Supporting Information for

Transition Metal-Free Catalytic Synthesis of 1,5-Diaryl-1,2,3-Triazoles

Sen W. Kwok, Joseph R. Fotsing, Rebecca J. Fraser, Valentin O. Rodionov, and Valery V. Fokin*

The Scripps Research Institute, 10550 North Torrey Pines Road,
La Jolla, California 92037, USA

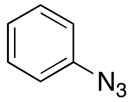
Email: fokin@scripps.edu

General Information

Melting points were recorded on either a Barnstead Electrothermal digital melting point apparatus (Model IA9300) or on Thomas-Hoover capillary melting apparatus and were uncorrected. High-resolution mass spectra (HRMS) were recorded at the mass spectrometry facility at The Scripps Research Institute, La Jolla, CA, USA. Analytical HPLC was performed on an Agilent HP 1100 series LC/MS with a variable wavelength diode array detector. Infrared spectra were recorded on Perkin Elmer Spectrum 100 FTIR spectrometer. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) and ^{19}F NMR (376 MHz) spectra were recorded on a Bruker AMX-400 or Varian Inova-400 spectrometers. Chemical shifts (*δ*) were reported as part per million (ppm). The proton signal of residual solvent (*δ* 7.26 for $CHCl_3$ and *δ* 2.05 for d_6-acetone) was used as the internal reference for ^{1}H spectra. For ^{13}C spectra, chemical shifts were reported relative to either the *δ* 77.00 resonance of $CDCl_3$ or to the *δ* 29.84 resonance of d_6-acetone. For the ^{19}F spectrum, chemical shifts were reported relative to the *δ* –164.9 resonance of C_6F_6, which was added as the internal reference. Coupling constants (*J*) were reported in Hertz (Hz). The following abbreviations for multiplicities were used: s-singlet, d-doublet, t-triplet, q-quartet, quin-quintet, sex-sextet, sep-septet, m-multiplet, dd-doublet of doublets, ddd-doublet of doublet of doublet, app-apparent, and br-broad signal. Flash column chromatography was performed using Merck Kieselgel 60 (230-400 mesh) silica gel. Analytical TLC was performed on precoated glass plates (Merck Kieselgel 60 F_{254}). All purchased chemicals were used as received without further purification.

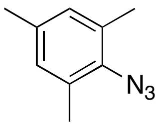
Preparation of aryl azides

Syntheses of aryl azides were conducted open to the atmosphere *in a well-ventilated hood away from direct light and behind a blast shield. All organic and inorganic azides should be handled and transferred either by glass pipette or plastic spoon and contact with metal should be avoided.* After purification, aryl azides were stored at 0-4 °C in the dark. With the exception of 4-azidopyridine (**f**) (see **S8**–**S9**), all aryl azides were prepared by diazotization of the corresponding aniline with nitrous acid, followed by treatment of the diazonium salts with sodium azide. A typical procedure for the preparation of aryl azides[1] is described below as exemplified for the synthesis of azidobenzene.[2] ^{1}H and ^{13}C NMR and IR spectra of aryl azides are consistent with the literature reports and are not included (except for one new compound, **j**).



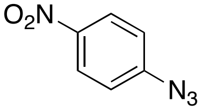
Azidobenzene (a)

To a 250-mL round bottom flask was charged with aniline (9.66 g, 0.10 mol) and water (110 mL). Concentrated HCl (17.4 mL, 0.21 mol) was added to the vigorously stirred reaction mixture in an ice-water bath. After stirring and cooling to 0 °C for 20–30 min, a freshly prepared, ice cold solution of $NaNO_2$ (7.16 g, 0.10 mol) in water (20–30 mL) was added dropwise to the reaction mixture while keeping the internal temperature between 0–5 °C. After addition of $NaNO_{2(aq)}$, the reaction mixture was stirred for an additional 10 min. A freshly prepared solution of sodium azide (6.75 g, 0.10 mol) in water (30–40 mL) was added dropwise to the reaction mixture via additional funnel while maintaining the internal temperature of the reaction mixture below 5 °C. Upon complete addition of the sodium azide solution, the reaction mixture was stirred for an additional 20–30 min at 0 °C, followed by stirring at rt for another 3 hr. The reaction mixture was extracted with ethyl acetate EtOAc (2×100 mL) (**Caution**: *extraction should never be performed with halogenated solvents such as DCM or* $CHCl_3$ *as these solvents can react with residual sodium azide to form diazidomethane or azidoform which are highly shock sensitive and energetic explosives.*[3] *After extraction, the pH of the aqueous layer should be checked with a pH paper to ensure that the solution is slightly basic (pH 8–10). If not, it should be adjusted with the addition of sat.* $NaHCO_{3(aq)}$ *prior to its disposal to a separate azide waste container*). The combined organic layers was dried over anhydrous $Na_2SO_{4(s)}$, filtered and concentrated under reduced pressure. The crude azidobenzene was further purified by flash column chromatography over a short plug of silica gel using hexanes as eluent to afford a yellow liquid (9.77 g, 80 mmol, 79%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (app t, J = 7.9 Hz, 2H), 7.15 (app td, J = 7.5, 0.8 Hz, 1H), 7.04 (app d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 129.7, 124.8, 119.0; FTIR (neat) 3065, 3036, 2418, 2257, 2122, 2090, 1938, 1593, 1490, 1455, 1340, 1293, 1279, 1174, 1129, 1075, 1025, 895, 810, 744, 685, 668 cm^{-1}.



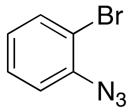
2-Azido-1,3,5-trimethylbenzene (mesityl azide)[4] **(b)**

Purification by flash column chromatography over a short plug of silica gel using hexanes as eluent afforded the titled compound as a yellow liquid (13.62 g, 85 mmol, 85%): ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 2H), 2.33 (s, 6H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.3, 134.3, 131.8, 129.5, 20.7, 18.0; FTIR (neat) 2974, 2952, 2919, 2860, 2114, 2088, 2056, 1589, 1477, 1449, 1377, 1314, 1277, 1177, 1100, 1032, 1016, 938, 851, 779, 714 cm^{-1}.



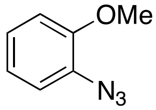
1-Azido-4-nitrobenzene[2] (**c**)

Vacuum filtration of the reaction mixture gave a grayish brown solid which was further purified by flash column chromatography over a short plug of silica gel using 1:1 dichloromethane/ hexanes as eluent to afford the titled compound as a fluffy yellow white powder (9.36 g, 57 mmol, 57%): mp: 69–71 °C (lit.[5] 69–70 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (app d, J = 9.0 Hz, 2H), 7.14 (app d, J = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 144.6, 125.6, 119.4; FTIR (neat) 3113, 3105, 3069, 2403, 2258, 2120, 2084, 1604, 1589, 1510, 1488, 1444, 1420, 1368, 1327, 1287, 1175, 1129, 1117, 1104, 990, 1008, 972, 950, 845, 811, 746, 699, 681 cm^{-1}.



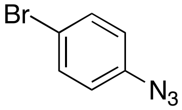
1-Azido-2-bromobenzene[6] (**d**)

(32 mmol scale) Purification by flash column chromatography over a short plug of silica gel using hexanes as eluent afforded the titled compound as a yellow liquid (5.82 g, 29 mmol, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (app d, J = 8.0 Hz, 1H), 7.35 (app t, J = 7.7 Hz, 1H), 7.17 (app d, J = 8.0 Hz, 1H), 7.01 (app t, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 133.8, 128.5, 125.9, 119.4, 113.8; FTIR (neat) 2442, 2117, 2093, 1579, 1471, 1438, 1309, 1294, 1163, 1147, 1118, 1038, 1027, 934, 846, 815, 742, 695 cm^{-1}.



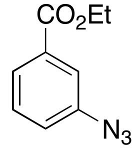
1-Azido-2-methoxybenzene[7] **(e)**

Purification by flash column chromatography over a short plug of silica gel using 5% EtOAc in hexanes as eluent afforded the titled compound as a yellow liquid (13.47 g, 90 mmol, 90%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.12 (app t, *J* = 7.8 Hz, 1H), 7.02 (app d, *J* = 7.5 Hz, 1H), 6.96–6.88 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.8, 128.2, 125.6, 121.2, 120.2, 112.0, 55.8; FTIR (neat) 3066, 3007, 2964, 2941, 2839, 2106, 1591, 1493, 1454, 1438, 1297, 1278, 1240, 1182, 1147, 1101, 1043, 1025, 925, 832, 781, 741, 659 cm^{-1}.



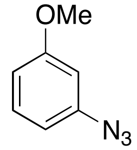
1-Azido-4-bromo-benzene[6] **(g)**

Purification by flash column chromatography over a short plug of silica gel using hexanes as eluent afforded the titled compound as a orange yellow liquid (18.10 g, 91 mmol, 91%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45 (app dt, *J* = 8.8, 2.5 Hz, 2H), 6.90 (app dt, *J* = 8.8, 2.5, Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 132.2, 125.7, 113.6, 110.7; FTIR (neat) 2414, 2253, 2122, 2084, 1881, 1583, 1480, 1423, 1406, 1288, 1270, 1175, 1126, 1110, 1071, 1008, 818, 692 cm^{-1}.



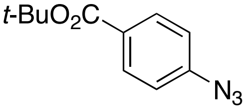
Ethyl-3-azidobenzoate[8] (**h**)

(50 mmol scale) Purification by flash column chromatography over a short plug of silica gel using 5% EtOAc in hexanes as eluent afforded the titled compound as a yellow liquid (8.36 g, 44 mmol, 87%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.81 (td, *J* = 7.8, 1.2 Hz, 1H), 7.70 (t, *J* = 1.8 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.19 (ddd, *J* = 8.0, 2.3, 1.0 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.6, 140.5, 132.2, 129.7, 125.9, 123.2, 119.9, 61.3, 14.3; FTIR (neat) 2983, 2101, 1718, 1604, 1586, 1483, 1441, 1392, 1367, 1292, 1250, 1172, 1138, 1096, 1079, 1020, 912, 900, 863, 809, 749, 702, 690, 676, 653 cm^{-1}.



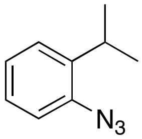
1-Azido-3-methoxybenzene[2] (**i**)

Purification by flash column chromatography over a short plug of silica gel using 5–10% EtOAc in hexanes as eluent afforded the titled compound as a yellow liquid (11.93 g, 80 mmol, 80%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 (app t, *J* = 8.1 Hz, 1H), 6.67 (ddd, *J* = 8.3, 2.4, 0.8 Hz, 1H), 6.65 (ddd, *J* = 8.0, 2.1, 0.9 Hz, 1H), 6.55 (app t, *J* = 2.2 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.8, 141.2, 130.4, 111.2, 110.6, 104.9, 55.3; FTIR (neat) 3006, 2960, 2943, 2836, 2190, 2102, 1600, 1586, 1487, 1466, 1450, 1436, 1295, 1284, 1225, 1182, 1162, 1108, 1037, 909, 842, 760, 680 cm^{-1}.



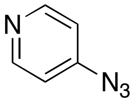
***tert*-Butyl-4-azidobenzoate (j)**

(30 mmol scale) Purification by flash column chromatography over a short plug of silica gel using 5% EtOAc in hexanes as eluent afforded the titled compound as an orange yellow liquid (5.17 g, 23.5 mmol, 79%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (app d, J = 8.7 Hz, 2H), 7.04 (app d, J = 8.7 Hz, 2H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 144.1, 131.2, 128.6, 118.6, 81.2, 28.2; FTIR (neat) 3004, 2978, 2933, 2122, 2087, 1709, 1602, 1503, 1474, 1457, 1416, 1392, 1367, 1280, 1254, 1160, 1129, 1107, 1014, 848, 765, 688 cm^{-1}.



1-Azido-2-isopropylbenzene[9] (k)

Purification by flash column chromatography over a short plug of silica gel using hexanes as eluent afforded the titled compound as a orange yellow liquid (12.13 g, 75 mmol, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ7.27–7.21 (m, 2H), 7.14–7.09 (m, 2H), 3.21 (sep, J = 6.9 Hz, 1H), 1.20 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 137.1, 126.9, 126.5, 124.9, 118.0, 27.9, 22.8; FTIR (neat) 2963, 2870, 2120, 2091, 1580, 1488, 1445, 1383, 1363, 1348, 1290, 1282, 1141, 1077, 1036, 934, 813, 746, 655 cm^{-1}.



4-Azidopyridine[10] **(f)**

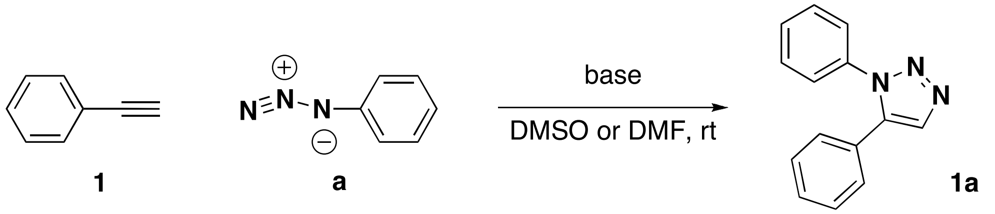
The titled compound was prepared based on the procedure reported by L'Abbe et al with modifications as described below.

To a 100-mL round bottom flask equipped with a stirbar was charged with sodium azide (4.92 g, 75.8 mmol) and water (34 mL). To the stirred solution was slowly added 4-chloropyridine hydrochloride (5.17 g, 34.5 mmol). A condenser was subsequently attached and the reaction mixture was refluxed open to atmosphere and away from light in a well-ventilated hood behind a blast shield (**CAUTION**: *since this procedure can generate hydrazoic acid* (HN_3)*, which can accumulate in the headspace, the reaction should be conducted open to the atmosphere in a well-ventilated hood and we do not recommend the synthesis of 4-azidopyridine using this modified procedure larger than the scale described here*). After refluxing for 24 h, the reaction mixture was cooled to rt and extracted with EtOAc (3×35 mL) (**CAUTION:** *extraction should never be performed with halogenated solvents such as DCM or* $CHCl_3$ *as these solvents can react with sodium azide to form diazidomethane or azidoform which are highly shock sensitive and energetic explosives.*[2] *After extraction, the pH of the aqueous layer should be checked with a pH paper to ensure that the solution is slightly basic (pH 8–10). If not, it should be adjusted with the addition of sat.* $NaHCO_{3(aq)}$ *prior to its disposal to a separate azide waste container*). The combined organic layer was dried over anhydrous $Na_2SO_{4(s)}$, filtered and concentrated under reduced pressure to afford the titled compound as a red brown liquid (3.18 g, 26.5 mmol, 77%), which was used without further purification: ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.51 (app dd, *J* = 4.6, 1.5 Hz, 2H), 6.92 (app dd, *J* = 4.7, 1.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 148.6, 114.0; FTIR (neat) 3408, 3038, 2430, 2272, 2135, 2093, 1579, 1564, 1493, 1415, 1343, 1297, 1278, 1214, 1136, 989, 811, 670 cm^{-1}.

Optimization of catalyst, solvent and substrate concentration

To a solution of phenylacetylene **1** (1 equiv) and azidobenzene **a** (1 equiv) in the selected solvent (5 mL) was added base catalyst (0.20 equiv) and the reaction mixture was stirred at rt under $N_{2(g)}$ to maintain a CO_2–free atmosphere. After 20 h, the reaction was quenched by pouring into ice-cold water (50 mL) in a 100-mL Erlenmeyer flask. After stirring for 2 h at rt, the product **1a** was isolated by vacuum filtration. Result from the optimization of catalyst, solvent and substrate concentration is summarized in Table 1.



Catalyst	mol %	Solvent	Conc (M)	Isolated yield (%)
2.8M $LiOH_{(aq)}$	20	DMSO	0.1	Trace (not isolated)
2.8M $NaOH_{(aq)}$	20	DMSO	0.1	52

2.8M $KOH_{(aq)}$	20	DMSO	0.1	55
2.8M $CsOH_{(aq)}$	20	DMSO	0.1	68
NMe_4OH (25 wt % solution in water)	20	DMSO	0.1	72
NBu_4OH (40 wt % solution in water)	20	DMSO	0.1	65
$BnNMe_3OH$ (40 wt % solution in water)	20	DMSO	0.1	75
NMe_4OH (25 wt % solution in water)	20	DMSO	0.25	85
NMe_4OH (25 wt % solution in water)	20	DMF	0.1	76
NMe_4OH (25 wt % solution in water)	20	DMF	0.25	46
t-BuOK powder	20	dry DMSO	0.1	74
2.6M $KOH_{(aq)}$	10	DMSO	0.3	86[a]
KOH powder	10	DMSO	0.3	91[a]
NMe_4OH (25 wt % solution in water)	10	DMSO	0.3	86[a]
$BnNMe_3OH$ (40 wt % solution in water)	10	DMSO	0.3	81[a]

Table 1. Results of the optimization of base, solvent and substrate concentration. [a] Reaction was performed at 4.2 mmol scale.

General procedure for the synthesis of 1,5-diarylsubstituted-1*H*-1,2,3-triazole

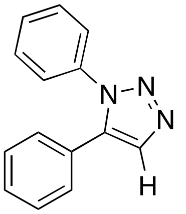
Method A

To a stirred DMSO solution (6–7 mL) of aryl alkyne (2.00–2.10 mmol) and aryl azide (2.00 mmol) was added tetramethylammonium hydroxide (0.20 mmol, 25 wt% solution in water) or benzyl trimethylammonium hydroxide (0.20 mmol, 40 wt% solution in water). Overall concentration of the reaction mixture (with respect to azide) should be between 0.25–0.30M. After addition of base catalyst, the reaction mixture was stirred at rt under an atmosphere of $N_{2(g)}$ (to maintain a CO_2-free environment) and monitored either by TLC or by LCMS. Upon complete consumption of aryl azide, the reaction was poured into water (3–20×vol of DMSO) and the suspension was stirred for 2–12 h. In the case where the desired product could not be isolated by filtration, it was extracted with EtOAc (1–2× vol of the suspension), the organic layer was dried over anhydrous

$Na_2SO_{4(s)}$, filtered, concentrated under reduced pressure, and followed by flash column chromatography over silica gel. If the products precipitated upon quenching and stirring in water, the desired products were isolated by vacuum filtration, washed with water (3×5 mL), air-dried for 1 h and then dried under high vacuum for at least 0.5–1 h. If the purity of the products remained unsatisfactory, the products were further purified either by flash column chromatography over silica gel or by trituration. In some cases, purity can be improved by re-suspending the precipitate in water (20 mL) and vigorously stirred for 24 h.

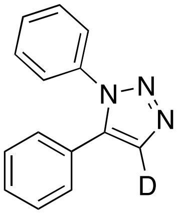
Method B

In the presence of base-labile substituent, dry DMSO and potassium *tert*-butoxide (0.20 equiv) were used instead. The sequence of addition and the overall concentration of the reaction mixture were the same as method A. After complete consumption of aryl azide, the reaction mixture was poured into ice-cold water, extracted with EtOAc, and purified by flash column chromatography over silica gel. Alternatively, small amount of saturated $NH_4Cl_{(aq)}$ solution can be added to adjust the pH of the aqueous DMSO suspension to neutral. The suspension was stirred for a few hours and the desired product was collected by vacuum filtration.



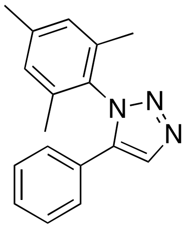
1,5-Diphenyl-1*H*-1,2,3-triazole (1a)

Using method A, a solution of azidobenzene (500 mg, 4.20 mmol) and phenylacetylene (461 μL, 4.20 mmol) in DMSO (16.8 mL) were allowed to react for 12 h. After quenching with water (300 mL) and stirring for 2 h, compound **1a** (810 mg, 3.60 mmol, 87%) was isolated as an off-white solid by vacuum filtration: mp 113–114 °C (lit.[11] 113–114 °C); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (s, 1H), 7.46–7.32 (m, 8H), 7.26–7.22 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.7, 136.6, 133.4, 129.3, 129.2, 128.8, 128.6, 126.7, 125.2; HRMS (ESI-TOF) (*m/z*): [M+H]$^+$ calcd for $C_{14}H_{12}N_3$, 222.1026; found, 222.1038.



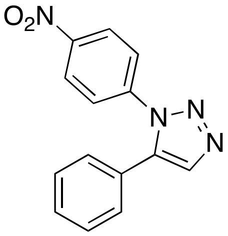
1,5-Diphenyl-4-[^{2}H]-1*H*-1,2,3-triazole (d-1a)

An inverse addition sequence based on Method B was carried out as follows: to anhydrous potassium *tert*-butoxide (9 mg, 0.08 mmol) in a 2.5-mL scintillation vial, equipped with a stirbar and a rubber septum, was added a solution of phenylacetylene (40.8 mg, 0.40 mmol) in d_6-DMSO (1 mL) and a solution of azidobenzene (47.6 mg, 0.40 mmol) in d_6-DMSO (1 mL) sequentially under a balloon of $N_{2(g)}$. The reaction mixture was stirred at rt under $N_{2(g)}$ for 5.5 h. After quenching with water (40 mL) and stirring for 2 h, compound **d-1a** (66 mg, 0.30 mmol, 74%) was isolated as an off-white solid by vacuum filtration: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 0.01H), 7.45–7.32 (m, 8H), 7.26–7.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 136.6, 129.3, 129.2, 128.8, 128.6, 126.8, 125.2; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{11}DN_3$, 223.1087; found, 223.1088. Based on ^{1}H NMR, the deuterium incorporation at the C4 position of 1*H*-1,2,3-triazole is greater than 98%.



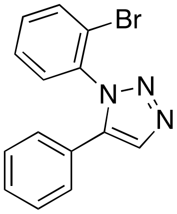
1-Mesityl-5-phenyl-1*H*-1,2,3-triazole (1b)

Using method A, a solution of 2-azido-1,3,5-trimethylbenzene (553 mg, 3.43 mmol) and phenylacetylene (396 μL, 3.60 mmol) in DMSO (11.4 mL) were allowed to react for 10 h. After quenching with water, extraction with EtOAc and concentration under reduced pressure, the crude was purified by flash column chromatography over silica gel, using 10% → 50% Et_2O/hexanes as eluent to give compound **1b** (543 mg, 2.06 mmol, 60%) as a light brown powder: mp 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.31–7.26 (m, 3H), 7.19–7.16 (m, 2H), 6.97 (br s, 2H), 2.35 (s, 3H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 138.2, 135.4, 132.7, 132.1, 129.3, 129.0, 128.9, 126.9, 126.6, 21.2, 17.5; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{18}N_3$, 264.1495; found, 264.1492.



1-(4-Nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole (1c)

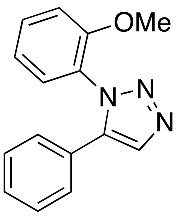
Using method A, a solution of 1-azido-4-nitrobenzene (334 mg, 2.04 mmol) and phenylacetylene (234 μL, 2.14 mmol) in DMSO (6.8 mL) were allowed to react for 12 h. After quenching with water and isolation by filtration, the brown red solid was purified by flash column chromatography over silica gel using 100% CH_2Cl_2 → 5% $MeOH/CH_2Cl_2$ as eluent to give compound **1c** (339 mg, 1.27 mmol, 62%) as a yellow powder: mp 164.5–165.5 °C (lit.[12] 164–165 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (app dt, J = 9.1, 2.4 Hz, 2H), 7.88 (s, 1H), 7.59 (app dt, J = 9.1, 2.4 Hz, 2H), 7.48–7.39 (m, 3H), 7.26–7.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 141.3, 138.0, 134.2, 129.9, 129.3, 128.7, 126.0, 125.3, 124.9; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{11}N_4O_2$, 267.0876; found, 267.0876.



1-(2-Bromophenyl)-5-phenyl-1*H*-1,2,3-triazole (1d)

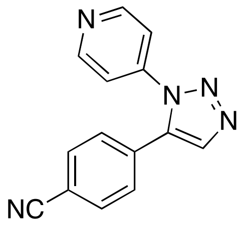
Using method A, a solution of 1-azido-2-bromobenzene (500 mg, 2.52 mmol) and phenylacetylene (278 μL, 2.53 mmol) in DMSO (8.4 mL) were allowed to react for 16 h. After quenching with water, extraction with EtOAc and concentration under reduced pressure, the crude was purified by flash column chromatography over silica gel using 10% → 50% EtOAc/hexanes as eluent. After the removal of solvent under reduced pressure, the yellow solid was vigorously stirred in water for 5h. Compound **1d** (488 mg, 1.62 mmol, 64%) was isolated as a yellow powder by vacuum filtration: mp 95–97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.67–7.65 (m, 1H), 7.46–7.25 (m, 6H), 7.21–

7.17 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 139.0, 136.0, 133.6, 132.2, 131.5, 129.4, 129.2, 128.7, 128.3, 127.7, 126.2, 121.5; HRMS (ESI-TOF) (*m/z*): [M+H]$^+$ calcd for C$_{14}$H$_{11}$^{79}BrN$_3$, 300.0131; found, 300.0134.



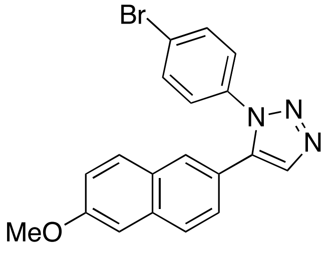
1-(2-Methoxyphenyl)-5-phenyl-1*H*-1,2,3-triazole (1e)

Using method A, a solution of 1-azido-2-methoxybenzene (525 mg, 3.52 mmol) and phenylacetylene (406 μL, 3.70 mmol) in DMSO (11.7 mL) were allowed to react for 5 h. After quenching with water (80 mL), stirring for 12 h, isolation by vacuum filtration, re-suspension and stirring in water (20 mL) for additional 5 h, compound **1e** (702 mg, 2.79 mmol, 79%) was isolated as a yellow powder by vacuum filtration: mp 105–107 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (s, 1H), 7.48–7.44 (m, 2H), 7.30–7.26 (m, 3H), 7.22–7.20 (m, 2H), 7.09 (app t, *J* = 7.7 Hz, 1H), 6.94 (app d, *J* = 8.8, 1.0 Hz, 1H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.7, 139.3, 132.1, 131.4, 128.8, 128.5, 128.4, 127.5, 127.4, 125.8, 121.0, 112.3, 55.4; HRMS (ESI-TOF) (*m/z*): [M+H]$^+$ calcd for C$_{15}$H$_{14}$N$_3$O, 252,1131; found, 252.1130.



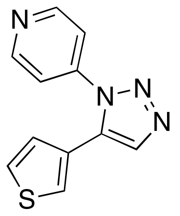
4-[1-(Pyridin-4-yl)-1*H*-1,2,3-triazol-5-yl]benzonitrile (2f)

Using method B, a solution of 4-azidopyridine (380 mg, 3.15 mmol) and 4-ethynylbenzonitrile (400 mg, 3.15 mmol) in dry DMSO (10 mL) were allowed to react for 20 h. After quenching with ice-cold water, extraction with EtOAc and concentration under reduced pressure, the crude was purified by flash column chromatography over silica gel, using 100% $CH_2Cl_2 \rightarrow$ 60% Et_2O/hexanes as eluent, to give compound **2f** (598 mg, 2.21 mmol, 70%) as light yellow solid: mp 170–171 °C; ^1H NMR (400 MHz, d_6-acetone) δ 8.75 (app ddd, J = 4.6, 1.6, 0.4 Hz, 2H), 8.14 (s, 1H), 7.89 (app dt, J = 8.1, 2.0 Hz 2H), 7.64 (app dt, J = 8.2, 2.0 Hz, 2H), 7.48 (app ddd, J = 4.6, 1.6, 0.4 Hz, 2H); ^{13}C NMR (100 MHz, d_6-acetone) δ 152.3, 144.0, 137.3, 135.5, 133.7, 132.0, 130.6, 119.9, 118.7, 114.0; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{10}N_5$, 248.0931; found, 248.0924.



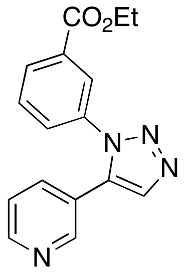
1-(4-Bromophenyl)-5-(6-methoxynapthalen-2-yl)-1*H*-1,2,3-triazole (3g)

Using method A, a solution of 1-azido-4-bromobenzene (367 mg, 1.85 mmol) and 2-ethynyl-6-methoxynaphthalene (366 mg, 1.95 mmol) in DMSO (6.2 mL) were allowed to react for 9 h. After quenching with water and isolation by filtration, the residue was further purified by flash column chromatography over silica gel, using 100% CH_2Cl_2 → 50% Et_2O/hexanes → 90% Et_2O/hexanes as eluent to give compound **3g** (395 mg, 1.04 mmol, 56%) as a yellow powder: mp 152–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.92 (s, 1H), 7.72–7.37 (m, 3H), 7.54 (app dt, *J* = 8.8, 2.4 Hz, 2H), 7.29 (app dt, *J* = 8.8, 2.4 Hz, 2H), 7.20 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.16 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.13 (d, *J* = 2.5 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 158.8, 137.9, 135.7, 134.6, 133.7, 132.6, 129.7, 128.4, 128.1, 127.6, 126.4, 126.0, 123.1, 121.3, 120.0, 105.6, 55.4; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{15}{}^{79}BrN_3O$, 380.0393; found, 380.0393.



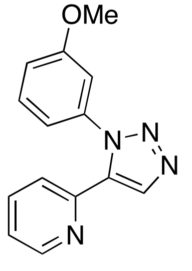
4-[5-(Thiophen-3-yl)-1*H*-1,2,3-triazol-1-yl]pyridine (4f)

Using method B, a solution of 4-azidopyridine (253 mg, 2.11 mmol) and 3-ethynylthiophene (218 μL, 2.21 mmol) in dry DMSO (7.0 mL) were allowed to react for 21 h. After quenching with water (20 mL) and stirring for 12 h, compound **4f** (330 mg, 1.45 mmol, 69%) was isolated as an off-white powder by vacuum filtration: mp 184–185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.72 (app dd, *J* = 4.5, 1.6 Hz, 2H), 7.84 (s, 1H), 7.41 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.38 (app dd, *J* = 4.6, 1.6 Hz, 2H), 7.32 (dd, *J* = 3.0, 1.3 Hz, 1H), 6.92 (dd, *J* = 5.0, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 151.3, 143.3, 134.0, 133.2, 127.5, 127.0, 125.9, 125.7, 118.4; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{11}H_9N_4S$, 229.0542; found, 229.0538.



Ethyl 3-[5-(pyridin-3-yl)-1*H*-1,2,3-triazol-1-yl]benzoate (5h)

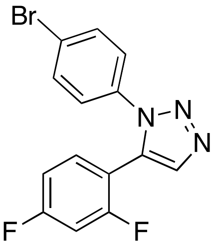
Using method B, a solution of ethyl 3-azidobenzoate (550 mg, 2.58 mmol) and 1-chloro-3-ethynylpyridine (300 mg, 2.91 mmol) in dry DMSO (8.6 mL) were allowed to react for 16 h. After quenching with ice-cold water, extraction with EtOAc and concentration under reduced pressure, the crude was further purified by flash column chromatography over silica gel, using 100% Et_2O as eluent to give compound **5h** (600 mg, 2.04 mmol, 79%) as solid: mp 75.5–77.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (app d, J = 3.6 Hz, 1H), 8.53 (d, J = 1.5 Hz, 1H), 8.14 (d, J = 7.3 Hz, 1H), 8.05 (br s, 1H), 7.94 (s, 1H), 7.55–7.48 (m, 3H), 7.31–7.26 (m, 1H), 4.34 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 150.4, 149.0, 136.2, 135.7, 134.7, 133.8, 132.3, 130.6, 129.7, 129.1, 126.1, 123.5, 122.8, 61.5, 14.2; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{15}N_4O_2$, 295.1189; found, 259.1199.



2-[1-(3-Methoxyphenyl)-1*H*-1,2,3-triazol-5-yl]pyridine (6i)

Using method A, a solution of 1-azido-3-methoxybenzene (302 mg, 2.02 mmol) and 2-ethynylpyridine (205 μL, 2.02 mmol) in DMSO (6.7 mL) were allowed to react for 15 h.

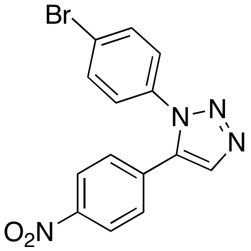
After quenching with water, extraction with EtOAc and concentration under reduced pressure, the crude was further purified by flash column chromatography over silica gel, using 100% CH_2Cl_2 → 5% $MeOH/CH_2Cl_2$ as eluent to give compound **6i** (470 mg, 1.86 mmol, 92%) as brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (dddd, J = 4.8, 1.7, 0.9, 0.4 Hz, 1H), 8.09 (d, J = 0.4 Hz, 1H), 7.65 (tdd, J = 8.1, 1.8, 0.4 Hz, 1H), 7.34–7.29 (m, 1H), 7.26 (dddd, J = 7.2, 4.9, 1.1, 0.4 Hz, 1H), 7.21 (dtd, J = 7.9, 1.0, 0.4 Hz, 1H), 7.01–6.98 (m, 2H), 6.90 (dddd, J = 7.9, 1.8, 1.0, 0.4 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 150.1, 146.6, 137.8, 137.2, 136.6, 134.5, 129.9, 123.6, 123.4, 117.5, 115.5, 110.8, 55.5; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{13}N_4O$, 253.1084; found, 253.1148.



1-(4-Bromophenyl)-5-(2,4-difluorophenyl)-1*H*-1,2,3-triazole (7g)

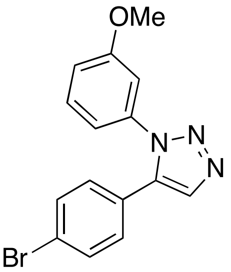
Using method A, a solution of 1-azido-4-bromobenzene (369 mg, 2.00 mmol) and 1-ethynyl-2,4-difluorobenzene (290 mg, 2.10 mmol) in DMSO (16.8 mL) were allowed to react for 9 h. After quenching with water and stirring for 5 h, compound **7g** (555 mg, 1.65 mmol, 83%) was isolated as a yellow powder by vacuum filtration: mp 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 1.0 Hz, 1H), 7.55 (app dt, J = 8.9, 2.5 Hz, 2H), 7.21 (app dt, J = 8.8, 2.5 Hz, 2H), 7.21–7.16 (m, 1H), 6.93 (dddd, J = 8.8, 7.8, 2.5, 1.1 Hz, 1H) 6.87 (ddd, J = 9.8, 8.6, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (dd, J_{CF} = 254, 11.6 Hz), 159.6 (dd, J_{CF} = 254, 12.2 Hz), 135.4, 134.8 (d, J_{CF} = 1.9 Hz), 132.6, 131.9 (dd, J_{CF} = 9.9, 3.5 Hz), 131.1, 125.7, 123.3, 112.3 (dd, J_{CF} = 21.8, 3.8 Hz), 111.0

(dd, J_{CF} = 15.0, 4.0 Hz), 105.1 (t, J_{CF} = 25.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$, relative to C_6F_6 at δ –164.9) δ –108.8 (d, J_{FF} = 8.4 Hz), –110.2 (d, J_{FF} = 8.6 Hz); HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{14}H_9{}^{79}BrF_2N_3$, 335.9942; found, 335.9942.



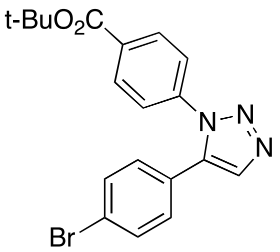
1-(4-Bromophenyl)-5-(4-nitrophenyl)-1*H*-1,2,3-triazole (8g)

Using method A, a solution of 1-azido-4-bromobenzene (0.367 g, 2.00 mmol) and 1-ethynyl-4-nitrobenzene (0.295 g, 2.00 mmol) in DMSO (6.7 mL) were allowed to react for 13 h. After quenching with water, extraction with EtOAc and concentration under reduced pressure, the crude was purified by flash column chromatography over silica gel, using 10% → 70% Et_2O/hexanes as eluent to give a reddish brown yellow powder. The solid was subsequently dissolved in a small amount of EtOAc and triturated with hexanes to give compound **8g** (0.256 g, 0.74 mmol, 37%) as a light brown powder: mp 172–173 °C (lit.[11] 173–174 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (app dt, J = 9.0, 2.2 Hz, 2H), 7.98 (s, 1H), 7.62 (app dt, J = 8.8, 2.4 Hz, 2H), 7.43 (app dt, J = 9.0, 2.2 Hz, 2H), 7.24 (app dt, J = 8.8, 2.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 135.6, 134.9 134.3, 133.0, 132.7, 129.3, 126.6, 124.3, 124.0; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{10}{}^{79}BrN_4O_2$, 344.9982; found, 344.9977.



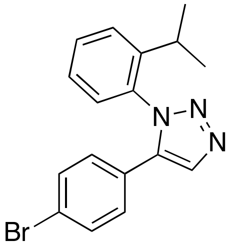
5-(4-Bromophenyl)-1-(3-methoxyphenyl)-1*H*-1,2,3-triazole (9i)

Using method A, a solution of 1-azido-3-methoxybenzene (252 mg, 1.69 mmol) and 1-bromo-4-ethynylbenzene (304 mg, 1.69 mmol) in DMSO (5.6 mL) were allowed to react for 24 h. After quenching with water, extraction with EtOAc and concentration under reduced pressure, the crude was purified by flash column chromatography over silica gel, using 30% Et_2O/hexanes as eluent to give compound **9i** (513 mg, 1.55 mmol, 92%) as an off-white solid: mp 148–149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.48 (app dt, J = 8.7, 2.2 Hz, 2H), 7.33–7.26 (m, 1H), 7.11 (app dt, J = 8.7, 2.2 Hz, 2H), 6.99 (ddd, J = 8.4, 2.5, 0.8 Hz, 1H), 6.95–6.94 (m, 1H), 6.84 (ddd, J = 7.9, 1.9, 0.9 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 137.2, 136.6, 133.3, 132.1, 130.2, 130.0, 125.6, 123.7, 117.3, 115.4, 110.8, 55.5; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{15}H_{13}{}^{79}BrN_3O$, 330.0236; found, 330.0235.



tert-Butyl 4-[5-(4-bromophenyl)-1*H*-1,2,3-triazol-1-yl]benzoate (9j)

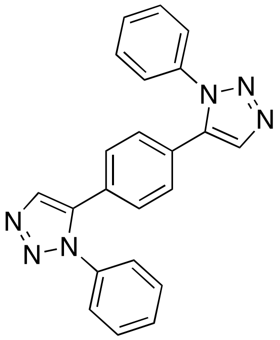
Using method B, a solution of *tert*-butyl 4-azidobenzoate (292 mg, 1.33 mmol) and 1-bromo-4-ethynylbenzene (253 mg, 1.39 mmol) in dry DMSO (4.4 mL) were allowed to react for 11 h. After quenching with ice-cold water (25 mL), saturated $NH_4Cl_{(aq)}$ (0.5 mL) was added to the suspension and the crude reaction mixture was stirred for 5 h. Compound **9j** (402 mg, 1.00 mmol, 76%) was then isolated as a yellow powder by vacuum filtration: mp 153–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (app dt, J = 8.6, 2.1 Hz, 2H), 7.86 (s, 1H), 7.50 (app dt, J = 8.5, 2.2 Hz, 2H), 7.40 (app dt, J = 8.6, 2.1 Hz, 2H), 7.09 (app dt, J = 8.5, 2.2 Hz, 2H), 1.60 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 139.3, 136.7, 133.7, 132.8, 132.3, 130.7, 130.1, 125.4, 124.6, 124.0, 81.9, 28.1; HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{19}{}^{79}BrN_3O_2$, 400.0655; found, 400.0650.



5-(4-Bromophenyl)-1-(2-isopropylphenyl)-1*H*-1,2,3-triazole (9k)

Using method A, a solution of 1-azido-2-isopropylbenzene (271 mg, 1.68 mmol) and 1-bromo-4-ethynylbenzene (304 mg, 1.68 mmol) in DMSO (5.7 mL) were allowed to react for 24 h. After quenching with water, extraction with EtOAc and concentration under reduced pressure, the crude was purified by flash column chromatography, using 100%

CH_2Cl_2 → 60% Et_2O/hexanes as eluent, to give compound **9k** (402 mg, 1.18 mmol, 70%) as a yellow viscous oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.53–7.39 (m, 2H), 7.41 (app dt, J = 8.8, 2.3 Hz, 2H), 7.30 (ddd, J = 7.9, 7.3, 1.6 Hz, 1H), 7.22 (dd, J = 7.9, 1.4, 1H), 7.03 (app dt, J = 8.8, 2.2 Hz, 2H), 2.43 (sep, J = 6.9 Hz, 1H), 0.98 (br s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 137.8, 134.1, 132.1, 132.0, 130.8, 129.2, 127.6, 127.1, 126.7, 125.4, 123.4, 28.0, 23.5 (br); HRMS (ESI-TOF) (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{17}{}^{79}BrN_3$, 342.0600; found, 342.0595.



1,4-Bis(1-phenyl-1*H*-triazol-5-yl)benzene (10a)

Using method A, a solution of azidobenzene (238 mg, 2.00 mmol) and 1,4-diethynylbenzene (132 mg, 1.03 mmol) in DMSO (6.7 mL) were allowed to react for 14.5 h. After quenching with water and isolation by vacuum filtration, the solid was triturated with a small amount of EtOAc/Et_2O/acetone (5 mL) to give compound **10a** (308 mg, 0.85 mmol, 85%) as a yellow powder: mp 267–269 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 2H), 7.47–7.43 (m, 6H), 7.36–7.34 (m, 4H), 7.21 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.7, 136.4, 133.6, 129.52, 129.49, 128.9, 127.6, 125.2; HRMS (ESI-TOF) (*m/ z*): $[M+H]^+$ calcd for $C_{22}H_{17}N_6$, 365.1509; found, 365.1506.

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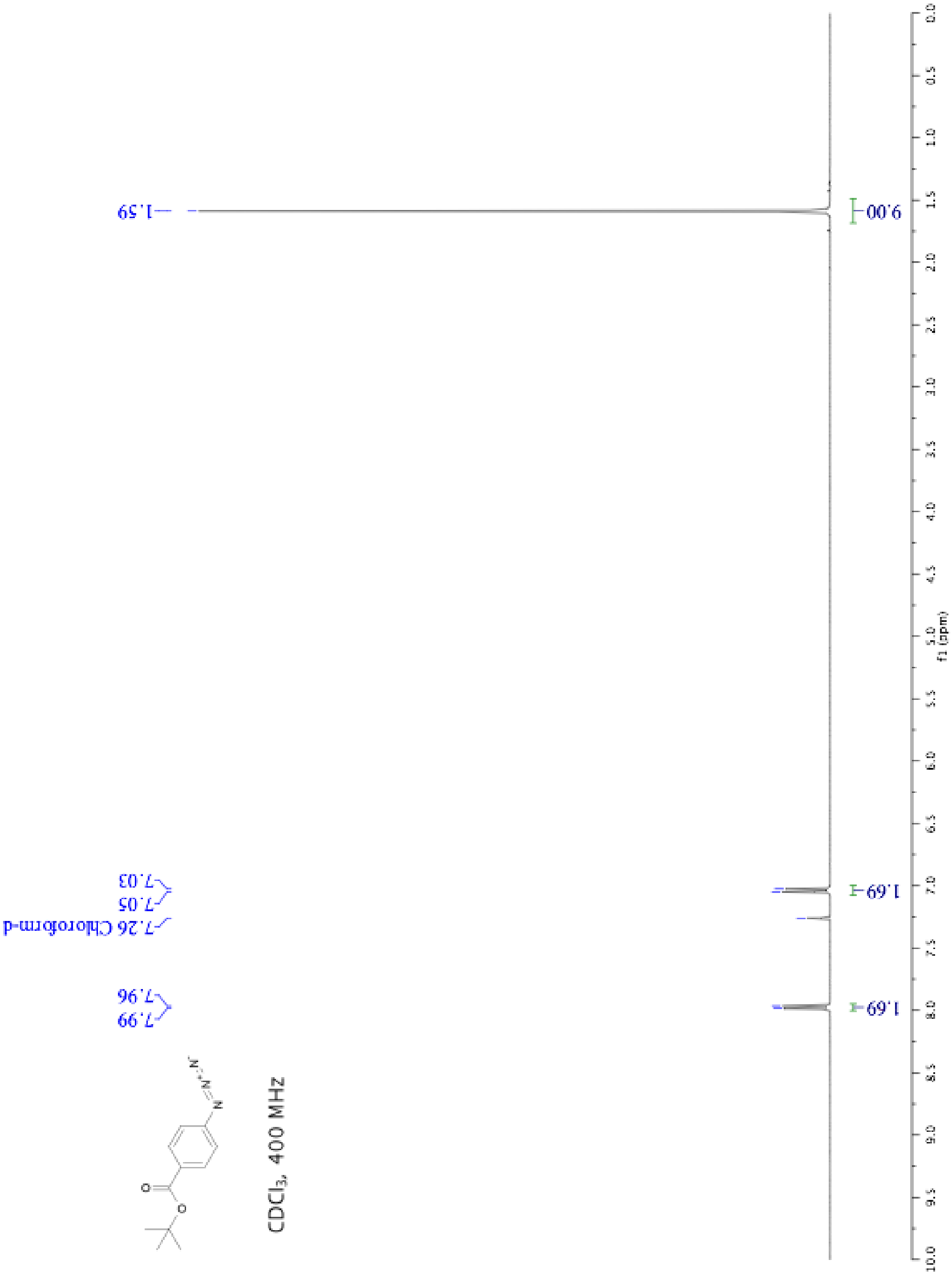
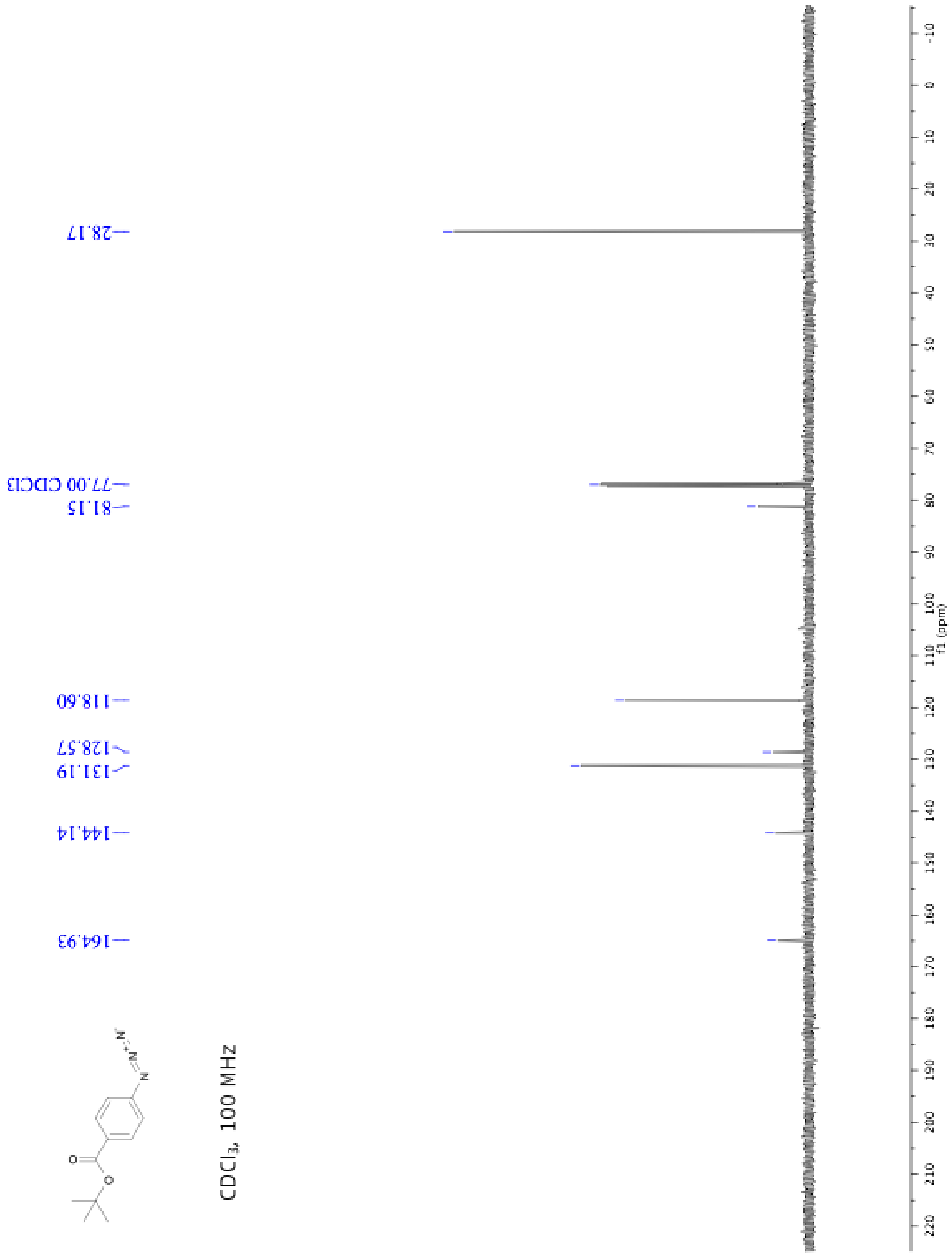
^{1}H NMR for compound **j**



^{13}C NMR for compound **j**



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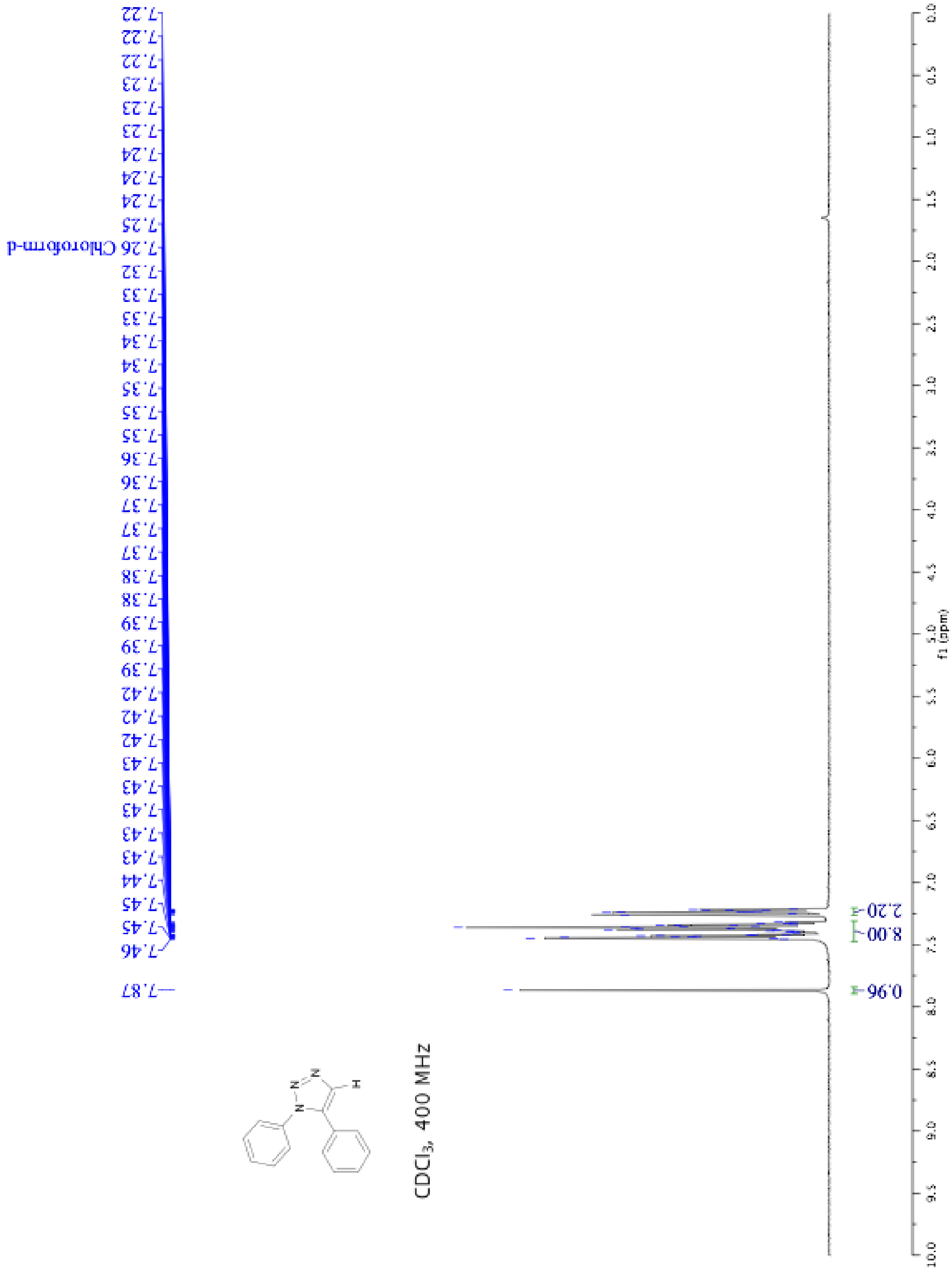

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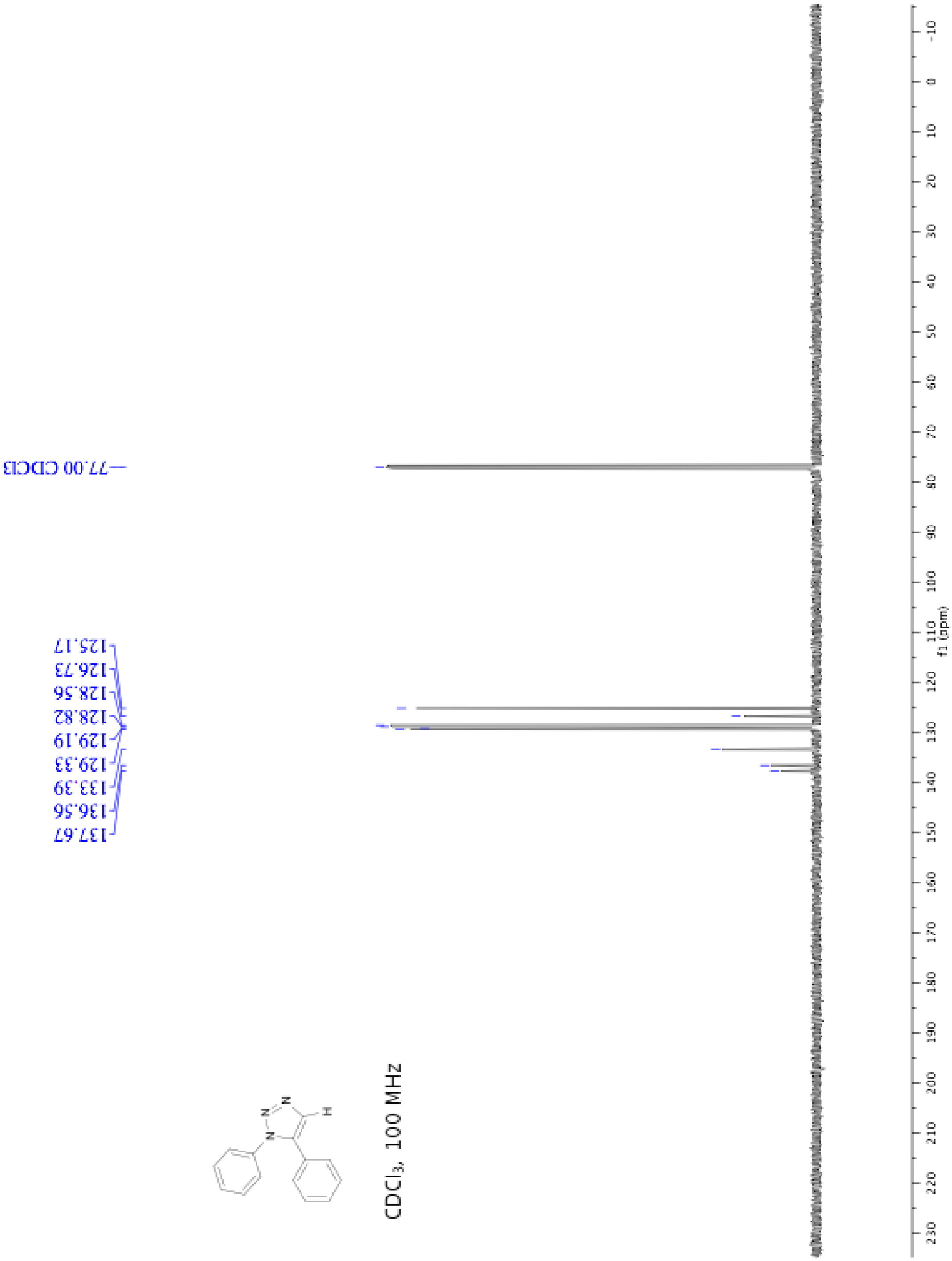

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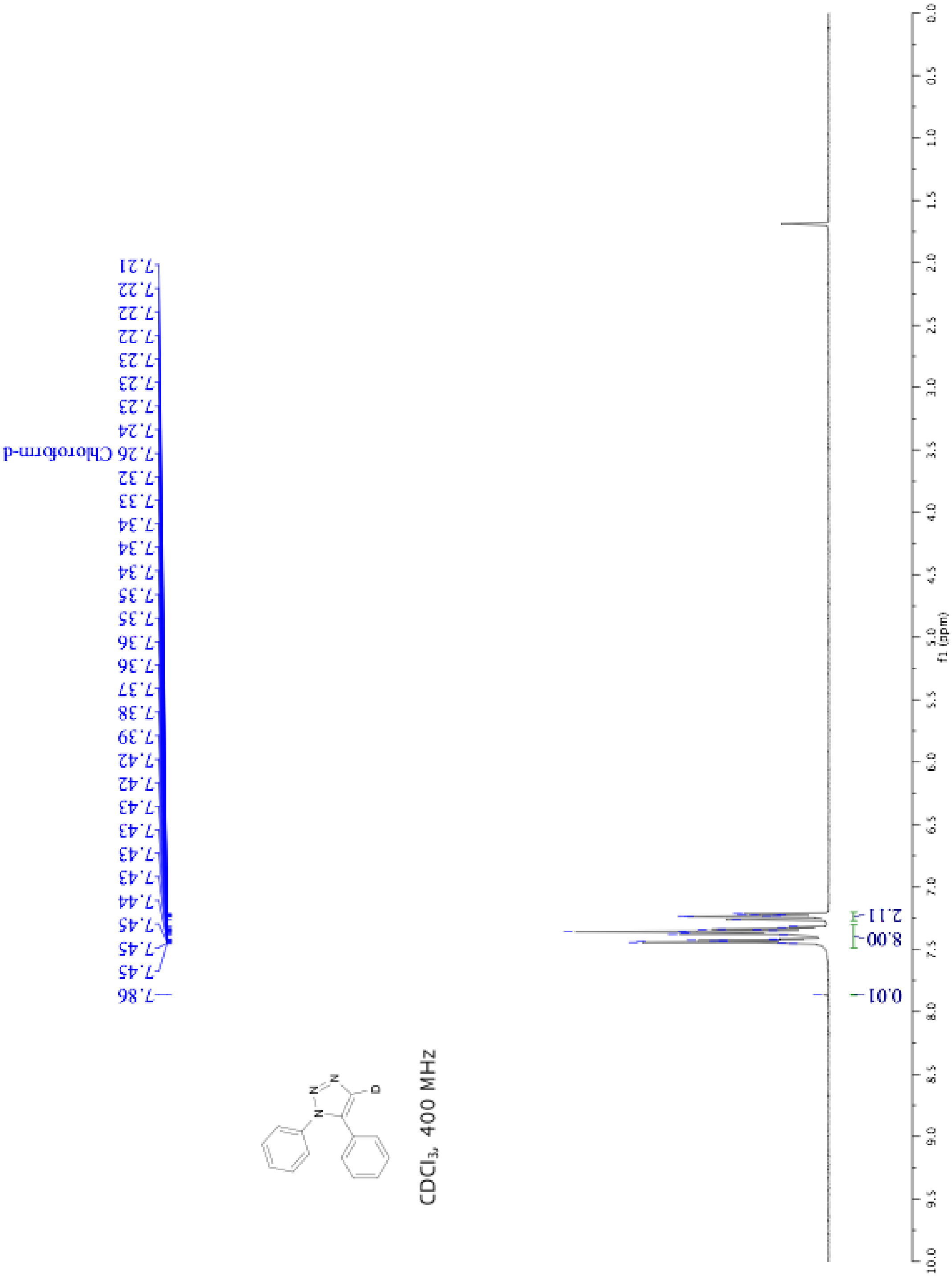

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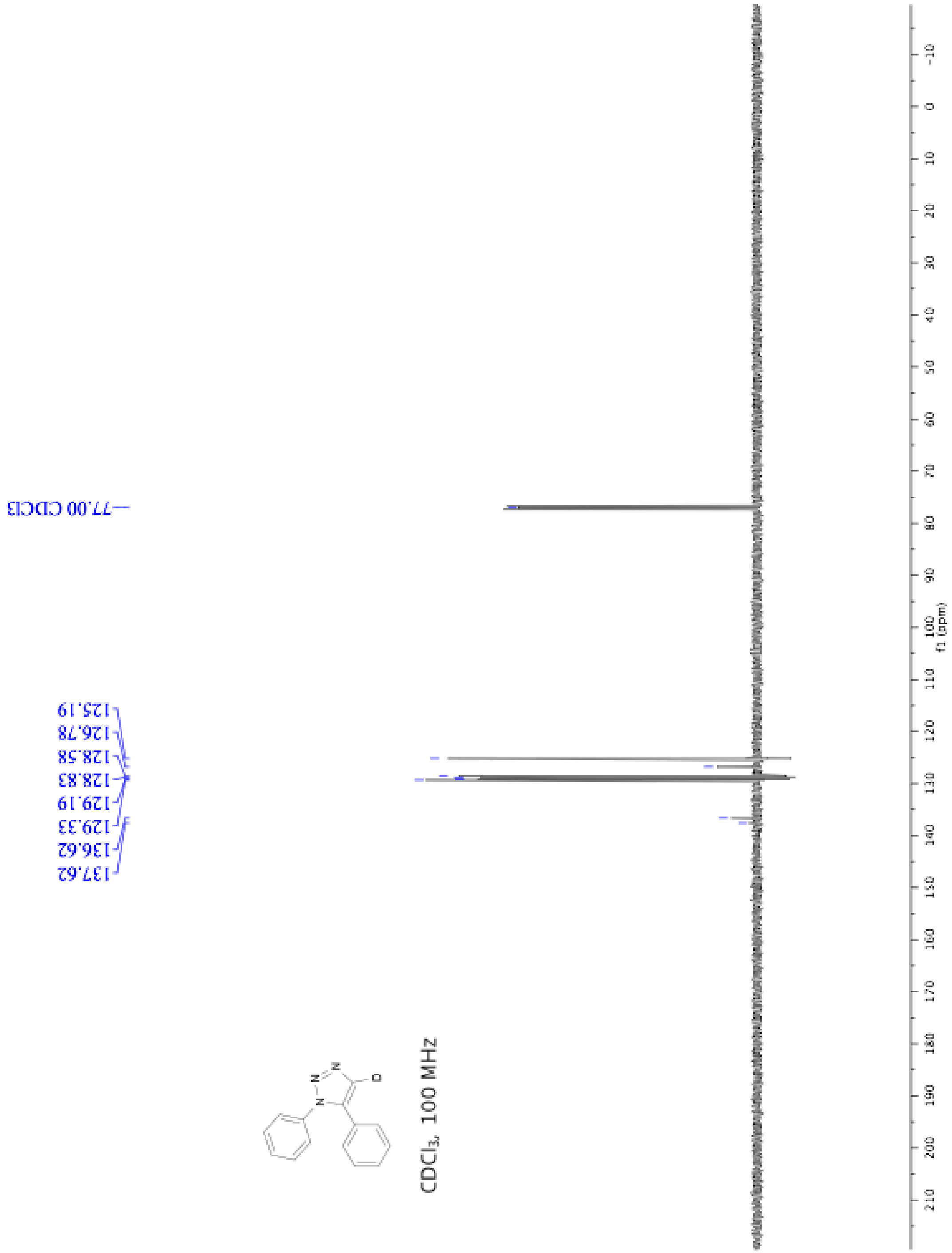
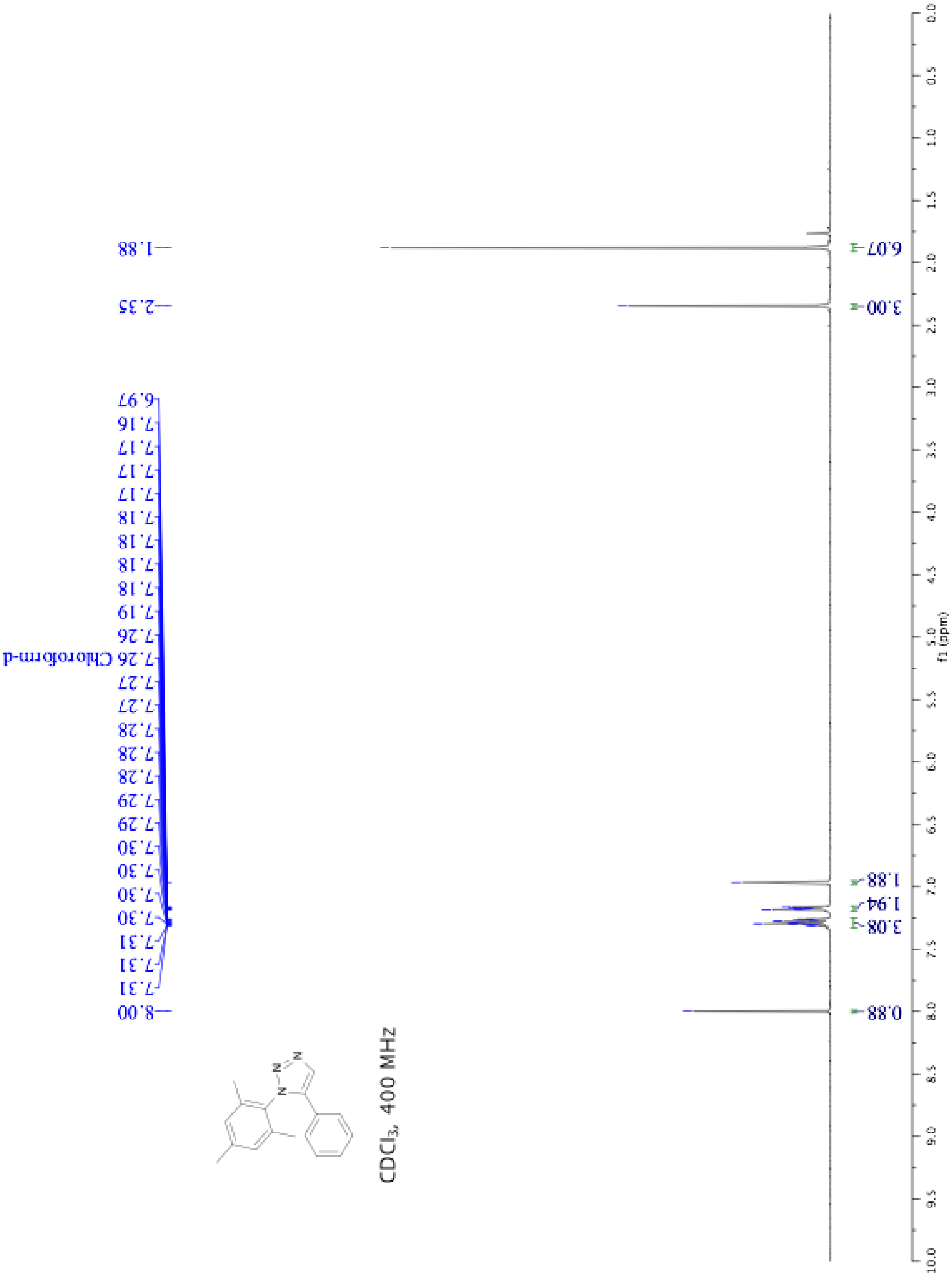


^{1}H NMR for compound **1b**



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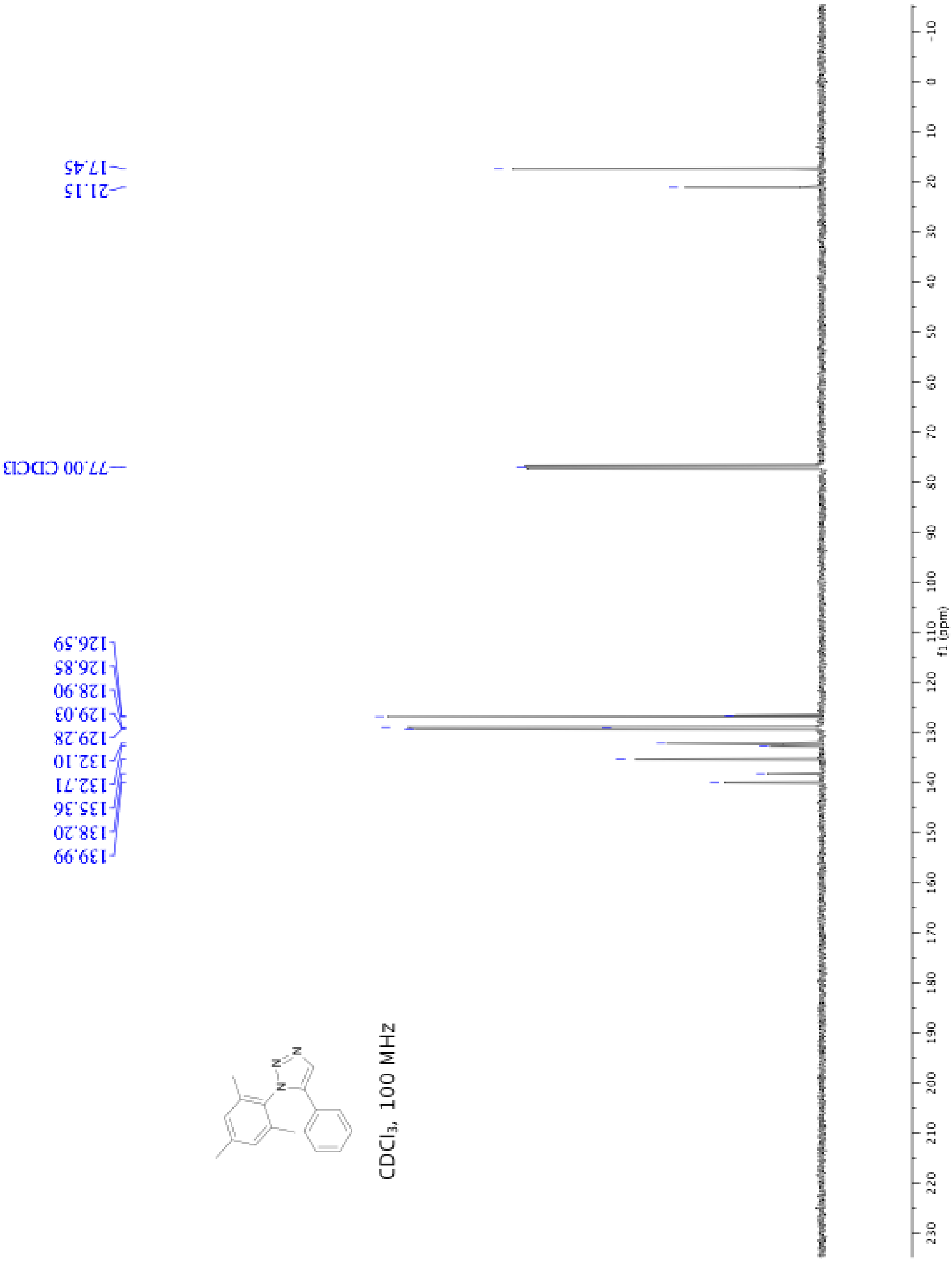

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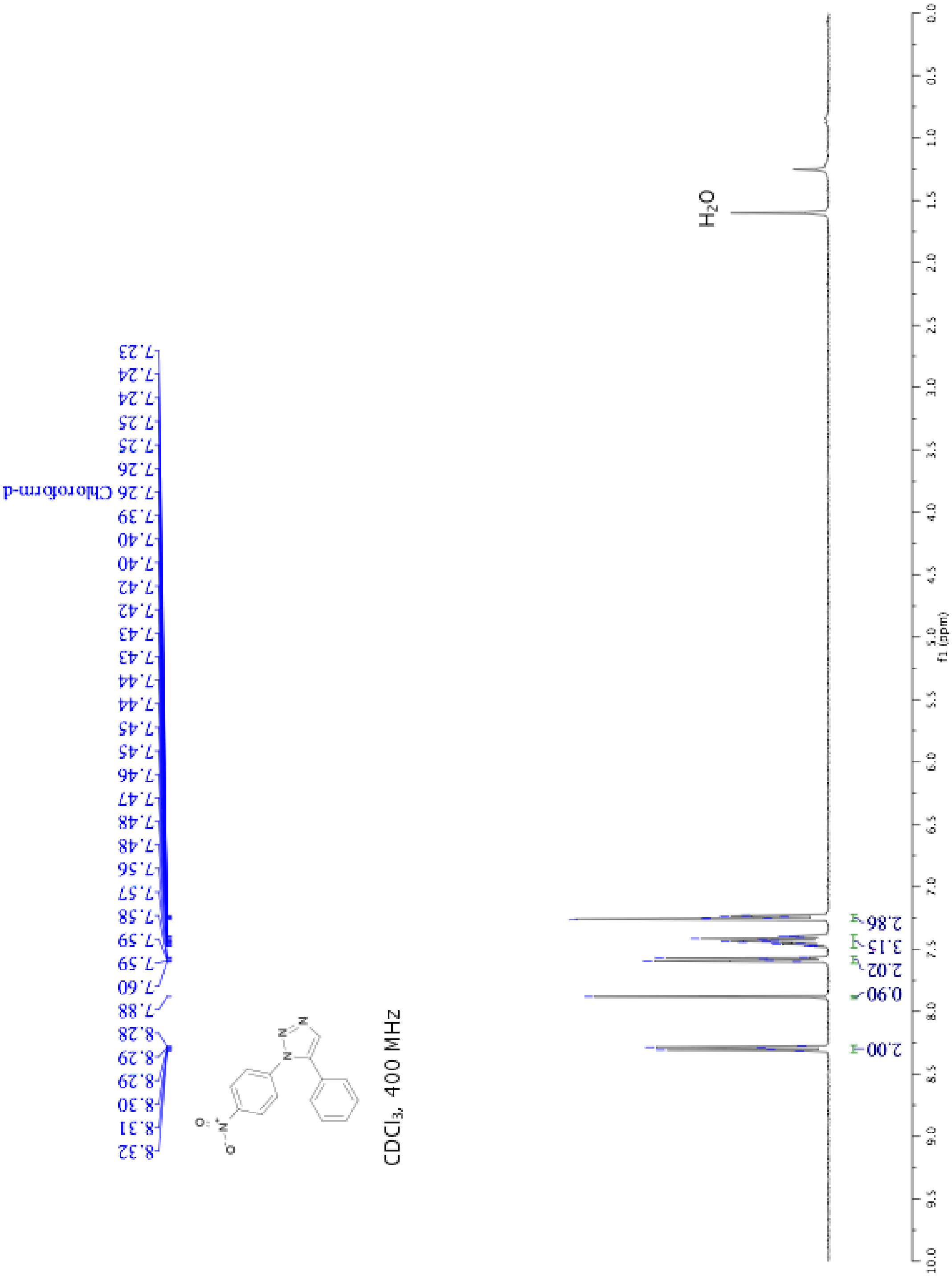

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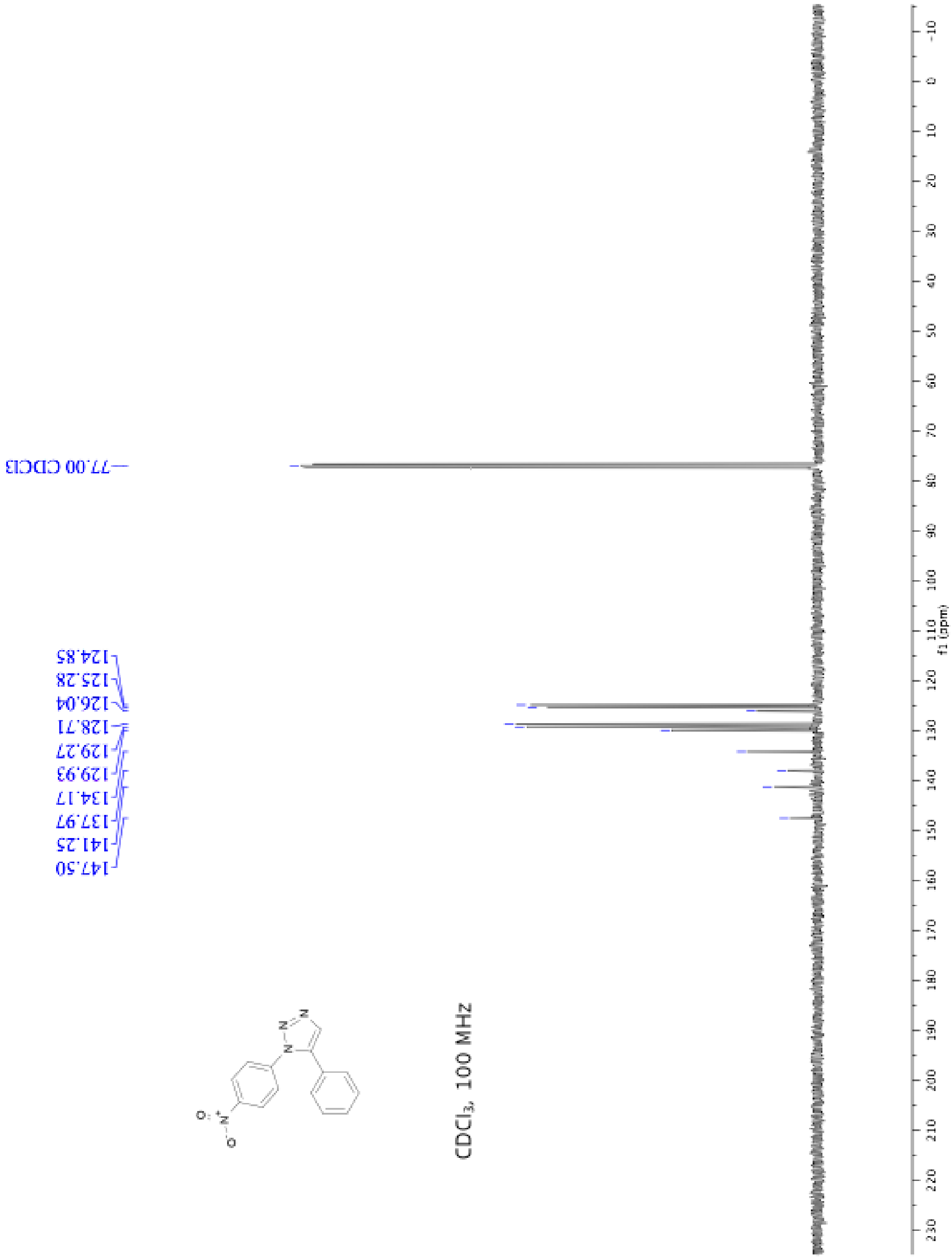

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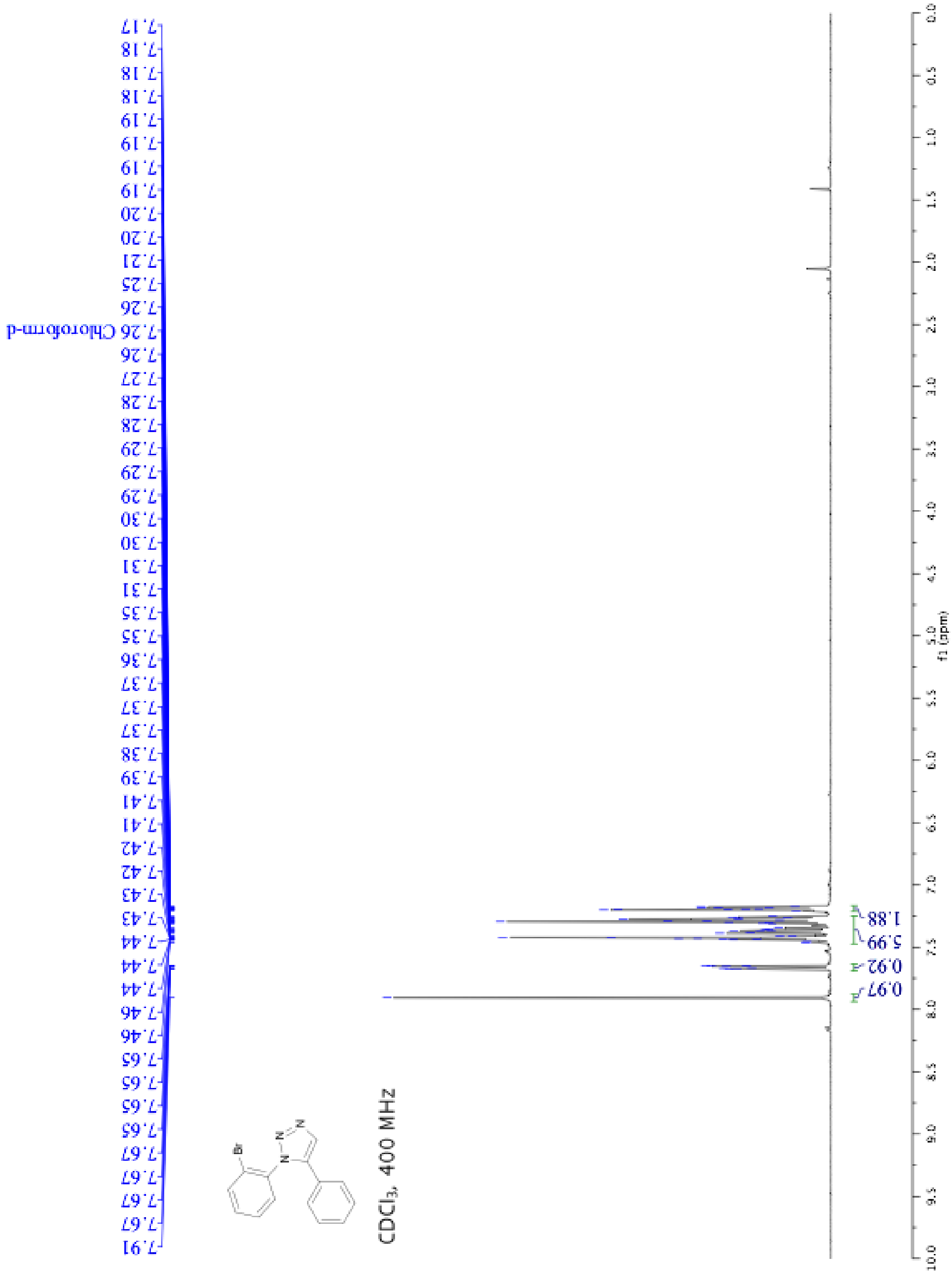

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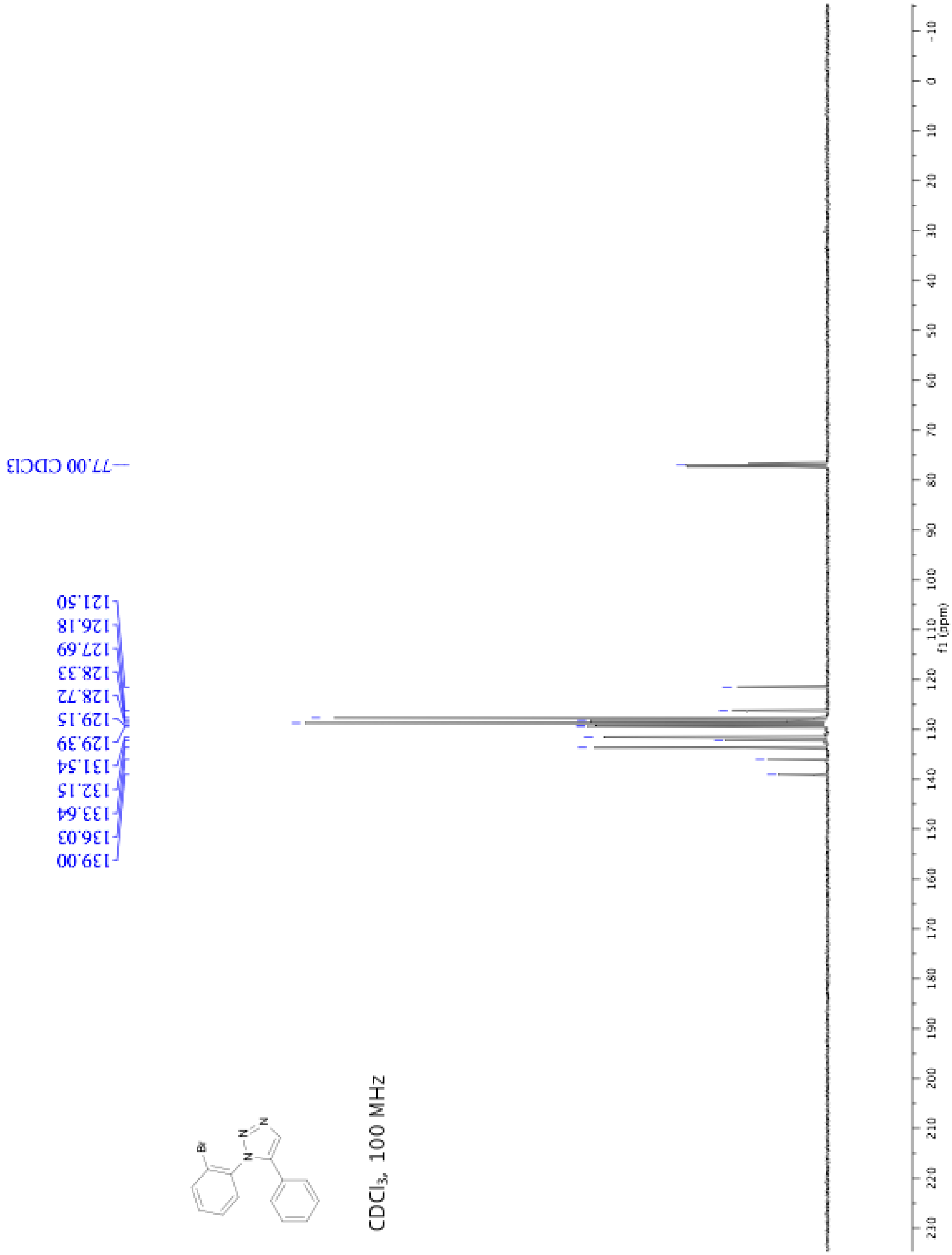

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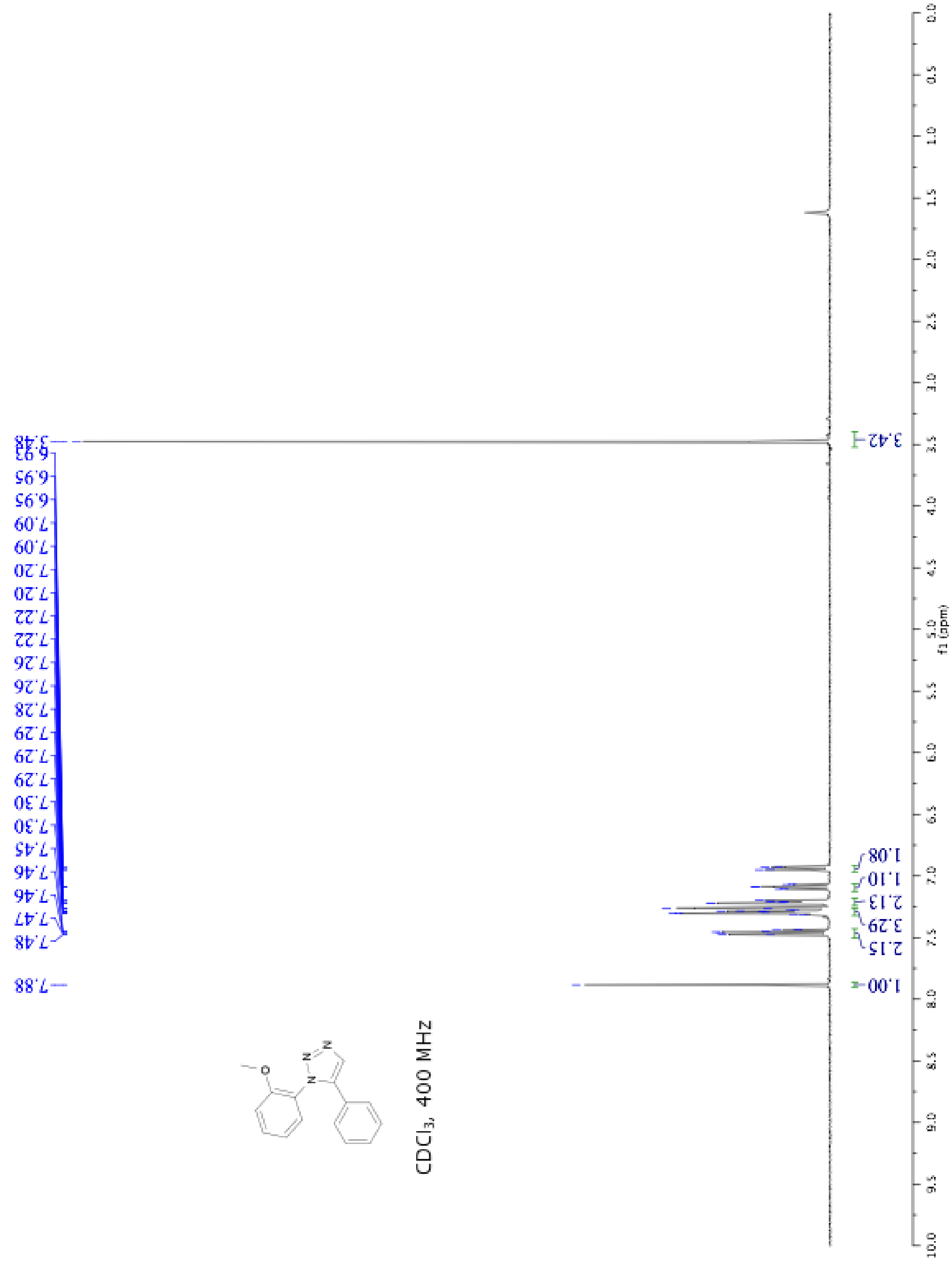
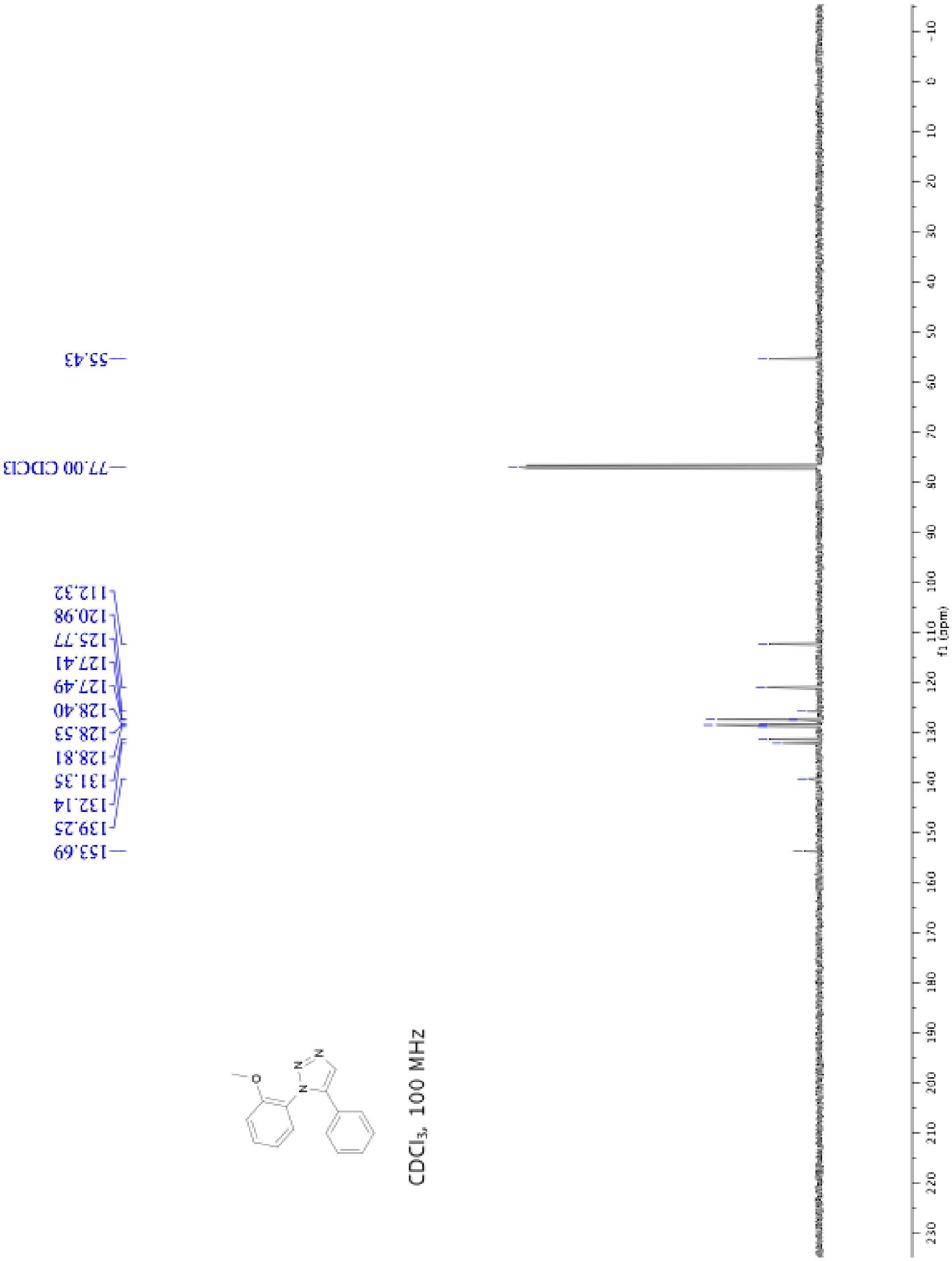
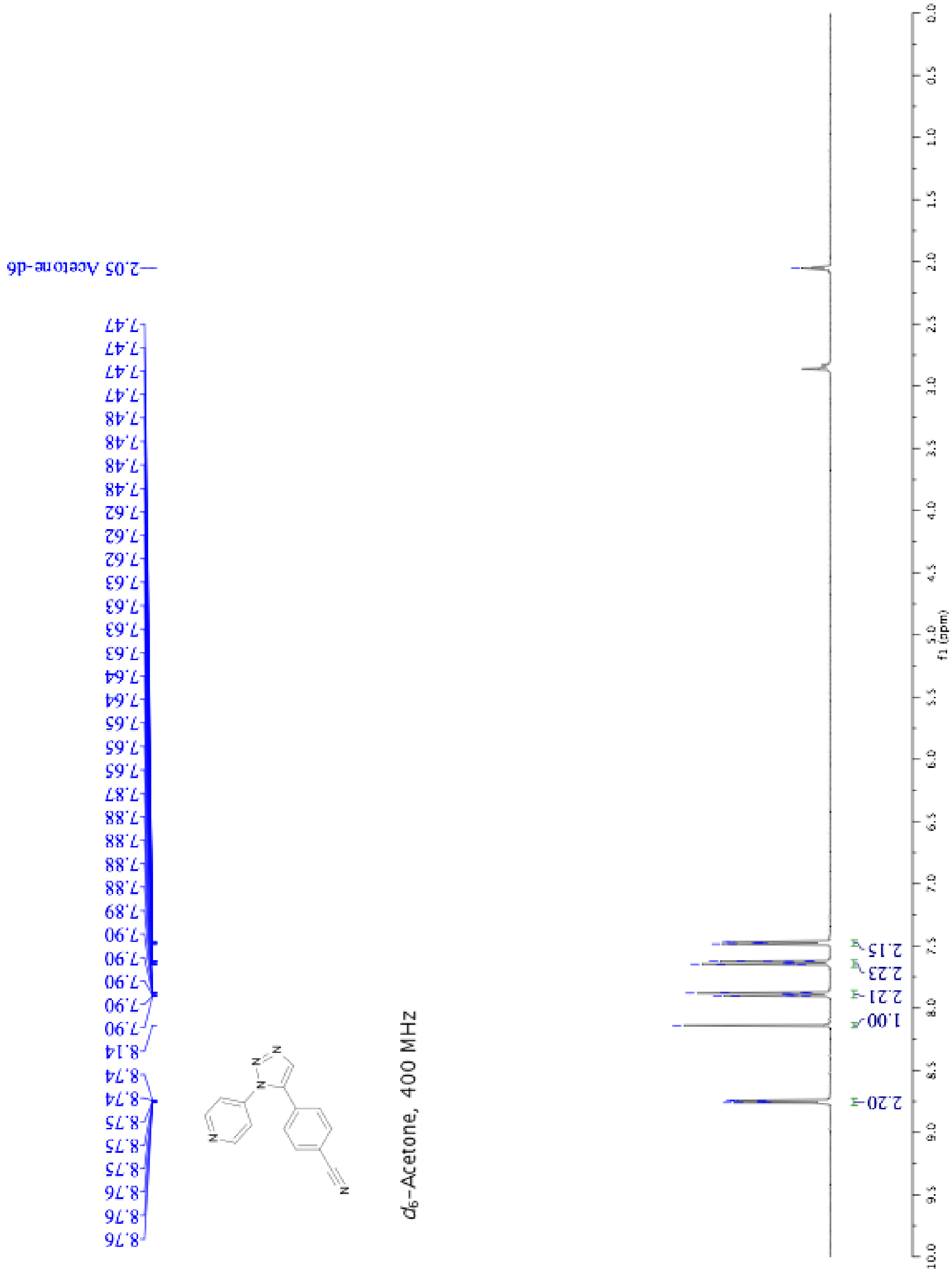


$CDCl_3$, 400 MHz

^{13}C NMR for compound **1e**



^{1}H NMR for compound **2f**



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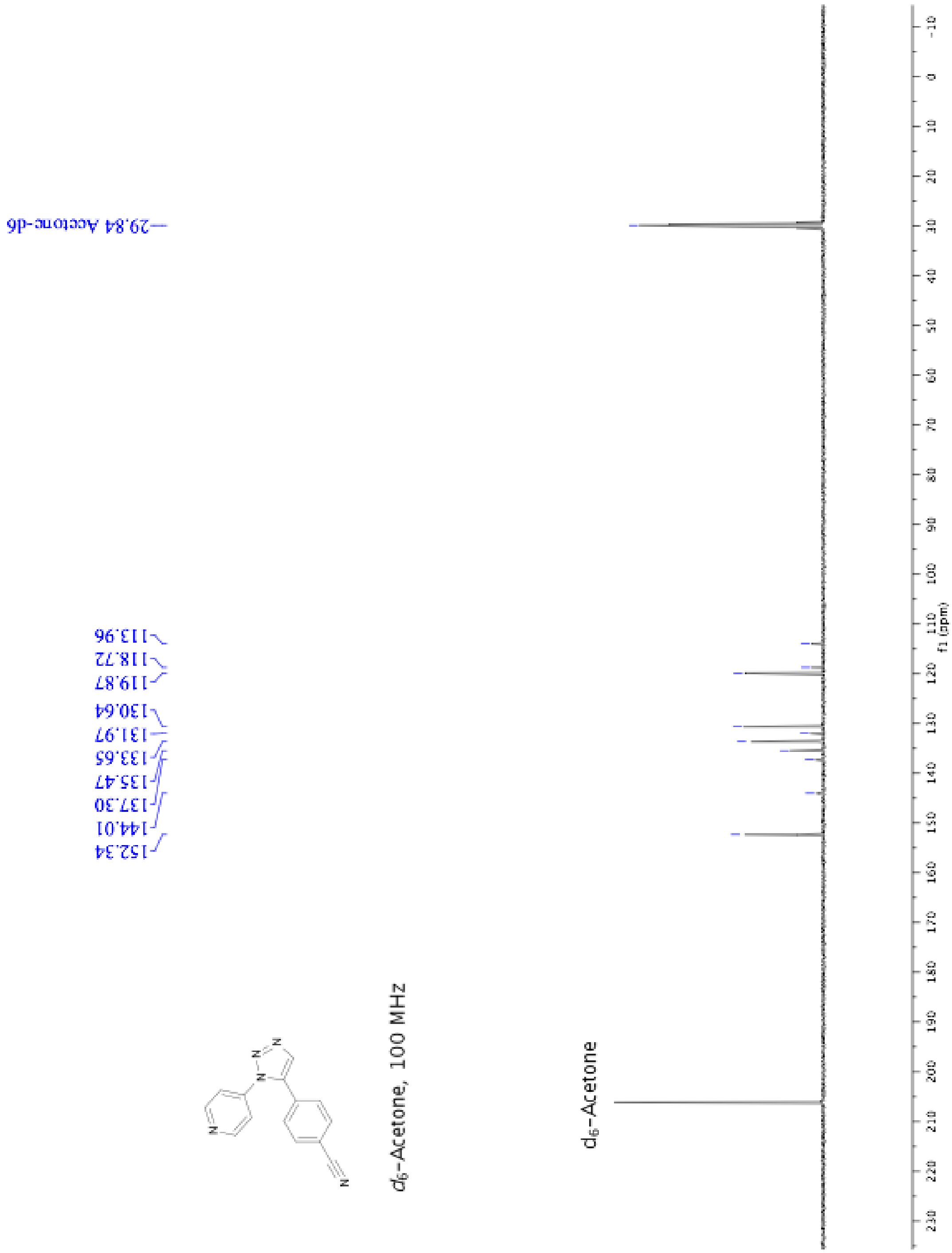

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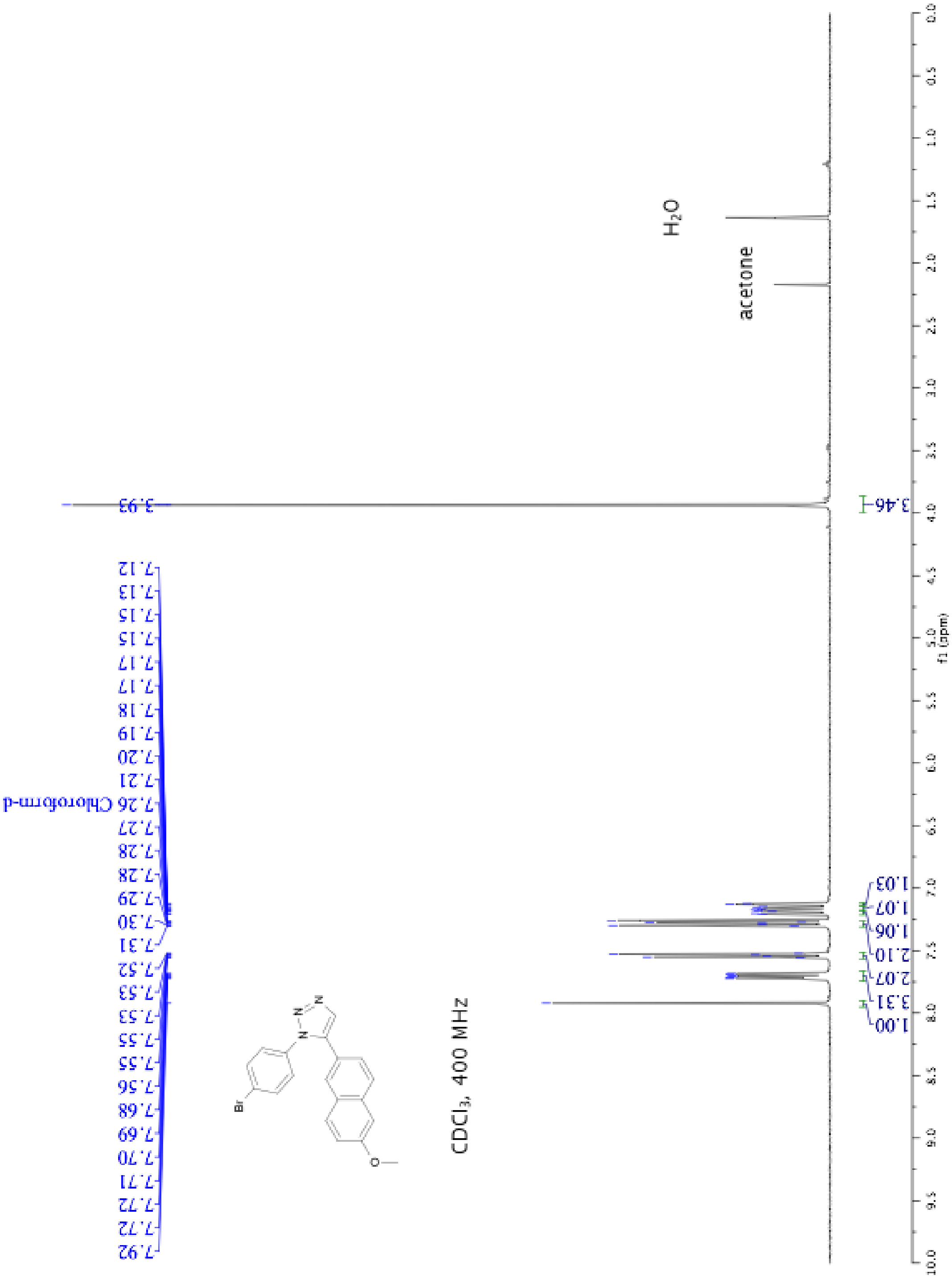

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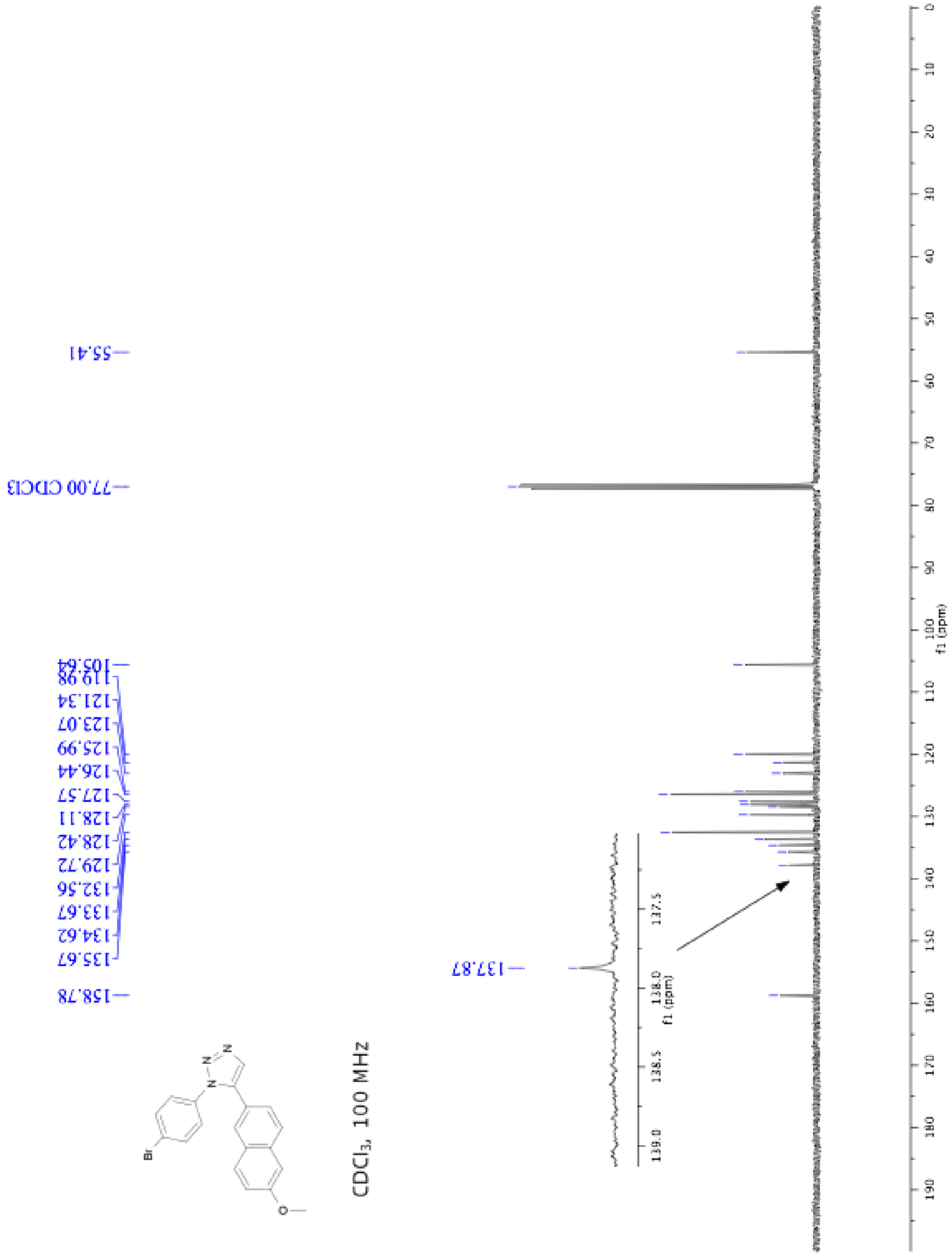

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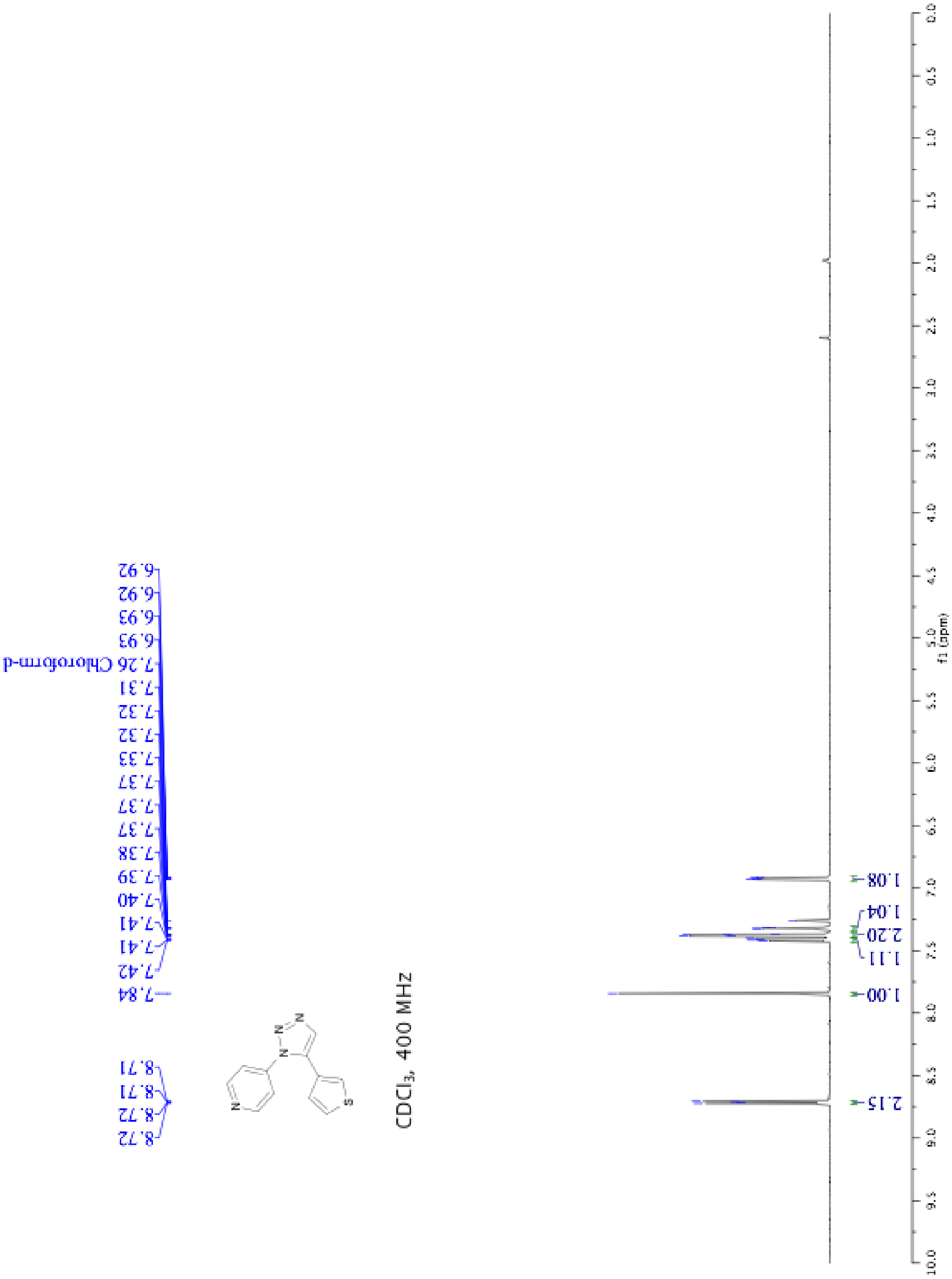

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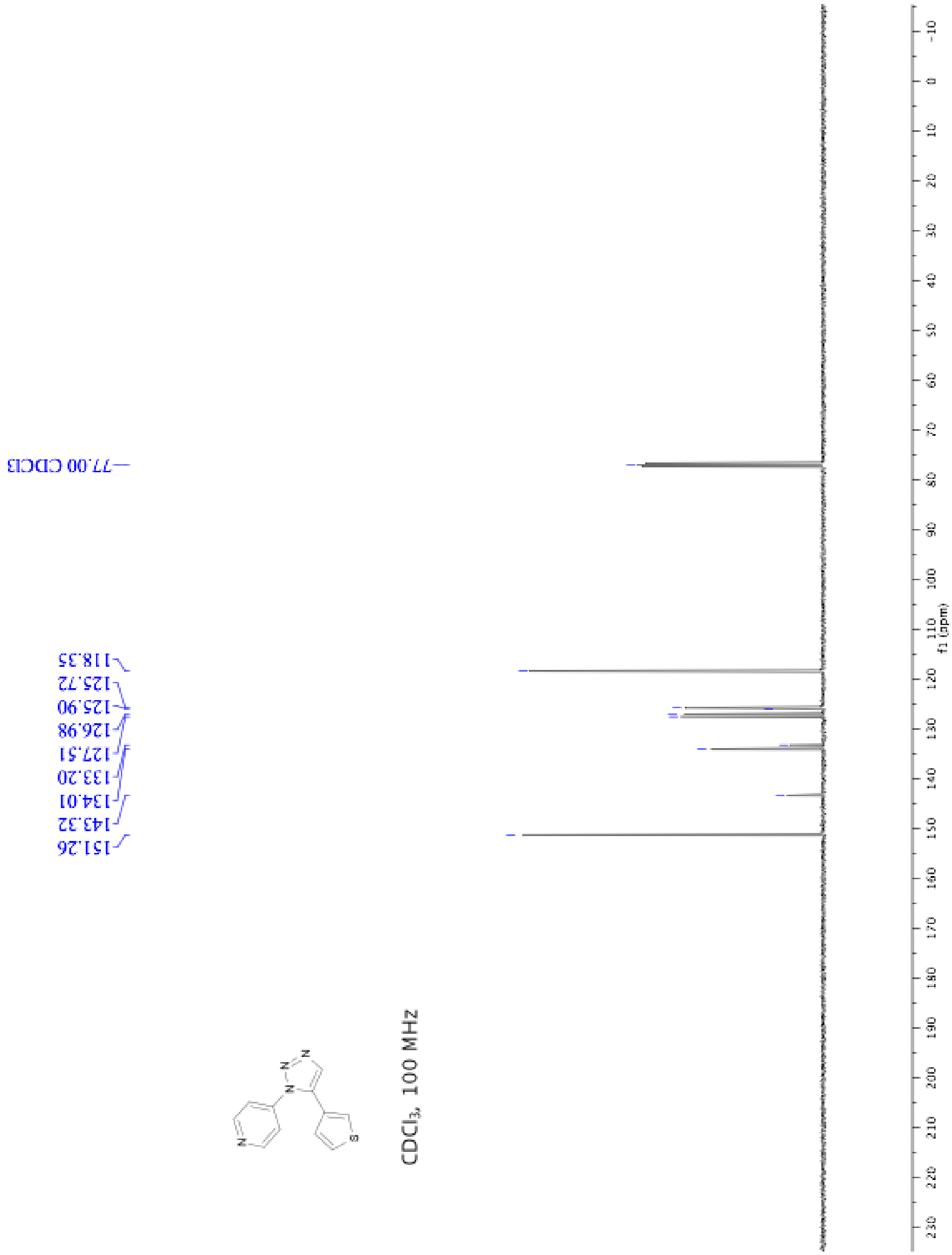

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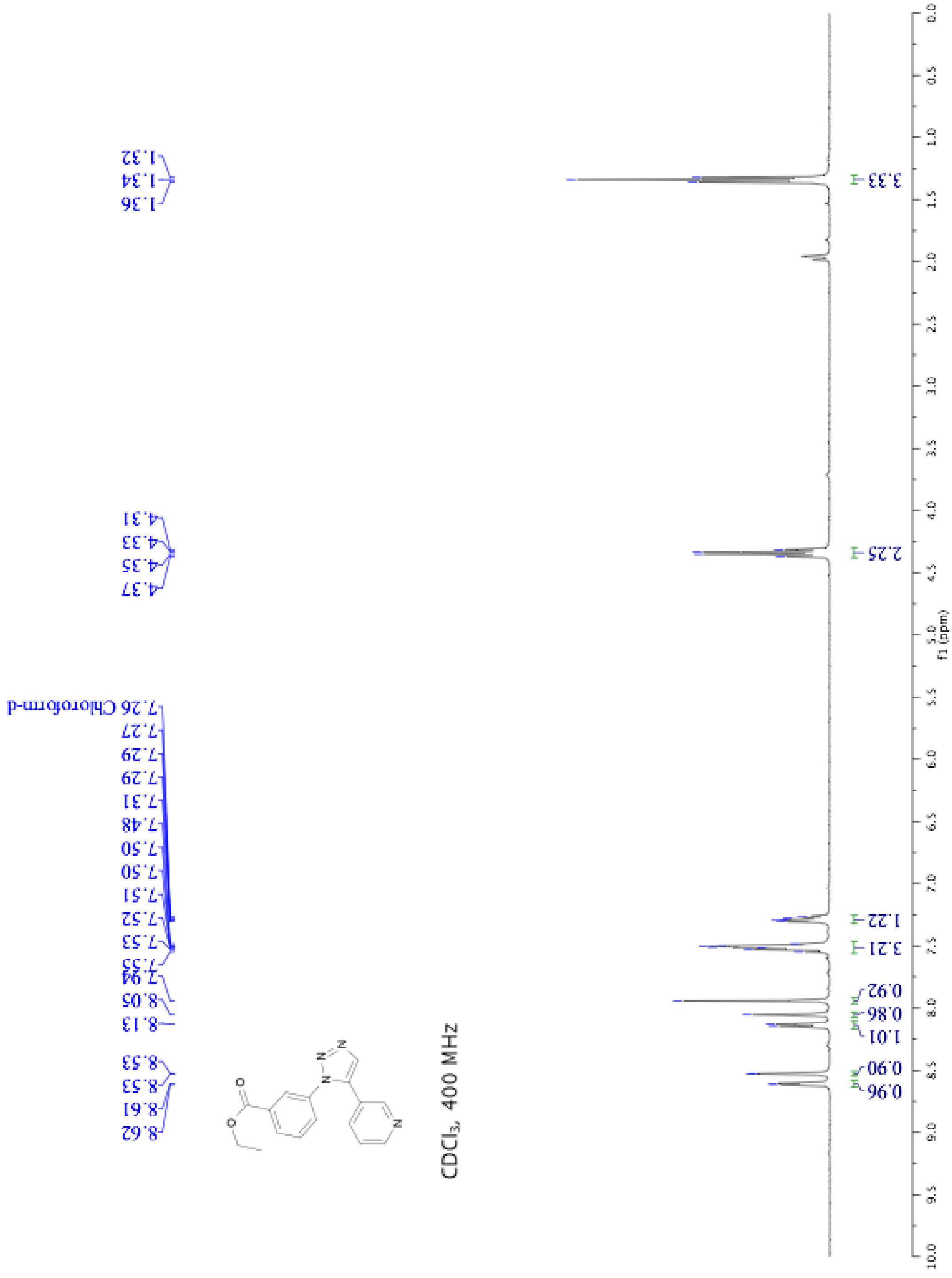
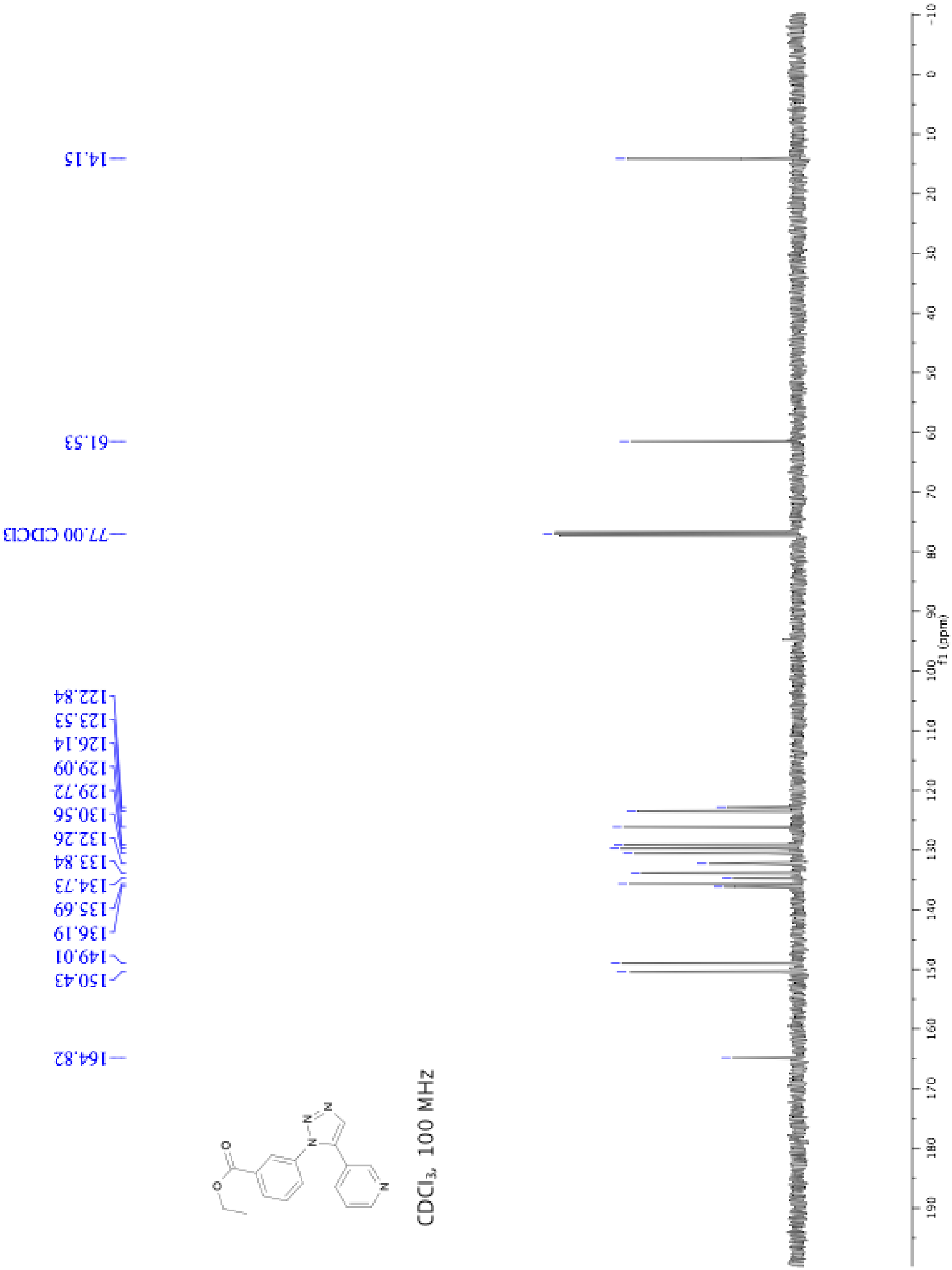


^{13}C NMR for compound **5h**



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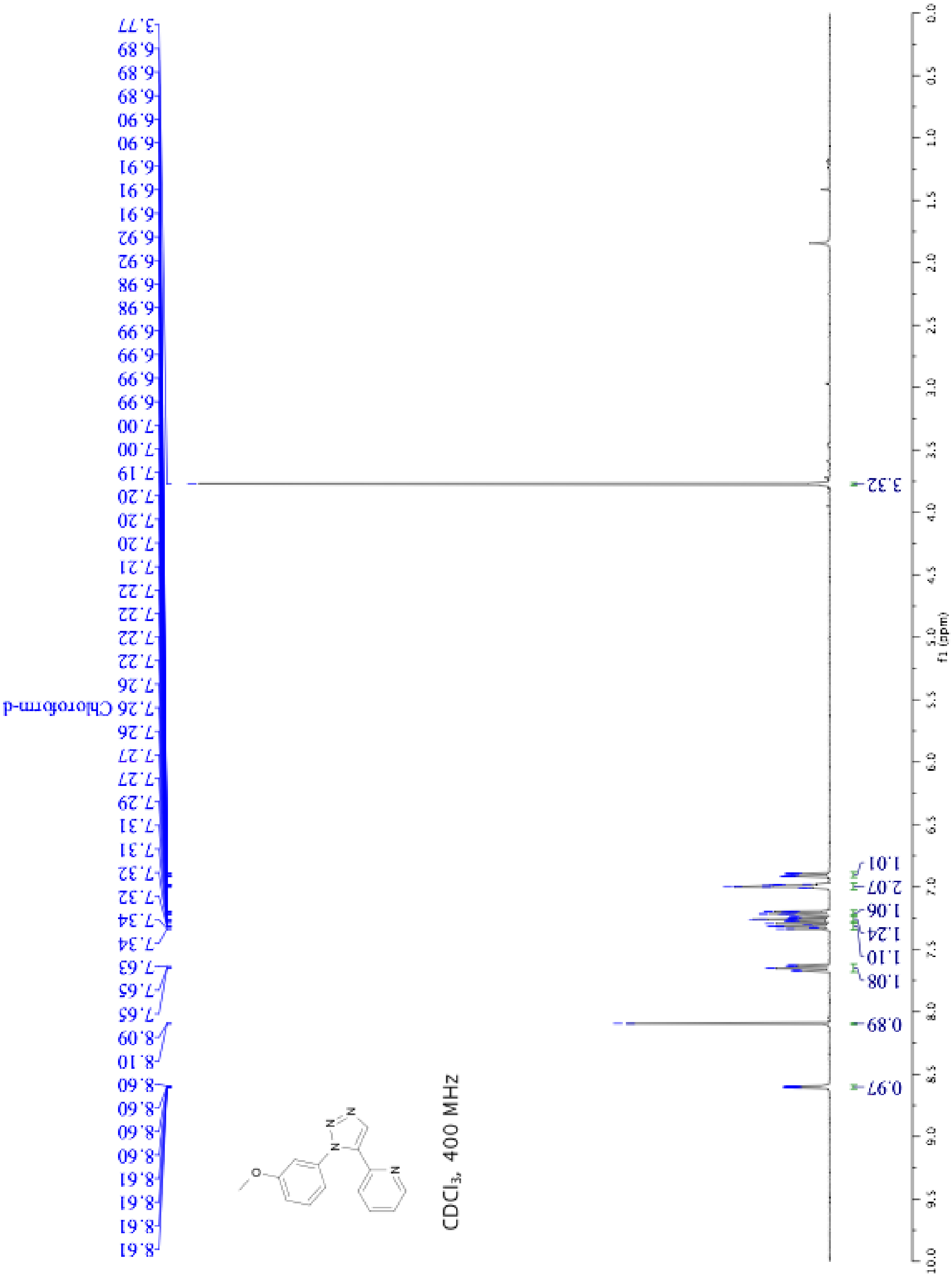
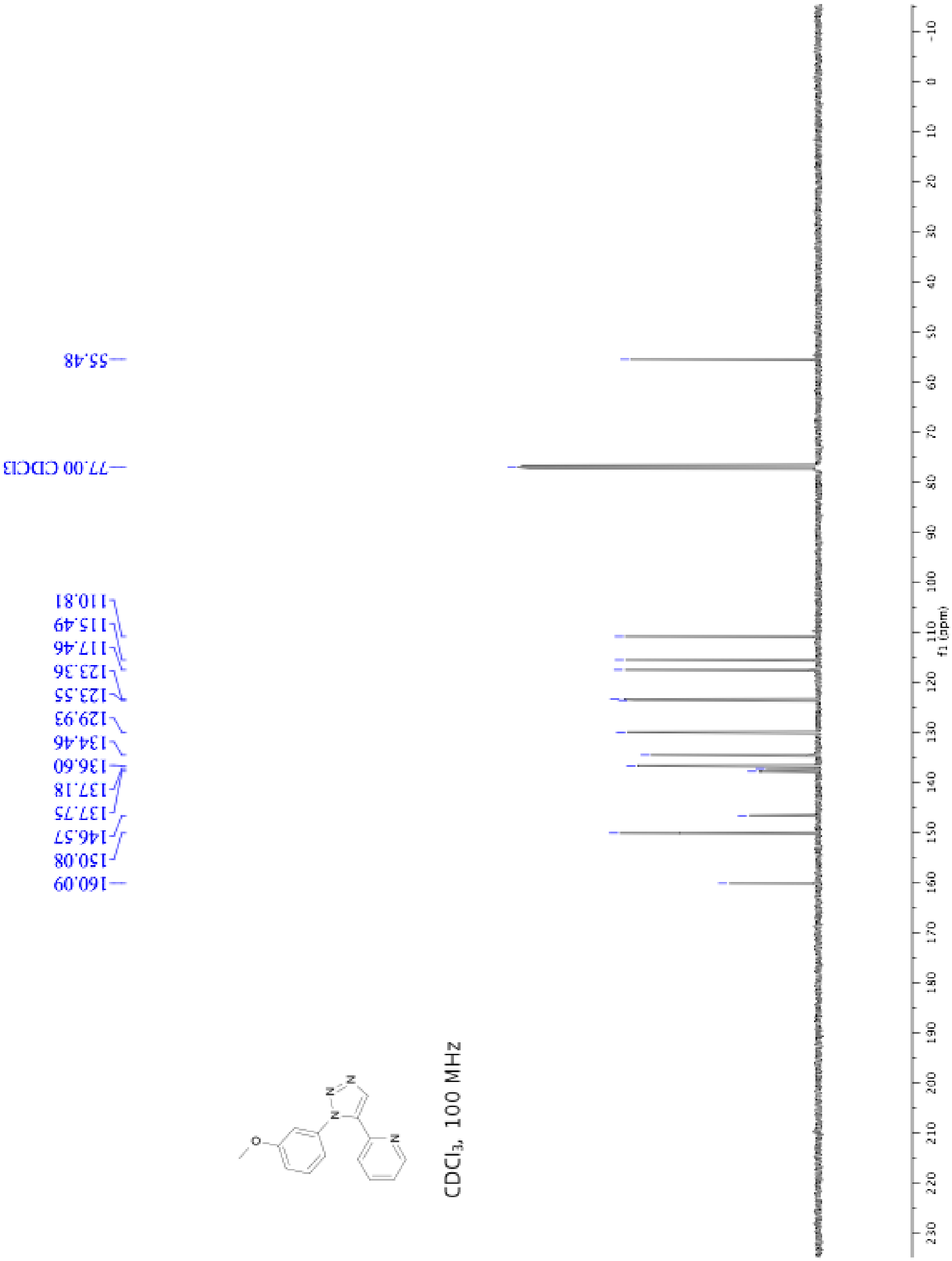
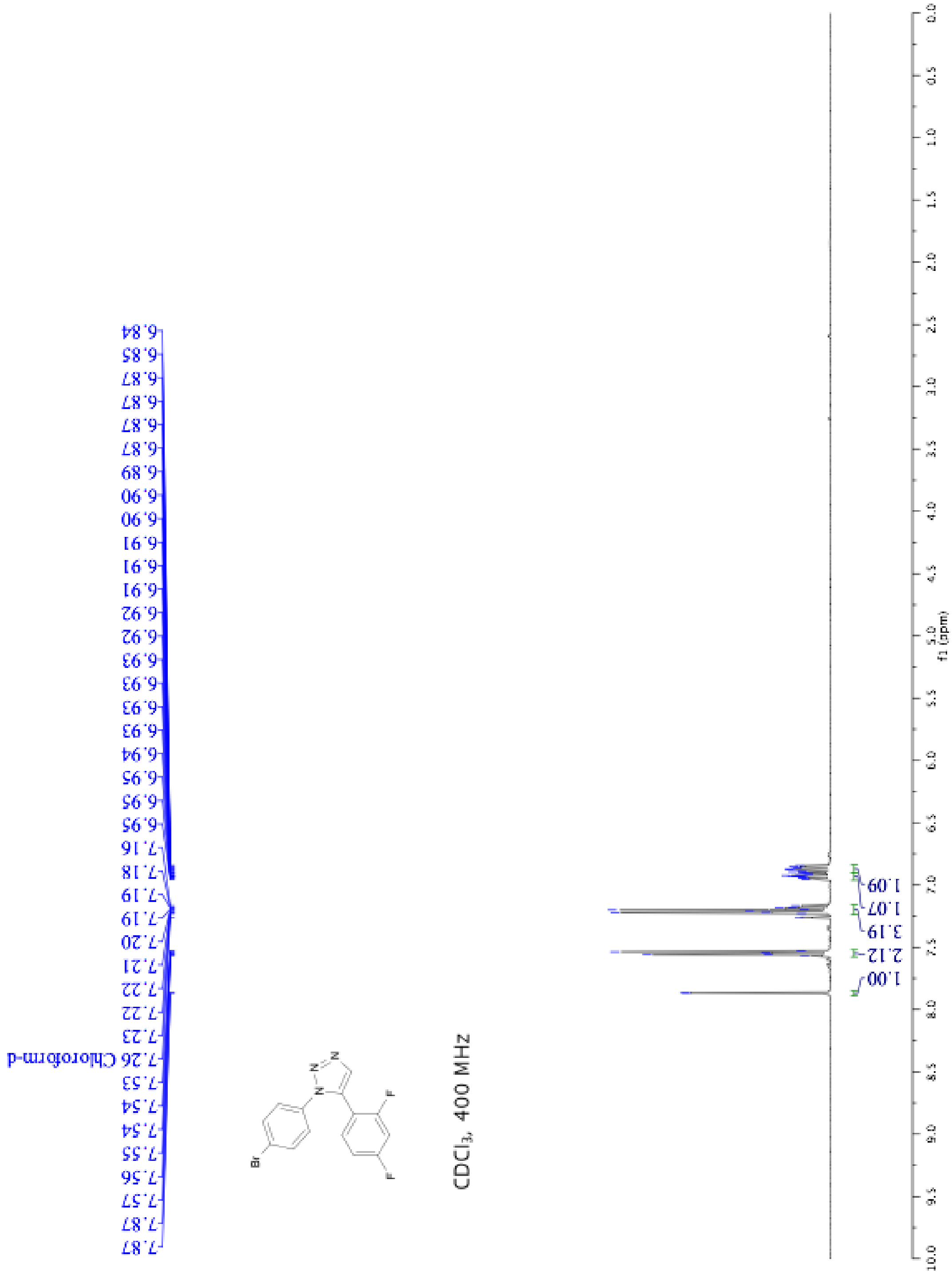


^{13}C NMR for compound **6i**



^{1}H NMR for compound **7g**



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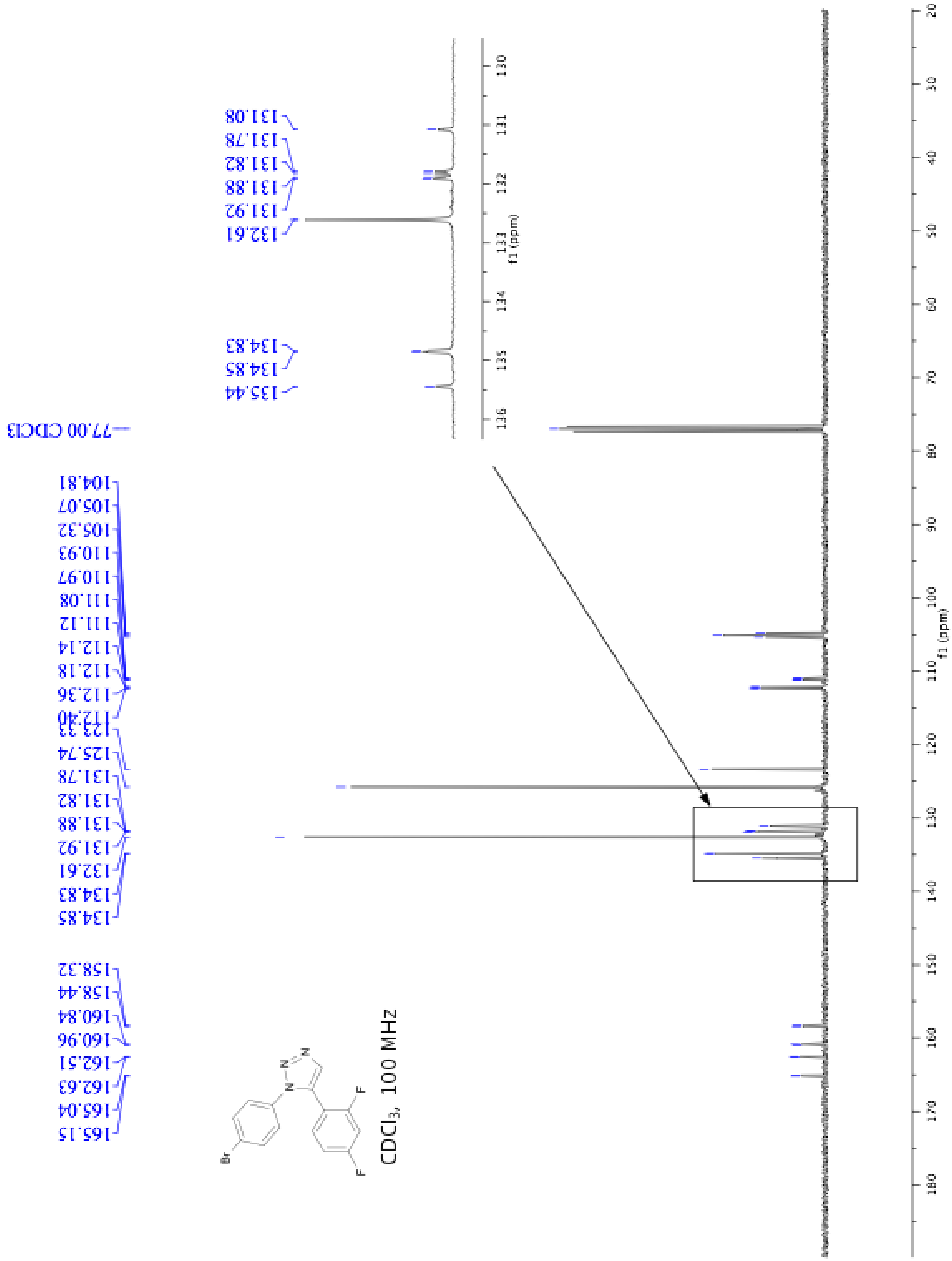
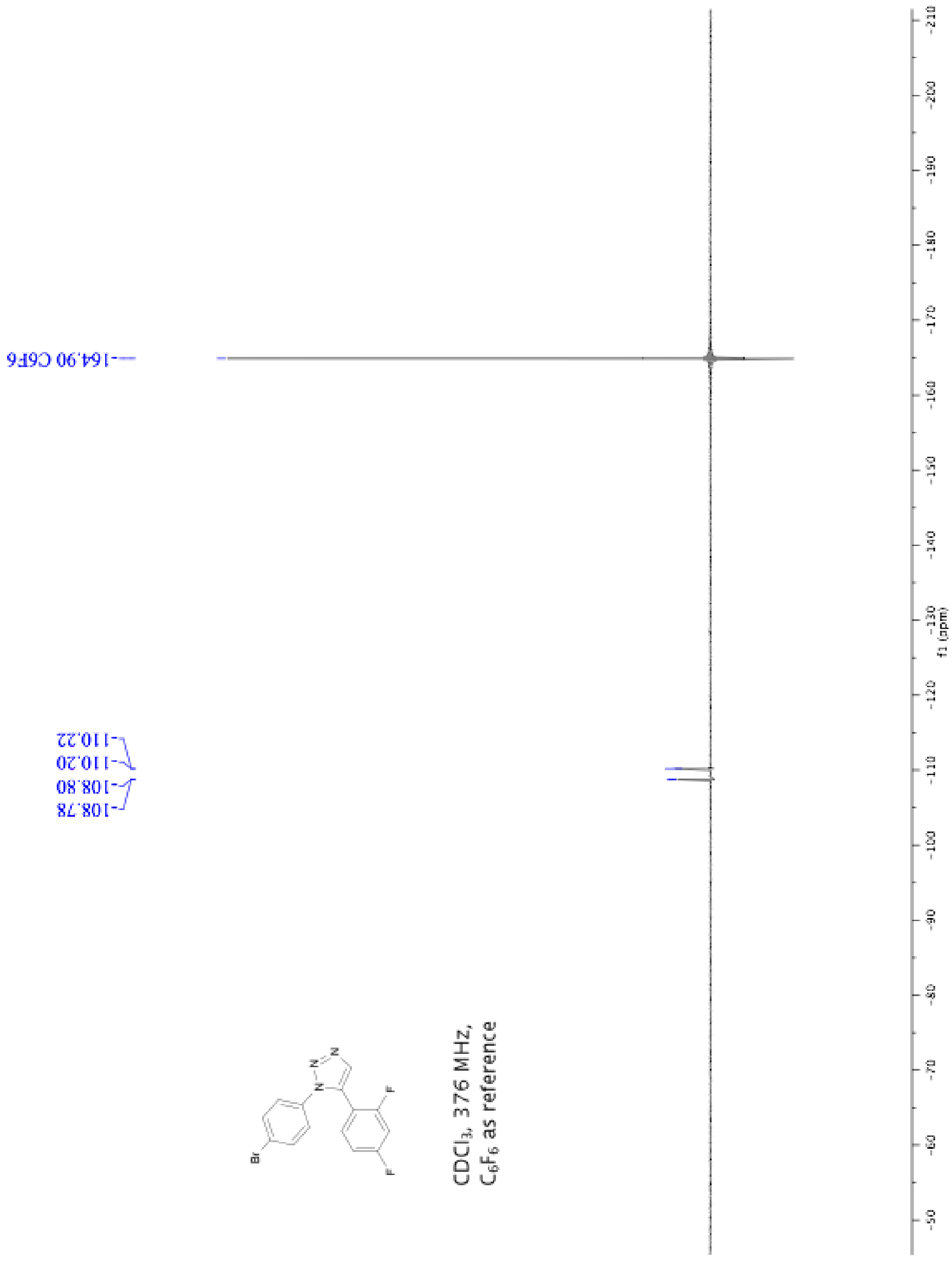


^{19}F NMR for compound **7g**



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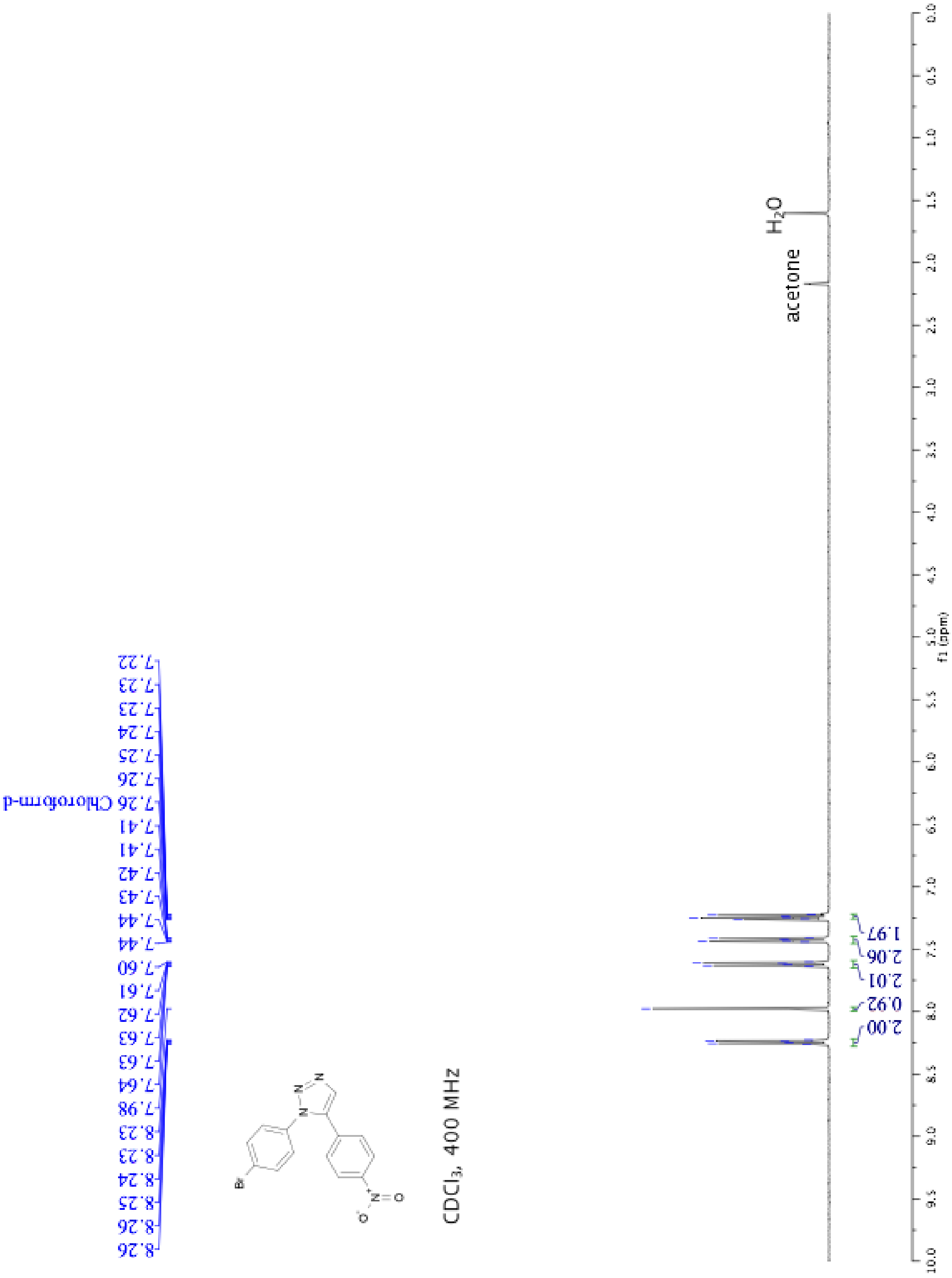

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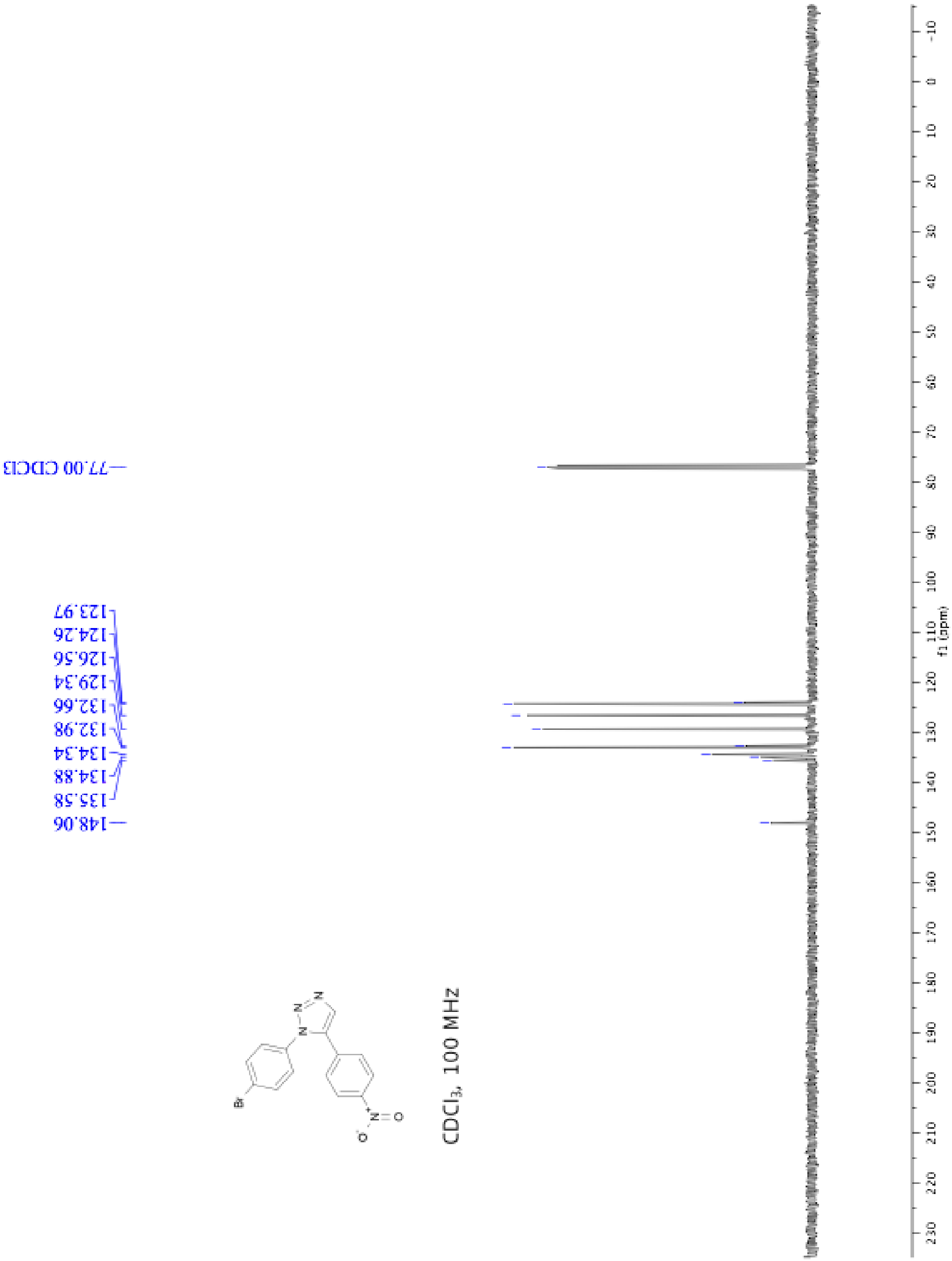

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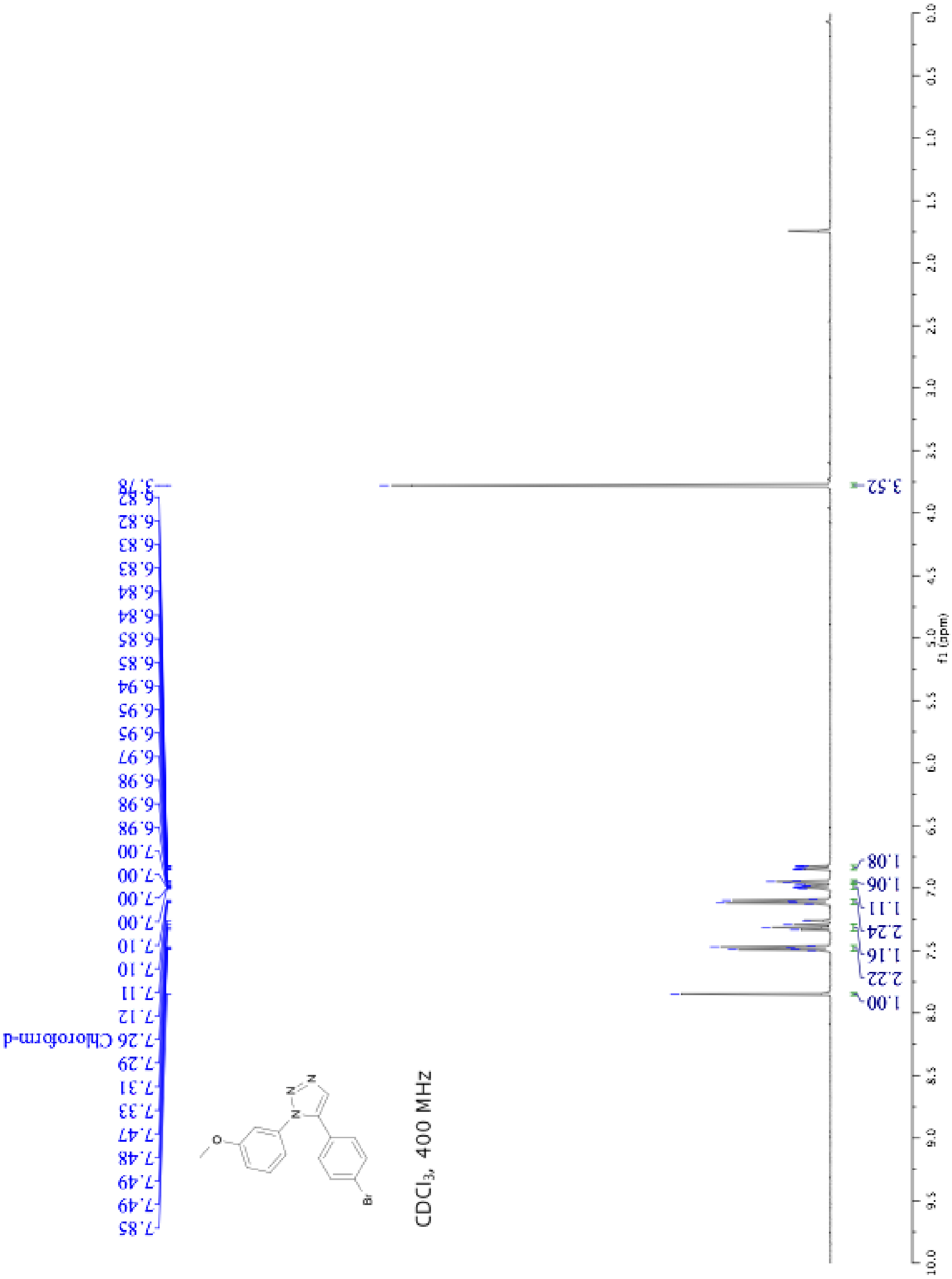

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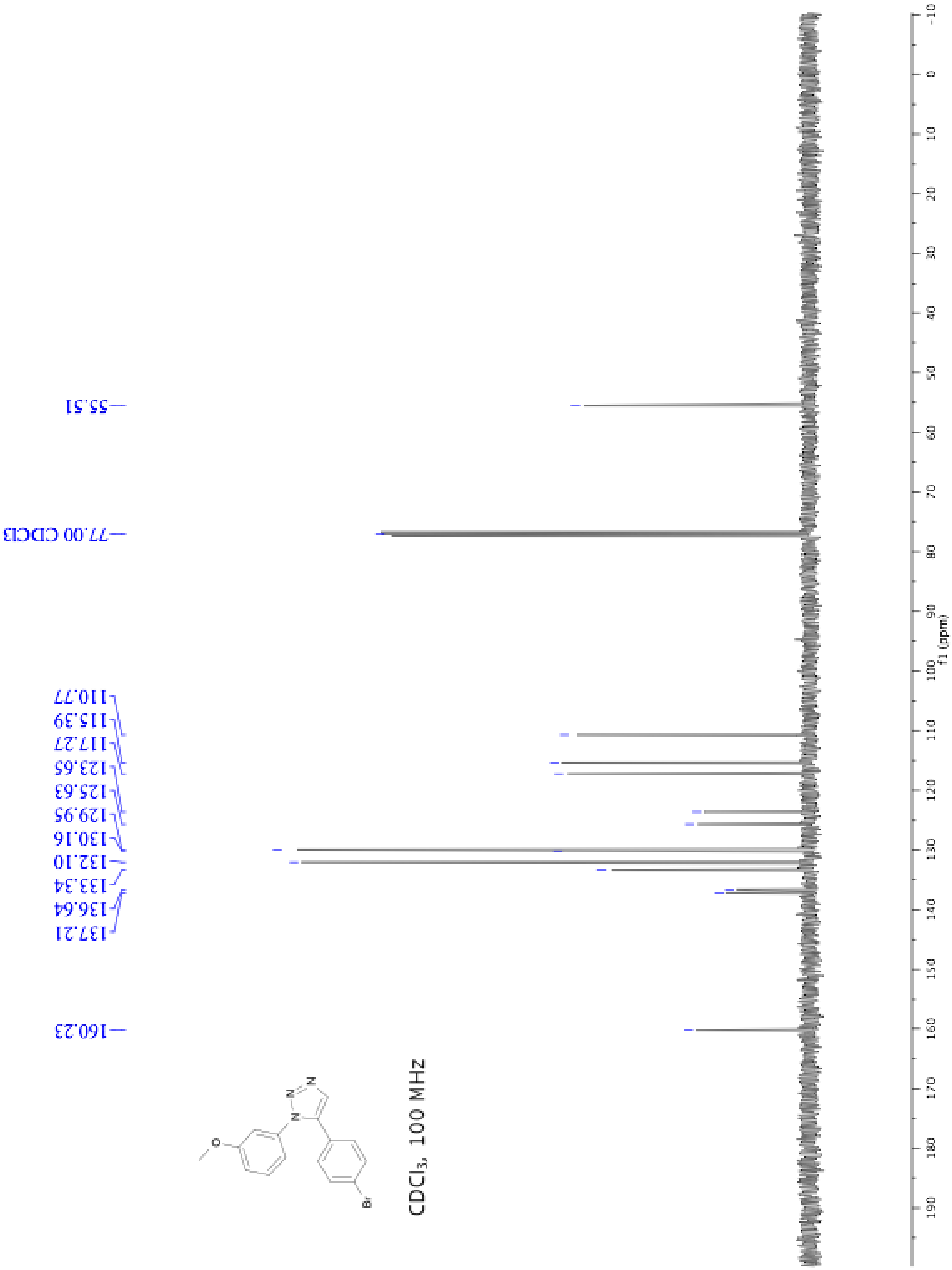

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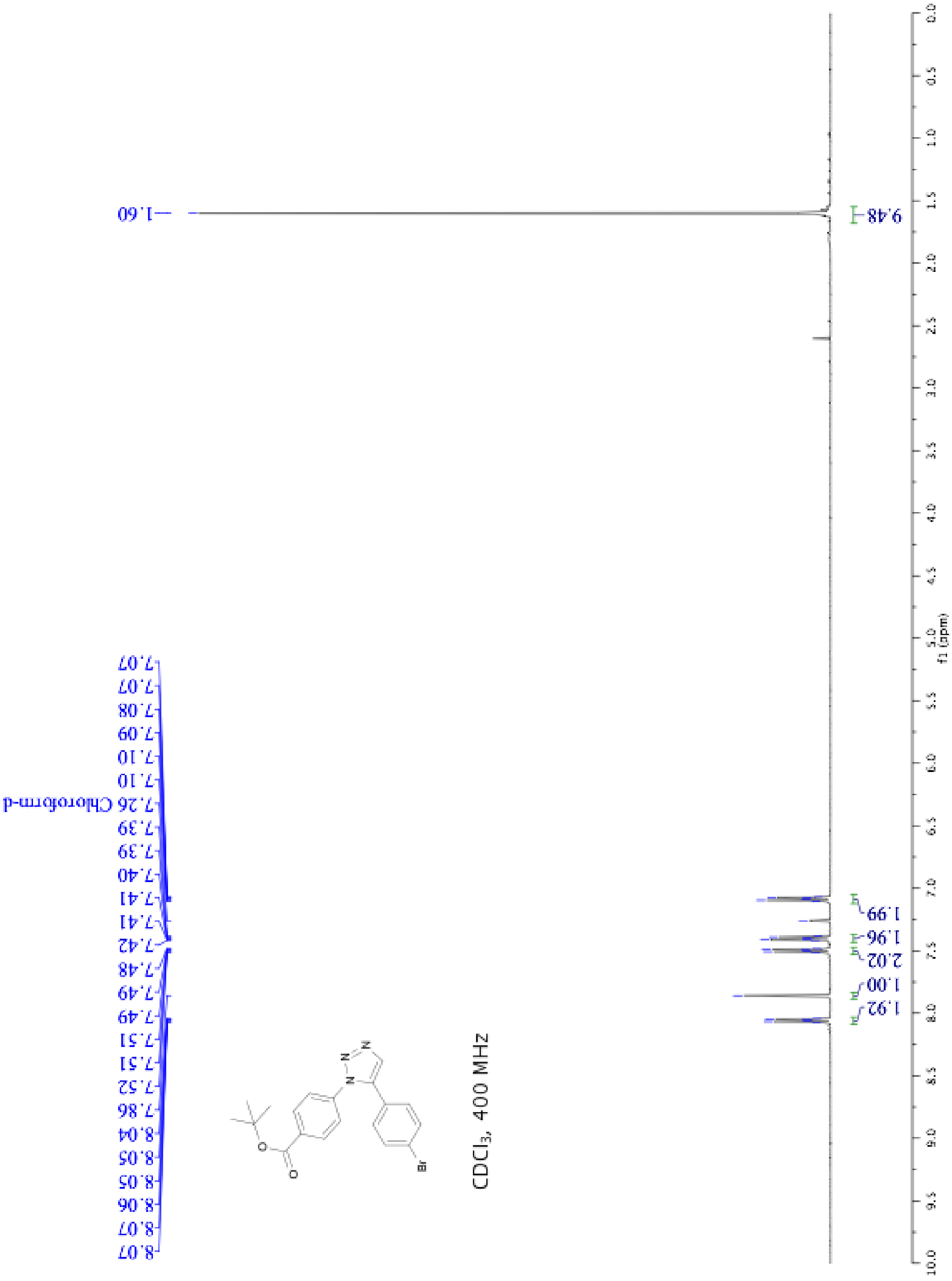

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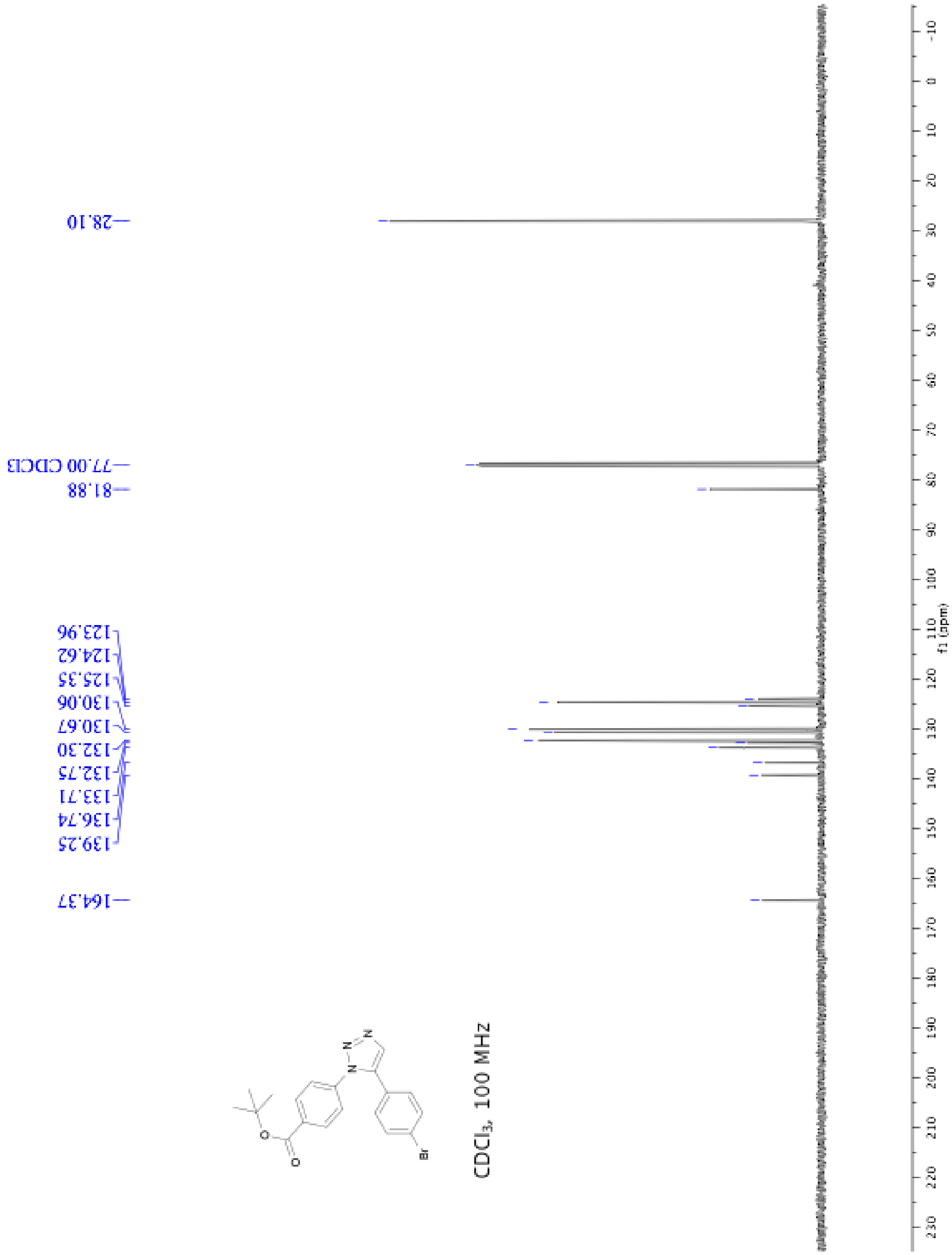

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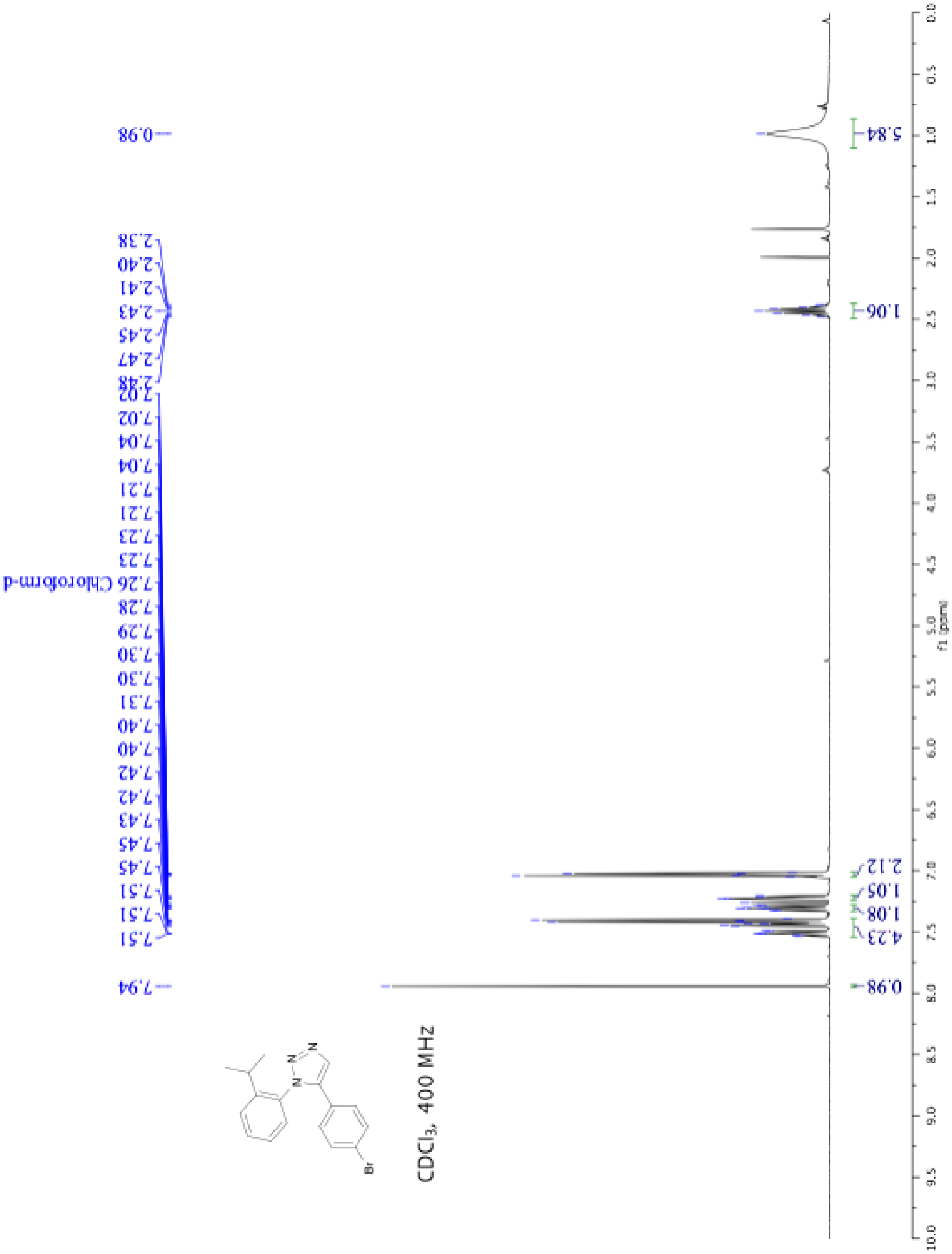

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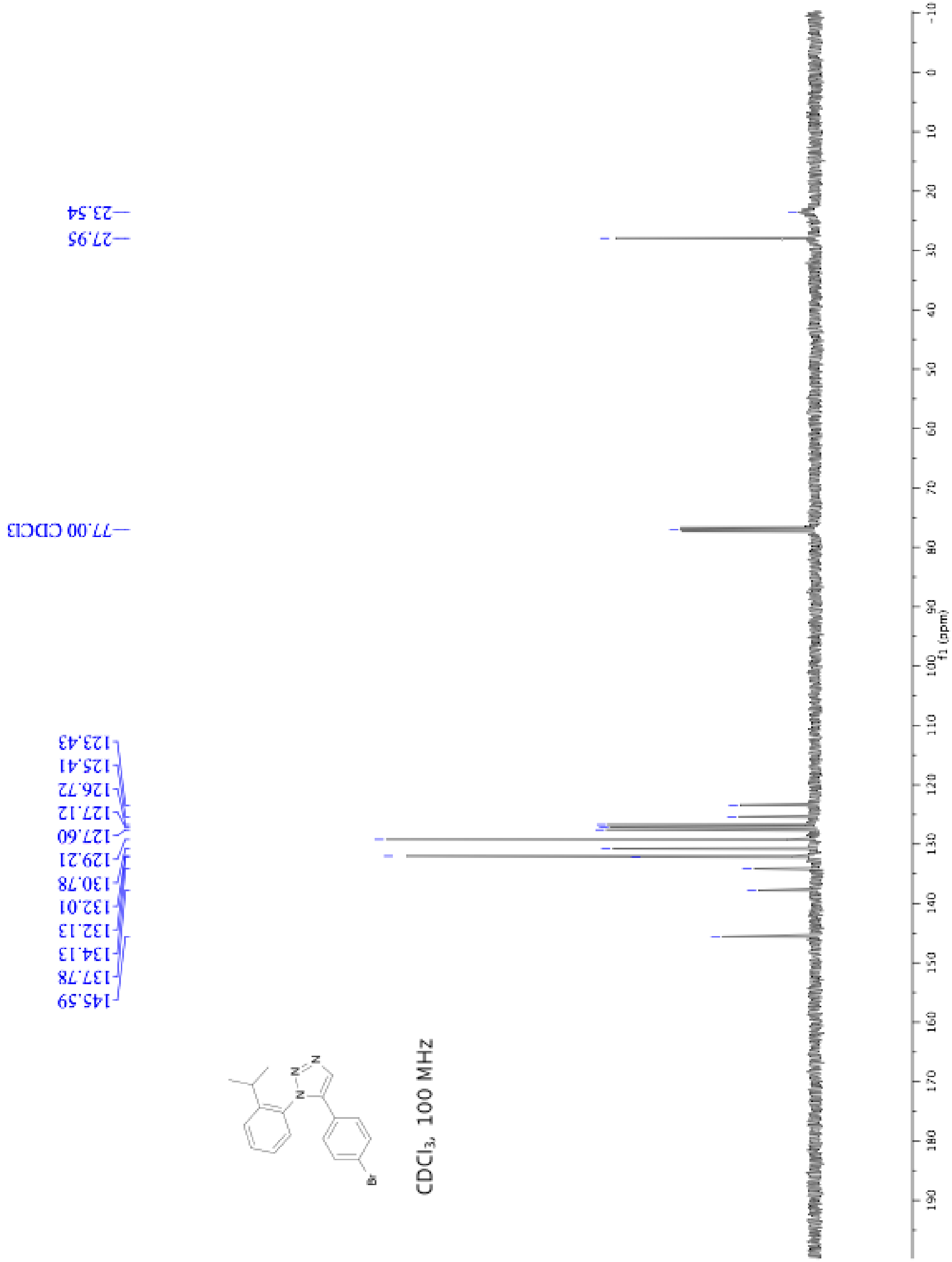

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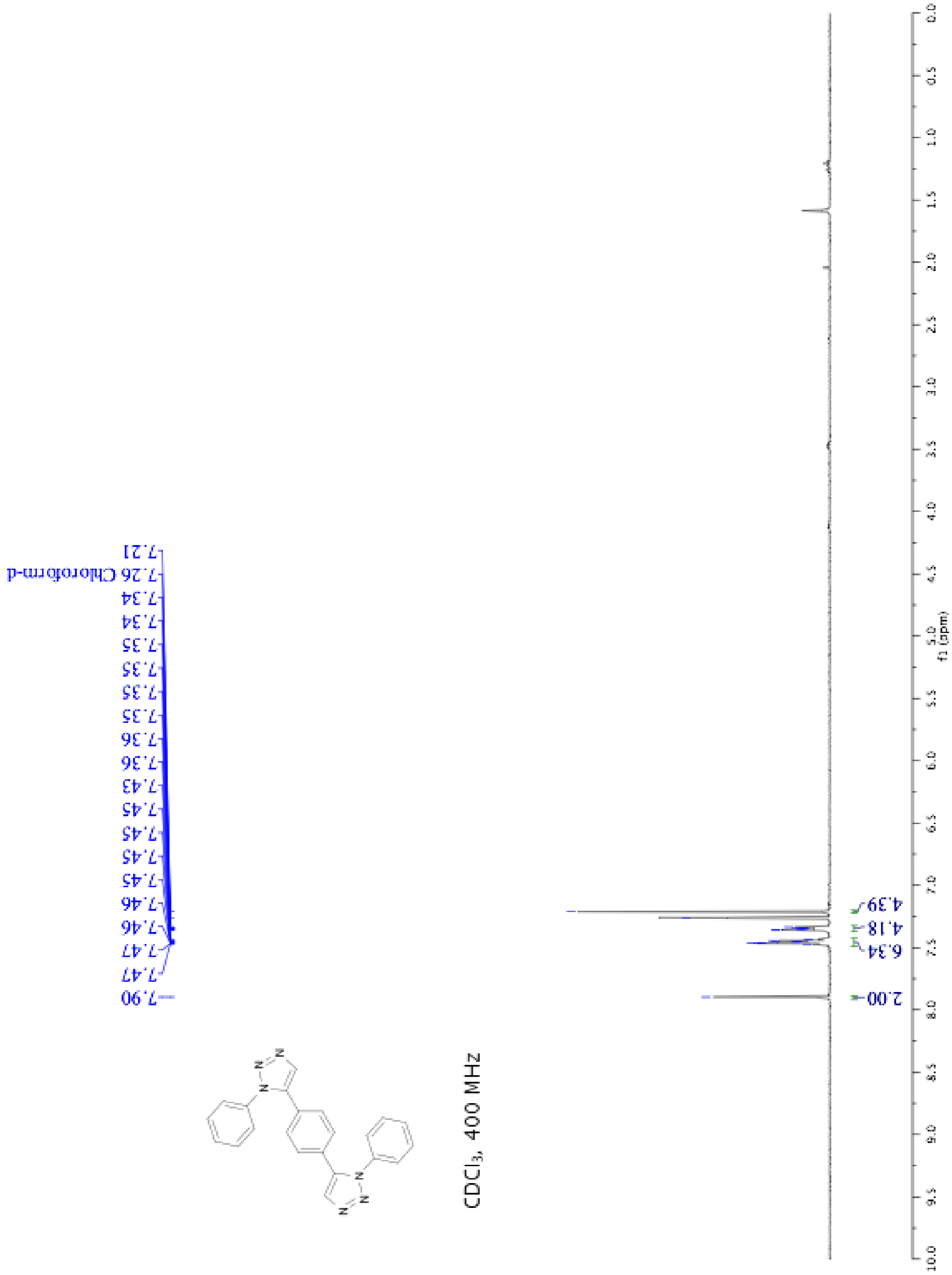

^{13}C NMR for compound **10a**