Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

A metal-catalyzed enyne-cyclization step for the synthesis of bi- and tricyclic scaffolds amenable to molecular library production

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General Methods

Unless otherwise noticed, all reactions were run under an argon atmosphere. All solvents were of HPLC quality, and were typically dried over molecular sieves.

All reactions were monitored by thin layer chromatography (TLC), reversed-phase high performance liquid chromatography (RP-HPLC), and reversed-phase ultra-performance liquid chromatography mass spectrometry (RP-HPLC/MS). All yields are unoptimized and generally represent the result of a single experiment.

TLC was conducted using Merck aluminum sheets covered with silica gel C-60 F_{254}. The plates were either visualized under UV-light (254 nm) or stained by dipping in a developing agent followed by heating. $KMnO_4$ dipping solution were used as the developing agents: $KMnO_4$ (1.5 g), K_2CO_3 (10 g), 5% NaOH aqueous solution (2.5 mL), H_2O (150 mL).

Column chromatography was performed using a glass column packed with Geduran® Si 60 silica gel (40-63 μm particles). A mixture of heptane and ethyl acetate was used as the liquid phase.

LC/MS analysis was performed on a Waters AQUITY UPLC system equipped with a C-18 column (*d* 1.7 μm, 2.1 × 50 mm, column temp: 65 °C), a PDA and SQD MS detector. A linear reversed phase gradient (5% to 100% organic in 2.4 min, hold for 0.1 min, total run-time 2.6 min) combining water and acetonitrile (buffered with 0.1% formic acid) was used.

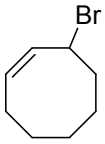
RP-HPLC was conducted on a Waters Alliance 2695 RP-HPLC system using a Symmetry C-18 column (*d* 2.5 μm, 4.6 × 75 mm, column temp: 25 °C), with detection at 215 nm and 254 nm. 0.1% TFA in H_2O (A) and 0.1% TFA in acetonitrile (B) were used (100% A to 100% B, total run-time 13 min) as the elusion phase.

^1H NMR and ^{13}C NMR were recorded using a Bruker Ascend-400 MHz instrument in DMSO-d_6 or $CDCl_3$ using the residual solvent peak as the internal standard. All 13C NMR spectra were proton decoupled. The chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (*J*) in Hz. Multiplicities of peaks in ^1H NMR are given as: s (singlet), brs (broad singlet), d (doublet), t (triplet), dd (double doublet), ddd (double double doublet) and m (multiplet).

Melting points were measure using a Stuart® SMP 30 capillary melting point apparatus.

Experimental Procedures and Characterization Data

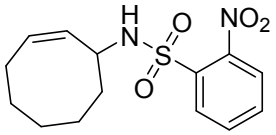
(*Z*)-3-Bromocyclooctene (3)



Cyclooctene (5.90 ml, 45.4 mmol), NBS (8.08 g, 45.37 mmol), and AIBN (75 mg, 0.45 mmol) were added to CCl_4 (45 mL) under argon atmosphere and heated to 80°C for 4 h. The solution was cooled to 25°C and the solvent was removed under reduced pressure. The product was distilled at 80°C (3 Torr) to give the title product (**3**) as colorless oil (5.33 g, 62%).[Lit] ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.75 (ddd, 1H, J = 10.5, 8.3, 1.3 Hz, CH=CH), 5.67 – 5.52 (m, 1H, CH=CH), 5.20 – 5.10 (m, 1H, CHBr), 2.33 – 1.98 (m, 3H; CH_2*CH=CHCHB*rCH_2), 1.97 – 1.87 (m, 1H, *CH_2CH=CHCHB*rCH_2), 1.68 – 1.38 (m, 5H, cyclooctene CH_2), 1.31 – 1.20 ppm (m, 1H, cyclooctene CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 132.9, 130.0, 50.3, 40.5, 28.6, 26.1, 25.3, 24.9.

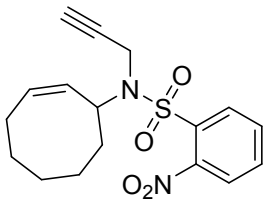
[Lit] C. W. Bond, A. J. Cresswell, S. G. Davies, A. M. Fletcher, W. Kurosawa, J. A. Lee, P. M. Roberts, A. J. Russell, A. D. Smith and J. E. Thomson, *J. Org. Chem.*, 2009, **74**, 6735.

(*Z*)-*N*-(Cyclooct-1-en-3-yl)-2-nitrobenzenesulfonamide (4)



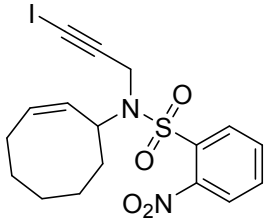
(*Z*)-3-Bromocyclooctene (**3**) (5.33 g, 28.2 mmol) was dissolved in dry DMF (110 mL). K_2CO_3 (4.80 g, 39.5 mmol) and 2-nitrobenzenesulfonamide (6.84 g, 33.8 mmol) were added to the solution and stirred for 1h at 60°C. The reaction mixture was cooled to 21°C and diluted with EtOAc (200 mL). The product was washed with sat. aq. NH_4Cl (2×200 mL) and 1M HCl (aq.) (2×150 mL). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The product was purified by flash chromatography (1:4, EtOAc/heptane) to give the product as a pale yellow powder (4.23 g, 49%), mp 82°C – 83°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.24 (s, 1H, NH), 8.00 (dd, 1H, J = 5.9, 3.4 Hz, phenyl H), 7.92 (dd, 1H, J = 5.7, 3.2 Hz, phenyl H), 7.88 – 7.80 (m, 2H, phenyl H), 5.52 – 5.43 (m, 1H, CH=CH), 5.31 – 5.18 (m, 1H, CH=CH), 4.21 – 4.11 (m, 1H, *NH*CH), 2.08 – 1.87 (m, 2H, cyclooctene CH_2), 1.69 – 1.36 (m, 5H, cyclooctene CH_2), 1.36 – 1.11 (m, 3H, cyclooctene CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.6, 134.0, 133.3, 132.3, 130.9, 129.8, 129.2, 124.0, 51.0, 36.5, 28.7, 26.0, 25.9, 23.8. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{14}H_{19}N_2O_4S$ 311.1066, found 311.1063.

(*Z*)-*N*-(Cyclooct-1-en-3-yl)-*N*-(prop-2-yn-1-yl)-2-nitrobenzenesulfonamide (1)



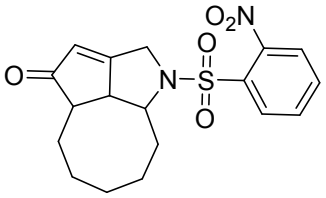
(*Z*)-*N*-(Cyclooct-1-en-3-yl)-2-nitrobenzenesulfonamide (**4**) (3.62 g, 11.67 mmol), and propargyl bromide (1.56 mL, 14.00 mmol), were dissolved in dry DMF (100 mL) and added K_2CO_3 (1.95 g, 14.00 mmol) under argon atmosphere. The temperature was raised to 60 °C and the reaction mixture was stirred for 1 h before sat. aq. NH_4Cl (100 mL) was added. The resulting mixture was extracted with EtOAc (3×100 mL) and the combined organic phases were washed with water (100 mL), then brine (100 mL), dried (Na_2SO_4), and concentrated *in vacuo*, yielding desired sulfonamide (**1**) (4.4 g, quant.) as a yellow powder, mp 89°C – 92°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09 (dd, 1H, *J* = 7.8, 1.5 Hz, phenyl H), 7.96 (dd, 1H, *J* = 7.8 and 1.4 Hz, phenyl H), 7.88 (td, 1H, *J* = 7.6 and 1.6 Hz, phenyl H), 7.83 (td, 1H, *J* = 7.6 and 1.5 Hz, phenyl H), 5.74 – 5.54 (m, 2H, CH=CH), 4.71 (ddd, 1H, *J* = 11.9, 7.4, 4.2 Hz, *N*CH), 4.28 (dd, 1H, *J* = 18.5 and 2.0 Hz, propargyl CH_2) and 4.23 (dd, 1H, *J* = 18.5 and 2.0 Hz, propargyl CH_2), 3.25 (t, 1H, *J* = 2.4 Hz, propargyl CH), 2.12 -1.97 (m, 2H, cyclooctene CH_2), 1.87 – 1.76 (m, 1H, cyclooctene CH_2), 1.69 – 1.51 (m, 4H, cyclooctene CH_2), 1.41 – 1.32 (m, 2H, cyclooctene CH_2), 1.30 – 1.20 (m, 1H, cyclooctene CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.6, 134.7, 132.3, 132.0, 130.3, 130.0, 127.6, 124.2, 80.6, 75.1, 55.6, 33.8, 33.1, 28.5, 25.6, 25.5, 23.9. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{21}N_2O_4S$ 349.1222, found 349.1219.

(*Z*)-*N*-(Cyclooct-1-en-3-yl)-*N*-(3-iodoprop-2-yn-1-yl)-2-nitrobenzenesulfonamide (5)



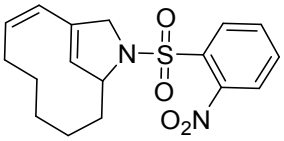
(*Z*)-*N*-(Cyclooct-1-en-3-yl)-*N*-(prop-2-yn-1-yl)-2-nitrobenzenesulfonamide (**1**) (4.07 g, 11.67 mmol) was dissolved in dry DMF (100 mL) under argon atmosphere and added *N*-iodosuccinimide (2.85 g, 12.67 mmol) and $AgNO_3$ (0.198 g, 1.17 mmol). The reaction mixture was stirred in the dark at 25°C for 2h, quenched by addition of sat. aq. $Na_2S_2O_3$ (100 mL), and extracted with EtOAc (4×50 mL). The combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated *in vacuo* to give desired iodide as yellow oil contaminated with succinimide and DMF. The compound was redissolved in diethyl ether (250 mL), washed with water (3×50 mL), then brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo* to give desired iodide (**5**) as a light yellow solid (3.5 g, 63%), mp 94°C – 96°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.05 (m, 1H, phenyl H), 7.97 (m, 1H, phenyl H), 7.90-7.82 (m, 2H, phenyl H), 5.64-5.58 (m, 2H, CH=CH), 4.74 (m, 1H, *N*CH), 4.37 (s, 2H, propargyl CH_2), 2.12-1.99 (m, 2H, cyclooctene CH_2), 1.81-1.72 (m, 1H, cyclooctene CH_2), 1.67-1.50 (m, 4H, cyclooctene CH_2), 1.42-1.20 (m, 3H, cyclooctene CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.5, 134.7, 132.2, 132.0, 130.2, 130.0, 127.6, 124.2, 88.9, 55.6, 34.9, 33.8, 28.5, 25.6, 25.5, 23.9, 11.2. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{20}IN_2O_4S$ 475.0188, found 475.0185.

1-((2-Nitrophenyl)sulfonyl)-1,2,2a1,4a,5,6,7,8,9,9a-decahydro-4H-1-azacycloocta[cd]pentalen-4-one (6)



(*Z*)-*N*-(Cyclooct-1-en-3-yl)-*N*-(prop-2-yn-1-yl)-2-nitrobenzenesulfonamide (**1**) (18 mg, 0.05 mmol) was dissolved in dry toluene (2 mL) at room temperature under nitrogen atmosphere and added powdered 4 Å activated molecular sieves (140 mg). $Co_2(CO)_8$ (21 mg, 0.06 mmol) was added to the reaction mixture, which was stirred at room temperature under a 1 atm of CO for 2 d (TLC indicated full consumption of the starting enyne substrate). The mixture was filtrated, and the filtrate was concentrated *in vacuo* to give brown crude, which was purified by flash chromatography (1:1, EtOAc/heptane) to give the product as a white solid (17 mg, 87%), mp 121°C – 123°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.02 (m, 1H, phenyl H), 7.68-7.65 (m, 2H, phenyl H), 7.61-7.59 (m, 1H, phenyl H), 5.95 (s, 1H, COCH=C), 4.61 (dt, 1H, *J* = 16 Hz and 1.2 Hz, CH_2NSO_2), 4.34 (d, 1H, *J* = 16 Hz, CH_2NSO_2), 3.68 (td, 1H, *J* = 10.8 Hz and 4.0 Hz, cyclooctane CH), 3.05-3.00 (m, 1H, cyclooctane CH), 2.38-2.33 (m, 1H, cyclooctane CH), 2.13-2.07 (m, 1H, cyclooctane CH_2), 1.96-1.92 (m, 1H, cyclooctane CH_2), 1.79-1.76 (m, 1H, cyclooctane CH_2), 1.61-1.55 (m, 2H, cyclooctane CH_2), 1.31-1.22 (m, 5H, cycloctane CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.8 (C=O), 175.2 (*COCH*=C), 148.1 (phenyl C), 148.0 (phenyl C), 133.9 (phenyl C), 131.9 (phenyl C), 130.6 (phenyl C), 124.3 (phenyl C), 124.3 (*CO*CH=*C*), 62.2 (cyclooctane CH), 54.2 (cyclooctane CH), 50.4 (cyclooctane CH), 50.2 (CH_2N SO_2), 34.4 (cyclooctane CH_2), 30.6 (cyclooctane CH_2), 27.3 (cyclooctane CH_2), 25.3 (cyclooctane CH_2), 24.2(cyclooctane CH_2). HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{18}H_{21}N_2O_5S$ 377.1171, found 377.1168.

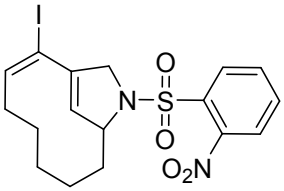
(*1Z,2Z*)-10-((2-Nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (7a)



(*Z*)-*N*-(Cyclooct-1-en-3-yl)-*N*-(prop-2-yn-1-yl)-2-nitrobenzenesulfonamide (**1**) (1.0 g, 2.87 mmol) and $PtCl_2$ (38.2 mg, 0.14 mmol) was added to dry toluene (150 ml) and heated to 80°C for 3 h. The solution was concentrated *in vacuo* and the product purified by flash chromatography (1:4, EtOAc/heptane) to give the product as a colorless oil (0.71 g, 71%). ^{1}H NMR (400 MHz, DMSO-d_6): δ= 8.01 – 7.96 (m, 2H, phenyl H), 7.94 – 7.81 (m, 2H, phenyl H), 5.99 (d, 1H, *J* = 11.0 Hz,*CH*=CH–*C(CH*$_2$*)=CH*), 5.79 (ddd, 1H, *J* = 11.1, 8.2, 6.2 Hz, CH=*CH–C(CH*$_2$*)=CH*), 5.64 (s, 1H, *CH=CH–C(CH*$_2$*)*=CH), 4.86 (s, 1H, *SO*$_2$*N*CH), 4.34 (d, 1H, *J* = 14.6 Hz, *CH=CH–C(*CH_2*)=CH*), 4.26 (dd, 1H, *J* = 14.6 and 4.4 Hz, *CH=CH–C(*CH_2*)=CH*), 2.27 – 2.15 (m, 1H, cyclodecadiene CH_2), 2.09 – 1.88 (m, 2H, cyclodecadiene CH_2), 1.63 – 1.49 (m, 3H, cyclodecadiene CH_2), 1.47 – 1.34 (m, 1H, cyclodecadiene CH_2), 1.33 – 1.15 (m, 3H, cyclodecadiene CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.5, 136.5, 135.1, 134.7, 133.0, 130.9,

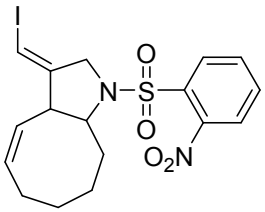
129.6, 129.0, 124.8, 124.2, 67.7, 58.5, 35.5, 28.5, 28.4, 25.6, 20.5; UPLC-MS (ESI) m/z: $[M+H]^+$ 349.2; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{21}N_2O_4S$ 349.1222, found 349.1238.

(*1E,2E*)-2-Iodo-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (7b)



(Z)-*N*-(Cyclooct-2-en-1-yl)-*N*-(3-iodoprop-2-yn-1-yl)-2-nitrobenzenesulfonami-de (**5**) (522 mg, 1.10 mmol) was dissolved in dry CH_2Cl_2 (12 mL) and cooled to 5°C, before PPh_3AuCl (27 mg, 5 mol%) was added , followed by $AgSbF_6$ (42 mg, 10 mol%) dissolved in dry toluene (0.2 mL). The reaction mixture was stirred at this temperature for 1 h and then filtered. The filtrate was washed with water (10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated *in vacuo* to give vinyl iodide (**7b**) as light yellow semisolid (458 mg, 88%) contaminated with trace amount of catalyst. Purification by flash column chromatography (4:5, CH_2Cl_2/heptane) afforded pure vinyl iodide. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.95 (m, 1H, phenyl H), 7.74-7.64 (m, 3H, phenyl H), 6.43 (dd, 1H, *J* = 6.3 and 8.1 Hz, CH=*CI–C(CH$_2$)=CH*), 5.75 (m, 1H, *CH=CI–C(CH$_2$)*=CH), 4.99 (m, 1H, *SO$_2$N*CH), 4.54 (td, 1H, *J* = 14.0 and 2.1 Hz, *CH=CI–C(*CH_2*)=CH*), 4.40 (ddd, 1H, *J* = 14.0, 4.7, 1.6 Hz, *CH=CI–C(*CH_2*)=CH*), 2.28 -2.16 (m, 2H, cyclodecadiene CH_2), 1.99-1.91 (m, 1H, cyclodecadiene CH_2), 1.68-1.59 (m, 2H, cyclodecadiene CH_2), 1.56-1.44 (m, 2H, cyclodecadiene CH_2), 1.41-1.25 (m, 2H, cyclodecadiene CH_2) 1.22-1.12 (m, 1H, cyclodecadiene CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 145.7, 138.3, 133.6, 132.4, 131.7, 130.8, 129.8, 126.7, 124.3, 85.2, 67.5, 56.7, 34.9, 29.5, 28.4, 27.6, 20.1. UPLC-MS (ESI) m/z: $[M+H]^+$ 475.0; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{21}IN_2O_4S$ 475.0188, found 475.0185.

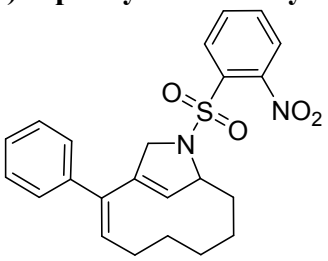
(3*Z*,4*Z*)-3-(Iodomethylene)-1-((2-nitrophenyl)sulfonyl)-2,3,3a,6,7,8,9,9a-octahydro-1H-cycloocta[*b*]pyrrole (8)



(Z)-*N*-(Cyclooct-2-en-1-yl)-*N*-(3-iodoprop-2-yn-1-yl)-2-nitrobenzenesulfonami-de (**5**) (20 mg, 0.04 mmol) was dissolved in dry THF (1 mL), followed by the adding of Cp*RuCl(COD) (2.29 mg, 10mol%). The reaction mixture was stirred at room temperature for 2 h and filtered through a pad of celite. The filtrate was concentrated *in vacuo.* Purification by flash column chromatography (1:4, EtOAc/heptane) afforded the product as a light yellow solid (12 mg, 60%), mp 136°C -139°C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.02-8.00 (m, 1H, phenyl H), 7.67-7.65 (m, 2H, phenyl H), 7.60-7.57 (m, 1H, phenyl H), 5.95 (dd, 1H, , *J* = 5.2 and 2.4 Hz, *I*CH=*C*), 5.71-5.64 (m, 1H, CH=CH), 5.48-

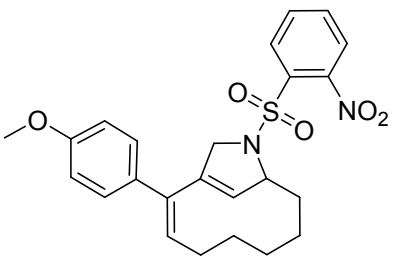
5.44 (m, 1H, CH=CH), 4.19 (dt, 1H, *J* = 15.6 and 2.0 Hz, CH_2NSO_2), 4.02 (dq, 1H, *J* = 15.6 and 1.2 Hz, CH_2NSO_2), 3.38-3.34 (m, 1H, *CH*=*CH*CH*CHNSO*$_2$), 3.27-3.20 (m, 1H, *CH*=*CHCH*CH*NSO*$_2$), 2.23-2.13 (m, 2H, cyclooctene CH_2), 2.08-2.01 (m, 1H, cyclooctene CH_2), 1.52-1.41 (m, 2H, cyclooctene CH_2), 1.21-1.14 (m, 3H, cyclooctene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5 (*ICH*=C), 148.2 (phenyl C), 133.8 (phenyl C), 133.4 (phenyl C), 133.3 (*CH*=CH), 131.8 (phenyl C), 130.4 (phenyl C), 126.7 (CH=*CH*), 124.2 (phenyl C), 70.2 (*I*CH=*C*), 68.2 (cyclooctene CH), 58.7 (CH_2N), 50.4 (cyclooctene CH), 30.9 (cyclooctene CH_2), 27.3 (cyclooctene CH_2), 25.0 (cyclooctene CH_2), 20.9 (cyclooctene CH_2). HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{20}IN_2O_4S$ 475.0188, found 475.0185.

(1*Z*,2*Z*)-10-((2-Nitrophenyl)sulfonyl)-2-phenyl-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (9a)



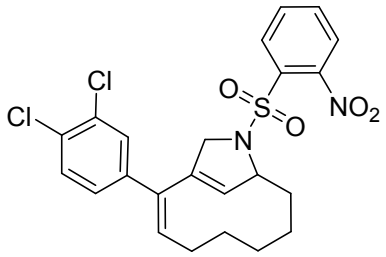
(1*E*,2*E*)-2-Iodo-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1] dodeca-1(12),2-diene **7b** (507 mg, 0.9 mmol), potassium carbonate (251 mg, 1.8 mmol), $Pd(II)OAc_2$ (20 mg, 0.09 mmol), phenylboronic acid (222 mg, 1.82 mmol), S-phos (75 mg, 0.18 mmol) were dissolved in DMF (2 mL) under argon atmosphere. The reaction mixture was heated to 50°C and stirred for 2 d, before saturated NH_4Cl aqueous solution (25 mL) was added, followed by extraction with EtOAc (3 × 50 mL). The combined organic phases were washed with water (3 × 25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (7:13, EtOAC/heptane) afforded the desired compound as a foam (145 mg, 38%) with minor impurities. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, 1H, *J* = 7.3 and 1.8 Hz, phenyl H), 7.74-7.64 (m, 3H, phenyl H), 7.33-7.20 (m, 5H, phenyl H), 6.31 (dd, 1H, *J* = 8.3 and 7.5 Hz, CH=*C–C=CHCHN*), 5.56 (m, 1H, *CH*=*C–C*=CH*CHN*), 5.10 (m, 1H, *CH*=*C–C*=*CH*CH*N*), 4.51 (ddd, 1H, *J* = 14.4, 4.6, 1.6 Hz, CH_2NSO_2) 4.43 (td, 1H, *J* = 14.4 and 2.1 Hz, CH_2NSO_2), 2.40-2.23 (m, 2H, cyclodecadiene CH_2), 2.09 (m, 1H, cyclodecadiene CH_2), 1.60-1.46 (m, 6H, cyclodecadiene CH_2), 1.30 (m, 1H, cyclodecadiene CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 136.6, 134.9, 133.6, 132.9, 131.7, 131.1, 130.8, 130.3, 128.7 (2), 127.6, 127.0, 125.5 (2), 124.4, 68.1, 58.4, 34.8, 28.5, 28.4, 25.0, 18.5. UPLC-MS (ESI) m/z: $[M+H]^+$ found 425.3; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{23}H_{25}N_2O_4S$ 425.1535, found 425.1536.

(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (9b)



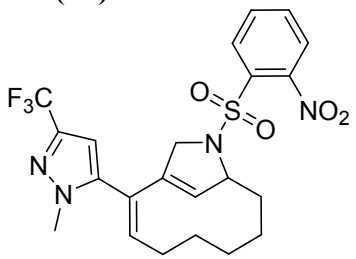
(1*E*,2*E*)-2-Iodo-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **7b** (207 mg, 0.37 mmol), potassium carbonate (103 mg, 0.74 mmol), Pd(II)OAc_2 (8 mg, 0.04 mmol), (4-methoxyphenyl)boronic acid (113 mg, 0.74 mmol), S-phos (31 mg, 0.07 mmol) was dissolved in DMF (4 mL) under argon atmosphere and heated to 50°C stirred overnight. 5% additional catalyst was added and the reaction was stirred for additional 6 h before saturated NH_4Cl aqueous solution (25 mL) was added, followed by extraction with EtOAc (3 × 50 mL). The combined organic phases were washed with water (3 × 25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (EtOAC/heptane, 4/6, v/v) afforded the desired compound as a foam (98 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, 1H, *J* = 7.5 and 1.7 Hz, phenyl H), 7.68 (m, 3H; phenyl H), 7.25 (d, 2H, *J* = 9.0 Hz, phenyl H), 6.81 (d, 2H, *J* = 9.0 Hz, phenyl H), 6.18 (dd, 1H, *J* = 8.2 and 7.6 Hz, CH=*C*–*C*=*CHCHN*), 5.53 (m, 1H, *CH*=*C*–*C*=CH*CHN*), 5.07 (m, 1H, *CH*=*C*–*C*=*CH*CH*N*), 4.49 (ddd, 1H, *J* = 14.3, 4.6, 1.5 Hz, CH_2*NSO*$_2$), 4.41 (td, 1H, *J* = 14.4 and 2.1 Hz, CH_2*NSO*$_2$), 3.79 (s, 3H, OCH_3), 2.29 (m, 2H, cyclodecadiene CH_2), 2.05 (m, 1H, cyclodecadiene CH_2), 1.62-1.25 (m, 7H, cyclodecadiene CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 148.6, 136.0, 135.1, 133.6, 132.8, 131.7, 131.0, 130.8, 130.2, 128.6, 126.6, 124.4, 114.0, 68.1, 58.4, 55.4, 34.8, 28.4, 28.4, 24.8, 18.4; UPLC-MS (ESI) m/z: $[M+H]^+$ found 455.3; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{24}H_{27}N_2O_5S$ 455.1640, found 455. 1643.

(1*Z*,2*Z*)-2-(3,4-Dichlorophenyl)-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (9c)



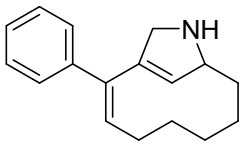
(1*E*,2*E*)-2-Iodo-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1] dodeca-1(12),2-diene **7b** (98 mg, 0.21 mmol), potassium carbonate (57 mg, 0.41 mmol), Pd(II)OAc_2 (5 mg, 0.021 mmol), (3,4-dichlorophenyl)boronic acid (79 mg, 0.41 mmol), S-phos (17 mg, 0.041 mmol) dissolved in DMF (2 mL) under argon atmosphere. The reaction mixture was heated to 50°C and stirred overnight. The resulting mixture added saturated NH_4Cl aqueous solution (25 mL) and extracted with EtOAc (3 × 25 mL). The combined organic phases were washed with water (3 × 25 mL) and brine (25 mL), dried Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (7:3, CH_2Cl_2/heptane) gave the desired compound as a white foam (56 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (m, 1H, phenyl H), 7.76-7.65 (m, 3H, phenyl H), 7.34 (d, 1H, *J* = 2.1 Hz, phenyl H), 7.33 (d, 1H, *J* = 8.4 Hz, phenyl H), 7.16 (dd, 1H, *J* = 8.4 and 2.1 Hz, phenyl H), 6.32 (dd, 1H, *J* = 8.3 and 7.5 Hz, CH=*C*–*C*=*CHCHN*), 5.58 (m, 1H, *CH*=*C*–*C*=CH*CHN*), 5.06 (m, 1H, *CH*=*C*–*C*=*CH*CH*N*), 4.49 (ddd, 1H, *J* = 14.5, 4.7, 1.5 Hz, CH_2*NSO*$_2$), 4.39 (td, 1H, *J* = 14.5 and 2.1 Hz, CH_2*NSO*$_2$), 2.39-2.21 (m, 2H, cyclodecadiene CH_2), 2.09 (m, 1H, cyclodecadiene CH_2), 1.65-1.42 (m, 6H, cyclodecadiene CH_2), 1.31-1.24 (m, 1H, cyclodecadiene CH_2); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, 77.0 ppm): δ= 148.6, 138.5, 134.6, 134.0, 133.8, 132.7, 132.7, 132.6, 132.0, 131.8, 131.3, 130.5, 130.2, 127.4, 124.7, 124.4, 68.1, 58.2, 34.8, 28.5, 28.2, 25.1, 18.5 ppm. UPLC-MS (ESI) m/z: $[M+H]^+$ found 493.1; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{23}H_{23}Cl_2N_2O_4$ 493.0756, found 493. 0750.

(1*Z*,2*E*)-2-(1-Methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (9d)



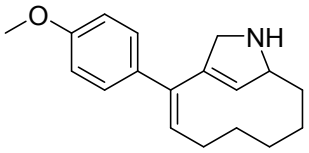
The crude iodo-functionalized bicycle (**9d**) (106 mg, 0.223 mmol), potassium carbonate (62 mg, 0.45 mmol), Pd(II)OAc_2 (5 mg, 0.021 mmol), (1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)boronic acid (87 mg, 0.45 mmol), S-phos (18 mg, 0.045 mmol) dissolved in DMF (2 mL) under argon atmosphere. The reaction mixture was heated to 50°C and stirred overnight. The resulting mixture added saturated aqueous solution NH_4Cl (25 mL) and extracted with EtOAc (3 × 25 mL). The combined organic phases were washed with water (3 × 25 mL) and brine (25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (9:11, EtOAc/heptane) gave desired compound as a yellow foam (64 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, 1H, *J* = 7.7 and 1.6 Hz, phenyl H), 7.75-7.61 (m, 3H, phenyl H), 6.30 (s, 1H, pyrazolyl H), 6.14 (dd, 1H, *J* = 8.7 and 6.8 Hz, CH=*C–C=CHCHN*), 5.66 (m, 1H, *CH=C–C=*CH*CHN*), 5.02 (m, 1H, *CH=C–C=CH*CH*N*) ,4.51 (ddd, 1H, *J* = 14.5, 4.7, 1.4 Hz, CH_2*NSO*$_2$), 4.39 (td, 1H, *J* = 14.5 and 2.0 Hz, CH_2*NSO*$_2$), 3.79 (s, 3H, CH_3), 2.41 (m, 1H, cyclodecadiene CH_2), 2.18 (m, 2H, cyclodecadiene CH_2), 1.69-1.34 (m, 6H, cyclodecadiene CH_2), 1.22 ppm (m, 1H, cyclodecadiene CH_2); ^{13}C NMR (100 MHz, , $CDCl_3$) δ 148.5, 143.2, 141.7 and 141.3 and 140.9 and 140.5 ($^2J_{C\text{-}F}$ = 38 Hz), 138.4, 134.0, 133.7, 132.3, 132.2, 131.8, 130.4, 125.6, 124.3, 122.6 and 119.9 ($^1J_{C\text{-}F}$ = 267 Hz), 104.2 and 104.2 ($^3J_{C\text{-}F}$ = 3 Hz), 67.8, 57.9, 38.8, 35.0, 28.5, 28.2, 25.5, 19.3. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{22}H_{24}F_3N_4O_4S$ 497.1470, found 497.1475.

(1*Z*,2*Z*)-2-Phenyl-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (10a)



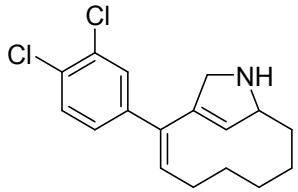
(1*Z*,2*Z*)-10-((2-Nitrophenyl)sulfonyl)-2-phenyl-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **9a** (110 mg, 0.26 mmol) was dissolved in DMF (2 mL) and added 2-mercaptoacetic acid (72 µl, 1.04 mmol) followed by LiOH (50 mg, 2.07 mmol). The reaction mixture was stirred at rt for 1 h, before saturated $NaHCO_3$ aqueous solution (25 mL) was added and the resulting mixture was extracted with EtOAc (3 × 25 mL). The combined organic phases were washed with water (3 × 25 mL) and brine (25 mL), dried (Na_2SO_4), and concentrated *in vacuo* to give desired amine **10a**. The crude was used in the next step without further purification. UPLC-MS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{22}N$ 240.2, found 240.2.

(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (10b)



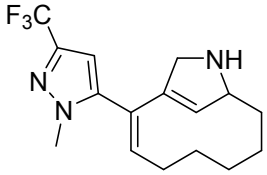
(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **9b** (510 mg, 1.12 mmol) was dissolved in DMF (5.5 ml) and added 2-mercaptoacetic acid (312 µl, 4.5 mmol) and LiOH (215 mg, 9 mmol).The reaction mixture was stirred at rt for 20 min, before saturated $NaHCO_3$ aqueous solution (75 mL) was added followed by extraction with EtOAc (3 × 75 mL). The combined organic phases were washed with water (3 × 25 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated *in vacuo* to give desired amine **10b**. The crude was used in the next step without further purification. UPLC-MS (ESI) m/z: $[M+H]^+$ calcd. for $C_{18}H_{24}NO$ 270.2, found 270.2.

(1*Z*,2*Z*)-2-(3,4-Dichlorophenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (10c)



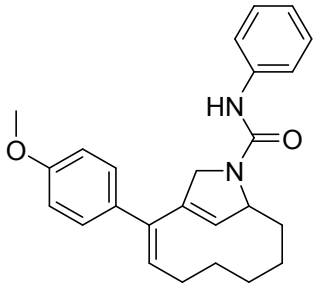
(1*Z*,2*Z*)-2-(3,4-Dichlorophenyl)-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **9c** (89 mg, 0.18 mmol) was dissolved in in DMF (0.9 ml) added 2-mercaptoacetic acid (25 µl, 0.36 mmol) and LiOH (17 mg, 0.72 mmol). The reaction mixture was stirred at rt and monitored by UPLC-MS. After 1 h and 45 min the reaction was almost complete, but formation of side-product was observed. Saturated $NaHCO_3$ aqueous solution (25 mL) was added and the resulting mixture was extracted with EtOAc (3 × 25 mL). The combined organic phases were washed with water (3 × 25 mL) and brine (25 mL), dried (Na_2SO_4), and concentrated in vacuo to give desired amine **10c** with some impurities. The crude was used in the next step without further purification. UPLC-MS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{20}Cl_2N$ 308.1, found 308.1.

(1*Z*,2*E*)-2-(1-Methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (10d)



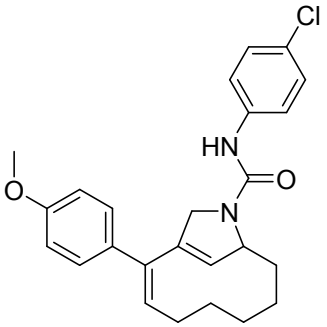
(1*Z*,2*E*)-2-(1-Methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-10-((2-nitrophenyl)sulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (**9d**) (55 mg, 0.11 mmol) was dissolved in DMF (1 ml) and added 2-mercaptoacetic acid (31 µl, 0.44 mmol) and LiOH (21 mg, 0.89 mmol). The reaction mixture was stirred for 1 h at 25 °C, before saturated $NaHCO_3$ aqueous solution (25 mL) was added followed by extraction with EtOAc (3 × 25 mL). The combined organic phases were washed with water (25 mL) and brine (25 mL), dried (Na_2SO_4). Concentration *in vacuo* afforded the desired amine **10d**, which was used in the next step without further purification. UPLC-MS (ESI) m/z: $[M+H]^+$ calcd. for $C_{16}H_{21}F_3N_3$ 312.2, found 312.2.

(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-N-phenyl-10-azabicyclo[7.2.1]dodeca-1(12),2-diene-10-carboxamide (11a)



(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10b** (30 mg, 0.11 mmol) was dissolved in DMF (1 mL) and phenyl isocyanate (19 mg, 0.18 mmol) was added followed by triethylamine (16 µl, 0.11 mmol). After stirring the reaction mixture at rt for 1 h, additional 4 mg of phenyl isocyanate was added, and the reaction mixture was stirred for another 1 h, after which full conversion of the starting amine was observed as monitored by UPLC-MS. Purification by preparative HPLC (acetonitrile/water, 0.1% HCOOH) afforded the desired urea **11a** (32 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, 2H, *J* = 7.6 Hz, phenyl H), 7.35 (d, 2H, *J* = 8.8 Hz, phenyl H), 7.28 (m, 2H, phenyl H), 7.02 (t, *J* = 7.4 Hz, 1H, phenyl H), 6.85 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.21 (m, 2H, NH and CH=*C–C=CHCHN*), 5.67 (m, 1H, *CH*=*C–C*=CH*CHN*), 5.08 (m, 1H, *CH*=*C–C*=*CH*CH*N*), 4.42 (m, 2H, CH_2*NCONH*), 3.81 (s, 3H, OCH_3), 2.36 (m, 2H, cyclodecadiene CH_2), 2.09 (m, 1H, cyclodecadiene CH_2), 1.63-1.31 (m, 7H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 153.4, 139.1, 136.7, 131.3, 129.0 (2), 129.0, 128.3, 126.8 (2), 123.1, 120.0, 119.7 (2), 114.0 (2), 64.7, 56.5, 55.5, 32.8, 28.6, 28.6, 25.0, 18.9. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{25}H_{29}N_2O_2$ 389.2229, found 389.2225.

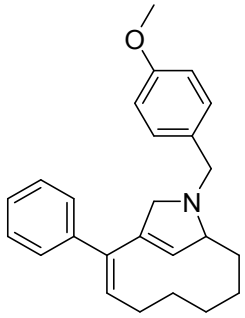
(1*Z*,2*Z*)-*N*-(4-Chlorophenyl)-2-(4-methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene-10-carboxamide (11b)



(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10b** (30 mg, 0.11 mmol) was dissolved in DMF (1 mL) and 4-chlorophenyl isocyanate (21 µl, 0.17 mmol) was added followed by triethylamine (16 µl, 0.11 mmol). After stirring the reaction mixture at rt for 1 h, additional 4 µl of chlorophenyl isocyanate was added, and the reaction mixture was stirred for another 1 h, after which full conversion of the starting amine was observed as monitored by UPLC-MS. Purification by preparative HPLC (acetonitrile/water, 0.1% HCOOH) afforded the desired urea **11b** (30 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.9 Hz, 2H, phenyl H), 7.34 (d, 2H, *J* = 8.8 Hz, phenyl H), 7.23 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.85 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.21 (m, 2H, NH and CH=*C–C=CHCHN*), 5.68 (m, 1H, *CH*=*C–C*=CH*CHN*), 5.07 (m, 1H, *CH*=*C–C*=*CH*CH*N*), 4.42 (m, 2H, CH_2*NCONH*), 3.80 (s, 3H, OCH_3), 2.34 (m, 2H, cyclodecadiene CH_2),

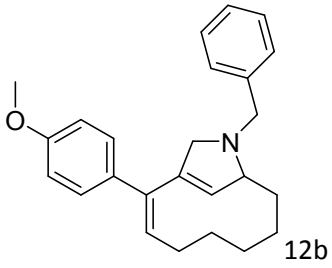
2.09 (m, 1H, cyclodecadiene CH_2), 1.63-1.33 (m, 7H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 153.1, 137.8, 136.6, 131.3, 129.0, 129.0 (2), 128.4, 127.9, 126.8 (2), 121.2, 120.8 (2), 114.0 (2), 64.8, 56.5, 55.5, 32.8, 28.6, 28.6, 25.0, 19.0. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{25}H_{28}ClN_2O_2$ 423.1839, found 423.1837.

(1*Z*,2*Z*)-10-(4-Methoxybenzyl)-2-phenyl-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (12a)



(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10a** (27 mg, 0.11 mmol) was dissolved in CH_2Cl_2 (1 mL) and added AcOH (1.3 µl, 0.022 mmol), sodium triacetoxyhydroborate (71 mg, 0.33 mmol), and anisaldehyde (26 mg, 0.19 mmol). The reaction mixture was stirred overnight at rt, before water was added followed by extraction with CH_2Cl_2 (3 × 25 mL). The combined organic phases were washed with brine (25 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by flash column chromatography (5:25:75, triethylamine/EtOAc/heptane) afforded desired amine **12a** (16 mg, 36%) with trace impurities. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.6 Hz, 2H, phenyl H), 7.30 (m, 4H, phenyl H), 7.20 (m, 1H, phenyl H), 6.85 (d, 2H, *J* = 8.6 Hz, phenyl H), 6.19 (dd, 1H, *J* = 8.4 and 6.8 Hz, CH=*C*–*C*=*CHCHN*), 5.61 (m, 1H, *CH*=*C*–*C*=CH*CHN*), 4.11 (m, 1H, *CH*=*C*–*C*=*CH*CH*N*), 3.93 (d, 1H, *J* = 13.5 Hz, benzyl CH_2), 3.91 (d, 1H, *J* = 13.5 Hz, benzyl CH_2), 3.82 (m, 1H, CH_2), 3.80 (s, 3H, OCH_3), 3.60 (td, 1H, *J* = 14.2 and 2.5 Hz, *CH*=*C*CH_2*N*), 2.43 (m, 1H, cyclodecadiene CH_2), 2.04 (m, 1H, cyclodecadiene CH_2), 1.72 (m, 2H, cyclodecadiene CH_2), 1.64-1.30 (m, 6H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 139.6, 138.5, 136.9, 133.4, 129.7, 129.5, 128.4, 128.4, 127.0, 125.8, 113.7, 70.4, 64.0, 58.7, 55.4, 34.8, 28.9, 28.5, 25.7, 20.0; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{25}H_{30}NO$ 360.2327, found 360.2342.

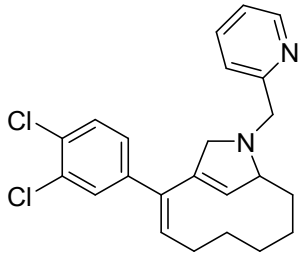
(1*Z*,2*Z*)-10-Benzyl-2-(4-methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (12b)



(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10b** (30 mg, 0.11 mmol), AcOH (1.3 µl, 0.022 mmol), sodium triacetoxyhydroborate (71 mg, 0.33 mmol), and benzaldehyde (18 mg, 0.17 mmol) were dissolved in DMA (1 mL). The reaction mixture was stirred at rt overnight. Purification by preparative HPLC (acetonitrile/H_2O, 0.1% HCOOH) afforded amine **12b** (23 mg, 57%) with traces of HCOOH. ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (m, 2H, phenyl H), 7.43

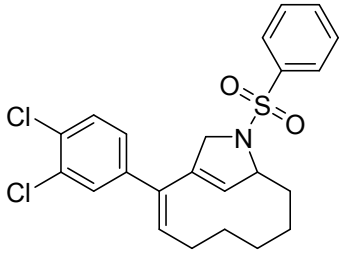
(m, 3H, phenyl H), 7.08 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.81 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.21 (t, 1H, *J* = 8.0 Hz, CH=*C*–*C*=*CHCHN*), 5.67 (m, 1H, *CH*=*C*–*C*=CH*CHN*), 4.71 (d, 1H, *J* = 16.4 Hz, *CH*=*C*CH_2*N*), 4.62 (m, 1H, *CH*=*C*–*C*=*CH*CH*N*), 4.54 (d, 1H, *J* = 13.0 Hz, benzyl CH_2), 4.26 (d, 1H, *J* = 13.0 Hz, benzyl CH_2), 3.89 (dd, 1H, *J* = 16.4 and 2.0 Hz, *CH*=*C*CH_2*N*), 3.81 (s, 3H, OCH_3), 2.30-2.11 (m, 3H, cyclodecadiene CH_2), 1.71-1.25 (m, 7H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 159.4, 135.3, 134.8, 130.8, 130.7, 130.3, 129.9, 129.7, 129.4, 129.1, 126.7, 114.1, 72.3, 60.8, 59.4, 55.5, 30.7, 28.2, 27.8, 24.6, 19.6; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{25}H_{30}NO$ 360.2327, found 360.2342.

(1*Z*,2*Z*)-2-(3,4-Dichlorophenyl)-10-(pyridin-2-ylmethyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (12c)



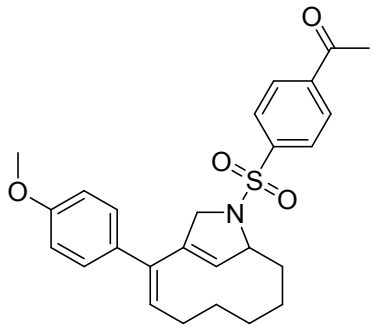
(1*Z*,2*Z*)-2-(3,4-Dichlorophenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10c** (31 mg, 0.10 mmol) was dissolved in CH_2Cl_2 (4 ml) and added 4Å molecular sieves, picolinaldehyde (30 mg, 0.28 mmol), and sodium triacetoxyhydroborate (44 mg, 0.21 mmol). The reaction mixture was stirred at rt for 1 h before being diluted with CH_2Cl_2 (25 mL). The organic phase was washed with water (25 mL) and brine (25 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by flash column chromatography (1:2:18, triethylamine/EtOAc/heptane) afforded the desired compound **12c** with minor impurities (10 mg, 24%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d,1 H, *J* = 4.6 Hz, pyridinyl H), 7.69 (m, 1H, pyridinyl H), 7.59 (m, 1H, pyridinyl H), 7.43 (d, 1H, *J* = 1.2 Hz, phenyl H), 7.32 (d, 1H, *J* = 8.4 Hz, phenyl H), 7.19 (m, 2H, phenyl and pyridinyl H), 6.22 (m, 1H, CH=*C*–*C*=*CHCHN*), 5.64 (m, 1H, *CH*=*C*–*C*=CH*CHN*), 4.35-4.02 (m, 4H, *CH*=*C*–*C*=*CH*CH*N, CH*=*C*CH_2*N*CH_2), 3.74 (d, 1H, *J* = 13.7 Hz, *CH*=*C*CH_2*NCH*$_2$), 2.42 (m, 1H, cyclodecadiene CH_2), 2.07 (m, 1H, cyclodecadiene CH_2), 1.89 (m, 1H, cyclodecadiene CH_2), 1.69-1.25 (m, 7H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 149.0, 137.2, 136.6, 132.4, 130.8, 130.2, 127.4, 125.7, 124.9, 122.5, 122.0, 121.7, 121.0, 119.1, 70.8, 63.7, 60.6, 31.6, 28.5, 28.1, 25.4, 19.8. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{23}H_{25}Cl_2N_2$ 399.1395, found 399.1401.

(1*Z*,*2Z*)-2-(3,4-Dichlorophenyl)-10-(phenylsulfonyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene (14a)



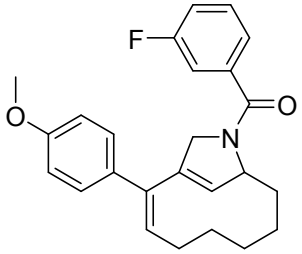
Triethylamine (19 µl, 0.14 mmol) and benzenesulfonyl chloride (15 µl, 0.14 mmol) were dissolved in dry CH_2Cl_2 (0.4 mL) under argon atmosphere and cooled to 0 °C. A solution of amine **10c** (0.9 mmol) in CH_2Cl_2 (0.5 mL) was added and the reaction mixture was allowed to warm to rt. After stirring for 1 h the reaction mixture was concentrated in vacuo. Purification by flash column chromatography (3: 17, EtOAc/heptane) afforded the desired sulfonamide **14a** (12 mg, 30%) with solvent traces. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (m, 2H, phenyl H), 7.65 (m, 1H, phenyl H), 7.57 (m, 2H, phenyl H), 7.25 (d, 1H, *J* = 8.4 Hz, phenyl H), 7.10 (d, 1H, *J* = 2.2 Hz, phenyl H), 6.89 (dd, 1H, *J* = 8.4 and 2.2 Hz, phenyl H), 6.28 (dd, 1H, *J* = 8.2 and 7.3 Hz, CH=*C–C=CHCHN*), 5.45 (m, 1H, *CH=C–C=*CH*CHN*), 4.89 (m, 1H, *CH=C–C=CH*CH*N*), 4.34 (ddd, 1H, *J* = 15.0, 4.6, 1.6 Hz, CH_2NSO_2), 4.22 (td, 1H, *J* = 15.0 and 2.0 Hz, CH_2NSO_2), 2.28 (m, 2H, cyclodecadiene CH_2), 2.06 (m, 1H, cyclodecadiene CH_2), 1.54 (m, 6H, cyclodecadiene CH_2), 1.23 (m, 1H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 138.0, 134.5, 134.3, 133.0, 132.7, 132.4, 132.2, 131.3, 130.4, 129.4, 127.3, 127.2, 124.5, 67.9, 58.2, 35.7, 28.6, 28.3, 25.2, 19.0; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{23}H_{24}Cl_2NO_2S$ 448.0905, found 448.0900.

1-(4-(((1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-dien-10-yl)sulfonyl) phenyl)ethan-1-one (14b)



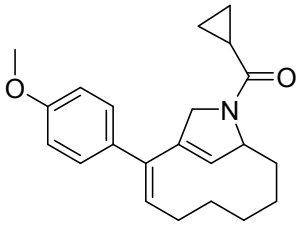
Triethylamine (23 µl, 0.16 mmol) and 4-acetylbenzenesulfonyl chloride (35 mg, 0.16 mmol) were dissolved in dry CH_2Cl_2 (0.5 mL) and the reaction mixture was cooled to 0 °C. (1Z,2Z)-2-(4-methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10b** (29 mg, 0.11 mmol) dissolved in dry CH_2Cl_2 (0.5 mL) was added to the reaction mixture, which was stirred and allowed to warm to rt over 1 h. Concentration *in vacuo* and purification by preparative HPLC (acetonitrile/H_2O, 0.1% HCCOH) afforded pure sulfonamide **14b** (20 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, 2H, *J* = 8.5 Hz, phenyl H), 7.96 (d, 2H, *J* = 8.5 Hz, phenyl H), 6.97 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.71 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.13 (dd, 1H, *J* = 8.1 and 7.5 Hz, CH=*C–C=CHCHN*), 5.43 (m, 1H, *CH=C–C=*CH*CHN*), 4.90 (m, 1H, *CH=C–C=CH*CH*N*), 4.35 (ddd, 1H, *J* = 14.8, 4.5, 1.5 Hz, CH_2NSO_2), 4.24 (td, 1H, *J* = 14.8 and 1.9 Hz, CH_2NSO_2), 3.78 (s, 3H, OCH_3), 2.68 (s, 3H, $COCH_3$), 2.25 (m, 2H, cyclodecadiene CH_2), 2.02 (m, 1H, cyclodecadiene CH_2), 1.63-1.36 (m, 6H, cyclodecadiene CH_2), 1.26 (m, 1H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 159.2, 142.3, 140.1, 135.7, 135.4, 130.9, 130.7, 129.1, 128.4, 127.7, 126.4, 113.9, 68.0, 58.3, 55.4, 35.6, 28.6, 28.5, 27.0, 25.0, 19.0; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{26}H_{30}NO_4S$ 452.1895, found 452.1897.

(3-Fluorophenyl)((1*Z*,2*Z*)-2-(4-methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-dien-10-yl)methanone (15a)



(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10b** (30 mg, 0.11 mmol), 3-fluorobenzoic acid (20 mg, 0.14 mmol), *N*-ethyl-*N*-diisopropylamine (24 µL, 0.14 mmol) were dissolved in dry DMF (1 ml) under argon atmosphere. TBTU (45 mg, 0.14 mmol) was added to the reaction mixture which was stirred at rt for 10 min. Purification by preparative HPLC (acetonitrile/H_2O, 0.1% HCOOH) afforded the desired amide **15a** (28 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) Rotamers 2/1. Rotamer I: δ 7.45-7.25 (m, 5H, phenyl H), 7.12 (m, 1H, phenyl H), 6.87 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.20 (m, 1H, CH=*C–C=CHCHN*), 5.72 (m, 1H, *CH=C–C=*CH*CHN*), 5.39 (m, 1H, *CH=C–C=CH*CH*N*), 4.47 (ddd, 1H, *J* = 14.8, 4.0, 1.4 Hz, CH_2*NCO*), 4.17 (d, 1H, *J* = 14.9 Hz, CH_2*NCO*), 3.78 (s, 3H, OCH_3), 2.58 (m, 1H, cyclodecadiene CH_2), 2.31 (m, 1H, cyclodecadiene CH_2), 2.09 (m, 1H, cyclodecadiene CH_2), 1.69-1.14 (m, 7H, cyclodecadiene CH_2). Rotamer II: δ 7.45-7.25 (m, 5H; phenyl H), 7.12 (m, 1H, phenyl H), 6.82 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.20 (m, 1H, CH=*C–C=CHCHN*), 5.53 (m, 1H, *CH=C–C=*CH*CHN*), 4.93 (m, 1H, CH_2*NSO*$_2$), 4.65 (m, 2H, CH_2*NSO*$_2$ and *CH=C–C=CH*CH*N*), 3.82 (s, 3H, OCH_3), 2.31 (m, 1H, , cyclodecadiene CH_2), 2.09 (m, 1H, , cyclodecadiene CH_2), 1.69-1.14 (m, 8H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$), major rotamer: 168.5 and 168.5 ($^4J_{C,F}$ = 2 Hz), 163.8 and 161.3 ($^1J_{C,F}$ = 246 Hz), 159.2, 139.2 and 139.1 ($^3J_{C,F}$ = 8 Hz), 136.6, 134.4, 131.8, 131.1 and 130.7 ($^2J_{C,F}$ = 22 Hz), 130.4 and 130.3 ($^3J_{C,F}$ = 8 Hz), 128.4, 126.7 (2), 122.7 and 122.7 ($^4J_{C,F}$ = 2 Hz), 116.9, 114.4 and 114.2 ($^2J_{C,F}$ = 22 Hz), 114.0 (2), 65.0, 59.4, 55.4, 32.2, 28.9, 28.6, 25.0, 19.3. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{25}H_{27}FNO_2$ 392.2026, found 392.2029.

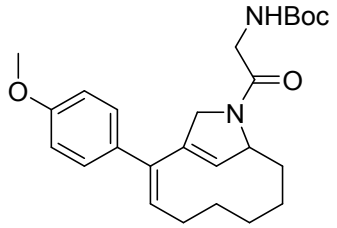
Cyclopropyl((1*Z*,2*Z*)-2-(4-methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-dien-10-yl) methanone (15b)



(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10b** (30 mg, 0.11 mmol), cyclopropanecarboxylic acid (12 mg, 0.14 mmol), and *N*-ethyl-*N*-diisopropylamine (24 µL, 0.14 mmol) were dissolved in dry DMF (1 ml) under argon atmosphere. TBTU (45 mg, 0.14 mmol) was added to the reaction mixture, which was stirred for another 10 min. Purification by preparative HPLC (acetonitrile/H_2O, 0.1% HCOOH) afforded amide **15b** (28 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$), rotamers 1:1, δ 7.37 (d, 2H, *J* = 8.8 Hz, aromatic H), 6.84 (d, 2H, *J* = 8.8 Hz, aromatic H), 6.19 (m, 1H, CH=*C–C=CHCHN*), 5.65 and 5.57 (m, 1H, *CH=C–C=*CH*CHN*), 5.11 (m, 1H, *CH=C–C=CH*CH*N*), 4.63-4.33 (m, 2H, CH_2*NCO*), 3.80/3.79 (s, 3H, OCH_3), 2.50-2.28 (m, 2H, cyclodecadiene CH_2), 2.10-2.04 (m, 1H, cyclopropyl CH), 1.73-1.24 (m, 8H, cyclodecadiene CH_2), 1.13-0.74 (m, 4H, cyclopropyl CH_2). ^{13}C NMR (100 MHz, $CDCl_3$), rotamer one: δ 172.3, 159.1,

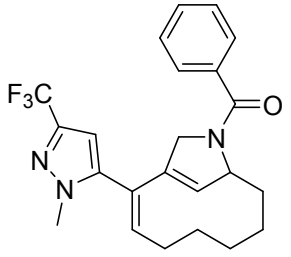
137.1, 135.9, 131.6, 130.6, 127.5, 126.7 (2), 113.9 (2), 64.3, 57.0, 55.4, 34.2, 28.7, 28.4, 25.0, 18.9, 12.7, 8.2, 7.7; rotamer two: 171.9, 159.2, 136.8, 134.1, 132.3, 131.4, 128.3, 126.8 (2), 114.0 (2), 64.8, 57.2, 55.4, 31.8, 28.6, 28.3, 24.5, 18.3, 12.7, 7.8, 7.4. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{22}H_{28}NO_2$ 338.2120, found 338.2128.

_t_-Butyl (2-((1*Z*,2*Z*)-2-(4-methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-dien-10-yl)-2-oxoethyl)carbamate (15c)



(1*Z*,2*Z*)-2-(4-Methoxyphenyl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10b** (30 mg, 0.11 mmol), (tert-butoxycarbonyl)glycine (24 mg, 0.14 mmol), and *N*-ethyl-*N*-diisopropylamine (24 µL, 0.14 mmol) were dissolved in dry DMF (1 ml) under argon atmosphere. TBTU (45 mg, 0.14 mmol) was added to the reaction mixture, which was stirred for another 10 min. Purification by preparative HPLC (acetonitrile/H_2O, 0.1% HCOOH) afforded pure amide **15c** (30 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$), rotamers 2:1, major rotamer: δ 7.32 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.85 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.21-6.19 (m, 1H, CH=*C*–*C*=*CHCHN*), 5.66 (d, 1H, *J* = 1.6 Hz *CH*=*C*–*C*=CH*CHN*), 5.48 (br s, 1H, NH), 5.14 (m, 1H, *CH*=*C*–*C*=*CH*CH*N*), 4.40-4.30 (m, 2H, CH_2*NCO*), 3.92-3.88 (m, 2H, *NCO*CH_2), 3.81 (s, 3H, OCH_3), 2.52-2.46 (m, 1H, cyclodecadiene CH_2), 2.30-2.07 (m, 2H, cyclodecadiene CH_2), 1.60-1.53 (m, 3H, cyclodecadiene CH_2), 1.44 (s, 9H, *t*-butyl CH_3), 1.42-1.28 (m, 4H, cyclodecadiene CH_2). Minor rotamer: δ 7.31 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.84 (d, 2H, *J* = 8.8 Hz, phenyl H), 6.20-6.18 (m, 1H, CH=*C*–*C*=*CHCHN*), 5.56 (d, 1H, *J* = 1.6 Hz, *CH*=*C*–*C*=CH*CHN*), 5.24 (br s, 1H, NH), 4.89 (m, 1H, *CH*=*C*–*C*=*CH*CH*N*), 4.55-4.34 (m, 2H, CH_2*NCO*), 4.10-3.92 (m, 2H, *NCO*CH_2), 3.80 (s, 3H, OCH_3), 2.31-2.07 (m, 3H, cyclodecadiene CH_2), 1.60-1.53 (m, 3H, cyclodecadiene CH_2), 1.44 (s, 9H, *t*-butyl CH_3), 1.42-1.28 (m, 4H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$), major rotamer: δ 166.7, 159.3, 156.0, 136.4, 134.0, 131.9, 131.1, 128.5, 126.7 (2), 114.0 (2), 79.7, 65.2, 55.8, 55.4, 43.1, 31.5, 28.5(3), 28.3,28.2, 24.9, 19.0. Minor rotamer: δ 167.4, 159.2, 156.0, 136.7, 135.6, 131.3, 130.3, 127.7, 126.7 (2), 113.9 (2), 79.8, 64.0, 56.9, 55.4, 42.8, 33.3, 28.5 (3), 28.3, 28.2, 24.5, 18.3. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{25}H_{35}N_2O_4$ 427.2597, found 427.2598 and 327.2067.

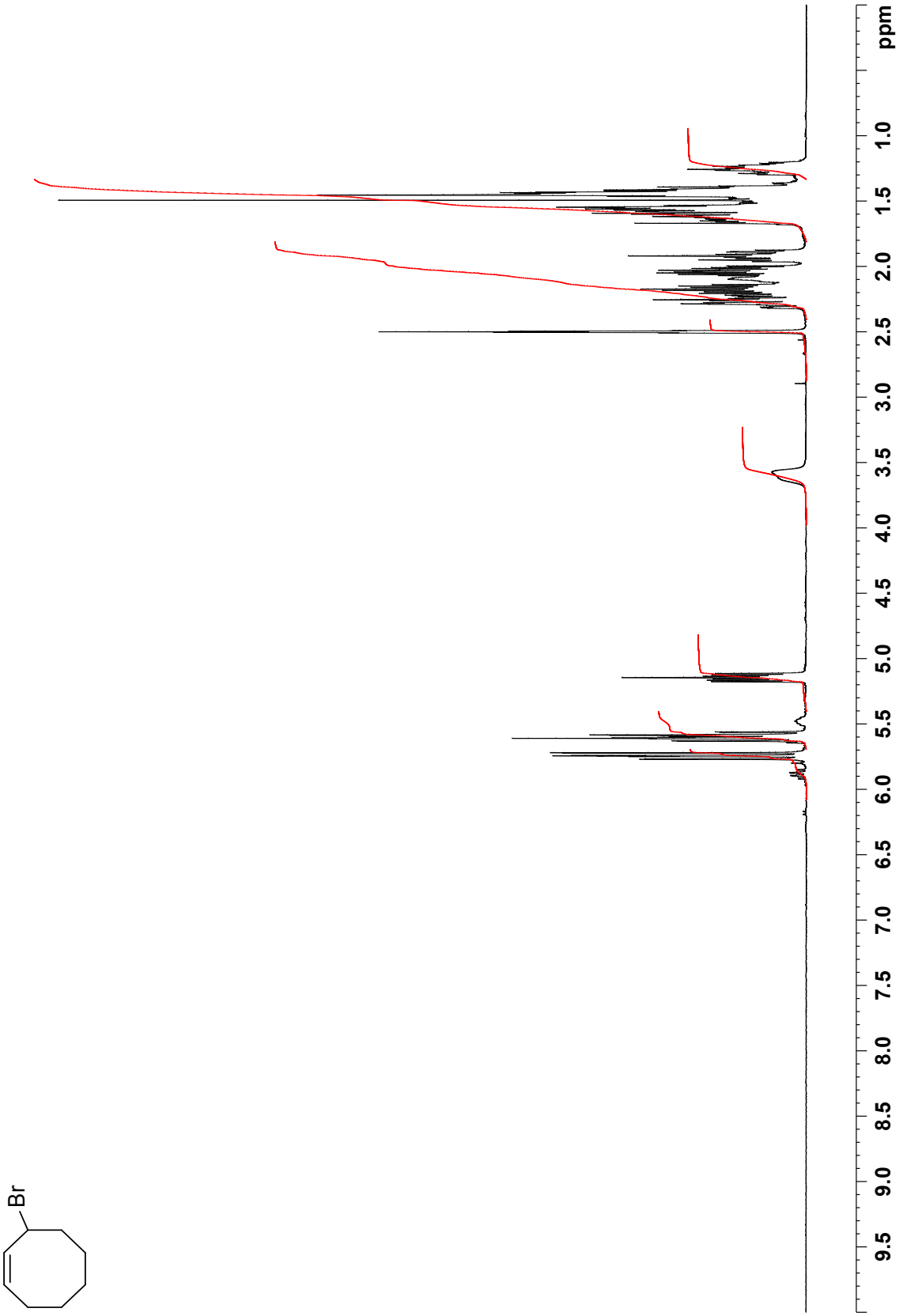
((1*Z*,2*E*)-2-(1-Methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-10-azabicyclo[7.2.1]dodeca-1(12),2-dien-10-yl)(phenyl)methanone (15d)



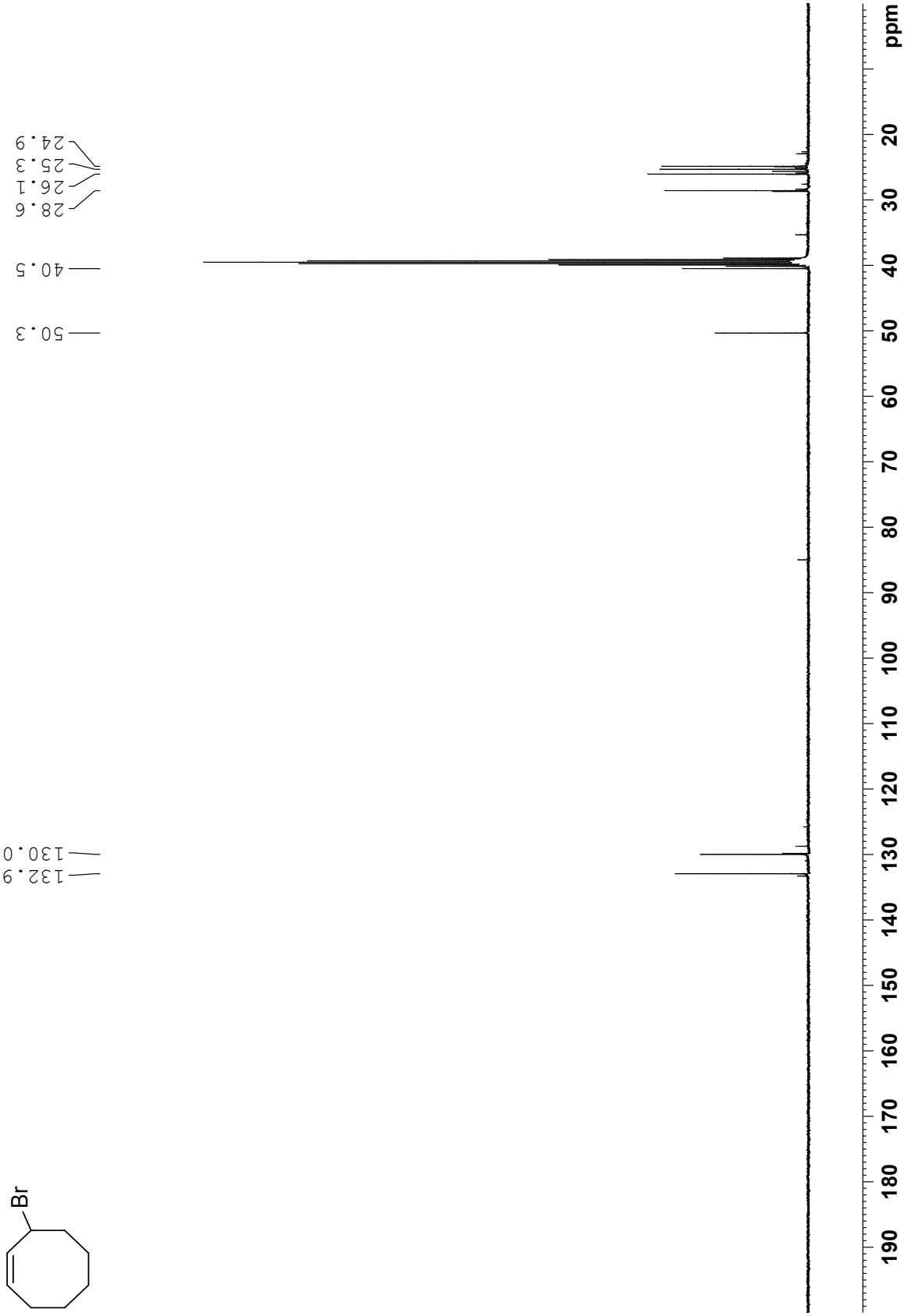
(1*Z*,2*E*)-2-(1-Methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-10-azabicyclo[7.2.1]dodeca-1(12),2-diene **10d** (34 mg, 0.11 mmol) was dissolved in dry DMF (1 mL) under argon atmosphere. TBTU (44 mg, 0.14 mmol) and DIPEA (18 mg, 0.14 mmol) were added. The reaction mixture was stirred for 1.5 h, before saturated NH_4Cl aqueous solution (25 mL) was added, followed by extraction with EtOAc (3 ×25 mL). The combined organic phases were washed with brine (25 mL), dried (MgSO4), and concentrated *in vacuo*. Purification by flash column chromatography (11: 9, EtOAc/heptane) afforded the desired amide **15d** (24 mg, 53%) with trace impurities. ^{1}H NMR (400 MHz, $CDCl_3$), rotamers 5:3, major rotamer, δ 7.53-7.40 (m, 5H, phenyl H), 6.34 (s, 1H, pyrazolyl H), 6.17-6.10 (m, 1H, CH=*C*–*C*=*CHCHN*), 5.87 (m, 1H, *CH*=*C*–*C*=CH*CHN*), 5.38 (m, 1H, *CH*=*C*–*C*=*CH*CH*N*), 4.51 (dd, 1H, *J* = 16.8 and 2.8 Hz, CH_2*NCO*), 4.14 (d, 1H, *J* = 16.8 Hz, CH_2*NCO*), 3.82 (s, 3H, *N*CH_3), 2.57-2.37 (m, 2H, cyclodecadiene CH_2), 2.23-2.18 (m, 1H, cyclodecadiene CH_2), 1.71-1.55 (m, 4H, cyclodecadiene CH_2), 1.37-1.21 (m, 3H, cyclodecadiene CH_2). ^{13}C NMR (100 MHz, $CDCl_3$), major rotamer, δ 170.3, 141.4 and 141.0 ($^2J_{C\text{-}F}$ = 35 Hz), 139.9, 138.2, 136.9, 133.3, 133.2, 130.2, 128.7 (2), 127.0 (2), 126.3, 122.6 and 119.9 ($^1J_{C\text{-}F}$ = 267 Hz), 104.3 and 104.3 ($^3J_{C\text{-}F}$ = 3 Hz), 64.7, 59.1, 38.8, 32.5, 28.9, 28.4, 25.8, 20.2. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{23}H_{25}F_3N_3O$ 416.1949, found 416.1948. HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{23}H_{25}F_3N_3O$ 416.1949, found 416.1948.

Characterization Spectra

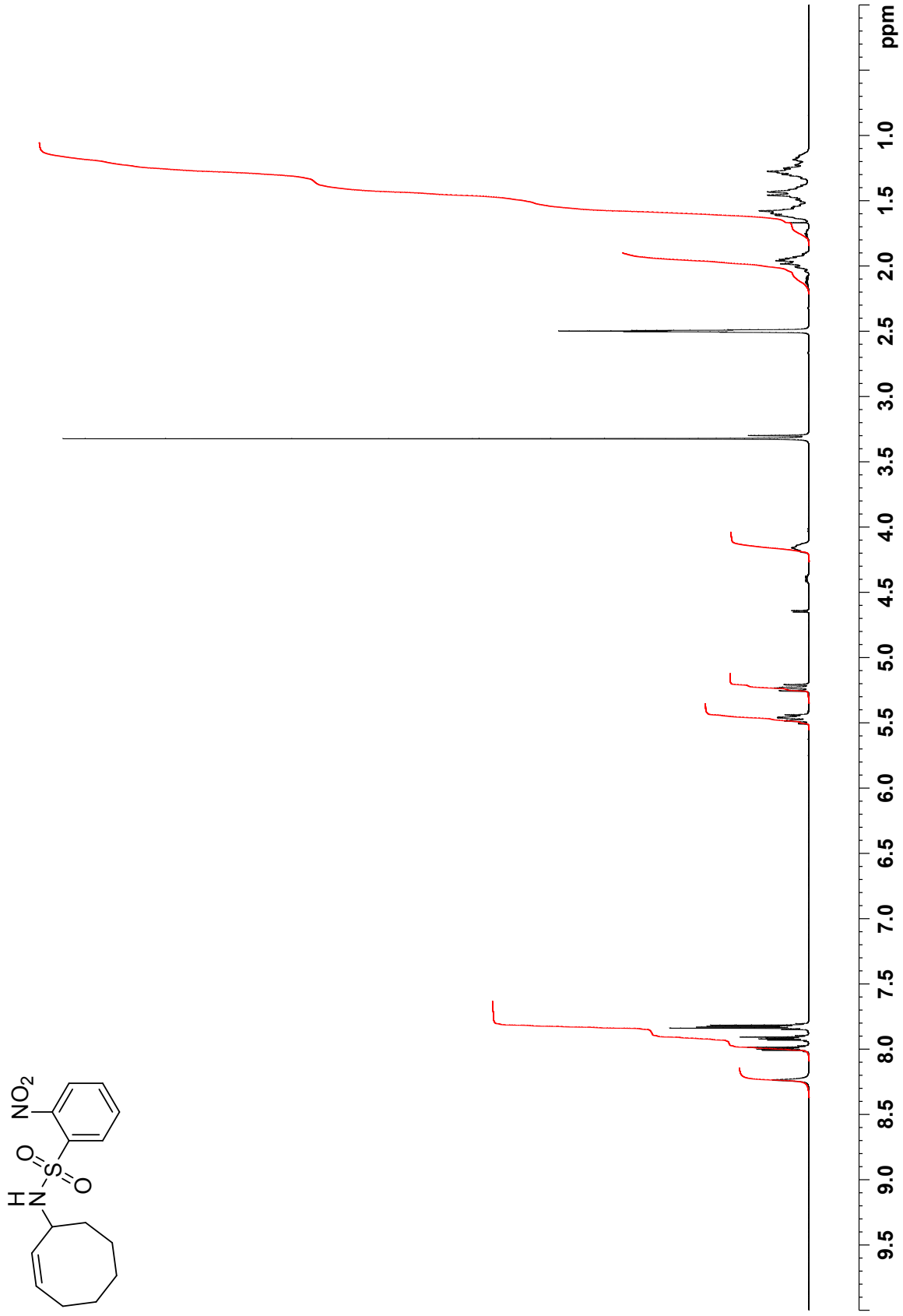
3, ^{1}H NMR (400 MHz, DMSO-d_6):


Br
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

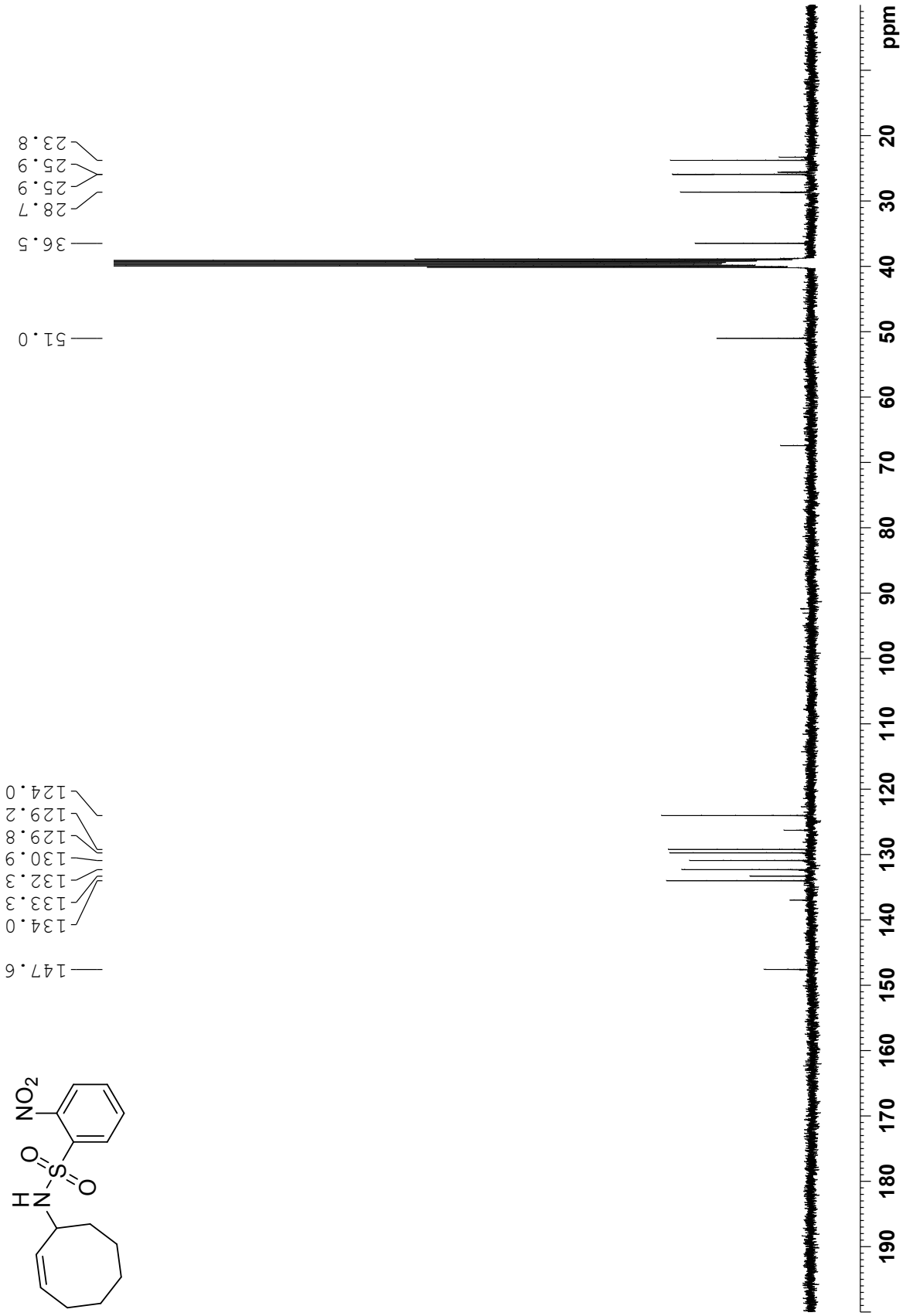
3, ^{13}C NMR (100 MHz, DMSO-d_6):



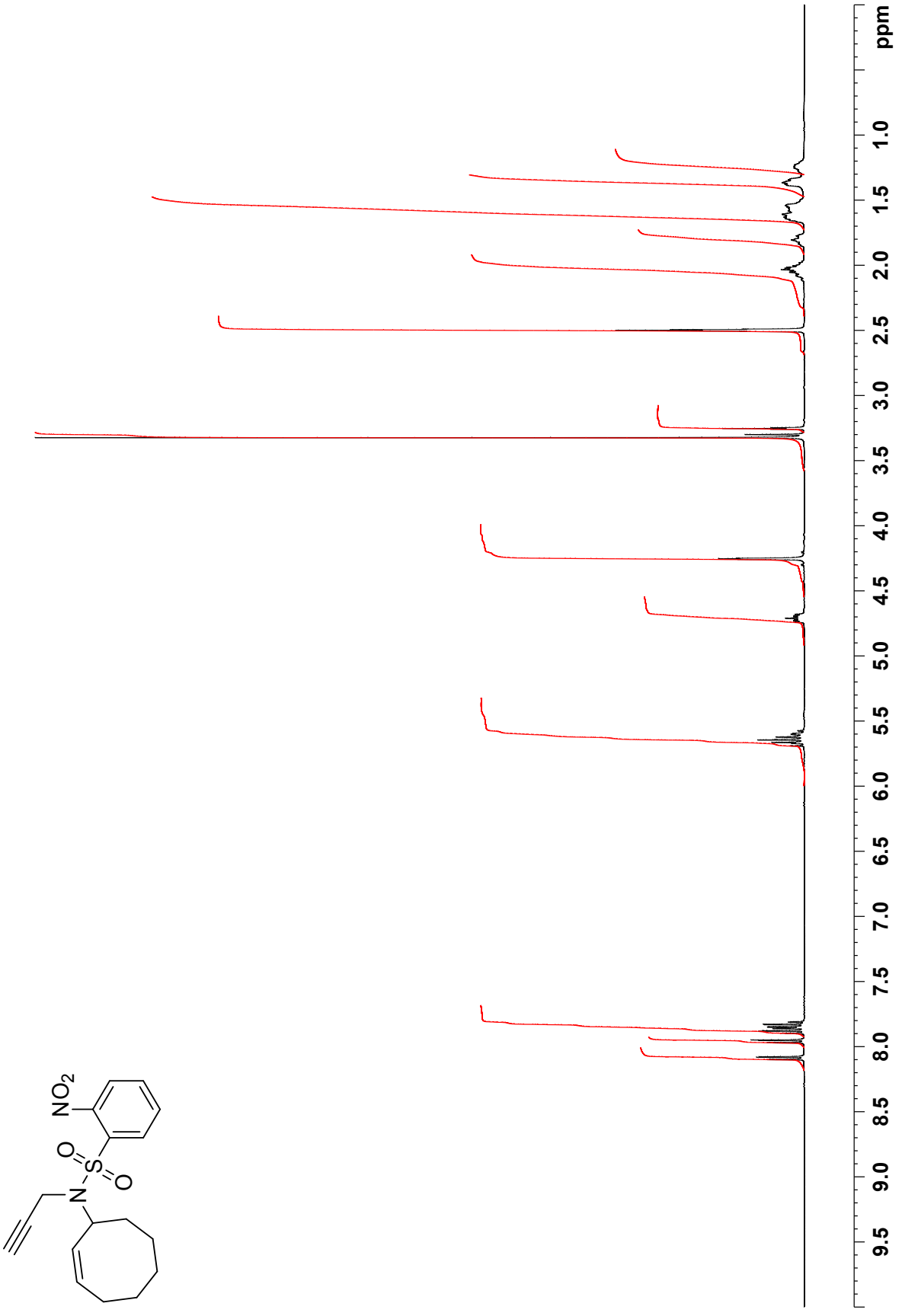
4, ^{1}H NMR (400 MHz, DMSO-d_6):



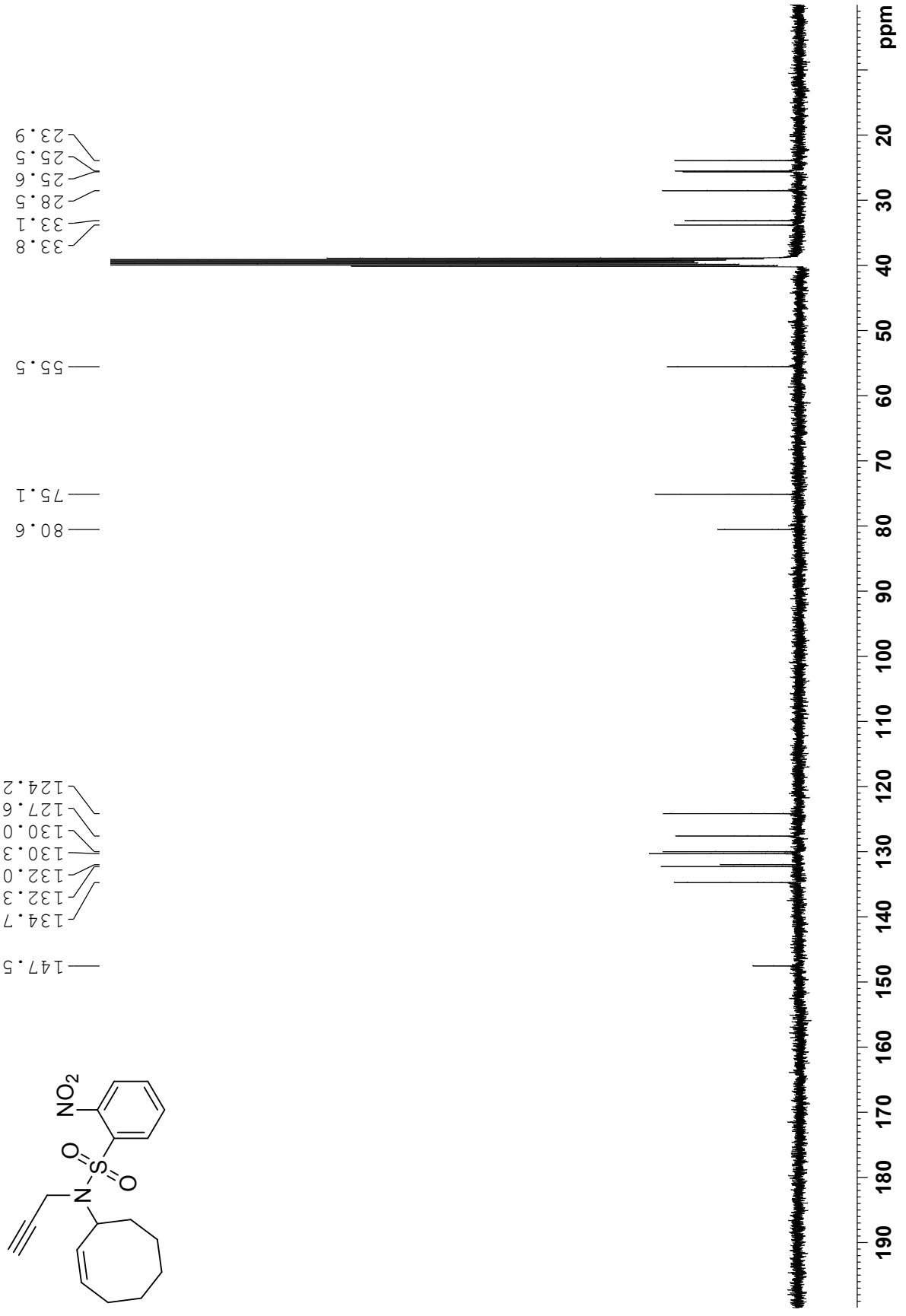
4, ^{13}C NMR (100 MHz, DMSO-d_6):



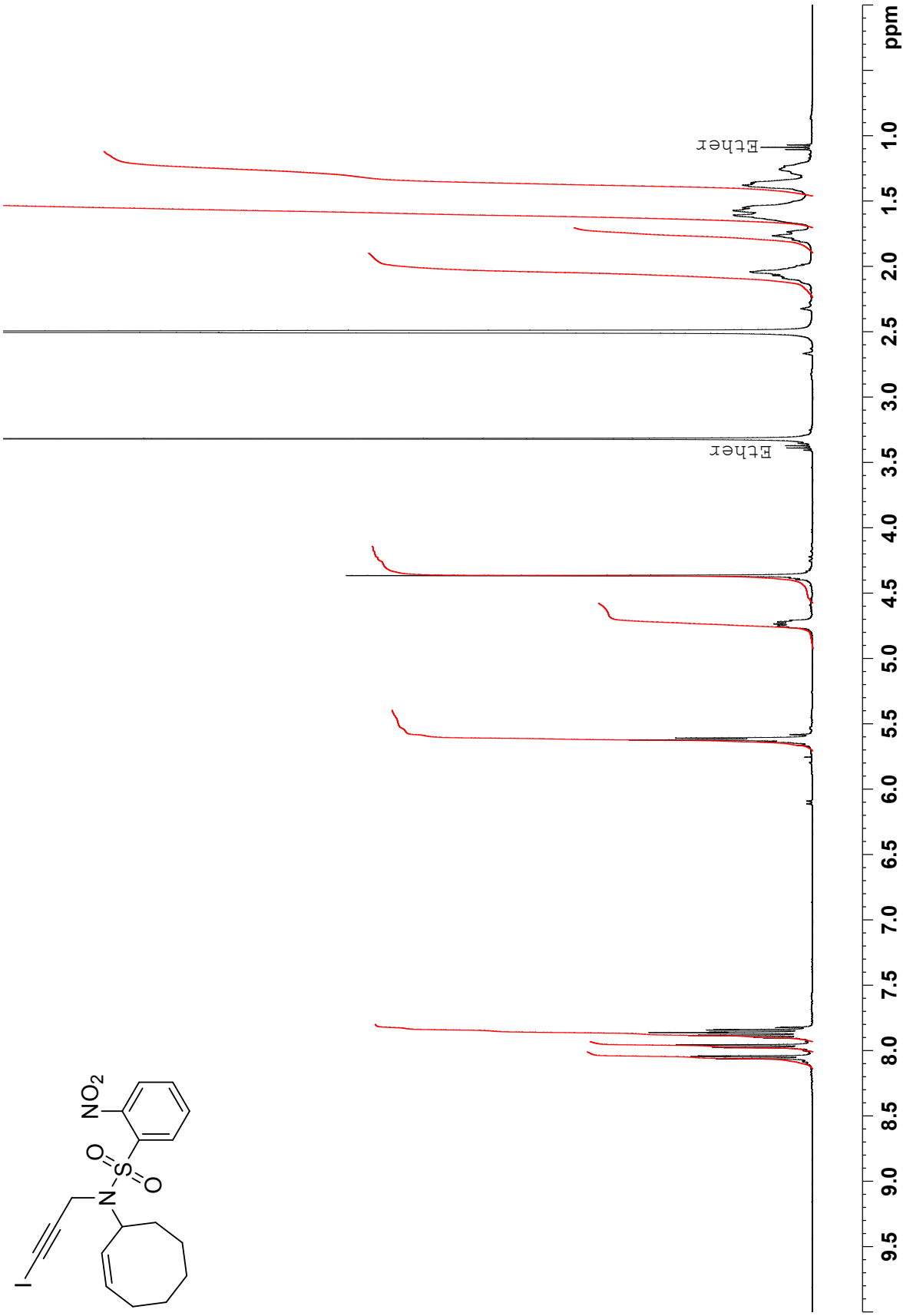
1, ^{1}H NMR (400 MHz, DMSO-d_6):



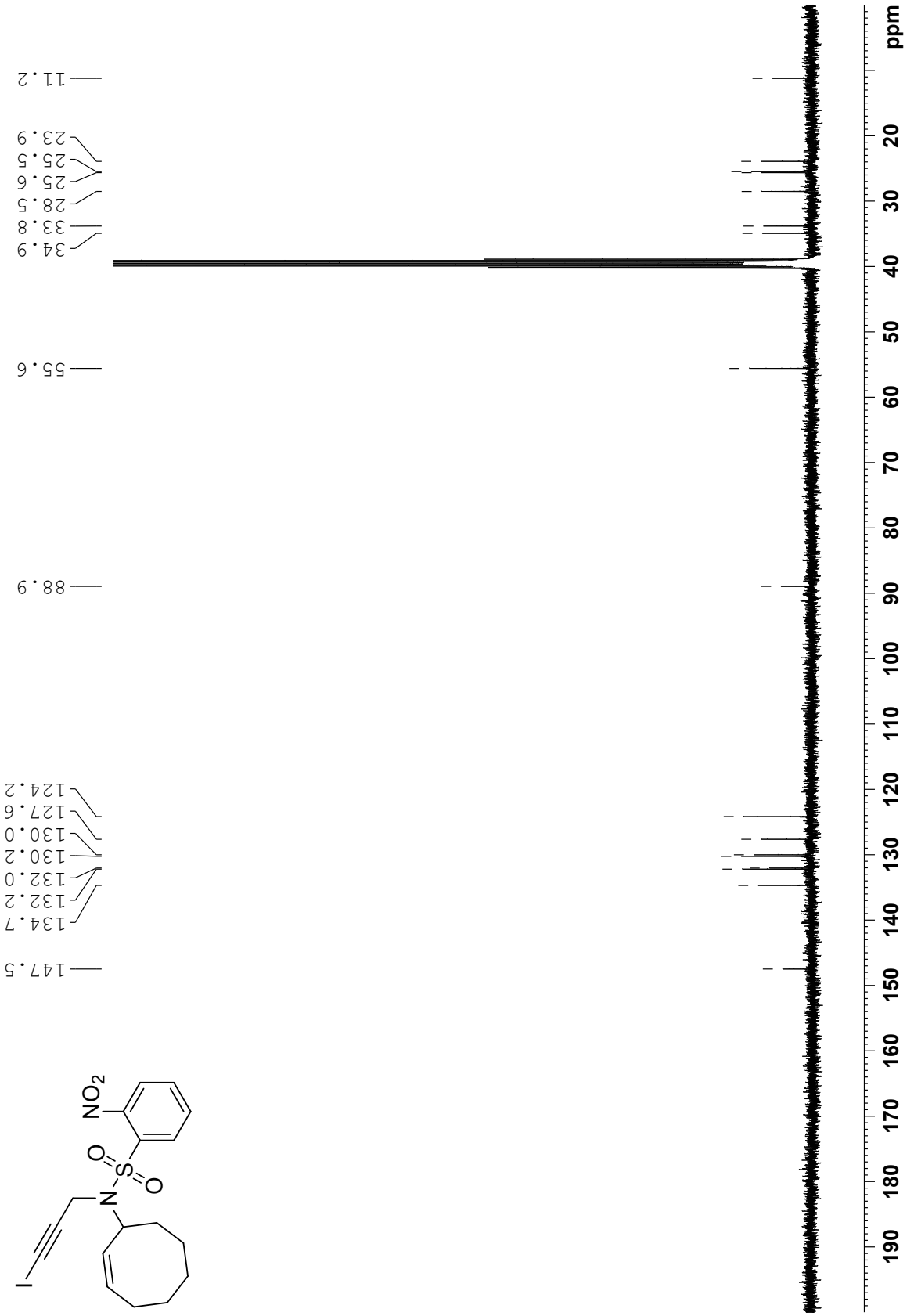
1, ^{13}C NMR (100 MHz, DMSO-d_6):



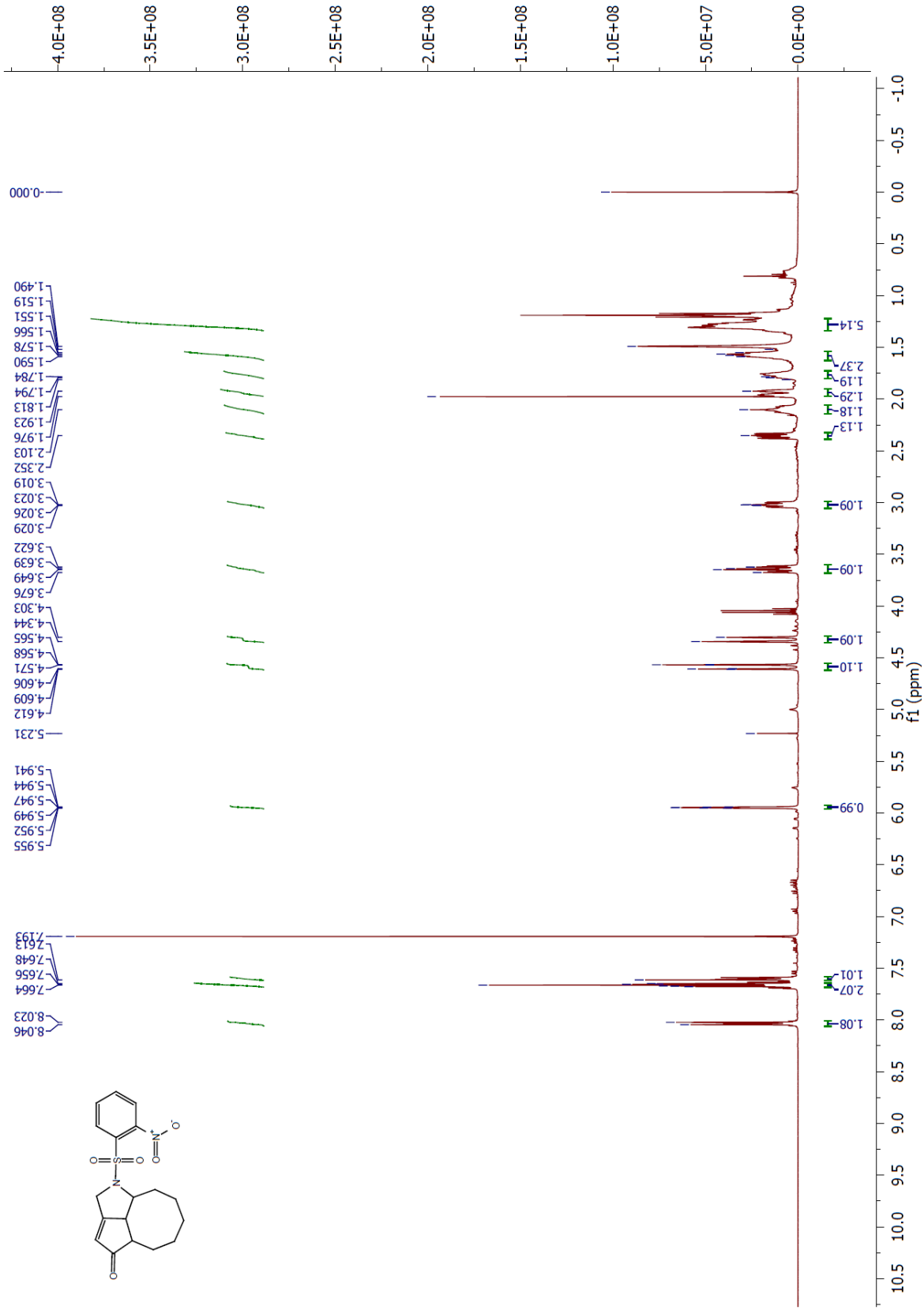
5, ^{1}H NMR (400 MHz, DMSO-d_6):



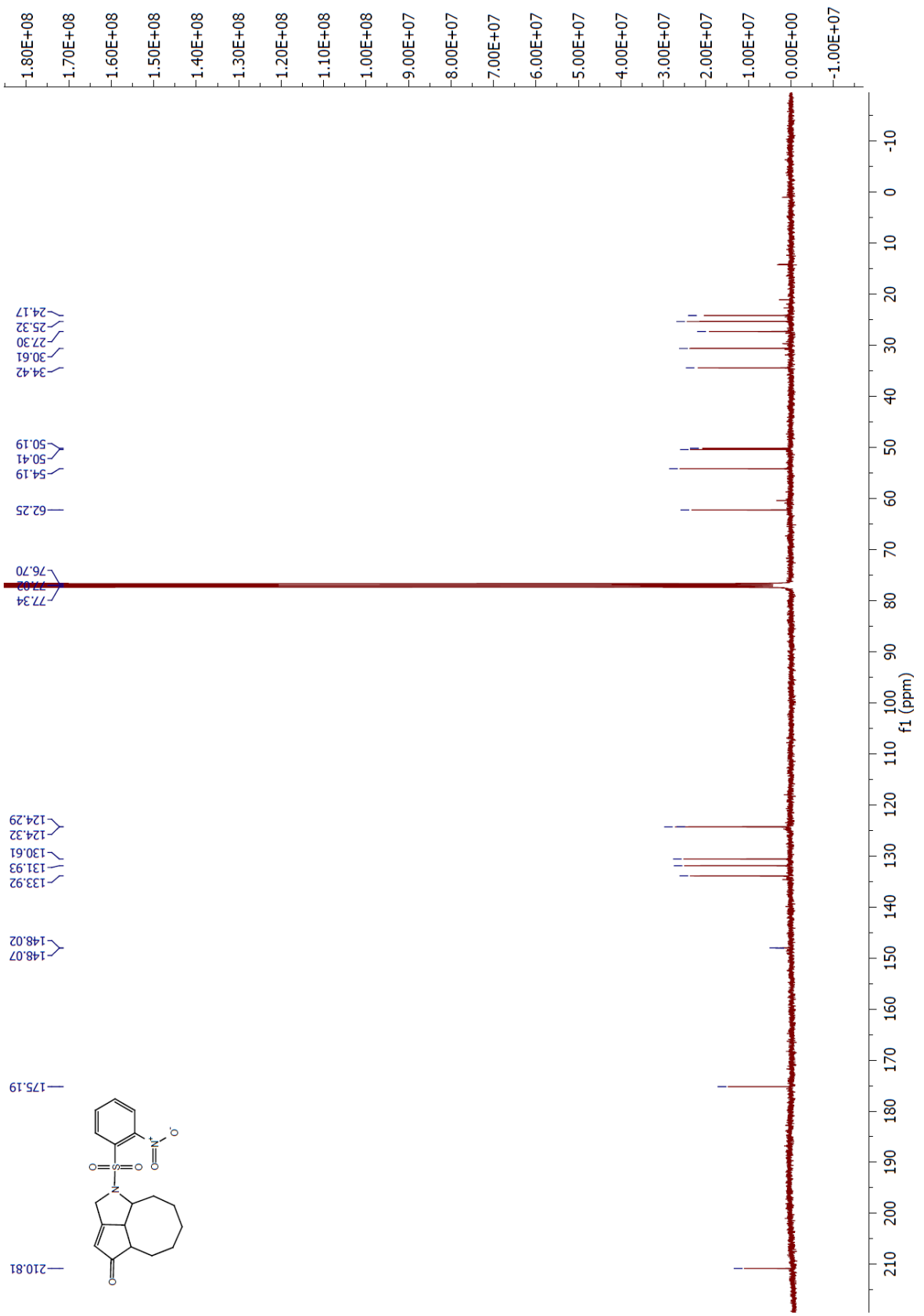
5, ^{13}C NMR (100 MHz, DMSO-d_6):



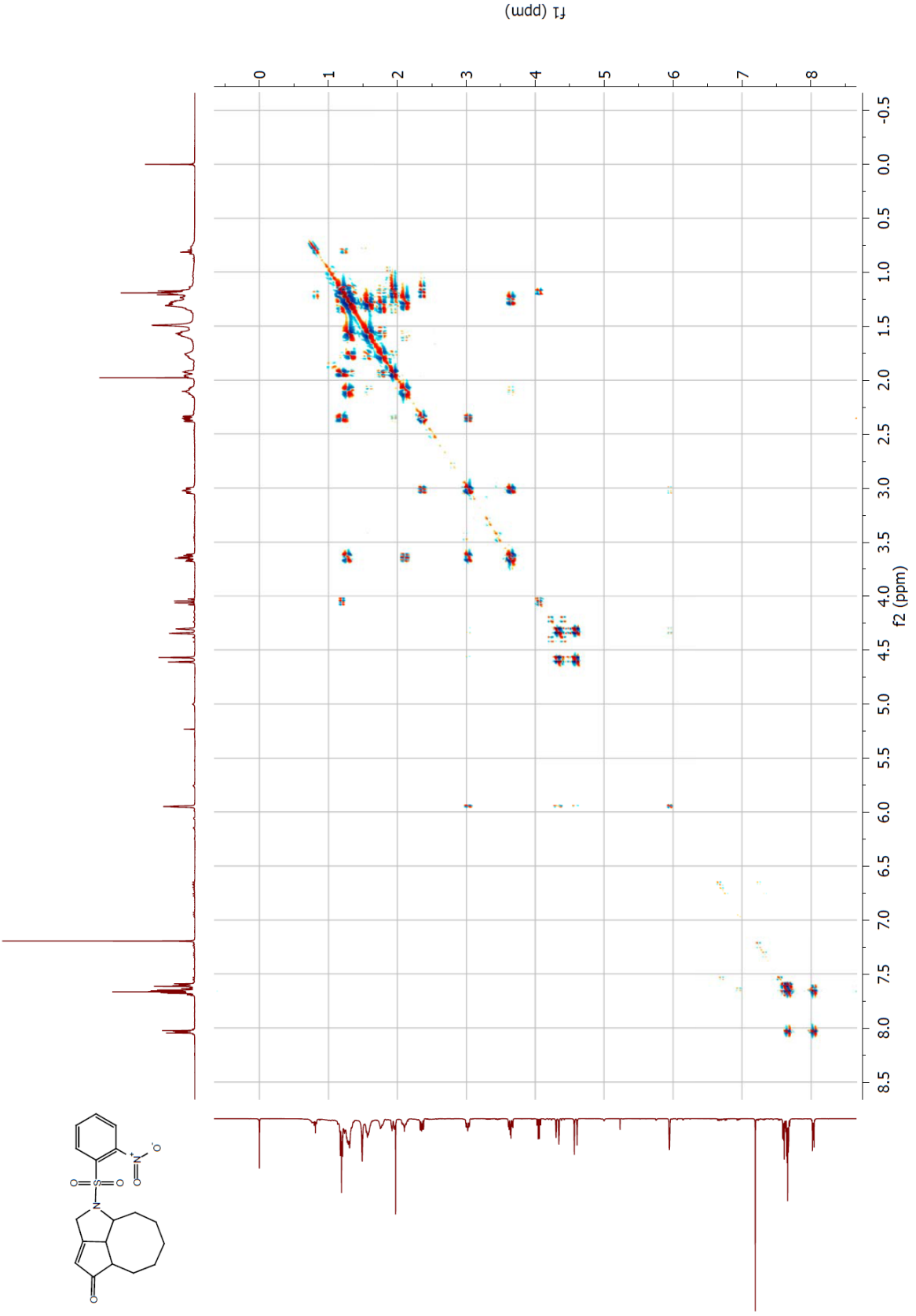
6, ^{1}H NMR (400 MHz, $CDCl_3$):



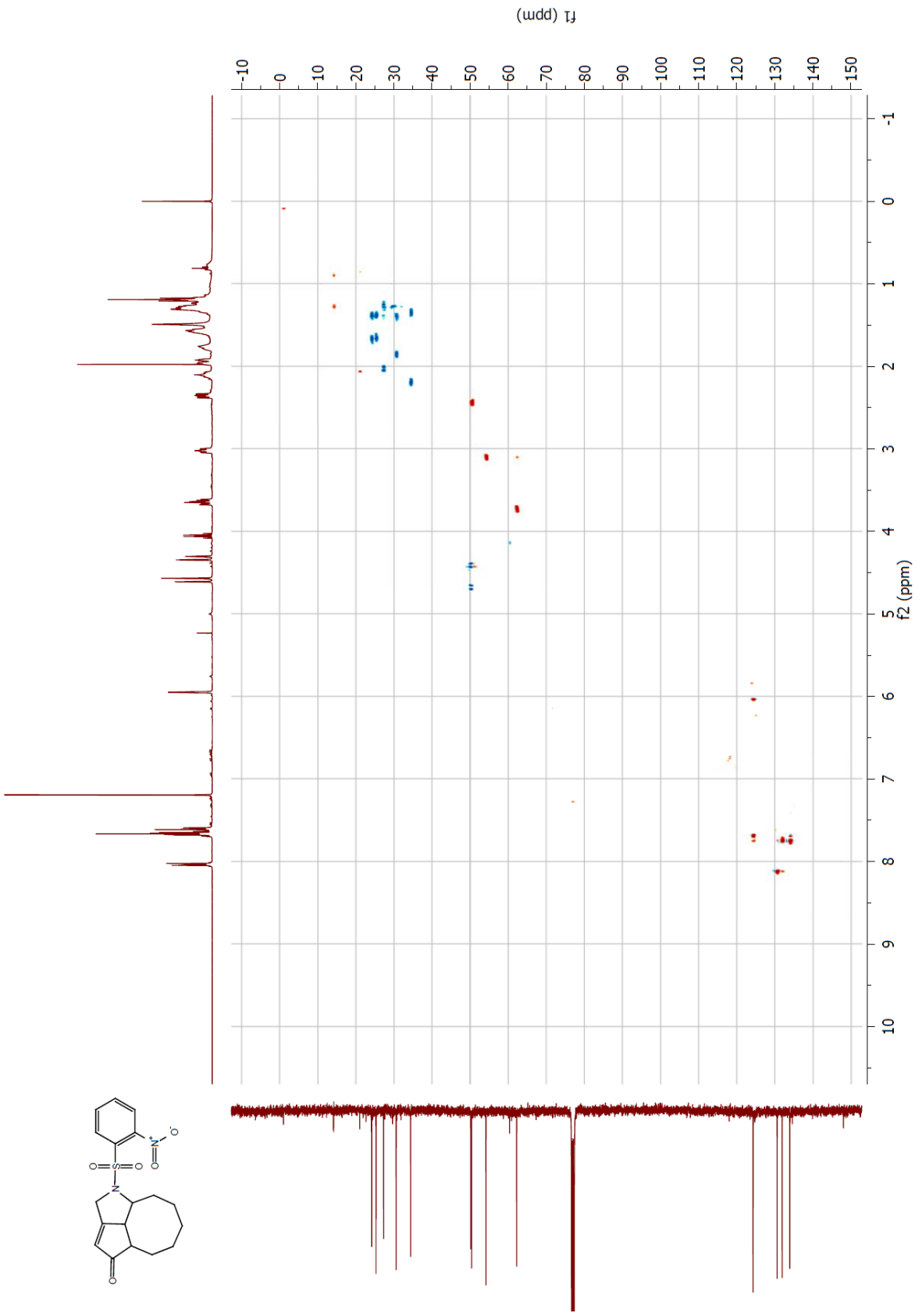
6, ^{13}C NMR (100 MHz, $CDCl_3$):



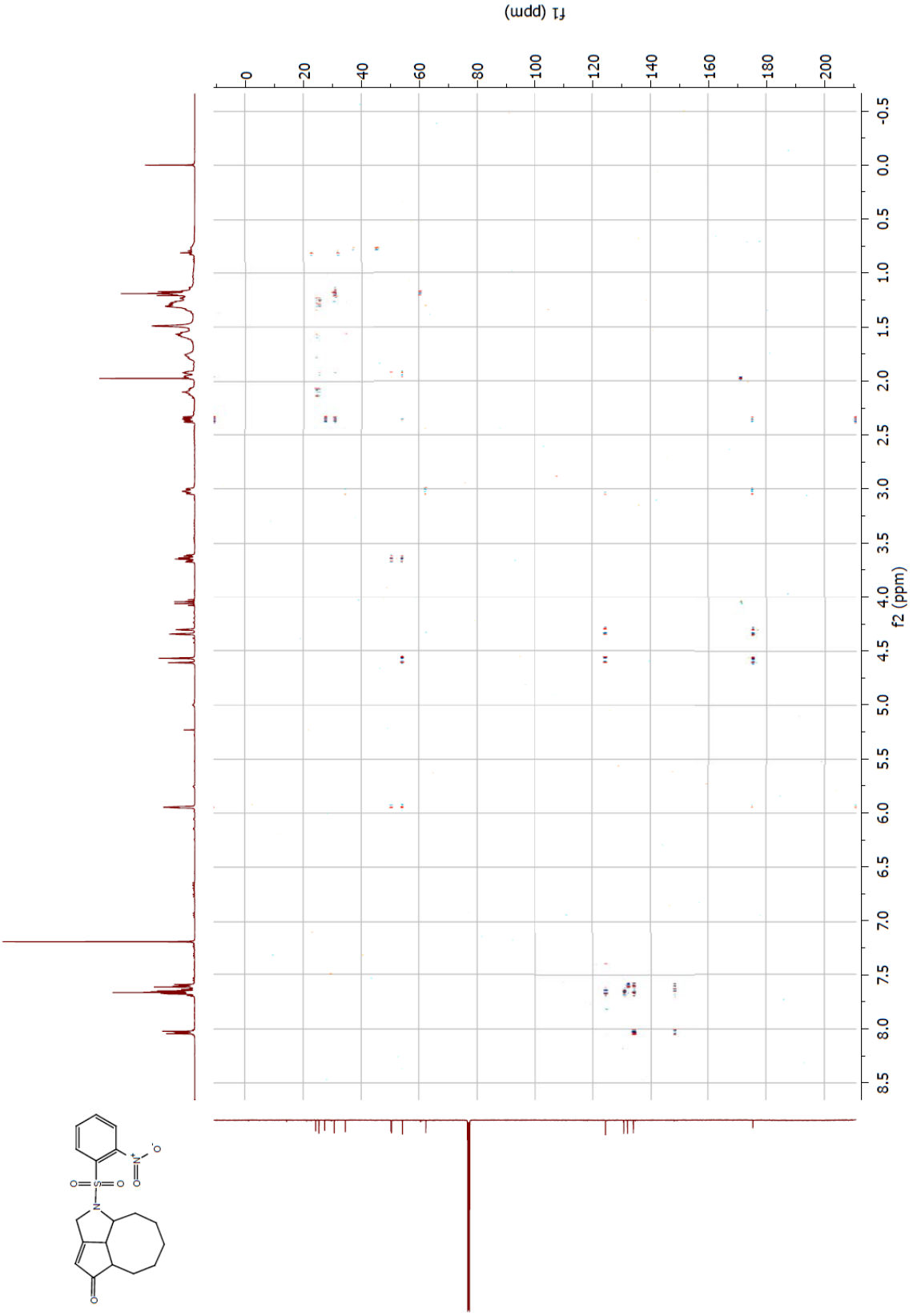
6, COSY (400 MHz, $CDCl_3$):



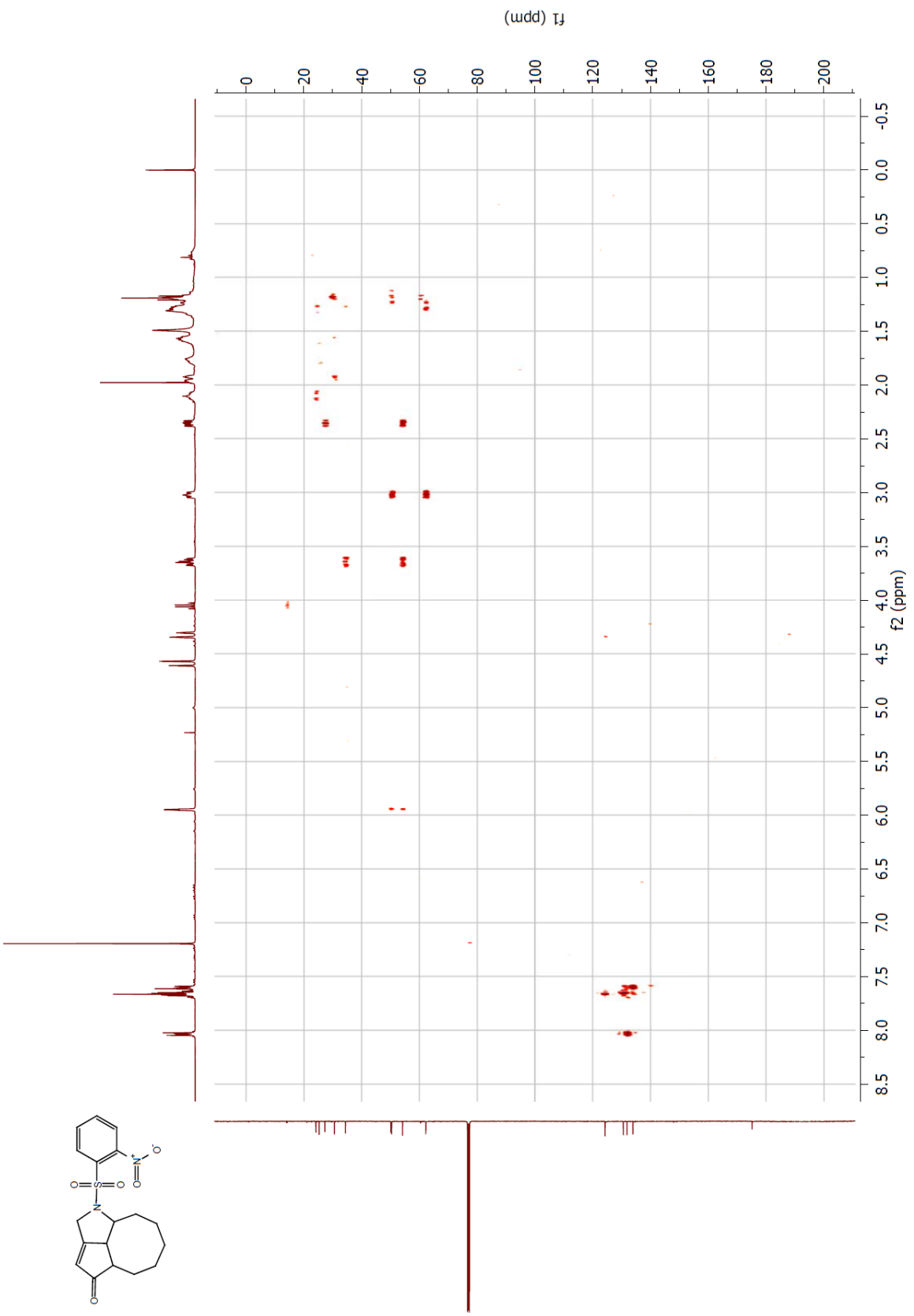
6, HSQC (400 MHz, $CDCl_3$):



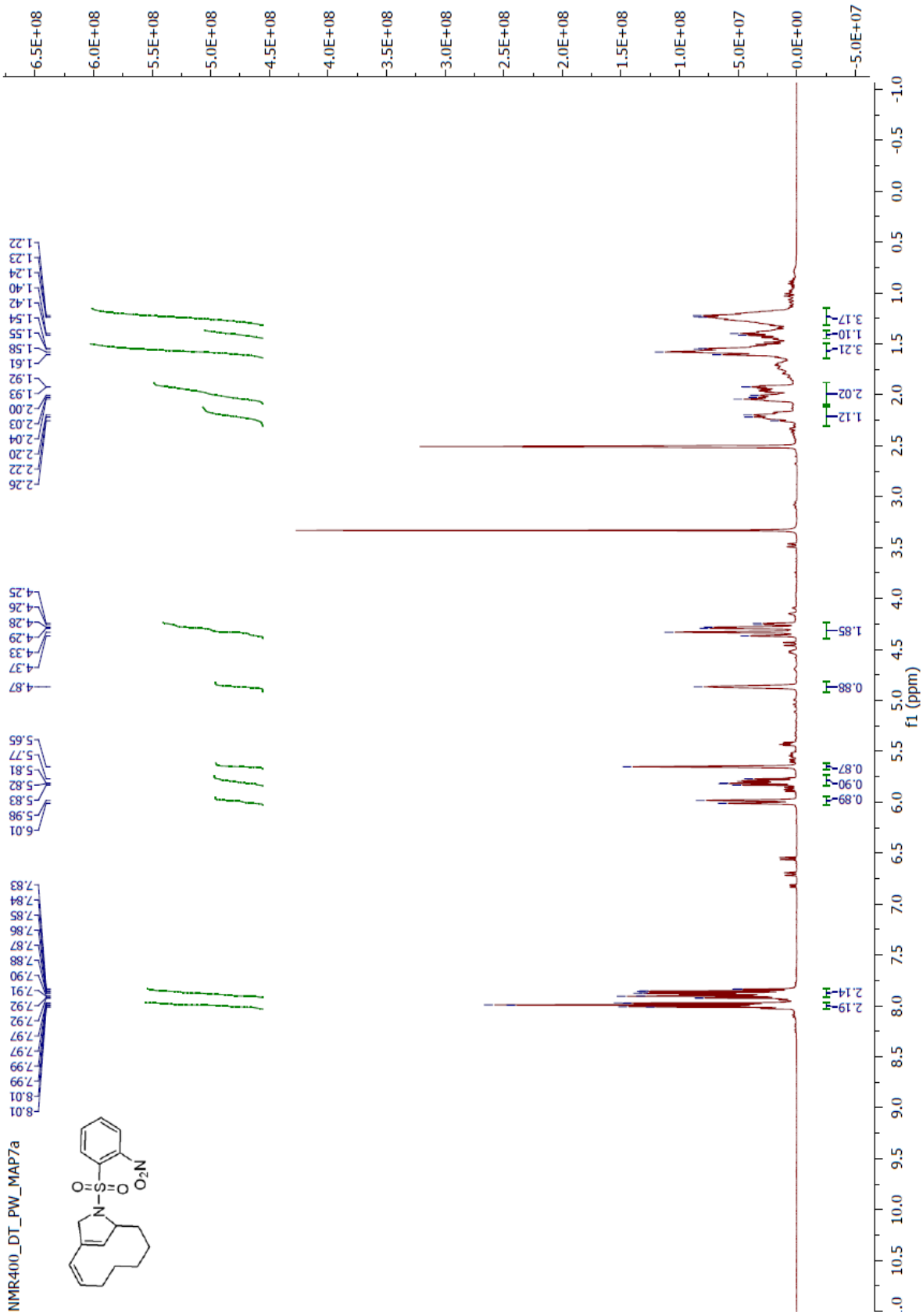
6, HMBC (400 MHz, $CDCl_3$):



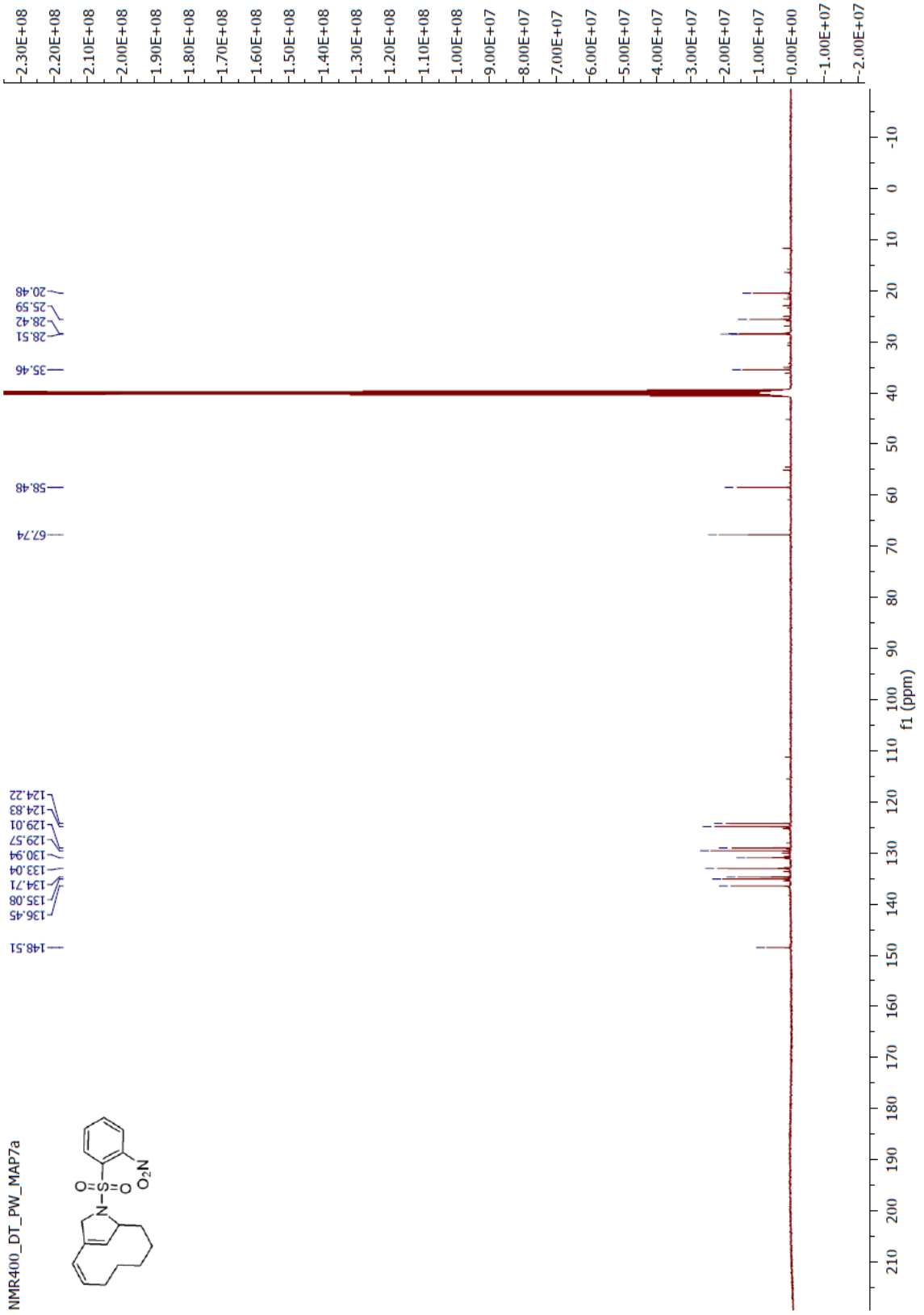
6, H2BC (400 MHz, $CDCl_3$):



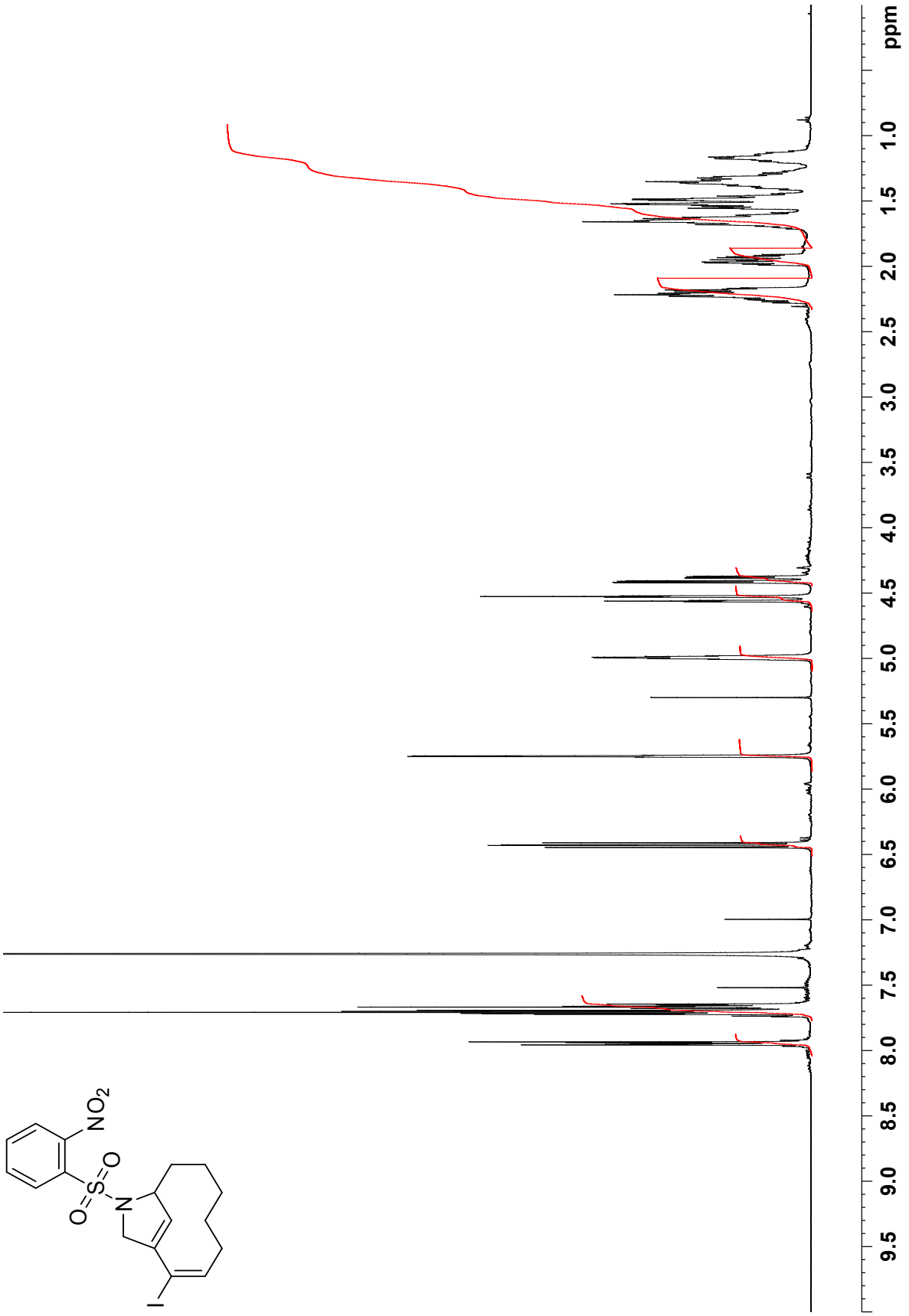
7a, ^{1}H NMR (400 MHz, DMSO-d_6):



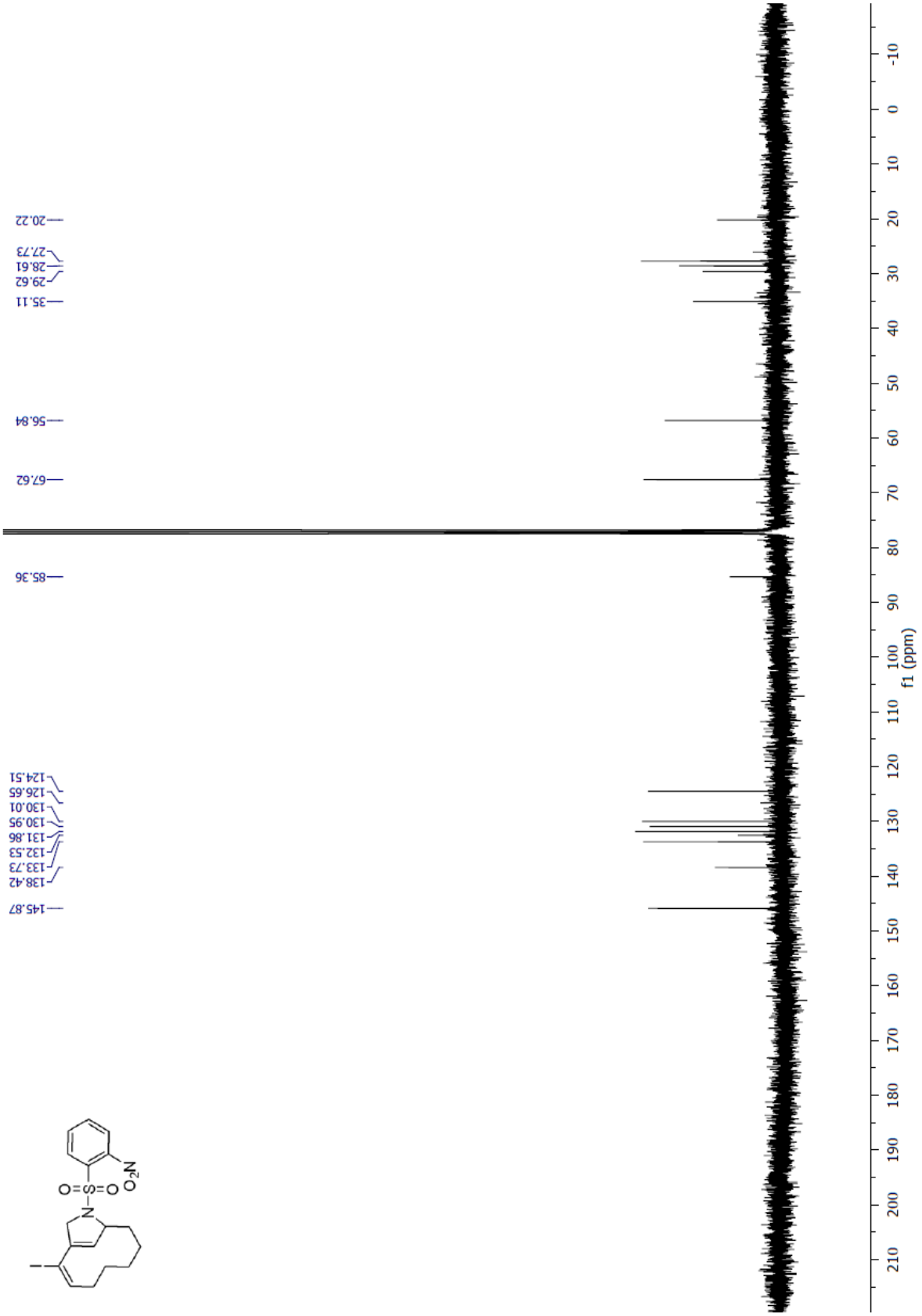
7a, ^{13}C NMR (100 MHz, DMSO-d_6):



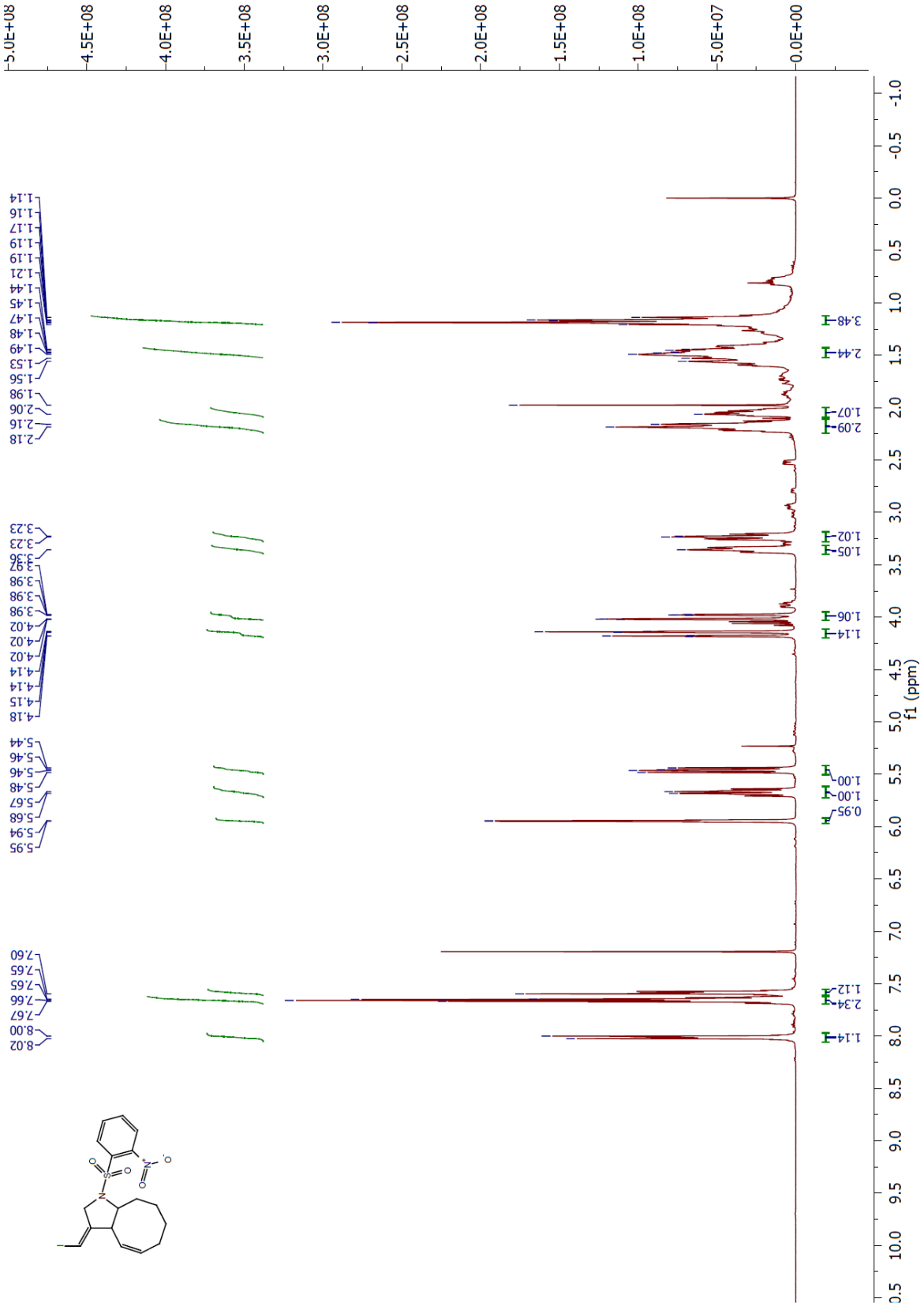
7b, ^{1}H NMR (400 MHz, $CDCl_3$):



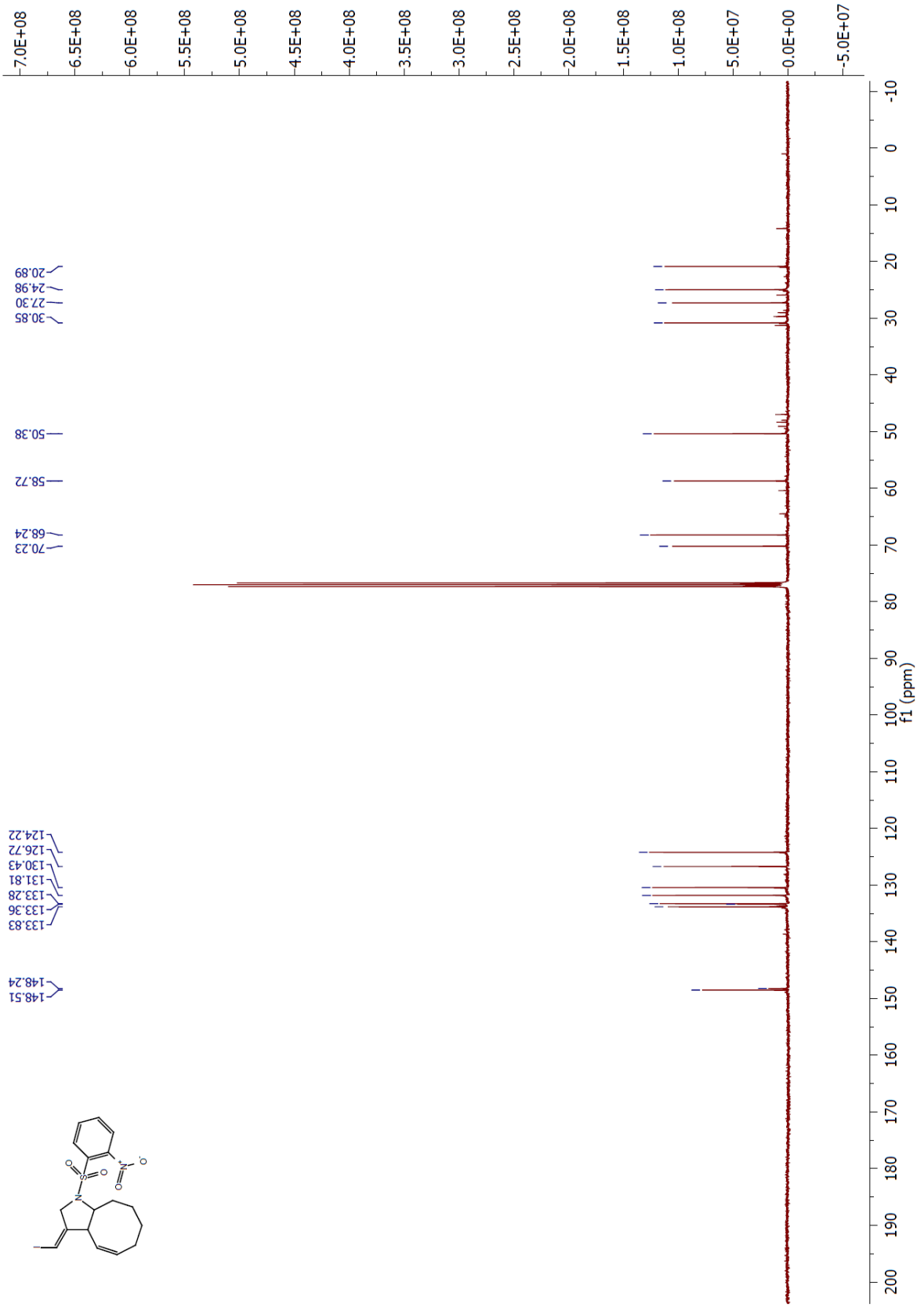
7b, ^{13}C NMR (100 MHz, $CDCl_3$):



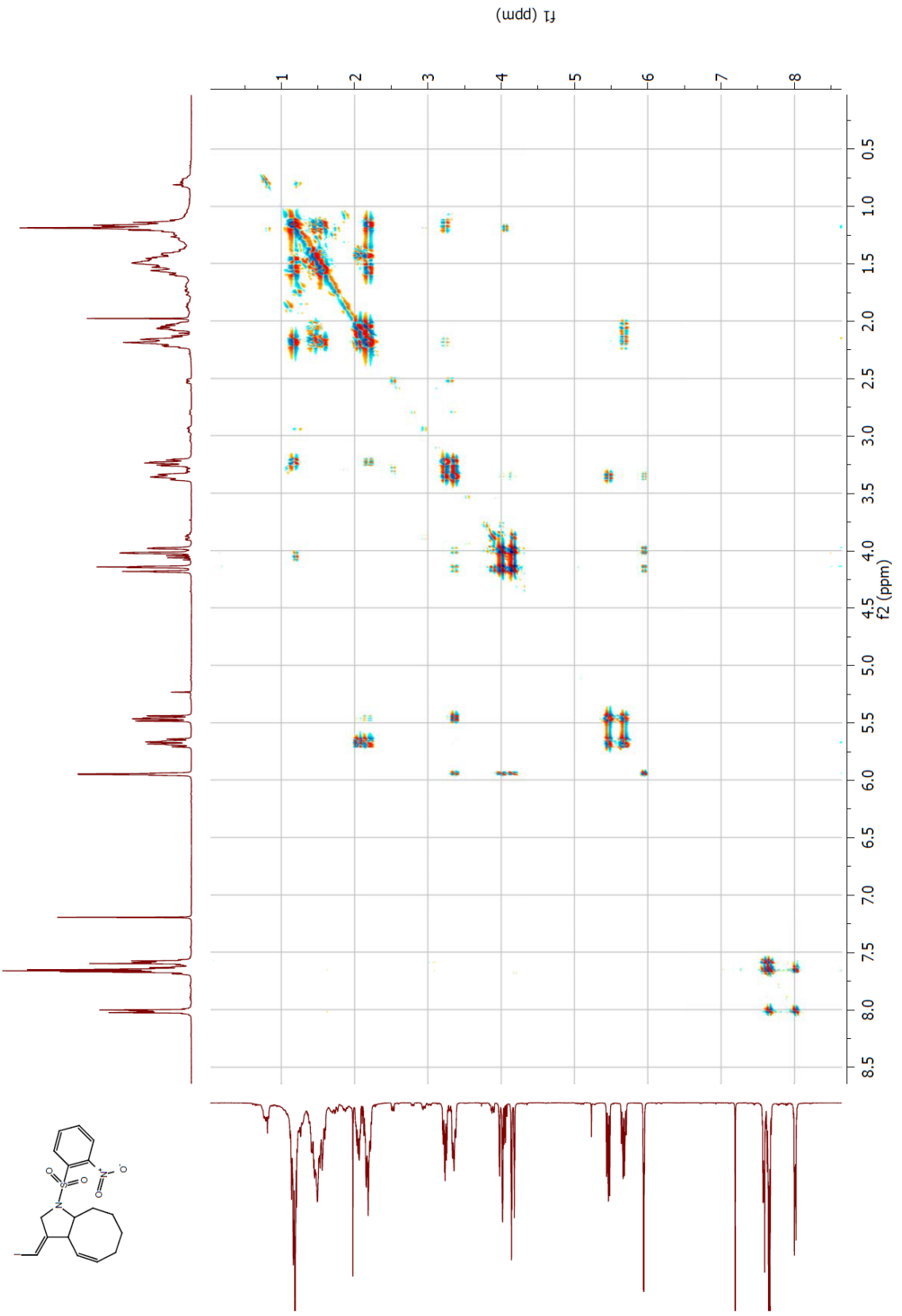
8, ^{1}H NMR (400 MHz, $CDCl_3$):



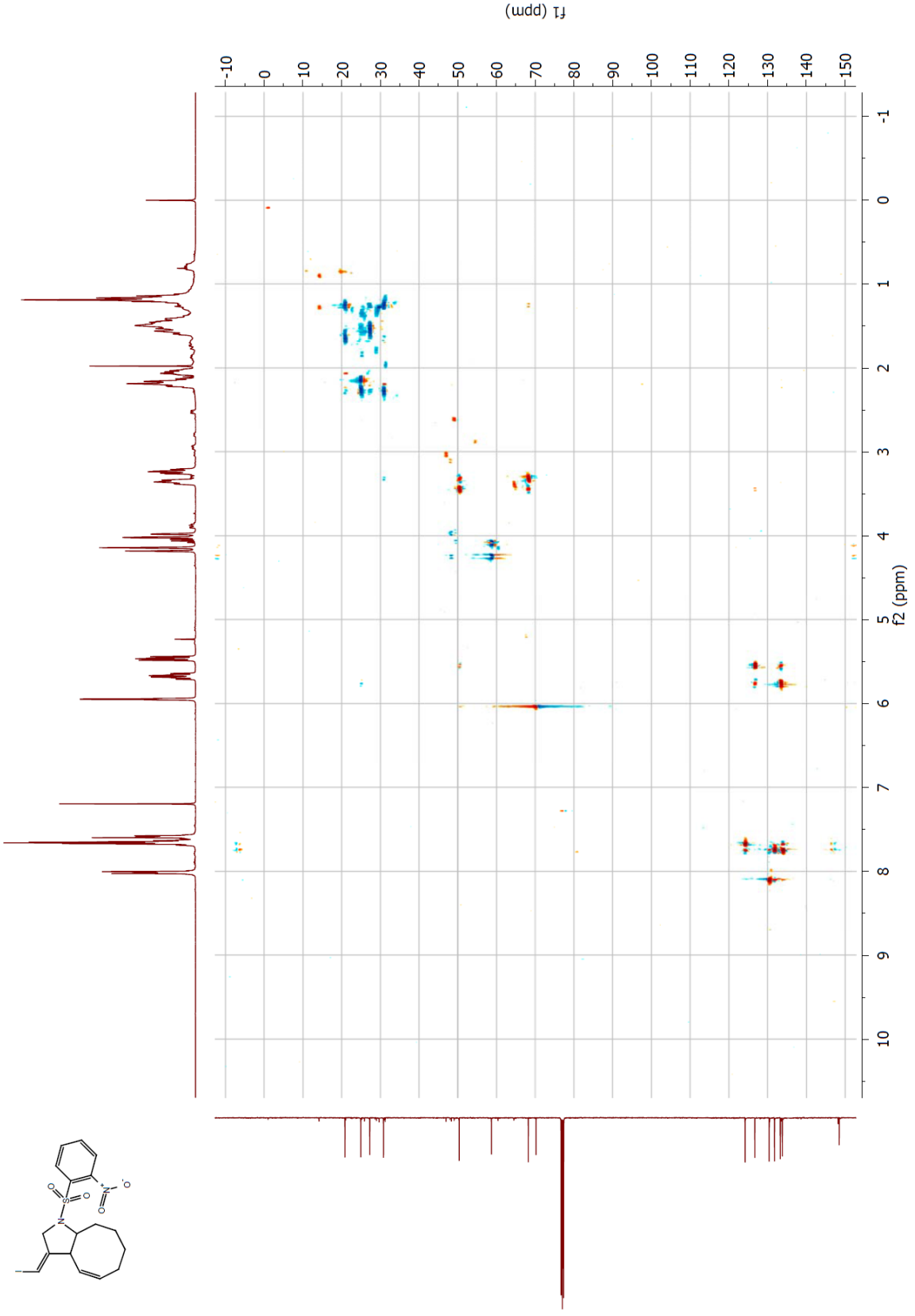
8, ^{13}C NMR (100 MHz, $CDCl_3$):



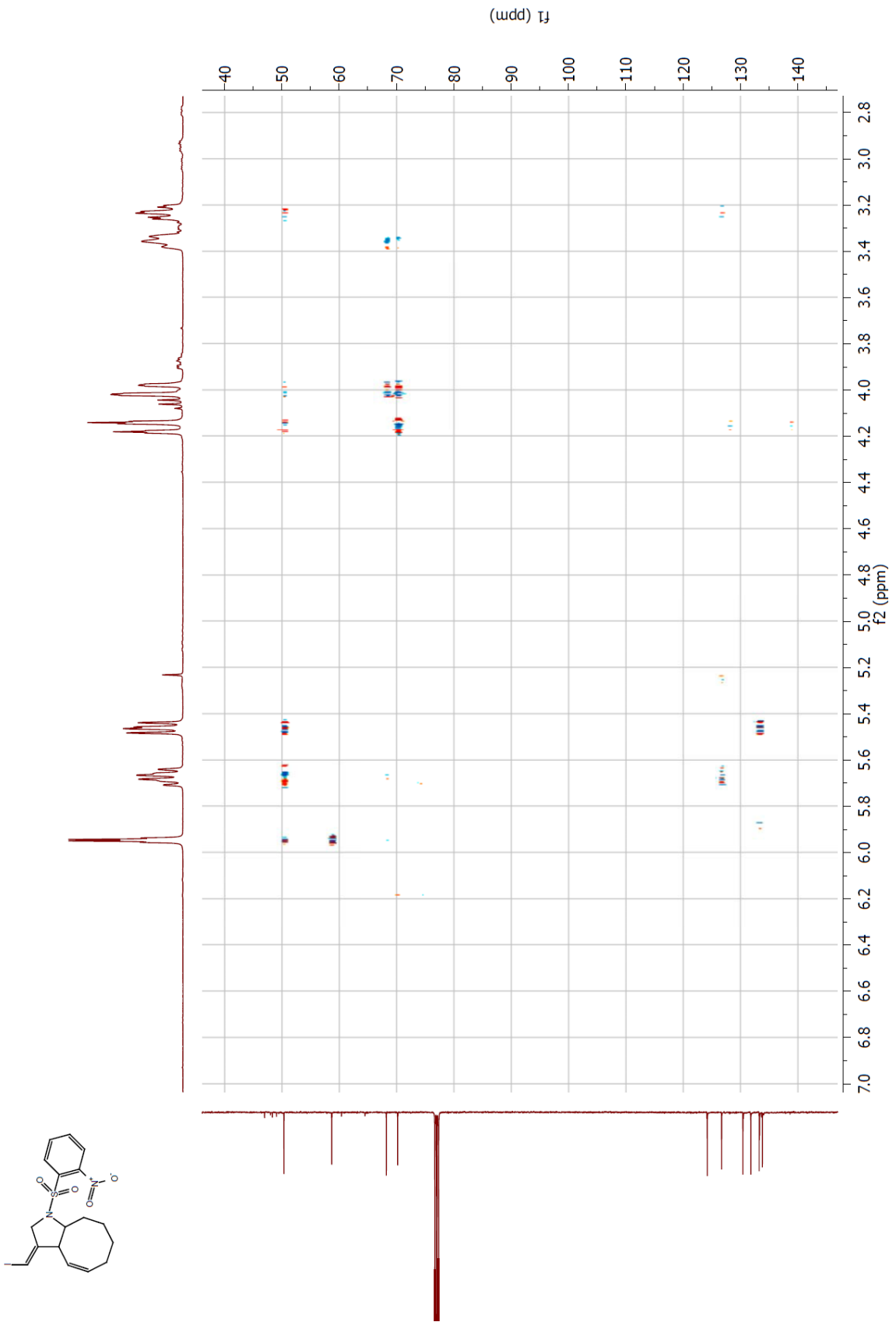
8, COSY (400 MHz, $CDCl_3$):



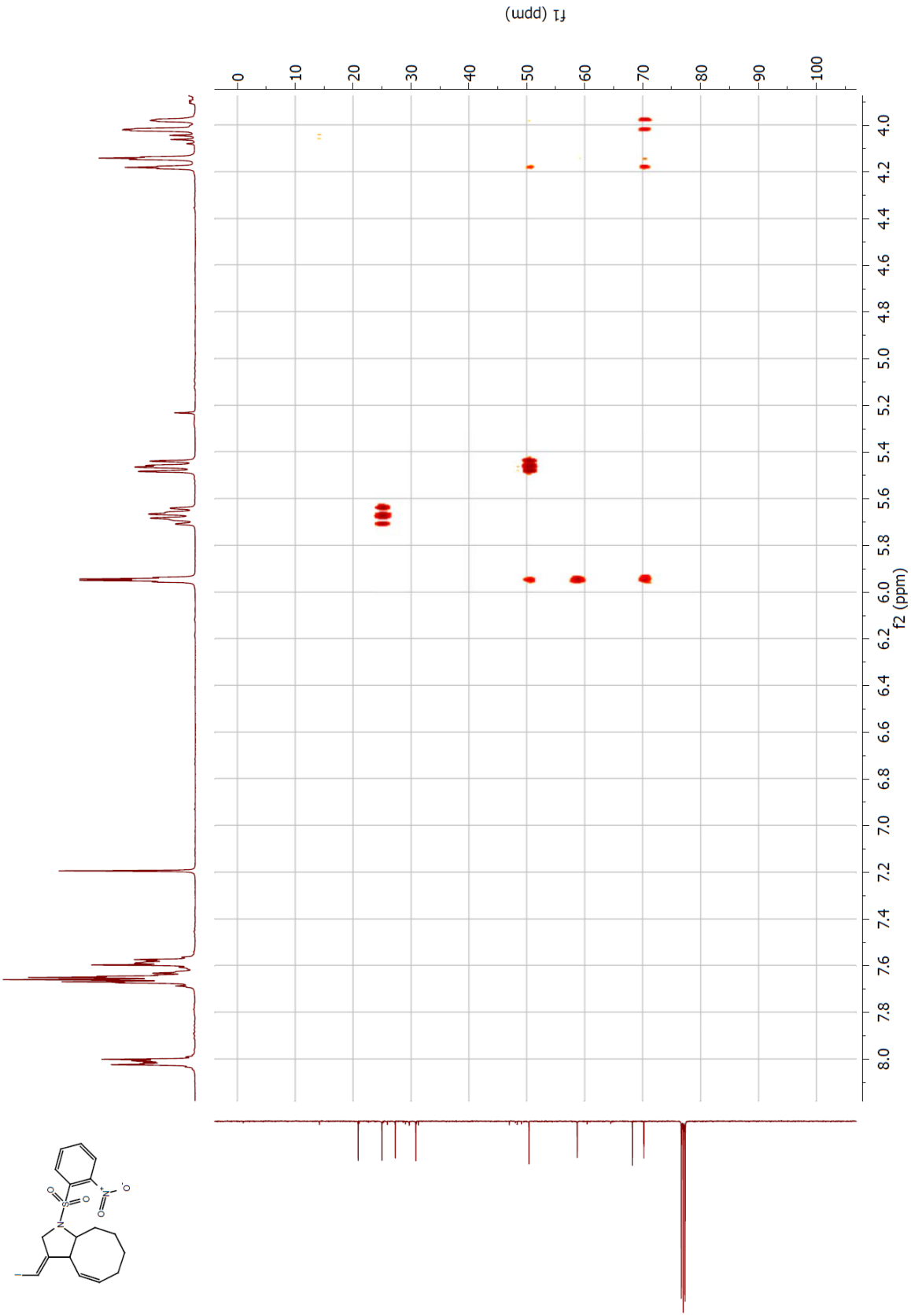
8, HSQC (400 MHz, $CDCl_3$):



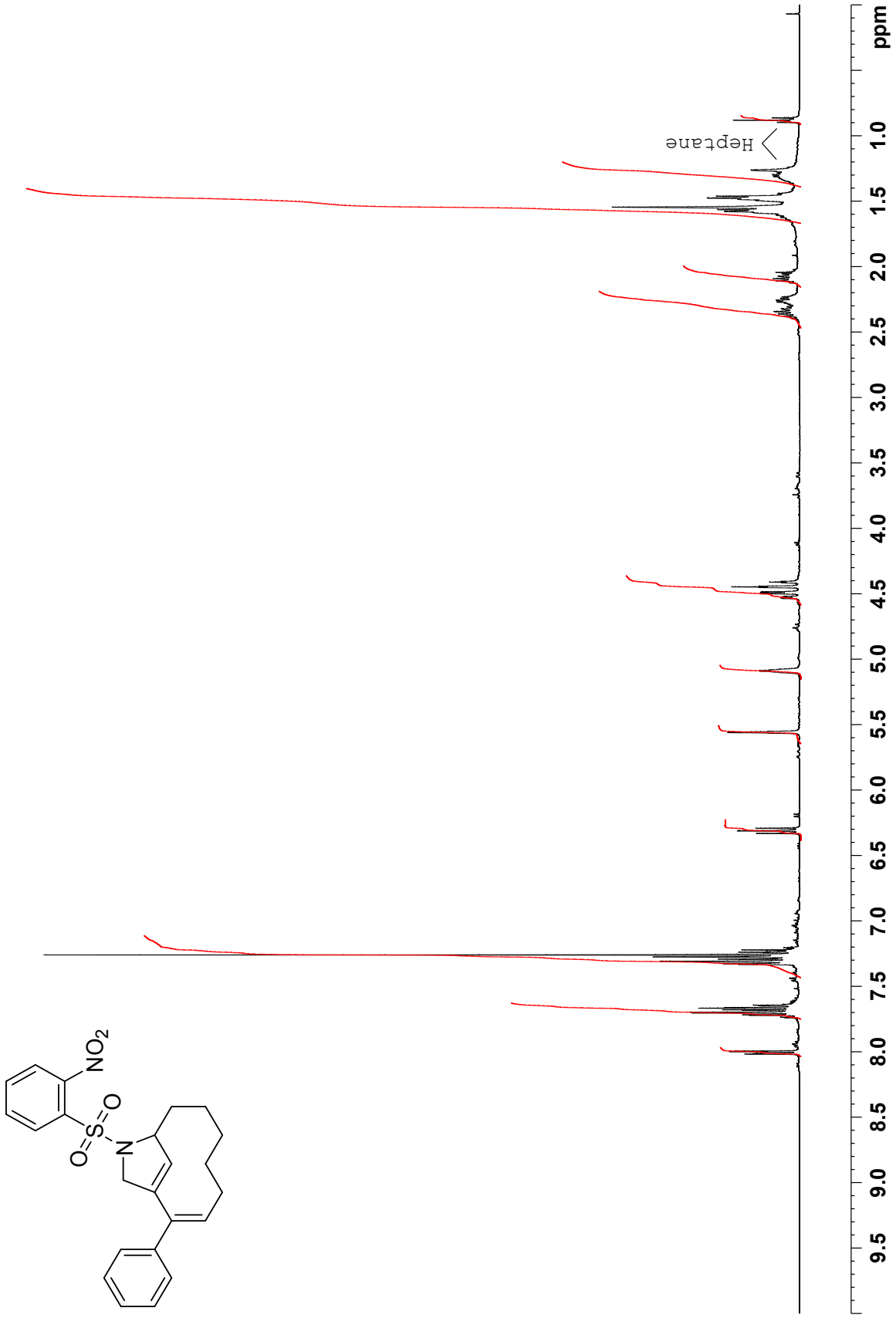
8, HMBC (400 MHz, $CDCl_3$):



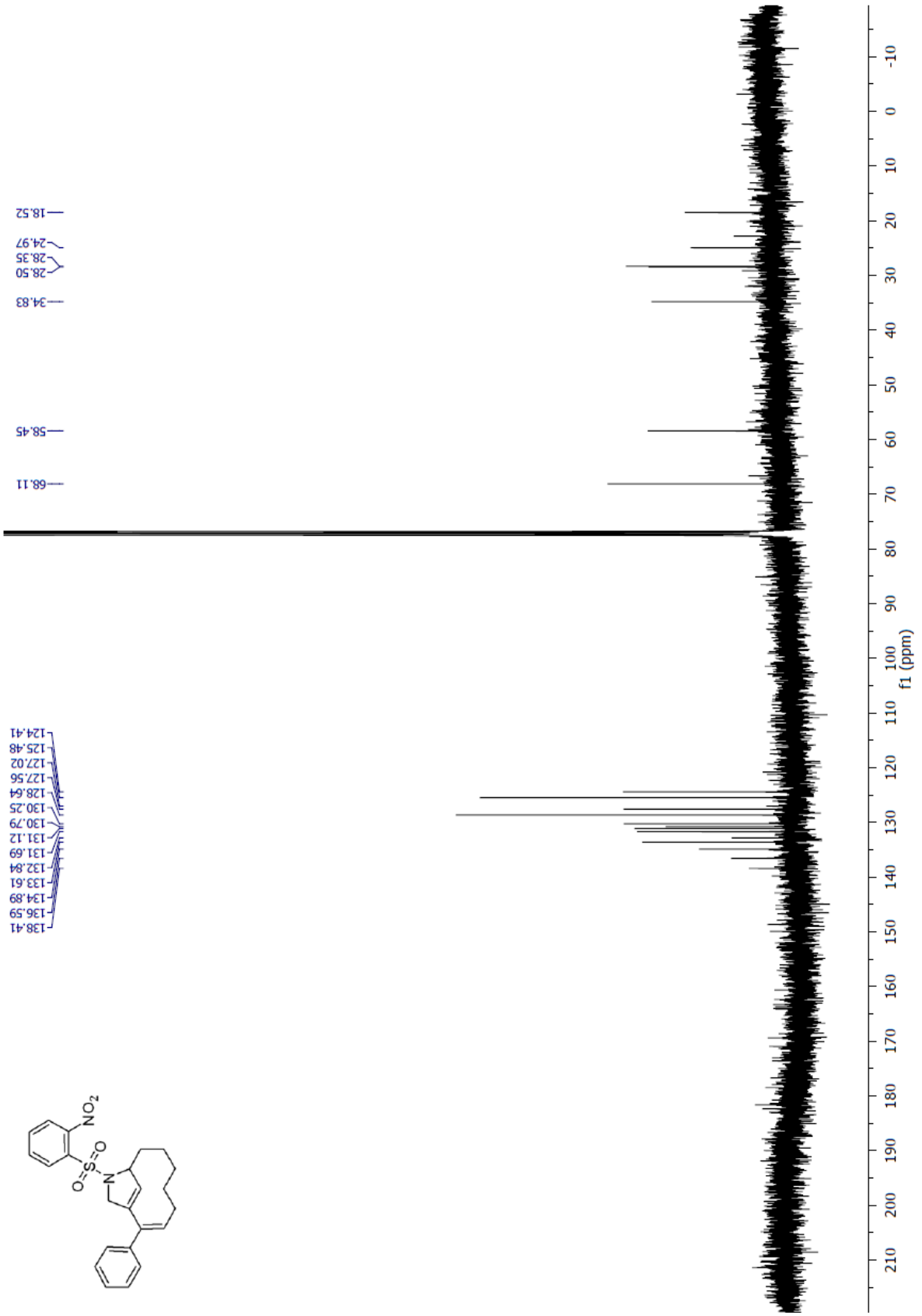
8, H2BC (400 MHz, $CDCl_3$):



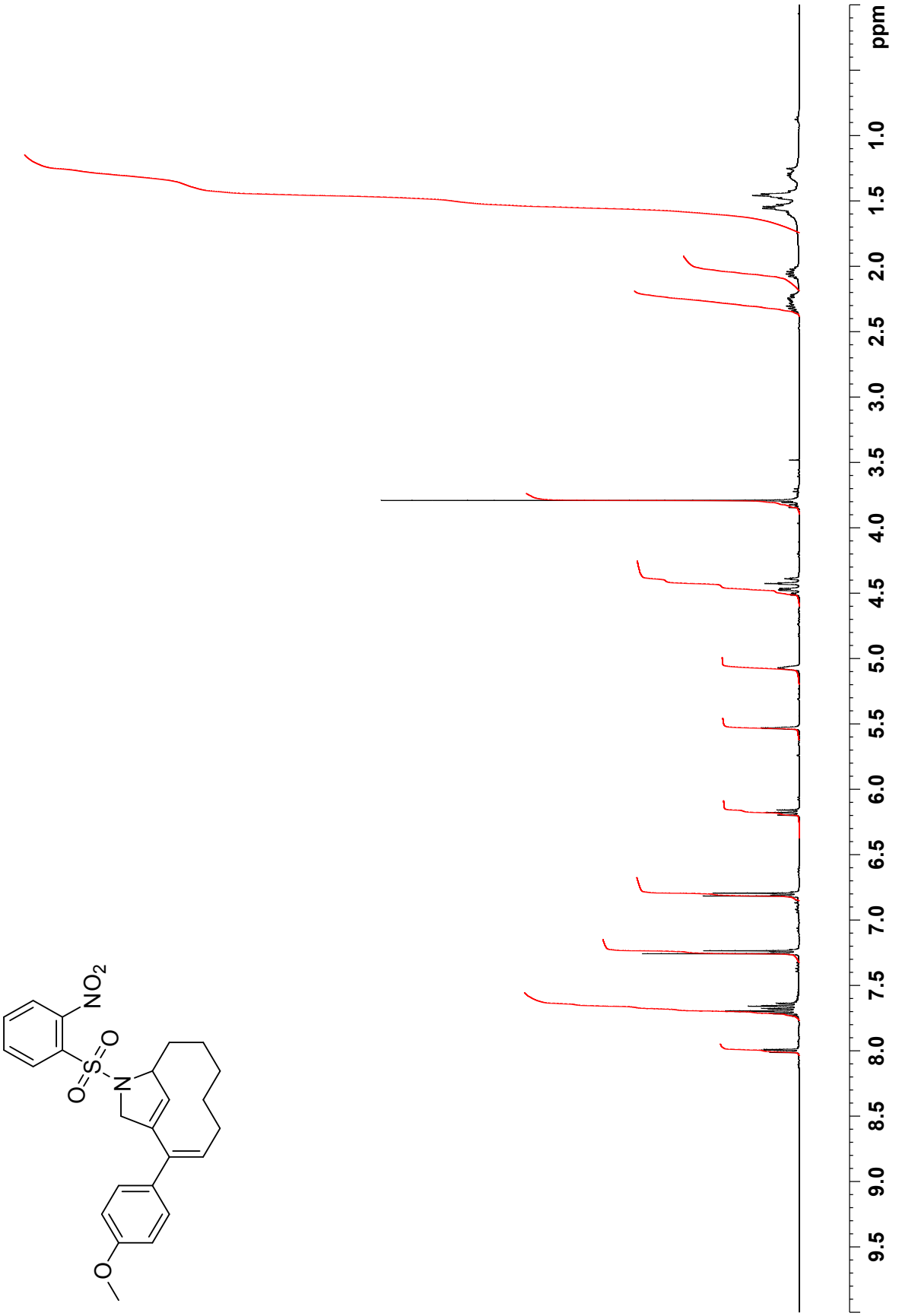
9a, ^{1}H NMR (400 MHz, $CDCl_3$):



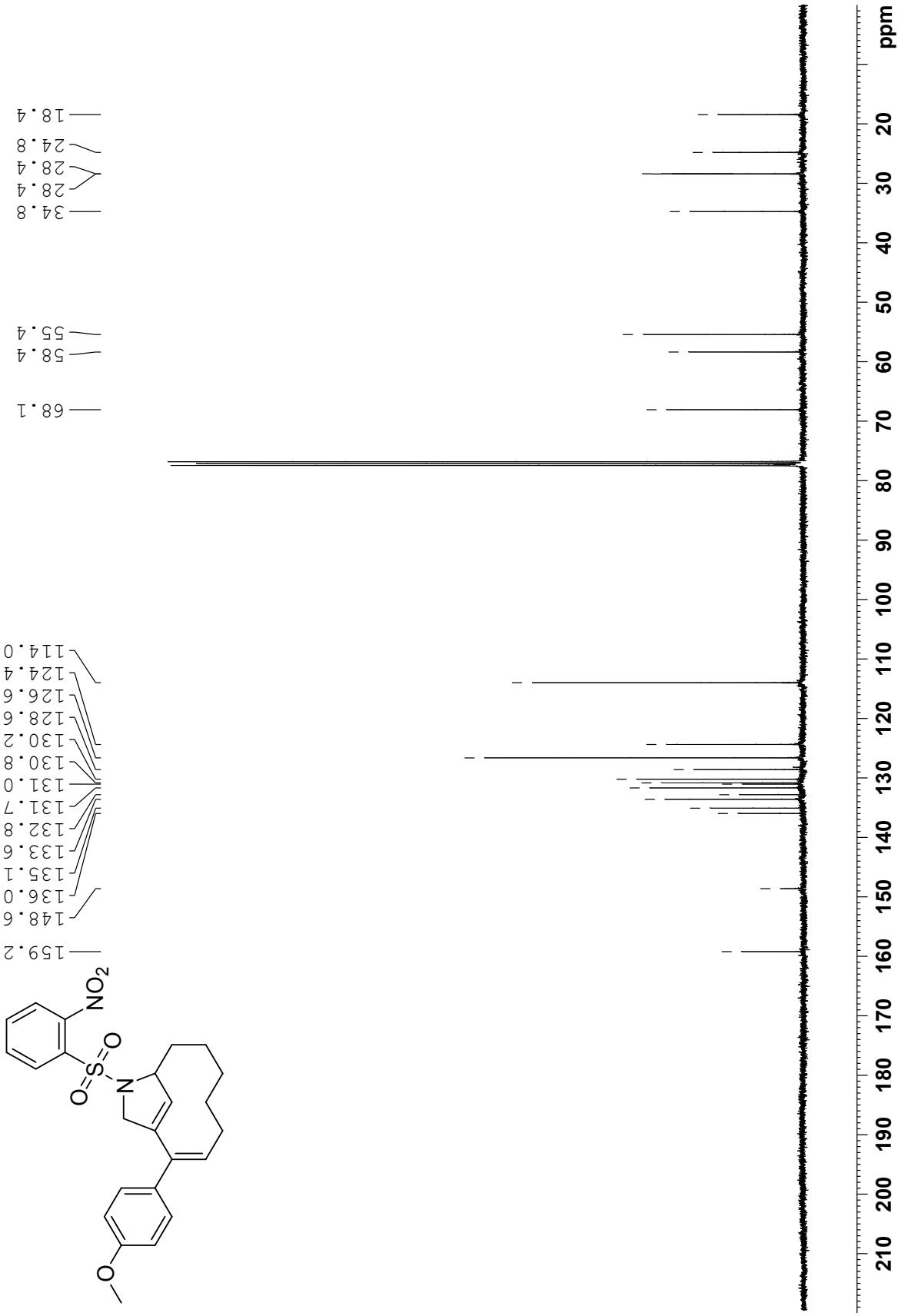
9a, ^{13}C NMR (100 MHz, $CDCl_3$):



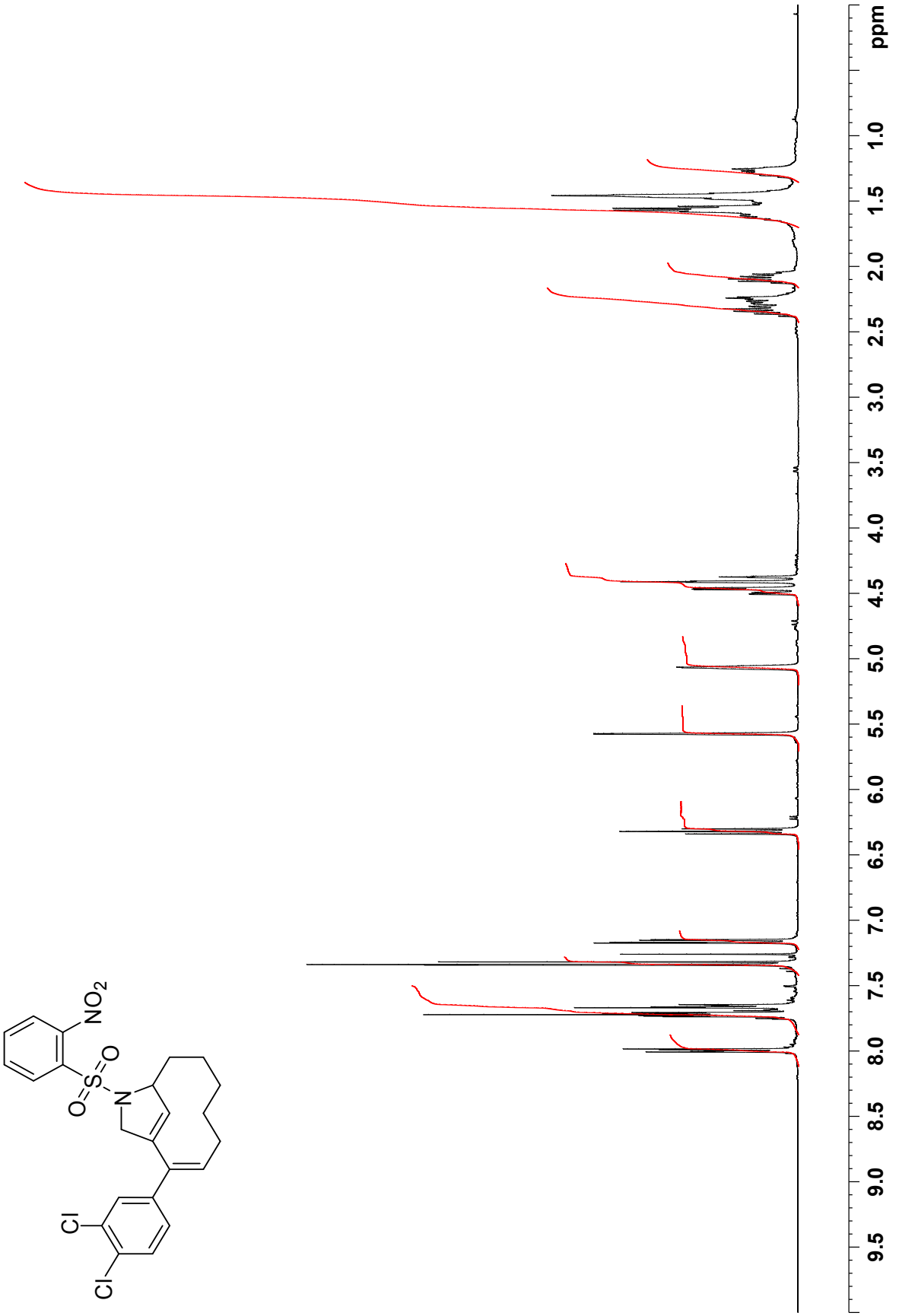
9b, ^{1}H NMR (400 MHz, $CDCl_3$):



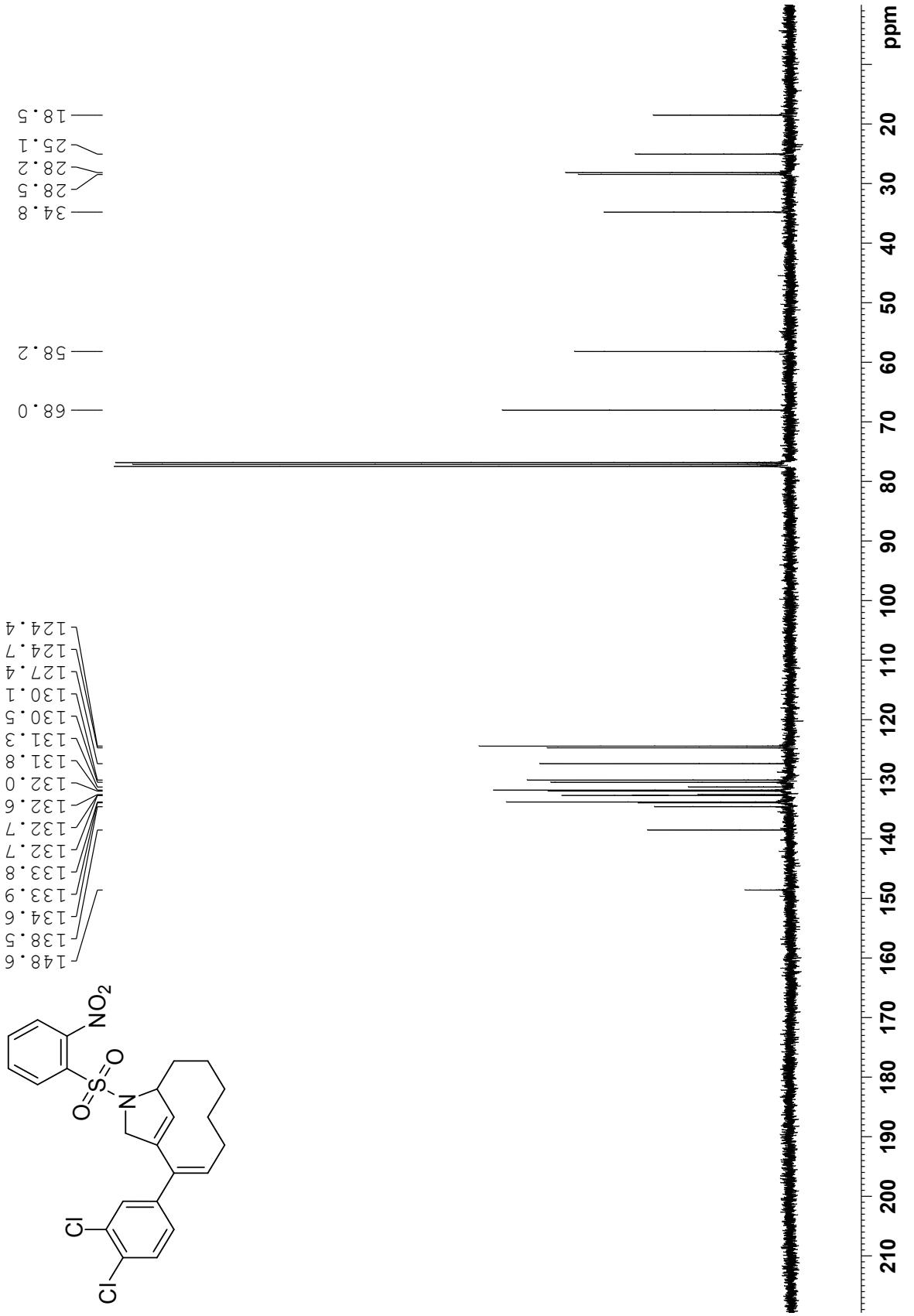
9b, ^{13}C NMR (100 MHz, $CDCl_3$):



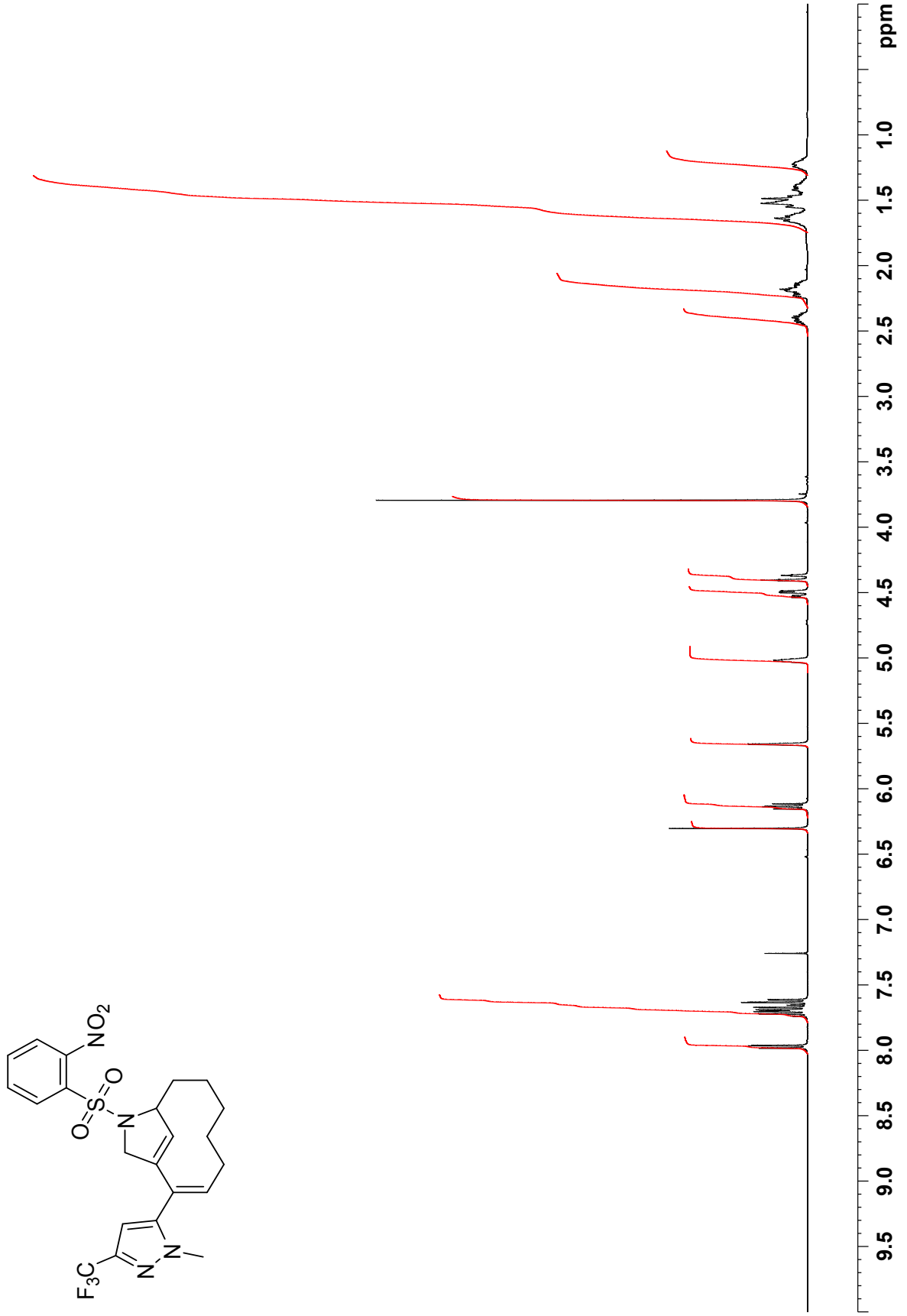
9c, ^{1}H NMR (400 MHz, $CDCl_3$):



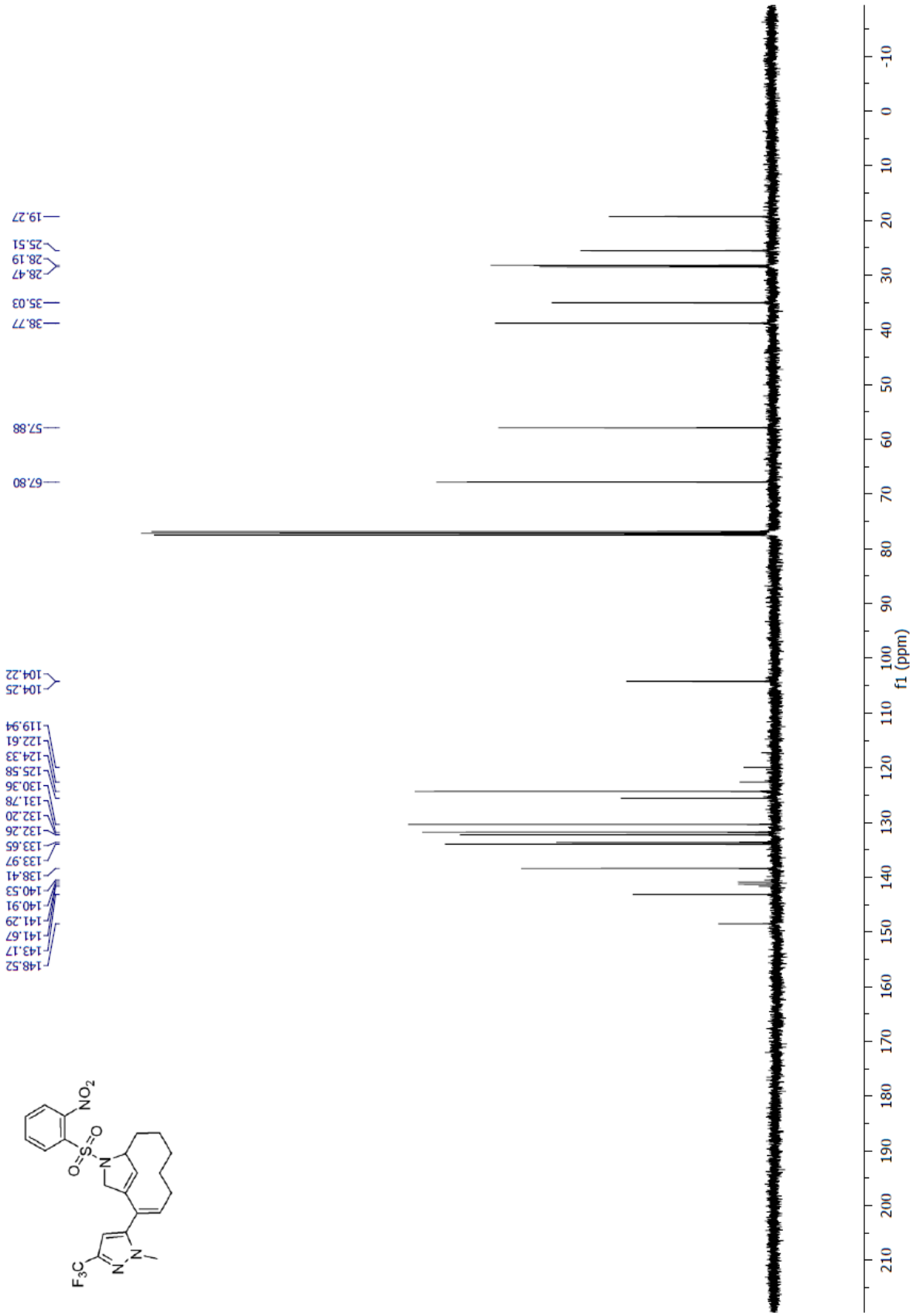
9c, ^{13}C NMR (100 MHz, $CDCl_3$):



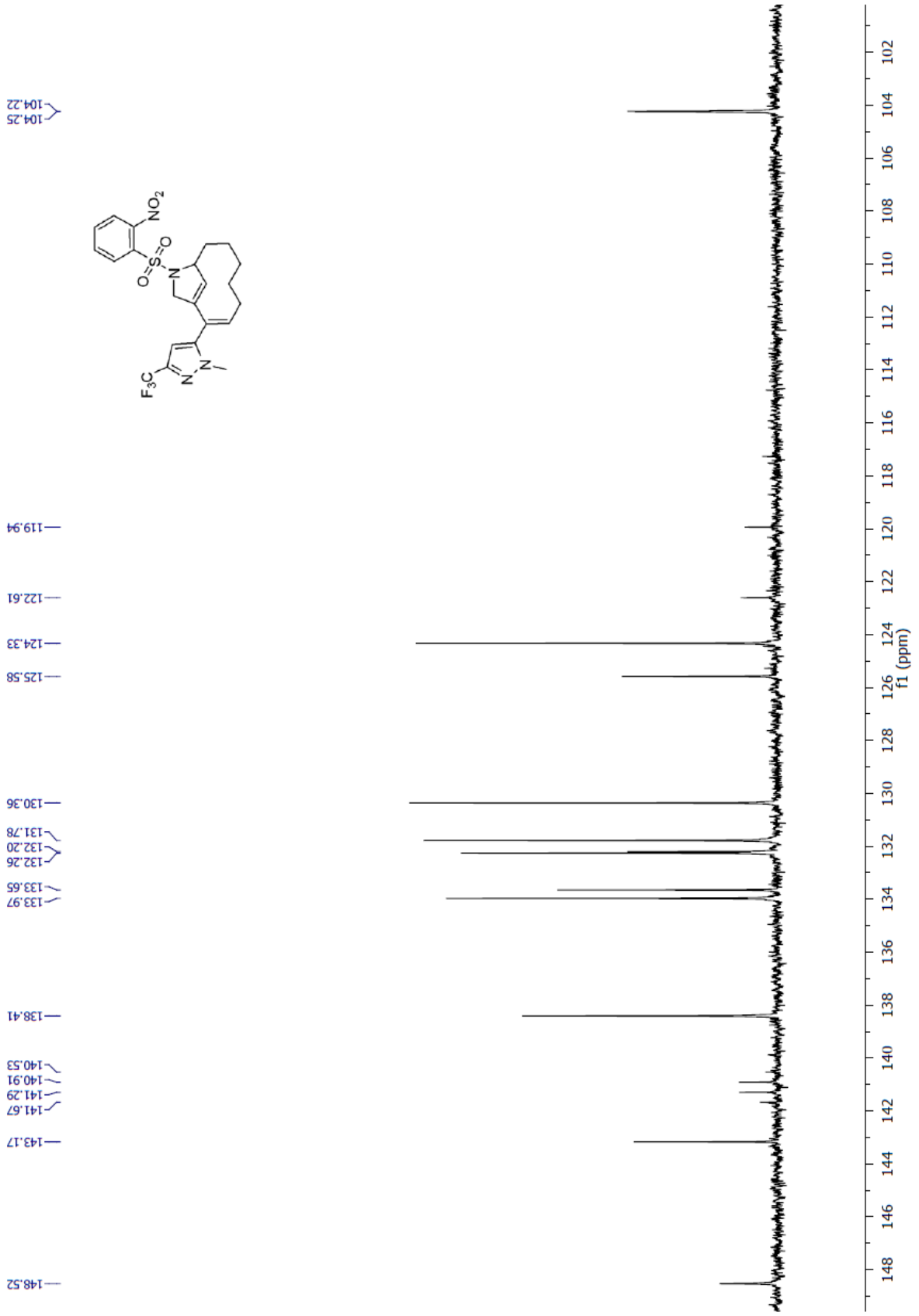
9d, ^{1}H NMR (400 MHz, $CDCl_3$):



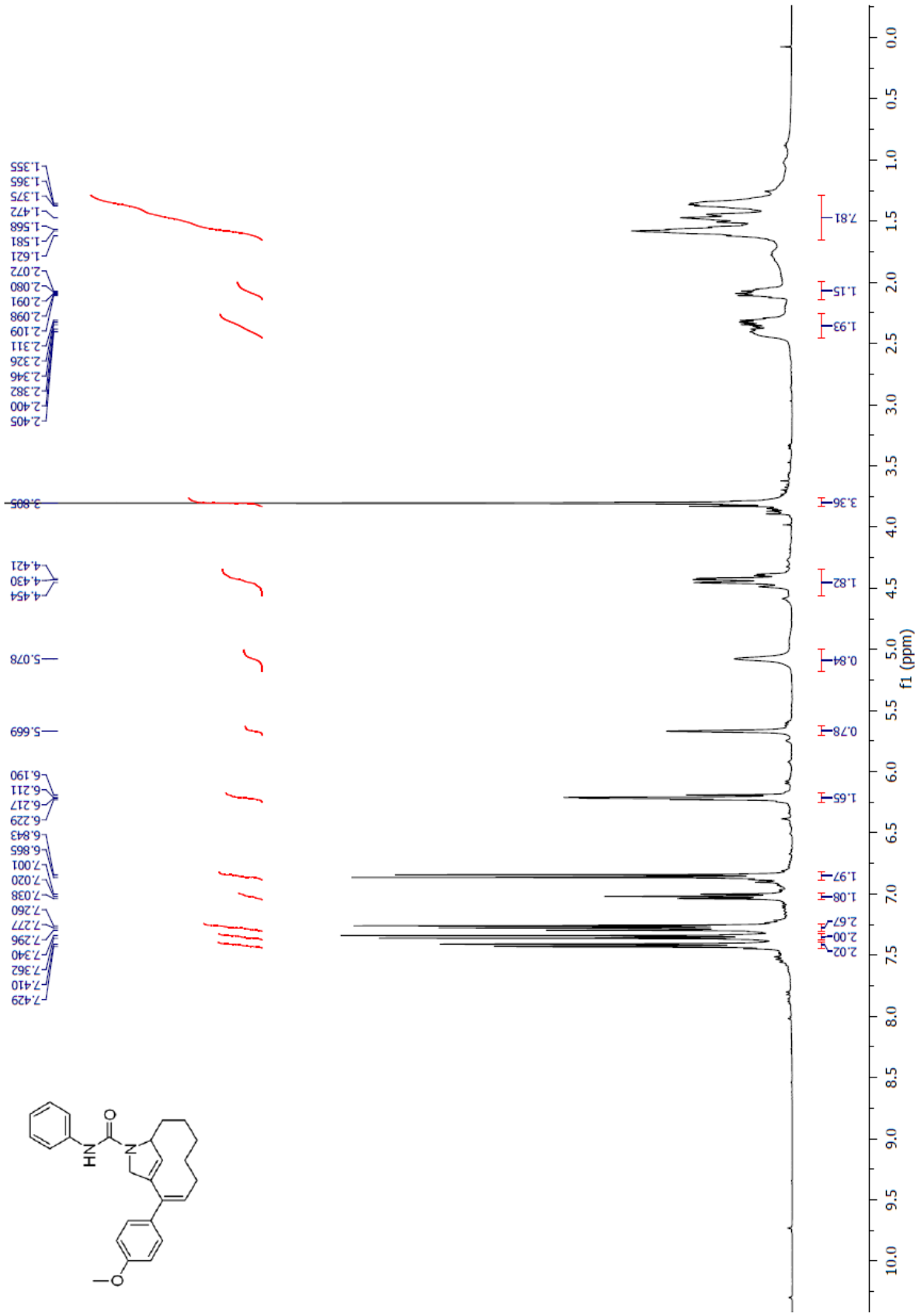
9d, ^{13}C NMR (100 MHz, $CDCl_3$):


19.27
25.51
28.19
28.47
35.03
38.77
57.88
67.80
104.25
104.22
119.94
122.61
124.33
125.58
130.36
131.78
132.20
132.26
133.65
133.97
138.41
140.53
140.91
141.29
141.67
143.17
148.52
NO2
O=S=O
N
N
F3C
f1 (ppm)

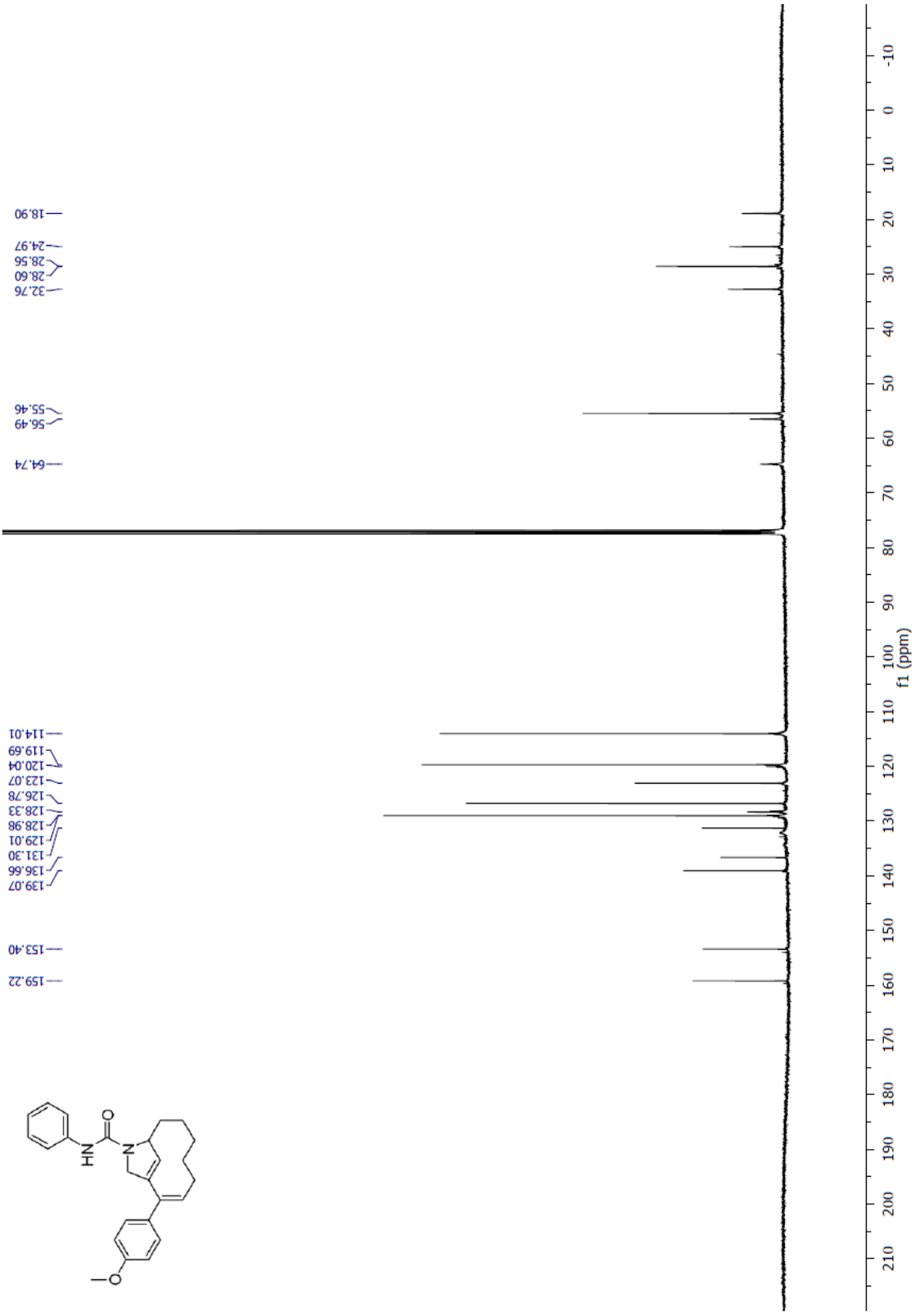
9d, ^{13}C NMR (100 MHz, $CDCl_3$), partially enlarged showing the C-F splitting peaks (100-150 ppm):



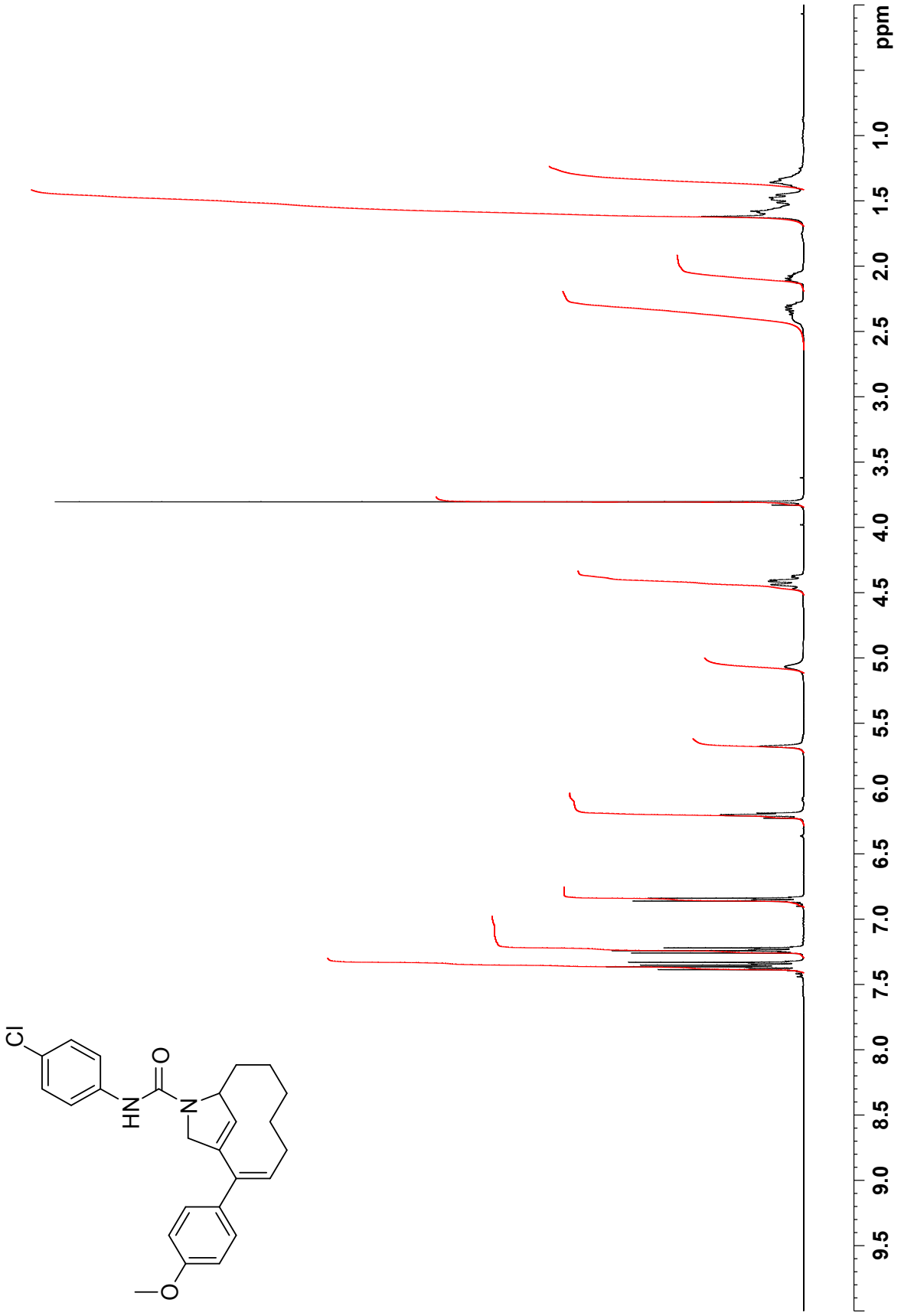
11a, ^{1}H NMR (400 MHz, $CDCl_3$):



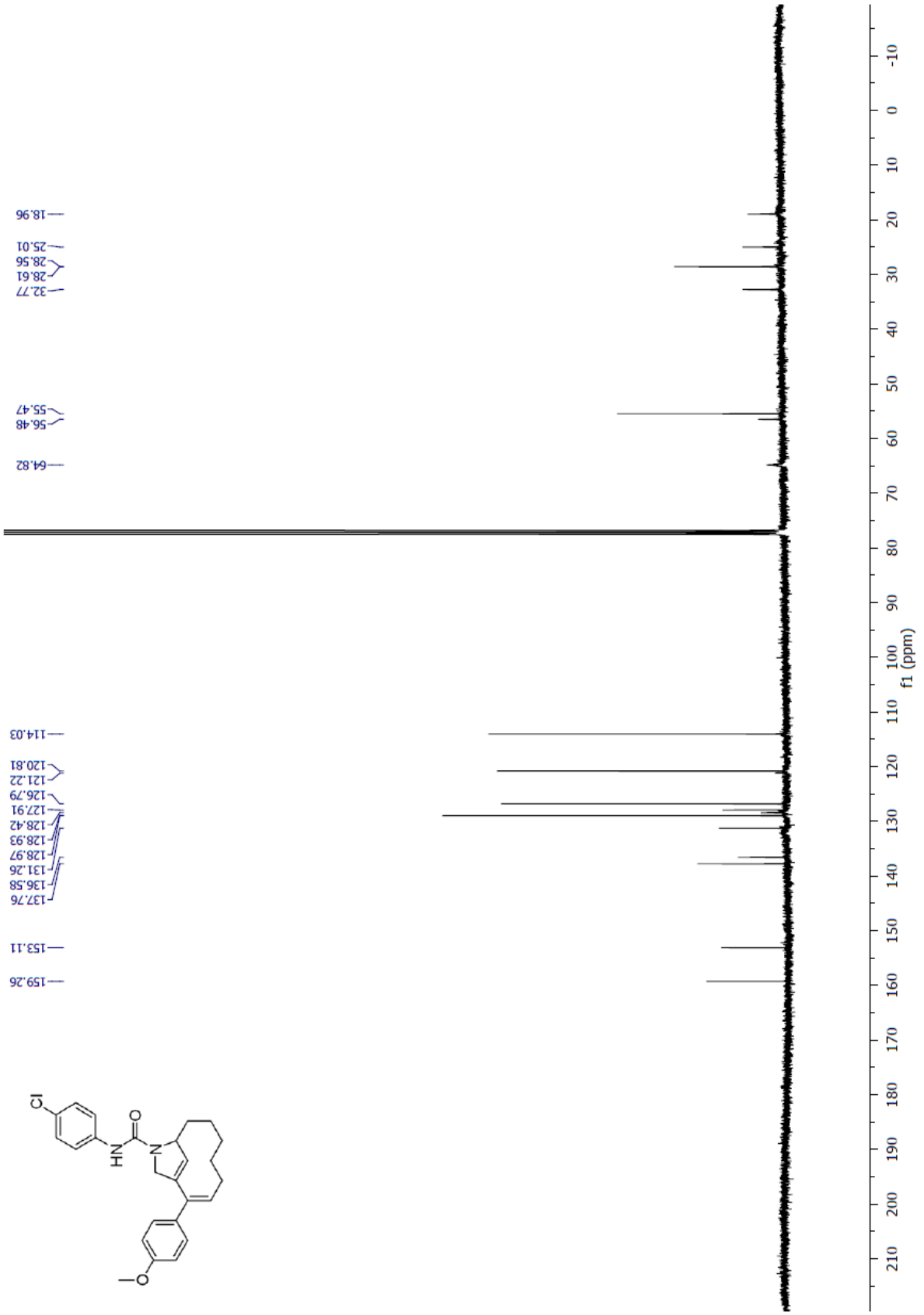
11a, ^{13}C NMR (100 MHz, $CDCl_3$):



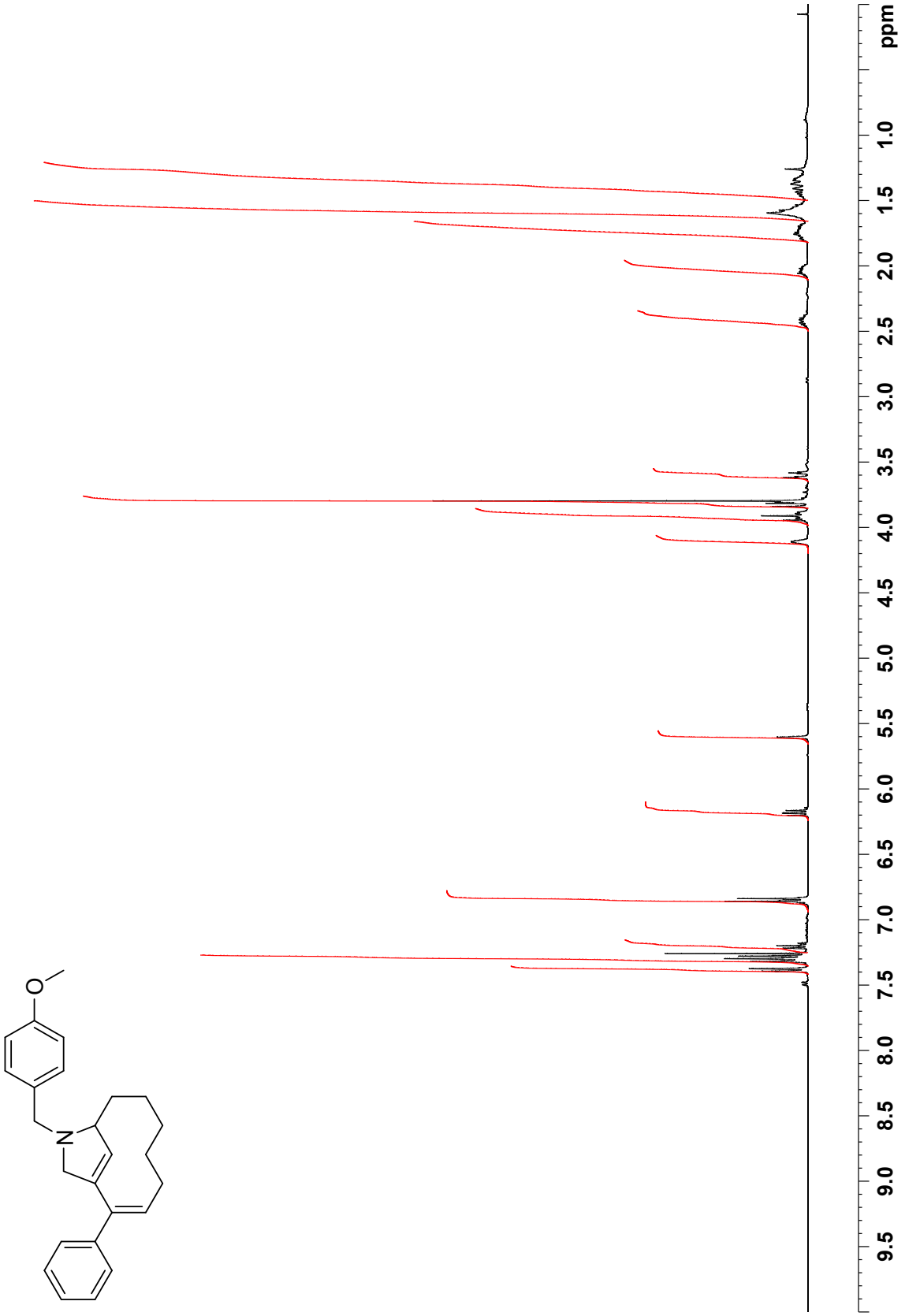
11b, ^{1}H NMR (400 MHz, $CDCl_3$):



11b, ^{13}C NMR (100 MHz, $CDCl_3$):

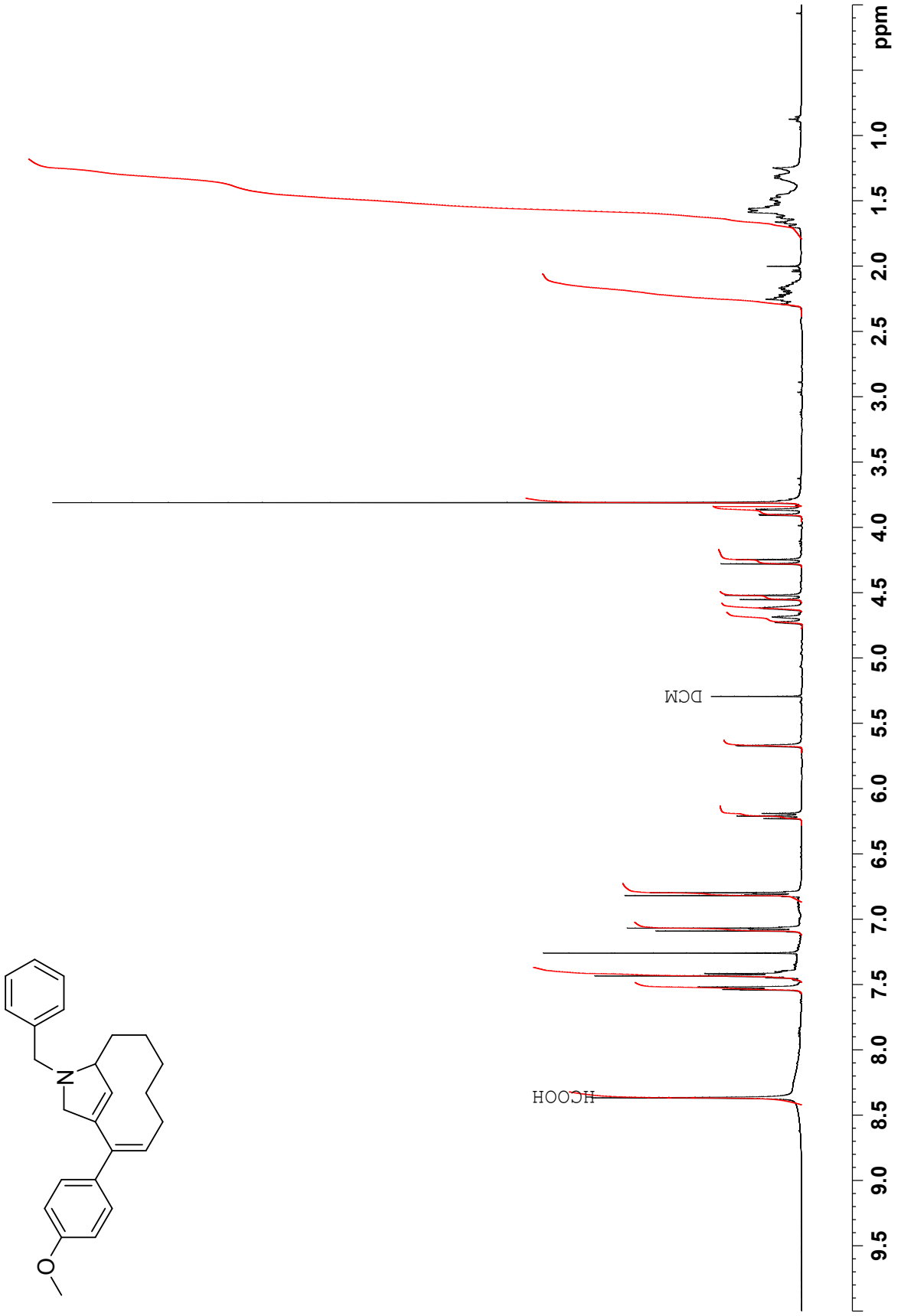


12a, ^{1}H NMR (400 MHz, $CDCl_3$):



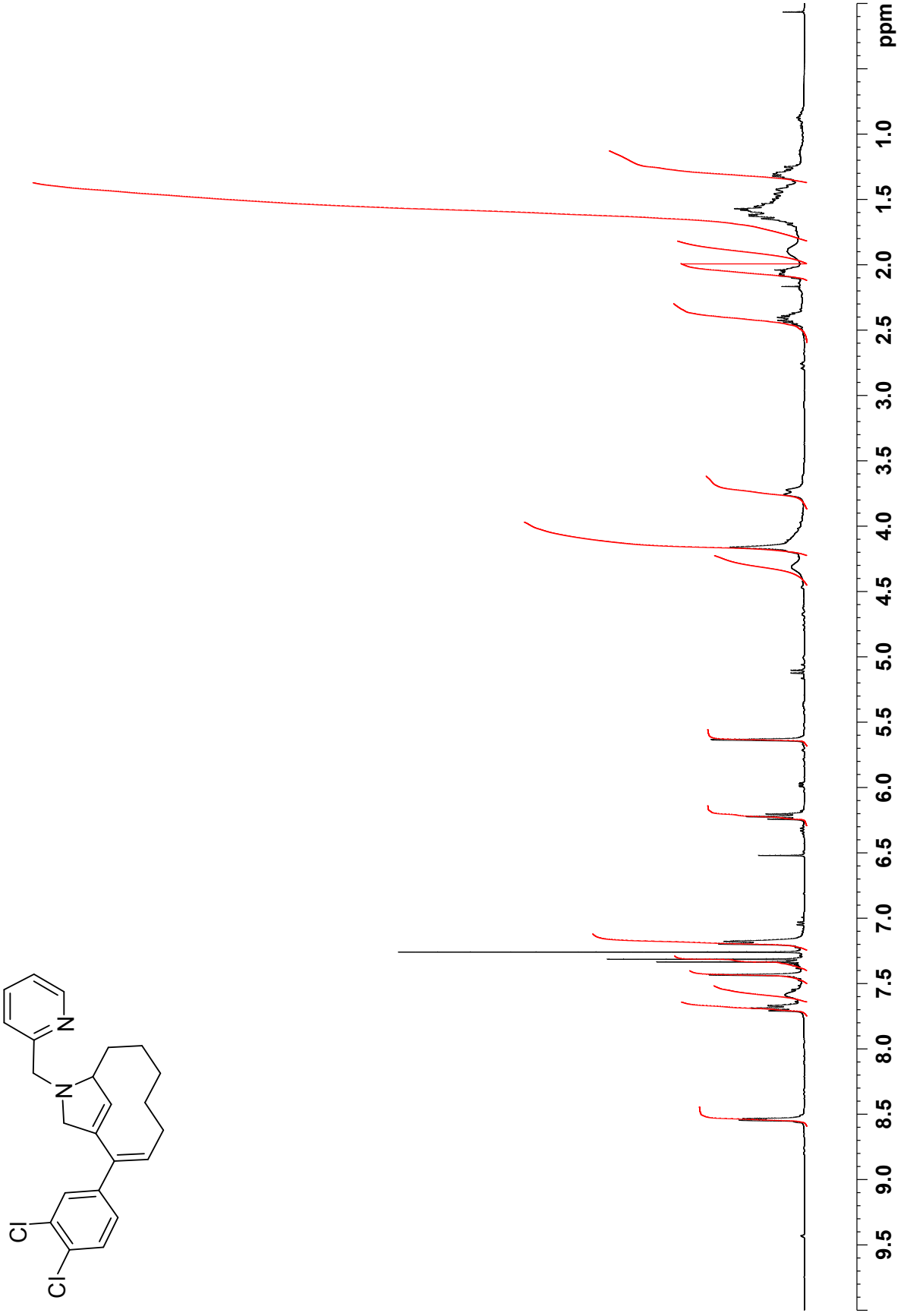
12a, ^{13}C NMR (100 MHz, $CDCl_3$):

12b, ^{1}H NMR (400 MHz, $CDCl_3$):

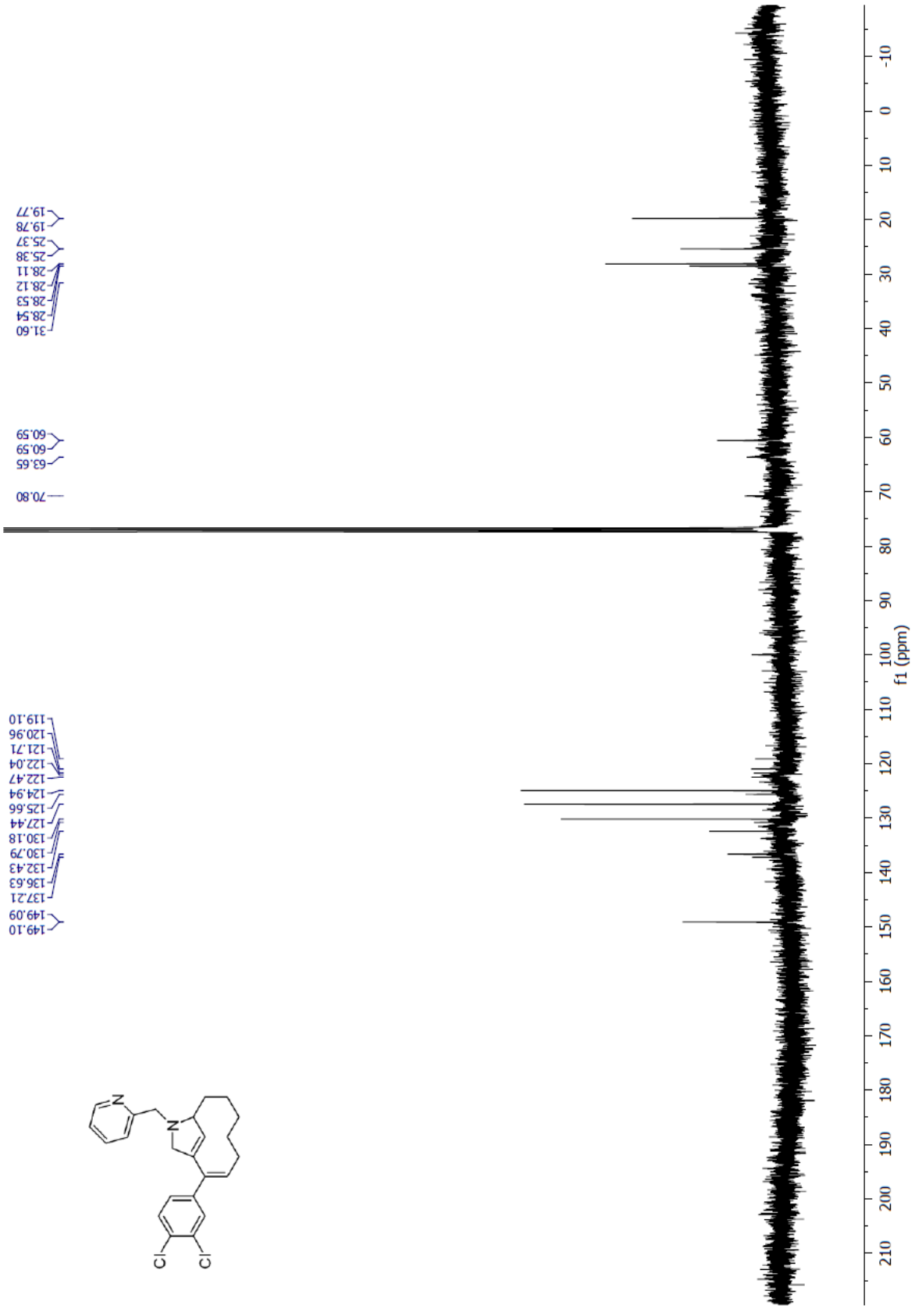


12b, ^{13}C NMR (100 MHz, $CDCl_3$):

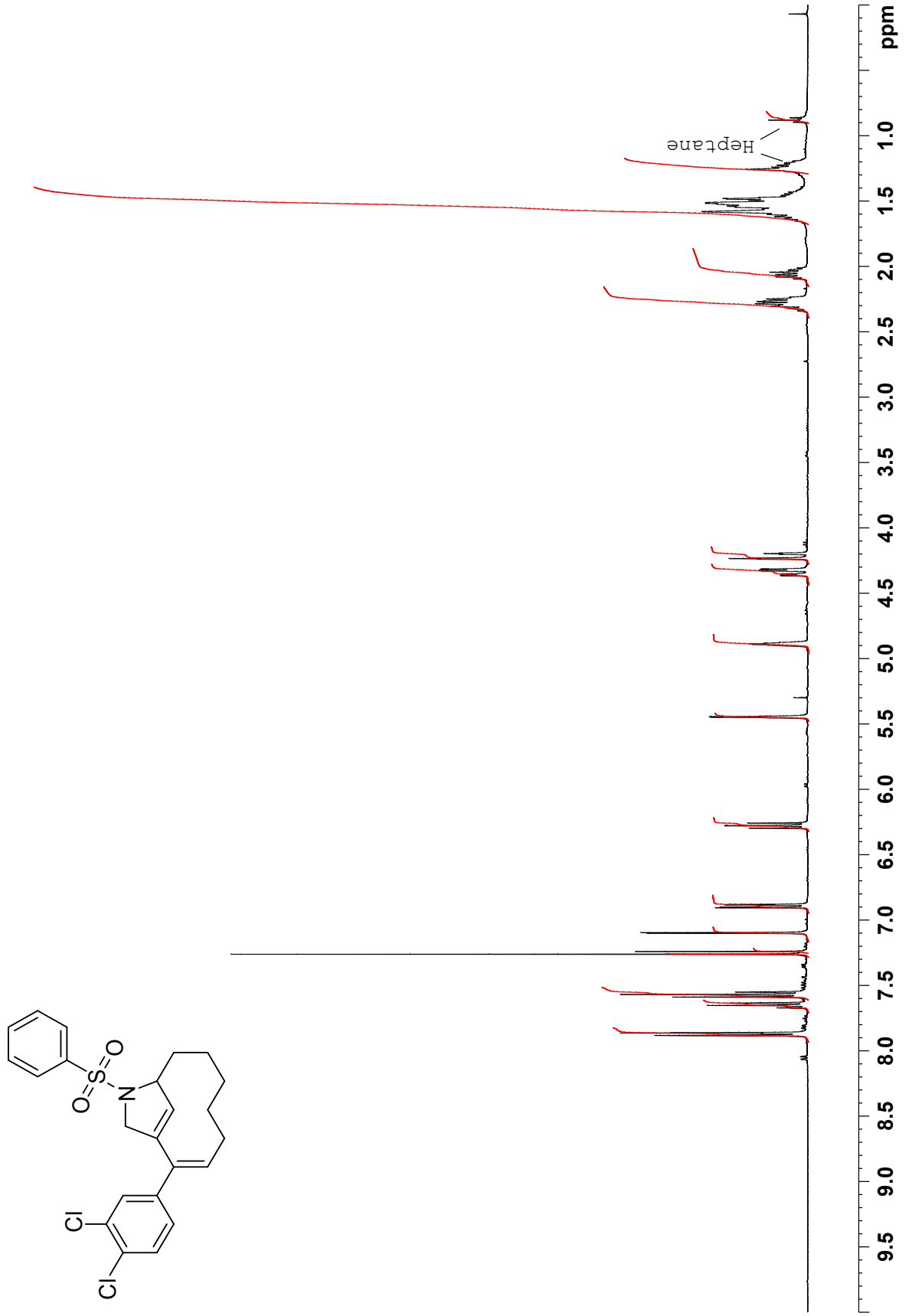
12c, ^{1}H NMR (400 MHz, $CDCl_3$):



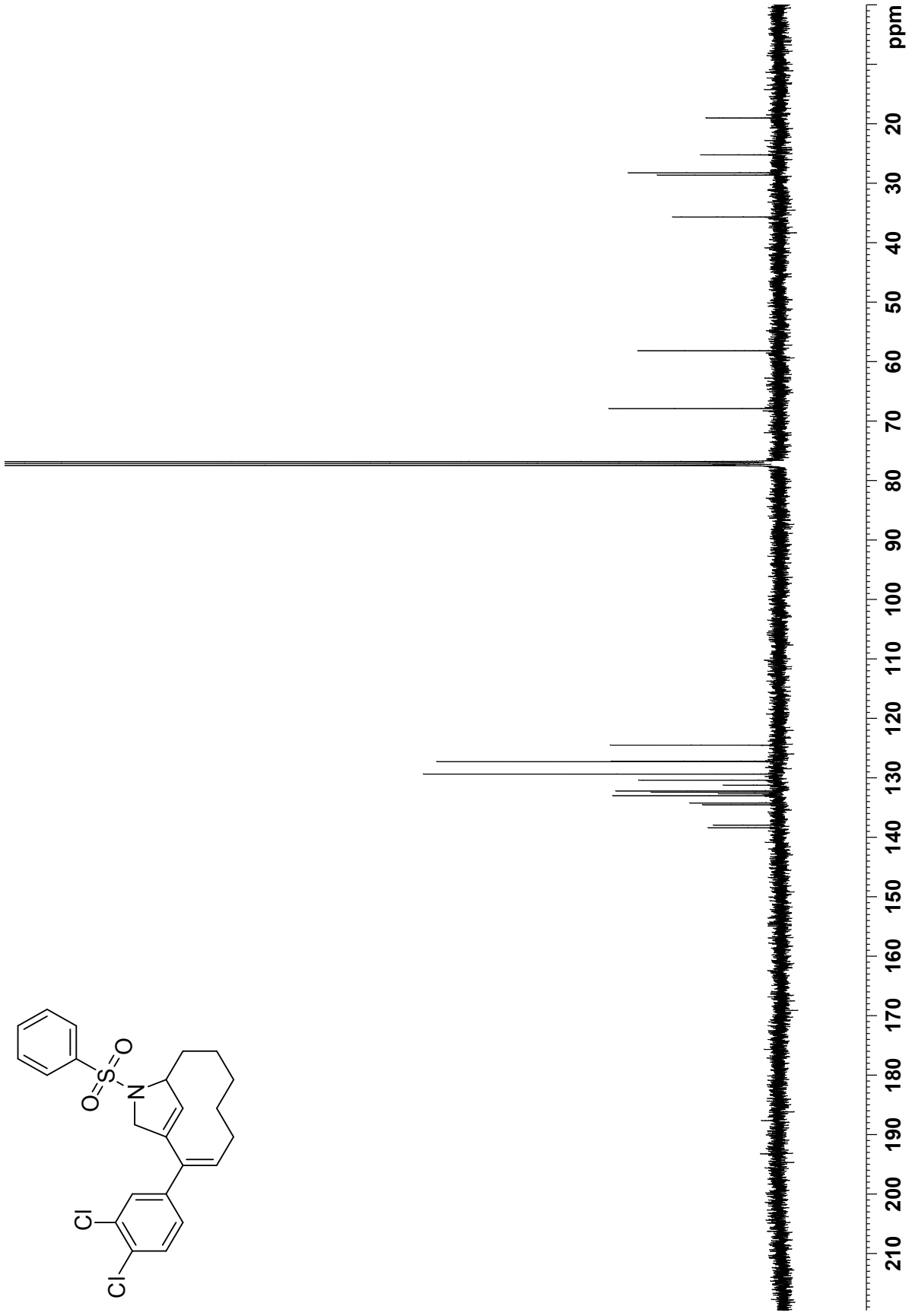
12c, ^{13}C NMR (100 MHz, $CDCl_3$):



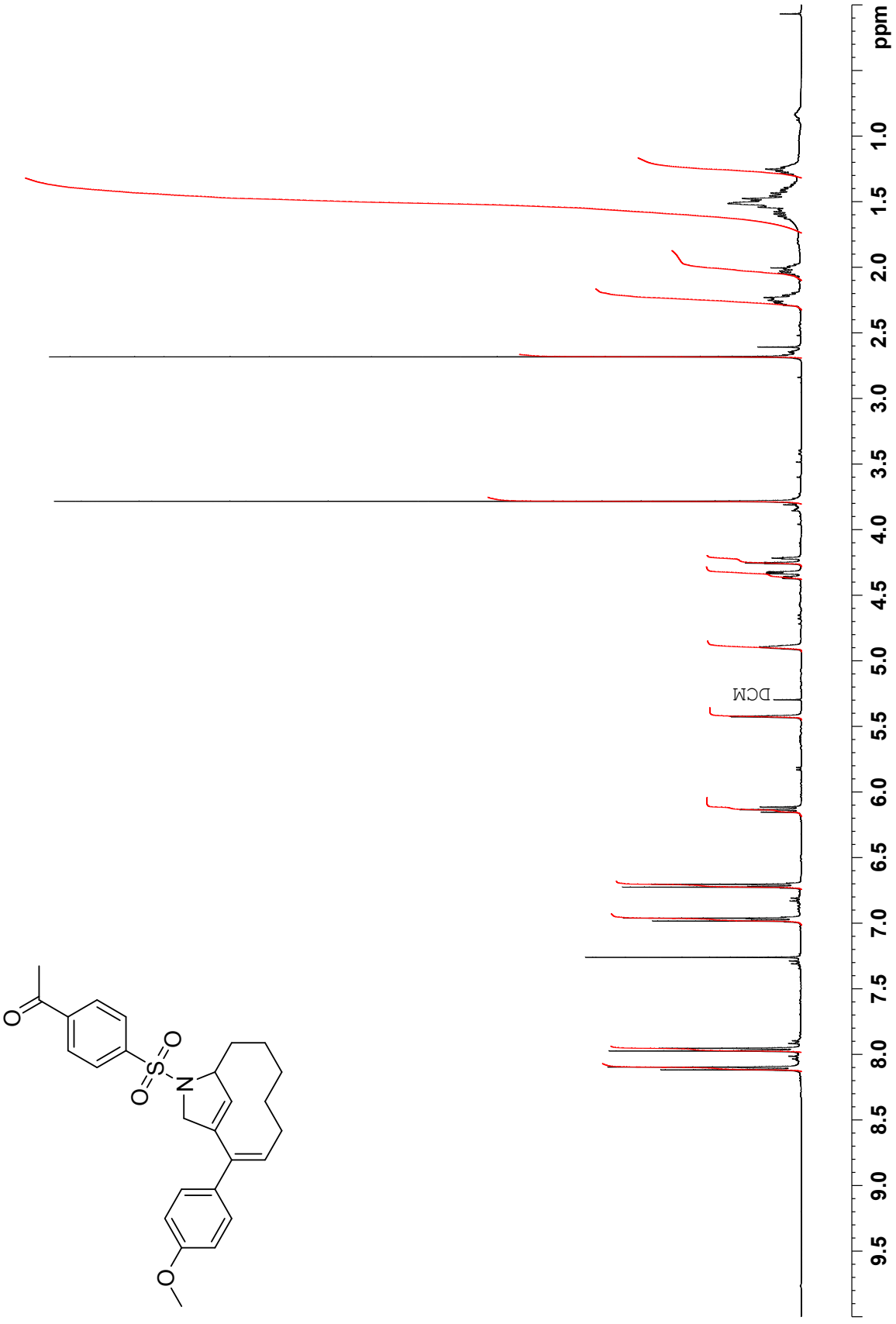
14a, ^{1}H NMR (400 MHz, $CDCl_3$):



14a, ^{13}C NMR (100 MHz, $CDCl_3$):

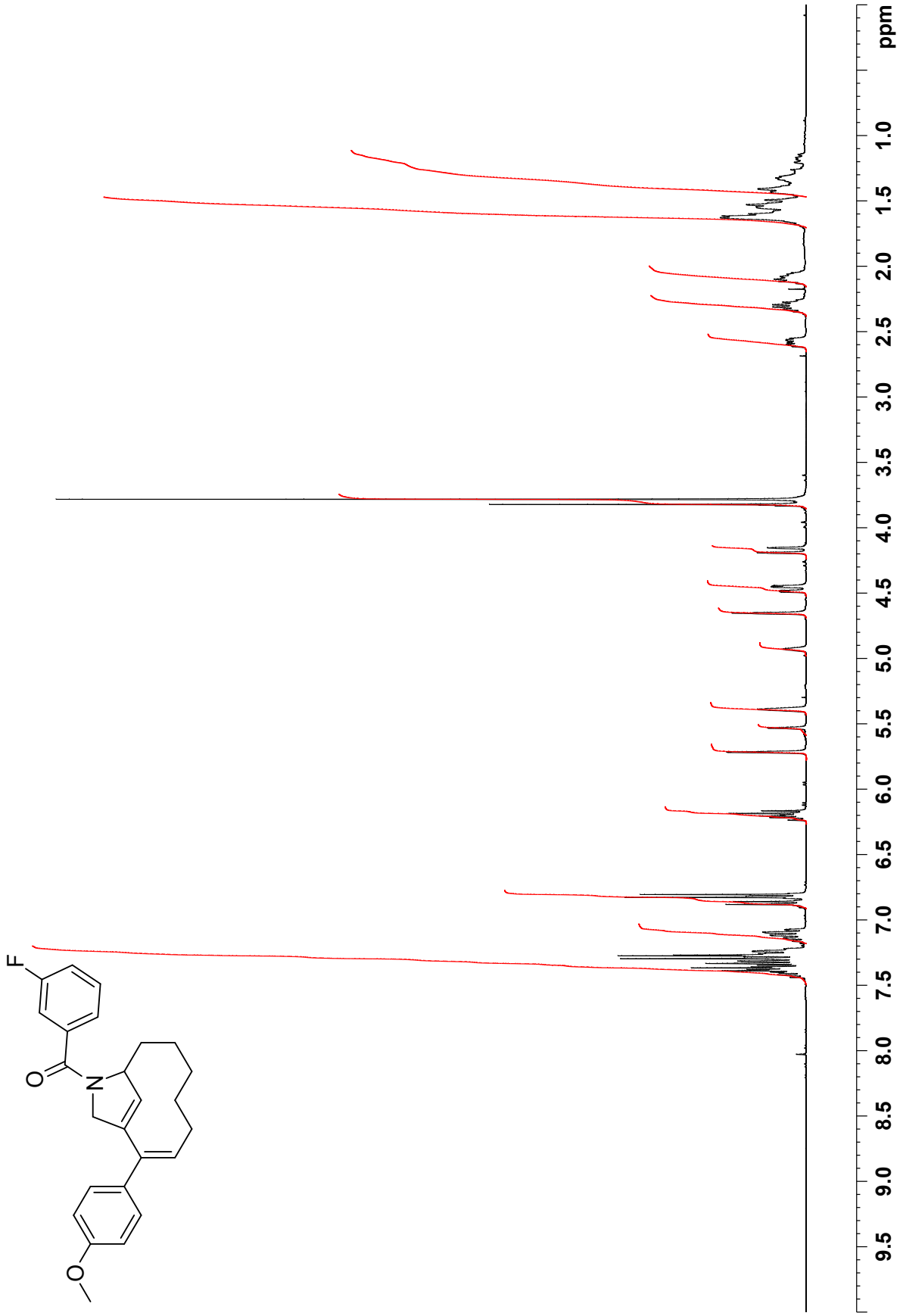


14b, ^{1}H NMR (400 MHz, $CDCl_3$):

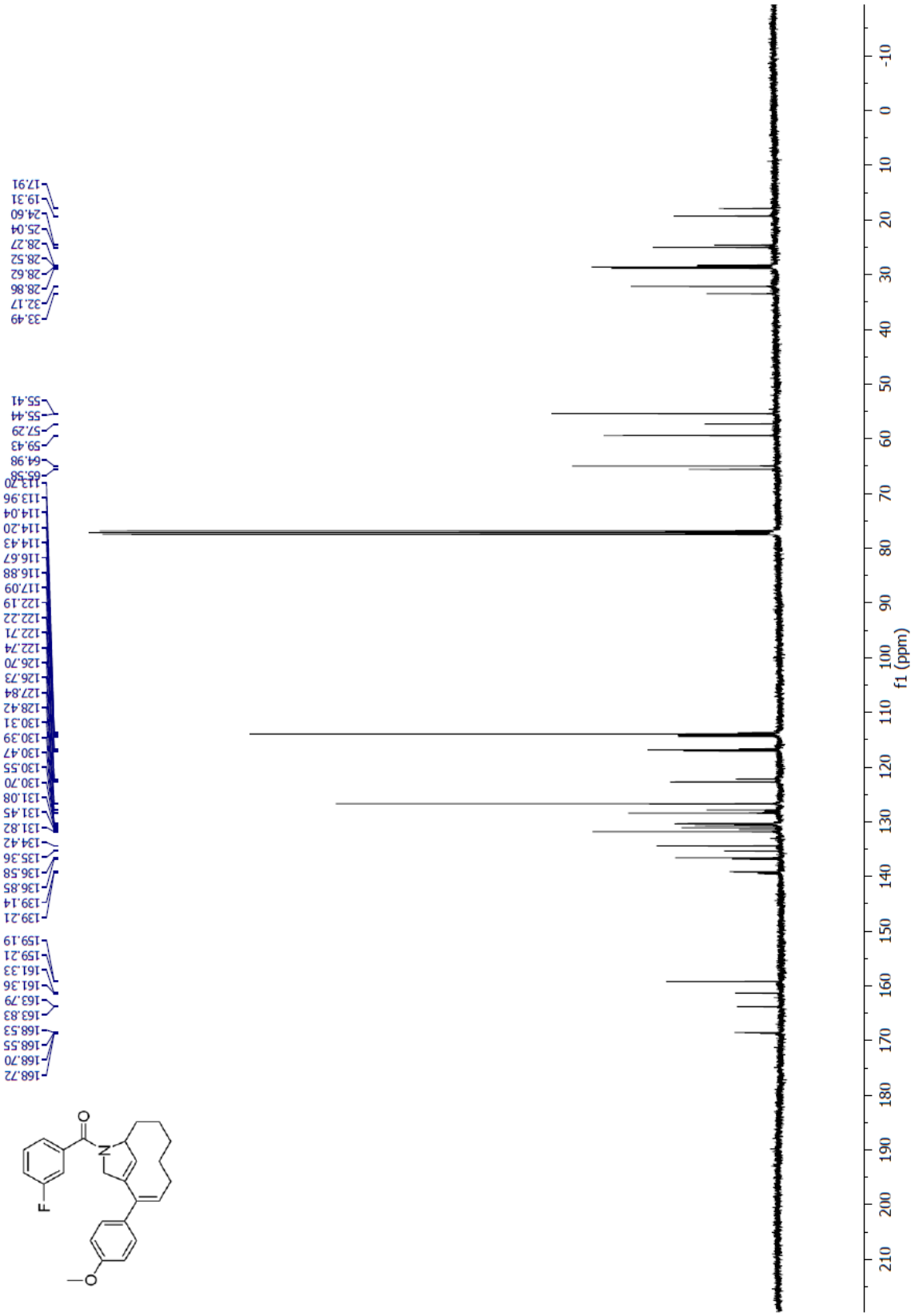


14b, ^{13}C NMR (100 MHz, $CDCl_3$):

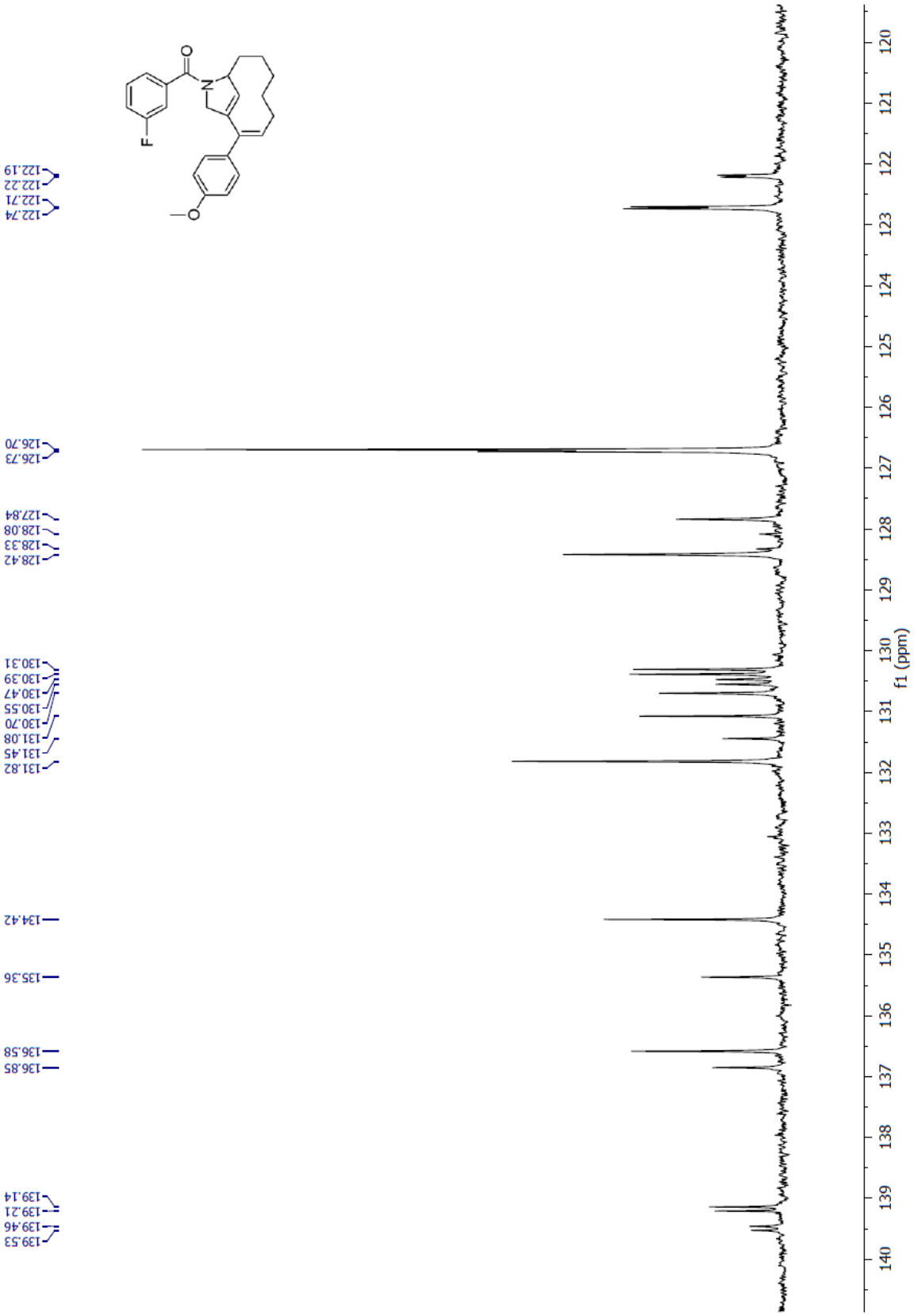
15a, ^{1}H NMR (400 MHz, $CDCl_3$):


F
O
N
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

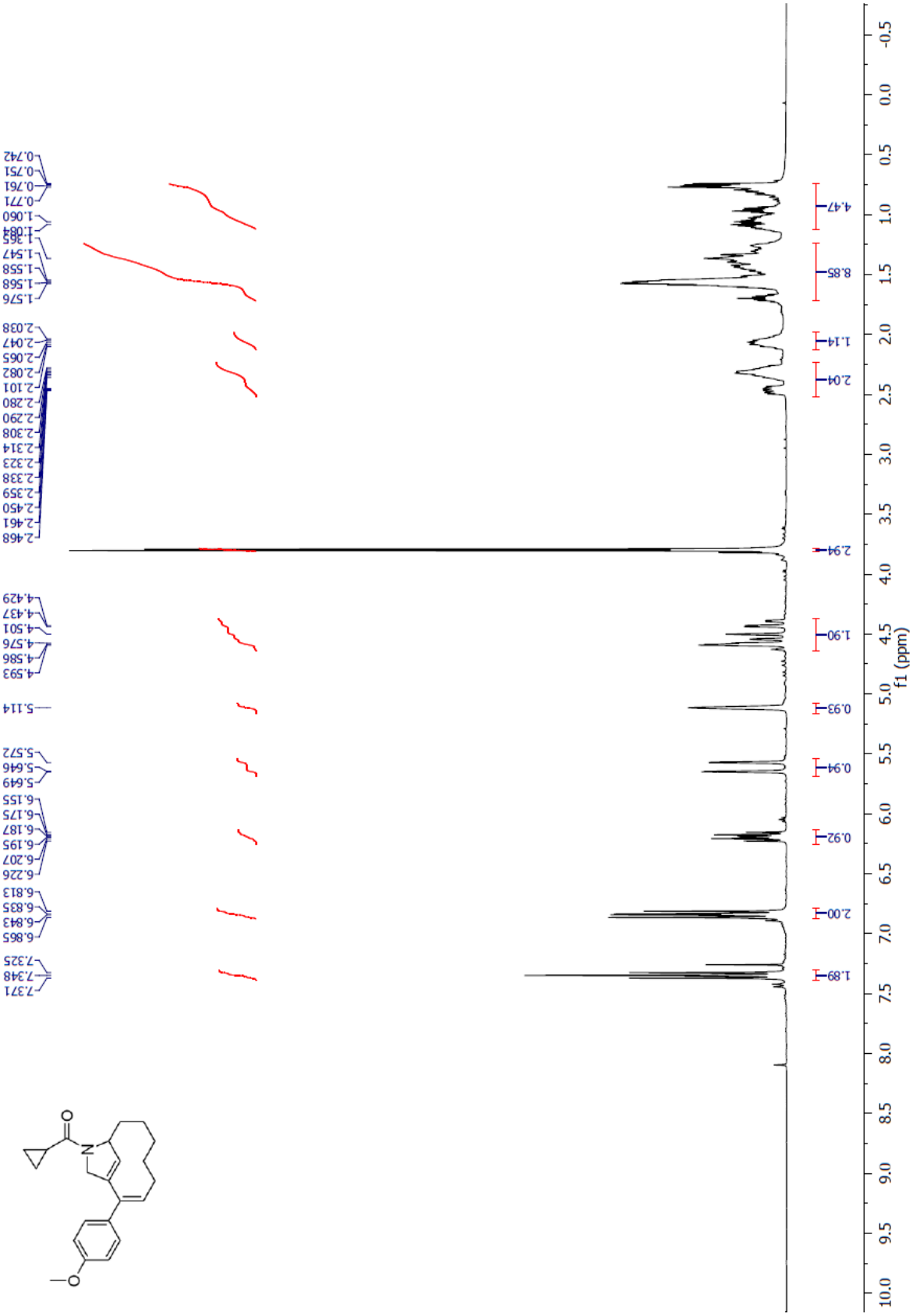
15a, ^{13}C NMR (100 MHz, $CDCl_3$):



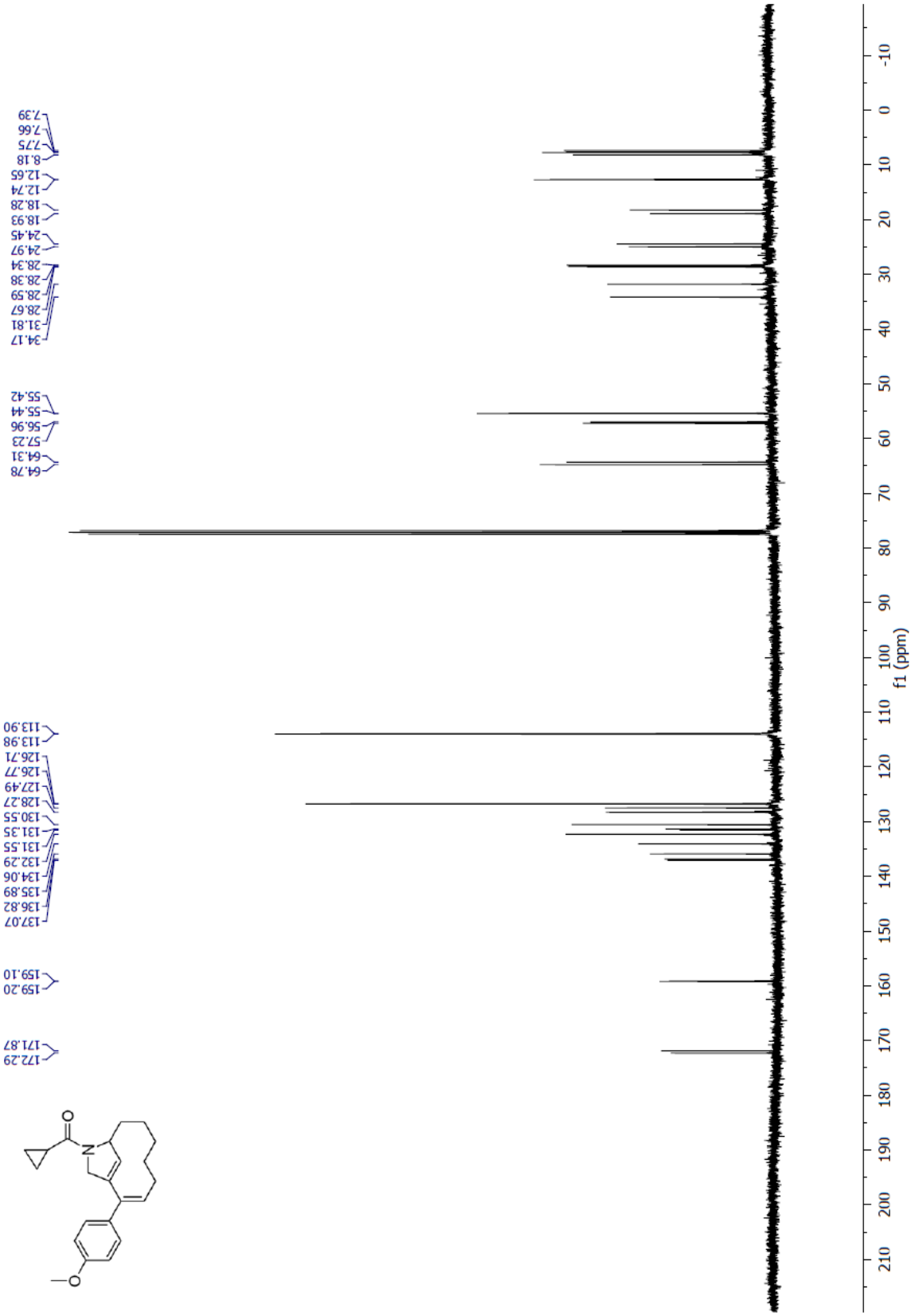
15a, ^{13}C NMR (100 MHz, $CDCl_3$), partially enlarged showing C-F splitting peaks (120-140 ppm):



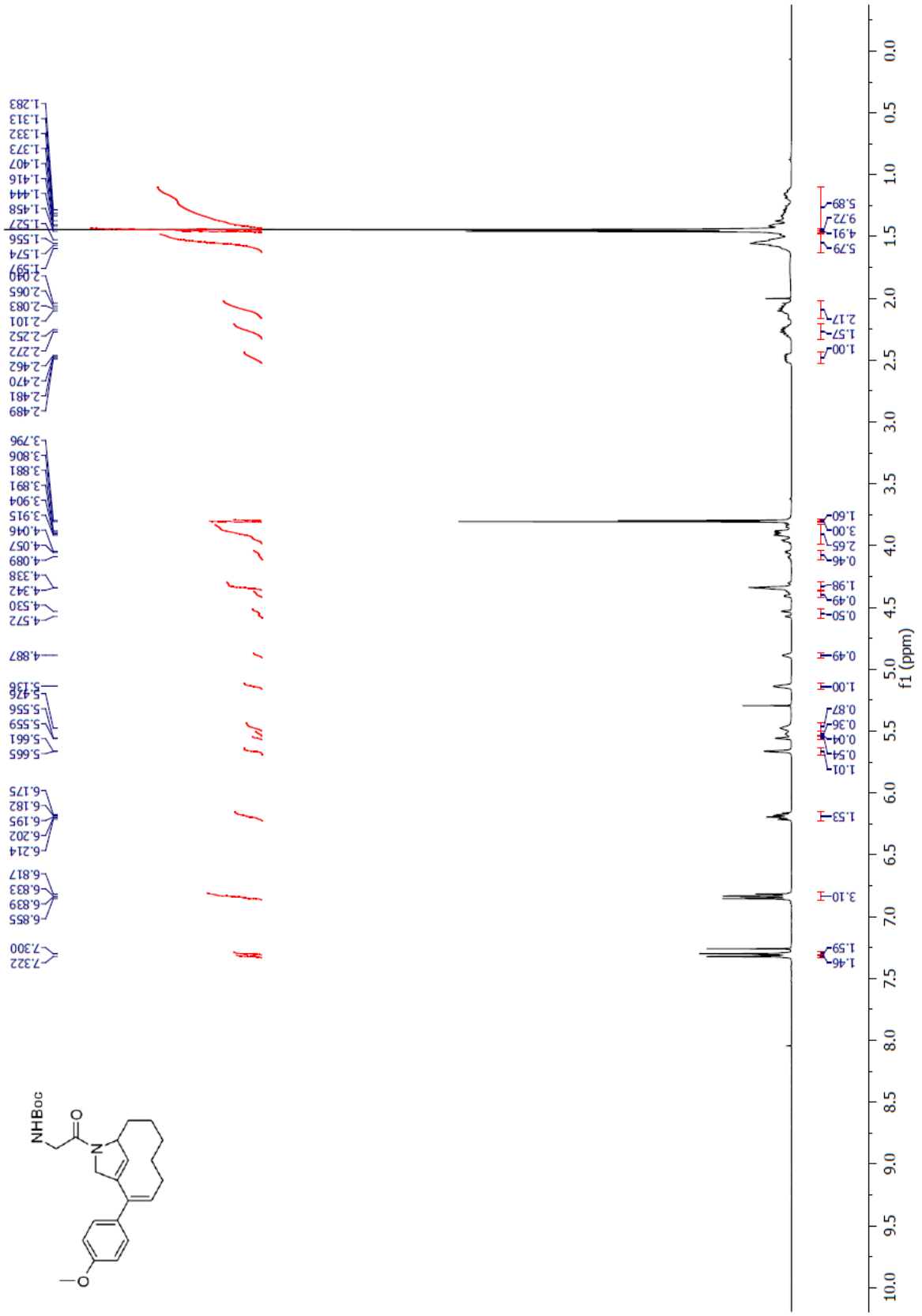
15b, ^{1}H NMR (400 MHz, $CDCl_3$):



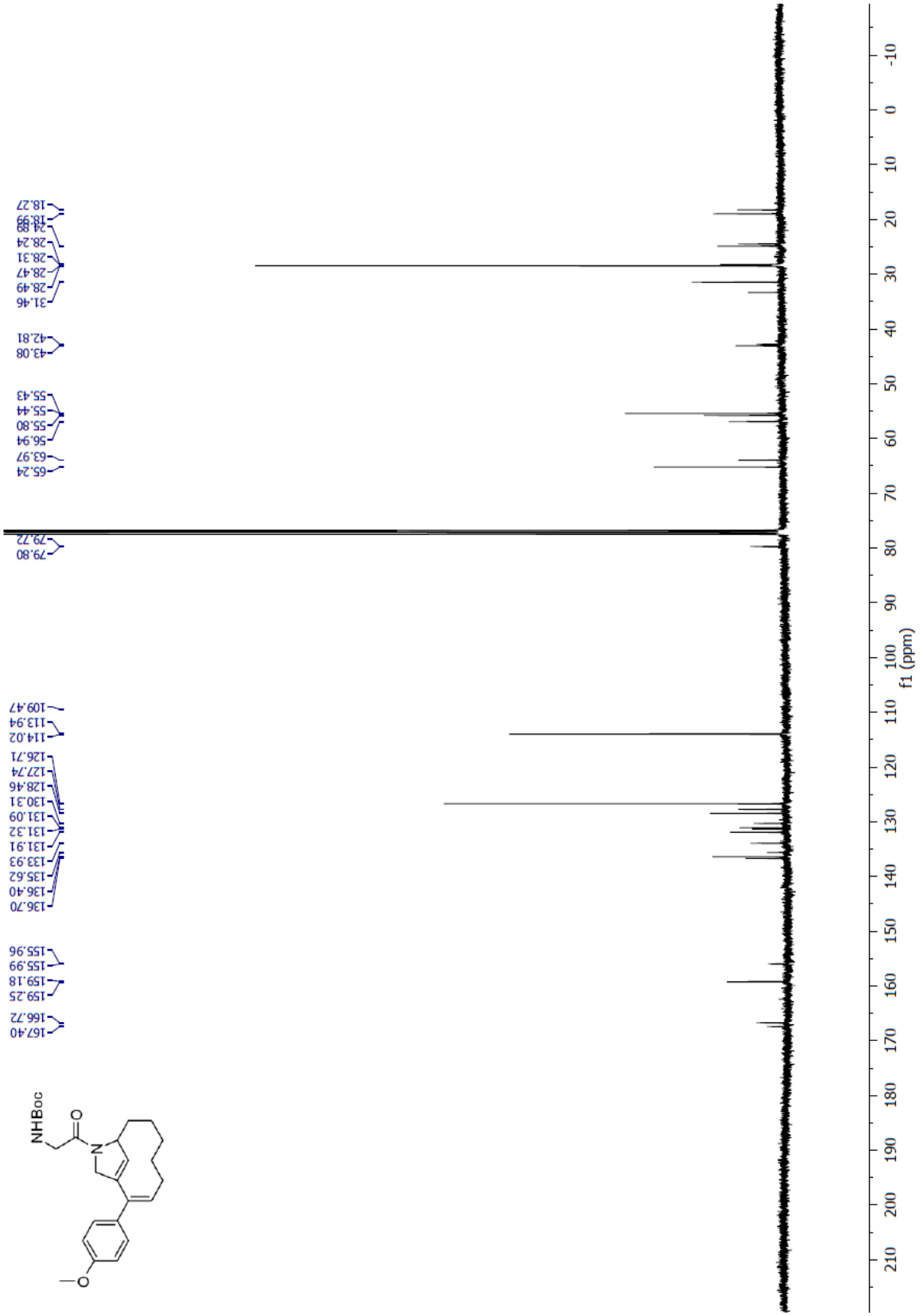
15b, ^{13}C NMR (100 MHz, $CDCl_3$):



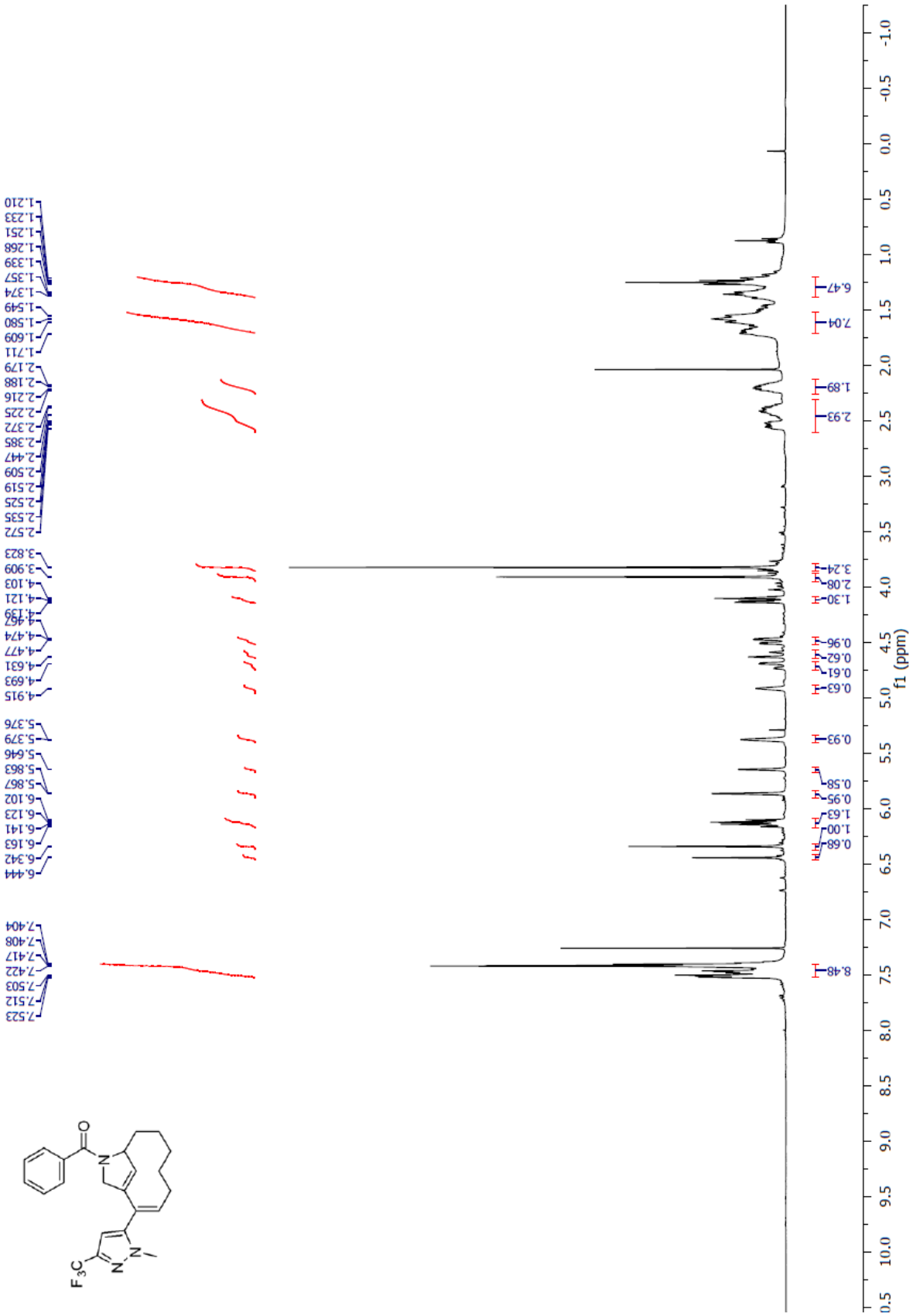
15c, ^{1}H NMR (400 MHz, $CDCl_3$):



15c, ^{13}C NMR (100 MHz, $CDCl_3$):



15d, ^{1}H NMR (400 MHz, $CDCl_3$):



15d, ^{13}C NMR (100 MHz, $CDCl_3$):