Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Electronic Supplementary Information

Dearomative C−C and C−N Bond Cleavage of 2-Arylindoles: Transition-Metal-Free Access to 2-Aminoarylphenones

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I. General Information

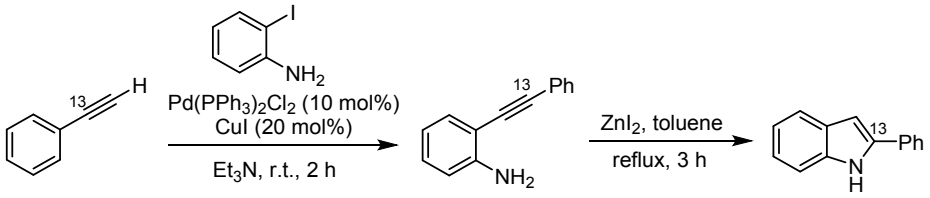
All reactions dealing with air- and moisture-sensitive compounds were carried out in dry reaction vessels under a nitrogen atmosphere. Column chromatography was conducted with 200-300 mesh silica gel. ^{1}H NMR (400 MHz) and ^{13}C NMR (125 MHz) were registered on Bruker 400 M or 500 M spectrometers. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the ^{1}H spectrum as 0.00 ppm, $CDCl_3$ resonance in the ^{13}C spectrum as 77.0 ppm. All coupling constants (*J* values) were reported in Hertz (Hz). The following abbreviations were used to describe peak splitting patterns when appropriate: br s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High resolution mass spectra (HRMS) were obtained on an ESI-LC-MS/MS spectrometer.

Materials. Unless otherwise noted, materials were purchased from Alfa Aesar, and other commercial suppliers and were used as received.

II. Preparation of Substrates

2-Phenylindole **1a** was purchased from Alfa Aesar. 2-Arylindoles **1b**-**1i**, **1k**-**1m**, **1o**, **1q**, **1s** and **1t** were prepared by Pd-catalyzed direct arylation of arenes with aryl boronic acids according to the literature procedure.[1] Other 2-arylindoles **1j**, **1n**, **1p**, **1r**, **1u** and **1v** were synthesized by the well-known Fischer indole synthesis.[2] ^{1}H and ^{13}C spectra of known compounds were in accordance with those described in literatures.

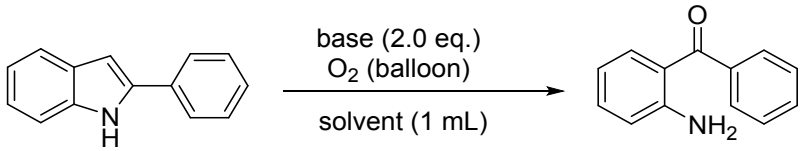
2-Phenyl-2-[^{13}C]indole ([^{13}C]-**1a**) was prepared according to the following procedure.[3,4] Phenyl-α-[^{13}C]acetylene was prepared according to the literature procedure.[5]



III. General Procedure

A 10 mL Schlenk tube equipped with a stirrer bar was charged with 2-arylindole (0.20 mmol), Cs_2CO_3 (130.3 mg, 0.40 mmol, 2.0 equiv) and DMSO (1.0 mL). The Schlenk tube was sealed with a rubber stopper in air and a balloon filled with O_2 was attached to it through a needle. Then, the reaction mixture was stirred at 120 °C for 16 h. Upon cooling to room temperature, the reaction mixture was directly subjected to flash chromatography on silica gel to afford the product.

IV. Screening of the Reaction Conditions



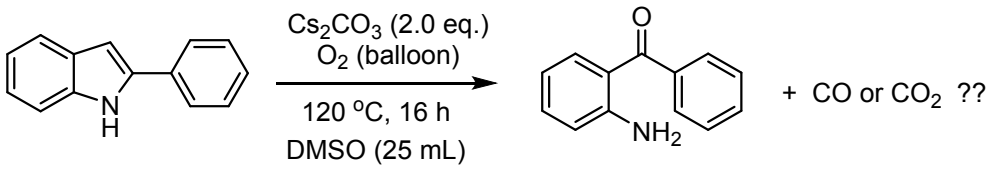
Entry	Base	Solvent	Additive	Time	Temp.	Yield (%)
1	Cs_2CO_3	DMSO		18 h	120 °C	51
2	Cs_2CO_3	Toluene		18 h	120 °C	NR
3	Cs_2CO_3	dioxane		18 h	120 °C	NR
4	Cs_2CO_3	DCE		18 h	120 °C	NR
5	Cs_2CO_3	CH_3CN		18 h	120 °C	NR
6	Cs_2CO_3	DMF		18 h	120 °C	20
7	Cs_2CO_3	NMP		18 h	120 °C	ND
8	K_3PO_4	DMSO		18 h	120 °C	NR
9	K_2CO_3	DMSO		18 h	120 °C	NR
10	KO^{t}Bu	DMSO		18 h	120 °C	NR
11	Na_2CO_3	DMSO		18 h	120 °C	NR
12	CsOAc	DMSO		18 h	120 °C	NR
13	LiOH	DMSO		18 h	120 °C	9
14	DBU	DMSO		18 h	120 °C	NR
15	TEA	DMSO		18 h	120 °C	NR

16	Pyridine	DMSO		18 h	120 °C	NR
17	Cs_2CO_3	DMSO (anhydrous)	4Å MS	18 h	120 °C	38
18	Cs_2CO_3	DMSO (anhydrous)		18 h	120 °C	44
19	Cs_2CO_3	DMSO (anhydrous)	H_2O (1.0 eq.)	18 h	120 °C	45
20	Cs_2CO_3	DMSO (anhydrous)	H_2O (5.0 eq.)	18 h	120 °C	47
21	Cs_2CO_3	DMSO (anhydrous)	H_2O (10.0 eq.)	18 h	120 °C	52
22	Cs_2CO_3	DMSO (anhydrous)	H_2O (15.0 eq.)	18 h	120 °C	48
23	Cs_2CO_3	DMSO		16 h	120 °C	56
24	Cs_2CO_3	DMSO		16 h	110 °C	18
25	Cs_2CO_3	DMSO		16 h	130 °C	51
26	Cs_2CO_3 (1.8 eq.)	DMSO		16 h	120 °C	49
27	Cs_2CO_3 (2.2 eq.)	DMSO		16 h	120 °C	56
28	Cs_2CO_3 (2.5 eq.)	DMSO		16 h	120 °C	56
29	Cs_2CO_3	DMSO (2 mL)		16 h	120 °C	43
30	Cs_2CO_3	DMSO	TBAC (1.0 eq.)	16 h	120 °C	trace
31	Cs_2CO_3	DMSO	TBAB (1.0 eq.)	16 h	120 °C	40
32	Cs_2CO_3	DMSO	TBAI (1.0	16 h	120 °C	33

			eq.)			
33	Cs_2CO_3	DMSO	H_2O (5.0 eq.)	16 h	120 °C	41
34	Cs_2CO_3	DMSO	BQ (2.0 eq.)	16 h	120 °C	NR
35	Cs_2CO_3	DMSO	$K_2S_2O_8$ (2.0 eq.)	16 h	120 °C	NR
36	Cs_2CO_3	DMSO	Oxone (2.0 eq.)	16 h	120 °C	NR
37	Cs_2CO_3	DMSO	TBHP (2.0 eq.)	16 h	120 °C	ND
38	Cs_2CO_3	DMSO	TEMPO (0.2 eq.)	16 h	120 °C	51
39	Cs_2CO_3	dioxane	TBAB (1.0 eq.)	16 h	120 °C	NR
40	Cs_2CO_3	DMSO	$Cu(OAc)_2$ (0.1 eq)	16 h	120 °C	54
41	Cs_2CO_3	DMSO	$Mn(Oac)_2$ (5 mol%)	16 h	120 °C	43
42	Cs_2CO_3	DMSO	$MnSO_4$ (5 mol%)	16 h	120 °C	53
43	Cs_2CO_3	DMSO	PPh_3 (20 mol%)	16 h	120 °C	48
44[b]	Cs_2CO_3	DMSO		16 h	120 °C	73
45[b,c]	Cs_2CO_3	DMSO		16 h	120 °C	78
46[b,d]	Cs_2CO_3	DMSO		16 h	120 °C	42

[a] Reaction conditions: **1a** (0.2 mmol), solvent (1 mL), base (2.0 equiv), degassed with O_2, 120 °C, 18 h, O_2 balloon, in a 50 mL Schlenk tube. NMR yields with CH_2Br_2 as an internal standard. NR = No reaction. ND = Not detected. [b] Without degassing with O_2. [c] Reaction was run in a 10 mL Schlenk tube. [d] Reaction was run in a 100 mL Schlenk tube.

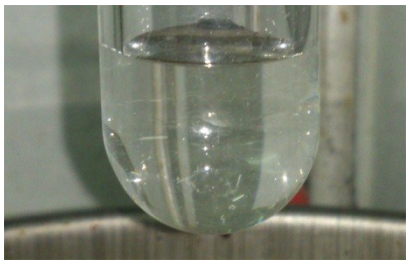
V. Mechanistic Studies



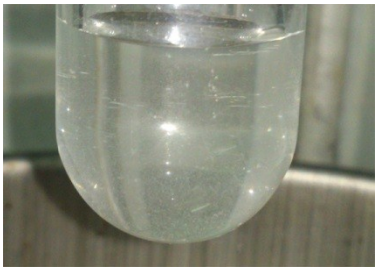
1a
5 mmol scale

2a

A 250 mL flask equipped with a stirrer bar was charged with 2-phenylindole (5.0 mmol), Cs_2CO_3 (10.0 mmol, 2.0 eq.) and DMSO (25 mL). The flask was attached to a balloon filled with O_2 and sealed with a rubber stopper. Then the reaction mixture was stirred at 120 °C for 16 h. After completion of the reaction, the gas in the attached balloon was bubbled through a solution of limewater via a long needle.



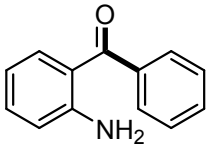
before bubbling



after bubbling

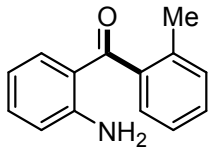
VI. Product Characterization

(2-aminophenyl)(phenyl)methanone (**2a**)[6]



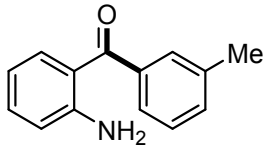
Yellow solid, 28.8 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.62 (m, 2H), 7.53-7.50 (m, 1H), 7.46-7.43 (m, 3H), 7.30-7.25 (m, 1H), 6.73 (d, J = 8.4 Hz, 1H), 6.61-6.58 (m, 1H), 6.08 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.0, 150.9, 140.1, 134.5, 134.2, 131.0, 129.1, 128.0, 118.2, 117.0, 115.5; MS (ESI) m/z: 198 ($[M+H]^+$).

(2-aminophenyl)(*o*-tolyl)methanone (**2b**)[7]



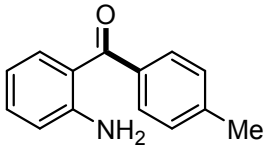
Yellow solid, 24.5 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 1H), 7.29-7.19 (m, 5H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.54-6.50 (m, 1H), 6.40 (br s, 2H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.3, 151.2, 140.6, 135.0, 134.8, 134.7, 130.5, 129.1, 127.1, 125.2, 118.4, 116.9, 115.6, 19.4; MS (EI) m/z: 212 ($[M+H]^+$).

(2-aminophenyl)(*m*-tolyl)methanone (**2c**)[7]



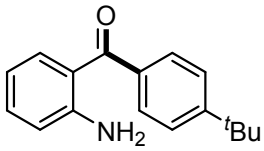
Yellow solid, 27.7 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.43 (m, 2H), 7.41-7.39 (m, 1H), 7.33-7.31 (m, 2H), 7.29-7.24 (m, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.61-6.57 (m, 1H), 6.07 (br s, 2H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.3, 150.8, 140.1, 137.9, 134.5, 134.1, 131.7, 129.5, 127.8, 126.3, 118.3, 116.9, 115.4, 21.3; MS (EI) m/z: 212 ($[M+H]^+$).

(2-aminophenyl)(*p*-tolyl)methanone (**2d**)[7]



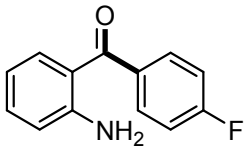
Yellow solid, 17.0 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.45 (dd, *J1* = 8.0 Hz, *J2* = 1.6 Hz, 1H), 7.30-7.24 (m, 3H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.62-6.58 (m, 1H), 5.99 (br s, 2H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.8, 150.7, 141.6, 137.2, 134.4, 133.9, 129.4, 128.7, 118.6, 116.9, 115.5, 21.5; MS (EI) m/z: 212 ($[M+H]^+$).

(2-aminophenyl)(4-(*tert*-butyl)phenyl)methanone (**2e**)[8]



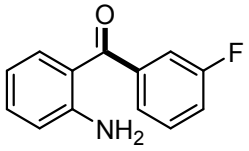
Yellow solid, 29.3 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.59 (m, 2H), 7.50-7.45 (m, 3H), 7.30-7.25 (m, 1H), 6.72 (d, J = 7.6 Hz, 1H), 6.62-6.58 (m, 1H), 6.01 (br s, 2H), 1.36 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.8, 154.7, 150.7, 137.2, 134.5, 133.9, 129.2, 125.0, 118.6, 116.9, 115.4, 34.9, 31.2; MS (EI) m/z: 254 ([M+H]$^+$).

(2-aminophenyl)(4-fluorophenyl)methanone (**2f**)[7]



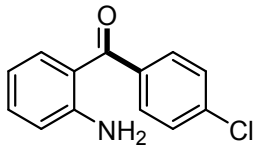
Yellow solid, 17.2 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.65 (m, 2H), 7.41 (dd, J = 1.2, 8.0 Hz, 1H), 7.31-7.27 (m, 1H), 7.15-7.11 (m, 2H), 6.74 (d, J = 8.4 Hz, 1H), 6.63-6.59 (m, 1H), 6.01 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 164.5 (J_{CF} = 250 Hz), 150.8, 136.2, 134.2, 134.1, 131.6 (J_{CF} = 9 Hz), 118.1, 117.1, 115.6, 115.2 (J_{CF} = 22 Hz); MS (EI) m/z: 216 ([M+H]$^+$).

(2-aminophenyl)(3-fluorophenyl)methanone (**2g**)[9]



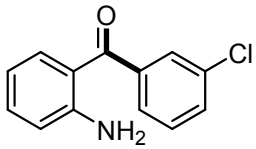
Yellow solid, 30.4 mg. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45-7.39 (m, 3H), 7.34-7.29 (m, 2H), 7.23-7.20 (m, 1H), 6.74 (d, J = 8.5 Hz, 1H), 6.61 (t, J = 7.5 Hz, 1H), 6.12 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 162.3 (J_{CF} = 246 Hz), 151.1, 142.2 (J_{CF} = 6 Hz), 134.5 (J_{CF} = 30 Hz), 129.8, 129.7, 124.7 (J_{CF} = 3 Hz), 117.9 (J_{CF} = 21 Hz), 117.6, 117.1, 116.0 (J_{CF} = 22 Hz), 115.6; MS (EI) m/z: 216 ([M+H]$^+$).

(2-aminophenyl)(4-chlorophenyl)methanone (**2h**)[7]



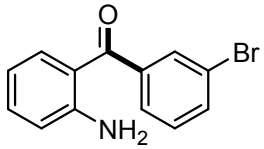
Yellow solid, 26.8 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.57 (m, 2H), 7.44-7.38 (m, 3H), 7.31-7.26 (m, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.62-6.58 (m, 1H), 6.01 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6, 151.0, 138.4, 137.3, 134.4, 134.2, 130.6, 128.4, 117.8, 117.1, 115.6; MS (EI) m/z: 232 ($[M+H]^+$).

(2-aminophenyl)(3-chlorophenyl)methanone (**2i**)[10]



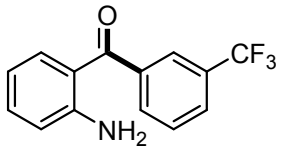
Yellow solid, 26.8 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.60 (m, 1H), 7.50-7.47 (m, 2H), 7.40-7.36 (m, 2H), 7.32-7.28 (m, 1H), 6.73 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.62-6.58 (m, 1H), 6.13 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 151.1, 141.8, 134.6, 134.3, 134.2, 130.9, 129.4, 128.9, 127.1, 117.5, 117.1, 115.6; MS (EI) m/z: 232 ($[M+H]^+$).

(2-aminophenyl)(3-bromophenyl)methanone (**2j**)



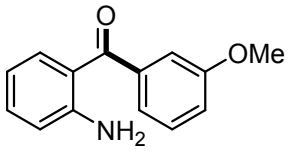
Yellow solid, 39.1 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.39 (dd, *J1* = 1.2 Hz, *J2* = 8.4 Hz, 1H), 7.34-7.28 (m, 2H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.63-6.59 (m, 1H), 6.12 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 151.1, 142.0, 134.6, 134.3, 133.8, 131.8, 129.6, 127.5, 122.3, 117.5, 117.1, 115.6; HRMS (ESI) m/z: Anal. Calcd. $C_{13}H_{11}BrNO$ $[M+H]^+$ 276.0018. Found 276.0017.

(2-aminophenyl)(3-(trifluoromethyl)phenyl)methanone (**2k**)[11]



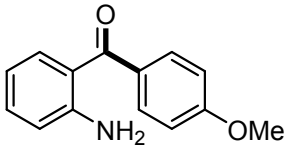
Yellow solid, 10.7 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.79 (t, J = 8.4 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.36-7.29 (m, 2H), 6.75 (d, J = 8.4 Hz, 1H), 6.61 (t, J = 7.6 Hz, 1H), 6.17 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 151.2, 140.8, 134.8, 134.2, 132.2, 130.8 (J_{CF} = 33 HZ), 128.7, 127.5 (J_{CF} = 4 HZ), 125.8 (J_{CF} = 4 HZ), 123.8 (J_{CF} = 271 HZ), 117.4, 117.2, 115.7; MS (EI) m/z: 266 ([M+H]$^+$).

(2-aminophenyl)(3-methoxyphenyl)methanone (**2l**)[7]



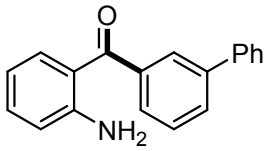
Yellow solid, 31.8 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 8.0, 1.2 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.30-7.26 (m, 1H), 7.19-7.17 (m, 2H), 7.07-7.04 (m, 1H), 6.73 (d, J = 7.6 Hz, 1H), 6.61-6.57 (m, 1H), 6.09 (br s, 2H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.8, 159.4, 150.9, 141.4, 134.5, 134.2, 129.0, 121.6, 118.1, 117.2, 116.9, 115.5, 113.8, 55.4; MS (EI) m/z: 228 ([M+H]$^+$).

(2-aminophenyl)(4-methoxyphenyl)methanone (**2m**)[7]



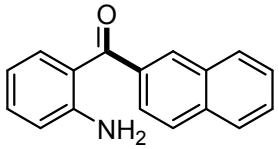
Yellow solid, 27.2 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.29-7.25 (m, 1H), 6.94 (d, J = 8.8 Hz, 2H), 6.72 (d, J = 8.0 Hz, 1H), 6.64-6.60 (m, 1H), 5.84 (br s, 2H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 162.3, 150.3, 133.9, 133.6, 132.3, 131.7, 119.0, 116.9, 115.5, 113.3, 55.4; MS (EI) m/z: 228 ([M+H]$^+$).

[1,1'-biphenyl]-3-yl(2-aminophenyl)methanone (**2n**)[9]



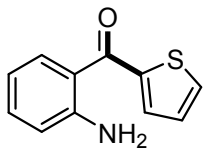
Yellow solid, 34.4 mg. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.61-7.59 (m, 3H), 7.53-7.49 (m, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.30-7.27 (m, 1H), 6.73 (d, *J* = 8.5 Hz, 1H), 6.61-6.58 (m, 1H), 6.13 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.0, 151.0, 141.1, 140.7, 140.3, 134.6, 134.3, 129.6, 128.8, 128.5, 127.9, 127.7, 127.6, 127.2, 118.1, 117.0, 115.6; MS (EI) m/z: 274 ($[M+H]^+$).

(2-aminophenyl)(naphthalen-2-yl)methanone (**2o**)[7]



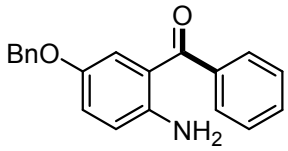
Yellow solid, 28.4 mg. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.92-7.88 (m, 3H), 7.78-7.76 (m, 1H), 7.59-7.50 (m, 3H), 7.32-7.29 (m, 1H), 6.76 (d, *J* = 8.5 Hz, 1H), 6.63-6.60 (m, 1H), 6.09 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.9, 150.9, 137.3, 134.6, 134.2, 132.3, 130.0, 129.0, 128.0, 127.7, 127.6, 126.6, 125.7, 118.5, 117.0, 115.6; MS (EI) m/z: 248 ($[M+H]^+$).

(2-aminophenyl)(thiophen-2-yl)methanone (**2p**)[12]



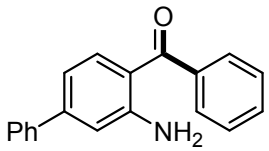
Yellow solid, 22.2 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.65 (dd, *J* = 1.2, 4.8 Hz, 1H), 7.57 (dd, *J* = 1.2, 4.0 Hz, 1H), 7.30 (m, 1H), 7.13 (m, 1H), 6.74-6.67 (m, 2H), 5.71 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 149.9, 144.8, 133.8, 133.6, 132.7, 127.5, 119.1, 117.0, 115.9; MS (EI) m/z: 204 ($[M+H]^+$).

(2-amino-5-(benzyloxy)phenyl)(phenyl)methanone (**2q**)[13]



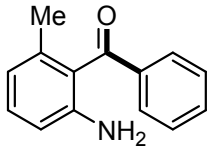
Yellow solid, 43.0 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.56 (m, 2H), 7.52-7.49 (m, 1H), 7.42-7.39 (m, 2H), 7.35-7.29 (m, 5H), 7.05 (dd, *J* = 2.8, 8.8 Hz, 1H), 7.00 (d, *J* = 2.8 Hz, 1H), 6.69 (d, *J* = 9.2 Hz, 1H), 5.75 (br s, 2H), 4.89 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.4, 148.7, 145.6, 139.8, 137.0, 131.1, 129.1, 128.5, 128.1, 127.9, 127.4, 124.0, 118.8, 118.4, 118.2, 71.0; MS (EI) m/z: 304 ($[M+H]^+$).

(3-amino-[1,1'-biphenyl]-4-yl)(phenyl)methanone (**2r**)



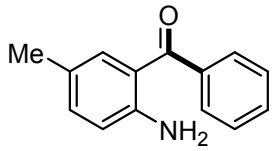
Yellow solid, 35.6 mg. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68-7.66 (m, 2H), 7.60 (d, *J* = 7.0 Hz, 2H), 7.55-7.52 (m, 2H), 7.49-7.43 (m, 4H), 7.40-7.37 (m, 1H), 6.94 (d, *J* = 1.5 Hz, 1H), 6.84 (dd, *J* = 1.5, 8.5 Hz, 1H), 6.21 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 151.3, 146.9, 140.2, 140.1, 135.2, 131.0, 129.0, 128.8, 128.2, 128.1, 127.2, 117.2, 115.2, 114.8; MS (ESI) m/z: Anal. Calcd. $C_{19}H_{16}NO$ $[M+H]^+$ 274.1226. Found 274.1227.

(2-amino-6-methylphenyl)(phenyl)methanone (**2s**)[14]



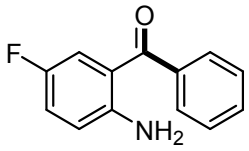
Yellow solid, 10.1 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.82 (m, 2H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.61 (t, *J* = 7.6 Hz, H), 3.91 (br s, 2H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.0, 144.7, 138.1, 136.4, 133.5, 130.4, 129.4, 128.8, 125.1, 120.4, 114.0, 20.5; MS (EI) m/z: 212 ($[M+H]^+$).

(2-amino-5-methylphenyl)(phenyl)methanone (**2t**)[15]



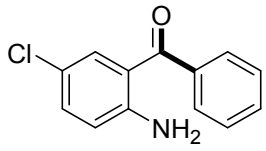
Yellow solid, 28.7 mg. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64-7.63 (m, 2H), 7.54-7.51 (m, 1H), 7.47-7.44 (m, 2H), 7.22 (s, 1H), 7.12 (dd, *J* = 1.5, 8.5 Hz, 1H), 6.67 (d, *J* = 8.5 Hz, 1H), 5.91 (br s, 2H), 2.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.0, 148.7, 140.2, 135.3, 134.0, 131.0, 129.1, 128.0, 124.6, 118.3, 117.1, 20.3; MS (EI) m/z: 212 ($[M+H]^+$).

(2-amino-5-fluorophenyl)(phenyl)methanone (**2u**)[16]



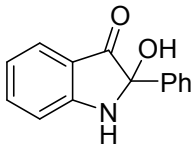
Yellow solid, 25.8 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (m, 2H), 7.56-7.52 (m, 1H), 7.48-7.45 (m, 2H), 7.14 (dd, *J* = 9.6, 2.8 Hz, 1H), 7.09-7.04 (m, 1H), 6.69 (dd, *J* = 4.4, 8.8 Hz, 1H), 5.90 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 153.2 (J_{CF} = 233 Hz), 147.3, 139.4, 131.4, 129.0, 128.2, 122.1 (J_{CF} = 23 Hz), 118.9 (J_{CF} = 22 Hz), 118.2 (J_{CF} = 7 Hz), 117.8 (J_{CF} = 5 Hz). MS (EI) m/z: 216 ($[M+H]^+$).

(2-amino-5-chlorophenyl)(phenyl)methanone (**2v**)[7]



Yellow solid, 27.0 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.59 (m, 2H), 7.55-7.51 (m, 1H), 7.47-7.44 (m, 2H), 7.38 (d, *J* = 12 Hz, 1H), 6.74 (d, *J* = 2.0 Hz, 1H), 6.56 (dd, *J* = 2.0, 8.4 Hz, 1H), 6.18 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 151.7, 140.3, 139.8, 135.8, 131.2, 129.0, 128.2, 116.6, 116.2, 116.0; MS (EI) m/z: 232 ($[M+H]^+$).

2-hydroxy-2-phenylindolin-3-one (**3**)[17]



Yellow solid, 15.8 mg. ^{1}H NMR (400 MHz, DMSO) δ 10.39 (s, 1H), 7.33-7.23 (m, 6H), 7.10 (d, *J* = 7.2 Hz, 1H), 6.96 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.61 (s, 1H); ^{13}C NMR (125 MHz, DMSO) δ 178.3, 141.8, 141.4, 133.6, 129.1, 127.9, 127.2, 125.3, 124.6, 121.9, 109.7, 77.2; MS (EI) m/z: 209 ($[M–OH+H]^{+}$).

VII. References

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S. Cockerill, V. C. L. Dowdell, E. A. Henderson, S. J. Keegan, R. D. Kelsey, M. J. Lockyer, J. N. Stables, L. J. Wilson, K. L. Powell, *J. Med. Chem.* **2006**, *49*, 2311.

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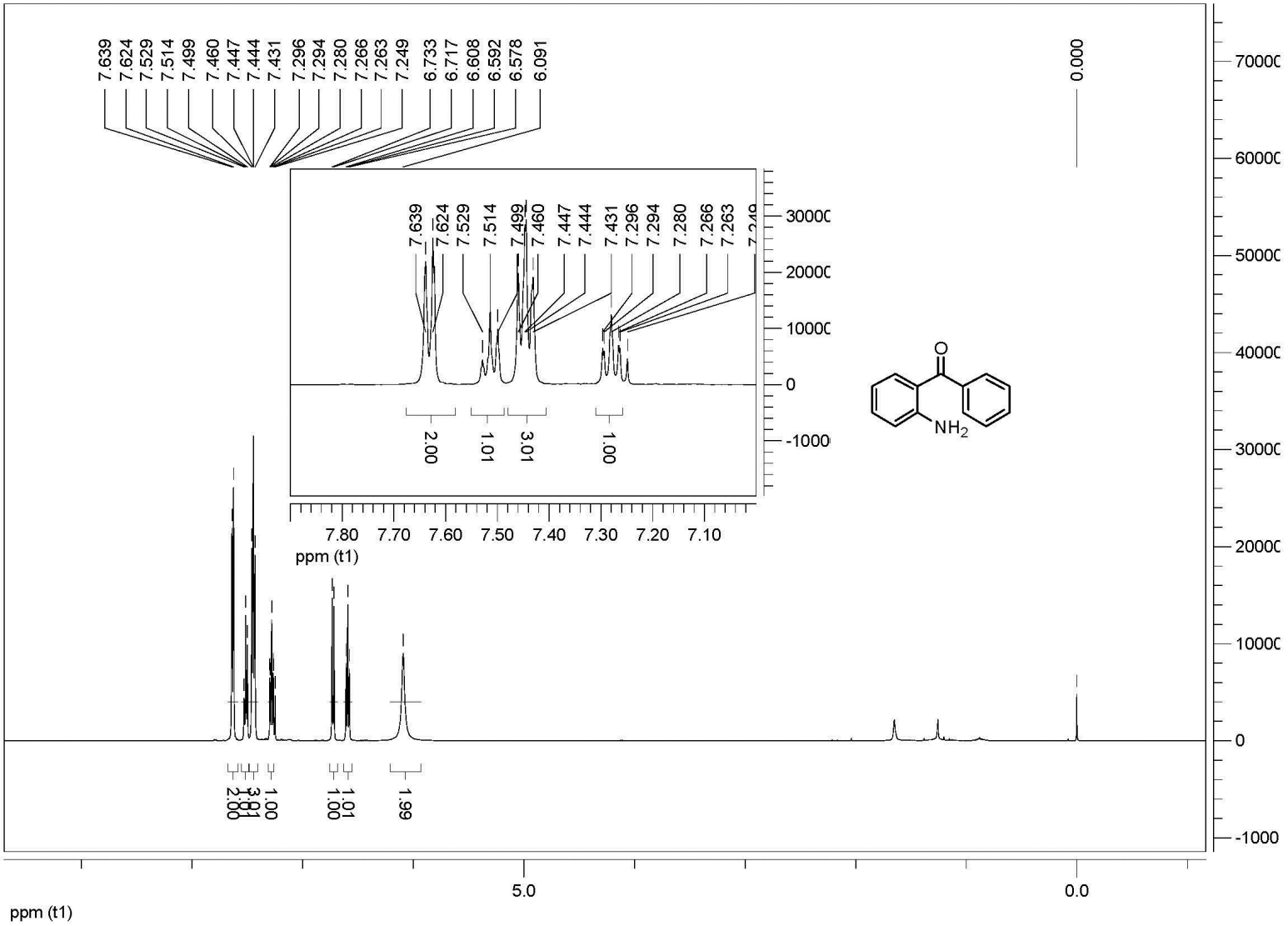
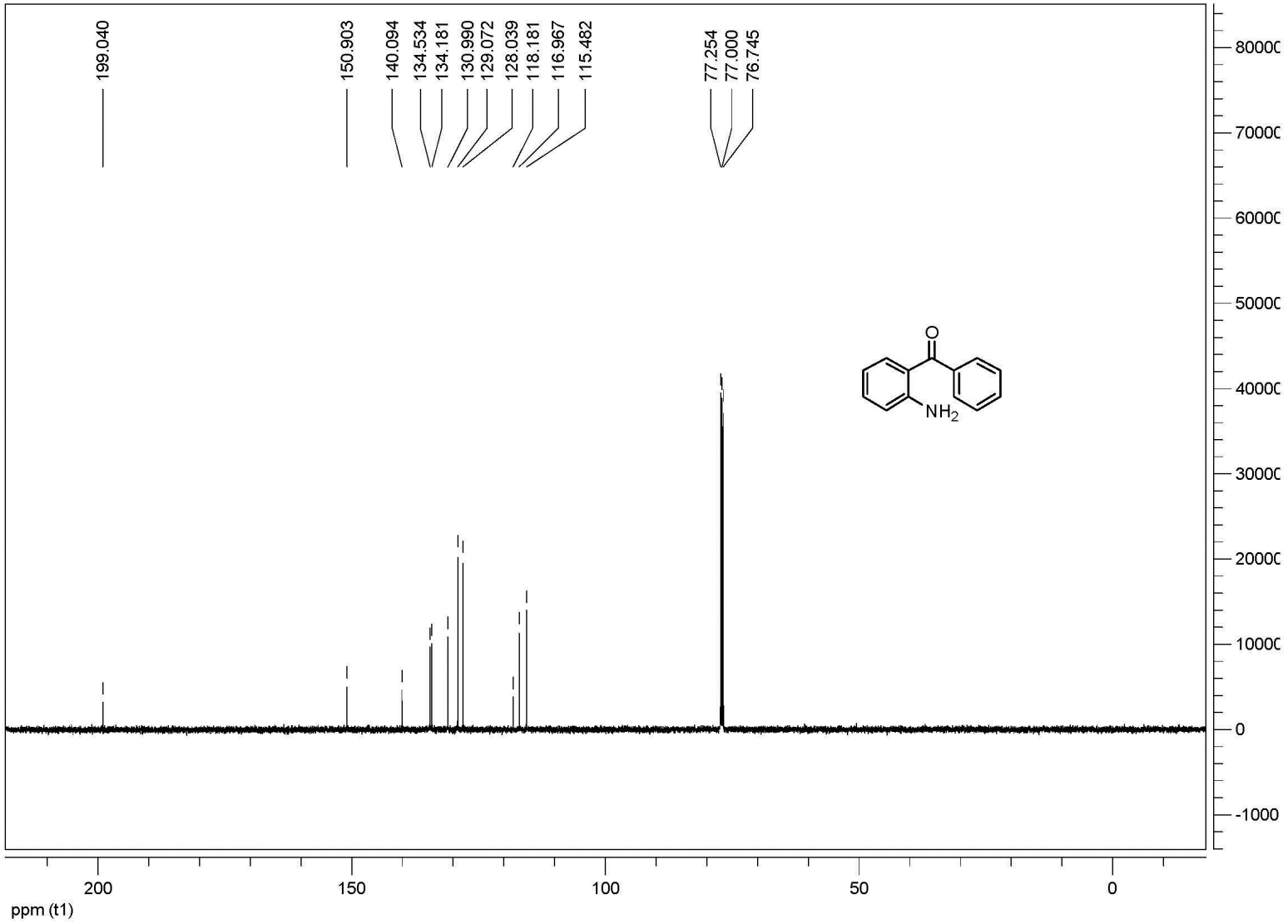
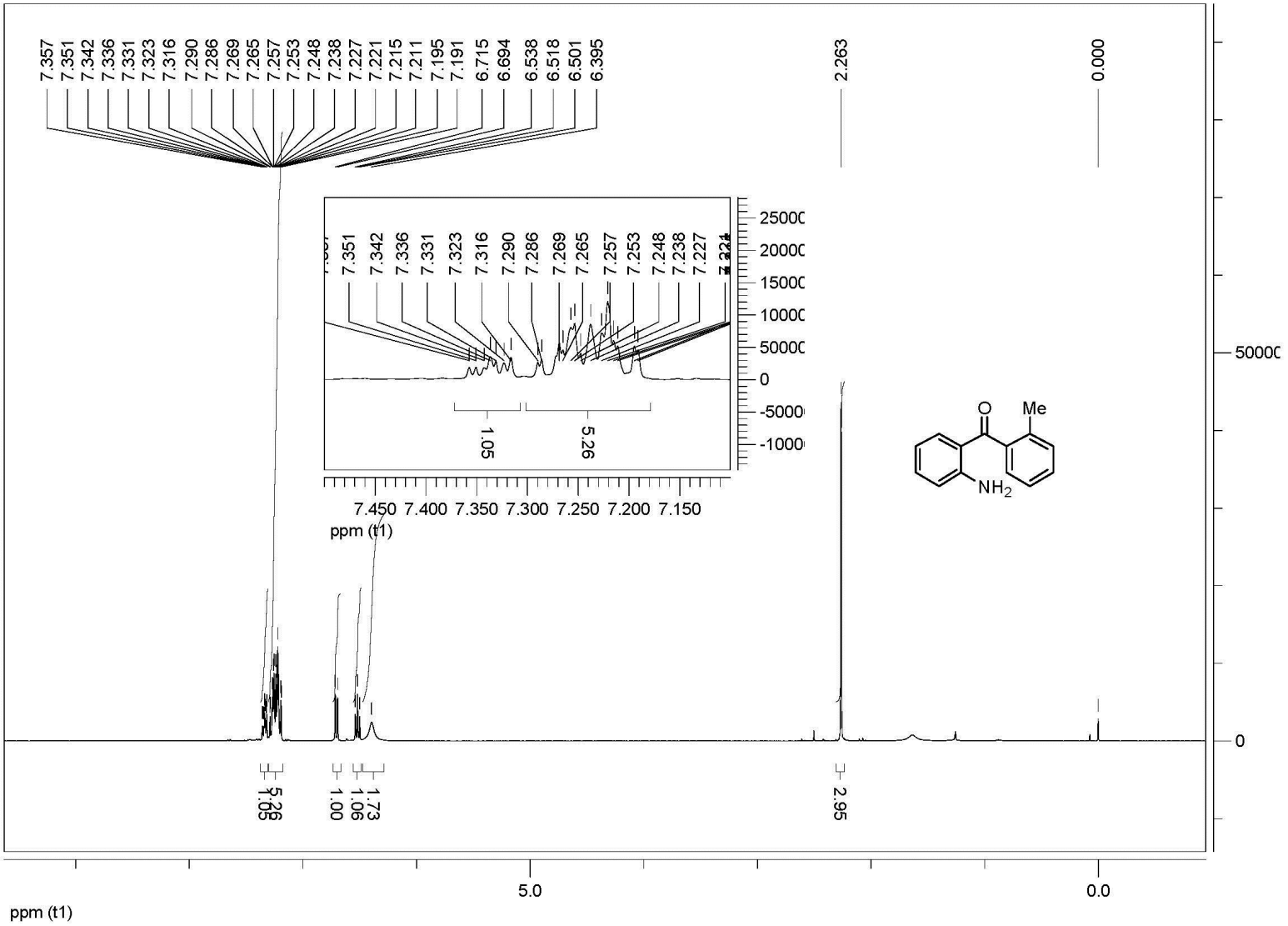
VIII. Copies of ^{1}H and ^{13}C NMR Spectra


7.639
7.624
7.529
7.514
7.499
7.460
7.447
7.444
7.431
7.296
7.294
7.280
7.266
7.263
7.249
6.733
6.717
6.608
6.592
6.578
6.091
0.000
2.00
1.01
3.01
1.00
7.80
7.70
7.60
7.50
7.40
7.30
7.20
7.10
ppm (t1)
NH2
2.00
3.01
1.00
1.01
1.00
1.99
5.0
0.0
ppm (t1)


199.040
150.903
140.094
134.534
134.181
130.990
129.072
128.039
118.181
116.967
115.482
77.254
77.000
76.745
O
NH2
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
200
150
100
50
0
ppm (t1)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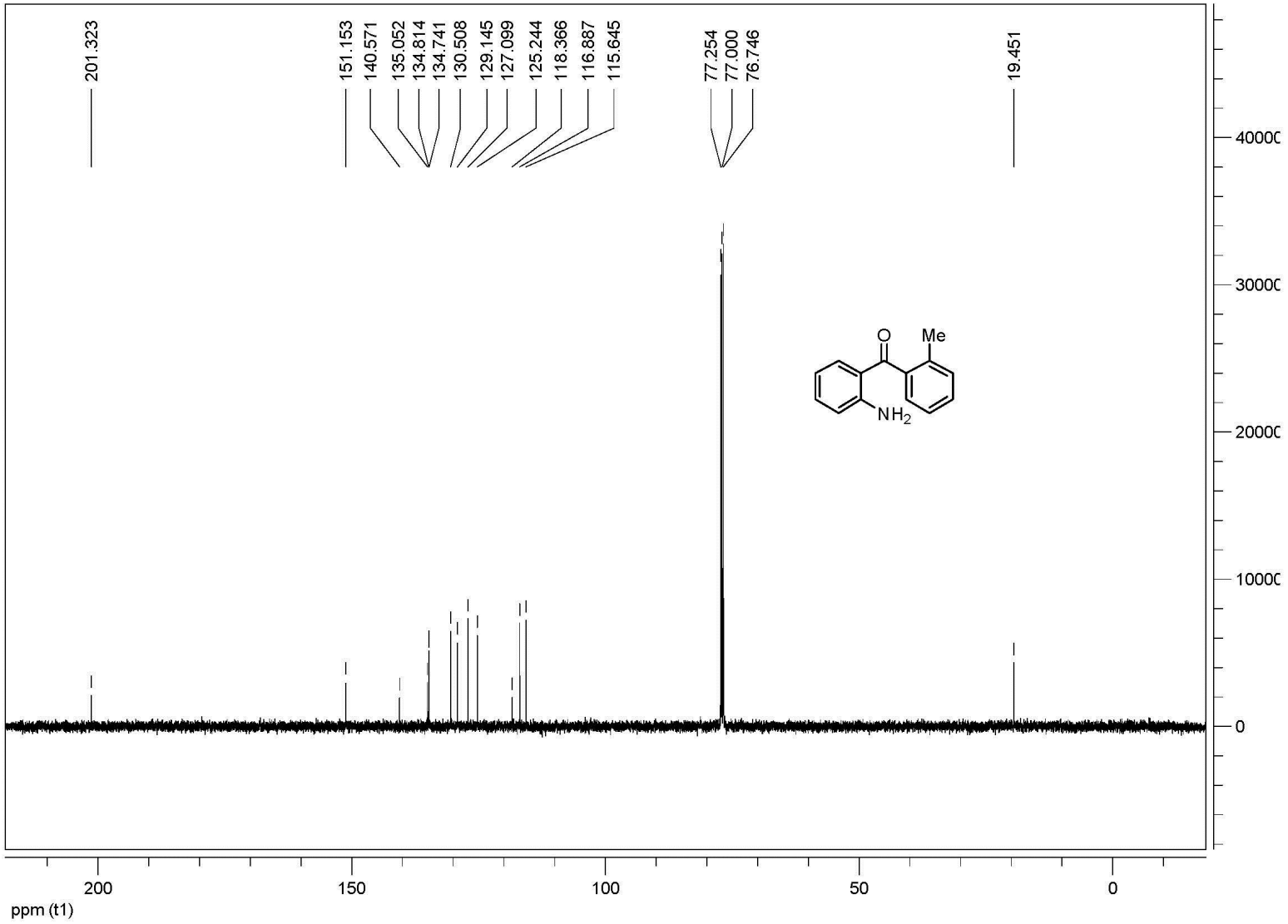
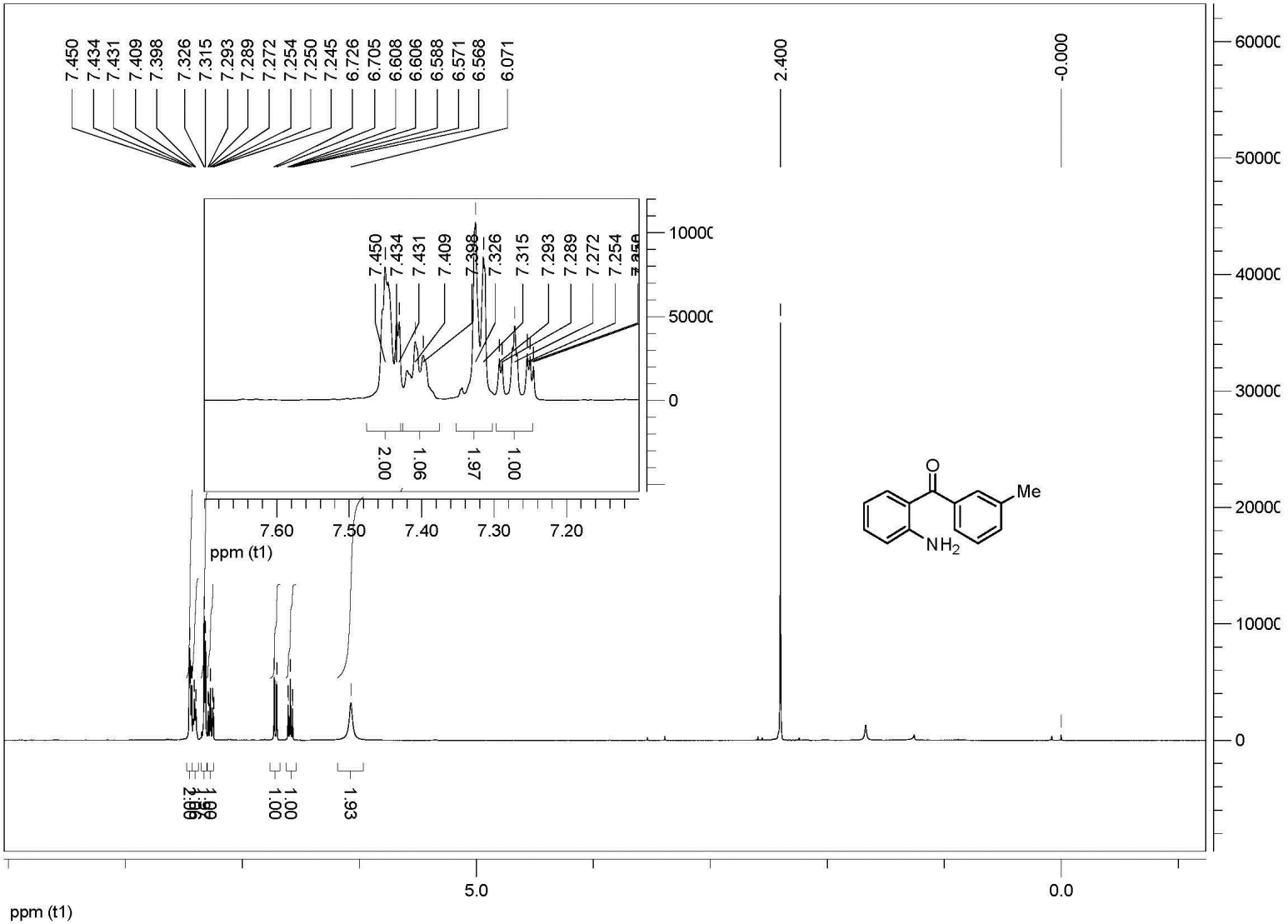
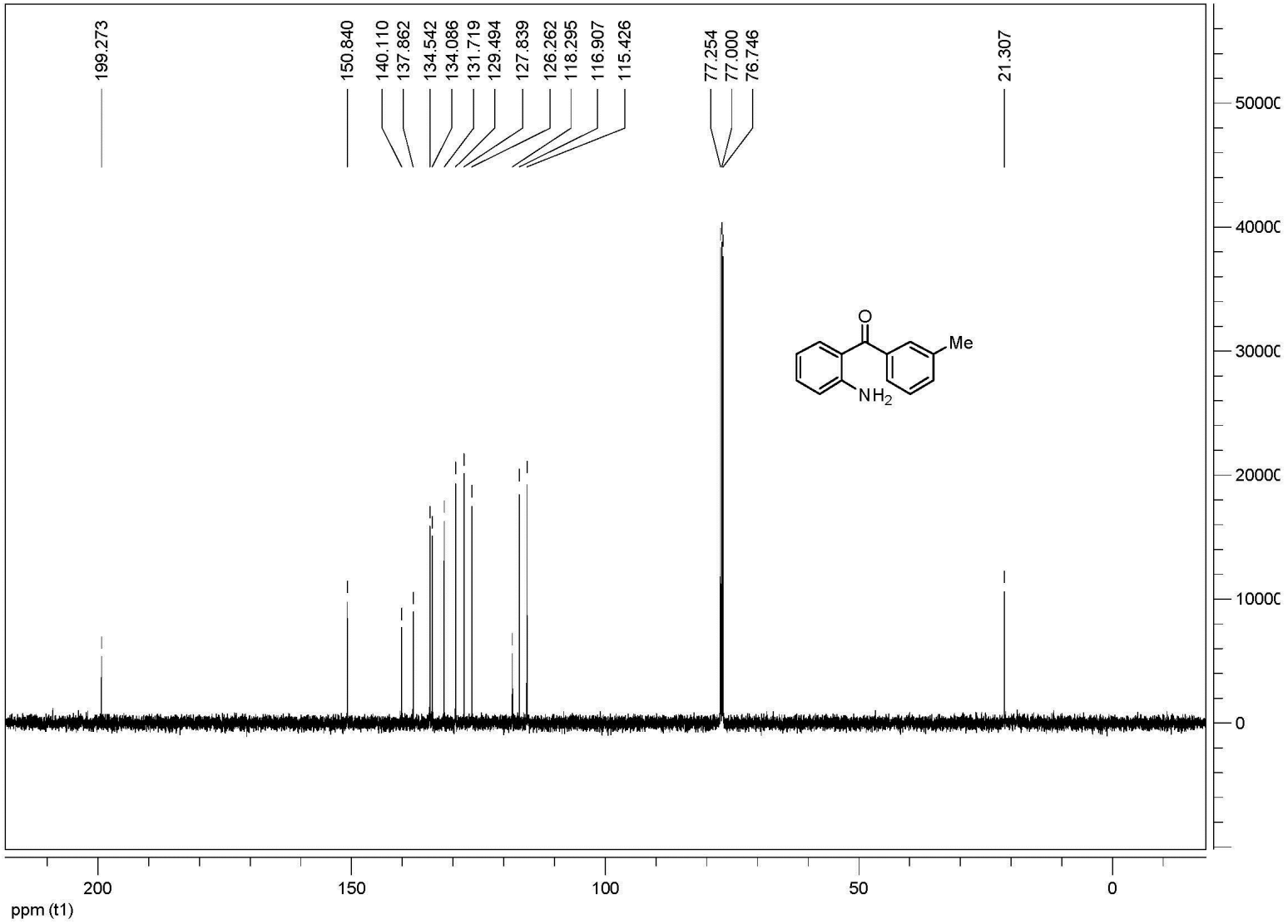
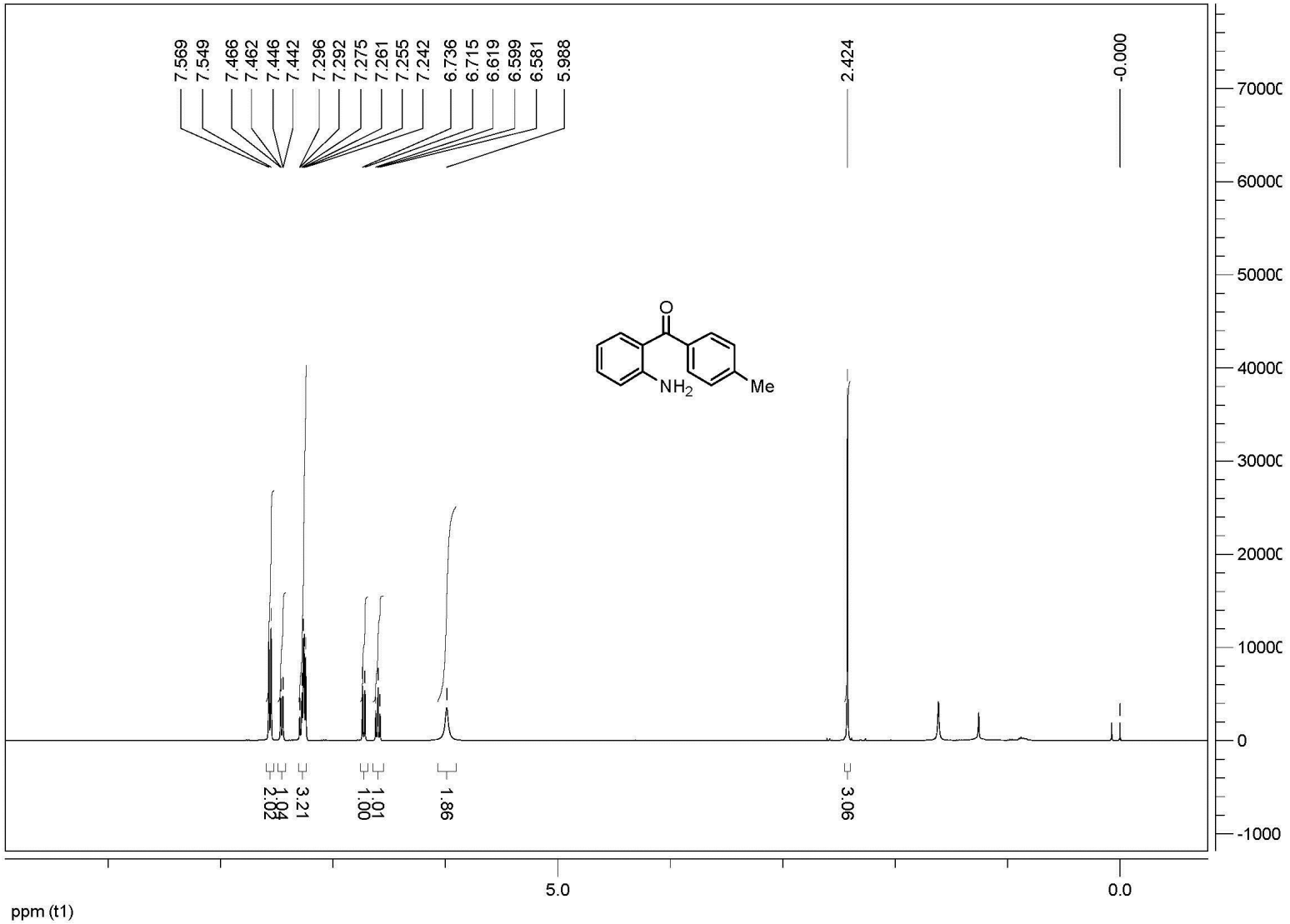
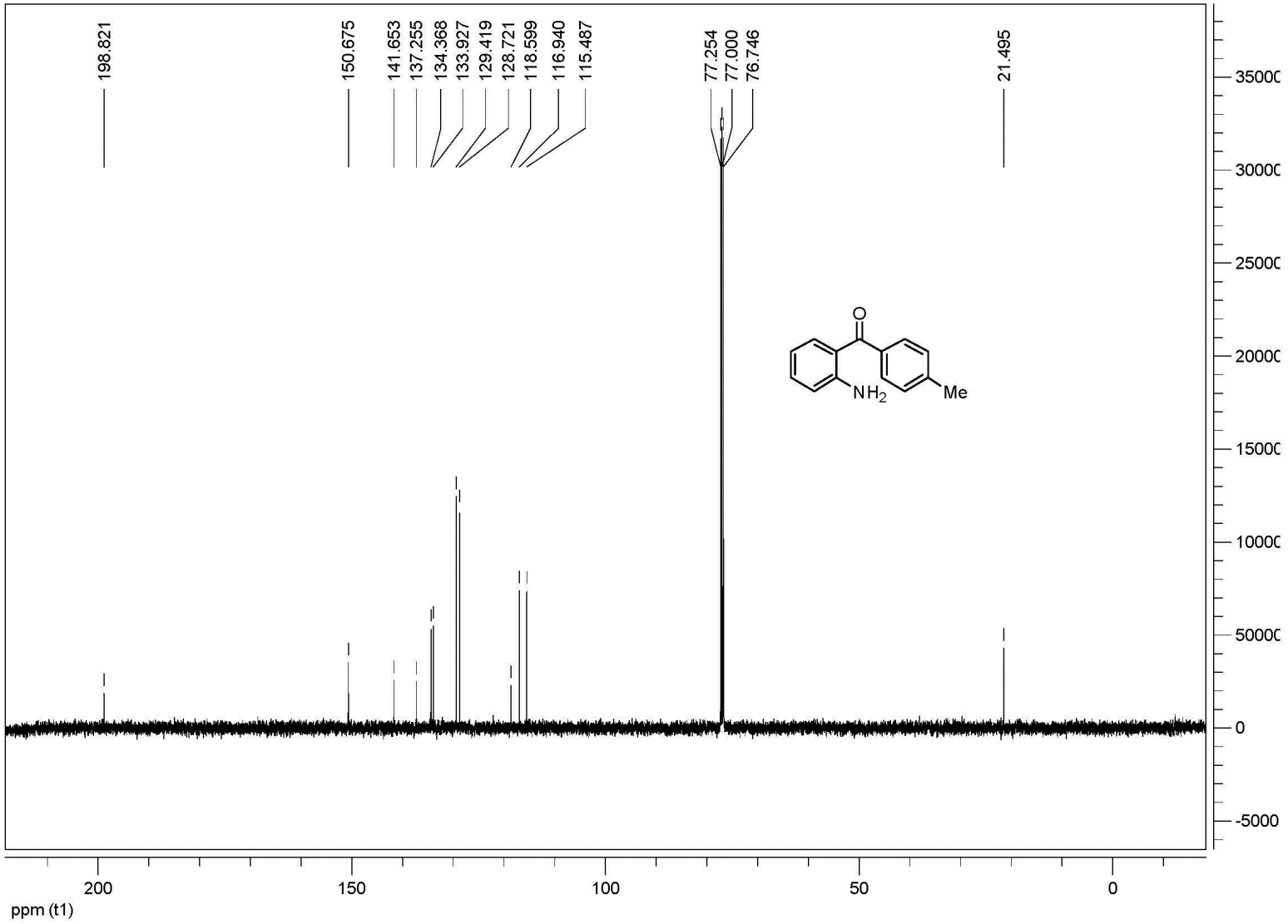
7.351
7.342
7.336
7.331
7.323
7.316
7.290
7.286
7.269
7.265
7.257
7.253
7.248
7.238
7.227
7.221
7.215
7.211
7.195
7.191
6.715
6.694
6.538
6.518
6.501
6.395
2.263
0.000
1.05
5.26
1.00
1.06
1.73
2.95
O
Me
NH2
7.450 7.400 7.350 7.300 7.250 7.200 7.150
ppm (t1)
5.0
0.0
ppm (t1)

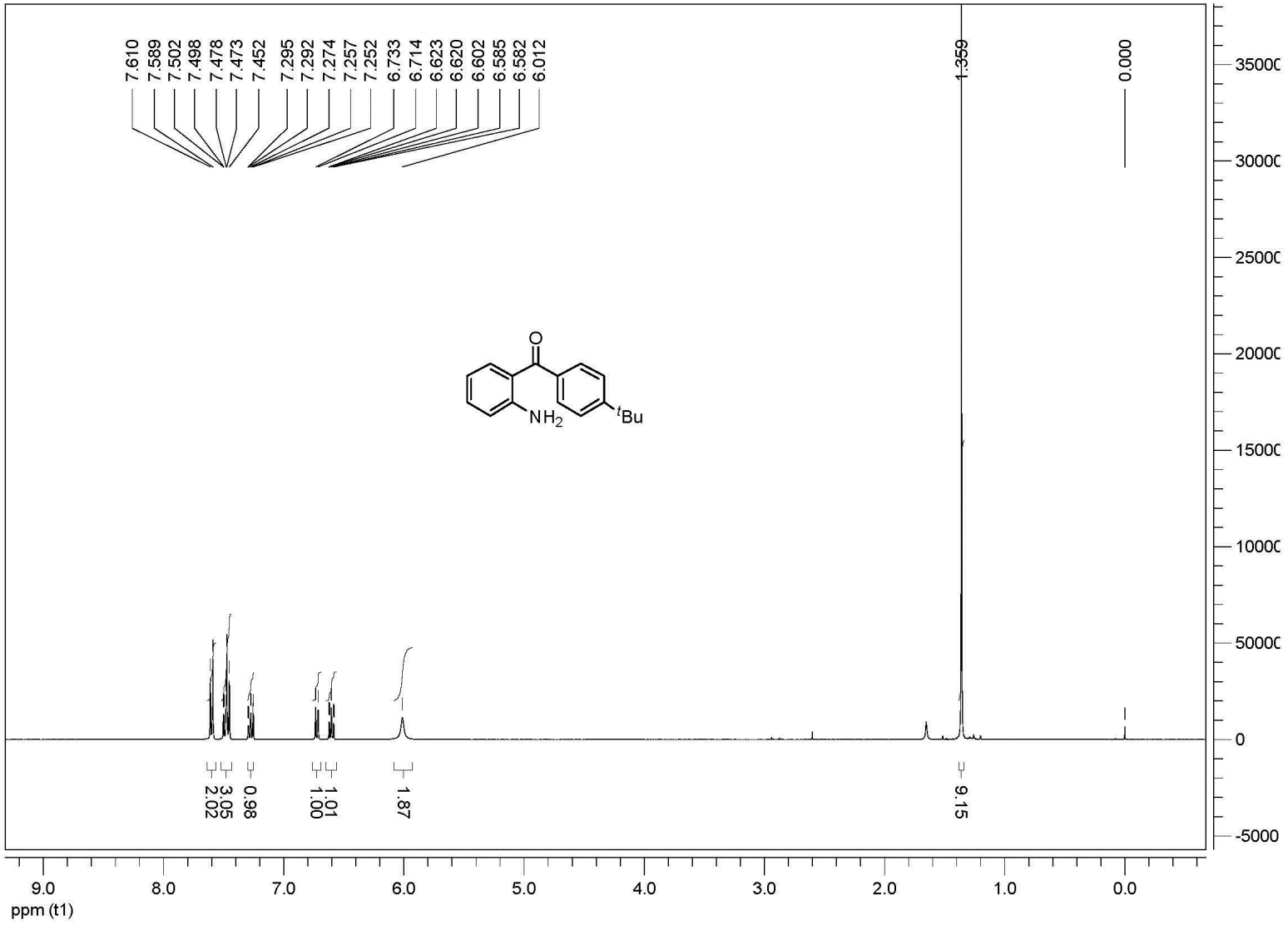

201.323
151.153
140.571
135.052
134.814
134.741
130.508
129.145
127.099
125.244
118.366
116.887
115.645
77.254
77.000
76.746
19.451
O
Me
NH2
4000
3000
2000
1000
0
200
150
100
50
0
ppm (t1)


7.450
7.434
7.431
7.409
7.398
7.326
7.315
7.293
7.289
7.272
7.254
7.250
7.245
6.726
6.705
6.608
6.606
6.588
6.571
6.568
6.071
2.400
-0.000
2.00
1.06
1.97
1.00
1.00
1.00
1.93
7.60
7.50
7.40
7.30
7.20
ppm (t1)
5.0
0.0
ppm (t1)
Me
NH2


199.273
150.840
140.110
137.862
134.542
134.086
131.719
129.494
127.839
126.262
118.295
116.907
115.426
77.254
77.000
76.746
21.307
O
Me
NH2
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)


7.569
7.549
7.466
7.462
7.446
7.442
7.296
7.292
7.275
7.261
7.255
7.242
6.736
6.715
6.619
6.599
6.581
5.988
2.424
-0.000
O
NH2
Me
2.02
2.04
3.21
1.01
1.00
1.86
3.06
7000
6000
5000
4000
3000
2000
1000
0
-1000
5.0
0.0
ppm (t1)


198.821
150.675
141.653
137.255
134.368
133.927
129.419
128.721
118.599
116.940
115.487
77.254
77.000
76.746
21.495
O
NH2
Me
35000
30000
25000
20000
15000
10000
5000
0
-5000
200
150
100
50
0
ppm (t1)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7.295
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7.274
7.257
7.252
6.733
6.714
6.623
6.620
6.602
6.585
6.582
6.012
1.359
0.000
O
NH2
tBu
2.02
3.05
0.98
1.00
1.01
1.87
9.15
35000
30000
25000
20000
15000
10000
5000
0
-5000
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7.0
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5.0
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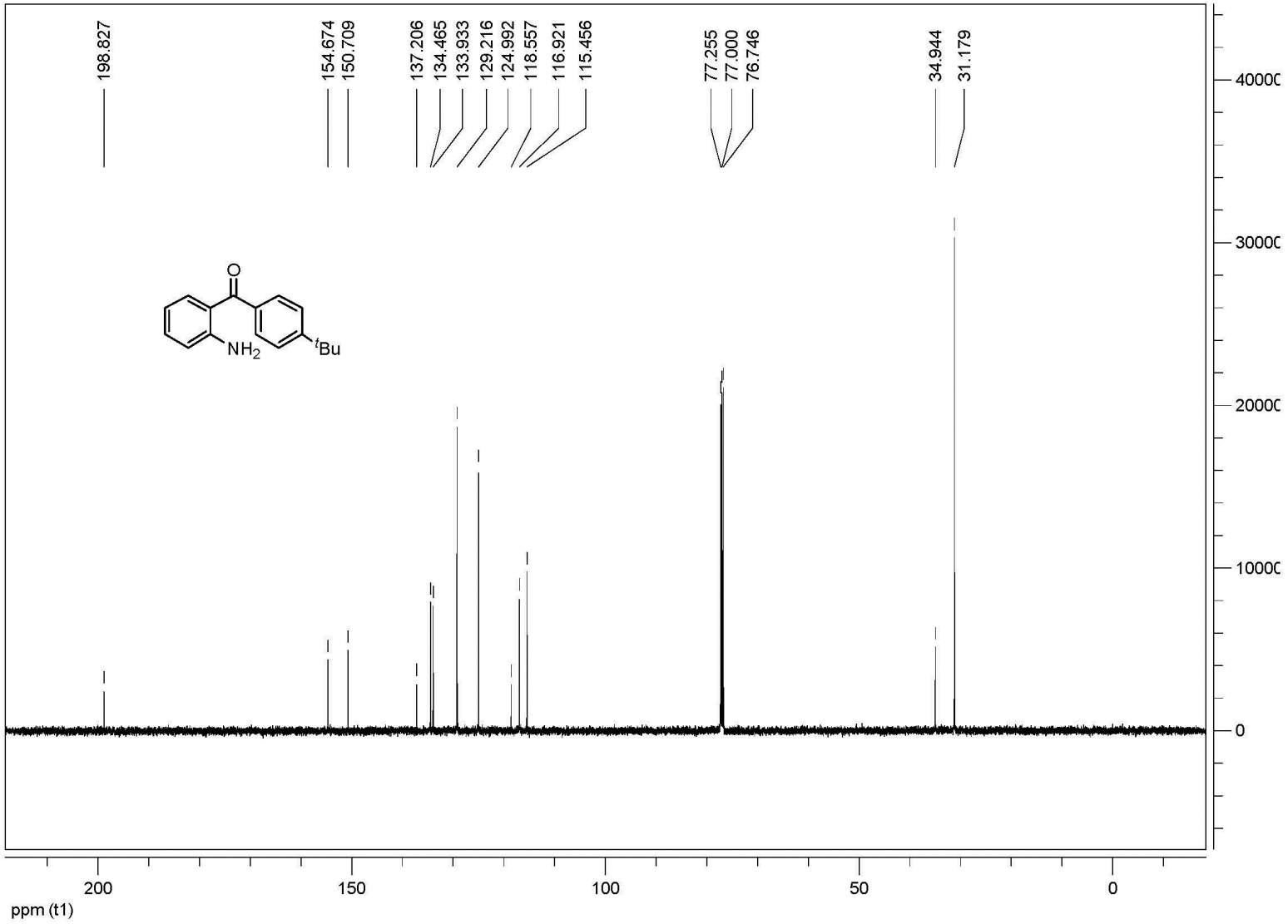
3.0
2.0
1.0
0.0
ppm (t1)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115.456
77.255
77.000
76.746
34.944
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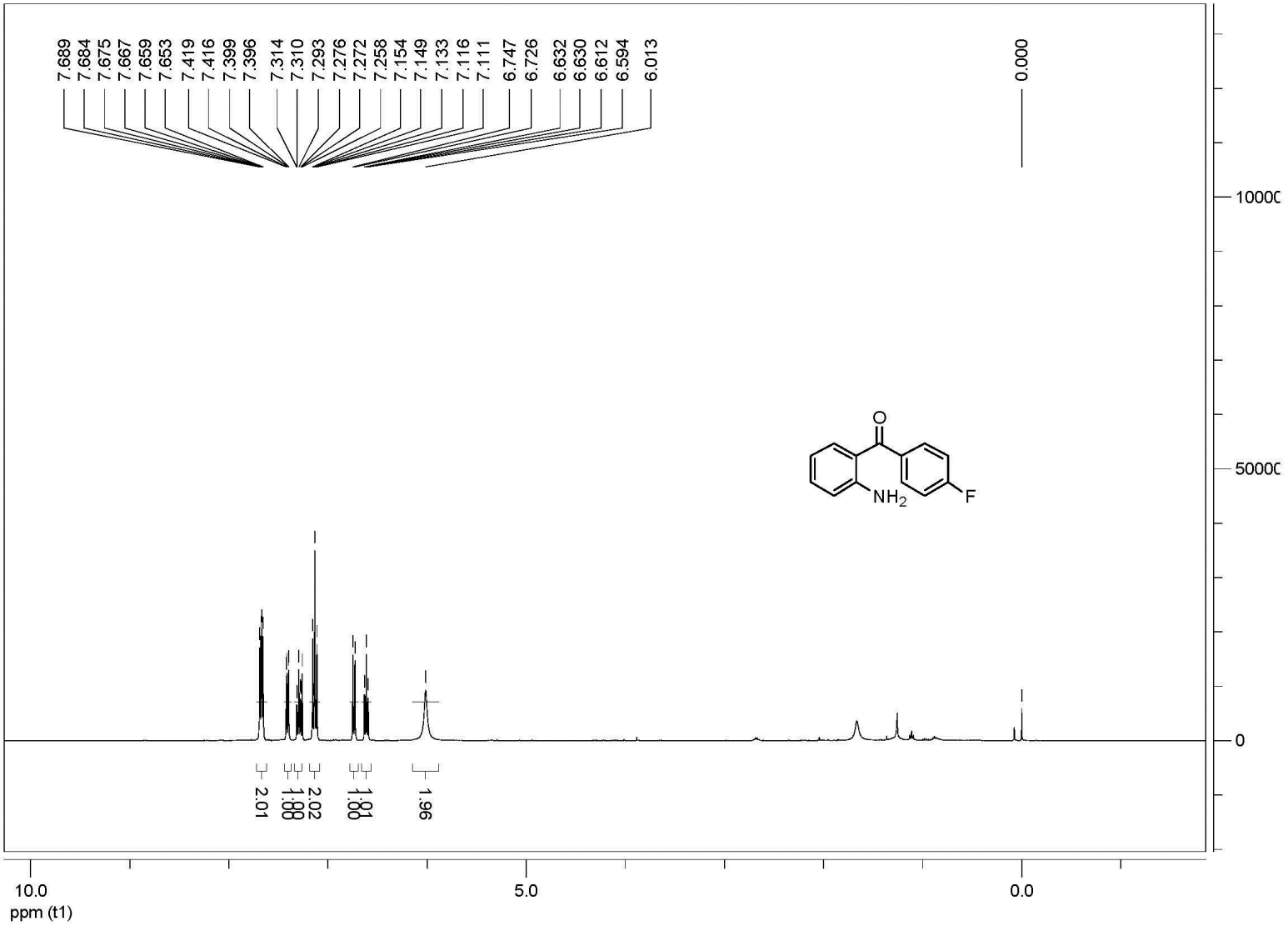
O
NH2
tBu
4000
3000
2000
1000
0
200
150
100
50
0
ppm (t1)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7.396
7.314
7.310
7.293
7.276
7.272
7.258
7.154
7.149
7.133
7.116
7.111
6.747
6.726
6.632
6.630
6.612
6.594
6.013
0.000
O
NH2
F
2.01
1.88
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1.81
1.80
1.96
10000
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ppm (t1)
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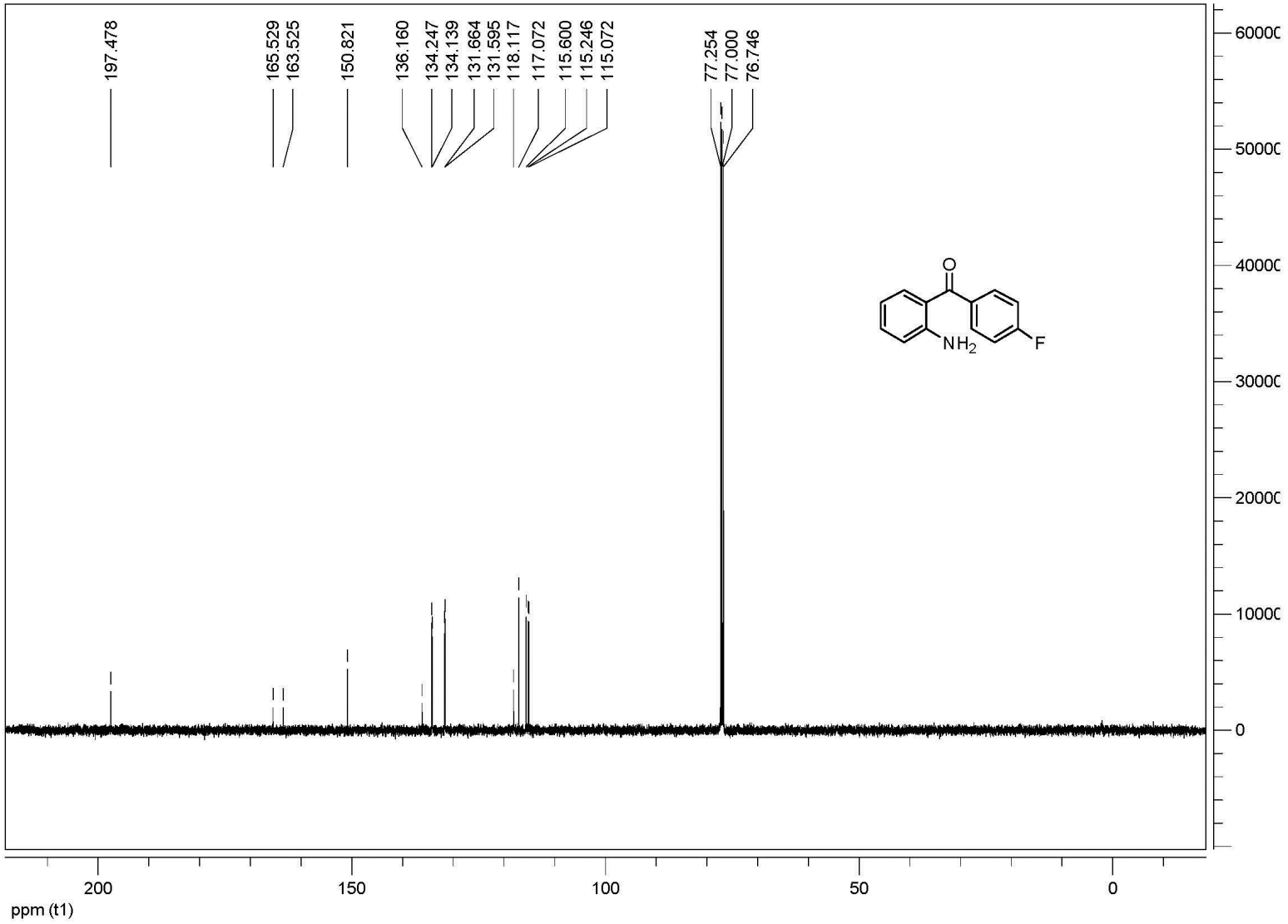
0.0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134.247
134.139
131.664
131.595
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117.072
115.600
115.246
115.072
77.254
77.000
76.746
O
NH2
F
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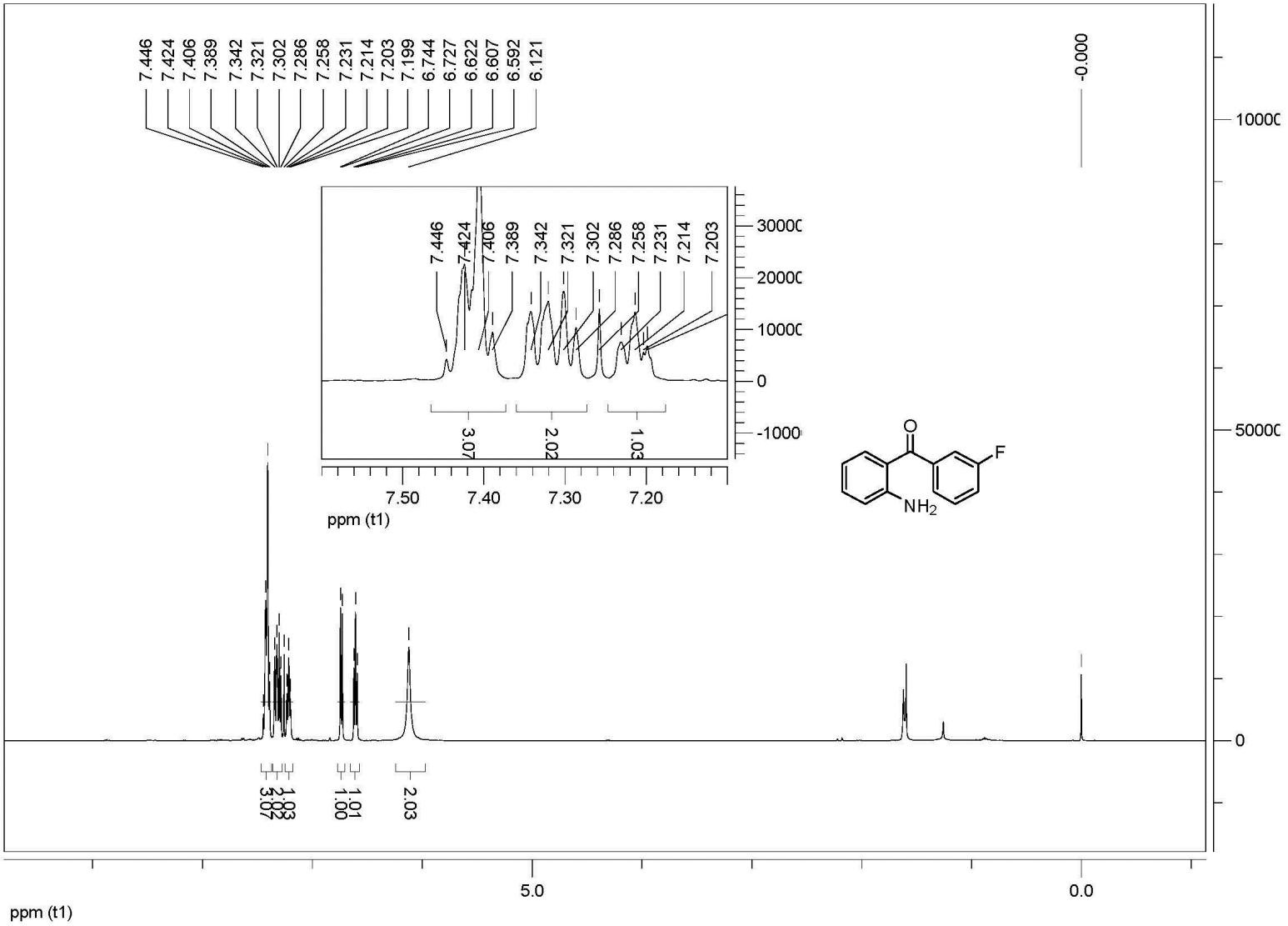
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)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7.302
7.286
7.258
7.231
7.214
7.203
7.199
6.744
6.727
6.622
6.607
6.592
6.121
-0.000
10000
50000
0
3.07
1.03
2.02
1.01
1.00
2.03
5.0
0.0
ppm (t1)
30000
20000
10000
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-10000
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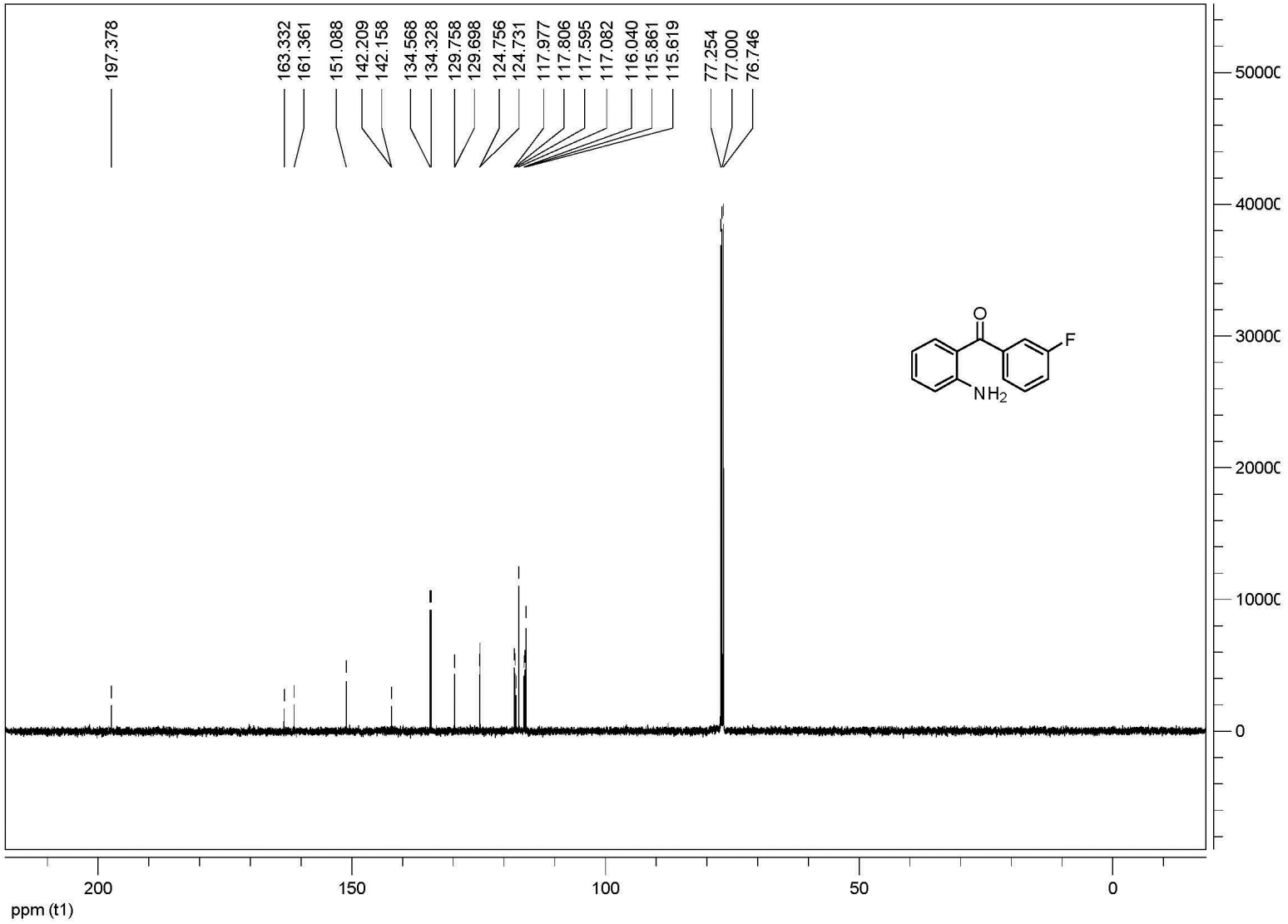
2.02
1.03
7.50
7.40
7.30
7.20
ppm (t1)
O
F
NH2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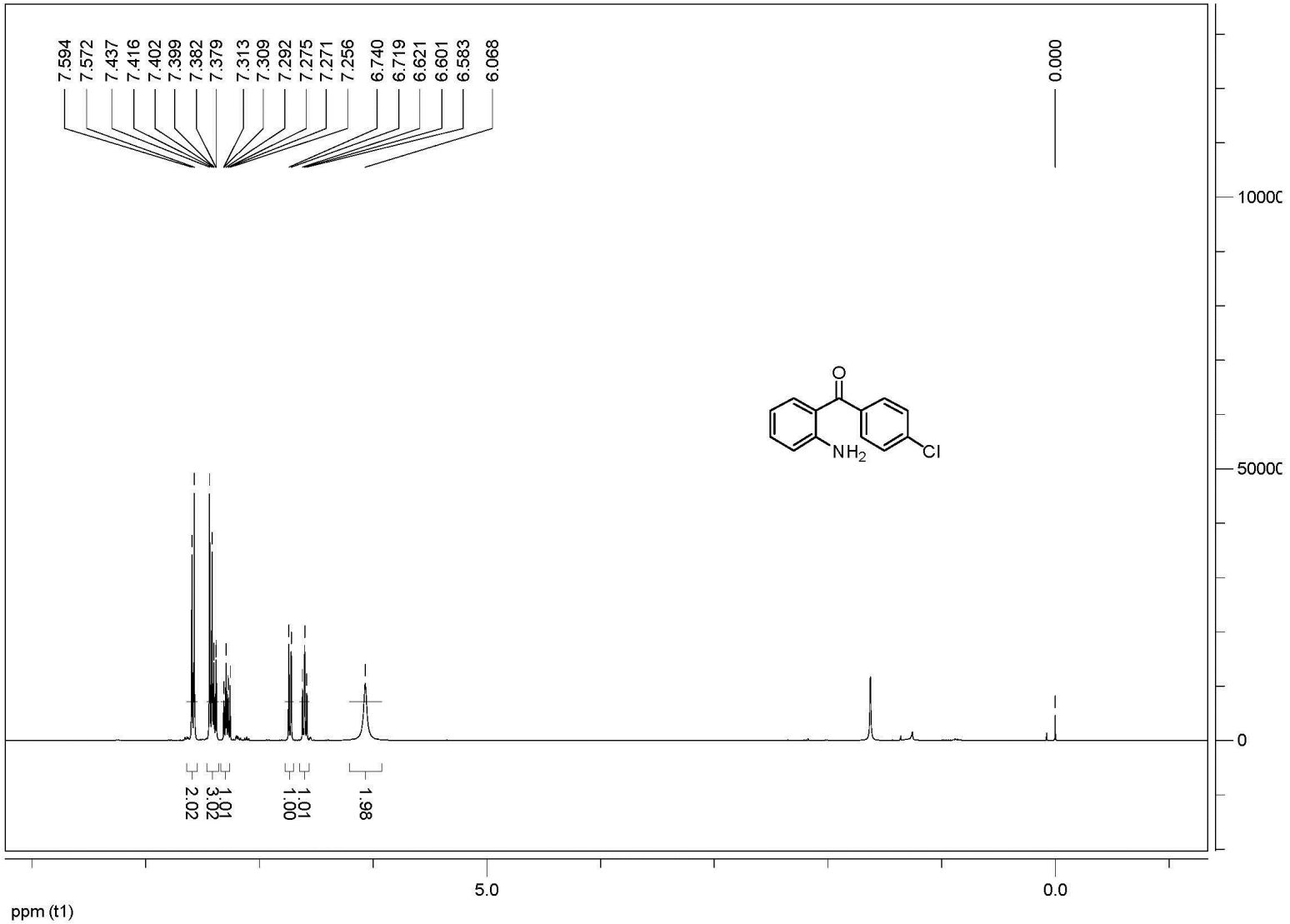
161.361
151.088
142.209
142.158
134.568
134.328
129.758
129.698
124.756
124.731
117.977
117.806
117.595
117.082
116.040
115.861
115.619
77.254
77.000
76.746
O
F
NH2
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)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7.572
7.437
7.416
7.402
7.399
7.382
7.379
7.313
7.309
7.292
7.275
7.271
7.256
6.740
6.719
6.621
6.601
6.583
6.068
0.000
O
NH2
Cl
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3.02
1.01
1.00
1.01
1.98
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5000
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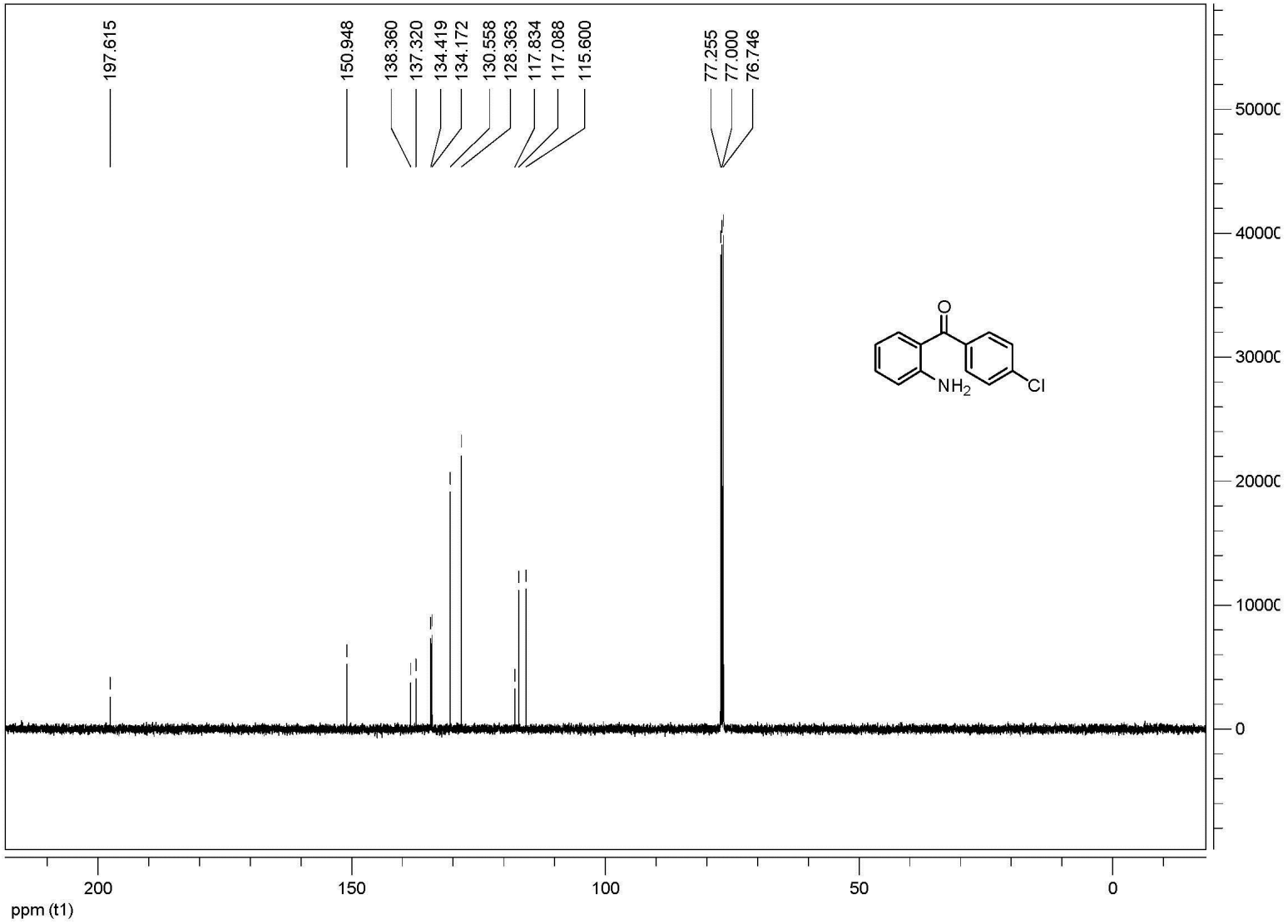
0.0
ppm (t1)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138.360
137.320
134.419
134.172
130.558
128.363
117.834
117.088
115.600
77.255
77.000
76.746
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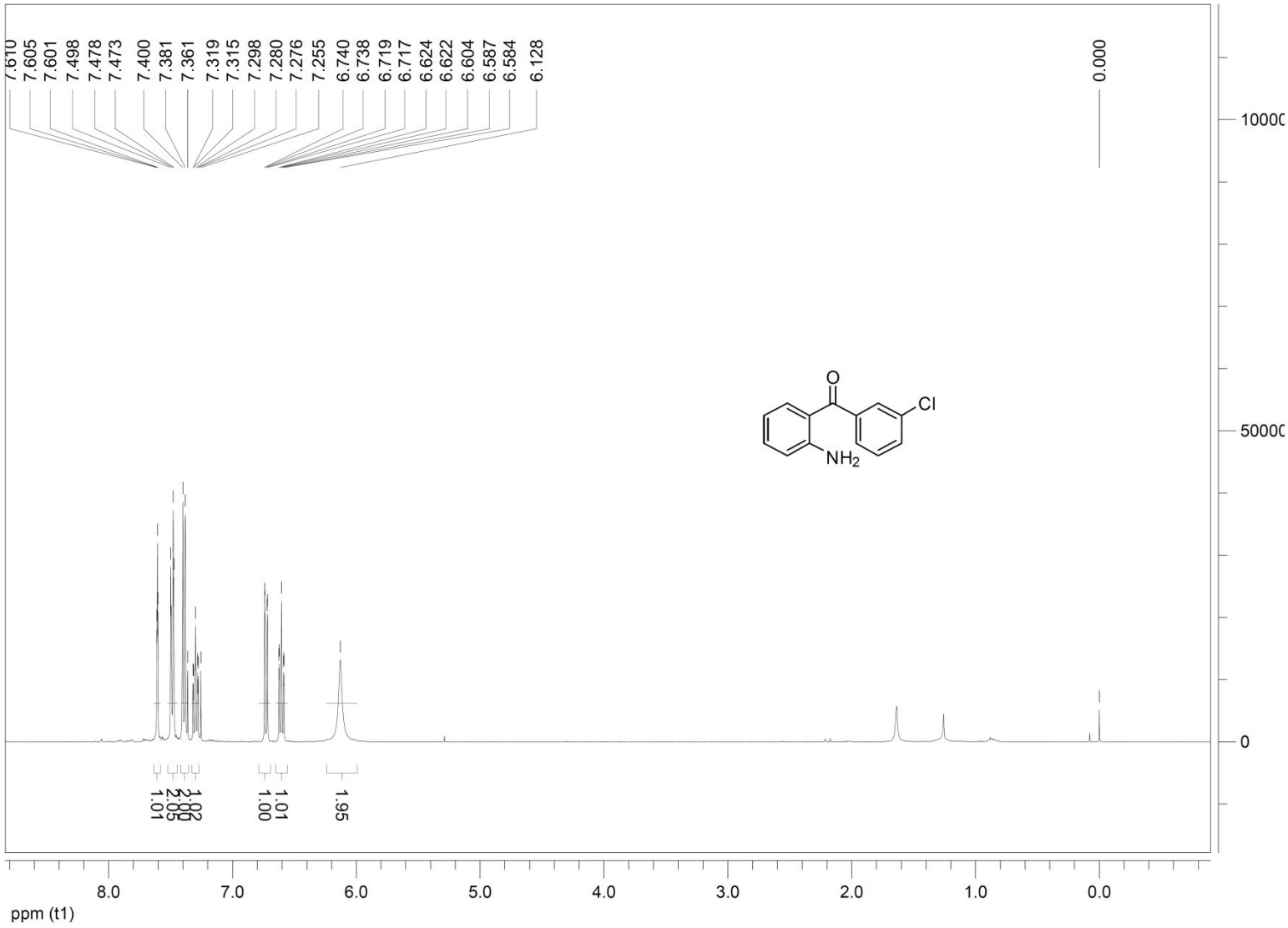
NH2
Cl
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)


7.610
7.605
7.601
7.498
7.478
7.473
7.400
7.381
7.361
7.319
7.315
7.298
7.280
7.276
7.255
6.740
6.738
6.719
6.717
6.624
6.622
6.604
6.587
6.584
6.128
0.000
O
Cl
NH2
1.01
2.08
3.02
1.00
1.01
1.95
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7.0
6.0
5.0
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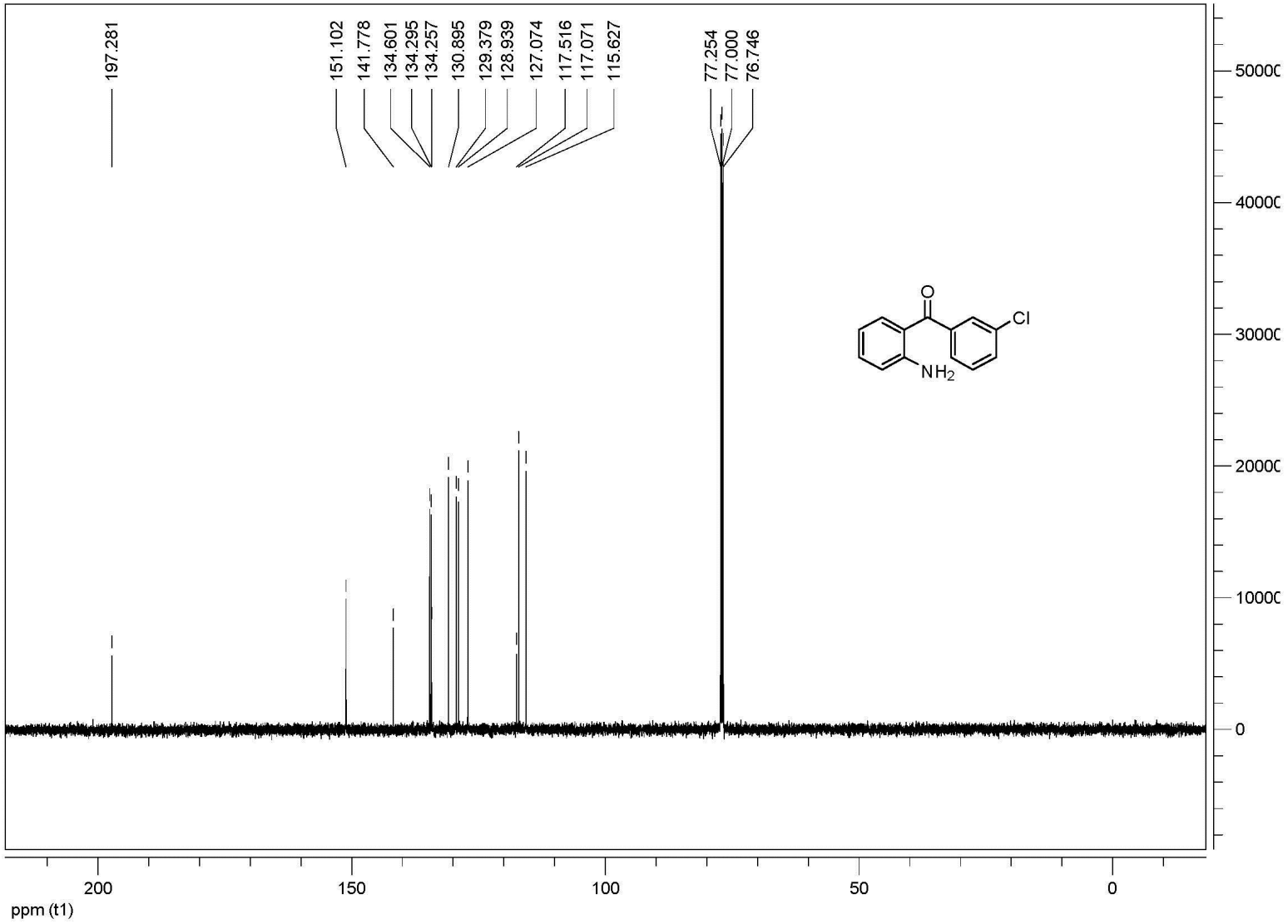
2.0
1.0
0.0
ppm (t1)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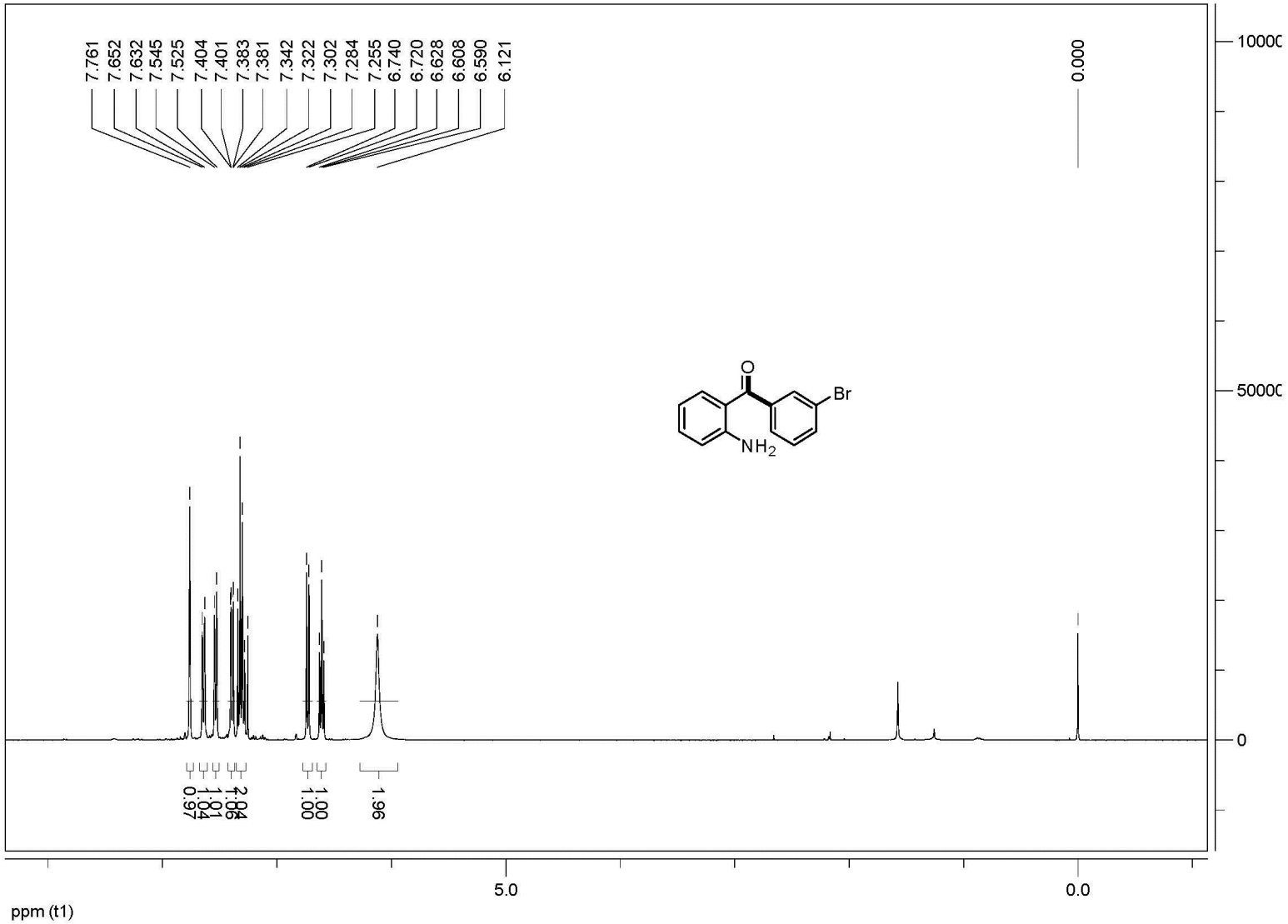
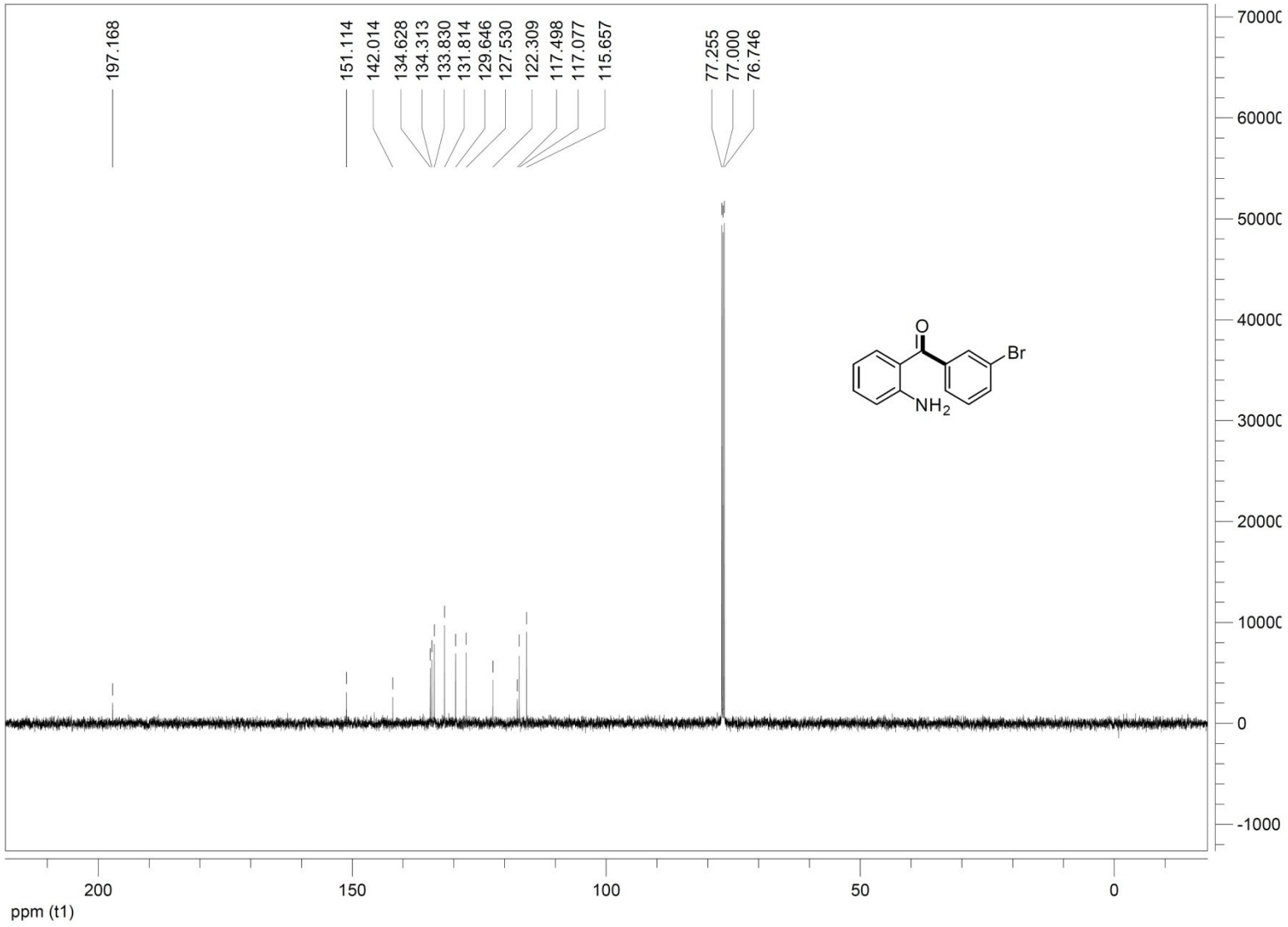
134.295
134.257
130.895
129.379
128.939
127.074
117.516
117.071
115.627
77.254
77.000
76.746
O
Cl
NH2
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)


7.761
7.652
7.632
7.545
7.525
7.404
7.401
7.383
7.381
7.342
7.322
7.302
7.284
7.255
6.740
6.720
6.628
6.608
6.590
6.121
0.000
O
Br
NH2
0.97
1.04
1.01
2.06
1.00
1.00
1.96
10000
5000
0
5.0
0.0
ppm (t1)


197.168
151.114
142.014
134.628
134.313
133.830
131.814
129.646
127.530
122.309
117.498
117.077
115.657
77.255
77.000
76.746
O
Br
NH2
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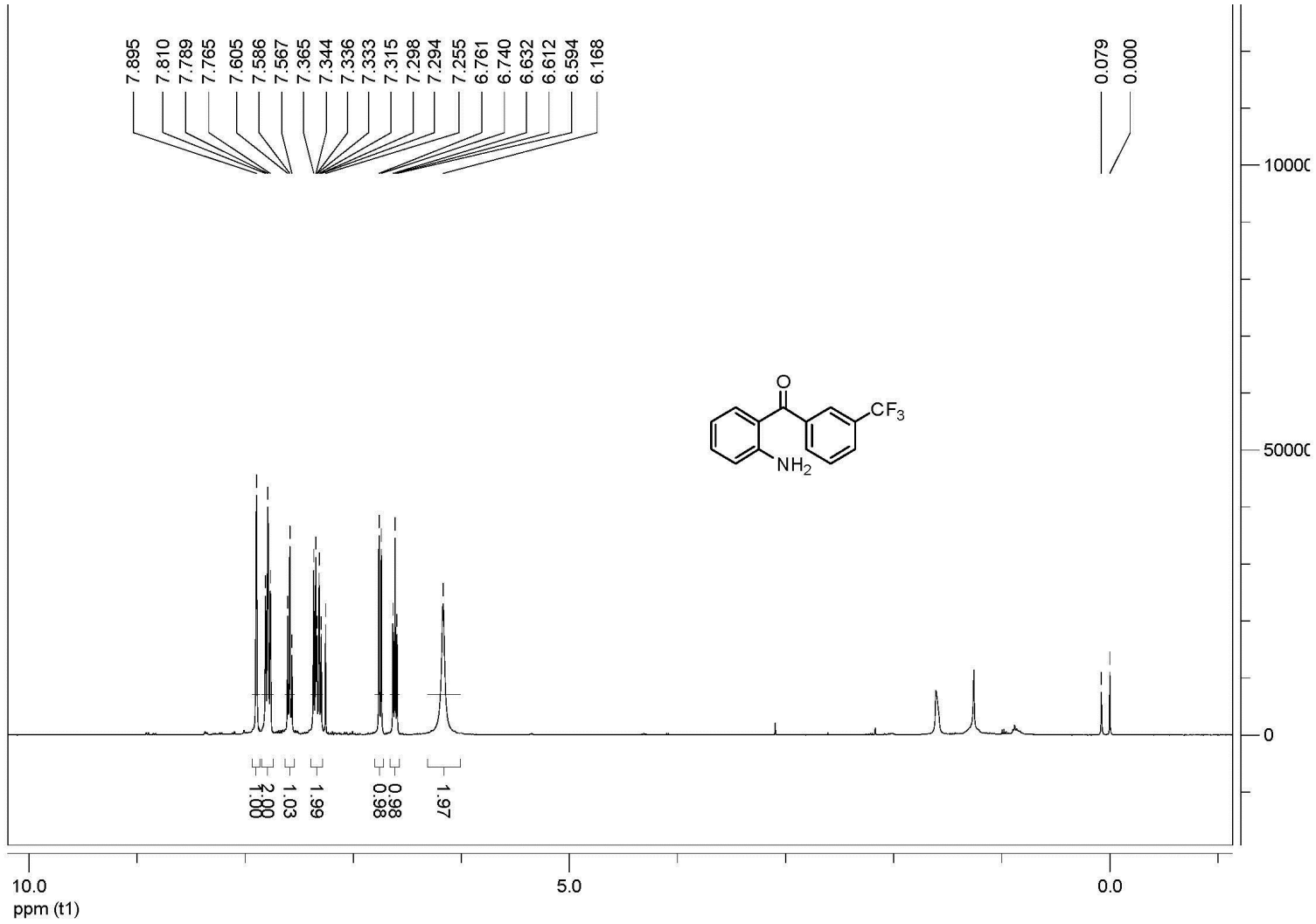
60000
50000
40000
30000
20000
10000
0
-1000
200
150
100
50
0
ppm (t1)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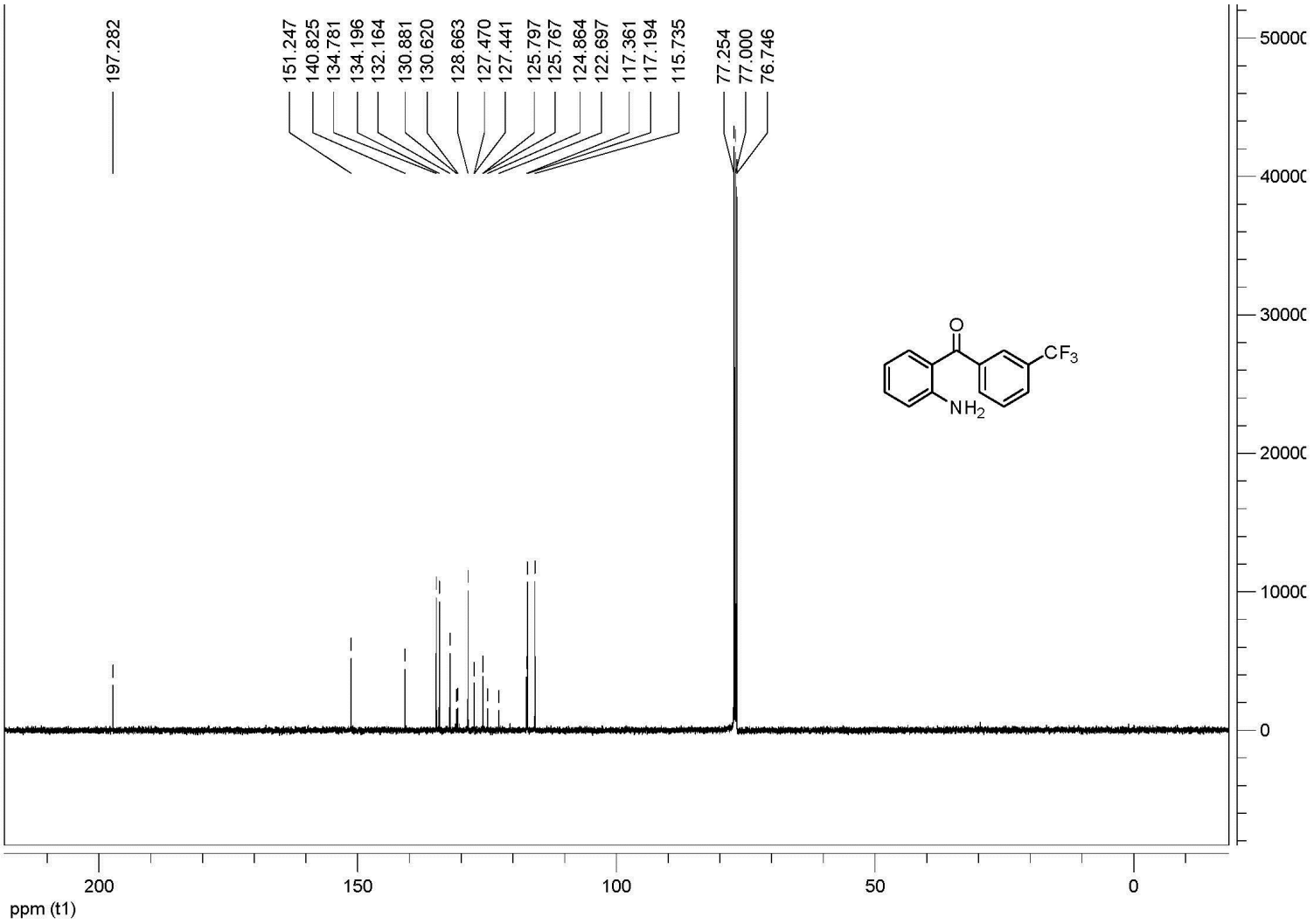
7.810
7.789
7.765
7.605
7.586
7.567
7.365
7.344
7.336
7.333
7.315
7.298
7.294
7.255
6.761
6.740
6.632
6.612
6.594
6.168
0.079
0.000
O
CF3
NH2
10000
5000
0
2.00
1.03
1.99
0.98
0.98
1.97
10.0
5.0
0.0
ppm (t1)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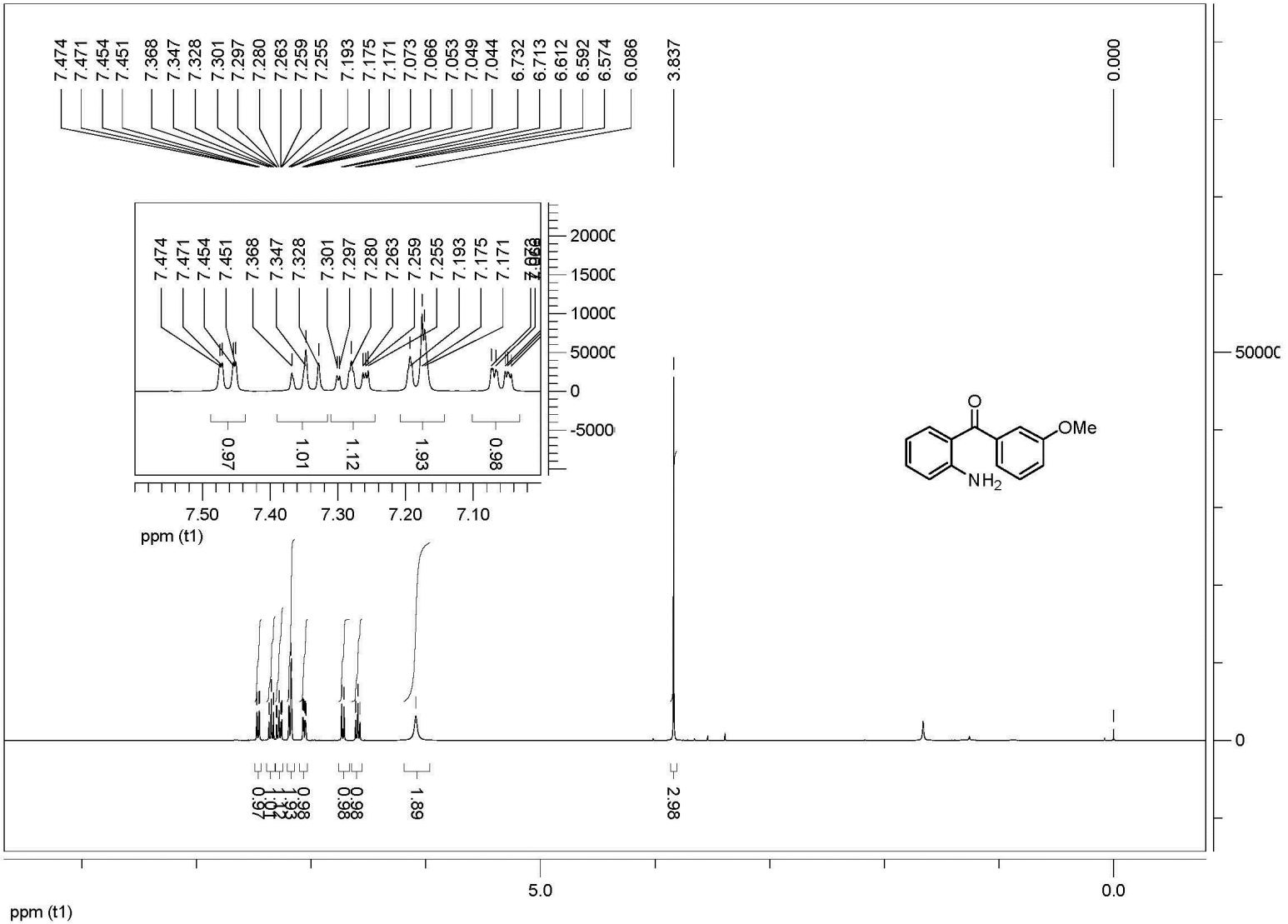
140.825
134.781
134.196
132.164
130.881
130.620
128.663
127.470
127.441
125.797
125.767
124.864
122.697
117.361
117.194
115.735
77.254
77.000
76.746
O
CF3
NH2
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)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7.471
7.454
7.451
7.368
7.347
7.328
7.301
7.297
7.280
7.263
7.259
7.255
7.193
7.175
7.171
7.073
7.066
7.053
7.049
7.044
6.732
6.713
6.612
6.592
6.574
6.086
3.837
0.000
ppm (t1)
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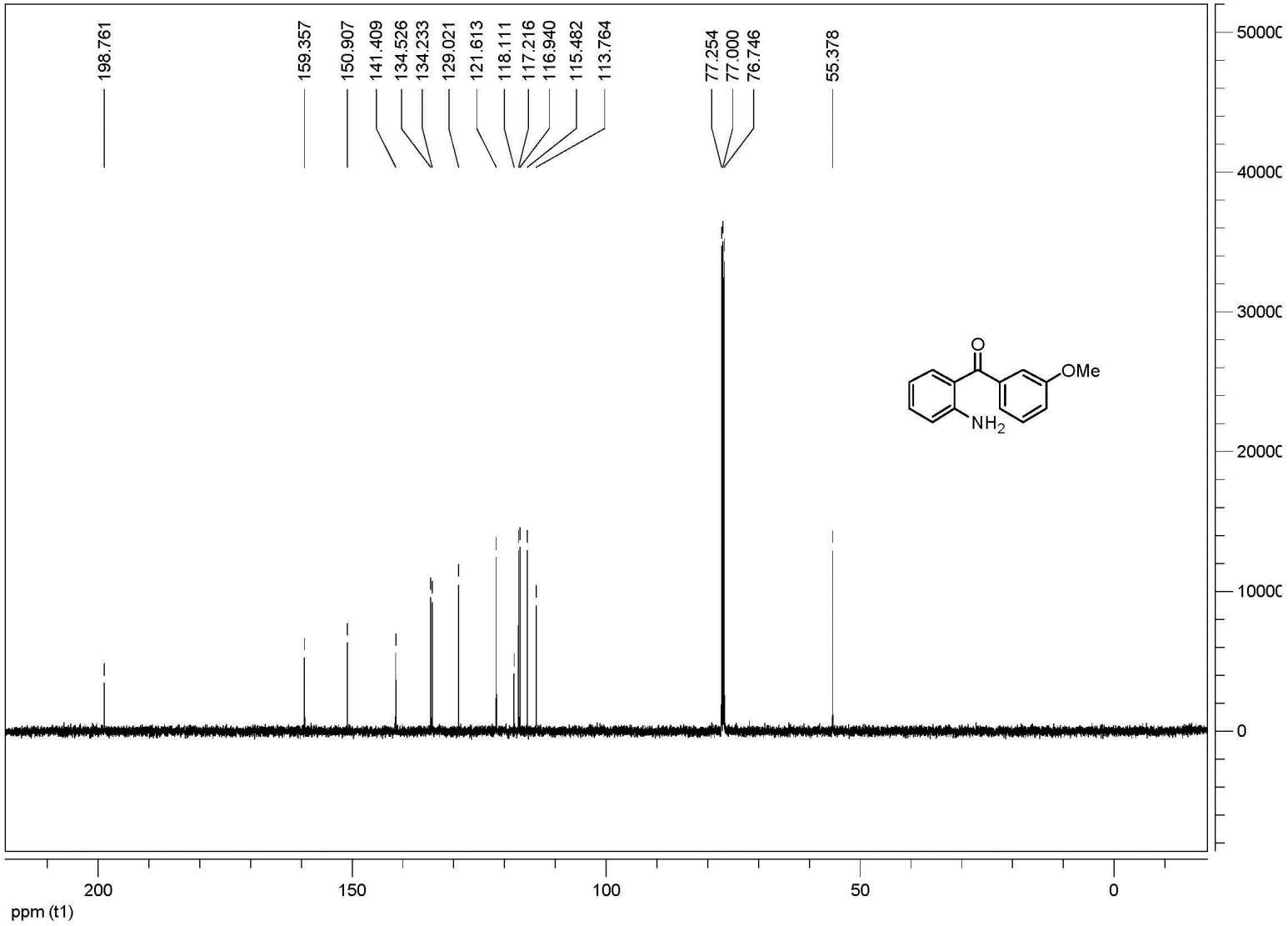
0.97
1.01
1.12
1.93
0.98
0.98
1.89
2.98
OMe
NH2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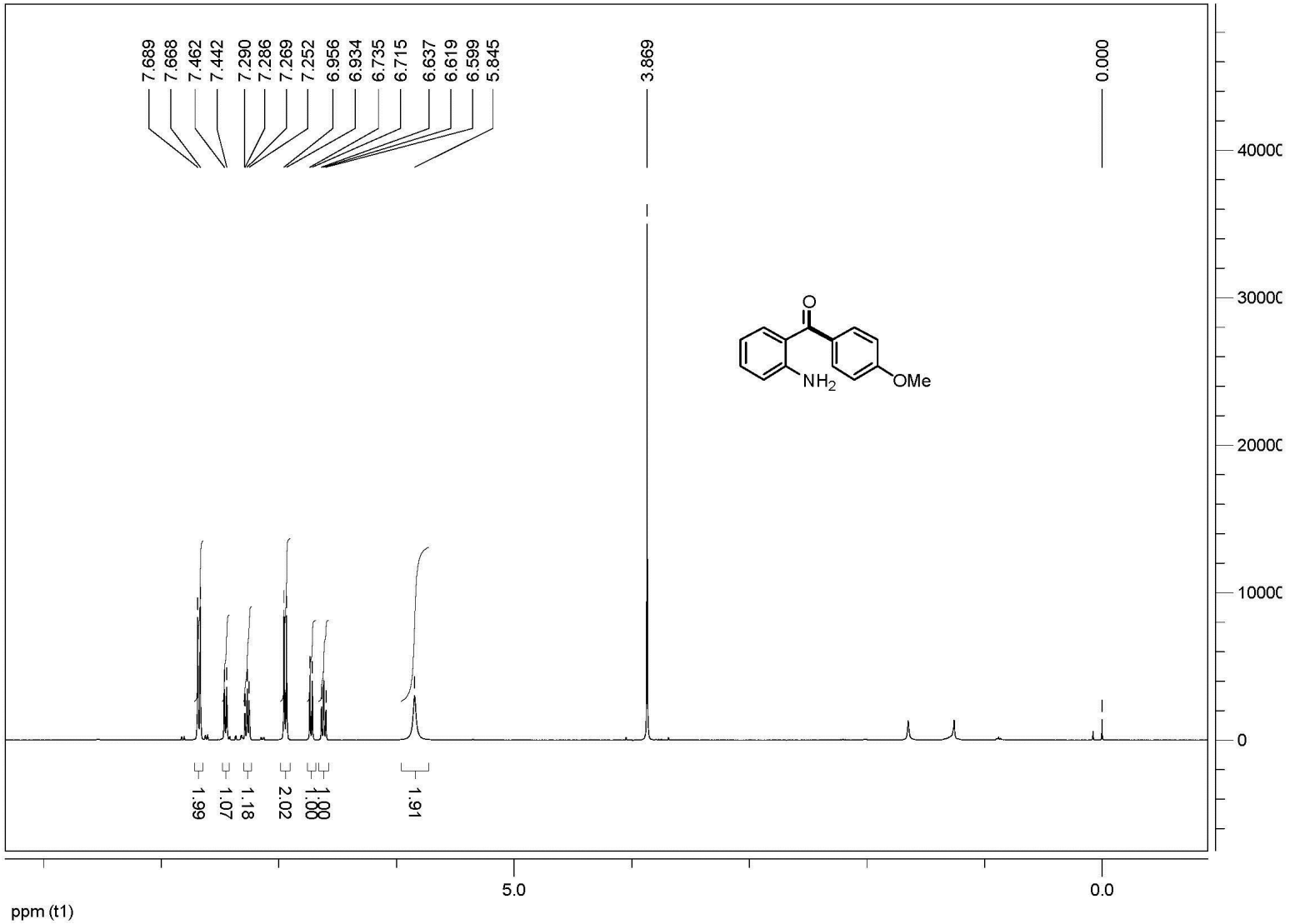
134.526
134.233
129.021
121.613
118.111
117.216
116.940
115.482
113.764
77.254
77.000
76.746
55.378
O
OMe
NH2
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)


7.689
7.668
7.462
7.442
7.290
7.286
7.269
7.252
6.956
6.934
6.735
6.715
6.637
6.619
6.599
5.845
3.869
0.000
O
NH2
OMe
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30000
20000
10000
0
1.99
1.07
1.18
2.02
1.91
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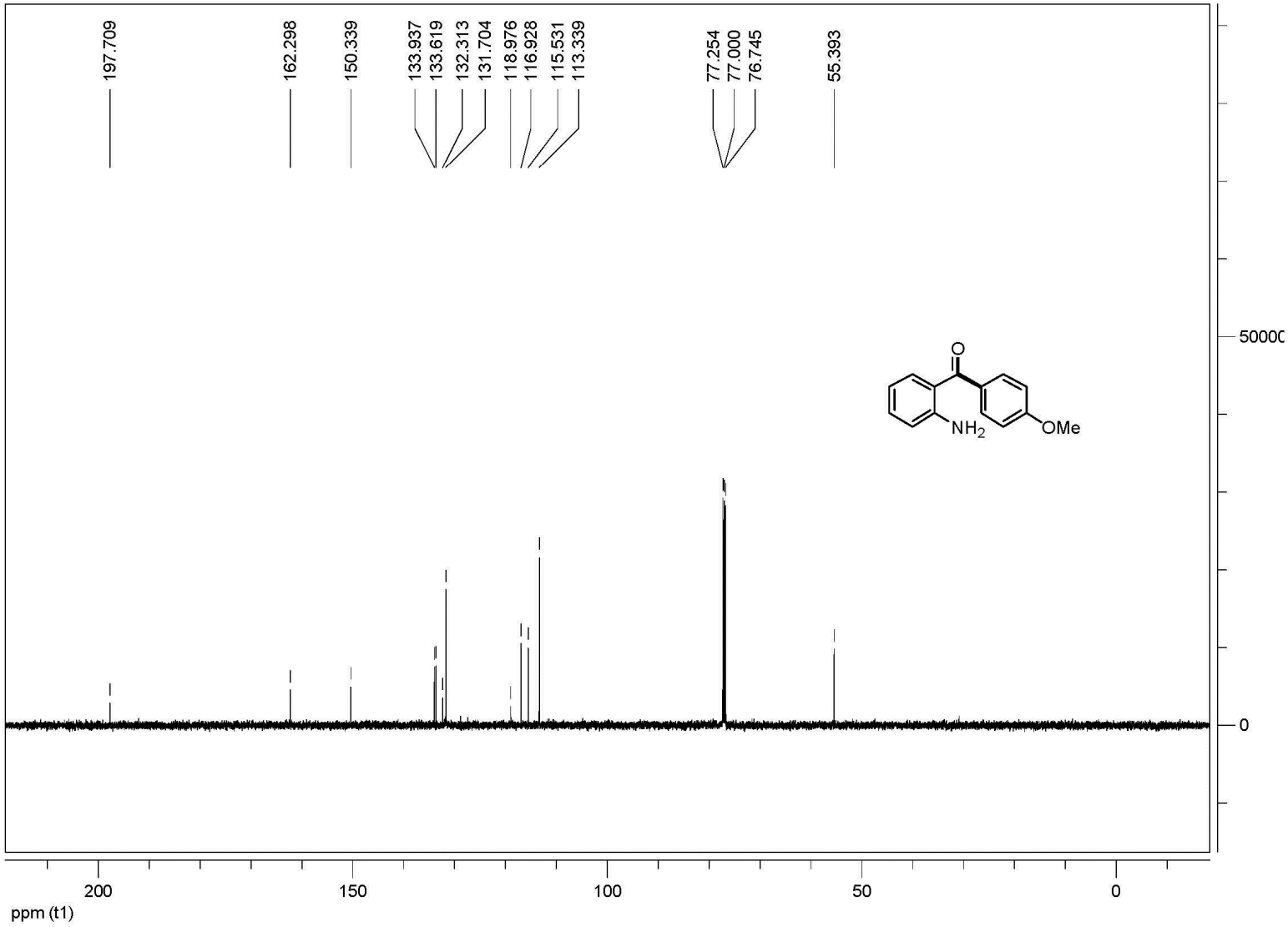
0.0
ppm (t1)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132.313
131.704
118.976
116.928
115.531
113.339
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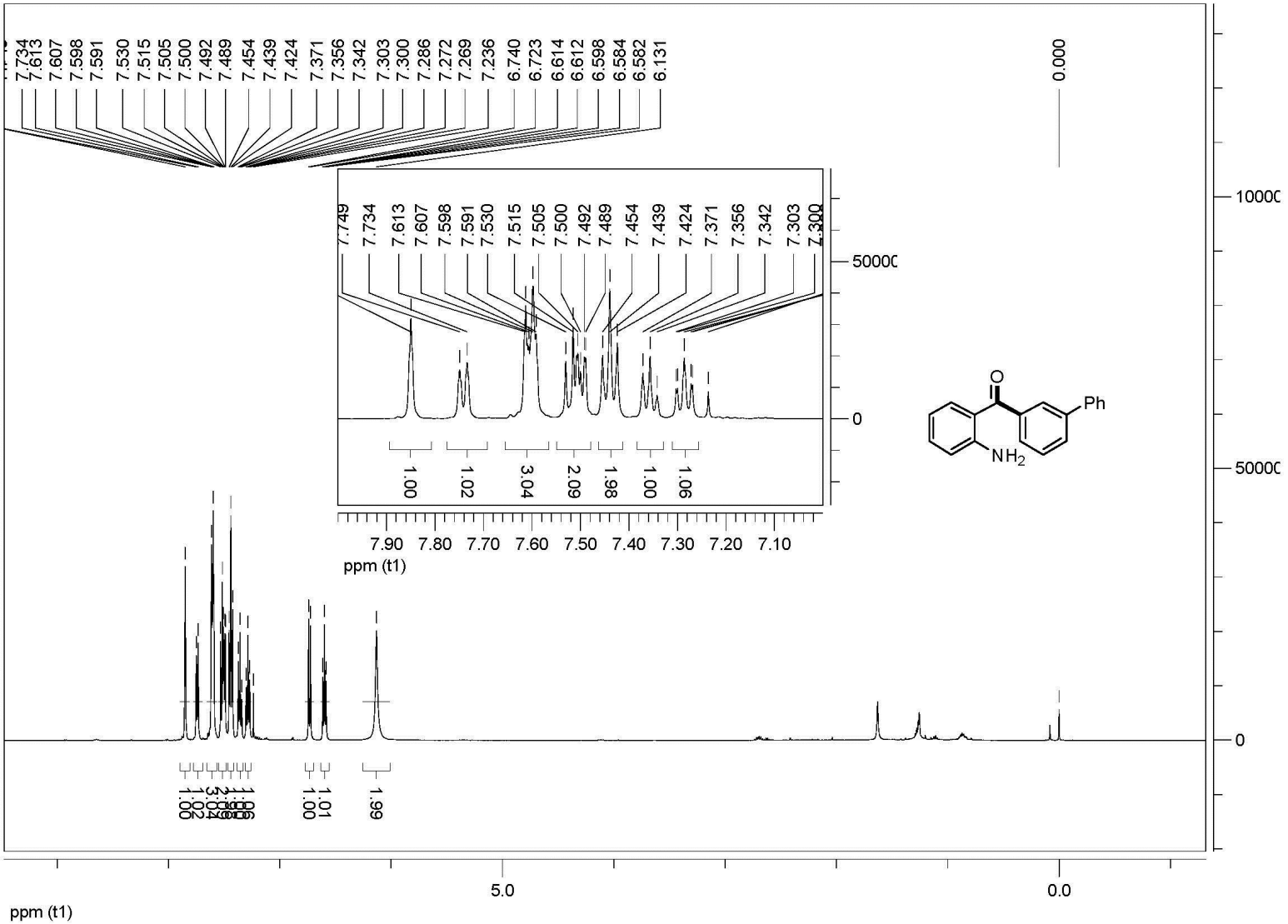
55.393
O
NH2
OMe
50000
0
200
150
100
50
0
ppm (t1)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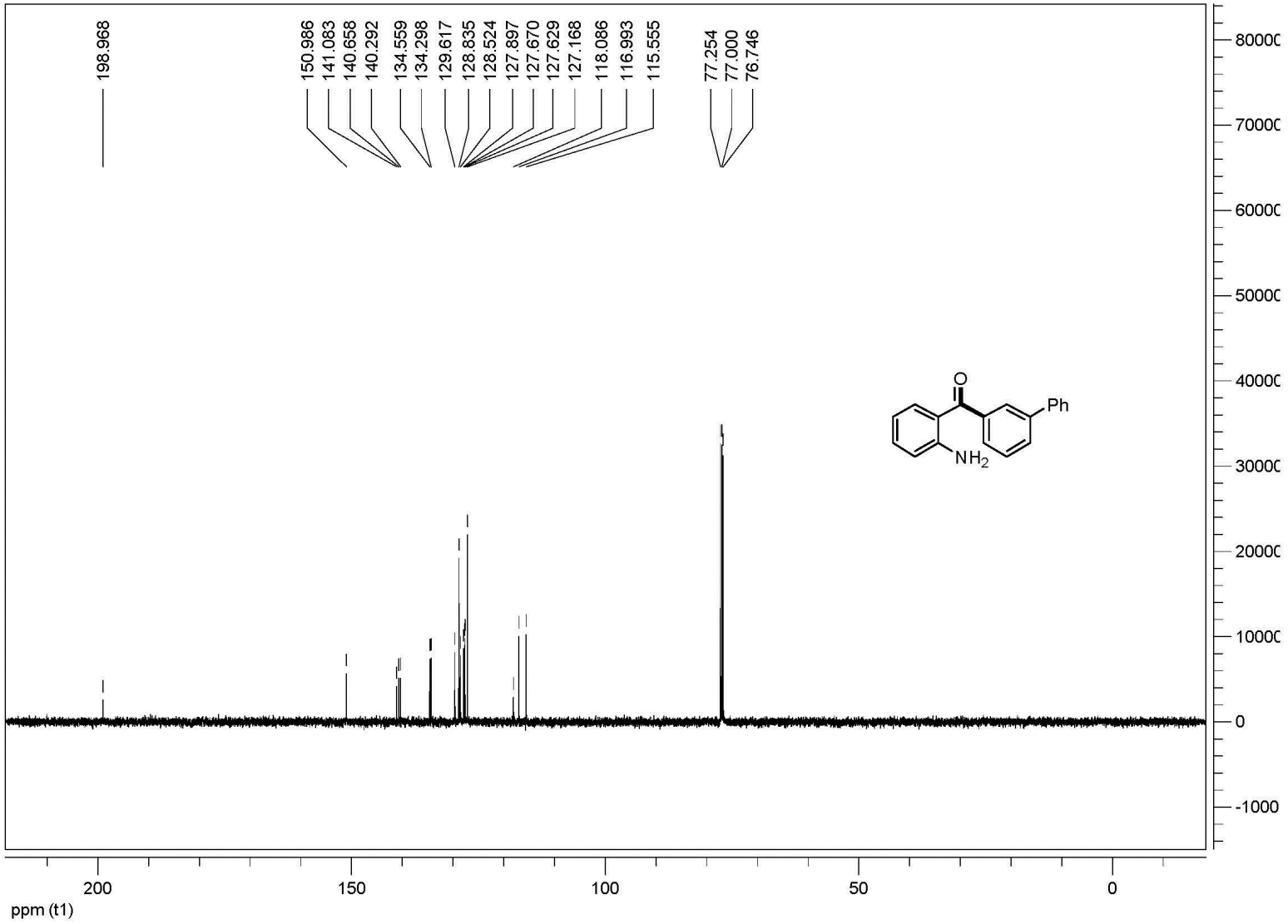
7.607
7.598
7.591
7.530
7.515
7.505
7.500
7.492
7.489
7.454
7.439
7.424
7.371
7.356
7.342
7.303
7.300
7.286
7.272
7.269
7.236
6.740
6.723
6.614
6.612
6.598
6.584
6.582
6.131
0.000
10000
50000
0
1.00
1.02
3.04
2.09
1.98
1.00
1.99
7.90 7.80 7.70 7.60 7.50 7.40 7.30 7.20 7.10
ppm (t1)
O
Ph
NH2
5.0
0.0
ppm (t1)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140.292
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134.298
129.617
128.835
128.524
127.897
127.670
127.629
127.168
118.086
116.993
115.555
77.254
77.000
76.746
O
Ph
NH2
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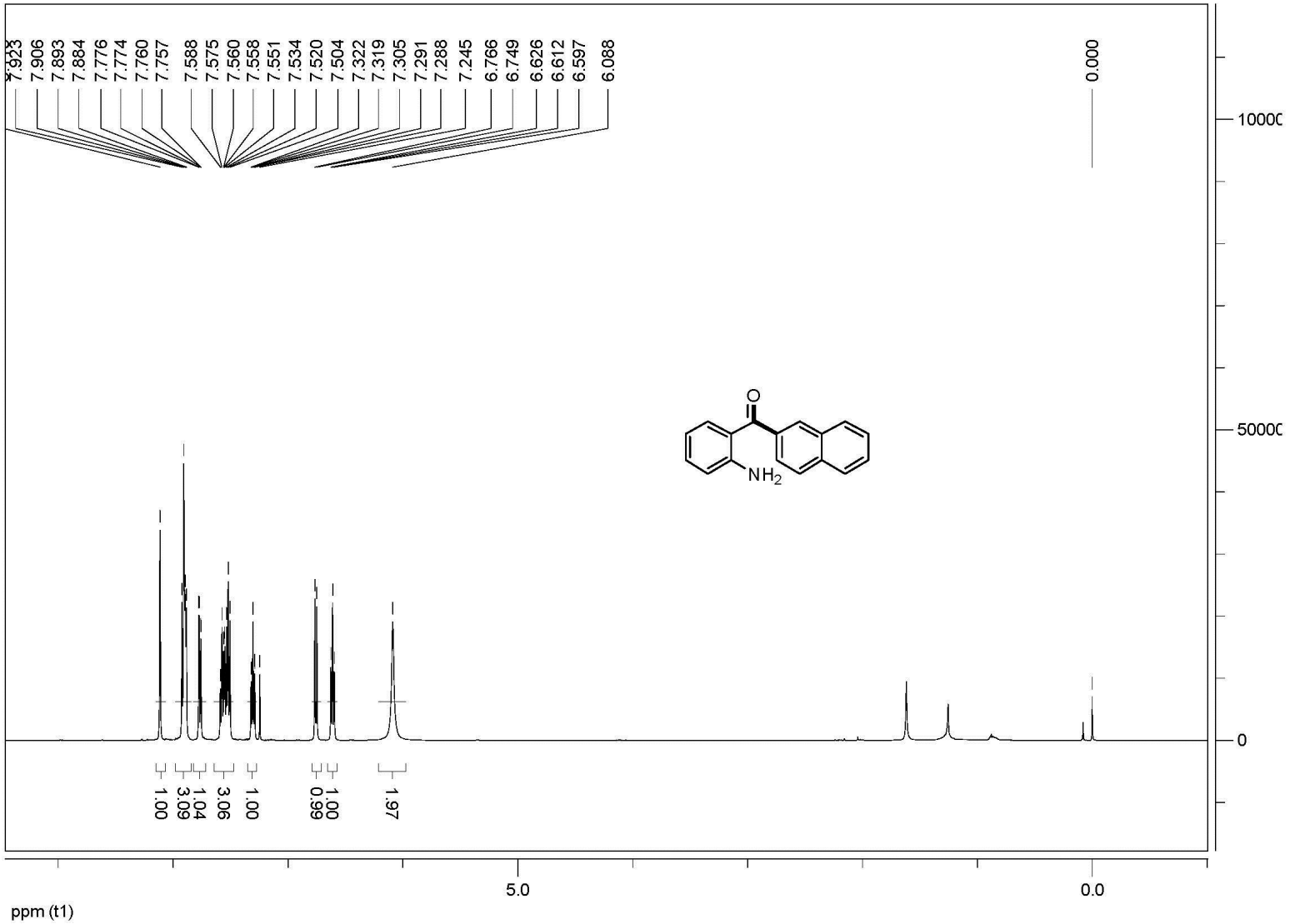
7000
6000
5000
4000
3000
2000
1000
0
-1000
200
150
100
50
0
ppm (t1)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7.757
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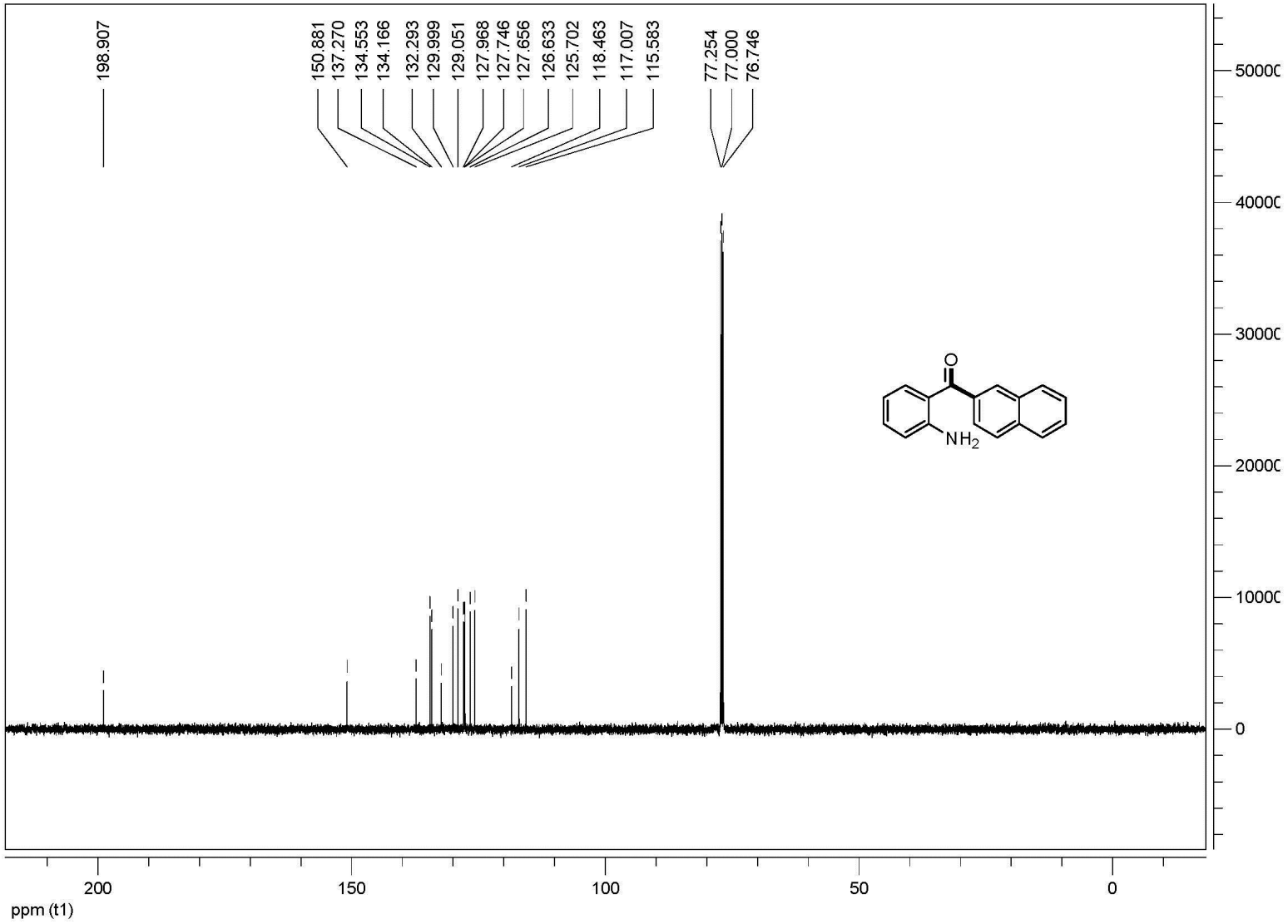
7.560
7.558
7.551
7.534
7.520
7.504
7.322
7.319
7.305
7.291
7.288
7.245
6.766
6.749
6.626
6.612
6.597
6.088
0.000
O
NH2
1.00
3.09
1.04
3.06
1.00
1.00
0.99
1.97
10000
5000
0
5.0
0.0
ppm (t1)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134.166
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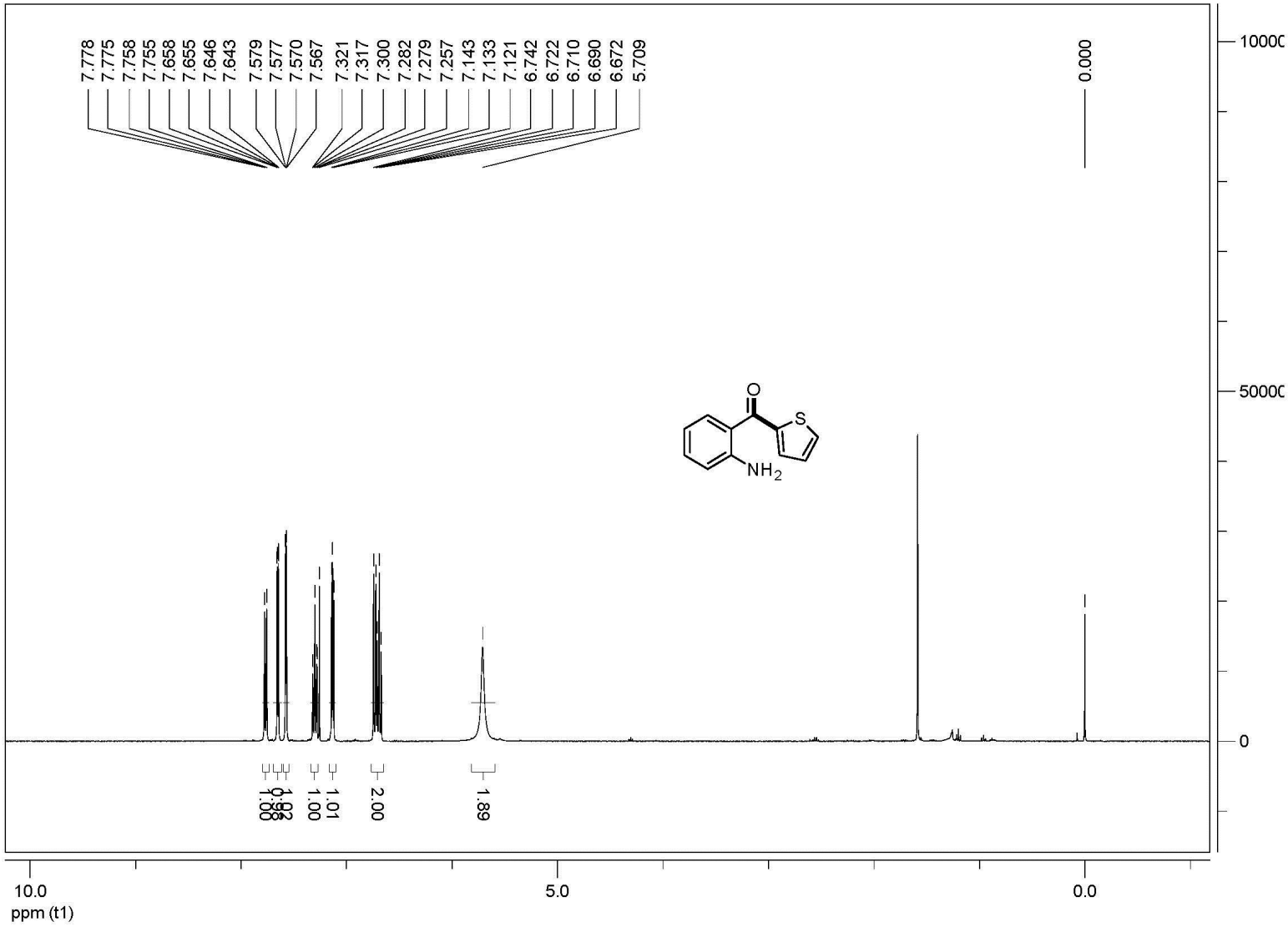
129.999
129.051
127.968
127.746
127.656
126.633
125.702
118.463
117.007
115.583
77.254
77.000
76.746
O
NH2
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)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7.775
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7.755
7.658
7.655
7.646
7.643
7.579
7.577
7.570
7.567
7.321
7.317
7.300
7.282
7.279
7.257
7.143
7.133
7.121
6.742
6.722
6.710
6.690
6.672
5.709
0.000
O
S
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1.01
2.00
1.89
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ppm (t1)
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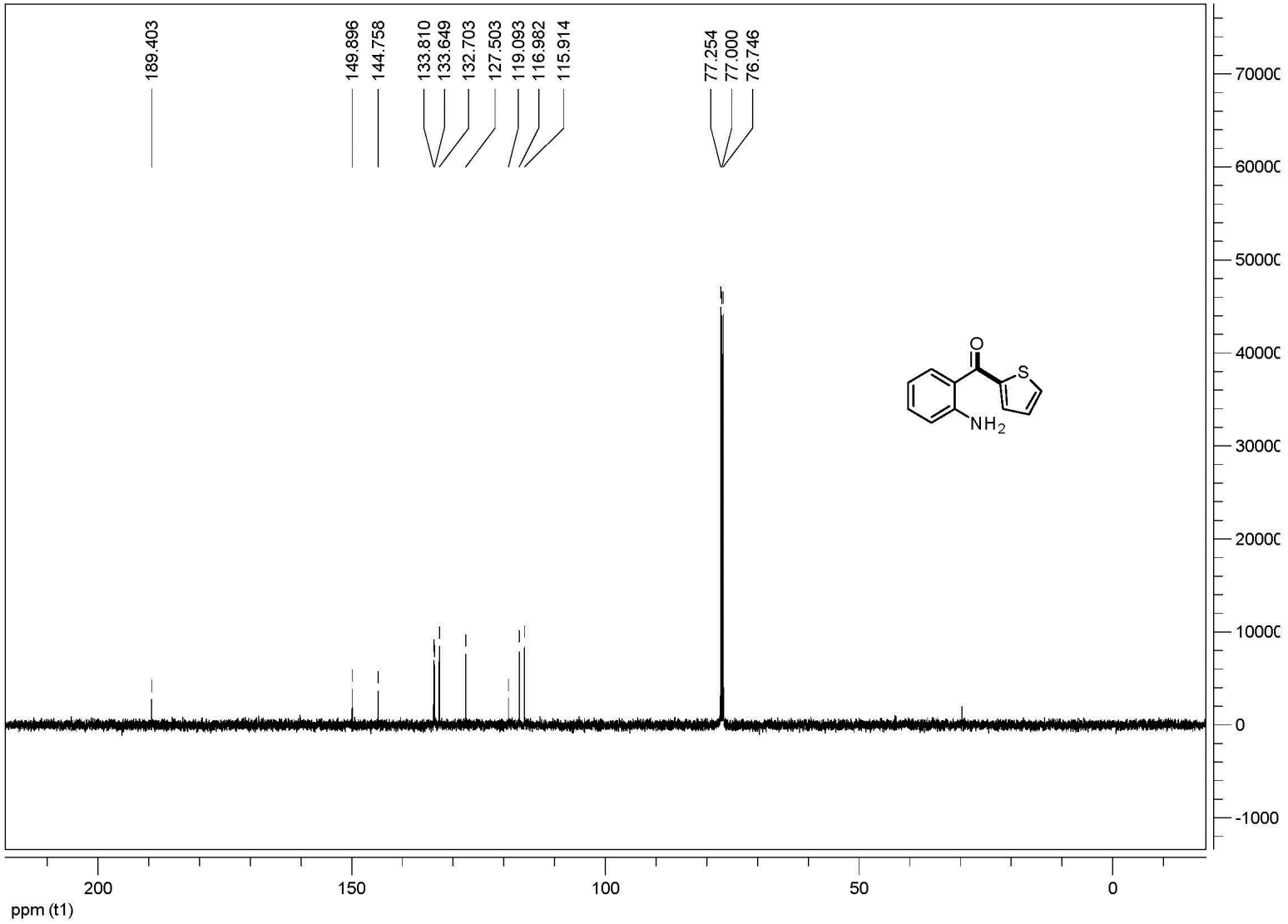
10000
5000
0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144.758
133.810
133.649
132.703
127.503
119.093
116.982
115.914
77.254
77.000
76.746
O
S
NH2
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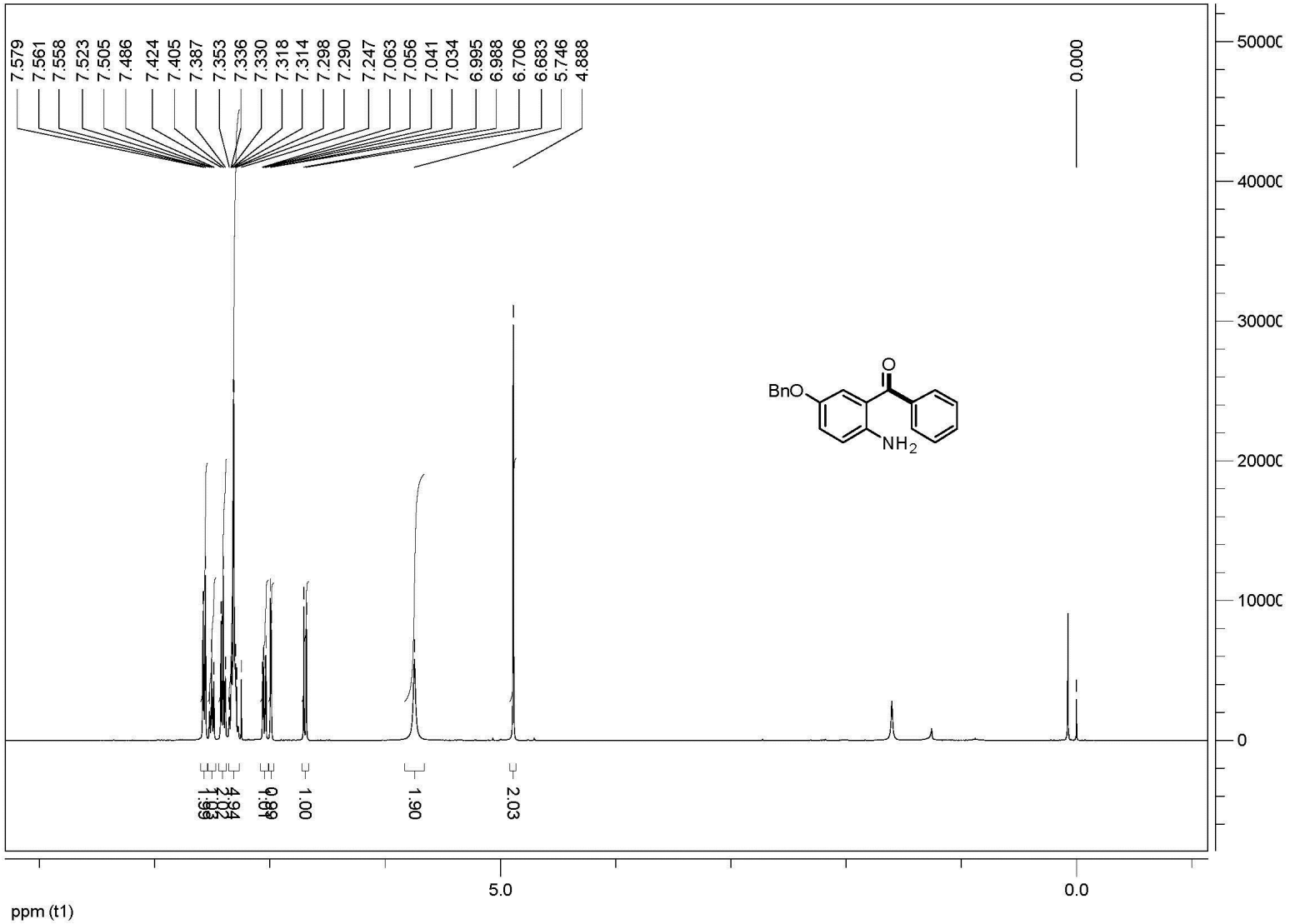
60000
50000
40000
30000
20000
10000
0
-1000
200
150
100
50
0
ppm (t1)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7.558
7.523
7.505
7.486
7.424
7.405
7.387
7.353
7.336
7.330
7.318
7.314
7.298
7.290
7.247
7.063
7.056
7.041
7.034
6.995
6.988
6.706
6.683
5.746
4.888
0.000
BnO
O
NH2
1.99
2.02
4.94
9.89
1.00
1.90
2.03
5000
4000
3000
2000
1000
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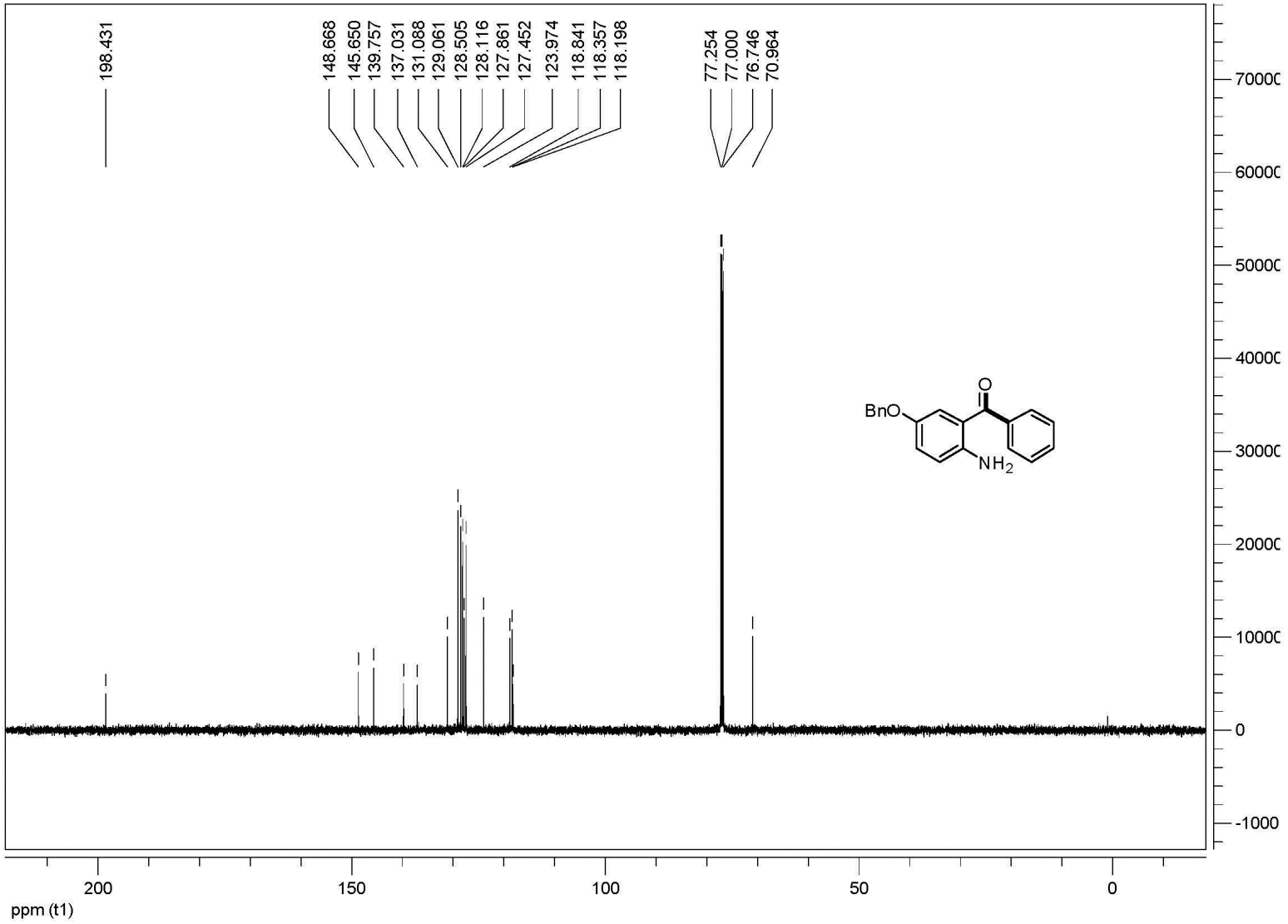
5.0
0.0
ppm (t1)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145.650
139.757
137.031
131.088
129.061
128.505
128.116
127.861
127.452
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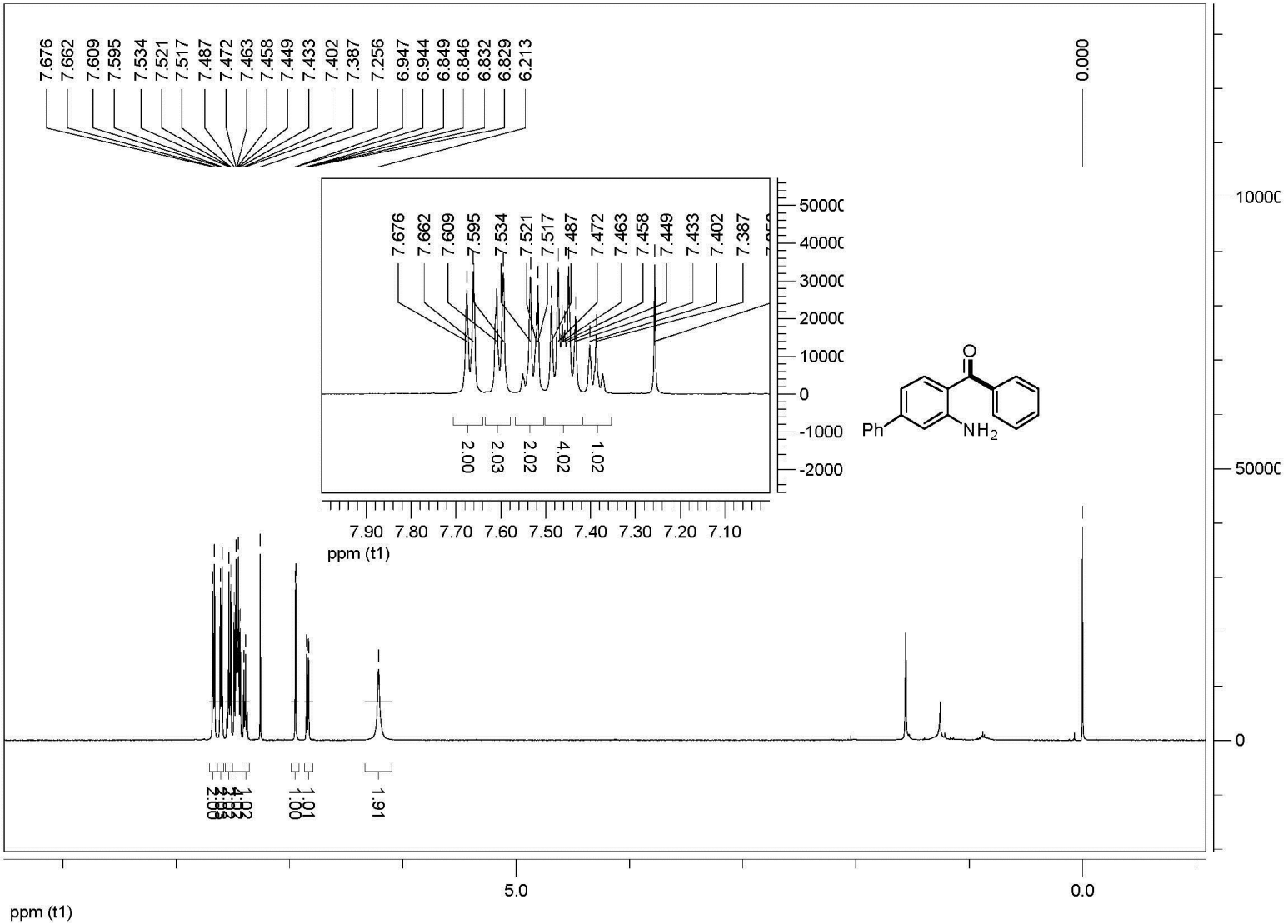
118.841
118.357
118.198
77.254
77.000
76.746
70.964
BnO
O
NH2
ppm (t1)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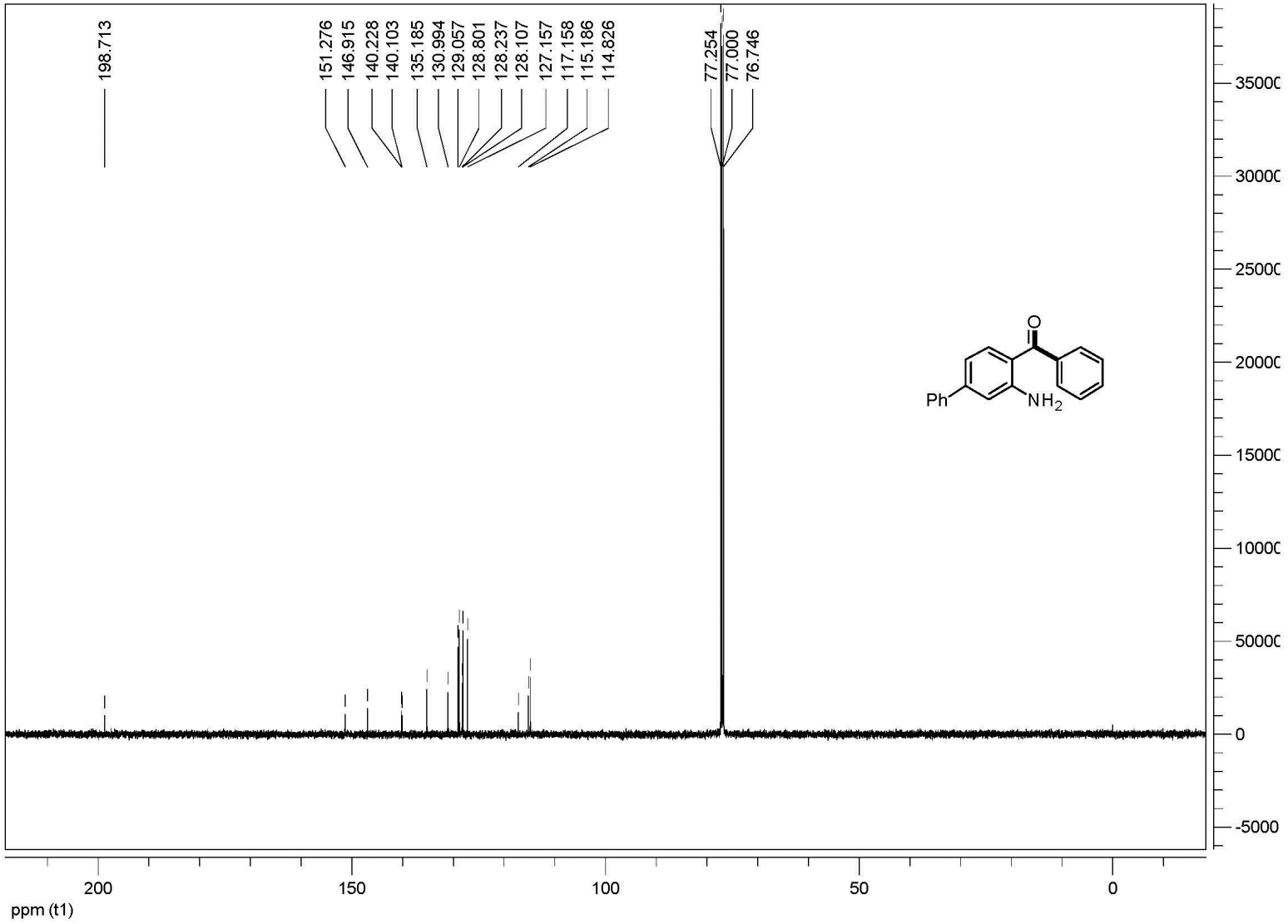
7.517
7.487
7.472
7.463
7.458
7.449
7.433
7.402
7.387
7.256
6.947
6.944
6.849
6.846
6.832
6.829
6.213
0.000
2.00
2.03
2.02
4.02
1.02
1.91
7.90 7.80 7.70 7.60 7.50 7.40 7.30 7.20 7.10
ppm (t1)
Ph
NH2
O
5.0
0.0
ppm (t1)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127.157
117.158
115.186
114.826
77.254
77.000
76.746
Ph
NH2
O
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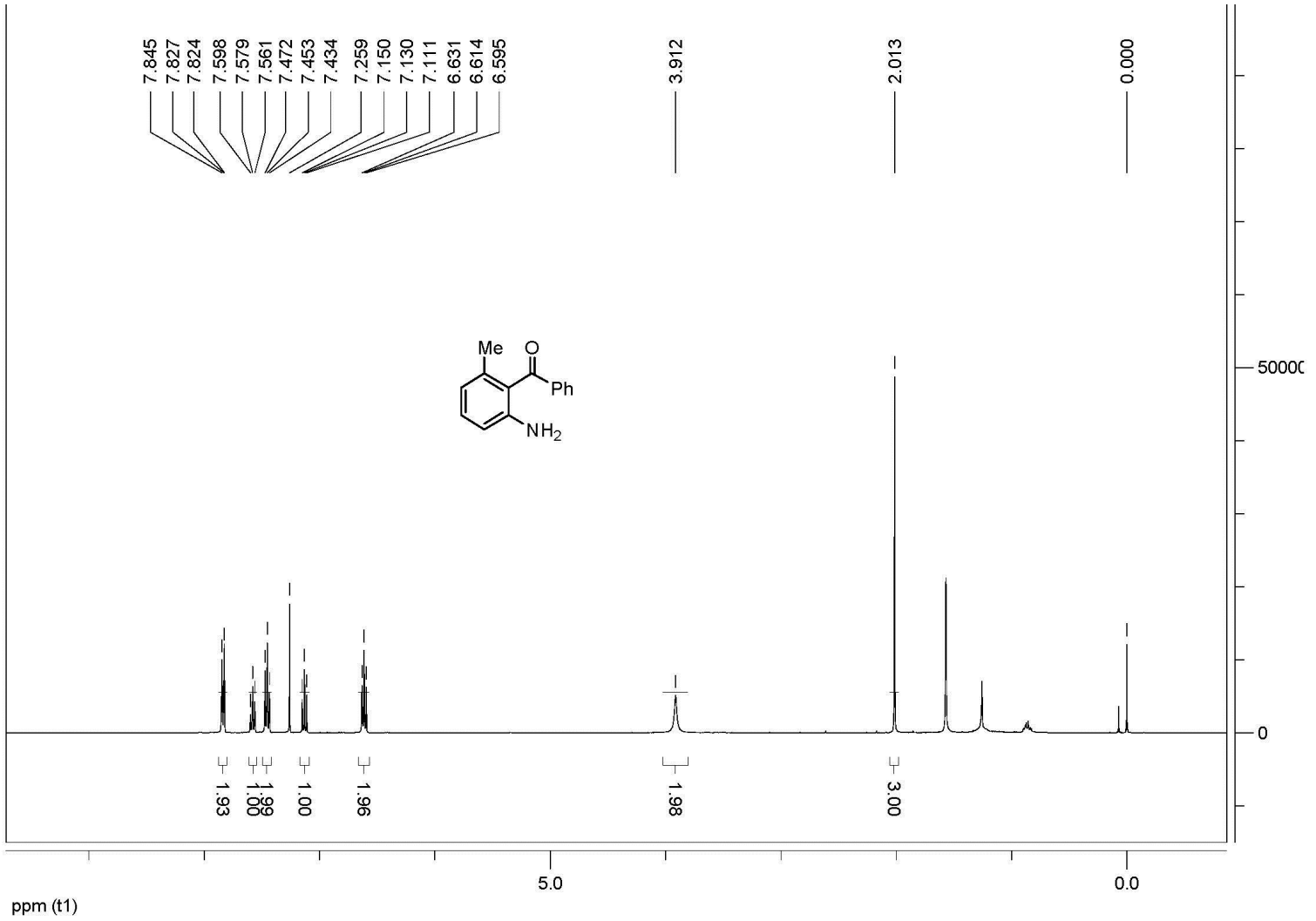
30000
25000
20000
15000
10000
5000
0
-5000
200
150
100
50
0
ppm (t1)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7.579
7.561
7.472
7.453
7.434
7.259
7.150
7.130
7.111
6.631
6.614
6.595
3.912
2.013
0.000
Me
O
Ph
NH2
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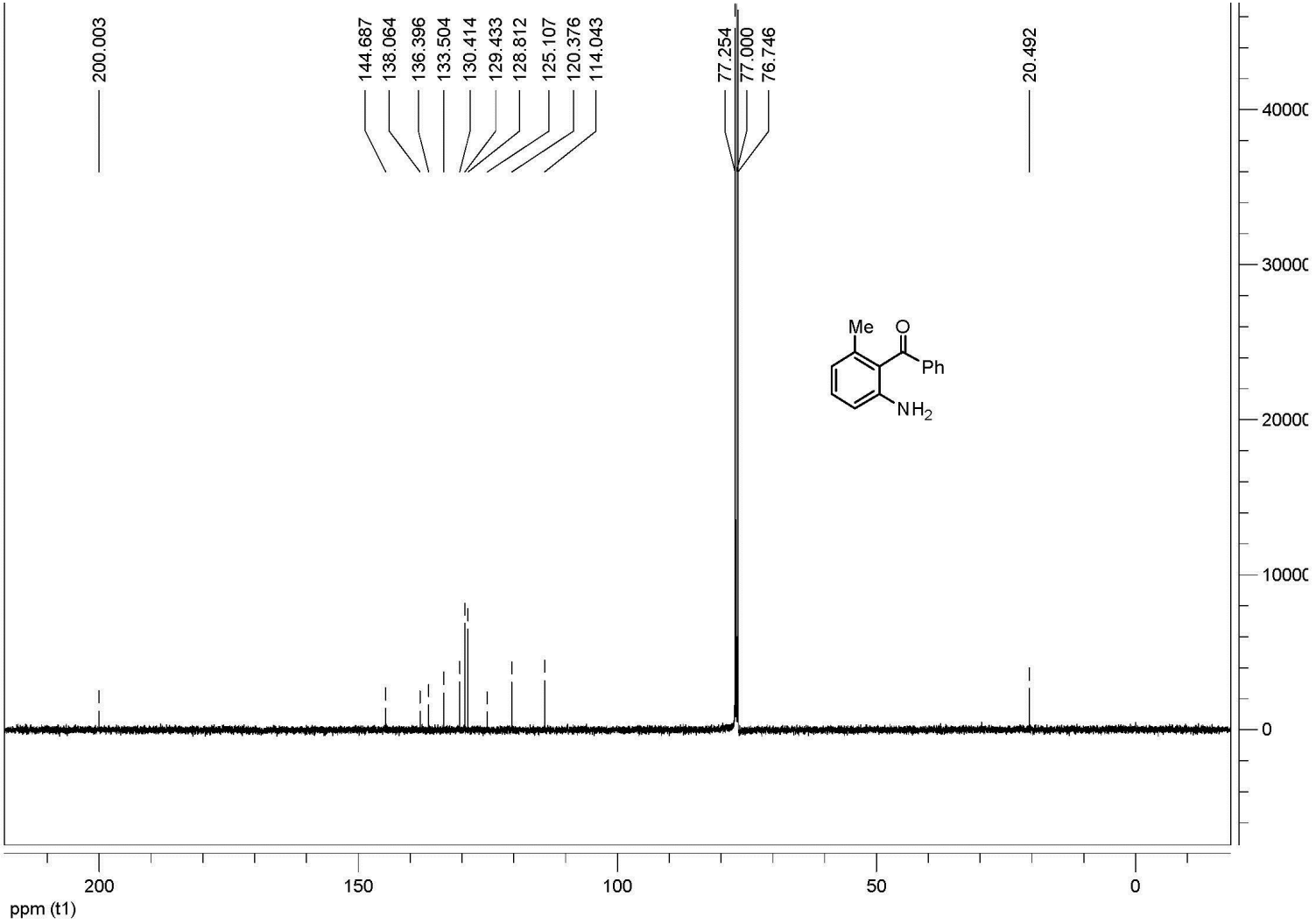
1.00
1.99
1.00
1.96
1.98
3.00
5.0
0.0
ppm (t1)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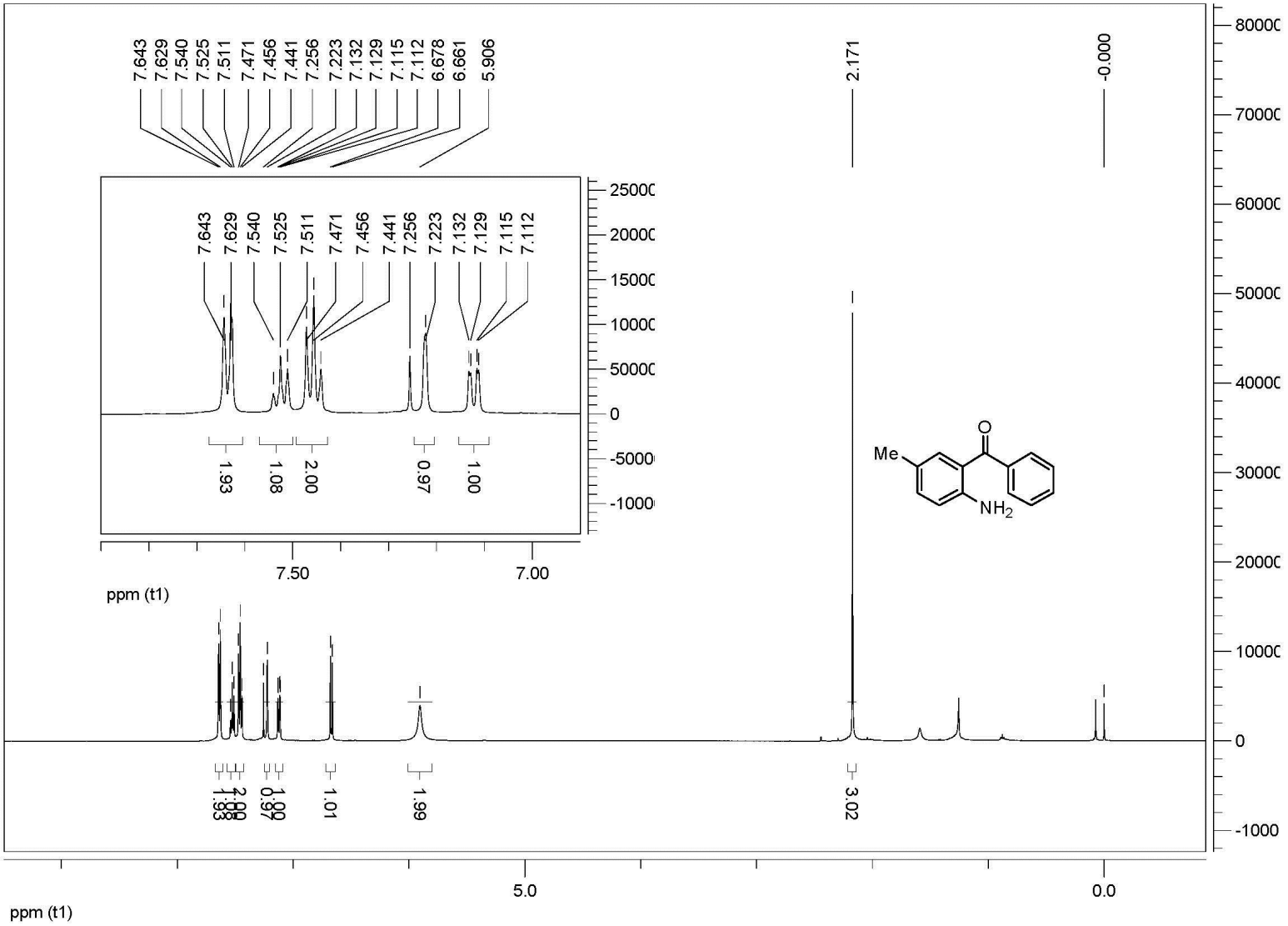
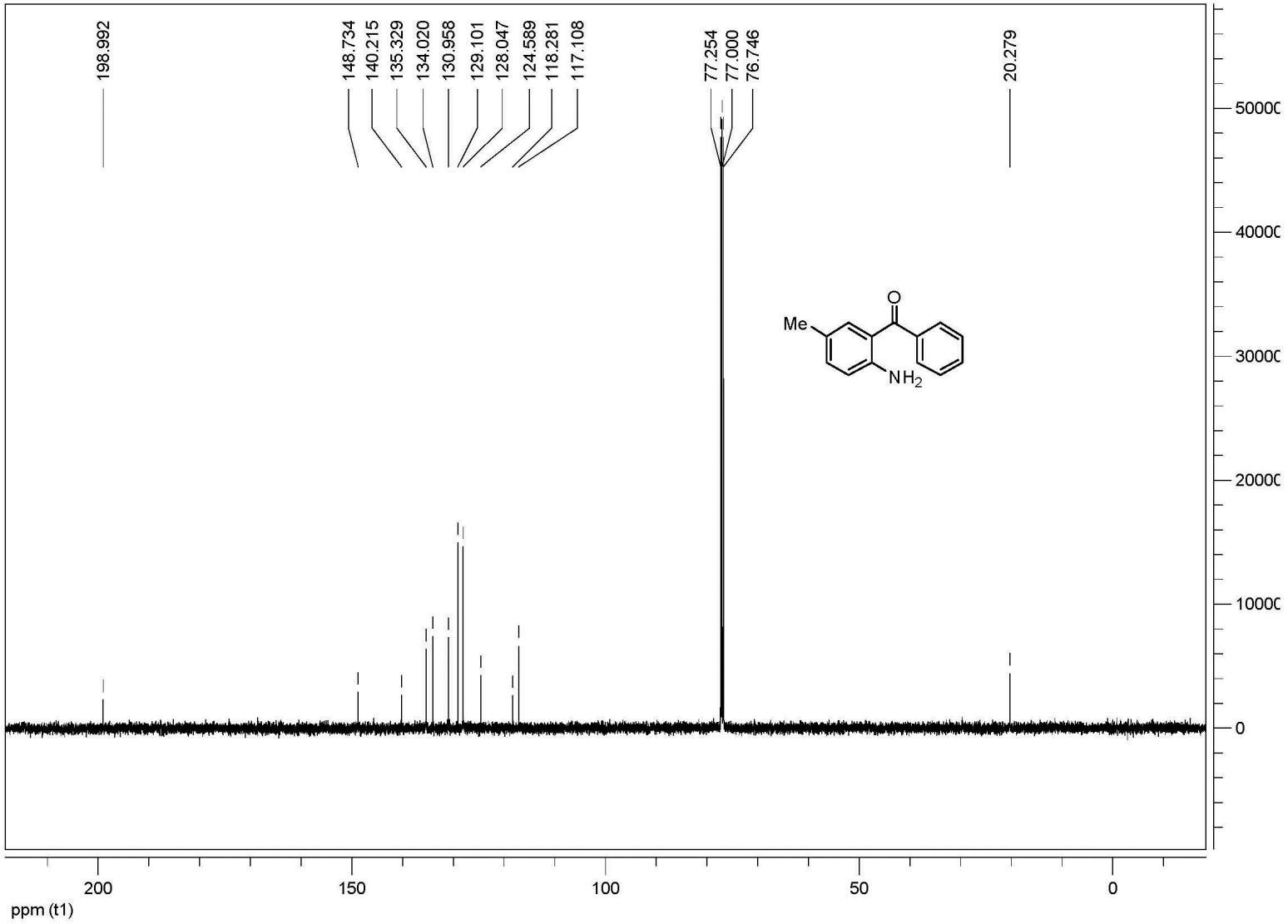
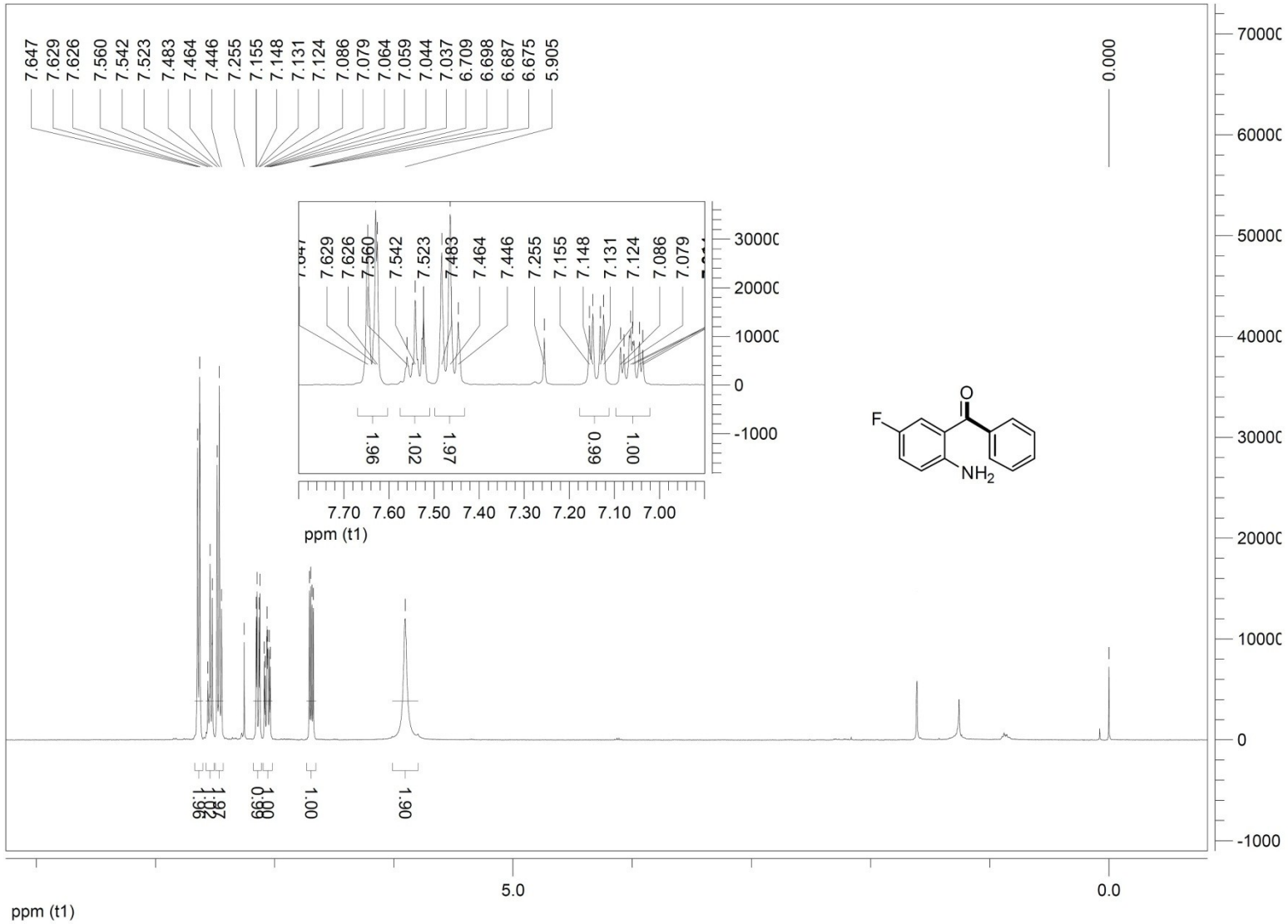
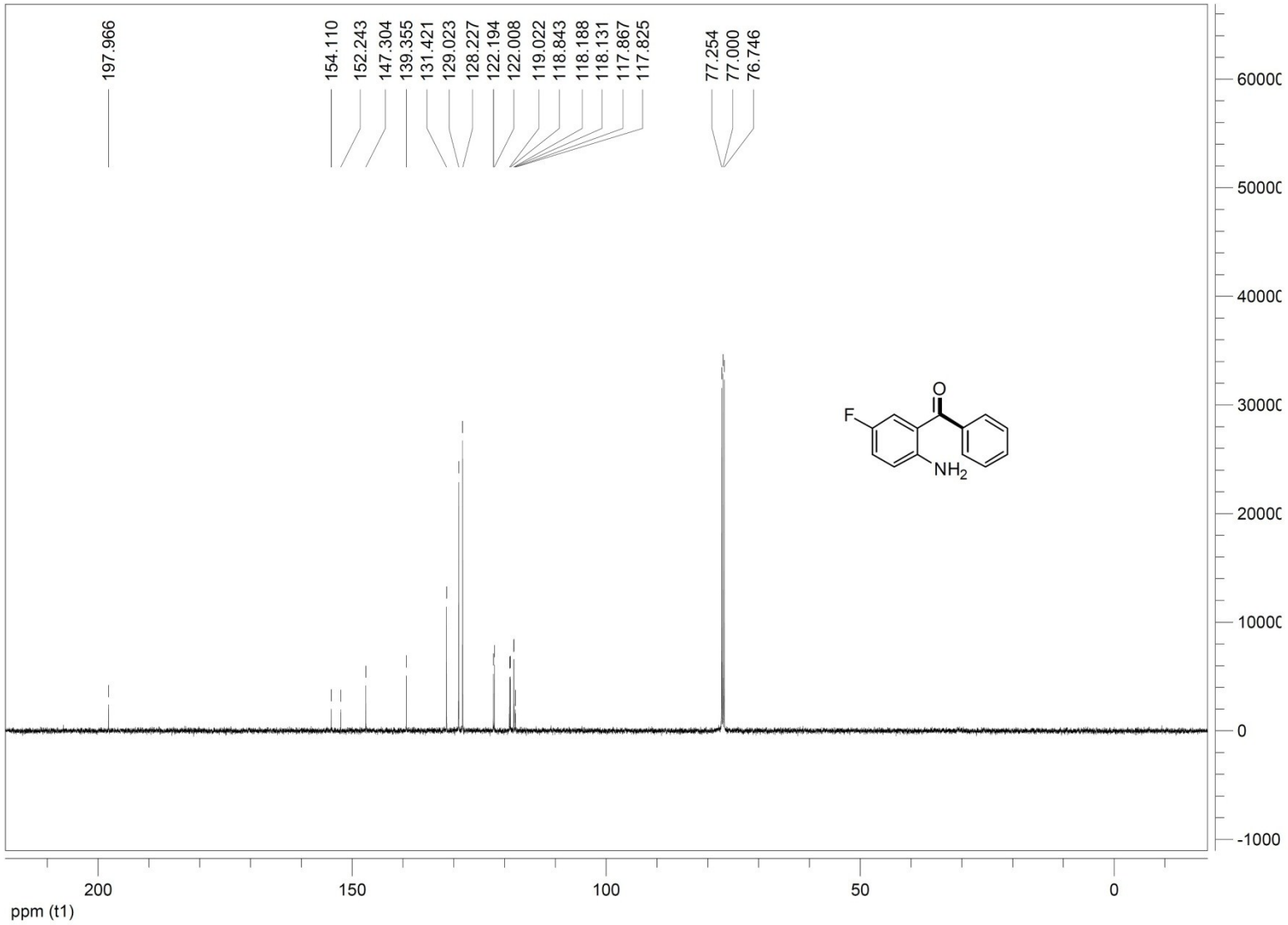
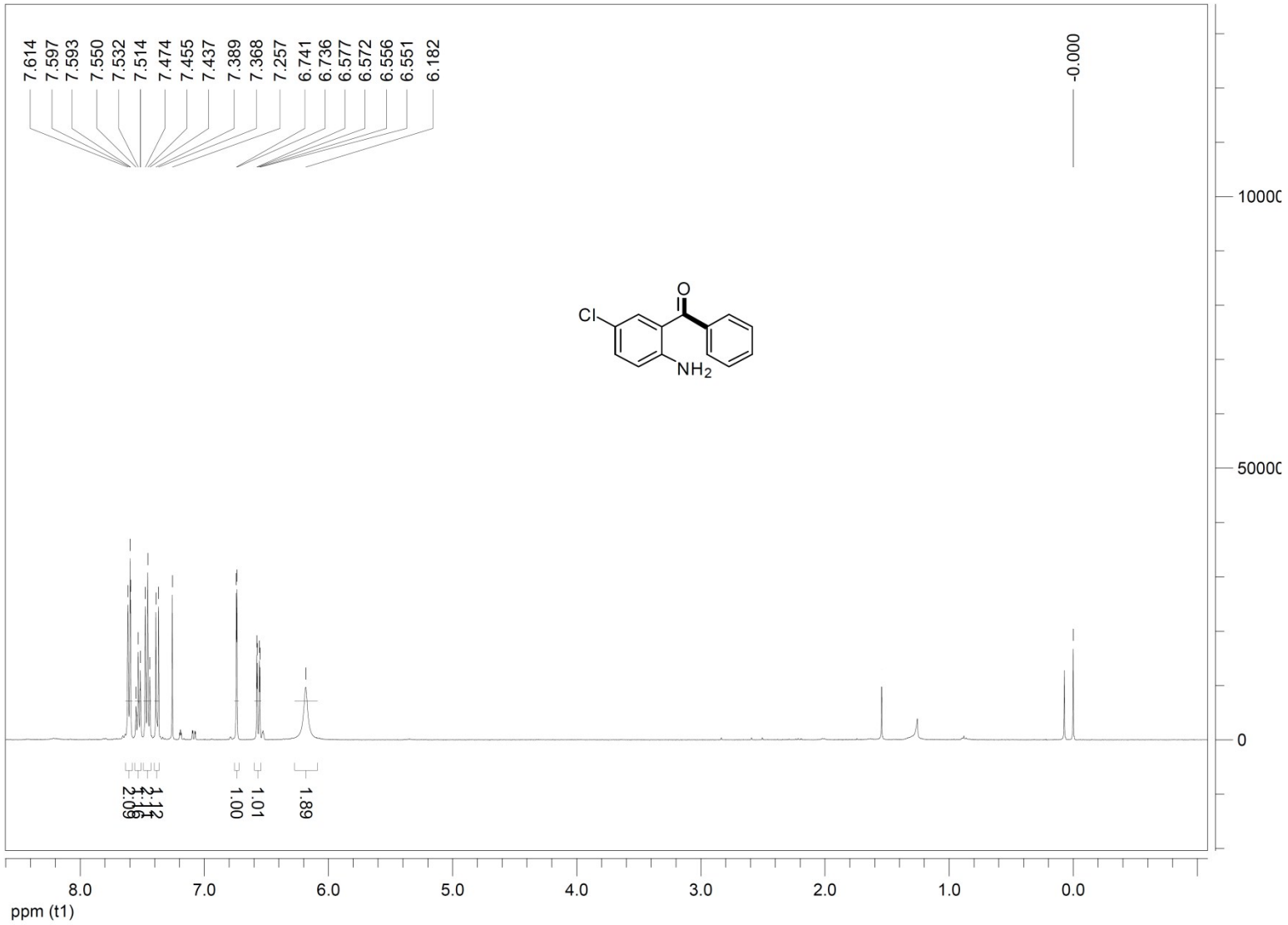
130.414
129.433
128.812
125.107
120.376
114.043
77.254
77.000
76.746
20.492
Me
O
Ph
NH2
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

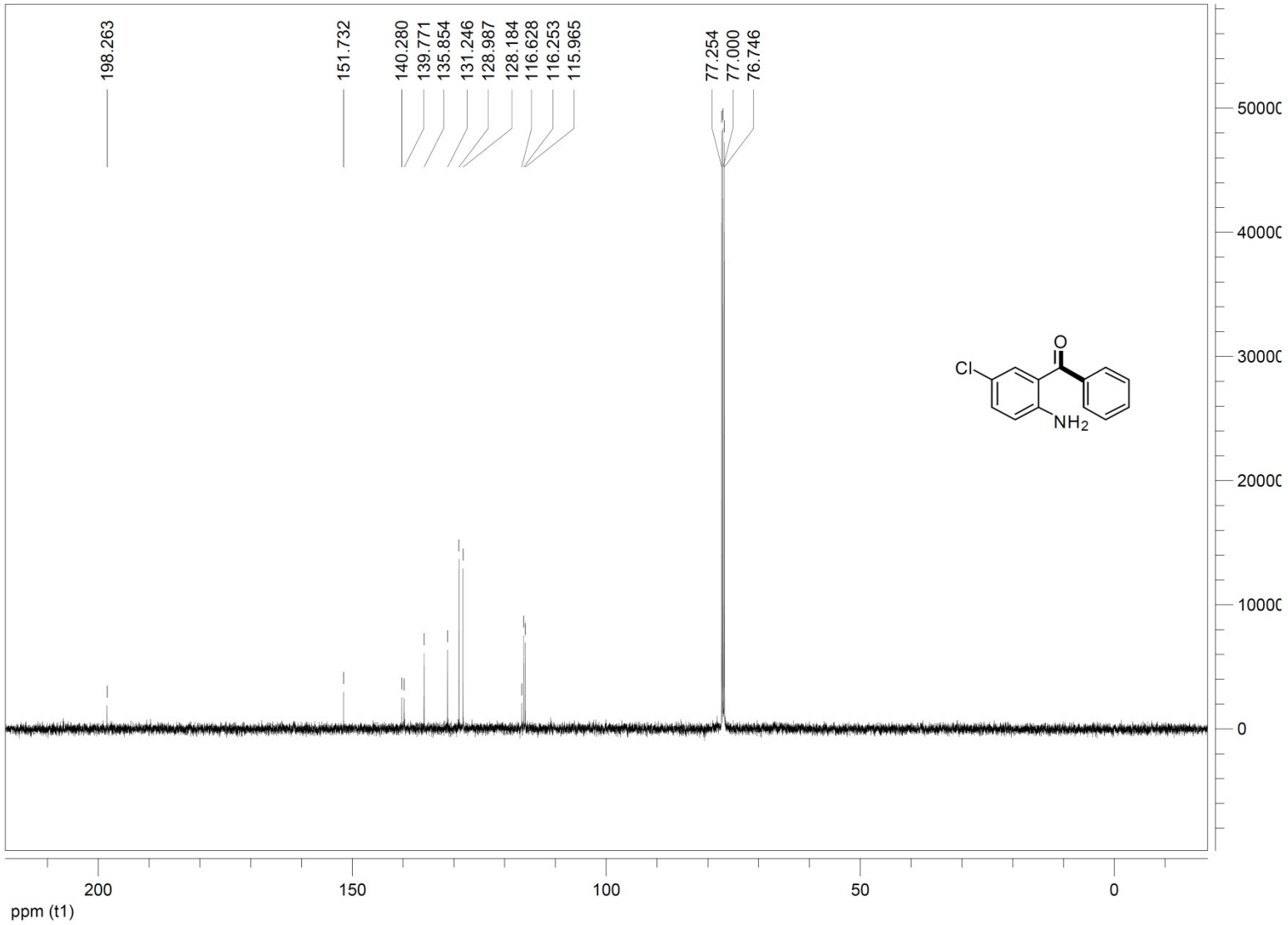

7.643
7.629
7.540
7.525
7.511
7.471
7.456
7.441
7.256
7.223
7.132
7.129
7.115
7.112
6.678
6.661
5.906
2.171
-0.000
1.93
1.08
2.00
0.97
1.00
7.50
7.00
ppm (t1)
1.01
1.69
3.02
5.0
0.0
ppm (t1)
Me
NH2
O

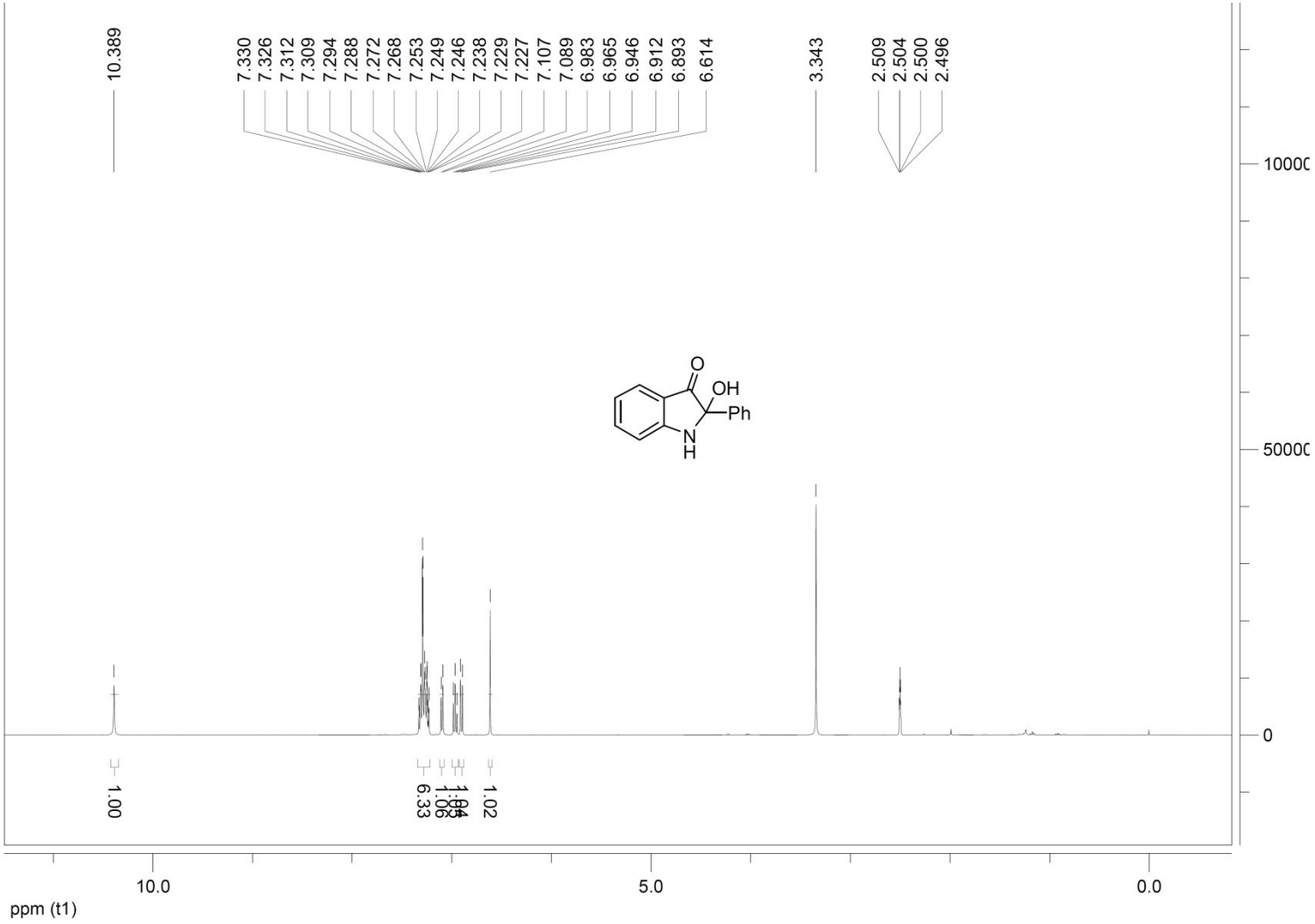

198.992
148.734
140.215
135.329
134.020
130.958
129.101
128.047
124.589
118.281
117.108
77.254
77.000
76.746
20.279
Me
O
NH2
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

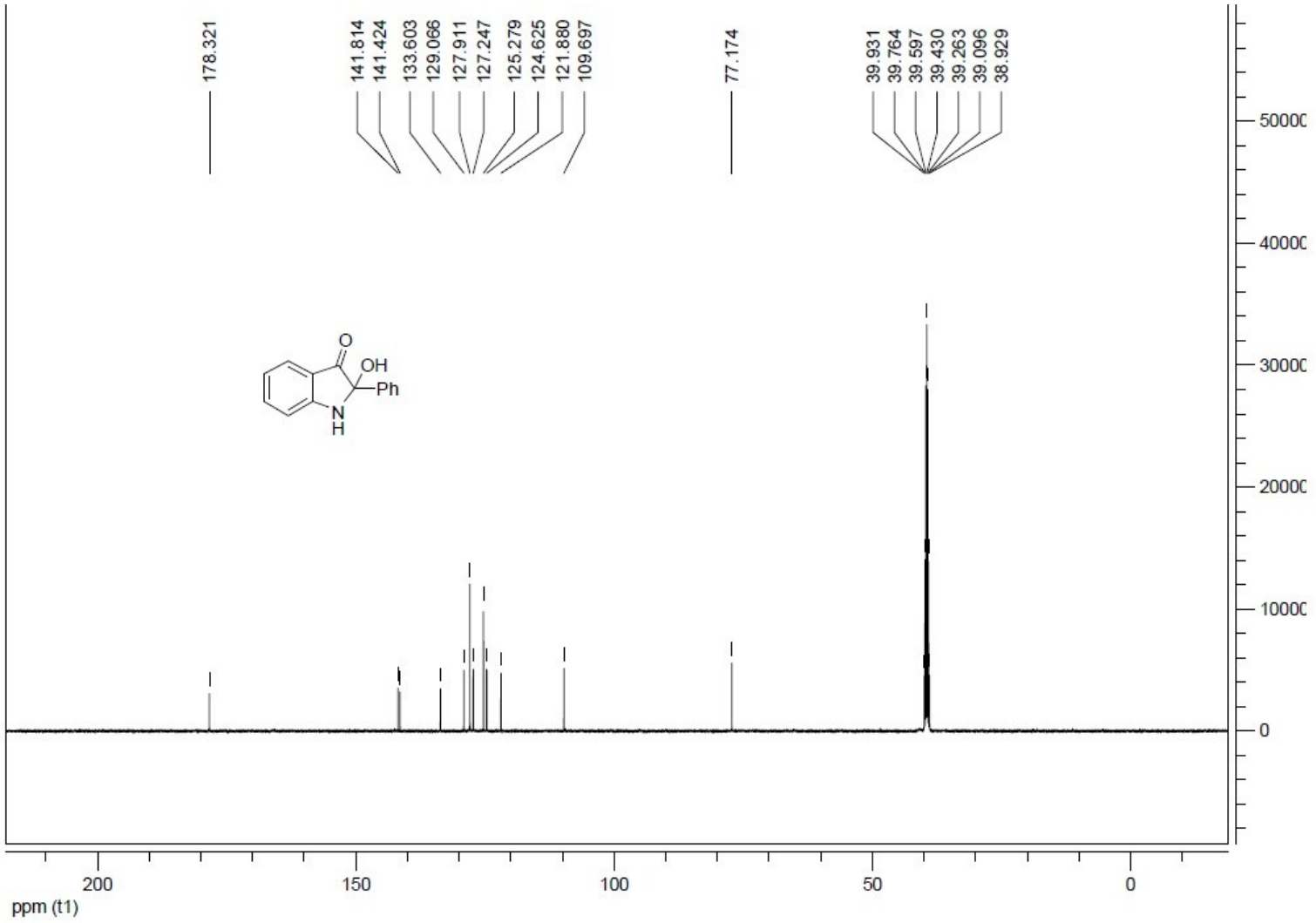

7.647
7.629
7.626
7.560
7.542
7.523
7.483
7.464
7.446
7.255
7.155
7.148
7.131
7.124
7.086
7.079
7.064
7.059
7.044
7.037
6.709
6.698
6.687
6.675
5.905
0.000
1.96
1.02
1.97
0.99
1.00
7.70 7.60 7.50 7.40 7.30 7.20 7.10 7.00
ppm (t1)
F
O
NH2
1.96
1.92
0.99
1.00
1.00
5.0
0.0
ppm (t1)


197.966
154.110
152.243
147.304
139.355
131.421
129.023
128.227
122.194
122.008
119.022
118.843
118.188
118.131
117.867
117.825
77.254
77.000
76.746
O
F
NH2
60000
50000
40000
30000
20000
10000
0
-1000
200
150
100
50
0
ppm (t1)


7.614
7.597
7.593
7.550
7.532
7.514
7.474
7.455
7.437
7.389
7.368
7.257
6.741
6.736
6.577
6.572
6.556
6.551
6.182
-0.000
Cl
O
NH2
10000
50000
0
2.09
2.16
2.12
1.00
1.01
1.89
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


198.263
151.732
140.280
139.771
135.854
131.246
128.987
128.184
116.628
116.253
115.965
77.254
77.000
76.746
Cl
O
NH2
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)


10.389
7.330
7.326
7.312
7.309
7.294
7.288
7.272
7.268
7.253
7.249
7.246
7.238
7.229
7.227
7.107
7.089
6.983
6.965
6.946
6.912
6.893
6.614
3.343
2.509
2.504
2.500
2.496
O
OH
Ph
N
H
1.00
6.33
1.02
10000
50000
0
10.0
5.0
0.0
ppm (t1)


178.321
141.814
141.424
133.603
129.066
127.911
127.247
125.279
124.625
121.880
109.697
77.174
39.931
39.764
39.597
39.430
39.263
39.096
38.929
O
OH
Ph
N
H
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)