Supporting Information

Bronsted Acid-mediated Thiazole Synthesis From Sulfoxonium Ylides

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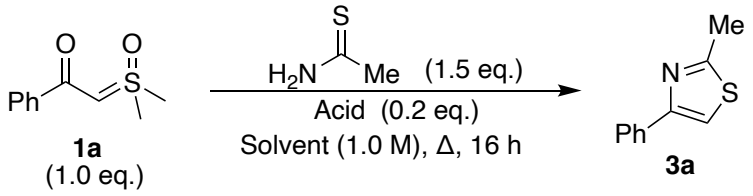
1.0 General Methods

Solvents, reagents, and consumables, such as TLC plates and column materials, were purchased from commercial suppliers and solvents/reagents were subsequently used without purification. ^{1}H, ^{13}C NMR spectroscopy was performed on a Varian 600 MHz spectrometer and chemical shifts are reported in ppm, usually referenced to TMS as an internal standard. LCMS measurements were performed on a Shimadzu LCMS-2020 equipped with a Phenomenex Kinetex 2.6uM EVO C18 100A 100 x 3.0 mm column and percentage purity measurements were run over 10 minutes in water/acetonitrile with 0.1% formic acid (5–95% over 10 min) with the UV detector set at 254 nm (Method A) or they were performed with Shimadzu LCMS-2020 equipped with a Phenomenex Kinetex 2.6uM EVO C18 100A 100 x 3.0 mm column and percentage purity measurements were run over 8 minutes in water/acetonitrile with 0.1% formic acid (5–95% over 10 min) with the UV detector set at 254 nm (Method B). ESI mass spectra were obtained using a Waters Xevo G2 Q-ToF HRMS (Wilmslow, UK) equipped with analytical flow ESI source. ESI experimental parameters were: capillary voltage 3.0 kV, sampling cone 35 au, extraction cone 4 au, source temperature 120 °C and desolvation gas 450 °C with a desolvation gas flow of 650 L h^{-1} and no cone gas. MS conditions were MS1 in resolution mode between 100-1500 Da. Accurate mass data were obtained using MassLynx software. All accurate mass data were within ±5 ppm from their theoretical value.

2.0 Optimisation of Acid-Mediated Thiazole Synthesis
2.1 Initial Solvent, Acid and Temperature Screen

Ylide **1a** (40 mg, 0.204 mmol,1.0 eq.), thioacetamide (23mg, 0.306 mmol, 1.5 eq.), acid (0.0408 mmol, 0.2 eq.) and solvent (0.2 mL, 1.0 M) were added to a microwave vial. The vessel was sealed and the resulting solution was heated to the specified temperature and stirred for 16 h.The reaction mixture was cooled to rt before 1,3,5-trimethoxybenzene (34 mg, 0.204 mmol, 1.0 eq.) was added as an internal standard and the reaction mixture concentrated under reduced pressure. ^{1}H NMR conversion was then calculated using the product methyl group signal relative to 1,3,5-trimethoxybenzene signals.

Table S1: Solvent, acid and temperature screen for the insertion of thioacetamide



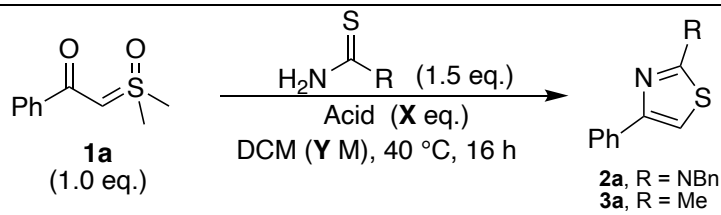
Entry	Solvent	Acid	Temperature (°C)	NMR Conversion (%)
1	MeCN	MsOH	40	33
2	MeCN	Diphenyl phosphate	40	34
3	THF	MsOH	70	14
4	EtOAc	Diphenyl phosphate	40	48
5	EtOH	Diphenyl phosphate	40	18
6	Acetone	Diphenyl phosphate	40	31
7	DMF	Diphenyl phosphate	40	34
8	Dioxane	Diphenyl phosphate	40	36
9	DCE	Diphenyl phosphate	40	51
10	DCE	Diphenyl phosphate	70	54
11	DCE	Diphenyl phosphate	40	42
12	Toluene	Diphenyl phosphate	rt	11
13	Toluene	Diphenyl phosphate	40	55
14	DCM	Diphenyl phosphate	rt	11

15	DCM	Diphenyl phosphate	40	59
16	DCM	AcOH	40	6
17	DCM	PTSA	40	33
18	DCM	HNO_3	40	47
19	DCM	Pyridine.HCl	40	48
20	DCM	MsOH	40	45
21	DCM	TFA	40	64

2.2 Acid Equivalence and Molarity Screen

Ylide **1a** (40 mg, 0.204 mmol,1.0 eq.), nucleophile (0.306 mmol, 1.5 eq.), acid (**X** eq.) and DCM (**Y** M) were added to a microwave. The vessel was sealed and the resulting solution was heated to 40 °C and stirred for 16 h. The reaction mixture was cooled to rt before 1,3,5 trimethoxybenzene (34 mg, 0.204 mmol, 1.0 eq.) was added as an internal standard and the reaction mixture concentrated under reduced pressure. ^{1}H NMR conversion was then calculated using product signals relative to 1,3,5-trimethoxybenzene signals.

Table S2: Acid equivalence and reaction molarity screen for the reaction of thioacetamide and *N*-benzyl thiourea



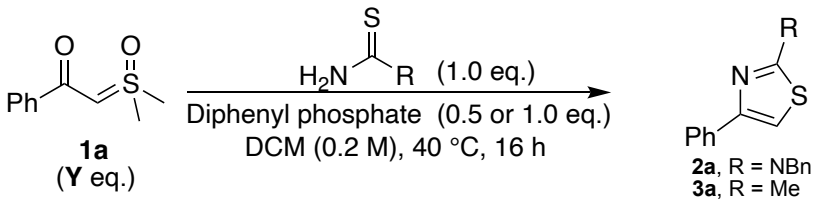
Entry	Acid	Acid (X eq.)	Molarity (Y M)	R	NMR Conversion (%)
1	TFA	1.0	1.0	Me	64
2	Diphenyl phosphate	1.0	1.0	Me	57
3	TFA	1.0	0.2	Me	69
4	Diphenyl phosphate	1.0	0.2	Me	70
5	TFA	1.0	0.2	NBn	68
6	Diphenyl phosphate	1.0	0.2	NBn	71

7	Diphenyl phosphate	0.25	0.2	Me	73
8	Diphenyl phosphate	0.50	0.2	Me	77
9	Diphenyl phosphate	0.50	0.2	NBn	73
10	Diphenyl phosphate	0.75	0.2	Me	70
11	Diphenyl phosphate	1.0	0.2	NBn	79

2.3 Ylide and acid equivalence screen

Ylide **1a** (**Y** eq.), nucleophile (0.204 mmol, 1.0 eq.), diphenyl phosphate (26 mg or 51 mg, 0.102 or 0.204 mmol, 0.5 or 1.0 eq.) and DCM (1.0 mL, 0.2 M) were added to a microwave vial. The vessel was sealed and the resulting solution was heated to 40 °C and stirred for 16 h. The reaction mixture was cooled to rt before 1,3,5-trimethoxybenzene (34 mg, 0.204 mmol, 1.0 eq.) was added as an internal standard and the reaction mixture concentrated under reduced pressure. ^{1}H NMR conversion was then calculated using product signals relative to 1,3,5-trimethoxybenzene signals.

Table S3: Ylide and acid equivalence screen

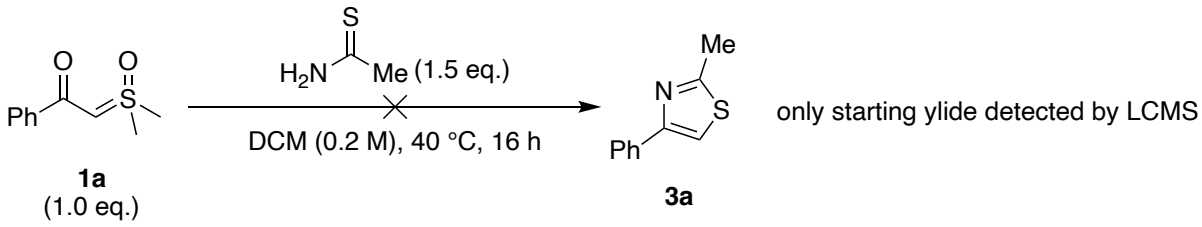


Entry	Ylide eq.	Diphenyl phosphate eq.	R	NMR Conversion (%)*
1	1.25	0.5	Me	82
2	1.25	1.0	NBn	88
3	1.5	0.5	Me	82
4	2.0	0.5	Me	77

2.4 Control Experiments and Proposed Mechanism

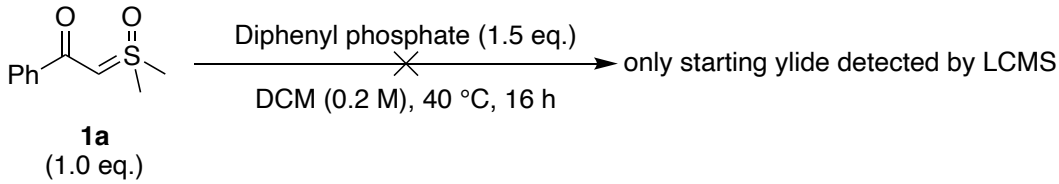
Ylide **1a** (40 mg, 0.204 mmol,1.0 eq.), thioacetamide (0.306 mmol or 0 mmol, 1.5 eq.), diphenyl phosphate (51 mg, 1.0 eq.) and DCM (1.0 mL, 0.2 M) were added to a microwave vial. The vessel was sealed and the resulting solution was heated to 40 °C and stirred for 16 h. The crude reaction mixture was then analysed using LCMS Method A.

Control experiment 1: Stirring sulfoxonium ylide **1a** with only thioacetamide at 40 °C



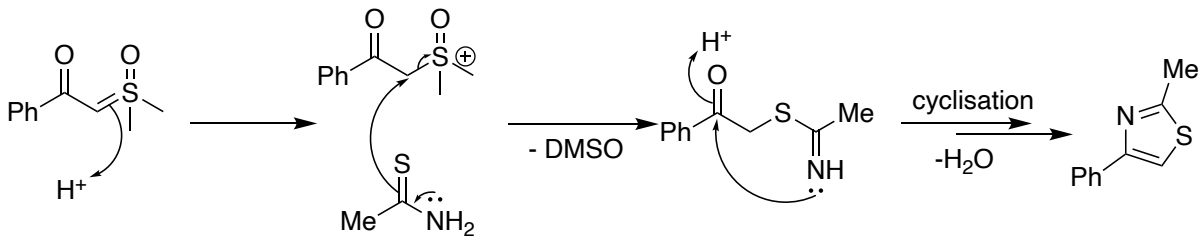
Scheme S1

Control experiment 2: Stirring sulfoxonium ylide **1a** with only diphenyl phosphate at 40 °C



Scheme S2

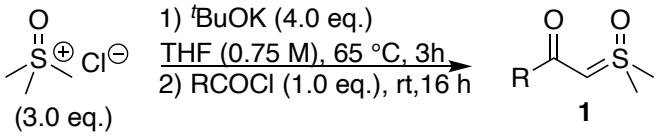
Based on these results and previously reported activation of ylides using diphenyl phosphate as an organocatalyst,[1] we speculate the following mechanism:



Scheme S3

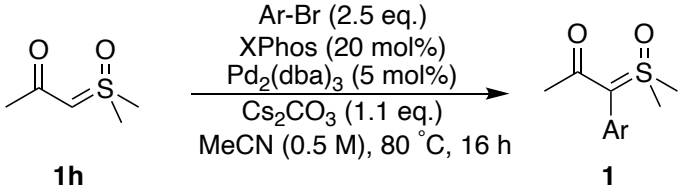
3.0 Experimental
3.1 Synthesis of Sulfoxonium Ylides

General procedure A: Synthesis of sulfoxonium ylides from acyl chlorides



To a mixture of dried trimethylsulfoxonium chloride (3.0 eq.) was added potassium *tert*-butoxide (4.0 eq.) in anhydrous THF (0.75 M). The resulting solution was heated to reflux and stirred for 3 h under an atmosphere of Ar. The reaction mixture was cooled to rt and acid chloride (1.0 eq.) added *via* dropwise addition. The resulting solution was stirred for 16 h at rt. The reaction mixture was concentrated under reduced pressure and to the resulting mixture was added water (50 mL) and DCM/IPA (3:1) (50 mL). The organic layer was collected and the aqueous layer extracted with DCM/IPA (3:1) (5 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated to give the crude product. The crude product was purified by trituration by dissolving in the minimum amount of boiling ethyl acetate, followed by precipitation with petroleum ether 40-60 °C. The solid was filtered, washed with a mixture of petroleum ether 40-60 °C:EtOAc (1:1), and dried to give the title compound.

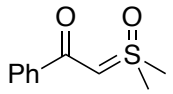
General procedure B: Synthesis of Alpha Arylated Sulfoxonium Ylides



Prepared according to a slightly modified literature procedure.[2] To an oven-dried microwave vial was added XPhos (38 mg, 0.08 mmol, 20 mol%), $Pd_2(dba)_3$ (18 mg, 0.02 mmol, 5 mol%), Cs_2CO_3 (143 mg, 0.44 mmol, 1.1 eq.) and anhydrous MeCN (0.4 mL) under Ar. To a separate oven-dried microwave vial was added ylide **1h** (54 mg, 0.4 mmol, 1.0 eq.), aryl bromide (2.5 eq.) and MeCN (0.4 mL) under Ar. Both the resulting solutions were stirred at rt for 10 min. After 10 min, the ylide and aryl bromide solution was added to the other vial which was transferred to a preheated hotplate and stirred at 80 °C for 16 h. The reaction mixture was then

filtered through Celite which was rinsed thoroughly with DCM. The volatiles were evaporated, and the crude reaction mixture was purified by automated column chromatography.

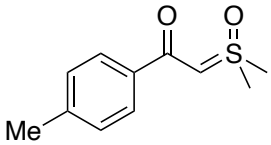
Benzoyl(dimethyloxosulphonio)methanide (1a)



1a

Performed according to general procedure **A**, trimethylsulfoxonium chloride (11.3 g, 88.2 mmol, 3.0 eq.), potassium *tert*-butoxide (13.2 g, 117.6 mmol, 4.0 eq.) and benzoyl chloride (3.4 mL, 29.4 mmol, 1.0 eq.) in anhydrous THF (118 mL) at 65 °C - rt for 16 h to give the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1a** as a light yellow solid (5.4 g, 93%). LCMS (Method A, UV, ESI) Rt = 1.40 min, $[M\text{-}H]^+$ m/z = 196.9, >99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.74-7.73 (m, 2H), 7.42-7.40 (m, 1H), 7.38-7.36 (m, 2H), 5.58 (s, 1H), 3.53 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 180.7, 139.9, 130.7, 128.5, 126.8, 72.6, 41.0; HRMS (ESI) m/z calcd for $C_{10}H_{13}O_2S$ $[M\text{-}H]^+$ 197.0636; found 197.0633. Spectroscopic data consistent with that reported in the literature.[3]

4-Methyl(dimethyloxosulphonio)methanide (1b)

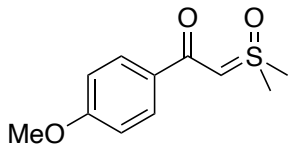


1b

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.83 g, 14.3 mmol, 3.0 eq.), potassium *tert*-butoxide (2.13 g, 19.0 mmol, 4.0 eq.) and 4-methylbenzoyl chloride (0.63 mL, 29.4 mmol, 1.0 eq.) in anhydrous THF (19 mL) at 65 ºC- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1b** as a white solid (770 mg, 77%). LCMS (Method A, UV, ESI) Rt = 2.08 min, $[M\text{-}H]^+$ m/z = 210.0, 98% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.64 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 5.54 (s, 1H), 3.52 (s, 6H), 2.30 (s, 3H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 180.7, 140.3, 137.2, 129.0, 126.8, 72.2, 41.0, 21.4; HRMS (ESI) m/z calcd for

$C_{11}H_{15}O_2S$ [M-H]$^+$ 211.0793; found 211.0800. Spectroscopic data consistent with that reported in the literature.[3]

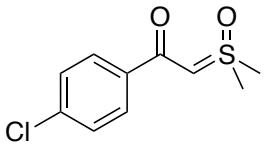
4-Methoxy(dimethyloxosulphonio)methanide (1c)



1c

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.71 g, 13.2 mmol, 3.0 eq.), potassium *tert*-butoxide (1.98 g, 17.7 mmol, 4.0 eq.) and 4-methoxybenzoyl chloride (0.60 mL, 4.42 mmol, 1.0 eq.) in anhydrous THF (18 mL) at 65 °C- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1c** as a white solid (901 mg, 91%). LCMS (Method A UV, ESI) R_t = 1.24 min, [M-H]$^+$ *m/z* = 226.9, 94% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.70 (d, J = 8.4 Hz, 2H), 6.91 (d, J = 8.4 Hz, 2H), 5.50 (s, 1H), 3.76 (s, 3H), 3.51 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 180.3, 161.4, 132.4, 128.5, 113.6, 71.6, 55.6, 41.1; HRMS (ESI) *m/z* calcd for $C_{11}H_{15}O_3S$ [M-H]$^+$ 227.0742; found 227.0752. Spectroscopic data consistent with that reported in the literature.[3]

4-Chloro(dimethyloxosulphonio)methanide (1d)

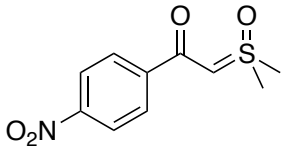


1d

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.67 g, 13.0 mmol, 3.0 eq.), potassium *tert*-butoxide (1.94 g, 17.3 mmol, 4.0 eq.) and 4-chlorobenzoyl chloride (0.56 mL, 29.4 mmol, 1.0 eq.) in anhydrous THF (17 mL) at 65 °C- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ethereum ether 40-60 °C gave ylide **1d** as a white solid (890 mg, 89%). LCMS (Method A, UV, ESI) R_t = 3.08 min, [M-H]$^+$ *m/z* = 230.9, 93% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.76 (d, J = 9.0 Hz, 2H), 7.44 (d, J = 9.0 Hz, 2H), 5.62 (s, 1H), 3.53 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 179.1, 138.6, 135.4, 128.6, 128.5, 73.1, 40.9; HRMS (ESI) *m/z* calcd for

$C_{10}H_{12}O_2SCl$ $[M-H]^+$ 231.0247; found 231.0257. Spectroscopic data consistent with that reported in the literature.[3]

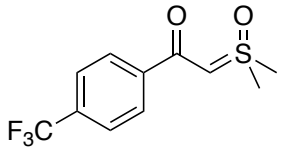
4-Nitrobenzoyl(dimethyloxosulphonio)methanide (1e)



1e

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.60 g, 12.4 mmol, 3.0 eq.), potassium *tert*-butoxide (1.86 g, 16.6 mmol, 4.0 eq.) and 4-nitrobenzoyl chloride (769 mg, 4.14 mmol, 1.0 eq.) in anhydrous THF (17 mL) at 65 °C- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1e** as an orange solid (657 mg, 66%). LCMS (Method A, UV, ESI) *Rt* = 2.87 min, $[M-H]^+$ *m/z* = 241.9, 94% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.24-8.23 (m, 2H), 7.98-7.97 (m, 2H), 5.80 (s, 1H), 3.57 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 177.9, 148.8, 145.5, 128.0, 123.8, 74.9, 40.8; HRMS (ESI) *m/z* calcd for $C_{10}H_{12}NO_4S$ $[M-H]^+$ 242.0487; found 242.0484. Spectroscopic data consistent with that reported in the literature.[3]

4-Trifluoromethyl(dimethyloxosulphonio)methanide (1f)

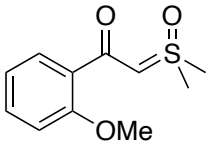


1f

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.46 g, 11.3 mmol, 3.0 eq.), potassium *tert*-butoxide (1.70 g, 15.1 mmol, 4.0 eq.) and 4-Trifluoromethylbenzoyl chloride (0.56 mL, 3.78 mmol, 1.0 eq.) in anhydrous THF (15 mL) at 65 °C- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1f** as a white solid (689 mg, 69%). LCMS (Method A, UV, ESI) *Rt* = 4.07 min, $[M-H]^+$ *m/z* = 265.0, 99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.94-7.93 (d, *J* = 7.8 Hz, 2H), 7.75-7.74 (d, *J* = 7.8 Hz, 2H), 5.72 (s, 1H), 3.56 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 178.8, 143.5, 130.6 (q, *J* = 31.6 Hz), 127.5, 125.5 (q, *J* = 3.6

Hz), 124.6 (q, J = 272.6 Hz), 74.0, 40.8; ^{19}F NMR (376 MHz, d_6-DMSO); δ -61.1; HRMS (ESI) *m/z* calcd for $C_{11}H_{12}O_2F_3S$ $[M\text{-}H]^+$ 265.0510; found 265.0508. Spectroscopic data consistent with that reported in the literature.[4]

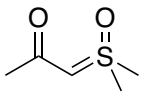
2-Methoxy(dimethyloxosulphonio)methanide (1g)



1g

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.71 g, 13.2 mmol, 3.0 eq.), potassium *tert*-butoxide (1.98 g, 17.7 mmol, 4.0 eq.) and 2-methoxybenzoyl chloride (0.66 mL, 4.42 mmol, 1.0 eq.) in anhydrous THF (18 mL) at 65 °C- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1g** as a white solid (865 mg, 87%). LCMS (Method A, UV, ESI) Rt = 1.18 min, $[M\text{-}H]^+$ *m/z* = 226.9, 98% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.66-7.65 (m, 1H), 7.34-7.32 (m, 1H), 7.01-7.00 (m, 1H), 6.94-6.91 (m, 1H), 5.44 (s, 1H), 3.79 (s, 3H), 3.50 (s, 6H);^{13}C NMR (151 MHz, d_6 -DMSO): δ179.3, 157.5, 131.4, 129.7, 129.4, 120.4, 112.2, 76.6, 55.9, 41.1; HRMS (ESI) *m/z* calcd for $C_{11}H_{15}O_3S$ $[M\text{-}H]^+$ 227.0742; found 227.0753. Spectroscopic data consistent with that reported in the literature.[3]

1-(Dimethyl-(oxo)-λ^6-sulfanylidene)propan-2-one (1h)

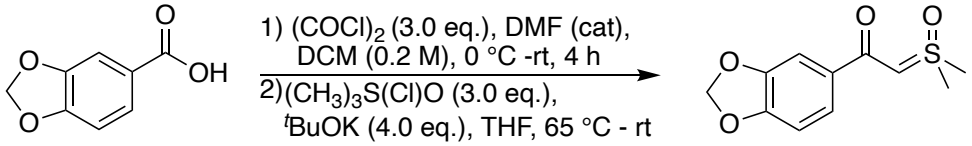


1h

Performed according to general procedure **A**, trimethylsulfoxonium chloride (3.86 g, 30 mmol, 3.0 eq.), potassium *tert*-butoxide (4.58 g, 19.0 mmol, 4.0 eq.) and acetyl chloride (728 µL, 10.2 mmol, 1.0 eq.) in anhydrous THF (40 mL) at 65 °C- rt for 16 h gave the crude product. Purification by automated flash column chromatography (12 g, SiO_2) using a 100:0-95:5 gradient of DCM/MeOH as eluent gave ylide **1h** as a yellow oil (583 mg, 43%); LCMS (UV, ESI) No sufficient chromophore present for analysis; ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.36 (s, 1H), 3.38 (s, 6H), 1.94 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 188.0, 69.2, 42.2, 27.8; HRMS

(ESI) *m/z* calcd for $C_5H_{11}O_2S$ $[M-H]^+$ 135.0480; found 135.0476. Spectroscopic data consistent with that reported in the literature.[3]

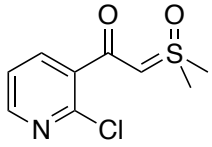
1-(Benzo[d][1,3]dioxol-5-yl)-2-(dimethyl(oxo)-λ⁶-sulfaneylidene)ethan-1-one (1i)



1i

To an oven-dried round-bottomed flask was added piperonylic acid (1.35 g, 8.13 mmol, 1.0 eq.) in anhydrous DCM (41 mL, 0.2 M) under Ar. The suspension was cooled to 0 °C with DMF (8 drops) and oxalyl chloride (2.06 mL, 24.4 mmol ,3.0 eq.) being added *via* dropwise addition. The resulting solution was allowed to warm to rt and stirred for 4 h. The organics were evaporated to give the crude acyl chloride which was immediately used without purification. Then, a solution of trimethylsulfoxonium chloride (3.14 g, 24.4 mmol, 3.0 eq.) and potassium *tert*-butoxide (3.65 g, 32.5 mmol, 4.0 eq.) in anhydrous THF (33 mL, 0.75 M) was heated to reflux for 3 h under an atmosphere of Ar. The reaction mixture was cooled to rt and the prepared acid chloride (1.0 eq.) dissolved in a minimum amount of anhydrous THF was added *via* dropwise addition. The resulting solution was stirred for 16 h at rt. The reaction mixture was concentrated under reduced pressure and to the resulting mixture was added water (50 mL) and DCM/IPA (3:1) (50 mL). The organic layer was collected and the aqueous layer extracted with DCM/IPA (3:1) (5 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated to give the crude product. Purification by automated flash column chromatography (24g, SiO_2) using a 100:0-5:95 gradient of DCM/MeOH as eluent gave ylide **1i** as a white solid (1.51g, 77%). LCMS (Method A, UV, ESI) Rt = 1.16 min, $[M-H]^+$ m/z = 240.9, 88% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.32-7.31 (m, 1H), 7.26 (s, 1H), 6.89 (d, J = 8.4 Hz, 1H), 6.03 (s, 2H), 5.52 (s, 1H), 3.50 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 179.7, 149.4, 147.6, 134.5, 121.5, 108.0, 107.0, 101.8, 71.9, 41.1; HRMS (ESI) *m/z* calcd for $C_{11}H_{13}O_4S$ $[M-H]^+$ 241.0535; found 241.0543. Spectroscopic data consistent with that reported in the literature.[5]

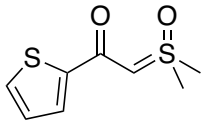
1-(2-Chloropyridin-3-yl)-2-(dimethyl(oxo)- λ^6-sulfaneylidene)ethan-1-one (1j)



1j

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.66 g, 12.9 mmol, 3.0 eq.), potassium *tert*-butoxide (1.94 g, 17.3 mmol, 4.0 eq.) and 2-chloronicotinoyl chloride (760 mg, 4.32 mmol, 1.0 eq.) in anhydrous THF (17 mL) at 65 °C- rt for 16 h gave ylide **1j** as an off-white solid (871 mg, 87%) that did not require purification. LCMS (Method A, UV, ESI) *Rt* = 1.23 min, $[M-H]^+$ *m/z* = 231.9, >99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.36 (dd, *J* = 4.8, 2.4 Hz, 1H), 7.81 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.41 (dd, *J* = 4.8, 3.0 Hz, 1H), 5.13 (s, 1H), 3.55 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 179.5, 149.8, 146.9, 138.1, 137.7, 123.5, 76.6, 40.8; HRMS (ESI) *m/z* calcd for $C_9H_{11}NO_2SCl$ $[M-H]^+$ 232.0199; found 232.0201.

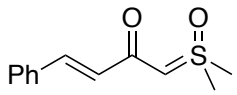
2-Thiophenecarbonyl(dimethyloxosulphonio)methanide (1k)



1k

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.91 g, 14.8 mmol, 3.0 eq.), potassium *tert*-butoxide (2.22 g, 19.8 mmol, 4.0 eq.) and 2-Thiophenecarbonyl chloride (0.53 mL, 4.9 mmol, 1.0 eq.) in anhydrous THF (20 mL) at 65 °C- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1k** as an off-white solid (823 mg, 83%). LCMS (Method A, UV, ESI) *Rt* = 0.89 min, $[M-H]^+$ *m/z* = 202.9, 98% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.60 (m, 1H), 7.44 (m, 1H), 7.05 (m, 1H), 5.49 (s, 1H), 3.52 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 174.6, 147.5, 129.7, 128.2, 127.0, 71.8, 41.1; HRMS (ESI) *m/z* calcd for $C_8H_{11}O_2S_2$ $[M-H]^+$ 203.0200; found 203.0198. Spectroscopic data consistent with that reported in the literature.[3]

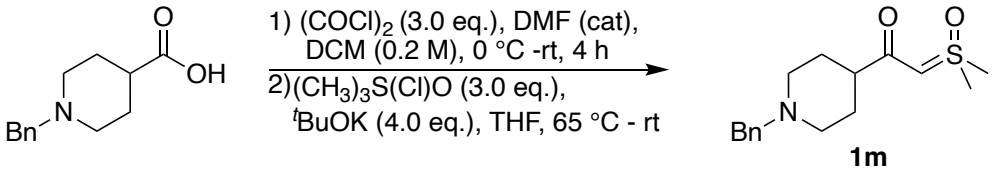
(*E*)-1-(Dimethyl(oxo)-λ^6-sulfanylidene)-4-phenylbut-3-en-2-one (1l)



1l

Performed according to general procedure **A**, trimethylsulfoxonium chloride (1.74 g, 13.5 mmol, 3.0 eq.), potassium *tert*-butoxide (2.02 g, 18.0 mmol, 4.0 eq.) and cinnamoyl chloride (749 mg, 4.5 mmol, 1.0 eq.) in anhydrous THF (18 mL) at 65 °C- rt for 16 h gave the crude product. Purification by automated flash column chromatography (24g, SiO_2) using a 100:0-5:95 gradient of DCM/MeOH as eluent gave ylide **1l** as a brown solid (341 mg, 34%). LCMS (Method A, UV, ESI) R_t = 2.45 min, $[M\text{-}H]^+$ *m/z* = 222.9, 89% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.55-7.53 (m, 2H), 7.36-7.34 (m, 2H), 7.31-7.29 (m, 1H), 7.21 (d, J = 16.2 Hz, 1H), 6.63 (d, J = 15.6 Hz, 1H), 5.01 (s, 1H), 3.50 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 178.8, 136.1, 135.2, 129.3, 129.2, 129.0, 128.9, 76.0, 40.9; HRMS (ESI) *m/z* calcd for $C_{12}H_{15}O_2S_s$ $[M\text{-}H]^+$ 223.0793; found 223.0804. Spectroscopic data consistent with that reported in the literature.[6]

1-(1-Benzylpiperidin-4-yl)-2-(dimethyl(oxo)- λ^6-sulfaneylidene)ethan-1-one (1m)

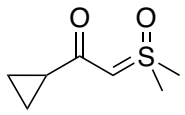


1m

To an oven-dried round-bottomed flask was added *N*-benzylpiperidine-4-carboxylic acid (1.38 g, 6.29 mmol, 1.0 eq.) in anhydrous DCM (31 mL, 0.2 M) under Ar. The suspension was cooled to 0 °C with DMF (6 drops) and oxalyl chloride (1.60 mL, 18.9 mmol, 3.0 eq.) being added *via* dropwise addition. The resulting solution was allowed to warm to rt and stirred for 4 h. The organics were evaporated to give the crude acyl chloride which was immediately used without purification. Then, a solution of trimethylsulfoxonium chloride (2.44 g, 18.9 mmol, 3.0 eq.) and potassium *tert*-butoxide (2.83 g, 25.2 mmol, 4.0 eq.) in anhydrous THF (25 mL, 0.75 M) was heated to reflux for 3 h under an atmosphere of Ar. The reaction mixture was cooled to rt and the prepared acid chloride (1.0 eq.) dissolved in a minium amount of THF was

added *via* dropwise addition. The resulting solution was stirred for 16 h at rt. The reaction mixture was concentrated under reduced pressure and to the resulting mixture was added water (50 mL) and DCM/IPA (3:1) (50 mL). The organic layer was collected and the aqueous layer extracted with DCM:IPA (3:1) (5 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated to give the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1m** as a light orange solid (767 mg, 51%). LCMS (Method A, UV, ESI) R_t = 0.76 min, $[M\text{-}H]^+$ *m/z* = 294.0, 99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.30-7.25 (m, 4H), 7.22-7.20 (m, 1H), 4.75 (s, 1H), 3.83 (m, 8H), 2.77-2.76 (m, 2H), 1.87-1.83 (m, 3H), 1.59-1.57 (m, 2H), 1.48-1.42 (dddd, *J* = 12.6, 12.6, 12.6, 3.6 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 191.7, 139.1, 129.2, 128.5, 127.2, 71.5, 62.9, 53.5, 46.8, 40.9, 29.4; HRMS (ESI) *m/z* calcd for $C_{16}H_{24}NO_2S$ $[M\text{-}H]^+$ 294.1528; found 294.1535.

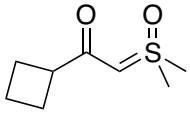
1-Cyclopropyl-2-(dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one (1n)



1n

Performed according to general procedure **A**, trimethylsulfoxonium chloride (2.41 g, 18.7 mmol, 3.0 eq.), potassium *tert*-butoxide (2.80 g, 25.0 mmol, 4.0 eq.) and cyclopropanecarbonyl chloride (0.57 mL, 6.2 mmol, 1.0 eq.) in anhydrous THF (25 mL) at 65 °C- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1n** as a white solid (876 mg, 88%). LCMS (Method A, UV, ESI) R_t = 0.55 min, $[M\text{-}H]^+$ *m/z* = 161.0, 86% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 4.88 (s, 1H), 3.39 (s, 6H), 1.49-1.45 (m, 1H), 0.62-0.60 (m, 2H), 0.51-0.48 (m, 2H);^{13}C NMR (151 MHz, d_6 -DMSO): δ 188.2, 72.4, 40.9, 18.7, 6.9; HRMS (ESI) *m/z* calcd for $C_7H_{13}O_2S$ $[M\text{-}H]^+$ 161.0636; found 161.0639.[5]

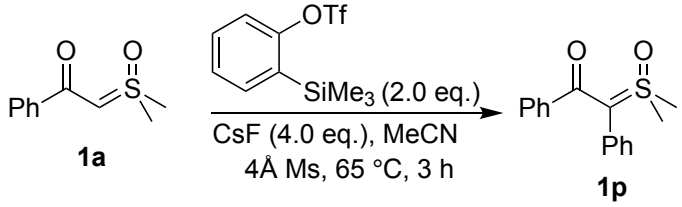
1-Cyclobutyl-2-(dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one (1o)



1o

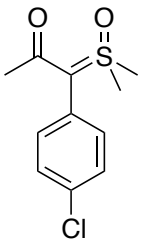
Performed according to general procedure **A**, trimethylsulfoxonium chloride (2.21 g, 17.2 mmol, 3.0 eq.), potassium *tert*-butoxide (2.58 g, 23.0 mmol, 4.0 eq.) and cyclobutylcarbonyl chloride (0.65 mL, 5.7 mmol, 1.0 eq.) in anhydrous THF (23 mL) at 65 °C- rt for 16 h gave the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1o** as a white solid (753 mg, 75%). LCMS (Method A, UV, ESI) Rt = 0.70 min, $[M\text{-}H]^+$ m/z = 175.0, 99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 4.66 (s, 1H), 3.40 (s, 6H), 2.89-2.83 (m, 1H), 2.06-2.00 (m, 2H), 1.91-1.87 (m, 2H), 1.83-1.75 (m, 1H), 1.68-1.62 (m, 1H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 190.8, 71.2, 43.6, 40.8, 25.3, 17.9; HRMS (ESI) m/z calcd for $C_8H_{15}O_2S$ $[M\text{-}H]^+$ 175.0793; found 175.0802. Spectroscopic data consistent with that reported in the literature.[3]

2-(Dimethyl(oxo)-λ^6-sulfaneylidene)-1,2-diphenylethan-1-one (1p)



Prepared using a modified literature procedure.[5] To an oven-dried round-bottomed flask was added Benzoyl(dimethyloxosulphonio)methanide (**1a**) (540 mg, 2.75 mmol, 1.0 eq.), dried CsF (1.67 g, 11.0 mmol, 4.0 eq.), 4Å powdered molecular sieves (540 mg) and anhydrous MeCN (22 mL, 0.2 M) under Ar. The resulting mixture was heated to 65 °C and vigorously stirred with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (1.3 mL, 5.5 mmol, 2.0 eq.) being added in four equal portions at hour intervals over 3h. Following complete addition, the mixture was stirred for a further 3h at 65 °C. The reaction mixture was then concentrated and filtered to give a residue. Purification by automated flash column chromatography (24g, SiO_2) using a 100:0-95:5 gradient of DCM/MeOH as eluent gave ylide **1p** (254 mg, 34%) as a brown solid. LCMS (Method A, UV, ESI) Rt = 3.08 min, $[M\text{-}H]^+$ m/z = 272.9, 93% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.19-7.14 (m, 6H), 7.12-7.08 (m, 4H), 3.60 (s, 6H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 181.6, 141.8, 135.3, 133.8, 129.0, 128.5, 128.4, 127.7, 127.2, 88.2, 41.9; HRMS (ESI) m/z calcd for $C_{16}H_{17}O_2S$ $[M\text{-}H]^+$ 273.0949; found 273.0959. Spectroscopic data consistent with that reported in the literature.[7]

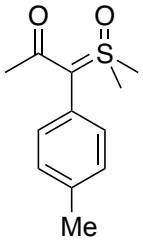
1-(4-Chlorophenyl)-1-(dimethyl(oxo)-λ^6-sulfaneylidene)propan-2-one (1q)



1q

Performed according to general procedure **B**, 1-bromo-4-chlorobenzene (192 mg, 1.0 mmol, 2.5 eq.) in anhydrous MeCN (0.8 mL) at 80 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-85:15 gradient of EtOAc/MeOH as eluent gave ylide **1q** (67 mg, 68%) as a colourless oil. LCMS (Method B, UV, ESI) R_t = 2.63 min, $[M-H]^+$ *m/z* = 245.0, 97% purity; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31-7.29 (m, 2H), 7.19-7.16 (m, 2H), 3.49 (s, 6H), 1.89 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 186.3, 135.5, 133.7, 130.9, 128.7, 84.3, 43.1, 26.5; HRMS (ESI) m/z calcd for $C_{11}H_{14}O_2SCl$ $[M-H]^+$ 245.0403; found 245.0397. Spectroscopic data consistent with that reported in the literature.[2]

1-(Dimethyl(oxo)-λ6-sulfaneylidene)-1-(p-tolyl)propan-2-one (1r)

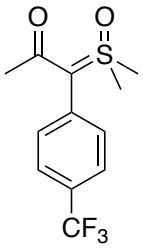


1r

Performed according to general procedure **B**, 4-bromotoluene (140 μL, 1.0 mmol, 2.5 eq.) in anhydrous MeCN (0.8 mL) at 80 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-90:10 gradient of EtOAc/MeOH as eluent gave ylide **1r** (39 mg, 44%) as an orange oil. LCMS (Method B, UV, ESI) R_t = 1.98 min, $[M-H]^+$ *m/z* = 225.0, 71% (chromophore strength was insufficient for accurate purity measurement); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.17-7.14 (m, 4H), 3.47 (s, 6H), 2.36 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 186.6, 137.7, 134.3, 129.4, 129.3, 85.6, 42.9,

26.5, 21.2; HRMS (ESI) m/z calcd for $C_{12}H_{17}O_2S$ $[M\text{-}H]^+$ 225.0949; found 225.0946. Spectroscopic data consistent with that reported in the literature.[2]

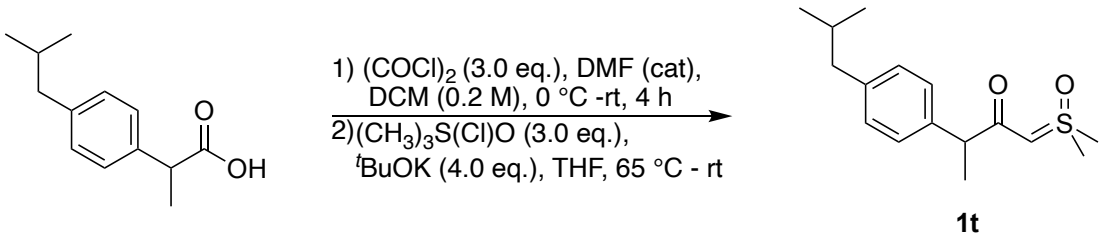
1-(Dimethyl(oxo)-λ^6-sulfaneylidene)-1-(4-(trifluoromethyl)phenyl)propan-2-one (1s)



1s

Performed according to general procedure **B**, 4-bromobenzotrifluoride (140 µL, 1.0 mmol, 2.5 eq.) in anhydrous MeCN (0.8 mL) at 80 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-90:10 gradient of EtOAc/MeOH as eluent gave ylide **1s** (75 mg, 67%) as a colourless oil. LCMS (Method B, UV, ESI) R_t = 3.16 min, $[M\text{-}H]^+$ *m/z* = 278.9, 94% purity; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.58 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 3.54 (s, 6H), 1.94 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 186.2, 136.4, 134.1, 129.1 (q, J = 32.5 Hz), 125.2 (q, J = 3.8 Hz), 124.2 (q, J = 272.1 Hz), 84.6, 43.3, 26.5; ^{19}F NMR (376 MHz, $CDCl_3$); δ -62.6; HRMS (ESI) m/z calcd for $C_{12}H_{14}O_2F_3S$ $[M\text{-}H]^+$ 279.0667; found 279.0670. Spectroscopic data consistent with that reported in the literature.[2]

1-(Dimethyl(oxo)-λ^6-sulfanylidene)-3-(4-isobutylphenyl)butan-2-one (1t)



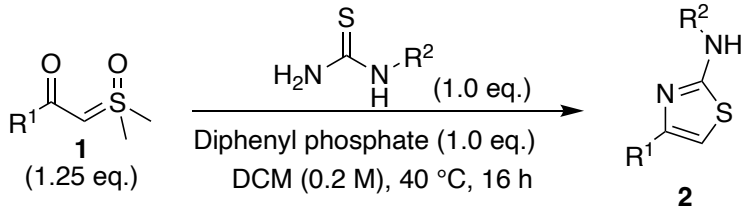
1t

To an oven-dried round-bottomed flask was added ibuprofen (1.10 g, 5.35 mmol, 1.0 eq.) in anhydrous DCM (27 mL, 0.2 M) under Ar. The suspension was cooled to 0 °C with DMF (5 drops) and oxalyl chloride (1.37 mL, 16.1 mmol, 3.0 eq.) being added *via* dropwise addition. The resulting solution was allowed to warm to rt and stirred for 4 h. The organics were evaporated to give the crude acyl chloride which was immediately used without purification.

Then, a solution of trimethylsulfoxonium chloride (2.06 g, 16.1 mmol, 3.0 eq.) and potassium *tert*-butoxide (2.40 g, 21.4 mmol, 4.0 eq.) in anhydrous THF (21 mL, 0.75 M) was heated to reflux for 3 h under an atmosphere of Ar. The reaction mixture was cooled to rt and the prepared acid chloride (1.0 eq.) dissolved in a minimum amount of anhydrous THF was added *via* dropwise addition. The resulting solution was stirred for 16 h at rt. The reaction mixture was concentrated under reduced pressure and to the resulting mixture was added water (50 mL) and DCM/IPA (3:1) (50 mL). The organic layer was collected and the aqueous layer extracted with DCM:IPA (3:1) (5 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated to give the crude product. Purification by trituration from boiling ethyl acetate using petroleum ether 40-60 °C gave ylide **1t** as a white solid (1.19 g, 79%). LCMS (Method B, UV, ESI) R_t = 3.44 min, $[M-H]^+$ *m/z* = 281.4, 87% purity; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.19 (d, J = 7.8 Hz, 2H), 7.07 (d, J = 7.8 Hz, 2H), 4.26 (s, 1H), 3.50 (q, J = 7.2 Hz, 1H), 3.36 (s, 3H), 3.32 (s, 3H), 2.44 (d, J = 7.2 Hz, 2H), 1.84 (sept, J = 6.6 Hz, 1H), 1.44 (d, J = 7.2 Hz, 3H), 0.90 (d, J = 6.6 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 192.3, 140.4, 139.7, 129.1, 127.3, 68.5, 49.7, 45.1, 42.2, 30.2, 22.4, 18.4; HRMS (ESI) *m/z* calcd for $C_{16}H_{25}NO_2S$ $[M-H]^+$ 281.1575; found 281.1581. Spectroscopic data consistent with that reported in the literature.[8]

3.2 Synthesis of 2-Aminothiazoles

General procedure C: Synthesis of 2-aminothiazoles

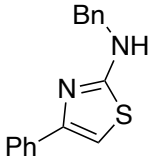


Ylide (0.51 mmol, 1.25 eq.), thiourea (0.408 mmol, 1.0 eq.), diphenyl phosphate (102 mg, 0.408 mmol, 1.0 eq.) and DCM (2.0 mL, 0.2M) were added to a microwave vial. The vessel was sealed and the resulting solution was heated to 40 °C and stirred for 16 h. The reaction mixture was cooled to rt and concentrated under reduced pressure. The subsequent residue was then purified by automated normal or reverse phase column chromatography to furnish the title compound.

General procedure D: Synthesis of 2-aminothiazoles including basic work-up

Ylide (0.510 mmol, 1.25 eq.), thiourea nucleophile (0.408 mmol, 1.0 eq.), diphenyl phosphate (102 mg, 0.408 mmol, 1.0 eq.) and DCM (2.0 mL, 0.2M) were added to a microwave vial. The vessel was sealed and the resulting solution was heated to 40 °C and stirred for 16 h. The reaction mixture was cooled to rt, before being diluted by the addition of DCM (20 mL) and H_2O (20 mL). To the mixture was added NaOH (20 mL, 2M), and the organic layer separated. The aqueous layer was extracted with DCM (5 x 15 mL) and the combined organics dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The subsequent residue was purified by automated column chromatography to furnish the title compound.

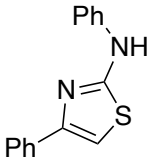
***N*-Benzyl-4-phenylthiazol-2-amine (2a)**



2a

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2a** (84 mg, 78%) as a white solid. LCMS (Method A, UV, ESI) R_t = 6.30 min, $[M\text{-}H]^+$ *m/z* = 267.1, 94% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.17 (t, J = 6.0 Hz, 1H), 7.81-7.79 (m, 2H), 7.39-7.37 (m, 2H), 7.35-7.31 (m, 4H), 7.25-7.22 (m, 2H), 7.04 (s, 1H), 4.49 (d, J = 6.0 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.8, 150.3, 139.7, 135.3, 128.9, 128.8, 128.0, 127.7, 127.4, 126.1, 101.6, 48.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{15}N_2S$ $[M\text{-}H]^+$ 267.0956; found 267.0960. Spectroscopic data consistent with that reported in the literature.[3]

***N*-4-Diphenylthiazol-2-amine (2b)**

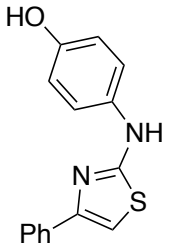


2b

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), *N*-phenylthiourea (62 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2b** (84 mg, 82%) as a yellow solid. LCMS (Method A, UV, ESI) R_t = 7.29 min, $[M\text{-}H]^+$ *m/z* = 253.1, 98% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 10.27 (s, 1H), 7.91-7.90 (m, 2H), 7.72-7.71 (m, 2H), 7.43-7.40 (m, 2H), 7.34-7.28 (m, 4H), 6.95 (m, 1H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 163.5, 150.5, 141.7, 135.0, 129.5, 129.1, 128.1, 126.1, 121.7, 117.2,

103.4; HRMS (ESI) *m/z* calcd for $C_{15}H_{13}N_2S$ $[M-H]^+$ 253.0799; found 235.0802. Spectroscopic data consistent with that reported in the literature.[3]

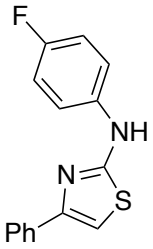
4-((4-Phenylthiazol-2-yl)amino)phenol (2c)



2c

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), *N*-(4-hydroxyphenyl)thiourea (69 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–75:25 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2c** (54 mg, 50%) as a brown solid. LCMS (Method A, UV,ESI) R_t = 5.59 min, $[M-H]^+$ *m/z* = 269.0, 96% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 9.90 (s, 1H), 9.11 (s, 1H), 7.87 (m, 2H), 7.46-7.45 (m, 2H), 7.39 (m, 2H), 7.28 (m, 1H), 7.21 (s, 1H), 6.74-6.72 (m, 2H); ^{13}C NMR (151 MHz, d_6-DMSO): δ 164.4, 152.8, 150.5, 135.1, 133.8, 129.0, 127.9, 126.1, 119.6, 115.9, 102.3; HRMS (ESI) *m/z* calcd for $C_{15}H_{13}N_2OS$ $[M-H]^+$ 269.0749; found 269.0761. Spectroscopic data consistent with that reported in the literature.[3]

***N*-(4-Fluorophenyl)-4-phenylthiazol-2-amine (2d)**

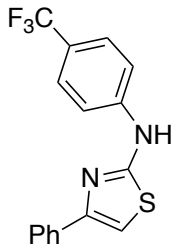


2d

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), *N*-(4-fluorophenyl)thiourea (69 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18)

using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2d** (80 mg, 73%) as a white solid. LCMS (Method A, UV,ESI) R_t = 7.38 min, $[M\text{-}H]^+$ *m/z* = 270.9, >99% purity; ^1H NMR (600 MHz, d_6-DMSO): δ 10.27 (s, 1H), 7.91-7.89 (m, 2H), 7.75-7.72 (m, 2H), 7.42-7.40 (m, 2H), 7.32-7.28 (m, 2H), 7.19-7.16 (m, 2H); ^{13}C NMR (151 MHz, d_6-DMSO): δ 163.6, 157.3 (d, J = 238.0 Hz), 150.5, 138.2 (d, J = 2.30 Hz), 134.9, 129.1, 128.0, 126.1, 118.8 (d, J = 7.7 Hz), 116.0 (d, J = 22.2 Hz), 103.3; ^{19}F NMR (376 MHz, d_6-DMSO); δ -122.12; HRMS (ESI) *m/z* calcd for $C_{15}H_{11}FN_2S$ $[M\text{-}H]^+$ 271.0705; found 271.0708. Spectroscopic data consistent with that reported in the literature.[3]

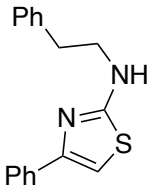
4-Phenyl-*N*-(4-(trifluoromethyl)phenyl)thiazol-2-amine (2e)



2e

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), 1-(4-(trifluoromethyl)phenyl)thiourea (90 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2e** (104 mg, 80%) as a white solid. LCMS (Method A, UV,ESI) R_t = 8.18 min, $[M\text{-}H]^+$ *m/z* = 320.9, 99% purity; ^1H NMR (600 MHz, d_6-DMSO): δ 10.68 (s, 1H), 7.94-7.91 (m, 4H), 7.70-7.68 (m, 2H), 7.44-7.41 (m, 3H), 7.33-7.31 (m, 1H); ^{13}C NMR (151 MHz, d_6-DMSO): δ 162.8, 150.7, 144.9, 134.8, 129.1, 128.8, 126.8 (q, J = 3.8 Hz), 126.2, 125.1 (q, J = 270.0 Hz), 121.4 (q, J = 31.9 Hz), 117.0, 104.6; ^{19}F NMR (376 MHz, d_6-DMSO); δ -59.9; HRMS (ESI) *m/z* calcd for $C_{16}H_{12}N_2F_3S$ $[M\text{-}H]^+$ 321.0673; found 321.0689. Spectroscopic data consistent with that reported in the literature.[9]

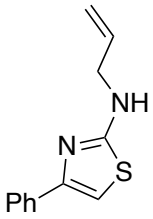
***N*-Phenethyl-4-phenylthiazol-2-amine (Fanetizole) (2f)**



2f

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), 2-phenylethylthiourea (74 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2f** (96 mg, 84%) as a white solid. LCMS (Method A, UV,ESI) R_t = 6.28 min, $[M-H]^+$ *m/z* = 281.0, >99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.83-7.81 (m, 2H), 7.73 (t, J = 5.4 Hz, 1H), 7.37-7.34 (m, 2H), 7.31-7.23 (m, 5H), 7.21-7.18 (m, 1H), 7.03 (s, 1H), 3.50-3.47 (m, 2H), 2.90 (t, J = 7.2 Hz, 2H); ^{13}C NMR (151 MHz, d_6-DMSO): δ 168.6, 150.5, 139.9, 135.4, 129.2, 128.9, 128.8, 127.7, 126.6, 126.1, 101.3, 46.6, 35.2; HRMS (ESI) *m/z* calcd for $C_{17}H_{16}N_2S$ $[M-H]^+$ 281.1112; found 281.1122. Spectroscopic data consistent with that reported in the literature.[3]

***N*-Allyl-4-phenylthiazol-2-amine (2g)**

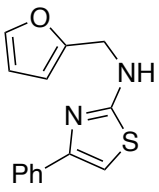


2g

Performed according to general procedure **D**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), *N*-allylthiourea (47 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–30:70 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2g** (66 mg, 75%) as a yellow solid. LCMS (Method A, UV, ESI) R_t = 4.63 min, $[M-H]^+$ *m/z* = 217.1, 99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.82-7.79 (m, 3H), 7.36-7.33

(m, 2H), 7.25-7.23 (m, 1H), 7.05 (s, 1H), 5.91 (ddt, J = 17.4, 10.2, 5.4 Hz, 1H), 5.25 (ddt, J= 17.4, 1.8, 1.8 Hz, 1H), 5.11 (ddt, J = 10.2, 1.8, 1.8 Hz, 1H), 3.92-3.90 (m, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.7, 150.4, 135.4, 135.3, 128.9, 127.7, 126.1, 116.3, 101.5, 47.2;HRMS (ESI) *m/z* calcd for $C_{12}H_{13}N_2S$ $[M\text{-}H]^+$ 217.0799; found 217.0805. Spectroscopic data consistent with that reported in the literature.[3]

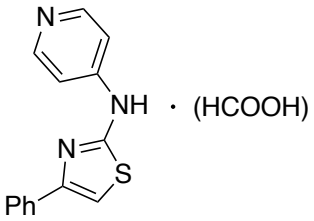
_N_-(Furan-2-ylmethyl)-4-phenylthiazol-2-amine (2h)



2h

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), furfurylthiourea (64 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2h** (80 mg, 76%) as a white solid. LCMS (Method A, UV, ESI) *Rt* = 5.85 min, $[M\text{-}H]^+$ *m/z* =257.0, 99% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.06 (t, J = 6.0 Hz, 1H), 7.82-7.81 (m, 2H), 7.56 (br s, 1H), 7.35 (m, 2H), 7.24 (m, 1H), 7.07 (br s, 1H), 6.39-6.38 (m, 1H), 6.35-6.34 (m, 1H), 4.49 (d, J = 6.0 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.3, 152.6, 150.2, 142.7, 135.3, 128.9, 127.7, 126.1, 110.9, 108.0, 101.9, 41.2; HRMS (ESI) *m/z* calcd for $C_{14}H_{13}N_2OS$ $[M\text{-}H]^+$ 257.0749; found 257.0752. Spectroscopic data consistent with that reported in the literature.[3]

4-Phenyl-_N_-(pyridin-4-yl)thiazol-2-amine formate (2i)

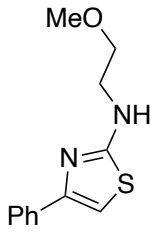


2i

Performed according to general procedure **C**, with a slight modification, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), *N*-4-pyridylthiourea (63 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 80 °C in DCE (2.0 mL, 0.2 M) for 72 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–10:90 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2i** (60 mg, 49%) as brown oil. LCMS (Method A, UV,ESI) R_t = 3.38 min, $[M\text{-}H]^+$ *m/z* = 253.9, 93% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.40 (d, J = 5.4 Hz, 2H), 8.14 (s, 1H), 7.94-7.93 (m, 2H), 7.67 (d, J = 5.4 Hz, 2H), 7.50 (s, 1H), 7.45-7.42 (m, 2H), 7.33-7.31 (m, 1H); ^{13}C NMR (151 MHz, d_6-DMSO): δ 162.4, 150.8, 150.6, 147.5, 134.7, 129.2, 128.3, 126.2, 111.6, 105.2; HRMS (ESI) *m/z* calcd for $C_{14}H_{12}N_3S$ $[M\text{-}H]^+$ 254.0752; found 254.0765.

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), *N*-4-pyridylthiourea (63 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave no crude product by LCMS analysis.

***N*-(2-Methoxyethyl)-4-phenylthiazol-2-amine (2j)**

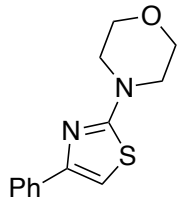


2j

Performed according to general procedure **D**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), 1,2-methoxyethylthiourea (55 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–90:10 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2j** (72 mg, 76%) as a yellow oil. LCMS (Method A, UV, ESI) R_t = 3.90 min, $[M\text{-}H]^+$ *m/z* = 235.0, 93% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.80-7.79 (m, 2H), 7.70 (t, J = 5.4 Hz, 1H), 7.34 (m, 2H), 7.24 (m, 1H), 7.02 (s, 1H), 3.50 (t, J = 5.4 Hz, 2H), 3.44 (td, J = 5.4, 5.4 Hz, 2H), 3.26 (s, 3H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.7, 150.3, 135.3,

128.9, 127.7, 126.0, 101.3, 70.7, 58.4, 44.4; HRMS (ESI) *m/z* calcd for $C_{12}H_{15}N_2OS$ $[M\text{-}H]^+$ 235.0905; found 235.0909. Spectroscopic data consistent with that reported in the literature.[3]

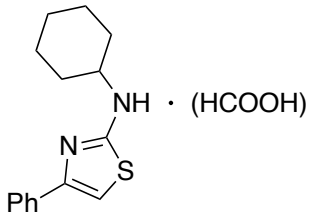
4-(4-Phenylthiazol-2-yl)morpholine (2k)



2k

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), morpholine-4-carbothioamide (60 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–30:70 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2k** (95 mg, 95%) as a yellow solid. LCMS (Method A, UV,ESI) R_t = 6.17 min, $[M\text{-}H]^+$ *m/z* = 247.1, 99% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.85-7.83 (m, 2H), 7.36 (m, 2H), 7.30 (s, 1H), 7.27 (m, 1H), 3.73-3.71 (m, 4H), 3.43-3.41 (m, 4H); ^{13}C NMR (151 MHz, *d6* -DMSO): δ 171.2, 151.0, 135.1, 129.0, 128.0, 126.2, 103.2, 65.9, 48.6; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}N_2OS$ $[M\text{-}H]^+$ 247.0905; found 247.0894. Spectroscopic data consistent with that reported in the literature.[3]

***N*-Cyclohexyl-4-phenylthiazol-2-amine formate (2l)**

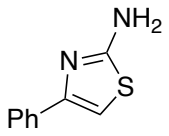


2l

Performed according to general procedure **C**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), *N*-cyclohexylthiourea (60 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) at 40 °C in DCM (2.0 mL, 0.2 M) for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent

gave thiazole **2l** (85 mg, 68%) as a yellow oil. LCMS (Method A, UV,ESI) R_t = 5.48 min, $[M-H]^+$ *m/z* = 259.0, 99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.80-7.78 (m, 2H), 7.55-7.54 (m, 1H), 7.36-7.33 (m, 2H), 7.25-7.22 (m, 1H), 6.98 (s, 1H), 3.51-3.46 (m, 1H), 1.98-1.96 (m, 2H), 1.72-1.69 (m, 2H), 1.58-1.54 (m, 1H), 1.35-1.13 (m, 5H) ; ^{13}C NMR (151 MHz, *d6* - DMSO): δ 167.9, 150.4, 135.5, 128.9, 127.6, 126.0, 100.8, 53.9, 32.8, 25.8, 24.9; HRMS (ESI) *m/z* calcd for $C_{15}H_{19}N_2S$ $[M-H]^+$ 259.1269; found 259.1266. Spectroscopic data consistent with that reported in the literature.[3]

2-Amino-4-phenylthiazole (2m)



2m

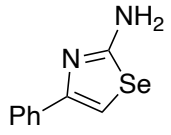
Performed according to general procedure **D**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), thiourea (31 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–50:50 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2m** (58 mg, 81%) as an off white solid. LCMS (Method A, UV, ESI) *Rt* = 2.27 min, $[M-H]^+$ *m/z* =177.1, 99% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.77-7.76 (m, 2H), 7.34 (m, 2H), 7.30 (m, 1H), 7.04 (s, 1H), 6.99 (s, 1H). ^{13}C NMR (151 MHz, d_6-DMSO): δ 173.4, 155.0, 140.1, 133.7, 132.4, 130.7, 106.7. HRMS (ESI) *m/z* calcd for $C_9H_9N_2S$ $[M-H]^+$ 177.0486; found 177.0490. Spectroscopic data consistent with that reported in the literature.[3]

Gram scale synthesis of 2-amino-4-phenylthiazole (2m):

Ylide **1a** (1.39 g, 7.08 mmol, 1.25 eq.), thiourea (432 mg, 5.67 mmol, 1.0 eq.), diphenyl phosphate (102 mg, 5.67 mmol, 1.0 eq.) and DCM (27.8 mL, 0.2M) were added to a round-bottomed flask. The resulting solution was heated to 40 °C and stirred for 16 h. The reaction mixture was cooled to rt, before being diluted by the addition of DCM (50 mL) and H_2O (50 mL). To the mixture was added NaOH (50 mL, 2M), and the organic layer separated. The aqueous layer was extracted with DCM (5 x 50 mL) and the combined organics dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–50:50 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2m**

(720 mg, 81%) as an off white solid with spectroscopic data concordant with that reported above.

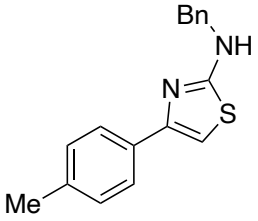
4-Phenyl-1,3-selenazol-2-amine (2n)



2n

Performed according to general procedure **D**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), selenourea (50 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-80:20 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave selenazole **2n** (60 mg, 65%) as a white solid. LCMS (Method B, UV, ESI) R_t = 1.58 min, $[M-H]^+$ *m/z* = 224.8, 98% purity; ^1H NMR (600 MHz, $CDCl_3$): δ 7.79-7.78 (m, 2H), 7.38-7.35 (m, 2H), 7.31 (br s, 1H), 7.30-7.27 (m, 1H), 5.19 (br s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.1, 152.0, 135.6, 128.6, 127.5, 126.4, 107.4; HRMS (ESI) m/z calcd for $C_9H_9N_2Se$ $[M-H]^+$ 224.9931; found 224.9929. Spectroscopic data consistent with that reported in the literature.[3]

***N*-Benzyl-4-(p-tolyl)thiazol-2-amine (2o)**

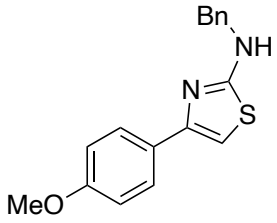


2o

Performed according to general procedure **C**, 4-methylbenzoyl(dimethyloxosulphonio)methanide **1b** (107 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2o** (92 mg, 81%) as a white solid. LCMS (Method A, UV, ESI) *Rt* = 6.67 min, $[M-H]^+$ *m/z* = 281.0, 99% purity;

^{1}H NMR (600 MHz, d_6-DMSO): δ 8.15 (t, J = 6.0 Hz, 1H), 7.69-7.68 (m, 2H), 7.38-7.36 (m, 2H), 7.33-7.30 (m, 2H), 7.24-7.22 (m, 1H), 7.15-7.14 (m, 2H), 6.96 (s, 1H), 4.48 (d, J = 6.0 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (151 MHz, d_6-DMSO): δ 168.7, 150.4, 139.7, 136.9, 132.7, 129.5, 128.7, 128.0, 127.4, 126.0, 100.7, 48.2, 21.3; HRMS (ESI) *m/z* calcd for $C_{17}H_{17}N_2S$ $[M-H]^+$ 281.1112; found 281.1104. Spectroscopic data consistent with that reported in the literature.[3]

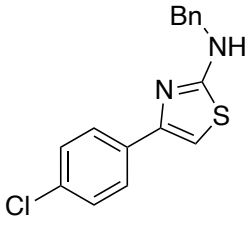
***N*-Benzyl-4-(4-methoxyphenyl)thiazol-2-amine (2p)**



2p

Performed according to general procedure **C**, 4-methoxybenzoyl(dimethyloxosulphonio)methanide **1c** (115 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2p** (104 mg, 86%) as a yellow solid. LCMS (Method A, UV, ESI) R_t = 6.03 min, $[M-H]^+$ *m/z* = 297.1, 97% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.14-8.12 (m, 1H), 7.73-7.71 (m, 2H), 7.38-7.36 (m, 2H), 7.33-7.31 (m, 2H), 7.24-7.22 (m, 1H), 6.91-6.89 (m, 2H), 6.87 (s, 1H), 4.47 (d, J = 6.0 Hz, 2H), 3.74 (s, 3H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.7, 159.1, 150.0, 139.7, 128.8, 128.1, 128.0, 127.4, 127.4, 114.3, 99.5, 55.5, 44.3; HRMS (ESI) *m/z* calcd for $C_{17}H_{17}N_2OS$ $[M-H]^+$ 297.1062; found 297.1078. Spectroscopic data consistent with that reported in the literature.[3]

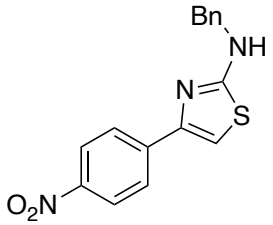
***N*-Benzyl-4-(4-chlorophenyl)thiazol-2-amine (2q)**



2q

Performed according to general procedure **C**, 4-chlorobenzoyl(dimethyloxosulphonio)methanide **1d** (118 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2q** (108 mg, 88%) as a white solid. LCMS (Method A, UV, ESI) R_t = 7.58 min, $[M\text{-}H]^+$ *m/z* = 300.9, 99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.22 (t, J = 6.0 Hz, 1H), 7.81 (m, 2H), 7.40 (m, 2H), 7.37 (m, 2H), 7.33-7.31 (m, 2H), 7.24-7.22 (m, 1H), 7.12 (s, 1H), 4.51 (d, J = 6.0 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.8, 149.0, 139.6, 134.1, 132.1, 128.9, 128.8, 128.0, 127.7, 127.4, 102.5, 48.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{14}N_2SCl$ $[M\text{-}H]^+$ 301.0566; found 301.566. . Spectroscopic data consistent with that reported in the literature.[3]

***N*-Benzyl-4-(4-nitrophenyl)thiazol-2-amine (2r)**

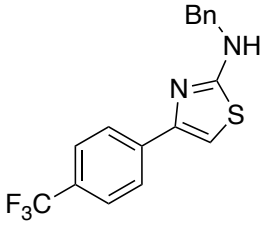


2r

Performed according to general procedure **C**, 4-nitrobenzoyl(dimethyloxosulphonio)methanide **1e** (123 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2r** (85 mg, 67%) as

an orange solid. LCMS (Method A, UV, ESI) R_t = 7.28 min, $[M\text{-}H]^+$ *m/z* = 311.9, 89% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.34 (t, J = 6.0 Hz, 1H), 8.23-8.21 (m, 2H), 8.07-8.05 (m, 2H), 7.47 (s, 1H), 7.39-7.37 (m, 2H), 7.34-7.32 (m, 2H), 7.25-7.23 (m, 1H), 4.52 (d, J = 6.0 Hz, 2H);^{13}C NMR (151 MHz, d_6-DMSO): δ 169.0, 148.3, 146.4, 141.3, 139.5, 128.8, 128.0, 127.5, 126.8, 124.5, 106.8, 48.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{14}N_3O_2S$ $[M\text{-}H]^+$ 312.0807; found 312.0811. Spectroscopic data consistent with that reported in the literature.[3]

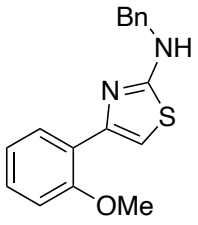
***N*-Benzyl-4-[4-(trifluoromethyl)phenyl]-1,3-thiazol-2-amine (2s)**



2s

Performed according to general procedure **C**, 4-trifluorobenzoyl(dimethyloxosulphonio)methanide **1f** (135 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2s** (116 mg, 85%) as a white solid. LCMS (Method A, UV, ESI) R_t = 7.96 min, $[M\text{-}H]^+$ *m/z* = 335.0, 96% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.27 (t, J = 6.0 Hz, 1H), 8.02 (m, 2H), 7.71 (m, 2H), 7.39 (m, 2H), 7.34-7.31 (m, 2H), 7.30 (s, 1H), 7.25-7.23 (m, 1H), 4.51 (d, J = 6.0 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.9, 148.8, 139.5, 138.9, 128.8, 128.0, 127.7 (q, J = 31.7 Hz), 127.5, 124.8 (q, J = 271.8 Hz), 126.5, 125.9 (q, J = 4.5 Hz), 104.5, 48.2; ^{19}F NMR (376 MHz, d_6-DMSO); δ -60.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}F_3N_2S$ $[M\text{-}H]^+$ 335.0830; found 335.0830.

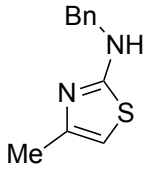
***N*-Benzyl-4-(2-methoxyphenyl)thiazol-2-amine (2t)**



2t

Performed according to general procedure **D**, 2-methoxybenzoyl(dimethyloxosulphonio)methanide **1g** (115 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-60:40 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2t** (90 mg, 74%) as a yellow oil; LCMS (Method A, UV, ESI) R_t = 5.33 min, $[M-H]^+$ *m/z* = 297.1, 93% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.07-8.03 (m, 2H), 7.38.7.37 (m, 2H), 7.33-7.30 (m, 2H), 7.24-7.21 (m, 2H), 7.13 (s, 1H), 7.04-7.03 (m, 1H), 6.96-6.94 (m, 1H), 4.48 (d, *J* = 6.0 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 166.9, 157.0, 146.2, 139.9, 129.8, 128.7, 128.6, 128.0, 127.4, 123.5, 120.8, 111.8, 105.8, 55.8, 48.2; HRMS (ESI) *m/z* calcd for $C_{11}H_{15}O_3S$ $[M-H]^+$ 227.0742; found 227.0753. Spectroscopic data consistent with that reported in the literature.[3]

***N*-Benzyl-4-methylthiazol-2-amine (2u)**

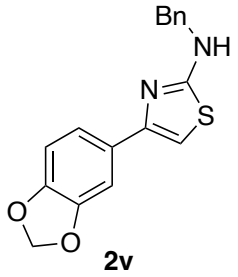


2u

Performed according to general procedure **D**, 1-(Dimethyl-(oxo)-λ^6-sulfanylidene)propan-2-one **1h** (68 mg, 0.51 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-50:50 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave thiazole **2u** (51 mg, 61%) as a white solid. LCMS (Method A, UV, ESI) R_t = 2.11 min, $[M-H]^+$ *m/z* = 205.0, 95% purity; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38-7.33 (m, 4H), 7.30-7.27 (m, 1H), 6.07 (br s,

1H), 6.04 (m, 1H), 4.45 (s, 2H), 2.19 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.7, 148.9, 137.7, 128.7, 127.7, 127.6, 100.8, 49.8, 17.3; HRMS (ESI) m/z calcd for $C_{11}H_{13}N_2S$ $[M\text{-}H]^+$ 205.0799; found 205.0800. Spectroscopic data consistent with that reported in the literature.[3]

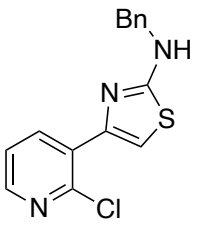
4-(Benzo[d][1,3]dioxol-5-yl)-*N*-benzylthiazol-2-amine (2v)



2v

Performed according to general procedure **C**, 1-(benzo[d][1,3]dioxol-5-yl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)ethan-1-one **1i** (123 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2t** (93 mg, 74%) as a brown solid; LCMS (Method A, UV, ESI) R_t = 6.15 min, $[M\text{-}H]^+$ *m/z* = 310.9, 99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.11 (t, J = 6.0 Hz, 1H), 7.38-7.31 (m, 6H), 7.24-7.22 (m, 1H), 6.91(br s, 1H), 6.89-6.87 (m, 1H), 6.00 (s, 2H), 4.47 (d, J = 6.0 Hz, 2H);^{13}C NMR (151 MHz, d_6-DMSO): δ 168.5, 150.0, 147.9, 147.0, 139.8, 129.9, 128.7, 128.0, 127.4, 119.9, 108.7, 106.4, 101.4, 100.1, 48.3; HRMS (ESI) *m/z* calcd for $C_{17}H_{15}N_2O_2S$ $[M\text{-}H]^+$ 311.0854; found 311.0863.[11]

***N*-Benzyl-4-(2-chloropyridin-3-yl)thiazol-2-amine (2w)**



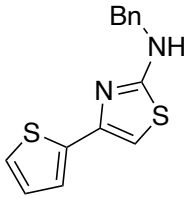
2w

Performed according to general procedure **C** with a slight modification, 1-(2-chloropyridin-3-yl)-2-(dimethyl(oxo)- λ^6-sulfaneylidene)ethan-1-one **1j** (123 mg, 0.510 mmol, 1.25 eq.), *N*-

benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (0.408 mmol, 1.0 eq.) in DCE (2.0 mL, 0.2 M) at 80 °C for 24 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2w** (102 mg, 82%) as a brown solid; LCMS (Method A, UV, ESI) R_t = 6.07 min, $[M-H]^+$ *m/z* = 301.9, 94% purity; ^1H NMR (600 MHz, d_6-DMSO): δ 8.31 (dd, J = 4.8, 2.4 Hz, 1H), 8.28 (dd, J = 7.8, 1.8 Hz, 1H), 8.25 (t, J = 6.0 Hz, 1H), 7.46 (dd, J = 7.8, 4.8 Hz, 1H), 7.38-7.36 (m, 2H), 7.34-7.31 (m, 2H), 7.27 (s, 1H), 7.25-7.23 (m, 1H), 4.49 (d, J = 6.0 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.0, 148.3, 147.5, 144.8, 140.2, 139.5, 130.5, 128.8, 128.0, 127.5, 123.7, 108.0, 48.2; HRMS (ESI) *m/z* calcd for $C_{15}H_{13}N_3SCl$ $[M-H]^+$ 302.0519; found 302.0517.

Performed according to general procedure **C**, 1-(2-chloropyridin-3-yl)-2-(dimethyl(oxo)- λ^6-sulfaneylidene)ethan-1-one **1j** (123 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (0.408 mmol, 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 24 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2w** (21 mg, 17 %) as a brown solid with spectroscopic data concordant with that reported above.

_N_-Benzyl-4-(thiophen-2-yl)thiazol-2-amine (2x)

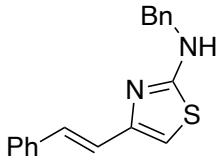


2x

Performed according to general procedure **C**, 2-thiophenecarbonyl(dimethyloxosulphonio)methanide **1k** (103 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2x** (86 mg, 78%) as a brown oil; LCMS (Method A, UV, ESI) R_t = 6.77 min, $[M-H]^+$ *m/z* = 272.9, 97% purity; ^1H

NMR (600 MHz, d_6-DMSO): δ 8.26 (t, J = 6.0 Hz, 1H), 7.39-7.36 (m, 4H), 7.33-7.31 (m, 2H), 7.25-7.22 (m, 1H), 7.03-7.01 (m, 1H), 6.88 (s, 1H), 4.43 (d, J = 6.0 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.9, 145.1, 139.6, 139.4, 128.8, 128.2, 128.1, 127.5, 125.3, 123.4, 100.0, 48.4; HRMS (ESI) *m/z* calcd for $C_{14}H_{13}N_2S_2$ $[M-H]^+$ 273.0520; found 273.0526. Spectroscopic data consistent with that reported in the literature.[3]

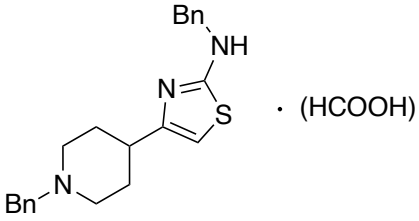
(*E*)-*N*-Benzyl-4-styrylthiazol-2-amine (2y)



2y

Performed according to general procedure **C**, (*E*)-1-(dimethyl(oxo)-λ^6-sulfaneylidene)-4-phenylbut-3-en-2-one **1l** (113 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-5:95 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2y** (99 mg, 83%) as a brown solid; LCMS (Method A, UV, ESI) R_t = 6.69 min, $[M-H]^+$ *m/z* = 293.0, 99% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.15 (t, J = 6.0 Hz, 1H), 7.50-7.49 (m, 2H), 7.38.7.37 (m, 2H), 7.34-7.31 (m, 4H), 7.25-7.20 (m, 2H), 7.11 (d, J = 15.6 Hz, 1H), 6.96 (d, J = 15.6 Hz, 1H), 6.63 (s, 1H), 4.48 (d, J = 6.0 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.7, 150.2, 139.6, 137.5, 129.2, 129.2, 128.8, 128.0, 127.8, 127.4, 126.7, 123.0, 106.2, 48.2; HRMS (ESI) *m/z* calcd for $C_{18}H_{17}N_2S$ $[M-H]^+$ 293.1112; found 293.1116.

***N*-Benzyl-4-(1-benzylpiperidin-4-yl)thiazol-2-amine formate (2z)**

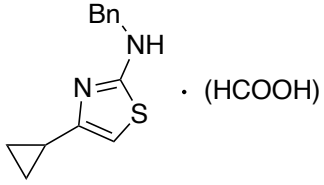


2z

Performed according to general procedure **D** with a slight modification, 1-(1-benzylpiperidin-4-yl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)ethan-1-one **1m** (113 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (204 mg, 0.916 mmol 2.0 eq.) in DCE (2.0 mL, 0.2 M) at 80 °C for 72 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-5:80:20 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2z** (67 mg, 40%) as a colourless oil; LCMS (Method A, UV, ESI) R_t = 3.19 min, $[M-H]^+$ *m/z* = 364.0, 93% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.92 (t, J = 6.0 Hz, 1H), 7.35-7.29 (m, 9H), 7.23-7.21 (m, 1H), 6.16 (s, 1H), 4.37 (d, J = 6.0 Hz, 2H), 3.69 (br s, 2H), 2.98-2.96 (m, 2H), 2.46-2.43 (m, 1H), 2.29 (br s, 2H), 1.88-1.86 (m, 2H), 1.64-1.58 (m, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): 168.8, 156.3, 139.7, 130.0, 128.8, 128.7, 128.1, 127.9, 127.4, 99.1, 61.9, 53.1, 48.3, 37.8, 30.7 (One ^{13}C resonance not resolved); HRMS (ESI) *m/z* calcd for $C_{22}H_{26}N_3S$ $[M-H]^+$ 364.1847; found 364.1853.

Performed according to general procedure **D** with a slight modification, 1-(1-benzylpiperidin-4-yl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)ethan-1-one **1m** (113 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (204 mg, 0.916 mmol 2.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-40:60 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave thiazole **2u** (47.5 mg, 32%) as a white solid with spectroscopic data concordant with that reported above.

_N_-Benzyl-4-cyclopropylthiazol-2-amine formate (2a')

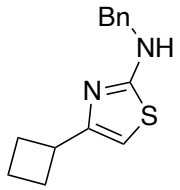


2a'

Performed according to general procedure **D**, 1-cyclopropyl-2-(dimethyl(oxo)-λ6-sulfaneylidene)ethan-1-one **1n** (82 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase

chromatography (15.5 g C18) using a 95:5-70:30 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2a'** (78 mg, 69%) as a cloudy oil; LCMS (Method A, UV, ESI) R_t = 3.30 min, $[M-H]^+$ *m/z* = 231.0, 92% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.31-7.30 (m, 4H), 7.24-7.21 (m, 1H), 6.17 (s, 1H), 4.34 (d, J = 6.0 Hz, 1H), 1.78-1.73 (m, 1H), 0.74-0.71 (m, 2H), 0.68-0.65 (m, 2H) (N-H triplet not resolved);^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.8, 152.7, 139.3, 128.7, 128.0, 127.5, 98.2, 48.4, 12.4, 7.4; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}N_2S$ $[M-H]^+$ 231.0956; found 231.0963.

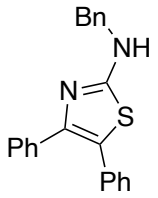
***N*-Benzyl-4-cyclobutylthiazol-2-amine (2b')**



2b'

Performed according to general procedure **D**, 1-cyclobutyl-2-(dimethyl(oxo)-λ6-sulfaneylidene)ethan-1-one **1o** (89 mg, 0.510 mmol, 1.25 eq.), *N*-benzylthiourea (68 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5-80:20 gradient of H_2O (0.1% formic acid)/acetonitrile (0.1% formic acid) as eluent gave thiazole **2b'** (61 mg, 61%) as a white solid. LCMS (Method A, UV, ESI) R_t = 3.74 min, $[M-H]^+$ *m/z* = 245.0, 95% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.95 (t, J = 6.0 Hz, 1H), 7.34-7.29 (m, 4H), 7.23-7.21 (m, 1H), 6.12 (s, 1H), 4.37 (d, J = 6.0 Hz, 2H), 3.31-3.26 (m, 1H), 2.13-2.05 (m, 4H), 1.90-1.83 (m, 1H), 1.78-1.74 (m, 1H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 169.1, 156.6, 139.7, 128.7, 128.0, 127.4, 99.2, 48.3, 37.0, 28.5, 18.4; HRMS (ESI) *m/z* calcd for $C_{14}H_{17}N_2S$ $[M-H]^+$ 245.1112; found 245.1124. Spectroscopic data consistent with that reported in the literature.[3]

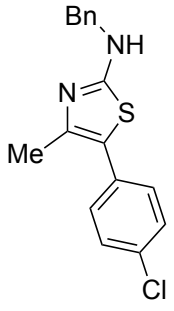
***N*-benzyl-4,5-diphenylthiazol-2-amine (2c')**



2c'

Performed according to general procedure **C** with a slight modification, 2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1,2-diphenylethan-1-one **1p** (64 mg, 0.236 mmol, 1.25 eq.), *N*-benzylthiourea (31.8 mg, 0.188 mmol, 1.0 eq.) and diphenyl phosphate (47 mg, 0.408 mmol, 1.0 eq.) in DCM (0.94 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-90:10 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave thiazole **2c'** (48 mg, 74%) as a white solid.LCMS (Method A, UV, ESI) R_t = 7.49 min, $[M-H]^+$ *m/z* = 343.1, 96% purity;^{1}H NMR (600 MHz, d_6-DMSO): δ 8.23 (t, J = 6.0 Hz, 1H), 7.39-7.33 (m, 6H), 7.28-7.21 (m, 7H), 7.19-7.18 (m, 2H), 4.48 (d, J = 6.0 Hz, 2H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 166.4, 145.4, 139.6, 135.9, 133.1, 129.4, 129.2, 128.9, 128.8, 128.5, 128.0, 127.8, 127.6, 127.5, 119.3, 48.0; HRMS (ESI) *m/z* calcd for $C_{22}H_{19}N_2S$ $[M-H]^+$ 343.1269; compound would not ionise using the general ESI procedure. Spectroscopic data consistent with that reported in the literature.[12]

***N*-Benzyl-5-(4-chlorophenyl)-4-methylthiazol-2-amine (2d')**

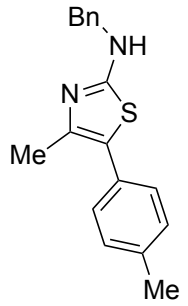


2d'

Performed according to general procedure **D**, 1-(4-chlorophenyl)-1-(dimethyl(oxo)-λ^6-sulfaneylidene)propan-2-one **1q** (69 mg, 0.273 mmol, 1.25 eq.), *N*-benzylthiourea (36 mg, 0.218 mmol, 1.0 eq.) and diphenyl phosphate (55 mg, 0.218 mmol 1.0 eq.) in DCM (1.1 mL,

0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-50:50 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave thiazole **2d'** (46 mg, 67%) as a white solid. LCMS (Method B, UV, ESI) R_t = 3.97 min, $[M-H]^+$ *m/z* = 315.1, 92% purity; ^1H NMR (600 MHz, $CDCl_3$): δ 7.39-7.35 (m, 4H), 7.33-7.31 (m, 3H), 7.28-7.27 (m, 2H), 5.39 (br s, 1H), 4.48 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.5, 144.3, 137.5, 132.3, 131.6, 129.8, 128.8, 128.7, 127.8, 127.2, 118.2, 49.8, 16.2; HRMS (ESI) m/z calcd for $C_{17}H_{16}N_2SCl$ $[M-H]^+$ 315.0723; found 315.0721.

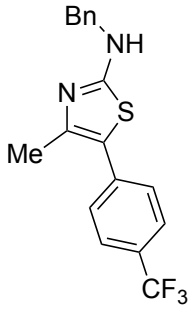
***N*-Benzyl-4-methyl-5-(p-tolyl)thiazol-2-amine (2e')**



2e'

Performed according to general procedure **D**, 1-(dimethyl(oxo)-λ6-sulfaneylidene)-1-(p-tolyl)propan-2-one **1r** (35 mg, 0.156 mmol, 1.25 eq.), *N*-benzylthiourea (21 mg, 0.125 mmol, 1.0 eq.) and diphenyl phosphate (31 mg, 0.125 mmol 1.0 eq.) in DCM (0.6 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-50:50 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave thiazole **2e'** (26 mg, 71%) as a white solid. LCMS (Method B, UV, ESI) R_t = 3.64 min, $[M-H]^+$ *m/z* = 296.4, 93% purity; ^1H NMR (600 MHz, d_6-DMSO): δ 8.03 (t, J = 6.0 Hz, 1H), 7.34-7.31 (m, 4H), 7.25-7.22 (m, 1H), 7.20-7.18 (m, 2H), 7.17-7.15 (m, 2H), 4.42 (m, 2H), 2.28 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (151 MHz, d_6-DMSO): δ 166.0, 143.2, 139.7, 135.9, 130.4, 129.7, 128.8, 128.3, 127.8, 127.4, 117.8, 47.8, 21.1, 16.8; HRMS (ESI) *m/z* calcd for $C_{18}H_{19}N_2S$ $[M-H]^+$ 295.1269; found 295.1277.

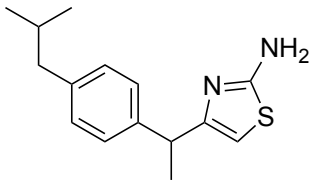
***N*-Benzyl-4-methyl-5-(4-(trifluoromethyl)phenyl)thiazol-2-amine (2f')**



2f'

Performed according to general procedure **D**, 1-(Dimethyl(oxo)-λ^6-sulfaneylidene)-1-(4-(trifluoromethyl)phenyl)propan-2-one **1s** (75 mg, 0.270 mmol, 1.25 eq.), *N*-benzylthiourea (36 mg, 0.216 mmol, 1.0 eq.) and diphenyl phosphate (54 mg, 0.216 mmol 1.0 eq.) in DCM (1.1 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4g, SiO_2) using a 100:0-50:50 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave thiazole **2f'** (29 mg, 39%) as a white solid. LCMS (Method B, UV, ESI) R_t = 4.48 min, $[M-H]^+$ *m/z* = 349.4, 94% purity; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.60 (d, J = 7.8 Hz, 2H), δ 7.46 (d, J = 8.4 Hz, 2H), 7.39-7.36 (m, 4H), 7.33-7.30 (m, 1H), 5.53 (br s, 1H), 4.49 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.8, 145.5, 137.4, 136.8, 128.8, 128.4, 127.8, 127.6, 125.5 (q, J = 3.6 Hz), 118, 49.8, 16.5 (two ^{13}C resonances not resolved); ^{19}F NMR (376 MHz, $CDCl_3$); δ -62.5; HRMS (ESI) m/z calcd for $C_{18}H_{16}N_2F_3S$ $[M-H]^+$ 349.0986; found 349.0973.

4-(1-(4-Isobutylphenyl)ethyl)thiazol-2-amine (2g')



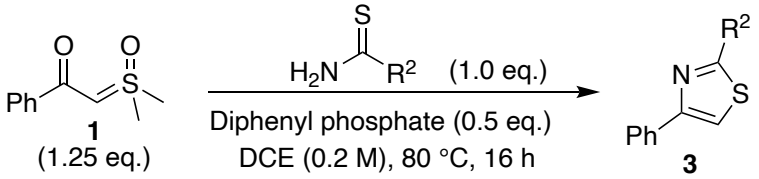
2g'

Performed according to general procedure **D**, 1-(dimethyl(oxo)-λ^6-sulfanylidene)-3-(4-isobutylphenyl)butan-2-one **1t** (143 mg, 0.51 mmol, 1.25 eq.), thiourea (31 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (102 mg, 0.408 mmol 1.0 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography

(4g, SiO_2) using a 100:0-80:20 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave thiazole **2g'** (57 mg, 54%) as a white solid. LCMS (Method B, UV, ESI) R_t = 3.36 min, $[M-H]^+$ *m/z* = 261.5, 97% purity; ^1H NMR (600 MHz, $CDCl_3$): δ 7.14 (d, J = 7.8 Hz, 2H), 7.07 (d, J = 7.8 Hz, 2H), 6.08 (s, 1H), 4.93 (s, 2H), 4.00 (q, J = 7.2 Hz, 1H), 2.44 (d, J = 7.2 Hz, 2H), 1.84 (sept, J = 6.6 Hz, 1H), 1.56 (d, J = 7.2 Hz, 3H), 0.90 (d, J = 6.6 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.8, 157.0, 142.3, 139.6, 129.1, 127.3, 102.0, 45.1, 41.7, 30.2, 22.4, 21.1; HRMS (ESI) *m/z* calcd for $C_{15}H_{21}N_2S$ $[M-H]^+$ 261.1425; found 261.1411.

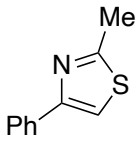
3.3 Synthesis of Thioamide-derived Thiazoles

General procedure E: Synthesis of thioamide-derived thiazoles



Benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), thioamide (0.408 mmol, 1.0 eq.), diphenyl phosphate (51 mg, 0.204 mmol, 1.0 eq.) and DCE (2.0 mL, 0.2M) were added to a microwave vial. The vessel was sealed and the resulting solution heated to 80 °C and stirred for 16 h. The reaction mixture was cooled to rt and concentrated under reduced pressure. The subsequent residue was purified by automated normal or reverse phase column chromatography to furnish the title compound.

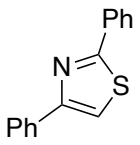
2-Methyl-4-phenylthiazole (3a)



3a

Performed according to general procedure **E** with a slight modification, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), thioacetamide (31 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (12 g, SiO_2) using a 100:0-95:5 gradient of petroleum ether 40-60 °C/EtOAc as eluent gave thiazole **3a** (49 mg, 69%) as a white solid. LCMS (Method A, UV, ESI) R_t = 5.59 min, $[M-H]^+$ *m/z* = 176.1, 78% purity. ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.92-7.91 (m, 3H), 7.42-7.39 (m, 2H), 7.32-7.29 (m, 2H), 7.20 (s, 3H); ^{13}C NMR (151 MHz, d_6 - DMSO): δ 165.9, 154.2, 134.6, 129.2, 128.3, 126.4, 114.2, 19.4; HRMS (ESI) *m/z* calcd for $C_{10}H_{10}NS$ $[M-H]^+$ 176.0534; found 176.0532. Spectroscopic data consistent with that reported in the literature.[3]

2,4-Diphenylthiazole (3b)

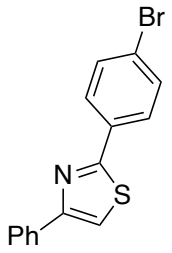


3b

Performed according to general procedure **E**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), thiobenzamide (56 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCE (2.0 mL, 0.2 M) at 80 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (1% formic acid)/acetonitrile (1% formic acid) as eluent gave thiazole **3b** (62 mg, 64%) as an off white solid. LCMS (Method A, UV, ESI) R_t = 8.03 min, $[M\text{-}H]^+$ *m/z* = 237.9, 97% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 8.17 (m, 1H), 8.05-8.01 (m, 4H), 7.54-7.50 (m, 3H), 7.48-7.45 (m, 2H), 7.38-7.35 (m, 1H); ^{13}C NMR (151 MHz, d_6 - DMSO): δ 167.4, 155.7, 134.5, 133.5, 130.8, 129.7, 129.3, 128.7, 126.7, 126.6, 115.1; HRMS (ESI) *m/z* calcd for $C_{11}H_{16}NS$ $[M\text{-}H]^+$ 238.0690; found 238.0701. Spectroscopic data consistent with that reported in the literature.[3]

Performed according to general procedure **E** with a slight modification, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), thiobenzamide (56 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (1% formic acid)/acetonitrile (1% formic acid) as eluent gave thiazole **3b** (39 mg, 40%) as an off white solid with spectroscopic data concordant with that reported above.

4-Phenyl-2-(4-bromophenyl)thiazole (3c)

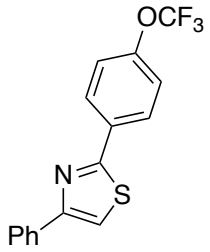


3c

Performed according to general procedure **E**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), 4-bromothiobenzamide (88 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCE (2.0 mL, 0.2 M) at 80 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (1% formic acid)/acetonitrile (1% formic acid) as eluent gave thiazole **3c** (72 mg, 56%) as an orange solid. LCMS (Method A, UV, ESI) R_t = 8.84 min, $[M-H]^+$ *m/z* =315.8, 97% purity; ^1H NMR (600 MHz, d_6-DMSO): δ 8.21 (s, 1H), 8.04-8.03 (m, 2H), 7.98-7.96 (m, 2H), 7.73-7.72 (m, 2H), 7.48-7.45 (m, 2H), 7.38-7.36 (m, 1H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 166.2, 155.8, 134.3, 132.7, 132.6, 129.3, 128.8, 128.6, 126.6, 124.1, 116.6; HRMS (ESI) *m/z* calcd for $C_{15}H_{11}BrNS$ $[M-H]^+$ 315.9805; found 315.9796. Spectroscopic data consistent with that reported in the literature.[13]

Performed according to general procedure **E** with a slight modification, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), 4-bromothiobenzamide (88 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (1% formic acid)/acetonitrile (1% formic acid) as eluent gave thiazole **3b** (39 mg, 40%) as an off white solid with spectroscopic data concordant with that reported above.

4-Phenyl-2-(4-(trifluoromethoxy)phenyl)thiazole (3d)

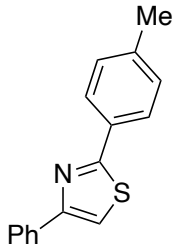


3d

Performed according to general procedure **E**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), 4-(trifluoromethoxy)thiobenzamide (90 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCE (2.0 mL, 0.2 M) at 80 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g

C18) using a 95:5–5:95 gradient of H_2O (1% formic acid)/acetonitrile (1% formic acid) as eluent gave thiazole **3d** (87 mg, 66%) as an orange solid. LCMS (Method A, UV, ESI) R_t = 8.89 min, $[M-H]^+$ *m/z* =321.9, 97% purity; ^1H NMR (600 MHz, d_6-DMSO): δ 8.22 (s, 1H), 8.16-8.14 (m, 2H), 8.05-8.03 (m, 2H), 7.53-7.52 (m, 2H), 7.48-7.46 (m, 2H), 7.39-7.36 (m, 1H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 165.7, 155.8, 149.9, 134.3, 132.6, 129.3, 128.8, 128.7, 126.6, 122.2, 120.5 (q, J = 257.6 Hz); ^{19}F NMR (376 MHz, d_6-DMSO); δ -56.7; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}F_3NOS$ $[M-H]^+$ 322.0513; found 322.0522.

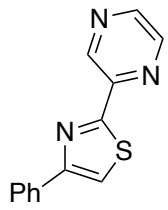
4-Phenyl-2-(*p*-tolyl)thiazole (3e)



3e

Performed according to general procedure **E**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), 4-methylthiobenzamide (88 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCE (2.0 mL, 0.2 M) at 80 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (1% formic acid)/acetonitrile (1% formic acid) as eluent gave thiazole **3e** (54 mg, 52%) as a brown solid. LCMS (Method A, UV, ESI) R_t = 8.49 min, $[M-H]^+$ *m/z* =252.0, 92% purity; ^1H NMR (600 MHz, d_6-DMSO): δ 8.12 (s, 1H), 8.04-8.02 (m, 2H), 7.92-7.90 (m, 2H), 7.47-7.45 (m, 2H), 7.37-7.33 (m, 3H), 2.36 (s, 3H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 167.5, 155.5, 140.7, 134.5, 130.9, 130.2, 129.3, 128.6, 126.6, 126.6, 114.6, 21.5; HRMS (ESI) *m/z* calcd for $C_{16}H_{14}NS$ $[M-H]^+$ 252.0847; found 252.0860. Spectroscopic data consistent with that reported in the literature.[3]

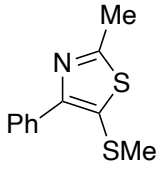
4-Phenyl-2-(pyrazin-2-yl)thiazole (3f)



3f

Performed according to general procedure **E**, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), pyrazine-2-thiocarboxamide (57 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCE (2.0 mL, 0.2 M) at 80 °C for 16 h gave the crude product. Purification by automated reverse phase chromatography (15.5 g C18) using a 95:5–5:95 gradient of H_2O (1% formic acid)/acetonitrile (1% formic acid) as eluent gave thiazole **3f** (35 mg, 36%) as an orange solid. LCMS (Method A, UV, ESI) R_t = 6.43 min, $[M-H]^+$ *m/z* =239.9, 89% purity;^{1}H NMR (600 MHz, d_6-DMSO): δ 9.45 (d, J = 1.2 Hz, 1H), 8.77 (d, J = 2.4 Hz, 1H), 8.73 (dd, J = 2.4, 1.8 Hz, 1H), 8.38 (s, 1H), 8.09-8.08 (m, 2H), 7.50-7.48 (m, 2H), 7.41-7.38 (m, 1H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 166.0, 156.6, 146.4, 146.3, 145.0, 141.1, 134.1, 129.3, 128.9, 126.6, 118.3; HRMS (ESI) *m/z* calcd for $C_{13}H_{10}N_3S$ $[M-H]^+$ 240.0595; found 240,0607. Spectroscopic data consistent with that reported in the literature.[3]

2-Methyl-5-(methylthio)-4-phenylthiazole (3a')



3a'

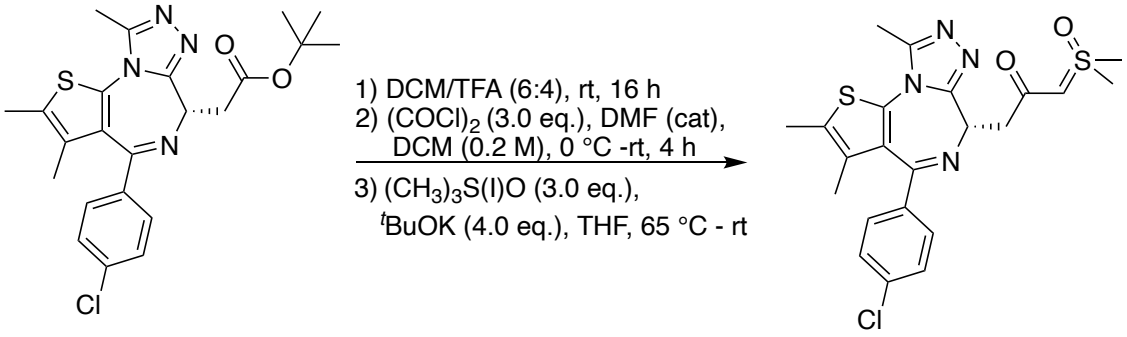
Performed according to general procedure **E** with a slight modification, benzoyl(dimethyloxosulphonio)methanide **1a** (100 mg, 0.510 mmol, 1.25 eq.), thioacetamide (31 mg, 0.408 mmol, 1.0 eq.) and diphenyl phosphate (51 mg, 0.204 mmol 0.5 eq.) in DCM (2.0 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (12 g, SiO_2) using a 100:0-95:5 gradient of pet ether 40-60 °C/EtOAc as eluent gave thiazole **3a'**(9 mg, 10%) as a white gum. LCMS (Method A, UV, ESI) R_t = 6.30 min, $[M-H]^+$ *m/z* = 221.9, 89% purity; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.90-7.89 (m, 2H), 7.45-

7.42 (m, 2H), 7.37-7.34 (m, 1H), 2.70 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.9, 154.4, 134.3, 128.7, 128.2, 128.1, 126.0, 21.9, 19.6; HRMS (ESI) *m/z* calcd for $C_{11}H_{12}NS_2$ $[M-H]^+$ 222.0411; found 222.0421. Spectroscopic data consistent with that reported in the literature.[14]

4.0 (+)- JQ1 derivatisation

4.1 Synthesis of (+)- JQ1 ylide and thiazole

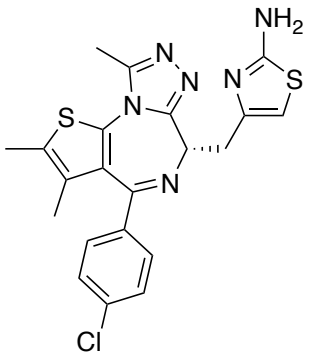
(*S*)-1-(4-(4-Chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-3-(dimethyl(oxo)-λ6-sulfaneylidene)propan-2-one (4a)



A mixture of (+)-JQ1 (1000 mg, 2.19 mmol, 1.0 eq.) in DCM (14.4 mL) was cooled to 0 °C. To the resulting solution was added TFA (9.6 mL) *via* dropwise addition before the mixture was allowed to warm to ambient temperature and stirred for 16 h. The mixture was concentrated under reduced pressure and redissolved in a 1:1 mixture of DCM/Et_2O. The solvent was removed under reduced pressure with this being repeated 5 times to give JQ1-COOH which was immediately used without further purification. Then, to an oven-dried round-bottomed flask was added JQ1-COOH (878 mg, 2.19 mmol, 1.0 eq.) in anhydrous DCM (11 mL, 0.2 M) under Ar. The suspension was cooled to 0 °C with DMF (3 drops) and oxalyl chloride (0.56 mL, 6.57 mmol, 3.0 eq.) being added *via* dropwise addition. The resulting solution was allowed to warm to rt and stirred for 4 h. The organics were evaporated to give the crude acyl chloride which was immediately used without purification. Then, a solution of trimethylsulfoxonium chloride (845 mg, 6.57 mmol, 3.0 eq.) and potassium *tert*-butoxide (982 mg, 8.76 mmol, 4.0 eq.) in anhydrous THF (9.0 mL, 0.75 M) was heated to reflux for 3 h under an atmosphere of Ar. The reaction mixture was cooled to rt and the prepared acid chloride (1.0 eq.) dissolved in a minium amount of anhydrous THF was added *via* dropwise addition. The resulting solution was stirred for 16 h at rt. The reaction mixture was concentrated under reduced pressure and to the resulting mixture was added water (50 mL) and DCM/IPA (3:1) (50 mL). The organic layer was collected and the aqueous layer extracted with DCM/IPA (3:1) (5 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated to give the crude product. Purification by automated flash column

chromatography (24g, SiO_2) using a 100:0-65:35 gradient of EtOAc/MeOH as eluent gave ylide **4a** as a brown solid (336 mg, 32%). LCMS (Method A, UV, ESI) R_t = 4.64 min, $[M-H]^+$ *m/z* = 475.0, 78% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.47-7.46 (m, 2H), 7.42-7.40 (m, 2H), 4.99 (s, 1H), 4.50-4.48 (m, 1H), 3.44-3.44 (m, 6H), 3.22 (dd, *J* = 15.6, 6.0 Hz, 1H), 3.13 (dd, *J* = 15.6, 7.2 Hz, 1H), 2.57 (s, 3H), 2.39 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 185.7, 163.1, 155.9, 150.2, 137.3, 135.6, 132.6, 131.1, 130.6, 130.3, 130.1, 128.9, 74.0, 54.1, 42.2, 40.9, 14.5, 13.1, 11.7; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}N_4O_2S_2Cl$ $[M-H]^+$ 475.1029; found 475.1019.

(*S*)-4-((4-(4-Chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)methyl)thiazol-2-amine (4b)



4b

Performed according to general procedure **B**, (*S*)-1-(4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-3-(dimethyl(oxo)-λ^6 sulfaneylidene)propan-2-one **4a** (61 mg, 0.128 mmol, 1.25 eq.), thiourea (8 mg, 0.105 mmol, 1.0 eq.) and diphenyl phosphate (26 mg, 0.105 mmol, 1.0 eq.) in DCM (0.25 mL, 0.2 M) at 40 °C for 16 h gave the crude product. Purification by automated flash column chromatography (4 g, SiO_2) using a 100:0-95:5 gradient of EtOAc/MeOH as eluent gave thiazole **4b** (25 mg, 54%) as an off-white solid. LCMS (Method A, UV, ESI) R_t = 4.45 min, $[M-H]^+$ *m/z* = 454.9, 92% purity; ^{1}H NMR (600 MHz, d_6-DMSO): δ 7.47-7.46 (m, 2H), 7.41-7.39 (m, 2H), 6.78 (m, 2H), 6.31 (s, 1H), 4.40 (m, 1H), 3.60 (dd, *J* = 14.4, 6.6 Hz, 1H), 3.43 (dd, *J* = 14.4, 7.2 Hz, 1H), 2.56 (s, 3H), 2.39 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (151 MHz, d_6 -DMSO): δ 168.5, 163.3, 155.5, 150.2, 149.0, 137.2, 135.6, 132.7, 131.2, 130.6, 130.2, 130.0, 128.9, 102.6, 56.5, 34.3, 14.5, 13.1, 11.8; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}N_6S_2Cl$ $[M-H]^+$ 455.0879; found 455.0884.

4.2 Determination of (+)- JQ1 thiazole stereochemistry

General procedure E: Preparation of NMR samples for enatiodiscrimination

NMR samples were prepared in $CDCl_3$ (500 µL) with **racemic 4b** or **4b** (1 mg, 0.0022 mmol, 1.0 eq.) and (-)-Pirkles alcohol (0.6 mg, 0.0022 mmol, 1.0 eq). Enatiodiscrimination and purity was then determined *via* the observed splitting between the three highlighted methyl singlets.

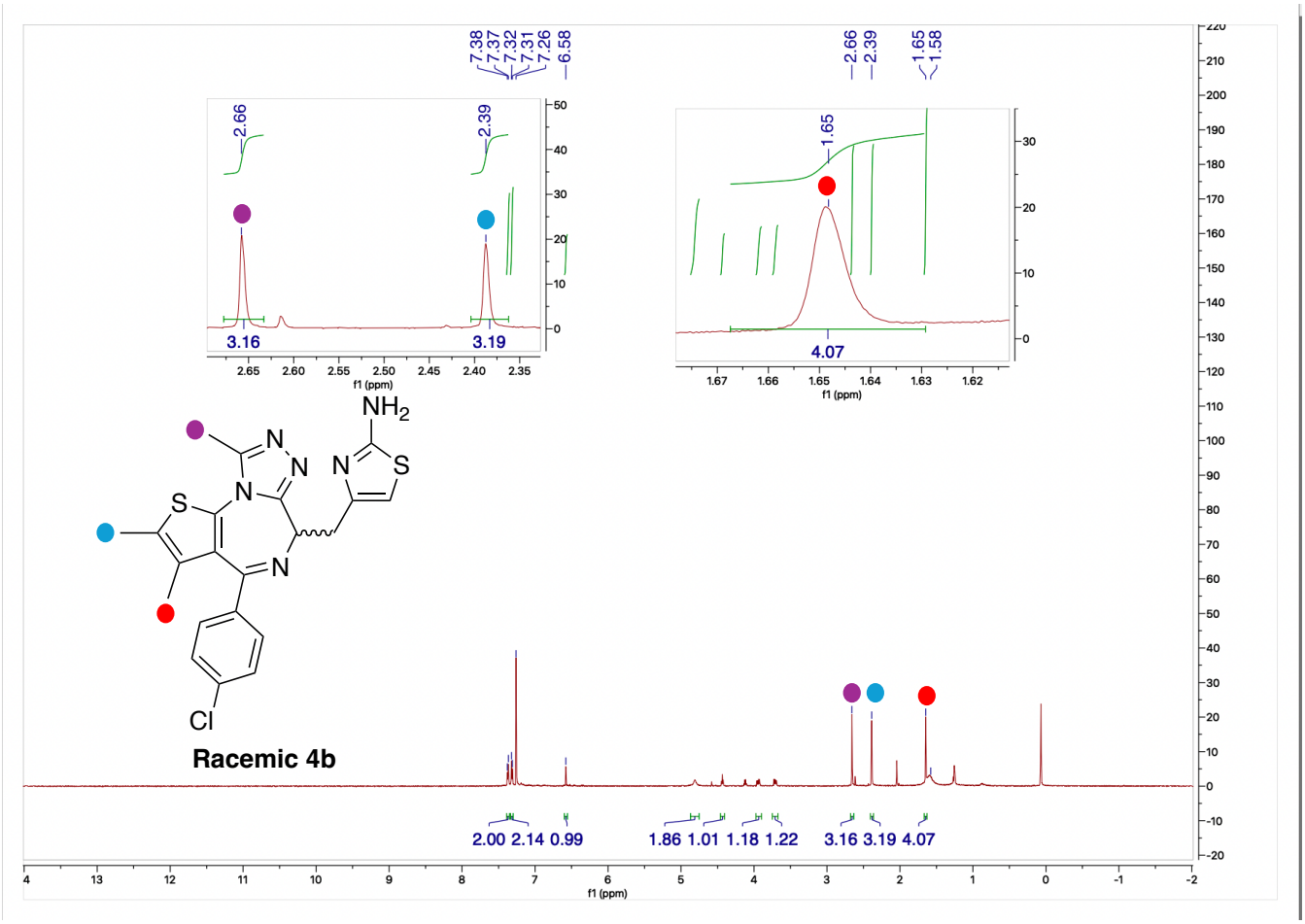


Figure S1: ^{1}H NMR spectrum of racemic **4b** in $CDCl_3$ (600 MHz)

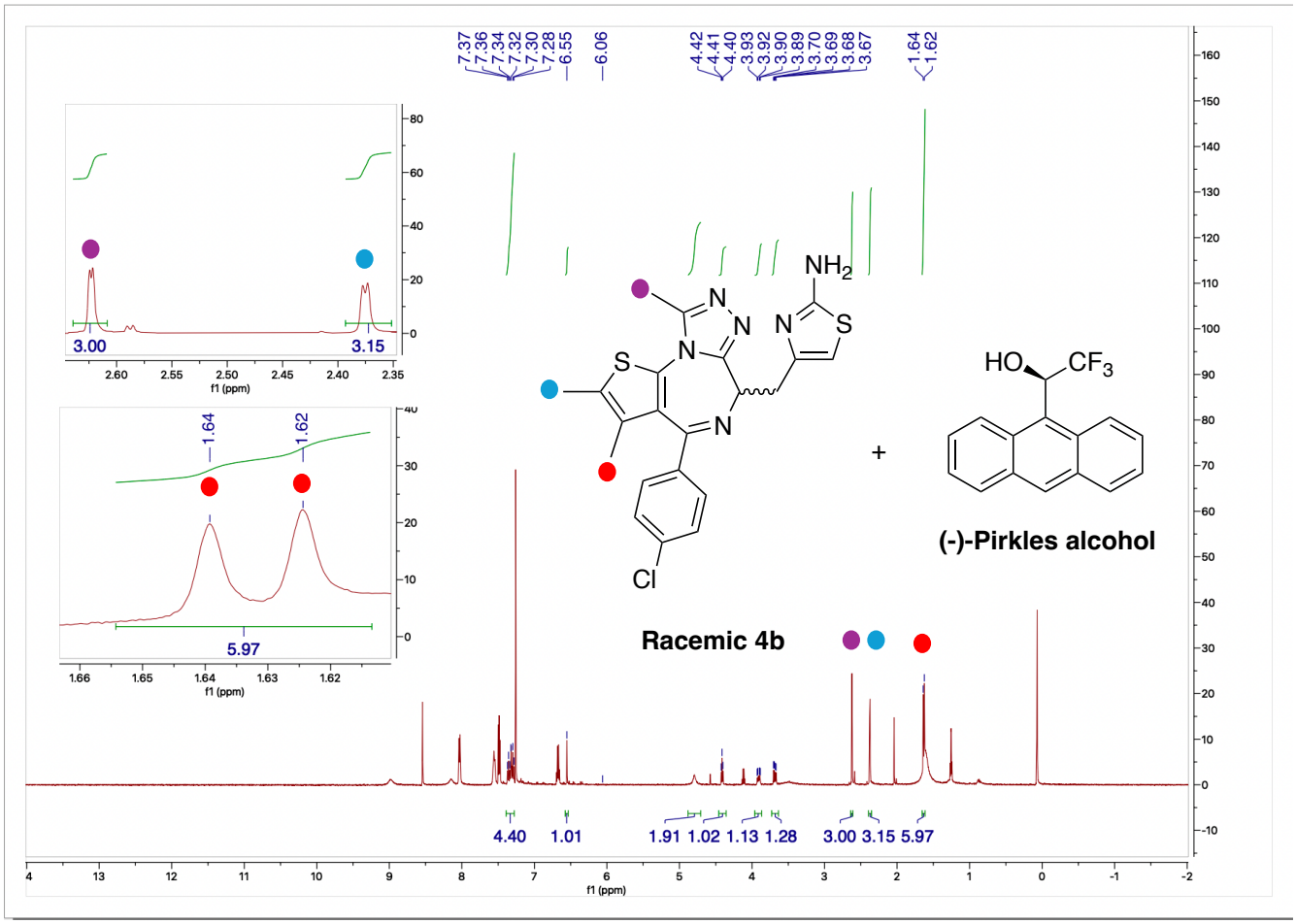


Figure S2: ^{1}H NMR spectrum of racemic **4b** in the presence of (-)- Pirkles alcohol in $CDCl_3$ (600 MHz)

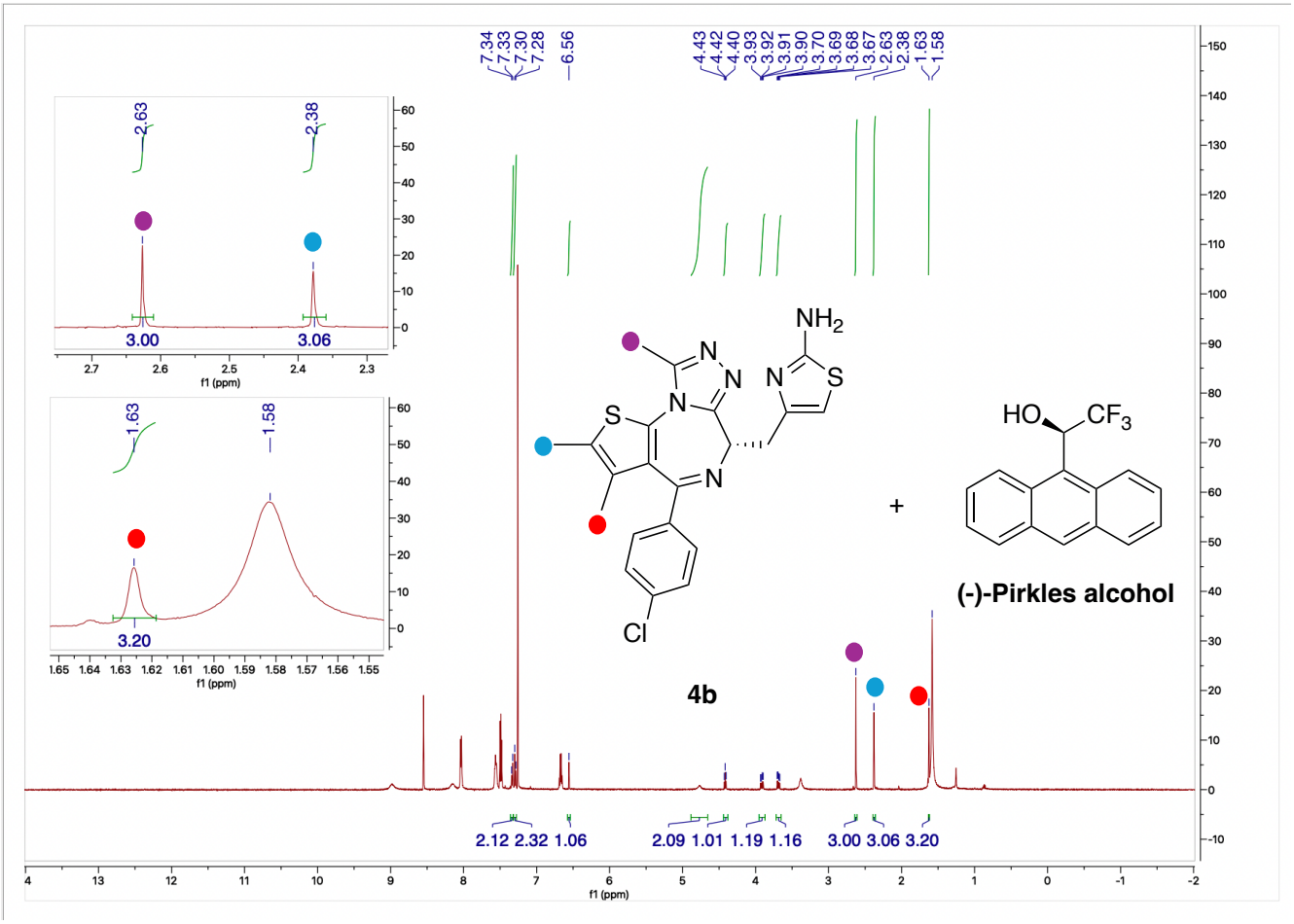


Figure S3: ^{1}H NMR spectrum of **4b** in the presence of (-)-Pirkles alcohol in $CDCl_3$ (600 MHz)

5.0 References

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6.0 NMR Spectra

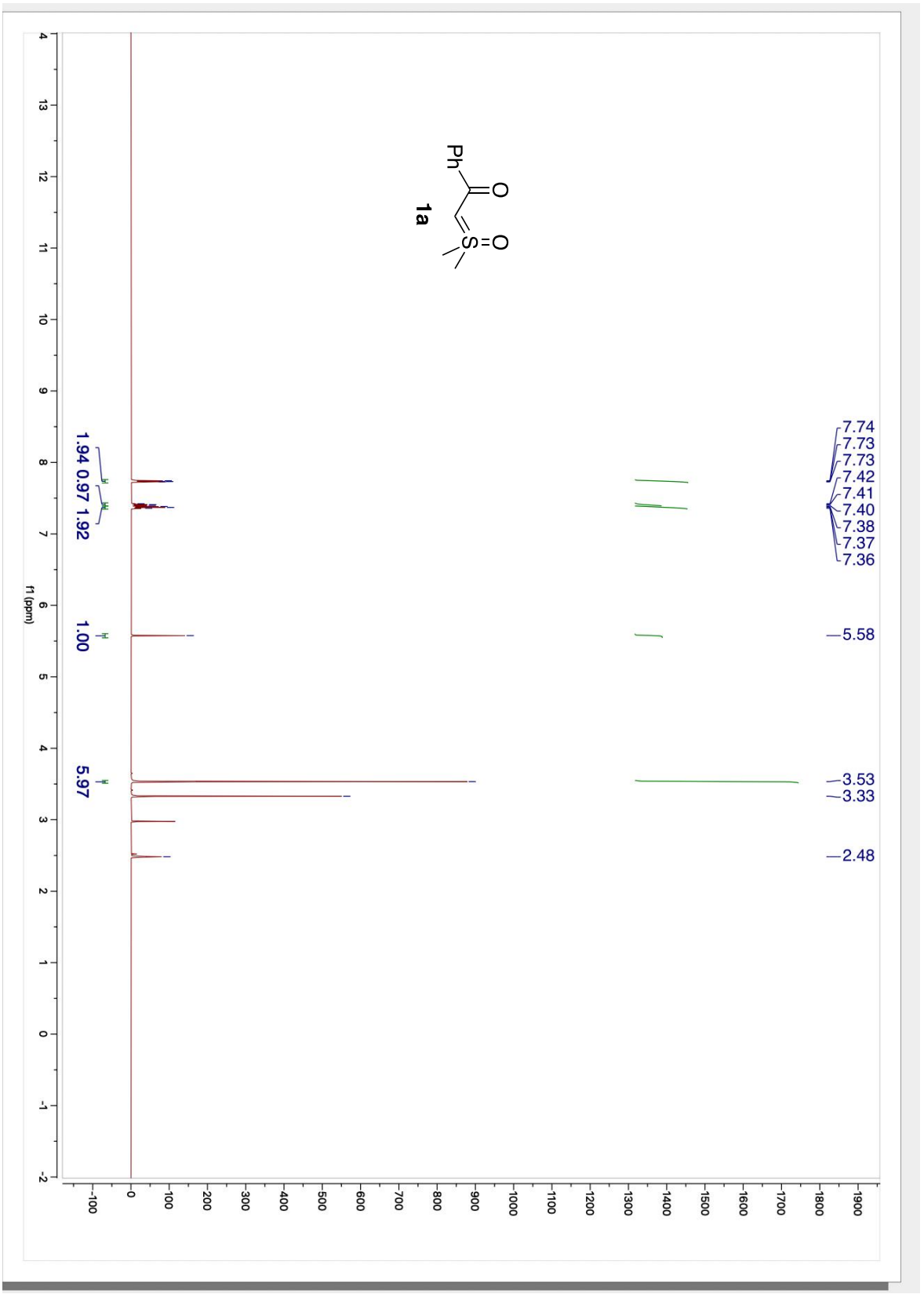

Figure S4: ^{1}H NMR spectrum of **1a** in d_6-DMSO (600 MHz)

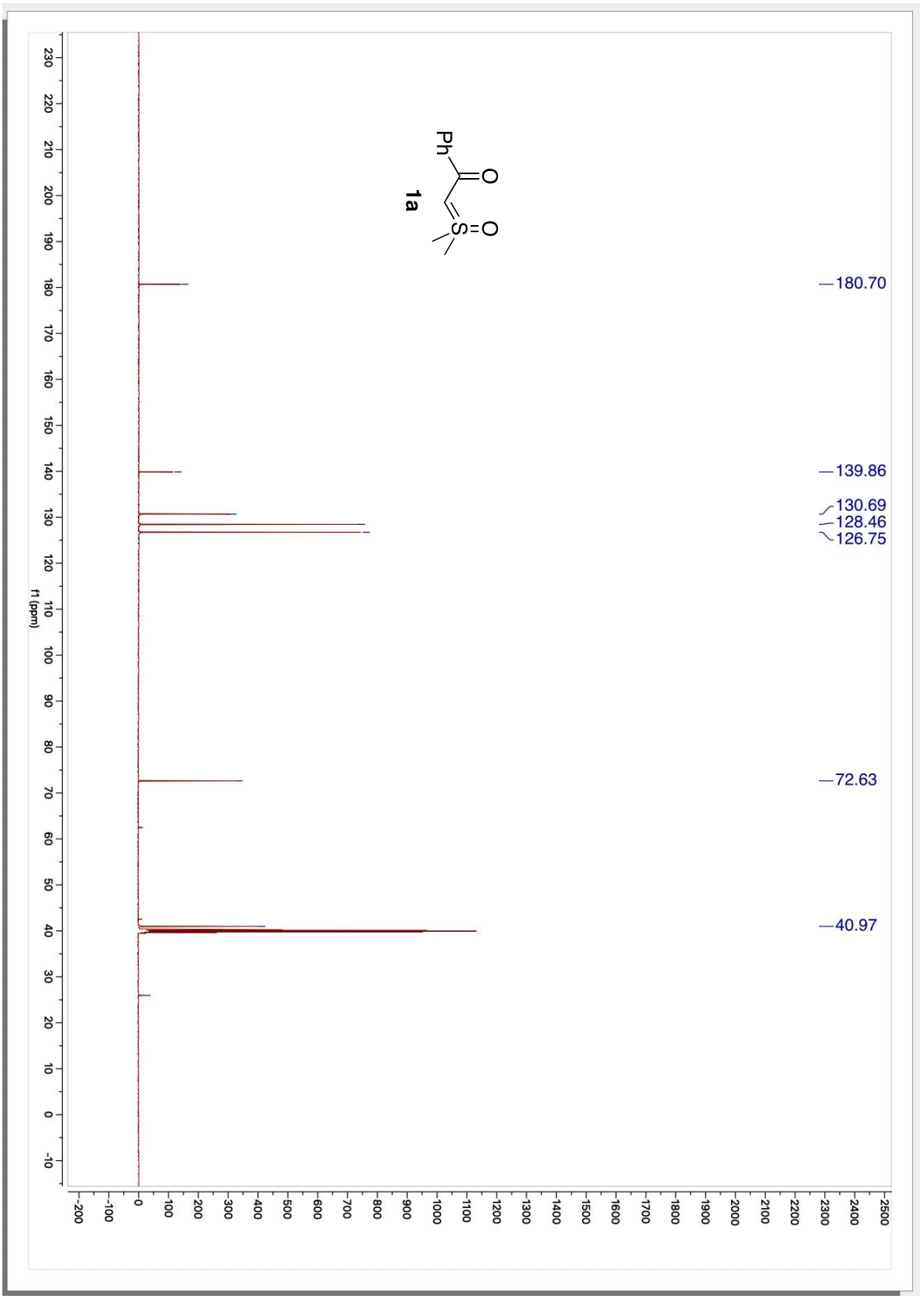

Figure S5: ^{13}C NMR spectrum of **1a** in d_6-DMSO (151 MHz)

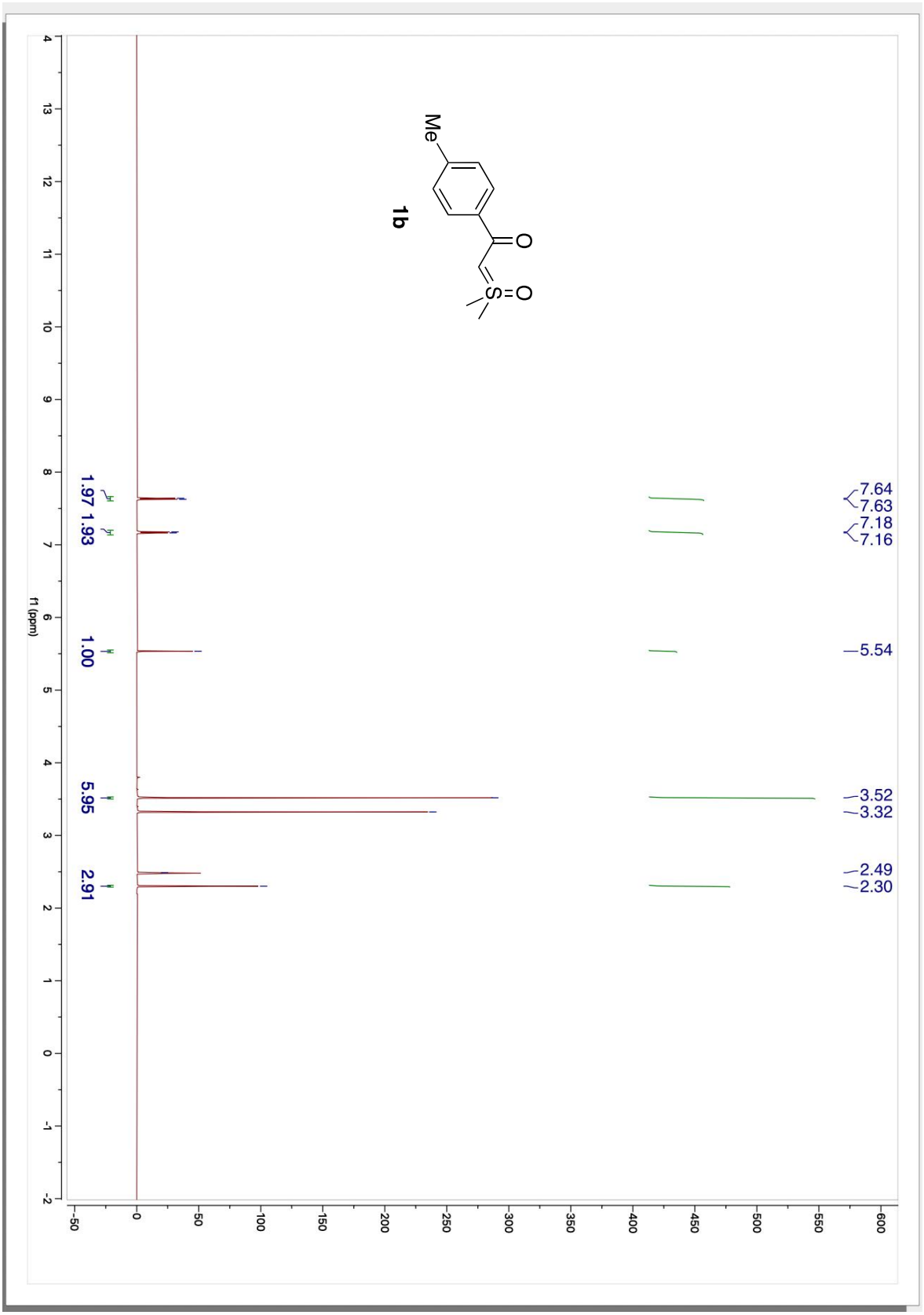

Figure S6: ^{1}H NMR spectrum of **1b** in d_6-DMSO (600 MHz)

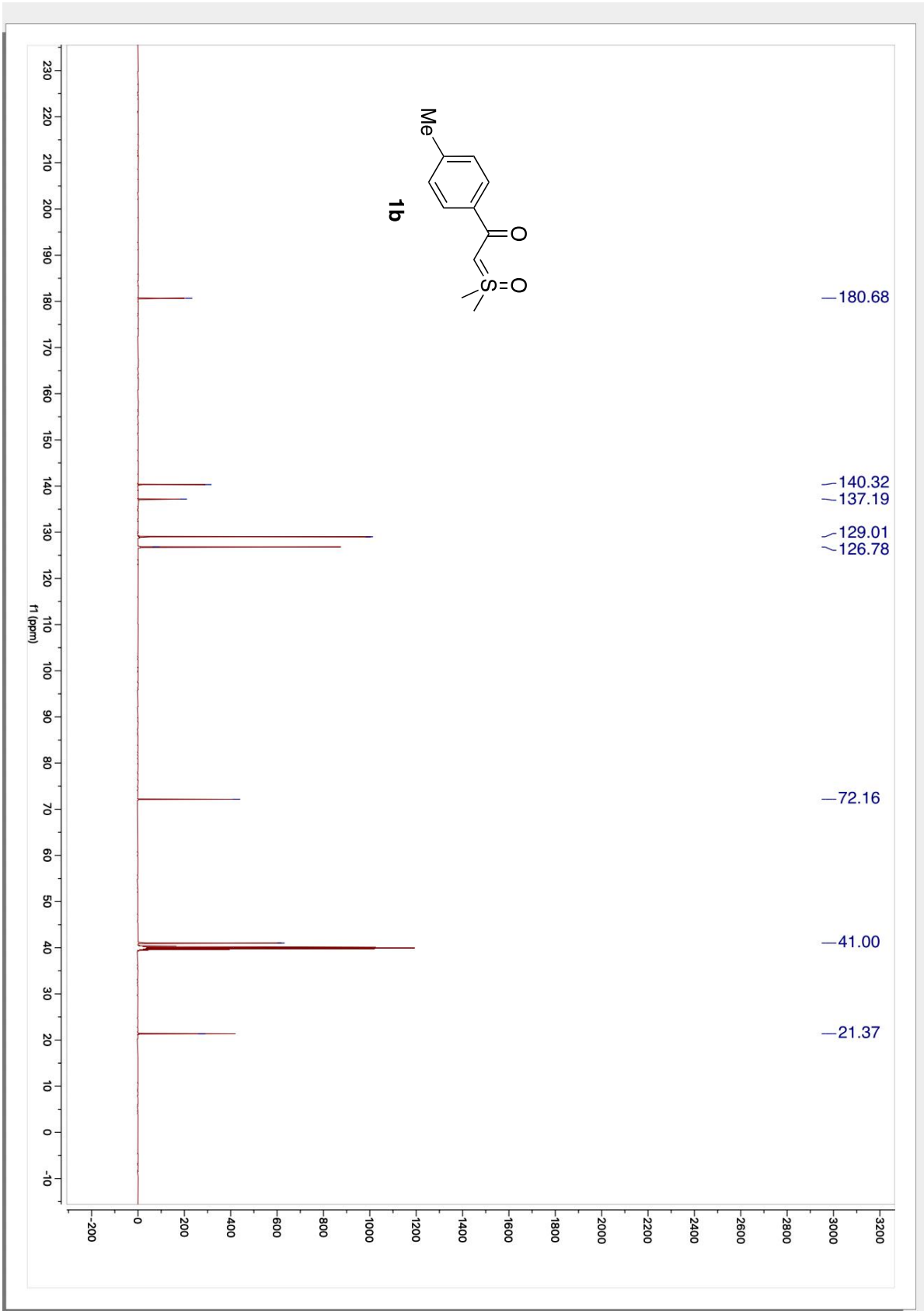

Figure S7: ^{13}C NMR spectrum of **1b** in d_6-DMSO (151 MHz)

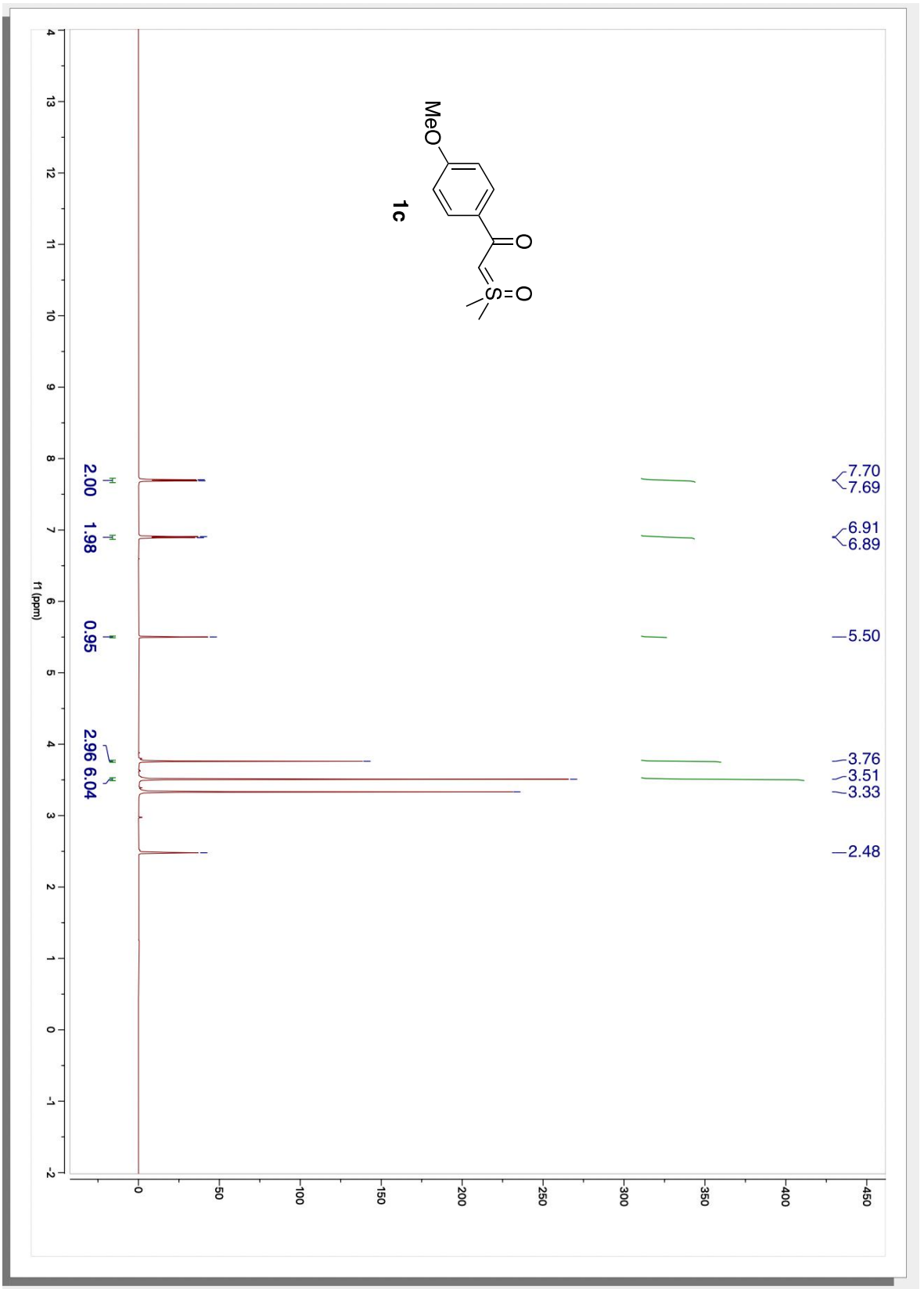

Figure S8: ^{1}H NMR spectrum of **1c** in d_6-DMSO (600 MHz)

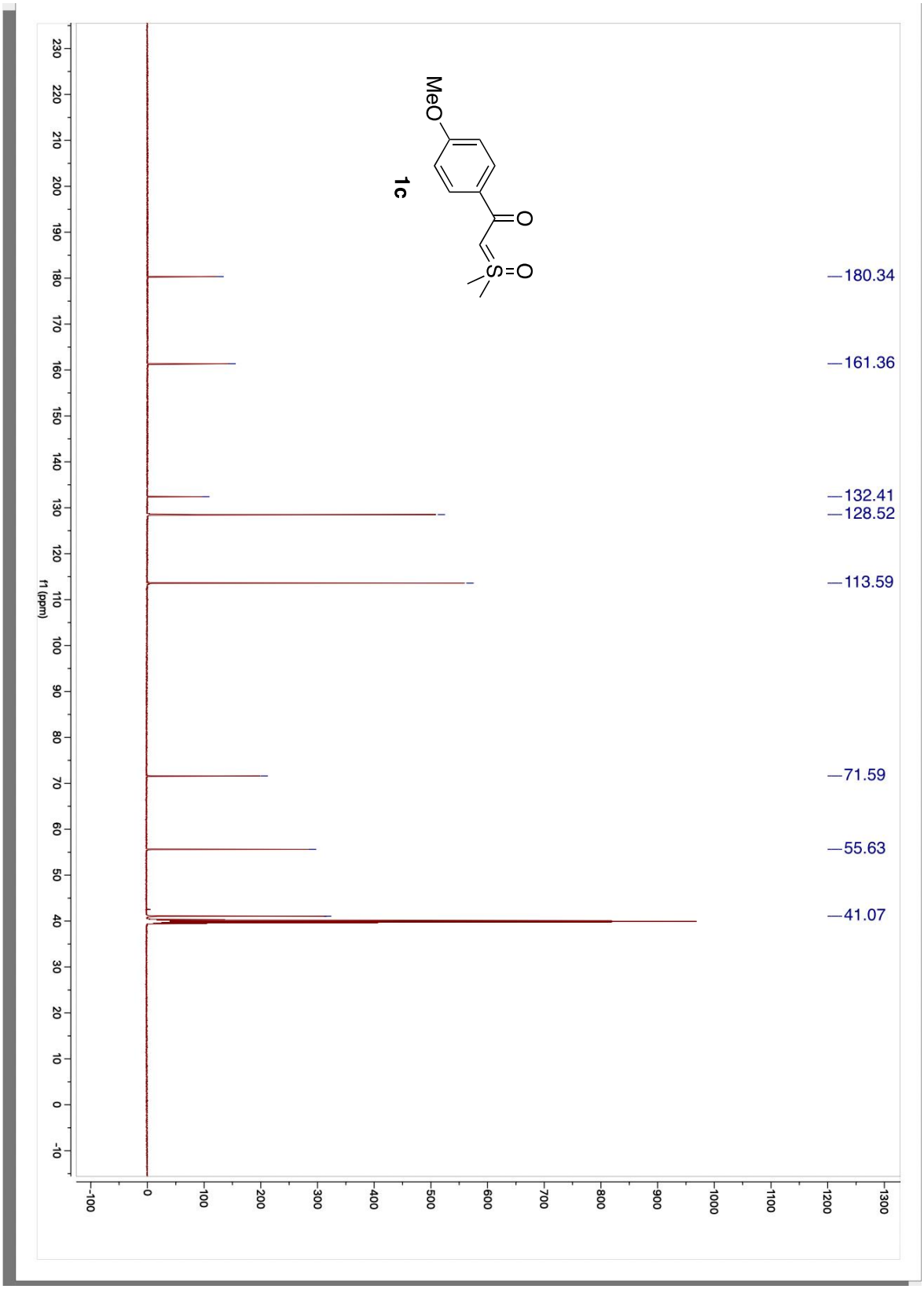

Figure S9: ^{13}C NMR spectrum of **1c** in d_6-DMSO (151 MHz)

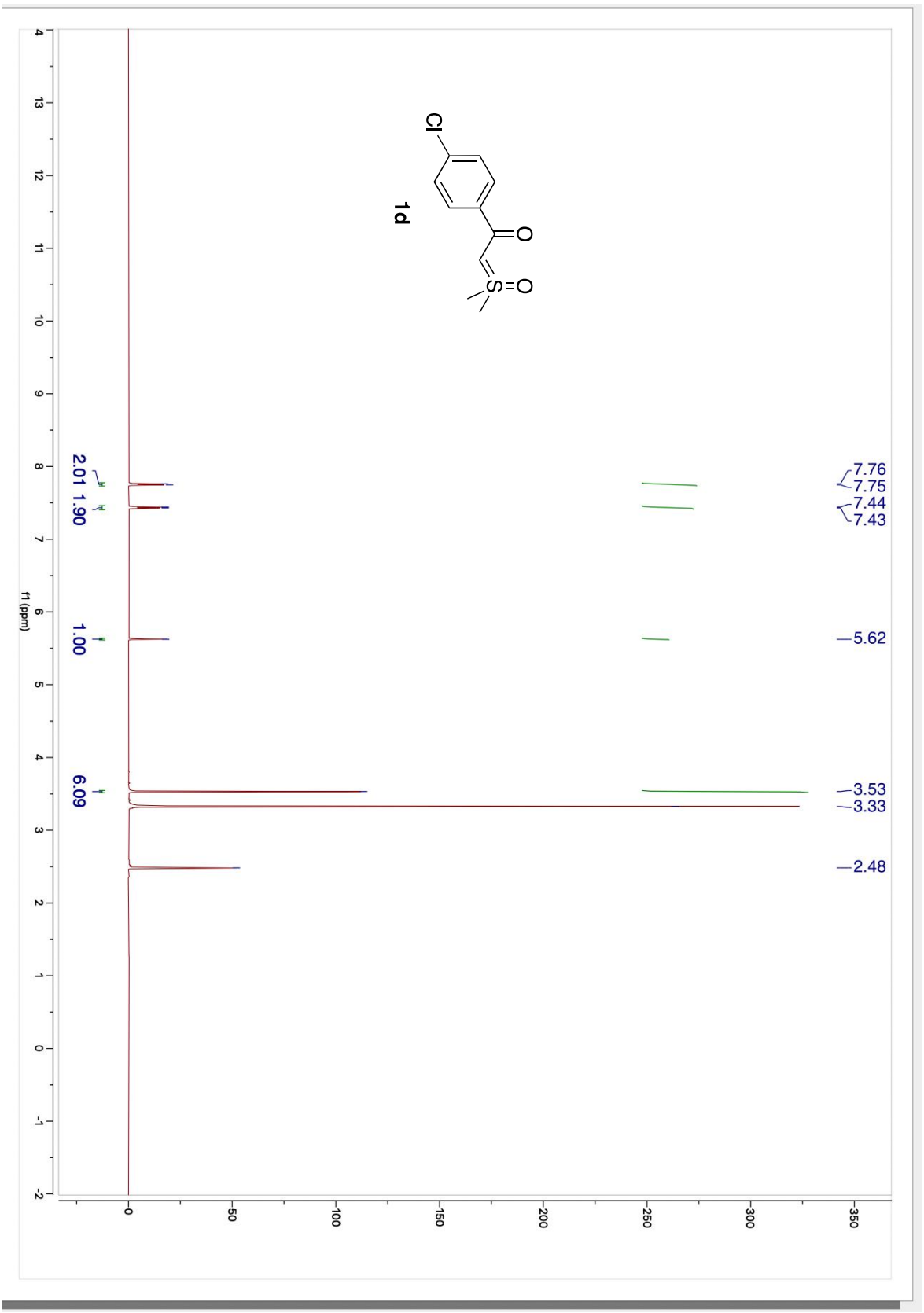

Figure S10: ^{1}H NMR spectrum of **1d** in d_6-DMSO (600 MHz)

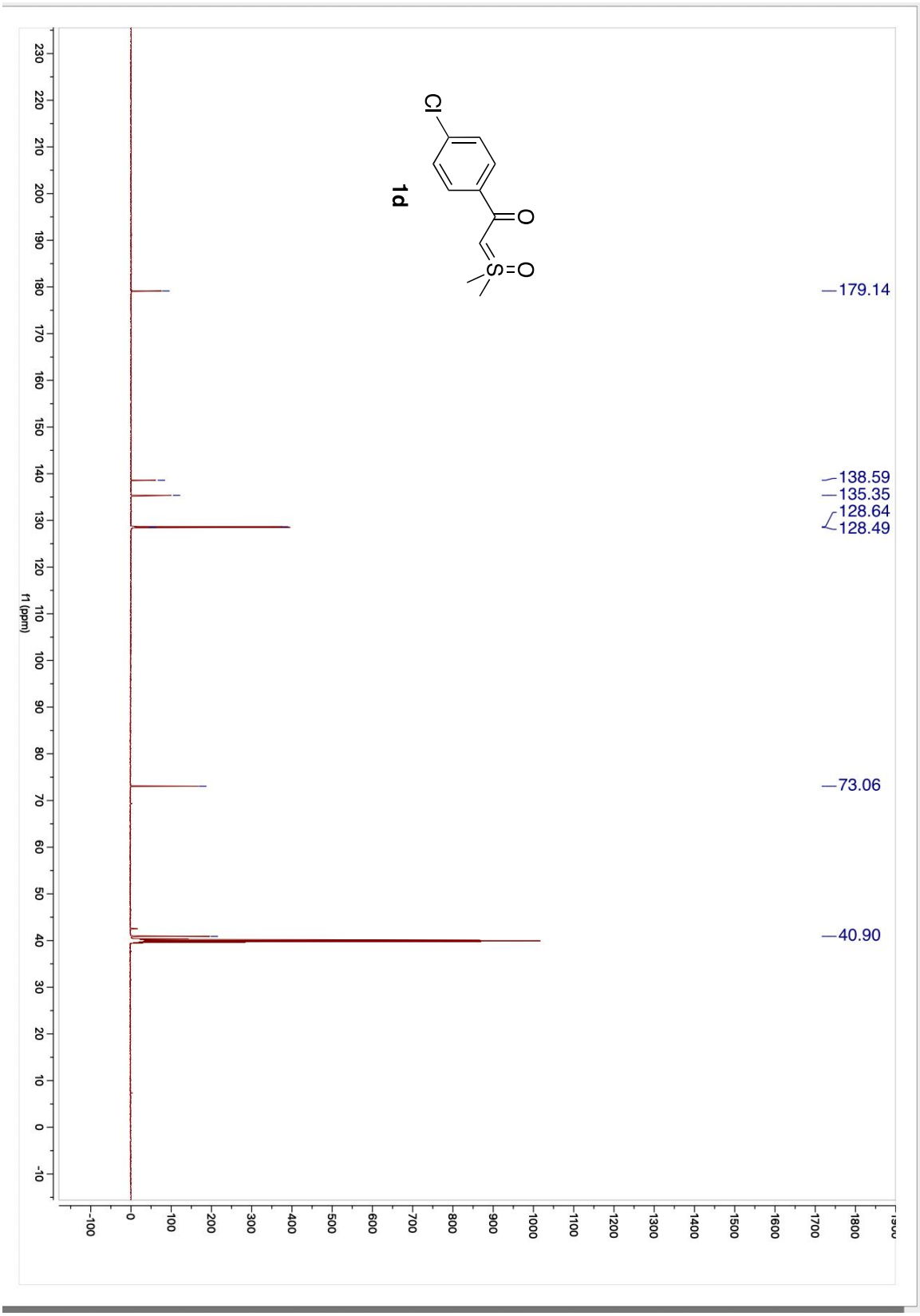

Figure S11: ^{13}C NMR spectrum of **1d** in d_6-DMSO (151 MHz)

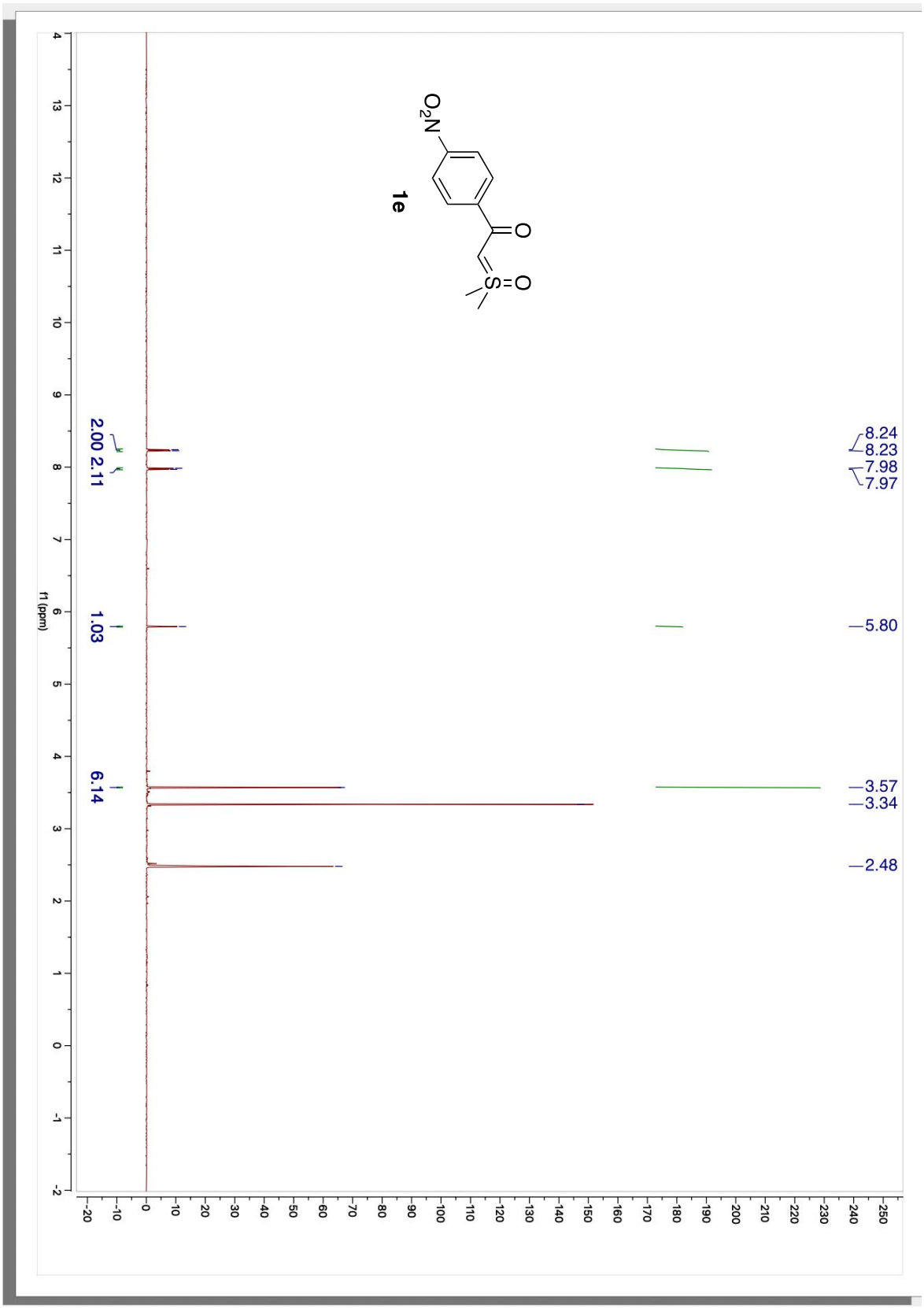

Figure S12: ^{1}H NMR spectrum of **1e** in d_6-DMSO (600 MHz)

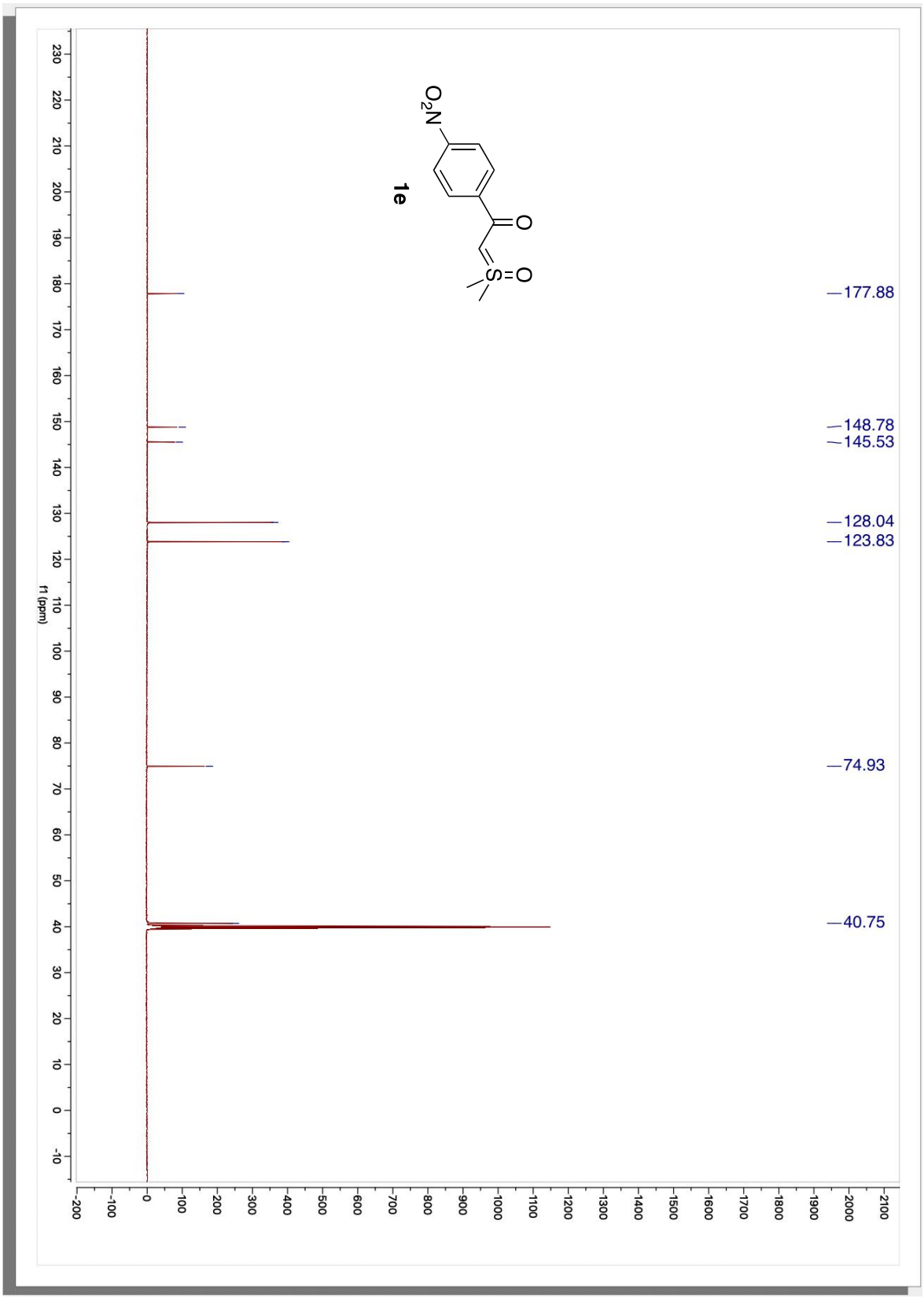

Figure S13: ^{13}C NMR spectrum of **1e** in d_6-DMSO (151 MHz)

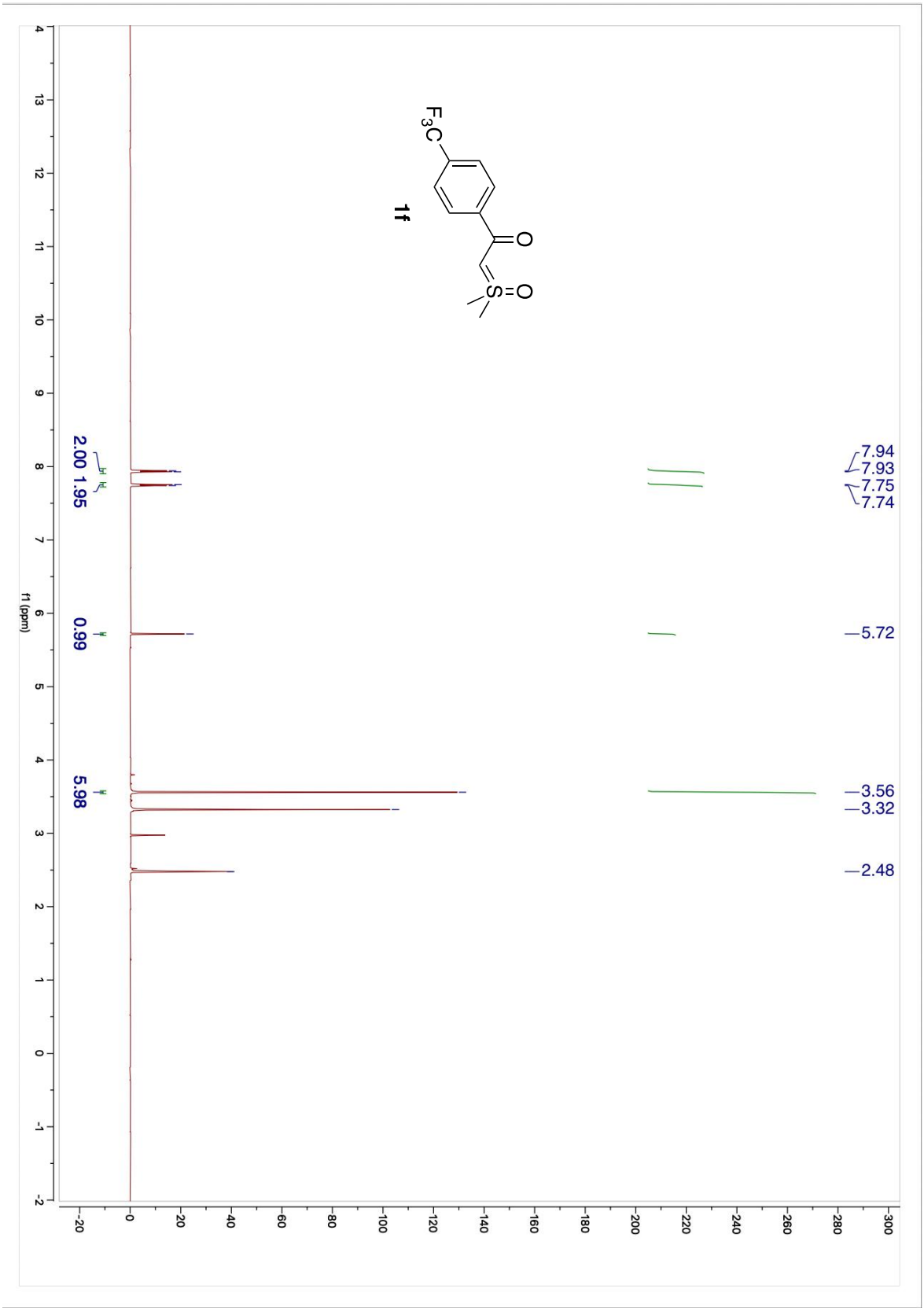

Figure S14: ^{1}H NMR spectrum of **1f** in d_6-DMSO (600 MHz)

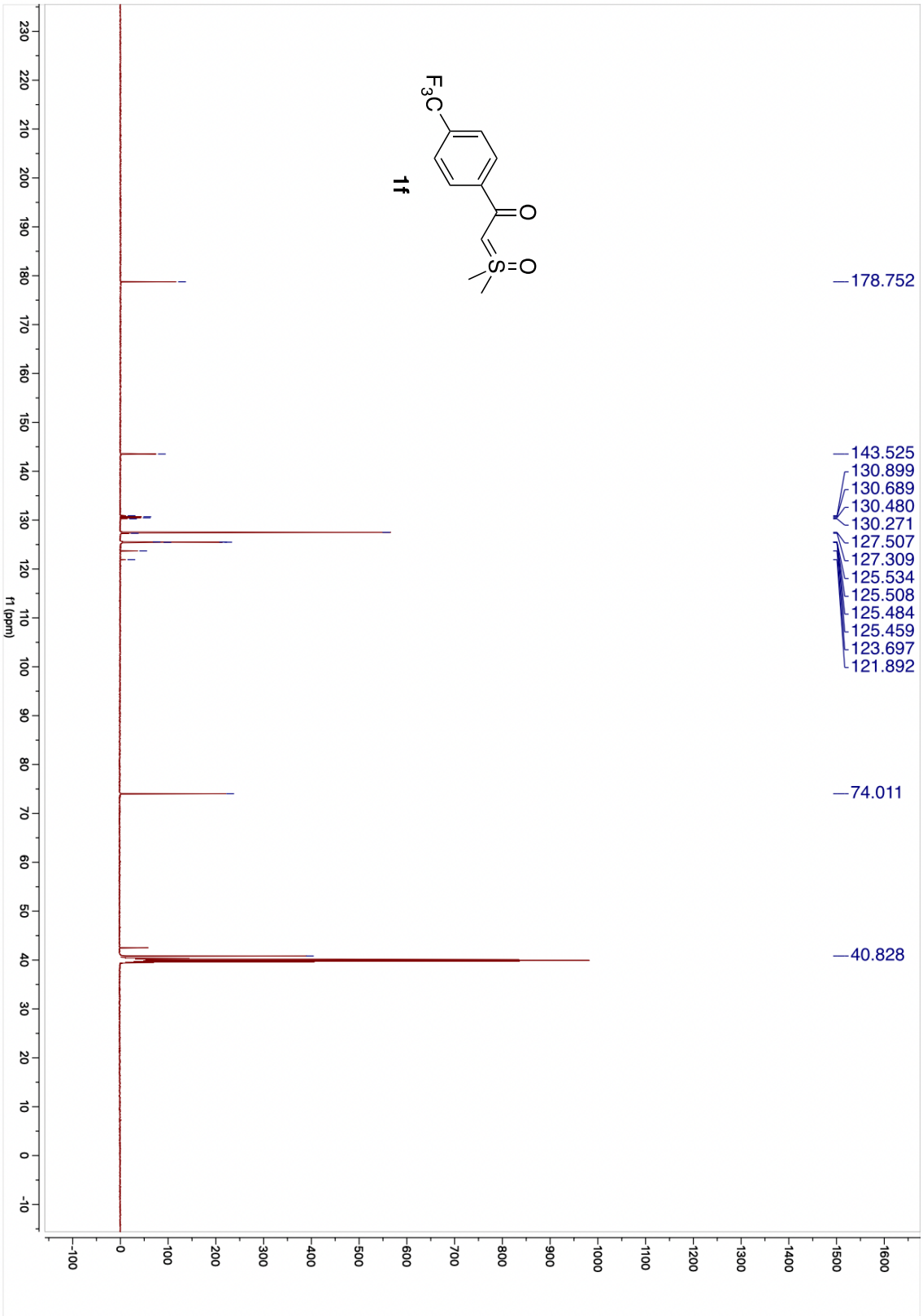

Figure S15: ^{13}C NMR spectrum of **1f** in d_6-DMSO (151 MHz)

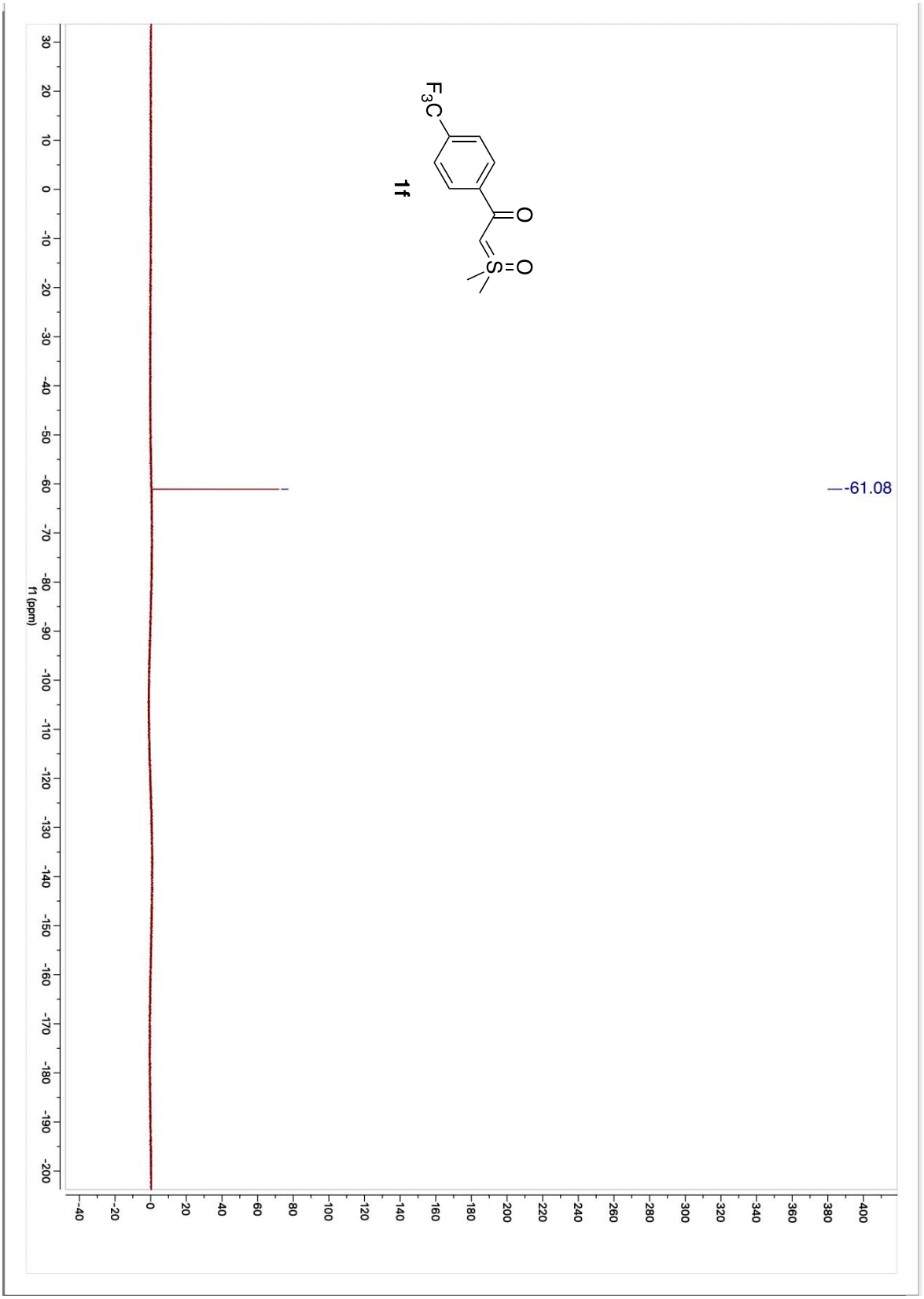

Figure S16: ^{19}F NMR spectrum of **1f** in d_6-DMSO (376 MHz)

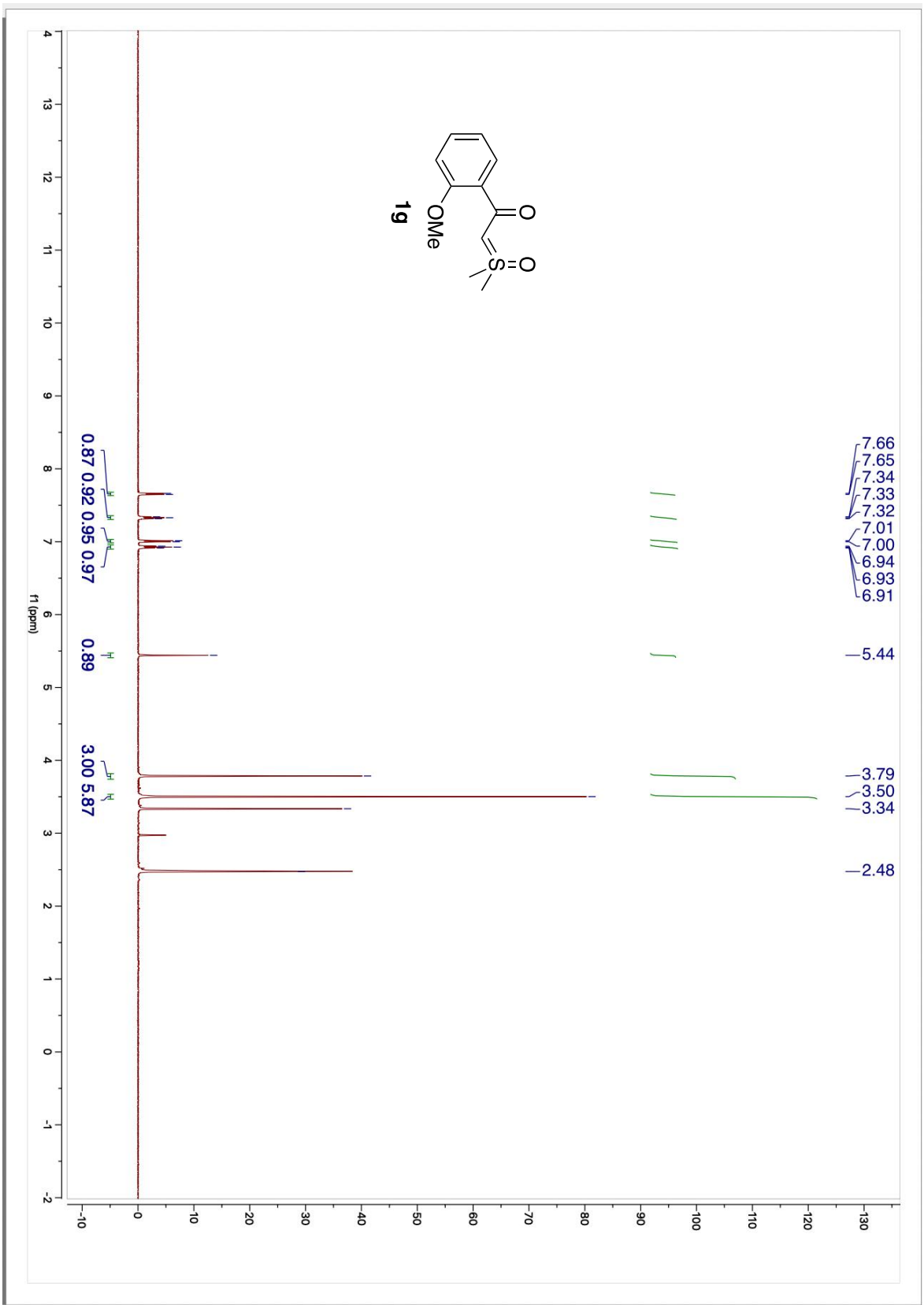

Figure S17: ^{1}H NMR spectrum of **1g** in d_6-DMSO (600 MHz)

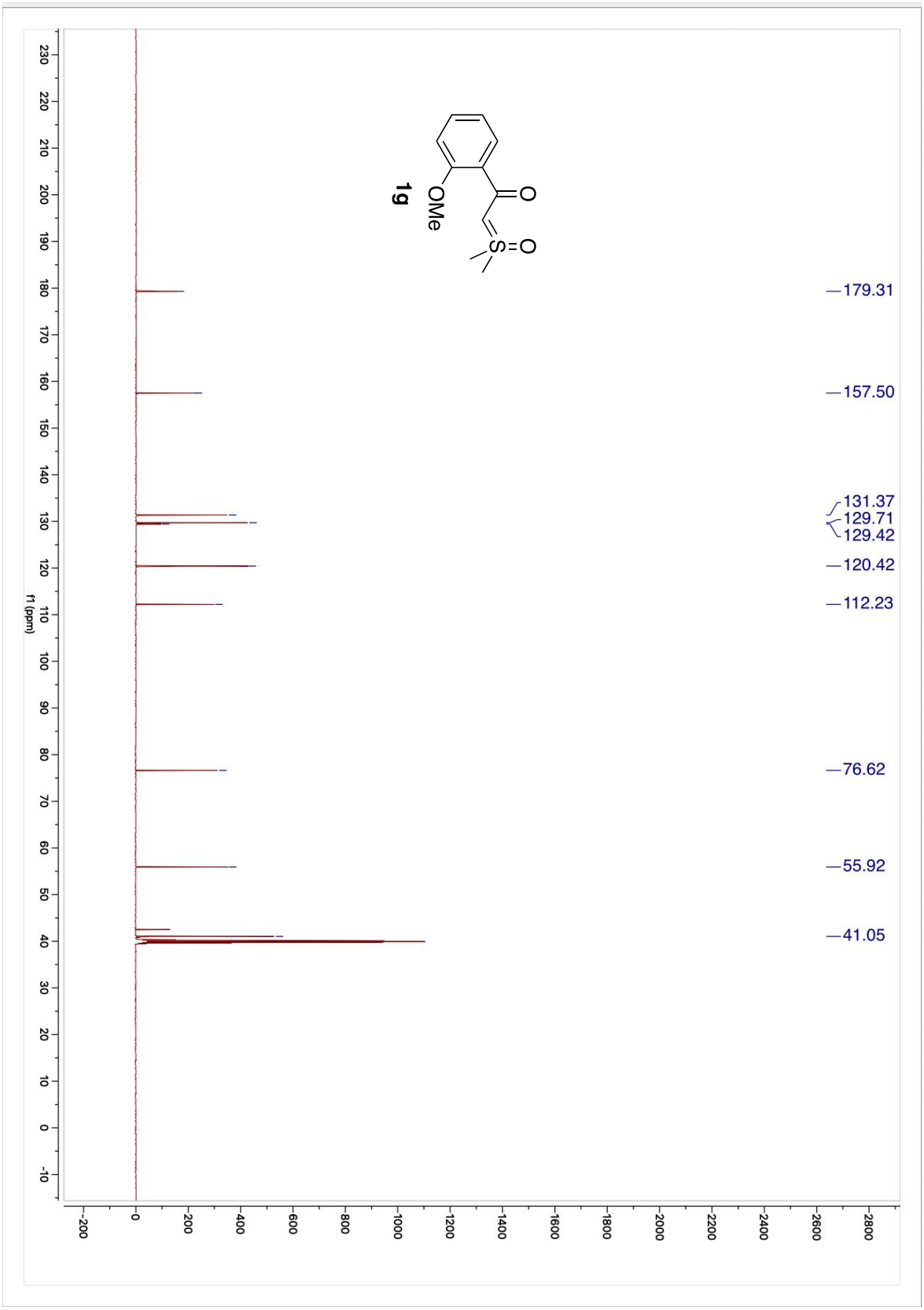

Figure S18: ^{13}C NMR spectrum of **1g** in d_6-DMSO (151 MHz)

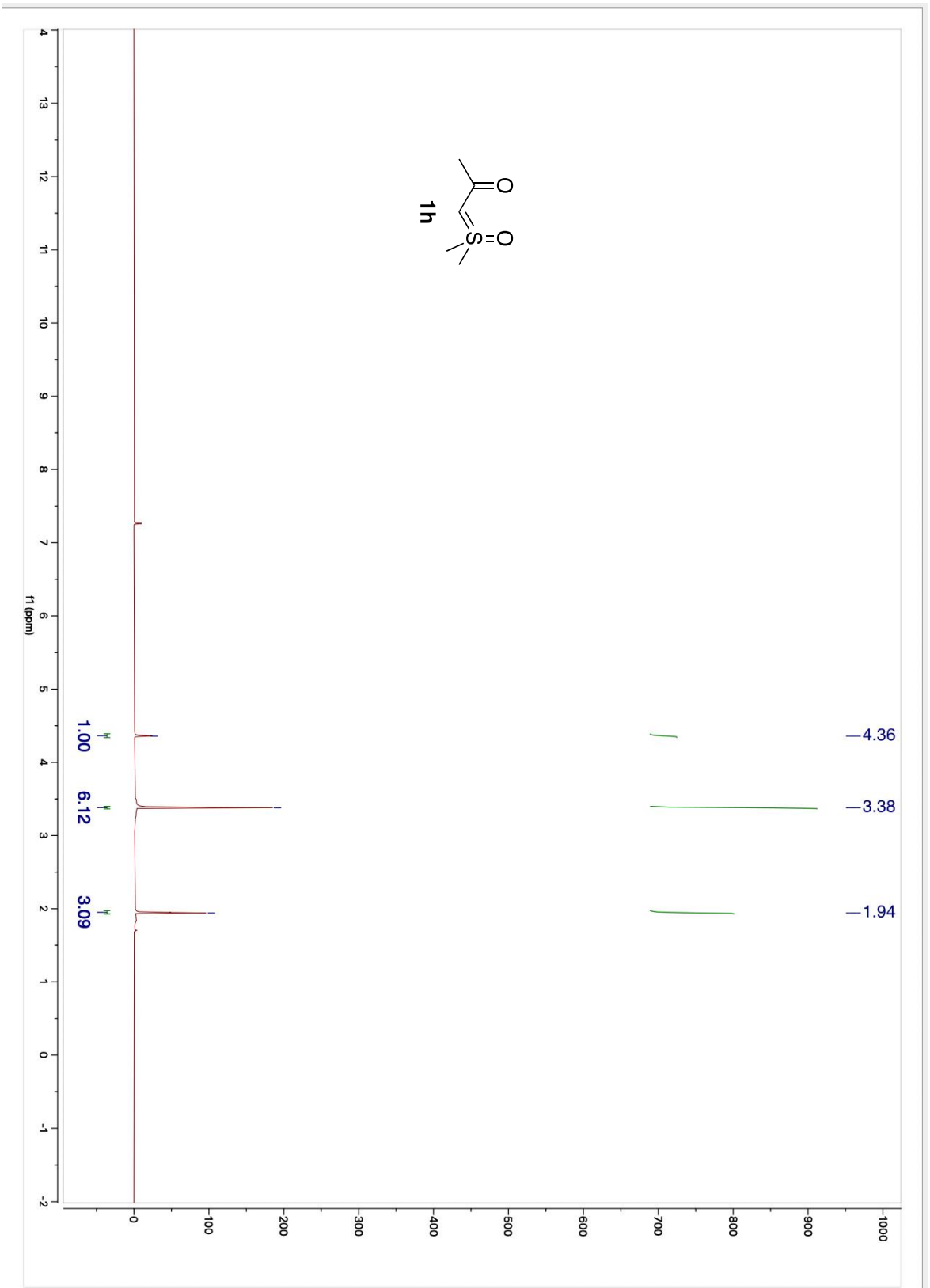

Figure S19: ^{1}H NMR spectrum of **1h** in $CDCl_3$ (600 MHz)

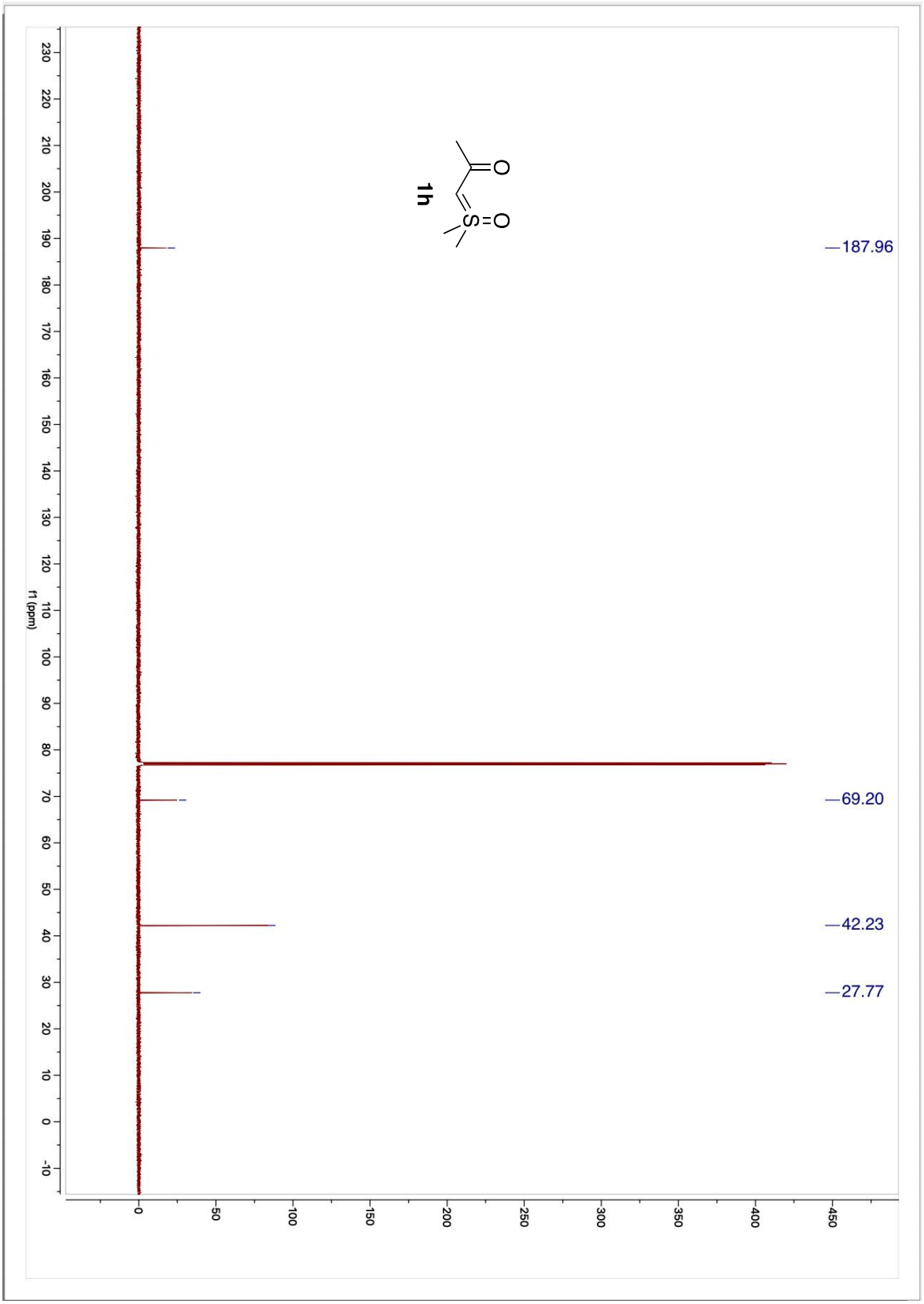

Figure S20: ^{13}C NMR spectrum of **1h** in $CDCl_3$ (151 MHz)

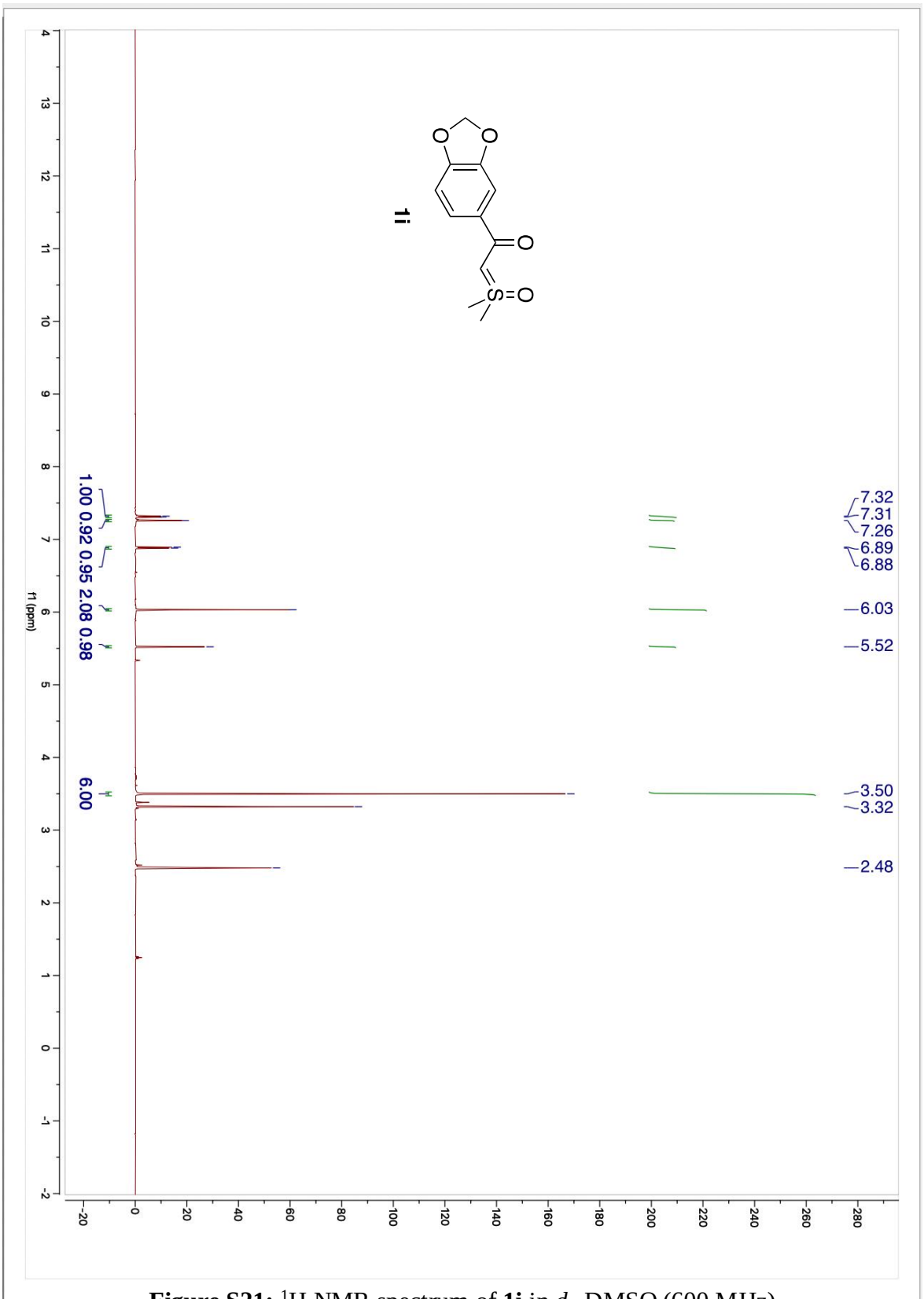

Figure S21: ^{1}H NMR spectrum of **1i** in d_6-DMSO (600 MHz)

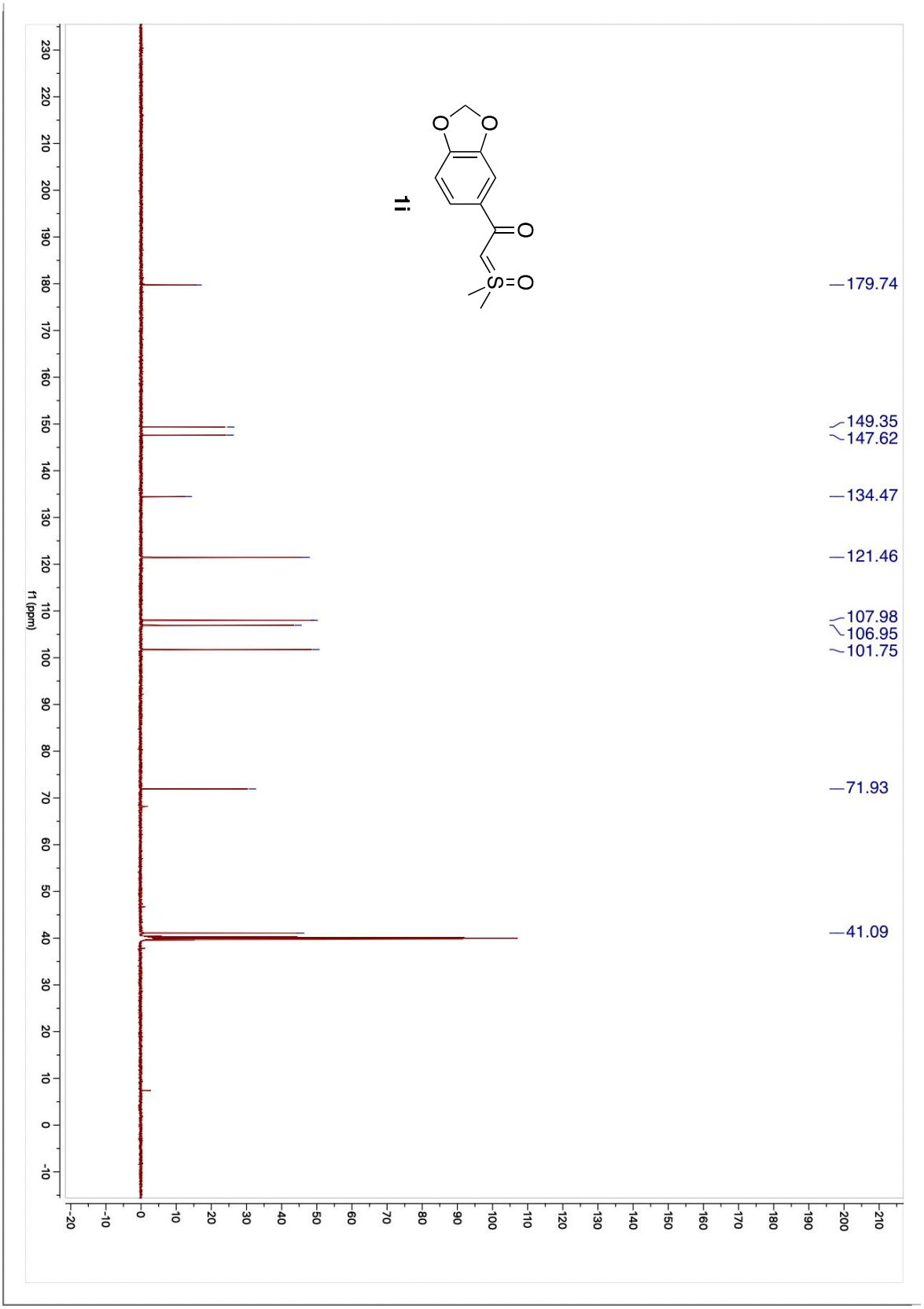

Figure S22: ^{1}H NMR spectrum of **1i** in d_6-DMSO (600 MHz)

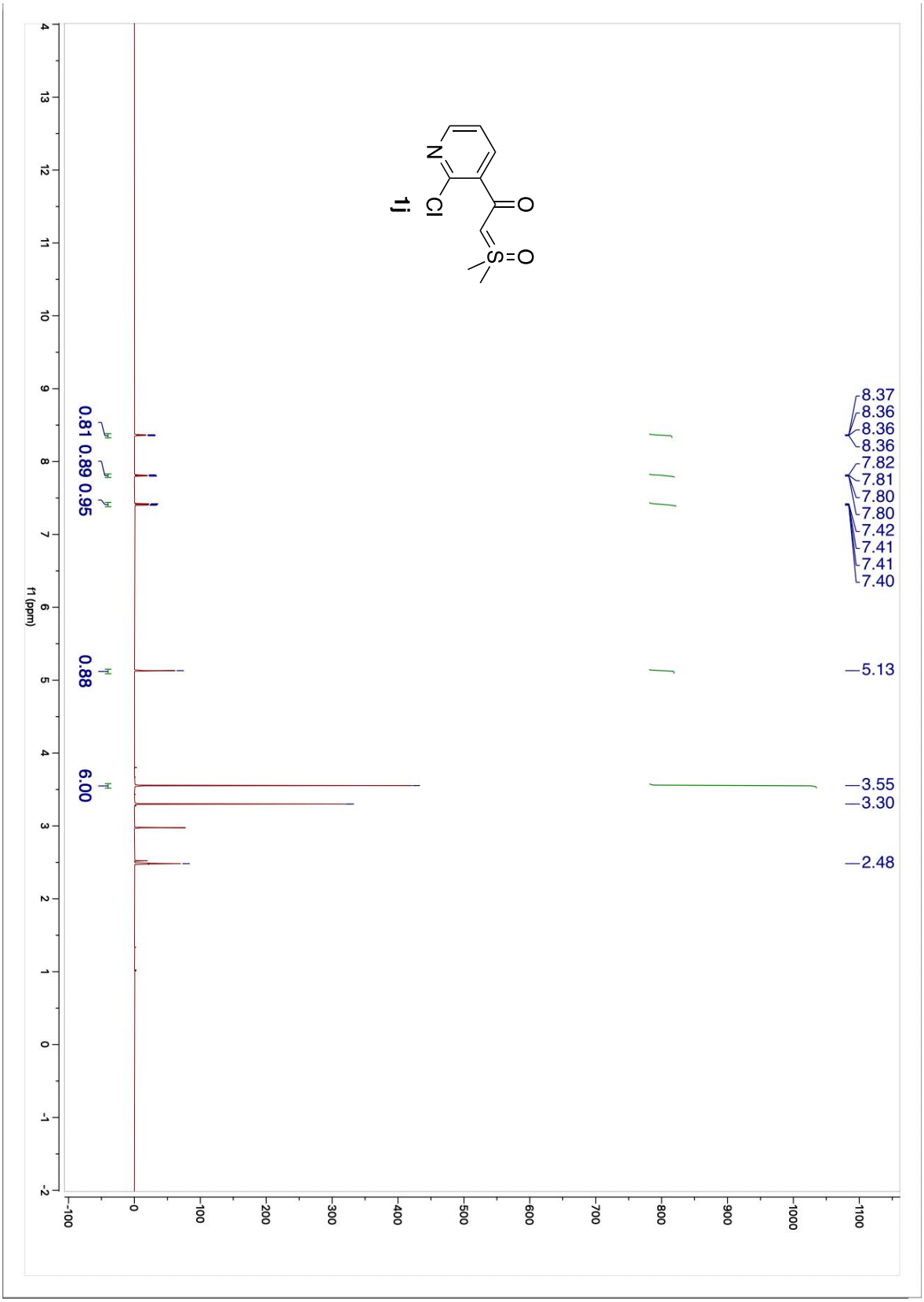

Figure S23: ^{1}H NMR spectrum of **1j** in d_6-DMSO (600 MHz)

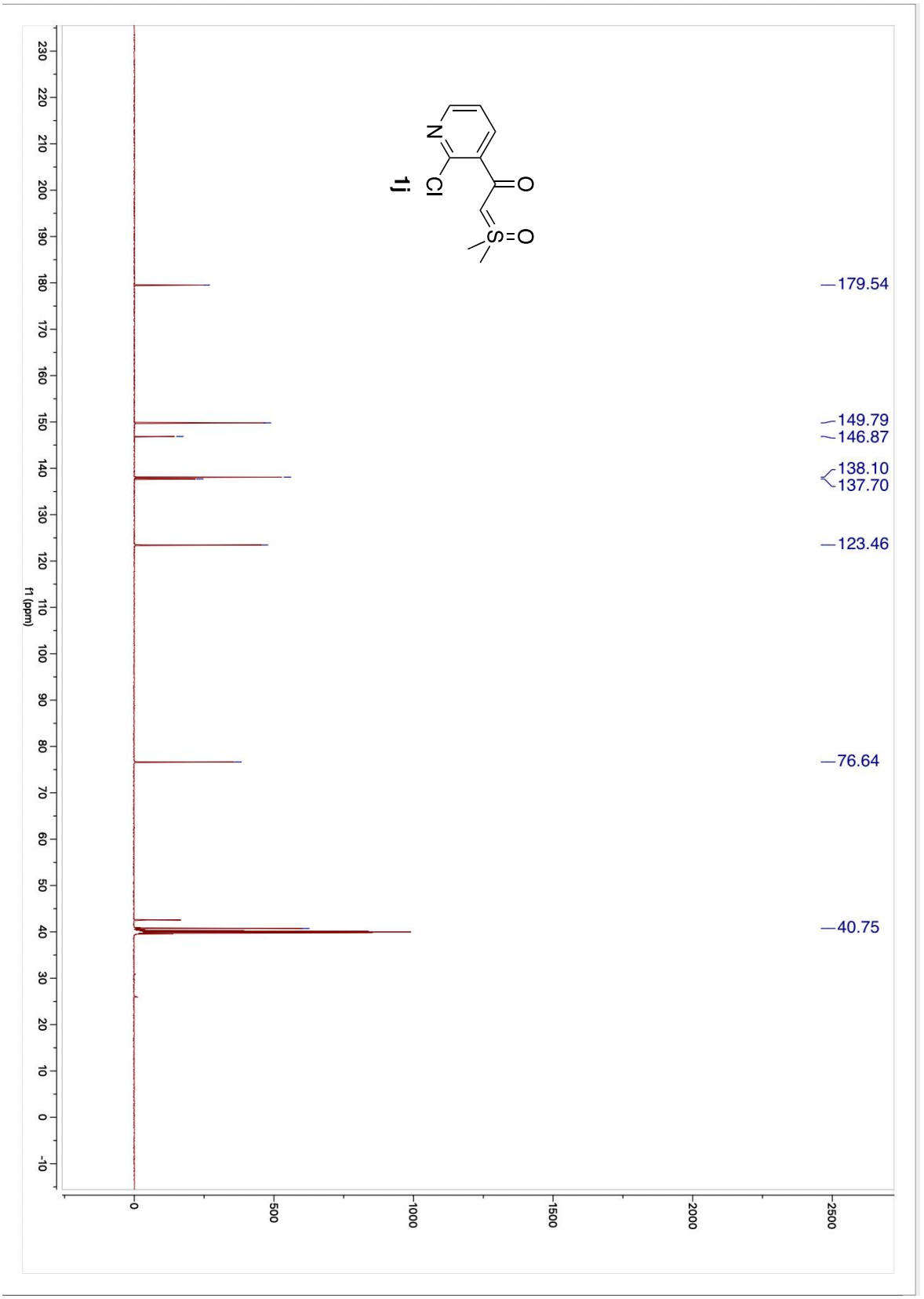

Figure S24: ^{13}C NMR spectrum of **1j** in d_6-DMSO (151 MHz)

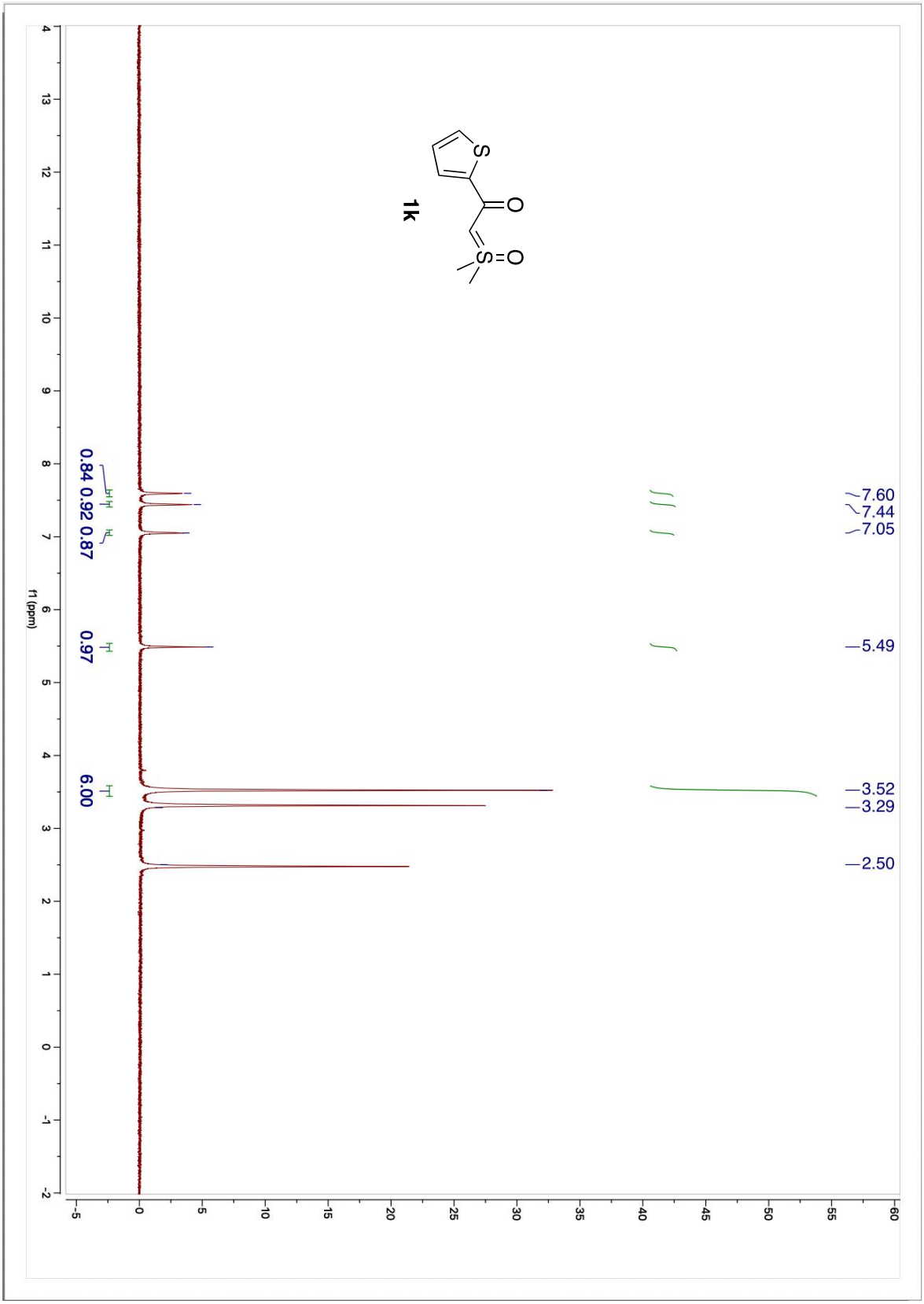

Figure S25: ^{1}H NMR spectrum of **1k** in d_6-DMSO (600 MHz)

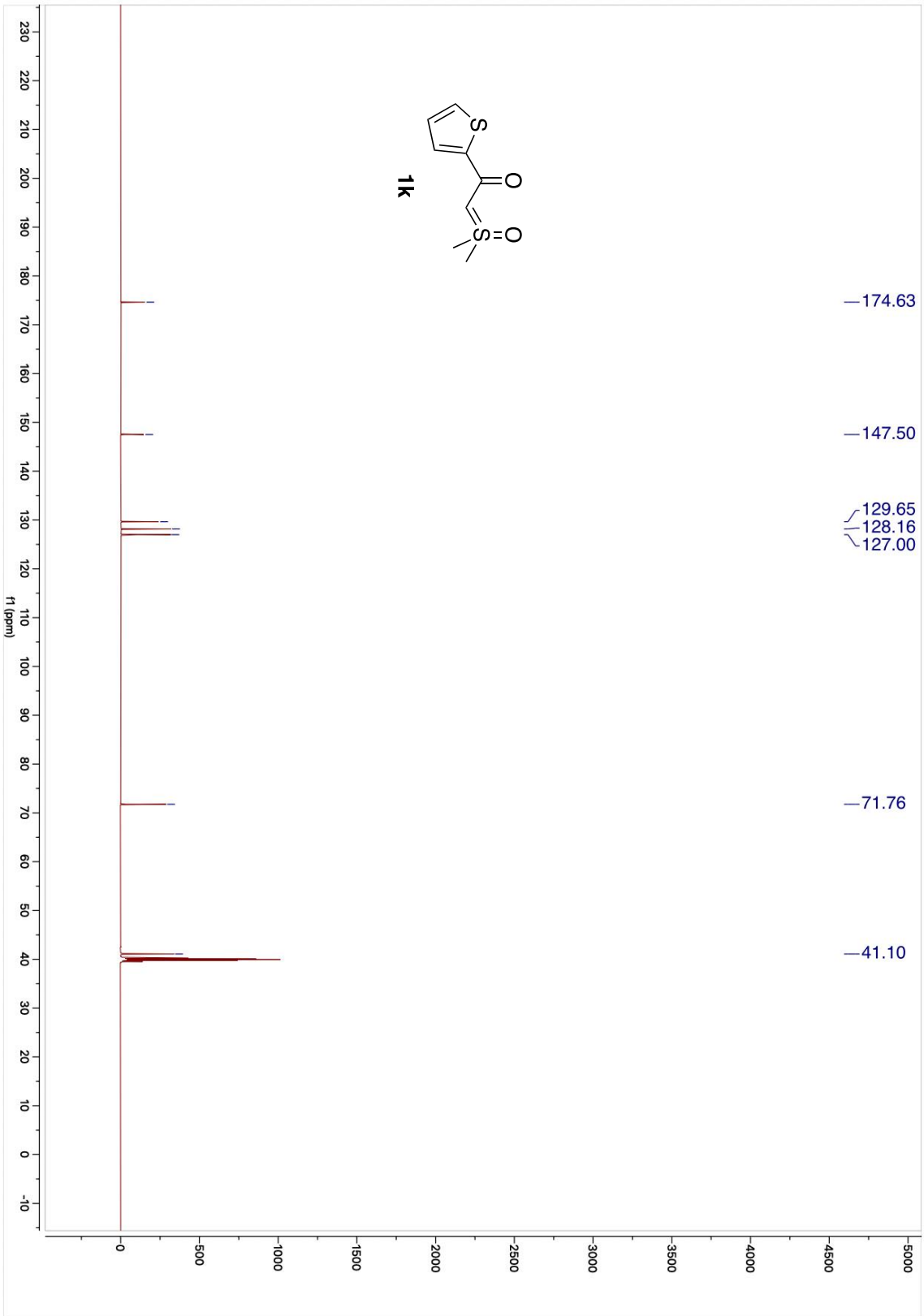

Figure S26: ^{13}C NMR spectrum of **1k** in d_6-DMSO (151 MHz)

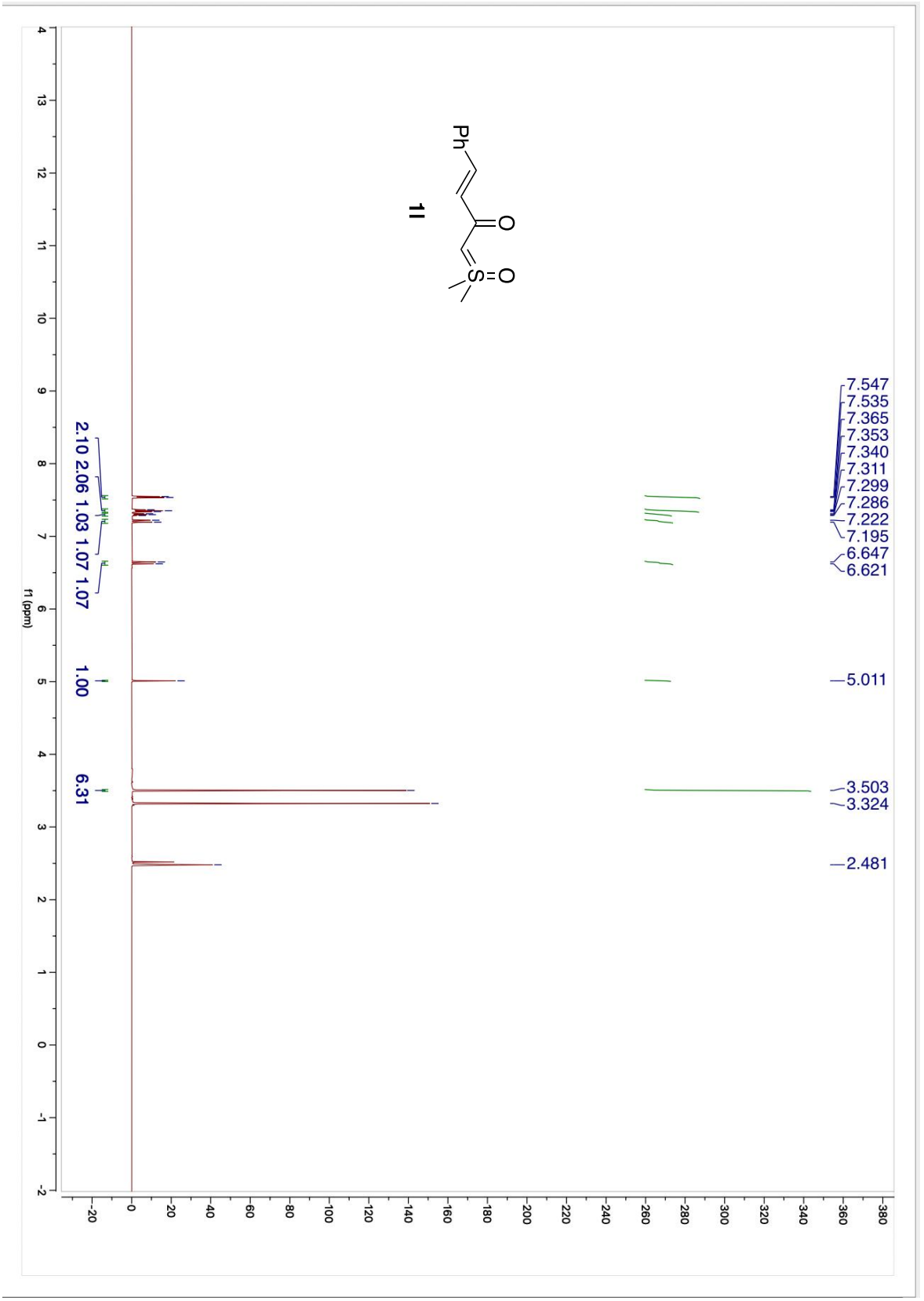

Figure S27: ^{1}H NMR spectrum of **1l** in d_6-DMSO (600 MHz)

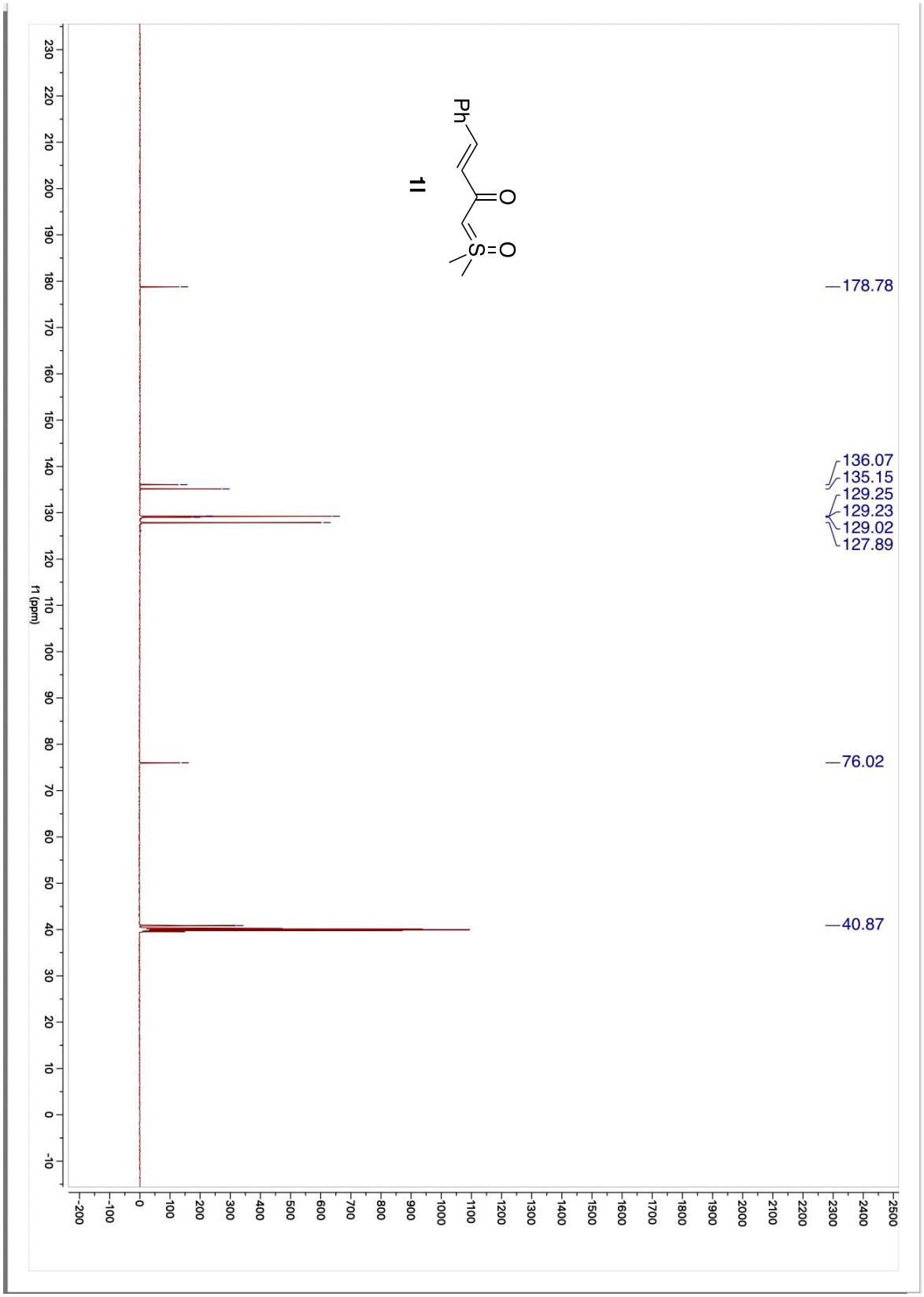

Figure S28: ^{13}C NMR spectrum of **1l** in d_6-DMSO (151 MHz)

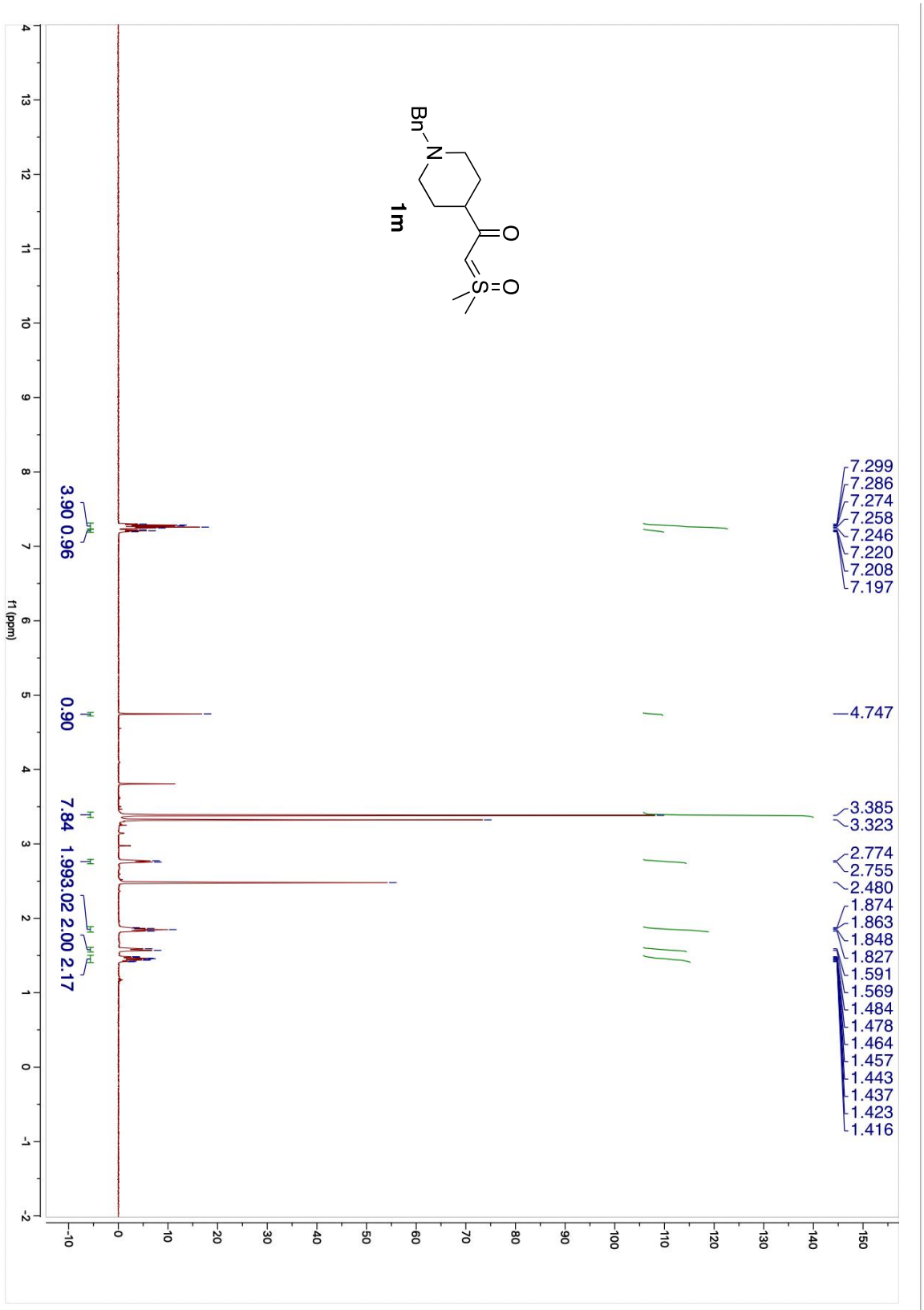

Figure S29: ^{1}H NMR spectrum of **1m** in d_6-DMSO (600 MHz)

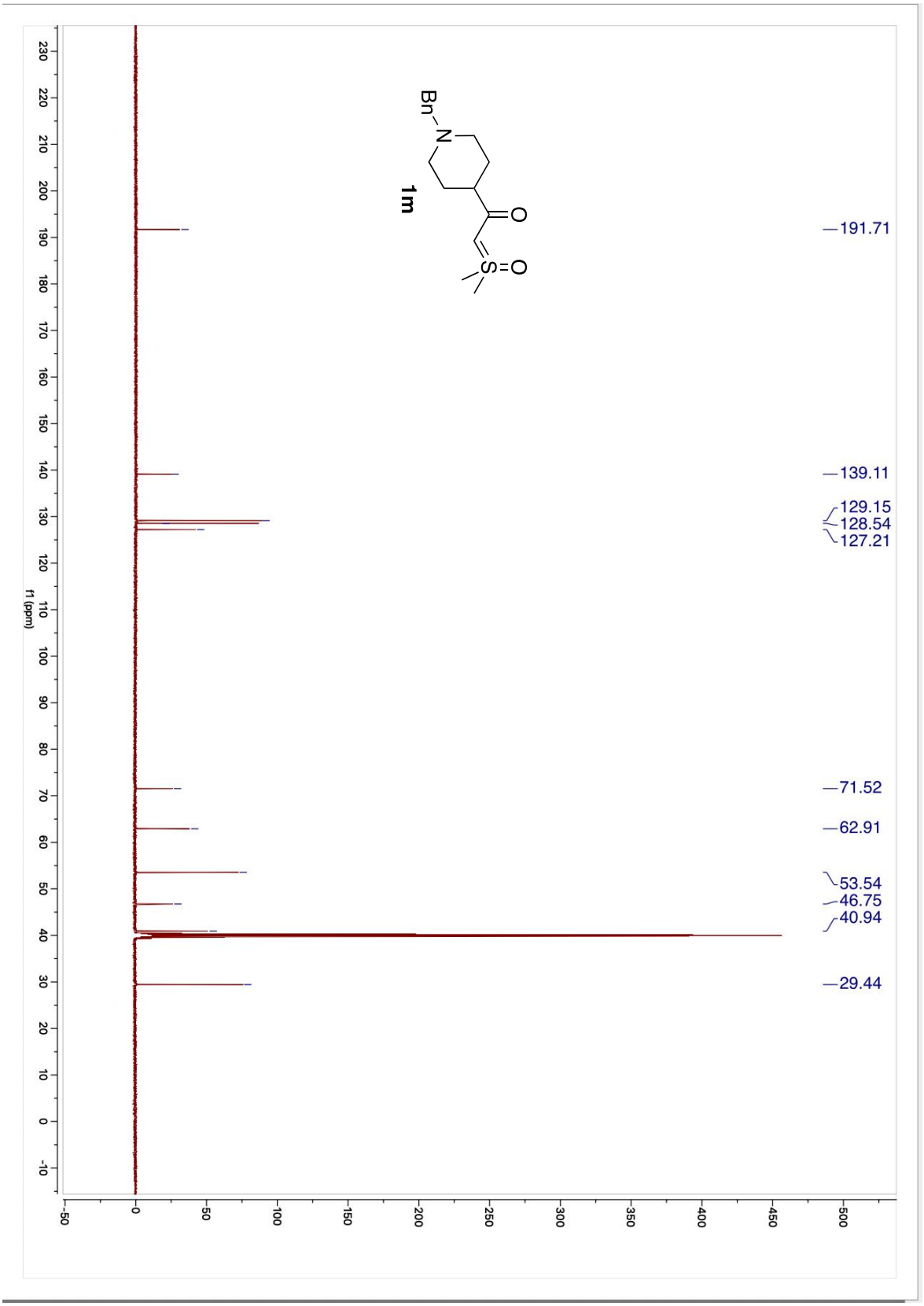

Figure S30: ^{13}C NMR spectrum of **1m** in d_6-DMSO (151 MHz)

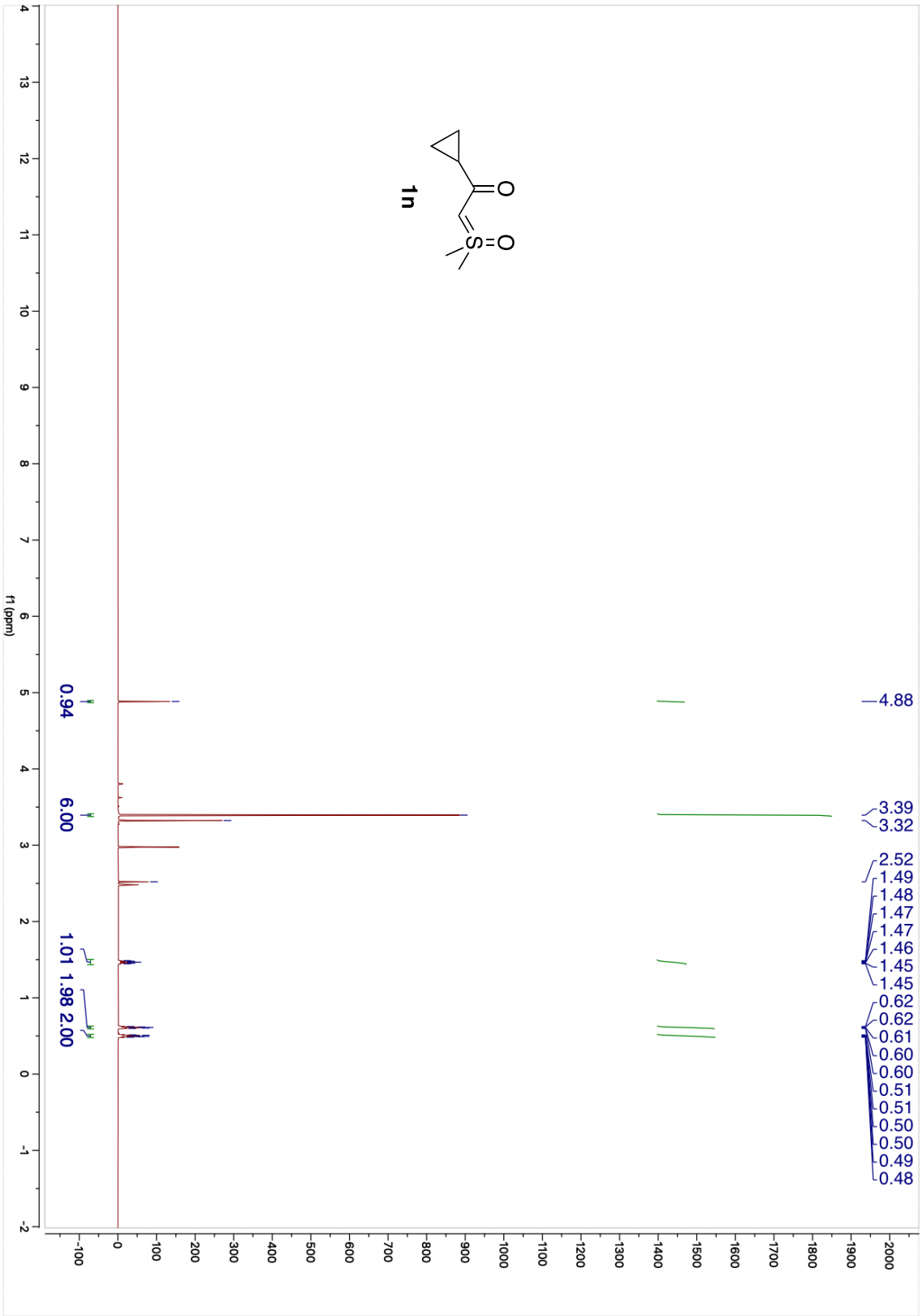

Figure S31: ^{1}H NMR spectrum of **1n** in d_6-DMSO (600 MHz)

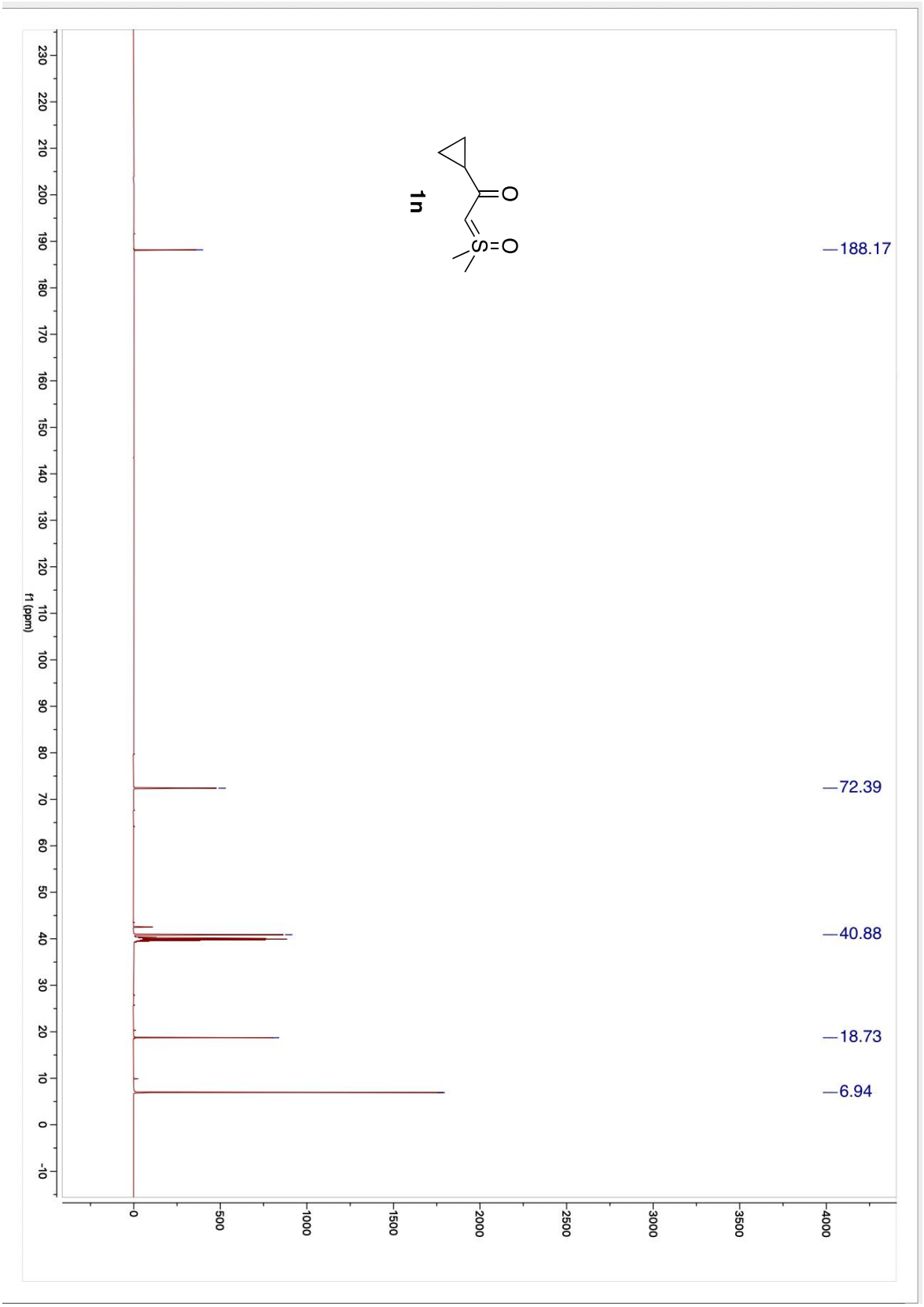

Figure S32: ^{13}C NMR spectrum of **1n** in d_6-DMSO (151 MHz)

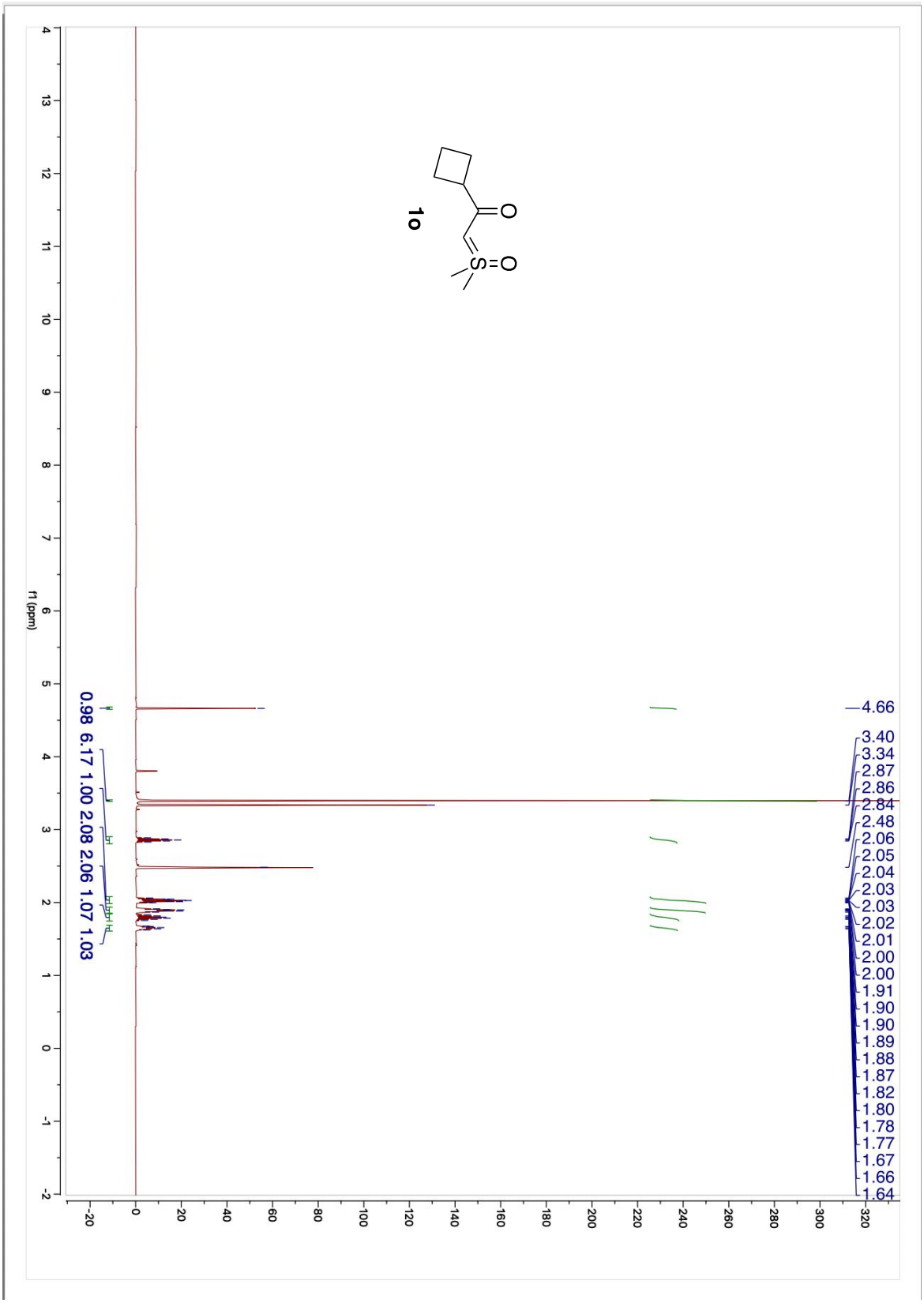

Figure S33: ^{1}H NMR spectrum of **1o** in d_6-DMSO (600 MHz)

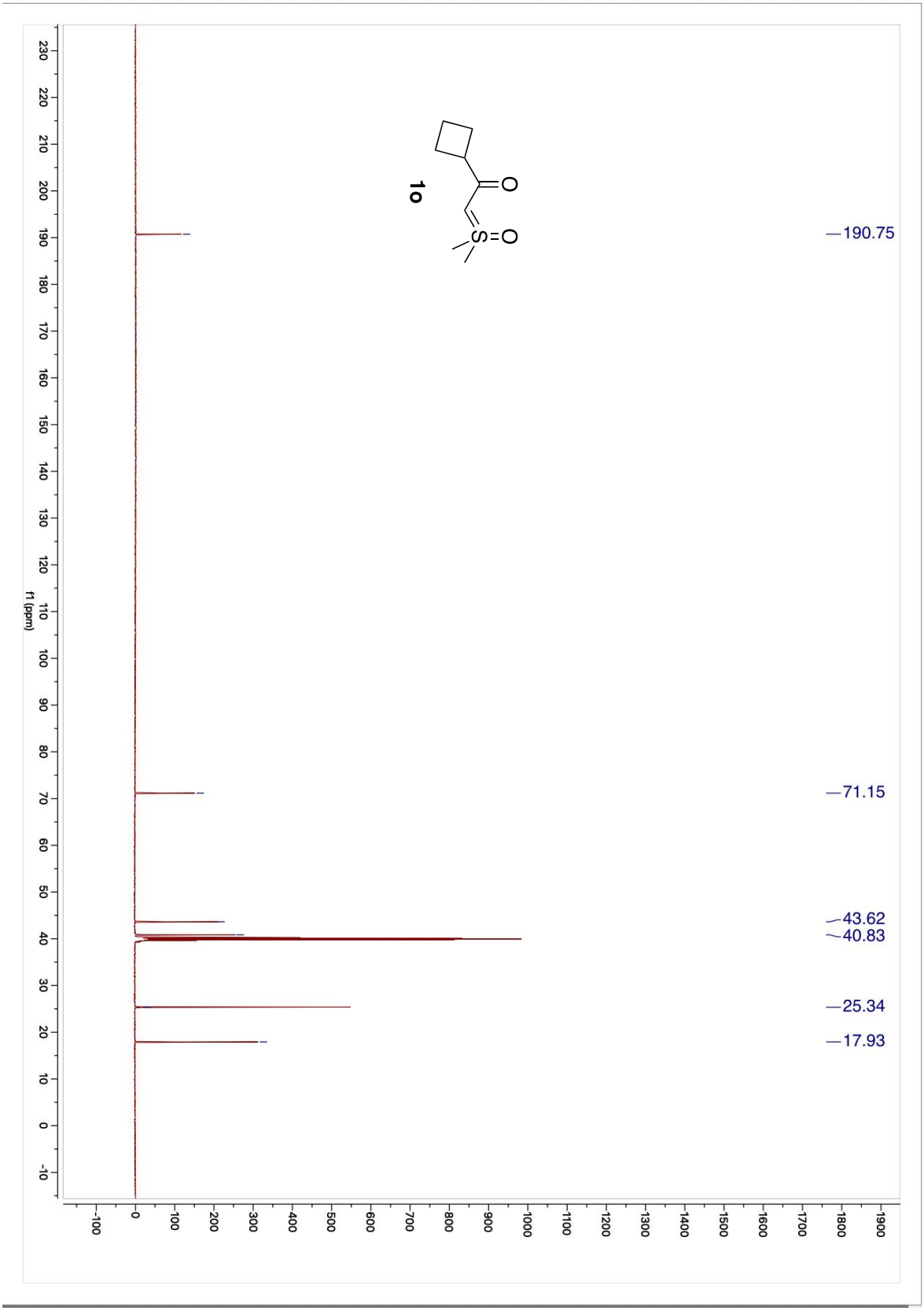

Figure S34: ^{13}C NMR spectrum of **1o** in d_6-DMSO (151 MHz)

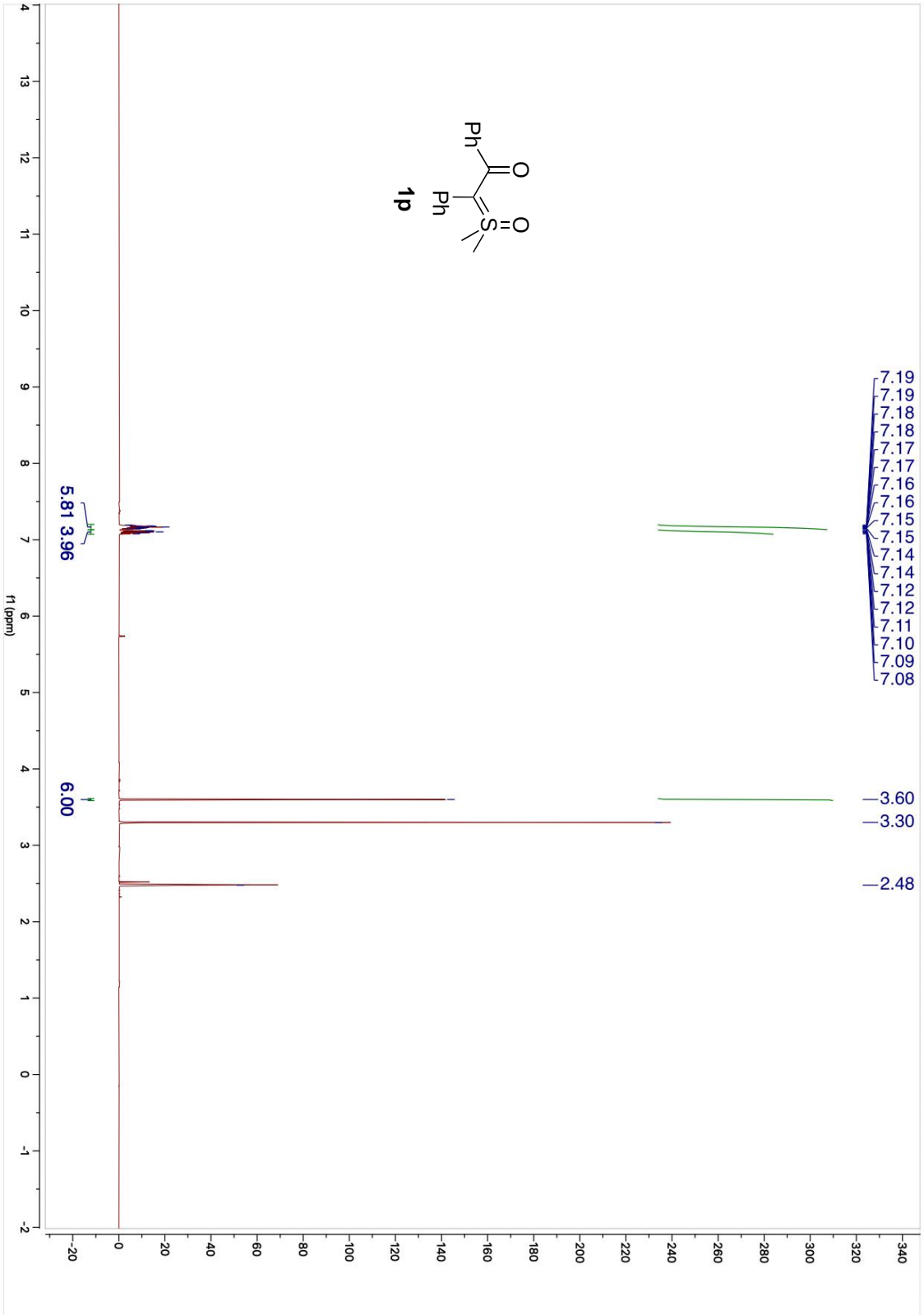

Figure S35: ^{1}H NMR spectrum of **1p** in d_6-DMSO (600 MHz)

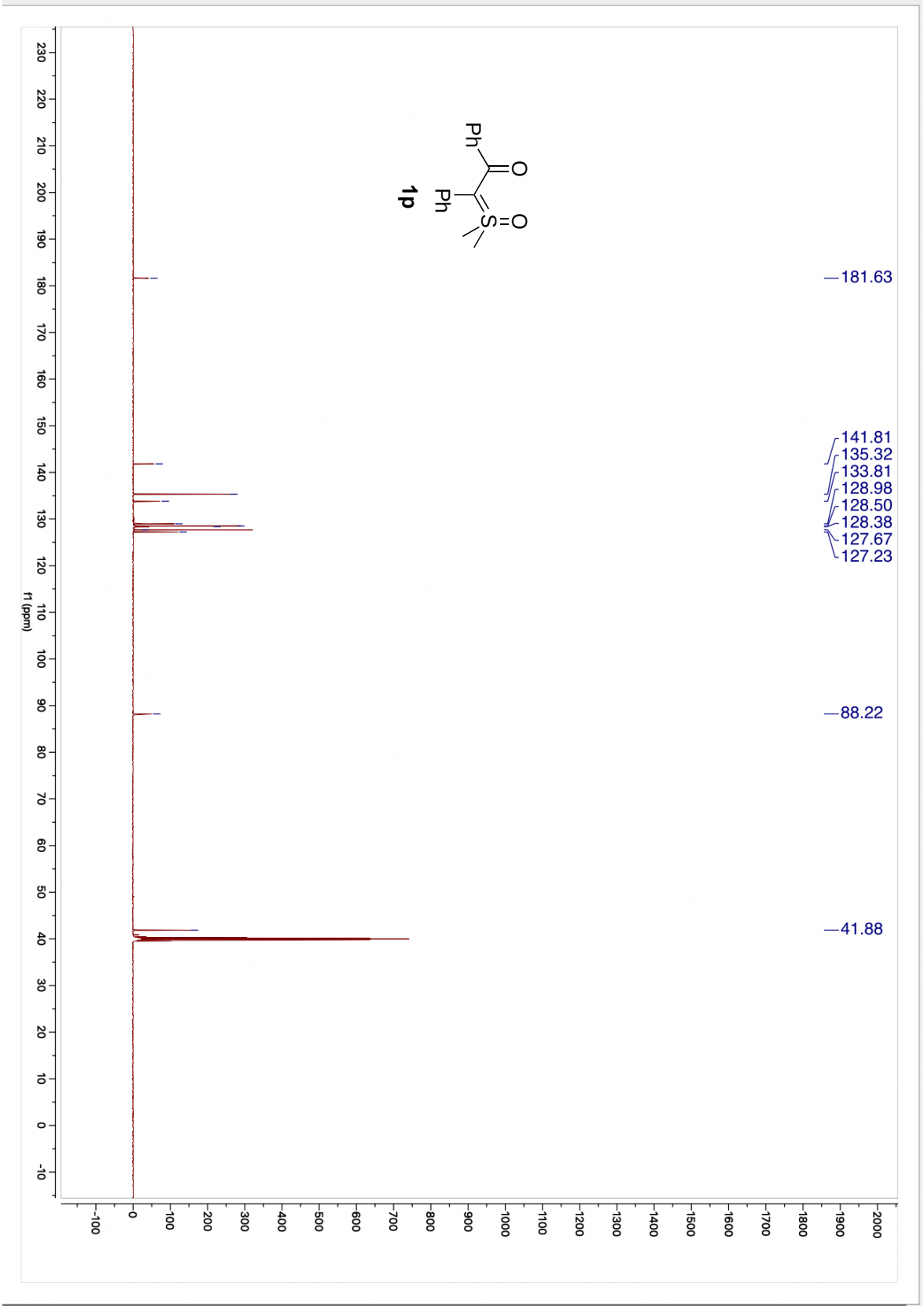

Figure S36: ^{13}C NMR spectrum of **1p** in d_6-DMSO (151 MHz)

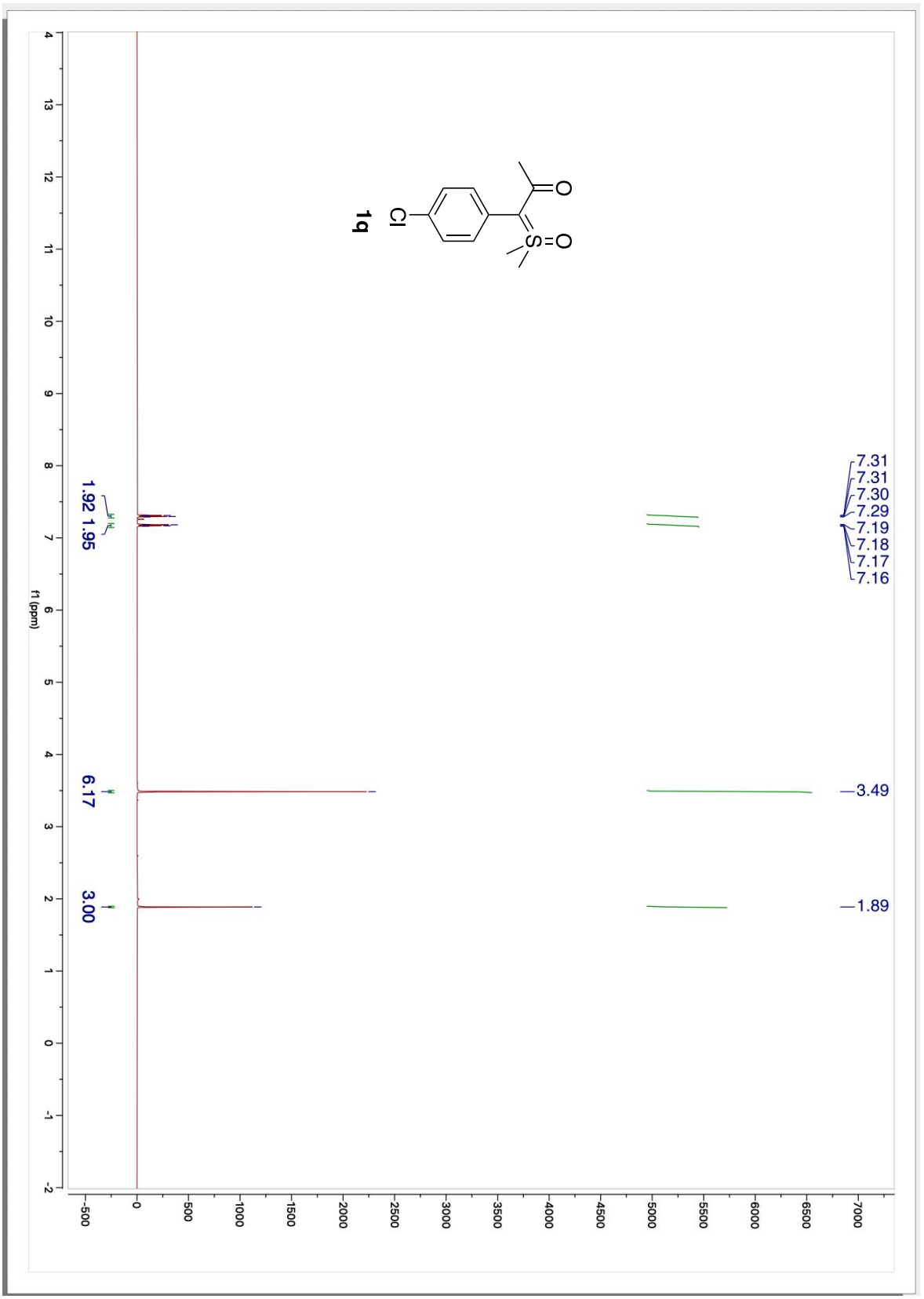

Figure S37: ^{1}H NMR spectrum of **1q** in $CDCl_3$ (600 MHz)

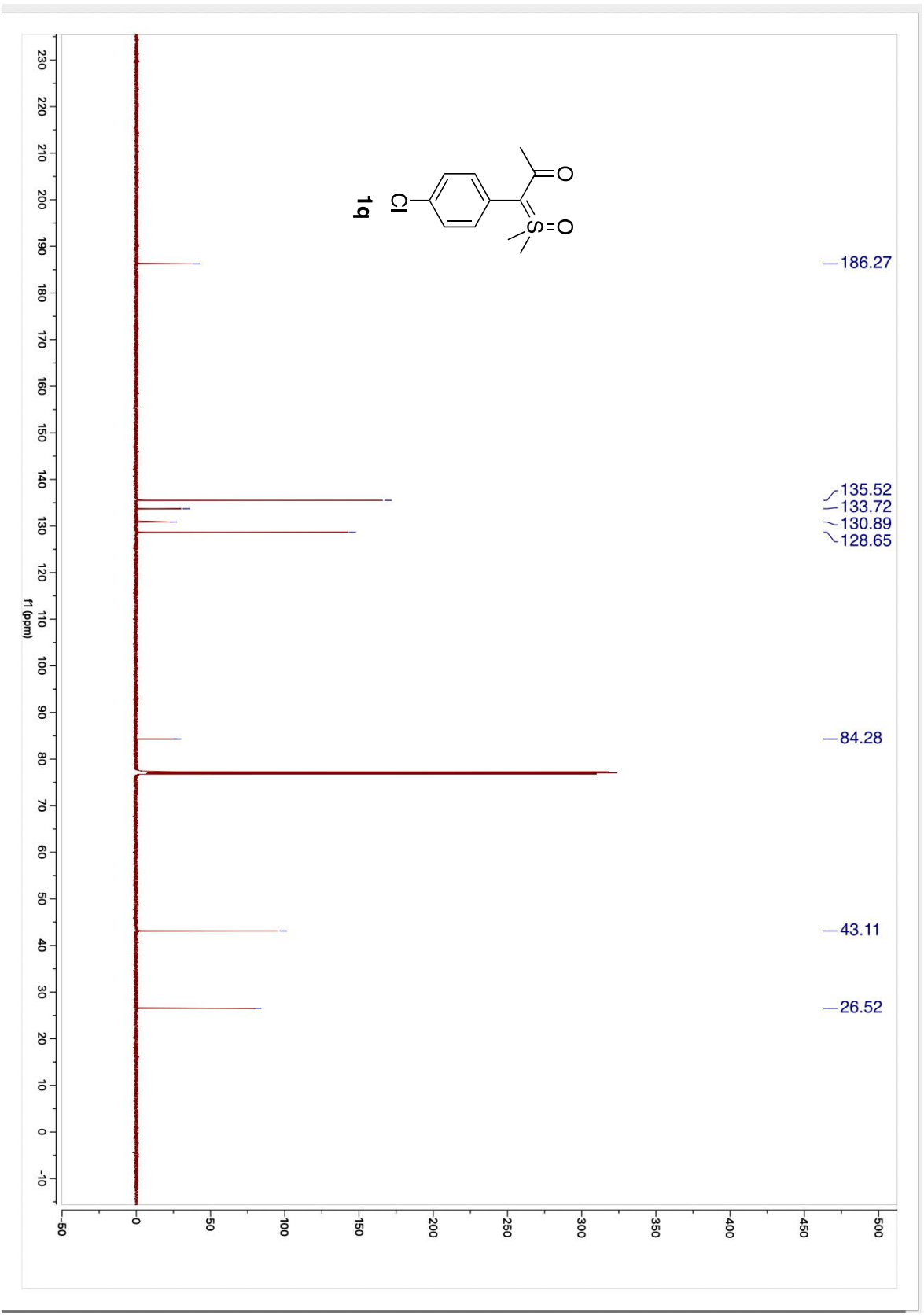

Figure S38: ^{13}C NMR spectrum of **1q** in $CDCl_3$ (151 MHz)

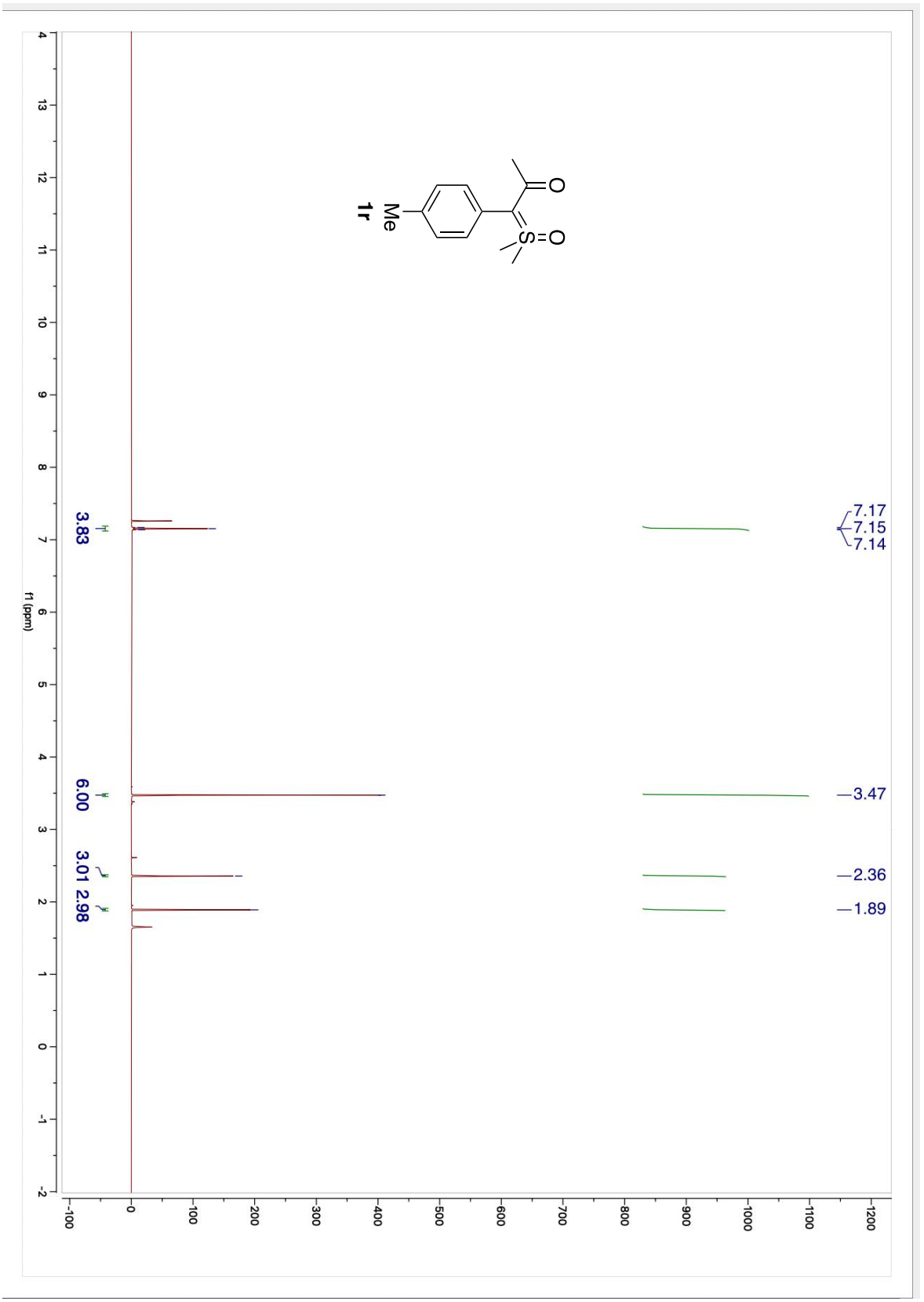

Figure S39: ^{1}H NMR spectrum of **1r** in $CDCl_3$ (600 MHz)

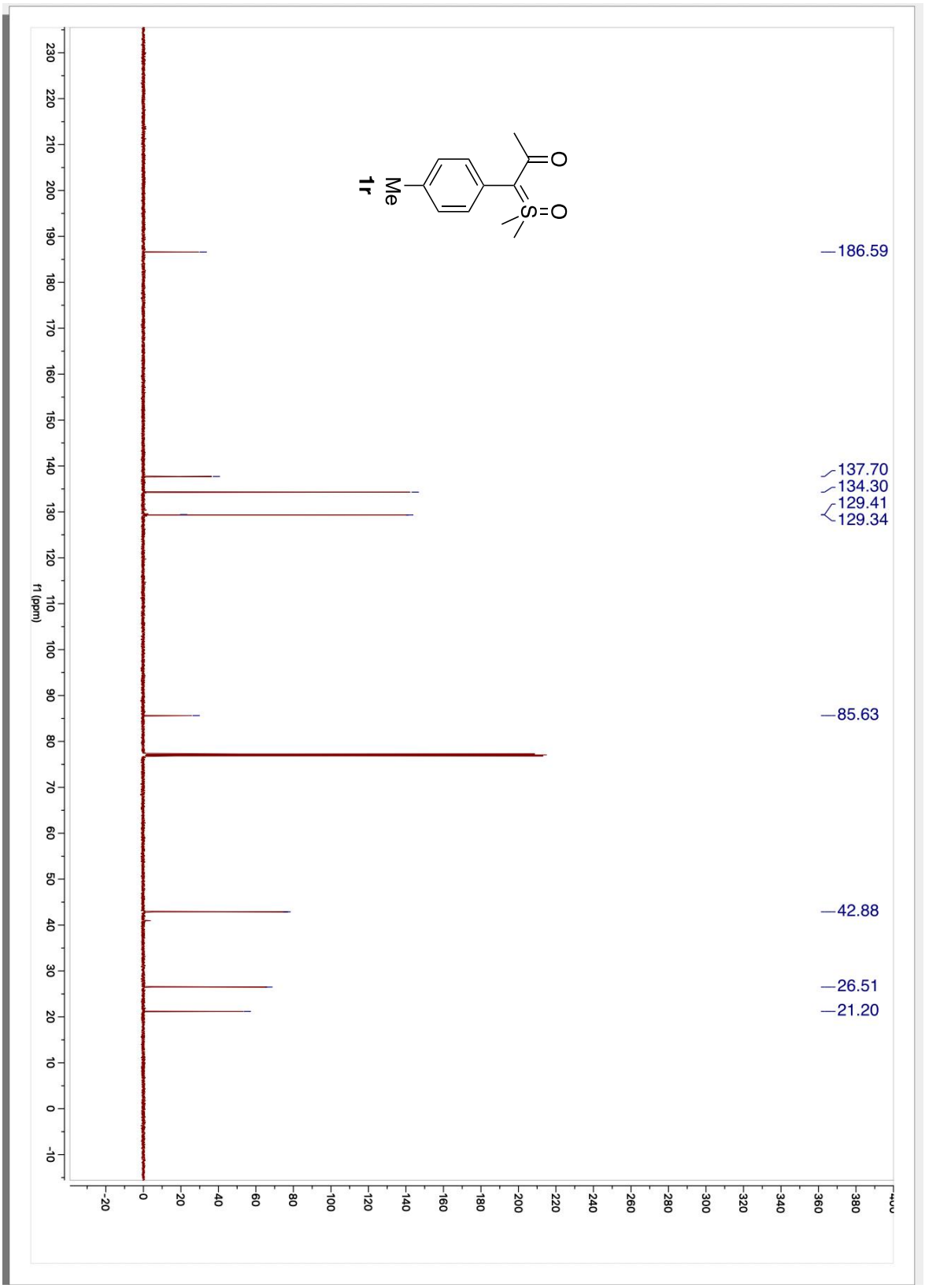

Figure S40: ^{13}C NMR spectrum of **1r** in $CDCl_3$ (151 MHz)

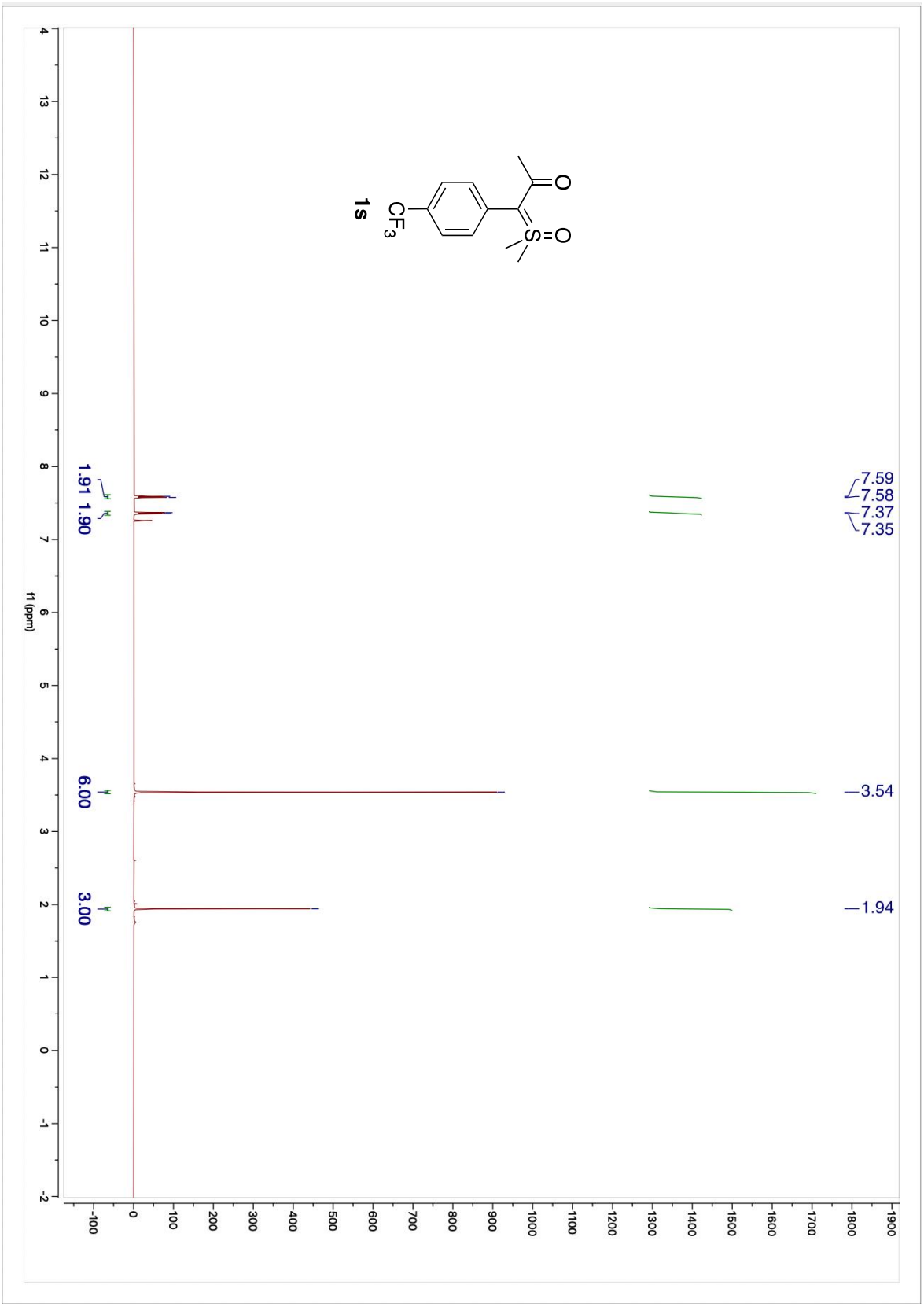

Figure S41: ^{1}H NMR spectrum of **1s** in $CDCl_3$ (600 MHz)

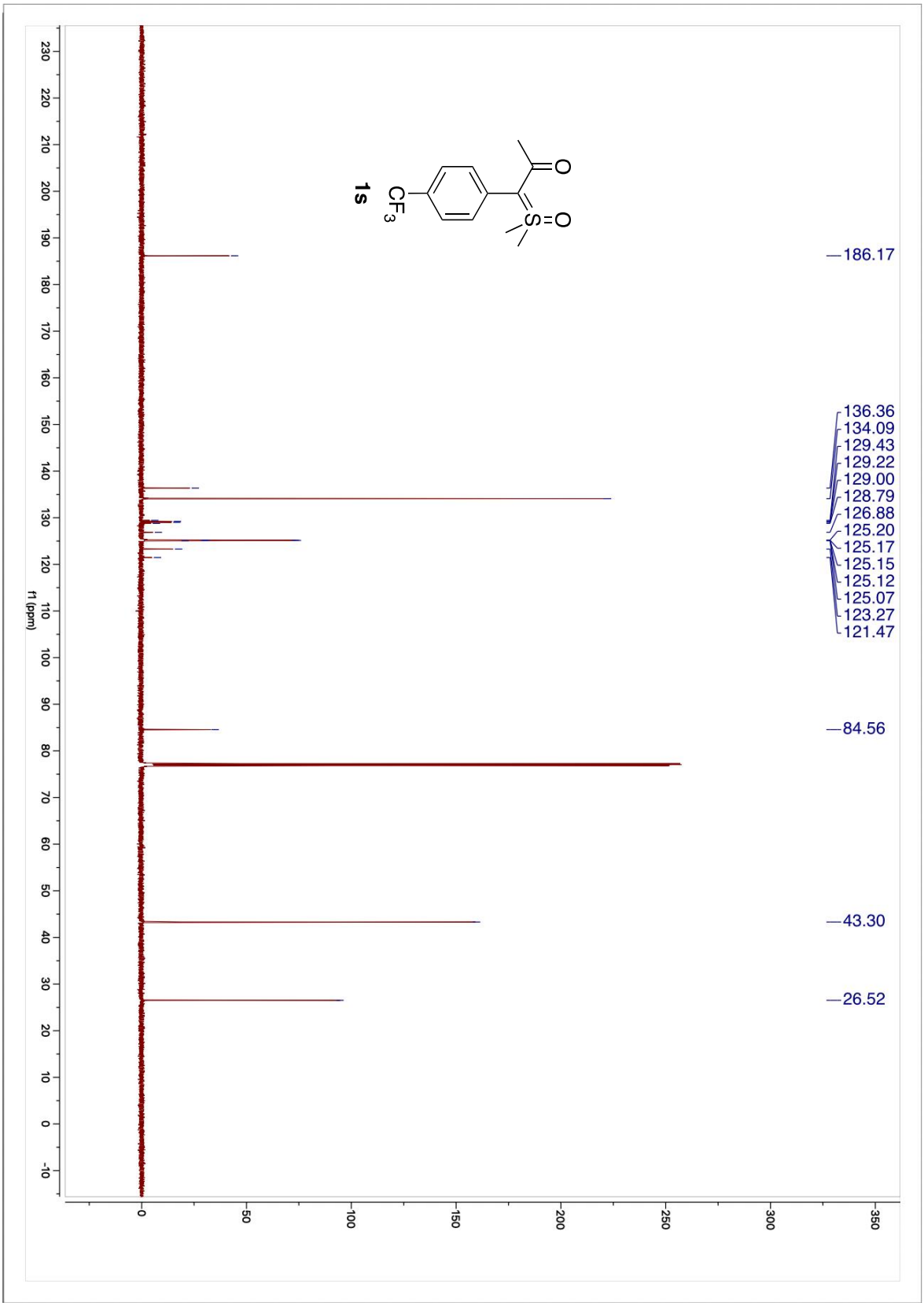

Figure S42: ^{13}C NMR spectrum of **1s** in $CDCl_3$ (151 MHz)

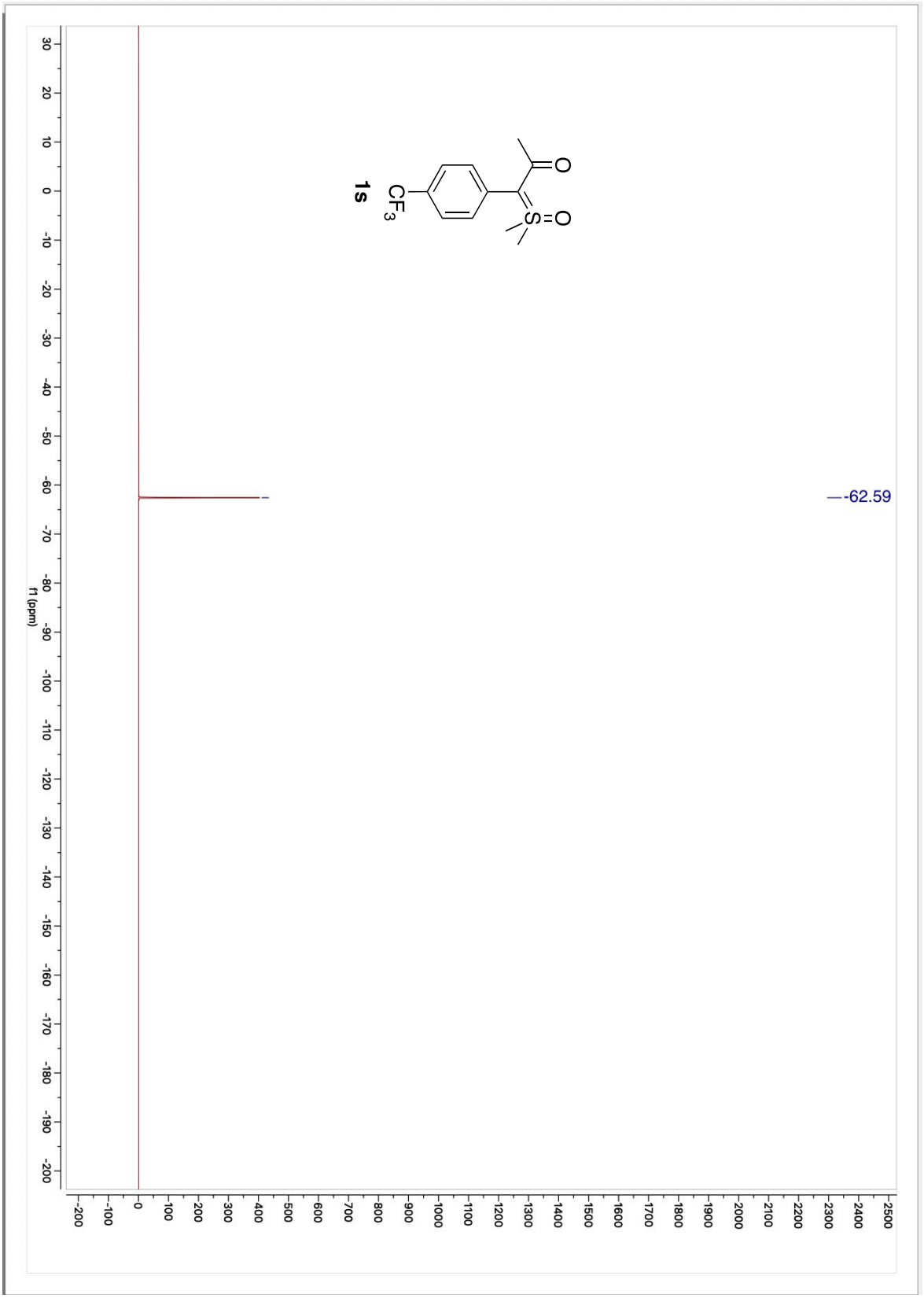

Figure S43: ^{19}F NMR spectrum of **1s** in $CDCl_3$ (376 MHz)

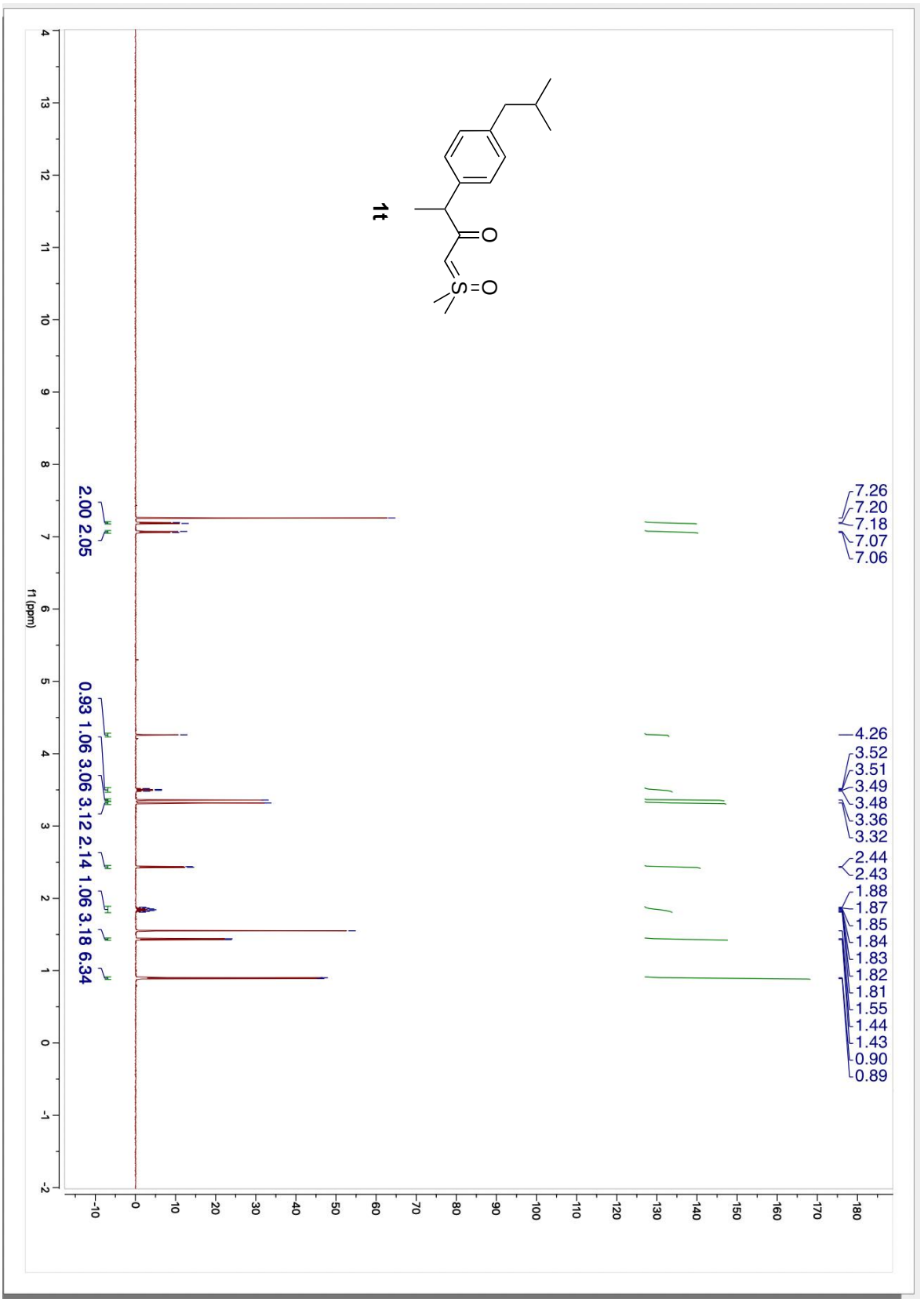

Figure S44: ^{1}H NMR spectrum of **1t** in $CDCl_3$ (600 MHz)

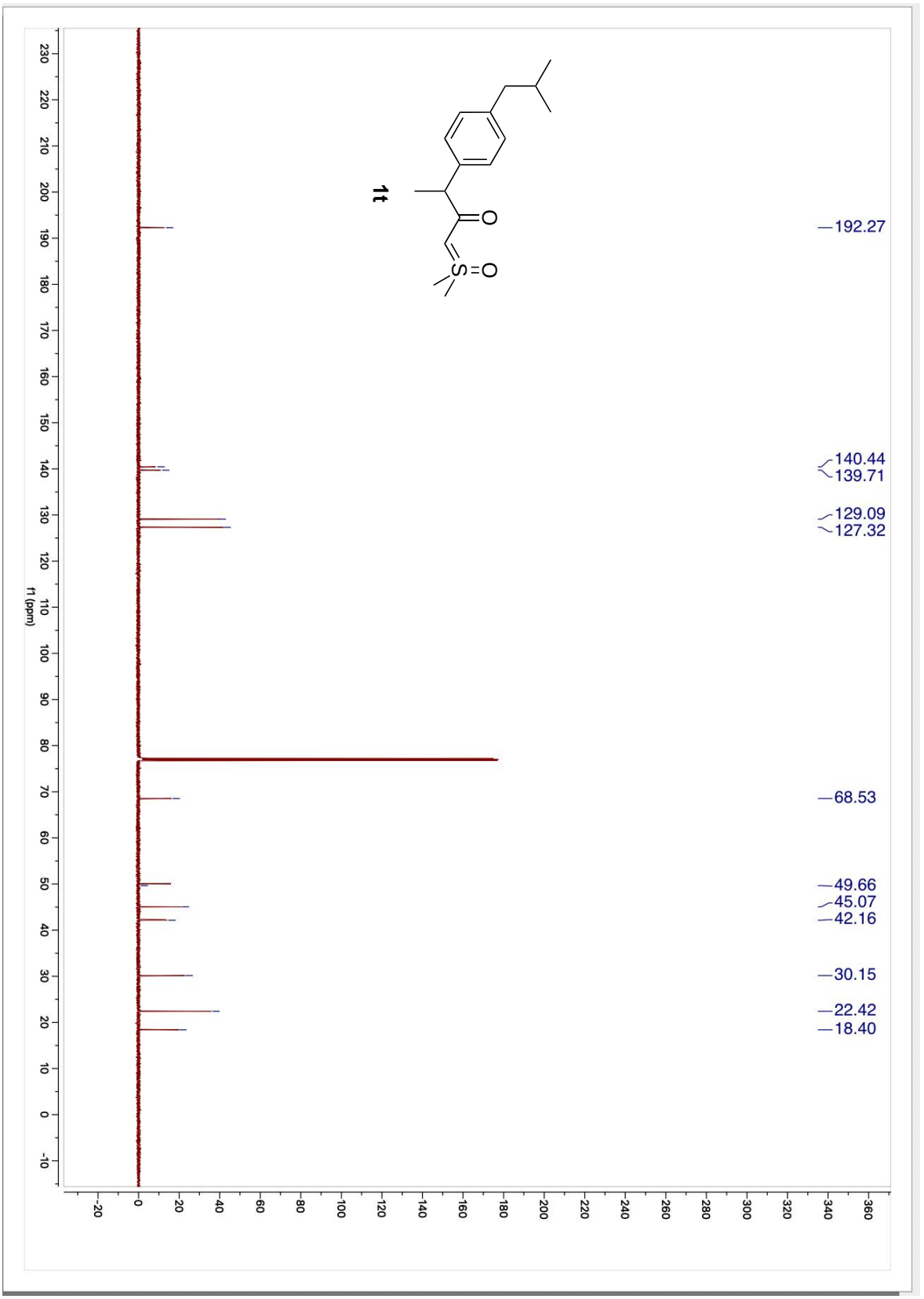

Figure S45: ^{13}C NMR spectrum of **1t** in $CDCl_3$ (151 MHz)

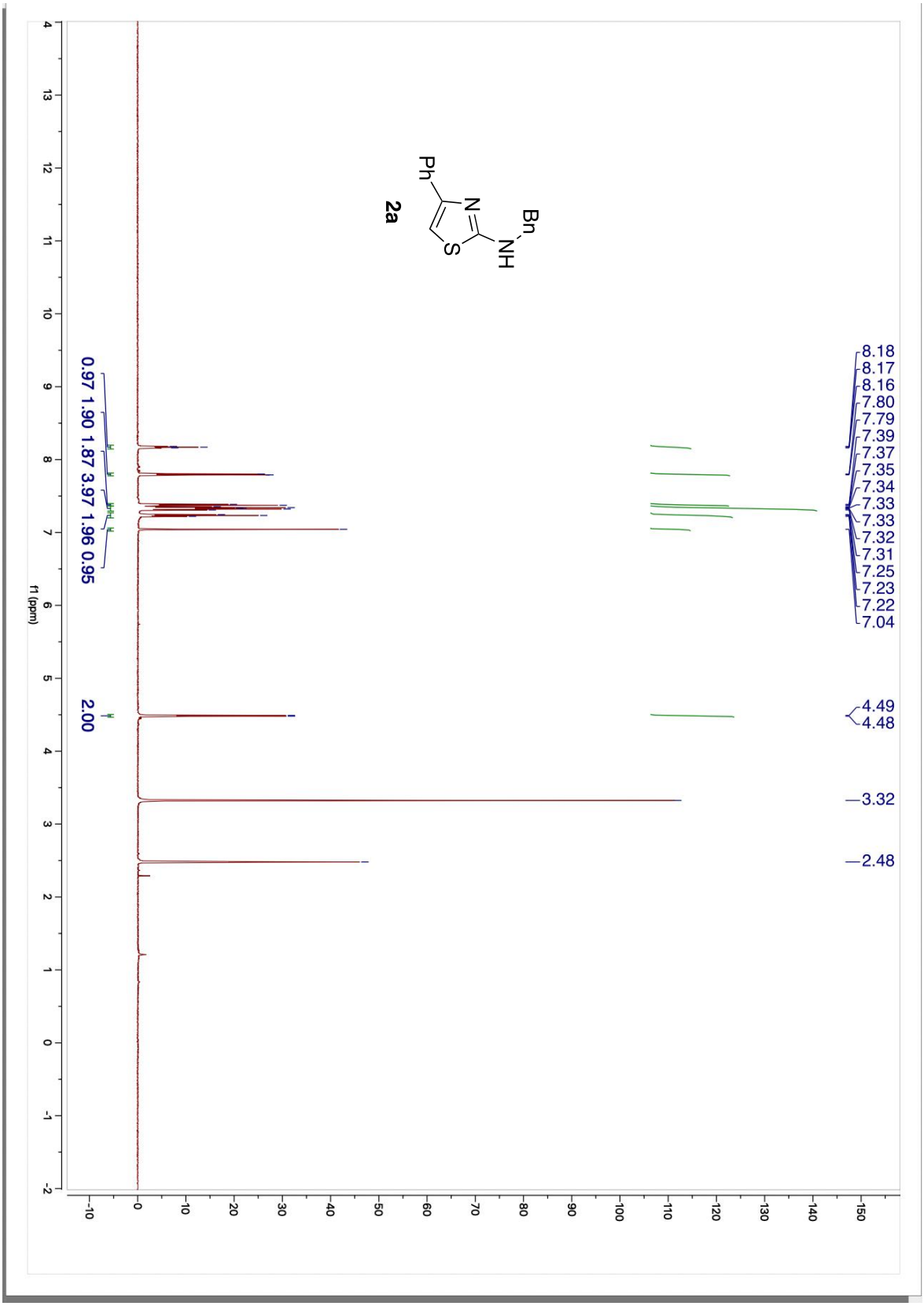

Figure S46: ^{1}H NMR spectrum of **2a** in d_6-DMSO (600 MHz)

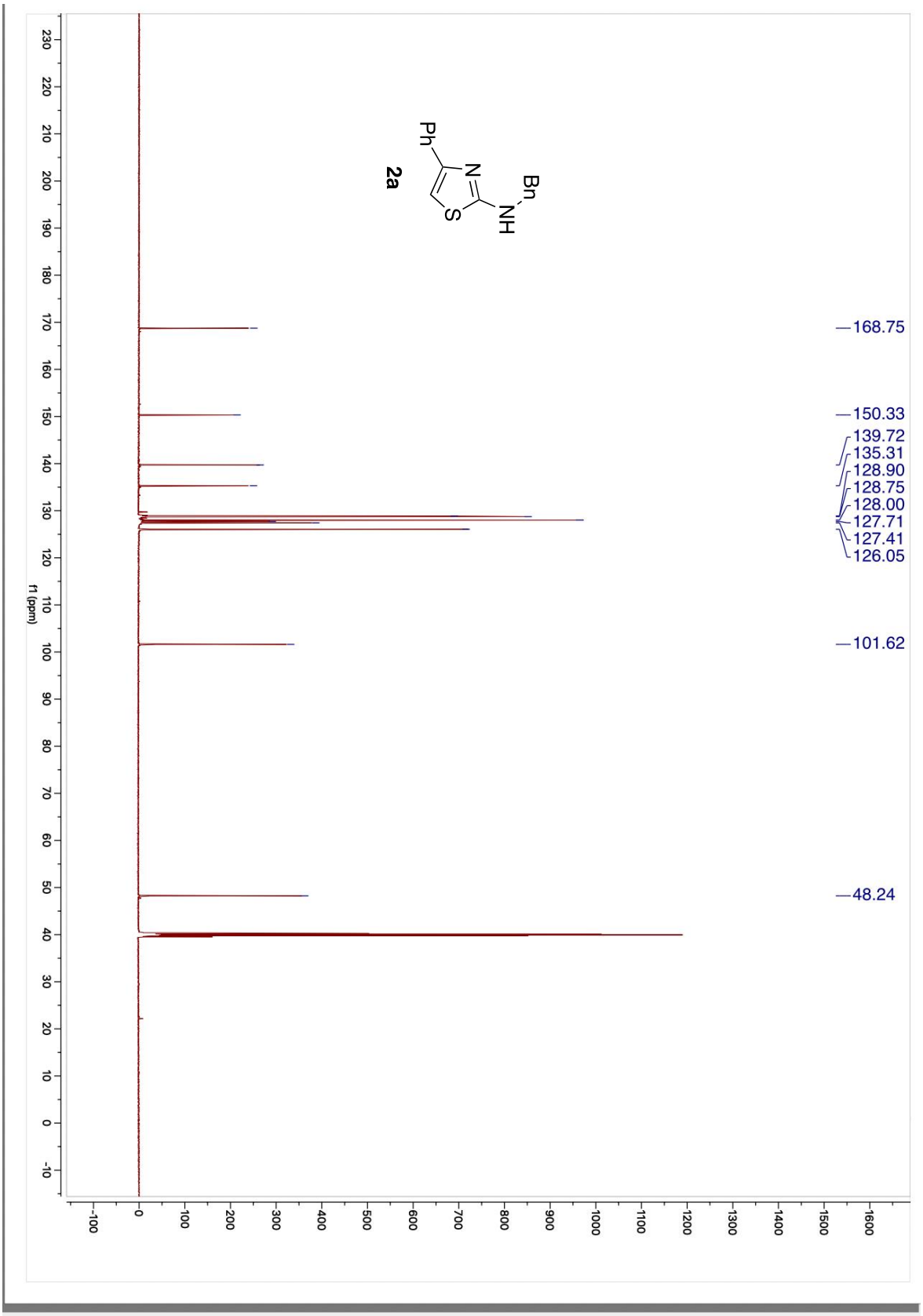

Figure S47: ^{13}C NMR spectrum of **2a** in d_6-DMSO (151 MHz)

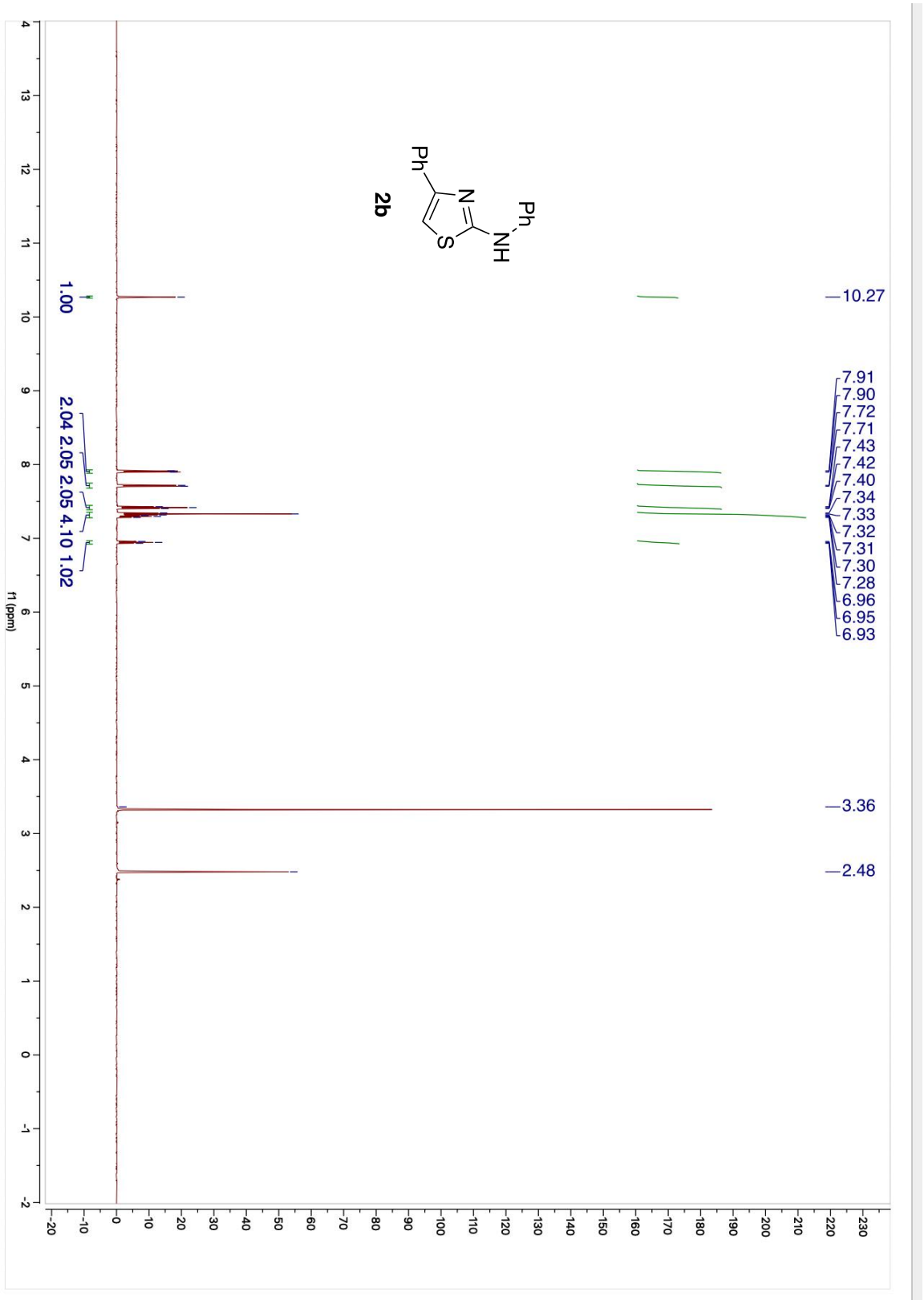

Figure S48: ^{1}H NMR spectrum of **2b** in d_6-DMSO (600 MHz)

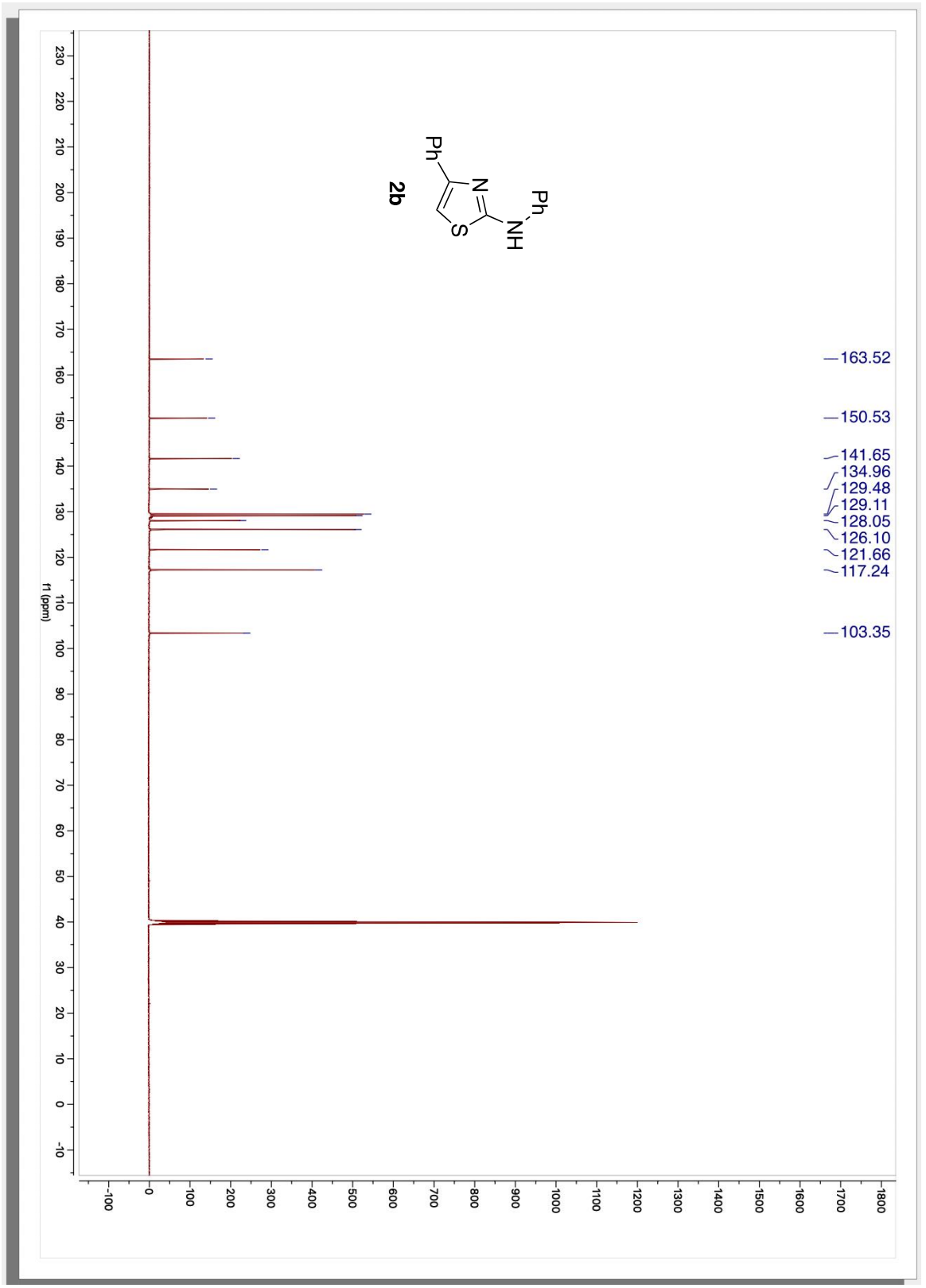

Figure S49: ^{13}C NMR spectrum of **2b** in d_6-DMSO (151 MHz)

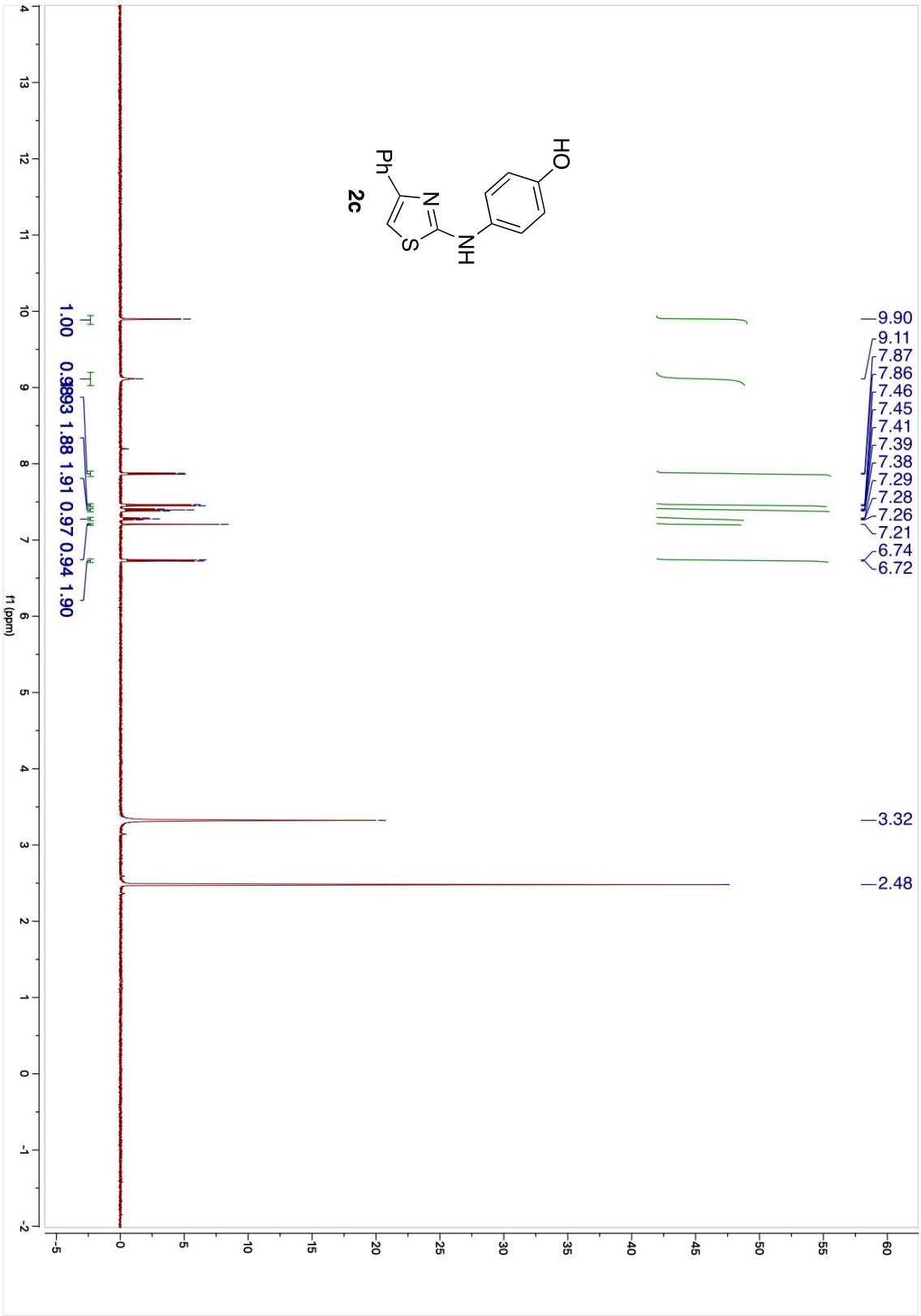

Figure S50: ^{1}H NMR spectrum of **2c** in d_6-DMSO (600 MHz)

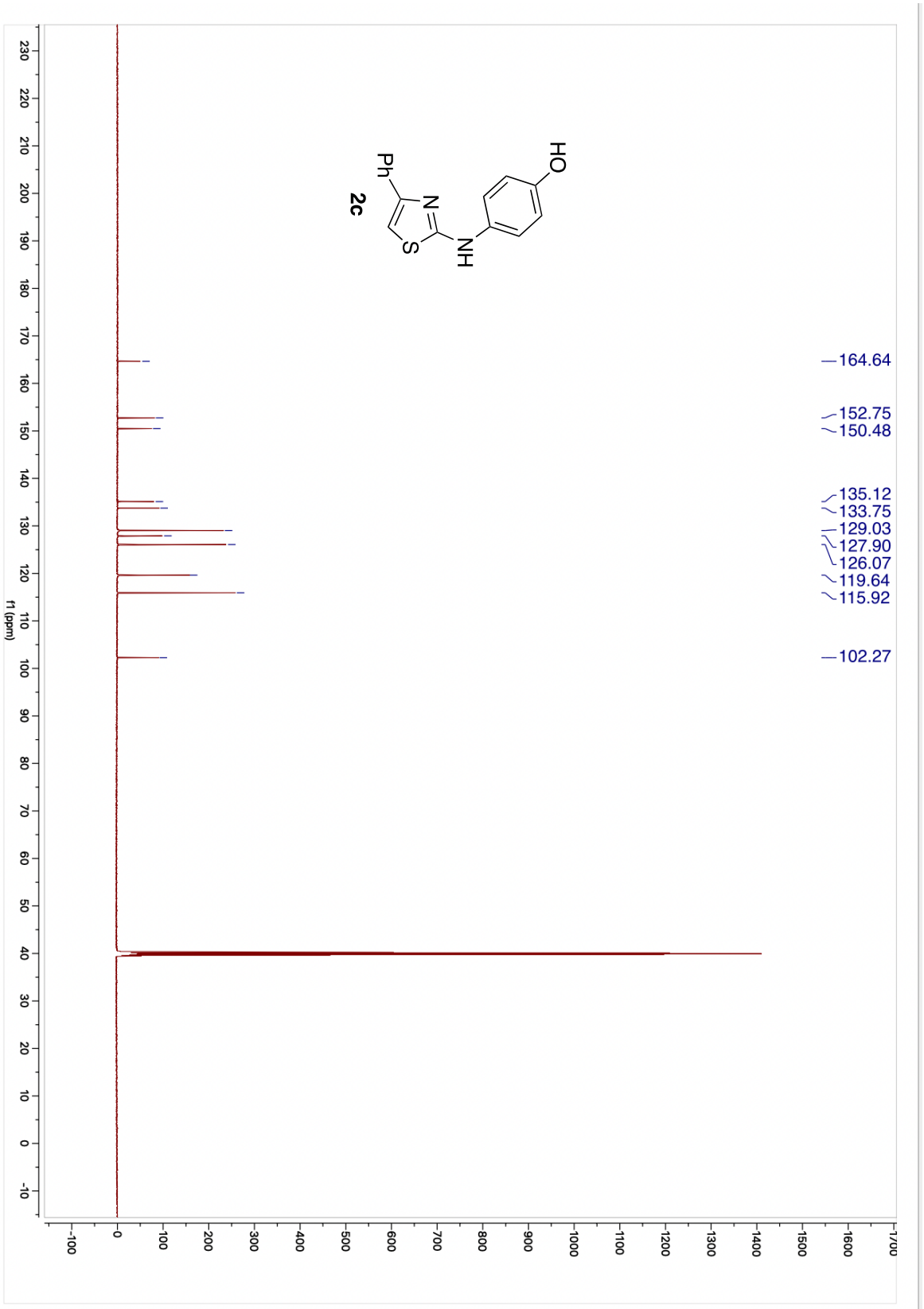

Figure S51: ^{13}C NMR spectrum of **2c** in d_6-DMSO (151 MHz)

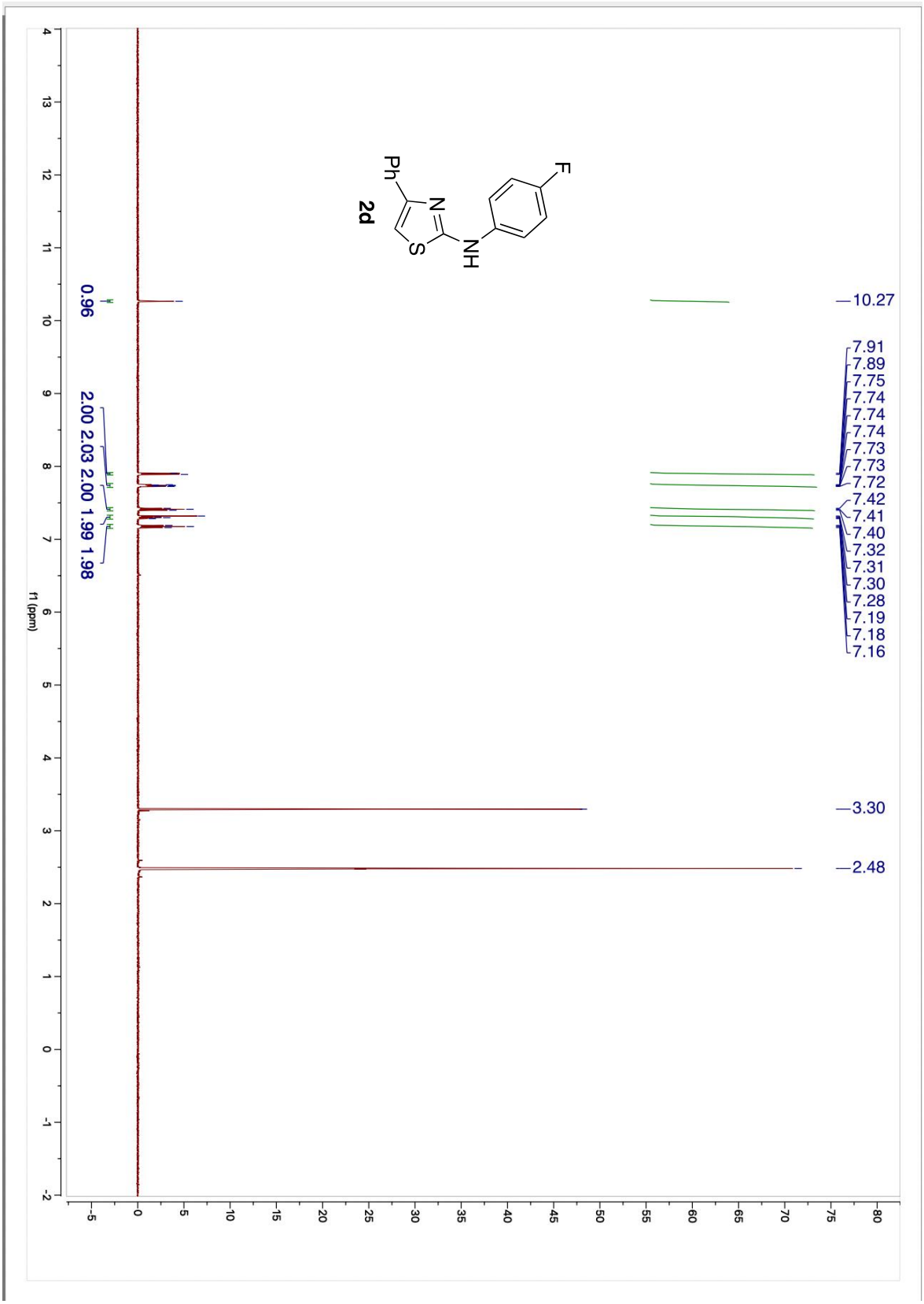

Figure S52: ^{1}H NMR spectrum of **2d** in d_6-DMSO (600 MHz)

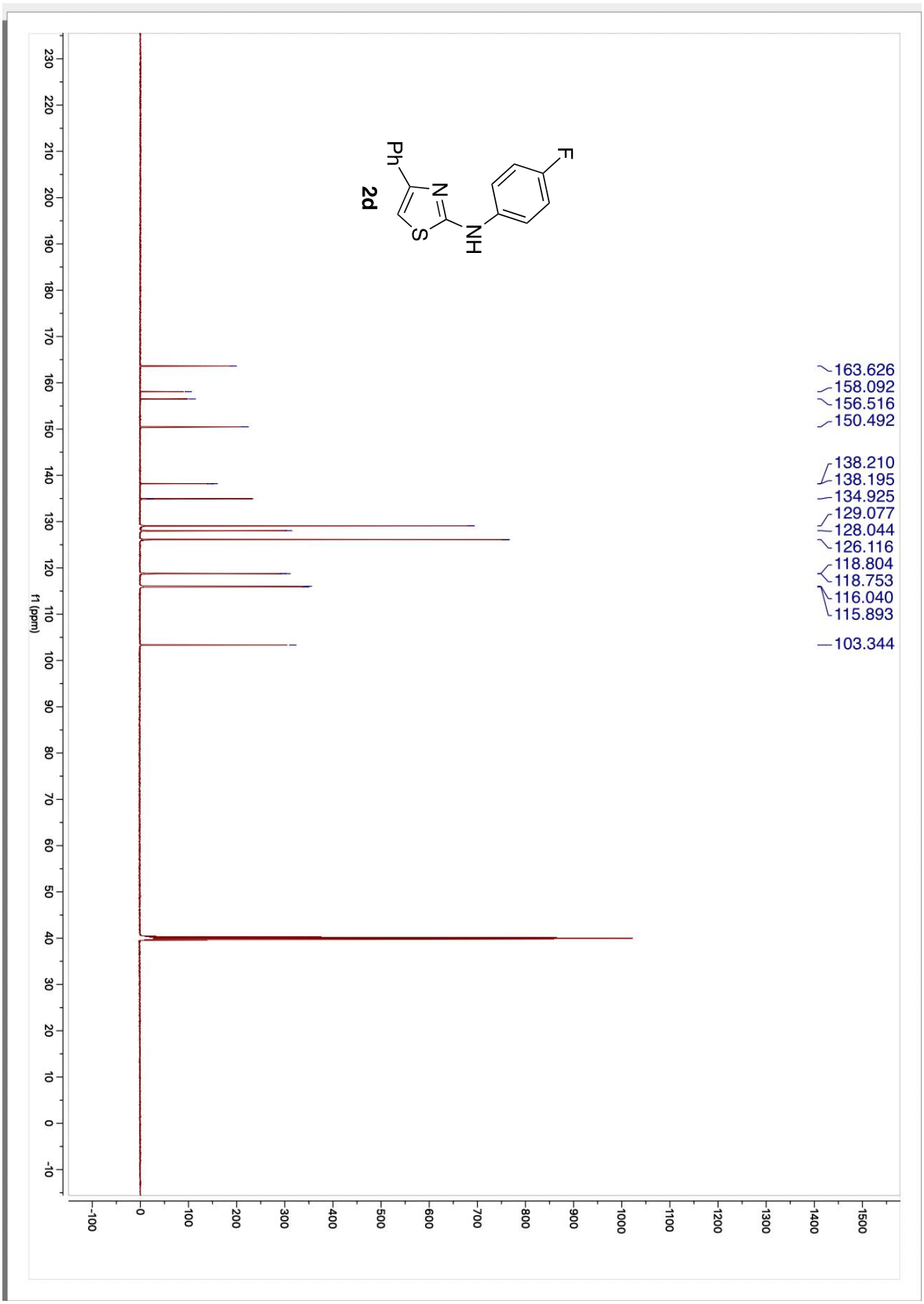

Figure S53: ^{13}C NMR spectrum of **2d** in d_6-DMSO (151 MHz)

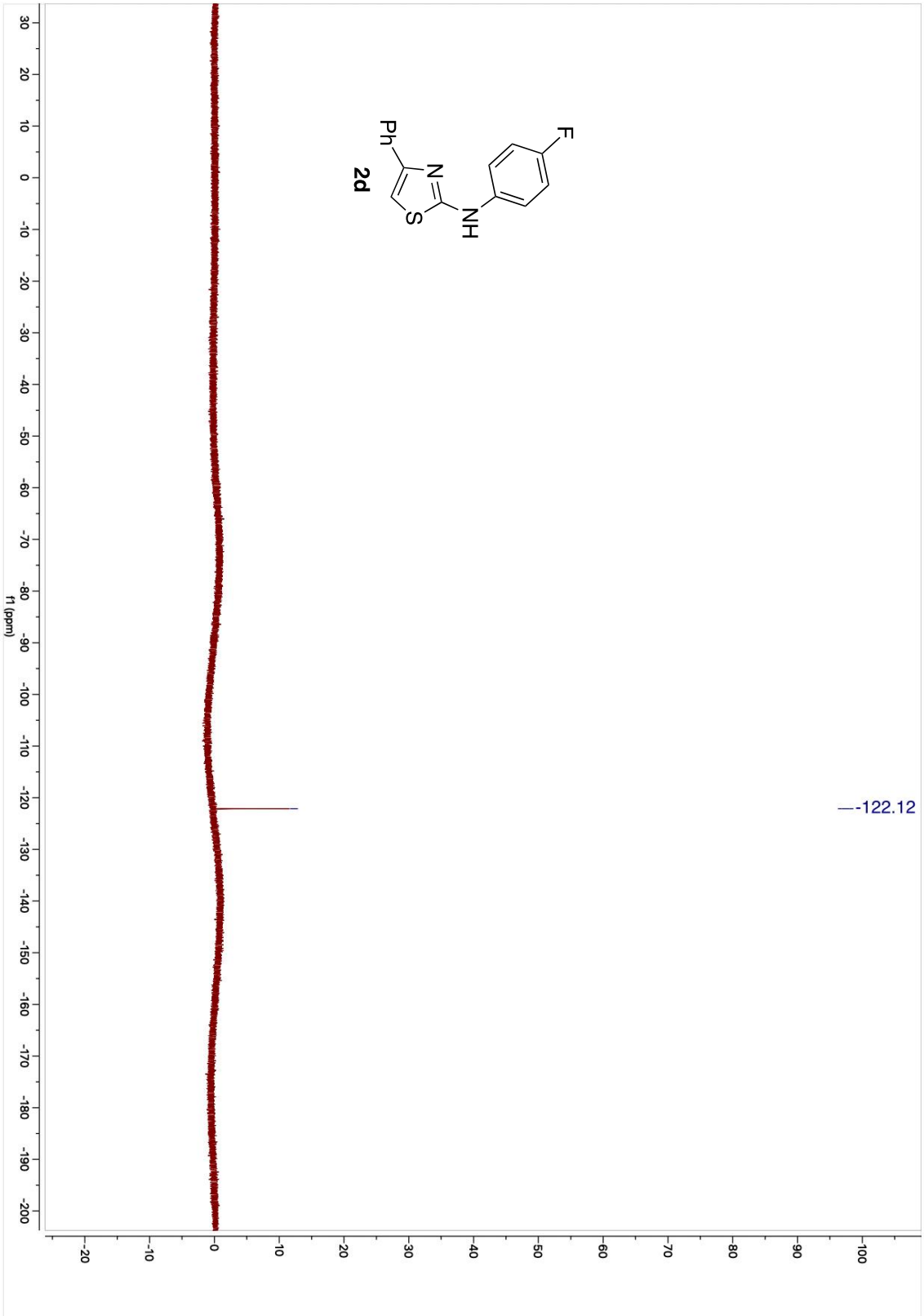

Figure S54: ^{19}F NMR spectrum of **2d** in d_6-DMSO (376 MHz)

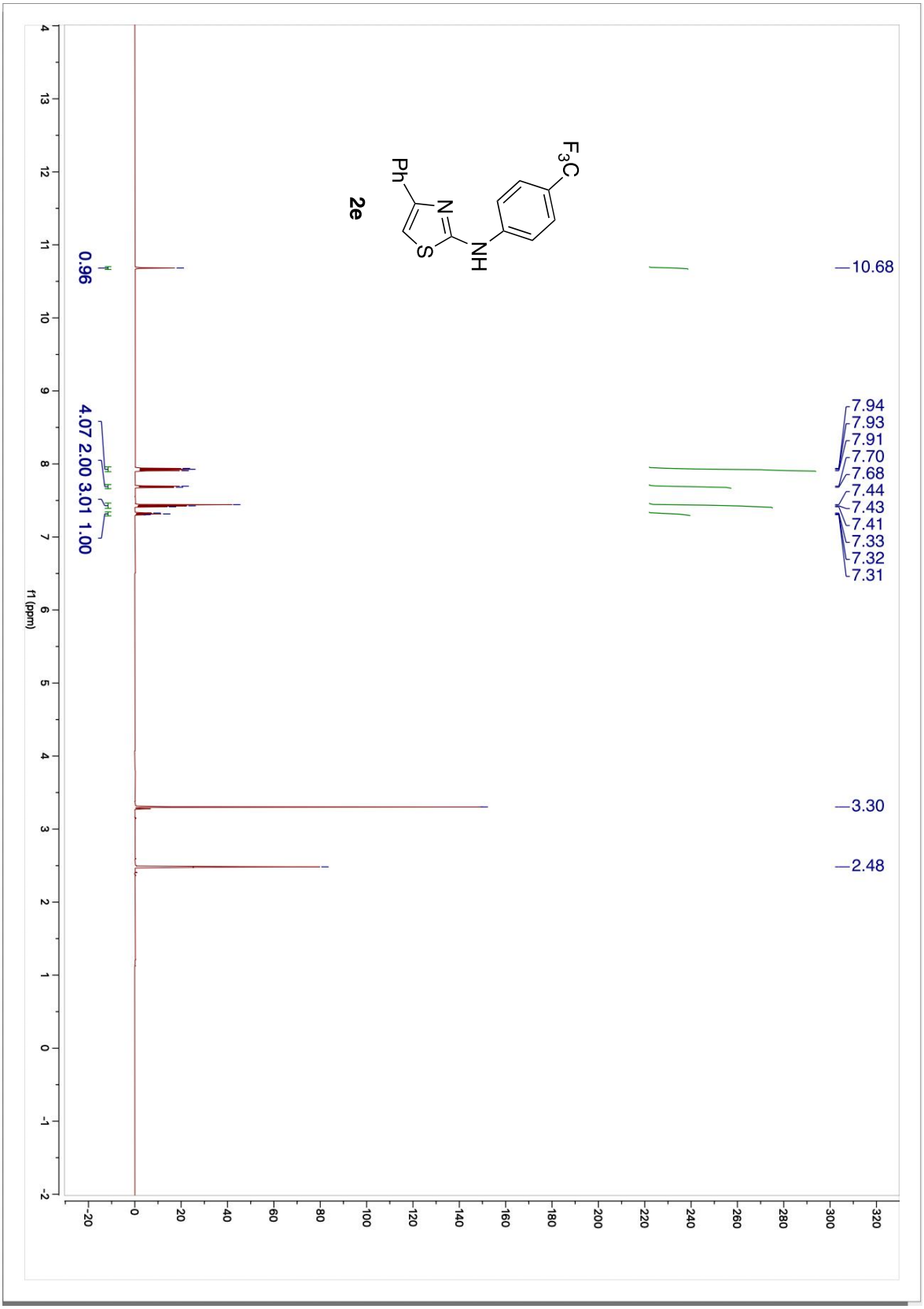

Figure S55: ^{1}H NMR spectrum of **2e** in d_6-DMSO (600 MHz)

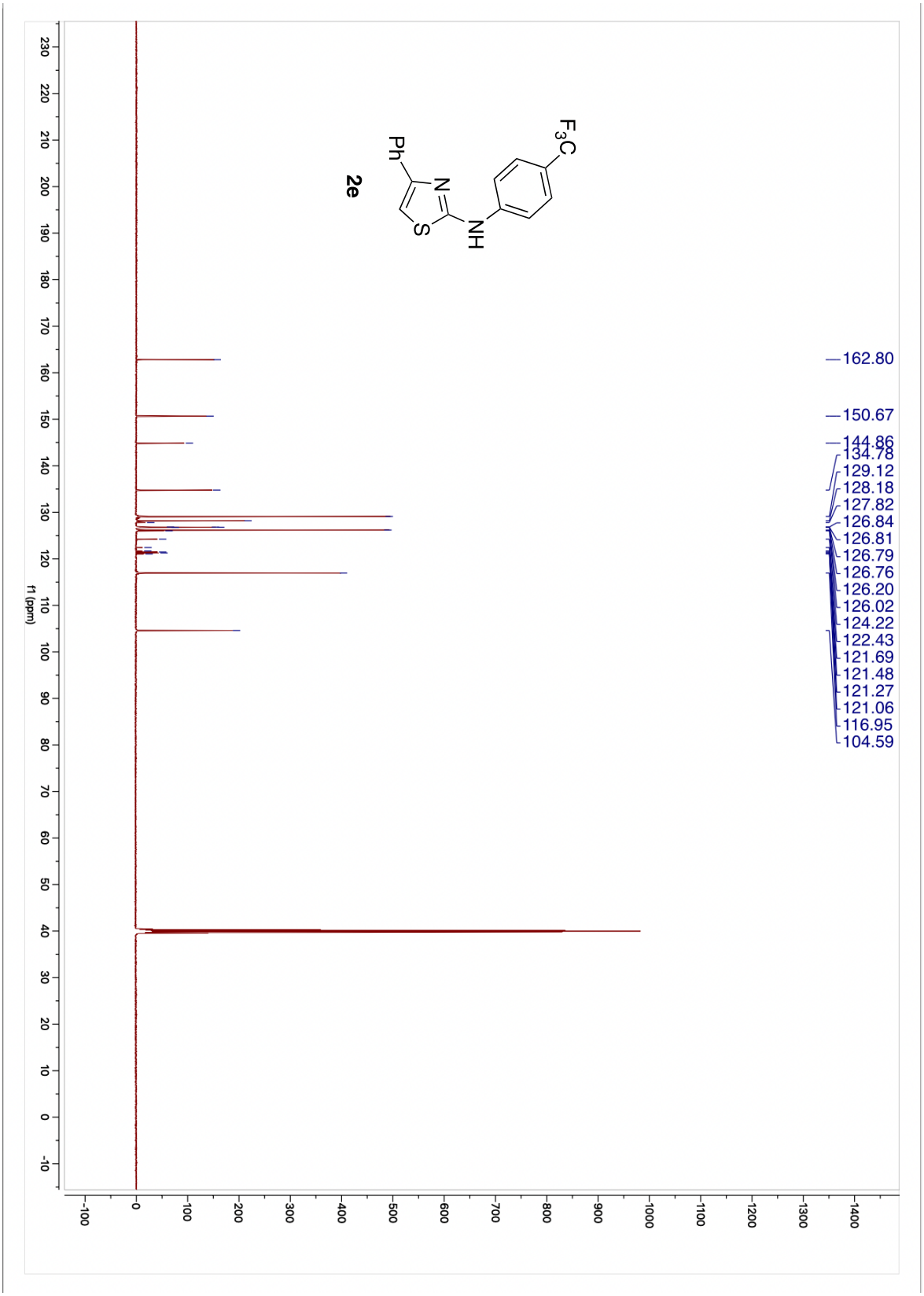

Figure S56: ^{13}C NMR spectrum of **2e** in d_6-DMSO (151 MHz)

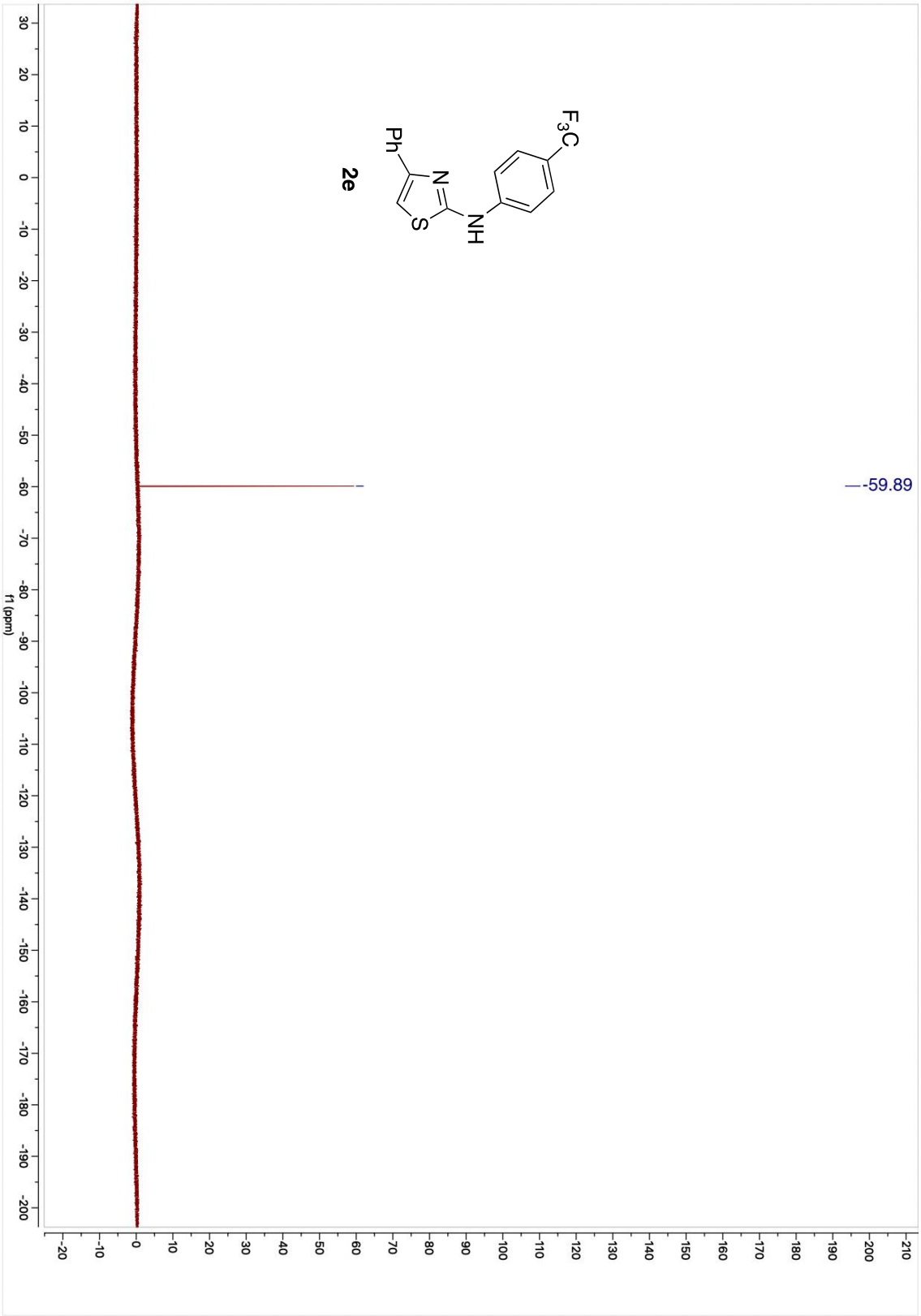

Figure S57: ^{19}F NMR spectrum of **2e** in d_6-DMSO (376 MHz)

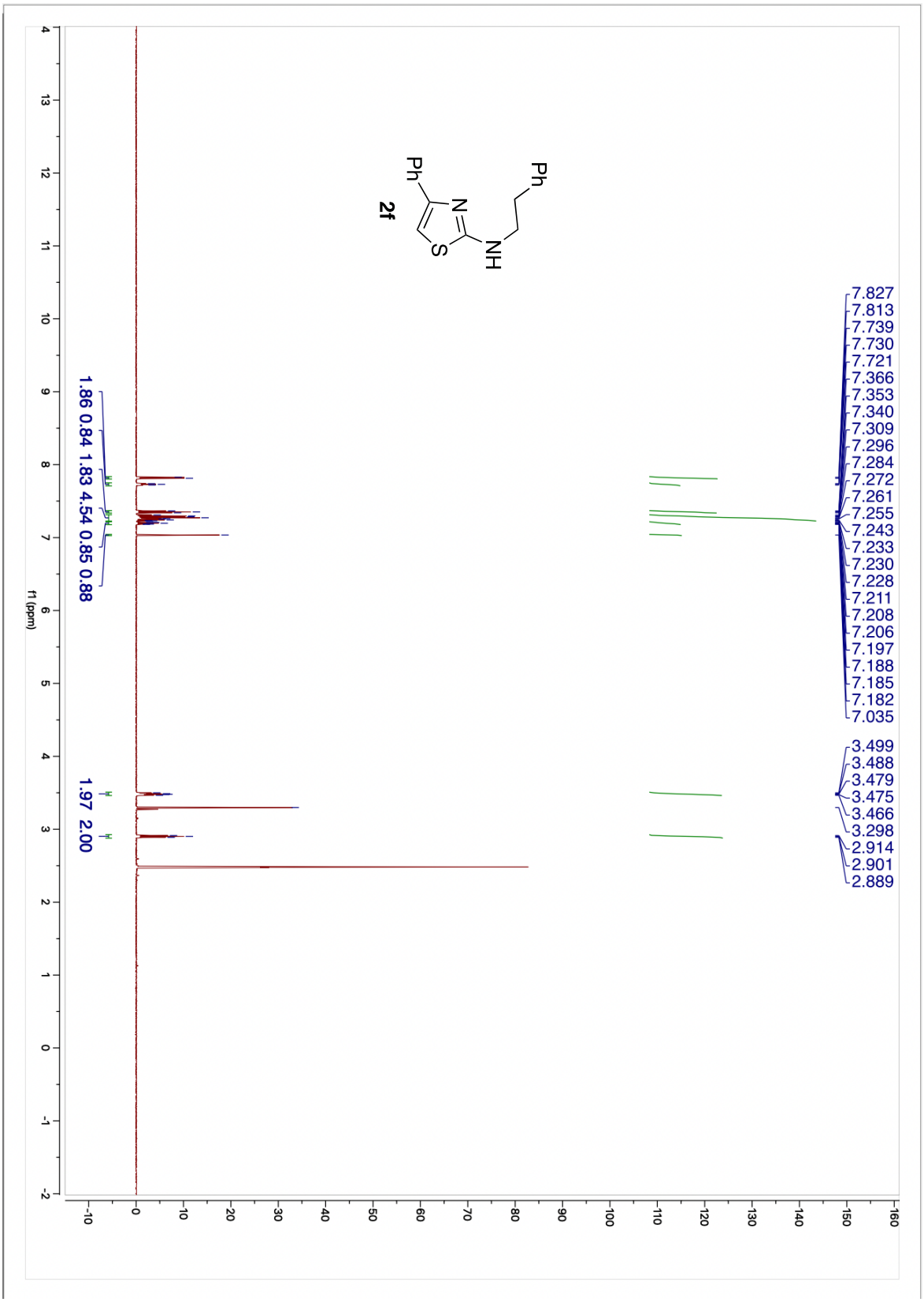

Figure S58: ^{1}H NMR spectrum of **2f** in d_6-DMSO (600 MHz)

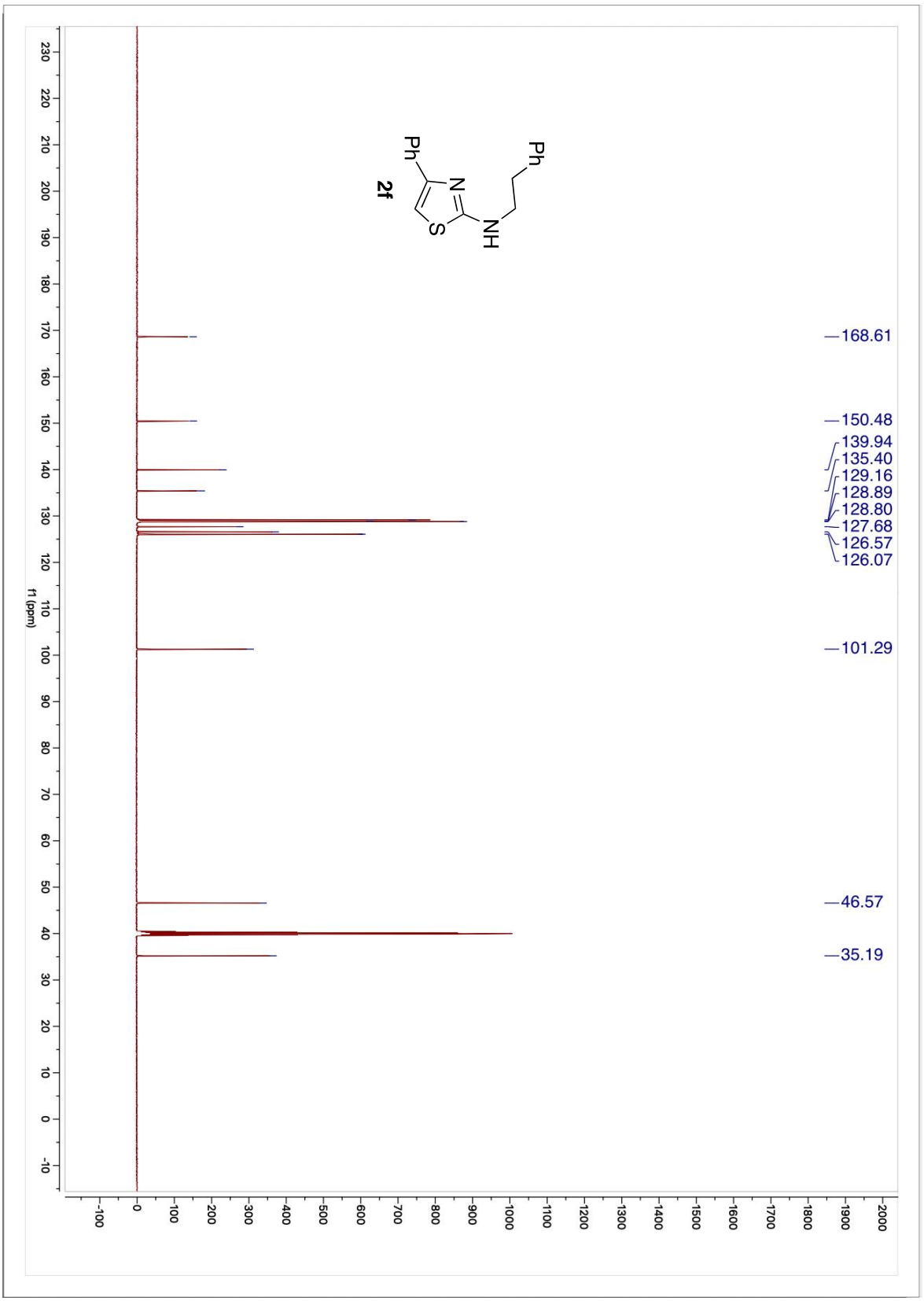

Figure S59: ^{13}C NMR spectrum of **2f** in d_6-DMSO (151 MHz)

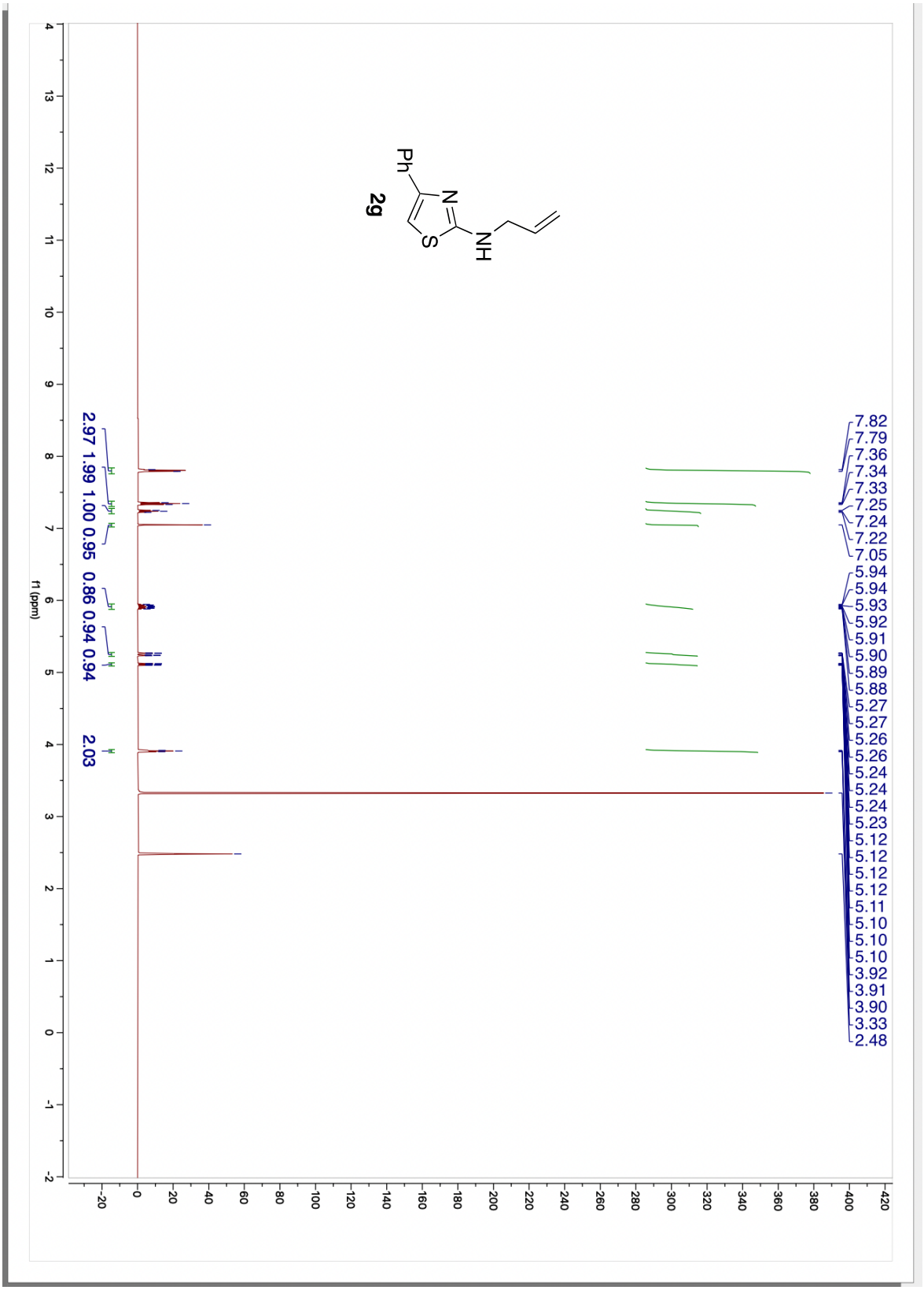

Figure S60: ^{1}H NMR spectrum of **2g** in d_6-DMSO (600 MHz)

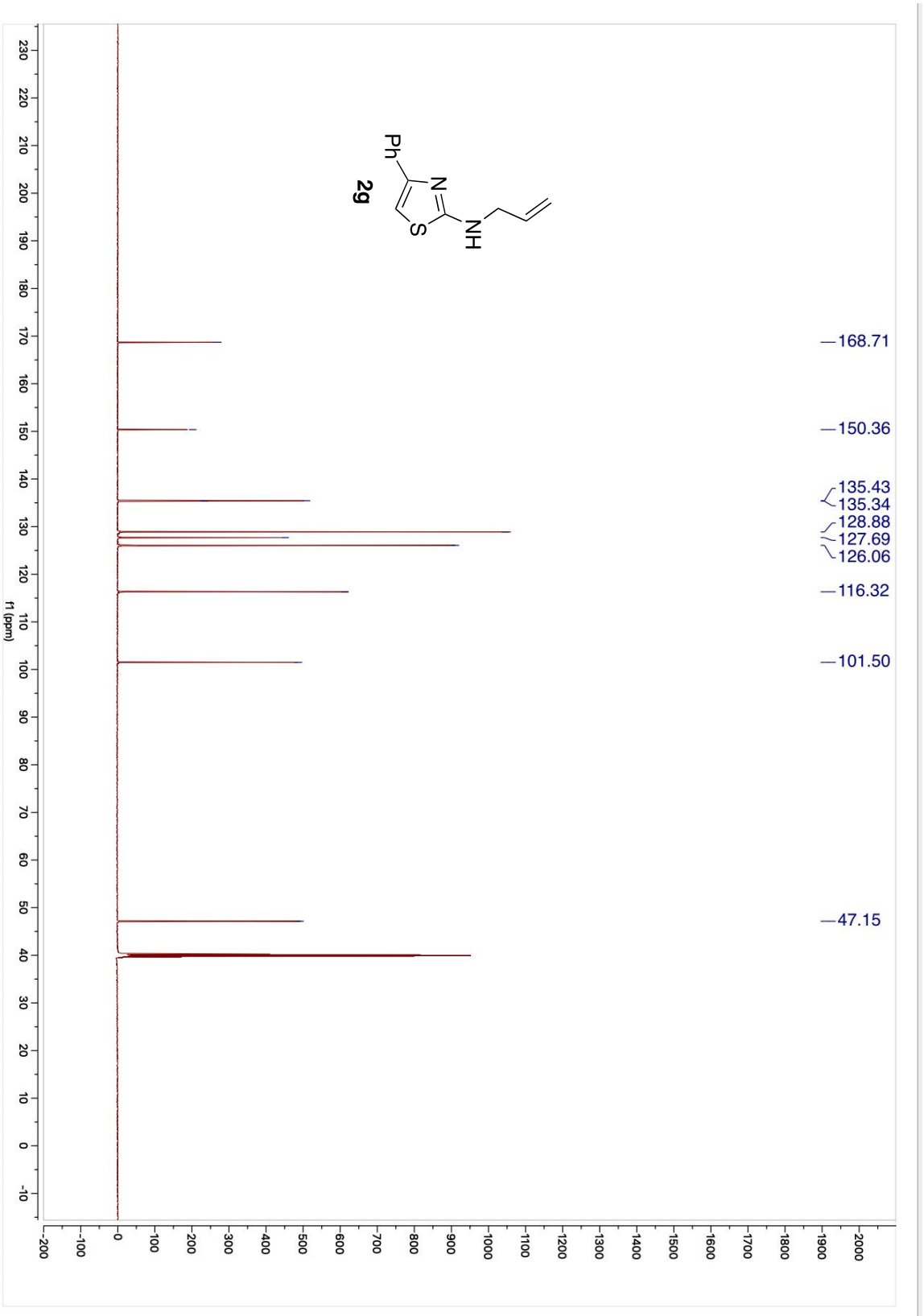

Figure S61: ^{13}C NMR spectrum of **2g** in d_6-DMSO (151 MHz)

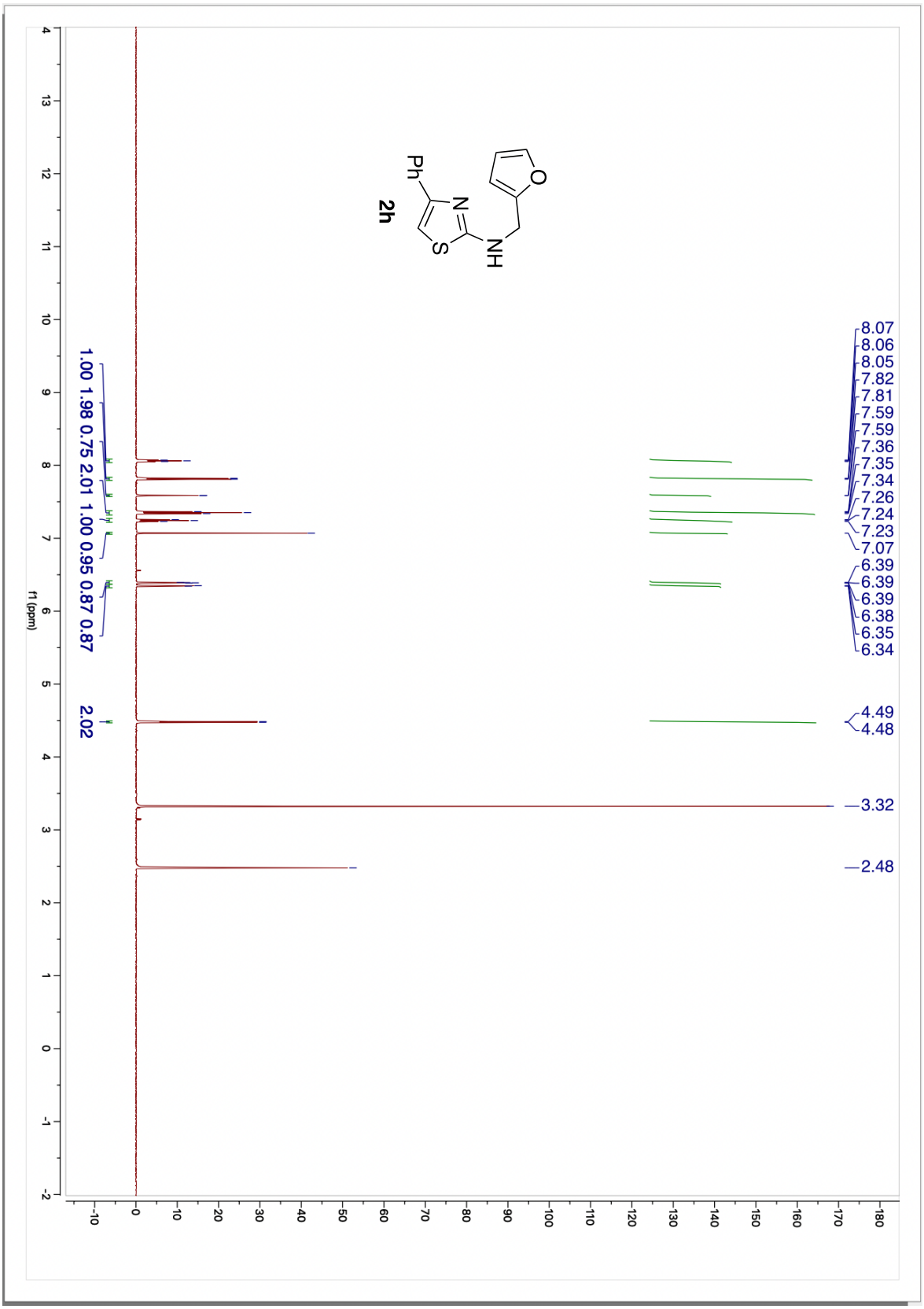

Figure S62: ^{1}H NMR spectrum of **2h** in d_6-DMSO (600 MHz)

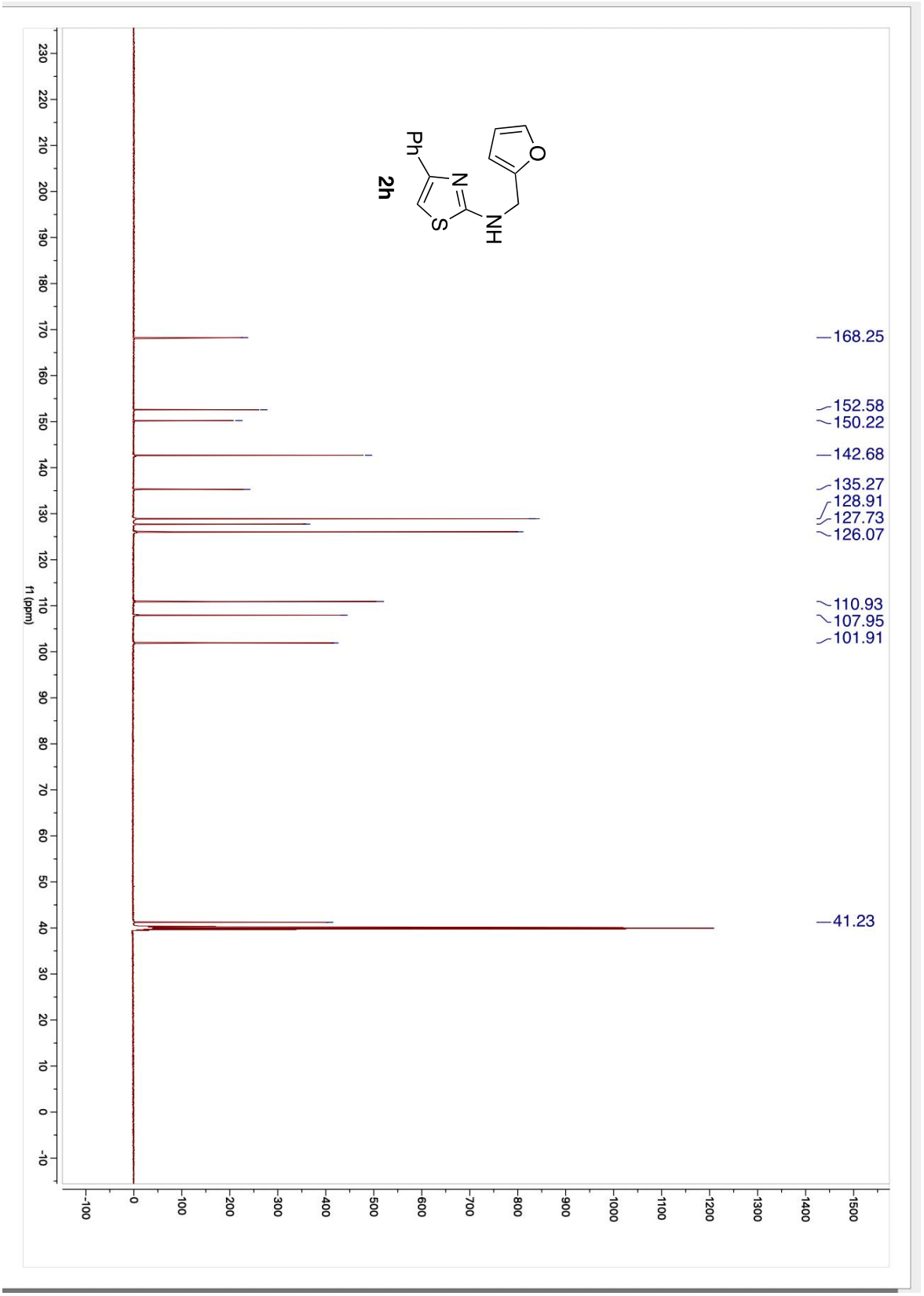

Figure S63: ^{13}C NMR spectrum of **2h** in d_6-DMSO (151 MHz)

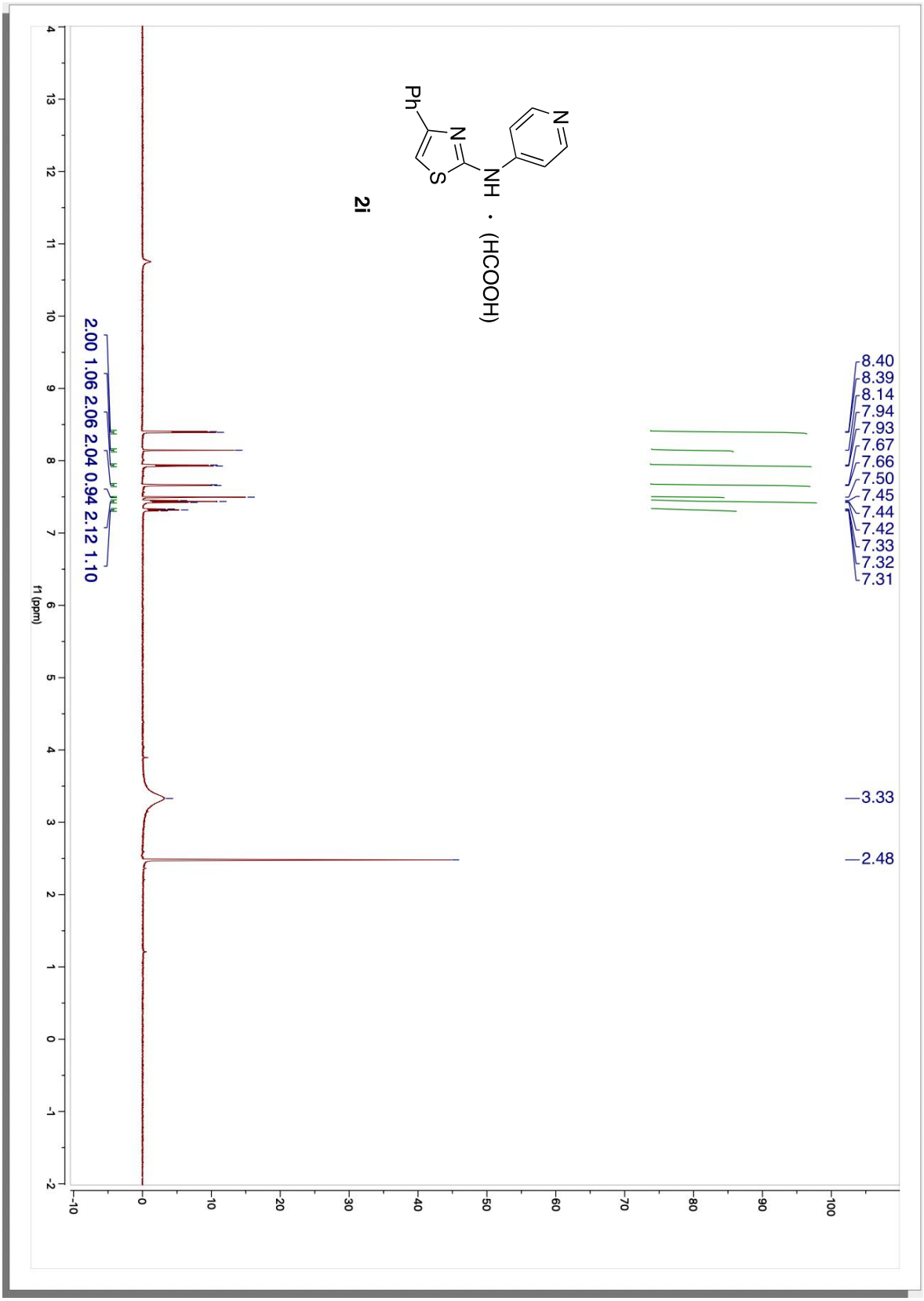

Figure S64: ^{1}H NMR spectrum of **2i** in d_6-DMSO (600 MHz)

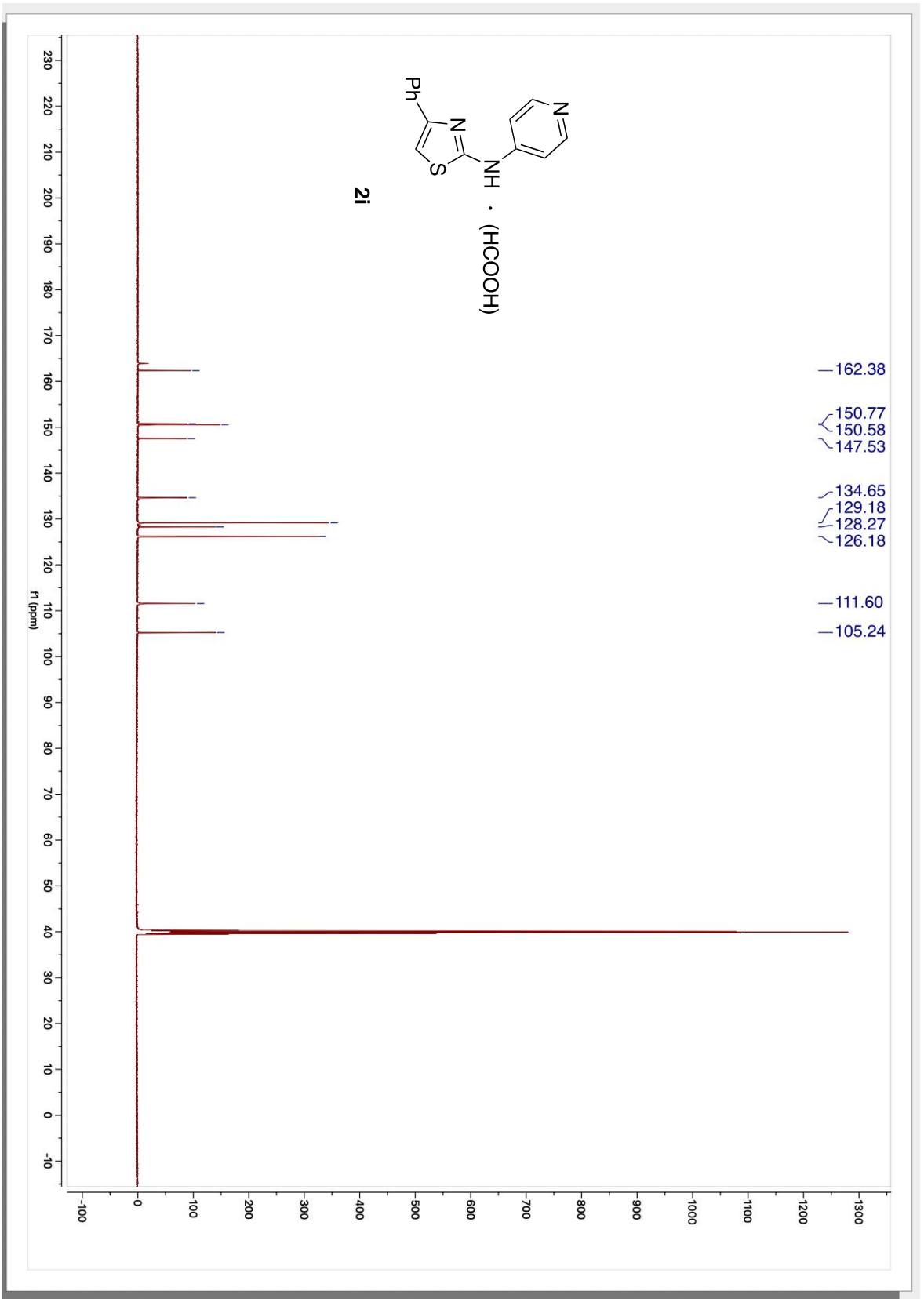

Figure S65: ^{13}C NMR spectrum of **2i** in d_6-DMSO (151 MHz)

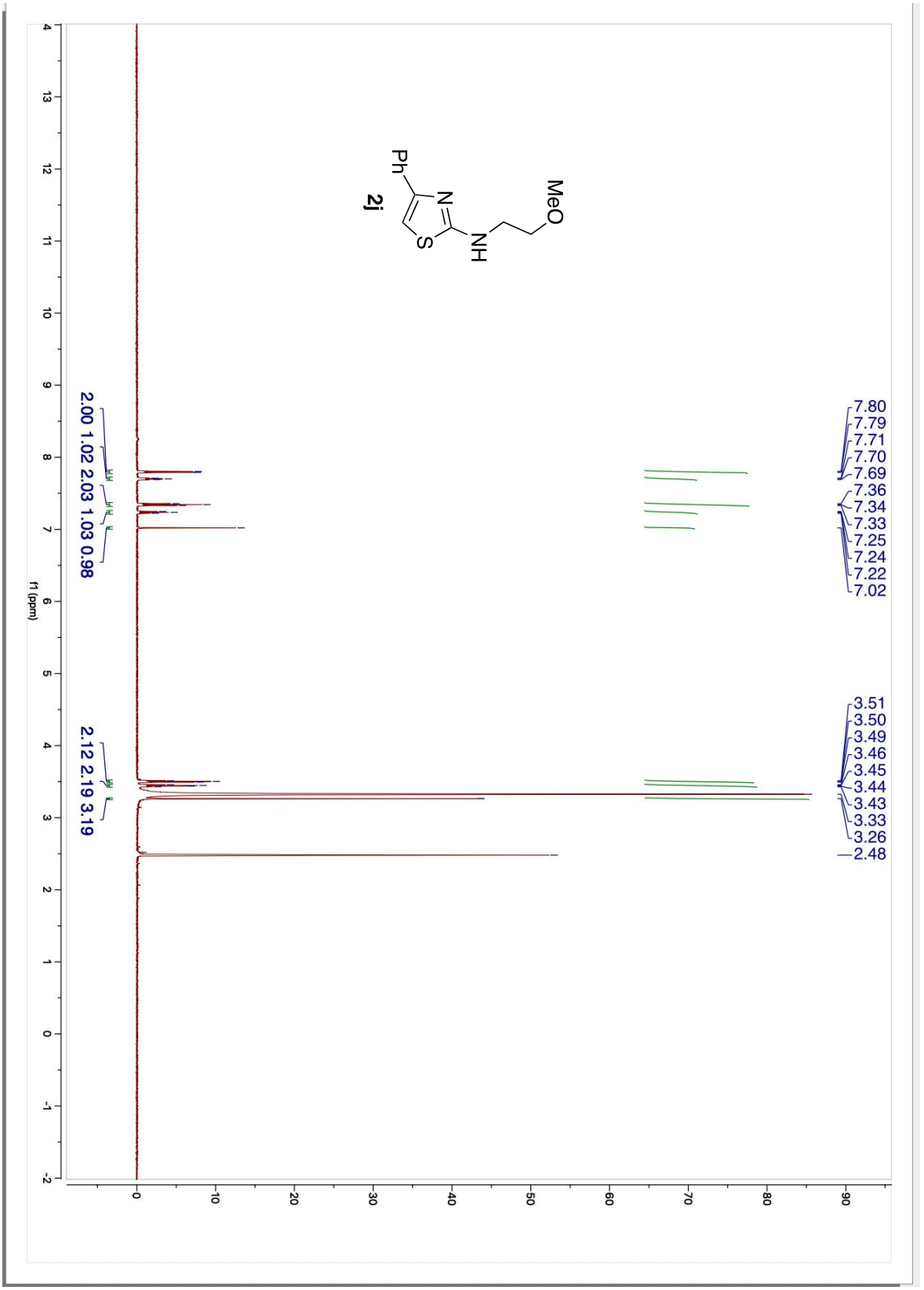

Figure S66: ^{1}H NMR spectrum of **2j** in d_6-DMSO (600 MHz)

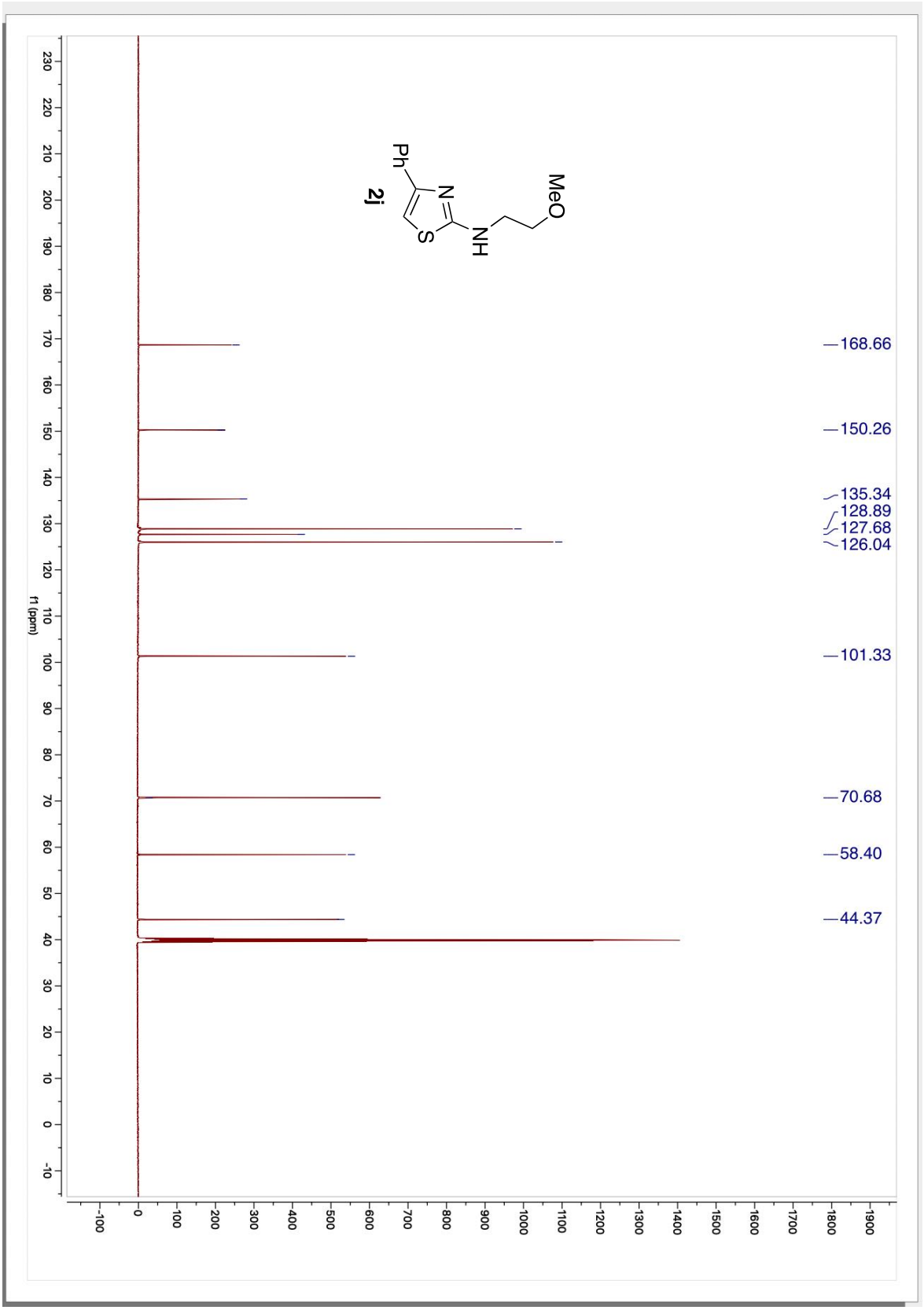

Figure S67: ^{13}C NMR spectrum of **2j** in d_6-DMSO (151 MHz)

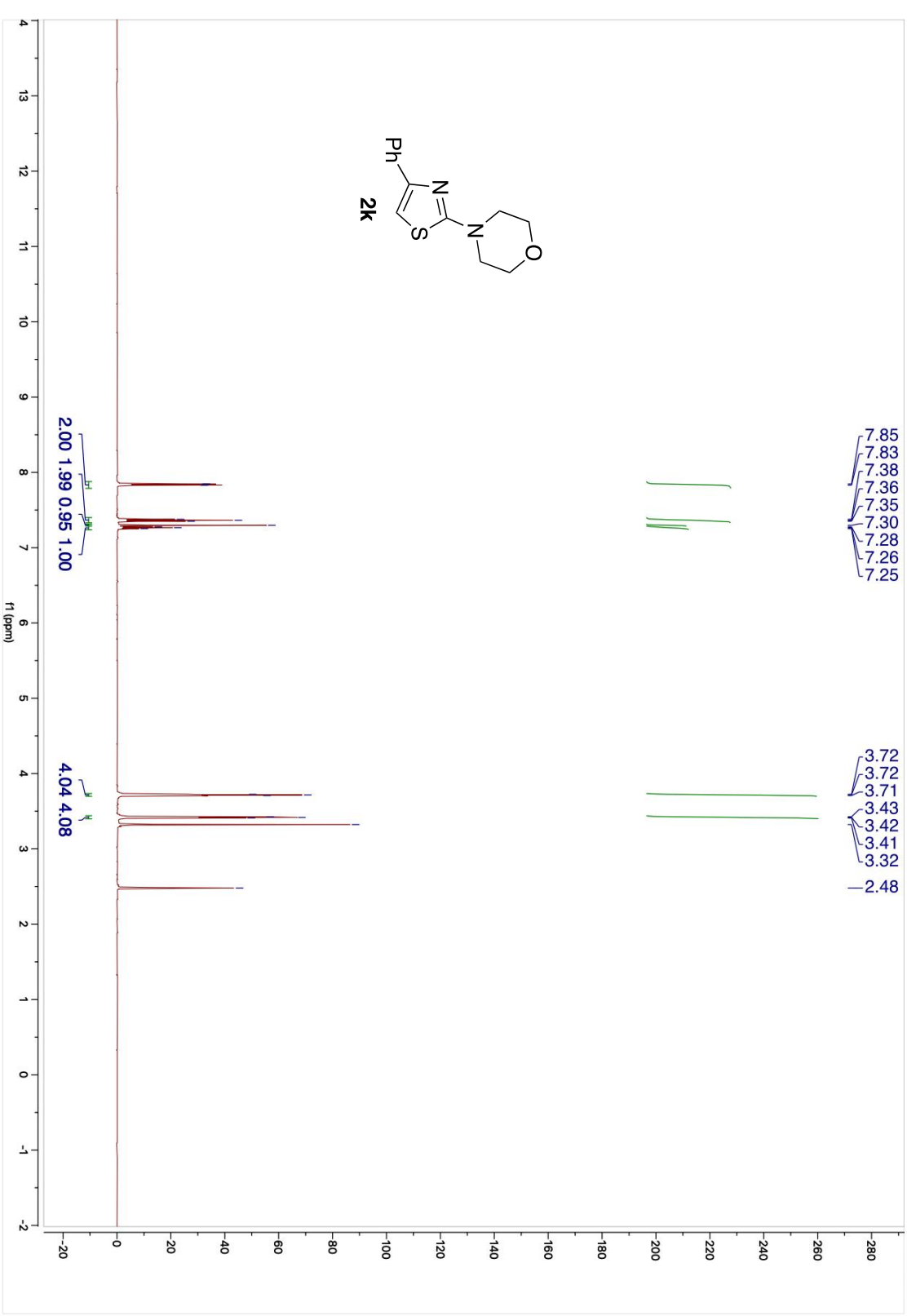

Figure S68: ^{1}H NMR spectrum of **2k** in d_6-DMSO (600 MHz)

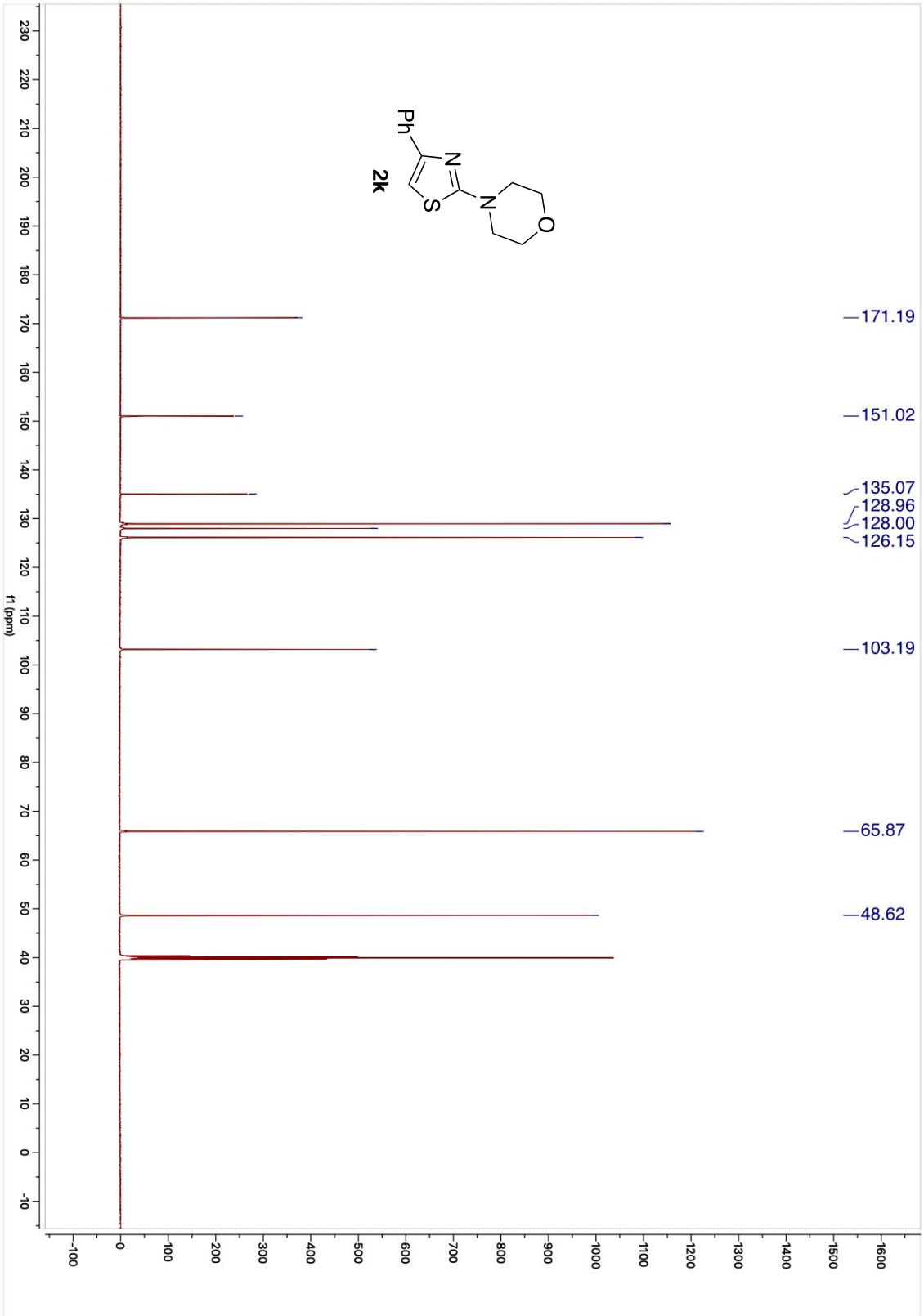

Figure S69: ^{13}C NMR spectrum of **2k** in d_6-DMSO (151 MHz)

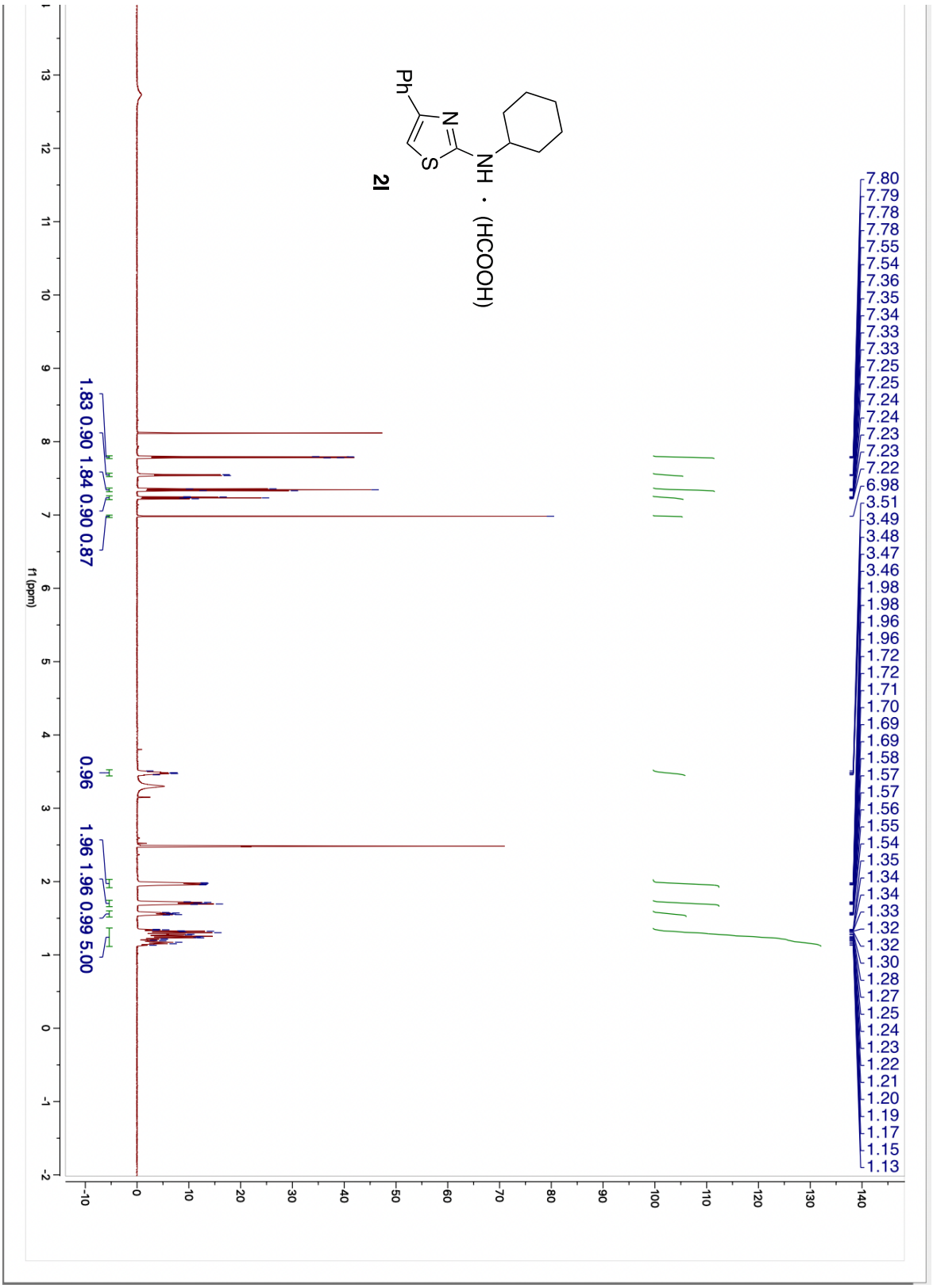

Figure S70: ^{1}H NMR spectrum of **2l** in d_6-DMSO (600 MHz)

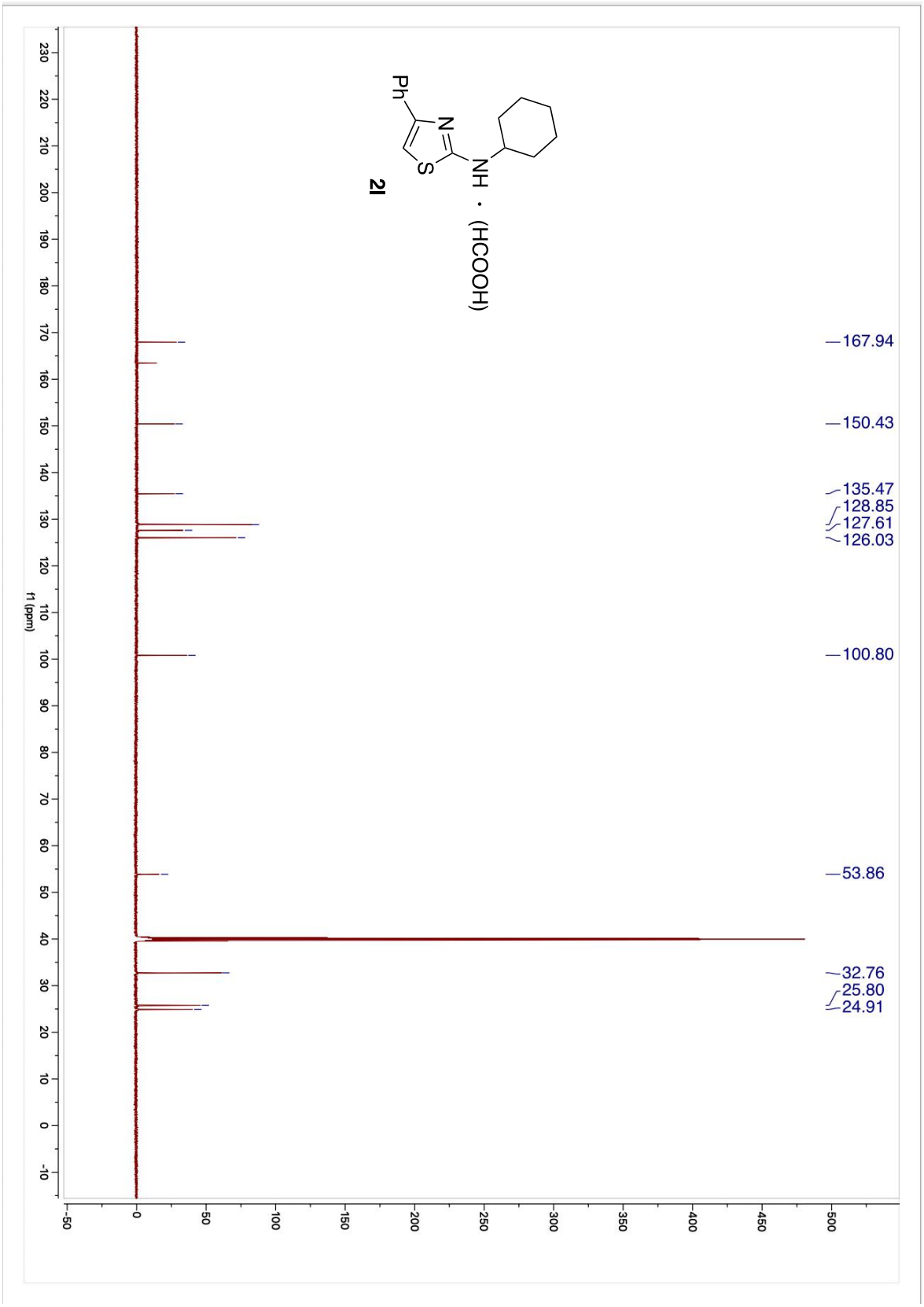

Figure S71: ^{13}C NMR spectrum of **2l** in d_6-DMSO (151 MHz)

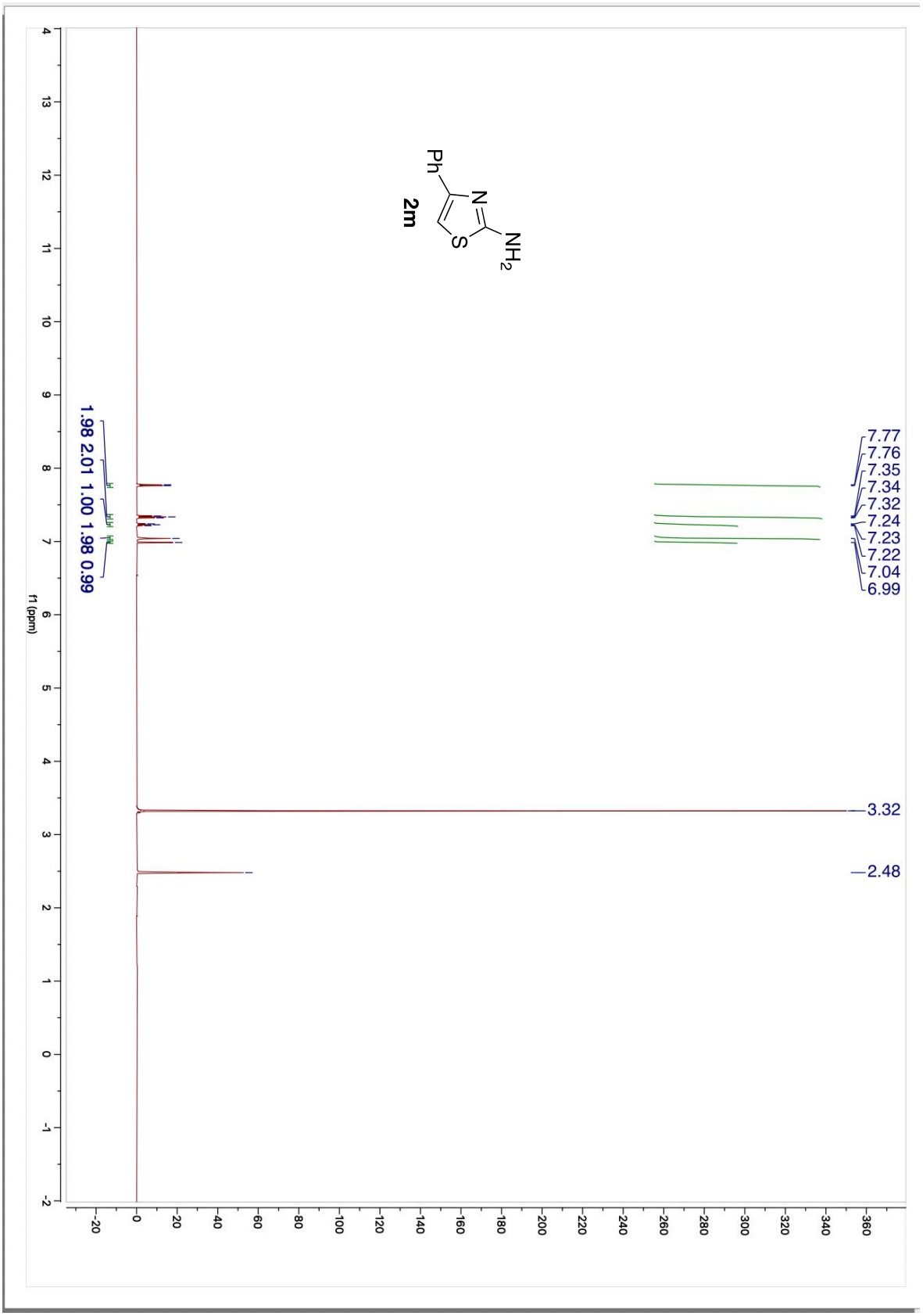

Figure S72: ^{1}H NMR spectrum of **2m** in d_6-DMSO (600 MHz)

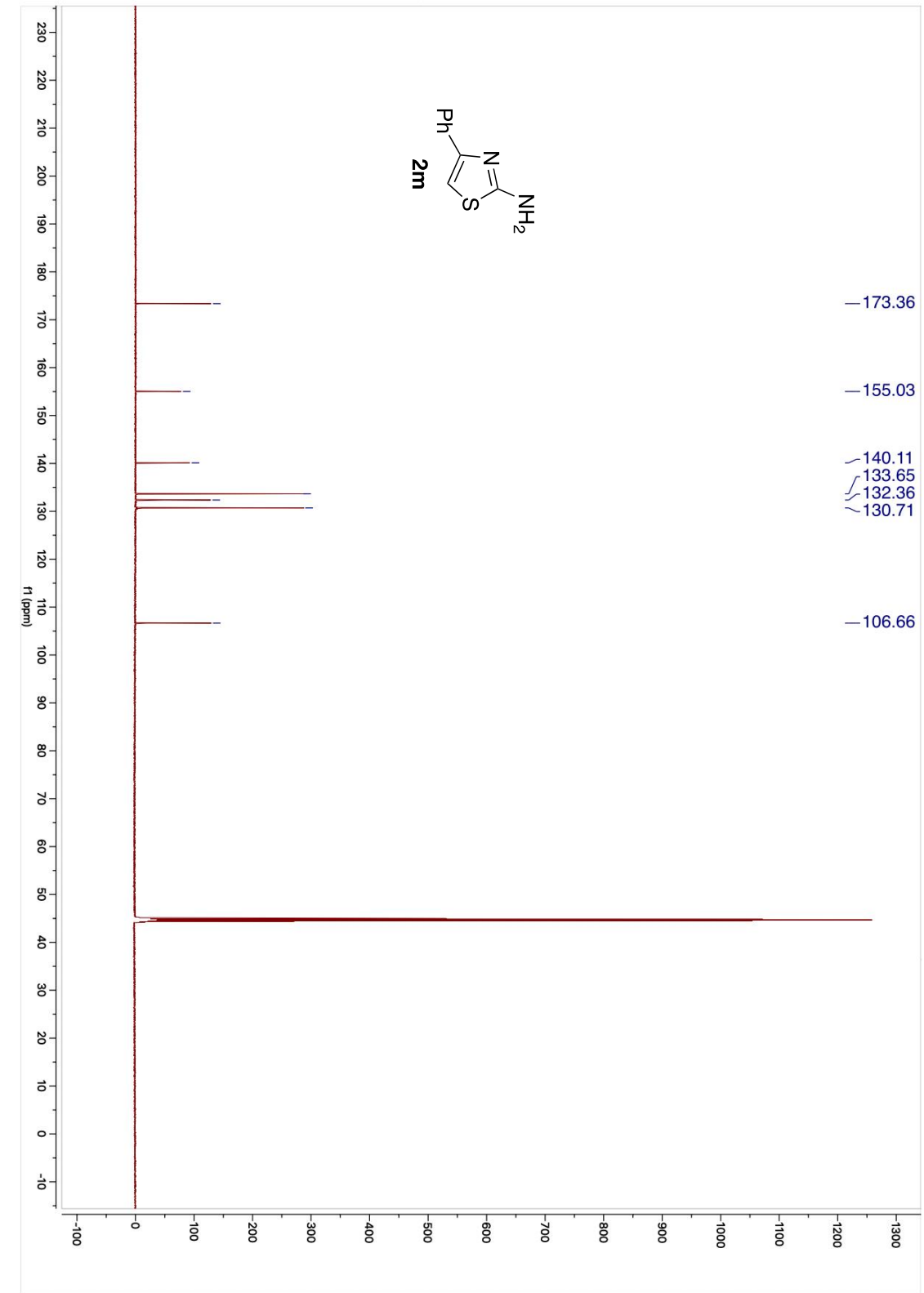

Figure S73: ^{13}C NMR spectrum of **2m** in d_6-DMSO (151 MHz)

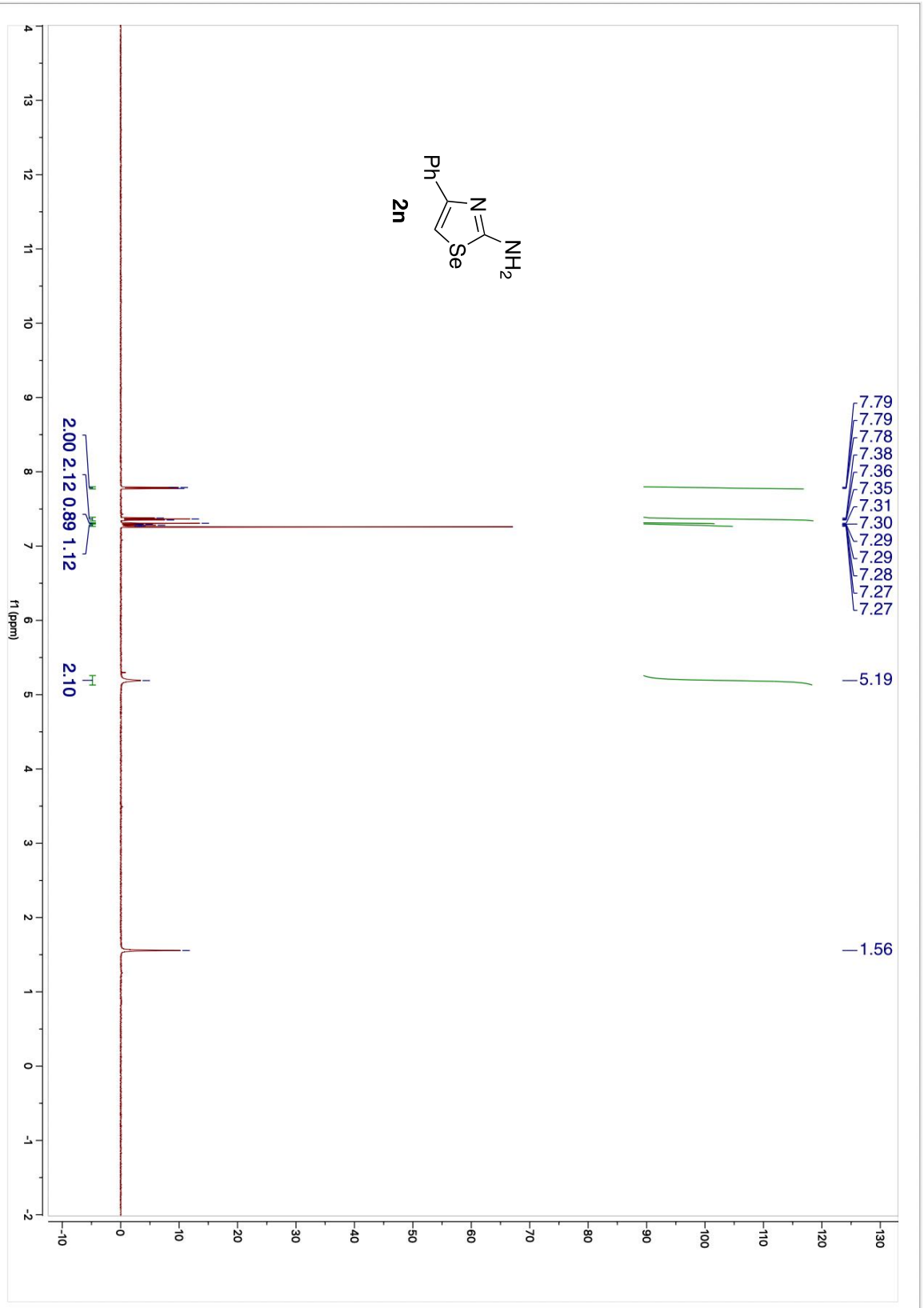

Figure S74: ^{1}H NMR spectrum of **2n** in $CDCl_3$ (600 MHz)

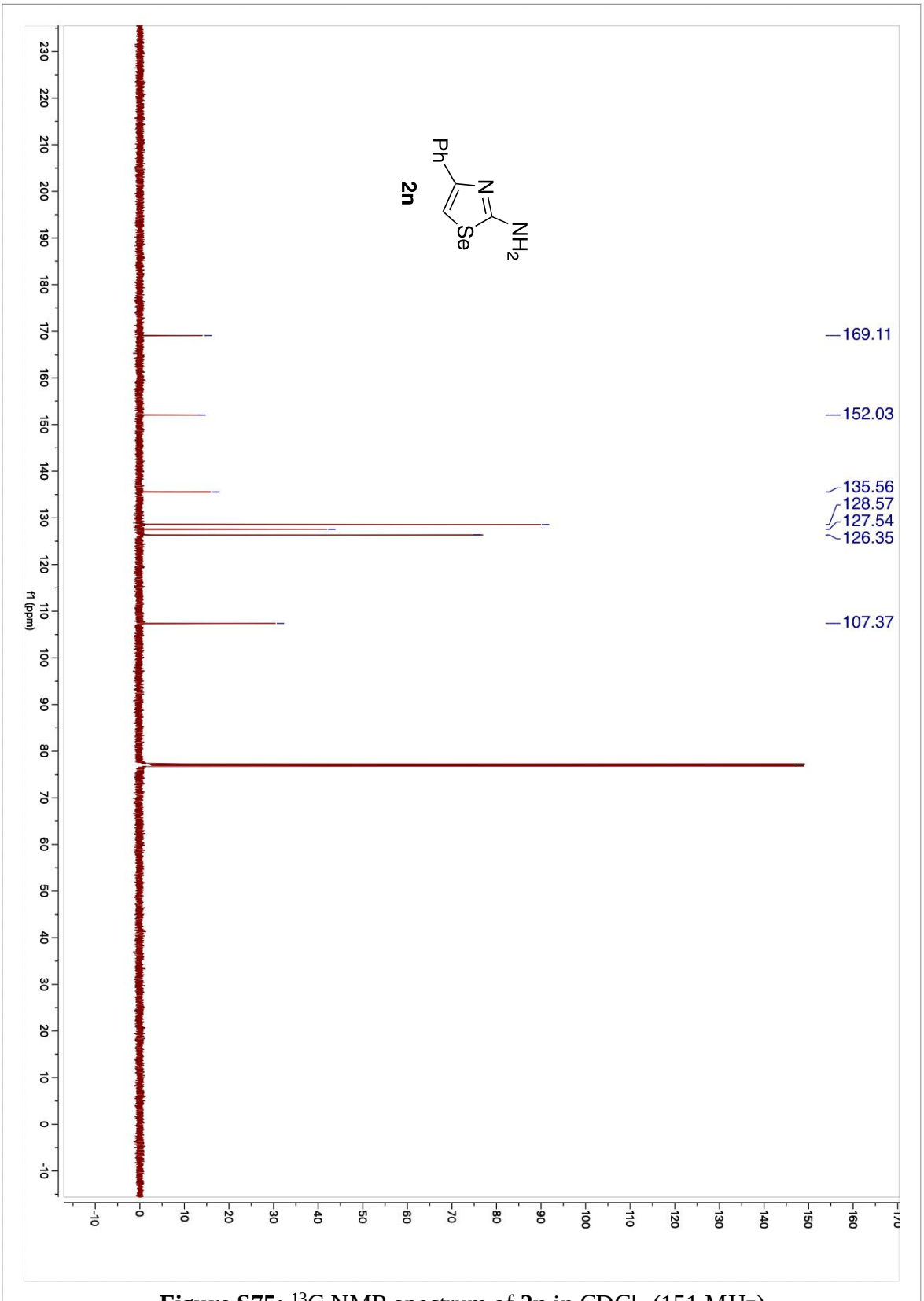

Figure S75: ^{13}C NMR spectrum of **2n** in $CDCl_3$ (151 MHz)

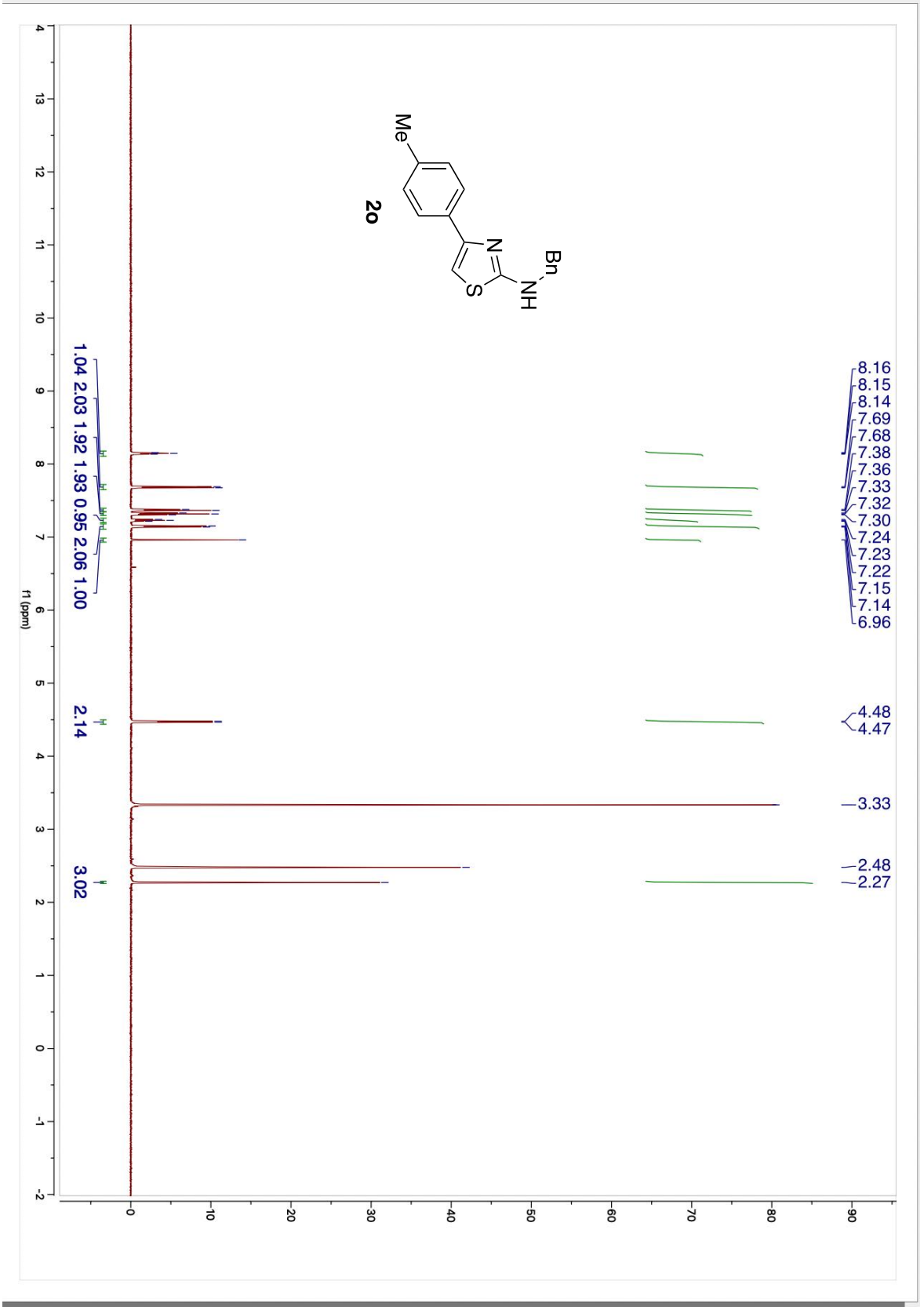

Figure S76: ^{1}H NMR spectrum of **2o** in d_6-DMSO (600 MHz)

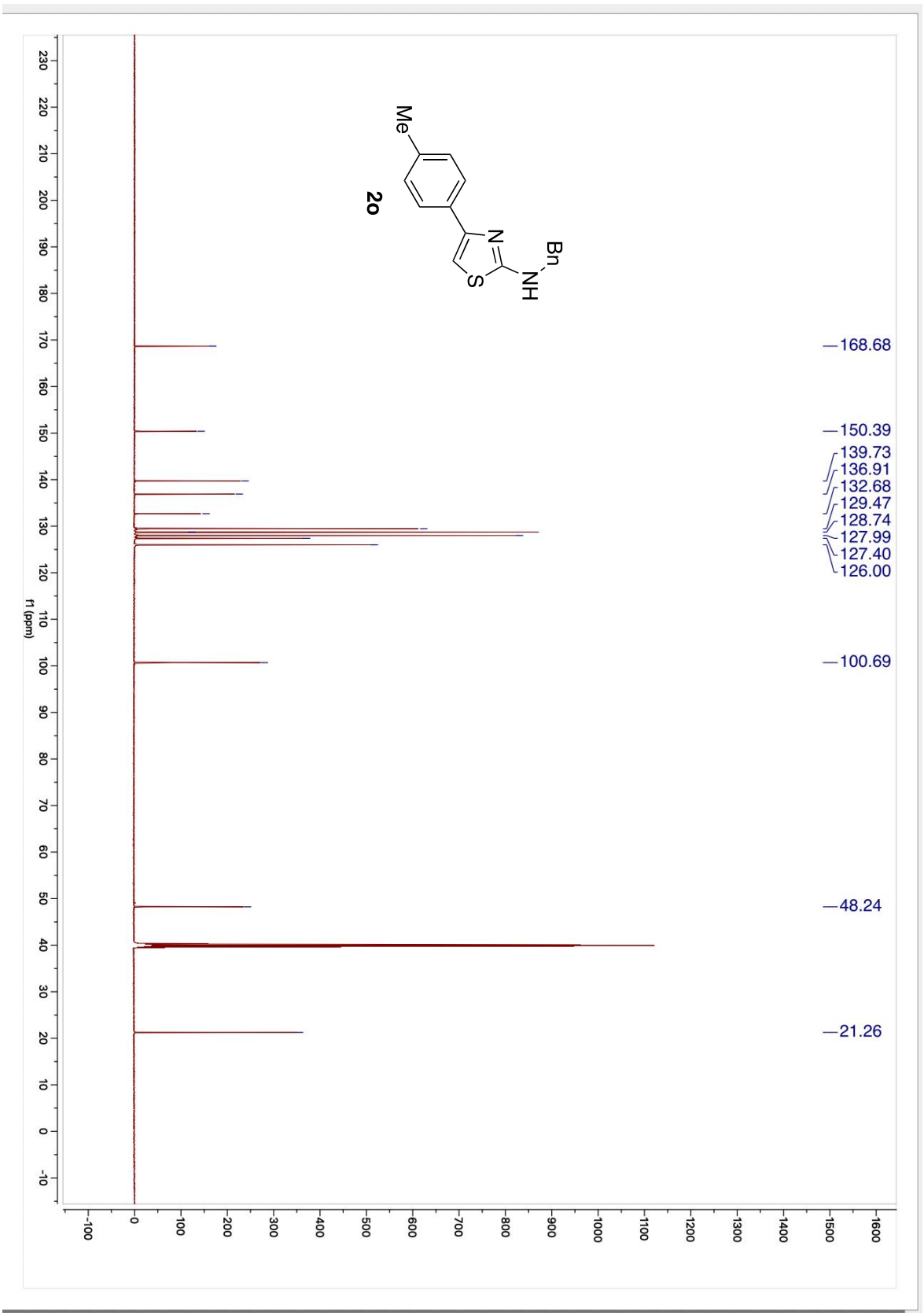

Figure S77: ^{13}C NMR spectrum of **2o** in d_6-DMSO (151 MHz)

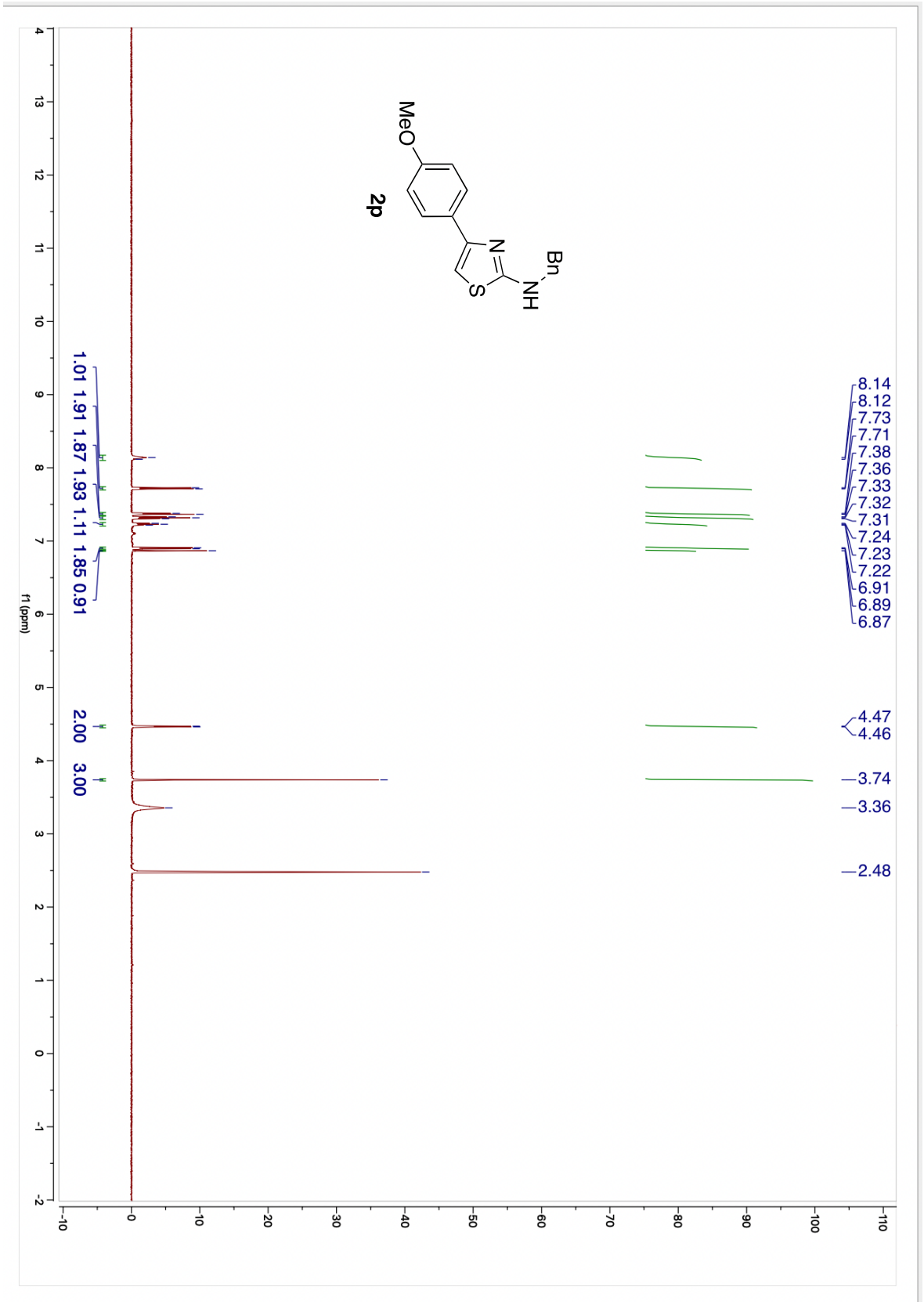

Figure S78: ^{1}H NMR spectrum of **2p** in d_6-DMSO (600 MHz)

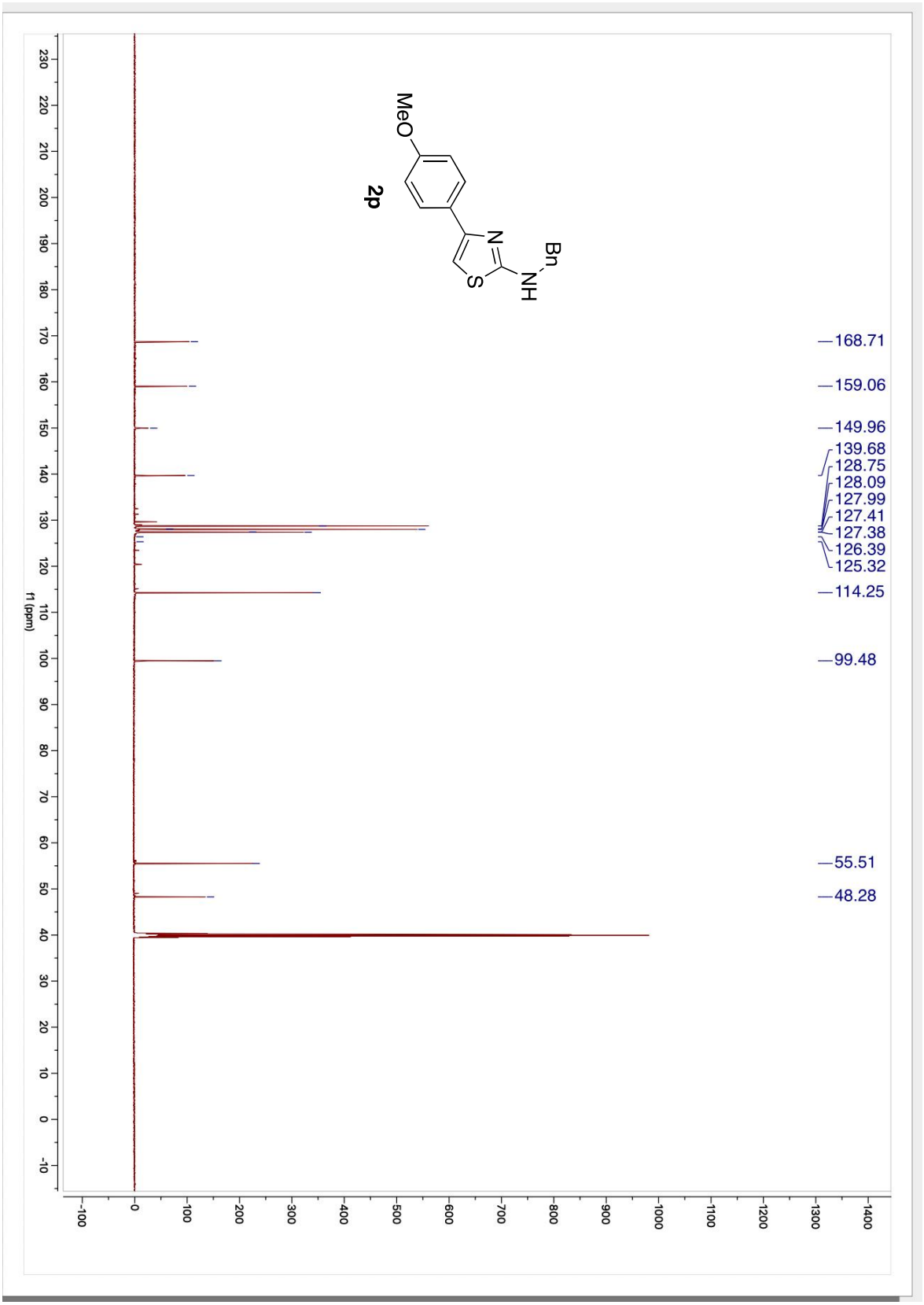

Figure S79: ^{13}C NMR spectrum of **2p** in d_6-DMSO (151 MHz)

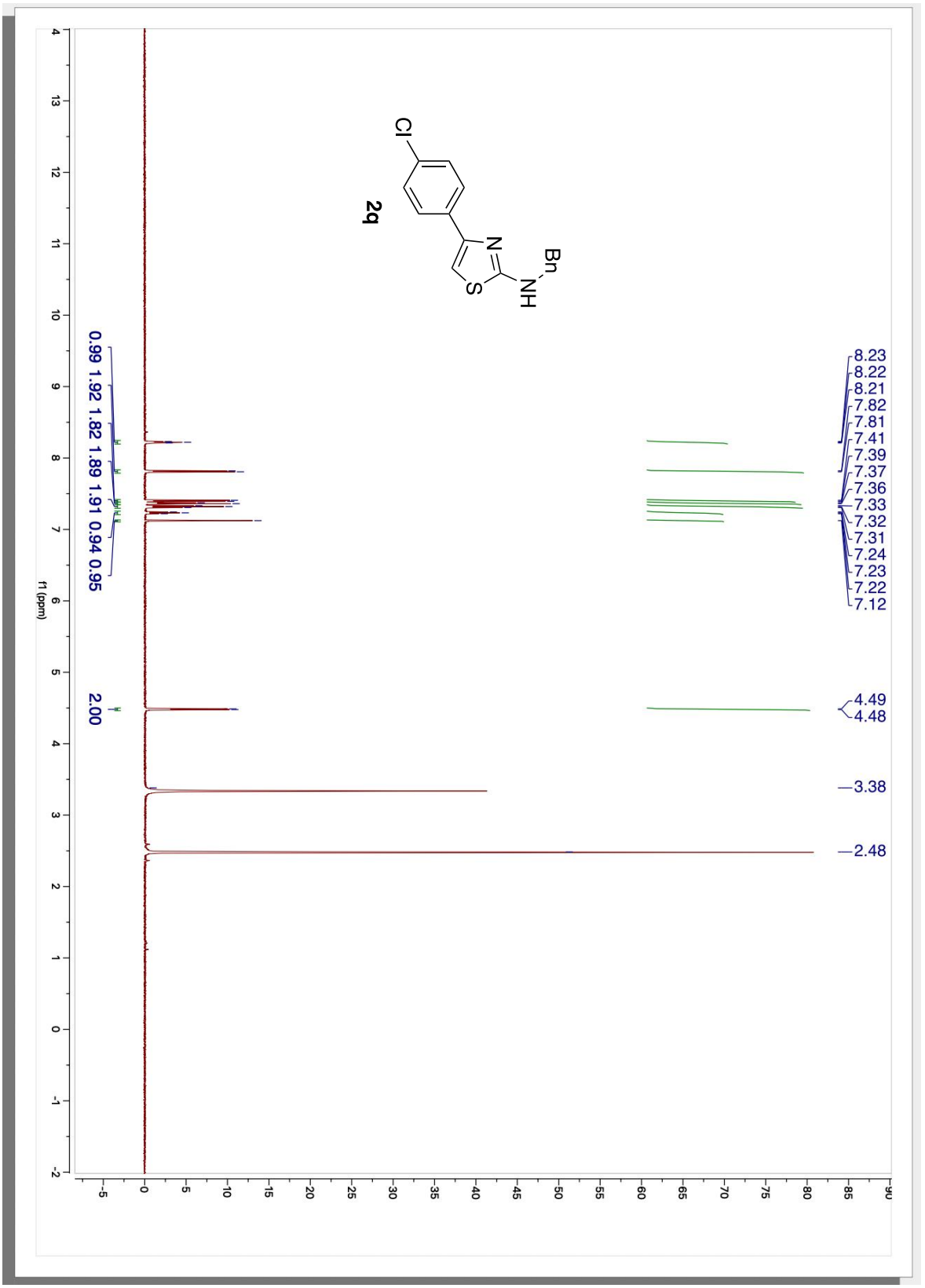

Figure S80: ^{1}H NMR spectrum of **2q** in d_6-DMSO (600 MHz)

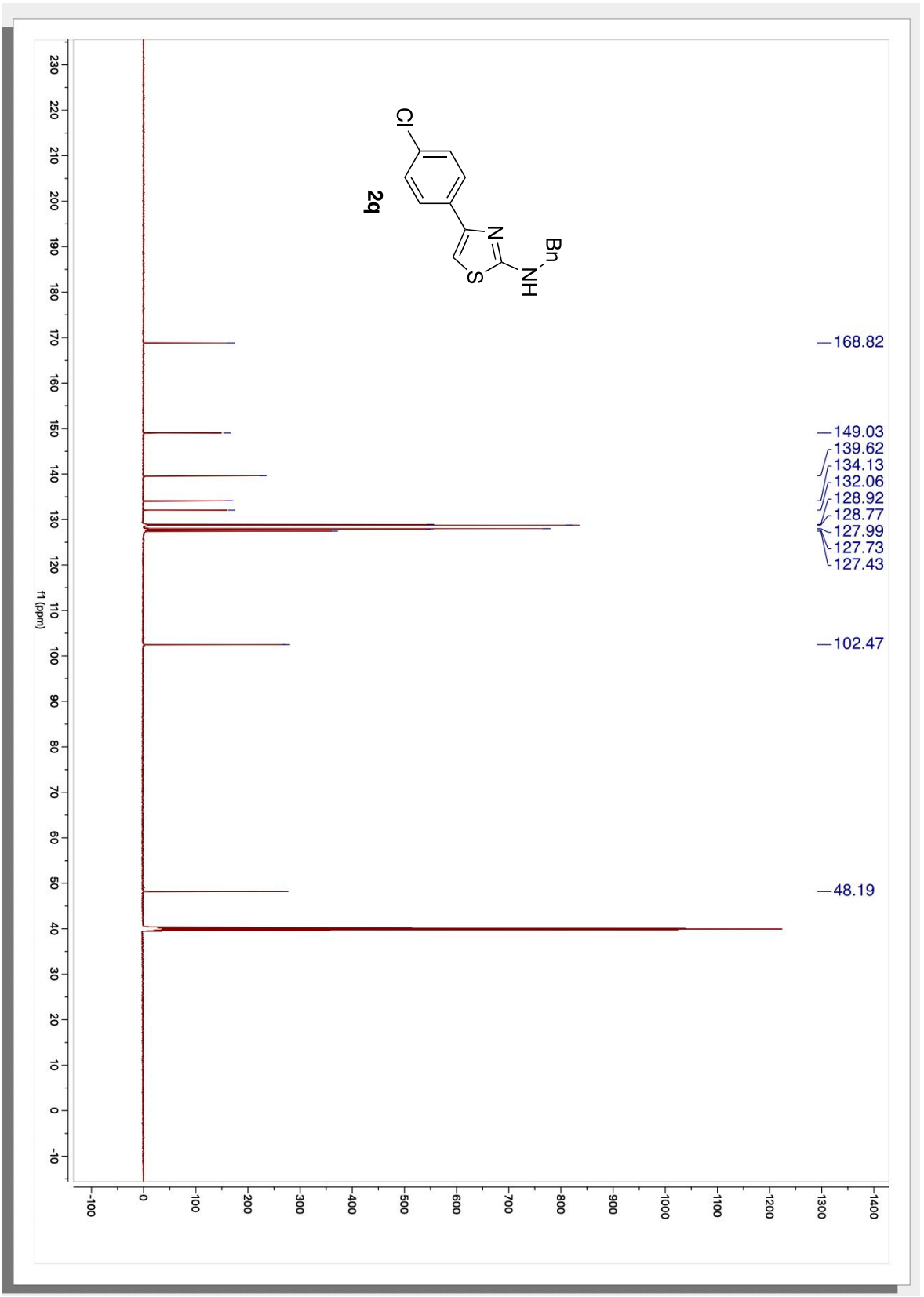

Figure S81: ^{13}C NMR spectrum of **2q** in d_6-DMSO (151 MHz)

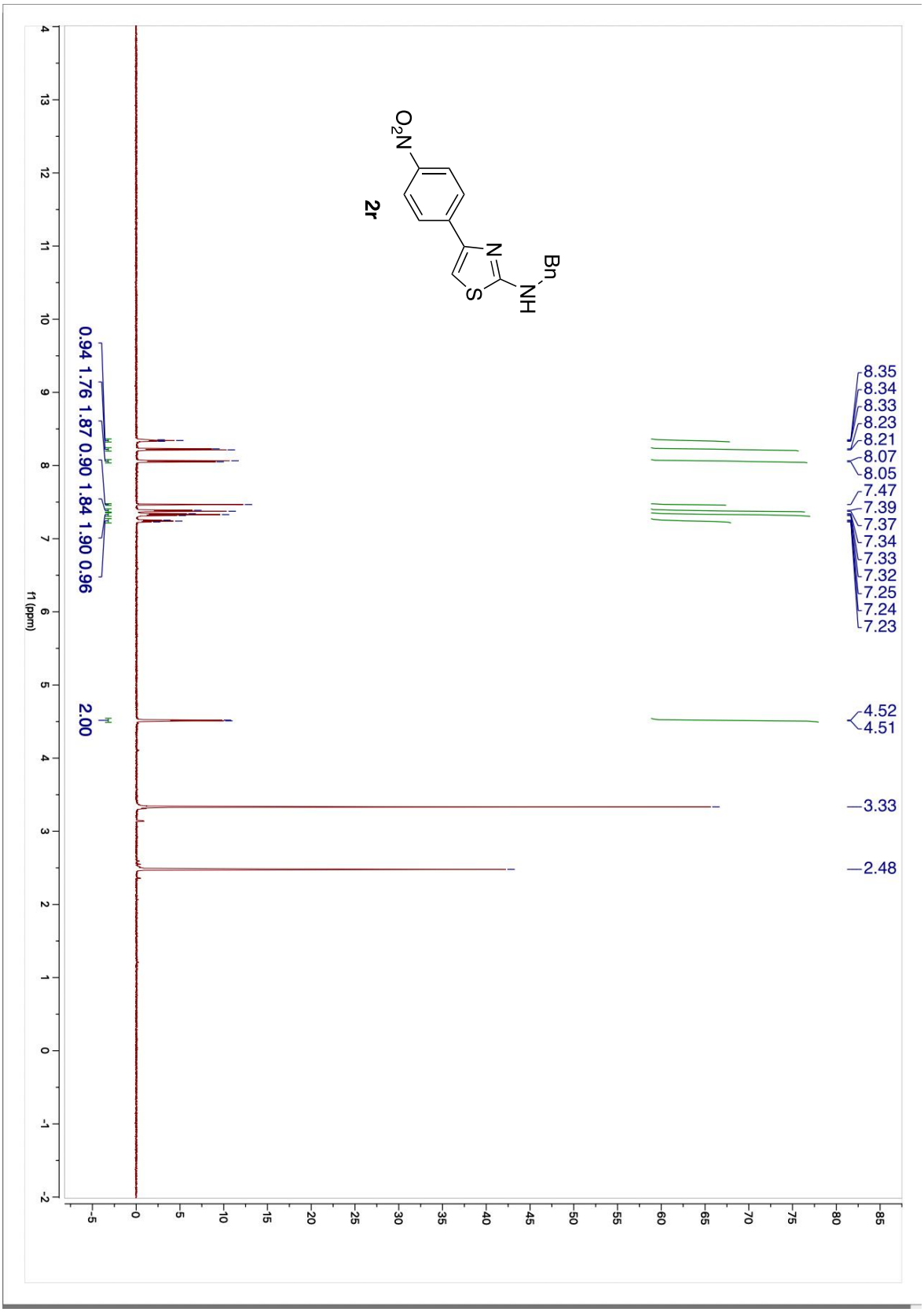

Figure S82: ^{1}H NMR spectrum of **2r** in d_6-DMSO (600 MHz)

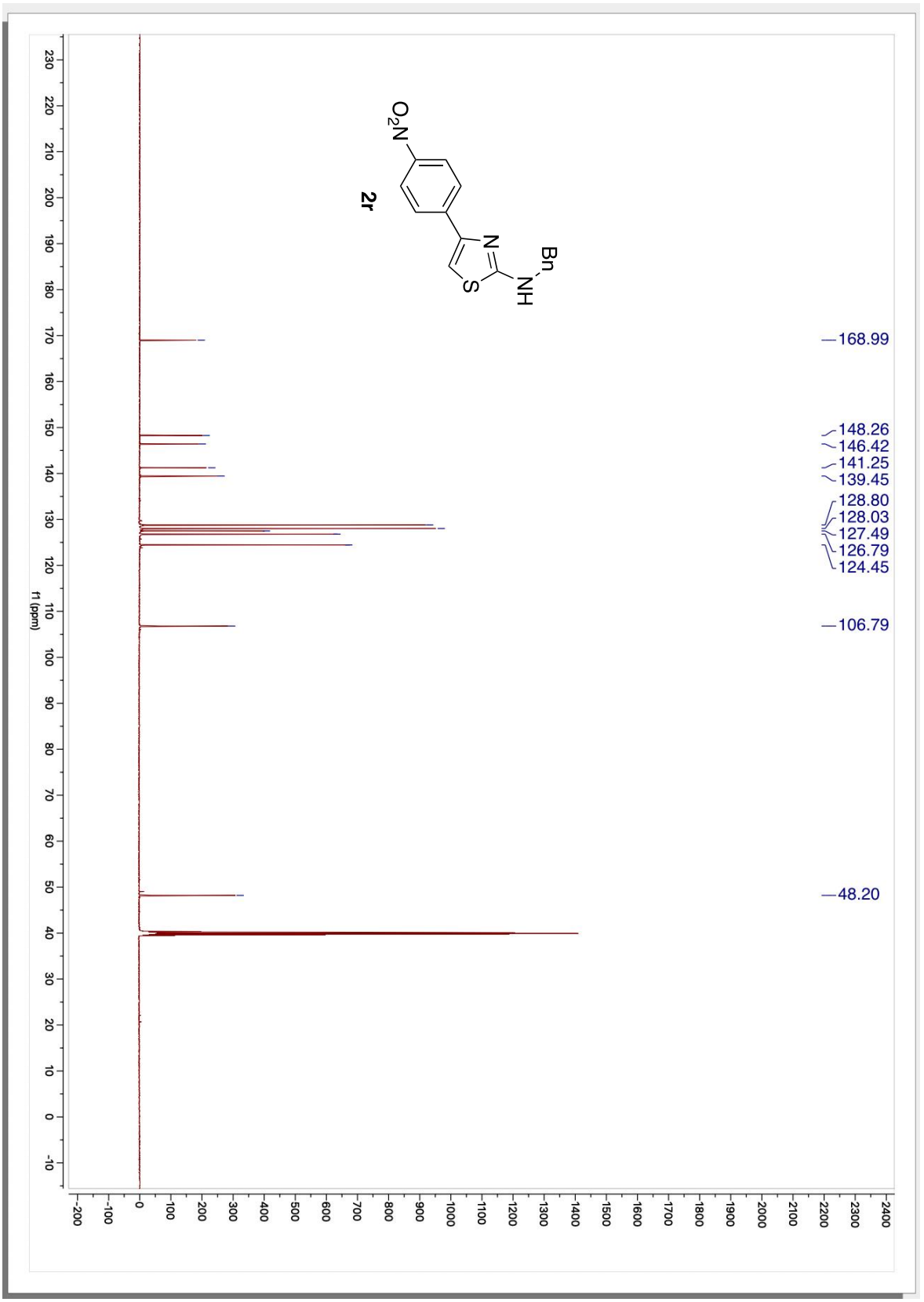

Figure S83: ^{13}C NMR spectrum of **2r** in d_6-DMSO (151 MHz)

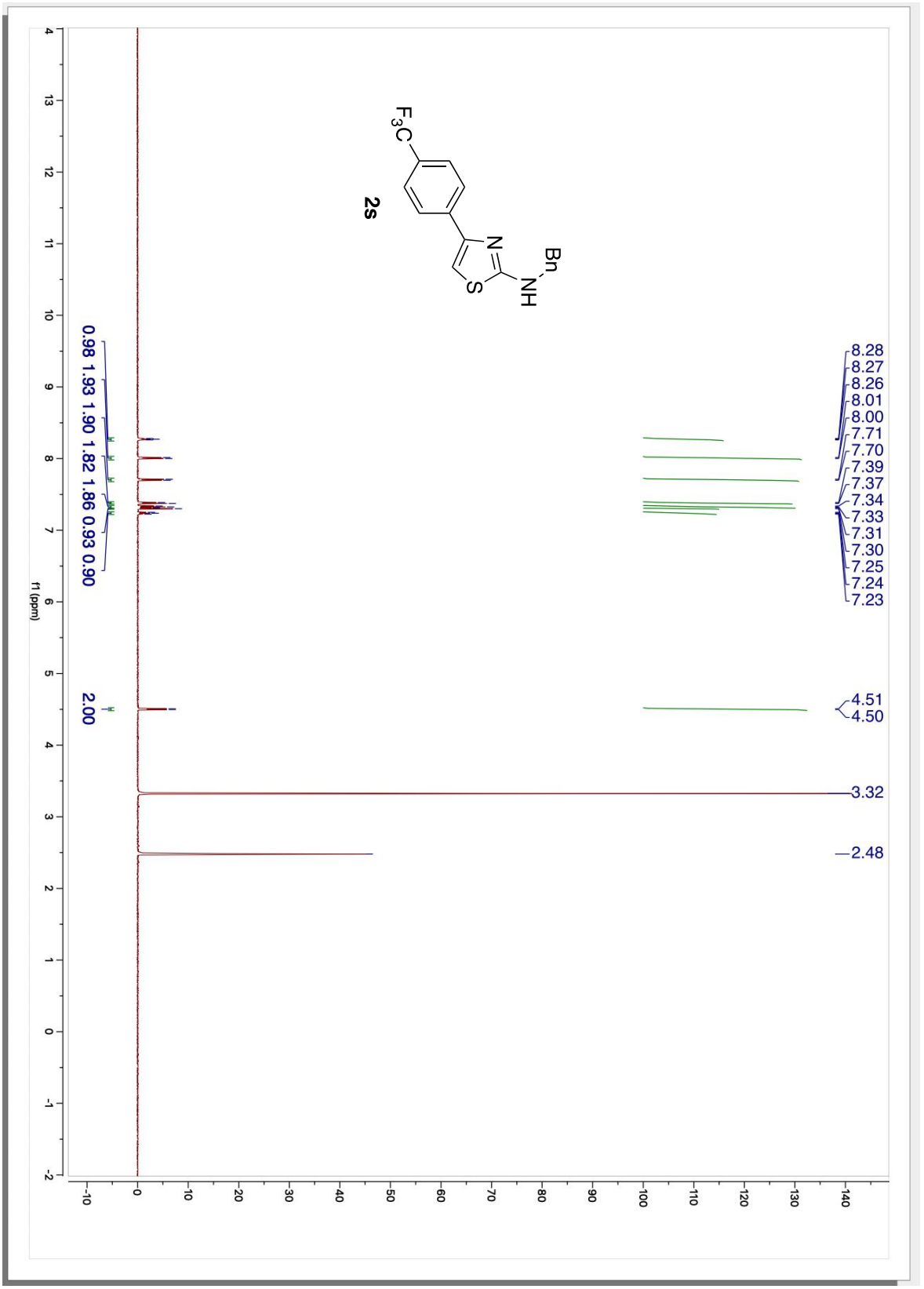

Figure S84: ^{1}H NMR spectrum of **2s** in d_6-DMSO (600 MHz)

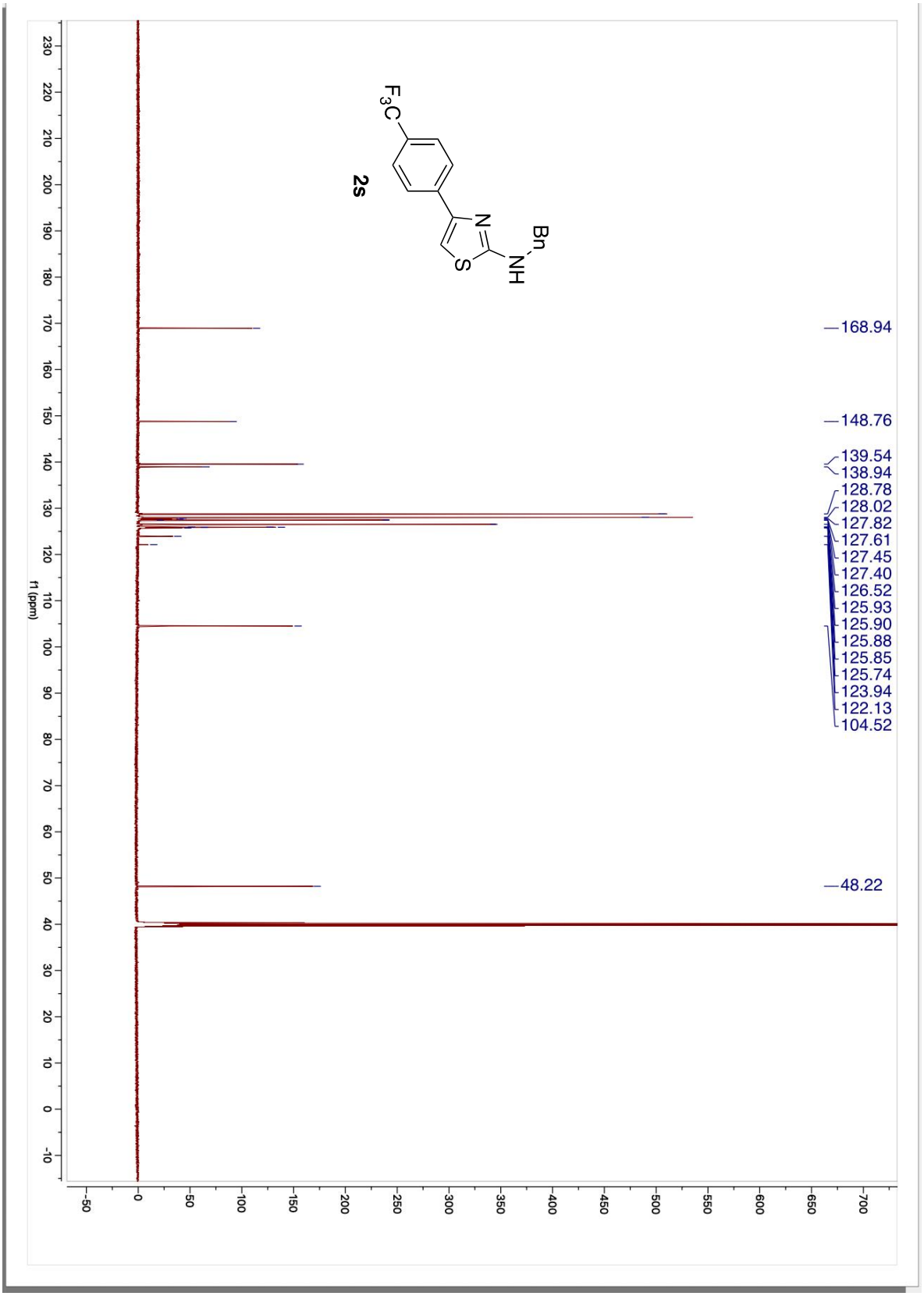

Figure S85: ^{13}C NMR spectrum of **2s** in d_6-DMSO (151 MHz)

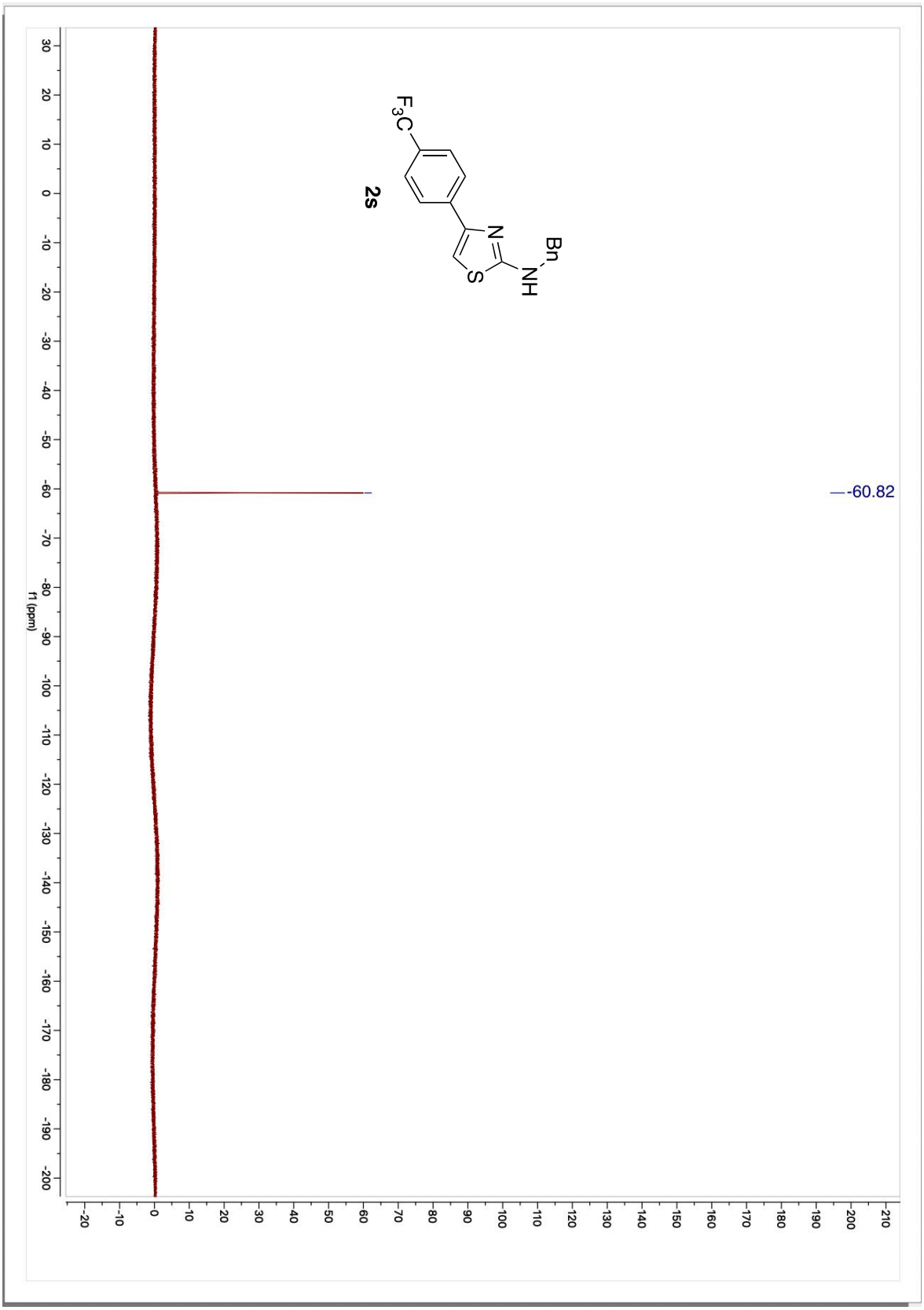

Figure S86: ^{19}F NMR spectrum of **2s** in d_6-DMSO (376 MHz)

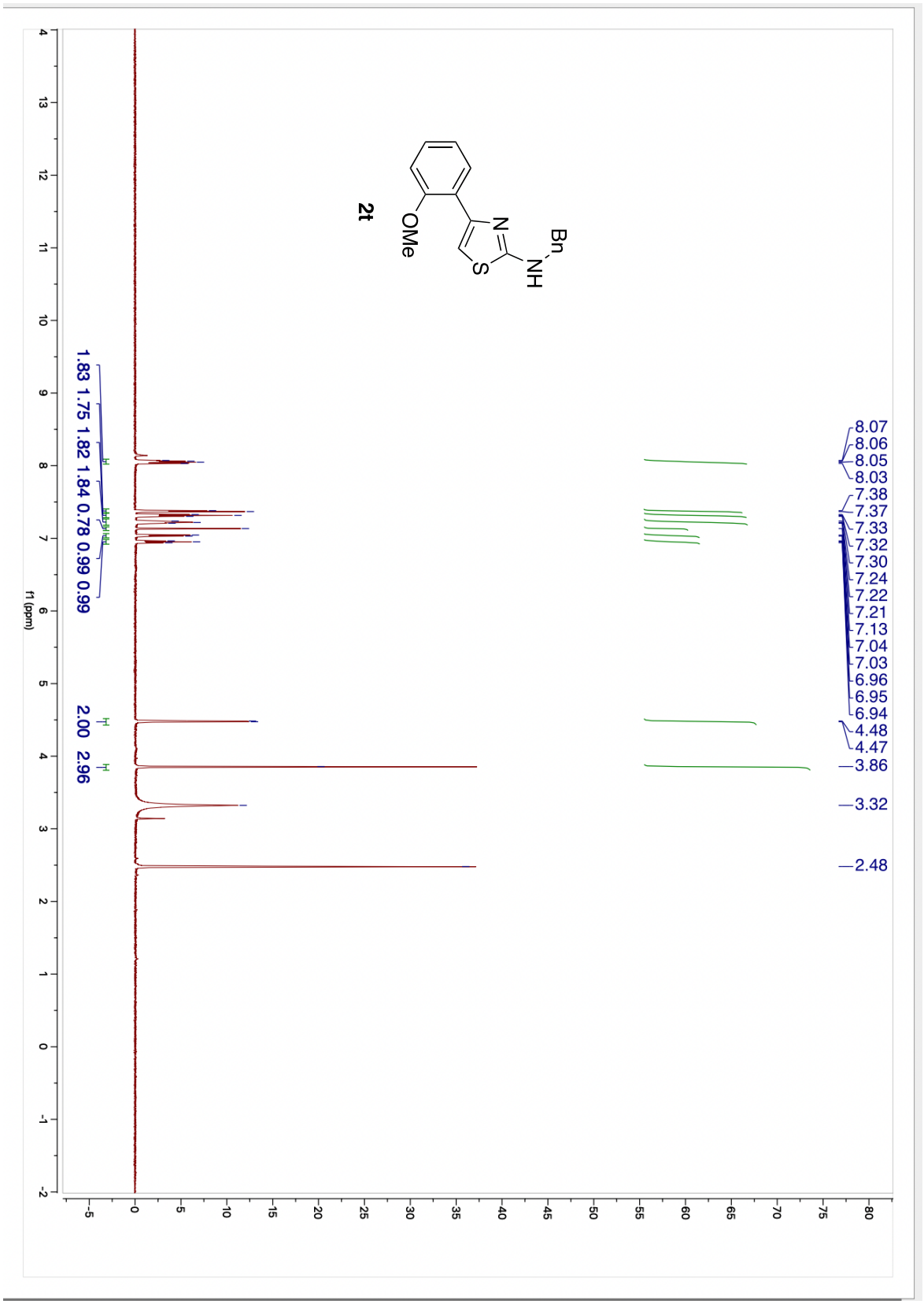

Figure S87: ^{1}H NMR spectrum of **2t** in d_6-DMSO (600 MHz)

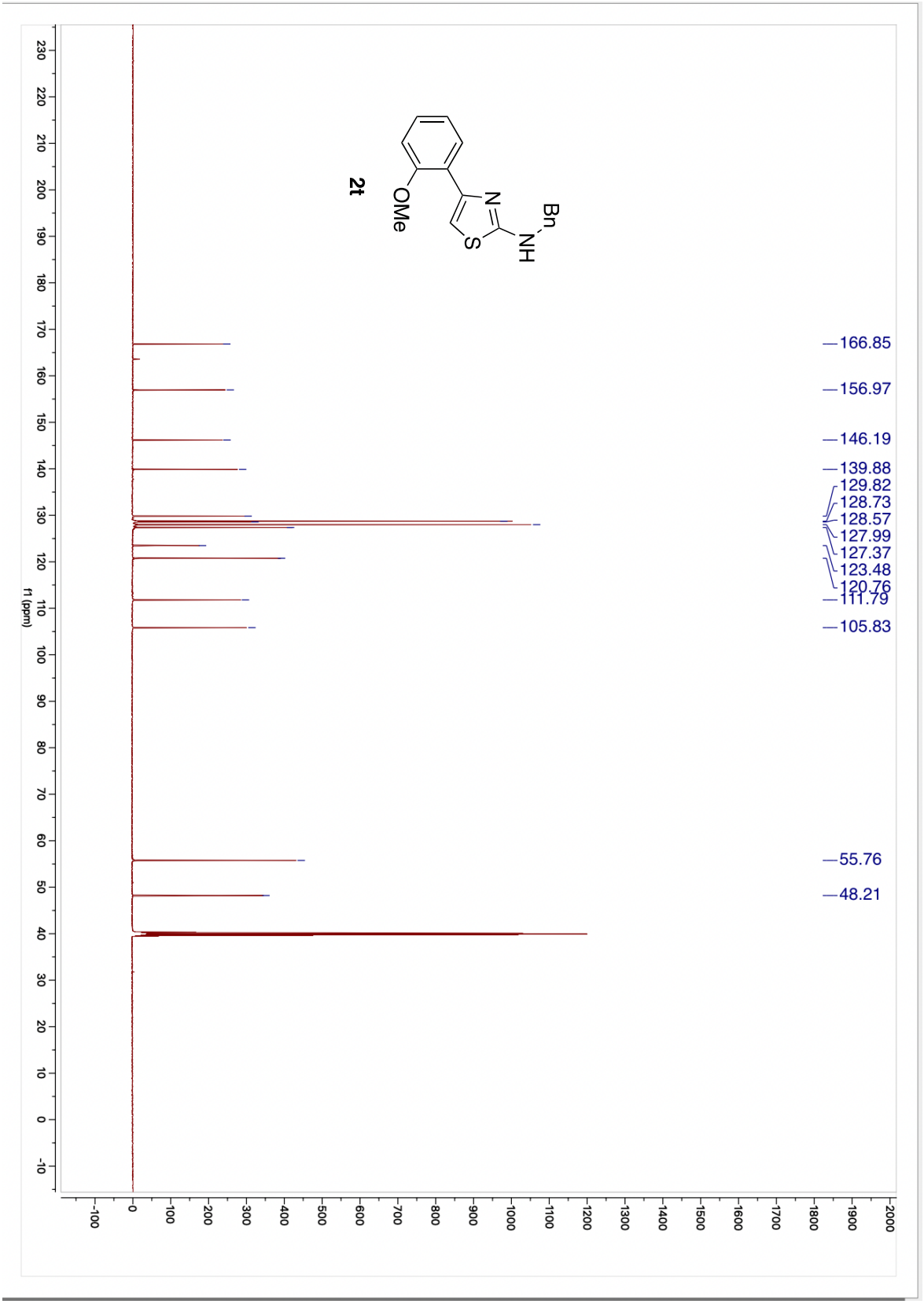

Figure S88: ^{13}C NMR spectrum of **2t** in d_6-DMSO (151 MHz)

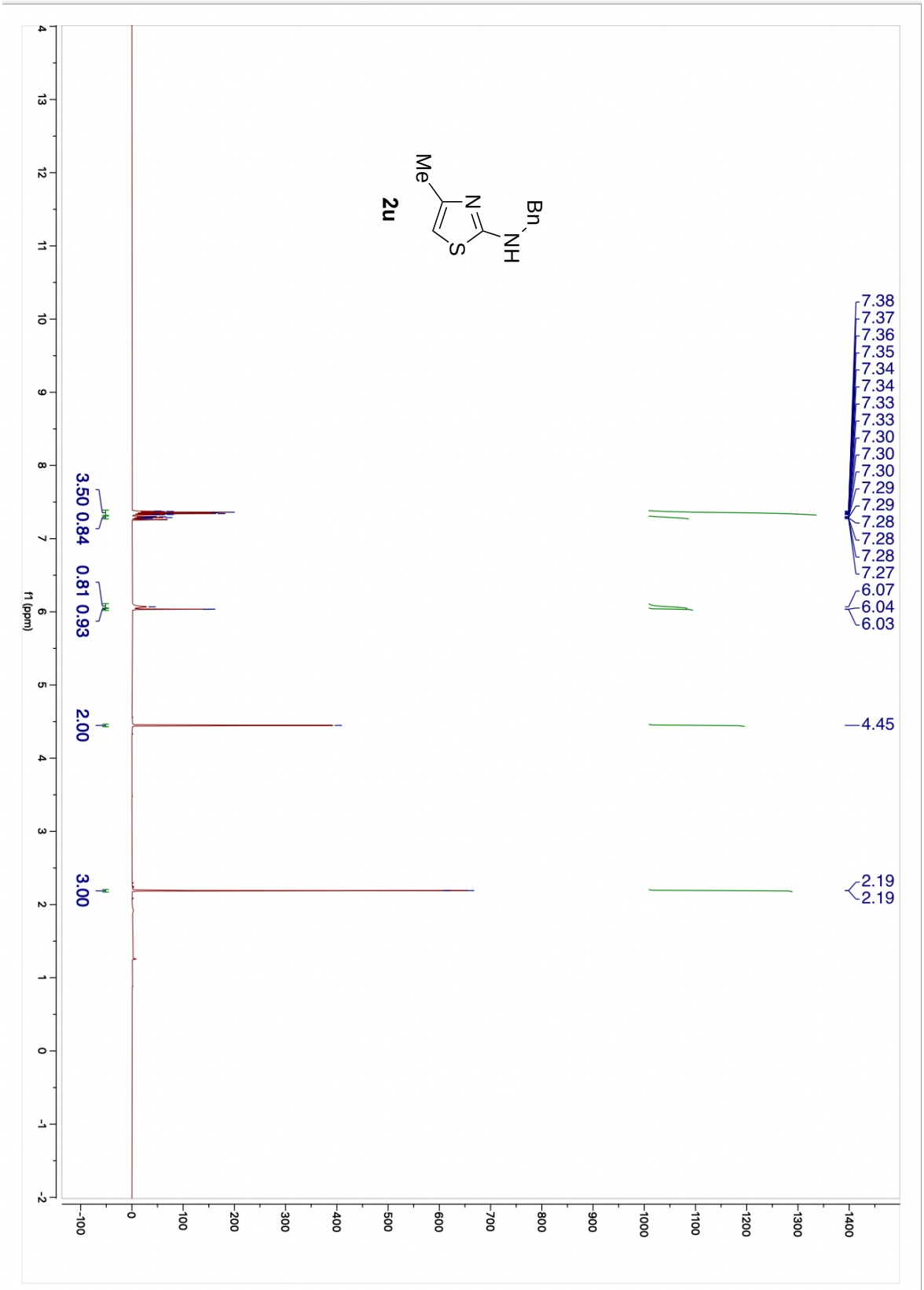

Figure S89: ^{1}H NMR spectrum of **2u** in $CDCl_3$ (600 MHz)

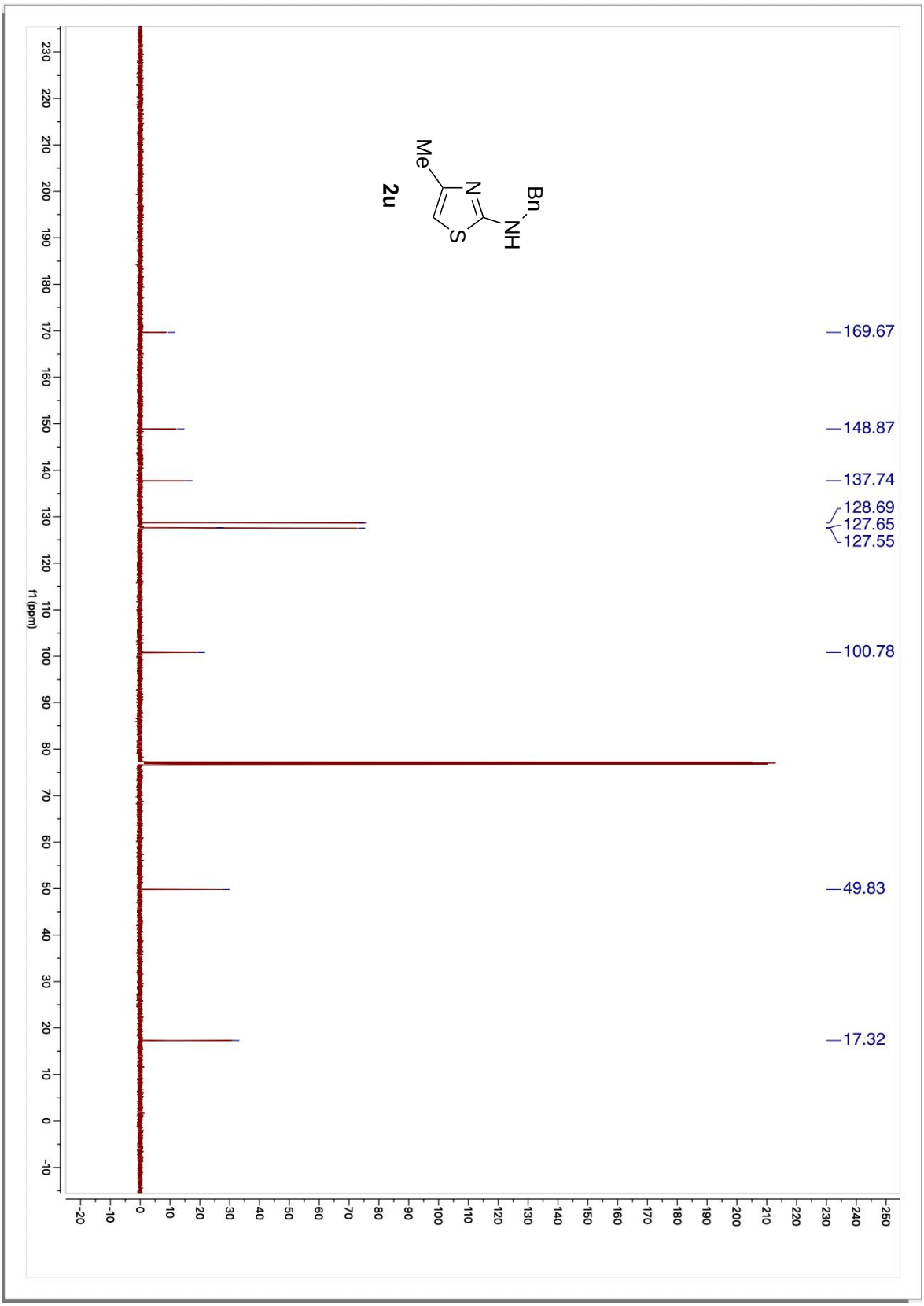

Figure S90: ^{13}C NMR spectrum of **2u** in $CDCl_3$ (151 MHz)

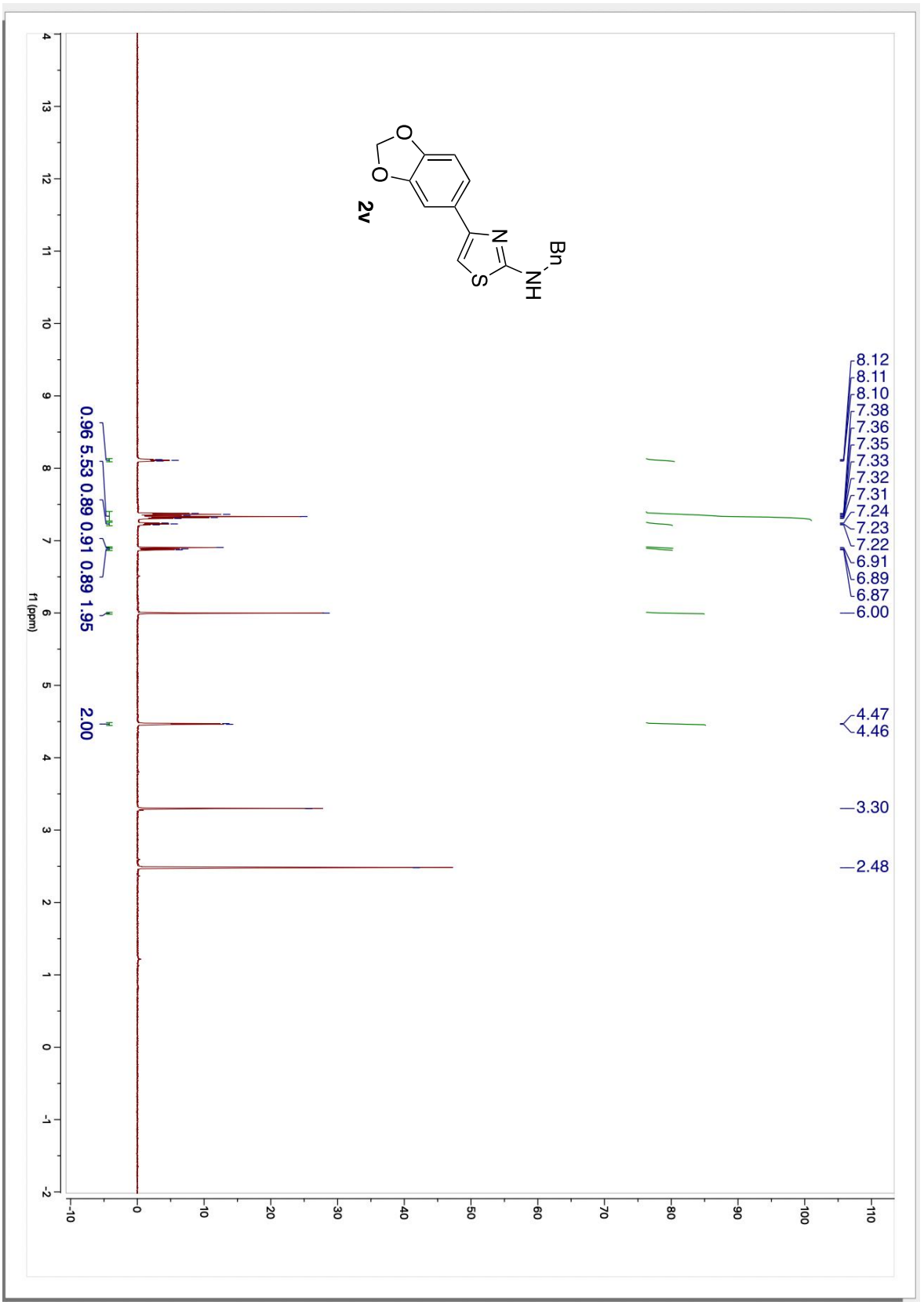

Figure S91: ^{1}H NMR spectrum of **2v** in d_6-DMSO (600 MHz)

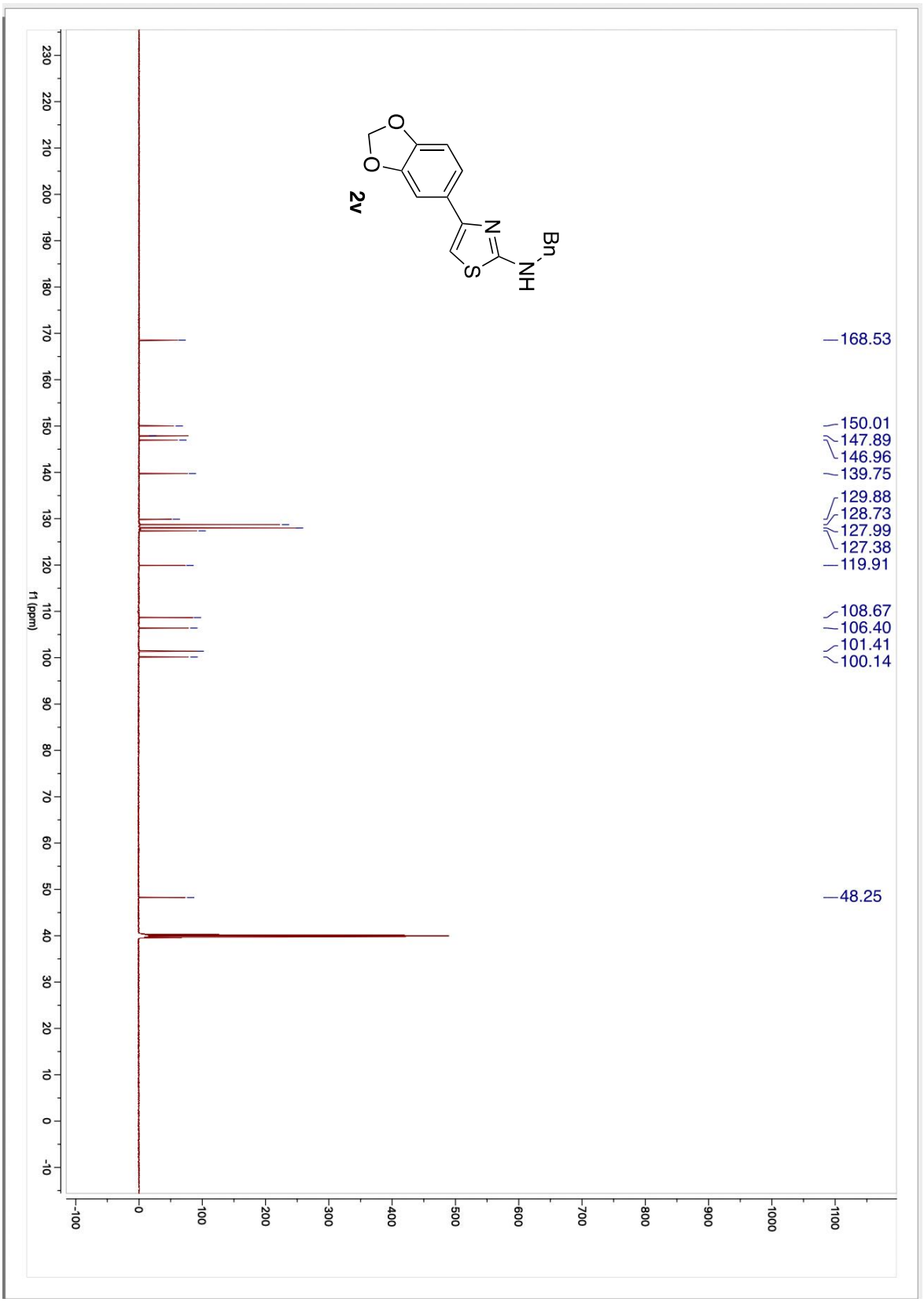

Figure S92: ^{13}C NMR spectrum of **2v** in d_6-DMSO (151 MHz)

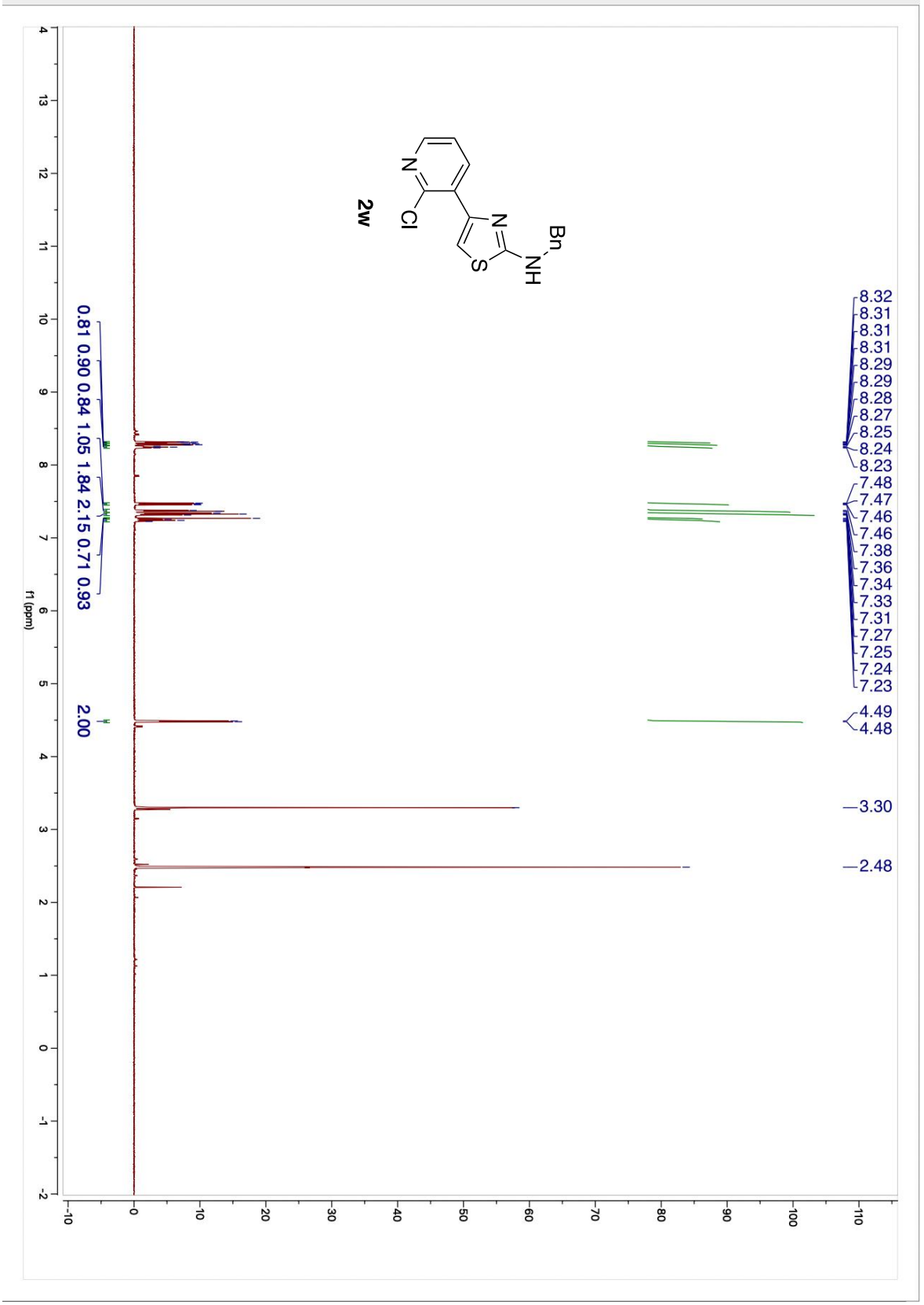

Figure S93: ^{1}H NMR spectrum of **2w** in d_6-DMSO (600 MHz)

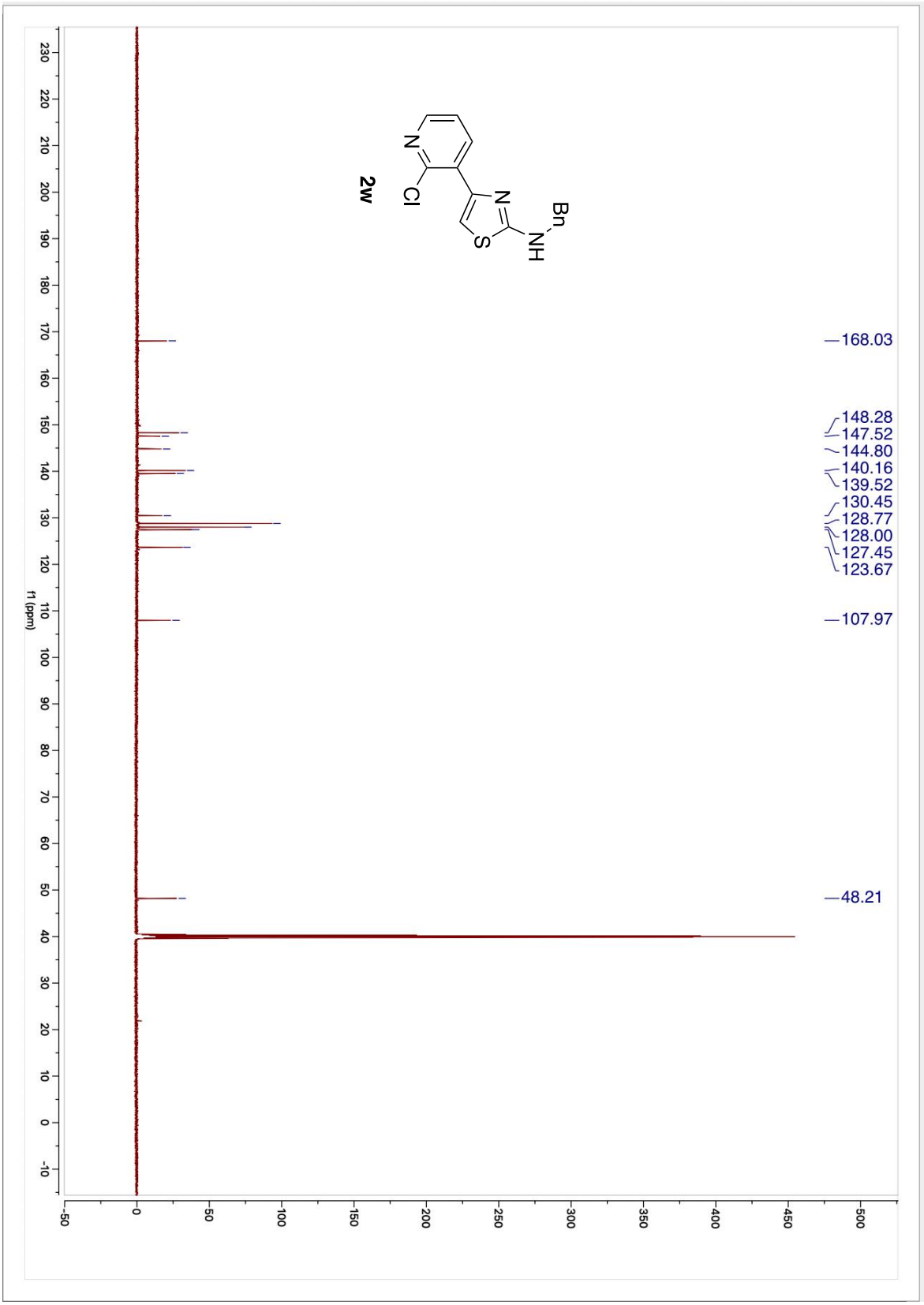

Figure S94: ^{13}C NMR spectrum of **2w** in d_6-DMSO (151 MHz)

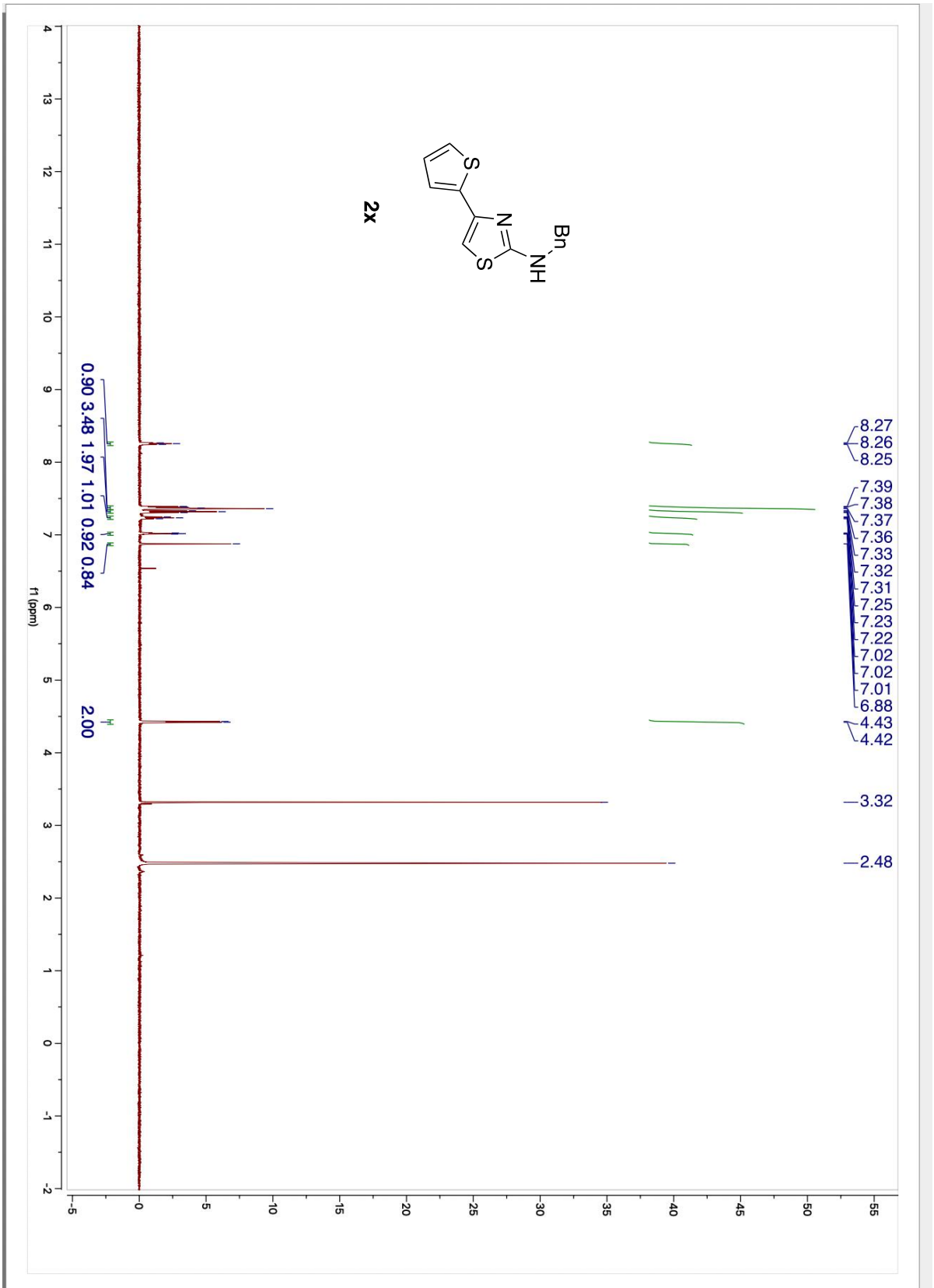

Figure S95: ^{1}H NMR spectrum of **2x** in d_6-DMSO (600 MHz)

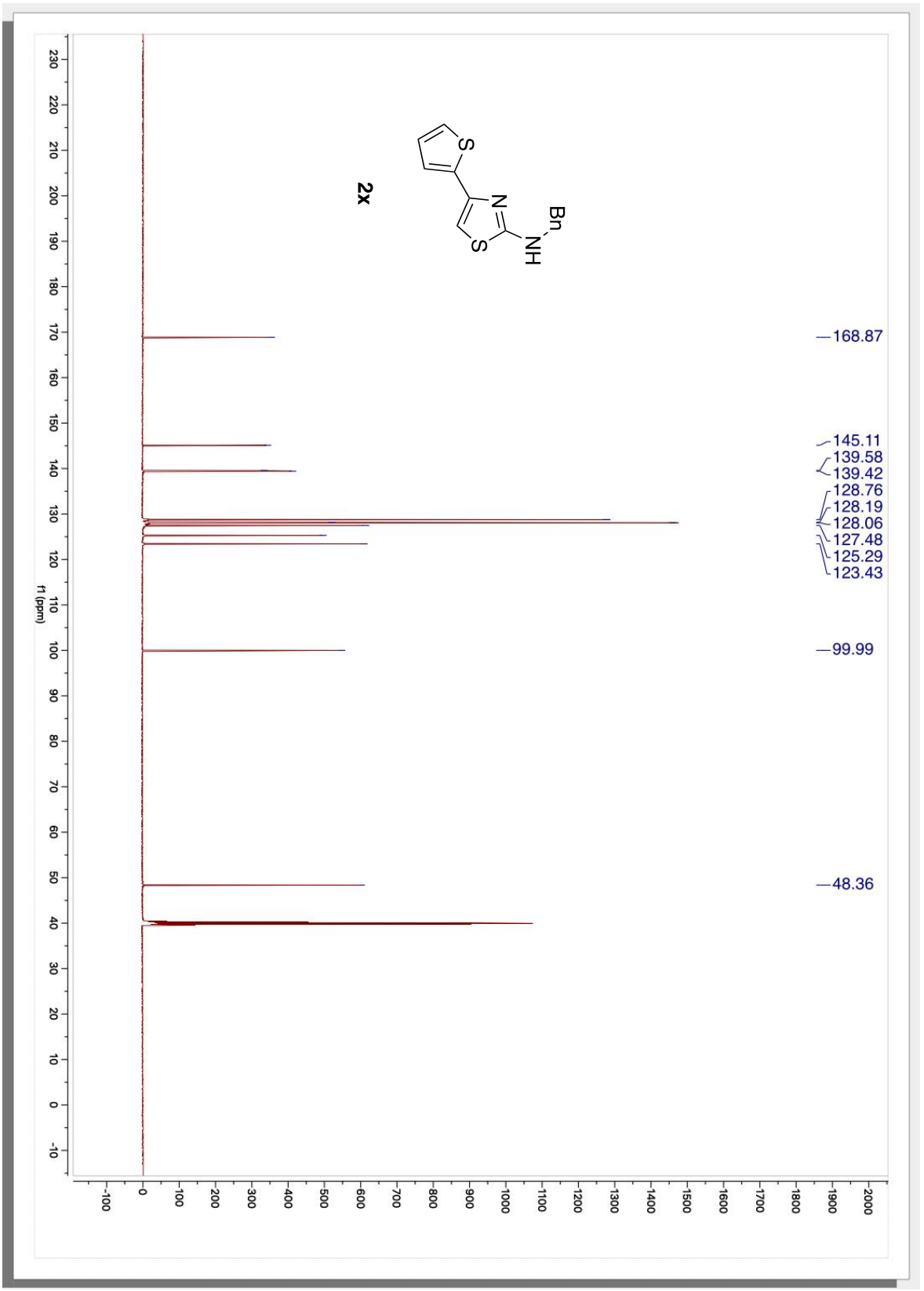

Figure S96: ^{13}C NMR spectrum of **2x** in d_6-DMSO (151 MHz)

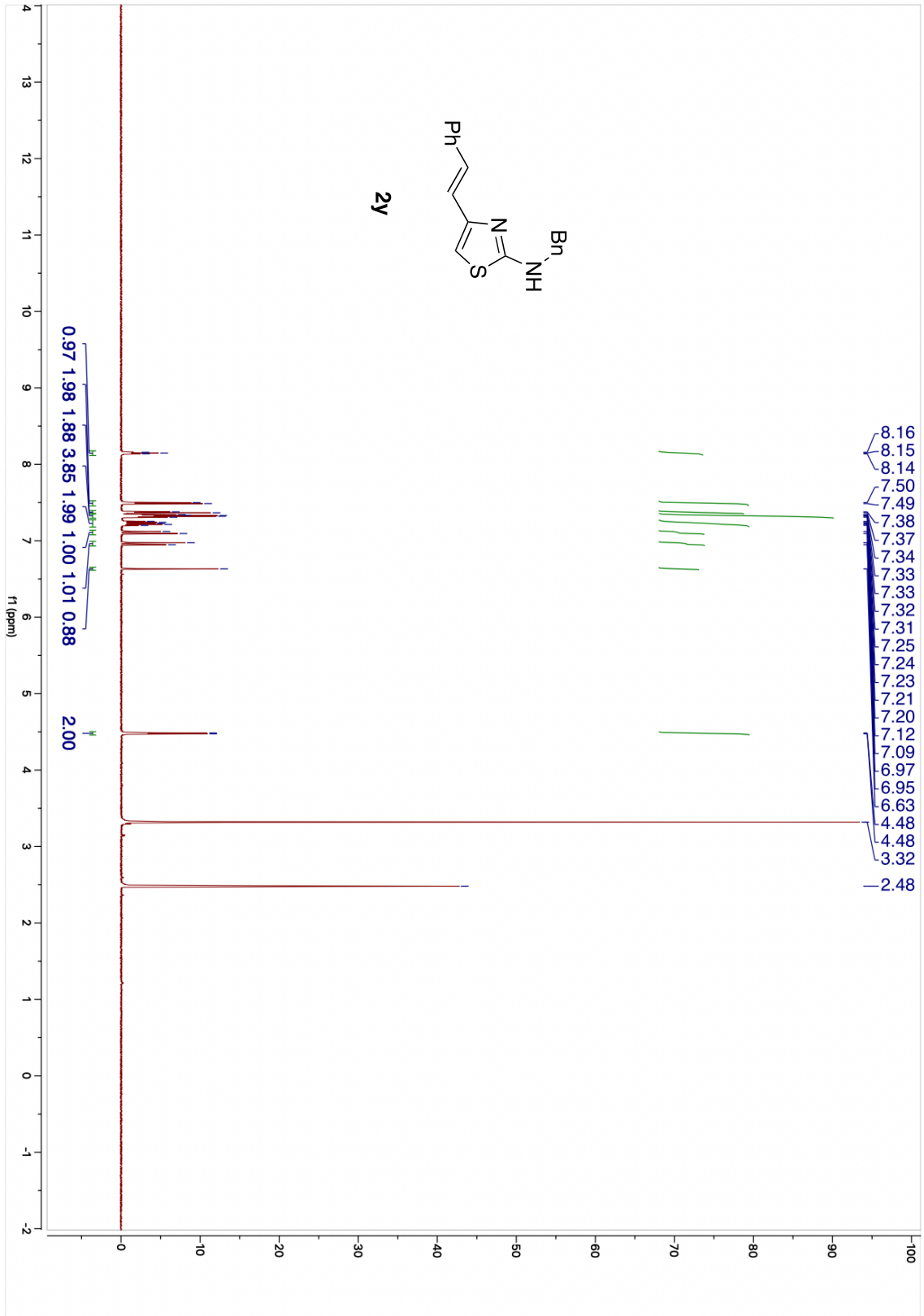

Figure S97: ^{1}H NMR spectrum of **2y** in d_6-DMSO (600 MHz)

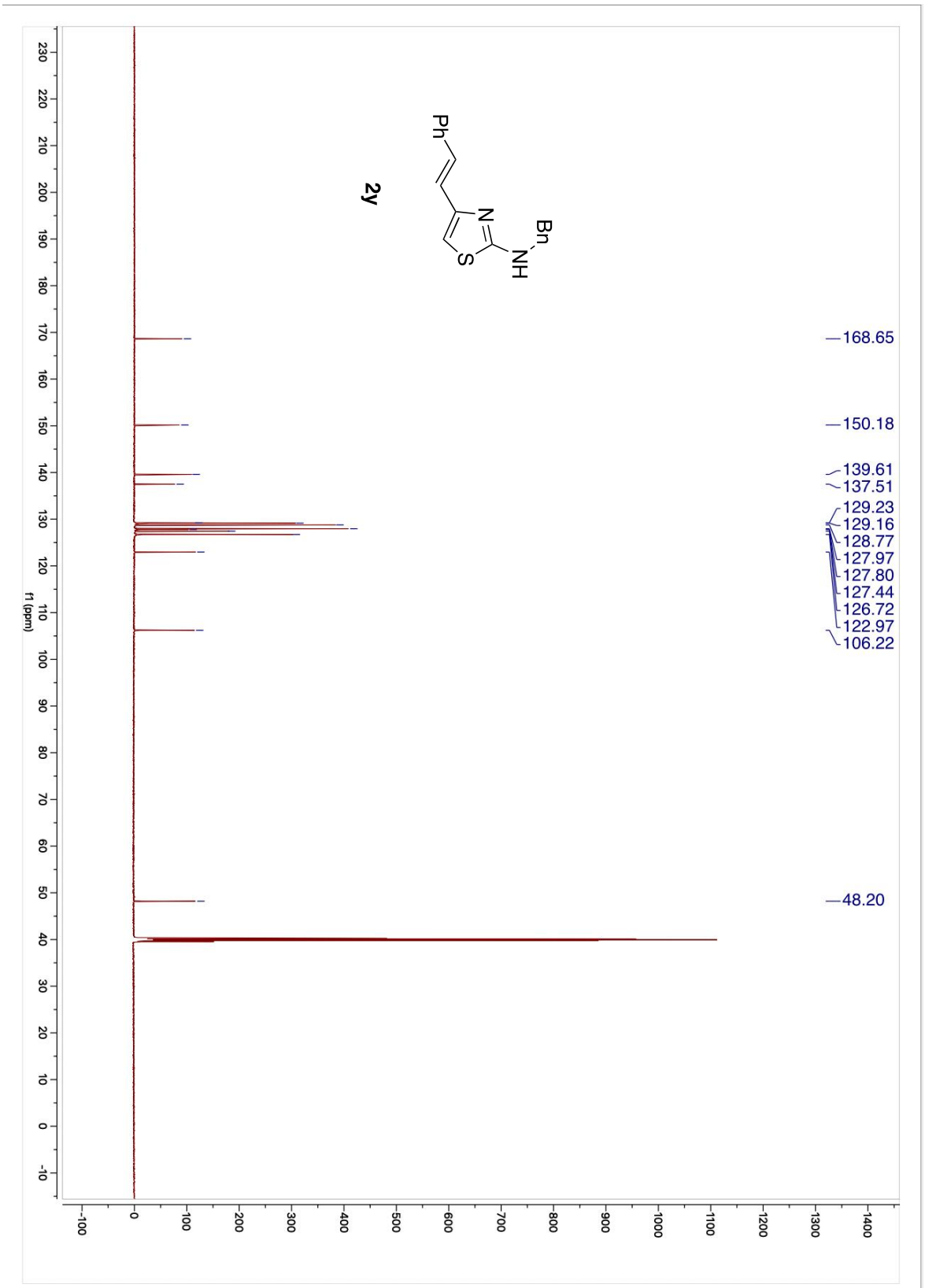

Figure S98: ^{13}C NMR spectrum of **2y** in d_6-DMSO (151 MHz)

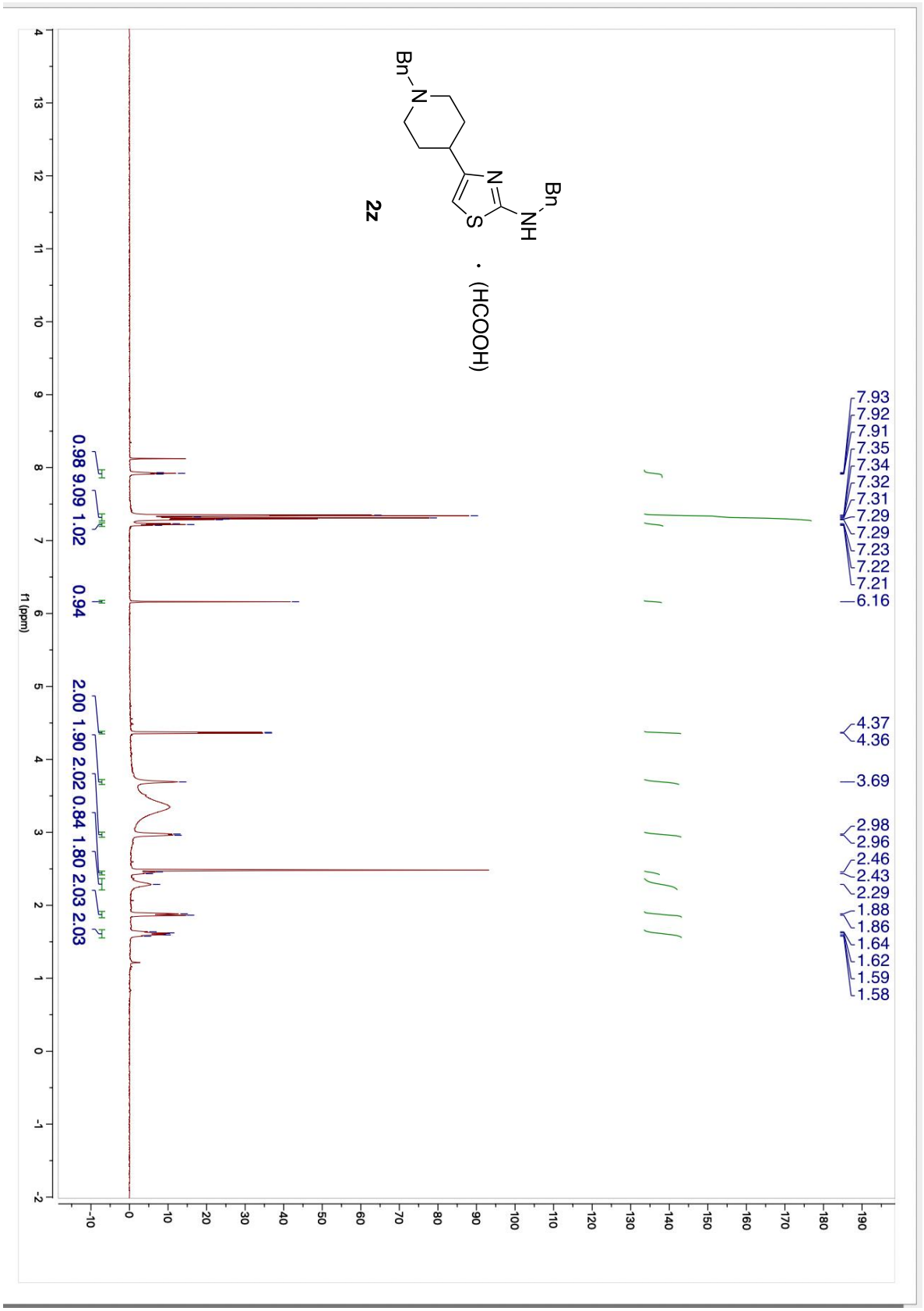

Figure S99: ^{1}H NMR spectrum of **2z** in d_6-DMSO (600 MHz)

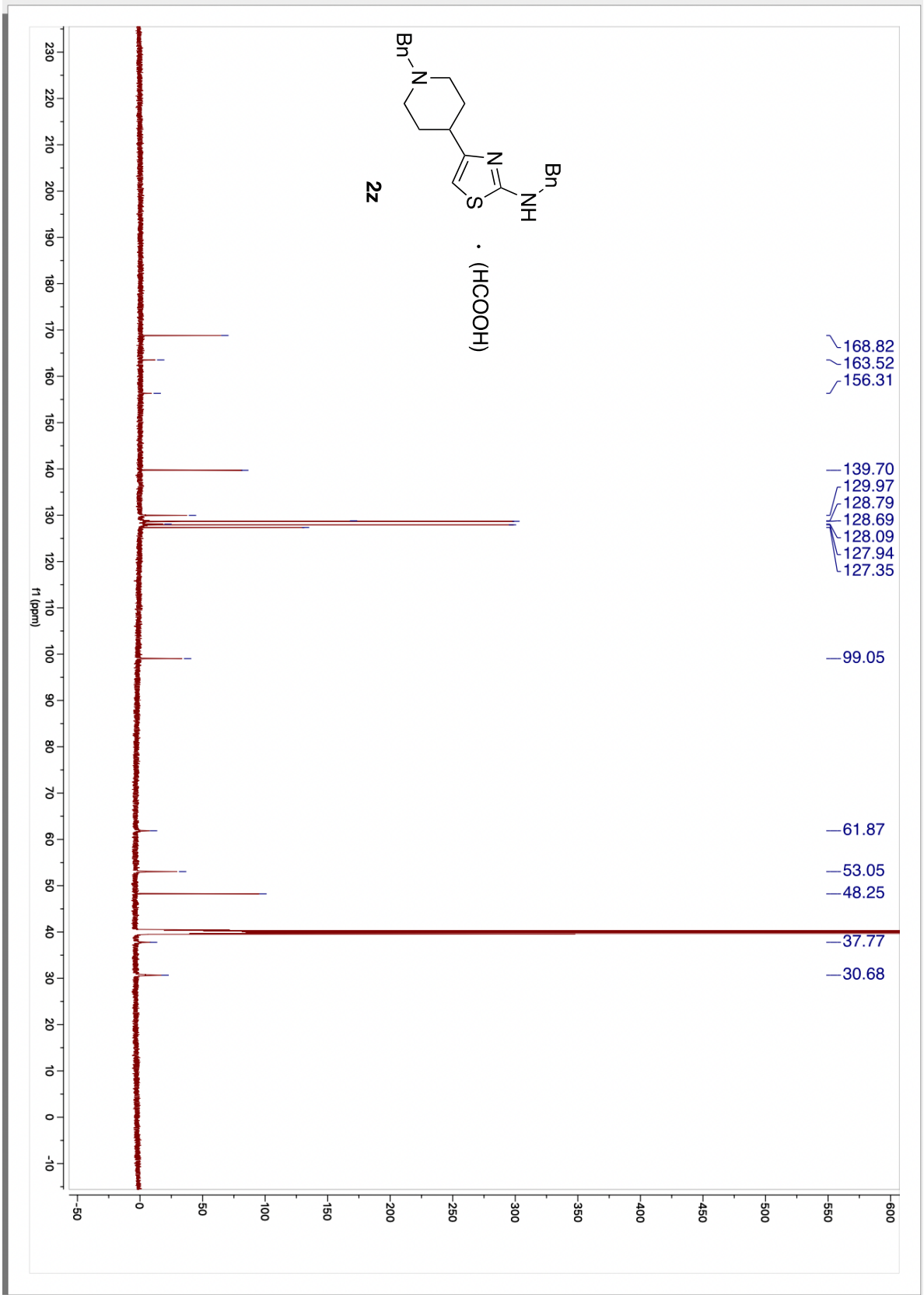

Figure S100: ^{13}C NMR spectrum of **2z** in d_6-DMSO (151 MHz)

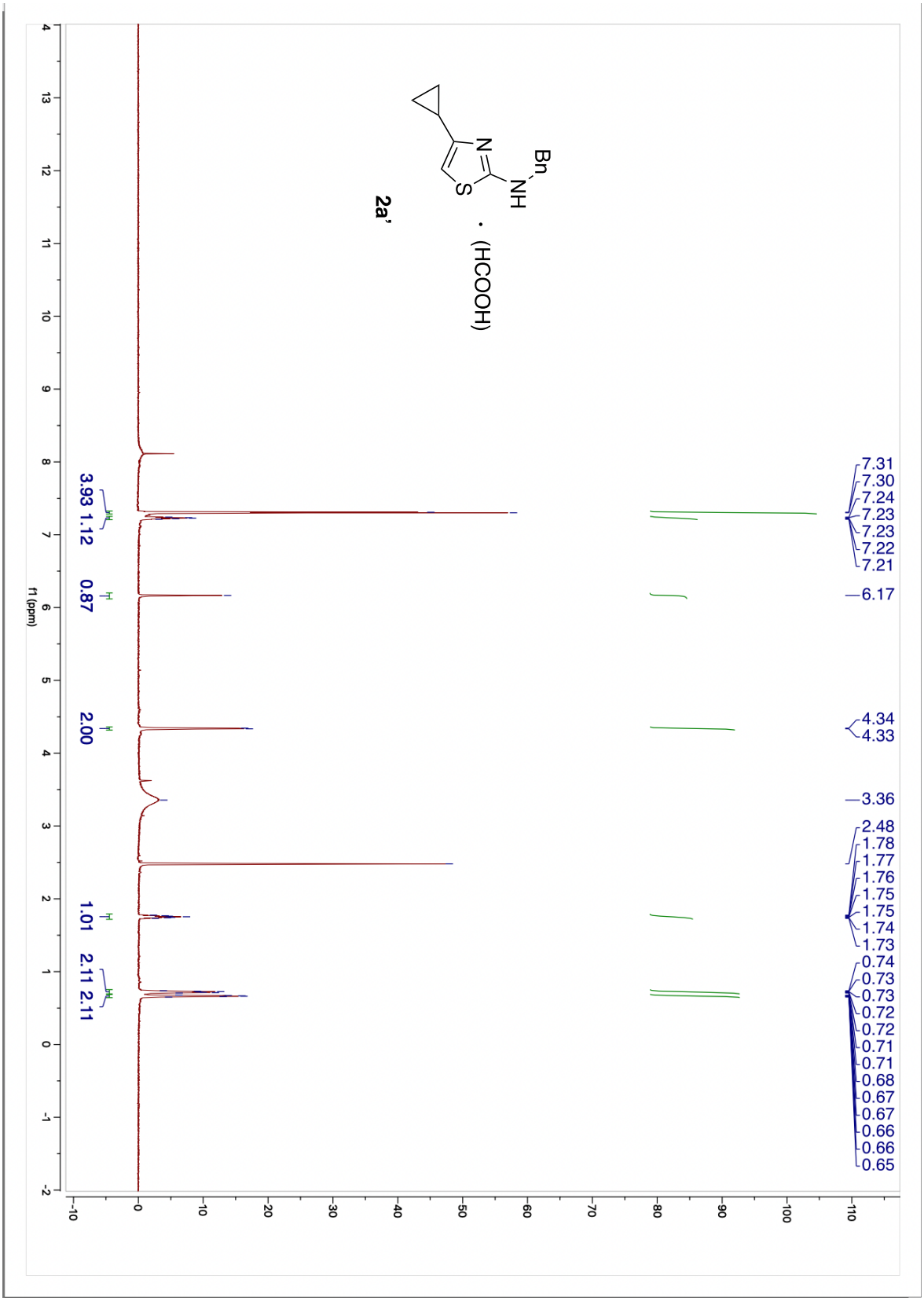

Figure S101: ^{1}H NMR spectrum of **2a'** in d_6-DMSO (600 MHz)

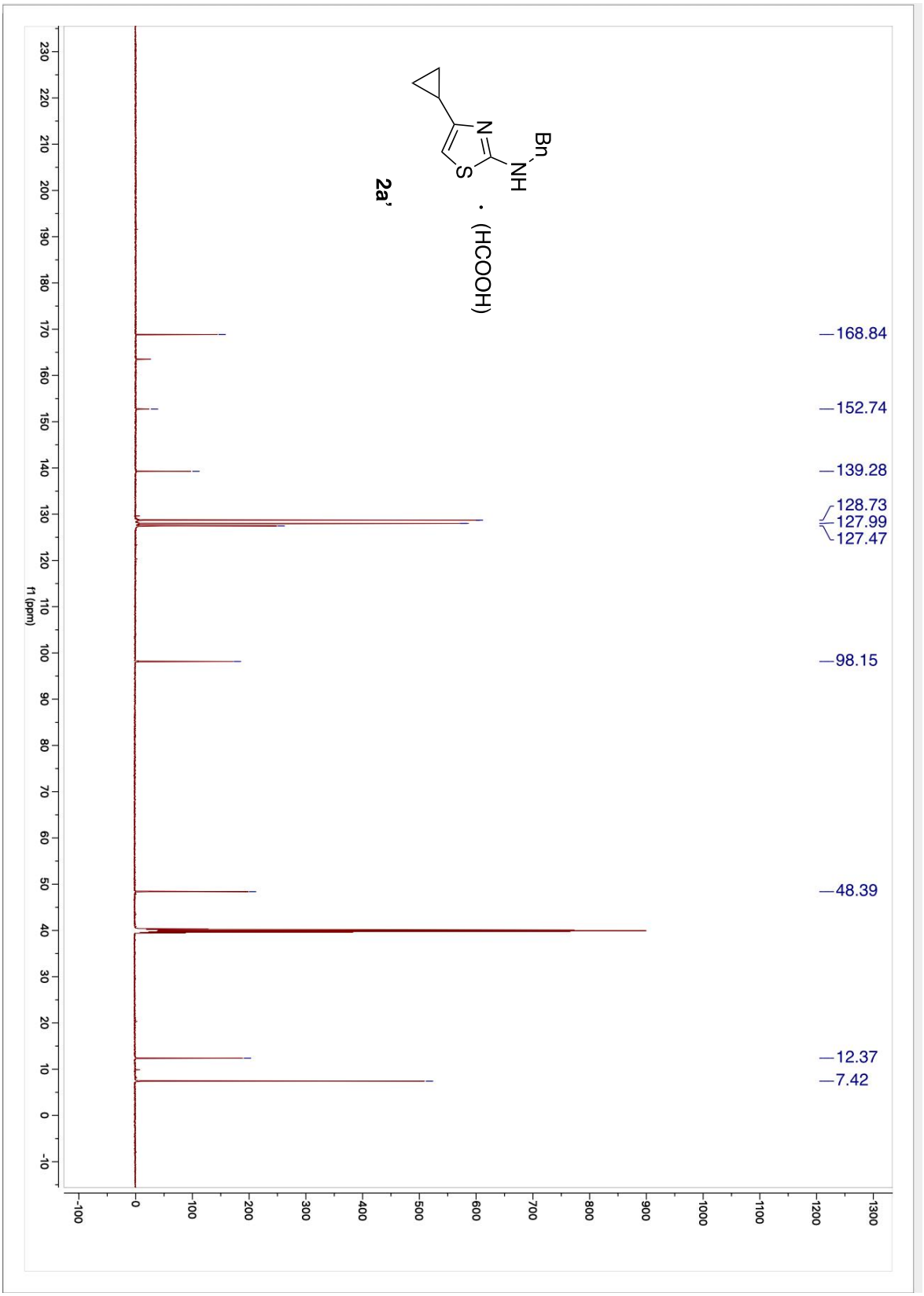

Figure S102: ^{13}C NMR spectrum of **2a'** in d_6-DMSO (151 MHz)

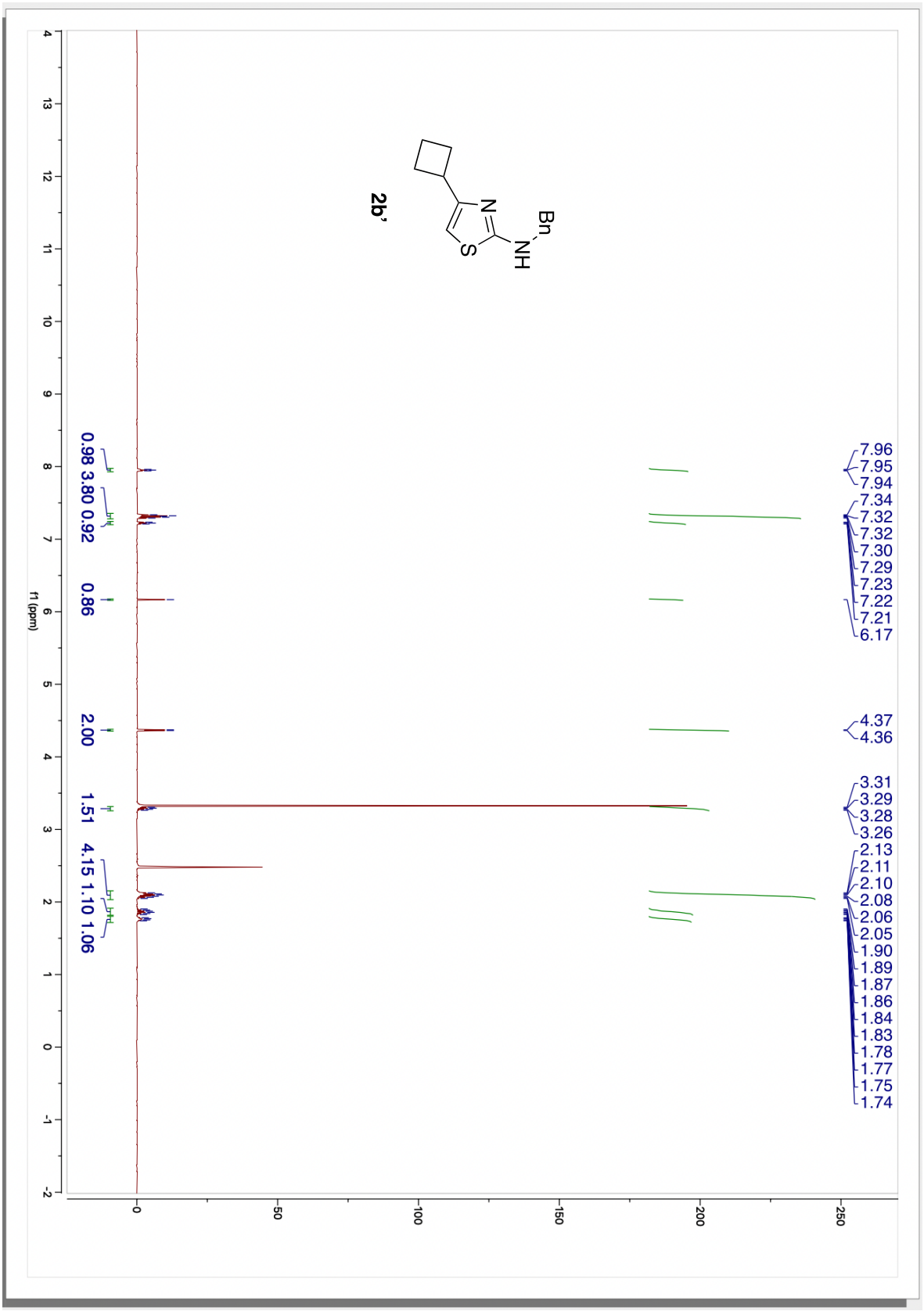

Figure S103: ^{1}H NMR spectrum of **2b'** in d_6-DMSO (600 MHz)

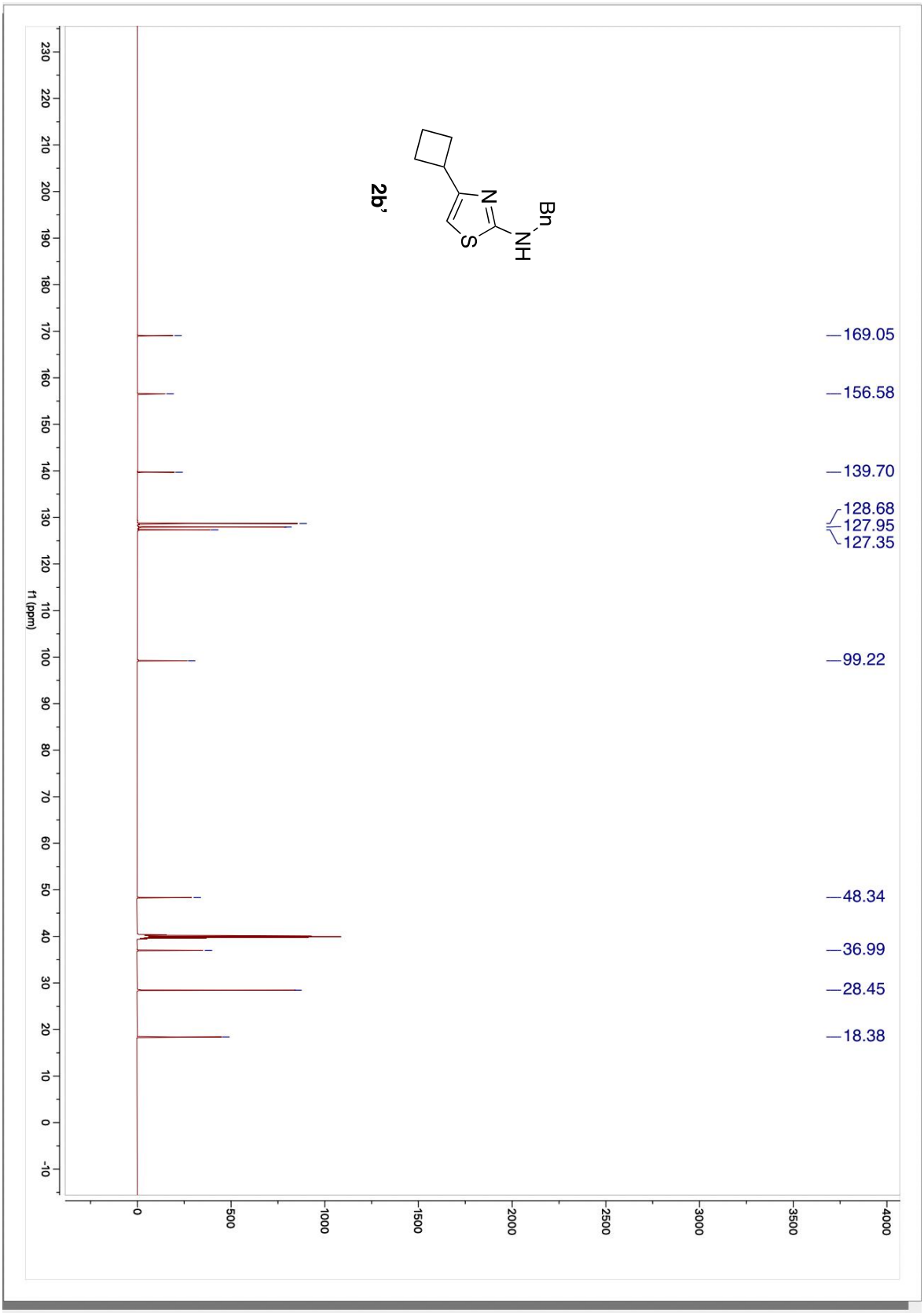

Figure S104: ^{13}C NMR spectrum of **2b'** in d_6-DMSO (151 MHz)

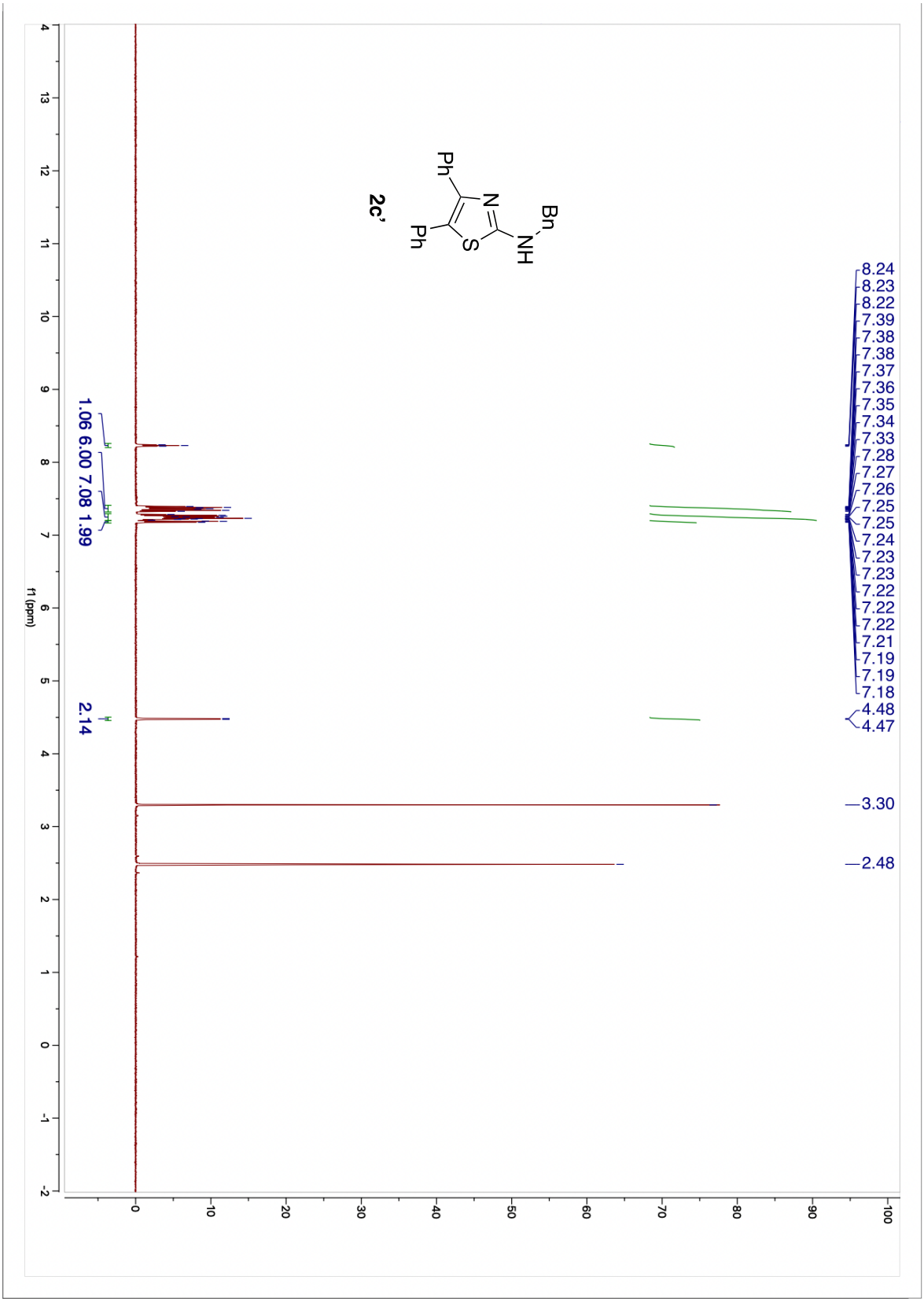

Figure S105: ^{1}H NMR spectrum of **2c'** in d_6-DMSO (600 MHz)

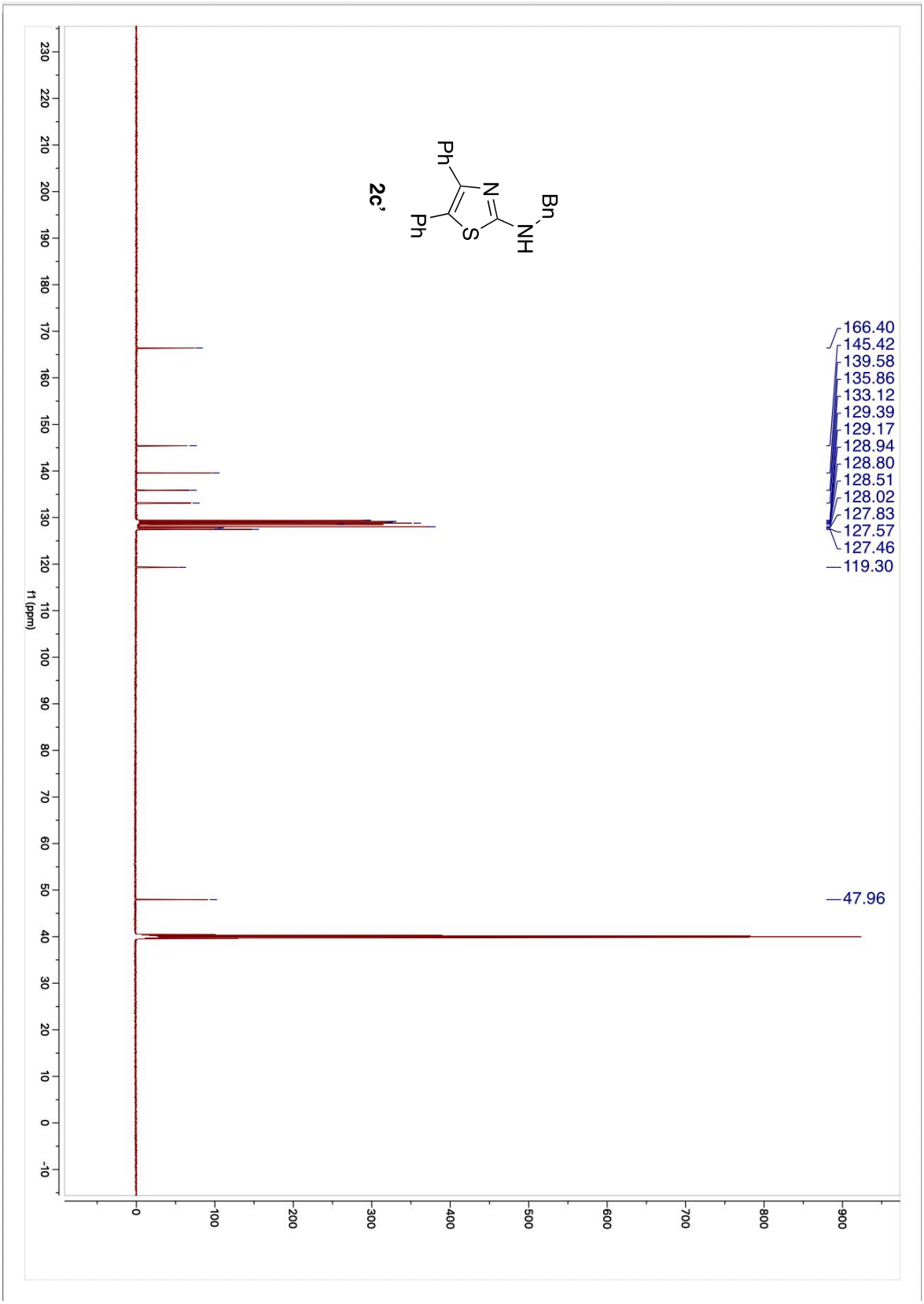

Figure S106: ^{13}C NMR spectrum of **2c'** in d_6-DMSO (151 MHz)

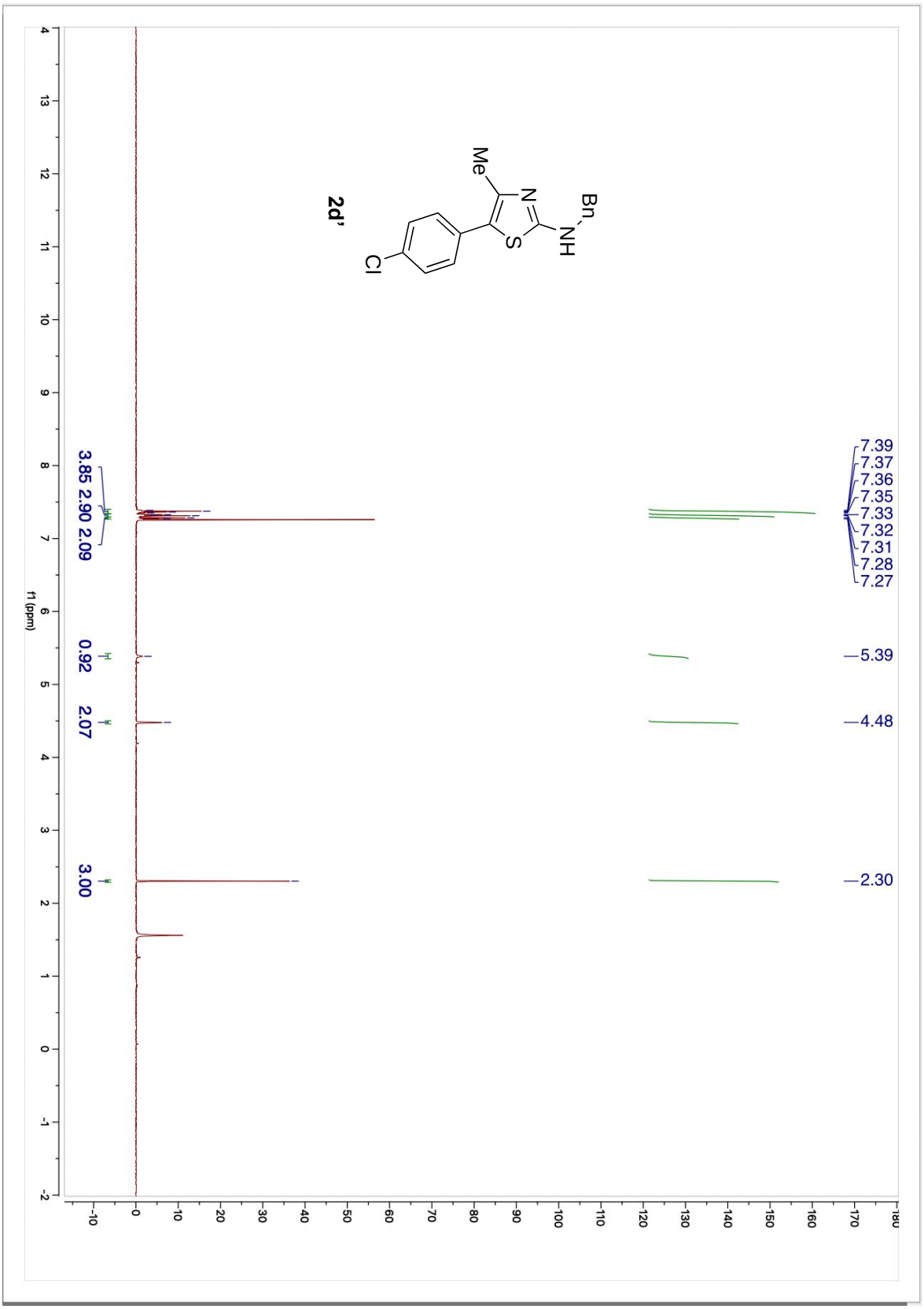

Figure S107: ^{1}H NMR spectrum of **2d'** in $CDCl_3$ (600 MHz)

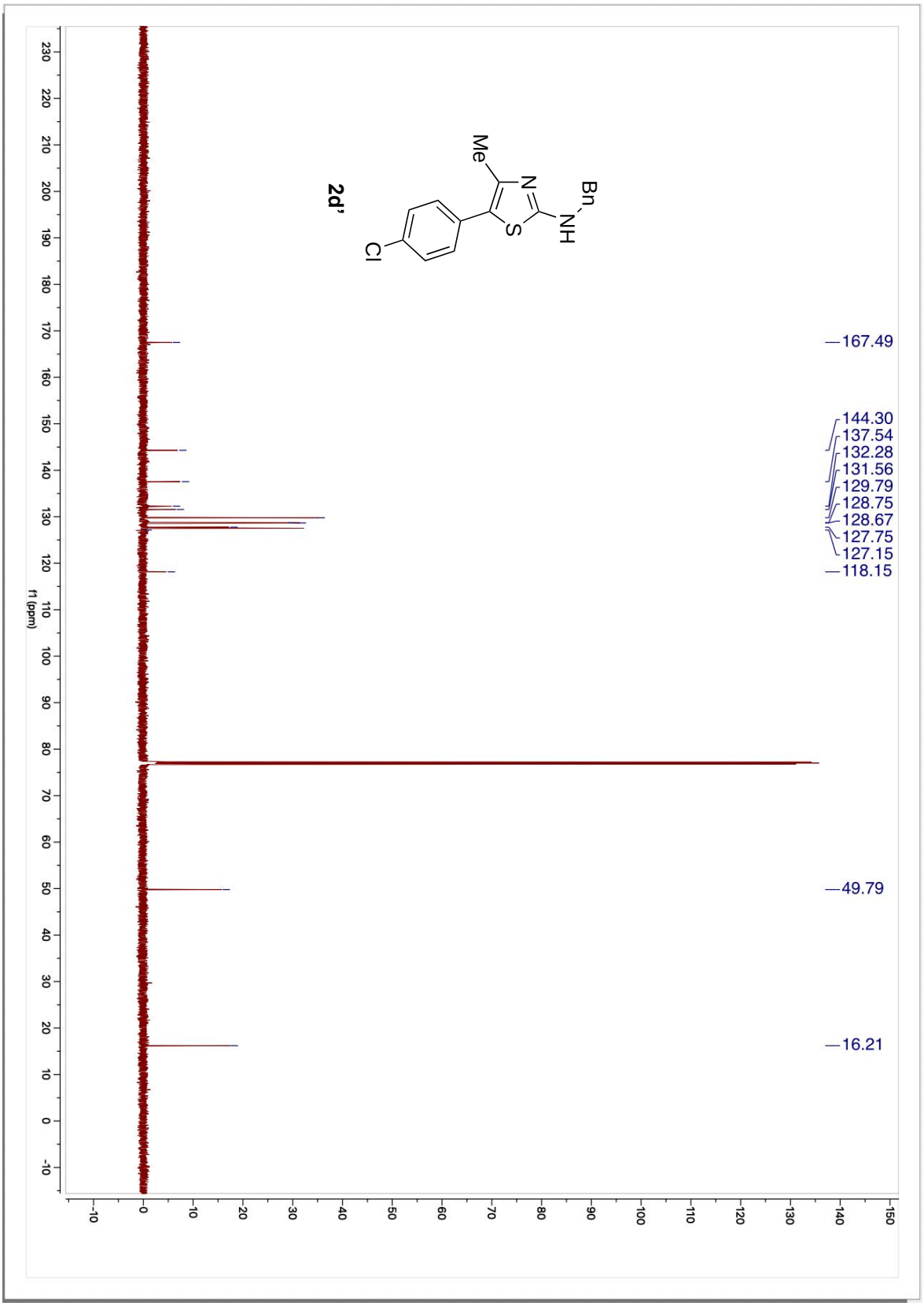

Figure S108: ^{13}C NMR spectrum of **2d'** in $CDCl_3$ (151 MHz)

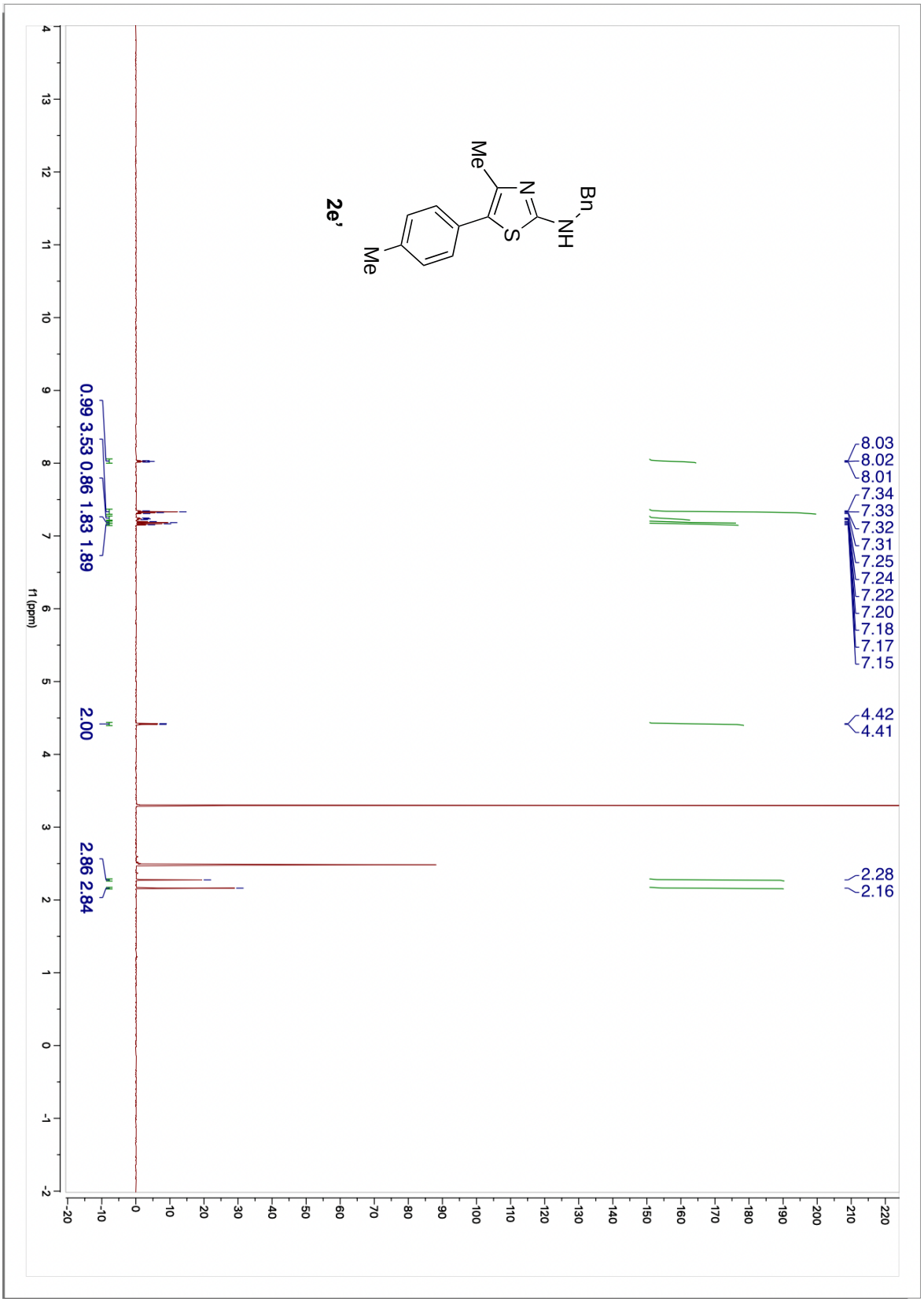

Figure S109: ^{1}H NMR spectrum of **2e'** in d_6-DMSO (600 MHz)

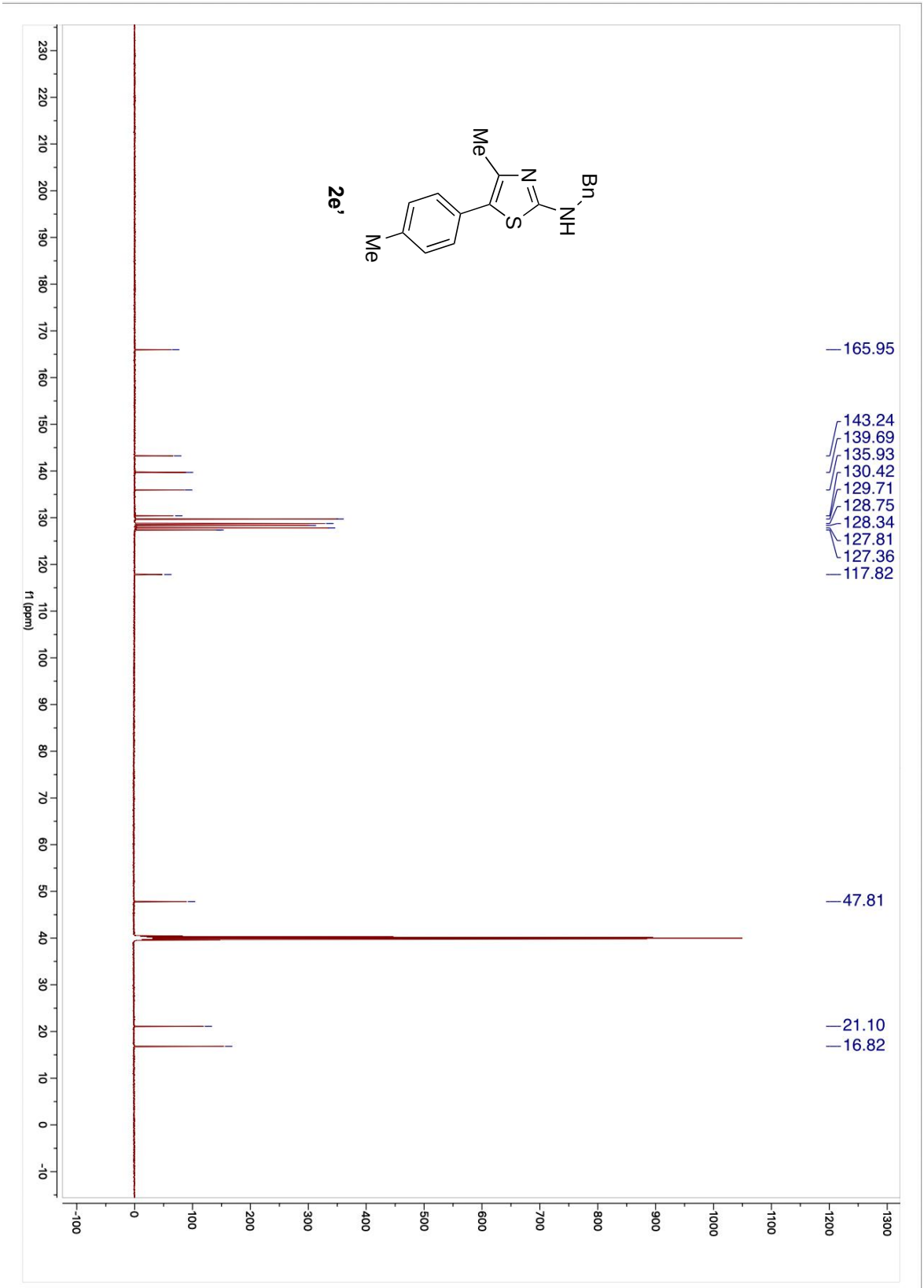

Figure S110: ^{13}C NMR spectrum of **2e'** in d_6-DMSO (151 MHz)

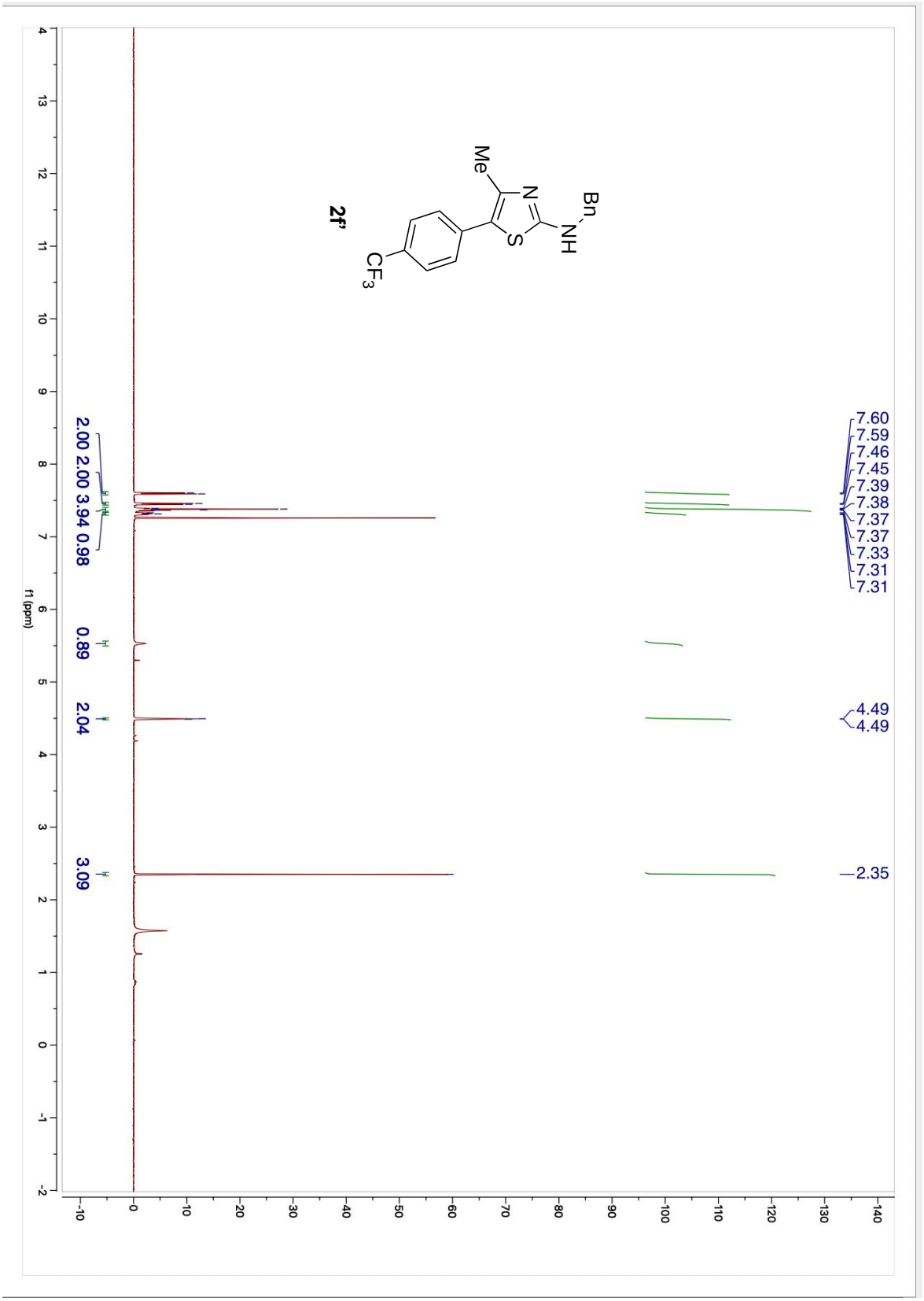

Figure S111: ^{1}H NMR spectrum of **2f'** in $CDCl_3$ (600 MHz)

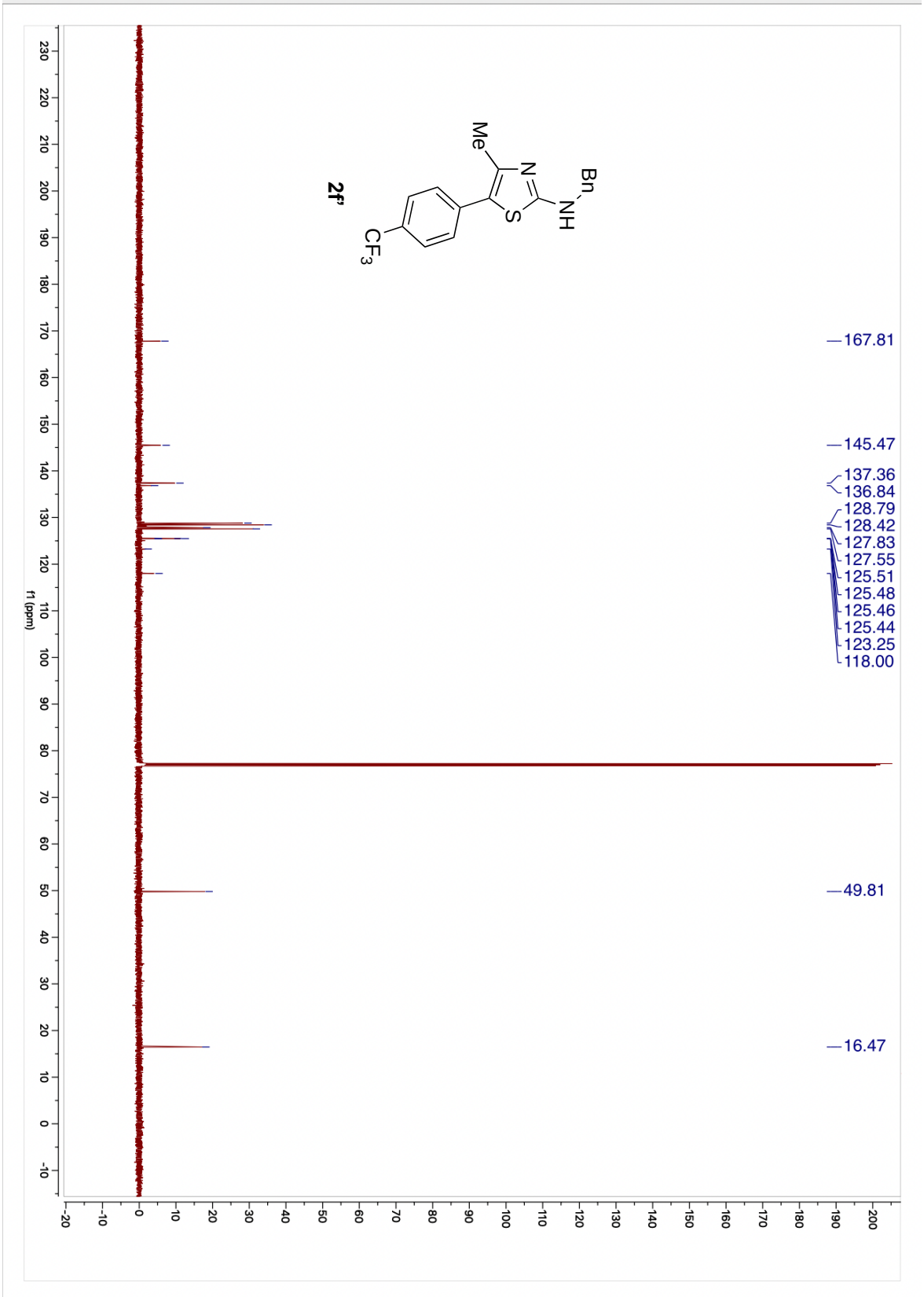

Figure S112: ^{13}C NMR spectrum of **2f'** in $CDCl_3$ (151 MHz)

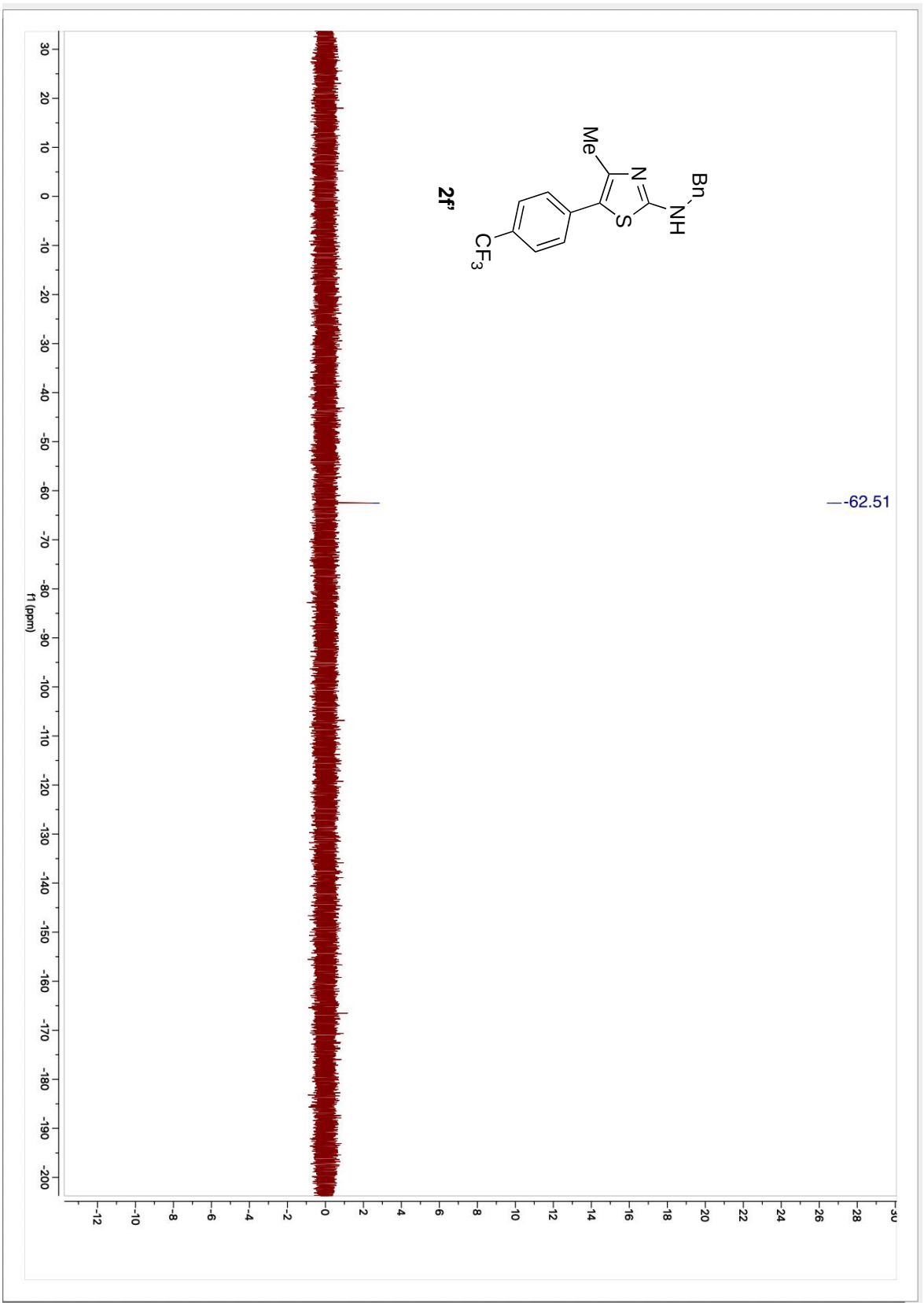

Figure S113: ^{19}F NMR spectrum of **2f'** in d_6-DMSO (376 MHz)

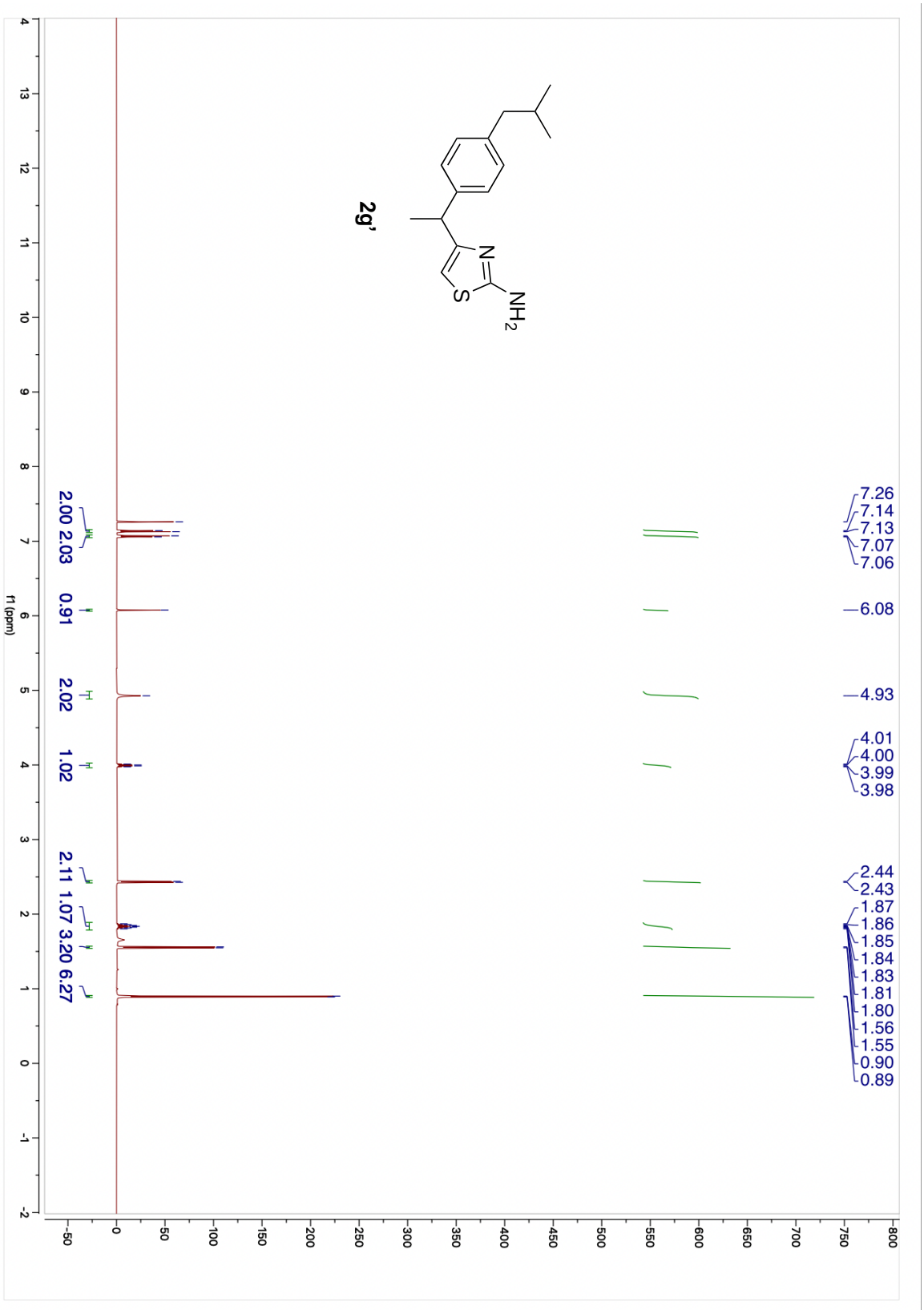

Figure S114: ^{1}H NMR spectrum of **2g'** in $CDCl_3$ (600 MHz)

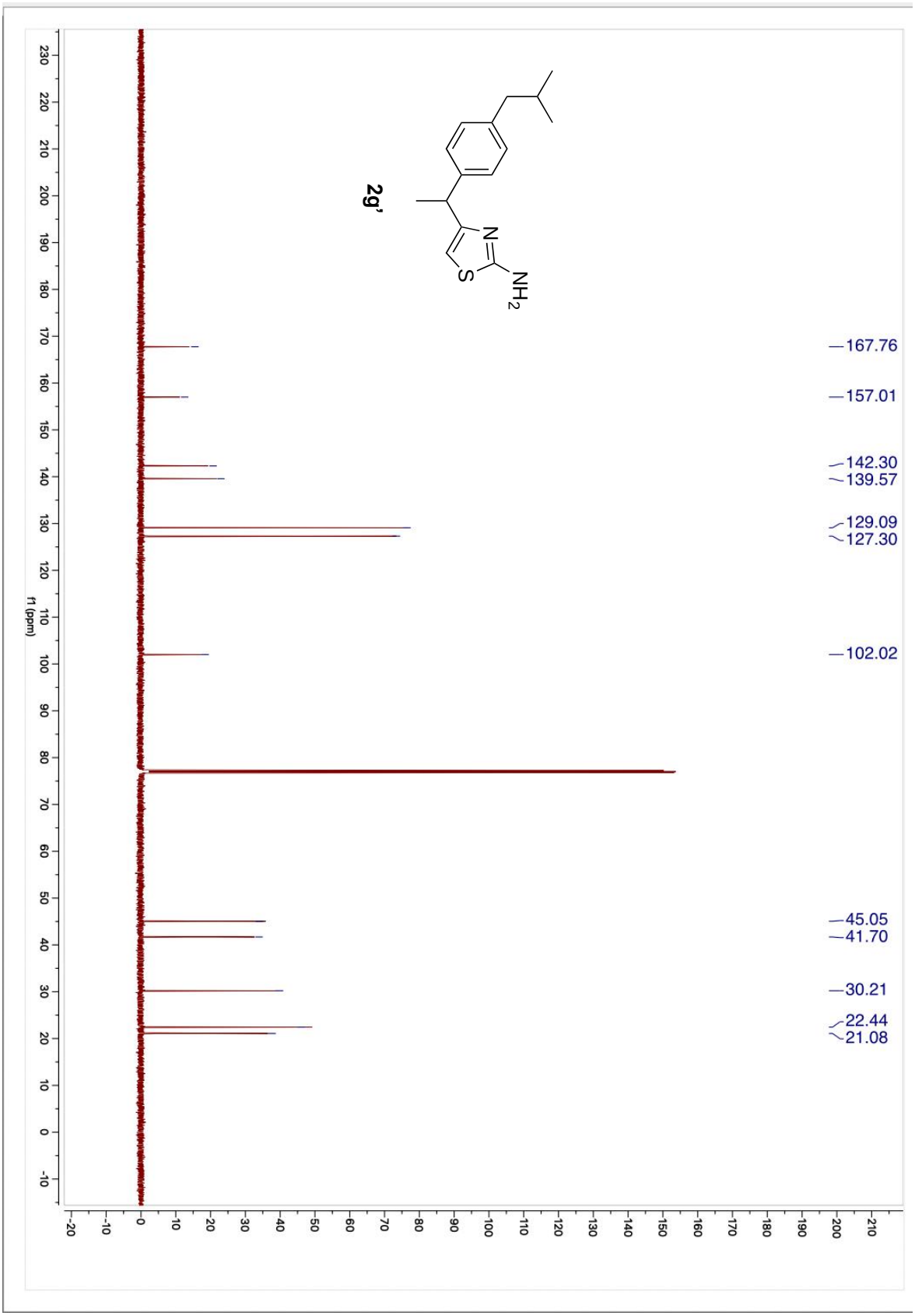

Figure S115: ^{1}H NMR spectrum of **2g'** in $CDCl_3$ (600 MHz)

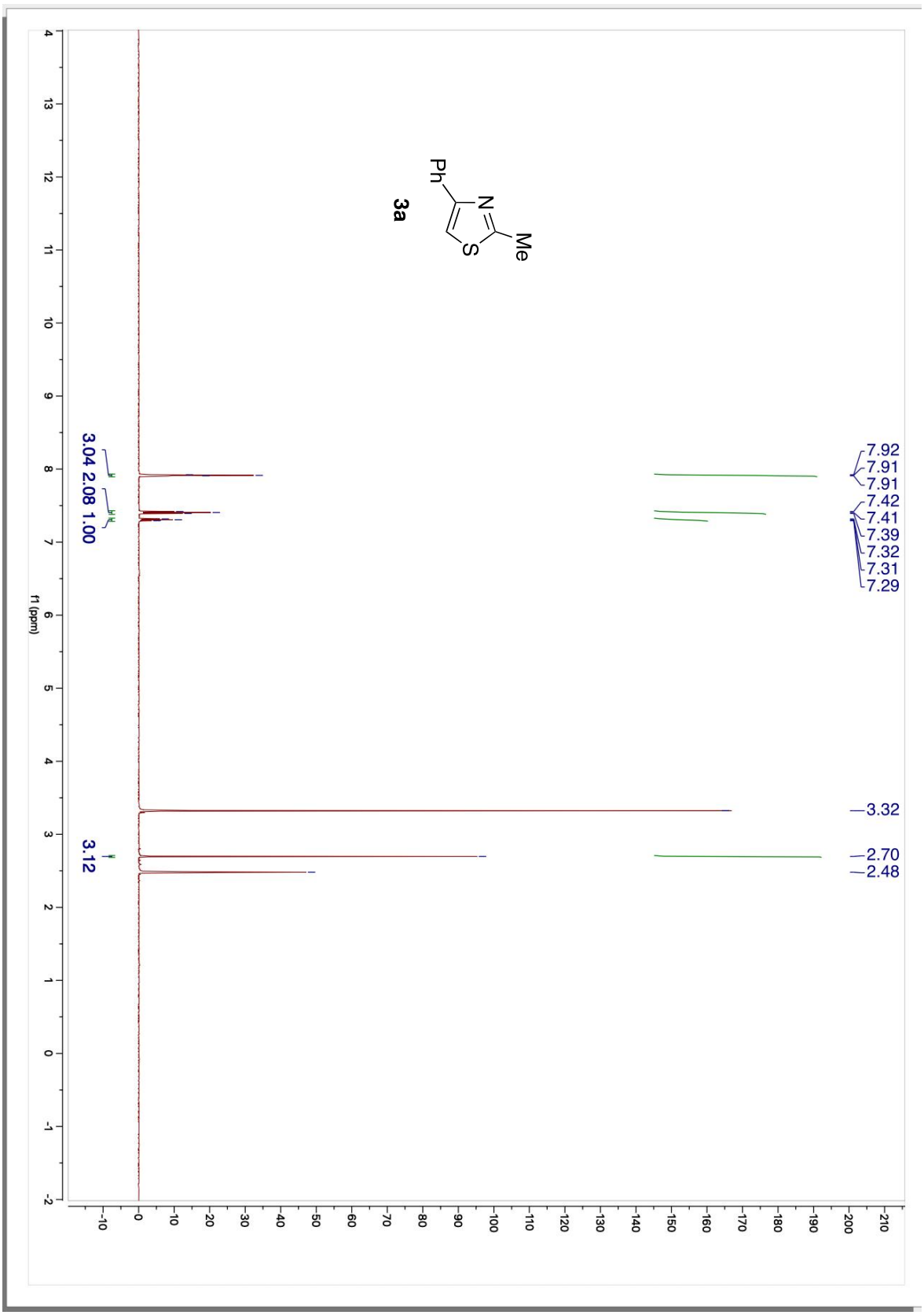

Figure S116: ^{1}H NMR spectrum of **3a** in d_6-DMSO (600 MHz)

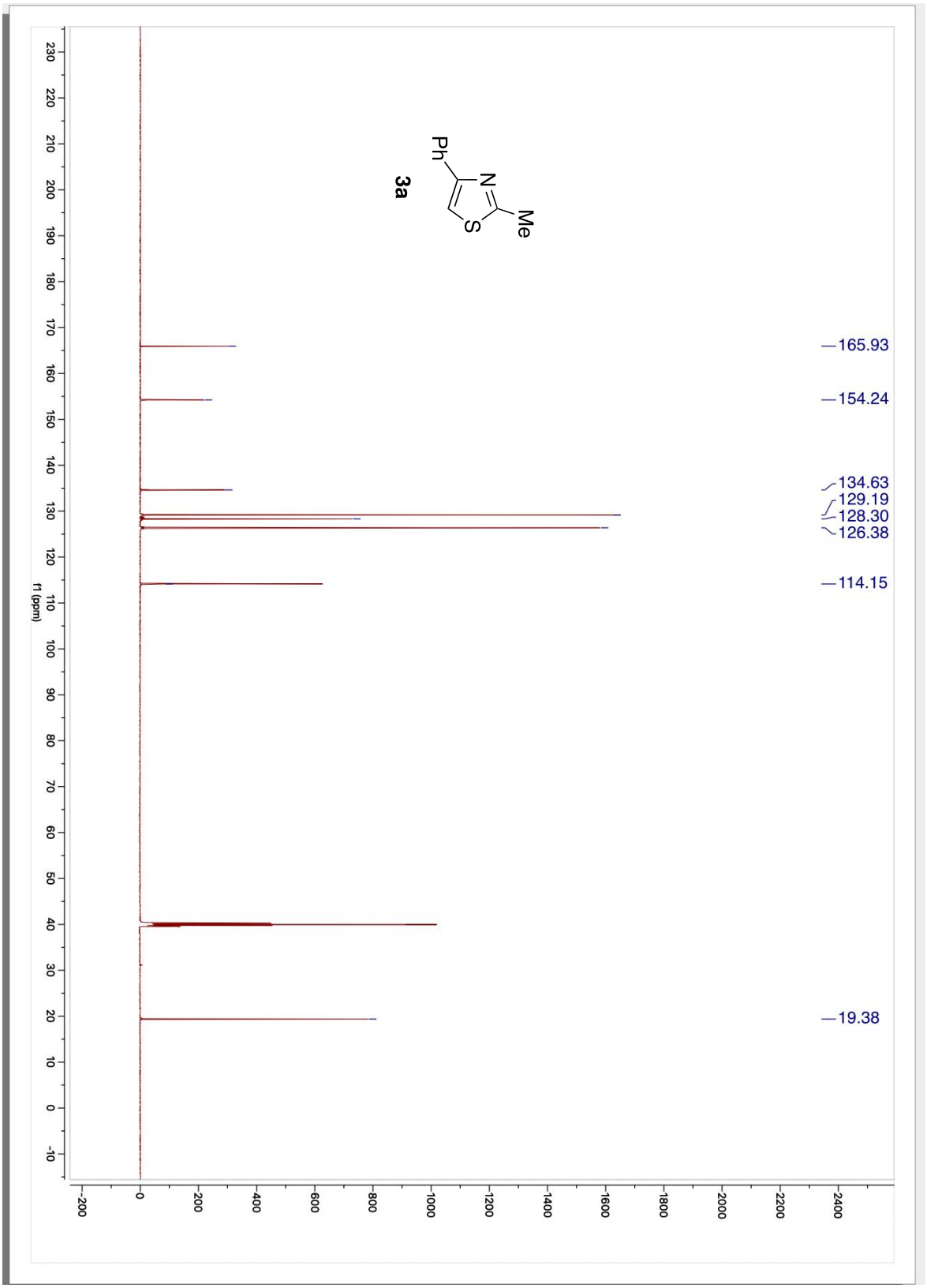

Figure S117: ^{13}C NMR spectrum of **3a** in d_6-DMSO (151 MHz)

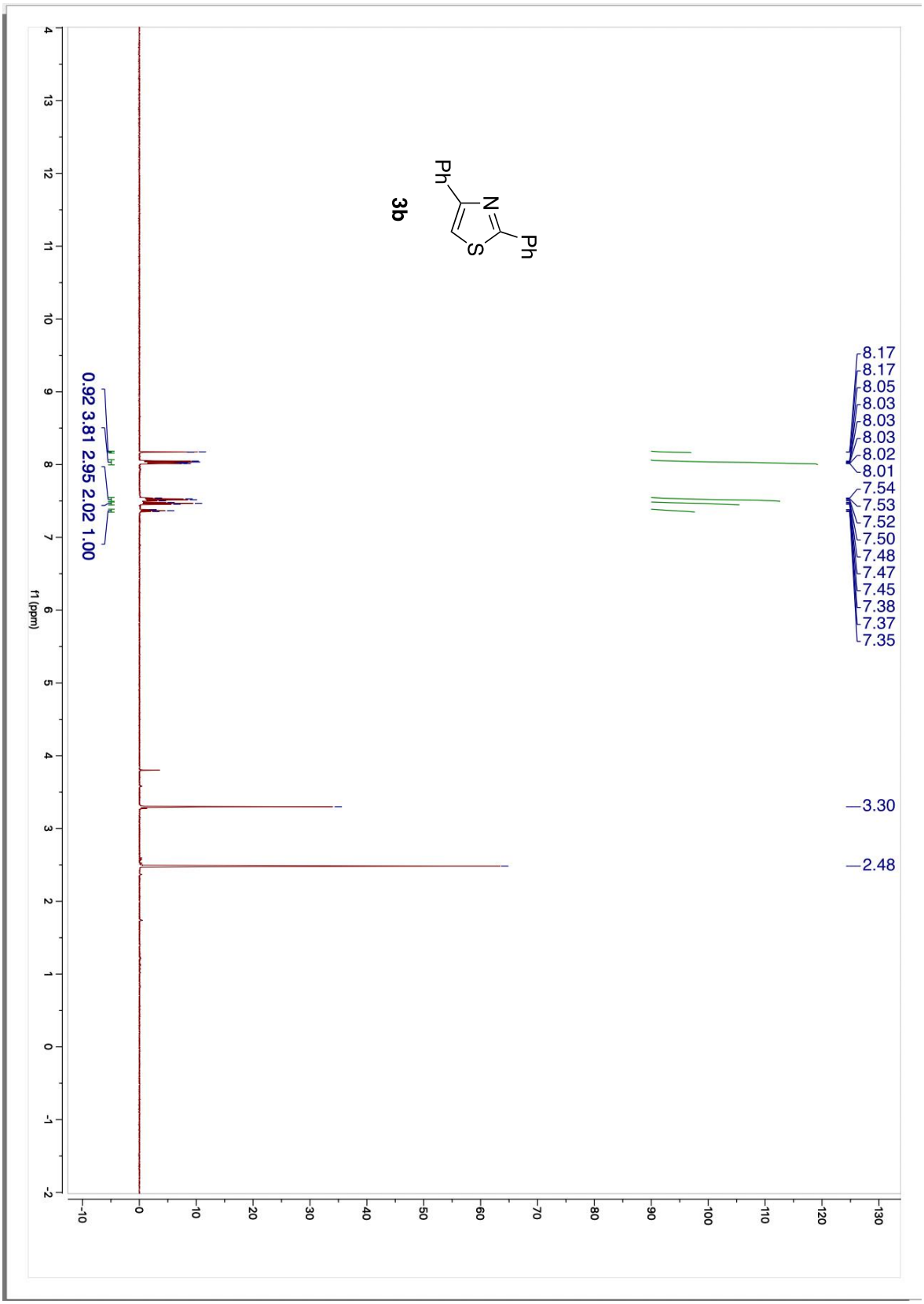

Figure S118: ^{1}H NMR spectrum of **3b** in d_6-DMSO (600 MHz)

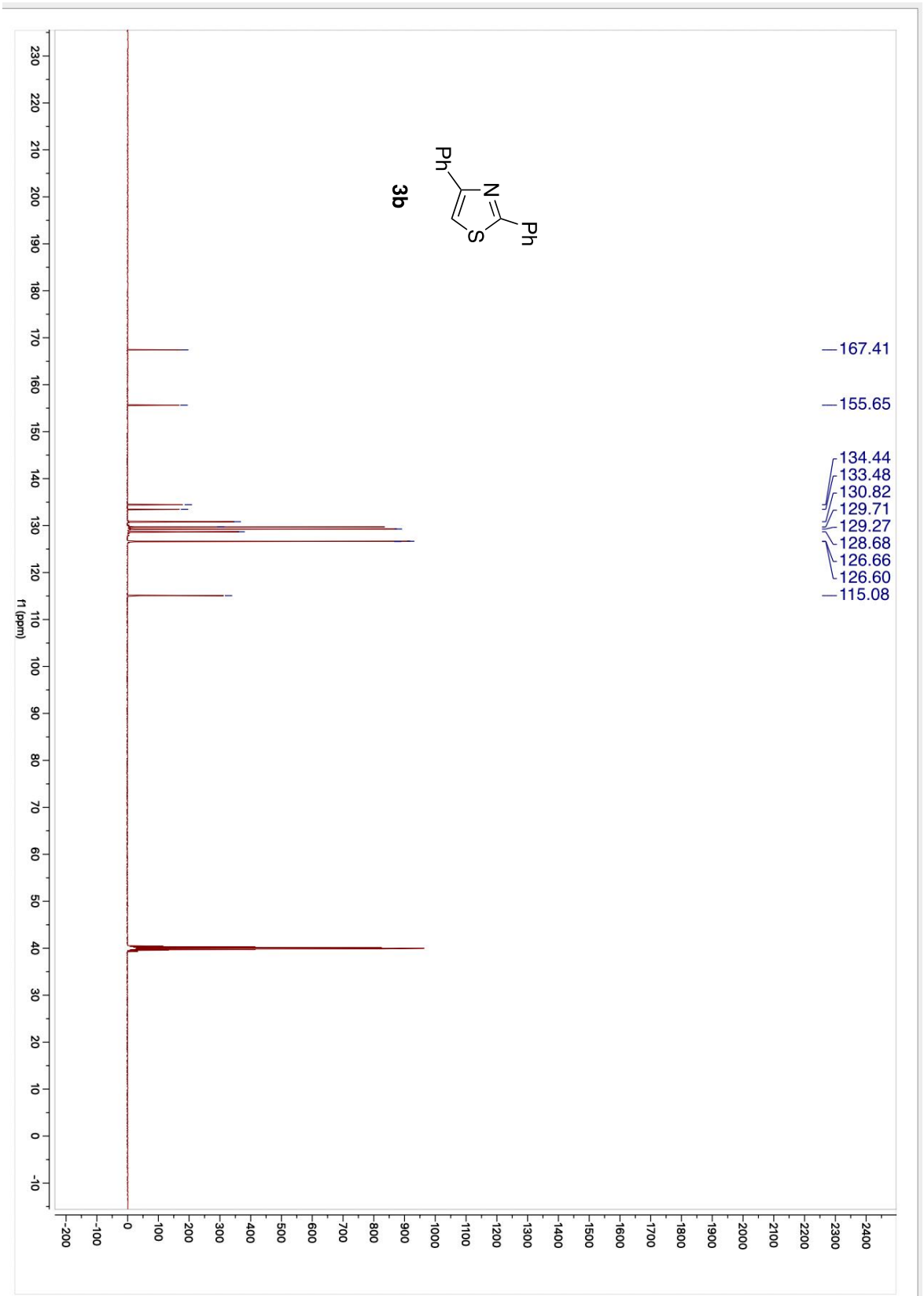

Figure S119: ^{13}C NMR spectrum of **3b** in d_6-DMSO (151 MHz)

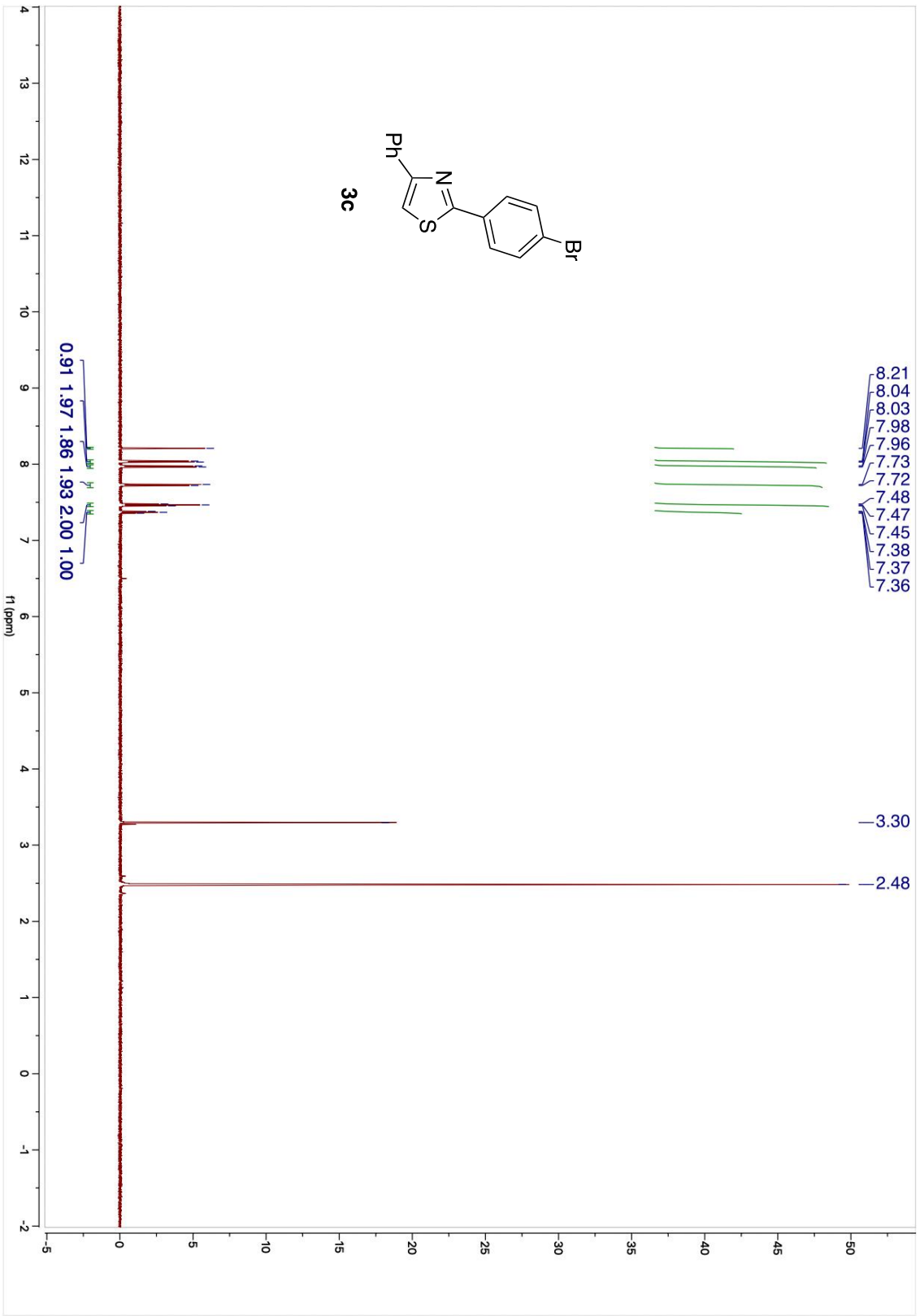

Figure S120: ^{1}H NMR spectrum of **3c** in d_6-DMSO (600 MHz)

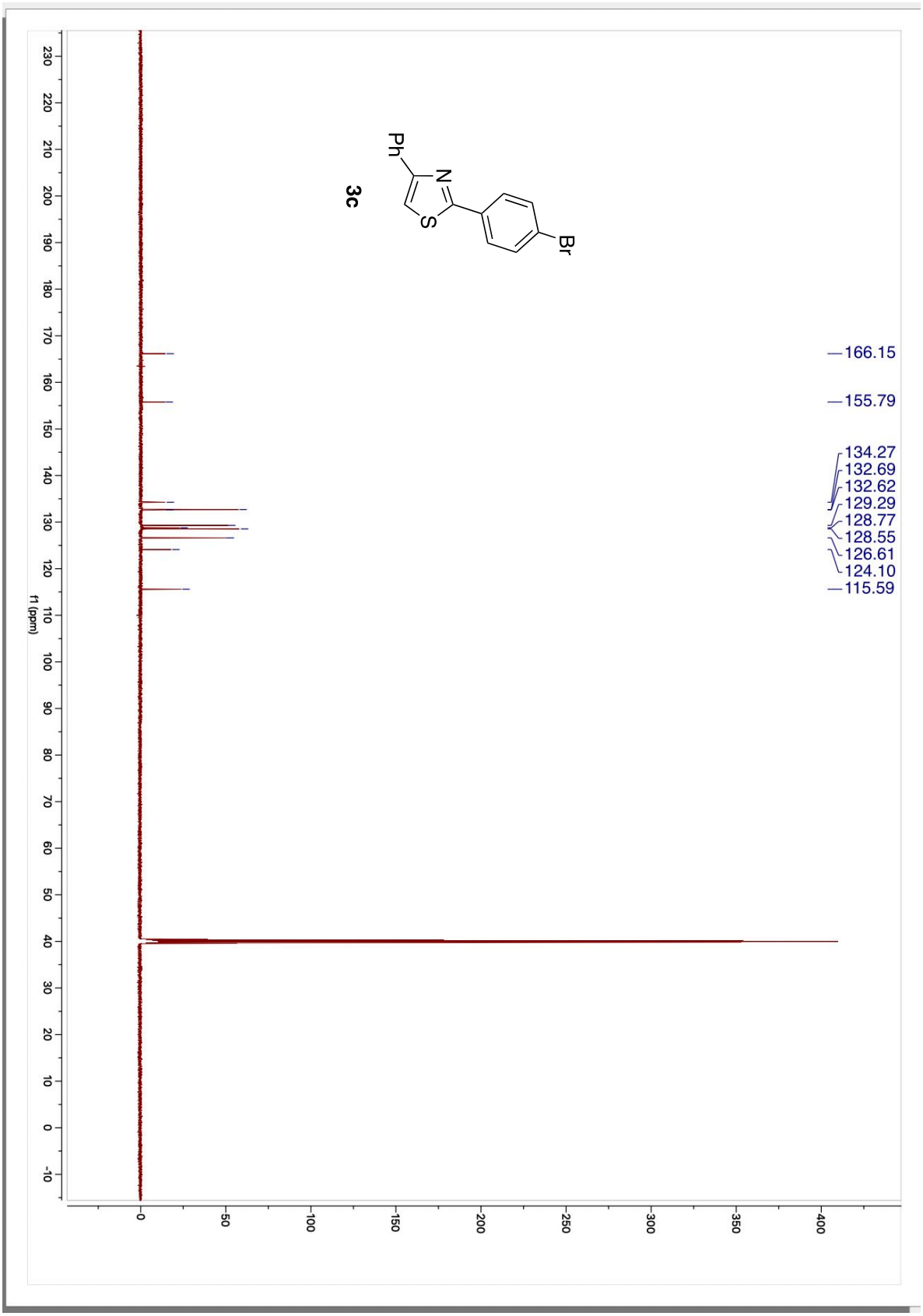

Figure S121: ^{13}C NMR spectrum of **3c** in d_6-DMSO (151 MHz)

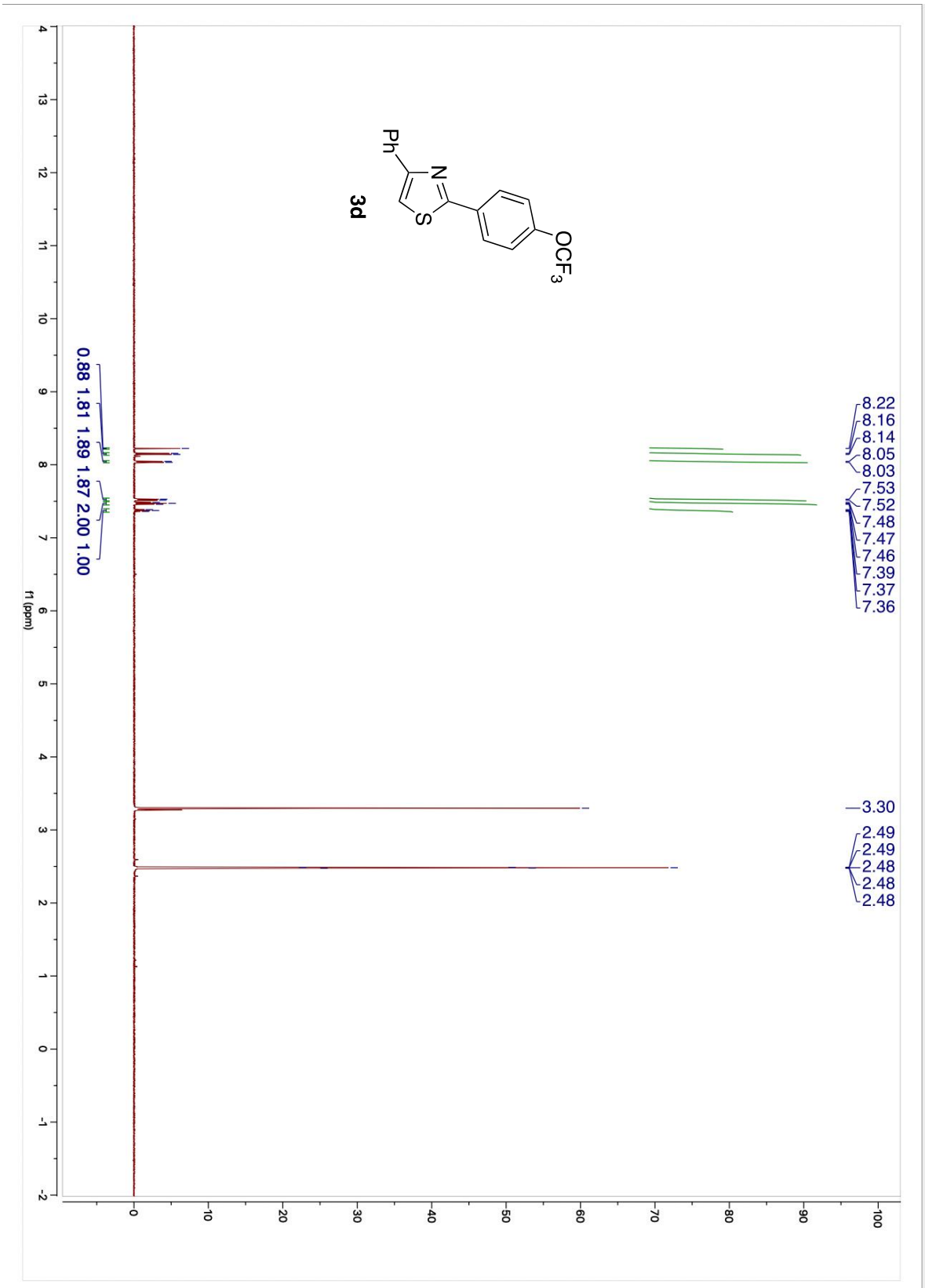

Figure S122: ^{1}H NMR spectrum of **3d** in d_6-DMSO (600 MHz)

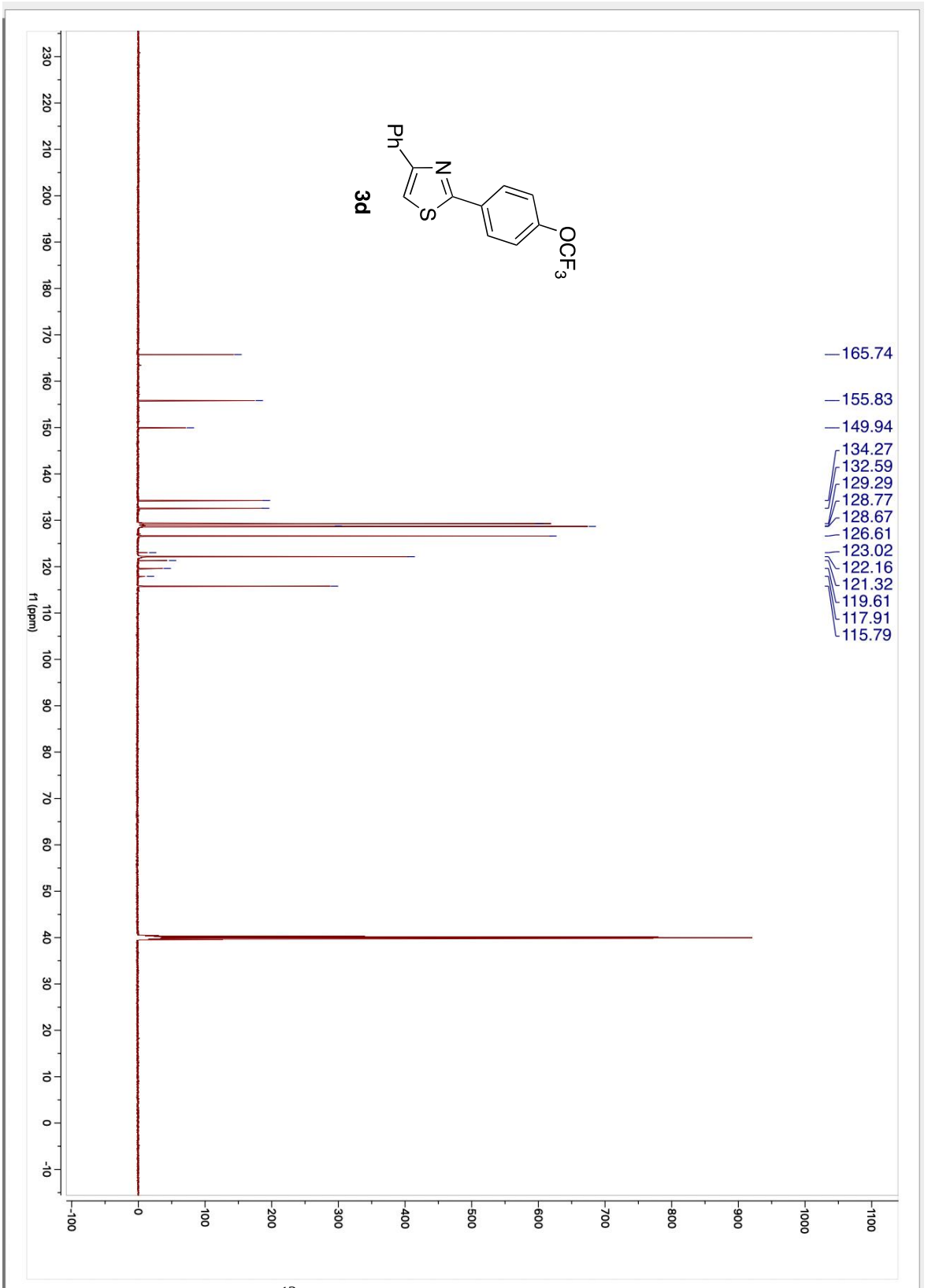

Figure S123: ^{13}C NMR spectrum of **3d** in d_6-DMSO (151 MHz)

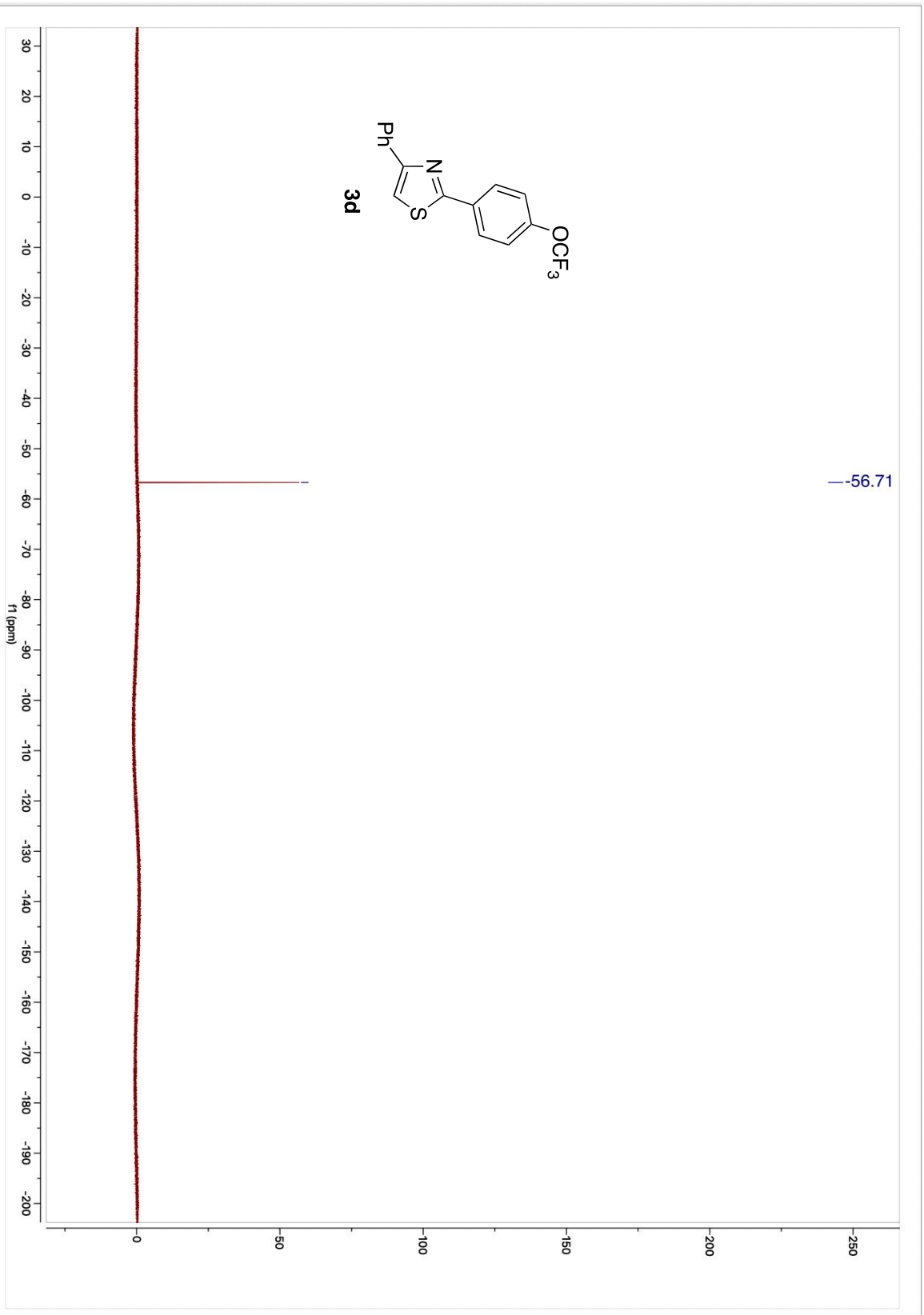

Figure S124: ^{19}F NMR spectrum of **3d** in d_6-DMSO (376 MHz)

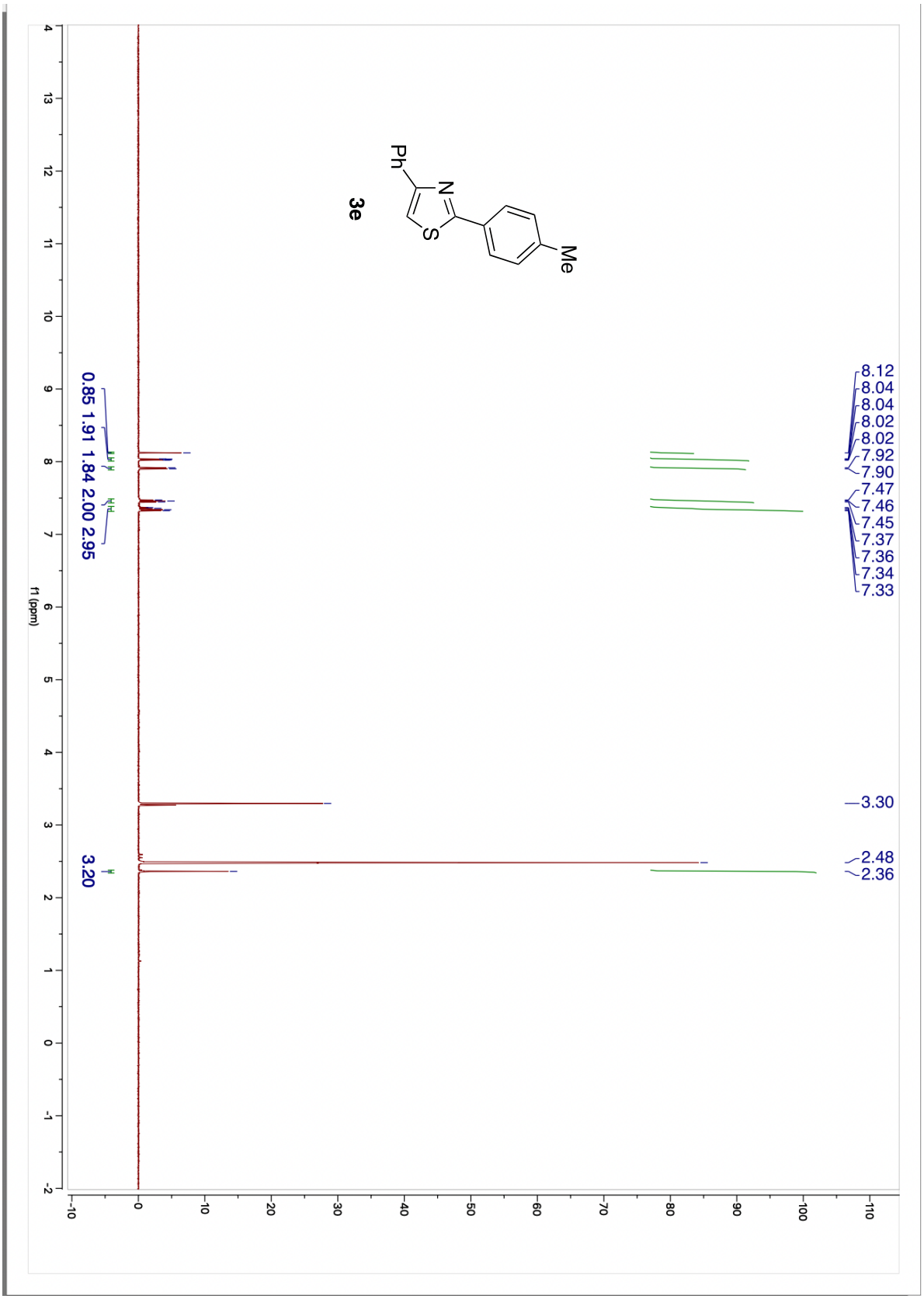

Figure S125: ^{1}H NMR spectrum of **3e** in d_6-DMSO (600 MHz)

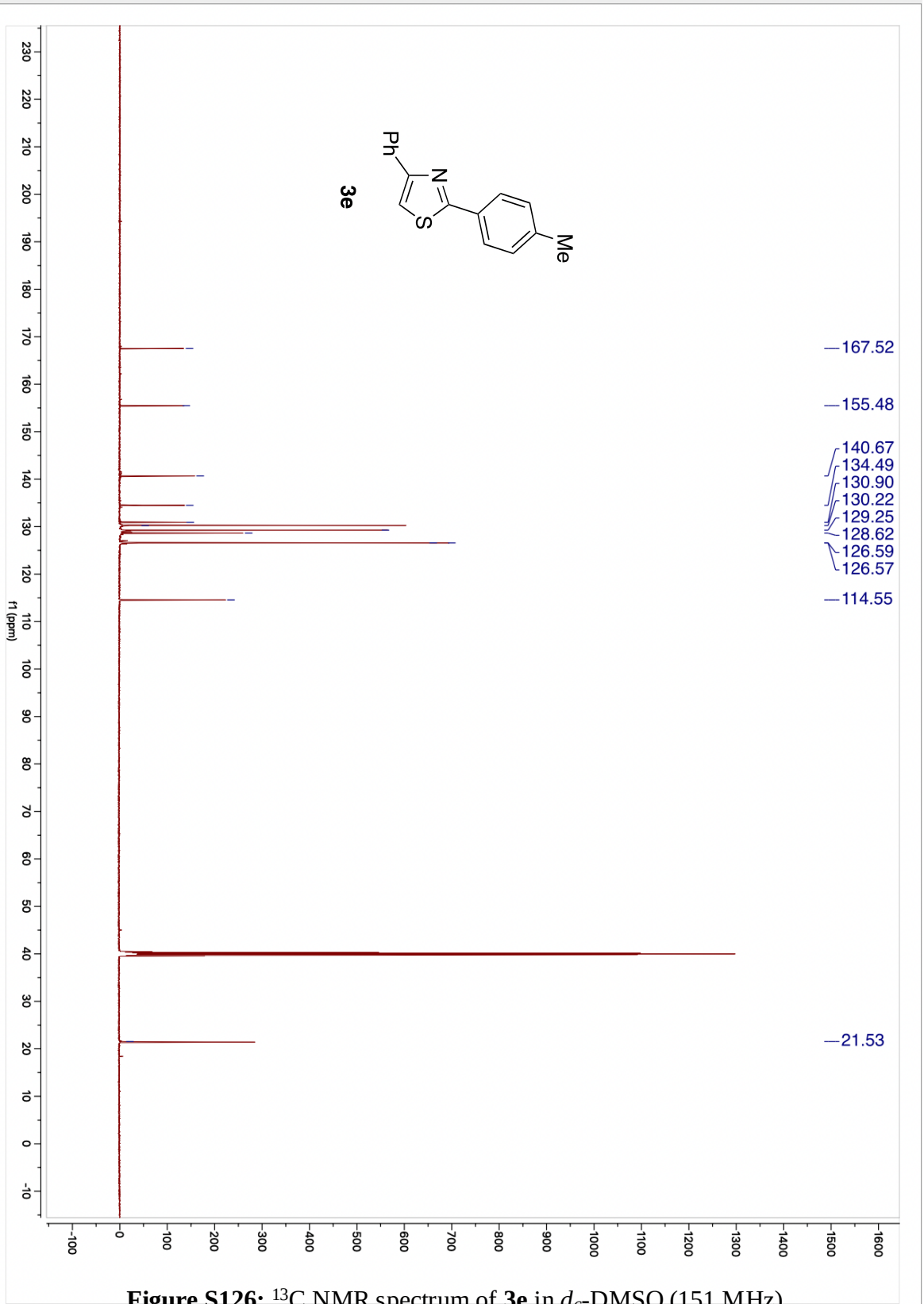

Figure S126: ^{13}C NMR spectrum of **3e** in d_6-DMSO (151 MHz)

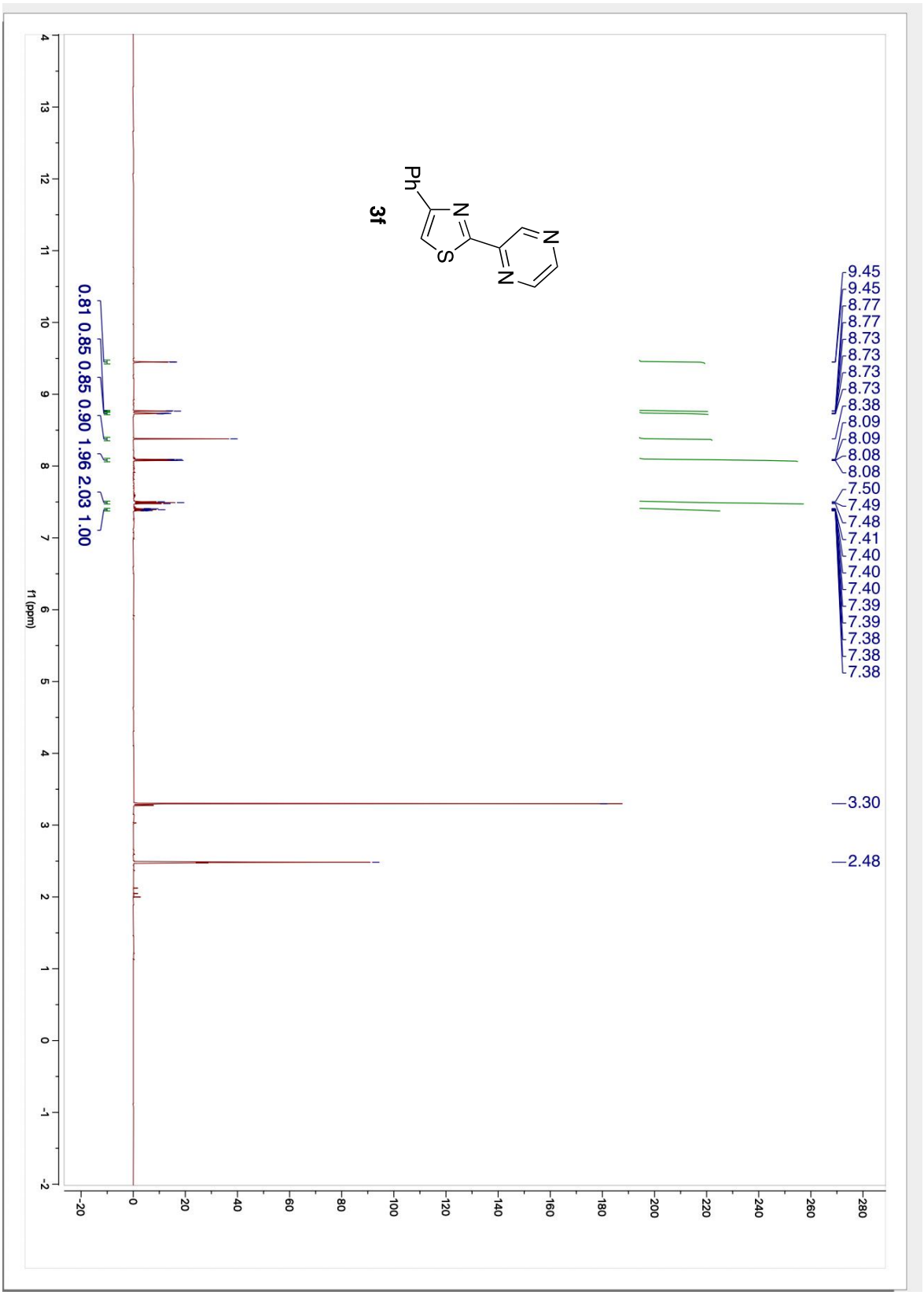

Figure S127: ^{1}H NMR spectrum of **3f** in d_6-DMSO (600 MHz)

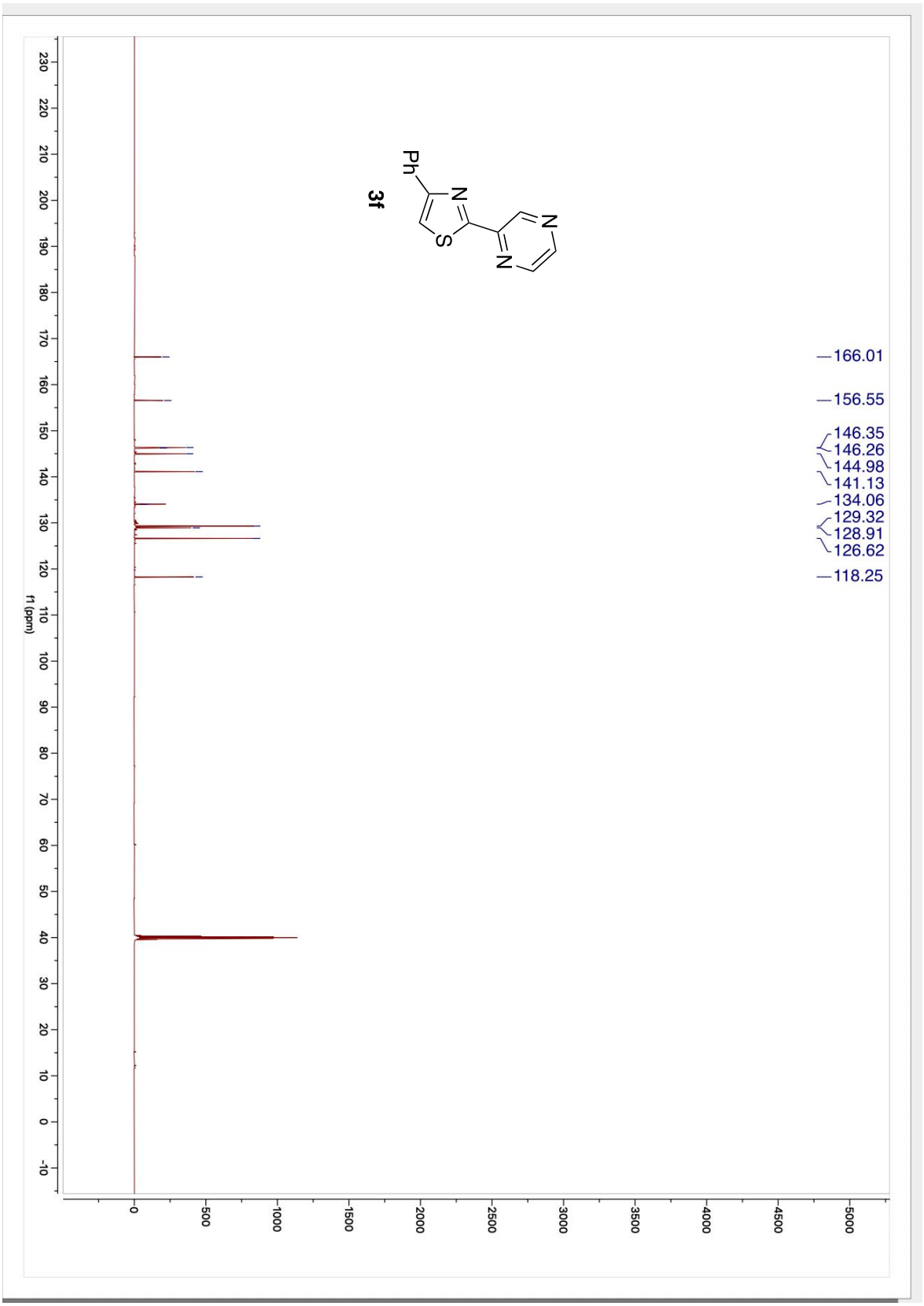

Figure S128: ^{13}C NMR spectrum of **3f** in d_6-DMSO (151 MHz)

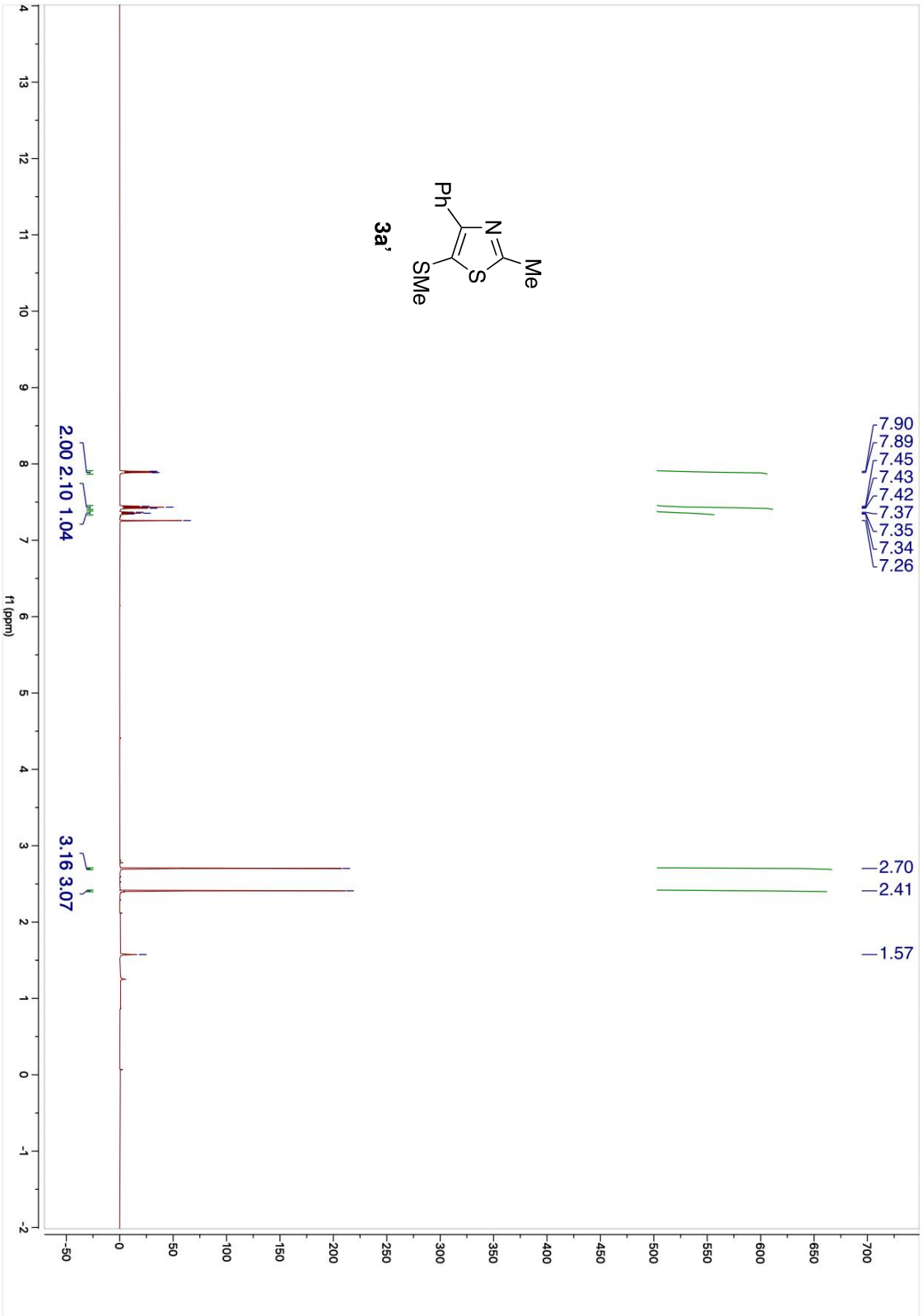

Figure S129: ^{1}H NMR spectrum of **3a'** in $CDCl_3$ (600 MHz)

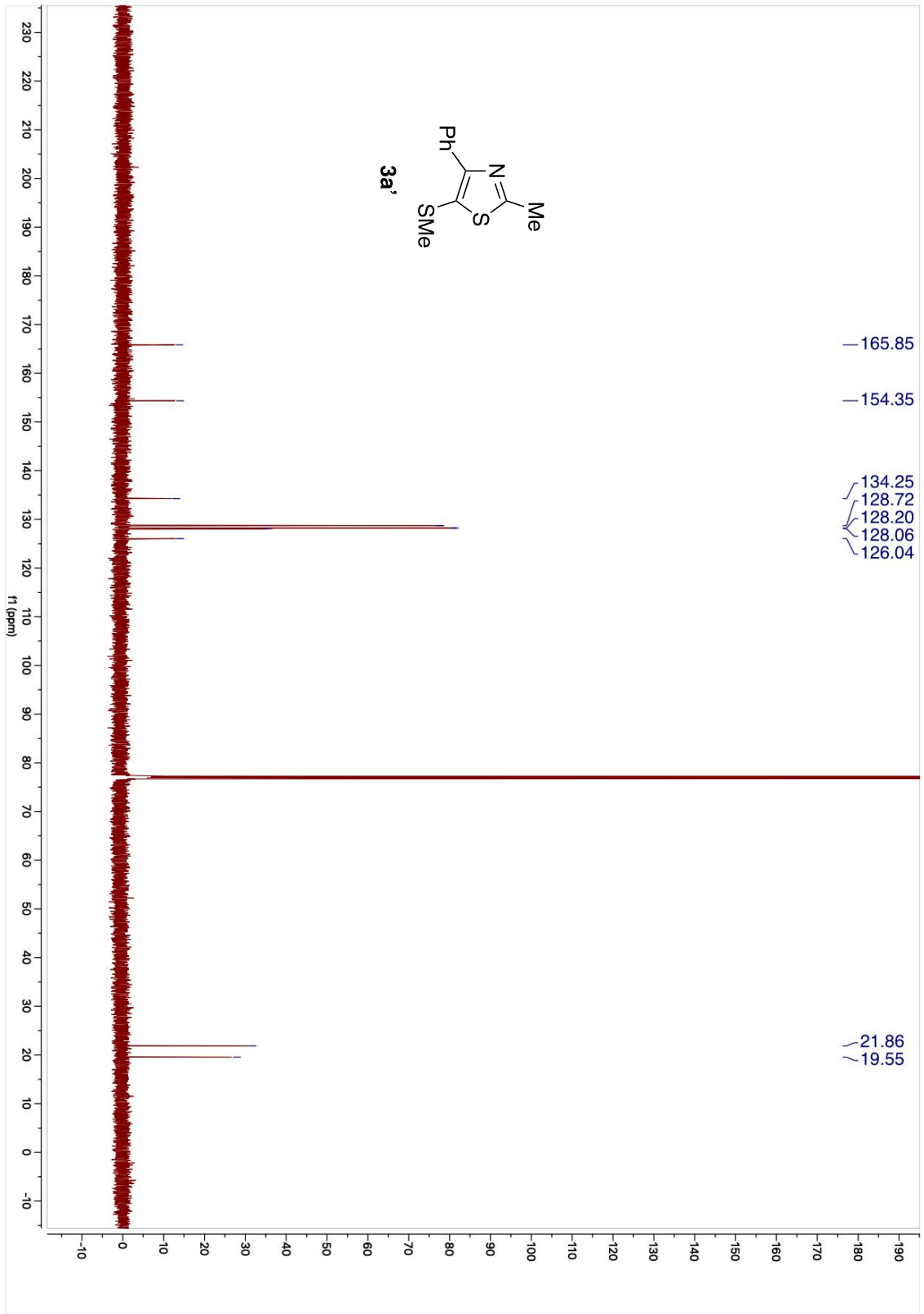

Figure S130: ^{13}C NMR spectrum of **3a'** in $CDCl_3$ (151 MHz)

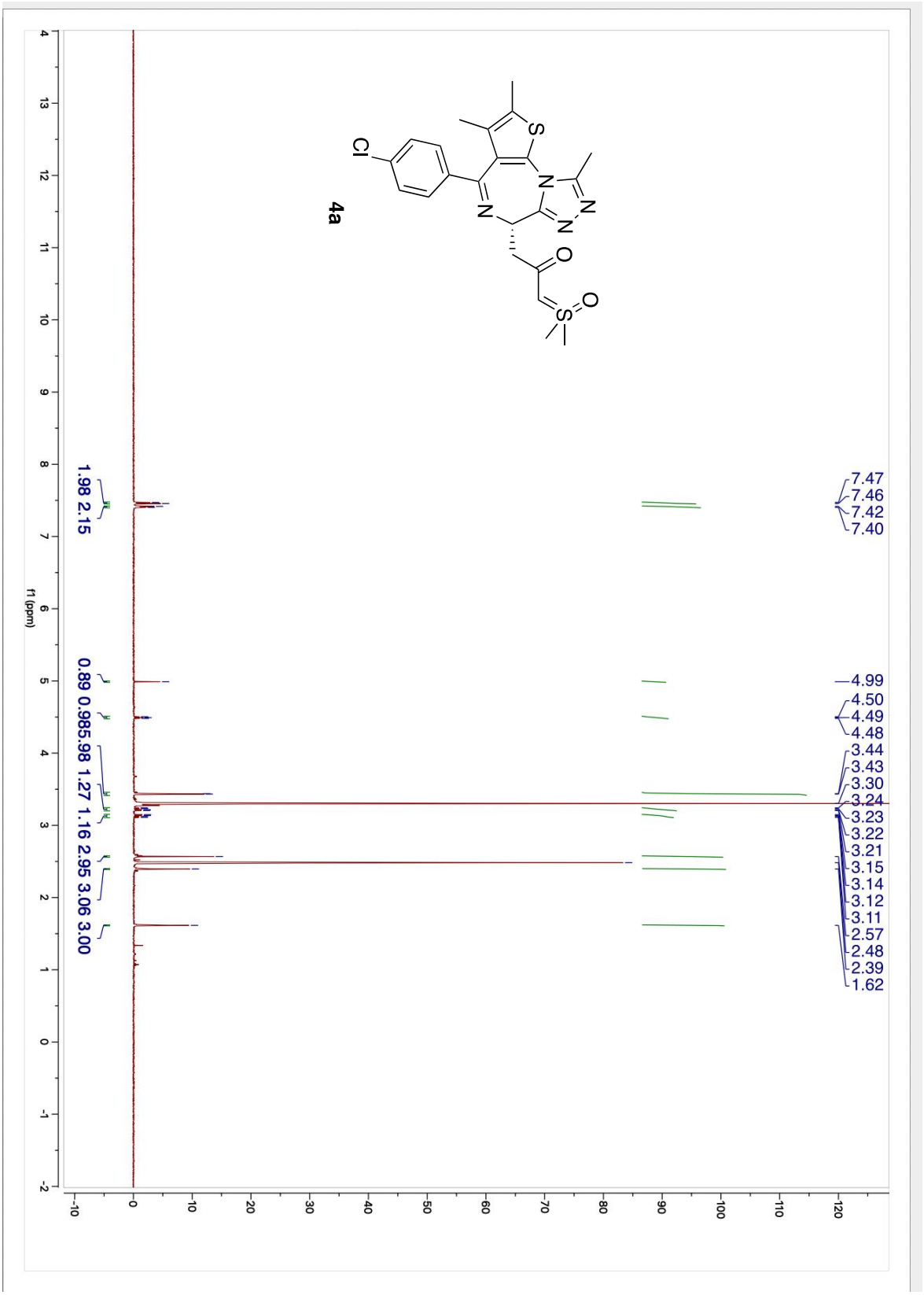

Figure S131: ^{1}H NMR spectrum of **4a** in d_6-DMSO (600 MHz) (600 MHz)

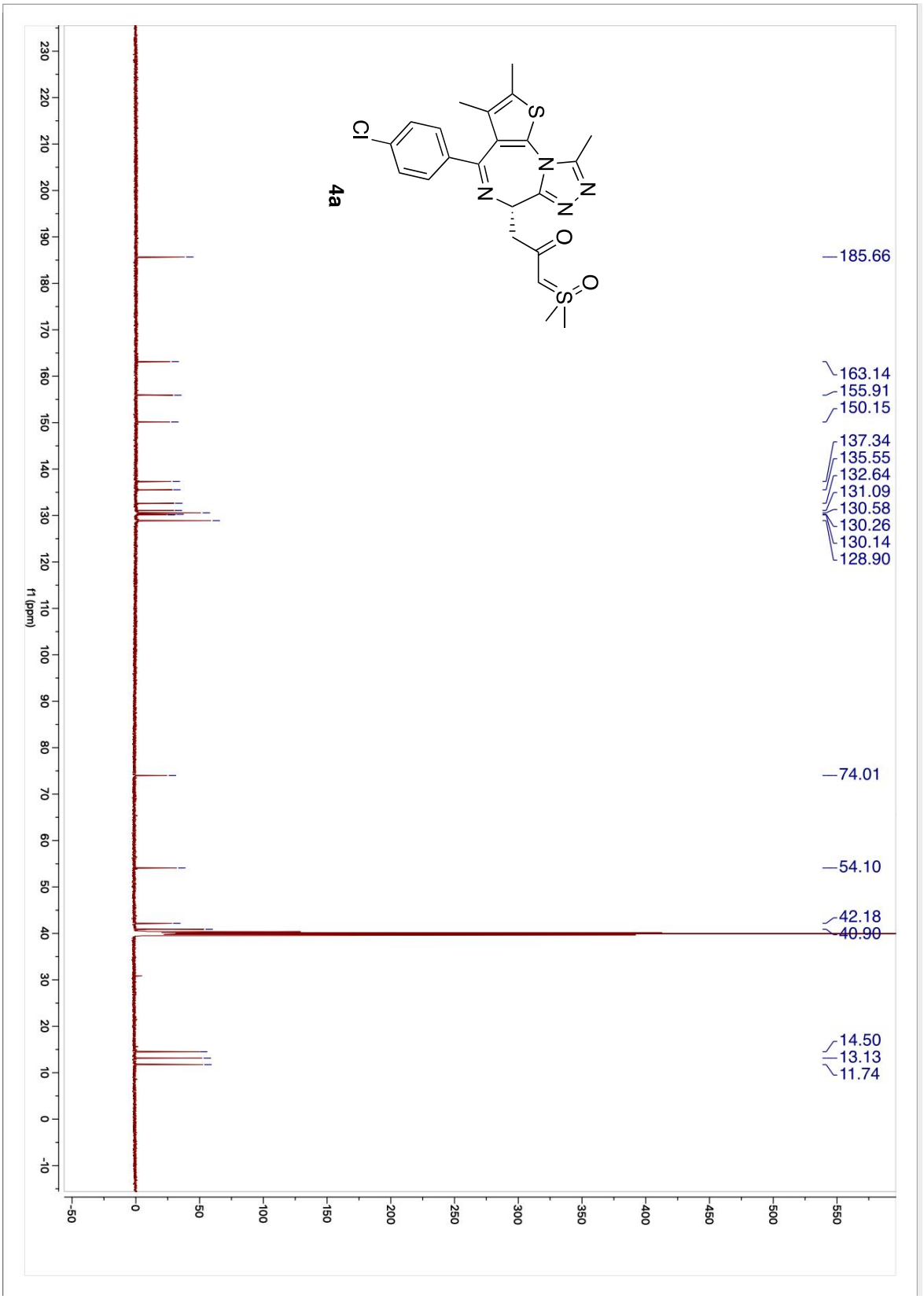

Figure S132: ^{13}C NMR spectrum of **3f** in d_6-DMSO (151 MHz)

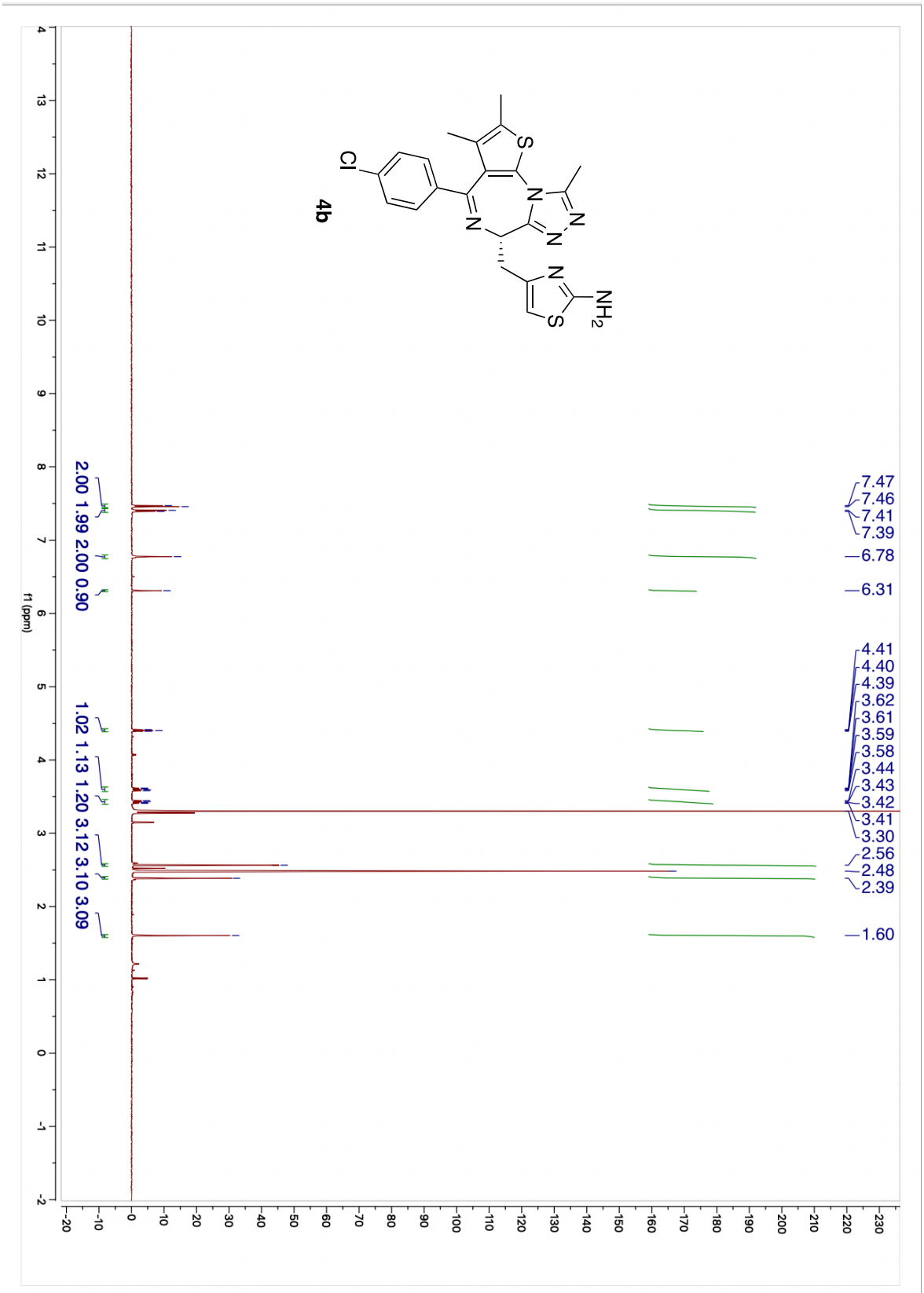

Figure S133: ^{1}H NMR spectrum of **4b** in d_6-DMSO (600 MHz)

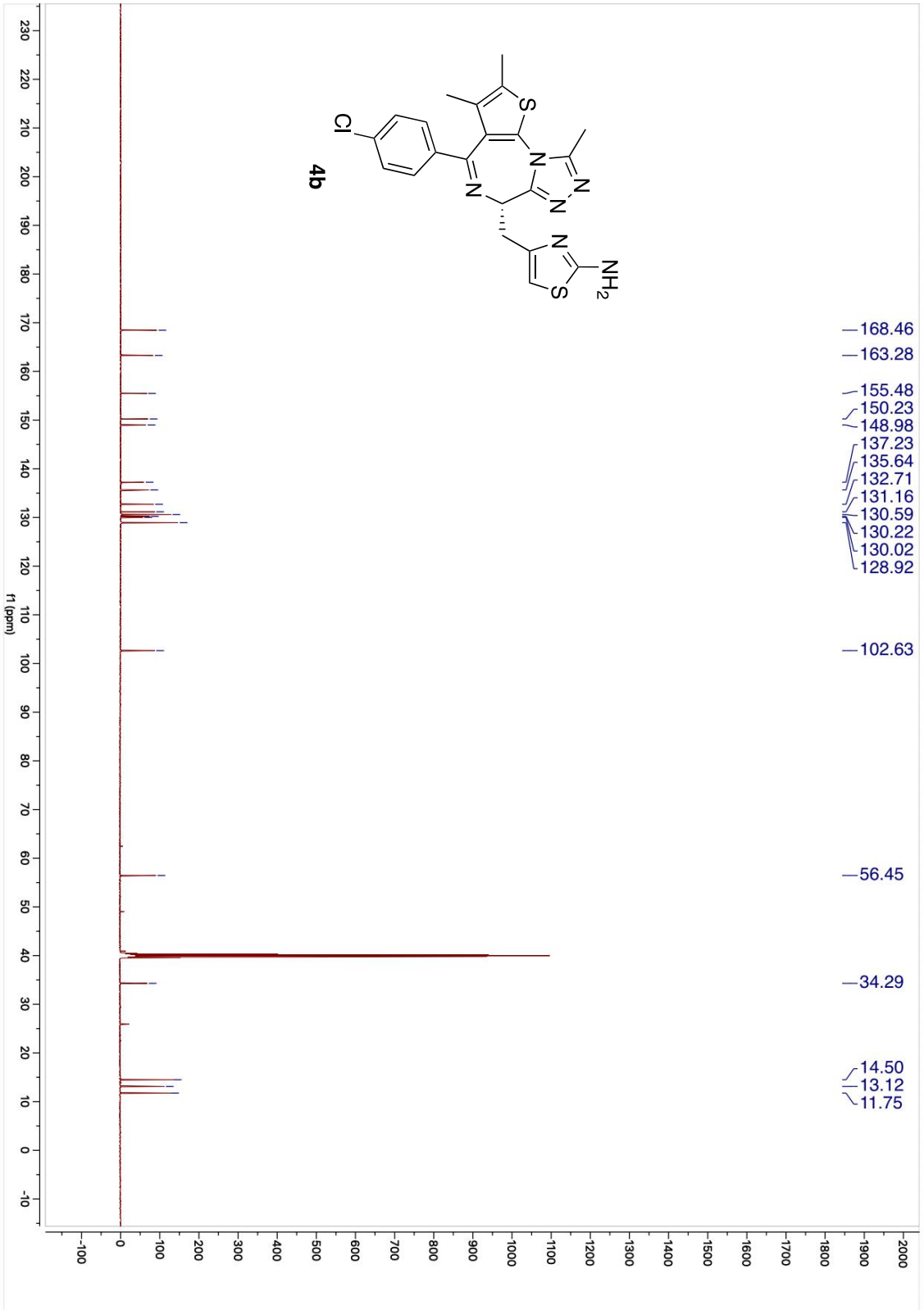

Figure S134: ^{13}C NMR spectrum of **4b** in d_6-DMSO (151 MHz)