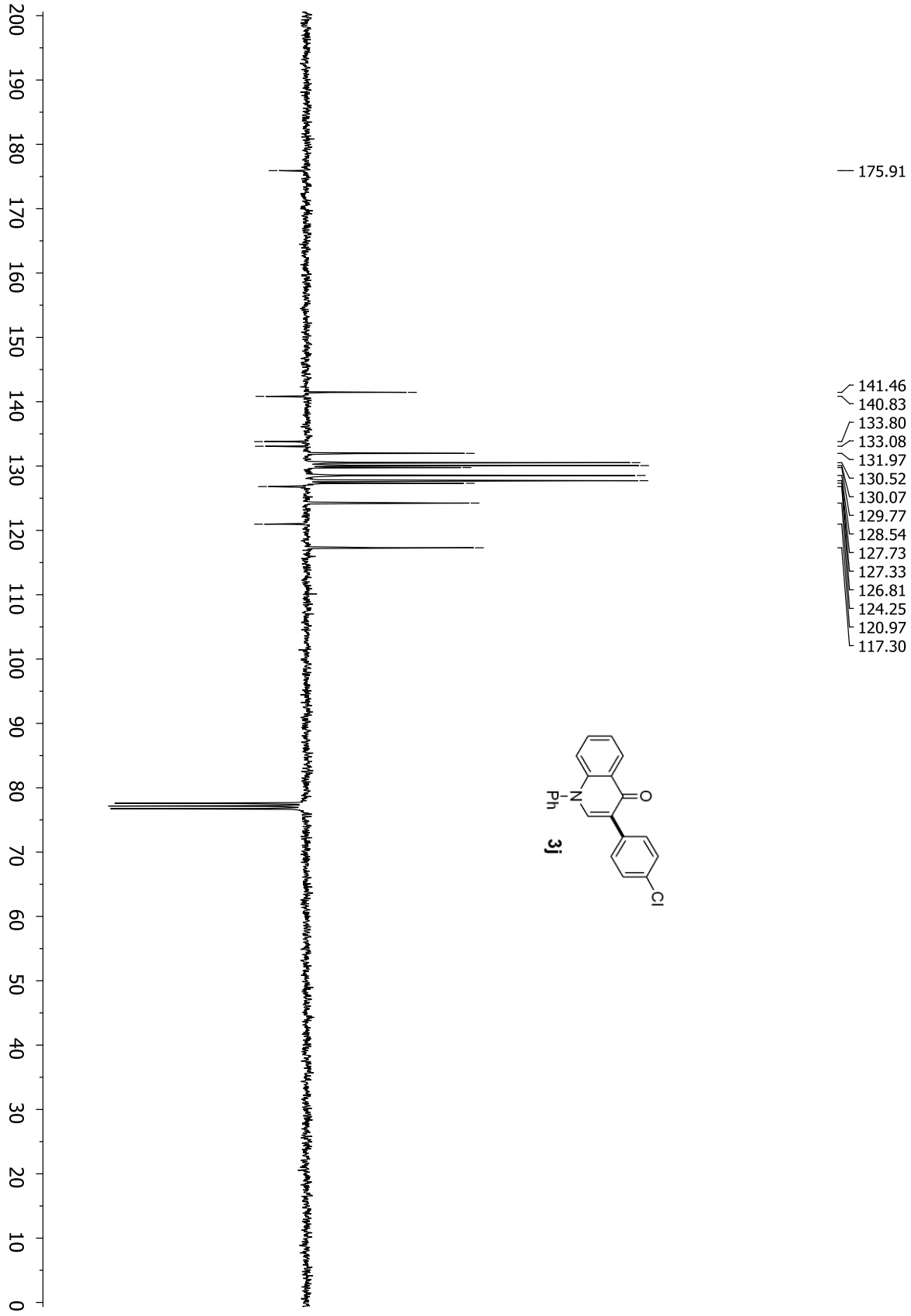
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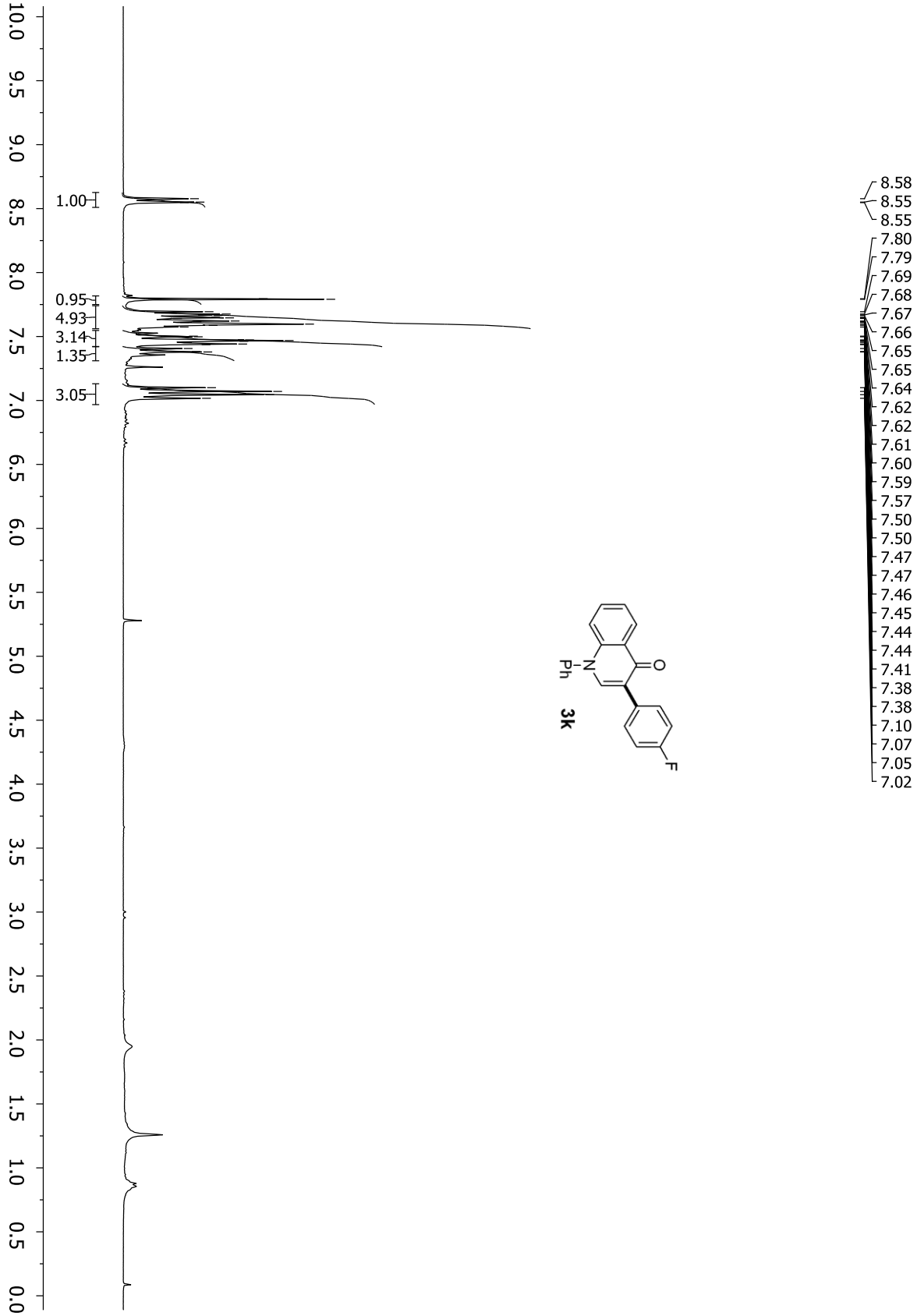
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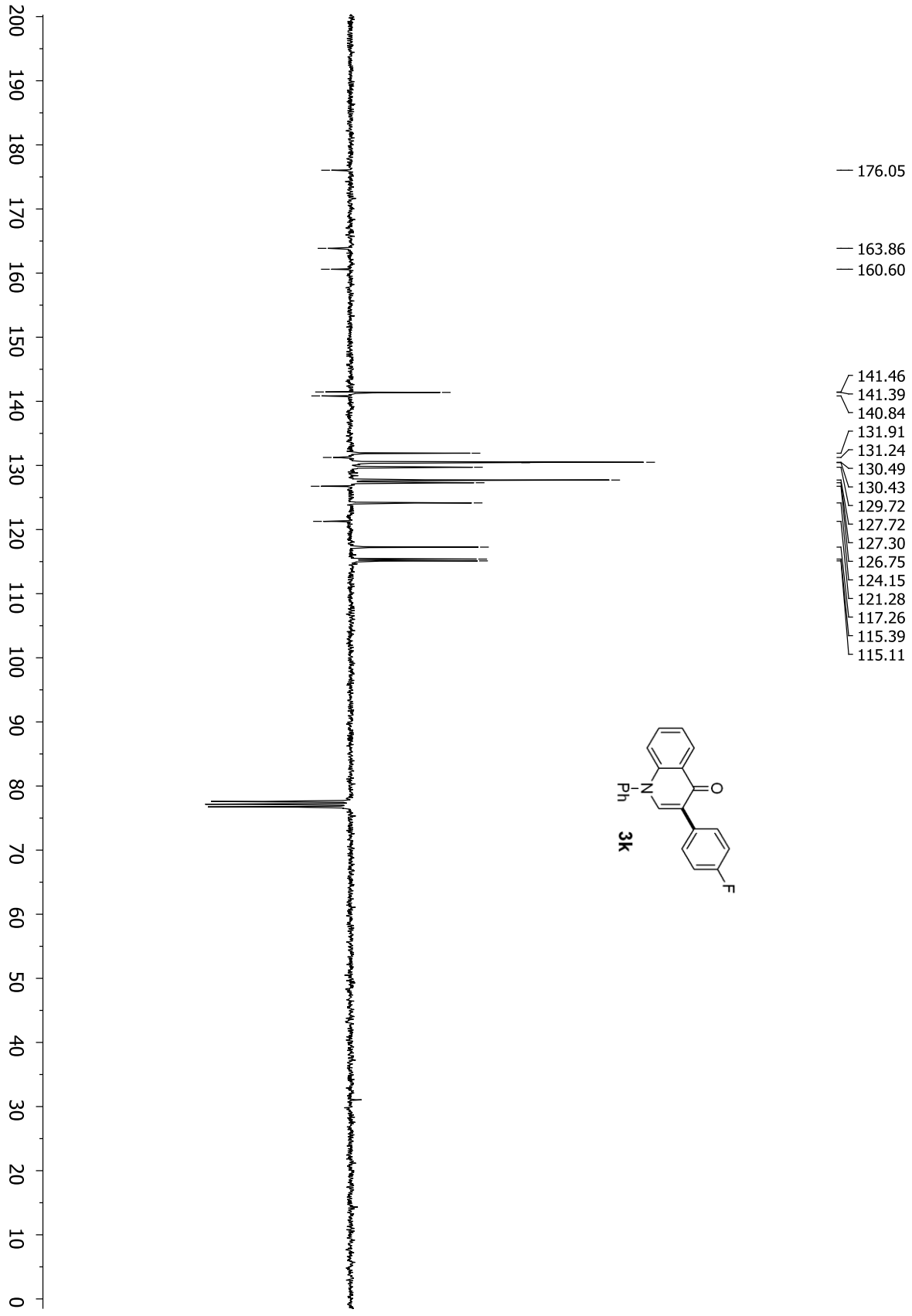
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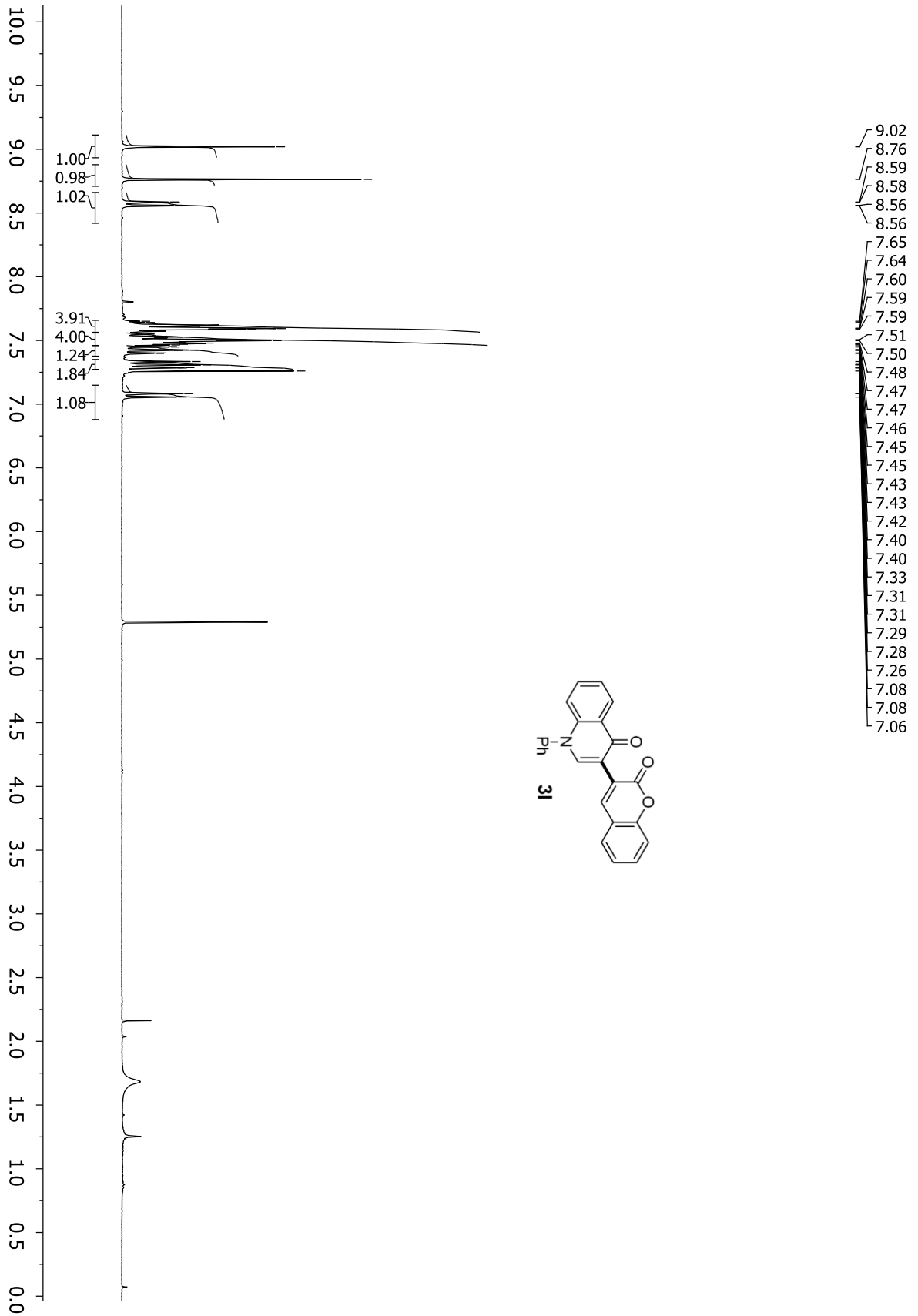
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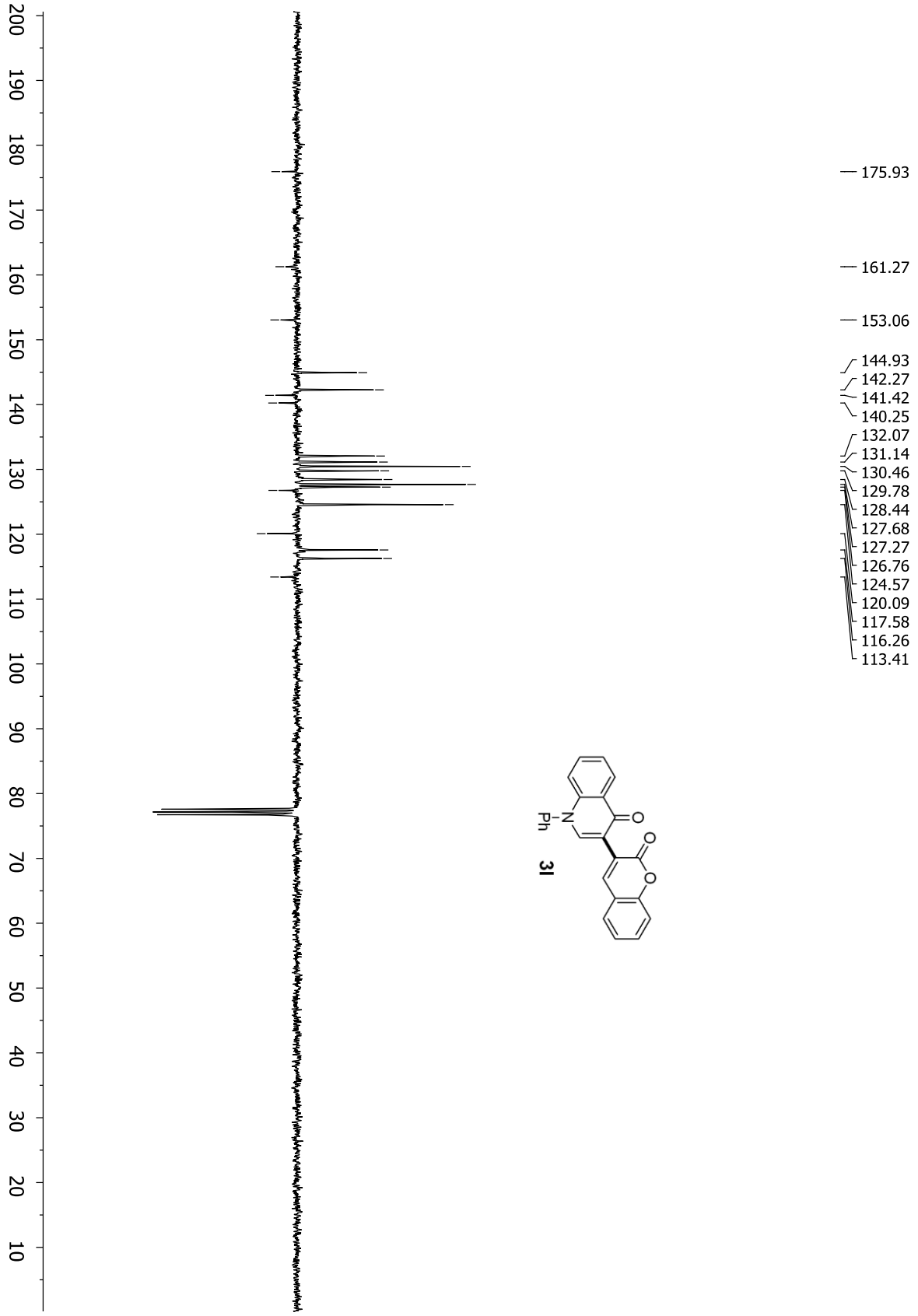
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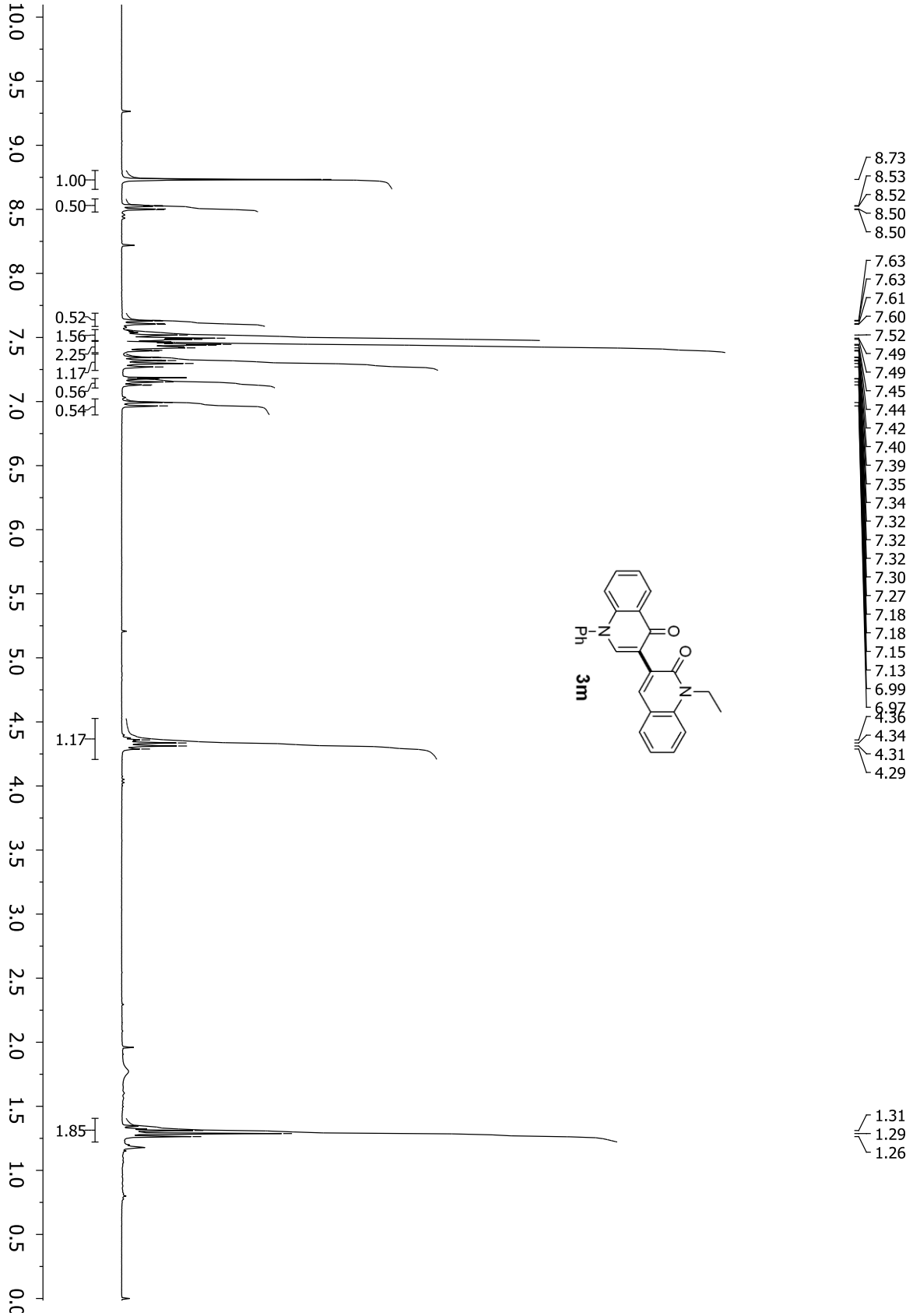
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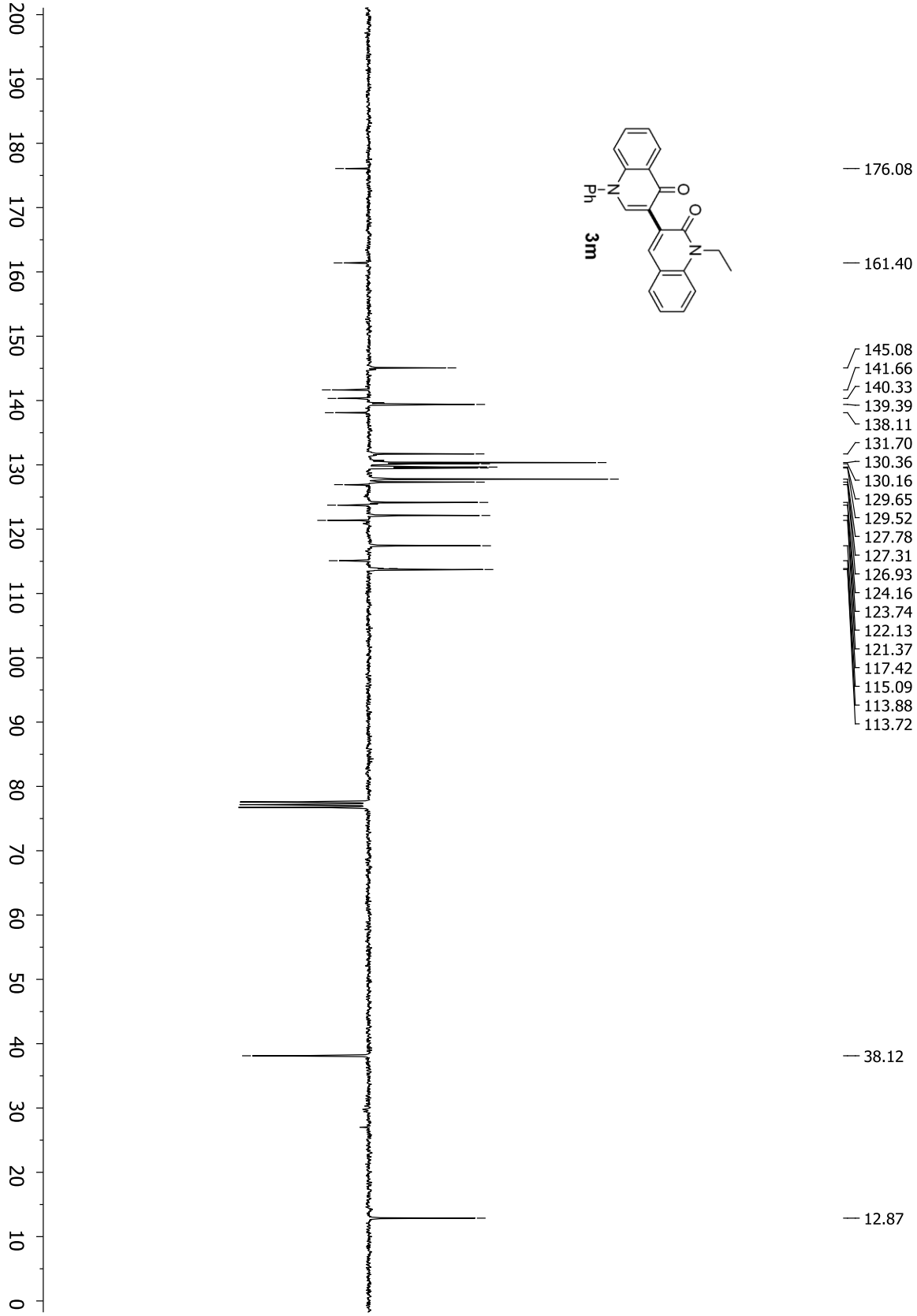
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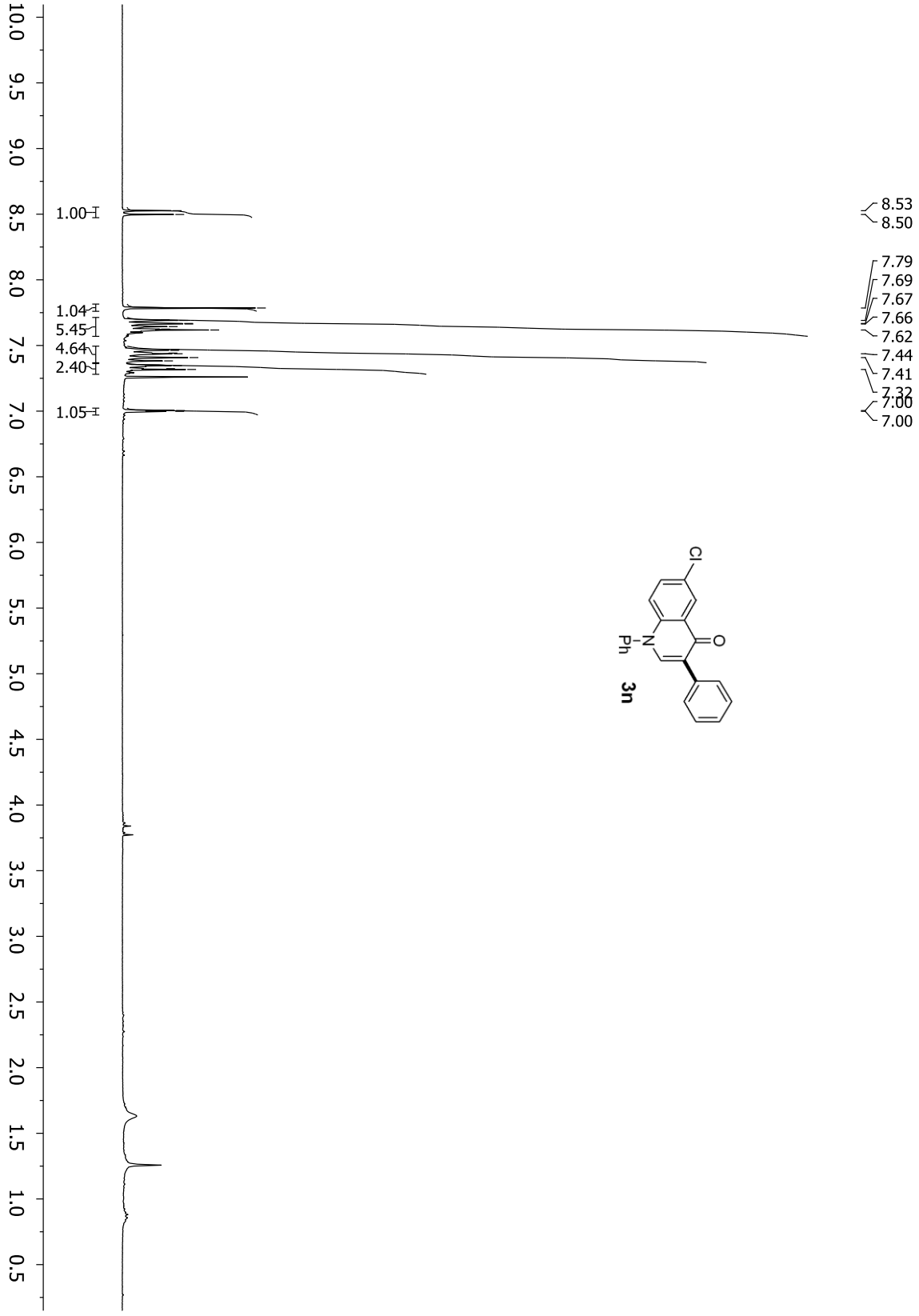
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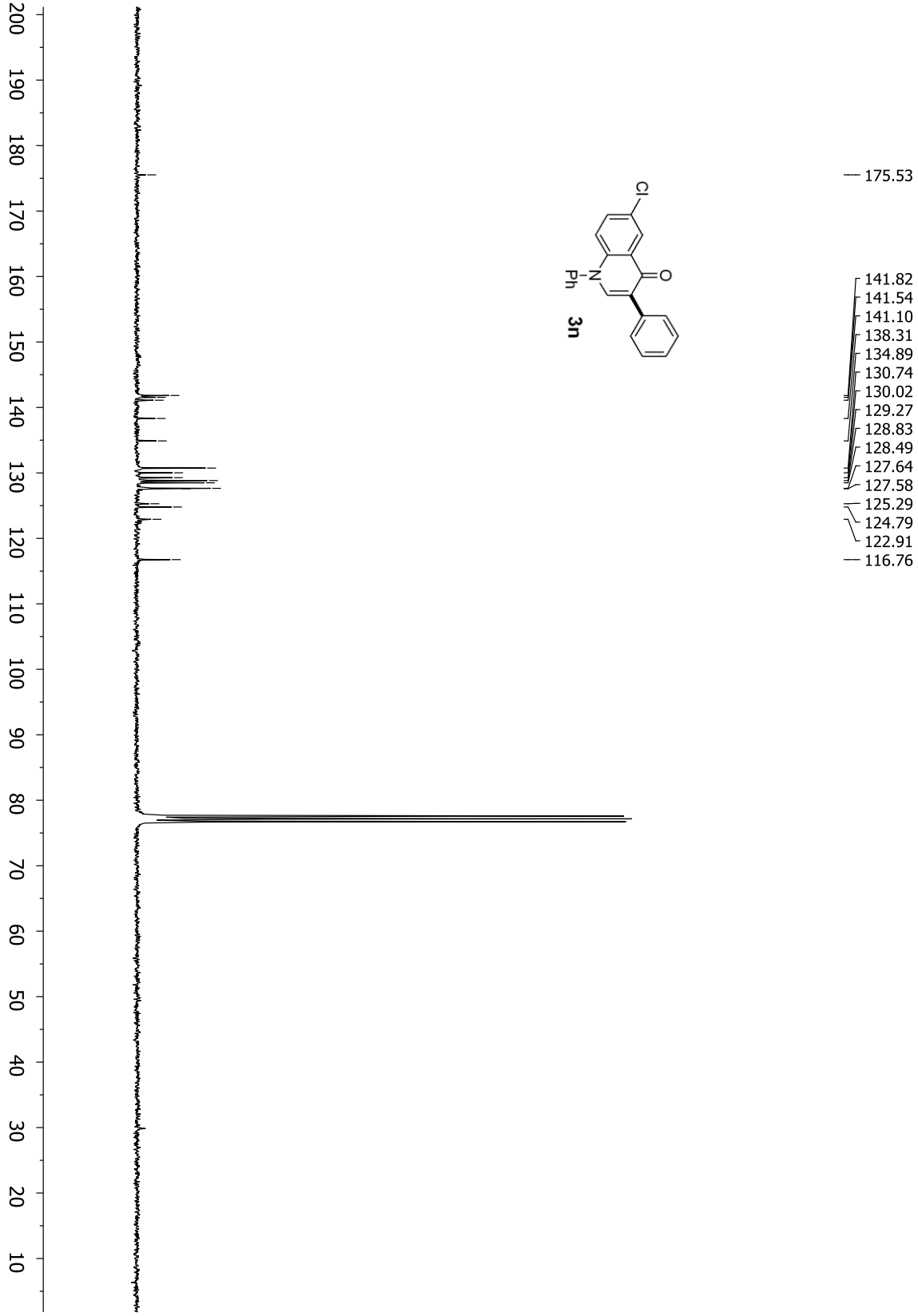
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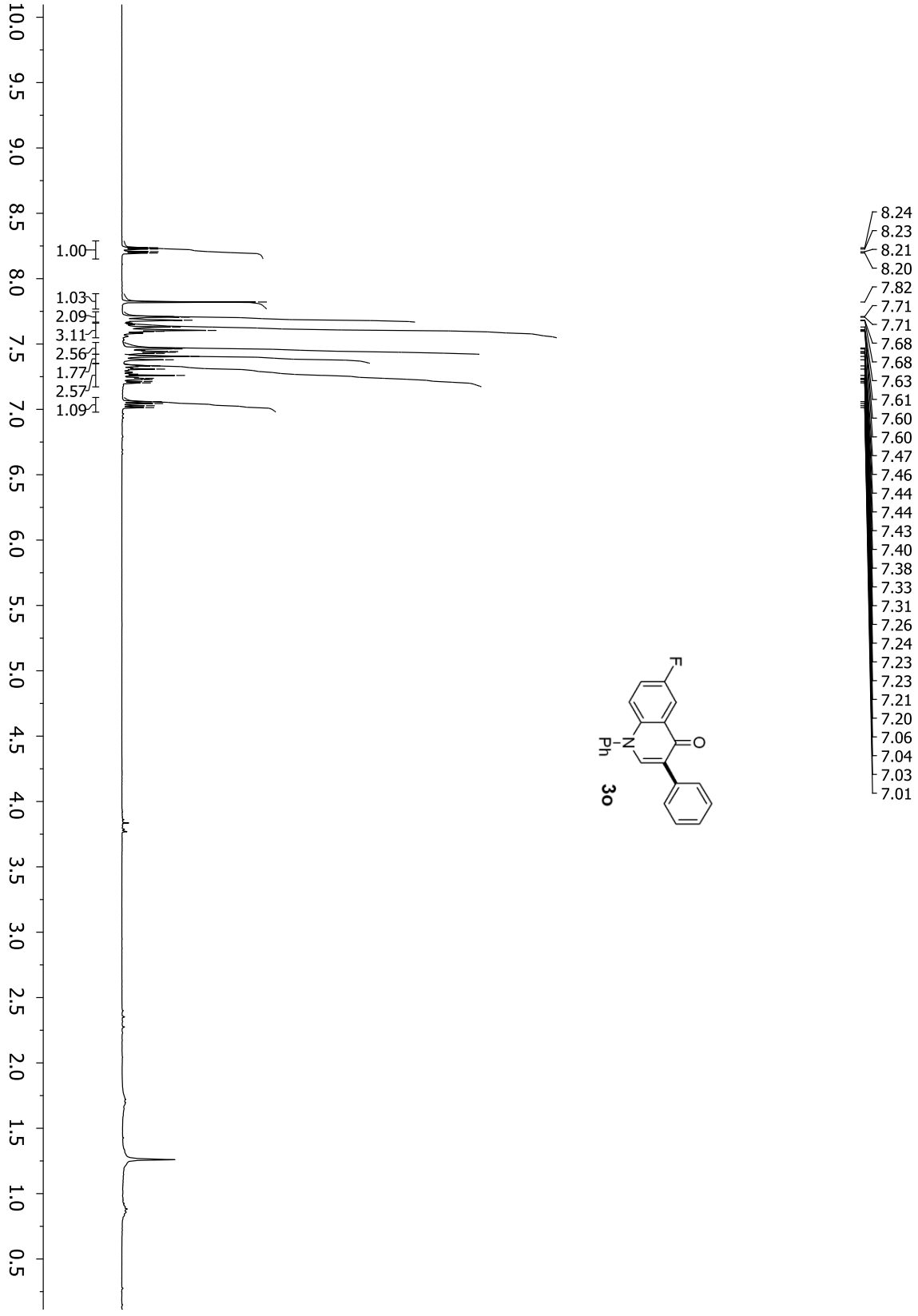
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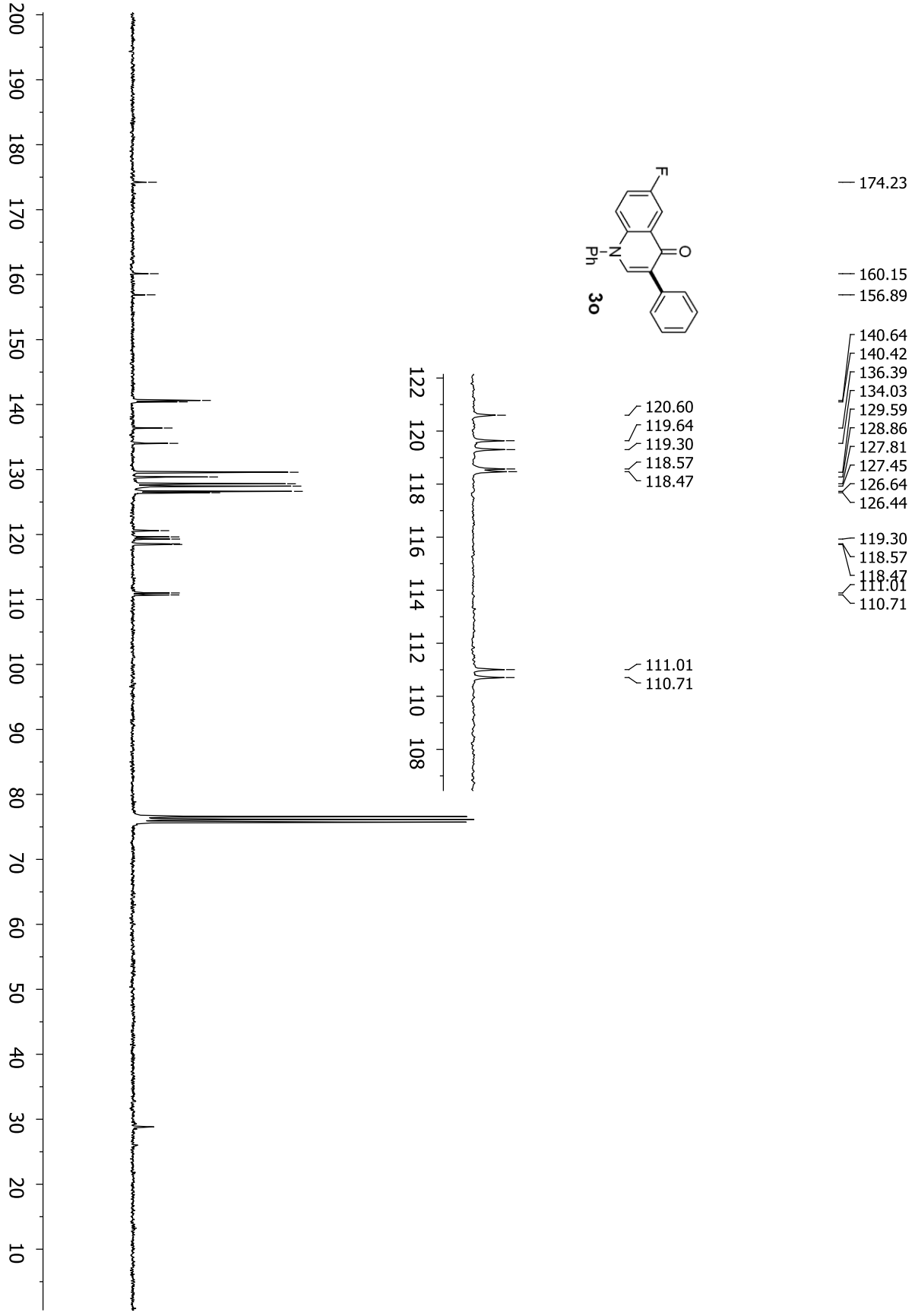
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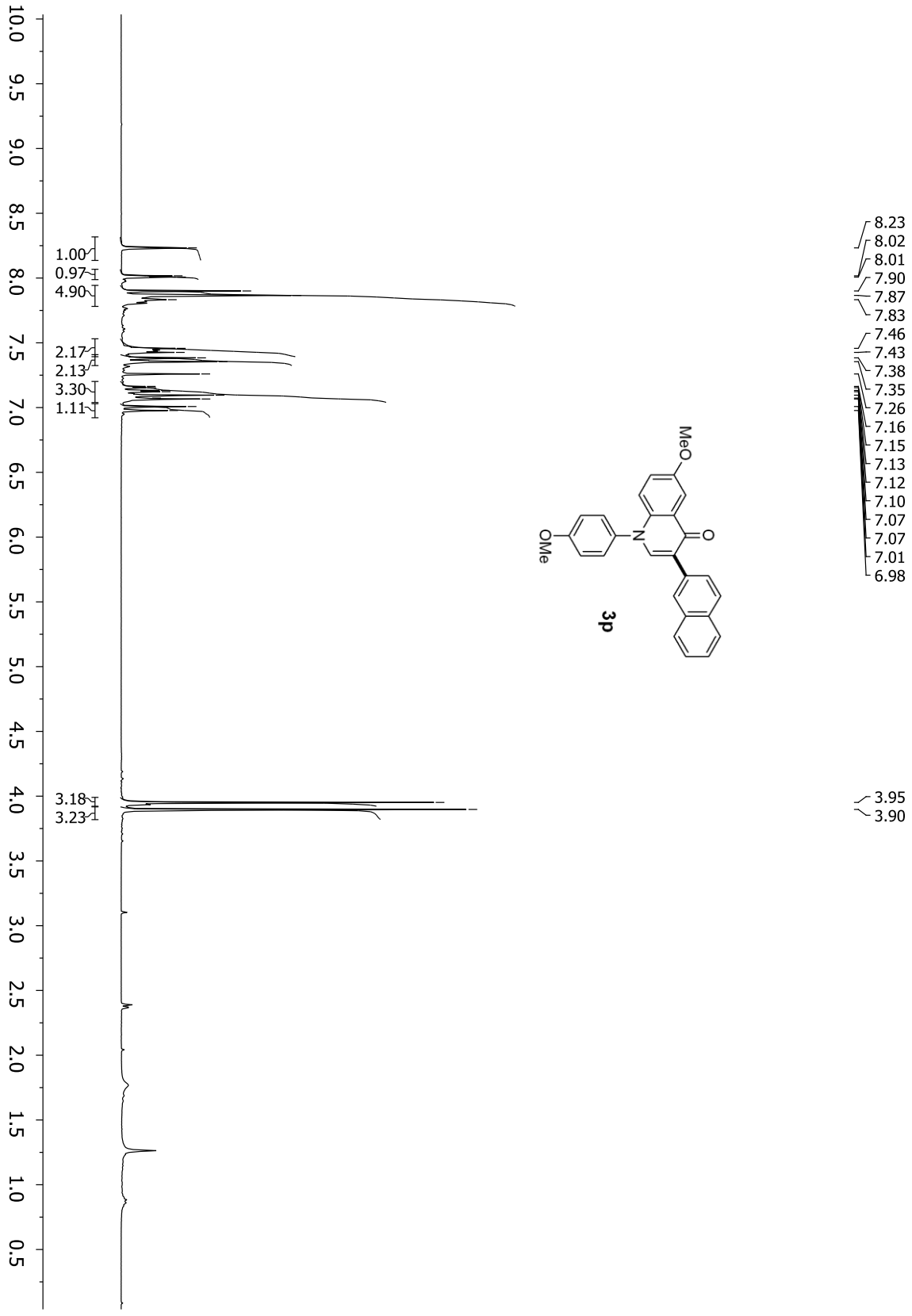
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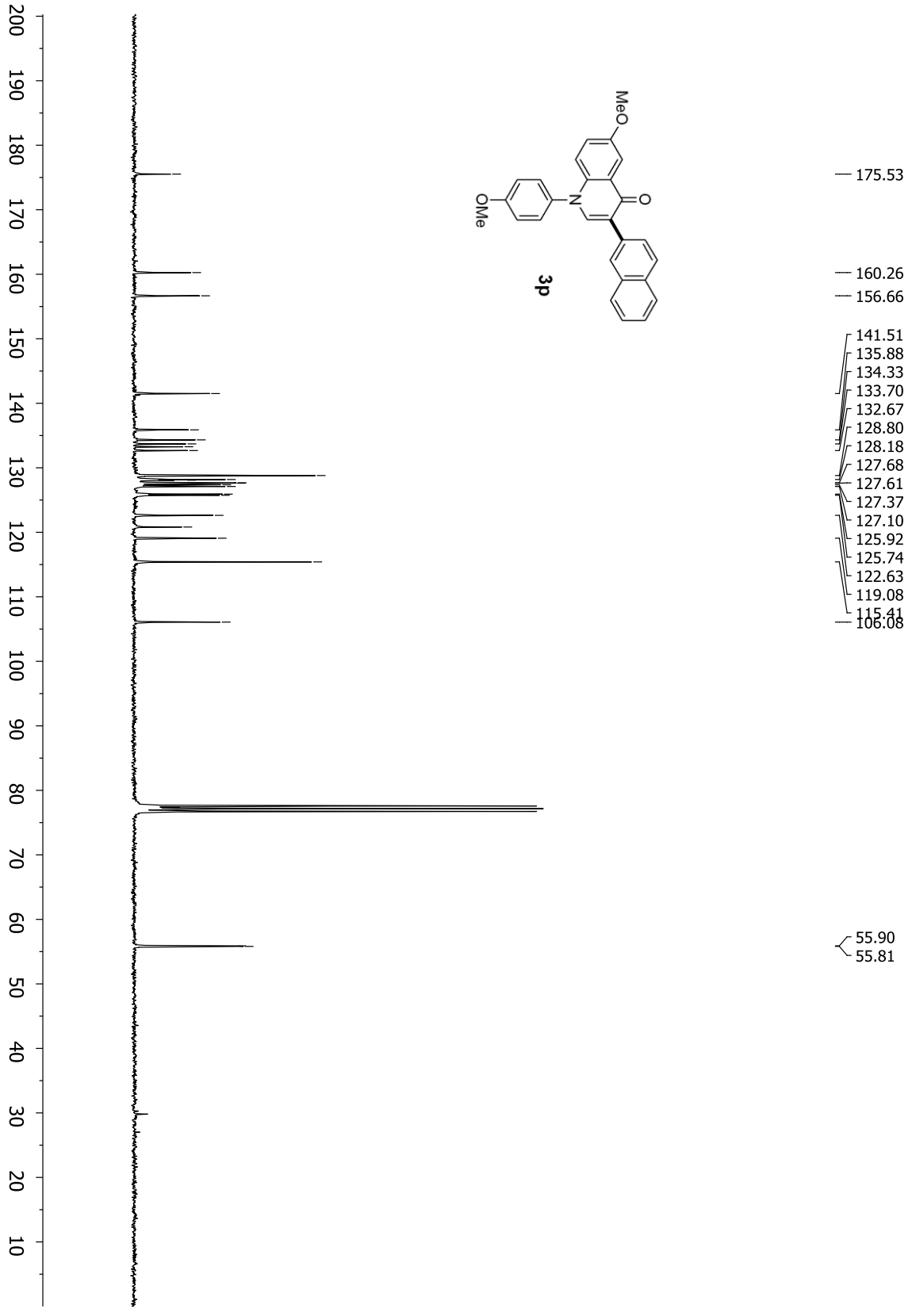
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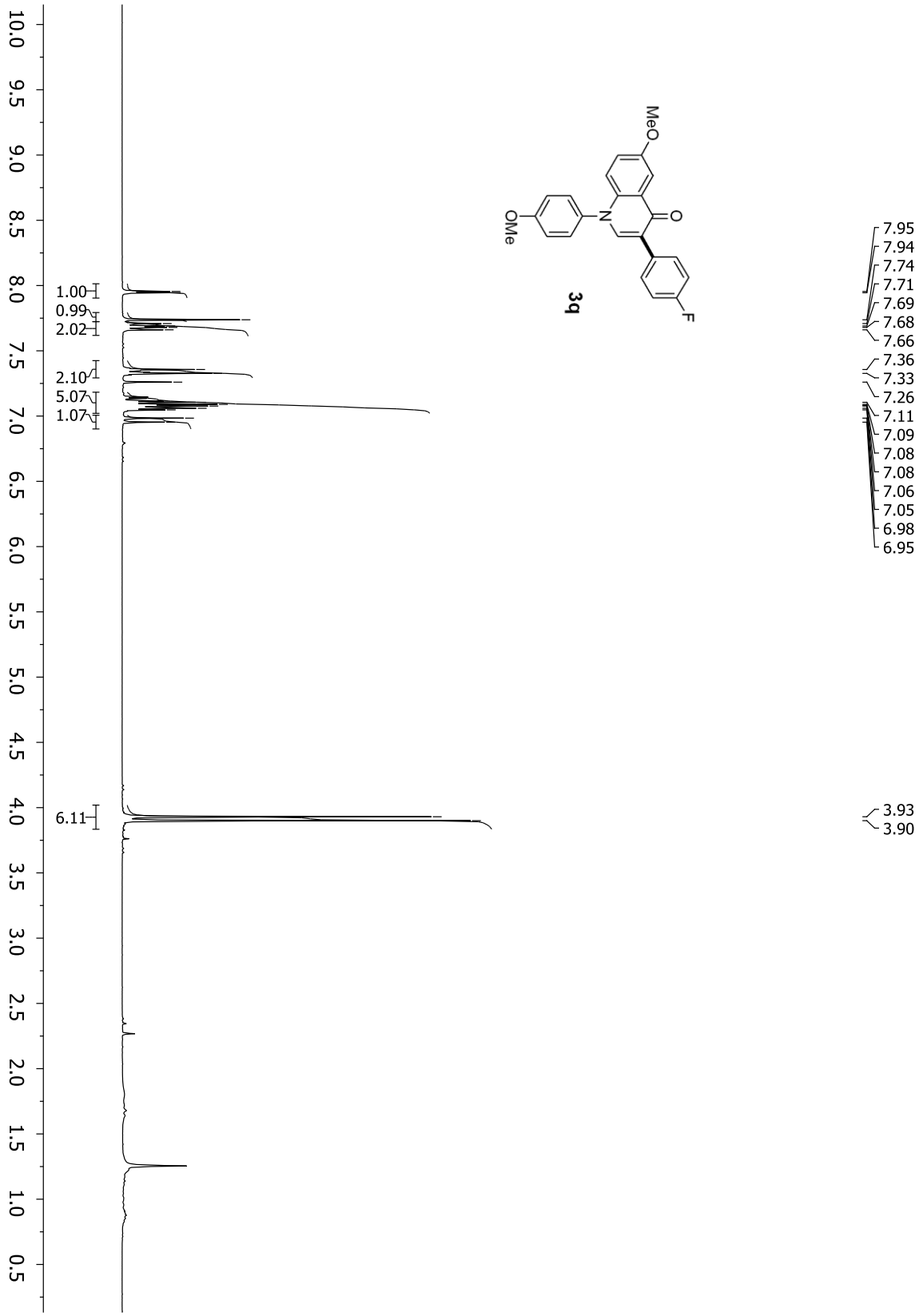
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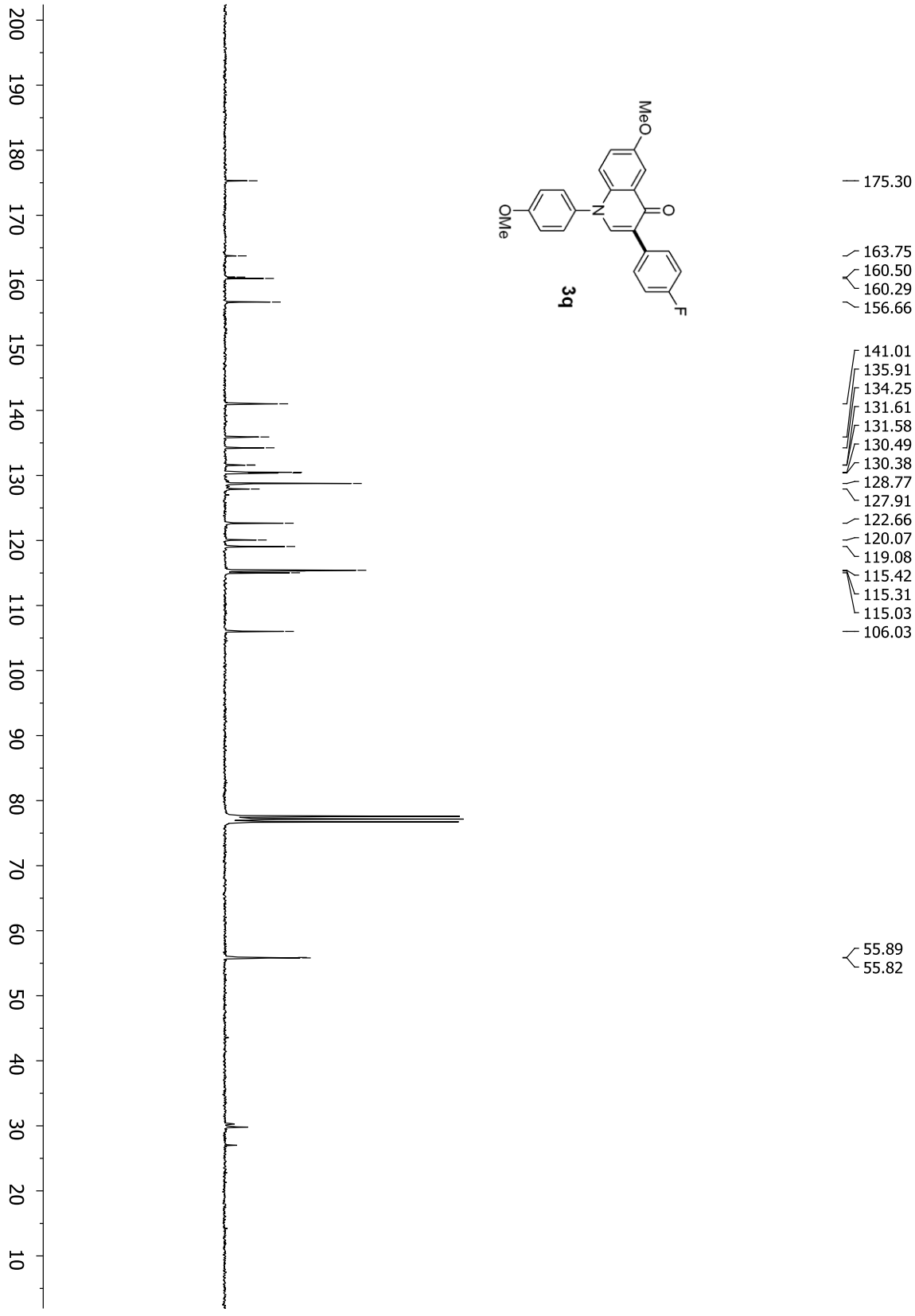
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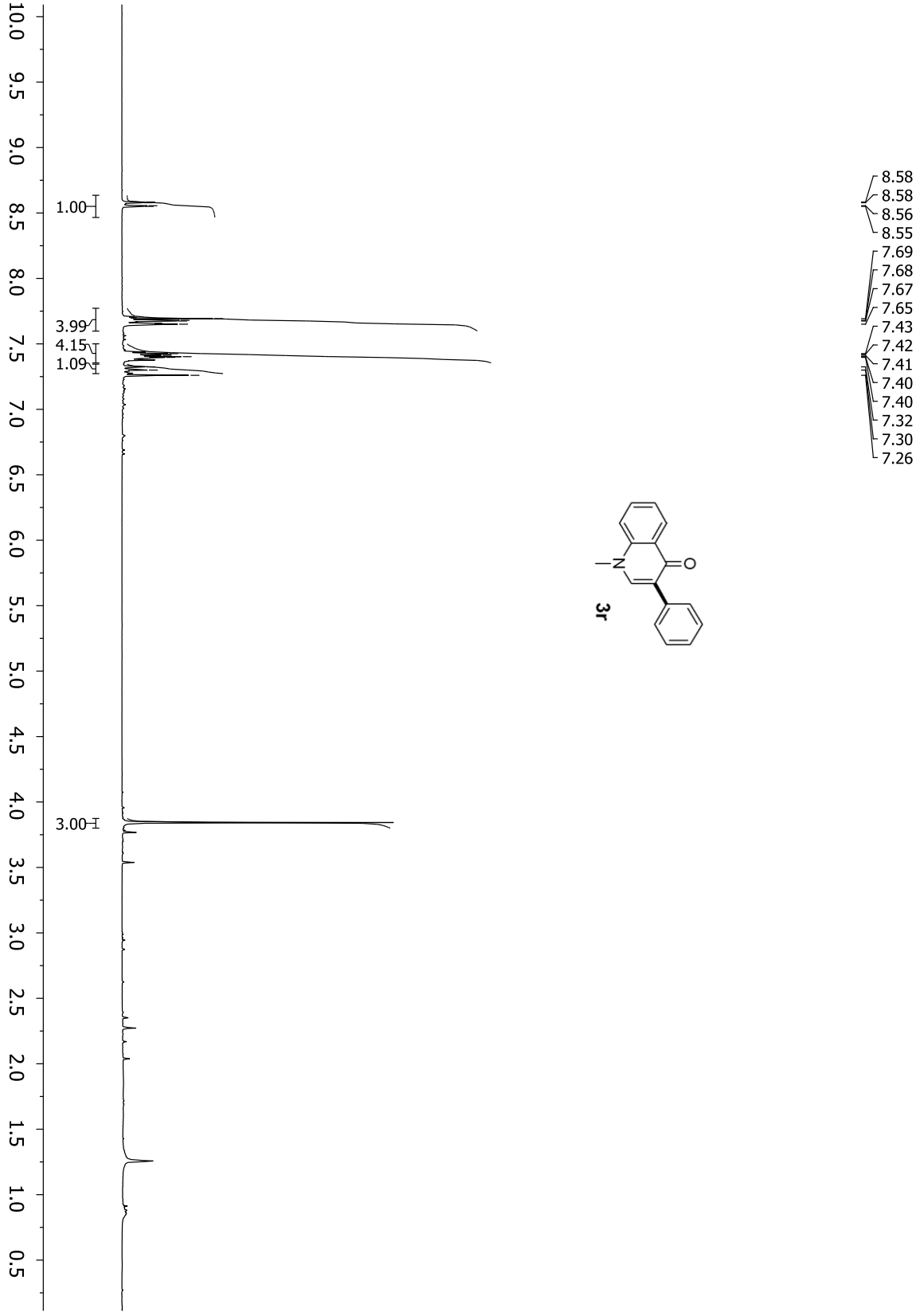
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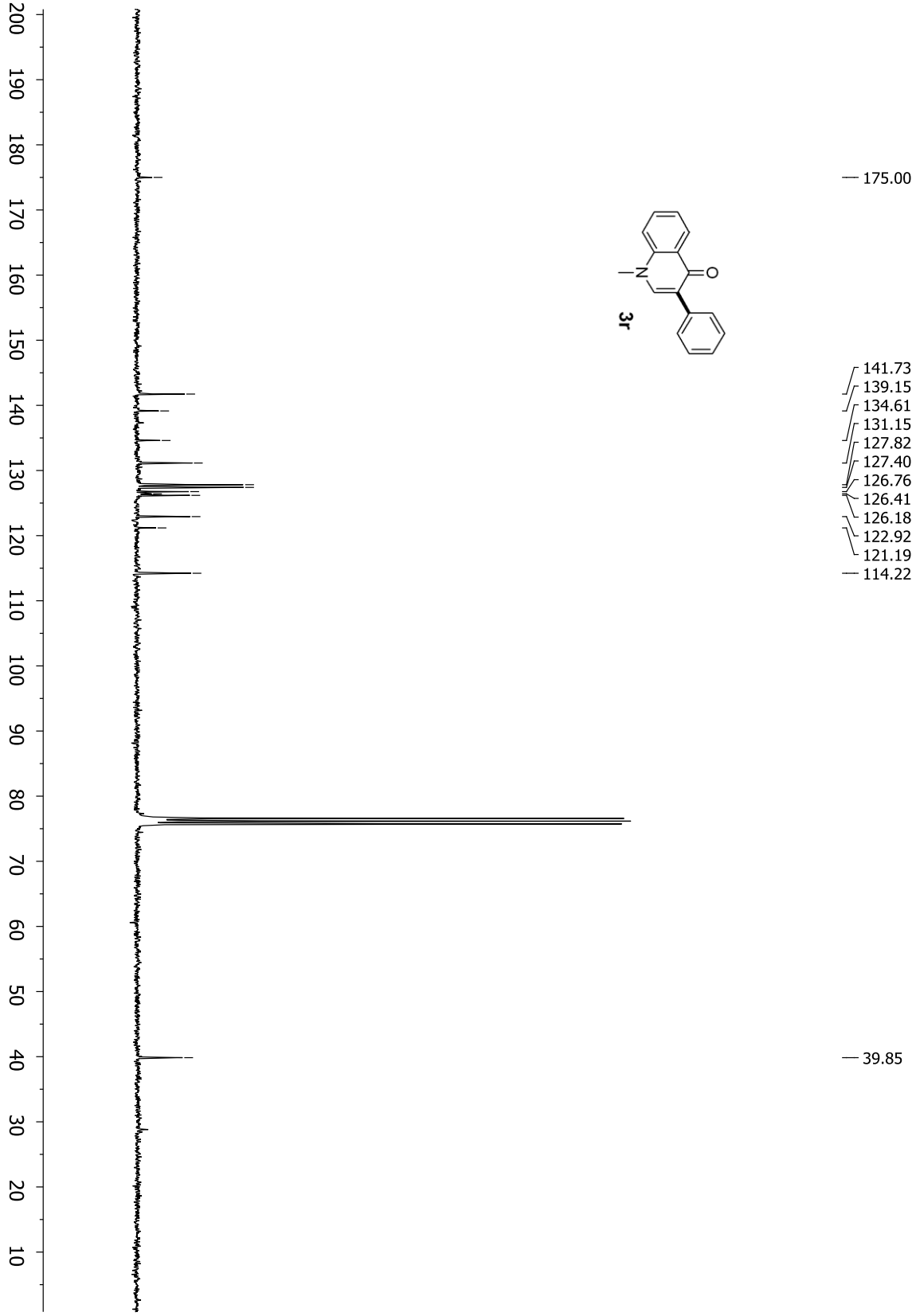
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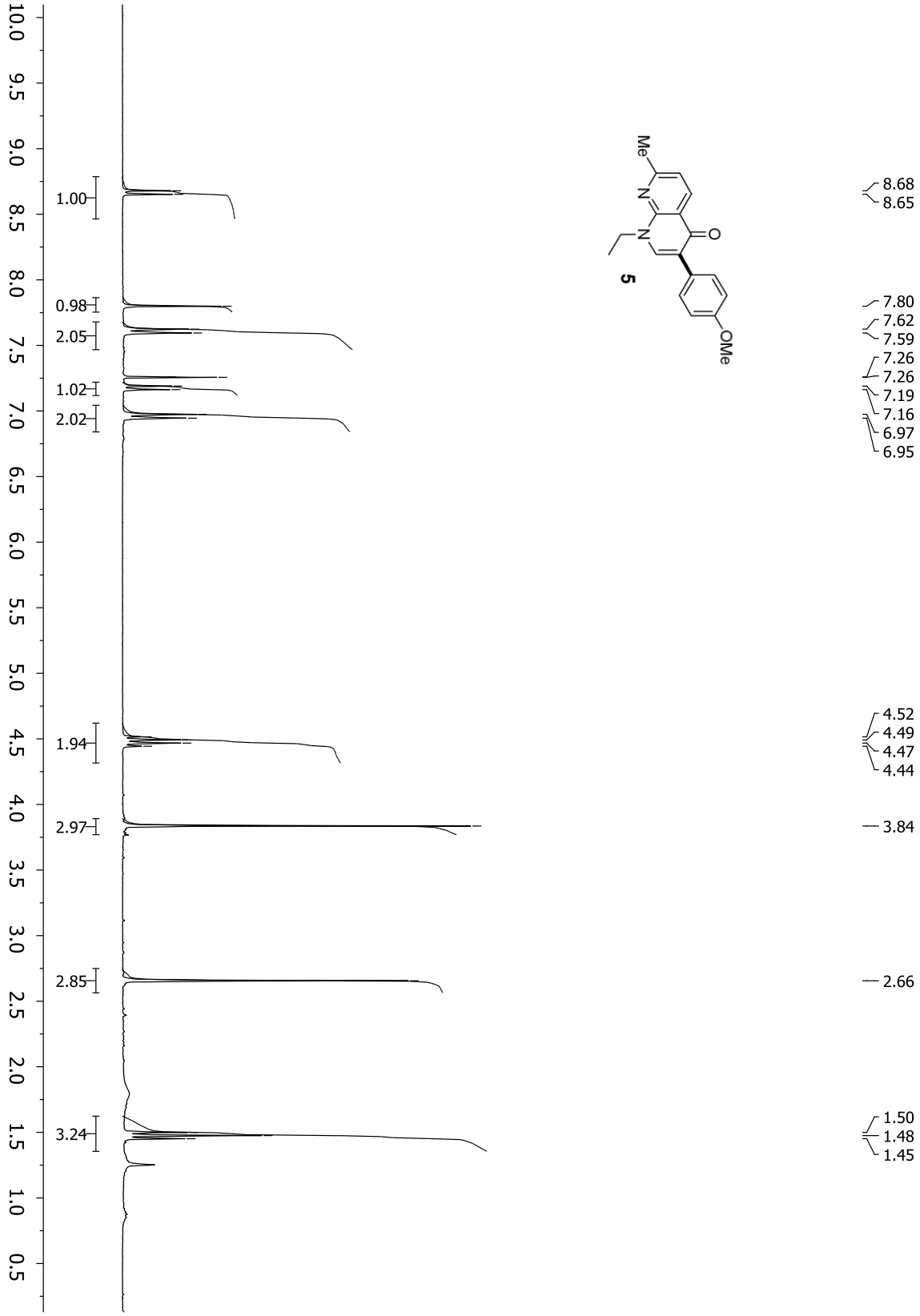
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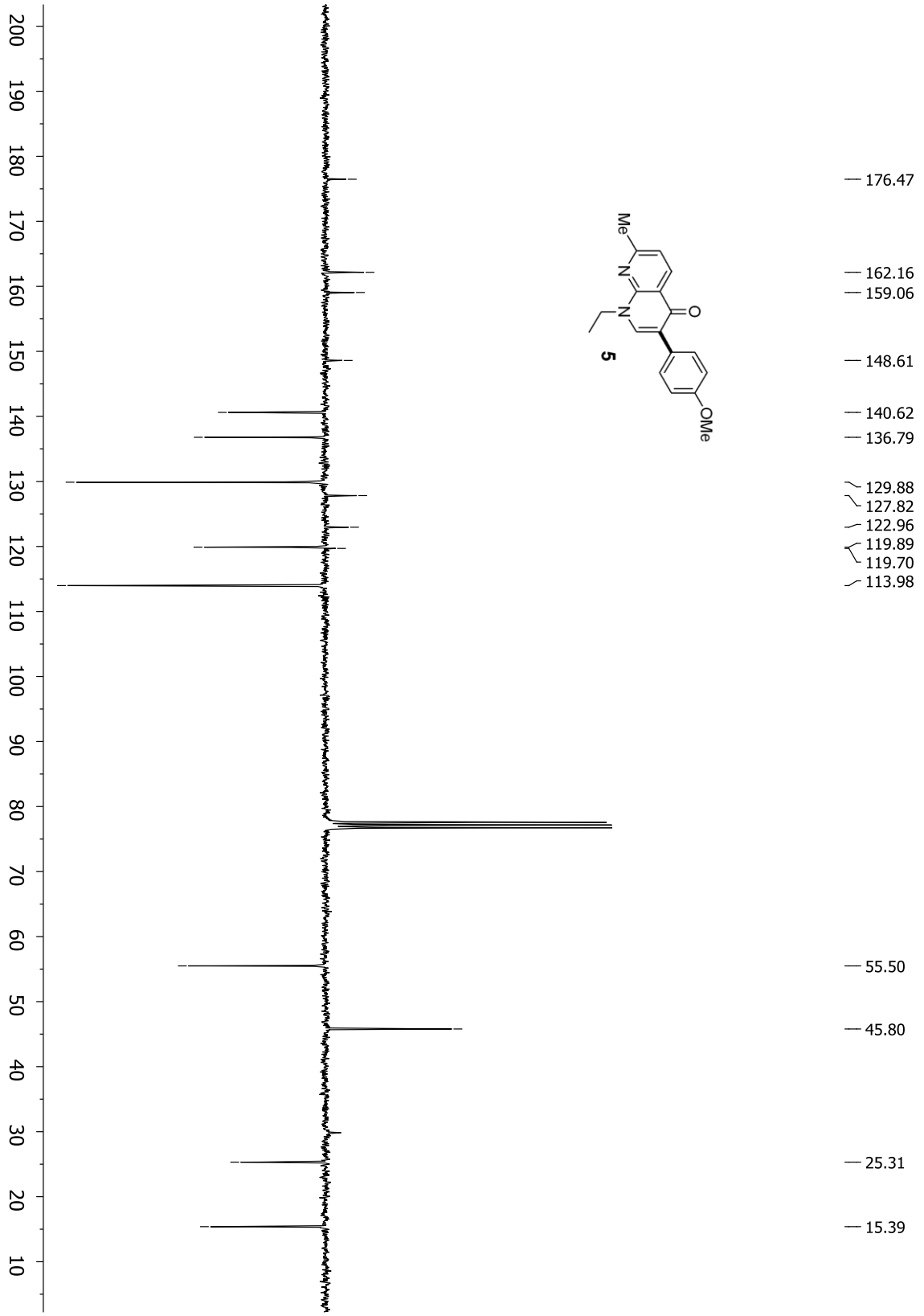
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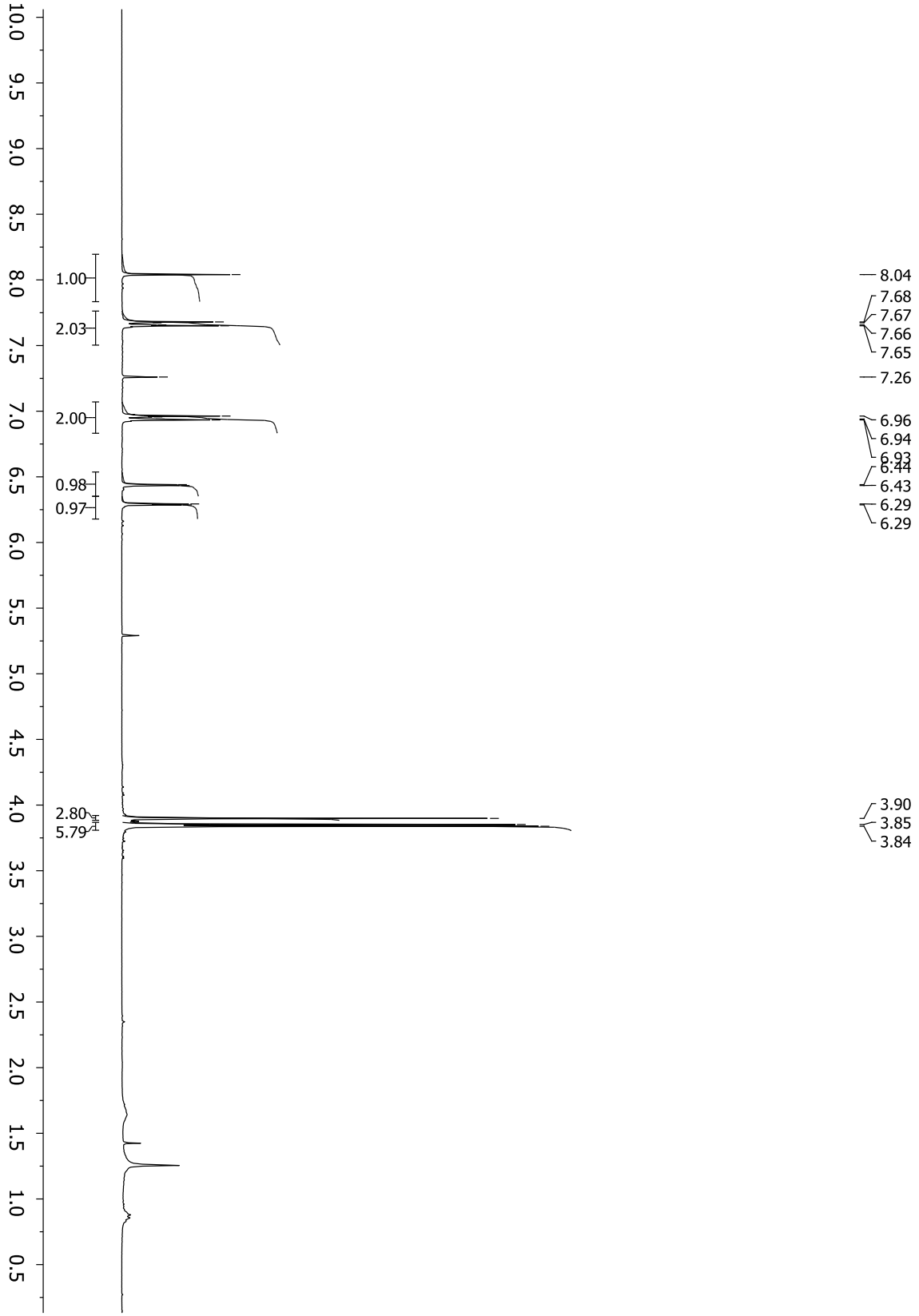
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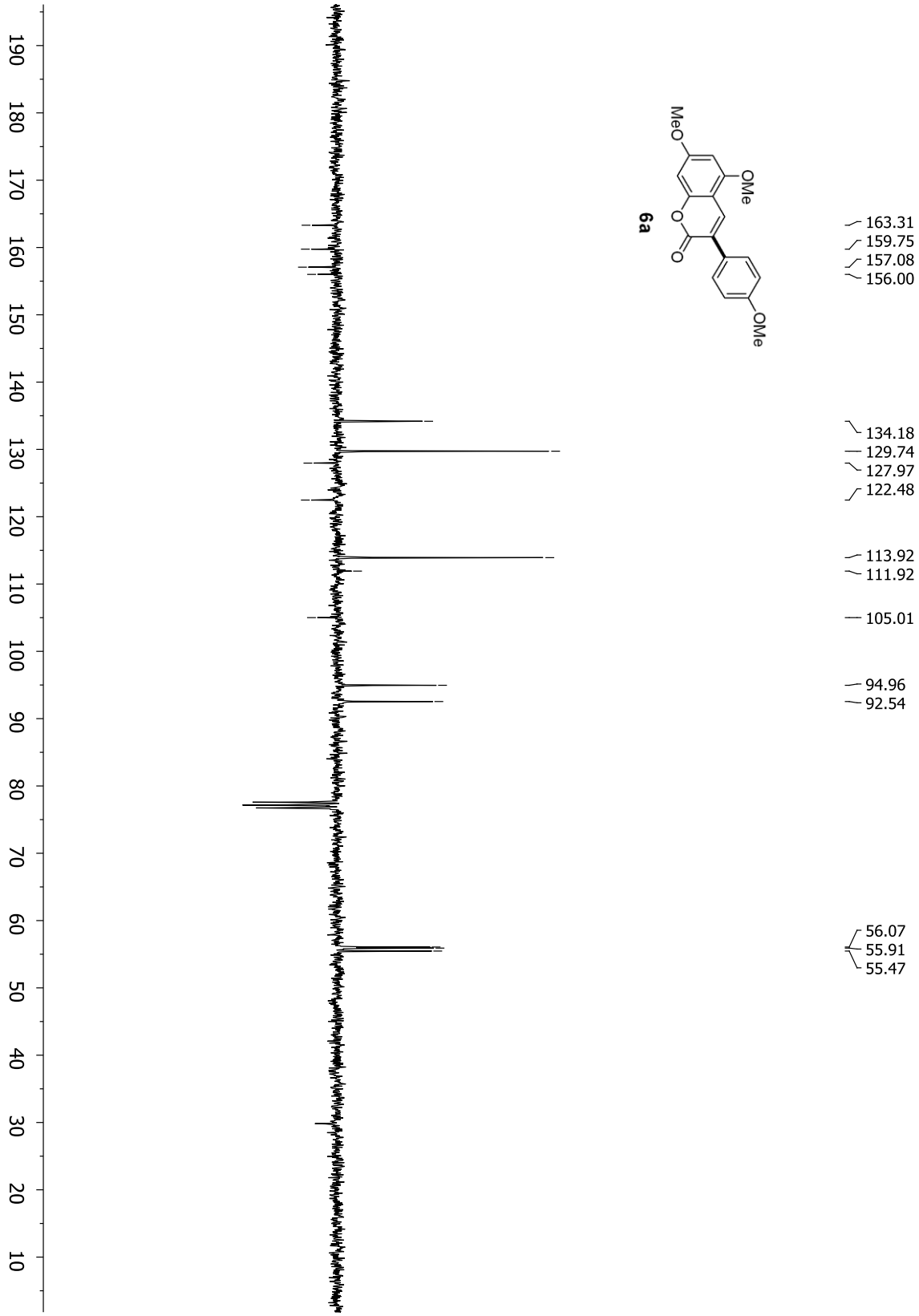
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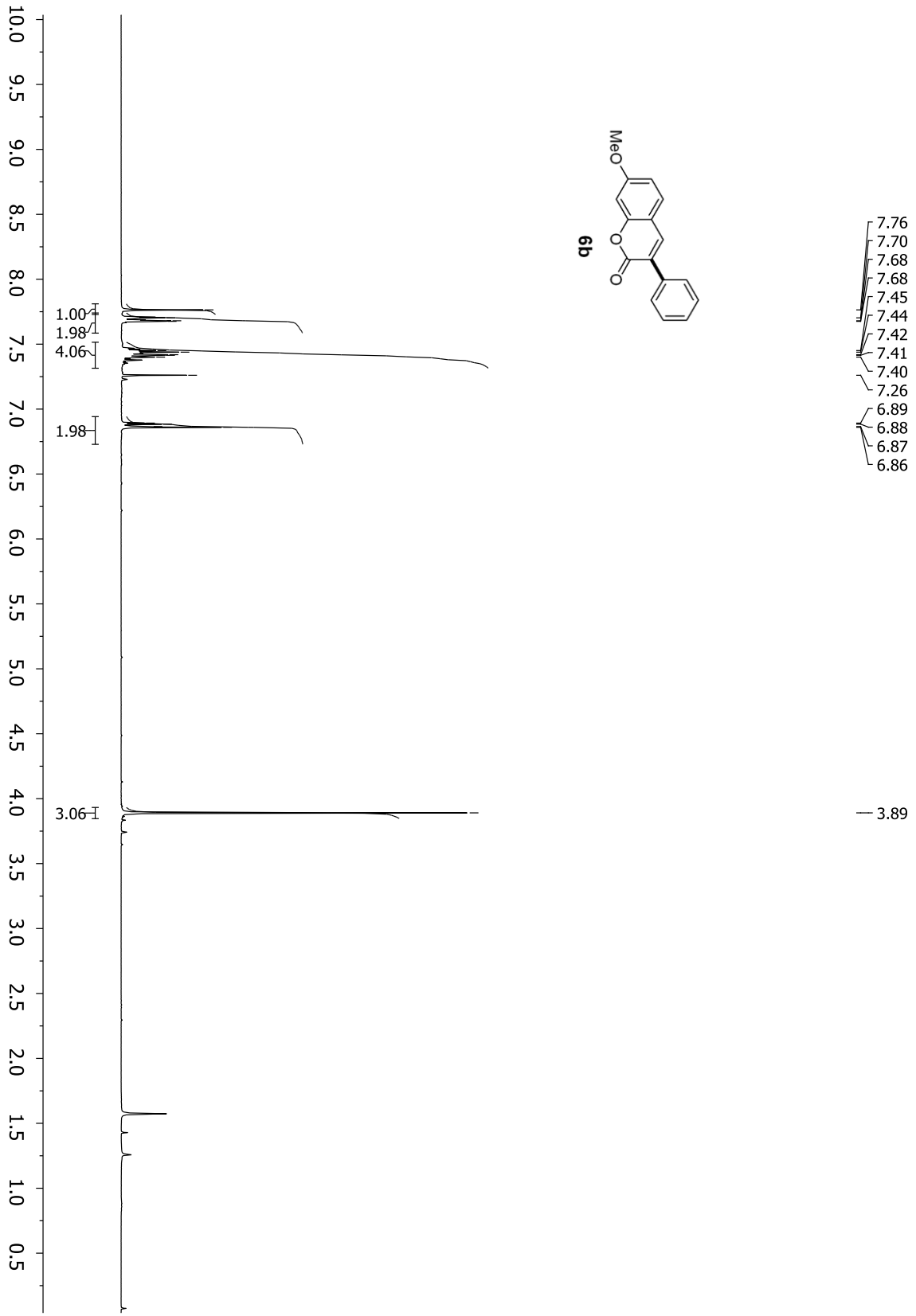
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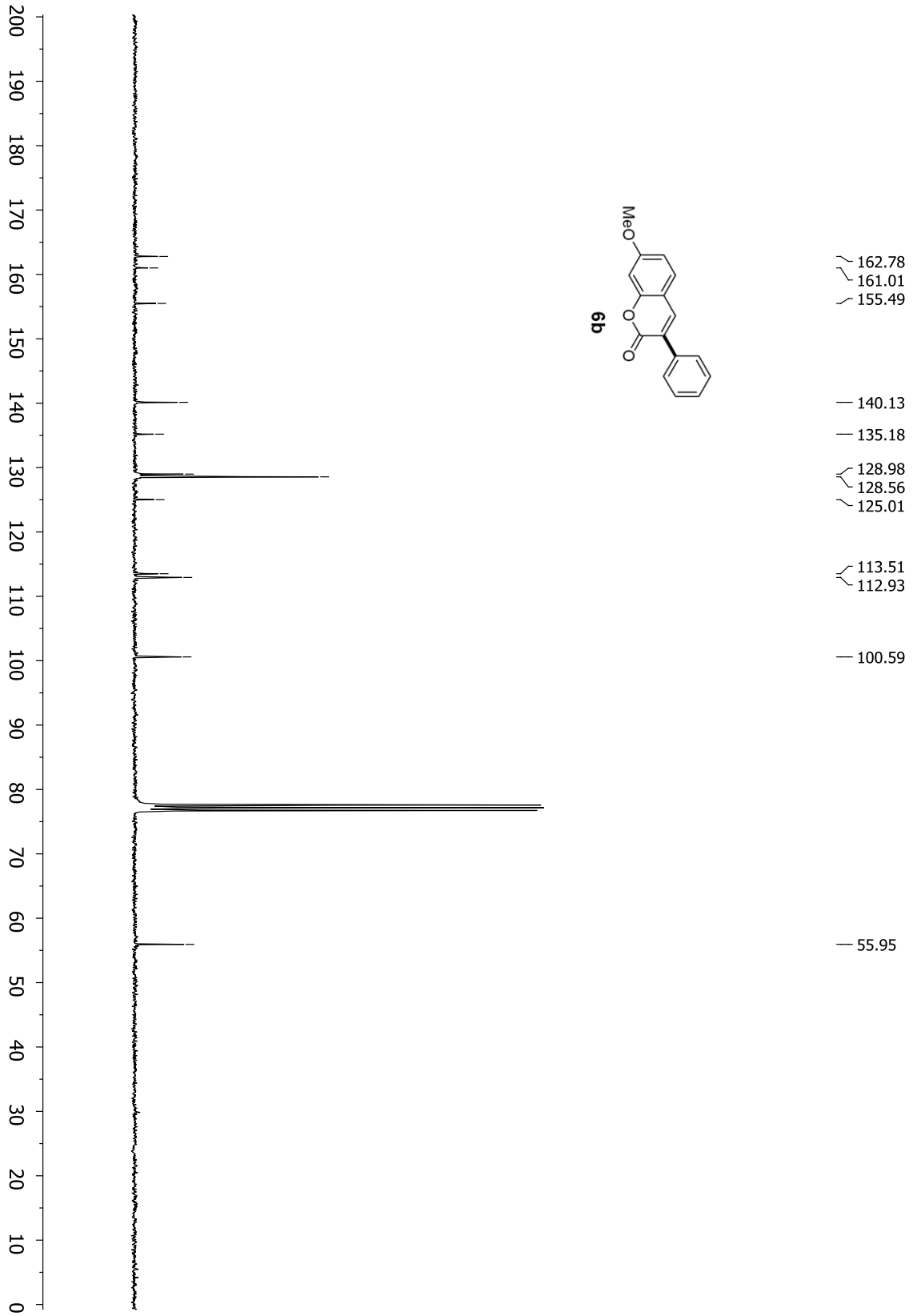
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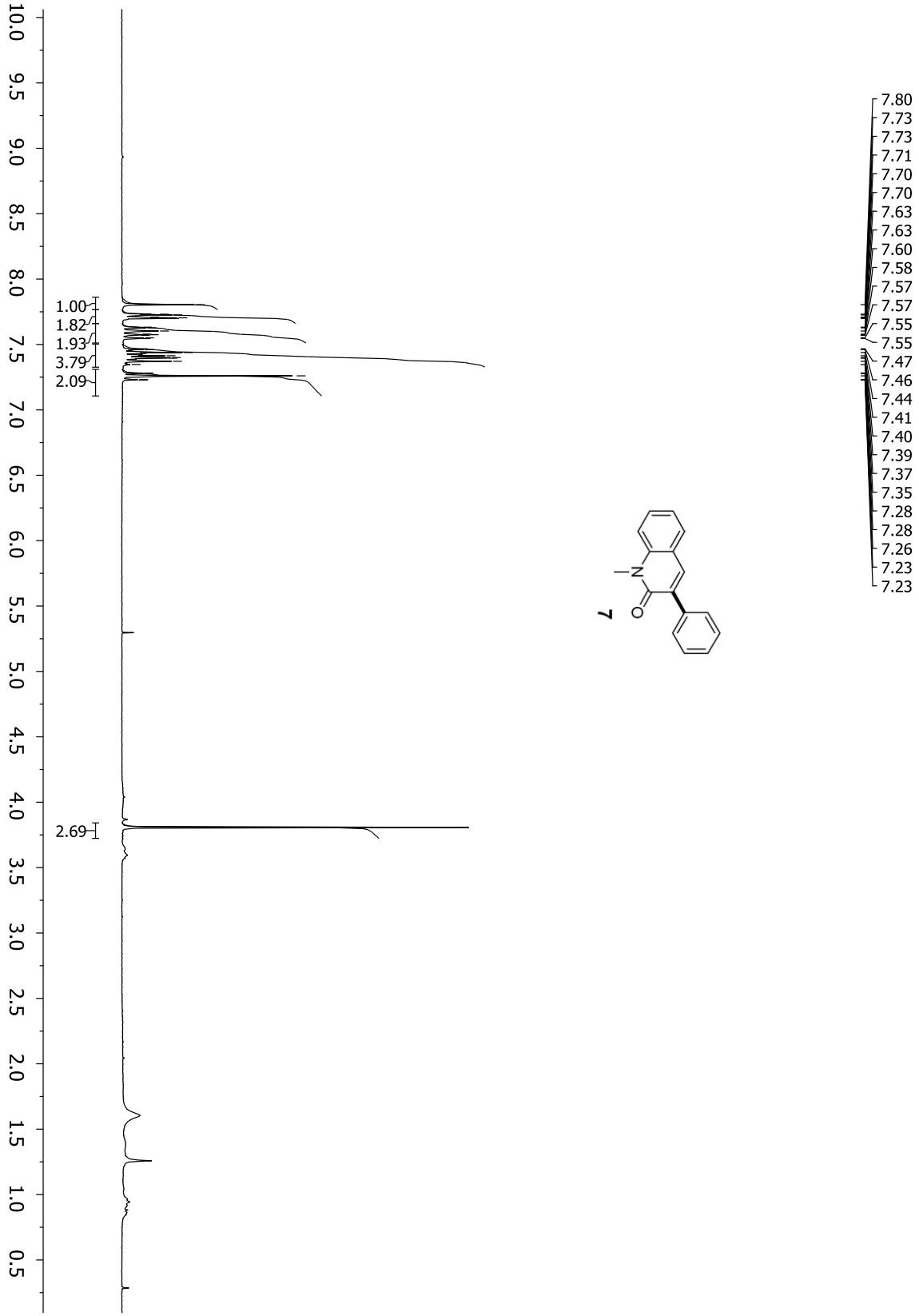
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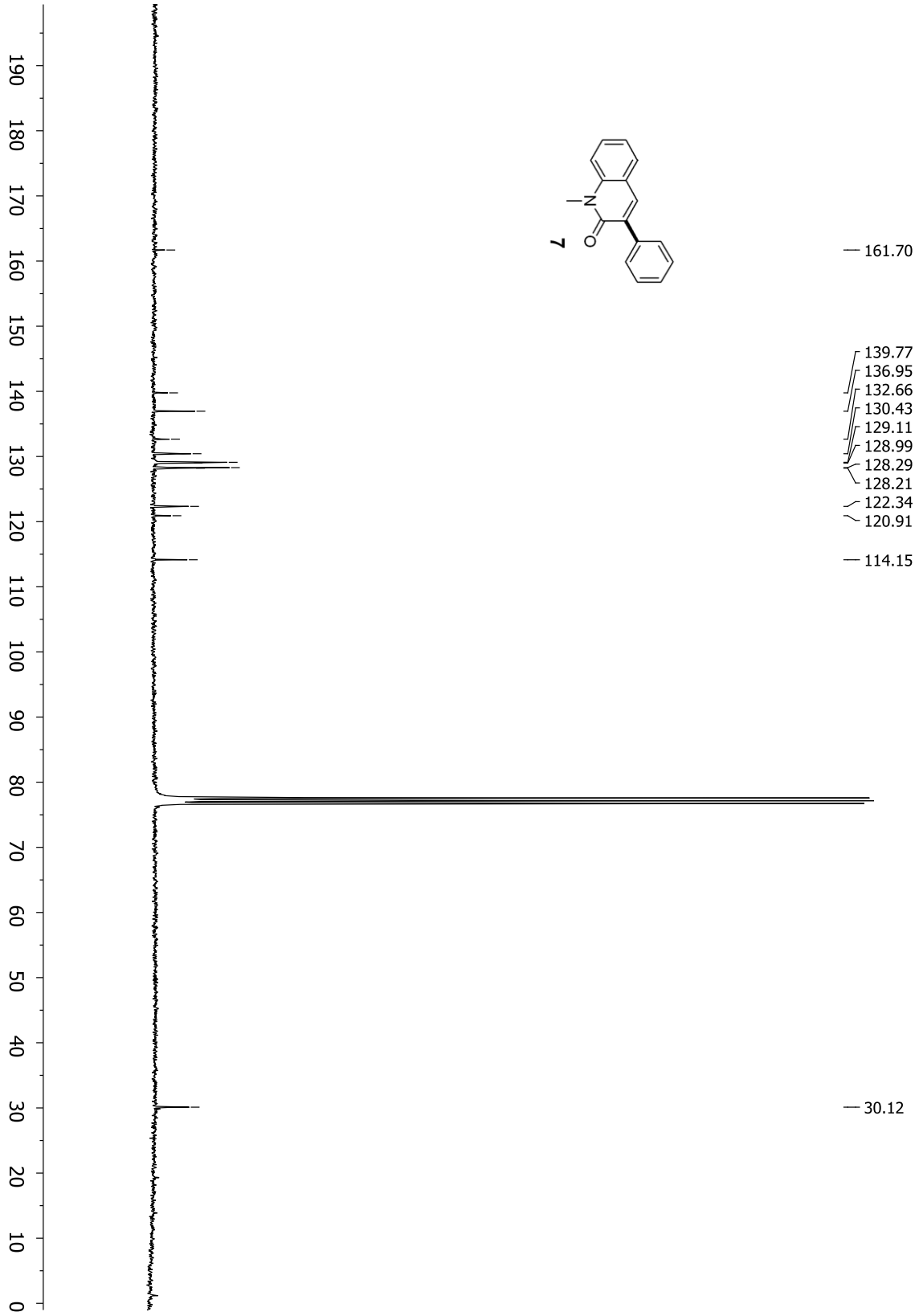
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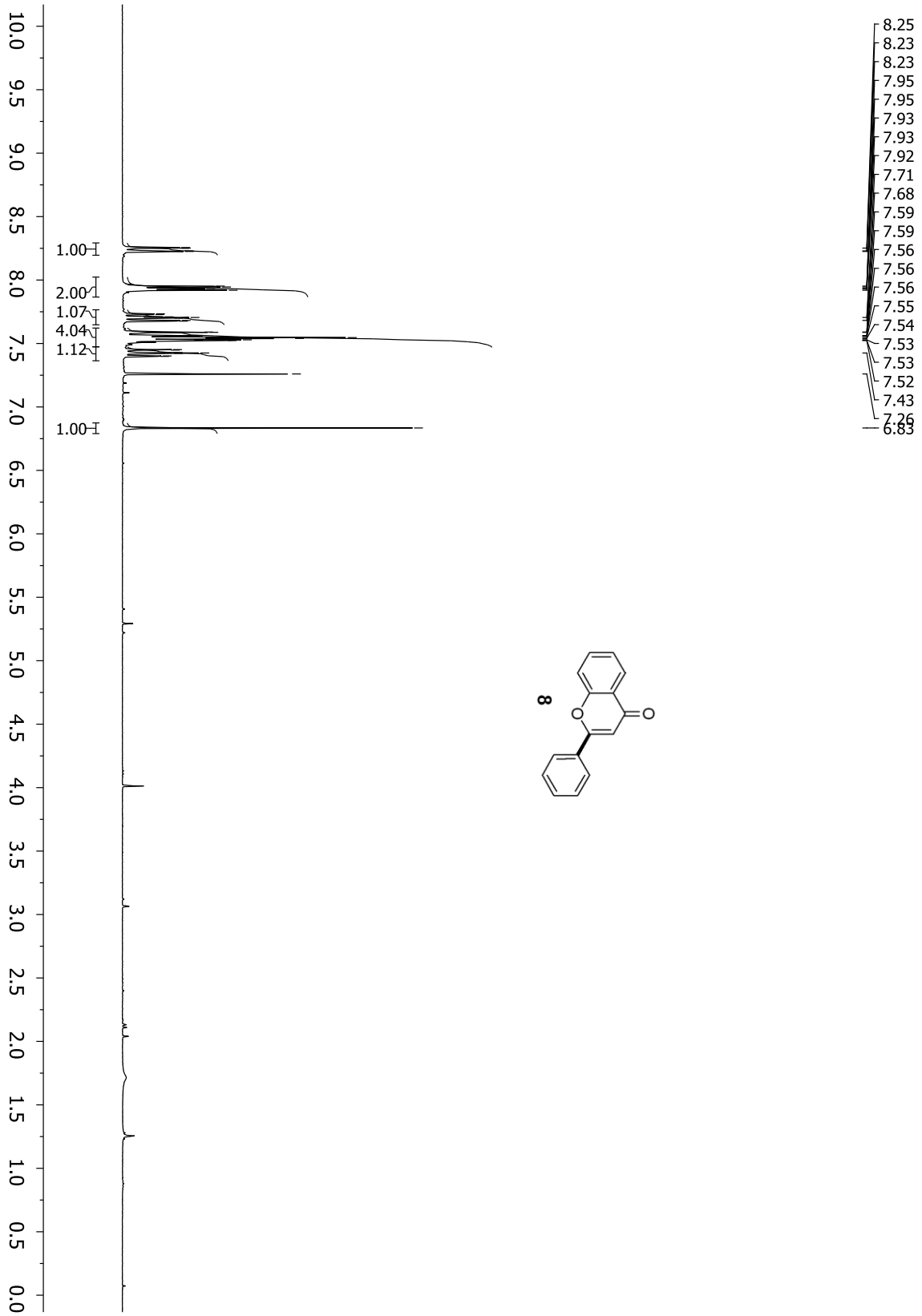
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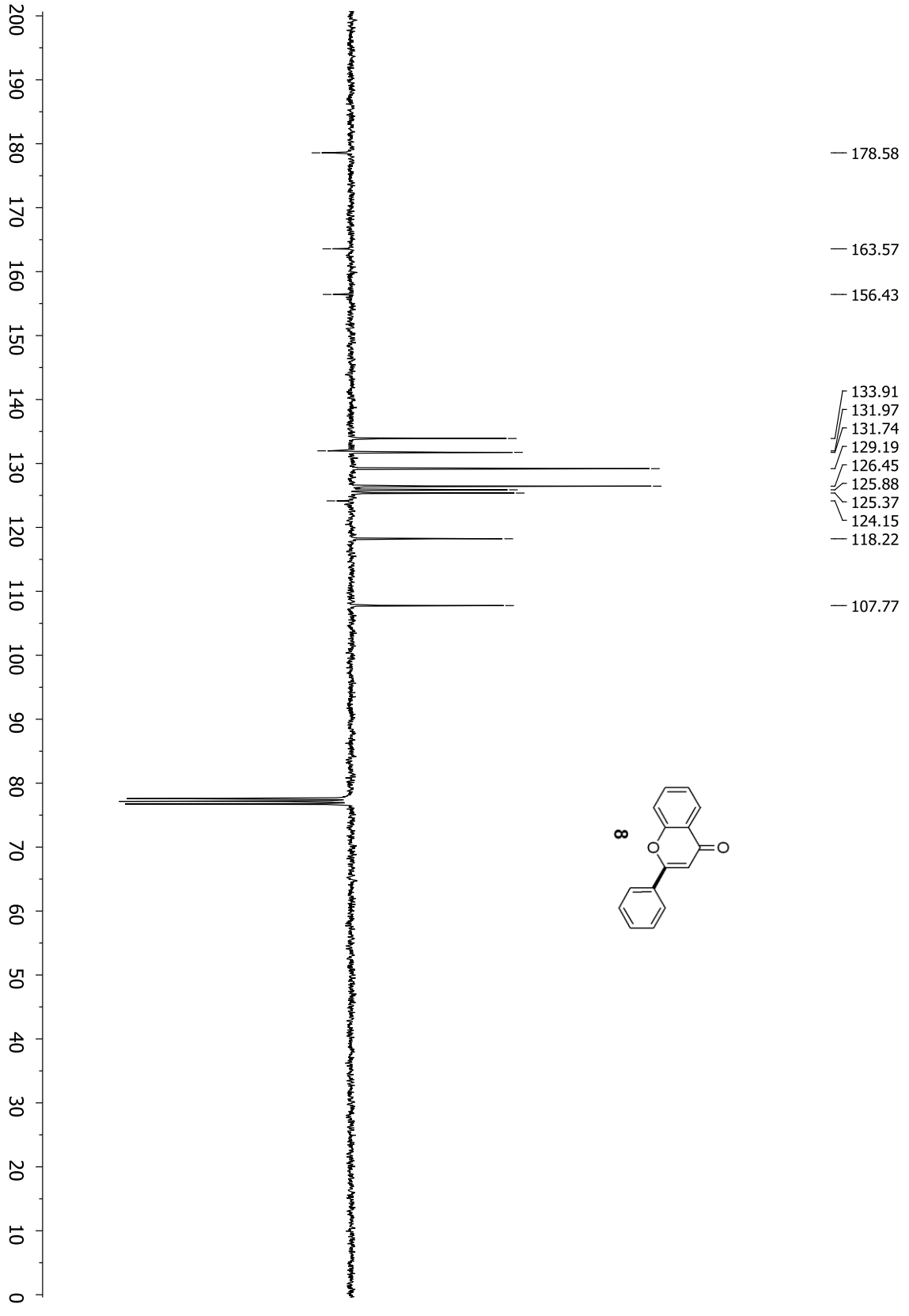
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