Supporting Information

Synthesis, characterization, and cycloaddition reactivity of a monocyclic aromatic 1,2,3,5-tetrazine

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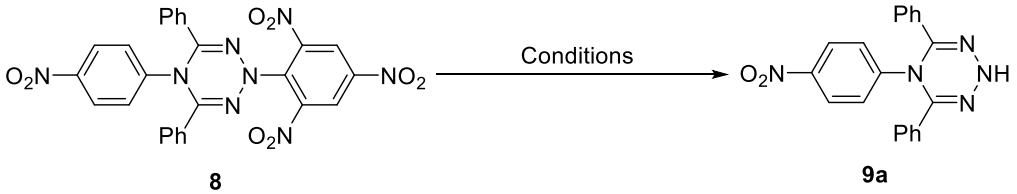
I. General Methods

General Methods. All reagents and solvents were used as supplied without further purification unless otherwise noted. All cycloaddition reactions were performed in anhydrous solvents unless otherwise noted. $CHCl_3$ was pre-treated with alumina for at least 24 h prior to use. Amidines were purchased as their hydrochloride salts and free-based by treatment with 2 M KOH (aq). Enamines and ynamines were prepared as reported in the literature.[1] Preparative TLC (PTLC) and column chromatography were conducted using Millipore SiO_2 60 F_{254} PTLC (0.5 mm) and Zeochem ZEOprep 60 ECO SiO_2 (40–63 μm), respectively. Analytical TLC was conducting using Millipore SiO_2 60 F254 TLC (0.250 mm) plates. ^1H and ^{13}C NMR spectra were obtained using a Bruker Avance III HD 600 MHz spectrometer equipped with either a 5 mm QCI or 5 mm CPDCH probe or a Bruker Avance III 500 MHz spectrometer equipped with a 5 mm BBFO probe. UV-Vis spectroscopy was performed on a Cary 3E spectrophotometer. Cyclic voltammetry was measured by using an IKA ElectraSyn 2.0 package. IR spectra were obtained using a Thermo Nicolet 380 FT-IR with a SmartOrbit Diamond ATR accessory. Mass spectrometry analysis was performed by direct sample injection on an Agilent G1969A ESI-TOF mass spectrometer. The single crystal X-ray diffraction studies were carried out on a Bruker Kappa APEX-II CCD diffractometer equipped with Mo Kα radiation (λ = 0.71073). Semiempirical computational studies (AM1, MNDO) were conducted with Gaussian09.[S2] Melting points (mp) are uncorrected.

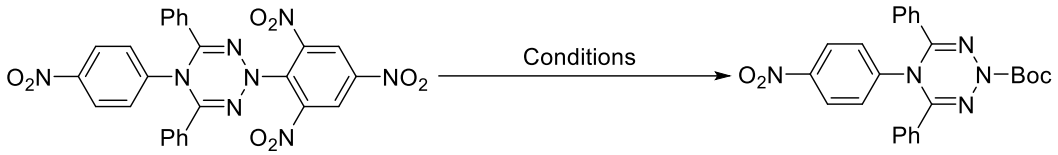
II. Condition screening for the synthesis of 9 and 10

Table S1. Condition screening for the synthesis of 9.



8 9a

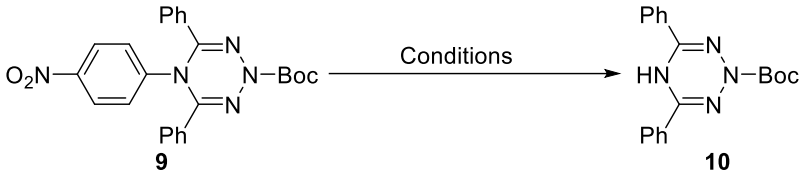
Entry	Conditions	Yield
1	KOH (5 equiv), PhSH (5 equiv), DMF, 25 °C, 2 h	Decomposition
2	NaOMe (5 equiv), DMF, 25 °C, 18 h	N. R.
3	PhSH (5 equiv), DMF, 25 °C, 40 min	N. R.
4	PhSH (5 equiv), DMF, 60 °C, 15 h	N. R.
5	K_2CO_3 (5 equiv), PhSH (5 equiv), DMF, 25 °C, 2 h	Decomposition
6	$KHCO_3$ (5 equiv), PhSH (5 equiv), DMF, 25 °C, 2 h	Trace
7	**$KHCO_3$ (5 equiv), *p*-$MeOC_6H_4SH$ (5 equiv), DMF, 25 °C, 2 h**	**25%**



8 **9**

Entry	Conditions	Yield
1	Et_3N (2.5 equiv), *p*-$MeOC_6H_4SH$ (2.5 equiv), CH_3CN, 25 °C, 1.5 h; then Et_3N (5 equiv), Boc_2O (5 equiv), 25 °C, 10 h	N. R., then Decomposition
2	Et_3N (2.5 equiv), *p*-$MeOC_6H_4SH$ (2.5 equiv), DMF, 25 °C, 1.5 h; then Et_3N (5 equiv), Boc_2O (5 equiv), 25 °C, 10 h	N. R., then Decomposition
3	NaH (10 equiv), *p*-$MeOC_6H_4SH$ (2.5 equiv), DMF, 25 °C, 1.5 h; then Boc_2O (5 equiv), 40 min	N. R., then Decomposition
4	Et_3N (2.5 equiv), *p*-$MeOC_6H_4SH$ (2.5 equiv), DMF, 25 °C, 1 h; then NaH (30 equiv), Boc_2O (30 equiv), 25 °C, 1 h	Trace
5	**Et_3N (2.5 equiv), *p*-$MeOC_6H_4SH$ (2.5 equiv), DMF, 25 °C, 1 h; then NaH (30 equiv), Boc_2O (30 equiv), -50 °C, 3 h**	**69-70%**
6	**Et_3N (2.5 equiv), *p*-$MeOC_6H_4SH$ (2.5 equiv), DMF, 25 °C, 1 h; then NaH (10 equiv), Boc_2O (10 equiv), -50 °C, 4 h**	**58-60%**

Table S2. Condition screening for the synthesis of 10.

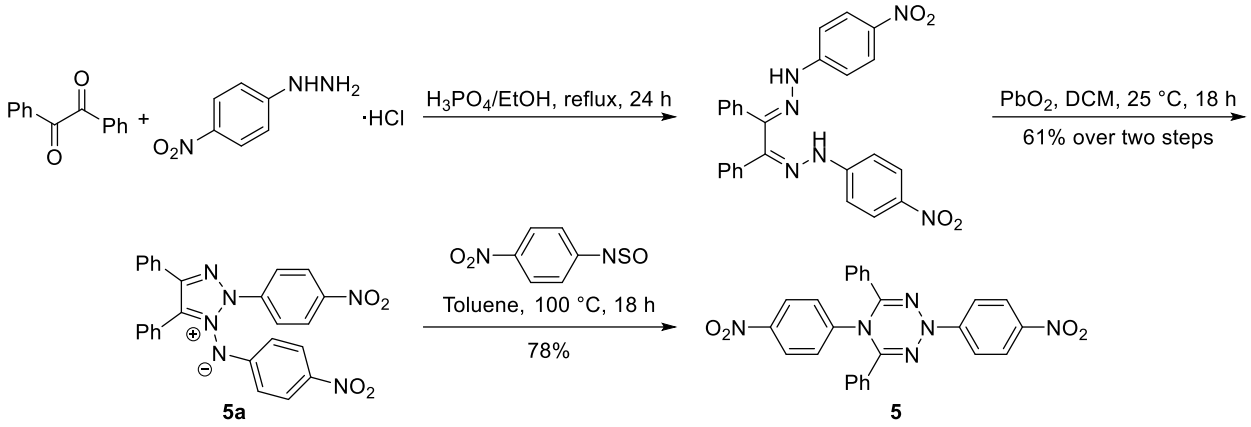


9 **10**

Entry	Nucleophile (5 equiv)	Base	Solvent	Temp	Time	Yield
1	*p*-$MeOC_6H_4SH$	K_2CO_3	DMF	120 °C	1 h	Decomposition
2	*p*-$MeOC_6H_4SH$	Et_3N	DMF	80 °C	16 h	Decomposition
3	*p*-$MeOC_6H_4SH$	DBU	DMF	80 °C	6 h	N. R.
4	**BnSH**	**DBU**	**DMF**	**50 °C**	**0.5 h**	**26-29%**
5	BnSH	DBU	DMF	25 °C	6 h	21%
6	BnSH	DBU	DMSO	25 °C	6 h	20%
7	BnSH	DBU	CH_3CN	25 °C	9 h	21%
8	BnSH	DBU	Acetone	25 °C	9 h	12%
9	EtSH	DBU	DMF	25 °C	1 h	17%
10	EtSH	DBU	DMF	25 °C	6 h	26-28%
11	EtSH (20 equiv)	DBU	DMF	25 °C	3 h	23%
12	Ph_3CSH	DBU	DMF	25 °C	14 h	N. R.
13	NaHS	DBU	DMF	25 °C	48 h	N. R.
14	*t*-BuSH	DBU	DMF	25 °C	26 h	N. R.
15	KSCN	DBU	DMF	25 °C	26 h	N. R.
16	EtSH	Et_3N	DMF	25 °C	24 h	N. R.
17	**EtSH**	**K_2CO_3**	**DMF**	**25 °C**	**6 h**	**29%**
18	$HSCH_2COOH$	K_2CO_3	DMF	25 °C	24 h	N. R.
19	$HSCH_2COOH$	DBU	DMF	25 °C	22 h	17%

III. Synthesis of 4,6-diphenyl-1,2,3,5-tetrazine (2)

Multi-gram scale synthesis of 5

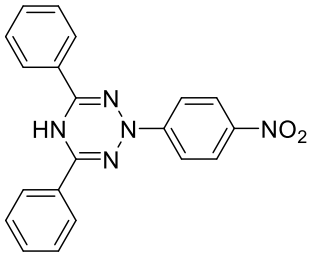


The synthesis of **5** was reported by Butler et al.[S3] and herein we describe a scaled synthesis from commercially available material.

Benzil (8.40 g, 40 mmol, 1.0 equiv) and *p*-nitrophenylhydrazine hydrochloride (22.80 g, 120 mmol, 3.0 equiv) were added to a 1 L round-bottom flask, and H_3PO_4/EtOH (400 mL, V/V = 6:4) was added, giving a suspension. The mixture was warmed at reflux at 120 °C for 24 h. The orange mixture was cooled to room temperature, diluted with 500 mL H_2O, and filtered through a Büchner funnel. The orange solid collected was washed with H_2O (500 mL × 2), air dried, and placed in a 1 L round-bottom flask. CH_2Cl_2 (400 mL) and PbO_2 (14.40 g, 60 mmol, 1.5 equiv) were added. The mixture was stirred at 25 °C for 18 h. The mixture was filtered through Celite and concentrated. The residue was purified by column chromatography (SiO_2, CH_2Cl_2 then EtOAc) to provide **5a** (11.73 g, 61%) as a red solid.

p-Nitroaniline (6.91 g, 50 mmol, 2.0 equiv) and anhydrous toluene (25 mL) were added to an oven-dried 250 mL round-bottom flask, and $SOCl_2$ (11.9 g, 7.26 mL, 100 mmol, 4.0 equiv) was added to the mixture under Ar. The mixture was warmed at 80 °C for 6 h. The mixture was cooled to room temperature and the solvent was removed to provide a yellow-green solid. The solid was placed in a 200 mL oven-dried bomb flask, followed by the addition of **5a** (11.47 g, 24 mmol, 1.0 equiv) and anhydrous toluene (150 mL). The flask was sealed, and the mixture was warmed at 100 °C for 16 h. The mixture was cooled and solvent was removed. The residue was purified by column chromatography (SiO_2, 50% CH_2Cl_2/hexanes) to provide **5** (8.95 g, 78%) as a yellow solid identical to material previously reported.[S3]

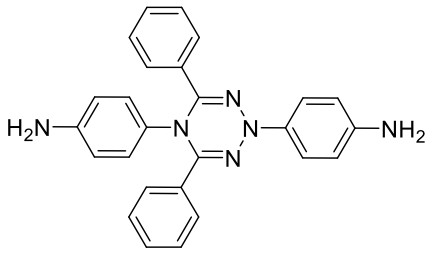
2-(4-Nitrophenyl)-4,6-diphenyl-2,5-dihydro-1,2,3,5-tetrazine (6).



6

A solution of **5** (120 mg, 0.25 mmol, 1.0 equiv) in CH_3CN (2.5 mL) was treated with KOH (70 mg, 1.25 mmol, 5 equiv) and PhSH (140 mg, 130 μL, 1.25 mmol, 5 equiv). The mixture was warmed at 80 °C for 42 h before it was cooled to room temperature and quenched with the addition of 10 mL of saturated aqueous NH_4Cl. The mixture was extracted with CH_2Cl_2 (50 mL × 2) and the organic phase was dried over Na_2SO_4. The solvent was removed and the residue was purified by column chromatography (SiO_2, 0–9% acetone/CH_2Cl_2) to provide **6** (44.0 mg, 49%) as a brown solid: mp 226–228 °C; ^{1}H NMR (600 MHz, DMSO-d_6, 298K) δ 10.27 (s, 1H), 8.20 (d, 2H, J = 9.1 Hz), 8.03 (d, 4H, J = 7.3 Hz), 7.64–7.57 (m, 8H); ^{13}C NMR (151 MHz, DMSO-d_6, 298K) δ 150.8, 149.2, 139.4, 131.7, 129.3, 128.7, 127.3, 125.3, 112.9; IR (film) ν_{max} 3667, 2984, 2890, 1591, 1479, 1393, 1321, 1249, 1061, 894 cm^{-1}; HRMS ESI-TOF *m/z* 357.1218 (M^+, $C_{20}H_{15}N_5O_2^+$ requires 357.1226).

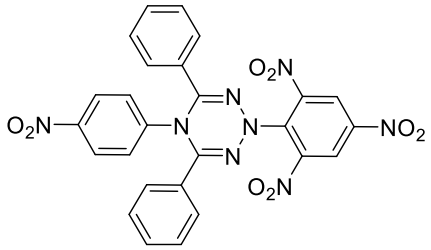
4,4'-(4,6-Diphenyl-1,2,3,5-tetrazine-2,5-diyl)dianiline (7).



7

A suspension of **5** (244 mg, 0.05 mmol, 1.0 equiv) and 10% Pd/C (12 mg) in EtOAc (1 mL) was stirred at 25 °C under a H_2 atmosphere for 16 h. The mixture was filtered, and the solvent was removed to provide **7** (18.8 mg, 90%) as an orange solid: mp 143–145 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.06–8.05 (m, 4H), 7.55 (d, 2H, J = 8.8 Hz), 7.43–7.38 (m, 6H), 6.93 (d, 2H, J = 8.8 Hz), 6.73 (d, 2H, J = 8.8 Hz), 6.44 (d, 2H, J = 8.8 Hz), 3.49 (br s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 143.1, 143.0, 142.3, 140.3, 135.6, 133.4, 129.9, 128.7, 127.3, 123.5, 117.7, 116.0, 115.7; IR (film) ν_{max} 3434, 3357, 3204, 3038, 1618, 1506, 1317, 1285, 1245, 1052, 822, 728, 692 cm^{-1}; HRMS ESI-TOF *m/z* 418.1901 (M^+, $C_{26}H_{22}N_6^+$ requires 418.1906).

5-(4-Nitrophenyl)-4,6-diphenyl-2-(2,4,6-trinitrophenyl)-2,5-dihydro-1,2,3,5-tetrazine (8).

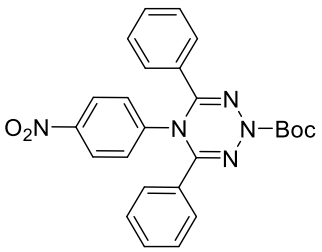


8

($^{n}Bu_4N)_2Ce(NO_3)_6$ was prepared as reported.[S4]

($^{n}Bu_4N)_2Ce(NO_3)_6$ (44.5 g, 44.5 mmol, 2.2 equiv) and TfOH (6.68 g, 4.0 mL, 44.5 mmol, 2.2 equiv) were sequentially added to a solution of **5** (10.64 g, 22.2 mmol, 1.0 equiv) in CH_2Cl_2 (400 mL) in a 1 L round-bottom flask. The mixture was stirred at 25 °C for 5 h before Et_3N (4.45 g, 44.5 mmol) was added to quench the reaction. The solvent was removed, and the mixture was triturated with Et_2O (200 mL). EtOAc (200 mL) was added and the mixture was stirred at 25 °C for 15 min. The mixture was then filtered over a Büchner funnel and the solid was washed with EtOAc/Et_2O (V/V = 1:3, 80 mL × 3). The filtrate was combined, and the solvent was removed. The residue was purified by column chromatography (SiO_2, 50–70% CH_2Cl_2/hexanes) to provide **8** (5.54 g, 44%) as a red solid: mp 226–228 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.66 (s, 2H), 8.05 (d, 2H, *J* = 9.2 Hz), 7.83 (d, 4H, *J* = 7.5 Hz), 7.60 (t, 2H, *J* = 7.3 Hz), 7.54 (t, 4H, *J* = 7.6 Hz), 7.02 (d, 2H, *J* = 9.2 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 147.7, 146.4, 144.0, 141.1, 140.5, 134.5, 132.9, 129.8, 129.7, 127.7, 125.6, 123.0, 119.8; IR (film) ν_{max} 3088, 2930, 1636, 1542, 1604, 1479, 1330, 1285, 849, 733, 706 cm^{-1}; HRMS ESI-TOF *m/z* 569.1166 ([M + H]$^+$, $C_{26}H_{16}N_8O_8$ + H^+ requires 569.1169). Differential scanning calorimetry revealed that **8** is of high thermal potential (2755.72 J/g) with an onset temperature of 241.6 °C, which is potentially explosive and shock sensitive. Although the authors have not been able to elicit detonation through the application of shock and friction, safety precautions should be exercised and heating within 100 °C of the thermal decomposition temperature of 242 °C should be avoided especially when **8** is synthesized on large scale.

***tert*-Butyl 5-(4-Nitrophenyl)-4,6-diphenyl-1,2,3,5-tetrazine-2(5*H*)-carboxylate (9).**

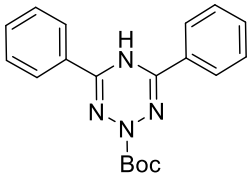


9

p-Methoxythiophenol (70.1 mg, 62 μL, 0.5 mmol, 2.5 equiv) and Et_3N (50.5 mg, 70 μL, 0.5 mmol, 2.5 equiv) were sequentially added to a solution of **8** (113 mg, 0.2 mmol, 1.0 equiv) in anhydrous DMF (4.0 mL) in a 25 mL round-bottom flask. The mixture was stirred at 25 °C under an Ar

atmosphere for 1 h. The mixture was then placed in a dropping funnel and added dropwise to a cooled mixture (-50 °C) of NaH (60% in mineral oil, pre-washed with hexanes, 240 mg, 6 mmol, 30 equiv) and Boc_2O (1.32 g, 6 mmol, 30 equiv) in anhydrous DMF (4.0 mL). The mixture was stirred at -50 °C for 3 h, warmed to 25 °C, and quenched by dropwise addition to a mixture of 40 mL of saturated aqueous $NaHCO_3$ and 40 mL of CH_2Cl_2. The mixture was extracted with CH_2Cl_2 (40 mL × 3) and the organic phase was combined and washed with saturated aqueous NaCl (40 mL), then dried over Na_2SO_4. The solvent was removed and the residue was purified by column chromatography (SiO_2, 30–80% CH_2Cl_2/hexanes) to provide **9** (64.1 mg, 70%) as a yellow solid. When the reaction was conducted on larger scales, 10 equiv of NaH and Boc_2O was used and the reaction required 4 h to run to completion. A typical yield of 58-60% was observed. For **9**: mp 204 °C (decomp.); ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.02 (d, 4H, *J* = 7.1 Hz), 7.98 (d, 2H, *J* = 9.4 Hz), 7.55 (t, 2H, *J* = 7.2 Hz), 7.51 (t, 4H, *J* = 7.3 Hz), 6.82 (d, 2H, *J* = 9.4 Hz), 1.64 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 151.6, 147.4, 143.7, 142.4, 131.7, 131.2, 129.5, 127.5, 125.4, 117.0, 84.6, 28.2; IR (film) ν_{max} 3056, 2925, 1753, 1591, 1510, 1366, 1344, 1245, 1272, 1052, 836, 746, 701 cm^{-1}; HRMS ESI-TOF *m/z* 358.1297 ([M – Boc + H]$^+$, $C_{20}H_{15}N_5O_2$ + H^+ requires 358.1304).

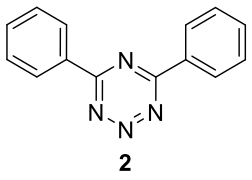
***tert*-Butyl 4,6-Diphenyl-1,2,3,5-tetrazine-2(5*H*)-carboxylate (10).**



10

Compound **9** (1.17 g, 2.5 mmol, 1 equiv) and K_2CO_3 (1.73 g, 12.5 mmol, 5 equiv) were added to a 100 mL round-bottom flask. DMF (25 mL) and EtSH (772 mg, 0.94 mL, 12.5 mmol, 5 equiv) were added to the mixture under an Ar atmosphere. The mixture was stirred at 25 °C for 6 h before being poured into a mixture of 100 mL of saturated aqueous NH_4Cl and 100 mL of CH_2Cl_2. The organic layer was washed with H_2O (100 mL), and dried over Na_2SO_4. The solvent was evaporated and the residue was purified by column chromatography (SiO_2, 100% CH_2Cl_2, then 44% CH_2Cl_2/12% EtOAc/44% hexanes) to provide **10** (247 mg, 29%) as a yellow solid: mp 163–165 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 7.81 (d, 4H, *J* = 7.3 Hz), 7.52 (t, 2H, *J* = 7.3 Hz), 7.47 (t, 4H, *J* = 7.5 Hz), 6.74 (br s, 1H), 1.63 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 152.8, 146.7, 131.7, 129.8, 129.1, 125.9, 82.4, 28.4; IR (film) ν_{max} 3213, 3061, 2966, 2926, 1685, 1658, 1456, 1411, 1312, 1146, 849, 769, 697 cm^{-1}; HRMS ESI-TOF *m/z* 337.1664 ([M + H]$^+$, $C_{19}H_{20}N_4O_2$ + H^+ requires 337.1665).

4,6-Diphenyl-1,2,3,5-tetrazine (2).



2

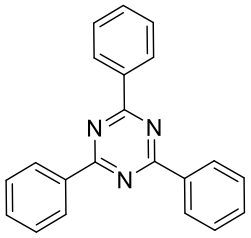
Compound **10** (247 mg, 0.74 mmol, 1 equiv) was added to a stirred mixture of MnO_2 (1.62 g, 18.2 mmol, 25 equiv) in anhydrous CH_2Cl_2 (7.3 mL). The mixture was stirred at 25 °C for 1 h and directly purified by column chromatography (SiO_2, CH_2Cl_2) within 15 min. The solvent was removed under a gentle stream of anhydrous N_2 to provide **2** (137 mg, 80%) as a yellow solid: mp 128 °C (decomp.); ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.77 (d, 4H, *J* = 7.2 Hz), 7.70 (t, 2H, *J* = 7.4 Hz), 7.62 (t, 4H, *J* = 7.7 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 163.2, 134.3, 132.0, 129.5, 129.4; IR (film) ν_{max} 3065, 3047, 2957, 2921, 2845, 1600, 1483, 1443, 1411, 1326, 1290, 1178, 917, 746, 683 cm^{-1}; UV (CH_3CN) λ_{max} 275 (ε 2.52 × 10^4 L·mol^{-1}·cm^{-1}), 396 (ε 4.90 × 10^2 L·mol^{-1}·cm^{-1}) nm; HRMS ESI-TOF *m/z* 235.0984 ([M + H]$^+$, $C_{14}H_{10}N_4$ + H^+ requires 235.0984). Differential scanning calorimetry revealed that **2** is of high thermal potential (744.17 J/g) with a low onset temperature of 138.1 °C, which is potentially explosive and shock sensitive. Although the authors have not been able to elicit detonation through the application of shock and friction, safety precautions should be exercised and extensive heating (>100 °C) should be avoided.

IV. Cycloaddition reactions with 4,6-diphenyl-1,2,3,5-tetrazine (2)

General procedure for the synthesis of 12a-n

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with the corresponding amidine **11a-n** (0.03 mmol, 1.5 equiv). The mixture was stirred at 25 °C for 2 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by column chromatography (SiO_2, EtOAc/hexanes) or PTLC (EtOAc/hexanes) to provide **12a-n** as desired products.

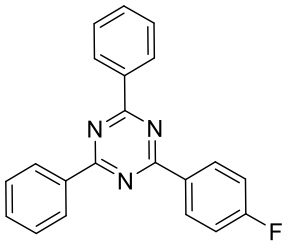
2,4,6-Triphenyl-1,3,5-triazine (12a).



12a

12a (5.97 mg, 98%, white solid): mp 222–224 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.79 (d, 6H, *J* = 7.4 Hz), 7.62 (t, 3H, *J* = 7.1 Hz), 7.59 (t, 6H, *J* = 7.3 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 171.8, 136.4, 132.7, 129.1, 128.8; IR (film) ν_{max} 2957, 2921, 2845, 1730, 1515, 1442, 1362, 1254, 1061, 1025, 742, 692 cm^{-1}; HRMS ESI-TOF *m/z* 310.1348 ([M + H]$^+$, $C_{21}H_{15}N_3$ + H^+ requires 310.1344).

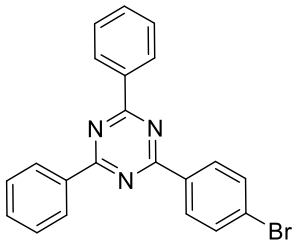
2-(4-Fluorophenyl)-4,6-diphenyl-1,3,5-triazine (12b).



12b

12b (6.45 mg, 99%, white solid): mp 208–210 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.80 (dd, 2H, *J* = 8.9, 5.6 Hz), 8.77 (dd, 4H, *J* = 8.3, 1.3 Hz), 7.62 (t, 2H, *J* = 7.2 Hz), 7.58 (t, 4H, *J* = 7.3 Hz), 7.25 (t, 2H, *J* = 8.6 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 171.8, 170.8, 166.0 (*J* = 251 Hz), 136.3, 132.7, 132.6 (*J* = 2.7 Hz), 131.4 (*J* = 8.9 Hz), 129.1, 128.8, 115.9 (*J* = 22 Hz); IR (film) ν_{max} 3056, 2921, 2849, 1604, 1519, 1443, 1362, 1227, 1142, 836, 764, 688 cm^{-1}; HRMS ESI-TOF *m/z* 328.1248 ($[M + H]^+$, $C_{21}H_{14}FN_3 + H^+$ requires 328.1250).

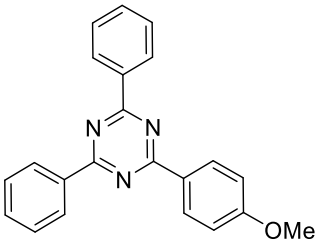
2-(4-Bromophenyl)-4,6-diphenyl-1,3,5-triazine (12c).



12c

12c (7.33 mg, 94%, white solid): mp 190–191 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.78 (d, 4H, *J* = 7.0 Hz), 8.67 (d, 2H, *J* = 8.6 Hz), 7.73 (d, 2H, *J* = 8.6 Hz), 7.65 (t, 2H, *J* = 7.2 Hz), 7.61 (t, 4H, *J* = 7.3 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 171.9, 171.0, 136.2, 135.4, 132.8, 132.1, 130.6, 129.1, 128.8, 127.6; IR (film) ν_{max} 3056, 2917, 2854, 1591, 1506, 1443, 1366, 1169, 1007, 836, 764, 688 cm^{-1}; HRMS ESI-TOF *m/z* 388.0449 ($[M + H]^+$, $C_{21}H_{14}BrN_3 + H^+$ requires 388.0452).

2-(4-Methoxyphenyl)-4,6-diphenyl-1,3,5-triazine (12d).

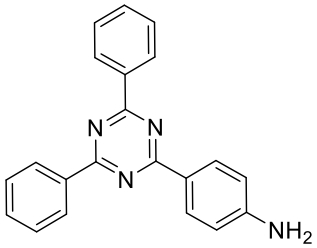


12d

12d (6.68 mg, 98%, white solid): mp 161–163 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.77 (dd, 4H, *J* = 8.2, 1.4 Hz), 8.75 (d, 2H, *J* = 8.9 Hz), 7.61 (t, 2H, *J* = 7.2 Hz), 7.57 (t, 4H, *J* = 7.2 Hz),

7.07 (d, 2H, *J* = 8.9 Hz), 3.93 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 171.5, 171.3, 163.5, 136.6, 132.5, 131.0, 129.0, 128.9, 128.7, 114.1, 55.6; IR (film) ν_{max} 3065, 2926, 2836, 1582, 1510, 1443, 1371, 1254, 1173, 769, 683 cm^{-1}; HRMS ESI-TOF *m/z* 340.1454 ($[M + H]^+$, $C_{22}H_{17}N_3O$ + H^+ requires 340.1450).

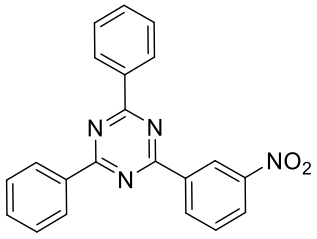
4-(4,6-Diphenyl-1,3,5-triazin-2-yl)aniline (12e).



12e

12e (6.31 mg, 97%, yellow solid): mp 197–199 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.76 (d, 4H, *J* = 6.8 Hz), 8.62 (d, 2H, *J* = 8.6 Hz), 7.60 (t, 2H, *J* = 7.1 Hz), 7.56 (t, 4H, *J* = 7.1 Hz), 6.81 (d, 2H, *J* = 8.6 Hz), 4.11 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 171.5, 171.3, 150.9, 136.8, 132.3, 131.1, 129.0, 128.7, 126.3, 114.6; IR (film) ν_{max} 3465, 3326, 3218, 2917, 2845, 1636, 1600, 1510, 1438, 1362, 1303, 1173, 764, 683 cm^{-1}; HRMS ESI-TOF *m/z* 325.1454 ($[M + H]^+$, $C_{21}H_{16}N_4$ + H^+ requires 325.1453).

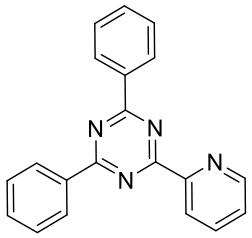
2-(3-Nitrophenyl)-4,6-diphenyl-1,3,5-triazine (12f).



12f

12f (6.62 mg, 94%, white solid): mp 194–196 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 9.56 (t, 1H, *J* = 1.9 Hz), 9.09 (dt, 1H, *J* = 7.7, 1.2 Hz), 8.77 (d, 4H, *J* = 7.1 Hz), 8.45 (ddd, 1H, *J* = 8.1, 2.2, 1.0 Hz), 7.76 (t, 1H, *J* = 7.9 Hz), 7.65 (t, 2H, *J* = 7.2 Hz), 7.60 (t, 4H, *J* = 7.4 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 172.2, 169.8, 148.9, 138.3, 135.8, 134.7, 133.1, 129.8, 129.2, 128.9, 126.9, 124.0; IR (film) ν_{max} 3088, 3061, 1591, 1515, 1506, 1438, 1366, 1348, 733, 693 cm^{-1}; HRMS ESI-TOF *m/z* 355.1193 ($[M + H]^+$, $C_{21}H_{14}N_4O_2$ + H^+ requires 355.1195).

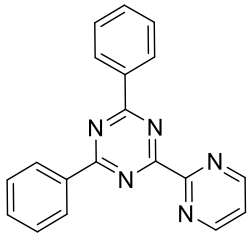
2,4-Diphenyl-6-(pyridin-2-yl)-1,3,5-triazine (12g).



12g

12g (5.39 mg, 87%, white solid): mp 210–212 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.97 (ddd, 1H, *J* = 4.7, 1.6, 0.8 Hz), 8.82–8.80 (m, 5H), 7.97 (td, 1H, *J* = 7.7, 1.7 Hz), 7.63 (t, 2H, *J* = 7.3 Hz), 7.58 (t, 4H, *J* = 7.3 Hz), 7.53 (ddd, 1H, *J* = 7.5, 4.7, 1.1 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 172.5, 171.2, 154.1, 150.6, 137.2, 136.0, 132.9, 129.4, 128.8, 126.3, 125.0; IR (film) ν_{max} 3061, 2921, 2849, 1591, 1524, 1452, 1371, 751, 688 cm^{-1}; HRMS ESI-TOF *m/z* = 311.1301 ([M + H]$^+$, $C_{20}H_{14}N_4$ + H$^+$ requires 311.1297).

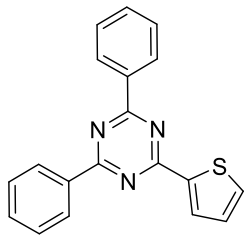
2,4-Diphenyl-6-(pyrimidin-2-yl)-1,3,5-triazine (12h).



12h

12h (6.02 mg, 97%, white solid): mp 200–203 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 9.12 (d, 2H, *J* = 4.8 Hz), 8.80 (d, 4H, *J* = 7.0 Hz), 7.63 (t, 2H, *J* = 7.3 Hz), 7.57 (t, 4H, *J* = 7.4 Hz), 7.54 (t, 1H, *J* = 4.8 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 173.0, 170.7, 162.6, 158.3, 135.6, 133.1, 129.5, 128.9, 122.2; IR (film) ν_{max} 3061, 3038, 1582, 1564, 1524, 1492, 1366, 755, 688 cm^{-1}; HRMS ESI-TOF *m/z* 312.1250 ([M + H]$^+$, $C_{19}H_{13}N_5$ + H$^+$ requires 312.1249).

2,4-Diphenyl-6-(thiophen-2-yl)-1,3,5-triazine (12i).

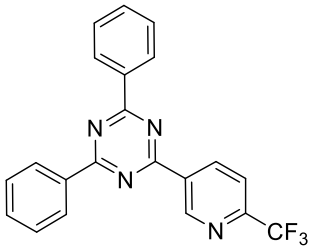


12i

12i (5.91 mg, 94%, white solid): mp 182–184 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.73 (dd, 4H, *J* = 8.3, 1.3 Hz), 8.38 (dd, 1H, *J* = 3.7, 1.2 Hz), 7.65 (dd, 1H, *J* = 4.9, 1.2 Hz), 7.61 (t, 2H, *J* = 7.2 Hz), 7.57 (t, 4H, *J* = 7.3 Hz), 7.25 (dd, 1H, *J* = 4.9, 3.7 Hz); ^{13}C NMR (151 MHz, $CDCl_3$,

298K) δ 171.7, 168.3, 142.3, 136.1, 132.7, 132.3, 131.6, 129.1, 128.8, 128.6; IR (film) ν_{max} 3097, 3043, 1578, 1542, 1519, 1438, 1398, 1371, 764, 697 cm^{-1}; HRMS ESI-TOF *m/z* 316.0908 ($[M + H]^+$, $C_{19}H_{13}N_3S + H^+$ requires 316.0908).

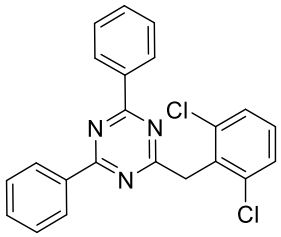
2,4-Diphenyl-6-(6-(trifluoromethyl)pyridin-3-yl)-1,3,5-triazine (12j).



12j

12j (7.43 mg, 91%, white solid): mp 166–168 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 9.97 (d, 1H, *J* = 1.6 Hz), 9.10 (dd, 1H, *J* = 8.0, 1.6 Hz), 8.71 (d, 4H, *J* = 7.0 Hz), 7.86 (d, 1H, *J* = 8.1 Hz), 7.63 (t, 2H, *J* = 7.3 Hz), 7.57 (t, 4H, *J* = 7.5 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 172.2, 169.1, 151.0, 150.8, 137.7, 135.5, 134.6, 133.2, 129.2, 128.9, 121.6 (q, *J* = 273 Hz), 120.4 (q, *J* = 2.6 Hz); IR (film) ν_{max} 3070, 1591, 1515, 1393, 1348, 1326, 1169, 1137, 1119, 1083, 760, 697, 683 cm^{-1}; HRMS ESI-TOF *m/z* 379.1170 ($[M + H]^+$, $C_{21}H_{13}F_3N_4 + H^+$ requires 379.1171).

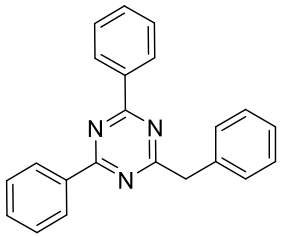
2-(2,6-Dichlorobenzyl)-4,6-diphenyl-1,3,5-triazine (12k).



12k

12k (7.65 mg, 98%, white solid): mp 151–152 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.56 (d, 4H, *J* = 7.1 Hz), 7.56 (t, 2H, *J* = 7.3 Hz), 7.50 (t, 4H, *J* = 7.5 Hz), 7.40 (d, 2H, *J* = 8.1 Hz), 7.23 (t, 1H, *J* = 8.1 Hz), 4.74 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 176.6, 171.5, 136.7, 136.1, 133.8, 132.6, 129.1, 128.73, 128.70, 128.1, 40.7; IR (film) ν_{max} 3052, 2917, 2849, 1515, 1429, 1357, 926, 787, 742, 683 cm^{-1}; HRMS ESI-TOF *m/z* 392.0718 ($[M + H]^+$, $C_{22}H_{15}Cl_2N_3 + H^+$ requires 392.0721).

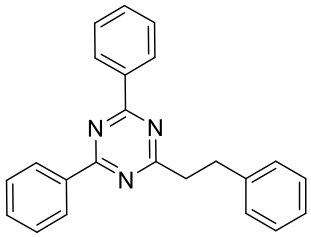
2-Benzyl-4,6-diphenyl-1,3,5-triazine (12l).



12l

12l (5.72 mg, 89%, white solid): mp 93–94 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.64 (d, 4H, *J* = 7.2 Hz), 7.58 (t, 2H, *J* = 7.3 Hz), 7.54–7.51 (m, 6H), 7.34 (t, 2H, *J* = 7.7 Hz), 7.26 (t, 1H, *J* = 7.4 Hz), 4.33 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 178.4, 171.7, 137.4, 136.1, 132.6, 129.6, 129.1, 128.8, 128.6, 126.9, 46.0; IR (film) ν_{max} 3065, 3029, 2917, 1587, 1519, 1447, 1362, 755, 710, 688 cm^{-1}; HRMS ESI-TOF *m/z* 324.1507 ($[M + H]^+$, $C_{22}H_{17}N_3 + H^+$ requires 324.1501).

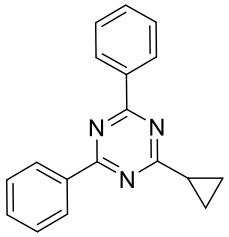
2-Phenethyl-4,6-diphenyl-1,3,5-triazine (12m).



12m

12m (6.60 mg, 98%, white solid): mp 77–79 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.66 (d, 4H, *J* = 7.1 Hz), 7.60 (t, 2H, *J* = 7.2 Hz), 7.55 (t, 4H, *J* = 7.4 Hz), 7.34 (d, 2H, *J* = 6.9 Hz), 7.31 (t, 2H, *J* = 7.6 Hz), 7.21 (t, 1H, *J* = 7.1 Hz), 3.38–3.35 (m, 2H), 3.34–3.31 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 179.1, 171.4, 141.4, 136.2, 132.6, 129.1, 128.8, 128.7, 128.6, 126.2, 40.8, 33.5; IR (film) ν_{max} 3061, 3025, 2921, 1587, 1519, 1447, 1366, 1178, 751, 692 cm^{-1}; HRMS ESI-TOF *m/z* 338.1663 ($[M + H]^+$, $C_{23}H_{19}N_3 + H^+$ requires 338.1657).

2-Cyclopropyl-4,6-diphenyl-1,3,5-triazine (12n).



12n

12n (5.36 mg, 98%, white solid): mp 81–83 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.63 (d, 4H, *J* = 7.1 Hz), 7.58 (t, 2H, *J* = 7.2 Hz), 7.53 (t, 4H, *J* = 7.4 Hz), 2.35–2.31 (m, 1H), 1.44–1.41 (m, 2H), 1.22–1.19 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 181.1, 170.8, 136.3, 132.4, 129.0,

128.7, 18.5, 11.9; IR (film) ν_{max} 3056, 2993, 2917, 1587, 1524, 1443, 1366, 935, 764, 706 cm^{-1}. HRMS ESI-TOF *m/z* 274.1350 ($[M + H]^+$, $C_{18}H_{15}N_3 + H^+$ requires 274.1344).

Reaction of 2 with 11l in protic solvent

A solution of amidine **11l** (4.0 mg, 0.03 mmol, 1.5 equiv) in CH_3CN/H_2O (V/V = 7:3, 0.5 mL) was added to **2** (4.68 mg, 0.02 mmol, 1 equiv), resulting in a suspension. The mixture was stirred at 25 °C for 2 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (17% EtOAc/hexanes) to provide **12l** (5.75 mg, 89%) as a white solid.

A solution of amidine **11l** (4.0 mg, 0.03 mmol, 1.5 equiv) in CH_3CN/H_2O (V/V = 3:7, 0.5 mL) was added to **2** (4.68 mg, 0.02 mmol, 1 equiv), resulting in a suspension. The mixture was stirred at 25 °C for 2 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (17% EtOAc/hexanes) to provide **12l** (6.09 mg, 94%) as a white solid.

Synthesis of 12l from 13a

Condition A

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with **13a** (4.59 mg, 0.03 mmol, 1.5 equiv) and the mixture was stirred at 25 °C for 48 h. The solvent was removed under a gentle stream of N_2 and the mixture was purified by PTLC (17% EtOAc/hexanes) to provide **12l** (3.02 mg, 47%) as a white solid.

Condition B

A 400 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous $CHCl_3$ (50 μL) was treated with **13a** (15.1 mg, 0.10 mmol, 5 equiv) and the mixture was stirred at 25 °C for 48 h. The solvent was removed under a gentle stream of N_2 and the mixture was purified by PTLC (17% EtOAc/hexanes) to provide **12l** (4.27 mg, 68%) as a white solid.

Synthesis of 12l from 13b

Condition A

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with **13b** (4.44 mg, 0.03 mmol, 1.5 equiv) and the mixture was warmed at 80 °C for 48 h in a sealed tube. The solvent was removed under a gentle stream of N_2 and the mixture was purified by PTLC (17% EtOAc/hexanes) to provide **12l** (2.23 mg, 35%) as a white solid.

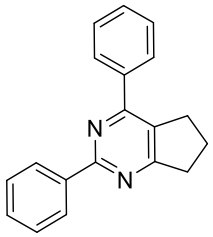
Condition B

A 400 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous $CHCl_3$ (50 μL) was treated with **13b** (14.9 mg, 0.10 mmol, 5 equiv) and the mixture was stirred at 25 °C for 48 h. The solvent was removed under a gentle stream of N_2 and the mixture was purified by PTLC (17% EtOAc/hexanes) to provide **12l** (2.72 mg, 43%) as a white solid.

General procedure for the synthesis of 15a-d

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with crushed 4Å molecular sieves (20 mg) and the corresponding enamine **14a-d** (0.024 mmol, 1.2 equiv). The mixture was stirred at 25 °C for 3 h, and then warmed at 60 °C for 24 h. The mixture was cooled and filtered through Celite. The solvent was removed under a gentle stream of N_2 and the mixture was purified by column chromatography (SiO_2, EtOAc/hexanes) to provide **15a-d** as desired products.

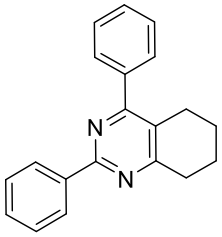
2,4-Diphenyl-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidine (15a).



15a

15a (4.53 mg, 83%, white solid): mp 72–73 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.55 (dd, 2H, *J* = 8.1, 1.5 Hz), 8.07 (d, 2H, *J* = 7.0 Hz), 7.55–7.46 (m, 6H), 3.25 (t, 2H, *J* = 7.3 Hz), 3.14 (t, 2H, *J* = 7.7 Hz), 2.22–2.17 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 176.7, 163.3, 159.5, 138.4, 138.3, 130.3, 130.0, 129.1, 128.9, 128.7, 128.6, 128.3, 34.6, 31.1, 23.1; IR (film) ν_{max} 3061, 2953, 2921, 2854, 1555, 1384, 1258, 1092, 1065, 1029, 804, 746, 697 cm^{-1}; HRMS ESI-TOF *m/z* 273.1396 ([M + H]$^+$, $C_{19}H_{16}N_2$ + H^+ requires 273.1392).

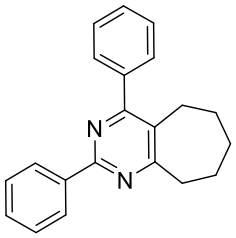
2,4-Diphenyl-5,6,7,8-tetrahydroquinazoline (15b).



15b

15b (2.47 mg, 43%, white solid): mp 103–105 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.47 (dd, 2H, *J* = 8.2, 1.6 Hz), 7.66 (dd, 2H, *J* = 7.4, 2.0 Hz), 7.51–7.42 (m, 6H), 3.04 (t, 2H, *J* = 6.6 Hz), 2.80 (t, 2H, *J* = 6.2 Hz), 1.99–1.95 (m, 2H), 1.81–1.77 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.7, 165.1, 161.4, 138.7, 138.2, 130.0, 129.04, 128.97, 128.4, 128.2, 128.1, 125.4, 32.8, 27.0, 22.9, 22.5; IR (film) ν_{max} 3052, 2930, 2858, 1542, 1497, 1420, 1398, 1258, 1164, 1029, 751, 692 cm^{-1}; HRMS ESI-TOF *m/z* 287.1552 ([M + H]$^+$, $C_{20}H_{18}N_2$ + H^+ requires 287.1548).

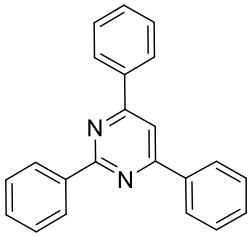
2,4-Diphenyl-6,7,8,9-tetrahydro-5*H*-cyclohepta[*d*]pyrimidine (15c).



15c

15c (3.59 mg, 60%, white solid): mp 119–121 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.49 (dd, 2H, *J* = 8.0, 1.6 Hz), 7.59 (dd, 2H, *J* = 8.1, 1.4 Hz), 7.53–7.41 (m, 6H), 3.18–3.16 (m, 2H), 2.89–2.87 (m, 2H), 1.96–1.92 (m, 2H), 1.83 (tt, 2H, *J* = 11.0, 4.6 Hz), 1.73-1.69 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 172.9, 164.5, 161.2, 139.4, 138.2, 130.6, 130.1, 129.4, 128.9, 128.5, 1284, 128.2, 39.5, 32.4, 29.3, 27.9, 26.3; IR (film) ν_{max} 3056, 2921, 2854, 1542, 1496, 1447, 1393, 1174, 764, 695 cm^{-1}; HRMS ESI-TOF *m/z* 301.1711 ($[M + H]^+$, $C_{21}H_{20}N_2 + H^+$ requires 301.1705).

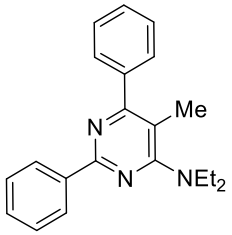
2,4,6-Triphenylpyrimidine (15d).



15d

15d (2.79 mg, 45%, white solid): mp 151–153 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.74 (dd, 2H, *J* = 8.1, 1.5 Hz), 8.30 (dd, 4H, *J* = 8.0, 1.6 Hz), 8.03 (s, 1H), 7.59–7.53 (m, 9H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 164.9, 164.7, 138.3, 137.7, 130.9, 130.8, 129.1, 128.62, 128.60, 127.4, 110.5; IR (film) ν_{max} 3056, 2926, 1591, 1573, 1523, 1492, 1362, 742, 683 cm^{-1}; HRMS ESI-TOF *m/z* 309.1391 ($[M + H]^+$, $C_{22}H_{16}N_2 + H^+$ requires 309.1392).

N,N-Diethyl-5-methyl-2,6-diphenylpyrimidin-4-amine (17a).

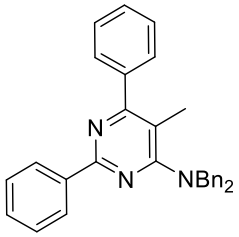


17a

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with ynamine **16a** (3.33 mg, 0.03 mmol, 1.5 equiv). The mixture was stirred at 25 °C for 1 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by column

chromatography (SiO_2, 10% EtOAc/hexanes) to provide **17a** (5.72 mg, 90%) as a white solid: mp 111–113 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.50 (dd, 2H, *J* = 8.1, 1.6 Hz), 7.70 (dd, 2H, *J* = 8.1, 1.3 Hz), 7.48–7.42 (m, 6H), 3.57 (q, 4H, *J* = 7.0 Hz), 2.23 (s, 3H), 1.30 (t, 6H, *J* = 7.0 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 166.4, 165.9, 159.9, 140.3, 138.9, 129.9, 129.8, 128.8, 128.3, 128.2, 128.1, 112.4, 44.2, 18.0, 13.6; IR (film) ν_{max} 3060, 2966, 2926, 2867, 1546, 1492, 1402, 1353, 1128, 1011, 764, 701 cm^{-1}; HRMS ESI-TOF *m/z* 318.1973 ([M + H]$^+$, $C_{21}H_{23}N_3$ + H^+ requires 318.1970).

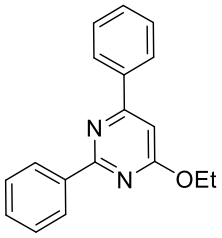
N,N-Dibenzyl-5-methyl-2,6-diphenylpyrimidin-4-amine (17b).



17b

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with ynamine **16b** (7.05 mg, 0.03 mmol, 1.5 equiv). The mixture was stirred at 25 °C for 24 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by column chromatography (SiO_2, 17% EtOAc/hexanes) to provide **17b** (8.09 mg, 92%) as a white solid: mp 126–128 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.44 (m, 2H), 7.68 (dd, 2H, *J* = 8.1, 1.4 Hz), 7.48–7.45 (m, 3H), 7.44–7.41 (m, 3H), 7.33–7.32 (m, 8H), 7.28–7.24 (m, 2H), 4.78 (s, 4H), 2.33 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 166.74, 166.72, 160.2, 140.0, 138.6, 138.5, 130.0, 129.9, 129.0, 128.7, 128.29, 128.26, 128.2, 127.9, 127.2, 112.5, 53.1, 18.0; IR (film) ν_{max} 3065, 3020, 2912, 1537, 1497, 1452, 1398, 1357, 1263, 1169, 1007, 737, 701 cm^{-1}; HRMS ESI-TOF *m/z* 442.2285 ([M + H]$^+$, $C_{31}H_{27}N_3$ + H^+ requires 442.2283).

4-Ethoxy-2,6-diphenylpyrimidine (19).

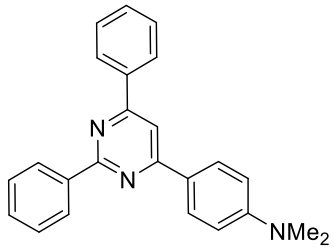


19

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous $CHCl_3$ (0.5 mL) was treated with ketene acetal **18** (11.6 mg, 0.1 mmol, 5 equiv). The mixture was heated at 60 °C for 24 h in a sealed tube. The solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (SiO_2, 25% EtOAc/hexanes) to provide **19** (3.30 mg, 60%) as a white solid: mp 61–62 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.59 (dd, 2H, *J* = 7.9, 1.9 Hz), 8.18 (dd, 2H, *J* = 7.9, 1.6 Hz), 7.53–7.49 (m, 6H), 7.01 (s, 1H), 4.62 (q, 2H, *J* = 7.1 Hz), 1.49 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 170.6, 164.9, 164.1, 138.1, 137.5, 130.7, 130.6, 128.9, 128.49, 128.48,

127.3, 101.4, 62.5, 14.7; IR (film) ν_{max} 3061, 2975, 2926, 1591, 1568, 1541, 1411, 1375, 1339, 1209, 1025, 760, 697 cm^{-1}; HRMS ESI-TOF *m/z* 277.1341 ($[M + H]^+$, $C_{18}H_{16}N_2O + H^+$ requires 277.1341).

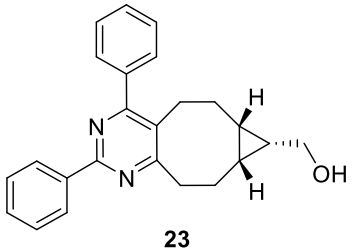
4-(2,6-Diphenylpyrimidin-4-yl)-*N*,*N*-dimethylaniline (21).



21

Compound **2** (4.68 mg, 0.02 mmol) was treated with **20** (100 μL) and the mixture was warmed at 80 °C for 72 h. The mixture was cooled to room temperature and purified by PTLC (SiO_2, 25% EtOAc/hexanes) to provide **21** (2.01 mg, 28%) as a yellow solid: mp 162–164 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.73 (dd, 2H, *J* = 8.2, 1.4 Hz), 8.28 (dd, 2H, *J* = 8.2, 1.4 Hz), 8.25 (d, 2H, *J* = 9.0 Hz), 7.92 (s, 1H), 7.57–7.49 (m, 6H), 6.86 (d, 2H, *J* = 7.4 Hz), 3.08 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 164.6, 164.3, 164.2, 138.7, 138.2, 130.6, 130.5, 129.0, 128.59, 128.55, 128.5, 127.3, 112.2, 108.8, 40.5; IR (film) ν_{max} 3056, 2953, 2912, 2849, 2804, 1613, 1587, 1564, 1519, 1492, 1357, 1200, 1169, 818, 755, 692 cm^{-1}; HRMS ESI-TOF *m/z* 352.1817 ($[M + H]^+$, $C_{24}H_{21}N_3 + H^+$ requires 352.1814).

((6aS,7S,7aR)-2,4-Diphenyl-6,6a,7,7a,8,9-hexahydro-5*H*-cyclopropa[5,6]cycloocta[1,2-*d*]pyrimidin-7-yl)methanol (23).



23

A 400 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous $CHCl_3$ (50 μL) was treated with **22** (12.00 mg, 0.08 mmol, 4 equiv). The mixture was stirred at 25 °C for 48 h. The solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (SiO_2, EtOAc) to provide **23** (6.93 mg, 97%) as a white solid: mp 93–95 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.48 (dd, 2H, *J* = 7.9, 1.7 Hz), 7.56 (dd, 2H, 7.9, 1.5 Hz), 7.51–7.43 (m, 6H), 3.80 (dd, 1H, 11.4, 7.4 Hz), 3.73 (dd, 1H, 11.3, 7.4 Hz), 3.34–3.29 (m, 1H), 3.18–3.14 (m, 1H), 3.01–2.96 (m, 1H), 2.80–2.76 (m, 1H), 1.69–1.52 (m, 2H), 1.26 (s, 1H), 1.20–1.12 (m, 2H), 1.08–0.99 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 171.7, 165.8, 139.6, 138.1, 130.2, 129.7, 129.0, 128.9, 128.5, 128.4, 128.3, 59.7, 36.8, 27.1, 24.7, 23.3, 22.6, 21.7, 19.7; IR (film) ν_{max} 3375, 3056, 2921, 2872, 1542, 1393, 1263, 1025, 769, 733, 697 cm^{-1}; HRMS ESI-TOF *m/z* 357.1968 ($[M + H]^+$, $C_{24}H_{24}N_2O + H^+$ requires 357.1967).

V. Comparison of reactivity between 2 and 24

(a) Reaction with amidine **11l**

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with amidine **11l** (5.10 mg, 0.03 mmol, 1.5 equiv). The mixture was stirred at 25 °C for 2 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by column chromatography (SiO_2, 17% EtOAc/hexanes) to provide **12l (**5.72 mg, 89%) as a white solid.

A 40 mM solution of **24** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous $CHCl_3/CH_3CN$ (V/V = 1:1, 0.5 mL) was treated with amidine **11l** (4.0 mg, 0.03 mmol, 1.5 equiv). No conversion was observed after 2 h.

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) and **24** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous $CHCl_3/CH_3CN$ (V/V = 1:1, 0.5 mL) was treated with amidine **11l** (2.68 mg, 0.03 mmol, 1.0 equiv). The mixture was stirred at 25 °C for 2 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (SiO_2, 17% EtOAc/hexanes) to provide **12l (**5.94 mg, 92%) as a white solid.

(b) Reaction with cyclooctyne **22**

A 5 mM solution of **24** (2.34 mg, 0.01 mmol, 1 equiv) in anhydrous CH_3CN (2 mL) was treated with cyclooctyne **22** (6.00 mg, 0.04 mmol, 4 equiv). The mixture was stirred at 25 °C for 10 min, and the solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (SiO_2, EtOAc) to provide **25** (3.32 mg, 93%) as a white solid.

A 5 mM solution of **2** (2.34 mg, 0.01 mmol, 1 equiv) in anhydrous CH_3CN (2 mL) was treated with cyclooctyne **22** (6.00 mg, 0.04 mmol, 4 equiv). No conversion was observed after 48 h.

A 5 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) and **24** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (4 mL) was treated with cyclooctyne **22** (3.00 mg, 0.02 mmol, 1 equiv). The mixture was stirred at 25 °C for 30 min, and the solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (SiO_2, EtOAc) to provide **25** (6.96 mg, 98%) as a white solid.

(c) Reaction with ynamine **16a**

A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with ynamine **16a** (3.33 mg, 0.03 mmol, 1.5 equiv). The mixture was stirred at 25 °C for 1 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to provide **17a** (5.72 mg, 90%) as a white solid.

A 40 mM solution of **24** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous $CHCl_3/CH_3CN$ (V/V = 1:1, 0.5 mL) was treated with ynamine **16a** (3.33 mg, 0.03 mmol, 1.5 equiv). The mixture was stirred at 25 °C for 1 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (SiO_2, 50% EtOAc/hexanes) to provide **26** (6.05 mg, 95%) as a white solid.

A 20 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) and **24** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous $CHCl_3/CH_3CN$ (V/V = 1:1, 1 mL) was treated with ynamine **16a** (2.22 mg, 0.02 mmol, 1.0 equiv). The mixture was stirred at 25 °C for 1 h, and the solvent was removed under a gentle

stream of N_2. The mixture was analyzed by ^1H NMR using mesitylene as an internal standard, resulting a 15% NMR yield of **17a** and a 53% NMR yield of **26**.

VI. LC-MS analysis of 2

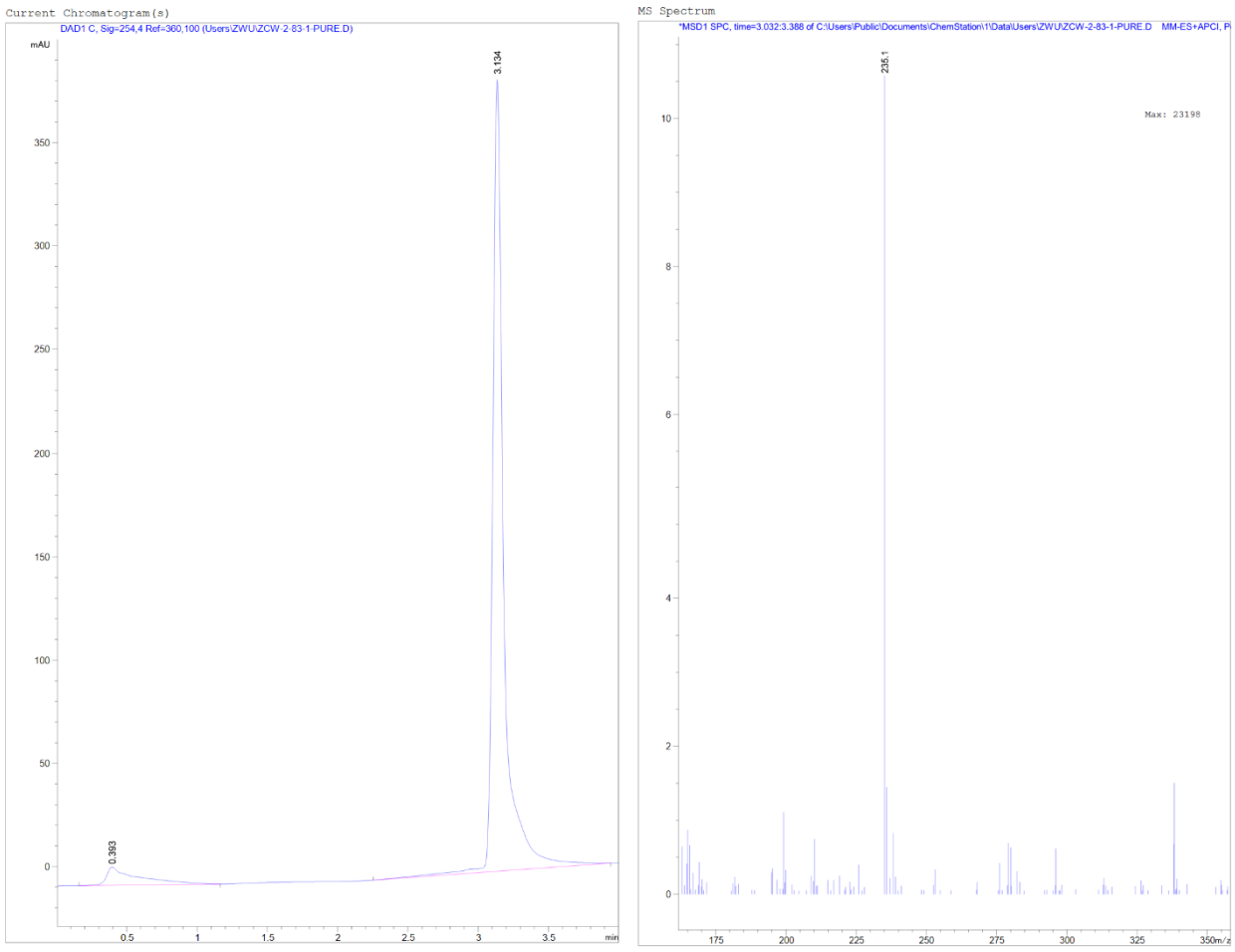


Figure S1. LC trace (left) and MS spectra (right) of 2.

VII. Decomposition kinetics of 2

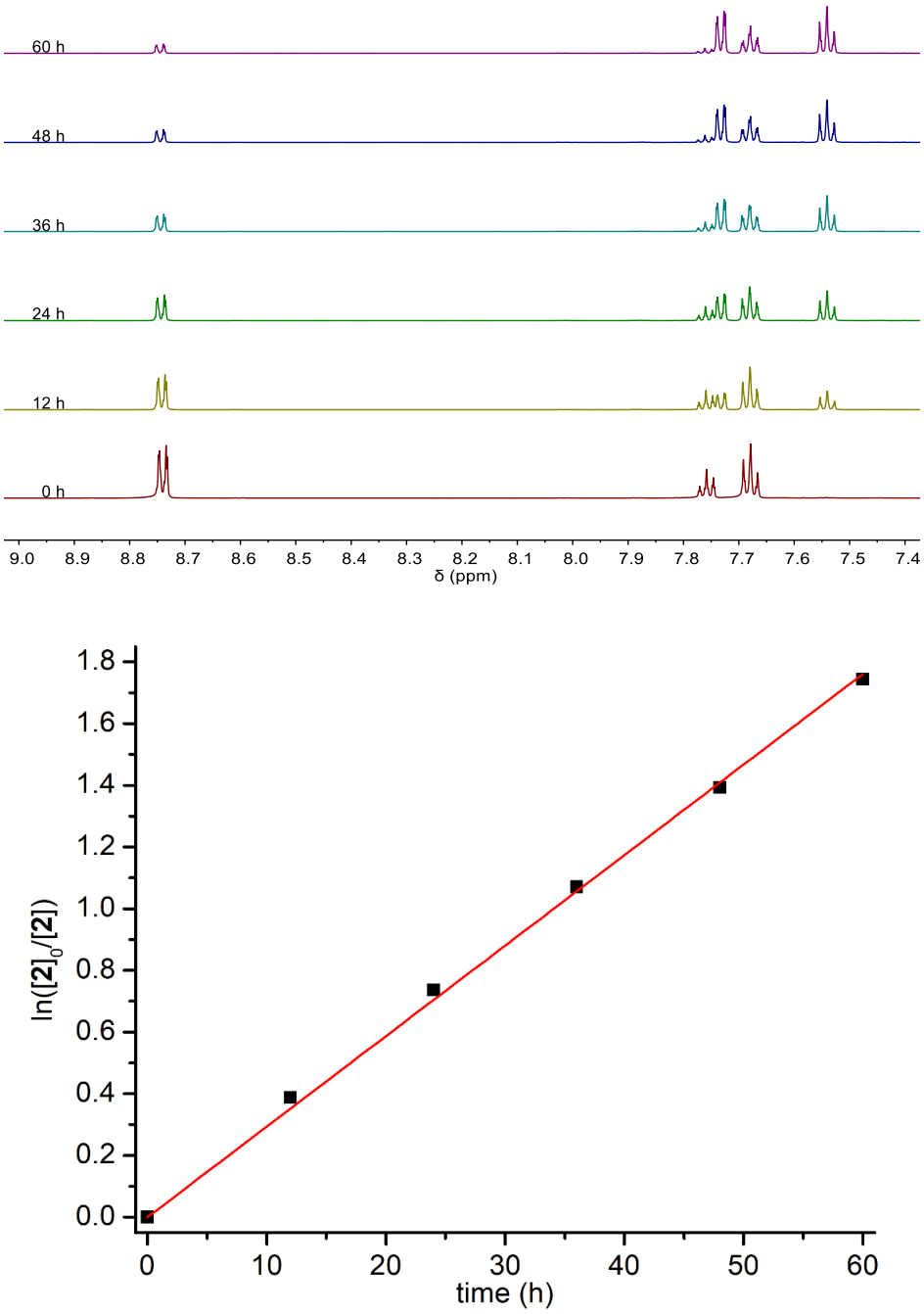


Figure S2. Kinetic study of decomposition of 2 (top: NMR spectra; bottom: linear fitting).

Experiment performed at 80 °C in CD_3CN. ^1H NMR spectra is recorded at 12 h intervals for 60 h. First order kinetics with k = (0.0293 ± 0.0003) h^{-1} (8.15 × 10^{-6} s^{-1}) was fitted with R^2 = 0.9995.

VIII. Kinetic study of the reaction between 2 and 11k

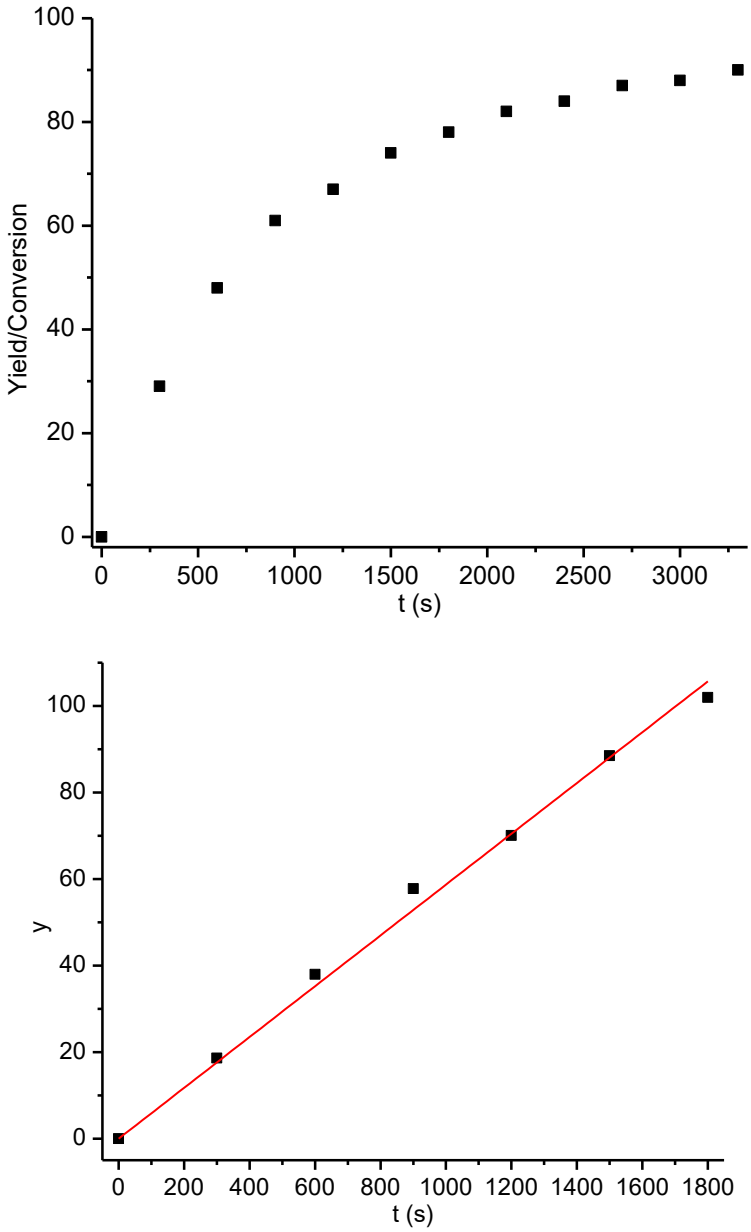


Figure S3. Kinetic study of reaction between 2 and 11k (top: reaction progress over time; bottom: linear fitting).

The kinetic study of the reaction between **2** (10 mM) and **11k** (20 mM) was conducted in CD_3CN at 25 °C. ^1H NMR spectra was recorded at 5 min intervals for 55 min. The second order rate constant was fitted by the following equation with the result of k = (5.87 ± 0.10)*10^{-2} $M^{-1}\cdot s^{-1}$ (R^2 = 0.9981).

$$y = \frac{1}{[\mathbf{2}]_0 - [\mathbf{11k}]_0} ln \frac{[\mathbf{11k}]_0([\mathbf{2}]_0 - [\mathbf{12k}])}{[\mathbf{2}]_0([\mathbf{11k}]_0 - [\mathbf{12k}])} = kt$$

IX. ^{15}N labeling experiments

Amidine $^{15}N_2$-**11l** was prepared as reported.[S5] A 40 mM solution of **2** (4.68 mg, 0.02 mmol, 1 equiv) in anhydrous CH_3CN (0.5 mL) was treated with $^{15}N_2$-**11l** (4.1 mg, 0.03 mmol, 1.5 equiv). The mixture was stirred at 25 °C for 2 h, and the solvent was removed under a gentle stream of N_2. The residue was purified by PTLC (17% EtOAc/hexanes) to provide ^{15}N-**12l** (6.06 mg, 94%) as a white solid: ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ 8.68–8.64 (m, 4H), 7.61–7.57 (m, 2H), 7.56–7.52 (m, 6H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.29–7.26 (m, 1H), 4.34 (d, *J* = 2.5 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ 177.8 (d, *J* = 1.7 Hz), 171.1 (m), 136.8, 135.54, 135.53 (d, *J* = 8.4 Hz), 132.0, 129.0, 128.5, 128.1, 128.0, 126.3, 45.4 (d, *J* = 9.2 Hz); HRMS ESI-TOF *m/z* 325.1475 ([M + H]$^+$, $C_{22}H_{17}N_2[^{15}N]$ + H$^+$ requires 325.1466).

Determination of ^{15}N content by HRMS: The reaction was conducted twice. From each reaction, four samples in parallel were subjected to HRMS analysis, where the ratio of signal intensity (peak area) of $C_{22}H_{17}N_3$ (M + H$^+$, 324), $C_{22}H_{17}N_2[^{15}N]$ (M + H$^+$, 325), and $C_{22}H_{17}N[^{15}N_2]$ was used to determine the ^{15}N content in the reaction product with the existence of natural occurring isotopes taken into account. Synthetic $C_{22}H_{17}N_3$ was also subjected to HRMS analysis as a control. The results are listed in Table S3. A 1.07–1.08 ratio of ^{15}N incorporation was determined by HRMS.

Table S3. HRMS analysis of ^{15}N labeling experiment.

Compound		Sample	m/z = 324	m/z = 325	m/z = 326
^{15}N-**12l**	Experiment 1	1	0.7%	91.2%	8.1%
		2	0.6%	90.3%	9.1%
		3	0.6%	91.7%	7.7%
		4	0.6%	91.1%	8.3%
		Average	0.6%	91.1%	8.3%
	Experiment 2	1	0.9%	92.1%	6.9%
		2	0.7%	93.0%	6.3%
		3	0.9%	91.7%	7.5%
		4	0.6%	92.1%	7.3%
		Average	0.8%	92.2%	7.0%
12l		1	100.2%	0.2%	-0.4%
		2	100.9%	-0.5%	-0.3%
		3	99.7%	0.8%	-0.4%
		4	100.0%	0.5%	-0.5%
		Average	100.2%	0.2%	-0.4%

The potential impact of the $^{15}NH_3$ released in the cycloaddition was also investigated, where no ^{15}N incorporation was observed when triazine **12l** or the reaction between **2** and **11l** was treated with excess $^{15}NH_3$. This observation indicates that the incorporation of ^{15}N only results from the reaction between tetrazine **2** and amidine $^{15}N_2$-**11l**.

Determination of ^{15}N content by ^{13}C NMR:

^{13}C NMR of the labeling reaction product was recorded and the signal of ^{13}C(a) (δ 135.5 ppm) was analyzed (Figure S4). A singlet (center) was observed when no ^{2}J (^{13}C-^{15}N) is present, representing a ^{13}C close to a ^{14}N. A doublet (sides) was also observed where ^{2}J (^{13}C-^{15}N, 8.4 Hz) is present, representing a ^{13}C close to a ^{15}N. The ratio between the intensity of the singlet and doublet was determined and provided the presence of ^{14}N (47%) and ^{15}N (53%). A 1.06 ratio of ^{15}N incorporation was determined by NMR.

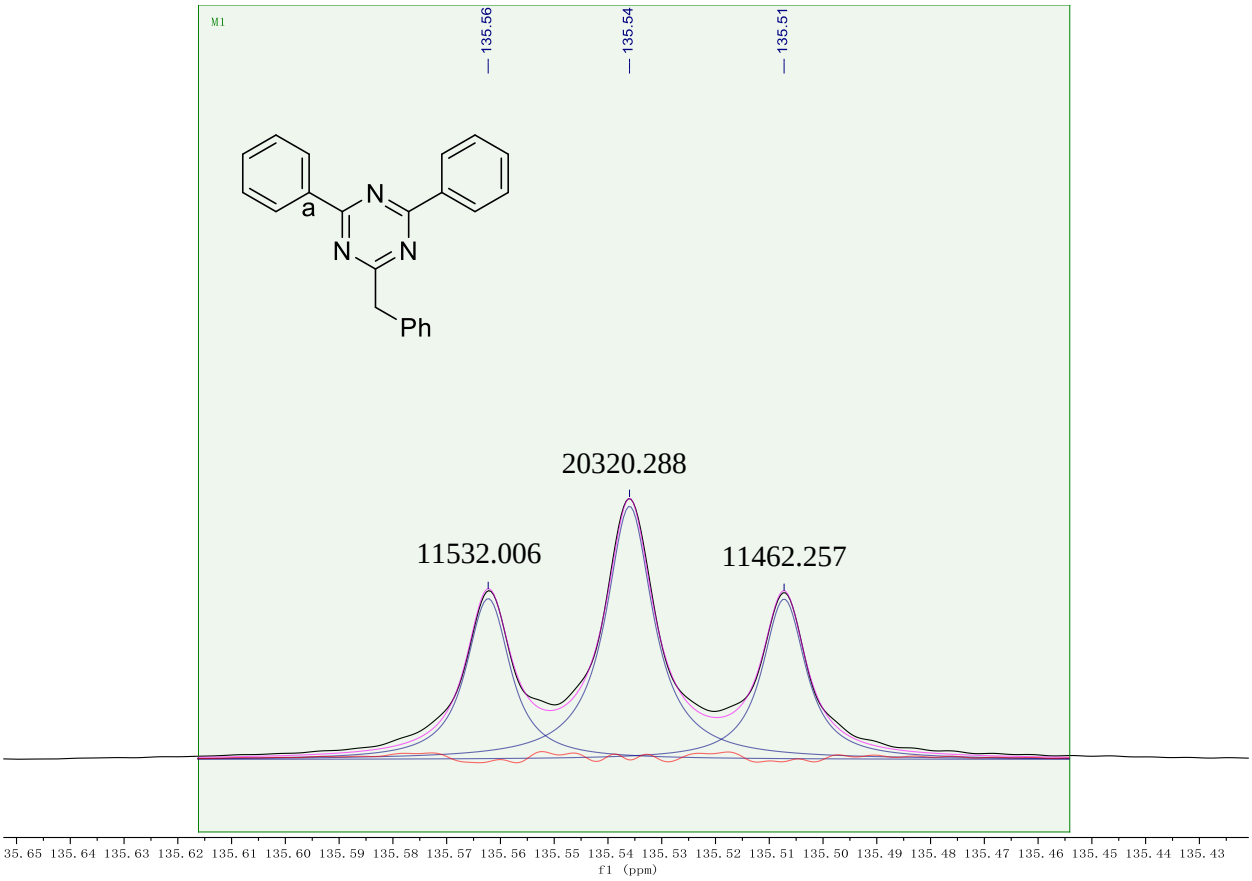


Figure S4. Determination of ^{15}N incorporation by ^{13}C NMR.

X. X-ray crystal data and structure refinement for 8, 10 and 2

X-ray information for 8

Crystal data and structure refinement for **8**.

Empirical formula	C53 H33 Cl3 N16 O16	
Molecular formula	2(C26 H16 N8 O8), C1 H1 Cl3	
Formula weight	1256.30	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 13.2215(4) Å	α= 90°.
	b = 31.0295(7) Å	β= 115.2070(10)°.
	c = 14.5700(4) Å	γ = 90°.
Volume	5408.2(3) $Å^3$	
Z	4	
Density (calculated)	1.543 Mg/m^3	
Absorption coefficient	0.259 mm^{-1}	
F(000)	2568	
Crystal size	0.15 x 0.125 x 0.125 mm^3	
Crystal color, habit	orange block	
Theta range for data collection	1.312 to 25.349°.	
Index ranges	-15<=h<=15, -37<=k<=36, -17<=l<=16	
Reflections collected	59891	
Independent reflections	9895 [R(int) = 0.0447]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.4903 and 0.4553	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9895 / 6 / 806	
Goodness-of-fit on F^2	1.020	
Final R indices [I>2sigma(I)]	R1 = 0.0496, wR2 = 0.1173	
R indices (all data)	R1 = 0.0700, wR2 = 0.1285	
Largest diff. peak and hole	1.110 and -0.999 $e.Å^{-3}$	

X-ray information for 10

Crystal data and structure refinement for **10**.

Empirical formula	C19 H20 N4 O2	
Formula weight	336.39	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 13.3231(7) Å	α= 90°.
	b = 9.9116(6) Å	β= 104.338(3)°.
	c = 14.2356(7) Å	γ = 90°.
Volume	1821.30(17) $Å^3$	
Z	4	
Density (calculated)	1.227 Mg/m^3	
Absorption coefficient	0.082 mm^{-1}	
F(000)	712	
Crystal size	0.25 x 0.17 x 0.1 mm^3	
Crystal color, habit	yellow block	
Theta range for data collection	2.954 to 28.301°.	
Index ranges	-17<=h<=17, -11<=k<=13, -18<=l<=18	
Reflections collected	14723	
Independent reflections	4497 [R(int) = 0.0437]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.6822	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4497 / 0 / 229	
Goodness-of-fit on F^2	1.013	
Final R indices [I>2sigma(I)]	R1 = 0.0474, wR2 = 0.0984	
R indices (all data)	R1 = 0.0793, wR2 = 0.1116	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.334 and -0.341 $e.Å^{-3}$	

X-ray information for 2

Crystal data and structure refinement for **2**.

Empirical formula	C14 H10 N4	
Molecular formula	C14 H10 N4	
Formula weight	234.26	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 3.8362(5) Å	α= 90°.
	b = 13.7755(18) Å	β= 90°.
	c = 20.821(2) Å	γ = 90°.
Volume	1100.3(2) $Å^3$	
Z	4	
Density (calculated)	1.414 Mg/m^3	
Absorption coefficient	0.089 mm^{-1}	
F(000)	488	
Crystal size	0.25 x 0.04 x 0.04 mm^3	
Crystal color, habit	yellow needle	
Theta range for data collection	1.773 to 25.661°.	
Index ranges	-4<=h<=4, -16<=k<=16, -25<=l<=15	
Reflections collected	7200	
Independent reflections	2090 [R(int) = 0.0520]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7454 and 0.6903	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2090 / 0 / 163	
Goodness-of-fit on F^2	1.002	
Final R indices [I>2sigma(I)]	R1 = 0.0475, wR2 = 0.0842	
R indices (all data)	R1 = 0.0825, wR2 = 0.0949	
Largest diff. peak and hole	0.181 and -0.193 $e.Å^{-3}$	

XI. Differential Scanning Calorimetry Characterization of 8 and 2

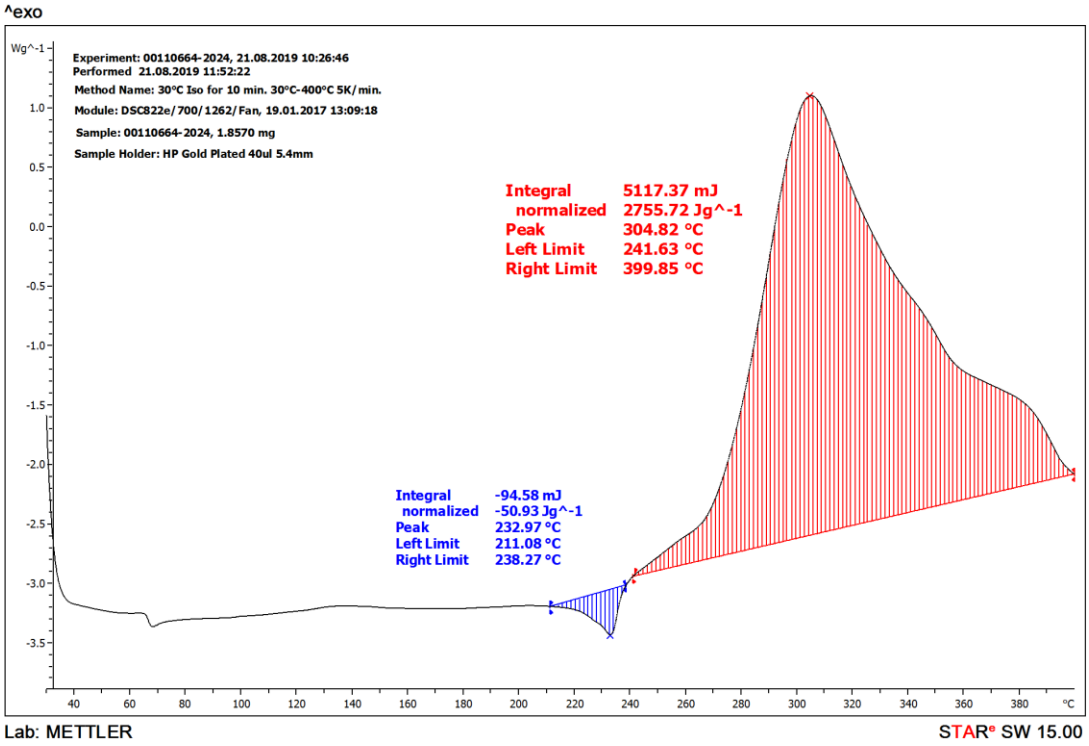


Figure S5. DSC measurement of compound 8.

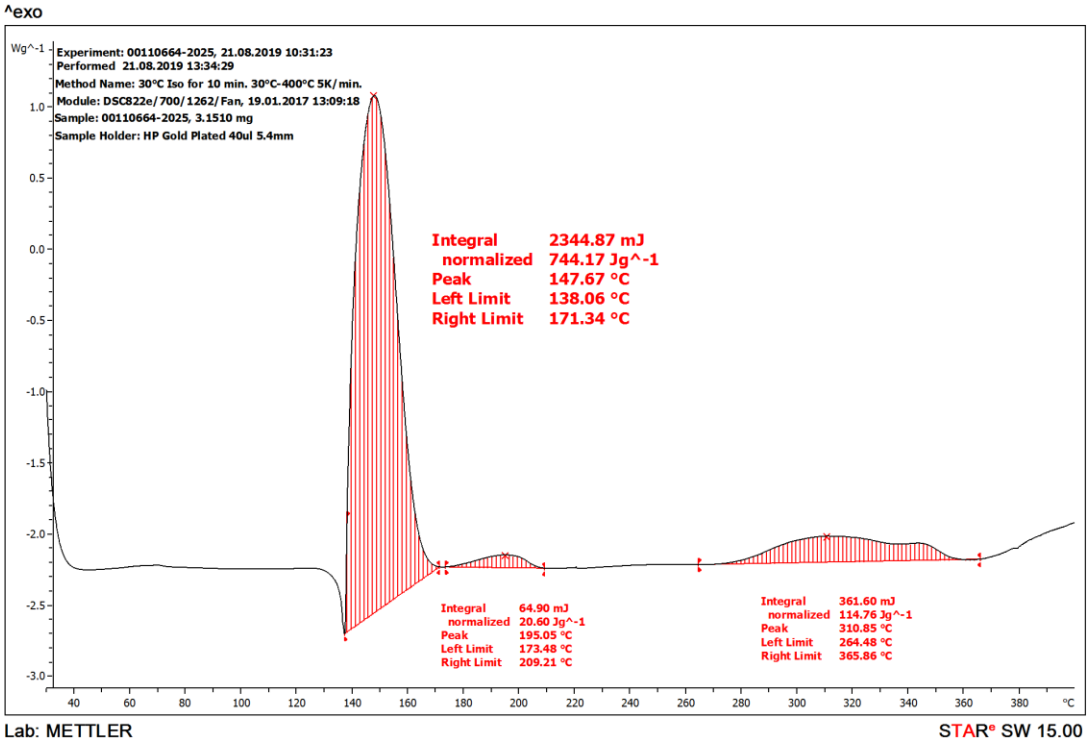


Figure S6. DSC measurement of compound 2.

XII. References

S1. (a) Zhao, X.; Liu, D.; Xie, F.; Zhang, W. *Tetrahedron* **2009**, *65*, 512. (b) Taylor, E. C.; Dumas, D. J. *J. Org. Chem.* **1981**, *46*, 1394. (c) White, W. A.; Weingarten, H. *J. Org. Chem.* **1967**, *32*, 213. (d) Carlson, R.; Nilsson, A. *Acta Chim. Scand.* **1984**, *38b*, 49. (e) Verkruijsse, H.; Bos, H.; de Noten, L.; Brandsma, L. *J. Royal Netherlands Chem. Soc.* **1981**, *100*, 244. (f) Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thairivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 1988.

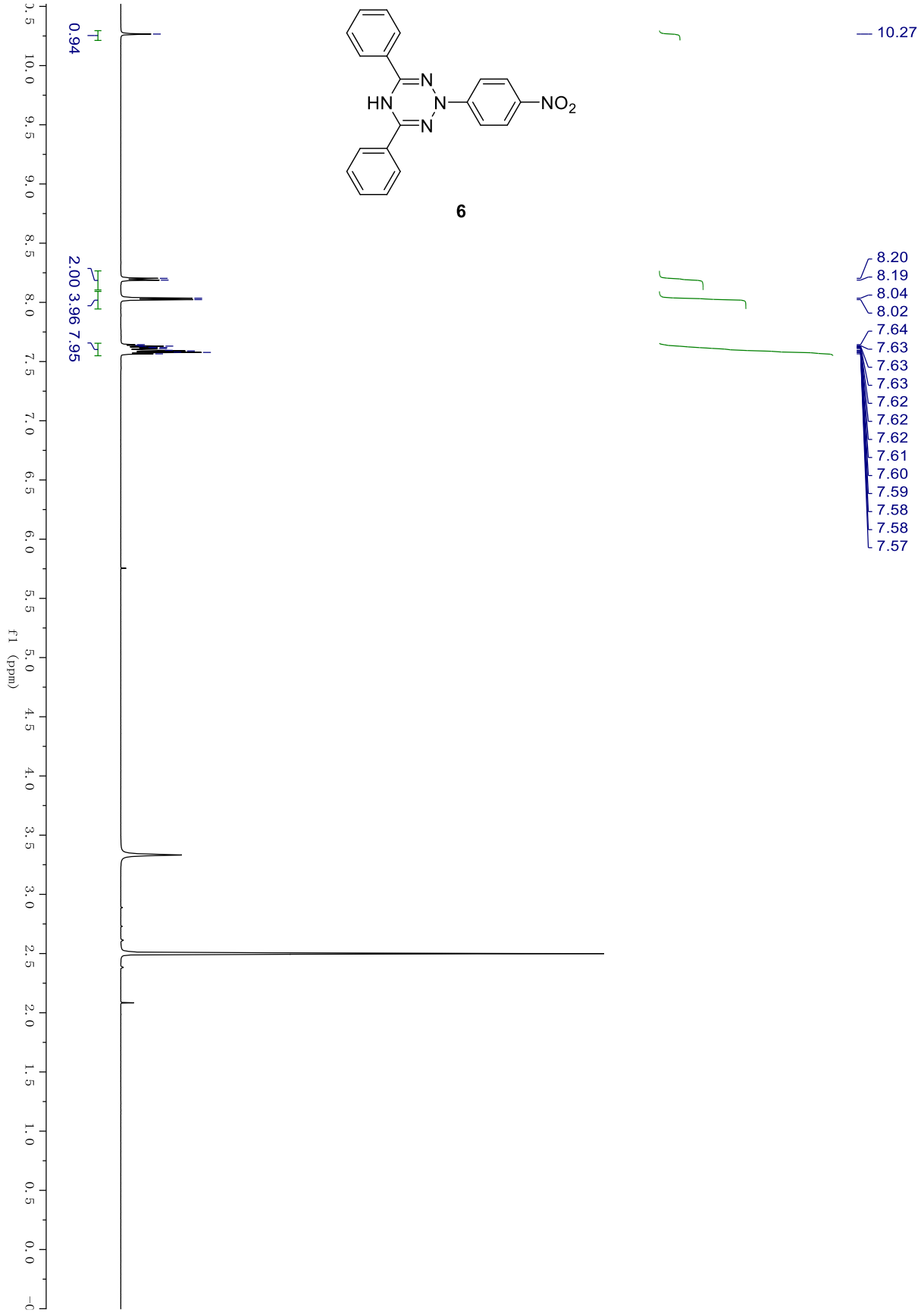
S2. Gaussian 09, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

S3. (a) Butler, R. N.; Cunningham, D.; McArdle, P.; O'Halloran, G. A. *J. Chem. Soc., Chem. Commun.* **1988**, *3*, 232. (b) Butler, R. N.; Evans, A. M.; McNeela, E. M.; Cunningham, D.; McArdIe, P. *J. Chem. Soc. Perkin Trans. 1*. **1990**, 2527.

S4. Muathen, H. A. *Indian J. Chem.* **1991**, *30B*, 521.

S5. Charushin, V. N.; van der Plas, H. C. *J. Org. Chem*. **1983**, *48*, 2667.

XIII. Spectra


0.94
2.00
3.96
7.95
10.27
8.20
8.19
8.04
8.02
7.64
7.63
7.63
7.63
7.62
7.62
7.62
7.61
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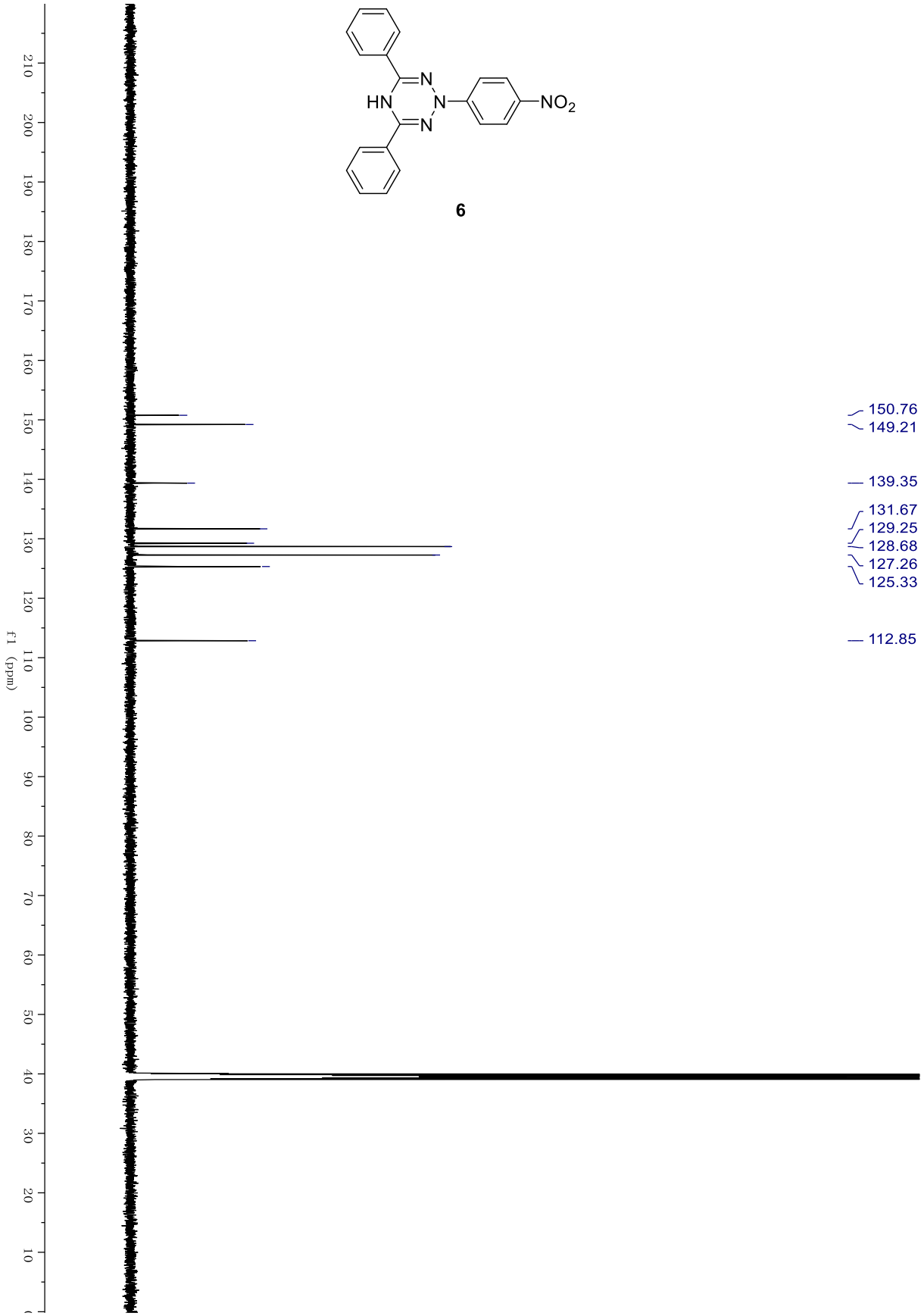
7.59
7.58
7.58
7.57
HN
N
N
N
NO2
6
f1 (ppm)


HN
N
N
N
NO2
6
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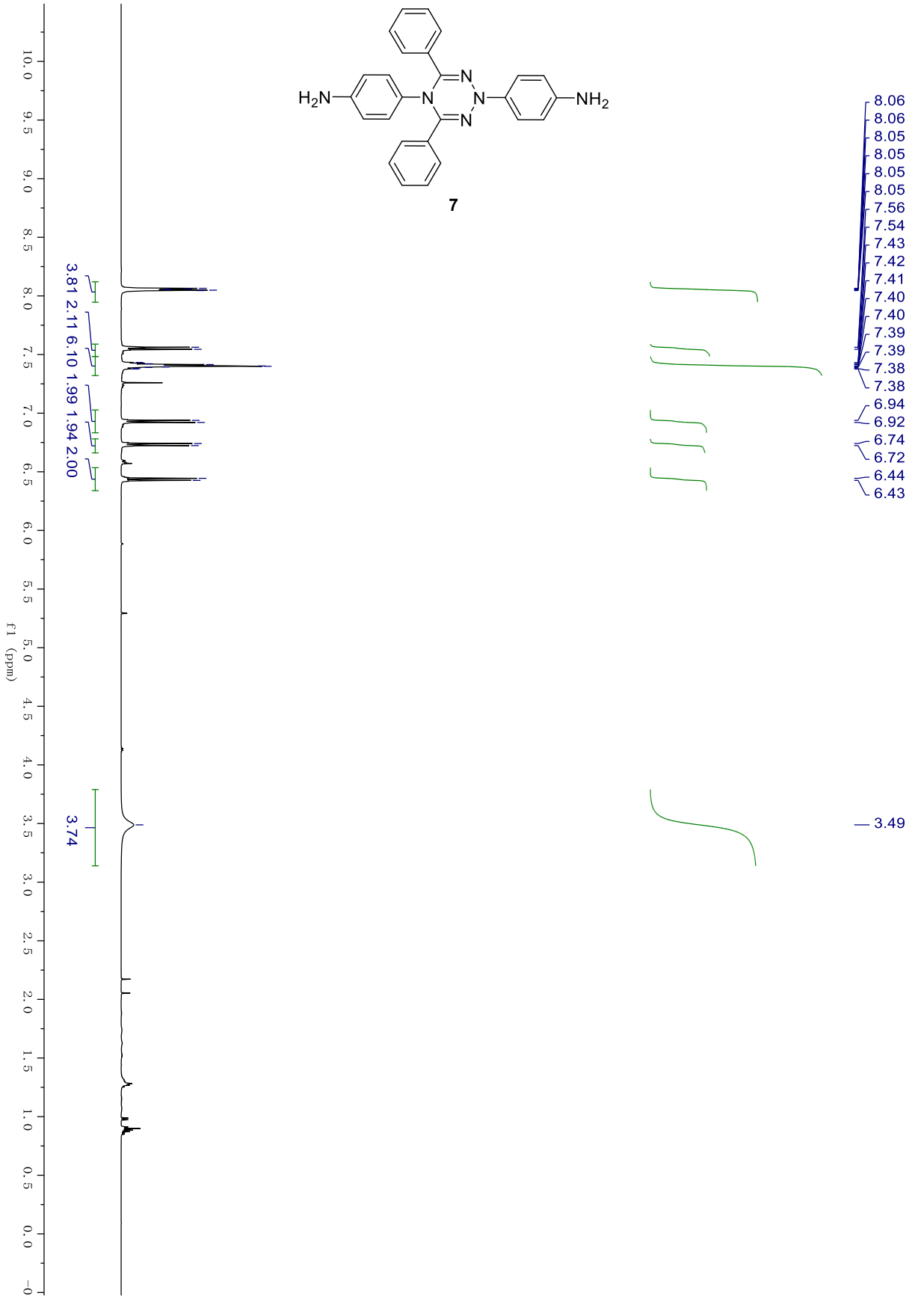
149.21
139.35
131.67
129.25
128.68
127.26
125.33
112.85
f1 (ppm)


7
8.06
8.06
8.05
8.05
8.05
8.05
7.56
7.54
7.43
7.42
7.41
7.40
7.40
7.39
7.39
7.38
7.38
6.94
6.92
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6.43
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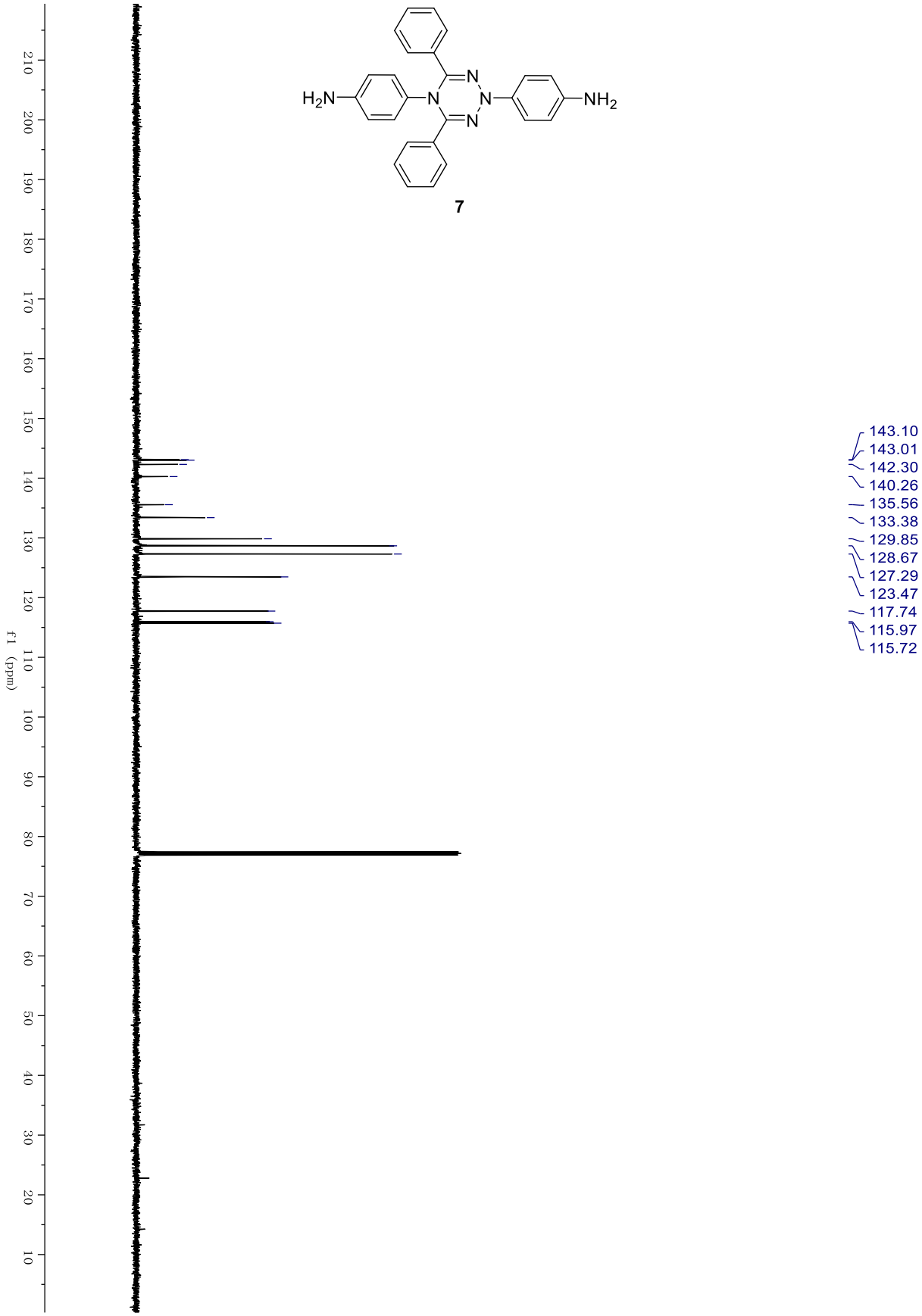
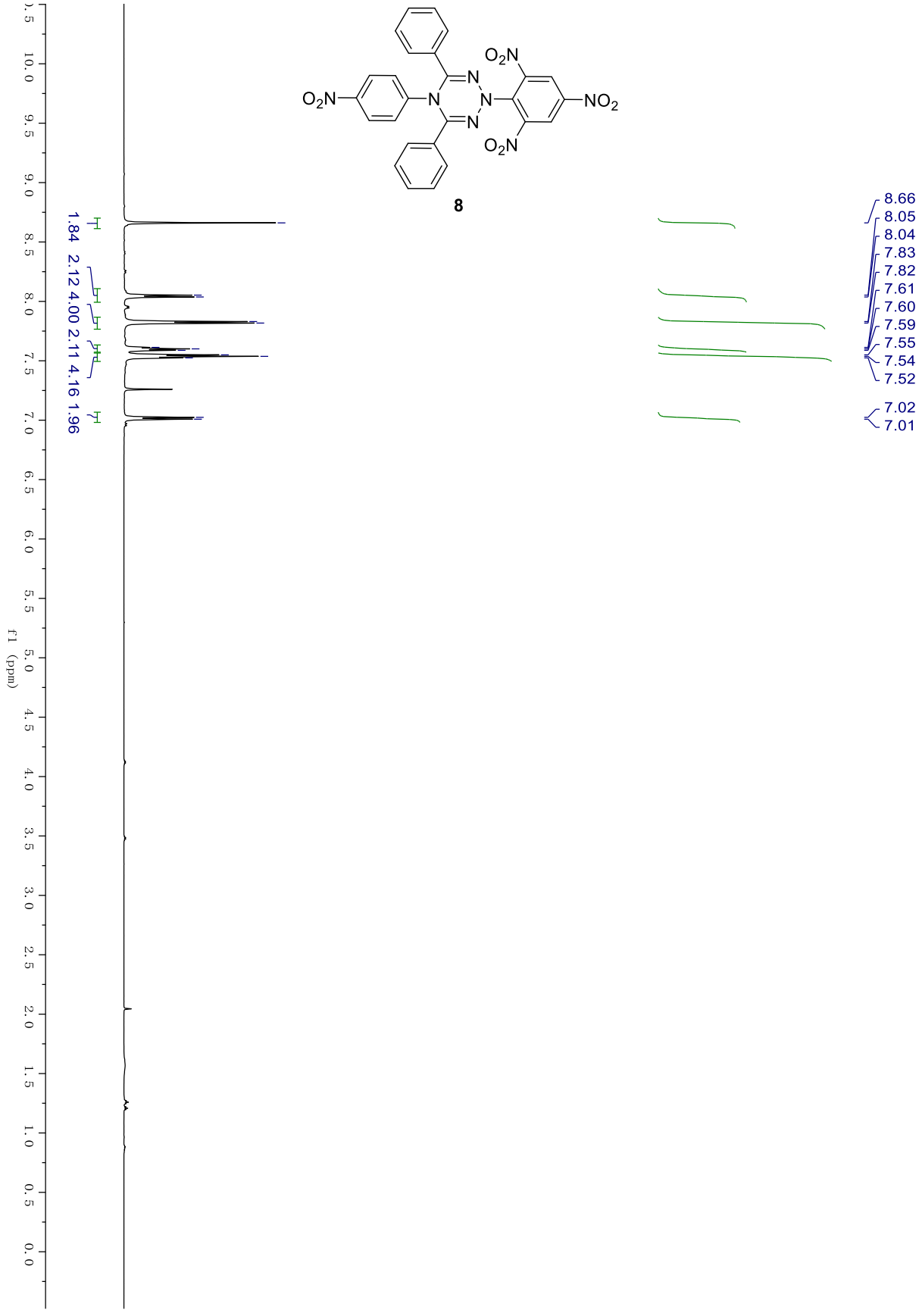
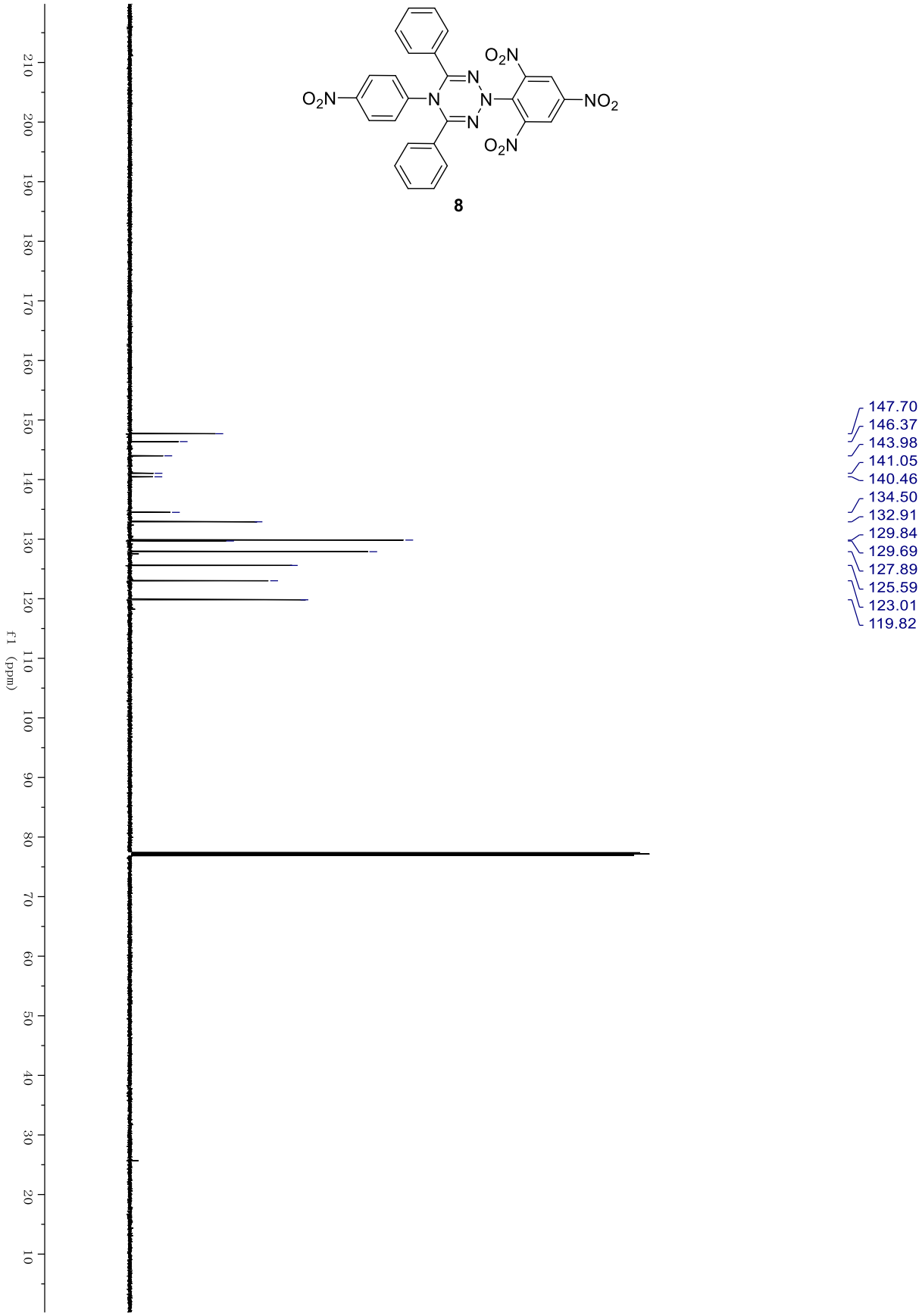
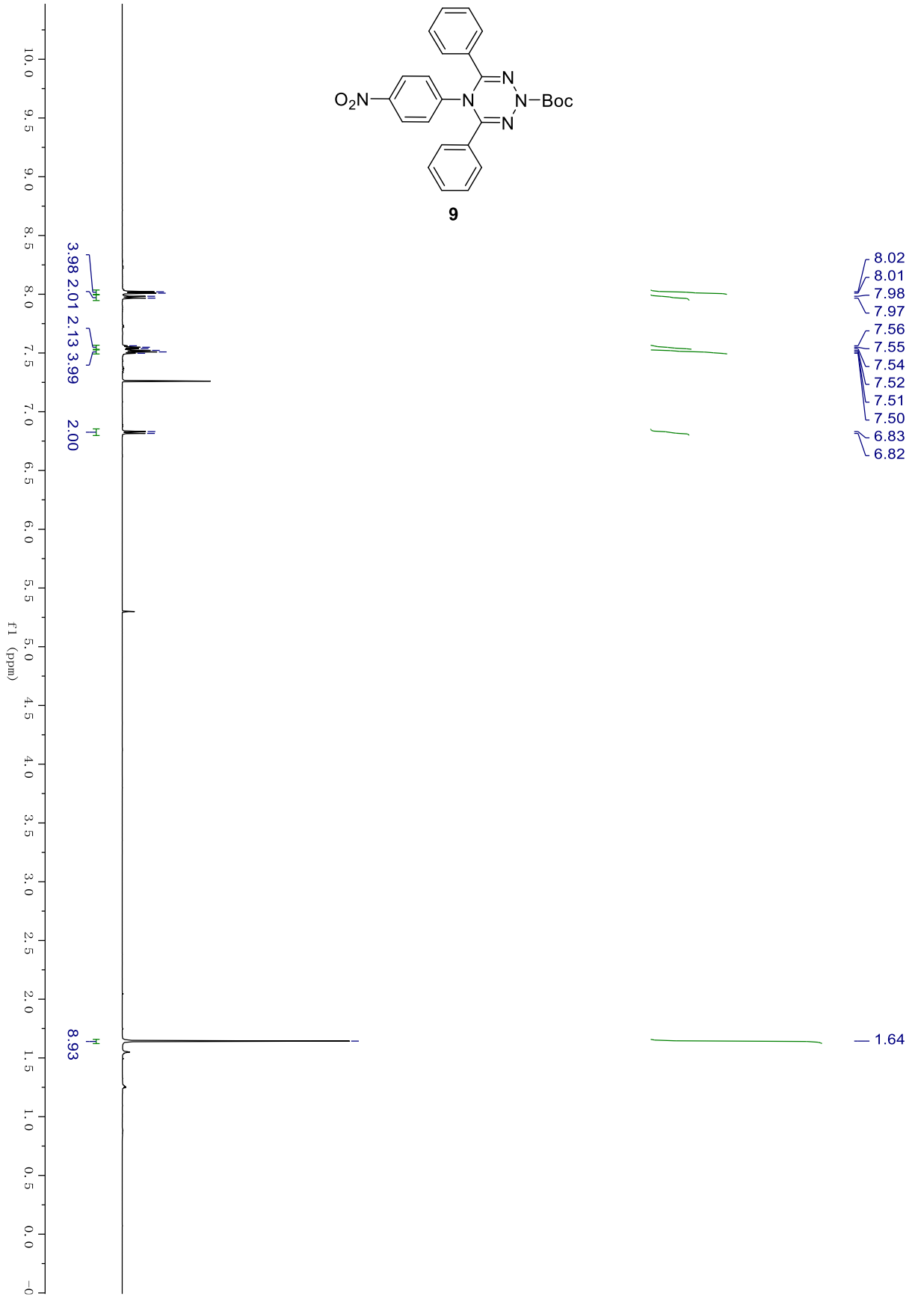
3.74
f1 (ppm)

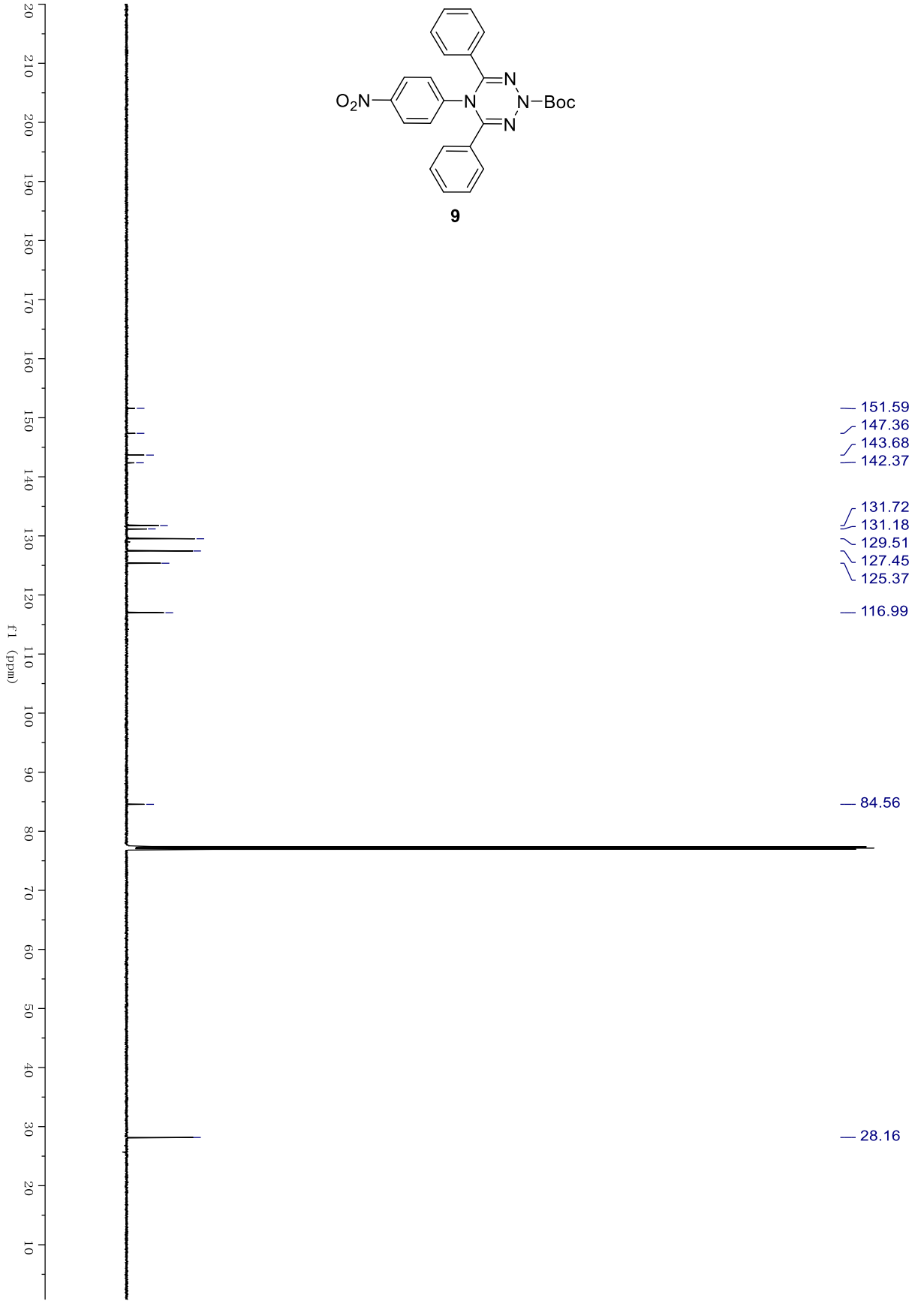

H2N
N
N
N
N
NH2
7
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
143.10
143.01
142.30
140.26
135.56
133.38
129.85
128.67
127.29
123.47
117.74
115.97
115.72


8.66
8.05
8.04
7.83
7.82
7.61
7.60
7.59
7.55
7.54
7.52
7.02
7.01
1.84 2.12 4.00 2.11 4.16 1.96
f1 (ppm)

8


O2N
N
N
N
N
NO2
O2N
O2N
8
147.70
146.37
143.98
141.05
140.46
134.50
132.91
129.84
129.69
127.89
125.59
123.01
119.82
f1 (ppm)


O2N
N
N
N
N
Boc
9
8.02
8.01
7.98
7.97
7.56
7.55
7.54
7.52
7.51
7.50
6.83
6.82
1.64
3.98
2.01
2.13
3.99
2.00
8.93
f1 (ppm)


O2N
N
N
N
N
Boc
9
151.59
147.36
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142.37
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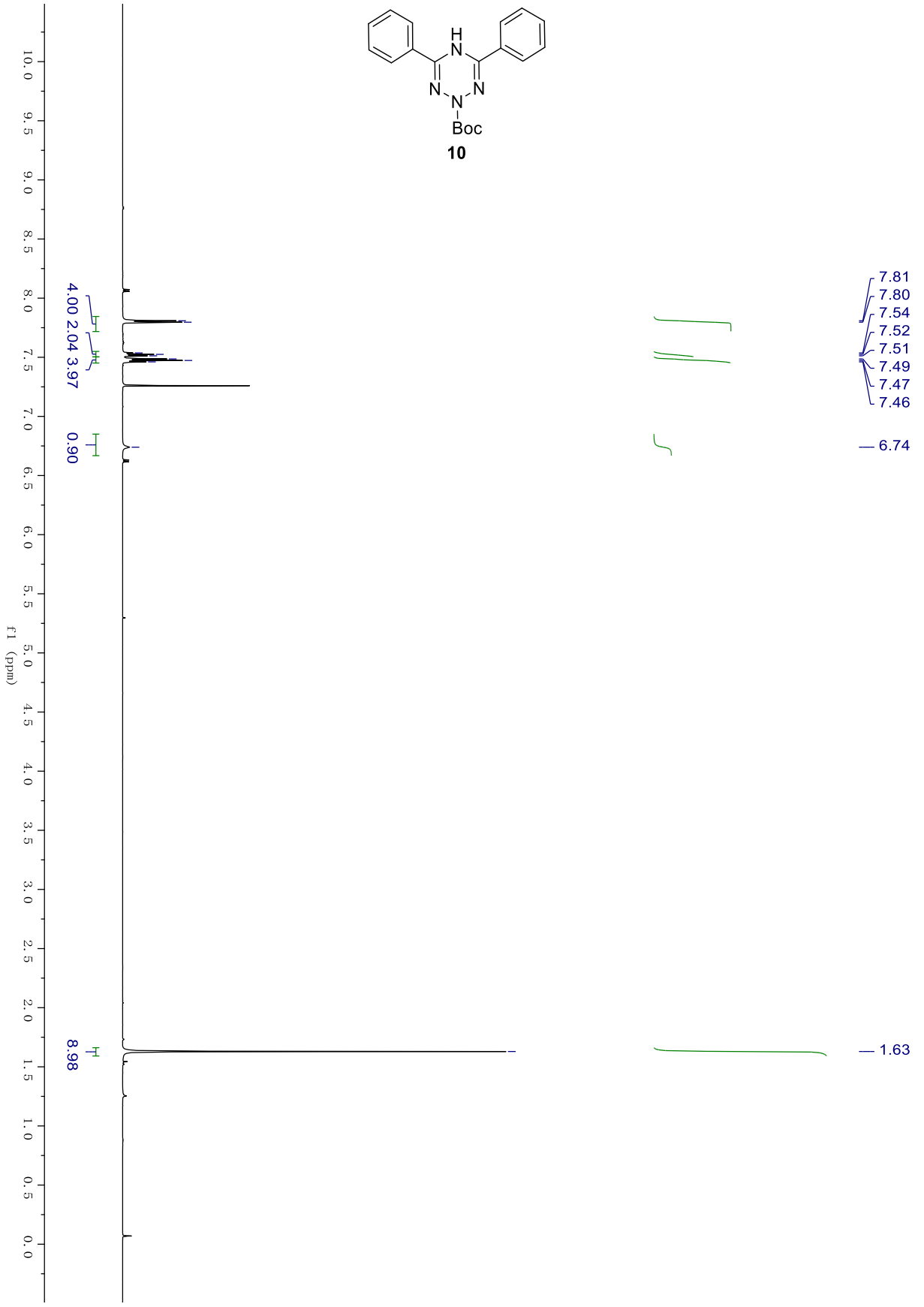
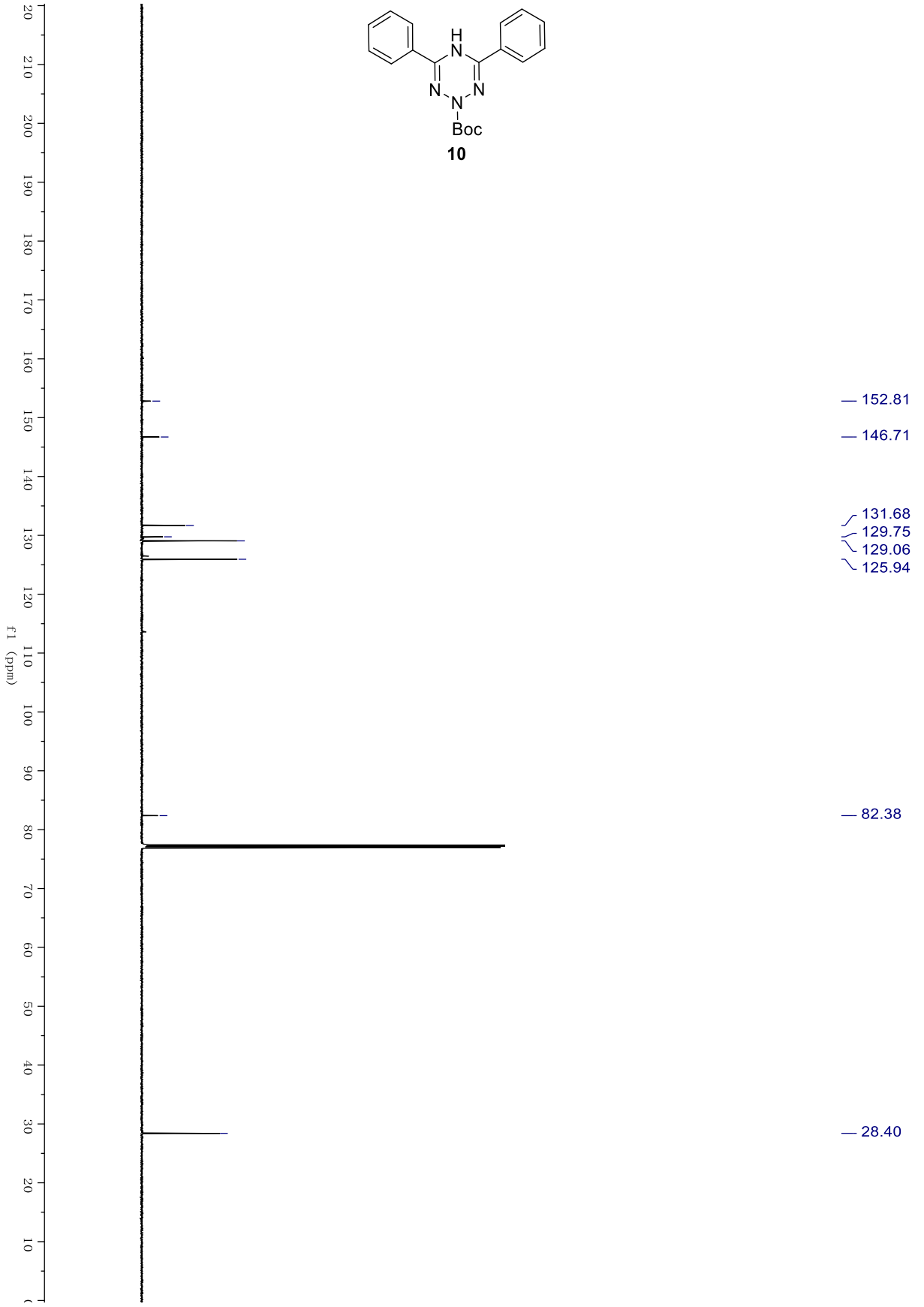
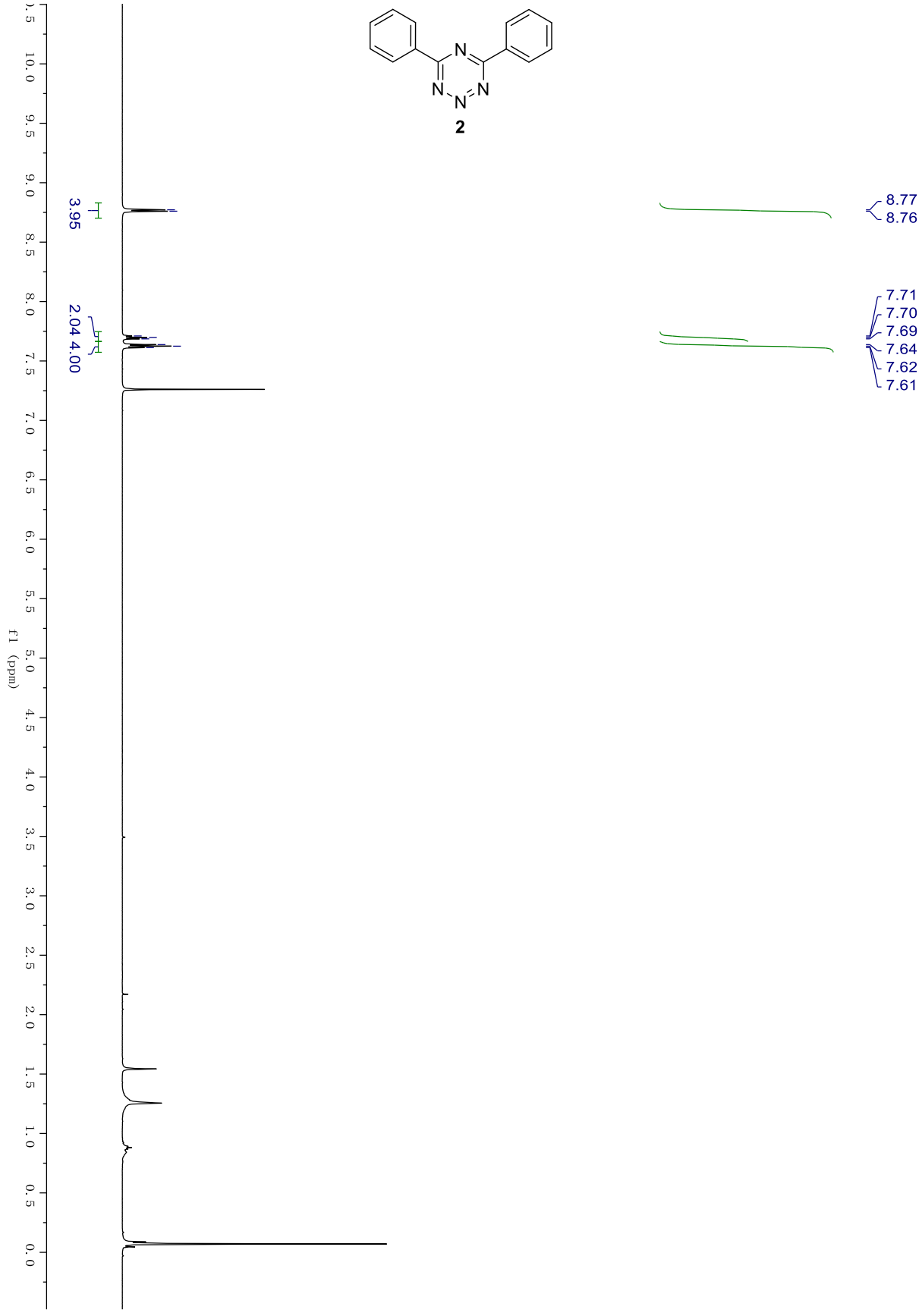
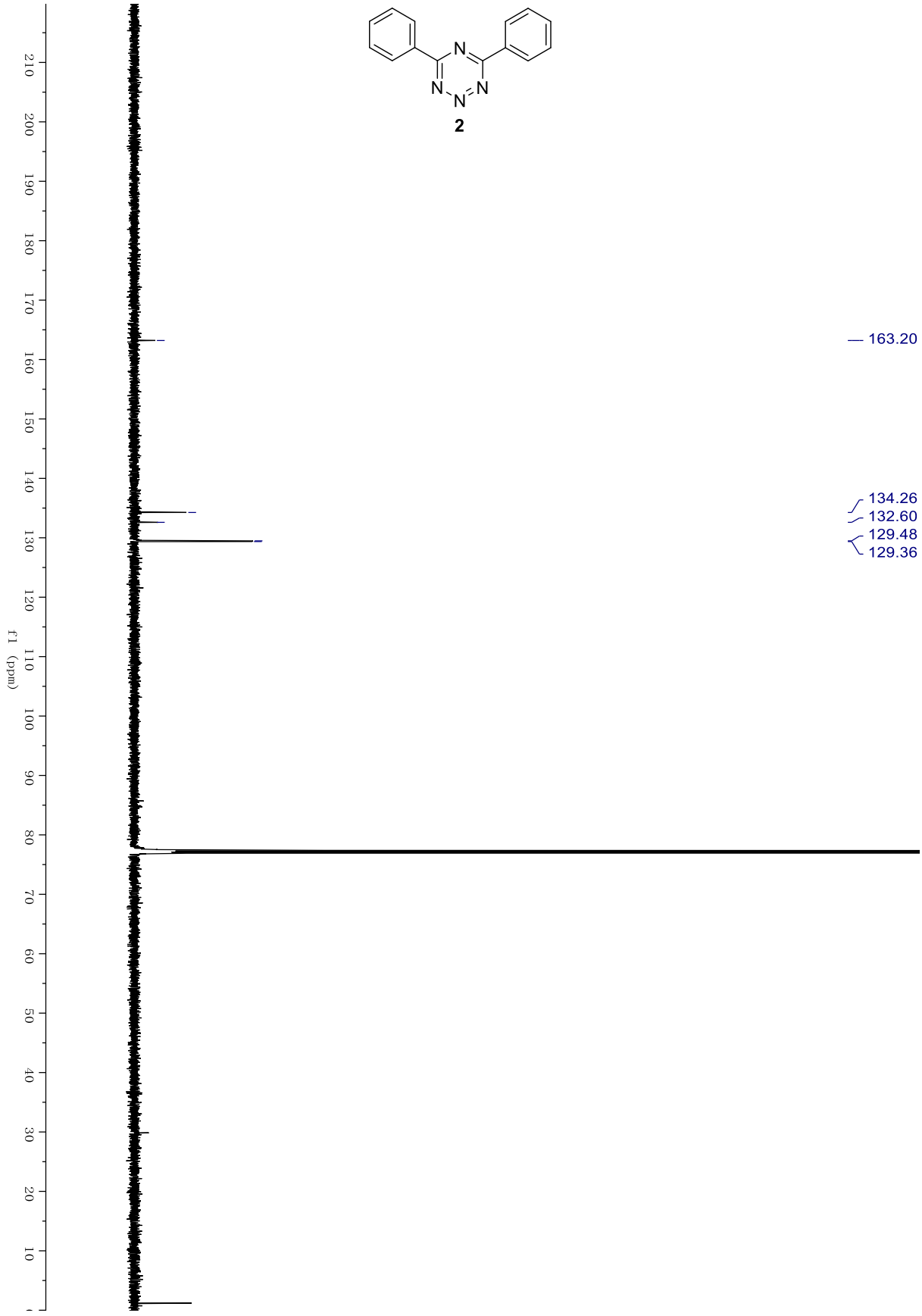
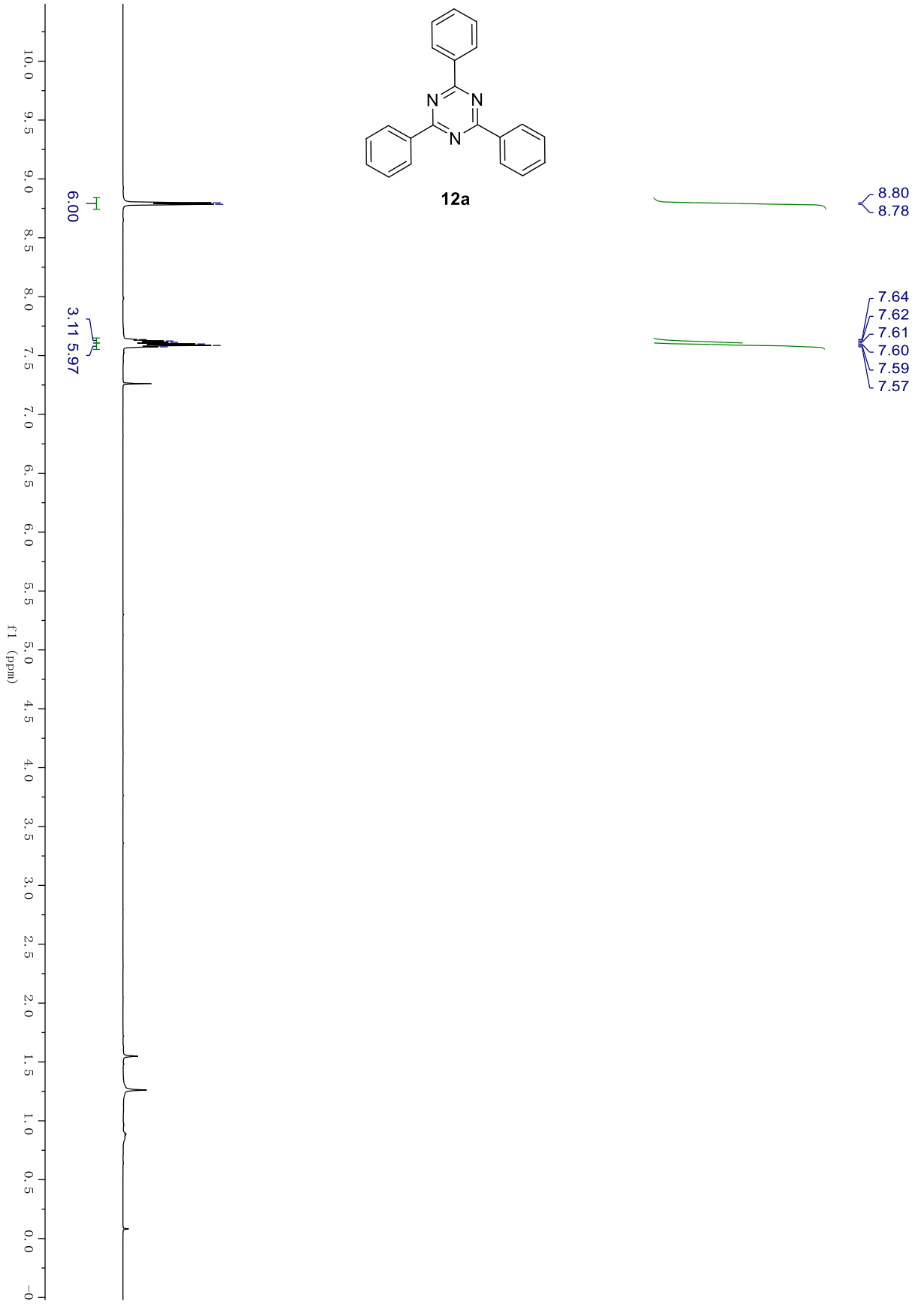
127.45
125.37
116.99
84.56
28.16
f1 (ppm)

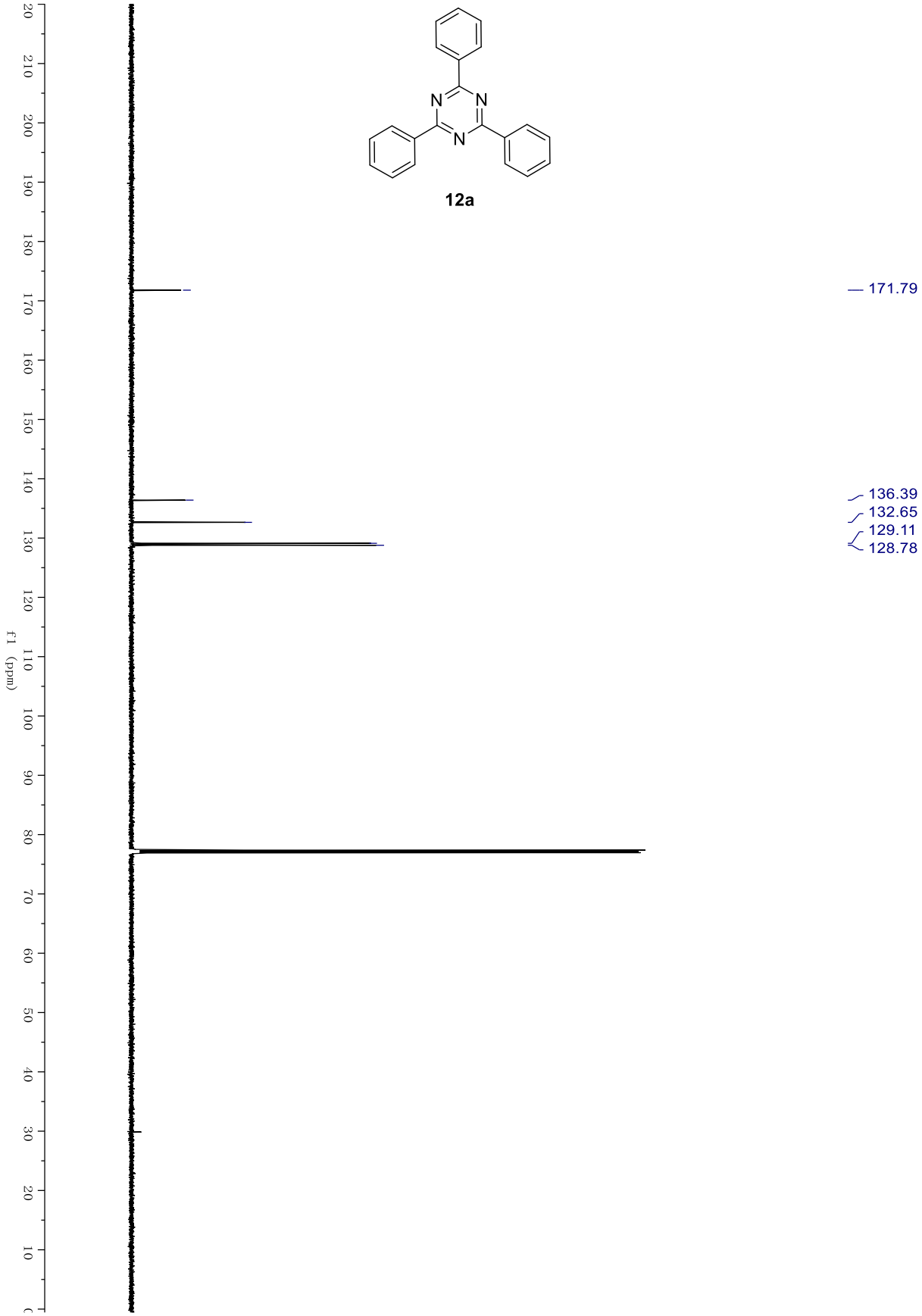

H
N
N
N
N
Boc
10
7.81
7.80
7.54
7.52
7.51
7.49
7.47
7.46
6.74
1.63
4.00
2.04
3.97
0.90
8.98
f1 (ppm)

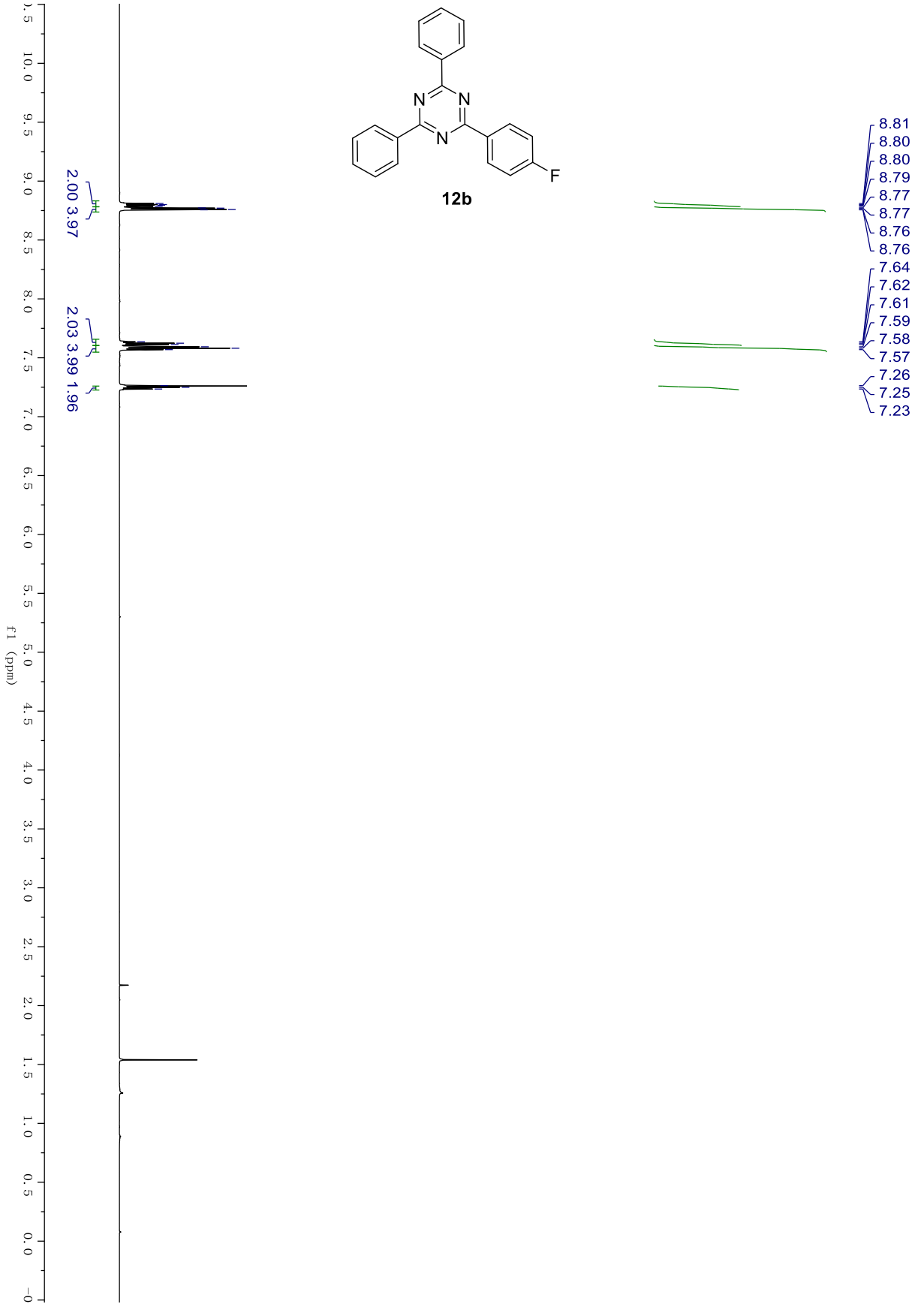

H
N
N
N
N
Boc
10
f1 (ppm)
152.81
146.71
131.68
129.75
129.06
125.94
82.38
28.40

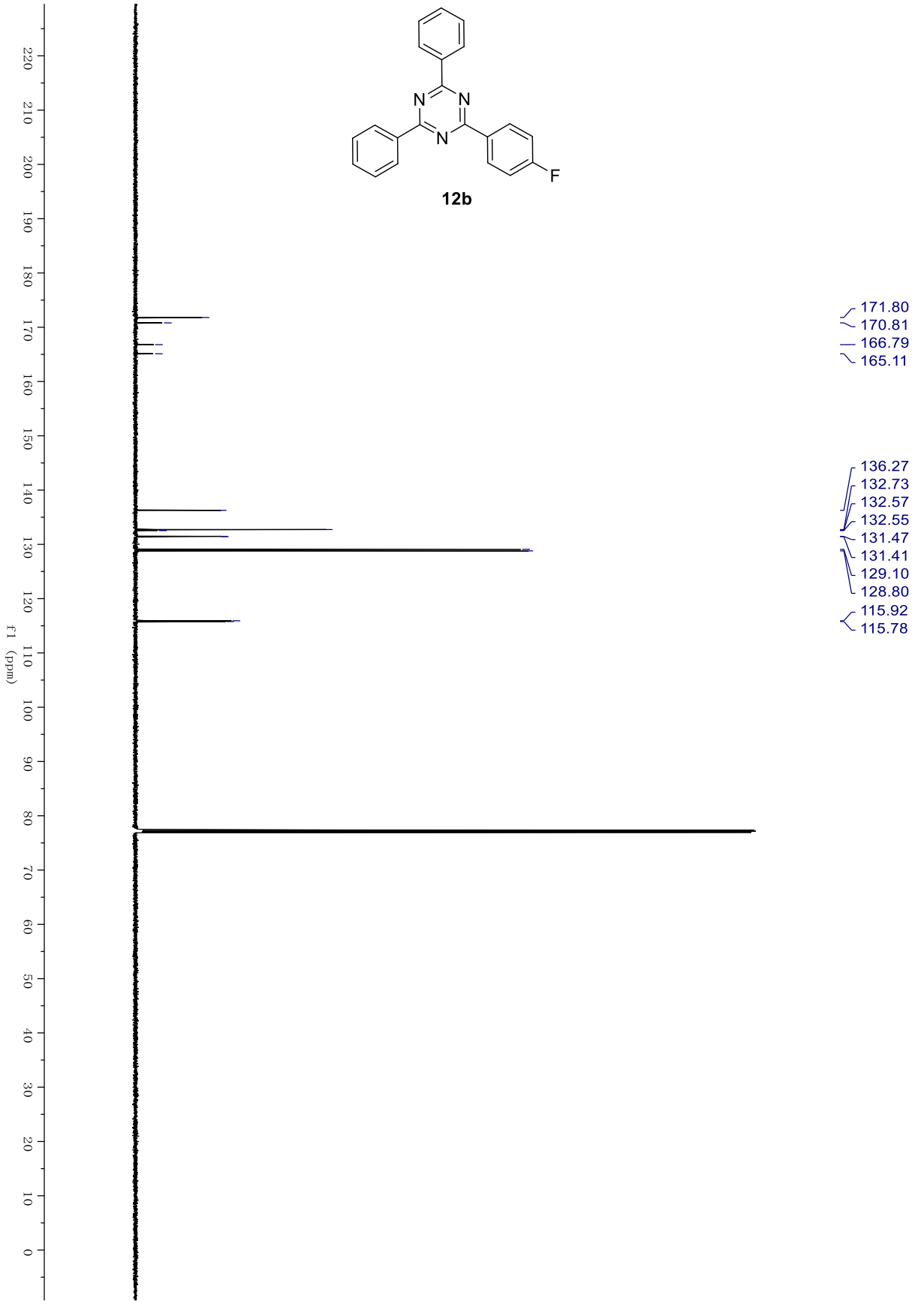

2
8.77
8.76
7.71
7.70
7.69
7.64
7.62
7.61
3.95
2.04
4.00
f1 (ppm)

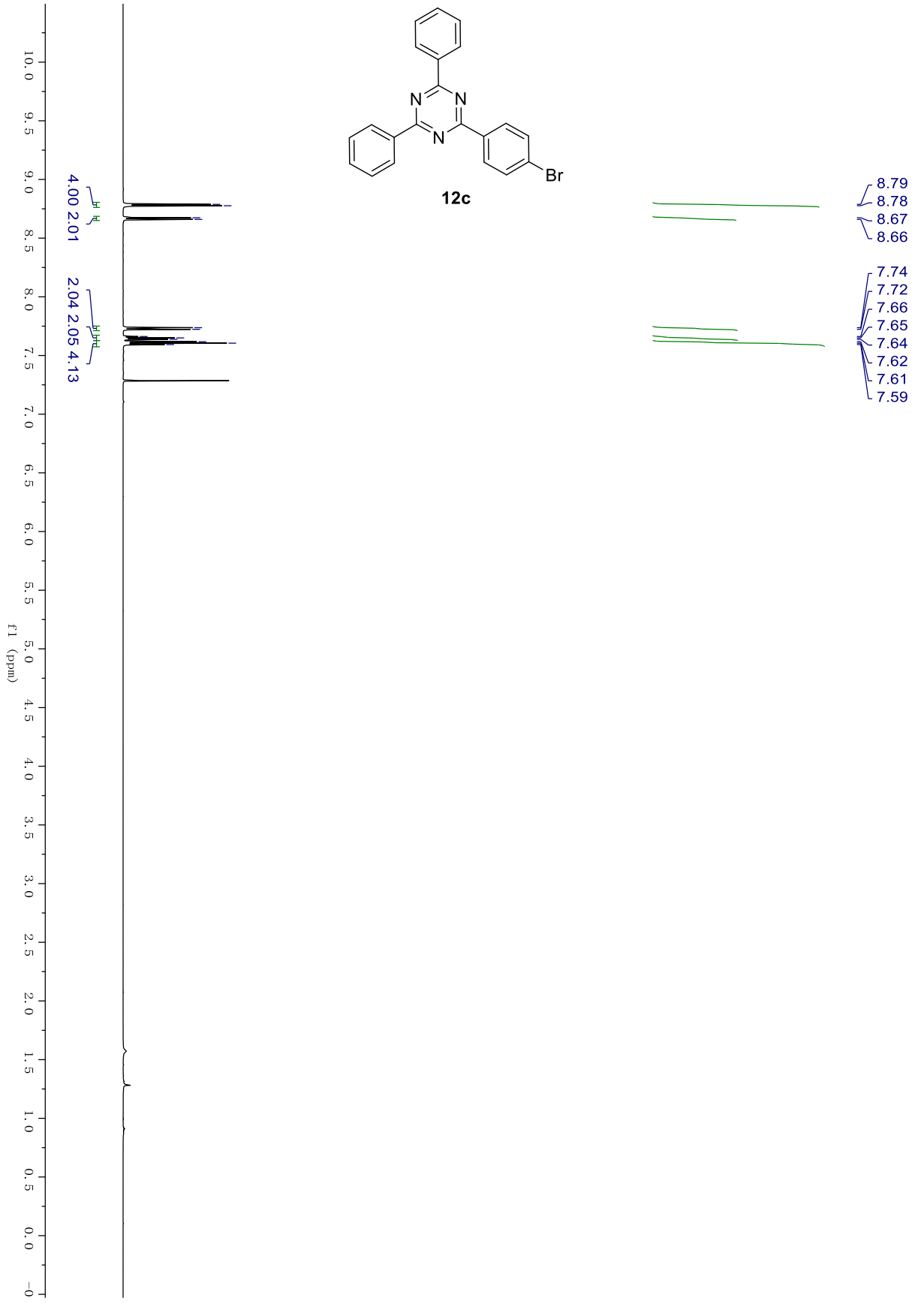

N
N
N
N
2
163.20
134.26
132.60
129.48
129.36
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

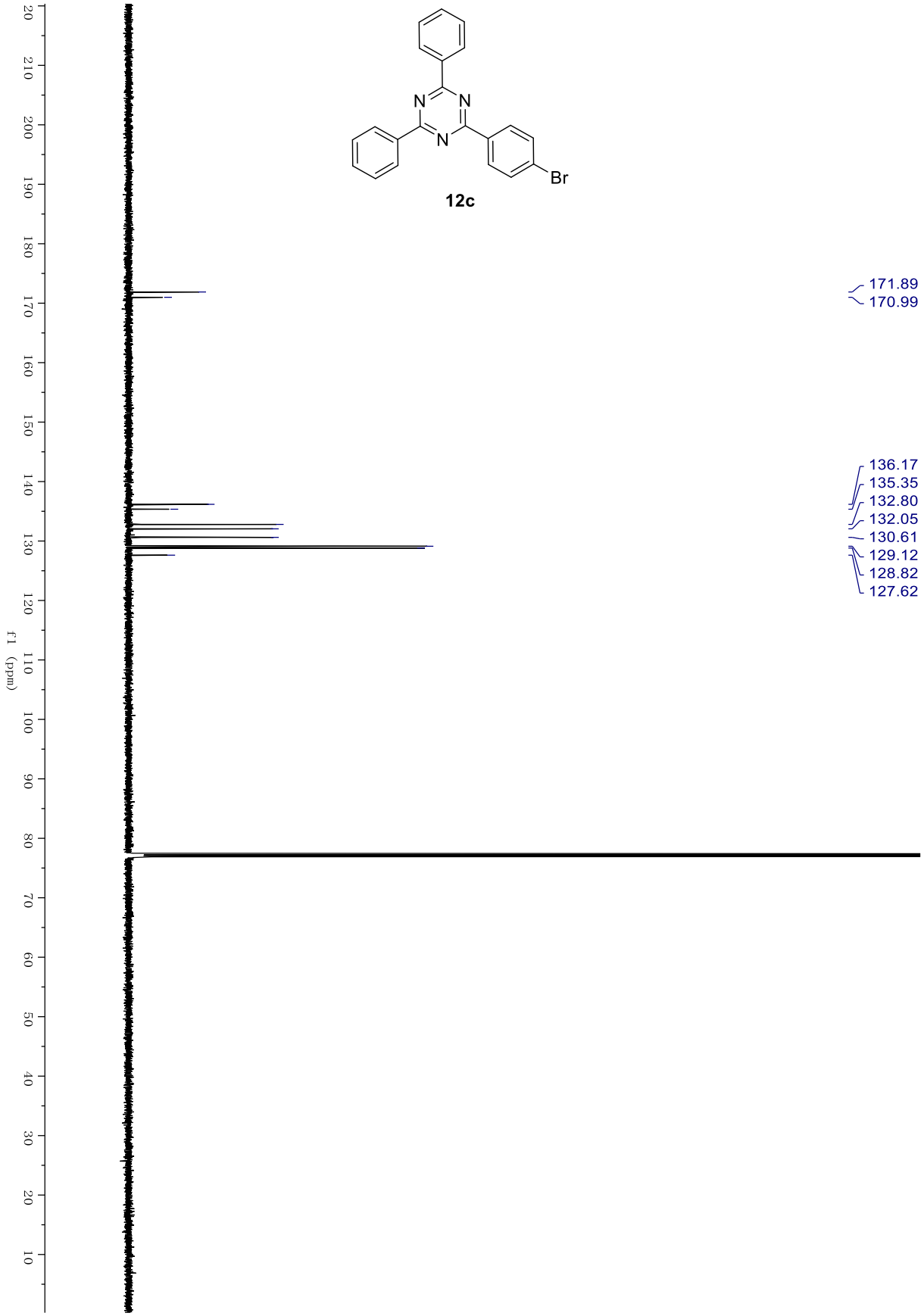

12a
8.80
8.78
7.64
7.62
7.61
7.60
7.59
7.57
6.00
3.11
5.97
f1 (ppm)


N
N
N
12a
171.79
136.39
132.65
129.11
128.78
f1 (ppm)


12b
F
8.81
8.80
8.80
8.79
8.77
8.77
8.76
8.76
7.64
7.62
7.61
7.59
7.58
7.57
7.26
7.25
7.23
2.00 3.97
2.03 3.99 1.96
f1 (ppm)


12b
171.80
170.81
166.79
165.11
136.27
132.73
132.57
132.55
131.47
131.41
129.10
128.80
115.92
115.78
f1 (ppm)


N
N
N
Br
12c
8.79
8.78
8.67
8.66
7.74
7.72
7.66
7.65
7.64
7.62
7.61
7.59
4.00 2.01
2.04 2.05 4.13
f1 (ppm)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N
N
Br
12c
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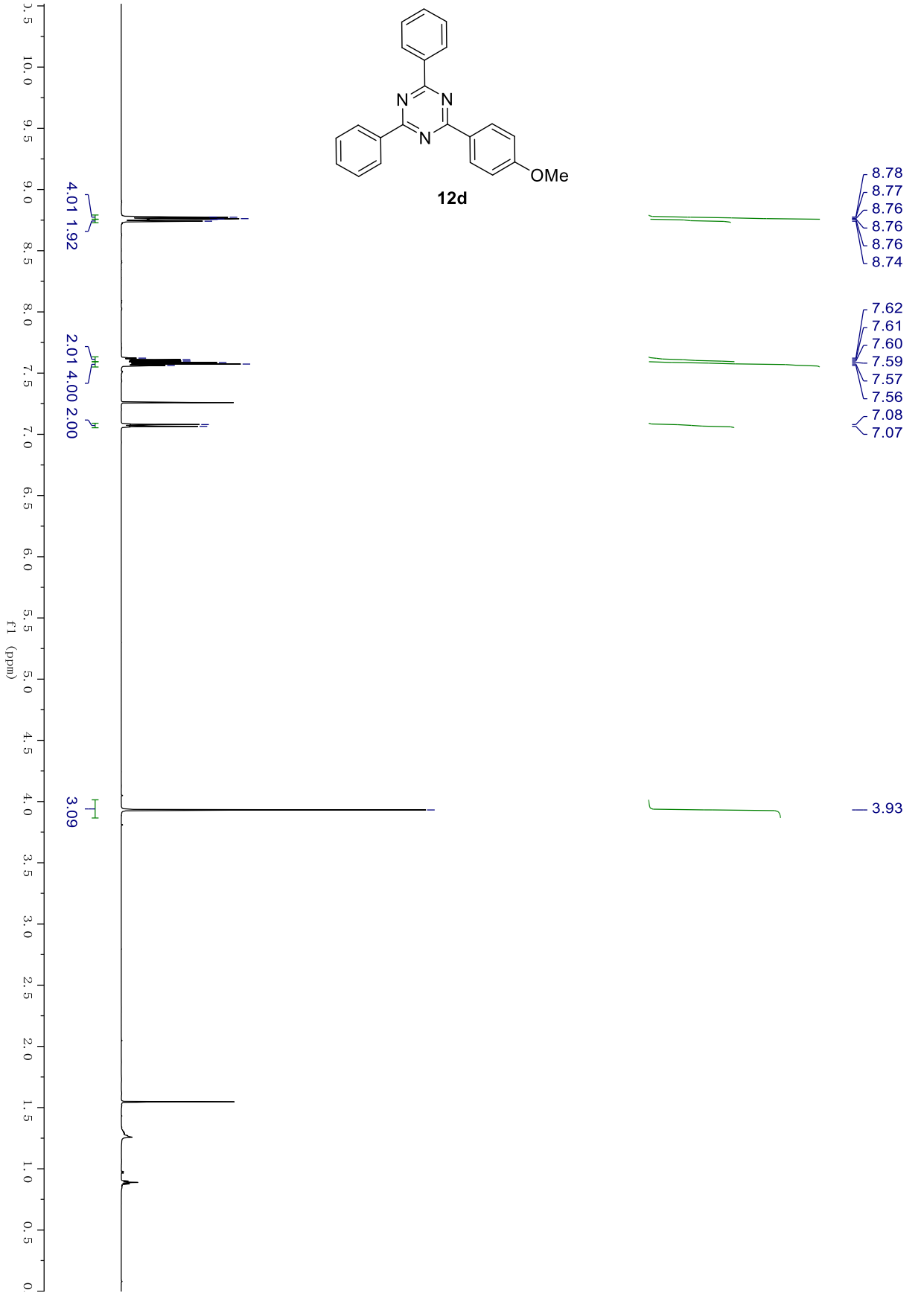
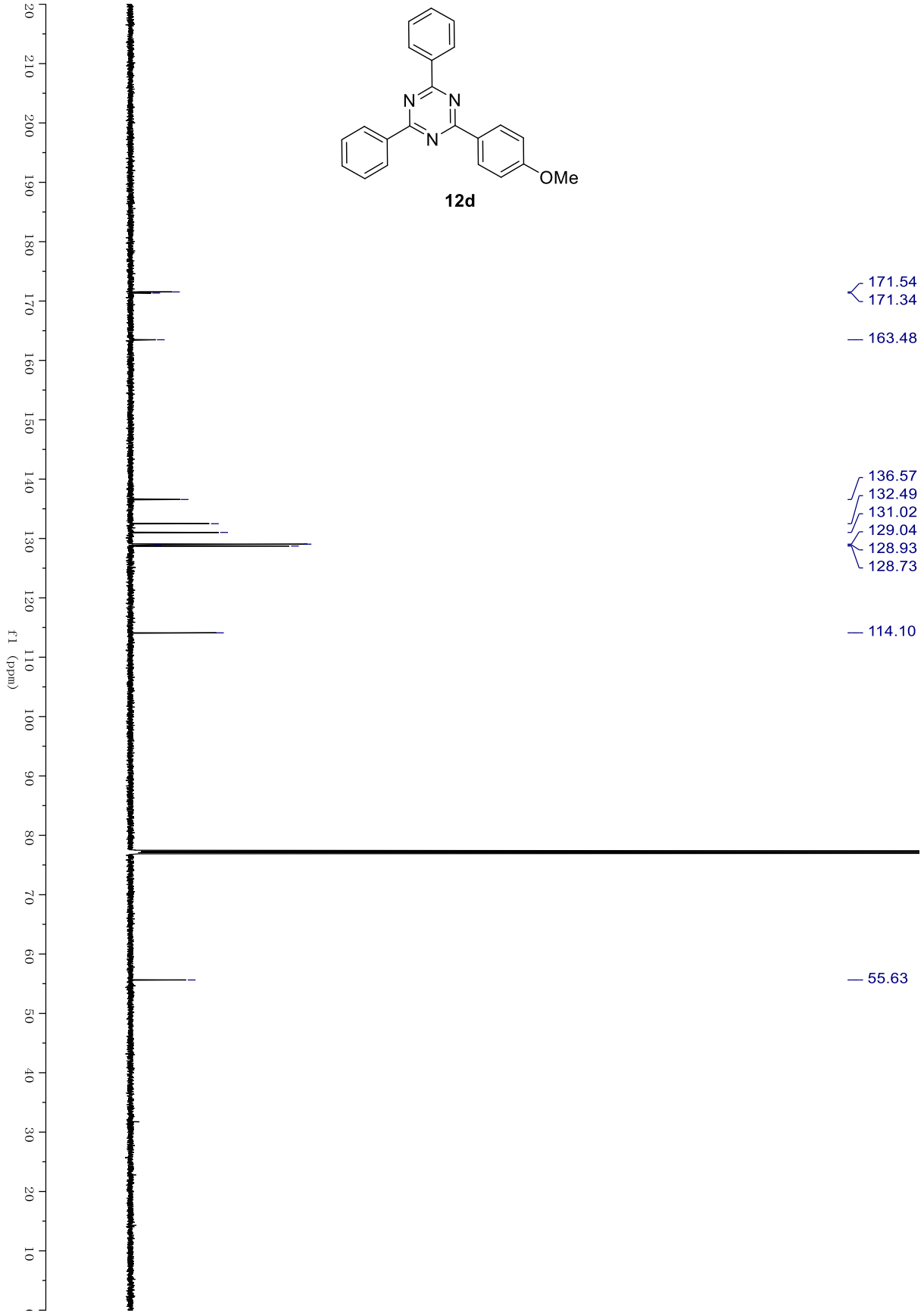
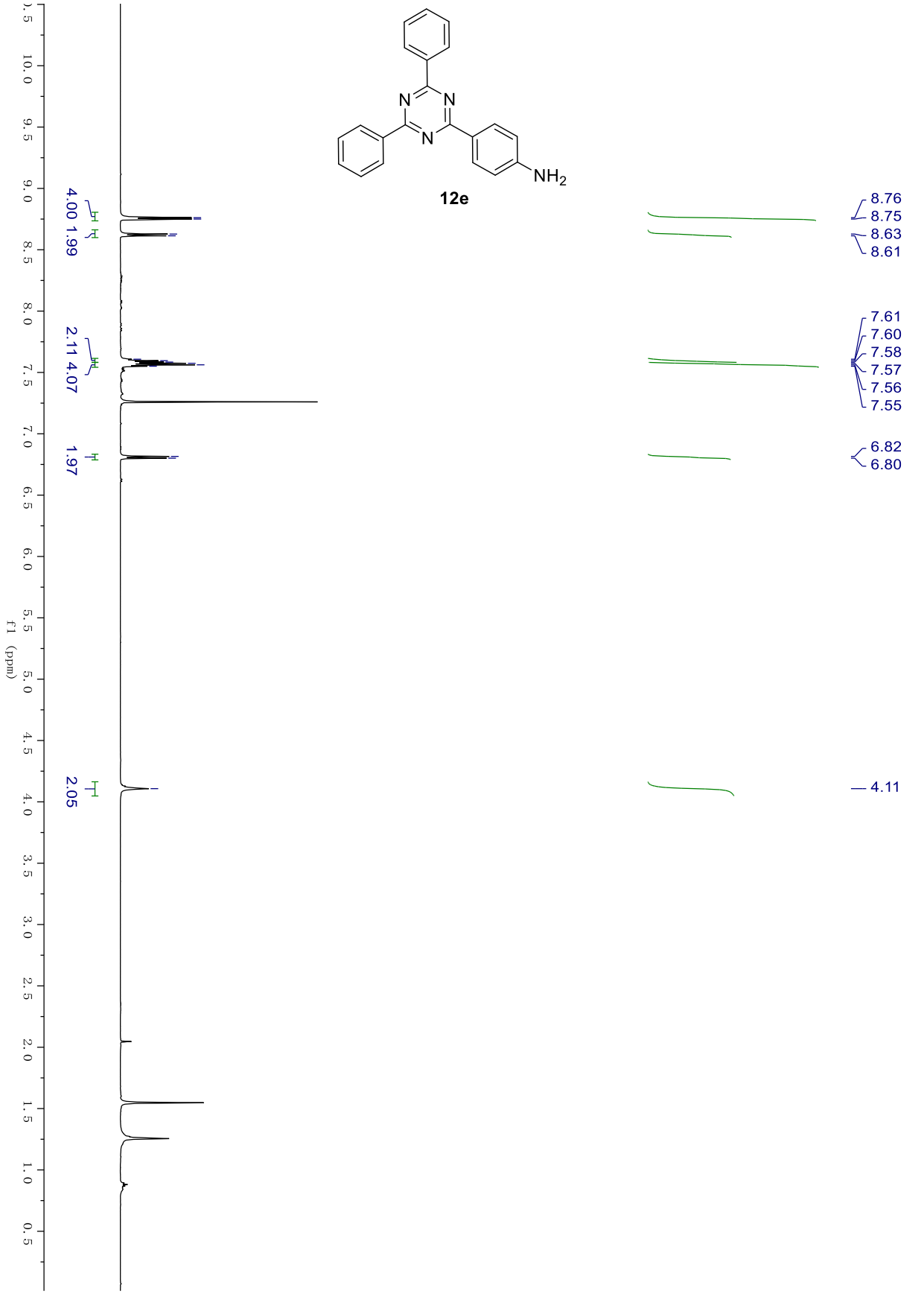
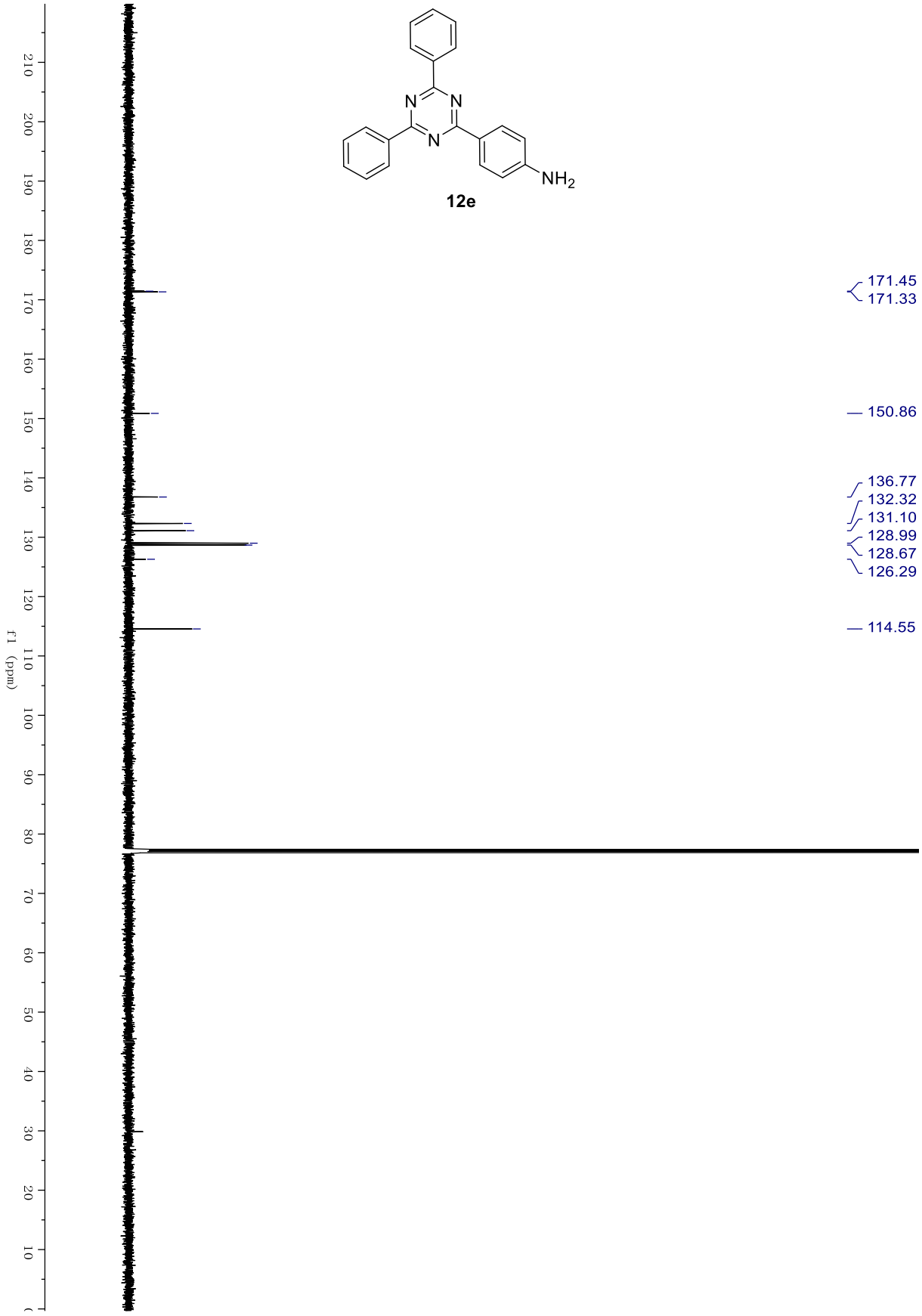
132.80
132.05
130.61
129.12
128.82
127.62
f1 (ppm)


12d
OMe
8.78
8.77
8.76
8.76
8.76
8.74
7.62
7.61
7.60
7.59
7.57
7.56
7.08
7.07
3.93
4.01
1.92
2.01
4.00
2.00
3.09
f1 (ppm)


N
N
N
OMe
12d
171.54
171.34
163.48
136.57
132.49
131.02
129.04
128.93
128.73
114.10
55.63
f1 (ppm)


12e
N
N
N
NH2
8.76
8.75
8.63
8.61
7.61
7.60
7.58
7.57
7.56
7.55
6.82
6.80
4.11
4.00
1.99
2.11
4.07
1.97
2.05
f1 (ppm)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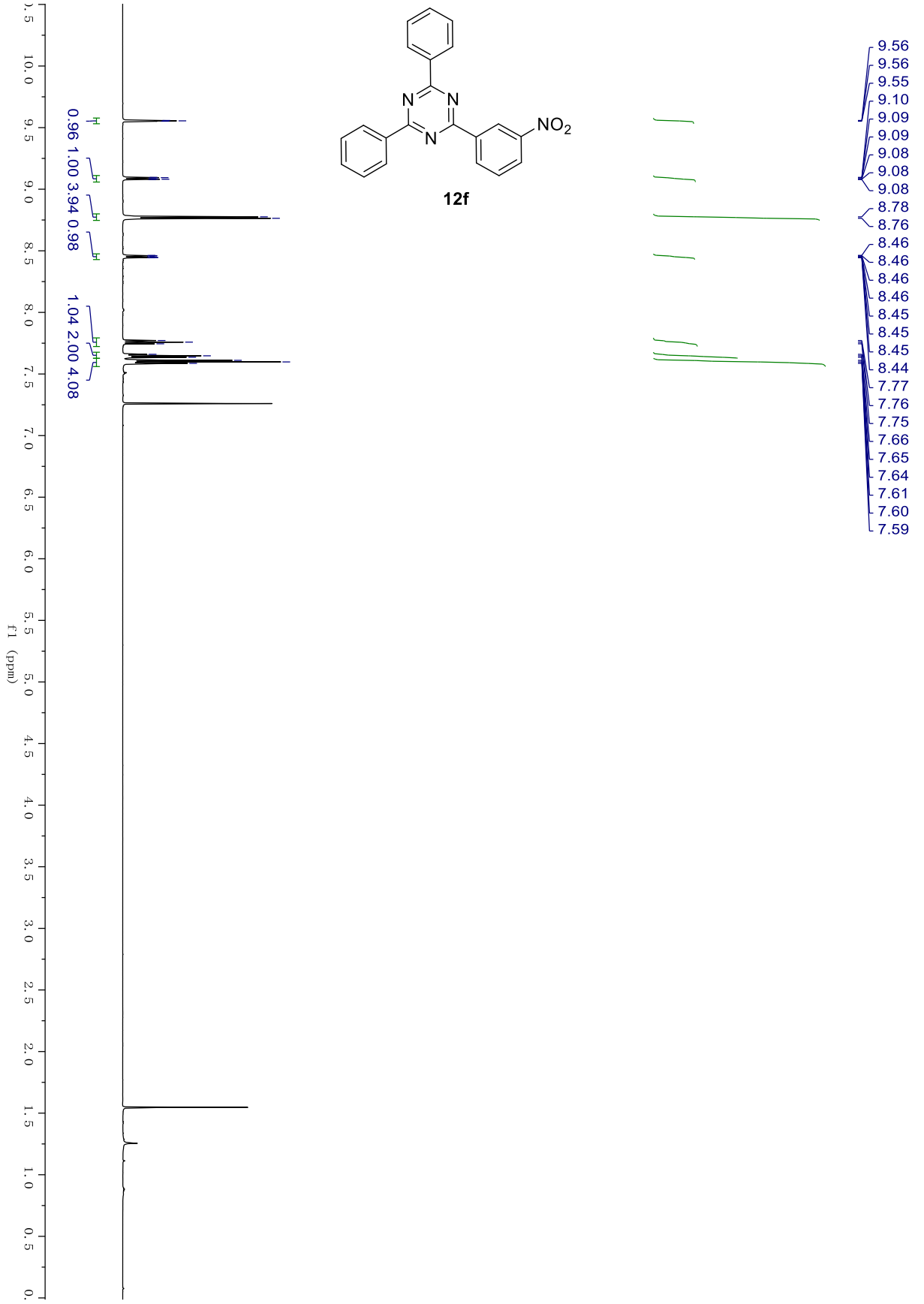
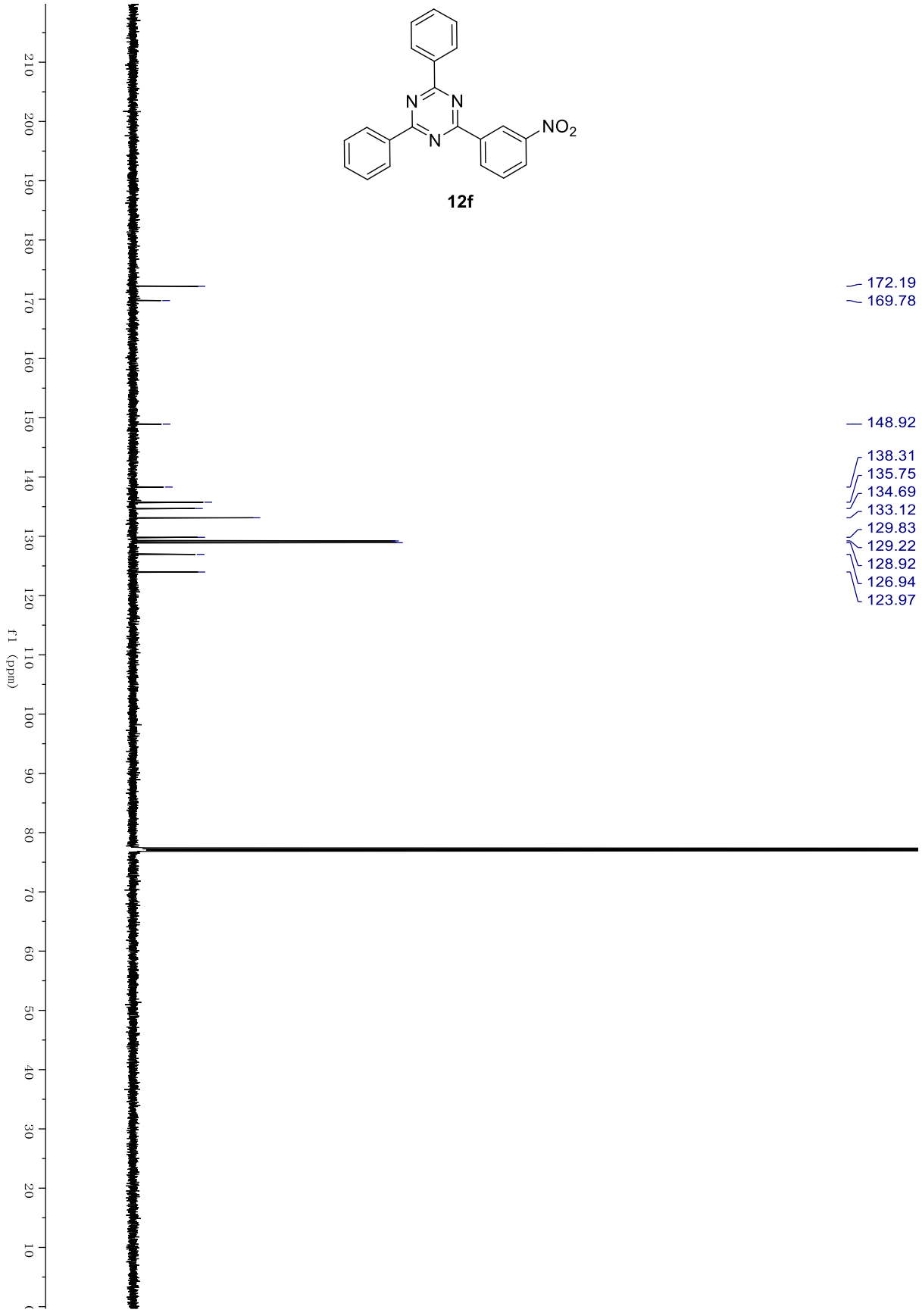
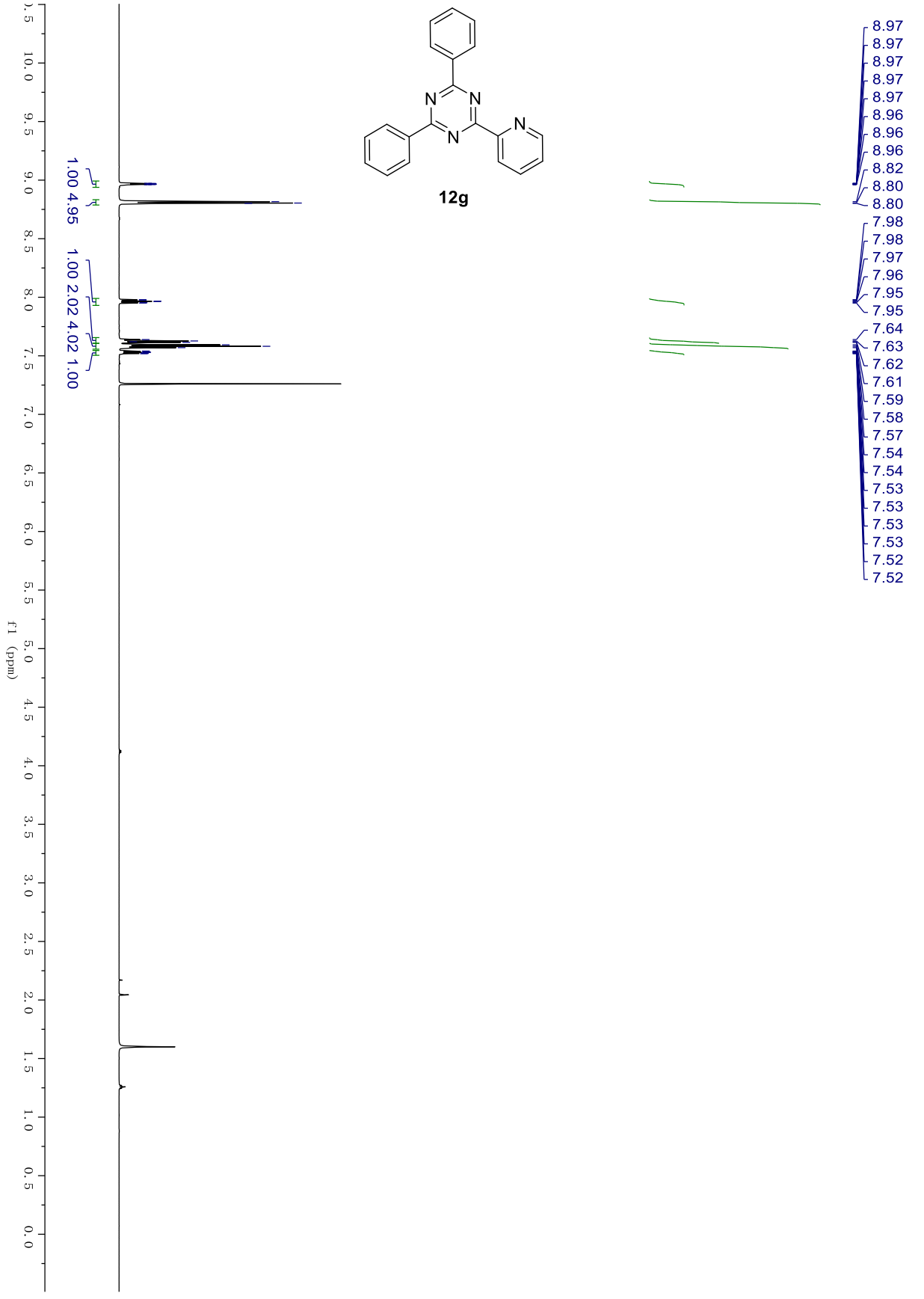
136.77
132.32
131.10
128.99
128.67
126.29
114.55
f1 (ppm)


9.56
9.56
9.55
9.10
9.09
9.09
9.08
9.08
9.08
8.78
8.76
8.46
8.46
8.46
8.46
8.45
8.45
8.45
8.44
7.77
7.76
7.75
7.66
7.65
7.64
7.61
7.60
7.59
0.96 1.00 3.94 0.98
1.04 2.00 4.08
N
N
N
NO2
12f
f1 (ppm)


N
N
N
NO2
12f
172.19
169.78
148.92
138.31
135.75
134.69
133.12
129.83
129.22
128.92
126.94
123.97
f1 (ppm)


12g
8.97
8.97
8.97
8.97
8.97
8.96
8.96
8.96
8.82
8.80
8.80
7.98
7.98
7.97
7.96
7.95
7.95
7.64
7.63
7.62
7.61
7.59
7.58
7.57
7.54
7.54
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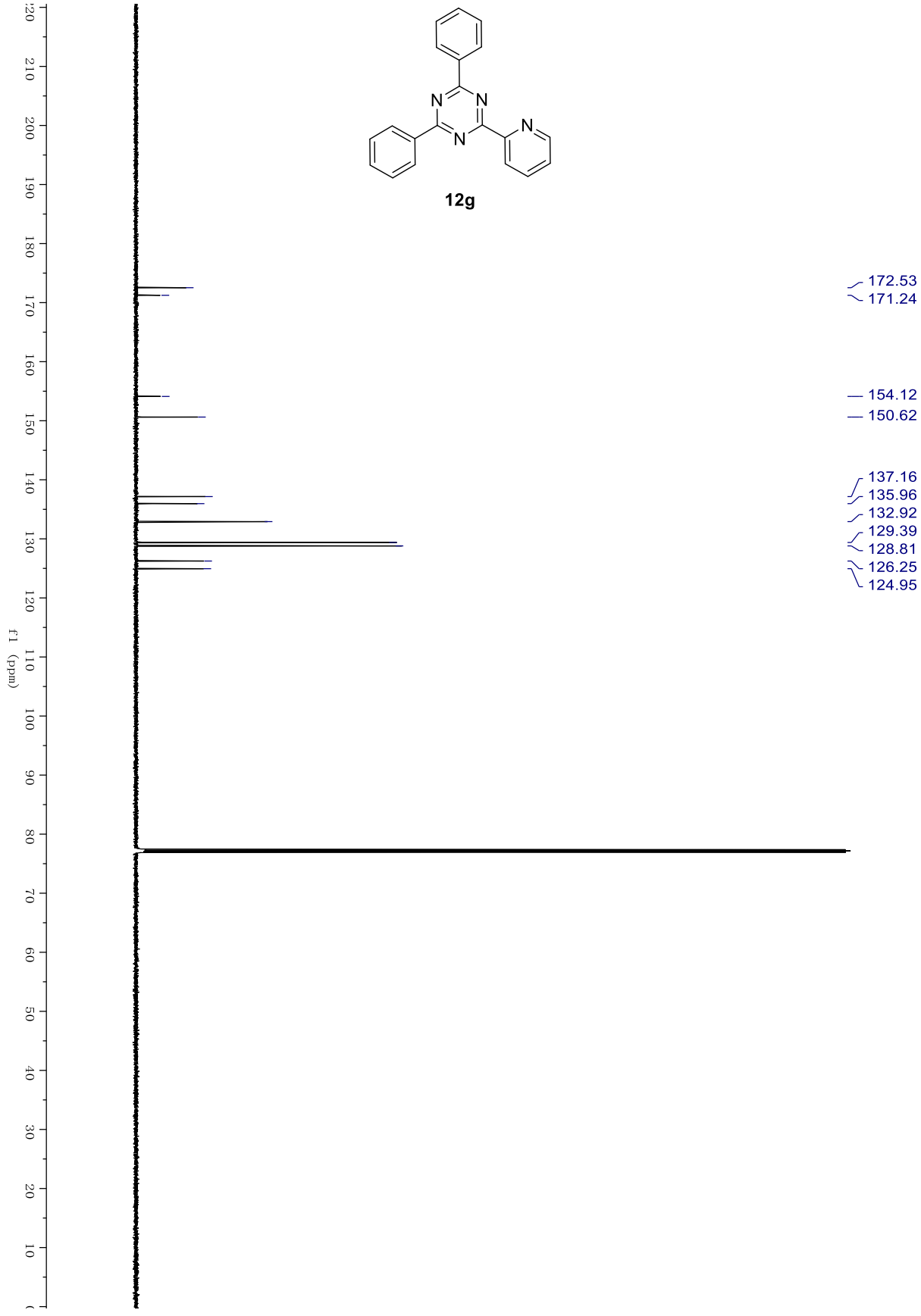
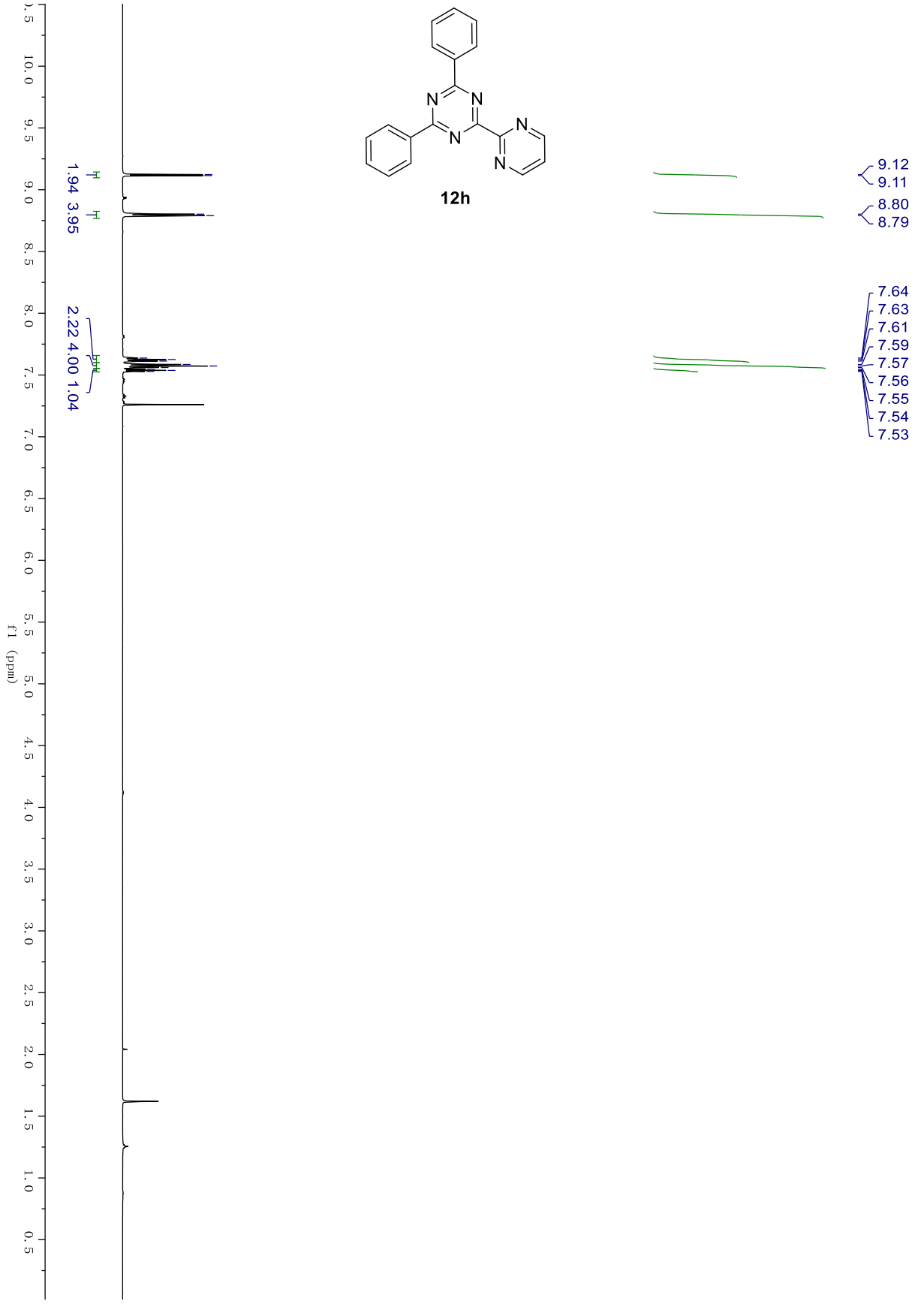
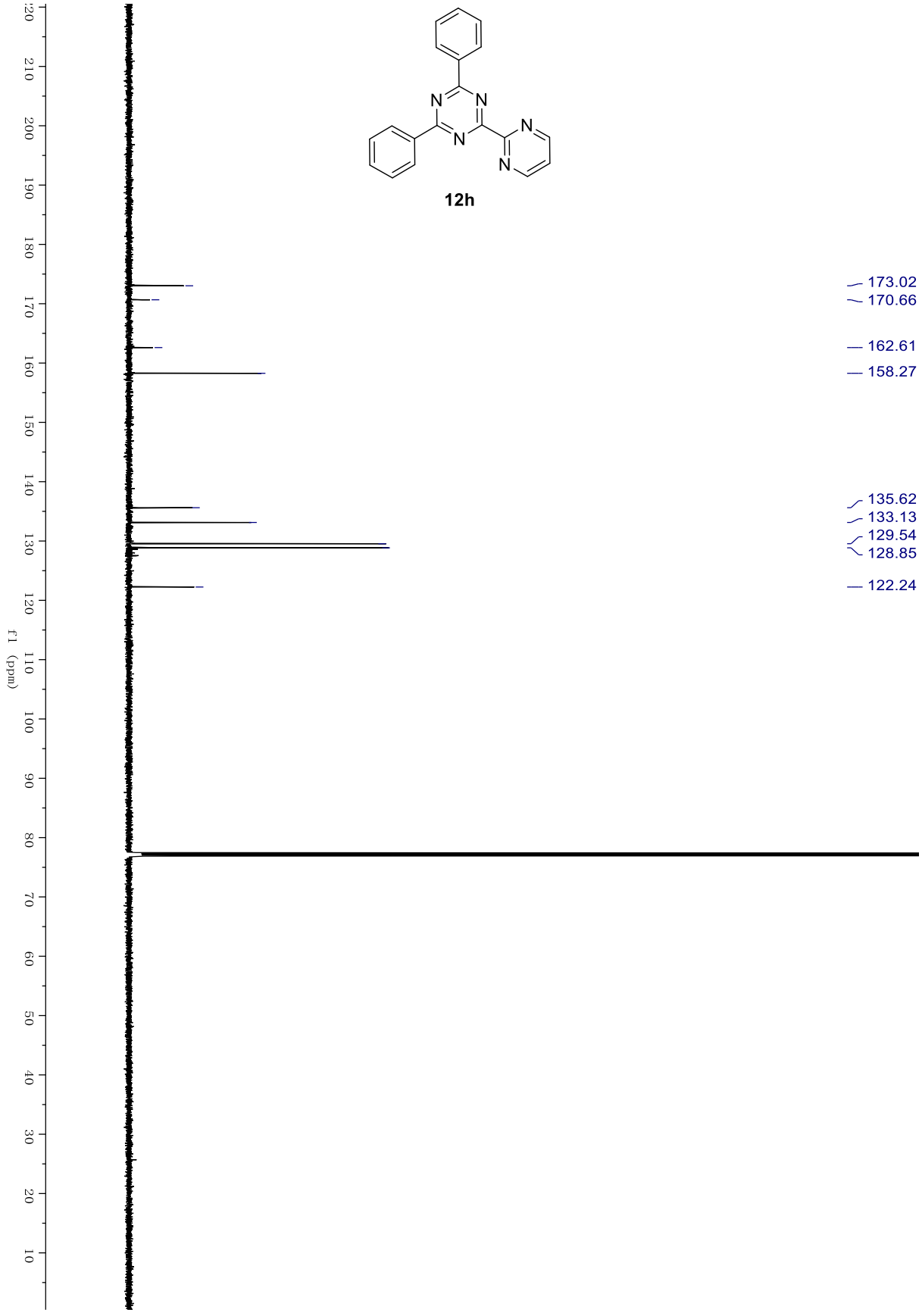
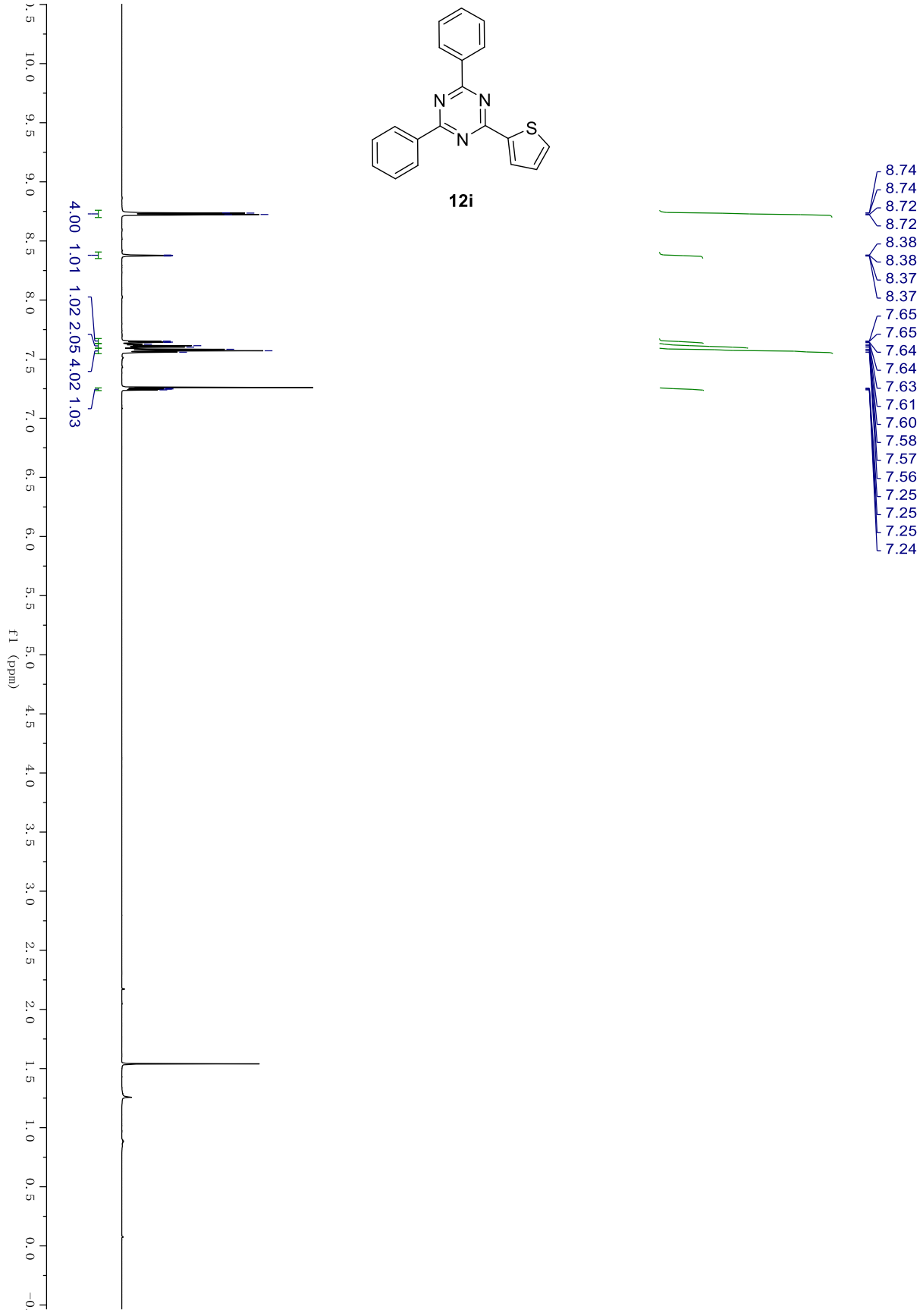
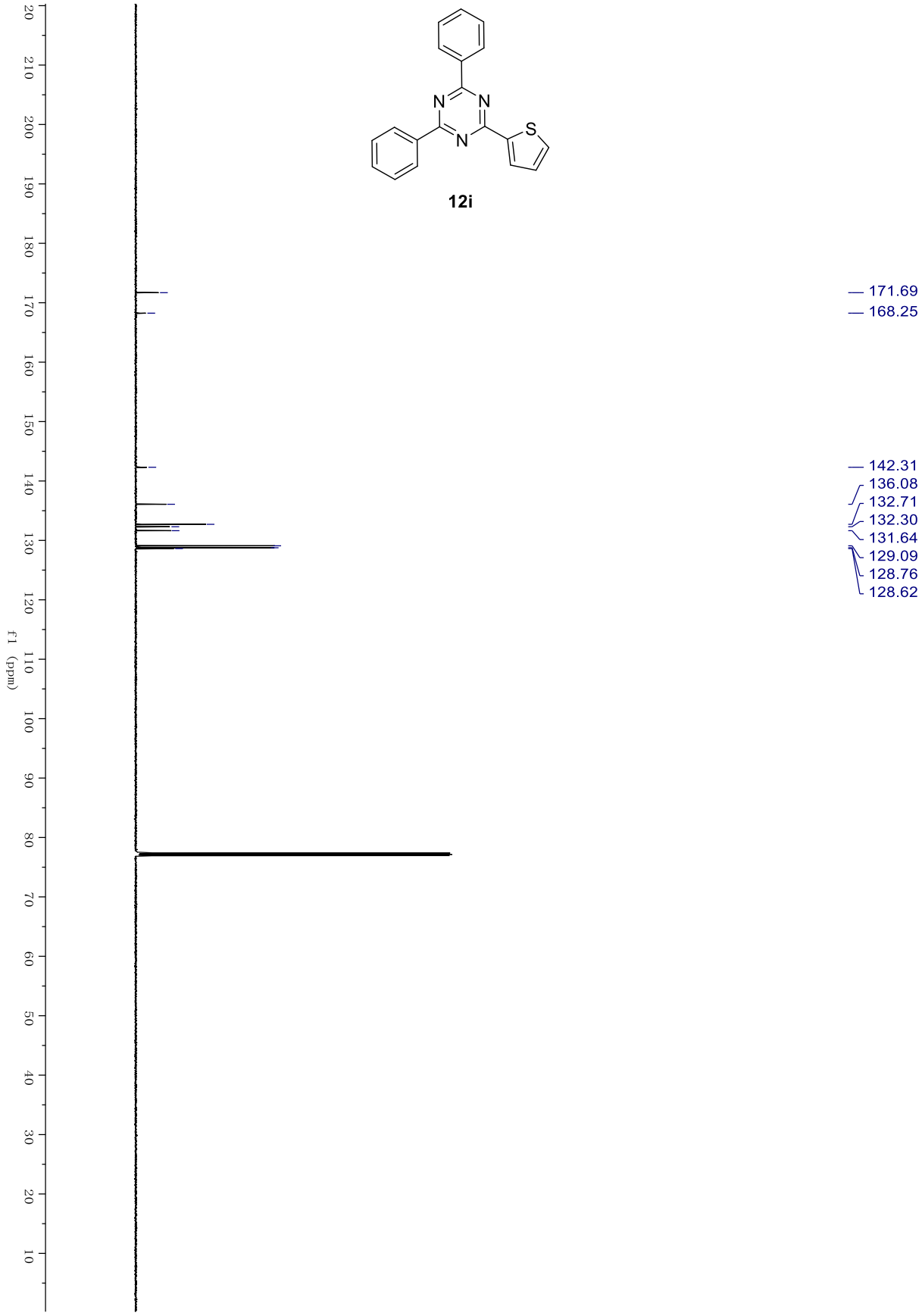
1.00 4.95
1.00 2.02 4.02 1.00
f1 (ppm)

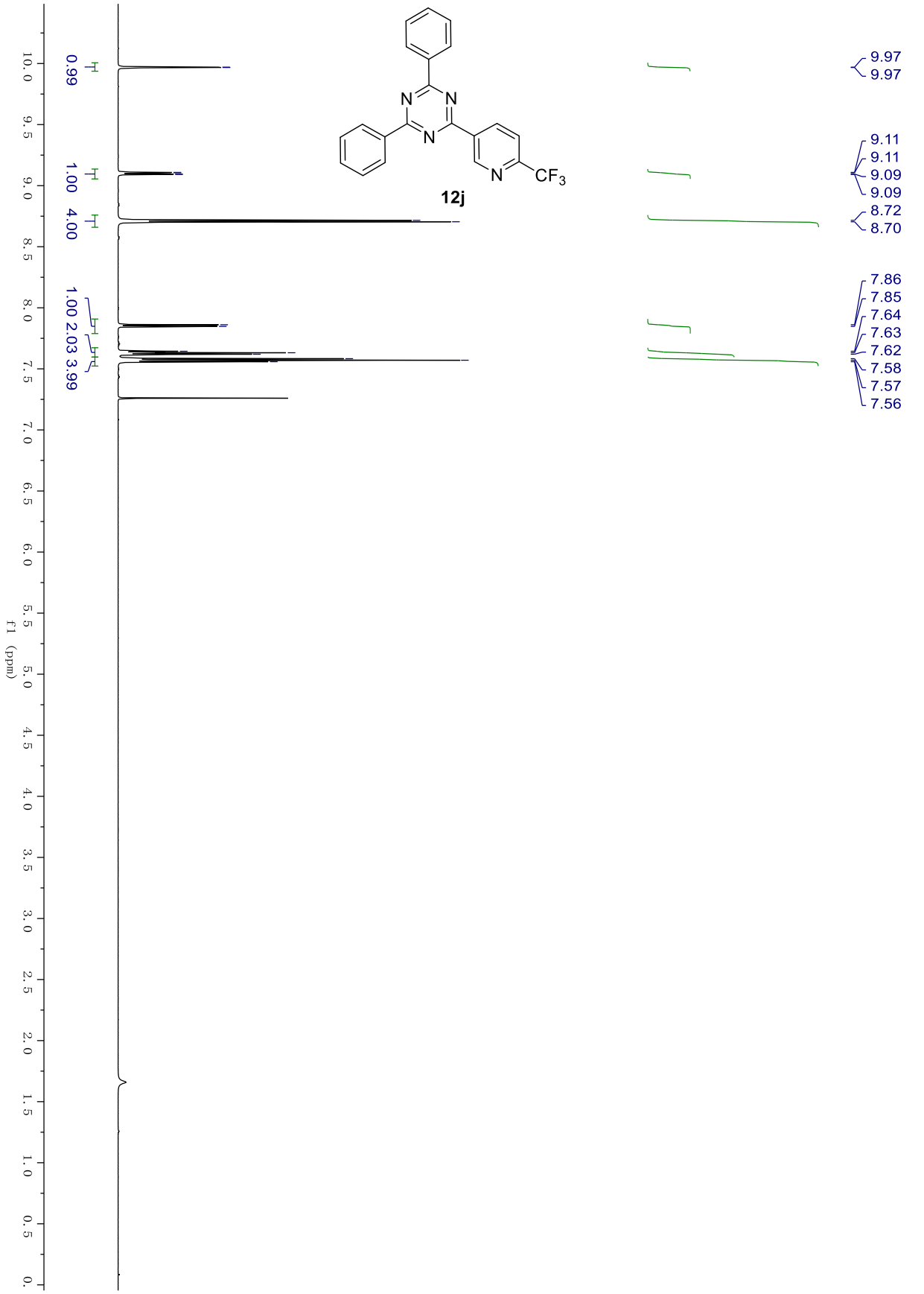

12g
172.53
171.24
154.12
150.62
137.16
135.96
132.92
129.39
128.81
126.25
124.95
f1 (ppm)

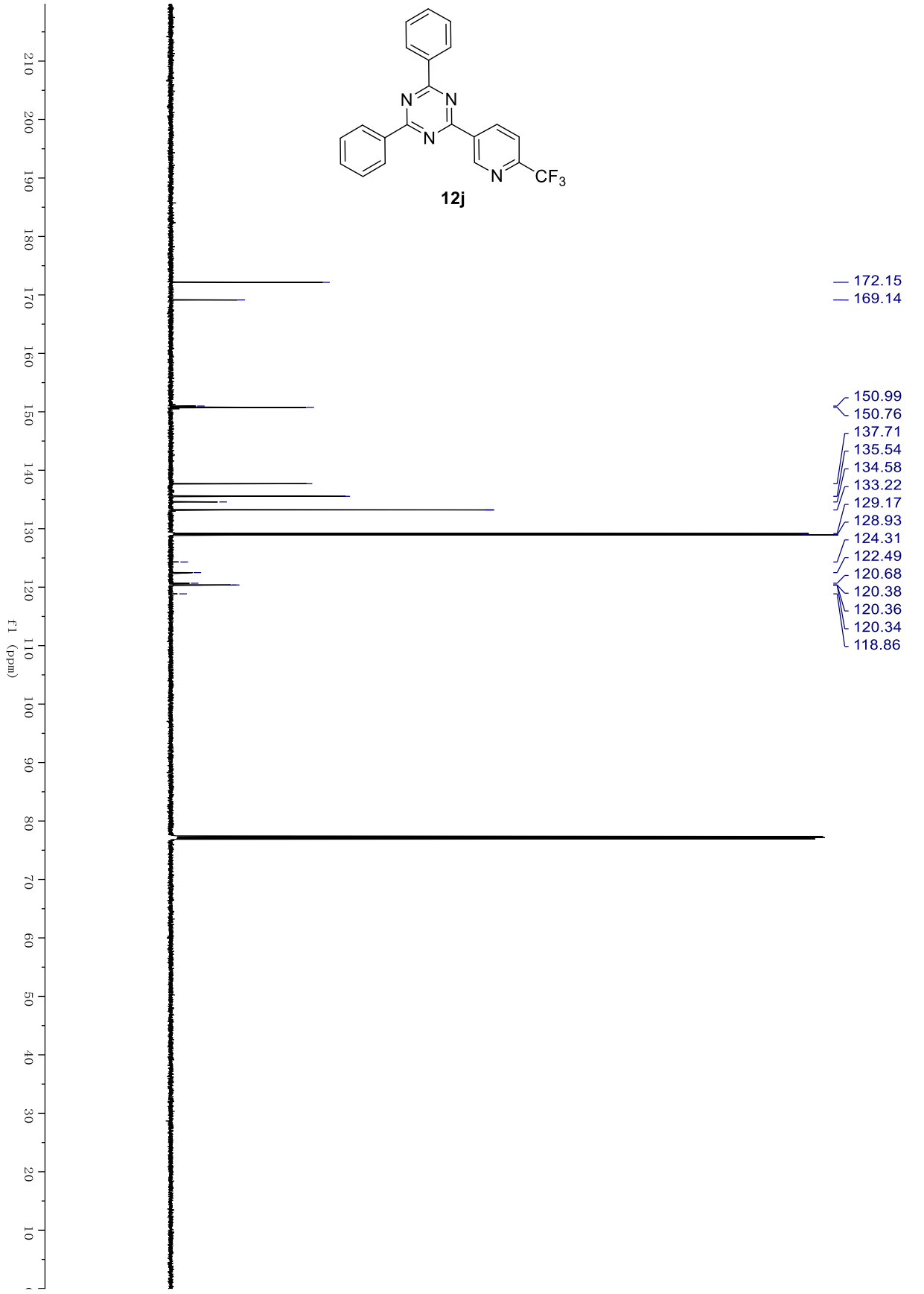

12h
9.12
9.11
8.80
8.79
7.64
7.63
7.61
7.59
7.57
7.56
7.55
7.54
7.53
1.94
3.95
2.22
4.00
1.04
f1 (ppm)

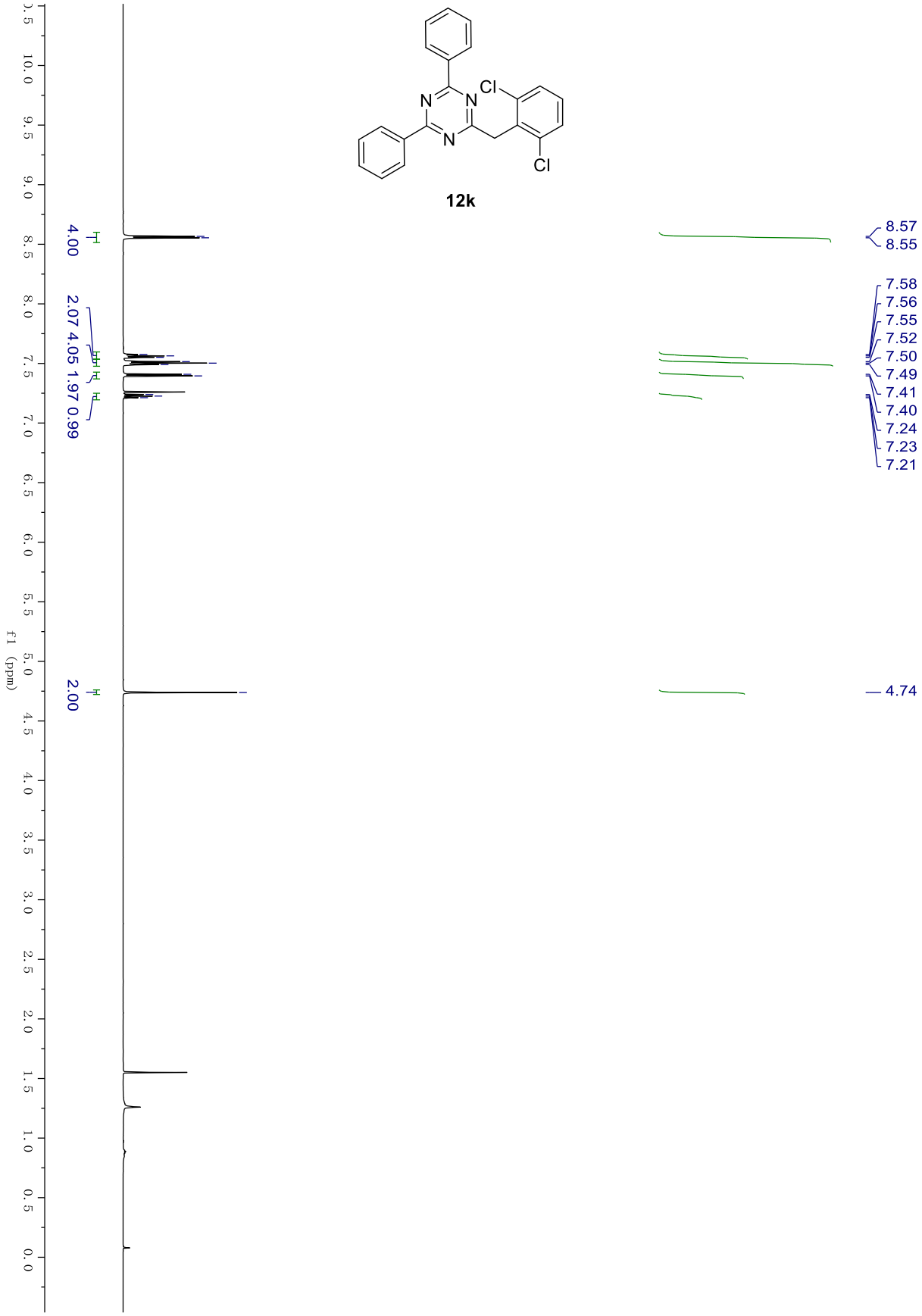

12h
173.02
170.66
162.61
158.27
135.62
133.13
129.54
128.85
122.24
f1 (ppm)

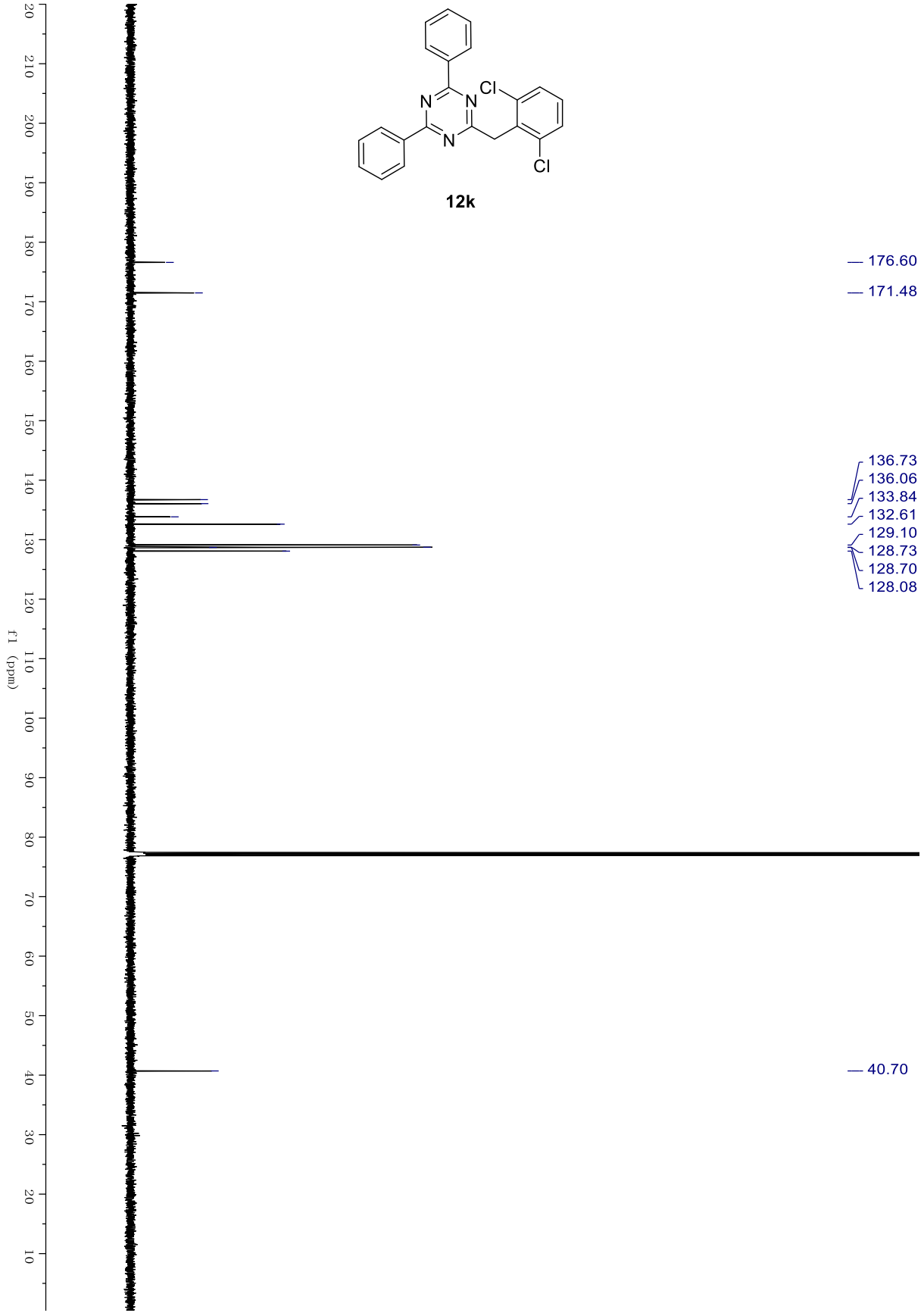

12i
8.74
8.74
8.72
8.72
8.38
8.38
8.37
8.37
7.65
7.65
7.64
7.64
7.63
7.61
7.60
7.58
7.57
7.56
7.25
7.25
7.25
7.24
4.00
1.01
1.02
2.05
4.02
1.03
f1 (ppm)

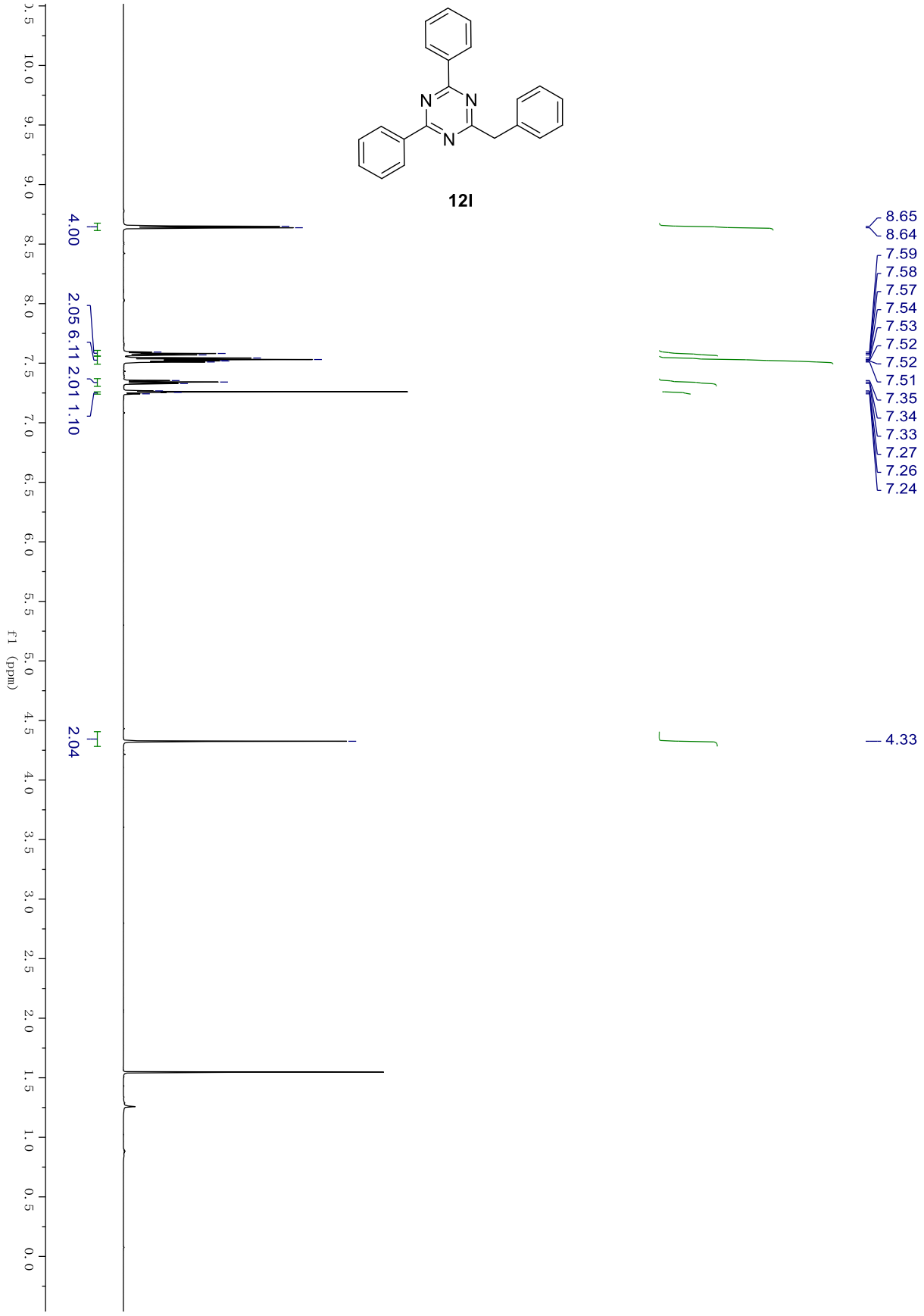

N
N
N
S
12i
171.69
168.25
142.31
136.08
132.71
132.30
131.64
129.09
128.76
128.62
f1 (ppm)

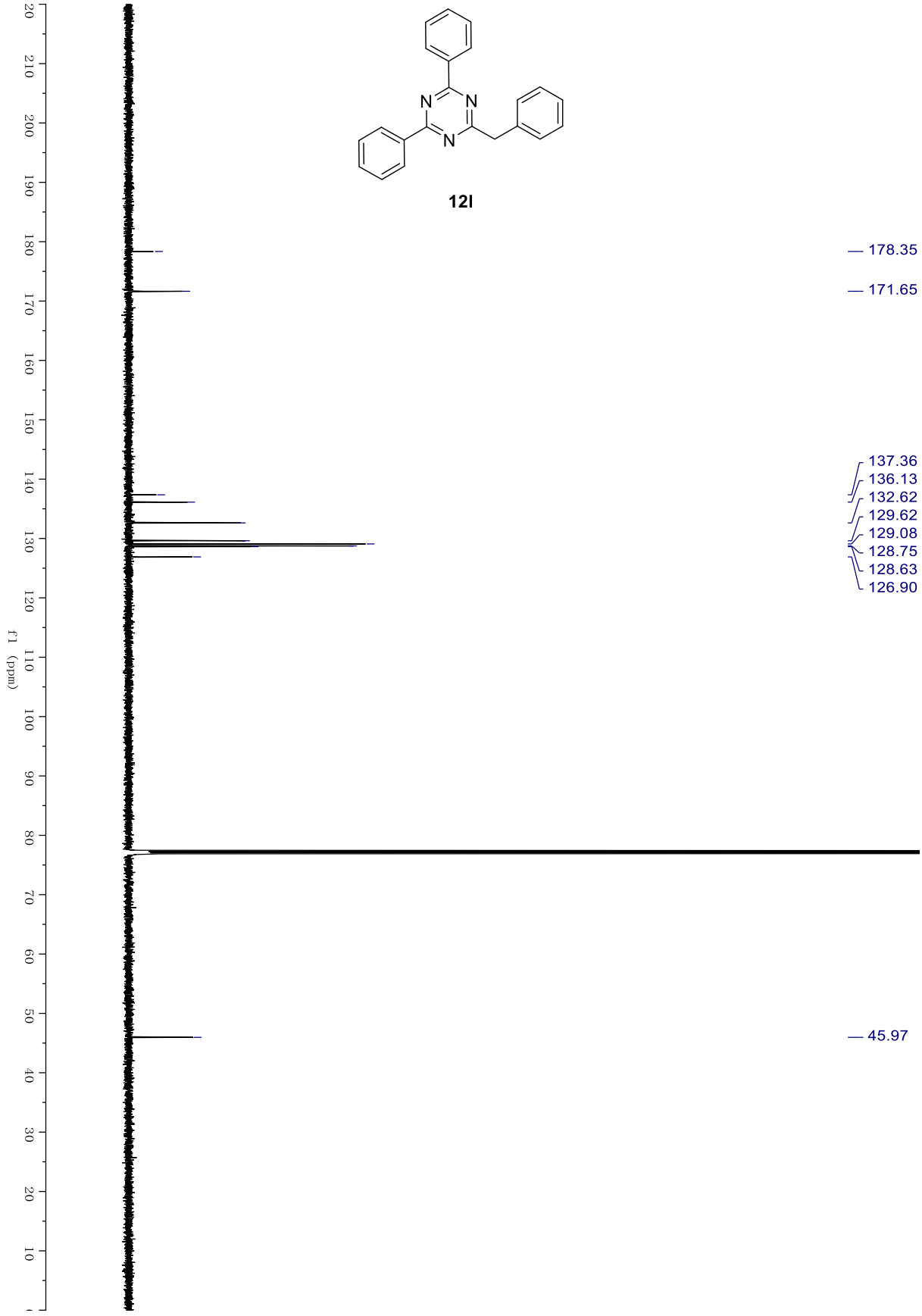

12j
N
N
N
N
CF3
9.97
9.97
9.11
9.11
9.09
9.09
8.72
8.70
7.86
7.85
7.64
7.63
7.62
7.58
7.57
7.56
0.99
1.00
4.00
1.00
2.03
3.99
f1 (ppm)

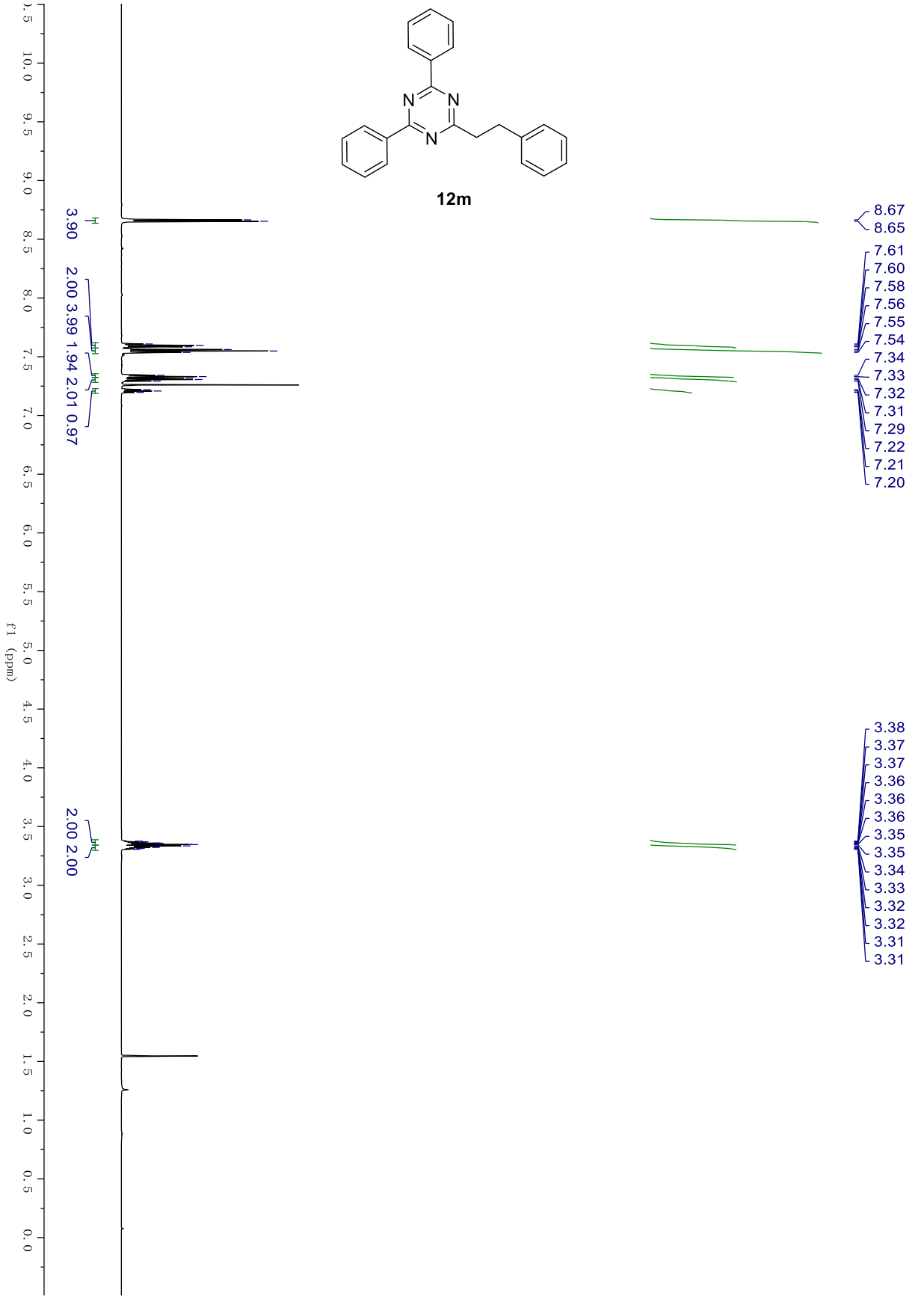

12j
172.15
169.14
150.99
150.76
137.71
135.54
134.58
133.22
129.17
128.93
124.31
122.49
120.68
120.38
120.36
120.34
118.86
f1 (ppm)

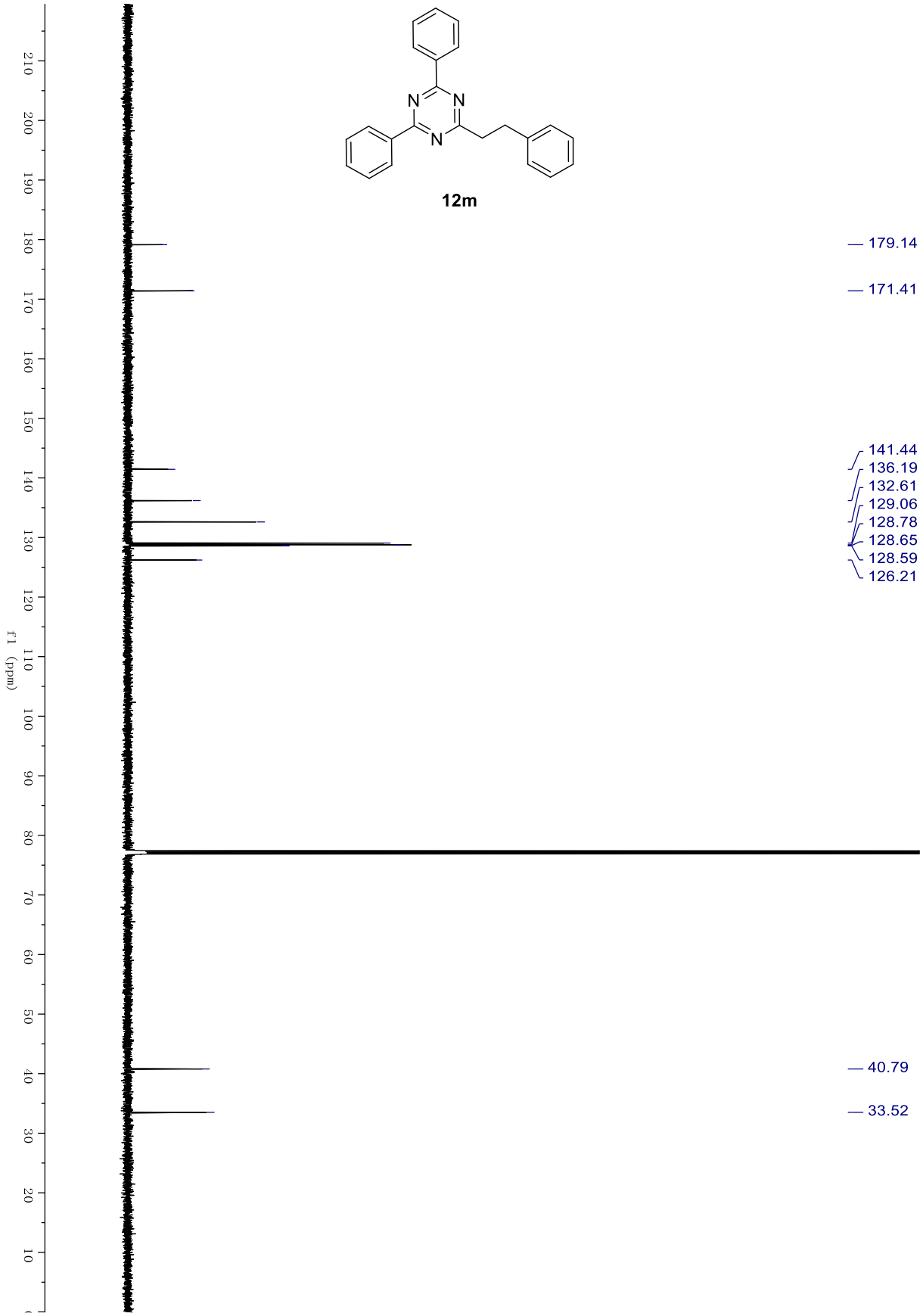

Cl
N
N
N
Cl
12k
8.57
8.55
7.58
7.56
7.55
7.52
7.50
7.49
7.41
7.40
7.24
7.23
7.21
4.74
4.00
2.07
4.05
1.97
0.99
2.00
f1 (ppm)

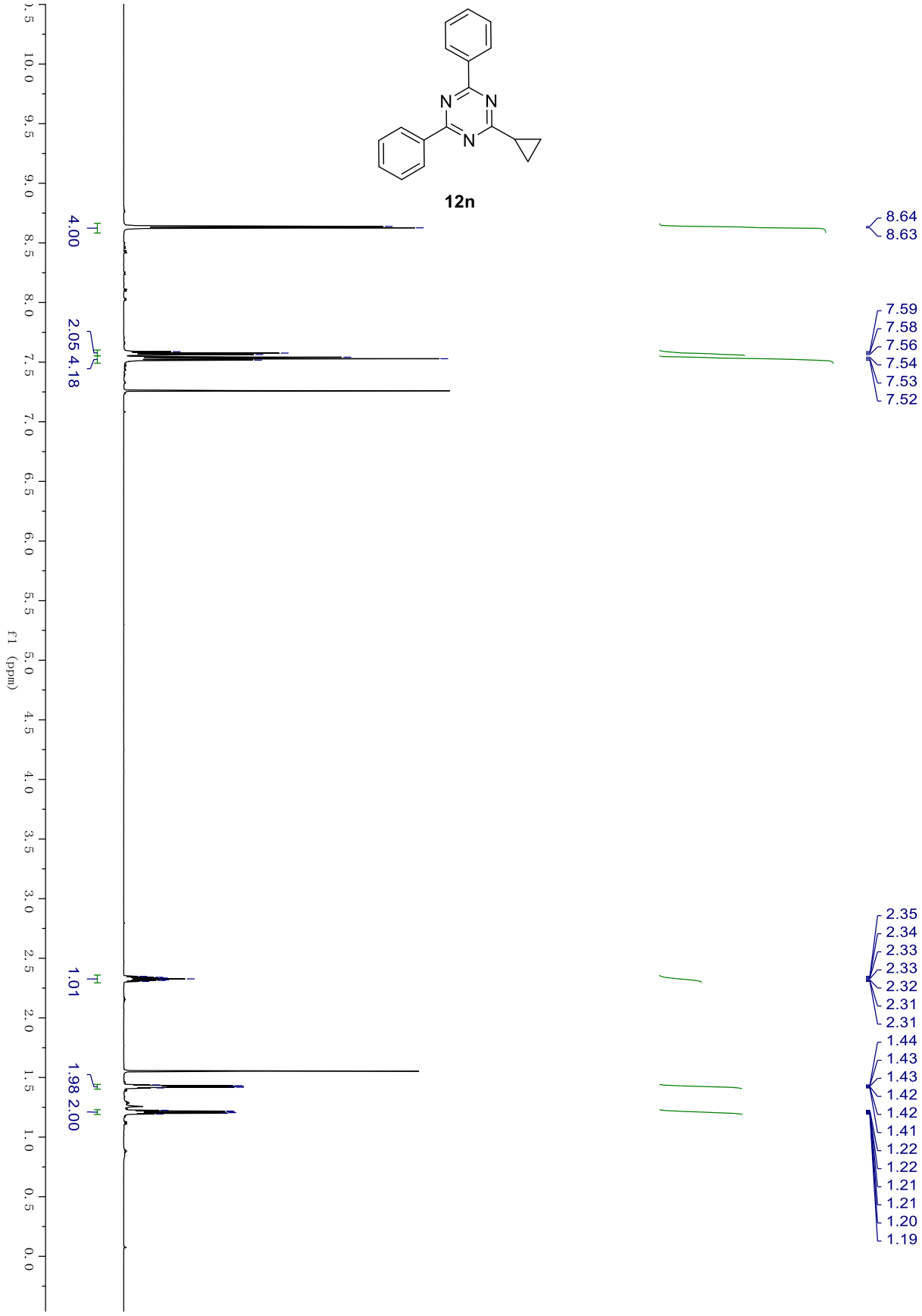

Cl
N
N
N
Cl
12k
176.60
171.48
136.73
136.06
133.84
132.61
129.10
128.73
128.70
128.08
40.70
f1 (ppm)

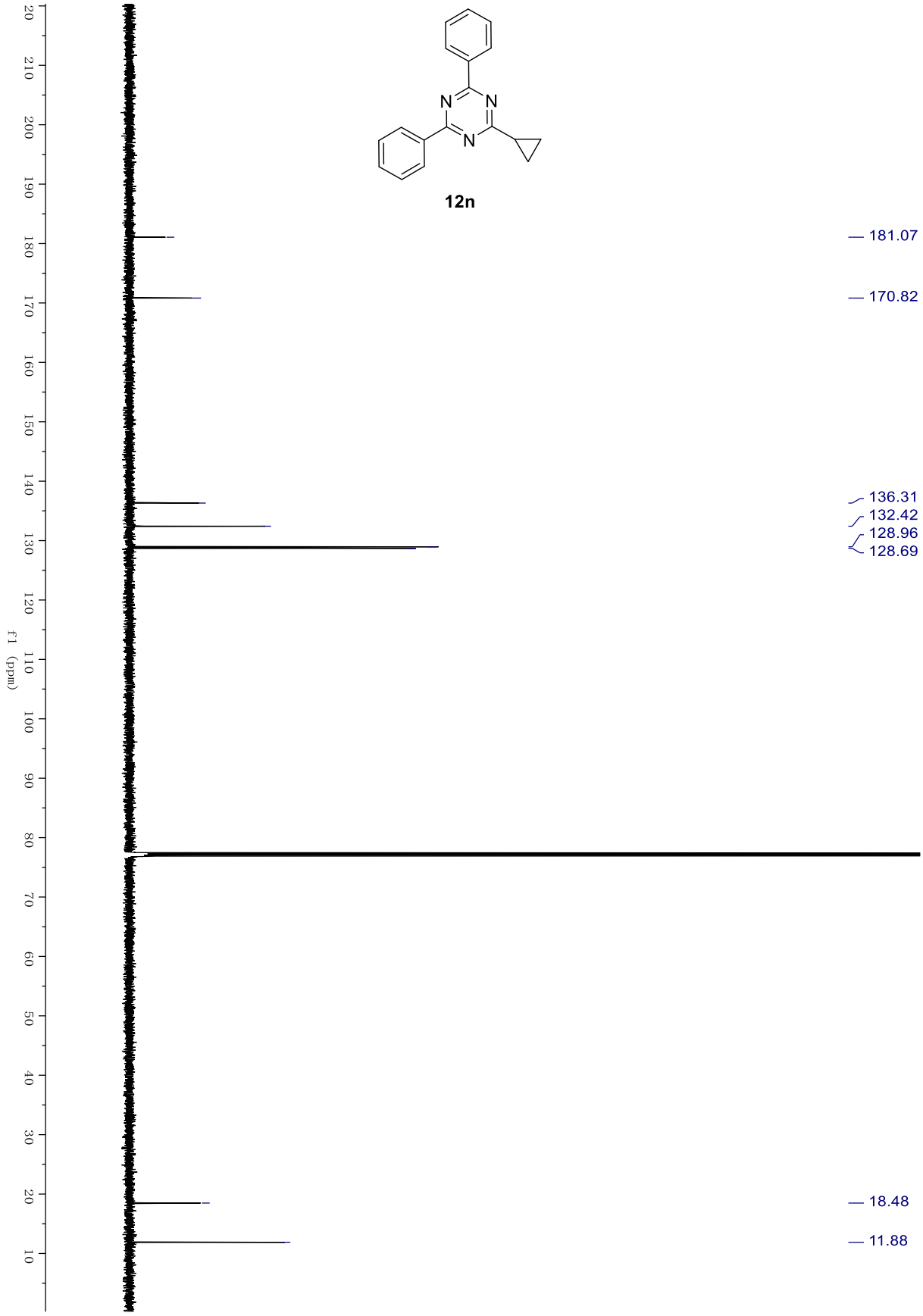

12l
8.65
8.64
7.59
7.58
7.57
7.54
7.53
7.52
7.52
7.51
7.35
7.34
7.33
7.27
7.26
7.24
4.33
4.00
2.05
6.11
2.01
1.10
2.04
f1 (ppm)

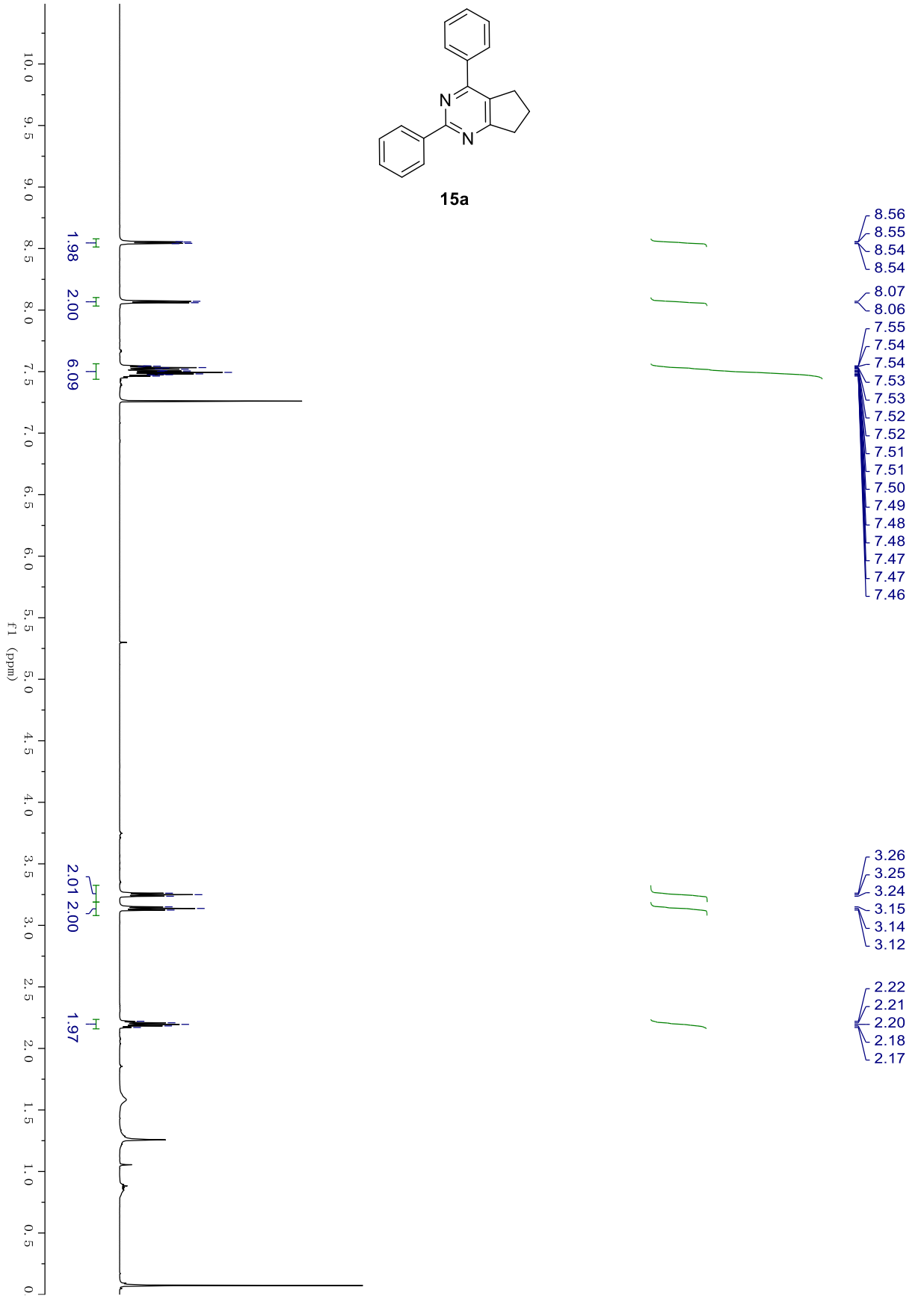

12l
178.35
171.65
137.36
136.13
132.62
129.62
129.08
128.75
128.63
126.90
45.97
f1 (ppm)

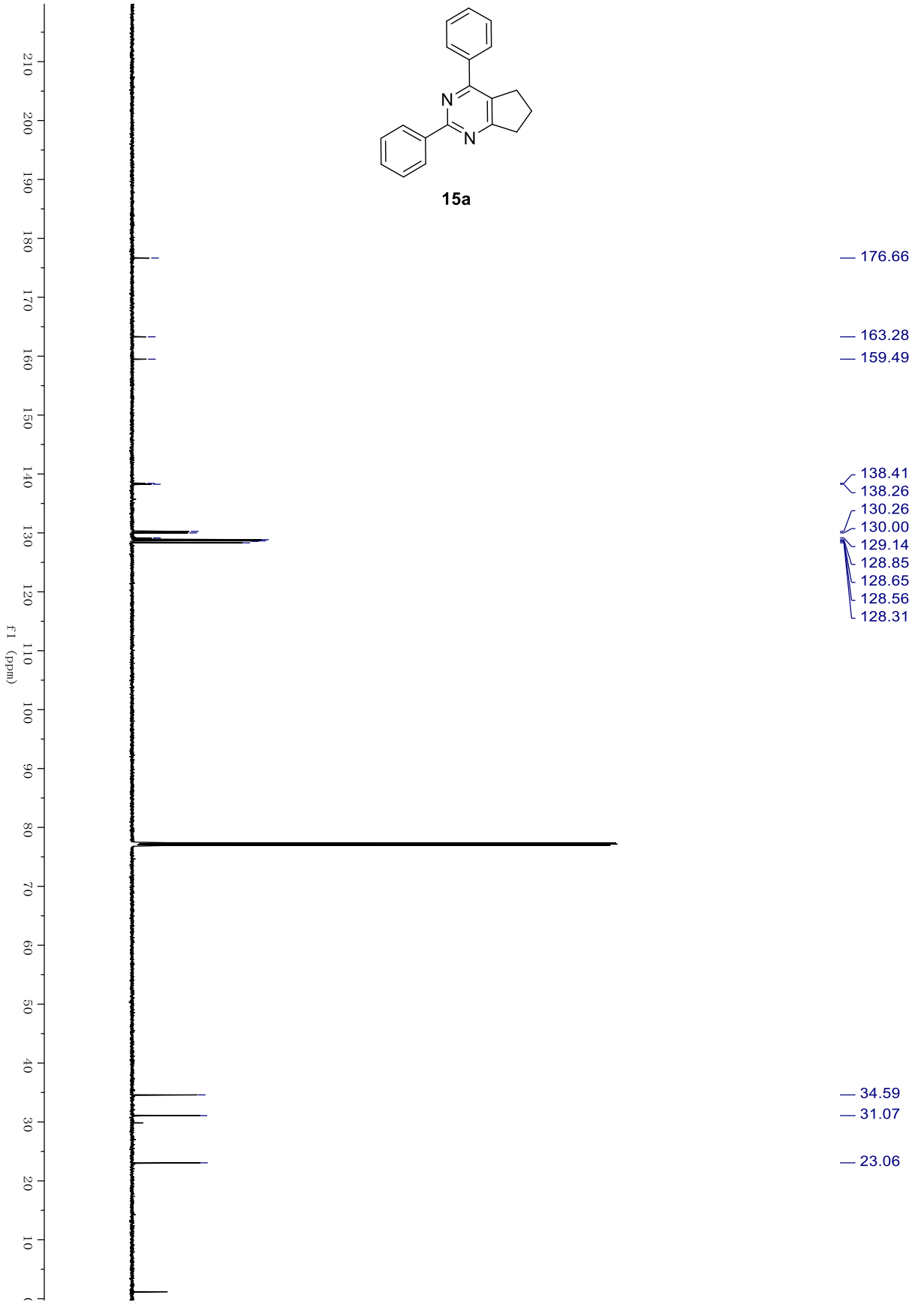

12m
8.67
8.65
7.61
7.60
7.58
7.56
7.55
7.54
7.34
7.33
7.32
7.31
7.29
7.22
7.21
7.20
3.38
3.37
3.37
3.36
3.36
3.36
3.35
3.35
3.34
3.33
3.32
3.32
3.31
3.31
3.90
2.00 3.99 1.94 2.01 0.97
2.00 2.00
f1 (ppm)

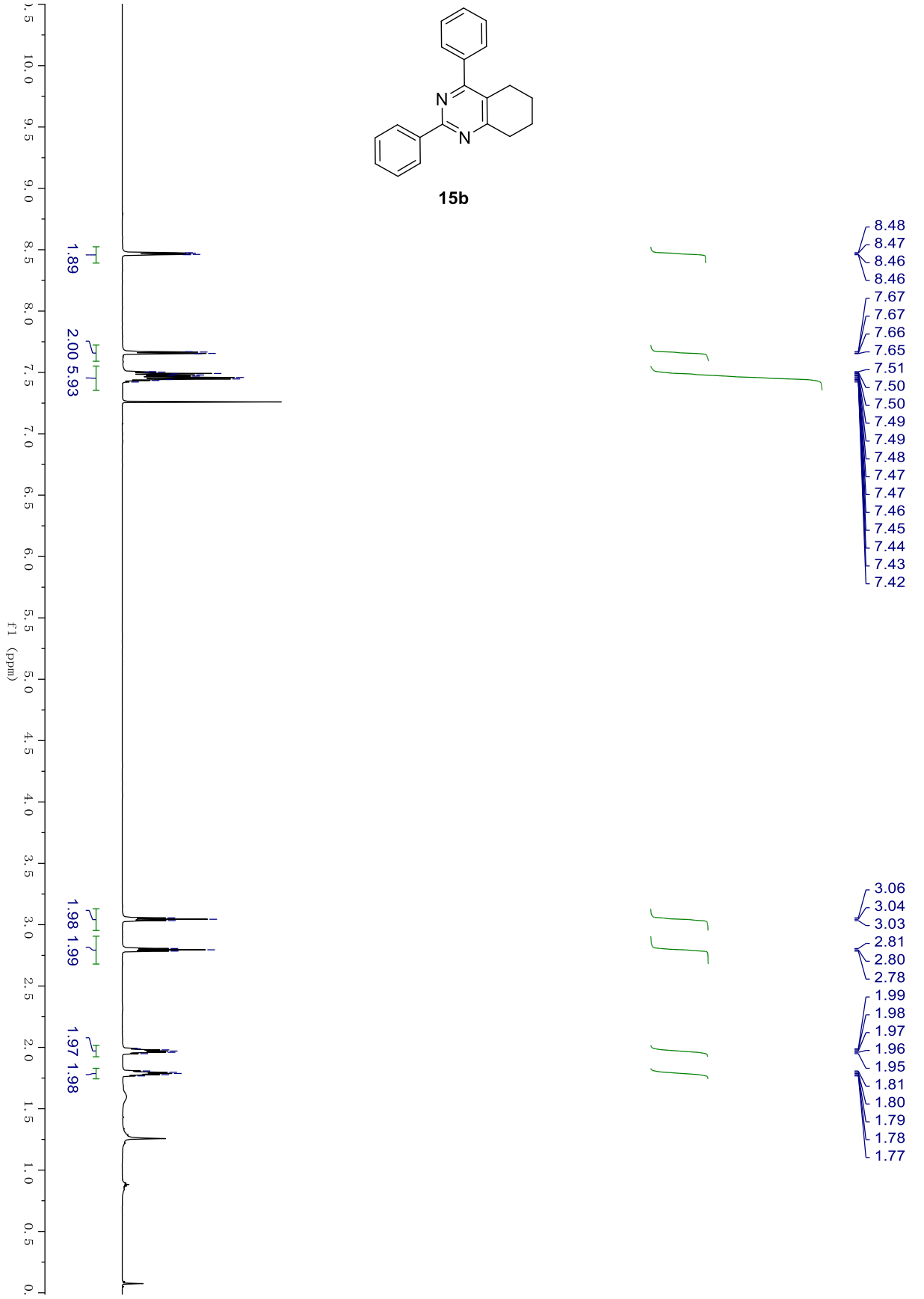

12m
179.14
171.41
141.44
136.19
132.61
129.06
128.78
128.65
128.59
126.21
40.79
33.52
f1 (ppm)

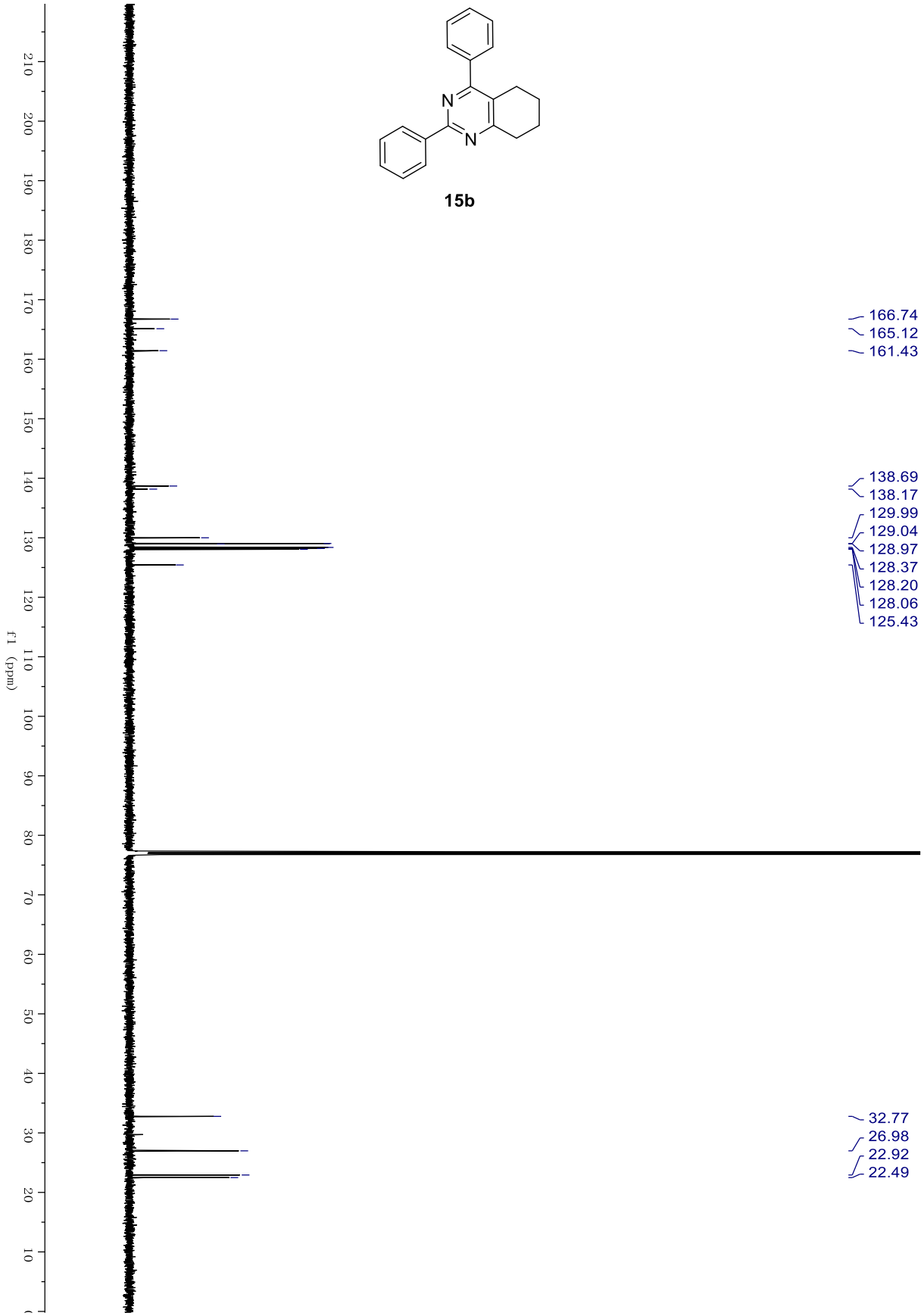

12n
8.64
8.63
7.59
7.58
7.56
7.54
7.53
7.52
2.35
2.34
2.33
2.33
2.32
2.31
2.31
1.44
1.43
1.43
1.42
1.42
1.41
1.22
1.22
1.21
1.21
1.20
1.19
4.00
2.05
4.18
1.01
1.98
2.00
f1 (ppm)

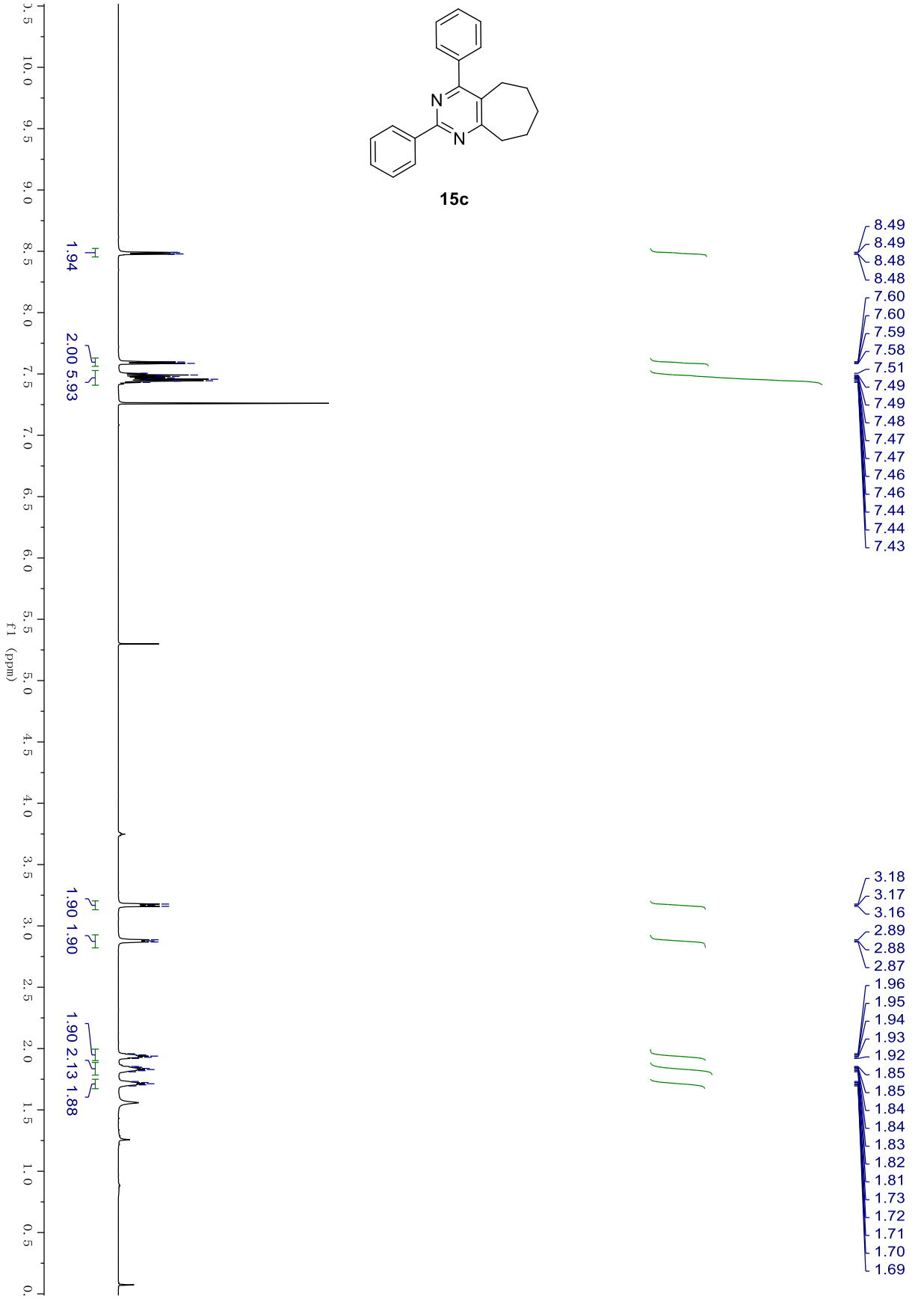

N
N
N
12n
181.07
170.82
136.31
132.42
128.96
128.69
18.48
11.88
f1 (ppm)

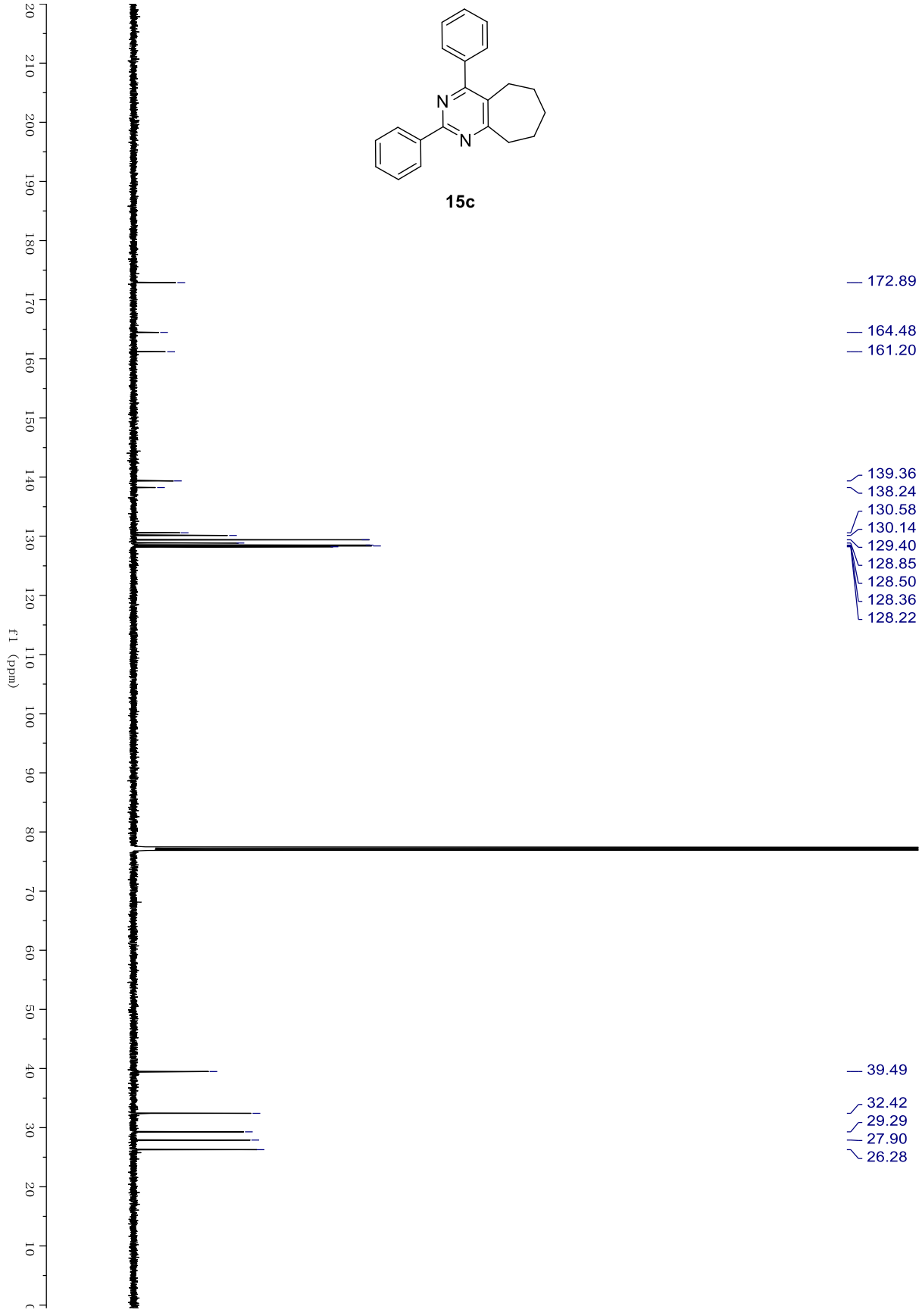

15a
N
N
8.56
8.55
8.54
8.54
8.07
8.06
7.55
7.54
7.54
7.53
7.53
7.52
7.52
7.51
7.51
7.50
7.49
7.48
7.48
7.47
7.47
7.46
3.26
3.25
3.24
3.15
3.14
3.12
2.22
2.21
2.20
2.18
2.17
1.98
2.00
6.09
2.01
2.00
1.97
f1 (ppm)

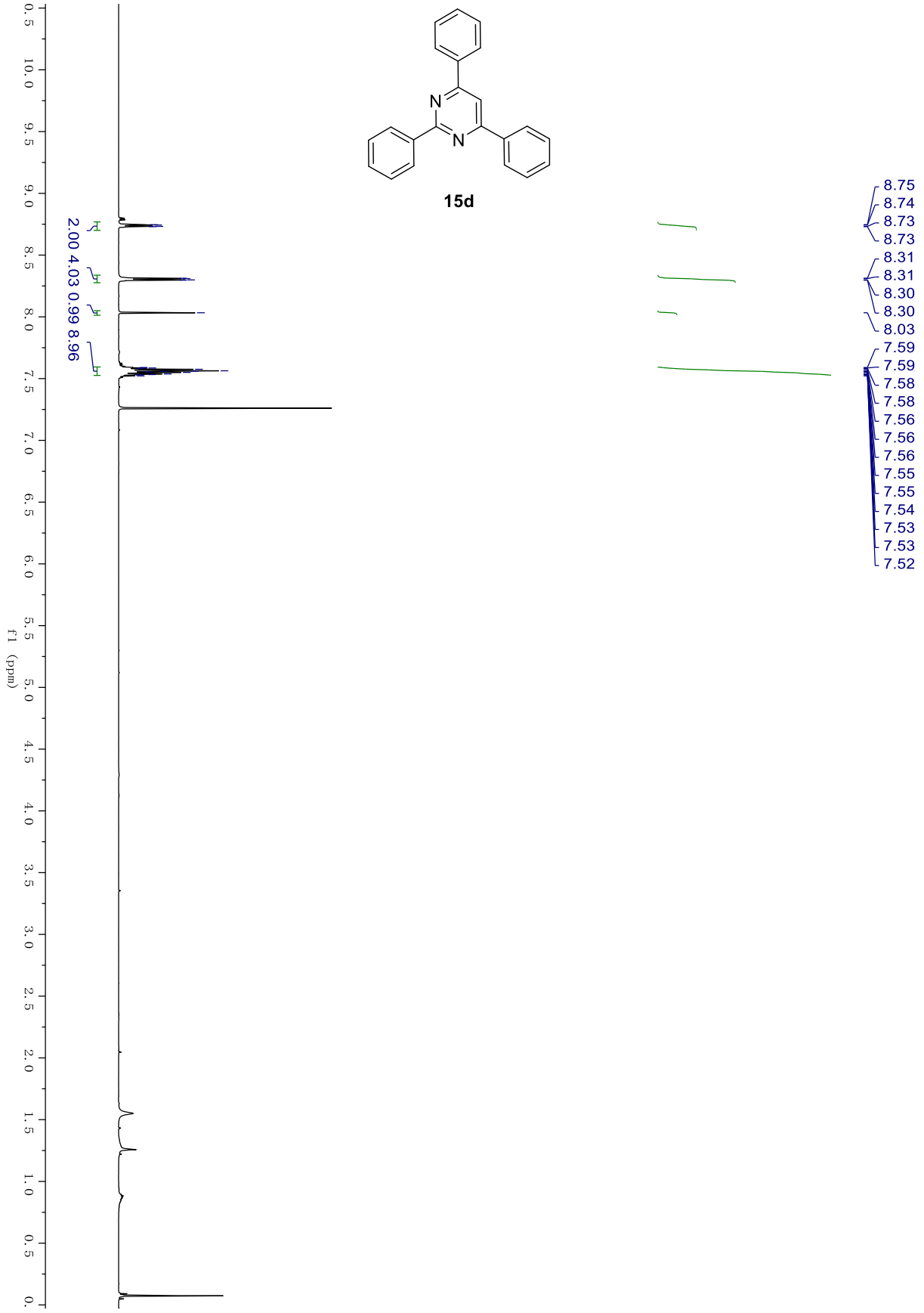

15a
176.66
163.28
159.49
138.41
138.26
130.26
130.00
129.14
128.85
128.65
128.56
128.31
34.59
31.07
23.06
f1 (ppm)

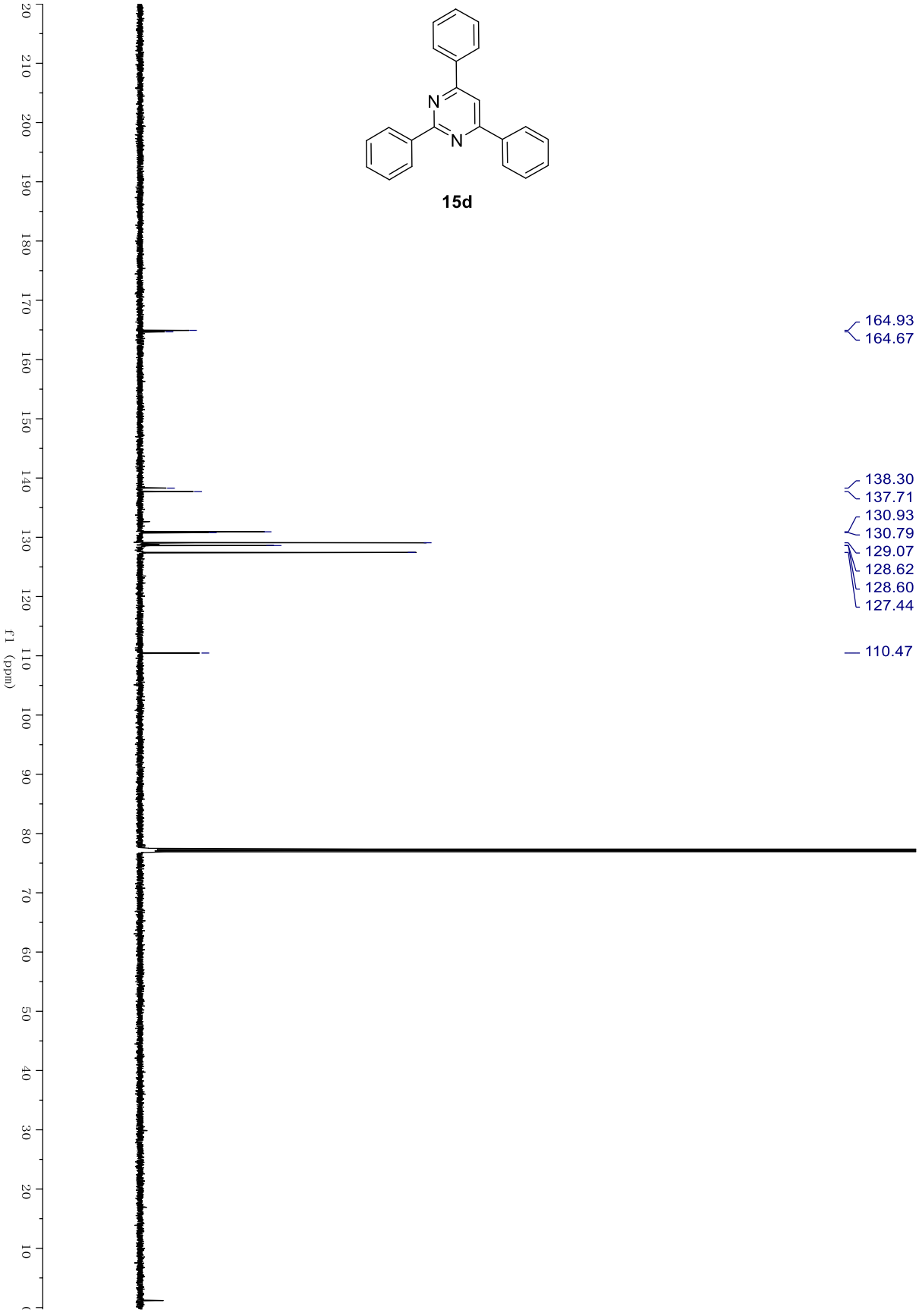

15b
N
N
8.48
8.47
8.46
8.46
7.67
7.67
7.66
7.65
7.51
7.50
7.50
7.49
7.49
7.48
7.47
7.47
7.46
7.45
7.44
7.43
7.42
3.06
3.04
3.03
2.81
2.80
2.78
1.99
1.98
1.97
1.96
1.95
1.81
1.80
1.79
1.78
1.77
1.89
2.00
5.93
1.98
1.99
1.97
1.98
f1 (ppm)

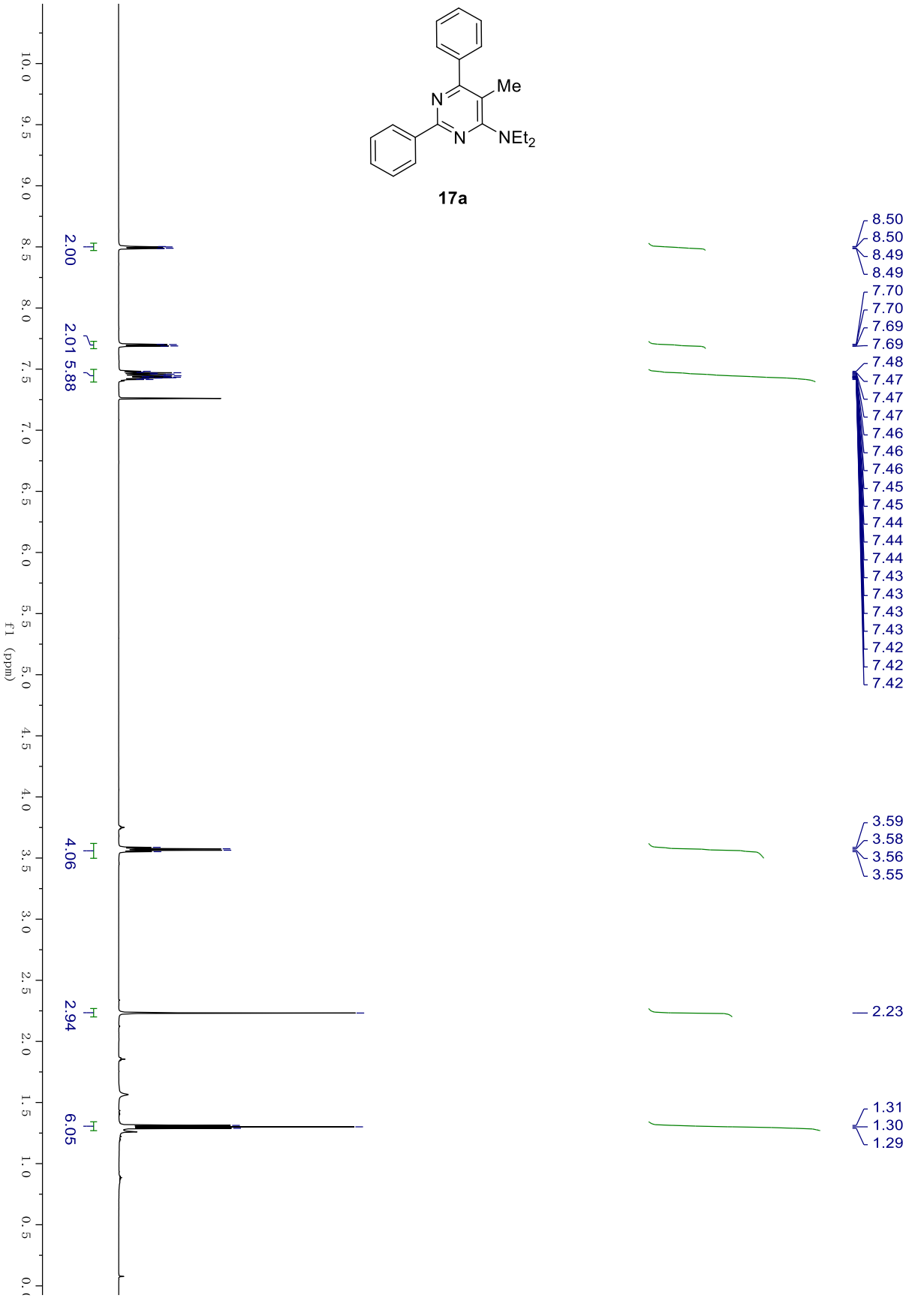

N
N
15b
166.74
165.12
161.43
138.69
138.17
129.99
129.04
128.97
128.37
128.20
128.06
125.43
32.77
26.98
22.92
22.49
f1 (ppm)

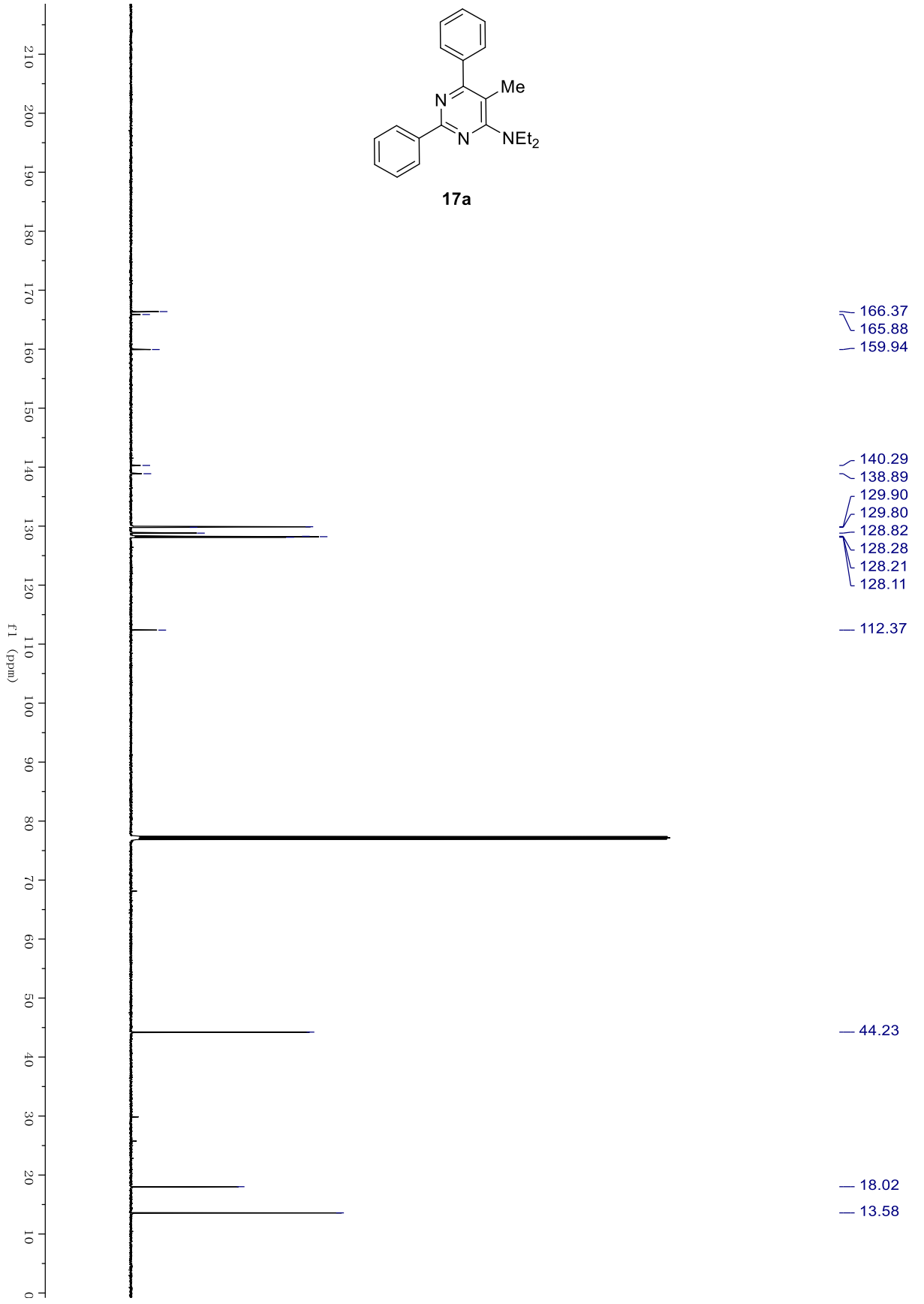

15c
N
N
8.49
8.49
8.48
8.48
7.60
7.60
7.59
7.58
7.51
7.49
7.49
7.48
7.47
7.47
7.46
7.46
7.44
7.44
7.43
3.18
3.17
3.16
2.89
2.88
2.87
1.96
1.95
1.94
1.93
1.92
1.85
1.85
1.84
1.84
1.83
1.82
1.81
1.73
1.72
1.71
1.70
1.69
1.94
2.00
5.93
1.90
1.90
1.90
2.13
1.88
f1 (ppm)

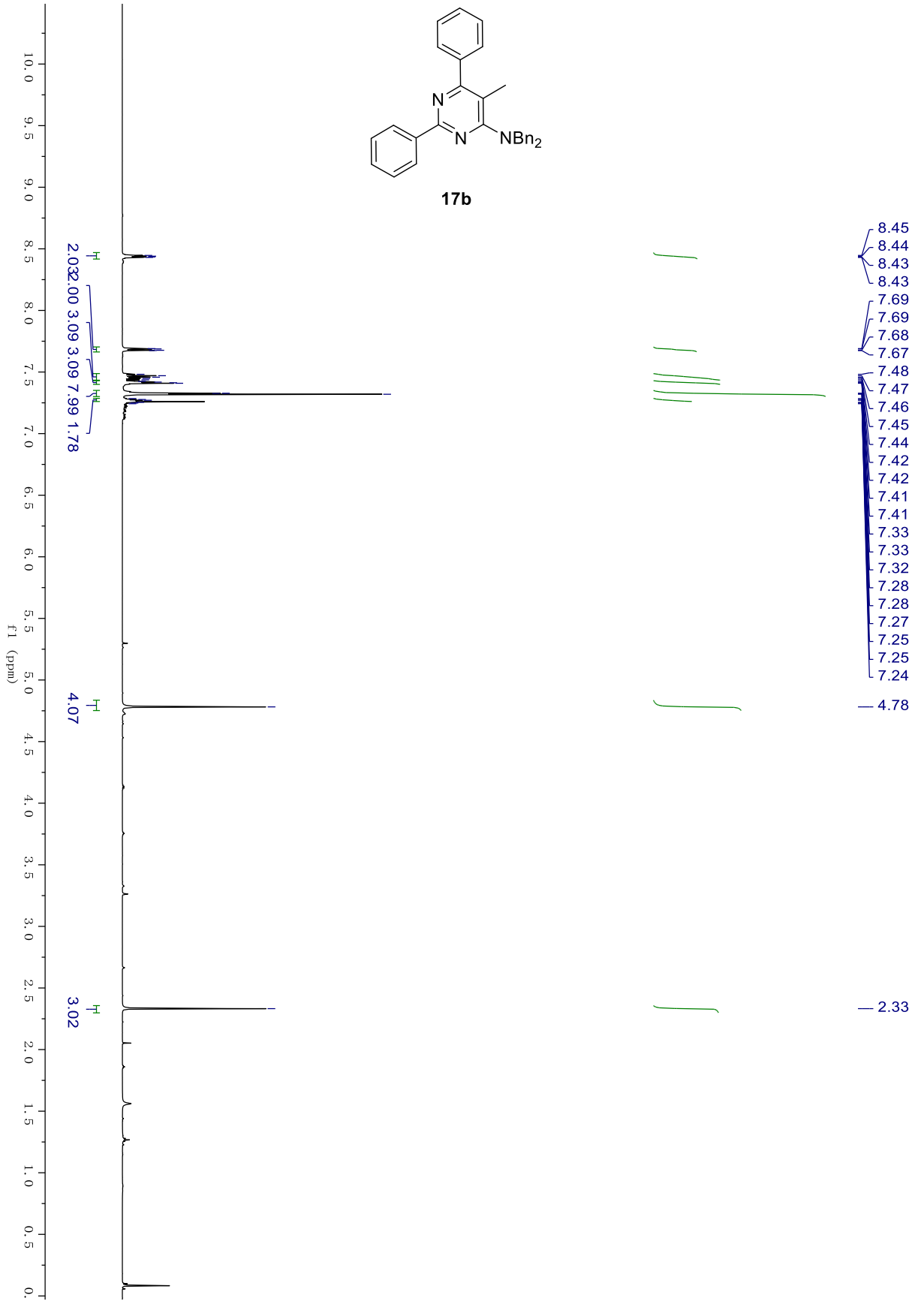

15c
172.89
164.48
161.20
139.36
138.24
130.58
130.14
129.40
128.85
128.50
128.36
128.22
39.49
32.42
29.29
27.90
26.28
f1 (ppm)

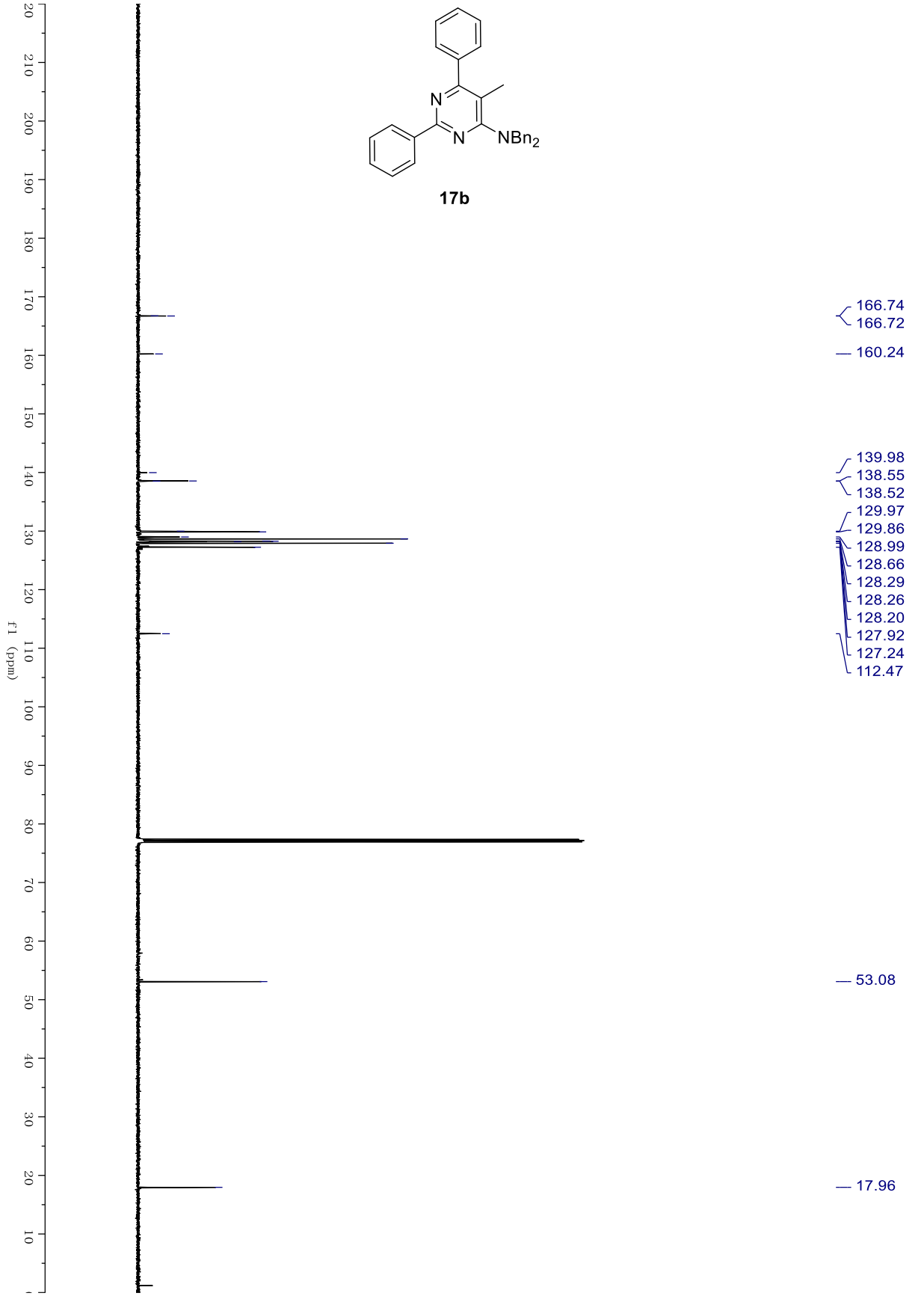

15d
2.00 4.03 0.99 8.96
8.75
8.74
8.73
8.73
8.31
8.31
8.30
8.30
8.03
7.59
7.59
7.58
7.58
7.56
7.56
7.56
7.55
7.55
7.54
7.53
7.53
7.52
f1 (ppm)

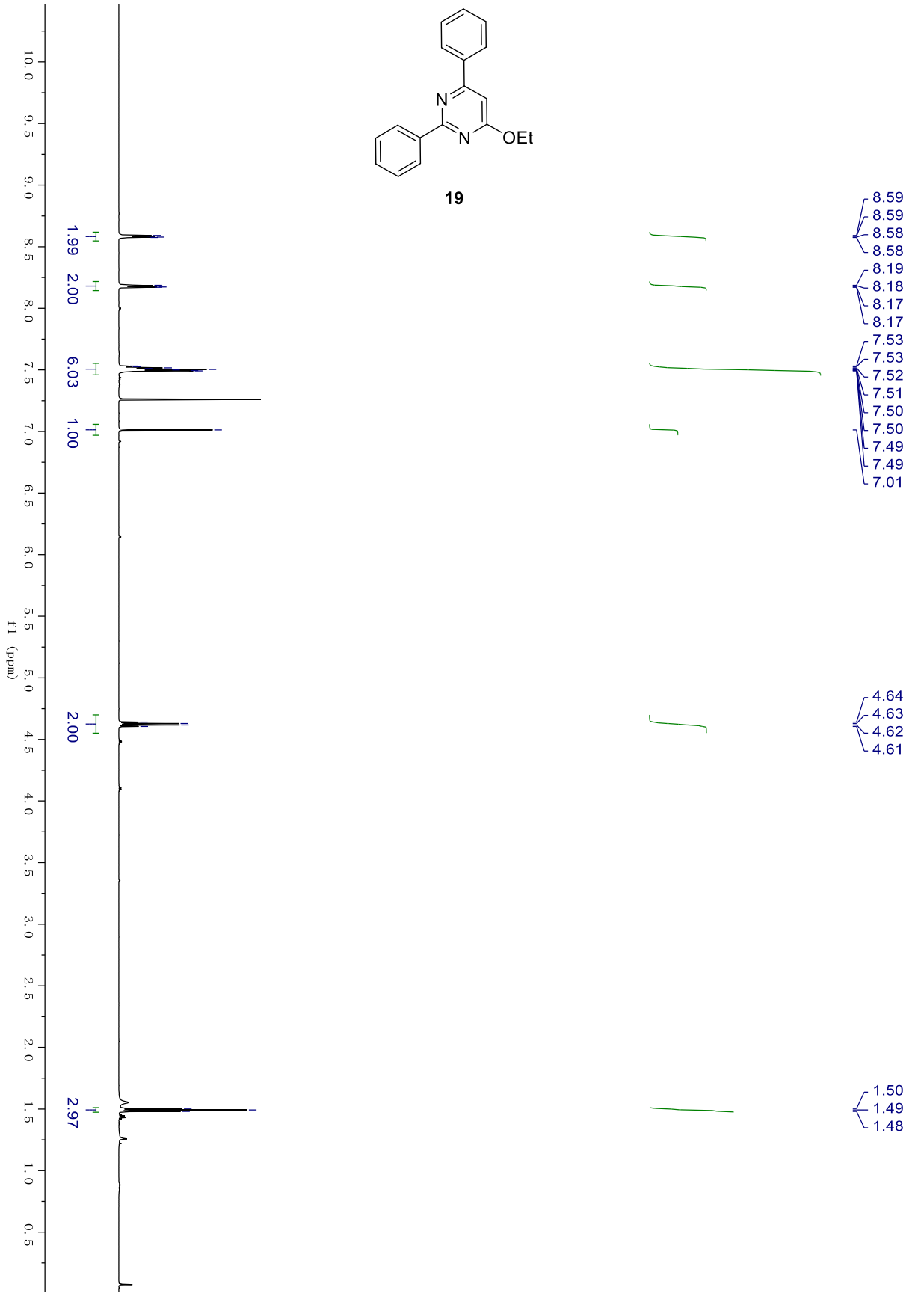

N
N
15d
164.93
164.67
138.30
137.71
130.93
130.79
129.07
128.62
128.60
127.44
110.47
f1 (ppm)

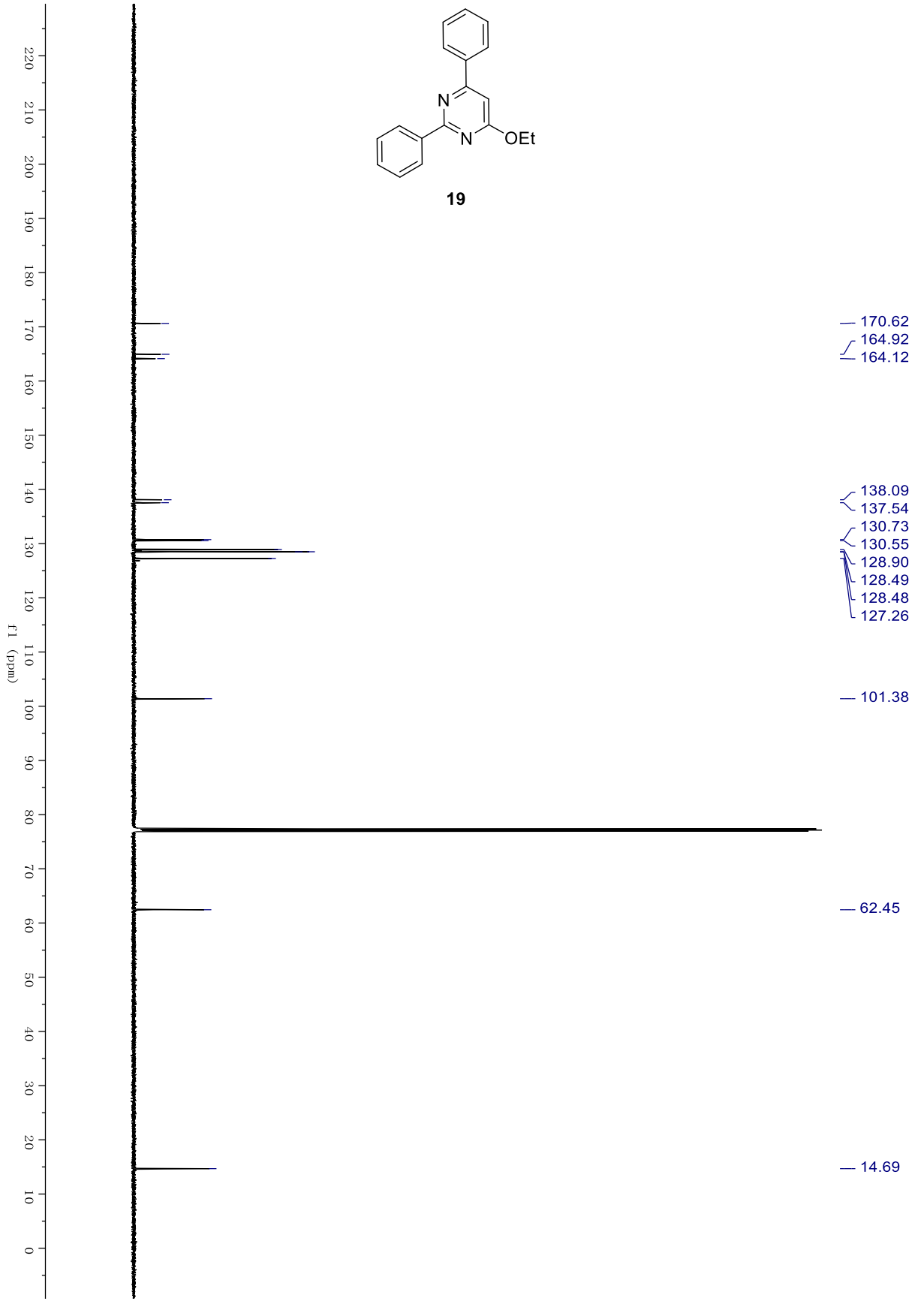

Me
N
N
NEt2
17a
8.50
8.50
8.49
8.49
7.70
7.70
7.69
7.69
7.48
7.47
7.47
7.47
7.46
7.46
7.46
7.45
7.45
7.44
7.44
7.44
7.43
7.43
7.43
7.43
7.42
7.42
7.42
3.59
3.58
3.56
3.55
2.23
1.31
1.30
1.29
2.00
2.01
5.88
4.06
2.94
6.05
f1 (ppm)

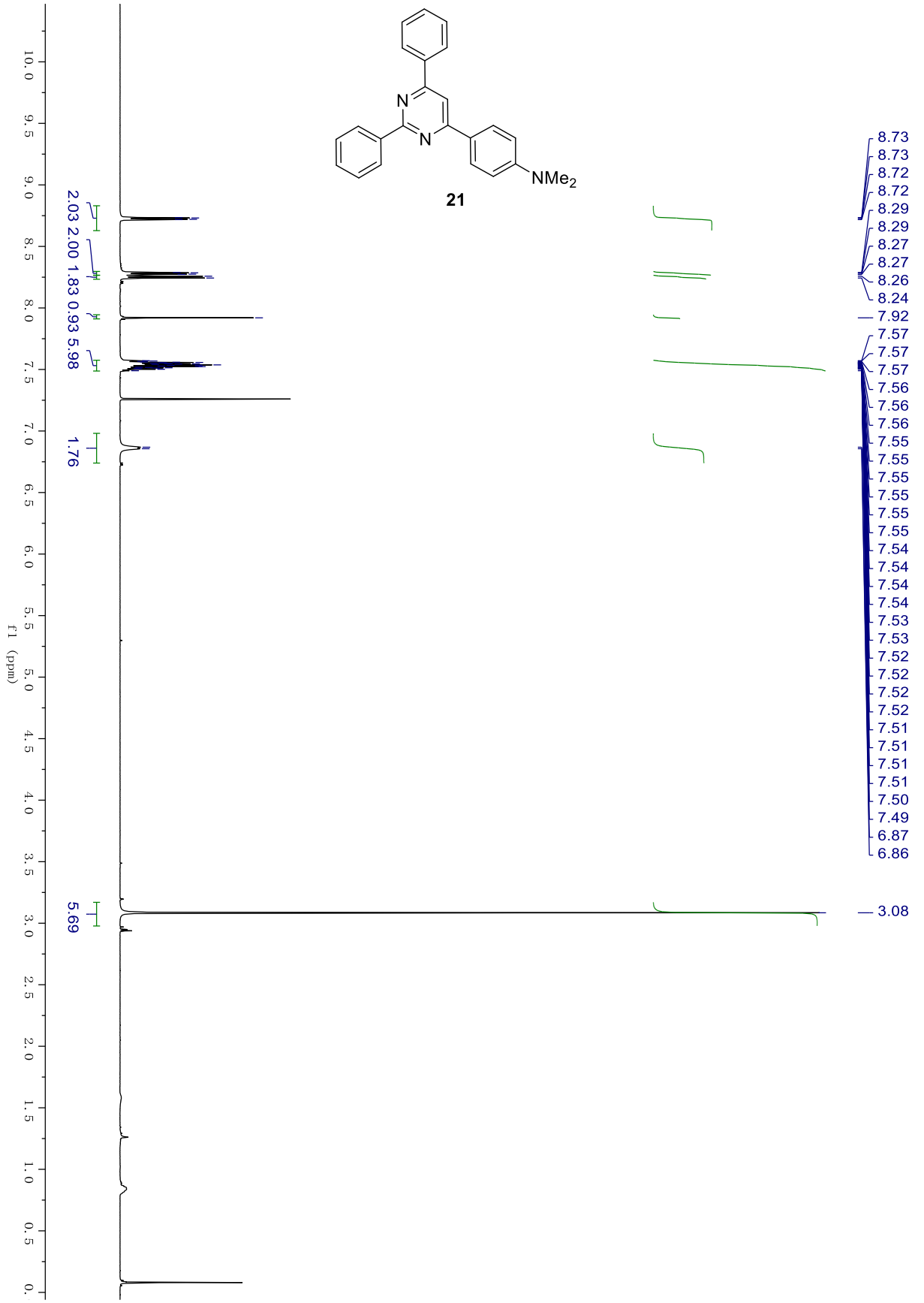

Me
N
N
NEt2
17a
166.37
165.88
159.94
140.29
138.89
129.90
129.80
128.82
128.28
128.21
128.11
112.37
44.23
18.02
13.58
f1 (ppm)


N
N
NBn2
17b
8.45
8.44
8.43
8.43
7.69
7.69
7.68
7.67
7.48
7.47
7.46
7.45
7.44
7.42
7.42
7.41
7.41
7.33
7.33
7.32
7.28
7.28
7.27
7.25
7.25
7.24
4.78
2.33
2.03
2.00
3.09
3.09
7.99
1.78
4.07
3.02
f1 (ppm)


N
N
NBn2
17b
166.74
166.72
160.24
139.98
138.55
138.52
129.97
129.86
128.99
128.66
128.29
128.26
128.20
127.92
127.24
112.47
53.08
17.96
f1 (ppm)


N
N
OEt
19
8.59
8.59
8.58
8.58
8.19
8.18
8.17
8.17
7.53
7.53
7.52
7.51
7.50
7.50
7.49
7.49
7.01
4.64
4.63
4.62
4.61
1.50
1.49
1.48
1.99
2.00
6.03
1.00
2.00
2.97
f1 (ppm)


N
N
OEt
19
170.62
164.92
164.12
138.09
137.54
130.73
130.55
128.90
128.49
128.48
127.26
101.38
62.45
14.69
f1 (ppm)


N
N
NMe2
21
8.73
8.73
8.72
8.72
8.29
8.29
8.27
8.27
8.26
8.24
7.92
7.57
7.57
7.57
7.56
7.56
7.56
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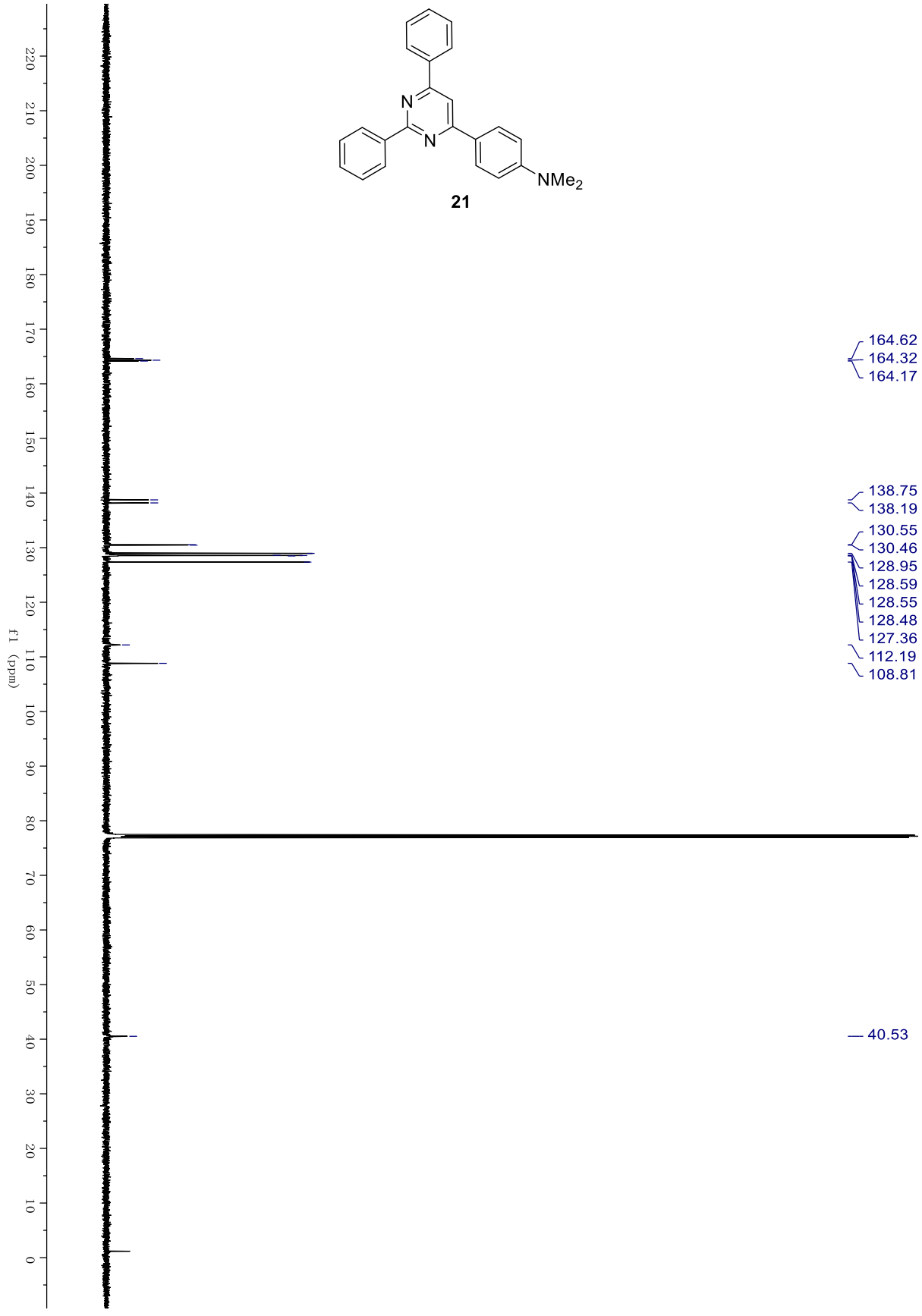
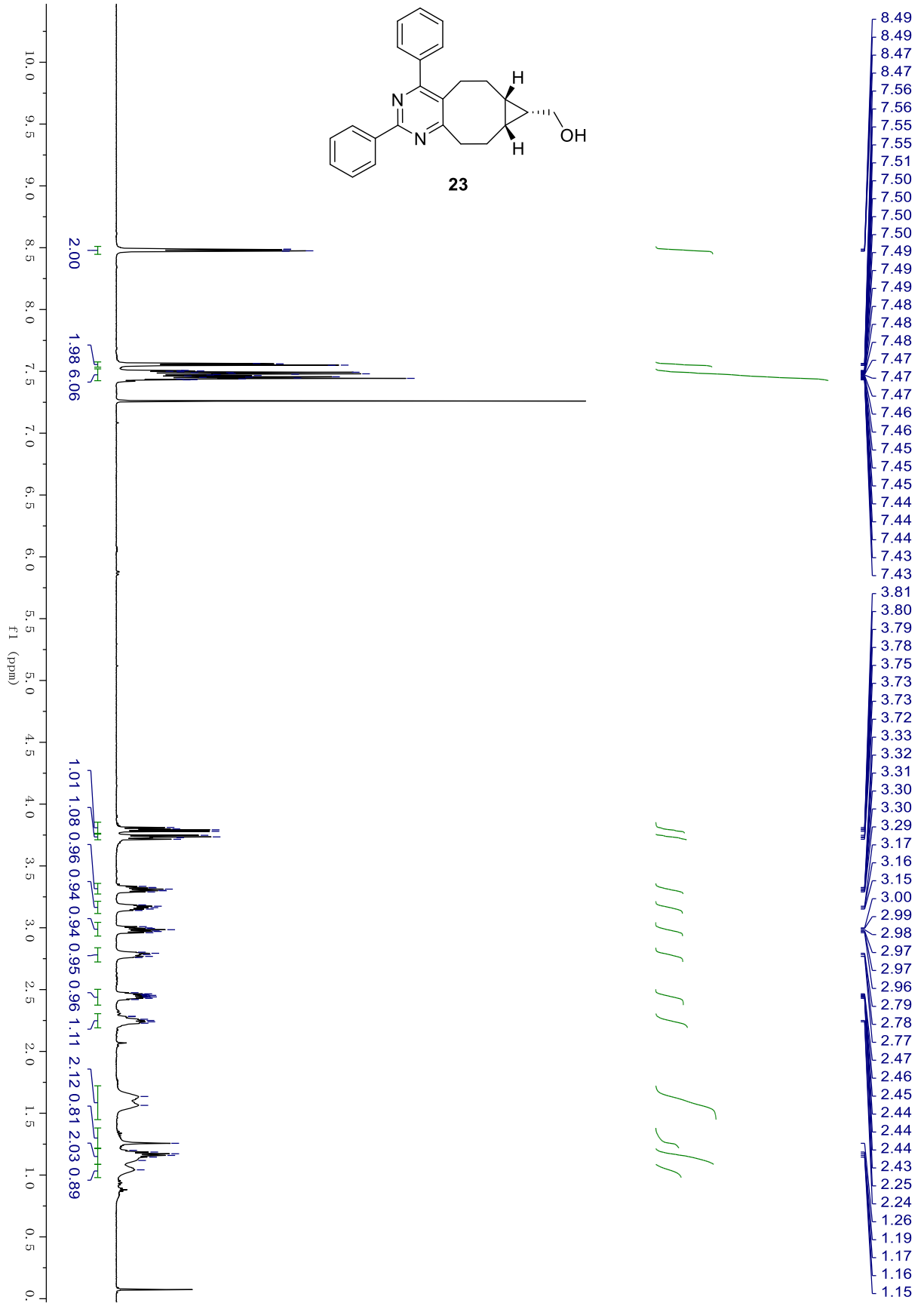
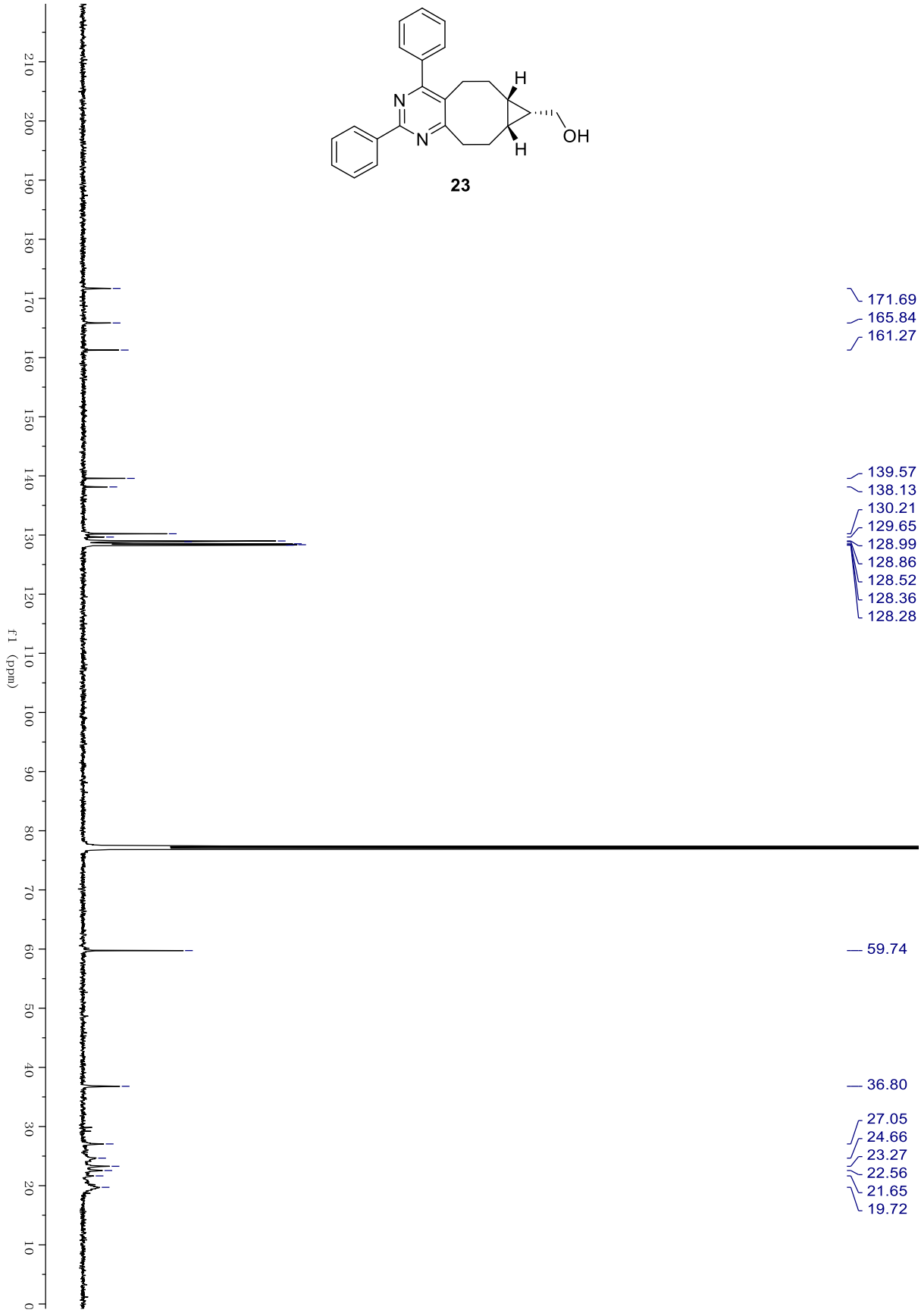
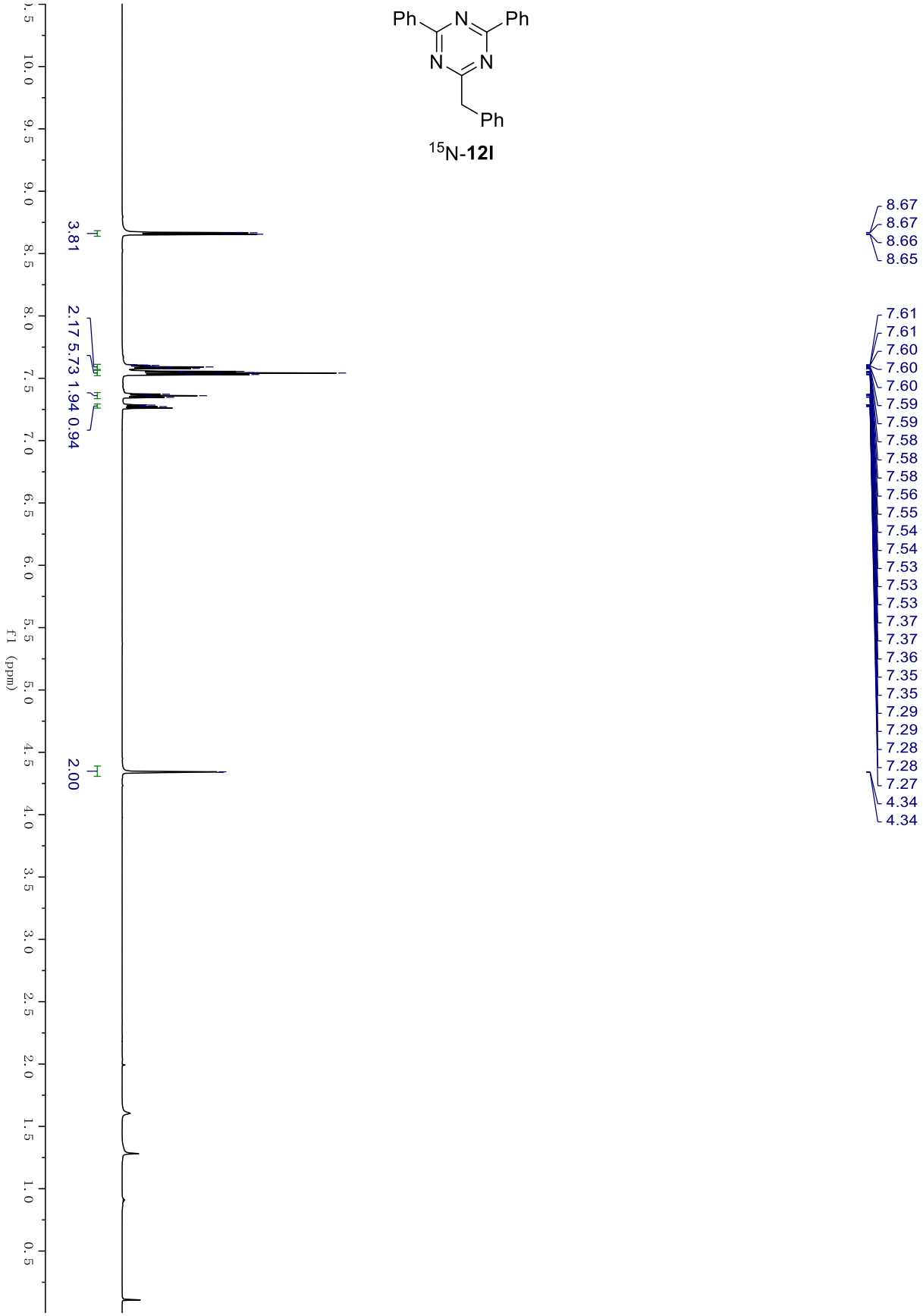
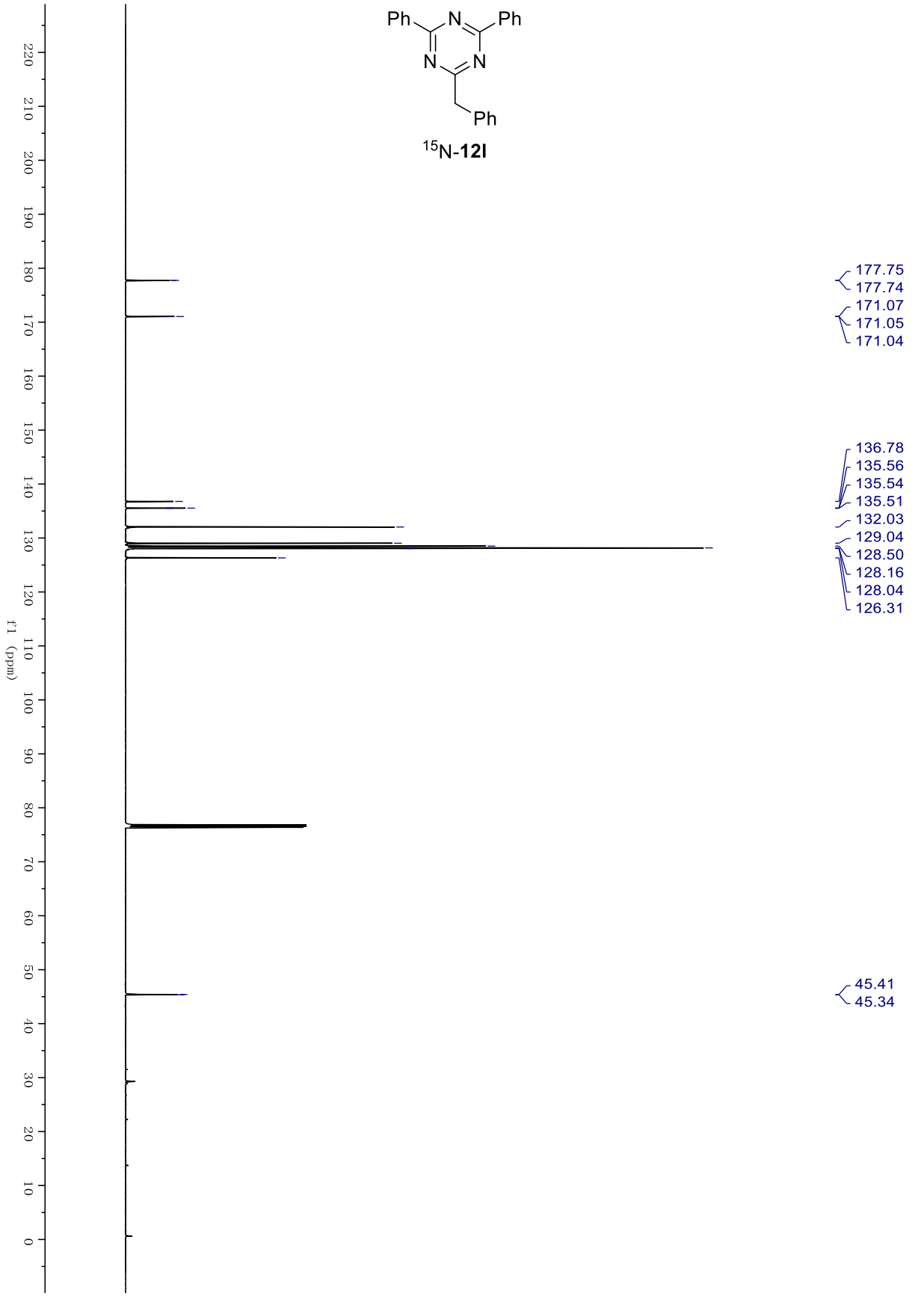
7.55
7.55
7.55
7.55
7.55
7.54
7.54
7.54
7.54
7.53
7.53
7.52
7.52
7.52
7.52
7.51
7.51
7.51
7.51
7.50
7.49
6.87
6.86
3.08
2.03 2.00 1.83 0.93 5.98
1.76
5.69
f1 (ppm)


N
N
NMe2
21
164.62
164.32
164.17
138.75
138.19
130.55
130.46
128.95
128.59
128.55
128.48
127.36
112.19
108.81
40.53
f1 (ppm)


N
N
H
H
OH
23
f1 (ppm)
2.00
1.98
6.06
1.01
1.08
0.96
0.94
0.94
0.95
0.96
1.11
2.12
0.81
2.03
0.89


N
N
H
H
OH
23
171.69
165.84
161.27
139.57
138.13
130.21
129.65
128.99
128.86
128.52
128.36
128.28
59.74
36.80
27.05
24.66
23.27
22.56
21.65
19.72
f1 (ppm)


Ph
N
Ph
N
N
Ph
15N-12l
8.67
8.67
8.66
8.65
7.61
7.61
7.60
7.60
7.60
7.59
7.59
7.58
7.58
7.58
7.56
7.55
7.54
7.54
7.53
7.53
7.53
7.37
7.37
7.36
7.35
7.35
7.29
7.29
7.28
7.28
7.27
4.34
4.34
3.81
2.17
5.73
1.94
0.94
2.00
f1 (ppm)


Ph
N
Ph
N
N
Ph
^{15}N-12l
177.75
177.74
171.07
171.05
171.04
136.78
135.56
135.54
135.51
132.03
129.04
128.50
128.16
128.04
126.31
45.41
45.34
f1 (ppm)