

SUPPORTING INFORMATION

Site-Selective C–H functionalization-Sulfinations-Sequence to Access Aryl Sulfonamides

Eva Maria Alvarez, Matthew B. Plutschack, Florian Berger, Tobias Ritter*

Max-Planck-Institut für Kohlenforschung

Kaiser-Wilhelm-Platz 1, D-45470 Mülheim an der Ruhr, Germany

*E-mail: ritter@mpi-muelheim.mpg.de

TABLE OF CONTENTS

TABLE OF CONTENTS	2
MATERIALS AND METHODS	9
Solvents.....	9
Chromatography.....	9
Spectroscopy and instruments.....	9
Starting materials	9
EXPERIMENTAL DATA	10
General procedure for thianthrenation of arenes.....	10
General procedure for sulfonamidation.....	10
Thianthrenation of arenes	11
Benzene-derived thianthrenium triflate TT-1	11
2-Phenylethyl acetate-derived thianthrenium tetrafluoroborate TT-2	12
o-Xylene-derived thianthrenium tetrafluoroborate TT-3	13
p-Xylene-derived thianthrenium tetrafluoroborate TT-4	13
Sulfonamidation of thianthrenium salts	14
(Phenylsulfonyl)methanol (1)	14
4-(Phenylsulfonyl)morpholine (2)	15
4-((4-Ethylphenyl)sulfonyl)morpholine (3).....	15
4-((4-Cyclopropylphenyl)sulfonyl)morpholine (4).....	16
4-((3,4-Dimethylphenyl)sulfonyl)morpholine (5).....	17
Methyl 2-methoxy-5-(morpholinosulfonyl)benzoate (6).....	18
4-((3,4-Dimethoxyphenyl)sulfonyl)morpholine (7).....	18
4-((4-Phenoxyphenyl)sulfonyl)morpholine (8).....	19
4-Methyl-N-(4-(morpholinosulfonyl)phenyl)benzenesulfonamide (9).....	20
4-((2,5-Dimethylphenyl)sulfonyl)morpholine (10).....	21
4-((5-((3s)-Adamantan-1-yl)-2-methylphenyl)sulfonyl)morpholine (11)	21
4'-(Morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12).....	22
4-((4-(4-Bromophenoxy)phenyl)sulfonyl)morpholine (13).....	23
2-Fluoro-6-(4-(morpholinosulfonyl)phenoxy)benzotrile (14).....	24
Pyriproxyfen morpholine sulfonamide derivative (15).....	25
Gemfibrozil methyl ester morpholine sulfonamide derivative (16).....	25
Flurbiprofen methyl ester morpholine sulfonamide derivative (17).....	26

Salicin pentaacetate morpholine sulfonamide derivative (18)	27
Bifonazole morpholine sulfonamide derivative (19)	28
Famoxadone morpholine sulfonamide derivative (20)	29
4-Sulfamoylphenethyl acetate (21)	30
4-(N-Heptylsulfamoyl)phenethyl acetate (22)	30
4-(N-Phenethylsulfamoyl)phenethyl acetate (23).....	31
4-(N-Cyclohexylsulfamoyl)phenethyl acetate (24)	32
4-(N-(2-(Diethylamino)ethyl)sulfamoyl)phenethyl acetate (25)	33
4-(N-(1-(4-Fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26).....	33
4-(N-Benzylsulfamoyl)phenethyl acetate (27).....	34
4-(Pyrrolidin-1-ylsulfonyl)phenethyl acetate (28)	35
4-(Morpholinosulfonyl)phenethyl acetate (29).....	36
4-(Piperidin-1-ylsulfonyl)phenethyl acetate (30)	37
4-((1,4-Dioxo-8-azaspiro[4.5]decan-8-yl)sulfonyl)phenethyl acetate (31).....	37
Ethyl 1-((4-(2-acetoxyethyl)phenyl)sulfonyl)piperidine-4-carboxylate (32)	38
4-((4-Methylpiperidin-1-yl)sulfonyl)phenethyl acetate (33)	39
4-(Thiomorpholinosulfonyl)phenethyl acetate (34).....	40
4-(N-(2-Methoxyethyl)-N-methylsulfamoyl)phenethyl acetate (35)	40
4-(N,N-Diethylsulfamoyl)phenethyl acetate (36)	41
4-(N,N-Dibenzylsulfamoyl)phenethyl acetate (37)	42
Sulfonyl diversification	43
Tert-butyl 2-((4-(2-acetoxyethyl)phenyl)sulfonyl)acetate (38)	43
4-(Benzylsulfonyl)phenethyl acetate (39).....	43
4-((2-Hydroxycyclohexyl)sulfonyl)phenethyl acetate (40)	44
4-((5-(Trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41)	45
4-(Fluorosulfonyl)phenethyl acetate (42)	46
SPECTROSCOPIC DATA.....	47
Benzene-derived thianthrenium salt (TT-1).....	47
¹ H NMR of benzene-derived thianthrenium salt (TT-1).....	47
¹³ C NMR of benzene-derived thianthrenium salt (TT-1)	48
¹⁹ F NMR of benzene-derived thianthrenium salt (TT-1).....	49
Phenethyl acetate-derived thianthrenium tetrafluoroborate (TT-2)	50
¹ H NMR of phenethyl acetate-derived thianthrenium tetrafluoroborate (TT-2)	50
¹³ C NMR of phenethyl acetate-derived thianthrenium tetrafluoroborate (TT-2).....	51
¹⁹ F NMR of phenethyl acetate-derived thianthrenium tetrafluoroborate (TT-2).....	52

o-Xylene-derived thianthrenium tetrafluoroborate (TT-3).....	53
¹ H NMR of o-xylene-derived thianthrenium tetrafluoroborate (TT-3).....	53
¹³ C NMR of o-xylene-derived thianthrenium tetrafluoroborate (TT-3).....	54
¹⁹ F NMR of o-xylene-derived thianthrenium tetrafluoroborate (TT-3).....	55
p-Xylene-derived thianthrenium tetrafluoroborate (TT-4).....	56
¹ H NMR of p-Xylene-derived thianthrenium tetrafluoroborate (TT-4).....	56
¹³ C NMR of p-xylene-derived thianthrenium tetrafluoroborate (TT-4).....	57
¹⁹ F NMR of p-xylene-derived thianthrenium tetrafluoroborate (TT-4).....	58
(Phenylsulfonyl)methanol (1).....	59
¹ H NMR of (phenylsulfonyl)methanol (1).....	59
¹³ C NMR of (phenylsulfonyl)methanol (1).....	60
¹ H- ¹³ C HSQC NMR of (phenylsulfonyl)methanol (1).....	61
¹ H- ¹³ C HMBC NMR of (phenylsulfonyl)methanol (1).....	62
4-(Phenylsulfonyl)morpholine (2).....	63
¹ H NMR of 4-(phenylsulfonyl)morpholine (2).....	63
¹³ C NMR of 4-(phenylsulfonyl)morpholine (2).....	64
4-((4-Ethylphenyl)sulfonyl)morpholine (3).....	65
¹ H NMR of 4-((4-ethylphenyl)sulfonyl)morpholine (3).....	65
¹³ C NMR of 4-((4-ethylphenyl)sulfonyl)morpholine (3).....	66
4-((4-Cyclopropylphenyl)sulfonyl)morpholine (4).....	67
¹ H NMR of 4-((4-cyclopropylphenyl)sulfonyl)morpholine (4).....	67
¹³ C NMR of 4-((4-cyclopropylphenyl)sulfonyl)morpholine (4).....	68
4-((3,4-Dimethylphenyl)sulfonyl)morpholine (5).....	69
¹ H NMR of 4-((3,4-dimethylphenyl)sulfonyl)morpholine (5).....	69
¹³ C NMR of 4-((3,4-dimethylphenyl)sulfonyl)morpholine (5).....	70
Methyl 2-methoxy-5-(morpholinosulfonyl)benzoate (6).....	71
¹ H NMR of methyl 2-methoxy-5-(morpholinosulfonyl)benzoate (6).....	71
¹³ C NMR of methyl 2-methoxy-5-(morpholinosulfonyl)benzoate (6).....	72
4-((3,4-Dimethoxyphenyl)sulfonyl)morpholine (7).....	73
¹ H NMR of 4-((3,4-dimethoxyphenyl)sulfonyl)morpholine (7).....	73
¹³ C NMR of 4-((3,4-dimethoxyphenyl)sulfonyl)morpholine (7).....	74
4-((4-Phenoxyphenyl)sulfonyl)morpholine (8).....	75

¹ H NMR of 4-((4-phenoxyphenyl)sulfonyl)morpholine (8)	75
¹³ C NMR of 4-((4-phenoxyphenyl)sulfonyl)morpholine (8).....	76
4-Methyl-N-(4-(morpholinosulfonyl)phenyl)benzenesulfonamide (9)	77
¹ H NMR of 4-methyl-N-(4-(morpholinosulfonyl)phenyl)benzenesulfonamide (9).....	77
¹³ C NMR of 4-methyl-N-(4-(morpholinosulfonyl)phenyl)benzenesulfonamide (9)	78
4-((2,5-Dimethylphenyl)sulfonyl)morpholine (10)	79
¹ H NMR of 4-((2,5-dimethylphenyl)sulfonyl)morpholine (10)	79
¹³ C NMR of 4-((2,5-dimethylphenyl)sulfonyl)morpholine (10).....	80
4-((5-((3s)-Adamantan-1-yl)-2-methylphenyl)sulfonyl)morpholine (11).....	81
¹ H NMR of 4-((5-((3s)-adamantan-1-yl)-2-methylphenyl)sulfonyl)morpholine (11).....	81
¹³ C NMR of 4-((5-((3s)-adamantan-1-yl)-2-methylphenyl)sulfonyl)morpholine (11)	82
4'-(Morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12)	83
¹ H NMR of 4'-(morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12).....	83
¹³ C NMR of 4'-(morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12)	84
¹⁹ F NMR of 4'-(morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12).....	85
4-((4-(4-Bromophenoxy)phenyl)sulfonyl)morpholine (13)	86
¹ H NMR of 4-((4-(4-bromophenoxy)phenyl)sulfonyl)morpholine (13)	86
¹³ C NMR of 4-((4-(4-bromophenoxy)phenyl)sulfonyl)morpholine (13).....	87
2-Fluoro-6-(4-(morpholinosulfonyl)phenoxy)benzotrile (14)	88
¹ H NMR of 2-fluoro-6-(4-(morpholinosulfonyl)phenoxy)benzotrile (14).....	88
¹³ C NMR of 2-fluoro-6-(4-(morpholinosulfonyl)phenoxy)benzotrile (14)	89
¹⁹ F NMR of 2-fluoro-6-(4-(morpholinosulfonyl)phenoxy)benzotrile (14).....	90
Pyriproxyfen morpholine sulfonamide derivative (15)	91
¹ H NMR of pyriproxyfen morpholine sulfonamide derivative (15)	91
¹³ C NMR of pyriproxyfen morpholine sulfonamide derivative (15).....	92
Gemfibrozil methyl ester morpholine sulfonamide derivative (16)	93
¹ H NMR gemfibrozil methyl ester morpholine sulfonamide derivative (16).....	93
¹³ C NMR of gemfibrozil methyl ester morpholine sulfonamide derivative (16)	94
Flurbiprofen methyl ester morpholine sulfonamide derivative (17)	95
¹ H NMR of flurbiprofen methyl ester morpholine sulfonamide derivative (17)	95
¹³ C NMR of flurbiprofen methyl ester morpholine sulfonamide derivative (17).....	96
¹⁹ F NMR of flurbiprofen methyl ester morpholine sulfonamide derivative (17)	97

Salicin pentaacetate morpholine sulfonamide derivative (18).....	98
¹ H NMR of salicin pentaacetate morpholine sulfonamide derivative (18).....	98
¹³ C NMR of salicin pentaacetate morpholine sulfonamide derivative (18).....	99
Bifonazole morpholine sulfonamide derivative (19)	100
¹ H NMR of bifonazole morpholine sulfonamide derivative (19)	100
¹³ C NMR of bifonazole morpholine sulfonamide derivative (19)	101
Famoxadone morpholine sulfonamide derivative (20)	102
¹ H NMR of famoxadone morpholine sulfonamide derivative (20).....	102
¹³ C NMR of famoxadone morpholine sulfonamide derivative (20).....	103
4-Sulfamoylphenethyl acetate (21)	104
¹ H NMR of 4-sulfamoylphenethyl acetate (21).....	104
¹³ C NMR of 4-sulfamoylphenethyl acetate (21)	105
4-(N-Heptylsulfamoyl)phenethyl acetate (22).....	106
¹ H NMR of 4-(N-heptylsulfamoyl)phenethyl acetate (22).....	106
¹³ C NMR of 4-(N-heptylsulfamoyl)phenethyl acetate (22)	107
4-(N-Phenethylsulfamoyl)phenethyl acetate (23).....	108
¹ H NMR of 4-(N-phenethylsulfamoyl)phenethyl acetate (23).....	108
¹³ C NMR of 4-(N-phenethylsulfamoyl)phenethyl acetate (23)	109
4-(N-Cyclohexylsulfamoyl)phenethyl acetate (24)	110
¹ H NMR of 4-(N-cyclohexylsulfamoyl)phenethyl acetate (24).....	110
¹³ C NMR of 4-(N-cyclohexylsulfamoyl)phenethyl acetate (24)	111
4-(N-(2-(Diethylamino)ethyl)sulfamoyl)phenethyl acetate (25)	112
¹ H NMR of 4-(N-(2-(diethylamino)ethyl)sulfamoyl)phenethyl acetate (25)	112
¹³ C NMR of 4-(N-(2-(diethylamino)ethyl)sulfamoyl)phenethyl acetate (25)	113
4-(N-(1-(4-Fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26).....	114
¹ H NMR of 4-(N-(1-(4-fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26).....	114
¹³ C NMR of 4-(N-(1-(4-fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26).....	115
¹⁹ F NMR of 4-(N-(1-(4-fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26).....	116
4-(N-Benzylsulfamoyl)phenethyl acetate (27)	117
¹ H NMR of 4-(N-benzylsulfamoyl)phenethyl acetate (27)	117
¹³ C NMR of 4-(N-benzylsulfamoyl)phenethyl acetate (27).....	118
4-(Pyrrolidin-1-ylsulfonyl)phenethyl acetate (28).....	119

¹ H NMR of 4-(pyrrolidin-1-ylsulfonyl)phenethyl acetate (28).....	119
¹³ C NMR of 4-(pyrrolidin-1-ylsulfonyl)phenethyl acetate (28)	120
4-(Morpholinosulfonyl)phenethyl acetate (29).....	121
¹ H NMR of 4-(morpholinosulfonyl)phenethyl acetate (29)	121
¹³ C NMR of 4-(morpholinosulfonyl)phenethyl acetate (29)	122
4-(Piperidin-1-ylsulfonyl)phenethyl acetate (30).....	123
¹ H NMR of 4-(piperidin-1-ylsulfonyl)phenethyl acetate (30).....	123
¹³ C NMR of 4-(piperidin-1-ylsulfonyl)phenethyl acetate (30)	124
4-((1,4-Dioxa-8-azaspiro[4.5]decan-8-yl)sulfonyl)phenethyl acetate (31).....	125
¹ H NMR of 4-((1,4-dioxa-8-azaspiro[4.5]decan-8-yl)sulfonyl)phenethyl acetate (31).....	125
¹³ C NMR of 4-((1,4-dioxa-8-azaspiro[4.5]decan-8-yl)sulfonyl)phenethyl acetate (31).....	126
Ethyl 1-((4-(2-acetoxyethyl)phenyl)sulfonyl)piperidine-4-carboxylate (32).....	127
¹ H NMR of ethyl 1-((4-(2-acetoxyethyl)phenyl)sulfonyl)piperidine-4-carboxylate (32)	127
¹³ C NMR of ethyl 1-((4-(2-acetoxyethyl)phenyl)sulfonyl)piperidine-4-carboxylate (32)	128
4-((4-Methylpiperidin-1-yl)sulfonyl)phenethyl acetate (33).....	129
¹ H NMR of 4-((4-methylpiperidin-1-yl)sulfonyl)phenethyl acetate (33)	129
¹³ C NMR of 4-((4-methylpiperidin-1-yl)sulfonyl)phenethyl acetate (33)	130
4-(Thiomorpholinosulfonyl)phenethyl acetate (34).....	131
¹ H NMR of 4-(thiomorpholinosulfonyl)phenethyl acetate (34).....	131
¹³ C NMR of 4-(thiomorpholinosulfonyl)phenethyl acetate (34)	132
4-(N-(2-Methoxyethyl)-N-methylsulfamoyl)phenethyl acetate (35)	133
¹ H NMR of 4-(N-(2-methoxyethyl)-N-methylsulfamoyl)phenethyl acetate (35).....	133
¹³ C NMR of 4-(N-(2-methoxyethyl)-N-methylsulfamoyl)phenethyl acetate (35)	134
4-(N,N-Diethylsulfamoyl)phenethyl acetate (36)	135
¹ H NMR of 4-(N,N-diethylsulfamoyl)phenethyl acetate (36)	135
¹³ C NMR of 4-(N,N-diethylsulfamoyl)phenethyl acetate (36)	136
4-(N,N-Dibenzylsulfamoyl)phenethyl acetate (37)	137
¹ H NMR of 4-(N,N-dibenzylsulfamoyl)phenethyl acetate (37).....	137
¹³ C NMR of 4-(N,N-dibenzylsulfamoyl)phenethyl acetate (37)	138
Tert-butyl 2-((4-(2-acetoxyethyl)phenyl)sulfonyl)acetate (38)	139
¹ H NMR of tert-butyl 2-((4-(2-acetoxyethyl)phenyl)sulfonyl)acetate (38).....	139
¹³ C NMR of tert-butyl 2-((4-(2-acetoxyethyl)phenyl)sulfonyl)acetate (38).....	140

4-(Benzylsulfonyl)phenethyl acetate (39).....	141
¹ H NMR of 4-(benzylsulfonyl)phenethyl acetate (39).....	141
¹³ C NMR of 4-(benzylsulfonyl)phenethyl acetate (39).....	142
4-((2-Hydroxycyclohexyl)sulfonyl)phenethyl acetate (40).....	143
¹ H NMR of 4-((2-hydroxycyclohexyl)sulfonyl)phenethyl acetate (40).....	143
¹³ C NMR of 4-((2-hydroxycyclohexyl)sulfonyl)phenethyl acetate (40).....	144
4-(N,N-4-((5-(Trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41).....	145
¹ H NMR of 4-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41).....	145
¹³ C NMR of 4-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41).....	146
¹⁹ F NMR of 4-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41).....	147
4-(Fluorosulfonyl)phenethyl acetate (42).....	148
¹ H NMR of 4-(fluorosulfonyl)phenethyl acetate (42).....	148
¹³ C NMR of 4-(fluorosulfonyl)phenethyl acetate (42).....	149
¹⁹ F NMR of 4-(fluorosulfonyl)phenethyl acetate (42).....	150
REFERENCES.....	151

MATERIALS AND METHODS

Unless otherwise noted, all reactions were carried out under ambient atmosphere and reaction progress was monitored by thin-layer chromatography (TLC). Concentration under reduced pressure was performed by rotary evaporation at 25–40 °C at an appropriate pressure. Purified compounds were further dried under high vacuum (0.010–0.005 mBar). Yields refer to spectroscopically pure compounds. All air- and moisture-sensitive manipulations were performed using oven-dried glassware (130 °C for a minimum of 12 hours) and standard Schlenk techniques under an atmosphere of argon.

Solvents

Anhydrous isopropanol was purchased from Sigma Aldrich (278475). Anhydrous MeCN and THF were obtained from a Phoenix Solvent Drying System from JC Meyer. All deuterated solvents were purchased from Euriso-Top.

Chromatography

Thin layer chromatography (TLC) was performed using EMD TLC plates pre-coated with 250 μm thickness silica gel 60 F₂₅₄ plates. Compound visualization was achieved by fluorescence quenching under 254 nm UV light, permanganate stain, cerium ammonium molybdate stain, or phosphomolybdic acid stain. Flash chromatography was performed using silica gel (40–63 μm particle size) purchased from Geduran.

Spectroscopy and instruments

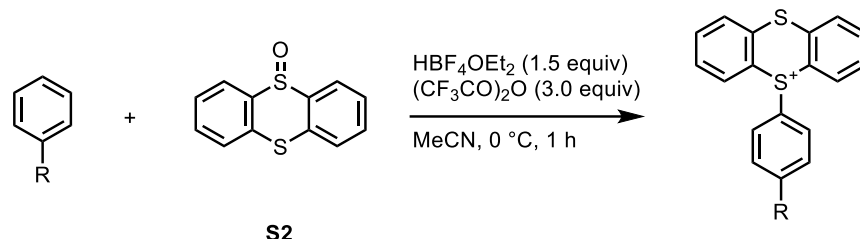
NMR spectra were recorded on a Bruker Ascend™ spectrometer operating at 500 MHz and 400 MHz for ¹H, 126 MHz and 101 MHz for ¹³C, and 471 MHz for ¹⁹F acquisitions. Chemical shifts are reported in ppm with the residual solvent signal as the internal standard. For ¹H NMR: CDCl₃, δ 7.26; CD₂Cl₂, δ 5.32; CD₃CN, δ 1.94; (CD₃)₂SO, δ 2.50. For ¹³C NMR: CDCl₃, δ 77.16; CD₂Cl₂, δ 53.84; CD₃CN, δ 1.32, 118.26; (CD₃)₂SO, δ 39.52. Data is reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad; coupling constants are reported in Hz.

Starting materials

All reagents were used as received from commercial suppliers unless otherwise stated. For convenient operation, Pd(dppf)Cl₂ was stored in a N₂-filled glovebox after being dried for more than 24 h under high-vacuum. Arylthianthrenium salts **TT-5** to **TT-20** and thianthrene-S-oxide (**S2**) were prepared according to our previous reports.¹⁻⁵

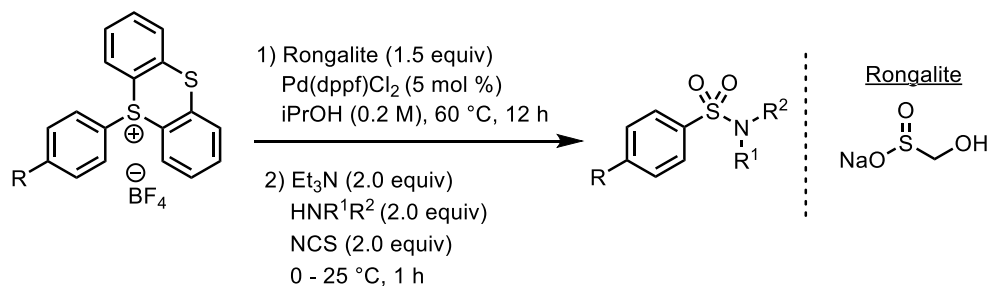
EXPERIMENTAL DATA

General procedure for thianthrenation of arenes



Under ambient atmosphere, a 20 mL glass-vial was charged with arene (0.50 mmol, 1.0 equiv) and dry MeCN (2.0 – 4.0 mL, $c = 0.25$ M). After cooling to 0 °C, $\text{HBF}_4 \cdot \text{OEt}_2$ (1.2 equiv + 1.0 equiv per basic functional group) was added to the vial while stirring the reaction mixture. Other acids may be used instead of $\text{HBF}_4 \cdot \text{OEt}_2$ like triflic acid (TfOH). For acid sensitive substrates $\text{BF}_3 \cdot \text{OEt}_2$ or trimethylsilyltriflate (TMSOTf) can be used. After all solids had dissolved, thianthrene-S-oxide (**S2**) (0.50 mmol, 1.0 equiv) was added in one portion to the solution at 0 °C, leading to a suspension. Subsequently, trifluoroacetic anhydride (0.21 mL, 0.32 g, 1.5 mmol, 3.0 equiv) was added in one portion at 0 °C, resulting in a color change to deep purple. The vial was sealed with a screw-cap. The mixture was stirred at 0 °C for 1 h, subsequently, the reaction mixture was warmed to 25 °C and stirred until all solid dissolved and the intensity of the purple color decreased. The solution was diluted with 5 mL DCM and poured onto a mixture of 30 mL DCM, 20 mL saturated aqueous Na_2CO_3 solution, and 10 mL water. After stirring for 5 min at 25 °C, the mixture was poured into a separatory funnel, and the layers were separated. The DCM layer was washed with aqueous NaBF_4 solution (2 x ca. 20 mL, 5 % w/w) and with water (2 x ca. 20 mL). Washing with NaBF_4 solution is only required if it is of interest that the product contains only one type of counterion, solutions containing other ions, like triflate or hexafluorophosphate may be used as well. The DCM layer was dried over Na_2SO_4 , filtered, and the solvent was removed under reduced pressure. In order to obtain analytically pure samples of thianthrenium salts, the residue was purified by chromatography on silica gel eluting with DCM / *i*-PrOH, subsequently, the product was dissolved in 2 mL DCM and precipitated with 20 mL Et_2O . The solid was dried in vacuo to afford the thianthrenium salt.

General procedure for sulfonamidation



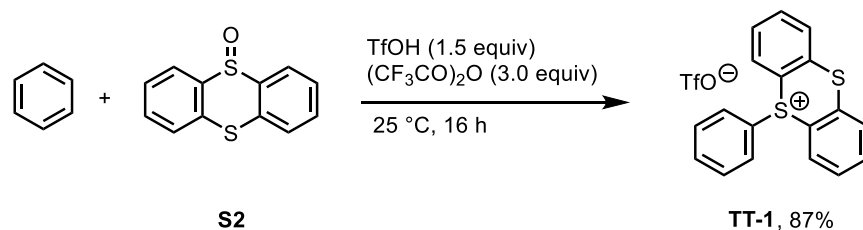
An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with an aryl thianthrenium salt (0.100 mmol, 1.00 equiv), $\text{Pd}(\text{dppf})\text{Cl}_2$ (4 mg, 5 μmol , 5 mol %), Rongalite (17 mg, 0.15 mmol

1.5 equiv) and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), the corresponding amine (0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel to afford the sulfonamide product.

NOTE: For convenience, we have stored and weighted the Pd(dppf)Cl₂, Rongalite, and **TT** salts in a N₂-filled glovebox.

Thianthrenation of arenes

Benzene-derived thianthrenium triflate **TT-1**



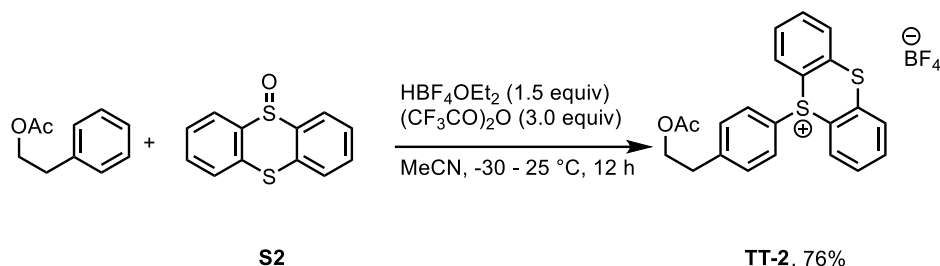
Under ambient atmosphere, a 4 mL glass-vial was charged with thianthrene-*S*-oxide (**S2**) (0.232 g, 1.00 mmol, 1.00 equiv), and benzene (1.0 mL, 0.88 g, 11 equiv). Then trifluoromethanesulfonic acid (132 μ L, 0.225 g, 1.50 mmol, 1.50 equiv) was added, followed by trifluoroacetic anhydride (418 μ L, 0.630 g, 3.00 mmol, 3.00 equiv). The vial was sealed with a screw-cap, and the mixture was stirred at 25 °C for 16 h. The reaction mixture was concentrated under reduced pressure, and subsequently, diluted with water (1 mL) and methanol (2 mL). The oily suspension was sonicated until the dark color dissipated and then swirled with heating (70 °C water bath) until a clear solution was obtained. Cooling with the vial open to the air resulted in the formation of a turbid solution, at which point the vial was capped and allowed to sit at 25 °C for an hour. The supernatant was pipetted off, the white crystalline solid was washed with 5 mL water, and dried under vacuum overnight yielding a first batch of crystals. The supernatant was concentrated in a rotary evaporator at 40 °C until a turbid suspension resulted. After cooling and standing for 1 h, the supernatant was removed, the resulting crystals were washed with 5 mL of water, and dried under vacuum overnight yielding a second batch of crystals. Total yield of **TT-1**: 0.385 g (87%).

NMR Spectroscopy:

¹H NMR (500 MHz, CD₃CN, 298 K, δ): 8.39 (dd, $J = 7.9, 1.1$ Hz, 2H), 7.96 (dd, $J = 7.8, 1.3$ Hz, 2H), 7.89 (td, $J = 7.7, 1.4$ Hz, 2H), 7.82 (td, $J = 7.7, 1.4$ Hz, 2H), 7.61 (tt, $J = 7.1, 1.0$ Hz, 1H), 7.51-7.45 (m, 2H), 7.16 – 7.08 (m, 2H).

¹³C {¹H} NMR (126 MHz, CD₃CN, 298 K, δ): 137.6, 136.1, 136.1, 133.9, 131.6, 131.5, 130.9, 128.9, 124.9,

119.5.

 ^{19}F (^1H) NMR (471 MHz, CD_3CN , 298 K, δ): -80.2 (s).HRMS-ESI (m/z) calc'd for $\text{C}_{18}\text{H}_{13}\text{S}_2^+$ [$\text{M}-\text{OTf}$] $^+$, 293.0453; found, 293.0452; deviation: $+0.51$ ppm.**2-Phenylethyl acetate-derived thianthrenium tetrafluoroborate TT-2**

Under ambient atmosphere, a 100 mL round bottom flask equipped with a magnetic stir bar was charged with 2-phenylethylacetate (1.64 g, 10.0 mmol, 1.00 equiv) and MeCN (40 mL, $c = 0.25$ M). Trifluoroacetic anhydride (4.17 mL, 6.30 g, 30.0 mmol, 3.00 equiv) was added at ambient temperature while stirring. After cooling to $0\text{ }^\circ\text{C}$, thianthrene-*S*-oxide (**S2**) (2.56 g, 11.0 mmol, 1.10 equiv) was added in one portion, followed by the addition of $\text{HBF}_4 \cdot \text{OEt}_2$ (2.04 mL, 2.43 g, 15.0 mmol, 1.50 equiv). The vial was sealed with a screw-cap, and the mixture was stirred at $0\text{ }^\circ\text{C}$ for 1 h, followed by stirring at $25\text{ }^\circ\text{C}$ for 12 h. The reaction mixture was concentrated under reduced pressure and subsequently diluted with DCM (50 mL). The solution was poured onto a saturated aqueous NaHCO_3 solution (50 mL), and the layers were separated. The organic phase was washed with aqueous NaBF_4 solution (2×50 mL, 10%). The organic phase was dried over MgSO_4 , and the solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel eluting with DCM / MeOH (1:0–20:1 (v/v)) to afford 3.54 g (76%) of **TT-2** as a yellow foam.

NMR Spectroscopy:

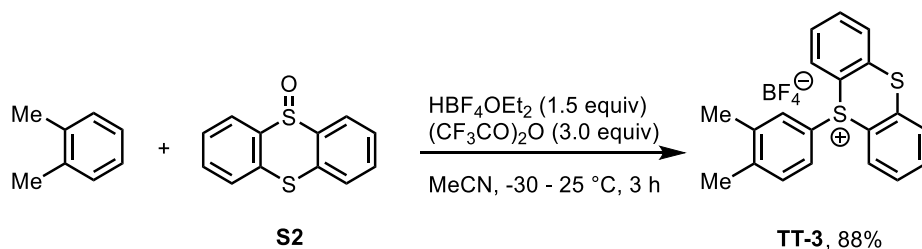
^1H NMR (500 MHz, CD_3CN , 298 K, δ): 8.36 (dd, $J = 7.9, 1.2$ Hz, 2H), 7.96 (dd, $J = 7.9, 1.1$ Hz, 2H), 7.89 (td, $J = 7.7, 1.4$ Hz, 2H), 7.82 (td, $J = 7.7, 1.4$ Hz, 2H), 7.37 (d, $J = 8.8$ Hz, 2H), 7.07 (d, $J = 8.7$ Hz, 2H), 4.19 (t, $J = 6.5$ Hz, 2H), 2.93 (t, $J = 6.5$ Hz, 2H), 1.90 (s, 3H).

^{13}C NMR (126 MHz, CD_3CN , 298 K, δ): 171.3, 145.6, 137.4, 136.0, 135.9, 132.1, 131.5, 130.9, 128.9, 122.5, 119.5, 64.4, 35.0, 20.9.

^{19}F NMR (471 MHz, CD_3CN , 298 K, δ): -151.60 (bs), -151.66 (bs).

HRMS-ESI (m/z) calc'd for $\text{C}_{22}\text{H}_{19}\text{O}_2\text{S}_2^+$ [$\text{M}-\text{BF}_4$] $^+$, 379.0820; found, 379.0821; deviation: $+0.26$ ppm.

o-Xylene-derived thianthrenium tetrafluoroborate TT-3



Under ambient atmosphere, a 20 mL glass-vial was charged with o-xylene (212 mg, 2.00 mmol, 1.00 equiv), thianthrene-S-oxide (**S2**) (465 mg, 2.00 mmol, 1.00 equiv), and MeCN (5.0 mL, c = 0.40 M). After cooling to –30 °C, HBF₄·OEt₂ (0.41 mL, 0.49 g, 3.0 mmol, 1.5 equiv) was added, followed by trifluoroacetic anhydride (0.83 mL, 1.3 g, 6.0 mmol, 3.0 equiv). The vial was sealed with a screw-cap, and the mixture was stirred at –30 °C for 1 h, followed by stirring at 25 °C for 2 h. The reaction mixture was concentrated under reduced pressure at 60 °C, and subsequently diluted with methanol (7 mL) while still warm. The slurry was swirled at 60 °C until all of the pink-purple color had dissipated. Cooling for 1 h to 25 °C and an additional 1 h at –20 °C resulted in clear colorless crystals. The supernatant was pipetted off. The white crystalline solid was dried under high vacuum yielding 0.715 g (88%) of thianthrenium salt **TT-3**.

NMR Spectroscopy:

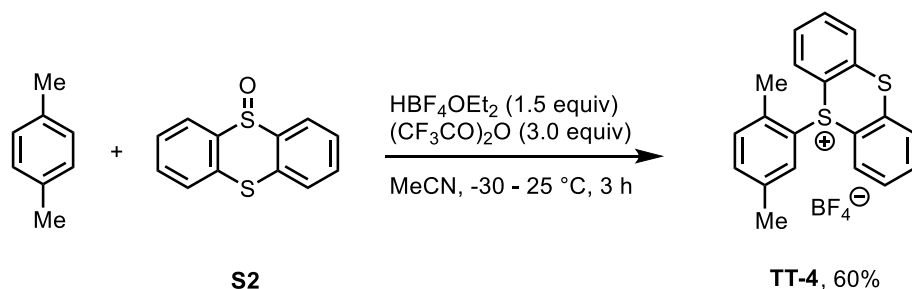
¹H NMR (500 MHz, CD₃CN, 298 K, δ): 8.33 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.94 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.87 (td, *J* = 7.7, 1.4 Hz, 2H), 7.80 (td, *J* = 7.6, 1.4 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 1H), 6.96 (d, *J* = 2.3 Hz, 1H), 6.83 (dd, *J* = 8.3, 2.4 Hz, 1H), 2.23 (s, 3H), 2.16 (s, 3H).

¹³C {¹H} NMR (126 MHz, CD₃CN, 298 K, δ): 144.4, 141.8, 137.8, 136.4, 136.2, 132.9, 132.0, 131.3, 129.7, 126.9, 121.6, 120.1, 20.3, 20.2.

¹⁹F NMR (471 MHz, CD₃CN, 298 K, δ): –152.25 (bs), –152.30 (bs).

HRMS-ESI(m/z) calc'd for C₂₀H₁₇S₂⁺ [M-BF₄]⁺, 321.0766; found, 321.0763; deviation: +0.97 ppm.

p-Xylene-derived thianthrenium tetrafluoroborate TT-4



Under ambient atmosphere, a 20 mL glass-vial was charged with p-xylene (212 mg, 2.00 mmol, 1.00 equiv), thianthrene-S-oxide **S2** (465 mg, 2.00 mmol, 1.00 equiv), and MeCN (5.0 mL, c = 0.40 M). After cooling to –

30 °C, HBF₄·OEt₂ (0.41 mL, 0.49 g, 3.0 mmol, 1.5 equiv) was added, followed by trifluoroacetic anhydride (0.83 mL, 1.3 g, 6.0 mmol, 3.0 equiv). The vial was sealed with a screw-cap, and the mixture was stirred at –30 °C for 3 h, followed by stirring at 25 °C for 19 h. The reaction mixture was concentrated under reduced pressure at 60 °C into a viscous oil, and purified by chromatography on silica gel eluting with DCM / *i*-PrOH (gradient from 1:0 to 25:2 (v/v)). The product **TT-4** was obtained as a foamy white solid in 60% yield (0.490 g).

NMR Spectroscopy:

¹H NMR (500 MHz, CD₃CN, 298 K, δ): 8.18 (dd, *J* = 8.0, 1.1 Hz, 2H), 7.93 (dd, *J* = 8.0, 1.1 Hz, 2H), 7.82 (td, *J* = 7.7, 1.3 Hz, 2H), 7.73 (td, *J* = 8.0, 1.3 Hz, 2H), 7.39 – 7.32 (m, 2H), 6.81 (d, *J* = 1.5 Hz, 1H), 2.60 (s, 3H), 2.19 (s, 3H).

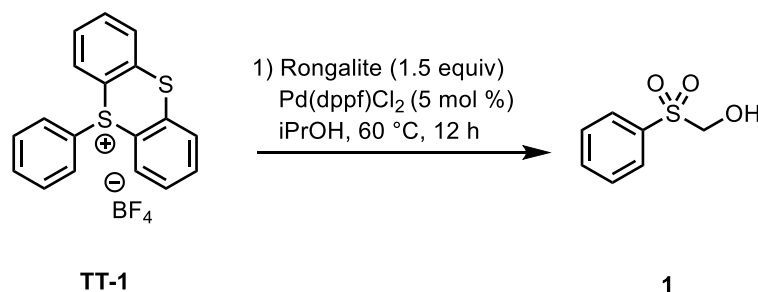
¹³C {¹H} NMR (126 MHz, CD₃CN, 298 K, δ): 139.5, 138.4, 137.8, 136.1, 135.6, 135.0, 134.6, 131.9, 131.0, 130.4, 122.0, 119.4, 21.0, 20.3.

¹⁹F NMR (471 MHz, CD₃CN, 298 K, δ): –151.52 (bs), –151.69 (bs).

HRMS-ESI(m/z) calc'd for C₂₀H₁₇S₂⁺ [M-BF₄]⁺, 321.0766; found, 321.0761; deviation: +1.56 ppm.

Sulfonamidation of thianthrenium salts

(Phenylsulfonyl)methanol (**1**)



A 4 mL oven dried borosilicate vial equipped with a magnetic stir bar was charged with **TT-1** (76.0 mg, 0.200 mmol, 1.00 equiv), Pd(dppf)Cl₂ (8 mg, 0.01 mmol, 5 mol %), Rongalite (35.4 mg, 0.300 mmol 1.50 equiv), and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (1.0 mL, *c* = 0.20 M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, the solvent was removed under reduced pressure.

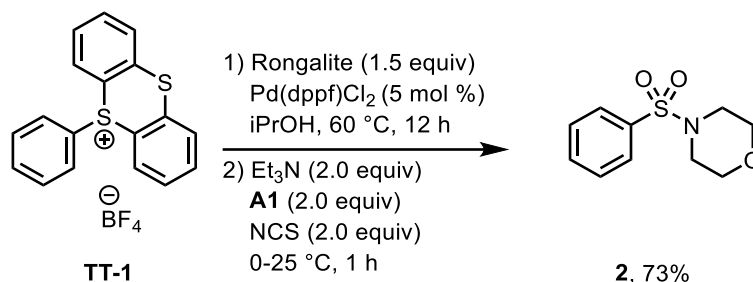
NMR Spectroscopy:

¹H NMR (400 MHz, CDCl₃, 298 K, δ): 7.95 – 7.93 (m, 2H), 7.72 – 7.68 (m, 1H), 7.60 (t, *J* = 7.7 Hz, 2H), 4.62 (s, 2H).

¹³C NMR (101 MHz, CDCl₃, 298 K, δ): 136.7, 134.4, 129.4, 129.0, 79.7.

HRMS-ESI (m/z) calc'd for C₇H₈O₃SN⁺ [M+Na]⁺, 195.0085; found, 195.0086; deviation: +0.60 ppm.

4-(Phenylsulfonyl)morpholine (**2**)



An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-1** (76.0 mg, 0.200 mmol, 1.00 equiv), Pd(dppf)Cl₂ (8 mg, 0.01 mmol, 5 mol %), Rongalite (34 mg, 0.30 mmol 1.5 equiv), and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (1.0 mL, c = 0.20 M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (56 μ L, 40 mg, 0.40 mmol, 2.0 equiv), morpholine (**A1**) (35 μ L, 35 mg, 0.40 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (53.4 mg, 0.400 mmol, 2.00 equiv) in THF (1.0 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 33 mg (73%) of **2** as a colorless solid.

R_f = 0.47 (hexanes / ethyl acetate, 1:1 (v/v)).

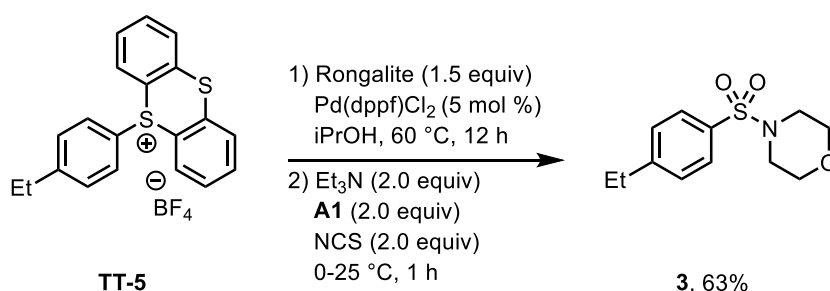
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.75 (d, J = 8.0 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.7 Hz, 2H), 3.73 (q, J = 5.1, 4.3 Hz, 4H), 3.02 – 2.96 (m, 4H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 134.9, 132.9, 129.0, 127.7, 65.9, 45.8.

HRMS-EI (m/z) calc'd for C₁₀H₁₃NO₃S⁺ [M]⁺, 227.0610; found, 227.0610; deviation: -0.02 ppm.

4-((4-Ethylphenyl)sulfonyl)morpholine (**3**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-5** (81.7 mg, 0.200 mmol, 1.00 equiv), Pd(dppf)Cl₂ (8 mg, 0.01 mmol, 5 mol %), Rongalite (35.4 mg, 0.300 mmol 1.50 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol

(1.0 mL, $c = 0.20$ M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (56 μ L, 40 mg, 0.40 mmol, 2.0 equiv), morpholine (**A1**) (35 μ L, 35 mg, 0.40 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (53.4 mg, 0.400 mmol, 2.00 equiv) in THF (1.0 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 32 mg (63%) of **3** as a colorless solid.

$R_f = 0.68$ (hexanes / ethyl acetate, 1:1 (v/v)).

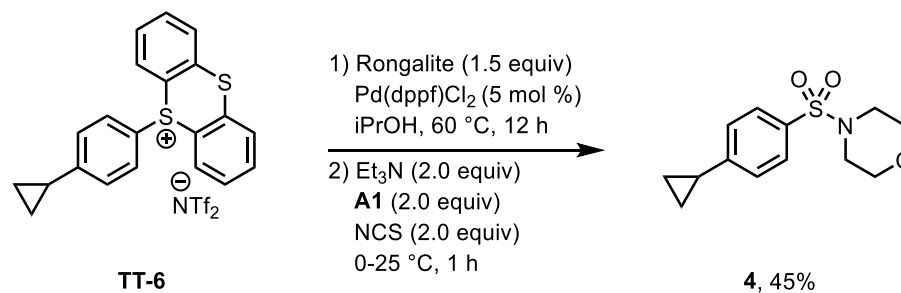
NMR Spectroscopy:

^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.66 (d, $J = 8.3$ Hz, 2H), 7.36 (d, $J = 8.3$ Hz, 2H), 3.77 – 3.70 (m, 4H), 3.02 – 2.95 (m, 4H), 2.73 (q, $J = 7.6$ Hz, 2H), 1.27 (t, $J = 7.6$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 149.9, 132.1, 128.4, 127.9, 66.0, 45.8, 28.7, 14.9.

HRMS-EI (m/z) calc'd for $\text{C}_{12}\text{H}_{17}\text{NO}_3\text{S}^+$ $[\text{M}]^+$, 255.0926; found, 255.0924; deviation: -0.96 ppm.

4-((4-Cyclopropylphenyl)sulfonyl)morpholine (**4**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-6** (61.4 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μ mol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (1.0 mL, $c = 0.20$ M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μ L, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 12 mg (45%) of **4** as a white solid.

$R_f = 0.62$ (hexanes / ethyl acetate, 1:1 (v/v)).

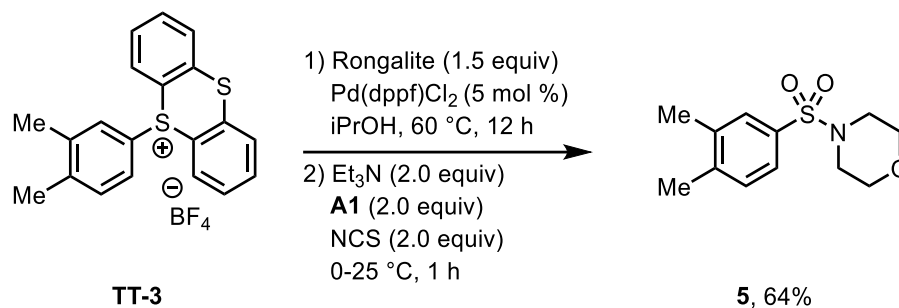
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.61 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 3.77 – 3.70 (m, 4H), 3.01 – 2.93 (m, 4H), 1.96 (ddd, *J* = 13.1, 8.3, 4.9 Hz, 1H), 1.15 – 1.04 (m, 2H), 0.79 (dt, *J* = 6.7, 4.9 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 150.6, 131.8, 128.1, 126.1, 66.2, 46.1, 15.8, 10.7.

HRMS-EI (m/z) calc'd for C₁₃H₁₇NO₃S⁺ [M]⁺, 267.0924; found, 267.0924; deviation: -0.28 ppm.

4-((3,4-Dimethylphenyl)sulfonyl)morpholine (**5**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-3** (81.7 mg, 0.200 mmol, 1.00 equiv), Pd(dppf)Cl₂ (8 mg, 0.01 mmol, 5 mol %), Rongalite (35.4 mg, 0.300 mmol 1.50 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (1.0 mL, *c* = 0.20 M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (56 μL, 40 mg, 0.40 mmol, 2.0 equiv), morpholine (**A1**) (35 μL, 35 mg, 0.40 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (53.4 mg, 0.400 mmol, 2.00 equiv) in THF (1.0 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 33 mg (64%) of **5** as a colorless solid.

R_f = 0.62 (hexanes / ethyl acetate, 1:1 (v/v)).

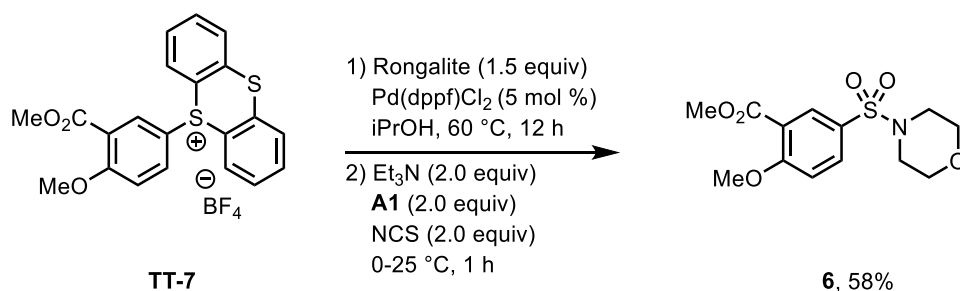
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.50 (s, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 1H), 3.77 – 3.71 (m, 4H), 3.02 – 2.95 (m, 4H), 2.34 (s, 6H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 142.8, 138.0, 132.2, 130.3, 128.7, 125.6, 66.2, 46.1, 20.0, 20.0.

HRMS-EI (m/z) calc'd for C₁₂H₁₇NO₃S⁺ [M]⁺, 255.0927; found, 255.0924; deviation: -1.31 ppm.

Methyl 2-methoxy-5-(morpholinosulfonyl)benzoate (**6**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-7** (93.6 mg, 0.200 mmol, 1.00 equiv), Pd(dppf)Cl₂ (8 mg, 0.01 mmol, 5 mol %), Rongalite (35.4 mg, 0.300 mmol 1.50 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (1.0 mL, c = 0.20 M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (56 μL, 40 mg, 0.40 mmol, 2.0 equiv), morpholine (**A1**) (35 μL, 35 mg, 0.40 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (53.4 mg, 0.400 mmol, 2.00 equiv) in THF (1.0 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-20:3 (v/v)) to afford 37 mg (58%) of **6** as a colorless solid.

R_f = 0.26 (hexanes / ethyl acetate, 1:1 (v/v)).

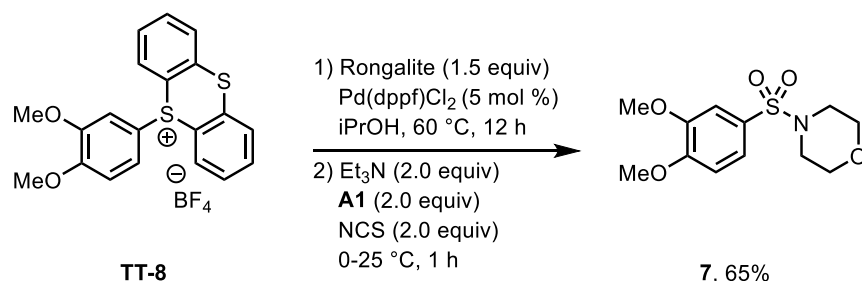
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 8.14 (t, *J* = 2.1 Hz, 1H), 7.83 (dt, *J* = 8.8, 2.1 Hz, 1H), 7.10 (dd, *J* = 8.8, 1.5 Hz, 1H), 3.97 (d, *J* = 1.7 Hz, 3H), 3.89 (d, *J* = 1.9 Hz, 3H), 3.75 – 3.70 (m, 4H), 3.00 – 2.95 (m, 4H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 165.0, 162.4, 133.3, 131.8, 126.7, 120.8, 112.4, 66.1, 56.6, 52.6, 46.1.

HRMS-EI (*m/z*) calc'd for C₁₃H₁₇NO₆S⁺ [M]⁺, 315.0772; found, 315.0771; deviation: -0.35 ppm.

4-((3,4-Dimethoxyphenyl)sulfonyl)morpholine (**7**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was

charged with **TT-8** (88.0 mg, 0.200 mmol, 1.00 equiv), Pd(dppf)Cl₂ (8 mg, 0.01 mmol, 5 mol %), Rongalite (35.4 mg, 0.300 mmol 1.50 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (1.0 mL, c = 0.20 M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (56 μL, 40 mg, 0.40 mmol, 2.0 equiv), morpholine (**A1**) (35 μL, 35 mg, 0.40 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (53.4 mg, 0.400 mmol, 2.00 equiv) in THF (1.0 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:2 (v/v)) to afford 37 mg (65%) of **7** as a white solid.

R_f = 0.25 (hexanes / ethyl acetate, 1:1 (v/v)).

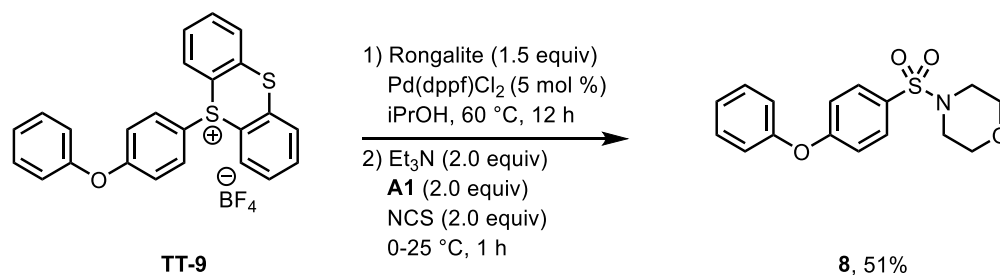
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.37 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.20 (d, *J* = 2.0 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 3.94 (d, *J* = 10.7 Hz, 6H), 3.76 – 3.72 (m, 4H), 3.03 – 2.97 (m, 4H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 153.0, 149.2, 126.9, 121.9, 110.8, 110.4, 66.2, 56.4, 56.3, 46.1.

HRMS-EI (m/z) calc'd for C₁₂H₁₇NO₅S⁺ [M]⁺, 287.0826; found, 287.0822; deviation: -1.41 ppm.

4-((4-Phenoxyphenyl)sulfonyl)morpholine (**8**)



An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-9** (94.4 mg, 0.200 mmol, 1.00 equiv), Pd(dppf)Cl₂ (8 mg, 0.01 mmol, 5 mol %), Rongalite (35.4 mg, 0.300 mmol 1.50 equiv), and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (1.0 mL, c = 0.20 M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (56 μL, 40 mg, 0.40 mmol, 2.0 equiv), morpholine (**A1**) (35 μL, 35 mg, 0.40 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (53.4 mg, 0.400 mmol, 2.00 equiv) in THF (1.0 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford to afford 33 mg (51%) of **8** as colorless solid.

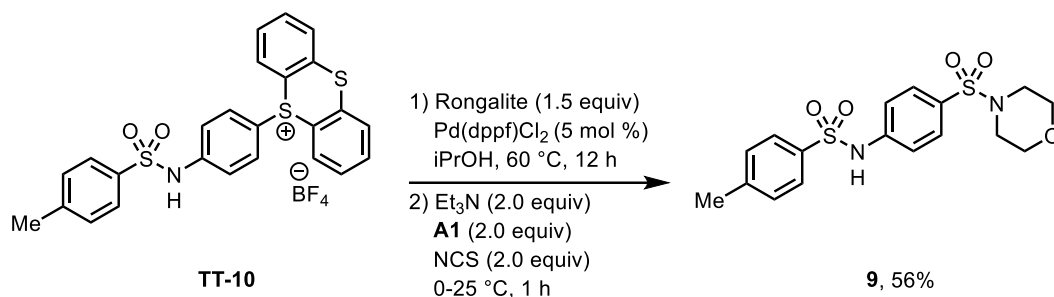
R_f = 0.77 (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.70 (d, *J* = 8.9 Hz, 2H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.07 (t, *J* = 9.4 Hz, 4H), 3.81 – 3.70 (m, 4H), 3.06 – 2.95 (m, 4H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 162.1, 155.1, 130.4, 130.2, 128.6, 125.2, 120.5, 117.7, 66.2, 46.1.

HRMS-EI (m/z) calc'd for C₁₆H₁₇NO₄S⁺ [M]⁺, 319.0875; found, 319.0873; deviation: -0.75 ppm.

4-Methyl-N-(4-(morpholinofulfonyl)phenyl)benzenesulfonamide (9)

In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-10** (54.9 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-4:1 (v/v)) to afford 22 mg (56%) of **9** as a white solid.

R_f = 0.38 (hexanes / ethyl acetate, 1:1 (v/v)).

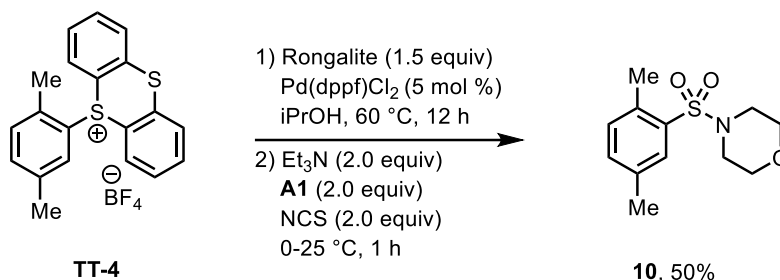
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.75 (d, *J* = 7.4 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.23 (m, 4H), 3.76 – 3.69 (m, 4H), 2.99 – 2.89 (m, 4H), 2.40 (s, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 145.0, 141.5, 135.7, 130.5, 130.2, 129.6, 127.4 119.2, 66.2, 46.1, 21.7.

HRMS-ESI (m/z) calc'd for C₁₇H₁₉N₂O₅S₂⁺ [M-H]⁺, 395.0744; found, 395.0741; deviation: -0.75 ppm.

4-((2,5-Dimethylphenyl)sulfonyl)morpholine (**10**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-4** (40.8 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 13 mg (50%) of **10** as a white solid.

R_f = 0.68 (hexanes / ethyl acetate, 1:1 (v/v)).

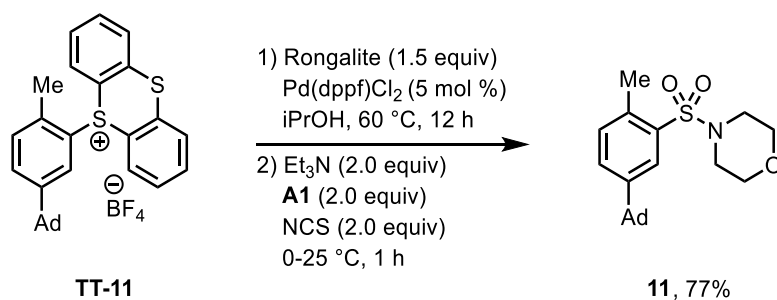
NMR Spectroscopy:

¹H NMR (500 MHz, CD₂Cl₂, 298 K, δ): 7.67 (s, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 3.71 – 3.66 (m, 4H), 3.12 – 3.05 (m, 4H), 2.57 (s, 3H), 2.38 (s, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 136.2, 135.1, 134.6, 134.0, 133.0, 130.9, 66.5, 45.4, 21.0, 20.5.

HRMS-EI (m/z) calc'd for C₁₂H₁₇NO₃S⁺ [M]⁺, 255.0925; found, 255.0924; deviation: -0.60 ppm.

4-((5-((3s)-Adamantan-1-yl)-2-methylphenyl)sulfonyl)morpholine (**11**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-11** (52.8 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c

= 0.2 M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μ L, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 29 mg (77%) of **11** as a colorless solid.

R_f = 0.74 (hexanes / ethyl acetate, 1:1 (v/v)).

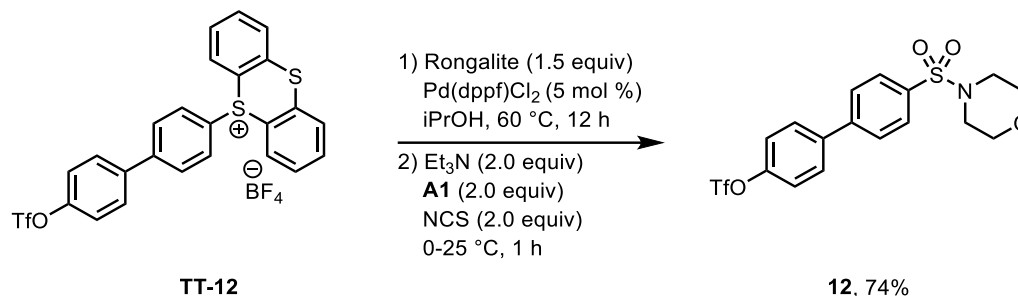
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.83 (s, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 6.0 Hz, 1H), 3.75 – 3.67 (m, 4H), 3.15 – 3.09 (m, 4H), 2.58 (s, 3H), 2.10 (s, 3H), 1.89 (s, 6H), 1.76 (q, J = 12.1 Hz, 6H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 149.9, 135.1, 134.4, 132.9, 129.9, 127.1, 66.5, 45.4, 43.1, 36.7, 36.2, 28.9, 20.5.

HRMS-ESI (m/z) calc'd for C₂₁H₂₉NO₃SNa⁺ [M+Na]⁺, 398.1757; found, 398.1760; deviation: +0.79 ppm.

4'-(Morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (**12**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-12** (60.4 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μ mol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μ L, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 33 mg (74%) of **12** as a white solid.

R_f = 0.70 (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

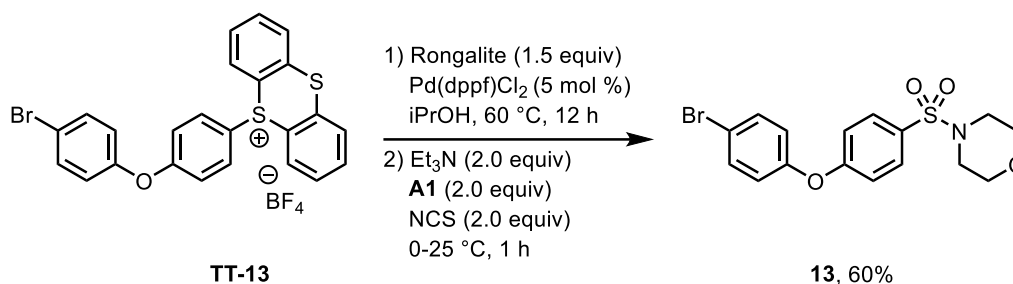
¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.85 (d, *J* = 8.4 Hz, 2H), 7.70 (dd, *J* = 24.4, 8.6 Hz, 4H), 7.41 (d, *J* = 8.7 Hz, 2H), 3.82 – 3.74 (m, 4H), 3.11 – 3.02 (m, 4H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 149.8, 144.1, 139.8, 134.8, 129.4, 128.7, 128.0, 122.2, 118.9 (q, *J* = 321 Hz, SO₂CF₃), 66.2, 46.1.

¹⁹F NMR (471 MHz, CDCl₃, 298 K, δ): -72.72 (s).

HRMS-ESI (m/z) calc'd for C₁₇H₁₇NO₆S₂F₃⁺ [M+H]⁺, 452.0444; found, 452.0444; deviation: -0.03 ppm.

4-((4-(4-Bromophenoxy)phenyl)sulfonyl)morpholine (**13**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-13** (110 mg, 0.200 mmol, 1.00 equiv), Pd(dppf)Cl₂ (8 mg, 0.01 mmol, 5 mol %), Rongalite (35.4 mg, 0.300 mmol 1.50 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (1.0 mL, c = 0.20 M) was added outside the glovebox and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (56 μL, 40 mg, 0.40 mmol, 2.0 equiv), morpholine (**A1**) (35 μL, 35 mg, 0.40 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (53.4 mg, 0.400 mmol, 2.00 equiv) in THF (1.0 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 48 mg (60%) of **13** as a colorless solid.

1 mmol scale reaction

An oven dried 100 mL round bottom flask equipped with a magnetic stir bar was charged with **TT-13** (550 mg, 1.00 mmol, 1.00 equiv), Pd(dppf)Cl₂ (40 mg, 0.050 mmol, 5.0 mol %), Rongalite (177 mg, 1.50 mmol 1.50 equiv), and sealed with a septum cap. The round bottom flask was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (5.0 mL, c = 0.20 M) was added and the reaction mixture was immediately placed in a preheated oil bath at 60 °C for 12 h. After cooling to 25 °C, triethylamine (0.300 mL, 120 mg, 2.00 mmol, 2.00 equiv), morpholine (**A1**) (0.200 mL, 175 mg, 2.00 mmol, 2.00 equiv), and a solution of *N*-chlorosuccinimide (268 mg, 2.00 mmol, 2.00 equiv) in THF (5.0 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 0.23g (58%) of **13** as a colorless solid.

$R_f = 0.65$ (hexanes / ethyl acetate, 1:1 (v/v)).

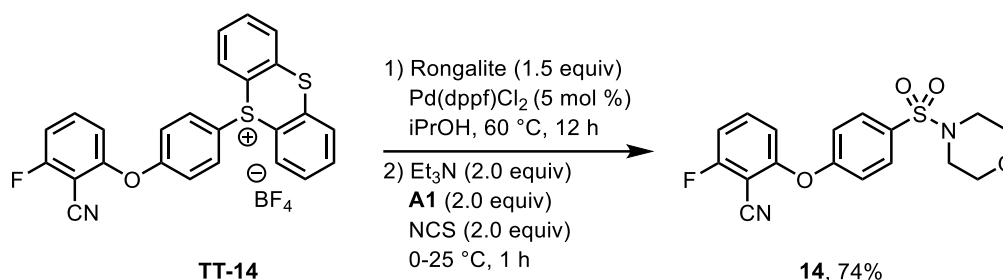
NMR Spectroscopy:

$^1\text{H NMR}$ (500 MHz, CDCl_3 , 298 K, δ): 7.71 (d, $J = 8.8$ Hz, 2H), 7.53 (d, $J = 8.8$ Hz, 2H), 7.07 (d, $J = 8.8$ Hz, 2H), 6.97 (d, $J = 8.8$ Hz, 2H), 3.80 – 3.71 (m, 4H), 3.05 – 2.93 (m, 4H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3 , 298 K, δ): 133.4, 130.3, 122.2, 117.8, 66.2, 46.1.

HRMS-ESI (m/z) calc'd for $\text{C}_{16}\text{H}_{17}\text{NO}_4\text{SBr}^+$ $[\text{M}+\text{H}]^+$, 398.0060; found, 398.0056; deviation: -0.85 ppm.

2-Fluoro-6-(4-(morpholinofonyl)phenoxy)benzonitrile (**14**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-14** (51.5 mg, 0.100 mmol, 1.00 equiv), $\text{Pd}(\text{dppf})\text{Cl}_2$ (4 mg, 5 μmol , 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.25 mL) and acetonitrile (0.25 mL, $c = 0.20$ M) were added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL , 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL , 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-20:3 (v/v)) to afford 27 mg (74%) of **14** as a colorless solid.

$R_f = 0.30$ (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

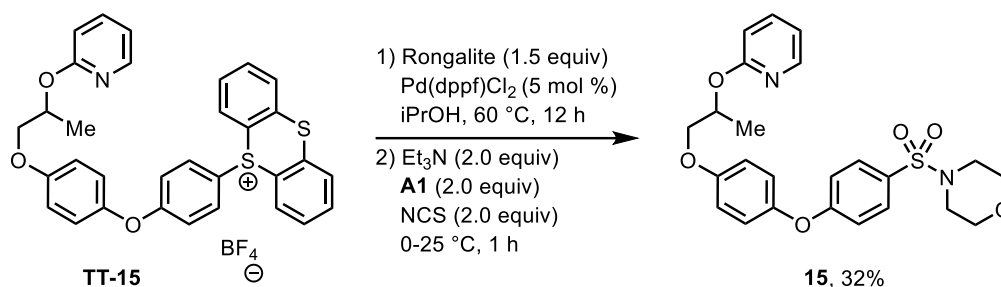
$^1\text{H NMR}$ (500 MHz, CDCl_3 , 298 K, δ): 7.80 (d, $J = 8.8$ Hz, 2H), 7.56 (td, $J = 8.5, 6.4$ Hz, 1H), 7.23 (d, $J = 8.8$ Hz, 2H), 7.03 (t, $J = 8.4$ Hz, 1H), 6.78 (d, $J = 8.5$ Hz, 1H), 3.78 – 3.73 (m, 4H), 3.05 – 2.98 (m, 4H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3 , 298 K, δ): 164.2 (d, $J = 261.1$ Hz), 158.9, 158.8, 135.4 (d, $J = 10.2$ Hz), 131.9, 130.5, 119.7, 114.0 (d, $J = 3.5$ Hz), 111.8, 111.7, 95.3 (d, $J = 18.0$ Hz), 66.2, 46.1.

$^{19}\text{F NMR}$ (471 MHz, CDCl_3 , 25 °C, δ): -103.28 – -103.43 (m).

HRMS-ESI (m/z) calc'd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_4\text{FS}^+$ $[\text{M}+\text{H}]^+$, 363.0802; found, 363.0809; deviation: +1.94 ppm.

Pyriproxyfen morpholine sulfonamide derivative (15)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-15** (62.2 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.25 mL) and acetonitrile (0.25 mL, *c* = 0.20 M) were added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 15 mg (32%) of **15** as a colorless oil.

R_f = 0.57 (hexanes / ethyl acetate, 1:1 (v/v)).

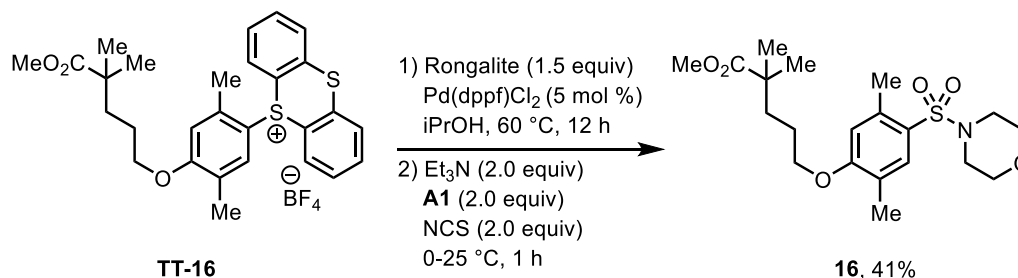
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 8.17 (ddd, *J* = 5.2, 2.1, 0.8 Hz, 1H), 7.66 (d, *J* = 8.9 Hz, 2H), 7.62 (ddd, *J* = 8.8, 7.1, 2.0 Hz, 1H), 7.03 - 6.96 (m, 6H), 6.90 (ddd, *J* = 7.1, 5.1, 1.0 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 5.66-5.60 (m, 1H), 4.22 (dd, *J* = 9.9, 5.4 Hz, 1H), 4.11 (dd, *J* = 9.9, 4.7 Hz, 1H), 3.78 - 3.71 (m, 4H), 3.02 - 2.96 (m, 4H), 1.50 (d, *J* = 6.4 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 163.2, 163.0, 156.4, 148.3, 146.9, 138.9, 130.1, 128.1, 121.9, 117.0, 116.8, 116.2, 111.8, 71.2, 69.3, 66.2, 46.1, 17.1.

HRMS-ESI (m/z) calc'd for C₂₄H₂₇N₂O₆S⁺ [M+H]⁺, 471.1584; found, 471.1305; deviation: +0.81 ppm.

Gemfibrozil methyl ester morpholine sulfonamide derivative (16)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-16** (56.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 17 mg (41%) of **16** as a colorless solid.

R_f = 0.54 (hexanes / ethyl acetate, 1:1 (v/v)).

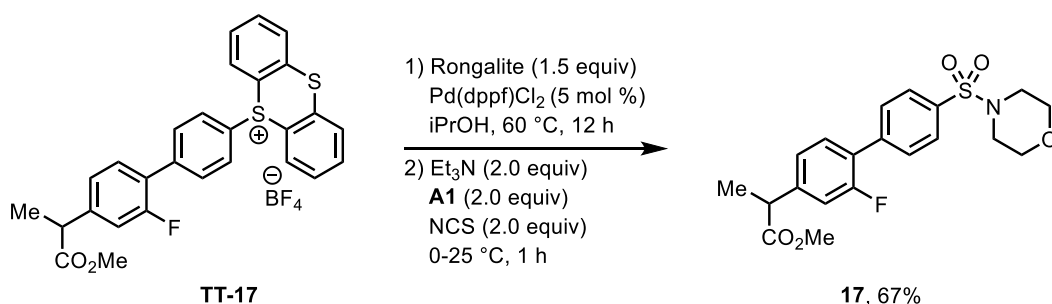
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.64 (s, 1H), 6.66 (s, 1H), 3.97 (t, *J* = 5.9 Hz, 2H), 3.72 – 3.69 (m, 4H), 3.67 (s, 3H), 3.13 – 3.07 (m, 4H), 2.58 (s, 3H), 2.20 (s, 3H), 1.78 – 1.69 (m, 4H), 1.22 (s, 6H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 178.3, 160.5, 138.1, 133.0, 125.3, 124.7, 114.4, 68.4, 66.4, 51.9, 45.4, 42.2, 37.1, 25.3, 25.1, 21.1, 15.8.

HRMS-ESI (*m/z*) calc'd for C₂₀H₃₂NO₆S⁺ [M+H]⁺, 414.1939; found, 414.1945; deviation: +1.51 ppm.

Flurbiprofen methyl ester morpholine sulfonamide derivative (**17**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-17** (56.0 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.25 mL) and acetonitrile (0.25 mL, c = 0.20 M) were added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v))

to afford 27 mg (67%) of **17** as colorless oil.

$R_f = 0.32$ (hexanes / ethyl acetate, 5:1 (v/v)).

NMR Spectroscopy:

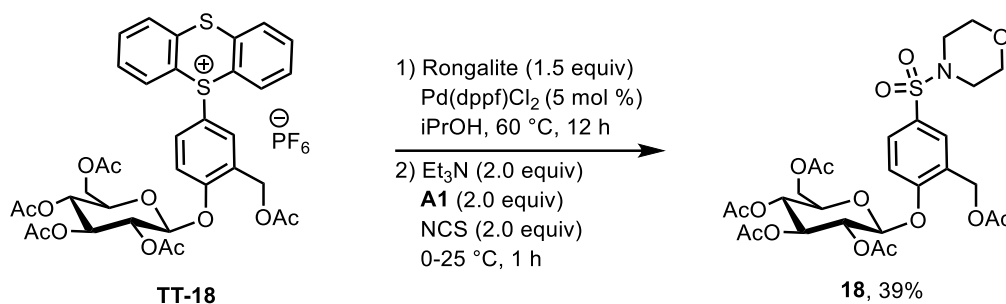
^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.81 (d, $J = 7.7$ Hz, 2H), 7.70 (d, $J = 8.2$ Hz, 2H), 7.40 (t, $J = 8.0$ Hz, 1H), 7.18 (dd, $J = 16.7, 9.9$ Hz, 2H), 3.81 – 3.73 (m, 5H), 3.70 (s, 3H), 3.08 – 3.00 (m, 4H), 1.54 (d, $J = 7.2$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 174.2, 159.8 (d, $J = 249.8$ Hz), 143.4 (d, $J = 7.8$ Hz), 134.2, 130.8 (d, $J = 3.4$ Hz), 129.7 (d, $J = 3.2$ Hz), 128.1, 126.0 (d, $J = 13.2$ Hz), 124.1 (d, $J = 3.4$ Hz), 115.7 (d, $J = 23.3$ Hz), 66.2, 52.4, 46.1, 45.1, 18.5.

^{19}F NMR (471 MHz, CDCl_3 , 298 K, δ): -117.1.

HRMS-ESI(m/z) calc'd for $\text{C}_{20}\text{H}_{22}\text{NO}_5\text{FSNa}^+ [\text{M}+\text{Na}]^+$, 430.1089; found, 430.1095; deviation: +1.29 ppm.

Salicin pentaacetate morpholine sulfonamide derivative (**18**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-18** (85.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol , 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.25 mL) and acetonitrile (0.25 mL, $c = 0.20$ M) were added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL , 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL , 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 25 mg (39%) of **18** as a colorless solid.

$R_f = 0.14$ (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

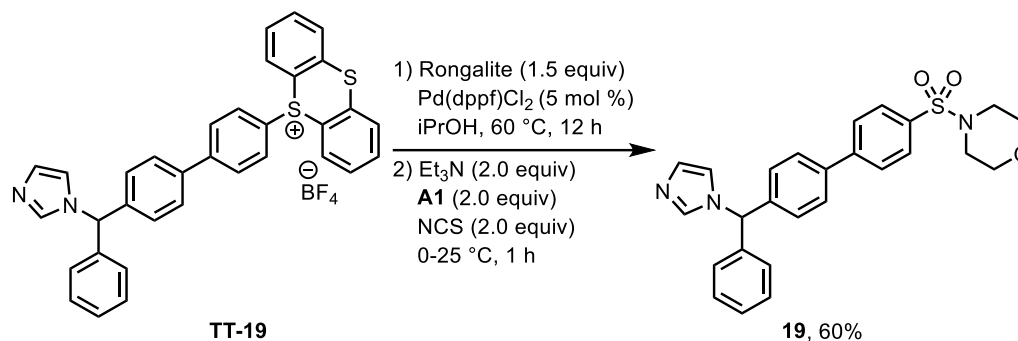
^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.72 (d, $J = 2.0$ Hz, 1H), 7.68 (dd, $J = 8.6, 2.2$ Hz, 1H), 7.17 (d, $J = 8.7$ Hz, 1H), 5.35 – 5.29 (m, 2H), 5.22 – 5.17 (m, 2H), 5.14 (d, $J = 13.6$ Hz, 1H), 5.04 (d, $J = 13.6$ Hz, 1H),

4.28 (dd, $J = 12.4, 5.2$ Hz, 1H), 4.20 (dd, $J = 12.4, 2.3$ Hz, 1H), 3.93 (ddd, $J = 9.9, 5.1, 2.4$ Hz, 1H), 3.78 – 3.69 (m, 4H), 3.01 – 2.93 (m, 4H), 2.11 (d, $J = 9.0$ Hz, 6H), 2.07 – 2.04 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 170.6, 170.5, 170.3, 169.5, 169.3, 157.6, 129.9, 129.6, 129.0, 127.5, 115.0, 98.6, 72.5, 72.4, 70.9, 68.2, 66.2, 61.9, 60.4, 46.1, 21.0, 20.8, 20.7.

HRMS-ESI (m/z) calc'd for $\text{C}_{27}\text{H}_{35}\text{NO}_{15}\text{SNa}^+$ [$\text{M}+\text{Na}$] $^+$, 668.1618; found, 668.1620; deviation: +0.20 ppm.

Bifonazole morpholine sulfonamide derivative (**19**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-19** (61.2 mg, 0.100 mmol, 1.00 equiv), $\text{Pd}(\text{dppf})\text{Cl}_2$ (4 mg, 5 μmol , 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.25 mL) and acetonitrile (0.25 mL, $c = 0.20$ M) were added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL , 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL , 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with DCM / $i\text{PrOH}$ (1:0-20:1 (v/v)) to afford 28 mg (60%) of **19** as yellow oil.

$R_f = 0.43$ (DCM / $i\text{PrOH}$, 10:1 (v/v)).

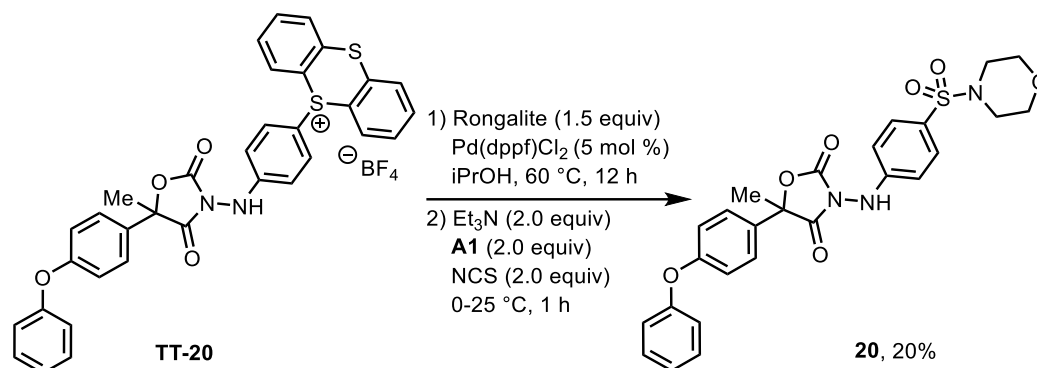
NMR Spectroscopy:

^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.82 (d, $J = 7.9$ Hz, 2H), 7.73 (d, $J = 7.9$ Hz, 2H), 7.60 (d, $J = 7.9$ Hz, 2H), 7.46 (s, 1H), 7.39 (q, $J = 6.4, 5.9$ Hz, 3H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.17 – 7.11 (m, 3H), 6.89 (s, 1H), 6.59 (s, 1H), 3.79 – 3.72 (m, 4H), 3.09 – 3.01 (m, 4H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 145.1, 139.7, 139.4, 138.7, 134.2, 129.2, 128.9, 128.8, 128.6, 128.3, 128.0, 127.9, 66.2, 64.9, 46.1.

HRMS-ESI (m/z) calc'd for $\text{C}_{26}\text{H}_{26}\text{N}_3\text{O}_3\text{S}^+$ [$\text{M}+\text{H}$] $^+$, 460.1684; found, 460.1689; deviation: +1.26 ppm.

Famoxadone morpholine sulfonamide derivative (20)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-20** (67.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was immediately placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A1**) (18 μL, 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 11 mg (20%) of **20** as a colorless oil.

$R_f = 0.35$ (hexanes / ethyl acetate, 1:1 (v/v)).

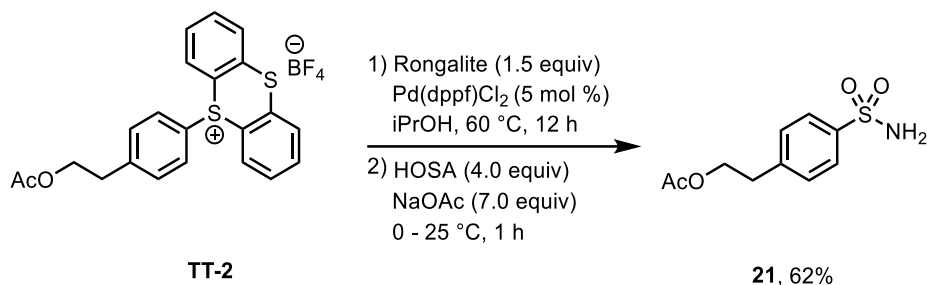
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.64 (d, $J = 8.7$ Hz, 2H), 7.54 (d, $J = 9.0$ Hz, 2H), 7.41 – 7.36 (m, 2H), 7.18 (t, $J = 7.9$ Hz, 1H), 7.09 – 7.02 (m, 4H), 6.78 (d, $J = 8.8$ Hz, 2H), 6.42 (s, 1H), 3.75 – 3.69 (m, 4H), 2.99 – 2.93 (m, 4H), 2.02 (s, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.7, 159.0, 156.2, 152.2, 148.3, 130.2, 130.1, 129.9, 129.0, 126.1, 124.4, 119.8, 118.8, 113.4, 85.6, 66.2, 46.1, 25.7.

HRMS-ESI (m/z) calc'd for C₂₆H₂₅N₃O₇SNa⁺ [M+Na]⁺, 546.1301; found, 546.1305; deviation: +0.81 ppm.

4-Sulfamoylphenethyl acetate (**21**)



An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (0.5 mL, c = 0.2 M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, a solution of hydroxylamine-*O*-sulfonic acid (45.2 mg, 0.400 mmol, 4.00 equiv) and sodium acetate (57.4 mg, 0.700 mmol, 7.00 equiv) in water (0.5 mL) was added dropwise through the septum under stirring. After stirring the reaction mixture at 25 °C for 1 h, the reaction mixture was washed with brine, dried over NaSO₄, and concentrated. The crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-4:1 (v/v)) to afford 15 mg (62%) of **21** as a colorless solid.

R_f = 0.24 (hexanes / ethyl acetate, 1:1 (v/v)).

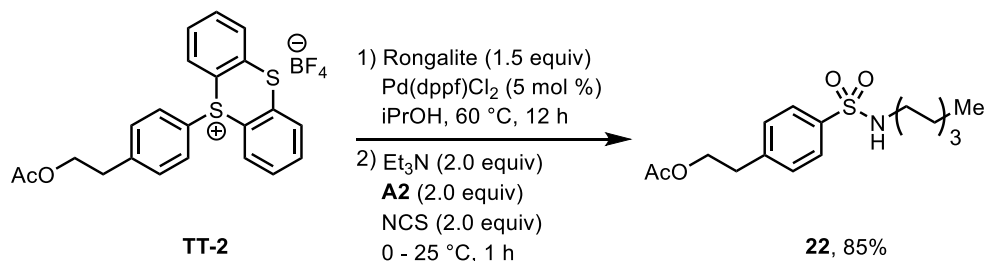
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.87 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 5.00 (s, 2H), 4.30 (t, *J* = 6.8 Hz, 2H), 3.01 (t, *J* = 6.8 Hz, 2H), 2.03 (s, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.1, 143.6, 140.4, 129.8, 126.8, 64.2, 35.0, 21.0.

HRMS-ESI (*m/z*) calc'd for C₁₀H₁₄NO₄S⁺ [M+H]⁺, 244.0635; found, 244.0638; deviation: +1.13 ppm.

4-(*N*-Heptylsulfamoyl)phenethyl acetate (**22**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating

block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), heptylamine (**A2**) (30 μ L, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 29 mg (85%) of **22** as a colorless oil.

R_f = 0.70 (hexanes / ethyl acetate, 1:1 (v/v)).

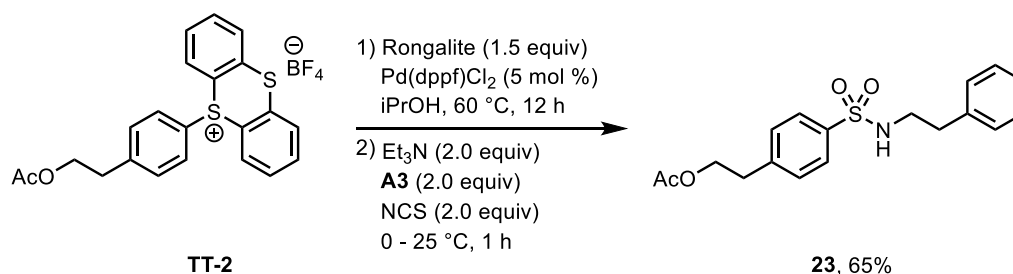
NMR Spectroscopy:

^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.80 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 4.52 (t, J = 6.1 Hz, 1H), 4.30 (t, J = 6.8 Hz, 2H), 3.01 (t, J = 6.8 Hz, 2H), 2.94 (q, J = 7.0 Hz, 2H), 2.03 (s, 3H), 1.44 (q, J = 7.1 Hz, 2H), 1.23 (dt, J = 20.1, 7.2 Hz, 8H), 0.85 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 171.0, 143.2, 138.4, 129.7, 127.4, 64.2, 43.4, 35.0, 31.7, 29.7, 28.8, 26.6, 22.6, 21.0, 14.1.

HRMS-ESI (m/z) calc'd for $\text{C}_{17}\text{H}_{27}\text{NO}_4\text{SNa}^+$ [$\text{M}+\text{Na}$] $^+$, 364.1557; found, 364.1553; deviation: -1.01 ppm.

4-(*N*-Phenethylsulfamoyl)phenethyl acetate (**23**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), $\text{Pd}(\text{dppf})\text{Cl}_2$ (4 mg, 5 μ mol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), phenethylamine (**A3**) (25.4 μ L, 0.200 mmol, 2.00 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 23 mg (65%) of **23** as a colorless solid.

R_f = 0.53 (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

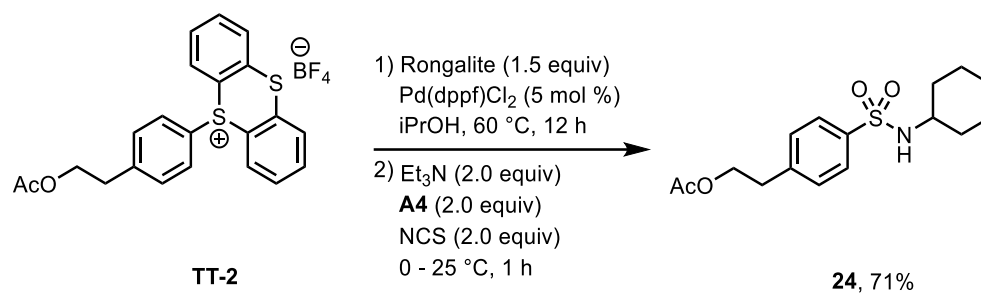
^1H NMR (500 MHz, CD_2Cl_2 , 298 K, δ): 7.72 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H), 7.27 (t, J = 7.2

Hz, 2H), 7.21 (t, $J = 7.3$ Hz, 1H), 7.08 (d, $J = 7.2$ Hz, 2H), 4.46 (d, $J = 6.1$ Hz, 1H), 4.28 (t, $J = 6.8$ Hz, 2H), 3.23 – 3.17 (m, 2H), 3.01 (t, $J = 6.8$ Hz, 2H), 2.74 (t, $J = 7.0$ Hz, 2H), 1.99 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 171.0, 143.4, 138.3, 137.7, 129.7, 128.9, 128.9, 127.4, 127.0, 64.2, 44.4, 36.0, 35.0, 21.0.

HRMS-ESI (m/z) calc'd for $\text{C}_{18}\text{H}_{21}\text{NO}_4\text{SNa}^+$ [$\text{M}+\text{Na}$] $^+$, 370.1088; found, 370.1084; deviation: -1.08ppm.

4-(*N*-Cyclohexylsulfamoyl)phenethyl acetate (**24**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol , 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL , 20 mg, 0.20 mmol, 2.0 equiv), cyclohexylamine (**A4**) (22.9 μL , 0.200 mmol, 2.00 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 23 mg (71%) of **24** as a colorless solid.

$R_f = 0.63$ (hexanes / ethyl acetate, 1:1 (v/v)).

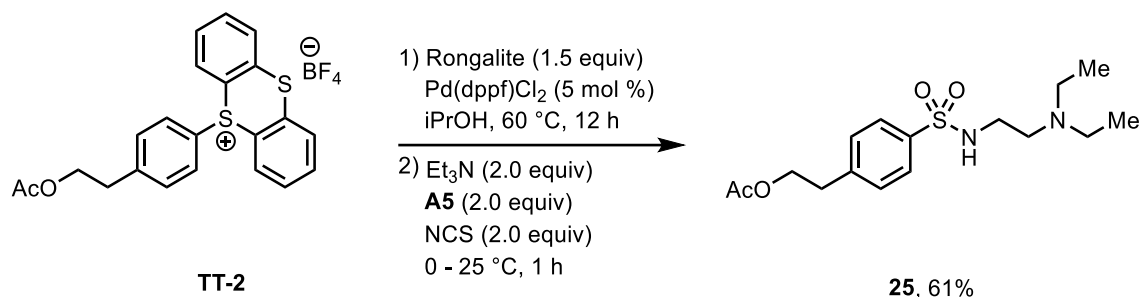
NMR Spectroscopy:

^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.81 (d, $J = 8.3$ Hz, 2H), 7.35 (d, $J = 8.3$ Hz, 2H), 4.50 (d, $J = 7.5$ Hz, 1H), 4.30 (t, $J = 6.9$ Hz, 2H), 3.19 – 3.11 (m, 1H), 3.01 (t, $J = 6.9$ Hz, 2H), 2.02 (s, 3H), 1.78 – 1.48 (m, 5H), 1.26 – 1.07 (m, 5H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 171.0, 143.0, 139.9, 129.6, 127.3, 64.2, 52.8, 35.0, 34.1, 25.3, 24.8, 21.0.

HRMS-ESI (m/z) calc'd for $\text{C}_{16}\text{H}_{23}\text{NO}_4\text{SNa}^+$ [$\text{M}+\text{Na}$] $^+$, 348.1240; found, 348.1240; deviation: +0.09 ppm.

4-(*N*-(2-(Diethylamino)ethyl)sulfamoyl)phenethyl acetate (**25**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), *N,N*-diethylethylenediamine (**A5**) (28 μL, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with DCM / iPrOH (1:0-20:1 (v/v)) to afford 21 mg (61%) of **25** as a yellow oil.

R_f = 0.45 (DCM / iPrOH, 10:1 (v/v)).

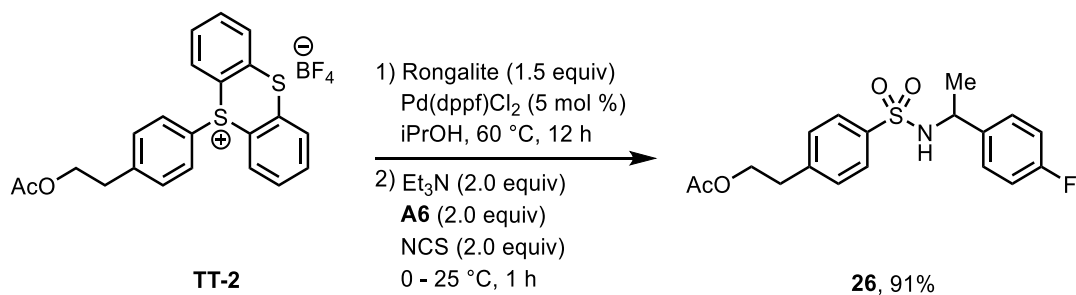
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.80 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 4.29 (t, *J* = 6.8 Hz, 2H), 2.98 (dt, *J* = 21.4, 6.3 Hz, 4H), 2.55 – 2.47 (m, 2H), 2.40 (q, *J* = 7.1 Hz, 4H), 2.02 (s, 3H), 0.91 (t, *J* = 7.1 Hz, 6H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.0, 143.2, 138.1, 129.6, 127.5, 64.3, 51.2, 46.5, 40.2, 35.0, 21.0, 11.6.

HRMS-ESI (m/z) calc'd for C₁₆H₂₇N₂O₄S⁺ [M+H]⁺, 343.1685; found, 343.1686; deviation: +0.42 ppm.

4-(*N*-(1-(4-Fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (**26**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), 4-fluoro- α -methylbenzylamine (**A6**) (27 μL, 27 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 33 mg (91%) of **26** as a colorless oil.

R_f = 0.52 (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

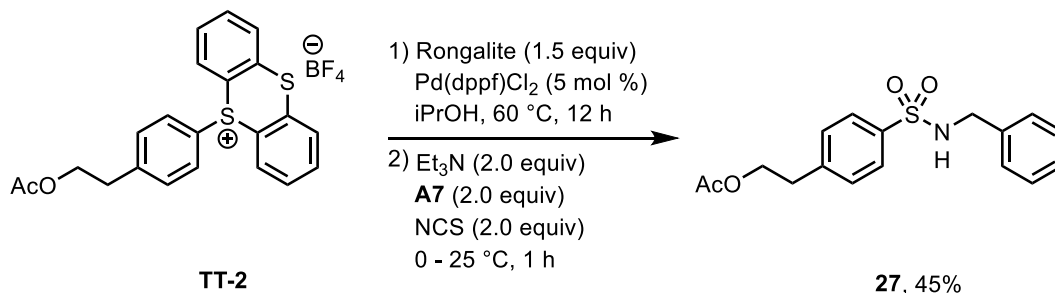
¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.62 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 7.05 (dd, *J* = 8.6, 5.3 Hz, 2H), 6.83 (t, *J* = 8.7 Hz, 2H), 5.21 (d, *J* = 7.0 Hz, 1H), 4.47 (p, *J* = 6.9 Hz, 1H), 4.27 (t, *J* = 6.9 Hz, 2H), 2.96 (t, *J* = 6.8 Hz, 2H), 2.04 (s, 3H), 1.39 (d, *J* = 6.9 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.0, 163.1, 161.0 (d, *J* = 245.9 Hz), 143.2, 139.0, 137.8, 129.4, 128.0 (d, *J* = 8.2 Hz), 127.4, 115.4 (d, *J* = 21.5 Hz), 64.3, 53.2, 35.0, 23.7, 21.0.

¹⁹F NMR (471 MHz, CDCl₃, 298 K, δ): -114.91.

HRMS-EI (m/z) calc'd for C₁₈H₂₀NO₄SF⁺ [M]⁺, 364.1032; found, 364.1024; deviation: -1.96 ppm.

4-(*N*-Benzylsulfamoyl)phenethyl acetate (**27**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), benzylamine (**A7**) (21.4 mg, 0.200 mmol, 2.00 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at

25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 15 mg (45%) of **27** as a colorless solid.

R_f = 0.59 (hexanes / ethyl acetate, 1:1 (v/v)).

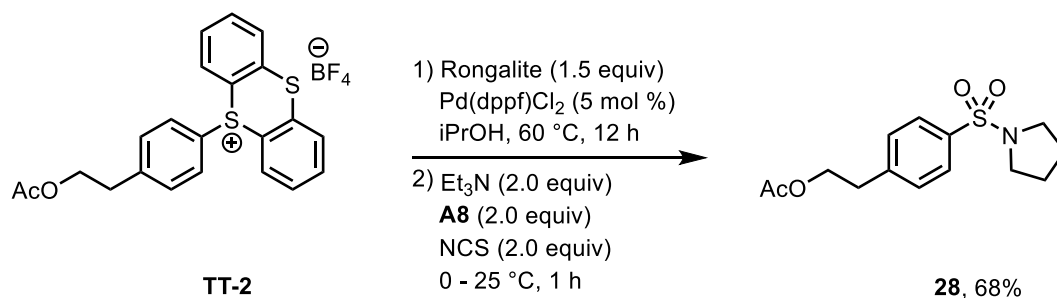
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.81 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.30 – 7.14 (m, 5H), 4.75 (t, J = 6.1 Hz, 1H), 4.31 (t, J = 6.8 Hz, 2H), 4.15 (d, J = 6.2 Hz, 2H), 3.01 (t, J = 6.8 Hz, 2H), 2.04 (s, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.0, 143.5, 138.4, 136.3, 129.8, 128.8, 128.1, 128.0, 127.5, 64.2, 47.4, 35.1, 21.0.

HRMS-ESI (m/z) calc'd for C₁₇H₁₉NO₄SNa⁺ [M+Na]⁺, 356.0925; found, 356.0927; deviation: +0.56 ppm.

4-(Pyrrolidin-1-ylsulfonyl)phenethyl acetate (**28**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μ mol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), pyrrolidine (**A8**) (16.9 μ L, 0.200 mmol, 2.00 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 20 mg (68%) of **28** as a yellow oil.

R_f = 0.41 (hexanes / ethyl acetate, 1:1 (v/v)).

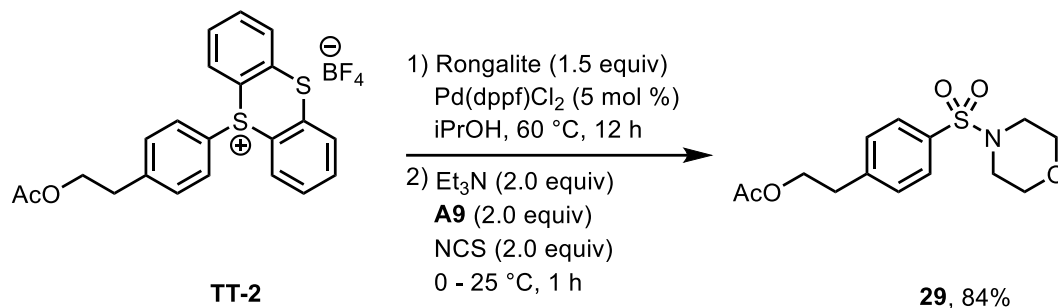
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.76 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 4.30 (t, J = 6.9 Hz, 2H), 3.32 – 3.19 (m, 4H), 3.01 (t, J = 6.9 Hz, 2H), 2.03 (s, 3H), 1.81 – 1.70 (m, 4H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 171.0, 143.2, 135.5, 129.6, 127.9, 64.2, 48.0, 35.0, 25.4, 21.0.

HRMS-EI (m/z) calc'd for $\text{C}_{14}\text{H}_{19}\text{NO}_4\text{S} [\text{M}]^+$, 297.1028; found, 297.1029; deviation: +0.37 ppm.

4-(Morpholinofonyl)phenethyl acetate (**29**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol , 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL , 20 mg, 0.20 mmol, 2.0 equiv), morpholine (**A9**) (18 μL , 18 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-4:1 (v/v)) to afford 27 mg (84%) of **29** as a white solid.

$R_f = 0.42$ (hexanes / ethyl acetate, 1:1 (v/v)).

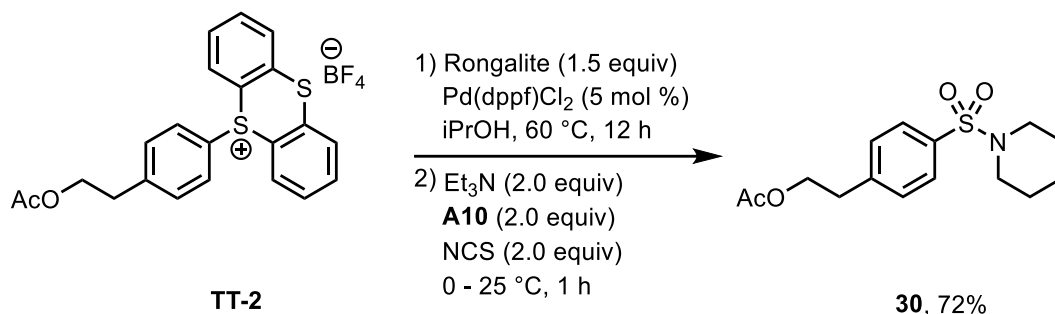
NMR Spectroscopy:

^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.67 (d, $J = 8.1$ Hz, 2H), 7.39 (d, $J = 8.1$ Hz, 2H), 4.29 (t, $J = 6.8$ Hz, 2H), 3.75 – 3.69 (m, 4H), 3.04 – 2.96 (m, 6H), 2.02 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 170.9, 143.8, 133.4, 129.7, 128.2, 66.2, 64.0, 46.0, 35.0, 21.0.

HRMS-ESI (m/z) calc'd for $\text{C}_{14}\text{H}_{19}\text{NO}_5\text{SNa}^+ [\text{M}+\text{Na}]^+$, 336.0877; found, 336.0876; deviation: -0.34ppm.

4-(Piperidin-1-ylsulfonyl)phenethyl acetate (**30**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), piperidine (**A10**) (20 μL, 17 mg, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 22 mg (72%) of **30** as colorless oil.

$R_f = 0.61$ (hexanes / ethyl acetate, 1:1 (v/v)).

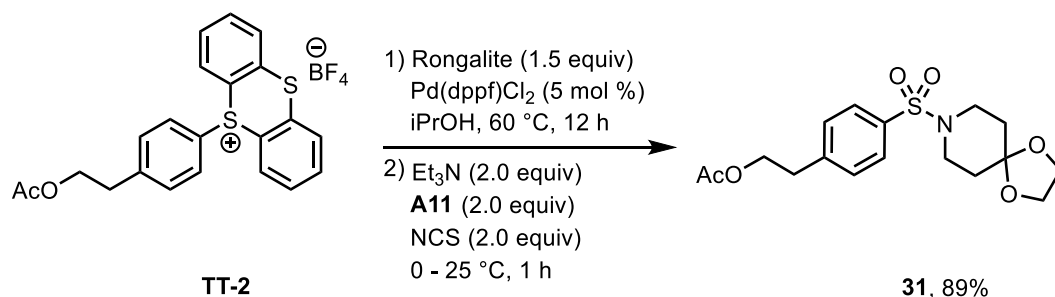
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.69 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 4.31 (t, *J* = 6.9 Hz, 2H), 3.04 – 2.96 (m, 6H), 2.04 (s, 3H), 1.69 – 1.60 (m, 4H), 1.45 – 1.38 (m, 2H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.0, 143.2, 134.7, 129.5, 128.0, 64.2, 47.0, 35.0, 25.3, 23.6, 21.0.

HRMS-EI (m/z) calc'd for C₁₅H₂₁NO₄S⁺ [M]⁺, 311.1189; found, 311.1186; deviation: -0.86 ppm.

4-((1,4-Dioxo-8-azaspiro[4.5]decan-8-yl)sulfonyl)phenethyl acetate (**31**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg,

0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), 4-piperidone ethylene ketal (**A11**) (25.6 μ L, 0.200 mmol, 2.00 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-4:1 (v/v)) to afford 33 mg (89%) of **31** as a colorless solid.

$R_f = 0.24$ (hexanes / ethyl acetate, 1:1 (v/v)).

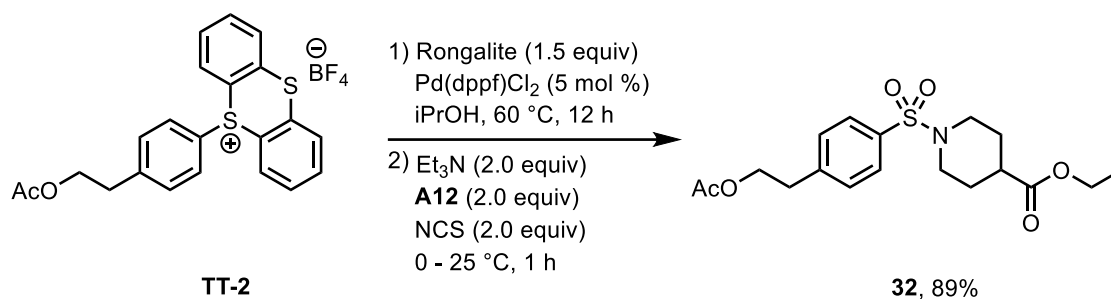
NMR Spectroscopy:

^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.68 (d, $J = 8.3$ Hz, 2H), 7.36 (d, $J = 8.3$ Hz, 2H), 4.30 (t, $J = 6.9$ Hz, 2H), 3.88 (s, 4H), 3.20 – 3.10 (m, 4H), 3.00 (t, $J = 6.8$ Hz, 2H), 2.03 (s, 3H), 1.80 – 1.74 (m, 4H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 171.0, 143.4, 134.9, 129.7, 127.9, 106.1, 64.5, 64.1, 44.6, 35.0, 34.5, 21.0.

HRMS-ESI (m/z) calc'd for $\text{C}_{17}\text{H}_{23}\text{NO}_6\text{SNa}^+$ [$\text{M}+\text{Na}$] $^+$, 392.1141; found, 392.1138; deviation: -0.56 ppm.

Ethyl 1-((4-(2-acetoxyethyl)phenyl)sulfonyl)piperidine-4-carboxylate (**32**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μ mol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), ethyl 4-piperidinecarboxylate (**A12**) (32 μ L, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-4:1 (v/v)) to afford 34 mg (89%) of **32** as a colorless solid.

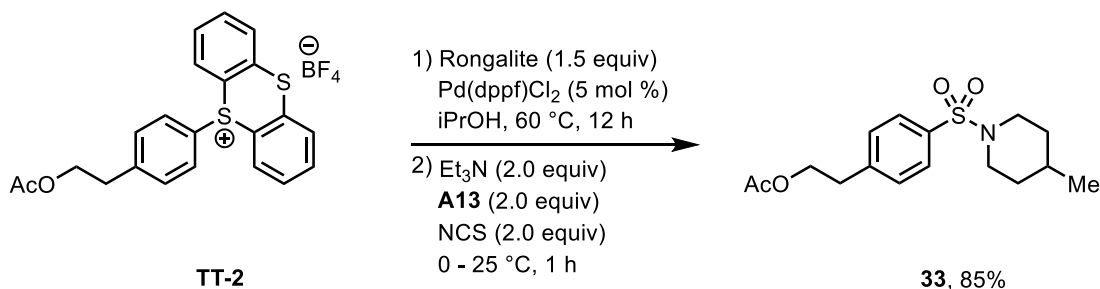
$R_f = 0.48$ (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.67 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 4.29 (t, *J* = 6.8 Hz, 2H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.60 (d, *J* = 11.9 Hz, 2H), 3.00 (t, *J* = 6.8 Hz, 2H), 2.47 (t, *J* = 10.1 Hz, 2H), 2.23 (ddd, *J* = 14.5, 10.5, 3.8 Hz, 1H), 2.02 (s, 3H), 1.98 – 1.91 (m, 2H), 1.84 – 1.75 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 173.9, 170.9, 143.5, 134.6, 129.6, 128.0, 64.1, 60.7, 45.5, 40.1, 35.0, 27.0, 21.0, 14.2.

HRMS-ESI(m/z) calc'd for C₁₈H₂₆NO₆S⁺ [M+H]⁺, 384.1469; found, 384.1475; deviation:+1.66 ppm.

4-((4-Methylpiperidin-1-yl)sulfonyl)phenethyl acetate (33)

In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), 4-methylpiperidine (**A13**) (25 μL, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 28 mg (85%) of **33** as a white solid.

R_f = 0.59 (hexanes / ethyl acetate, 1:1 (v/v)).

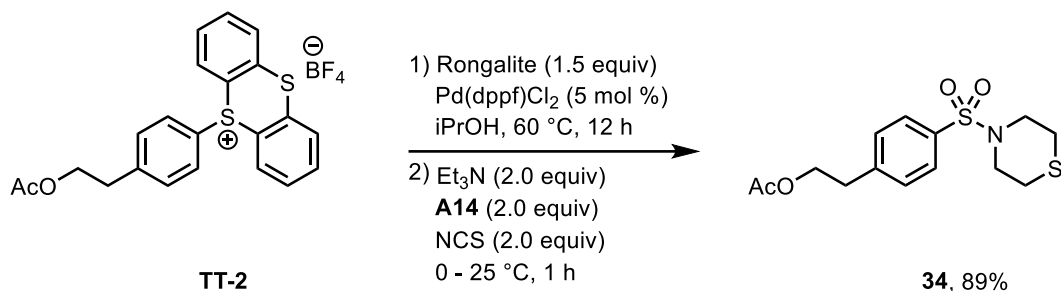
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.67 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 4.29 (t, *J* = 6.9 Hz, 2H), 3.72 (d, *J* = 11.1 Hz, 2H), 3.00 (t, *J* = 6.8 Hz, 2H), 2.24 (t, *J* = 11.1 Hz, 2H), 2.02 (s, 3H), 1.65 (d, *J* = 10.6 Hz, 2H), 1.32 – 1.22 (m, 3H), 0.89 (d, *J* = 4.9 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.0, 143.2, 134.8, 129.5, 128.0, 64.2, 46.5, 35.0, 33.4, 30.2, 21.6, 21.0.

HRMS-ESI (m/z) calc'd for C₁₆H₂₄NO₄S⁺ [M+H]⁺, 326.1420; found, 326.1420; deviation:+0.17 ppm.

4-(Thiomorpholinofonyl)phenethyl acetate (**34**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, c = 0.2 M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL, 20 mg, 0.20 mmol, 2.0 equiv), thiomorpholine (**A14**) (22 μL, 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-4:1 (v/v)) to afford 29 mg (89%) of **34** as a yellow solid.

$R_f = 0.31$ (hexanes / ethyl acetate, 1:1 (v/v)).

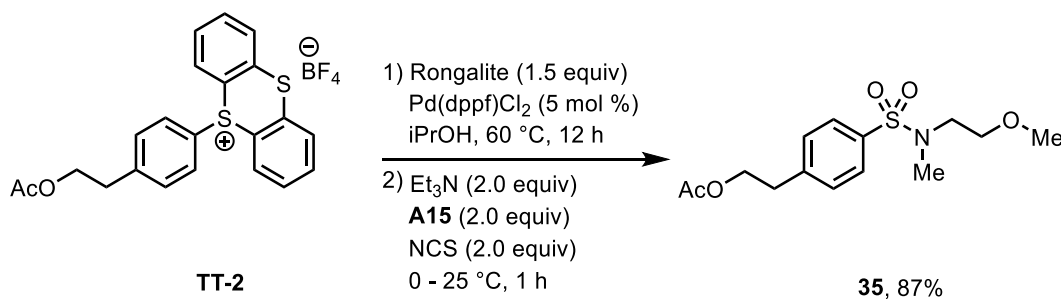
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.67 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 4.31 (t, *J* = 6.8 Hz, 2H), 3.45 – 3.21 (m, 4H), 3.02 (t, *J* = 6.8 Hz, 2H), 2.74 – 2.66 (m, 4H), 2.04 (s, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.0, 143.7, 135.2, 129.8, 127.8, 64.1, 48.0, 27.5, 21.0.

HRMS-ESI (*m/z*) calc'd for C₁₄H₂₀NO₄S₂⁺ [M+H]⁺, 330.0828; found, 330.0828; deviation: +0.03 ppm.

4-(*N*-(2-Methoxyethyl)-*N*-methylsulfamoyl)phenethyl acetate (**35**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg,

0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), (2-methoxyethyl)methylamine (**A15**) (21.7 μ L, 0.200 mmol, 2.00 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-6:4 (v/v)) to afford 27 mg (87%) of **35** as a yellow oil.

$R_f = 0.62$ (hexanes / ethyl acetate, 1:1 (v/v)).

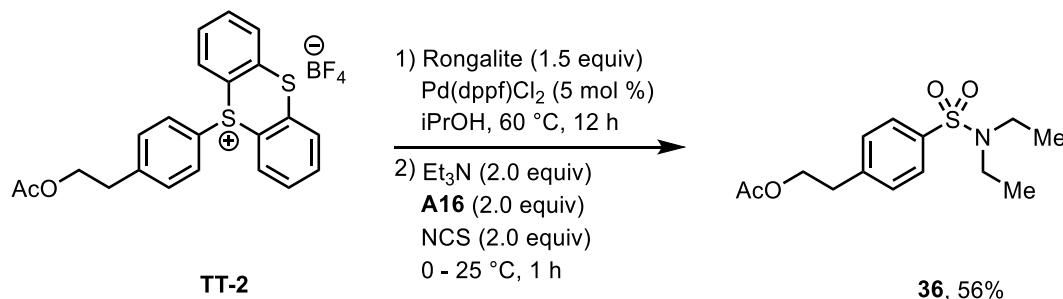
NMR Spectroscopy:

^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.72 (d, $J = 8.3$ Hz, 2H), 7.36 (d, $J = 8.3$ Hz, 2H), 4.29 (t, $J = 6.8$ Hz, 2H), 3.54 (t, $J = 5.6$ Hz, 2H), 3.31 (s, 3H), 3.21 (t, $J = 5.6$ Hz, 2H), 3.00 (t, $J = 6.8$ Hz, 2H), 2.83 (s, 3H), 2.03 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 171.0, 143.2, 136.3, 129.6, 127.7, 71.5, 64.2, 58.9, 49.8, 36.4, 35.0, 21.0.

HRMS-ESI (m/z) calc'd for $\text{C}_{14}\text{H}_{22}\text{NO}_5\text{S}^+$ $[\text{M}+\text{H}]^+$, 316.1212; found 316.1213; deviation: +0.35 ppm.

4-(*N,N*-Diethylsulfamoyl)phenethyl acetate (**36**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μ mol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μ L, 20 mg, 0.20 mmol, 2.0 equiv), diethylamine (**A16**) (20.8 μ L, 0.200 mmol, 2.00 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 17 mg (56%) of **36** as a colorless oil.

$R_f = 0.60$ (hexanes / ethyl acetate, 1:1 (v/v)).

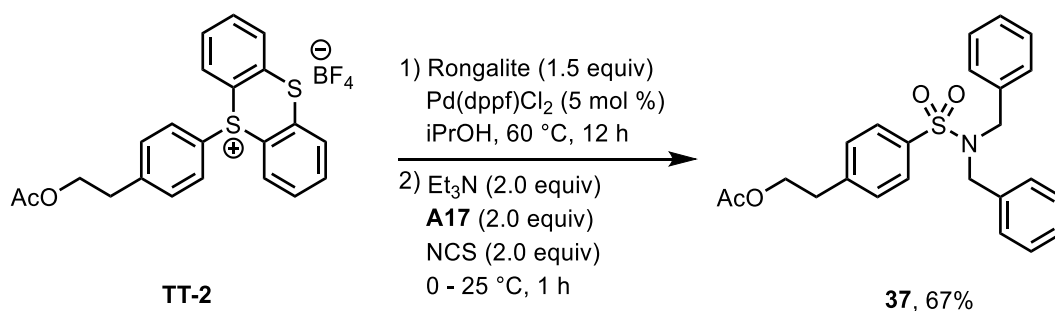
NMR Spectroscopy:

$^1\text{H NMR}$ (500 MHz, CDCl_3 , 298 K, δ): 7.74 (d, $J = 8.2$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 4.29 (t, $J = 6.9$ Hz, 2H), 3.23 (q, $J = 7.1$ Hz, 4H), 2.99 (t, $J = 6.9$ Hz, 2H), 2.02 (s, 3H), 1.12 (t, $J = 7.1$ Hz, 6H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3 , 298 K, δ): 171.0, 142.8, 138.9, 129.6, 127.4, 64.2, 42.2, 35.0, 21.0, 14.3.

HRMS-ESI (m/z) calc'd for $\text{C}_{14}\text{H}_{22}\text{NO}_4\text{S}^+$ $[\text{M}+\text{H}]^+$, 300.1265; found, 300.1264; deviation: -0.51 ppm.

4-(*N,N*-Dibenzylsulfamoyl)phenethyl acetate (**37**)



In an argon-filled glovebox, an oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol , 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv), and the sealed vial was taken out from the glovebox. Anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added outside the glovebox, and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (28 μL , 20 mg, 0.20 mmol, 2.0 equiv), dibenzylamine (**A17**) (40 μL , 0.20 mmol, 2.0 equiv), and a solution of *N*-chlorosuccinimide (26.7 mg, 0.200 mmol, 2.00 equiv) in THF (0.5 mL) were added sequentially through the septum. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-10:1 (v/v)) to afford 28 mg (67%) of **37** as a colorless solid.

$R_f = 0.72$ (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

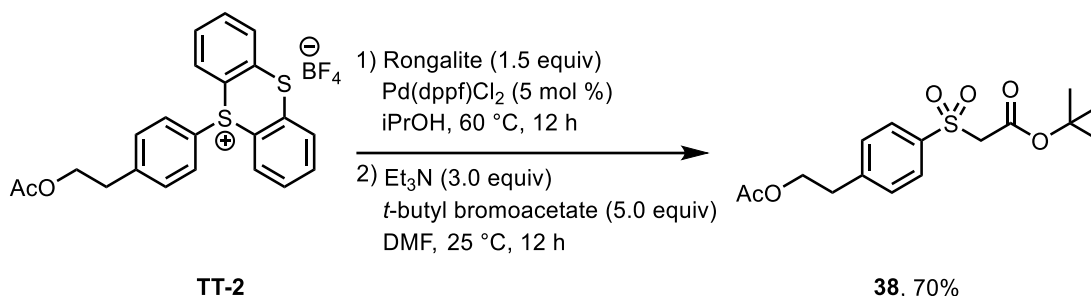
$^1\text{H NMR}$ (500 MHz, CDCl_3 , 298 K, δ): 7.78 (d, $J = 7.2$ Hz, 2H), 7.35 (d, $J = 7.5$ Hz, 2H), 7.24 – 7.19 (m, 6H), 7.07 – 7.01 (m, 4H), 4.33 (d, $J = 5.7$ Hz, 6H), 3.03 (t, $J = 6.7$ Hz, 2H), 2.05 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3 , 298 K, δ): 171.0, 143.2, 139.2, 135.7, 129.7, 128.7, 128.6, 127.8, 127.6, 64.3, 50.6, 35.0, 21.1.

HRMS-EI (m/z) calc'd for $\text{C}_{24}\text{H}_{25}\text{NO}_4\text{S}^+$ $[\text{M}]^+$, 423.1502; found 423.1504; deviation: +0.56 ppm.

Sulfonyl diversification

Tert-butyl 2-((4-(2-acetoxyethyl)phenyl)sulfonyl)acetate (**38**)



An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (0.5 mL, c = 0.2 M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (42 μL, 30 mg, 0.30 mmol, 3.0 equiv) was added and the mixture stirred for 30 min. Following this, the solvent was removed *in vacuo* and *tert*-butylbromoacetate (45 μL, 59 mg, 0.30 mmol, 3.0 equiv) and DMF (0.5 mL) were added. The resulting mixture was stirred for 1 h. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 24 mg (70%) of **38** as a yellow oil.

$R_f = 0.46$ (hexanes / ethyl acetate, 1:1 (v/v)).

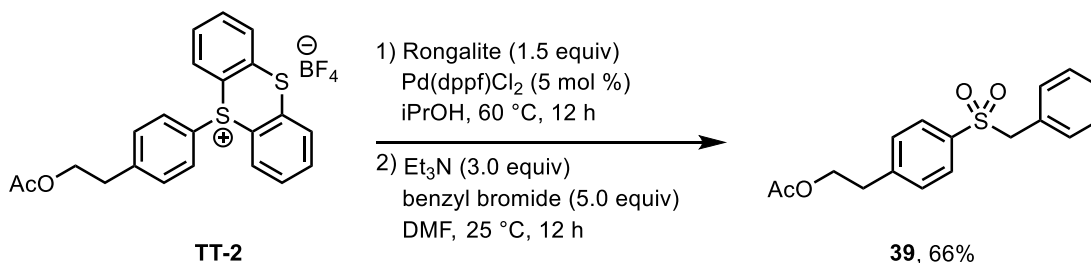
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.87 (d, $J = 7.8$ Hz, 2H), 7.42 (d, $J = 8.0$ Hz, 2H), 4.30 (t, $J = 6.7$ Hz, 2H), 4.02 (s, 2H), 3.03 (t, $J = 6.7$ Hz, 2H), 2.01 (s, 3H), 1.35 (s, 9H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 170.9, 161.4, 145.1, 137.3, 129.7, 128.9, 83.7, 64.1, 62.2, 35.1, 27.8, 21.0

HRMS-ESI (m/z) calc'd for C₁₆H₂₁O₆S⁺ [M-H]⁺, 341.1064; found, 341.1064; deviation: +0.11 ppm.

4-(Benzylsulfonyl)phenethyl acetate (**39**)



An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (0.5 mL, c = 0.2 M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (42 μL, 30 mg, 0.30 mmol, 3.0 equiv) was added and the mixture stirred for 30 min. Following this, the solvent was removed *in vacuo* and benzyl bromide (35 μL, 50 mg, 0.30 mmol, 3.0 equiv) and DMF (0.5 mL) were added. The resulting mixture was stirred for 1 h. After stirring the reaction mixture at 25 °C for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 21 mg (66%) of **39** as a white solid.

R_f = 0.51 (hexanes / ethyl acetate, 1:1 (v/v)).

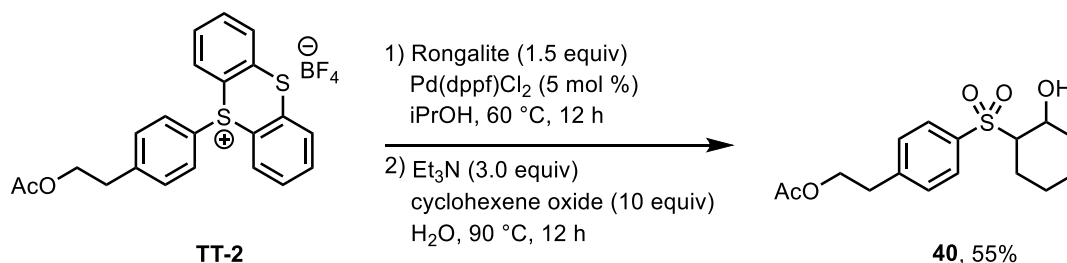
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.55 (d, *J* = 8.1 Hz, 2H), 7.34 – 7.22 (m, 5H), 7.12 – 7.05 (m, 2H), 4.33 – 4.26 (m, 4H), 2.99 (t, *J* = 6.8 Hz, 2H), 2.02 (s, 3H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 170.9, 144.6, 136.3, 130.9, 129.5, 129.0, 128.9, 128.7, 128.3, 64.1, 63.0, 35.1, 21.0.

HRMS-ESI (*m/z*) calc'd for C₁₇H₁₉O₄S⁺ [M+H]⁺, 319.0994; found, 319.0999; deviation: +1.40 ppm.

4-((2-Hydroxycyclohexyl)sulfonyl)phenethyl acetate (**40**)



An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μmol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (0.5 mL, c = 0.2 M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (42 μL, 30 mg, 0.30 mmol, 3.0 equiv) was added and the mixture stirred for 30 min. Following this, the solvent was removed *in vacuo* and cyclohexene oxide (100 μL, 96.4 mg, 1.00 mmol, 10.0 equiv) and H₂O (0.5 mL) added. The resulting mixture was heated at 90 °C and stirred at this temperature for 12 h. After cooling to 25 °C, sat. NH₄Cl (10 mL) and subsequently CH₂Cl₂ (10 mL) were added, the two phases separated and the aqueous layer extracted with CH₂Cl₂ (2 x 10 mL). The combined organic extracts were dried (MgSO₄), filtered and the

solvent removed under reduced pressure. The crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 18 mg (55%) of **40** as a colorless oil.

R_f = 0.38 (hexanes / ethyl acetate, 1:1 (v/v)).

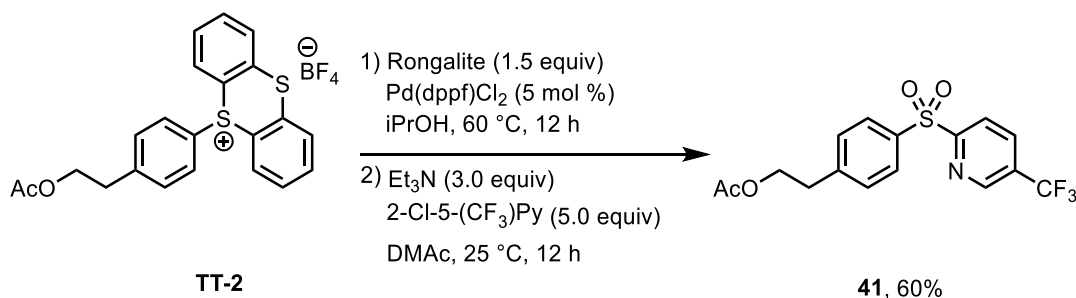
NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 7.83 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.2 Hz, 2H), 4.32 (t, J = 6.8 Hz, 2H), 3.90 (td, J = 10.3, 4.9 Hz, 1H), 3.05 (t, J = 6.8 Hz, 2H), 2.97 (ddd, J = 12.5, 9.7, 4.1 Hz, 1H), 2.17 – 2.10 (m, 1H), 2.04 (s, 3H), 1.90 (dd, J = 12.7, 3.8 Hz, 1H), 1.75 – 1.69 (m, 2H), 1.36 – 1.14 (m, 4H).

¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 171.0, 145.2, 135.2, 129.9, 129.4, 69.1, 68.4, 64.0, 35.1, 34.3, 25.9, 24.7, 23.7, 21.0.

HRMS-ESI (m/z) calc'd for C₁₆H₂₃O₅S⁺ [M+H]⁺, 327.1257; found, 327.1261; deviation: +1.26 ppm.

4-((5-(Trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (**41**)



An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl₂ (4 mg, 5 μ mol, 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (0.5 mL, c = 0.2 M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 °C for 12 h. After cooling to 25 °C, triethylamine (42 μ L, 30 mg, 0.30 mmol, 3.0 equiv) was added and the mixture stirred for 30 min. Following this, the solvent was removed *in vacuo* and 2-chloro-5-(trifluoromethyl)pyridine (89 mg, 0.50 mmol, 5.0 equiv) and DMAc (0.5 mL) were added. The resulting mixture was stirred for 12 h. After stirring the reaction mixture at 25 °C for 12 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 22 mg (60%) of **41** as a white solid.

R_f = 0.63 (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

¹H NMR (500 MHz, CDCl₃, 298 K, δ): 8.90 (s, 1H), 8.33 (dd, J = 8.3, 0.9 Hz, 1H), 8.20 – 8.14 (m, 1H), 8.03 – 7.97 (m, 2H), 7.44 – 7.37 (m, 2H), 4.27 (t, J = 6.8 Hz, 2H), 3.00 (t, J = 6.8 Hz, 2H), 2.00 (s, 3H).

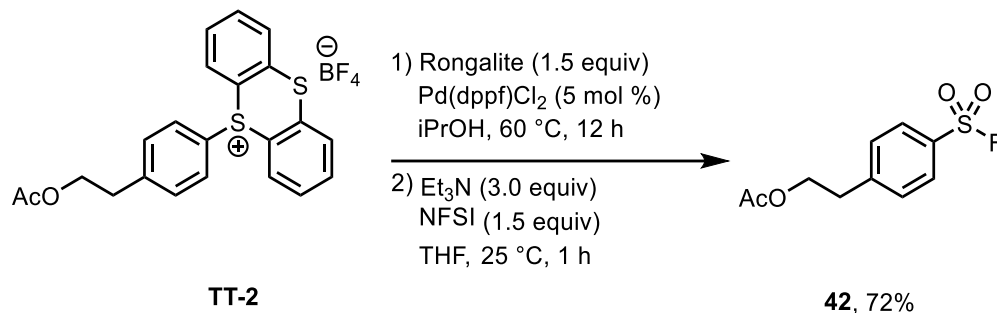
¹³C NMR (126 MHz, CDCl₃, 298 K, δ): 170.9, 162.1, 147.4 (q, J = 3.9 Hz), 145.5, 136.2, 135.7 (q, J = 3.6

Hz), 129.9, 129.6, 129.4 (d, $J = 33.6$ Hz), 122.5 (d, $J = 273.4$ Hz), 64.0, 35.1, 21.0.

^{19}F NMR (471 MHz, CDCl_3 , 298 K, δ): -62.68.

HRMS-ESI (m/z) calc'd for $\text{C}_{16}\text{H}_{15}\text{NO}_4\text{SF}_3^+$ $[\text{M}+\text{H}]^+$, 374.0666; found, 374.0668; deviation: +0.62 ppm.

4-(Fluorosulfonyl)phenethyl acetate (**42**)



An oven dried borosilicate 4 mL reaction vial equipped with a magnetic stir bar was charged with **TT-2** (46.6 mg, 0.100 mmol, 1.00 equiv), Pd(dppf)Cl_2 (4 mg, 5 μmol , 5 mol %), Rongalite (17 mg, 0.15 mmol 1.5 equiv) and sealed with a septum cap. The vial was evacuated and flushed with argon three times. Under positive pressure of argon, anhydrous isopropanol (0.5 mL, $c = 0.2$ M) was added through the septum and the reaction mixture was placed in a preheated metal heating block at 60 $^\circ\text{C}$ for 12 h. After cooling to 25 $^\circ\text{C}$, triethylamine (42 μL , 30 mg, 0.30 mmol, 3.0 equiv) was added and the mixture stirred for 30 min. Following this, addition of NFSI (47 mg, 0.15 mmol, 1.5 equiv) in THF (0.5 mL) was added sequentially through the septum and stirred for 1 h. After stirring the reaction mixture at 25 $^\circ\text{C}$ for 1 h, the solvent was removed under reduced pressure, and the crude product was purified by chromatography on silica gel eluting with hexanes / EtOAc (1:0-5:1 (v/v)) to afford 18 mg (72%) of **42** as a colorless oil.

$R_f = 0.69$ (hexanes / ethyl acetate, 1:1 (v/v)).

NMR Spectroscopy:

^1H NMR (500 MHz, CDCl_3 , 298 K, δ): 7.95 (d, $J = 8.3$ Hz, 2H), 7.48 (d, $J = 8.2$ Hz, 2H), 4.33 (t, $J = 6.6$ Hz, 2H), 3.07 (t, $J = 6.6$ Hz, 2H), 2.03 (s, 3H).

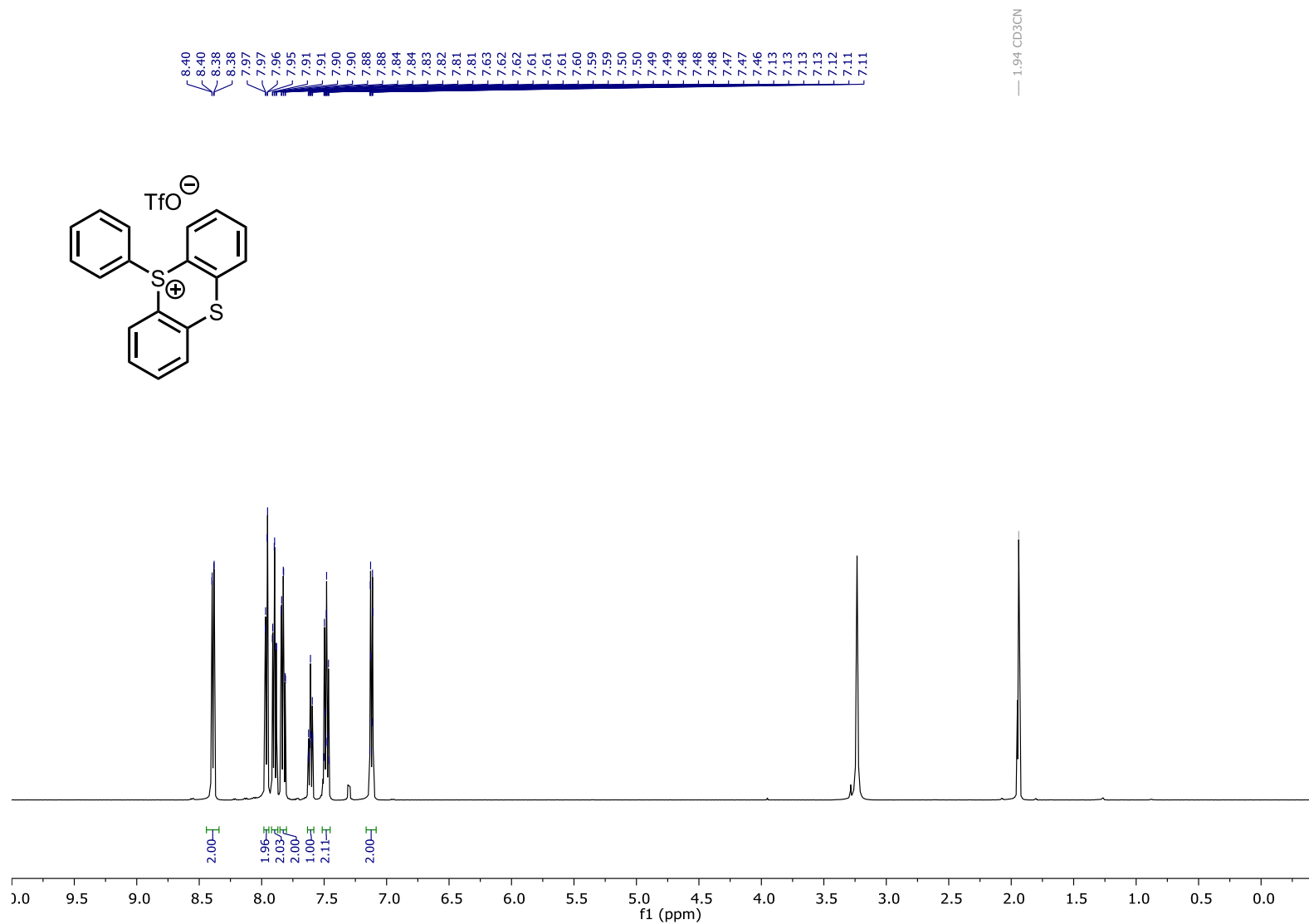
^{13}C NMR (126 MHz, CDCl_3 , 298 K, δ): 170.9, 147.0, 131.3 (d, $J = 24.7$ Hz), 130.3, 128.8, 63.8, 35.2, 21.0.

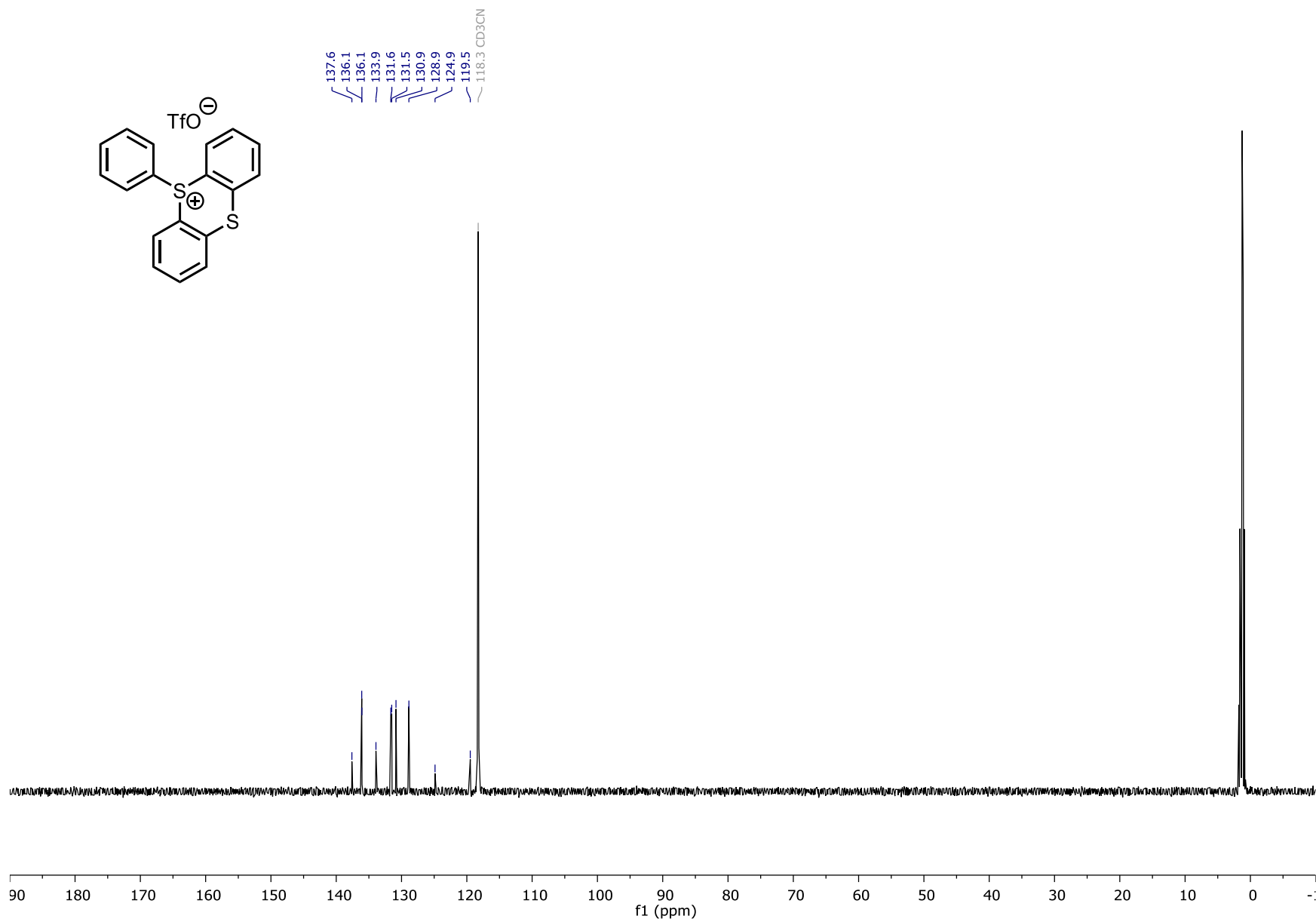
^{19}F NMR (471 MHz, CDCl_3 , 298 K, δ): 66.16.

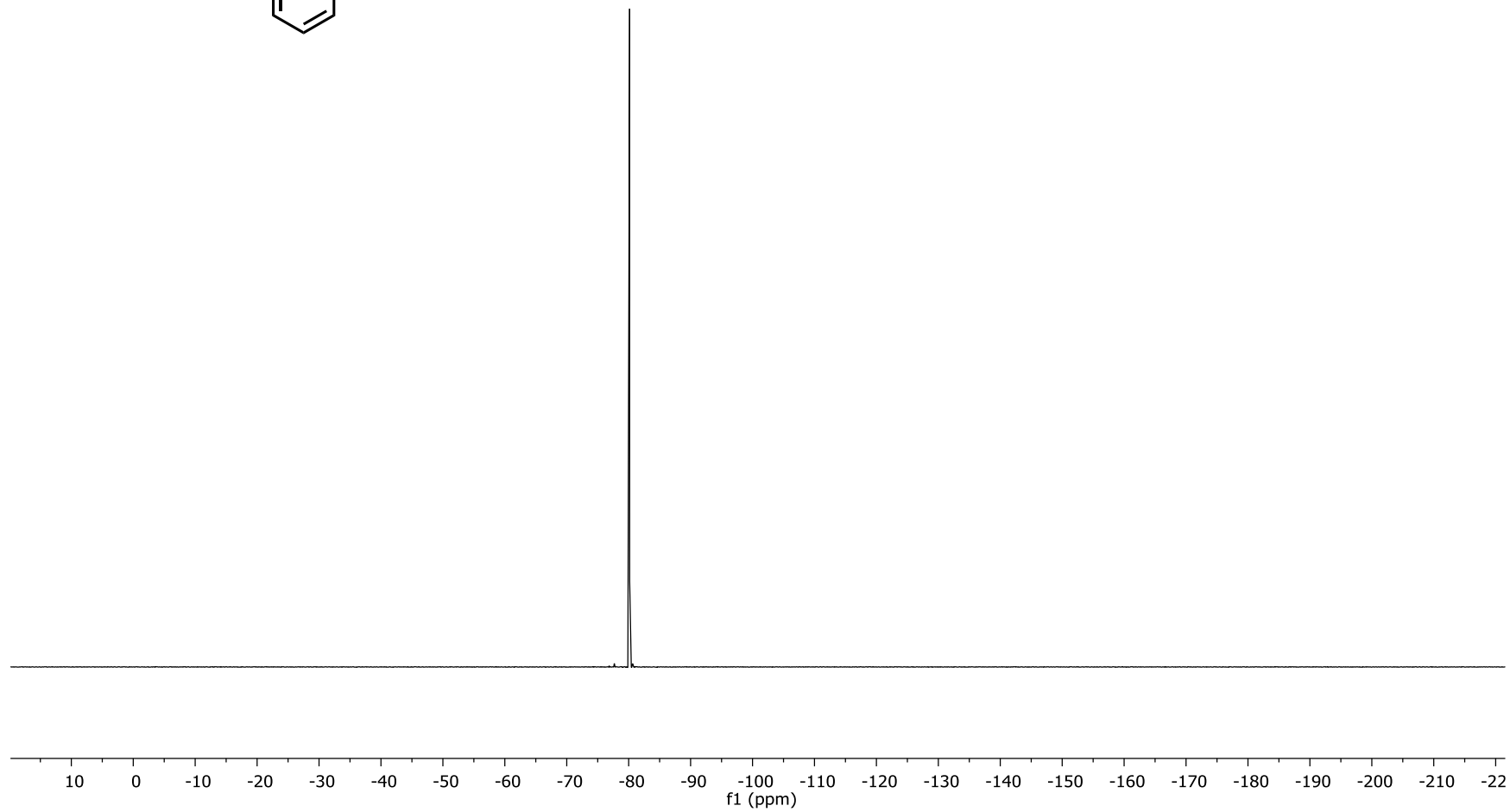
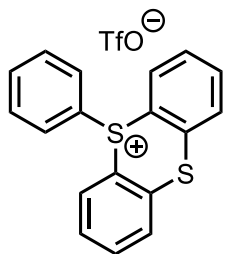
HRMS-ESI (m/z) calc'd for $\text{C}_{10}\text{H}_{12}\text{O}_4\text{SF}^+$ $[\text{M}+\text{H}]^+$, 247.0434; found, 247.0435; deviation: +0.43 ppm.

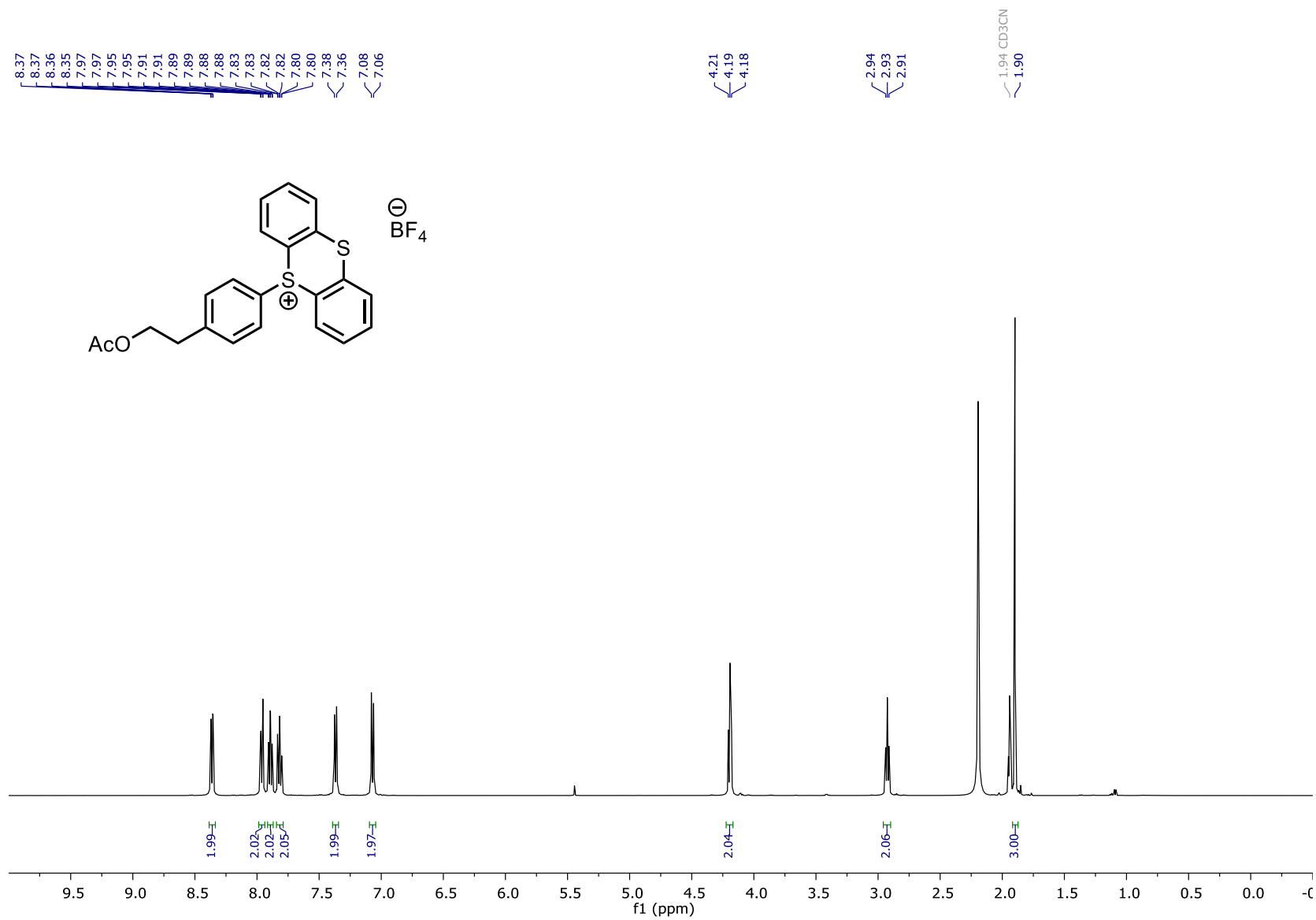
SPECTROSCOPIC DATA

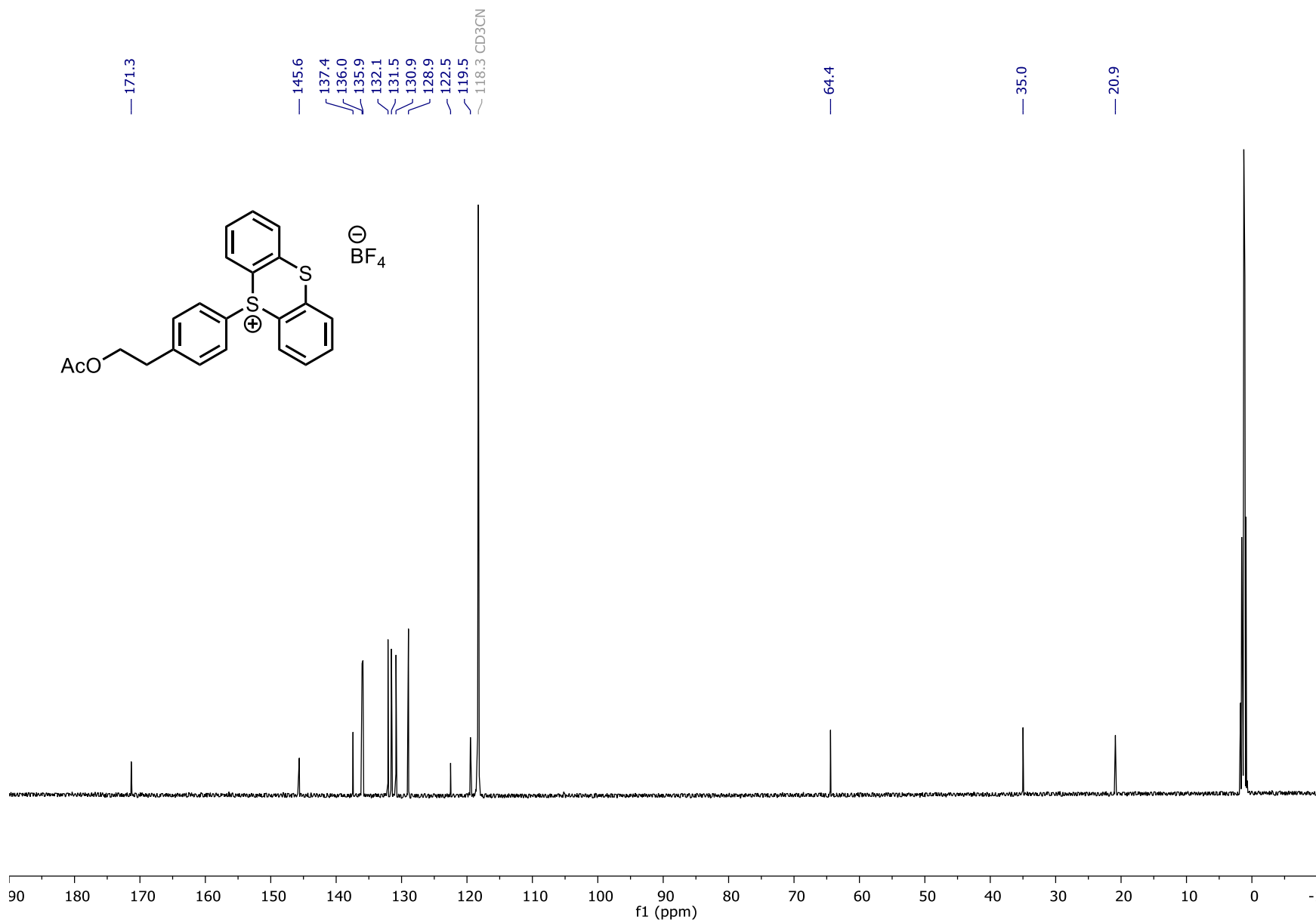
Benzene-derived thianthrenium salt (TT-1)

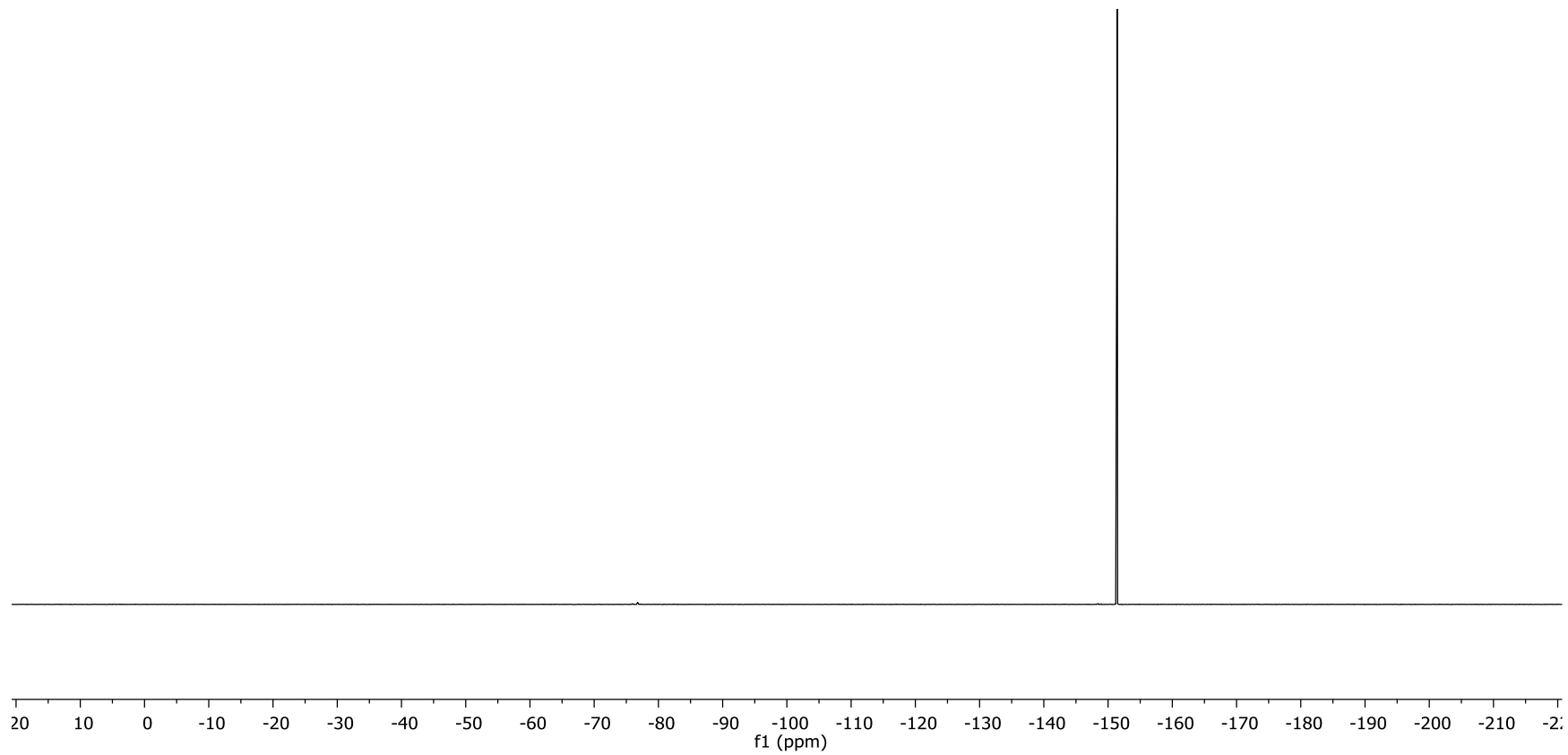
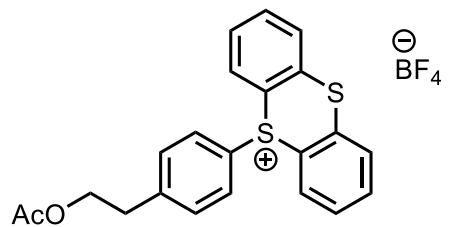
 ^1H NMR of benzene-derived thianthrenium salt (TT-1)CD₃CN, 500 MHz, 298 K

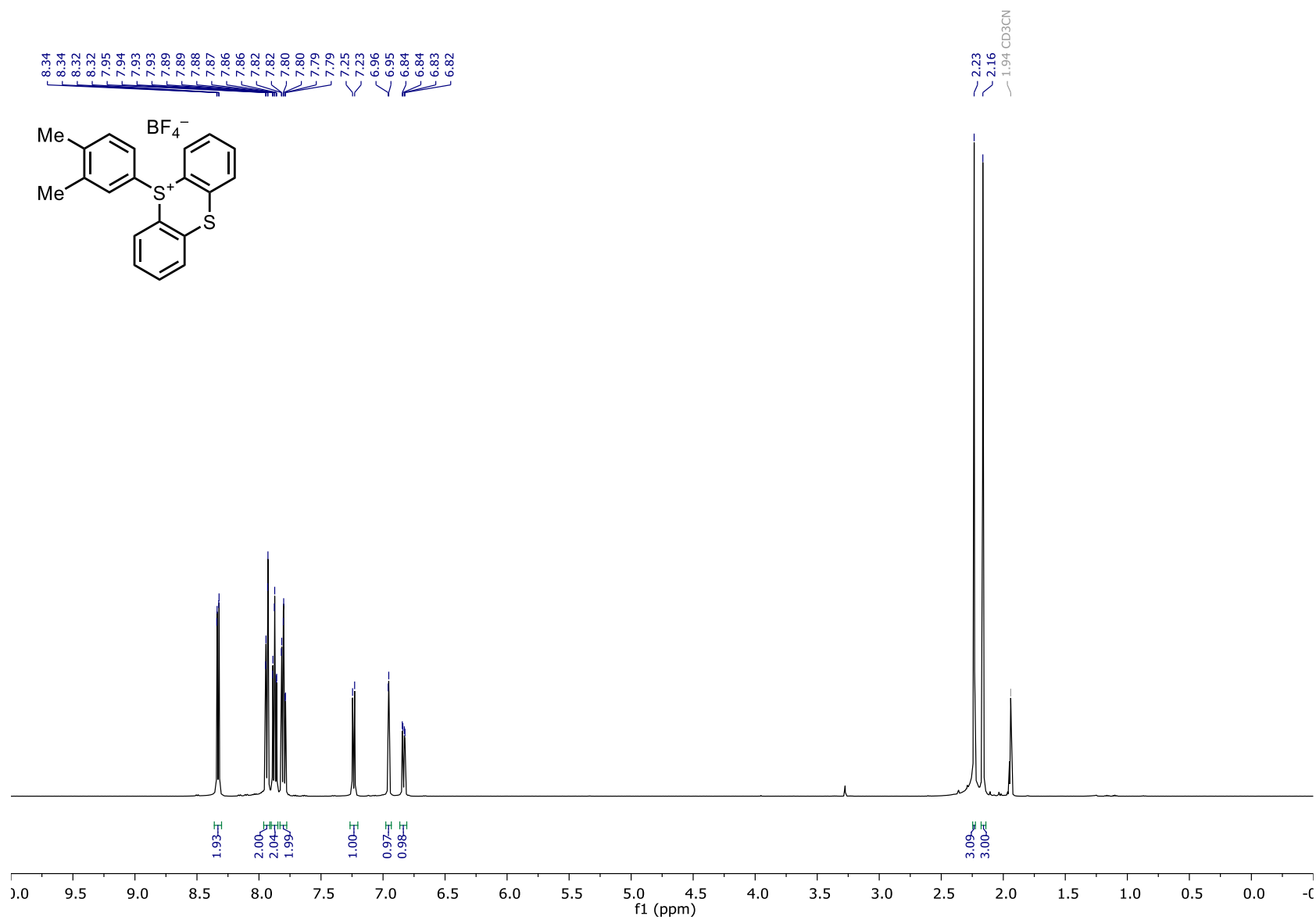
^{13}C NMR of benzene-derived thianthrenium salt (TT-1)CD₃CN, 126 MHz, 298 K

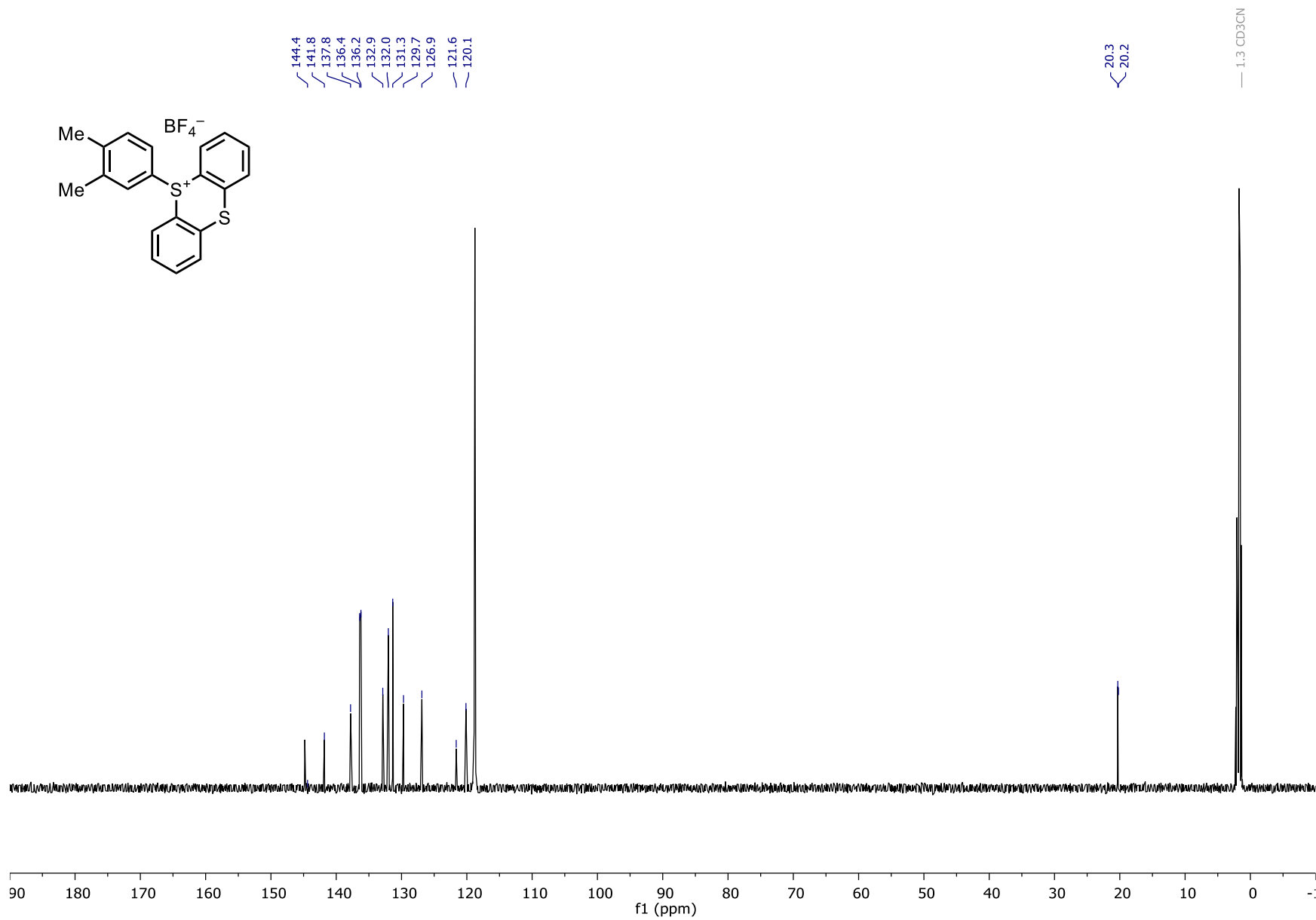
^{19}F NMR of benzene-derived thianthrenium salt (TT-1)CD₃CN, 471 MHz, 298 K

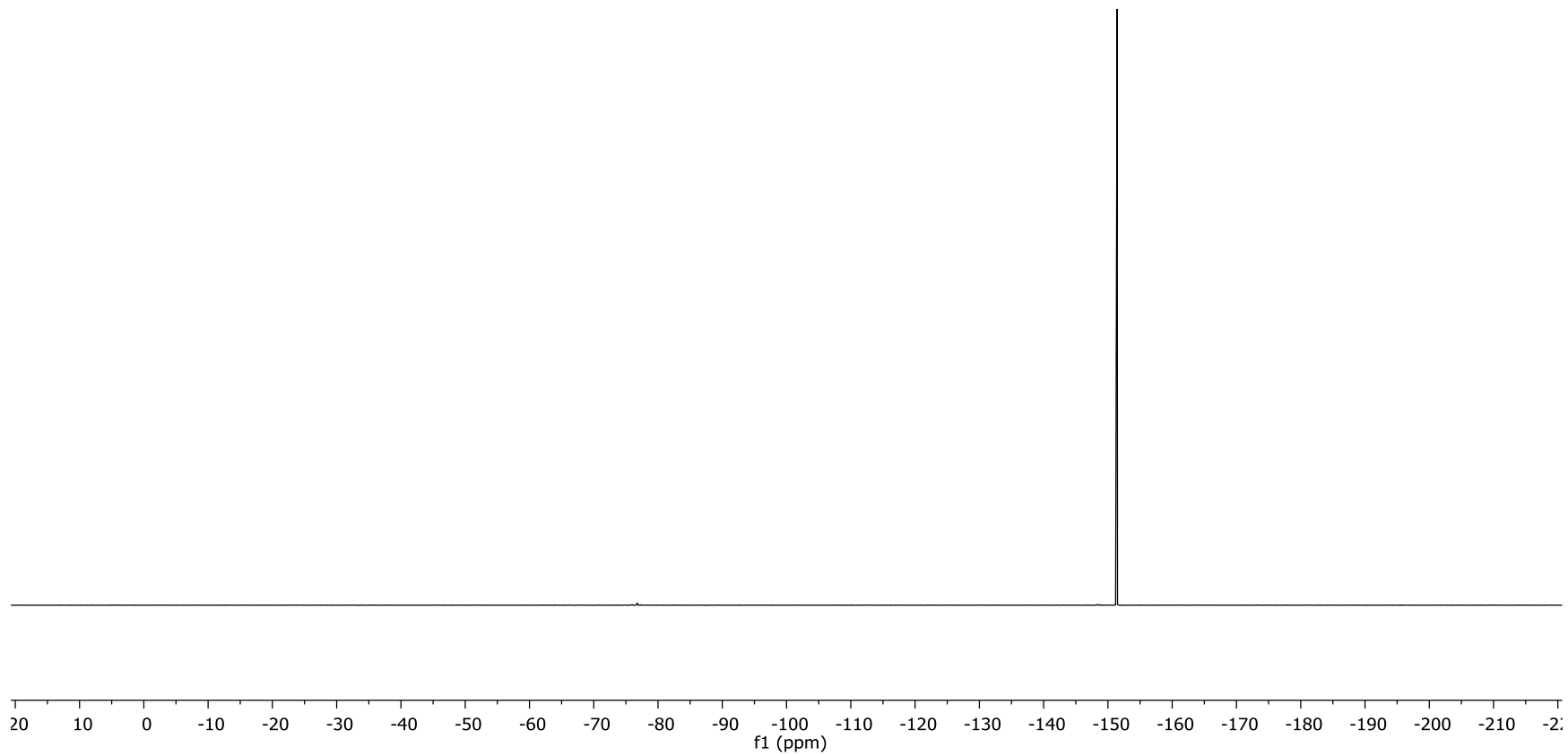
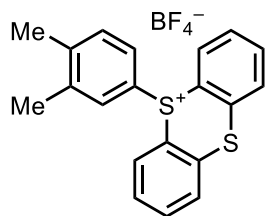
Phenethyl acetate-derived thianthrenium tetrafluoroborate (TT-2)**¹H NMR of phenethyl acetate-derived thianthrenium tetrafluoroborate (TT-2)**CD₃CN, 500 MHz, 298 K

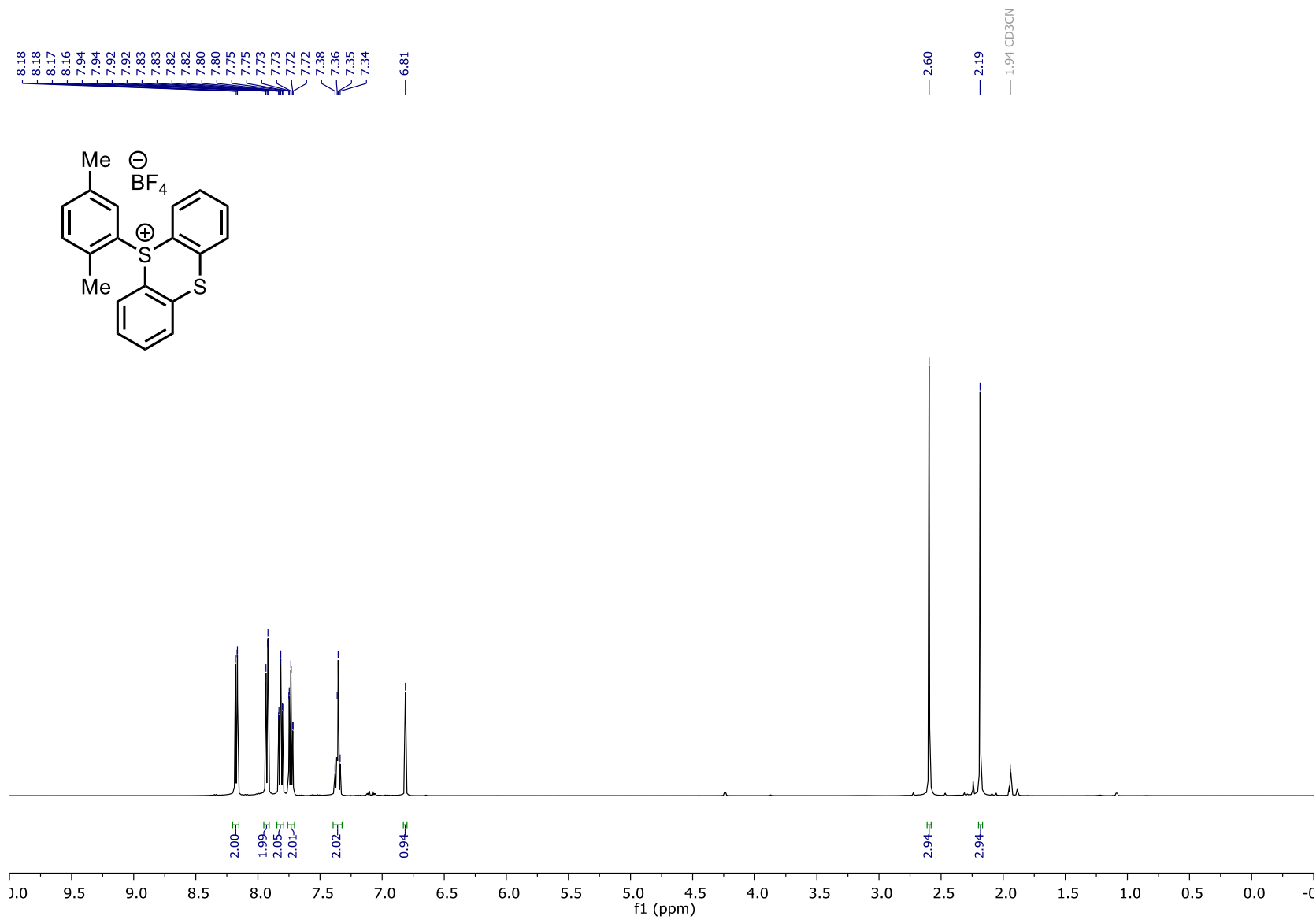
^{13}C NMR of phenethyl acetate-derived thianthrenium tetrafluoroborate (TT-2)CD₃CN, 126 MHz, 298 K

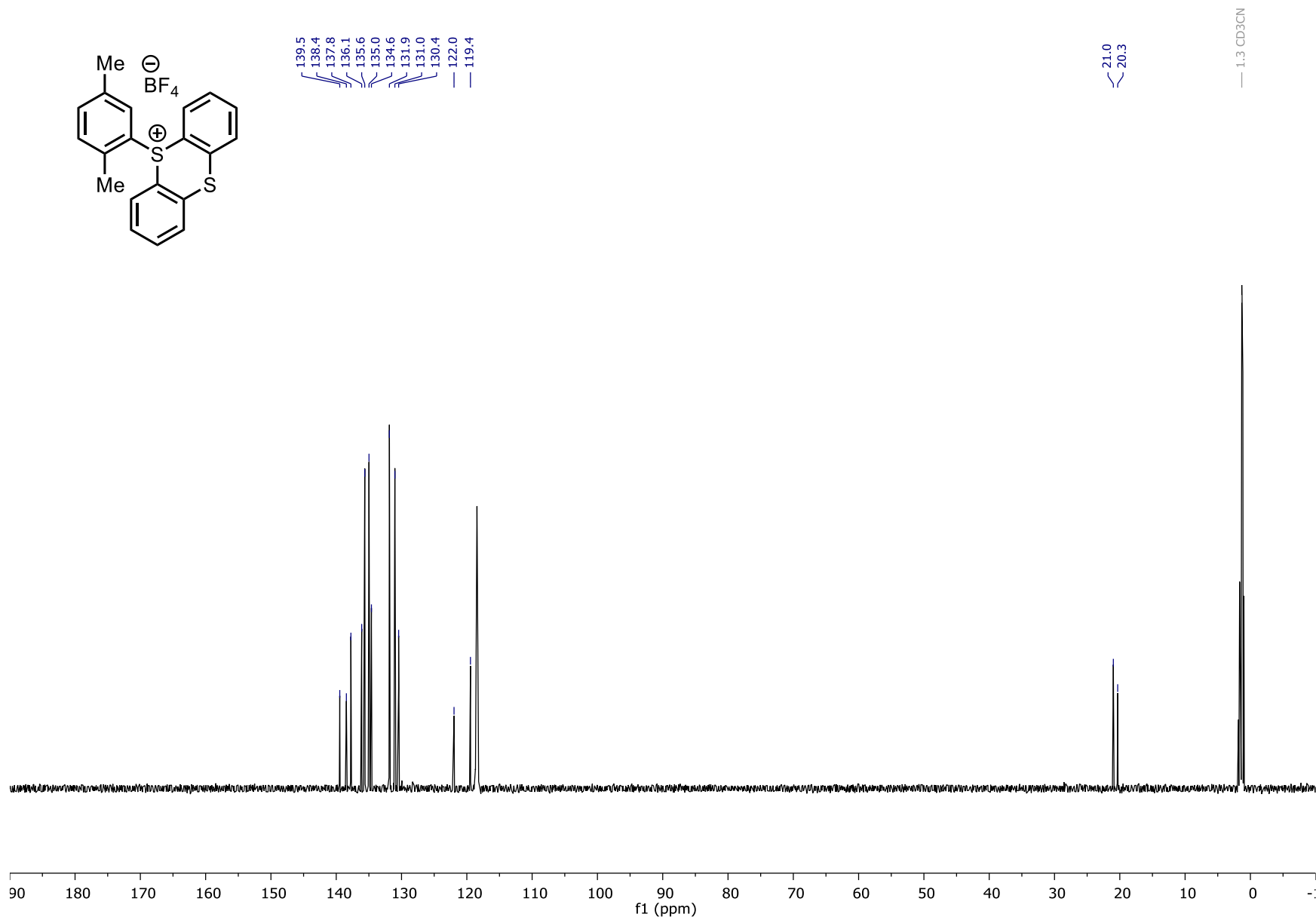
^{19}F NMR of phenethyl acetate-derived thianthrenium tetrafluoroborate (TT-2)CD₃CN, 471 MHz, 298 K

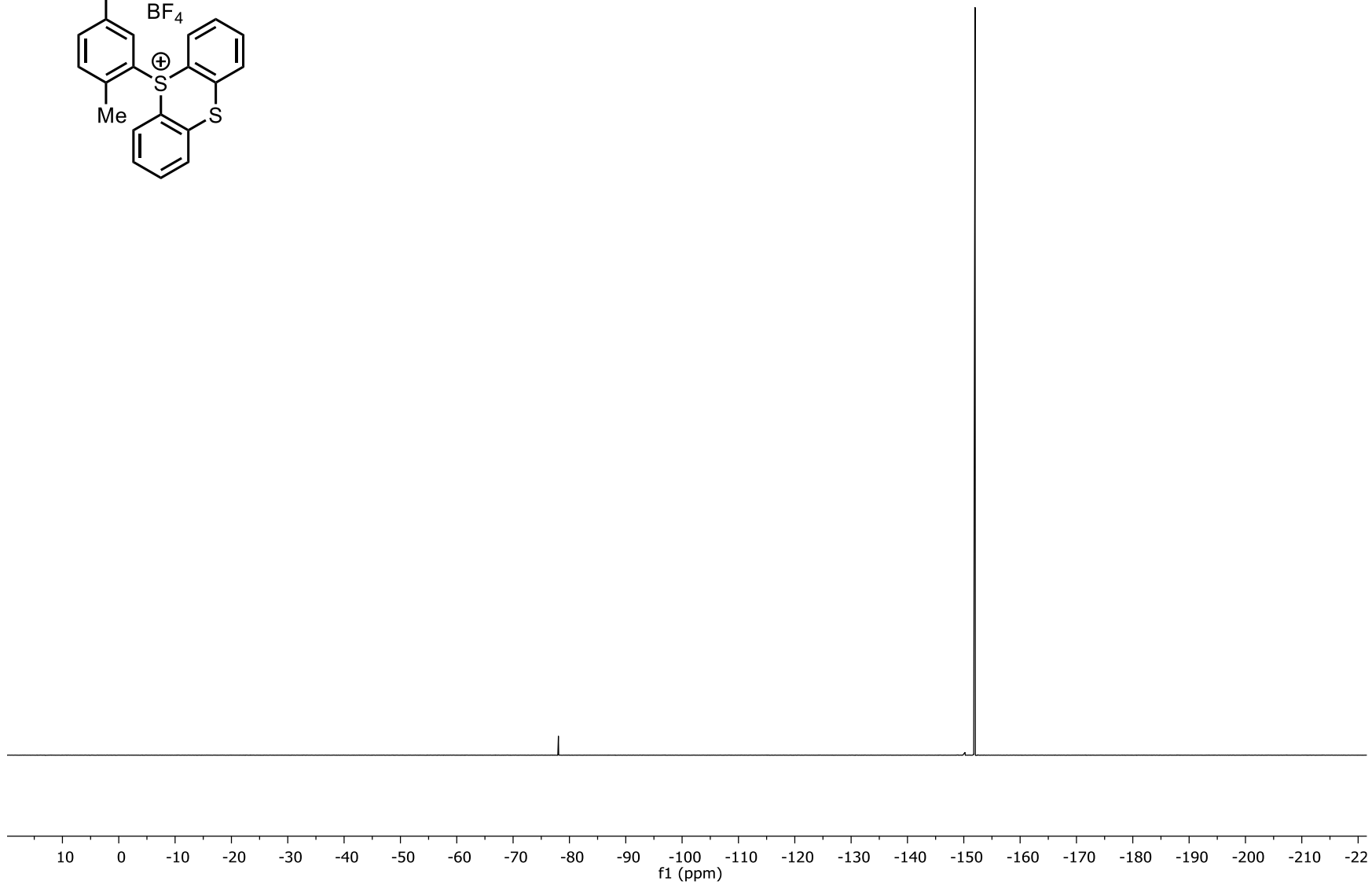
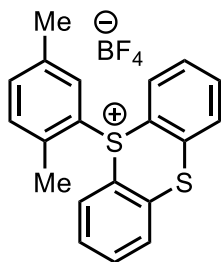
o-Xylene-derived thianthrenium tetrafluoroborate (TT-3)**¹H NMR of o-xylene-derived thianthrenium tetrafluoroborate (TT-3)**CD₃CN, 500 MHz, 298 K

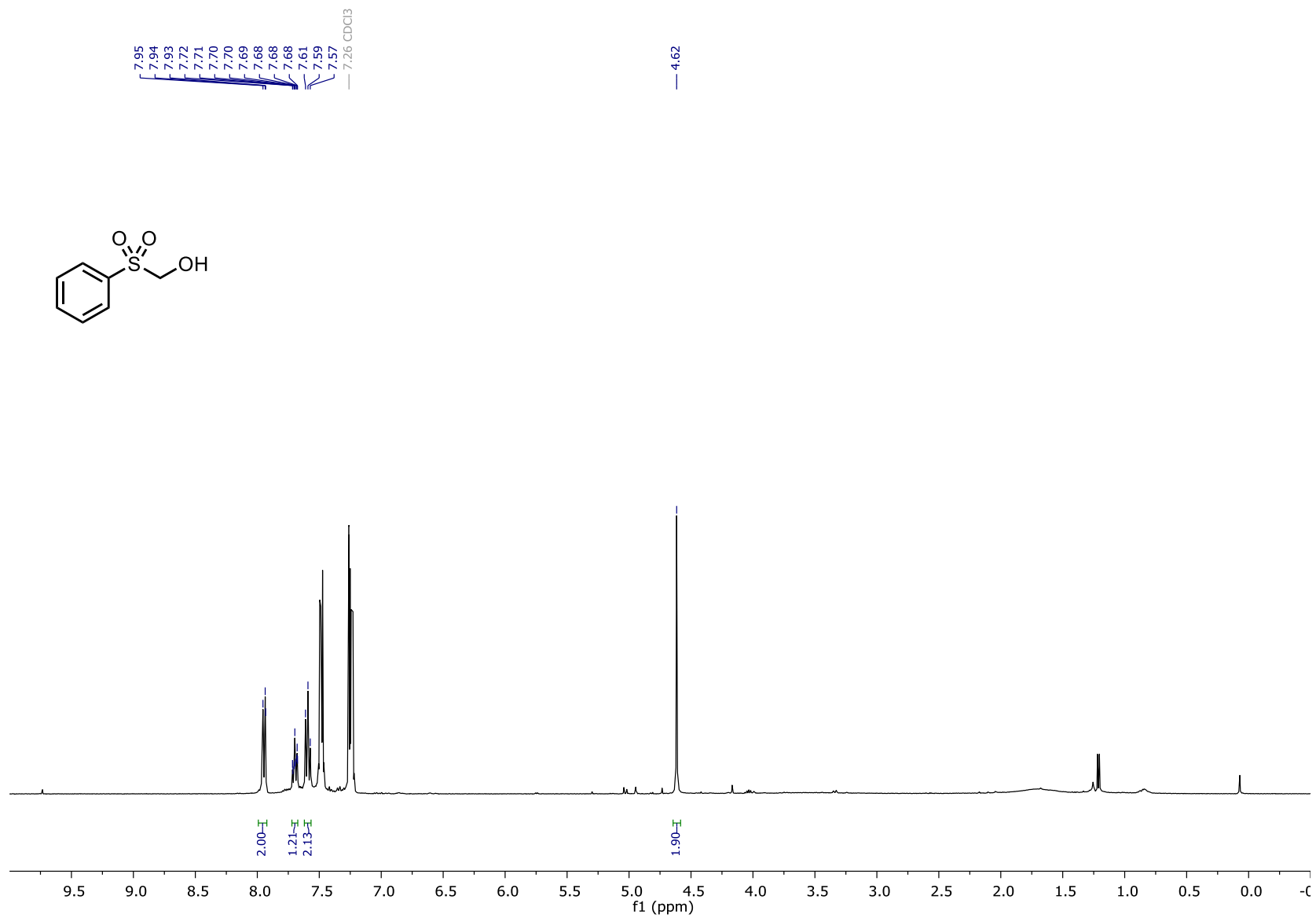
^{13}C NMR of *o*-xylene-derived thianthrenium tetrafluoroborate (TT-3)CD₃CN, 126 MHz, 298 K

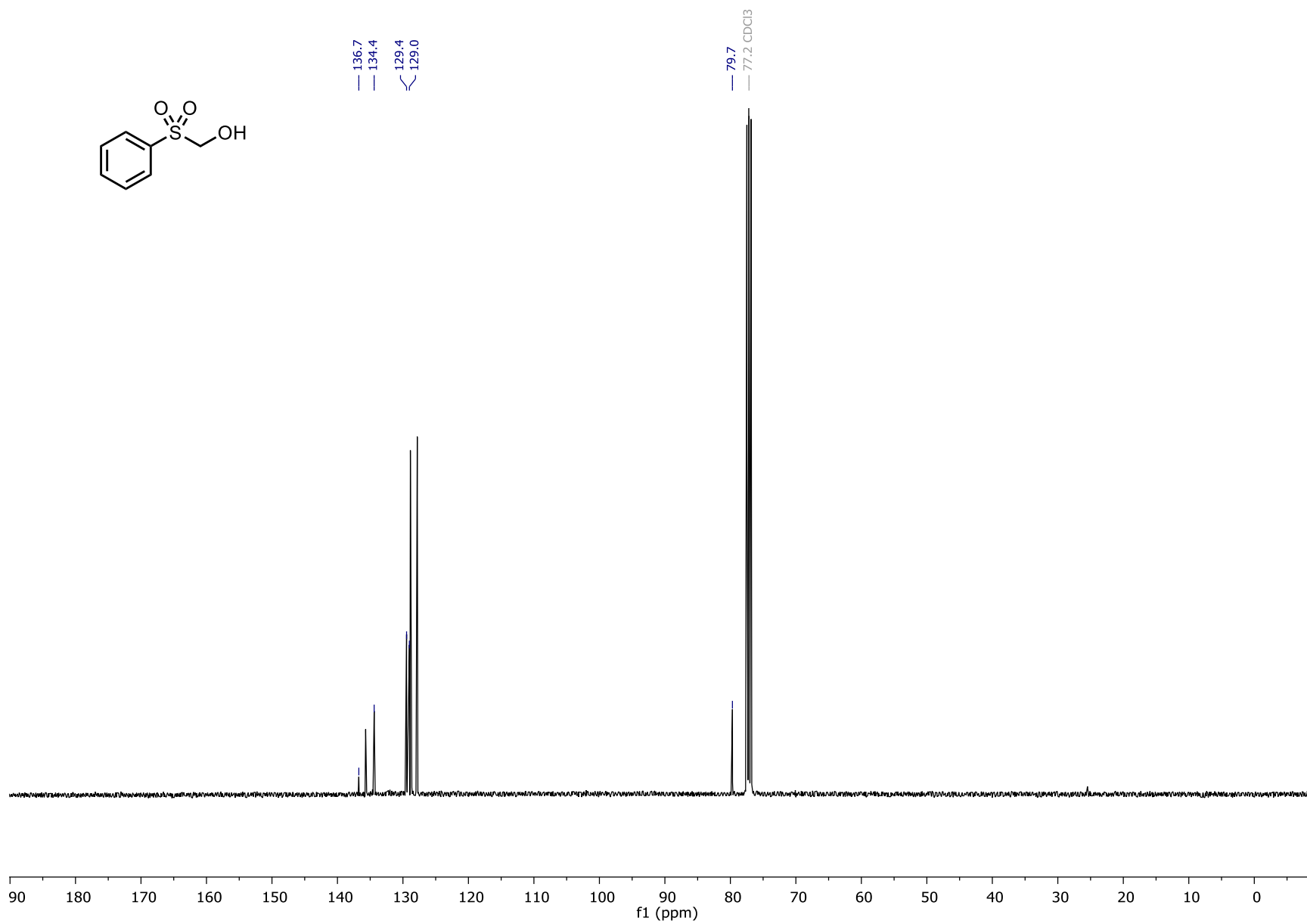
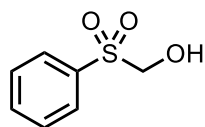
^{19}F NMR of *o*-xylene-derived thianthrenium tetrafluoroborate (TT-3)CD₃CN, 471 MHz, 298 K

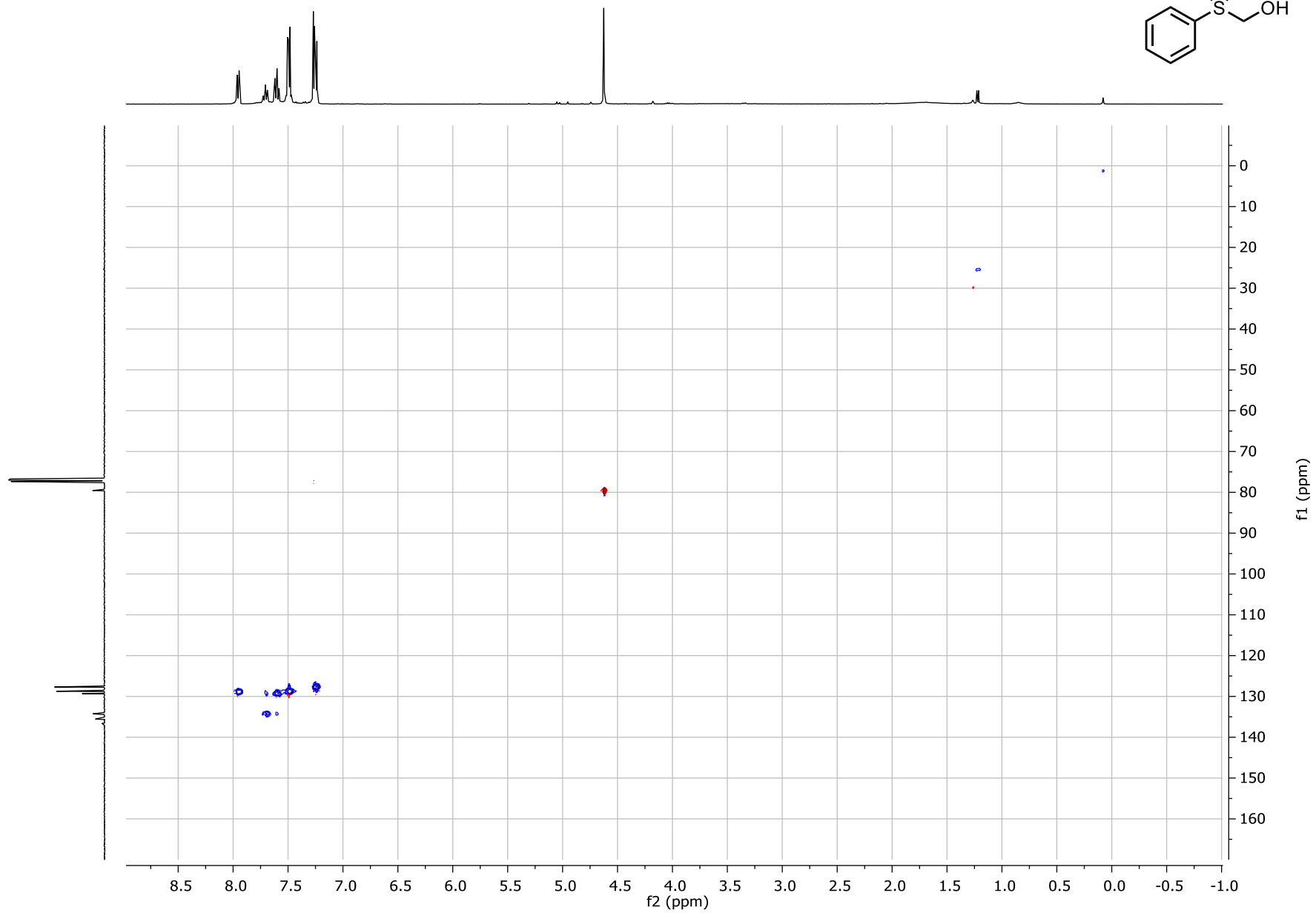
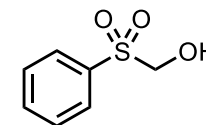
p-Xylene-derived thianthrenium tetrafluoroborate (TT-4)**¹H NMR of p-Xylene-derived thianthrenium tetrafluoroborate (TT-4)**CD₃CN, 500 MHz, 298 K

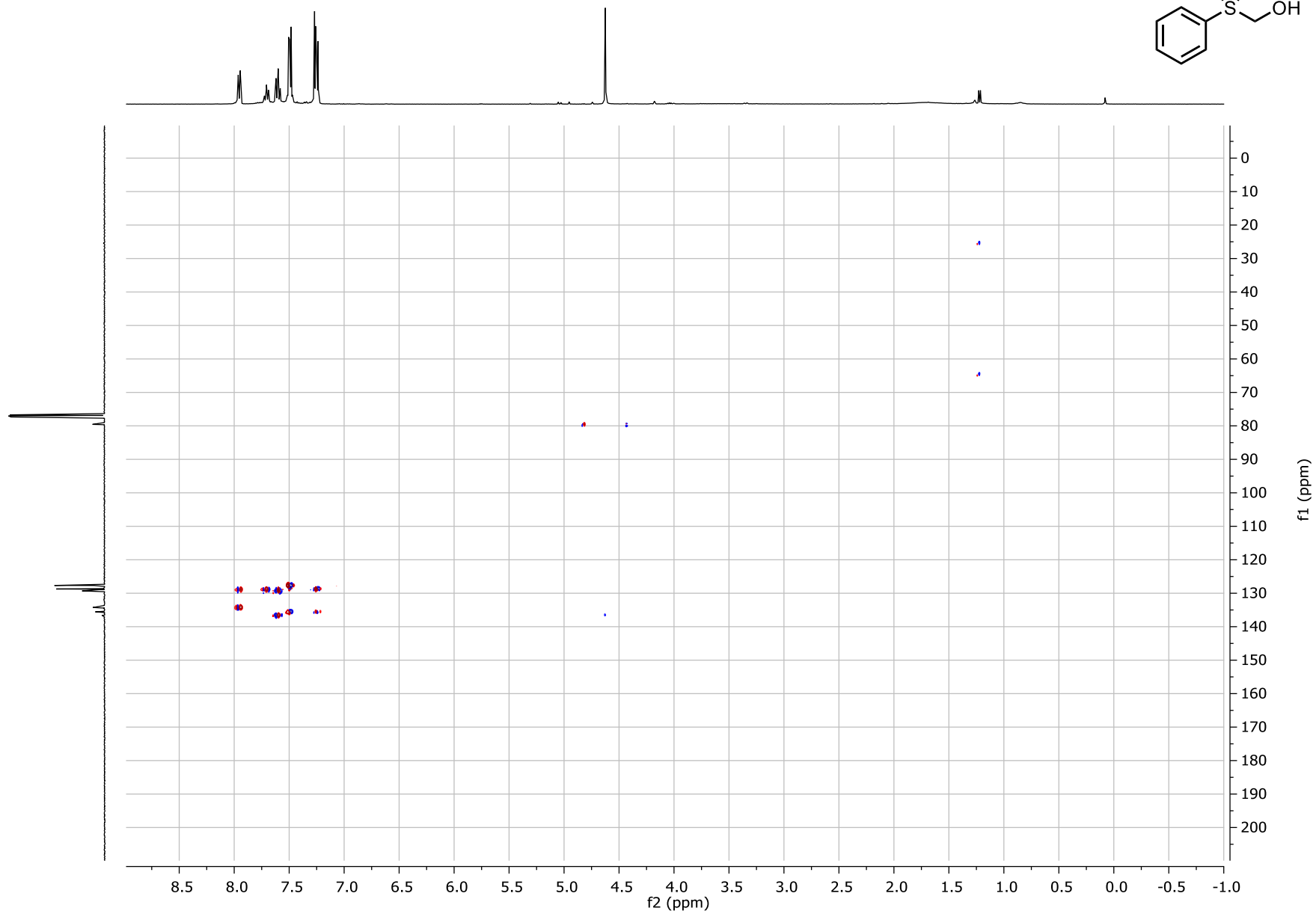
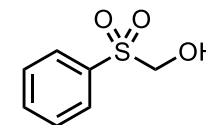
^{13}C NMR of p-xylene-derived thianthrenium tetrafluoroborate (TT-4)CD₃CN, 126 MHz, 298 K

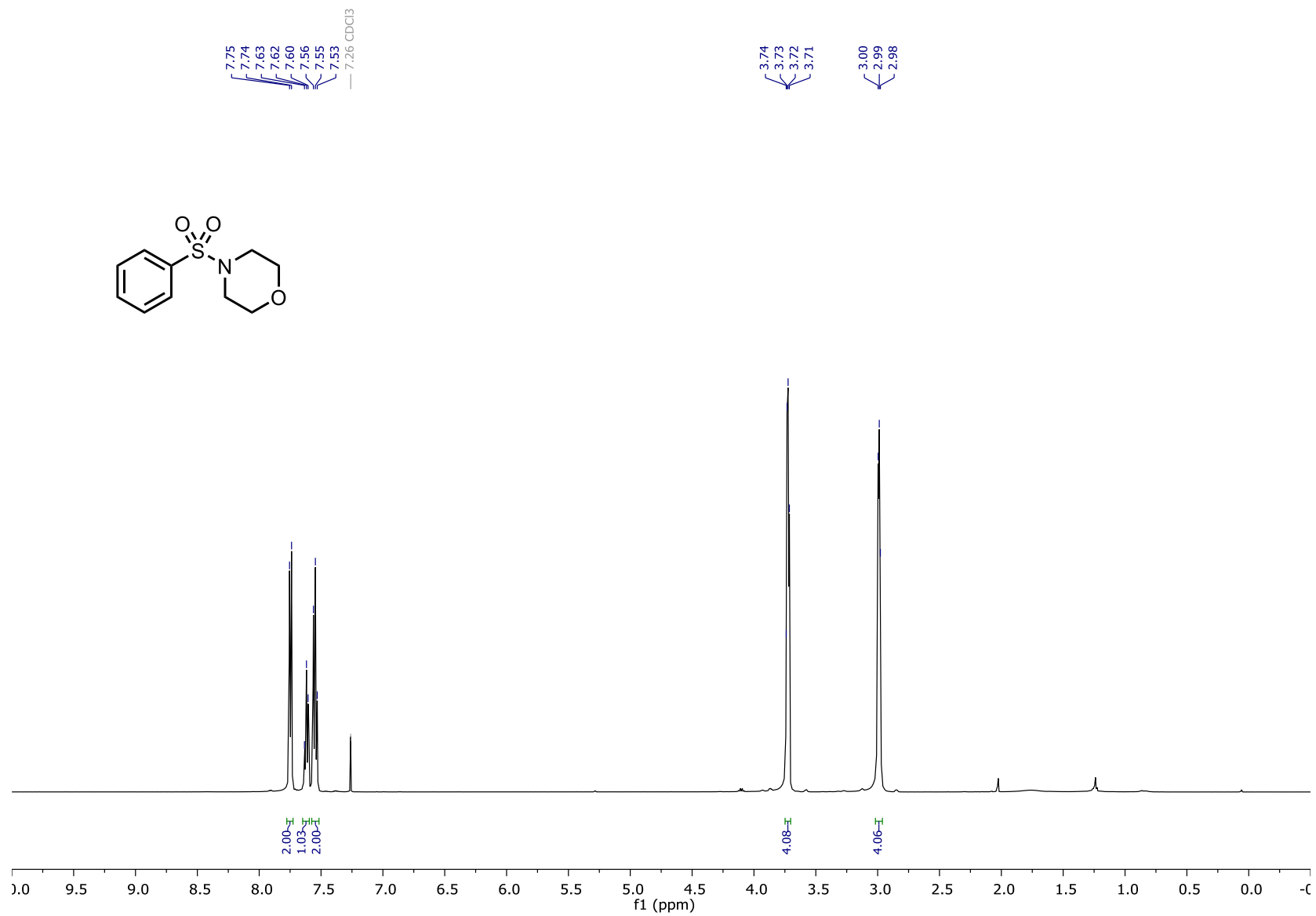
^{19}F NMR of p-xylene-derived thianthrenium tetrafluoroborate (TT-4)CD₃CN, 471 MHz, 298 K

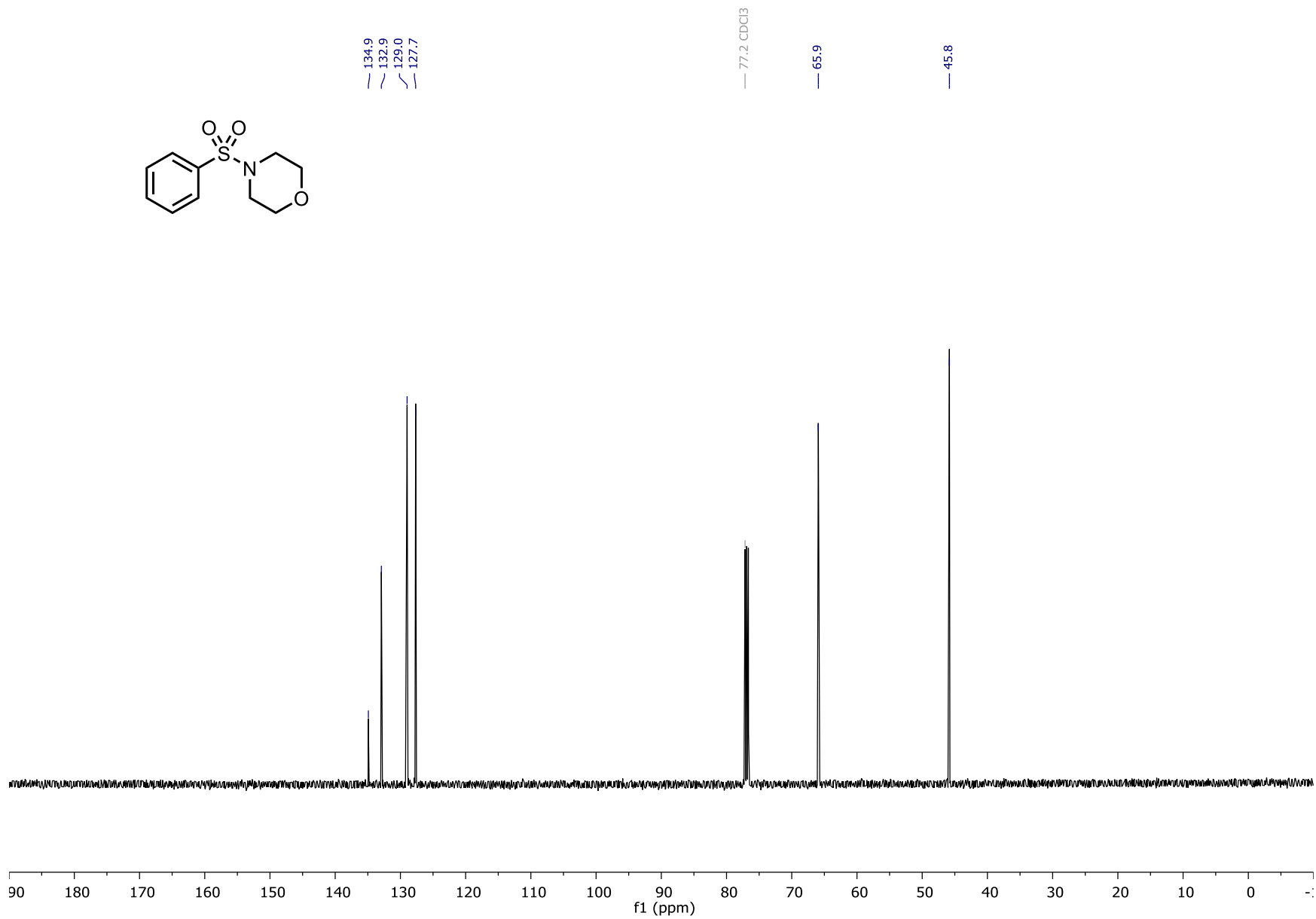
(Phenylsulfonyl)methanol (1)**¹H NMR of (phenylsulfonyl)methanol (1)**CDCl₃, 400 MHz, 298 K

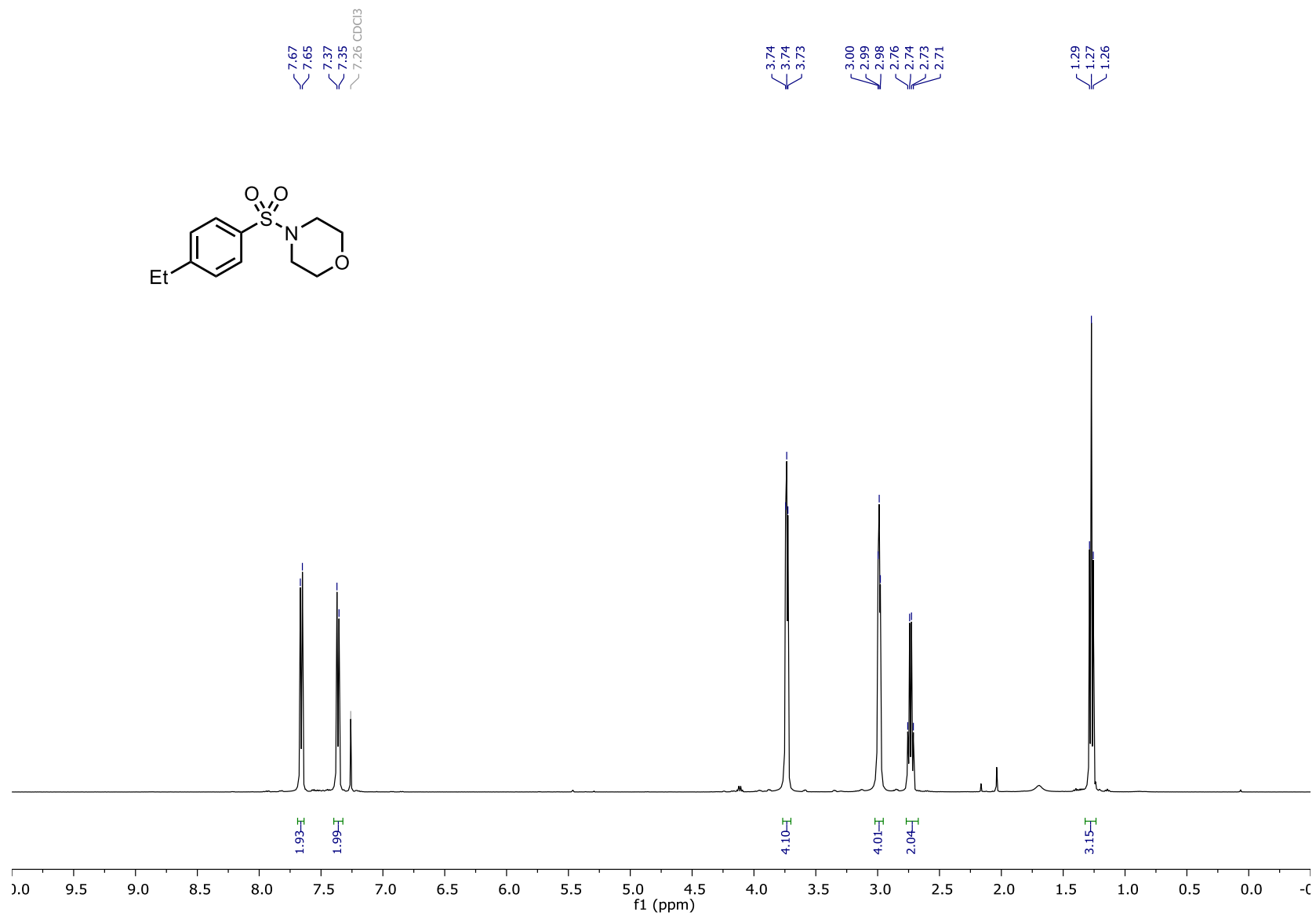
^{13}C NMR of (phenylsulfonyl)methanol (1)CDCl₃, 101 MHz, 298 K

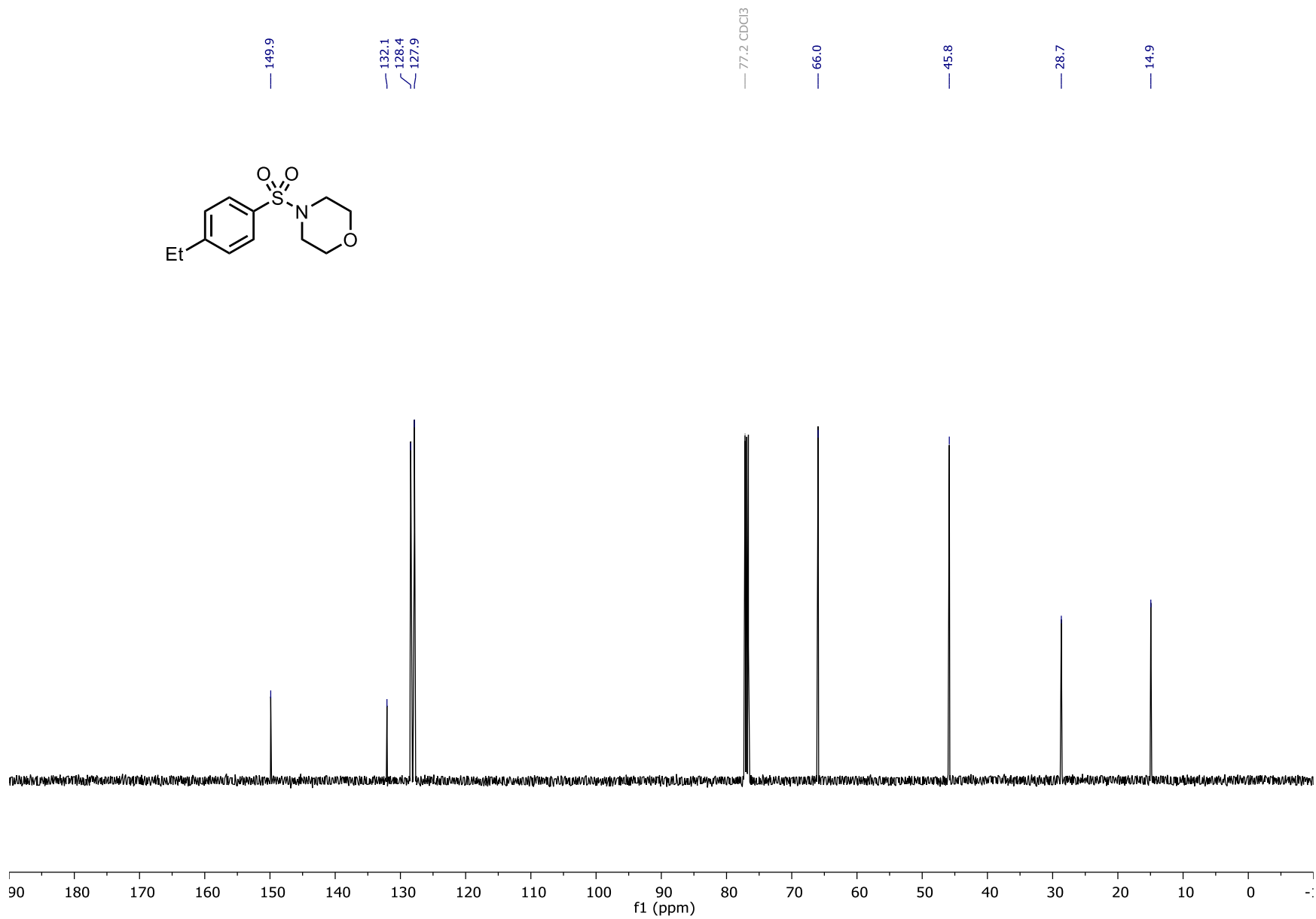
^1H - ^{13}C HSQC NMR of (phenylsulfonyl)methanol (1)

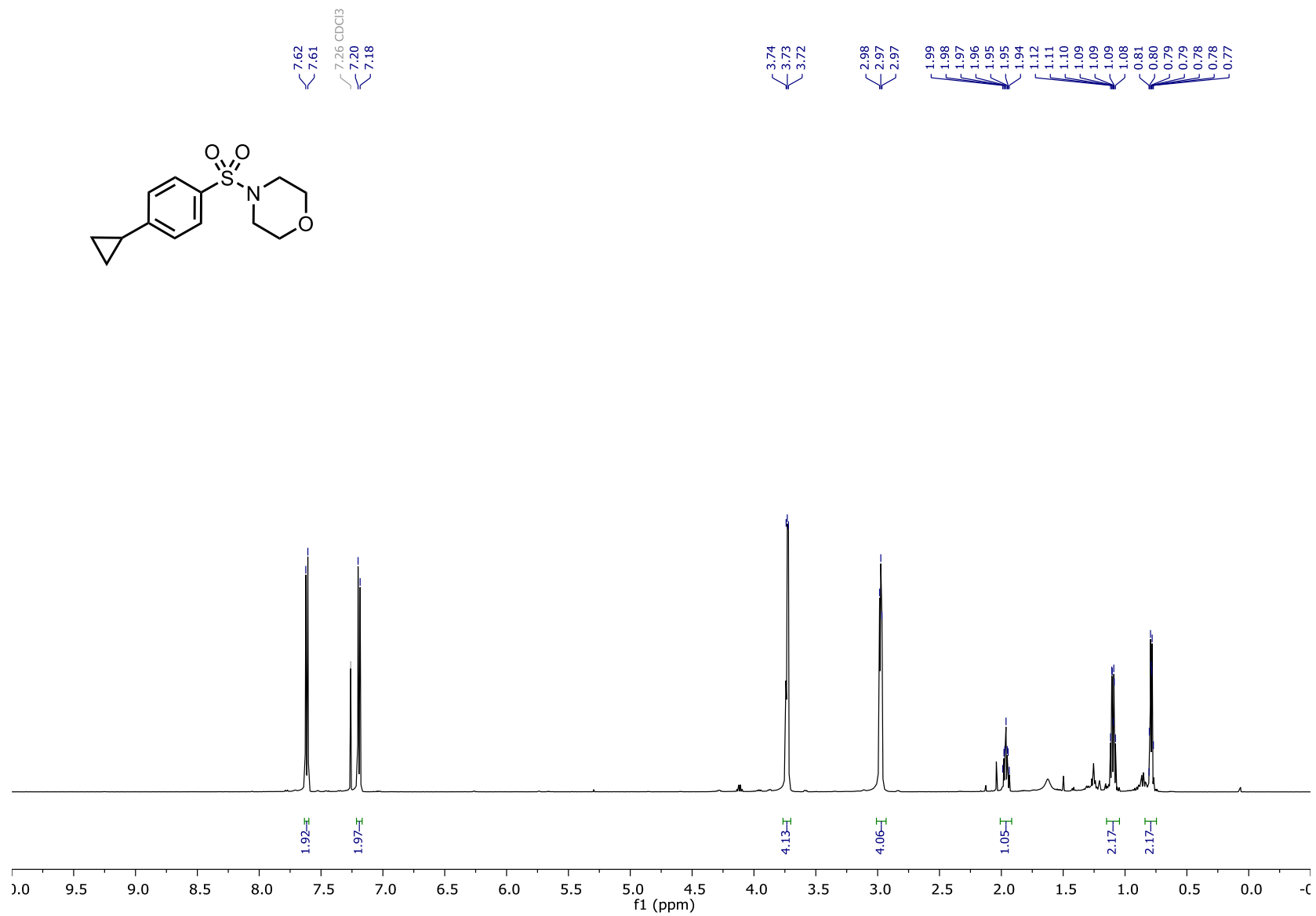
^1H - ^{13}C HMBC NMR of (phenylsulfonyl)methanol (1)

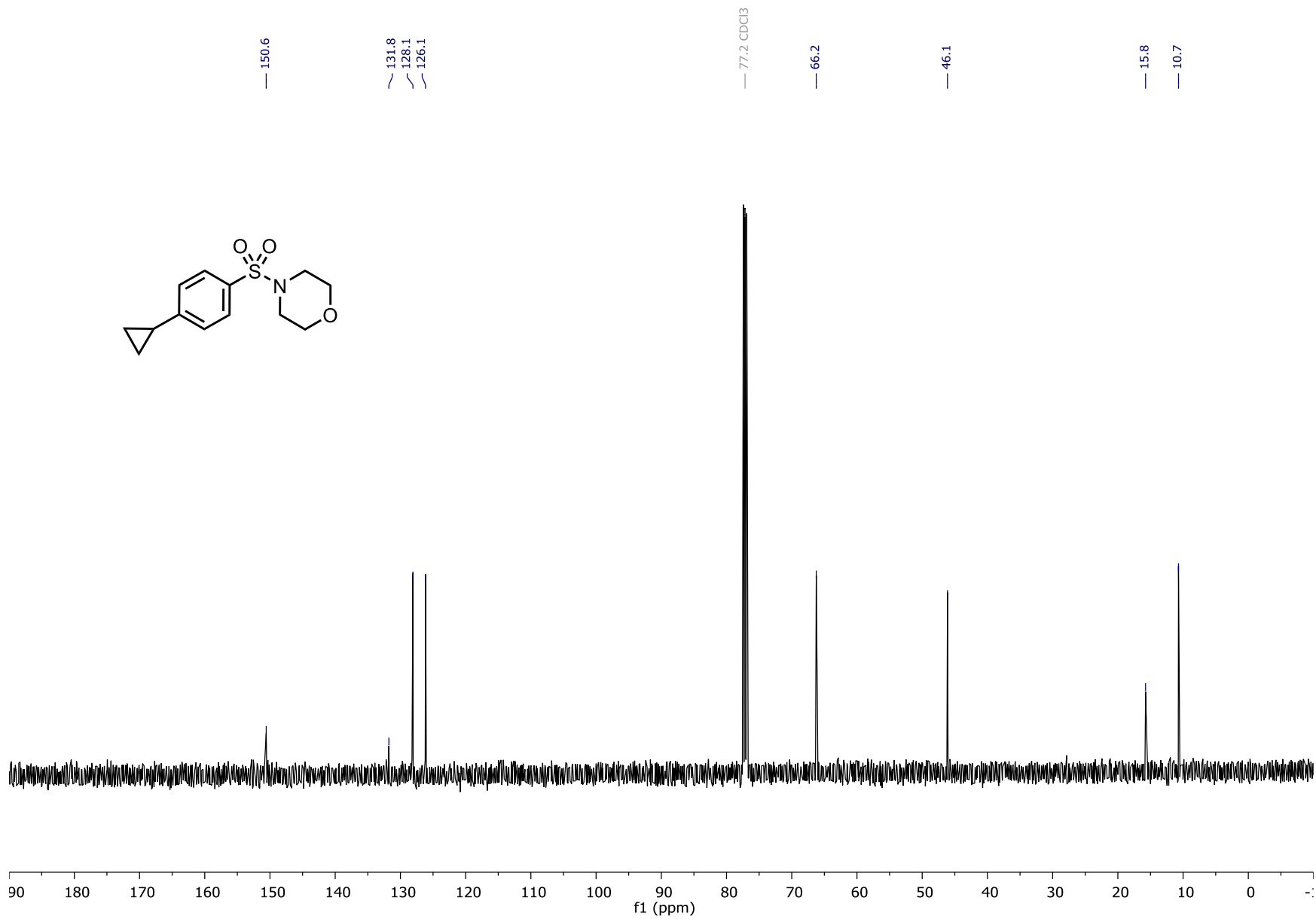
4-(Phenylsulfonyl)morpholine (2)**¹H NMR of 4-(phenylsulfonyl)morpholine (2)**CDCl₃, 500 MHz, 298 K

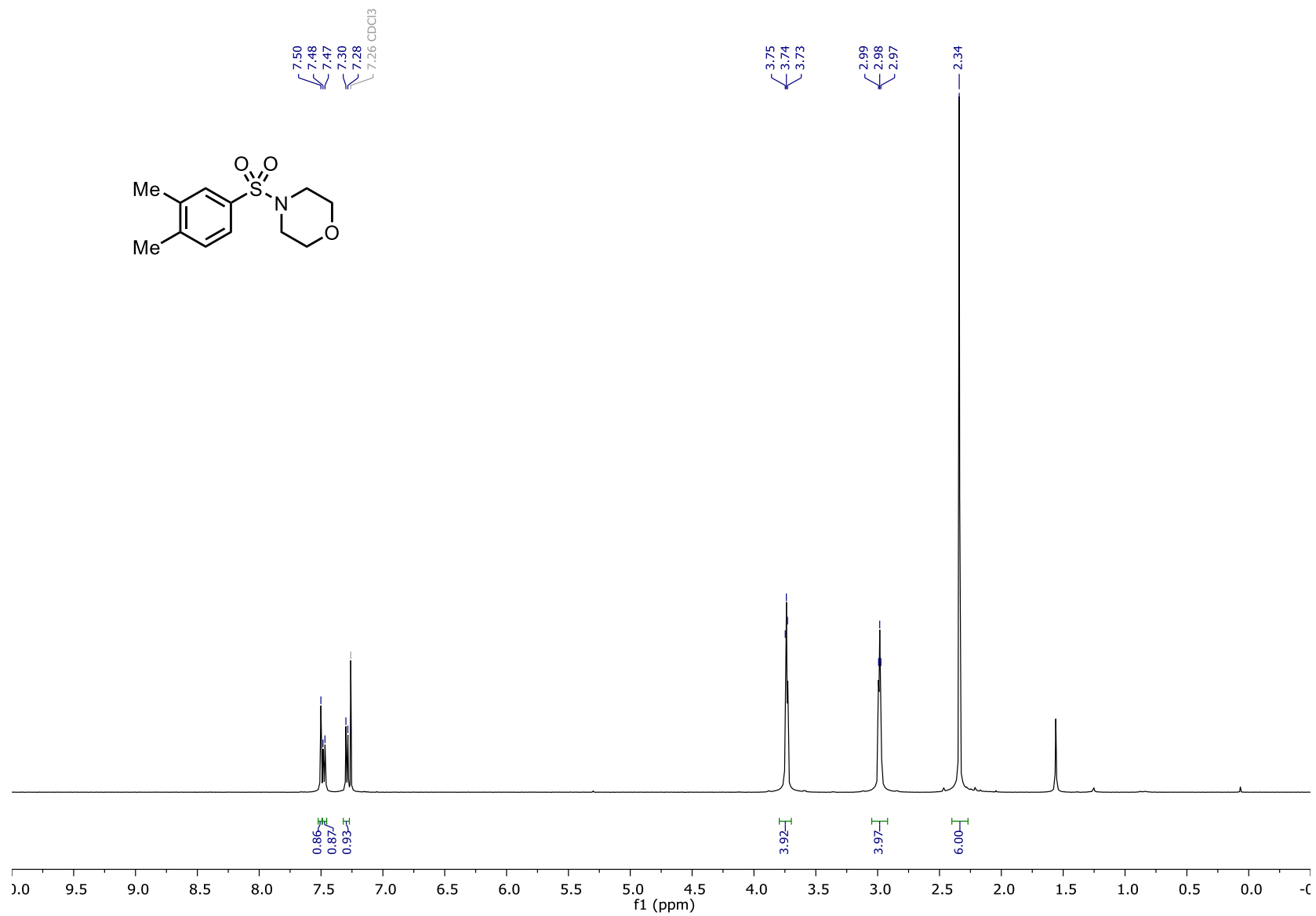
¹³C NMR of 4-(phenylsulfonyl)morpholine (2)CDCl₃, 126 MHz, 298 K

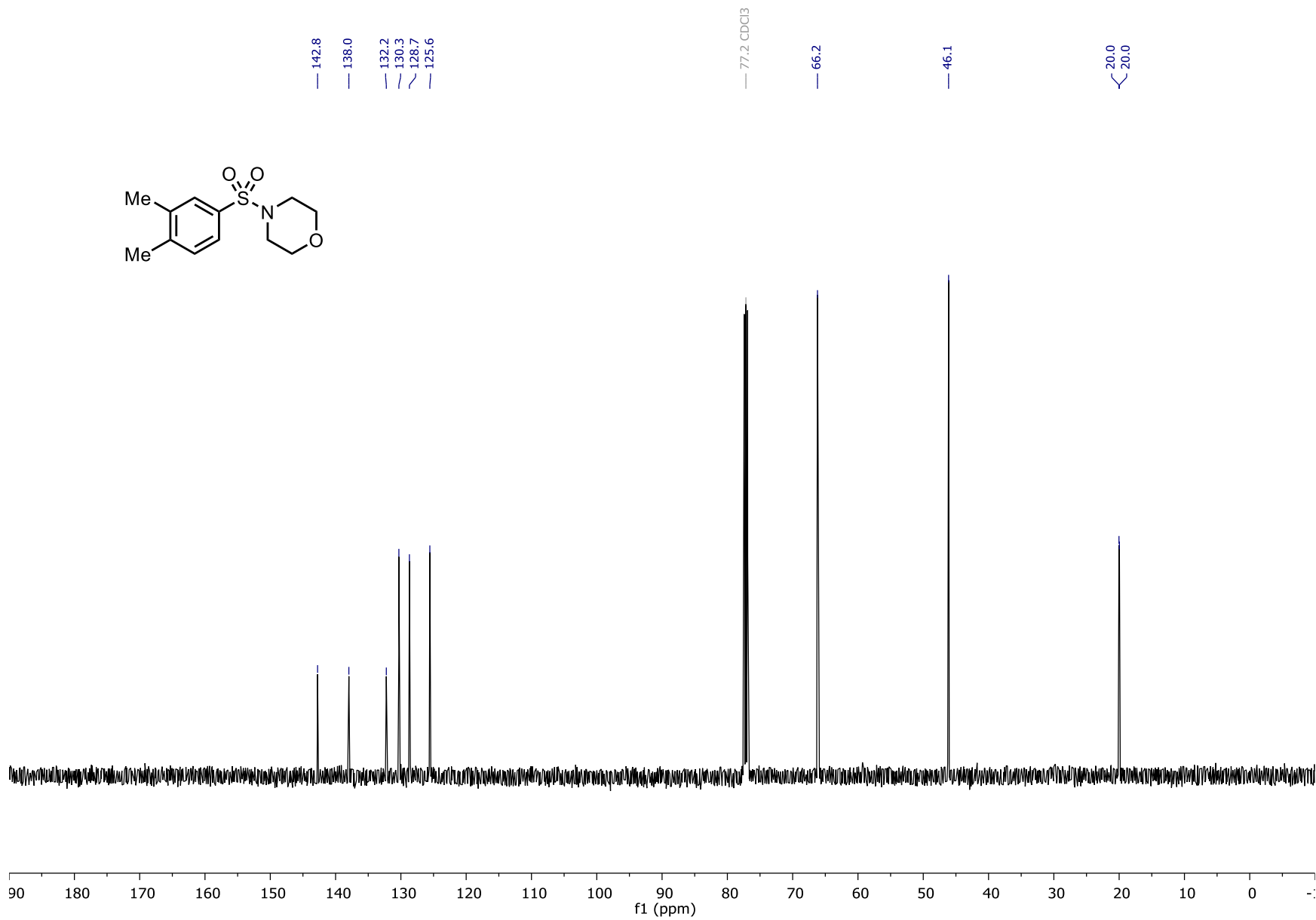
4-((4-Ethylphenyl)sulfonyl)morpholine (3)**¹H NMR of 4-((4-ethylphenyl)sulfonyl)morpholine (3)**CDCl₃, 500 MHz, 298 K

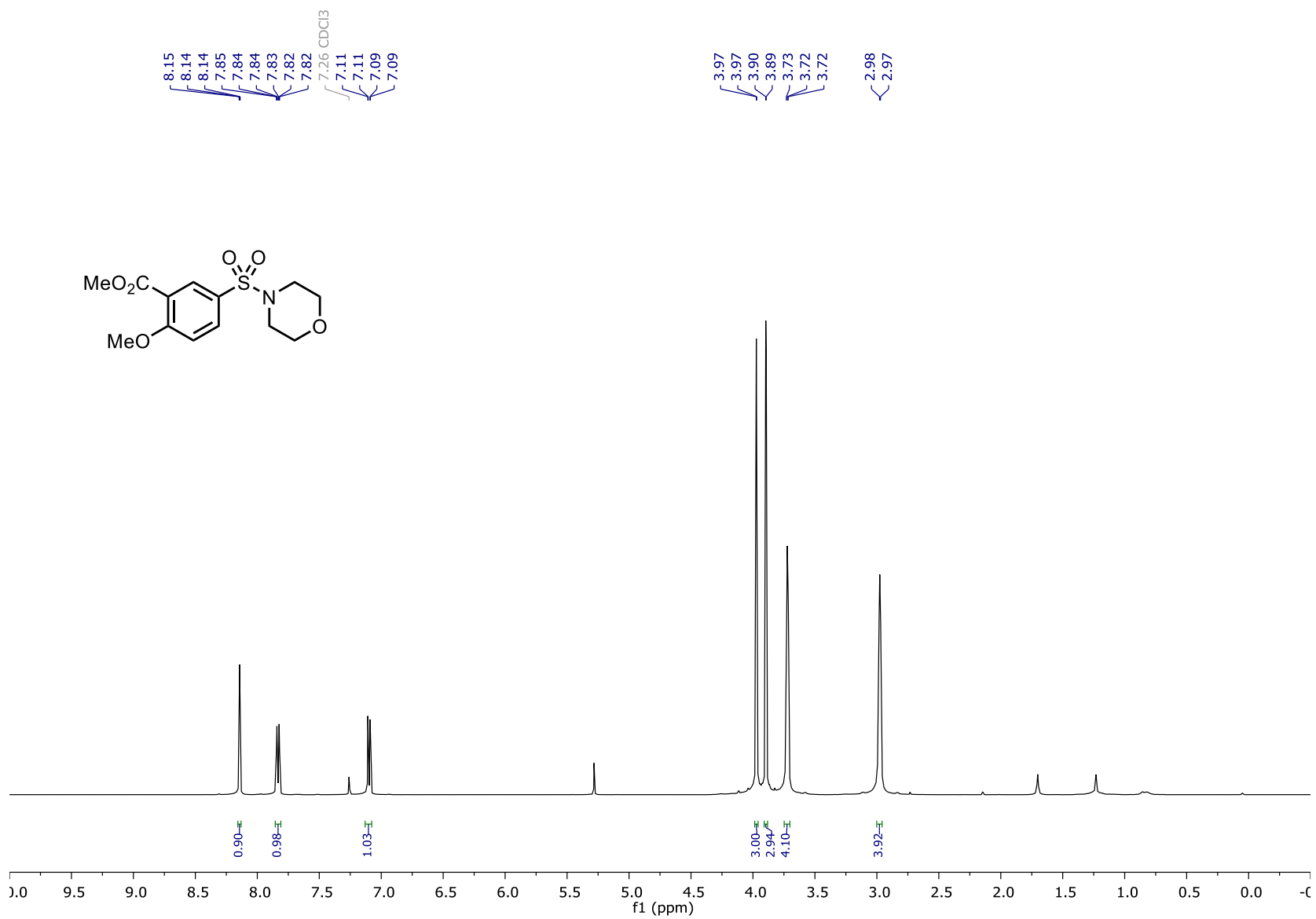
^{13}C NMR of 4-((4-ethylphenyl)sulfonyl)morpholine (3)CDCl₃, 126 MHz, 298 K

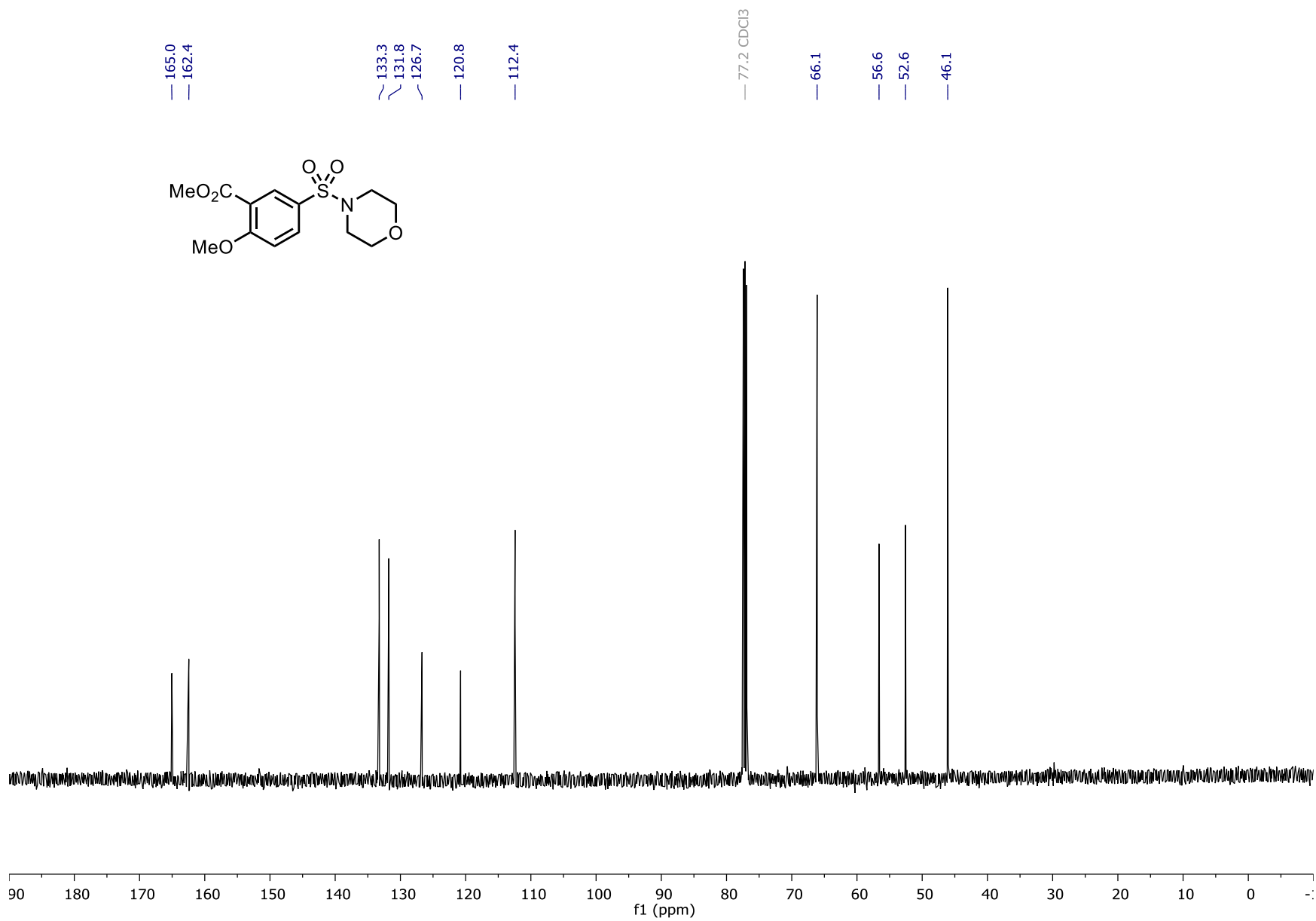
4-((4-Cyclopropylphenyl)sulfonyl)morpholine (4)**¹H NMR of 4-((4-cyclopropylphenyl)sulfonyl)morpholine (4)**CDCl₃, 500 MHz, 298 K

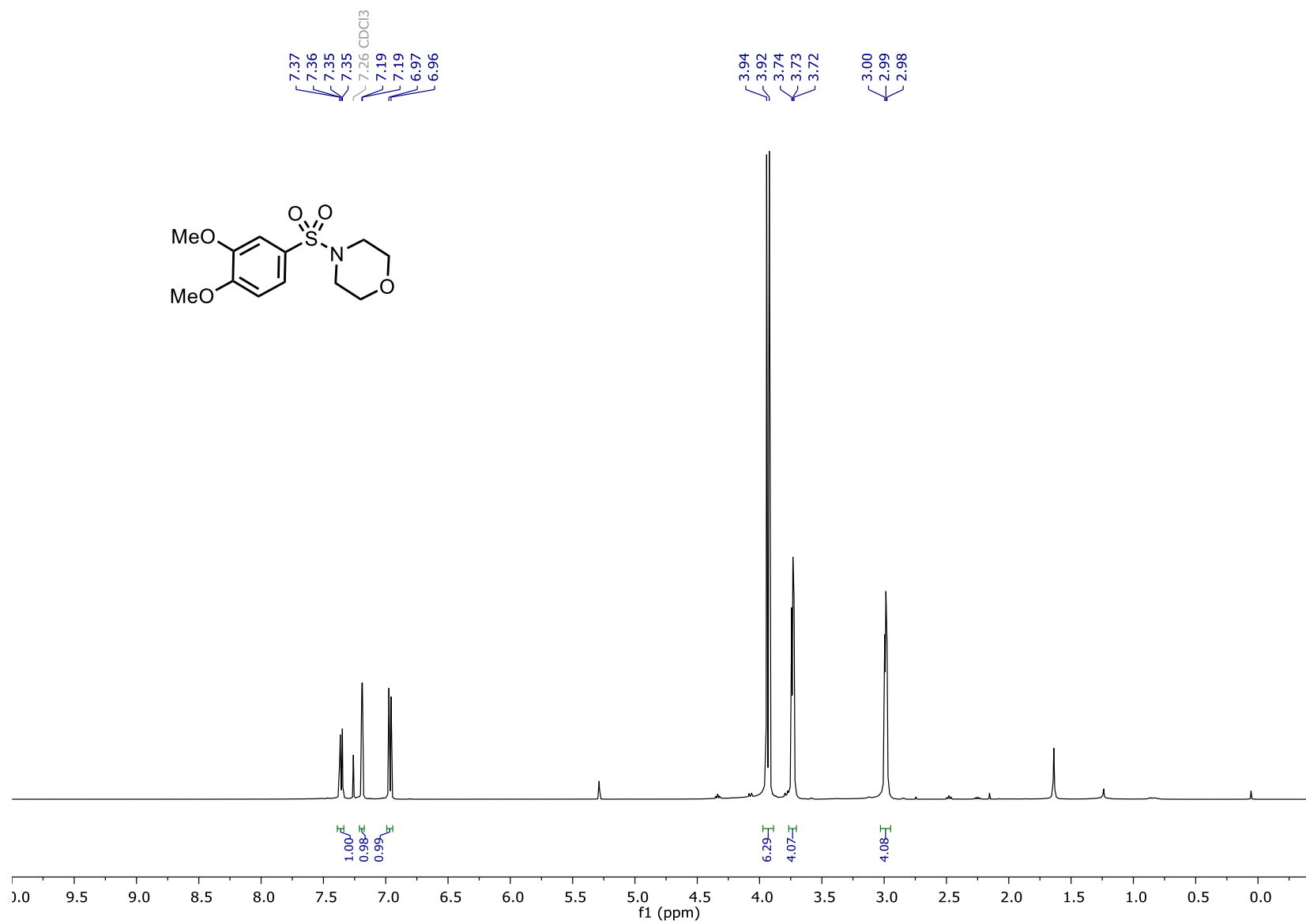
^{13}C NMR of 4-(4-cyclopropylphenyl)sulfonylmorpholine (4)CDCl₃, 126 MHz, 298 K

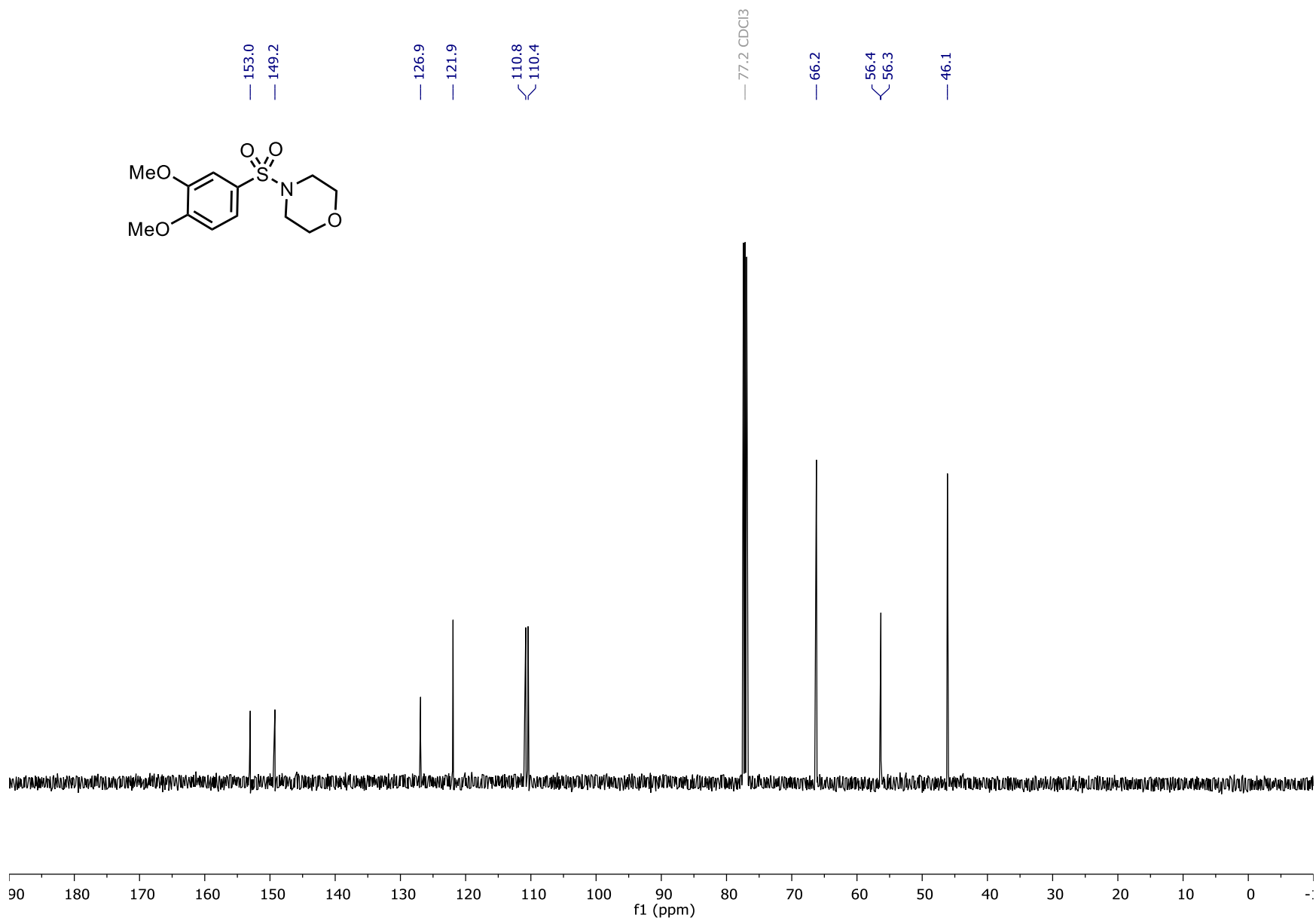
4-((3,4-Dimethylphenyl)sulfonyl)morpholine (5)**¹H NMR of 4-((3,4-dimethylphenyl)sulfonyl)morpholine (5)**CDCl₃, 500 MHz, 298 K

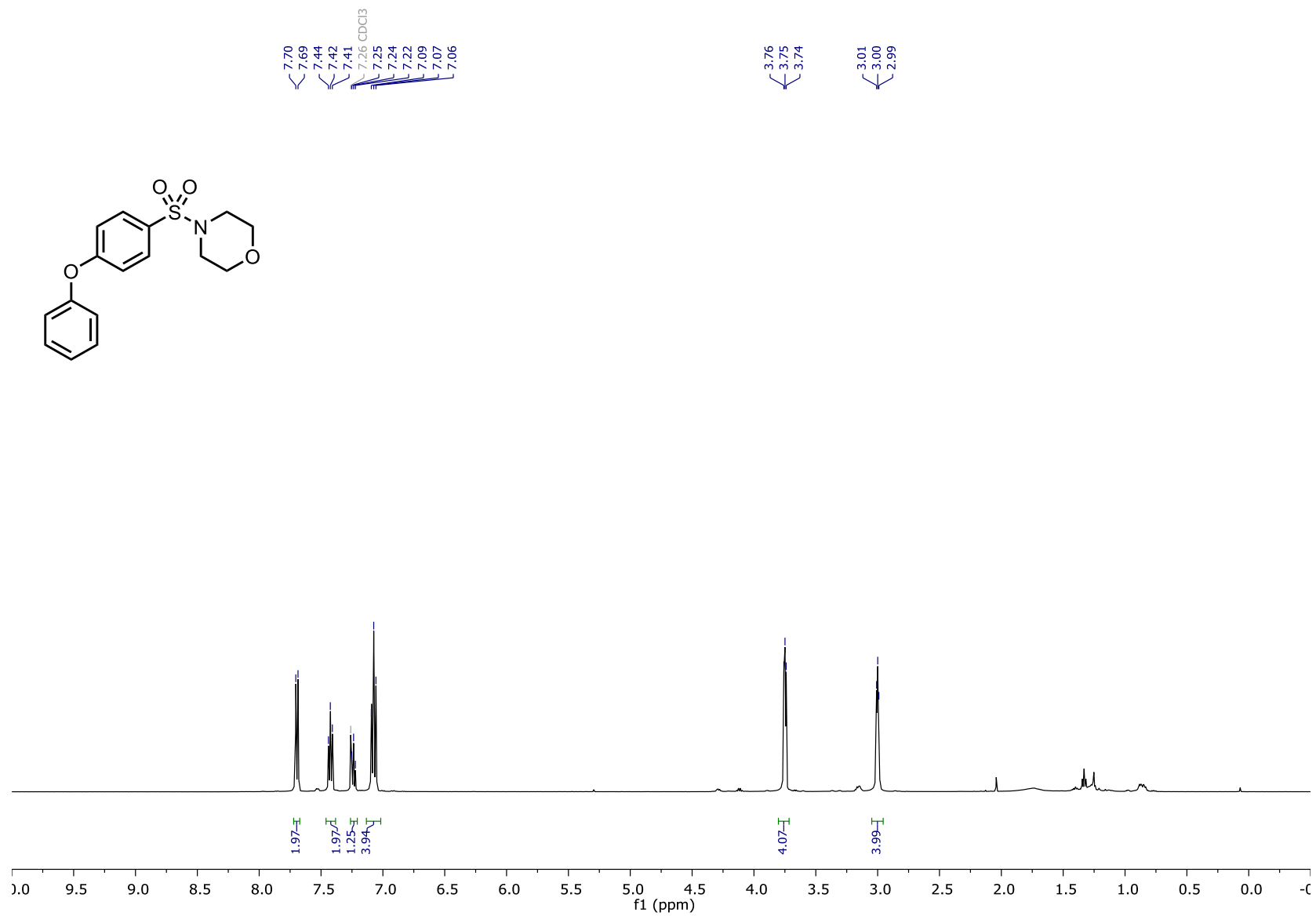
^{13}C NMR of 4-((3,4-dimethylphenyl)sulfonyl)morpholine (5)CDCl₃, 126 MHz, 298 K

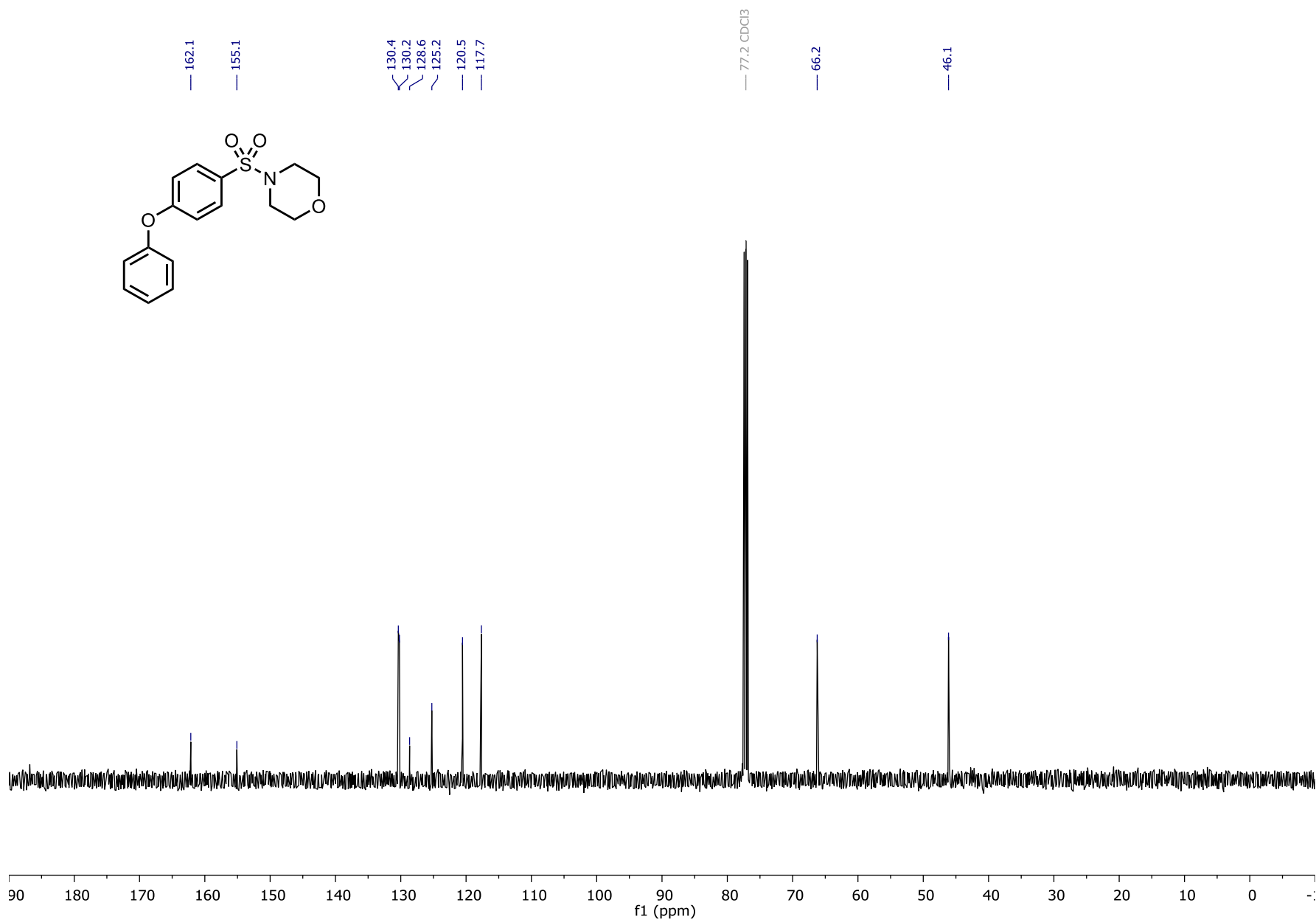
Methyl 2-methoxy-5-(morpholinosulfonyl)benzoate (6)**¹H NMR of methyl 2-methoxy-5-(morpholinosulfonyl)benzoate (6)**CDCl₃, 500 MHz, 298 K

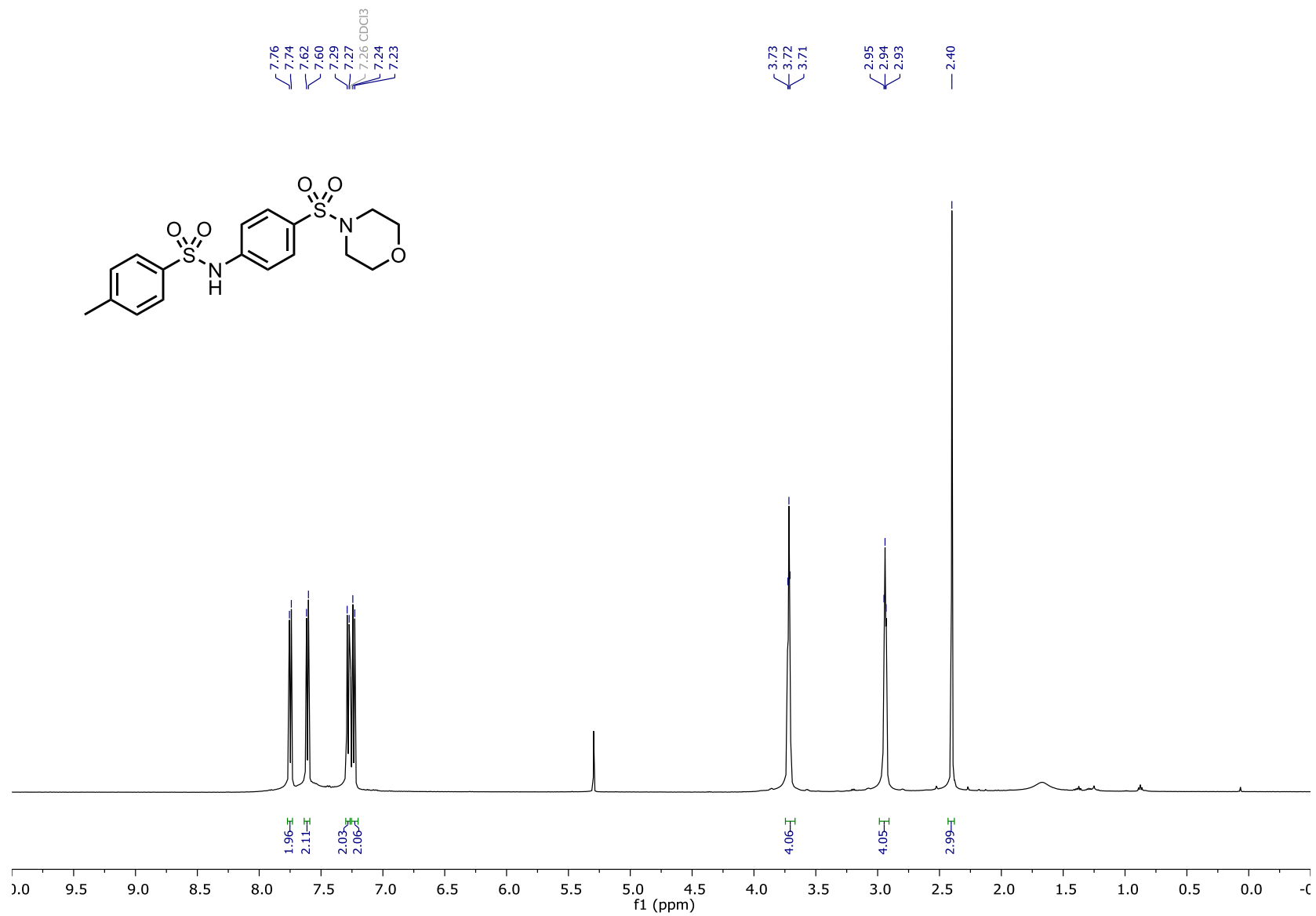
^{13}C NMR of methyl 2-methoxy-5-(morpholinosulfonyl)benzoate (6)CDCl₃, 126 MHz, 298 K

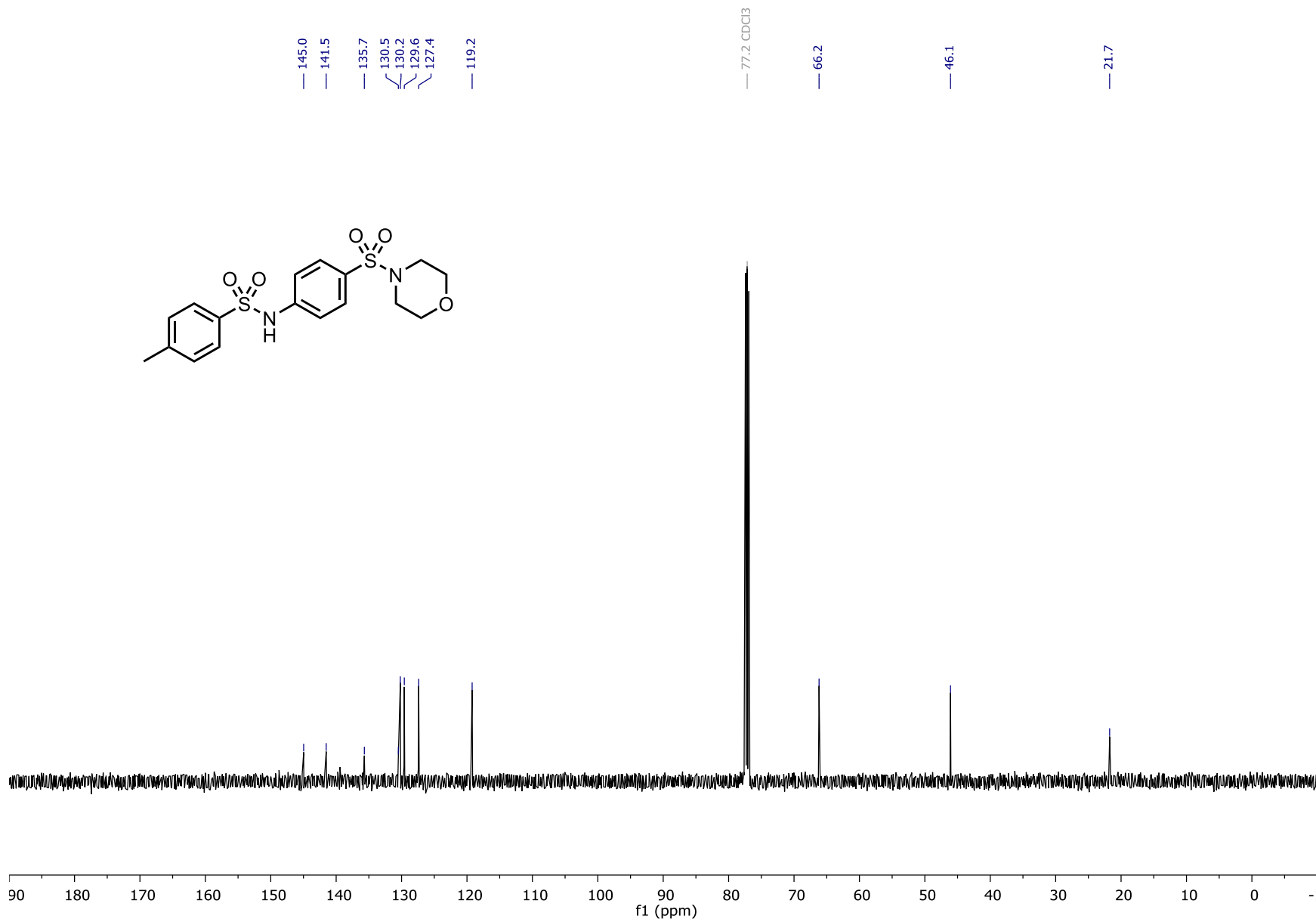
4-((3,4-Dimethoxyphenyl)sulfonyl)morpholine (7)**¹H NMR of 4-((3,4-dimethoxyphenyl)sulfonyl)morpholine (7)**CDCl₃, 500 MHz, 298 K

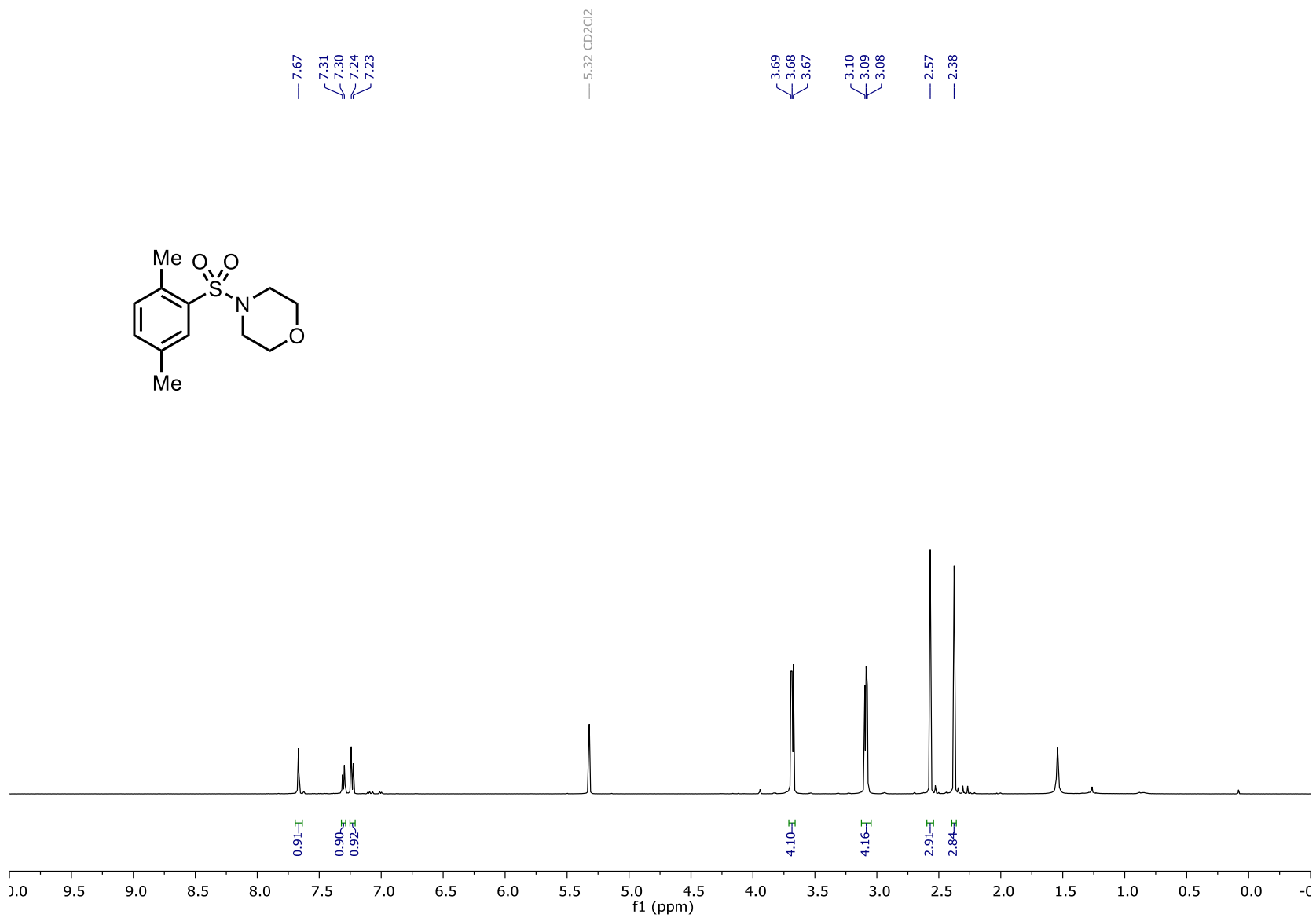
^{13}C NMR of 4-((3,4-dimethoxyphenyl)sulfonyl)morpholine (7)CDCl₃, 126 MHz, 298 K

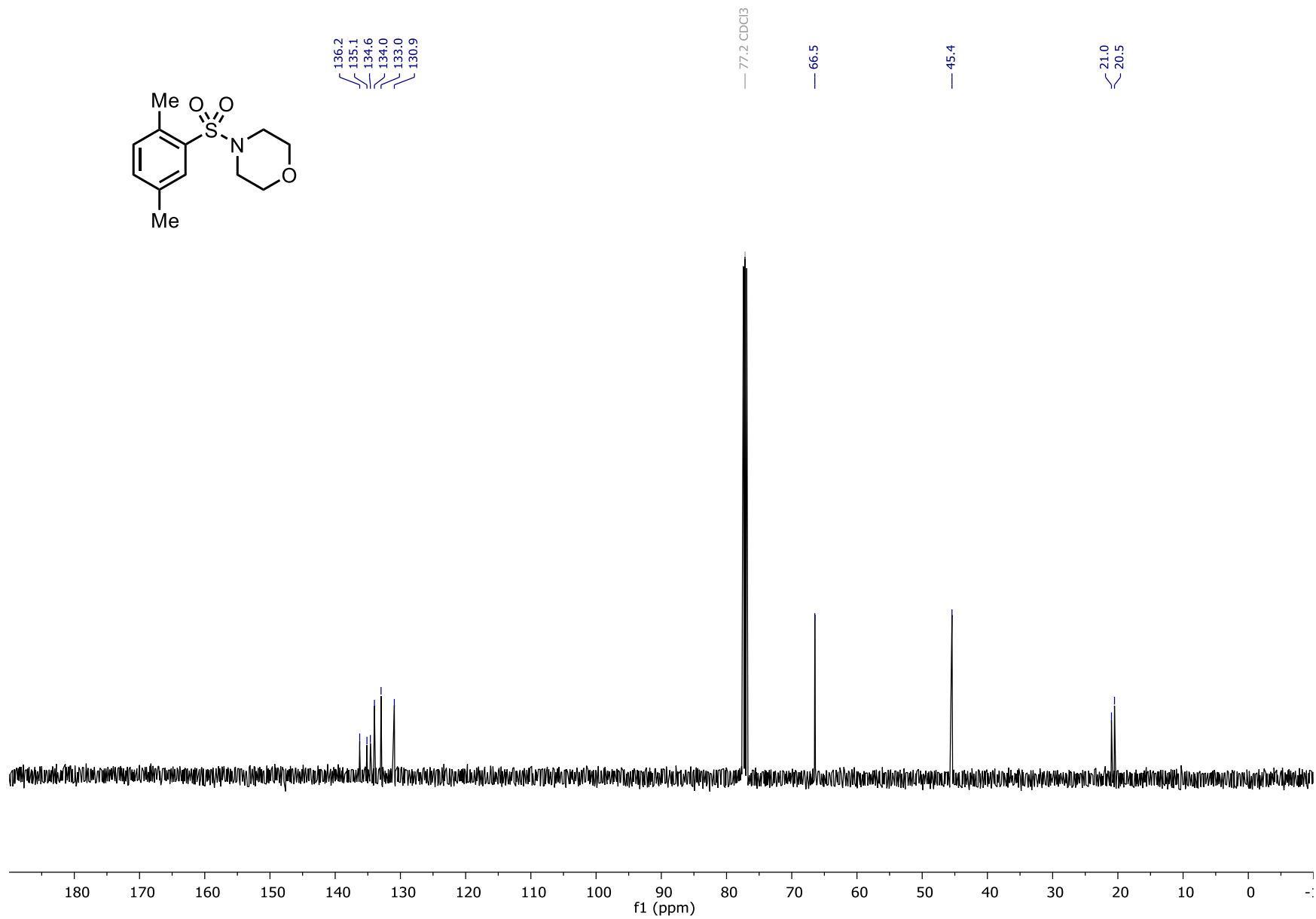
4-((4-Phenoxyphenyl)sulfonyl)morpholine (8)**¹H NMR of 4-((4-phenoxyphenyl)sulfonyl)morpholine (8)**CDCl₃, 500 MHz, 298 K

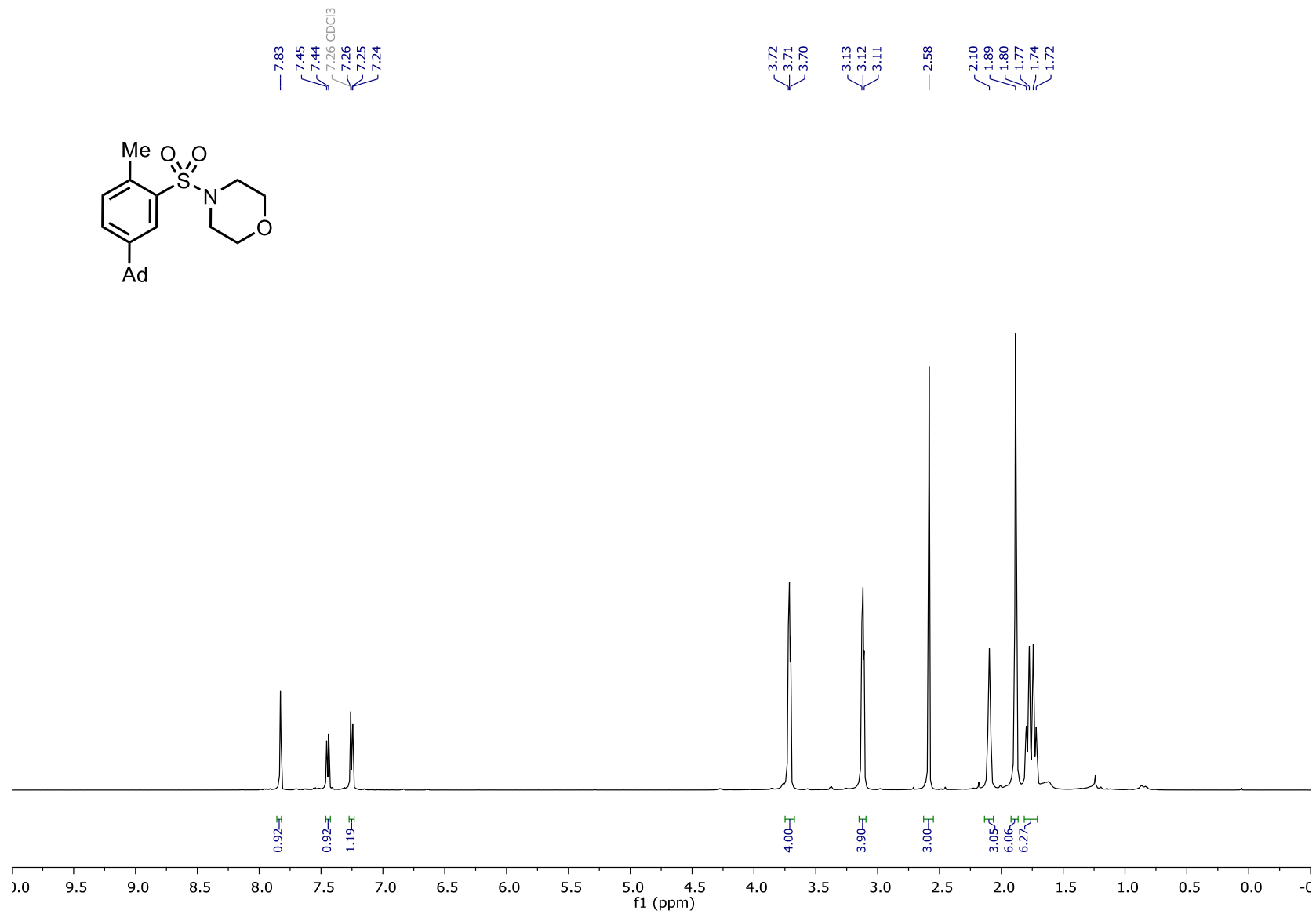
^{13}C NMR of 4-((4-phenoxyphenyl)sulfonyl)morpholine (8)CDCl₃, 126 MHz, 298 K

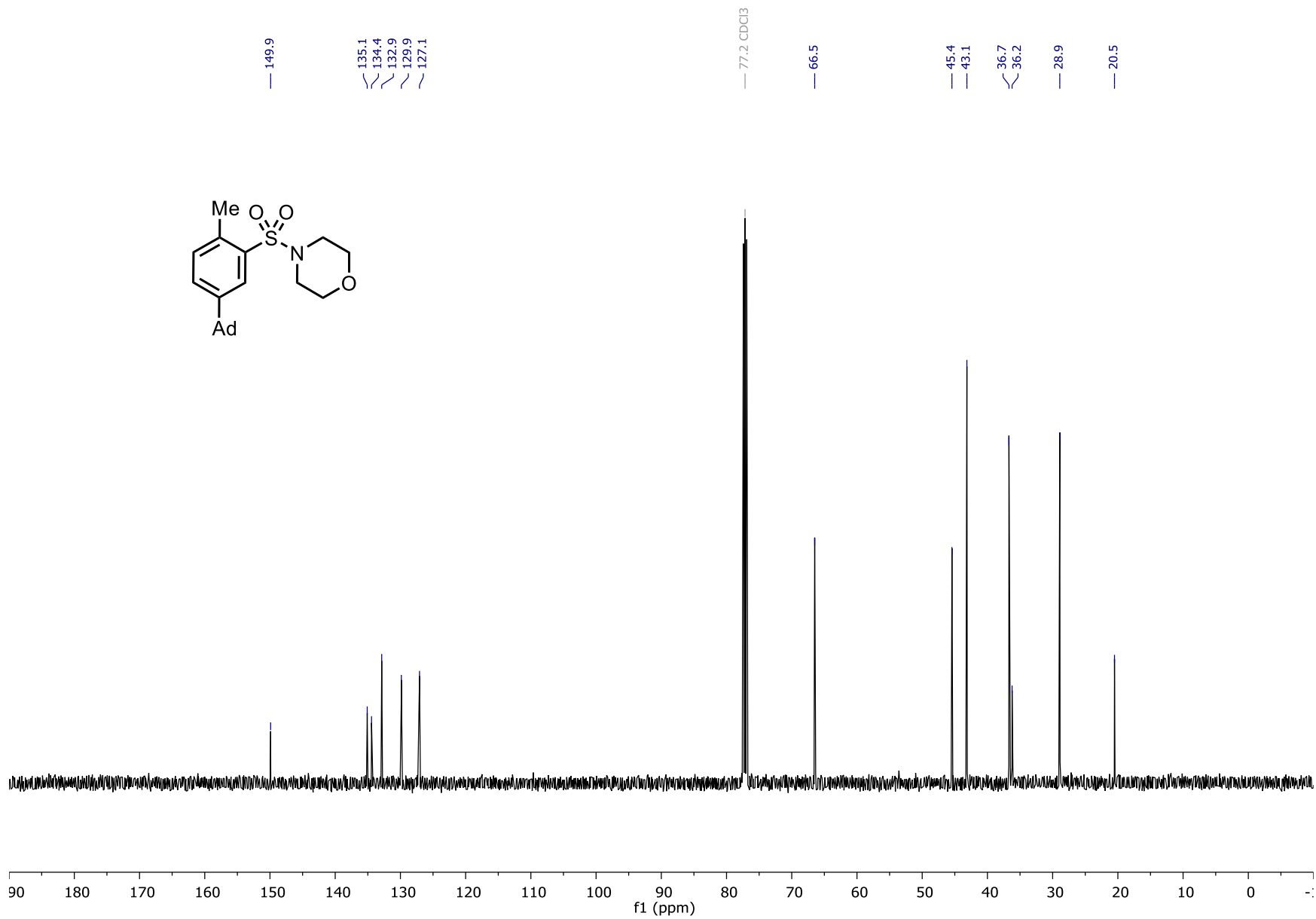
4-Methyl-N-(4-(morpholinosulfonyl)phenyl)benzenesulfonamide (9)**¹H NMR of 4-methyl-N-(4-(morpholinosulfonyl)phenyl)benzenesulfonamide (9)**CDCl₃, 500 MHz, 298 K

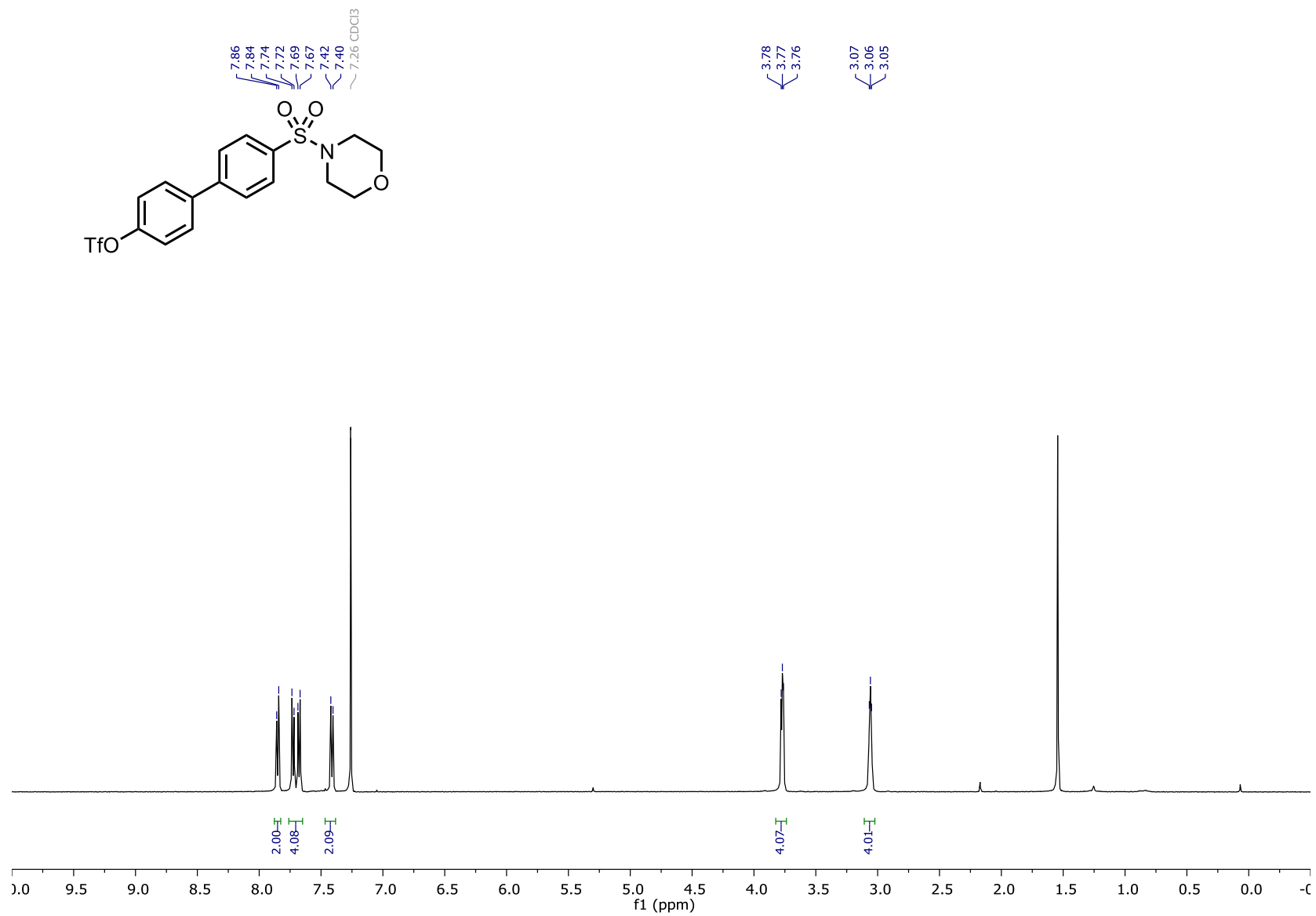
^{13}C NMR of 4-methyl-N-(4-(morpholinofonyl)phenyl)benzenesulfonamide (9)CDCl₃, 126 MHz, 298 K

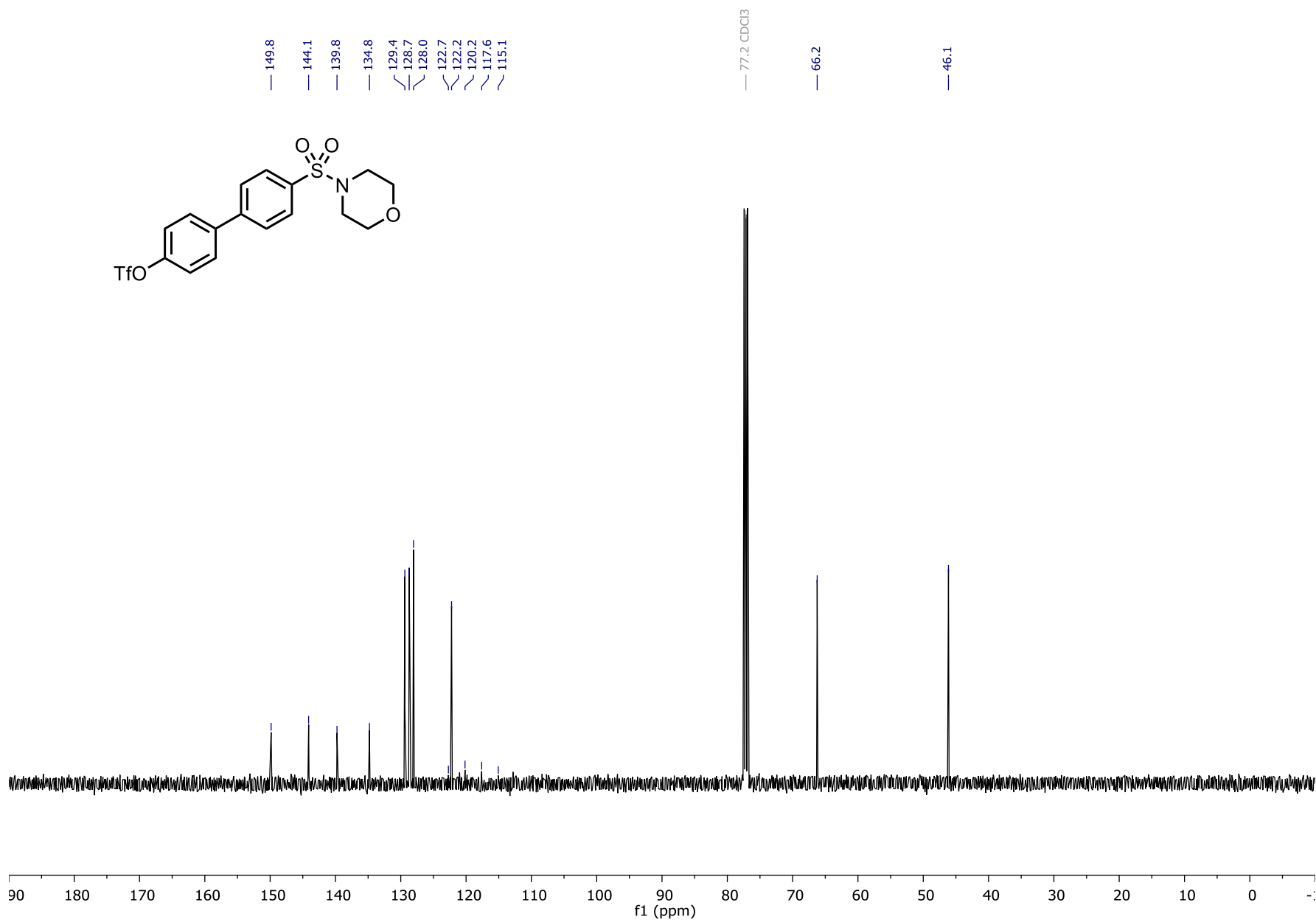
4-((2,5-Dimethylphenyl)sulfonyl)morpholine (10)**¹H NMR of 4-((2,5-dimethylphenyl)sulfonyl)morpholine (10)**CD₂Cl₂, 500 MHz, 298 K

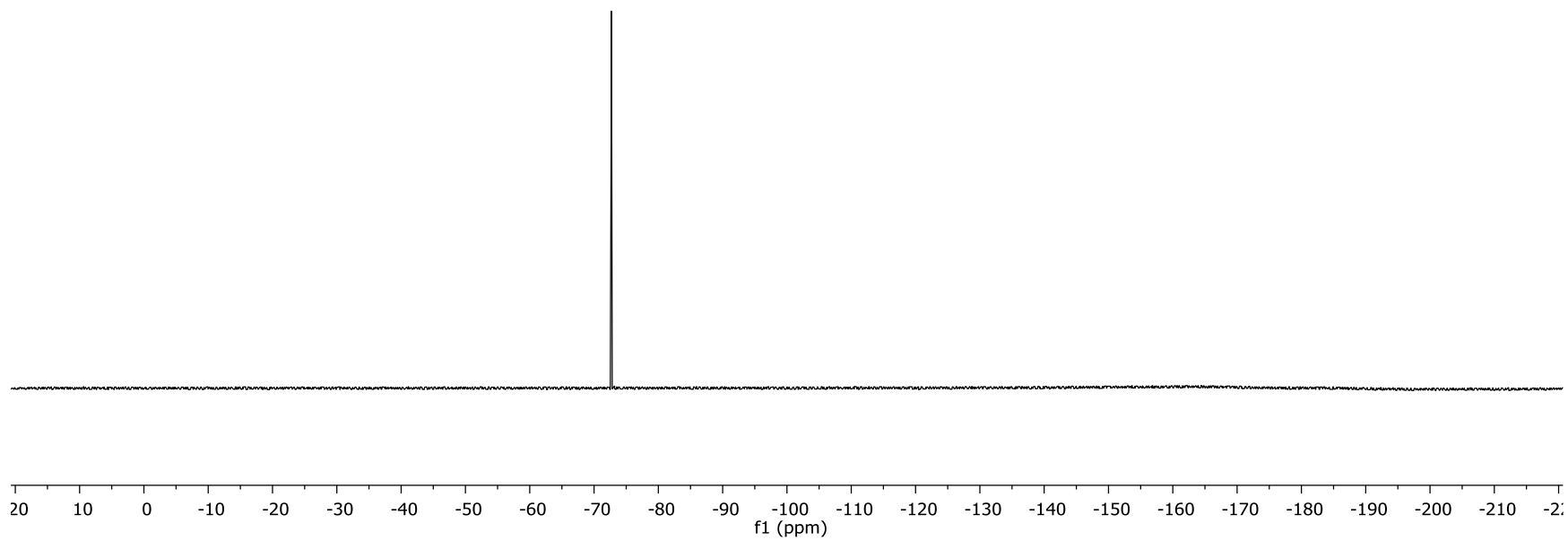
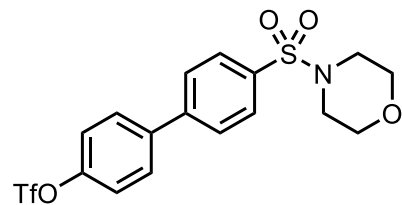
^{13}C NMR of 4-((2,5-dimethylphenyl)sulfonyl)morpholine (10)CDCl₃, 126 MHz, 298 K

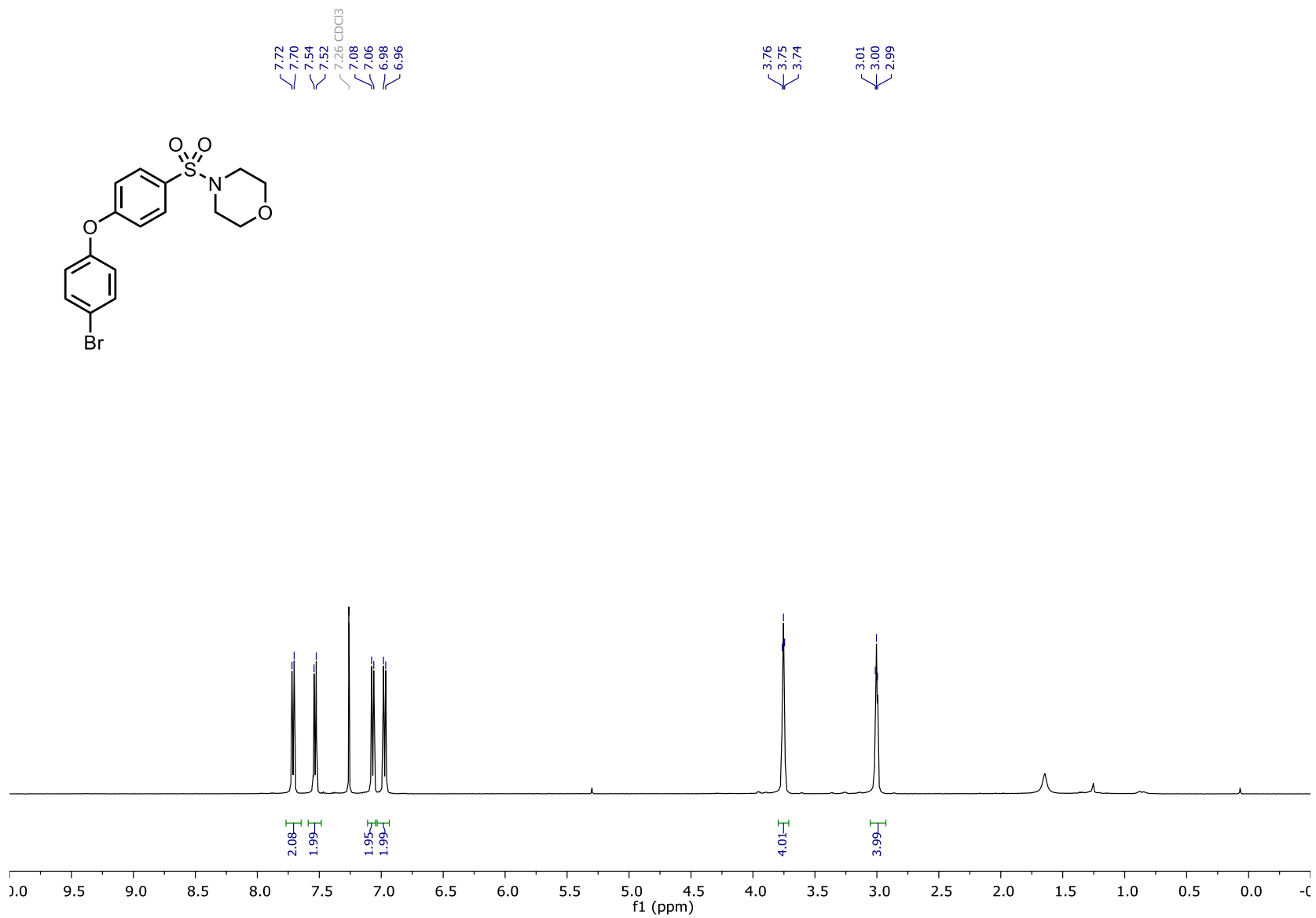
4-((5-((3s)-Adamantan-1-yl)-2-methylphenyl)sulfonyl)morpholine (11)**¹H NMR of 4-((5-((3s)-adamantan-1-yl)-2-methylphenyl)sulfonyl)morpholine (11)**CDCl₃, 500 MHz, 298 K

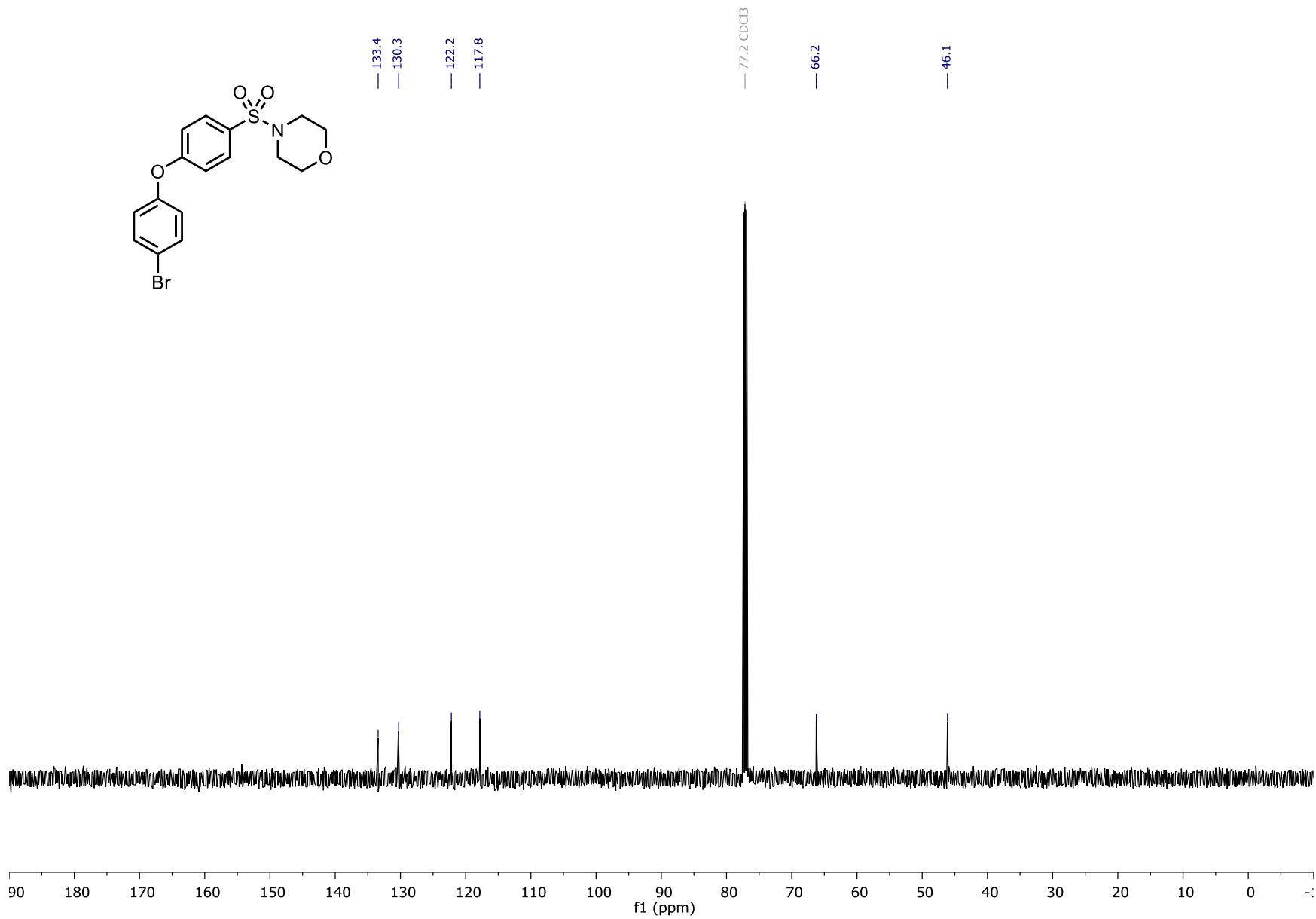
^{13}C NMR of 4-((5-((3s)-adamantan-1-yl)-2-methylphenyl)sulfonyl)morpholine (11)CDCl₃, 126 MHz, 298 K

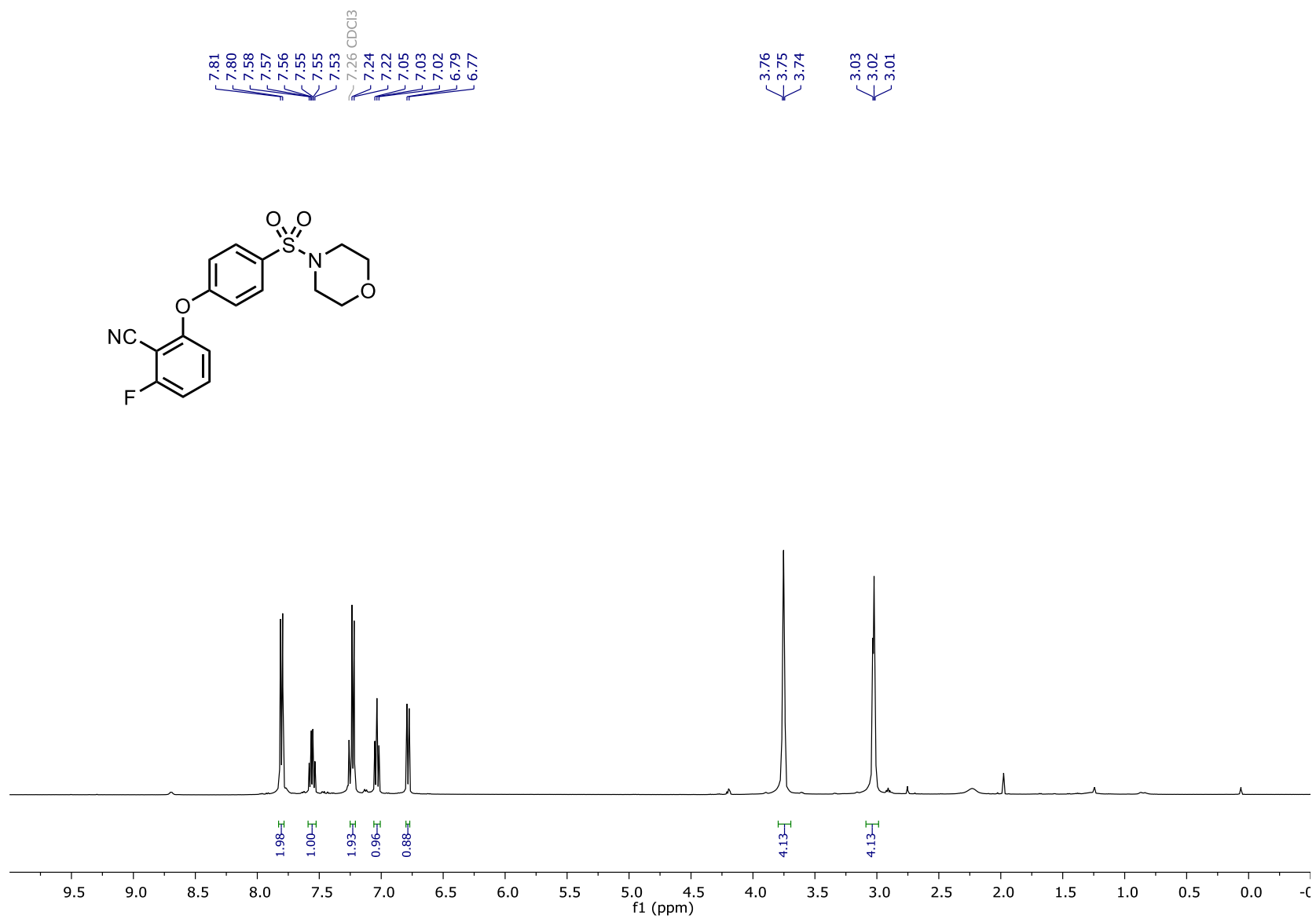
4'-(Morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12)**¹H NMR of 4'-(morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12)**CDCl₃, 500 MHz, 298 K

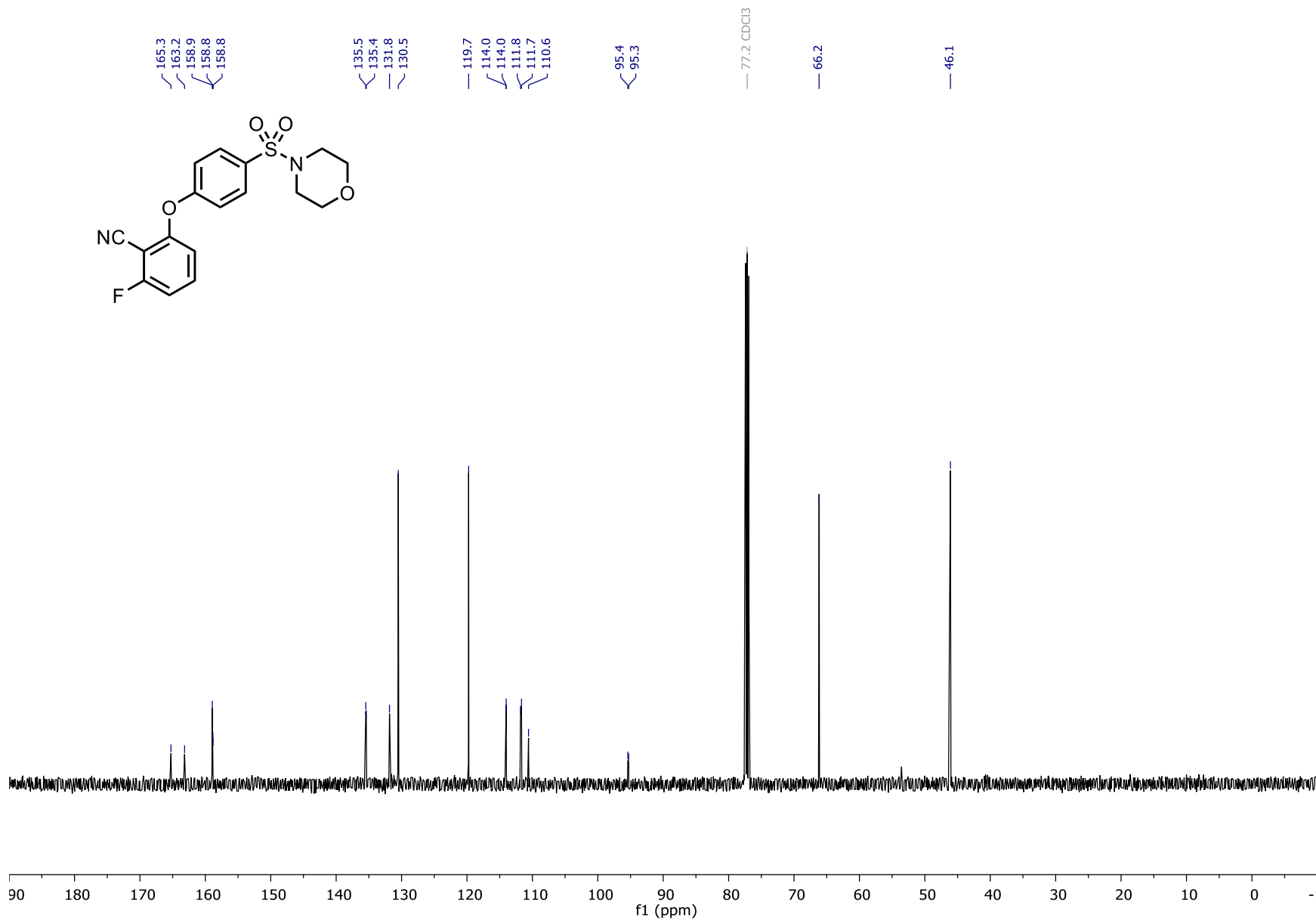
^{13}C NMR of 4'-(morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12)CDCl₃, 126 MHz, 298 K

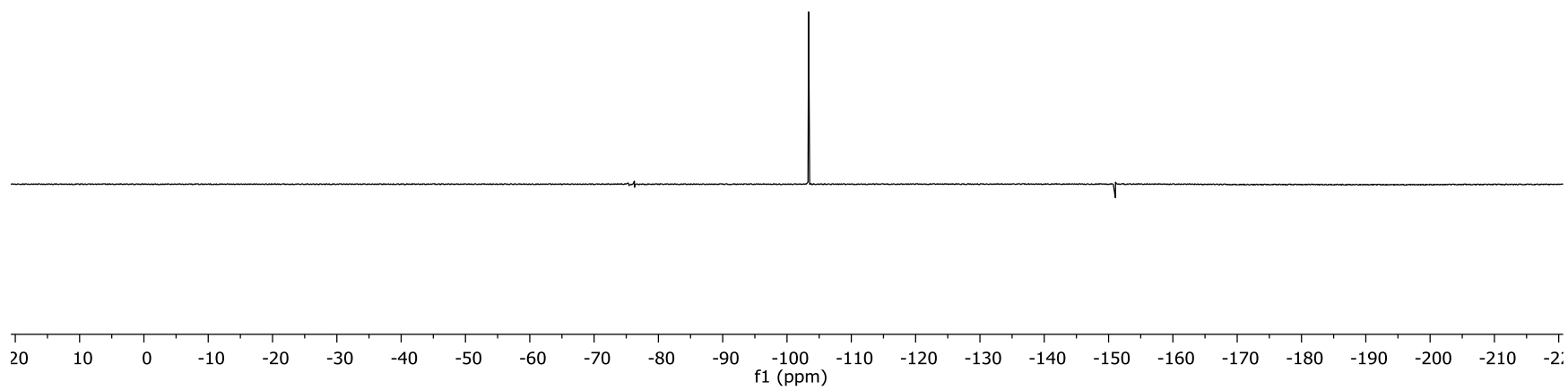
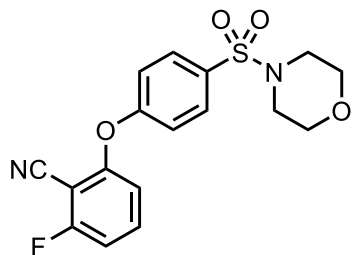
¹⁹F NMR of 4'-(morpholinosulfonyl)-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (12)CD₃Cl, 471 MHz, 298 K

4-((4-(4-Bromophenoxy)phenyl)sulfonyl)morpholine (13)**¹H NMR of 4-((4-(4-bromophenoxy)phenyl)sulfonyl)morpholine (13)**CDCl₃, 500 MHz, 298 K

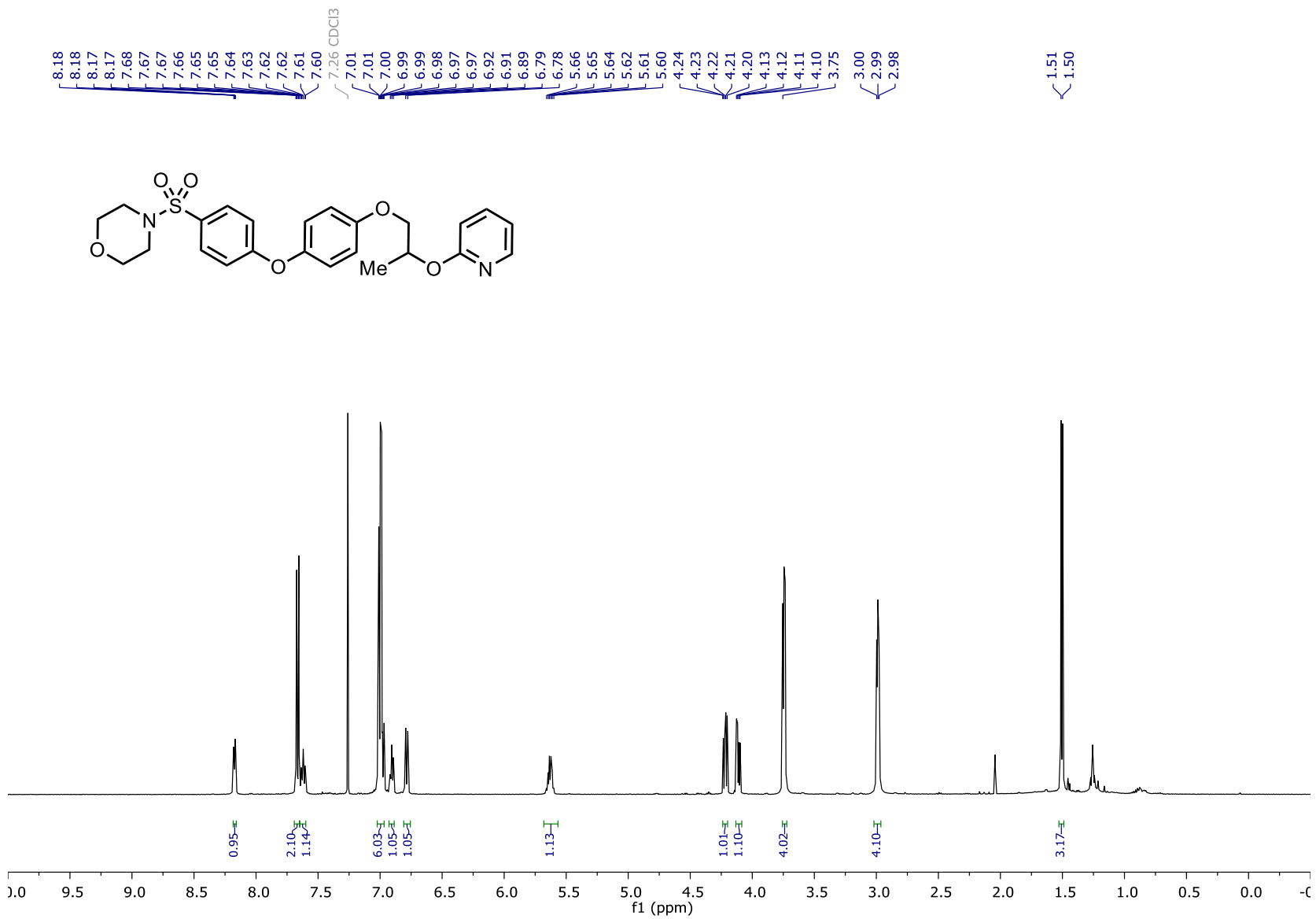
^{13}C NMR of 4-((4-(4-bromophenoxy)phenyl)sulfonyl)morpholine (13)CDCl₃, 126 MHz, 298 K

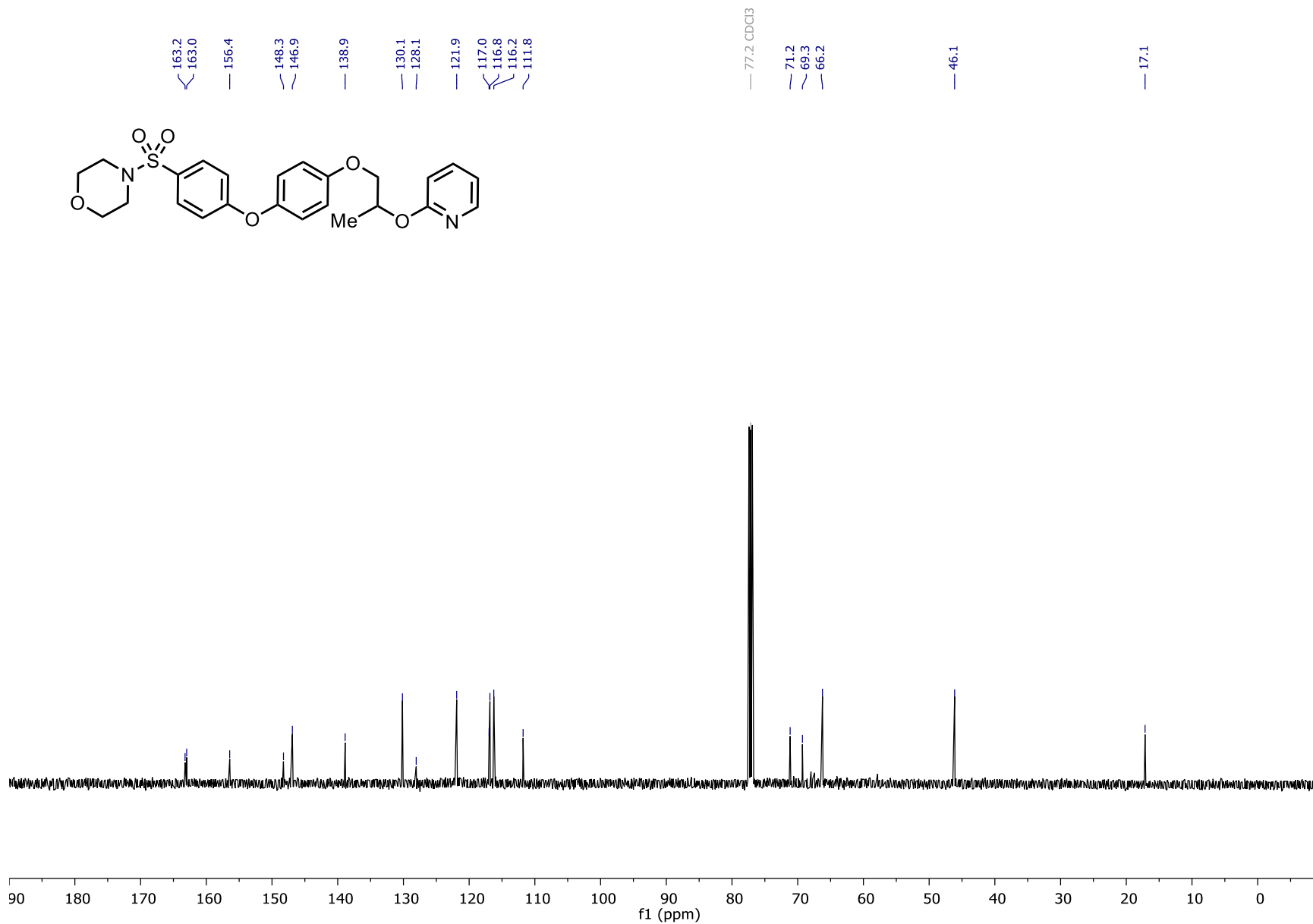
2-Fluoro-6-(4-(morpholinosulfonyl)phenoxy)benzonitrile (14)**¹H NMR of 2-fluoro-6-(4-(morpholinosulfonyl)phenoxy)benzonitrile (14)**CDCl₃, 500 MHz, 298 K

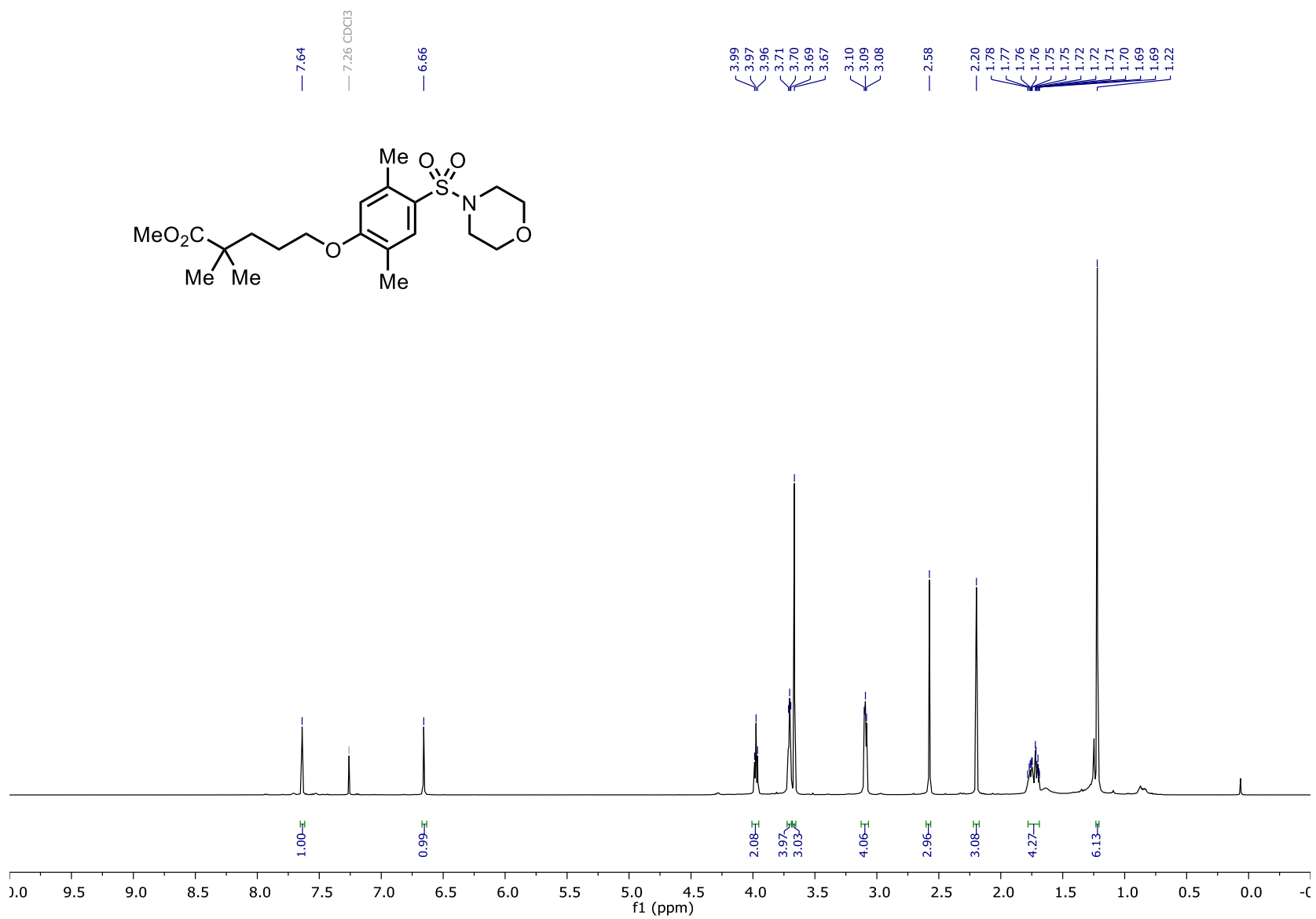
¹³C NMR of 2-fluoro-6-(4-(morpholinosulfonyl)phenoxy)benzonitrile (14)CDCl₃, 126 MHz, 298 K

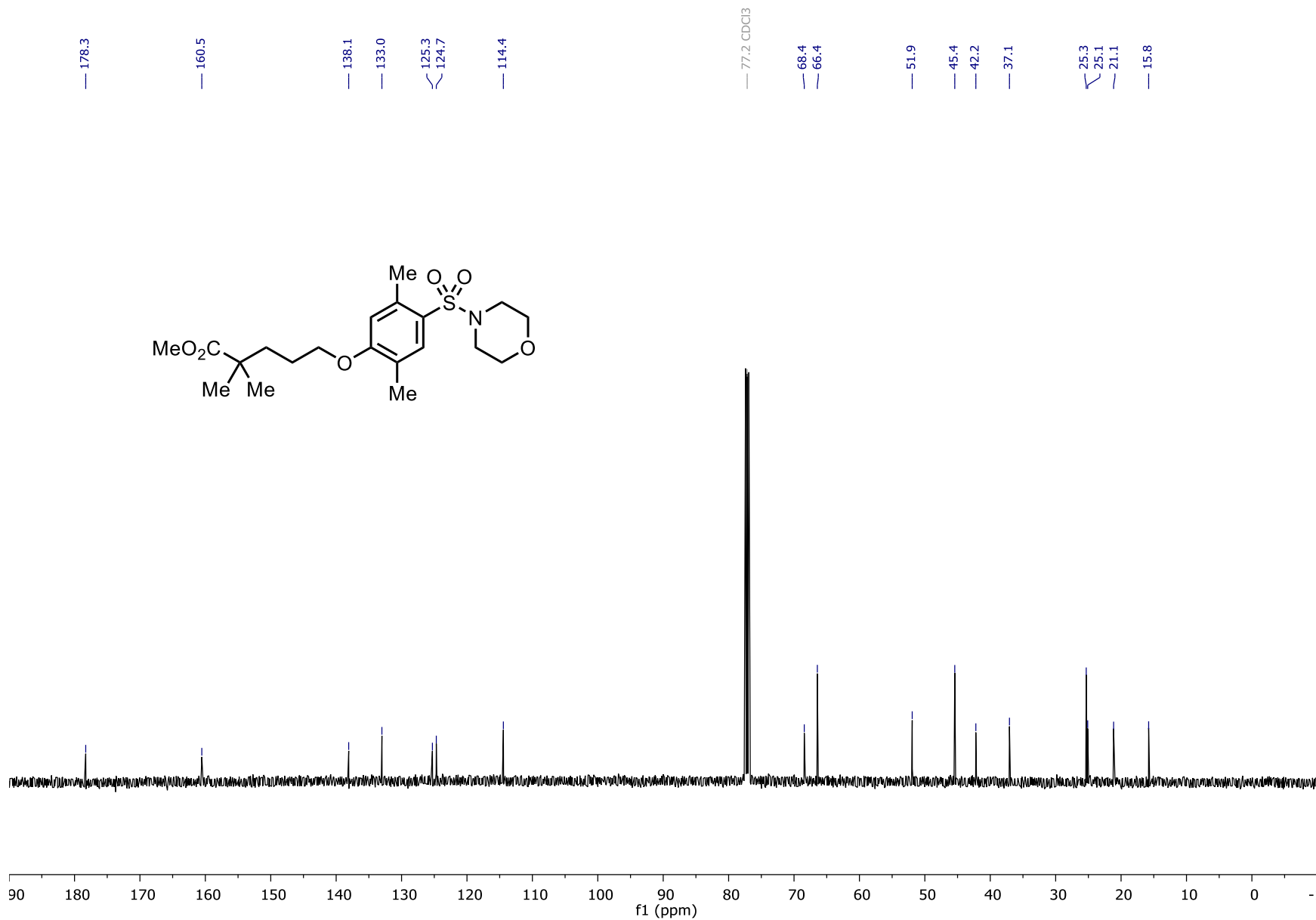
^{19}F NMR of 2-fluoro-6-(4-(morpholinylsulfonyl)phenoxy)benzonitrile (14)CDCl₃, 471 MHz, 298 K

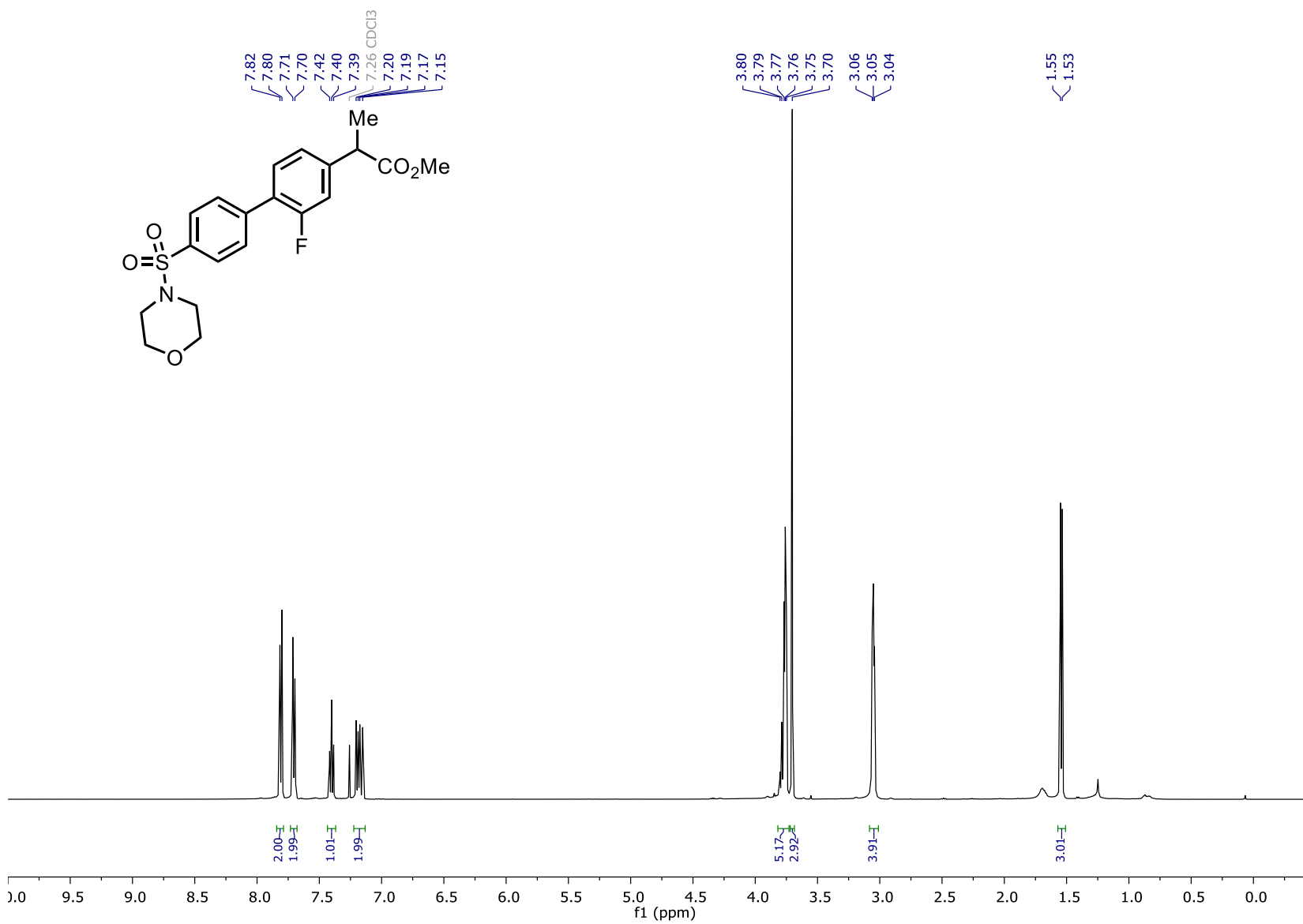
Pyriproxyfen morpholine sulfonamide derivative (15)

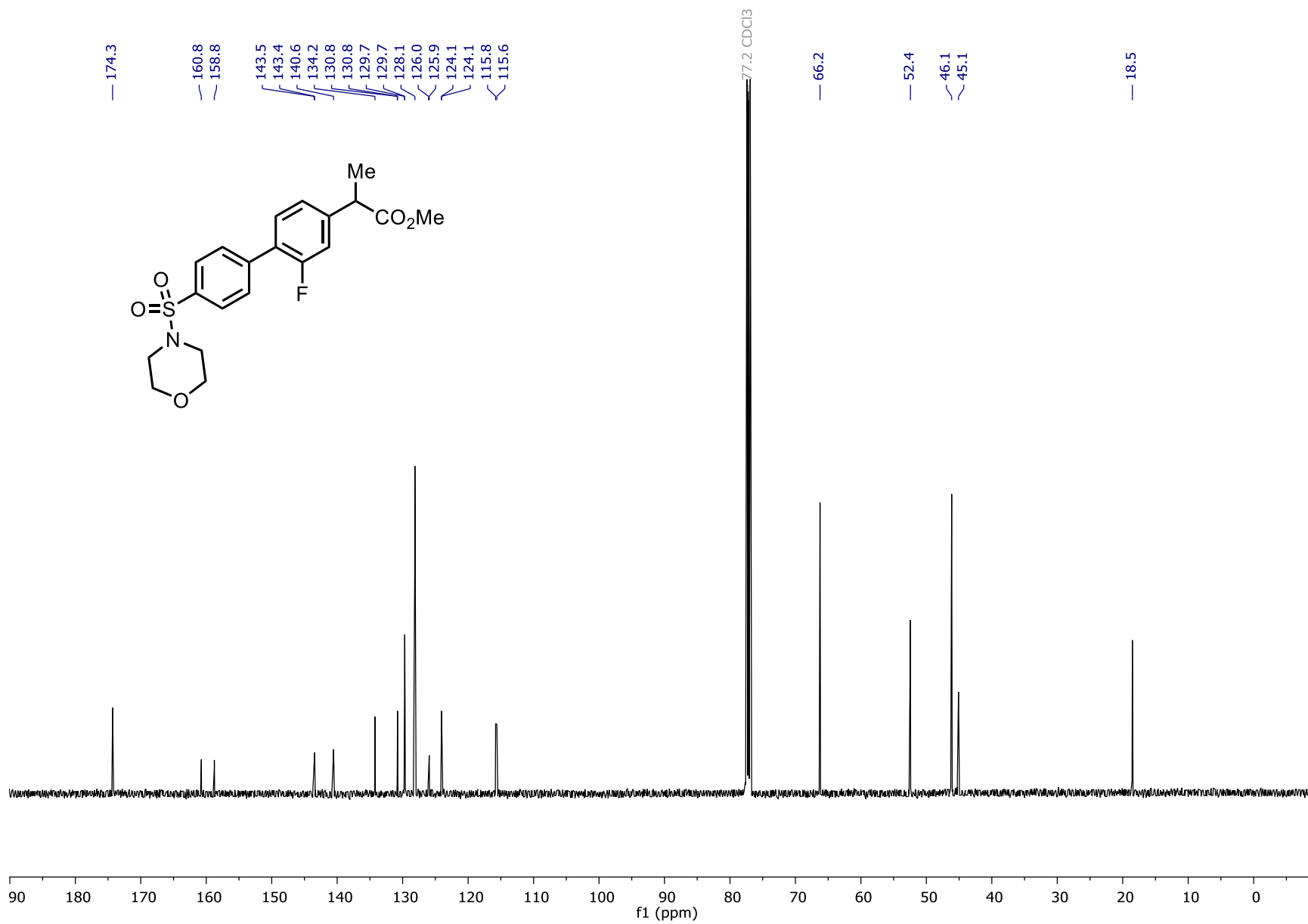
¹H NMR of pyriproxyfen morpholine sulfonamide derivative (15)CDCl₃, 500 MHz, 298 K

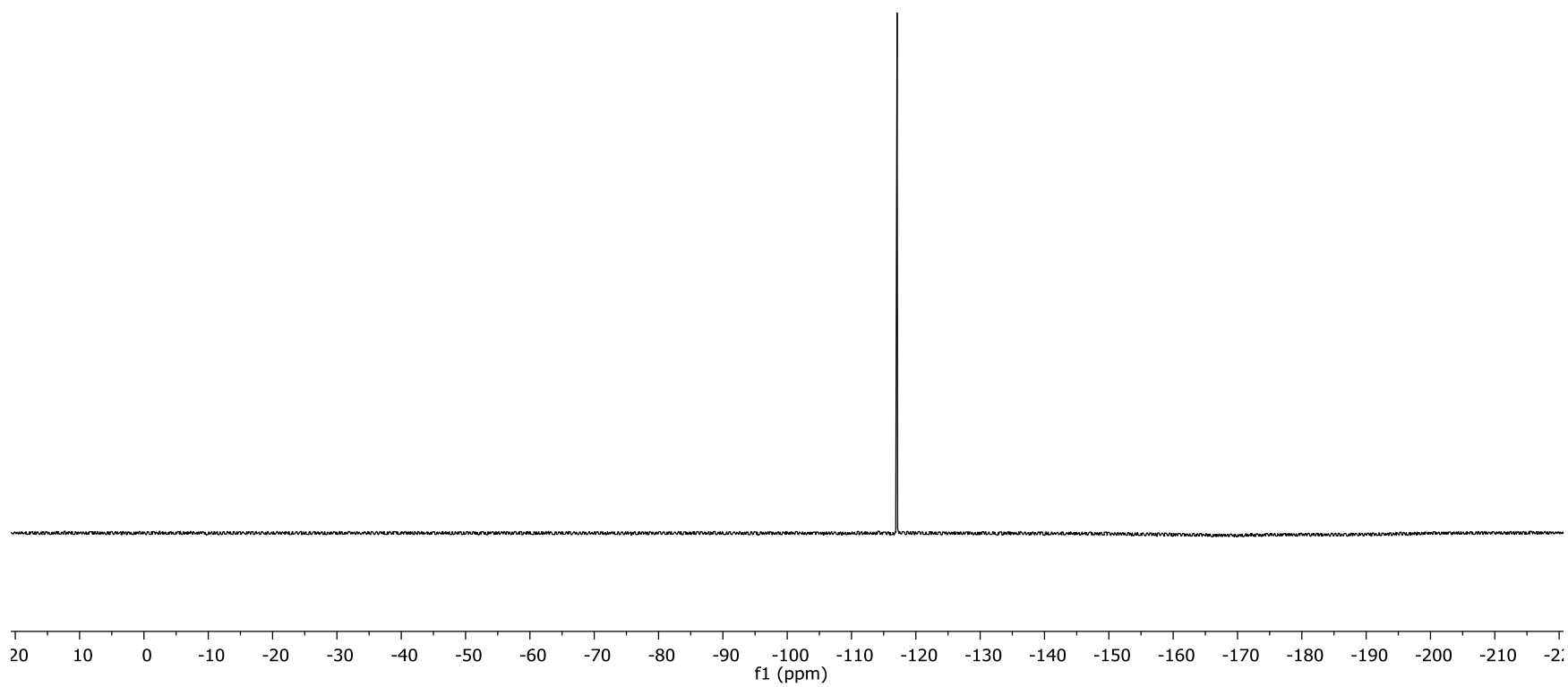
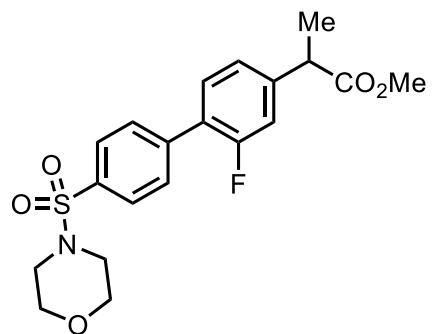
¹³C NMR of pyriproxyfen morpholine sulfonamide derivative (15)CDCl₃, 126 MHz, 298 K

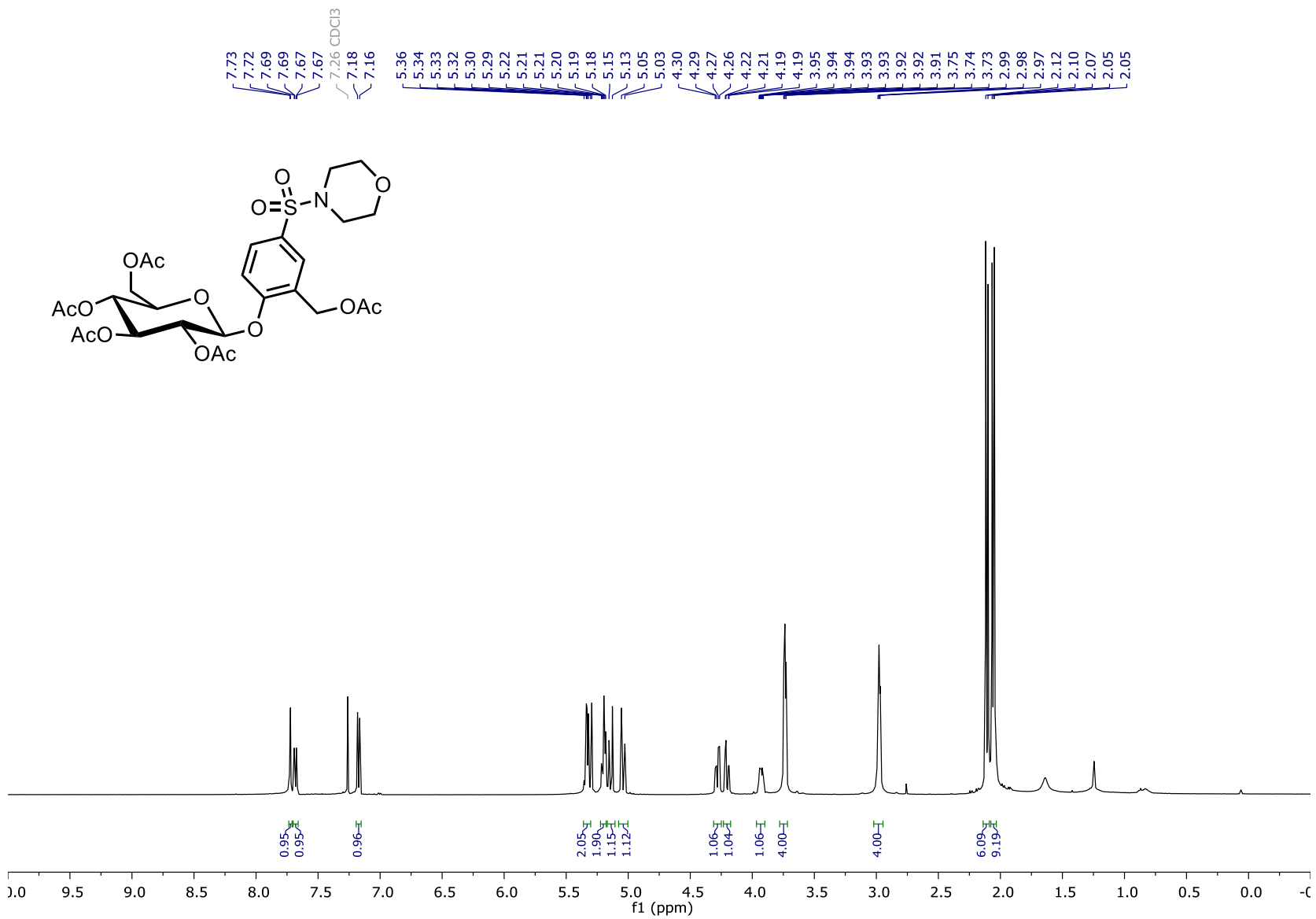
Gemfibrozil methyl ester morpholine sulfonamide derivative (16)**¹H NMR gemfibrozil methyl ester morpholine sulfonamide derivative (16)**CDCl₃, 500 MHz, 298 K

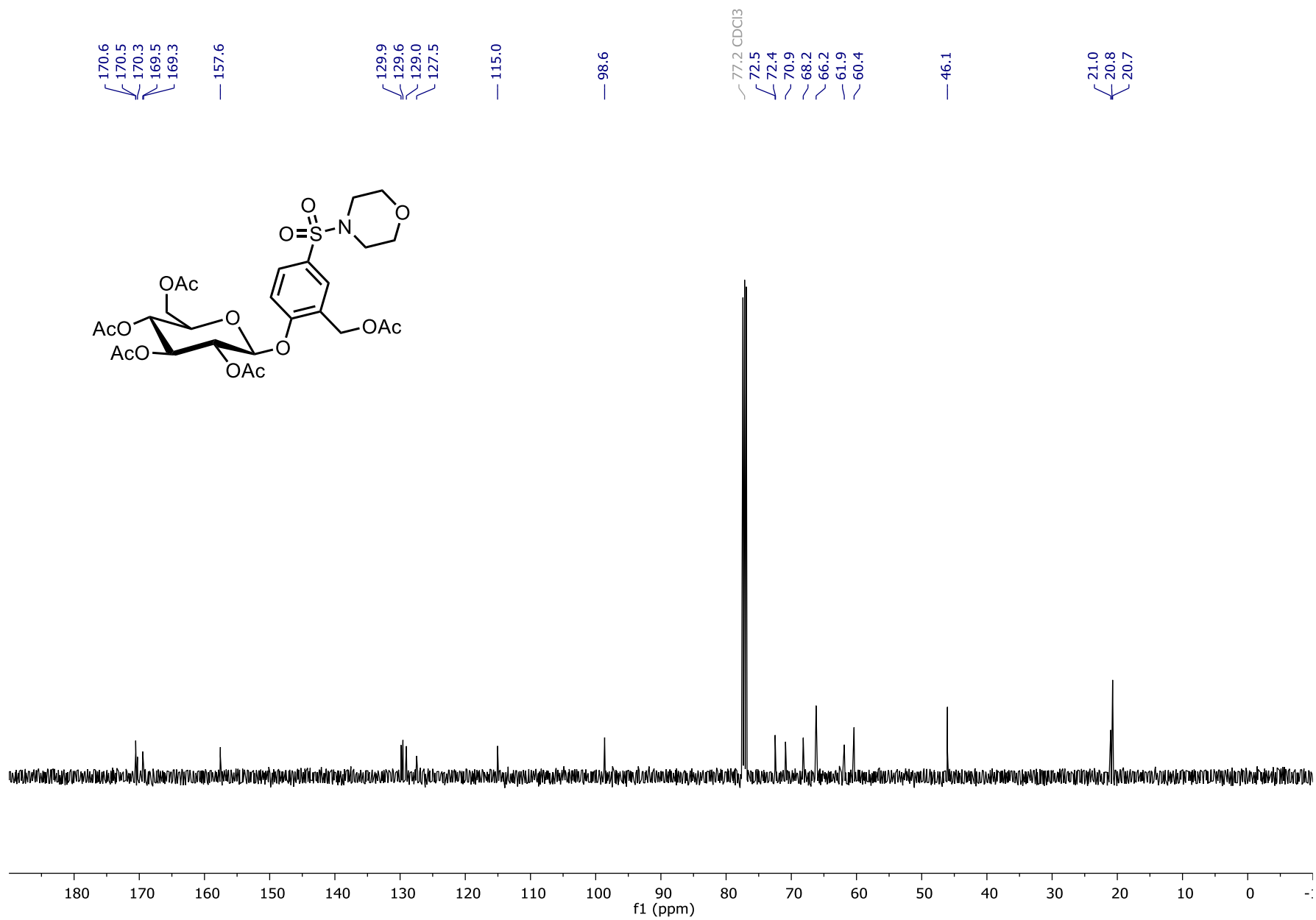
^{13}C NMR of gemfibrozil methyl ester morpholine sulfonamide derivative (16)CDCl₃, 126 MHz, 298 K

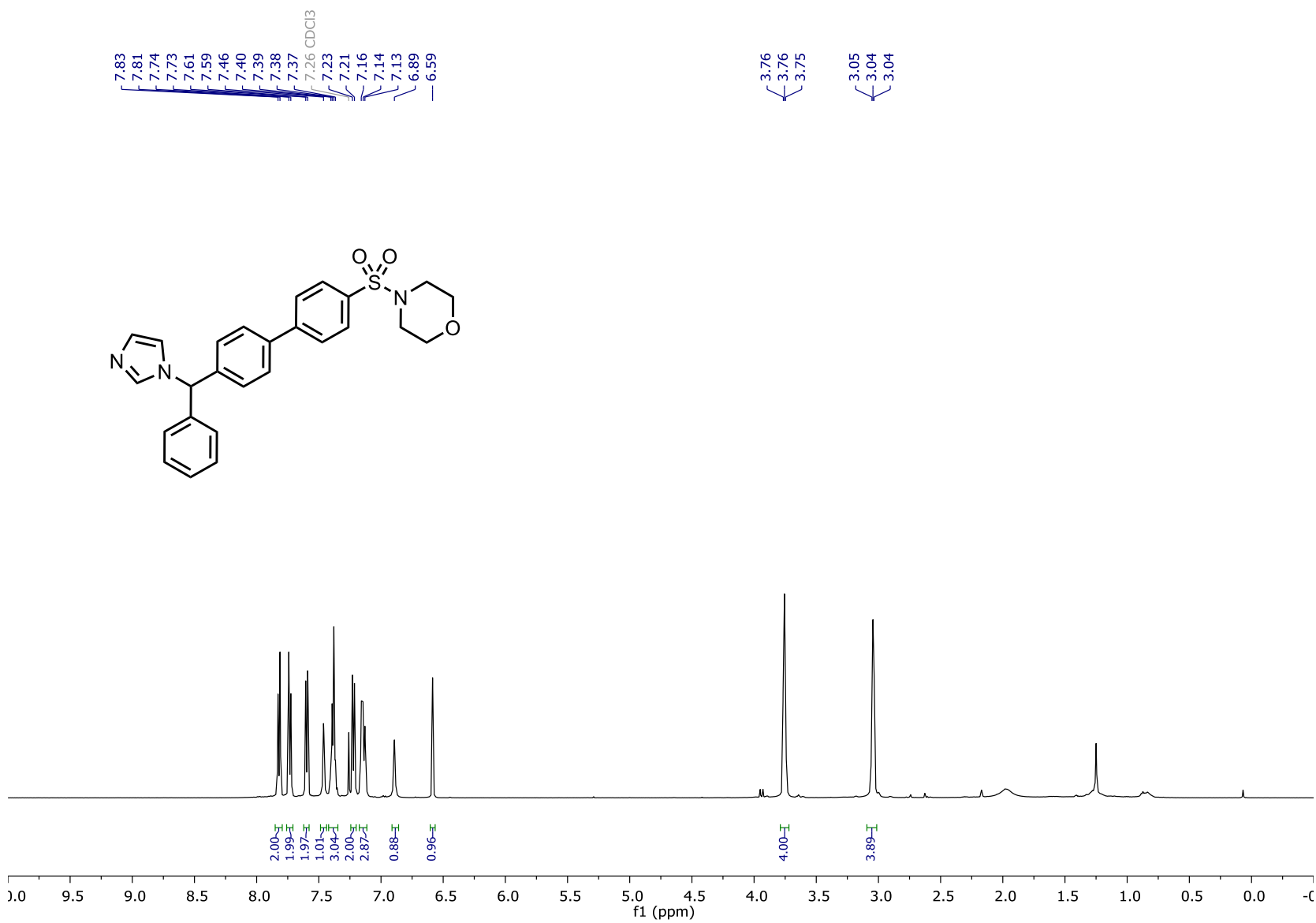
Flurbiprofen methyl ester morpholine sulfonamide derivative (17)**¹H NMR of flurbiprofen methyl ester morpholine sulfonamide derivative (17)**CDCl₃, 500 MHz, 298 K

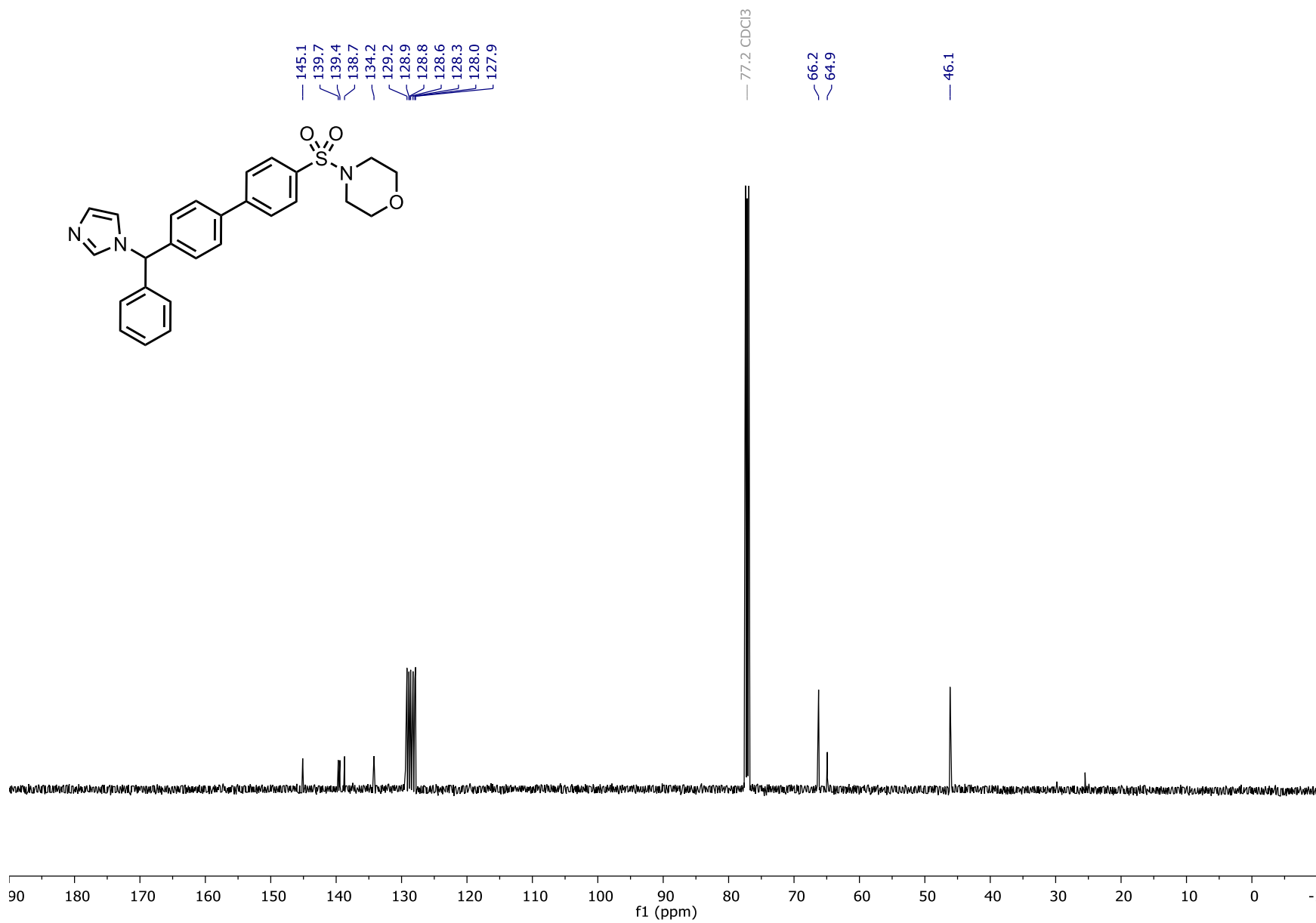
^{13}C NMR of flurbiprofen methyl ester morpholine sulfonamide derivative (17)CDCl₃, 126 MHz, 298 K

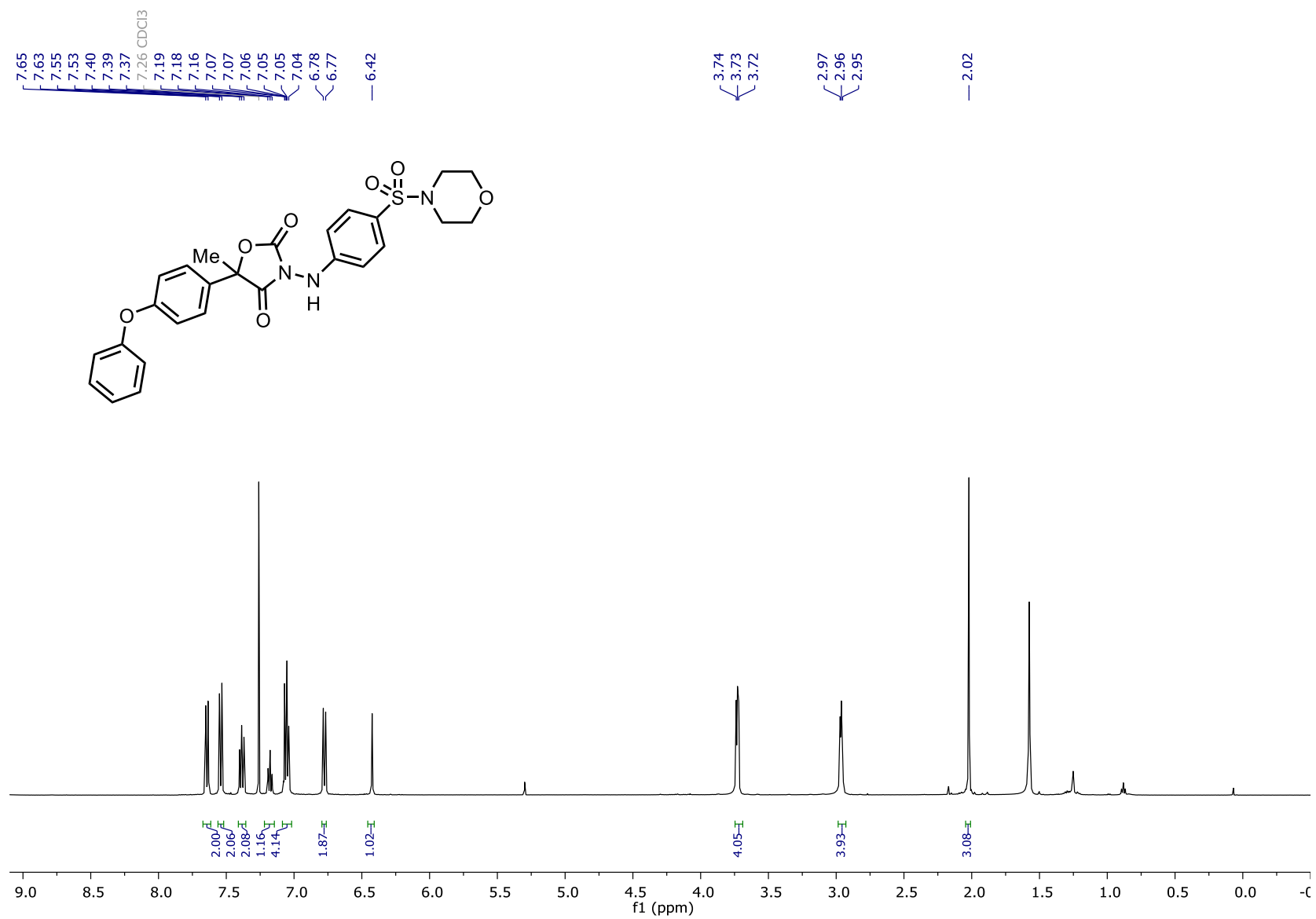
^{19}F NMR of flurbiprofen methyl ester morpholine sulfonamide derivative (17)CDCl₃, 471 MHz, 298 K

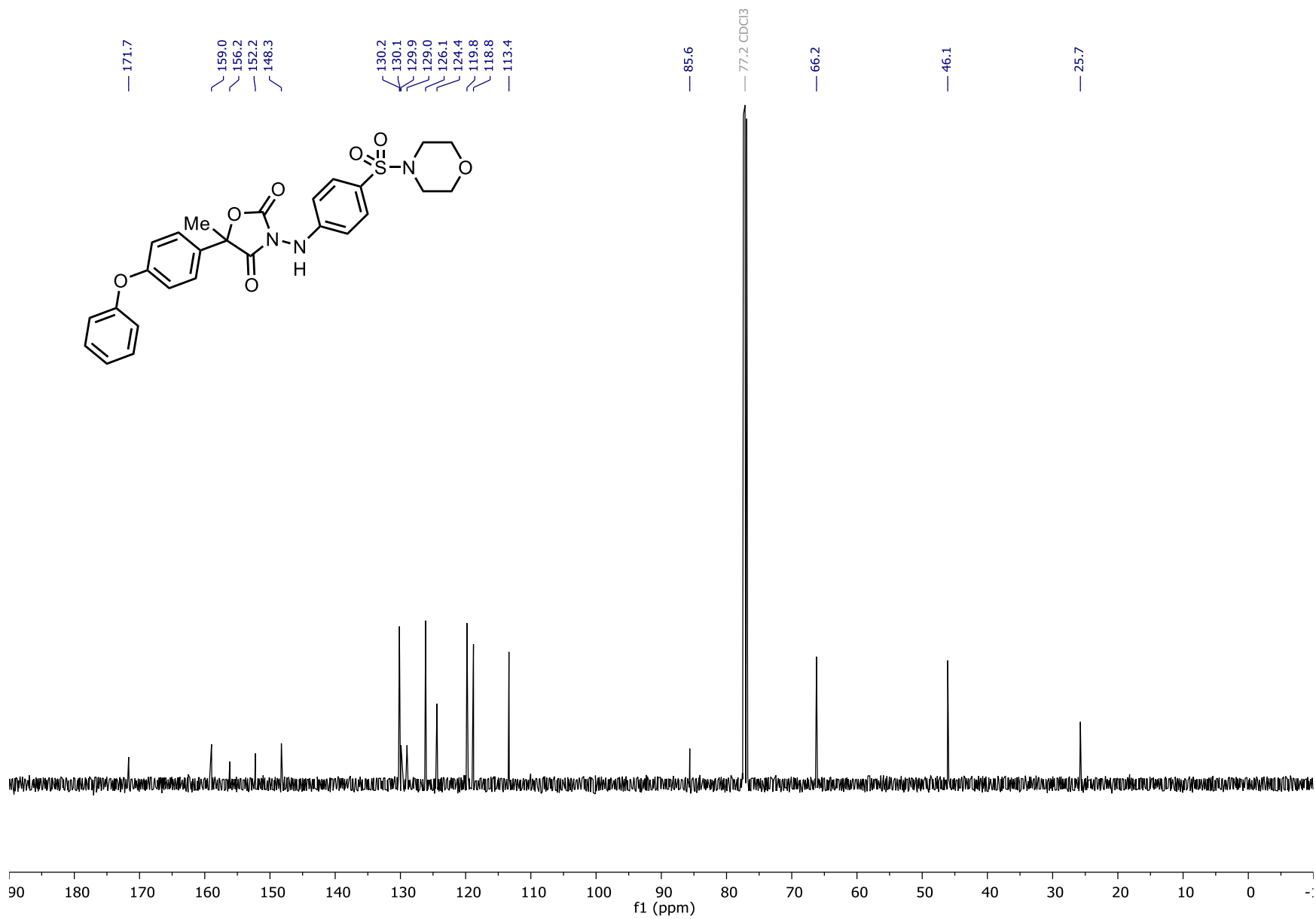
Salicin pentaacetate morpholine sulfonamide derivative (18)**¹H NMR of salicin pentaacetate morpholine sulfonamide derivative (18)**CDCl₃, 500 MHz, 298 K

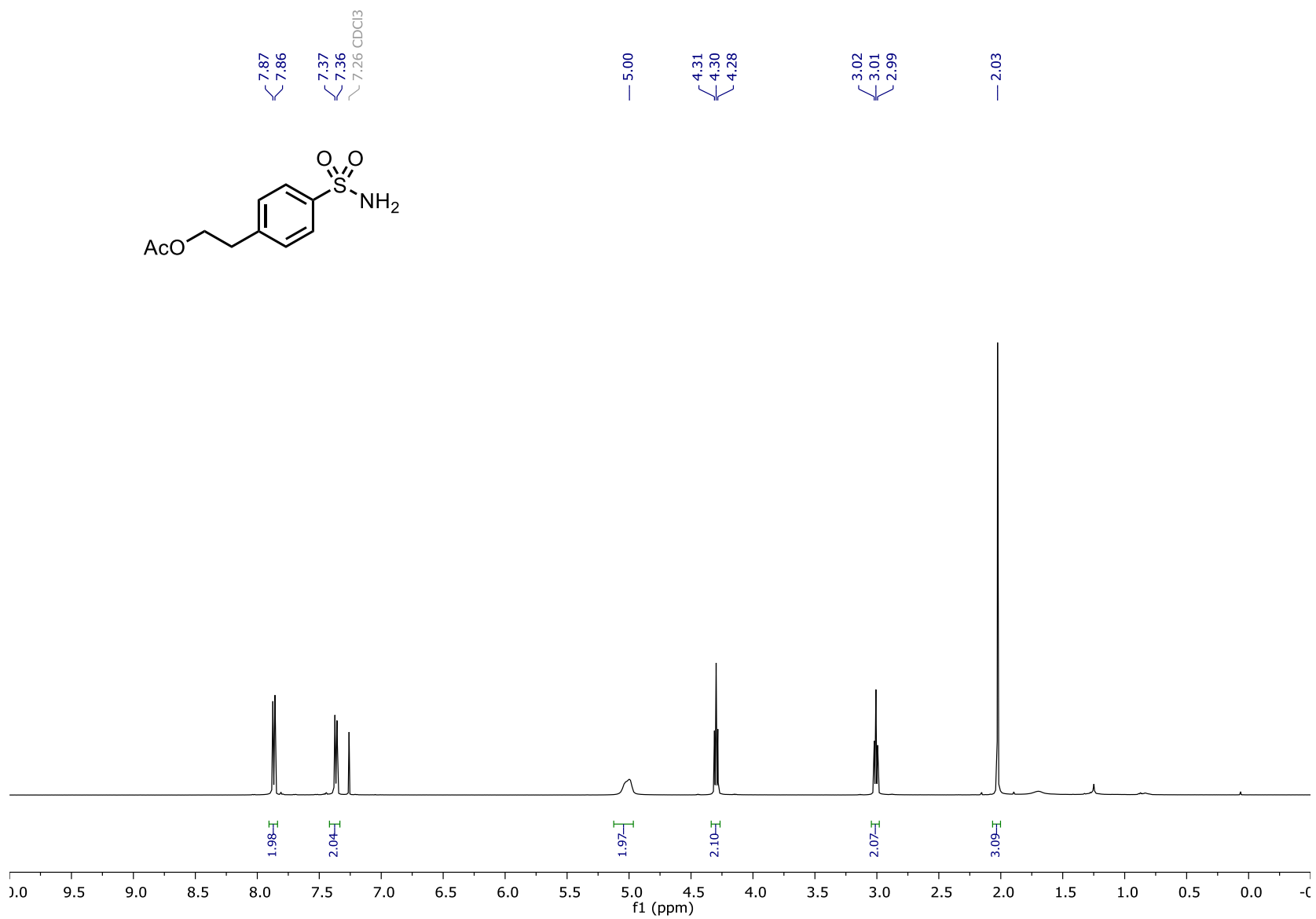
¹³C NMR of salicin pentaacetate morpholine sulfonamide derivative (18)CDCl₃, 126 MHz, 298 K

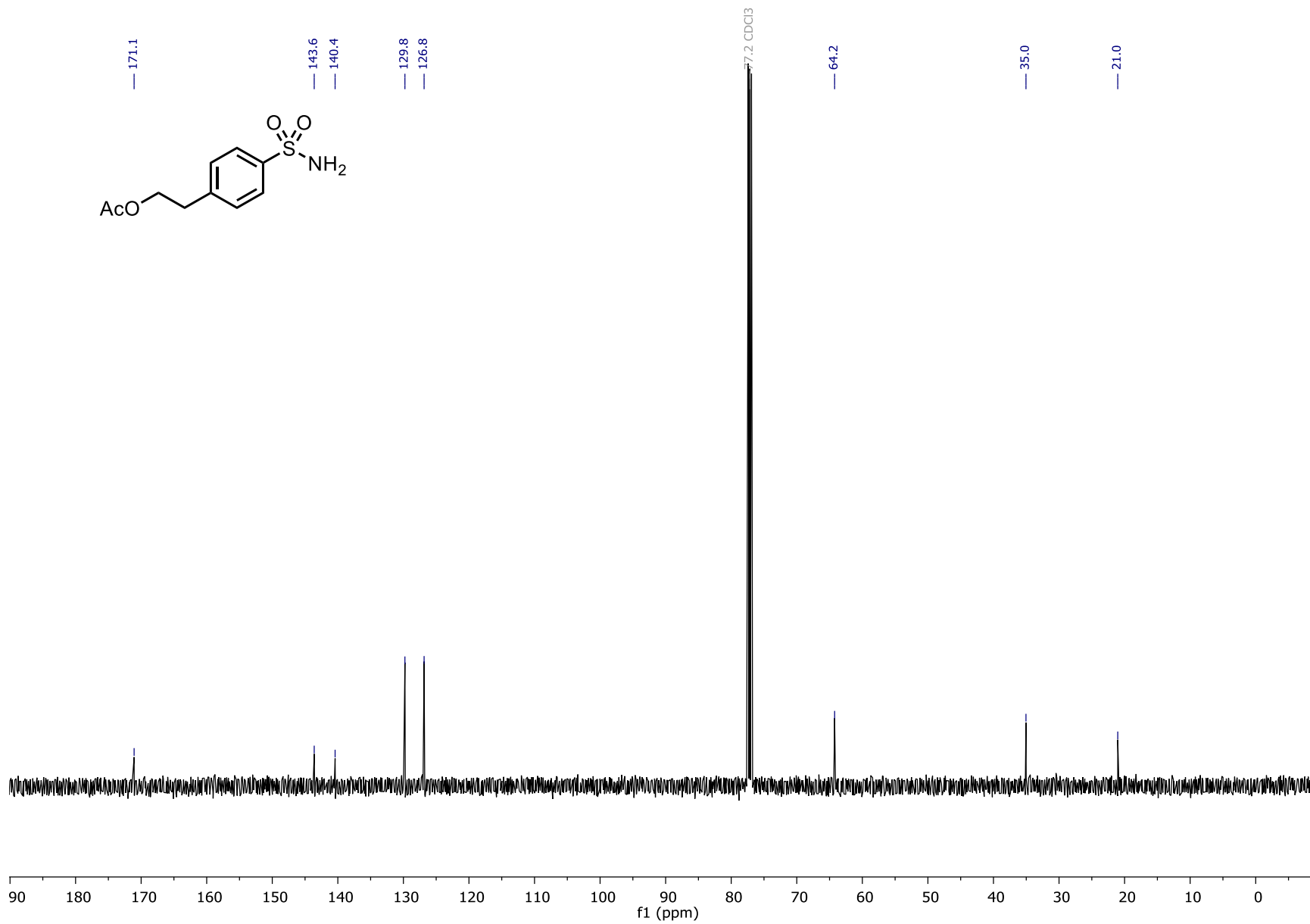
Bifonazole morpholine sulfonamide derivative (19)**¹H NMR of bifonazole morpholine sulfonamide derivative (19)**CDCl₃, 500 MHz, 298 K

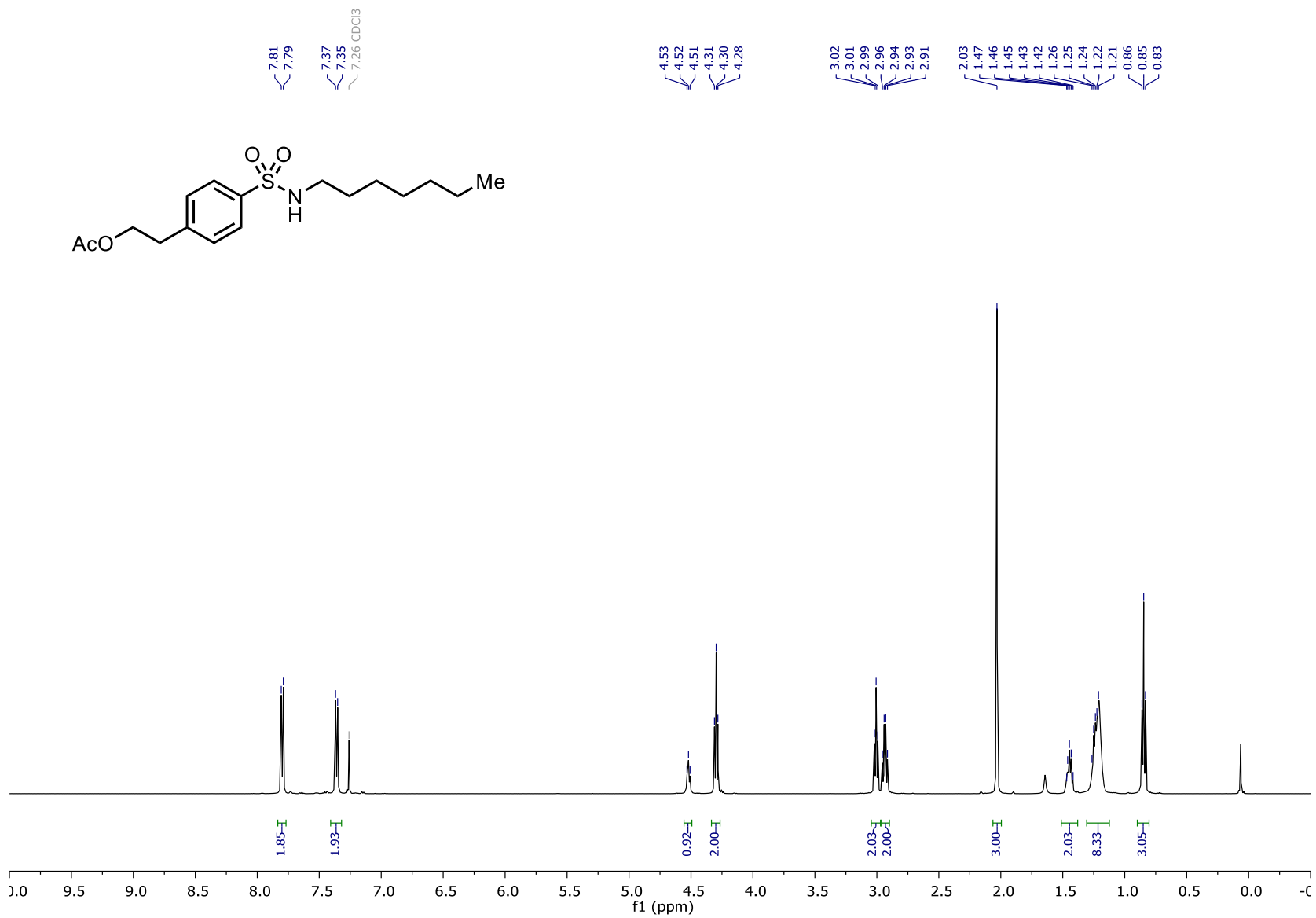
¹³C NMR of bifonazole morpholine sulfonamide derivative (19)CDCl₃, 126 MHz, 298 K

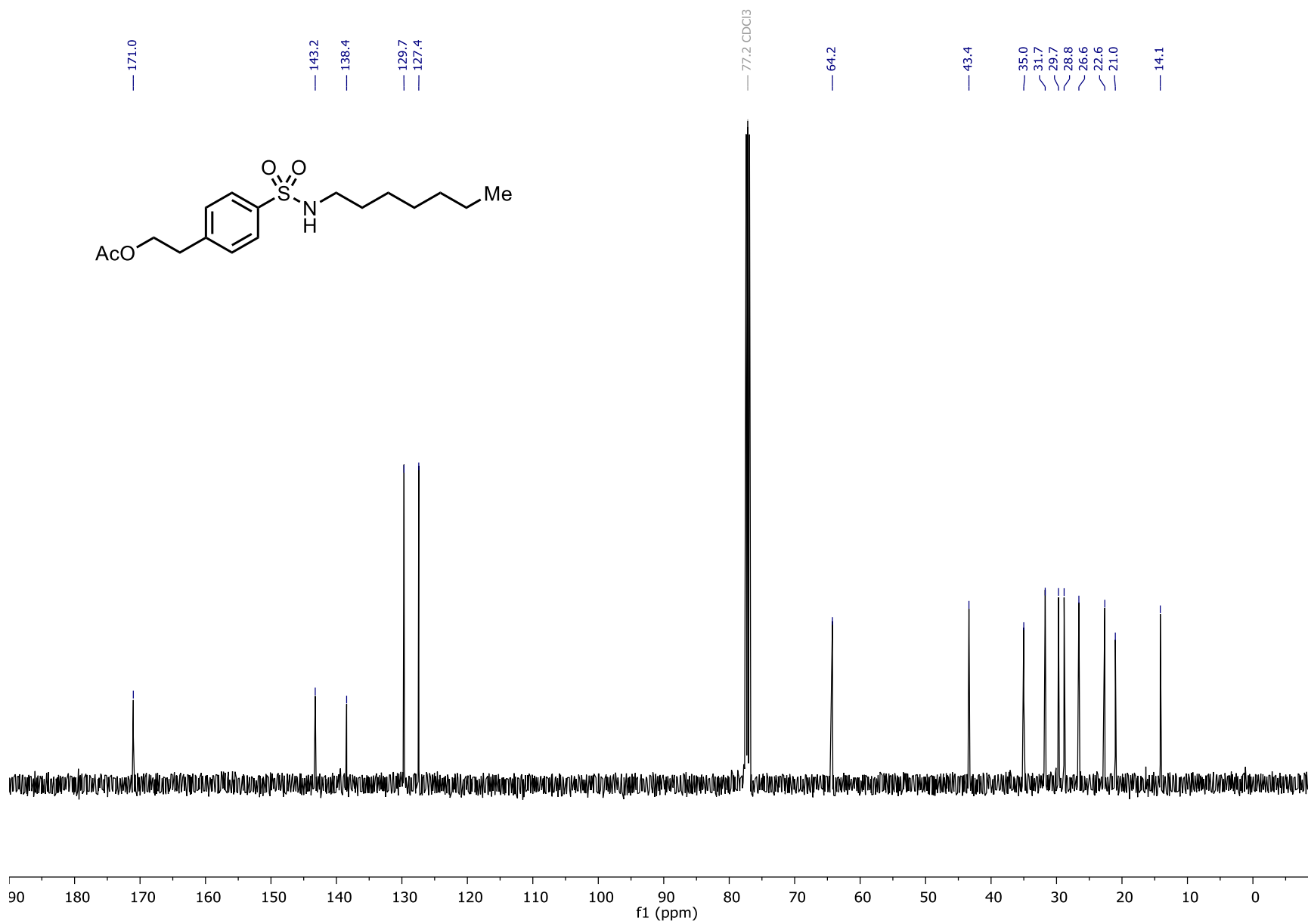
Famoxadone morpholine sulfonamide derivative (20)**¹H NMR of famoxadone morpholine sulfonamide derivative (20)**CDCl₃, 500 MHz, 298 K

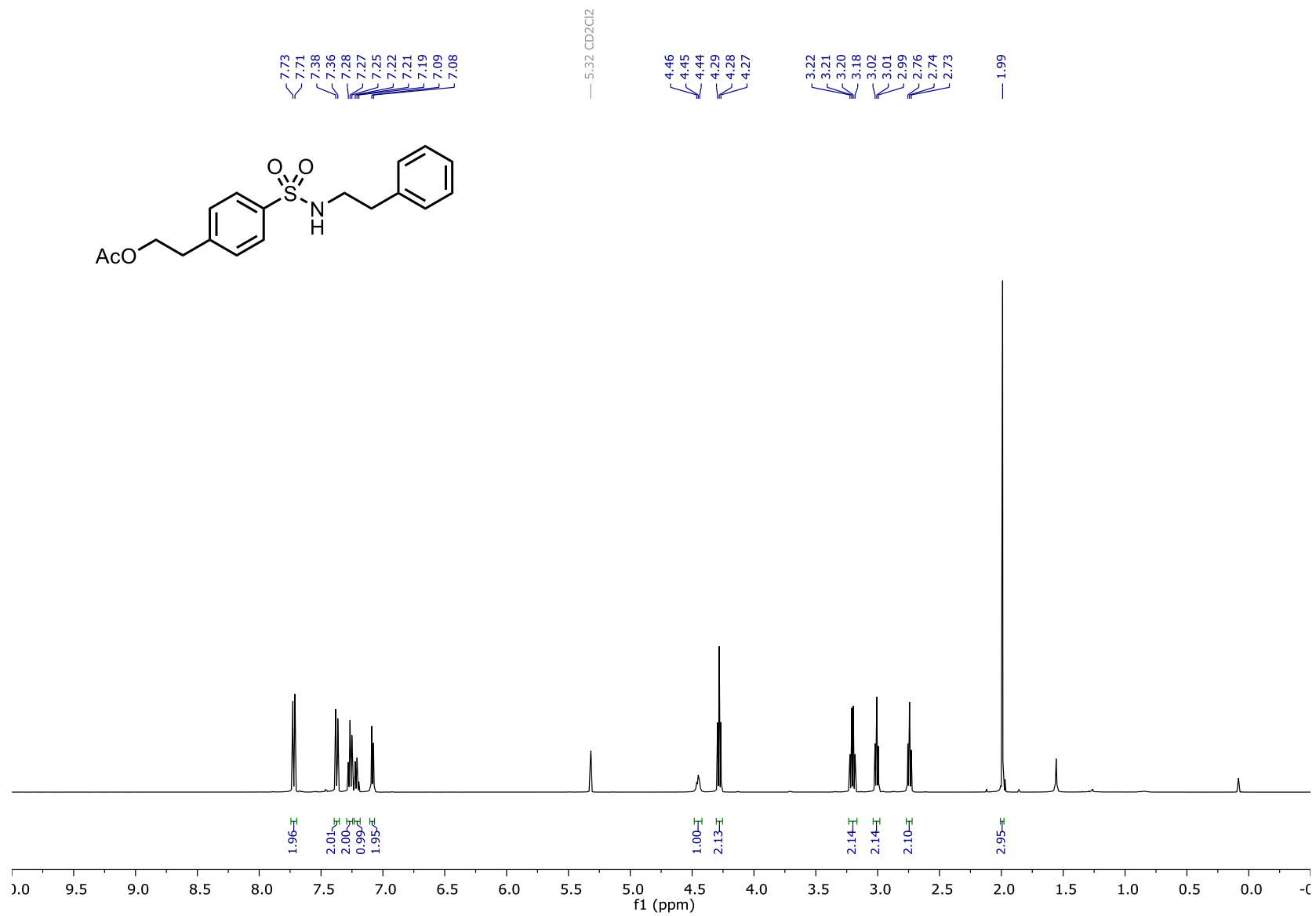
¹³C NMR of famoxadone morpholine sulfonamide derivative (20)CDCl₃, 126 MHz, 298 K

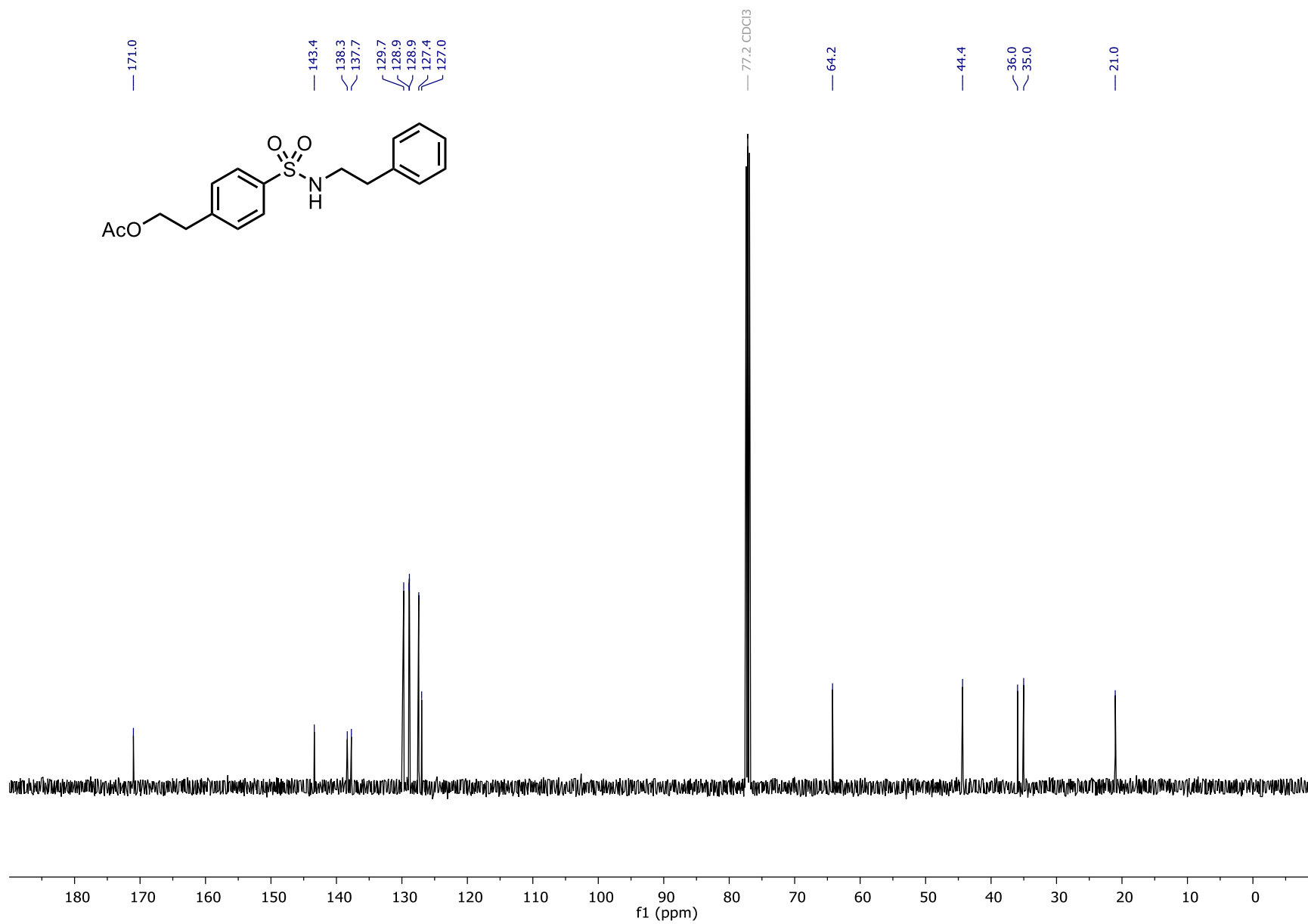
4-Sulfamoylphenethyl acetate (21)**¹H NMR of 4-sulfamoylphenethyl acetate (21)**CDCl₃, 500 MHz, 298 K

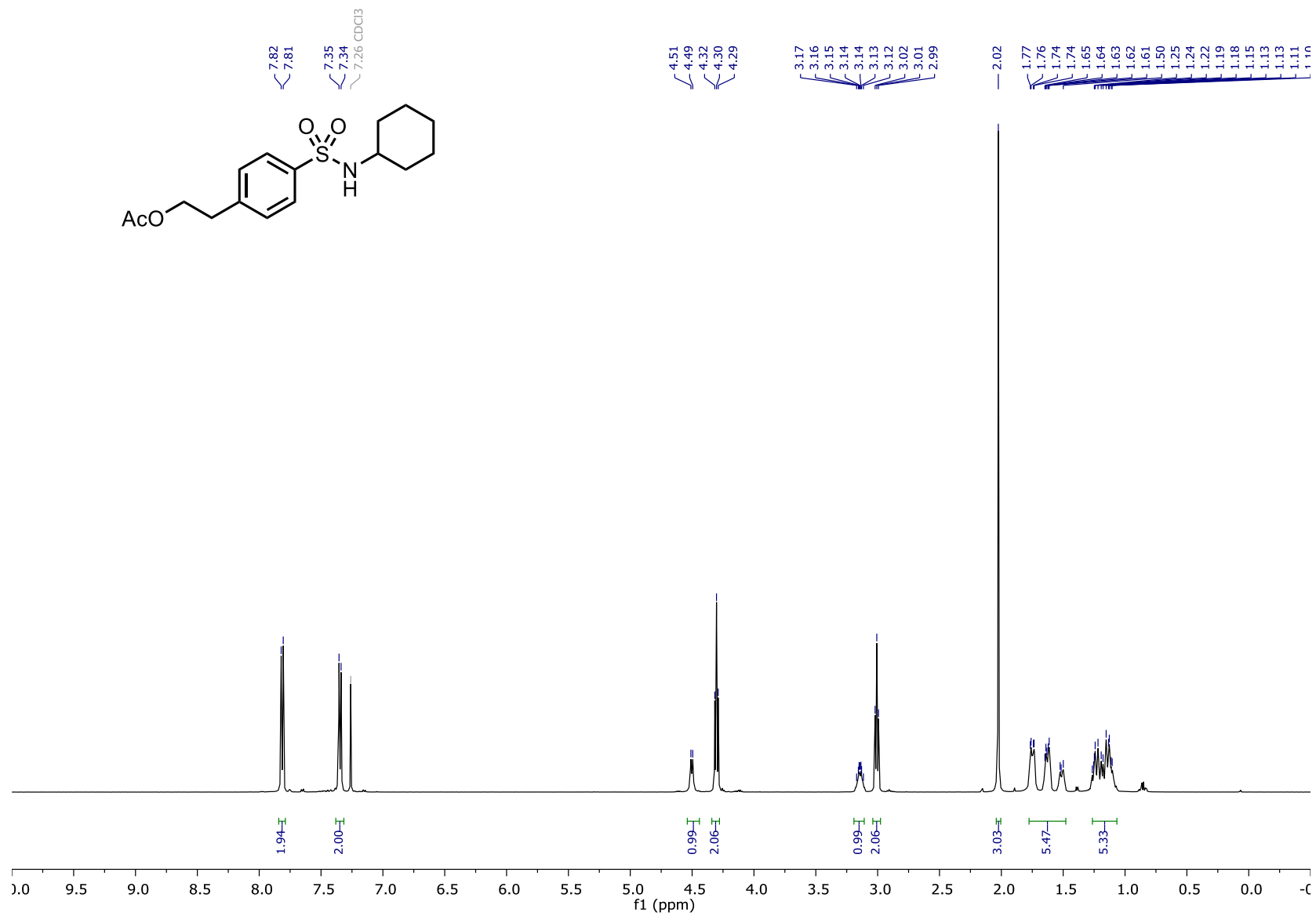
^{13}C NMR of 4-sulfamoylphenethyl acetate (21)CDCl₃, 126 MHz, 298 K

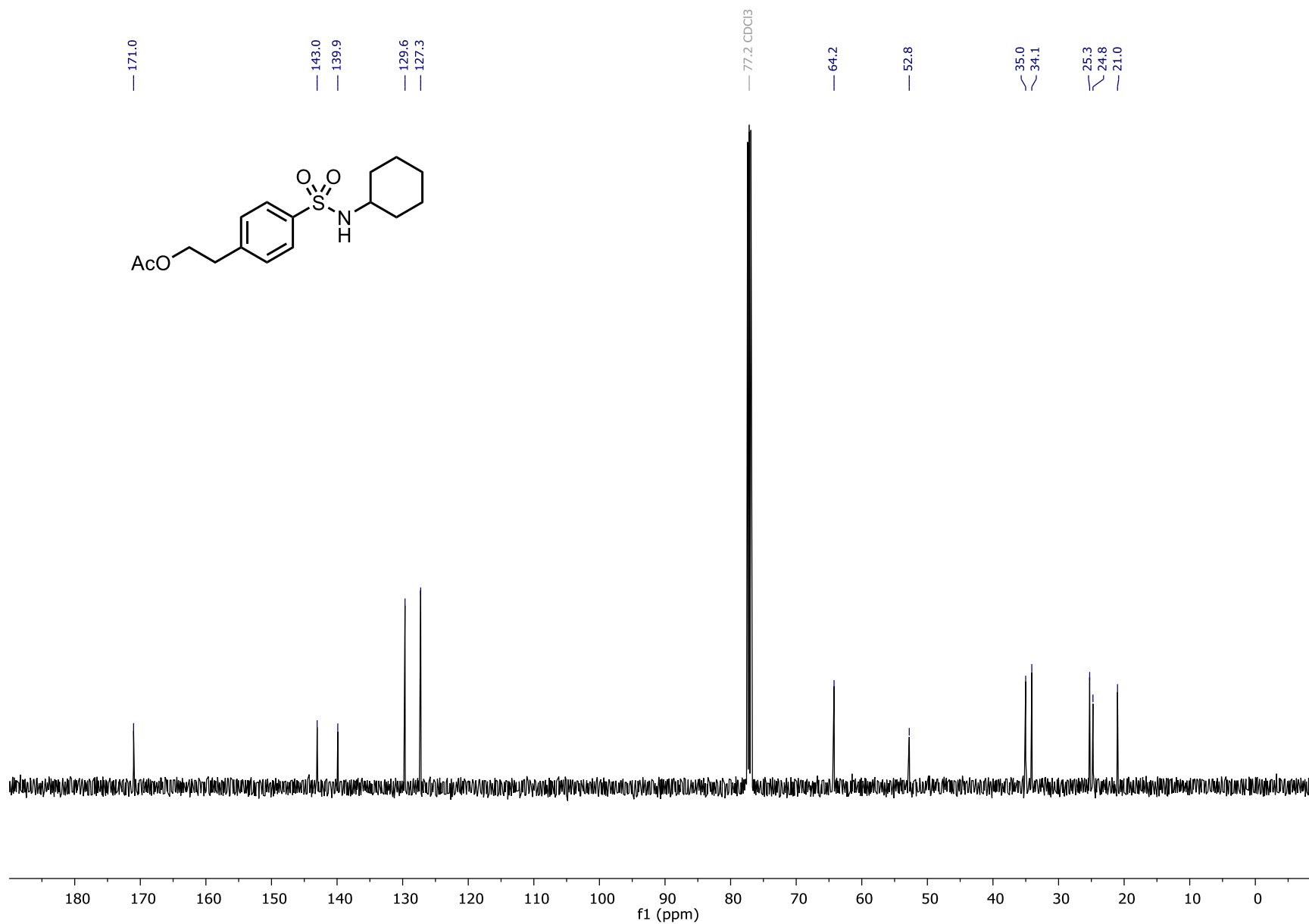
4-(N-Heptylsulfamoyl)phenethyl acetate (22)**¹H NMR of 4-(N-heptylsulfamoyl)phenethyl acetate (22)**CDCl₃, 500 MHz, 298 K

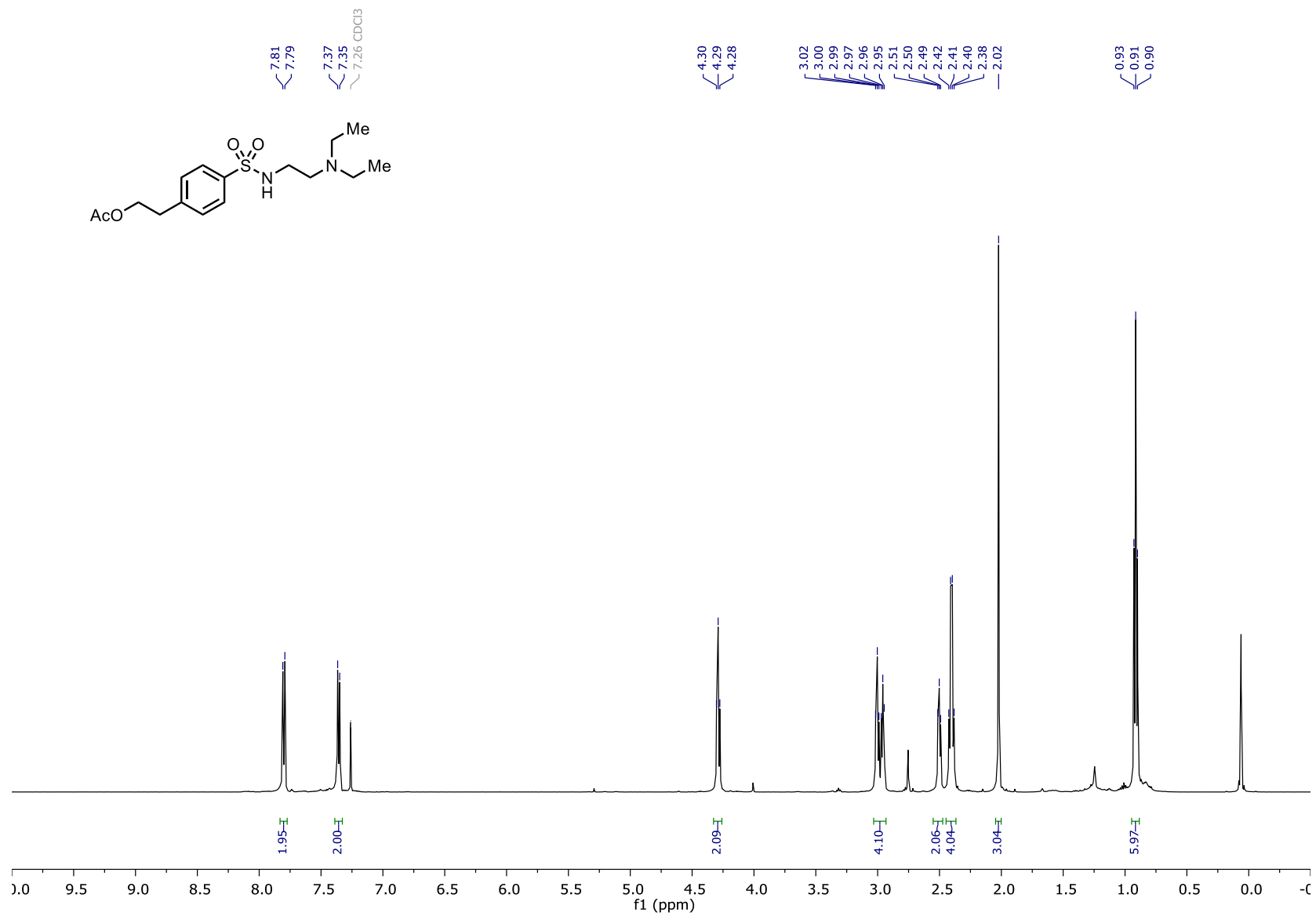
^{13}C NMR of 4-(N-heptylsulfamoyl)phenethyl acetate (22)CDCl₃, 126 MHz, 298 K

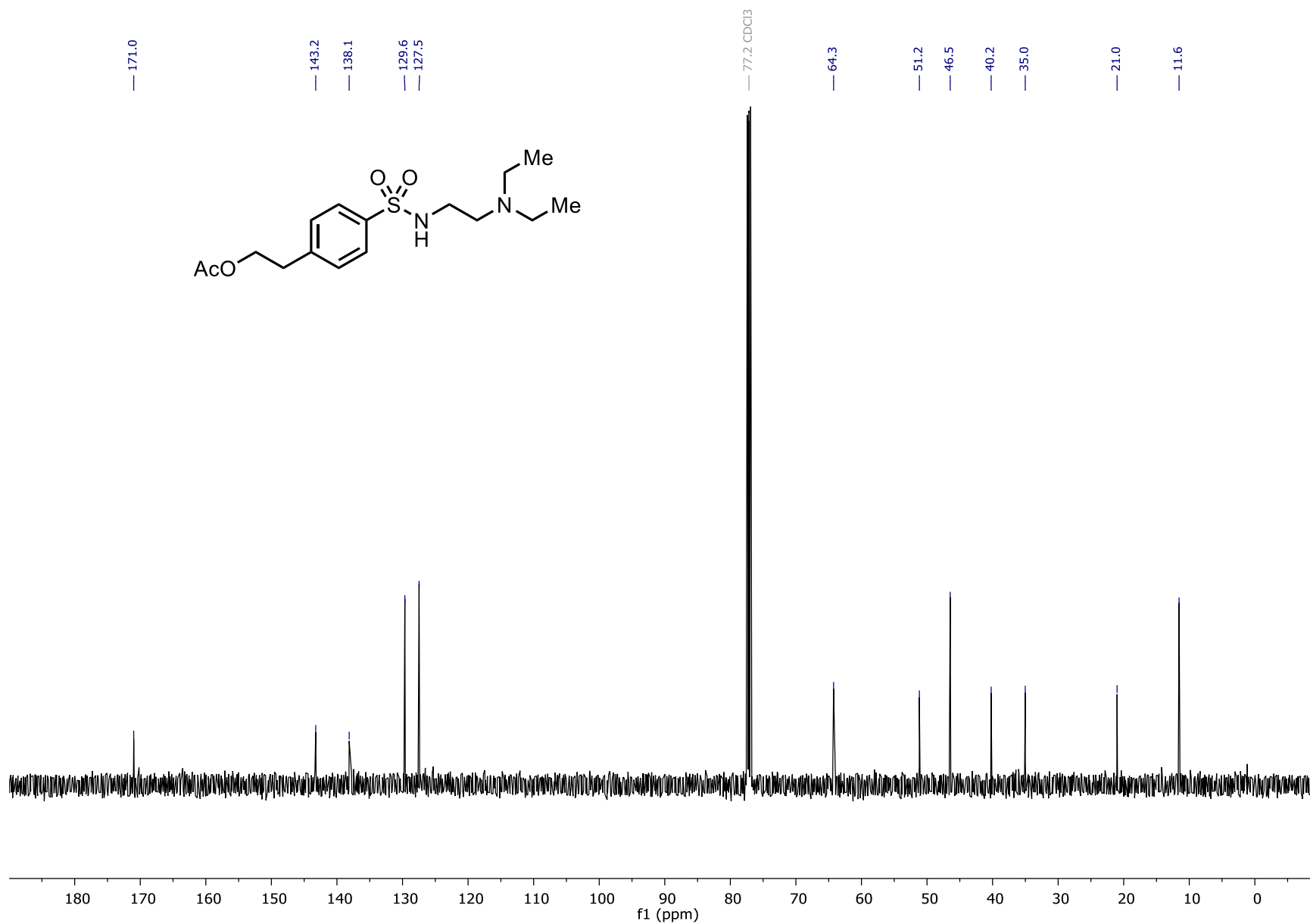
4-(N-Phenethylsulfonyl)phenethyl acetate (23)**¹H NMR of 4-(N-phenethylsulfonyl)phenethyl acetate (23)**CD₂Cl₂, 500 MHz, 298 K

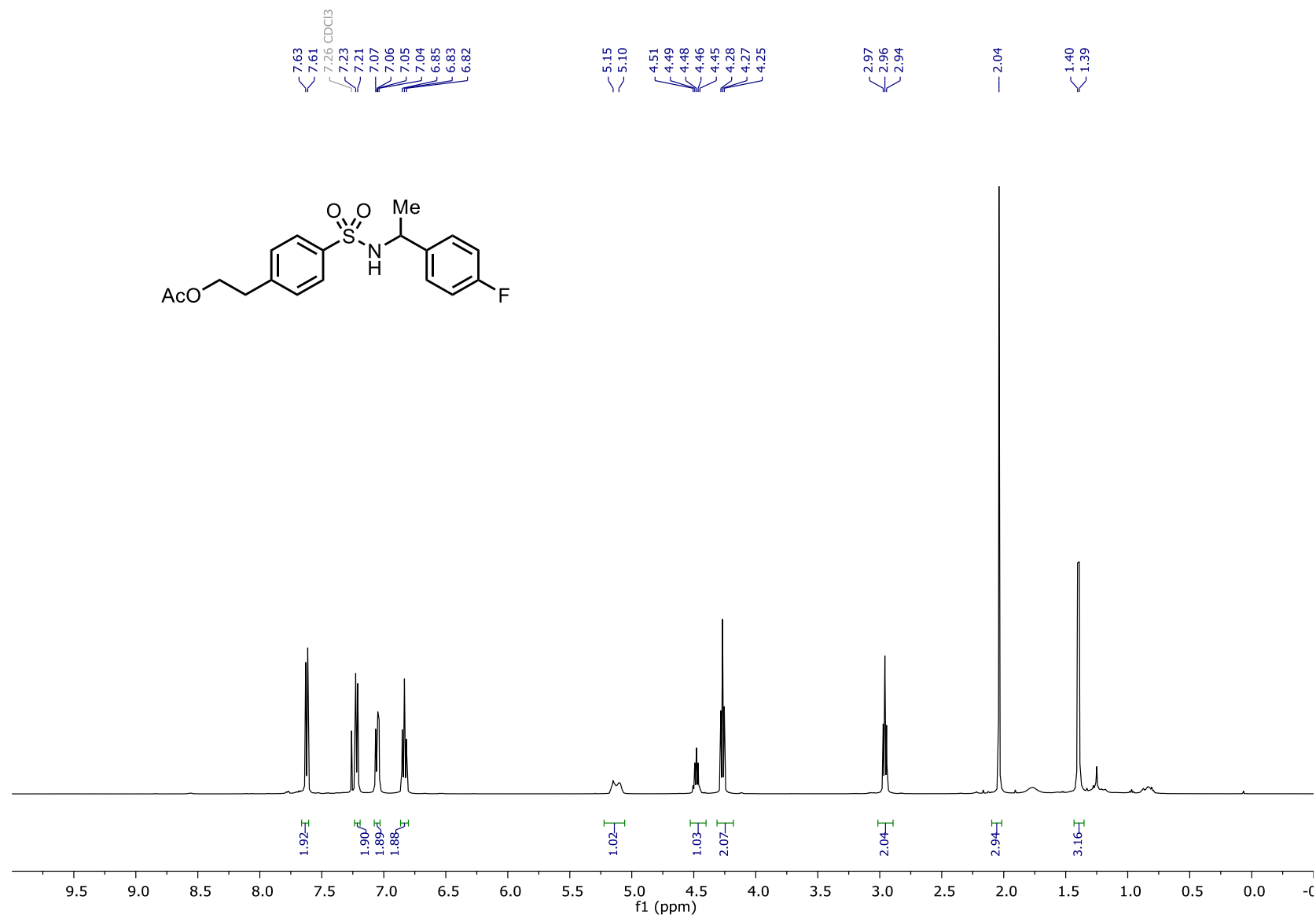
^{13}C NMR of 4-(N-phenethylsulfamoyl)phenethyl acetate (23)CDCl₃, 126 MHz, 298 K

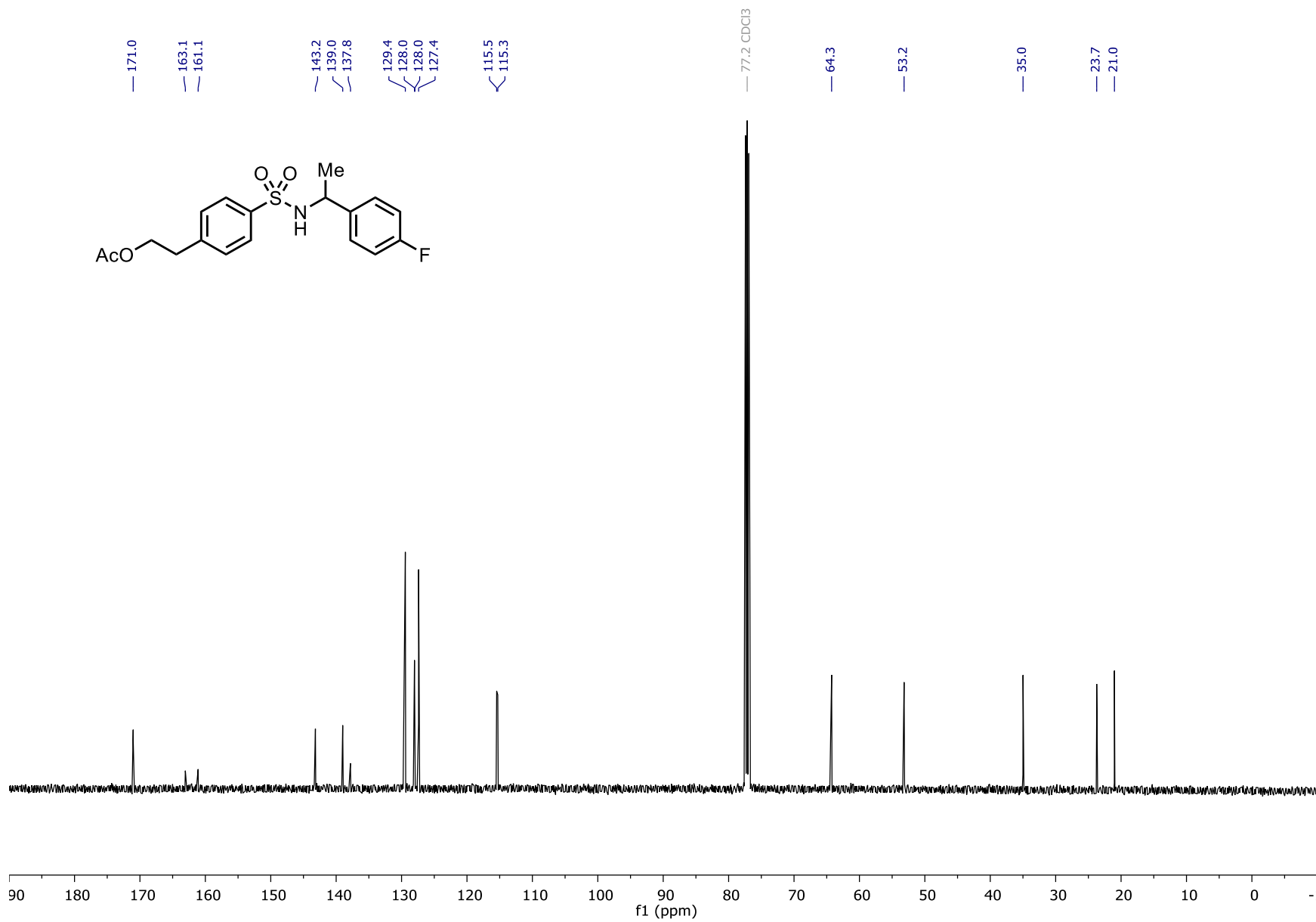
4-(N-Cyclohexylsulfamoyl)phenethyl acetate (24)**¹H NMR of 4-(N-cyclohexylsulfamoyl)phenethyl acetate (24)**CDCl₃, 500 MHz, 298 K

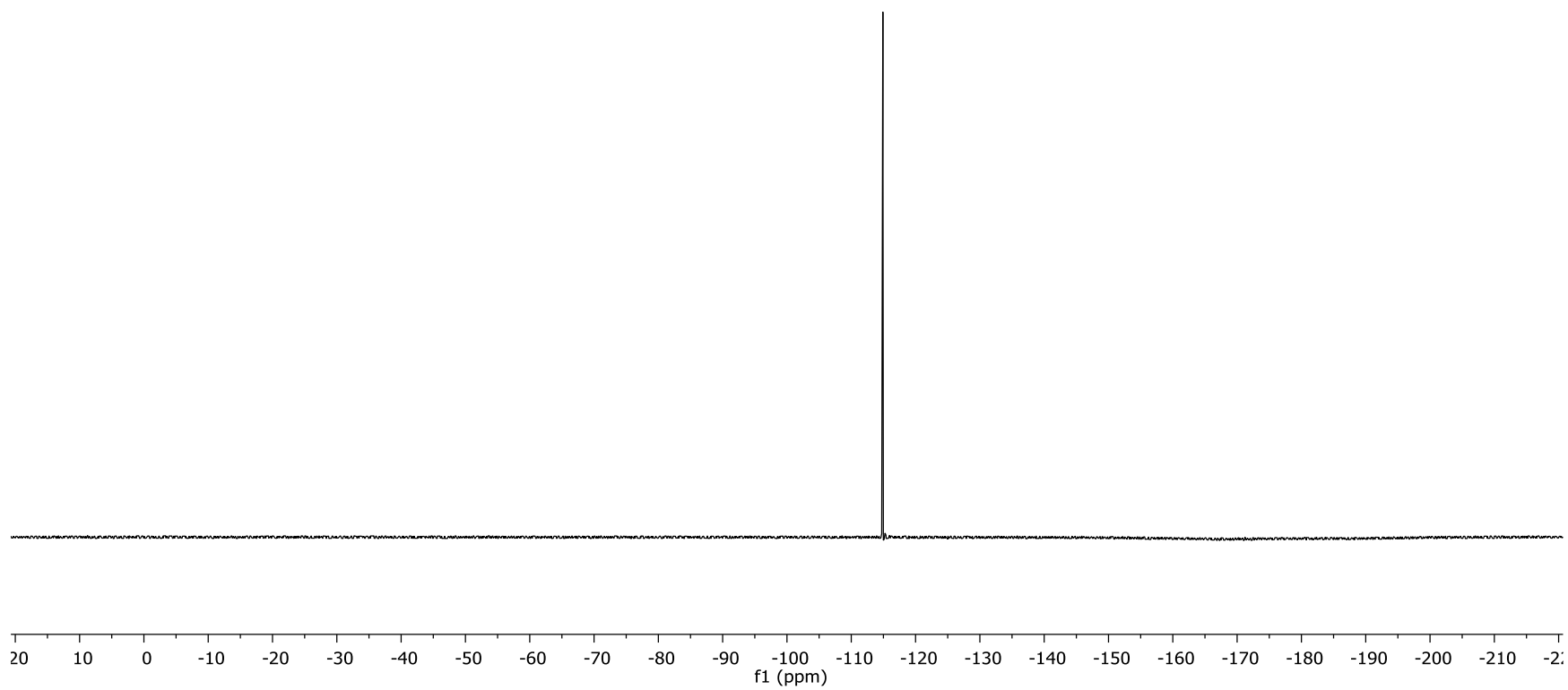
^{13}C NMR of 4-(N-cyclohexylsulfamoyl)phenethyl acetate (24)CDCl₃, 126 MHz, 298 K

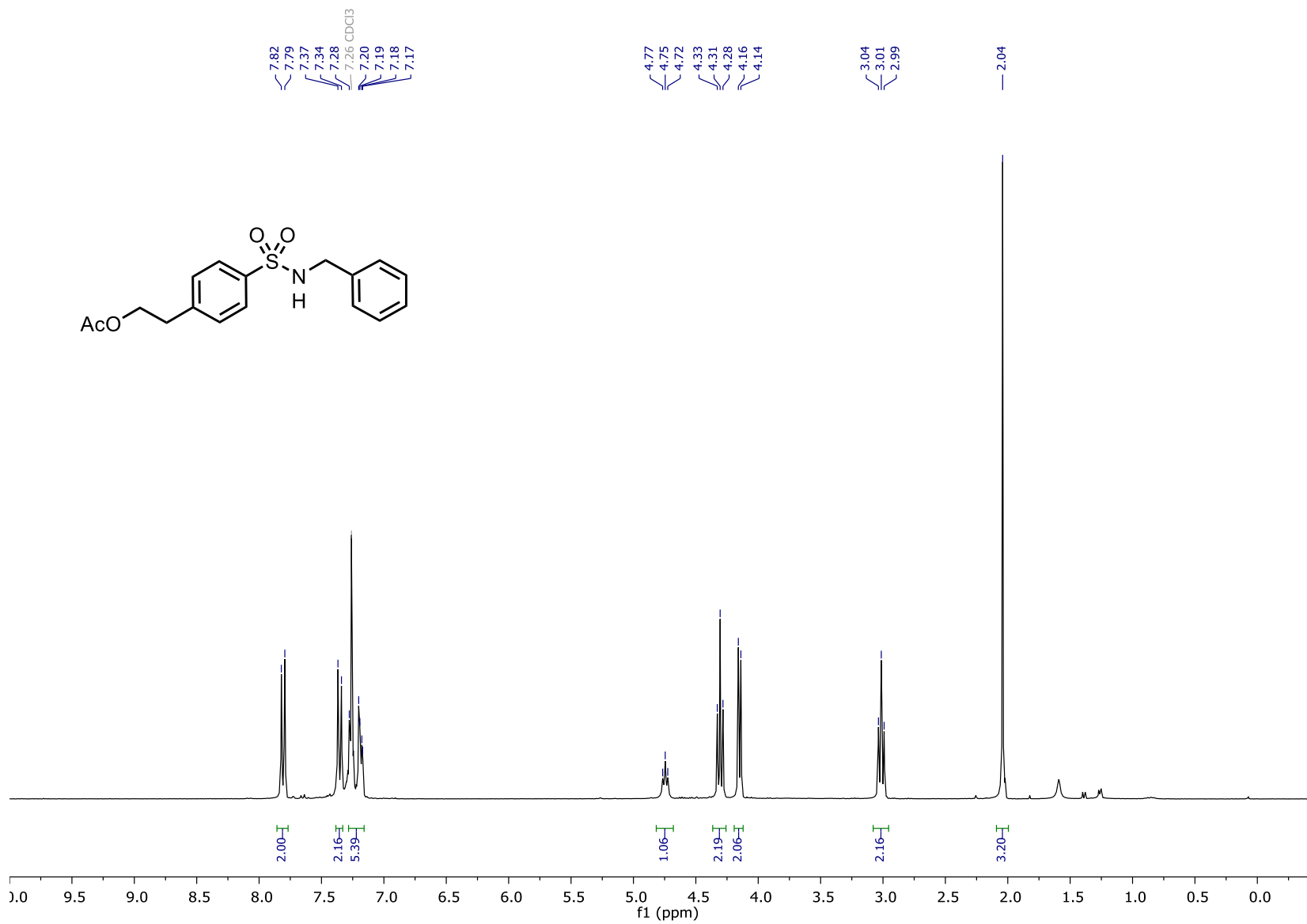
4-(N-(2-(Diethylamino)ethyl)sulfamoyl)phenethyl acetate (25)**¹H NMR of 4-(N-(2-(diethylamino)ethyl)sulfamoyl)phenethyl acetate (25)**CDCl₃, 500 MHz, 298 K

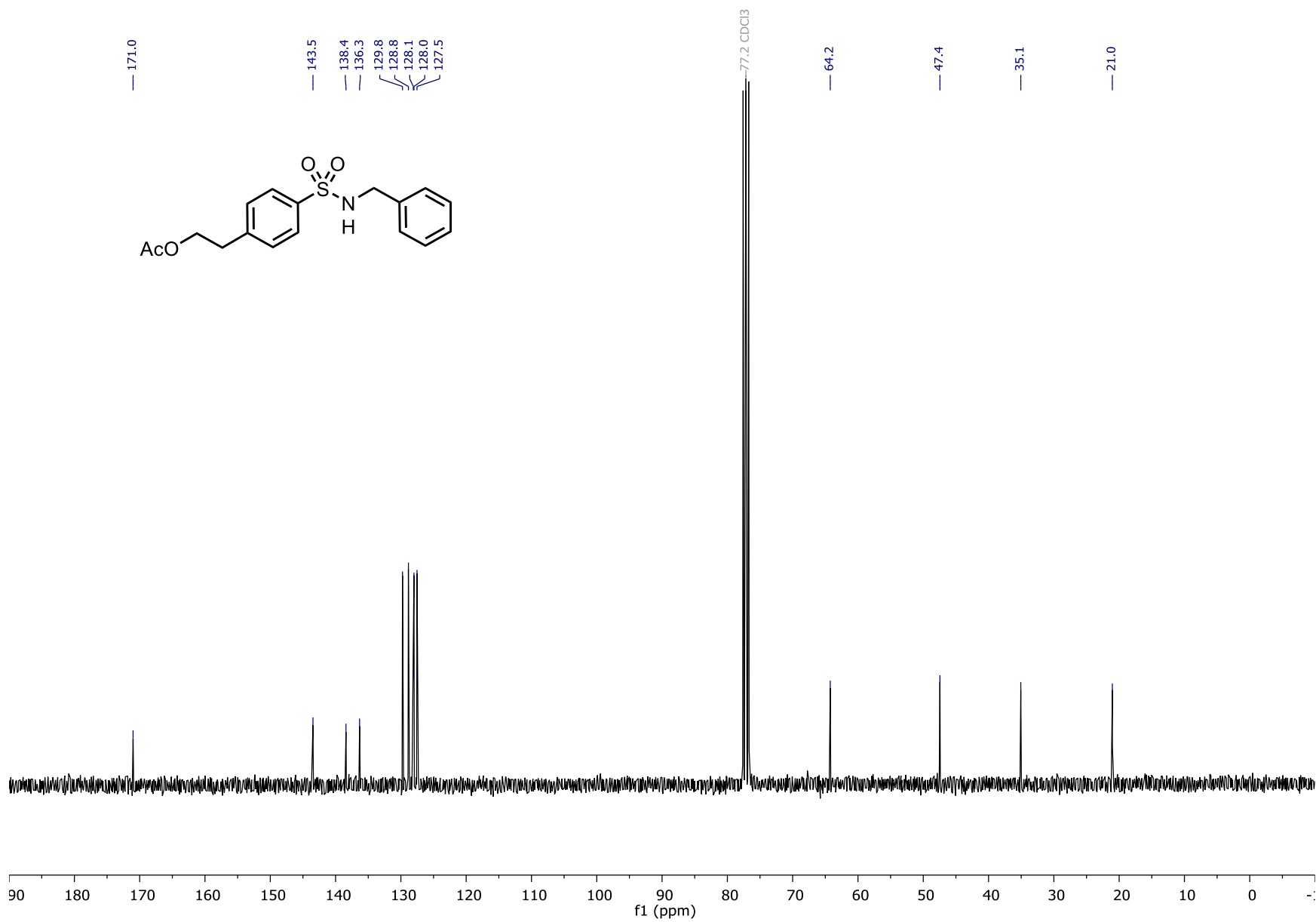
^{13}C NMR of 4-(N-(2-(diethylamino)ethyl)sulfamoyl)phenethyl acetate (25)CDCl₃, 126 MHz, 298 K

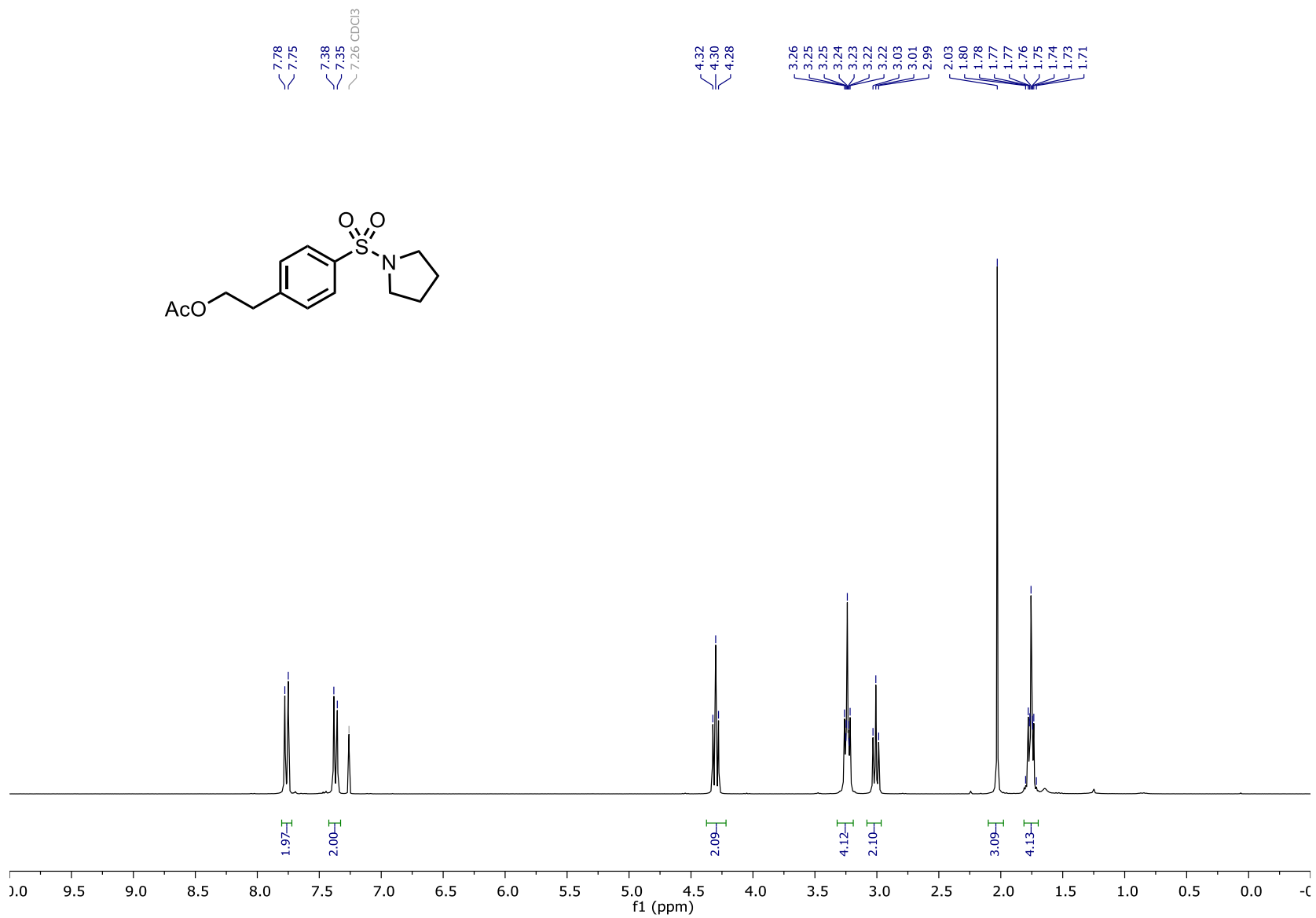
4-(N-(1-(4-Fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26)**¹H NMR of 4-(N-(1-(4-fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26)**CDCl₃, 500 MHz, 298 K

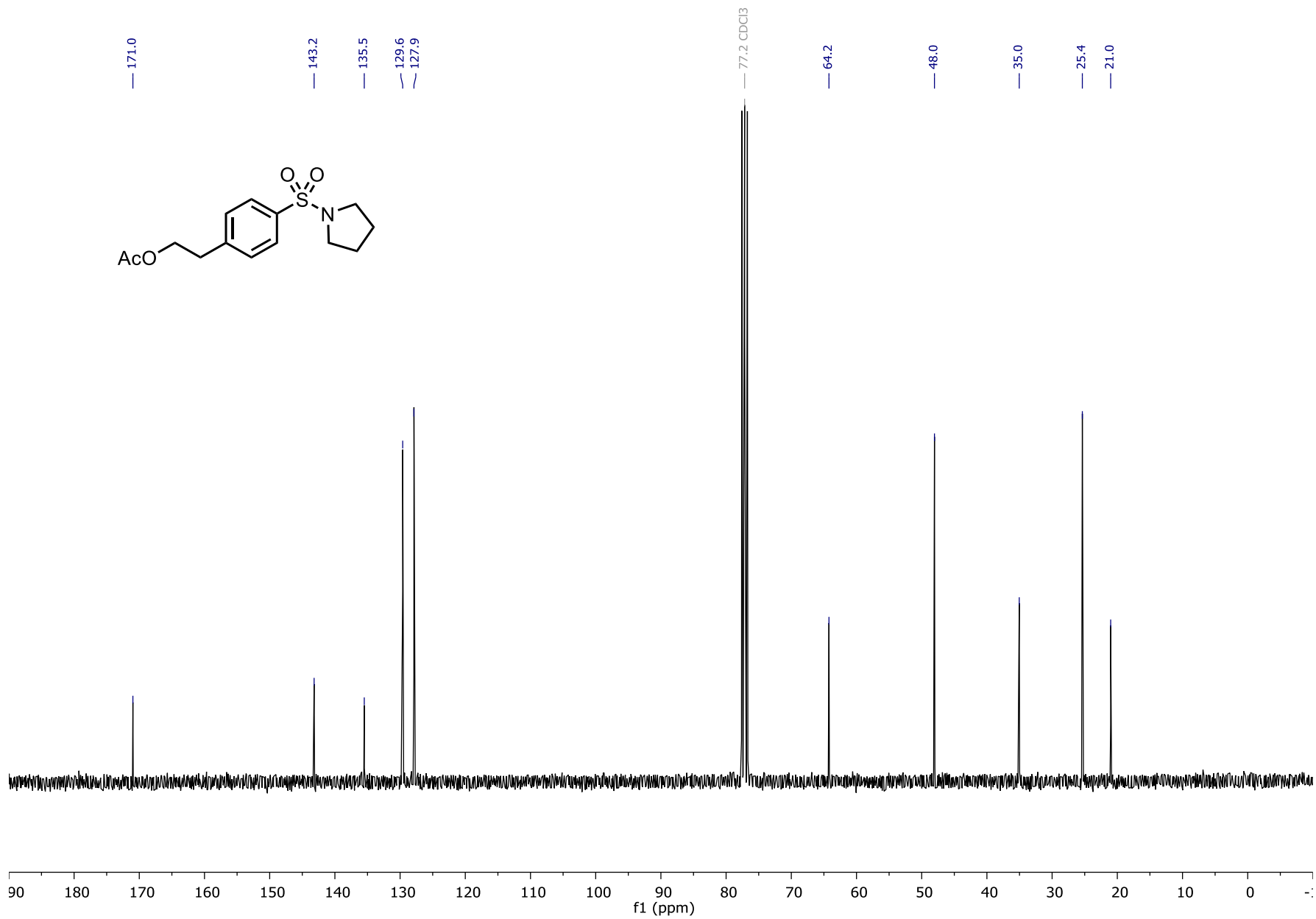
¹³C NMR of 4-(N-(1-(4-fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26)CDCl₃, 126 MHz, 298 K

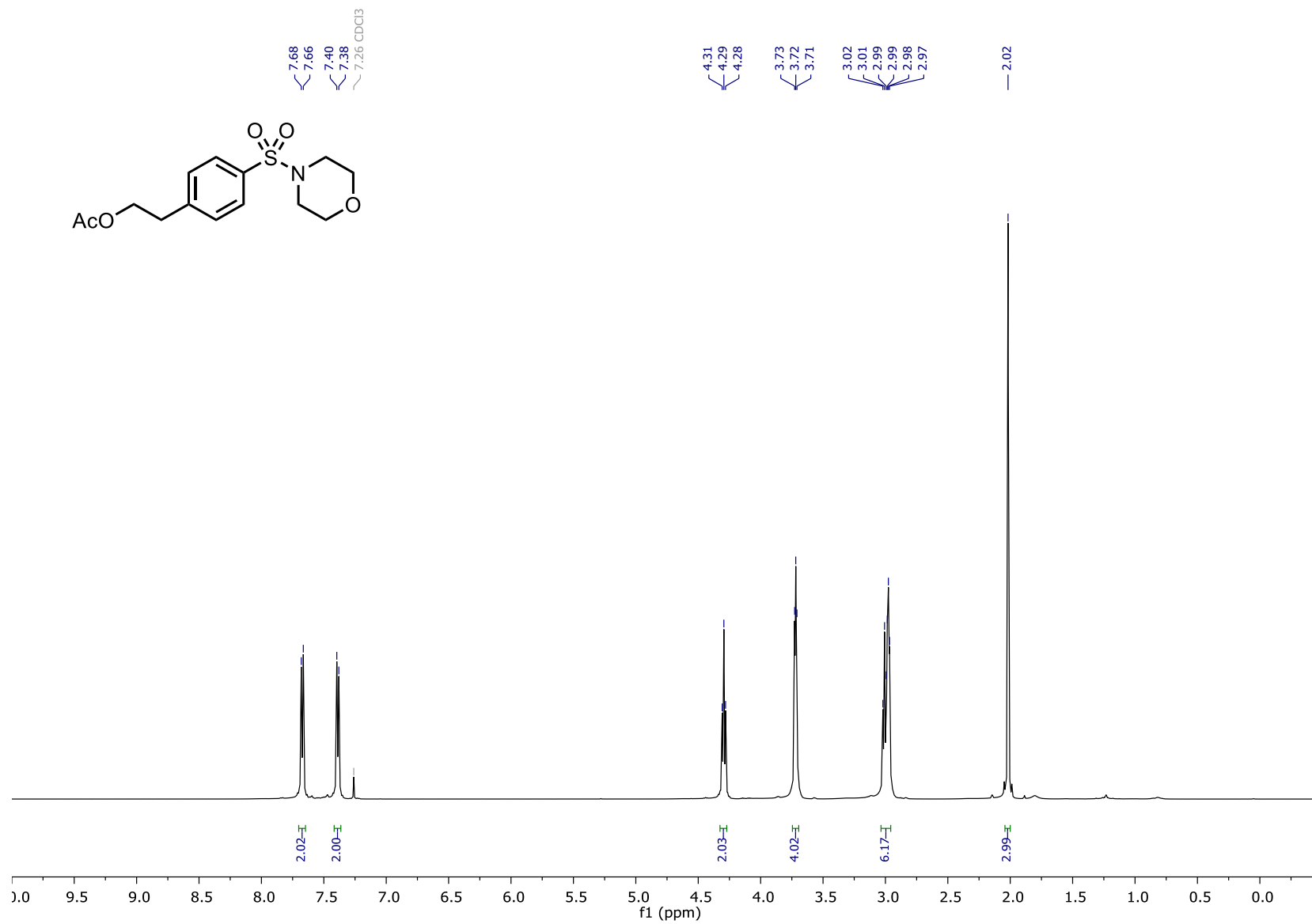
^{19}F NMR of 4-(*N*-(1-(4-fluorophenyl)ethyl)sulfamoyl)phenethyl acetate (26)CDCl₃, 471 MHz, 298 K

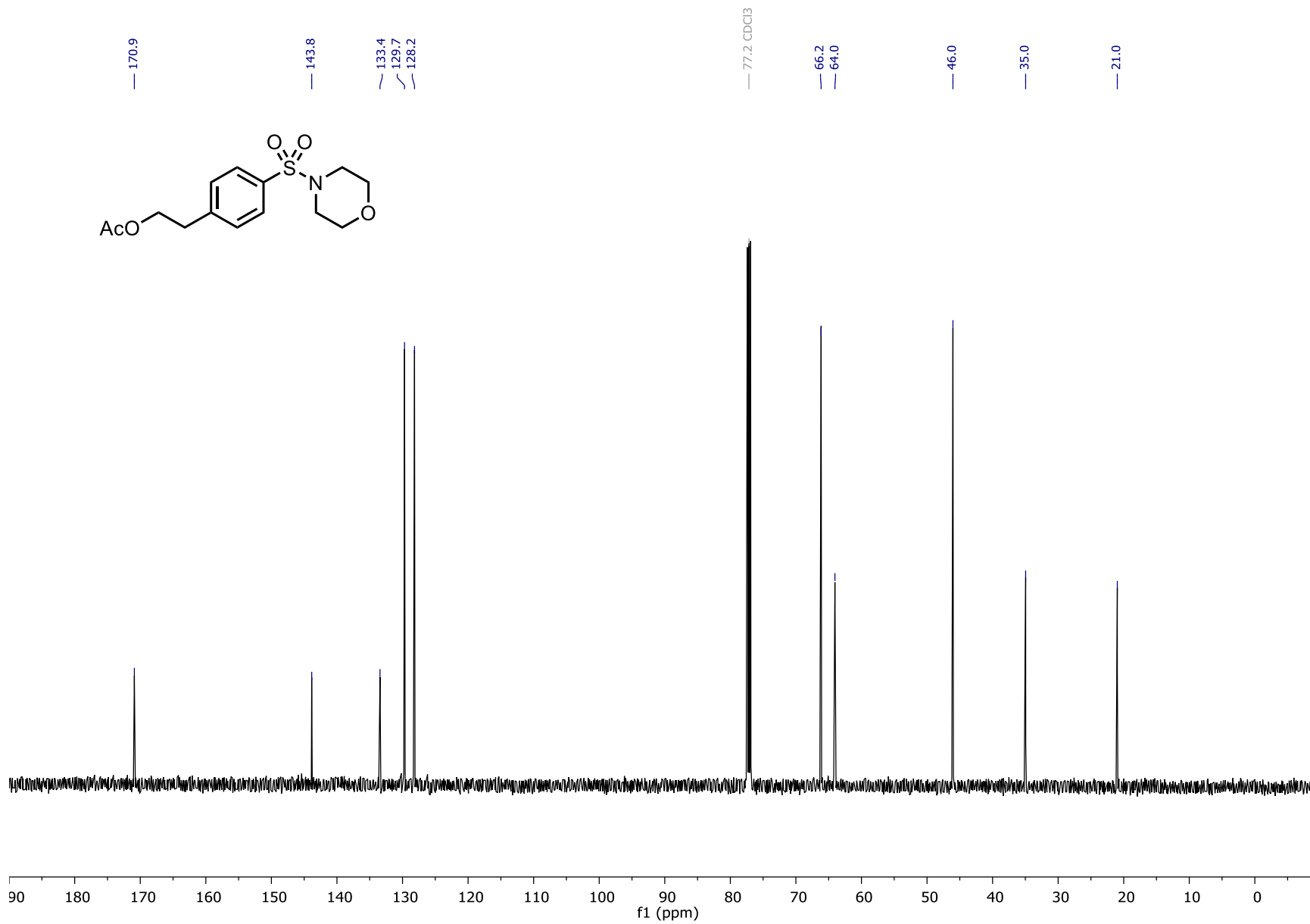
4-(N-Benzylsulfonyl)phenethyl acetate (27)**¹H NMR of 4-(N-benzylsulfonyl)phenethyl acetate (27)**CDCl₃, 500 MHz, 298 K

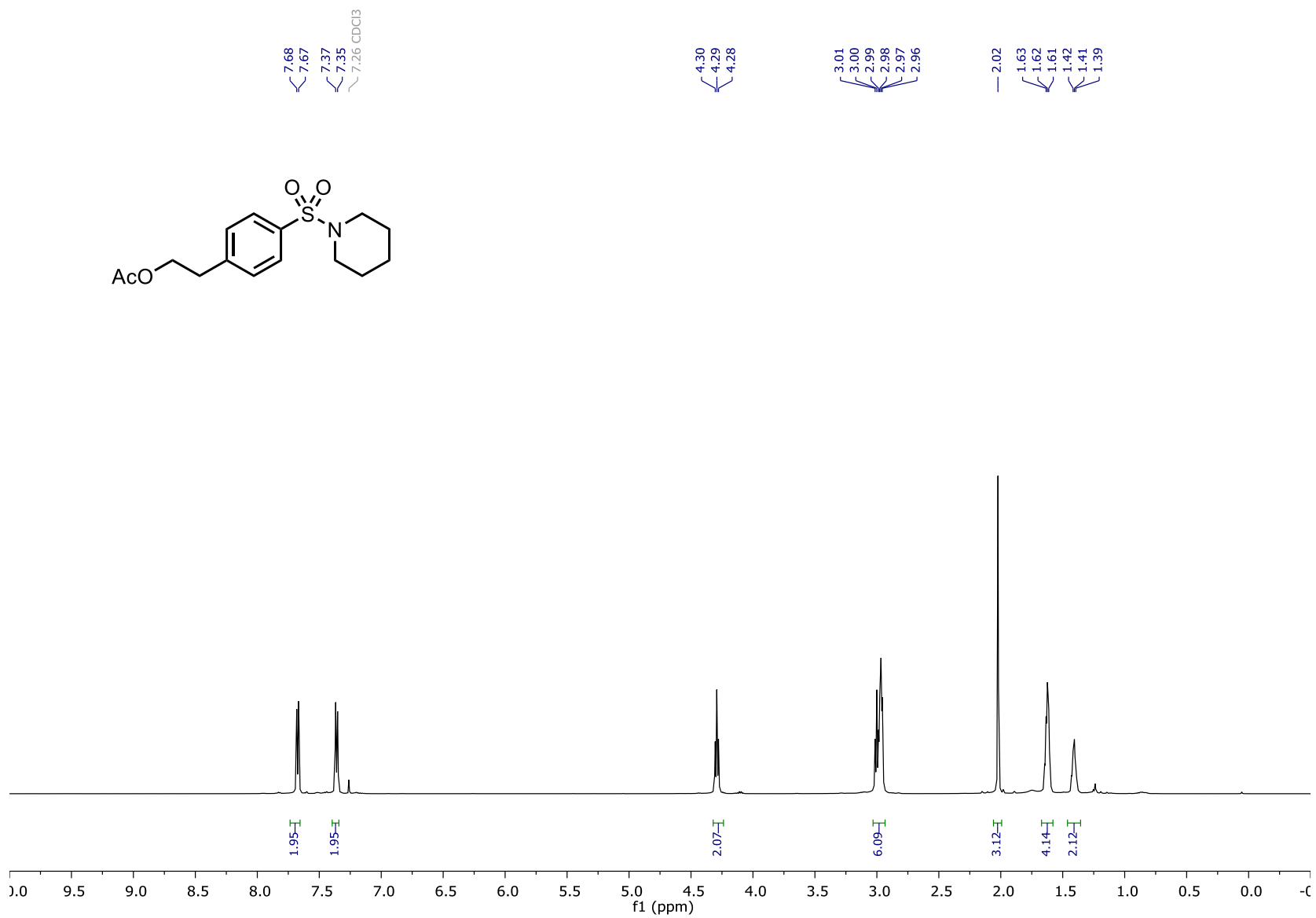
^{13}C NMR of 4-(N-benzylsulfamoyl)phenethyl acetate (27)CDCl₃, 126 MHz, 298 K

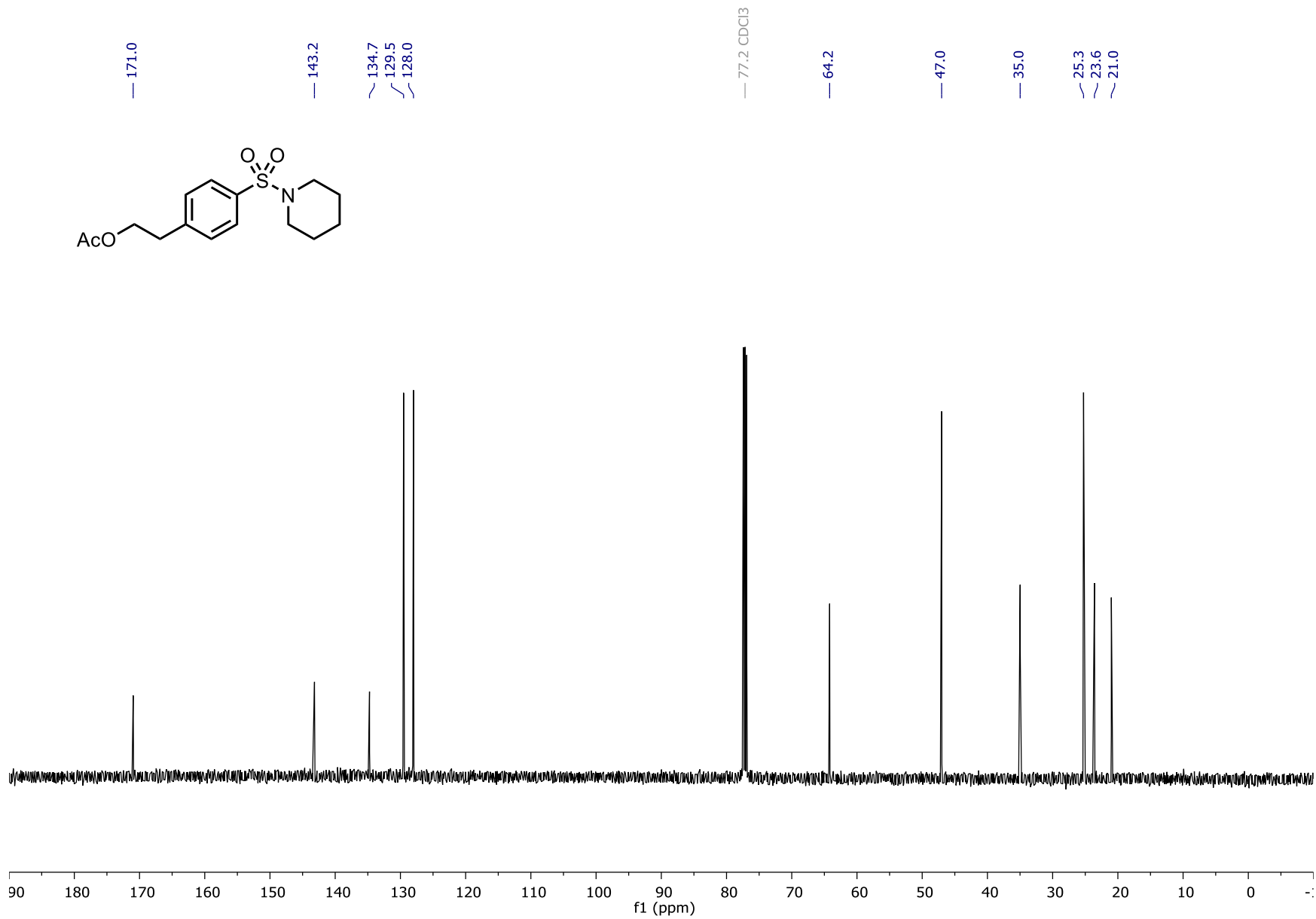
4-(Pyrrolidin-1-ylsulfonyl)phenethyl acetate (28)**¹H NMR of 4-(pyrrolidin-1-ylsulfonyl)phenethyl acetate (28)**CDCl₃, 500 MHz, 298 K

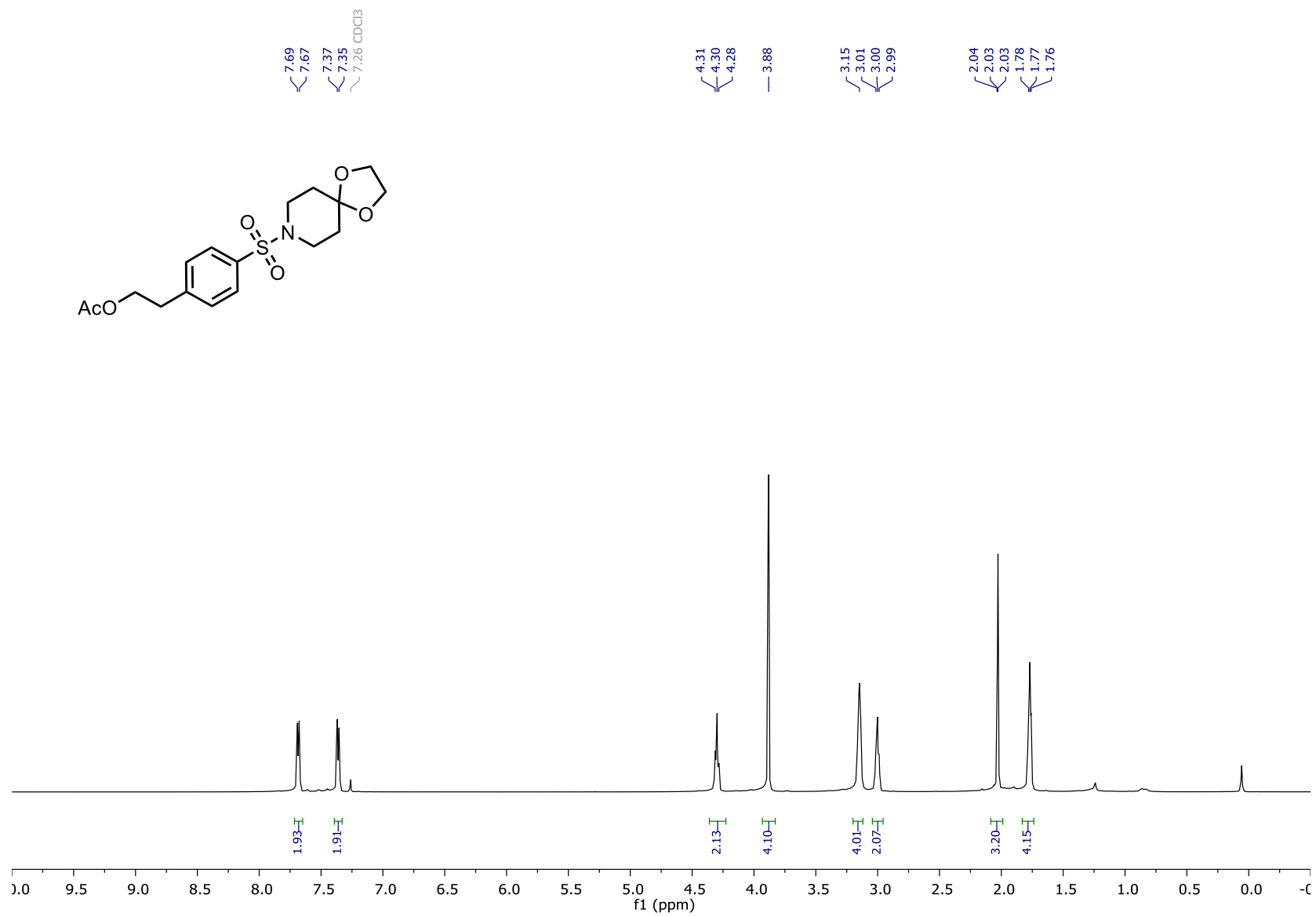
^{13}C NMR of 4-(pyrrolidin-1-ylsulfonyl)phenethyl acetate (28)CDCl₃, 126 MHz, 298 K

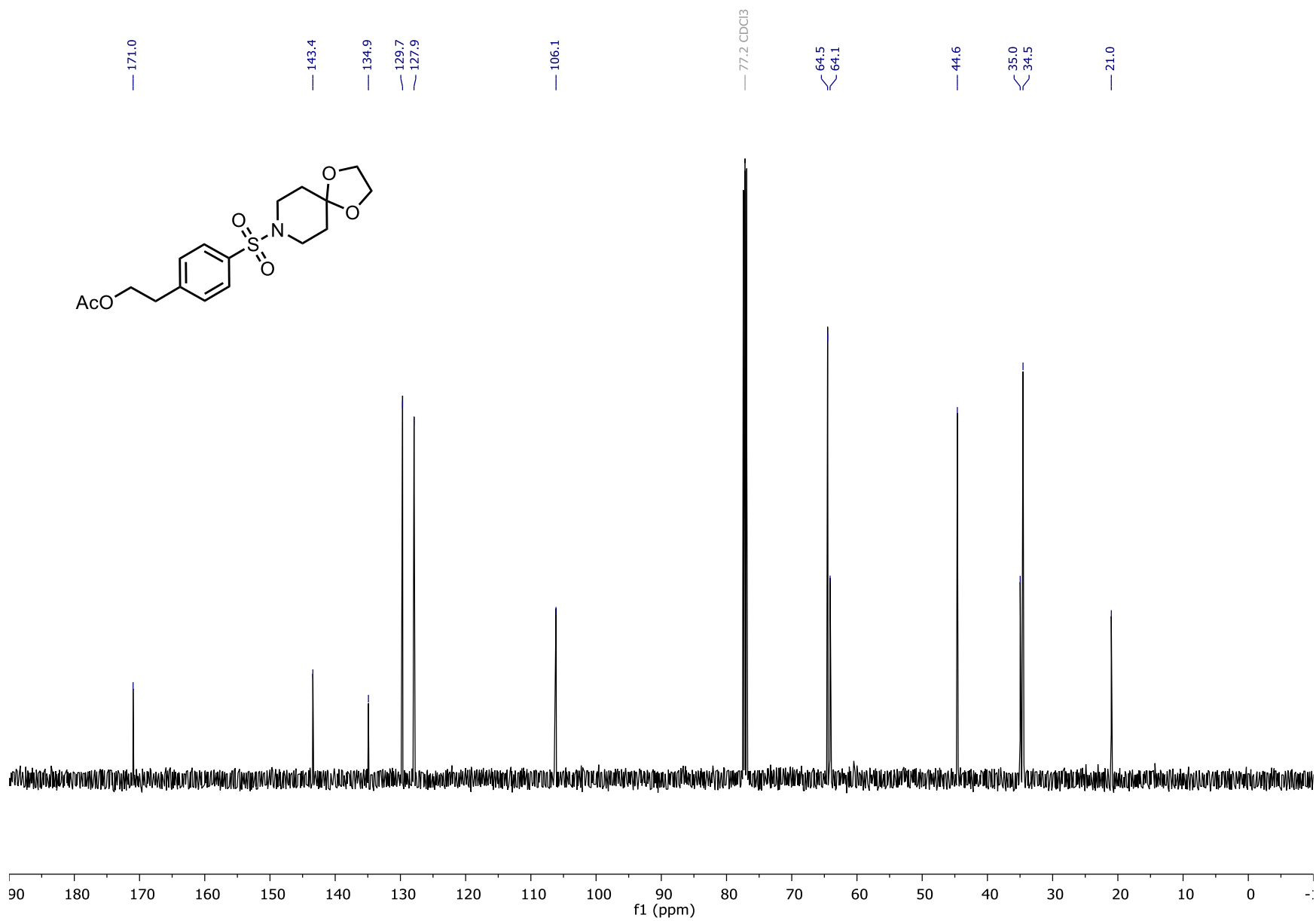
4-(Morpholinosulfonyl)phenethyl acetate (29)**¹H NMR of 4-(morpholinosulfonyl)phenethyl acetate (29)**CDCl₃, 500 MHz, 298 K

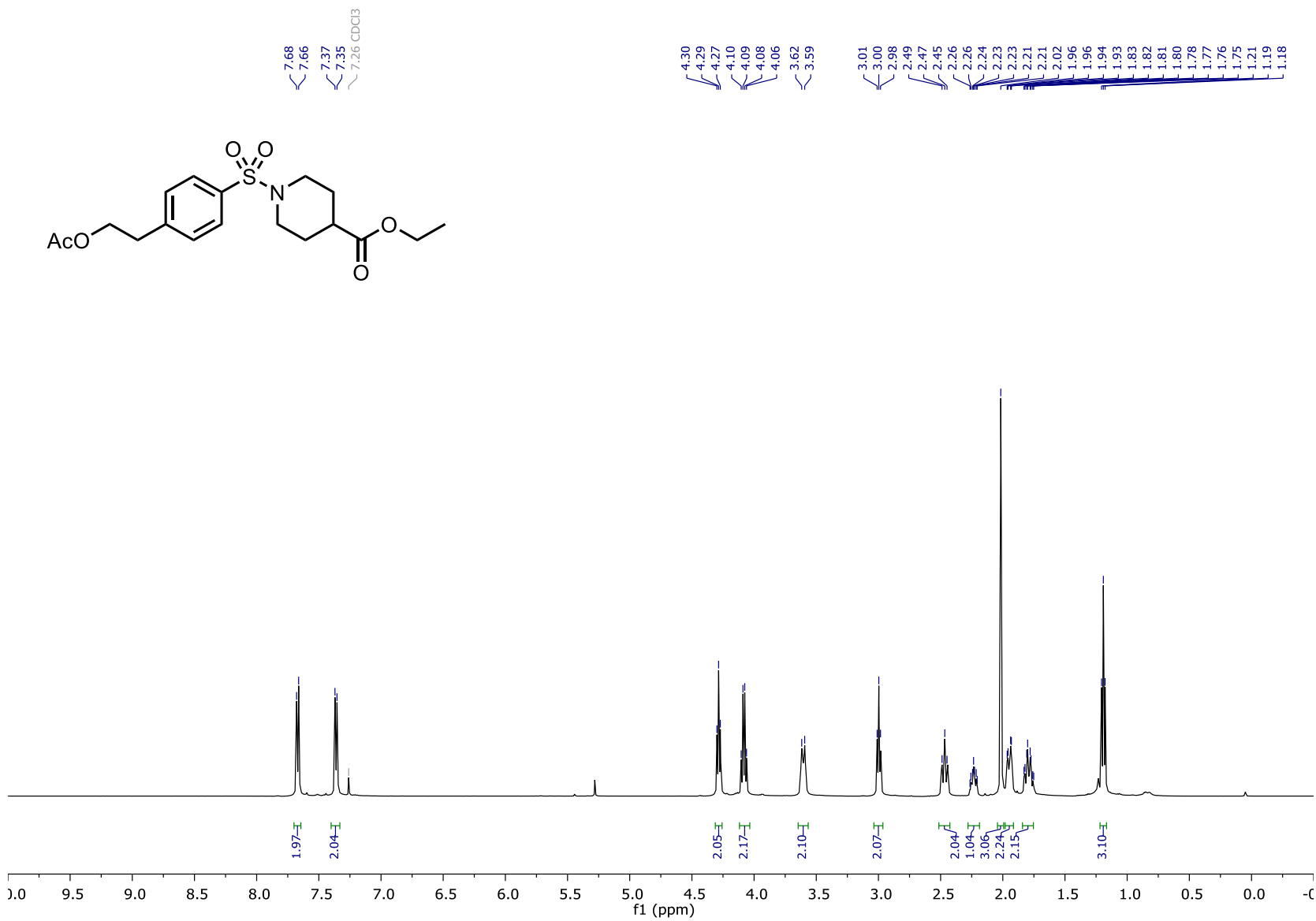
^{13}C NMR of 4-(morpholinosulfonyl)phenethyl acetate (29)CDCl₃, 126 MHz, 298 K

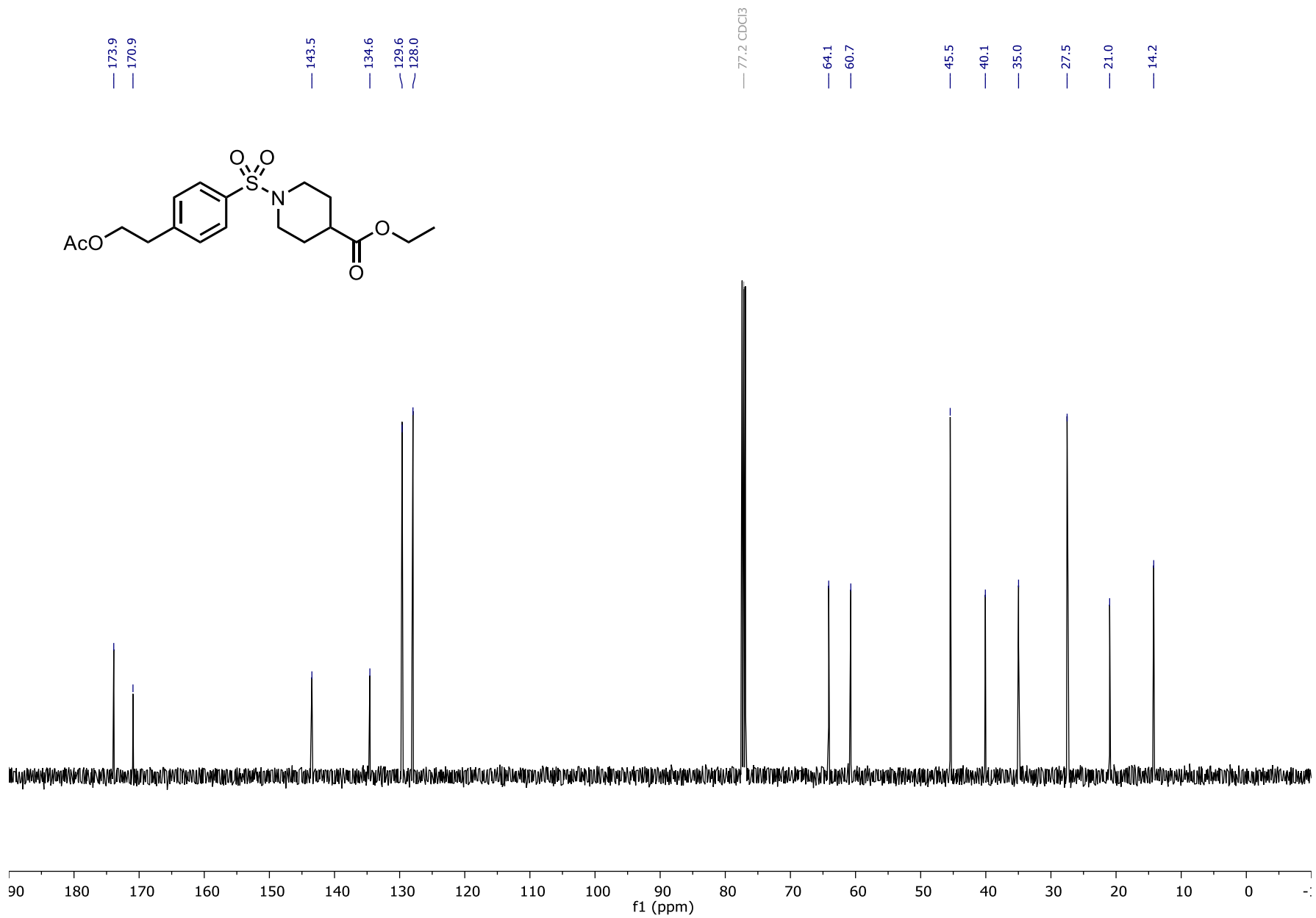
4-(Piperidin-1-ylsulfonyl)phenethyl acetate (30)**¹H NMR of 4-(piperidin-1-ylsulfonyl)phenethyl acetate (30)**CDCl₃, 500 MHz, 298 K

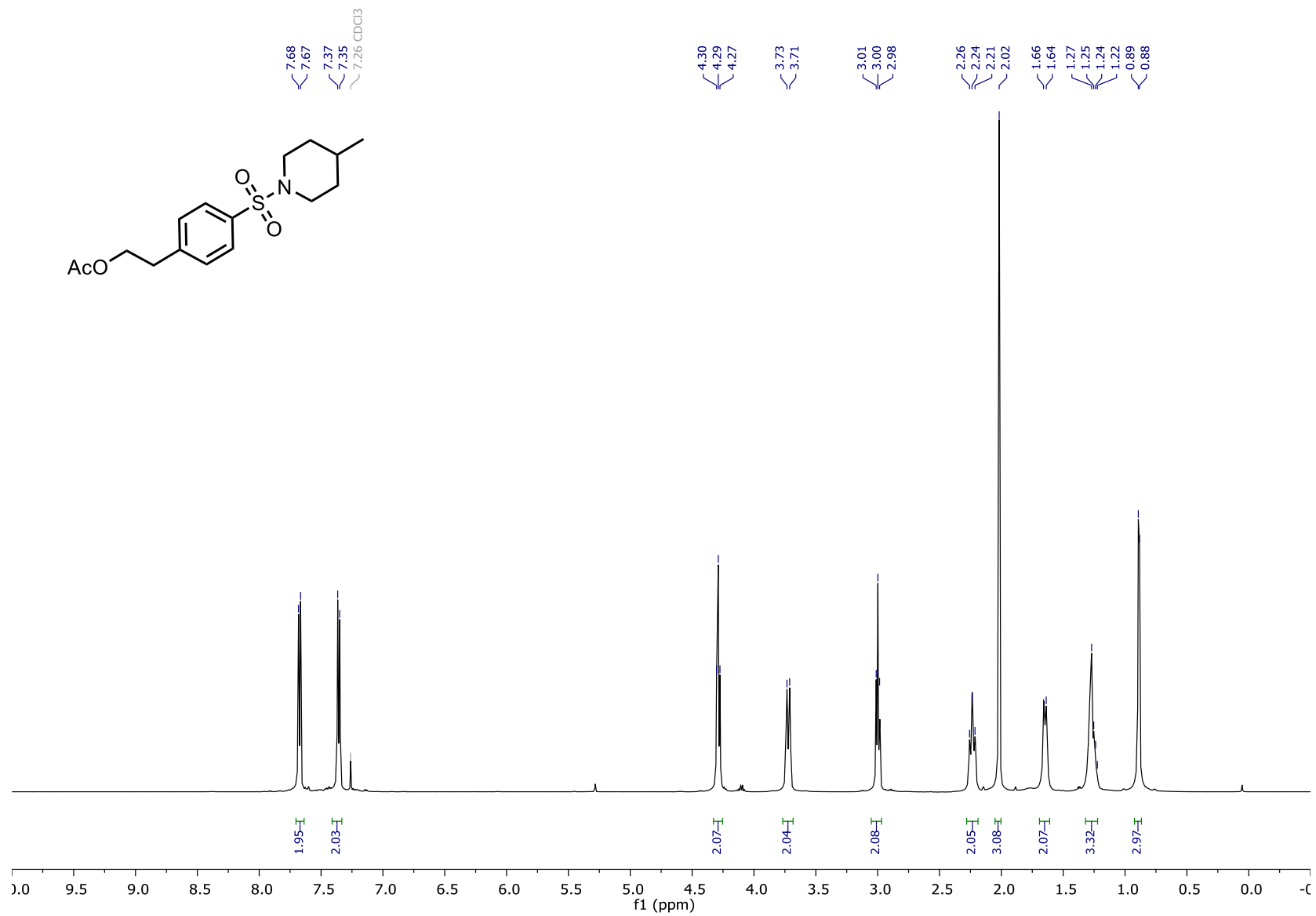
¹³C NMR of 4-(piperidin-1-ylsulfonyl)phenethyl acetate (30)CDCl₃, 126 MHz, 298 K

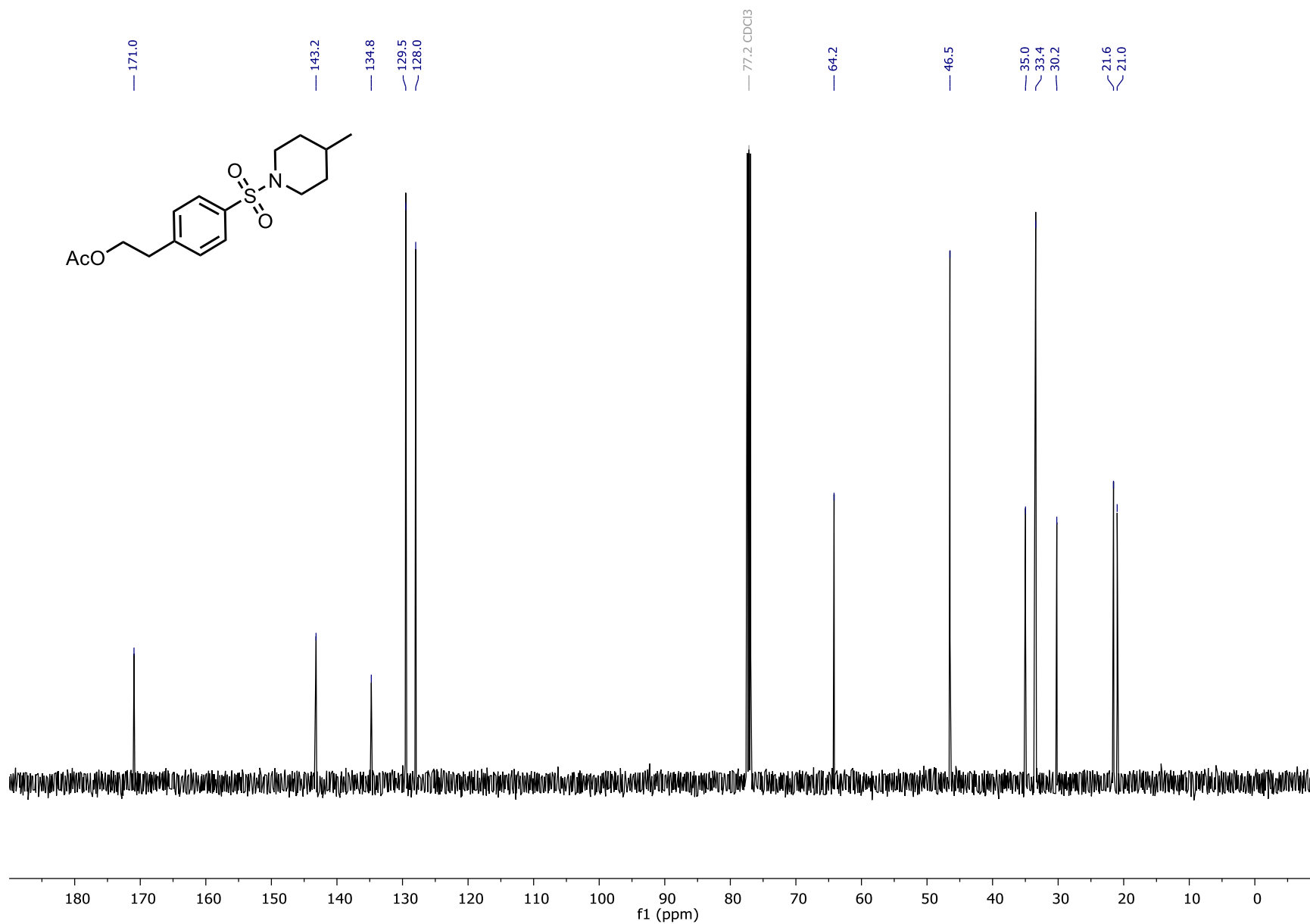
4-((1,4-Dioxa-8-azaspiro[4.5]decan-8-yl)sulfonyl)phenethyl acetate (31)**¹H NMR of 4-((1,4-dioxa-8-azaspiro[4.5]decan-8-yl)sulfonyl)phenethyl acetate (31)**CDCl₃, 500 MHz, 298 K

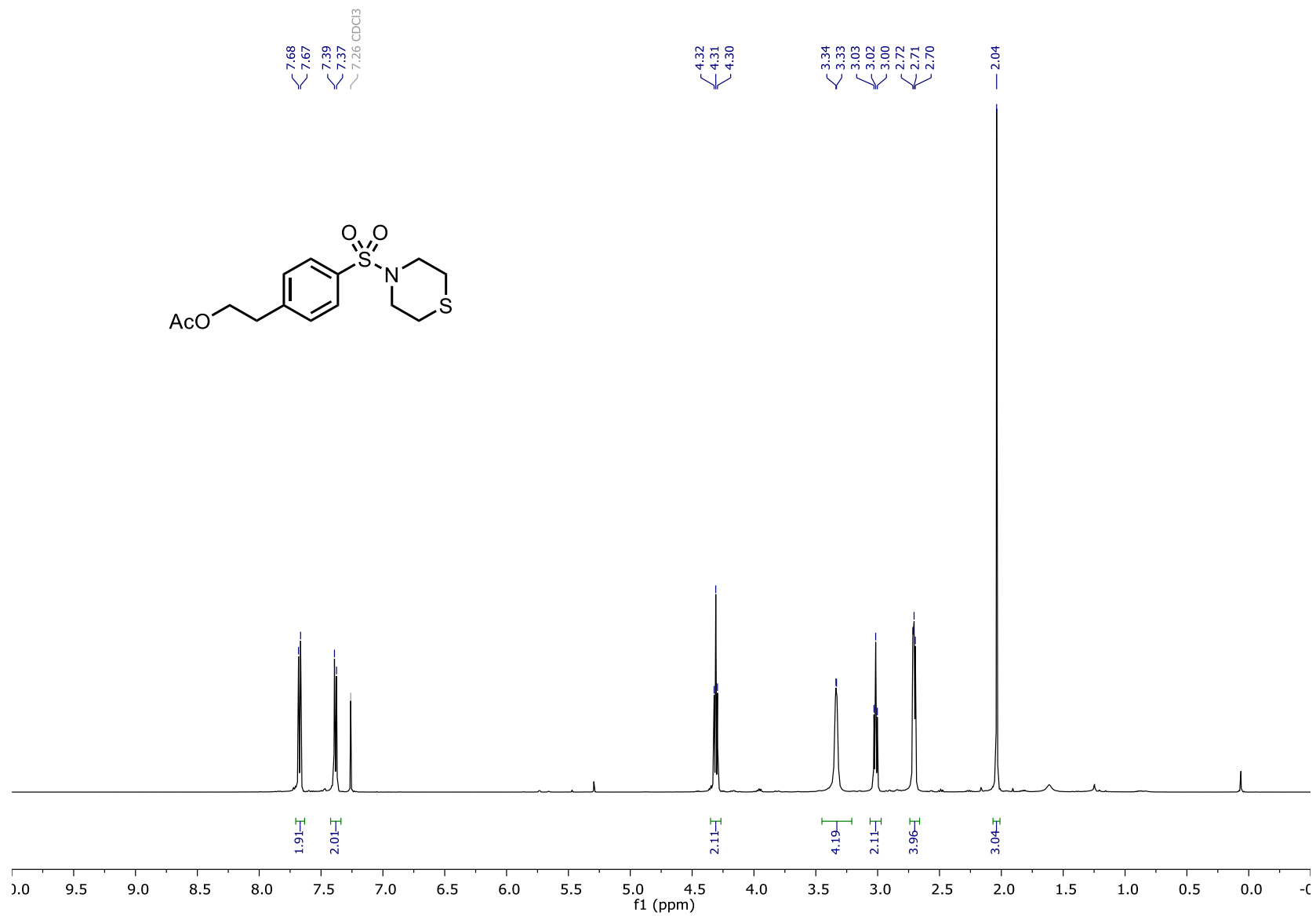
^{13}C NMR of 4-((1,4-dioxa-8-azaspiro[4.5]decan-8-yl)sulfonyl)phenethyl acetate (31)CDCl₃, 126 MHz, 298 K

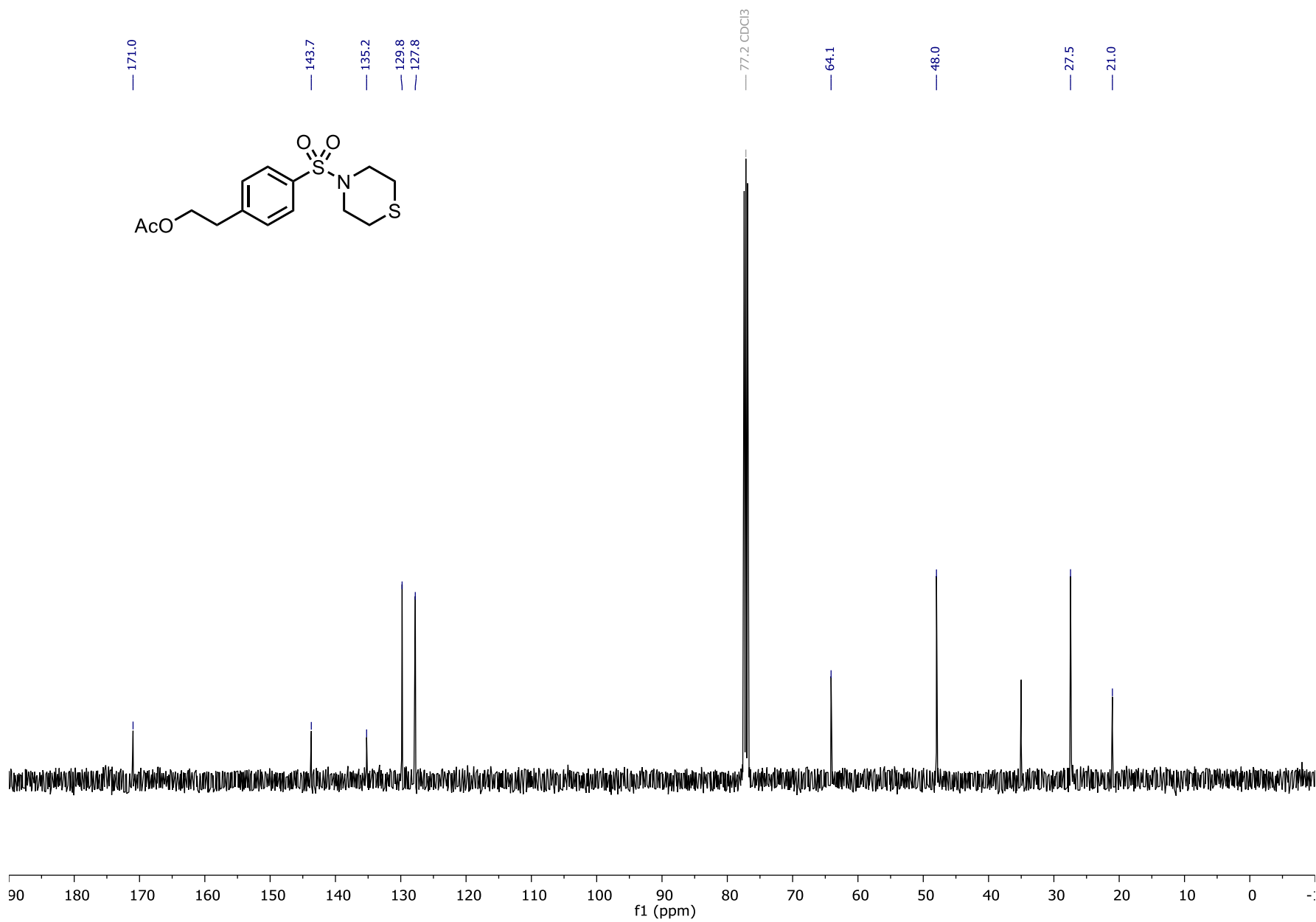
Ethyl 1-((4-(2-acetoxyethyl)phenyl)sulfonyl)piperidine-4-carboxylate (32)**¹H NMR of ethyl 1-((4-(2-acetoxyethyl)phenyl)sulfonyl)piperidine-4-carboxylate (32)**CDCl₃, 500 MHz, 298 K

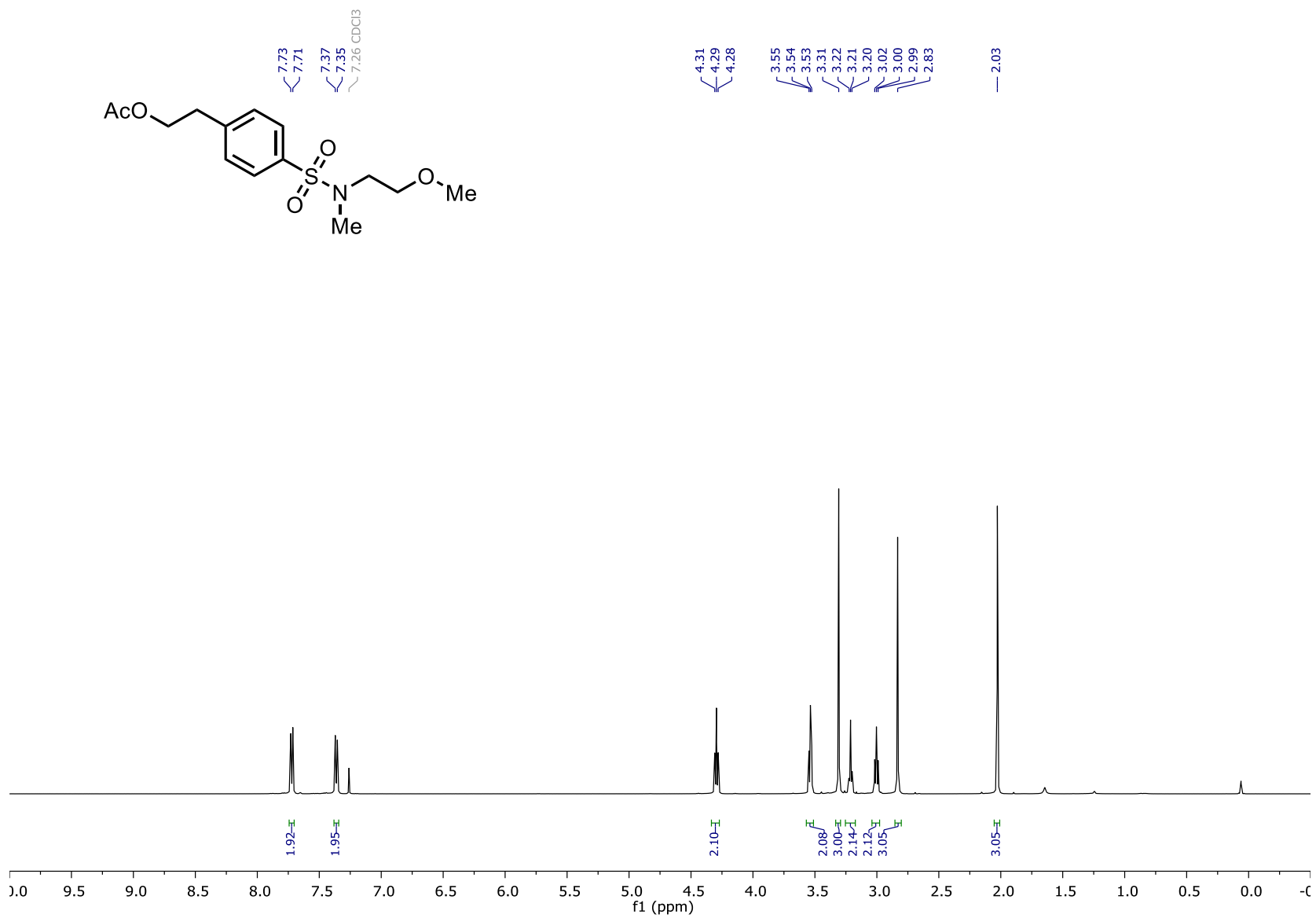
¹³C NMR of ethyl 1-((4-(2-acetoxyethyl)phenyl)sulfonyl)piperidine-4-carboxylate (32)CDCl₃, 126 MHz, 298 K

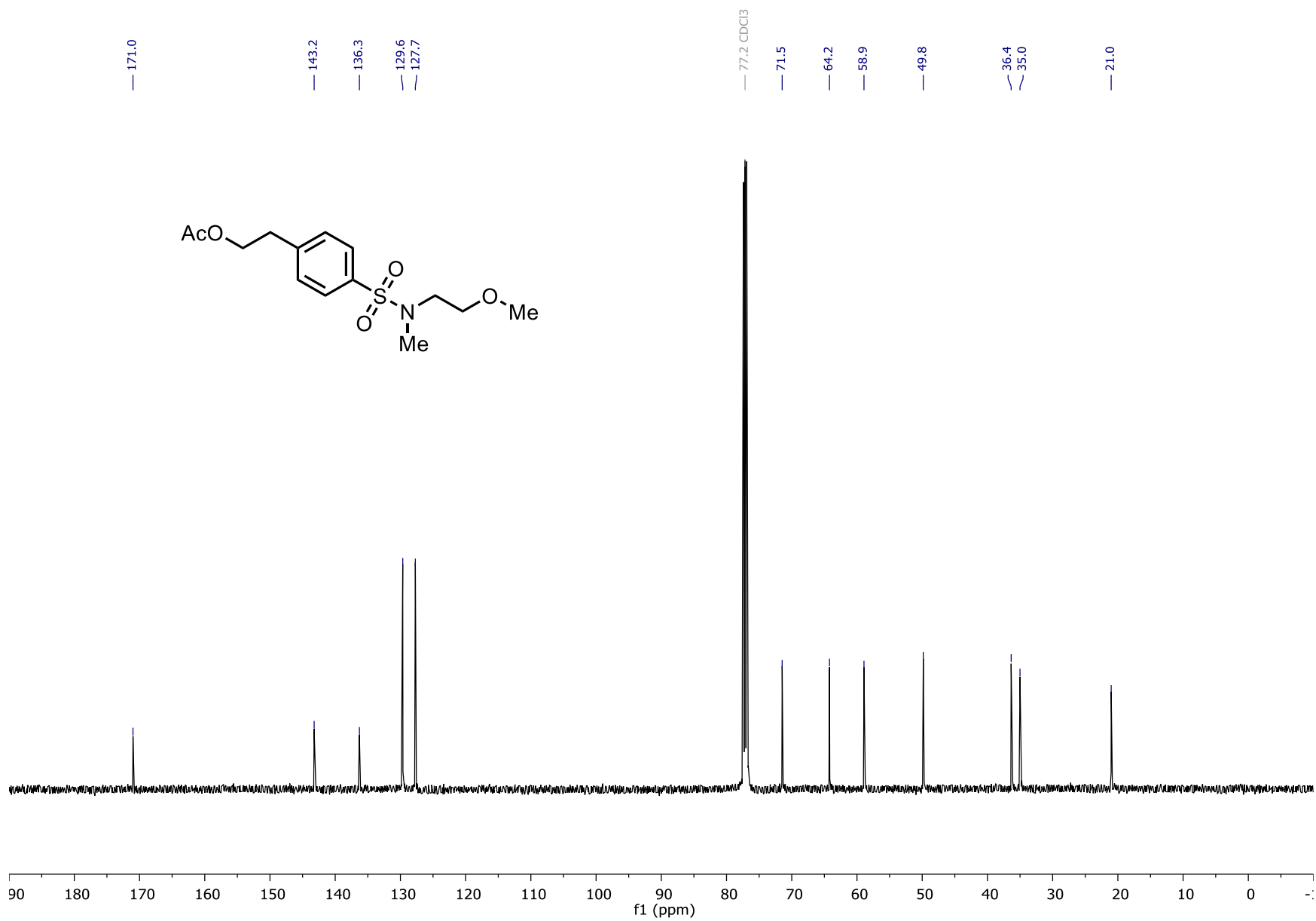
4-((4-Methylpiperidin-1-yl)sulfonyl)phenethyl acetate (33)**¹H NMR of 4-((4-methylpiperidin-1-yl)sulfonyl)phenethyl acetate (33)**CDCl₃, 500 MHz, 298 K

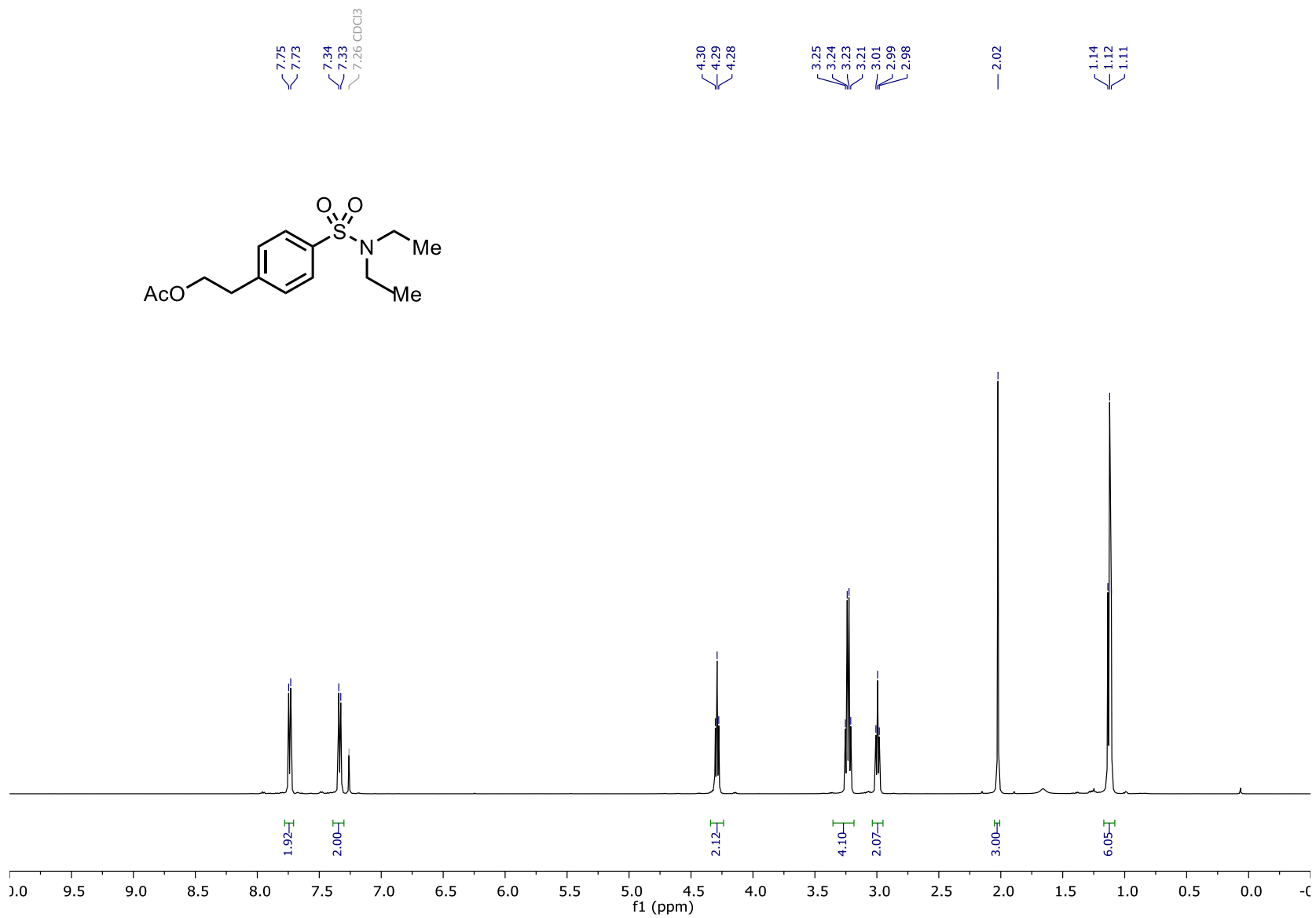
¹³C NMR of 4-(4-methylpiperidin-1-yl)sulfonylphenethyl acetate (33)CDCl₃, 126 MHz, 298 K

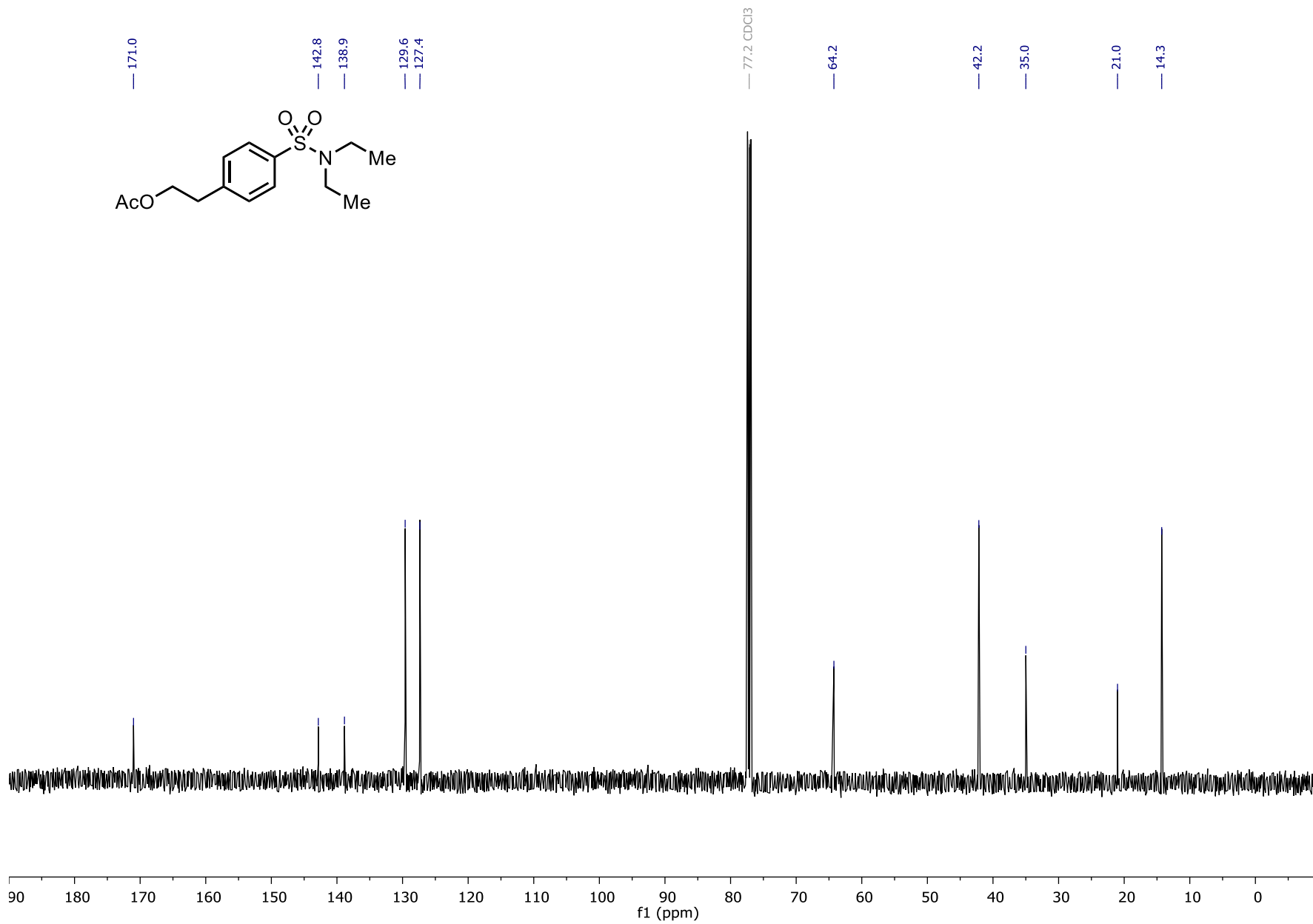
4-(Thiomorpholinosulfonyl)phenethyl acetate (34)**¹H NMR of 4-(thiomorpholinosulfonyl)phenethyl acetate (34)**CDCl₃, 500 MHz, 298 K

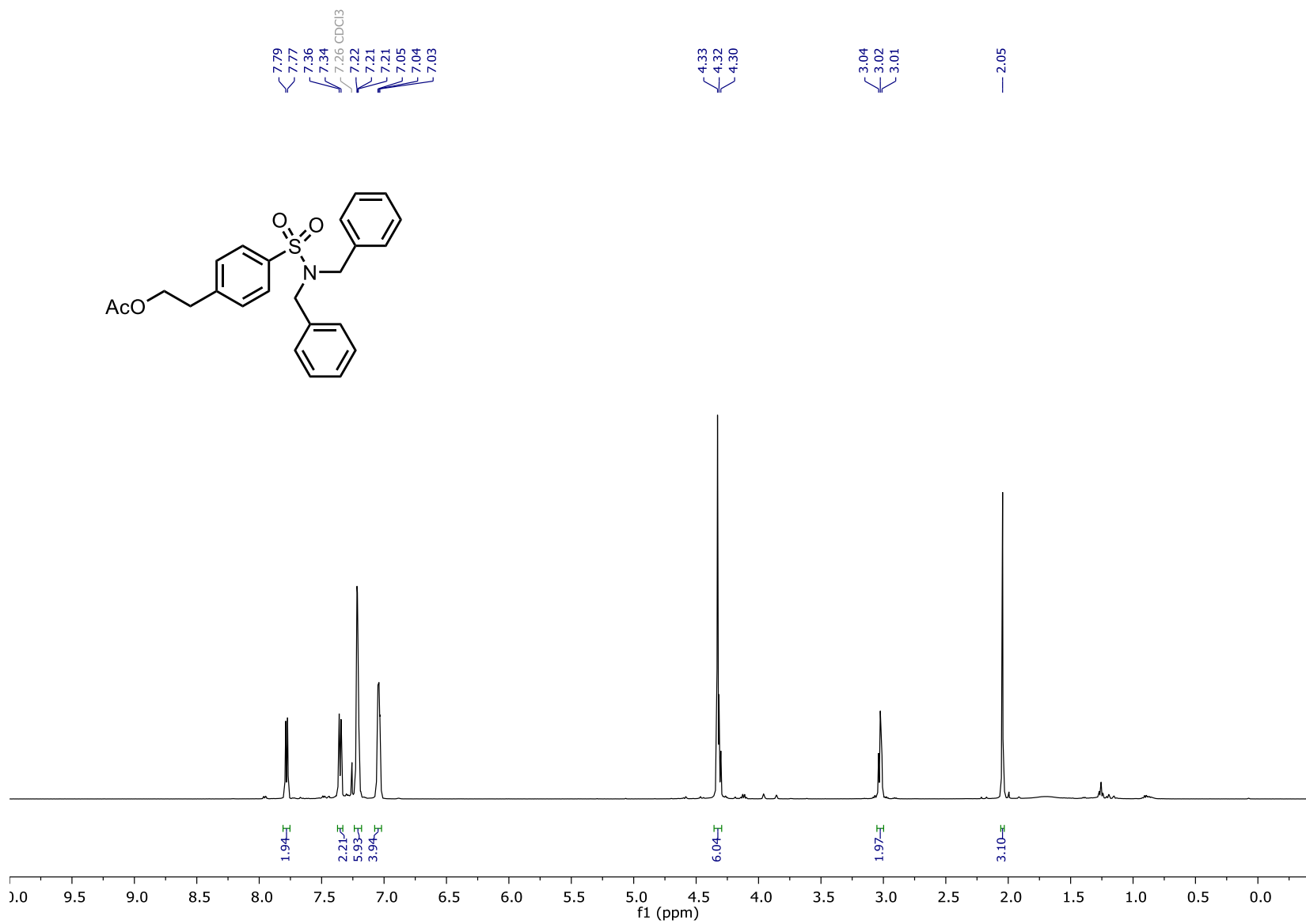
¹³C NMR of 4-(thiomorpholin sulfonyl)phenethyl acetate (34)CDCl₃, 126 MHz, 298 K

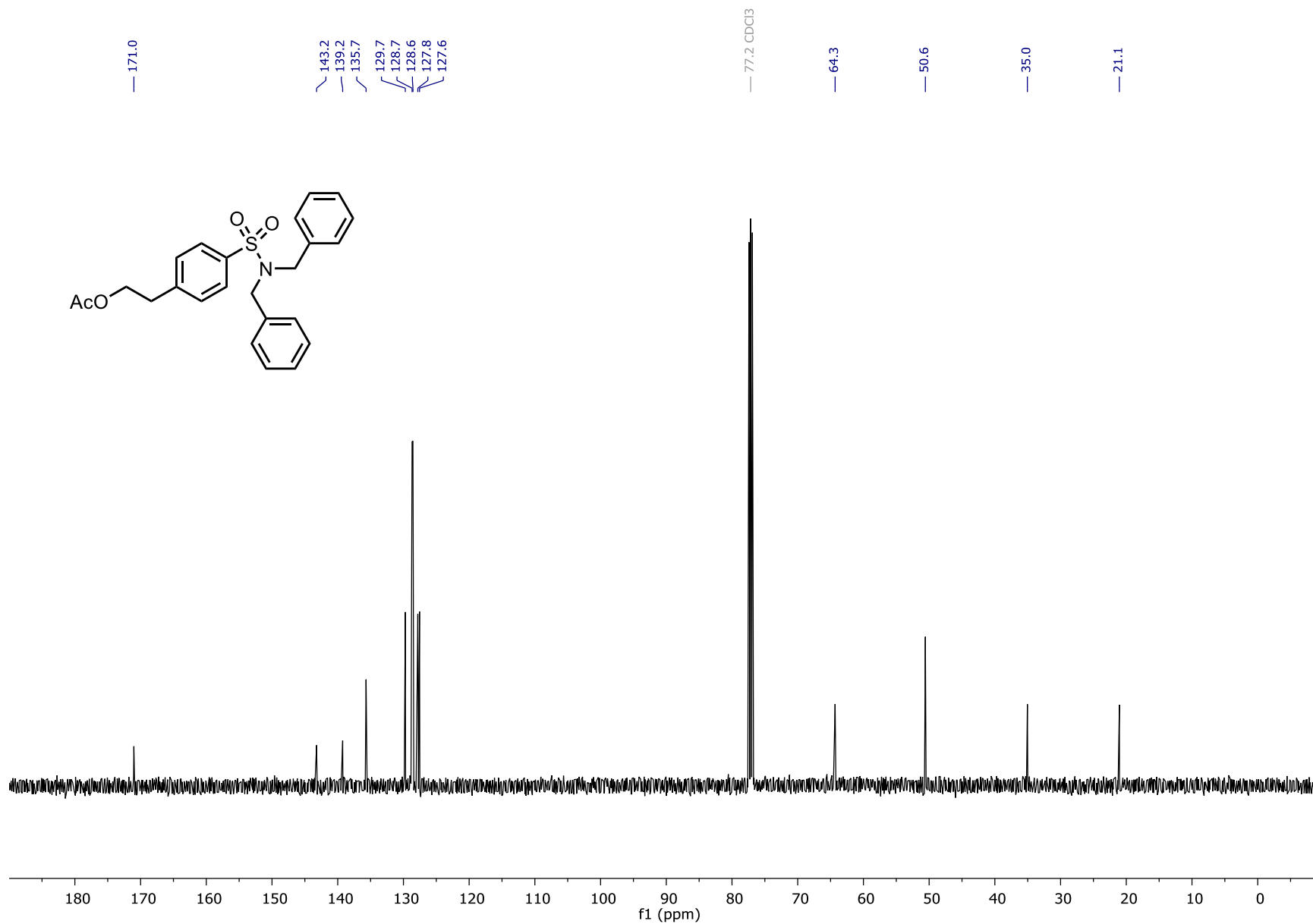
4-(N-(2-Methoxyethyl)-N-methylsulfonyl)phenethyl acetate (35)**¹H NMR of 4-(N-(2-methoxyethyl)-N-methylsulfonyl)phenethyl acetate (35)**CDCl₃, 500 MHz, 298 K

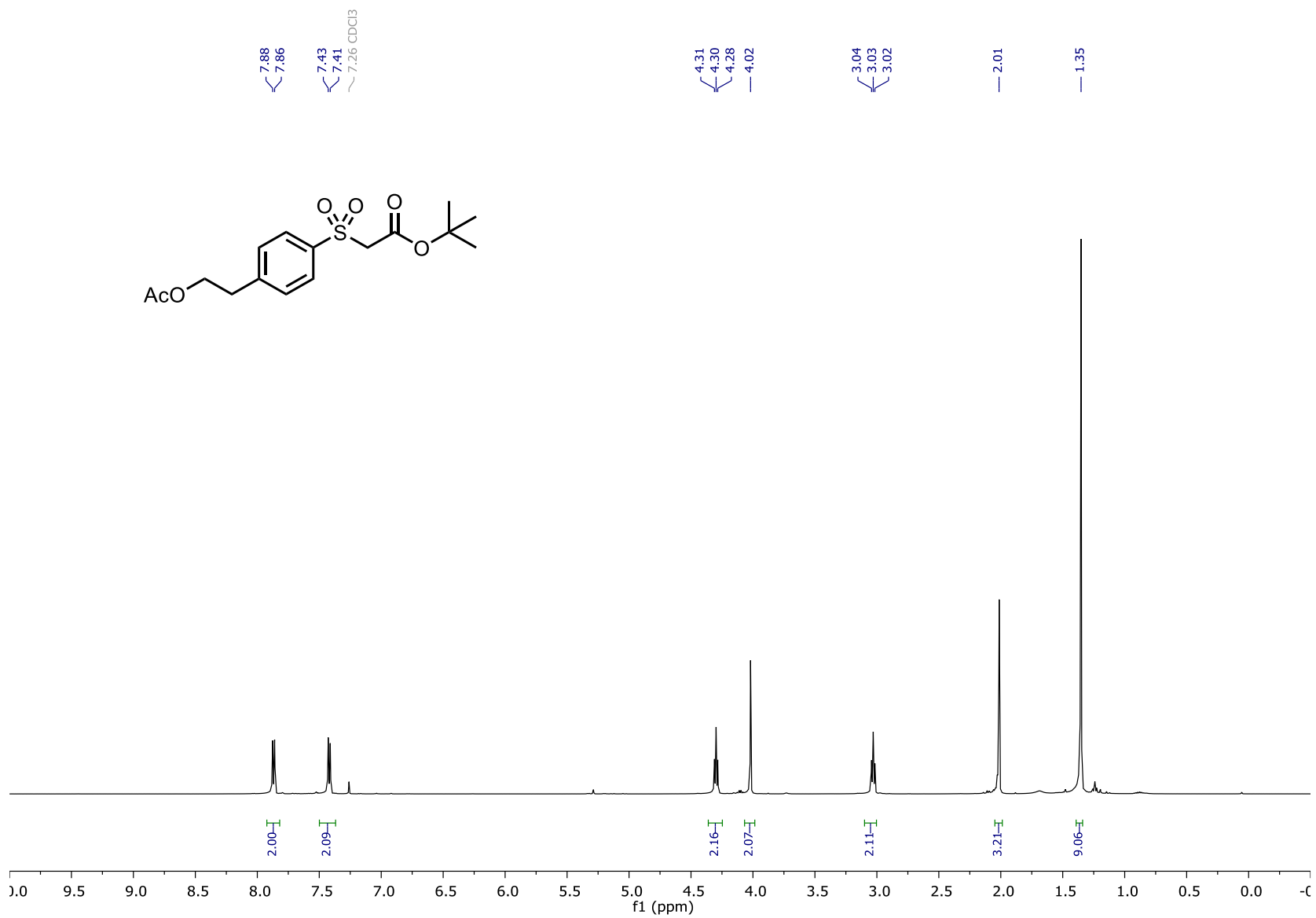
¹³C NMR of 4-(N-(2-methoxyethyl)-N-methylsulfonyl)phenethyl acetate (35)CDCl₃, 126 MHz, 298 K

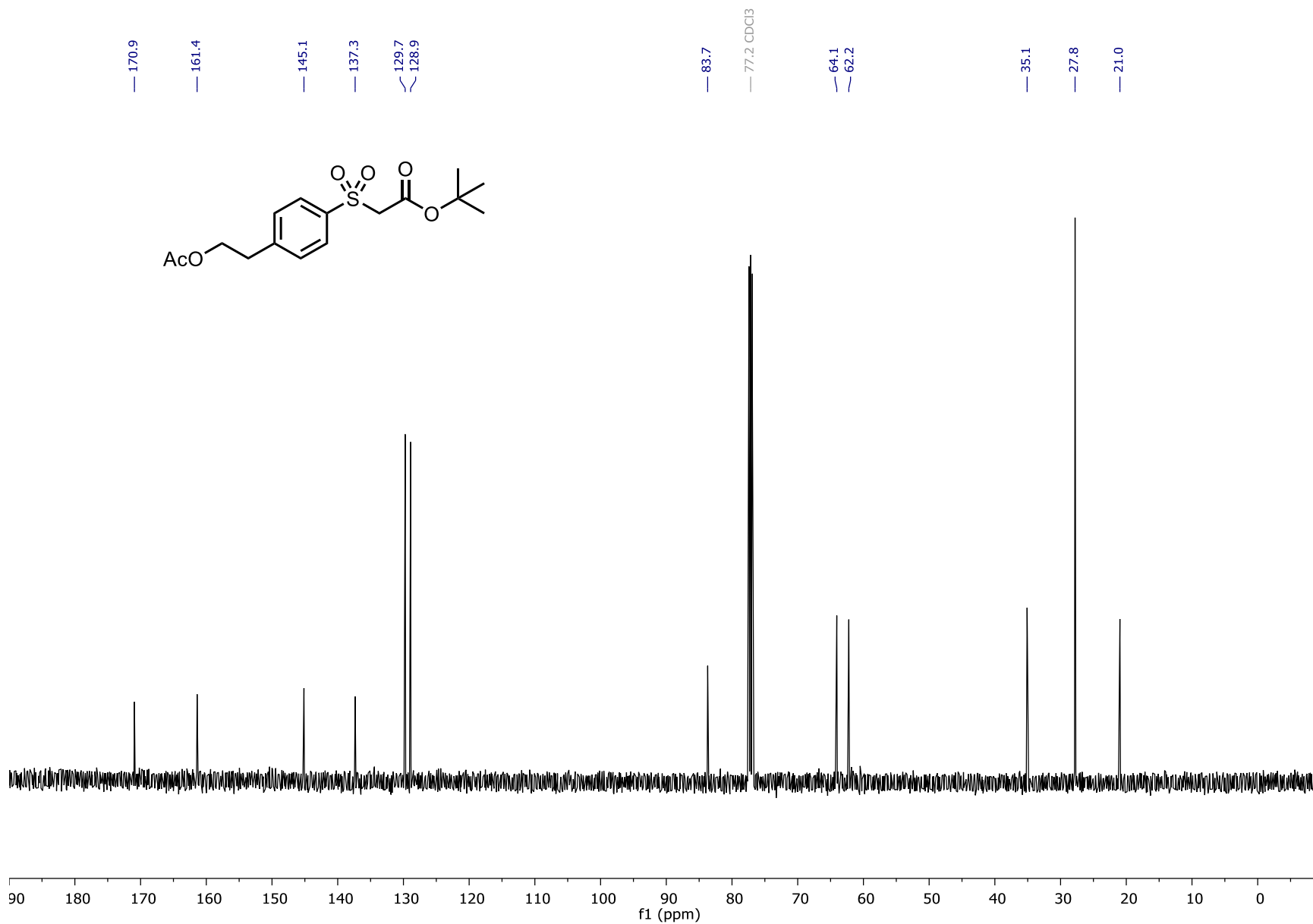
4-(N,N-Diethylsulfamoyl)phenethyl acetate (36)**¹H NMR of 4-(N,N-diethylsulfamoyl)phenethyl acetate (36)**CDCl₃, 500 MHz, 298 K

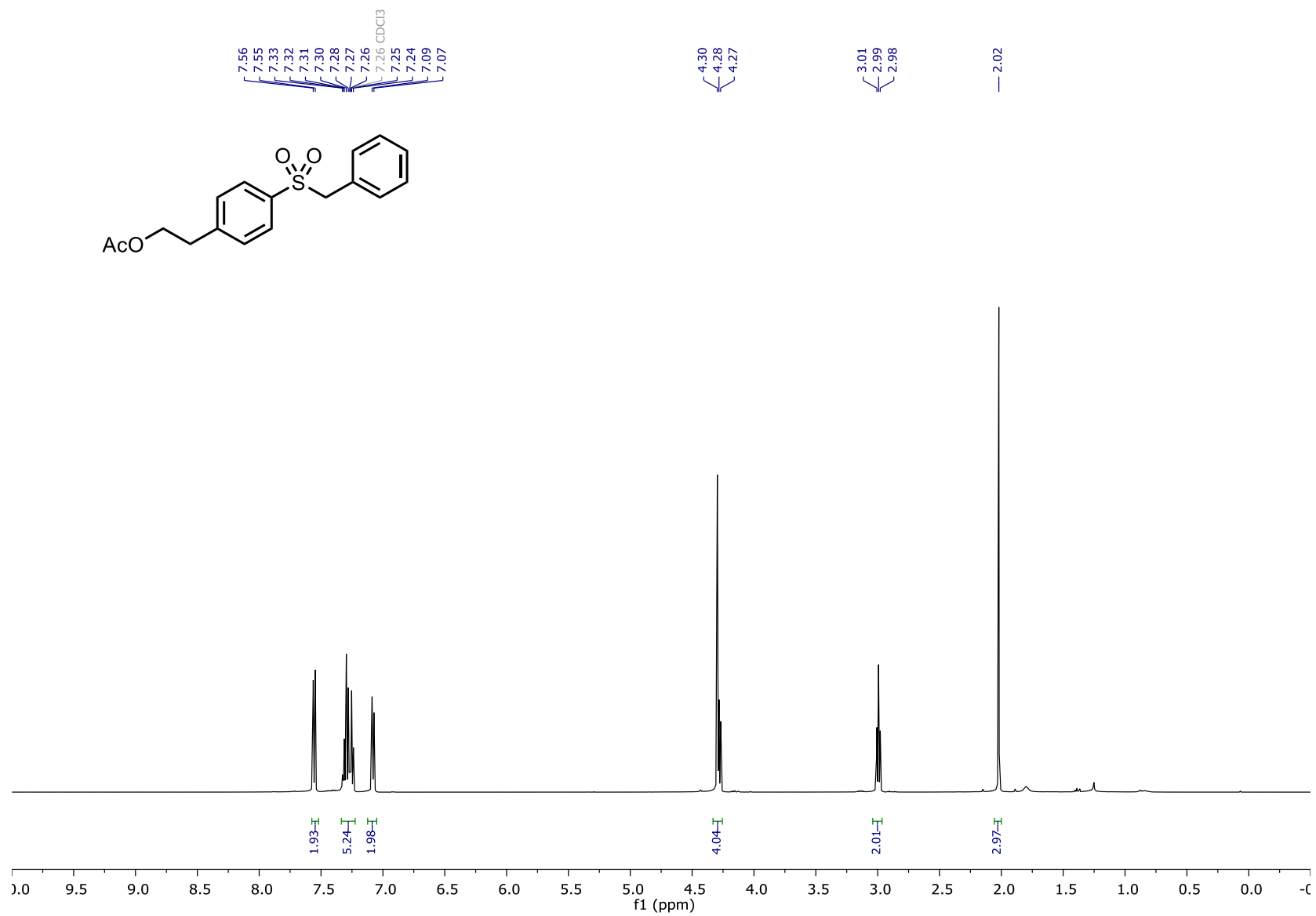
^{13}C NMR of 4-(N,N-diethylsulfamoyl)phenethyl acetate (36)CDCl₃, 126 MHz, 298 K

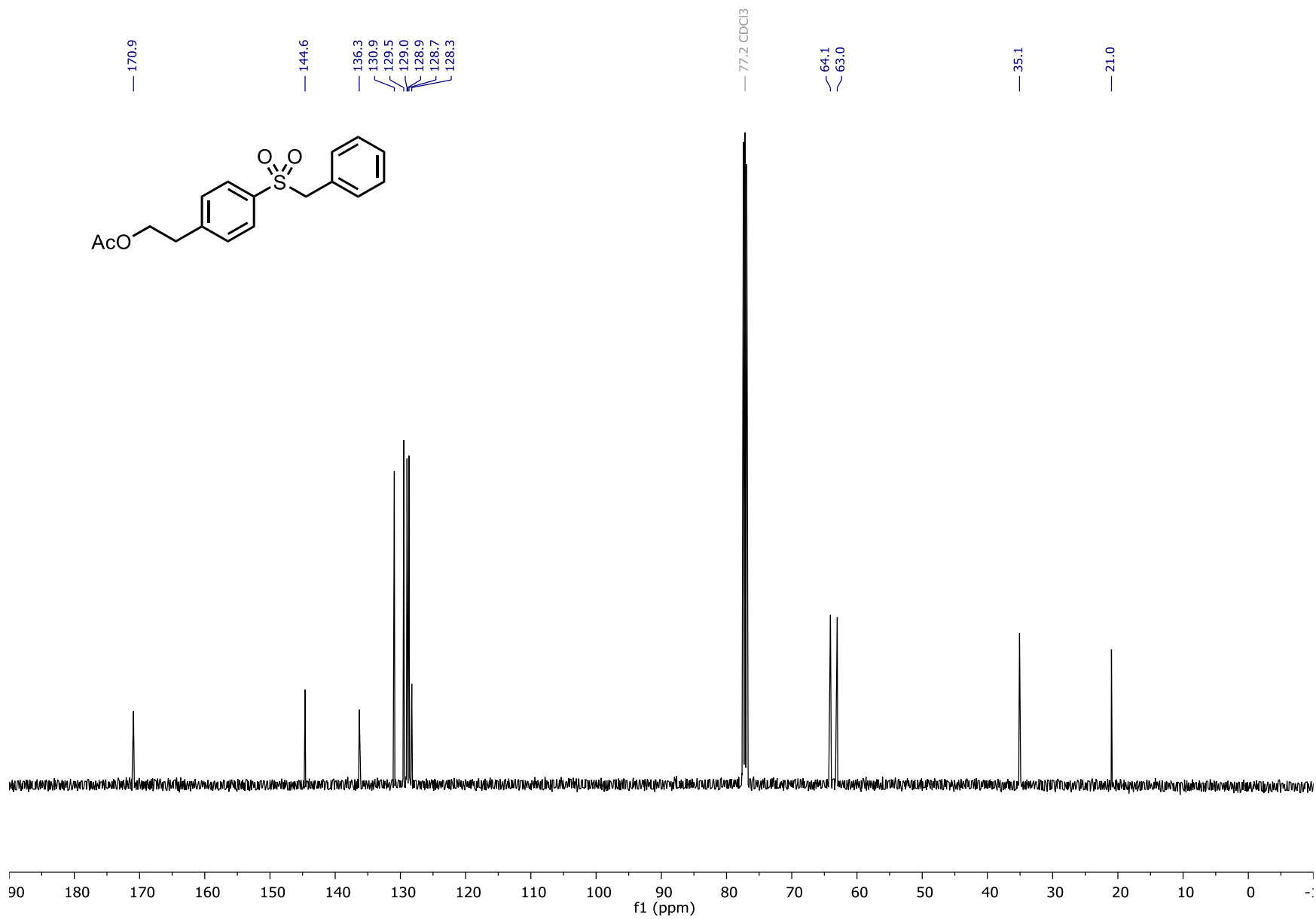
4-(N,N-Dibenzylsulfamoyl)phenethyl acetate (37)**¹H NMR of 4-(N,N-dibenzylsulfamoyl)phenethyl acetate (37)**CDCl₃, 500 MHz, 298 K

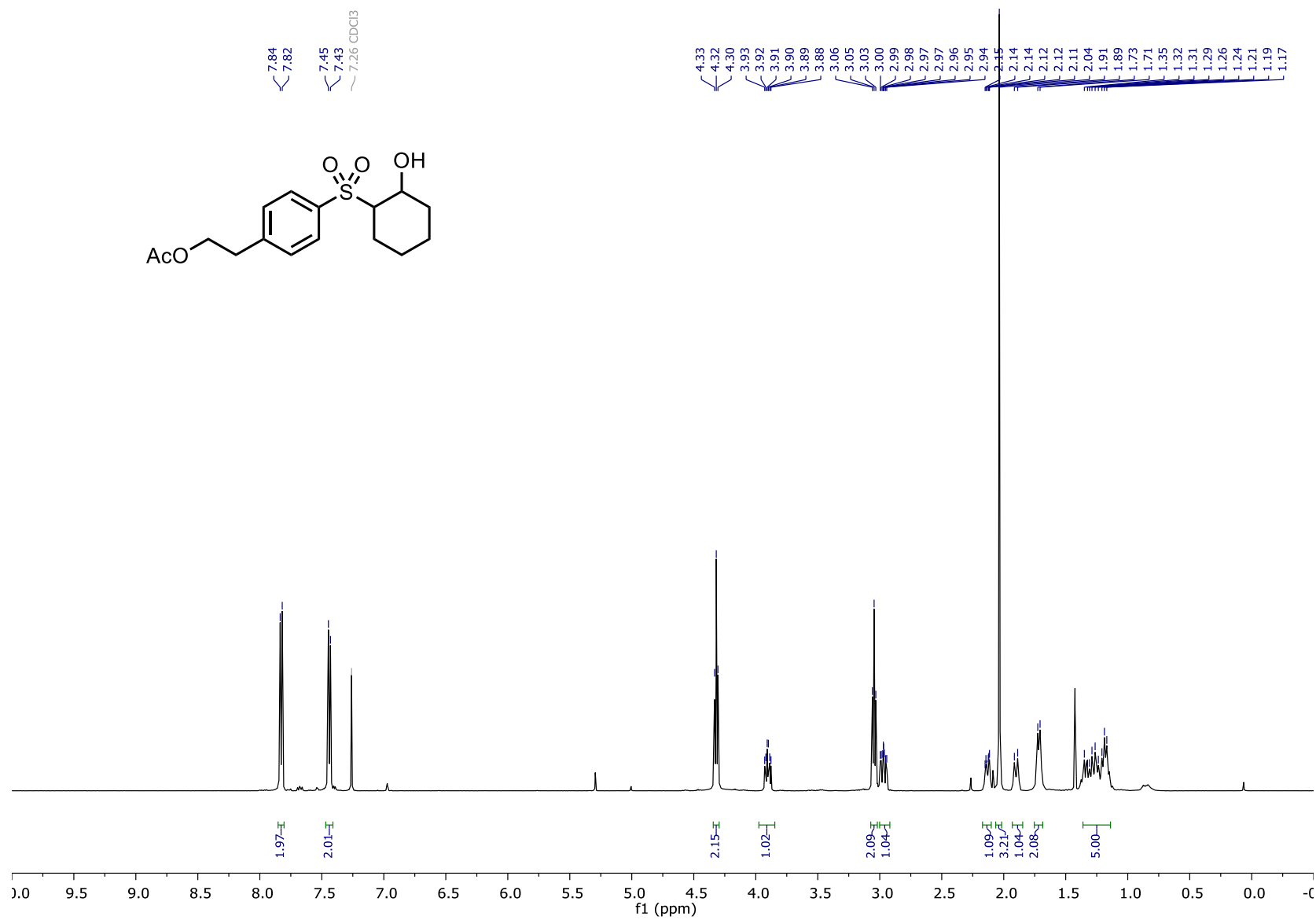
¹³C NMR of 4-(N,N-dibenzylsulfamoyl)phenethyl acetate (37)CDCl₃, 126 MHz, 298 K

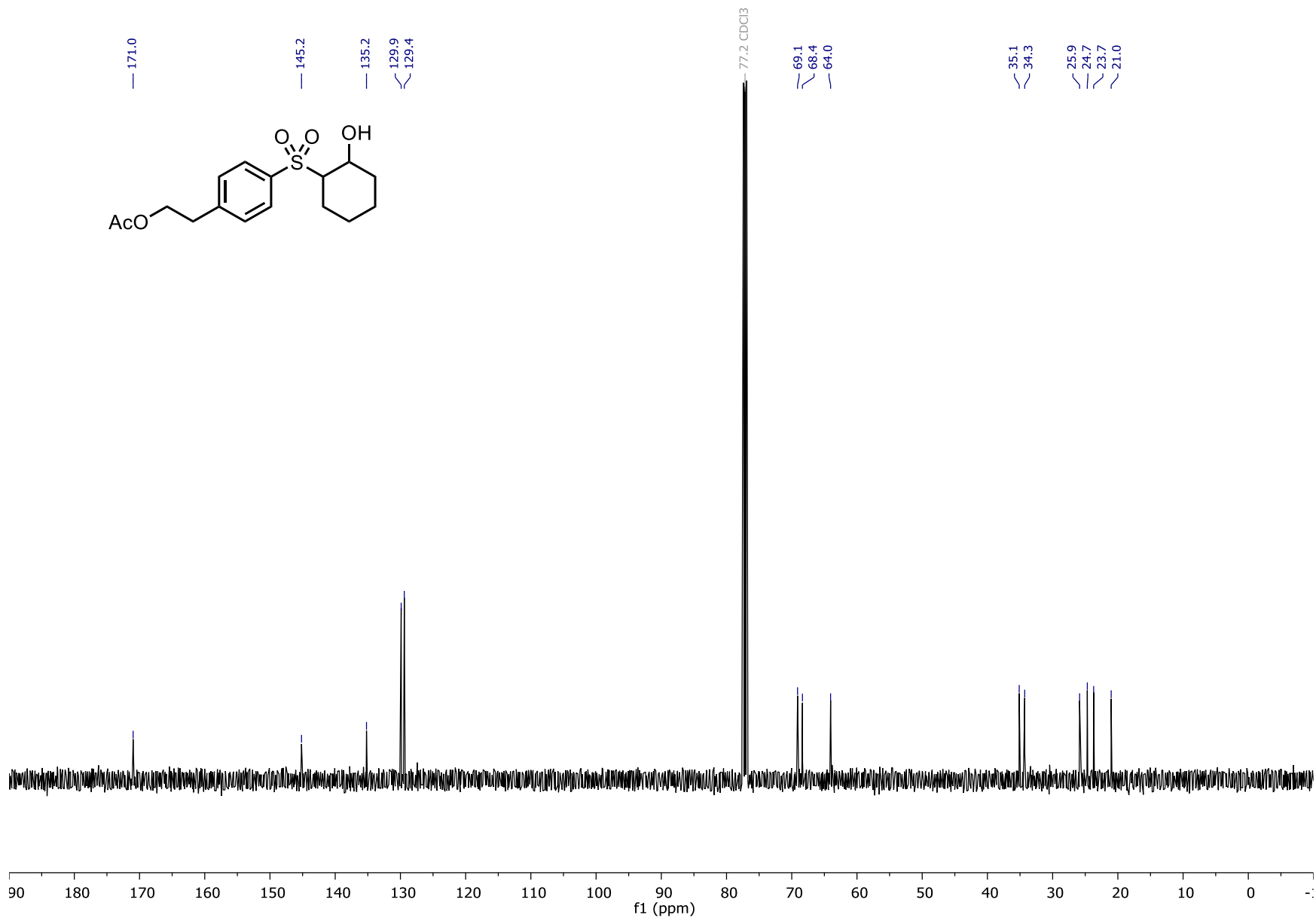
Tert-butyl 2-((4-(2-acetoxyethyl)phenyl)sulfonyl)acetate (38)**¹H NMR of tert-butyl 2-((4-(2-acetoxyethyl)phenyl)sulfonyl)acetate (38)**CDCl₃, 500 MHz, 298 K

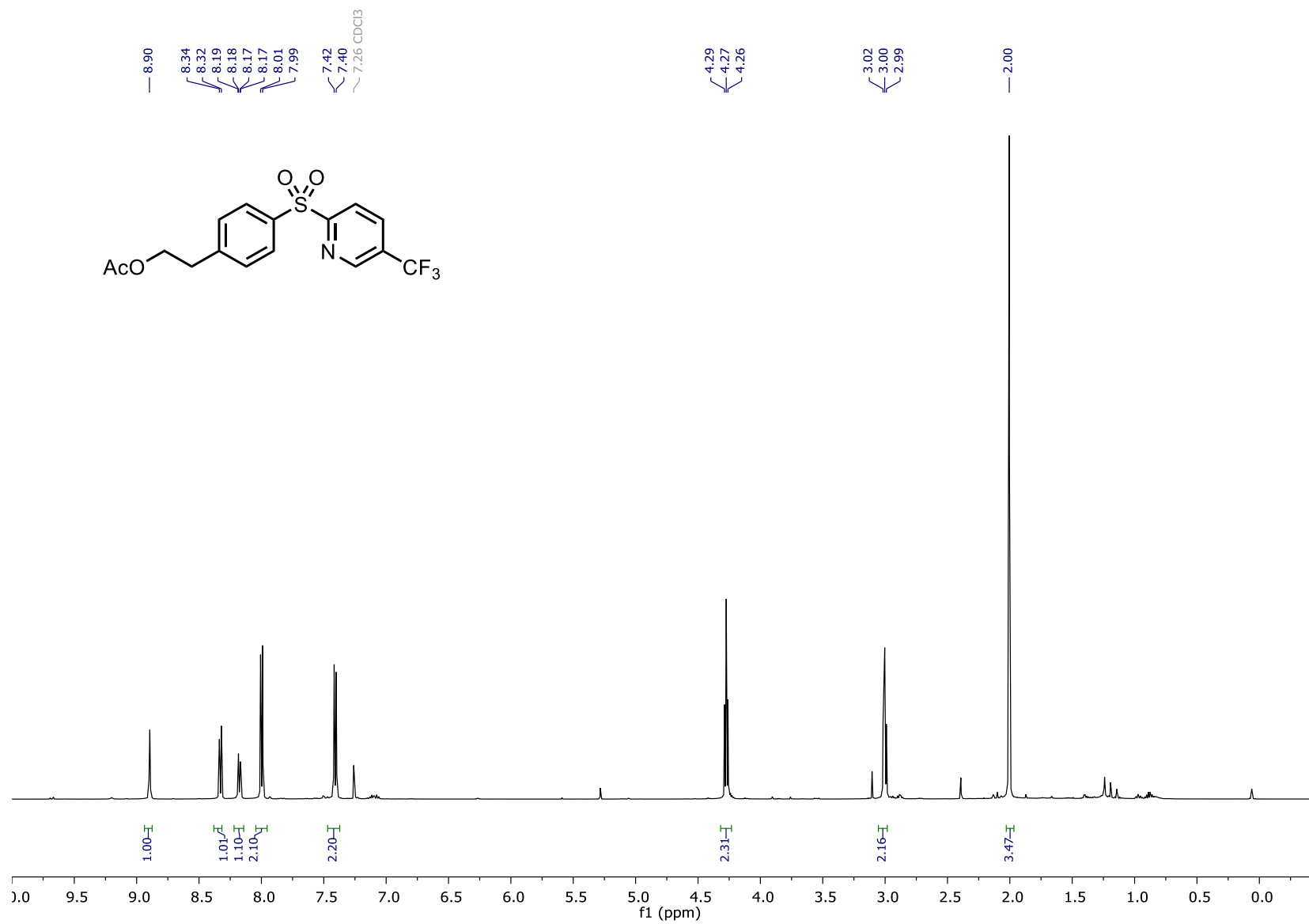
¹³C NMR of tert-butyl 2-((4-(2-acetoxyethyl)phenyl)sulfonyl)acetate (38)CDCl₃, 126 MHz, 298 K

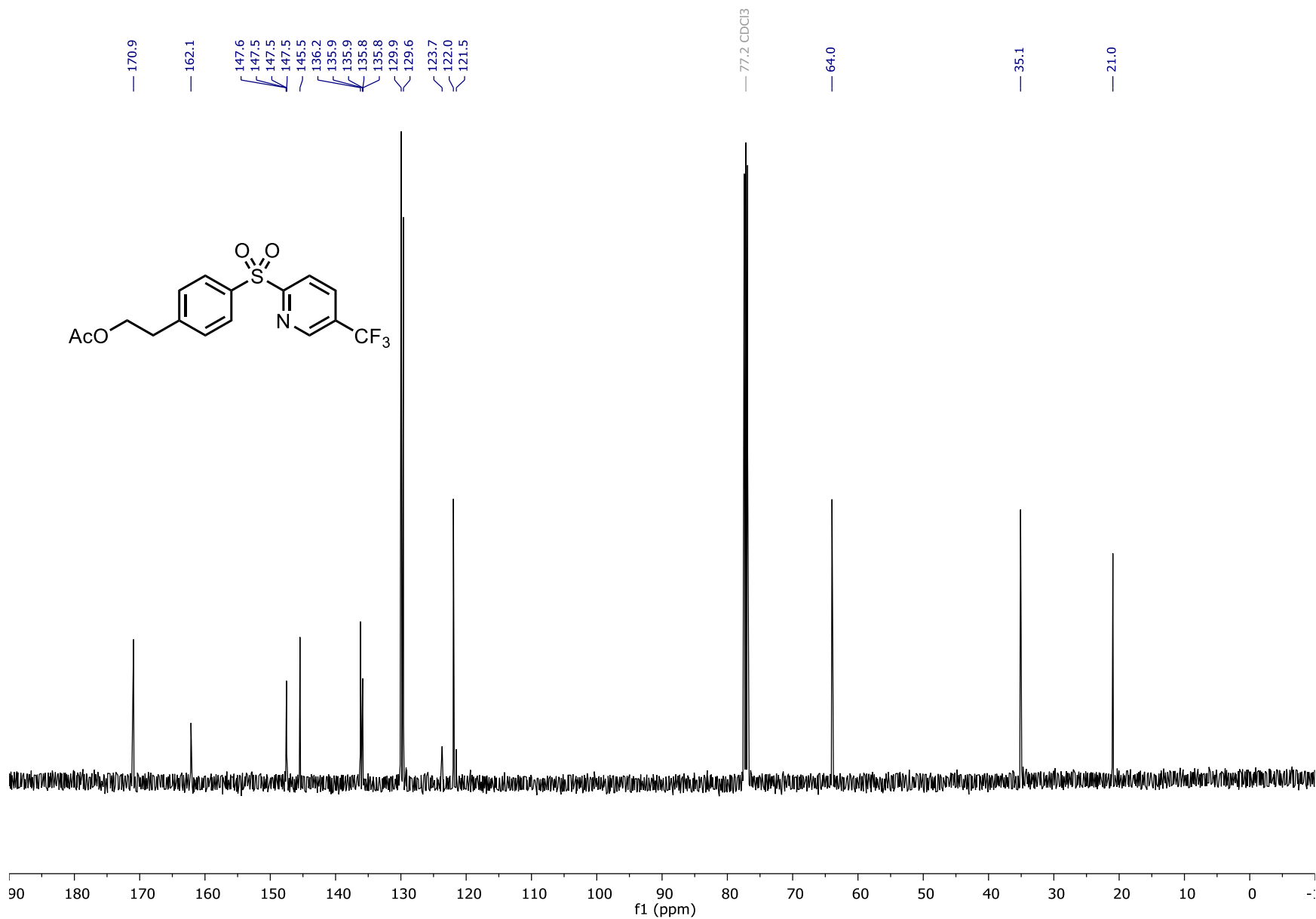
4-(Benzylsulfonyl)phenethyl acetate (39)**¹H NMR of 4-(benzylsulfonyl)phenethyl acetate (39)**CDCl₃, 500 MHz, 298 K

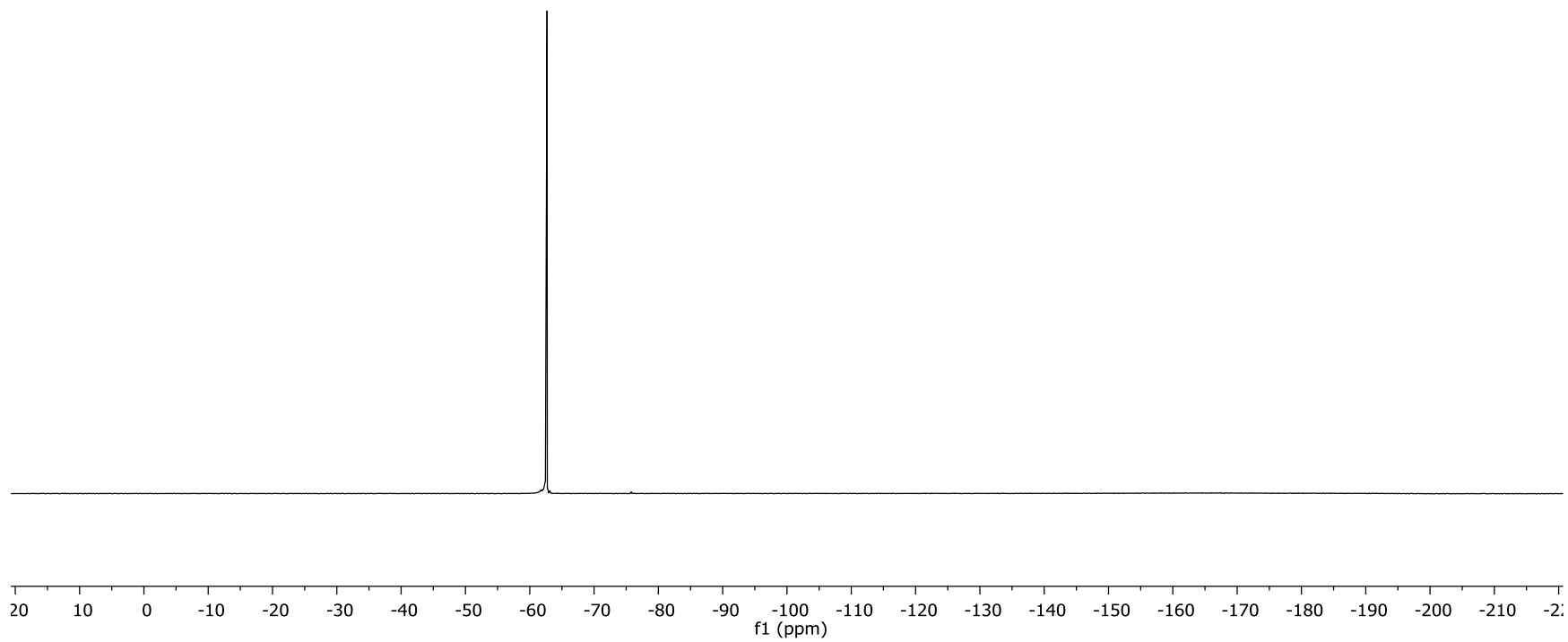
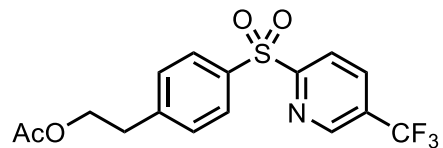
¹³C NMR of 4-(benzylsulfonyl)phenethyl acetate (39)CDCl₃, 126 MHz, 298 K

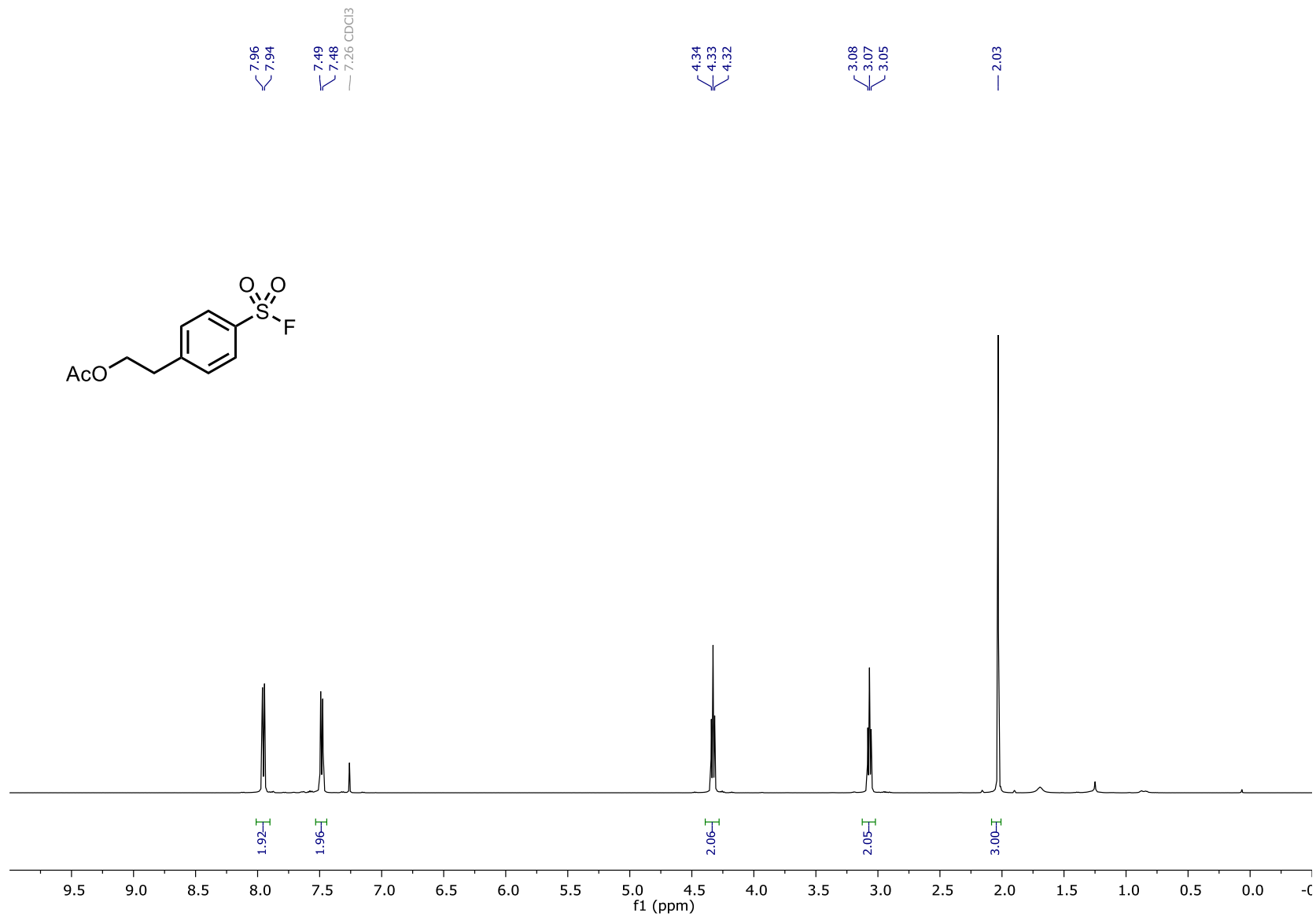
4-((2-Hydroxycyclohexyl)sulfonyl)phenethyl acetate (40)**¹H NMR of 4-((2-hydroxycyclohexyl)sulfonyl)phenethyl acetate (40)**CDCl₃, 500 MHz, 298 K

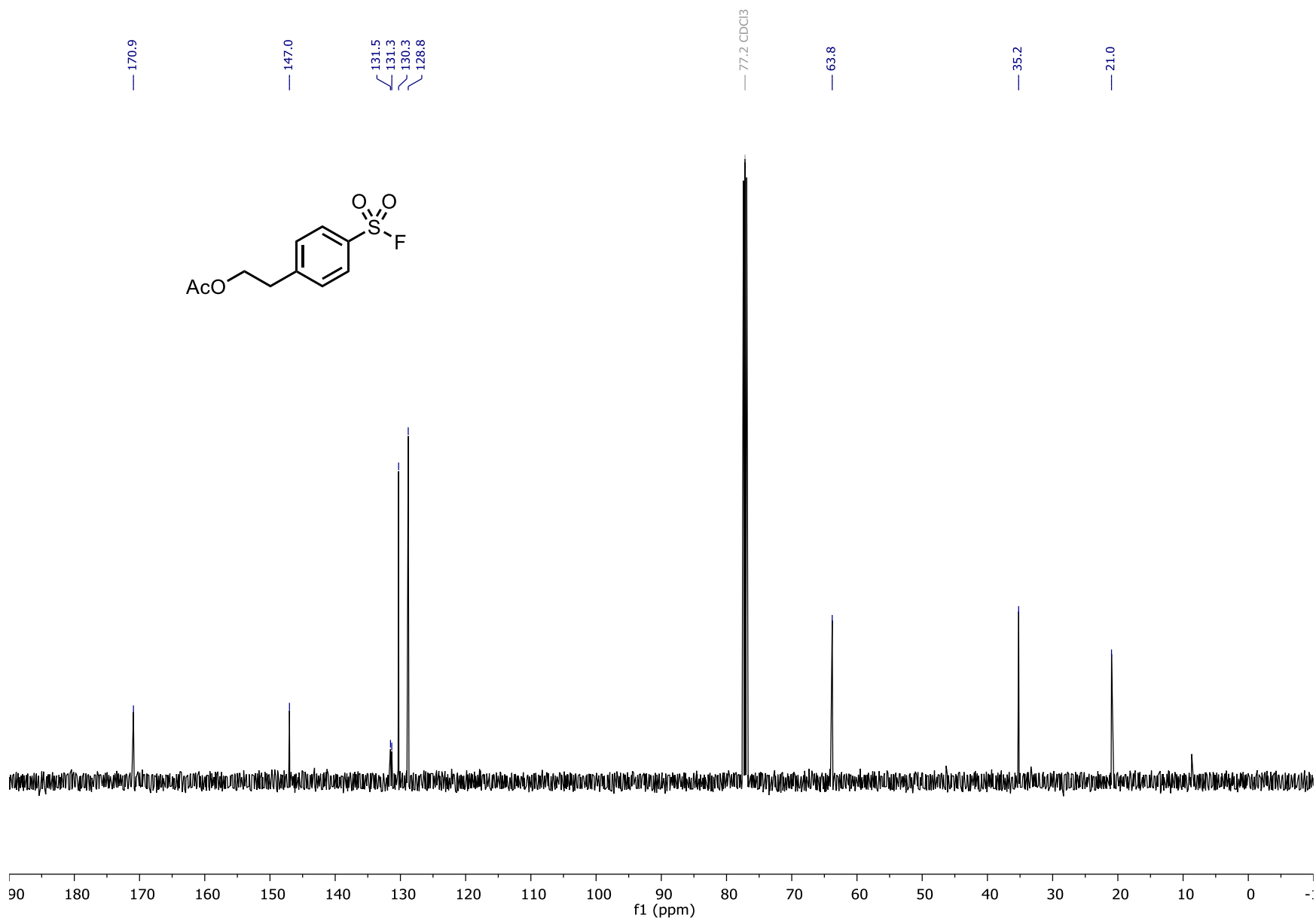
¹³C NMR of 4-((2-hydroxycyclohexyl)sulfonyl)phenethyl acetate (40)CDCl₃, 126 MHz, 298 K

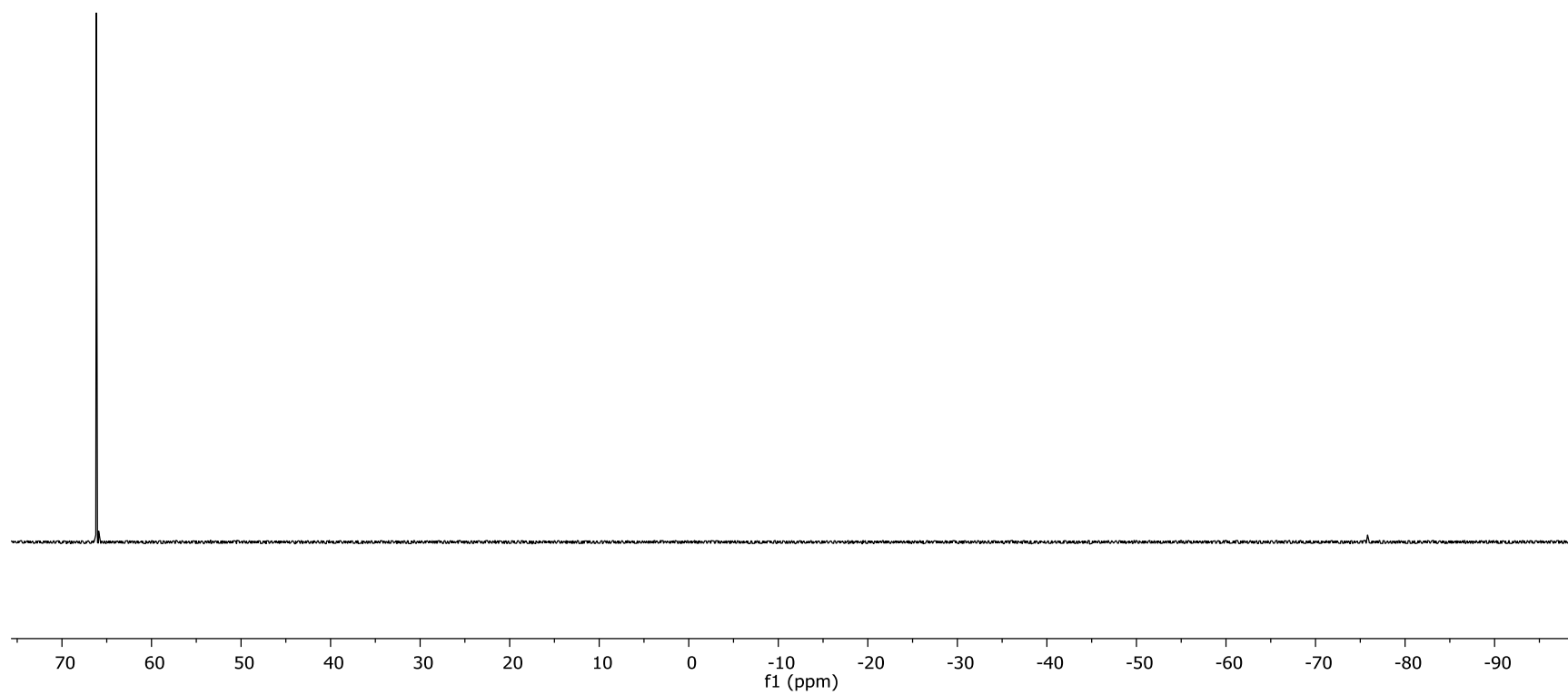
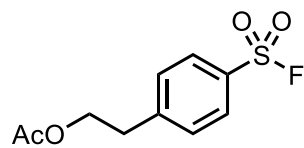
4-(N,N-4-((5-(Trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41)**¹H NMR of 4-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41)**CDCl₃, 500 MHz, 298 K

^{13}C NMR of 4-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41)CDCl₃, 126 MHz, 298 K

^{19}F NMR of 4-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)phenethyl acetate (41)CDCl₃, 471 MHz, 298 K

4-(Fluorosulfonyl)phenethyl acetate (42)**¹H NMR of 4-(fluorosulfonyl)phenethyl acetate (42)**CDCl₃, 500 MHz, 298 K

^{13}C NMR of 4-(fluorosulfonyl)phenethyl acetate (42)CDCl₃, 126 MHz, 298 K

^{19}F NMR of 4-(fluorosulfonyl)phenethyl acetate (42)CDCl₃, 471 MHz, 298 K

REFERENCES

- ¹ Berger, F.; Plutschack, M. B.; Riegger, J.; Yu, W.; Speicher, S.; Ho, M.; Frank, N.; Ritter, T. Site-selective and versatile aromatic C–H functionalization by thianthrenation. *Nature* **2019**, *567*, 223-228.
- ² Engl P. S.; Häring A. P.; Berger F.; Berger G.; Pérez-Bitrián A.; Ritter T. C-N Cross-Couplings for Site-Selective Late-Stage Diversification via Aryl Sulfonium Salts. *J. Am. Chem. Soc.* **2019**, *141*, 13346-13351.
- ³ Ye, F.; Berger, F.; Jia, H.; Ford, J.; Wortman, A.; Borgel, J.; Genicot, C.; Ritter, T. Aryl Sulfonium Salts for Site-Selective Late-Stage Trifluoromethylation. *Angew. Chem. Int. Ed.* **2019**, *58*, 14615-14619.
- ⁴ Sang, R.; Korkis, S.; Su, Wanqi.; Ye, F.; Engl, P.; Berger F.; Ritter, T. Site-Selective C-H Oxygenation via Aryl Sulfonium Salts. *Angew. Chem. Int. Ed.* **2019**, *58*, 16161-16166.
- ⁵ Li, J.; Chen, J.; Sang, R.; Ham, W-S.; Plutschack, M. B.; Berger, F.; Chhabra S.; Schnegg A.; Genicot C.; Ritter T. Photoredox catalysis with aryl sulfonium salts enables site-selective late-stage fluorination. *Nat. Chem.* **2020**, *12*, 56-62.