Strain-release C-C bond cleavage enables the [2,3]-sigmatropic rearrangement of tertiary allylamines

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Supporting information

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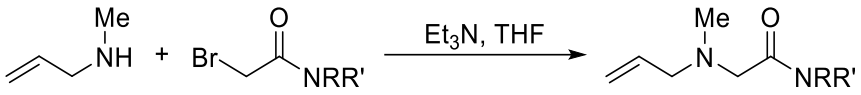
General information

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on 400, 100, and 376 MHz spectrometers, or on 500, 125, and 471 MHz spectrometers, respectively. The chemical shifts of ^{1}H NMR and ^{13}C NMR spectra were referenced internally with tetramethylsilane (δ H 0.00, δ C 0.0) or residual protio solvent signals $CDCl_3$ (δ C 77.2). The chemical shifts of ^{19}F NMR spectra were referenced to external $CFCl_3$. NMR multiplicities were abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. High resolution mass spectra (HRMS) were recorded on an LC-TOF spectrometer using electron spray ionization (ESI) techniques. High pressure liquid chromatography (HPLC) analyses were performed on an instrument equipped with an isostatic pump using a chiral column (OD-H, 250 × 4.6 mm) with isopropanol/hexane as mobile phase, and the UV detection was monitored at 254 nm. The chiral HPLC methods were calibrated with the corresponding racemic mixtures. Optical rotations were measured on a polarimeter with a sodium lamp at λ = 589 nm and reported as $[\alpha]_D^{T°C}$ (c = g/100 mL, solvent). Melting points are uncorrected. X-ray crystallography analysis of single crystals was performed on a Rigaku SuperNova single crystal X-ray diffractometer.

Allylamines **1a**-**y**[1] and 1-sulfonylbicyclo[1.1.0]butanes **2a**-**e**[2] were prepared according to literature procedures.

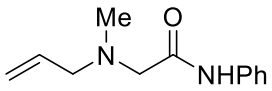
Abbreviations: Bn = benzyl, DCE = 1,2-dichloroethane, DMF = *N*,*N*-dimethylformamide, DMSO = dimethyl sulfoxide, EDCI = 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, Et = ethyl, HOBt = 1-hydroxybenzotriazole, Me = methyl, Ph = phenyl, Pr = propyl, THF = tetrahydrofuran.

Preparation of tertiary allylamines



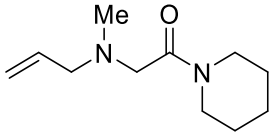
1f or **1g**

To a solution of *N*-allylmethylamine (356 mg, 5.0 mmol), triethylamine (556 mg, 0.76 mL, 5.5 mmol) in THF (10 mL) at room temperature was added the alkyl halide (5.0 mmol). The mixture was stirred for 14 h, filtered, and concentrated. The resulting residue was subjected to silica gel chromatography, using a mixture of ethyl acetate and petroleum ether (1:10~1:4) as the eluent, to give a tertiary allylamine product.



1f

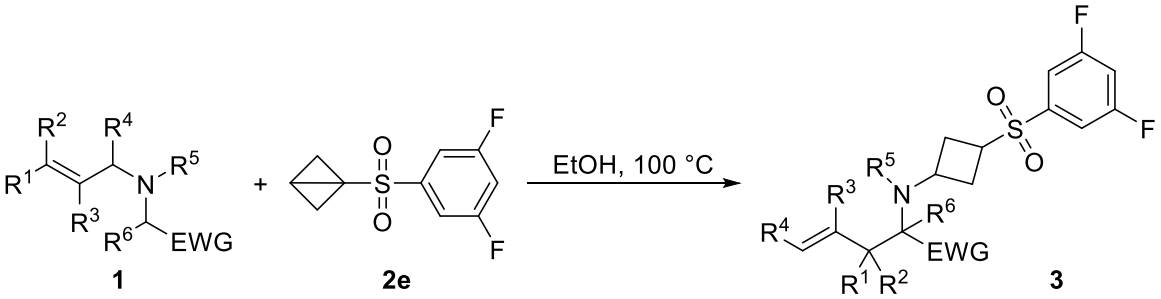
2-(Allyl(methyl)amino)-*N*-phenylacetamide (**1f**). Colorless oil (541 mg, 53% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (br, s, 1H), 7.60-7.57 (m, 2H), 7.35-7.31 (m, 2H), 7.13-7.08 (m, 1H), 5.93-5.83 (m, 1H), 5.29-5.21 (m, 2H), 3.18-3.15 (m, 4H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 137.8, 134.3, 129.1, 124.3, 119.6, 119.1, 60.9, 60.9, 43.3; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{12}H_{17}ON_2$ 205.1335; Found 205.1329.



1g

2-(Allyl(methyl)amino)-1-(piperidin-1-yl) ethan-1-one (**1g**). Yellow oil (638 mg, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.90-5.82 (m, 1H), 5.22-5.13 (m, 2H), 3.54-3.48 (m, 4H), 3.17 (s, 2H), 3.06-3.05 (m, 2H), 2.28 (s, 3H), 1.66-1.61 (m, 2H), 1.58-1.51 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 135.4, 118.0, 60.8, 60.1, 46.8, 43.0, 42.5, 26.6, 25.8, 24.7; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{11}H_{21}ON_2$ 197.1648; Found 197.1644.

General procedure for the 1-sulfonylbicyclo[1.1.0]butane-mediated [2,3]-sigmatropic rearrangement of tertiary allylamines

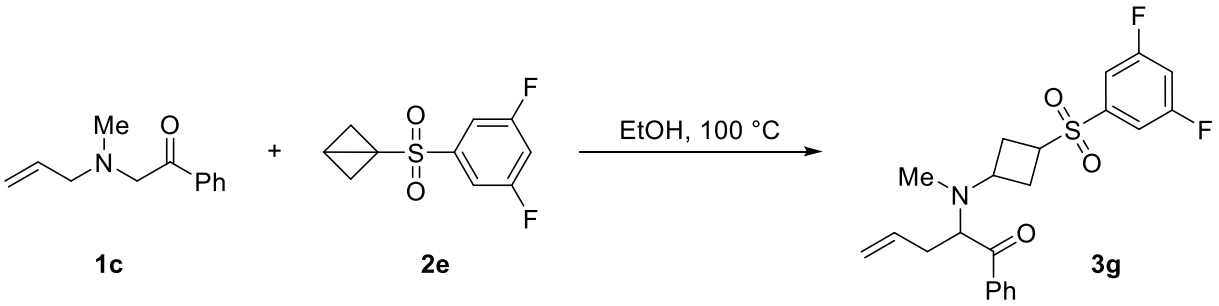


1 **2e** **3**

To a stirred solution of allylamine **1** (0.20 mmol) in ethanol (1.0 mL) was added bicyclo[1.1.0]butane **2e** (55.2 mg, 0.24 mmol). The mixture was stirred in a sealed tube at 100 ˚C (oil bath) for 20 h. The mixture was concentrated and purified by silica gel chromatography, using a mixture of ethyl acetate and petroleum ether (1:2 to 1:10) as the eluent, to give homoallylic amine **3**.

Except compounds **3e**, **3i**, **3j**, **3k**, **3o**, **3p**, **3t**, and **3aa-ac**, the products were obtained as a mixture of *cis*- and *trans*-isomers and their ratios were determined by ^{1}H NMR spectroscopic analysis. The relative stereochemistry of compounds *cis*-**3o** and *trans*-**3o** was assigned by single crystal X-ray analysis (see below), and that of the rest of the products was assigned by analogy.

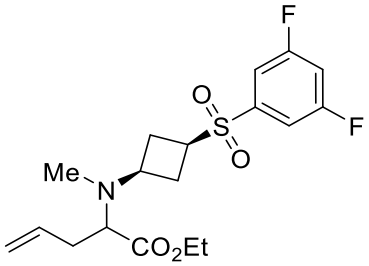
A 2-mmol scale reaction



1c **2e** **3g**

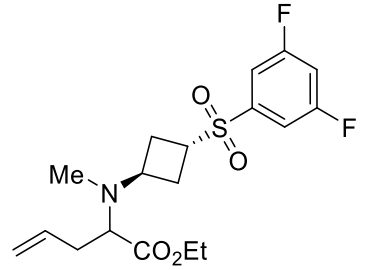
To a stirred solution of allylamine **1c** (379 mg, 2.0 mmol) in ethanol (10 mL) was added bicyclo[1.1.0]butane **2e** (552 mg, 2.4 mmol). The mixture was stirred in a sealed tube at 100 ˚C (oil bath) for 20 h. The mixture was concentrated and purified by silica gel chromatography, using a mixture of ethyl acetate and petroleum ether (1:5) as the eluent, to give homoallylic amine **3g** as a brown oil (747 mg, 89%).

Analytical data for the products (Table 2 and Scheme 2)



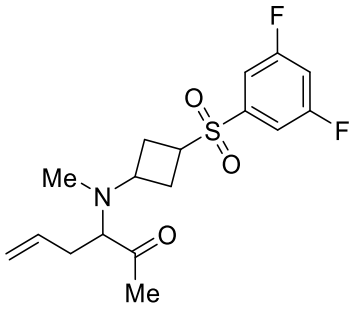
cis-**3e**

(*cis*)-Ethyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)pent-4-enoate (*cis*-**3e**). Colorless oil (17.6 mg, 23% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.39 (m, 2H), 7.13-7.08 (m, 1H), 5.80-5.70 (m, 1H), 5.12-5.03 (m, 2H), 4.13 (q, J = 7.2 Hz, 2H), 3.46-3.38 (m, 1H), 3.28-3.18 (m, 2H), 2.53-2.41 (m, 3H), 2.39-2.26 (m, 3H), 2.24 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 163.0 (dd, J = 254.2, 11.2 Hz), 141.8 (t, J = 8.0 Hz), 134.5, 117.3, 111.9 (dd, J = 19.6, 8.3 Hz), 109.5 (t, J = 24.8 Hz), 62.7, 60.4, 51.9, 50.4, 34.0, 32.1, 29.4, 29.0, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{18}H_{24}F_2NO_4S$ 388.1389; Found 388.1387.



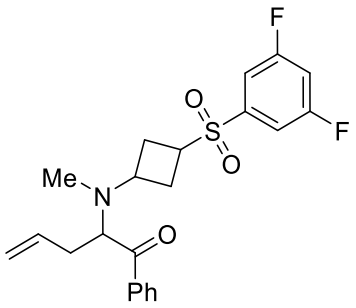
trans-**3e**

(*trans*)-Ethyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)pent-4-enoate (*trans*-**3e**). Colorless oil (47.5 mg, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.42 (m, 2H), 7.14-7.09 (m, 1H), 5.79-5.68 (m, 1H), 5.13-5.03 (m, 2H), 4.23-4.10 (m, 2H), 3.68-3.58 (m, 2H), 3.28 (t, J = 8.0 Hz, 1H), 2.65-2.54 (m, 2H), 2.53-2.47 (m, 1H), 2.37-2.30 (m, 3H), 2.21 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 163.0 (dd, J = 254.4, 11.3 Hz), 141.5 (t, J = 7.7 Hz), 134.4, 117.5, 112.1 (dd, J = 19.6, 8.3 Hz), 109.5 (t, J = 24.8 Hz), 62.1, 60.6, 54.8, 52.9, 33.6, 32.1, 28.7, 28.3, 14.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{18}H_{24}F_2NO_4S$ 388.1389; Found 388.1383.



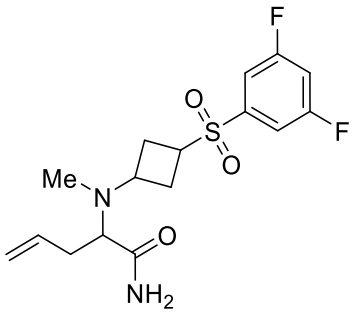
cis/trans-**3f**

(*cis*/*trans*)-3-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)hex-5-en-2-one, (inseparable mixture of *cis*-**3f** and *trans*-**3f**, *cis*/*trans* = 27:73). Colorless oil (44.3 mg, 62% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.42 (m, 2H), 7.15-7.10 (m, 1H), 5.76-5.68 (m, 1H), 5.09-5.00 (m, 2H), 3.73-3.65 (m, 1.5H), 3.47-3.40 (m, 0.3H), 3.27-3.21 (m, 1.2 H), 2.65-2.58 (m, 1.7H), 2.51-2.27 (m, 4H), 2.20-2.13 (m, 6.3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.5, 163.1 (dd, J = 254.4, 11.4 Hz), 163.0 (dd, J = 254.4, 11.4 Hz), 141.8 (t, J = 7.9 Hz), 141.4 (t, J = 6.7 Hz), 135.4, 135.3, 117.4, 117.2, 112.0 (dd, J = 20.8, 7.4 Hz), 111.8 (dd, J = 20.8, 7.3 Hz), 109.6 (t, J = 25.0 Hz), 109.5 (t, J = 25.0 Hz), 68.9, 68.2, 66.4, 54.6, 52.8, 51.6, 50.2, 32.8, 32.5, 31.2, 29.4, 29.3, 29.1, 28.9. 28.6, 28.5; ^{19}F NMR (471 MHz, $CDCl_3$) δ -104.7, -104.8; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{17}H_{22}F_2NO_3S$ 358.1283; Found 358.1279.



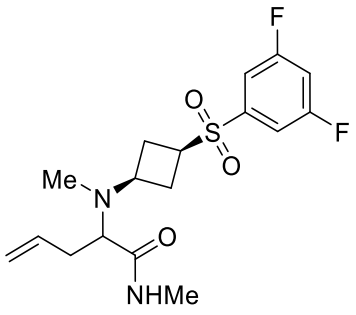
cis/trans-**3g**

(*cis*/*trans*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-1-phenylpent-4-en-1-one (inseparable mixture of *cis*-**3g** and *trans*-**3g**, *cis/trans* = 24:76). Brown oil (82.2 mg, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.90 (m, 2H), 7.60-7.54 (m, 1H), 7.49-7.44 (m, 2H), 7.42-7.36 (m, 2H), 7.13-7.06 (m, 1H), 5.79-5.69 (m, 1H), 5.12-4.99 (m, 2H), 4.26-4.21 (m, 1H), 3.72-3.66 (m, 0.8H), 3.62-3.55 (m, 0.8H), 3.41-3.25 (m, 0.2H), 3.31-3.25 (m, 0.2H), 2.70-2.58 (m, 1.3H), 2.56-2.44 (m, 2H), 2.42-2.32 (m, 2.7H), 2.31 (s, 0.8H), 2.21 (s, 2.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 199.0, 163.0 (dd, J = 254.4, 11.3 Hz), 141.8 (t, J = 7.9 Hz), 141.4 (t, J = 8.0 Hz), 137.4, 137.2, 135.1, 135.0, 133.3, 128.8, 128.8, 128.5, 128.4, 117.7, 117.5, 112.1 (dd, J = 19.7, 8.2 Hz), 111.8 (d, J = 7.9 Hz), 109.6 (t, J = 24.8 Hz), 109.5 (t, J = 24.7 Hz), 64.2, 63.4, 54.8, 53.0, 51.2, 50.5, 32.8, 32.1, 30.7, 30.3, 29.4, 29.0, 28.7, 28.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.8, -104.8; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{22}H_{24}F_2NO_3S$ 420.1440; Found 420.1437.



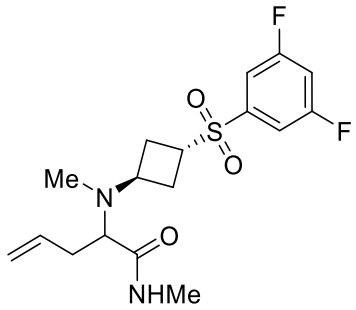
cis/trans-**3h**

(*cis*/*trans*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)pent-4-enamide (inseparable mixture of *cis*-**3h** and *trans*-**3h**, *cis*/*trans* = 45:55). Yellow oil (50.9 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.41 (m, 2H), 7.16-7.10 (m, 1H), 6.98 + 6.89 (s, 1H), 6.14 + 6.03 (s, 1H), 5.92-5.80 (m, 1H), 5.15-5.00 (m, 2H), 3.78-3.66 (m, 1H), 3.52-3.43 (m, 0.6H), 3.36-3.30 (m, 0.4H), 3.28-3.21 (m, 1 H), 2.72-2.57 (m, 2H), 2.47-2.28 (m, 4H), 2.25 + 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 174.7, 163.0 (dd, J = 254.4, 11.3 Hz), 163.0 (dd, J = 254.4, 11.3 Hz), 141.6 (t, J = 7.8 Hz), 141.2 (t, J = 7.8 Hz), 136.5, 136.0, 117.2, 117.0, 112.0 (dd, J = 19.6, 8.4 Hz), 111.8 (dd, J = 19.7, 8.3 Hz), 109.6 (t, J = 24.8 Hz), 109.6 (t, J = 24.8 Hz), 63.4, 63.2, 54.5, 52.6, 51.7, 50.1, 33.0, 32.9, 30.4, 29.2, 28.9, 28.7, 28.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.5, -104.6; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{16}H_{21}F_2N_2O_3S$ 359.1236; Found 359.1240.



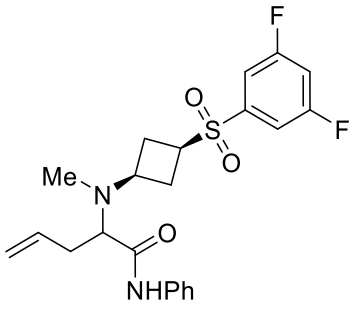
cis-**3i**

(*cis*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-*N*-methylpent-4-enamide (*cis*-**3i**). Colorless oil (32.7 mg, 44% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.38 (m, 2H), 7.16-7.09 (m, 2H), 5.92-5.81 (m, 1H), 5.12-5.00 (m, 2H), 3.51-3.42 (m, 1H), 3.38-3.32 (m, 1H), 3.23 (s, 1H), 2.84 (d, J = 5.2 Hz, 3H), 2.78-2.70 (m, 1H), 2.48-2.27 (m, 5H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 163.0 (dd, J = 254.6, 11.4 Hz), 141.6 (t, J = 7.8 Hz), 136.7, 117.0, 111.8 (dd, J = 19.6, 8.3 Hz), 109.7 (t, J = 24.8 Hz), 63.4, 51.8, 50.1, 33.0, 30.7, 29.3, 29.0, 26.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.6; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{17}H_{23}F_2N_2O_3S$ 373.1392; Found 373.1385.



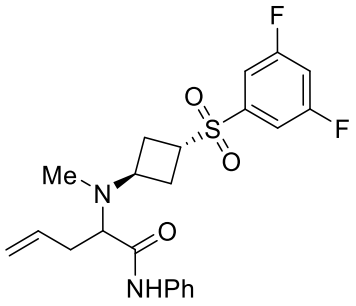
trans-**3i**

(*trans*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-*N*-methylpent-4-enamide (*trans*-**3i**). Colorless oil (15 mg, 20%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.42 (m, 2H), 7.14-7.10 (m, 1H), 6.93 (br, 1H), 5.92-5.84 (m, 1H), 5.13-5.04 (m, 2H), 3.74-3.68 (m, 1H), 3.68-3.62 (m, 1H), 3.16 (t, J = 6.5 Hz, 1H), 2.81 (d, J = 5.0 Hz, 3H), 2.74-2.68 (m, 1H), 2.64-2.56 (m, 2H), 2.33-2.23 (m, 3H), 2.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 163.1 (dd, J = 254.5, 11.1 Hz), 141.4 (t, J = 7.9 Hz), 136.7, 117.0, 112.1 (dd, J = 20.9, 7.4 Hz), 109.7 (t, J = 24.8 Hz), 63.5, 54.5, 52.7, 33.0, 30.6, 28.9, 28.3, 26.1; ^{19}F NMR (471 MHz, $CDCl_3$) δ -104.7; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{17}H_{23}F_2N_2O_3S$ 373.1392; Found 373.1416.



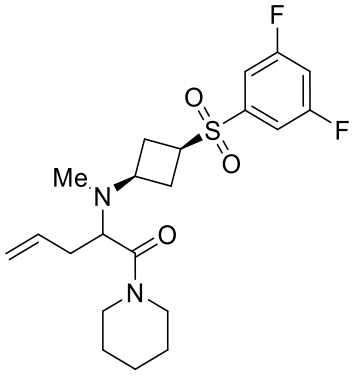
cis-**3j**

(*cis*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-*N*-phenylpent-4-enamide (*cis*-**3j**). Yellow oil (22.8 mg, 26% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (br, s, 1H), 7.63-7.59 (m, 2H), 7.43-7.38 (m, 2H), 7.37-7.32 (m, 2H), 7.14-7.07 (m, 2H), 5.97-5.87 (m, 1H), 5.16-5.03 (m, 2H), 3.55-3.47 (m, 1H), 3.41-3.37 (m, 2H), 2.86-2.79 (m, 1H), 2.56-2.48 (m, 2H), 2.46-2.35 (m, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 163.1 (dd, J = 254.8, 11.4 Hz), 141.6 (t, J = 7.8 Hz), 137.8, 136.6, 129.1, 124.3, 119.7, 117.2, 111.9 (dd, J = 19.7, 8.4 Hz), 109.7 (t, J = 24.9 Hz), 64.1, 51.8, 50.2, 33.2, 30.3, 29.0, 28.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.5; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{22}H_{25}F_2N_2O_3S$ 435.1549; Found 435.1548.



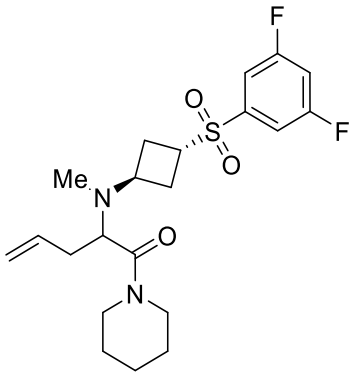
trans-**3j**

(*trans*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-*N*-phenylpent-4-enamide (*trans*-**3j**). Yellow oil (42.4 mg, 49% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (br, 1H), 7.53-7.50 (m, 2H), 7.47-7.43 (m, 2H), 7.34-7.30 (m, 2H), 7.14-7.08 (m, 2H), 6.00-5.88 (m, 1H), 5.18-5.08 (m, 2H), 3.83-3.75 (m, 1H), 3.72-3.65 (m, 1H), 3.32 (t, J =6.8 Hz 1H), 2.82-2.75 (m, 1H), 2.69-2.60 (m, 2H), 2.40-2.31 (m, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 163.1 (dd, J = 254.5, 11.2 Hz), 141.2 (t, J = 7.8 Hz), 137.6, 136.4, 129.1, 124.3, 119.6, 117.3, 112.0 (dd, J = 19.6, 8.3 Hz), 109.7 (t, J = 24.8 Hz), 64.2, 54.5, 52.6, 33.3, 30.0, 29.0, 28.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.6; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{22}H_{25}F_2N_2O_3S$ 435.1549; Found 435.1544.



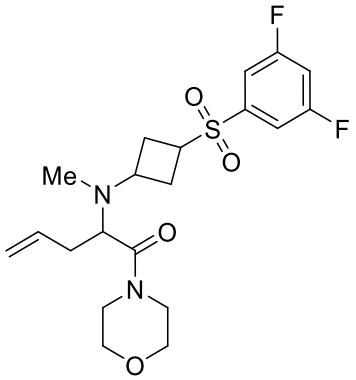
cis-**3k**

(*cis*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-1-(piperidin-1-yl)pent-4-en-1-one (*cis*-**3k**). Colorless oil (16.9 mg, 20% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.38 (m, 2H), 7.13-7.07 (m, 1H), 5.79-5.69 (m, 1H), 5.08-4.99 (m, 2H), 3.80-3.74 (m, 1H), 3.61-3.55 (m, 1H), 3.53-3.50 (m, 1H), 3.45-3.38 (m, 1H), 3.35-3.27 (m, 3H), 2.61-2.42 (m, 3H), 2.30 (s, 3H), 2.27-2.17 (m, 3H), 1.70-1.44 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 163.0 (dd, J = 254.3, 11.3 Hz), 141.9 (t, J = 8.0 Hz), 136.0, 117.0, 111.8 (dd, J = 19.7, 8.3 Hz), 109.5 (t, J = 24.8 Hz), 61.6, 50.6, 50.4, 47.0, 43.3, 33.4, 30.3, 29.5, 28.6, 26.7, 26.0, 24.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.8; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{21}H_{29}F_2N_2O_3S$ 427.1862; Found 427.1861.



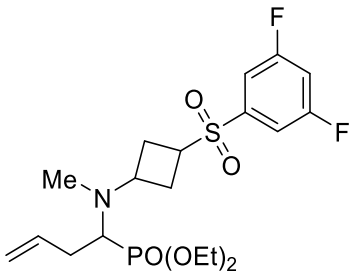
trans-**3k**

(*trans*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-1-(piperidin-1-yl)pent-4-en-1-one (*trans*-**3k**). Colorless oil (34.3 mg, 40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.42 (m, 2H), 7.14-7.09 (m, 1H), 5.78-5.68 (m, 1H), 5.11-5.00 (m, 2H), 3.72-3.60 (m, 3H), 3.58-3.50 (m, 2H), 3.45-3.32 (m, 2H), 2.64-2.53 (m, 3H), 2.42-2.34 (m, 2H), 2.24-2.18 (m, 4H), 1.69-1.48 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 163.0 (dd, J = 254.4, 11.3 Hz), 141.5 (t, J = 7.8 Hz), 135.7, 117.1, 112.0 (dd, J = 19.6, 8.2 Hz), 109.5 (t, J = 24.8 Hz), 60.5 , 54.2, 53.1, 47.0, 43.2, 32.3, 30.9, 28.8, 28.1, 26.8, 25.9, 24.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.8; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{21}H_{29}F_2N_2O_3S$ 427.1862; Found 427.1855.



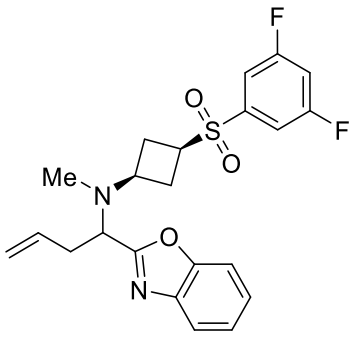
cis/trans-**3l**

(*cis*/*trans*)-2-((3-((3,5-Difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-1-morpholinopent-4-en-1-one (inseparable mixture of *cis*-**3l** and *trans*-**3l**, *cis*/*trans* = 35:65). Colorless oil (55.7 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.39 (m, 2H), 7.15-7.09 (m, 1H), 5.78-5.67 (m, 1H), 5.12-5.00 (m, 2H), 3.83-3.80 (m, 0.4H), 3.74-3.59 (m, 7H), 3.54-3.40 (m, 3.3H), 3.33-3.25 (m, 0.3H), 2.67-2.52 (m, 2.7H), 2.50-2.33 (m, 2H), 2.29 (s, 1H), 2.25-2.16 (m, 3.3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 169.5, 163.1 (dd, J = 254.4, 11.3 Hz), 163.0 (dd, J = 254.4, 11.3 Hz), 141.7 (t, J = 7.9 Hz), 141.4 (t, J = 7.9 Hz), 135.7, 135.4, 117.5, 117.3, 112.0 (dd, J = 19.6, 8.3 Hz), 111.8 (dd, J = 19.6, 8.3 Hz), 109.6 (t, J = 24.7 Hz), 109.5 (t, J = 24.8 Hz), 67.1, 67.1, 67.0, 67.0, 61.7, 60.9, 54.2, 53.0, 50.4, 50.3, 46.4, 42.5, 42.4, 33.4, 32.4, 30.3, 29.6, 29.5, 28.8, 28.3, 28.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.7; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{20}H_{27}F_2N_2O_4S$ 429.1654; Found 429.1661.



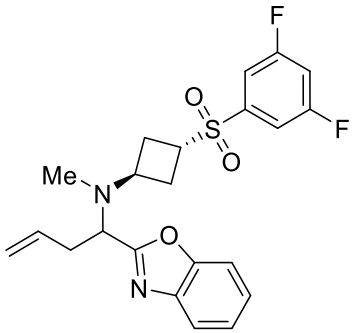
cis/trans-**3n**

(*cis*/*trans*)-Diethyl (1-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)but-3-en-1-yl)phosphonate (inseparable mixture of *cis*-**3n** and *trans*-**3n**, *cis*/*trans* = 41:59). Colorless oil (61.4 mg, 68% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.39 (m, 2H), 7.14-7.08 (m, 1H), 5.86-5.75 (m, 1H), 5.14-5.04 (m, 2H), 4.18-4.07 (m, 4H), 3.90-3.82 (m, 0.6H), 3.65-3.58 (m, 0.6H), 3.54-3.47 (m, 0.4H), 3.44-3.35 (m, 0.4H), 2.97-2.87 (m, 1H), 2.61-2.52 (m, 1H), 2.50-2.23 (m, 8H), 1.36-1.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (dd, *J* = 254.3, 11.4 Hz), 163.0 (dd, *J* = 254.2, 11.3 Hz), 141.8 (t, *J* = 7.9 Hz), 141.6 (t, *J* = 7.9 Hz), 135.9 (d, *J* = 5.8 Hz), 135.8 (d, *J* = 5.9 Hz), 117.0, 117.0, 112.0 (dd, *J* = 19.6, 8.3 Hz), 111.8 (dd, *J* = 19.6, 8.3 Hz), 109.5 (t, *J* = 24.9 Hz), 109.4 (t, *J* = 25.0 Hz), 62.6 (d, *J* = 7.3 Hz), 62.3 (d, *J* = 7.4 Hz), 61.6 (d, *J* = 7.4 Hz), 61.4 (d, *J* = 7.6 Hz), 57.5 (d, *J* = 144.4 Hz), 57.2 (d, *J* = 144.9 Hz), 55.0 (d, *J* = 6.4 Hz), 52.8, 52.1 (d, *J* = 6.4 Hz), 50.1, 32.8 (d, *J* = 2.8 Hz), 32.6 (d, *J* = 2.1 Hz), 31.3 (d, *J* = 6.7 Hz), 31.0 (d, *J* = 6.5 Hz), 29.5 (d, *J* = 2.3 Hz), 29.2, 28.7 (d, *J* = 2.3 Hz), 28.4, 16.7 (d, *J* = 5.6 Hz), 16.7 (d, *J* = 5.7 Hz), 16.6 (d, *J* = 5.8 Hz), 16.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9, -104.9; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{19}H_{29}F_2NO_5PS$ 452.1467; Found 452.1465.



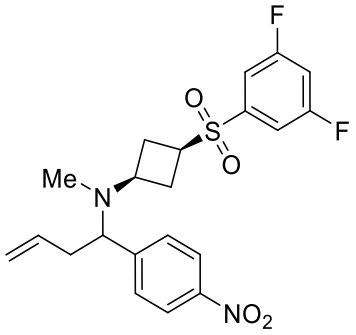
cis-**3o**

(*cis*)-*N*-(1-(Benzo[*d*]oxazol-2-yl)but-3-en-1-yl)-3-((3,5-difluorophenyl)sulfonyl)-*N*-methylcyclobutan-1-amine (*cis*-**3o**). White solid (22.2 mg, 26% yield), melting point: 103-105 ˚C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72-7.69 (m, 1H), 7.53-7.50 (m, 1H), 7.43-7.39 (m, 2H), 7.36-7.31 (m, 2H), 7.12-7.08 (m, 1H), 5.84-5.76 (m, 1H), 5.15-5.02 (m, 2H), 4.01 (t, *J* = 7.5 Hz, 1H), 3.46-3.39 (m, 1H), 3.17-3.11 (m, 1H), 2.88-2.81 (m, 1H), 2.74-2.68 (m, 1H), 2.50-2.39 (m, 3H), 2.25-2.20 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 163.0 (dd, *J* = 254.5, 11.4 Hz), 150.5, 141.6 (t, *J* = 8.1 Hz), 140.7, 134.1, 125.2, 124.5, 120.2, 117.8, 111.9 (dd, *J* = 20.6, 7.3 Hz), 110.8, 109.5 (t, *J* = 24.8 Hz), 58.2, 51.9, 50.3, 34.7, 32.2, 29.1, 29.0; ^{19}F NMR (471 MHz, $CDCl_3$) δ -104.8; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{22}H_{23}F_2N_2O_3S$ 433.1392; Found 433.1391.



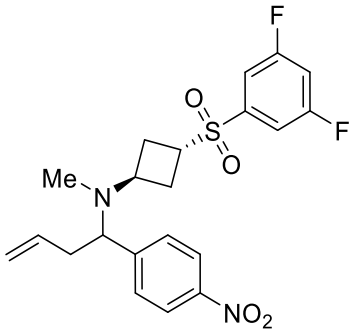
trans-**3o**

(*trans*)-*N*-(1-(Benzo[*d*]oxazol-2-yl)but-3-en-1-yl)-3-((3,5-difluorophenyl)sulfonyl)-*N*-methylcyclobutan-1-amine (*trans*-**3o**). White solid (60.0 mg, 69% yield), melting point: 103-105 ˚C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75-7.73 (m, 1H), 7.56-7.53 (m, 1H), 7.46-7.43 (m, 2H), 7.38-7.33 (m, 2H), 7.12-7.07 (m, 1H), 5.83-5.75 (m, 1H), 5.15-5.02 (m, 2H), 4.03 (t, J = 8.0 Hz, 1H), 3.71-3.66 (m, 1H), 3.58-3.52 (m, 1H), 2.88-2.82 (m, 1H), 2.74-2.68 (m, 2H), 2.59-2.53 (m, 1H), 2.39-2.33 (m, 2H), 2.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 163.0 (dd, J = 254.4, 11.4 Hz), 150.6, 141.3 (t, J = 9.0 Hz), 140.7, 134.2, 125.3, 124.5, 120.3, 117.9, 112.1 (dd, J = 20.9, 7.4 Hz), 110.8, 109.6 (t, J = 25.4 Hz), 57.7, 54.5, 52.9, 34.3, 32.2, 28.4, 28.2; ^{19}F NMR (471 MHz, $CDCl_3$) δ -104.7; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{22}H_{23}F_2N_2O_3S$ 433.1392; Found 433.1393.



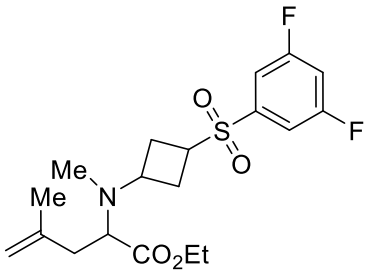
cis-**3p**

(*cis*)-3-((3,5-Difluorophenyl)sulfonyl)-*N*-methyl-*N*-(1-(4-nitrophenyl)but-3-en-1-yl)cyclobutan-1-amine (*cis*-**3p**). White solid (16.3 mg, 19% yield), melting point: 114-115 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19-8.16 (m, 2H), 7.43-7.40 (m, 2H), 7.37-7.35 (m, 2H), 7.14-7.08 (m, 1H), 5.67-5.57 (m, 1H), 5.05-4.97 (m, 2H), 3.74-3.70 (m, 1H), 3.45-3.36 (m, 1H), 2.99-2.89 (m, 1H), 2.70-2.63 (m, 1H), 2.59-2.39 (m, 3H), 2.35-2.28 (m, 1H), 2.19-2.12 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (dd, J = 254.4, 11.3 Hz), 147.3, 141.7 (t, J = 7.2 Hz), 134.7, 129.4, 124.0, 123.5, 117.7, 111.9 (dd, J = 19.6, 8.3 Hz), 109.6 (t, J = 24.9 Hz), 64.1, 51.6, 50.5, 35.7, 31.9, 29.1, 29.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.7; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{21}H_{23}F_2N_2O_4S$ 437.1341; Found 437.1340.



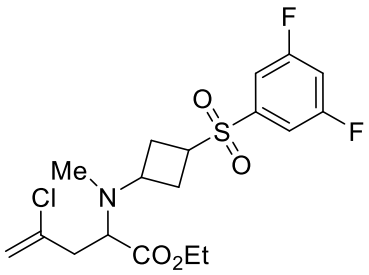
trans-**3p**

(*trans*)-3-((3,5-Difluorophenyl)sulfonyl)-*N*-methyl-*N*-(1-(4-nitrophenyl)but-3-en-1-yl)cyclobutan-1-amine (*trans*-**3p**). White solid (26.5 mg, 30% yield), melting point 114-115 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22-8.17 (m, 2H), 7.47-7.41 (m, 2H), 7.37-7.33 (m, 2H), 7.15-7.09 (m, 1H), 5.69-5.58 (m, 1H), 5.06-4.97 (m, 2H), 3.72 (dd, *J* = 8.8, 6.8 Hz, 1H), 3.69-3.62 (m, 1H), 3.43-3.35 (m, 1H), 2.68-2.52 (m, 3H), 2.49-2.37 (m, 2H), 2.32-2.25 (m, 1H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (dd, *J* = 254.3, 11.3 Hz), 147.3, 146.2, 141.4 (t, *J* = 7.8 Hz), 134.9, 129.4, 123.4, 117.5, 112.0 (dd, *J* = 19.7, 8.3 Hz), 109.6 (t, *J* = 24.8 Hz), 63.5, 54.1, 53.0, 35.1, 31.8, 28.6, 28.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.7; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{21}H_{23}F_2N_2O_4S$ 437.1341; Found 437.1346.



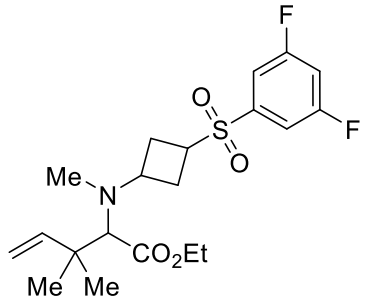
cis/trans-**3q**

(*cis*/*trans*)-Ethyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-4-methylpent-4-enoate (inseparable mixture of *cis*-**3q** and *trans*-**3q**, *cis*/*trans* = 21:79). Colorless oil (62.6 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.41 (m, 2H), 7.14-7.09 (m, 1H), 4.79-4.77 (m, 1H), 4.72-4.61 (m, 1H), 4.20-4.09 (m, 2H), 3.65-3.57 (m, 1.7H), 3.43-3.39 (m, 1.2H), 3.25-3.17 (m, 0.2H), 2.67-2.56 (m, 1.6H), 2.55-2.47 (m, 1H), 2.46-2.41 (m, 0.5H), 2.38-2.30 (m, 2H), 2.29-2.24 (m, 1.5H), 2.21-2.20 (m, 2.3H), 1.73 (s, 3H), 1.32-1.23 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 171.3, 163.0 (dd, *J* = 254.2, 11.4 Hz), 163.0 (dd, *J* = 253.9, 11.1 Hz), 141.9, 141.8, 141.5 (t, *J* = 7.8 Hz), 112.8, 112.1 (dd, *J* = 19.6, 8.3 Hz), 111.8 (dd, *J* = 19.6, 8.3 Hz), 109.5 (t, *J* = 24.8 Hz), 109.4 (t, *J* = 25.0 Hz), 61.4, 60.7, 60.4, 60.3, 54.7, 53.0, 51.8, 50.4, 37.8, 37.5, 32.2, 32.1, 29.5, 28.9, 28.7, 28.3, 22.5, 22.4, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9, -104.9; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{19}H_{26}F_2NO_4S$ 402.1545; Found 402.1551.



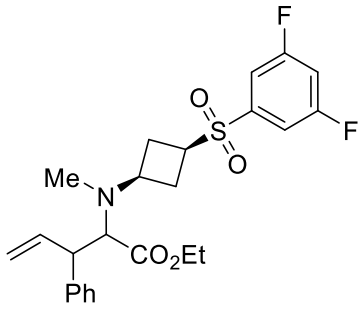
cis/trans-**3r**

(*cis*/*trans*)-Ethyl 4-chloro-2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)pent-4-enoate (inseparable mixture of *cis*-**3r** and *trans*-**3r**, *cis*/*trans*= 20:80). Yellow oil (43.0 mg, 51% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.40 (m, 2H), 7.14-7.09 (m, 1H), 5.23-5.19 (m, 2H), 4.26-4.12 (m, 2H), 3.70-3.58 (m, 2.6H), 3.47-3.21 (m, 0.4H), 2.79-2.74 (m, 1H), 2.66-2.56 (m, 2.6H), 2.48-2.27 (m, 2.4H), 2.21+2.16 (s, 3H), 1.33-1.25 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.5, 163.0 (dd, J = 254.3, 11.4 Hz), 163.0 (dd, J = 254.3, 11.5 Hz), 141.7 (t, J = 7.7 Hz), 141.5 (t, J = 8.0 Hz), 138.8, 115.2, 115.1, 112.1 (dd, J = 19.5, 8.4 Hz), 112.1, 111.8, 109.5 (t, J = 24.8 Hz), 109.5, 60.8, 60.7, 60.2, 59.2, 54.7, 52.9, 52.1, 50.3, 39.1, 38.9, 32.1, 31.9, 29.5, 29.0, 28.7, 28.1, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9, -104.9; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{18}H_{23}ClF_2NO_4S$ 422.0999; Found 422.1003.



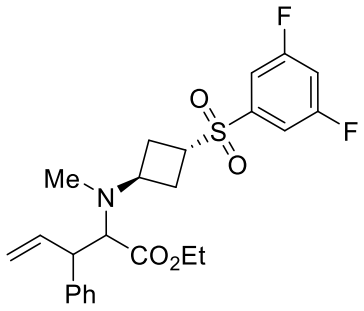
cis/trans-**3s**

(*cis*/*trans*)-Ethyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-3,3-dimethylpent-4-enoate (inseparable mixture of *cis*-**3s** and *trans*-**3s**, *cis*/*trans* = 30:70). Colorless oil (44.9 mg, 54% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.41 (m, 2H), 7.14-7.08 (m, 1H), 6.16-6.08 (m, 1H), 5.03-4.98 (m, 2H), 4.19-4.09 (m, 2H), 3.65-3.60 (m, 1.4H), 3.42-3.22 (m, 0.6H), 2.93-2.92 (m, 1H), 2.61-2.51 (m, 1.5H), 2.46-2.36 (m, 0.8H), 2.36-2.17 (m, 4.7H), 1.31-1.24 (m, 3H), 1.14 (d, J = 2.4 Hz, 3H), 1.07 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.2, 163.1 (dd, J = 254.2, 11.4 Hz), 163.0 (dd, J = 254.2, 11.2 Hz), 145.3, 145.1, 141.9 (t, J = 8.1 Hz), 141.6 (t, J = 7.6 Hz), 112.4, 112.1 (dd, J = 19.5, 8.3 Hz), 111.8 (d, J = 8.2 Hz), 109.5 (t, J = 25.0 Hz), 109.4 (t, J = 25.0 Hz), 71.0, 70.2, 59.9, 56.2, 53.0, 52.7, 50.1, 40.0, 39.9, 35.2, 35.0, 29.6, 28.7, 28.6, 28.3, 26.2, 26.1, 24.2, 24.1, 14.6, 14.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.0, -105.0; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{20}H_{28}F_2NO_4S$ 416.1702; Found 416.1705.



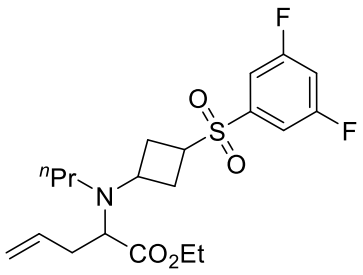
cis-**3t**

(*cis*)-Ethyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-3-phenylpent-4-enoate (*cis*-**3t**, inseparable mixture of *syn*- and *anti*-isomers). Colorless oil (12.6 mg, 14% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.38 (m, 2H), 7.29-7.26 (m, 2H), 7.20 (t, J = 7.5 Hz, 1H), 7.16 (d, J = 7.5 Hz, 2H), 7.11-7.07 (m, 1H), 5.88-5.81 (m, 1H), 5.09-5.02 (m, 2H), 4.24-4.10 (m, 2H), 3.80-3.76 (m, 1H), 3.55 (d, J = 11.5 Hz, 1H), 3.46-3.40 (m, 1H), 3.39-3.33 (m, 1H), 2.51-2.45 (m, 1H), 2.42-2.36 (m, 1H), 2.11 (s, 3H), 2.07-1.97 (m, 2H), 1.31 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 163.0 (dd, J = 254.4, 11.3 Hz), 141.6 (t, J = 8.3 Hz), 140.9, 138.3, 128.5, 128.2, 126.6, 117.0, 112.0 (dd, J = 20.9, 7.4 Hz), 109.5 (t, J = 24.6 Hz), 65.6, 60.4, 54.7, 53.1, 49.4, 31.8, 28.3, 28.0, 14.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ -105.0; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{24}H_{28}F_2NO_4S$ 464.1702; Found 464.1711.



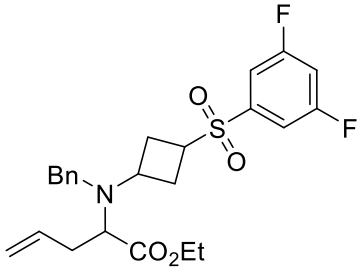
trans-**3t**

(*trans*)-Ethyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-3-phenylpent-4-enoate (*trans*-**3t**, inseparable mixture of *syn*- and *anti*- isomers). Colorless oil (37.5 mg, 40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.42 (m, 2H), 7.28-7.25 (m, 2H), 7.20-7.15 (m, 3H), 7.13-7.09 (m, 1H), 6.11-6.03 (m, 1H), 5.09-5.00 (m, 2H), 3.94-3.83 (m, 2H), 3.80-3.76 (m, 1H), 3.68-3.58 (m, 2H), 3.56-3.48 (m, 1H), 2.67-2.57 (m, 2H), 2.38-2.31 (m, 2H), 2.27 (s, 3H), 0.99 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 163.1 (dd, J = 254.3, 11.3 Hz), 141.6 (t, J = 7.5 Hz), 140.6, 138.9, 128.6, 128.5, 127.0, 116.3, 112.1 (dd, J = 19.6, 8.2 Hz), 109.5 (t, J = 24.8 Hz), 66.7, 60.1, 54.9, 53.0, 48.9, 31.7, 28.5, 28.3, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{24}H_{28}F_2NO_4S$ 464.1702; Found 464.1707.



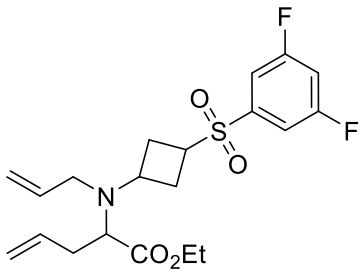
cis/trans-**3w**

(*cis*/*trans*)-Ethyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(propyl)amino)pent-4-enoate (inseparable mixture of *cis*-**3w** and *trans*-**3w**, *cis*/*trans* = 24:76). Yellow oil (41.6 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.40 (m, 2H), 7.12-7.08 (m, 1H), 5.79-5.70 (m, 1H), 5.11-5.02 (m, 2H), 4.17-4.09 (m, 2H), 3.92-3.89 (m, 0.8H), 3.62-3.58 (m, 0.8H), 3.47-3.44 (m, 0.2H), 3.39-3.30 (m, 1H), 2.70-2.58 (m, 2.7H), 2.53-2.44 (m, 2.5H), 2.41-2.26 (m, 3H), 1.45-1.37 (m, 2H), 1.30-1.24 (m, 3H), 0.89-0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 163.0 (dd, J = 254.2, 11.3 Hz), 142.0 (t, J = 8.3 Hz), 141.6 (t, J = 8.4 Hz), 134.8, 117.2, 112.1 (dd, J = 19.7, 8.3 Hz), 111.8 (dd, J = 19.7, 8.1 Hz), 109.5 (t, J = 24.8 Hz), 109.4 (t, J = 24.5 Hz), 61.7, 61.6, 60.6, 60.5, 53.2, 50.9, 49.9, 49.4, 49.0, 34.6, 34.5, 30.9, 30.2, 29.7, 29.2, 23.0, 22.8, 14.5, 11.8, 11.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.0, -105.0; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{20}H_{28}F_2NO_4S$ 416.1702; Found 416.1691.



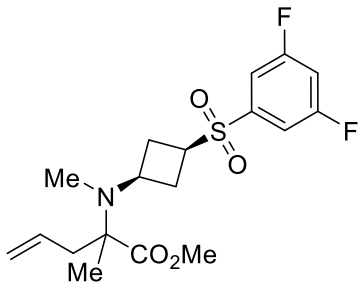
cis/trans-**3x**

(*cis*/*trans*)-Ethyl 2-(benzyl(3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)amino)pent-4-enoate (inseparable mixture of *cis*-**3x** and *trans*-**3x**, *cis*/*trans* = 71:29). Yellow oil (27.8 mg, 30% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.38 (m, 2H), 7.37-7.17 (m, 5H), 7.11-7.06 (m, 1H), 5.76-5.66 (m, 1H), 5.09-5.01 (m, 2H), 4.22-4.12 (m, 2H), 4.06-3.93 (m, 1.7H), 3.76-3.64 (m, 0.3H), 3.63-3.48 (m, 2H), 3.44-3.30 (m, 1.3H), 2.80-2.74 (m, 0.3 H), 2.64-2.57 (m, 1H), 2.54-2.47 (m, 1.4H), 2.43-2.33 (m, 2.1H), 2.25-2.20 (m, 0.6H), 2.18-2.12 (m, 0.3H), 1.33-1.26 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 163.0 (dd, J = 254.2, 11.3 Hz), 141.5 (t, J = 6.4 Hz), 139.8, 134.7, 129.4, 128.4, 128.4, 127.2, 117.4, 112.0 (dd, J = 19.5, 8.3 Hz), 111.7, 109.5 (t, J = 24.9 Hz), 70.3, 64.0, 61.7, 61.2, 60.7, 60.6, 53.3, 51.5, 50.9, 50.3, 34.6, 34.5, 31.6, 30.7, 30.0, 29.8, 29.3, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9, -104.9; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{24}H_{28}F_2NO_4S$ 464.1702; Found 464.1697.



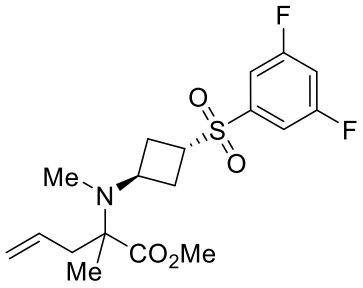
cis/trans-**3y**

(*cis*/*trans*)-Ethyl 2-(allyl(3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)amino)pent-4-enoate (inseparable mixture of *cis*-**3y** and *trans*-**3y**, *cis*/*trans* = 19:81). Colorless oil (38.0 mg, 46% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.39 (m, 2H), 7.14-7.07 (m, 1H), 5.81-5.69 (m 2H), 5.22-5.02 (m, 4H), 4.19-4.10 (m, 2H), 3.95-3.87 (m, 0.8H), 3.63-3.55 (m, 0.8H), 3.50-3.32 (m, 2.4H), 3.18-3.06 (m, 1H), 2.62-2.53 (m, 2H), 2.52-2.47 (m, 1.3H), 2.41-2.29 (m, 2.7H), 1.31-1.23 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 172.5, 163.1 (dd, J = 254.2, 11.3 Hz), 142.0 (t, J = 9.0 Hz), 141.7 (t, J = 8.3 Hz), 137.3, 137.1, 134.8, 134.7, 117.3, 117.3, 117.0, 116.8, 112.1 (dd, J = 19.7, 8.2 Hz), 111.5 (dd, J = 19.8, 8.3 Hz), 109.5 (t, J = 24.7 Hz), 109.4 (t, J = 25.1 Hz), 61.6, 61.3, 60.6, 60.6, 53.3, 50.9, 50.3, 50.2, 50.0, 44.5, 38.6, 34.5, 30.8, 30.0, 29.6, 29.2, 22.0, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9, -105.0, -105.0; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{20}H_{26}F_2NO_4S$ 414.1545; Found 414.1551.



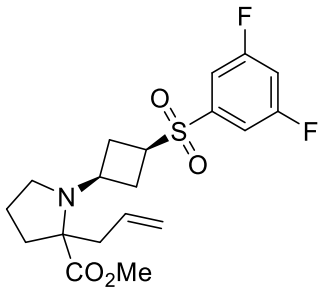
cis-**3aa**

(*cis*)-Methyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-2-methylpent-4-enoate (*cis*-**3aa**). Colorless oil (8.3 mg, 11% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.38 (m, 2H), 7.12-7.07 (m, 1H), 5.74-5.63 (m, 1H), 5.10-5.05 (m, 2H), 3.68 (s, 3H), 3.56-3.49 (m, 1H), 3.40-3.32 (m, 1H), 2.74-2.63 (m, 2H), 2.48 (d, J = 7.2 Hz, 2H), 2.38 (s, 3H), 2.26-2.21 (m, 2H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 163.0 (dd, J = 254.4, 11.4 Hz), 141.9 (t, J = 7.7 Hz), 133.2, 118.8, 111.8 (dd, J = 19.6, 8.2 Hz), 109.5 (t, J = 24.8 Hz), 66.5, 52.1, 51.0, 49.2, 41.6, 31.1, 30.3, 29.2, 19.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.8; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{18}H_{24}F_2NO_4S$ 388.1389; Found 388.1387.



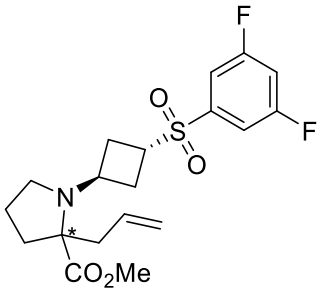
trans-**3aa**

(*trans*)-Methyl 2-((3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)(methyl)amino)-2-methylpent-4-enoate (*trans*-**3aa**). Colorless oil (40.5 mg, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.41 (m, 2H), 7.14-7.08 (m, 1H), 5.74-5.63 (m, 1H), 5.12-5.07 (m, 2H), 4.07-3.98 (m, 1H), 3.69 (s, 3H), 3.59-3.52 (m, 1H), 2.57-2.45 (m, 4H), 2.47 (d, J = 9.0 Hz, 2H), 2.28 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 163.0 (dd, J = 254.3, 11.4 Hz), 141.6 (t, J = 7.9 Hz), 133.2, 118.7, 112.0 (dd, J = 20.8, 7.4 Hz), 109.5 (t, J = 24.8 Hz), 66.3, 53.2, 52.0, 51.7, 41.8, 30.3, 29.1, 28.9, 19.3; ^{19}F NMR (471 MHz, $CDCl_3$) δ -104.90; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{18}H_{24}F_2NO_4S$ 388.1389; Found 388.1381.



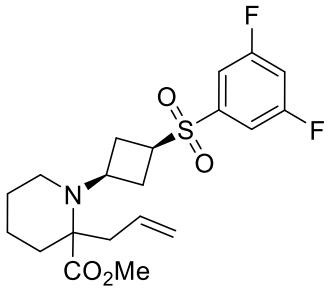
cis-**3ab**

(*cis*)-Methyl 2-allyl-1-(3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)pyrrolidine-2-carboxylate (*cis*-**3ab**). Colorless oil (19.7 mg, 25% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.38 (m, 2H), 7.11-7.07 (m, 1H), 5.74-5.66 (m, 1H), 5.09-5.05 (m, 2H), 3.64 (s, 3H), 3.52-3.45 (m, 1H), 3.41-3.35 (m, 1H), 3.10-3.06 (m, 1H), 2.93-2.88 m, 1H), 2.73 (q, J = 10.0 Hz, 1H), 2.66 (q, J = 10.0 Hz, 1H), 2.58 (dd, J = 14.0, 7.5 Hz, 1H), 2.30-2.24 (m, 2H), 2.19-2.11 (m, 2H), 1.87-1.76 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.3, 163.0 (dd, J = 254.1, 11.4 Hz), 142.1 (t, J = 7.6 Hz), 133.8, 118.3, 111.8 (dd, J = 20.9, 7.4 Hz), 109.4 (t, J = 24.8 Hz), 69.4, 51.8, 51.3, 46.8, 46.1, 39.9, 34.4, 30.4, 27.8, 21.9; ^{19}F NMR (471 MHz, $CDCl_3$) δ -105.0; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{19}H_{24}F_2NO_4S$ 400.1389; Found 400.1387.



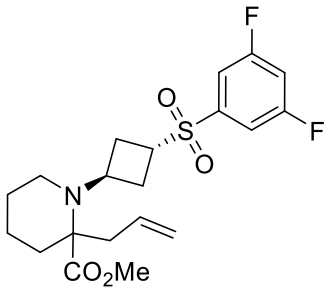
trans-**3ab**

(*trans*)-Methyl 2-allyl-1-(3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)pyrrolidine-2-carboxylate (*trans*-**3ab**). Colorless oil (50.6 mg, 63% yield), $[\alpha]_D^{20}$= -1.2 (*c* = 0.50, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.43 (m, 2H), 7.13-7.09 (m, 1H), 5.74-5.66 (m, 1H), 5.11-5.06 (m, 2H), 3.95-3.89 (m, 1H), 3.68 (s, 3H), 3.63-3.58 (m, 1H), 2.99-2.95 (m, 1H), 2.86-2.82 (m, 1H), 2.65-2.45 (m, 5H), 2.31-2.26 (m, 1H), 2.18-2.12 (m, 1H), 1.87-1.75 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 163.0 (dd, *J* = 254.1, 11.4 Hz), 141.6 (t, *J* = 7.9 Hz), 133.7, 118.3, 112.0 (dd, *J* = 20.8, 7.4 Hz), 109.4 (t, *J* = 24.9 Hz), 69.6, 53.6, 51.8, 49.6, 46.1, 39.6, 34.4, 29.9, 27.5, 21.8; ^{19}F NMR (471 MHz, $CDCl_3$) δ -105.0; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{19}H_{24}F_2NO_4S$ 400.1389; Found 400.1382. The ee was determined to be 19% by HPLC analysis (Chiralpak OD-H column, λ = 254 nm, hexane/isopropanol = 90/10, flow rate =1.0 mL/min): t_R(major) = 7.9 min, t_R(minor) = 9.1 min.



cis-**3ac**

(*cis*)-Methyl 2-allyl-1-(3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)piperidine-2-carboxylate (*cis*-**3ac**). Colorless oil (14.5 mg, 18% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.39 (m, 2H), 7.12-7.06 (m, 1H), 5.78-5.68 (m, 1H), 5.10-5.04 (m, 2H), 3.78-3.68 (m, 1H), 3.66 (s, 3H), 3.37-3.28 (m, 1H), 3.02-2.97 (m, 1H), 2.88-2.81 (m, 1H), 2.65-2.50 (m, 3H), 2.40-2.35 (m, 1H), 2.31-2.18 (m, 2H), 1.96-1.91 (m, 1H), 1.69-1.60 (m, 2H), 1.56-1.52 (m, 1H), 1.48-1.39 (m, 1H), 1.33-1.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 163.0 (dd, *J* = 254.1, 11.3 Hz), 142.2 (t, *J* = 7.7 Hz), 133.1, 118.4, 111.8 (dd, *J* = 19.6, 8.2 Hz), 109.3 (t, *J* = 24.8 Hz), 66.6, 51.7, 51.1, 48.1, 42.7, 41.1, 33.9, 30.1, 28.7, 25.9, 22.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.1; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{20}H_{26}F_2NO_4S$ 414.1545; Found 414.1542.

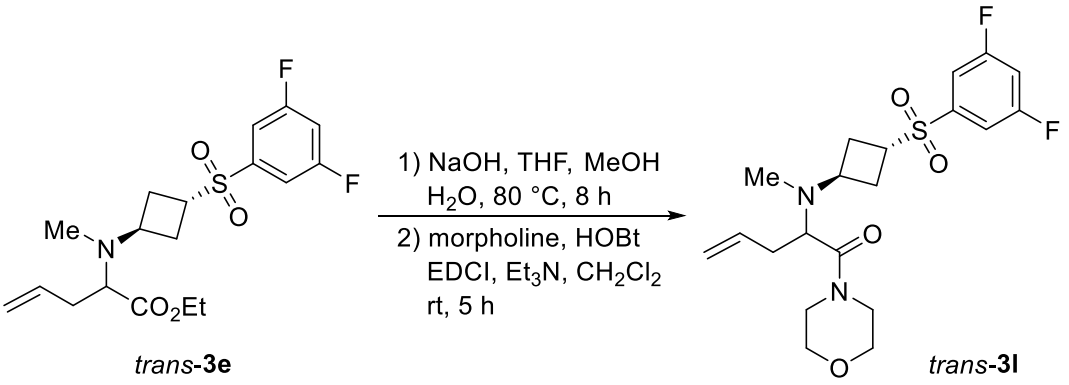


trans-**3ac**

(*trans*)-Methyl 2-allyl-1-(3-((3,5-difluorophenyl)sulfonyl)cyclobutyl)piperidine-2-carboxylate (*trans*-**3ac**). Colorless oil (45.9 mg, 55% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.42 (m, 2H), 7.14-7.07 (m, 1H), 5.79-5.69 (m, 1H), 5.16-5.11 (m, 2H), 4.29-4.20 (m, 1H), 3.67 (s, 3H), 3.53-3.46 (m, 1H), 2.81-2.72 (m, 2H), 2.62-2.47 (m, 4H), 2.45-2.38 (m, 2H), 1.98-1.92 (m, 1H), 1.63-1.52 (m, 3H), 1.47-1.37 (m, 1H), 1.35-1.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 163.0 (dd, J = 254.1, 11.4 Hz), 141.9 (t, J = 7.9 Hz), 132.9, 118.6, 112.1 (dd, J = 19.4, 8.3 Hz), 109.4 (t, J = 25.0 Hz), 66.5, 53.3, 51.7, 50.6, 42.4, 40.9, 33.8, 30.0, 28.2, 25.8, 21.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.1; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{20}H_{26}F_2NO_4S$ 414.1545; Found 414.1536.

Chemical transformations of the products (Scheme 3)

(1) Hydrolysis followed by amination[1]



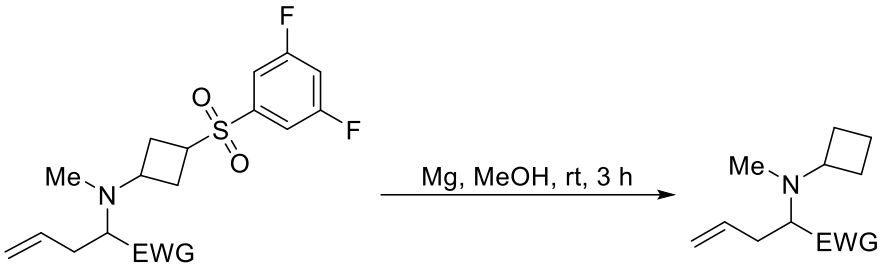
trans-**3e** *trans*-**3l**

To a solution of ester *trans*-**3e** (38.7 mg, 0.10 mmol) in tetrahydrofuran (1.0 mL) and methanol (1.0 mL) were added sodium hydroxide (20.0 mg, 0.50 mmol) and water (1.0 mL). The mixture was heated at 80 ˚C for 8 h, cooled to room temperature, added hydrochloric acid (1.0 M) until pH = 7.0, and extracted with ethyl acetate (3 × 5 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated to give a crude acid.

The crude acid was transferred into a 10 mL round-bottom flask, to which were added morpholine (10.5 mg, 0.12 mmol), HOBt (20.3 mg, 0.15 mmol), EDCI (28.8 mg, 0.15 mmol), and triethylamine (15.2 mg, 0.15 mmol). The mixture was stirred at room temperature for 3 h, concentrated, and subjected to silica gel chromatography, using a mixture of ethyl acetate and petroleum ether (1:2) as the eluent, to give amide *trans*-**3l** (22.7 mg, 53% yield, 2 steps) as s colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.42 (m, 2H), 7.14-7.10 (m, 1H), 5.77-5.68 (m, 1H), 5.12-5.04 (m, 2H), 3.75-3.51 (m, 10H), 3.46-3.42 (m, 1H), 2.66-2.55 (m, 3H), 2.44-2.38 (m, 2H), 2.26-2.23 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 163.1 (dd, J = 254.6, 11.4 Hz), 141.4 (t, J = 8.0 Hz), 135.2, 117.6, 112.1 (dd, J

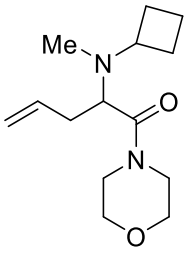
= 19.7, 8.2 Hz), 109.6 (t, J = 24.8 Hz), 67.2, 67.0, 60.8, 54.3, 53.0, 46.4, 42.5, 32.4, 30.5, 28.8, 28.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.7; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{20}H_{27}F_2N_2O_4S$ 429.1654; Found 429.1665.

(2) Desulfonylation[2]



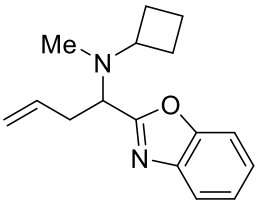
3l, EWG = $CON(CH_2CH_2)_2O$ **4a**
3o, EWG = benzo[*d*]oxazol-2-yl **4b**

Amine **3l** or **3o** (0.10 mmol) was dissolved in methanol (2.5 mL) and freshly activated magnesium turnings (97.2 mg, 4.0 mmol) were added. After sonication for 5 min, the reaction mixture was stirred at room temperature until completion. The mixture was diluted with ethyl acetate (5 mL), washed successively with saturated aqueous NH_4Cl (5 mL) and brine (5 mL), dried over anhydrous sodium sulfate, concentrated under reduced pressure, and purified by silica gel chromatography to give compound **4a** or **4b**.



4a

2-(Cyclobutyl(methyl)amino)-1-morpholinopent-4-en-1-one (**4a**). Yellow oil (19.9 mg, 79% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81-5.71 (m, 1H), 5.09-4.99 (m, 2H), 3.85-3.75 (m, 2H), 3.74-3.65 (m, 3H), 3.63-3.58 (m, 1H), 3.50-3.42 (m, 3H), 3.19-3.11 (m, 1H), 2.69-2.61 (m, 1H), 2.25-2.18 (m, 1H), 2.16 (s, 3H), 2.02-1.95 (m, 2H), 1.89-1.76 (m, 2H), 1.69-1.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 136.4, 116.8, 67.2, 67.1, 60.4, 57.3, 46.4, 42.5, 33.0, 28.8, 28.7, 27.6, 14.3; HRMS (ESI) m/z: (M + H)+ Calcd for $C_{14}H_{25}N_2O_2$ 253.1911; Found 253.1904.



4b

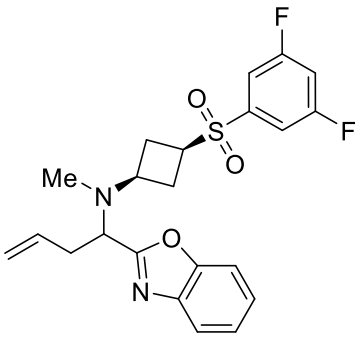
N-(1-(Benzo[*d*]oxazol-2-yl)but-3-en-1-yl)-*N*-methylcyclobutanamine (**4b**). Colorless oil (21.2 mg, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.71 (m, 1H), 7.55-7.51 (m, 1H), 7.35-7.30 (m, 2H), 5.86-5.76 (m, 1H), 5.13-4.98 (m, 2H), 4.07-4.03 (m, 1H), 3.08-3.00 (m, 1H), 2.90-2.82 (m, 1H), 2.72-2.65 (m, 1H), 2.25-2.13 (m, 4H), 1.99-1.80 (m, 3H), 1.70-1.56 (m, 2H);^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 150.6, 140.9, 134.7, 124.9, 124.3, 120.2, 117.4, 110.8, 57.9, 57.8, 34.7, 32.7, 28.3, 28.0, 14.1; HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{16}H_{21}N_2O$ 257.1648; Found 257.1643.

References

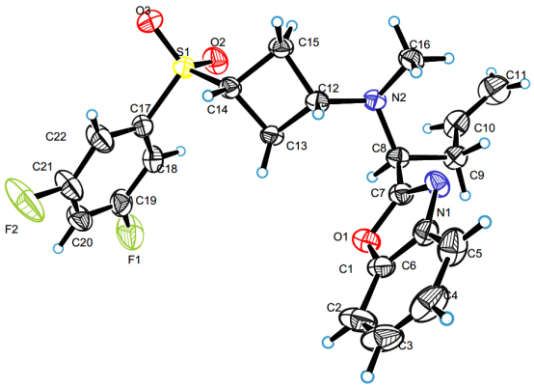
1. J. Zhang, Z.-X. Chen, T. Du, B. Li, Y. Gu and S.-K. Tian, *Org. Lett.*, 2016, **18**, 4872−4875.
2. R. Gianatassio, J. M. Lopchuk, J. Wang, C.-M. Pan, L. R. Malins, L. Prieto, T. A. Brandt, M. R. Collins, G. M. Gallego, N. W. Sach, J. E. Spangler, H. Zhu, J. Zhu and P. S. Baran, *Science*, 2016, **351**, 241−246.

Crystal data of compound *cis*-3o

The crystal of *cis*-**3o** were obtained by leaving alone its solution in hexane and $CHCl_3$ at room temperature in the open air for seven days. The relative configuration of compound *cis*-**3o** were assigned by single crystal X-ray analysis. The crystal data of compound *cis*-**3o** have been deposited in CCDC with number 2069934.



cis-**3o**



Molecular structure of *cis*-**3o** was obtained by single-crystal X-ray diffraction studies with the ellipsoid contour at 35% probability levels.

Table 1 Crystal data and structure refinement for drh12-99-11.

Identification code	drh12-99-11
Empirical formula	$C_{22}H_{22}F_2N_2O_3S$
Formula weight	432.47
Temperature/K	291(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.21316(16)
b/Å	17.3615(2)
c/Å	10.31999(14)
α/°	90
β/°	98.3484(13)
γ/°	90
Volume/Å^3	2165.05(5)
Z	4
ρ_{calc}g/cm^3	1.327
μ/mm^{-1}	1.703
F(000)	904.0
Crystal size/mm^3	0.21 × 0.2 × 0.16
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.316 to 139.78
Index ranges	$-14 \le h \le 14$, $-16 \le k \le 20$, $-9 \le l \le 12$

Reflections collected	8742
Independent reflections	4001 [R_{int} = 0.0168, R_{sigma} = 0.0183]
Data/restraints/parameters	4001/1/273
Goodness-of-fit on F^2	1.030
Final R indexes [I>=2σ (I)]	R_1 = 0.0468, wR_2 = 0.1295
Final R indexes [all data]	R_1 = 0.0515, wR_2 = 0.1348
Largest diff. peak/hole / e $Å^{-3}$	0.34/-0.26

Table 2 Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for drh12-99-11. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
S1	6447.7(4)	2758.3(3)	1964.6(5)	60.57(19)
O1	3996.5(12)	4539.4(8)	6089.7(14)	62.6(4)
N2	3112.9(12)	3874.7(9)	2957.7(14)	47.6(4)
N1	2243.1(13)	4144.5(11)	5650.5(14)	56.5(4)
O2	6175.6(14)	3311.7(11)	935.9(14)	78.0(5)
O3	6561.2(15)	1965.7(11)	1606.9(18)	88.0(6)
F1	9454.6(15)	4714.2(11)	3386(3)	134.5(8)
C12	3987.9(15)	3337.8(10)	3443.0(17)	48.6(4)
C8	3161.2(16)	4573.0(11)	3773.8(17)	49.7(4)
C7	3111.8(16)	4412.9(11)	5191.4(18)	51.8(4)
C13	5194.3(15)	3616.0(11)	3557.0(18)	50.7(4)
C14	5478.9(17)	2815.2(11)	3070.5(18)	52.0(4)
C15	4251.1(17)	2709.2(11)	2486(2)	55.2(5)
C6	2576.9(18)	4097.7(12)	7005.6(18)	58.2(5)
C1	3647.5(18)	4344.4(11)	7261.8(19)	56.7(5)
C9	2275.7(18)	5169.0(12)	3270(2)	59.6(5)
F2	9690(2)	2351.5(16)	5535(3)	171.2(13)
C16	2047.7(17)	3476.8(13)	2768(2)	61.7(5)
C17	7686.8(17)	3061.2(13)	2930(2)	59.4(5)
C18	8080.5(18)	3795.2(14)	2767(2)	69.4(6)
C19	9033.0(19)	4009.1(16)	3547(3)	80.0(7)
C10	2223(2)	5361.8(14)	1858(2)	76.6(7)
C5	2007(2)	3855.9(18)	7987(2)	85.9(8)
C20	9591(2)	3543.9(18)	4473(3)	85.5(8)
C22	8213(2)	2562.4(17)	3862(3)	87.5(8)
C2	4224(3)	4365.5(15)	8523(3)	89.6(9)
C4	2600(4)	3891.6(19)	9250(3)	100.9(11)

C3	3667(4)	4136.6(17)	9494(3)	101.4(11)
C21	9159(2)	2826.5(19)	4616(3)	97.1(9)
C11	1320(3)	5405.3(19)	1016(3)	106.6(10)

Table 3 Anisotropic Displacement Parameters ($Å^2×10^3$) for drh12-99-11. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	60.3(3)	72.0(4)	46.5(3)	-11.5(2)	-2.2(2)	11.0(2)
O1	65.3(8)	60.8(8)	58.4(8)	-2.7(6)	-1.8(6)	-8.6(6)
N2	49.6(8)	50.2(8)	42.4(7)	-0.9(6)	4.9(6)	-3.8(6)
N1	46.1(8)	85.9(12)	36.8(8)	6.3(7)	3.9(6)	-0.5(8)
O2	77.9(10)	111.3(13)	43.3(7)	8.9(8)	3.4(7)	12.7(9)
O3	84.6(11)	85.5(12)	88.4(12)	-40.7(10)	-6.7(9)	19.0(9)
F1	73.6(10)	94.9(12)	229(3)	14.6(14)	3.4(13)	-18.7(9)
C12	54.8(10)	49.6(9)	40.8(9)	3.8(7)	5.2(7)	-3.5(8)
C8	52.7(10)	51.9(10)	45.2(9)	-1.2(7)	9.4(7)	-6.2(8)
C7	57.0(10)	53.1(10)	45.0(9)	-3.8(8)	6.3(8)	-0.2(8)
C13	53.0(10)	54.1(10)	42.8(9)	-6.3(7)	-0.7(7)	-2.8(8)
C14	58.4(11)	50.0(10)	44.5(9)	1.0(7)	-2.8(8)	3.9(8)
C15	60.1(11)	45.2(10)	57.8(11)	-4.4(8)	0.1(9)	-5.4(8)
C6	67.3(12)	67.2(12)	40.7(9)	4.0(8)	9.2(8)	18.1(10)
C1	74.7(13)	46.3(10)	45.4(10)	-4.7(8)	-3.3(9)	3.9(9)
C9	67.0(12)	57.4(11)	55.0(11)	2.8(9)	11.2(9)	4.3(9)
F2	123.3(18)	186(2)	174(2)	81.9(19)	-82.6(17)	-28.8(15)
C16	54.2(11)	68.0(13)	61.4(12)	-7.2(10)	3.4(9)	-10.6(9)
C17	53.8(11)	69.5(13)	53.8(11)	-5.2(9)	4.1(8)	9.1(9)
C18	54.3(12)	76.3(15)	79.1(15)	5.9(12)	14.9(10)	10.5(10)
C19	50.7(12)	76.1(15)	115(2)	-5.2(14)	16.8(13)	-1.7(11)
C10	97.6(18)	70.3(14)	63.9(14)	14.1(11)	18.4(13)	16.5(13)
C5	88.7(17)	109(2)	66.3(15)	21.5(14)	31.6(13)	24.8(15)
C20	51.0(12)	109(2)	93.4(18)	-12.2(16)	0.2(12)	-7.4(13)
C22	73.6(16)	85.6(17)	93.6(19)	15.9(15)	-20.3(14)	-6.7(13)
C2	124(2)	70.4(15)	61.3(15)	-4.8(12)	-29.7(15)	-5.2(15)
C4	165(3)	94(2)	51.2(14)	17.7(13)	40.9(18)	41(2)
C3	173(4)	78.1(18)	45.6(13)	-2.1(12)	-10.1(17)	14(2)
C21	71.7(16)	114(2)	94(2)	21.8(17)	-24.9(15)	-2.7(15)
C11	139(3)	108(2)	66.9(16)	13.7(15)	-4.5(17)	20(2)

Table 4 Bond Lengths for drh12-99-11.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	O2	1.4346(17)	C14	C15	1.544(3)
S1	O3	1.4365(18)	C6	C1	1.365(3)
S1	C14	1.762(2)	C6	C5	1.375(3)
S1	C17	1.767(2)	C1	C2	1.388(3)
O1	C7	1.336(2)	C9	C10	1.488(3)
O1	C1	1.382(3)	F2	C21	1.350(3)
N2	C12	1.451(2)	C17	C18	1.381(3)
N2	C8	1.472(2)	C17	C22	1.382(3)
N2	C16	1.461(2)	C18	C19	1.366(4)
N1	C7	1.309(3)	C19	C20	1.357(4)
N1	C6	1.401(2)	C10	C11	1.303(4)
F1	C19	1.348(3)	C5	C4	1.398(4)
C12	C13	1.539(3)	C20	C21	1.369(4)
C12	C15	1.536(3)	C22	C21	1.374(4)
C8	C7	1.499(3)	C2	C3	1.349(5)
C8	C9	1.532(3)	C4	C3	1.360(5)
C13	C14	1.535(3)			

Table 5 Bond Angles for drh12-99-11.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O2	S1	O3	118.16(11)	C1	C6	N1	107.88(17)
O2	S1	C14	109.67(9)	C1	C6	C5	121.8(2)
O2	S1	C17	107.77(11)	C5	C6	N1	130.4(2)
O3	S1	C14	108.61(11)	O1	C1	C2	129.5(2)
O3	S1	C17	108.86(10)	C6	C1	O1	108.42(16)
C14	S1	C17	102.65(9)	C6	C1	C2	122.1(2)
C7	O1	C1	104.24(16)	C10	C9	C8	114.34(18)
C12	N2	C8	111.41(14)	C18	C17	S1	119.41(17)
C12	N2	C16	109.83(15)	C18	C17	C22	121.9(2)
C16	N2	C8	115.27(15)	C22	C17	S1	118.68(19)
C7	N1	C6	104.37(16)	C19	C18	C17	117.4(2)
N2	C12	C13	118.27(15)	F1	C19	C18	118.8(3)
N2	C12	C15	116.53(15)	F1	C19	C20	117.8(2)
C15	C12	C13	89.13(14)	C20	C19	C18	123.4(3)
N2	C8	C7	113.68(15)	C11	C10	C9	125.3(3)
N2	C8	C9	113.22(15)	C6	C5	C4	115.1(3)
C7	C8	C9	109.26(16)	C19	C20	C21	117.1(2)
O1	C7	C8	120.24(17)	C21	C22	C17	116.9(3)
N1	C7	O1	115.08(16)	C3	C2	C1	116.6(3)
N1	C7	C8	124.68(17)	C3	C4	C5	122.7(3)

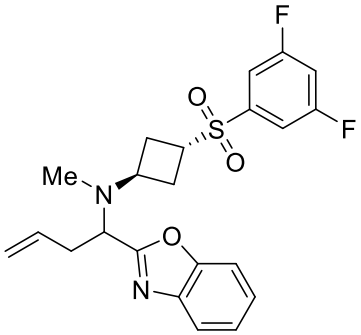
C14	C13	C12	87.16(14)	C2	C3	C4	121.8(3)
C13	C14	S1	117.89(14)	F2	C21	C20	118.6(3)
C13	C14	C15	88.99(14)	F2	C21	C22	118.2(3)
C15	C14	S1	116.49(14)	C20	C21	C22	123.2(3)
C12	C15	C14	86.93(14)				

Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for drh12-99-11.

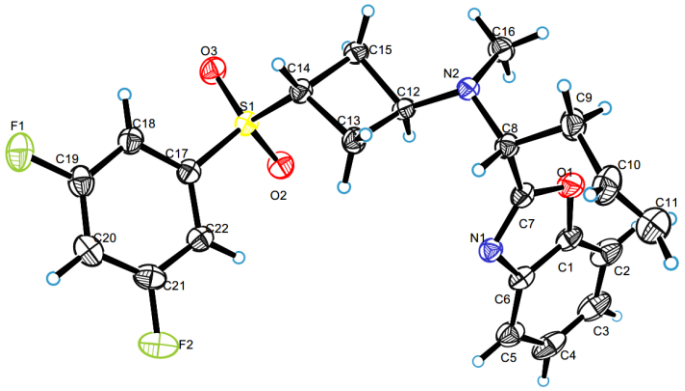
Atom	*x*	*y*	*z*	U(eq)
H12	3847	3107	4270	58
H8	3880	4815	3730	60
H13A	5308	4032	2964	61
H13B	5533	3730	4445	61
H14	5682	2464	3810	62
H15A	4080	2852	1571	66
H15B	3952	2207	2648	66
H9A	1559	4975	3418	71
H9B	2419	5637	3779	71
H16A	2072	3059	2163	93
H16B	1475	3831	2424	93
H16C	1896	3279	3592	93
H18	7712	4131	2150	83
H10	2889	5459	1550	92
H5	1280	3681	7822	103
H20	10238	3705	4989	103
H22	7940	2071	3974	105
H2	4956	4529	8691	108
H4	2250	3742	9952	121
H3	4024	4147	10354	122
H11A	637	5312	1284	128
H11B	1358	5530	147	128

Crystal data of compound *trans*-3o

The crystal of *trans*-**3o** were obtained by leaving alone its solution in hexane and $CHCl_3$ at room temperature in the open air for seven days. The relative configuration of compound *trans*-**3o** were assigned by single crystal X-ray analysis. The crystal data of compound *trans*-**3o** have been deposited in CCDC with number 2069936.



trans-**3o**



Molecular structure of *trans*-**3o** was obtained by single-crystal X-ray diffraction studies with the ellipsoid contour at 35% probability levels.

Table 7 Crystal data and structure refinement for drh12-99-12.

Identification code	drh12-99-12
Empirical formula	$C_{22}H_{22}F_2N_2O_3S$
Formula weight	432.47
Temperature/K	291(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	10.36756(12)
b/Å	11.59613(14)
c/Å	17.36693(19)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2087.91(4)
Z	4
ρ_{calc}g/cm^3	1.376
μ/mm^{-1}	1.766
F(000)	904.0
Crystal size/mm^3	0.22 × 0.17 × 0.16
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.17 to 139.646
Index ranges	-12 ≤ h ≤ 10, -13 ≤ k ≤ 12, -21 ≤ l ≤ 15

Reflections collected	7580
Independent reflections	3856 [R_{int} = 0.0190, R_{sigma} = 0.0224]
Data/restraints/parameters	3856/1/273
Goodness-of-fit on F^2	1.089
Final R indexes [I>=2σ (I)]	R_1 = 0.0361, wR_2 = 0.0996
Final R indexes [all data]	R_1 = 0.0367, wR_2 = 0.1003
Largest diff. peak/hole / e $Å^{-3}$	0.25/-0.21
Flack parameter	0.027(7)

Table 8 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for drh12-99-12. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
S1	3904.7(6)	7881.7(5)	4943.3(3)	42.58(19)
O2	5208(2)	8253.1(19)	5077.6(13)	57.3(5)
F2	6134(2)	4090.2(19)	4353.5(14)	79.0(6)
N2	3815(2)	8458.8(19)	7659.4(12)	39.6(5)
F1	2076(2)	4737(2)	3254.5(13)	78.0(6)
O3	3085(2)	8585.7(18)	4471.2(12)	56.3(5)
N1	6910(2)	7495.1(19)	7686.4(13)	43.0(5)
O1	6550(2)	8944(2)	8504.9(14)	61.2(6)
C8	4667(2)	7745(2)	8136.6(14)	42.2(6)
C7	6068(3)	8066(2)	8100.6(15)	46.5(6)
C15	3074(3)	8834(2)	6298.7(16)	45.7(6)
C12	4111(2)	8350(2)	6841.3(14)	39.0(5)
C18	2939(3)	6143(3)	4073.7(16)	48.3(6)
C1	7855(3)	8941(3)	8335.7(19)	54.0(7)
C6	8087(3)	8046(2)	7835.3(17)	48.1(6)
C13	3923(3)	7138(2)	6486.5(14)	46.3(6)
C19	3045(3)	5077(3)	3720.0(17)	55.0(7)
C17	3971(3)	6485(2)	4528.7(14)	43.3(6)
C21	5077(3)	4762(3)	4270.4(19)	55.5(7)
C14	3113(3)	7694(2)	5835.4(15)	42.4(6)
C22	5050(3)	5811(3)	4643.4(17)	48.9(6)
C20	4088(4)	4374(3)	3804.0(18)	58.7(8)
C16	3781(3)	9683(2)	7873.1(19)	55.5(7)
C5	9315(3)	7810(4)	7571(2)	64.9(9)
C9	4227(3)	7697(3)	8979.5(17)	62.3(8)
C2	8829(4)	9658(3)	8603(3)	77.5(11)

C10	4905(5)	6727(4)	9415(2)	83.3(12)
C4	10283(3)	8529(4)	7846(3)	79.2(13)
C3	10044(4)	9429(4)	8342(3)	82.0(12)
C11	5898(6)	6788(5)	9829(3)	104.0(16)

Table 9 Anisotropic Displacement Parameters ($Å^2×10^3$) for drh12-99-12. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	40.9(3)	46.3(3)	40.5(3)	3.4(2)	-0.2(2)	-4.6(3)
O2	45.4(11)	61.1(12)	65.4(12)	-5.0(10)	3.9(9)	-15.1(9)
F2	67.8(13)	65.2(11)	104.1(16)	9.0(11)	15.3(12)	17.8(11)
N2	36.5(11)	41.4(11)	40.9(10)	-3.6(8)	-2.6(9)	1.4(9)
F1	80.7(14)	77.9(13)	75.5(13)	-16.0(11)	-14.4(11)	-23.1(12)
O3	67.6(14)	53.6(11)	47.9(10)	10.7(9)	-6.8(10)	5.4(10)
N1	37.8(11)	47.1(11)	44.1(11)	-0.2(9)	-2.7(8)	-2.0(9)
O1	47.3(12)	64.2(13)	72.0(13)	-14.9(11)	-11.9(10)	0.8(10)
C8	38.9(13)	45.6(14)	42.2(13)	-0.6(11)	-2.2(10)	-3.9(11)
C7	39.8(13)	53.2(14)	46.3(13)	3.4(11)	-7.3(10)	-3.3(11)
C15	47.1(15)	45.2(14)	44.8(13)	3.0(10)	-2.5(12)	9.6(12)
C12	36.1(13)	38.0(12)	42.9(12)	1.2(10)	-3.5(10)	2.2(10)
C18	43.6(14)	56.5(16)	45.0(13)	-0.1(12)	0.9(11)	-5.3(12)
C1	41.9(15)	53.2(16)	66.8(18)	5.1(14)	-15.3(13)	-6.1(13)
C6	38.9(13)	52.4(15)	52.8(15)	11.9(12)	-7.5(11)	-1.6(12)
C13	58.8(16)	40.2(12)	39.9(12)	1.0(10)	-6.1(11)	4.6(13)
C19	56.2(18)	60.0(17)	48.7(15)	-5.4(13)	3.4(13)	-14.9(15)
C17	40.9(14)	50.5(13)	38.4(11)	3.5(10)	3.8(11)	-3.9(12)
C21	51.6(16)	51.6(16)	63.3(17)	9.4(14)	15.4(14)	5.3(14)
C14	38.6(12)	47.5(14)	41.2(12)	0.8(10)	-2.7(10)	-3.7(11)
C22	42.7(14)	55.7(16)	48.3(14)	6.6(12)	4.1(11)	-2.4(13)
C20	70(2)	49.4(15)	56.8(16)	-1.7(12)	15.5(15)	-8.8(15)
C16	56.1(17)	45.5(14)	65.0(17)	-13.7(12)	-7.2(15)	3.6(13)
C5	51.3(17)	82(2)	61.3(17)	18.2(17)	3.8(14)	6.2(17)
C9	59.6(18)	86(2)	41.9(14)	0.0(15)	3.3(13)	-4.5(17)
C2	62(2)	63(2)	108(3)	-0.3(19)	-32(2)	-11.0(18)
C10	90(3)	107(3)	52.1(18)	19(2)	-9.9(19)	-9(3)
C4	38.9(17)	107(3)	92(3)	49(3)	-5.9(16)	-7.0(18)
C3	54(2)	81(3)	110(3)	23(3)	-26(2)	-16.6(19)
C11	118(4)	115(4)	79(3)	4(3)	-13(3)	31(3)

Table 10 Bond Lengths for drh12-99-12.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	O2	1.437(2)	C12	C13	1.547(3)
S1	O3	1.436(2)	C18	C19	1.384(5)
S1	C17	1.773(3)	C18	C17	1.388(4)
S1	C14	1.767(3)	C1	C6	1.375(5)
F2	C21	1.352(4)	C1	C2	1.388(5)
N2	C8	1.468(3)	C6	C5	1.381(4)
N2	C12	1.459(3)	C13	C14	1.549(3)
N2	C16	1.468(3)	C19	C20	1.362(5)
F1	C19	1.349(4)	C17	C22	1.380(4)
N1	C7	1.311(4)	C21	C22	1.378(5)
N1	C6	1.401(3)	C21	C20	1.382(5)
O1	C7	1.334(3)	C5	C4	1.389(6)
O1	C1	1.384(4)	C9	C10	1.527(6)
C8	C7	1.500(4)	C2	C3	1.364(7)
C8	C9	1.534(4)	C10	C11	1.257(7)
C15	C12	1.536(3)	C4	C3	1.376(7)
C15	C14	1.548(4)			

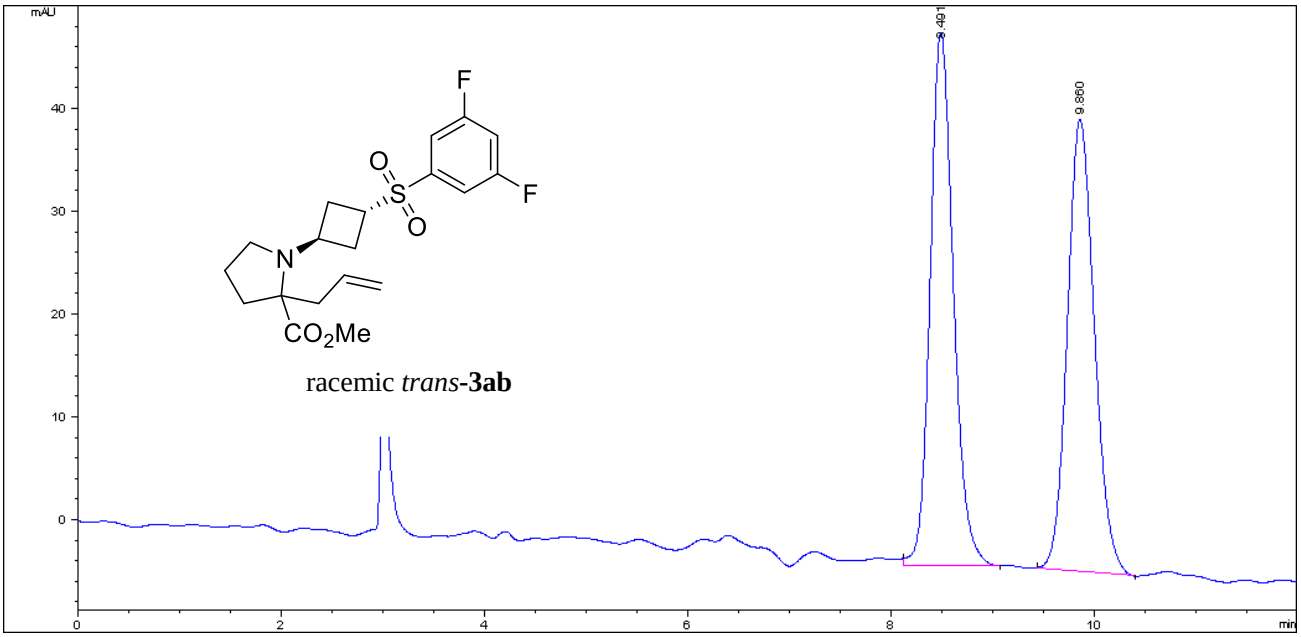
Table 11 Bond Angles for drh12-99-12.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O2	S1	C17	107.65(13)	C1	C6	N1	108.0(2)
O2	S1	C14	109.35(13)	C1	C6	C5	121.4(3)
O3	S1	O2	118.61(14)	C5	C6	N1	130.6(3)
O3	S1	C17	108.07(13)	C12	C13	C14	88.91(19)
O3	S1	C14	107.22(13)	F1	C19	C18	117.9(3)
C14	S1	C17	105.15(12)	F1	C19	C20	118.7(3)
C8	N2	C16	114.7(2)	C20	C19	C18	123.4(3)
C12	N2	C8	112.0(2)	C18	C17	S1	117.6(2)
C12	N2	C16	109.6(2)	C22	C17	S1	119.4(2)
C7	N1	C6	104.4(2)	C22	C17	C18	123.0(3)
C7	O1	C1	104.6(2)	F2	C21	C22	118.4(3)
N2	C8	C7	114.8(2)	F2	C21	C20	118.4(3)
N2	C8	C9	112.3(2)	C22	C21	C20	123.2(3)
C7	C8	C9	109.7(2)	C15	C14	S1	111.25(19)
N1	C7	O1	115.1(2)	C15	C14	C13	89.43(19)
N1	C7	C8	122.9(2)	C13	C14	S1	116.08(19)
O1	C7	C8	122.0(3)	C21	C22	C17	116.7(3)

C12	C15	C14	89.34(19)	C19	C20	C21	117.2(3)
N2	C12	C15	114.8(2)	C6	C5	C4	115.7(4)
N2	C12	C13	116.1(2)	C10	C9	C8	111.3(3)
C15	C12	C13	89.98(19)	C3	C2	C1	116.4(4)
C19	C18	C17	116.5(3)	C11	C10	C9	128.2(5)
O1	C1	C2	129.7(3)	C3	C4	C5	122.7(4)
C6	C1	O1	107.9(2)	C2	C3	C4	121.4(4)
C6	C1	C2	122.4(3)				

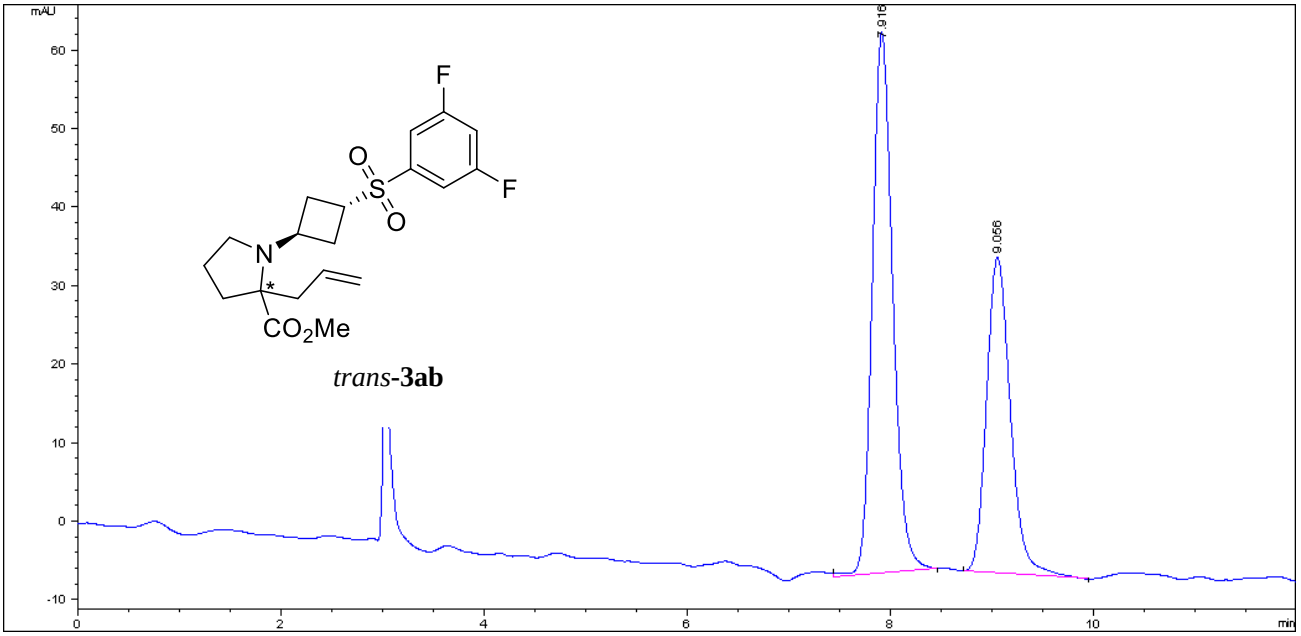
Table 12 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for drh12-99-12.

Atom	*x*	*y*	*z*	U(eq)
H8	4602	6957	7937	51
H15A	3354	9502	6007	55
H15B	2253	8979	6548	55
H12	4965	8664	6721	47
H18	2214	6605	4010	58
H13A	3438	6613	6811	56
H13B	4717	6785	6309	56
H14	2260	7339	5780	51
H22	5726	6052	4957	59
H20	4132	3662	3558	70
H16A	3518	9756	8401	83
H16B	3179	10082	7548	83
H16C	4625	10012	7810	83
H5	9483	7209	7231	78
H9A	4414	8428	9227	75
H9B	3302	7576	8998	75
H2	8663	10262	8941	93
H10	4536	5999	9370	100
H4	11127	8397	7687	95
H3	10725	9892	8504	98
H11A	6312	7492	9897	125
H11B	6219	6128	10066	125



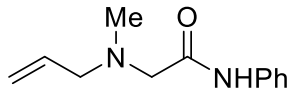
racemic *trans*-**3ab**

Number	Time (min)	Area (mAU.s)	Height (mAU)	Width (min)	Symmetry factor	Area (%)
1	8.491	827.2	51.9	0.2444	0.823	50.309
2	9.86	817	44	0.2879	0.846	49.691



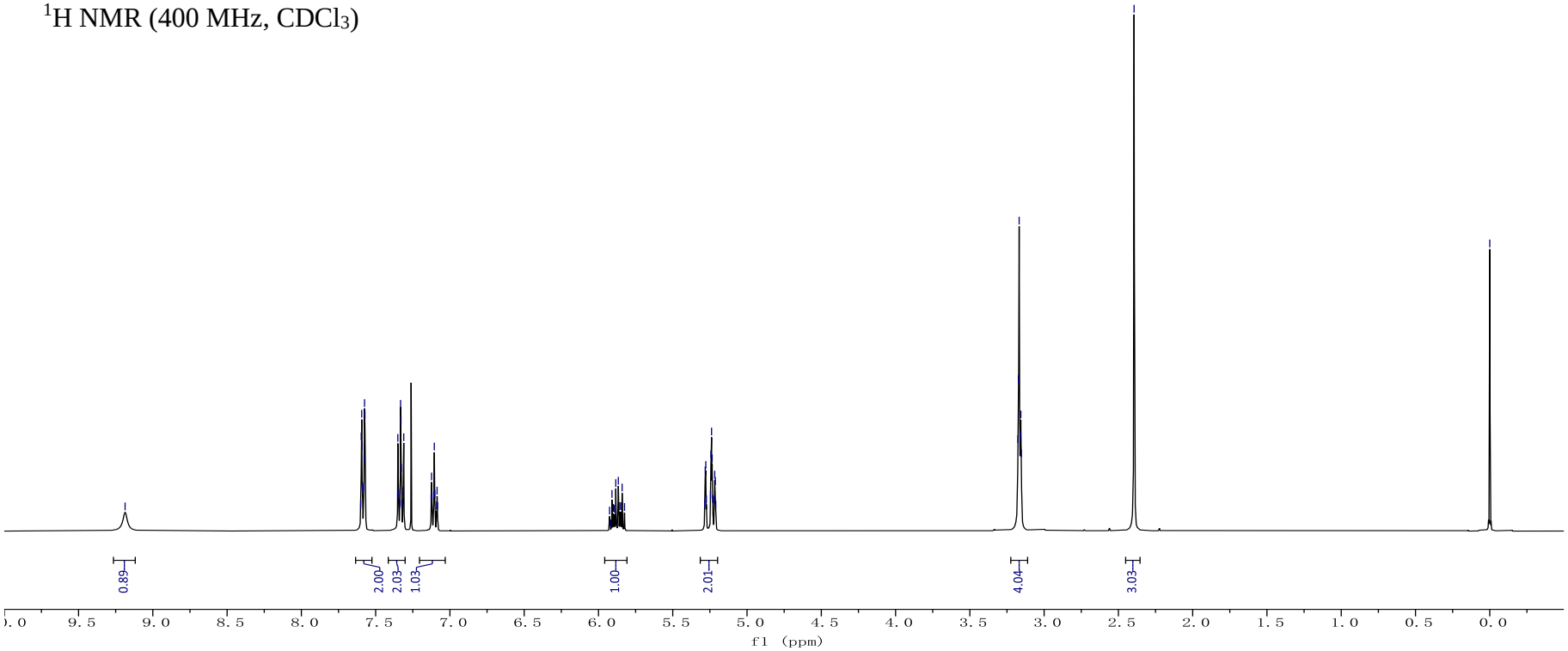
trans-**3ab**

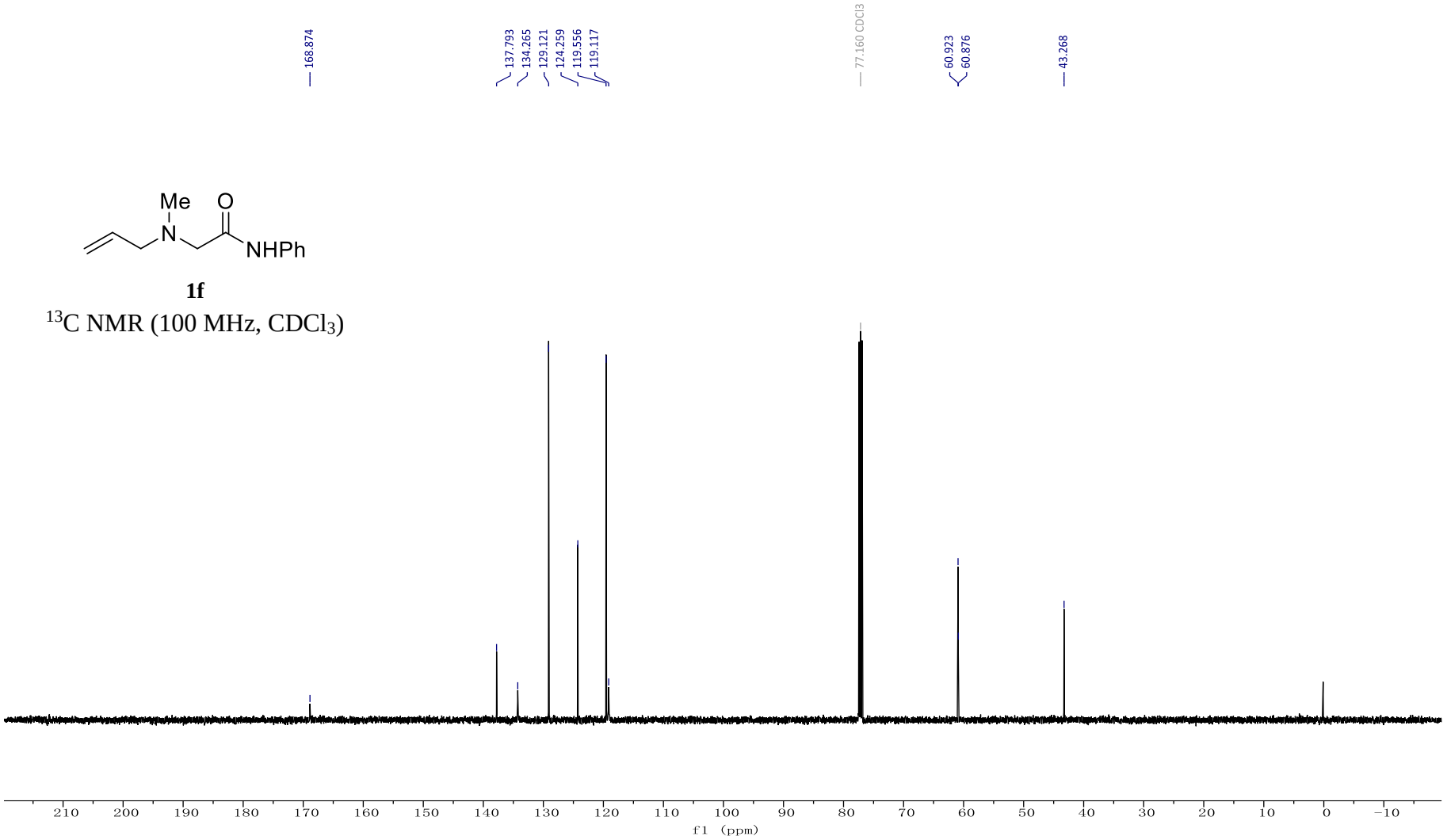
Number	Time (min)	Area (mAU.s)	Height (mAU)	Width (min)	Symmetry factor	Area (%)
1	7.916	971.8	69	0.2182	0.816	59.670
2	9.056	656.8	40.3	0.2515	0.786	40.330



1f

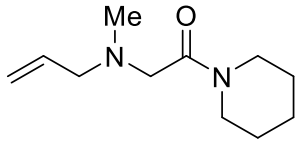
^{1}H NMR (400 MHz, $CDCl_3$)





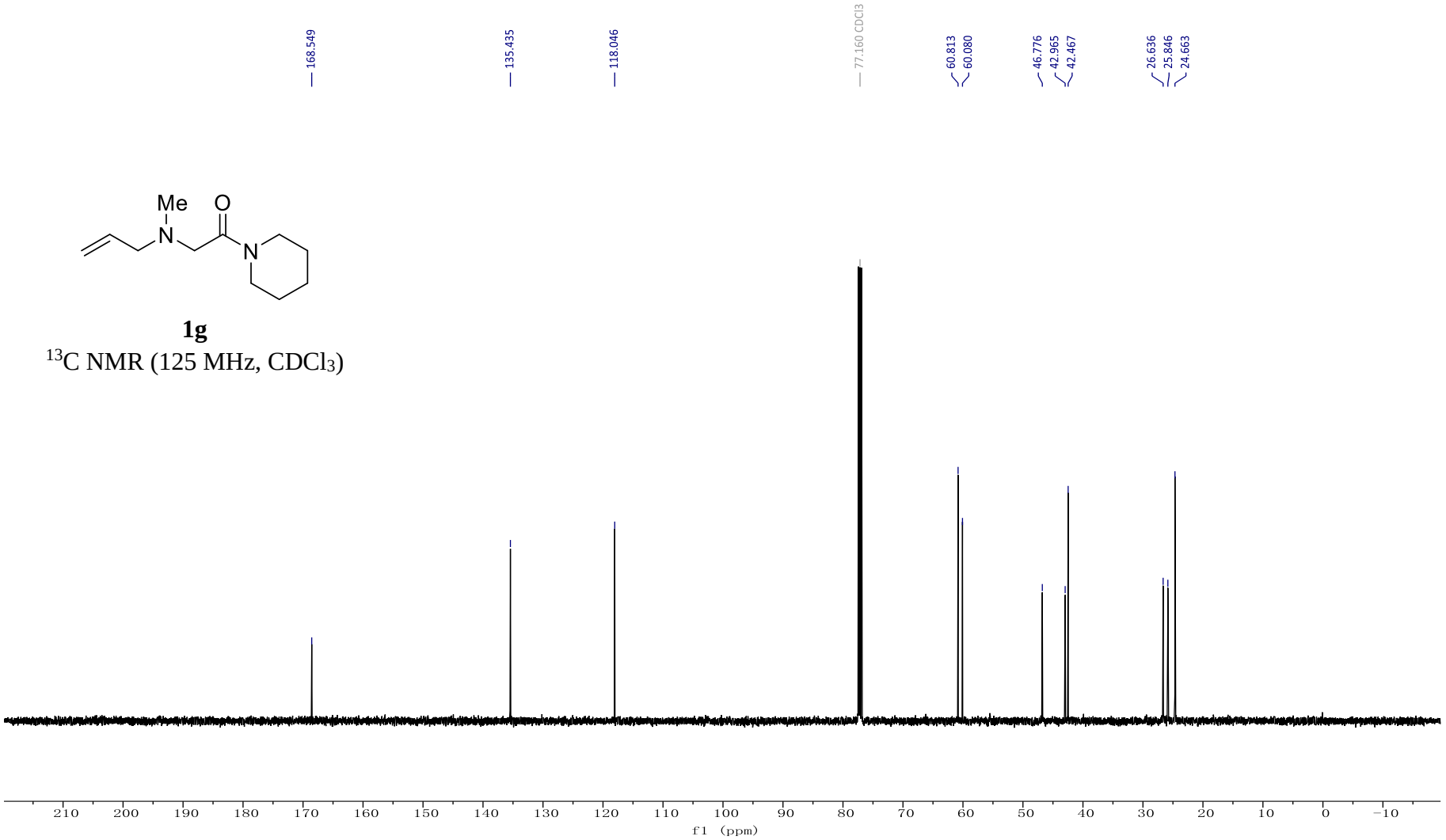
1f

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



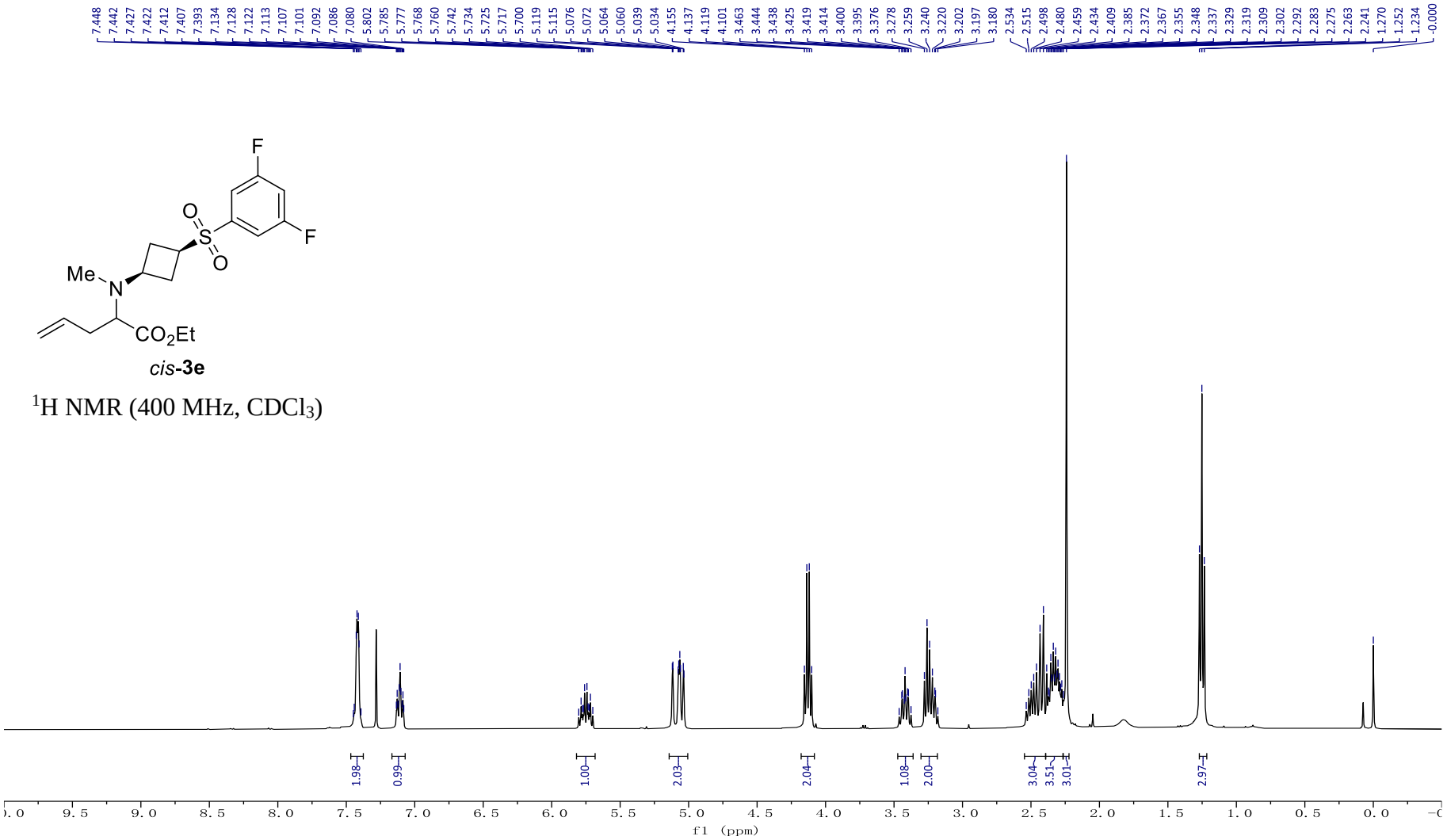
1g

^{1}H NMR (500 MHz, $CDCl_3$)



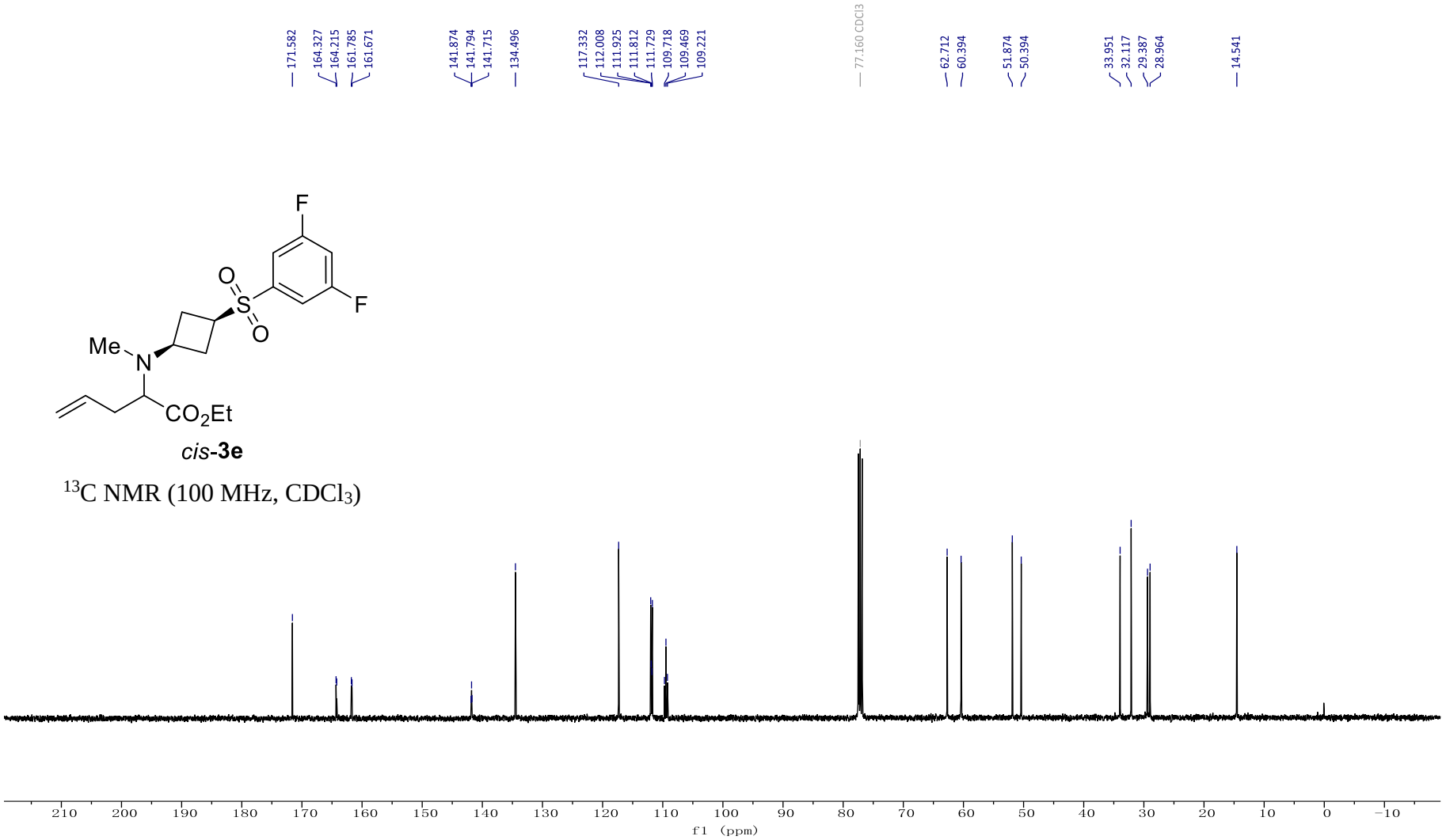
1g

^{13}C NMR (125 MHz, $CDCl_3$)



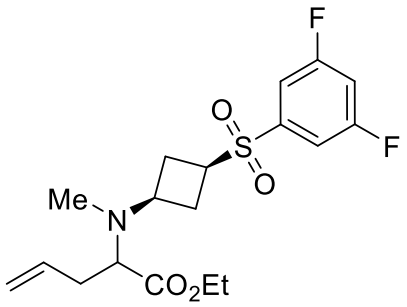
cis-**3e**

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



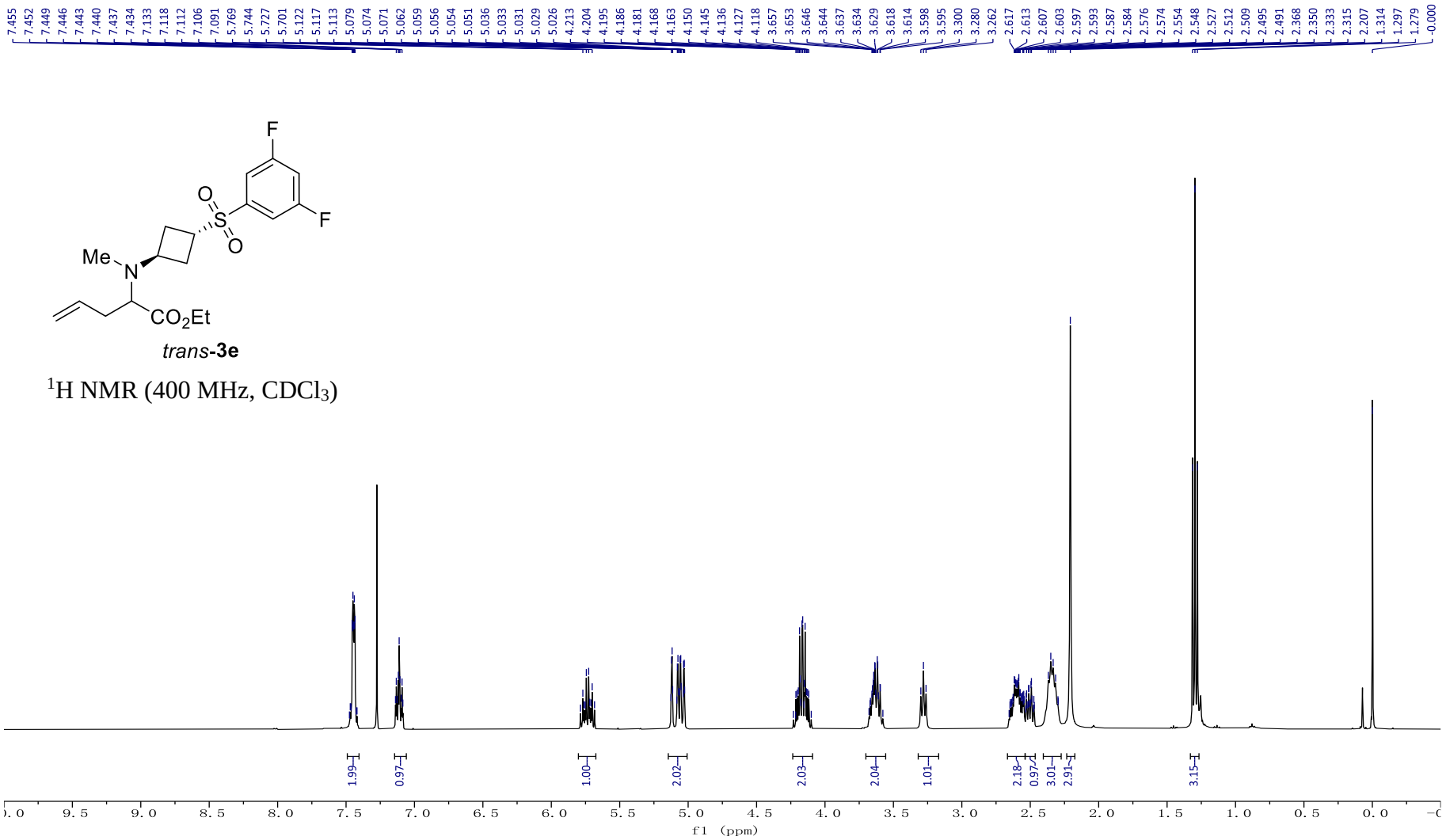
cis-**3e**

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



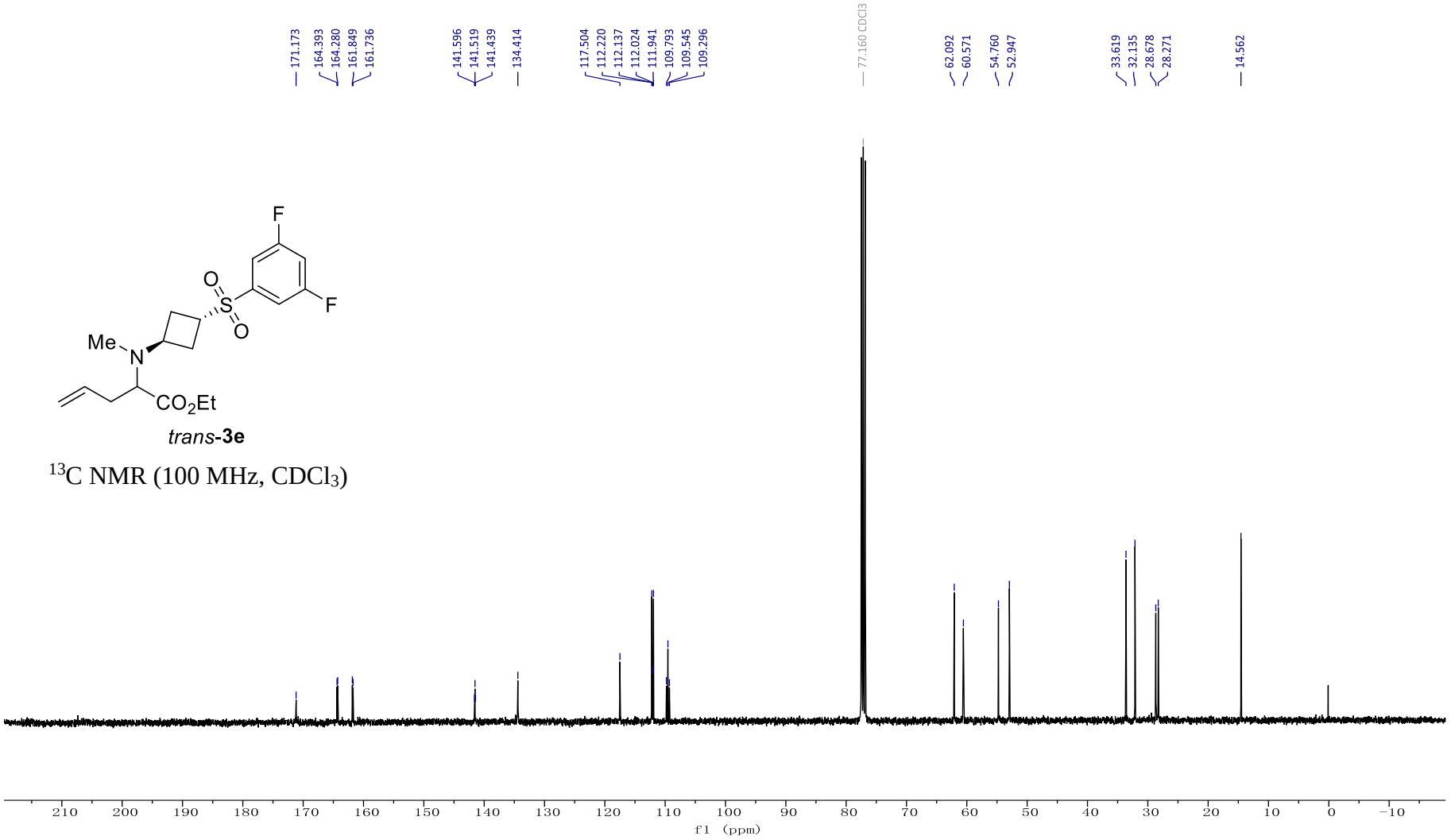
cis-**3e**

^{19}F NMR (376 MHz, $CDCl_3$)



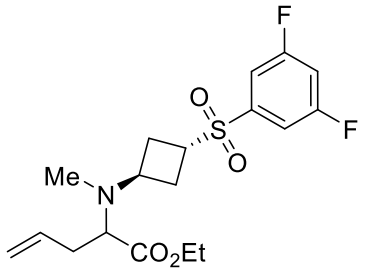
trans-**3e**

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



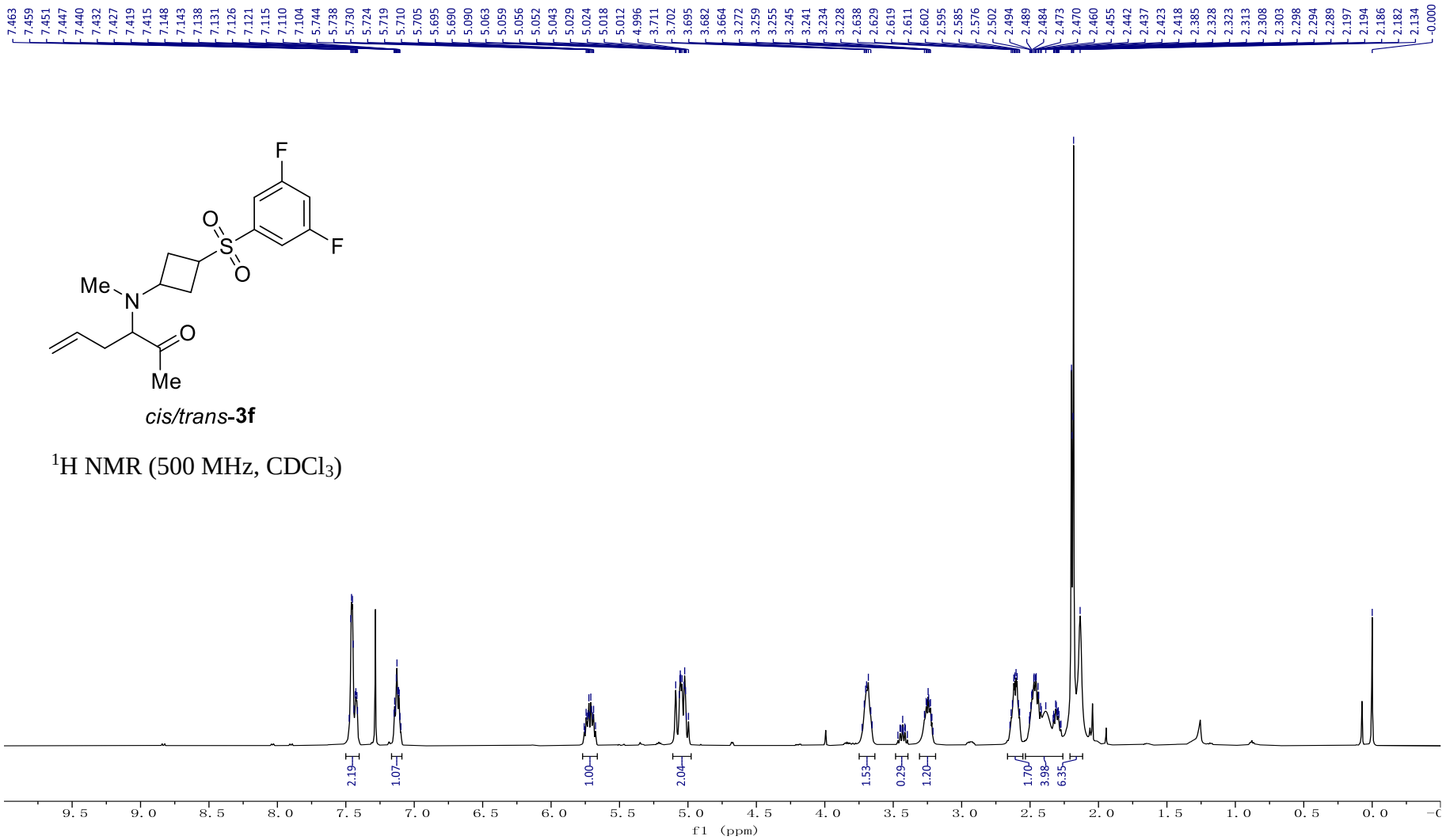
trans-**3e**

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



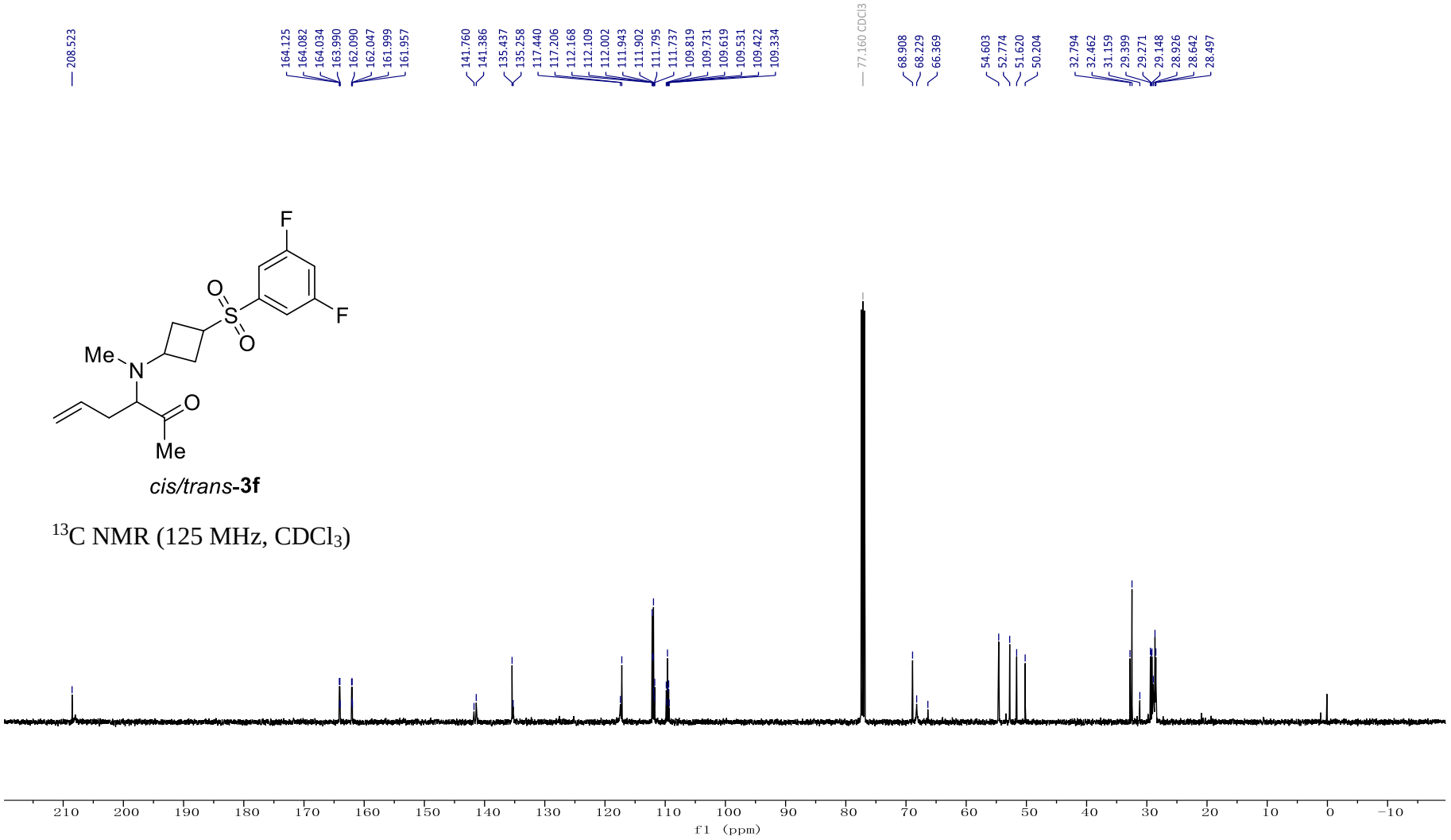
trans-**3e**

^{19}F NMR (376 MHz, $CDCl_3$)



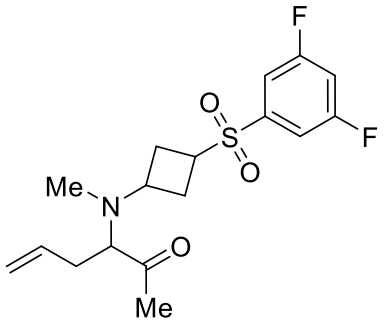
cis/trans-**3f**

^{1}H NMR (500 MHz, $CDCl_3$)



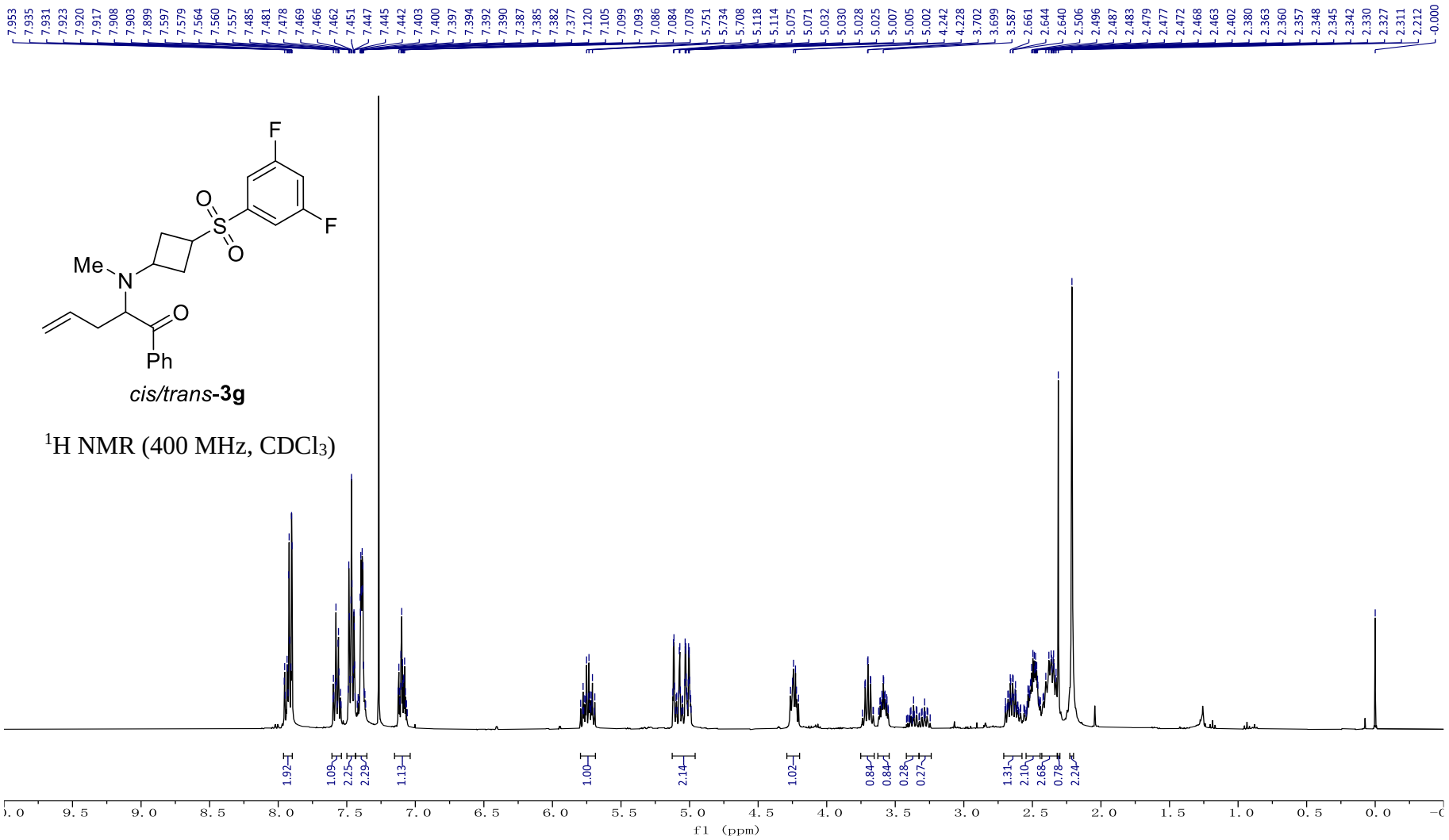
cis/trans-**3f**

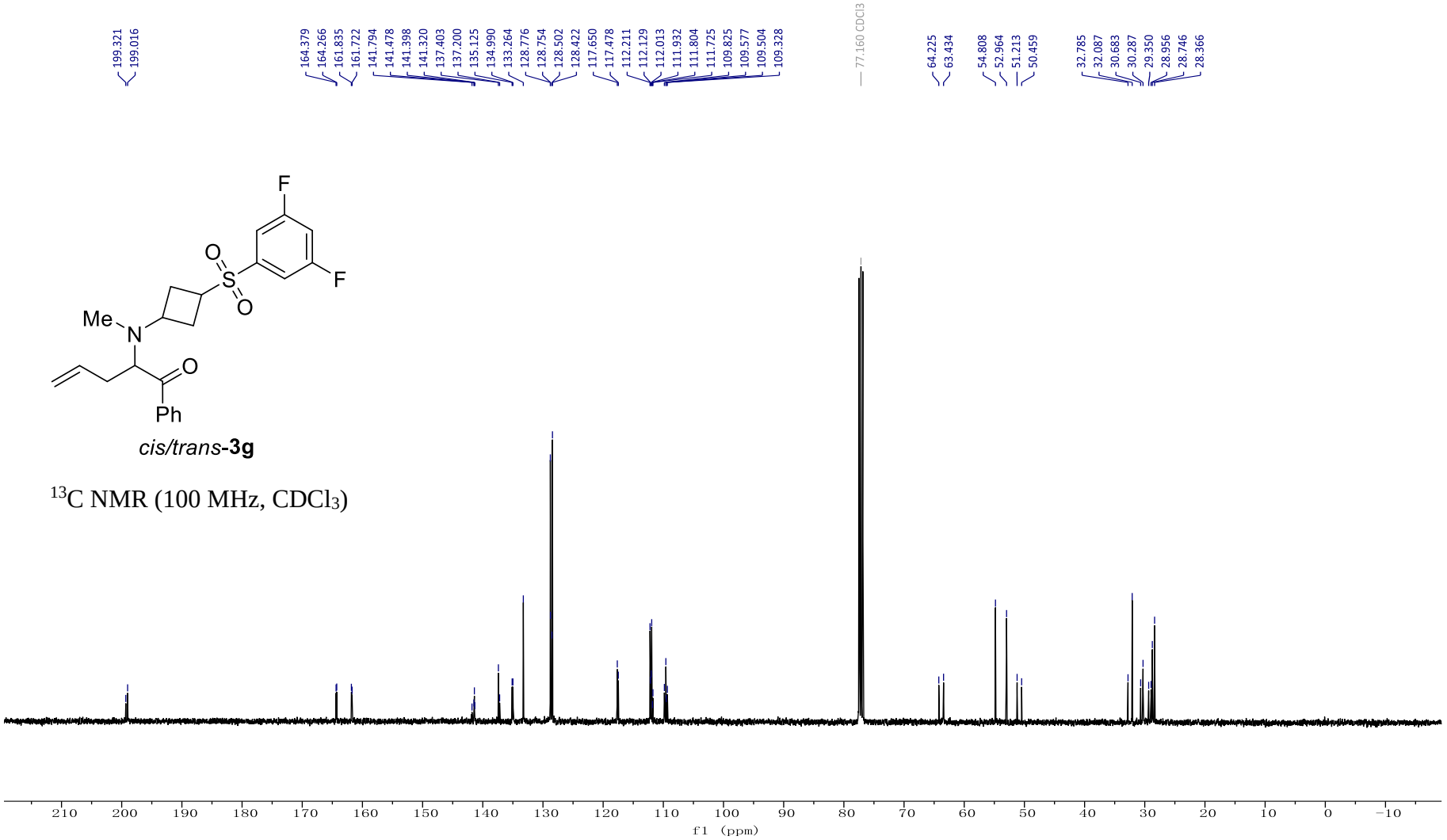
^{13}C NMR (125 MHz, $CDCl_3$)



cis/trans-**3f**

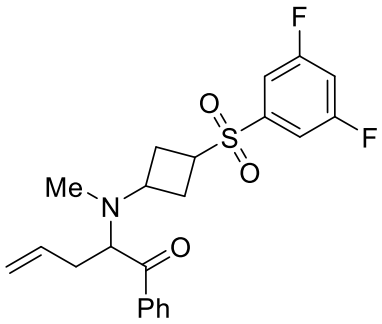
^{19}F NMR (471 MHz, $CDCl_3$)


F
O
S
O
F
Me
N
O
Ph
cis/trans-3g
1H NMR (400 MHz, CDCl3)
f1 (ppm)



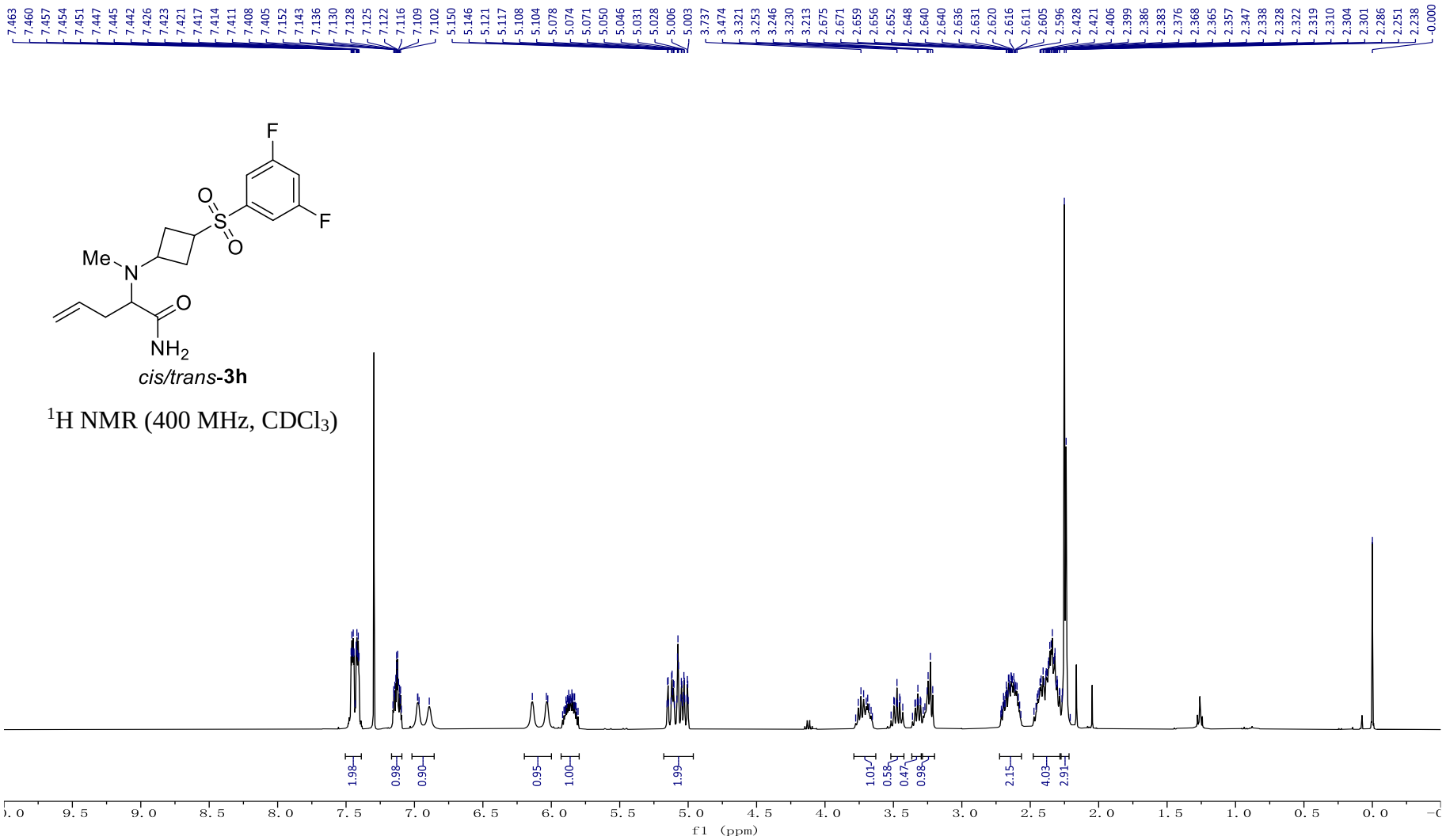
cis/trans-**3g**

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



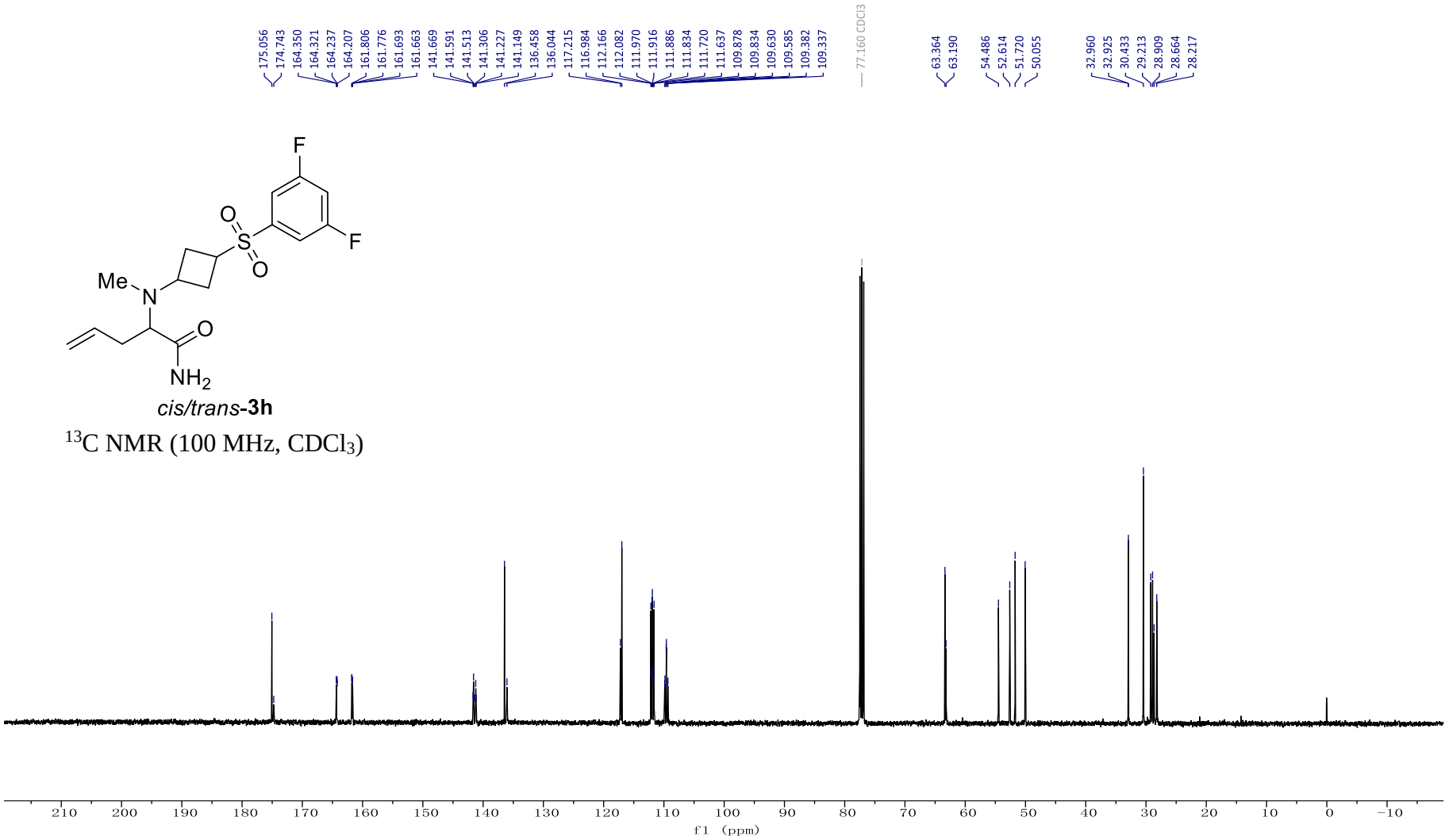
cis/trans-**3g**

^{19}F NMR (376 MHz, $CDCl_3$)



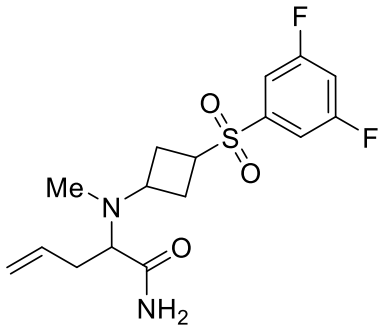
cis/trans-**3h**

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



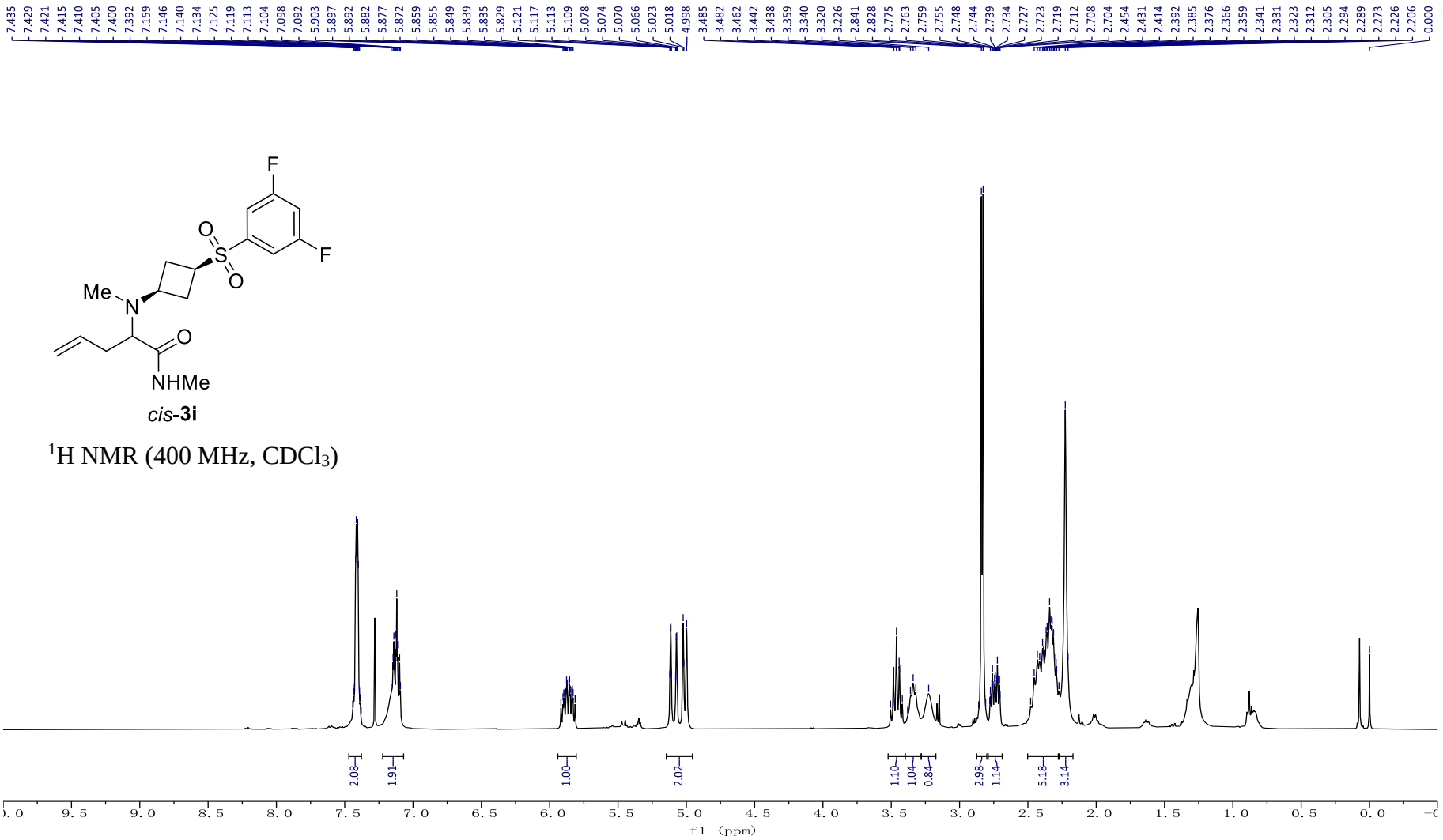
cis/trans-**3h**

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



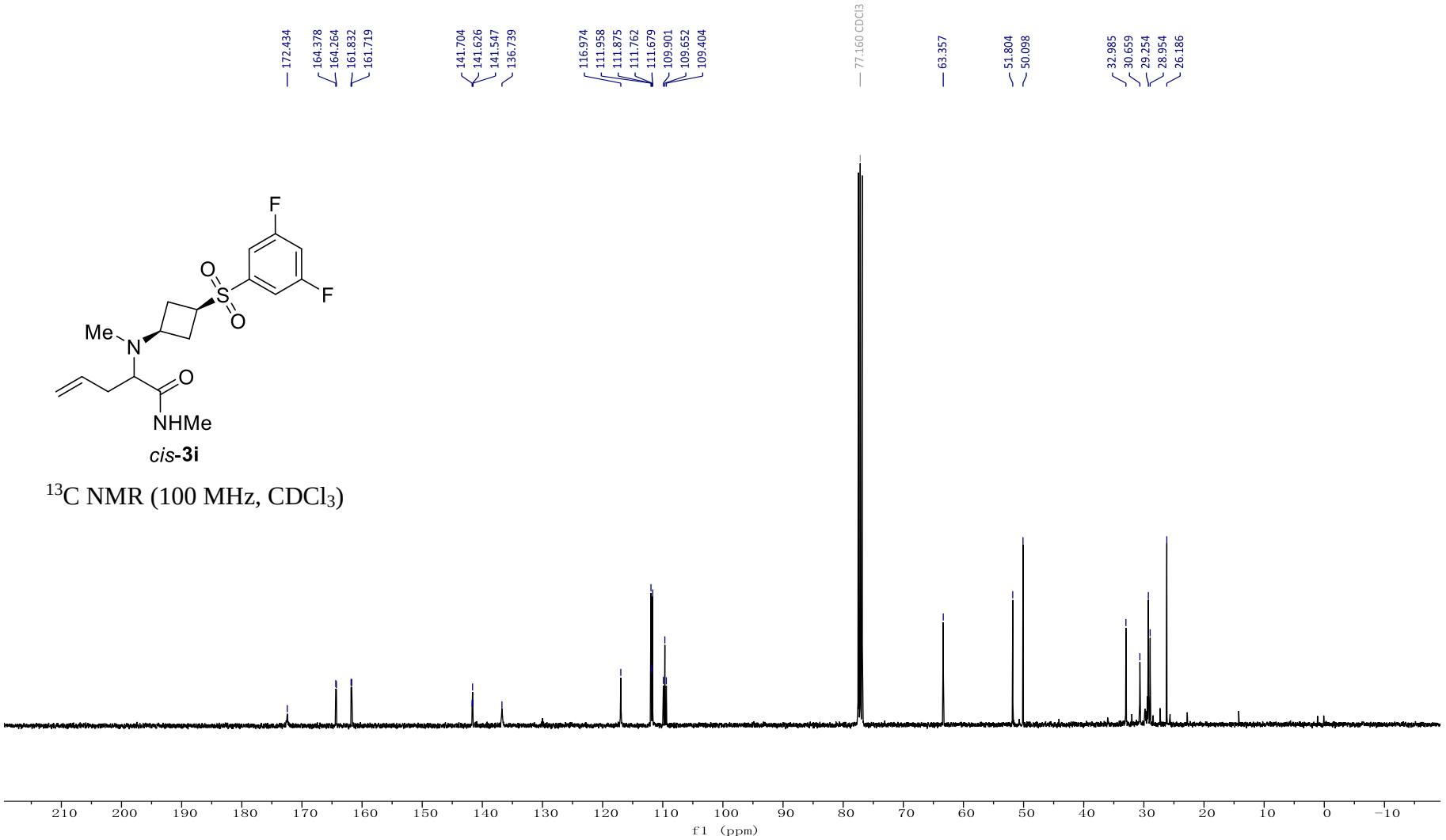
cis/trans-**3h**

^{19}F NMR (376 MHz, $CDCl_3$)



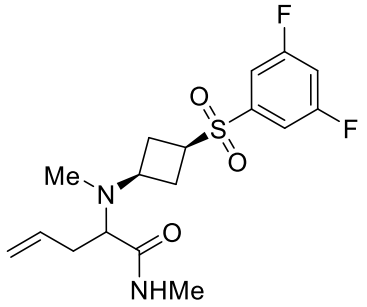
cis-**3i**

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



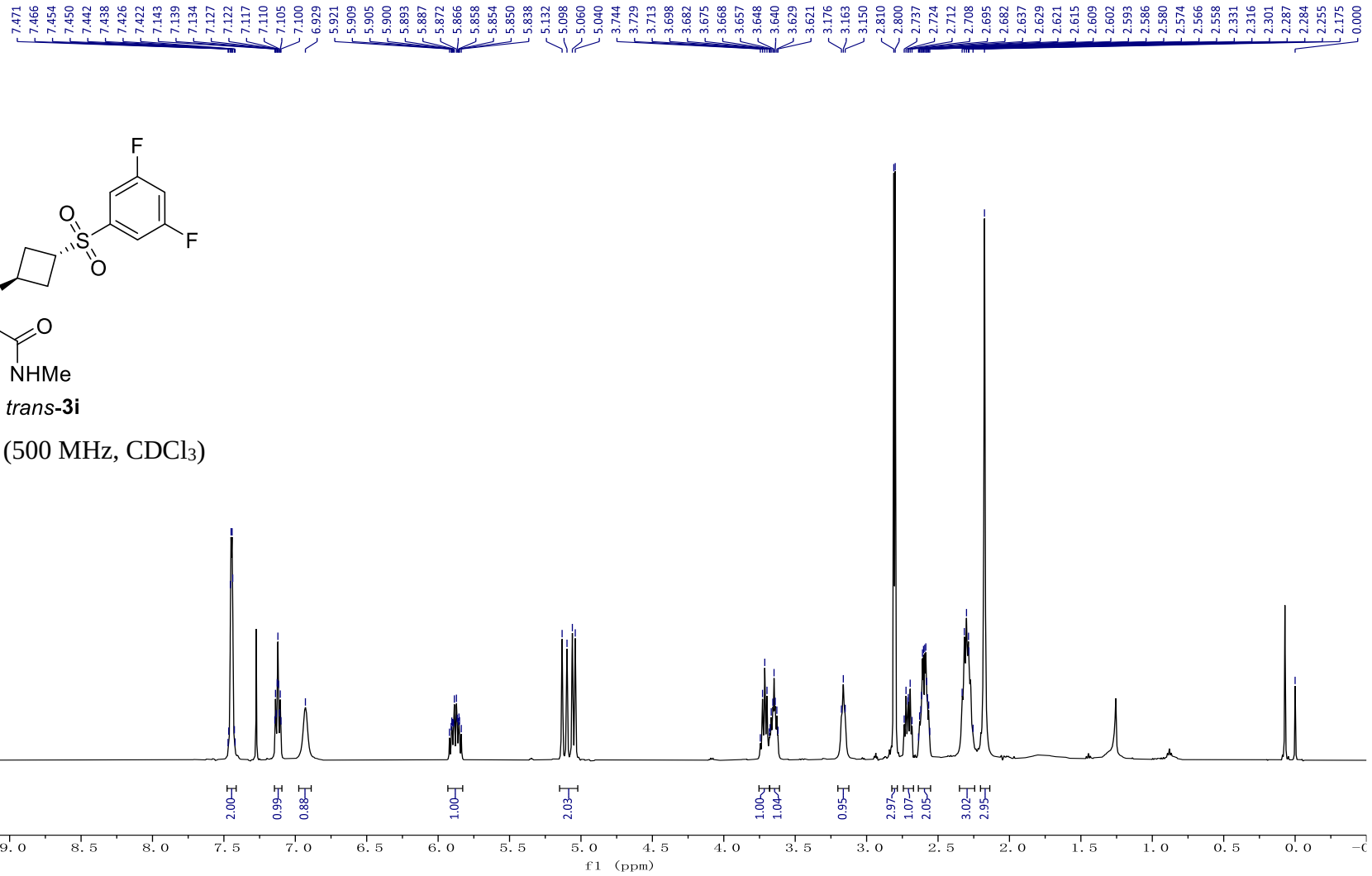
cis-**3i**

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



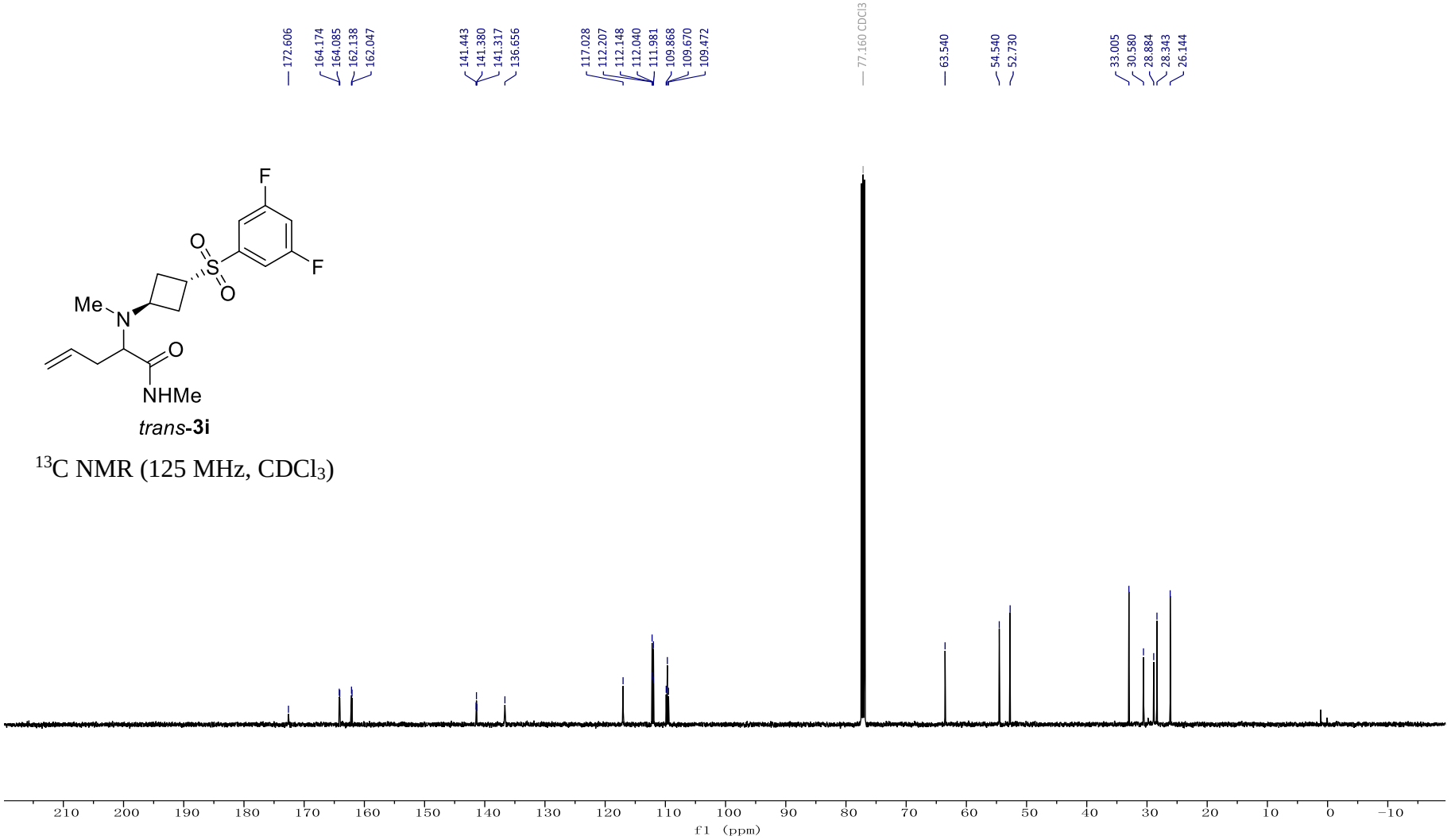
cis-**3i**

^{19}F NMR (376 MHz, $CDCl_3$)



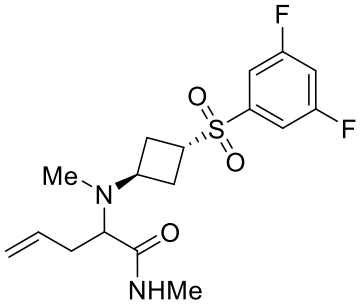
trans-**3i**

^{1}H NMR (500 MHz, $CDCl_3$)



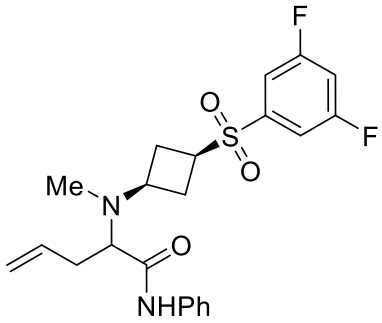
trans-**3i**

^{13}C NMR (125 MHz, $CDCl_3$)



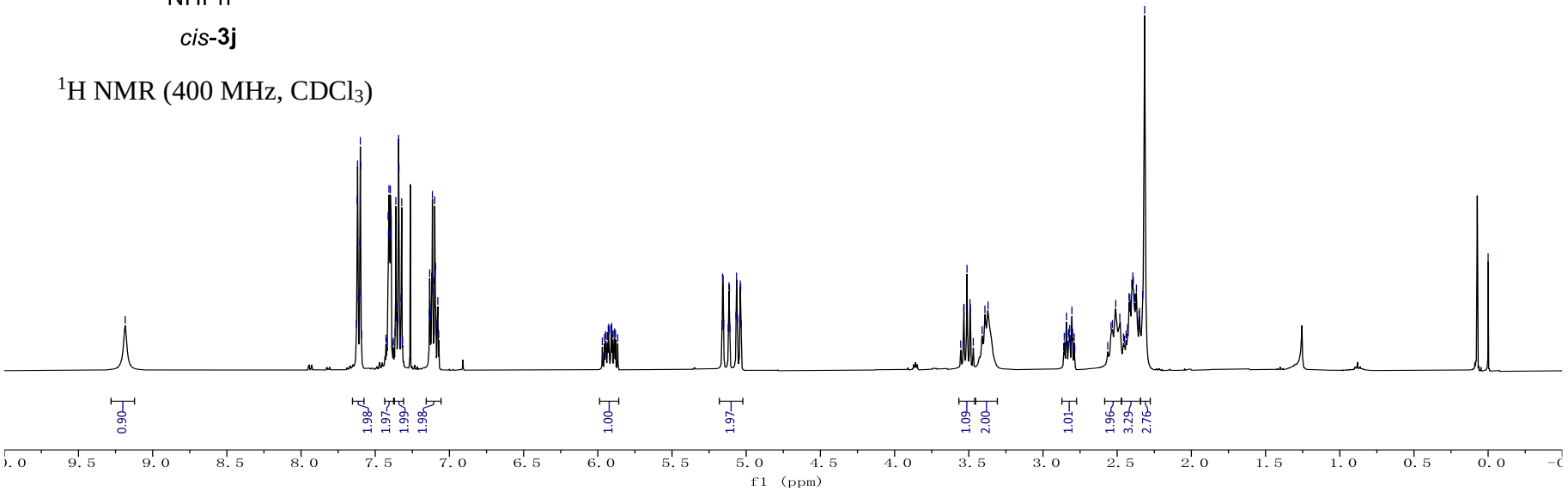
trans-**3i**

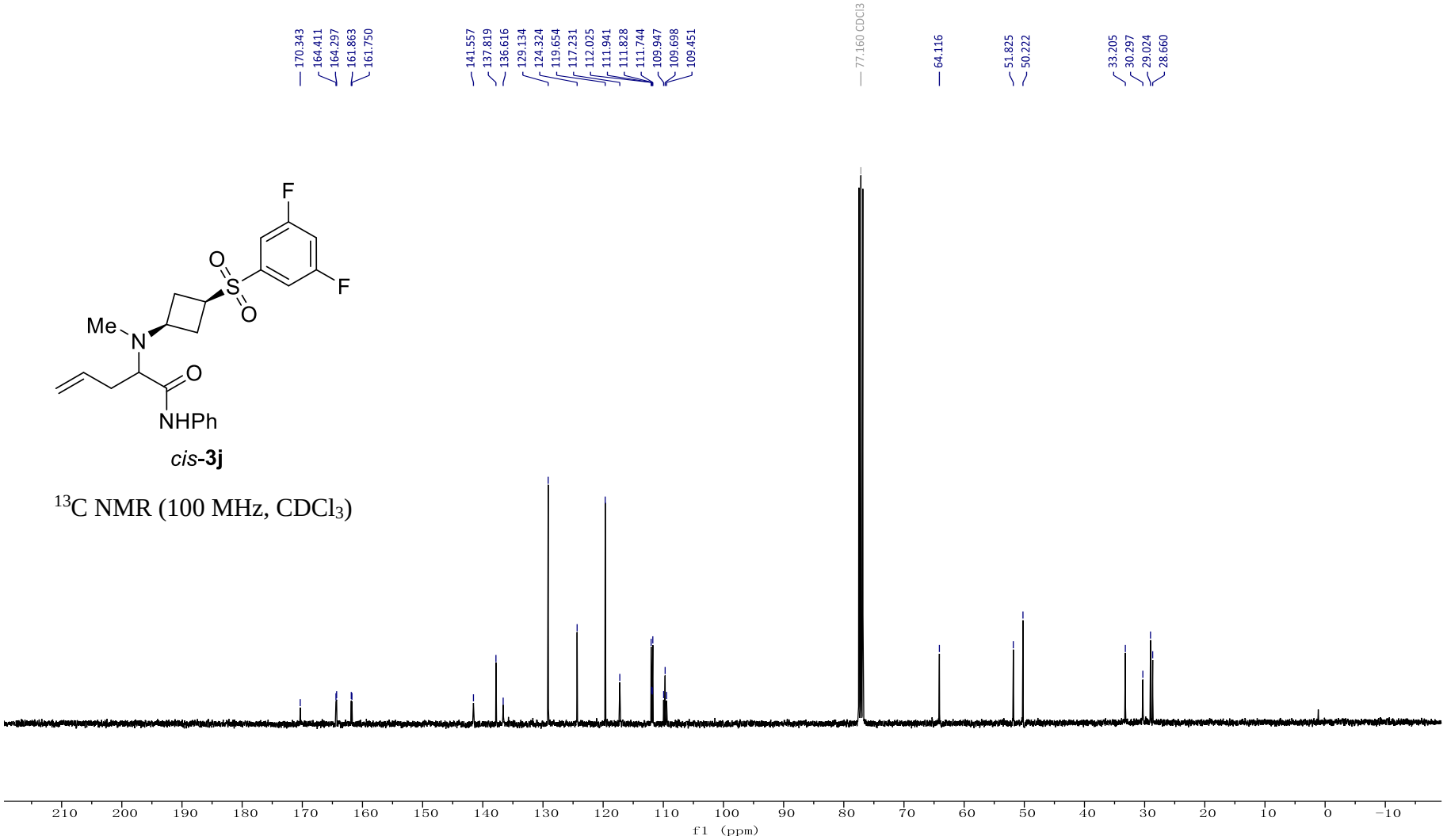
^{19}F NMR (471 MHz, $CDCl_3$)



cis-**3j**

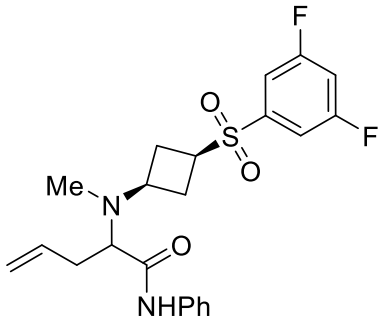
^{1}H NMR (400 MHz, $CDCl_3$)





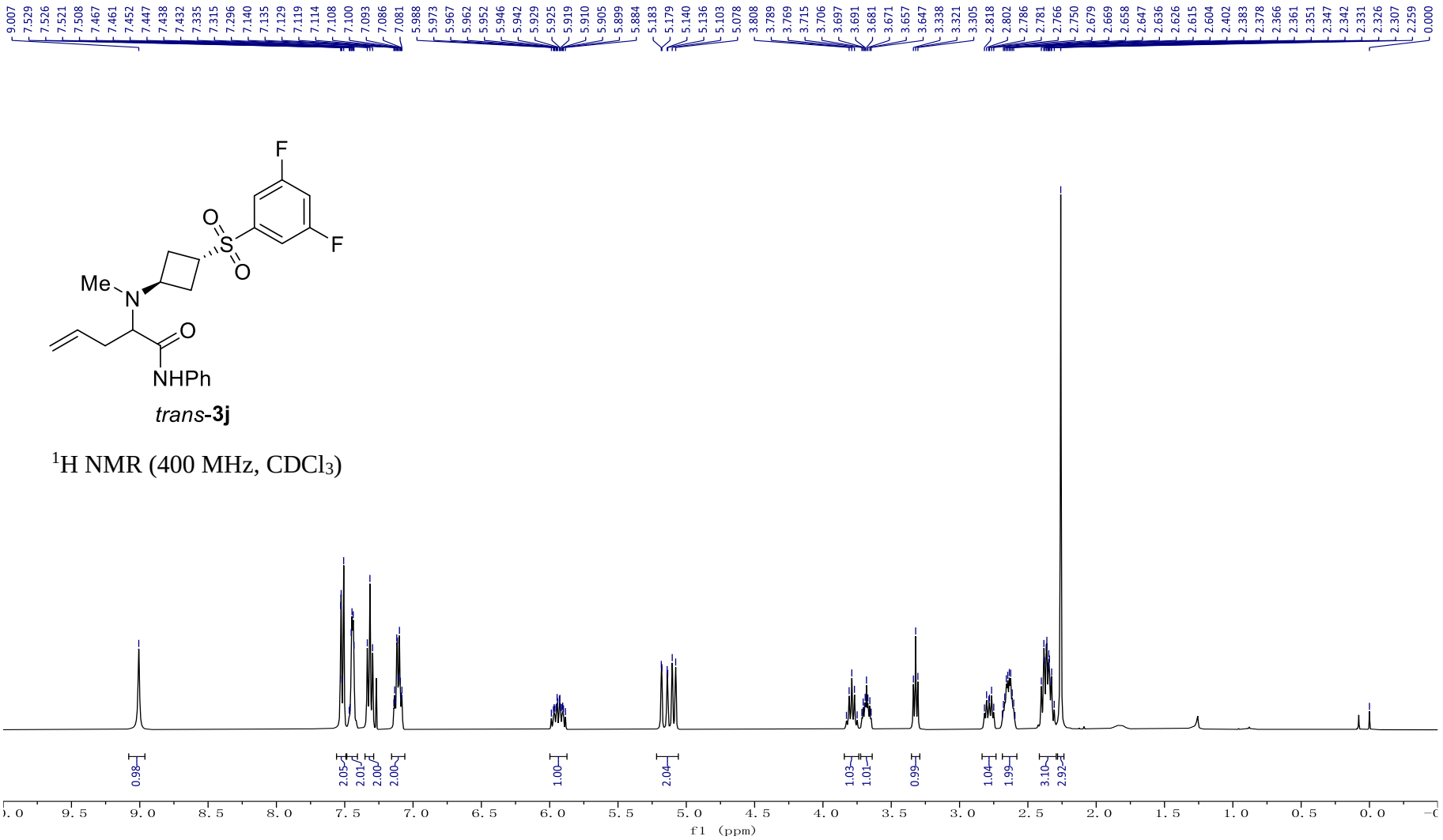
cis-**3j**

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



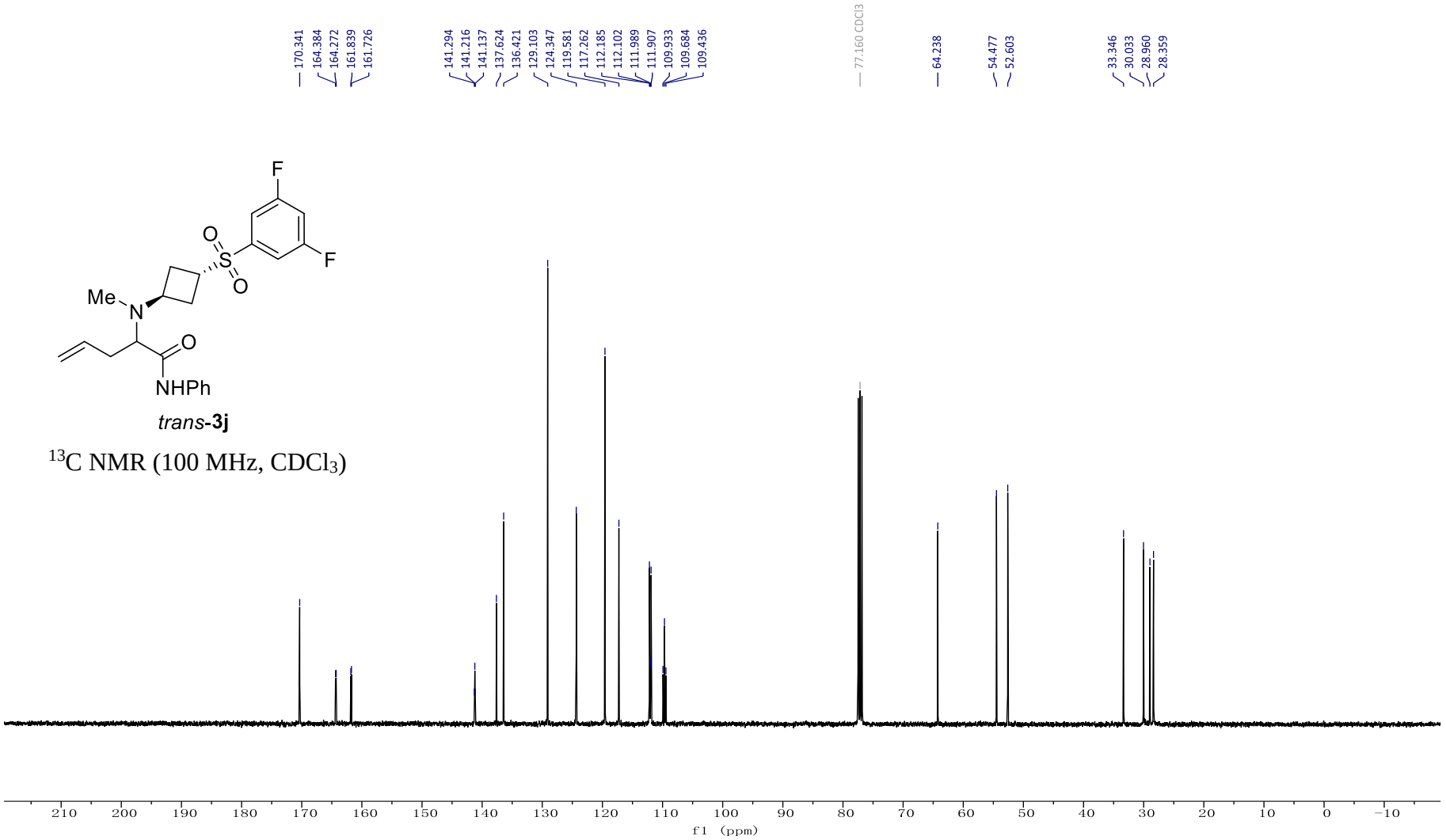
cis-**3j**

^{19}F NMR (376 MHz, $CDCl_3$)



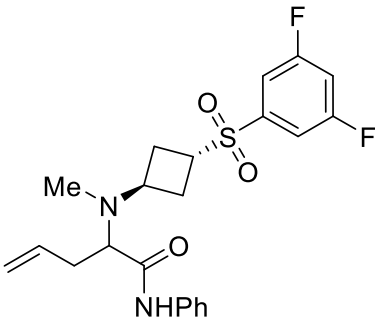
trans-**3j**

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



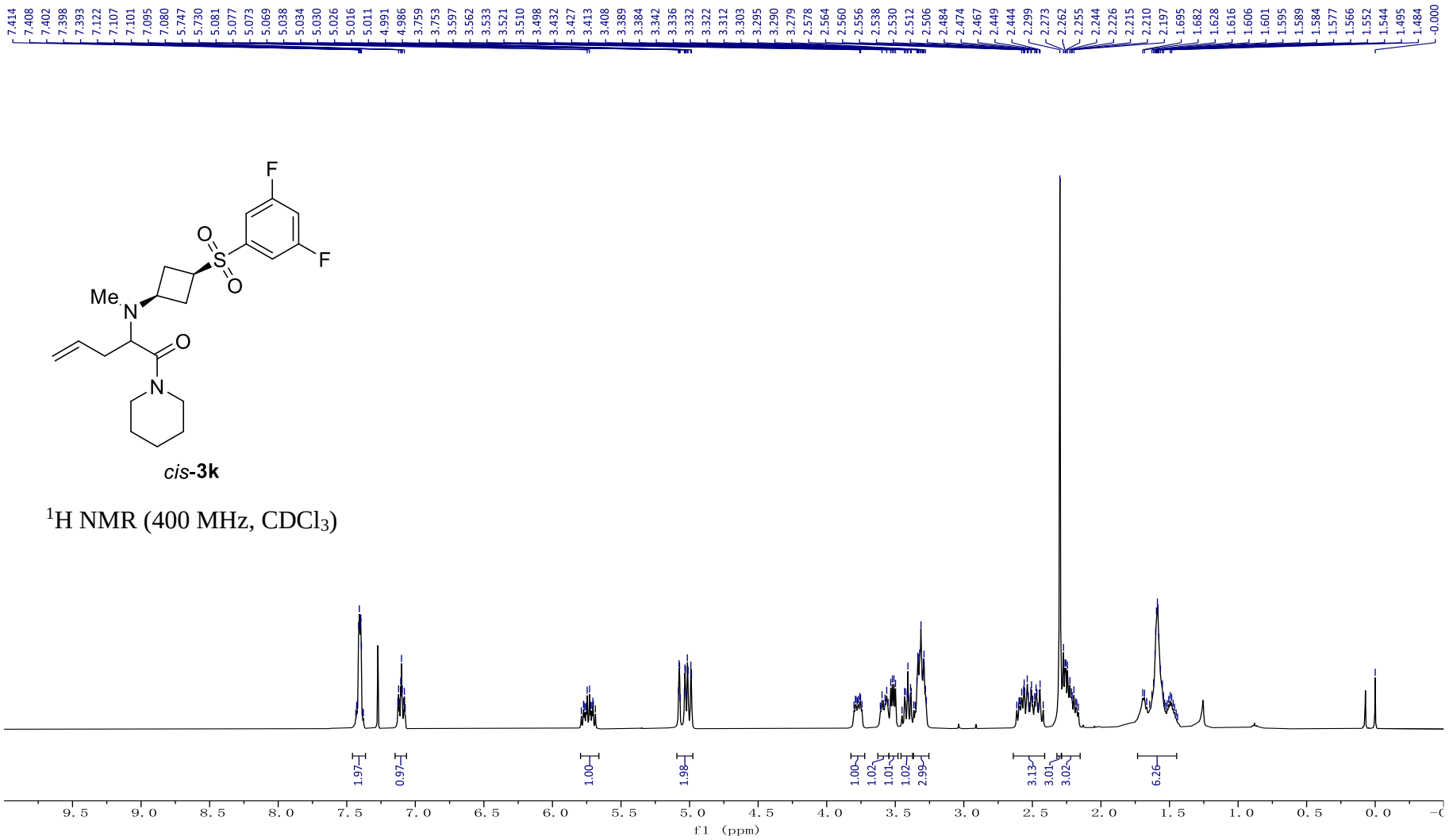
trans-**3j**

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



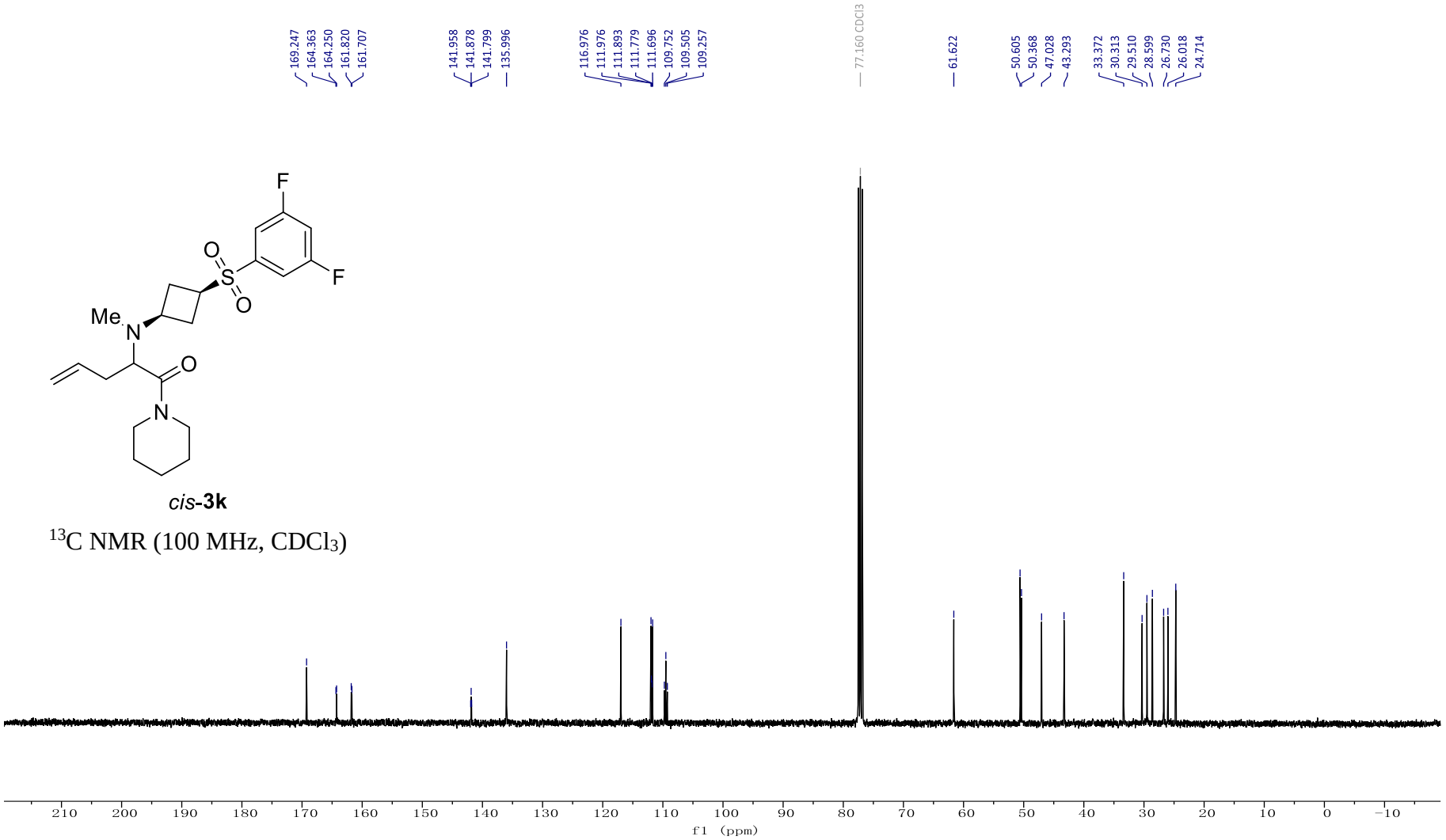
trans-**3j**

^{19}F NMR (376 MHz, $CDCl_3$)



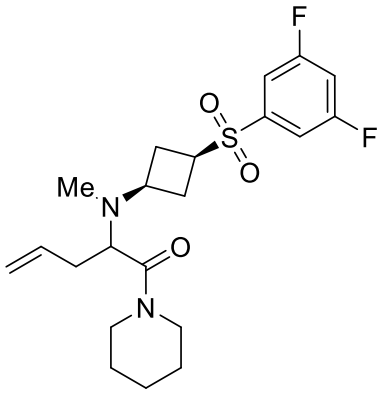
cis-**3k**

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



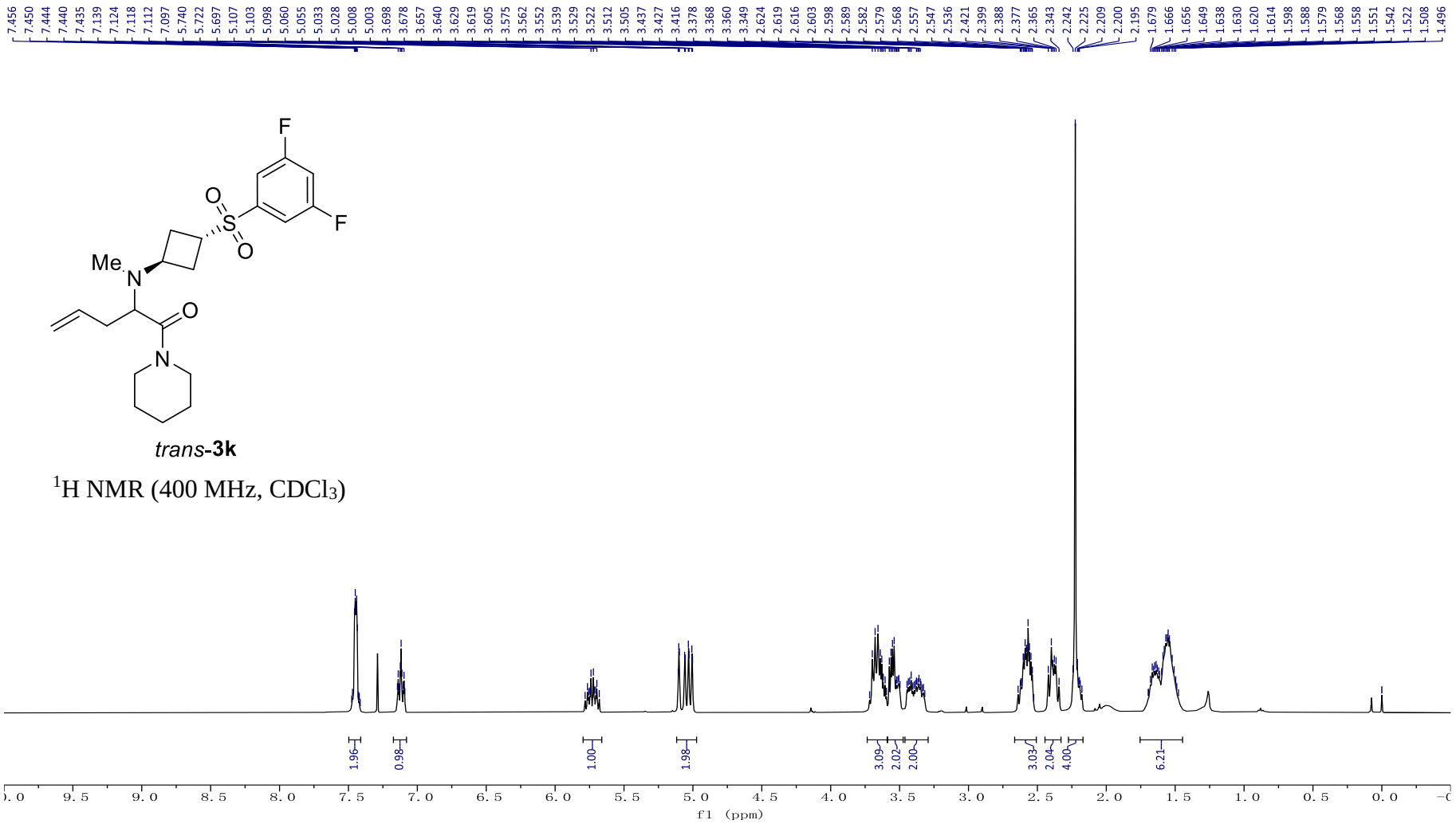
cis-**3k**

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



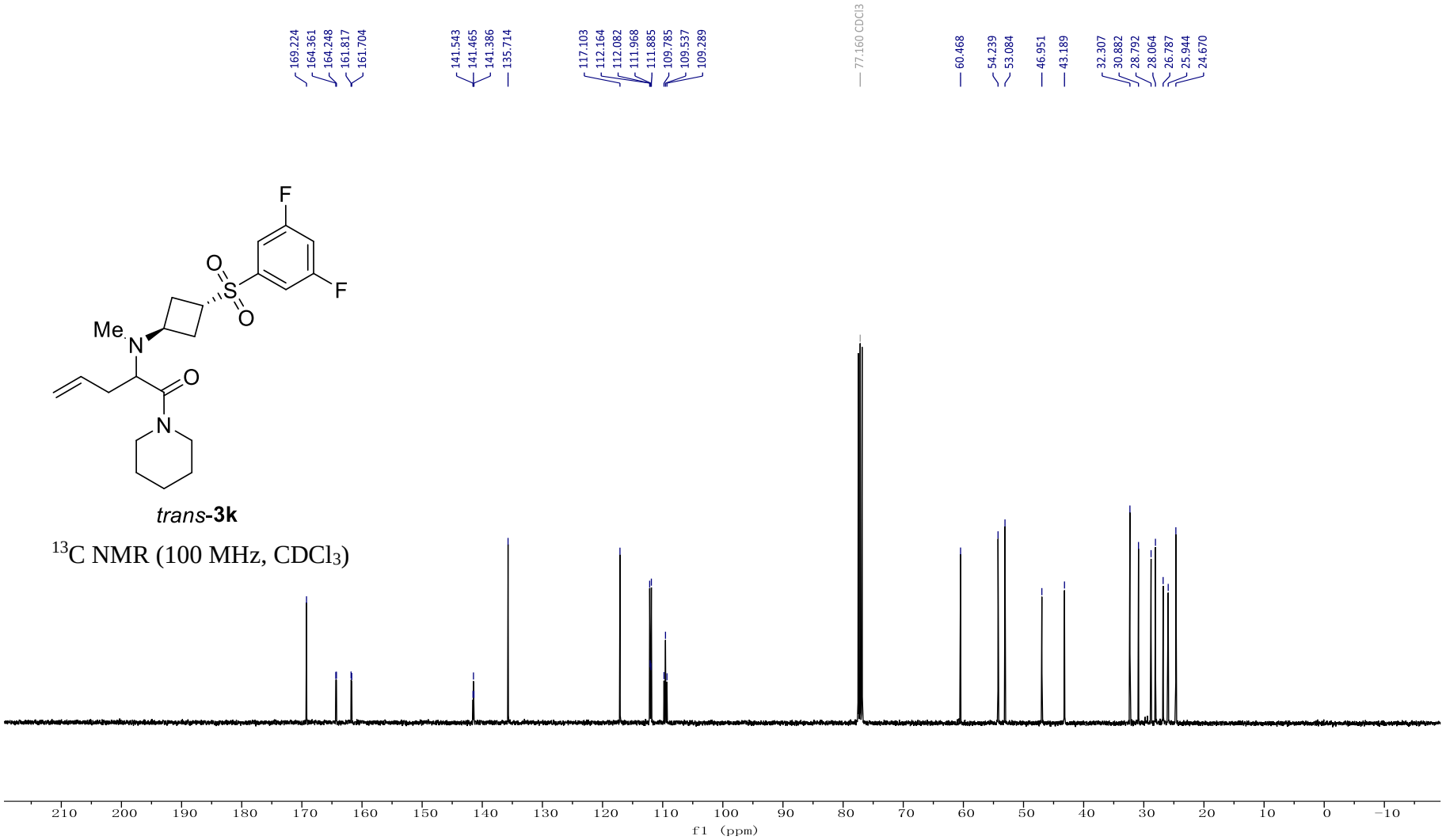
cis-**3k**

^{19}F NMR (376 MHz, $CDCl_3$)



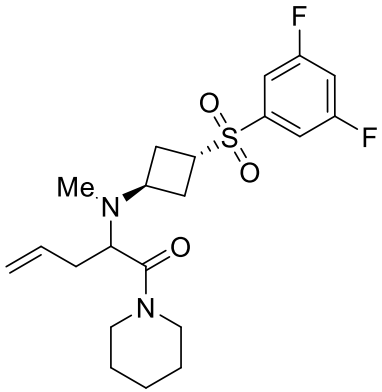
trans-**3k**

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



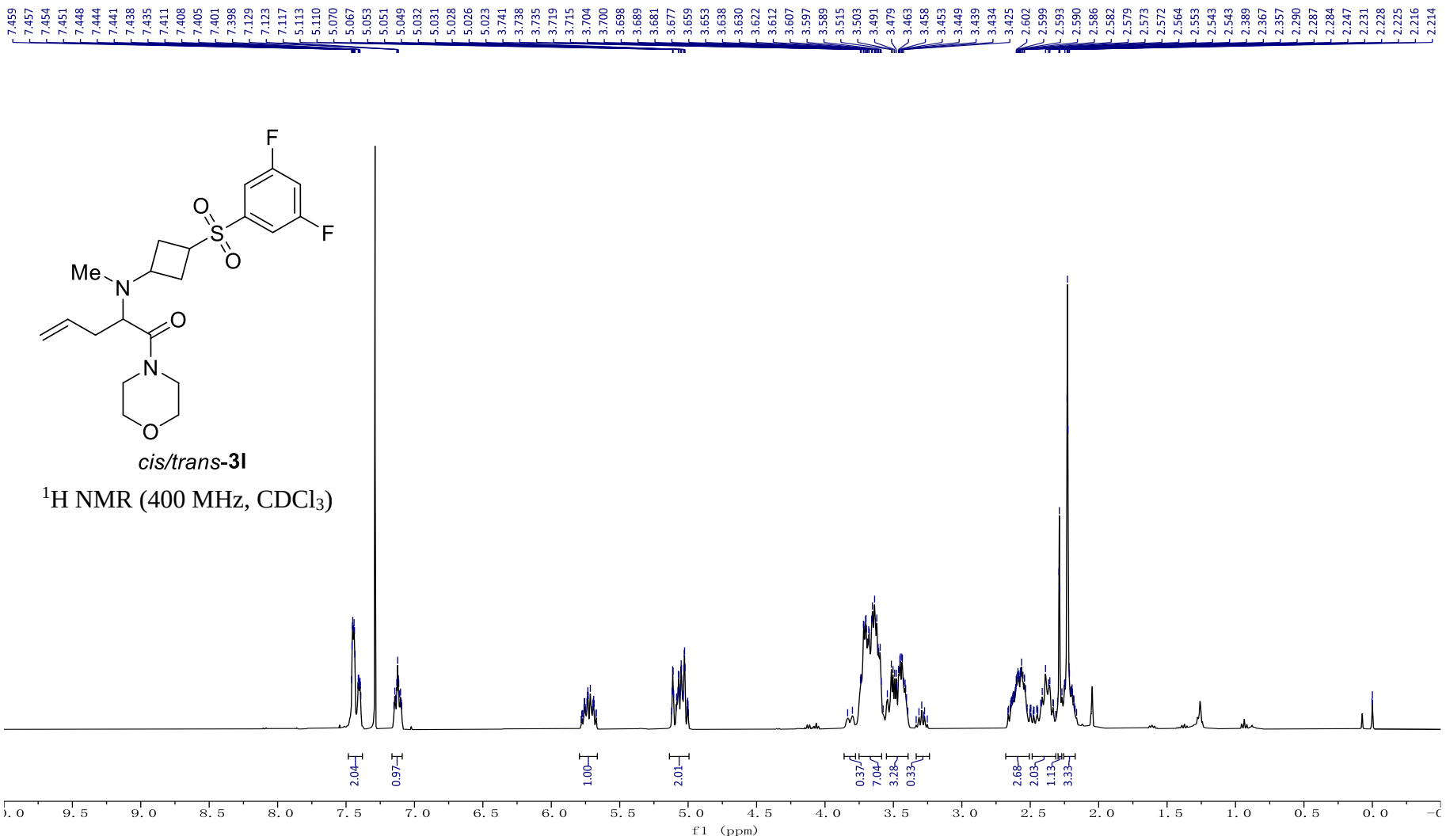
trans-**3k**

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



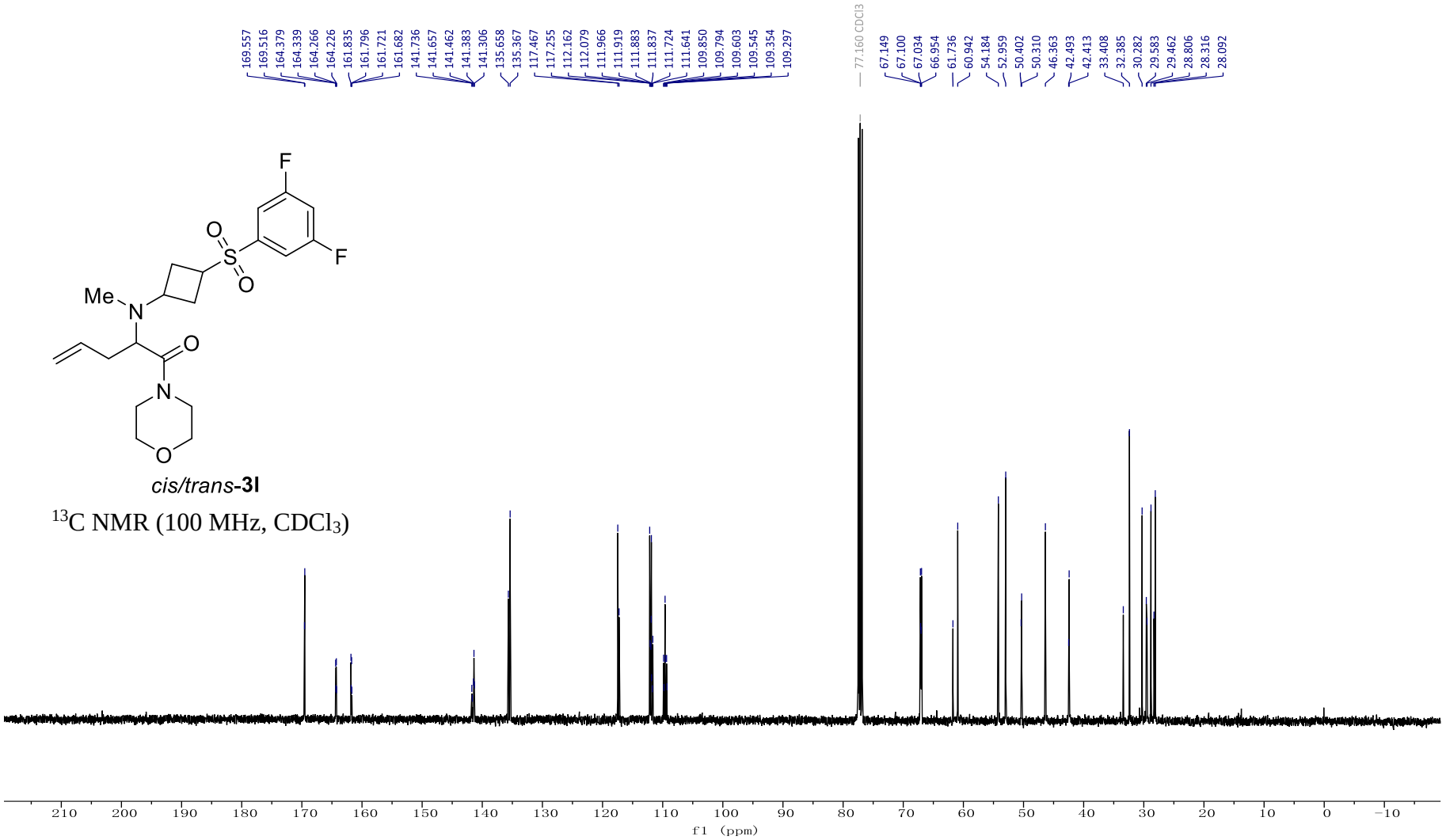
trans-**3k**

^{19}F NMR (376 MHz, $CDCl_3$)



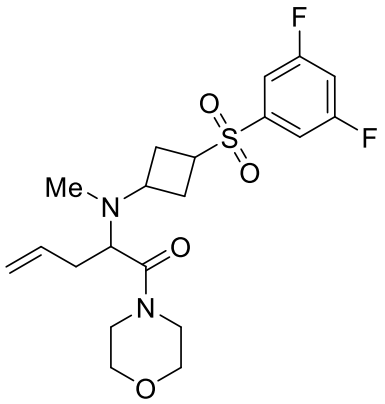
cis/trans-**3l**

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



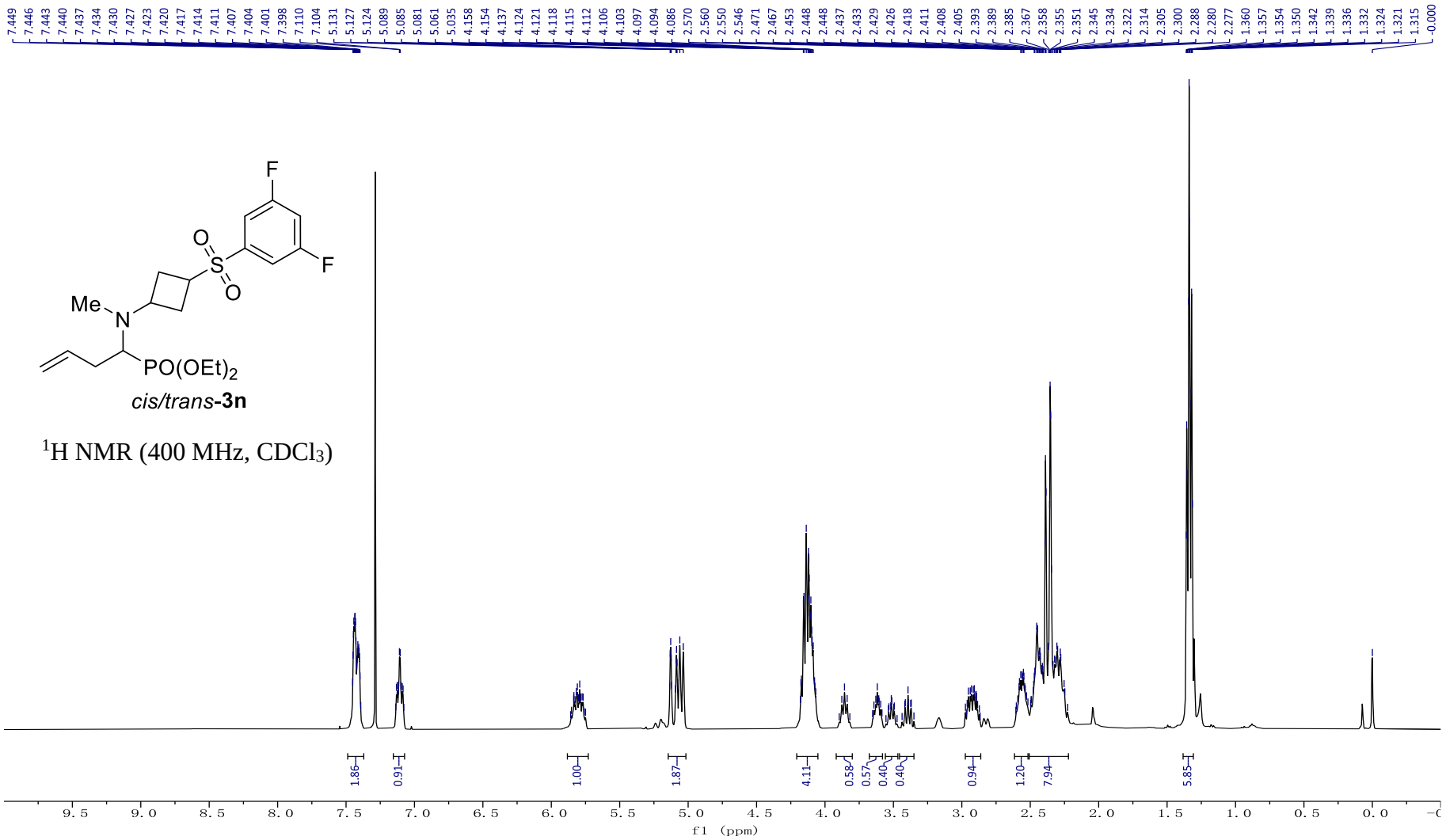
cis/trans-**3l**

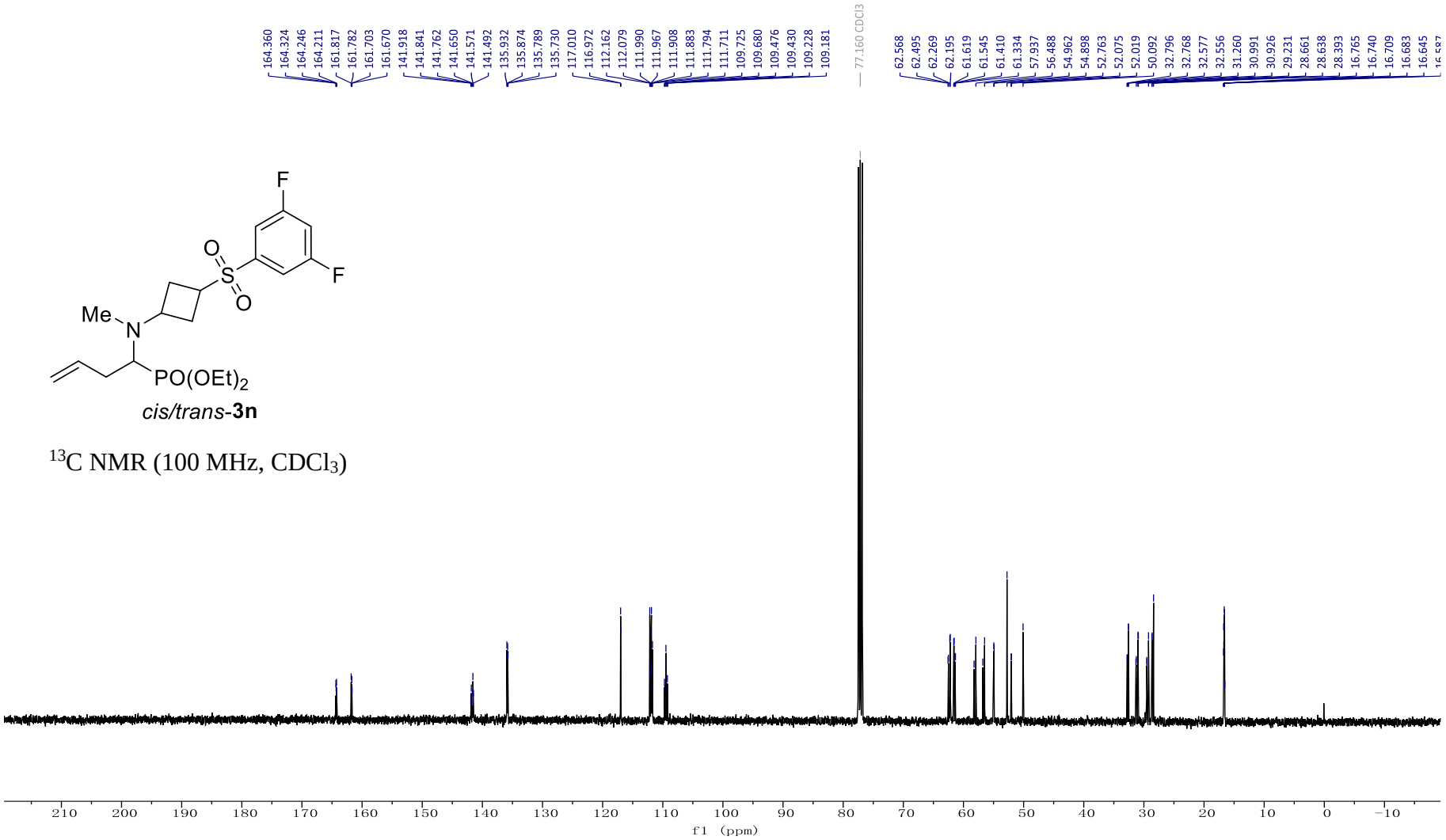
^{13}C NMR (100 MHz, $CDCl_3$)



cis/trans-**3l**

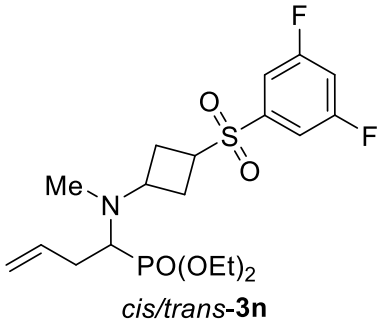
^{19}F NMR (376 MHz, $CDCl_3$)


F
O
S
O
F
Me
N
PO(OEt)2
cis/trans-3n
1H NMR (400 MHz, CDCl3)
f1 (ppm)



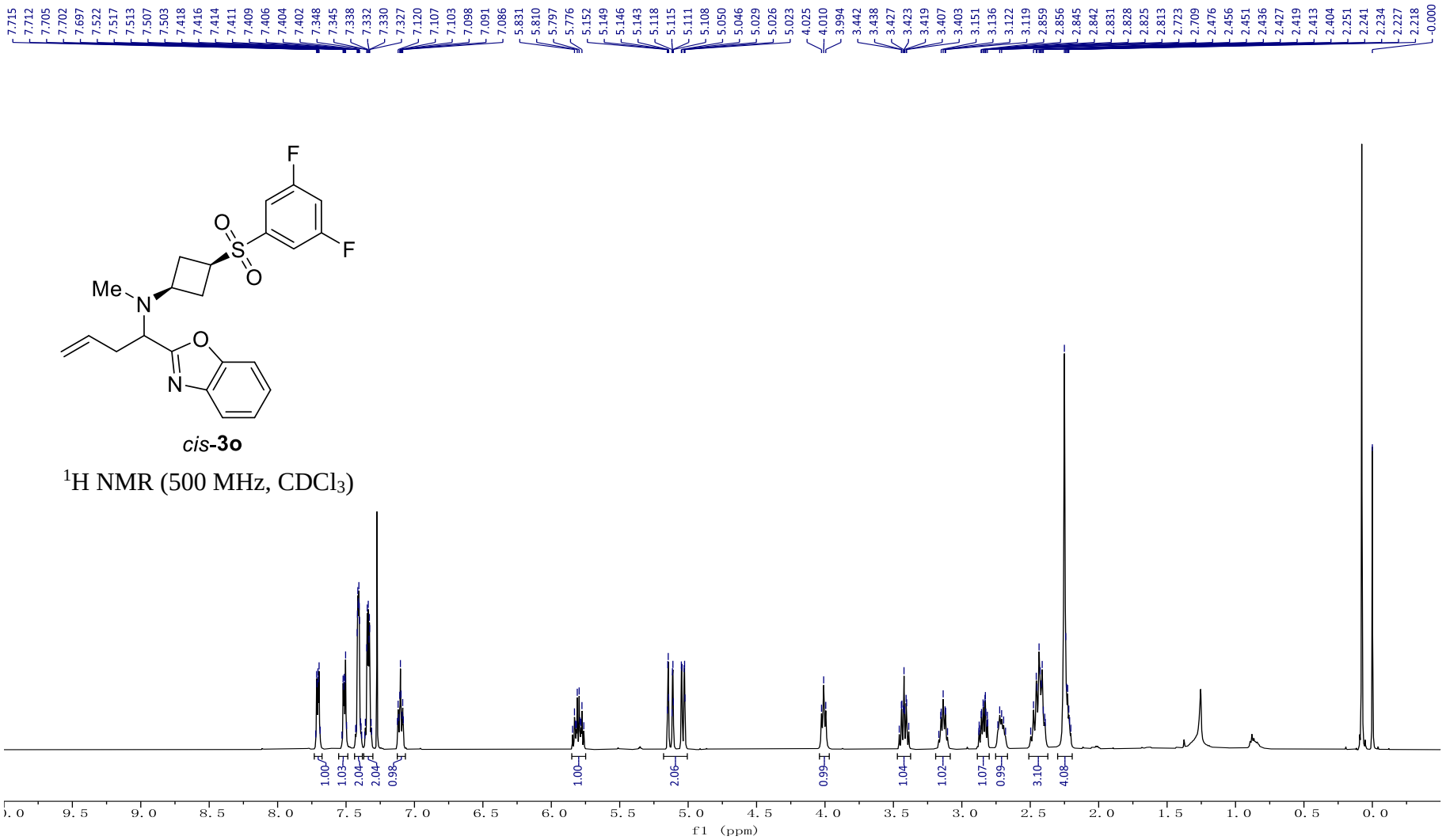
cis/trans-**3n**

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



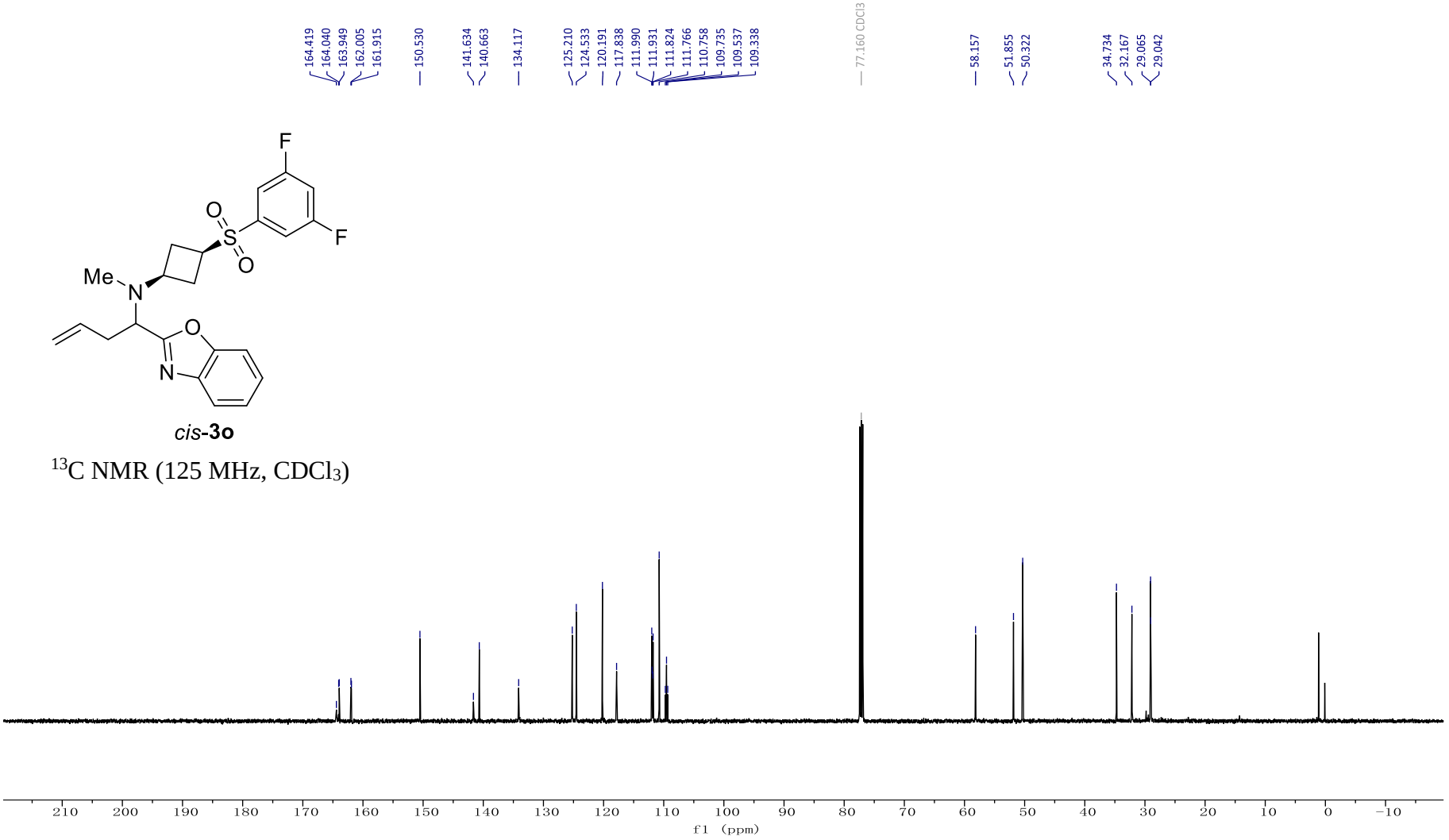
cis/trans-**3n**

^{19}F NMR (376 MHz, $CDCl_3$)



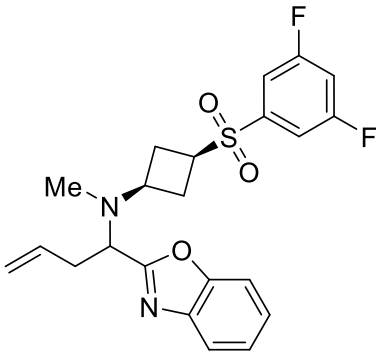
cis-**3o**

^{1}H NMR (500 MHz, $CDCl_3$)



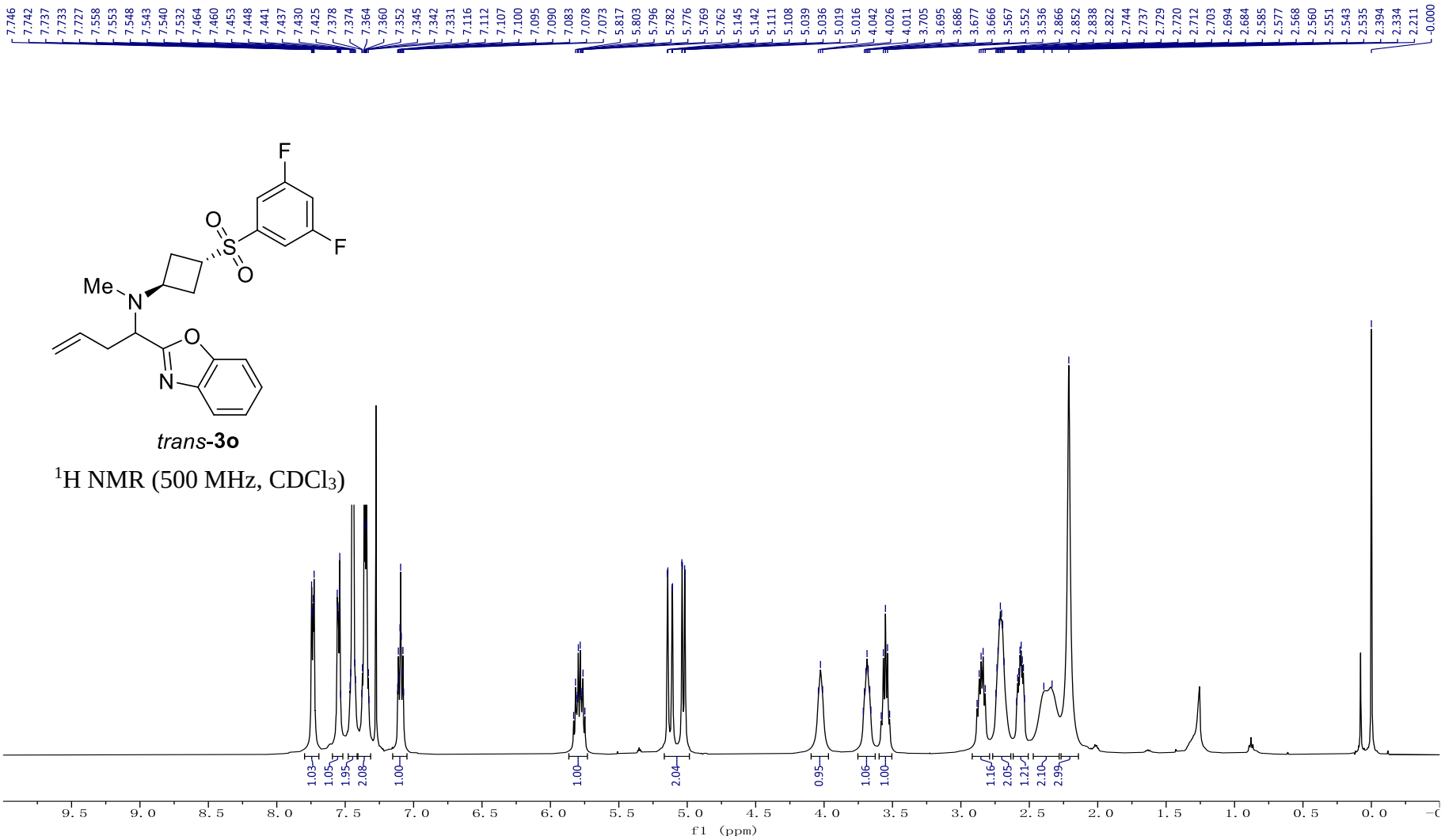
cis-**3o**

^{13}C NMR (125 MHz, $CDCl_3$)



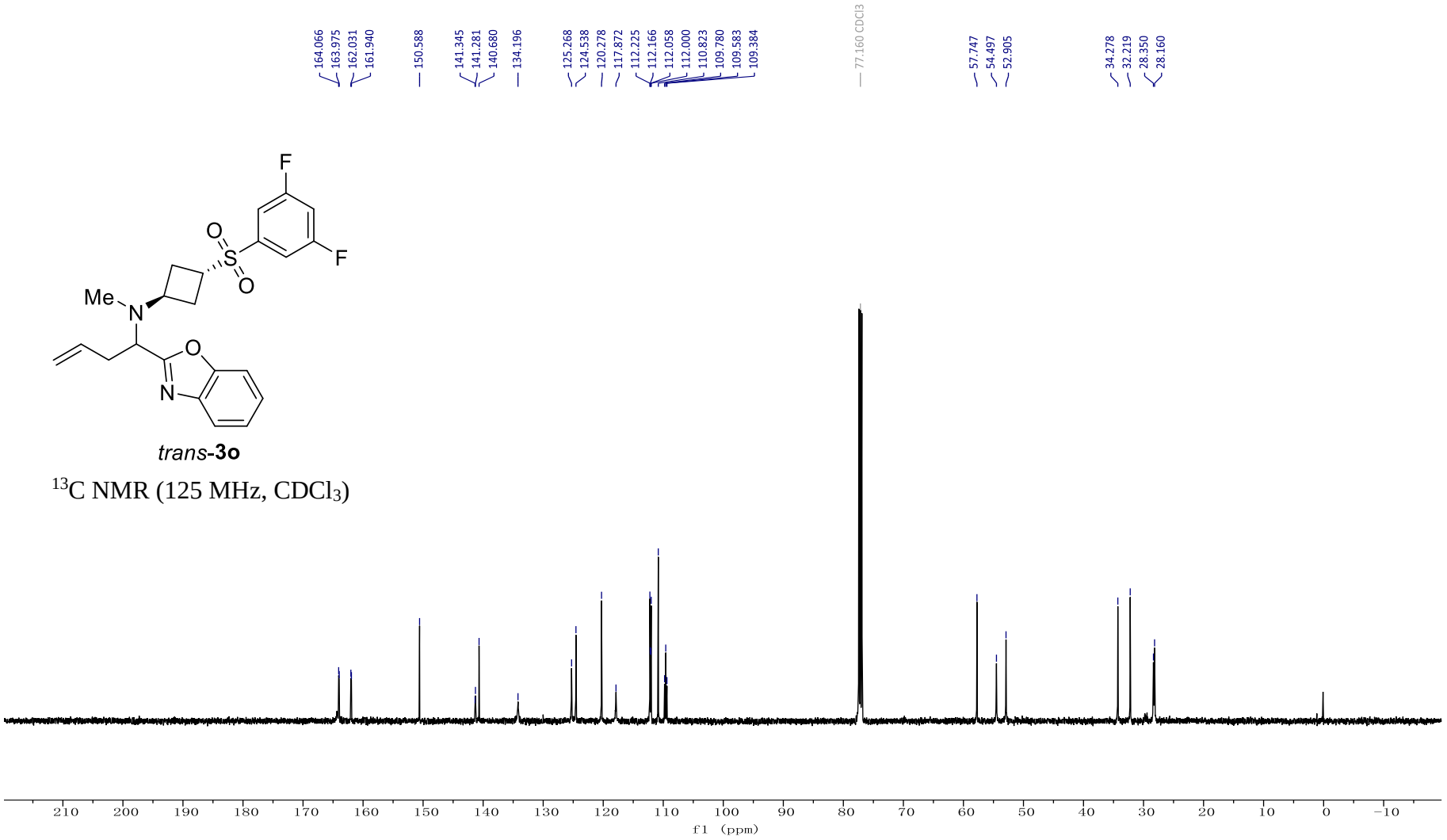
cis-**3o**

^{19}F NMR (471 MHz, $CDCl_3$)



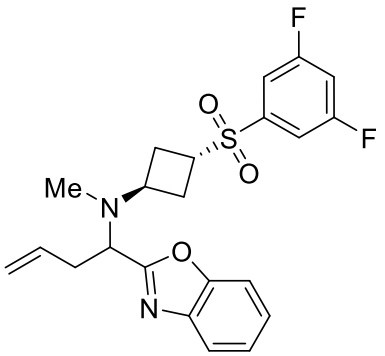
trans-**3o**

^{1}H NMR (500 MHz, $CDCl_3$)



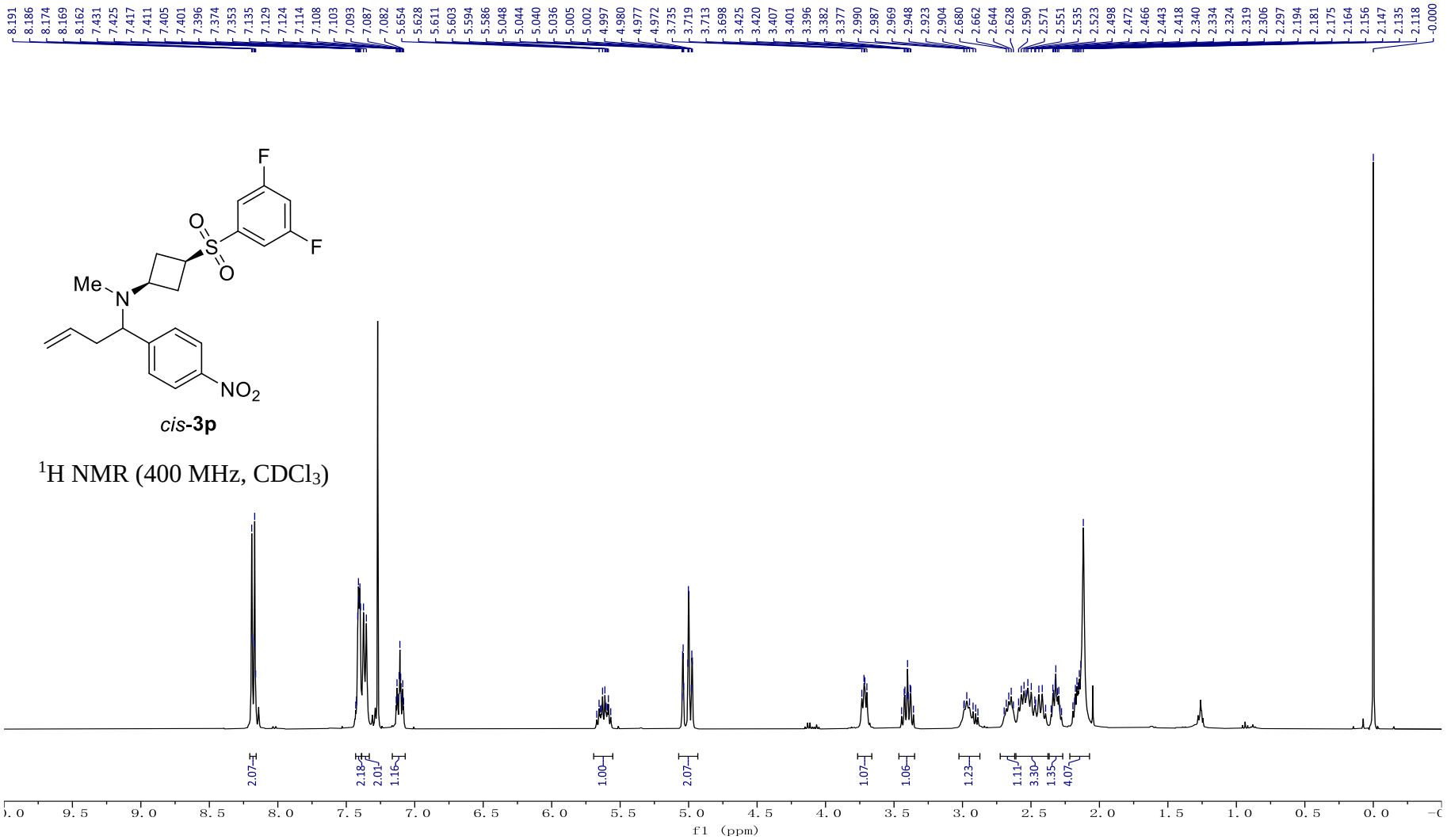
trans-**3o**

^{13}C NMR (125 MHz, $CDCl_3$)



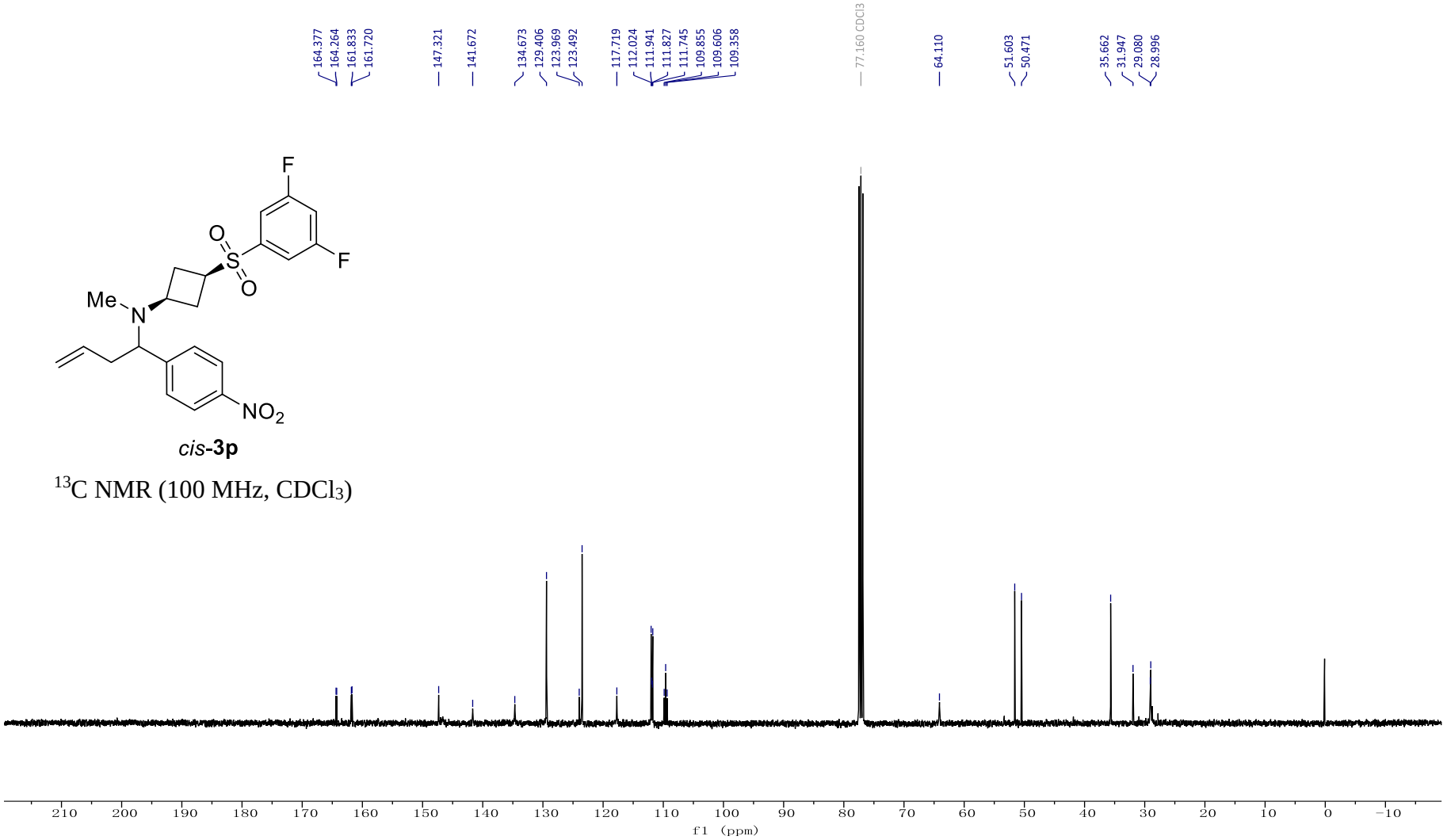
trans-**3o**

^{19}F NMR (471 MHz, $CDCl_3$)



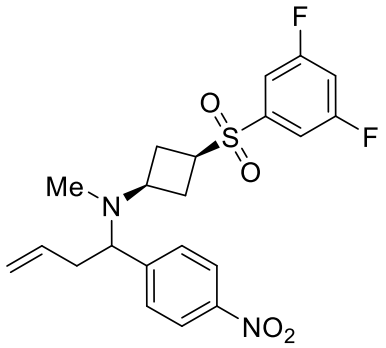
cis-**3p**

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



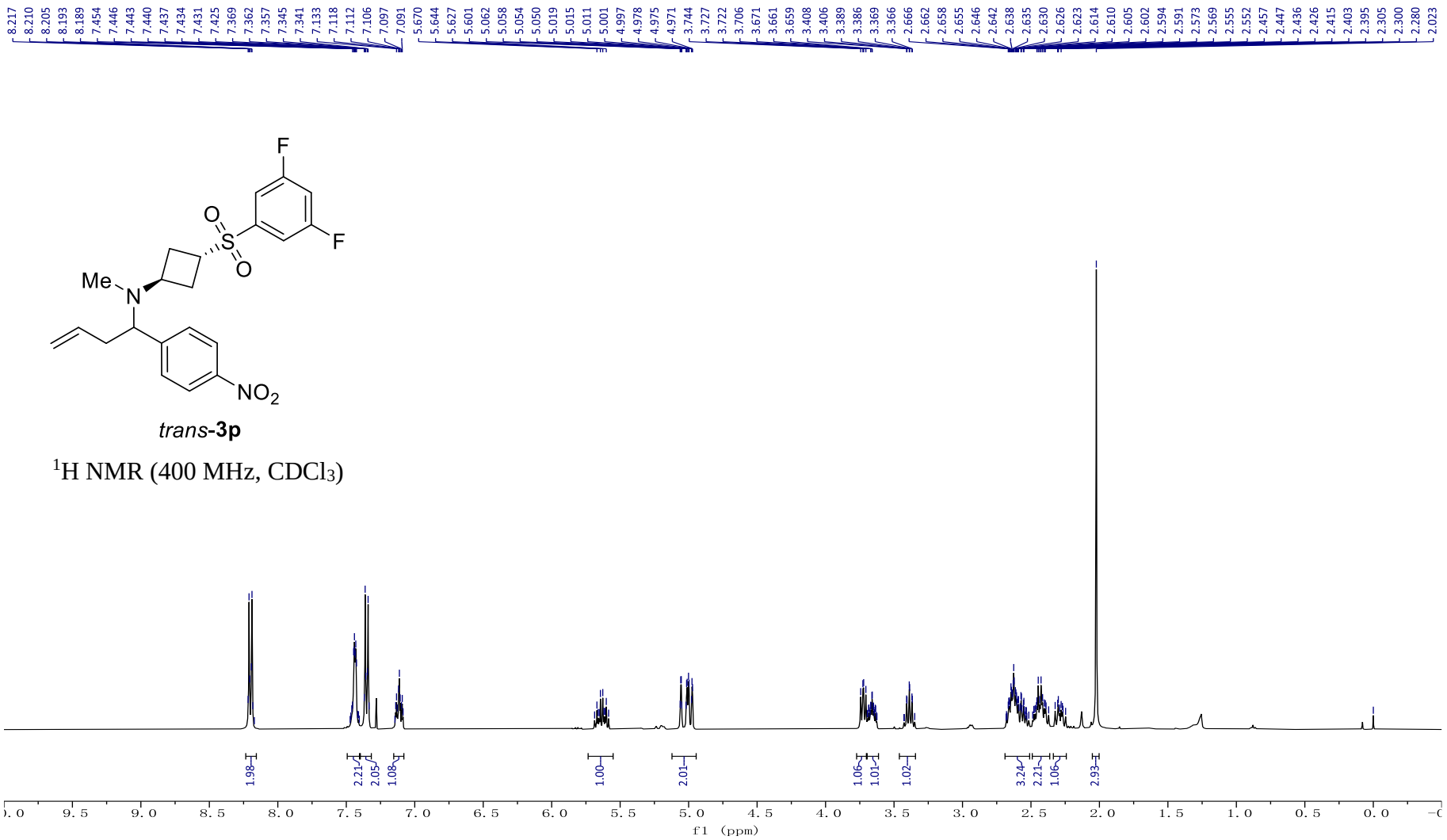
cis-**3p**

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



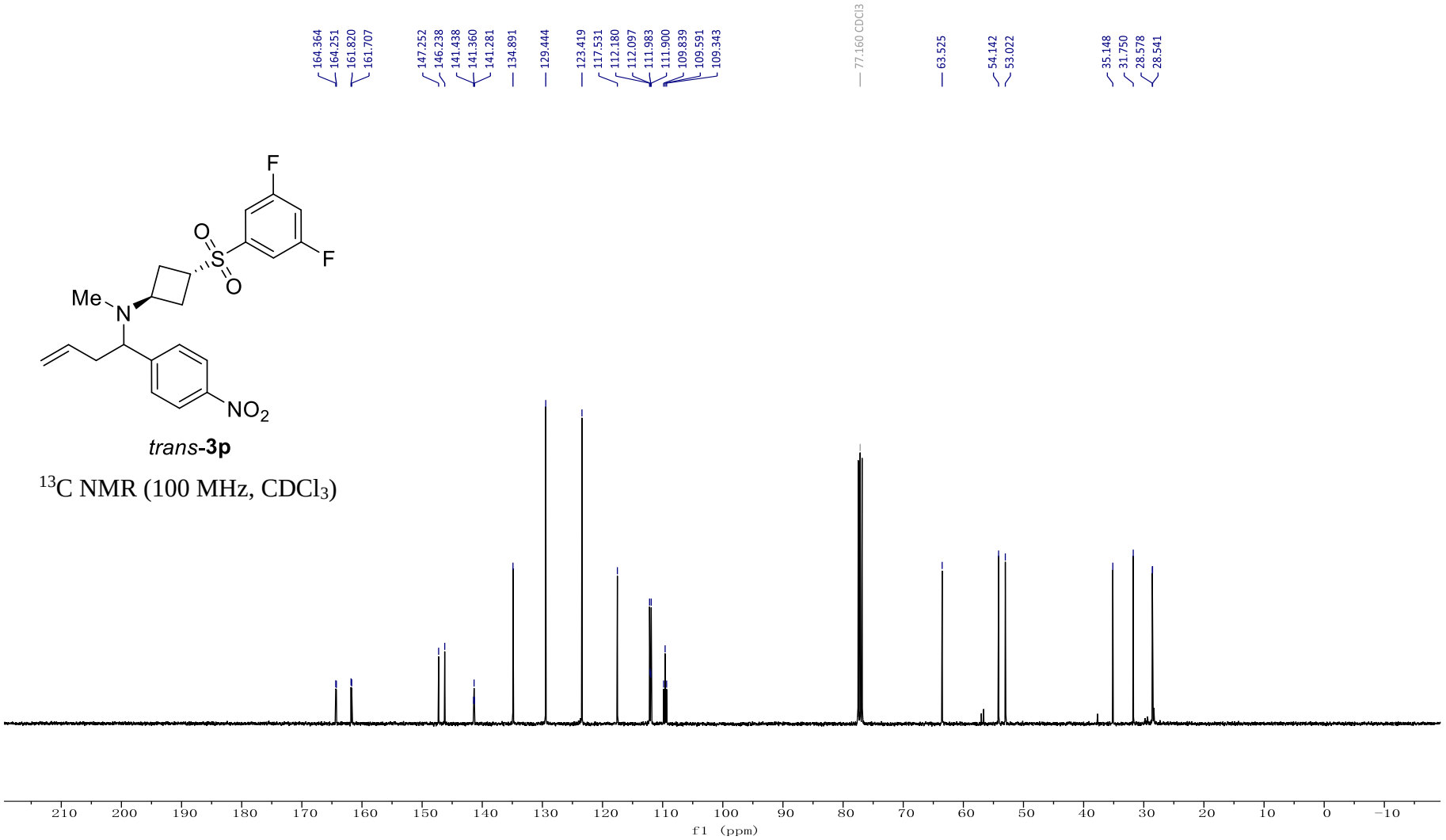
cis-**3p**

^{19}F NMR (376 MHz, $CDCl_3$)



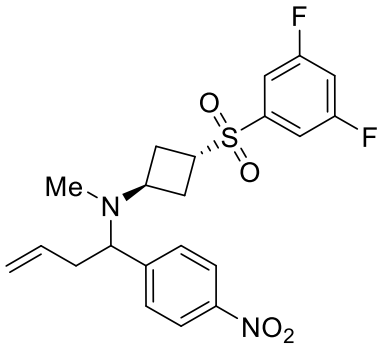
trans-**3p**

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



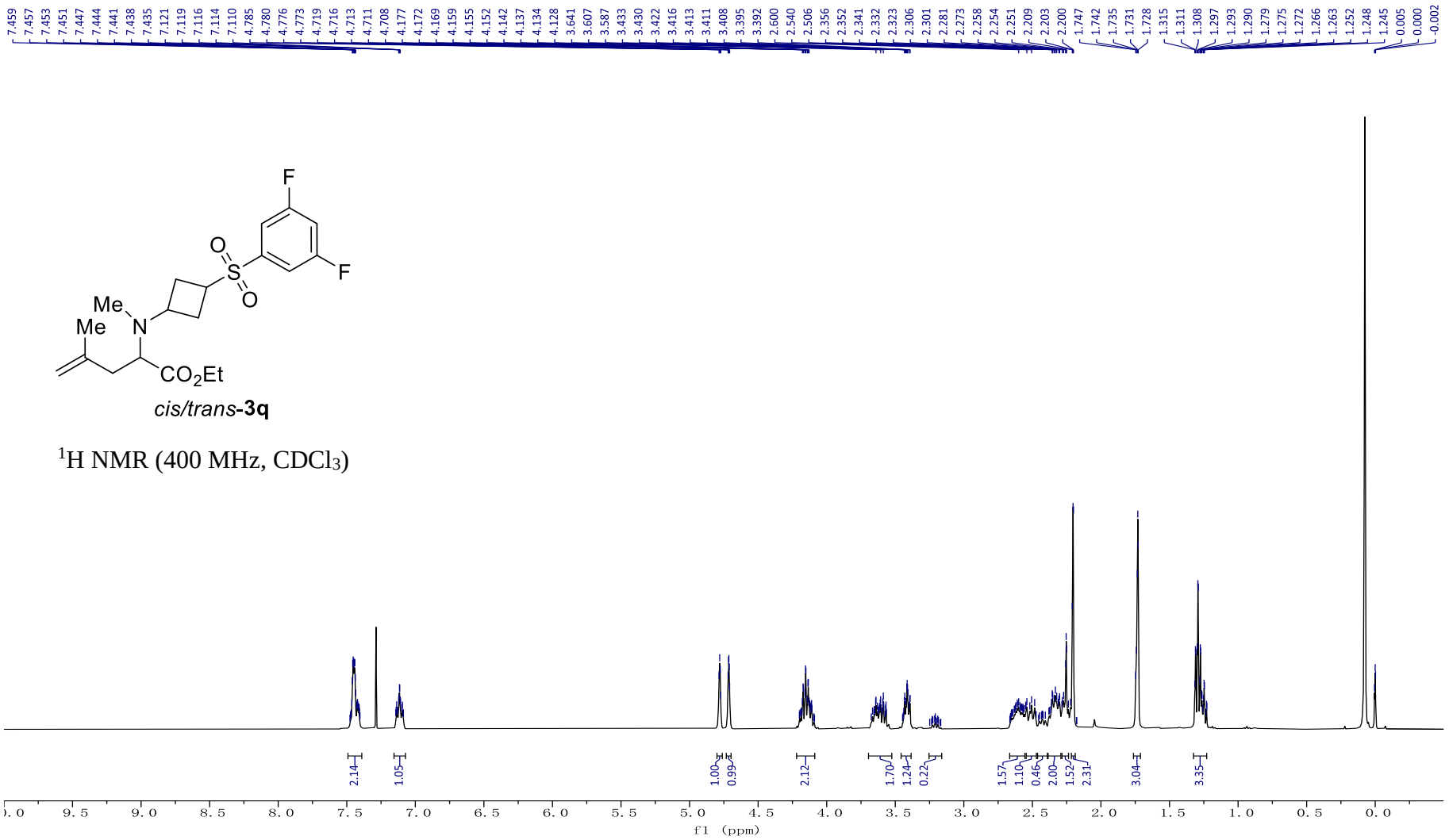
trans-**3p**

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



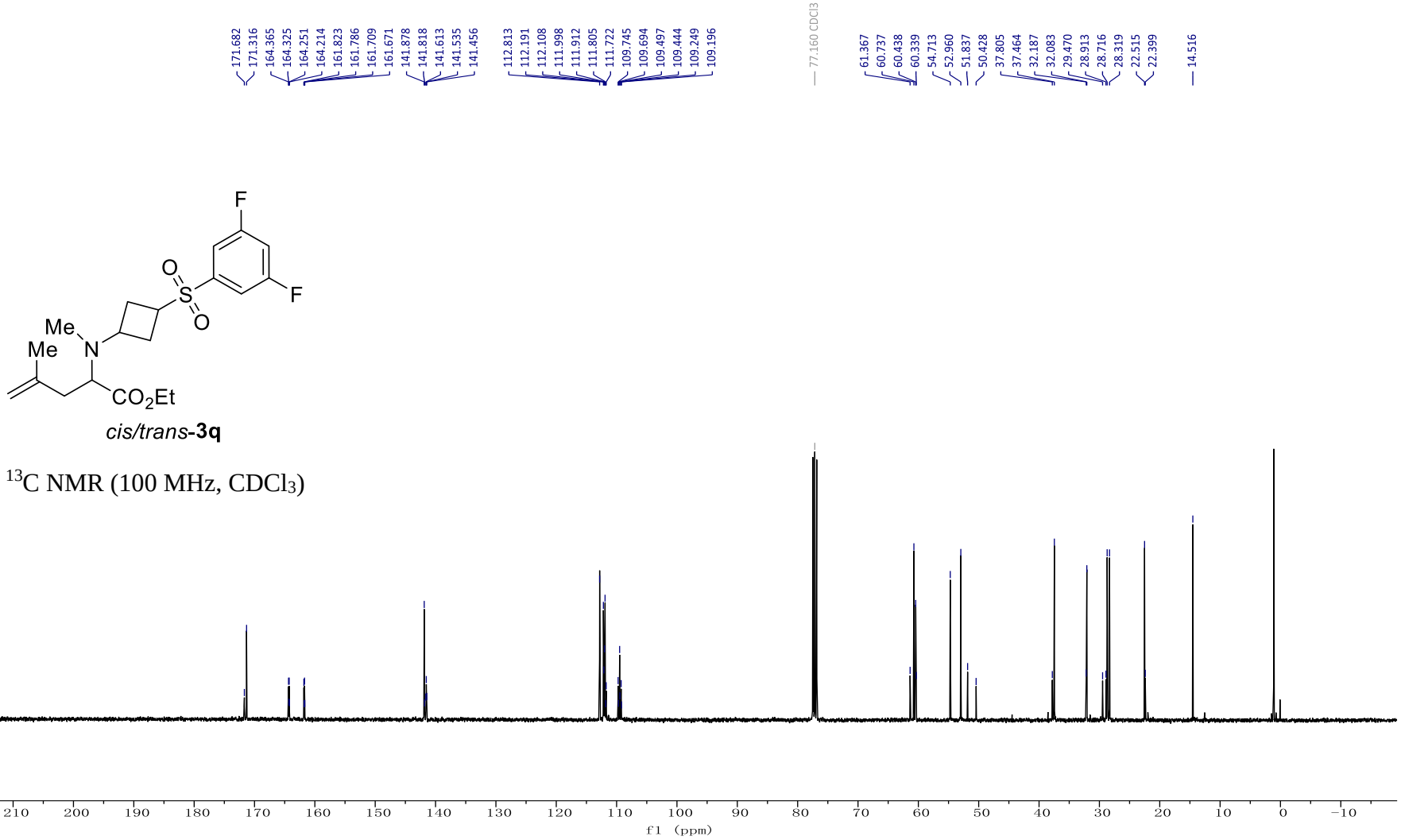
trans-**3p**

^{19}F NMR (376 MHz, $CDCl_3$)



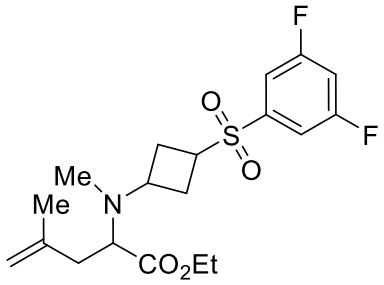
cis/trans-**3q**

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



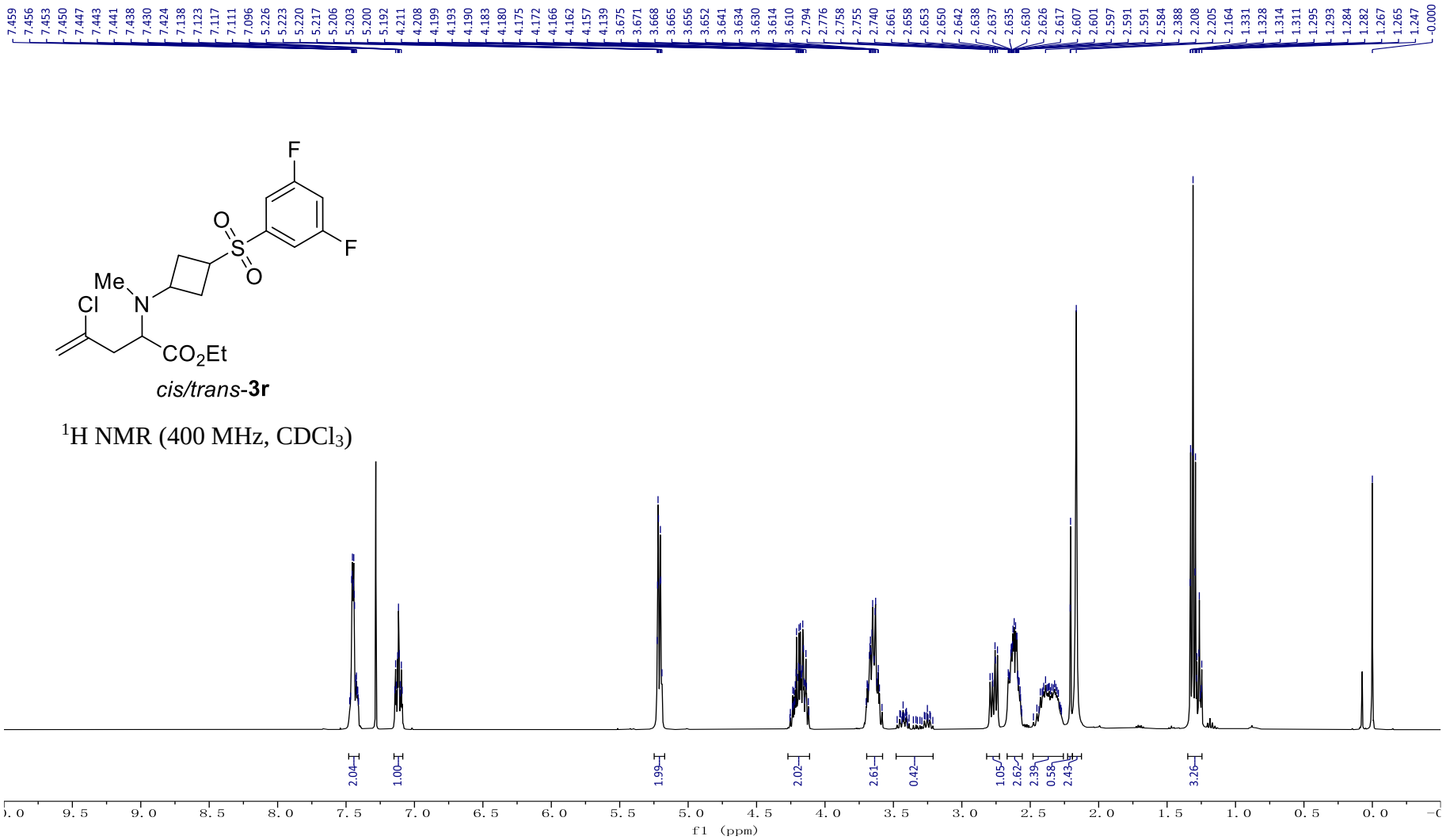
cis/trans-**3q**

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



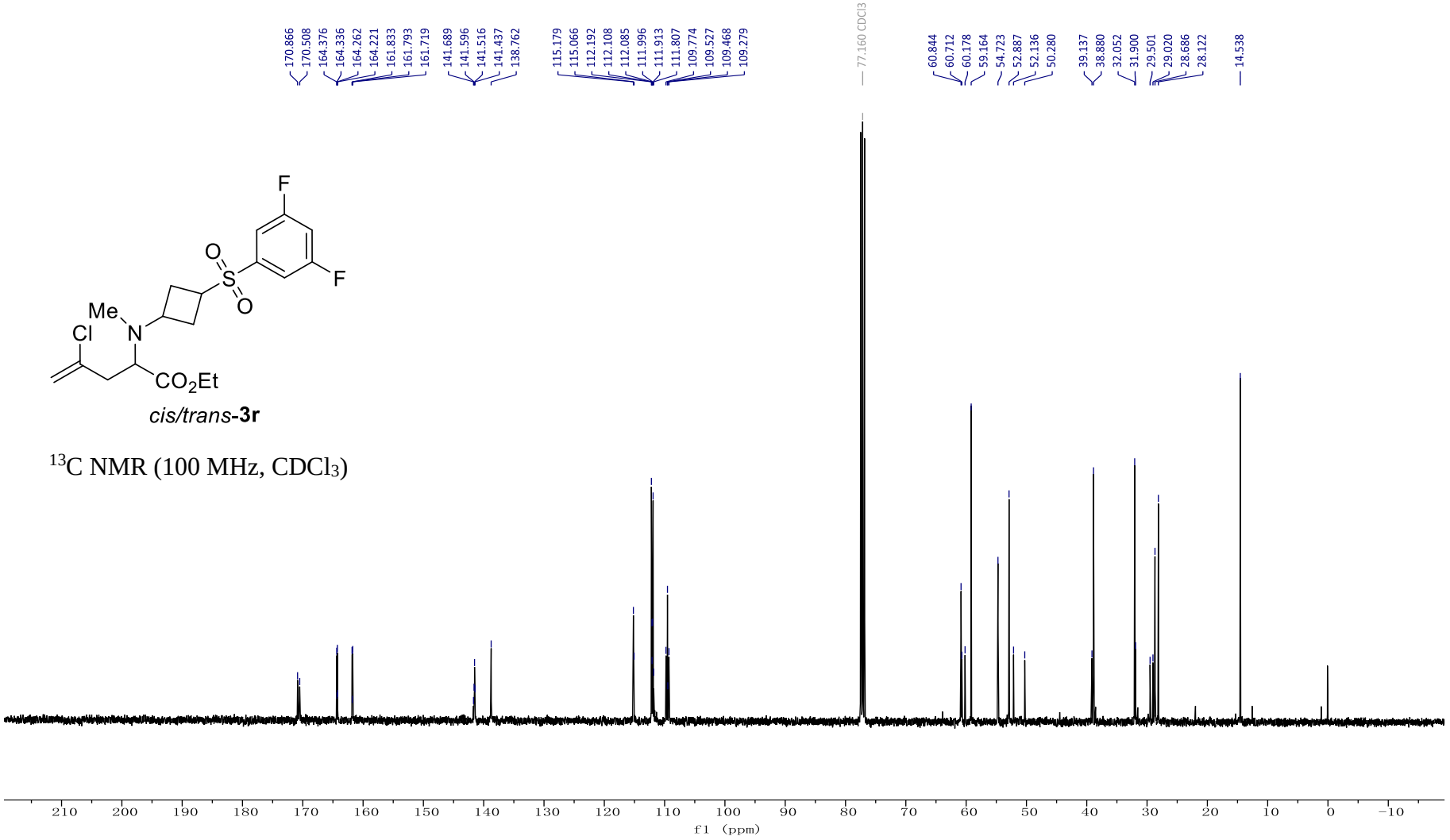
cis/trans-**3q**

^{19}F NMR (376 MHz, $CDCl_3$)



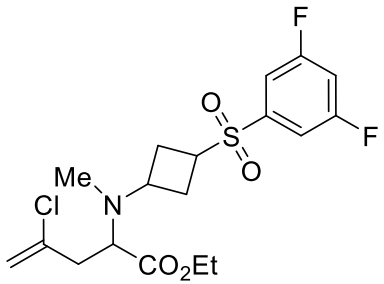
cis/trans-**3r**

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



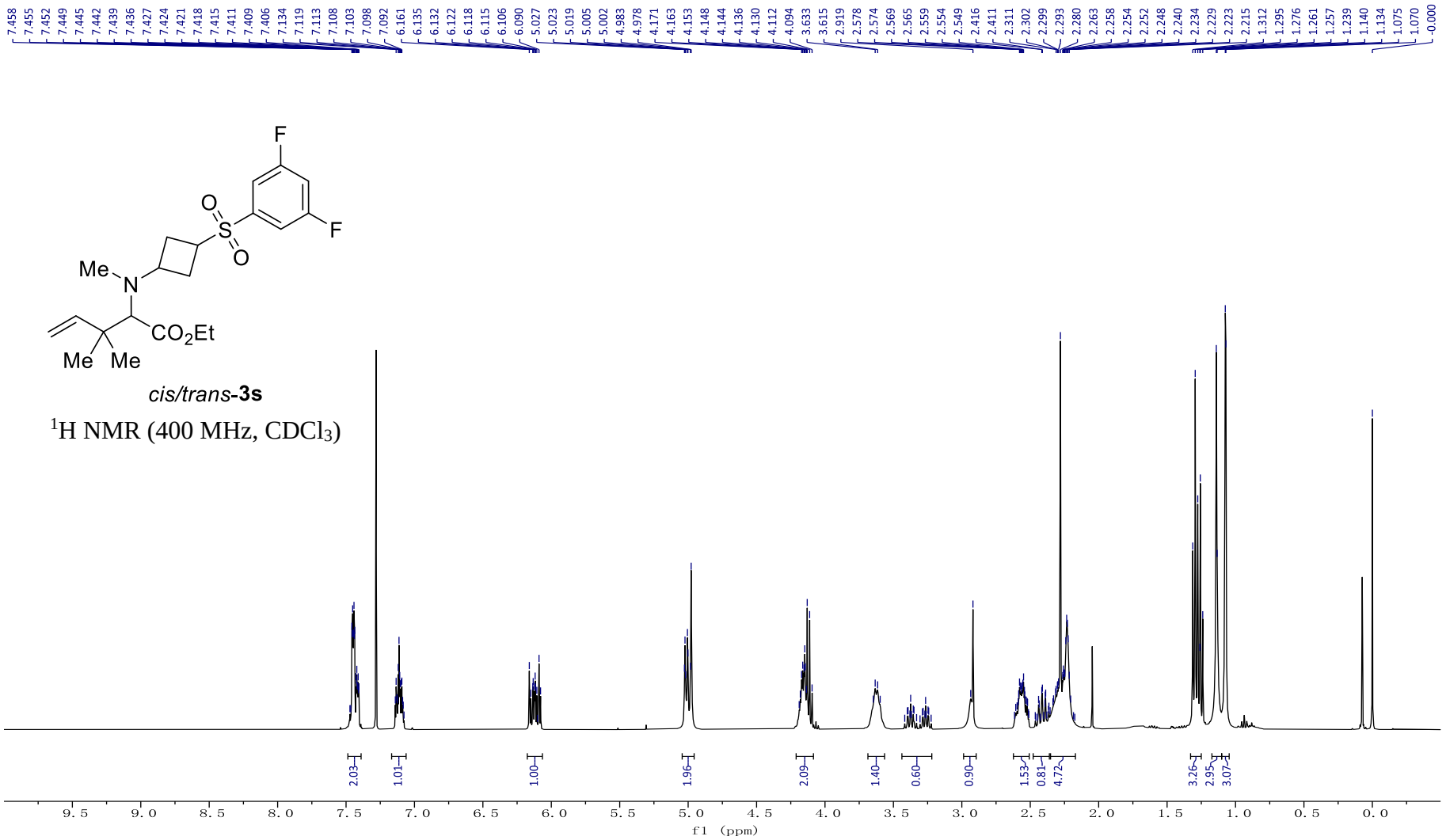
cis/trans-**3r**

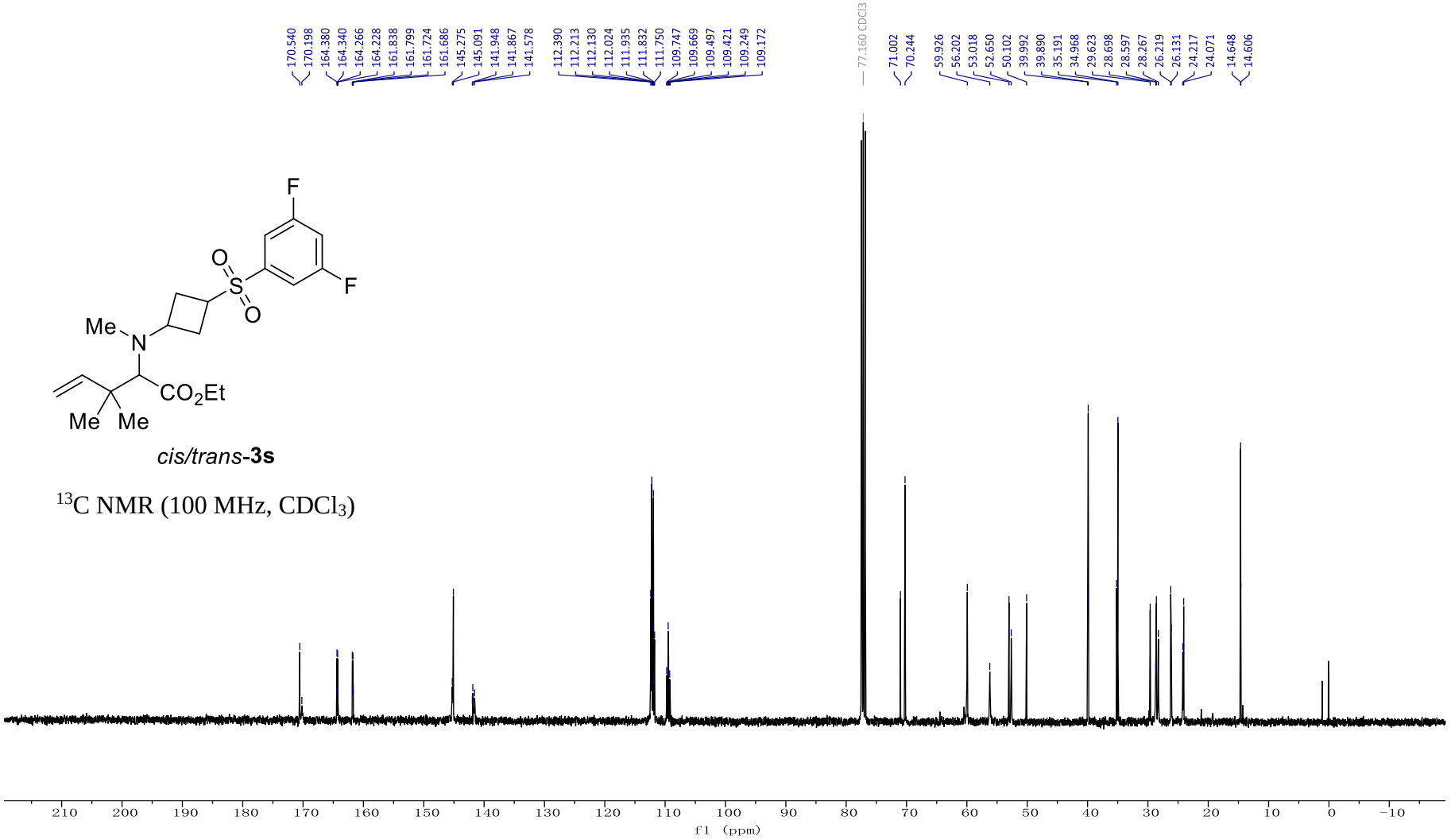
^{13}C NMR (100 MHz, $CDCl_3$)



cis/trans-**3r**

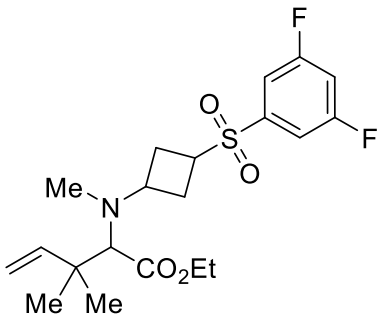
^{19}F NMR (376 MHz, $CDCl_3$)


F
O
S
O
F
Me
N
CO2Et
Me
Me
cis/trans-3s
1H NMR (400 MHz, CDCl3)
f1 (ppm)



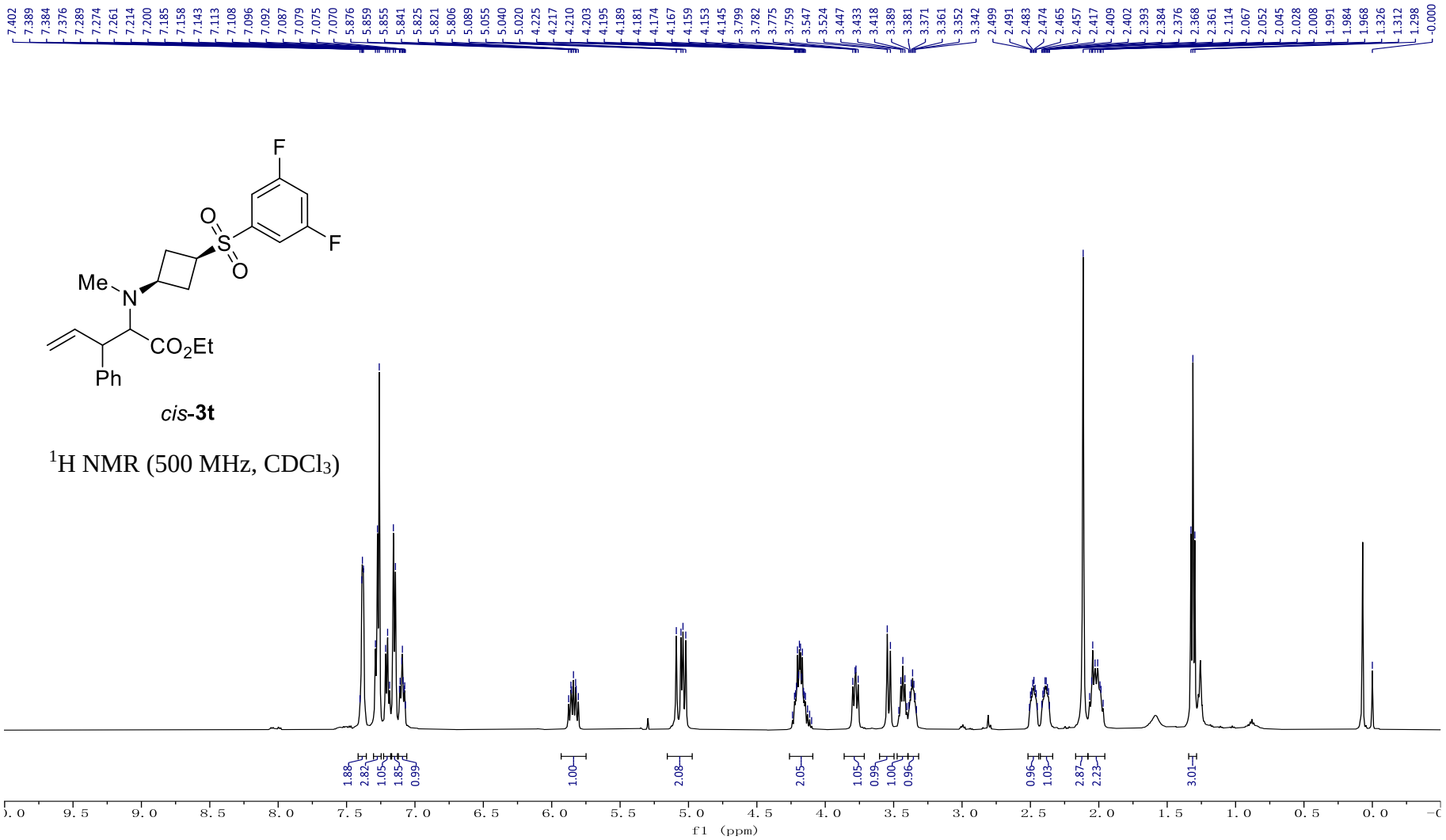
cis/trans-**3s**

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



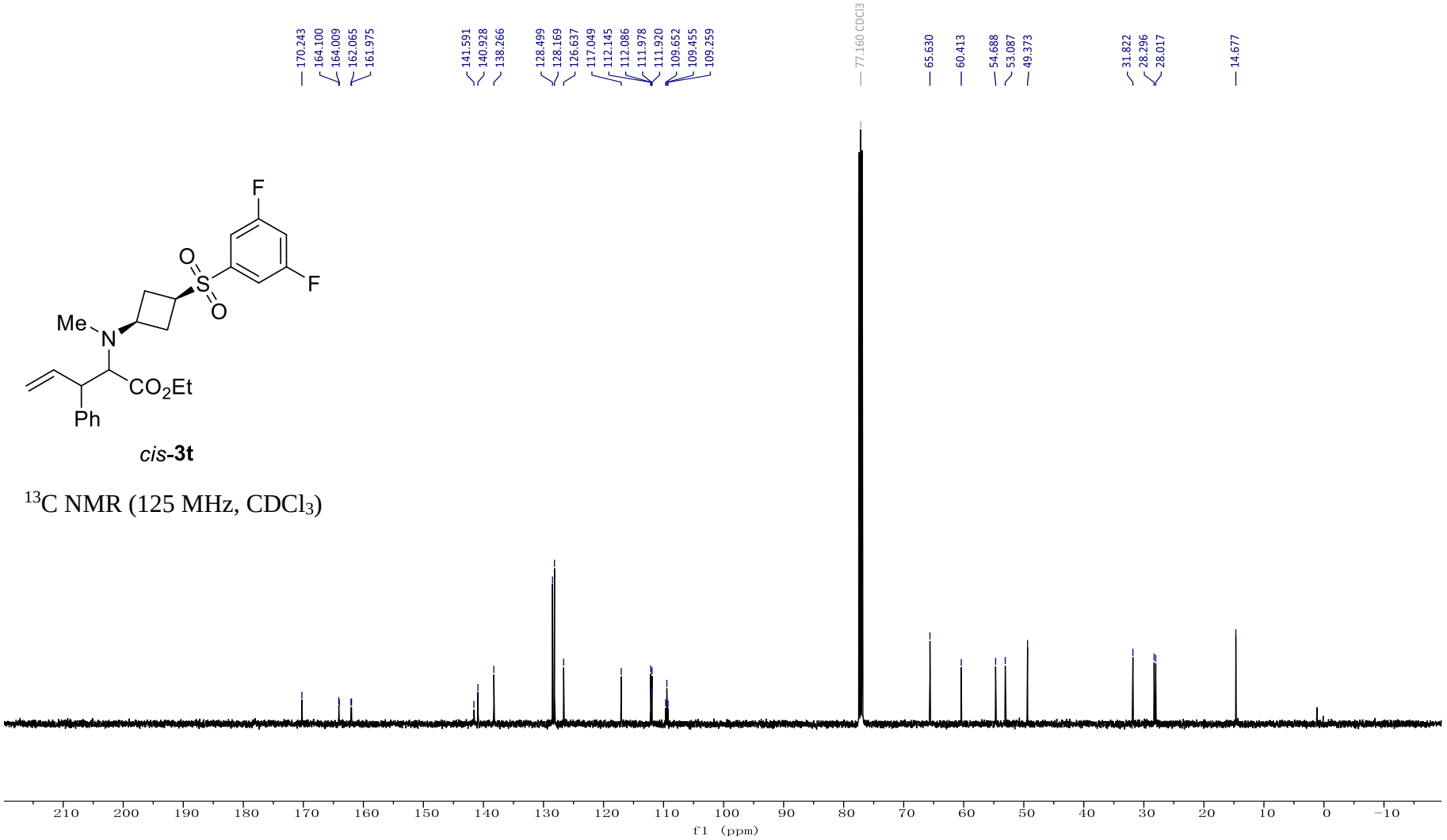
cis/trans-**3s**

^{19}F NMR (376 MHz, $CDCl_3$)



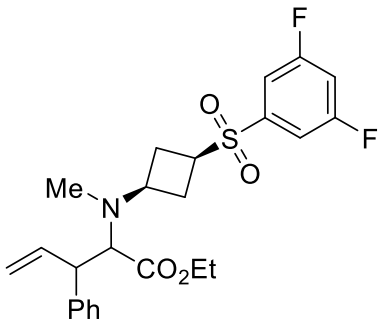
cis-**3t**

^{1}H NMR (500 MHz, $CDCl_3$)



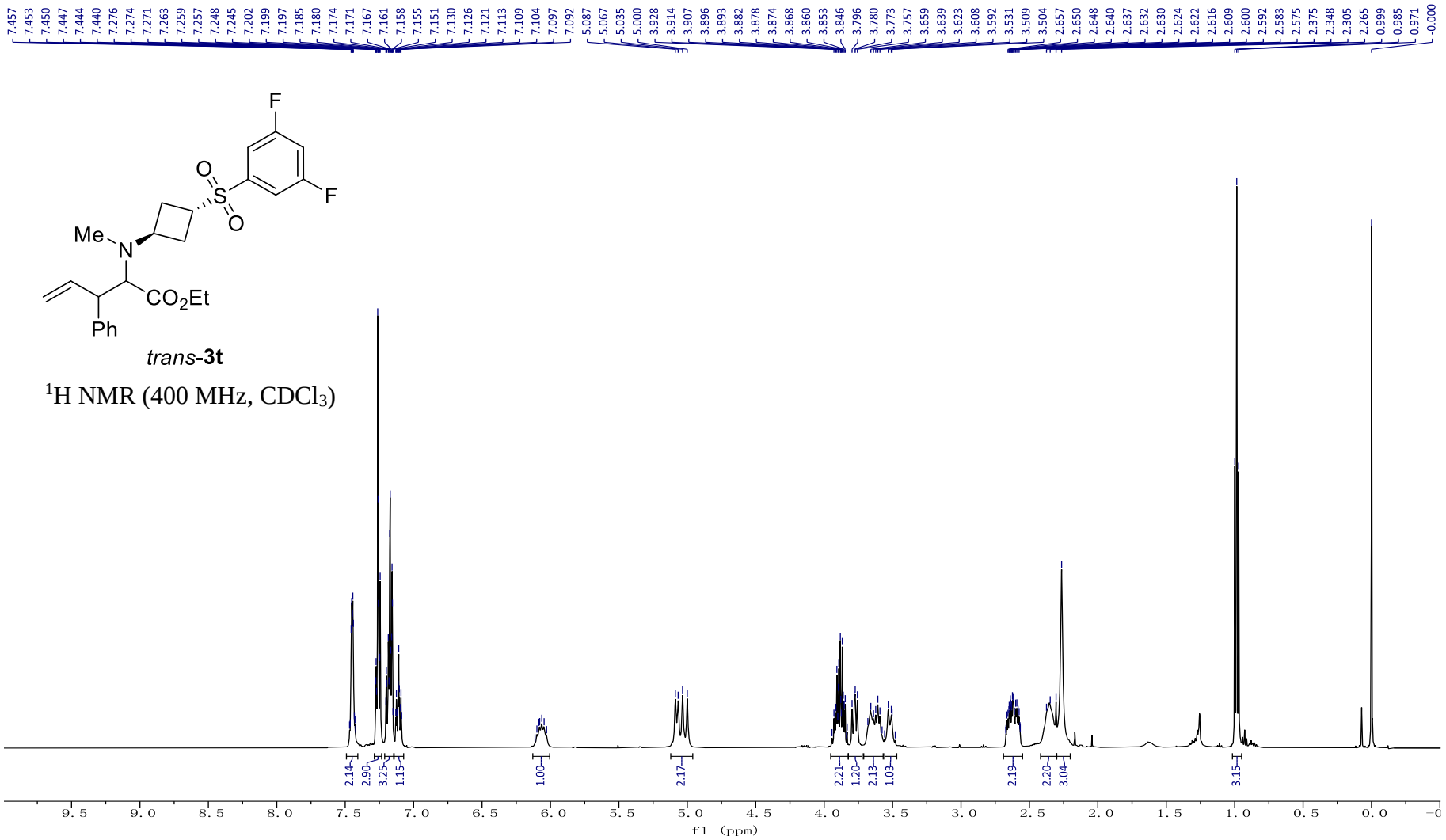
***cis*-3t**

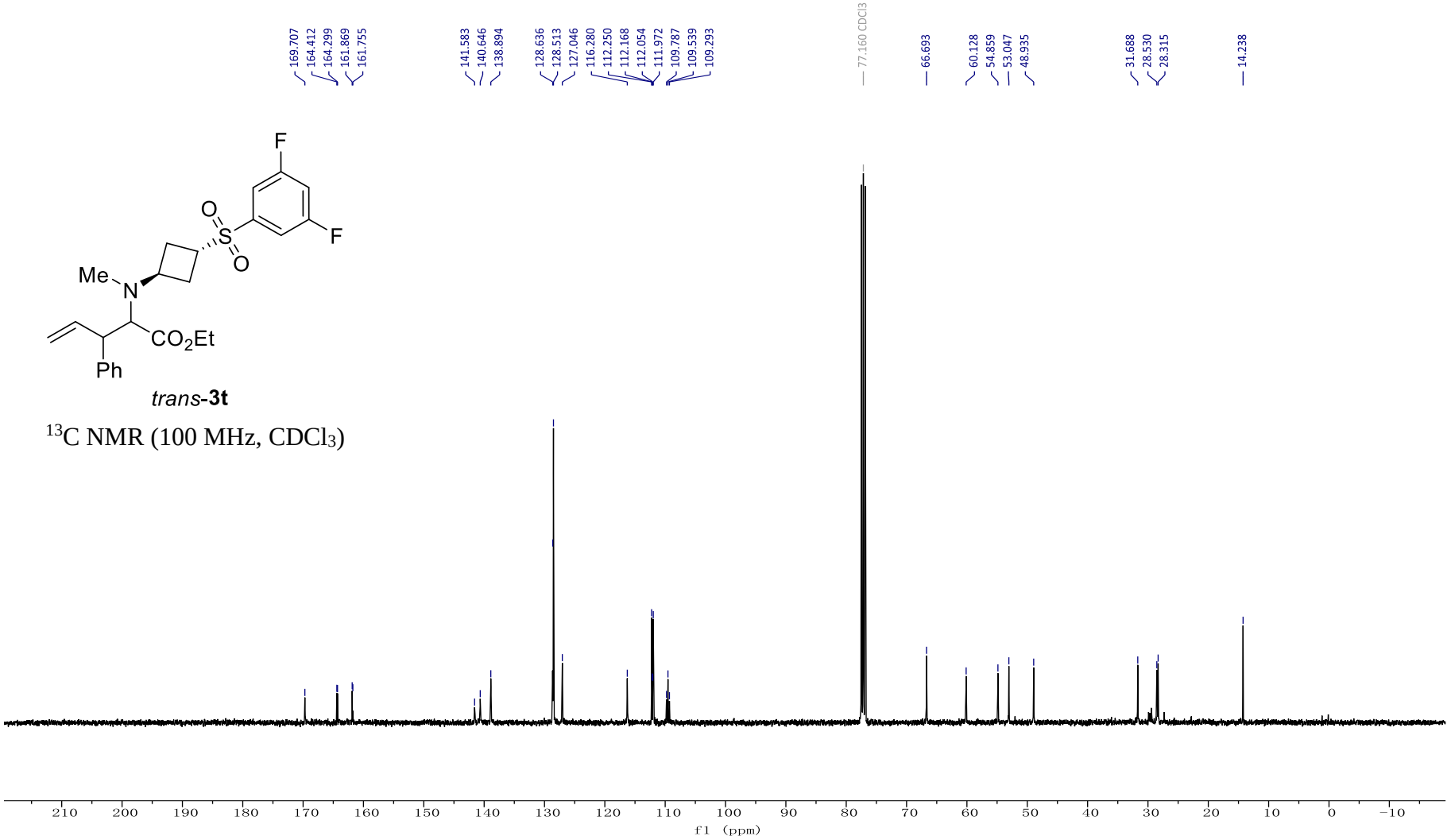
^{13}C NMR (125 MHz, $CDCl_3$)



cis-**3t**

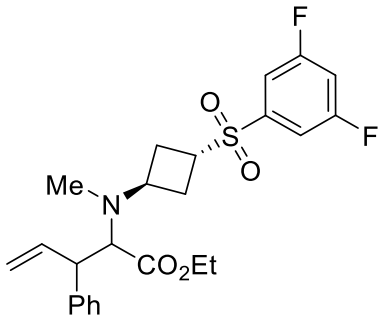
^{19}F NMR (471 MHz, $CDCl_3$)


F
O
S
O
F
Me
N
CO2Et
Ph
trans-3t
1H NMR (400 MHz, CDCl3)
f1 (ppm)



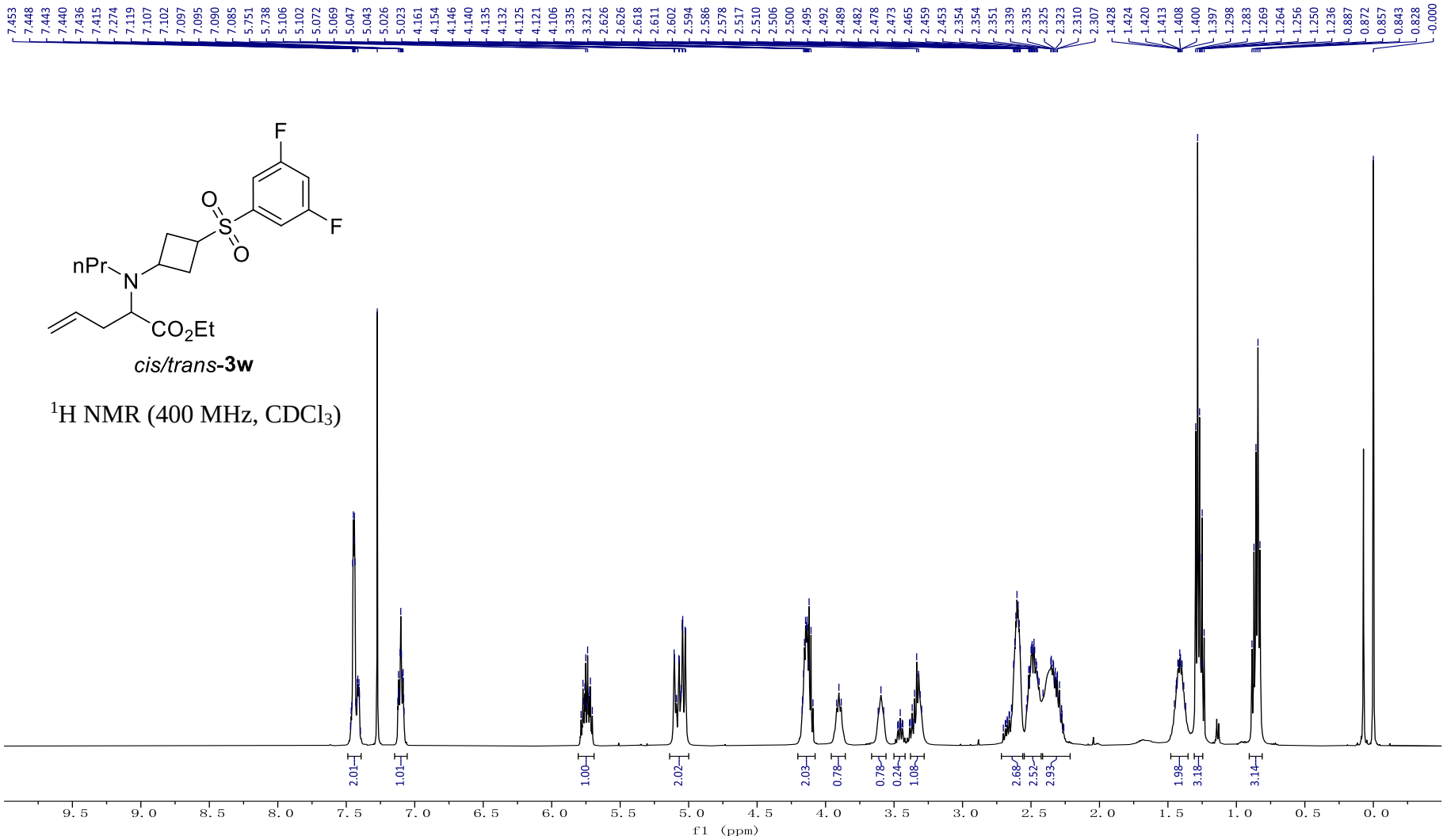
trans-**3t**

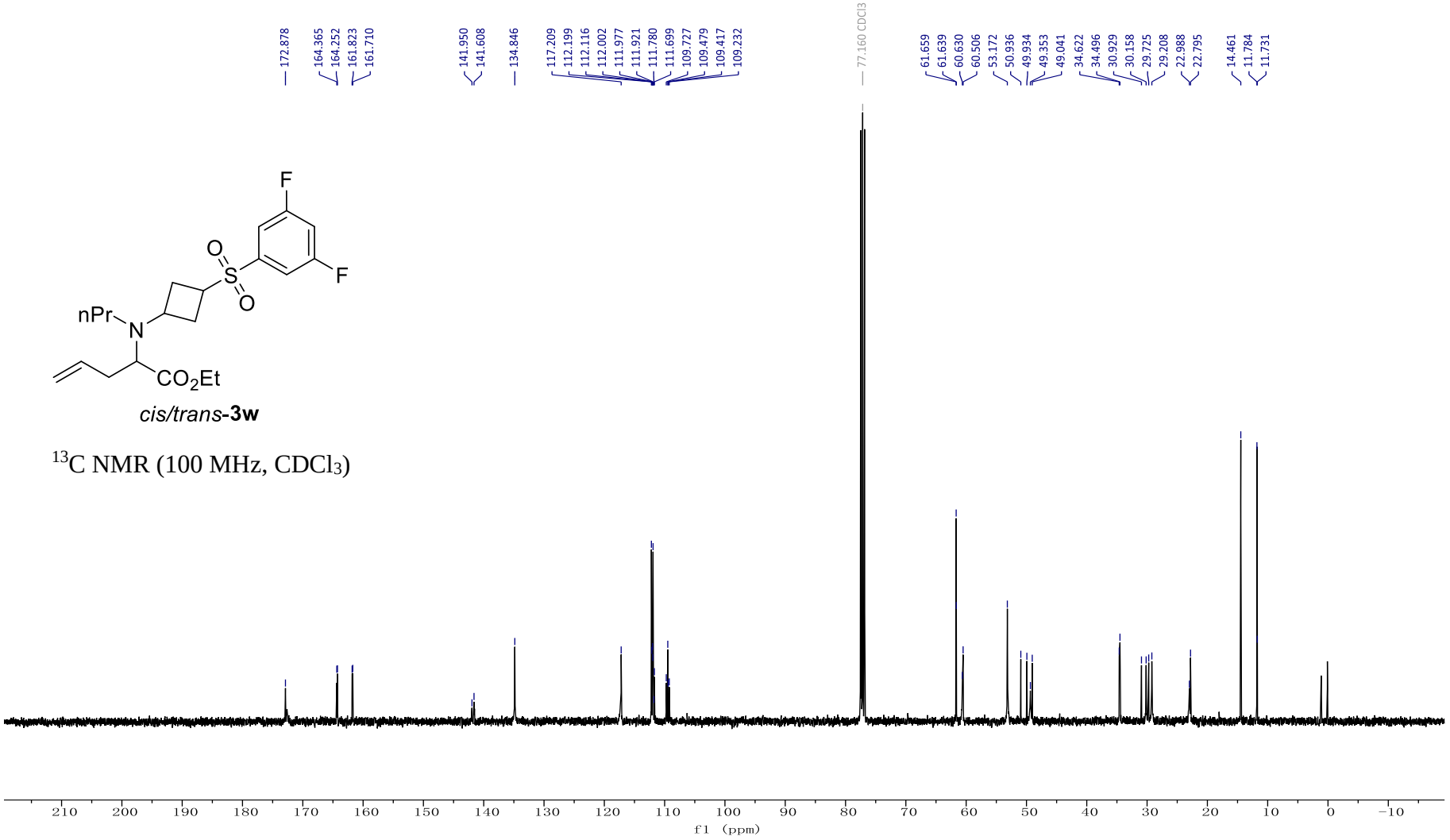
^{13}C NMR (100 MHz, $CDCl_3$)



trans-**3t**

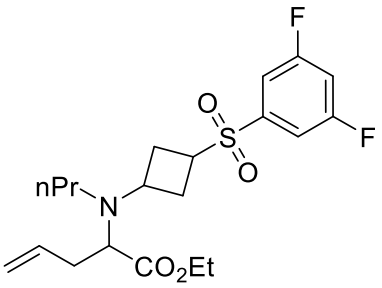
^{19}F NMR (376 MHz, $CDCl_3$)


7.453 7.448 7.443 7.440 7.436 7.415 7.274 7.119 7.107 7.102 7.097 7.095 7.090 7.085 5.751 5.738 5.106 5.102 5.072 5.069 5.047 5.043 5.026 5.023 4.161 4.154 4.146 4.140 4.135 4.132 4.125 4.121 4.106 3.335 3.321 2.626 2.626 2.618 2.611 2.602 2.594 2.586 2.578 2.517 2.510 2.506 2.500 2.495 2.492 2.489 2.482 2.478 2.473 2.465 2.459 2.453 2.354 2.354 2.351 2.339 2.335 2.325 2.323 2.310 2.307 1.428 1.424 1.420 1.413 1.408 1.400 1.397 1.298 1.283 1.269 1.264 1.256 1.250 1.236 0.887 0.872 0.857 0.843 0.828 -0.000
F
O
S
O
F
nPr
N
CO2Et
cis/trans-3w
1H NMR (400 MHz, CDCl3)
2.01 1.01 1.00 2.02 2.03 0.78 0.78 0.24 1.08 2.68 2.52 2.93 1.98 3.18 3.14
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



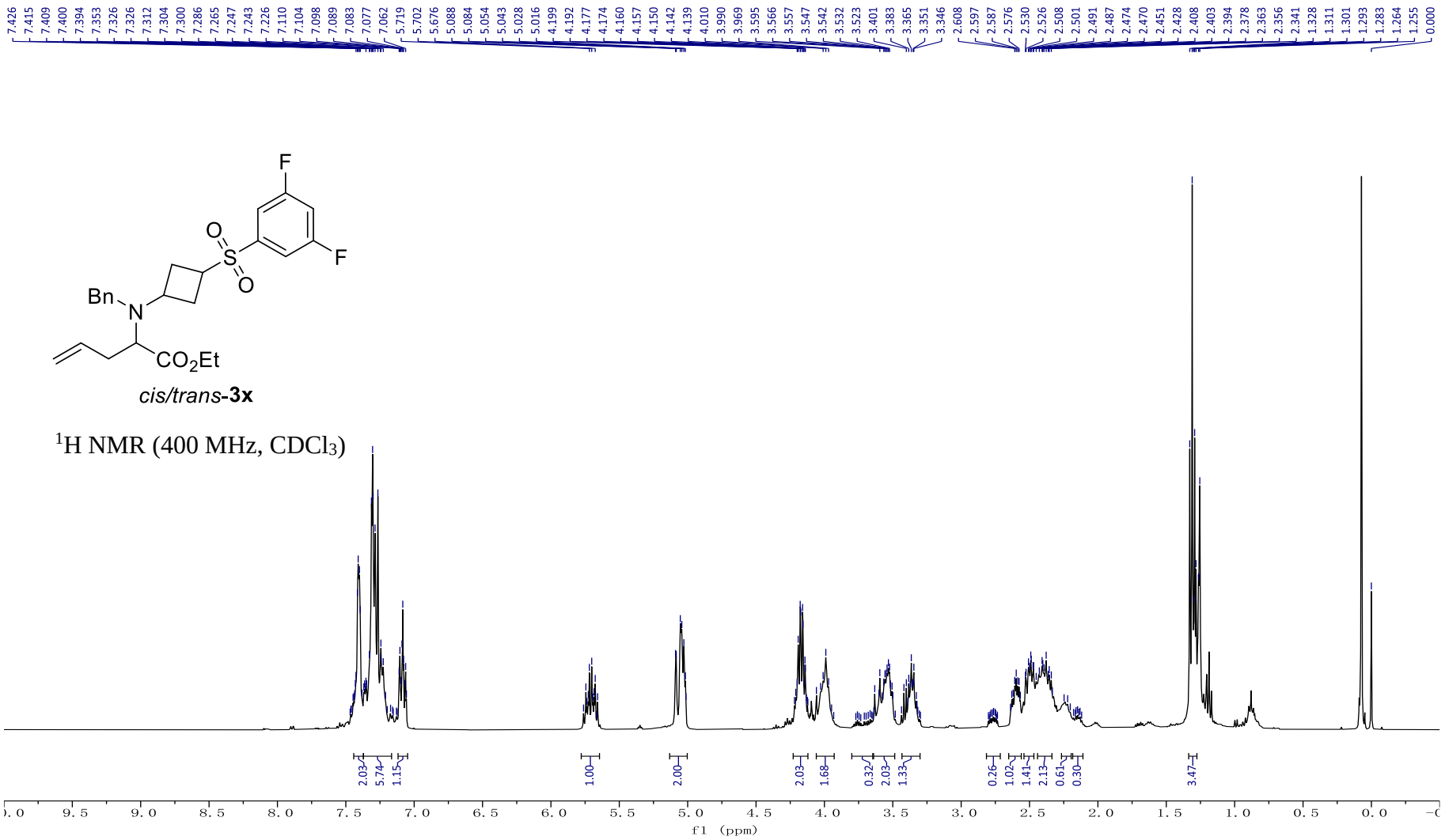
cis/trans-**3w**

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



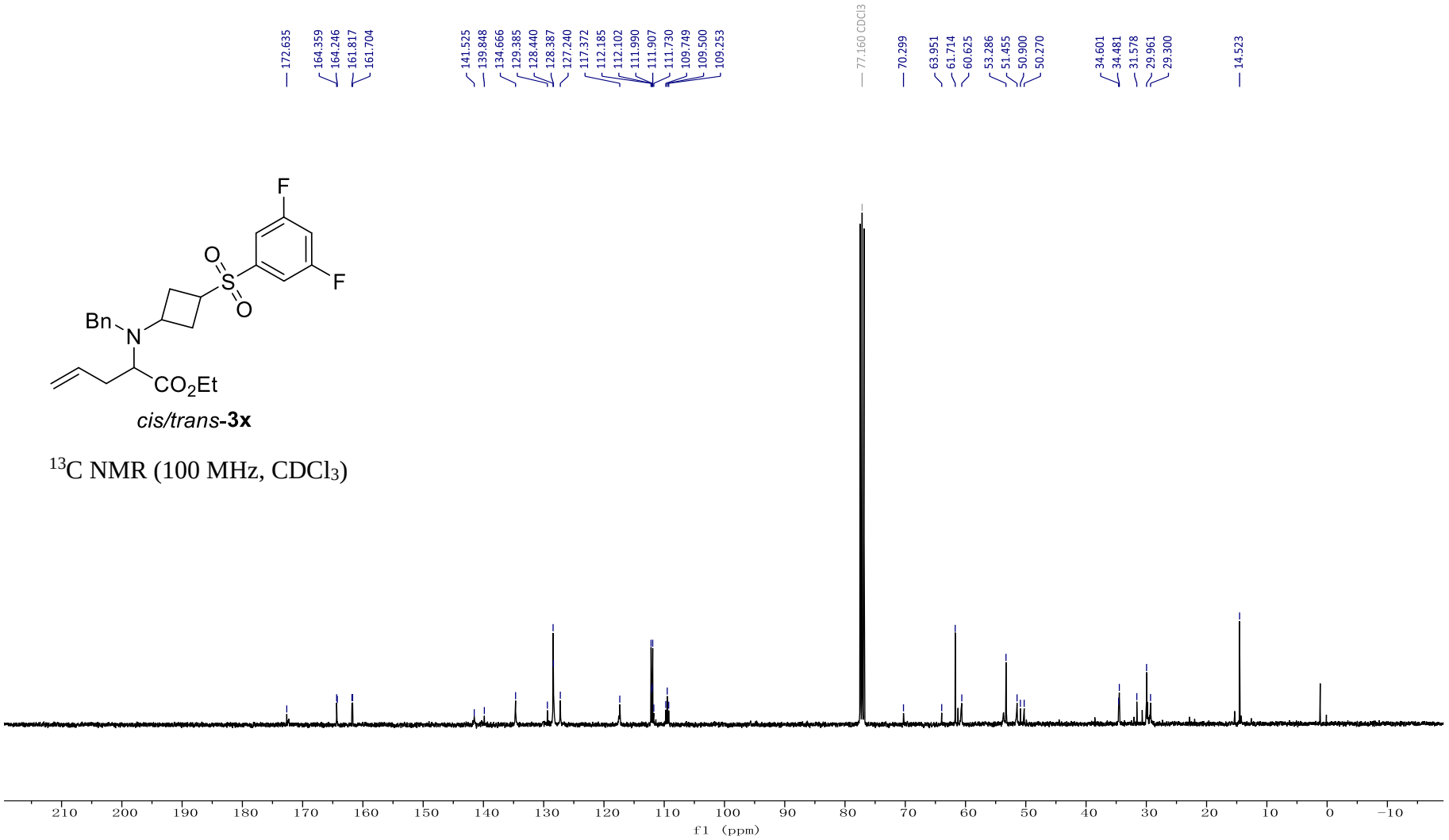
cis/trans-**3w**

^{19}F NMR (376 MHz, $CDCl_3$)



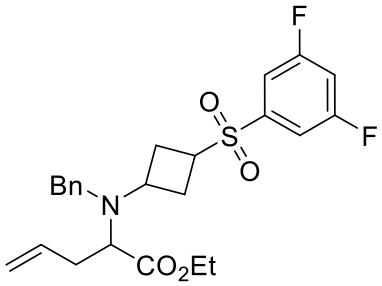
cis/trans-**3x**

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



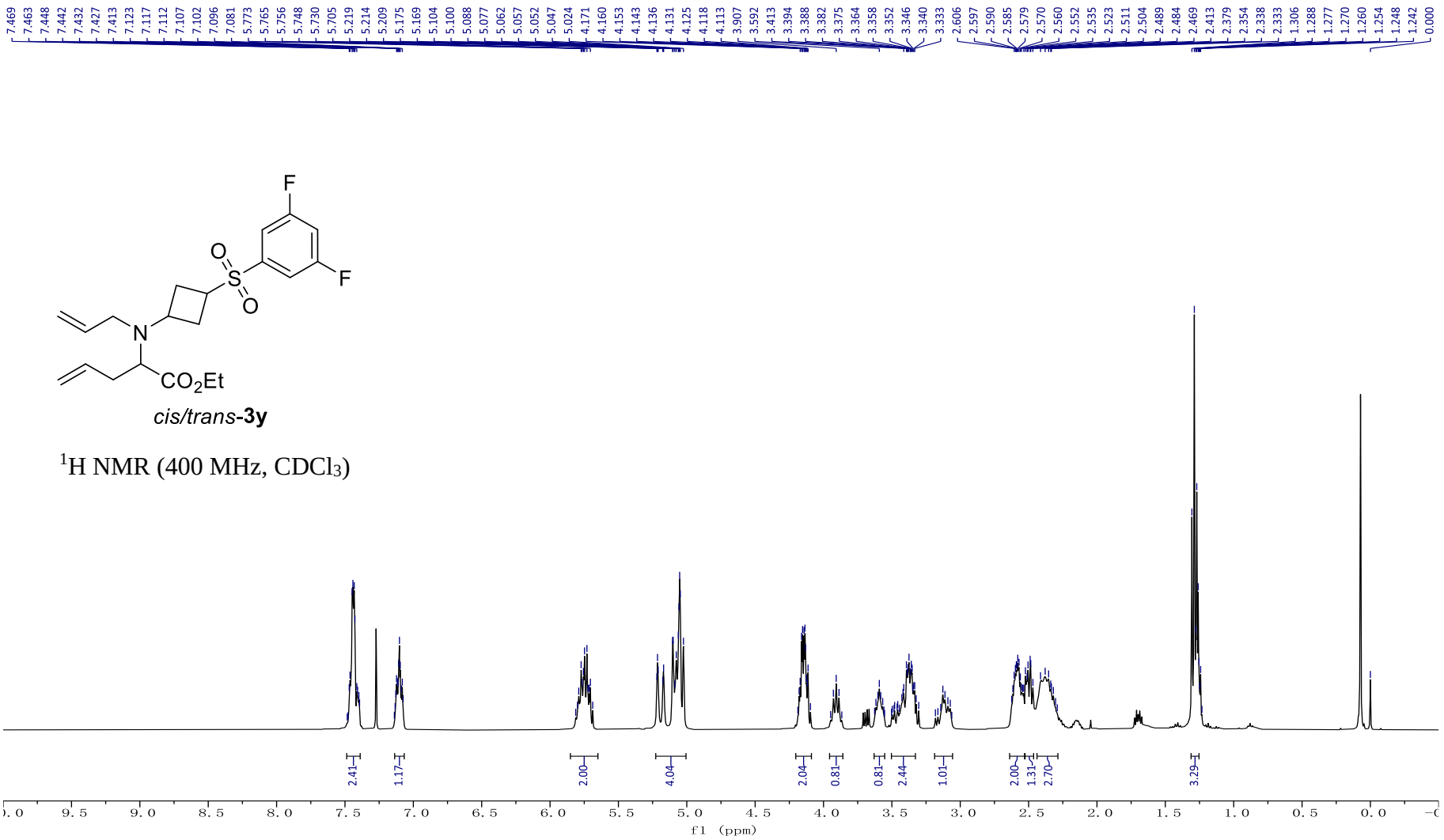
cis/trans-**3x**

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



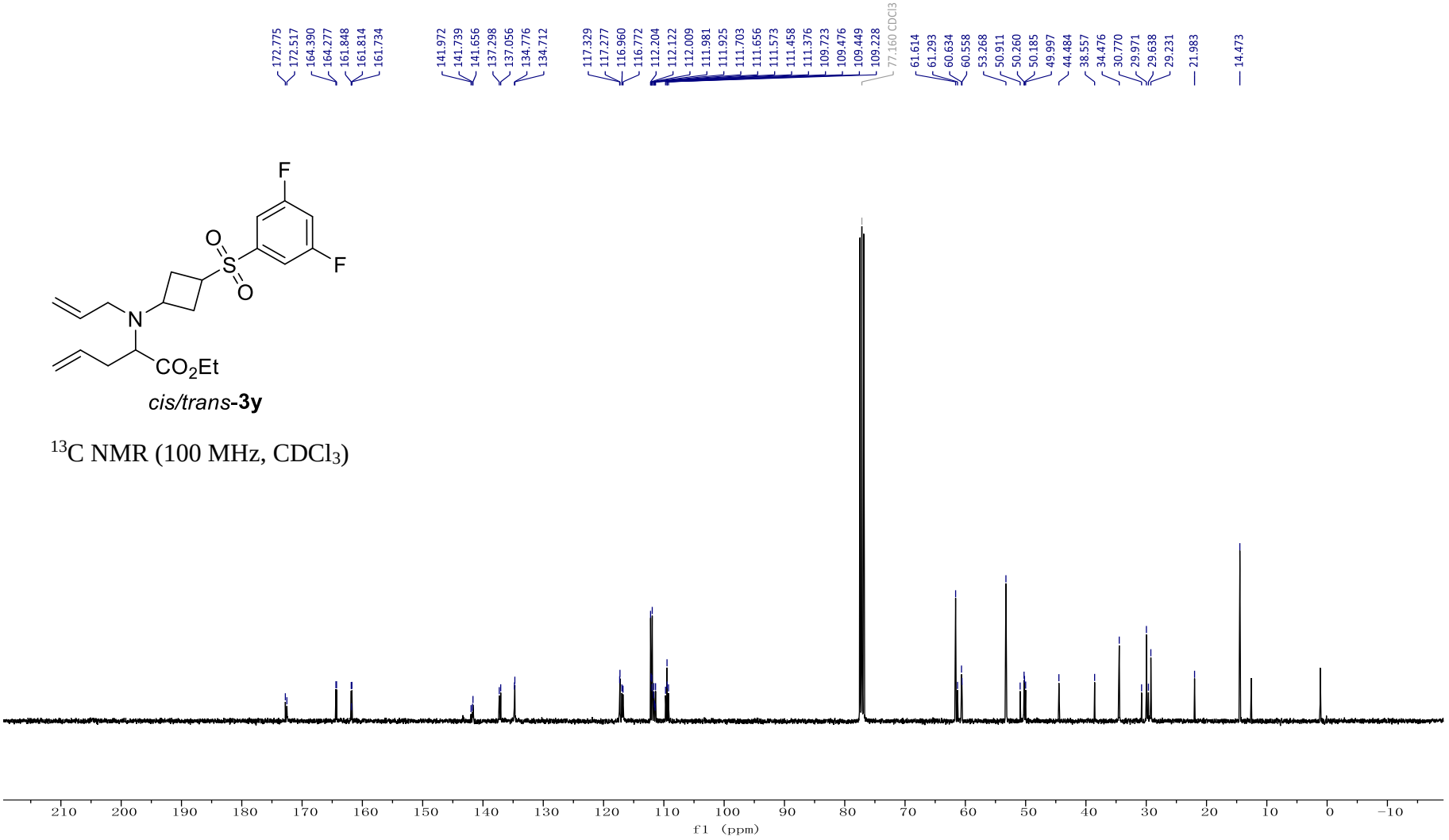
cis/trans-**3x**

^{19}F NMR (376 MHz, $CDCl_3$)



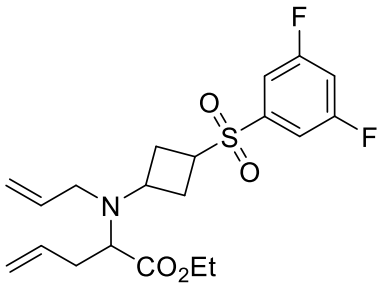
cis/trans-**3y**

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



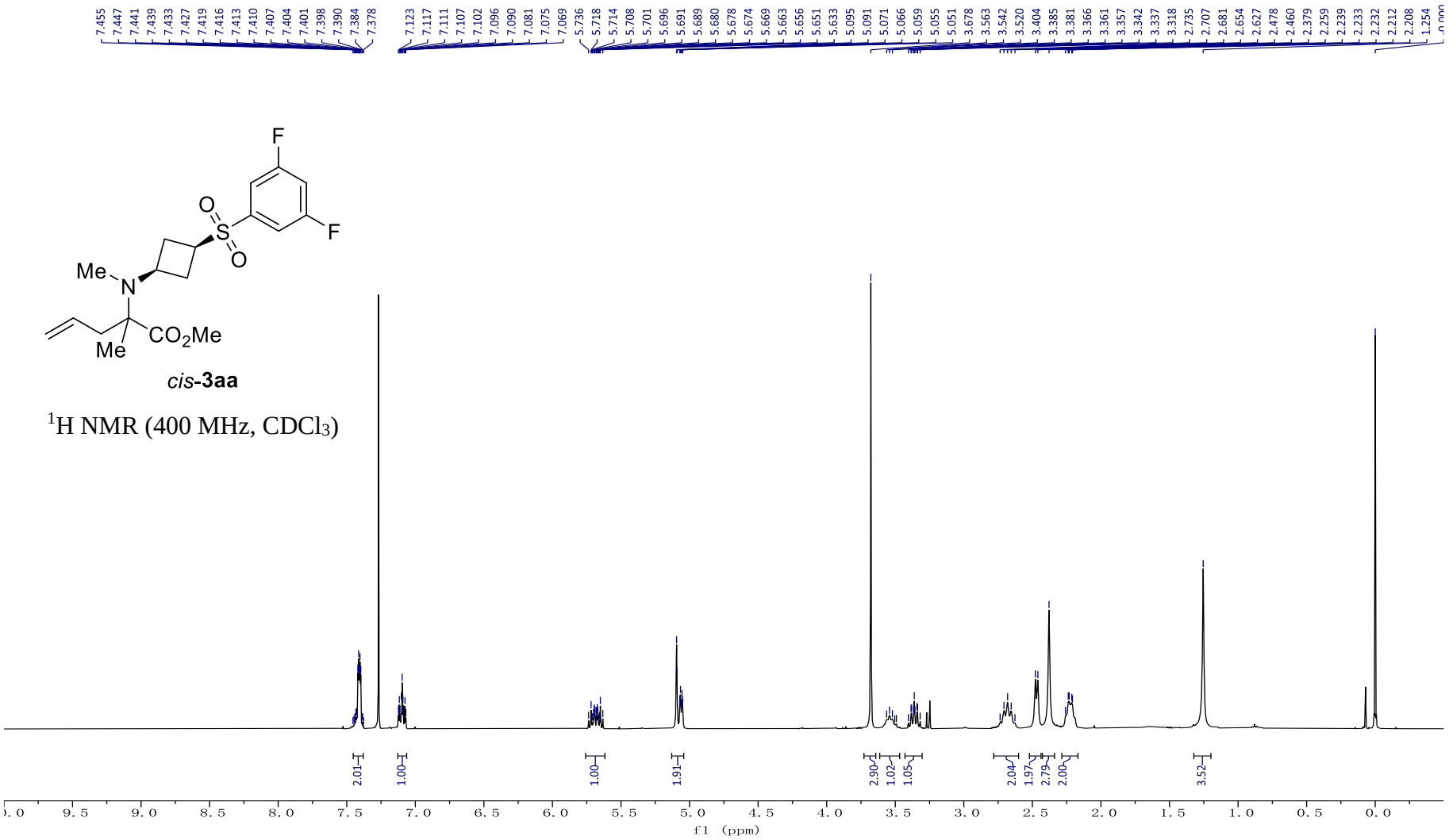
cis/trans-**3y**

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



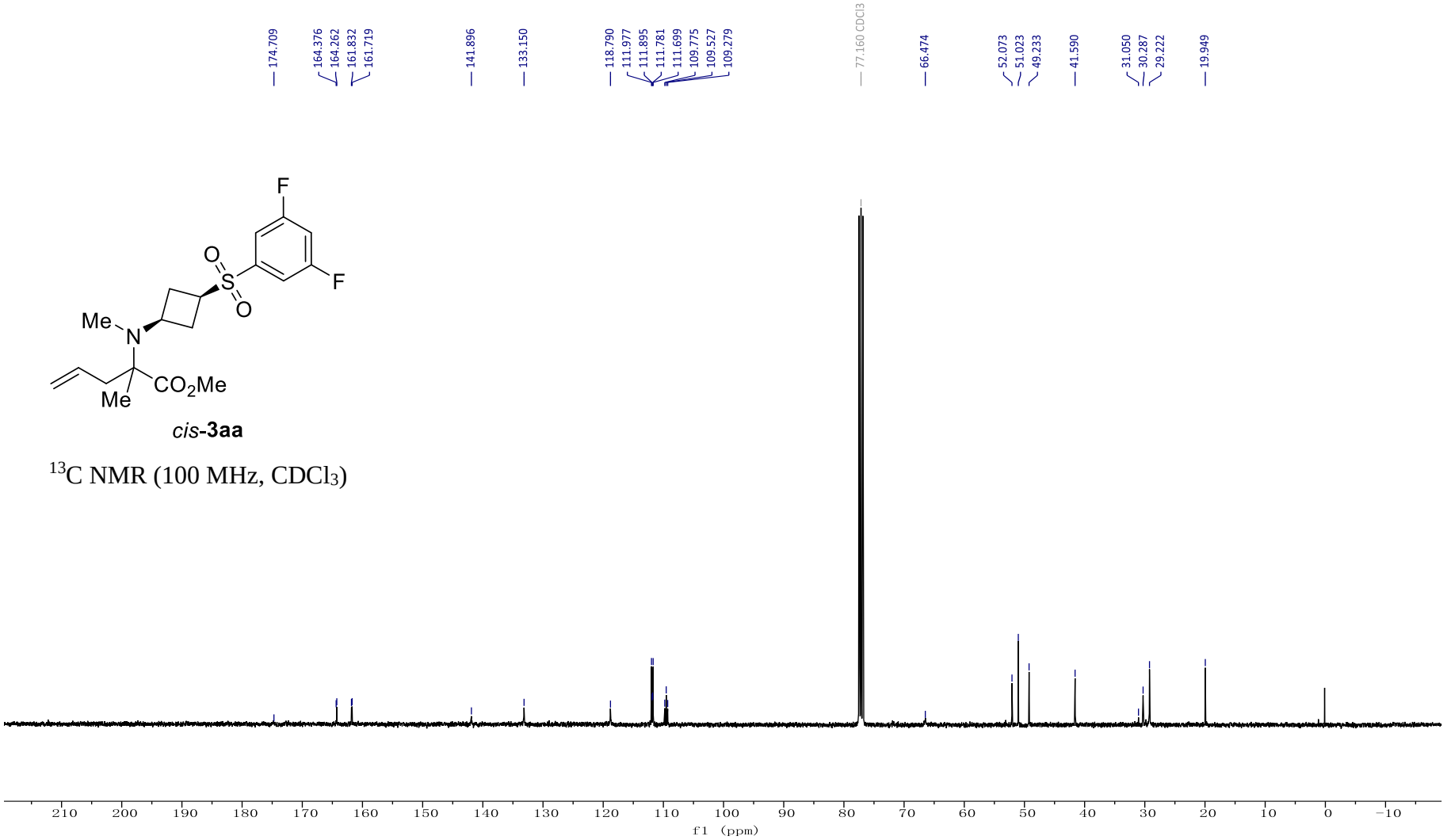
cis/trans-**3y**

^{19}F NMR (376 MHz, $CDCl_3$)



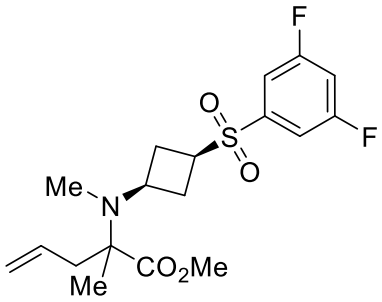
cis-**3aa**

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



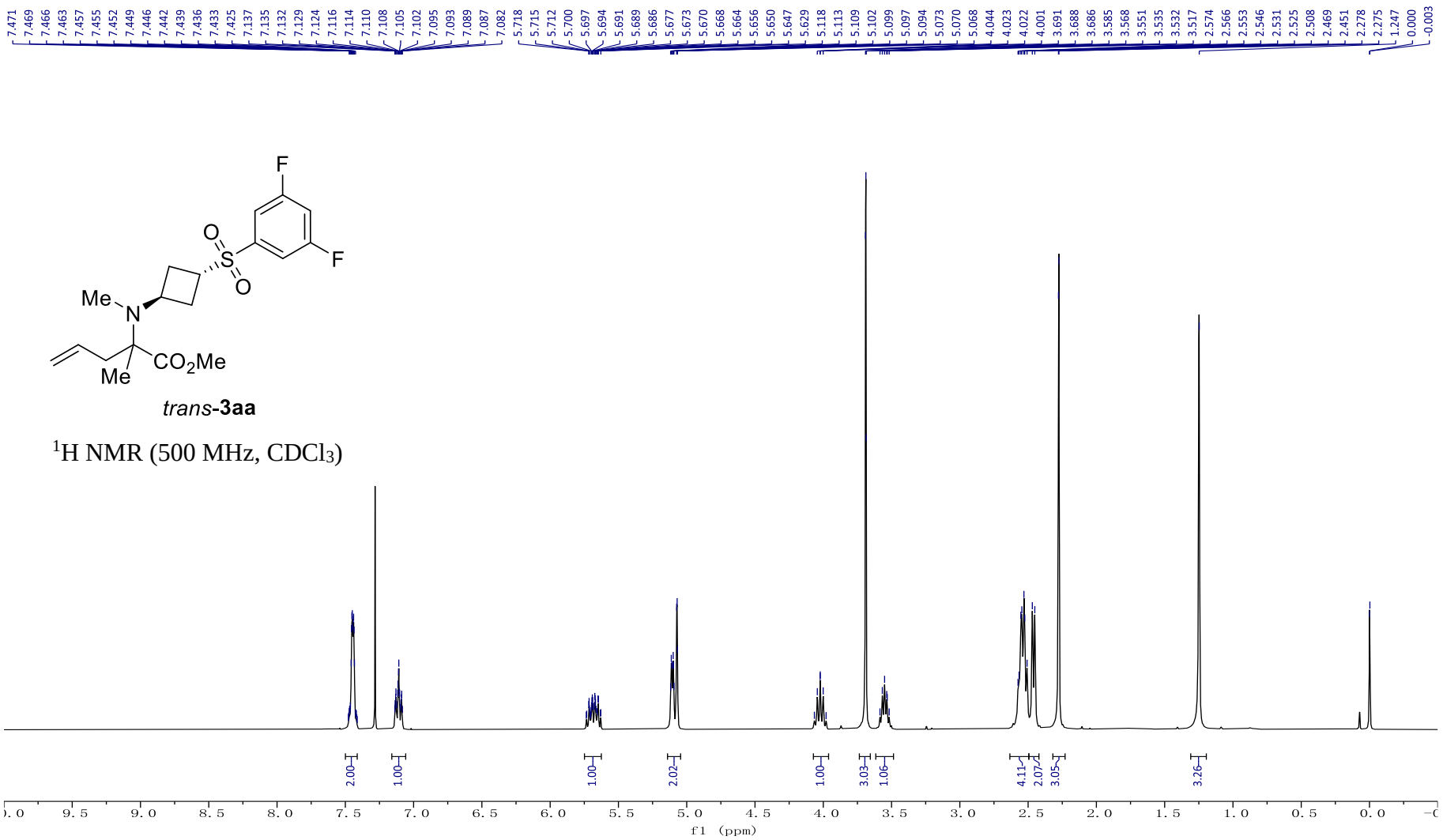
cis-**3aa**

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



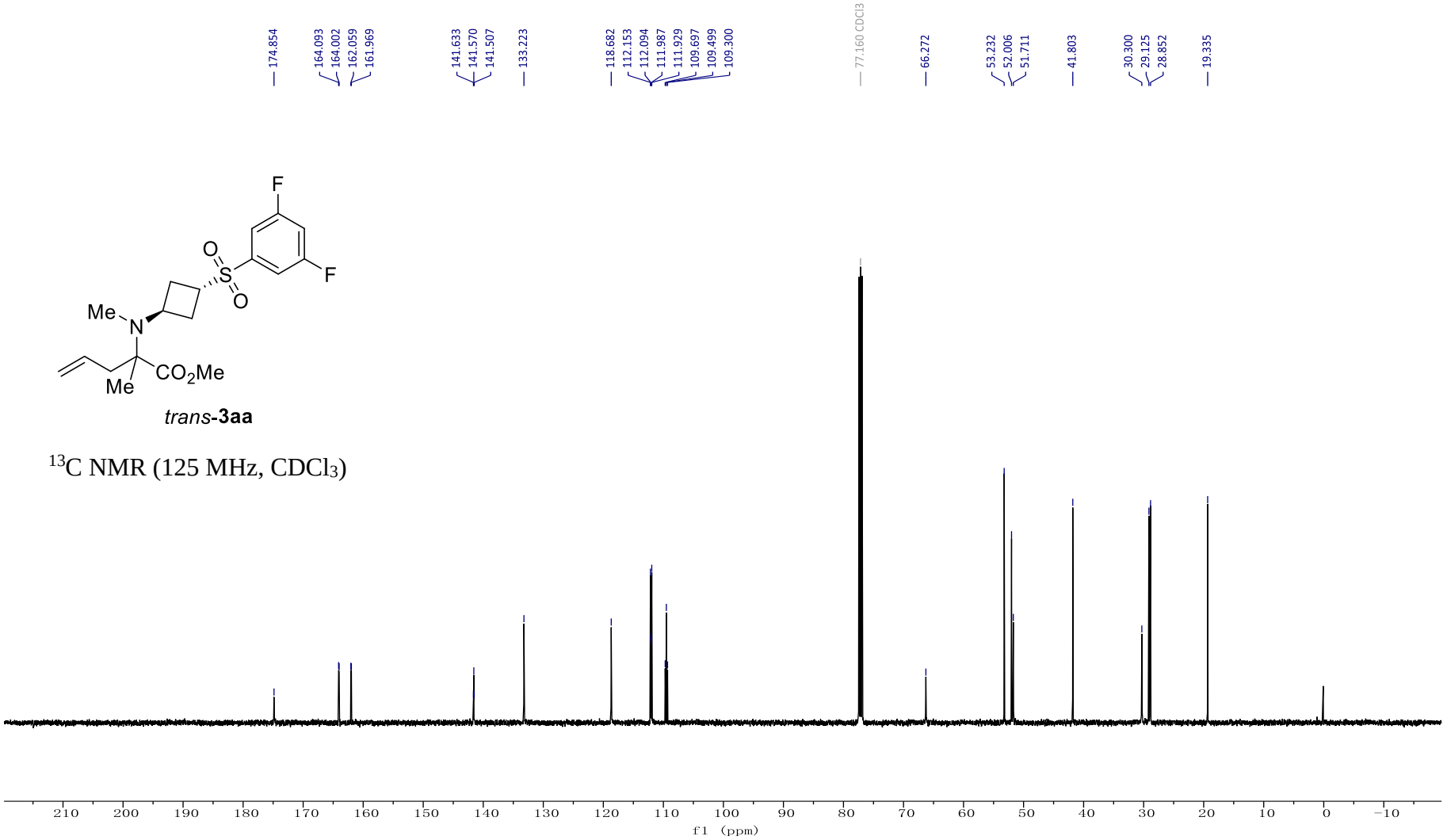
***cis*-3aa**

^{19}F NMR (376 MHz, $CDCl_3$)



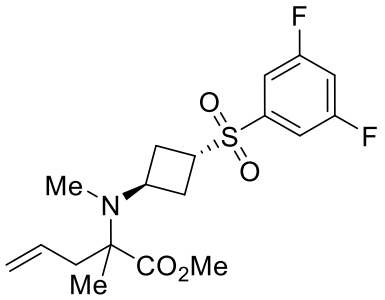
trans-**3aa**

^{1}H NMR (500 MHz, $CDCl_3$)



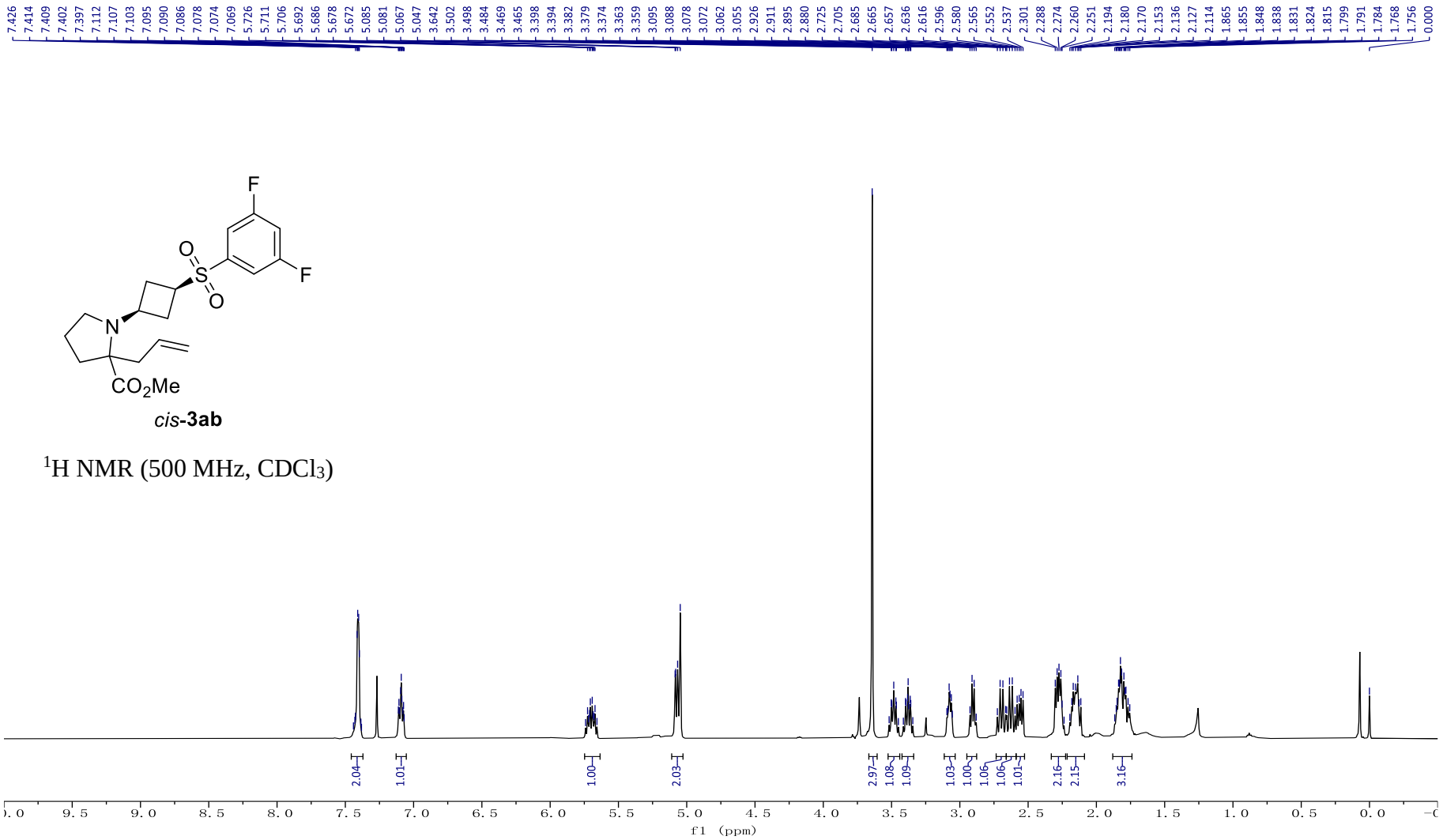
trans-**3aa**

^{13}C NMR (125 MHz, $CDCl_3$)



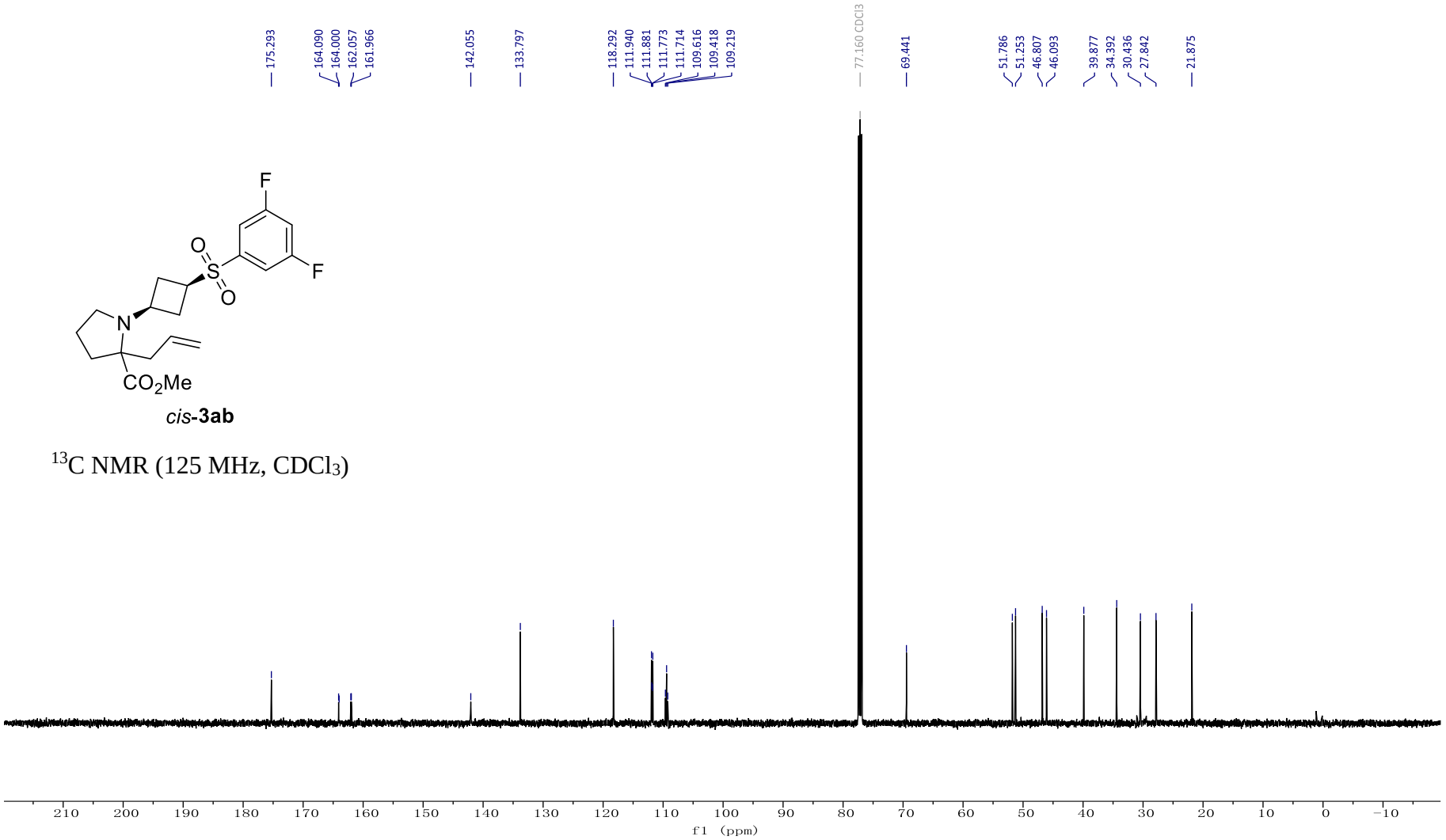
trans-**3aa**

^{19}F NMR (471 MHz, $CDCl_3$)



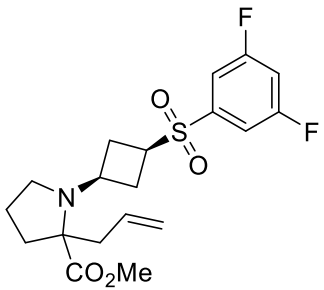
cis-**3ab**

^{1}H NMR (500 MHz, $CDCl_3$)



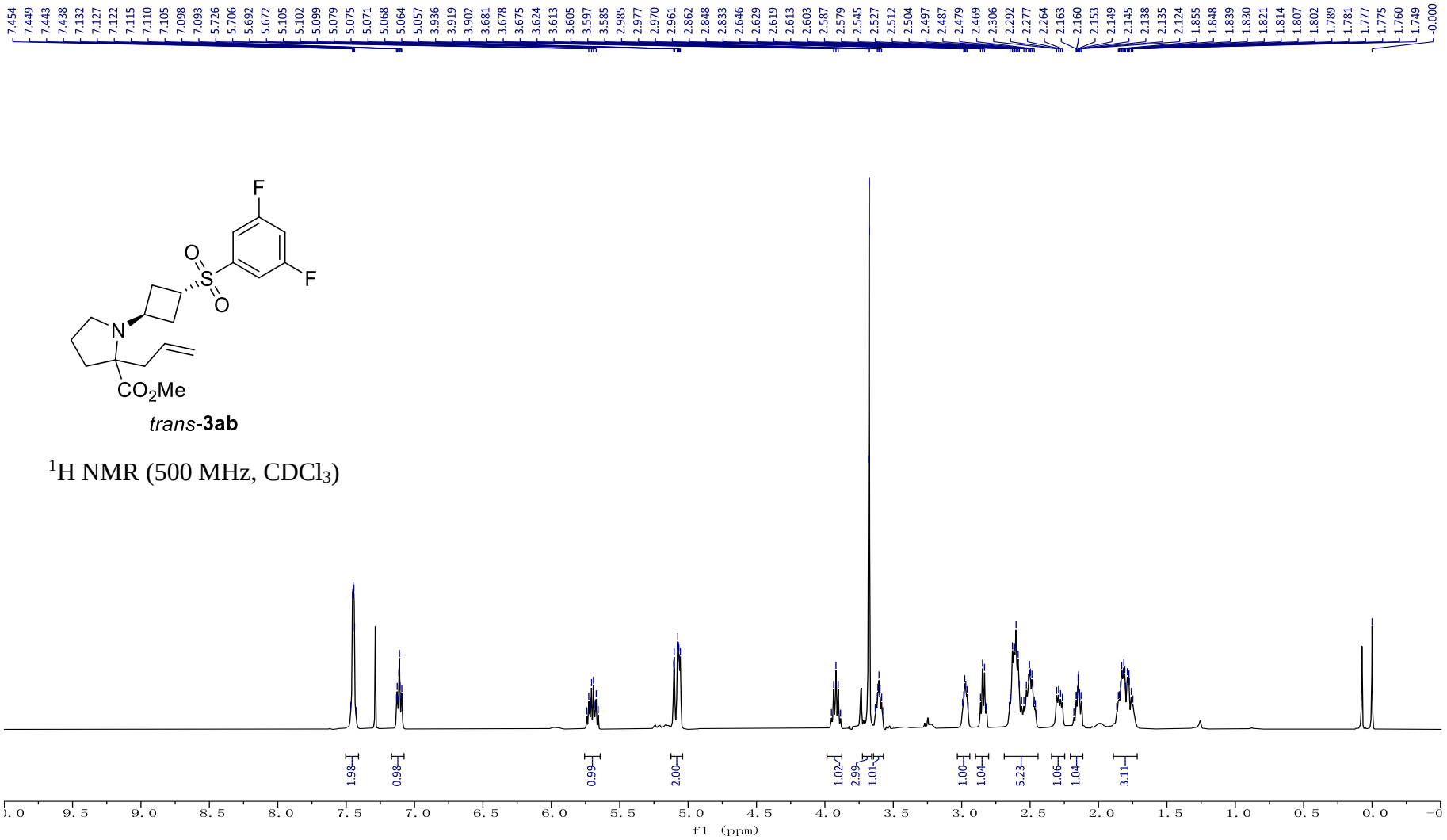
cis-**3ab**

^{13}C NMR (125 MHz, $CDCl_3$)



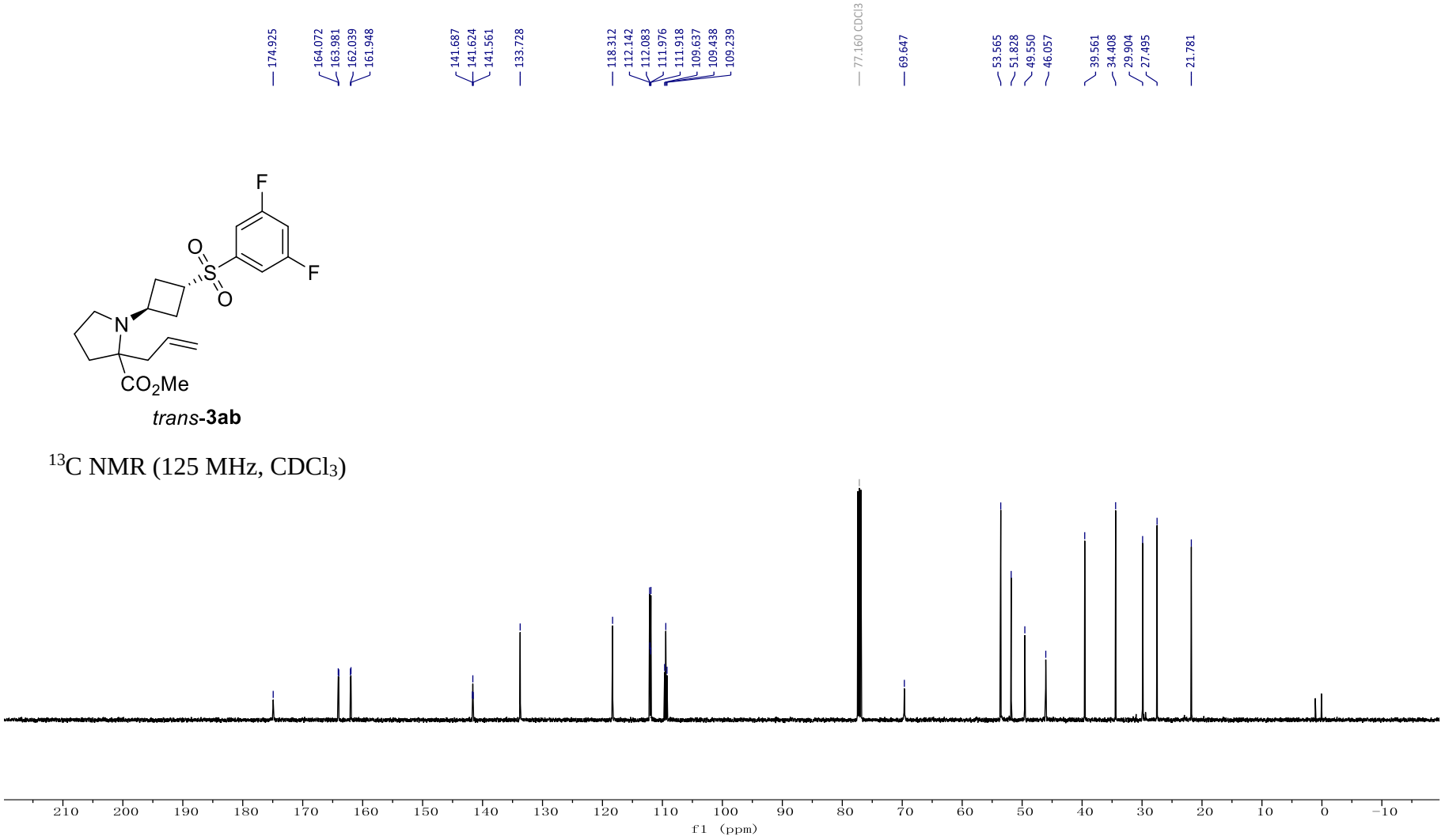
cis-**3ab**

^{19}F NMR (471 MHz, $CDCl_3$)



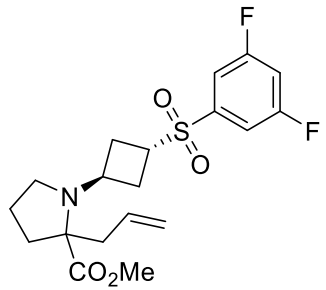
trans-**3ab**

^{1}H NMR (500 MHz, $CDCl_3$)



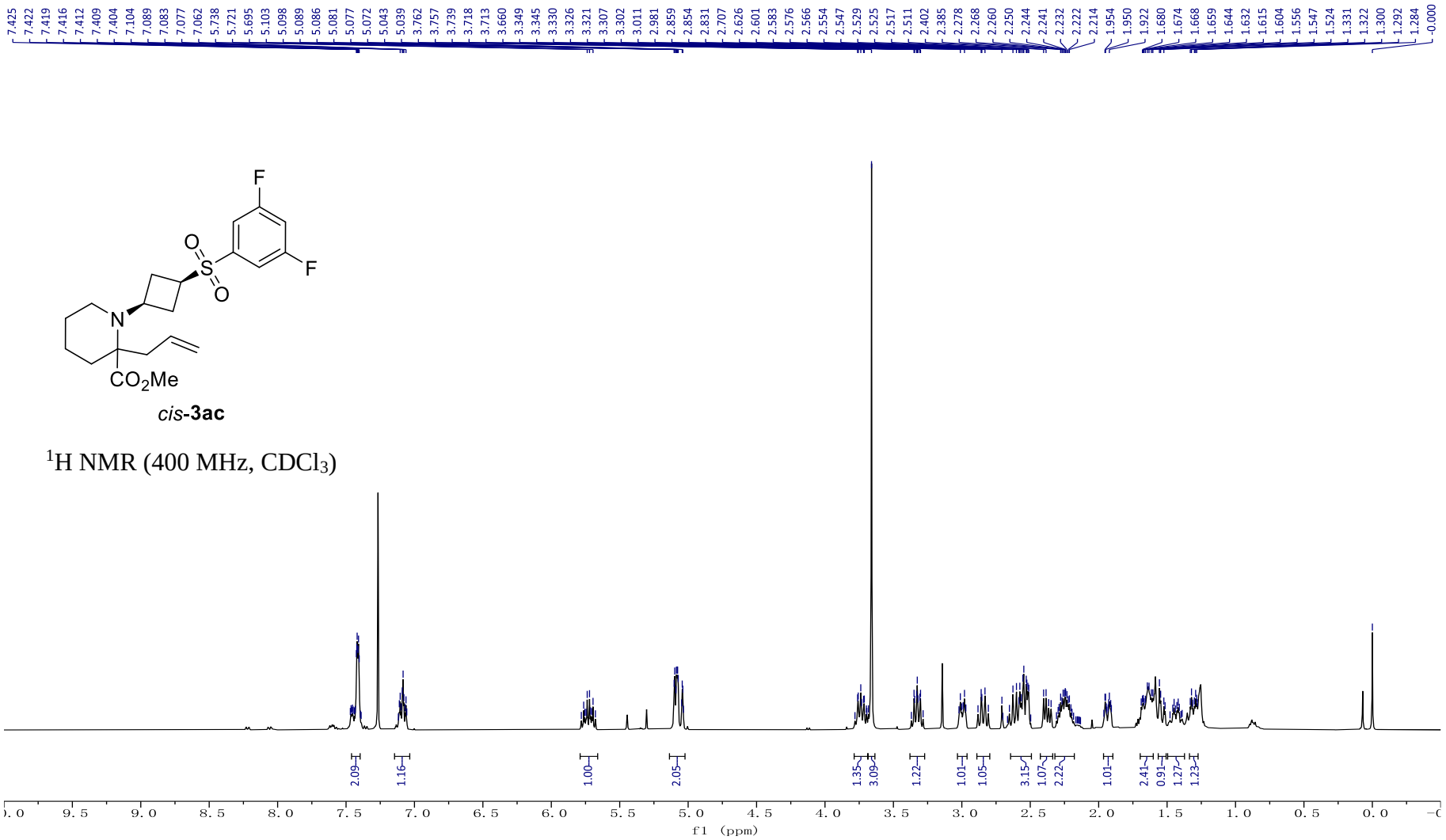
trans-**3ab**

^{13}C NMR (125 MHz, $CDCl_3$)



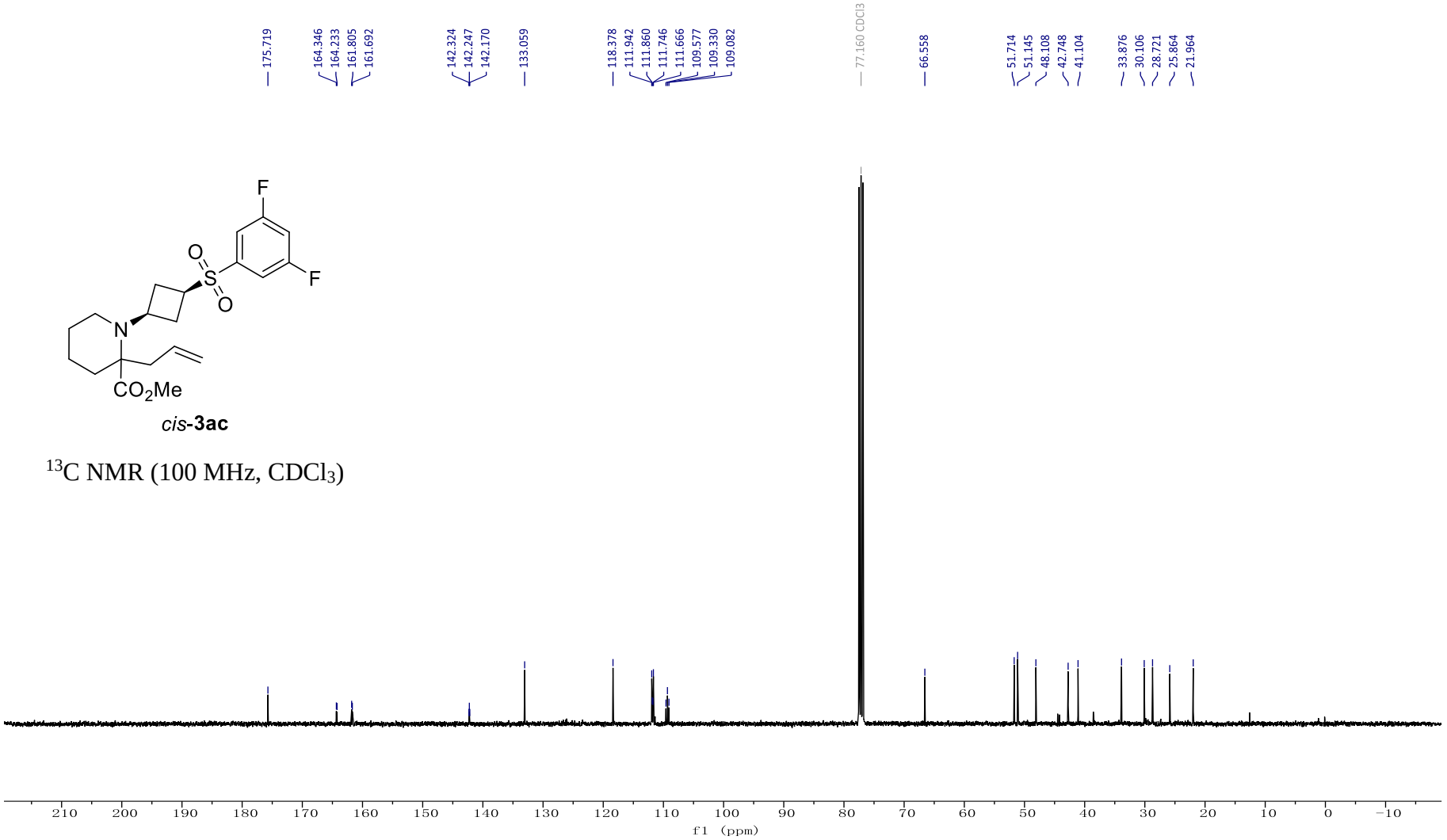
trans-**3ab**

^{19}F NMR (471 MHz, $CDCl_3$)



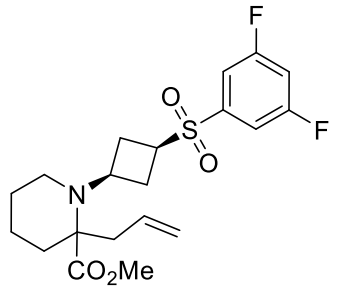
cis-**3ac**

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



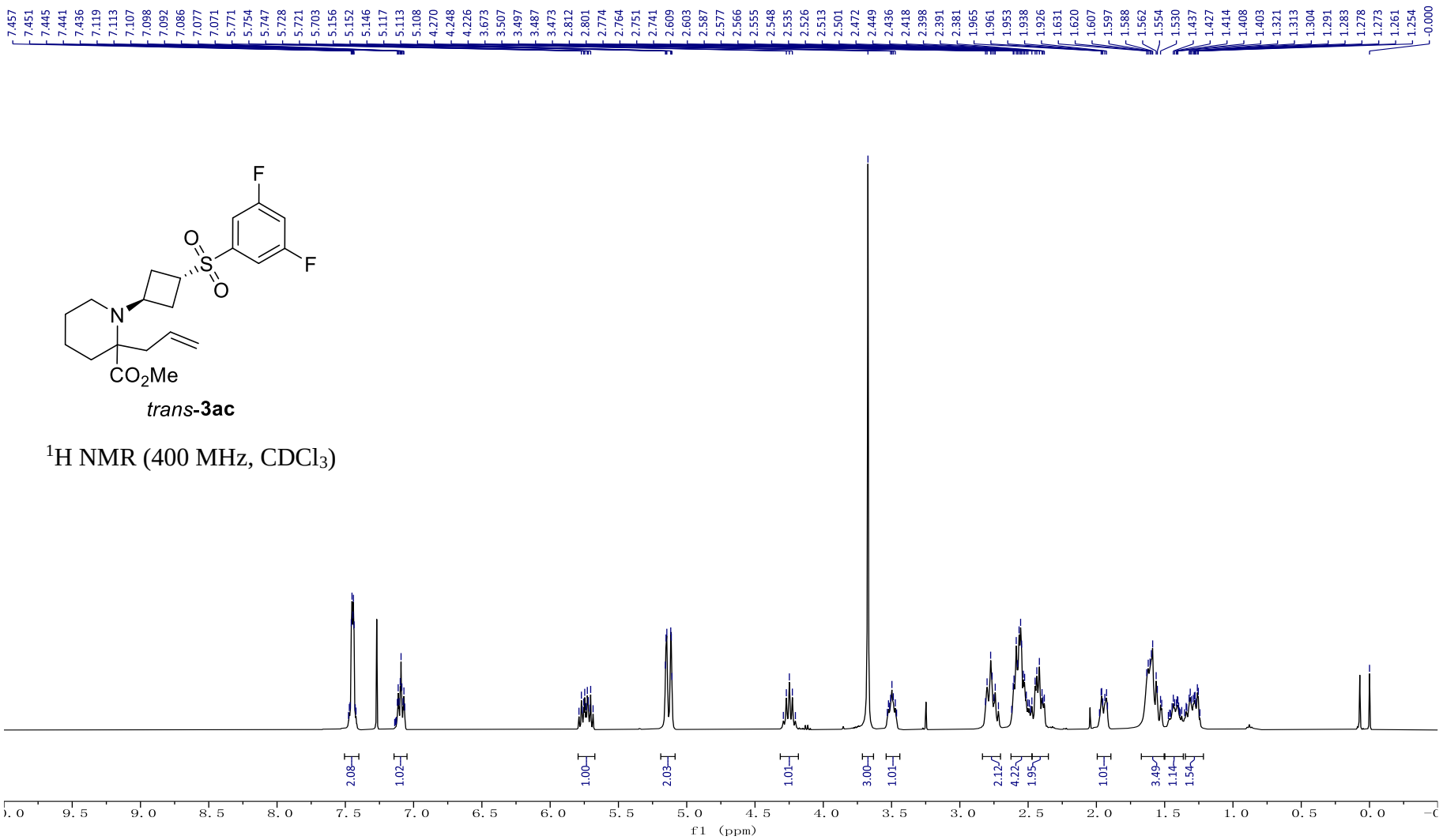
cis-**3ac**

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



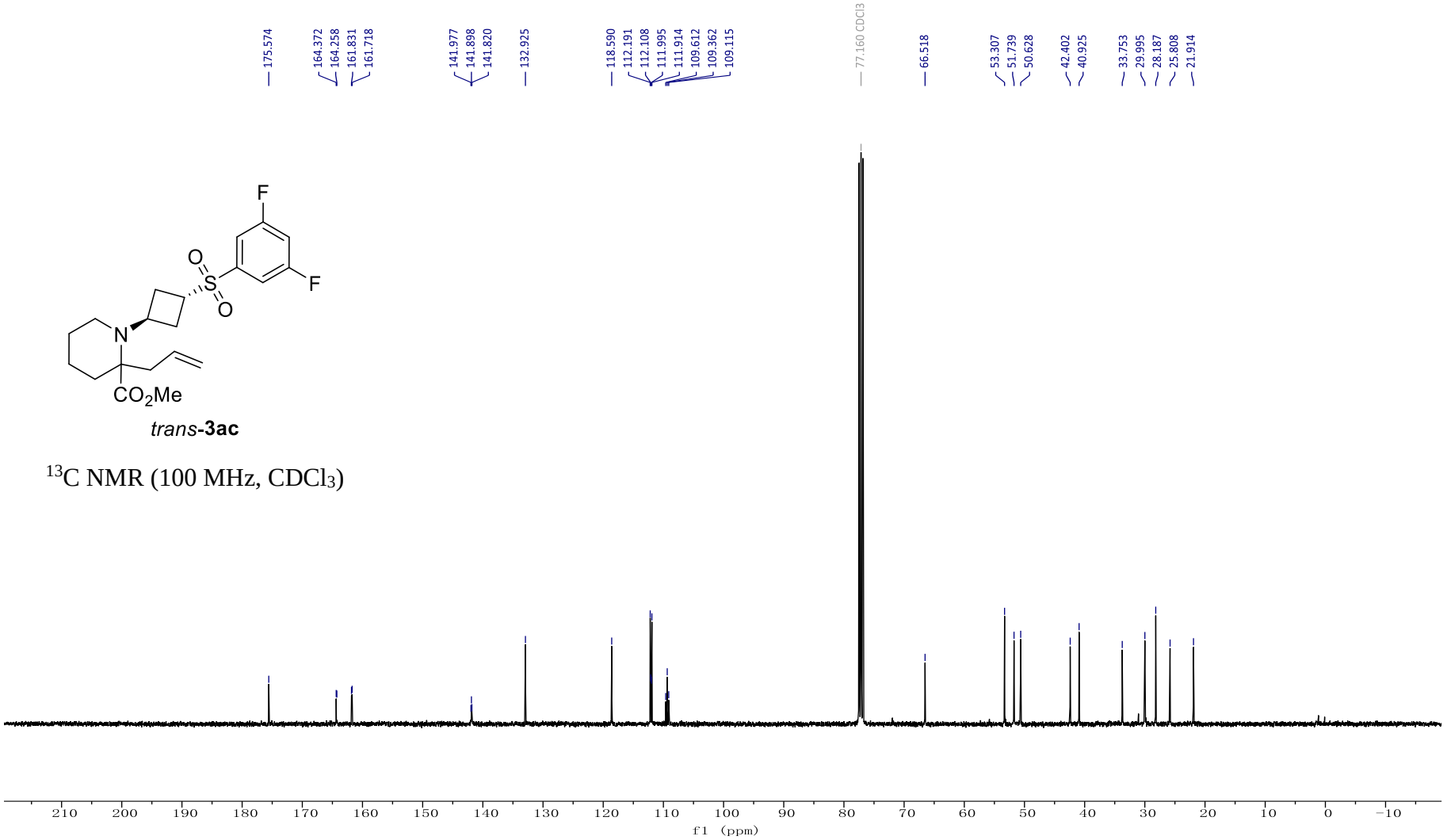
cis-**3ac**

^{19}F NMR (376 MHz, $CDCl_3$)



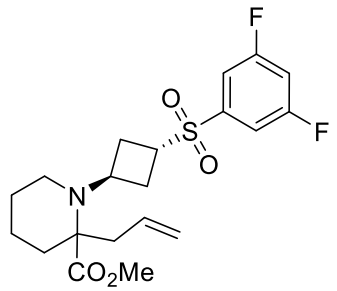
trans-**3ac**

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



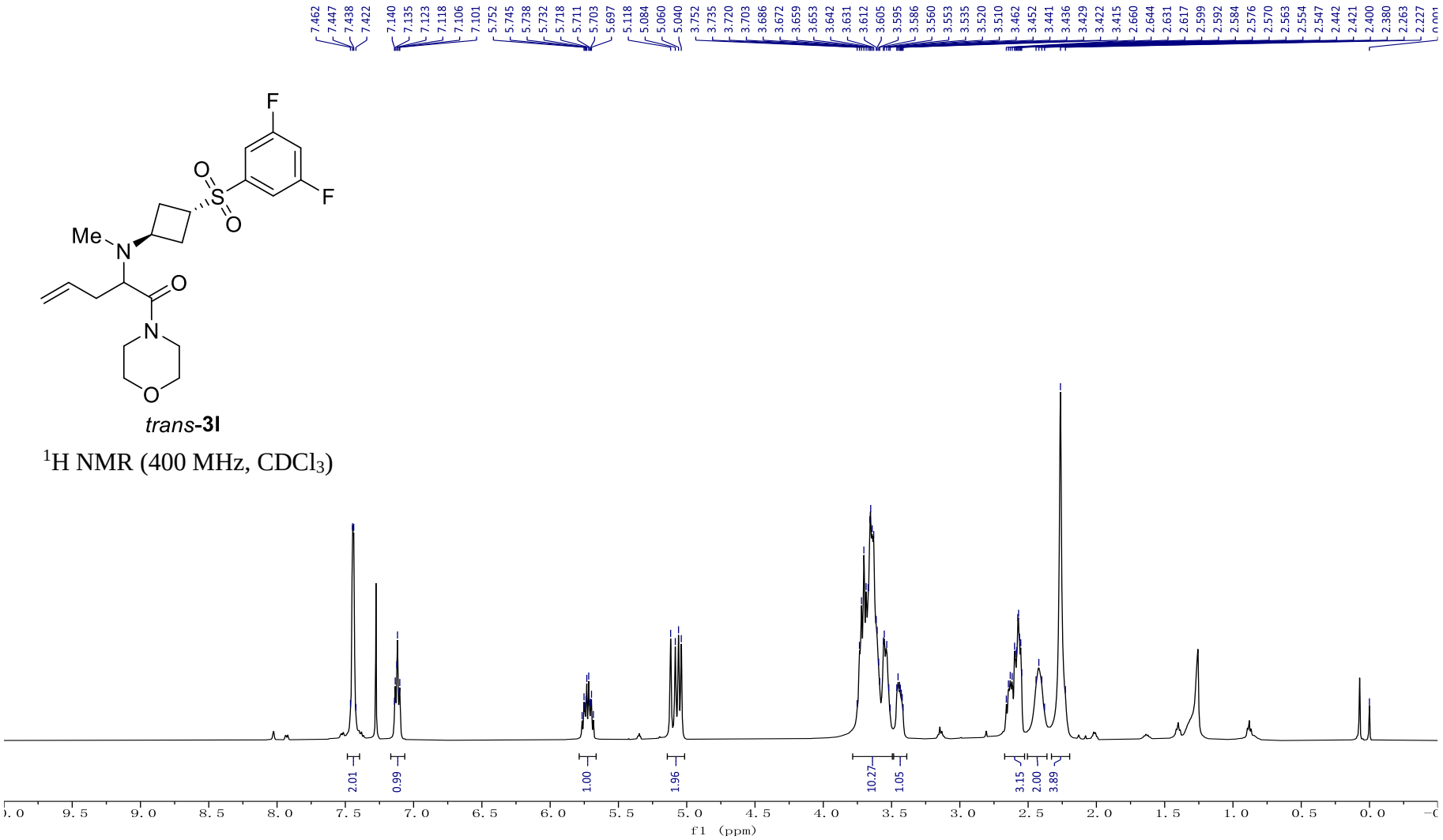
trans-**3ac**

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



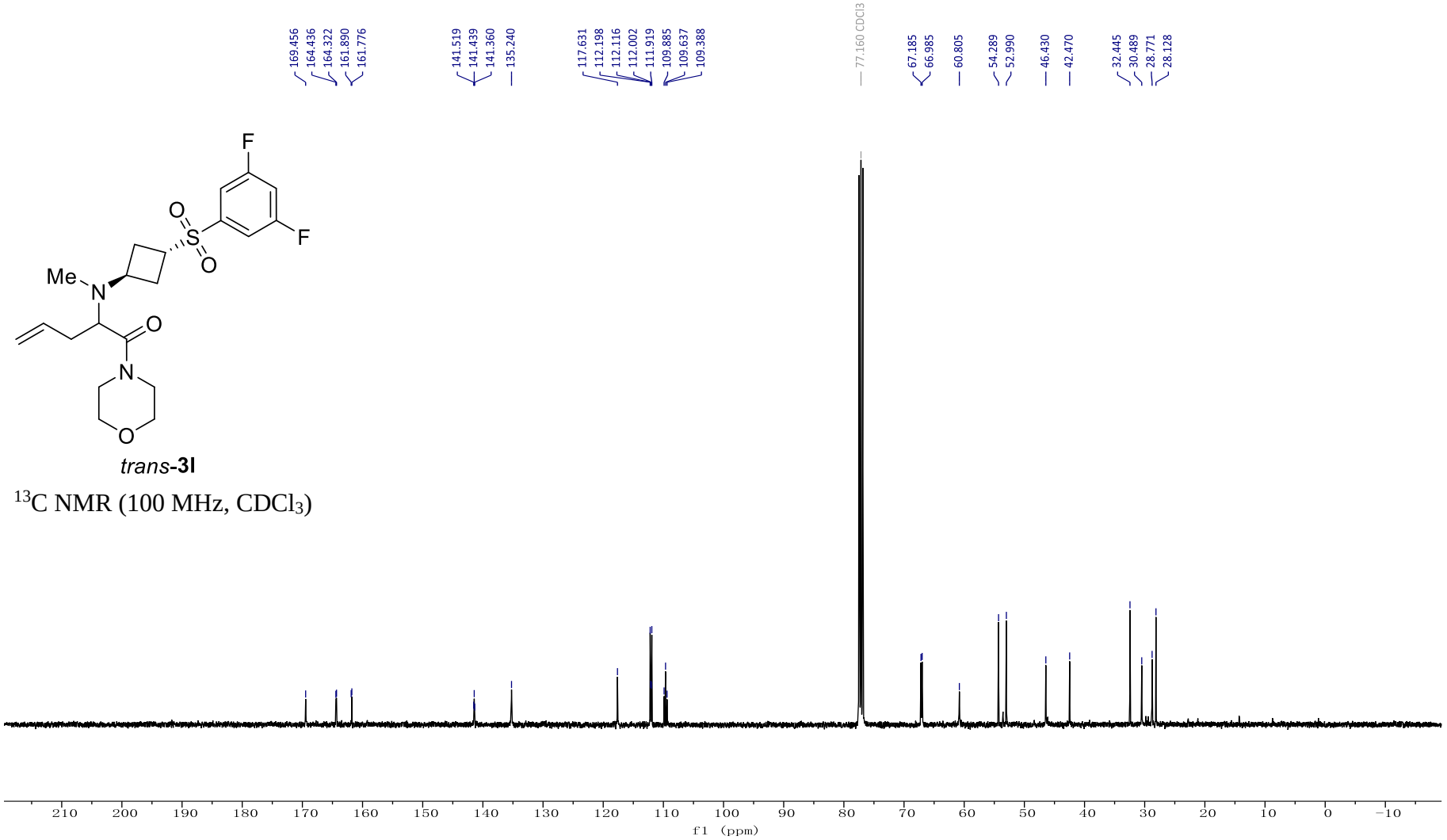
trans-**3ac**

^{19}F NMR (376 MHz, $CDCl_3$)



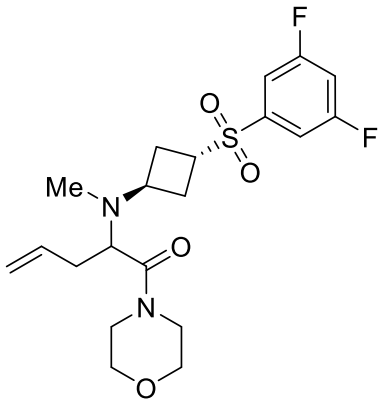
trans-**3l**

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



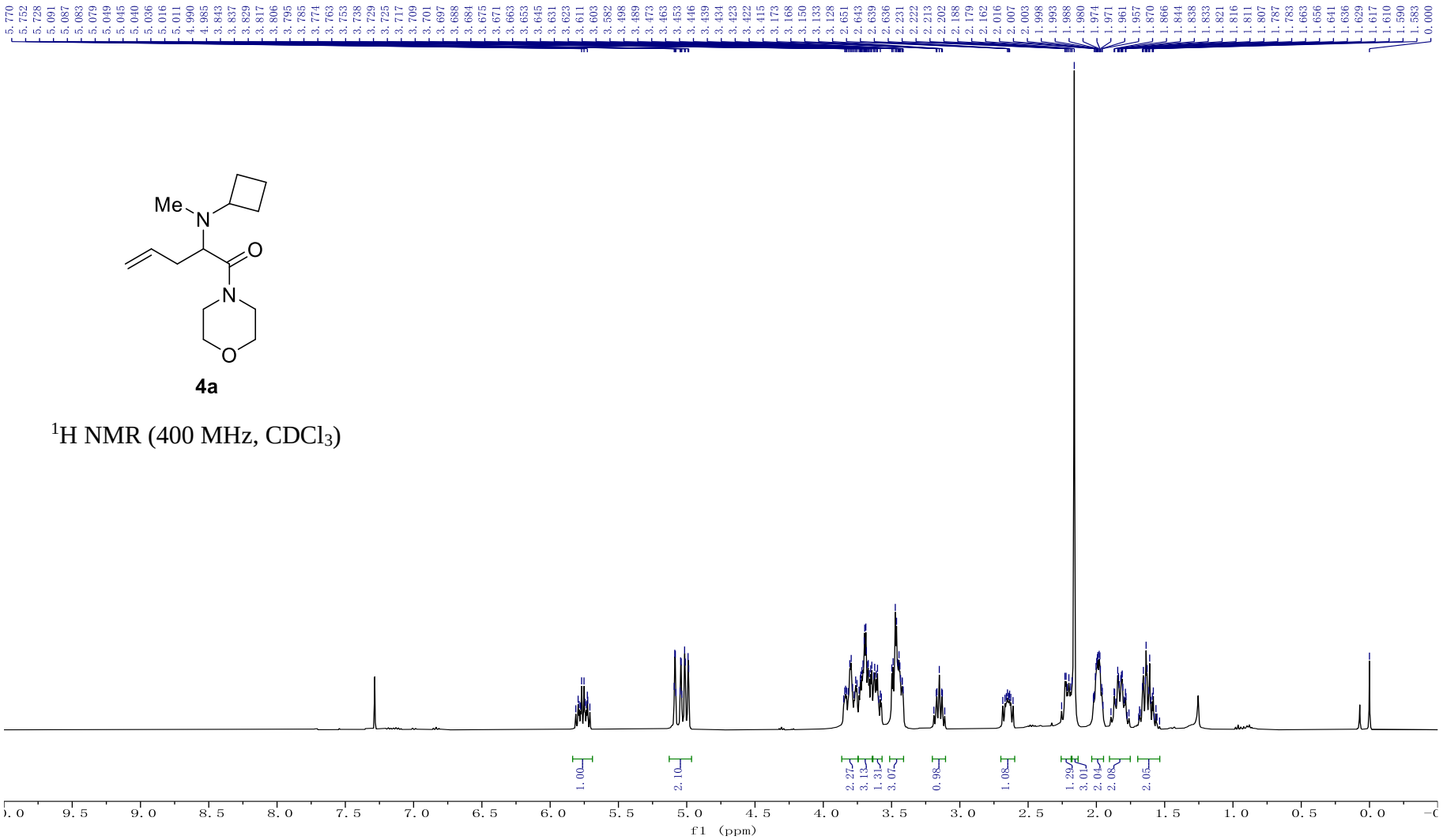
trans-**3l**

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

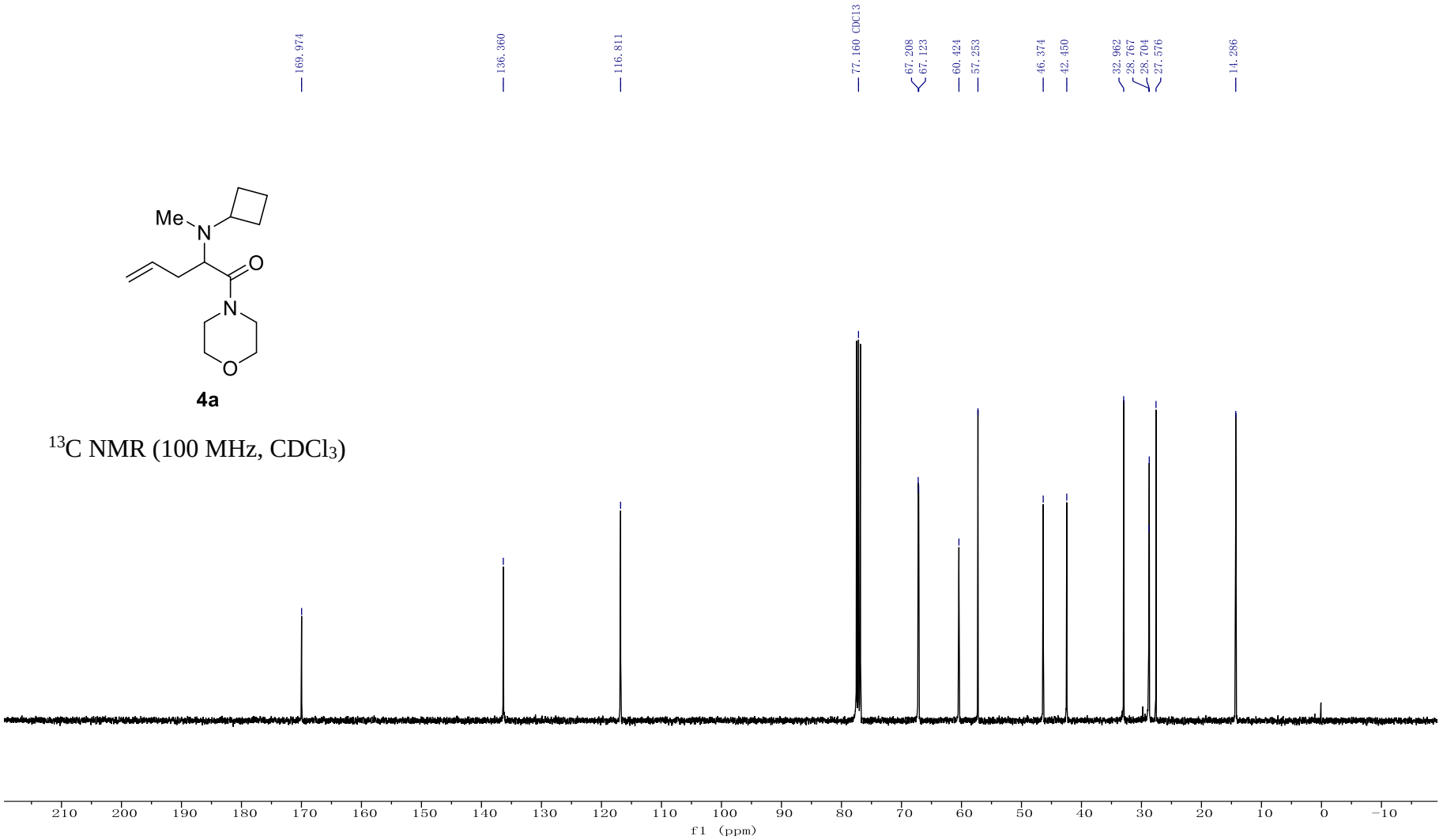


trans-**3l**

^{19}F NMR (376 MHz, $CDCl_3$)

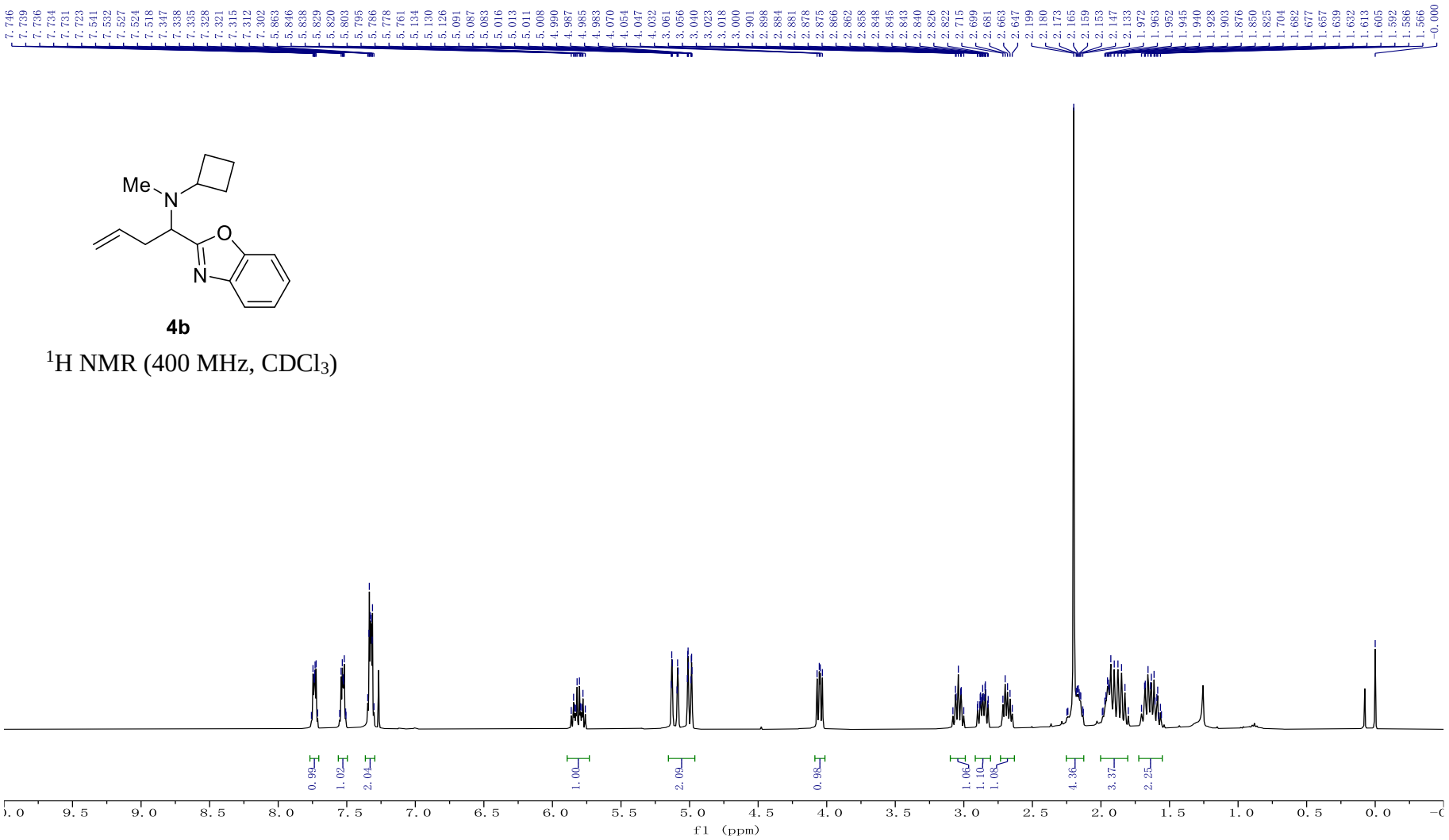


^{1}H NMR (400 MHz, $CDCl_3$)



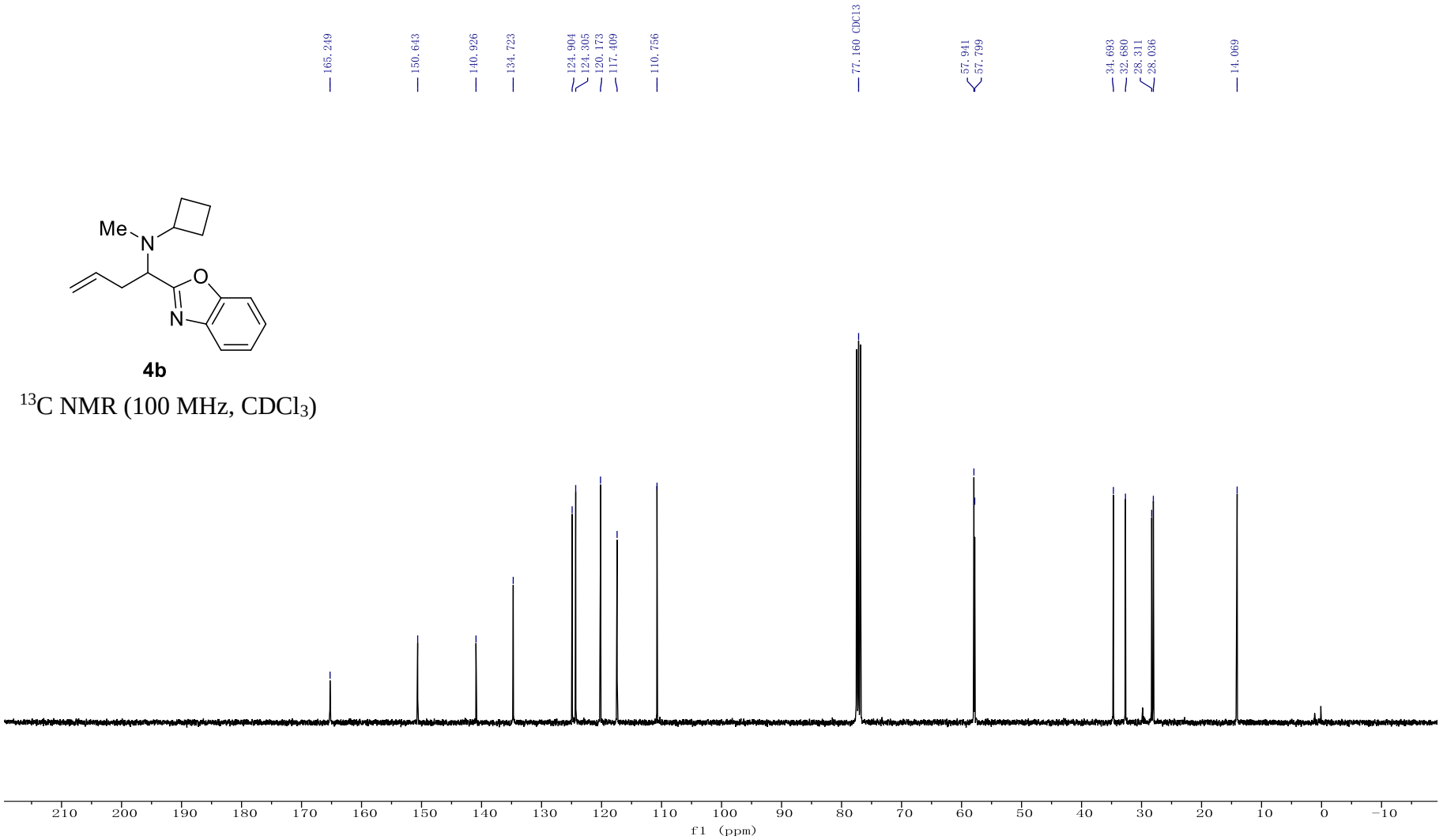
4a

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



4b

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



4b

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