Molecular engineering of 3-Arylated Tetrazo[1,2-*b*]indazoles: Divergent Synthesis and Structure-property Relationships

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General conditions

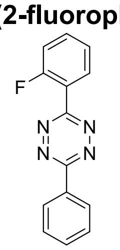
All reagents were purchased from commercial suppliers and used without purifications expect for the 3-(methylthio)-6-(2-fluorophenyl)-[1,2,4,5]-tetrazine which was synthesized according to the literature.[1] All experiments were carried out under an inert atmosphere using Schlenk technics or under air using a microwave reaction vessel. Microwave heating was carried out using a CEM Discover microwave reactor. The microwave reactions were run in closed reaction vessels with magnetic stirring and with the temperature controlled via IR detection. Flash chromatography was performed on silica gel (40-63 µm). The identity and purity of the products were established at the "Chemical Analysis Platform and Molecular Synthesis University of Burgundy" (PACSMUB Platform – SATT SAYENS) using high-resolution mass spectrometry, elemental analysis and multinuclear NMR. ^{1}H (500 or 400 MHz), ^{13}C (125 or 100 MHz), ^{19}F (470 or 376 MHz) spectra were recorded on Bruker AVANCE III instruments in $CDCl_3$, CD_2Cl_2 or DMSO-*d6* solution. Chemical shifts are reported in ppm relative to $CDCl_3$ (^{1}H: 7.26 and ^{13}C: 77.16); CD_2Cl_2 (^{1}H: 5.32 ppm and ^{13}C: 54.00 ppm) or DMSO-*d6* (^{1}H: 2.50 ppm and ^{13}C: 39.52 ppm) and coupling constants *J* are given in Hz. High resolution mass spectra (HRMS) were obtained on a Orbitrap Exploris 240 mass spectrometer (thermo Scientific) equipped with an electrospray ionization source (HESI). UV-visible absorption spectra were recorded with a Varian UV-vis spectrophotometer Cary 50 scan using quartz cells (Hellma).

General procedures

Procedure for the synthesis of 3-(2-fluorophenyl)-6-aryl-[1,2,4,5]-tetrazine

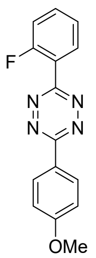
To an oven dried Schlenk tube equipped with a magnetic stirring bar was sequentially charged with of 3-(methylthio)-6-(2-fluorophenyl)-[1,2,4,5]-tetrazine (1.0 equiv.), [$PdCl_2$(dppf))] (15 mol%), arylboronic acid (2.0 equiv.) and Ag_2O (2.0 equiv.). After 3 cycles of vacuum purge with argon, DMF [0.1 M] solvent was added by syringe. After heating under argon at 60 °C for 20 h, the DMF was removed by rotary evaporation under vacuum. The crude was purified by column chromatography.

3-(2-fluorophenyl)-6-phenyl-[1,2,4,5]-tetrazine (1)[2] CAS: 1893365-27-9



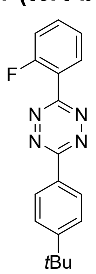
Purification on silica gel (pentane/CH_2Cl_2: 5/4) to give 95% isolated yield (24 mg, as a purple solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.68–8.66 (m, 2H), 8.33 (td, *J* = 7.6 and 1.6 Hz, 1H), 7.67–7.59 (m, 4H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.33 (dd, *J* = 10.8 and 8.5 Hz, 1H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –112.0.

3-(2-fluorophenyl)-6-(4-methoxyphenyl)-[1,2,4,5]-tetrazine (2)



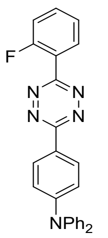
Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 72% isolated yield (273 mg, as a purple solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.64 (d, *J* = 8.9 Hz, 2H), 8.32 (td, *J* = 7.6 and 1.7 Hz, 1H), 7.63–7.59 (m, 1H), 7.40 (td, *J* = 7.7 and 0.8 Hz, 1H), 7.33 (dd, *J* = 10.8 and 8.4 Hz, 1H), 7.12 (d, *J* = 8.9 Hz, 2H), 3.97 (s, 3H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –112.3.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 163.8, 163.5 (d, *J* = 5.9 Hz), 162.9, 162.6 (d, *J* = 259.0 Hz), 133.8 (d, *J* = 8.7 Hz), 131.2 (d, *J* = 1.1 Hz), 130.2, 124.9 (d, *J* = 3.9 Hz), 124.1, 121.0 (d, *J* = 9.9 Hz), 117.5 (d, *J* = 21.7 Hz), 115.0, 55.7.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{15}H_{12}FN_4O$: 283.09897; Found: 283.09869.

3-(4-(*tert*-butyl)phenyl)-6-(2-fluorophenyl)-[1,2,4,5]-tetrazine (3)



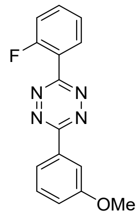
Purification on silica gel (pentane/CH_2Cl_2: 8/2) to give 71% isolated yield (26 mg, as a purple solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.61 (d, *J* = 8.6 Hz, 2H), 8.34 (td, *J* = 7.6 and 1.7 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.62–7.60 (m, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.33 (dd, *J* = 10.7 and 9.0 Hz, 1H), 1.41 (s, 9H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –112.0.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 163.8 (d, *J* = 5.9 Hz), 163.2, 162.6 (d, *J* = 259.3 Hz), 156.8, 134.0 (d, *J* = 8.7 Hz), 131.3 (d, *J* = 0.8 Hz), 128.8, 128.2, 126.5, 124.9 (d, *J* = 3.9 Hz), 120.9 (d, *J* = 9.8 Hz), 117.6 (d, *J* = 21.7 Hz), 35.3, 31.2.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{18}H_{18}N_4$: 309.15100; Found: 309.15104.

4-(6-(2-fluorophenyl)-[1,2,4,5]-tetrazin-3-yl)-*N,N*-diphenylaniline (4)



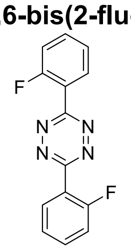
Purification on silica gel (pentane/CH_2Cl_2: 4/6 to 3/7) to give 61% isolated yield (341 mg, as a reddish solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.49 (d, *J* = 8.9 Hz, 2H), 8.31 (td, *J* = 7.7 and 1.7 Hz, 1H), 7.62–7.57 (m, 1H), 7.40–7.30 (m, 6H), 7.22 (d, *J* = 7.5 Hz, 4H), 7.18–7.15 (m, 4H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –112.2.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 163.1 (d, *J* = 5.9 Hz), 162.8, 162.5 (d, *J* = 259.0 Hz), 152.3, 146.5, 133.7 (d, *J* = 8.6 Hz), 131.1 (d, *J* = 0.9 Hz), 129.8, 129.5, 126.2, 124.8, 124.8 (d, *J* = 3.9 Hz), 123.3, 121.1 (d, *J* = 9.9 Hz), 120.8, 117.5 (d, *J* = 21.7 Hz).
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{26}H_{19}FN_5$: 420.16190; Found: 420.16159.

3-(2-fluorophenyl)-6-(3-methoxyphenyl)-[1,2,4,5]-tetrazine (5)



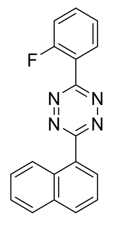
Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 55% isolated yield (207 mg, as a purple solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.34 (td, *J* = 7.6 and 1.8 Hz, 1H), 8.27 (dt, *J* = 7.7 and 1.3 Hz, 1H), 8.20 (dd, *J* = 2.7 and 1.6 Hz, 1H), 7.64–7.60 (m, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.40 (td, *J* = 7.7 and 1.2 Hz, 1H), 7.35–7.31 (m, 1H), 7.18 (ddd, *J* = 8.2, 2.6 and 1.0 Hz, 1H), 3.94 (s, 3H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –111.9.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 164.0, 163.1, 162.7 (d, *J* = 259.6 Hz), 160.5, 134.2 (d, *J* = 8.7 Hz), 132.9, 131.4, 130.6, 124.9 (d, *J* = 4.0 Hz), 120.9, 120.8 (d, *J* = 9.7 Hz), 119.9, 117.6 (d, *J* = 21.6 Hz), 112.4, 55.7.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{15}H_{12}FN_4O$: 283.09897; Found: 283.09869.

3,6-bis(2-fluorophenyl)-[1,2,4,5]-tetrazine (6)[2] CAS: 108350-48-7



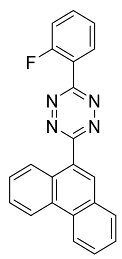
Purification on silica gel (pentane/ethyl acetate: 97/3) to give 17% isolated yield (20 mg, as a purple solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.36 (t, *J* = 7.6 Hz, 2H), 7.63 (q, *J* = 7.5 and 6.6 Hz, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 19.2 Hz, 2H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –111.6.

3-(2-fluorophenyl)-6-(naphth-9-yl)-[1,2,4,5]-tetrazine (7)



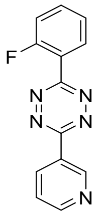
Purification on silica gel (pentane/CH_2Cl_2: 50/50) to give 32% isolated yield (130 mg, as a pink solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 9.28 (bs, 1H), 8.71 (dd, *J* = 8.7 and 1.8 Hz, 1H), 8.38 (td, *J* = 7.6 and 1.8 Hz, 1H), 8.08 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 7.9 Hz, 1H), 7.95 (d, *J* = 7.9 Hz, 1H), 7.65–7.58 (m, 3H), 7.43 (td, *J* = 7.6 and 1.1 Hz, 1H), 7.35 (ddd, *J* = 11.0, 8.3 and 1.1 Hz, 1H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –111.8.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 163.8 (d, *J* = 5.9 Hz), 163.4, 162.6 (d, *J* = 259.5 Hz), 135.6, 134.0 (d, *J* = 8.9 Hz), 133.3, 131.3, 129.6 (d, *J* = 1.6 Hz), 129.3, 128.8, 128.5, 127.9, 127.0, 124.8 (d, *J* = 3.7 Hz), 123.8, 120.7 (d, *J* = 9.7 Hz), 117.4 (d, *J* = 21.6 Hz).
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{22}H_{14}FN_4$: 353.11970; Found: 353.11969.

3-(2-fluorophenyl)-6-(phenanthren-9-yl)-[1,2,4,5]-tetrazine (8)



Purification on silica gel (pentane/CH_2Cl_2: 3/1) to give 53% isolated yield (250 mg, as a pink solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.83 (t, *J* = 8.1 Hz, 2H), 8.77 (d, *J* = 8.4 Hz, 1H), 8.73 (s, 1H), 8.44 (td, *J* = 7.6 and 1.2 Hz, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.82–7.76 (m, 2H), 7.73–7.64 (m, 3H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.40–7.36 (m, 1H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –111.7.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 166.4, 163.2 (d, *J* = 5.9 Hz), 162.8 (d, *J* = 259.8 Hz), 134.3 (d, *J* = 8.7 Hz), 133.7, 132.1, 131.5, 131.1, 130.8, 130.3, 129.1, 128.8, 128.2, 127.7, 127.5, 127.4, 126.2, 125.0 (d, *J* = 3.8 Hz), 123.3, 122.9, 120.7 (d, *J* = 9.8 Hz), 117.7 (d, *J* = 21.6 Hz).
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{22}H_{14}FN_4$: 353.11970; Found: 353.11969.

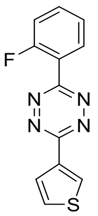
3-(2-fluorophenyl)-6-(pyridin-3-yl)-[1,2,4,5]-tetrazine (9)



Purification on silica gel (pentane/CH_2Cl_2: 5/1 to 0/1) to give 22% isolated yield (73 mg, as a purple solid).

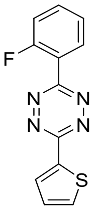
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 9.87 (s, 1H), 8.92 (d, *J* = 8.0 Hz, 1H), 8.89 (d, *J* = 4.3 Hz, 1H), 8.35 (td, *J* = 7.7 and 1.6 Hz, 1H), 7.67–7.62 (m, 1H), 7.57 (dd, *J* = 7.9 and 4.9 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.34 (dd, *J* = 10.5 and 8.7 Hz, 1H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –111.7.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 164.4 (d, *J* = 5.9 Hz), 162.7 (d, *J* = 260.0 Hz), 162.2, 153.5, 149.6, 135.3, 134.5 (d, *J* = 8.8 Hz), 131.4, 127.7, 125.0 (d, *J* = 3.9 Hz), 124.1, 120.5 (d, *J* = 9.8 Hz), 117.7 (d, *J* = 21.6 Hz).
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{13}H_9FN_5$: 254.08365; Found: 254.08359.

3-(2-fluorophenyl)-6-(thiophen-3-yl)-[1,2,4,5]-tetrazine (10)



Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 50% isolated yield (173.2 mg, as a purple solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.68 (dd, *J* = 3.0 and 1.0 Hz, 1H), 8.31 (td, *J* = 7.7 and 1.7 Hz, 1H), 8.11 (dd, *J* = 5.1 and 1.0 Hz, 1H), 7.64–7.59 (m,1H), 7.54 (dd, *J* = 5.1 and 3.0 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.32 (dd, *J* = 10.5 and 8.7 Hz, 1H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –112.1.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 163.5 (d, *J* = 5.9 Hz), 162.6 (d, *J* = 259.3 Hz), 160.9, 134.8, 134.0 (d, *J* = 8.7 Hz), 131.2, 130.8, 127.7, 126.8, 124.9 (d, *J* = 3.8 Hz), 120.9 (d, *J* = 9.9 Hz), 117.5 (d, *J* = 21.6 Hz).
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{12}H_8FN_4S$: 259.04482; Found: 259.04478.

3-(2-fluorophenyl)-6-(thiophen-2-yl)-[1,2,4,5]-tetrazine (11)

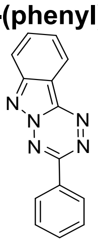


Purification on silica gel (pentane/CH_2Cl_2: 3.5/1.5) to give 23% isolated yield (30.0 mg, as a purple solid).
^{1}H NMR (500 MHz, CD_2Cl_2): δ (ppm) = 8.34 (dd, *J* = 3.8 and 1.2 Hz, 1H), 8.27 (td, *J* = 7.7 and 1.8 Hz, 1H), 7.77 (dd, *J* = 4.9 and 1.2 Hz, 1H), 7.67–7.61 (m, 1H), 7.45–7.39 (m, 1H), 7.36–7.30 (m, 2H).
^{19}F{^{1}H} NMR (470 MHz, CD_2Cl_2): δ (ppm) = –113.0.
^{13}C NMR (125 MHz, CD_2Cl_2): δ (ppm) = 164.0 (d, *J* = 5.5 Hz), 162.9 (d, *J* = 259.8 Hz), 161.8, 136.3, 134.4 (d, *J* = 8.7 Hz), 133.7, 132.3, 131.7, 129.7, 125.4 (d, *J* = 3.7 Hz), 121.4 (d, *J* = 10.1 Hz), 117.9 (d, *J* = 21.6 Hz).
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{12}H_8FN_4S$: 259.04482; Found: 259.04537.

Procedure for the synthesis of 3-(aryl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole

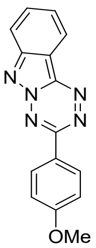
As a typical experiment, the 3-aryl-6-(2-fluorophenyl)-[1,2,4,5]-tetrazine (1.0 equiv), sodium azide (3.0 equiv), were introduced in a microwave reaction vessel equipped with a magnetic stirring bar. The DMF [0.125 M] was added, and the reaction mixture was heated at 130 °C under air for 1h. After cooling down to room temperature, the solvent was removed under vacuum. The crude product was purified by silica gel column chromatography to afford the corresponding product.

3-(phenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (12)[3] CAS: 2914972-57-7



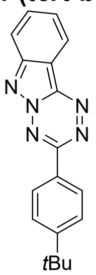
Purification on silica gel (Pentane/CH_2Cl_2: 2/8) to give 44% isolated yield (27 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.66–8.63 (m, 3H), 8.15 (d, *J* = 8.5 Hz, 1H), 7.93 (t, *J* = 7.7 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.65–7.63 (m, 3H).

3-(4-methoxyphenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (13)



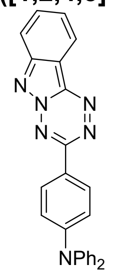
Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 52% isolated yield (36 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.64 (d, *J* = 8.8 Hz, 2H), 8.60 (d, *J* = 8.1 Hz, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.88 (t, *J* = 7.7 Hz, 1H), 7.73 (t, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 8.9 Hz, 2H), 3.49 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 163.2, 157.6, 148.2, 141.0, 131.8, 130.4, 126.4, 124.8, 121.1, 118.5, 114.7, 114.2, 55.6.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{15}H_{12}N_5O$: 278.10364; Found: 278.10362.

3-(4-(*tert*-butyl)phenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (14)



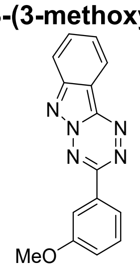
Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 64% isolated yield (50 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.62–8.59 (m, 3H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.89 (t, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 1.41 (s, 9H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 157.7, 156.1, 148.3, 141.2, 132.0, 129.6, 128.4, 126.5, 126.3, 121.1, 118.5, 114.1, 35.2, 31.3.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{18}H_{18}N_5$: 304.15567; Found: 304.15566.

4-([1,2,4,5]-tetrazo[1,6-*b*]indazol-3-yl)-*N,N*-diphenylaniline (15)



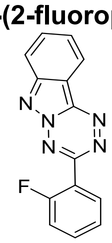
Purification on silica gel (pentane/CH_2Cl_2: 50/50) to give 55% isolated yield (54 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.58 (d, *J* = 8.1 Hz, 1H), 8.49 (d, *J* = 8.9 Hz, 2H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.86 (t, *J* = 7.7 Hz, 1H), 7.7 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 4H), 7.21 (d, *J* = 7.7 Hz, 4H), 7.18–7.14 (m, 4H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 157.7, 151.8, 148.1, 146.7, 140.8, 131.7, 129.7, 129.6, 126.3, 126.0, 124.6, 124.3, 121.1, 120.9, 118.4, 114.2.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{26}H_{19}N_6$: 415.16657; Found: 415.16614.

3-(3-methoxyphenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (16)



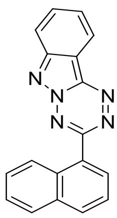
Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 47% isolated yield (33 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.61 (d, *J* = 8.1 Hz, 1H), 8.27 (dt, *J* = 7.8 and 1.3 Hz, 1H), 8.19–8.18 (m, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.91–7.87 (m, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.16–7.13 (m, 1H), 3.95 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 159.4, 156.4, 147.4, 140.4, 132.7, 131.2, 129.3, 125.6, 120.3, 120.2, 118.2, 117.6, 113.1, 111.6, 54.7.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{15}H_{12}N_5O$: 278.10364 ; Found: 278.10362.

3-(2-fluorophenyl)-[1,2,4,5]-tetrazo-[1,2-*b*]-indazole (17)[3] CAS: 2914972-58-8



Purification on silica gel (pentane/CH_2Cl_2: 2/8) to give 47% isolated yield (31 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.66 (dt, *J* = 8.1 and 1.0 Hz, 1H), 8.32 (td, *J* = 7.7 and 1.8 Hz, 1H), 8.18 (dt, *J* = 8.5 and 0.7 Hz, 1H), 7.96 (ddd, *J* = 8.4, 7.0 and 1.2 Hz, 1H), 7.81–7.78 (m, 1H), 7.67–7.62 (m, 1H), 7.43 (td, *J* = 7.6 and 1.2 Hz, 1H), 7.35 (ddd, *J* = 11.0, 8.4 and 1.2 Hz, 1H).
^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) = –112.0.

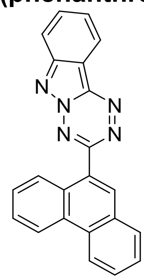
3-(1-naphthyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (18)



Purification on silica gel (pentane/CH_2Cl_2: 50/50) to give 41% isolated yield (30 mg, as an orange solid).

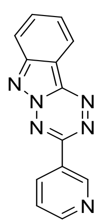
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 9.30 (br, 1H), 8.69 (dd, *J* = 8.7 and 1.8 Hz, 1H), 8.65 (dt, *J* = 8.1 and 1.1 Hz, 1H), 8.17 (dt, *J* = 8.5 and 0.9 Hz, 1H), 8.06 (t, *J* = 7.4 Hz, 2H), 7.94–7.90 (m, 2H), 7.75 (ddd, *J* = 7.9, 7.0 and 0.9 Hz, 1H), 7.94–7.90 (m, 2H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 157.7, 148.5, 141.4, 135.4, 133.4, 132.2, 129.9, 129.7, 129.6, 129.2, 128.3, 128.0, 127.0, 126.7, 124.3, 121.3, 118.6, 114.2.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{18}H_{12}FN_5$: 298.10872; Found: 298.10858.

3-(phenanthren-9-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (19)



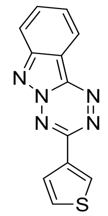
Purification on silica gel (pentane/CH_2Cl_2: 50/50) to give 64% isolated yield (55.7 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.84 (d, *J* = 8.3 Hz, 1H), 8.78 (d, *J* = 8.3 Hz, 1H), 8.73–8.70 (m, 2H), 8.62 (s, 1H), 8.22 (dt, *J* = 8.5 and 0.9 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.96 (ddd, *J* = 8.4, 7.1 and 1.2 Hz, 1H), 7.82–7.75 (m, 3H), 7.71–7.68 (m, 2H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 160.4, 148.5, 141.0, 133.6, 132.4, 1331.9, 131.1, 131.0, 129.2, 129.1, 128.9, 127.6, 127.4, 127.4, 127.4, 126.9, 126.3, 123.3, 122.9, 121.5, 118.8, 114.1.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{22}H_{14}FN_5$: 348.12437; Found: 348.12436.

6-(pyridine-3-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (20)



Purification on silica gel (pentane/CH_2Cl_2: 5/1 to 0/1) to give 59% isolated yield (37 mg, as a purple solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 9.87 (s, 1H), 8.92 (d, *J* = 8.0 Hz, 1H), 8.89 (d, *J* = 4.3 Hz, 1H), 8.35 (td, *J* = 7.7 and 1.6 Hz, 1H), 7.67–7.62 (m, 1H), 7.57 (dd, *J* = 7.9 and 4.9 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.34 (dd, *J* = 10.5 and 8.7 Hz, 1H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 156.1, 152.9, 149.4, 148.8, 141.8, 135.7, 132.6, 128.7, 127.1, 124.0, 121.5, 118.8, 114.1.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{13}H_9N_6$: 249.08832; Found: 249.08823.

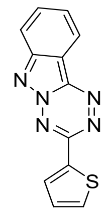
6-(thiophen-3-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (21)



Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 24% isolated yield (15 mg, as an orange solid).

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.68 (dd, *J* = 3.0 and 1.0 Hz, 1H), 8.60 (td, *J* = 8.1 and 1.1 Hz, 1H), 8.13 (dt, *J* = 8.5 and 0.9 Hz, 1H), 8.10 (dd, *J* = 5.1 and 1.2 Hz, 1H), 7.89 (ddd, *J* = 8.3, 7.1 and 1.2 Hz, 1H), 7.73 (ddd, *J* = 8.1, 7.1 and 0.9 Hz, 1H), 7.52 (dd, *J* = 5.1 and 3.0 Hz, 1H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 155.2, 148.3, 141.0, 135.4, 132.0, 130.5, 127.4, 126.9, 126.7, 121.2, 118.6, 114.3.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{12}H_8N_5S$: 254.04949; Found: 254.04944.

6-(thiophen-2-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (22)

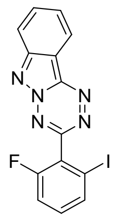


Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 36% isolated yield (23 mg, as an orange solid).

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.59 (d, *J* = 8.1 Hz, 1H), 8.33 (dd, *J* = 3.7 and 1.3 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.89 (t, *J* = 7.8 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.69 (dd, *J* = 5.0 and 1.3 Hz, 1H), 7.28 (dd, *J* = 5.0, 3.8 Hz, 1H).
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 155.9, 148.8, 141.6, 136.9, 132.7, 132.5, 131.6, 129.4, 127.2, 121.4, 119.0, 114.9.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{12}H_8N_5S$: 254.04949; Found: 254.04936.

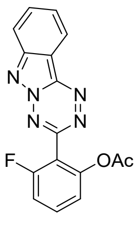
Procedure for the direct halogenation / acetoxylation of 3-(2-fluorophenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole
As a typical experiment, an oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with 3-(2-fluorophenyl)-[1,2,4,5]-tetrazo-[1,2-*b*]-indazole (1.0 equiv), NIS or PIDA (2.0 equiv), $[Pd(OAc)_2]$ (10 mol%), and HOAc [0.5 M] under air. The mixture was stirred at 110 °C for 30 min microwave irradiation (200 Watts). The solvent was removed under vacuum and the crude product was purified by column chromatography on silica using an appropriate ratio of eluent to afford the desired product.

6-(2-fluoro-6-iodophenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (23)



Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 66% isolated yield (64.5 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.70 (dt, *J* = 8.1 and 1.1 Hz, 1H), 8.22 (dt, *J* = 8.1 and 1.0 Hz, 1H), 7.97 (ddd, *J* = 8.2, 7.0 and 1.2 Hz, 1H), 7.86–7.83 (m, 1H), 7.80 (ddd, *J* = 8.1, 7.0 and 0.9 Hz, 1H), 7.32–7.29 (m, 2H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –108.8.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 162.5 (d, *J* = 255.6 Hz), 157.5, 148.3, 141.4, 135.3 (d, *J* = 3.6 Hz), 133.4 (d, *J* = 8.7 Hz), 132.7, 127.4 (d, *J* = 16.9 Hz), 127.2, 121.7, 118.9, 116.2 (d, *J* = 21.4 Hz), 113.9, 97.9.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{14}H_8FIN_5$: 391.98029; Found: 391.98019.

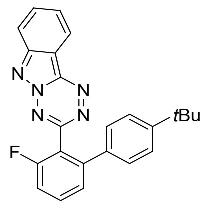
6-(2-fluoro-6-acetoxyphenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (24)



Purification on silica gel (pentane/ethyl acetate: 7/3) to give 25% isolated yield (20 mg, as an orange solid).
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.71 (d, *J* = 8.1 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.00 (t, *J* = 7.4 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.68–7.61 (m, 1H), 7.29 (d, *J* = 11.3 Hz, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 2.25 (s, 3H).
^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –112.6.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 169.1, 162.4 (d, *J* = 255.6 Hz), 154.2 (d, *J* = 2.2 Hz), 150.2 (d, *J* = 4.6 Hz), 148.6, 148.6, 132.7, 132.6, 127.0, 121.6, 119.8 (d, *J* = 3.6 Hz), 118.8, 116.3 (d, *J* = 15.2 Hz), 114.3 (d, *J* = 21.7 Hz), 113.9, 20.9.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{16}H_{11}FN_5O_2$: 324.08913; Found: 324.08897.

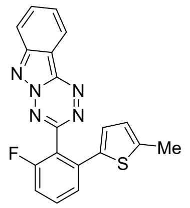
Procedure for the direct arylation of 3-(2-fluorophenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole
As a typical experiment, an oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with 3-(2-fluorophenyl)-[1,2,4,5]-tetrazo-[1,2-*b*]-indazole (1.0 equiv), 4-*tert*-Butylphenylboronic acid or 2-methylthiophene (3.0 equiv), $[MCl_2Cp^*]_2$ (M = Rh, Ir; 5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (3.0 equiv) and dichloroethane [0.5 M] under air. The mixture was stirred at 140 °C for 5 h or 24 h. The solvent was removed under vacuum and the crude product was purified by column chromatography on silica using an appropriate ratio of eluent to afford the desired product.

2-(fluoro)-6-(1-(4-*tert*-butyl)phenyl))-[1,2,4,5]-tetrazo[1,2-*b*]indazole (25)



Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 58% isolated yield (57 mg, as an orange solid).
^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.62 (d, *J* = 8.1 Hz, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.92 (ddd, *J* = 8.4, 7.0 and 1.2 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.63–7.59 (m, 1H), 7.37 (dd, *J* = 7.8 and 1.1 Hz, 1H), 7.31–7.27 (m, 1H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 1.19 (s, 9H).
^{19}F {^1H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –114.7.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 162.3 (d, *J* = 251.0 Hz), 157.1, 150.6, 148.4, 144.6, 140.6, 132.5, 132.1 (d, *J* = 9.2 Hz), 129.1, 162.8, 126.4 (d, *J* = 3.3 Hz), 125.5, 121.6, 118.8, 114.8 (d, *J* = 21.6 Hz), 113.8, 34.6, 31.3.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{24}H_{21}FN_5$: 398.17755; Found: 398.17739.

2-(fluoro)-6-(5-(2-methylthiophenyl))-[1,2,4,5]-tetrazo[1,2-*b*]indazole (26)



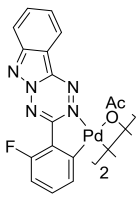
Purification on silica gel (pentane/CH_2Cl_2: 1/1) to give 49% isolated yield (44 mg, as an orange solid).
^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.66 (d, *J* = 8.1 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.95 (t, *J* = 7.8 Hz, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.57 (td, *J* = 8.1 and 5.8 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 8.3 Hz, 1H), 6.63 (d, *J* = 3.5 Hz, 1H), 6.48–6.46 (m, 1H), 2.30 (s, 3H).
^{19}F {^1H} NMR (470 MHz, $CDCl_3$): δ (ppm) = –113.8.
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 162.3 (d, *J* = 250.5 Hz), 156.7, 148.5, 142.0, 140.9, 137.8 (d, *J* = 3.0 Hz), 137.3 (d, *J* = 2.2 Hz), 132.5, 132.1 (d, *J* = 9.3 Hz), 127.9, 126.9, 125.9, 125.9 (d, *J* = 3.2 Hz), 121.6, 120.9 (d, *J* = 15.8 Hz), 118.8, 114.9 (d, *J* = 21.6 Hz), 113.9, 15.3.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{19}H_{12}FN_5S$: 362.08702; Found: 362.08680.

Procedure for the metallacycle formation by *o*-C–H activation of 3-(2-fluorophenyl)-[1,2,4,5]-tetrazo-[1,2-*b*]-indazole

*Palladacycles **A-x** (x = 1, 2 and 3)*

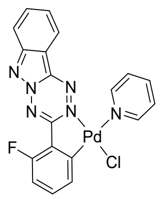
An oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with $[Pd(OAc)_2]$ (83 mg, 0.37 mmol, 1 equiv) and **(17)** (100 mg, 0.37 mmol, 1 equiv) was added HOAc [9.25 mM]. After heating at 80 °C under argon for 16 h, the brown solution was concentrated under vacuum. The crude mixture was dissolved in CH_2Cl_2 and then was filtrated through a pad of Celite (with CH_2Cl_2). The solvent was removed under vacuum and the mixture was recrystallized in dichloromethane/pentane mixture to afford **(Pd_2)** as a dark brown powder (120 mg, 75% yield).
LiCl (10 mg, 0.23 mmol, 10 equiv) was added to a solution of (**(Pd_2)** (20 mg, 0.023 mmol, 1 equiv) in chloroform (5 ml, [4.65 mM]). After 30 min stirring, the solvent was removed under vacuum and then dichloromethane was added [4.65 mM] for a better solubility. Pyridine (4 µl, 0.05 mmol, 2 equiv) was added and the solution was stirred for additional 30 min giving a bright orange solution. The solution was washed with water then the crude was purified by column chromatography (CH_2Cl_2/MeOH: 90/10). The second fraction was recrystallized in dichloromethane/pentane to afford a mixture of isomers as an orange powder (16 mg, 71% yield).

Metallacycles (Pd_2)



Recrystallisation with pentane/CH_2Cl_2 mixture to give 75% isolated yield (120 mg, as a dark brown powder).
^1H NMR (500 MHz, CD_2Cl_2): δ (ppm) = 8.41 (d, *J* = 8.0 Hz, 2H), 8.27 (d, *J* = 8.5 Hz, 2H), 8.07–8.01 (m, 2H), 7.92–7.83 (m, 2H), 6.57 (d, *J* = 7.5 Hz, 2H), 6.18 (dd, *J* = 10.8 and 8.1 Hz, 2H), 5.80 (td, *J* = 7.9, 5.0 and 1.0 Hz, 2H), 2.35 (s, 6H).
^{19}F{^1H} NMR (470 MHz, CD_2Cl_2): δ (ppm) = –108.1.
The low solubility of the dimeric palladacycle in different solvents did not allow to measure satisfying ^{13}C NMR.
HRMS + p ESI (m/z) $[M+H]^+$ calcd for $C_{32}H_{21}F_2N_{10}O_4Pd_2$: 858.97848; Found: 858.97532.

Metallacycle (Pd)

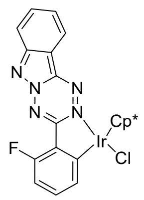


Purification on silica gel (CH_2Cl_2/MeOH: 90/10) to give 71% isolated yield (21.5 mg, as an orange solid). *Only data from the major isomer is provided*.
^1H NMR (500 MHz, CD_2Cl_2): δ (ppm) = 8.93 (d, *J* = 5.5 Hz, 2H), 8.22 (d, *J* = 8.5 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.96 (q, *J* = 7.9 Hz, 2H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 6.7 Hz, 2H), 7.30 (td, *J* = 8.0 and 5.4 Hz, 1H), 6.98 (dd, *J* = 10.9 and 8.3 Hz, 1H).
^{19}F{^1H} NMR (470 MHz, CD_2Cl_2): δ (ppm) = –108.7.
The low solubility of the palladacycle in different solvents did not allow to measure satisfying ^{13}C NMR.
HRMS + p ESI (m/z) $[M-Cl]^+$ calcd for $C_{19}H_{12}FN_6Pd$: 449.01368; Found: 449.01383.

Iridacycle (Ir) and rhodacycle (Rh)

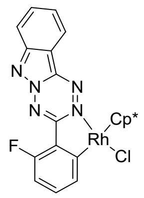
As a typical experiment, an oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with 3-(2-fluorophenyl)-[1,2,4,5]-tetrazo-[1,2-*b*]-indazole ligand **(17)** (1.0 equiv), $[MCl_2Cp^*]_2$ (0.5 equiv, M = Ir or Rh) precursor, and KOAc (4.0 equiv) as the base. After 3 cycles of vacuum purge with argon, MeOH [0.094 M] solvent was added. The mixture was stirred at 60 °C for 14 h, and then filtered through Celite and washed with CH_2Cl_2. The solvent was removed under vacuum and the crude product was purified by column chromatography on silica using an appropriate ratio of eluent to afford the desired metallacycle.

Metallacycle (Ir)



Purification on silica gel (heptane/ethyl acetate: 9/1) to give 33%.
^{1}H NMR (500 MHz, CD_2Cl_2): δ (ppm) = 8.55 (d, *J* = 8.1 Hz, 1H), 8,15 (d, *J* = 8.5 Hz, 1H), 7,96 (t, *J* = 7.7 Hz, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 7,38 (td, *J* = 7.8 and 5.3 Hz, 1H), 6.87 (dd, *J* = 11.3 and 8.1 Hz, 1H), 1.79 (s, 15H).
^{19}F {^{1}H} NMR (470 MHz, CD_2Cl_2): δ (ppm) = –109.3.
^{13}C NMR (125 MHz, CD_2Cl_2): δ (ppm) = 167.7 (d, *J* = 7.7 Hz), 166.0 (d, *J* = 4.4 Hz), 163.5 (d, *J* = 266.0 Hz), 149.1, 140.1, 135.1 (d, *J* = 8.1 Hz), 132.6, 132.1 (d, *J* = 3.3 Hz), 127.8, 123.6 (d, *J* = 4.6 Hz), 121.1, 119.7, 114.6, 110.6 (d, *J* = 20.2 Hz), 92.3, 9.2.
HRMS + p ESI (m/z) [M-Cl]$^+$ calcd for $C_{24}H_{22}FIrN_5$: 592.14830; Found: 592.14714.

Metallacycle (Rh)

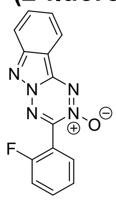


Purification on silica gel (heptane/ethyl acetate: 9/1) to give 31%.
^{1}H NMR (500 MHz, CD_2Cl_2): δ (ppm) = 8.59 (d, *J* = 8.1 Hz, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 7.97 (ddd, *J* = 8.3, 7.1, and 1.1 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.44 (td, *J* = 7.8 and 5.1 Hz, 1H), 6.91 (dd, *J* = 11.4 and 8.1 Hz, 1H), 1.74 (s, 15H).
^{19}F{^{1}H} NMR (470 MHz, CD_2Cl_2): δ (ppm) = –109.4.
^{13}C NMR (125 MHz, CD_2Cl_2): δ (ppm) = 181.7 (dd, *J* = 32.7 and 5.6 Hz), 164.5 (dd, *J* = 8.0 and 4.0 Hz), 162.7 (d, *J* = 266.8 Hz), 149.3, 140.3, 134.0 (d, *J* = 7.8 Hz), 132.9, 132.8 (d, *J* = 3.5 Hz), 127.9, 123.4 (d, *J* = 4.5 Hz), 121.4, 119.5, 114.5, 111.4 (d, *J* = 20.5 Hz), 98.7 (d, *J* = 6.2 Hz), 9.4.
HRMS + p ESI (m/z) [M-Cl]$^+$ calcd for $C_{24}H_{22}FRhN_5$: 502.09088; Found: 502.09054.

***N*-Oxides (17-O1 and 17-O2)**

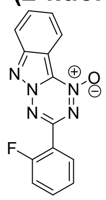
In a dry Schlenk under argon was added H_2O_2 (1.55 ml, 15.1 mmol, 10 equiv.) to trifluoromethanesulfonic anhydride (2.1 ml, 15.1 mmol, 10 equiv.) in dry CH_2Cl_2 (10 ml), and stirred for 5 min at 0°C. Then 3-(2-fluorophenyl)-[1,2,4,5]-tetrazo-[1,2-*b*]-indazole **(17)** (400 mg, 1.5 mmol, 1 equiv.) was added to the solution at 0°C and stirred for 5h. The solvent was removed under vacuum. The product was purified through silica gel column chromatography (CH_2Cl_2/Petroleum Ether: 40/60) to afford **17-O2** (135 mg, 32%, yellow powder) as the first eluted compound and **17-O1** (148 mg, 35%, red powder) as the second.

3-(2-fluorophenyl)-3*H*-5λ^4-[1,2,4,5]tetrazino[1,6-*b*]indazole 2-oxide (17-O1)



^{1}H NMR (400 MHz, DMSO-*d*6): δ (ppm) = 8.19 (dd, *J* = 8.4 and 1.1 Hz, 1H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.74 (ddd, *J* = 9.4, 7.2 and 1.5 Hz, 2H), 7.71–7.64 (m, 1H), 7.51–7.45 (m, 1H), 7.45–7.37 (m, 2H).
^{19}F NMR (376 MHz, DMSO-*d*6): δ (ppm) = –109.0.
^{13}C NMR (101 MHz, DMSO-*d*6): δ (ppm) = 161.9, 159.4, 149.5, 147.2, 137.0, 134.8 (d, *J* = 8.6 Hz), 132.9, 132.1, 125.2 (d, *J* = 3.4 Hz), 124.8, 121.0, 117.9, 116.9 (d, *J* = 13.7 Hz), 116.6 (d, *J* = 20.3 Hz), 110.9.
HRMS + ASAP (m/z) [M+H]$^+$ calcd for $C_{14}H_9N_5OF$: 282.07856; Found: 282.07850

3-(2-fluorophenyl)-3*H*-5 λ^4-[1,2,4,5]tetrazino[1,6-*b*]indazole 1-oxide (17-O2)



^{1}H NMR (400 MHz, DMSO-*d*6): δ (ppm) = 8.39 (dt, *J* = 8.2 and 1.1 Hz, 1H), 8.16 (dt, *J* = 8.6 and 0.9 Hz, 1H), 8.09 (td, *J* = 7.7 and 1.8 Hz, 1H), 7.87 (ddd, *J* = 8.4, 7.0 and 1.2 Hz, 1H), 7.78–7.69 (m, 2H), 7.55–7.45 (m, 2H).
^{19}F NMR (376 MHz, DMSO-*d*6): δ (ppm) = –111.9.
^{13}C NMR (101 MHz, DMSO-*d*6): δ (ppm) = 161.5, 158.9, 154.6 (d, *J* = 4.6 Hz), 145.2, 134.2 (d, *J* = 8.8 Hz), 131.6, 131.0, 126.8, 125.2 (d, *J* = 3.8 Hz), 120.6, 119.7 (d, *J* = 9.9 Hz), 117.9, 117.3 (d, *J* = 21.5 Hz), 109.6.
HRMS + ASAP (m/z) [M+H]$^+$ calcd for $C_{14}H_9N_5OF$: 282.07856; Found: 282.07840

UV-Vis analysis

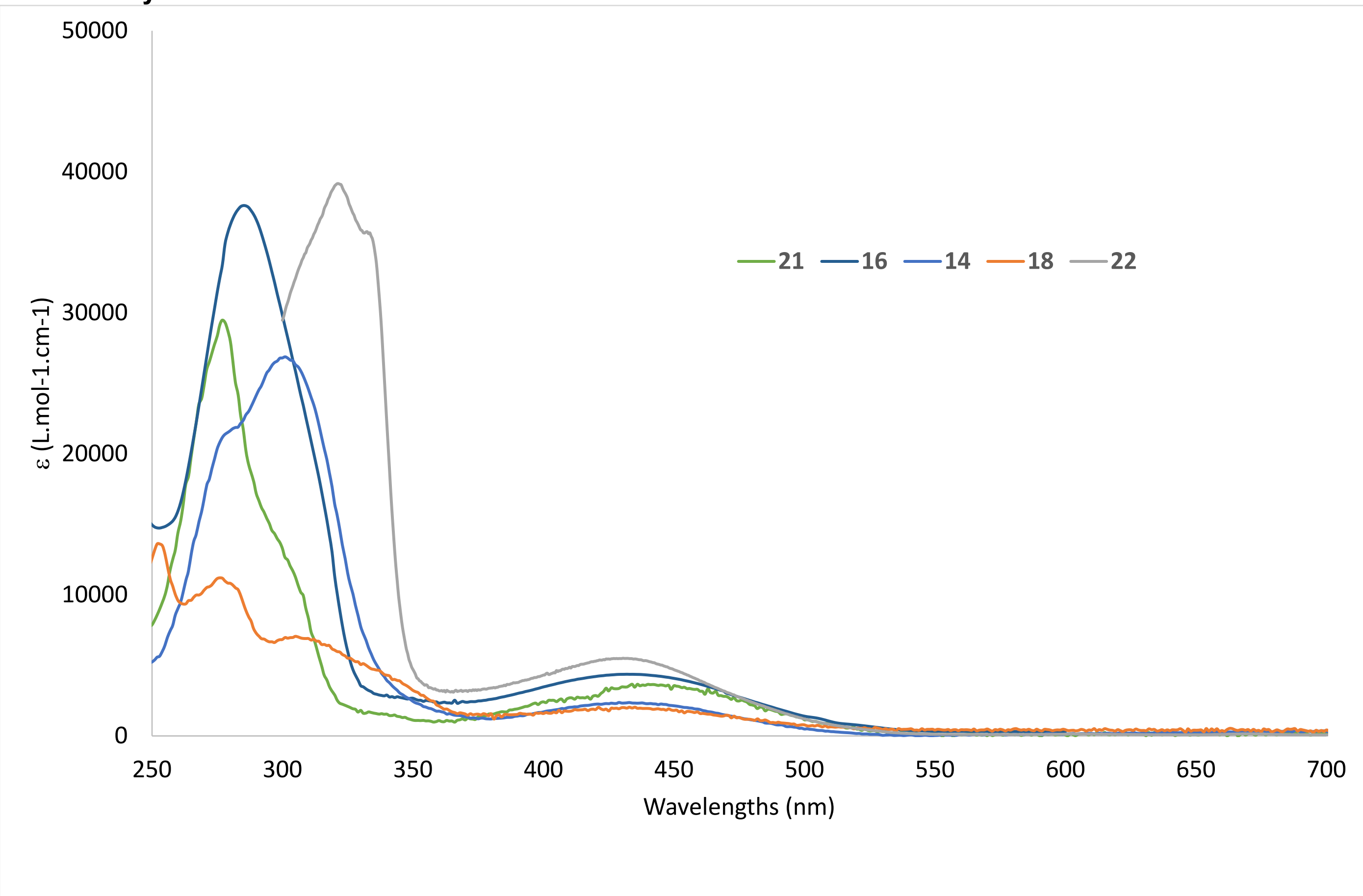


*Figure S-1. Absorption spectra of [1,2,4,5]-tetrazo[1,2-*b*]indazole **14**, **16**, **18**, **21** and **22** recorded in CH_2Cl_2 at 25 °C*

Table S-1: Photophysical and redox data for the 3-arylated tetrazo[1,2-*b*]indazoles and complexes.

	λ_{abs}[a] [nm]	ε[a] [$M^{-1}cm^{-1}$]	$E^{red\ 1}$[b] [V]	$E^{red\ 2}$[b] [V]	E^{ox}[b] [V]
13	426	5500	–0.82	–1.60	-
14	431	2400	–0.82	-	-
15	459	7800	–0.84	-	1.18
16	432	4300	–0.79	–1.58	-
17-O1	428	3700	–0.81	-	-
17-O2	516	4100	–0.89	-	-
18	417	2000	–0.78	-	-
19	432	4900	–0.76	-	-
20	434	4027	–0.73	-	-
21	434	3600	–0.81	-	-
22	430	5500	–0.89		
Pd_2	471	10600			
Pd	480	4500			
Ir	554	3900			
Rh	531	2800			

[a] In CH_2Cl_2 [10^{-5} M]. [b] 10^{-3} M in CH_2Cl_2 with $Et_4N^+BF_4^-$ [0.1 M] at a scan rate of 100 mV.s^{-1}. Half wave Potentials ($E_{1/2}$) *vs* SCE. For the photophysical analysis of **11** and **16** see reference 3.

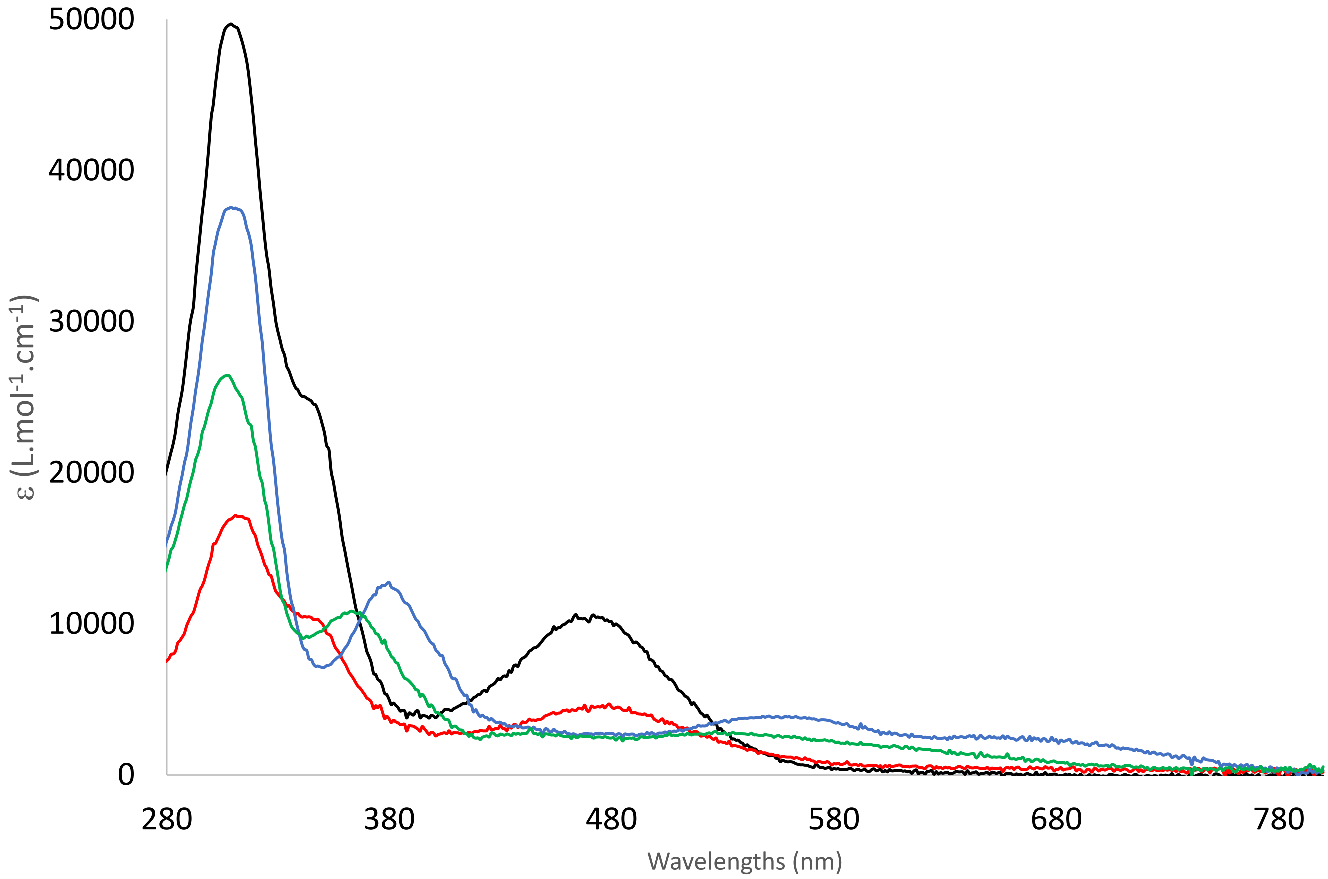
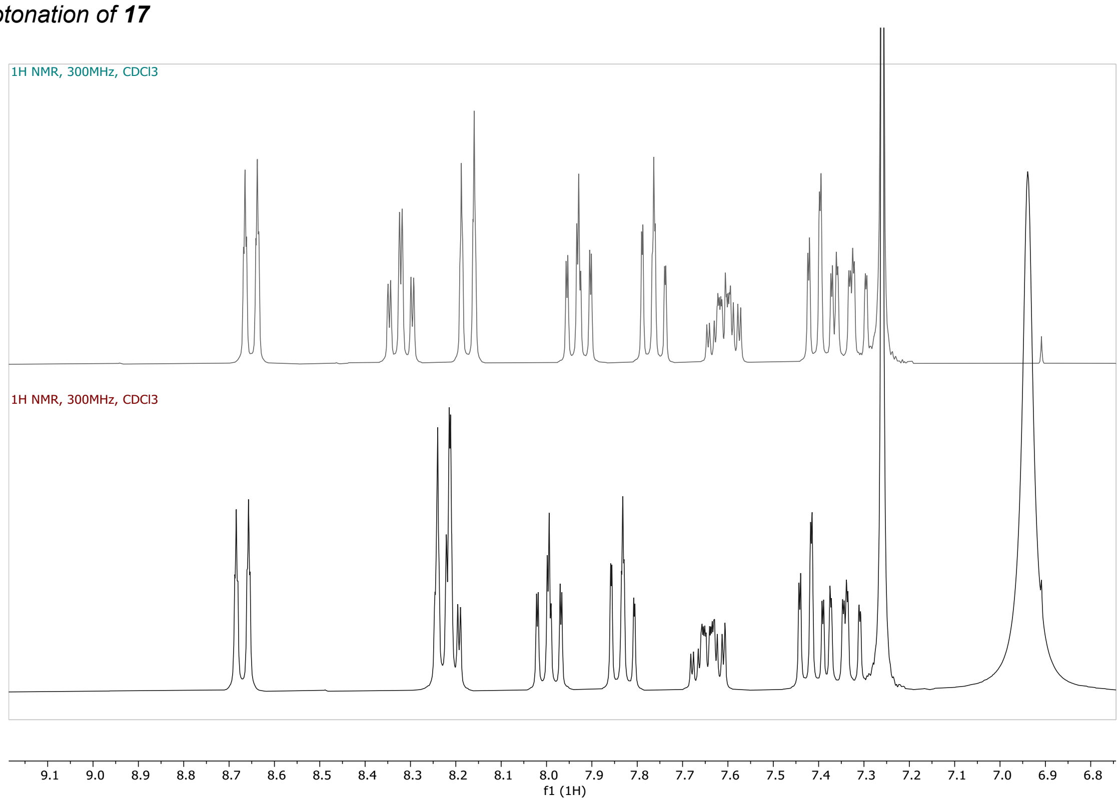


Figure S-2. *Absorption spectra of metallacyles **Pd_2** (black), **Pd** (red), **Ir** (blue), **Rh** (green) recorded in CH_2Cl_2 at 25 °C*

*Selective protonation of **17***



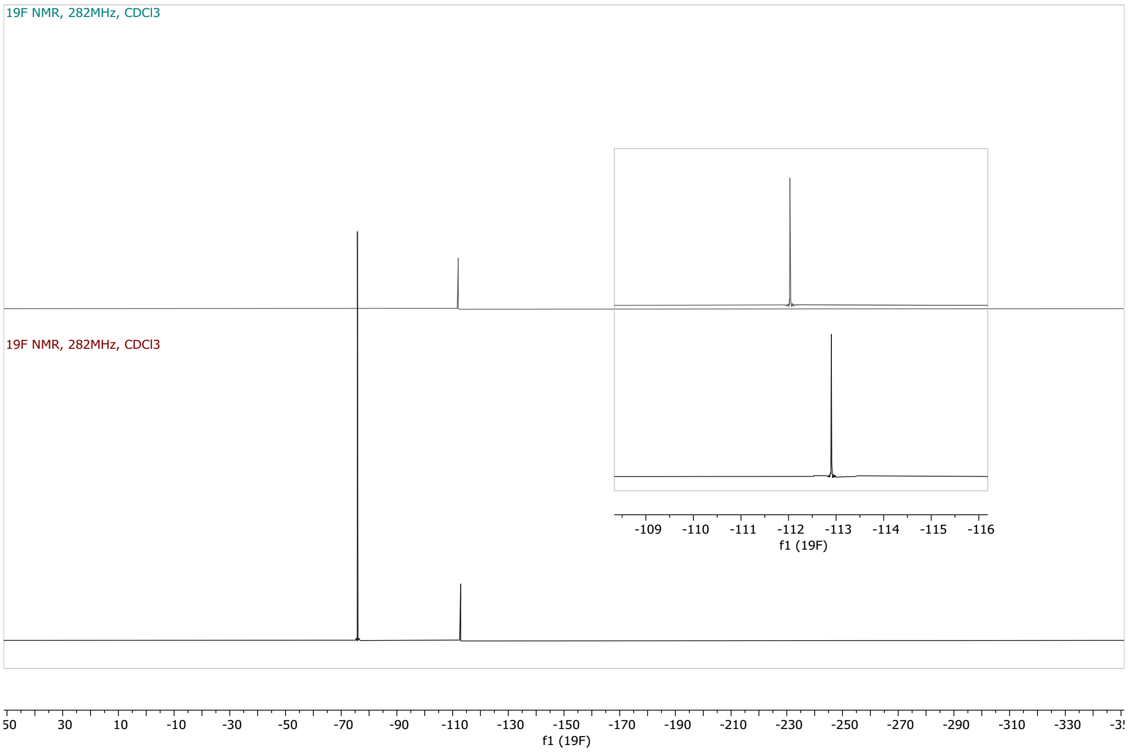


Figure S-3. *NMR spectra of **17** (up) and **17** + trifluoroacetic acid (down) (peak at –76 ppm refers to trifluoroacetic acid).*

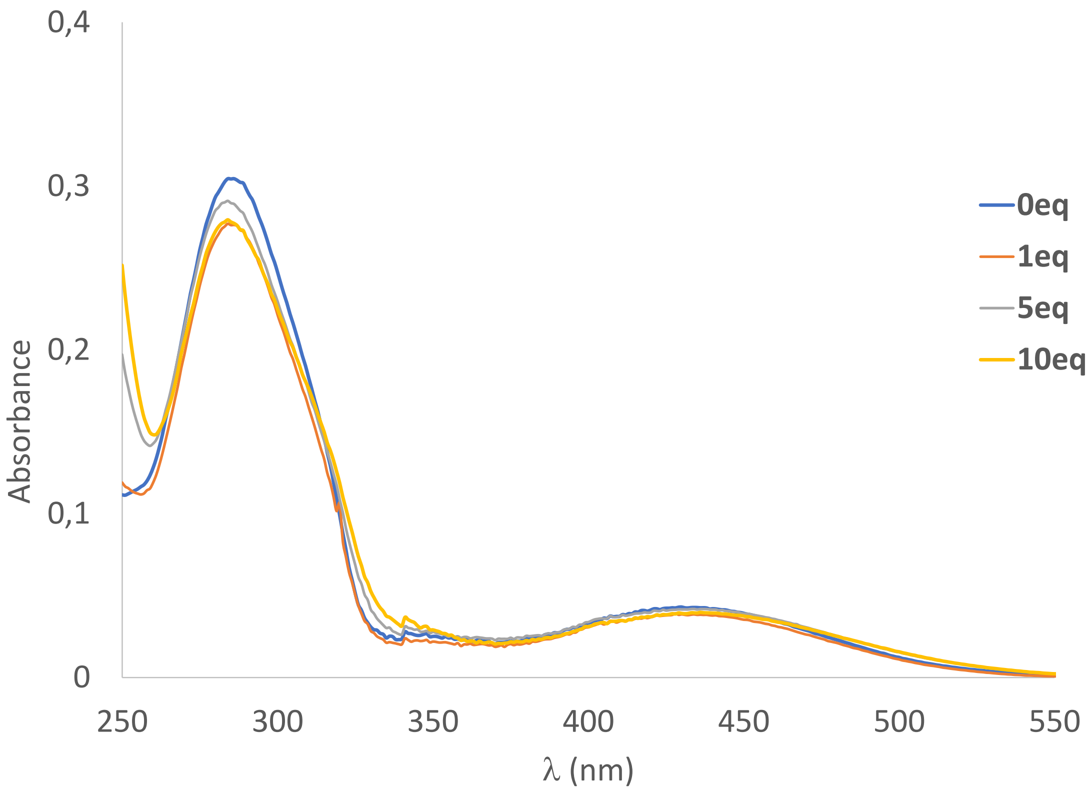


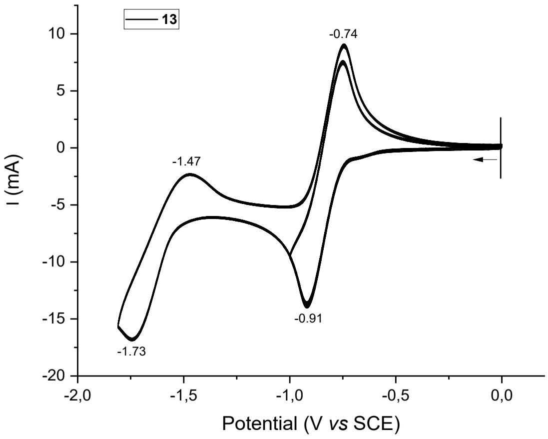
Figure S-4. *UV-vis absorption spectra of a diluted solution of **17** in DCM (10^{-5}M) with increasing amount of trifluoroacetic acid.*

Voltammetric analysis

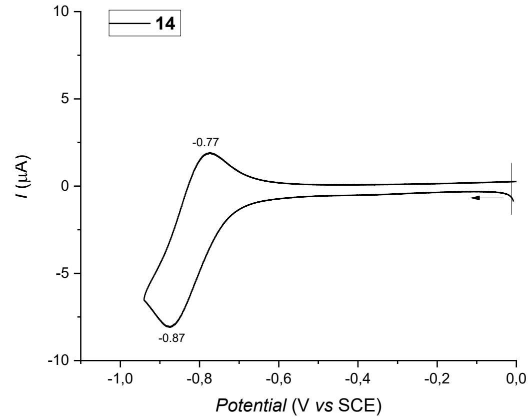
Voltammetric analyses were performed in a standard three-electrode cell using Schlenk techniques under argon at room temperature (T = 20°C ± 3°C) with Biologic SP-300 potentiostat connected to an interfaced computer that employed EC-Lab (v. 11.25) software. The supporting electrolyte tetraethylammonium tetrafluoroborate ($TEABF_4$) was degassed under vacuum before use and then dissolved in CH_2Cl_2 to a concentration of 0.1 $mol.L^{-1}$. The reference electrode was a saturated calomel electrode (SCE) separated from the analyzed solution by a sintered glass disk filled with the background solution (V = 5 mL). The auxiliary electrode was a platinum foil separated from the analyzed solution by a sintered glass disk filled with the background solution (V = 5 mL). For all voltammetric measurements, the working electrode was a platinum electrode (Ø = 1.6 mm) dipped in the compartment (V = 5 mL). Before each voltammetric analysis, the Pt electrode was polished with a diamond suspension.

*For the voltammetric analysis of **1**, **11** and **16** see reference 3.*

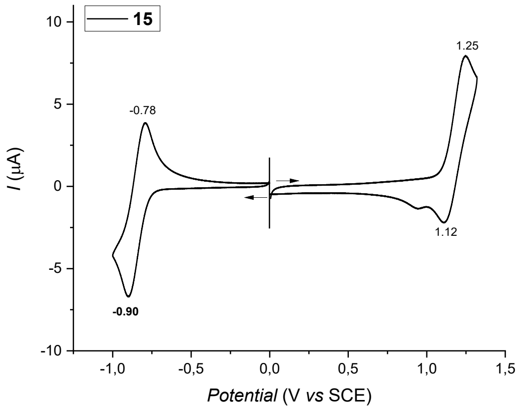
3-(4-methoxyphenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (13)



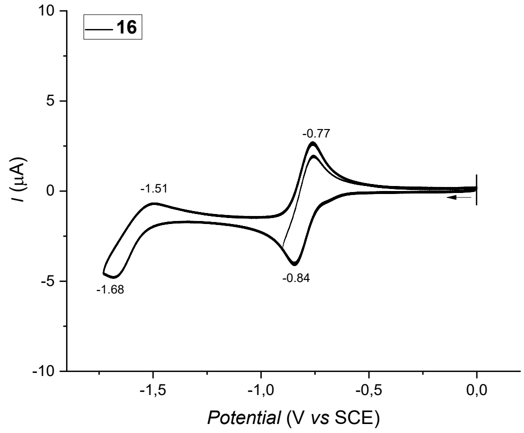
3-(4-*tert*-butylphenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (14)



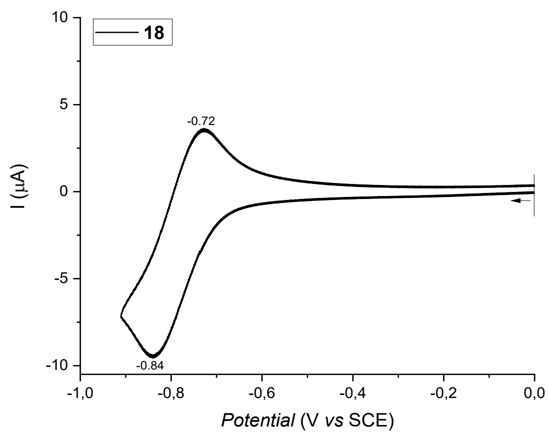
4-([1,2,4,5]-tetrazo[1,2-*b*]indazol-3-yl)-*N*,*N*-diphenylaniline (15)



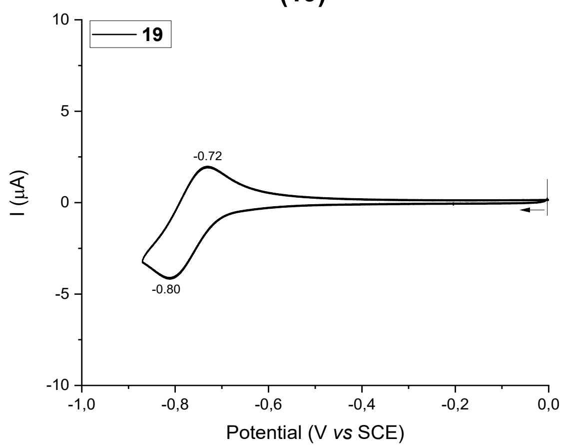
3-(3-methoxyphenyl)-[1,2,4,5]-tetrazo[1,2-*b*] indazole (16)



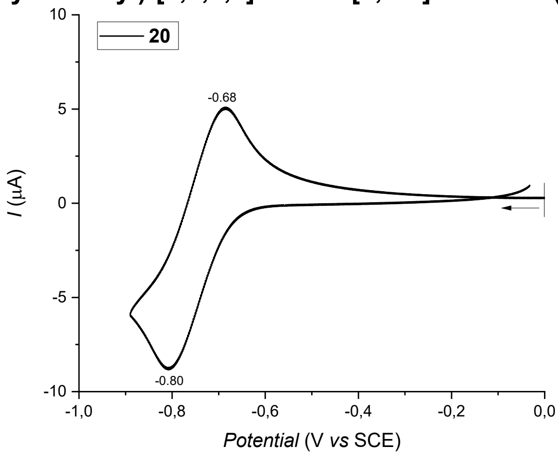
3-(1-naphtyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (18)



3-(phenanthren-9-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (19)



6-(pyridin-3-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (20)



6-(thiophen-3-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (21)

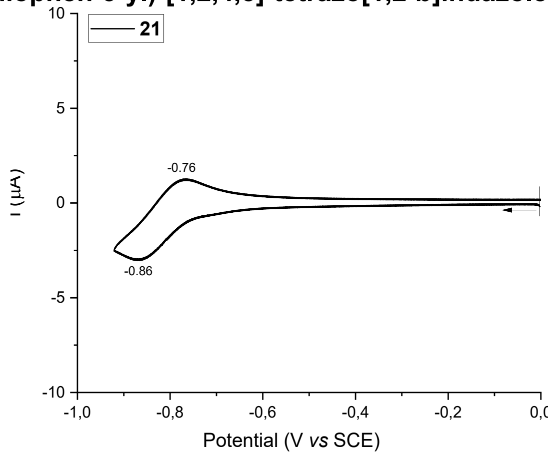
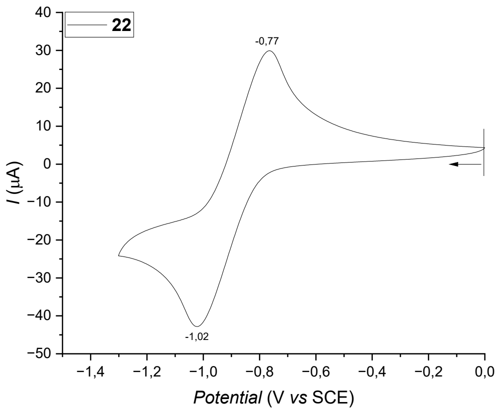
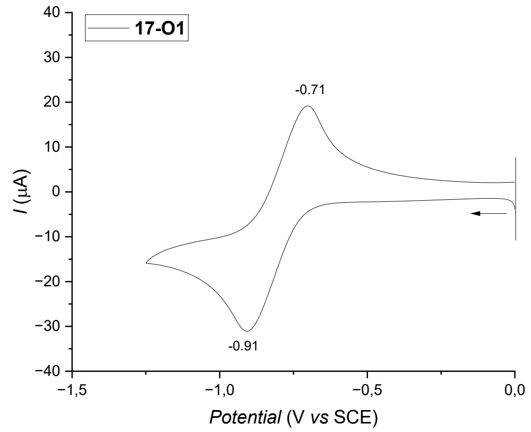


Figure S-5. *Voltammetric analysis of **13**-**16** and **18**-**22.** Recorded with 1.10^{-3} M in CH_2Cl_2 (0.1 M $TEABF_4$), v = 100 mV.s^{-1}, WE: Pt, Ø = 1.6 mm.*

6-(thiophen-2-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (22)



3-(2-fluorophenyl)-3*H*-5λ^4-[1,2,4,5]tetrazino[1,6-*b*]indazole 2-oxide (17-O1)



3-(2-fluorophenyl)-3*H*-5λ^4-[1,2,4,5]tetrazino[1,6-*b*]indazole 1-oxide (17-O2)

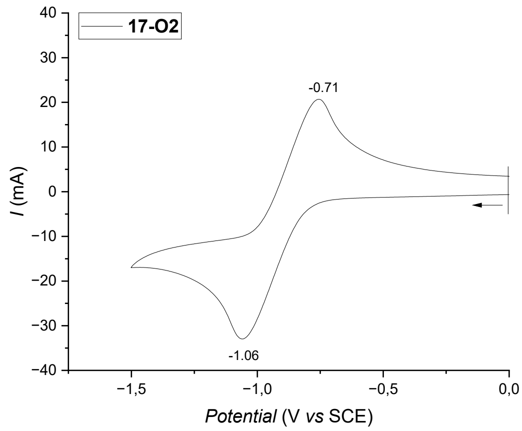
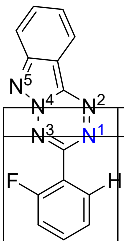


Figure S-6. *Voltammetric analysis of **17**-**O1** and **17**-**O2.** Recorded with 5.10^4 M in CH_2Cl_2 (0.1 M $TBAPF_6$), v = 200 mV.s^{-1}, WE: Pt, Ø = 2 mm.*

Computational details

All Quantum mechanics calculations were performed using the Gaussian 16 package.[4] Energy and forces were computed by density functional theory with the hybrid B3LYP exchange-correlation functional,[5] in dichloromethane described by the PCM approach. Geometries were optimized and characterized with the def2-SVP basis set and associated pseudo-potential for **Pd** and 6-31+G(d,p) basis set for all other atoms. Gibbs free energies have been computed at 298K and 1 atm using unscaled density functional frequencies at the same level. More accurate energies were then computed using the def2-TZVP basis set and associated pseudo-potential for **Pd** and 6-311++G(2df,2pd) basis set for all other atoms. TD-DFT calculations were performed with a tightened self-consistent field convergence criterion (10^{-10} au) with the B3LYP/6-311++G(d,p) level in dichloromethane using geometries obtained at the B3LYP/6-31+G(d,p) level. The first 12 singlet excited states were computed for organic molecules and the first 36 singlet excited states were computed for organometallics complexes **Ir** and **Rh**.

Table S-Th1. *Relative Gibbs free energies (in kcal mol-1) for the different protonation sites of* ***17.***



N1	N2	N3	N4	N5
0.0	11.8	13.8	66.7	8.5

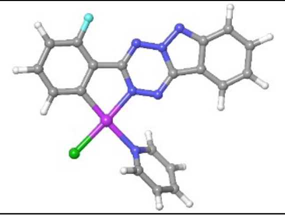
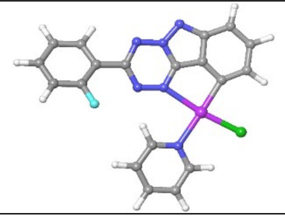
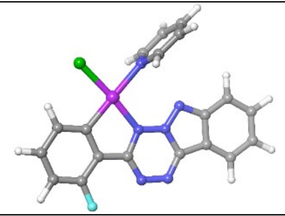
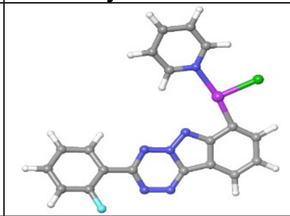
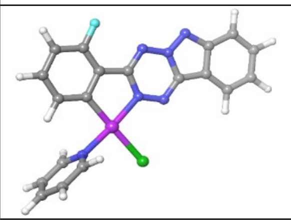
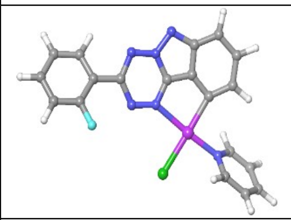
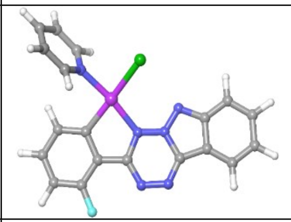
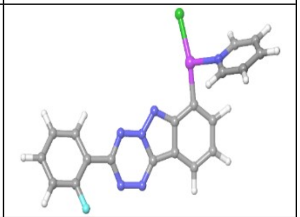
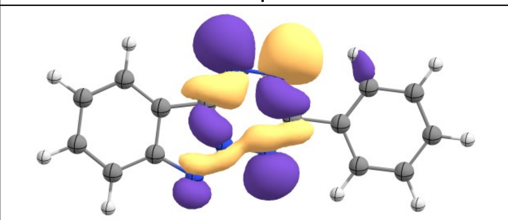
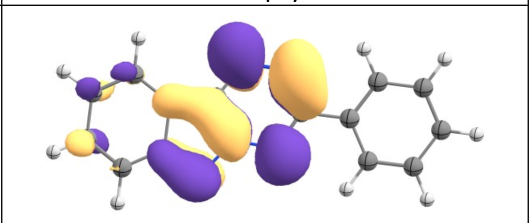
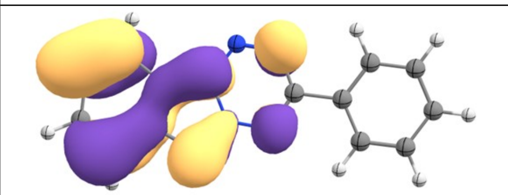
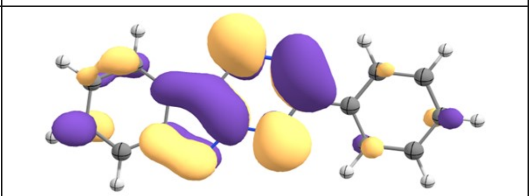
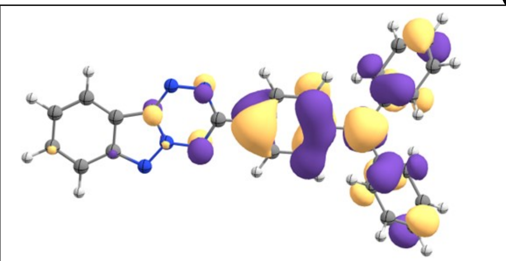
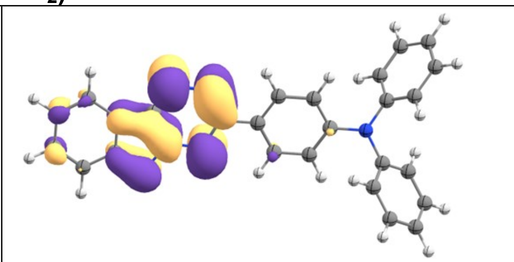
	N1	N2	N3	N5	C adjacent to N5
Cis				Does not exist	
	ΔG = 0.0 kcal mol-1	ΔG = 24.5 kcal mol-1	ΔG = 9.3 kcal mol-1		ΔG = 26.5 kcal mol-1
Trans				Does not exist	
	ΔG = 0.6 kcal mol-1	ΔG = 26.5 kcal mol-1	ΔG = 12.5 kcal mol-1		ΔG = 26.5 kcal mol-1

Figure S-Th1. *All Metallacycles* ***Pd*** *formed at various nitrogens of tetrazoindazole with the indication of their relative Gibbs free energies (in kcal mol-1). Color scheme: Pd (plum), Cl (green), F (cyan), N (blue), C (grey), H (white).*

λ (nm)	Occupied		Empty
12 (R = H)			
427.1 $S_0 \rightarrow S_1$ f=0.0062		→	
419.1 $S_0 \rightarrow S_2$ f=0.2000		→	
15 (R = 4-NPh_2)			
600.5 $S_0 \rightarrow S_1$ f=0.1164		→	

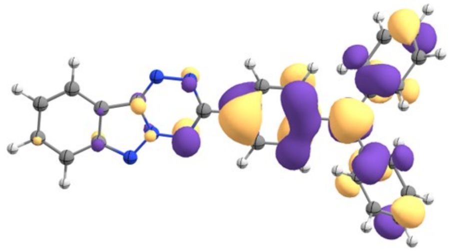
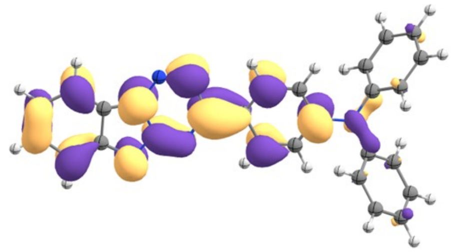
441.9 $S_0 \rightarrow S_2$ f=1.0976		→	

Figure S-Th2. *Natural transition orbitals of the transition around 430 nm for **12** and **15**. Isovalue: 0.05 au.*

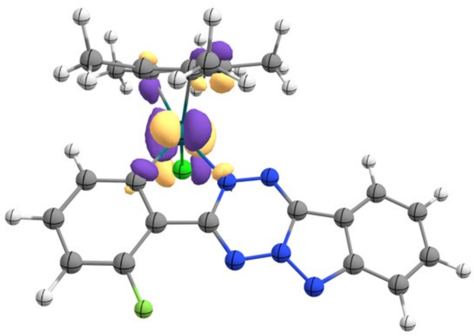
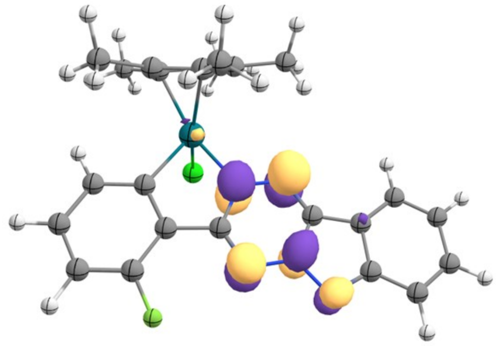
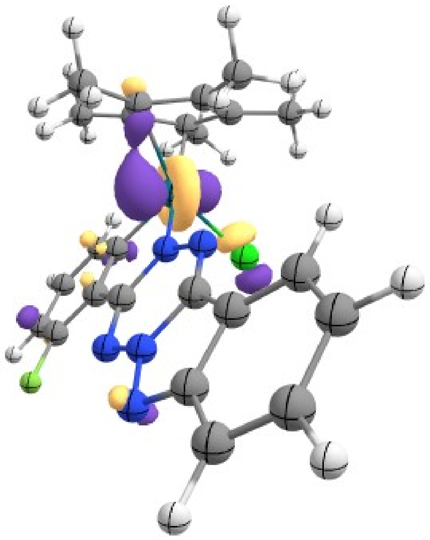
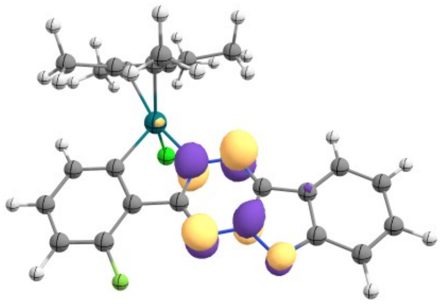
648.16 $S_0 \rightarrow S_1$ f=0.0413		→	
551.63 $S_0 \rightarrow S_2$ f=0.0762		→	

Figure S-Th3. *Natural transition orbitals for the rhodacycle **Rh** (Cp)Rh(2F-TzInd). Isovalue: 0.07 au.*

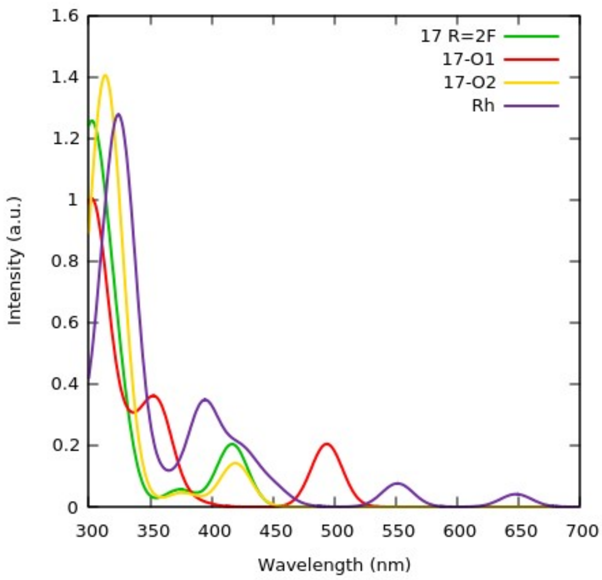


Figure S-Th4. *Simulation UV-vis absorption spectra for **17**, **17-O1**, **17-O2** and **Rh**. Geom: B3LYP/6-311++G(d,p), TD: B3LYP/6-311++G(d,p).*

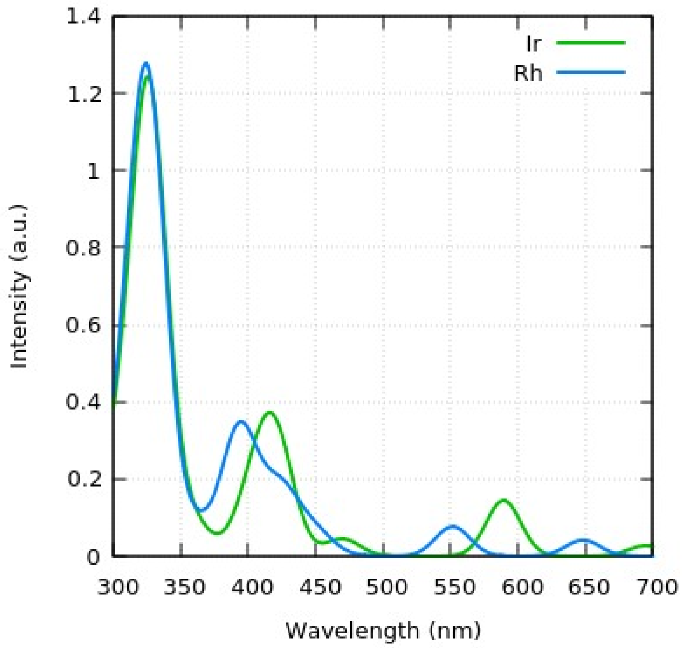
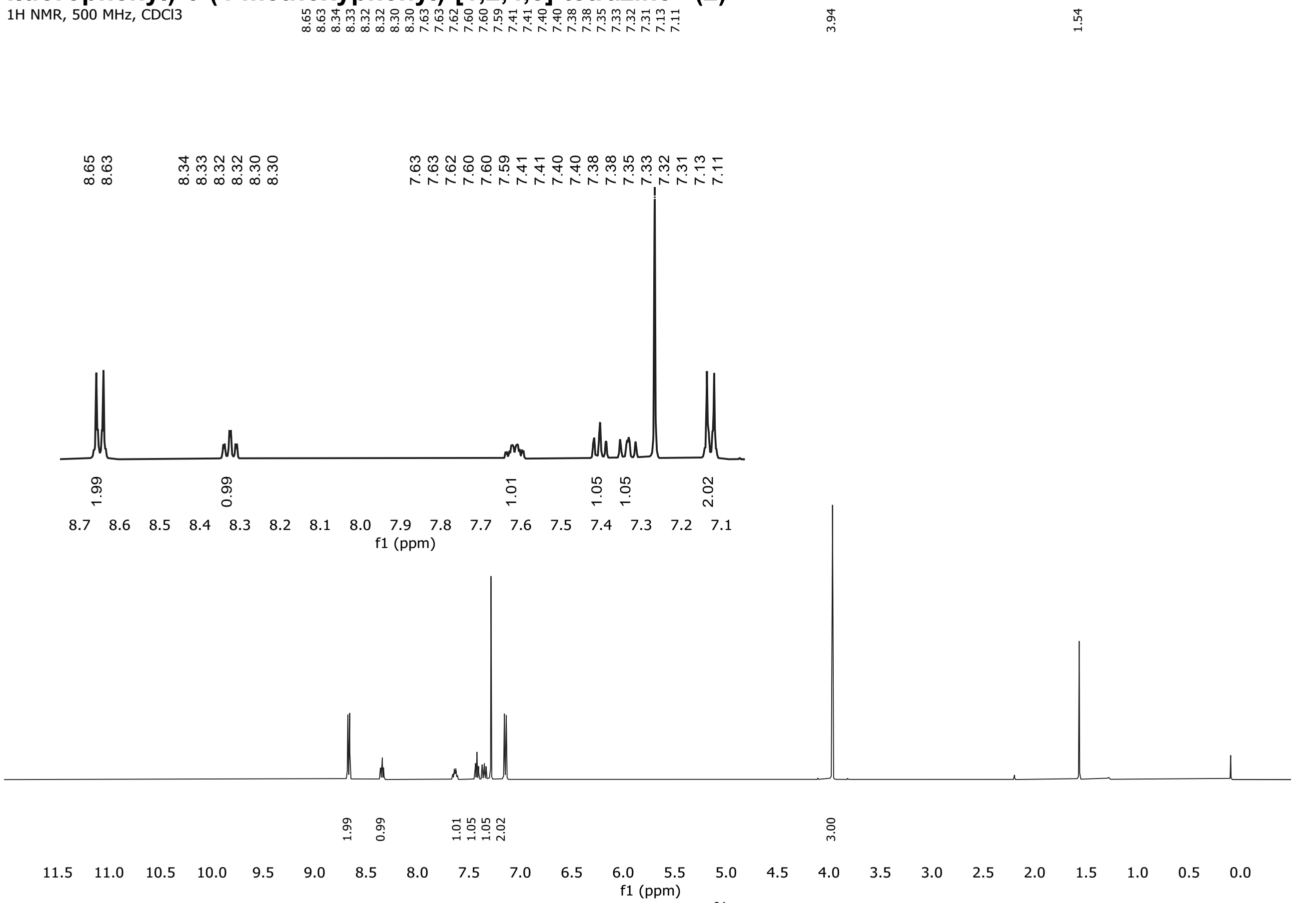


Figure S-Th5. *Simulation UV-vis absorption spectra for* ***Ir*** *and* ***Rh****. Geom: B3LYP/6-311++G(d,p), TD: B3LYP/6-311++G(d,p).*

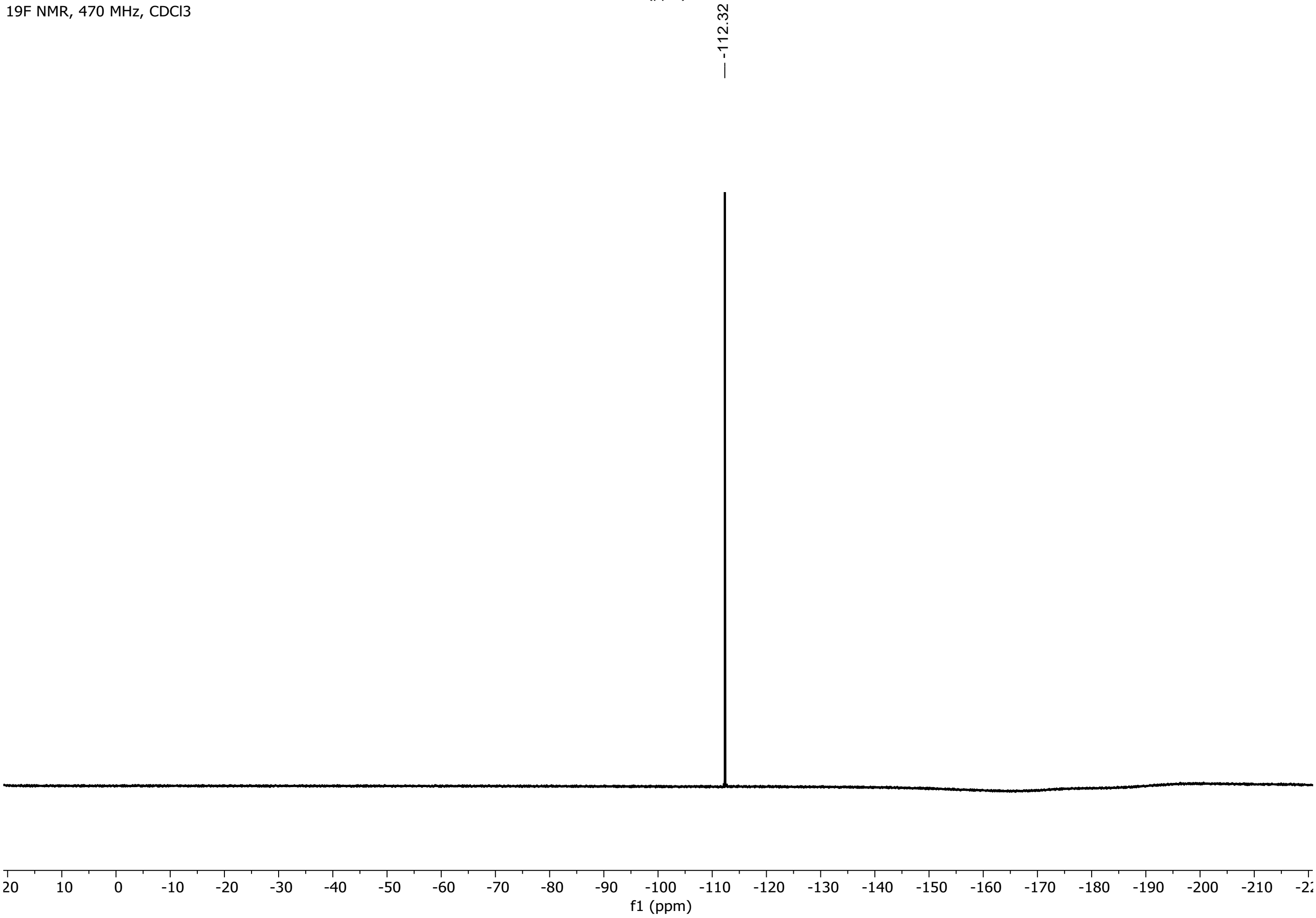
Copy of NMR spectrum of the new compounds

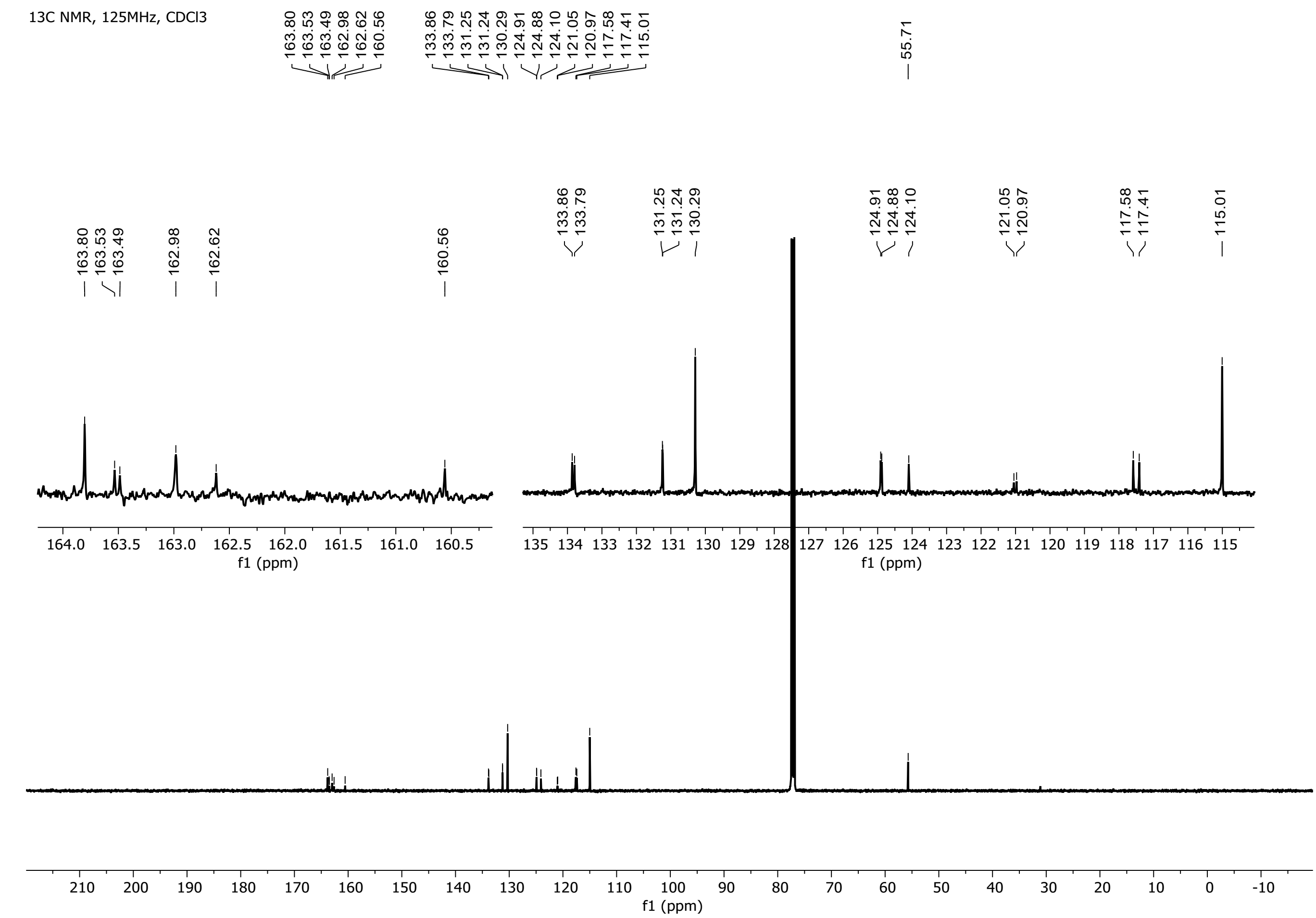
3-(2-fluorophenyl)-6-(4-methoxyphenyl)-[1,2,4,5]-tetrazine (2)

1H NMR, 500 MHz, CDCl3

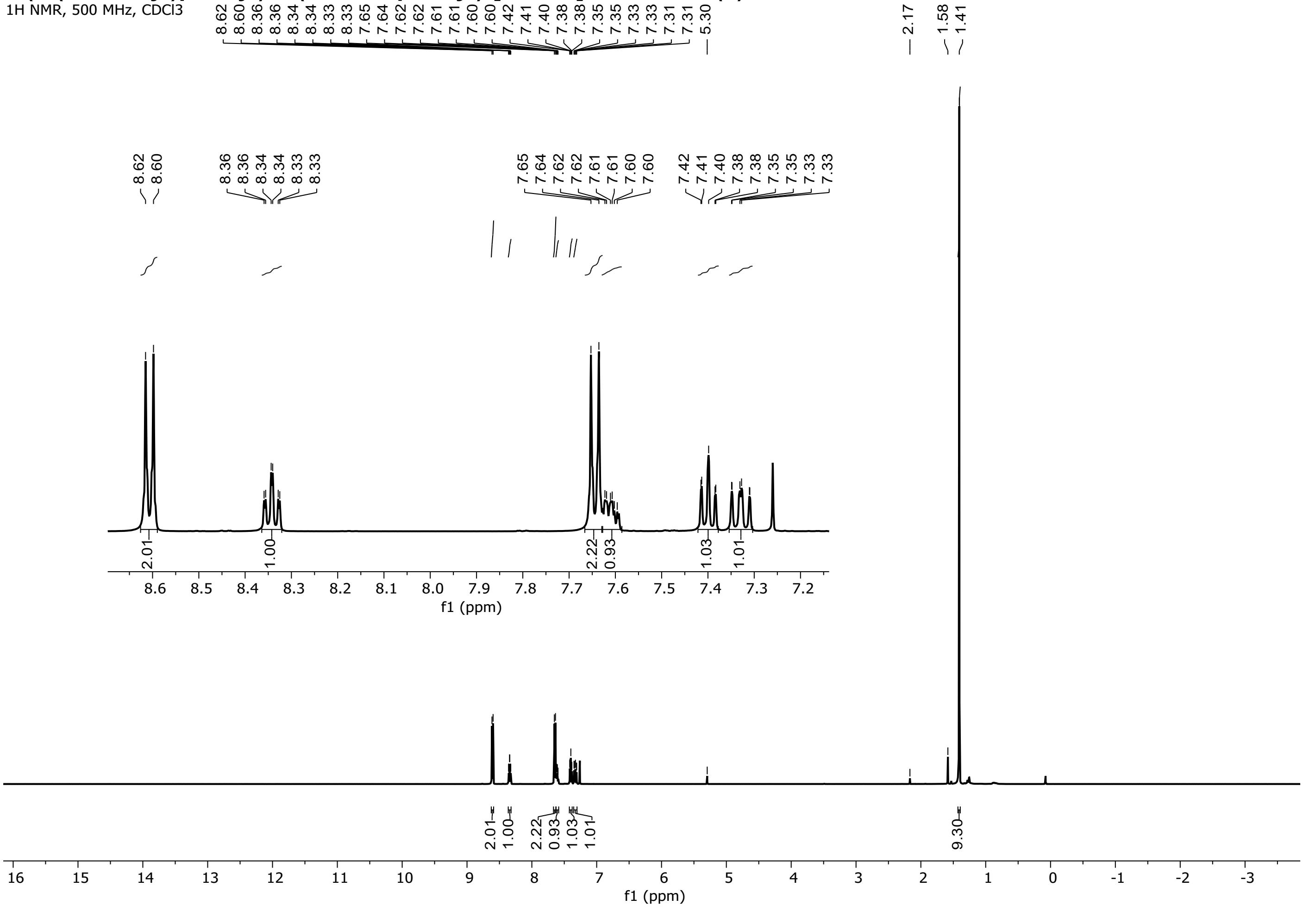


19F NMR, 470 MHz, CDCl3

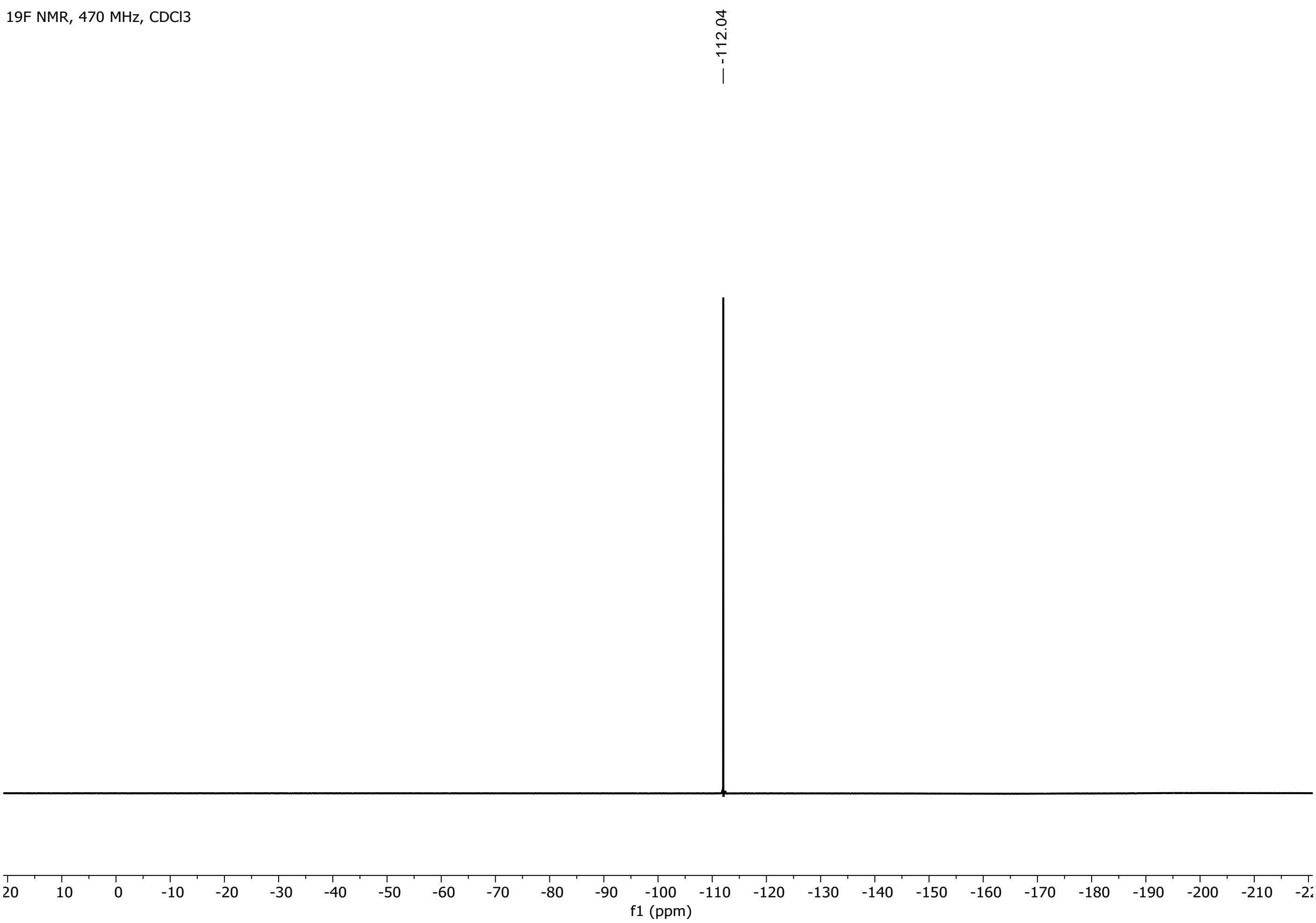




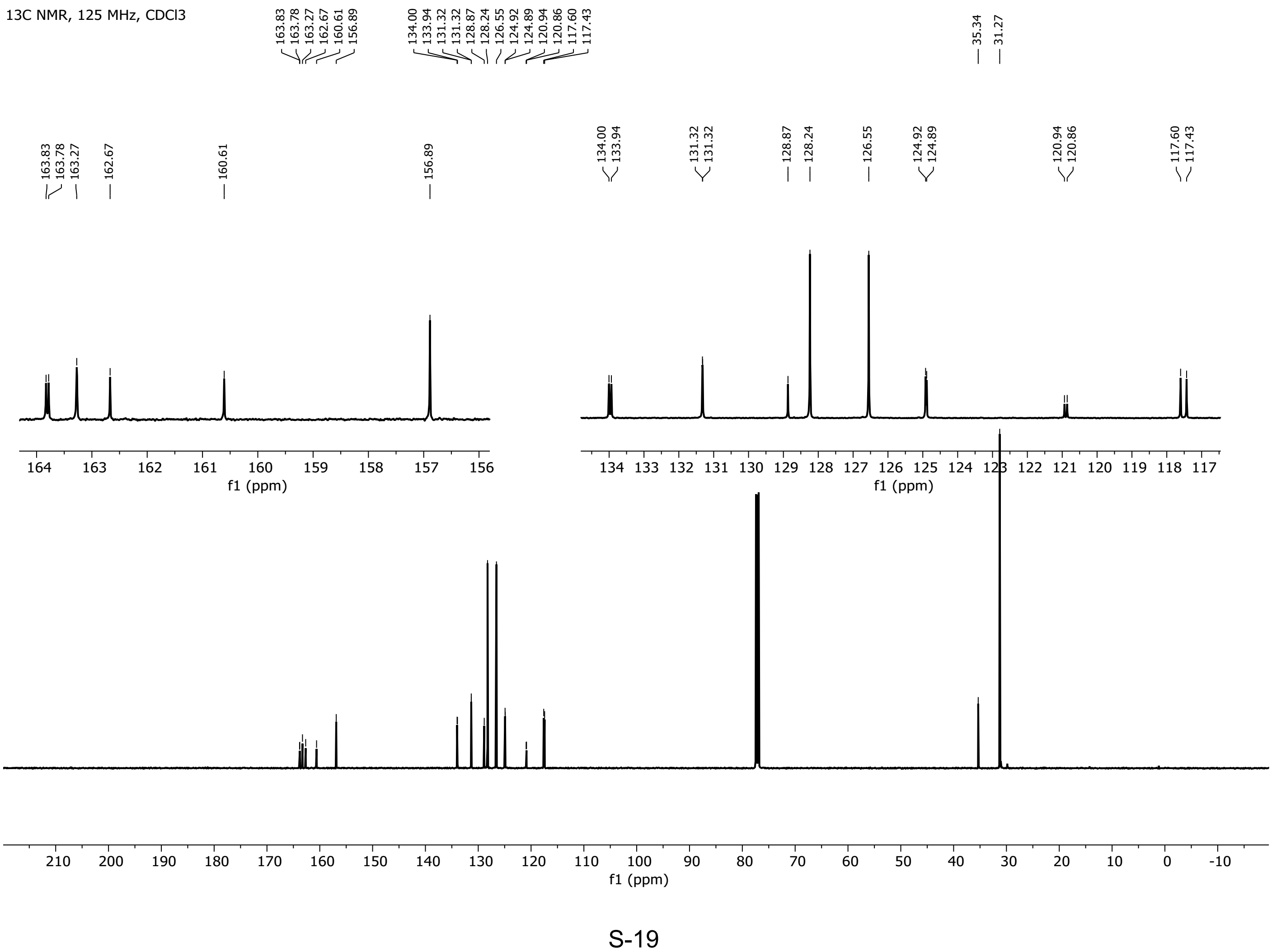
3-(4-(*tert*-butyl)phenyl)-6-(2-fluorophenyl)-[1,2,4,5]-tetrazine (3)



19F NMR, 470 MHz, CDCl3

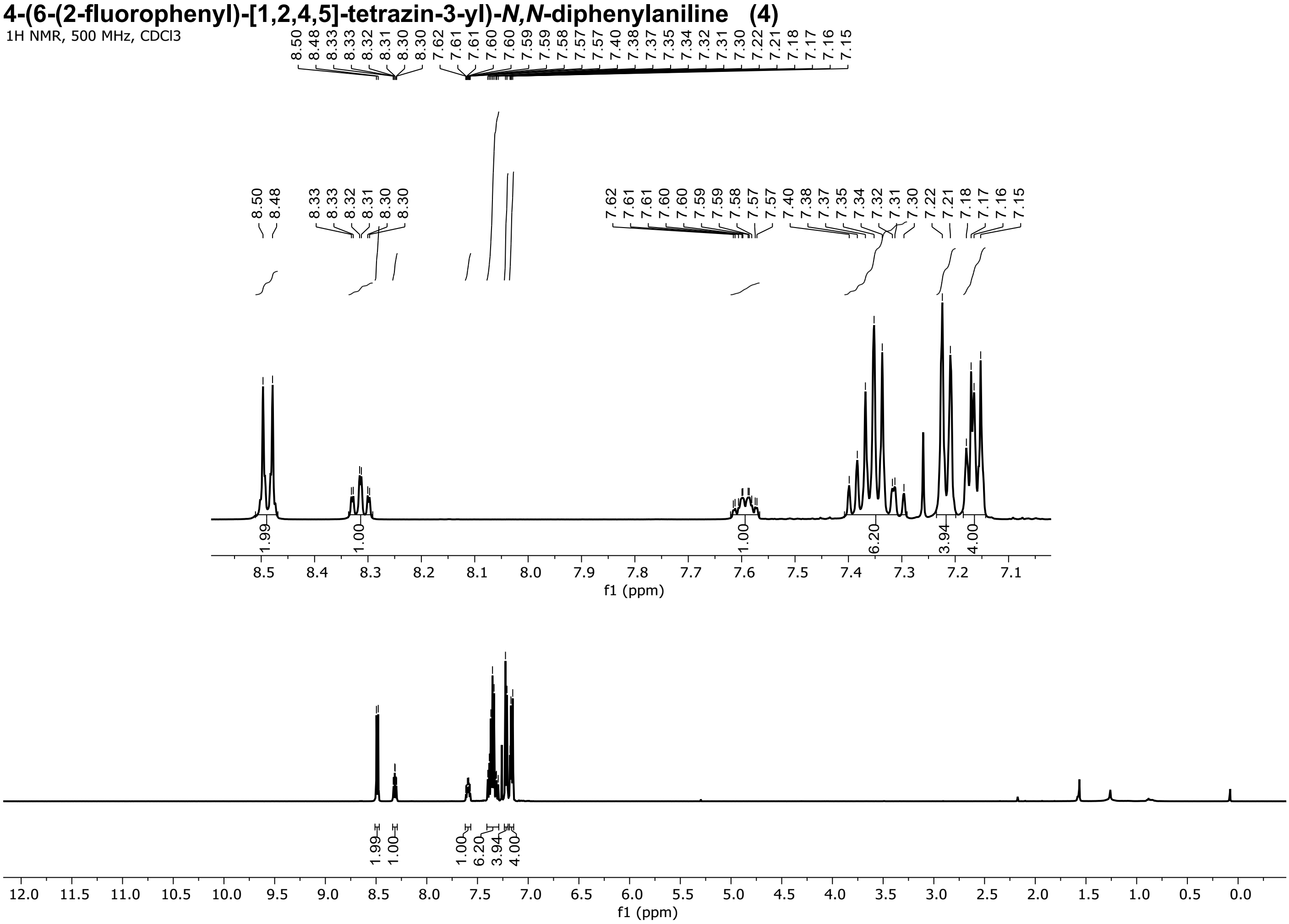


13C NMR, 125 MHz, CDCl3

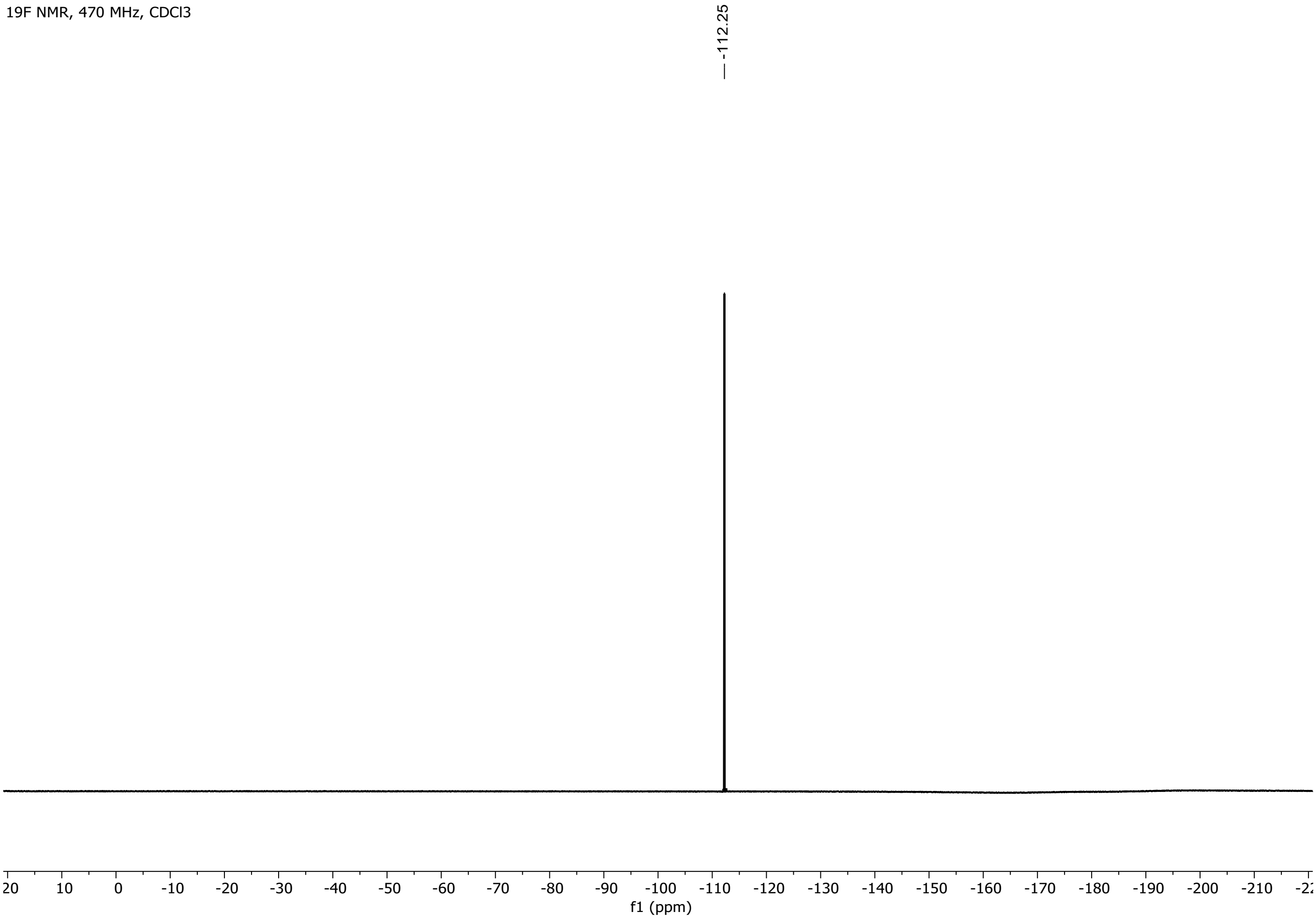


4-(6-(2-fluorophenyl)-[1,2,4,5]-tetrazin-3-yl)-*N,N*-diphenylaniline (4)

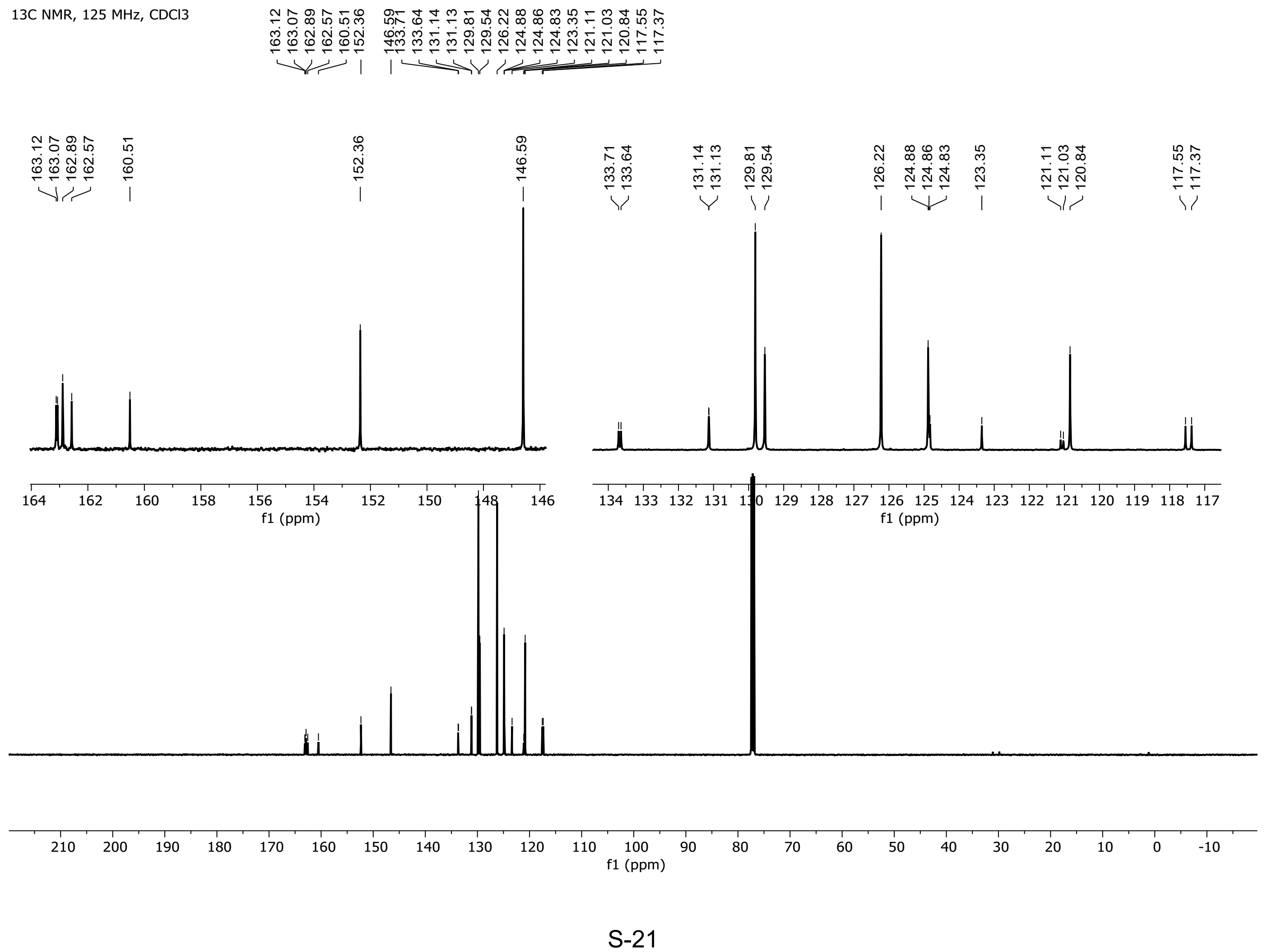
1H NMR, 500 MHz, CDCl3



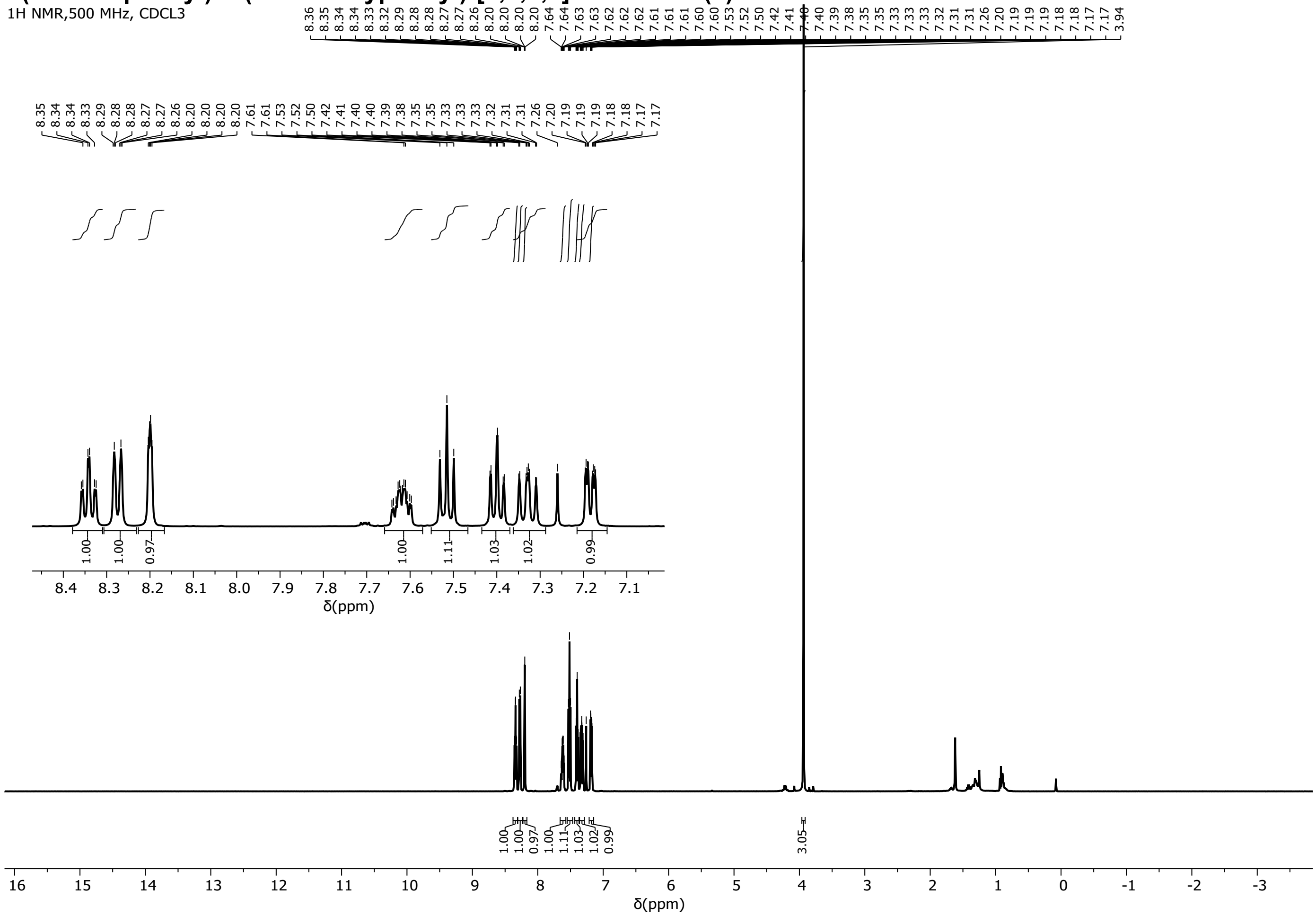
19F NMR, 470 MHz, CDCl3

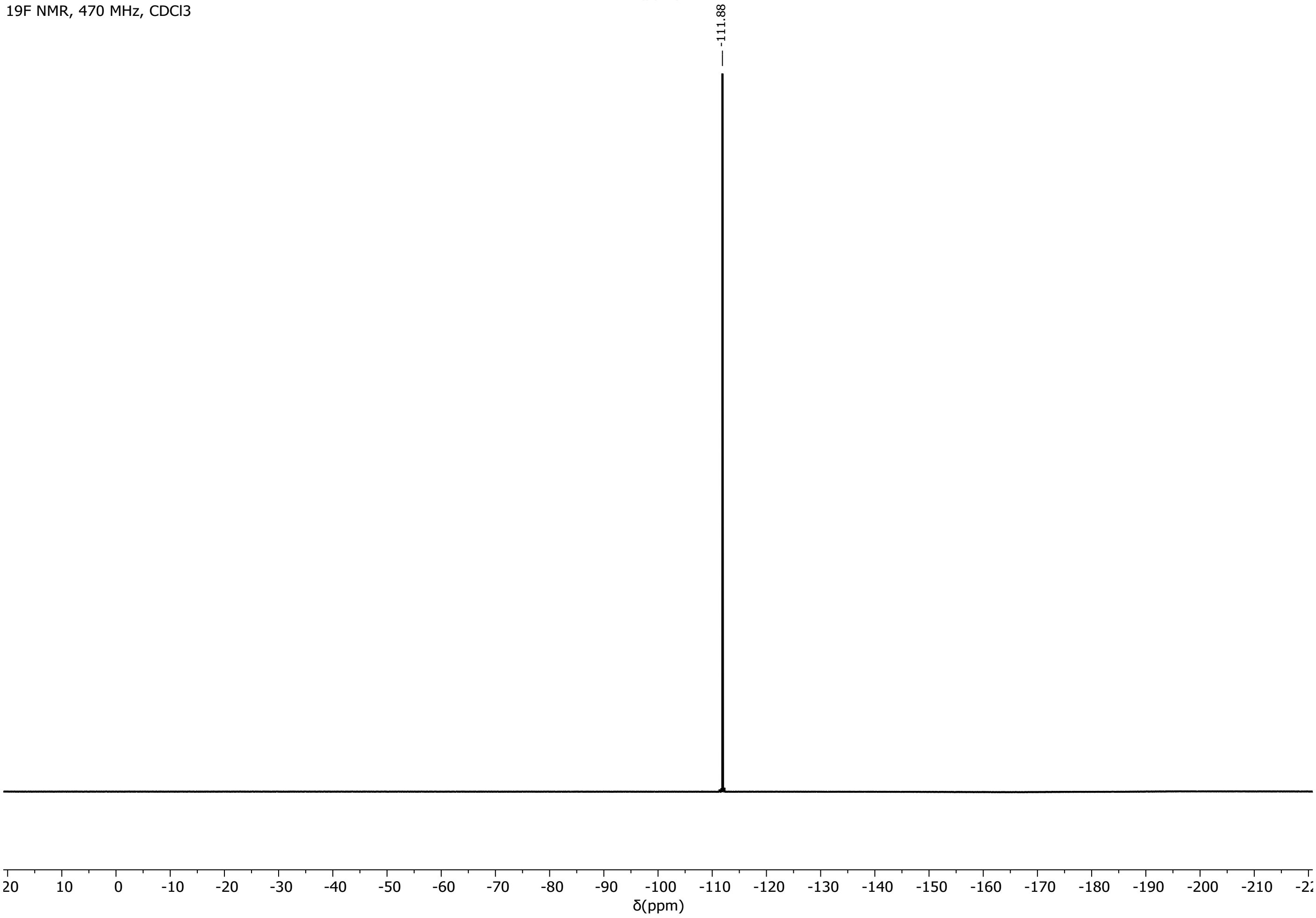


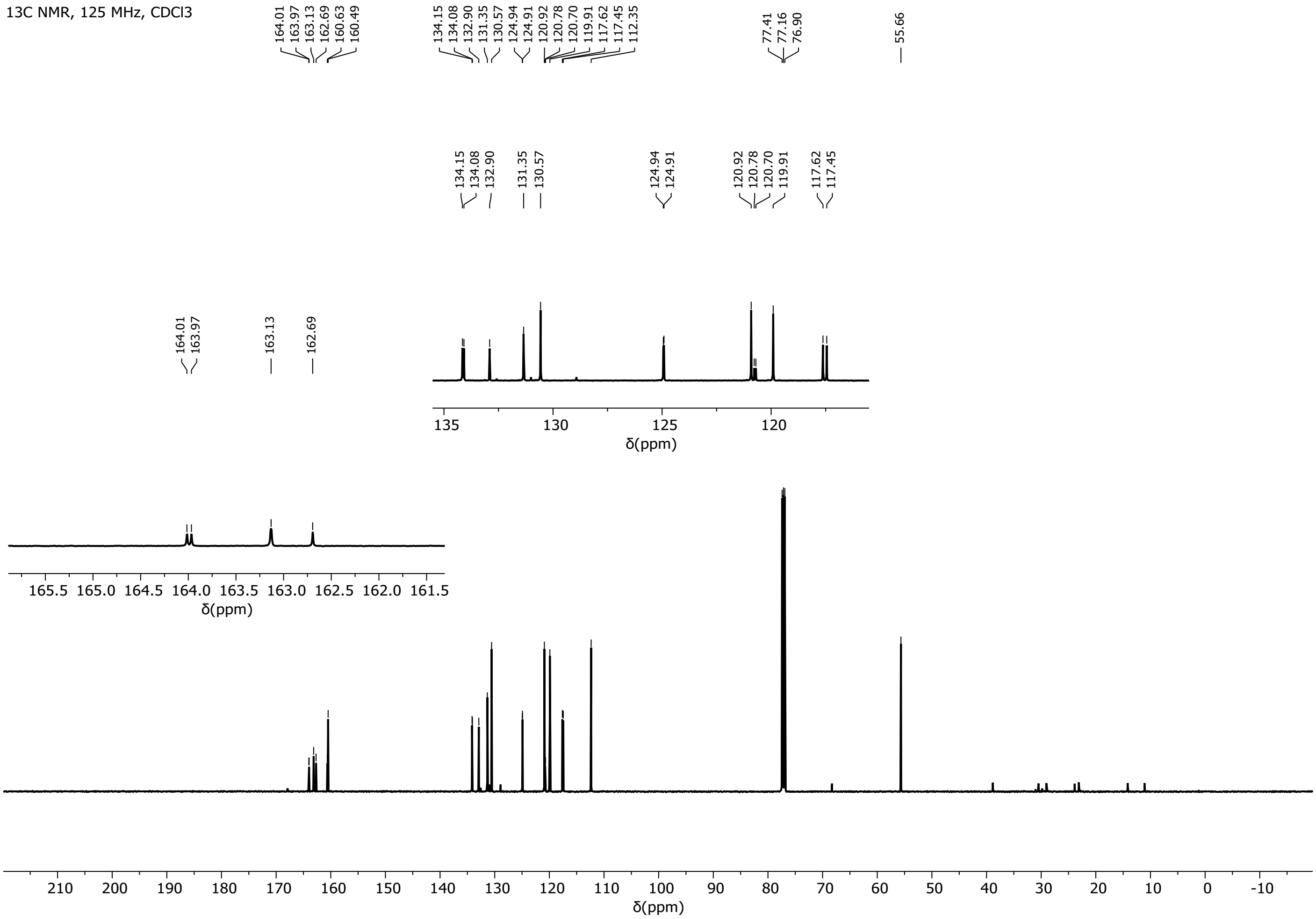
13C NMR, 125 MHz, CDCl3



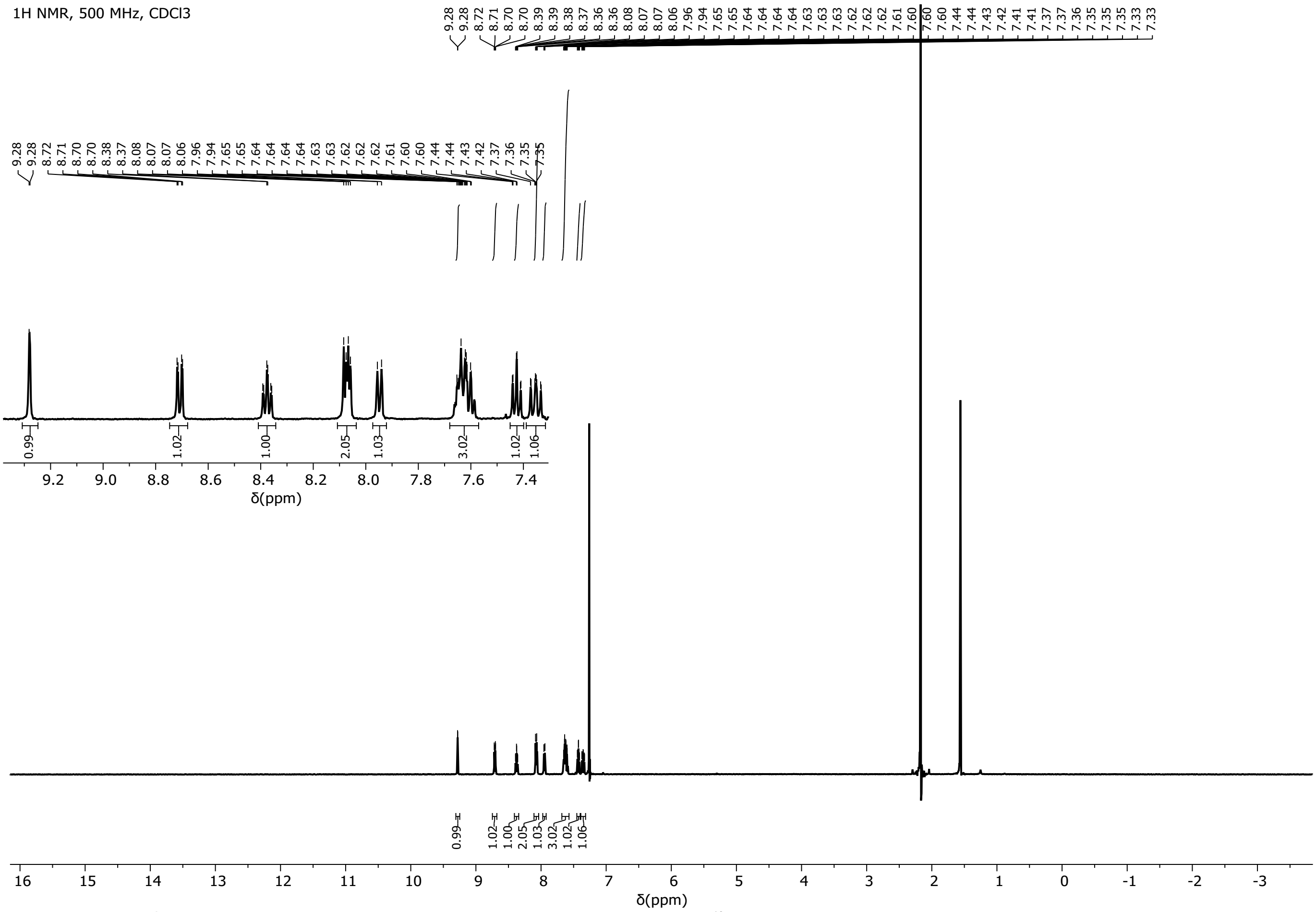
3-(2-fluorophenyl)-6-(3-methoxyphenyl)-[1,2,4,5]-tetrazine (5)

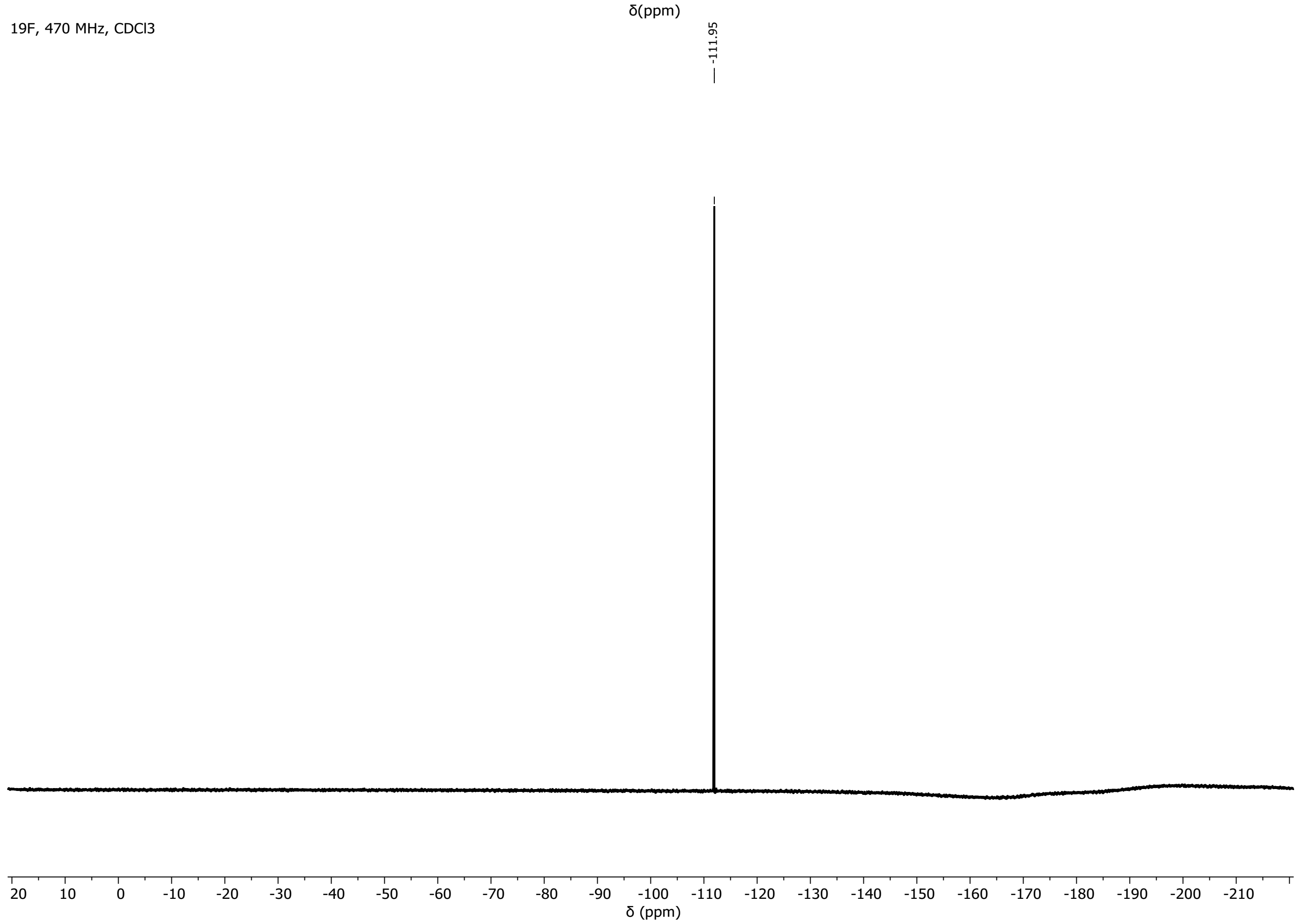


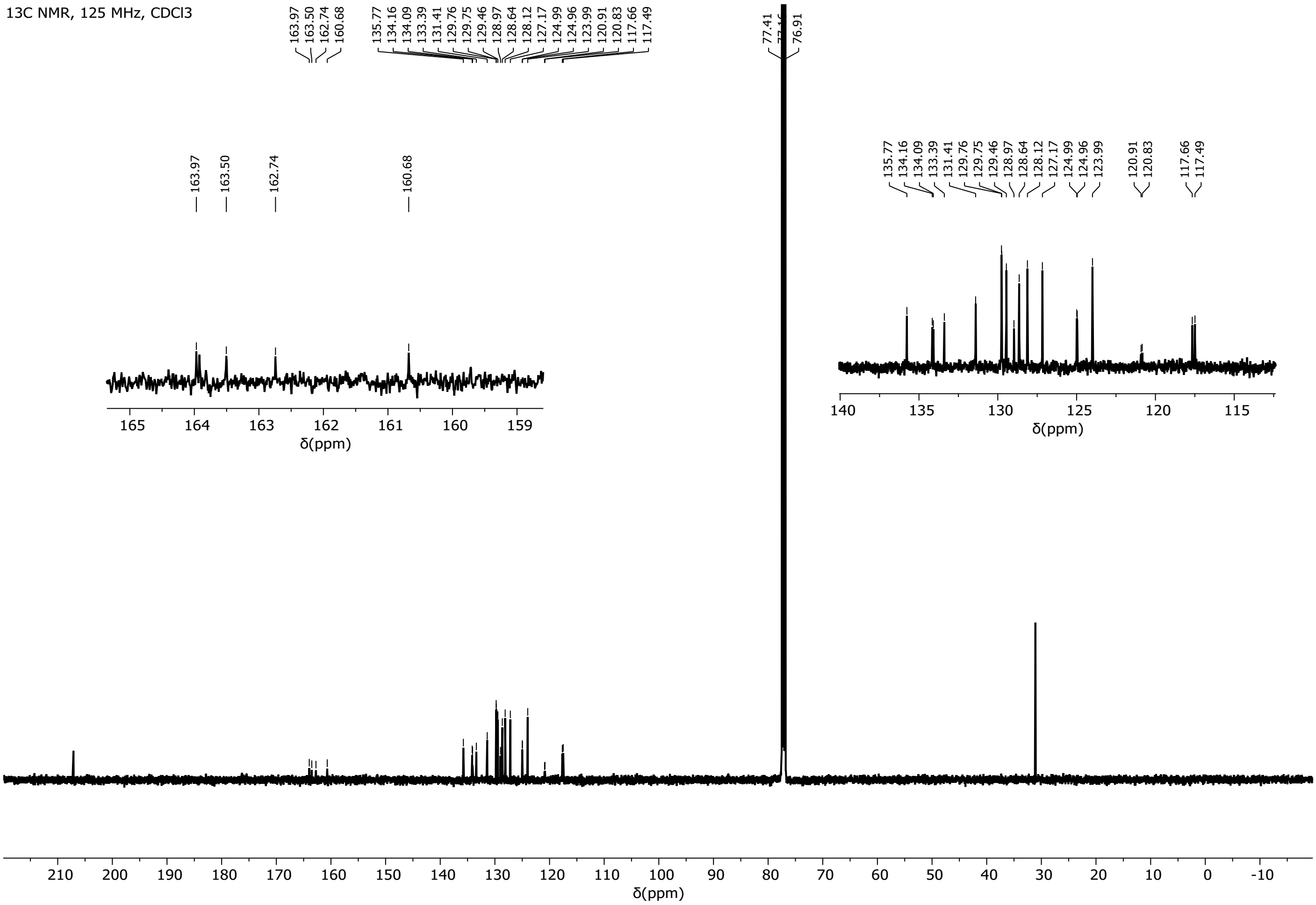




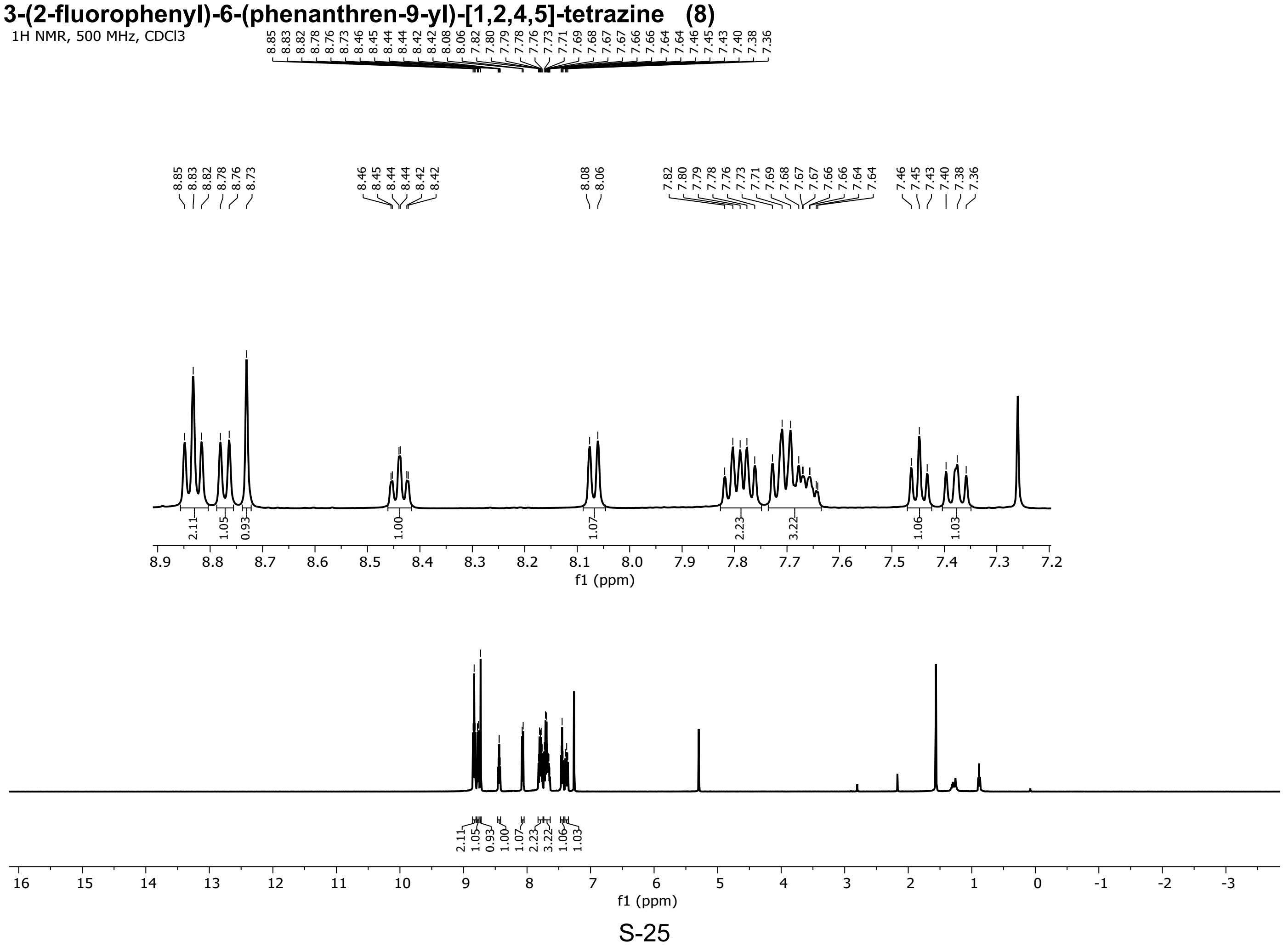
3-(2-fluorophenyl)-6-(napht-9-yl)-[1,2,4,5]-tetrazine (7)


1H NMR, 500 MHz, CDCl3
0.99
1.02
1.00
2.05
1.03
3.02
1.02
1.06
δ(ppm)

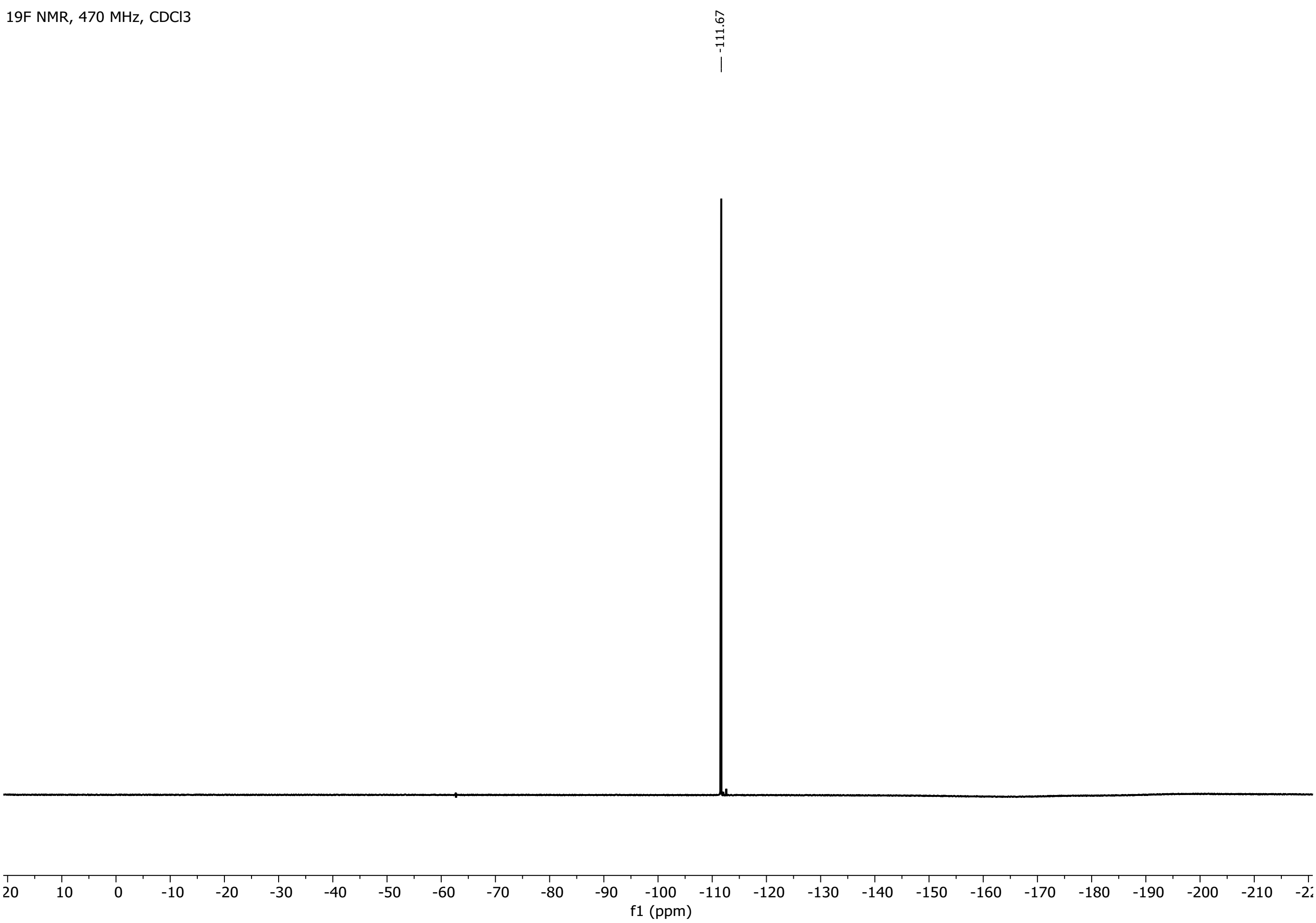

19F, 470 MHz, CDCl3
-111.95
δ (ppm)



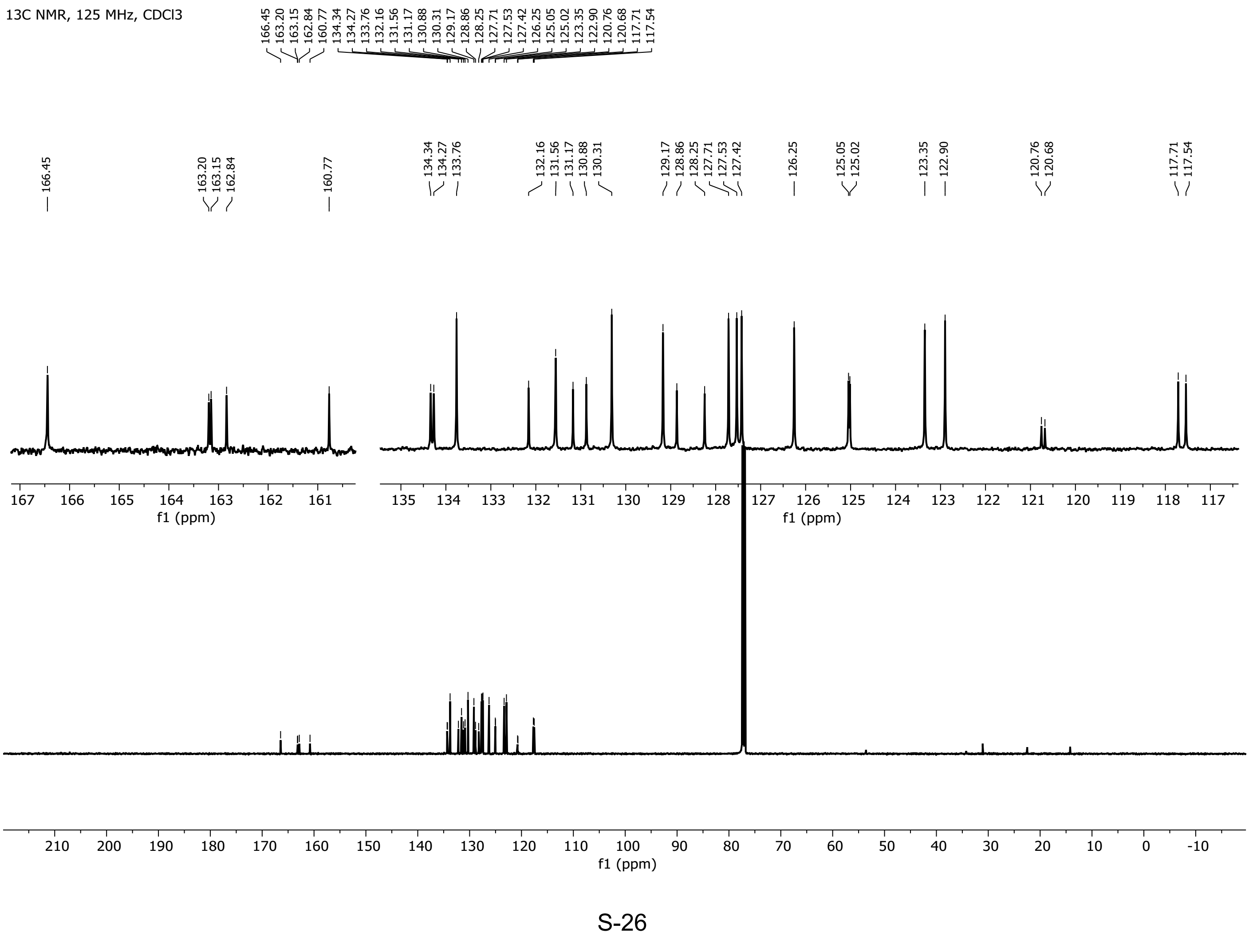
3-(2-fluorophenyl)-6-(phenanthren-9-yl)-[1,2,4,5]-tetrazine (8)



19F NMR, 470 MHz, CDCl3

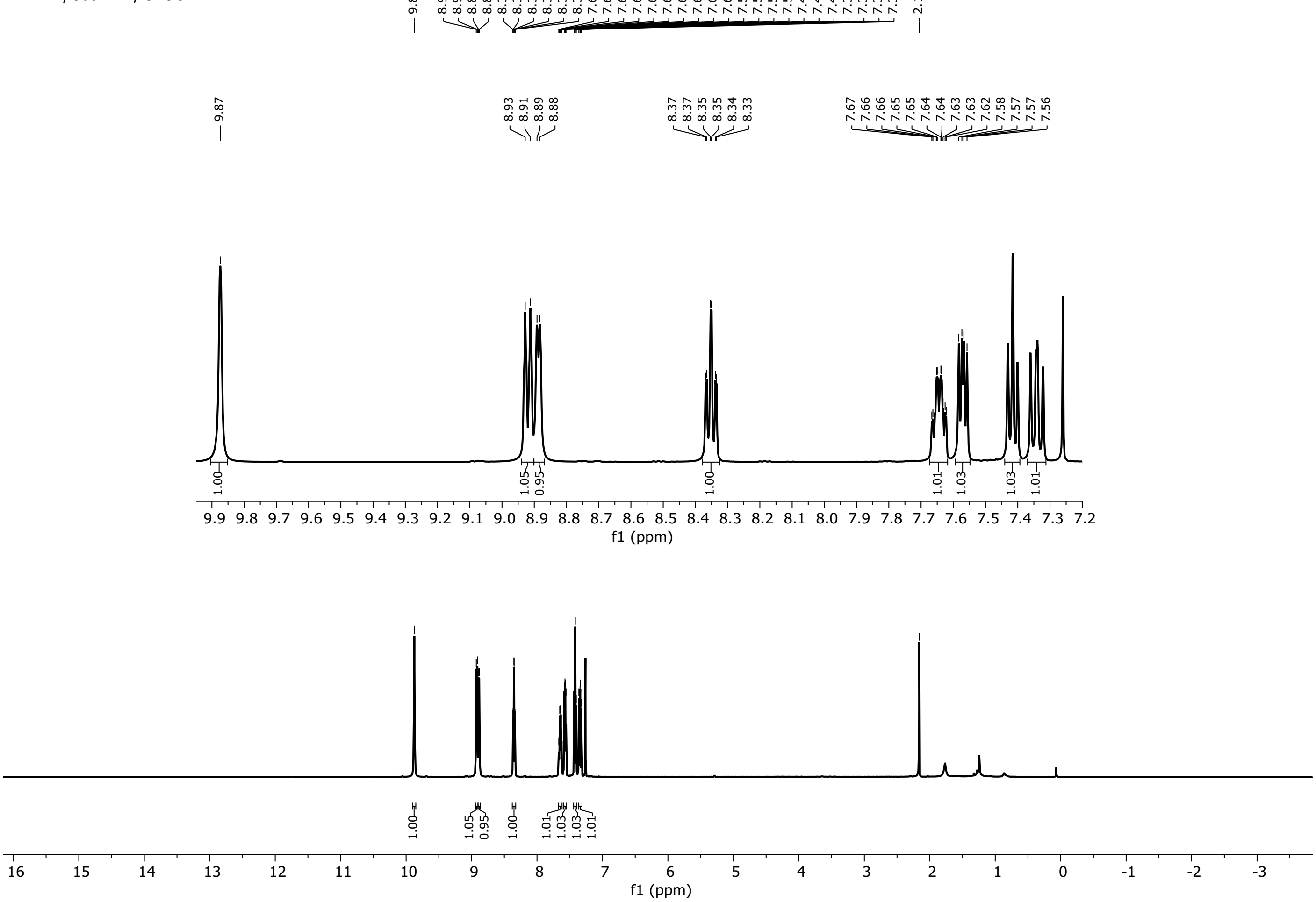


13C NMR, 125 MHz, CDCl3

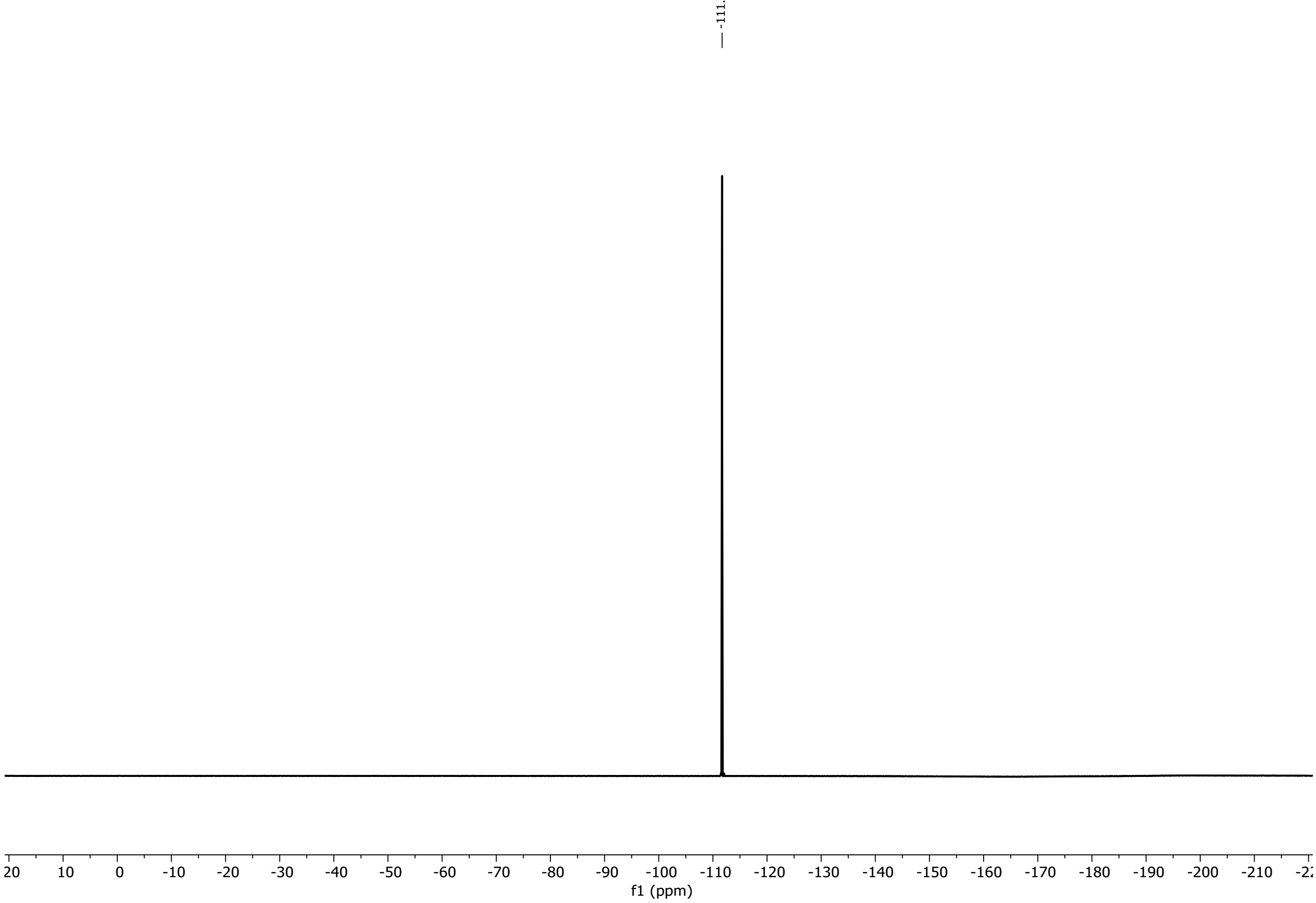


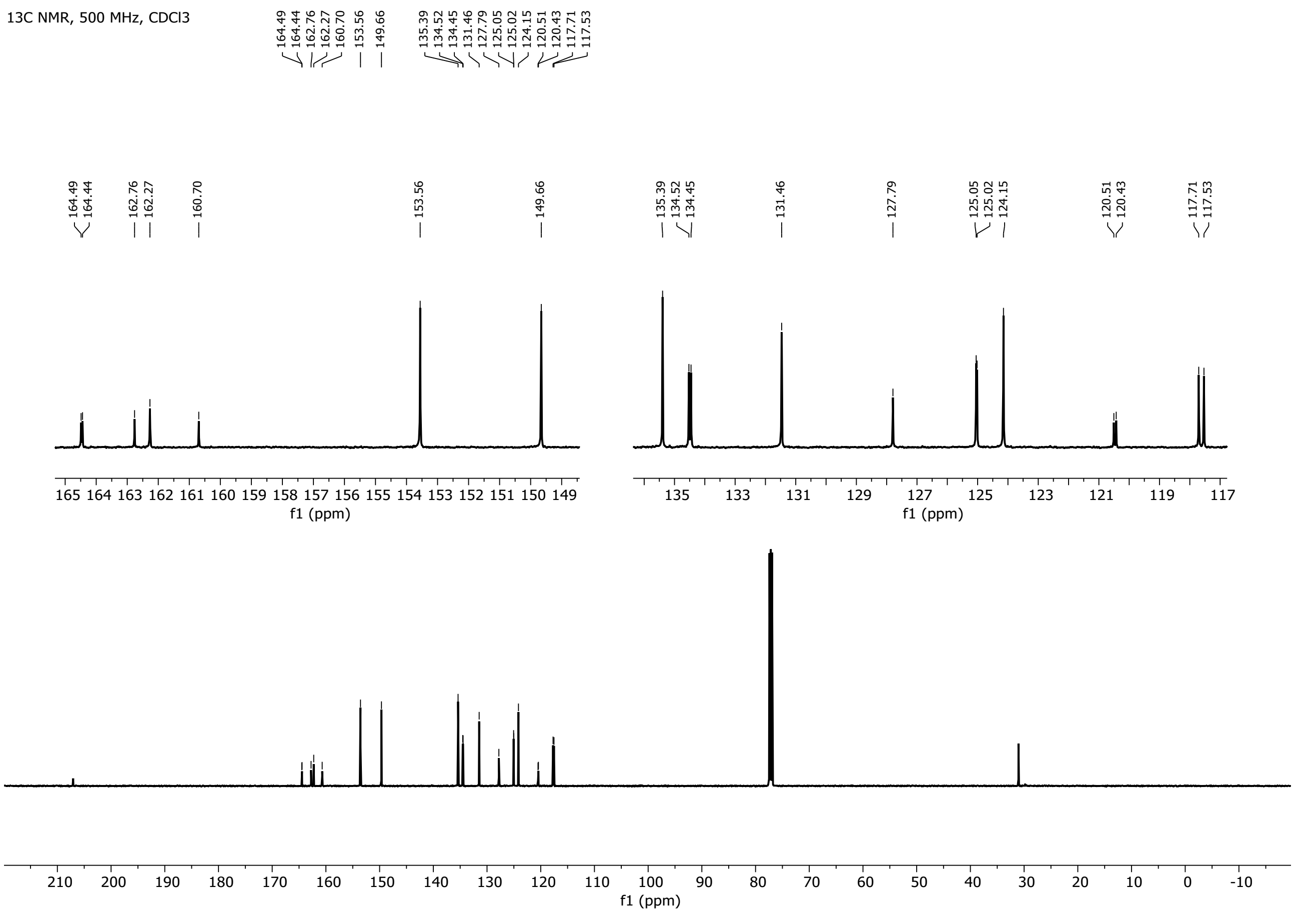
3-(2-fluorophenyl)-6-(pyridine-3-yl)-[1,2,4,5]-tetrazine (9)

1H NMR, 500 MHz, CDCl3

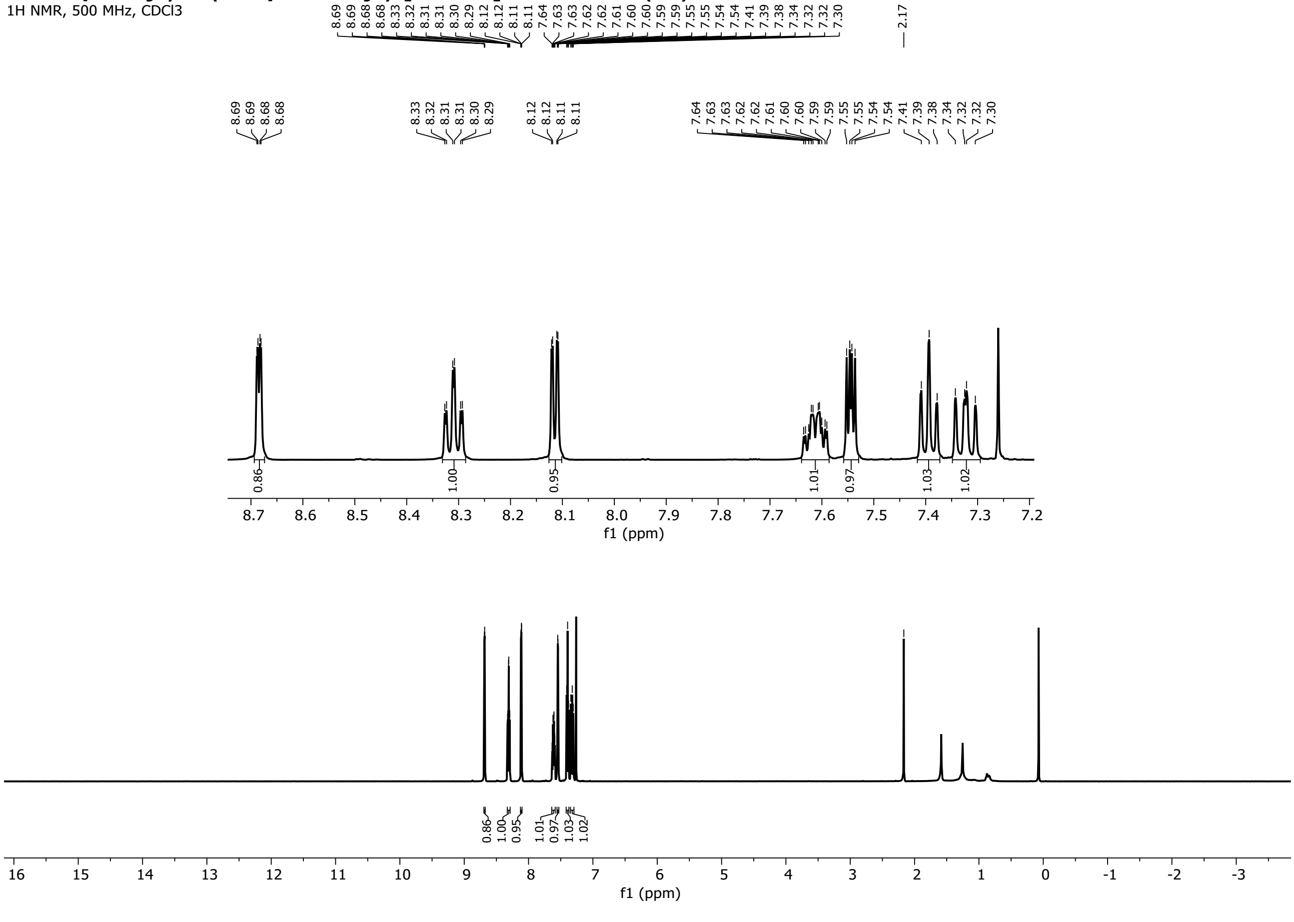


19F NMR, 470 MHz, CDCl3

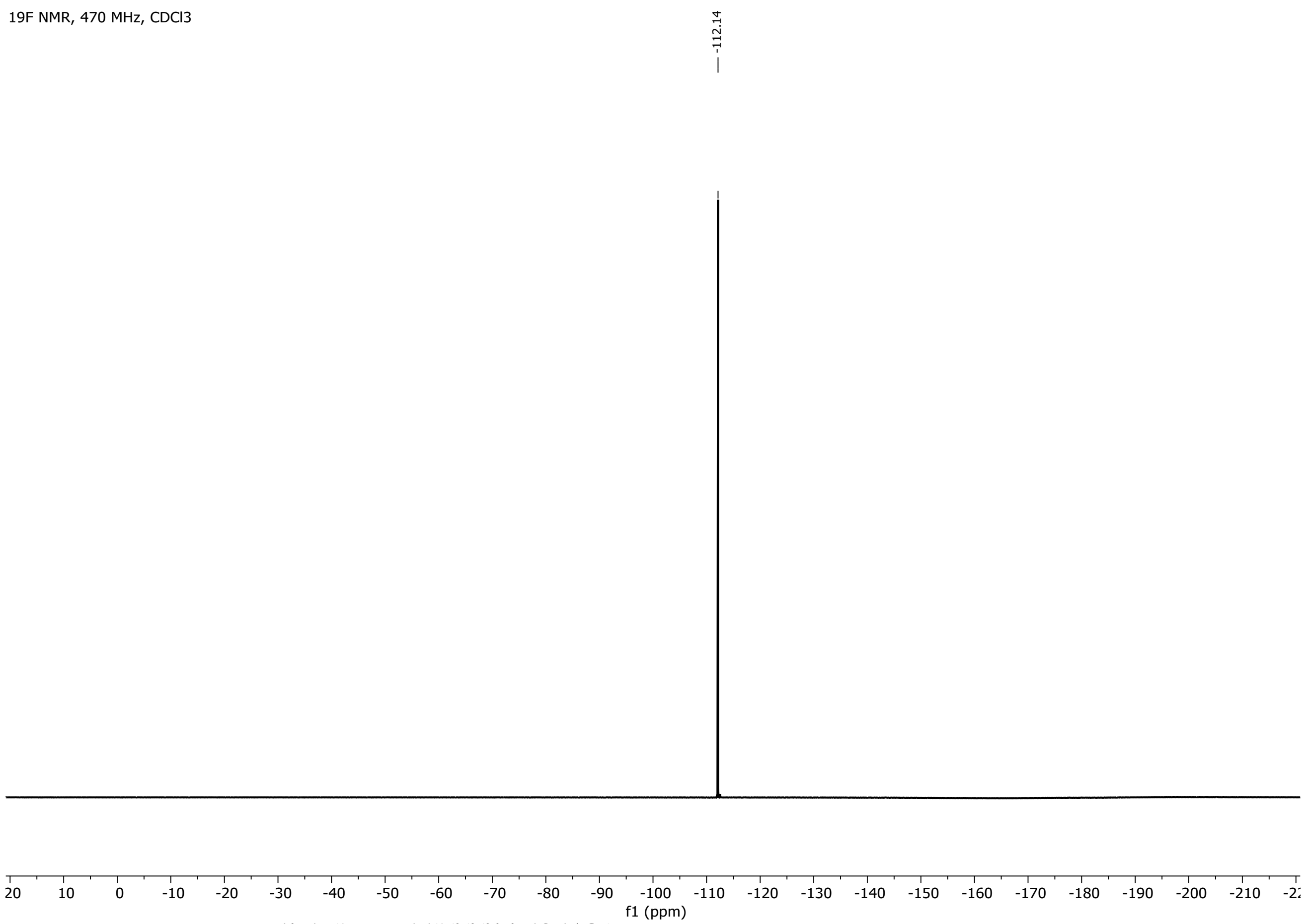




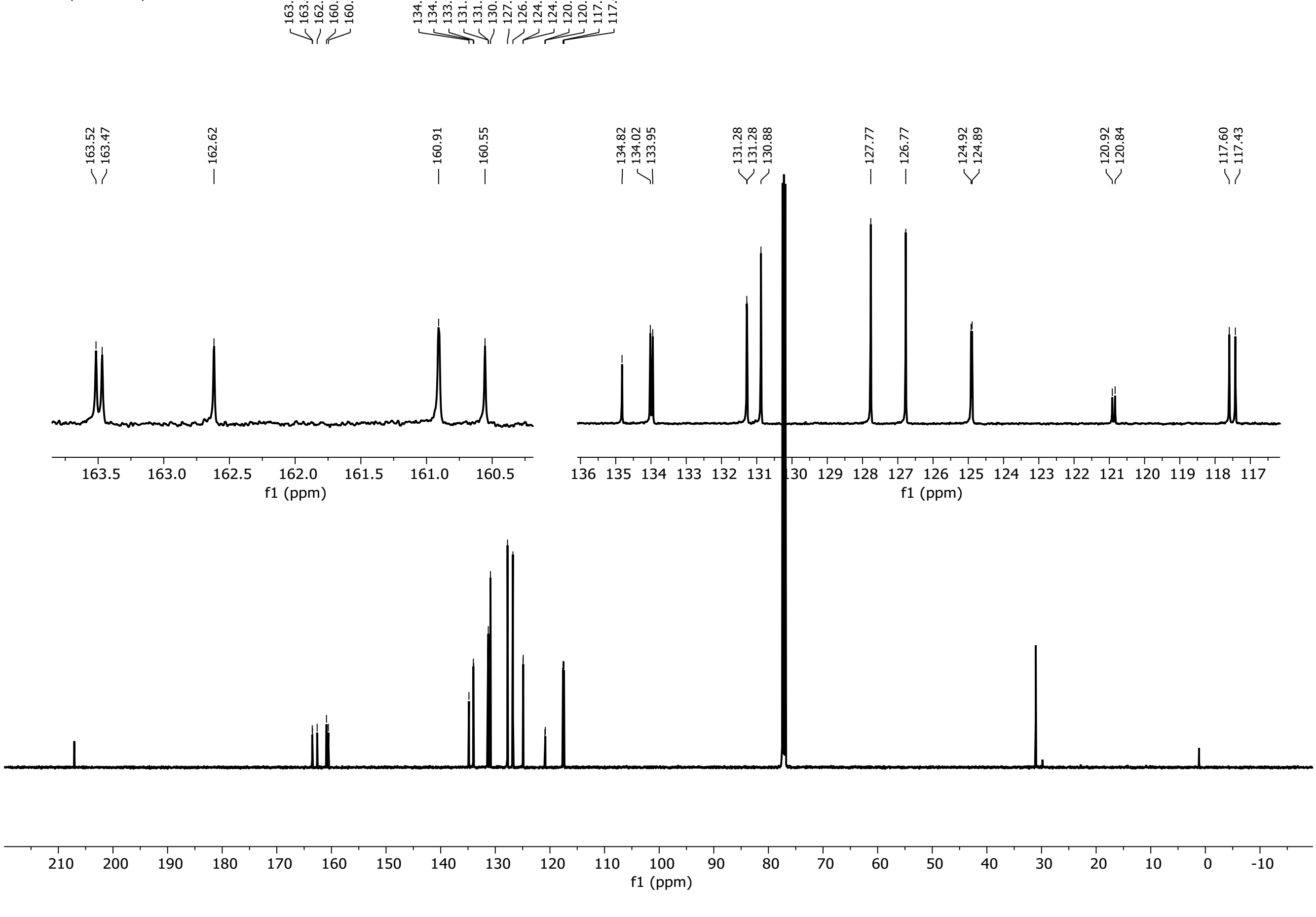
3-(2-fluorophenyl)-6-(thiophen-3-yl)-[1,2,4,5]-tetrazine (10)



19F NMR, 470 MHz, CDCl3

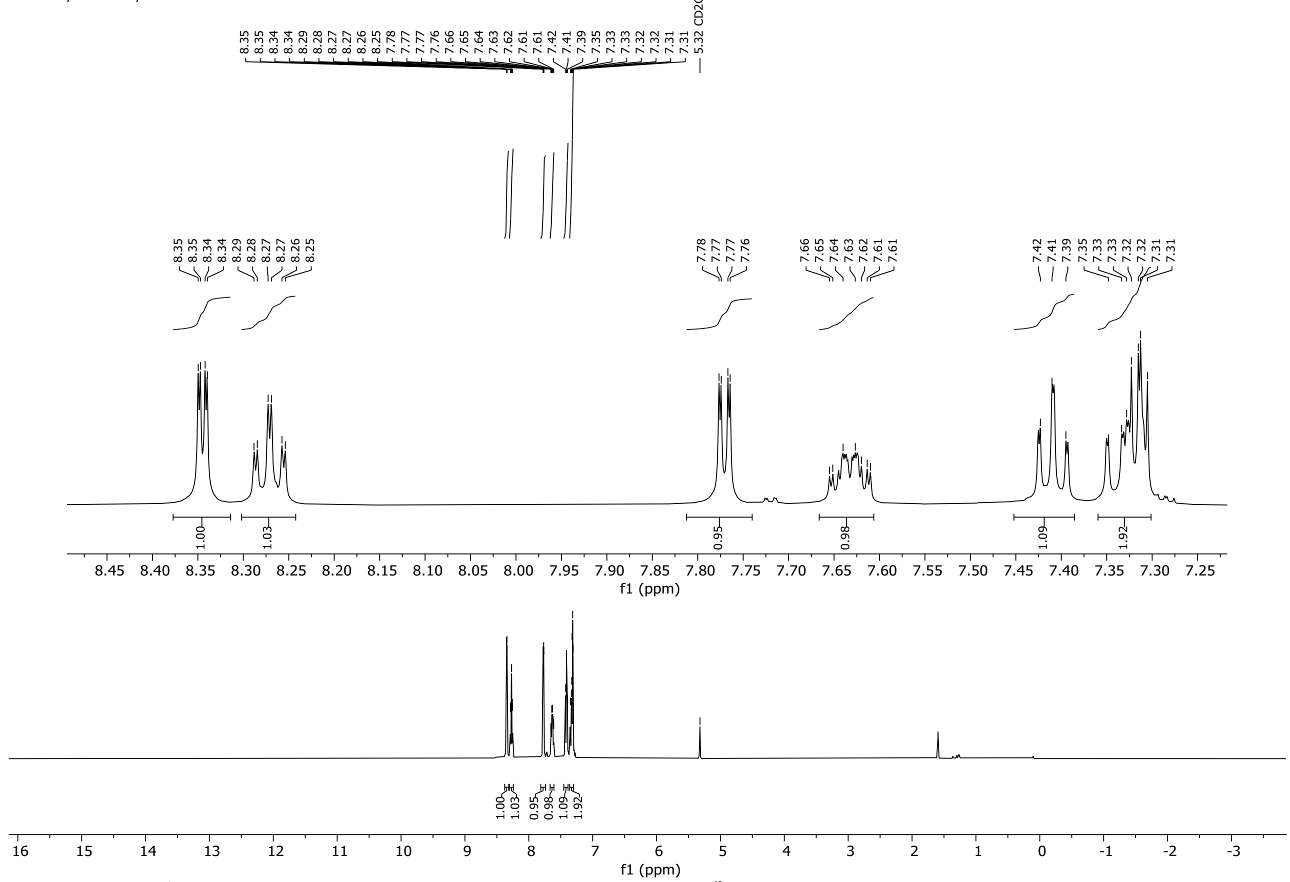


13C NMR, 125 MHz, CDCl3

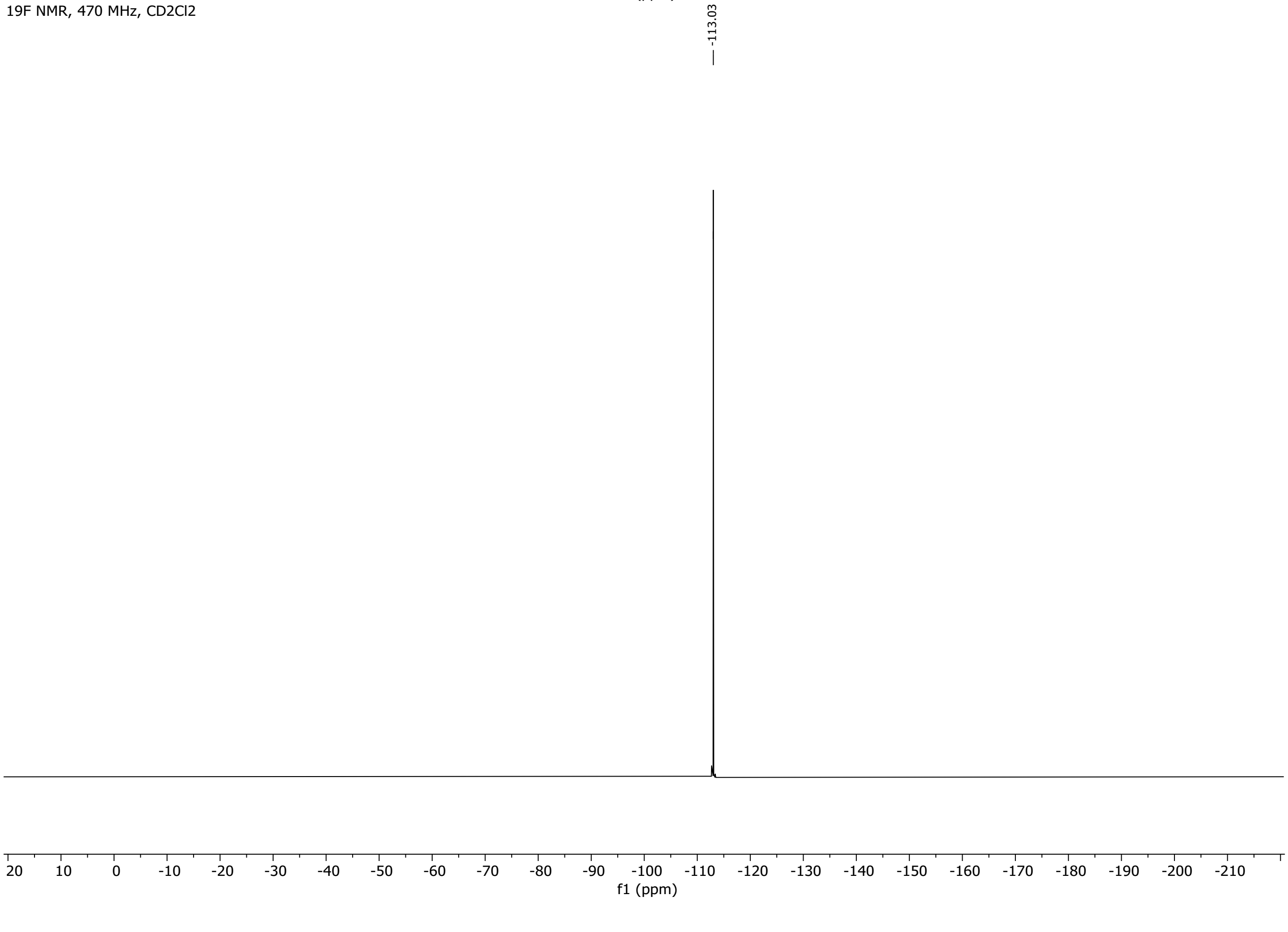


3-(2-fluorophenyl)-6-(thiophen-2-yl)-[1,2,4,5]-tetrazine (11)

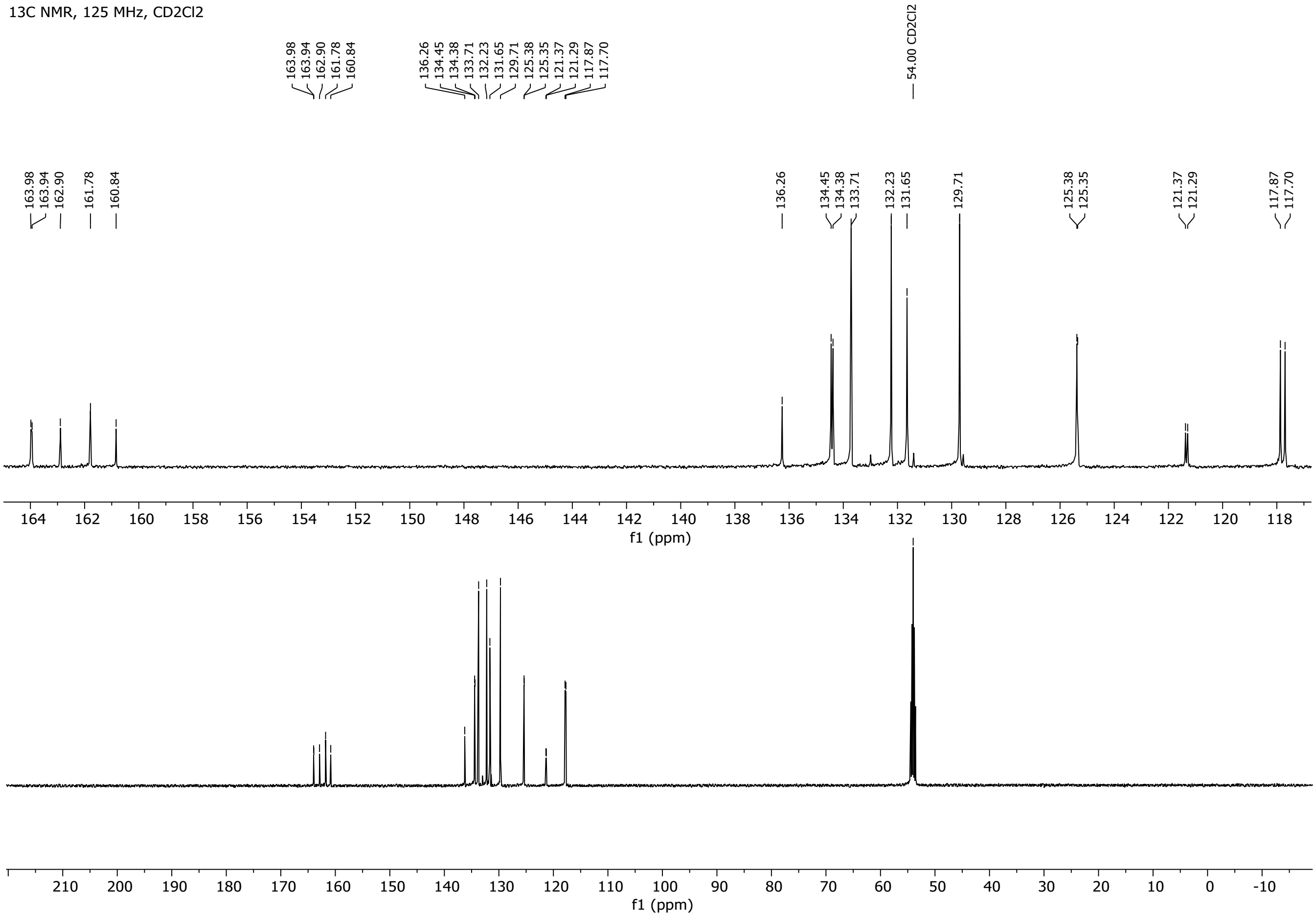
1H NMR, 500 MHz, CD2Cl2



19F NMR, 470 MHz, CD2Cl2

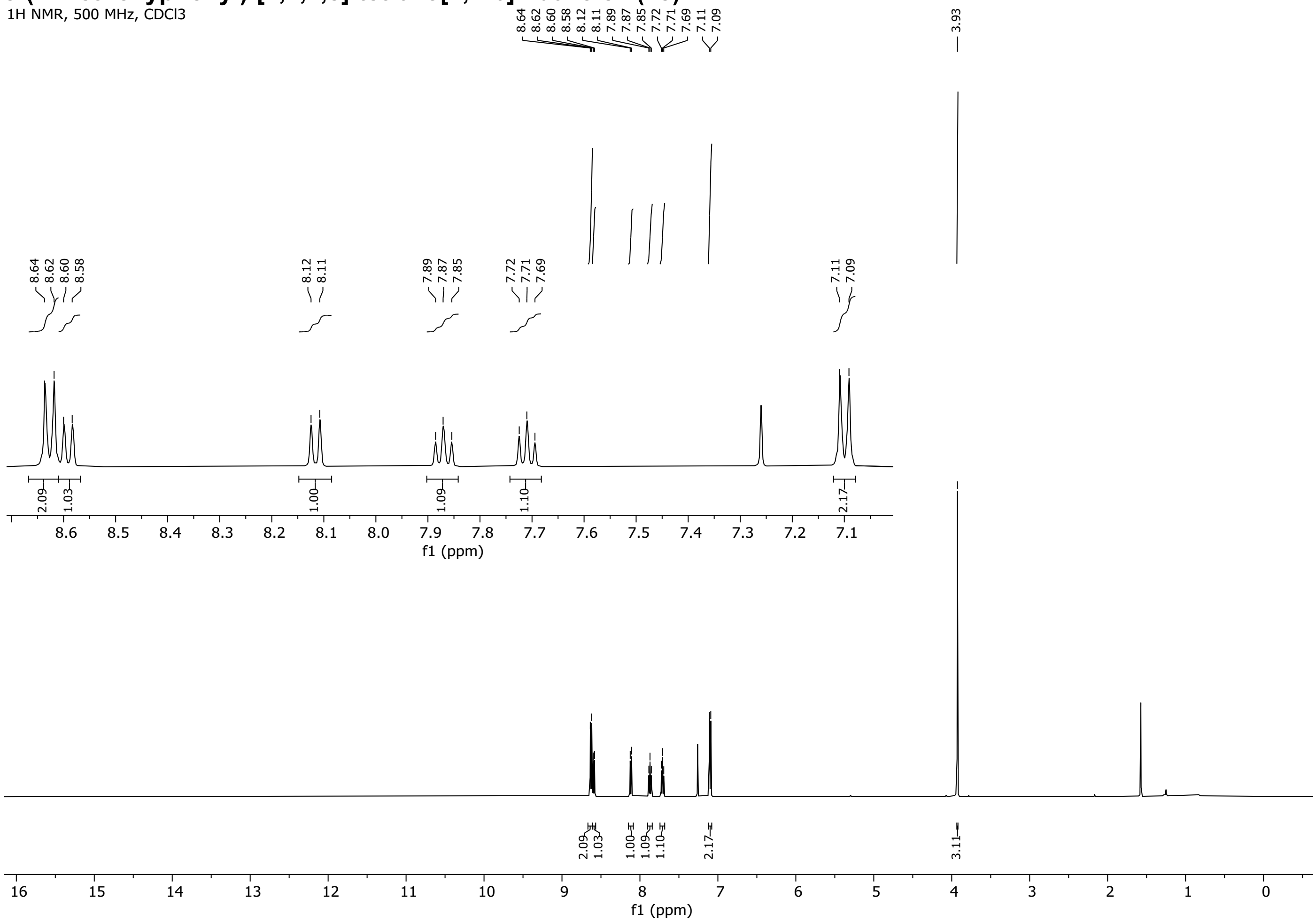


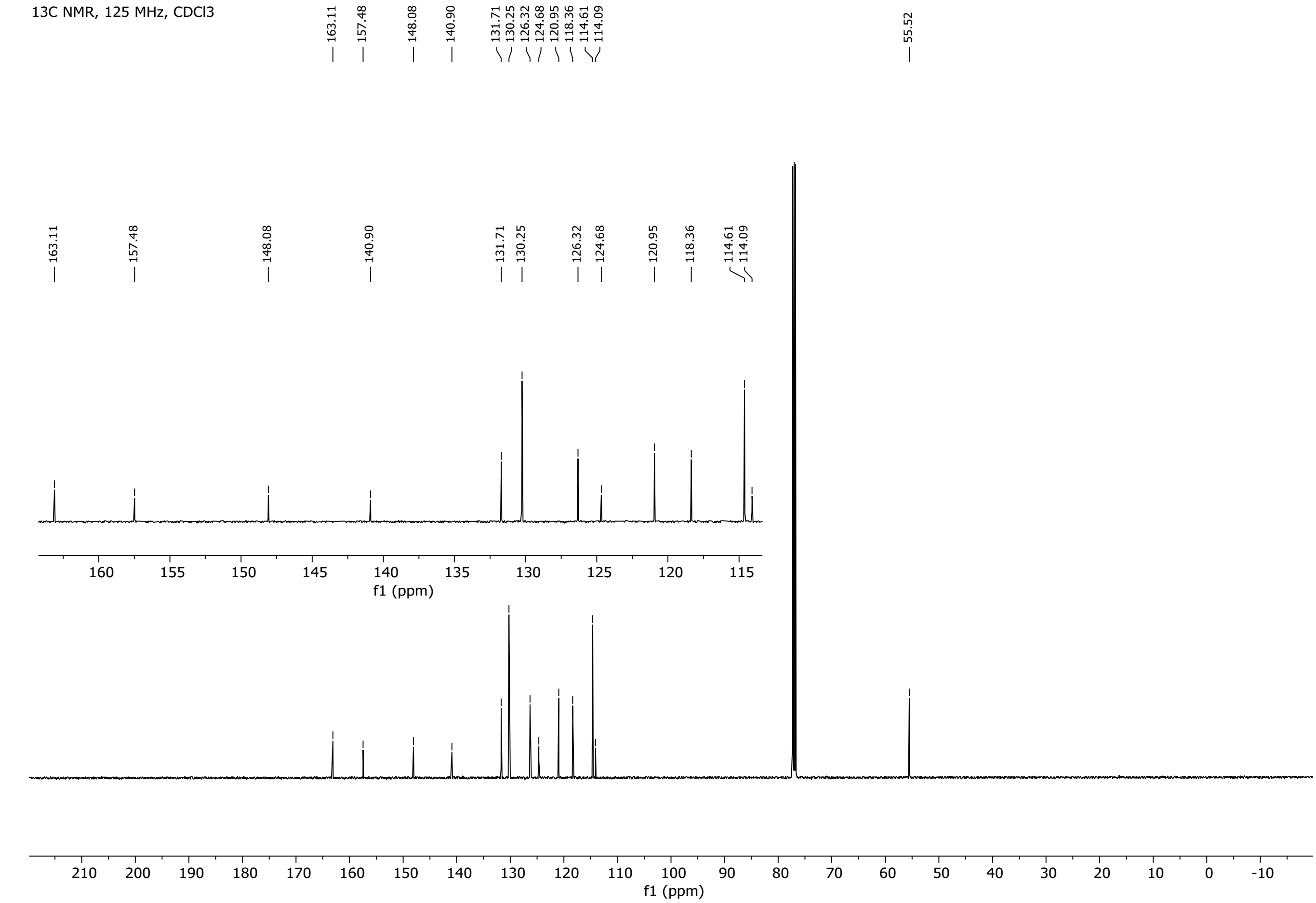
13C NMR, 125 MHz, CD2Cl2



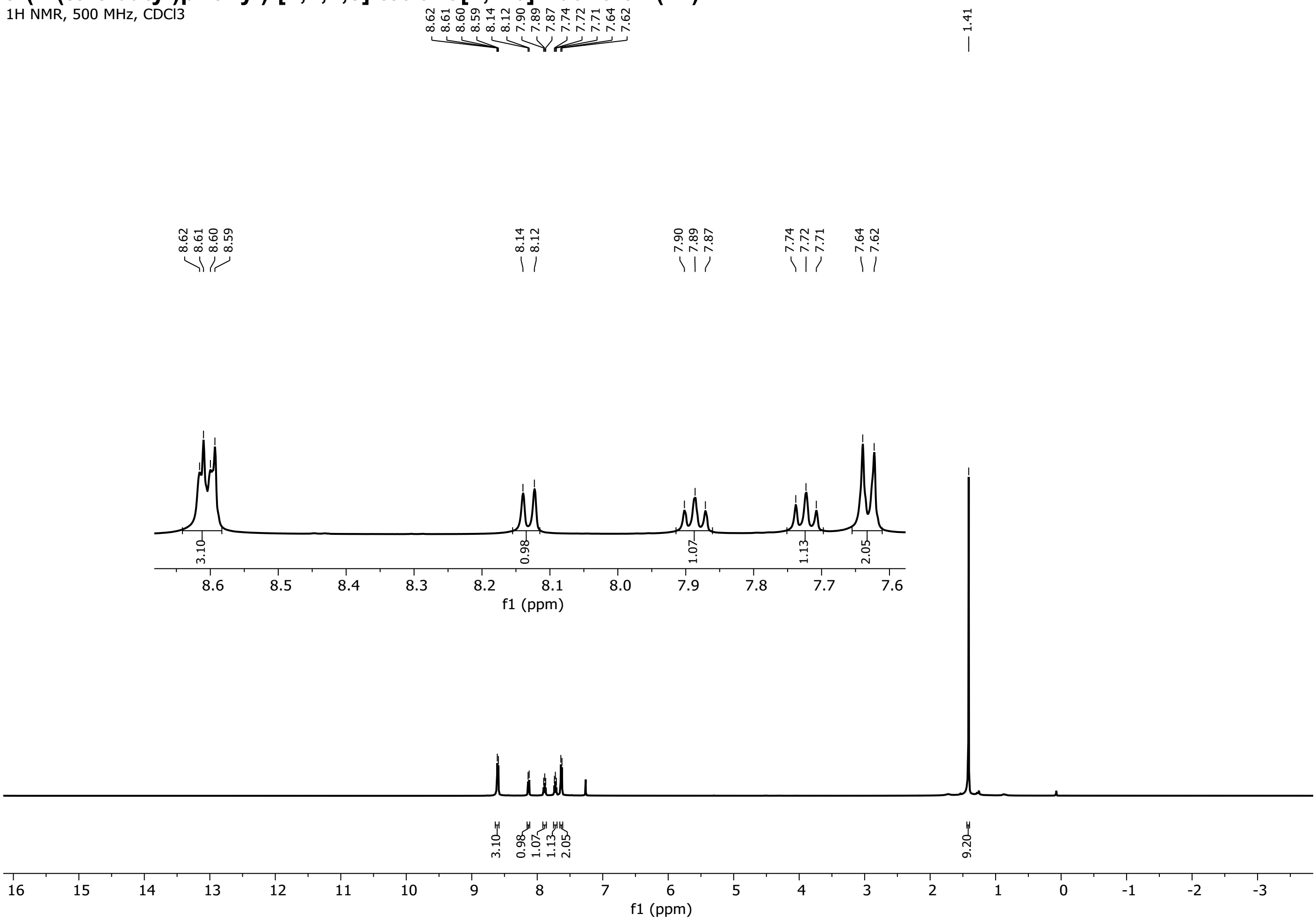
3-(4-methoxyphenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (13)

1H NMR, 500 MHz, CDCl3

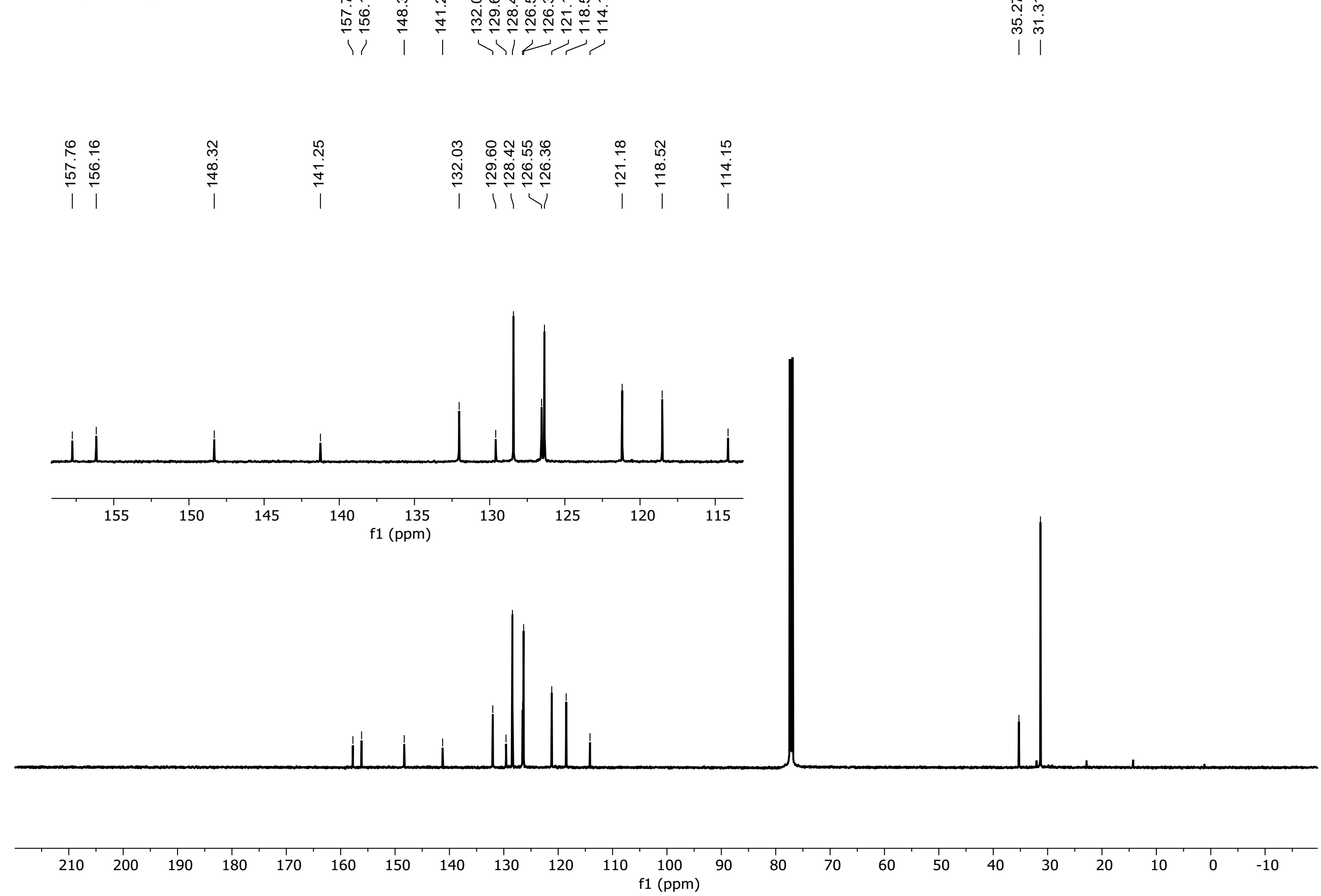




3-(4-(*tert*-butyl)phenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (14)

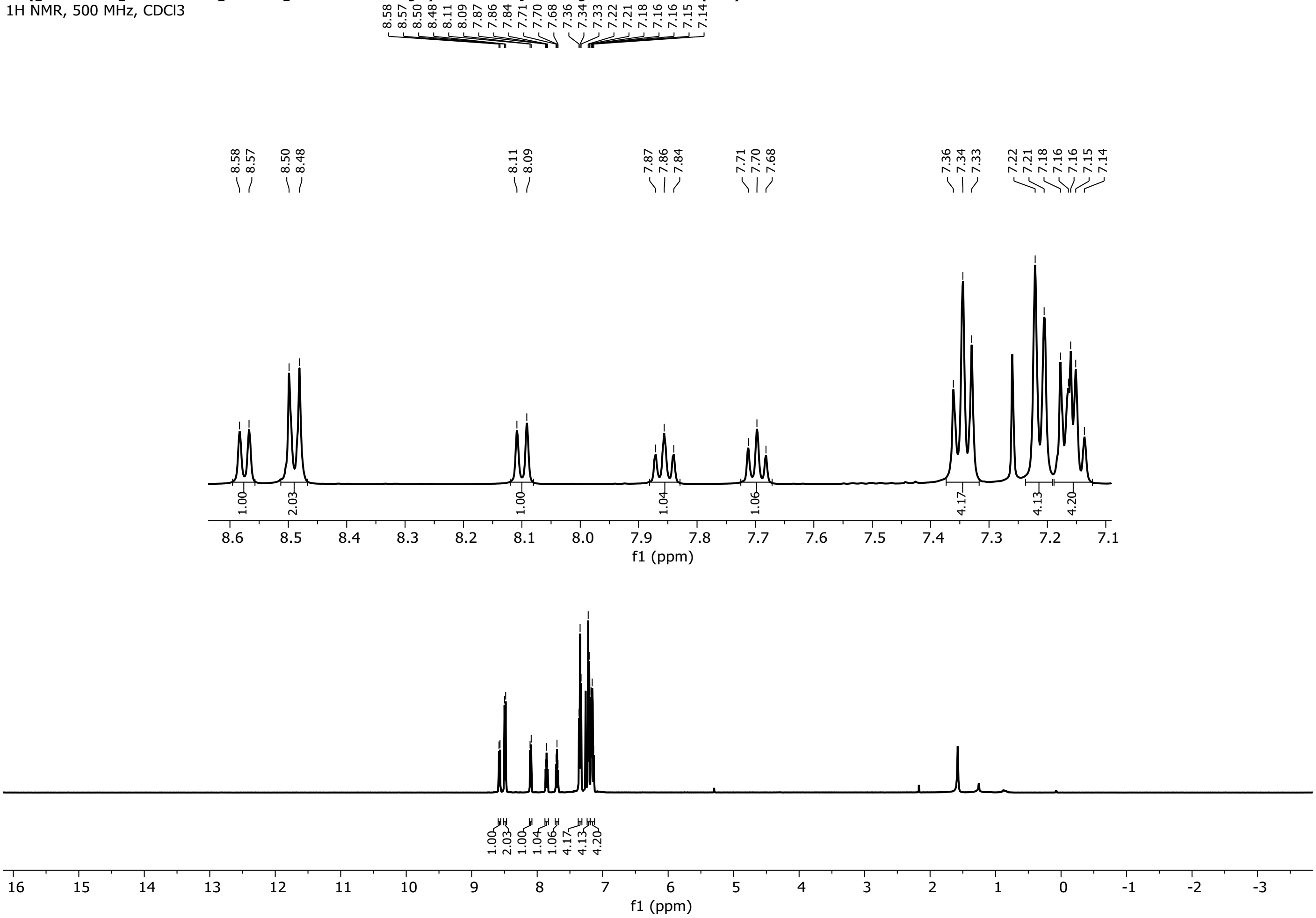


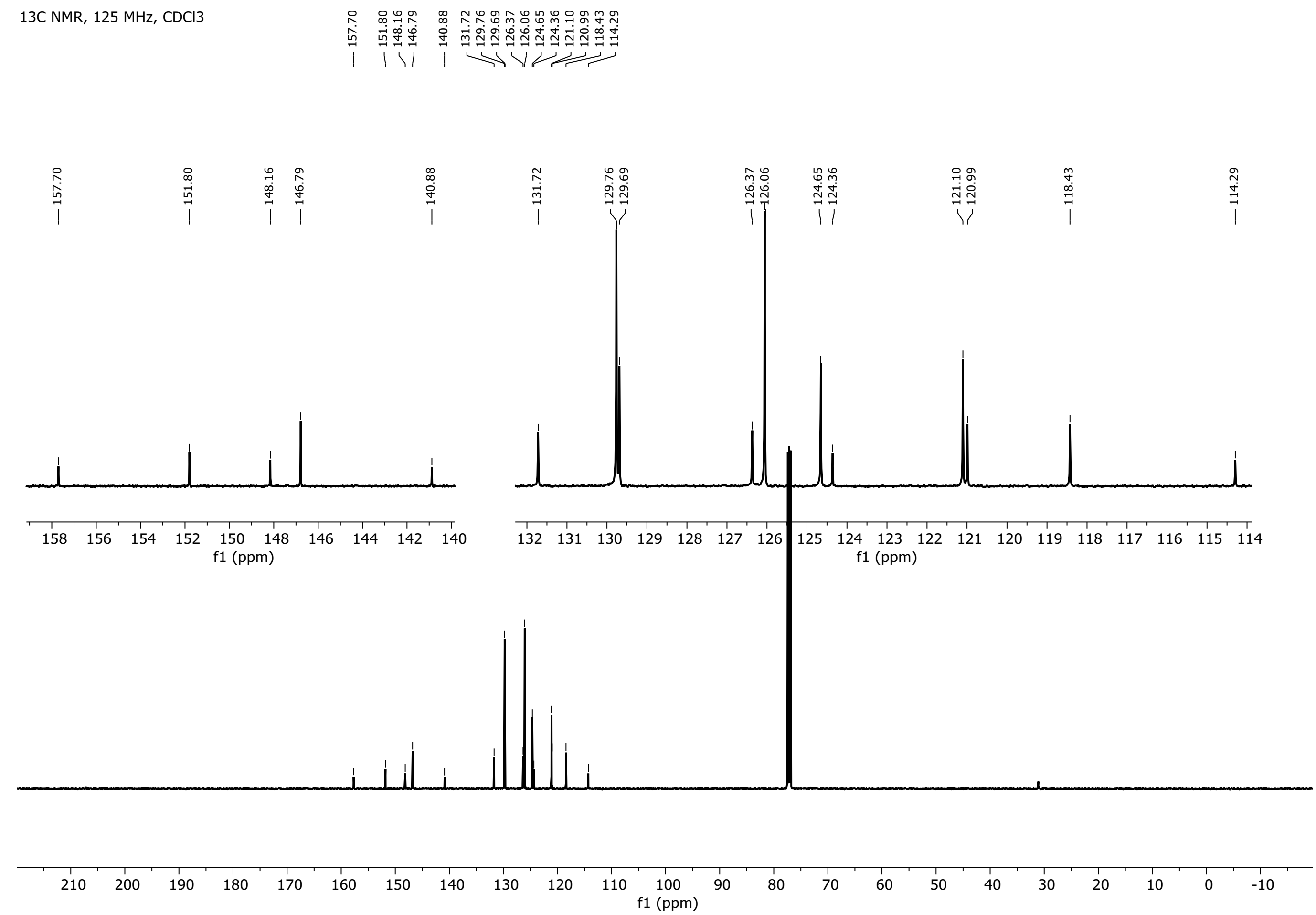
13C NMR, 125 MHz, CDCl3



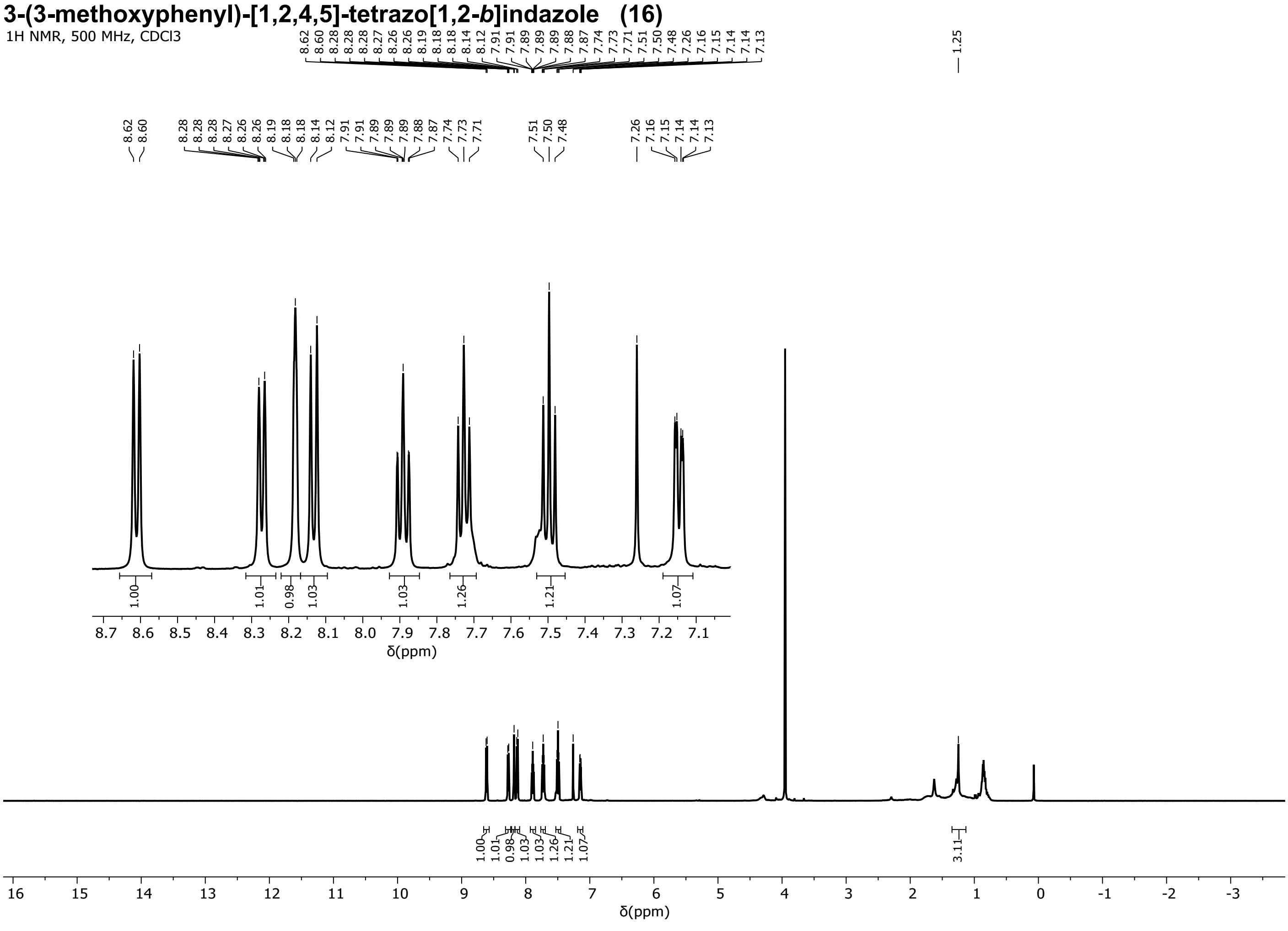
4-([1,2,4,5]-tetrazo[1,2-*b*]indazol-3-yl)-*N*,*N*-diphenylaniline (15)

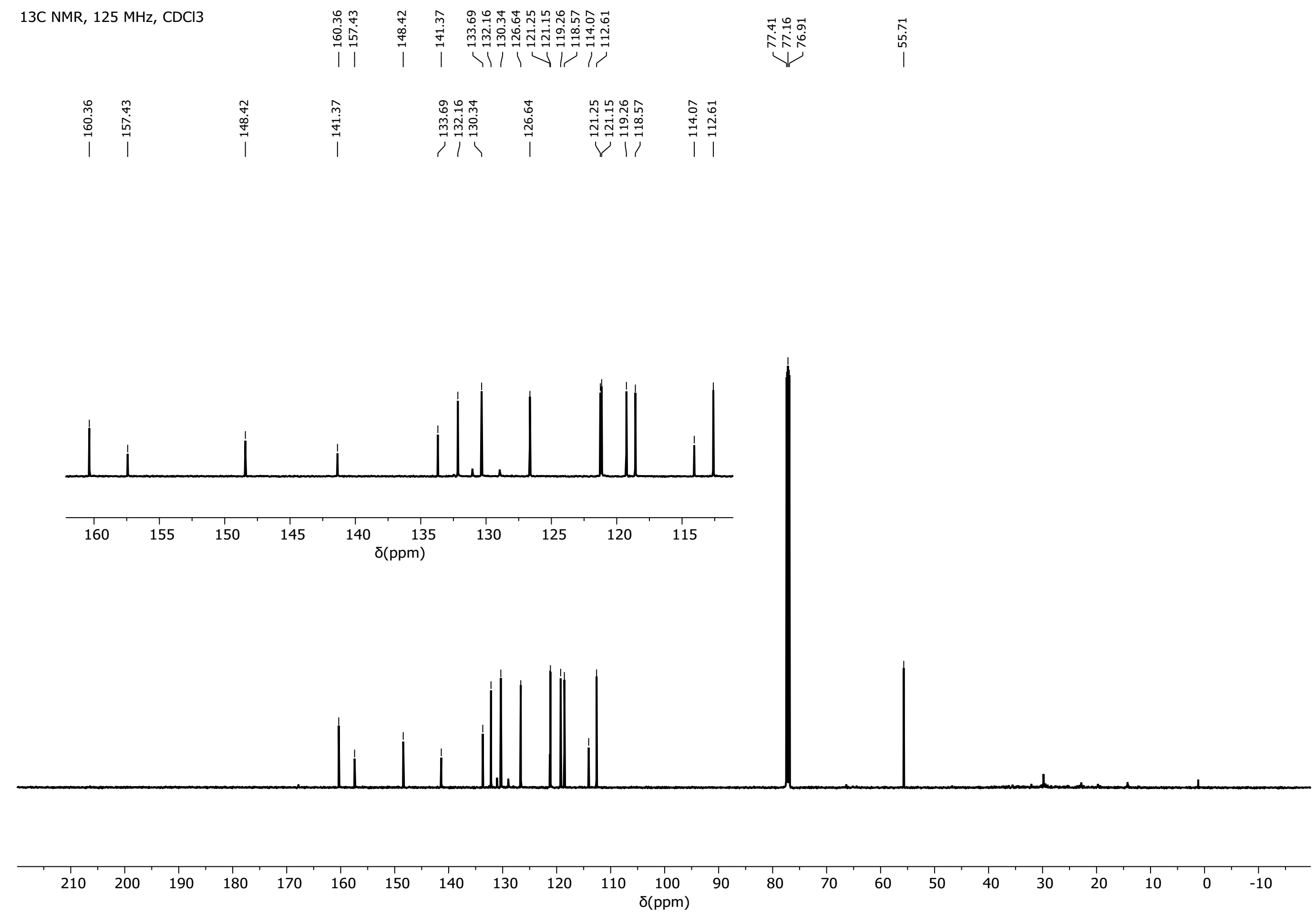
1H NMR, 500 MHz, CDCl3



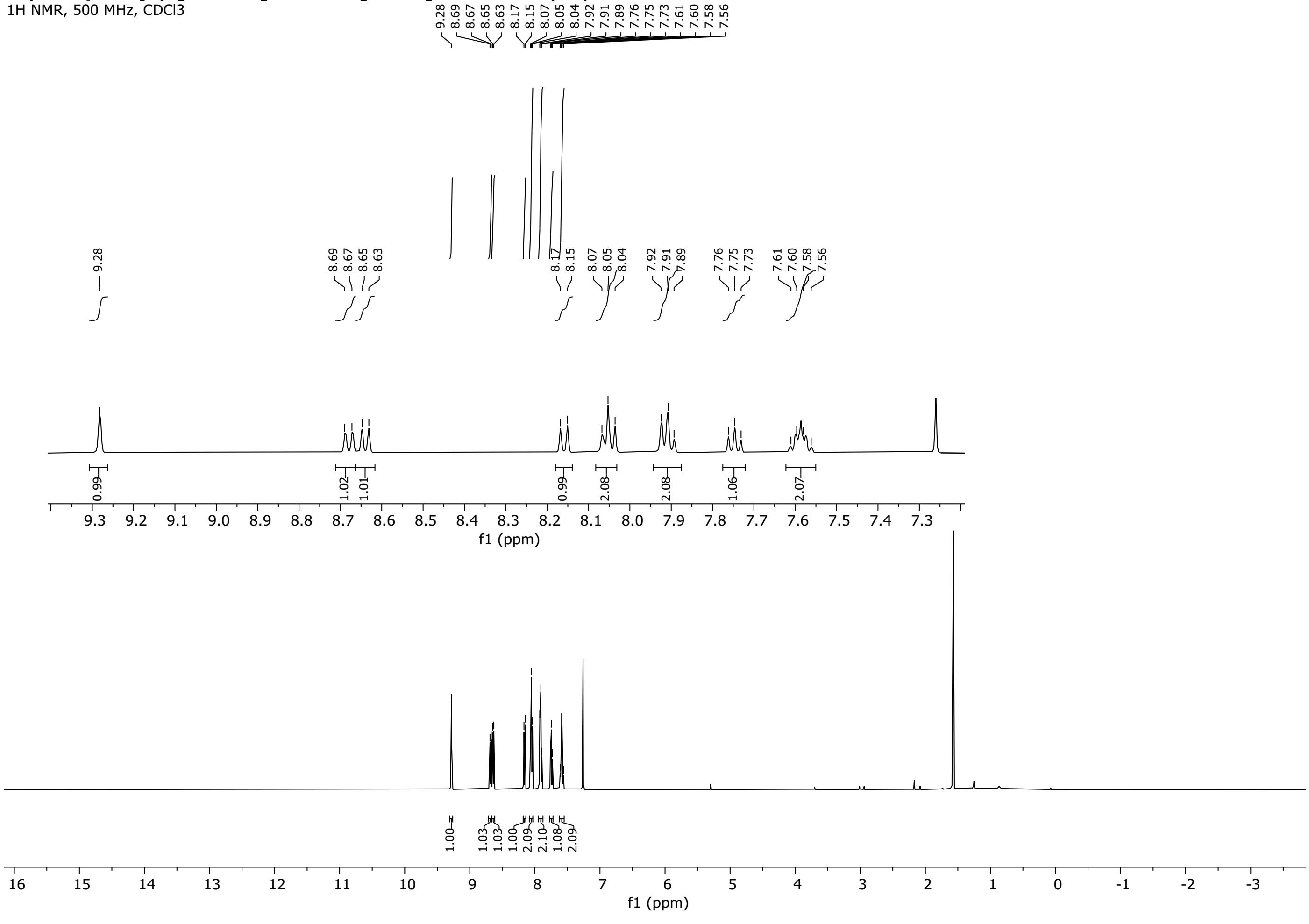


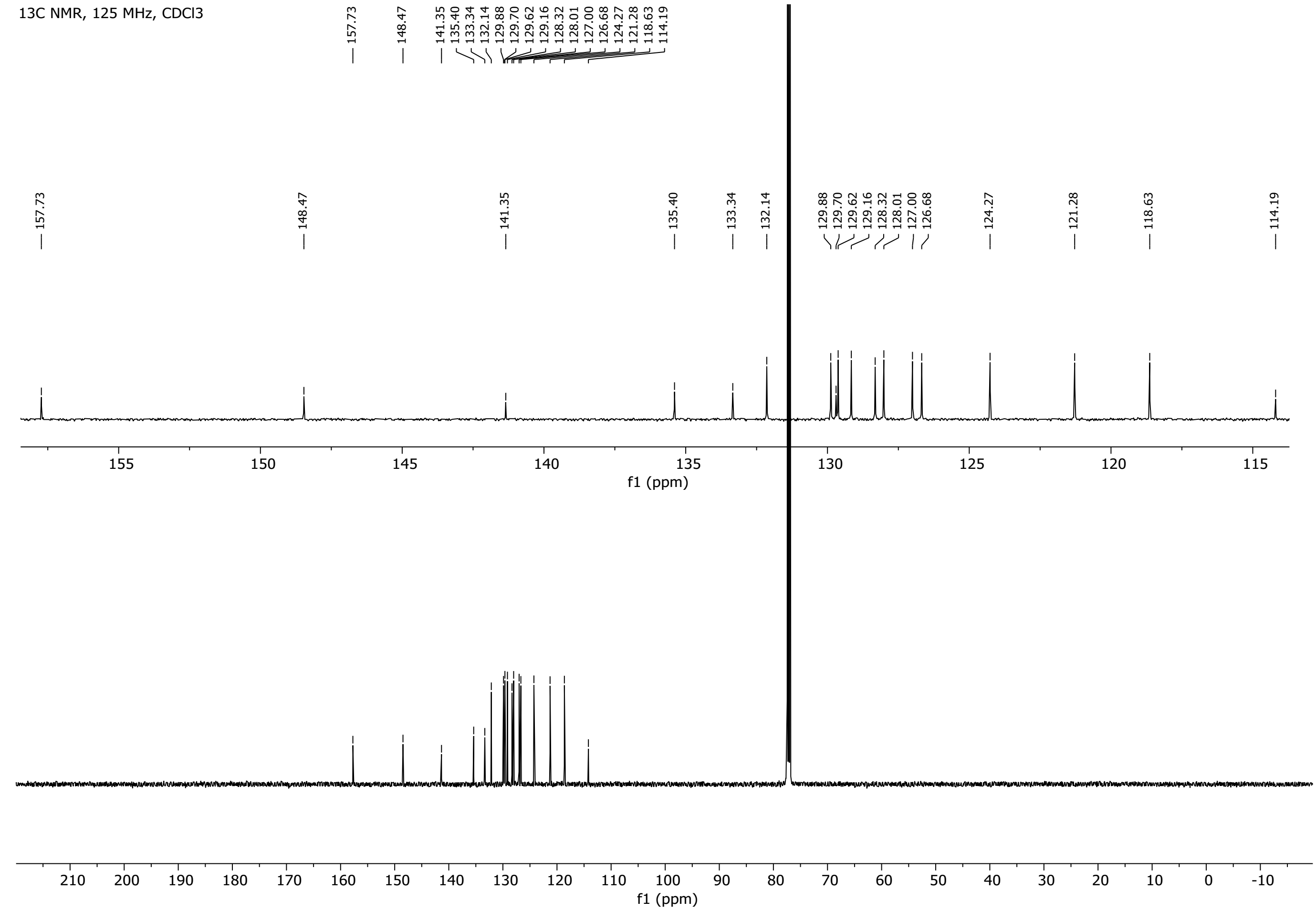
3-(3-methoxyphenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (16)



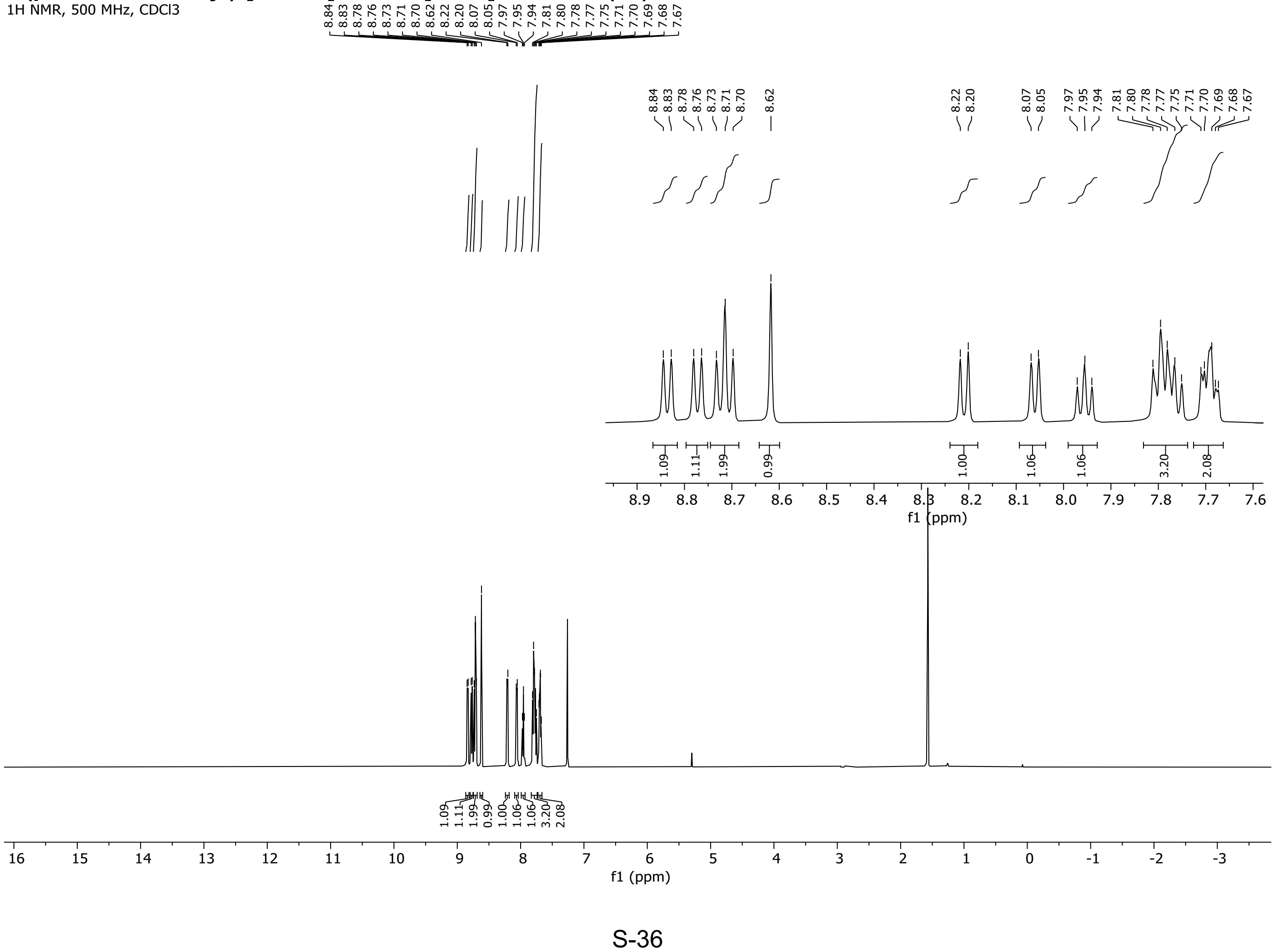


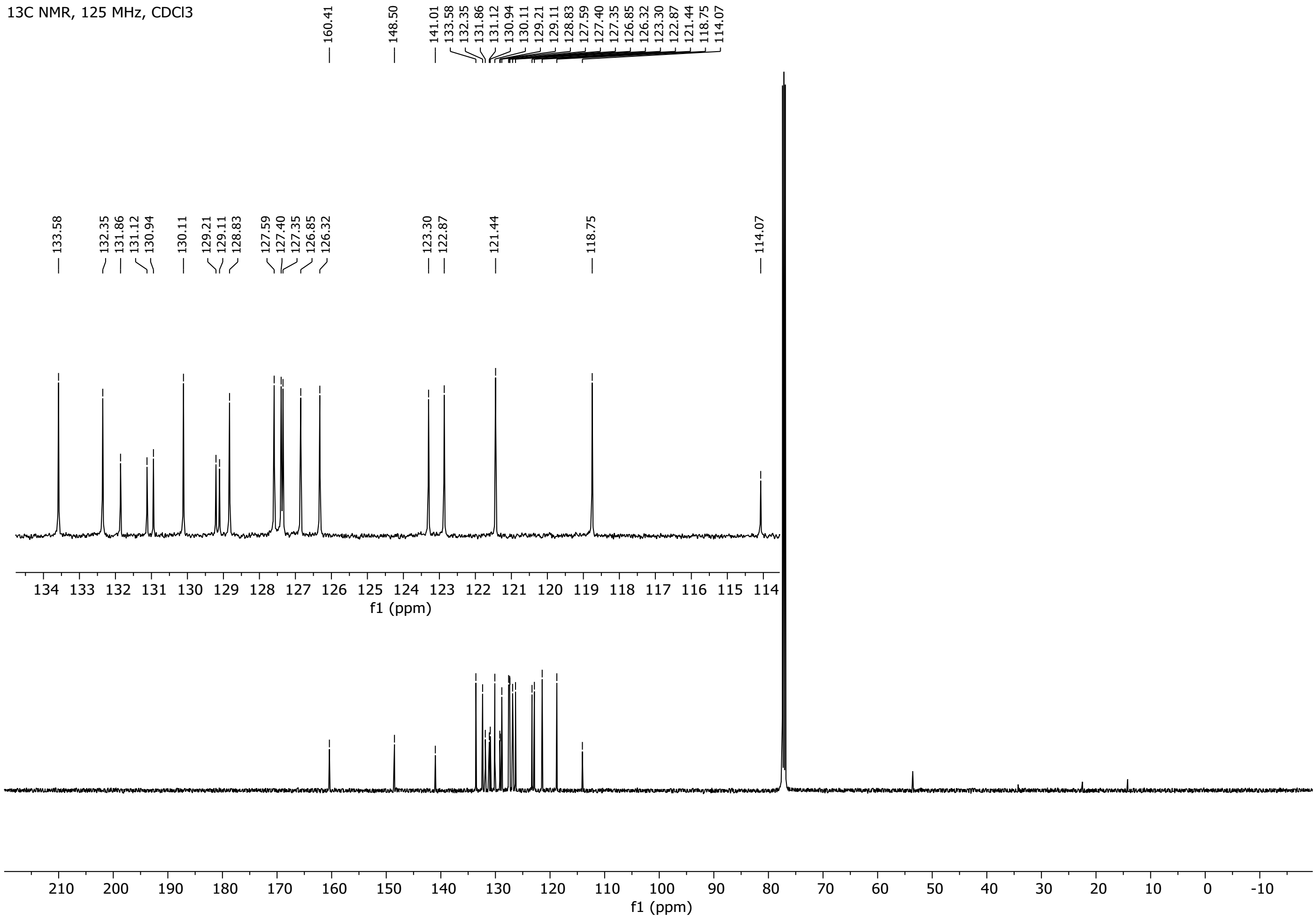
3-(1-naphthyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (18)



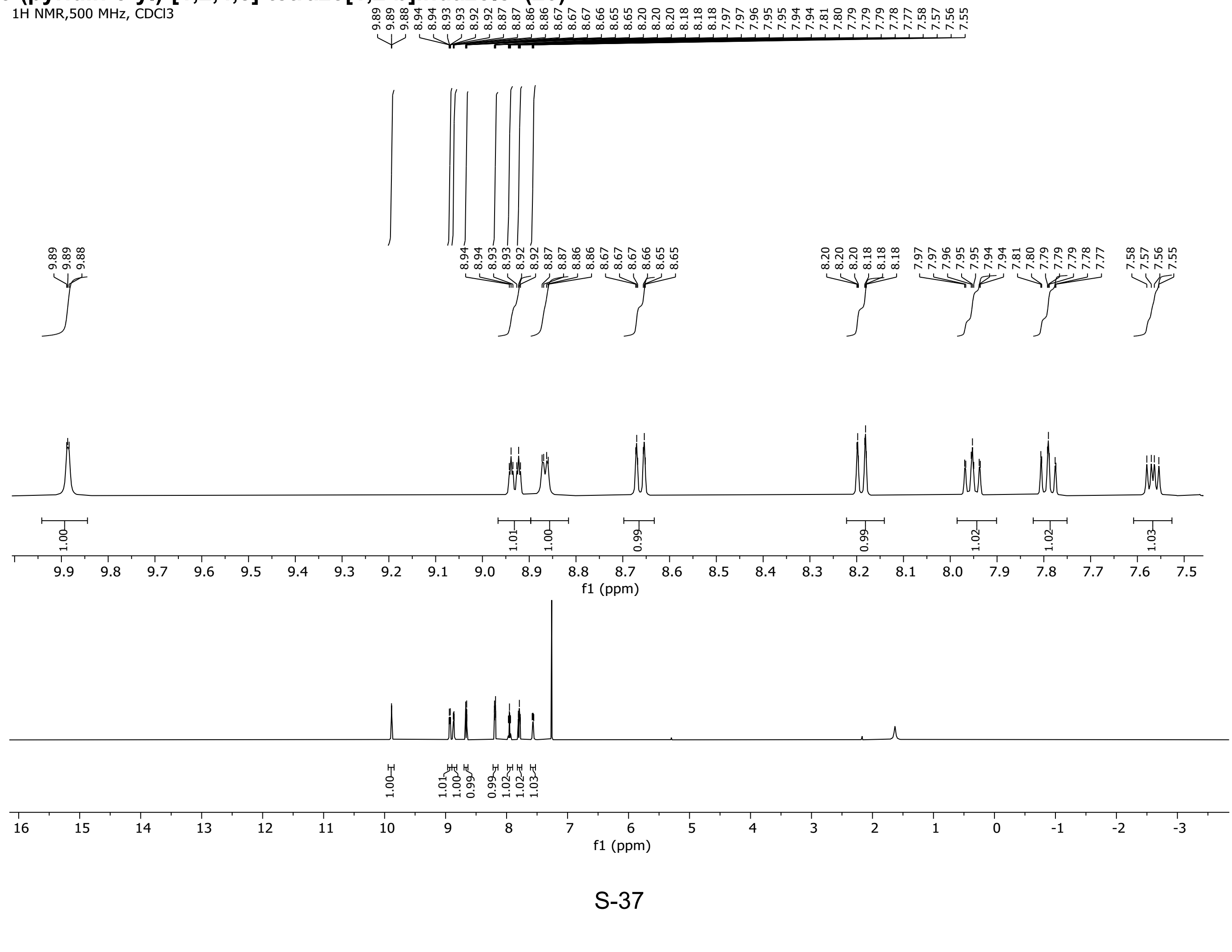


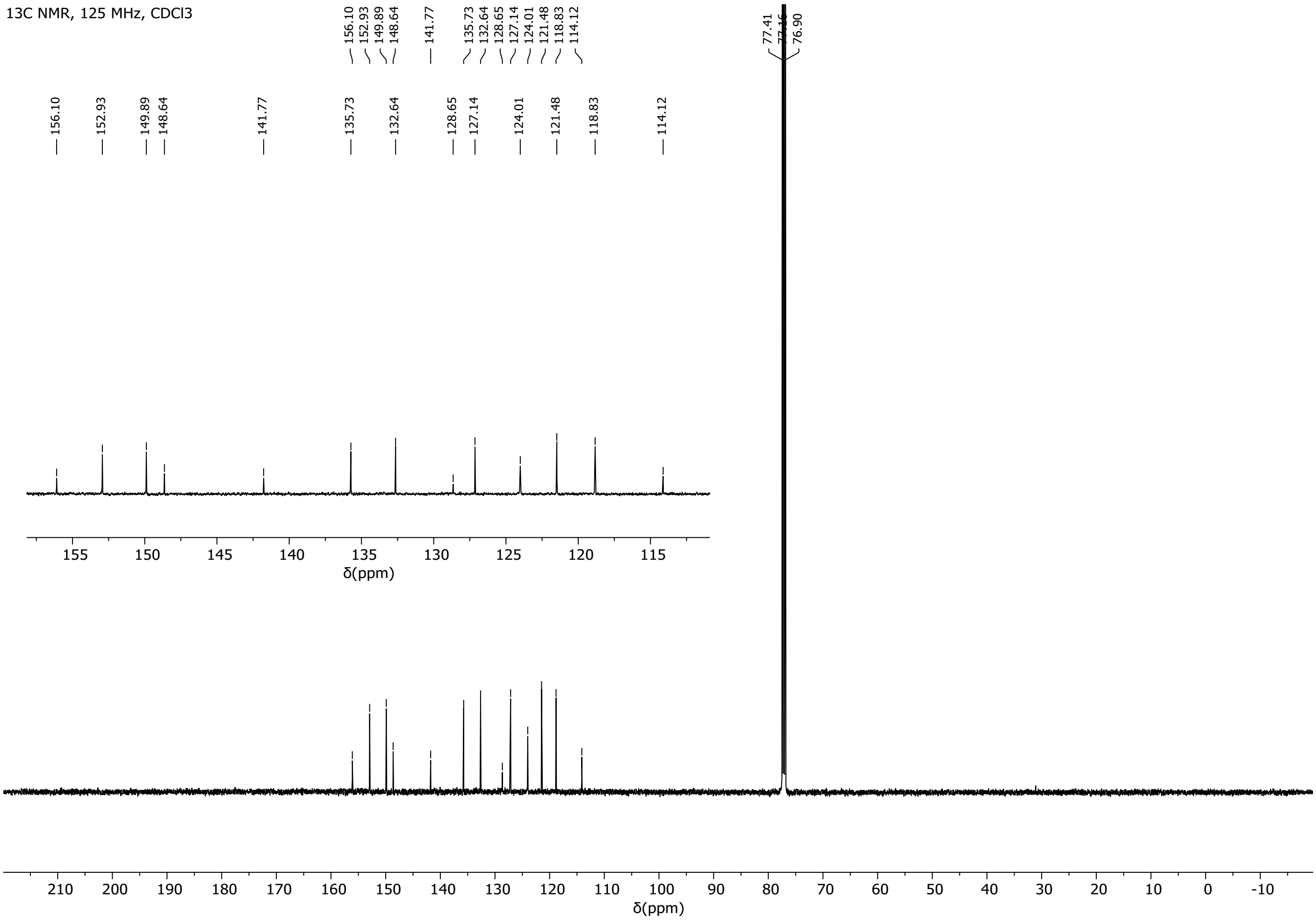
3-(phenanthren-9-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (19)



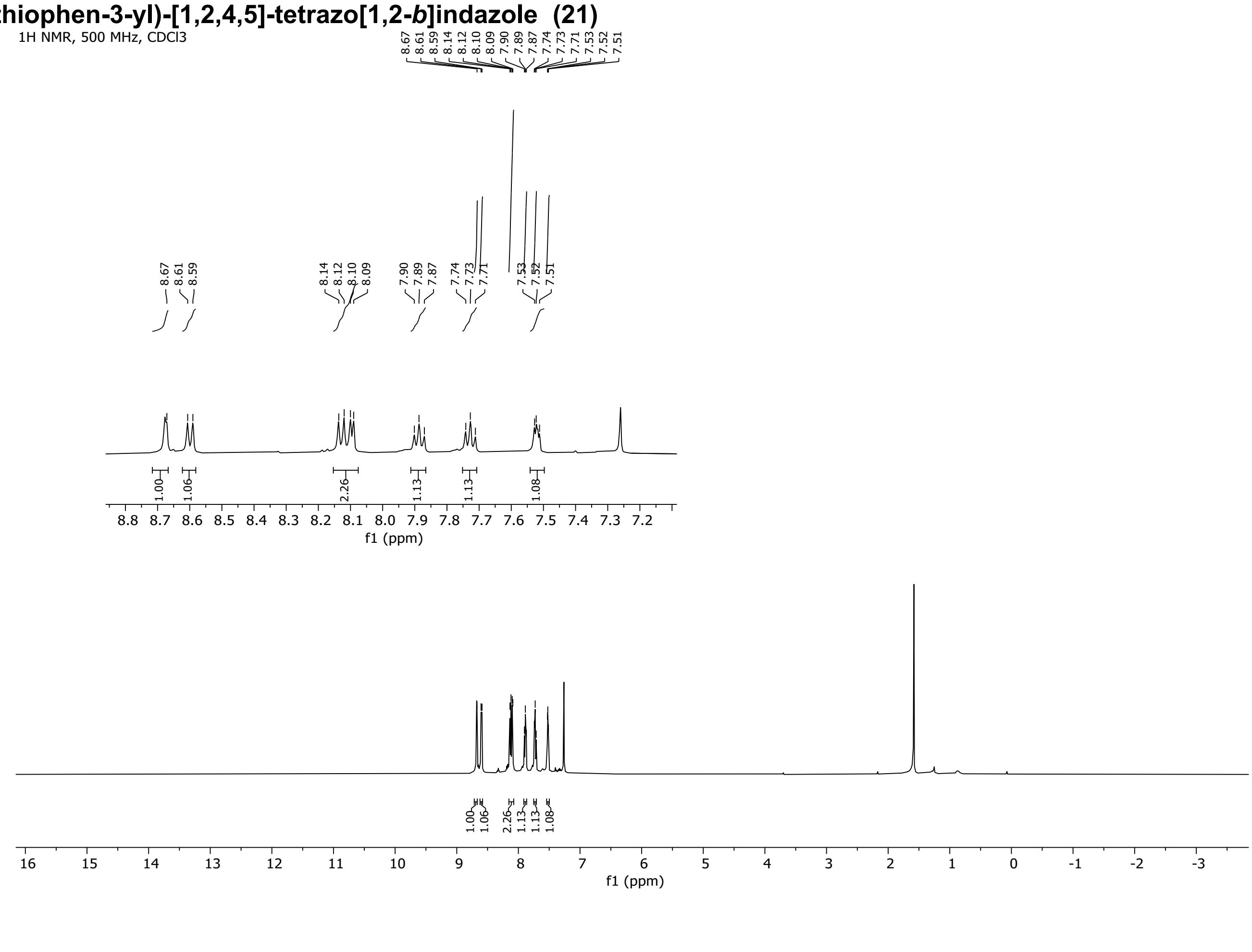


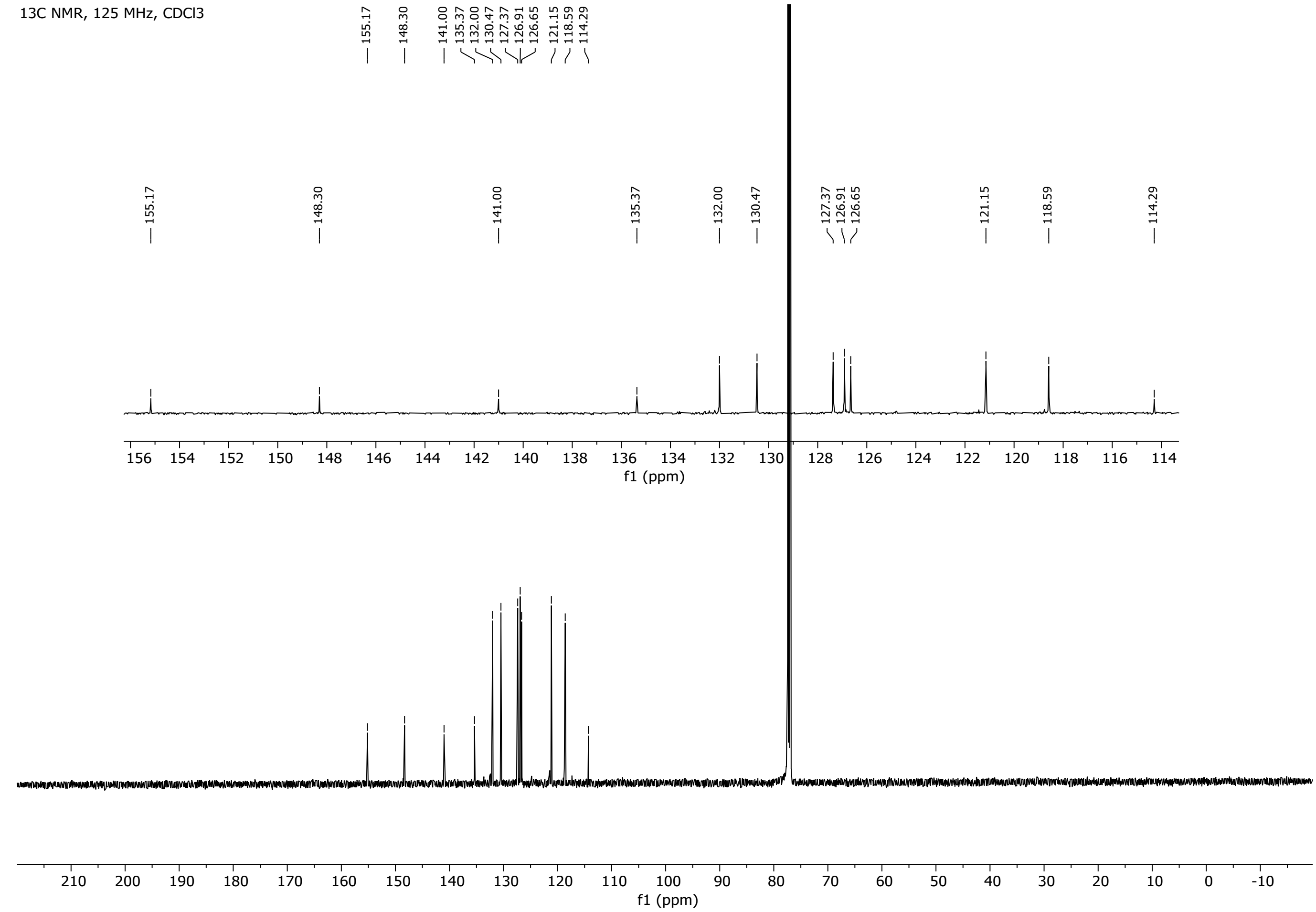
6-(pyridin-3-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (20)



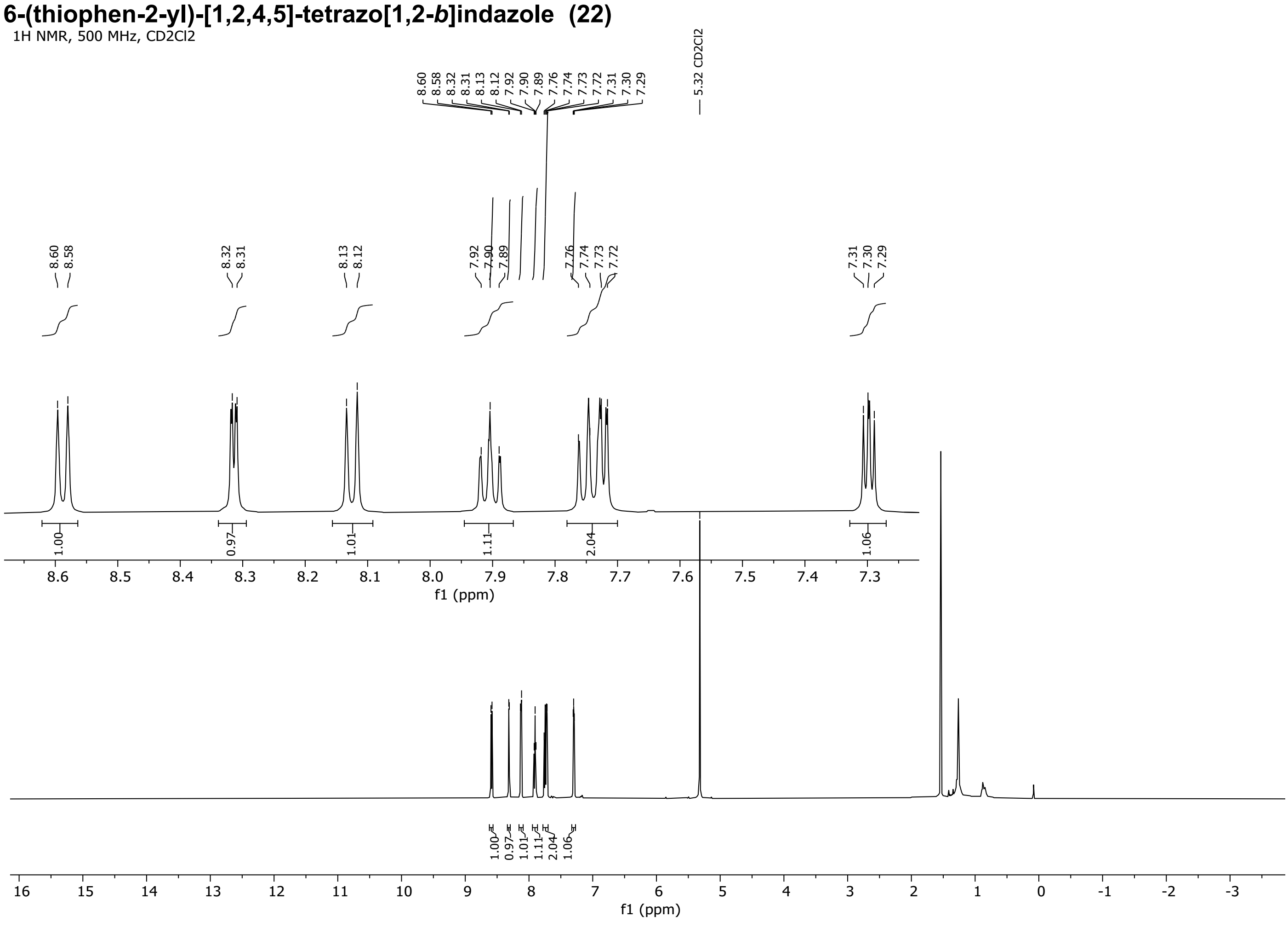


6-(thiophen-3-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (21)

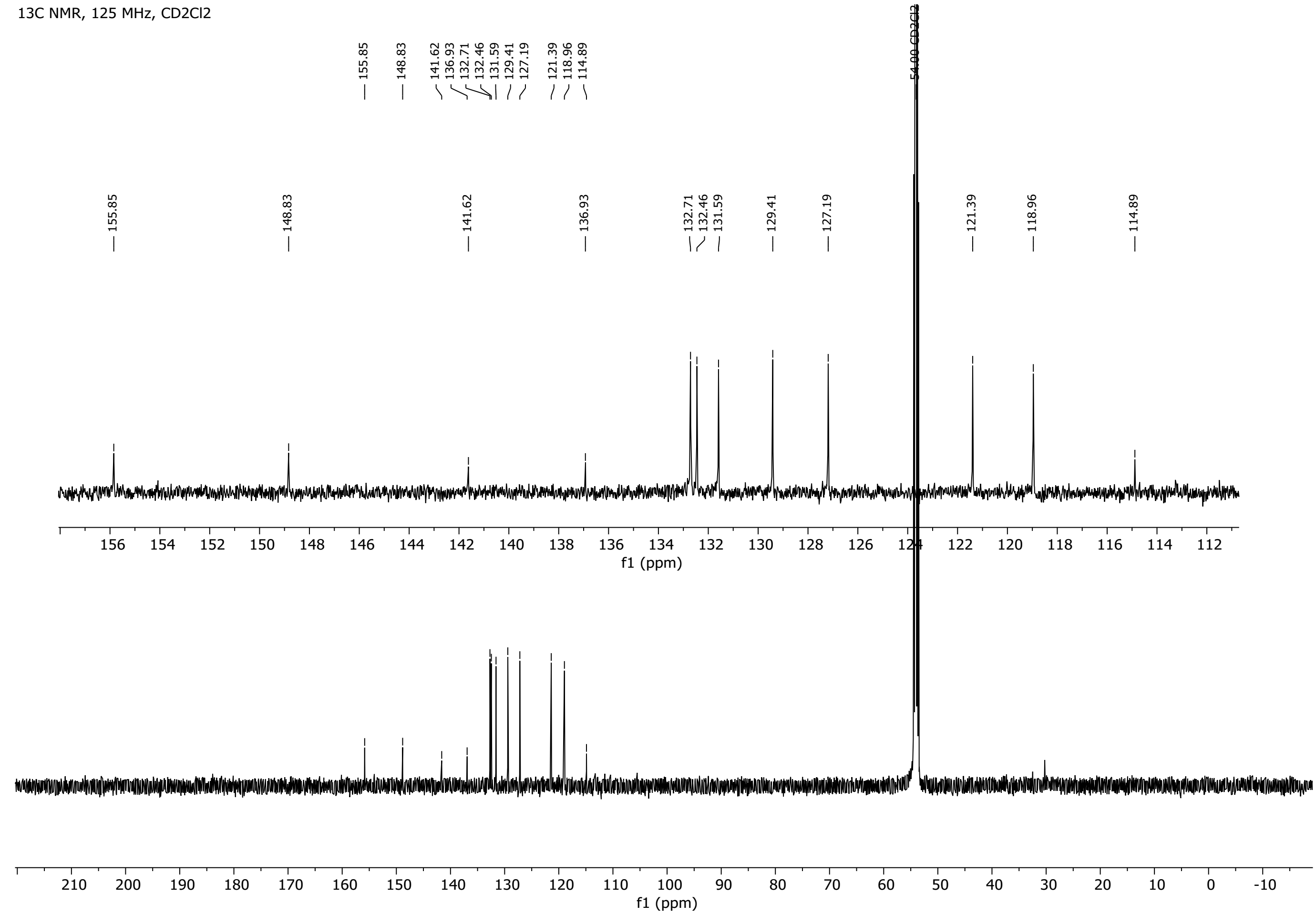




6-(thiophen-2-yl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (22)

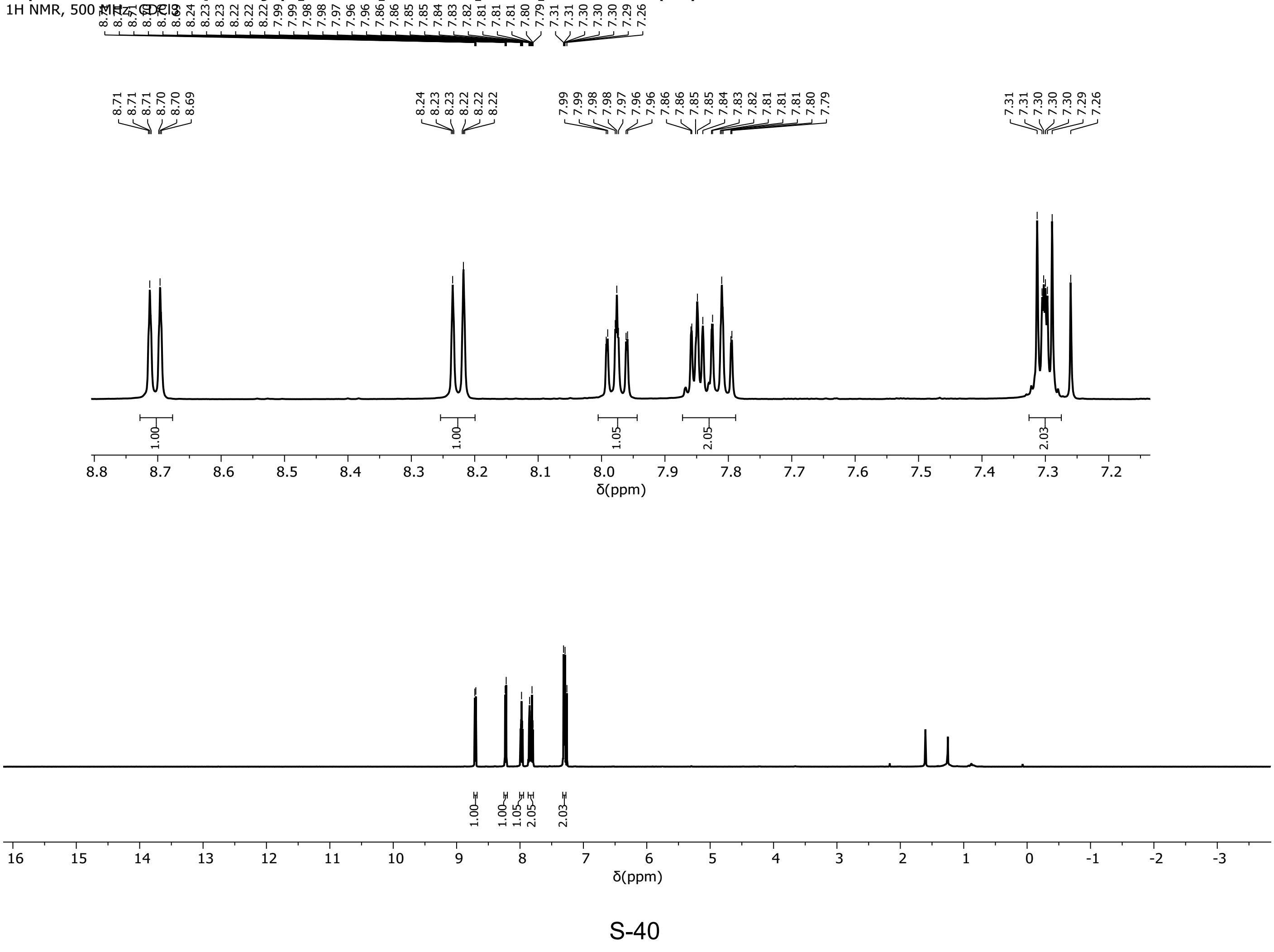


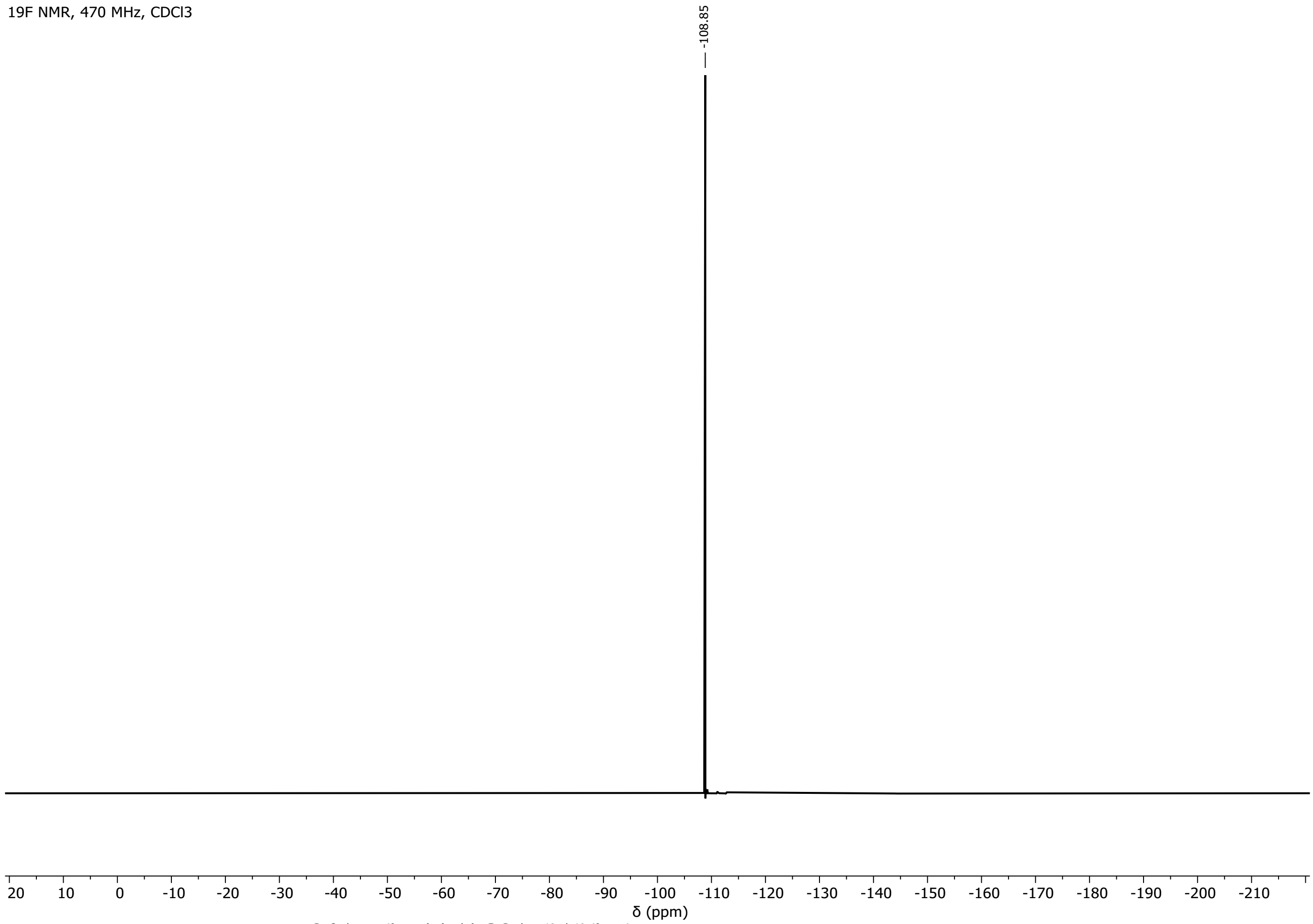
13C NMR, 125 MHz, CD2Cl2



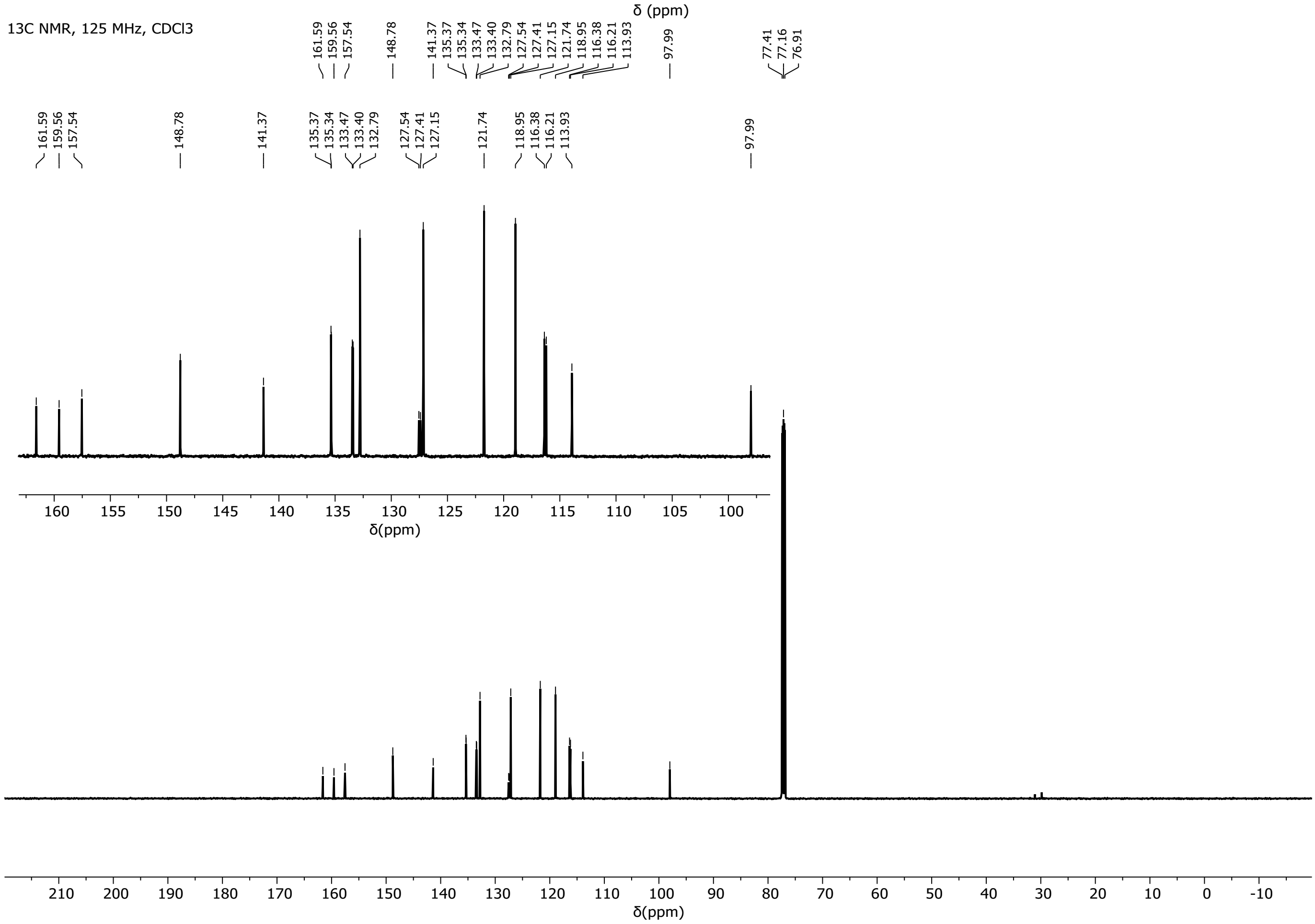
6-(2-fluoro-6-iodophenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (23)

1H NMR, 500 MHz, CDCl3





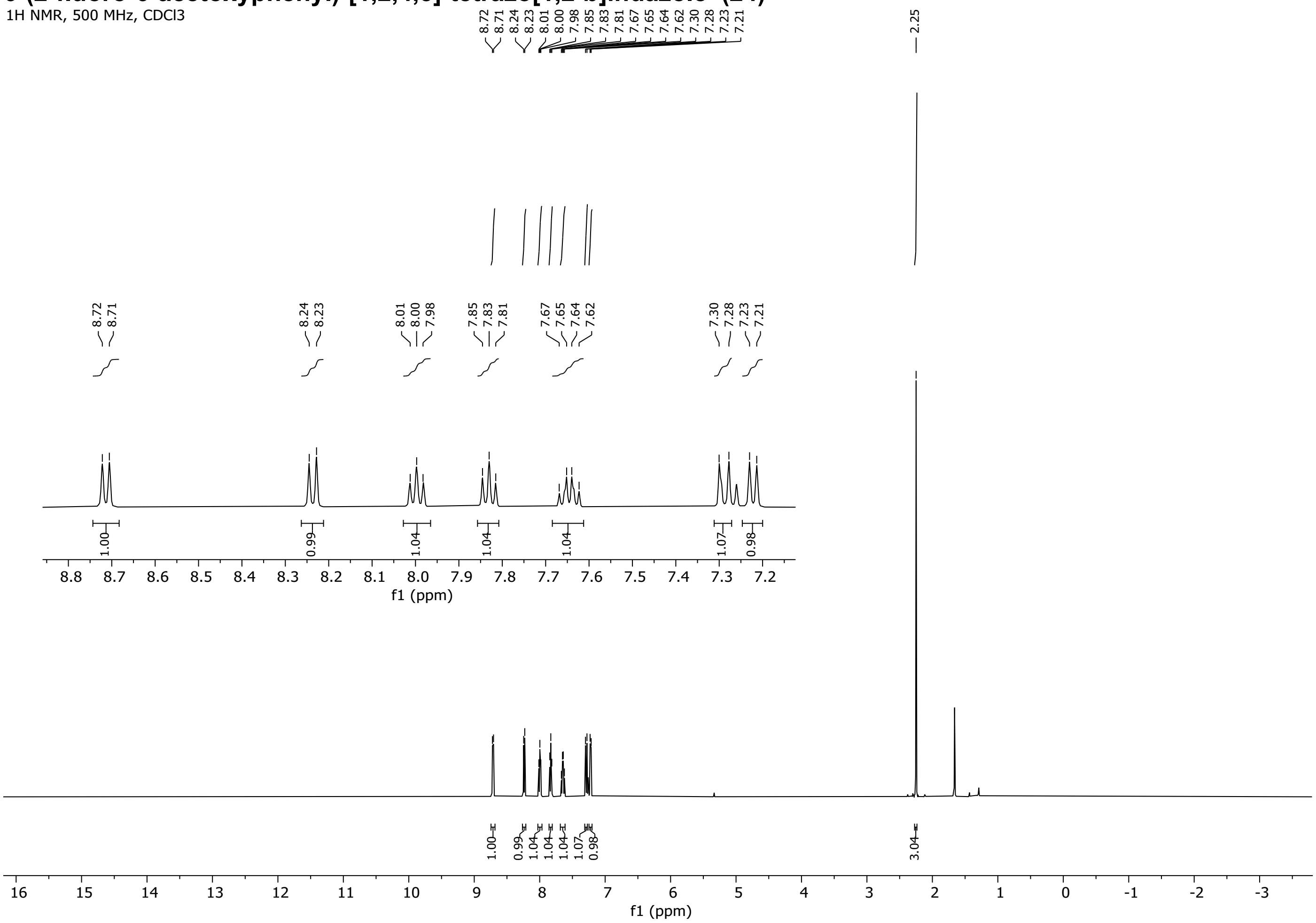
19F NMR, 470 MHz, CDCl3
-108.85
δ (ppm)



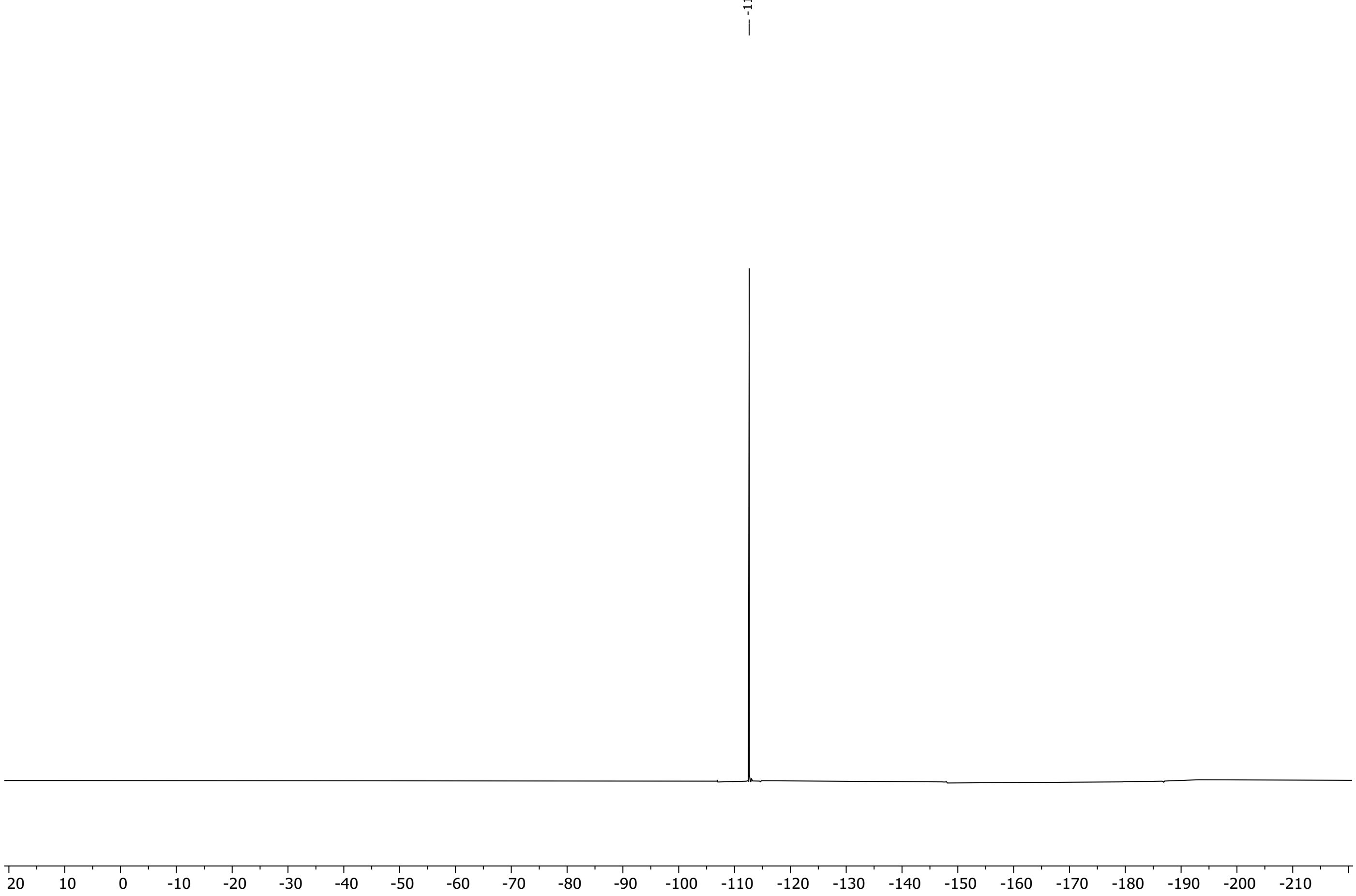
13C NMR, 125 MHz, CDCl3
161.59
159.56
157.54
148.78
141.37
135.37
135.34
133.47
133.40
132.79
127.54
127.41
127.15
121.74
118.95
116.38
116.21
113.93
97.99
77.41
77.16
76.91
δ(ppm)

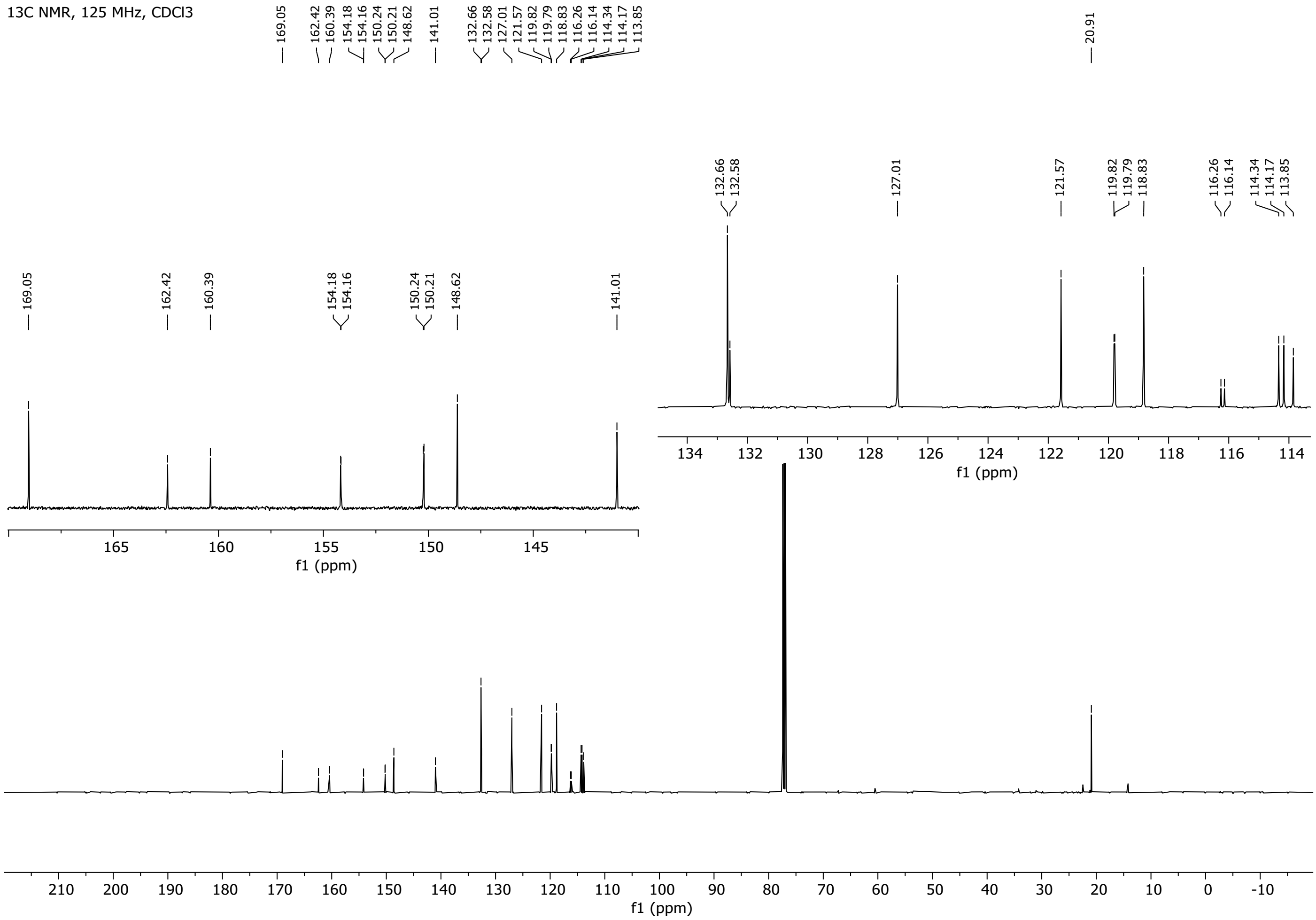
6-(2-fluoro-6-acetoxyphenyl)-[1,2,4,5]-tetrazo[1,2-*b*]indazole (24)

1H NMR, 500 MHz, CDCl3

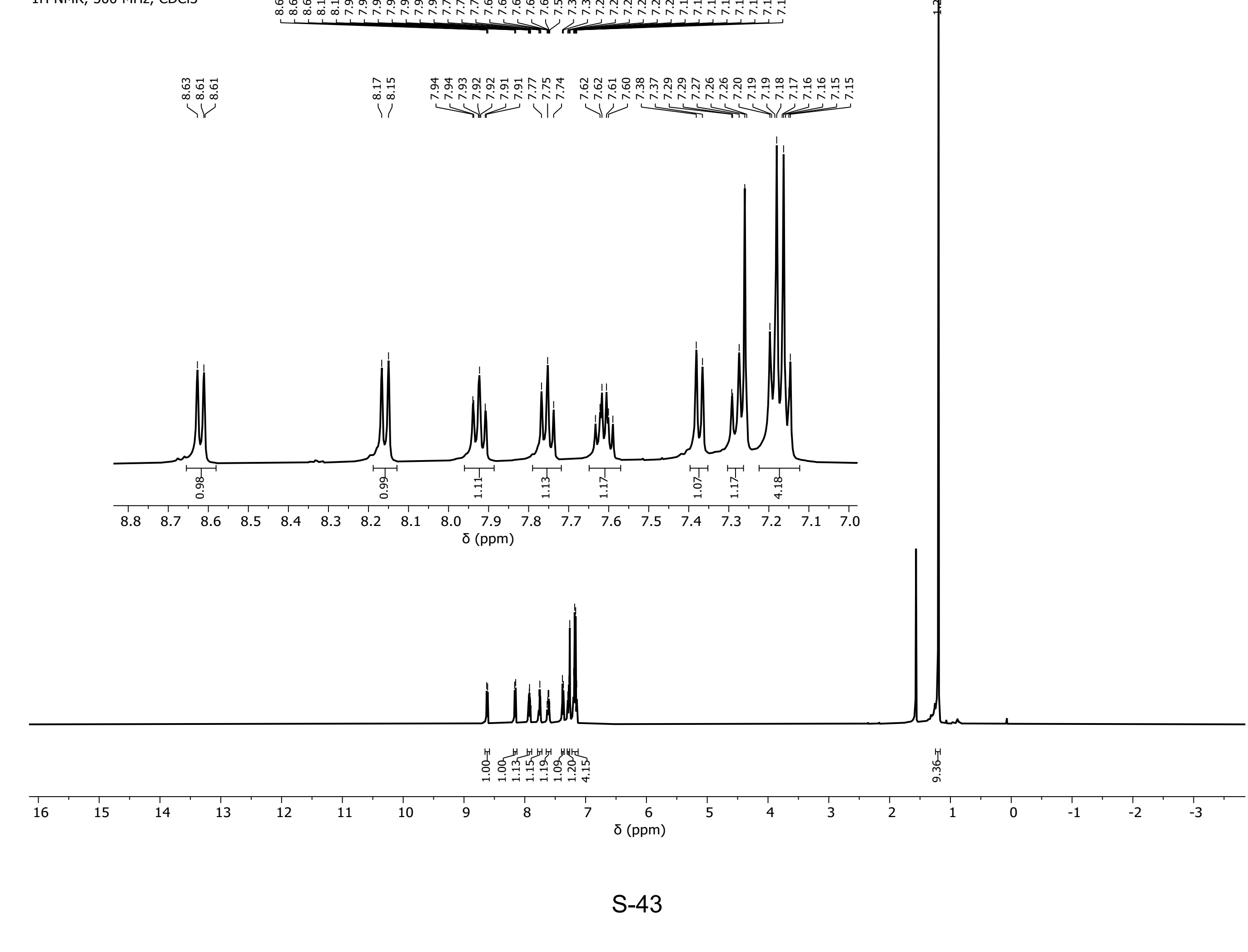


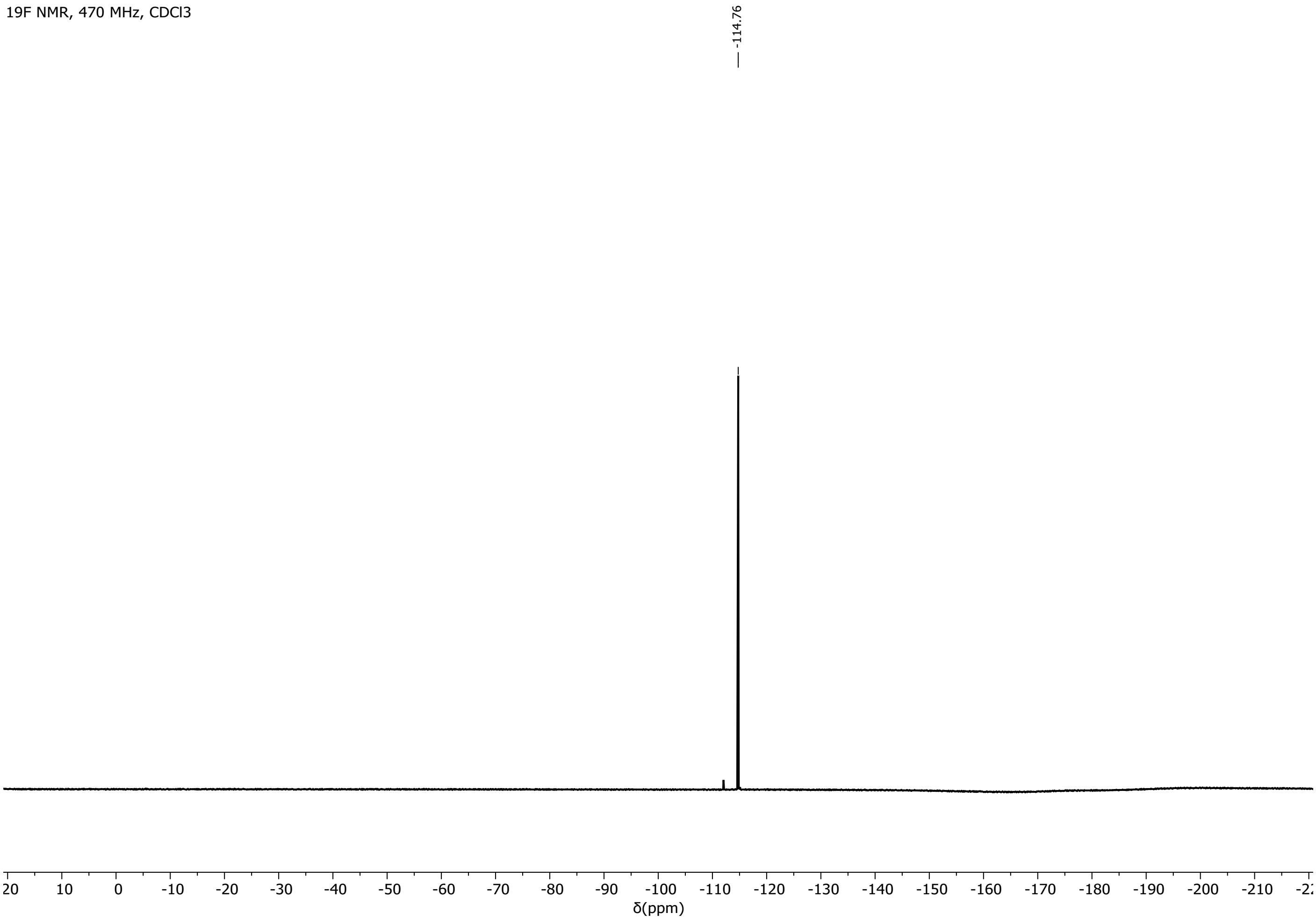
19F NMR, 470 MHz, CDCl3

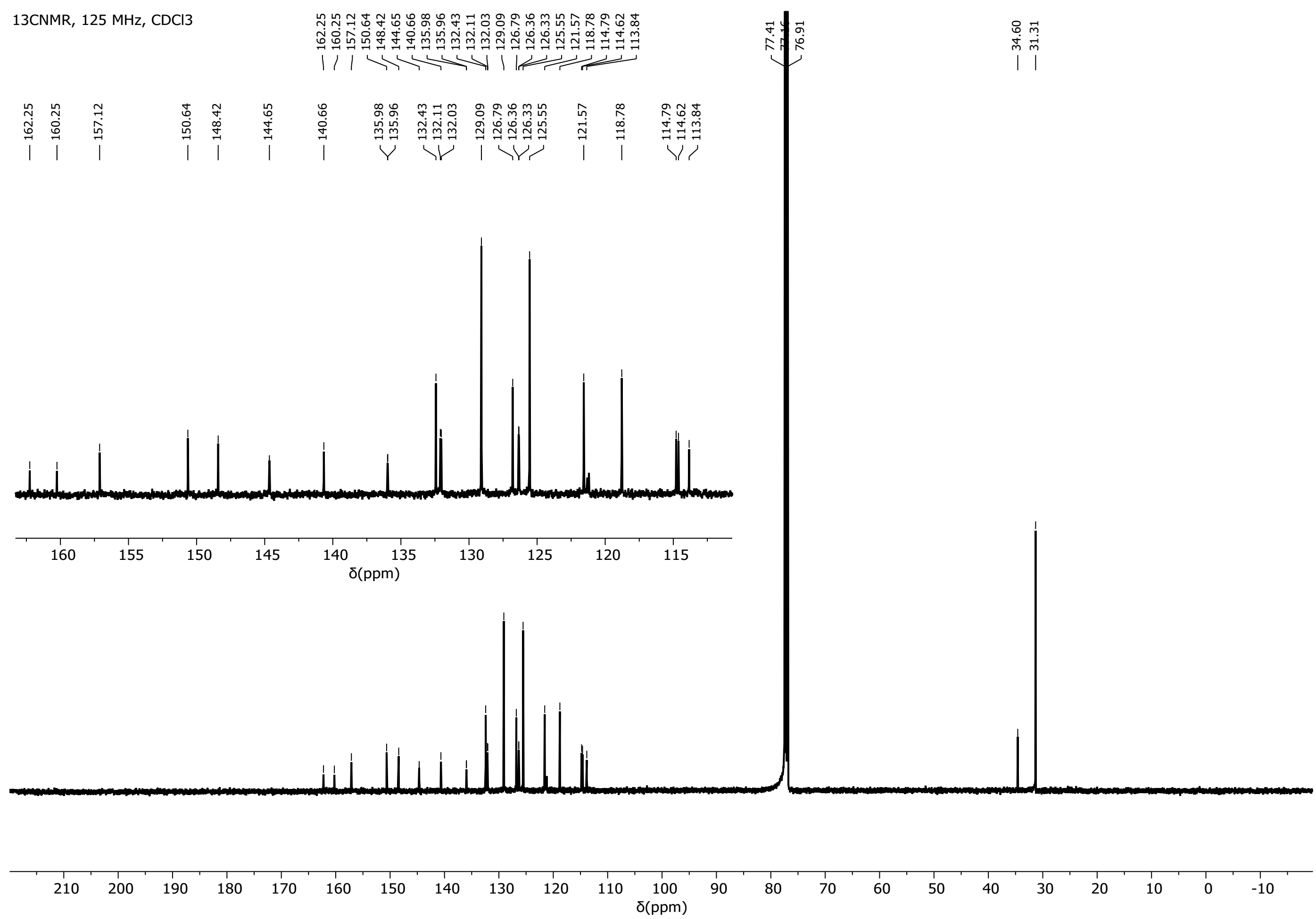




2-(fluoro)-6-(1-(4-*tert*-butyl)phenyl))-[1,2,4,5]-tetrazo[1,2-*b*]indazole (25)

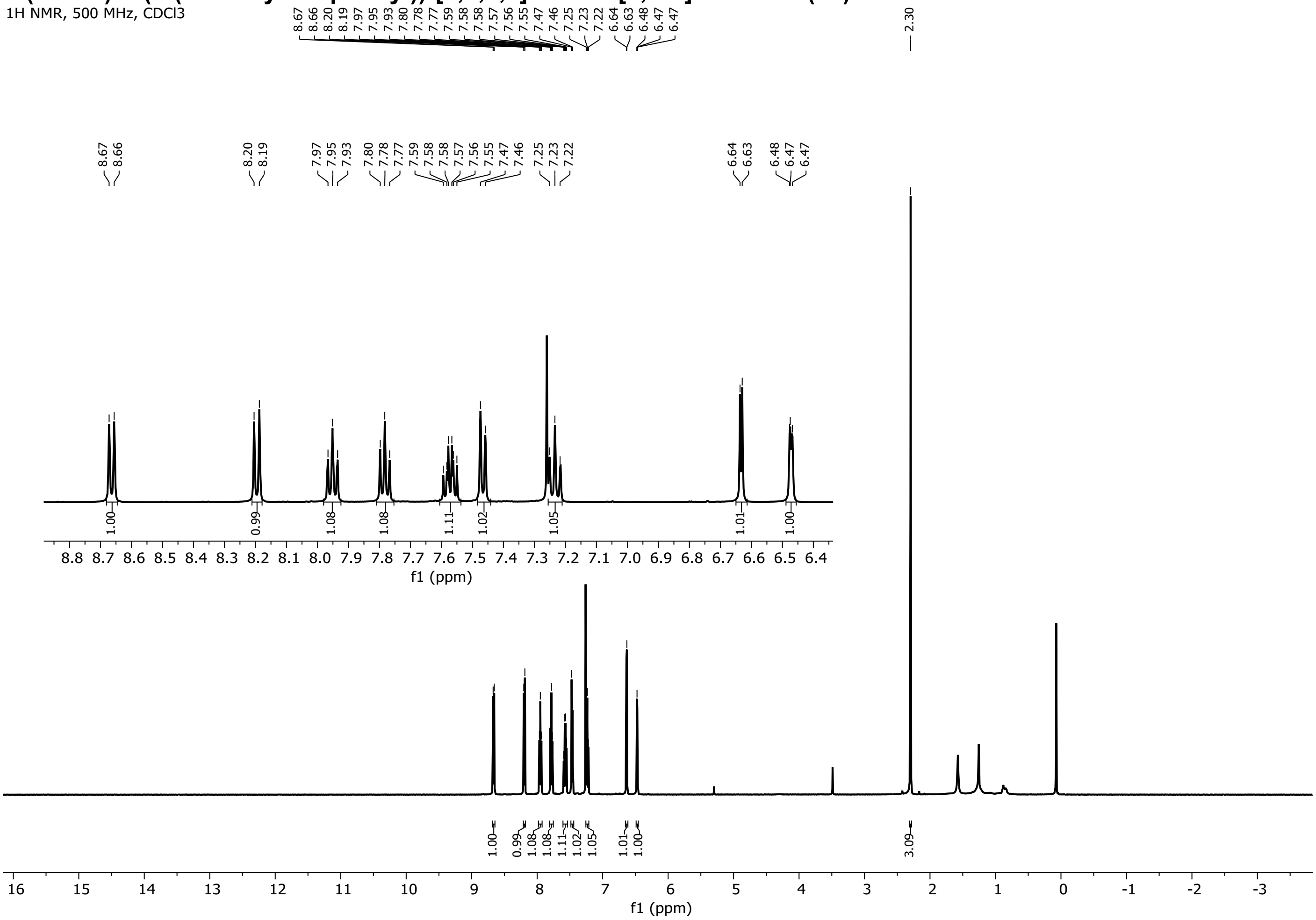


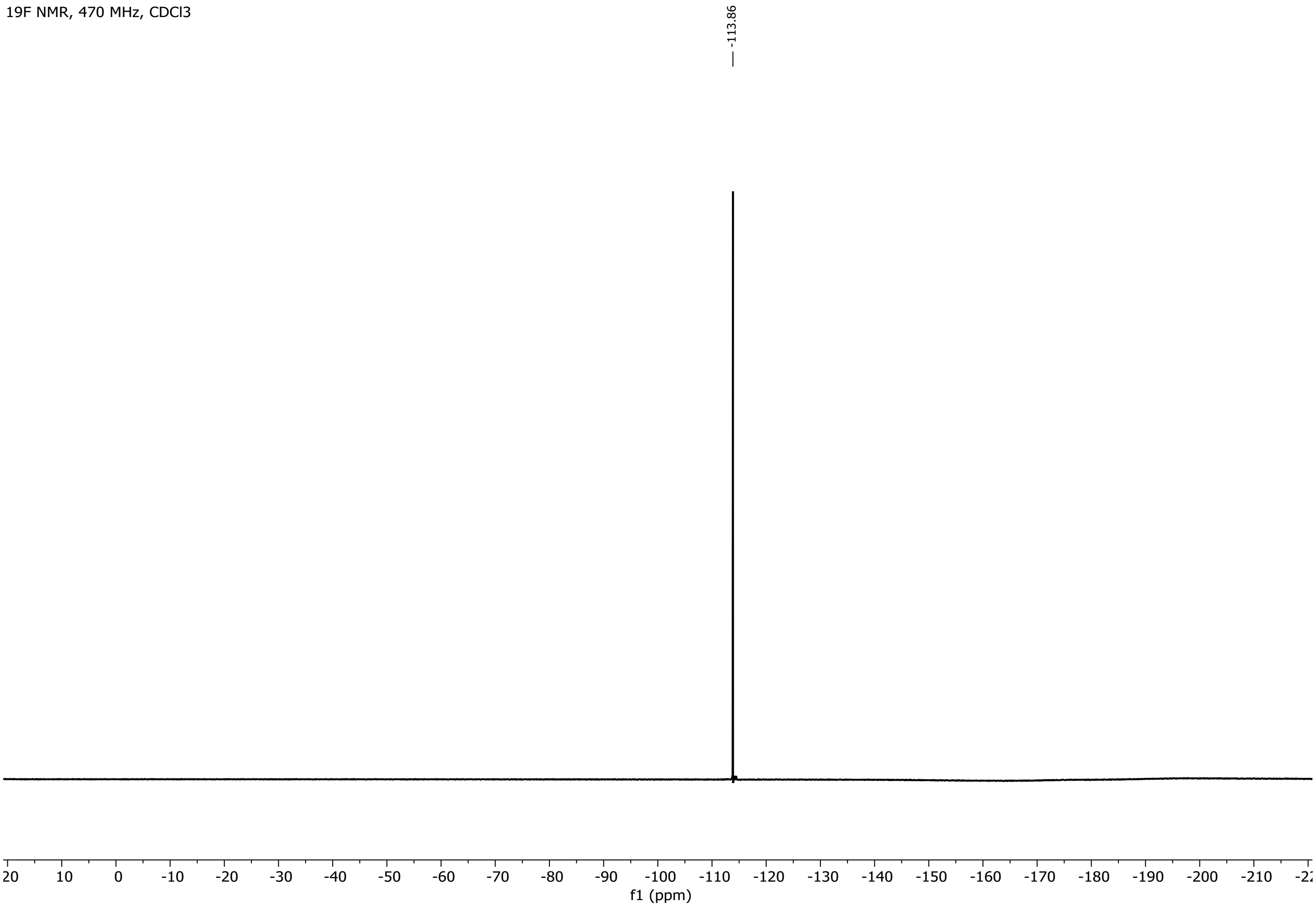

19F NMR, 470 MHz, CDCl3
-114.76
δ(ppm)

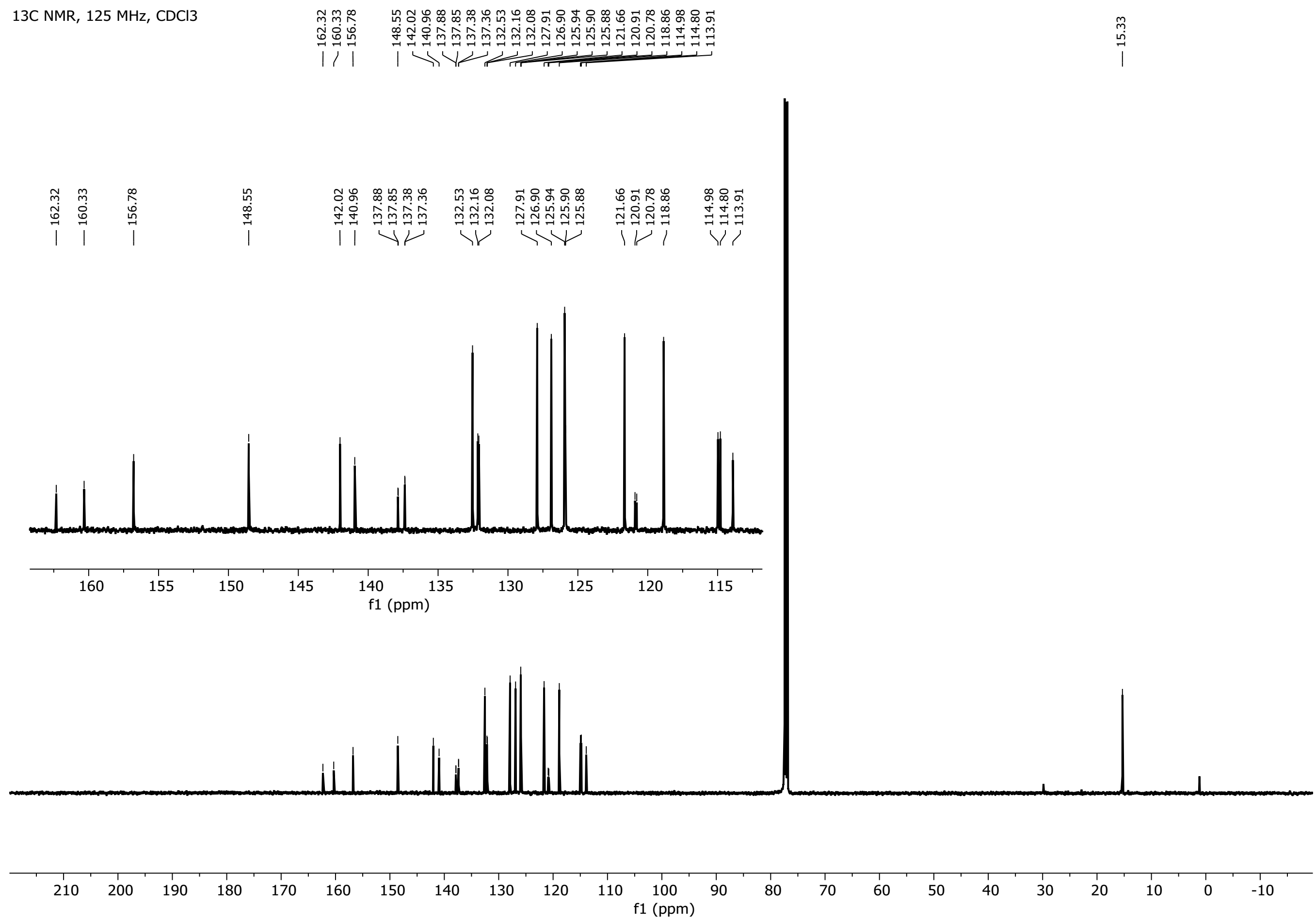

13CNMR, 125 MHz, CDCl3
162.25
160.25
157.12
150.64
148.42
144.65
140.66
135.98
135.96
132.43
132.11
132.03
129.09
126.79
126.36
126.33
125.55
121.57
118.78
114.79
114.62
113.84
77.41
76.91
34.60
31.31
δ(ppm)

2-(fluoro)-6-(5-(2-methylthiophenyl))-[1,2,4,5]-tetrazo[1,2-*b*]indazole (26)

1H NMR, 500 MHz, CDCl3

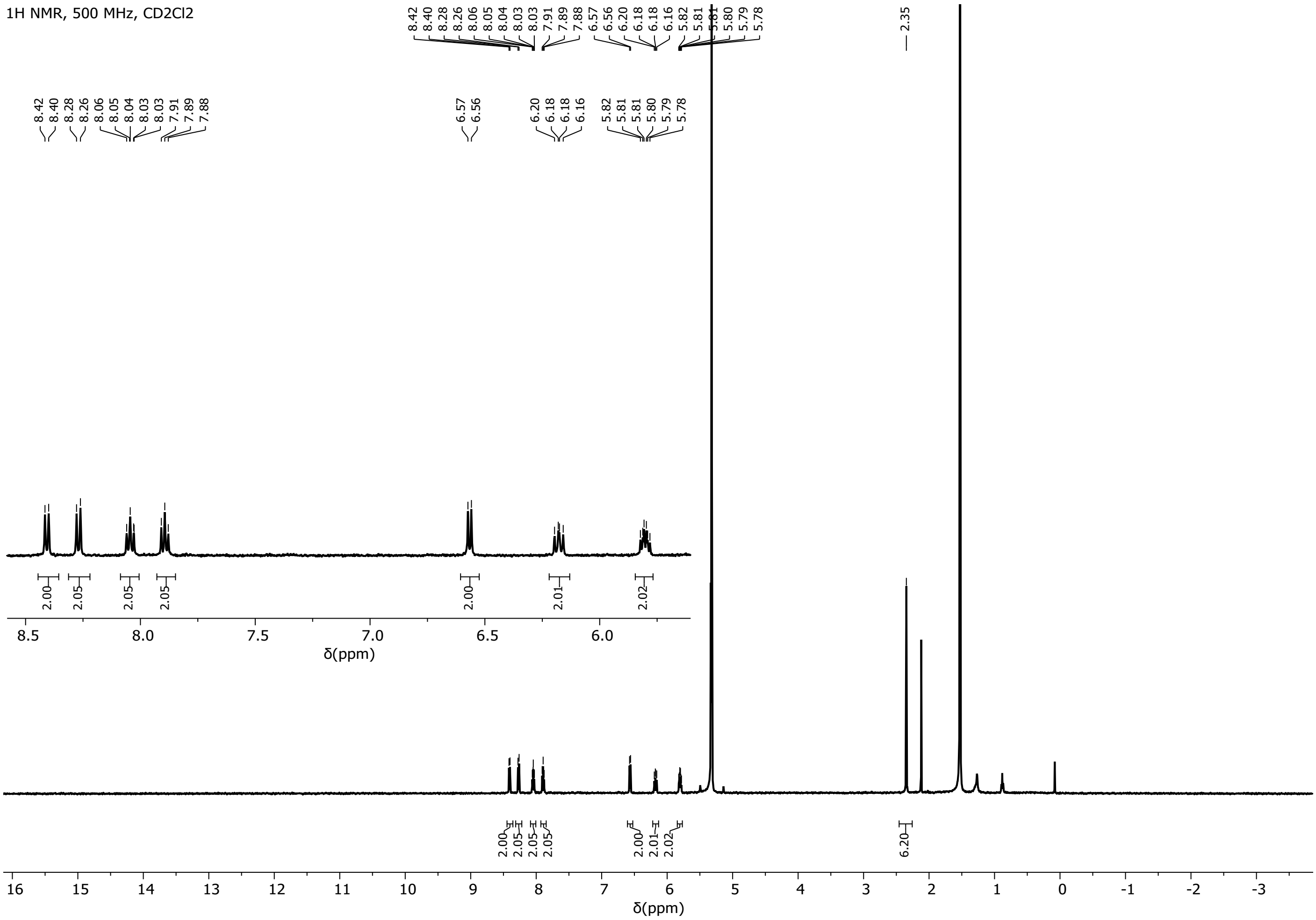




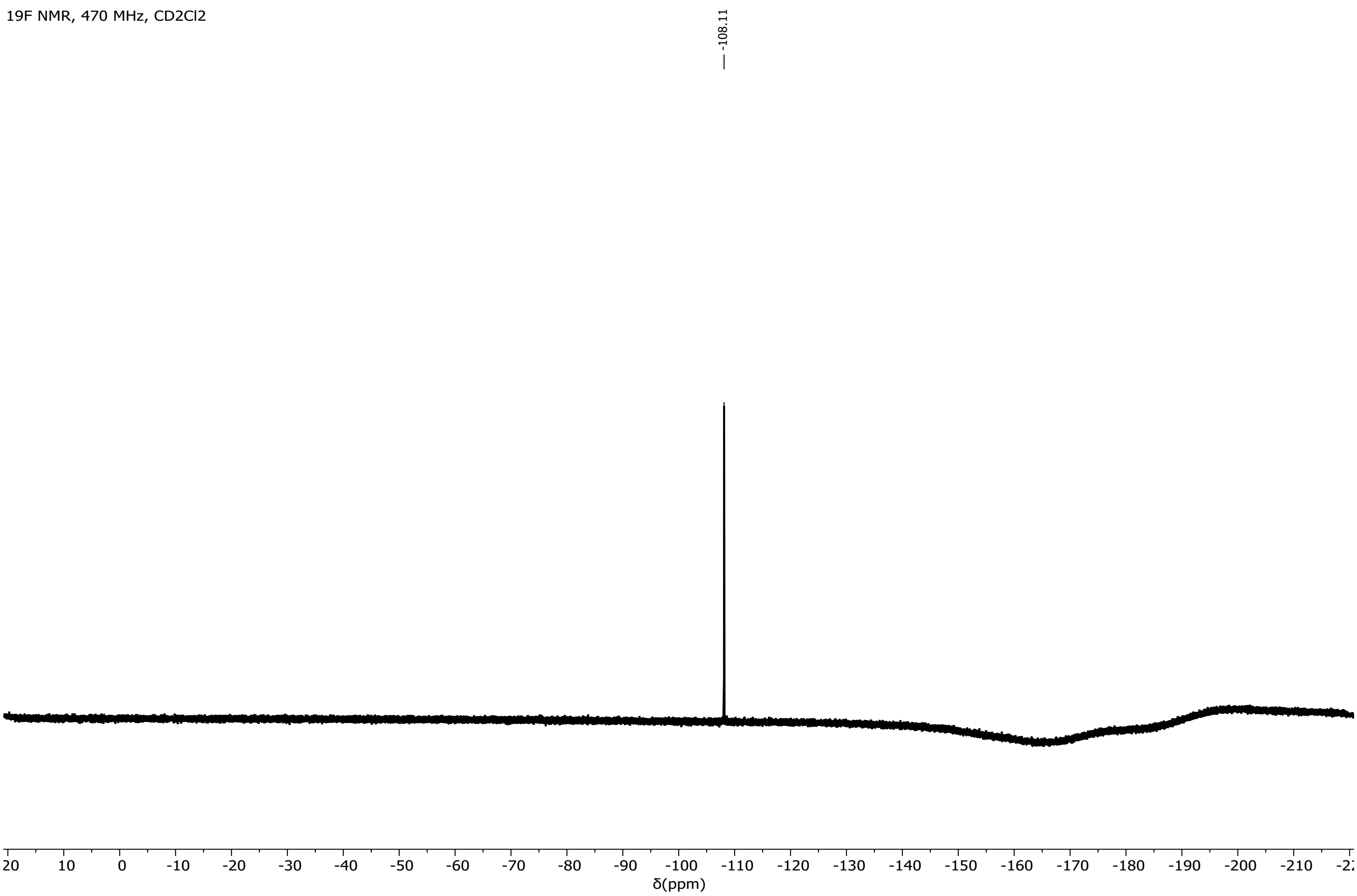


Dimeric palladacycle (Pd_2)

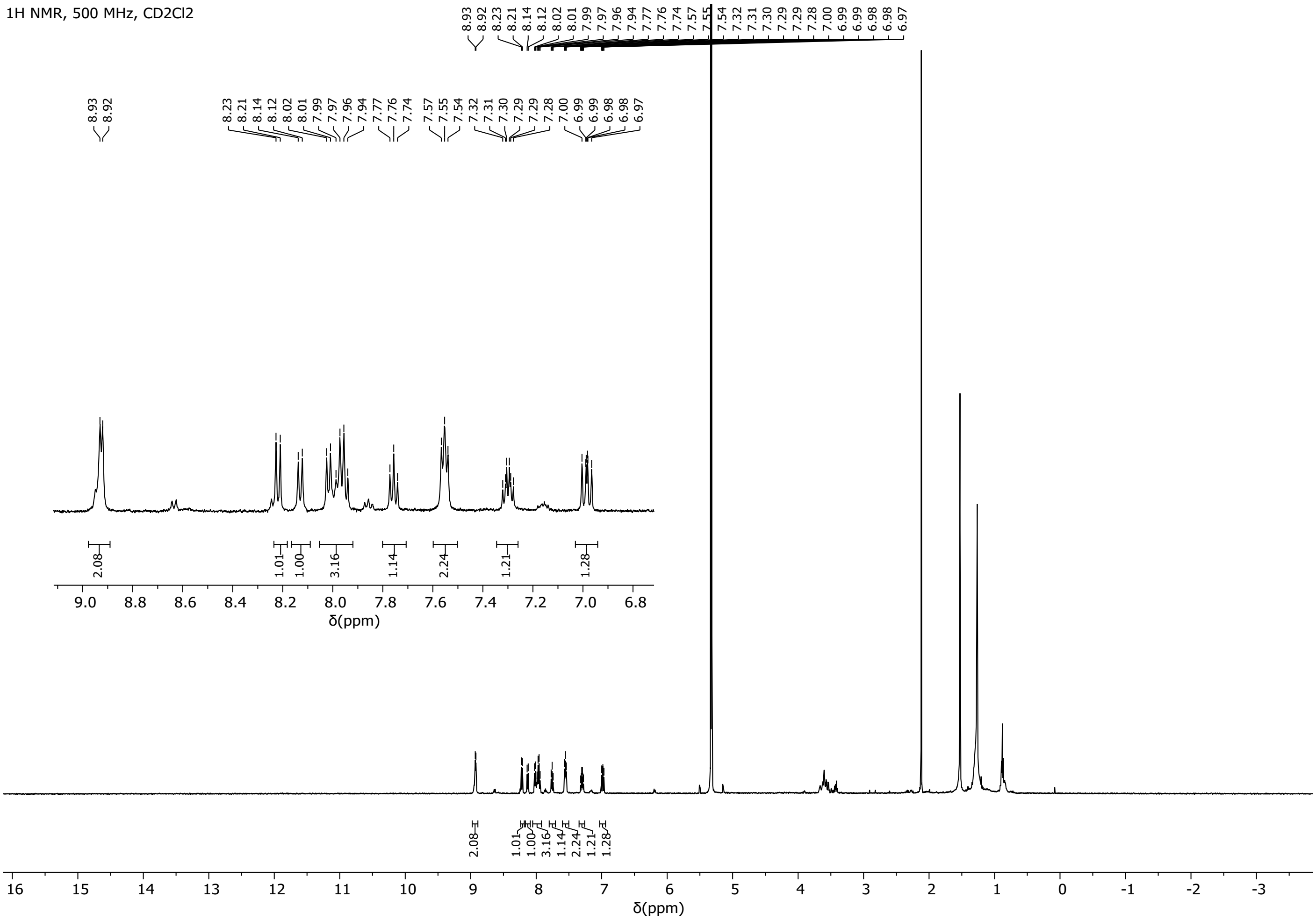
1H NMR, 500 MHz, CD2Cl2

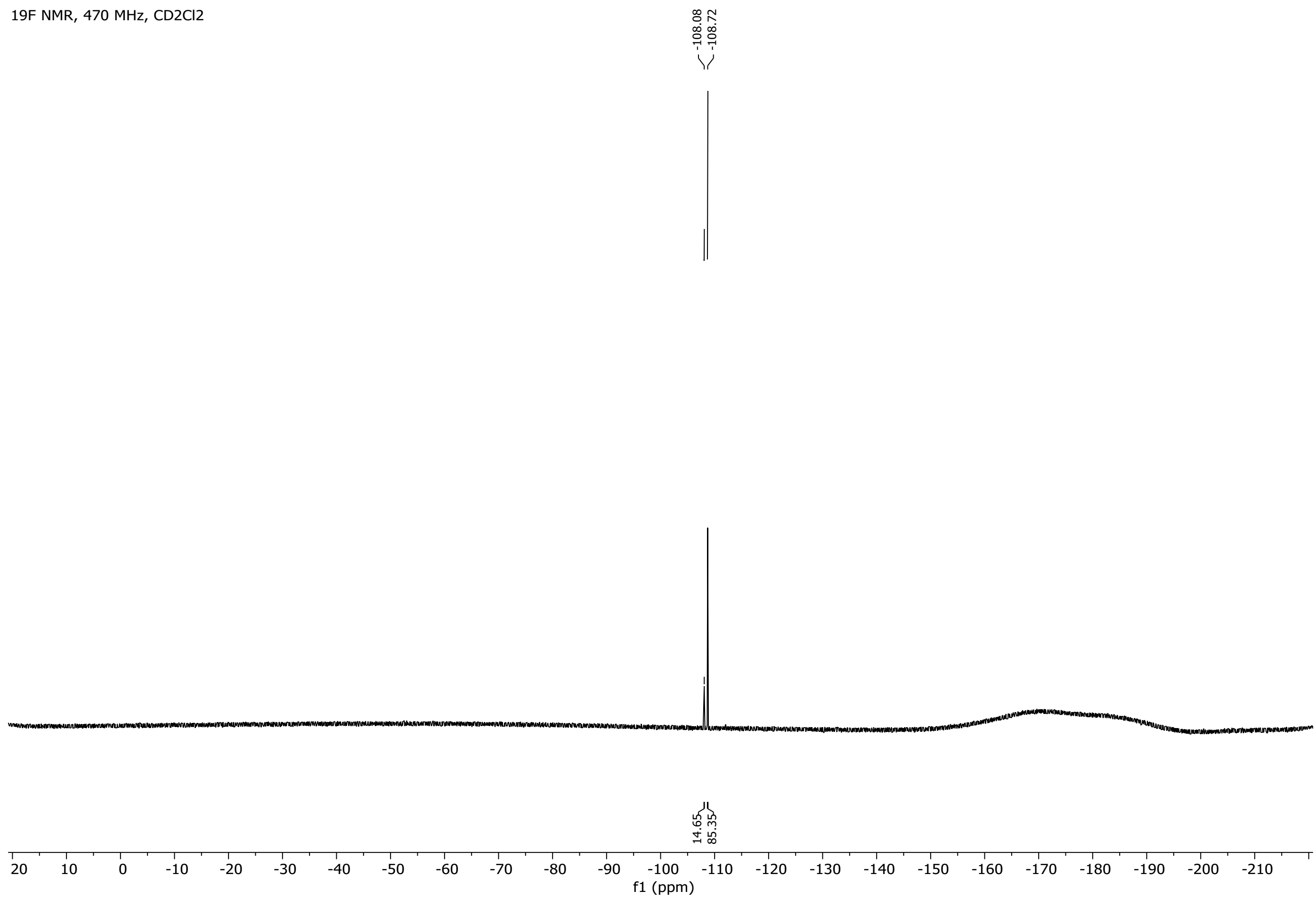


19F NMR, 470 MHz, CD2Cl2



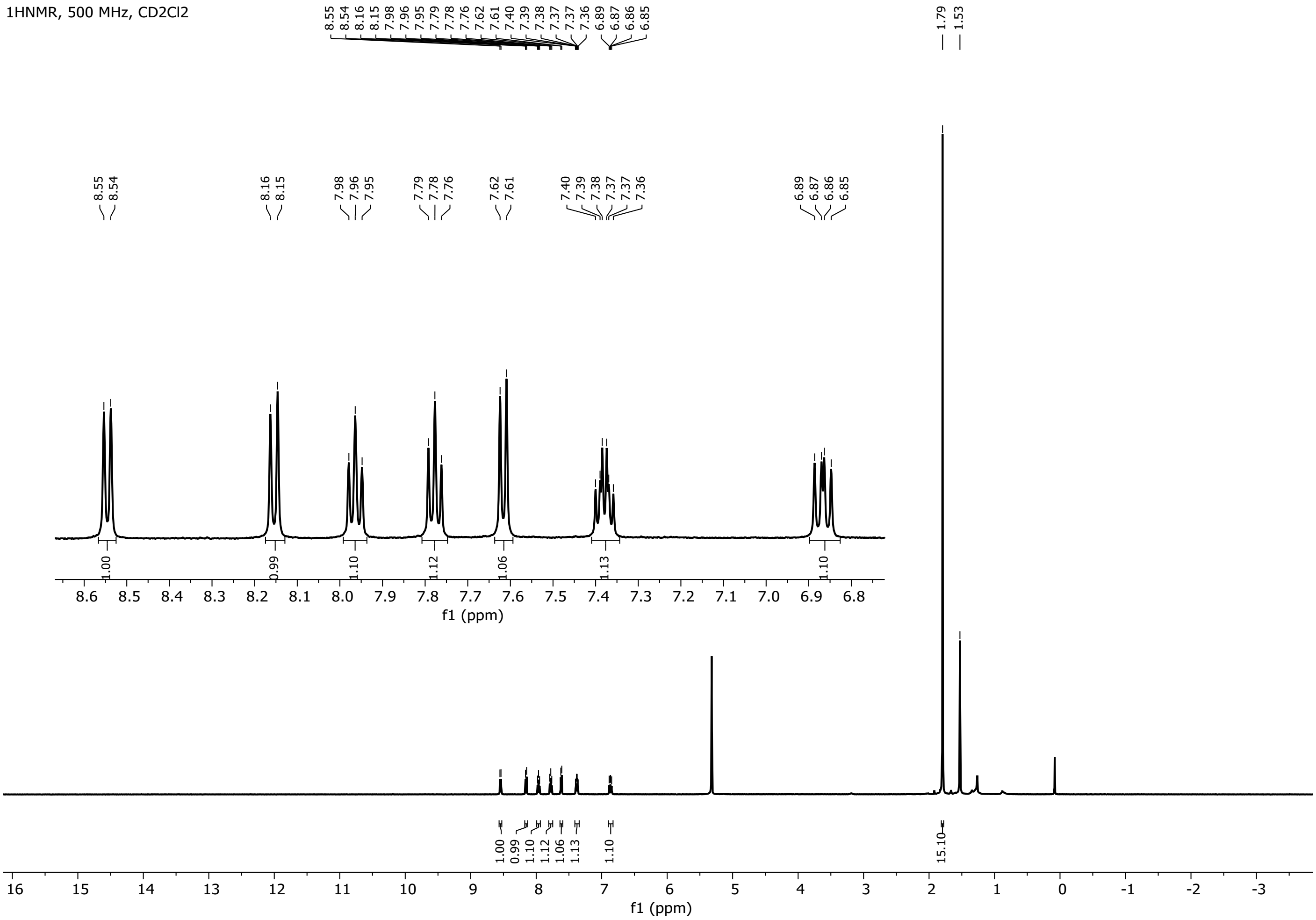
Metallacycle (Pd)



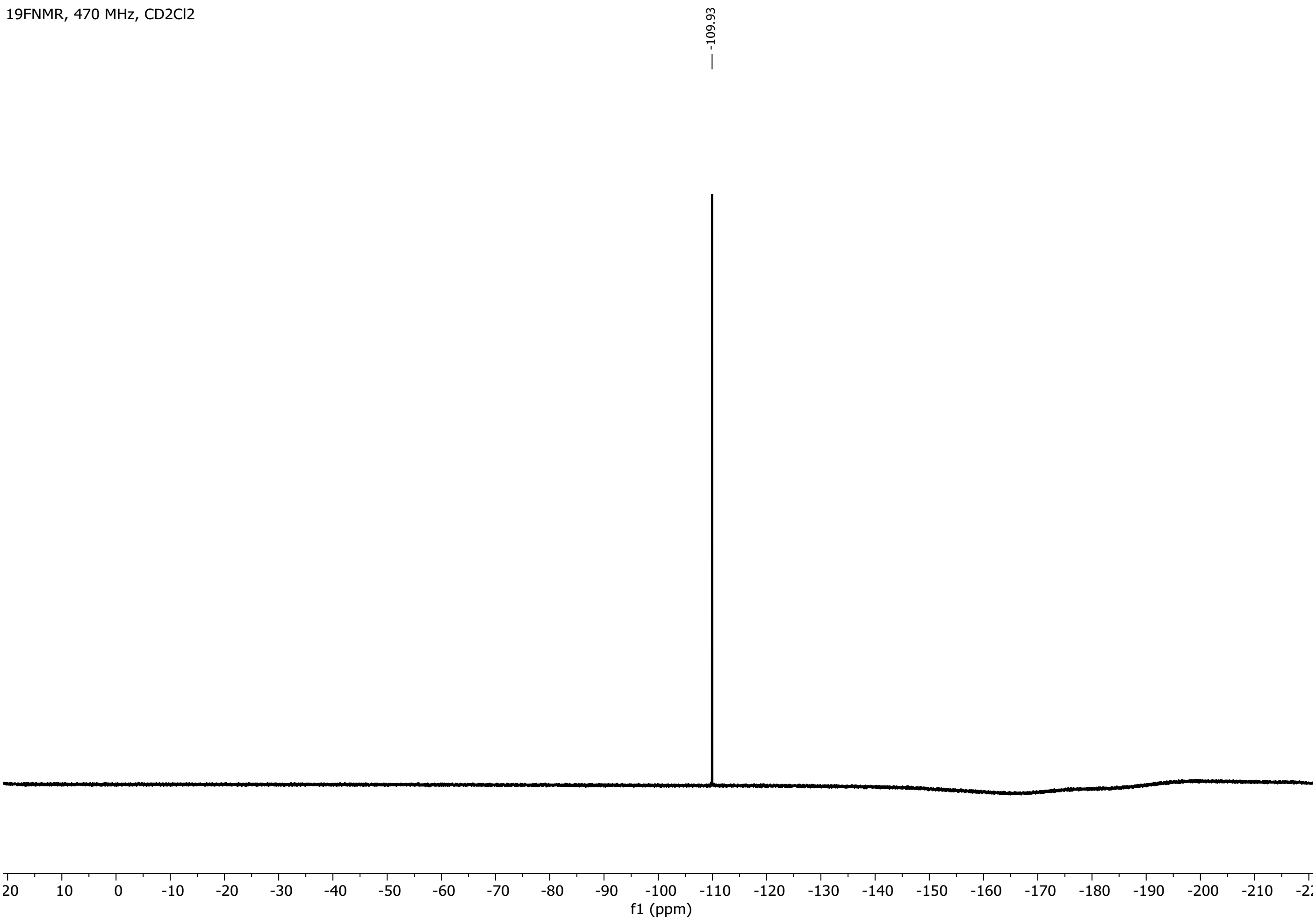


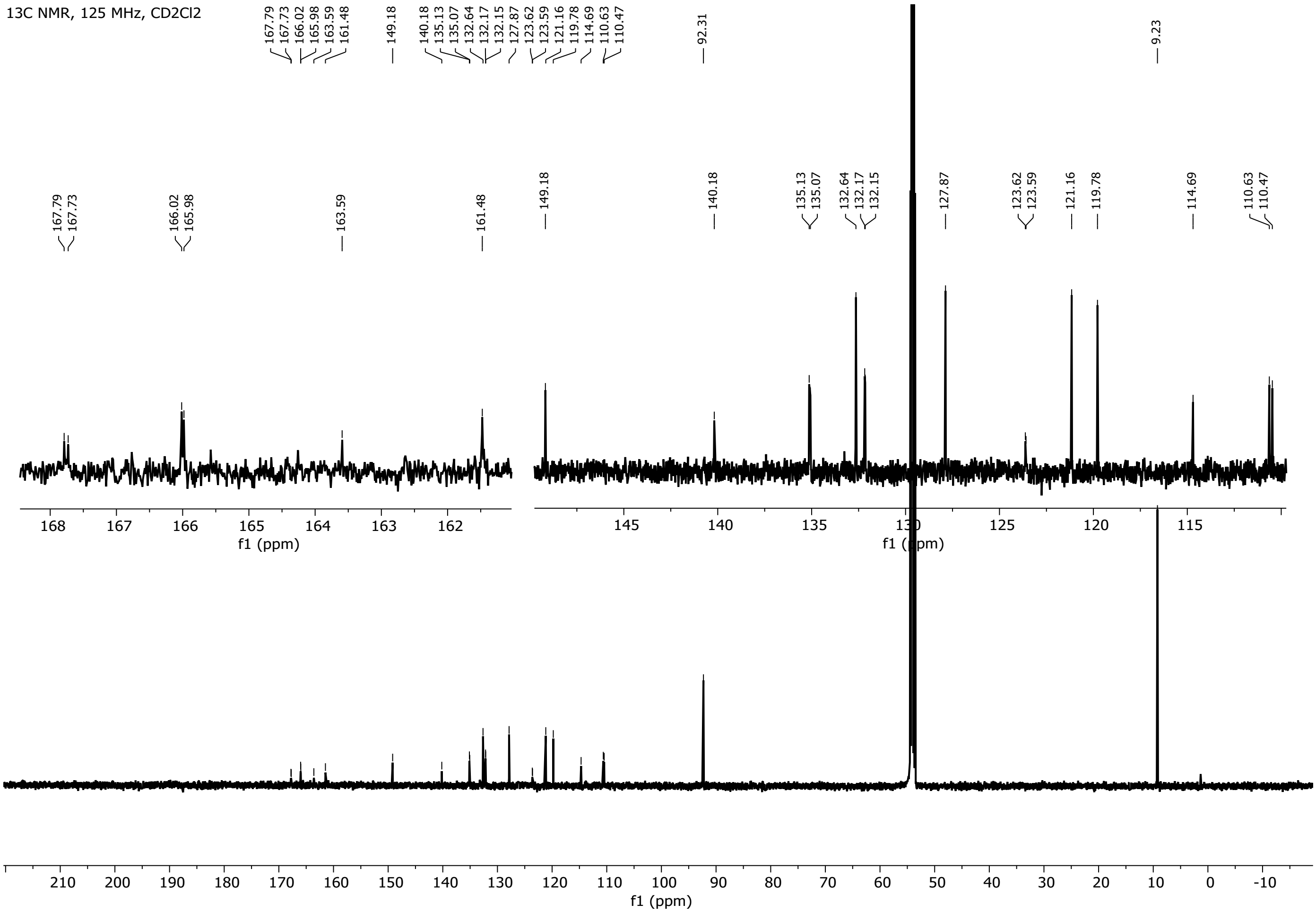
Metallacycle (Ir)

1HNMR, 500 MHz, CD2Cl2

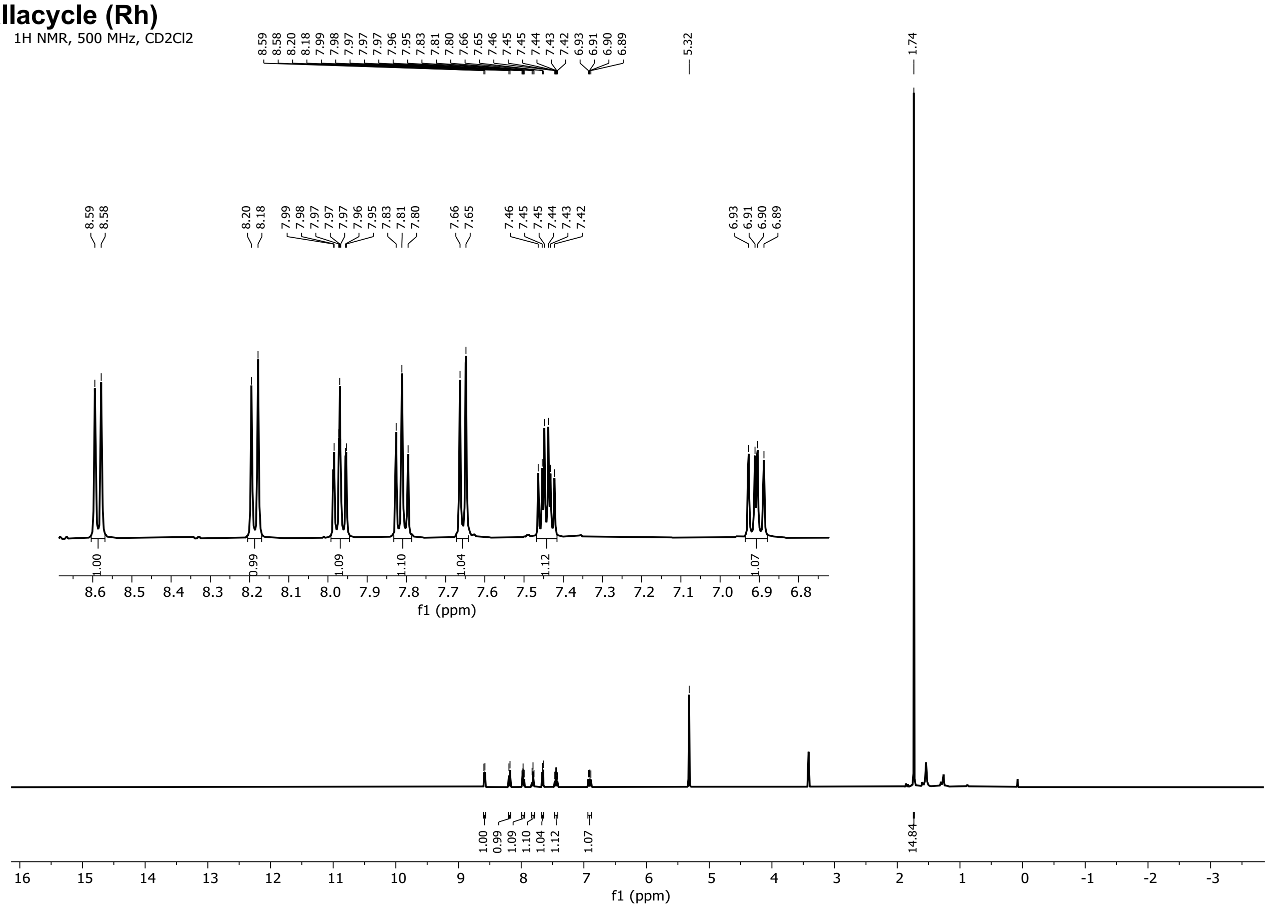


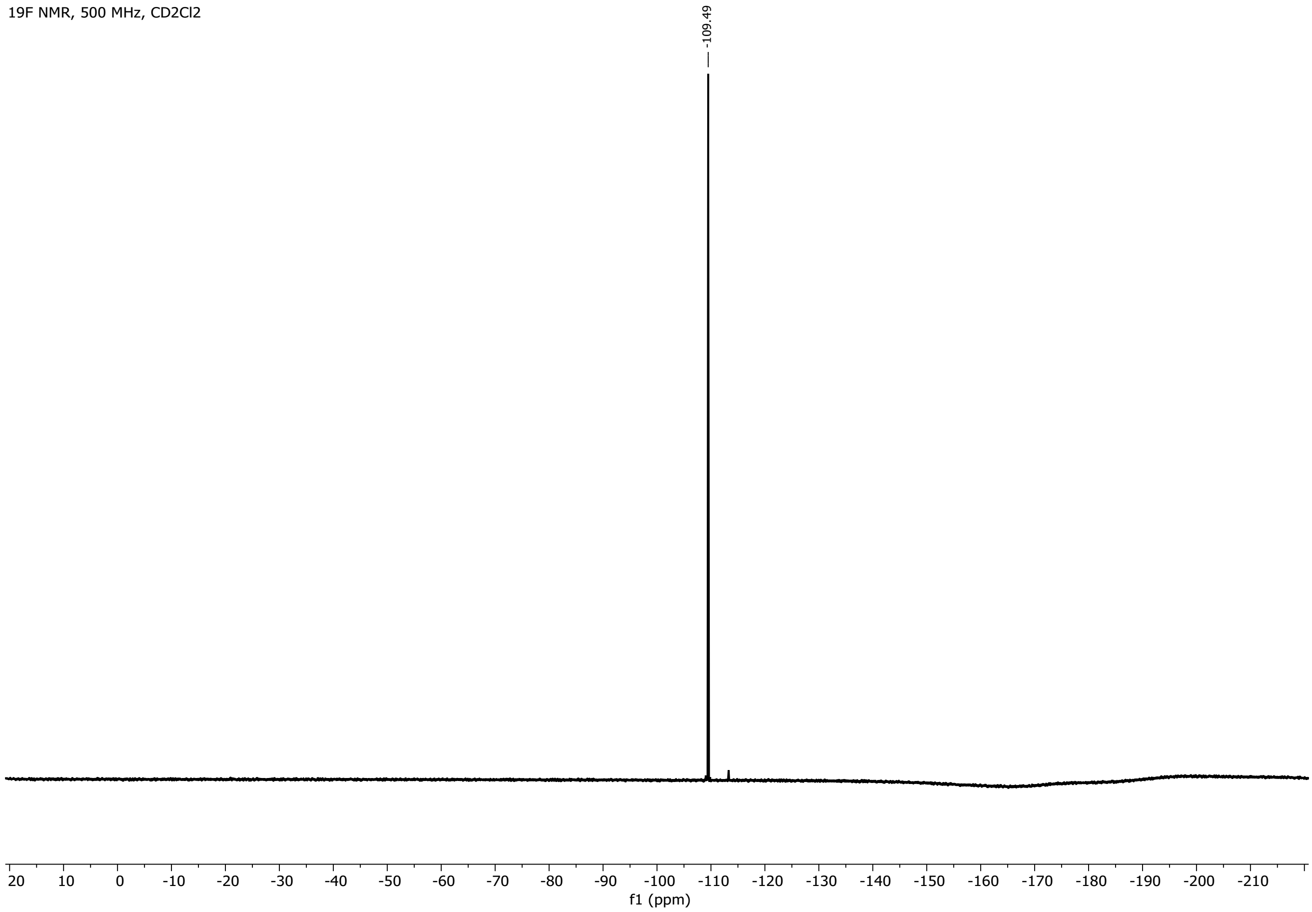
19FNMR, 470 MHz, CD2Cl2

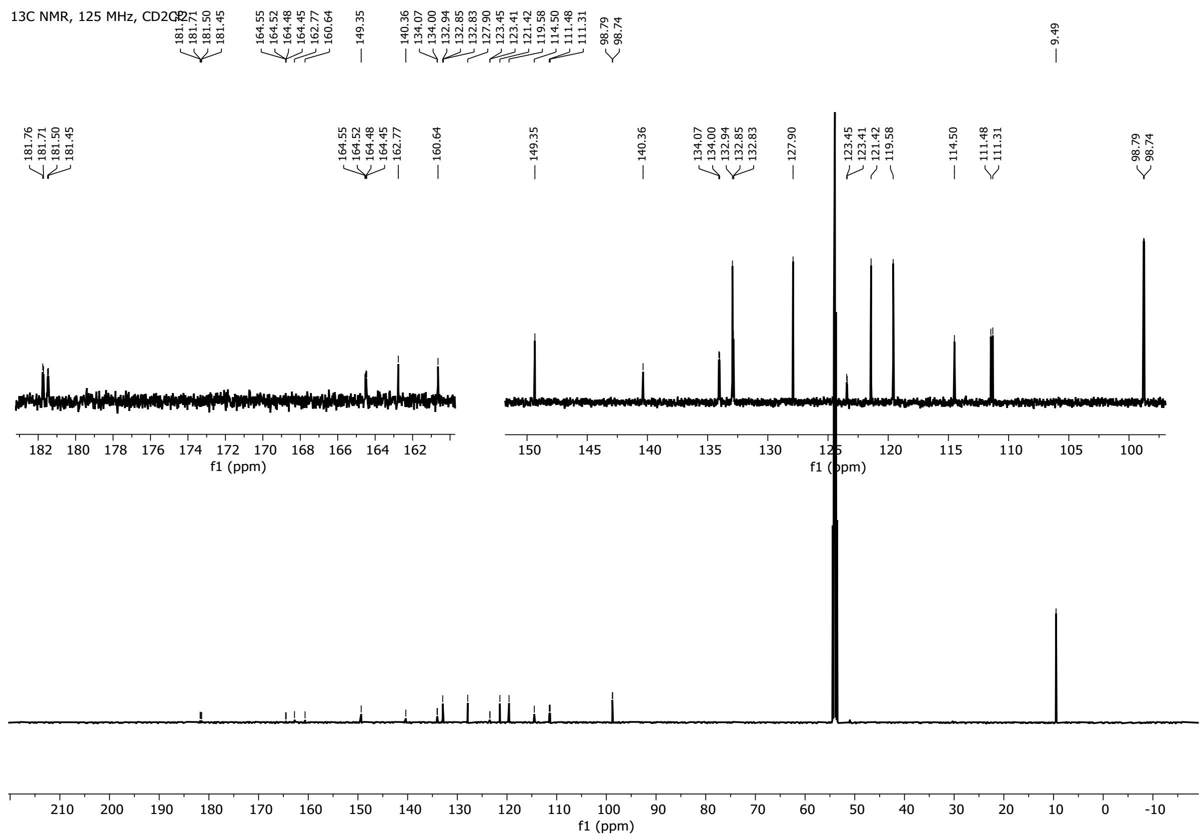




Metallacycle (Rh)

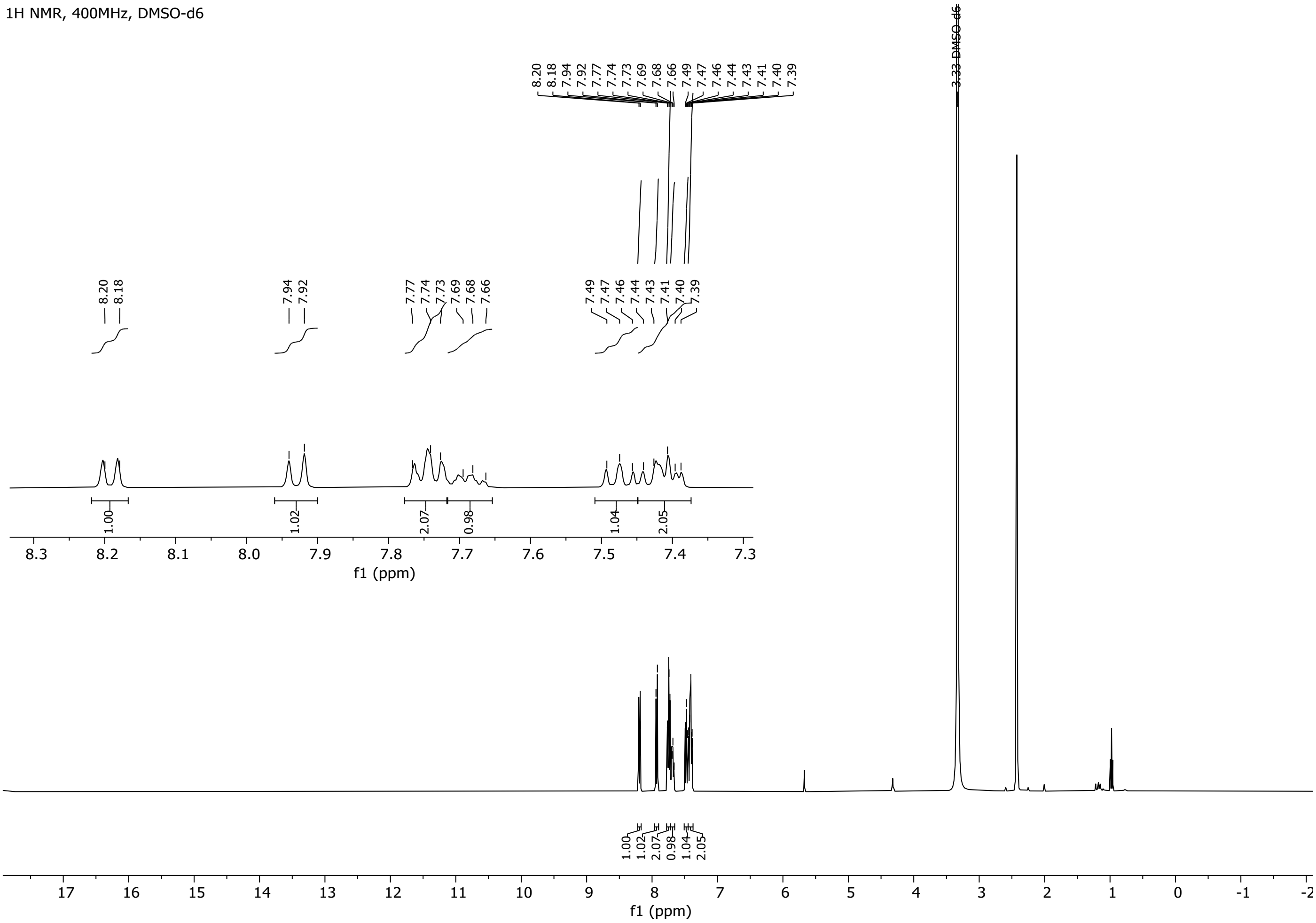




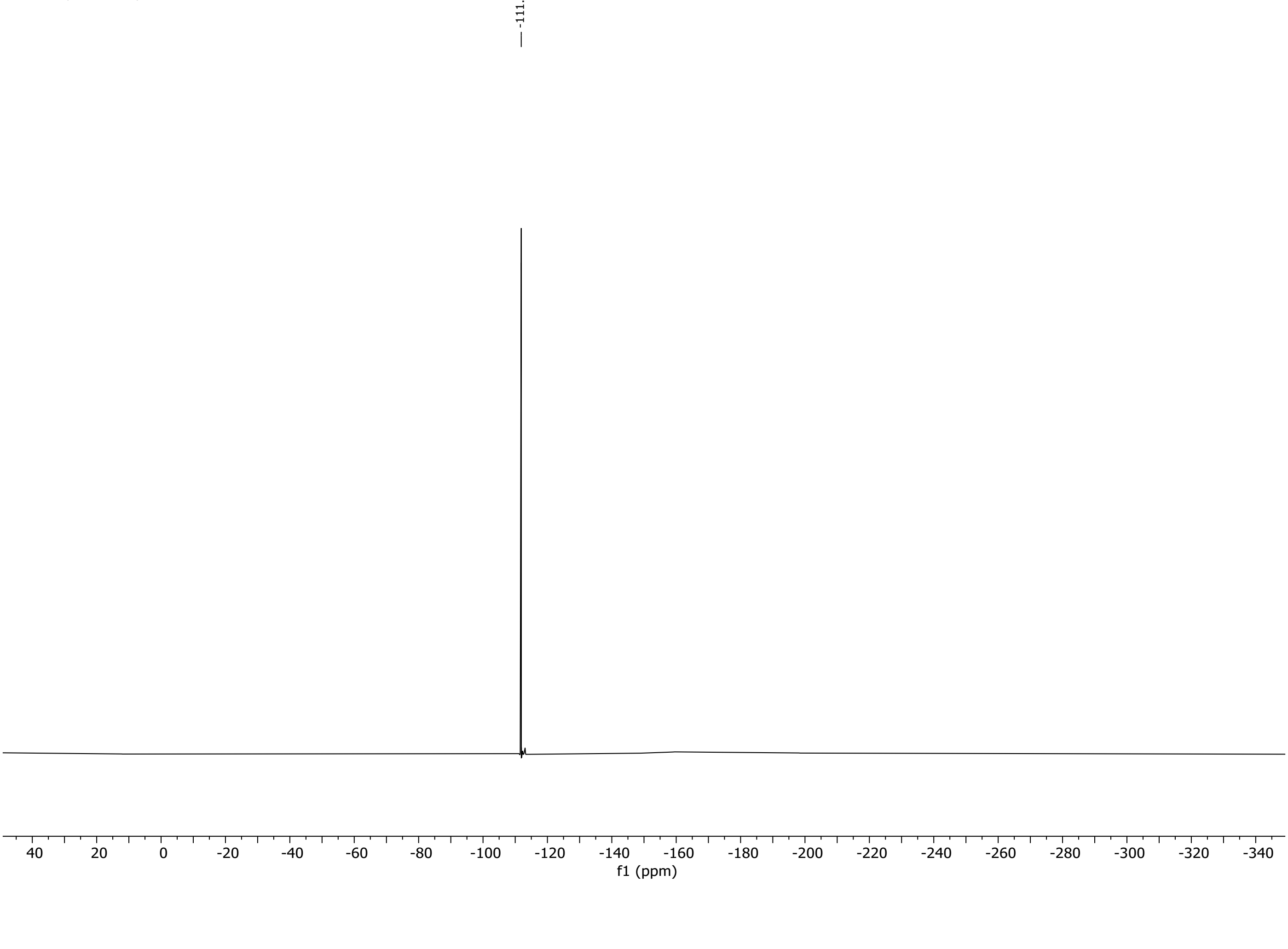


3-(2-fluorophenyl)-3*H*-5λ⁴-[1,2,4,5]tetrazino[1,6-*b*]indazole 2-oxide (17-O1)

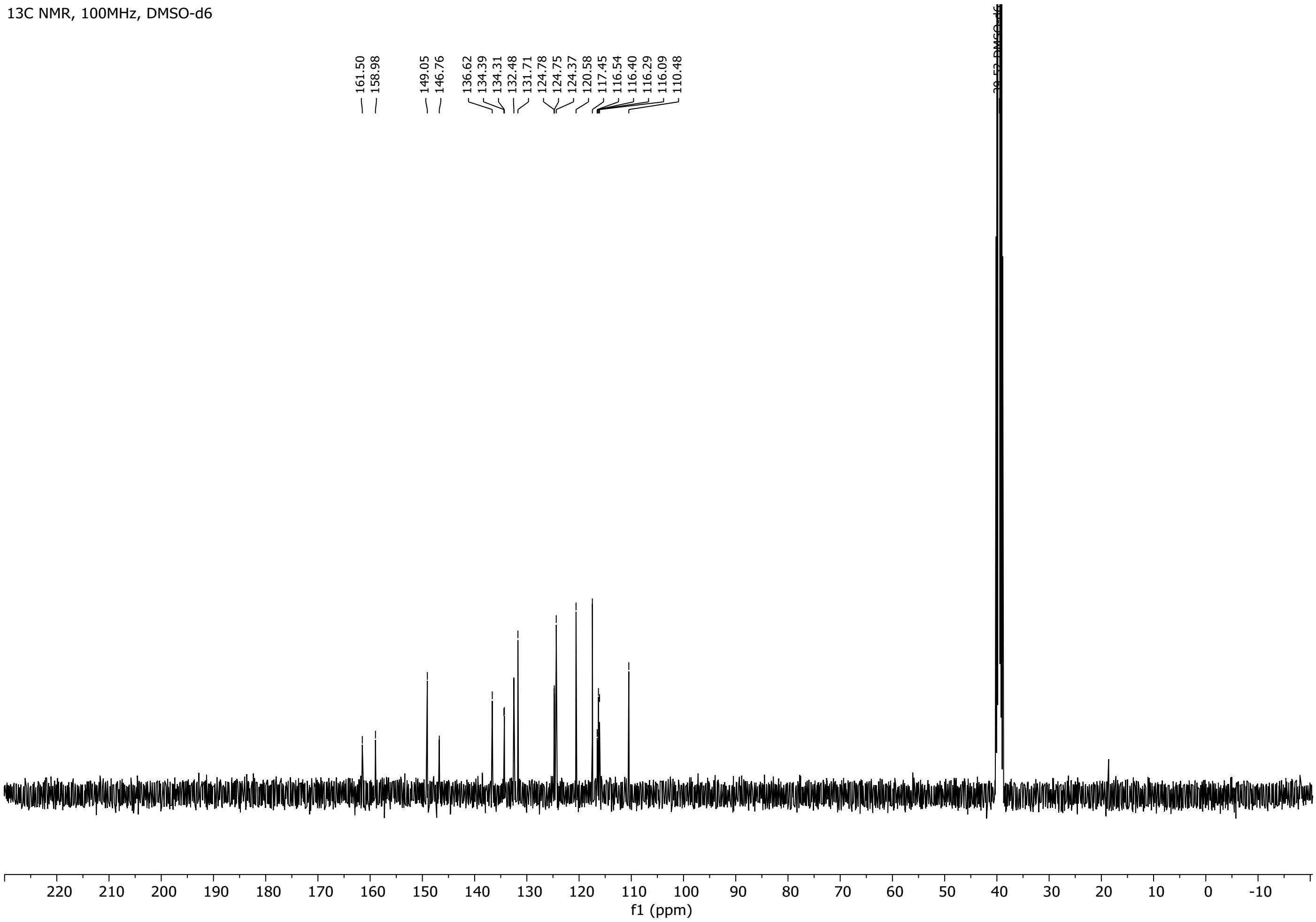
1H NMR, 400MHz, DMSO-d6



19F NMR, 376 MHz, DMSO-d6

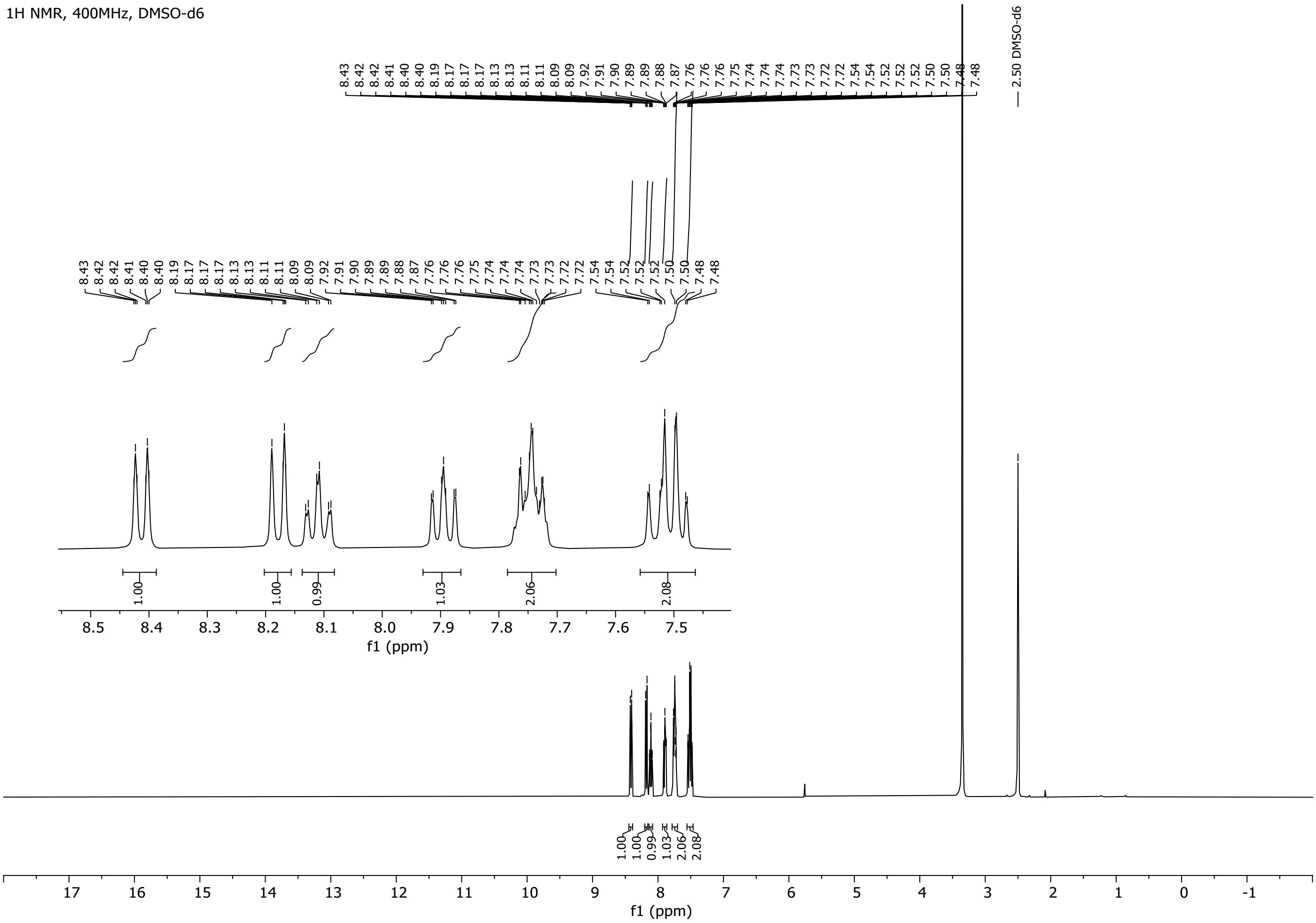


13C NMR, 100MHz, DMSO-d6

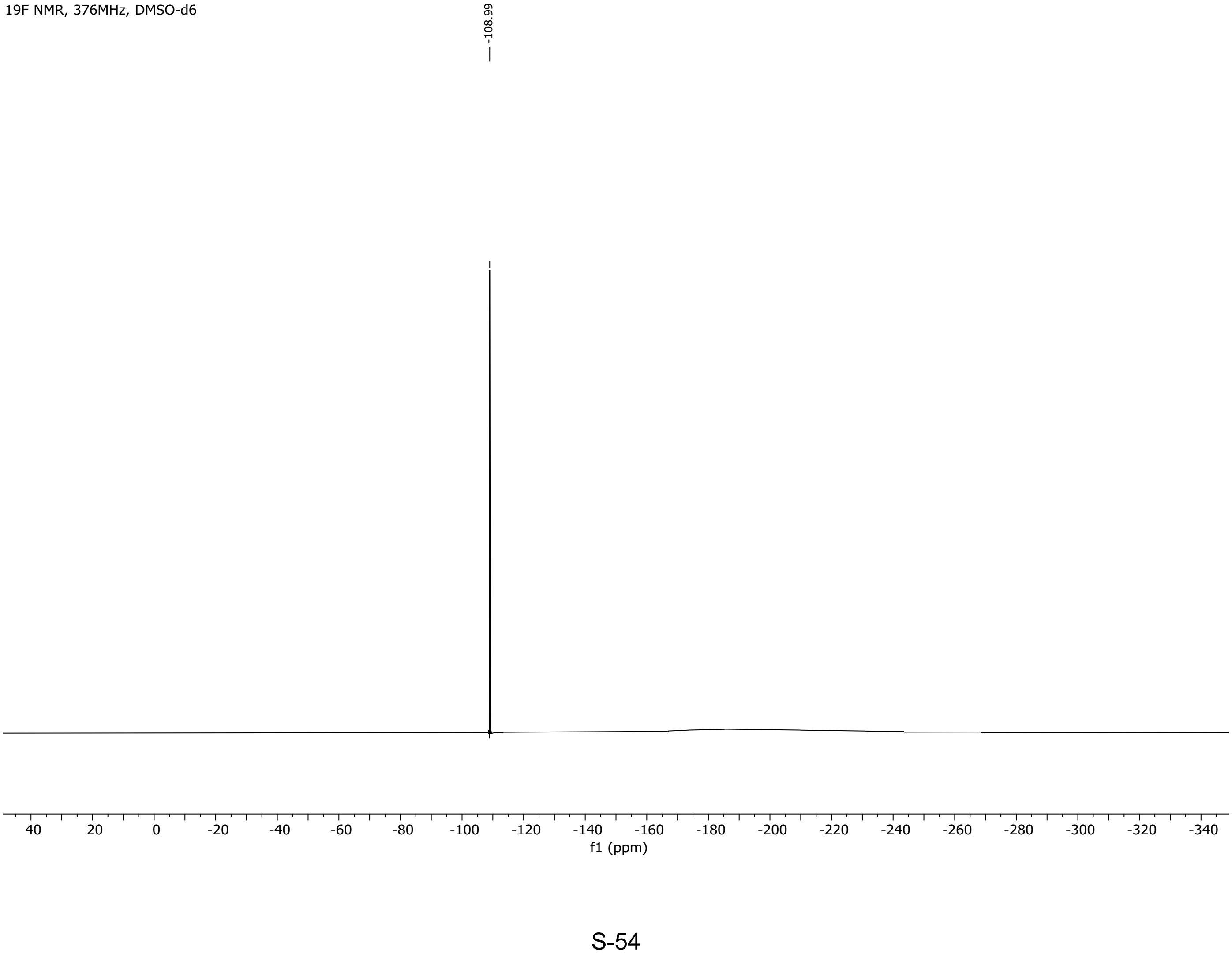


3-(2-fluorophenyl)-3*H*-5λ4-[1,2,4,5]tetrazino[1,6-*b*]indazole 1-oxide (17-O2)

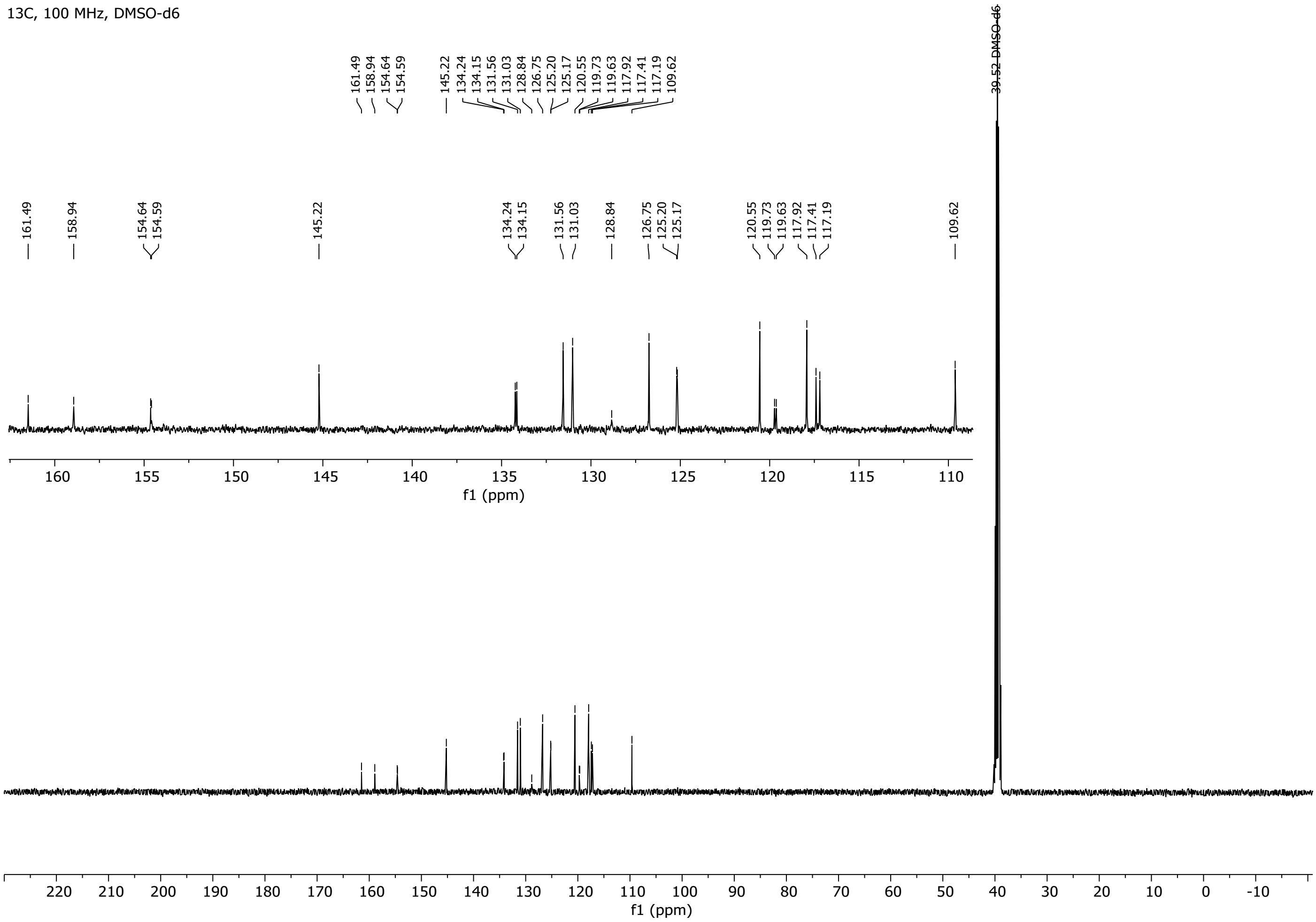
1H NMR, 400MHz, DMSO-d6



19F NMR, 376MHz, DMSO-d6



13C, 100 MHz, DMSO-d6



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[5] a) A. D. Becke *J. Chem. Phys.* **1993**, *98*, 5648–5652; b) C. Lee, W. Yang, R. G. Parr *Phys. Rev. B* **1988**, *37*, 785–789; c) S. H. Vosko, L. Wilk, M. Nusair *Can. J. Phys.* **1980**, *58*, 1200–1211.d) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98 (45)*, 11623–11627