Electronic Supplementary Information (ESI)

Indoleninyl-substituted pyrimido[1,2-*b*]indazoles *via* a facile condensation reaction

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General details

All chemicals and reagents were purchased from Acros Organics, Merck Millipore and Sigma Aldrich, Malaysia. The solvents were used as received without further purification unless noted. The Nuclear Magnetic Resonance (NMR) spectra of compounds were collected on 400 MHz JEOL ECX 400II MHz, 400 MHz BRUKER DMX NMR, and 600 MHz BRUKER DMX NMR instruments. Chemical shifts and coupling constants (*J*) are reported in δ and Hz units, respectively. Melting points were measured on a Mel-Temp II Laboratory Devices. High Resolution Mass Spectrometry (HRMS) spectra were obtained from an Agilent 6530 Accurate-Mass Q-TOF LC/MS system. The UV-vis absorption spectra were recorded on a Shimadzu UV-2600 UV-Vis spectrophotometer at room temperature.

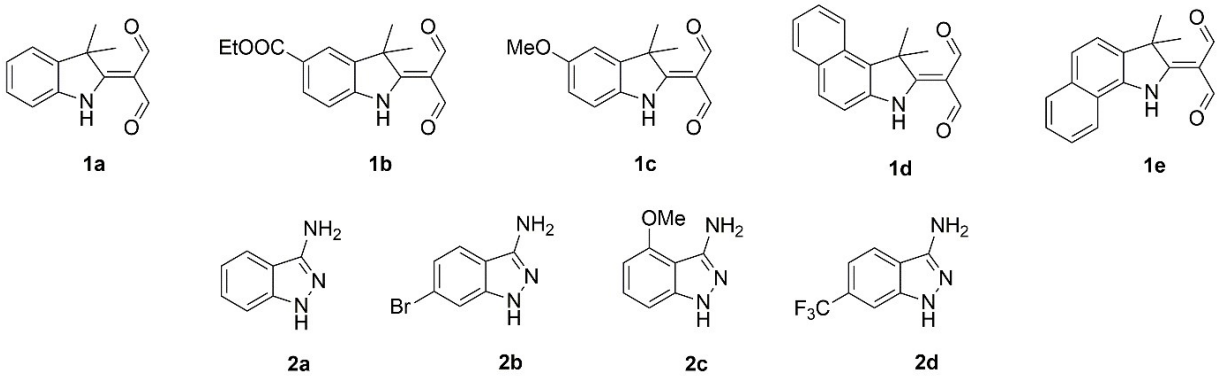

Fig. S1: Chemical structures of **1a-e** and **2a-d**.

Synthetic procedure for the preparation of 1e.

2-(3,3-dimethyl-1*H*-benzo[*g*]indol-2(3*H*)-ylidene)malonaldehyde (1e): To a solution of 2,3,3-trimethyl-3*H*-benzo[*g*]indole (5 mmol, 1 equiv.) in DMF (50 mL), $POCl_3$ (15 mmol, 3 equiv.) was added dropwise at 0 – 5 ºC. Upon completion, the mixture was heated at 95 ºC for 9 h under a vigorous stirring. After being cooled down to room temperature, crushed ice (200 g) was added and the solution was slowly neutralized using 2 M NaOH. The solid was filtered and discarded. The filtrate was left at room temperature overnight. The solid was filtered, washed with warm distilled water and dried at 60 ºC. Brown solid. Yield: 12%. mp = 159 – 161 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 14.31 (bs, 1H, N-H), 9.83 (s, 1H, CHO), 9.79 (s, 1H, CHO), 7.98 (d, 1H, J = 8.0 Hz, Ar-H), 7.95 (d, 1H, J = 8.0 Hz, Ar-H), 7.79 (d, 1H, J = 8.4 Hz, Ar-H), 7.66 (t, 1H, J = 7.2 Hz, Ar-H), 7.58 (t, 1H, J = 6.8 Hz, Ar-H), 7.49 (d, 1H, J = 8.4 Hz, Ar-H), 1.83 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.69, 187.94, 180.08, 136.98, 134.57, 133.55, 128.88, 127.38, 126.64, 126.34, 120.81, 120.60, 119.45, 110.07, 52.63, 22.88. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{17}H_{16}NO_2$: 266.1176; found: 266.1185.

General procedure for the preparation of 3a-t.

A mixture of **1** (0.30 mmol, 1.0 equiv.) and **2** (0.33 mmol, 1.1 equiv.) dissolved in ethanol/acetic acid (5 mL, v/v = 4:1) was heated at 78 ºC for 5 h (monitored by TLC). Upon completion, the solvent was partially evaporated. The solids were collected by filtration, washed with diethyl ether and dried to provide product **3**.

3-(3,3-dimethyl-3*H*-indol-2-yl)pyrimido[1,2-*b*]indazole (3a): Yellow solid. Yield: 68%. mp = 197 – 199 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.59 (d, 1H, J = 1.6 Hz, CHN), 9.55 (d, 1H, J = 1.2 Hz, CHN), 8.36 (d, 1H, J = 8.4 Hz, Ar-H), 7.88 (d, 1H, J = 8.8 Hz, Ar-H), 7.78 (d, 1H, J = 7.6 Hz, Ar-H), 7.69 (t, 1H, J = 7.6 Hz, Ar-H), 7.45 (m, 2H, Ar-H), 7.38 (m, 2H, Ar-H), 1.68 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.63, 152.77, 152.51, 147.04, 145.74, 143.23, 132.65, 130.55, 128.27, 126.95, 121.79, 121.53, 121.06, 120.88, 118.39, 116.34, 113.65, 53.70, 24.63. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{20}H_{17}N_4$: 313.1448; found: 313.1448. X-ray quality crystals were grown from a DMF solution after two weeks.

Ethyl 3,3-dimethyl-2-(pyrimido[1,2-*b*]indazol-3-yl)-3*H*-indole-5-carboxylate (3b): Yellow solid. Yield: 55%. mp = 200 – 202 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (d, 1H, J = 2.0 Hz, CHN), 9.55 (d, 1H, J = 2.4 Hz, CHN), 8.37 (dt, 1H, J = 8.0, 0.8 Hz, Ar-H), 8.18 (dd, 1H, J = 8.4, 1.6 Hz, Ar-H), 8.10 (d, 1H, J = 0.8 Hz, Ar-H), 7.88 (d, 1H, J = 8.4 Hz, Ar-H), 7.81 (d, 1H, J = 8.0 Hz, Ar-H), 7.71 (m, 1H, Ar-H), 7.40 (m, 1H, Ar-H), 4.46 (q, 2H, CH_2), 1.72 (s, 6H, CH_3), 1.46 (t, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.63, 166.55, 156.22, 152.45, 147.05, 145.86, 143.41, 133.31, 131.04, 130.59, 128.96, 122.60, 122.19, 121.23, 121.02, 117.95, 116.36, 113.70, 61.34, 53.99, 24.58, 14.50. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{23}H_{21}N_4O_2$: 385.1664; found: 385.1583.

3-(5-methoxy-3,3-dimethyl-3*H*-indol-2-yl)pyrimido[1,2-*b*]indazole (3c): Yellow solid. Yield: 47%. mp = 182 – 184 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (d, 1H, J = 2.4 Hz, CHN), 9.52 (d, 1H, J = 1.6 Hz, CHN), 8.35 (d, 1H, J = 8.0 Hz, Ar-H), 7.87 (d, 1H, J = 8.8 Hz, Ar-H), 7.69 (m, 2H, Ar-H), 7.37 (td, 1H, J = 8.0, 1.2 Hz, Ar-H), 6.96 (m, 2H, Ar-H), 3.90 (s, 3H, OCH_3), 1.66 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.49, 159.43, 152.41, 149.04, 146.62, 145.85, 143.10, 132.17, 130.54, 122.15, 121.81, 120.91, 118.66, 116.33, 113.71, 113.09, 107.64, 55.88, 53.83, 24.85. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{21}H_{19}N_4O$: 343.1553; found: 343.1551.

3-(1,1-dimethyl-1*H*-benzo[*e*]indol-2-yl)pyrimido[1,2-*b*]indazole (3d): Yellow solid. Yield: 62%. mp = 183 – 185 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (d, 1H, J = 2.0 Hz, CHN), 9.63 (d, 1H, J = 2.0 Hz, CHN), 8.73 (d, 1H, J = 8.0 Hz, Ar-H), 8.18 (d, 1H, J = 8.4 Hz, Ar-H), 8.03 (d, 1H, J = 8.4 Hz, Ar-H), 7.97 (s, 2H, Ar-H), 7.89 (d, 1H, J = 8.8 Hz, Ar-H), 7.70 (t, 1H, J = 7.2 Hz, Ar-H), 7.66 (t, 1H, J = 7.6 Hz, Ar-H), 7.56 (t, 1H, J = 7.6 Hz, Ar-H), 7.39 (t, 1H, J = 7.6 Hz, Ar-H), 1.93 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.36, 152.52, 150.17, 145.84, 143.17, 140.59, 133.20, 132.41, 130.54, 129.98, 129.74, 127.95, 126.83, 125.34, 122.73, 121.79, 120.88, 120.63, 118.14, 116.34, 113.68, 55.41, 24.17. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{24}H_{19}N_4$: 363.1604; found: 363.1612.

3-(3,3-dimethyl-3*H*-benzo[*g*]indol-2-yl)pyrimido[1,2-*b*]indazole (3e): Yellow solid. Yield: 60%. mp = 227 – 229 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (d, 1H, J = 2.0 Hz, CHN), 9.69 (d, 1H, J = 2.0 Hz, CHN), 8.76 (d, 1H, J = 8.8 Hz, Ar-H), 8.38 (dt, 1H, J = 8.0, 1.2 Hz, Ar-H), 7.95 (d, 1H, J = 8.0 Hz, Ar-H), 7.89 (d, 1H, J = 1.2 Hz, Ar-H), 7.87 (d, 1H, J = 2.0 Hz, Ar-H), 7.70 (m, 2H, Ar-H), 7.58 (m, 2H, Ar-H), 7.39 (td, 1H, J = 6.8, 0.8 Hz, Ar-H), 1.74 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.44, 152.45, 148.31, 146.10, 143.89, 143.17, 133.91, 132.52, 130.64, 128.23, 127.66, 127.45, 126.99, 126.22, 123.38, 121.86, 120.96, 118.86, 118.69, 116.33, 113.73, 54.73, 24.26. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{24}H_{19}N_4$: 363.1604; found: 363.1612.

8-bromo-3-(3,3-dimethyl-3*H*-indol-2-yl)pyrimido[1,2-b]indazole (3f): Yellow solid. Yield: 77%. mp = 202 – 204 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.57 (d, 1H, J = 1.8 Hz, CHN), 9.56 (d, 1H, J = 2.4 Hz, CHN), 8.50 (d, 1H, J = 1.2 Hz, Ar-H), 7.78 (m, 3H, Ar-H), 7.45 (m, 2H, Ar-H), 7.38 (td, 1H, J = 7.2, 1.2 Hz, Ar-H), 1.68 (s, 6H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.34, 152.64, 150.81, 147.01, 146.34, 142.39, 133.95, 132.79, 128.33, 127.11, 123.18, 121.61, 121.07, 118.86, 118.06, 114.86, 114.80, 53.70, 24.59. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{20}H_{16}N_4Br$: 391.0558; found: 391.0559.

Ethyl 2-(8-bromo-pyrimido[1,2-*b*]indazol-3-yl)-3,3-dimethyl-3*H*-indole-5-carboxylate (3g): Yellow solid. Yield: 67%. mp = 208 – 210 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (d, 1H, J = 2.0 Hz, CHN), 9.56 (d, 1H, J = 2.4 Hz, CHN), 8.50 (m, 1H, Ar-H), 8.18 (dd, 1H, J = 8.0, 1.6 Hz, Ar-H), 8.11 (d, 1H, J = 1.2 Hz, Ar-H), 7.81 (m, 3H, Ar-H), 4.46 (q, 2H, CH_2), 1.72 (s, 6H, CH_3), 1.46 (t, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.39, 166.56, 156.38, 151.05, 147.09, 146.24, 142.57, 134.26, 133.38, 130.60, 129.00, 123.27, 122.60, 121.36, 118.51, 118.21, 115.09, 114.91, 61.36, 53.99, 24.53, 14.50. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{23}H_{20}N_4O_2Br$: 463.0769; found: 463.0763.

8-bromo-3-(5-methoxy-3,3-dimethyl-3*H*-indol-2-yl)pyrimido[1,2-*b*]indazole (3h): Yellow solid. Yield: 73%. mp = 226 – 228 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.53 (d, 1H, J = 2.0 Hz, CHN), 9.50 (d, 1H, J = 2.0 Hz, CHN), 8.49 (s, 1H, Ar-H), 7.75 (m, 3H, Ar-H), 6.96 (m, 2H, Ar-H), 3.90 (s, 3H, OCH_3), 1.66 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.17, 159.55, 150.73, 149.04, 146.57, 146.43, 142.27, 133.90, 132.25, 123.21, 122.26, 119.17, 118.08, 114.94, 114.78, 113.17, 107.65, 55.89, 53.82, 24.82. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{21}H_{18}N_4OBr$: 421.0664; found: 421.0663.

8-bromo-3-(1,1-dimethyl-1*H*-benzo[*e*]indol-2-yl)pyrimido[1,2-*b*]indazole (3i): Yellow solid. Yield: 73%. mp = 238 – 240 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.66 (d, 1H, J = 2.4 Hz, CHN), 9.64 (d, 1H, J = 1.8 Hz, CHN), 8.50 (d, 1H, J = 1.2 Hz, Ar-H), 8.17 (d, 1H, J = 8.4 Hz, Ar-H), 8.02 (d, 1H, J = 8.4 Hz, Ar-H), 7.97 (s, 2H, Ar-H), 7.76 (d, 1H, J = 8.4 Hz, Ar-H), 7.72 (dd, 1H, J = 9.0, 1.8 Hz, Ar-H), 7.65 (t, 1H, J = 7.2 Hz, Ar-H), 7.56 (t, 1H, J = 7.2 Hz, Ar-H), 1.93 (s, 6H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ 179.04, 150.81, 150.05, 146.44, 142.33, 140.62, 133.93, 133.26, 132.54, 130.00, 129.80, 127.92, 126.88, 125.43, 123.18, 122.73, 120.61, 118.61, 118.06, 114.89, 114.80, 55.40, 24.13. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{24}H_{18}N_4Br$: 441.0716; found: 441.0634.

8-bromo-3-(3,3-dimethyl-3*H*-benzo[*g*]indol-2-yl)pyrimido[1,2-*b*]indazole (3j): Yellow solid. Yield: 78%. mp = 256 – 258 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.80 (d, 1H, J = 2.4 Hz, CHN), 9.73 (d, 1H, J = 1.6 Hz, CHN), 8.85 (d, 1H, J = 8.4 Hz, Ar-H), 8.51 (d, 1H, J = 0.8 Hz, Ar-H), 7.96 (d, 1H, J = 8.0 Hz, Ar-H), 7.92 (d, 1H, J = 8.0 Hz, Ar-H), 7.78 (m, 3H, Ar-H), 7.60 (m, 2H, Ar-H), 1.76 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.26, 150.77, 147.80, 146.59, 143.84, 142.37, 134.10, 133.92, 132.77, 128.25, 128.00, 127.31, 127.15, 126.34, 123.42, 123.26, 118.90, 118.79, 118.10, 114.98, 114.93, 54.72, 24.27. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{24}H_{18}N_4Br$: 441.0715; found: 441.0711.

3-(3,3-dimethyl-3*H*-indol-2-yl)-10-methoxypyrimido[1,2-*b*]indazole (3k): Orange solid. Yield: 61%. mp = 212 – 214 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (d, 1H, J = 2.4 Hz, CHN), 9.58 (d, 1H, J = 2.4 Hz, CHN), 7.77 (dd, 1H, J = 7.6, 1.2 Hz, Ar-H), 7.61 (dd, 1H, J = 8.0, 0.8 Hz, Ar-H), 7.45 (m, 3H, Ar-H), 7.37 (td, 1H, J = 7.2, 0.8 Hz, Ar-H), 6.66 (d, 1H, J = 7.2 Hz, Ar-H), 4.17 (s, 3H, OCH_3), 1.67 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.68, 155.76, 154.10, 152.85, 147.11, 146.30, 142.90, 132.68, 131.67, 128.31, 126.95, 121.60, 121.12, 117.94, 108.70, 105.44, 99.79, 56.19, 53.76, 24.62. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{21}H_{19}N_4O$: 343.1559; found: 343.1568.

Ethyl 2-(10-methoxypyrimido[1,2-*b*]indazol-3-yl)-3,3-dimethyl-3*H*-indole-5-carboxylate (3l): Yellow solid. Yield: 94%. mp = 194 – 196 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.67 (d, 1H, J = 2.4 Hz, CHN), 9.58 (d, 1H, J = 2.4 Hz, CHN), 8.16 (dd, 1H, J = 8.4, 1.6 Hz, Ar-H), 8.09 (d, 1H, J = 1.6 Hz, Ar-H), 7.80 (d, 1H, J = 8.0 Hz, Ar-H), 7.62 (t, 1H, J = 8.4 Hz, Ar-H), 7.45 (d, 1H, J = 8.8 Hz, Ar-H), 6.66 (d, 1H, J = 7.6 Hz, Ar-H), 4.45 (q, 2H, CH_2), 4.17 (s, 3H, OCH_3), 1.70 (s, 6H, CH_3), 1.45 (t, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.58, 166.51, 156.44, 155.69, 154.19, 147.04, 146.03, 142.94, 133.05, 131.80, 130.43, 128.71, 122.44, 121.17, 117.39, 108.64, 105.42, 99.83, 61.20, 56.11, 53.88, 24.41, 14.41. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{24}H_{23}N_4O_3$: 415.1770; found: 415.1771.

10-methoxy-3-(5-methoxy-3,3-dimethyl-3*H*-indol-2-yl)pyrimido[1,2-*b*]indazole (3m): Yellow solid. Yield: 68%. mp = 258 – 260 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (d, 1H, J = 2.4 Hz, CHN), 9.55 (d, 1H, J = 2.4 Hz, CHN), 7.68 (d, 1H, J = 9.2 Hz, Ar-H), 7.60 (dd, 1H, J = 8.4, 0.8 Hz, Ar-H), 7.44 (d, 1H, J = 8.4 Hz, Ar-H), 6.95 (m, 2H, Ar-H), 6.66 (d, 1H, J = 7.2 Hz, Ar-H), 4.17 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 1.64 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.47, 159.37, 155.73, 153.98, 149.03, 146.66, 146.28, 142.72, 132.11, 131.54, 122.14, 118.15, 113.03, 108.65, 107.63, 105.43, 99.73, 56.17, 55.86, 53.83, 24.78. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{22}H_{21}N_4O_2$; found: 373.1664; found: 373.1673.

3-(1,1-dimethyl-1*H*-benzo[*e*]indol-2-yl)-10-methoxypyrimido[1,2-*b*]indazole (3n): Yellow solid. Yield: 83%. mp = 241 – 243 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (d, 1H, J = 2.4 Hz, CHN), 9.67 (d, 1H, J = 2.4 Hz, CHN), 8.17 (d, 1H, J = 8.4 Hz, Ar-H), 8.02 (d, 1H, J = 8.4 Hz, Ar-H), 7.96 (s, 2H, Ar-H), 7.65 (m, 2H, Ar-H), 7.55 (td, 1H, J = 7.2, 1.2 Hz, Ar-H), 7.46 (d, 1H, J = 8.8 Hz, Ar-H), 6.67 (d, 1H, J = 7.2 Hz, Ar-H), 4.18 (s, 3H, OCH_3), 1.91 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.42, 155.77, 154.09, 150.25, 146.41, 142.84, 140.63, 133.23, 132.48, 131.67, 130.04, 129.77, 128.00, 126.87, 125.35, 122.81, 120.74, 117.70, 108.69, 105.47, 99.81, 56.20, 55.46, 24.13. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{25}H_{21}N_4O$: 393.1710; found: 393.1724.

3-(3,3-dimethyl-3*H*-benzo[*g*]indol-2-yl)-10-methoxypyrimido[1,2-*b*]indazole (3o): Yellow solid. Yield: 70%. mp = 206 – 208 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.94 (d, 1H, J = 1.6 Hz, CHN), 9.74 (d, 1H, J = 2.4 Hz, CHN), 8.81 (d, 1H, J = 8.0 Hz, Ar-H), 7.96 (d, 1H, J = 8.0 Hz, Ar-H), 7.90 (d, 1H, J = 8.4 Hz, Ar-H), 7.72 (td, 1H, J = 6.8, 1.6 Hz, Ar-H), 7.65 (m, 3H, Ar-H), 7.47 (d, 1H, J = 8.4 Hz, Ar-H), 6.70 (d, 1H, J = 7.6 Hz, Ar-H), 4.19 (s, 3H, OCH_3), 1.75 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.47, 155.78, 153.78, 148.05, 146.60, 143.83, 142.78, 133.89, 132.58, 131.83, 128.20, 127.67, 127.36, 127.00, 126.22, 123.42, 118.84, 118.07, 108.52, 105.44, 99.90, 56.19, 54.74, 24.17. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{25}H_{21}N_4O$: 393.1715; found: 393.1716.

3-(3,3-dimethyl-3*H*-indol-2-yl)-8-(trifluoromethyl)pyrimido[1,2-*b*]indazole (3p): Yellow solid. Yield: 50%. mp = 209 – 211 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (d, 1H, J = 1.6 Hz, CHN), 9.64 (d, 1H, J = 2.0 Hz, CHN), 8.47 (d, 1H, J = 8.8 Hz, Ar-H), 8.18 (s, 1H, Ar-H), 7.81 (d, 1H, J = 7.6 Hz, Ar-H), 7.54 (dd, 1H, J = 8.8, 1.2 Hz, Ar-H), 7.47 (m, 3H, Ar-H), 1.70 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.32, 152.25, 151.14, 146.98, 146.85, 143.24, 133.11, 132.48 (q, J = 31.5 Hz), 128.51, 127.43, 125.63 (q, J = 271.7 Hz), 122.37, 121.69, 121.22, 119.15, 117.70 (q, J = 1.9 Hz), 115.07, 114.77 (q, J = 4.8 Hz), 53.81, 24.67. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.32. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{21}H_{16}N_4F_3$: 381.1321; found: 381.1234.

Ethyl 3,3-dimethyl-2-(8-(trifluoromethyl)pyrimido[1,2-*b*]indazol-3-yl)-3*H*-indole-5-carboxylate (3q): Yellow solid. Yield: 56%. mp = 222 – 224 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.74 (d, 1H, J = 2.0 Hz, CHN), 9.65 (d, 1H, J = 2.0 Hz, CHN), 8.48 (d, 1H, J = 8.4 Hz, Ar-H), 8.19 (s, 1H, Ar-H), 8.18 (d, 1H, J = 1.6 Hz, Ar-H), 8.13 (d, 1H, J = 0.8 Hz, Ar-H), 7.86 (d, 1H, J = 8.0 Hz, Ar-H), 7.56 (dd, 1H, J = 8.8, 1.6 Hz, Ar-H), 4.46 (q, 2H, CH_2), 1.75 (s, 6H, CH_3), 1.46 (t, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.19, 166.42, 156.25, 151.19, 147.03, 146.59, 143.27, 133.35, 132.54 (q, J = 32.2 Hz), 130.54, 129.08, 125.52 (q, J = 271.7 Hz), 122.53, 122.30, 121.37, 118.92, 117.72 (q, J = 3.0 Hz), 114.97, 114.81 (q, J = 4.6 Hz), 61.28, 53.97, 24.44, 14.42. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.38. HRMS (ESI): m/z [M + H]$^+$ calcd $C_{24}H_{20}N_4O_2F_3$: 453.1538; found: 453.1562.

3-(5-methoxy-3,3-dimethyl-3*H*-indol-2-yl)-8-(trifluoromethyl)pyrimido[1,2-*b*]indazole (3r): Yellow solid. Yield: 63%. mp = 210 – 212 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (d, 1H, J = 2.0 Hz, CHN), 9.60 (d, 1H, J = 2.4 Hz, CHN), 8.46 (d, 1H, J = 8.8 Hz, Ar-H), 8.17 (s, 1H, Ar-H), 7.72 (d, 1H, J = 8.8 Hz, Ar-H), 7.53 (dd, 1H, J = 8.4, 1.2 Hz, Ar-H), 6.97 (m, 2H, Ar-H), 3.90 (s, 3H, OCH_3), 1.68 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.01, 159.76, 151.01, 148.92, 146.79, 145.91, 143.03, 132.52, 132.36 (q, J = 31.4 Hz), 125.65 (q, J = 271.7 Hz), 122.29 (2C), 119.29, 117.62 (q, J = 2.9 Hz), 115.08, 114.71 (q, J = 4.8 Hz), 113.30, 107.68, 55.91, 53.85, 24.84. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.29. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{22}H_{18}N_4OF_3$: 411.1233; found: 411.1160.

3-(1,1-dimethyl-1*H*-benzo[*e*]indol-2-yl)-8-(trifluoromethyl)pyrimido[1,2-*b*]indazole (3s): Yellow solid. Yield: 59%. mp = 217 – 219 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.79 (d, 1H, J = 2.0 Hz, CHN), 9.74 (d, 1H, J = 2.0 Hz, CHN), 8.49 (d, 1H, J = 8.8 Hz, Ar-H), 8.20 (m, 2H, Ar-H), 8.04 (m, 3H, Ar-H), 7.68 (t, 1H, J = 7.2 Hz, Ar-H), 7.58 (m, 2H, Ar-H), 1.96 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.98, 151.18, 149.32, 146.88, 143.17, 140.66, 133.44, 133.00, 132.52 (q, J = 31.4 Hz), 130.14, 130.07, 127.93, 127.12, 125.75, 125.63 (q, J = 271.7 Hz), 122.82, 122.38, 120.41, 118.70, 117.75 (q, J = 2.8 Hz), 115.09, 114.79 (q, J = 4.8 Hz), 55.53, 24.25. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.32. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{25}H_{18}N_4F_3$: 431.1284; found: 431.1195.

3-(3,3-dimethyl-3*H*-benzo[*g*]indol-2-yl)-8-(trifluoromethyl)pyrimido[1,2-*b*]indazole (3t): Yellow solid. Yield: 79%. mp = 280 – 282 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.78 (d, 1H, J = 2.0 Hz, CHN), 9.76 (d, 1H, J = 2.0 Hz, CHN), 8.80 (d, 1H, J = 8.0 Hz, Ar-H), 8.48 (d, 1H, J = 8.8 Hz, Ar-H), 8.19 (s, 1H, Ar-H), 7.95 (d, 1H, J = 8.0 Hz, Ar-H), 7.92 (d, 1H, J = 8.0 Hz, Ar-H), 7.71 (t, 1H, J = 7.2 Hz, Ar-H), 7.59 (m, 3H, Ar-H), 1.77 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.12, 151.06, 147.72, 146.96, 143.90, 143.13, 133.92, 132.88, 132.45 (q, J = 32.4 Hz), 128.28, 128.18, 127.31, 127.22, 126.39, 125.65 (q, J = 271.7 Hz), 123.40, 122.34, 119.30, 118.78, 117.68 (q, J = 2.9 Hz), 115.10, 114.73 (q, J = 4.8 Hz), 54.77, 24.25. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.29. HRMS (ESI): m/z $[M + H]^+$ calcd $C_{25}H_{18}N_4F_3$: 431.1284; found: 431.1208.

X-ray crystallography

X-ray intensity data for a yellow crystal of **3a** (0.09 × 0.22 × 0.28 mm) were measured at T = 294 K on Rigaku/Oxford Diffraction XtaLAB Synergy diffractometer (Dualflex, AtlasS2) fitted with CuKα radiation (λ = 1.54178 Å) so that θ_{max} = 67.7° (= 100% completeness). Data reduction, including absorption correction, was accomplished with CrysAlisPro.[S1] The structure was solved by direct-methods[S2] and refined (anisotropic displacement parameters and H atoms in the riding model approximation) on F^2.[S3] A weighting scheme of the form $w = 1/[\sigma^2(F_o^2) + (0.108P)^2 + 0.413P]$, where $P = (F_o^2 + 2F_c^2)/3$, was introduced towards the end of the refinement. The molecular structure diagram was generated with ORTEP for Windows[S4] with 35% displacement ellipsoids, and the packing diagrams were drawn with DIAMOND.[S5] Additional data analysis was made with PLATON.[S6]

S1 Rigaku Oxford Diffraction, CrysAlis PRO, Yarnton, Oxfordshire, England (2017).

S2 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr*., 2008, **64**, 112-122.

S3 G. M. Sheldrick, *Acta Crystallogr*., *Sect. C: Struct. Chem*., 2015, **71**, 3-8.

S4 L. J. Farrugia, *J. Appl. Crystallogr*., 2012, **45**, 849-854.

S5 K. Brandenburg, DIAMOND, Crystal Impact GbR, Bonn, Germany, 2006.

S6 A. L. Spek, *Acta Crystallogr. Sect. E: Crystallogr*. *Commun*., 2020, **76**, 1-10.

Table S1: Crystallographic data and refinement details for **3a**

CCDC deposition number	2082645
Formula	$C_{20}H_{16}N_4$
Molecular weight	312.37
Crystal system	monoclinic
Space group	$P2_1/m$
a/Å	7.2371(1)
b/Å	6.8632(1)
c/Å	16.2164(3)
β/°	101.478(1)
V/Å^3	789.36(2)
Z	2
D_c/g cm^{-3}	1.314
μ/mm^{-1}	0.634
Measured data	10920
Unique data	1774
Observed data ($I \geq 2.0\sigma(I)$)	1622
No. parameters	143
R, obs. data; all data	0.069; 0.194
R_w, obs. data; all data	0.072; 0.198
Largest diff. peak/ hole /e Å^{-3}	0.84 / -0.28

Details of the molecular packing in the crystal of 3a

Molecules are connected into a linear chain *via* C–H···N interactions.

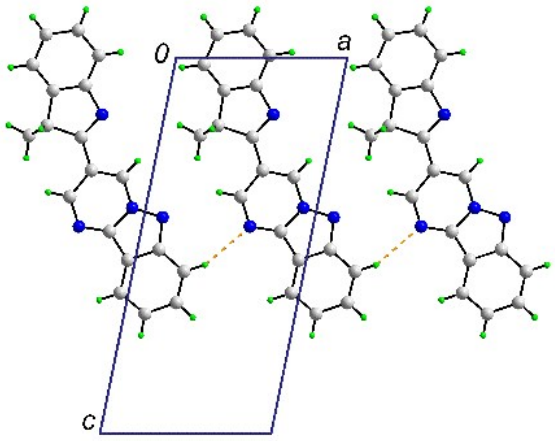

Fig. S2: Molecular packing in the crystal of **3a**. [C18–H18···N2^{i}: H18···N2^{i} = 2.51 Å, C18···N2^{i} = 3.382(4) Å with angle at H18 = 157° for symmetry operation (i): 1+*x*, *y*, *z*].

The links between chains include π(N3,N4,C12,C14,C19)…π(N3,N4,C12,C14,C19)^{ii} [Cg…Cg = 3.5825(5) Å; symmetry operation ii: 2-*x*, -½+*y*, 1-*z*] and π(N2,N3,C10-C13)…π(C14-C19)^{ii} [Cg…Cg = 3.5880(5) Å] contacts between centrosymmetrically-related molecules shown as purple dashed lines in the unit-cell diagram (viewed slightly off-set from -*a*), to establish layers in the *ab*-plane. The closest links between layers along the *c*-axis to consolidate the three-dimensional packing are C7…C7^{iii} contacts (blue dashed lines) between parallel (C3-C8) rings, vertical separation = 3.4316(11) Å [Cg…Cg = 4.0412(11) Å], which are off-set from each other by 2.134 Å for symmetry operation (iii): 1-*x*, -½+*y*, -*z*.

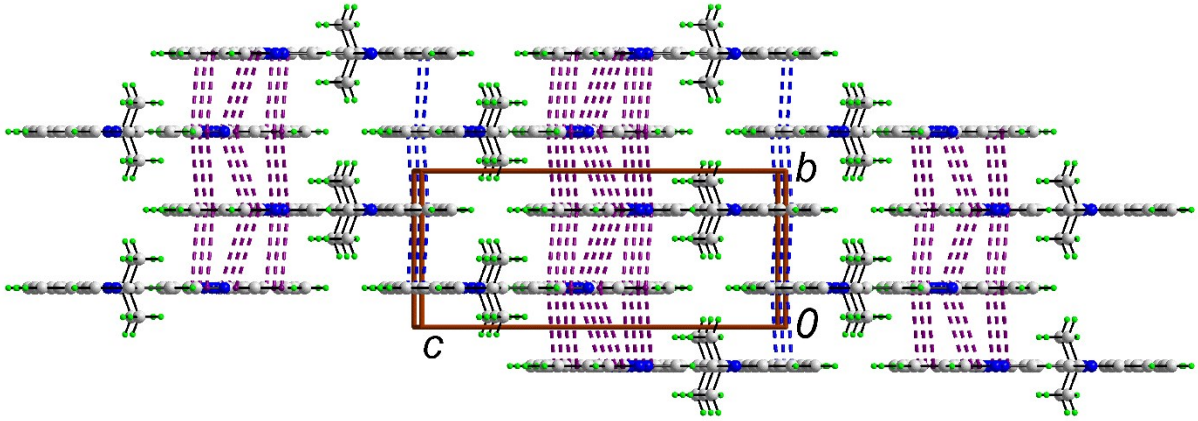

Fig. S3: Unit cell contents for **3a**.

Table S2: UV-vis absorption parameters of **3a** and **3d**

Compound	Solvent	Absorption, λ_{max} (nm) / ε ($\times 10^4$ M^{-1} cm^{-1})	λ_{onset} (nm)	$E_{gap} = 1240 / \lambda_{onset}$ (eV)
3a	$CHCl_3$	328 (6.52)	383.0	3.24
3d	AcOH	346 (6.32)	438.8	2.83
	$CHCl_3$	350 (6.49)	430.4	2.88
	DMF	347 (6.74)	427.5	2.90
	MeOH	346 (6.33)	430.0	2.88
	THF	348 (6.73)	424.2	2.92

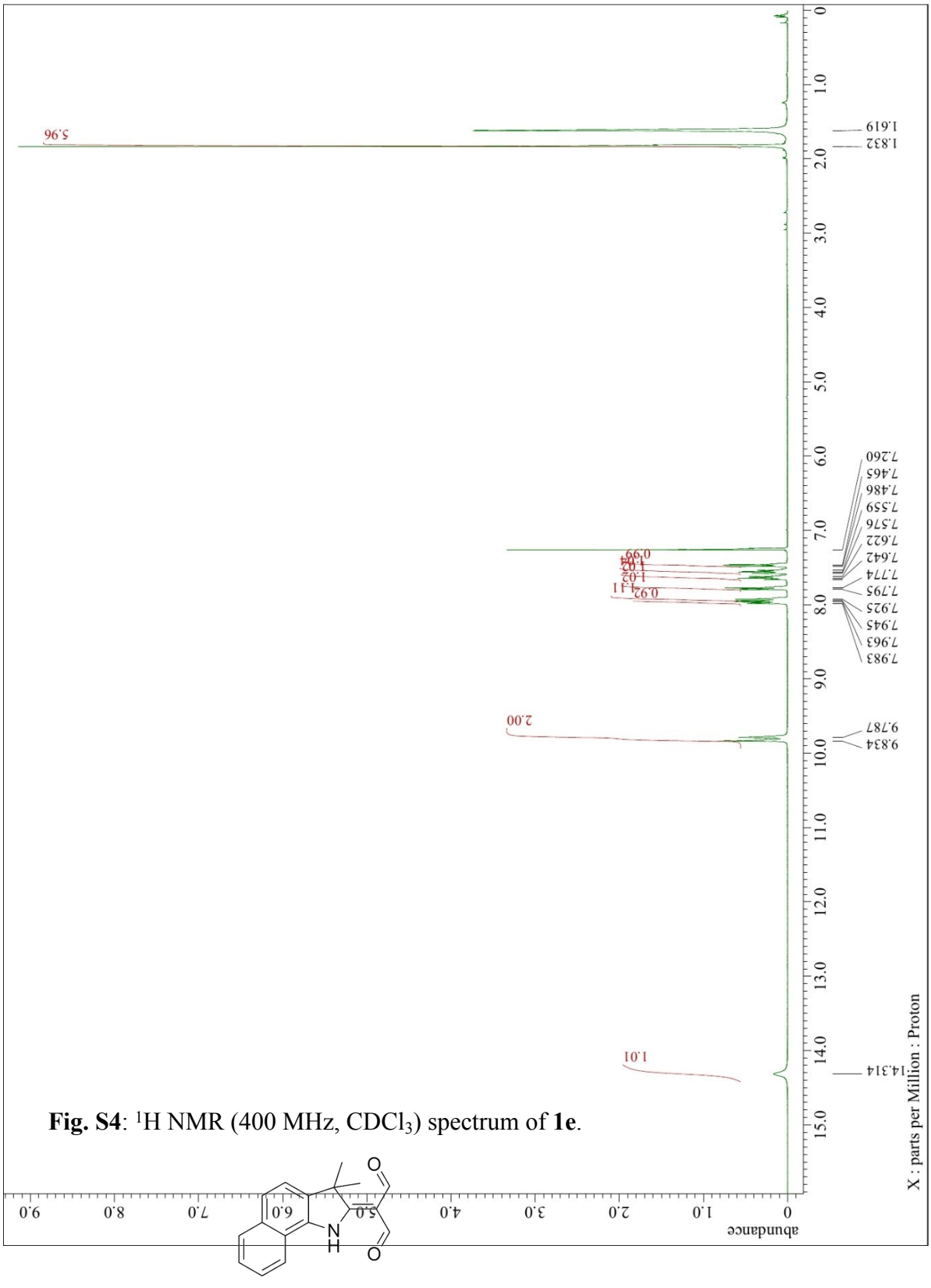

Fig. S4: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **1e**.

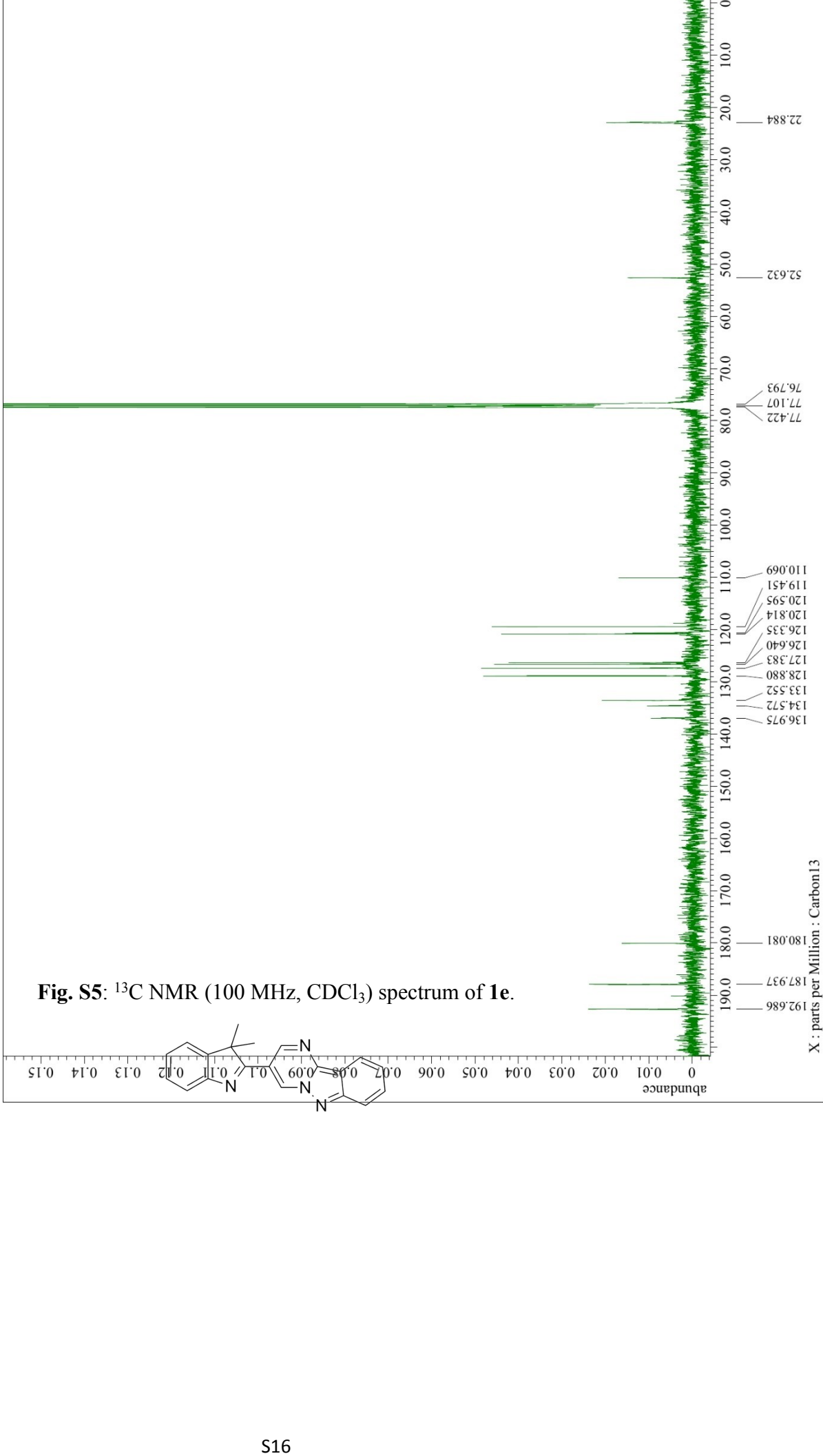

Fig. S5: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **1e**.

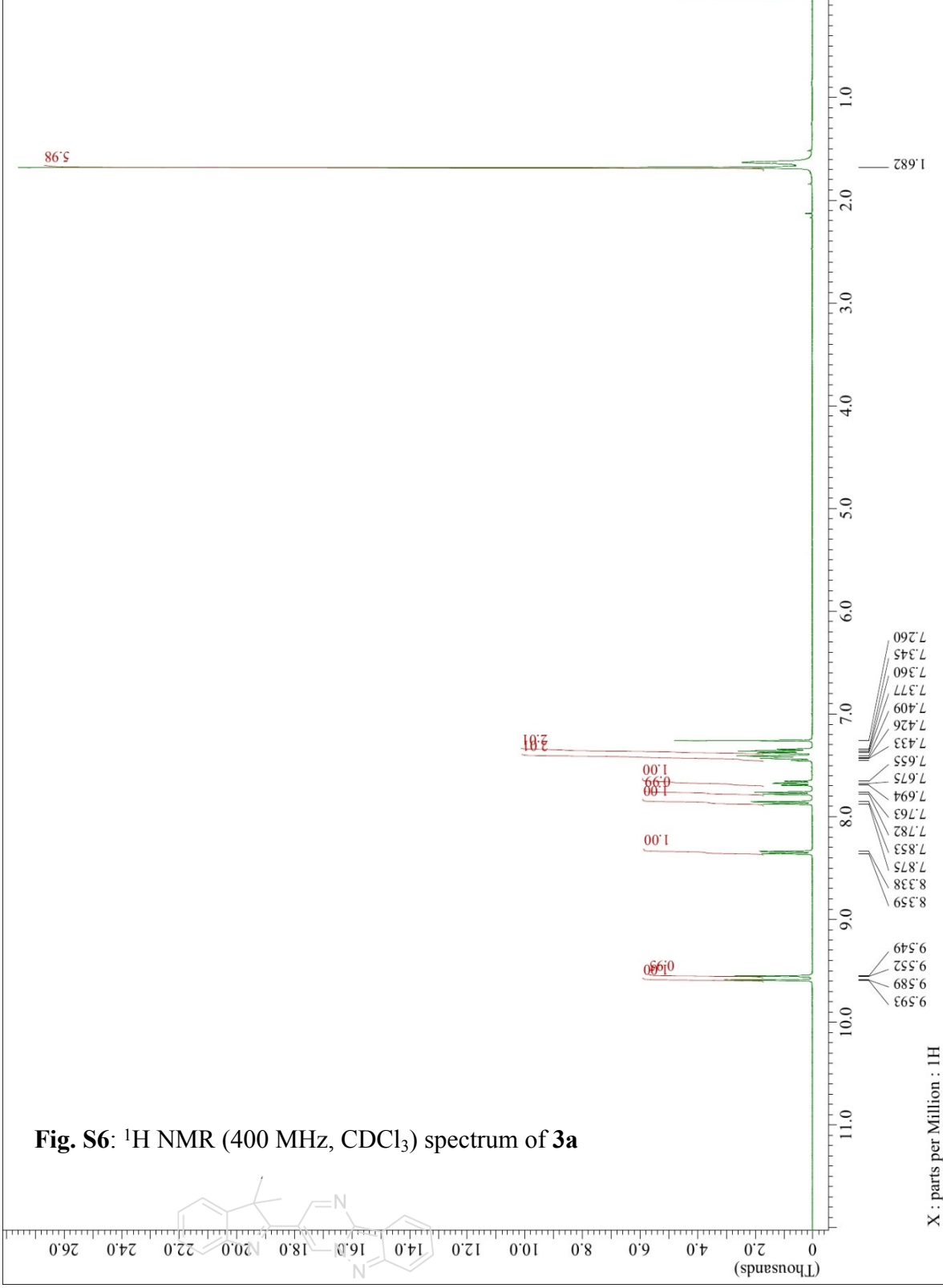

Fig. S6: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3a**

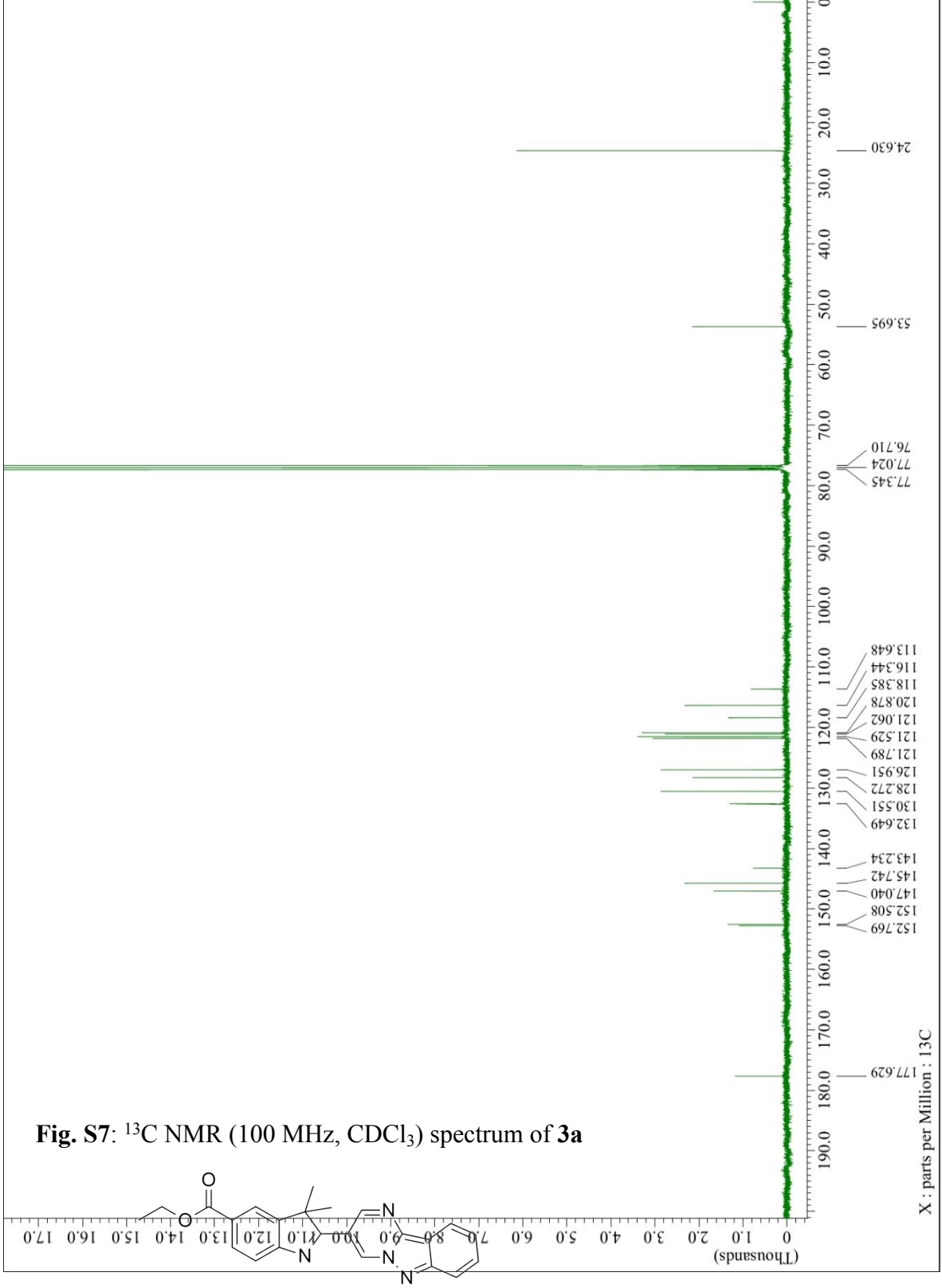

Fig. S7: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3a**

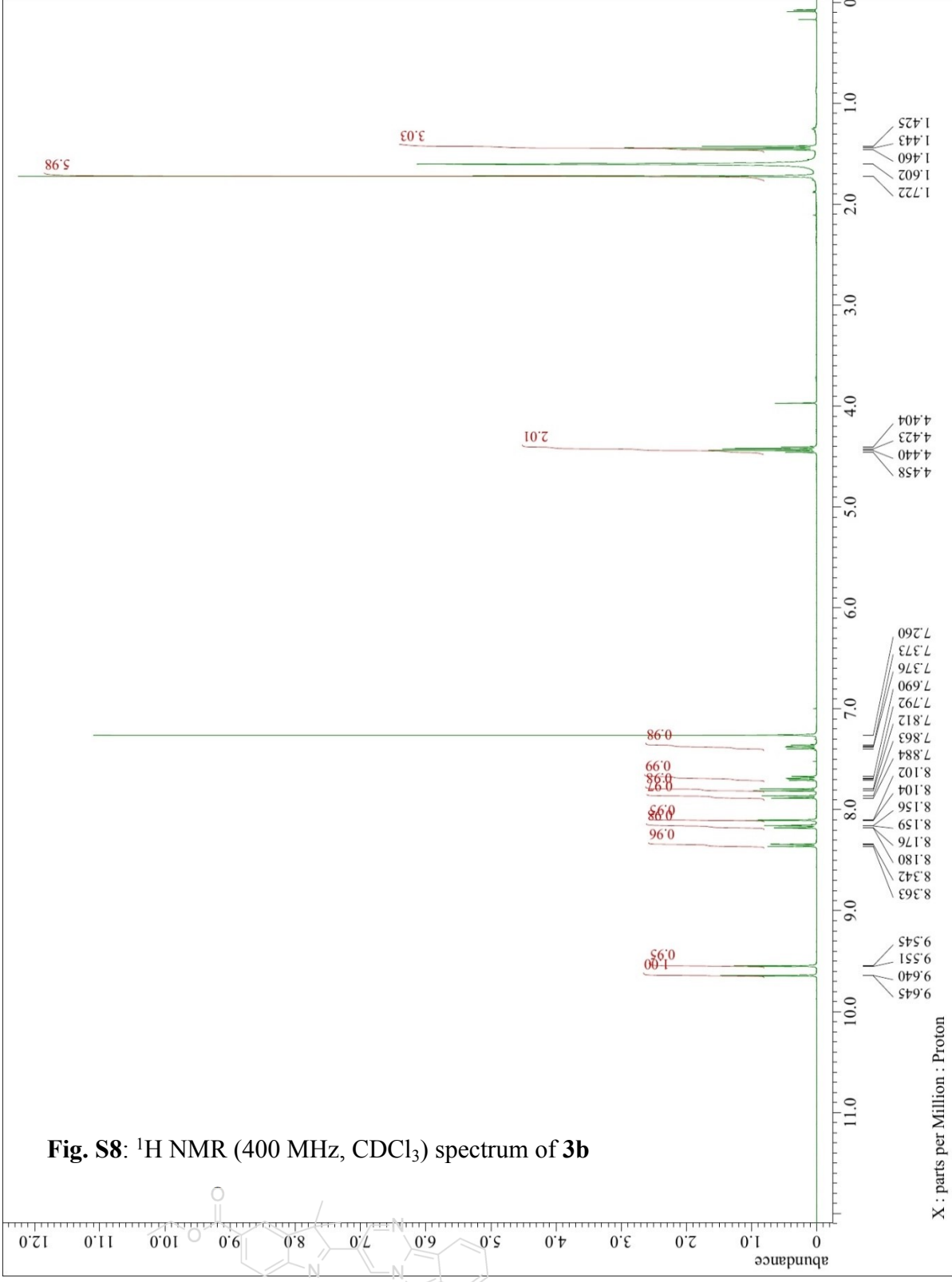

Fig. S8: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3b**

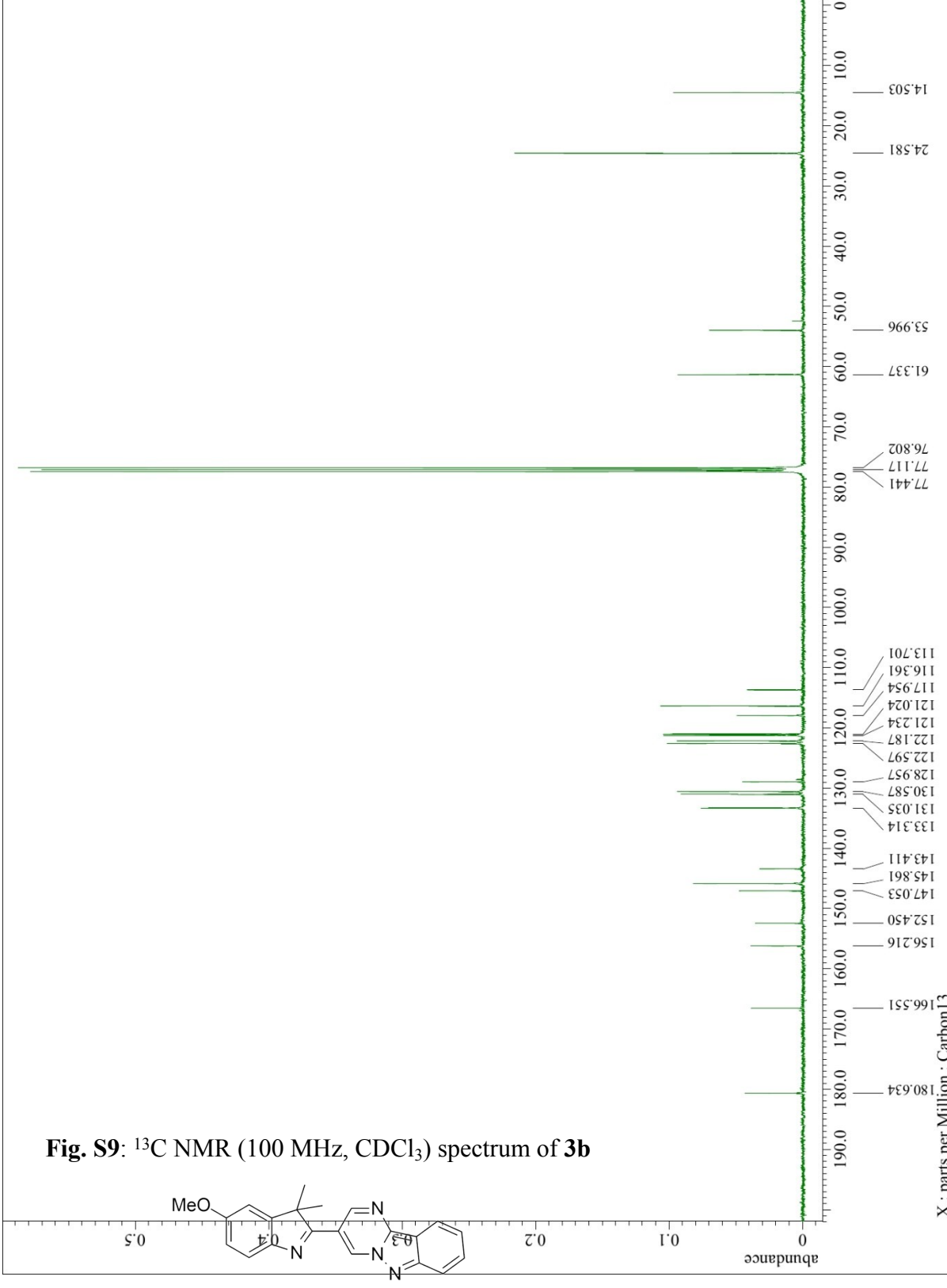

Fig. S9: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3b**

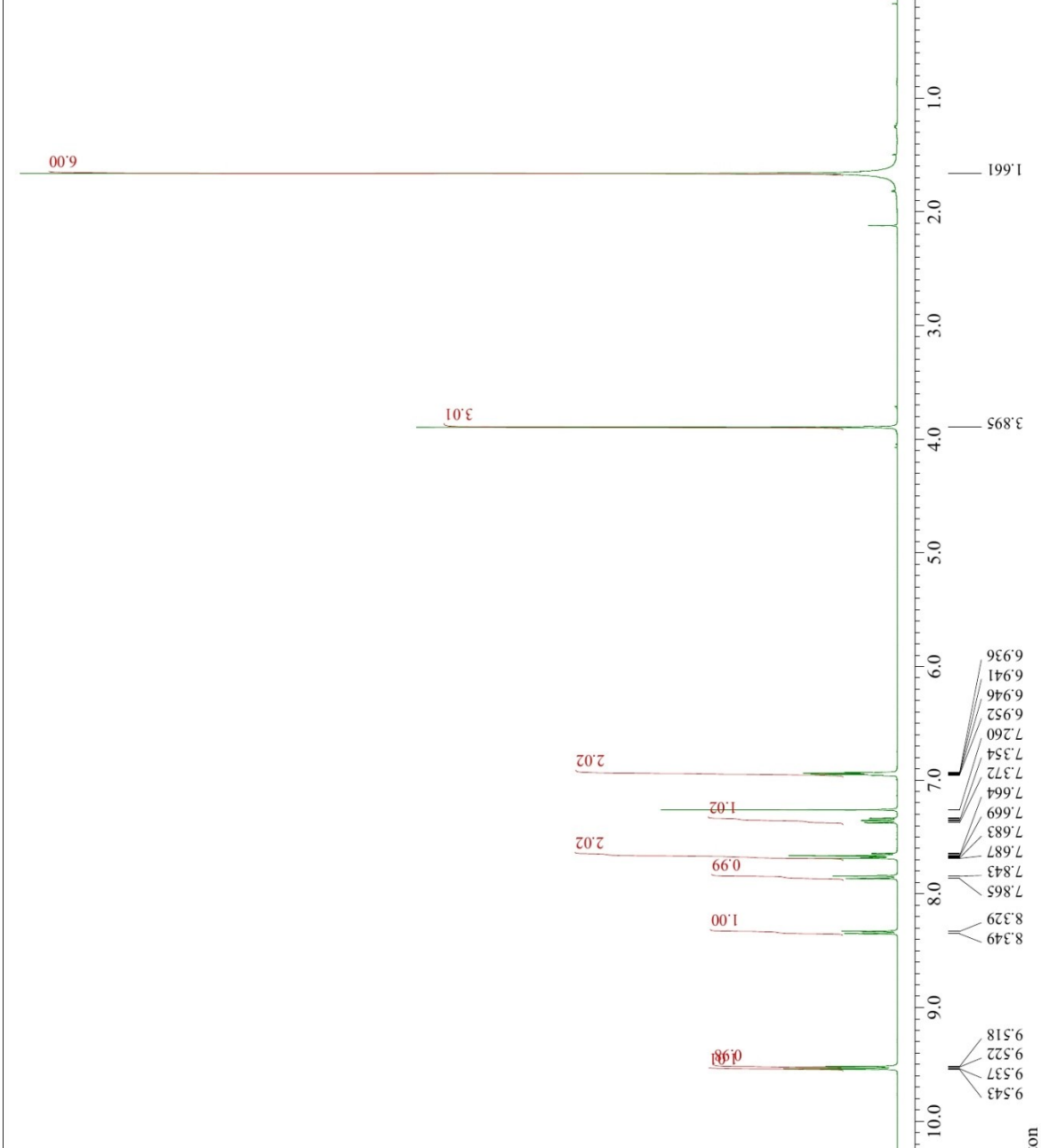

Fig. S10: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3c**

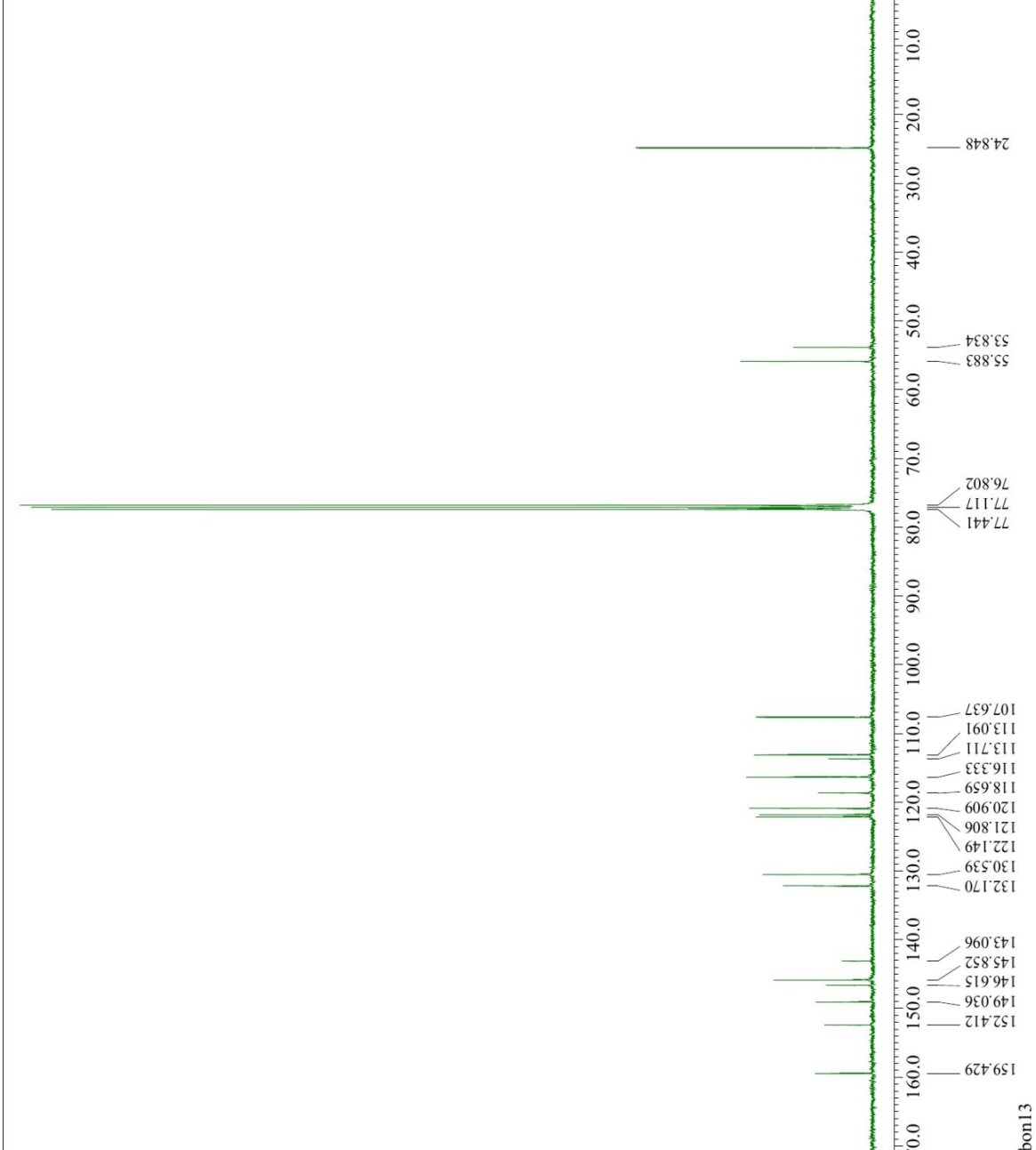

Fig. S11: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3c**

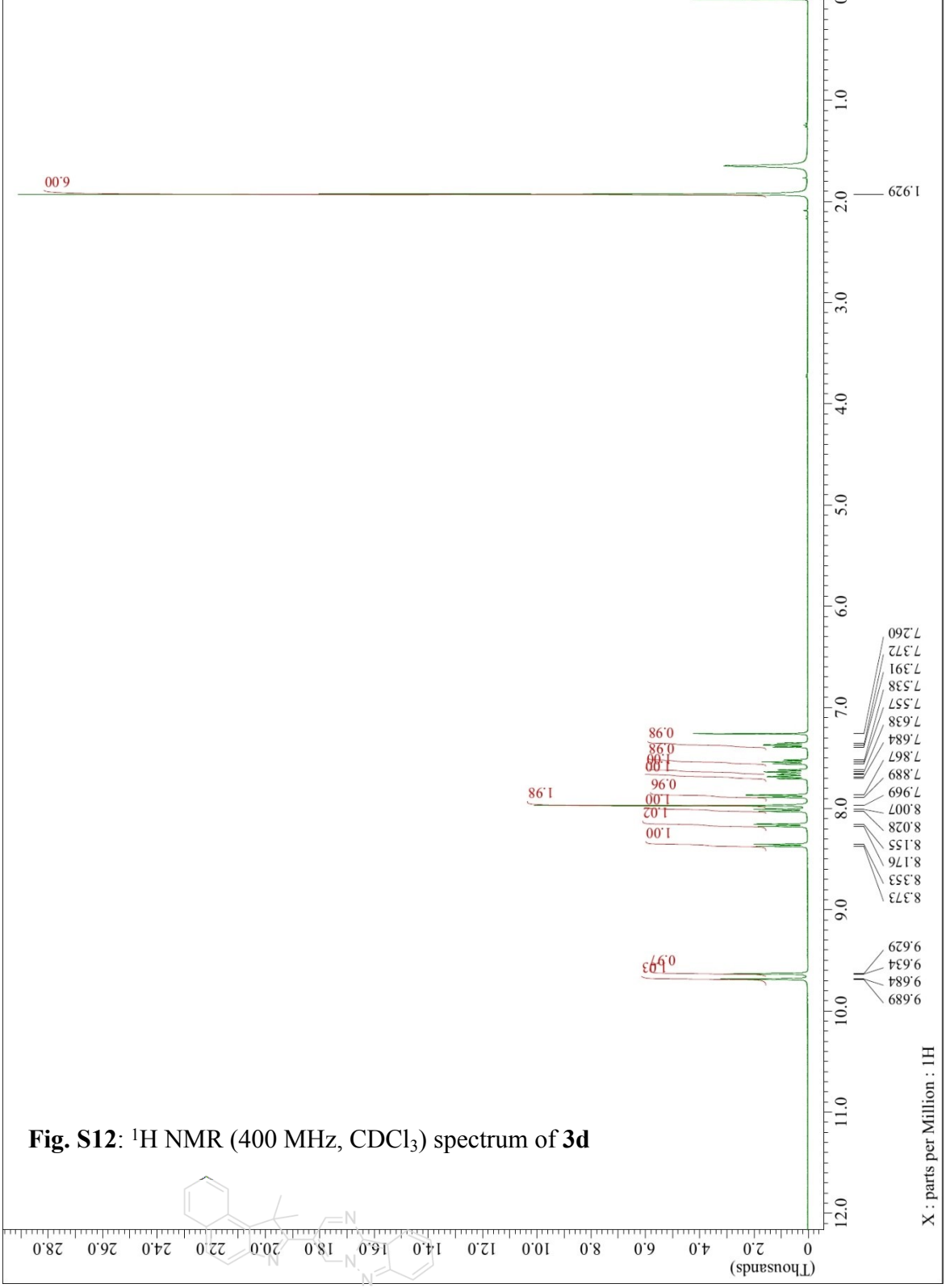

Fig. S12: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3d**

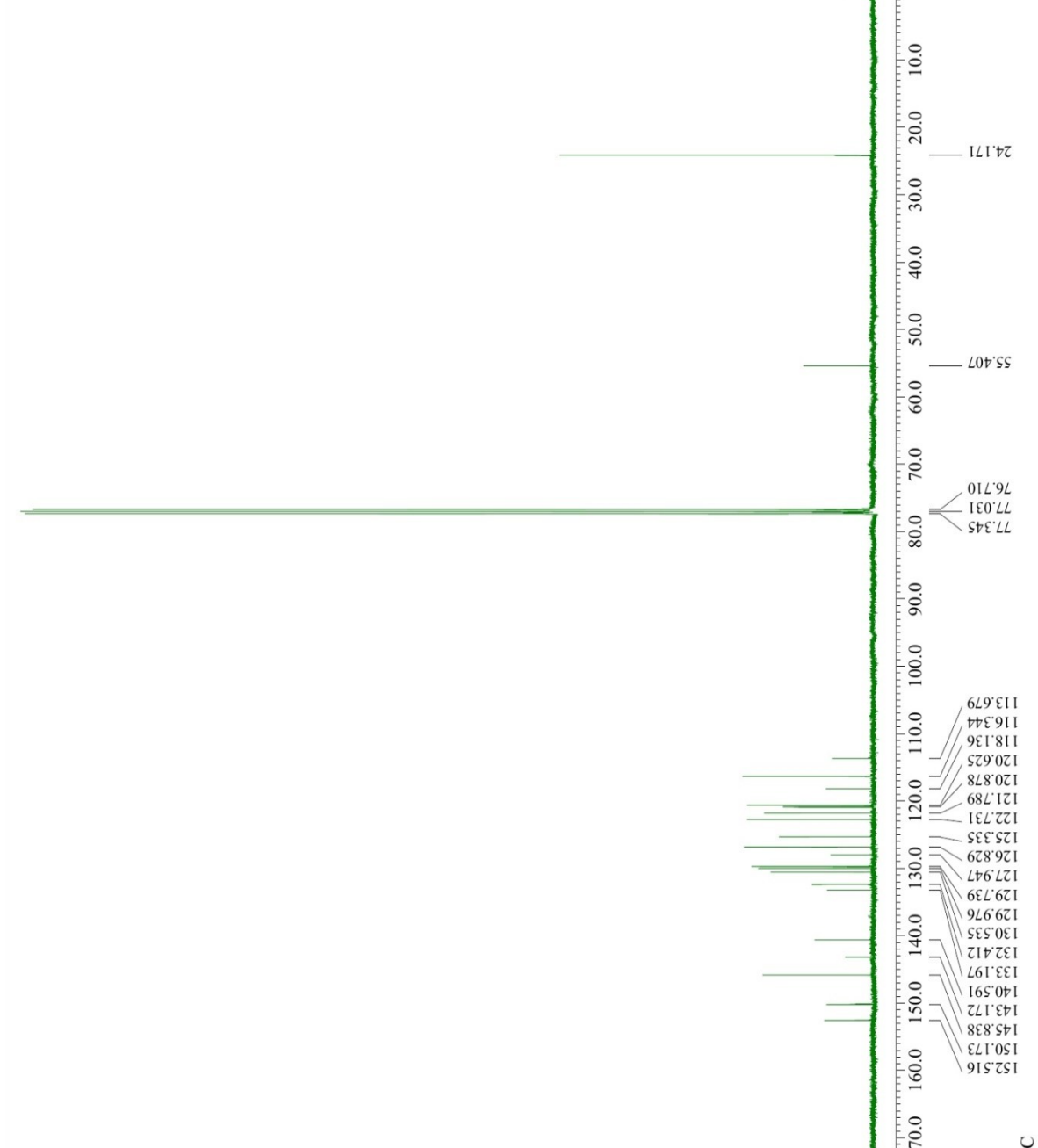

Fig. S13: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3d**

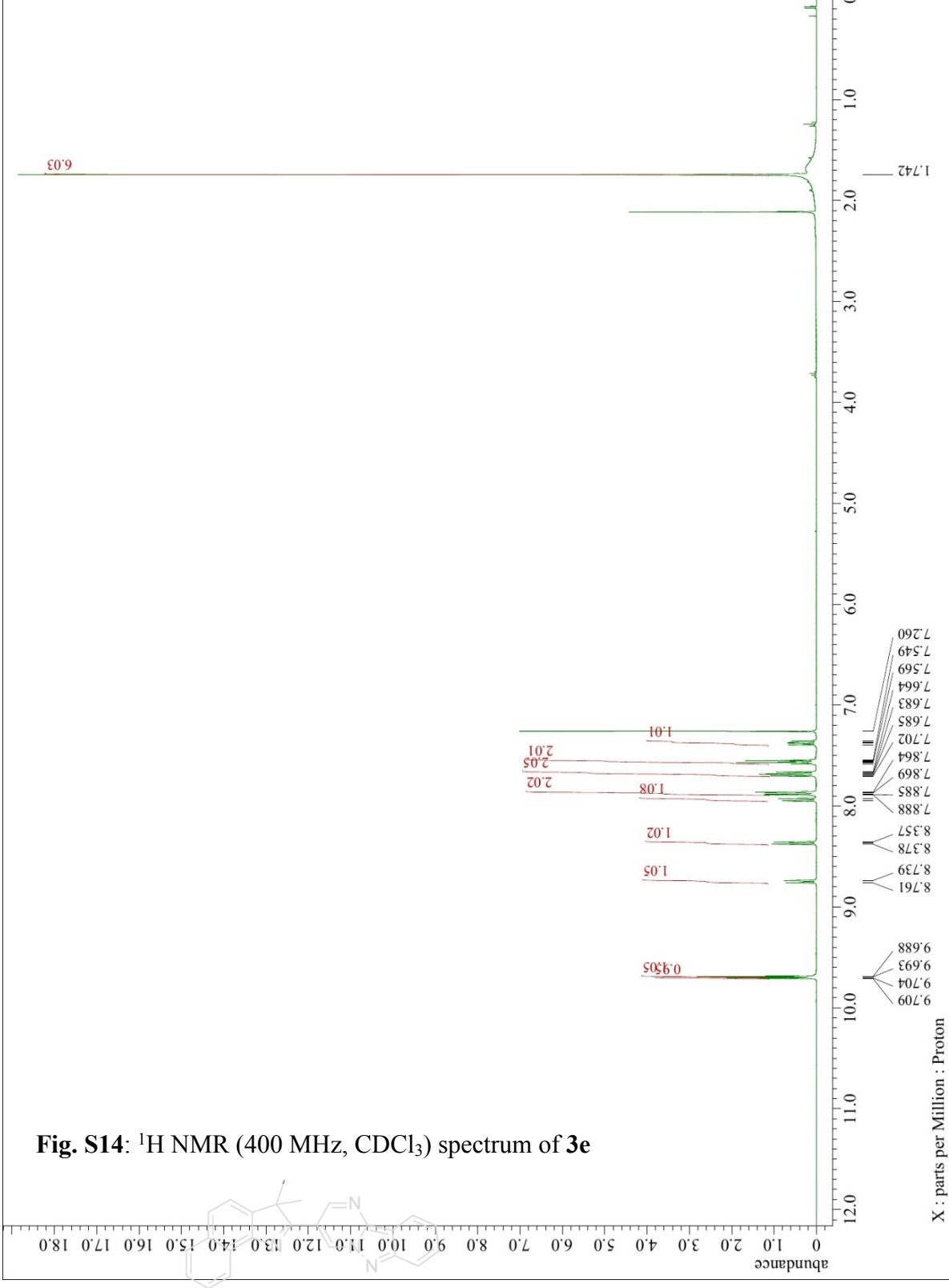

Fig. S14: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3e**

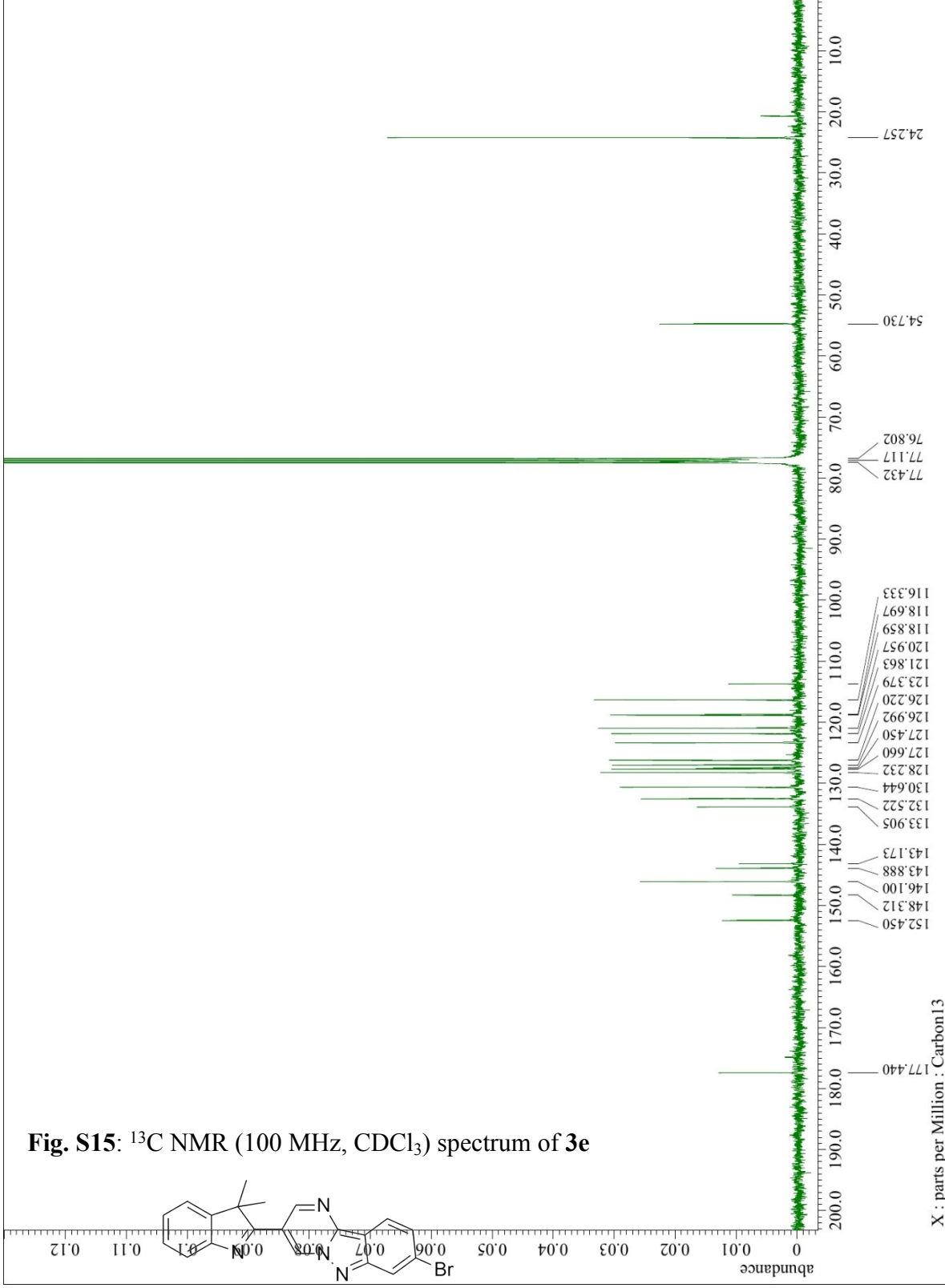

Fig. S15: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3e**

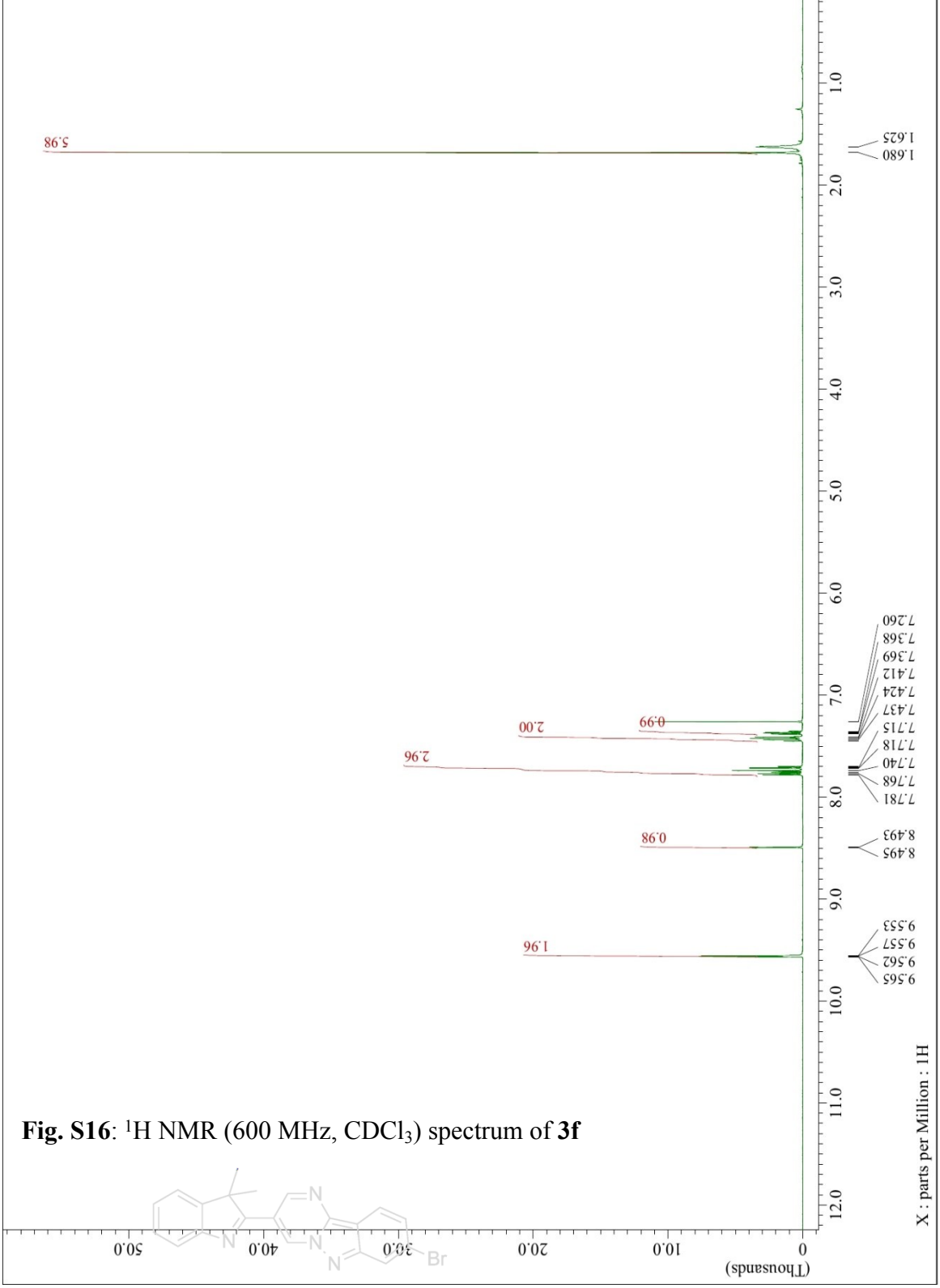

Fig. S16: ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **3f**

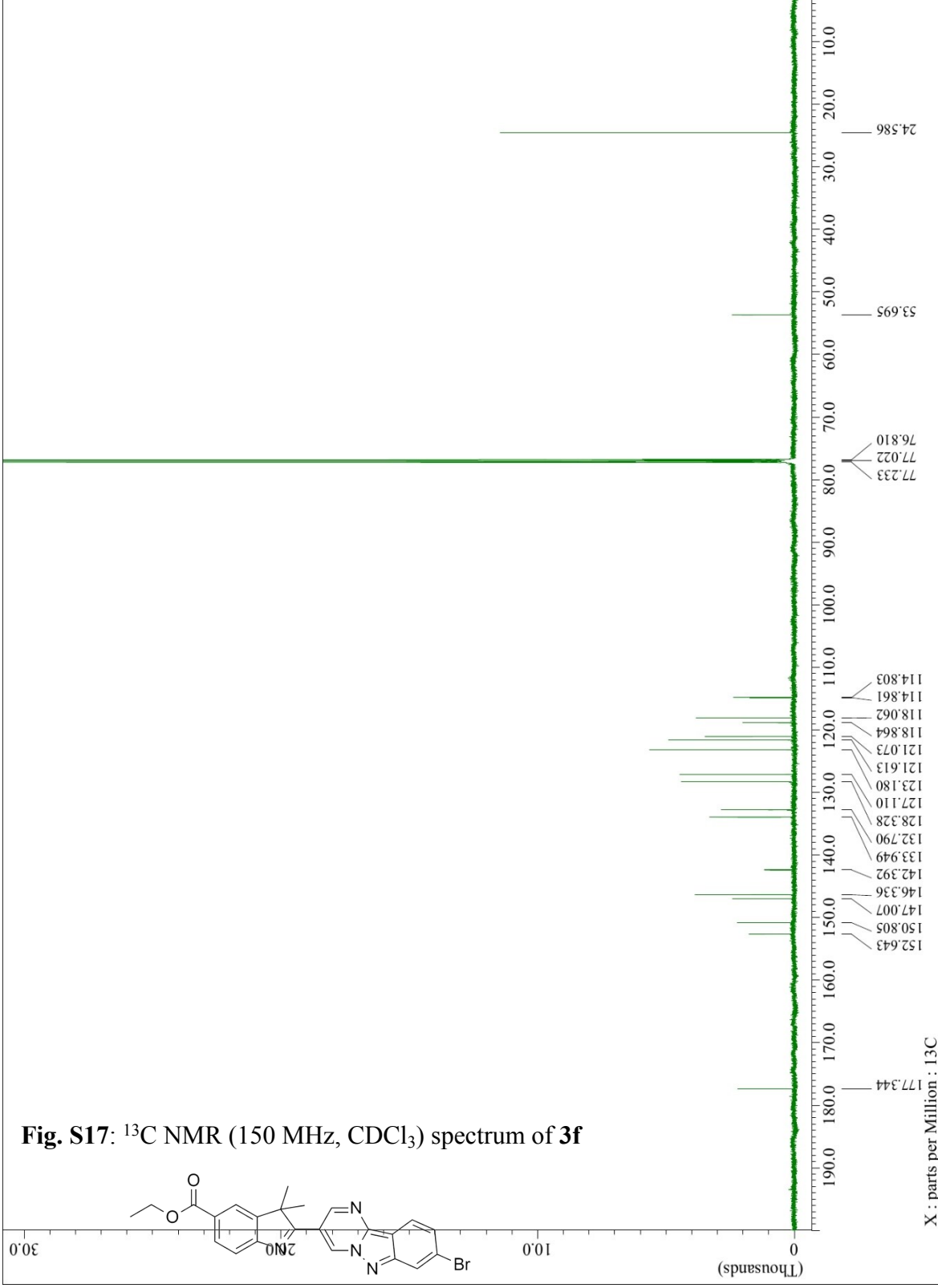

Fig. S17: ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of **3f**

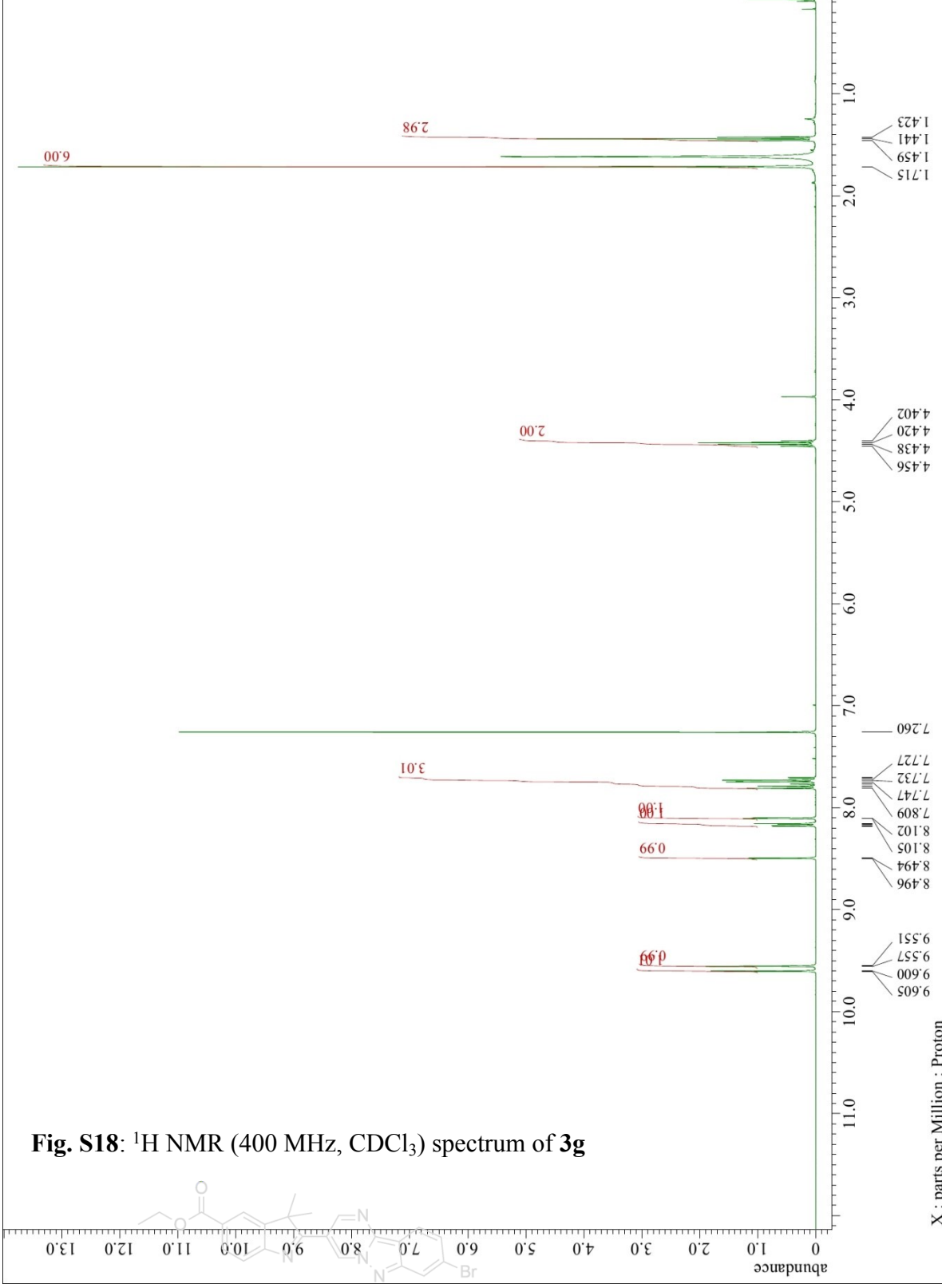

Fig. S18: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3g**

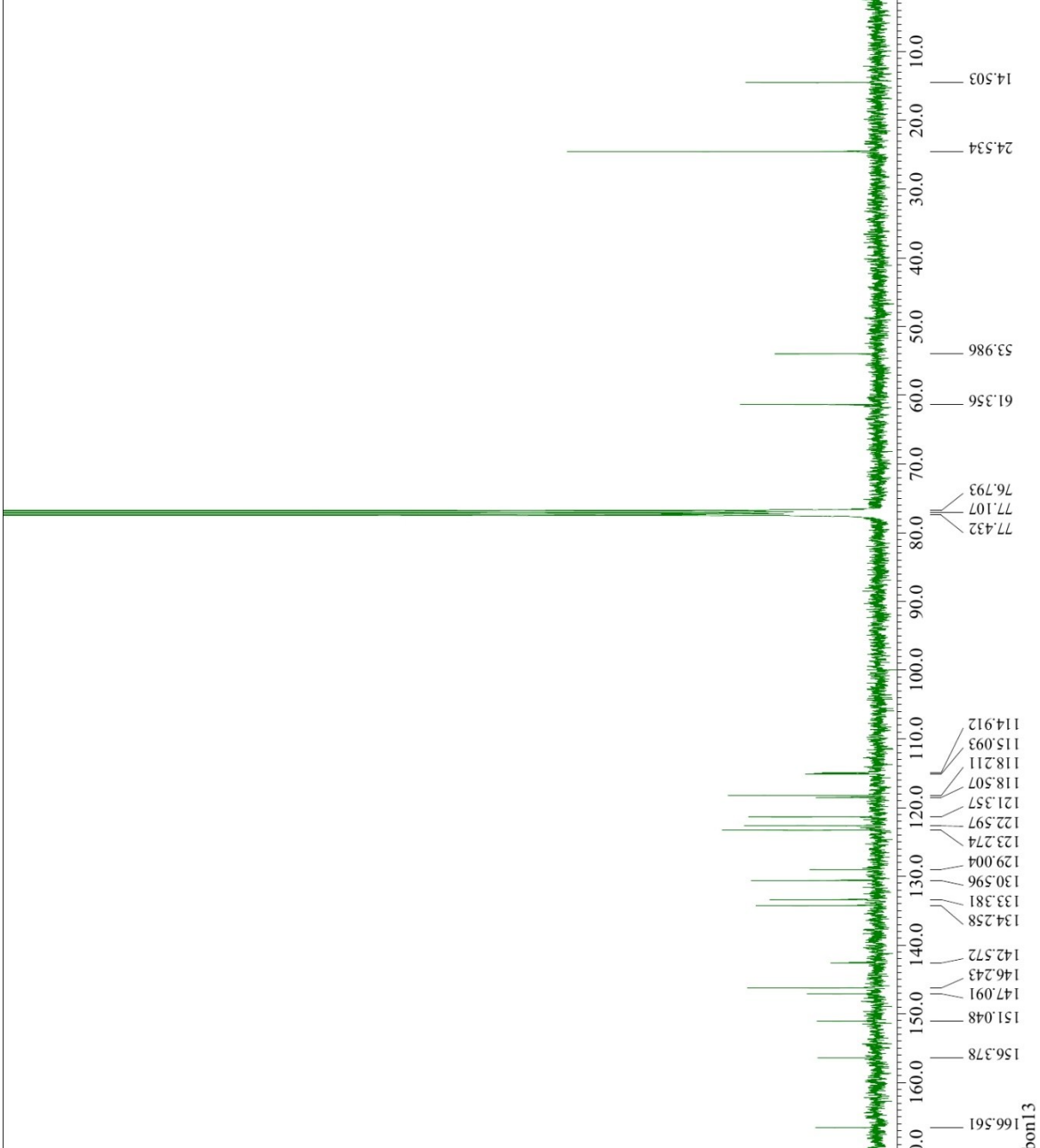

Fig. S19: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3g**

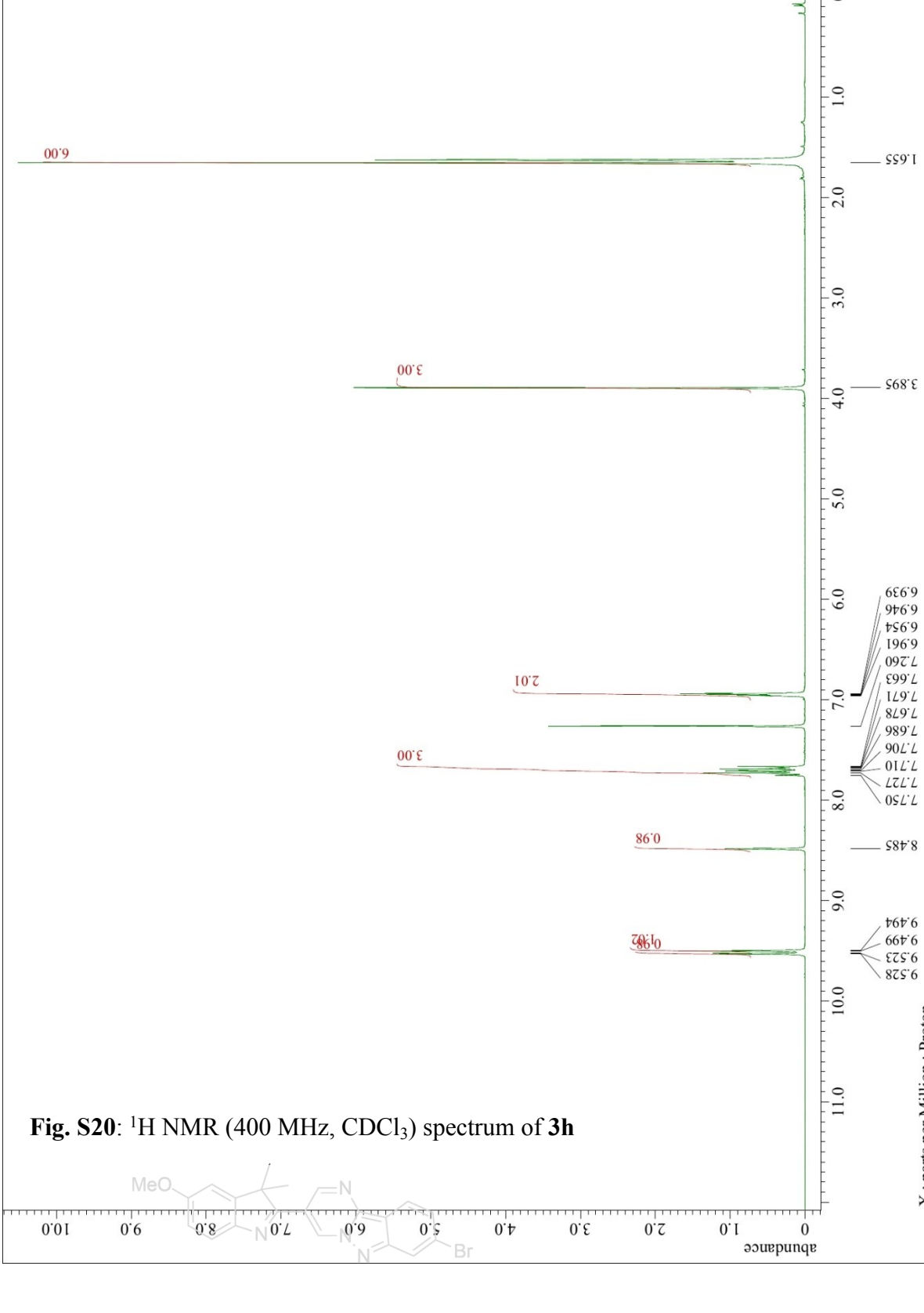

Fig. S20: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3h**

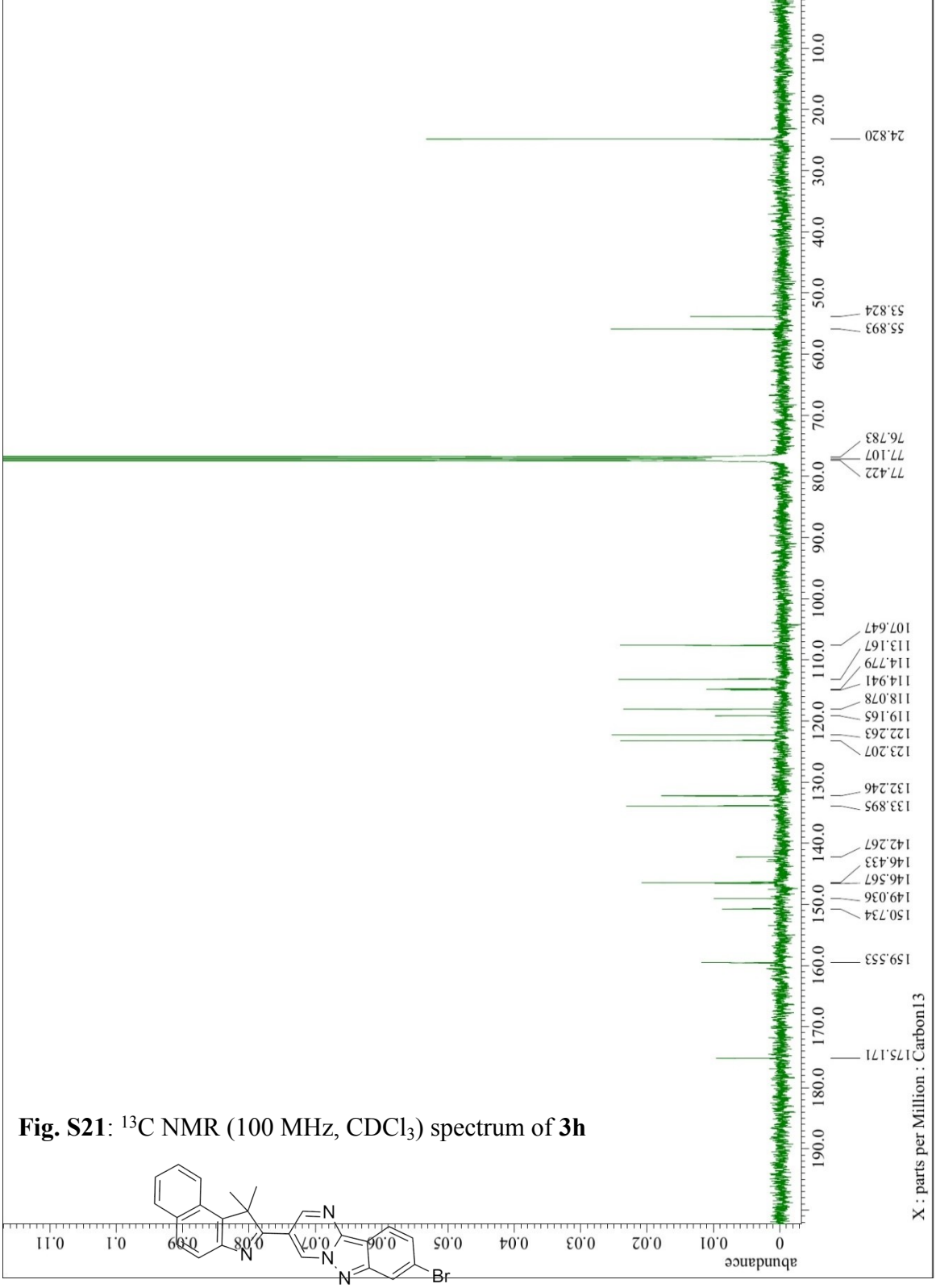

Fig. S21: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3h**

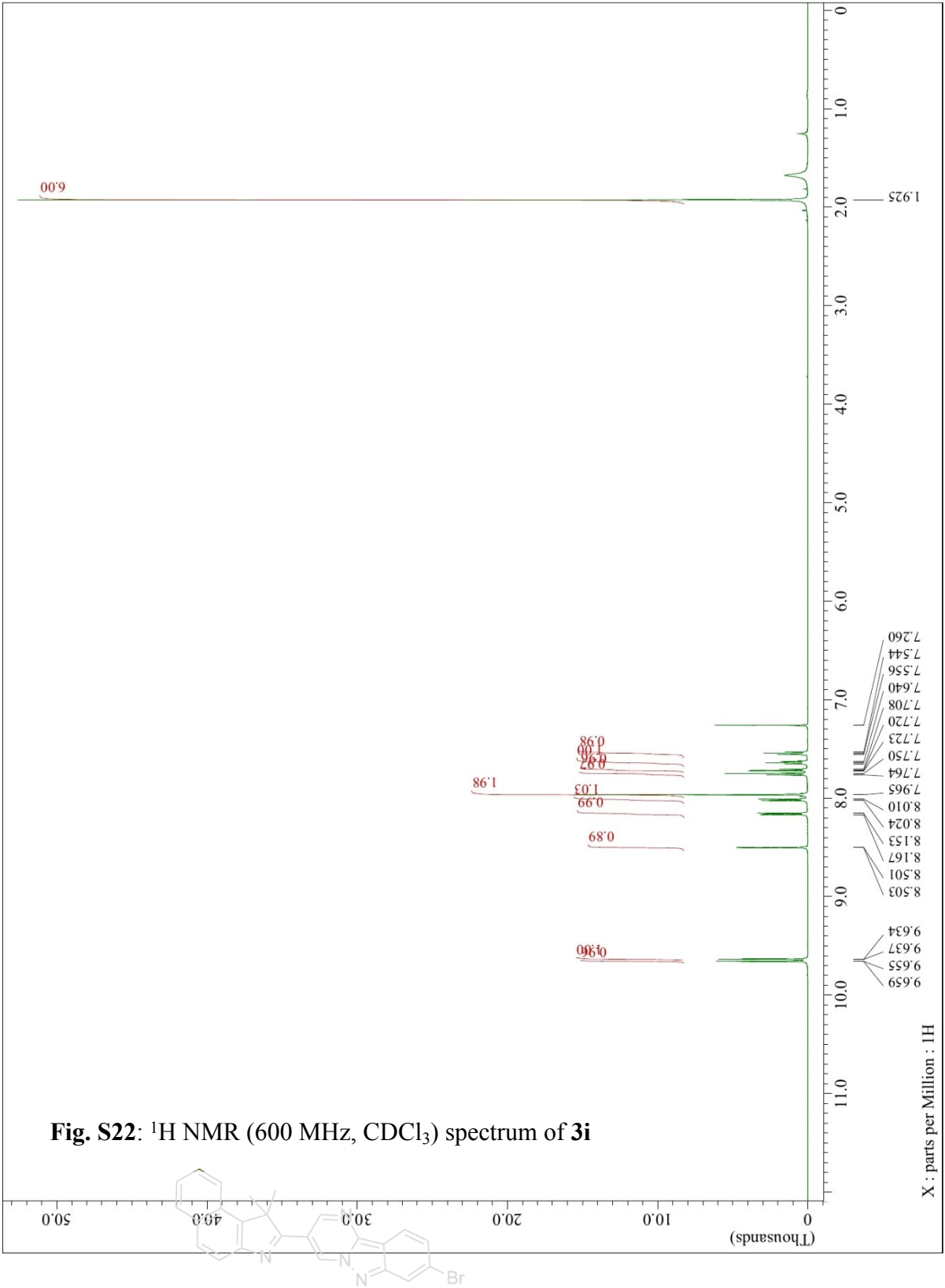

Fig. S22: ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **3i**

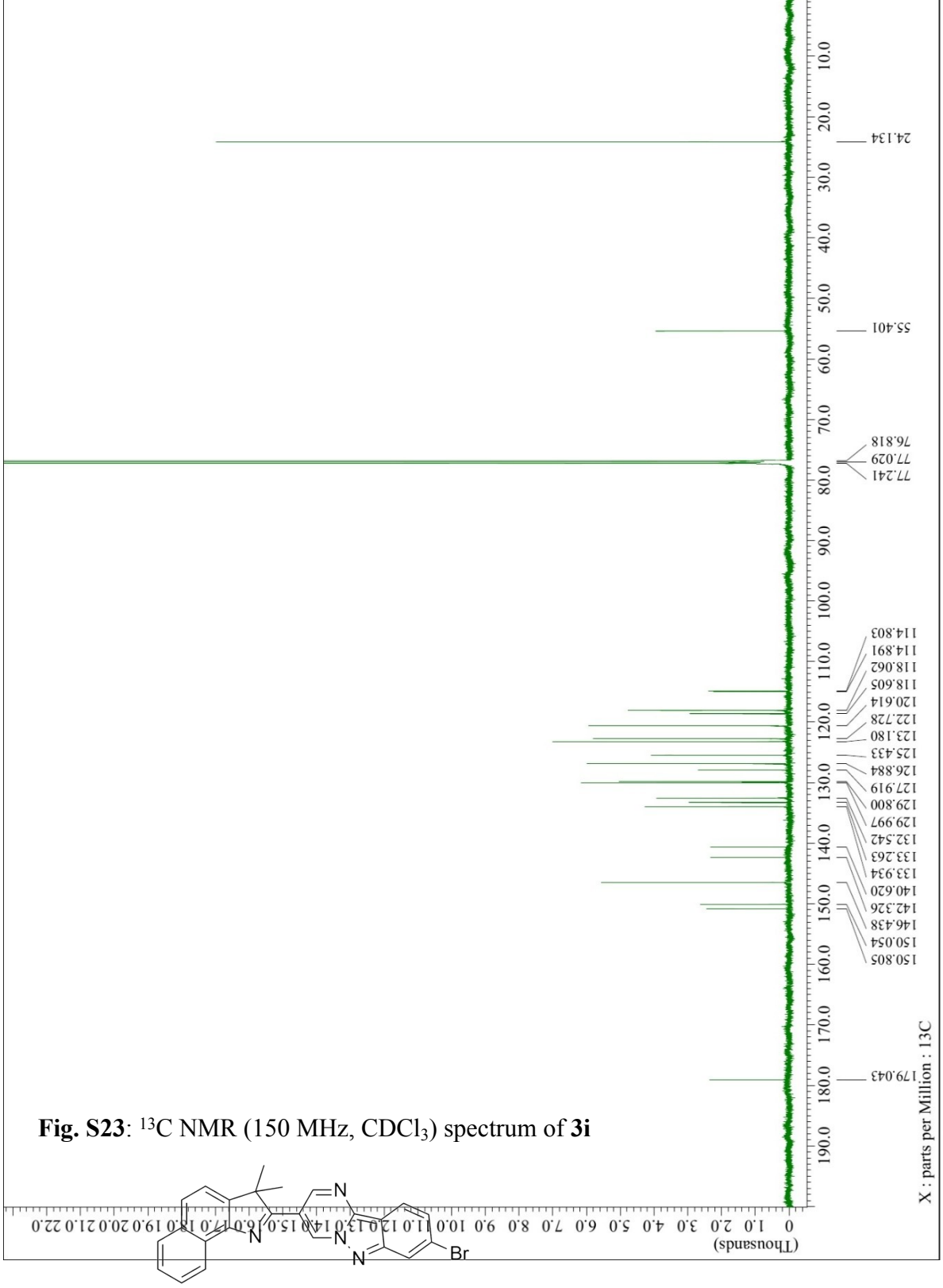

Fig. S23: ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of **3i**

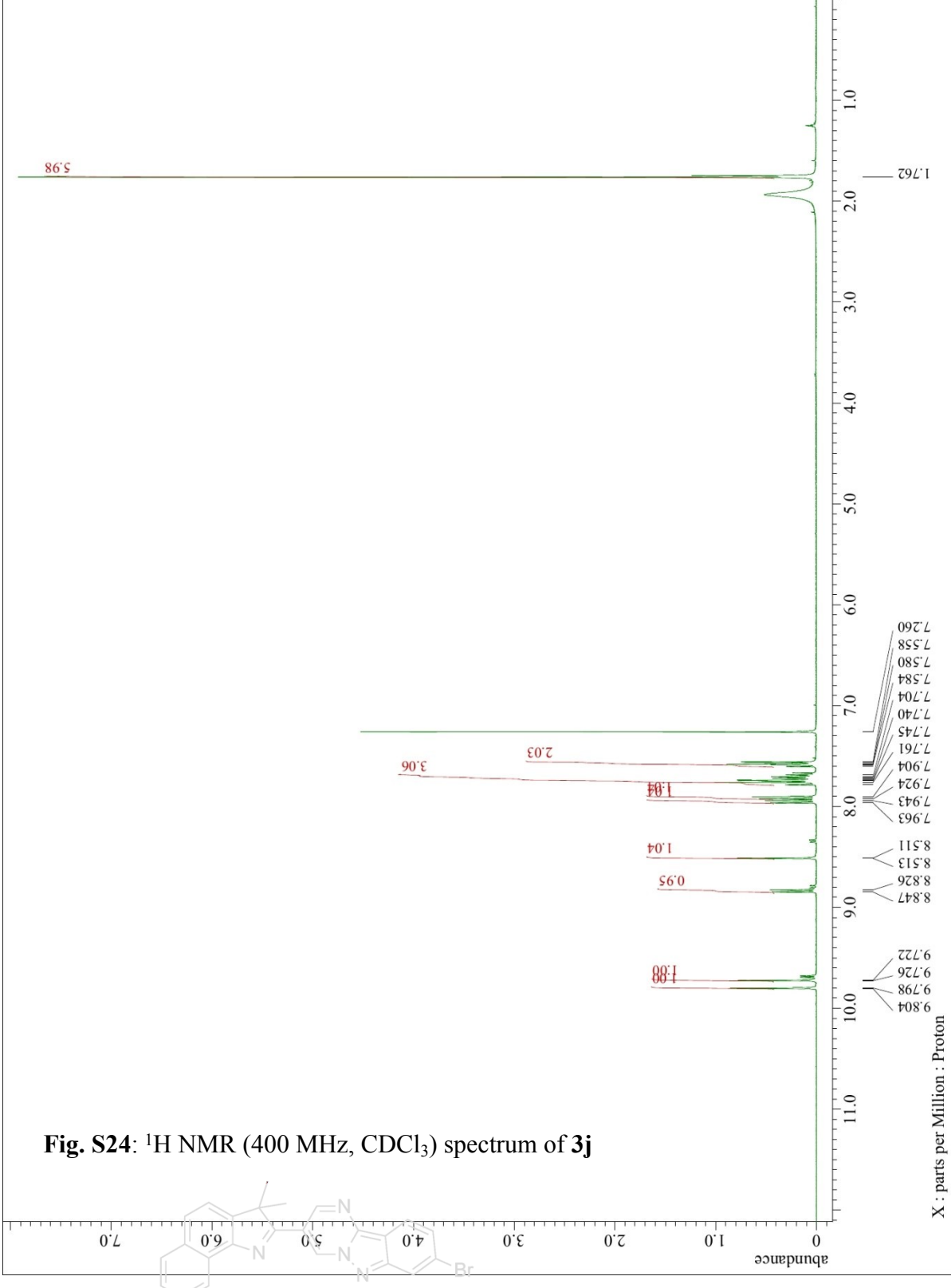

Fig. S24: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3j**

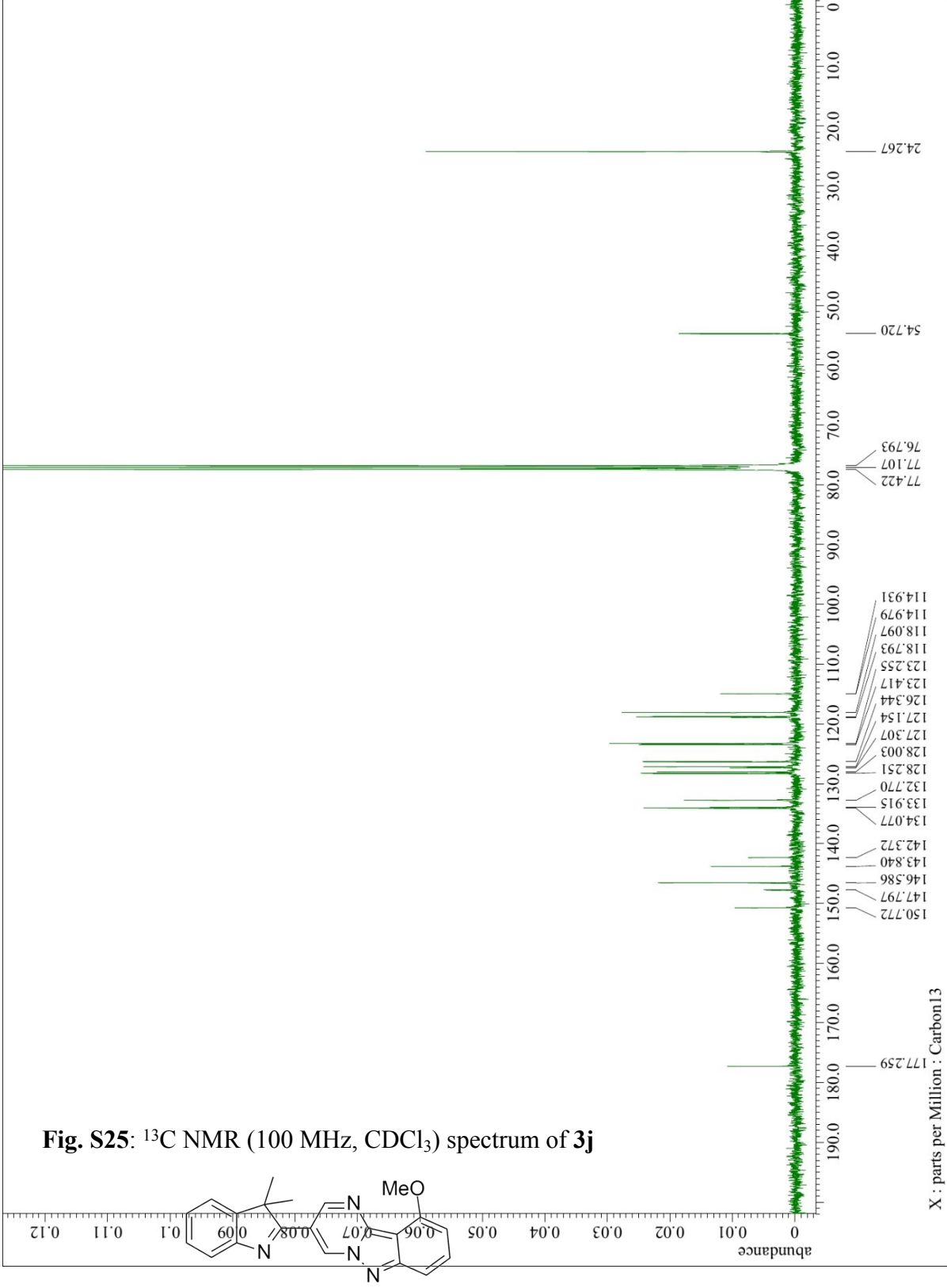

Fig. S25: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3j**

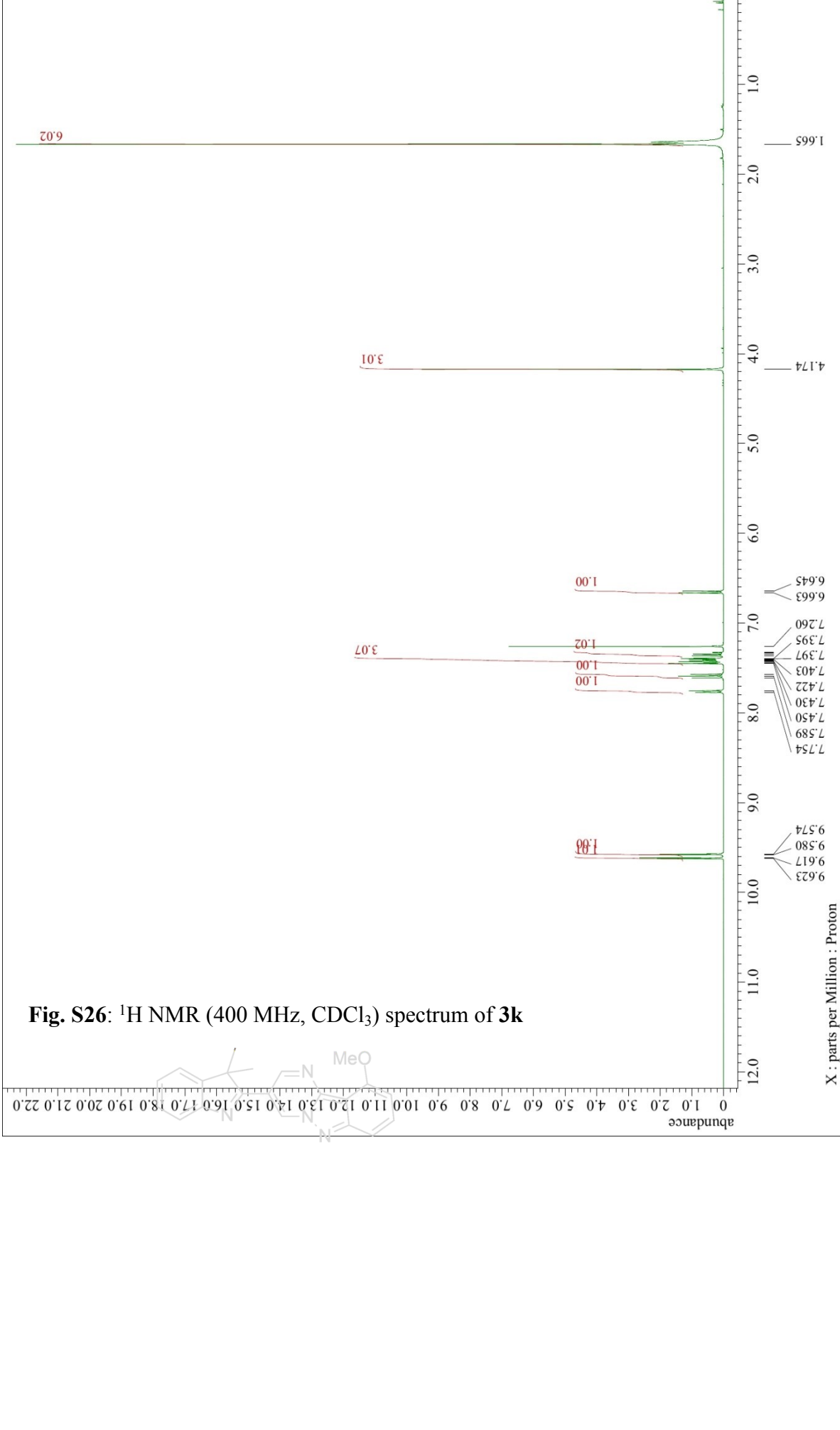

Fig. S26: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3k**

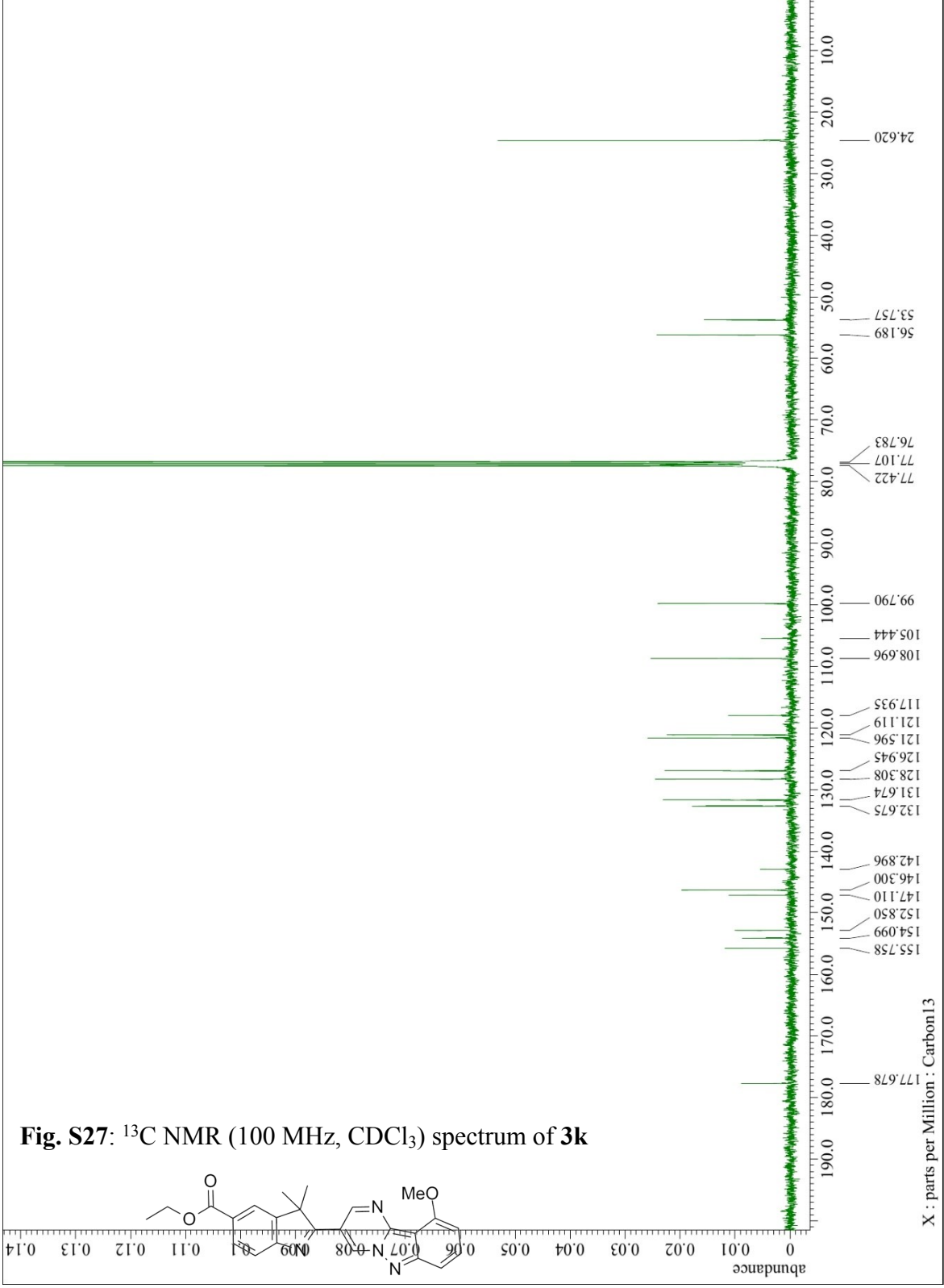

Fig. S27: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3k**

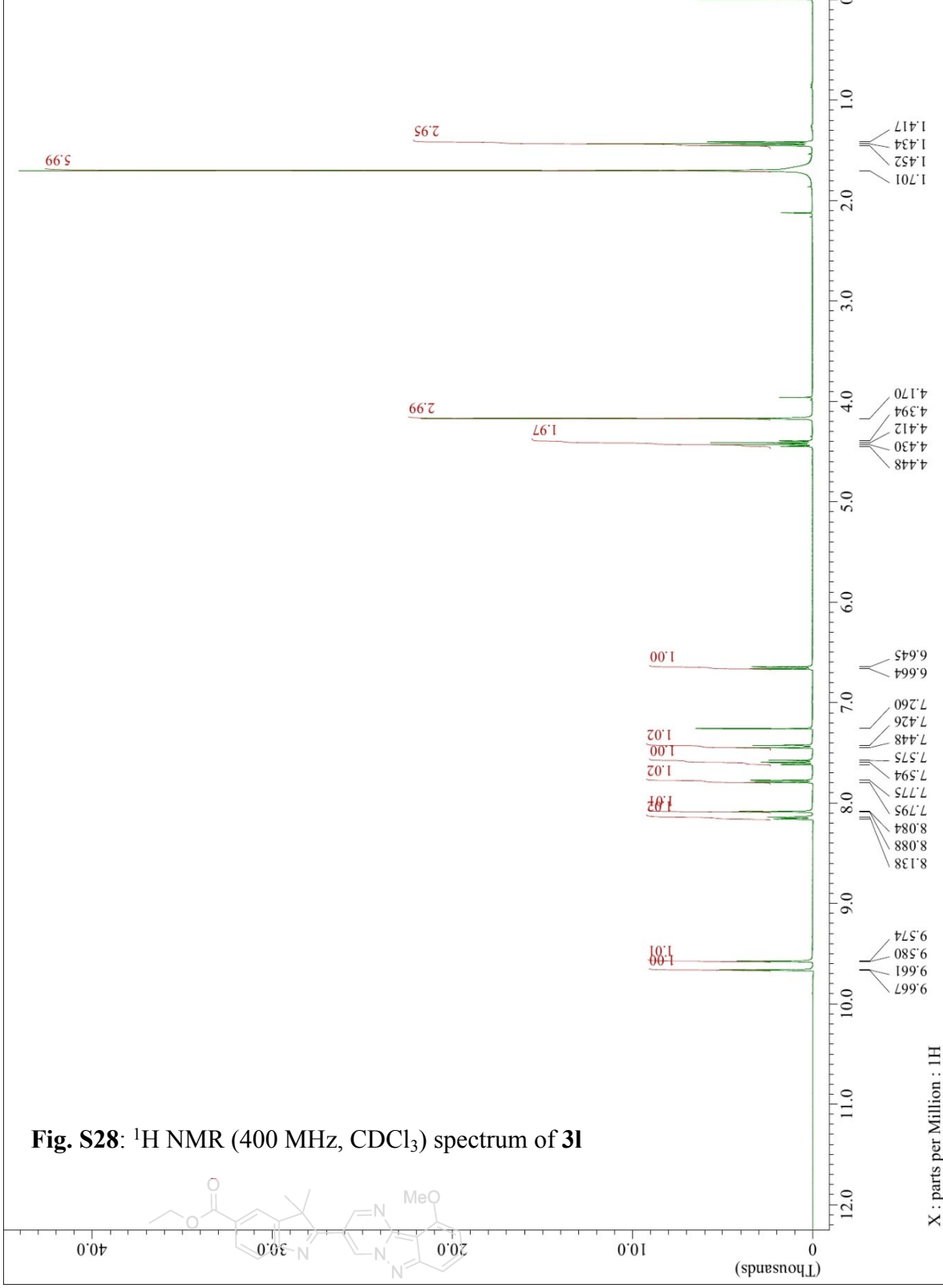

Fig. S28: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3l**

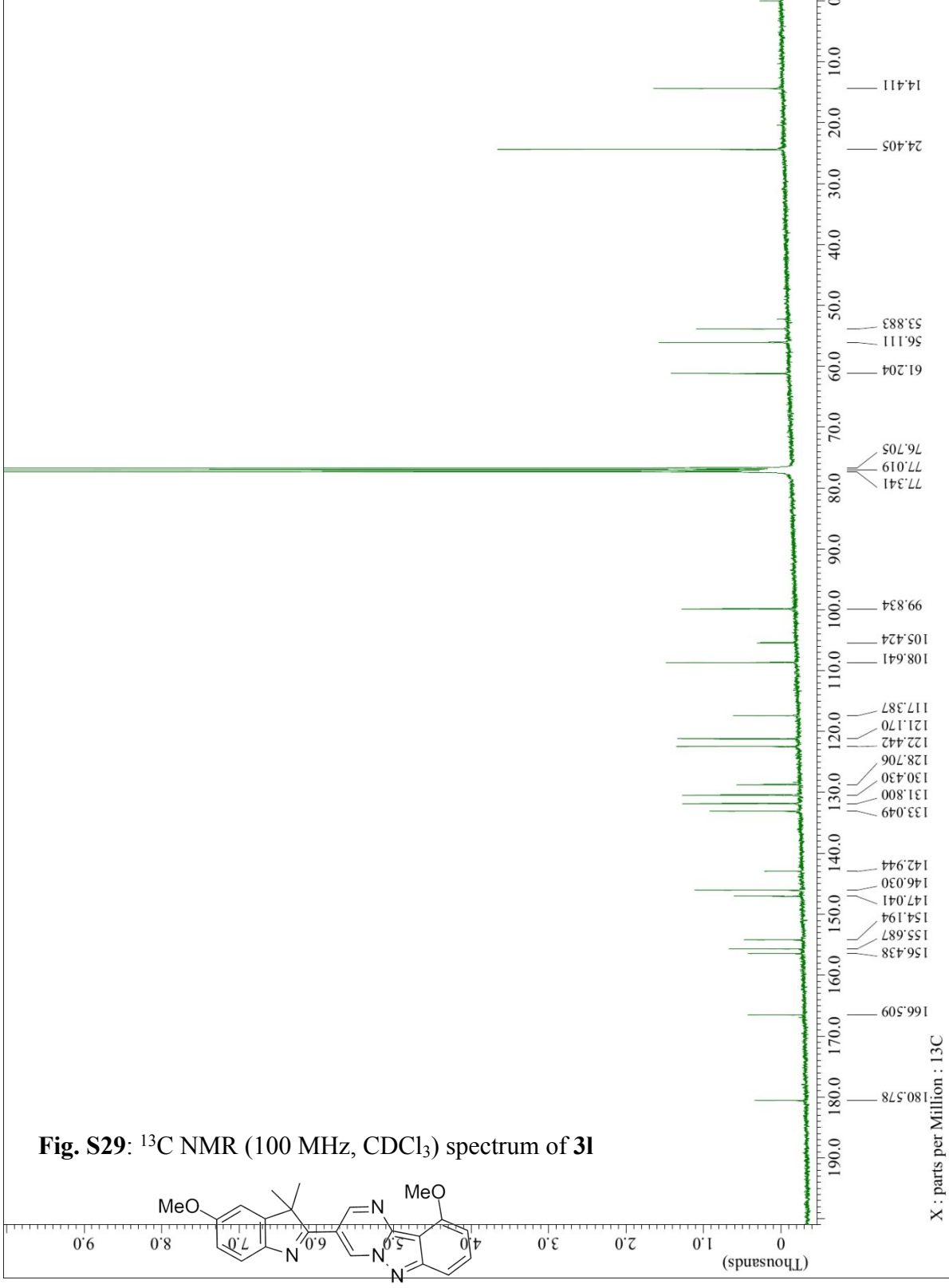

Fig. S29: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3l**

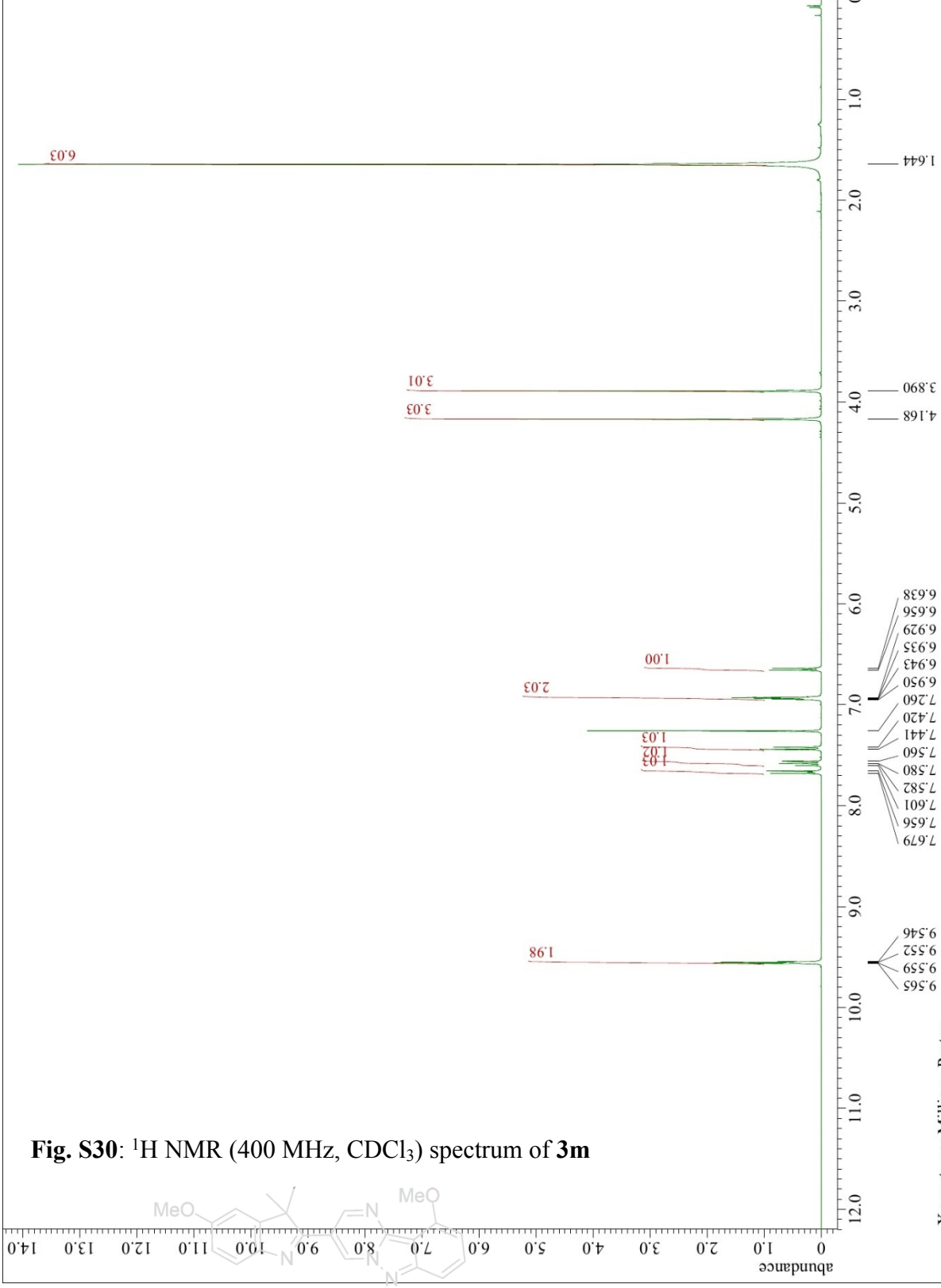

Fig. S30: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3m**

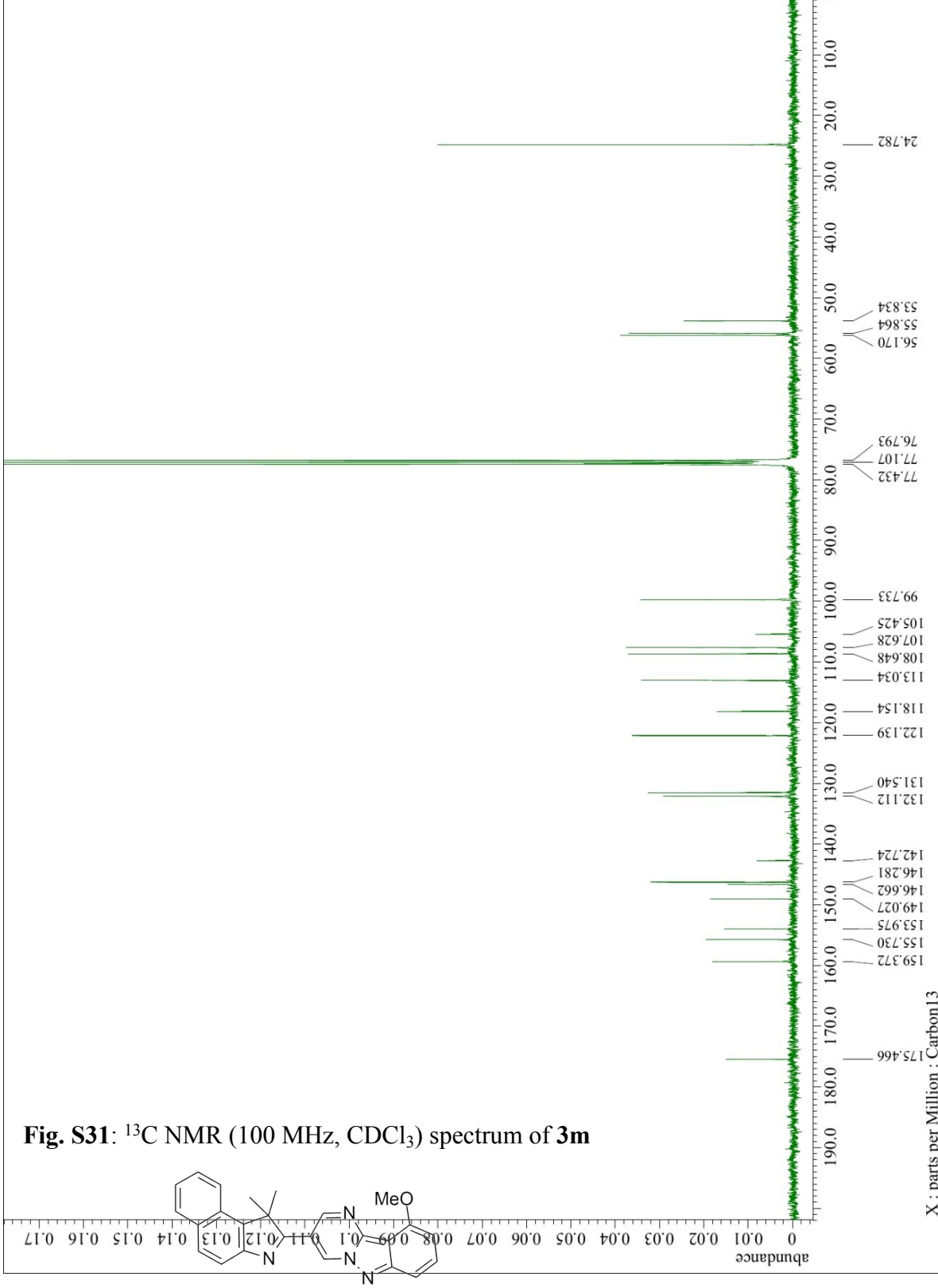

Fig. S31: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3m**

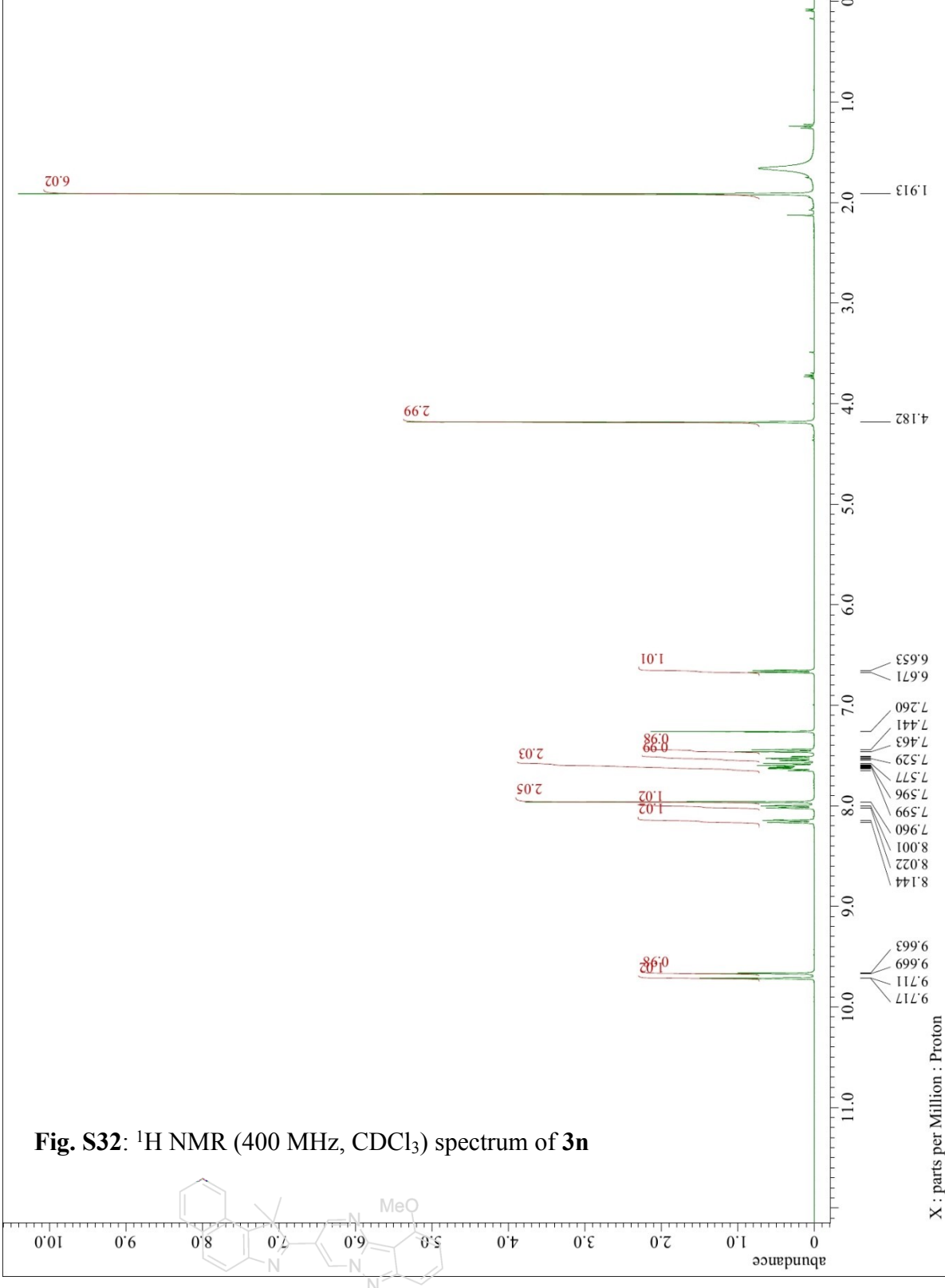

Fig. S32: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3n**

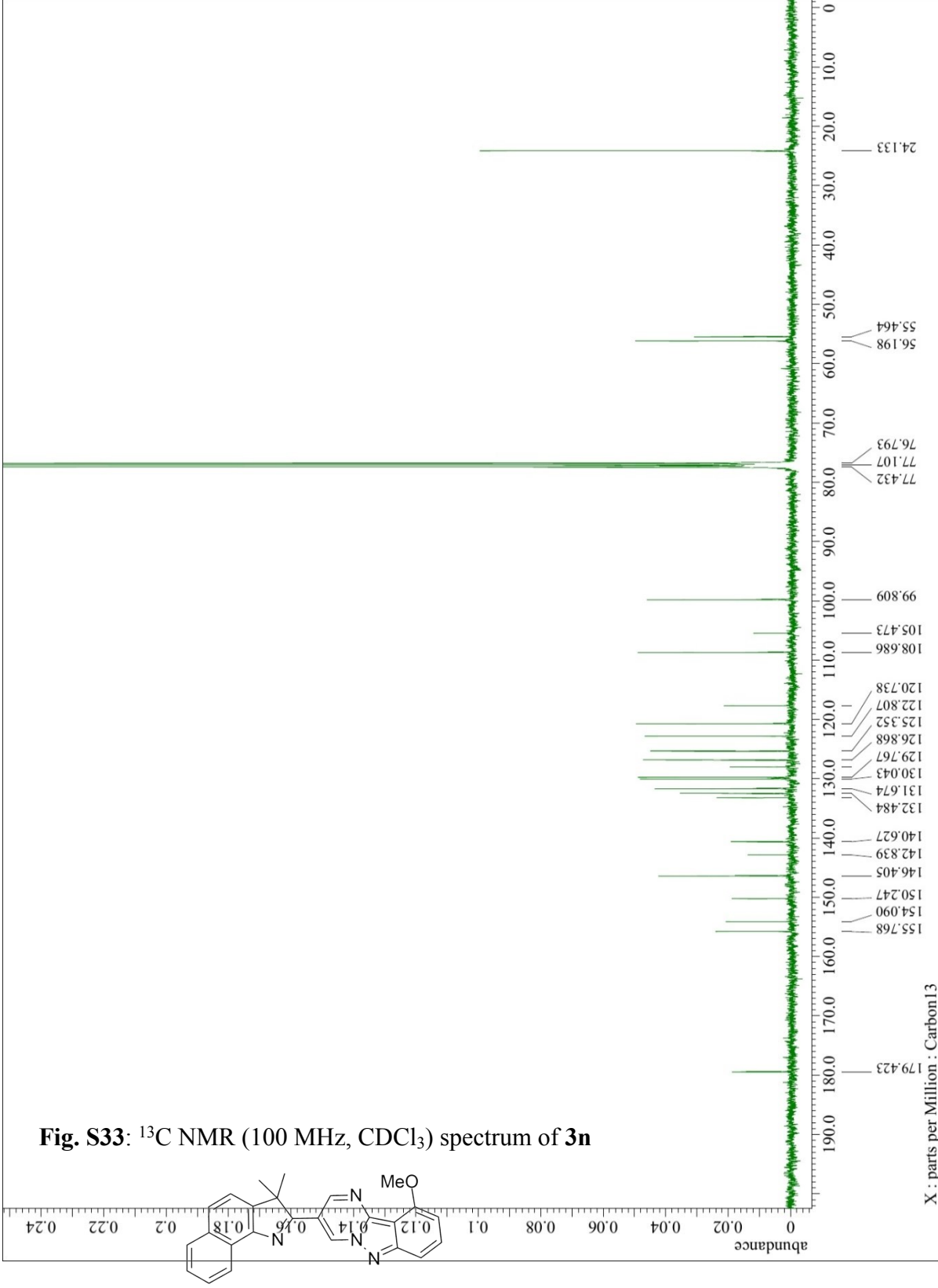

Fig. S33: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3n**

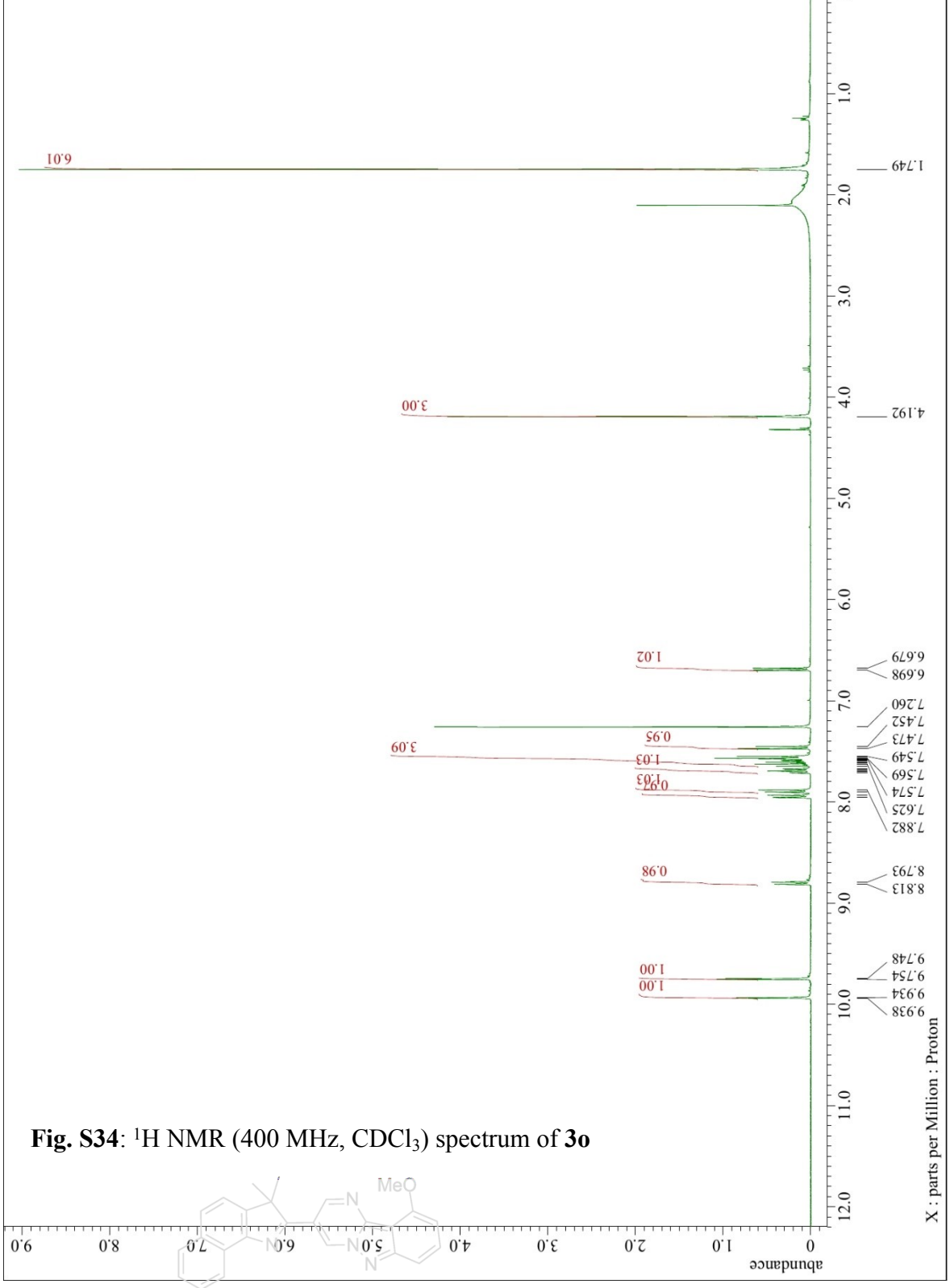

Fig. S34: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3o**

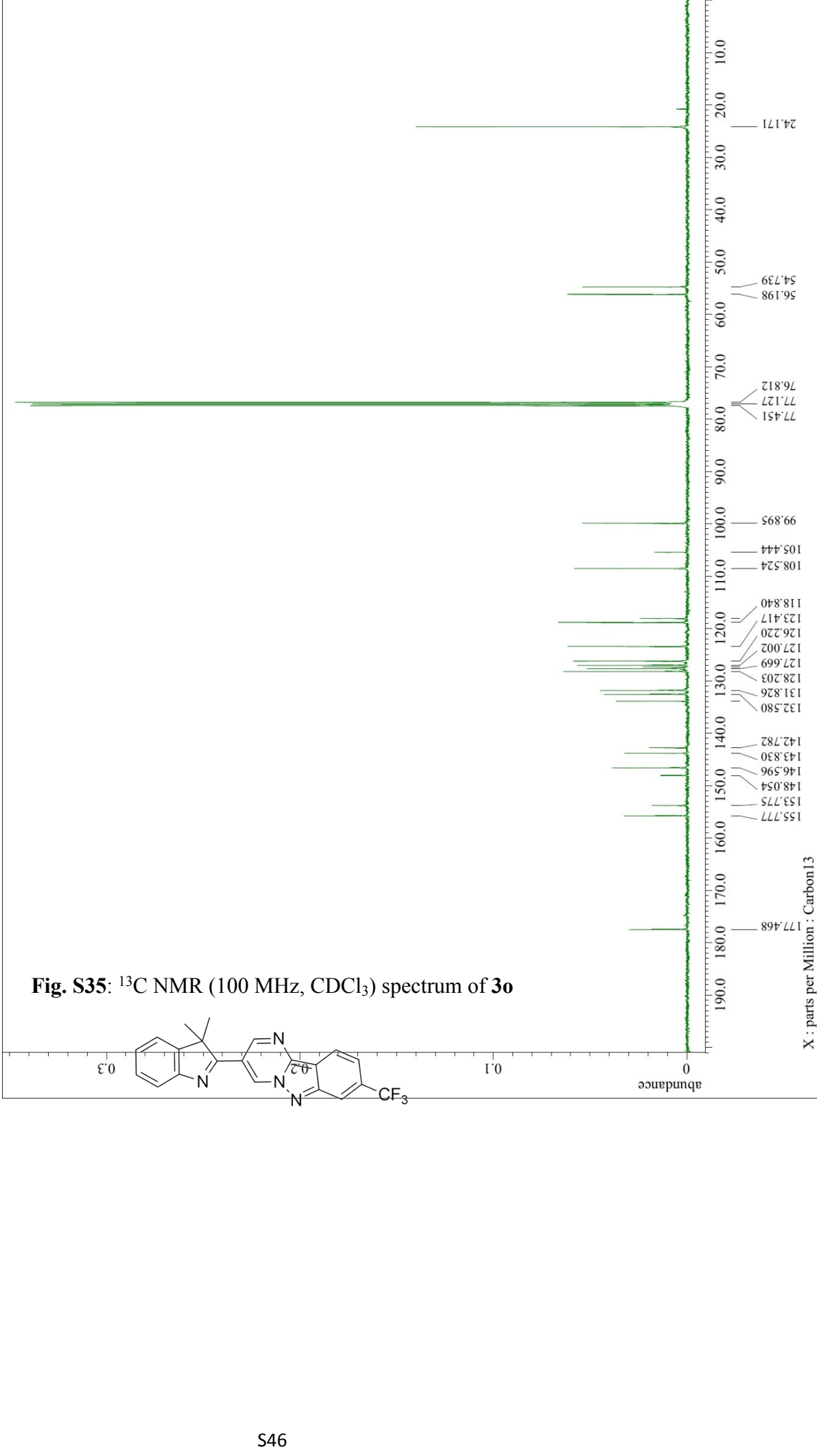

Fig. S35: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3o**

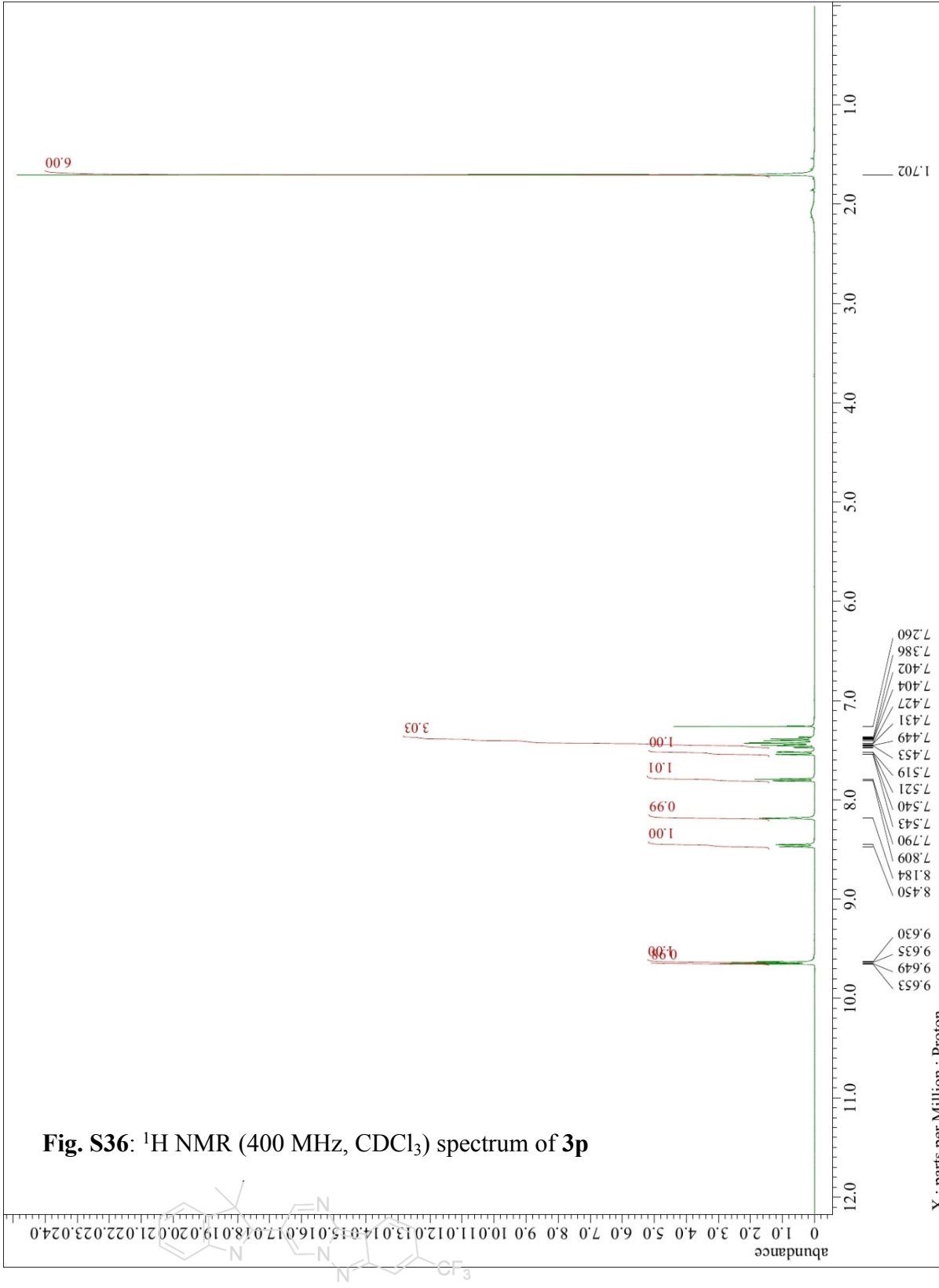

Fig. S36: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3p**

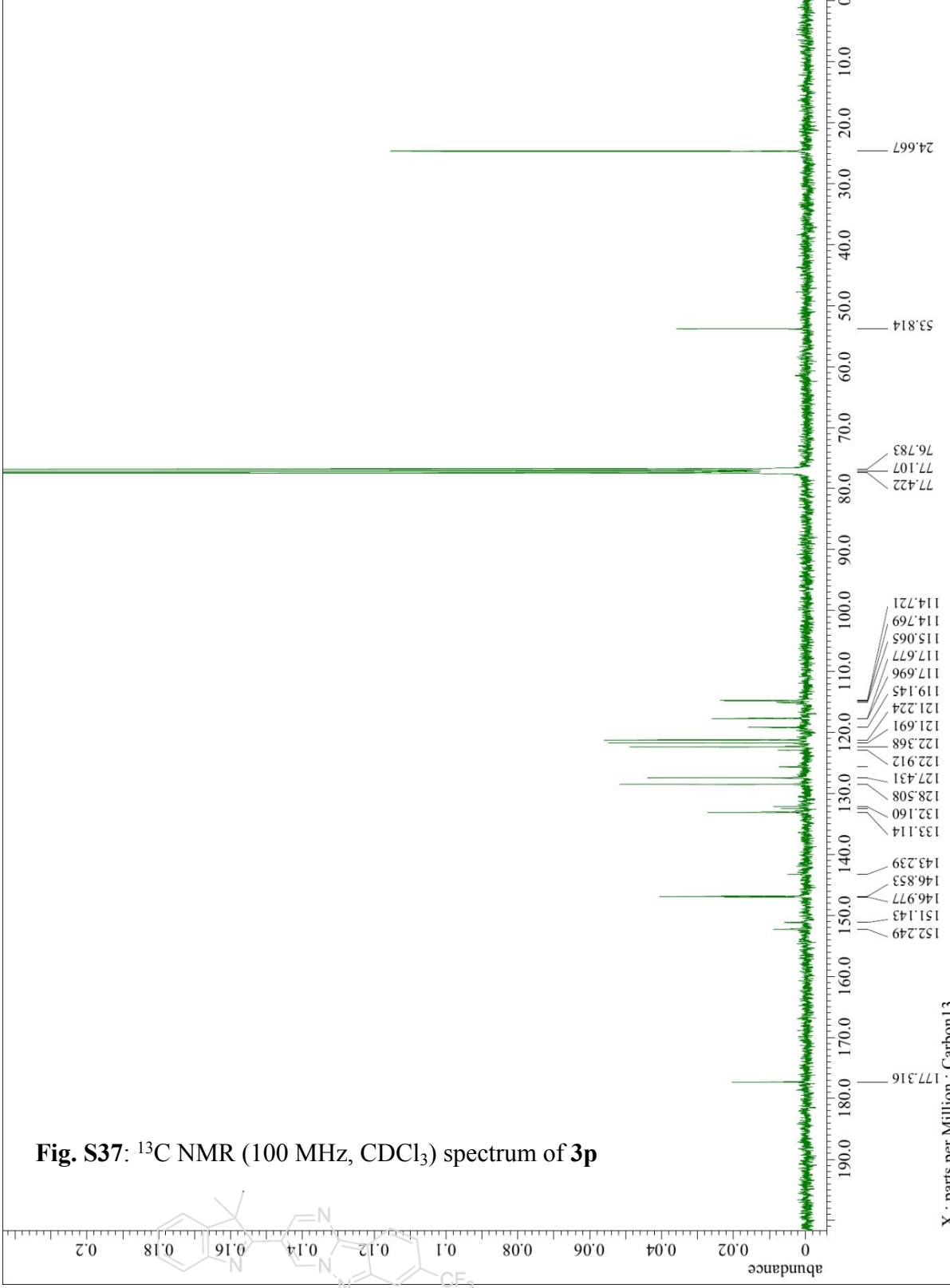

Fig. S37: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3p**

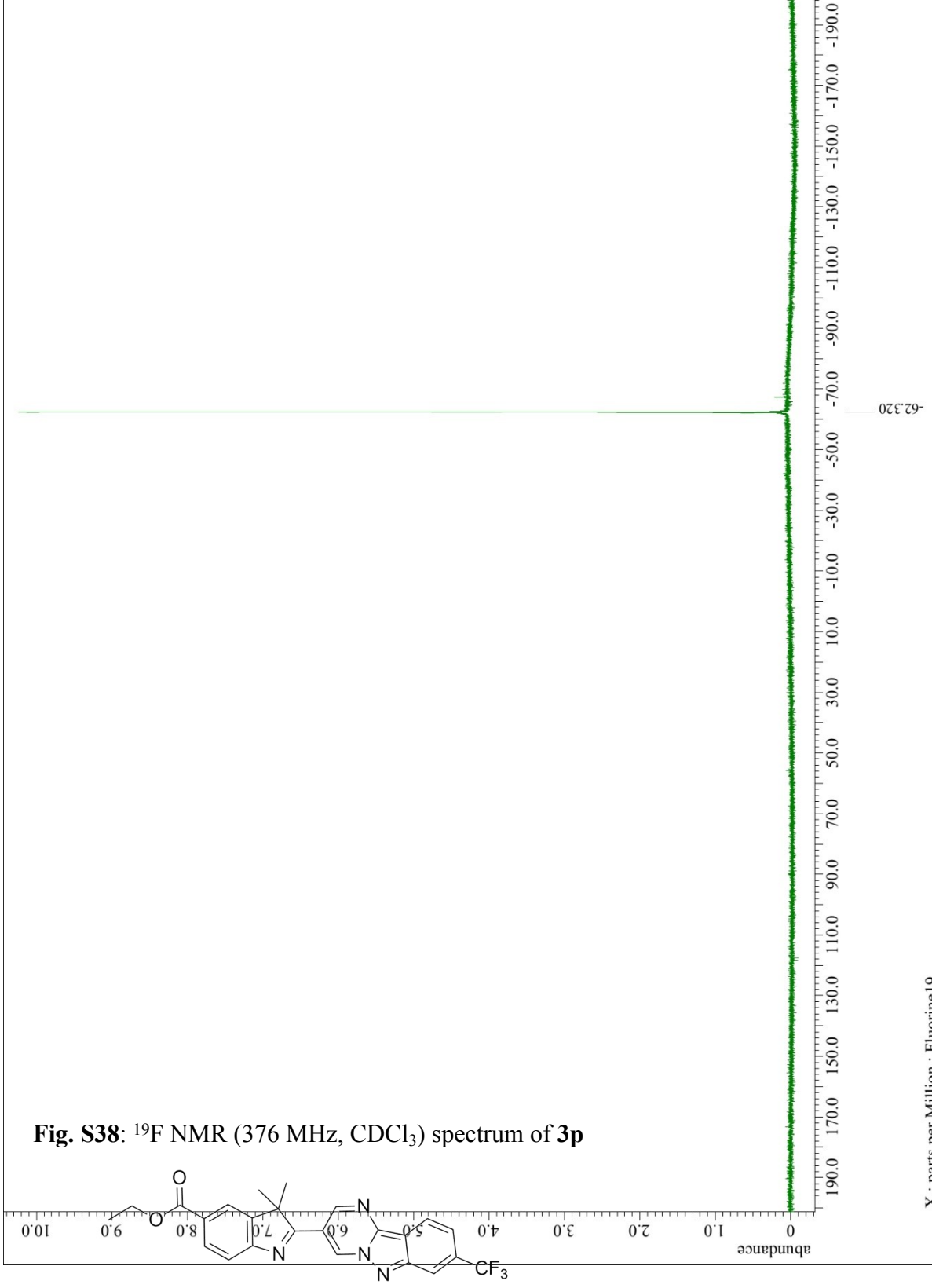

Fig. S38: ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3p**

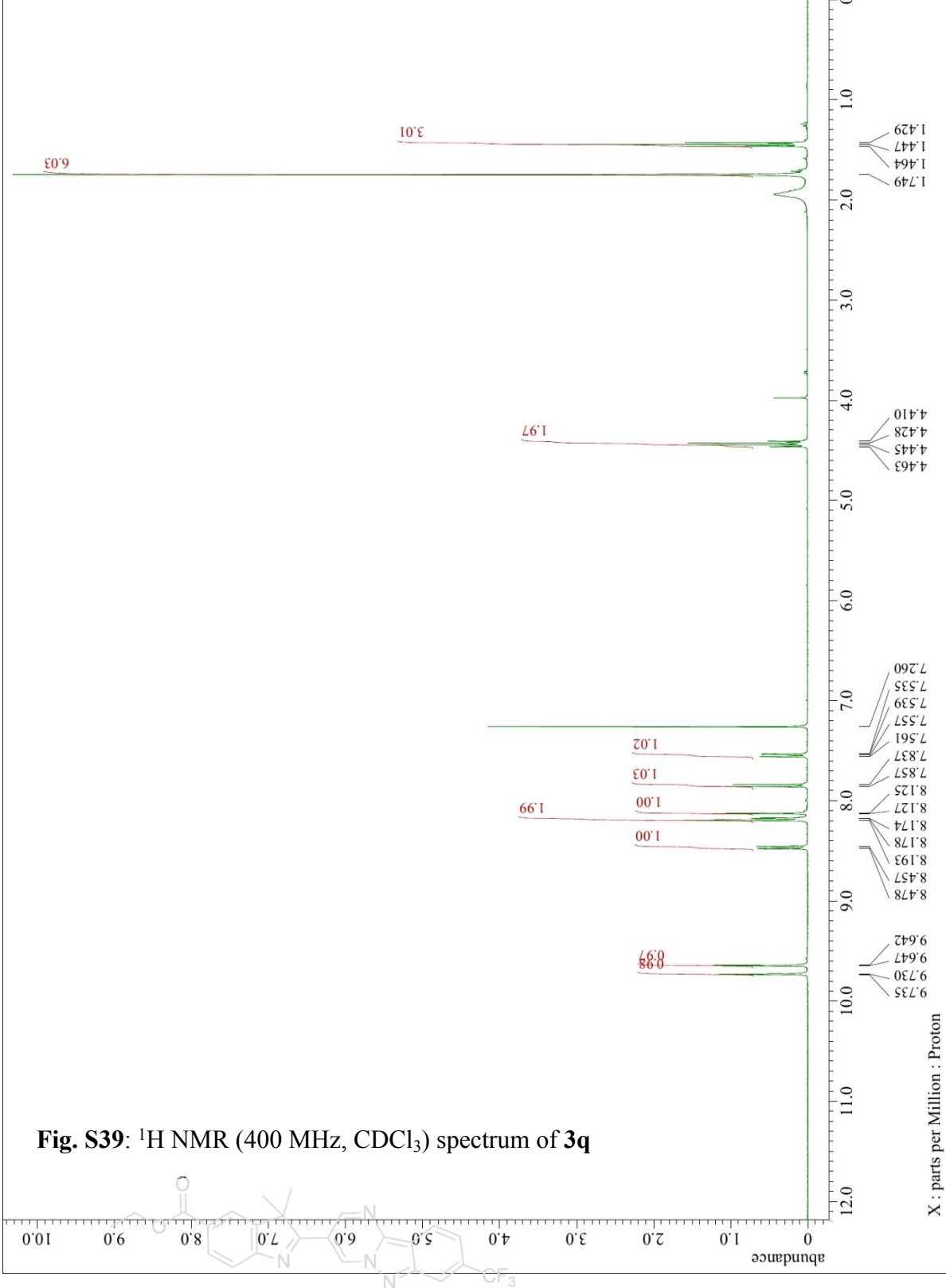

Fig. S39: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3q**

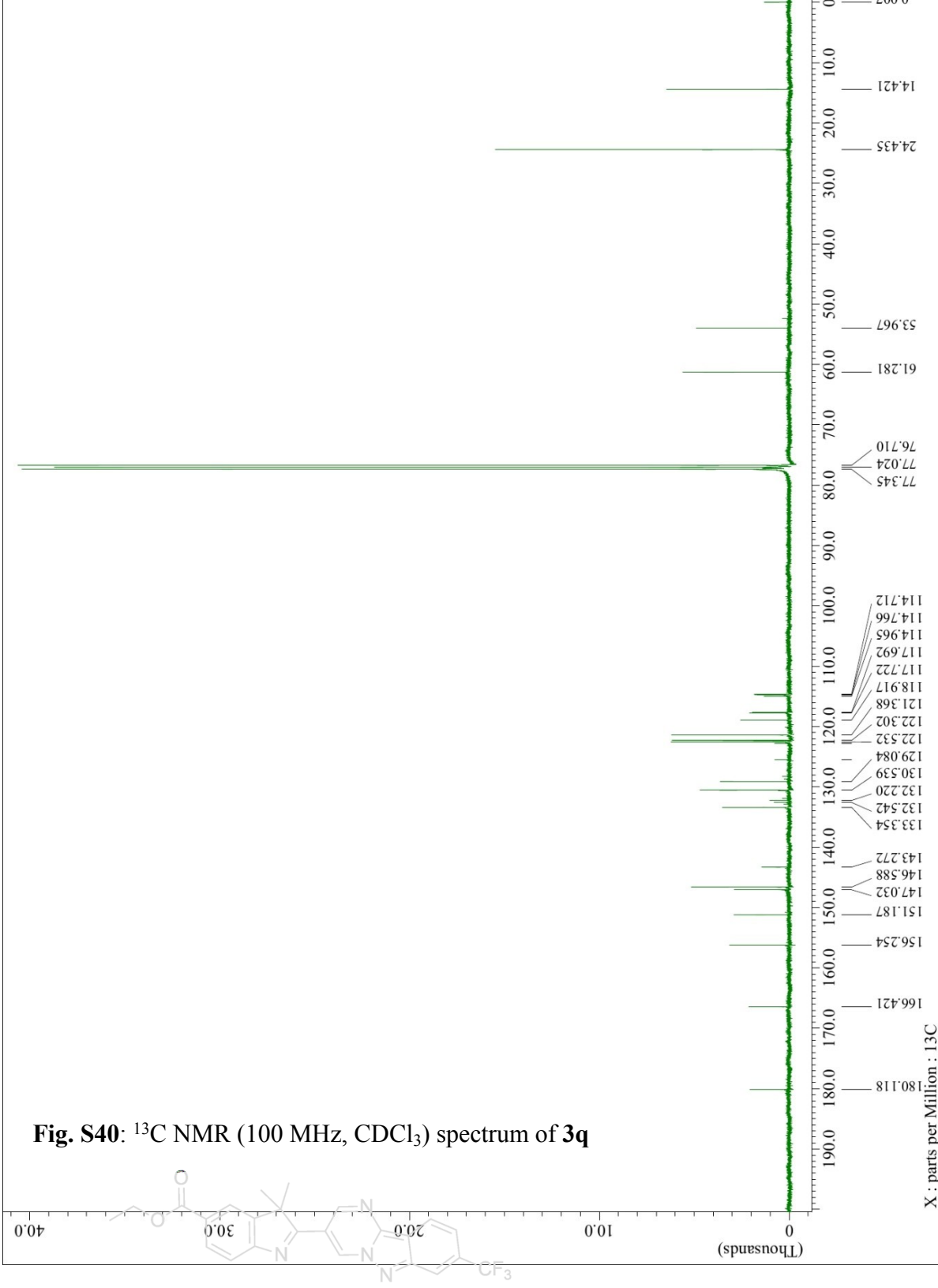

Fig. S40: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3q**

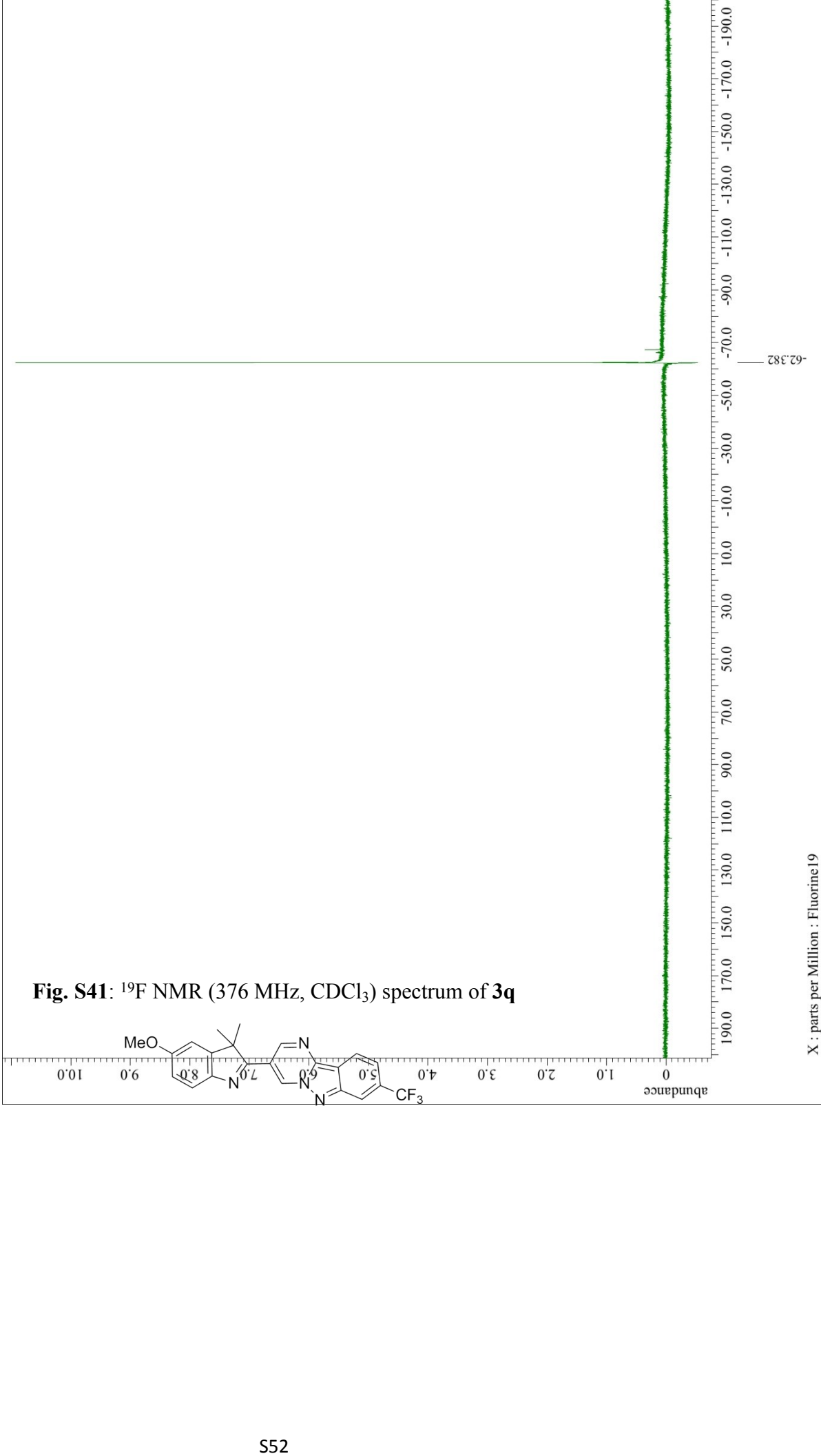

Fig. S41: ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3q**

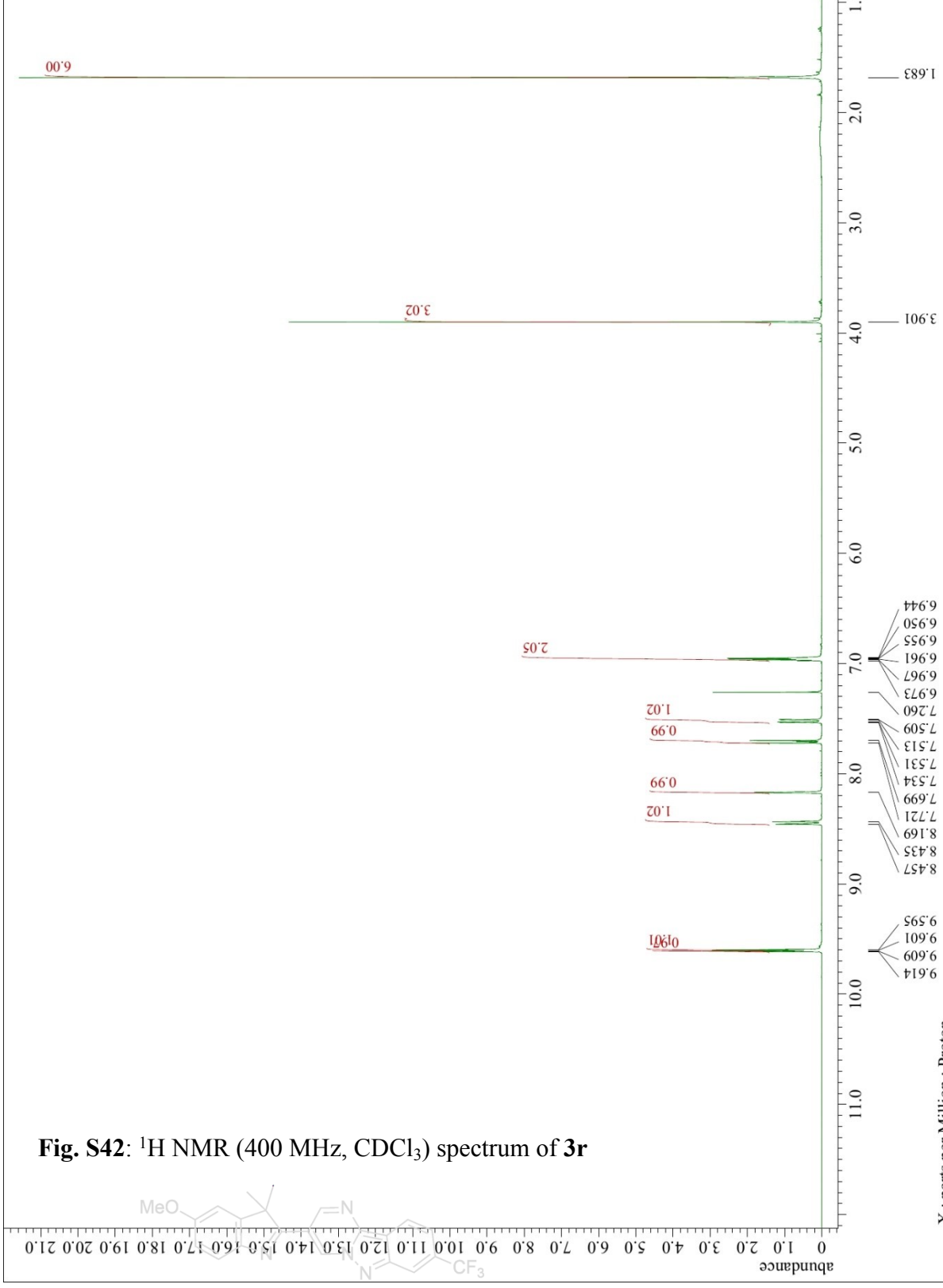

Fig. S42: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3r**

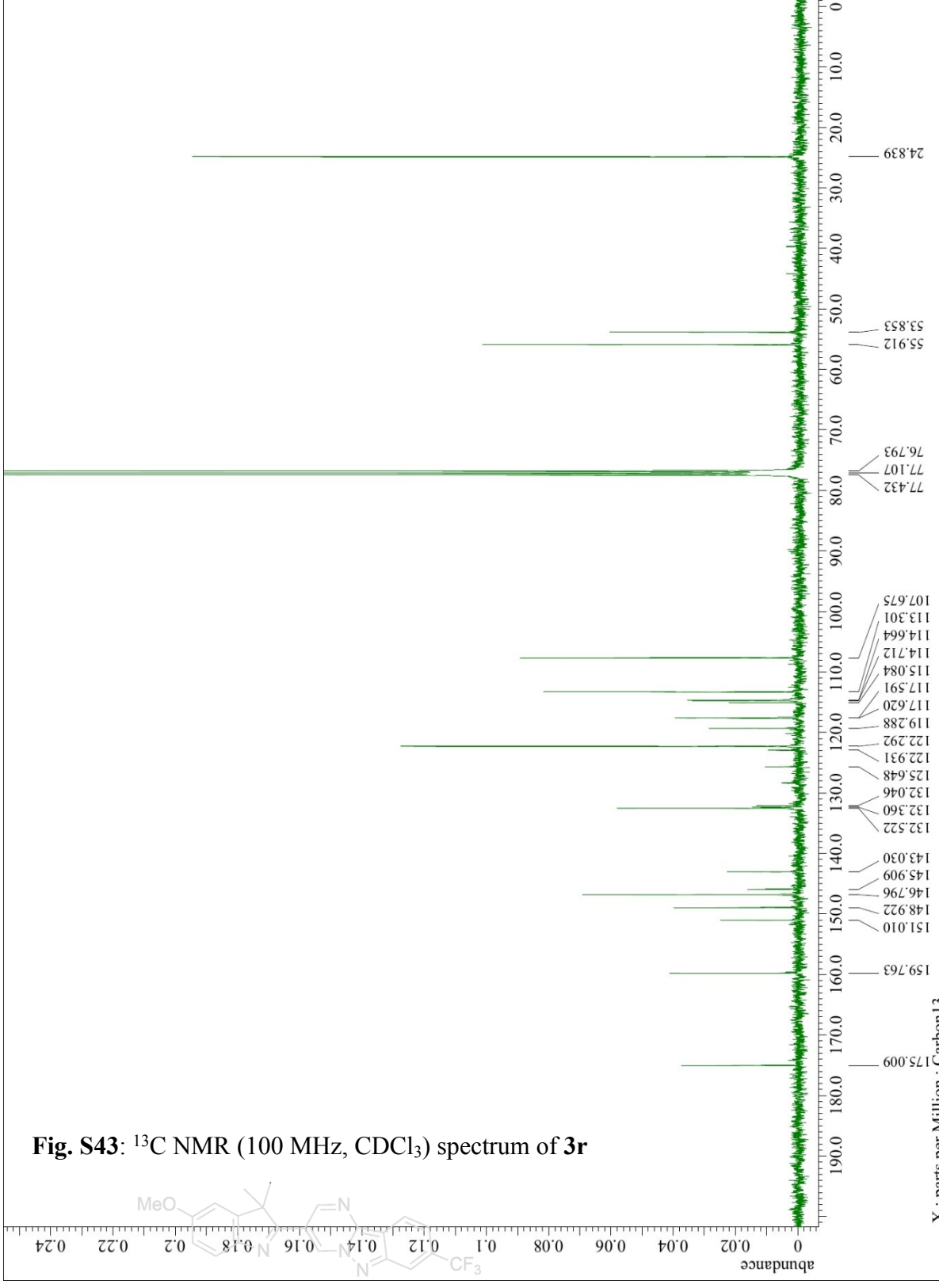

Fig. S43: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3r**

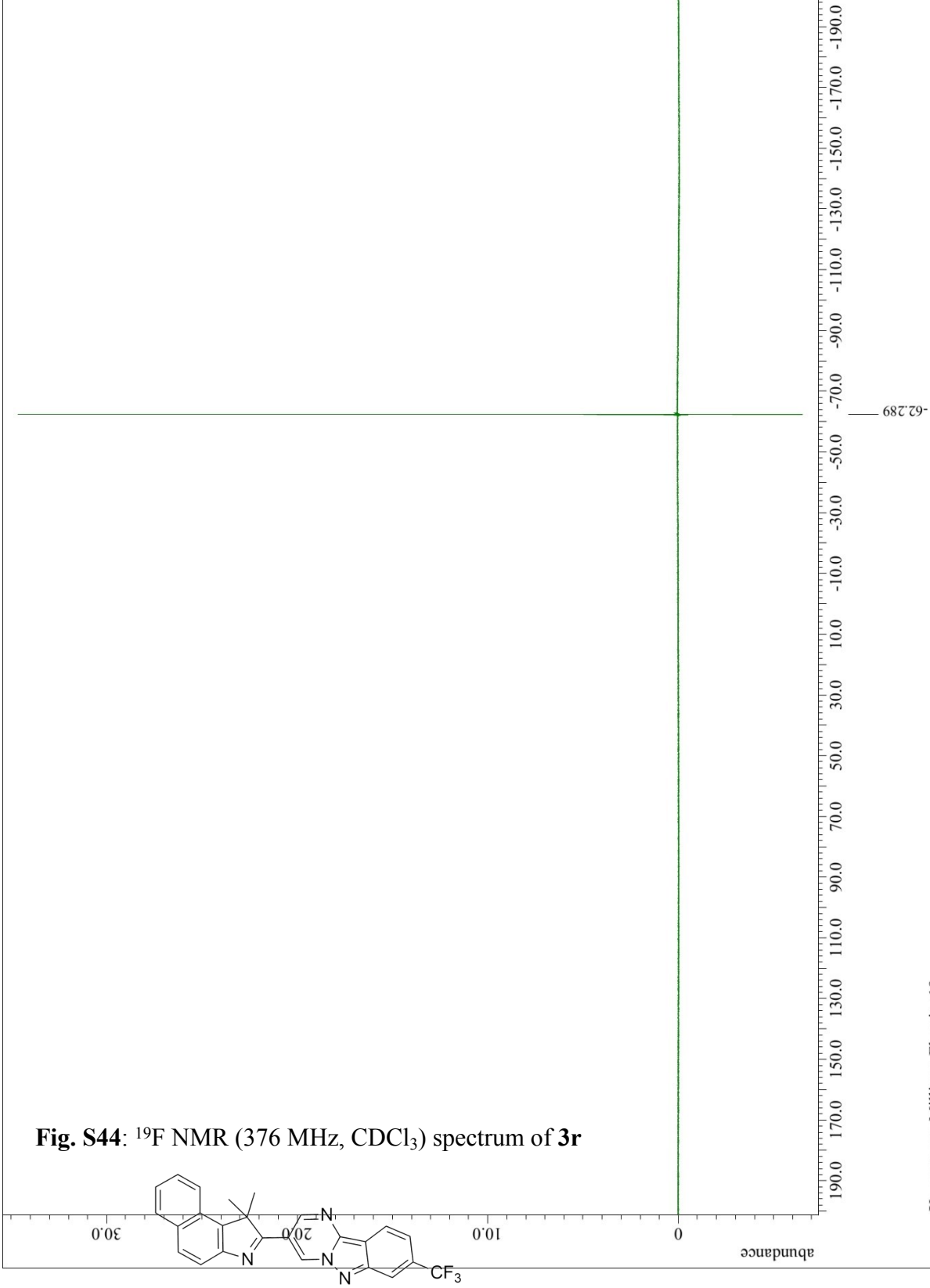

Fig. S44: ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3r**

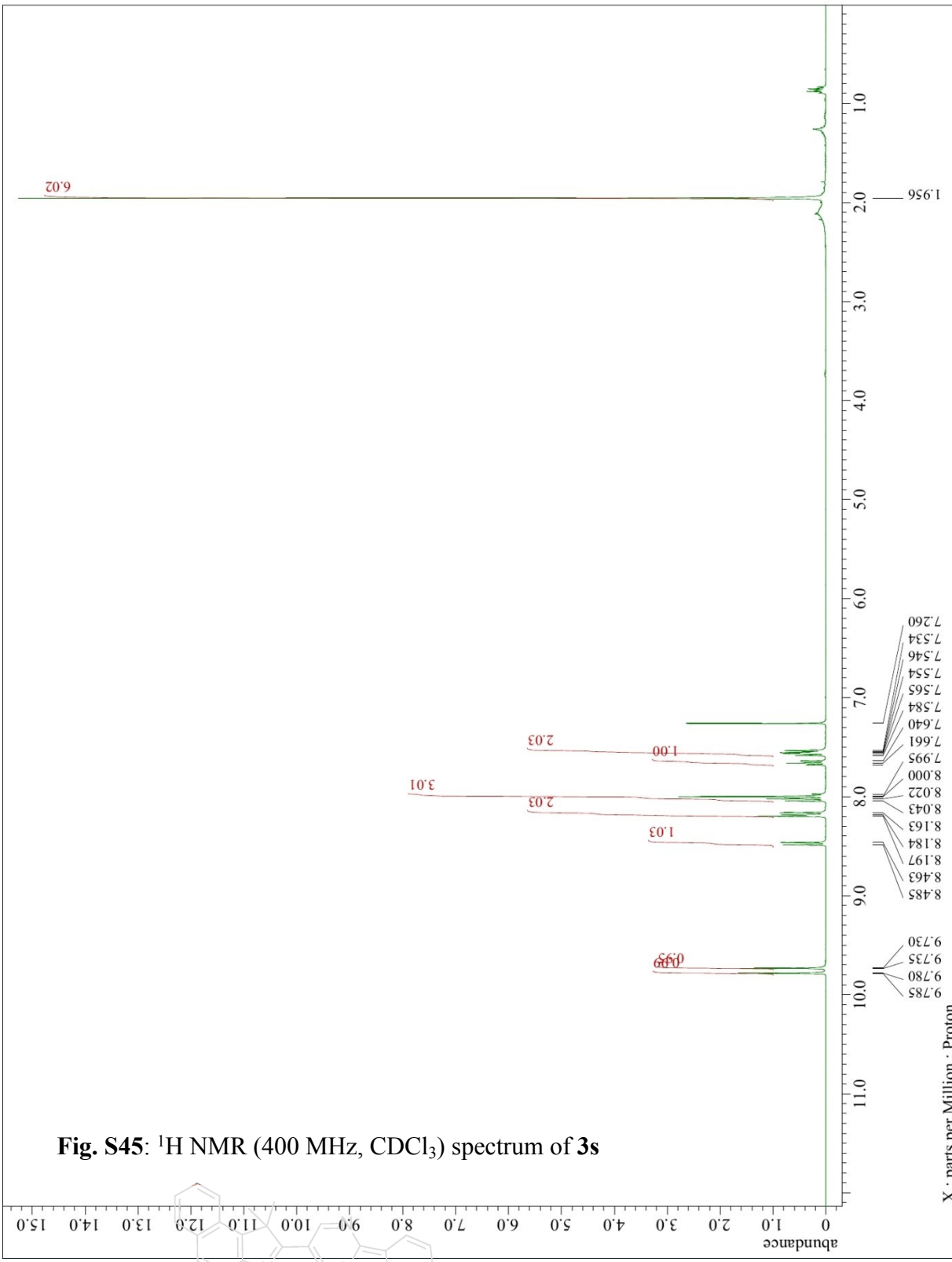

Fig. S45: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3s**

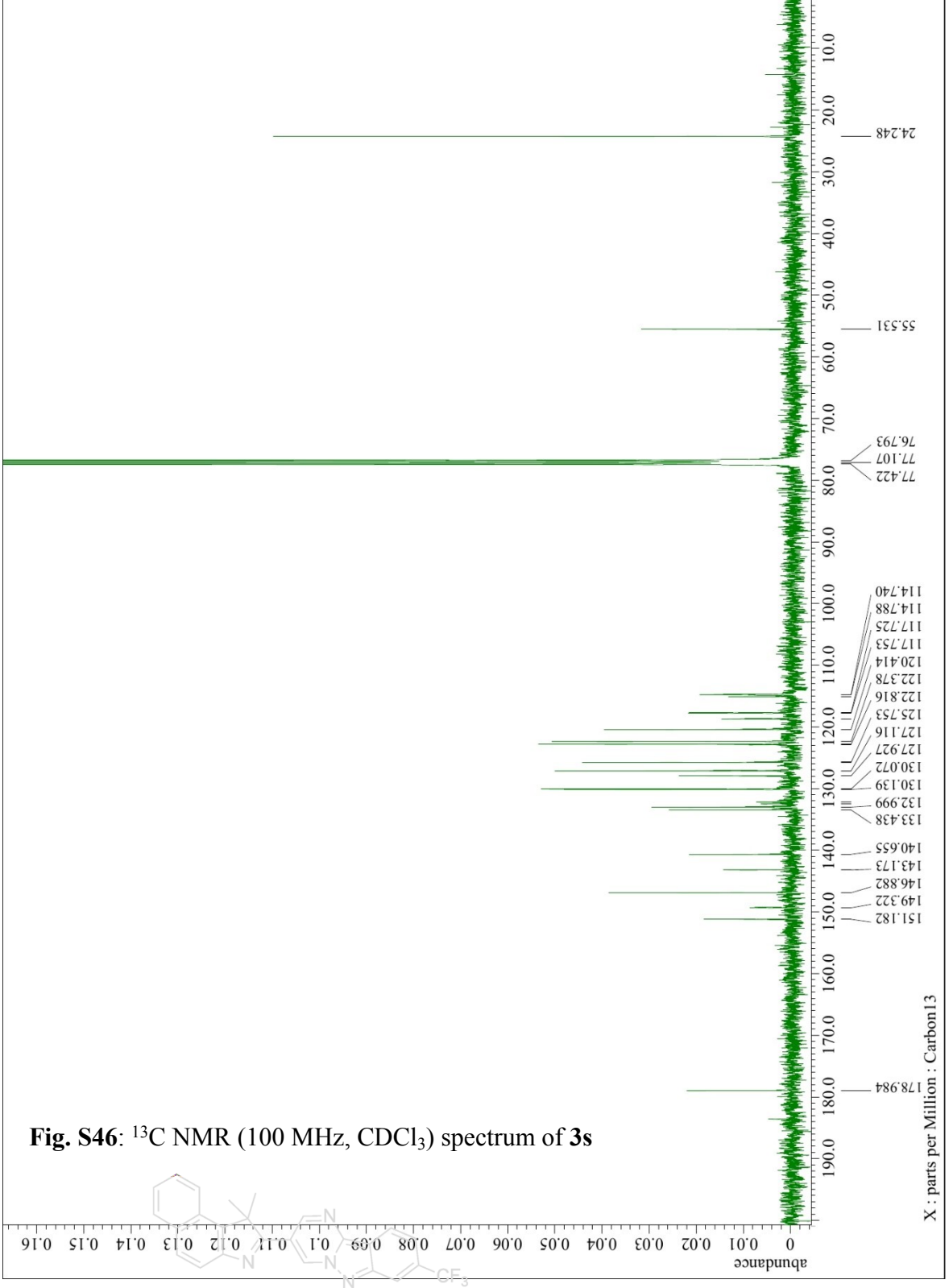

Fig. S46: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3s**

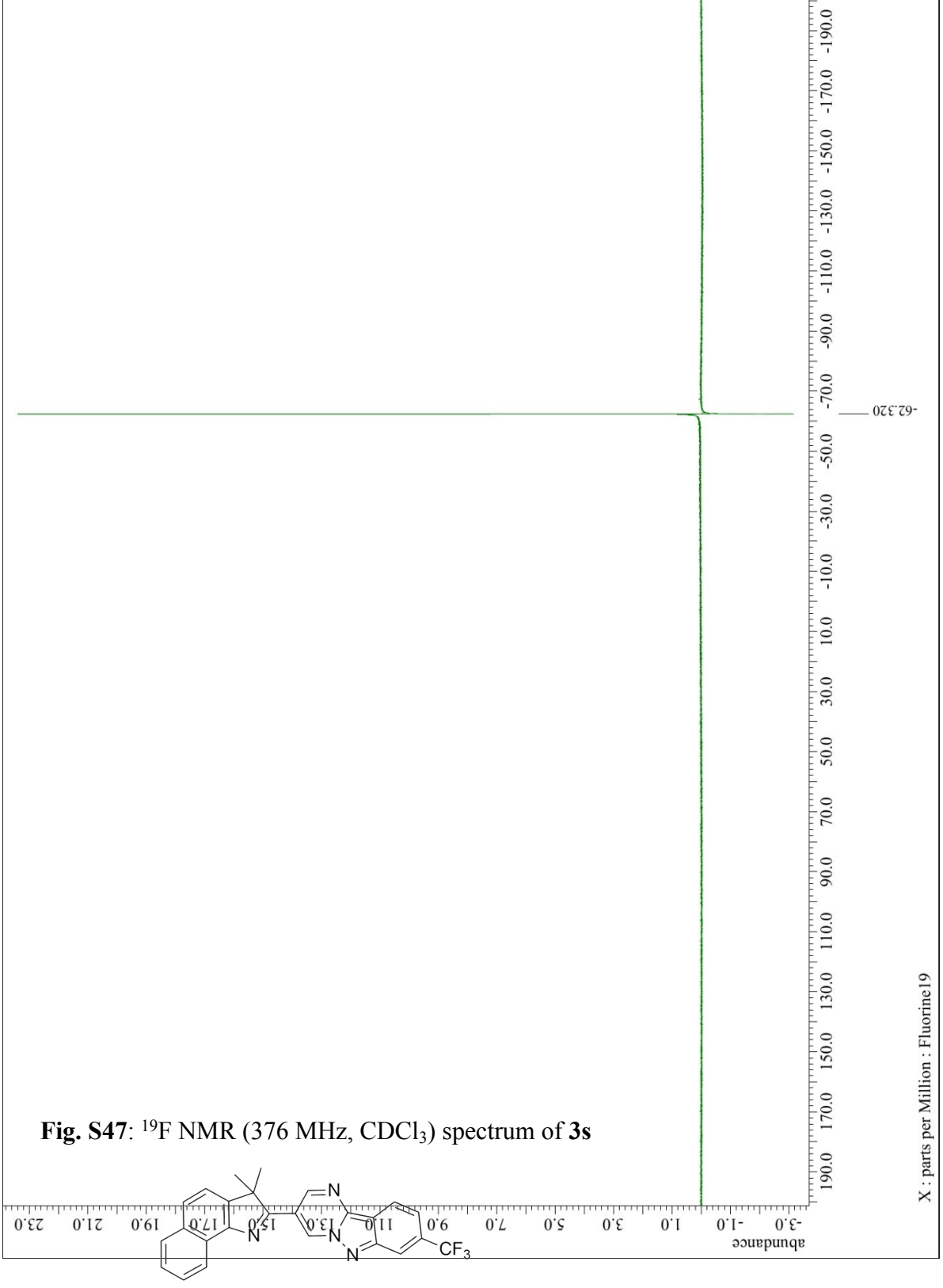

Fig. S47: ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3s**

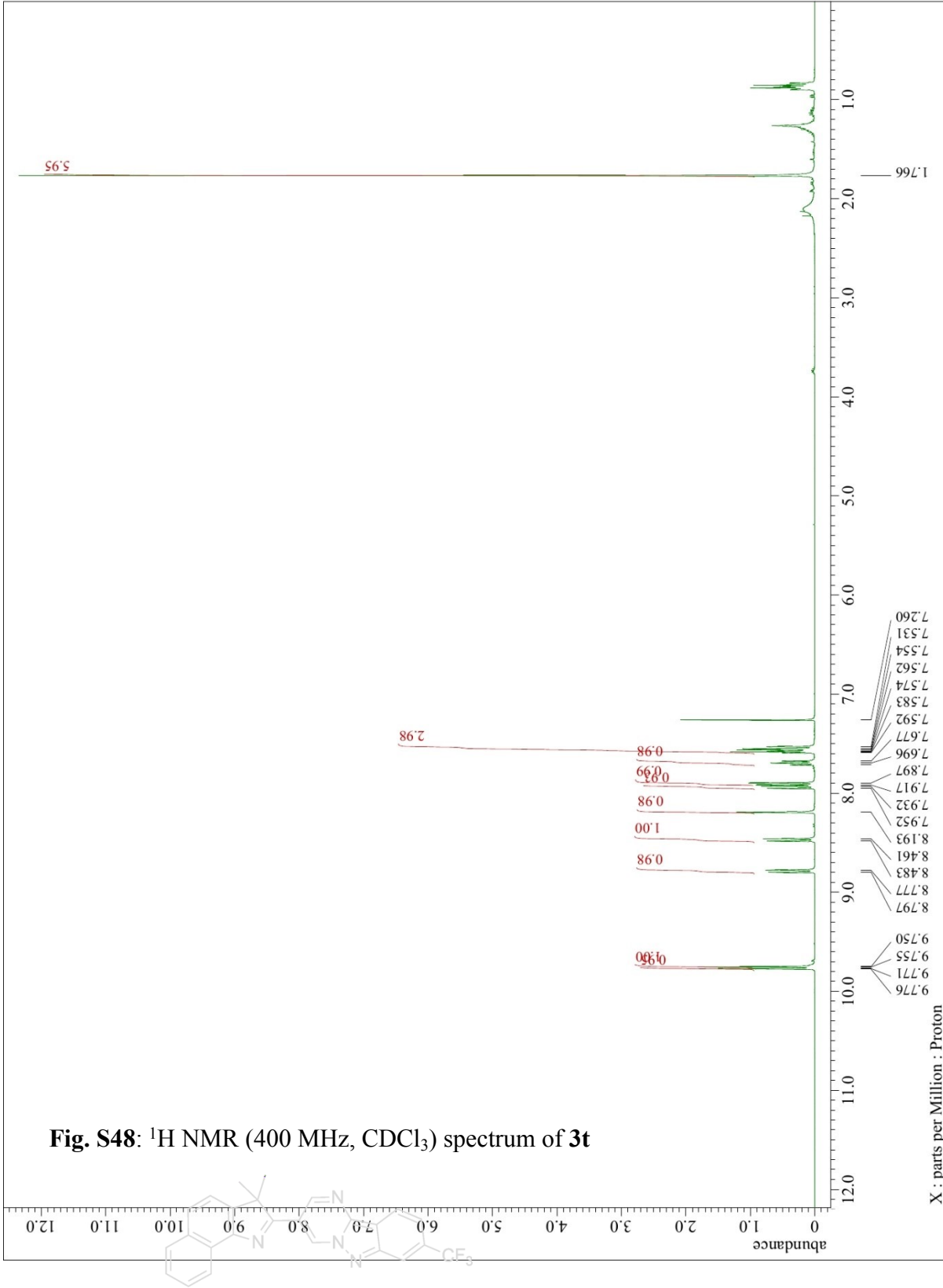

Fig. S48: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3t**

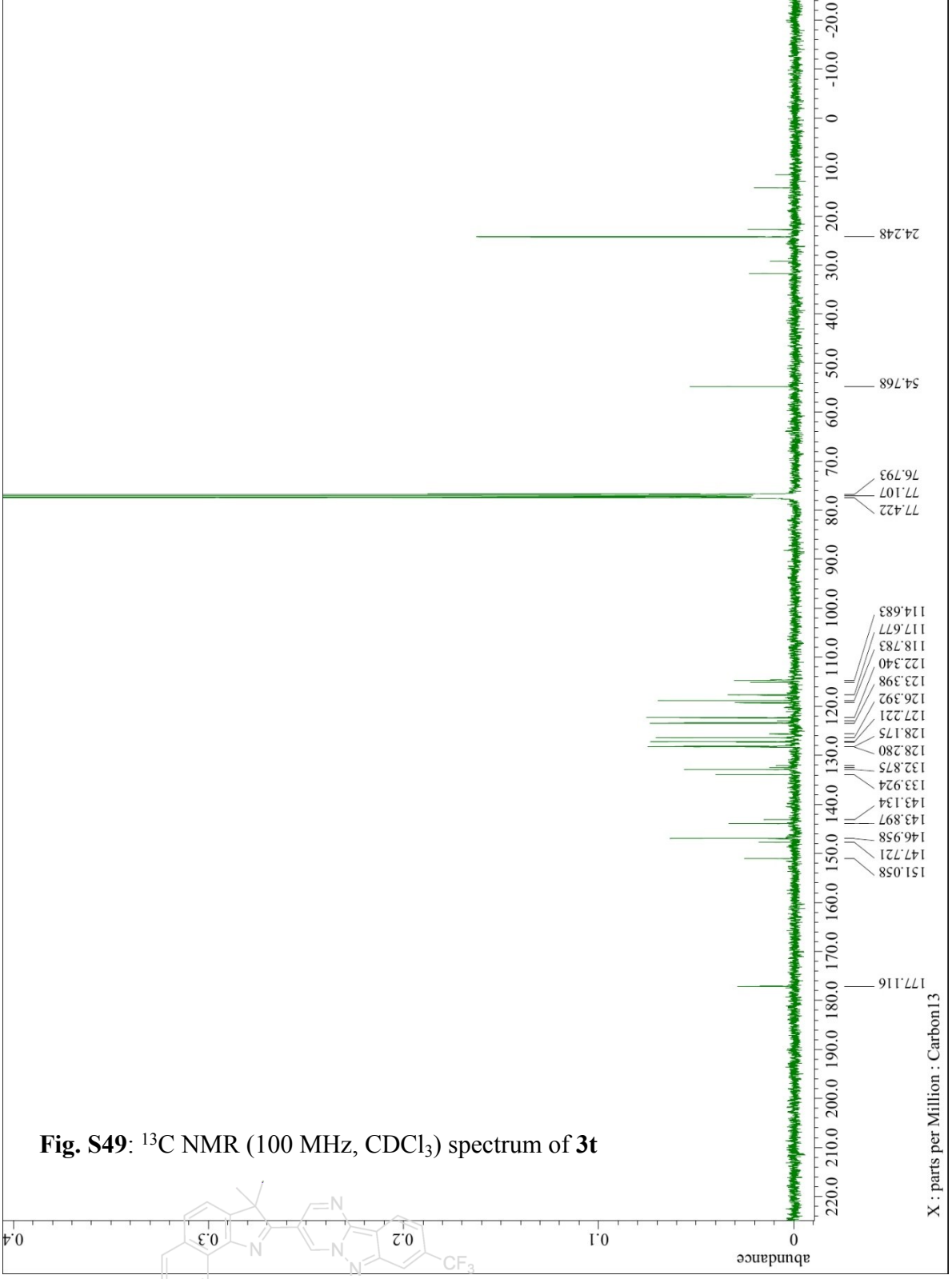

Fig. S49: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3t**

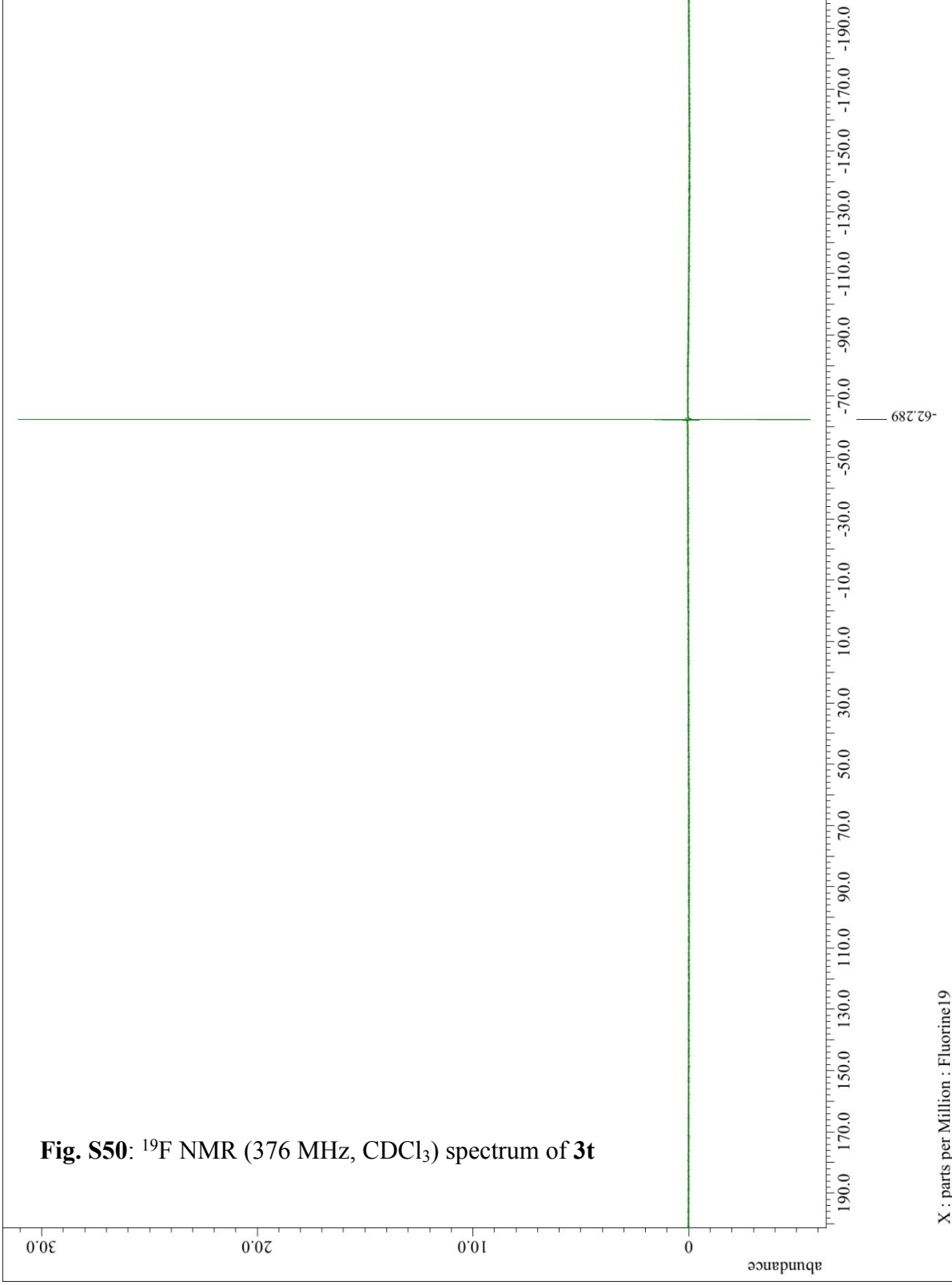

Fig. S50: ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3t**