Progressive Structural Modification to a Zinc-Actuated Photoinduced Electron Transfer (PeT) Switch in the Context of Intracellular Zinc Imaging

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Electronic Supplementary Information (ESI)

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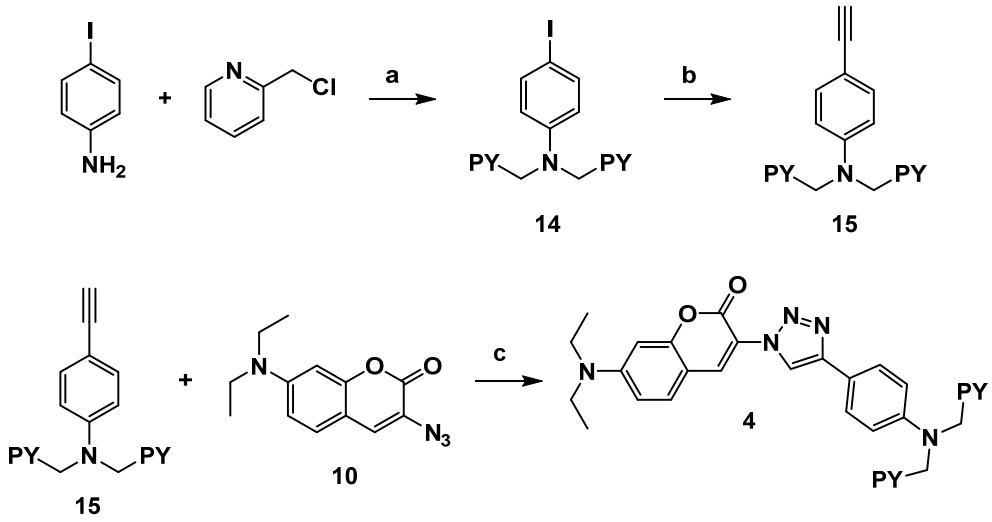
(1) Materials and general methods

Reagents and solvents were used as received from commercial sources. For absorption and fluorescence studies, spectroscopic grade organic solvents (CH_3CN and DMSO) and deionized water obtained from a NANOpure Diamond water system were used. TLC was performed on silica gel 60 F254 plates. Flash column chromatography was performed using 40-63 μm (230-400 mesh) silica gel or alumina (80-200 mesh, pH 9-10) as the stationary phase. ^1H and ^{13}C NMR spectra were acquired at 300/500/600 and 125/150 MHz, respectively. Chemical shifts are reported in δ (ppm) values relative to the residual internal $CHCl_3$ (δ_H 7.26; δ_C 77.2). High resolution mass spectra were obtained at the Mass Spectrometry Laboratory at FSU. Absorption and emission titrations were performed on a Varian Cary100 UV-VIS spectrophotometer and a Cary Eclipse fluorimeter, respectively, in quartz semi-micro cuvettes fitted with rubber septa. The cyclic voltammograms were acquired in CH_3CN (spectroscopic grade) containing Bu_4NPF_6 (100 mM) as supporting electrolyte using an electrochemical analyzer. Compound **10** was prepared according to the procedure reported by Wang and coworkers.[1]

(2) Syntheses and characterizations



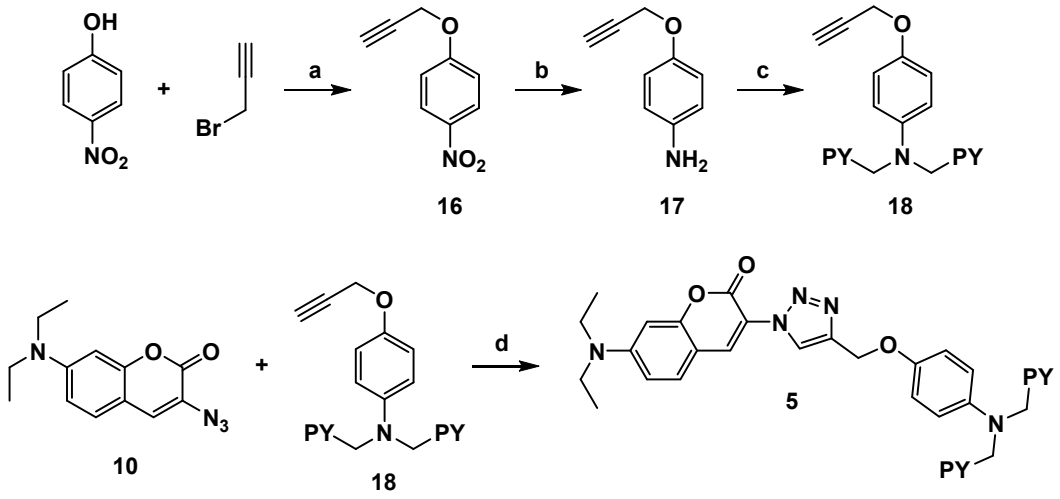
Scheme S1. Synthesis of compound **4**. Reagents and conditions: a) PTC (phase transfer catalyst), NaOH, water, rt, 24 h, 25%; b) (1) ethynyltrimethylsilane, $PdCl_2(PPh_3)_2$, CuI, Et_3N, THF, rt, overnight; (2) Bu_4NF, THF, rt, ~ 1 h, 96%; c) CuCl, THF, rt, overnight, 70%.

Compound 14.[2] 4-Iodoaniline (2.19 g, 10 mmol) was added to a round-bottom flask followed by a NaOH solution (6 mL, 5 M) and hexadecyltrimethylammonium chloride (40 mg, 0.13 mmol). 2-(Chloromethyl)pyridine hydrochloride (3.3 g, 20 mmol) dissolved in water (1 mL) was then added, and the reaction mixture was stirred vigorously for 24 h at rt before being diluted with dichloromethane (DCM) and extracting with DCM × 3. The organic layers were combined and washed once with basic (pH > 10) saturated brine before being dried over anhydrous Na_2SO_4 and concentrated. The pure product was isolated on a silica gel column by eluting with ethyl acetate in hexanes followed by 2% CH_3OH in EtOAc to give **14** in 25% yield (1.0 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm 8.60 (d, *J* = 4.7 Hz, 2H), 7.65 (td, *J* = 7.7, 1.7 Hz, 2H), 7.40 (d, *J* = 9.0 Hz, 2H), 7.23-7.15 (m, 4H), 6.50 (d, *J* = 9.0 Hz, 2H), 4.79 (s, 4H).

Compound 15.[3] To a flame-dried round-bottom flask, compound **14** (253 mg, 0.63 mmol), THF (2.6 mL), and Et_3N (1.3 mL) were added sequentially. The solution was bubbled with argon for ~5 min before ethynyltrimethylsilane (100 µL, 0.7 mmol) was added and the reaction mixture was allowed to stir at rt under argon. To the stirring solution, bis(triphenylphosphine)palladium(II) dichloride (13 mg, 0.019 mmol) and CuI (7 mg, 0.005 mmol) were added and the reaction mixture was stirred under argon overnight before being diluted with EtOAc and washed with a basic (pH > 10) EDTA solution (0.1 M) × 2. The organic layer was then dried over anhydrous sodium sulfate and concentrated. The crude product was filtered through a short silica column (i.e., a 'plug') with DCM. The collected product was then dissolved in THF (5 mL) and cooled in an ice bath. Tetrabutylammonium fluoride (220 mg) was dissolved in a small amount of THF and added dropwise to the reaction mixture, which was then allowed to stir at rt for 40 min. A small amount of sodium sulfate was added and the reaction mixture was stirred for another 10 min before being loaded directly onto a short alumina column and eluted with DCM. After concentration, compound **15** (180 mg, 96%) was isolated in pure form. ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm 8.61 (d, *J* = 5.5 Hz, 2H), 7.67 (td, *J* = 7.7, 1.7 Hz, 2H), 7.31-7.17 (m, 6H), 6.65 (d, *J* = 9.0 Hz, 2H), 4.84 (s, 4H), 2.95 (s, 1H).

Compound 4. In a Schlenk flask were placed alkyne **15** (0.050 g, 0.17 mmol), azide **10** (0.054 g, 0.21 mmol), and 20 mol% CuCl (3 mg). The flask was put under vacuum using a Schlenk line. The flask was back-filled with argon and then, degassed THF (1.5 mL) was added via a syringe. The resulting mixture was stirred overnight at rt. The reaction was quenched by the addition of 10% NH_4OH aqueous solution (2 mL). The desired product precipitated from the solution as a yellow powder. The solid was recovered through vacuum filtration, rinsed with basic 0.1 M EDTA solution, water and acetonitrile to afford

compound **4** in pure form (0.065 g, 70% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm 8.62-8.60 (m, 3H), 8.41 (s, 1H), 7.71-7.61 (m, 4H), 7.41 (d, *J* = 8.7 Hz, 1H), 7.29-7.25 (m, 3H), 7.18 (t, *J* = 6.6 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 6.68 (d, *J* = 9.0 Hz, 1H), 6.54 (s, 1H), 4.86 (s, 4H), 3.45 (q, *J* = 6.9 Hz, 4H), 1.23 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 158.7, 157.1, 155.9, 151.6, 149.9, 148.4, 148.0, 137.1, 134.4, 130.1, 127.3, 122.3, 121.0, 119.8, 119.1, 117.3, 112.9, 110.2, 107.4, 97.2, 57.5, 45.2, 12.6; HRMS (ESI+) (*m*/*z*): $[M+H]^+$ calcd for $C_{33}H_{32}N_7O_2$ 558.2618, found 558.2605.



Scheme S2. Synthesis of compound **5**. Reagents and conditions: a) K_2CO_3, CH_3CN, > 95%; b) $SnCl_2$, HCl, 88%; c) 2-pyridinecarboxaldehyde, $NaBH(OAc)_3$, 1,2-dichloroethane, rt, 70%; d) CuCl (10 mol%), THF, > 95%.

Compound 16.[4] p-Nitrophenol (1.0 g, 7.19 mmol) was dissolved in CH_3CN (100 mL) in a round-bottom flask. K_2CO_3 (995 mg, 7.21 mmol) was added, and the reaction mixture was stirred for 10 min at rt. Propargyl bromide (80% in toluene, 1.08 g, 7.2 mmol) was added via a syringe and the reaction mixture was heated under reflux overnight. After allowing to cool to rt, the product precipitated out of solution and was filtered. Compound **16** was isolated as a white solid (100%, 1.3 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm 8.26 (d, *J* = 9.3 Hz, 2H), 7.08 (d, *J* = 9.3 Hz, 2H), 4.81 (d, *J* = 2.4 Hz, 2H), 2.60 (t, *J* = 2.4 Hz, 1H).

Compound 17.[4] $SnCl_2{\cdot}2H_2O$ (3.4 g, 15 mmol) was added to a round-bottom flask and dissolved in HCl (37%, 12 mL). Compound **16** (354 mg, 2 mmol) was added to the stirring reaction mixture in portions.

The reaction mixture was then stirred for 4 h at rt before it was cooled in an ice bath. The mixture was basified by slow addition of a NaOH solution and then extracted with diethyl ether × 3. The combined ether layers were washed twice with saturated $NaHCO_3$, dried with sodium sulfate and concentrated to give **17** in 88% yield (259 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm 6.83 (d, *J* = 9.0 Hz, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 4.60 (d, *J* = 2.4 Hz, 2H), 2.49 (t, *J* = 2.4 Hz, 1H).

Compound 18. Compound **17** (74 mg, 0.5 mmol), 1,2-dichoroethane (1.25 mL), 2-picolylchloride (134 mg, 1.25 mmol), and $NaBH(OAc)_3$ (244mg, 1.12 mmol) were added to a round-bottom flask. The reaction mixture was stirred overnight under argon before it was quenched by dropwise addition of a saturated $NaHCO_3$ solution. The mixture was then diluted with EtOAc and washed with sat. $NaHCO_3$ × 3, dried with sodium sulfate, and concentrated. The crude product was further purified by silica gel column eluting with EtOAc in DCM (0 to 100% EtOAc) to give compound **18** in 70% (115 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 8.58-8.57 (m, 2H), 7.61 (td, *J* = 4.8, 1.2 Hz, 2H), 7.28 (d, *J* = 4.5 Hz, 2H), 7.15-7.14 (m, 2H), 6.84 (d, *J* = 5.7 Hz, 2H), 6.66 (d, *J* = 5.4 Hz, 2H), 4.78 (s, 4H), 4.56 (d, *J* = 1.5 Hz, 2H), 2.48 (t, *J* = 1.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm 159.2, 149.9, 149.7, 143.5, 136.9, 122.1, 121.0, 116.3, 113.8, 79.3, 75.3, 58.0, 56.7; HRMS (EI+) (*m*/*z*): $[M]^+$ calcd for $C_{21}H_{19}ON_3$ 329.1528, found 329.1531.

Compound 5. Alkyne **18** (60 mg, 0.18 mmol), THF (0.45 mL), azide **10** (49 mg, 0.19 mmol) and CuCl (1.8 mg, 0.018 mmol) were added sequentially to a round-bottom flask. The reaction mixture was stirred at rt under argon for 6 h before being diluted with EtOAc. The reaction mixture was then washed with basic EDTA (0.1 M, pH > 10) × 3, dried with sodium sulfate, and concentrated to give compound **5** in 100% yield (106 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm 8.65-8.53 (m, 3H), 8.38 (s, 1H), 7.63 (t, *J* = 7.5 Hz, 2H), 7.42 (d, *J* = 8.7 Hz, 1H), 7.32-7.24 (m, 2H), 7.21-7.10 (m, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 6.73-6.63 (m, 3H), 6.58-6.53 (m, 1H), 5.16 (s, 2H), 4.77 (s, 4H), 3.49 (q, *J* = 7.2 Hz, 4H), 1.28 (t, *J* = 7.2 Hz, 6H); HRMS (ESI+) (*m*/*z*): $[M+H]^+$ calcd for $C_{34}H_{34}N_7O_3$ 588.2723, found 588.2723.

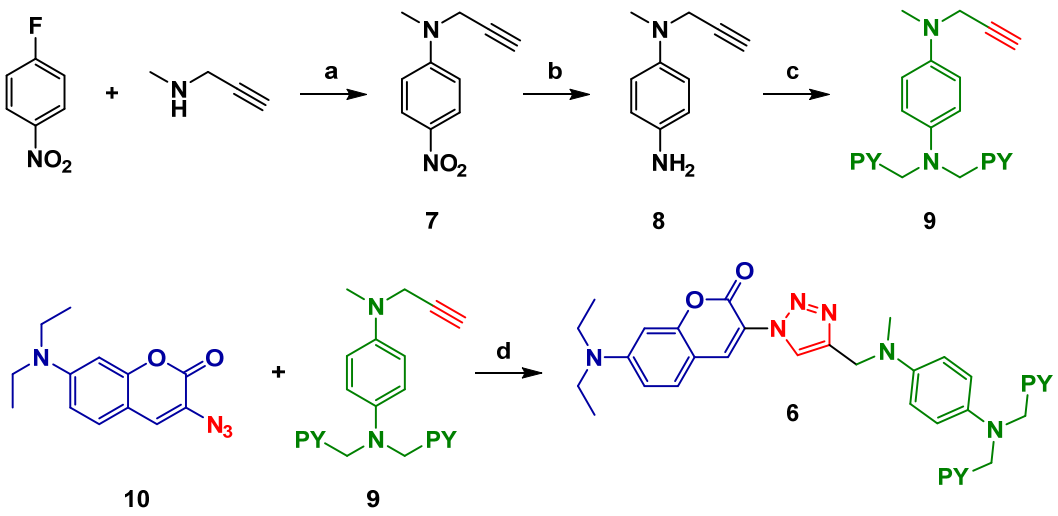


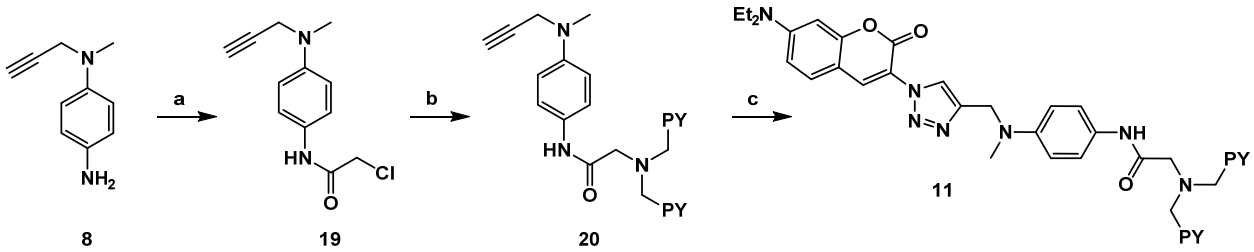
Figure 8 (reproduced in the ESI). Synthesis of compound **6**. Reagents and conditions: a) *N*-methylpropargylamine (1 molar equiv.), K_2CO_3, DMSO, 50 °C, overnight, 72%; b) $SnCl_2$, HCl (37%), overnight, 70%; c) 2-picolylbromide hydrobromide, Na_2CO_3, EtOH, reflux, overnight, 26%; d) CuCl (20 mol%), THF, under argon, overnight, 60%.

Compound 7.[5] *N*-Methylpropargylamine (0.150 g, 2.17 mmol), *p*-fluoronitrobenzene (0.306 g, 2.17 mmol), K_2CO_3 (0.360 g, 2.61 mmol), Et_3N (0.12 mL, 0.87 mmol), and DMSO (3 mL) were added to a vial. The mixture was stirred overnight at 50 °C. The heterogeneous mixture was poured into 30 mL of cold water, resulting in a yellow precipitate. The yellow solid was recovered by vacuum filtration and rinsed with cold water and isopropanol to give 0.289 g (72% yield) of pure product. ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 8.17-8.12 (m, 2H), 6.77-6.71 (m, 2H), 4.15 (d, *J* = 2.5 Hz, 2H), 3.14 (s, 3H), 2.26 (t, *J* = 2.5 Hz, 1H).

Compound 8. $SnCl_2 \cdot 2H_2O$ (2.546 g, 0.01 mol) and 37.4% HCl (8.7 mL) were added to a round-bottom flask. Then compound **7** (0.290 g, 1.47 mmol) was added portion-wise. After completion of addition, the mixture was stirred overnight at rt. The crude mixture was diluted with cold water, basified with aq 1 M NaOH and then extracted twice with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo to give 0.171 g (70% yield) of a dark brown solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 6.82-6.77 (m, 2H), 6.71-6.66 (m, 2H), 3.94 (d, *J* = 2.5 Hz, 2H), 3.40 (bs, 1H), 2.86 (s, 3H), 2.17 (t, *J* = 2.0 Hz, 1H).

Compound 9. Compound **8** (0.050 g, 0.31 mmol) was dissolved in EtOH (5 mL) and transferred to a round-bottom flask. Then Na_2CO_3 (0.134 g, 1.26 mmol) and 2-(bromomethyl)pyridine hydrobromide (0.157 g, 0.62 mmol) were added. The mixture was stirred at reflux for 24 h. The crude mixture was filtered and concentrated in vacuo. The residue was taken in DCM and washed with water. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The desire compound was isolated via silica column chromatography (EtOAc to 5% MeOH in EtOAc) as a yellow solid (0.028 g, 26% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 8.57 (dq, *J* = 4.5, 1.0 Hz, 2H), 7.60 (td, *J* = 8.0, 2.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.17-7.12 (m, 2H), 6.80-6.75 (m, 2H), 6.68-6.63 (m, 2H), 4.76 (s, 4H), 3.90 (d, *J* = 2.0 Hz, 2H), 2.82 (s, 3H), 2.15 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 159.4, 149.6, 142.1, 141.4, 136.9, 122.0, 121.1, 117.4, 113.9, 79.6, 72.4, 57.9, 43.9, 39.4; HRMS (ESI+) calcd from $C_{22}H_{22}N_4Na_1$ $[M+Na]^+$ 365.1742, found 365.1741.

Compound 6. Under argon protection, alkyne **9** (0.025 g, 0.07 mmol), dry THF (1 mL), azide **10** (0.024 g, 0.09 mmol) and 20 mol % CuCl were added to a two-neck round bottom flask. The mixture was stirred overnight at rt. The reaction was quenched by the addition of 10% NH_4OH (2 mL). The mixture was stirred for 5 min and then extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The desired compound was recrystallized from hot EtOAc to give 0.026 g (60% yield) of a brown powder. ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 8.56 (d, *J* = 4.5 Hz, 2H), 8.32 (s, 1H), 8.27 (s, 1H), 7.61 (td, *J* = 7.5, 1.5 Hz, 2H), 7.38 (d, *J* = 9.0 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 2H), 7.14 (dd, *J* = 7.0, 5.0 Hz, 2H), 6.79-6.72 (m, 2H), 6.68-6.61 (m, 3H), 6.53 (d, *J* = 2.5 Hz, 1H), 4.74 (s, 4H), 4.53 (s, 2H), 3.44 (q, *J* = 7.0 Hz, 4H), 2.88 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 159.5, 157.0, 155.8, 151.6, 149.6, 137.0, 134.8, 130.1, 122.9, 122.0, 121.2, 117.1, 116.2, 114.3, 110.1, 107.1, 97.0, 58.0, 50.0, 45.1, 39.4, 12.5; HRMS (ESI+) calcd from $C_{35}H_{36}N_8Na_1O_2$ $[M+Na]^+$ 623.2859, found 623.2852.



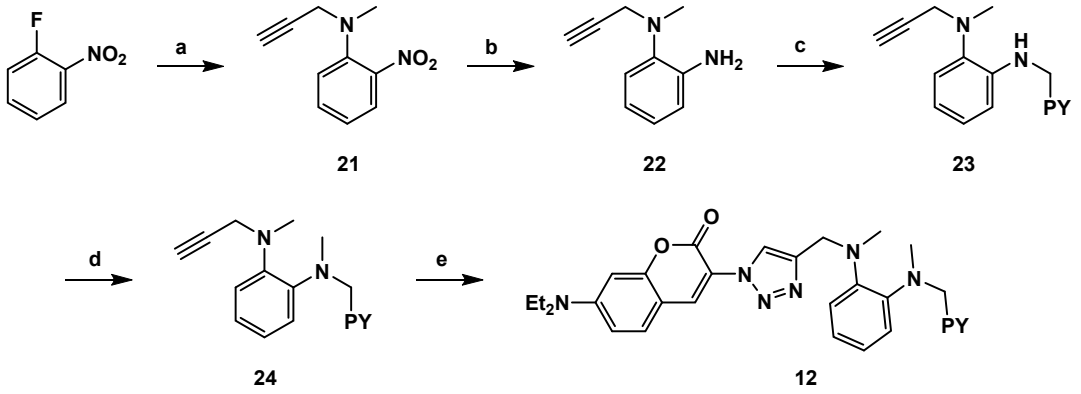
Scheme S3. Synthesis of compound **11**. Reagents and conditions: a) Et_3N, chloroacetyl chloride, THF, Ar, 0-5 °C to rt, 6 h, 66%; b) (1) K_2CO_3, THF, Ar, rt, 10 min; (2) DPA, 30 °C, 6 h, 58%; c) azide **10**, THF, 20 mol% CuCl, Ar, rt, overnight, 28%.

Compound 19. Under argon protection, compound **8** (0.200 g, 1.25 mmol) and dry THF (2 mL) were added to a two-neck round-bottom flask. The resulting solution was cooled to 0-5 °C in an ice bath. Then, Et_3N (0.24 mL, 1.25 mmol) was added dropwise, followed by the dropwise addition of a solution of chloroacetyl chloride (0.20 mL, 2.50 mmol) in dry THF (3 mL). The resulting mixture was stirred at rt for 6 h. The crude mixture was filtered and concentrated under reduced pressure. The residue was taken in DCM in a separatory funnel and washed with water. The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. Compound **19** was isolated as a yellow solid on a silica gel column eluted by DCM in 66% yield (0.194 g). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 8.11 (bs, 1H), 7.45-7.38 (m, 2H), 6.89-6.80 (m, 2H), 4.17 (s, 2H), 4.04 (d, *J* = 2.5 Hz, 2H), 2.96 (s, 3H), 2.18 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 163.8, 146.7, 127.9, 122.0, 114.8, 79.0, 72.4, 43.0, 42.8, 38.9; HRMS (ESI+) calcd from $C_{12}H_{14}Cl_1N_2O_1$ $[M+H]^+$ 237.0795, found 237.0781.

Compound 20. Under argon protection, compound **19** (0.075 g, 0.32 mmol), dry THF (15 mL), and K_2CO_3 (0.044 g, 0.32 mmol) were added to a round-bottom flask. The resulting mixture was stirred 10 min at rt prior the addition of di(2-picolyl)amine (114 µL, 0.63 mmol). The mixture was stirred at 30 °C for 6 h. The crude mixture was filtered and concentrated in vacuo. The residue was taken in EtOAc in a separatory funnel and washed with water. The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The desired compound was isolated on a silica column (up to 5% MeOH in EtOAc) as a yellow solid (0.074 g, 58% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 10.70 (s, 1H), 8.59 (dq, *J* = 4.5, 0.5 Hz, 2H), 7.68-7.62 (m, 2H), 7.58 (td, *J* = 7.5, 2.0 Hz, 2H), 7.29-7.24 (m, 2H), 7.15 (ddd, *J* = 7.5, 5.0, 1.0 Hz, 2H), 6.87-6.82 (m, 2H), 4.00 (d, *J* = 2.0 Hz, 2H), 3.89 (s, 4H), 3.42 (s, 2H), 2.91 (s, 3H), 2.15 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 169.2, 158.2, 149.4, 145.7, 136.6, 130.4, 123.2,

122.5, 120.9, 115.1, 79.2, 72.2, 60.4, 58.6, 43.0, 38.9; HRMS (ESI+) calcd from $C_{24}H_{25}N_5Na_1O_1$ $[M+Na]^+$ 422.1957, found 422.1967.

Compound 11. Under argon protection, compound **20** (0.050 g, 0.13 mmol), dry THF (4 mL), compound **10** (0.040 g, 0.16 mmol), and 20 mol % CuCl (3 mg, 0.03 mmol) were added to a two-neck round-bottom flask. The mixture was stirred overnight at rt. The reaction was quenched by the addition of NH_4OH (10%, 4 mL). The mixture was stirred for 5 min and then extracted twice with DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude mixture was subjected to separation on an alumina column (up to 5% MeOH in EtOAc) to give a yellow solid (0.023 g, 28% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 10.62 (s, 1H), 8.60 (dq, *J* = 5.0, 1.0 Hz, 2H), 8.30 (s, 1H), 8.29 (s, 1H), 7.63-7.57 (m, 4H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.31-7.27 (m,2H), 7.16 (ddd, *J* = 7.5, 5.0, 1.5 Hz, 2H), 6.85-6.80 (m 2H), 6.65 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.52 (d, *J* = 2.5 Hz, 1H), 4.67 (s, 2H), 3.91 (s, 4H), 3.47-3.39 (m, 6H), 3.04 (s, 3H), 1.22 (t, *J* = 7.5 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 169.1, 158.3, 157.1, 155.9, 151.6, 149.5, 146.0, 145.1, 136.7, 135.0, 130.1, 129.4, 123.3, 122.7, 122.6, 121.2, 117.1, 113.8, 110.1, 107.1, 97.1, 60.6, 58.7, 49.1, 45.1, 39.1, 12.5; HRMS (ESI+) calcd from $C_{37}H_{39}N_9Na_1O_3$ $[M+Na]^+$ 680.3074, found 680.3066.



Scheme S4. Synthesis of compound **12**. Reagents and conditions: a) *N*-methylpropargylamine, K_2CO_3, Et_3N, DMSO, 50 °C, overnight, 66%; b) (1) EtOAc, 0-5 °C; (2) $SnCl_2{\cdot}2H_2O$, 0-5 °C to rt, 24 h, 91%; c) 2-pyridinecarboxaldehyde, $NaBH(OAc)_3$, DCE, Ar, rt, overnight, 87%; d) (1) formaldehyde 37 wt%, AcOH, CH_3CN, rt, 30 min; (2) $NaCNBH_3$, 0-5 °C to rt, overnight, 58%; e) azide **10**, THF, 20 mol% CuCl, Ar, rt, overnight, 71%.

Compound **21**. *N*-Methylpropargylamine (0.150 g, 2.17 mmol), 1-fluoro-2-nitrobenzene (0.306 g, 2.17 mmol), K_2CO_3 (0.360 g, 2.61 mmol), Et_3N (0.12 mL, 0.87 mmol) and DMSO (3 mL) were added to a vial. The mixture was stirred overnight at 50 °C. The crude mixture was diluted with water and extracted with DCM. The organic layer was washed twice with water. The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo. The desired product was isolated on a silica column (hexanes:DCM 1:1) as a yellow oil (0.273 g, 66% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 7.75 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.47 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.29 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.00 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H), 3.93 (dd, *J* = 2.5, 0.3 Hz, 2H), 2.88 (s, 3H), 2.31 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 144.9, 142.3, 133.3, 126.2, 121.2, 121.1, 78.5, 73.9, 44.7, 40.3; HRMS (ESI+) calcd from $C_{10}H_{11}N_2O_2$ $[M+H]^+$ 191.0820, found 191.0813.

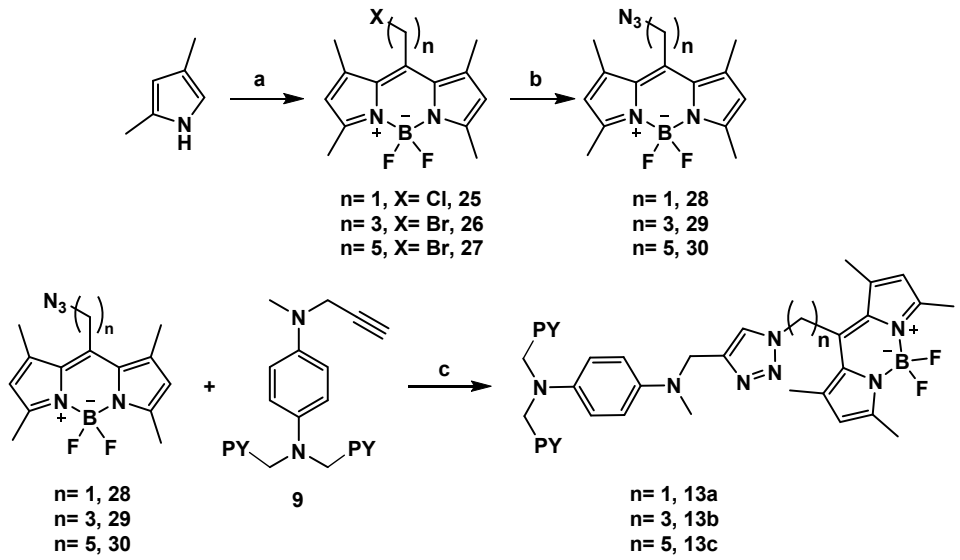
Compound 22. Compound **21** (0.140 g, 0.74 mmol) and EtOAc (2 mL) were placed in a round-bottom flask. The resulting solution was cooled to 0-5 °C in an ice bath. A dispersion of $SnCl_2{\cdot}2H_2O$ (0.830 g, 3.68 mmol) in EtOAc (3 mL) was slowly added into the flask over a period of about 30 min. Upon complete addition, the ice bath was removed and the reaction was stirred at rt for 24 h. The crude mixture was diluted with EtOAc and then a saturated $NaHCO_3$ aqueous solution was carefully added. The heterogeneous mixture was placed in a separatory funnel and the organic layer isolated. The aqueous phase was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo to give a brown viscous oil (0.107 g, 91% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 7.13 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.96 (td, *J* = 8.0, 1.5 Hz, 1H), 6.77-6.72 (m, 2H), 3.95 (bs, 2H), 3.72 (d, *J* = 2.5 Hz, 2H), 2.80 (s, 3H), 2.25 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 141.6, 138.1, 125.1, 121.2, 118.4, 115.3, 79.9, 72.7, 44.3, 40.0.

Compound 23. Compound **22** (0.100 g, 0.62 mmol) was transferred into a two-neck round-bottom flask as a solution in DCM, then the solvent was evaporated. Under argon protection, $NaBH(OAc)_3$ (0.304 g, 1.44 mmol), 2-pyridinecarboxaldehyde (0.167 g, 1.56 mmol), and 1,2-dichloroethane (3 mL) were added to the flask. The mixture was stirred at rt overnight. The reaction was quenched by the slow addition of a saturated $NaHCO_3$ aqueous solution. The crude mixture was extracted twice with DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Compound **23** was isolated on a silica column eluted by (EtOAc) as a brown oil (0.137 g, 87% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 8.61-8.57 (m, 1H), 7.63 (td, *J* = 6.0, 1.5 Hz, 1H), 7.34 (d, *J* = 6.5 Hz, 1H), 7.19-7.14 (m, 2H), 7.00-6.96 (m, 1H), 6.71 (td, *J* = 6.0, 1.0 Hz, 1H), 6.55 (dd, *J* = 6.5, 1.0 Hz, 1H), 5.51 (bs, 1H), 4.51 (s, 2H), 3.76 (d, *J* = 2.0 Hz, 2H), 2.83 (s, 3H), 2.26 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz)

δ/ppm 159.5, 149.3, 142.9, 137.9, 136.8, 125.5, 122.0, 121.3, 121.0, 117.0, 110.6, 80.0, 72.8, 49.7, 44.6, 40.3; HRMS (ESI+) calcd from $C_{16}H_{18}N_3$ $[M+H]^+$ 252.1501, found 252.1504.

Compound 24. Compound **23** (0.075 g, 0.30 mmol), a formaldehyde solution 37 wt % in water (0.25 mL), acetonitrile (1 mL), and glacial acetic acid (0.26 mL) were added to a vial. The mixture was stirred at rt for 30 min. Then the mixture was cooled to 0-5 °C in an ice bath. $NaCNBH_3$ (0.023 g, 0.37 mmol) was added in two portions over a period of 30 min. The mixture was stirred overnight at rt. The reaction was quenched by adding a saturated $NaHCO_3$ aqueous solution and then extracted twice with DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The desired compound was isolated on a silica column (hexanes:EtOAc 1:1) as a yellow solid (0.046 g, 58% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 8.54 (dq, *J* = 4.5, 0.5 Hz, 1H), 7.58 (td, *J* = 7.5, 1.5 Hz, 1H), 7.23-7.19 (m, 1H), 7.13 (ddd, *J* = 7.5, 5.0, 1.0 Hz, 1H), 7.09-7.04 (m, 1H), 7.01-6.92 (m, 3H), 4.50 (s, 2H), 4.16 (d, *J* = 2.0 Hz, 2H), 2.87 (s, 3H), 2.78 (s, 3H), 2.16 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 159.4, 149.0, 144.7, 143.0, 136.4, 123.2, 122.6, 122.3, 121.8, 120.8, 119.6, 80.1, 72.3, 59.9, 42.6, 39.4, 38.8; HRMS (ESI+) calcd from $C_{17}H_{20}N_3$ $[M+H]^+$ 266.1657, found 266.1657.

Compound 12. Compound **24** (0.045 g, 0.17 mmol) was transferred into a two-neck round-bottom flask as a solution in DCM, then the solvent was evaporated. Under argon protection, dry THF (2 mL), compound **10** (0.055 g, 0.21 mmol) and 20 mol % CuCl (3 mg, 0.03 mmol) were added to the flask. The resulting mixture was stirred overnight at rt. The reaction was quenched by the addition of NH_4OH (10%, 2 mL). The mixture was stirred for 5 min and then extracted twice with DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Compound **12** was isolated on a silica column (hexanes:EtOAc 1:1). A yellow solid was recovered (0.063 g, 71% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm 8.53 (dq, *J* = 5.0, 0.5 Hz, 1H), 8.30 (s, 1H), 8.00 (s, 1H), 7.57 (td, *J* = 8.0, 2.0 Hz, 1H), 7.38 (d, *J* = 9.0 Hz, 1H), 7.24-7.20 (m, 1H), 7.12 (ddd, *J* = 7.5, 5.0, 1.0 Hz, 1H), 6.99-6.91 (m, 4H), 6.66 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.53 (d, *J* = 2.5 Hz, 1H), 4.68 (s, 2H), 4.56 (s, 2H), 3.44 (q, *J* = 7.0 Hz, 4H), 2.84 (s, 3H), 2.82 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ/ppm 159.4, 157.0, 155.9, 151.6, 149.0, 144.8, 143.9, 136.5, 134.9, 130.0, 123.2, 122.9, 122.8, 122.4, 121.9, 120.3, 119.8, 117.2, 110.0, 107.1, 97.1, 60.0, 48.6, 45.1, 39.8, 39.5, 12.5; HRMS (ESI+) calcd from $C_{30}H_{34}N_7O_2$ $[M+H]^+$ 524.2774, found 524.2784.



Scheme S5. Synthesis of compounds **13a-c**. Reagents and conditions: (a) chloroacetyl chloride (**25**), 4-bromobutyryl chloride (**26**), 6-bromohexanoyl chloride (**27**), DCM, Et_3N, boron trifluoride diethyl etherate, rt, 14 h, 24-37%; (b) Sodium azide, DMF, 50 °C, overnight, 89-98%; (c) $Cu(OAc)_2 \cdot H_2O$, sodium ascorbate, EtOH, rt 16 h, 31-59%.

Compound 25.[6, 7] In a dry round-bottom flask, chloroacetyl chloride (1.76 mmol, 0.14 mL) was added to dry dichloromethane (10 mL). The solution was placed on ice to cool down to 0 °C. Then, 2,4-dimethyl pyrrole (3.80 mmol, 0.40 mL) was added dropwise. Upon full addition, the reaction mixture was stirred for 30 min at 0 °C, followed by 30 min at rt. The reaction mixture was then cooled to 0 °C, and triethylamine (0.74 mL) was added slowly. The solution was stirred at rt for 10 min. To this mixture, boron trifluoride diethyl etherate (8.9 mmol, 1.10 mL) was slowly added, and the reaction was stirred under argon at rt for 14 h. The resulting mixture was diluted with dichloromethane (30 mL) and washed with water (40 mL x 3). The organic layer was concentrated and loaded onto a silica column. The pure product was acquired using an elution of 1:1 hexanes:dichloromethane. The final product was acquired in a yield of 37% as a dark purple-green powder (195 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 6.10 (s, 2H), 4.79 (s, 2H), 2.54 (s, 12 H).

Compound 26.[8] In a dry round-bottom flask, 4-bromobutyryl chloride (1.76 mmol, 0.20 mL) was added to dry dichloromethane (10 mL). The solution was placed on ice to cool down to 0 °C. Then, 2,4-dimethyl pyrrole (3.80 mmol, 0.40 mL) was added dropwise. Upon full addition, the reaction mixture

was stirred for 30 min at 0 °C, followed by 30 min at rt. The reaction mixture was then cooled to 0 °C, and triethylamine (0.70 mL) was added slowly. The solution was stirred at rt for 10 more min. To this mixture, boron trifluoride diethyl etherate (6.0 mmol, 0.80 mL) was slowly added, and the reaction was stirred under argon at rt for 14 h. The resulting mixture was diluted with dichloromethane (30 mL) and washed with water (40 mL x 3). The organic layer was concentrated and loaded onto a silica column. The pure product was acquired using an elution of 1:1 hexanes: dichloromethane in a yield of 24% as an orange powder (24 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 6.06 (s, 2H), 3.57 (t, *J* = 6.0 Hz, 2H), 3.13 (t, *J* = 8.4 Hz, 2H), 2.52 (s, 6H), 2.45 (s, 6H), 2.19-2.14 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 154.7, 144.4, 140.5, 131.7, 122.1, 34.3, 33.1, 27.5, 16.9, 14.7.

Compound 27.[9] In a dry round-bottom flask, 6-bromohexanoyl chloride (1.83 mmol, 0.28 mL) was added to dry dichloromethane (10 mL). The solution was placed on ice to cool down to 0 °C. Then, 2,4-dimethyl pyrrole (4.86 mmol, 0.50 mL) was added dropwise. Upon full addition, the reaction mixture was stirred for 30 min at 0 °C, followed by 30 min at rt. The reaction mixture was then cooled to 0 °C, and triethylamine (0.70 mL) was added slowly. The solution was stirred at rt for 10 min. To this mixture, boron trifluoride diethyl etherate (8.1 mmol, 1.00 mL) was slowly added, and the reaction was stirred under argon at rt for 14 h. The resulting mixture was diluted with dichloromethane (30 mL) and washed with water (40 mL x 3). The organic layer was concentrated and loaded onto a silica column. The pure product was acquired using an elution of 1:1 hexanes: dichloromethane. The final product was acquired in a yield of 33% as an orange-red powder (238 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 6.04 (s, 2H), 3.42 (t, *J* = 6.6 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.51 (s, 6H), 2.39 (s, 6H), 1.91 (quint, *J* = 7.2 Hz, 2H), 1.62-1.64 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 154.1, 146.1, 140.4, 131.6, 121.8, 33.5, 32.4, 31.0, 28.7, 28.3, 16.5, 14.6.

Compound 28.[7] Compound **25** (0.18 mmol, 54.0 mg) was dissolved in ethanol (30 mL). To this mixture, sodium azide (0.85 mmol, 54.0 mg) was added. The round-bottom flask was then wrapped with aluminum foil and placed under argon. The reaction was stirred at 40 °C for 18 h. The solvent was removed under reduced pressure. The crude mixture was then dissolved with dichloromethane and washed twice with water. The organic layer was dried using sodium sulfate and concentrated. The crude material was then purified on a silica gel column using an elution of 3:10 dichloromethane in hexanes. The final product was obtained as an orange-red solid in 98% yield (54 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 6.11 (s, 2H), 4.61 (s, 2H), 2.53 (s, 6H), 2.46 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm 156.9, 141.4, 133.3, 132.2, 122.8, 44.8, 16.3, 14.9.

Compound 29.[10] Compound **26** (0.28 mmol, 105 mg) was dissolved in DMF (3.0 mL), and sodium azide (1.0 mmol, 65.0 mg) was slowly added to the round-bottom flask. The solution stirred at 50 °C for 12 h. The reaction mixture was then diluted with ethyl acetate (40 mL), and was then washed with saturated ammonium chloride (40 mL x 4). The organic layer was dried with anhydrous sodium sulfate and concentrated under reduced pressure. The pure compound was acquired in 89% yield as an orange-red powder (84 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm 6.06 (s, 2H), 3.49 (t, *J* = 6.3 Hz, 2H), 3.04 (t, *J* = 8.4 Hz, 2H), 2.52 (s, 6H), 2.43 (s, 6H), 1.92-1.82 (m, 2H).

Compound 30.[9] Compound **27** (0.39 mmol, 154 mg) was dissolved in DMF (3.0 mL), and sodium azide (2.33 mmol, 152 mg) was slowly added to a round-bottom flask. The solution was stirred at 50 °C for 12 h. The reaction mixture was then diluted with ethyl acetate (40 mL), and was washed with saturated ammonium chloride (40 mL x 4). The organic layer was dried with anhydrous sodium sulfate and concentrated under reduced pressure. The pure compound was acquired in 99% yield as an orange-red powder (140 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 6.06 (s, 2H), 3.31 (t, *J* = 6.5 Hz, 2H), 2.96 (t, *J* = 8.0 Hz, 2H), 2.51 (s, 6H), 2.41 (s, 6H), 1.69-1.63 (m, 4H), 1.60-1.56 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 154.2, 145.1, 140.4, 131.6, 121.9, 51.4, 31.6, 28.9, 28.4, 27.6, 16.6, 14.7.

Compound 13a. Compound **28** (0.13 mmol, 39.3 mg) was dissolved in ethanol (2.0 mL). To this solution, copper(II) acetate monohydrate (0.013 mmol, 2.6 mg) was added, followed by sodium ascorbate (0.065 mmol, 12.9 mg) and compound **10** (0.13 mmol, 44.1 mg). The reaction was stirred at rt for 16 h. The solvent was removed under reduced pressure, and was purified via silica gel column, eluted by 2% (v/v) triethylamine in dichloromethane. The pure product was acquired with a 31% yield as an orange-brown solid (26 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 8.57 (dq, *J* = 2.5, 1.0 Hz, 2H), 7.60 (td, *J* = 6.0, 2.0 Hz, 2H), 7.27 (s, 1H), 7.25 (s, 1H), 7.24 (s, 1H), 7.15 (ddd, *J* = 4.0, 1.5, 1.0 Hz, 2H), 6.76 (d, *J* = 9.0 Hz, 2H), 6.67 (d, *J* = 9.5 Hz, 2H), 6.07 (s, 2H), 5.73 (s, 2H), 4.72 (s, 4H), 4.36 (s, 2H), 2.74 (s, 3H), 2.55 (s, 6H), 2.12 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm 159.6, 157.8, 149.8, 146.1, 141.6, 137.0, 132.5, 130.1, 122.2, 121.3, 120.9, 117.1, 114.2, 58.1, 50.7, 45.8, 39.7, 15.8, 15.0; HRMS (ESI+) calculated for $[C_{36}H_{39}B_1F_2N_9]^+$ = 646.3390, found 646.3404.

Compound 13b. Compound **29** (0.253 mmol, 83.7 mg) was dissolved in ethanol (2.0 mL) and 1,4-dioxane (0.2 mL). To this solution, copper(II) acetate monohydrate (0.025 mmol, 5.0 mg) was added, followed by sodium ascorbate (0.126 mmol, 25.0 mg) and compound **10** (0.253 mmol, 86.5 mg). The reaction was stirred at rt for 16 h. The solvent was removed under reduced pressure. The residual was

purified on a silica gel column, eluted by 2% (v/v) triethylamine in dichloromethane. The pure product was acquired with a 38% yield as an orange solid (64 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 8.55 (ddd, *J* = 5.0, 3.0, 0.5 Hz, 2H), 7.55 (td, *J* = 6.0, 2.0 Hz, 2H), 7.31 (s, 1H), 7.26 (d, *J* = 7.5 Hz, 2H), 7.11-7.13 (m, 2H), 6.64-6.71 (m, 4H), 5.99 (s, 2H), 4.72 (s, 4H), 4.47 (s, 2H), 4.42 (t, *J* = 6.5 Hz, 2H), 2.90 (t, *J* = 8.5 Hz, 2H), 2.84 (s, 3H), 2.48 (s, 6H), 2.12 (s, 6H), 2.06-2.10 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm 159.6, 154.8, 149.8, 146.3, 143.9, 141.9, 141.5, 140.4, 137.1, 131.5, 122.3, 121.4, 116.0, 114.6, 58.2, 50.3, 39.7, 32.5, 25.8, 16.4, 14.8; HRMS (ESI+) calculated for $[C_{38}H_{42}B_1F_2N_9]^+$ = 673.3624, found 673.3641.

Compound 13c. Compound **30** (0.110 mmol, 39.0 mg) was dissolved in a mixture of ethanol (2.0 mL) and 1,4-dioxane (0.2 mL). To this solution, copper(II) acetate monohydrate (0.011 mmol, 2.2 mg) was added, followed by sodium ascorbate (0.0540 mmol, 11.0 mg) and compound **10** (0.110 mmol, 37.0 mg). The reaction was stirred at rt for 16 h. The solvent was removed under reduced pressure, and was purified on a silica gel column, eluted with 2% (v/v) triethylamine in dichloromethane. The pure product was acquired with a 59% yield as an orange solid (43 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 8.56 (ddd, *J* = 2.0, 1.5, 1.0 Hz, 2H), 7.59 (td, *J* = 6.0, 1.5 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.23 (s, 1H), 7.14 (ddd, *J* = 4.0, 1.5, 1.0 Hz, 2H), 6.71-6.69 (m, 2H), 6.67-6.64 (m, 2H), 6.04 (s, 2H), 4.74 (s, 4H), 4.46 (s, 2H), 4.29 (t, *J* = 7.0 Hz, 2H), 2.90 (t, *J* = 8.5 Hz, 2H), 2.81 (s, 3H), 2.50 (s, 6H), 2.36 (s, 6H), 1.91 (quint, *J* = 7.5 Hz, 2H), 1.68-1.59 (m, 4H), 1.46 (quint, *J* = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm 159.6, 154.1, 149.7, 145.8, 142.1, 141.4, 140.3, 136.8, 131.47, 122.1, 121.8, 121.6, 1212, 116.0, 114.4, 58.1, 50.1, 50.0, 39.3, 31.3, 30.2, 28.2, 27.1, 16.5, 14.6; HRMS (ESI+) calculated for $[C_{40}H_{45}B_1F_2N_9]^+$ = 701.3937, found 701.3921.

(3) Spectroscopic studies

DMSO stock solutions (1 mL) of compounds **4**, **5**, **6**, **11**, **12**, **13a-c** were prepared and stored frozen. Prior usage, the solutions were allowed to thaw at rt. Absorption and emission spectra were recorded on a Varian Cary100 UV-VIS spectrophotometer and Varian Cary Eclipse Fluorometer, respectively. Fluorescence quantum yield values were reported relative to quinine bisulphate (ϕ(1N H_2SO_4) = 0.54)[11] or 4-methyl-7-diethylaminocoumarin (ϕ(EtOH) = 0.73).[12] Zinc(II) titration experiments were conducted as previously described.[13]

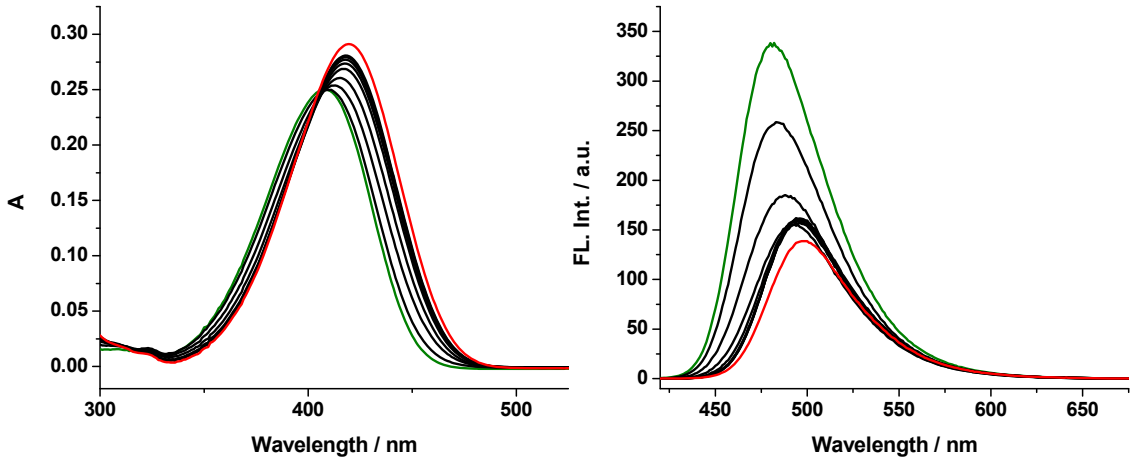


Fig. S1 Left. Absorption spectra of **3** (8.0 μM) in the presence of $Zn(ClO_4)_2$ (0 – 26 μM) in CH_3CN. Right. Fluorescence spectra of **3** (8.0 μM) in the presence of $Zn(ClO_4)_2$ (0 – 14 μM) in CH_3CN. The initial and final spectra of each titration experiment are coded green and red, respectively.

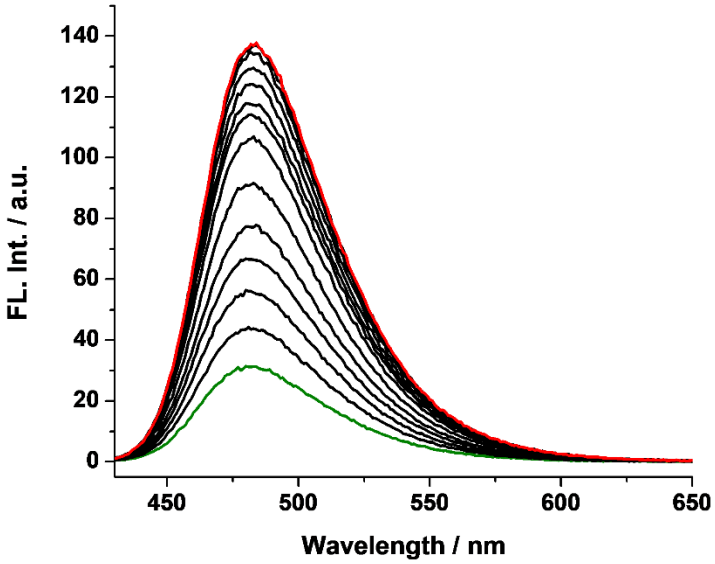


Fig. S2 Fluorescence spectra of **5** (3.0 μM, λ_{ex} = 410 nm) in the presence of $Zn(ClO_4)_2$ (0 – 6.4 μM) in acetonitrile. The initial and final spectra of each titration experiment are coded green and red, respectively.

For metal ion selectivity studies of compounds **6** and **11**, an aqueous buffer containing HEPES (25 mM) and NaCl (25 mM) at pH = 7.3 was first prepared. This buffer was used to prepare a 1:1 v/v HEPES:CH_3CN mixed solvent. Using the 1:1 mixed solvent, stock solutions of the following metal ions in the form of the perchlorate salts were prepared: Na(I), K(I), Mg(II), Ca(II), Mn(II), Fe(II), Cd(II) and Cu(II). Compounds **6** and **11** were stored frozen as DMSO stock solutions (1 mM). A working solution was prepared by diluting appropriate volumes of compound **6** or **11** and a metal ion stock solution to a volume of 1 mL in 1:1 v/v HEPES:CH_3CN mixed solvent. The final concentrations were: 10 µM dye and 1 mM metal ion for Na(I), K(I), Mg(II) and Ca(II), and 50 µM for Mn(II), Fe(II), Cd(II) and Cu(II). The emission spectra of the working solutions were recorded. After that, 50 µM of $Zn(ClO_4)_2$ was added to the working solution and the emission spectrum was reacquired.

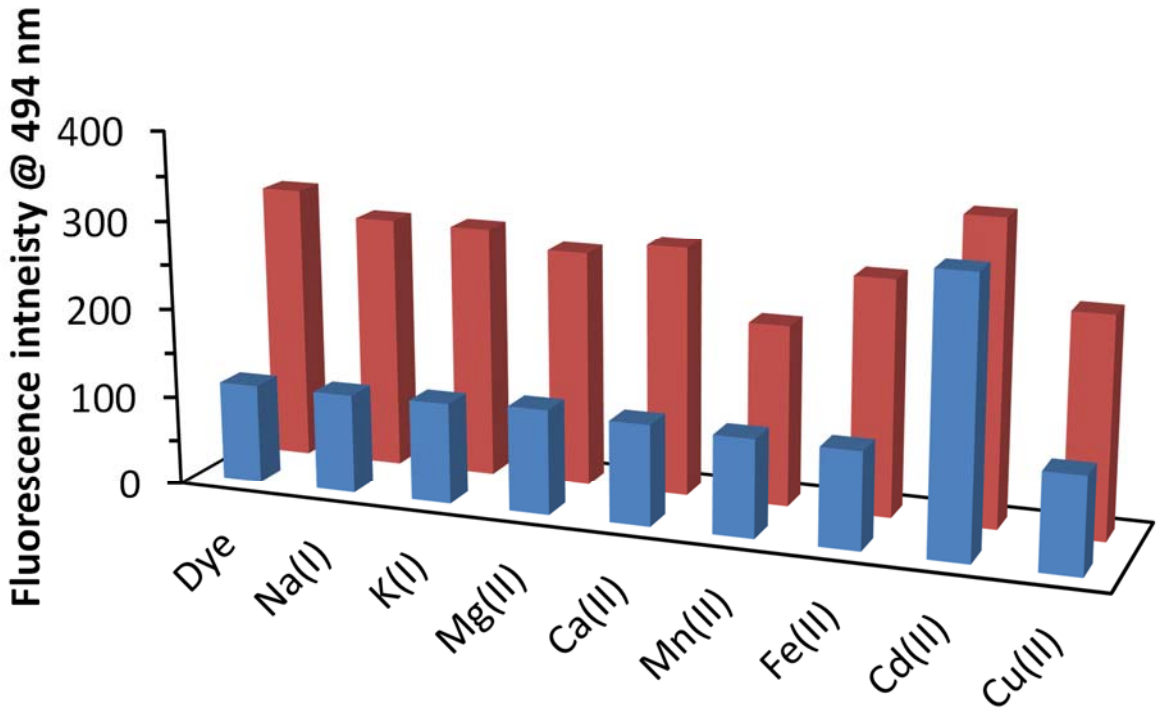


Fig. S3 Fluorescence spectroscopic responses of compound **6** (10 µM, λ_{ex} = 405 nm) to various metal ions in HEPES buffer solution at pH 7.3 (HEPES 25 mM, NaCl 25 mM). Blue bars represent the fluorescence intensity at 494 nm in the presence of various metal ions (perchlorate salts). Metal ion concentrations of Na(I), Ca(II), Mg(II) were 1 mM, and for other ions 50 µM. Orange bars represent the intensity at 494 nm following the addition of $ZnCl_2$ (50 µM).

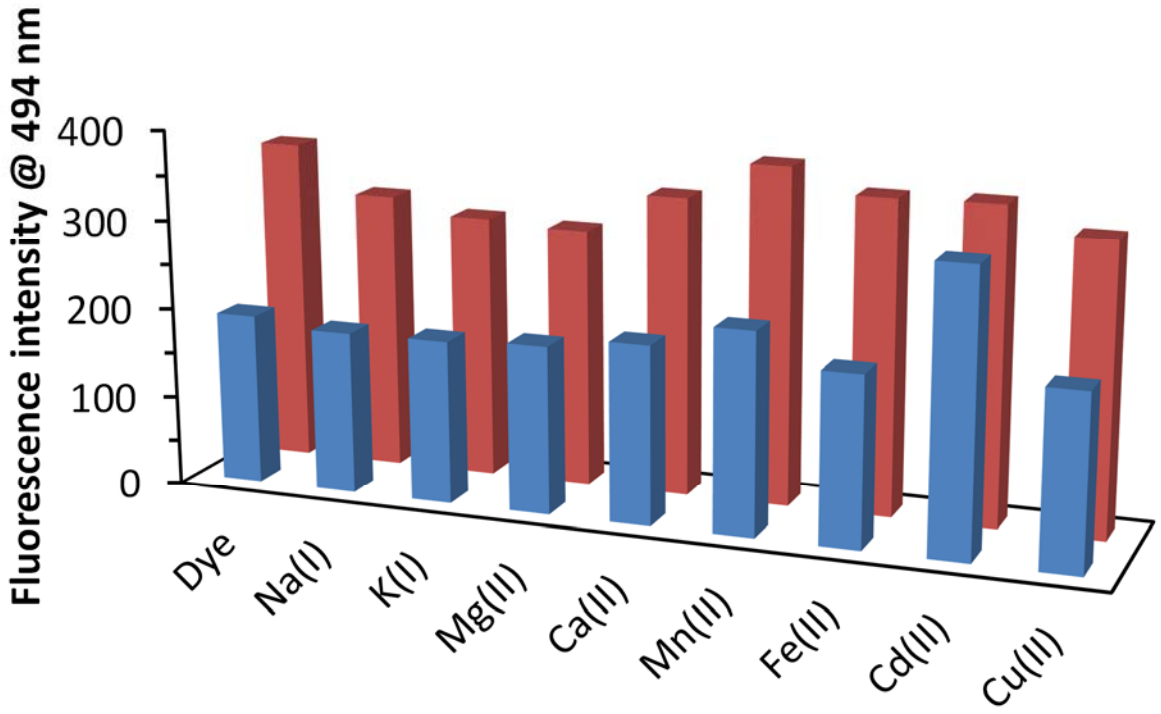


Fig. S4 Fluorescence spectroscopic responses of compound **11** (10 μM, λ_{ex} = 405 nm) to various metal ions in HEPES buffer solution at pH 7.3 (HEPES 25 mM, NaCl 25 mM). Blue bars represent the fluorescence intensity at 494 nm in the presence of various metal ions (perchlorate salts). Metal ion concentrations of Na(I), Ca(II), Mg(II) were 1 mM, and for other ions 50 μM. Orange bars represent the intensity at 494 nm following the addition of $ZnCl_2$ (50 μM).

(4) Cyclic voltammetry

The cyclic voltammograms were acquired in CH_3CN (spectroscopic grade) containing Bu_4NPF_6 (100 mM) as supporting electrolyte using an electrochemical analyzer. The data were collected at a concentration of 1.0 mM in a single cell with a glassy carbon working electrode, a Pt wire counter electrode, and a Ag/AgCl reference electrode. The cyclic voltammograms were collected at a scan rate of 100 mV/s.

(5) Cell culture and fluorescence microscopy

In an incubator at 37 °C, 5% CO_2 and 95% humidity, a HeLa S3 culture was maintained in a 75-cm^2 culture flask using RPMI supplemented with 11% fetal bovine serum and 1x penicillin, streptomycin and amphotericin B as the culture medium.

HeLa cells were plated on Bioptechs Delta T4 dishes the night before the imaging experiment and incubated at 37 °C, 5% CO_2, and 95% humidity in an incubator. On the day of the experiment, the media was aspirated and the cells washed with 1 mL of fresh media, and then incubated for 30 min in 1 mL of media containing a few micromolar of a dye. After incubation, the dye-containing media was aspirated, the cells were rinsed twice with 1 mL of fresh media, before 1 mL of fresh media containing either 50 µM $ZnCl_2$ and 5 µM sodium pyrithione or just 5 µM pyrithione was added. The dish was mounted on the stage of the microscope and imaged. Imaging was performed on an Olympus FluoView FV1000 Laser Scanning Confocal Microscope. A 60x objective and a 405-nm diode or a 488-nm argon-ion laser were used.

(6) Copies of ^{1}H and ^{13}C NMRs of synthesized compounds

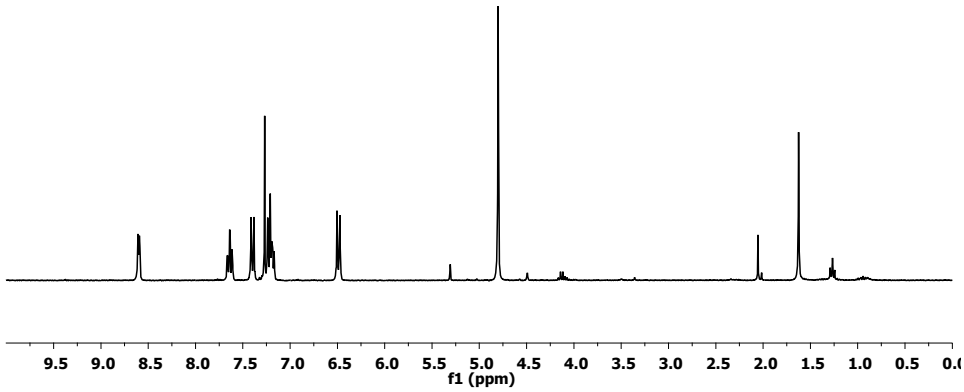


Fig. S5 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **14**.

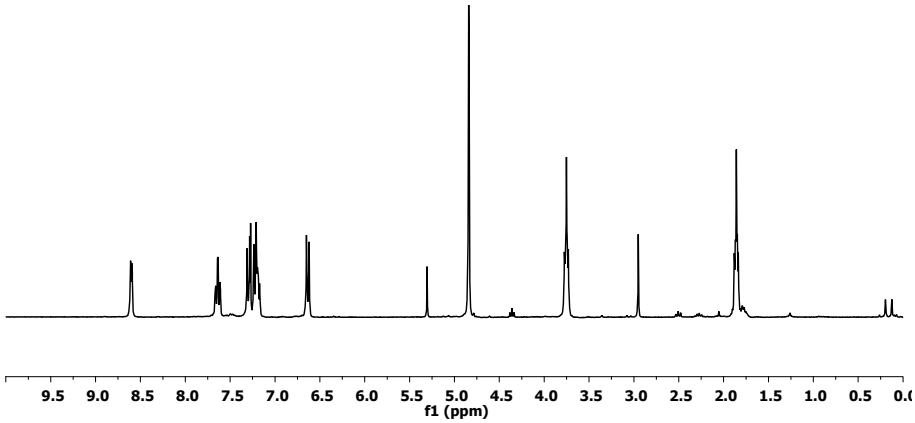


Fig. S6 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **15**.

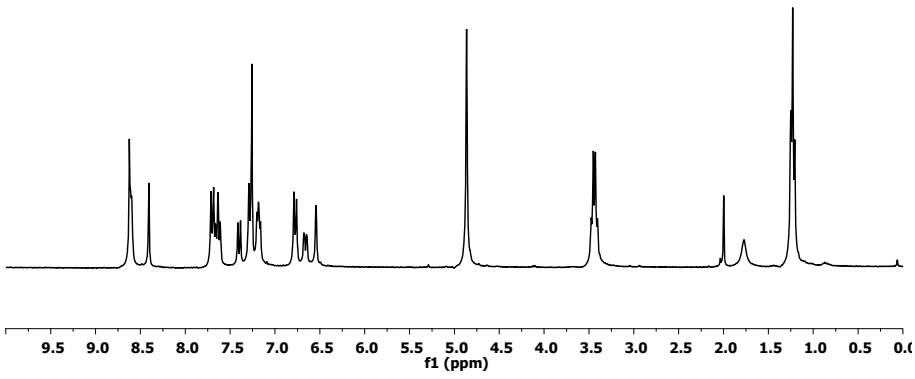


Fig. S7 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **4**.

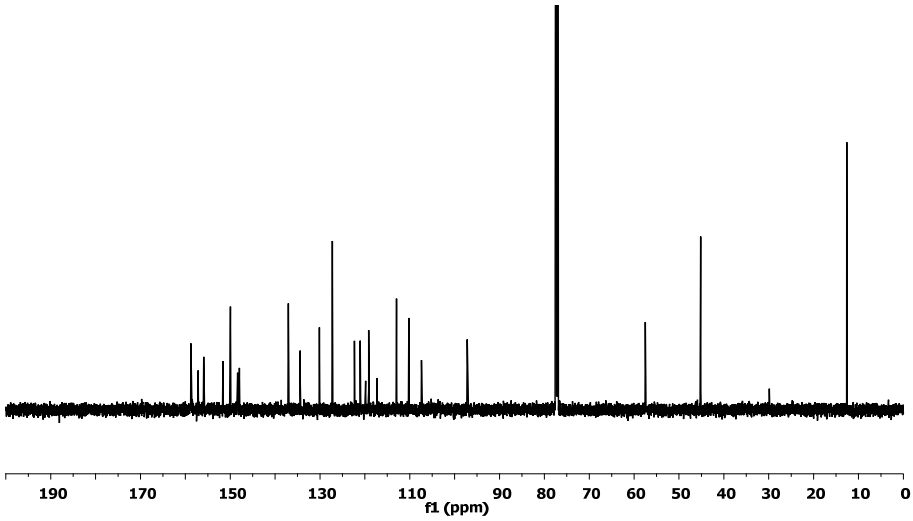


Fig. S8 ^{13}C NMR (150 MHz, $CDCl_3$) of compound **4**.

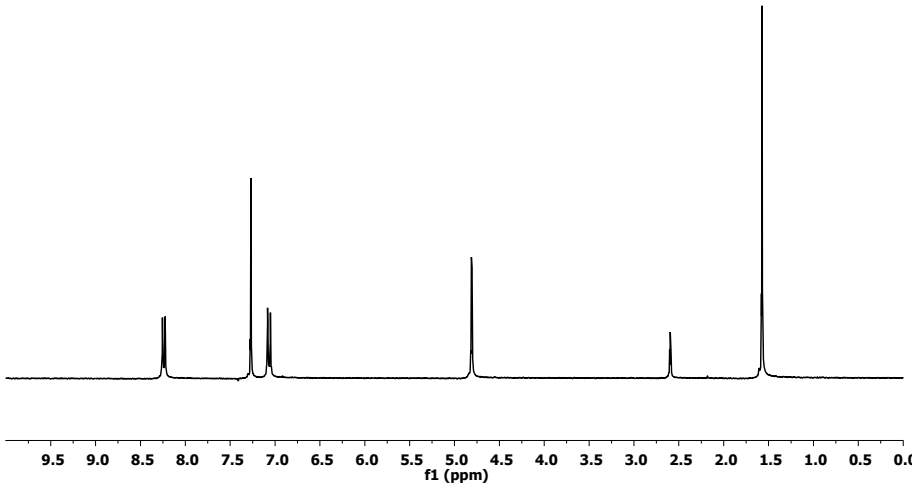


Fig. S9 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **16**.

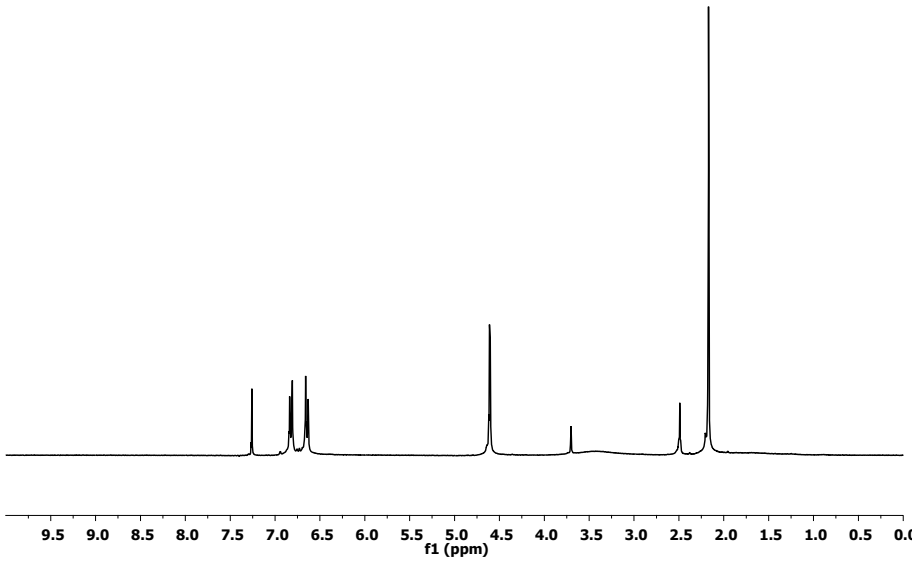


Fig. S10 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **17**.

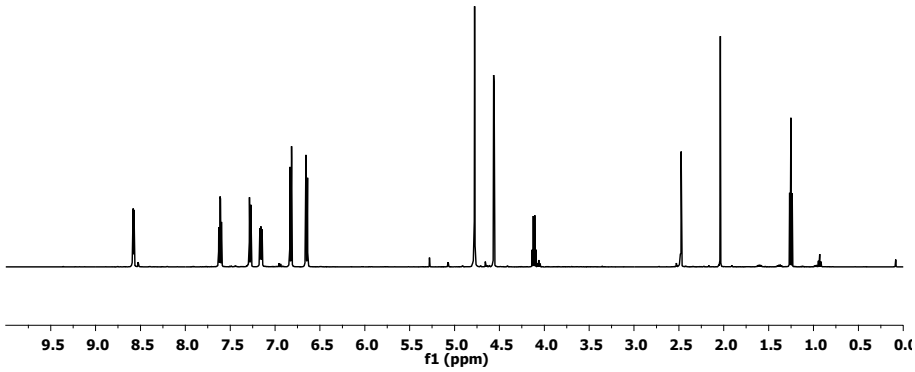


Fig. S11 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **18**.

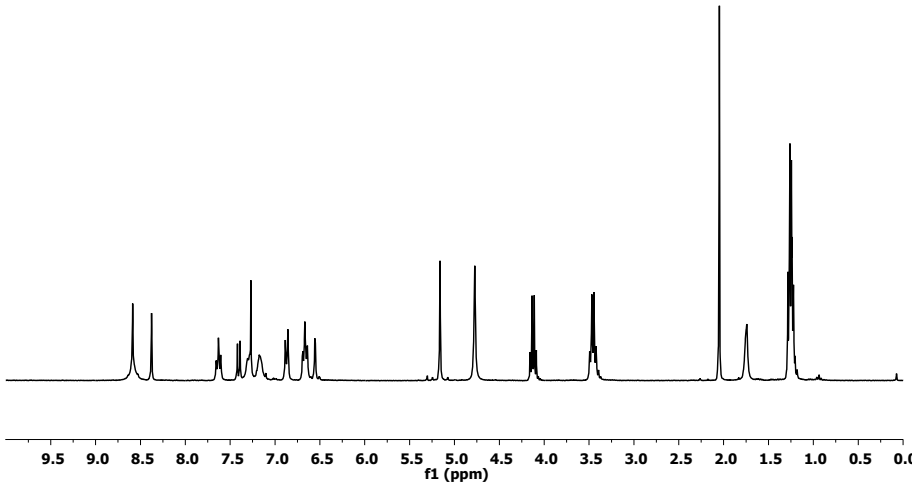


Fig. S12 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **5**.

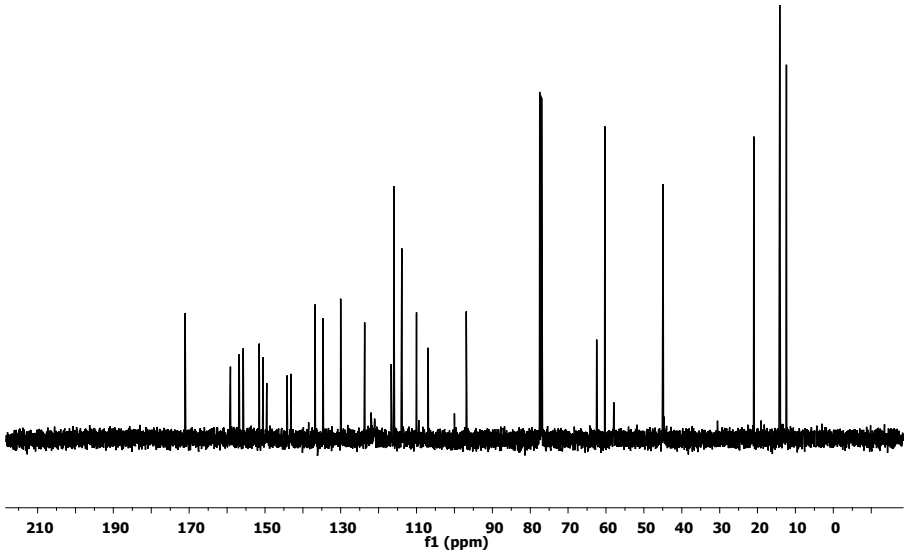


Fig. S13 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **5**.

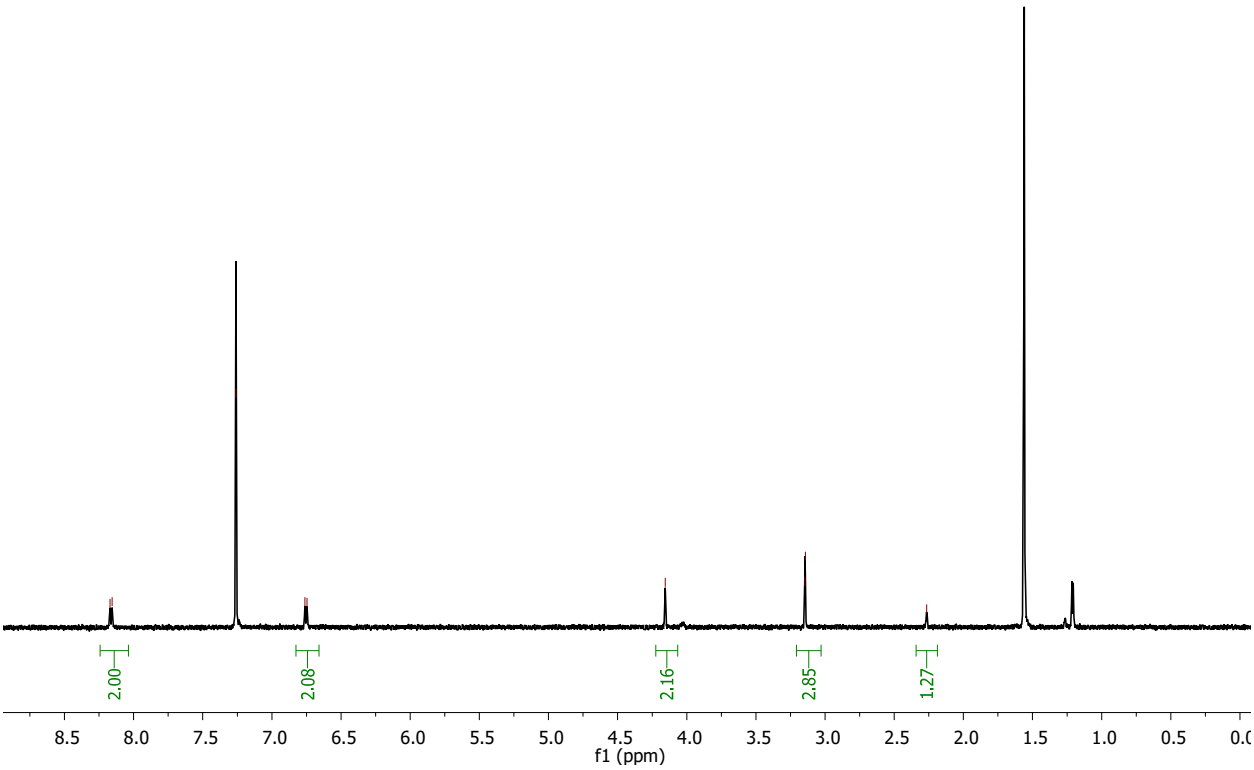


Fig. S14 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **7**.

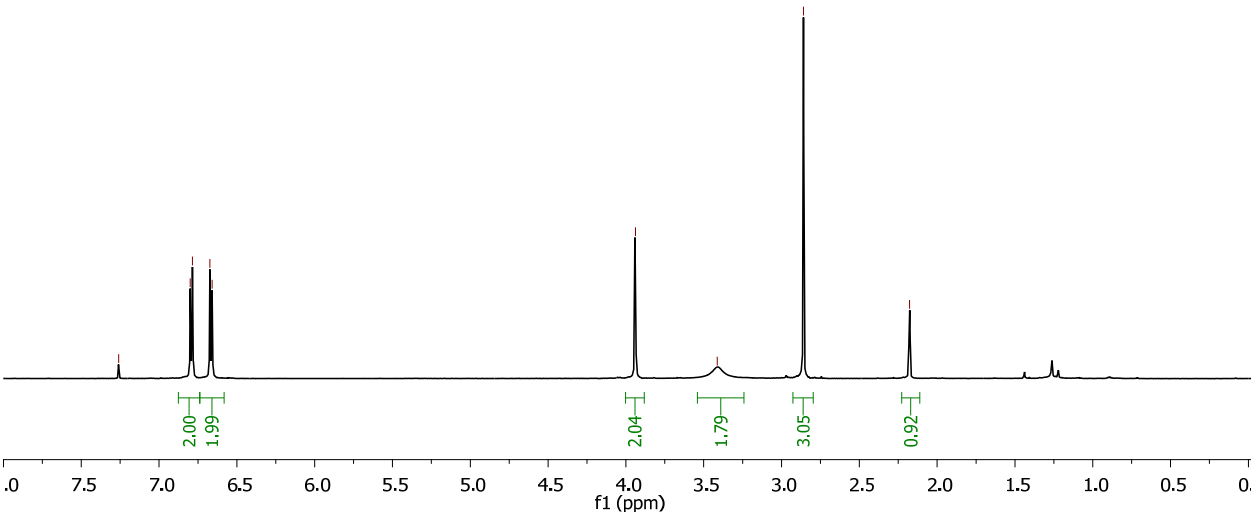


Fig. S15 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **8**.

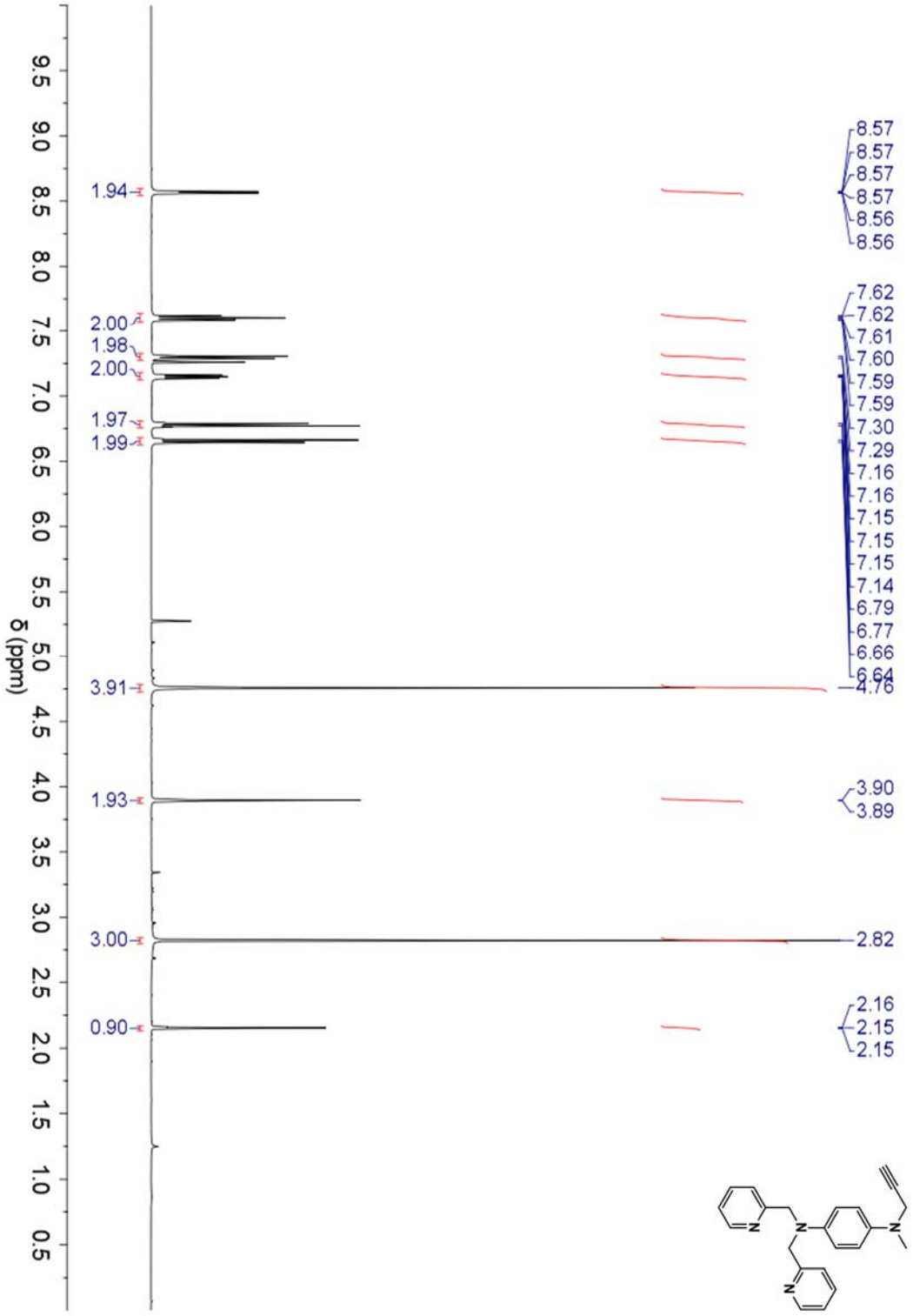


Fig. S16 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **9**.

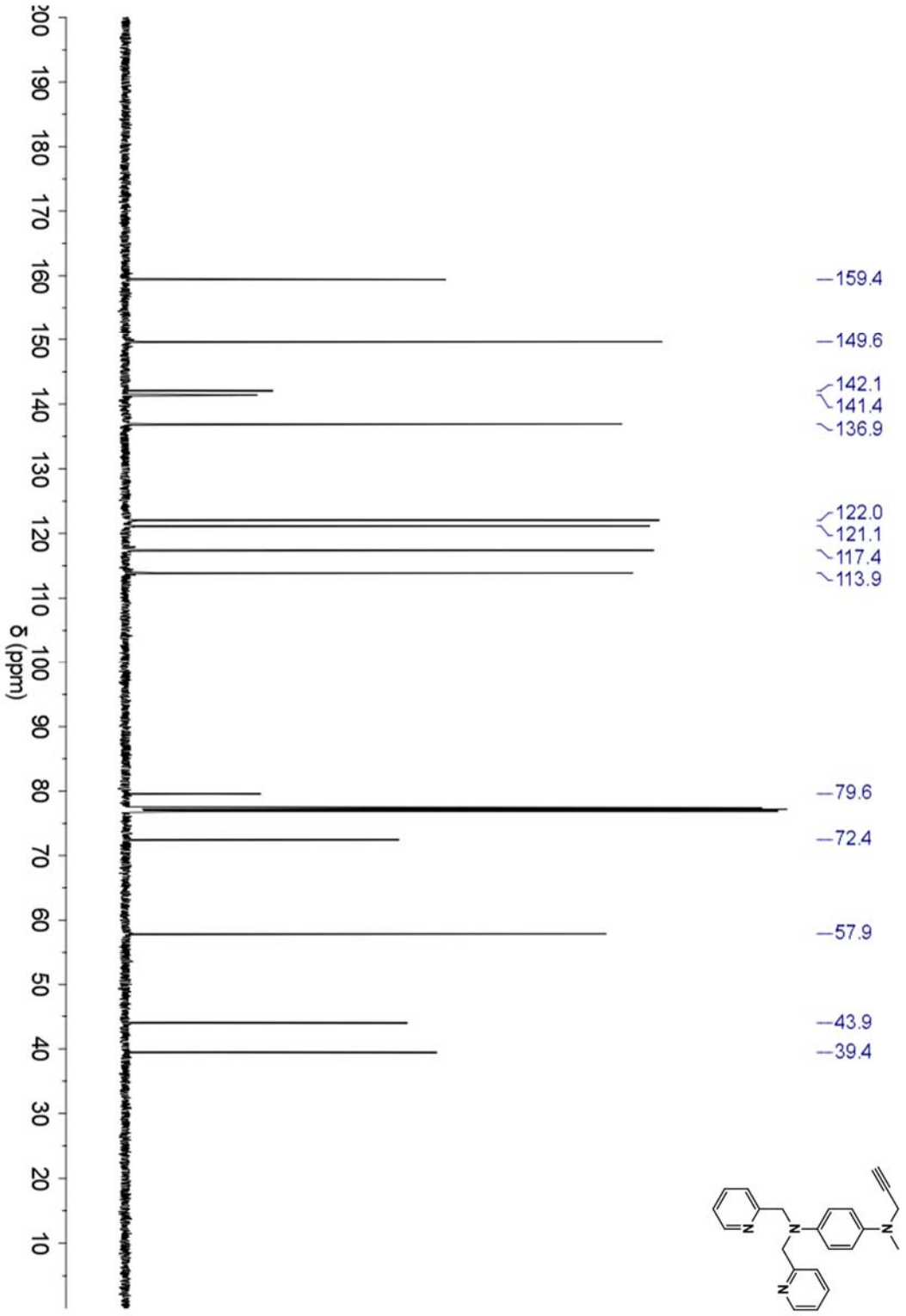


Fig. S17 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **9**.

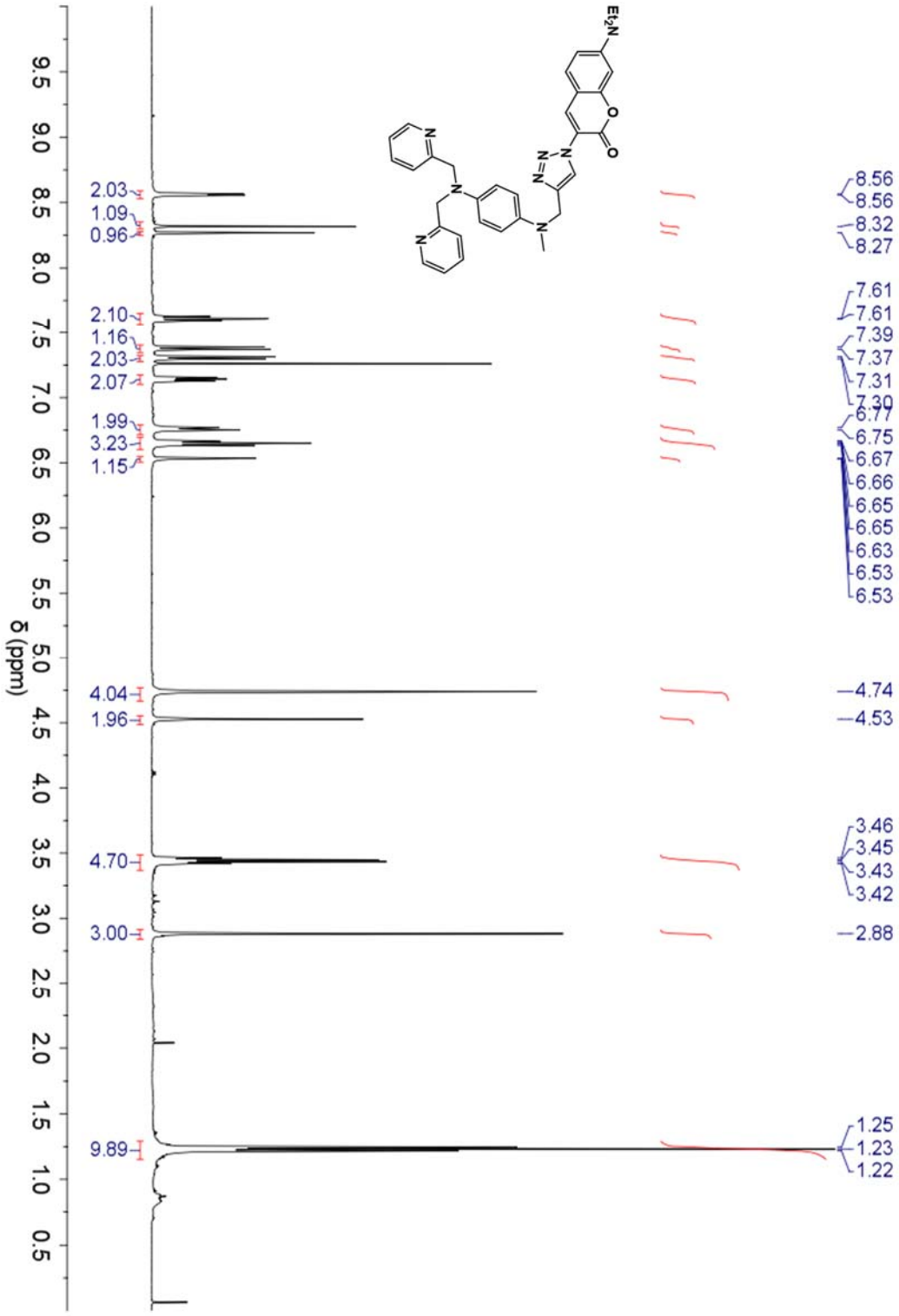


Fig. S18 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **6**.

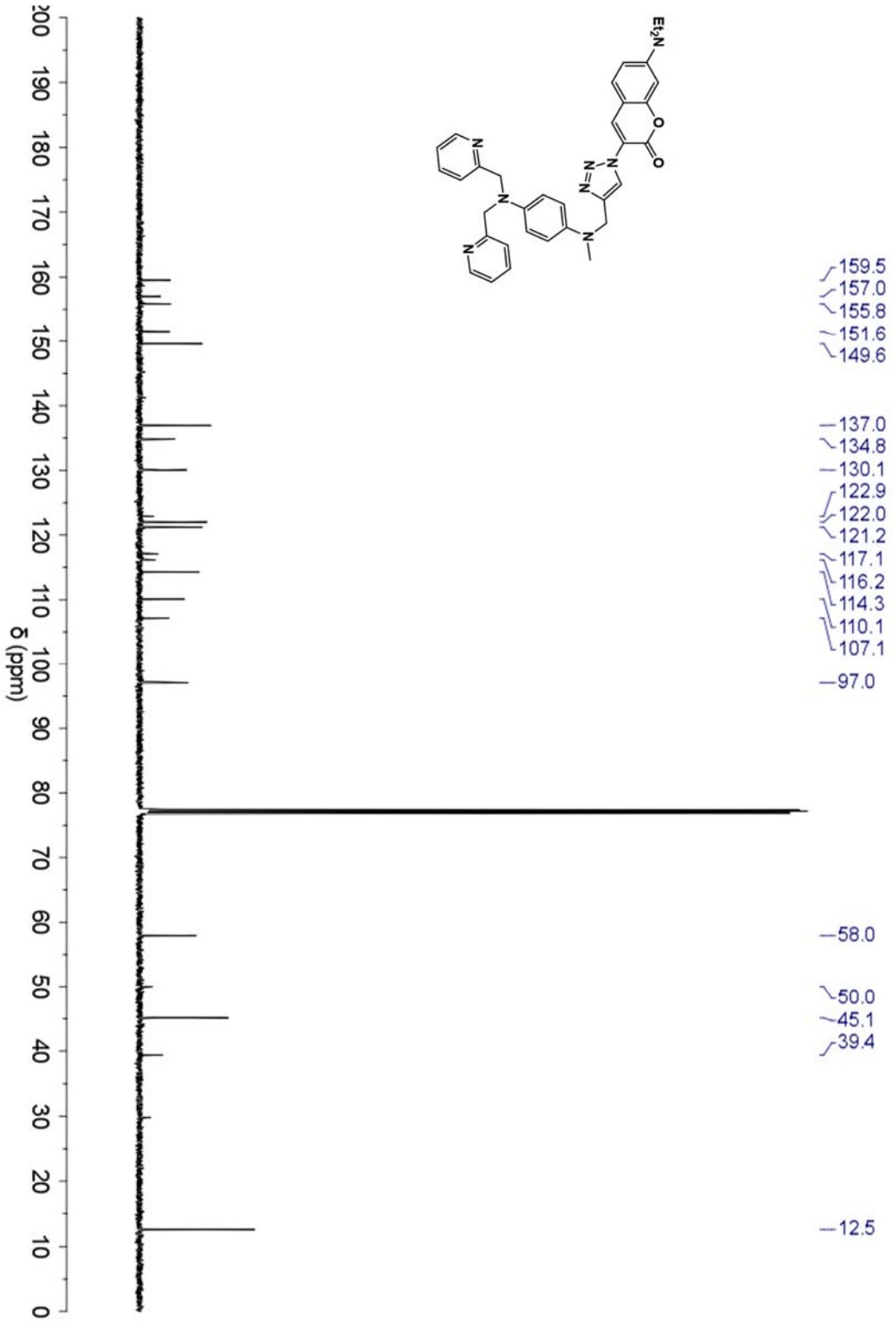


Fig. S19 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **6**.

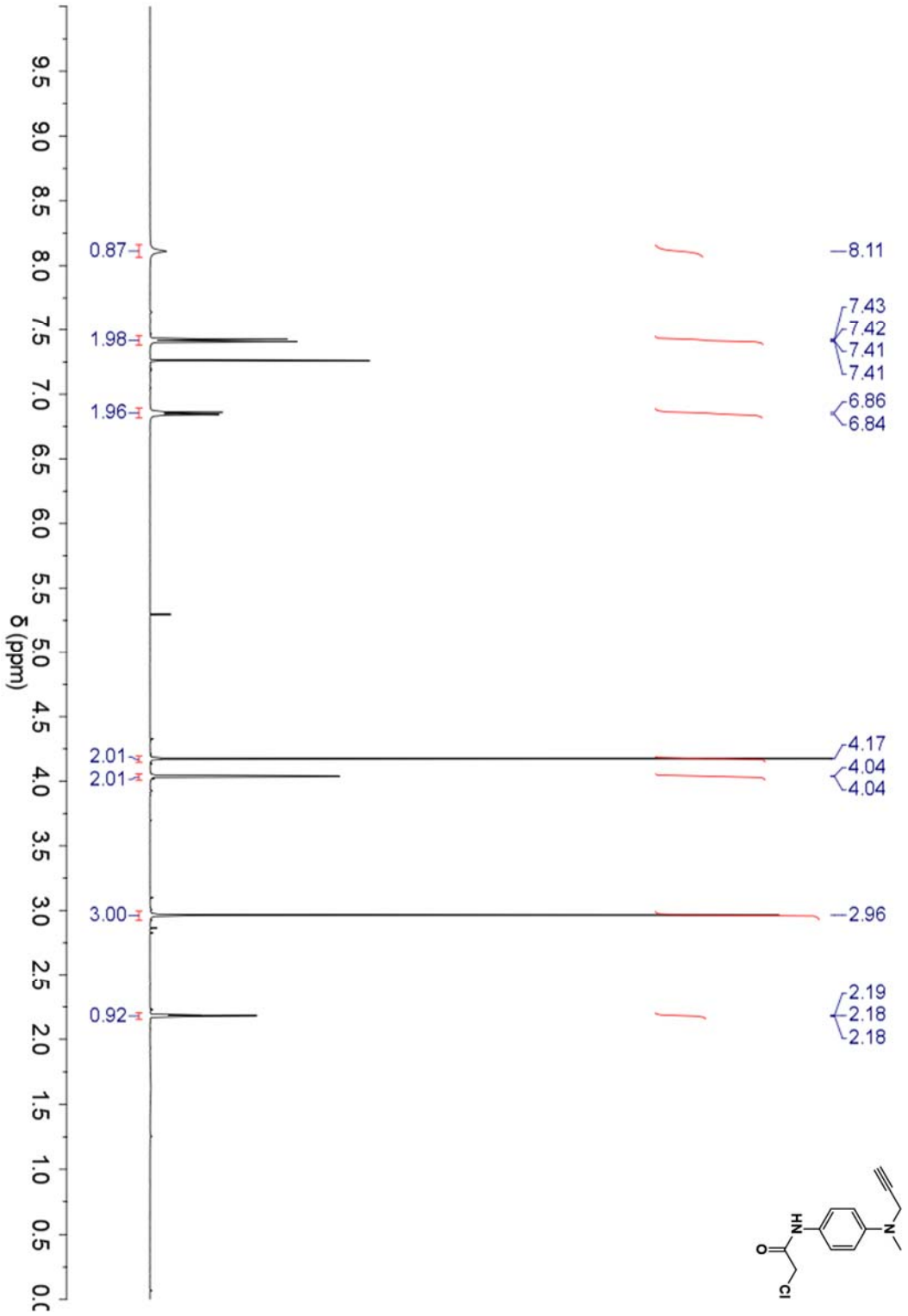


Fig. S20 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **19**.

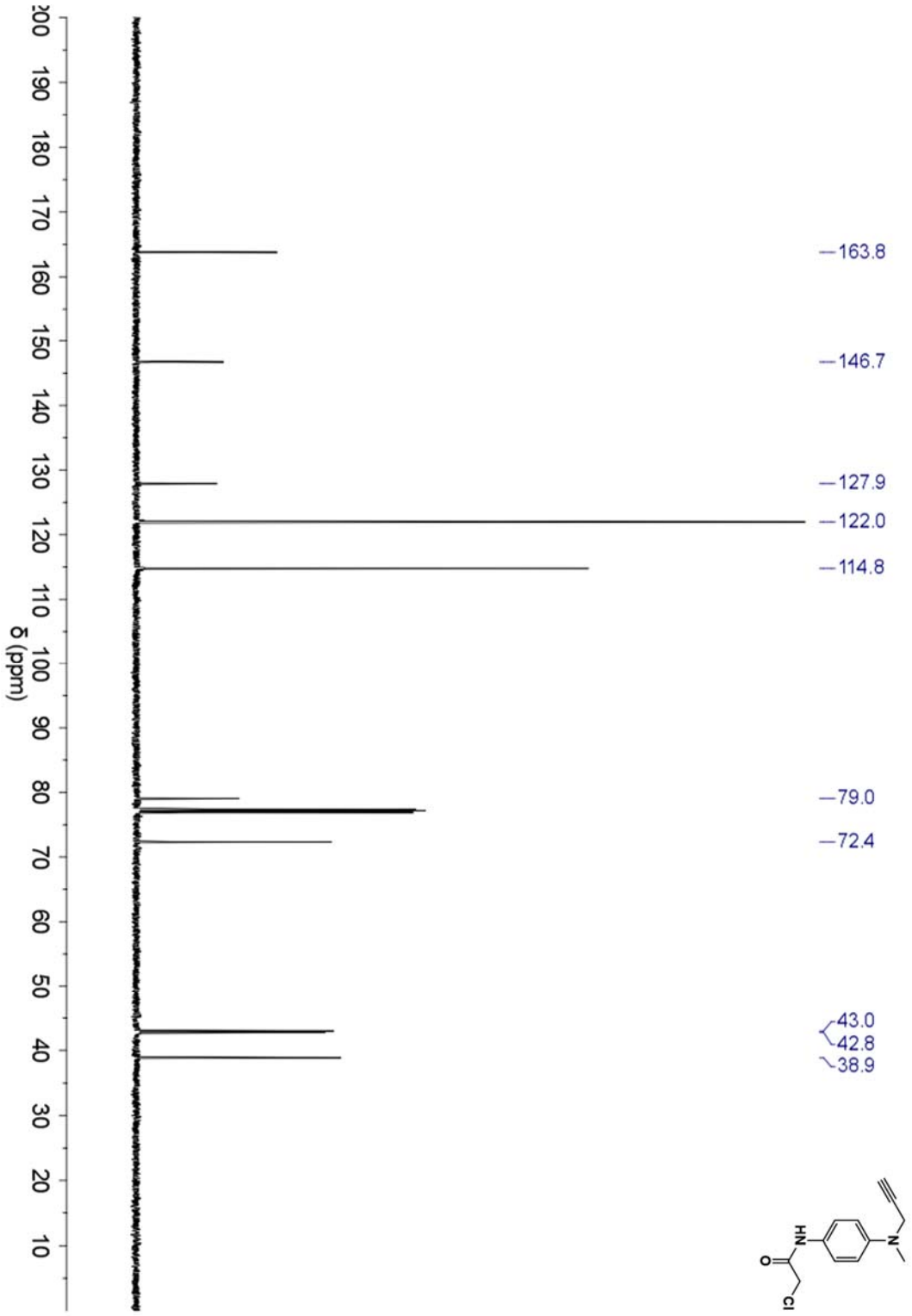


Fig. S21 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **19**.

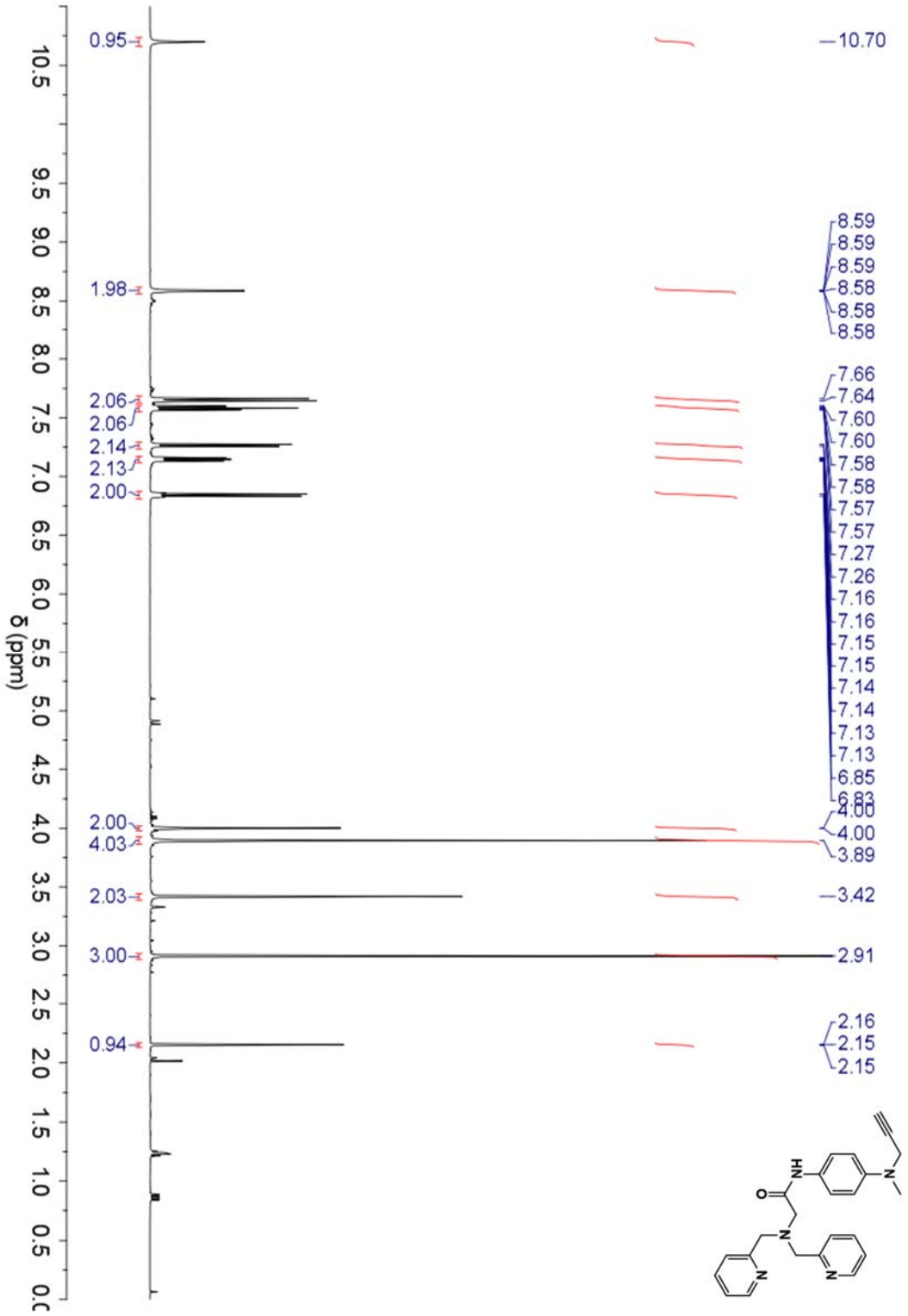


Fig. S22 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **20**.

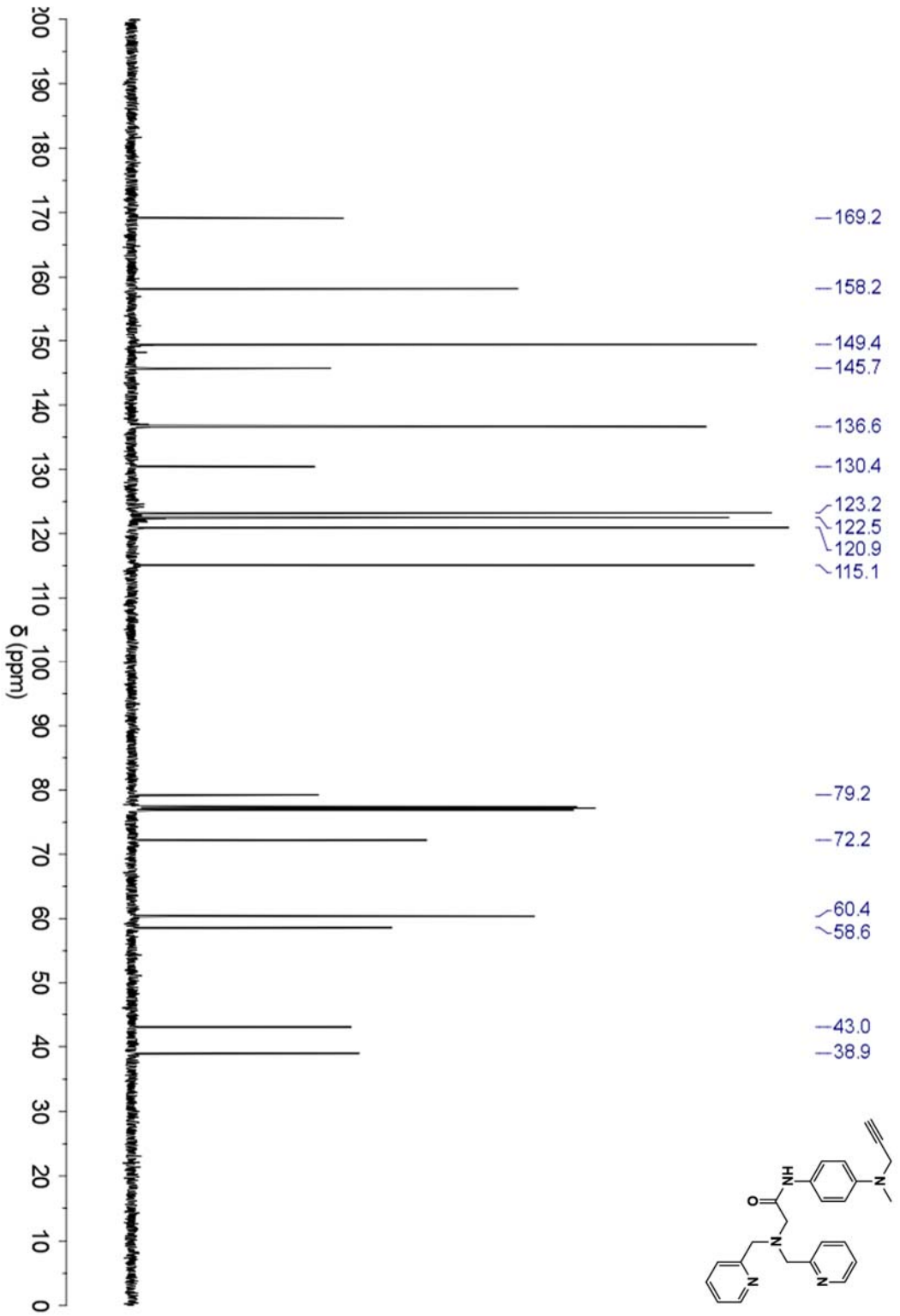


Fig. S23 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **20**.

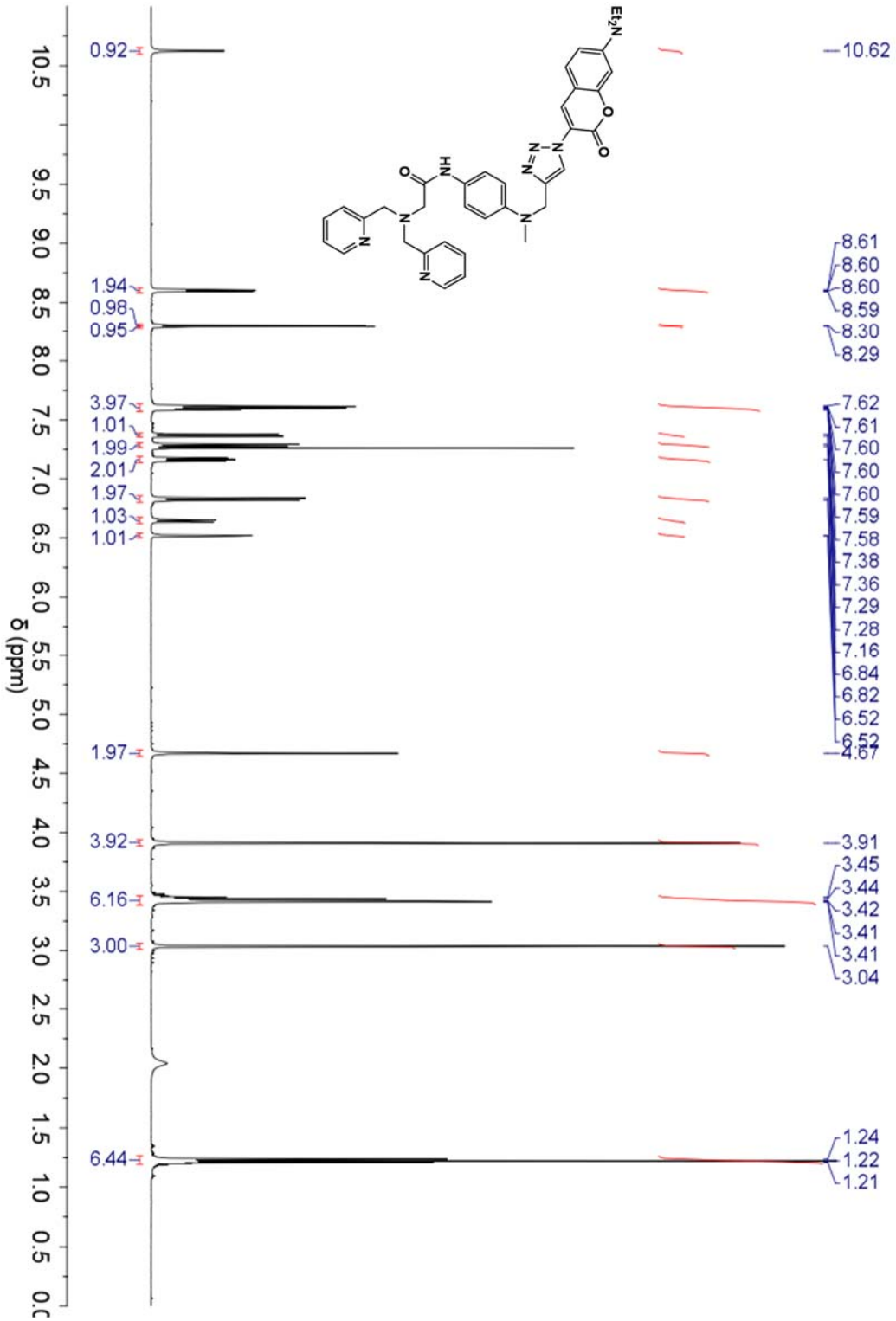


Fig. S24 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **11**.

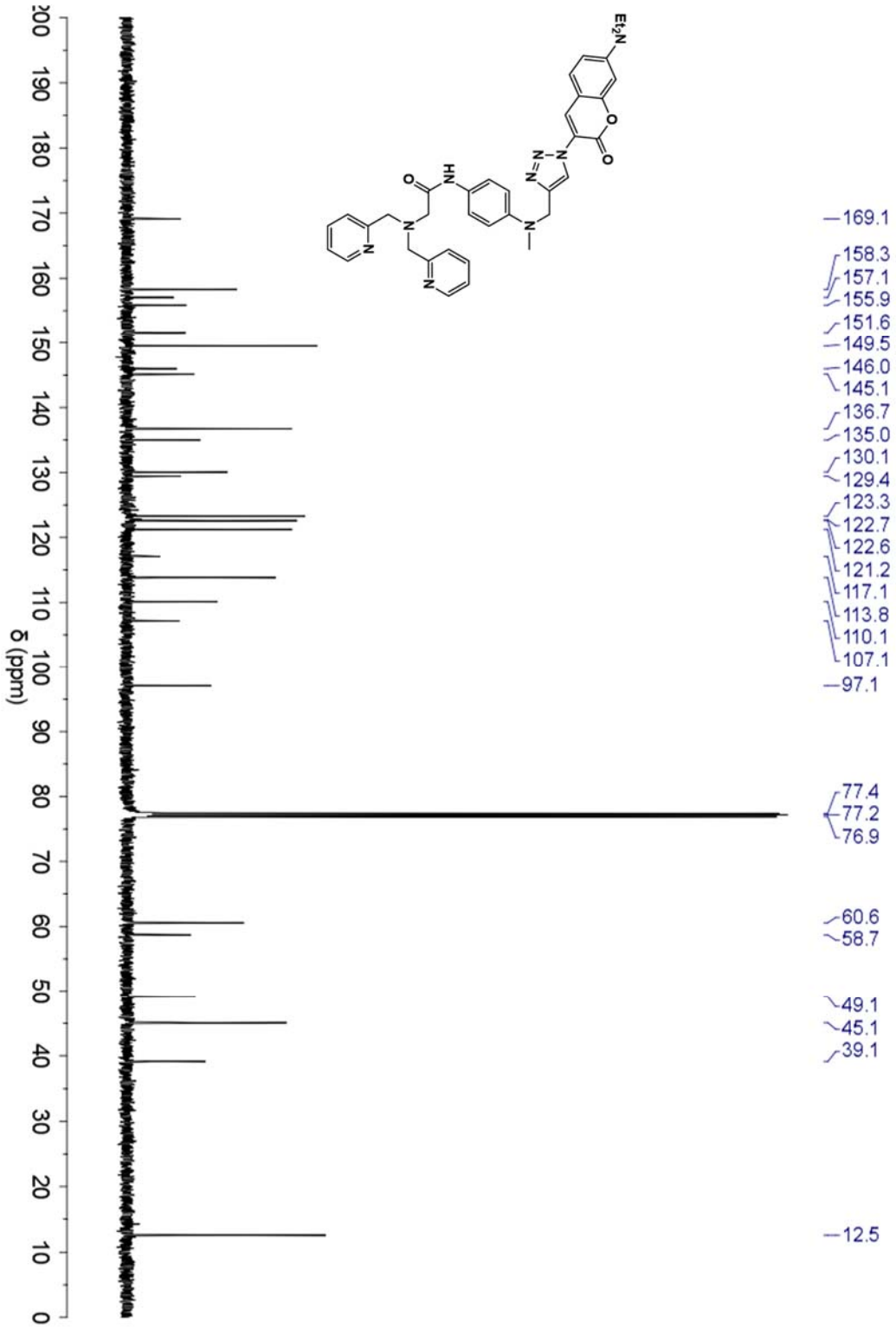


Fig. S25 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **11**.

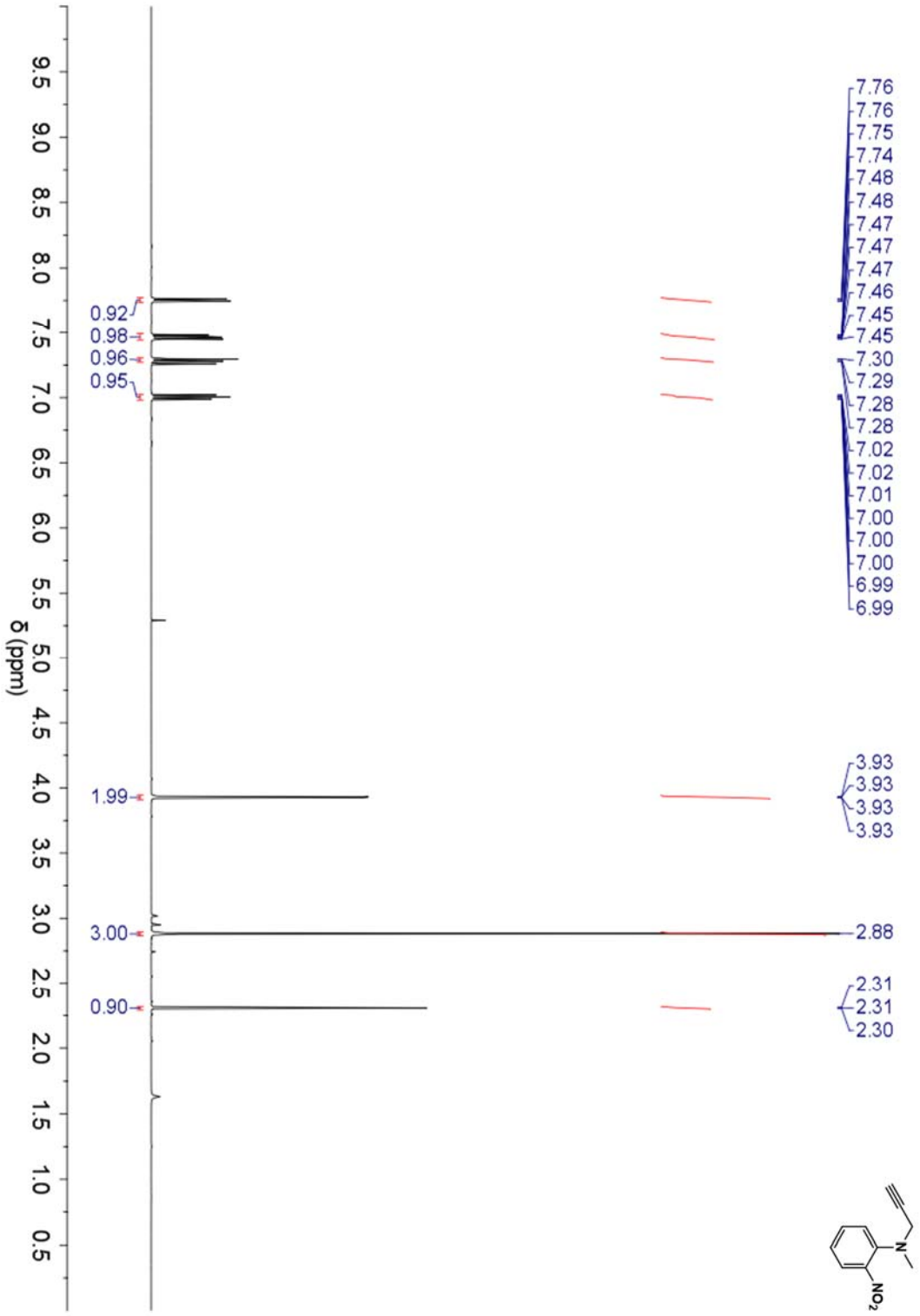


Fig. S26 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **21**.

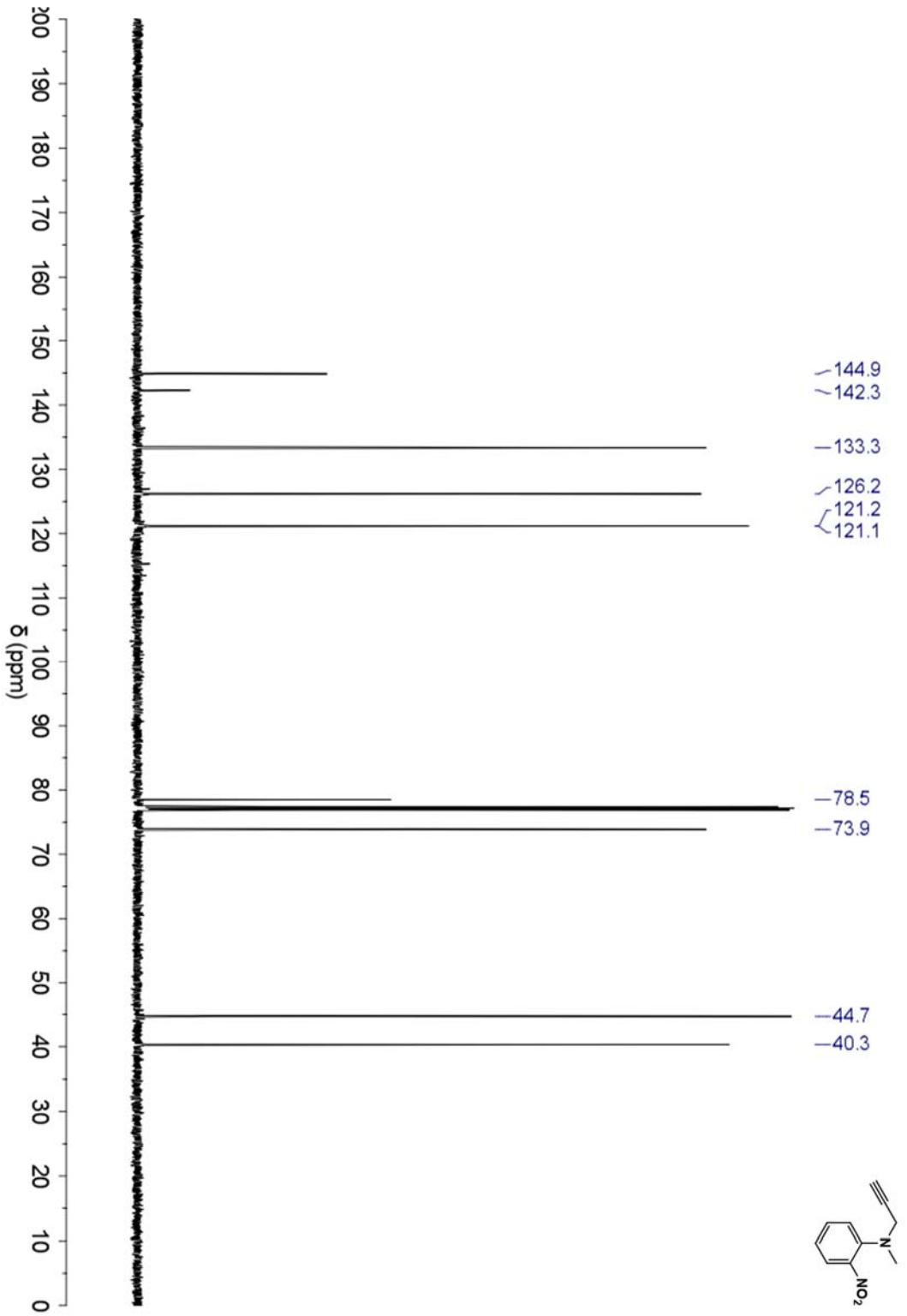


Fig. S27 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **21**.

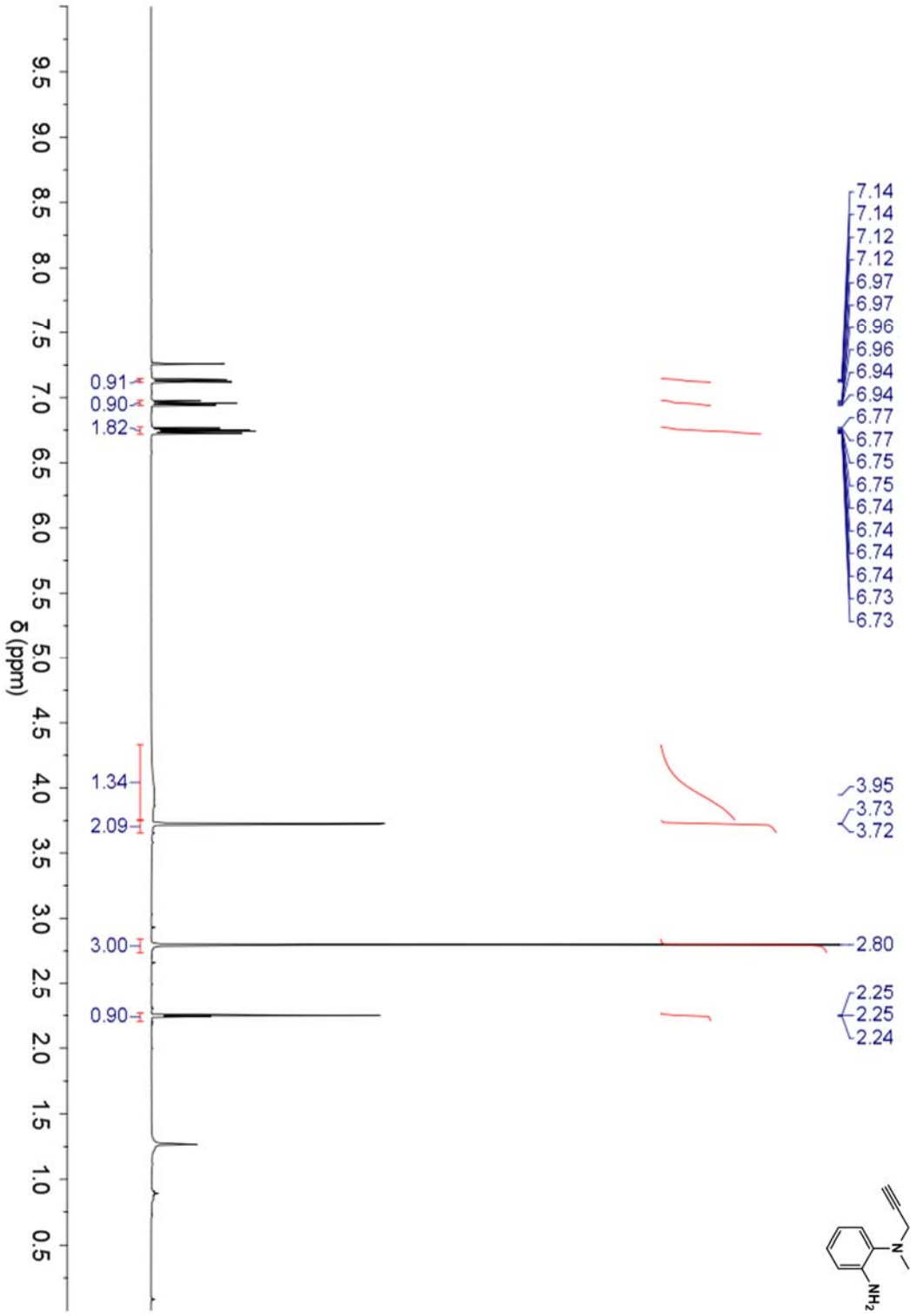


Fig. S28 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **22**.

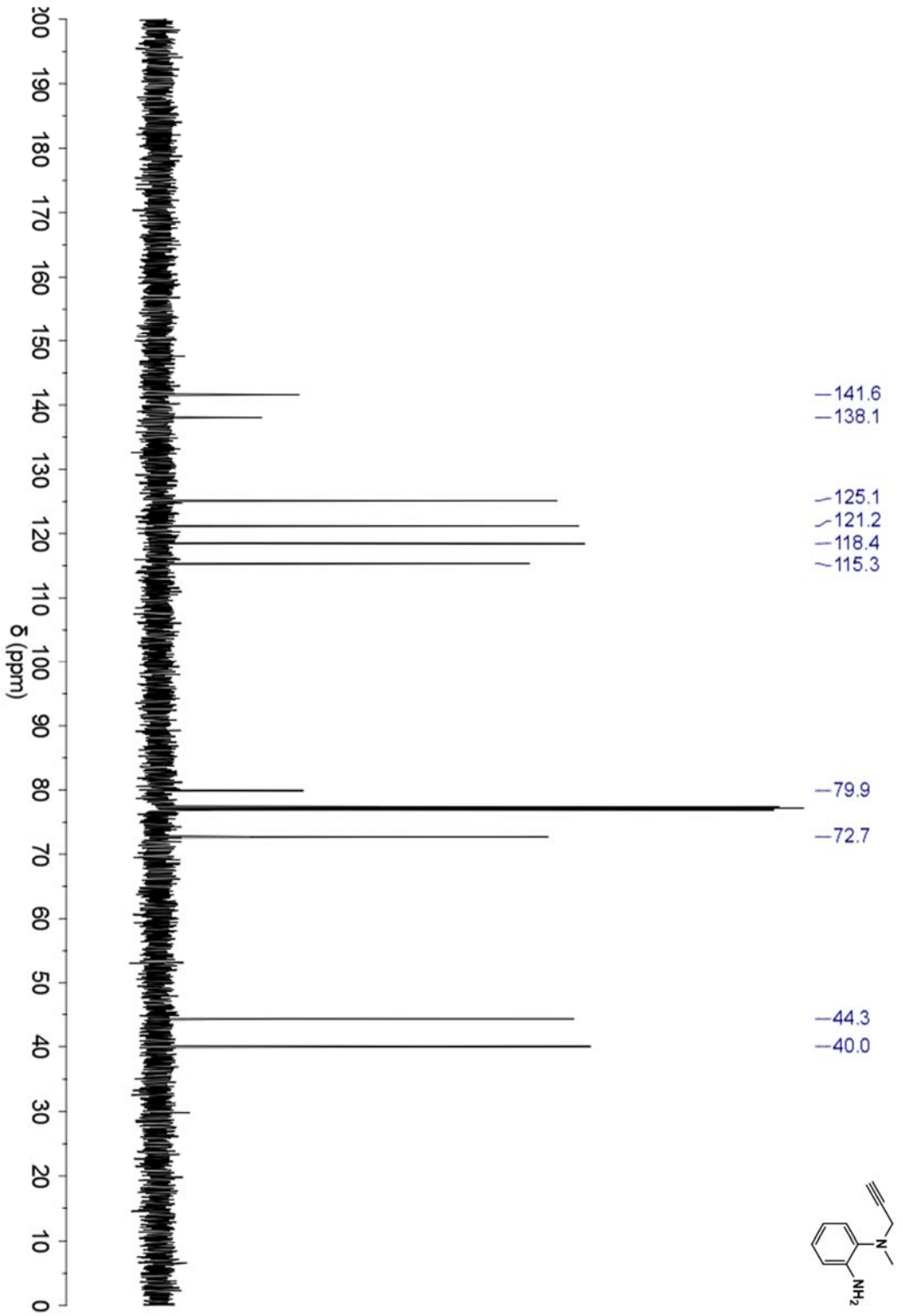


Fig. S29 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **22**.

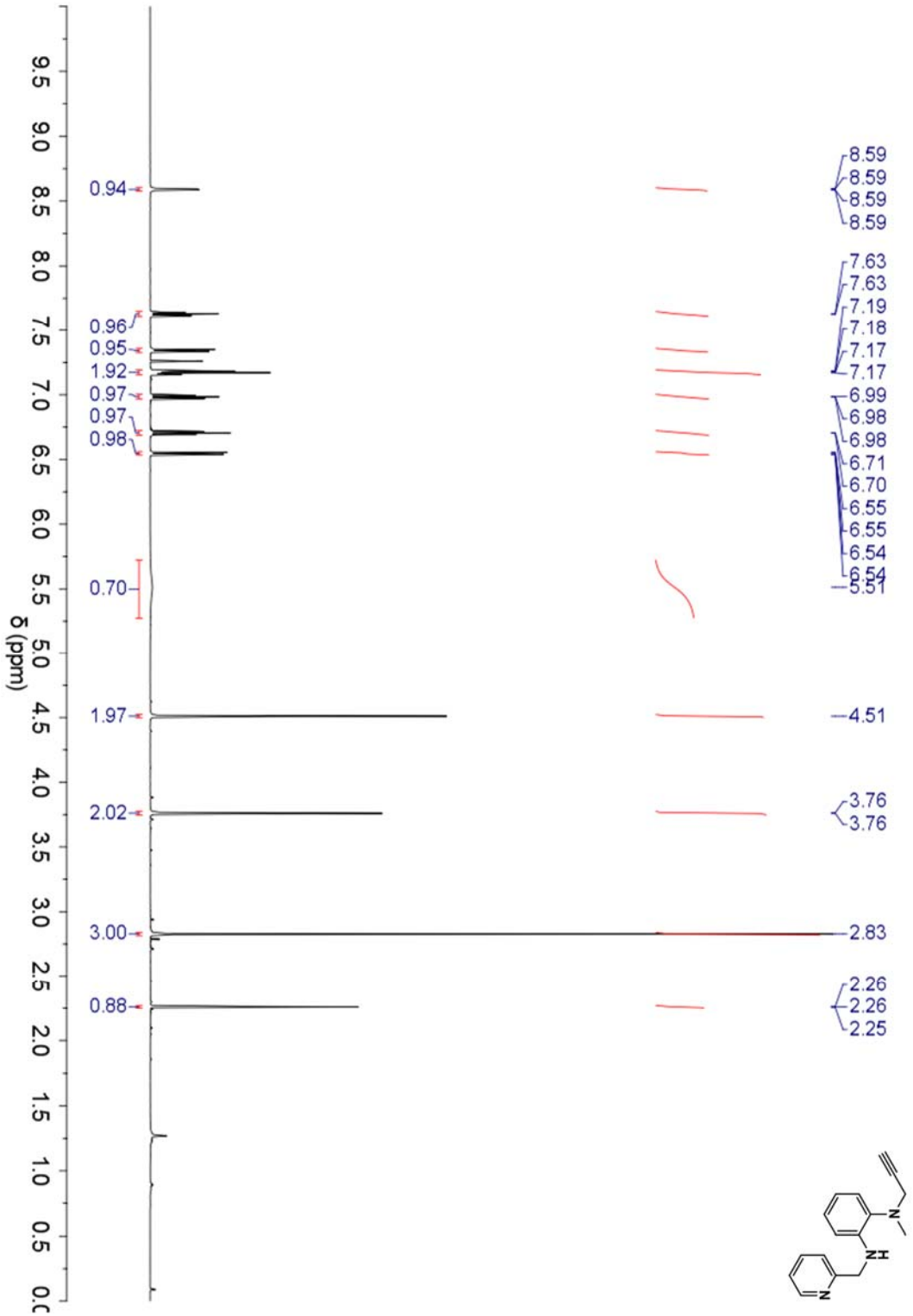


Fig. S30 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **23**.

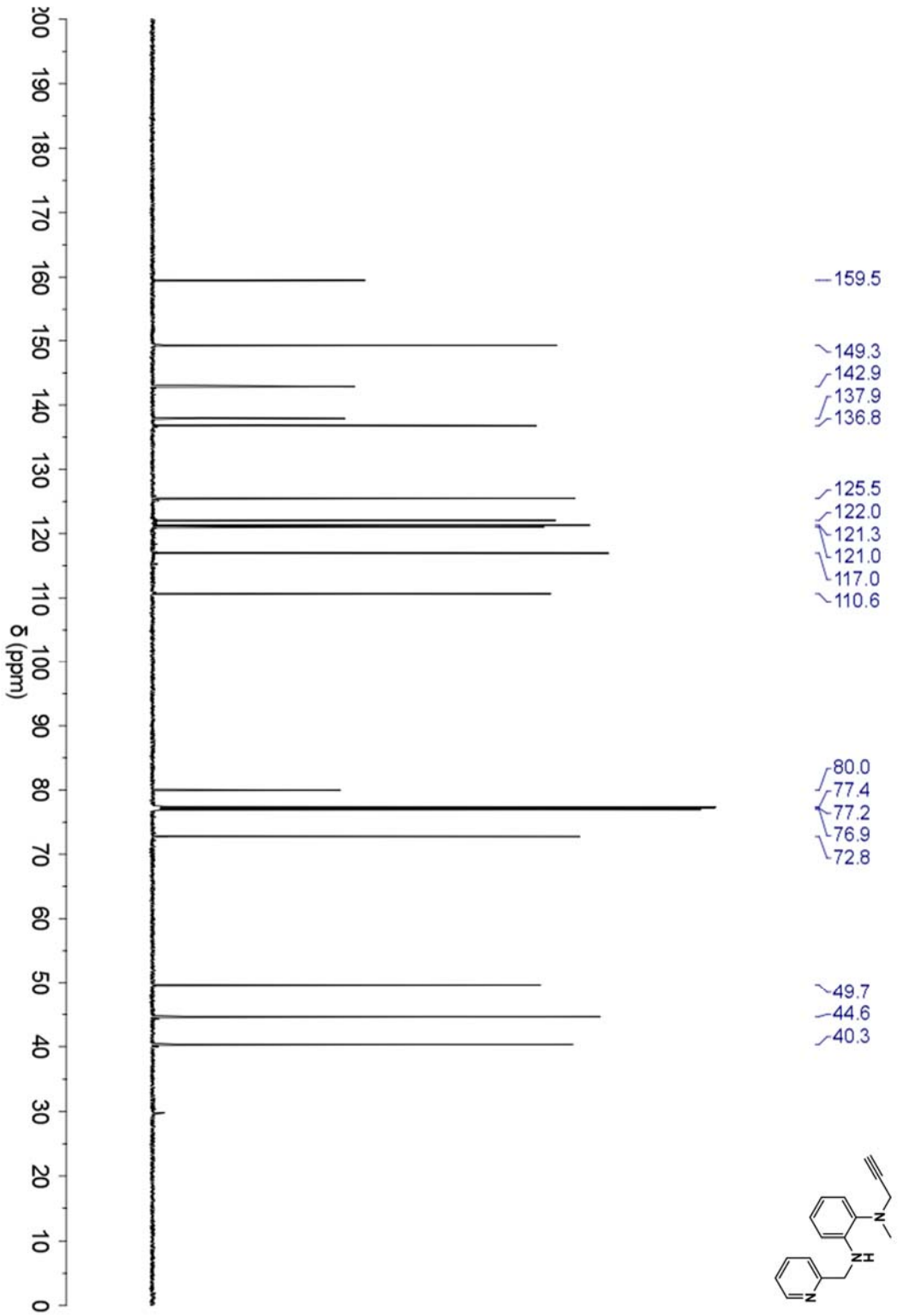


Fig. S31 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **23**.

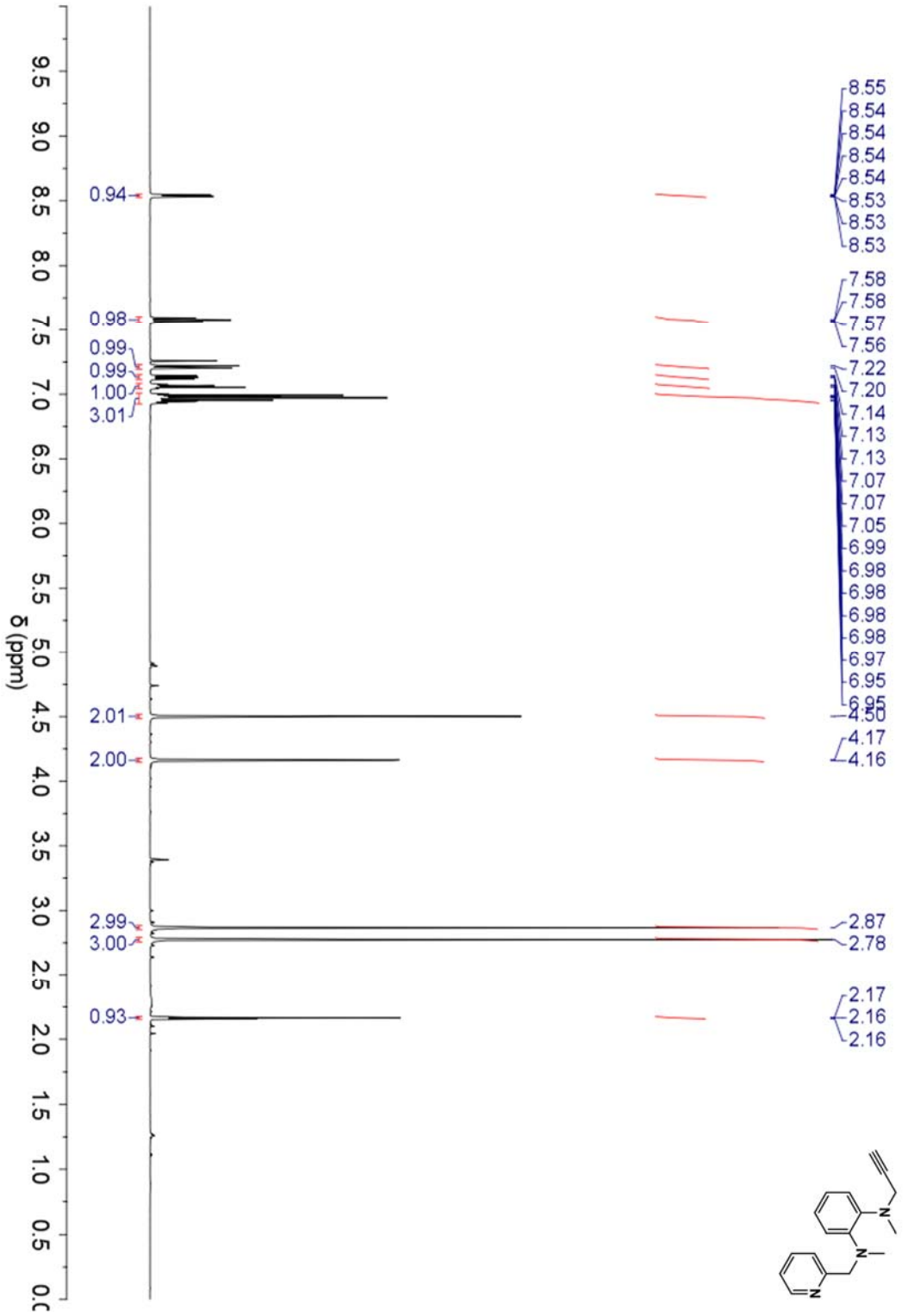


Fig. S32 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **24**.

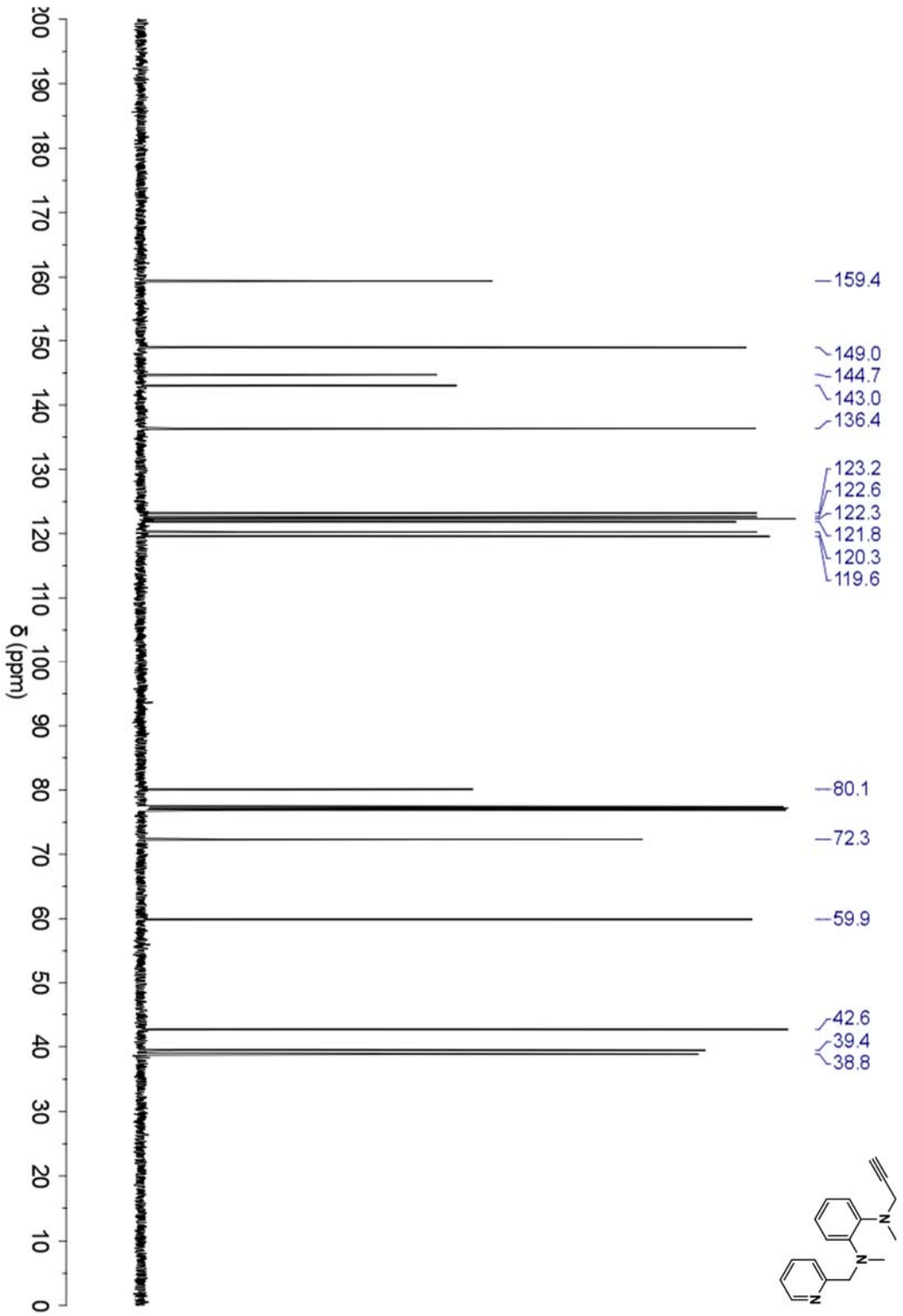


Fig. S33 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **24**.

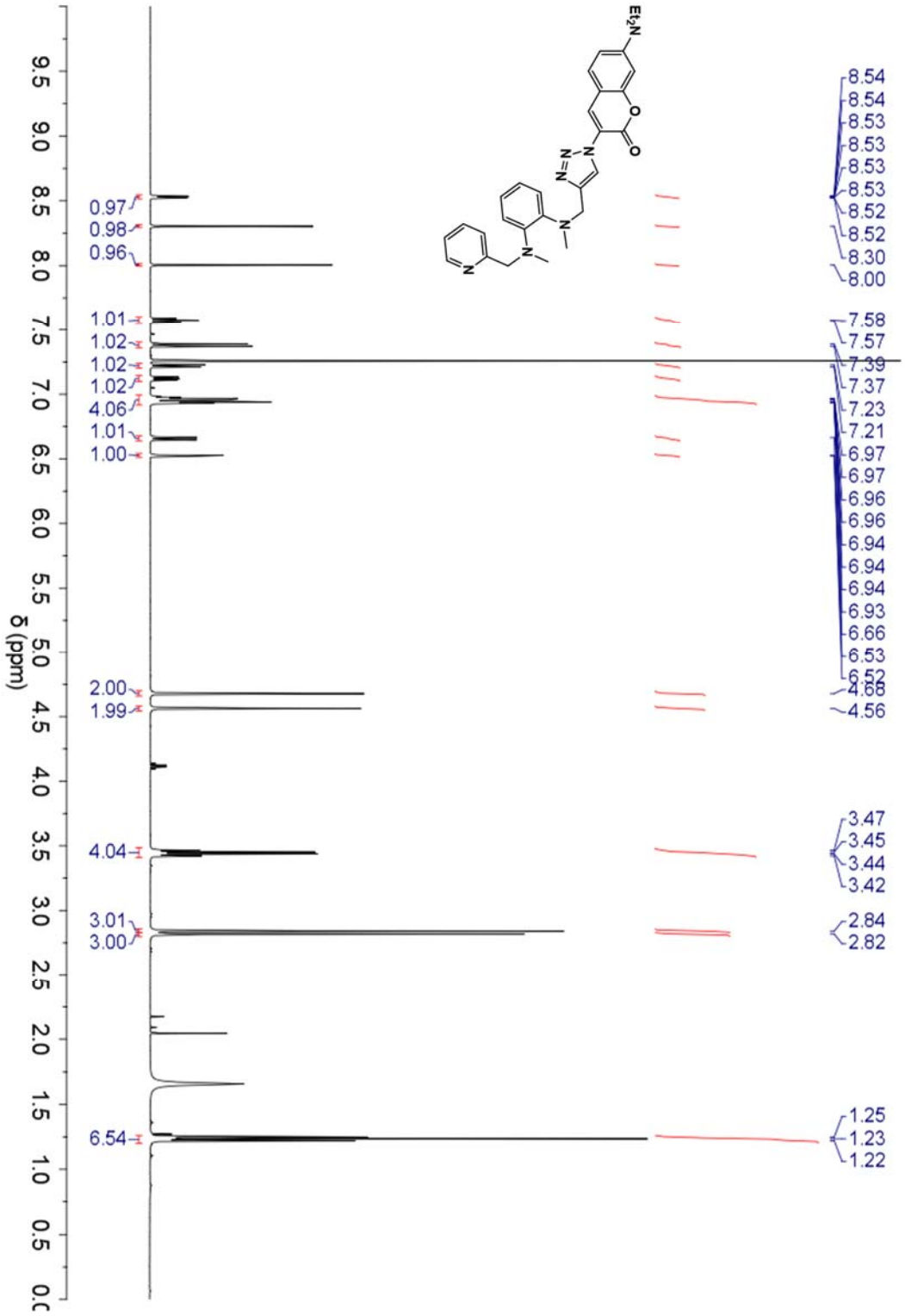


Fig. S34 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **12**.

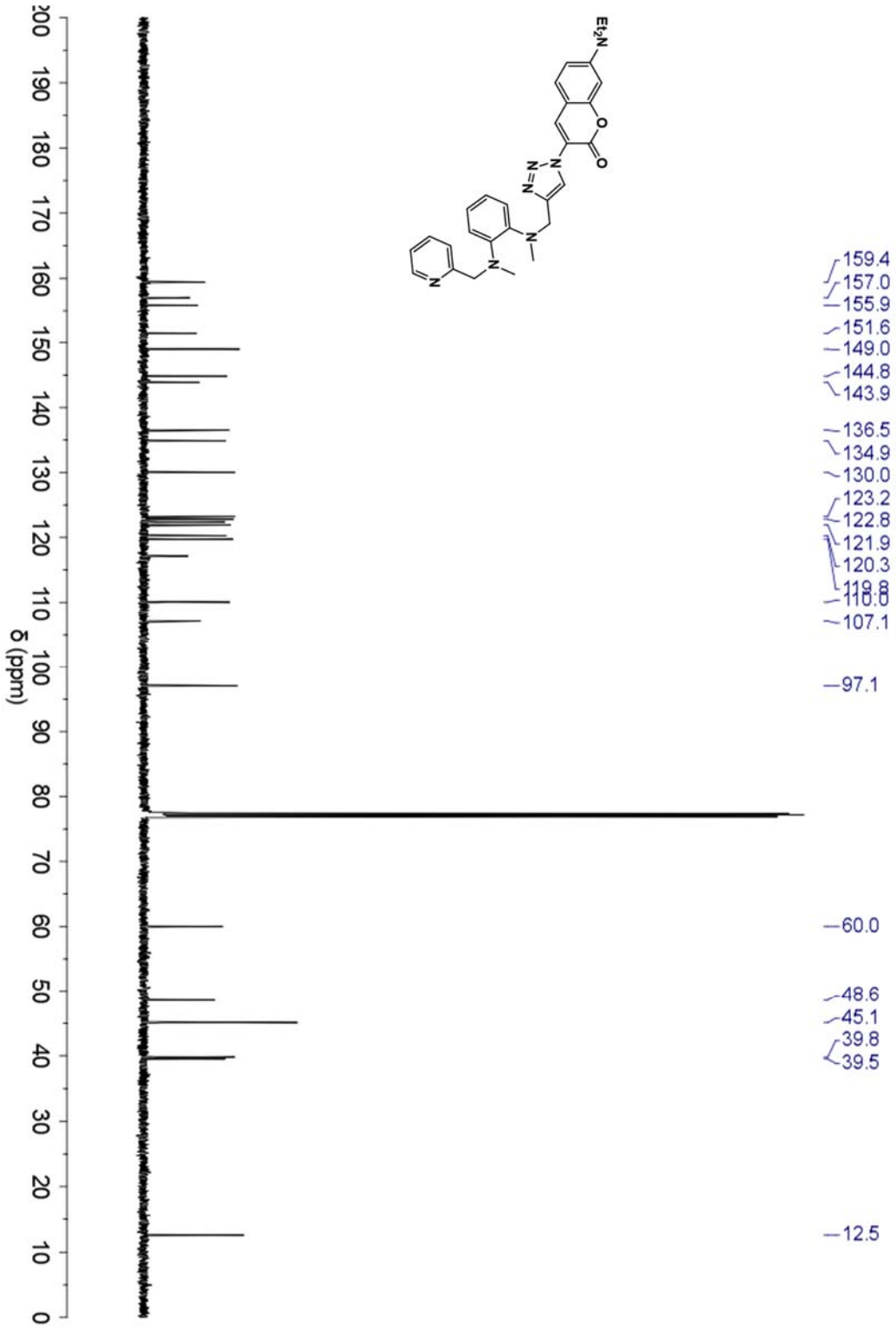


Fig. S35 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **12**.

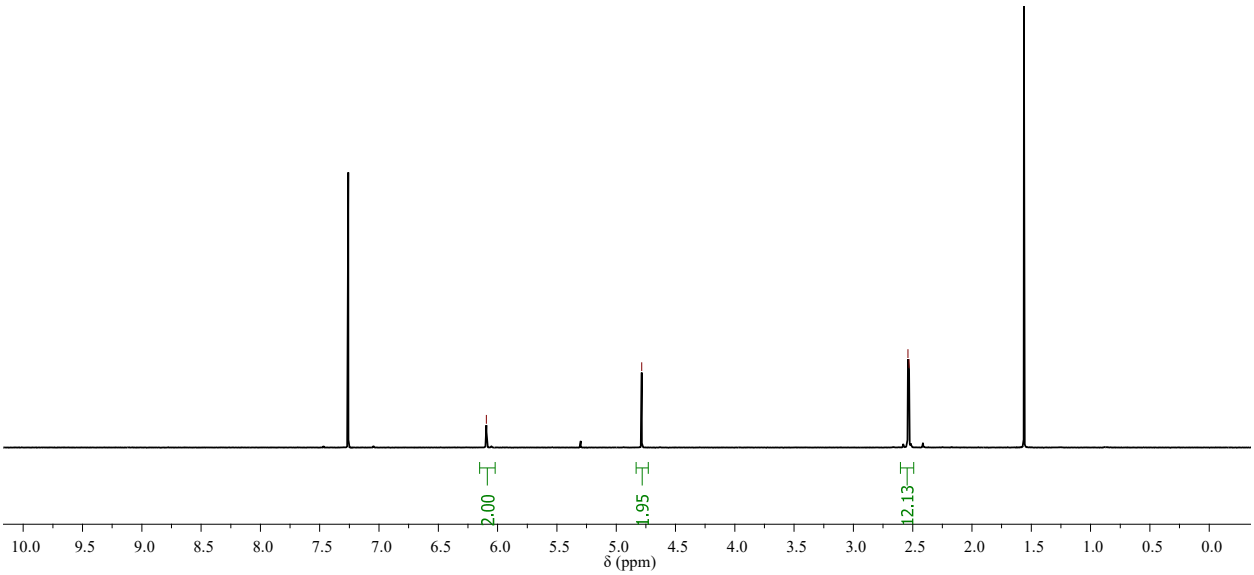


Fig. S36 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **25**.

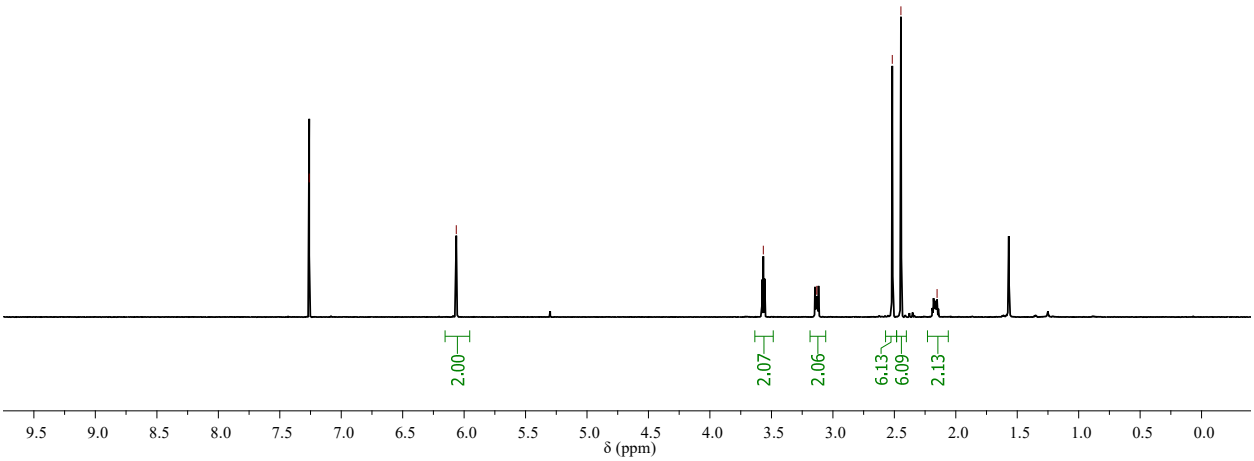


Fig. S37 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **26**.

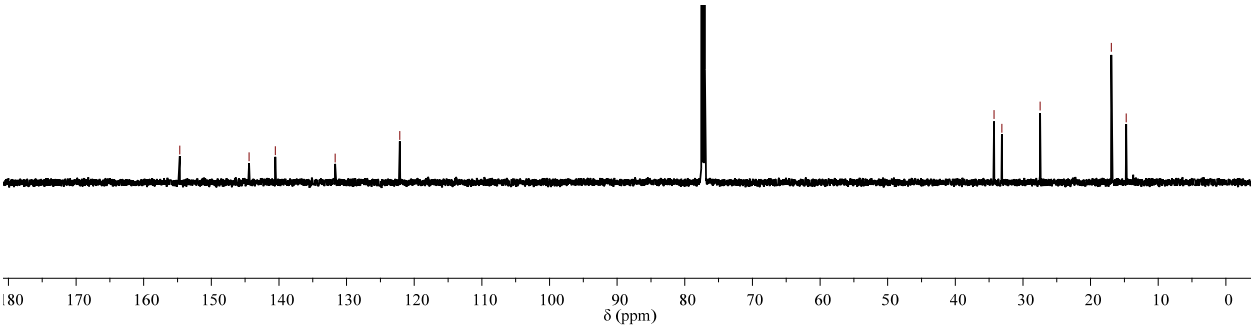


Fig. S38 ^{13}C NMR (150 MHz, $CDCl_3$) of compound **26**.

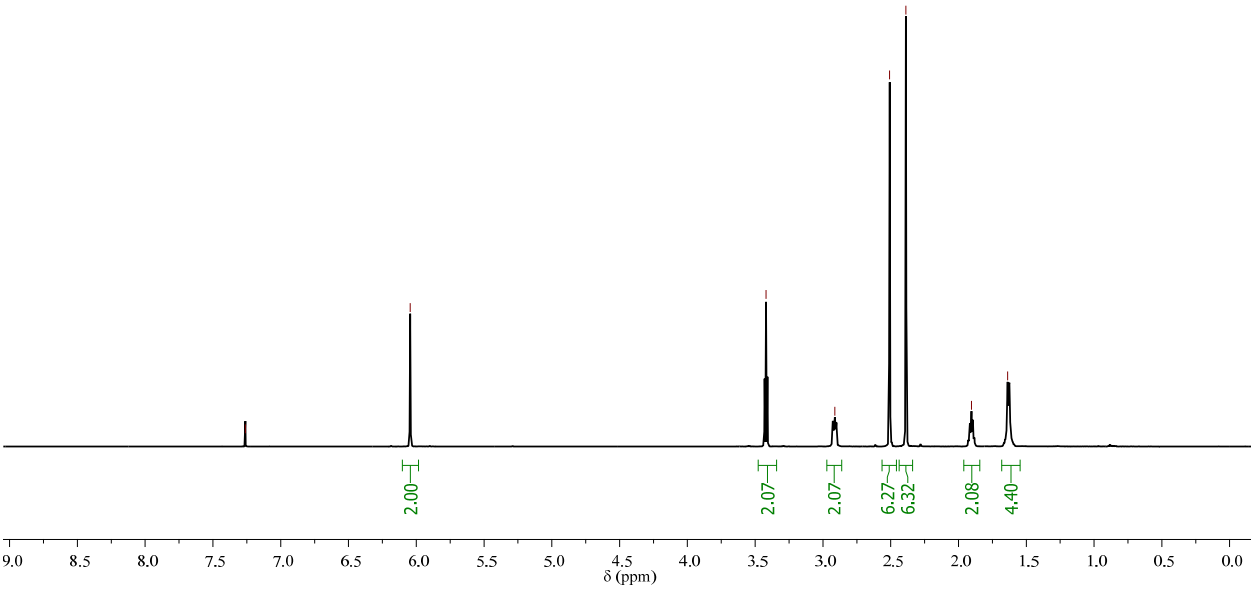


Fig. S39 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **27**.

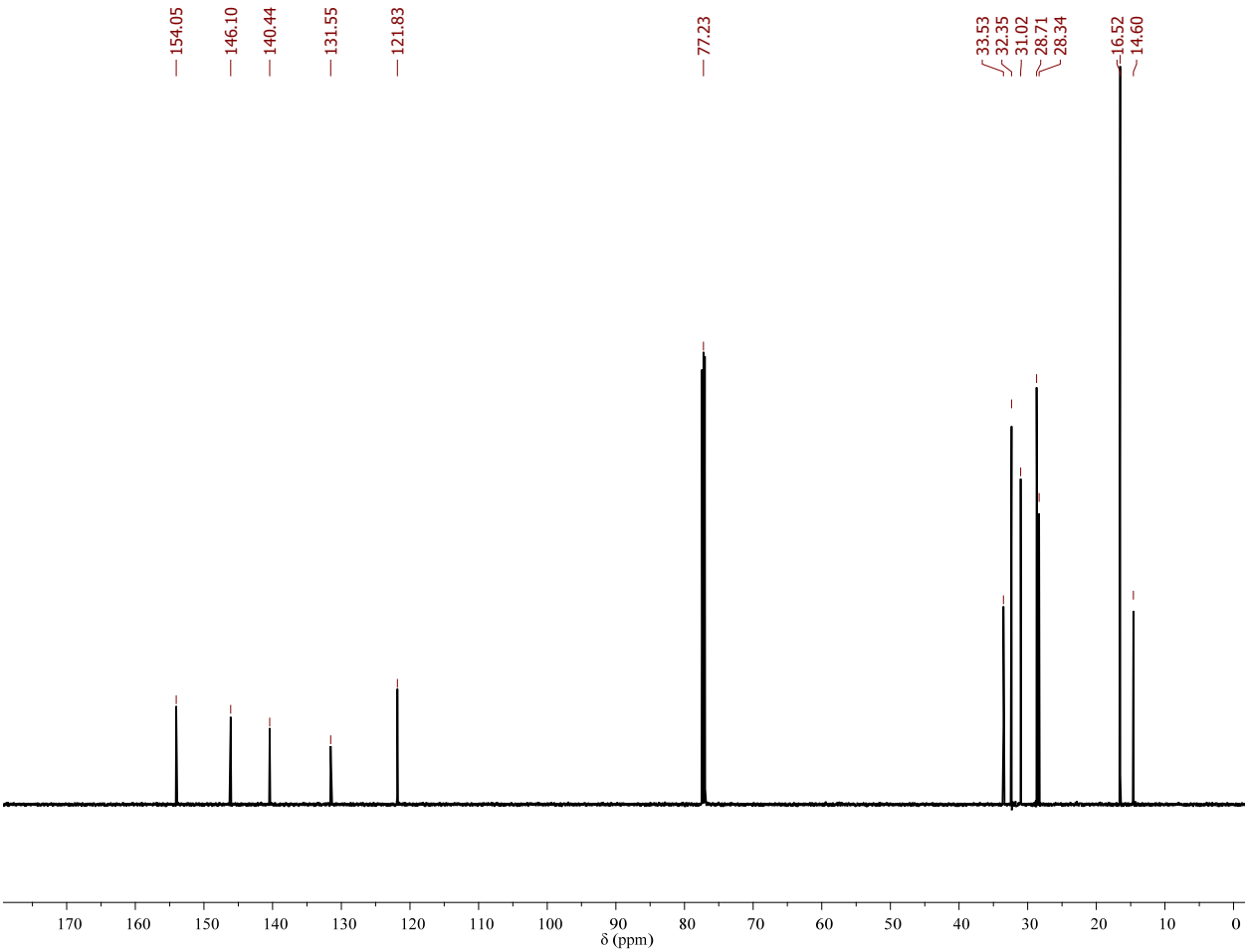


Fig. S40 ^{13}C NMR (150 MHz, $CDCl_3$) of compound **27**.

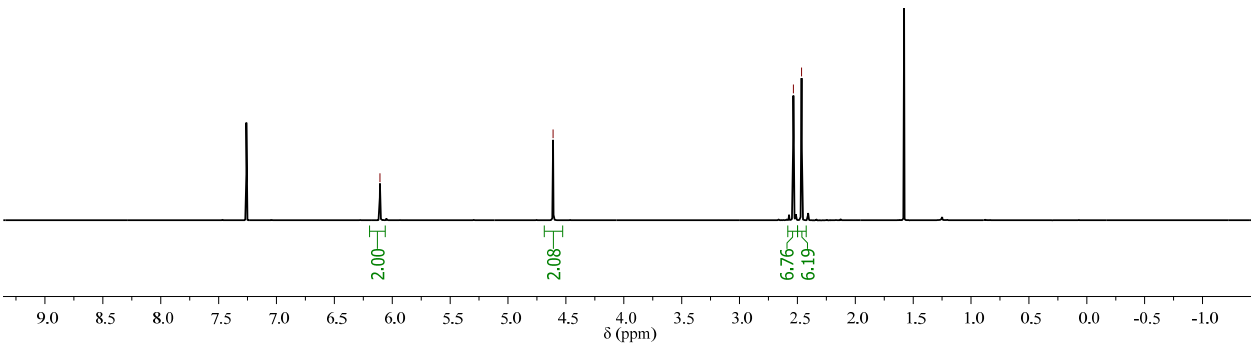


Fig. S41 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **28**.

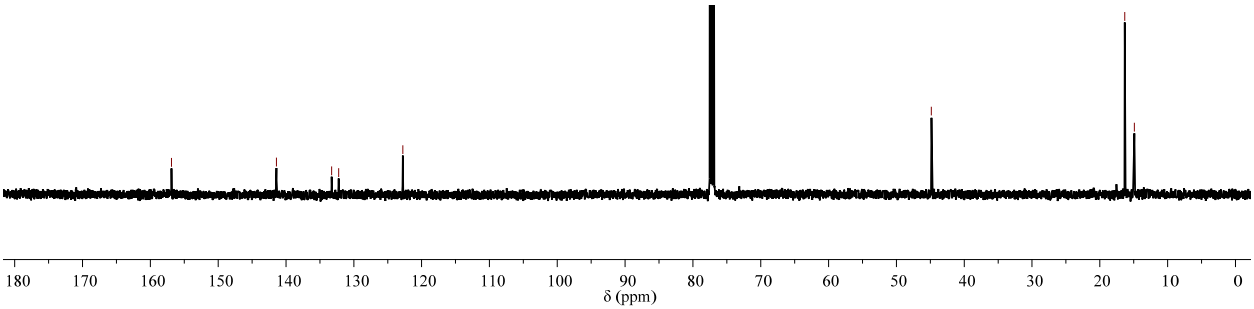


Fig. S42 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **28**.

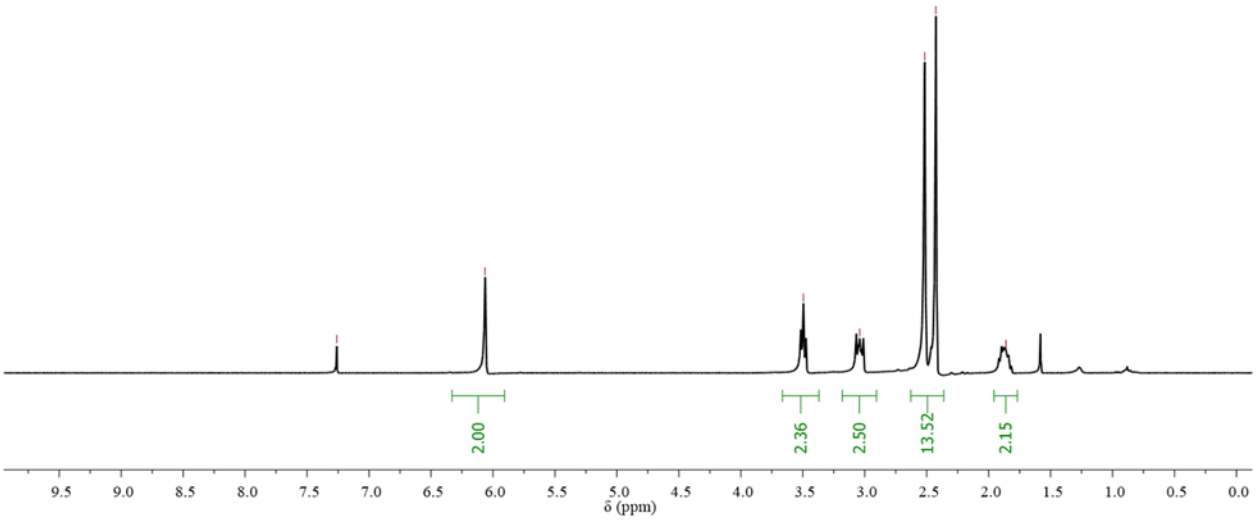


Fig. S43 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **29**.

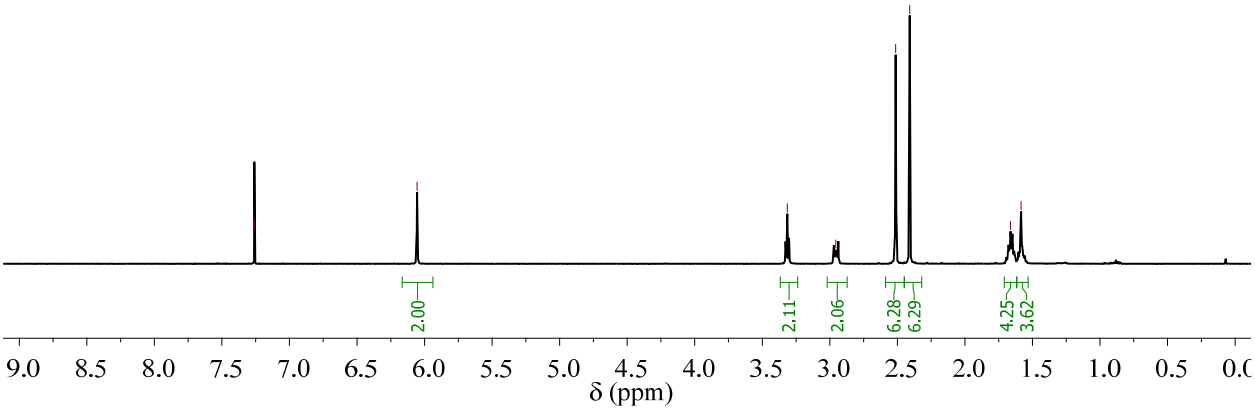


Fig. S44 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **30**.

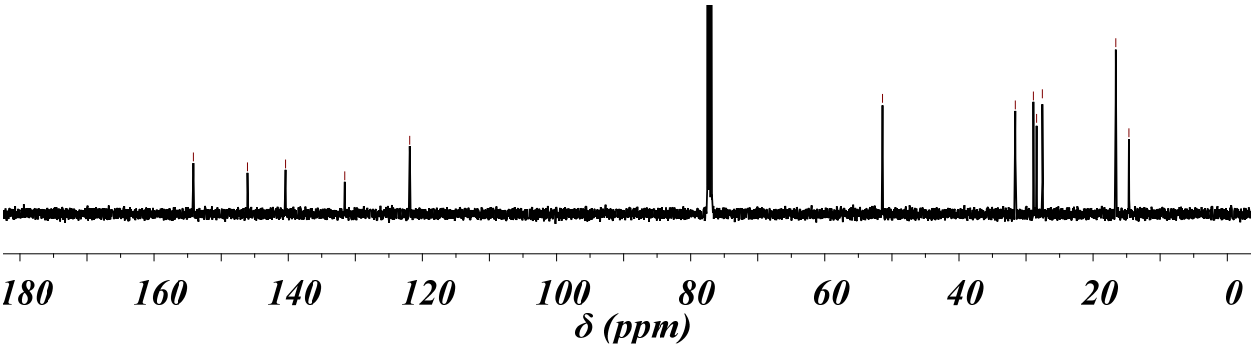


Fig. S45 ^{13}C NMR (150 MHz, $CDCl_3$) of compound **30**.

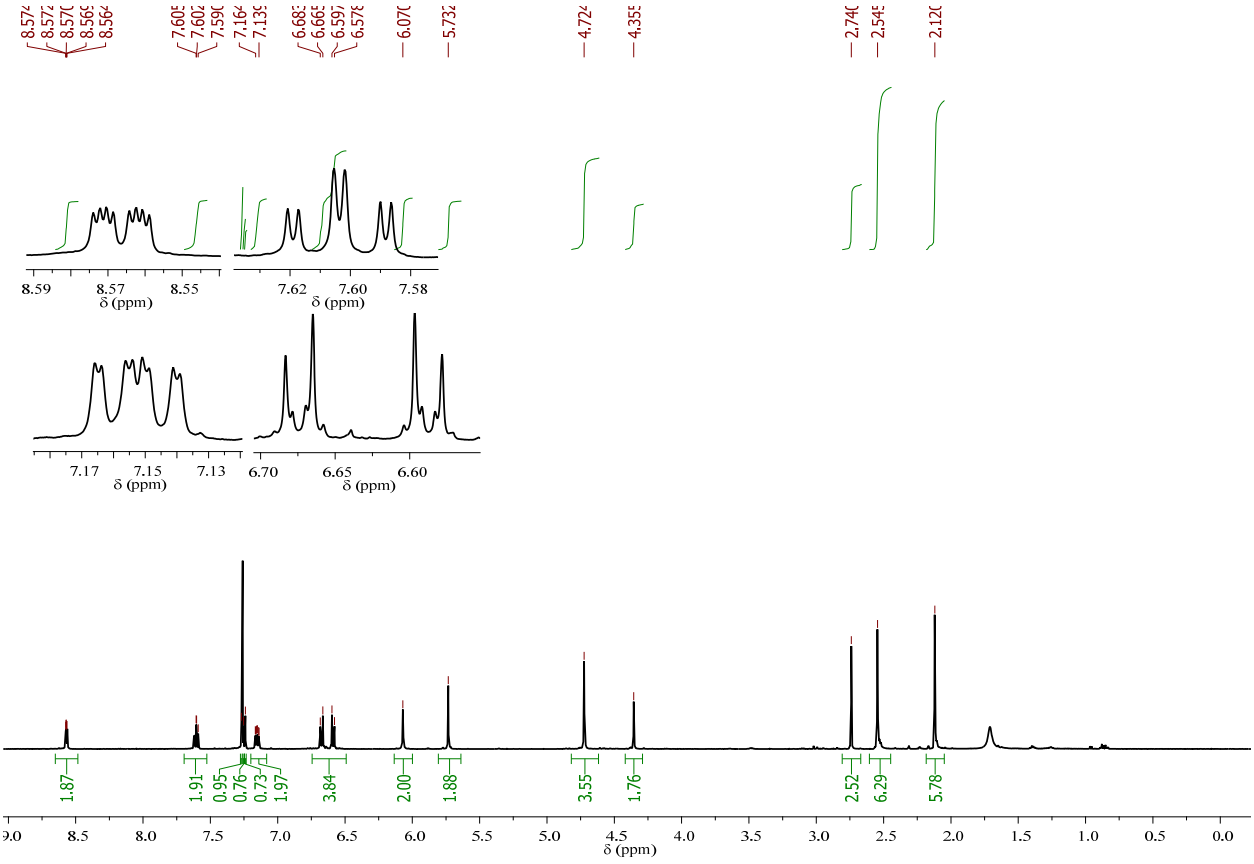


Fig. S46 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **13a**.

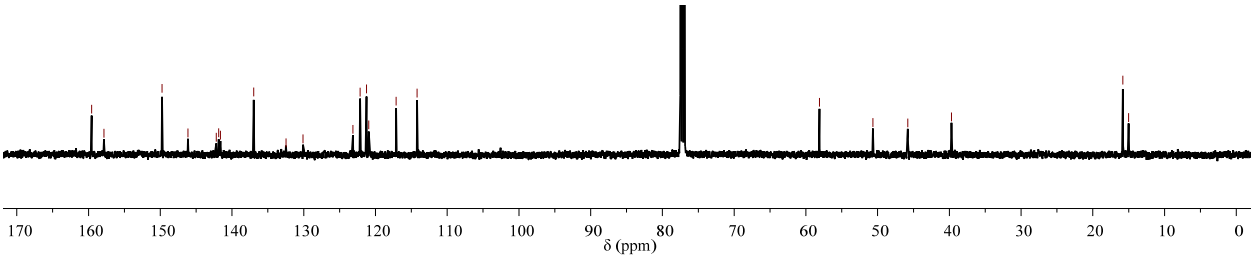


Fig. S47 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **13a**.

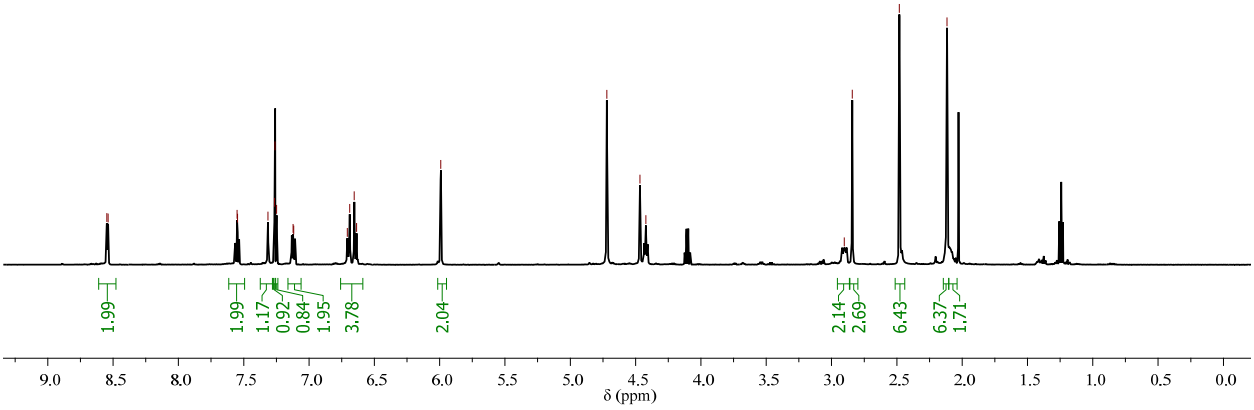


Fig. S48 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **13b**.

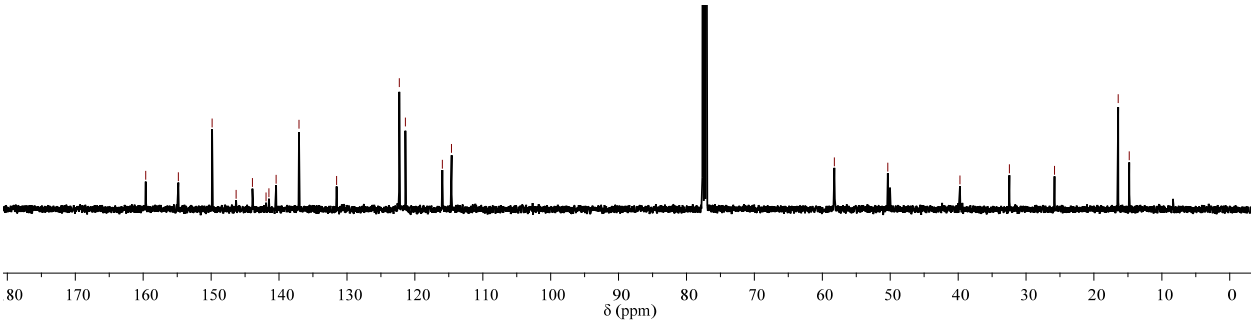


Fig. S49 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **13b**.

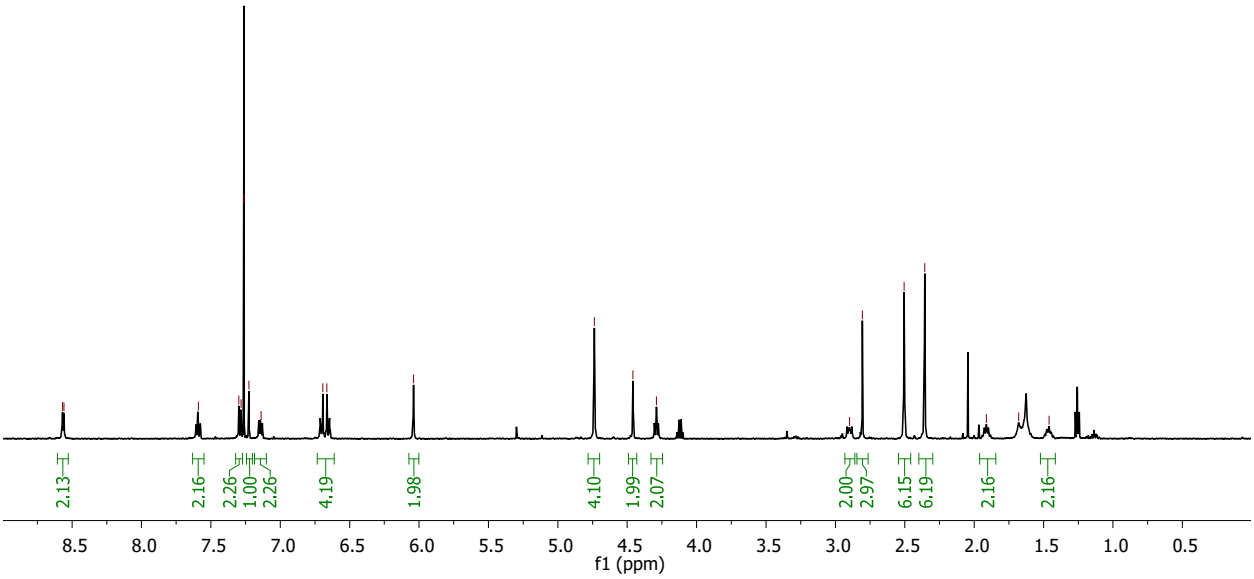


Fig. S50 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **13c**.

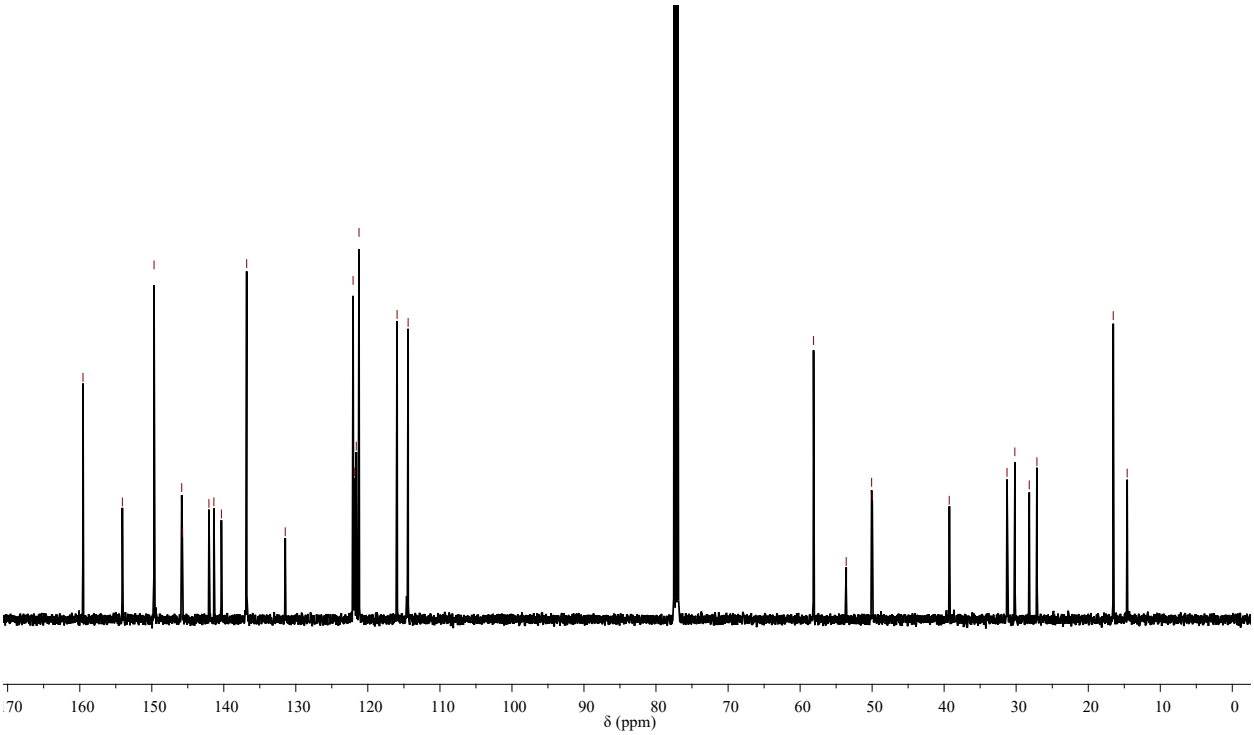


Fig. S51 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **13c**.

(7) References

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