Supporting Information

Silver-Catalyzed Late-Stage Fluorination

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Materials and Methods

Solvents other than acetone were dried by passage through alumina.[1] Except as indicated otherwise, reactions were monitored by thin layer chromatography (TLC) using EMD TLC plates pre-coated with 250 μm thickness silica gel 60 F254 plates and visualized by fluorescence quenching under UV light. Flash chromatography was performed on Whatman Silica Gel 60 μm (230–400 mesh) particle size using a forced flow of eluant at 0.3–0.5 bar pressure.[2] NMR spectra were recorded on either a Varian Unity/Inova 500 spectrometer operating at 500 MHz and 125 MHz for ^{1}H and ^{13}C acquisitions, respectively, or a Varian Mercury 400 spectrometer operating at 400 HMz and 375 MHz for ^{1}H and ^{19}F acquisitions, respectively. Chemical shifts are reported in ppm with the solvent resonance as the internal standard. Data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad; coupling constants in Hz; integration. High-resolution mass spectra were obtained on Jeol AX-505 or SX-102 spectrometers at the Harvard University Mass Spectrometry Facilities. Triethylamine was distilled over calcium hydride. Silver oxide was purchased from Strem and used as received. Acetone (CHROMASOLV® Plus, for HPLC, ≥99.9%), *n*-butyllithium, isopropylmagnesium chloride, tetrakis(triphenylphosphine)palladium, lithium chloride, 4-(dimethylamino)pyridine, di-*tert*-butyl dicarbonate, trifluoromethanesulfonic anhydride, pyridine, bis(tributyltin), *N*-phenylbis(trifluoromethanesulfonimide) and silver triflate were purchased from Aldrich and used as received. 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) was donated from Air Products and Chemicals. Ammonium hexafluorophosphate and tributyltin chloride were purchased from Alfa Aesar and used as received. All deuterated reagents and solvents were purchased from Cambridge Isotope Laboratories and used as received. NMR spectroscopic data of known compounds correspond to the data given in the appropriate references. NMR spectra of new compounds are attached. Ag-catalyzed fluorination reactions were carried out under ambient atmosphere with vigorous stirring. Freshly prepared arylstannanes and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate)[3] were used for fluorination reactions.

[1] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **15**, 1518 **(**1996).

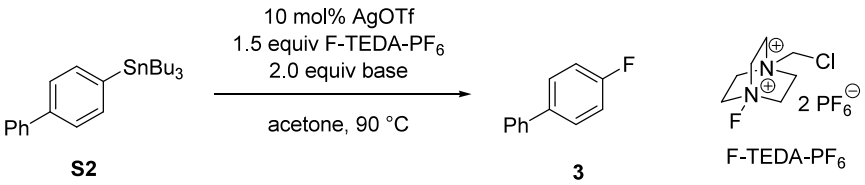
[2] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **43**, 2925 (1978).

[3] T. Furuya, A. E. Strom, T. Ritter, *J. Am. Chem. Soc.* **131**, 1662 (2009).

Experimental Data

Experimental Procedures and Compound Characterization

Effect of bases on the Ag-catalyzed fluorination reaction

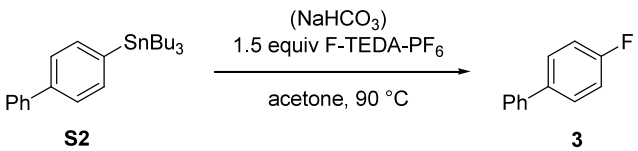


To 4-(biphenyl)tributylstannane (**S2**) (8.9 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver triflate (0.51 mg, 0.0020 mmol, 10 mol%), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv) and base (0.040 mmol, 2.0 equiv). The reaction mixture was stirred at 90 ºC for 2 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S1.

Table S1: Effect of bases on the Ag-catalyzed fluorination reaction

Base	Yield [%] (^{19}F NMR)	Base	Yield [%] (^{19}F NMR)
None	30	$Ba(OH)_2$	71
$NaHCO_3$	85	Na_2CO_3	59
$KHCO_3$	26	K_2CO_3	4
NaOH	12	Cs_2CO_3	3
KOH	9	K_3PO_4	3

Background reaction without AgOTf



To 4-(biphenyl)tributylstannane (**S2**) (8.9 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv) in the presence and absence of sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv). The reaction mixture was stirred at

90 ºC for 2 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S2.

Table S2: Background reaction without AgOTf

$NaHCO_3$	Yield [%] (^{19}F NMR)
None	1
2.0 equiv	4

Effect of silver source and additives on the Ag-catalyzed fluorination reaction

1 **2** **2a**

To ethyl 4-(tributylstannyl)benzoate (**1**) (8.8 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver catalyst, additive and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv). The reaction mixture was stirred in a sealed vial at 65 ºC or 90 ºC for the indicated time and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of ethyl 4-fluorobenzoate (–108.4 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S3.

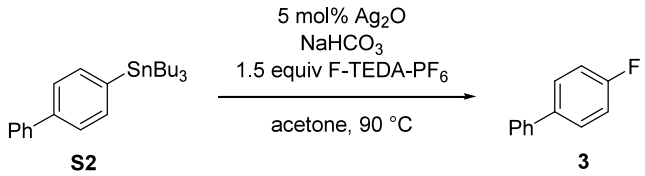
Table S3: Effect of silver source and additives on the Ag-catalyzed fluorination reaction

Ag catalyst		Base (2.0 equiv)	Additive (1.0 equiv)	Temp, time	**2**[a]	**2a**[a]
10 mol%	AgOTf	None	none	65 °C, 3 h	30%	68%
10 mol%	AgOTf	$NaHCO_3$	none	65 °C, 3 h	85%	9%
5 mol%	Ag_2O	$NaHCO_3$	none	65 °C, 5 h	87%	9%
5 mol%	Ag_2O	$NaHCO_3$	NaOTf	65 °C, 3 h	90%	5%
5 mol%	Ag_2O[b]	$NaHCO_3$	NaOTf	65 °C, 3 h	92%	2%
1 mol%	Ag_2O	$NaHCO_3$	NaOTf	90 °C, 18 h	92%	2%
1 mol%	Ag_2O[b]	$NaHCO_3$	NaOTf	90 °C, 18 h	75%	20%

a) Yields were determined by ^{19}F NMR and ^{1}H NMR using 1-fluoro-3-nitrobenzene as a

standard. b) 5.0 equiv MeOH was used.

Effect of $NaHCO_3$ on the Ag-catalyzed fluorination reaction



S2 **3**

To 4-(biphenyl)tributylstannane (**S2**) (8.9 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver oxide (0.23 mg, 0.0010 mmol, 5.0 mol%), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv) and sodium bicarbonate. The reaction mixture was stirred at 90 ºC for 2 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S4.

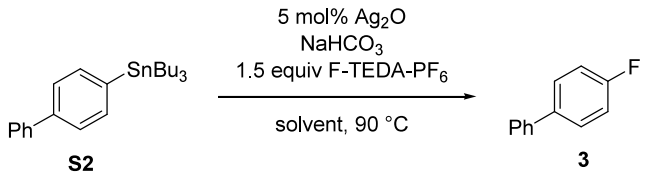
Table S4: Effect of $NaHCO_3$ on the Ag-catalyzed fluorination reaction

$NaHCO_3$ [equiv]	Yield [%] (^{19}F NMR)
0.5	59
1.0	70
2.0 (from Merck)	85
2.0 (from Mallinckrodt)	86
2.0 (washed with acetone)	86
5.0 equiv	85

Table S5: Impurities of $NaHCO_3$ used in fluorination

Maximum impurities and specifications	Merck	Mallinckrodt
Assay ($NaHCO_3$)	99.7-100.3%	100.0%
Insoluble matter	0.015%	<0.003%
Chloride	0.003%	<0.003%
Phosphate	0.001%	<0.001%
Sulfur compounds (as SO_4)	0.003%	<0.003%
Heavy Metals (as Pb)	5 ppm	<0.0005%
Ammonium	5 ppm	<0.0005%
Calcium	0.02%	<0.02%
Iron	0.001%	<0.001%
Potassium	0.005%	<0.005%

Effect of solvents on the Ag-catalyzed fluorination reaction



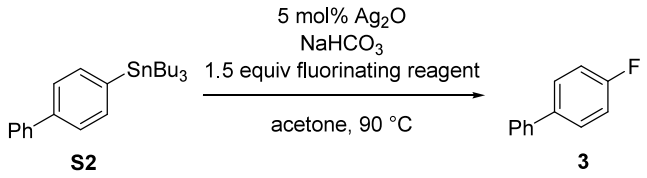
S2 **3**

To 4-(biphenyl)tributylstannane (**S2**) (8.9 mg, 0.020 mmol, 1.0 equiv) in the indicated solvent (0.4 mL) at 23 ºC was added silver oxide (0.23 mg, 0.0010 mmol, 5.0 mol%), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv). The reaction mixture was stirred at 90 ºC for 2 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S6.

Table S6: Effect of solvents on the Ag-catalyzed fluorination reaction

Solvent	Yield [%] (^{19}F NMR)	Solvent	Yield [%] (^{19}F NMR)
acetone	85	benzene	0
DMF	69	DMSO	0
EtOAc	42	MeCN	45
THF	29	DME	5
CH_2Cl_2	0	3-pentanone	25

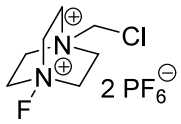
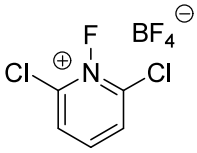
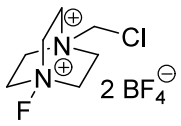
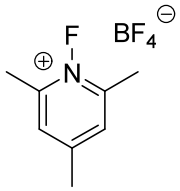
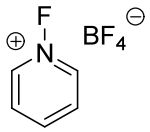
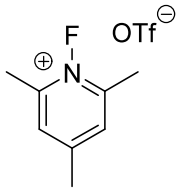
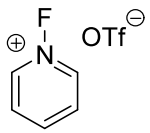
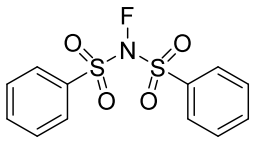
Effect of fluorinating reagents on the Ag-catalyzed fluorination reaction



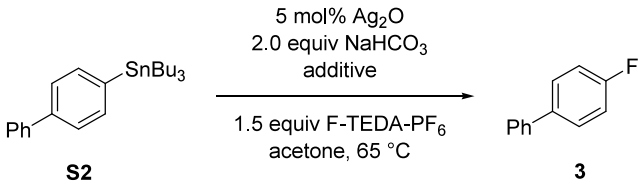
S2 **3**

To 4-(biphenyl)tributylstannane (**S2**) (8.9 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver oxide (0.23 mg, 0.0010 mmol, 5.0 mol%), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv) and fluorinating reagent (0.0300 mmol, 1.5 equiv). The reaction mixture was stirred at 90 ºC for 2 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S7.

Table S7: Effect of fluorinating reagents on the Ag-catalyzed fluorination reaction

Fluorinating reagent	Yield [%] (^{19}F NMR)	Fluorinating reagent	Yield [%] (^{19}F NMR)
	85		0
	70		0
	0		0
	0		0

Effect of additives on the Ag-catalyzed fluorination reaction



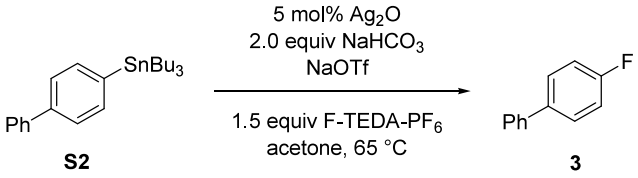
S2 **3**

To 4-(biphenyl)tributylstannane (**S2**) (8.9 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver oxide (0.23 mg, 0.0010 mmol, 5.0 mol%), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv) and additive. The reaction mixture was stirred at 65 ºC for 5 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S8.

Table S8: Effect of additives on the Ag-catalyzed fluorination reaction

Additive [1 equiv]	Yield [%] (^{19}F NMR)	Additive	Yield [%] (^{19}F NMR)
None	76	3Å MS	15
2,6-lutidine	44	NaOTf (0.5 equiv)	82
LiCl	0	NaOTf (1.0 equiv)	85
BaO	78	NaOTf (2.0 equiv)	85

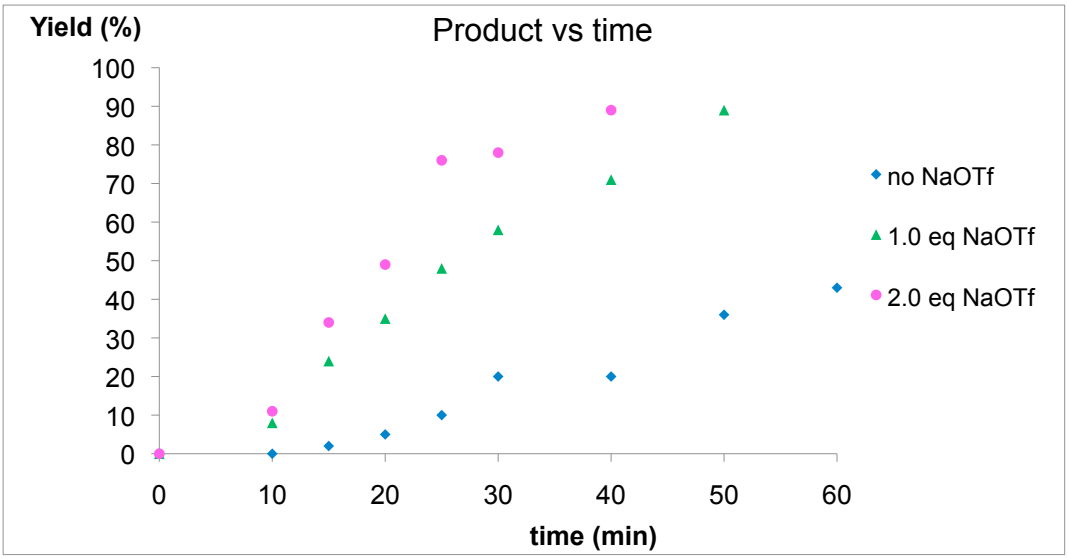
Effect of NaOTf on the Ag-catalyzed fluorination reaction



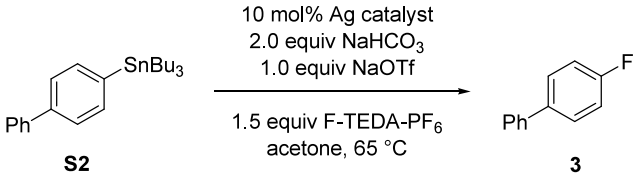
S2 **3**

To 4-(biphenyl)tributylstannane (**S2**) (44.4 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate, and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (705 mg, 0.150 mmol, 1.50 equiv). 3-Nitrofluorobenzene (10.0 μL, 0.188 mmol) was added to the reaction as the standard. The reaction mixture was stirred at 65 ºC in a sealed vial. For each data point, an aliquot of the reaction mixture was removed from the reaction vessel and quenched with 1N HCl. The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Results are reported in Figure S1.

Figure S1: Effect of NaOTf on the Ag-catalyzed fluorination reaction



Effect of silver salts on the Ag-catalyzed fluorination reaction

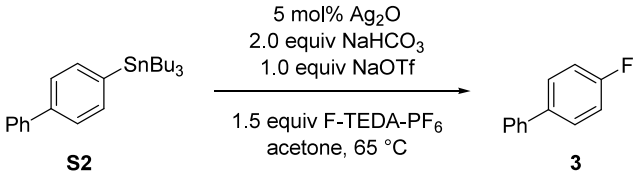


To 4-(biphenyl)tributylstannane (**S2**) (8.9 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver salt (10 mol%), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv), sodium trifluoromethanesulfonate (3.4 mg, 0.020 mmol, 1.0 equiv), and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv). The reaction mixture was stirred at 65 ºC for 5 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S9.

Table S9: Effect of silver salts on the Ag-catalyzed fluorination reaction

Silver salt	Yield [%] (^{19}F NMR)
Ag_2O	85
AgOTf	85
$AgBF_4$	84
$AgPF_6$	85

Effect of concentration[a] on the Ag-catalyzed fluorination reaction



S2 **3**

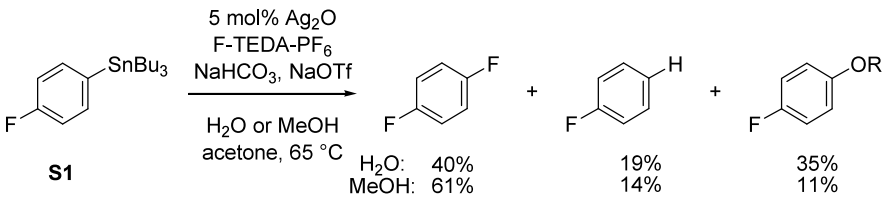
To 4-(biphenyl)tributylstannane (**S2**) (44.4 mg, 0.100 mmol, 1.00 equiv) in acetone at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred at 65 ºC for 5 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (10.0 μL, 0.188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S10.

Table S10: Effect of concentration[a] on the Ag-catalyzed fluorination reaction

Concentration[a] (M)	Yield [%] (^{19}F NMR)
0.025	82
0.050	85
0.10	79
0.20	65

a) concentration of 4-(biphenyl)tributylstannane

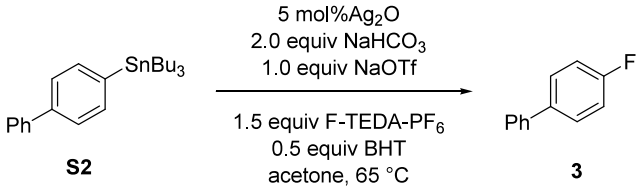
C–O bond formation in the Ag-catalyzed fluorination reaction



To 4-(fluorophenyl)tributylstannane (**S1**) (38.6 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), water or methanol (25.0 equiv), and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred at 65 ºC for 5 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorophenol (–128.0 ppm, 6%) or 4-fluoroanisole (–126.0 ppm, 3%) with that of 3-nitrofluorobenzene (–112.0 ppm).

Effect of BHT on the Ag-catalyzed fluorination reaction

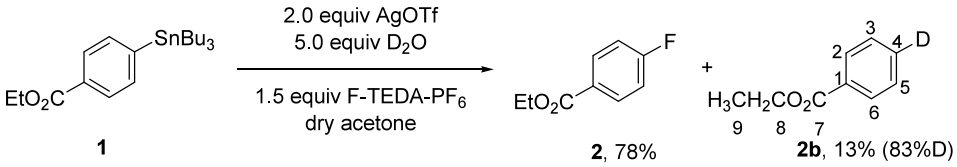
Addition of the radical scavengers of butylated hydroxytoluene (BHT) and galvinoxyl, free radical did not influence the yield of fluorination product, which suggests that the mechanism is unlikely to proceed via long-lived free radical intermediates.



To 4-(biphenyl)tributylstannane (**S2**) (8.9 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver oxide (0.23 mg, 0.0010, 5.0 mol%), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv), sodium trifluoromethanesulfonate (3.4 mg, 0.020 mmol, 1.0 equiv), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv), and 2,6-di-*tert*-butyl-4-methylphenol (BHT) (2.2 mg, 0.010 mmol, 0.50 equiv). The reaction mixture was stirred at 65 ºC for 5 hr in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of 4-fluorobiphenyl (–118.1 ppm, 80%) with that of 3-nitrofluorobenzene (–112.0 ppm).

^{2}H-labeling experiment

A ^{2}H-labeling experiment with D_2O was carried out to interrogate the source of protodestannylation.

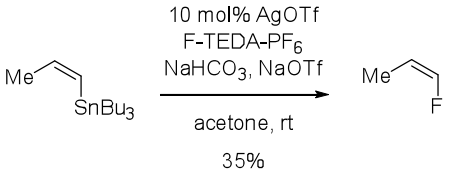


To ethyl 4-(tributylstannyl)benzoate (**1**) (44.0 mg, 0.100 mmol, 1.00 equiv) in dry acetone (2 mL) at 23 ºC was added silver triflate (51.2 mg, 0.200 mmol, 2.00 equiv), deuterium oxide (10 μL) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred at 23 ºC for 20 min. The solvent was concentrated in vacuo. The residue was purified by preparative TLC with hexane/EtOAc 3:1 (v/v) to afford 13.1 mg ethyl 4-fluorobenzoate (78%) and 2.0 mg 4-deutero-ethyl benzoate (13% yield). The amount of ^{2}H-incorporation was determined to be 83% at C-4 by integration of the proton resonances at 7.57–7.53 ppm (H-4) and 7.44 ppm (H-3, H-5) in $CDCl_3$.

4-deutero-ethyl benzoate: R_f = 0.30 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.05 (d, J = 8.5 Hz, 2H, H-3, H-5), 7.57–7.53 (m, 0.17 H, H-4), 7.44 (d, J = 8.0 Hz, 2H, H-2, H-6), 4.37 (q, J = 7.0 Hz, 2H, H-8), 1.39 (t, J = 9.0 Hz, 3H, H-9). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 166.63 (C-7), 132.59 ($J_{C\text{-}D}$ = 28 Hz, C-4), 130.50 (C-1), 129.52 (C-3, C-5), 128.29 (C-2, C-6), 60.93 (C-8), 14.32 (C-9). ^{2}H NMR (92 MHz, $CHCl_3$, 23 ºC, δ): 7.61. The proton and carbon NMR resonances were assigned by ^{1}H-^{1}H COSY, HSQC and HMBC experiments.

Stereospecific fluorination of (*Z*)-β-tributylstannylpropene

To distinguish between a stereospecific fluorination, consistent with stereospecific transmetallation and stereospecific reductive elimination from a high-valent silver fluoride, and an electrophilic substitution mechanism, fluorination of (*Z*)-β-tributylstannylpropene was carried out. The observation of only (*Z*)-β-fluoropropene is consistent with a stereospecific reductive elimination from a high-valent silver fluoride.

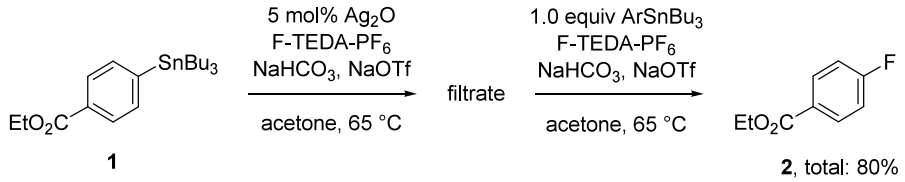


To (*Z*)-β-tributylstannylpropene (6.6 mg, 0.020 mmol, 1.0 equiv) in acetone-d_6 (0.4 mL) at 23 ºC was added silver triflate (0.51 mg, 0.0020 mmol, 10 mol%), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv), sodium trifluoromethanesulfonate (3.4 mg, 0.020 mmol, 1.0 equiv), and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv). The reaction mixture was stirred for 3 hr at room temperature in a sealed vial. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of (*Z*)-β-fluoropropene (–133.5 ppm, dd, J = 86 Hz, 44 Hz,

35%) with that of 3-nitrofluorobenzene (–112.0 ppm). No (*E*)-β-fluoropropene (–131.3 ppm, dd, J = 89 Hz, 22 Hz) was observed. The low yield of the fluorination product may be due to the low boiling point (bp: –20 ºC) of the product.

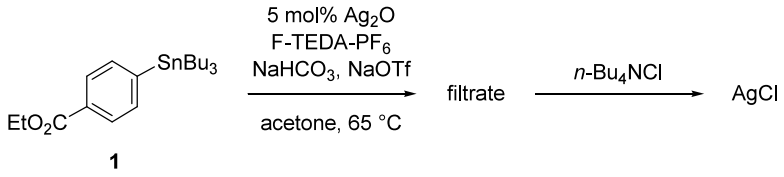
Evidence for a homogeneous silver catalysis

To determine the presence of a soluble Ag(I) species, the reaction suspension was filtered through Celite, the filtrate was added to the same amount of all reagents except silver catalyst, fluorination proceeded. Also precipitates were observed when tetrabutylammonium chloride or tetrabutylammonium iodide was added to the filtrate.



1 **2**, total: 80%

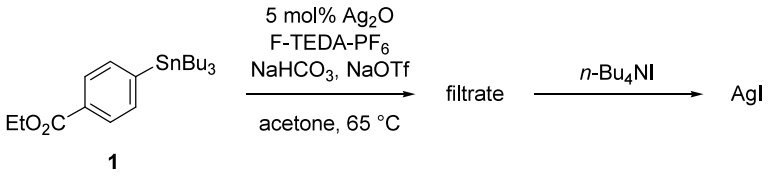
To ethyl 4-(tributylstannane)benzoate (**1**) (8.8 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver oxide (0.23 mg, 0.0010 mmol, 5.0 mol%), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv), sodium trifluoromethanesulfonate (3.4 mg, 0.020 mmol, 1.0 equiv), and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 °C, the reaction mixture was filtered through a pad of celite and the filtrate was added to ethyl 4-(tributylstannane)benzoate (8.8 mg, 0.020 mmol, 1.00 equiv), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv), sodium trifluoromethanesulfonate (3.4 mg, 0.020 mmol, 1.0 equiv), and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv) in acetone (0.4 mL) at 23 ºC. The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.00 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of ethyl 4-fluorobenzoate (–108.4 ppm, 80%) with that of 3-nitrofluorobenzene (–112.0 ppm).



1

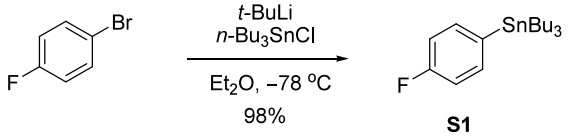
To ethyl 4-(tributylstannane)benzoate (**1**) (44.0 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred at 65 ºC in a sealed vial. After 30 min, the black solid of Ag_2O was no longer

observable and a colorless precipitate was observed. The reaction mixture was further stirred for 4 h at 65 ºC and subsequently cooled to 23 ºC. The reaction mixture was filtered through a pad of celite, eluting with acetone. Tetrabutylammonium chloride (5.5 mg, 0.020 mmol) was added to the filtrate and a white precipitate was observed immediately. The reaction mixture was stirred for 20 min at 23 °C and the precipitate was collected on a sintered glass funnel, washed with H_2O (3 × 1 mL), acetone (3 × 1 mL) and dried in vacuo to afford 1.31 mg of AgCl as a colorless powder (92% yield based on Ag_2O). The AgCl was soluble in concentrated ammonia solution.



To ethyl 4-(tributylstannane)benzoate (**1**) (44.0 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred at 65 ºC in a sealed vial. After 30 min, the black solid of Ag_2O was no longer observable and a colorless precipitate was observed. The reaction mixture was further stirred for 4 h at 65 °C and subsequently cooled to 23 ºC. The reaction mixture was filtered through a pad of celite, eluting with acetone. Tetrabutylammonium iodide (7.4 mg, 0.020 mmol) was added to the filtrate and a yellow precipitate was observed immediately. The reaction mixture was stirred for 20 min at 23 °C and the precipitates were collected on a sintered glass funnel, washed with H_2O (3 × 1 mL), acetone (3 × 1 mL) and dried in vacuo to afford 2.15 mg of AgI as a yellow powder (92% yield based on Ag_2O). The AgI was insoluble in concentrated ammonia solution.

Tributyl(4-fluorophenyl)stannane[4] (S1)

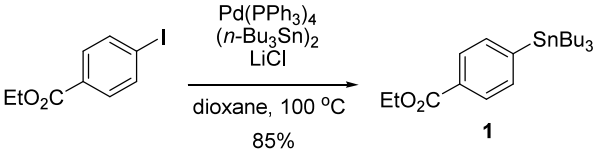


To 1-bromo-4-fluorobenzene (1.75 g, 10.0 mmol, 1.00 equiv) in Et_2O (25 mL) at –78 ºC was added *t*-BuLi (1.7 M in pentane, 11.8 mL, 20 mmol, 2.0 equiv). The reaction mixture was stirred at –78 ºC for 30 min before the addition of *n*-Bu_3SnCl (3.26 g, 10.0 mmol, 1.00 equiv). The reaction mixture was warmed to 23 ºC and stirred for 1 hr before being filtered through a plug of neutral alumina. The filtrate was concentrated in vacuo to afford 3.76 g of the title compound as a colorless oil (98% yield).

[4] J. Justicia, J. E. Oltra, J. M. Querva, *J. Org. Chem.* **69**, 5803 (2004).

R_f = 0.63 (hexanes). NMR Spectroscopy: ^{1}H NMR (600 MHz, $CDCl_3$, 23 ºC, δ): 7.41 (dd, *J* = 8.4 Hz, 6.6 Hz, 2H), 7.04 (dd, *J* = 9.6 Hz, 8.4 Hz, 2H), 1.59–1.46 (m, 6H), 1.36–1.30 (m, 6H), 1.11–1.09 (m, 6H), 0.89 (t, *J* = 6.0 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 23 ºC, δ): 163.24 (d, *J* = 245 Hz), 137.83 (d, *J* = 6.9 Hz), 136.65 (d, *J* = 4.6 Hz), 115.11 (d, *J* = 19.0 Hz), 29.07, 27.38, 13.66, 9.65. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –114.1. These spectroscopic data correspond to previously reported data.[4]

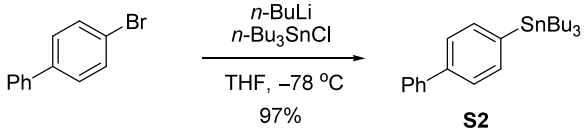
Ethyl 4-(tributylstannyl)benzoate[5] (1)



To ethyl 4-iodobenzoate (275 mg, 1.00 mmol, 1.00 equiv) in dioxane (10 mL) at 23 ºC was added lithium chloride (210 mg, 5.00 mmol, 5.00 equiv), tetrakis(triphenylphosphine)palladium (57.8 mg, 0.0500 mmol, 5.00 mol%) and bis(tri-*n*-butyltin) (1.0 mL, 2.0 mmol, 2.0 equiv). After stirring for 21 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 20:1 (v/v), to afford 374 mg of the title compound as a colorless oil (85% yield).

R_f = 0.20 (hexanes). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.96 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 4.37 (q, *J* = 6.0 Hz, 2H), 1.58–1.50 (m, 6H), 1.40–1.30 (m, 9H), 1.10–1.06 (m, 6H), 0.88 (t, *J* = 7.3 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ):167.06, 149.45, 136.36, 129.92, 128.33, 60.79, 29.02, 27.31, 14.34, 13.64, 9.64. These spectroscopic data correspond to previously reported data.[5]

(4-Biphenyl)tributylstannane[6] (S2)



To 4-bromobiphenyl (1.00 g, 4.31 mmol, 1.00 equiv) in THF (10 mL) at –78 ºC was added *n*-BuLi (2.5 M in hexane, 1.7 mL, 4.3 mmol, 1.0 equiv). The reaction mixture was stirred at –78 ºC for 30 min before the addition of *n*-Bu_3SnCl (1.41 g, 4.31 mmol, 1.00 equiv). After stirring for 1 hr at –78 ºC, the reaction mixture was warmed to 23 ºC and the solvent was removed in vacuo. The residue was dissolved in 20 mL of Et_2O and filtered through a plug of neutral alumina. The filtrate was concentrated in vacuo to afford 1.85 g of the title compound as a colorless oil (97% yield).

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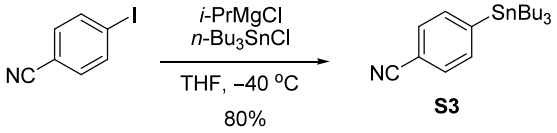
[5] C. Gosmini, J. Périchon, *Org. Biomol. Chem*. **3**, 216 (2005).

[6] Y. Dienes, *et al*, *Chem. Eur. J.* **13**, 7487 (2007).

R_f = 0.58 (hexanes). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.65–7.57 (m, 6H), 7.48 (dd, *J* = 7.8 Hz, 7.8 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 1H), 1.64–1.54 (m, 6H), 1.40–1.34 (m, 6H), 1.18–1.08 (m, 6H), 0.93 (t, *J* = 7.3 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 23 ºC, δ): 141.31, 140.76, 136.89, 128.71, 127.14, 127.08, 126.96, 126.63, 29.16, 27.44, 13.71, 9.62. These spectroscopic data correspond to previously reported data.[6]

Tributyl(4-cyanophenyl)stannane[7] (S3)

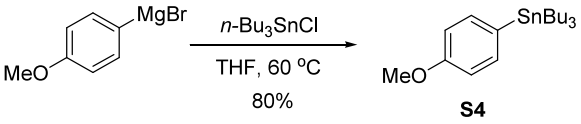


S3

To 4-iodobenzonitrile (458 mg, 2.00 mmol, 1.00 equiv) in THF (6 mL) at –40 ºC was added *i*-PrMgCl (2.0 M in Et_2O, 1.1 mL, 2.2 mmol, 1.1 equiv). The reaction mixture was stirred for 1 hr at –40 ºC and *n*-Bu_3SnCl (783 mg, 2.40 mmol, 1.20 equiv) was added. After stirring for 1 hr at –40 ºC, the reaction mixture was warmed to 23 ºC and quenched with saturated aqueous NH_4Cl (6 mL), and Et_2O (4 mL) was added. The phases were separated and the aqueous phase was extracted with Et_2O (2 × 10 mL). The combined organic phases were washed with brine (50 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with hexanes, to afford 629 mg of the title compound as a colorless oil (80% yield).

R_f = 0.25 (hexanes/EtOAc 50:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.56–7.55 (m, 4H), 1.54–1.50 (m, 6H), 1.34–1.30 (m, 6H), 1.11–1.07 (m, 6H), 0.89 (t, *J* = 7.3 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 150.33, 136.86, 130.70, 119.22, 111.55, 28.95, 27.27, 13.61, 9.73**.** These spectroscopic data correspond to previously reported data.[7]

(4-Methoxyphenyl)tributylstannane[3] (S4)



S4

To tributyltin chloride (652 mg, 2.00 mmol, 1.00 equiv) in THF (2 mL) at 23 ºC was added 4-methoxyphenylmagnesium bromide (0.50 M in THF, 8.0 mL, 4.0 mmol, 2.0 equiv). After stirring for 1 hr at 60 ºC, the reaction mixture was cooled to 0 ºC and quenched with saturated aqueous NH_4Cl (10 mL), and Et_2O (10 mL) was added. The phases were separated and the aqueous phase was extracted with Et_2O (2 × 10 mL). The combined organic phases were washed with brine (10 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by fractional distillation to afford 637 mg of the title compound as a colorless oil (80% yield).

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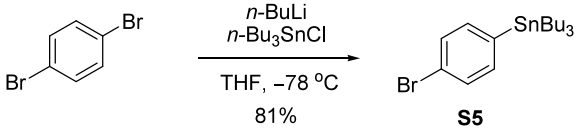
[7] M. Kosugi, T. Ohya, T. Migita, *Bull. Chem. Soc. Jpn.* **56**, 3855 (1983).

R_f = 0.20 (hexanes). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.37 (d, *J* = 7.0 Hz, 2H), 6.90 (d, *J* = 7.0 Hz, 2H), 3.80 (s, 3H), 1.56–1.50 (m, 6H), 1.35–1.31 (m, 6H), 1.04–1.00 (m, 6H), 0.89 (t, *J* = 6.0 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 23 ºC, δ): 159.67, 137.47, 132.00, 113.89, 54.94. 29.09, 27.37, 13.67, 9.58. These spectroscopic data correspond to previously reported data.[3]

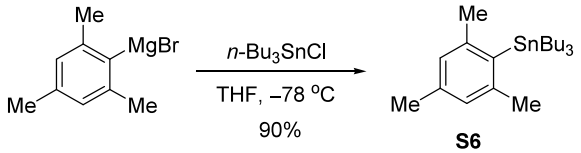
(4-Bromophenyl)tributylstannane[8] (S5)



To *p*-dibromobenzene (932 mg, 4.00 mmol, 1.00 equiv) in THF (10 mL) at –78 ºC was added *n*-BuLi (2.5 M in hexane, 1.6 mL, 4.0 mmol, 1.0 equiv). The reaction mixture was stirred at –78 ºC for 30 min before the addition of *n*-Bu_3SnCl (1.30 g, 4.00 mmol, 1.00 equiv). After stirring for 1 hr at –78 ºC, the reaction mixture was warmed to 23 ºC and the solvent was removed in vacuo. The residue was purified by fractional distillation to afford 1.45 g of the title compound as a colorless oil (81% yield).

R_f = 0.50 (hexanes). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.46 (d, *J* = 7.0 Hz, 2H), 7.32 (d, *J* = 7.0 Hz, 2H), 1.56–1.50 (m, 6H), 1.35–1.31 (m, 6H), 1.08–1.04 (m, 6H), 0.89 (t, *J* = 7.5 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 140.62, 137.89, 130.97, 122.75, 29.01, 27.32. 13.65, 9.62. These spectroscopic data correspond to previously reported data.[8]

Tributyl(2,4,6-trimethylphenyl)stannane[9] (S6)



To 2,4,6-trimethylphenylmagnesium bromide (1.0 M in THF, 5.0 mL, 5.0 mmol, 1.0 equiv) in THF (15 mL) at –78 ºC was added *n*-Bu_3SnCl (1.63 g, 5.0 mmol, 1.00 equiv). After stirring for 1 hr at 23 ºC, the solvent was removed in vacuo and the residue was purified by fractional distillation to afford 1.85 g of the title compound as a colorless oil (90% yield).

R_f = 0.76 (hexanes). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 6.83 (s, 2H), 2.36 (s, 6H), 2.26 (s, 3H), 1.55–1.46 (m, 6H), 1.35–1.30 (m, 6H), 1.09–1.06 (m, 6H), 0.89 (t, *J* = 7.3 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 145.19, 138.32, 137.83, 127.57, 29.17, 27.44, 25.53, 20.91, 13.62, 12.48. These spectroscopic data correspond to previously reported data.[9]

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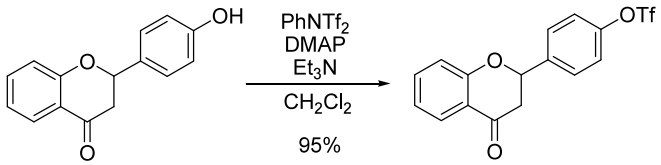
[8] K. L. Juara, H. S. Hundal, R. D. Handa, *Indian. J. Chem.* **5**, 211 (1967).

[9] A. F. Littke, L. Schwarz, G. C. Fu, *J. Am. Chem. Soc.* **124**, 6343 (2002).

4'-(Trifluoromethanesulfonyl)flavanone (S7)

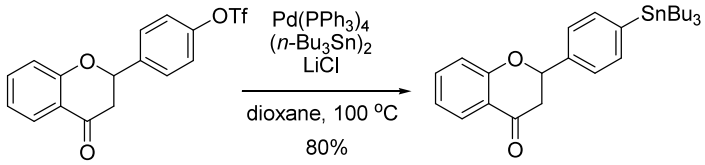


S7

To 4'-hydroxyflavanone (240 mg, 1.00 mmol, 1.00 equiv) in CH_2Cl_2 (2.0 mL) at 23 ºC was added triethylamine (418 μL, 3.00 mmol, 3.00 equiv), 4-(dimethylamino)pyridine (12 mg, 0.10 mmol, 0.10 equiv), and *N*-phenylbis(trifluoromethanesulfonimide) (535 mg, 1.50 mmol, 1.50 equiv). The reaction mixture was stirred for 3 hr at 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 10:1 (v/v), to afford 353 mg of the title compound as a colorless solid (95% yield).

R_f = 0.50 (hexane/EtOAc 10:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.94 (dd, *J* = 8.0 Hz, 1.5 Hz, 1H), 7.60 (dd, *J* = 7.0 Hz, 2.5 Hz, 2H), 7.56–7.52 (m, 1H), 7.36 (dd, *J* = 7.0 Hz, 2.0 Hz, 2H), 7.11–7.06 (m, 2H), 5.52 (dd, *J* = 13.0 Hz, 3.0 Hz, 1H), 3.04 (dd, *J* = 17.0 Hz, 3.5 Hz, 1H), 2.92 (dd, *J* = 17.0 Hz, 3.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 191.07, 161.09, 149.42, 139.34, 136.40, 127.99, 127.15, 122.02, 121.86, 120.87, 118.70 (q, *J* = 320 Hz), 118.04, 78.44, 44.68. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –75.05. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 373.0352. Found, 373.0354.

4'-(Tributylstannyl)flavanone (S8)



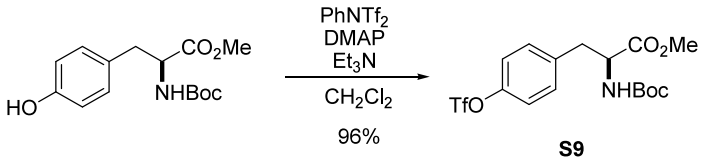
S7 **S8**

To 4-(trifluoromethanesulfonyl)flavanone (**S7**) (200 mg, 0.538 mmol, 1.00 equiv) in dioxane (5 mL) at 23 ºC was added lithium chloride (113 mg, 2.69 mmol, 5.00 equiv), tetrakis(triphenylphosphine)palladium (31 mg, 0.027 mmol, 5.0 mol%) and bis(tri-*n*-butyltin) (0.55 mL, 0.11 mmol, 2.0 equiv). After stirring for 3 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 20:1 (v/v), to afford 222 mg of the title compound as a colorless oil (80% yield).

R_f = 0.30 (hexane/EtOAc 10:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.94 (dd, *J* = 8.5 Hz, 1.5 Hz, 1H), 7.56–7.50 (m, 3H), 7.45 (dd, *J* = 7.5 Hz, 3.5 Hz, 2H), 7.08–7.05 (m, 2H), 5.47 (dd, *J* = 13.5 Hz, 3.0 Hz, 1H), 3.13 (dd, *J* = 17.0 Hz, 3.0 Hz, 1H), 2.91 (dd, *J* = 17.0 Hz, 3.0 Hz, 1H), 1.59–1.53 (m, 6H), 1.39–1.32 (m, 6H), 1.10–1.03 (m, 6H), 0.91 (d, *J* = 7.3 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 192.11, 161.64,

143.19, 138.18, 136.89, 136.15, 127.03, 125.61, 121.54, 120.94, 118.13, 79.75, 44.53, 29.05, 27.36, 13.65, 9.59. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 515.1966. Found, 515.1978.

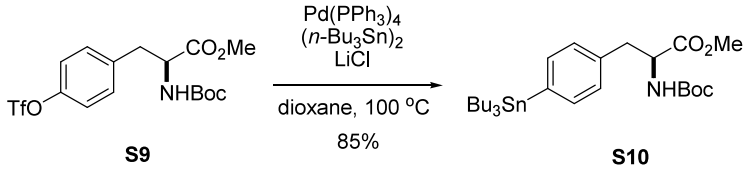
_N_-Boc-4-(trifluoromethanesulfonyl)-_L_-phenylalanine methyl ester (S9)



To *N*-Boc-*L*-tyrosine methyl ester (295 mg, 1.00 mmol, 1.00 equiv) in CH_2Cl_2 (2 mL) at 23 ºC was added triethylamine (418 μL, 3.00 mmol, 3.00 equiv), 4-(dimethylamino)pyridine (12 mg, 0.10 mmol, 0.10 equiv), and *N*-phenylbis(trifluoromethanesulfonimide) (535 mg, 1.50 mmol, 1.50 equiv). The reaction mixture was stirred for 3 hr at 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 3:1 (v/v), to afford 410 mg of the title compound as a colorless solid (96% yield).

R_f = 0.25 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.23–7.20 (m, 4H), 5.08–5.05 (m, 1H), 4.60 (m, 1H), 3.72 (s, 3H), 3.20–3.01 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 171.88, 154.93, 148.57, 136.92, 131.09, 121.29, 118.69 (q, J = 320 Hz), 80.16, 54.18, 52.33, 37.85, 28.19. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –74.90. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 450.0805. Found, 450.0806.

_N_-Boc-4-(tributylstannyl)-_L_-phenylalanine methyl ester[10] (S10)



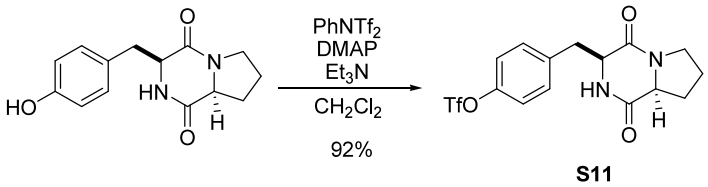
To *N*-Boc-4-(trifluoromethanesulfonyl)-*L*-phenylalanine methyl ester (**S9**) (214 mg, 0.500 mmol, 1.00 equiv) in dioxane (5 mL) at 23 ºC was added lithium chloride (105 mg, 2.50 mmol, 5.00 equiv), tetrakis(triphenylphosphine)palladium (29 mg, 0.025 mmol, 5.0 mol%), and bis(tri-*n*-butyltin) (0.51 mL, 0.10 mmol, 2.0 equiv). After stirring for 5 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 4:1 (v/v), to afford 242 mg of the title compound as a colorless oil (85% yield).

R_f = 0.50 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.38 (d, J = 7.5 Hz, 2H), 7.08 (d, J = 7.5 Hz, 2H), 4.97 (d, J = 8.0 Hz, 1H), 4.60–5.57

[10] D. S. Wilbur, D. K. Hamlin, R. R. Srivastava, H. D. Burns, *Bioconjugate Chem.* **4**, 574 (1993).

(m, 1H), 3.71 (s, 3H), 3.09–3.02 (m, 2H), 1.56–1.50 (m, 6H), 1.41 (s, 9H), 1.36–1.29 (m, 6H), 1.05–0.98 (m, 6H), 0.89 (t, J = 7.3 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 172.42, 155.07, 140.30, 136.62, 135.54, 128.86, 79.83, 54.34, 52.13, 38.31, 29.04, 28.26, 27.33, 13.63, 9.51. These spectroscopic data correspond to previously reported data.[10]

4-(Trifluoromethanesulfonyl)maculosin (S11)

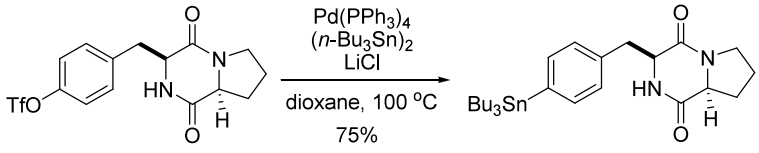


S11

To maculosin (100 mg, 0.384 mmol, 1.00 equiv) in CH_2Cl_2 (1 mL) at 23 ºC was added triethylamine (0.16 mL, 1.2 mmol, 3.0 equiv), 4-(dimethylamino)pyridine (4.7 mg, 0.038 mmol, 0.10 equiv), and *N*-phenylbis(trifluoromethanesulfonimide) (206 mg, 0.576 mmol, 1.50 equiv). The reaction mixture was stirred for 3 hr at 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with EtOAc/MeOH 10:1 (v/v), to afford 138 mg of the title compound as a colorless solid (92% yield).

R_f = 0.50 (EtOAc/MeOH 10:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.38–7.36 (m, 2H), 7.28–7.24 (m, 2H), 6.29 (br s, 1H), 4.32 (dd, J = 8.0 Hz, 3.0 Hz, 1H), 4.07 (t, J = 8.0 Hz, 1H), 3.61–3.56 (m, 1H), 3.55–3.51 (m, 2H), 3.00 (dd, J = 14.5 Hz, 8.0 Hz, 1H), 2.34–2.31 (m, 1H), 2.02–1.99 (m, 1H), 1.94–1.88 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 169.52, 164.45, 148.74, 136.75, 131.28, 121.81, 118.69 (q, J = 320 Hz), 59.06, 56.15, 45.39, 36.15, 28.34, 22.38. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –76.44. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 393.0727. Found, 393.0738.

4-(Tributylstannyl)maculosin (S12)



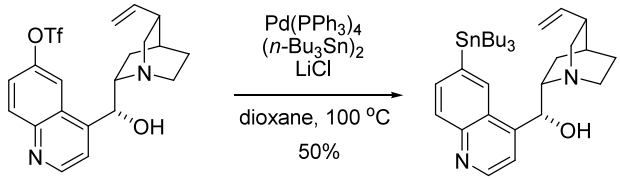
S11 **S12**

To 4-(trifluoromethanesulfonyl)maculosin (**S11**) (100 mg, 0.255 mmol, 1.00 equiv) in dioxane (2 mL) at 23 ºC was added lithium chloride (53.5 mg, 1.28 mmol, 5.00 equiv), tetrakis(triphenylphosphine)palladium (14.7 mg, 0.0127 mmol, 5.00 mol%) and bis(tri-*n*-butyltin) (0.26 mL, 0.51 mmol, 2.0 equiv). After stirring for 24 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with EtOAc/$CHCl_3$ 3:1 (v/v), to afford 102 mg of the title compound as a colorless oil (75% yield).

R_f = 0.30 (EtOAc/$CHCl_3$ 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC,

δ): 7.39–7.38 (m, 2H), 7.17–7.15 (m, 2H), 6.51 (dd, *J* = 10.0 Hz, 3.5 Hz, 1H), 4.23–4.20 (m, 1H), 3.64–3.58 (m, 1H), 3.41–3.36 (m, 1H), 3.11 (dd, *J* = 14.0 Hz, 7.0 Hz, 1H), 3.03 (dd, *J* = 14.0 Hz, 4.0 Hz, 1H), 2.86 (dd, *J* = 10.5 Hz, 6.5 Hz, 1H), 2.15–2.11 (m, 1H), 1.94–1.91 (m, 1H), 1.83–1.75 (m, 1H), 1.66–1.61 (m, 1H), 1.56–1.44 (m, 6H), 1.35–1.25 (m, 6H), 1.10–0.97 (m, 6H), 0.88 (d, *J* = 7.3 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 169.29, 164.84, 140.98, 136.77, 134.75, 129.47, 59.06, 57.69, 45.06, 40.44, 29.01, 28.85, 27.27, 21.68, 13.61, 9.52. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 535.2341. Found, 535.2347.

6-Demethoxy-6-(tributylstannyl)quinine[3] (S13)

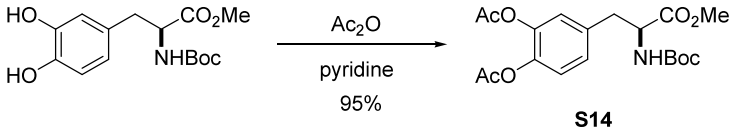


S13

To 6-(trifluoromethanesulfonyl)cupreine[3] (221 mg, 0.500 mmol, 1.00 equiv) in dioxane (5 mL) at 23 ºC was added lithium chloride (106 mg, 2.50 mmol, 5.00 equiv), tetrakis(triphenylphosphine)-palladium (29.0 mg, 0.0250 mmol, 5.00 mol%) and bis(tri-*n*-butyltin) (504 μL, 1.00 mmol, 2.00 equiv). After stirring for 24 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with EtOAc/MeOH 19:1 (v/v), to afford 146 mg of the title compound as colorless oil (50% yield).

R_f = 0.25 (EtOAc/MeOH 9:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.86 (d, *J* = 4.5 Hz, 1H), 8.07 (s, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 4.5 Hz, 1H), 6.26 (s br, 1H), 5.62–5.53 (m, 1H), 5.03 (d, *J* = 17.0 Hz, 1H), 5.01 (d, *J* = 10.0 Hz, 1H), 4.27 (s br, 1H), 3.54–3.45 (m, 2H), 3.20 (dd, *J* = 10.0 Hz, 10.0 Hz, 1H), 3.10 (d, *J* = 13 Hz, 1H), 2.65 (s br, 1H), 2.10–1.97 (m, 3H), 1.80 (s br, 1H), 1.66–1.47 (m, 6H), 1.44–1.12 (m, 13H), 0.87 (t, *J* = 6.0 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 149.87, 148.03, 144.62, 143.43, 137.94, 136.88, 130.22, 129.02, 124.47, 118.43, 117.01, 68.14, 60.84, 55.61, 44.72, 37.69, 29.09, 27.28, 26.83, 25.01, 19.67, 13.65, 9.86. These spectroscopic data correspond to previously reported data.[3]

***N*-Boc-*O*-acetyl-DOPA methyl ester (S14)**



S14

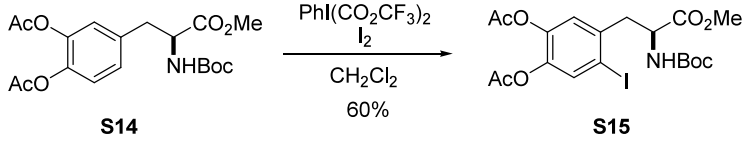
To *N*-Boc-DOPA methyl ester [11] (311 mg, 1.00 mmol, 1.00 equiv) in pyridine (5 mL) at 0 ºC

[11] S. Tang, L. J. Martinez, A. Sharma, M. Chai, *Org. Lett.* **8**, 4421 (2006).

was added acetic anhydride (0.38 mL, 4.0 mmol, 4.0 equiv). The reaction mixture was stirred for 1 hr at 0 ºC and stirred for 6 hr at 23 ºC. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with sat. $NaHCO_3$ (aq) (2 × 20 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 3:1 (v/v), to afford 375 mg of the title compound as a colorless oil (95% yield).

R_f = 0.19 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.09 (d, *J* = 8.5 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.95 (br s, 1H), 5.05 (d, *J* = 7.5 Hz, 1H), 4.57–4.53 (m, 1H), 3.68 (s, 3H), 3.07–3.03 (m, 2H), 2.25 (s, 6H), 1.40 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 171.91, 168.09, 167.96, 154.95, 141.82, 140.94, 134.86, 127.25, 124.16, 123.24, 79.93, 54.12, 52.24, 37.53, 28.15, 20.51, 20.51. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 418.1472. Found, 418.1475.

_N_-Boc-_O_-acetyl-6-iodo-DOPA methyl ester (S15)

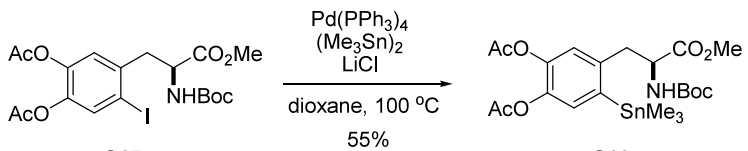


S14 **S15**

To *N*-Boc-*O*-acetyl-DOPA methyl ester (**S14**) (198 mg, 0.500 mmol, 1.00 equiv) in CH_2Cl_2 (5 mL) at 0 ºC was added [bis(trifluoroacetoxy)iodo]benzene (258 mg, 0.600 mmol, 1.20 equiv) and iodine (152 mg, 0.600 mmol, 1.20 equiv). The reaction mixture was stirred for 1 hr at 0 ºC and stirred for 6 hr at 23 ºC. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with sat. $Na_2S_2O_3$ (aq) (2 × 20 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel eluting with hexanes/EtOAc 3:1 (v/v) to afford 156 mg of the title compound as a colorless solid (60% yield).

R_f = 0.20 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.65 (br s, 1H), 7.04 (br s, 1H), 5.08 (d, *J* = 8.5 Hz, 1H), 4.62–4.61 (m, 1H), 3.71 (s, 3H), 3.23–3.09 (m, 2H), 2.26 (s, 6H), 1.39 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 172.06, 167.75, 167.69, 154.91, 142.17, 141.13, 138.22, 133.84, 124.52, 95.79, 80.07, 53.34, 52.51, 42.59, 28.21, 20.54, 20.50. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 544.0439. Found, 544.0434.

_N_-Boc-_O_-acetyl-6- trimethylstannyl -DOPA methyl ester (S16)



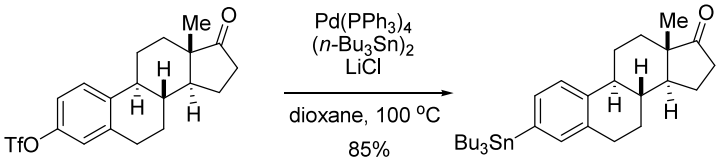
S15 **S16**

To *N*-Boc-*O*-acetyl-6-iodo-DOPA methyl ester (**S15**) (104 mg, 0.200 mmol, 1.00 equiv) in

dioxane (2 mL) at 23 ºC was added lithium chloride (42 mg, 1.0 mmol, 5.0 equiv), tetrakis(triphenylphosphine)palladium (69 mg, 0.060 mmol, 30 mol%) and bis(trimethyltin) (132 mg, 0.400 mmol, 2.00 equiv). After stirring for 5 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 5:1 (v/v), to afford 62 mg of the title compound as a colorless oil (55% yield).

R_f = 0.30 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.18 (br s, 1H), 7.01 (br s, 1H), 4.90 (d, J = 7.5 Hz, 1H), 4.53–4.51 (m, 1H), 3.69 (s, 3H), 3.10–2.98 (m, 2H), 2.28 (s, 3H), 2.26 (s, 3H), 1.39 (s, 9H), 0.35 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 172.54, 168.35, 168.12, 155.02, 142.17, 141.86, 141.61, 140.46, 130.61, 123.46, 80.09, 54.23, 52.35, 40.43, 28.18, 20.64, 20.62, –7.88. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 582.1120. Found, 582.1119.

3-Deoxy-3-(tributylstannyl)estrone[3] (S17)

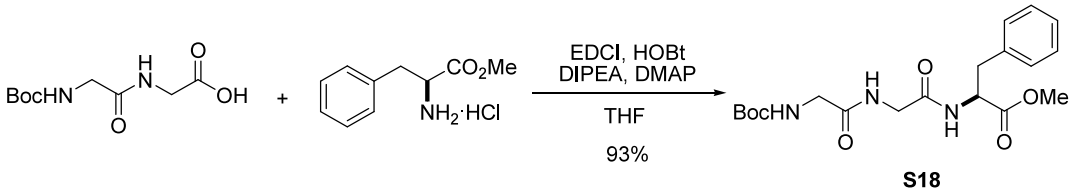


S17

To 3-(trifluoromethanesulfonyl)estrone[3] (402 mg, 1.00 mmol, 1.00 equiv) in dioxane (10 mL) at 23 ºC was added lithium chloride (210 mg, 5.00 mmol, 5.00 equiv), tetrakis(triphenylphosphine)palladium (57.8 mg, 0.0500 mmol, 5.00 mol%) and bis(tri-*n*-butyltin) (1.0 mL, 2.0 mmol, 2.0 equiv). After stirring for 14 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 19:1 (v/v), to afford 463 mg of the title compound as a colorless oil (85% yield).

R_f = 0.48 (hexanes/EtOAc 19:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.30–7.12 (m, 3H), 2.93–2.90 (m, 2H), 2.50 (dd, J = 19.0 Hz, 8.5 Hz, 1H), 2.44–2.41 (m, 1H), 2.36–2.30 (m, 1H), 2.17–1.95 (m, 4H), 1.68–1.42 (m, 12H), 1.38–1.28 (m, 6H), 1.06–0.96 (m, 6H), 0.95–0.87 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 220.90, 139.49, 138.74, 137.33, 135.90, 133.97, 124.84, 50.57, 47.99, 44.49, 38.08, 35.85, 31.63, 29.37, 29.09, 27.40, 26.57, 25.51, 21.57, 13.84, 13.67, 9.50. These spectroscopic data correspond to previously reported data.[3]

_N_-Boc-glycylglycyl-_L_-phenylalanine methyl ester[12] (S18)

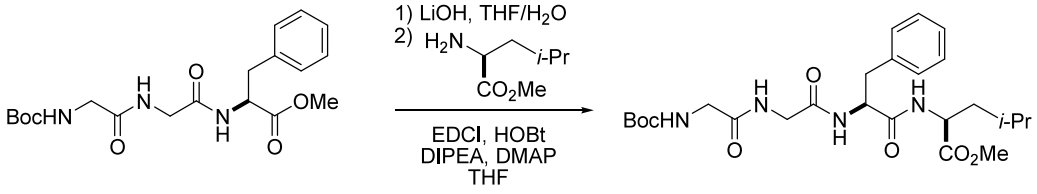


S18

To *N*-Boc-glycylglycine (696 mg, 3.00 mmol, 1.00 equiv) in THF (10 mL) at 0 ºC was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (1.15 g, 6.00 mmol, 2.00 equiv), 1-hydroxybenzotriazole (HOBt) (810 mg, 6.00 mmol, 2.00 equiv), *N*,*N*-diisopropylethylamine (1.56 mL, 9.00 mmol, 3.00 equiv) and 4-(dimethylamino)pyridine (36 mg, 0.030 mmol, 0.10 equiv) and *L*-phenylalanine methyl ester (647 mg, 3.00 mmol, 1. 00 equiv). The reaction mixture was stirred for 1 hr at 0 ºC and stirred for 12 hr at 23 ºC. The reaction mixture was diluted with EtOAc (40 mL) and washed with water (2 × 20 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with CH_2Cl_2/MeOH 10:1 (v/v), to afford 1.10 g of the title compound as a colorless oil (93% yield).

R_f = 0.50 (CH_2Cl_2/MeOH 10:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.29–7.21 (m, 2H), 7.13–7.11 (m, 2H), 7.02 (d, *J* = 8.0 Hz, 1H), 5.46 (br s, 1H), 4.82 (dd, *J* = 14.0 Hz, 6.5 Hz, 1H), 3.94 (dd, *J* = 16.5 Hz, 5.5 Hz, 1H), 3.88 (dd, *J* = 16.5 Hz, 6.0 Hz, 1H), 3.80 (d, *J* = 5.0 Hz, 2H), 3.69 (s, 3H), 3.13 (dd, *J* = 14.0 Hz, 6.0 Hz, 1H), 3.04 (dd, *J* = 14.0 Hz, 7.0 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 171.79, 170.07, 168.53, 156.07, 135.78, 129.15, 128.49, 127.05, 80.16, 53.36, 52.30, 44.01, 42.75, 37.71, 28.24.

_N_-Boc-glycylglycyl-_L_-phenylalanyl-_L_-leucine methyl ester (S19)



S18 **S19**

To *N*-Boc-glycylglycyl-*L*-phenylalanine methyl ester (**S18**) (786 mg, 2.00 mmol, 1.00 equiv) in THF (4 mL) and water (2 mL) at 0 ºC was added LiOH (96 mg, 4.0 mmol, 2.0 equiv). The reaction mixture was stirred for 2 hr at 0 ºC. The reaction mixture was diluted with EtOAc (15 mL) and acidified to pH 2–3 with 1 N HCl. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo.

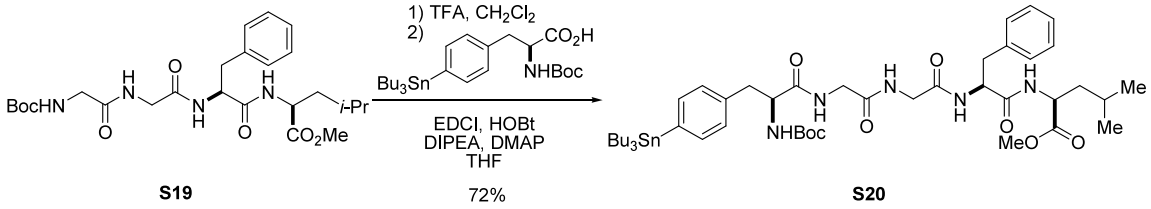
To the residue was added THF (10 mL) at 0 ºC and subsequently

[12] W. Cui, C. Wang, M. Zhao, S. Peng, *Prep. Biochem. Biotech.* **33**, 217 (2003).

1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (764 g, 4.00 mmol, 2.00 equiv), 1-hydroxybenzotriazole (HOBt) (540 mg, 4.00 mmol, 2.00 equiv), *N,N*-diisopropylethylamine (1.00 mL, 6.00 mmol, 3.00 equiv), and 4-(dimethylamino)pyridine (24 mg, 0.020 mmol, 0.10 equiv) and *L*-leucine methyl ester (544 mg, 3.00 mmol, 1.50 equiv). The reaction mixture was stirred for 1 hr at 0 ºC and further stirred for 12 hr at 23 ºC. The reaction mixture was diluted with EtOAc (40 mL) and washed with water (2 × 20 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with CH_2Cl_2/MeOH 10:1 (v/v), to afford 880 mg of the title compound as a colorless solid (88% yield).

R_f = 0.50 (CH_2Cl_2/MeOH 10:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.40 (br s, 1H), 7.27–7.12 (m, 7H), 5.57 (br s, 1H), 4.95–4.93 (m, 1H), 4.59–4.54 (m, 1H), 3.96–3.85 (m, 4H), 3.70 (s, 3H), 3.11 (dd, *J* = 13.5 Hz, 5.5 Hz, 1H), 2.98 (dd, *J* = 13.5 Hz, 7.0 Hz, 1H), 1.63–1.51 (m, 3H), 1.45 (s, 9H), 0.89 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 172.95, 170.78, 169.74, 168.41, 156.13, 136.36, 129.37, 128.42, 126.87, 80.05, 54.15, 52.21, 50.83, 43.89, 42.99, 41.05, 38.71, 28.34, 24.77, 22.69, 21.86. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 529.2633. Found, 529.2630.

_N_-Boc-4-(tributylstannyl)-_L_-phenylalanyl-glycylglycyl-_L_-phenylalanyl-_L_-leucine methyl ester (S20)



S19 72% **S20**

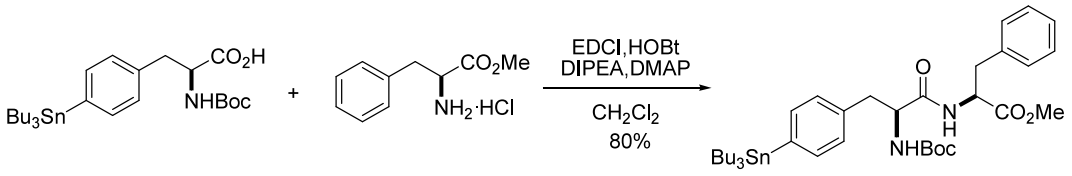
To *N*-Boc-glycylglycyl-*L*-phenylalanyl-*L*-leucine methyl ester (**S19**) (101 mg, 0.200 mmol, 1.00 equiv) in CH_2Cl_2 (2 mL) at 0 ºC was added trifluoroacetic acid (0.20 mL). The reaction mixture was stirred for 2 hr at 0 ºC. The reaction mixture was concentrated in vacuo.

To the residue was added THF (10 mL) at 0 ºC and subsequently 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (76.7 mg, 0.400 mmol, 2.00 equiv), 1-hydroxybenzotriazole (HOBt) (54 mg, 0.40 mmol, 2.0 equiv), *N,N*-diisopropylethylamine (0.20 mL, 0.60 mmol, 3.0 equiv) and 4-(dimethylamino)pyridine (2.4 mg, 0.020 mmol, 0.10 equiv) and *N*-Boc-4-(tributylstannyl)-*L*-phenylalanine[13] (111 mg, 0.200 mmol, 1.00 equiv). The reaction mixture was stirred for 1 hr at 0 ºC and stirred for 12 hr at 23 ºC. The reaction mixture was diluted with EtOAc (40 mL) and washed with water (2 × 20 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue is purified by chromatography on silica gel, eluting with CH_2Cl_2/MeOH 10:1 (v/v), to afford 135 mg of the title compound as a colorless solid (72% yield).

R_f = 0.50 (CH_2Cl_2/MeOH 10:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.52 (br s, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.24–7.13 (m, 8H), 7.01 (br s, 1H), 5.29 (br s,

1H), 4.91–4.89 (m, 1H), 4.58–4.54 (m, 1H), 4.37–4.35 (m, 1H), 3.98–3.85 (m, 4H), 3.69 (s, 3H), 3.18–3.03 (m, 3H), 2.95–2.90 (m, 1H), 1.62–1.48 (m, 9H), 1.40 (s, 9H), 1.39–1.28 (m, 6H), 1.05–1.01 (m, 6H), 0.89–0.86 (m, 15H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 173.03, 172.37, 170.76, 168.89, 168.24, 155.68, 139.90, 136.52, 136.42, 129.56, 128.96, 128.21, 126.62, 79.73, 55.38, 53.98, 52.15, 50.81, 43.06, 41.11, 39.23, 38.74, 29.01, 28.27, 27.32, 24.74, 22.74, 22.05, 13.61, 9.47. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 966.4373. Found, 966.4386.

_N_-Boc-4-(tributylstannyl)-_L_-phenylalanyl-_L_-phenylalanine methyl ester (S21)



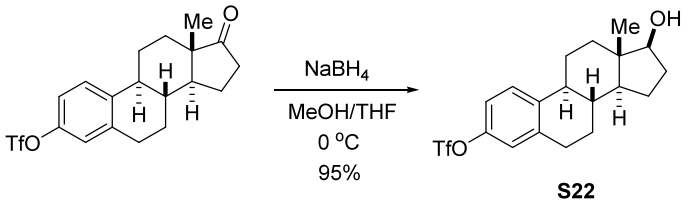
S21

To *N*-Boc-4-(tributylstannyl)-*L*-phenylalanin [13] (1.67 g, 3.00 mmol, 1.00 equiv) and *L*-phenylalanine methyl ester hydrochloride (647 mg, 3.00 mmol, 1.00 equiv) in CH_2Cl_2 (30 mL) at 0 ºC was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (1.15 g, 6.00 mmol, 2.00 equiv), 1-hydroxybenzotriazole (HOBt) (810 mg, 6.00 mmol, 2.00 equiv), *N,N*-diisopropylethylamine (1.56 mL, 9.00 mmol, 3.00 equiv) and 4-(dimethylamino)pyridine (36 mg, 0.30 mmol, 0.10 equiv). After stirring for 1 hr at 0 ºC, the reaction mixture was warmed to 23 ºC and further stirred for 12 hr. The reaction mixture was quenched with water (20 mL), and CH_2Cl_2 (10 mL) was added. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were washed with brine (10 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 3:1 (v/v), to afford 1.72 g of the title compound as a colorless foam (80% yield).

R_f = 0.30 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.39 (d, *J* = 8.0 Hz, 2H), 7.23–7.21 (m, 3H), 7.15 (d, *J* = 7.5 Hz, 2H), 6.97 (dd, *J* = 7.5 Hz, 2.0 Hz, 2H), 6.38 (d, *J* = 7.5 Hz, 1H), 4.90 (br s, 1H), 4.80 (br s, 1H), 4.35 (br s, 1H), 3.68 (s, 3H), 3.09–2.99 (m, 4H), 1.55–1.50 (m, 6H), 1.38 (s, 9H), 1.36–1.29 (m, 6H), 1.05–1.01 (m, 6H), 0.87 (t, *J* = 7.3 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 171.38, 170.83, 155.27, 140.29, 136.74, 136.06, 135.64, 129.19, 128.99, 128.49, 127.06, 80.12, 55.47, 53.21, 52.20, 38.04, 37.92, 29.03, 28.18, 27.33, 13.61, 9.50. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 739.3103. Found, 739.3069.

[13] D. S. Wilbur, D. K. Hamlin, R. R. Srivastava, H. D. Burns, *Bioconjugate Chem.* **4**, 574 (1993).

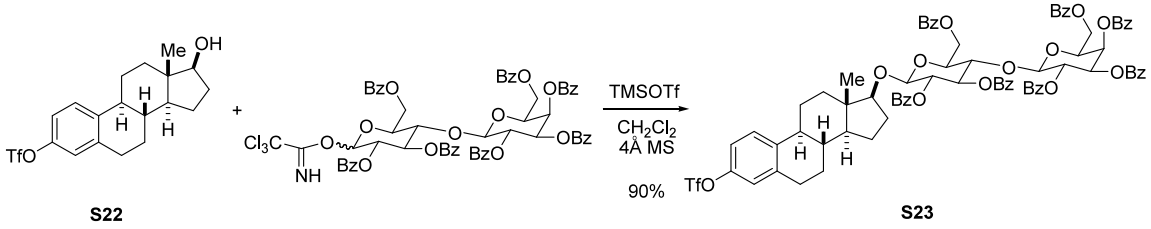
3-(Trifluoromethanesulfonyl)-β-estradiol[14] (S22)



To 3-(trifluoromethanesulfonyl)estrone[3] (402 mg, 1.00 mmol, 1.00 equiv) in MeOH/THF (1.0 mL/1.0 mL) at 0 ºC was added sodium borohydride (76 mg, 2.0 mmol, 2.0 equiv) and the reaction mixture was stirred for 0.5 hr at 0 ºC. The reaction mixture was quenched with sat. NH_4Cl (aq) (10 mL) and EtOAc (10 mL) was added. The phases were separated and the aqueous phase was extracted with EtOAc (2 × 10 mL). The combined organic phases were washed with brine (10 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 3:1 (v/v), to afford 384 mg of the title compound as a colorless solid (95% yield).

R_f = 0.25 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.33 (d, *J* = 8.5 Hz, 1H), 7.02 (dd, *J* = 8.5 Hz, 2.5 Hz, 1H), 6.96 (d, *J* = 3.0 Hz, 1H), 3.74 (t, *J* = 8.5 Hz, 1H), 2.89 (dd, *J* = 9.0 Hz, 4.0 Hz, 2H), 2.35–2.30 (m, 1H), 2.25–2.20 (m, 1H), 2.15–2.11 (m, 1H), 1.99–1.89 (m, 2H), 1.74–1.69 (m, 1H), 1.54–1.17 (m, 8H), 0.79 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 147.43, 140.85, 139.49, 127.12, 121.09, 118.72 (q, *J* = 319 Hz), 118.07, 81.71, 50.00, 44.05, 43.13, 38.19, 36.55, 30.51, 29.47, 26.74, 26.05, 23.06. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –73.39. These spectroscopic data correspond to previously reported data.[14]

3-(Trifluoromethanesulfonyl)-β-estradiol-β-heptabenzoyllactose (S23)



A mixture of 3-(trifluoromethanesulfonyl)-β-estradiol (**S22**) (202 mg, 0.500 mmol, 1.00 equiv), 1-*O*-[2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-D-glucopyranosyl] trichloroacetimidate[15] (909 mg, 0.750 mmol, 1.50 equiv), and powdered 4 Å molecular sieves in CH_2Cl_2 (5 mL) was stirred for 1 hr at 23 ºC. To the reaction mixture was added TMSOTf (4.5 μL, 0.025 mmol, 0.050 equiv) and stirring was continued for 1.0 hr before the

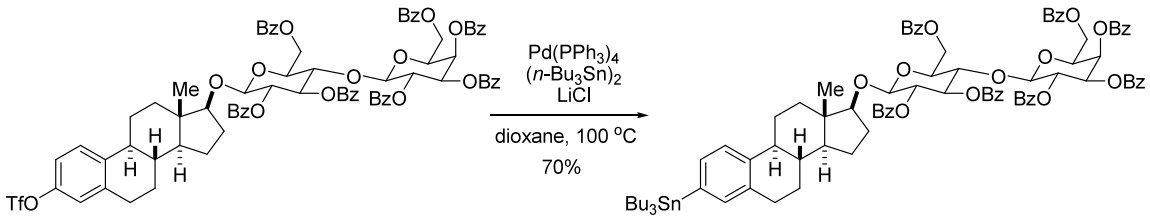
[14] E. D. Hostetler, S. D. Jonson, M. J. Welch, J. A. Katzenellenbogen, *J. Org. Chem.* **64**, 178 (1999).

[15] G. Biswas, *et al*, *Chem. Eur. J.* **14**, 9161 (2008).

addition of Et_3N (0.1 mL). The reaction mixture was filtered. The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 3:1 (v/v), to afford 655 mg of the title compound as a colorless foam (90% yield).

R_f = 0.32 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.02–7.96 (m, 10H), 7.91 (dd, *J* = 8.5 Hz, 1.0 Hz, 2H), 7.73 (dd, *J* = 8.5 Hz, 1.0 Hz, 2H), 7.63–7.30 (m, 18H), 7.22 (dd, *J* = 8.5 Hz, 7.5 Hz, 2H), 7.17 (dd, *J* = 8.5 Hz, 7.5 Hz, 2H), 6.97 (dd, *J* = 8.5 Hz, 2.5 Hz, 1H), 6.92–6.91 (m, 1H), 5.81 (dd, *J* = 9.5 Hz, 9.5 Hz, 1H), 5.74–5.71 (m, 2H), 5.47 (dd, *J* = 9.5 Hz, 8.0 Hz, 1H), 5.38 (dd, *J* = 10.5 Hz, 3.5 Hz, 1H), 4.89 (d, *J* = 8.0 Hz, 1H), 4.75 (d, *J* = 8.5 Hz, 1H), 4.63–4.60 (m, 1H), 4.49 (dd, *J* = 12.0 Hz, 5.0 Hz, 1H), 4.23 (dd, *J* = 9.5 Hz, 9.5 Hz, 1H), 3.91 (dd, *J* = 7.0 Hz, 6.5 Hz, 1H), 3.84–3.82 (m, 1H), 3.75 (dd, *J* = 11.0 Hz, 6.5 Hz, 1H), 3.69 (dd, *J* = 11.0 Hz, 6.5 Hz, 1H), 3.58 (dd, *J* = 9.0 Hz, 8.0 Hz, 1H), 2.83–2.81 (m, 2H), 2.11–2.01 (m, 2H), 1.98–1.88 (m, 1H), 1.82–1.78 (m, 1H), 1.68–1.51 (m, 3H), 1.31–1.21 (m, 4H), 1.18–1.10 (m, 2H), 0.58 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 165.81, 165.57, 165.41, 165.39, 165.20, 165.11, 164.78, 147.40, 140.65, 139.40, 133.52, 133.38, 133.34, 133.30, 133.24, 133.15, 133.12, 129.99, 129.74, 129.71, 129.67, 129.63, 129.59, 129.49, 129.41, 128.86, 128.71, 128.62, 128.56, 128.49, 128.31, 128.23, 127.09, 121.06, 118.71 (q, *J* = 319 Hz), 118.03, 101.83, 100.99, 89.95, 76.32, 73.00, 72.94, 71.94, 71.74, 71.40, 69.93, 67.53, 62.55, 61.12, 49.61, 43.91, 43.07, 37.78, 37.05, 29.42, 28.67, 26.62, 25.77, 22.96, 11.32. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –73.38. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + NH_4]^+$, 1474.4498. Found, 1474.4486.

3-Deoxy-3-tributylstannyl-β-estradiol-β-heptabenzoyllactose (S24)



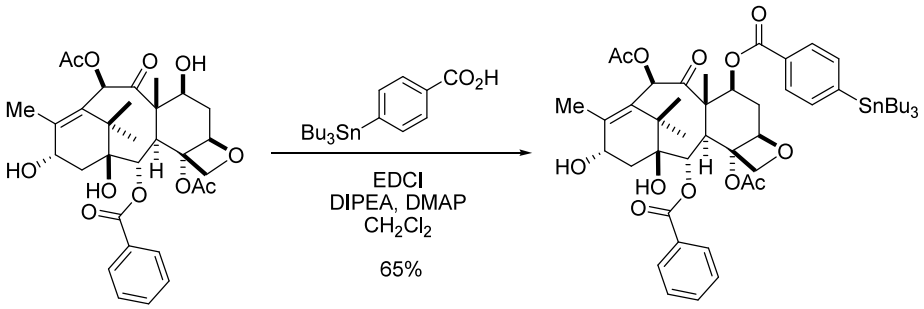
S23 **S24**

To 3-(trifluoromethanesulfonyl)-β-estradiol-β-heptabenzoyllactose (**S23**) (200 mg, 0.137 mmol, 1.00 equiv) in dioxane (2 mL) at 23 ºC was added lithium chloride (28.7 mg, 0.683 mmol, 5.00 equiv), tetrakis(triphenylphosphine)palladium (7.9 mg, 0.069 mmol, 5.0 mol%) and bis(tri-*n*-butyltin) (0.14 mL, 0.27 mmol, 2.0 equiv). After stirring for 21 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 4:1 (v/v), to afford 154 mg of the title compound as a colorless oil (70% yield).

R_f = 0.29 (hexane/EtOAc 4:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.04–7.97 (m, 10H), 7.93 (dd, *J* = 8.0 Hz, 1.0 Hz, 2H), 7.74 (dd, *J* = 8.0 Hz, 1.0 Hz, 2H), 7.66–7.31 (m, 18H), 7.22 (dd, *J* = 8.5 Hz, 8.5 Hz, 2H), 7.18–7.14 (m, 4H), 5.82 (dd, *J* =

10.0 Hz, 9.0 Hz, 1H), 5.77–5.73 (m, 2H), 5.49 (dd, *J* = 10.0 Hz, 8.0 Hz, 1H), 5.40 (dd, *J* = 10.0 Hz, 3.0 Hz, 1H), 4.90 (d, *J* = 8.0 Hz, 1H), 4.78 (d, *J* = 8.0 Hz, 1H), 4.64–4.61 (m, 1H), 4.51 (dd, *J* = 12.0 Hz, 5.0 Hz, 1H), 4.24 (dd, *J* = 9.5 Hz, 9.5 Hz, 1H), 3.93 (dd, *J* = 7.0 Hz, 6.5 Hz, 1H), 3.86–3.84 (m, 1H), 3.78 (dd, *J* = 11.5 Hz, 6.5 Hz, 1H), 3.71 (dd, *J* = 11.5 Hz, 6.5 Hz, 1H), 3.60 (dd, *J* = 9.0 Hz, 8.0 Hz, 1H), 2.83–2.80 (m, 2H), 2.13–2.01 (m, 2H), 1.98–1.92 (m, 1H), 1.83–1.84 (m, 1H), 1.75–1.49 (m, 9H), 1.37–1.24 (m, 10H), 1.18–0.97 (m, 8H), 0.91 (t, *J* = 7.3 Hz, 9H), 0.57 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ)[16]: 165.81, 165.55, 165.42, 165.37, 165.19, 165.11, 164.77, 139.88, 138.31, 137.25, 136.04, 133.71, 133.50, 133.36, 133.28, 133.21, 133.11, 133.08, 129.98, 129.71, 129.65, 129.61, 129.58, 129.48, 129.39, 128.83, 128.68, 128.61, 128.54, 128.47, 128.27, 128.21, 124.79, 101.78, 100.95, 90.04, 76.33, 72.97, 71.92, 71.74, 71.39, 69.91, 67.54, 62.59, 61.14, 49.78, 44.29, 43.16, 38.11, 37.29, 29.41, 29.05, 28.65, 27.37, 27.0, 25.62, 22.94, 13.63, 11.32, 9.45. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 1621.5667. Found, 1621.5740.

Taxol derivative (S25)



S25

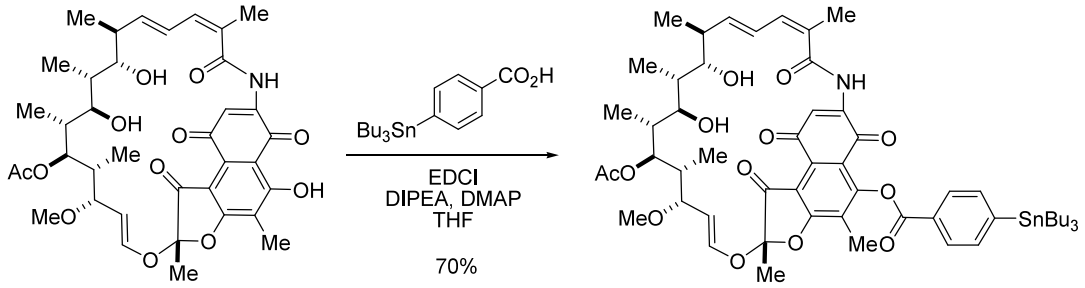
To baccatin III (58.6 mg, 0.100 mmol, 1.00 equiv) in CH_2Cl_2 (1 mL) at 0 ºC was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (95.5 mg, 0.500 mmol, 5.00 equiv), *N,N*-diisopropylethylamine (0.10 mL, 0.60 mmol, 6.0 equiv) and 4-(dimethylamino)pyridine (1.2 mg, 0.010 mmol, 0.10 equiv) and 4-(tributylstannyl)benzoic acid (**S30**) (61.8 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred for 1 hr at 0 ºC and further stirred for 12 hr at 23 ºC. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed with water (2 × 1.0 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 1:1 (v/v), to afford 63.7 mg of the title compound as a colorless solid (65% yield).

R_f = 0.30 (hexane/EtOAc 1:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.13 (d, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.62 (dd, *J* = 7.5 Hz, 7.0 Hz, 1H), 7.53–7.48 (m, 4H), 6.45 (s, 1H), 5.78 (dd, *J* = 10.0 Hz, 7.5 Hz, 1H), 5.69 (d, *J* = 7.5 Hz, 1H), 5.01 (d, *J* = 8.5 Hz, 1H), 4.87 (t, *J* = 7.5 Hz, 1H), 4.35 (d, *J* = 8.5 Hz, 1H), 4.20 (d, *J* = 8.5 Hz, 1H), 4.10 (d, *J* = 7.0 Hz, 1H), 2.82–2.75 (m, 1H), 2.32–2.30 (m, 2H), 2.31 (s, 3H), 2.17 (s, 4H), 1.97 (s, 3H), 1.94 (s, 3H), 1.94–1.88 (m, 1H), 1.61–1.50 (m, 6H), 1.36–1.29 (m, 6H),

[16] Only 60 peaks were observed due to the overlap of peaks.

1.16 (s, 3H), 1.09–1.01 (m, 9H), 0.88 (t, J = 7.5 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 202.86, 170.62, 168.36, 167.05, 165.69, 149.33, 144.70, 136.19, 133.69, 131.94, 130.11, 129.62, 129.31, 128.64, 128.55, 84.06, 80.65, 78.72, 76.39, 75.47, 74.49, 72.16, 67.94, 56.48, 47.18, 42.78, 38.48, 33.43, 29.02, 27.32, 26.62, 22.57, 20.51, 20.14, 15.17, 13.64, 10.93, 9.63. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$,1033.3625. Found,1033.3622.

Rifamycin S derivative (S26)

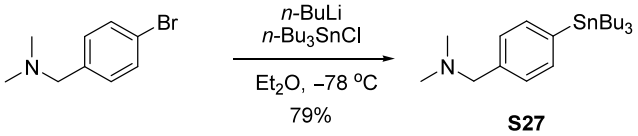


S26

To rifamycin S (139 mg, 0.200 mmol, 1.00 equiv) in THF (1 mL) at 0 ºC was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (76.4 mg, 0.400 mmol, 2.00 equiv), *N,N*-diisopropylethylamine (0.10 mL, 0.60 mmol, 3.0 equiv) and 4-(dimethylamino)pyridine (2.4 mg, 0.020 mmol, 0.10 equiv) and 4-(tributylstannyl)benzoic acid (**S30**) (124 mg, 0.300 mmol, 1.50 equiv). The reaction mixture was stirred for 1 hr at 0 ºC and further stirred for 12 hr at 23 ºC. The reaction mixture was diluted with EtOAc (5 mL) and washed with water (2 × 1.0 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 2:1 (v/v), to afford 153 mg of the title compound as a colorless solid (70% yield).

R_f = 0.30 (hexane/EtOAc 2:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.26 (s, 1H), 8.18–8.16 (m, 2H), 7.80 (s, 1H), 7.67 (d, J = 8.0 Hz, 2H), 6.28–6.15 (m, 3H), 5.89 (dd, J = 15.5 Hz, 7.0 Hz, 1H), 5.14 (dd, J = 12.5 Hz, 7.0 Hz, 1H), 4.70 (d, J = 10.5 Hz, 1H), 3.71 (d, J = 5.0 Hz, 1H), 3.61 (d, J = 10.0 Hz, 1H), 3.40–3.37 (m, 2H), 3.12 (s, 3H), 3.05–3.02 (m, 1H), 2.34 (s, 3H), 2.32–2.29 (m, 1H), 2.04 (s, 3H), 1.95 (s, 3H), 1.81–1.80 (m, 1H), 1.77 (s, 3H), 1.69–1.67 (m, 1H), 1.61–1.53 (m, 6H), 1.39–1.32 (m, 6H), 1.09–1.01 (m, 9H), 0.91 (t, J = 7.5 Hz, 9H), 0.84 (d, J = 7.0 Hz, 3H), 0.68 (d, J = 7.0 Hz, 3H), 0.18 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 192.47, 182.12, 177.67, 173.29, 172.95, 169.43, 164.59, 156.01, 151.97, 144.31, 141.81, 139.93, 136.79, 136.68, 133.54, 132.24, 130.66, 129.35, 127.65, 124.06, 118.61, 116.36, 115.86, 114.63, 108.65, 81.12, 73.50, 73.21, 56.98, 38.82, 37.39, 37.34, 32.81, 29.01, 27.33, 21.91, 21.04, 19.94, 16.97, 13.65, 11.44, 11.11, 9.72, 8.84, 8.36. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$,1090.4333. Found,1090.4289.

Tributyl[{(4-dimethylamino)methyl}phenyl]stannane[3] (S27)

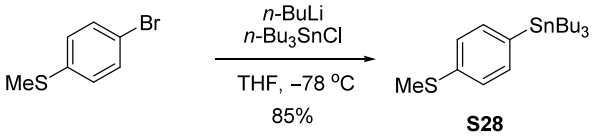


S27

To (4-bromobenzyl)dimethylamine (2.14 g, 10.0 mmol, 1.00 equiv) in Et_2O (25 mL) at 23 ºC was added *n*-BuLi (2.4 M in hexane, 4.17 mL, 10 mmol, 1.0 equiv). The reaction mixture was warmed to 23 ºC and stirred for 2.0 hr before the addition of *n*-Bu_3SnCl (3.25 g, 10.0 mmol, 1.00 equiv) at –78 ºC. After stirring for 1.0 hr at 23 ºC, the reaction mixture was concentrated in vacuo. The residue was purified by chromatography on silica gel eluting with hexanes/EtOAc 1:1 (v/v) to afford 3.35 g of the title compound as a colorless oil (79% yield).

R_f = 0.20 (hexanes/EtOAc 1:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.42 (d, *J* = 6.5 Hz, 2H), 7.27 (d, *J* = 6.5 Hz, 2H), 3.41 (s, 2H), 2.26 (s, 6H), 1.64–1.48 (m, 6H), 1.40–1.30 (m, 6H), 1.15–0.99 (m, 6H), 0.90 (t, *J* = 6.0 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 23 ºC, δ): 140.30, 138.40, 136.36, 128.72, 64.40, 45.36, 29.07, 27.35, 13.64, 9.52. These spectroscopic data correspond to previously reported data.[3]

4-(Tributylstannyl)thioanisole[17] (S28)



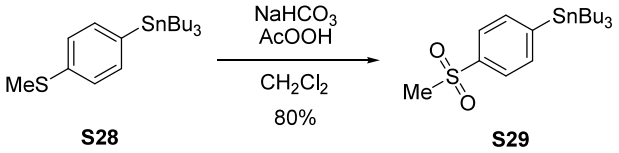
S28

To 4-bromothioanisole (1.02 g, 5.00 mmol, 1.00 equiv) in THF (5.0 mL) at –78 ºC was added *n*-BuLi (2.5 M in hexane, 2.0 mL, 5.0 mmol, 1.0 equiv). The reaction mixture was stirred at –78 ºC for 30 min before the addition of *n*-Bu_3SnCl (1.63 g, 5.00 mmol, 1.00 equiv). After stirring for 2 hr at –78 ºC, the reaction mixture was warmed to 23 ºC and the solvent was removed in vacuo. The residue was purified by fractional distillation to afford 1.76 g of the title compound as a colorless oil (85% yield).

R_f = 0.60 (hexanes). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.42–7.32 (m, 2H), 7.24–7.22 (m, 2H), 2.48 (s, 3H), 1.64–1.54 (m, 6H), 1.40–1.34 (m, 6H), 1.20–1.08 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 23 ºC, δ): 138.17, 137.88, 136.76, 126.07, 29.05, 27.35, 15.56, 13.66, 9.55. These spectroscopic data correspond to previously reported data.[17]

[17] J.L. Wardell, S. Ahmed, *J. Organomet. Chem.* **78**, 395 (1974).

(4-Methylsulfonylphenyl)tributylstannane (S29)

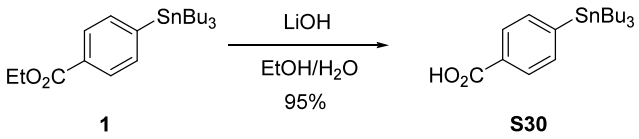


S28 **S29**

To 4-(tributylstannyl)thioanisole (**S28**) (207 mg, 0.500 mmol, 1.00 equiv) in CH_2Cl_2 (5.0 mL) at 0 ºC was added sodium bicarbonate (168 mg, 2.00 mmol, 4.00 equiv) and peracetic acid (0.21 mL, 32 wt. % in dilute acetic acid, 1.0 mmol, 2.0 equiv). The reaction mixture was warmed to 23 ºC and stirred for 50 min before being filtered through a plug of basic alumina. The filtrate was concentrated in vacuo and purified by preparative TLC eluting with hexanes/EtOAc 5:1 (v/v) to afford 178 mg of the title compound as a colorless oil (80% yield).

R_f = 0.30 (hexanes/EtOAc 6:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.85–7.84 (m, 2H), 7.70–7.62 (m, 2H), 3.05 (s, 3H), 1.60–1.44 (m, 6H), 1.36–1.28 (m, 6H), 1.16–1.04 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 23 ºC, δ): 151.32, 139.94, 137.12, 125.85, 44.47, 28.95, 27.28, 13.61, 9.74. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + NH_4]^+$, 464.1639. Found, 464.1655.

4-(Tributylstannyl)benzoic acid[18] (S30)



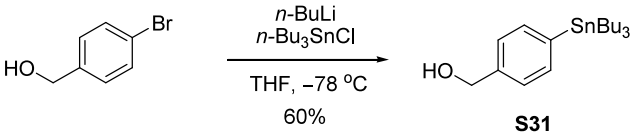
1 **S30**

To ethyl 4-(tributylstannyl)benzoate (**1**) (88 mg, 0.20 mmol, 1.0 equiv) in EtOH/H_2O (0.95 mL/0.050 mL) at 23 ºC was added LiOH (4.8 mg, 0.40 mmol, 2.0 equiv). The reaction mixture was stirred for 4 hr at 23 ºC. The reaction mixture was diluted with EtOAc (15 mL) and acidified to pH 2–3 with 1 N HCl. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and purified by preparative TLC eluting with hexanes/EtOAc 1:1 (v/v) to afford 78 mg of the title compound as a colorless oil (95% yield).

R_f = 0.30 (hexanes/EtOAc 2:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 10.78 (br s, 1H), 8.04 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.5 Hz, 2H), 1.60–1.52 (m, 6H), 1.38–1.32 (m, 6H), 1.15–1.08 (m, 6H), 0.89 (t, *J* = 7.5 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 23 ºC, δ): 172.82, 151.14, 136.51, 128.88, 128.73, 29.02, 27.32, 13.64, 9.67. These spectroscopic data correspond to previously reported data.[18]

[18] C. Ramesh, *et al*, *J. Med. Chem.* **53**, 1004 (2010).

4-(Tributylstannyl)benzyl alcohol[19] (S31)

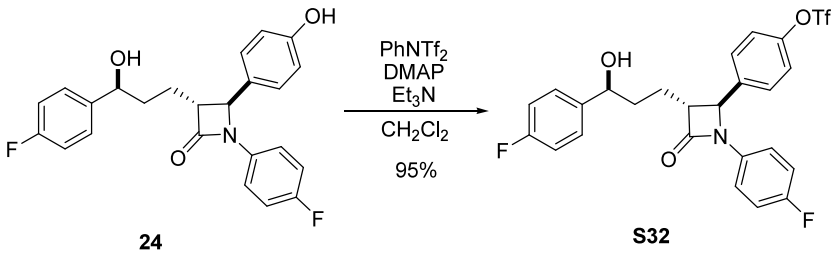


S31

To 4-bromobenzyl alcohol (558 mg, 3.00 mmol, 1.00 equiv) in THF (5.0 mL) at –78 ºC was added *n*-BuLi (2.5 M in hexane, 2.4 mL, 6.0 mmol, 2.0 equiv). The reaction mixture was stirred at –78 ºC for 60 min before the addition of *n*-Bu_3SnCl (587 g, 6.00 mmol, 2.00 equiv). After stirring for 2 hr at –78 ºC, the reaction mixture was warmed to 23 ºC and quenched with saturated aqueous NH_4Cl (10 mL). The phases were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with brine (30 mL) and dried (Na_2SO_4). The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel eluting with hexanes/EtOAc 4:1 (v/v) to afford 716 mg of the title compound as a colorless oil (60% yield).

R_f = 0.30 (hexanes/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.48 (d, *J* = 7.5 Hz, 2H), 7.33 (d, *J* = 7.5 Hz, 2H), 4.67 (m, 2H), 1.59–1.52 (m, 6H), 1.38–1.30 (m, 6H), 1.09–1.02 (m, 6H), 0.90 (t, *J* = 6.0 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 23 ºC, δ): 141.31, 140.49, 136.66, 126.58, 65.39, 29.05, 27.34, 13.63, 9.53. These spectroscopic data correspond to previously reported data.[19]

(Trifluoromethanesulfonyl)ezetimibe (S32)



24 **S32**

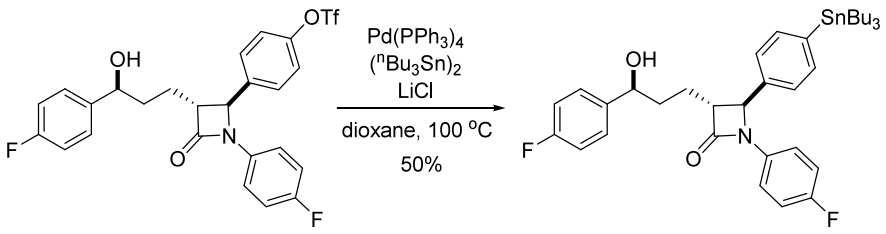
To ezetimibe (**24**) (205 mg, 0.500 mmol, 1.00 equiv) in CH_2Cl_2 (2 mL) at 23 ºC was added triethylamine (209 μL, 1.50 mmol, 3.00 equiv), 4-(dimethylamino)pyridine (6.0 mg, 0.050 mmol, 0.10 equiv) and *N*-phenylbis(trifluoromethanesulfonimide) (196 mg, 0.550 mmol, 1.10 equiv) and the reaction mixture was stirred for 3 hr at 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 2:1 (v/v), to afford 258 mg of the title compound as a colorless solid (95% yield).

R_f = 0.20 (hexane/EtOAc 2:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.43–7.40 (m, 2H), 7.31–7.28 (m, 4H), 7.21–7.19 (m, 2H), 7.03–6.94 (m, 4H), 4.72 (dd, *J* = 6.5 Hz, 6.0 Hz, 1H), 4.68 (d, *J* = 2.5 Hz, 1H), 3.07 (dt, *J* = 7.5 Hz, 2.0 Hz, 1H), 2.63 (br s, 1H), 2.04–1.89 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 166.89, 162.15

[19] Y. Huang, P. S. Hammond, L. Wu, R. H. Mach, *J. Med. Chem.* **44**, 4404 (2001).

(d, J = 244 Hz), 159.12 (d, J = 243 Hz), 149.31, 139.92, 138.18, 133.36, 127.65, 127.31 (d, J = 8.3 Hz), 122.31, 118.63 (q, J = 319 Hz), 118.25 (d, J = 8.3 Hz), 115.99 (d, J = 22.8 Hz), 115.31 (d, J = 21.0 Hz), 72.99, 60.45, 60.29, 36.44, 24.99. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –73.25, –115.14, –117.72. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 564.0875. Found, 564.0849.

(Tributylstannyl)ezetimibe (25)

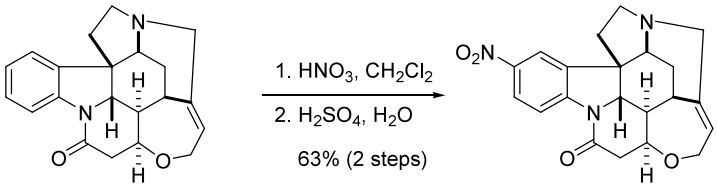


S32 **25**

To (trifluoromethanesulfonyl)ezetimibe (**S32**) (54.1 mg, 0.100 mmol, 1.00 equiv) in dioxane (1 mL) at 23 ºC was added lithium chloride (21.0 mg, 0.500 mmol, 5.00 equiv), tetrakis(triphenylphosphine)palladium (5.8 mg, 0.0050 mmol, 5.0 mol%) and bis(tri-*n*-butyltin) (0.10 mL, 0.20 mmol, 2.0 equiv). After stirring for 12 hr at 100 ºC, the reaction mixture was cooled to 23 ºC and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexanes/EtOAc 3:1 (v/v), to afford 34 mg of the title compound as a colorless oil (50% yield).

R_f = 0.30 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.47 (d, J = 8.0 Hz, 2H), 7.32–7.24 (m, 6H), 7.03 (dd, J = 9.0 Hz, 9.0 Hz, 2H), 6.94 (dd, J = 9.0 Hz, 9.0 Hz, 2H), 4.74 (dd, J = 6.5 Hz, 6.0 Hz, 1H), 4.60 (d, J = 2.5 Hz, 1H), 3.12 (dt, J = 7.5 Hz, 2.0 Hz, 1H), 2.36 (br s, 1H), 2.04–1.91 (m, 4H), 1.59–1.53 (m, 6H), 1.39–1.30 (m, 6H), 1.13–1.03 (m, 6H), 0.89 (d, J = 7.5 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 167.61, 162.17 (d, J = 244 Hz), 158.97 (d, J = 241 Hz), 142.99, 140.05 (d, J = 2.8 Hz), 137.21, 136.98, 133.91 (d, J = 2.6 Hz), 127.37 (d, J = 8.1 Hz), 125.25, 118.39 (d, J = 8.1 Hz), 115.79 (d, J = 22.8 Hz), 115.32 (d, J = 21.9 Hz), 73.05, 61.48, 60.18, 36.59, 29.03, 27.32, 25.04, 13.63, 9.59. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –115.32, –118.50. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + K]^+$, 722.2228. Found, 722.2204.

2-Nitrostrychnine[20] (S33)



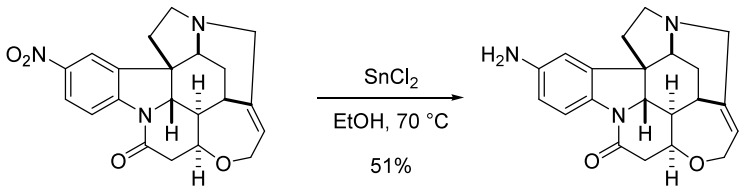
27 **S33**

To strychnine (**27**) (5.00 g, 15.0 mmol, 1.00 equiv) in CH_2Cl_2 (75 mL) at 23 ºC was added nitric acid (15.7 M, 0.955 mL, 15.0 mmol, 1.00 equiv) dropwise over 2 min. After stirred for 10 min, precipitates were filtered off, washed with CH_2Cl_2 (2 × 10 mL), and dried in vacuo to give the nitrate salt as a white powder (4.50 g). This material was used in the next step without further purification.

To strychnine nitrate (4.50 g, 11.3 mmol) in water (9.0 mL) at 0 ºC was added conc. H_2SO_4 (25 mL) dropwise over 20 min. The reaction mixture was warmed to 15 ºC and stirred for 2 hr. The reaction mixture was cooled to 0 ºC and water (30 mL) was added. The reaction mixture was basified at 0 ºC by dropwise addition of sat. NH_4OH (aq) and stirred for 20 min at 65 ºC. The reaction mixture was cooled to 23 ºC and precipitates were filtered off, washed with H_2O (3 × 10 mL), and dried in vacuo to afford 3.60 g of the title compound as a yellow powder (63% over 2 steps).

R_f = 0.10 (CH_2Cl_2/MeOH 95:5 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.19–8.17 (m, 2H), 8.03 (s, 1H), 5.93–5.89 (m, 1H), 4.33–4.27 (m, 1H), 4,16 (dd, *J* = 14 Hz, 7.5 Hz, 1H), 4.06 (dd, *J* = 14 Hz, 6.5 Hz, 1H), 4.02–3.97 (m, 2H), 3.70 (d, *J* = 15 Hz, 1H), 3.27–3.14 (m, 3H), 2.93–2.84 (m, 1H), 2.75–2.66 (m, 2H), 2.44–2.37 (m, 1H), 1.99–1.86 (m, 2H), 1.44 (d, *J* = 15 Hz, 1H), 1.32–1.26 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 169.72, 147.38, 144.32, 140.92, 134.56, 127.41, 125.51, 118.55, 115.62, 77.15, 64.72, 61.18, 60.42, 52.62, 51.47, 50.26, 48.15, 42.94, 42.47, 31.50, 26.94. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 380.16048. Found, 380.15998.

2-Aminostrychnine[20] (S34)



S33 **S34**

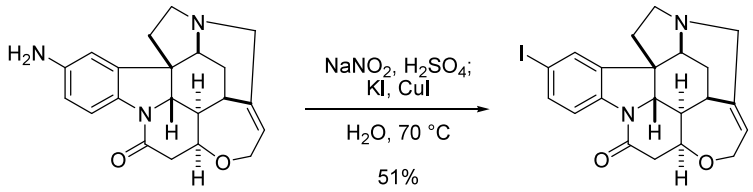
To 2-nitrostrychnine (**S33**) (3.60 g, 9.49 mmol, 1.00 equiv) in EtOH (95 mL) at 23 ºC was added $SnCl_2$ (9.00 g, 47.5 mmol, 5.00 equiv). The reaction mixture was stirred at 70 ºC for 12 hr and cooled to 23 ºC. A solution of 5% KOH (aq) (20 mL) was added to the reaction

[20] P. Rosenmund, *Chem. Ber.* **94**, 3342 (1961).

mixture and the suspension was filtered through a pad of celite. The filtrate was concentrated in vacuo to remove EtOH and the aqueous solution was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic phase was dried (Na_2SO_4) and concentrated in vacuo to afford 1.69 g of the title compound as a colorless powder (51%).

R_f = 0.05 (CH_2Cl_2/MeOH 9:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.88 (d, *J* = 9.0 Hz, 1H), 6.58 (dd, *J* = 8.5 Hz, *J* = 2.5 Hz, 1H), 6.50 (d, *J* = 2.5 Hz, 1H), 5.95–5.91 (m, 1H), 4.29–4.25 (m, 1H), 4,14 (dd, *J* = 14 Hz, 7.5 Hz, 1H), 4.05 (dd, *J* = 14 Hz, 6.5 Hz, 1H), 3.94 (br s, 1H), 3.81 (d, *J* = 11 Hz, 1H), 3.73 (d, *J* = 15 Hz, 1H), 3.70–3.50 (br s, 2H), 3.27–3.23 (m, 1H), 3.15 (br s, 1H), 3.09 (dd, *J* = 17 Hz, 8.5 Hz, 1H), 2.90–2.83 (m, 1H), 2.77 (d, *J* = 15 Hz, 1H), 2.63 (dd, *J* = 17 Hz, 3.5 Hz, 1H), 2.38–2.30 (m, 1H), 1.93–1.87 (m, 2H), 1.48 (d, *J* = 14 Hz, 1H), 1.29–1.22 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 168.39, 143.39, 139.61, 134.54, 133.54, 128.21, 117.12, 115.23, 109.05, 77.77, 64.46, 60.19, 60.02, 52.53, 51.99, 50.32, 48.05, 42.40, 42.25, 31.45, 26.60. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 350.18630. Found, 350.18651.

2-Iodostrychnine[20] (28)

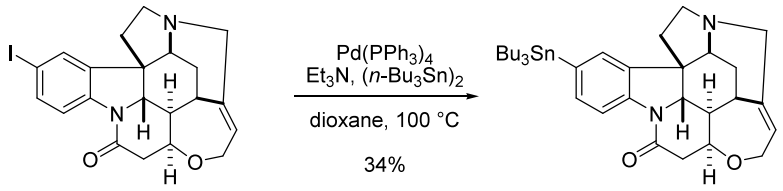


S34 **28**

To 2-aminostrychnine (**S34**) (692 mg, 1.98 mmol, 1.00 equiv) in 4N H_2SO_4 (aq) (2.0 mL) at 23 ºC was added a solution of $NaNO_2$ (164 mg, 2.38 mmol, 1.20 equiv) in water (0.6 mL) dropwise over 2 min and stirred at 70 ºC for 10 min to form a solution of the corresponding diazonium salt. To a solution of CuI (1.32 g, 6.93 mmol, 3.5 equiv) in sat. KI aq (6.0 mL) at 70 ºC was added above prepared solution of diazonium salt dropwise over 10 min and further stirred at 70 ºC for 30 min. The reaction mixture was cooled to 23 ºC and sat. NH_4OH (aq) was added (5 mL). The aqueous suspension was extracted with $CHCl_3$ (3 × 15 mL) and the combined organic phase was washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with CH_2Cl_2/MeOH 96:4 (v/v), to afford 465 mg of the title compound as an orange powder (51%).

R_f = 0.40 (CH_2Cl_2/MeOH 9:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.82 (d, *J* = 9.0 Hz, 1H), 7.50 (dd, *J* = 8.5 Hz, *J* = 1.5 Hz, 1H), 7.40 (d, *J* = 1.5 Hz, 1H), 5.90–5.85 (m, 1H), 4.28–4.21 (m, 1H), 4,11 (dd, *J* = 14 Hz, 7.5 Hz, 1H), 4.02 (dd, *J* = 14 Hz, 6.5 Hz, 1H), 3.85 (br s, 1H), 3.82 (d, *J* = 11 Hz, 1H), 3.66 (d, *J* = 15 Hz, 1H), 3.21–3.14 (m, 1H), 3.12 (br s, 1H), 3.08 (dd, *J* = 17 Hz, 8.5 Hz, 1H), 2.87–2.77 (m, 1H), 2.69 (d, *J* = 15 Hz, 1H), 2.61 (dd, *J* = 17 Hz, 3.5 Hz, 1H), 2.37–2.29 (m, 1H), 1.88–1.80 (m, 2H), 1.42 (d, *J* = 14 Hz, 1H), 1.24–1.17 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 169.25, 141.94, 139.95, 137.36, 135.31, 131.25, 127.49, 118.05, 86.86, 77.32, 64.51, 60.16, 60.13, 52.50, 51.66, 50.18, 47.99, 42.68, 42.33, 31.37, 26.73. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 461.07205. Found, 461.07296.

2-Tributylstannylstrychnine (29)



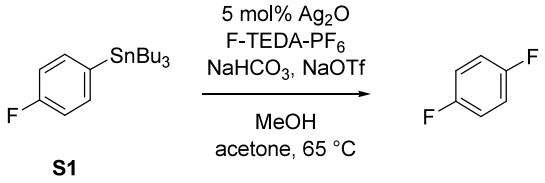
28 **29**

To 2-iodostrychnine (**28**) (880 mg, 1.91 mmol, 1.00 equiv) in dioxane (3.6 mL) at 23 ºC was added tetrakis(triphenylphosphine)palladium (22 mg, 0.019 mmol, 1.0 mol%), triethylamine (0.444 mL, 3.82 mmol, 2.00 equiv), and bis(tri-*n*-butyltin) (1.44 mL, 2.87 mmol, 1.50 equiv). The reaction mixture was stirred for 2 hr at 100 ºC and cooled to 23 ºC. The reaction mixture was filtered through a pad of celite and the filtrate was concentrated in vacuo. The residue was purified by chromatography on silica gel eluting with acetone/benzene 1:1 (v/v) to afford 400 mg of the title compound as a colorless oil (34%).

R_f = 0.25 (acetone/benzene 1:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.04 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.22 (s, 1H), 5.97–5.89 (m, 1H), 4.29–4.24 (m, 1H), 4,14 (dd, *J* = 14 Hz, 7.0 Hz, 1H), 4.05 (dd, *J* = 14 Hz, 7.0 Hz, 1H), 3.97 (br s, 1H), 3.83 (d, *J* = 10 Hz, 1H), 3.72 (d, *J* = 15 Hz, 1H), 3.24–3.20 (m, 1H), 3.15–3.07 (m, 2H), 2.92–2.83 (m, 1H), 2.74 (d, *J* = 15 Hz, 1H), 2.65 (dd, *J* = 17 Hz, 3.0 Hz, 1H), 2.40–2.31 (m, 1H), 1.93–1.86 (m, 2H), 1.60–1.43 (m, 7H), 1.40–1.25 (m, 7H), 1.10–0.95 (m, 6H), 0.87 (t, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 169.13, 142.21, 140.23, 137.08, 136.55, 132.02, 129.89, 127.54, 115.81, 77.60, 64.55, 60.22, 59.91, 52.66, 51.95, 50.35, 48.17, 42.83, 42.45, 31.57, 29.04, 27.28, 26.73, 13.66, 9.67. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 625.28105. Found, 625.28033.

Silver-catalyzed fluorination of arylstannanes

Effect of MeOH in the Ag-catalyzed fluorination reaction



S1

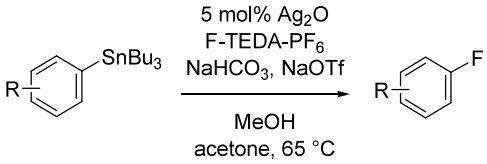
To (4-fluorophenyl)tributylstannane (**S1**) (7.7 mg, 0.020 mmol, 1.0 equiv) in acetone (0.4 mL) at 23 ºC was added silver oxide (0.23 mg, 0.0010 mmol, 5.0 mol%), sodium bicarbonate (3.4 mg, 0.040 mmol, 2.0 equiv), sodium trifluoromethanesulfonate (3.4 mg, 0.020 mmol, 1.0 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14 mg, 0.030 mmol, 1.5 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (2.0 μL, 0.0188 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of

fluorobenzene (–115.3 ppm), 1,4-difluorobenzene (–121.6 ppm) and 4-fluoroanisole (–126.0 ppm) with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S11.

Table S11: Effect of MeOH in the Ag-catalyzed fluorination reaction

MeOH [equiv]	ArF [%] (^{19}F NMR)	ArH [%] (^{19}F NMR)	ArOMe [%] (^{19}F NMR)
None	74	12	<1
1.0	75	7	<1
2.0	79	6	<1
5.0	78	5	2
10.0	70	4	3

General procedure

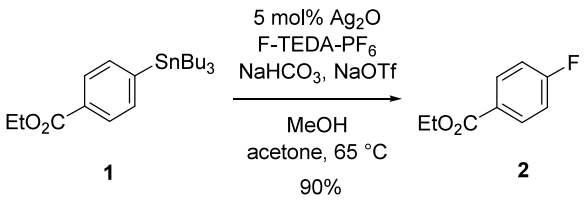


To arylstannane (0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv) and MeOH (20 μL, 0.50 mmol, 5.0 equiv). The reaction mixture was stirred for 4 hr at 65 ºC in a sealed vial and subsequently cooled to 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (10.0 μL, 0.0939 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-d_6, 23 ºC) resonance of an arylfluoride with that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S12.

Table S12. Synthesis of arylfluorides

R	^{19}F chemical shift[3]	Yield [%] (^{19}F NMR)
4-Phenyl (**3**)	–118.1 ppm	88
4-CN (**4**)	–105.0 ppm	89
4-OMe (**5**)	–126.8 ppm	76
4-Br (**6**)	–117.1 ppm	77
2,4,6-Trimethyl (**7**)	–129.7 ppm	78

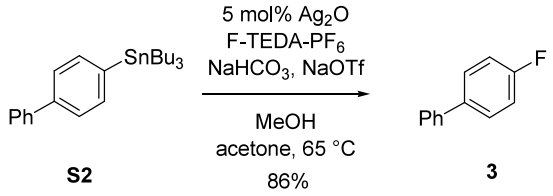
Ethyl 4-fluorobenzoate[21] (2)



To ethyl 4-(tributylstannyl)benzoate (**1**) (44.0 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv) and MeOH (20 μL, 0.50 mmol, 5.0 equiv). The reaction mixture was stirred for 4 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 3:1 (v/v), to afford 15.1 mg of the title compound as a colorless solid (90% yield).

R_f = 0.30 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.06 (dd, *J* = 9.0 Hz, 5.5 Hz, 2H), 7.10 (dd, *J* = 9.0 Hz, 8.5 Hz, 2H), 4.37 (q, *J* = 7.0 Hz, 2H), 1.39 (t, *J* = 9.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 165.68 (d, *J* = 252 Hz), 165.65, 132.04 (d, *J* = 10 Hz), 126.72, 115.42 (d, *J* = 22 Hz), 61.07, 14.30. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –108.4. These spectroscopic data correspond to previously reported data.[21]

4-Fluorobiphenyl[22] (3)



To (4-biphenyl)tributylstannane (**S2**) (44.4 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv) and MeOH (20 μL, 0.50 mmol, 5.0 equiv). The reaction mixture was stirred for 4 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with

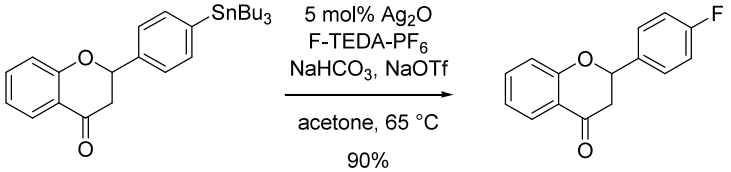
[21] C. Cai, *et al*, *Org. Lett.* **8**, 5161 (2006).

[22] T. Furuya, H. M. Kaiser, T. Ritter, *Angew. Chem. Int. Ed*. **47**, 5993 (2008).

hexane/EtOAc 19:1 (v/v), to afford 14.8 mg of the title compound as a colorless solid (86% yield).

R_f = 0.60 (hexanes/EtOAc 19:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.60–7.54 (m, 4H), 7.47 (dd, *J* = 7.5 Hz, 7.0 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.14 (dd, *J* = 8.0 Hz, 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 162.44 (d, *J* = 244 Hz), 140.25, 137.30, 128.80, 128.75 (d, *J* = 8.5 Hz), 127.24, 127.00, 115.59 (d, *J* = 21 Hz). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –118.1. These spectroscopic data correspond to previously reported data.[22]

4'-(Fluoro)flavanone[23] (8)

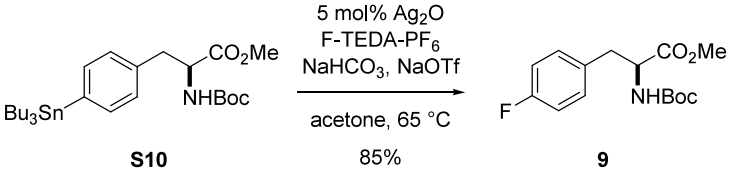


S8 **8**

To 4'-(trifluoromethanesulfonyl)flavanone (**S8**) (51.4 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 5:1 (v/v), to afford 21.8 mg of the title compound as a colorless solid (90% yield).

R_f = 0.50 (hexane/EtOAc 5:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.93 (dd, *J* = 8.0 Hz, 1.5 Hz, 1H), 7.53–7.46 (m, 3H), 7.14–7.04 (m, 4H), 5.87 (dd, *J* = 13.0 Hz, 2.5Hz, 1H), 3.06 (dd, *J* = 16.5 Hz, 2.5Hz, 1H), 2.88 (dd, *J* = 16.5 Hz, 3.5Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 191.68, 162.79 (d, *J* = 247 Hz), 161.37, 136.25, 134.57 (d, *J* = 3.6 Hz) 128.01 (d, *J* = 9.1 Hz), 127.06, 121.74, 120.87, 118.06, 115.78 (d, *J* = 22 Hz), 78.90, 44.64. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –115.5. These spectroscopic data correspond to previously reported data.[23]

***N*-Boc-4-(fluoro)-*L*-phenylalanine methyl ester[24] (9)**



S10 **9**

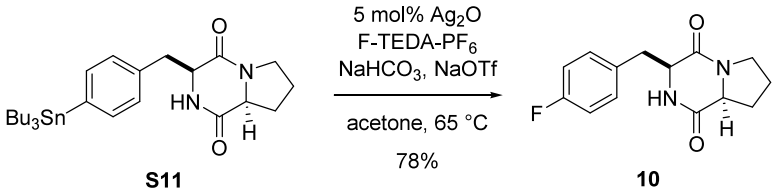
[23] D. Dauzonne, C. Monneret, *Synthesis* **11**, 1305 (1997).

[24] M. Schumacher, G. Coste, L. Miesch, *Synthesis* **6**, 1014 (2009).

To *N*-Boc-4-(tributylstannyl)-*L*-phenylalanine methyl ester (**S10**) (56.9 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 5:1 (v/v), to afford 25.2 mg of the title compound as a colorless solid (85% yield).

R_f = 0.30 (hexane/EtOAc 5:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.08 (dd, *J* = 8.5 Hz, 5.5 Hz, 2H), 6.98–6.96 (m, 2H), 4.98 (d, *J* = 7.5 Hz, 1H), 4.57–4.54 (m, 1H), 3.70 (s, 3H), 3.09 (dd, *J* = 14.0 Hz, 5.5 Hz, 1H), 3.00 (dd, *J* = 14.0 Hz, 5.5 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 172.16, 161.97 (d, *J* = 243 Hz), 154.99, 131.75, 130.75 (d, *J* = 8.1 Hz), 115.35 (d, *J* = 21 Hz), 80.00, 54.40, 52.23, 37.61, 28.25. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –118.5. These spectroscopic data correspond to previously reported data.[24]

4-(Fluoro)maculosin[25] (10)



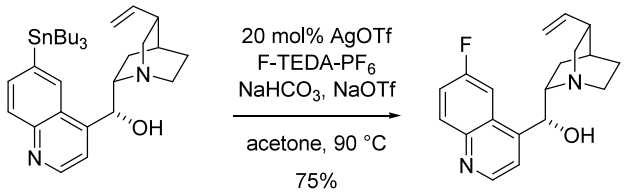
S11 **10**

To 4-(tributylstannyl)maculosin (**S11**) (37.3 mg, 0.0698 mmol, 1.00 equiv) in acetone (1.4 mL) at 23 ºC was added silver oxide (0.81 mg, 0.0035 mmol, 5.0 mol%), sodium bicarbonate (11.8 mg, 0.140 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (11.9 mg, 0.0698 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (49.3 mg, 0.105 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with CH_2Cl_2/MeOH 10:1 (v/v), to afford 14.3 mg of the title compound as a colorless oil (78% yield).

R_f = 0.30 (CH_2Cl_2/MeOH 10:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.18 (dd, *J* = 8.0 Hz, 5.5 Hz, 1H), 7.01 (t, *J* = 9.0 Hz, 2H), 6.18 (m, 1H), 4.21–4.18 (m, 1H), 3.67–3.61 (m, 1H), 3.42–3.37 (m, 1H), 3.14–3.02 (m, 3H), 2.25–2.20 (m, 1H), 1.98–1.92 (m, 1H), 1.86–1.69 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 168.93, 164.55, 162.31 (d, *J* = 246 Hz), 131.38 (d, *J* = 8.3 Hz) 130.94 (d, *J* = 3.6 Hz), 115.74 (d, *J* = 22 Hz), 59.03, 57.82, 45.23, 39.70, 28.78, 21.66. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –117.5. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 263.1190. Found, 263.1192.

[25] M. Bobylev, L. Bobyleva, G. Strobel, *J. Agri. Food. Chem*. **44**, 3960 (1996).

6-Demethoxy-6-fluoroquinine[3] (11)

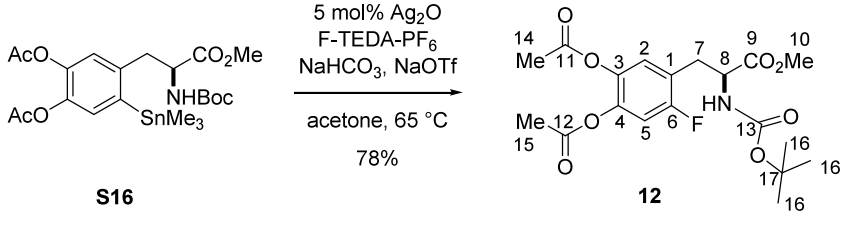


S13 **11**

To 6-demethoxy-6-(tributylstannyl)quinine (**S13**) (29.2 mg, 0.0500 mmol, 1.00 equiv) in acetone (1 mL) at 23 ºC was added silver triflate (2.56 mg, 0.0100 mmol, 20.0 mol%), sodium bicarbonate (8.4 mg, 1.0 mmol, 2.0 equiv), sodium trifluoromethanesulfonate (17.0 mg, 1.00 mmol, 2.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (47.0 mg, 1.00 mmol, 2.00 equiv). The reaction mixture was stirred for 2 hr at 90 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with CH_2Cl_2/MeOH 9:1 (v/v), to afford 11.7 mg of the title compound as a colorless solid (75% yield).

R_f = 0.40 (CH_2Cl_2/MeOH 9:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, CD_3CN, 23 ºC, δ): 8.85 (d, *J* = 4.2 Hz, 1H), 8.10 (dd, *J* = 9.0 Hz, 5.4 Hz, 1H), 7.97 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H,), 7.65 (d, *J* = 4.2 Hz, 1H), 7.54 (ddd, *J* = 9.0 Hz, 9.0 Hz, 3.0 Hz, 1H), 5.83 (d, *J* = 3.0 Hz, 1H), 5.78–5.72 (m, 1H), 5.06 (d, *J* = 17.4 Hz, 1H), 4.99 (d, *J* = 10.2 Hz, 1H), 3.92–3.86 (m, 1H), 3.48–3.43 (m, 1H), 3.35 (dd, *J* = 13.2 Hz, 7.2 Hz, 1H), 3.06–3.00 (m, 2H), 2.68 (s br, 1H), 2.05–1.99 (m, 3H), 1.84–1.78 (m, 1H), 1.65–1.58 (m, 1H). ^{13}C NMR (125 MHz, CD_3CN, 23 ºC, δ): 161.48 d, *J* = 244 Hz), 150.63, 146.83 (d, *J* = 6.1 Hz), 146.45, 139.78, 133.81 (d, *J* = 9.9 Hz), 126.76 (d, *J* = 9.9 Hz), 120.78, 120.18 (d, *J* = 26 Hz), 116.68, 108.25 (d, *J* = 24 Hz), 68.99, 61.30, 55.61, 4.78, 38.38, 27.87, 25.32, 20.44. ^{19}F NMR (375 MHz, CD_3CN, 23 ºC, δ): –113.6. These spectroscopic data correspond to previously reported data.[3]

***N*-Boc-*O*-acetyl-6-fluoro-DOPA methyl ester (12)**



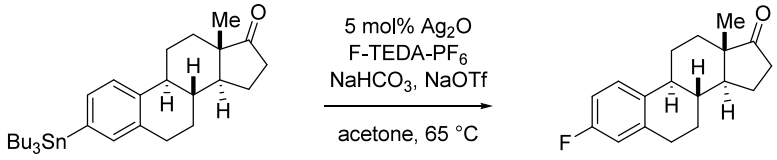
S16 **12**

To *N*-Boc-*O*-acetyl-6-trimethylstannyl-DOPA methyl ester (**S16**) (22.4 mg, 0.0400 mmol, 1.00 equiv) in acetone (0.8 mL) at 23 ºC was added silver oxide (0.46 mg, 0.0020 mmol, 5.0 mol%), sodium bicarbonate (6.7 mg, 0.080 mmol, 2.0 equiv), sodium trifluoromethanesulfonate (6.9 mg, 0.040 mmol, 1.0 equiv) and

1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (28.2 mg, 0.0600 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 3:1 (v/v), to afford 12.9 mg of the title compound as a colorless solid (78% yield).

R_f = 0.30 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 6.98 (d, *J* = 7.0 Hz, 1H, H-2), 6.95 (d, *J* = 9.5 Hz, 1H, H-5), 5.08 (d, *J* = 7.5 Hz, 1H, NH), 4.57–4.55 (m, 1H, H-8), 3.72 (s, 3H, H-10), 3.18–3.02 (m, 2H, H-7), 2.27 (s, 3H, H-15), 2.26 (s, 3H, H-14), 1.41 (s, 9H, H-16). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 171.89 (C-9), 168.10 (C-12), 167.74 (C-11), 158.19 (d, *J* = 245 Hz, C-6), 154.96 (C-13), 141.46 (C-4), 137.99 (C-3), 125.48 (d, *J* = 5.4 Hz, C-2), 121.64 (d, *J* = 18 Hz, C-1), 110.02 (d, *J* = 27 Hz, C-5), 80.07 (C-17), 53.35 (C-8), 52.47 (C-10), 31.59 (C-7), 28.20 (C-16), 20.59 (C-15), 20.51 (C-14). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –117.98. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 436.1378. Found, 436.1373. The proton and carbon NMR resonances were assigned by ^{1}H-^{1}H COSY, HSQC and HMBC experiments.

3-Deoxy-3-fluoroestrone[26] (13)



S17 **13**

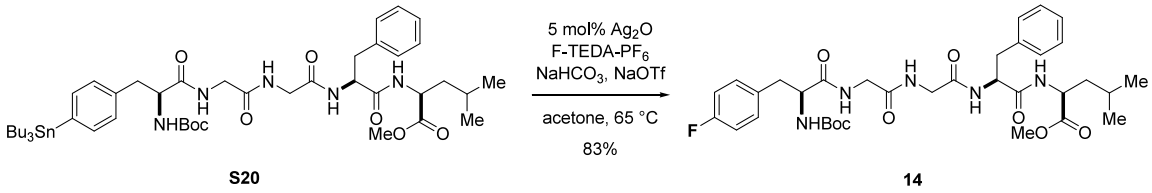
To 3-deoxy-3-(tributylstannyl)estrone (**S17**) (54.4 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 9:1 (v/v), to afford 22.0 mg of the title compound as a colorless solid (81% yield).

R_f = 0.33 (hexane/EtOAc 9:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.23 (dd, *J* = 8.0 Hz, 6.0 Hz, 1H), 6.85–6.77 (m, 2H), 2.92–2.88 (m, 2H), 2.51 (dd, *J* = 19.0 Hz, 9.0 Hz, 1H), 2.42–2.38 (m, 1H), 2.29–2.23 (m, 1H), 2.18–1.94 (m, 4H), 1.67–1.41 (m, 6H,), 0.91 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 220.69, 160.99 (d, *J* = 242 Hz), 138.65 (d, *J* = 7.3 Hz), 135.31, 126.76 (d, *J* = 7.3 Hz), 115.10 (d, *J* = 20 Hz), 112.48 (d, *J* = 20 Hz), 50.38, 47.92, 43.98, 38.10, 35.82, 31.52, 29.45, 26.30, 25.88, 21.56, 13.81. ^{19}F

[26] D. F. Morrow, R. M. Hofer, *J. Med. Chem.* **9**, 249 (1966).

NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –118.5. These spectroscopic data correspond to previously reported data.[26]

4-(Fluoro)-leu-enkephalin (14)

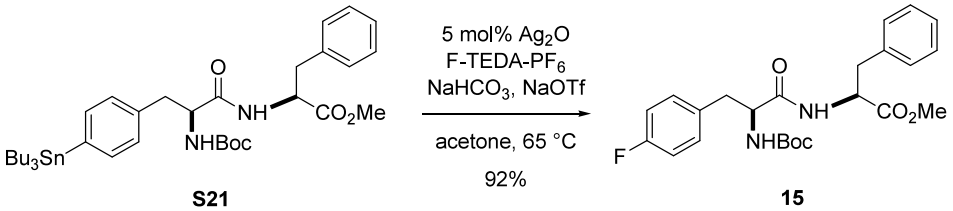


S20 **14**

To *N*-Boc-4-(tributylstannyl)-*L*-phenylalanyl-glycylglycyl-*L*-phenylalanyl-*L*-leucine methyl ester (**S20**) (18.9 mg, 0.0200 mmol, 1.00 equiv) in acetone (0.4 mL) at 23 ºC was added silver oxide (0.23 mg, 0.0010 mmol, 5.0 mol%), sodium bicarbonate (3.36 mg, 0.0400 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (3.42 mg, 0.0200 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14.1 mg, 0.0300 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with CH_2Cl_2/MeOH 10:1 (v/v), to afford 11.2 mg of the title compound as a colorless solid (83% yield).

R_f = 0.40 (CH_2Cl_2/MeOH 10:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.86 (br s, 1H), 7.60 (br s, 1H), 7.50 (br s, 1H), 7.23–7.15 (m, 5H), 7.07–7.04 (m, 2H), 6.92–6.88 (m, 2H), 5.77 (br s, 1H), 5.07 (br s, 1H), 4.63–4.58 (m, 2H), 4.18–4.00 (m, 4H), 3.70 (s, 3H), 3.14–3.10 (m, 1H), 3.03–2.99 (m, 2H), 2.92–2.88 (m, 1H), 1.58–1.51 (m, 3H), 1.40 (s, 9H), 0.88 (d, J = 6.0 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 173.02, 171.99, 170.72, 168.79, 168.28, 161.82 (d, J = 243 Hz), 155.76, 136.49, 132.33, 130.82 (d, J = 8.1 Hz), 129.52, 128.34, 126.78, 115.22 (d, J = 21 Hz), 80.05, 55.50, 54.16, 52.18, 50.81, 43.07, 41.18, 39.0, 38.13, 29.68, 28.33, 24.77, 22.71, 22.03. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –118.5. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$, 672.3403. Found, 672.3397.

***N*-Boc-4-(fluoro)-*L*-phenylalanyl-*L*-phenylalanine methyl ester[27] (15)**



S21 **15**

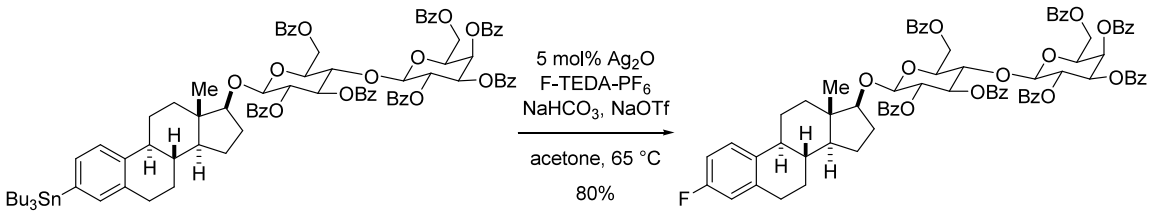
To *N*-Boc-4-(Tributylstannyl)-*L*-phenylalanyl-*L*-phenylalanine methyl ester (**S21**) (1.43 g,

[27] H. Kreuzfeld, C. Döbler, C. Fischer, W. Baumann, *Am. Acids* **17**, 369 (1999).

2.00 mmol, 1.00 equiv) in acetone (40 mL) at 23 ºC was added silver oxide (23.2 mg, 0.100 mmol, 5.00 mol%), sodium bicarbonate (336 mg, 4.00 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (342 mg, 2.00 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (1.41 g, 3.00 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by chromatography on silica gel, eluting with hexane/EtOAc 2:1 (v/v), to afford 817 mg of the title compound as a colorless solid (92% yield).

R_f = 0.30 (hexane/EtOAc 2:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.28–7.22 (m, 3H), 7.16–7.13 (m, 2H), 7.03–7.93 (m, 4H), 6.38 (d, *J* = 6.5 Hz, 1H), 5.06 (br s, 1H), 4.78 (br s, 1H), 4.32 (br s, 1H), 3.68 (s, 3H), 3.09–2.99 (m, 4H), 1.41 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 171.32, 170.61, 161.82 (d, *J* = 244 Hz), 155.17, 135.52, 132.19, 130.79 (d, *J* = 7.3 Hz), 129.12, 128.49, 127.08, 115.59 (d, *J* = 21 Hz), 80.13, 55.60, 53.17, 52.22, 37.85, 37.48, 28.17. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –118.8. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 467.1953. Found, 467.1942.

3-Deoxy-3-fluoro-β-estradiol-β-heptabenzoyllactose (16)



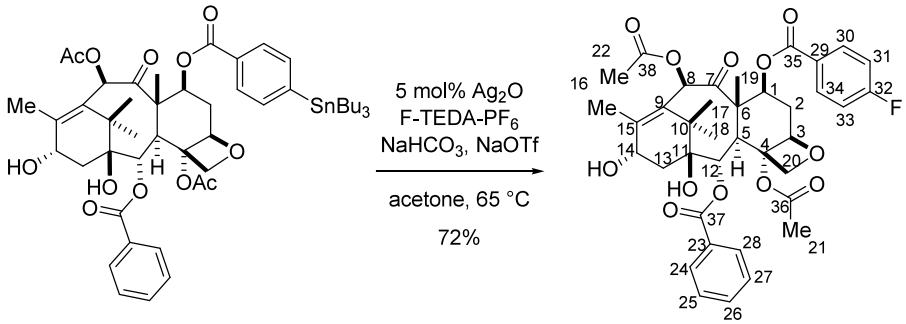
S24 **16**

To 3-deoxy-3-tributylstannyl-β-estradiol-β-heptabenzoyllactose (**S24**) (53.3 mg, 0.0333 mmol, 1.00 equiv) in acetone (0.6 mL) at 23 ºC was added silver oxide (0.38 mg, 0.0017 mmol, 5.0 mol%), sodium bicarbonate (5.54 mg, 0.0666 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (5.67 mg, 0.0333 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (23.5 mg, 0.0500 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 3:1 (v/v), to afford 35.0 mg of the title compound as a colorless oil (80% yield).

R_f = 0.30 (hexane/EtOAc 3:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.02–7.96 (m, 10H), 7.91 (dd, *J* = 8.0 Hz, 1.0 Hz, 2H), 7.73 (dd, *J* = 8.0 Hz, 1.0 Hz, 2H), 7.65–7.30 (m, 18H), 7.22 (dd, *J* = 8.5 Hz, 7.5 Hz, 2H), 7.16–7.11 (m, 3H), 6.80–6.78 (m, 1H), 6.72 (dd, *J* = 10.0 Hz, 2.5 Hz, 1H), 5.81 (dd, *J* = 9.5 Hz, 9.0 Hz, 1H), 5.75–5.71 (m, 2H), 5.47 (dd, *J* = 10.0 Hz, 8.5 Hz, 1H), 5.38 (dd, *J* = 10.0 Hz, 3.5 Hz, 1H), 4.88 (d, *J* = 8.0 Hz, 1H), 4.76 (d, *J* = 8.0 Hz, 1H), 4.62–4.60 (m, 1H), 4.50 (dd, *J* = 11.5 Hz, 5.0 Hz, 1H), 4.23 (dd,

J = 10.0 Hz, 9.0 Hz, 1H), 3.91 (dd, *J* = 6.5 Hz, 6.5 Hz, 1H), 3.84–3.82 (m, 1H), 3.75 (dd, *J* = 11.5 Hz, 7.0 Hz, 1H), 3.69 (dd, *J* = 11.5 Hz, 7.0 Hz, 1H), 3.58 (dd, *J* = 9.0 Hz, 8.0 Hz, 1H), 2.79–2.77 (m, 2H), 2.06–2.03 (m, 2H), 1.98–1.92 (m, 1H), 1.83–1.78 (m, 1H), 1.68–1.54 (m, 4H), 1.30–1.22 (m, 4H), 1.15–1.01 (m, 2H), 0.57 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 165.82, 165.57, 165.43, 165.39, 165.20, 165.12, 164.79, 160.84 (d, *J* = 242 Hz), 138.78 (d, *J* = 7.3 Hz), 135.71, 133.52, 133.37, 133.34, 133.29, 133.23, 133.14, 133.09, 129.99, 129.74, 129.73, 129.71, 129.66, 129.63, 129.59, 129.49, 129.40, 128.84, 128.69, 128.62, 128.56, 128.49, 128.29, 128.22, 126.68 (d, *J* = 8.1 Hz), 114.98 (d, *J* = 20 Hz), 112.20 (d, *J* = 21 Hz), 101.81, 100.98, 90.02, 76.32, 72.98, 72.96, 71.94, 71.74, 71.39, 69.92, 67.54, 62.57, 61.13, 49.60, 43.79, 43.11, 38.15, 37.16, 29.50, 28.67, 26.85, 25.99, 22.96, 11.33. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –120.5. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + NH_4]^+$, 1344.4963. Found, 1344.4962.

Fluorinated Taxol derivative (17)



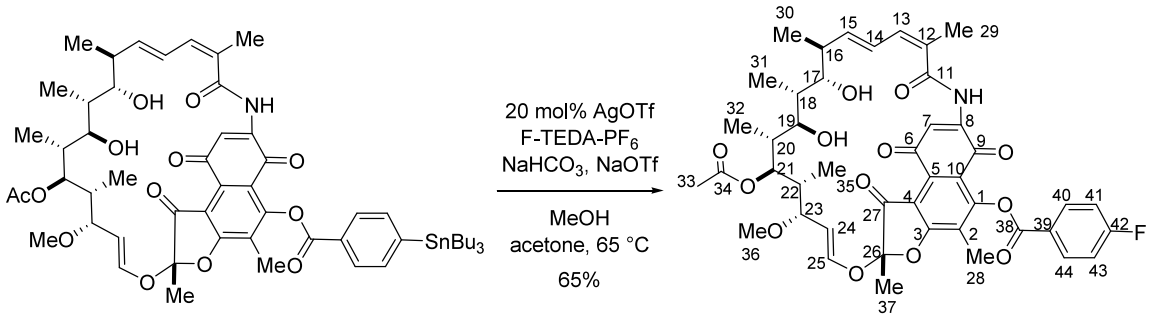
S25 **17**

To taxol derivative (**S25**) (19.6 mg, 0.0200 mmol, 1.00 equiv) in acetone (0.4 mL) at 23 ºC was added added silver oxide (0.23 mg, 0.0010 mmol, 5.0 mol%), sodium bicarbonate (3.36 mg, 0.0400 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (3.42 mg, 0.0200 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (14.1 mg, 0.0300 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 1:2 (v/v), to afford 10.2 mg of the title compound as a colorless solid (72% yield).

R_f = 0.30 (hexane/EtOAc 1:2 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.12 (d, *J* = 7.5 Hz, 2H, H-24, H-28), 7.93 (dd, *J* = 8.5 Hz, 5.5 Hz, 2H, H-30, H-34), 7.62 (dd, *J* = 7.5 Hz, 7.0 Hz, 1H, H-26), 7.49 (dd, *J* = 8.0 Hz, 7.5 Hz, 2H, H-25, H-27), 7.08 (dd, *J* = 8.5 Hz, 8.0 Hz, 2H, H-31, H-33), 6.40 (s, 1H, H-8), 5.76 (dd, *J* = 10.5 Hz, 7.0 Hz, 1H, H-1), 5.68 (d, *J* = 7.0 Hz, 1H, H-12), 5.01 (d, *J* = 9.0 Hz, 1H, H-3), 4.88–4.85 (m, 1H, H-14), 4.35 (d, *J* = 8.5 Hz, 1H, H-20), 4.20 (d, *J* = 8.5 Hz, 1H, H-20), 4.09 (d, *J* = 7.0 Hz, 1H, H-5), 2.82–2.75 (m, 1H, H-2), 2.32–2.30 (m, 2H, H-13), 2.31 (s, 3H, H-22), 2.15 (s, 3H, H-21), 2.10 (d, *J* = 5.0 Hz, 1H, OH-14), 1.99 (s, 3H, H-16), 1.93 (s, 3H, H-19), 1.94–1.88 (m, 1H, H-2), 1.15 (s, 3H, H-17), 1.08 (s, 3H, H-18). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 202.94 (C-7), 170.65 (C-36), 168.44 (C-38), 167.06 (C-37), 165.65 (d, *J* = 252 Hz, C-32), 164.35

(C-35), 144.66 (C-15), 133.73 (C-26), 132.33 (d, *J* = 9.1 Hz, C-30, C-34), 131.91 (C-9), 130.11 (C-24, C-28), 129.27 (C-23), 128.67 (C-25, C-27), 126.52 (C-29), 115.24 (d, *J* = 22 Hz, C-31, C-33), 83.99 (C-3), 80.61 (C-4), 78.72 (C-11), 76.39 (C-20), 75.45 (C-8), 74.44 (C-12), 72.49 (C-1), 67.95 (C-14), 56.42 (C-6), 47.19 (C-5), 42.78 (C-10), 38.47 (C-13), 33.40 (C-2), 26.62 (C-18), 22.56 (C-22), 20.52 (C-16), 20.14 (C-17), 15.19 (C-21), 10.94 (C-19). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –108.72. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$,709.2655. Found, 709.2641. The proton and carbon NMR resonances were assigned by COSY, HSQC and HMBC experiments.

Fluorinated rifamycin S derivative (18)



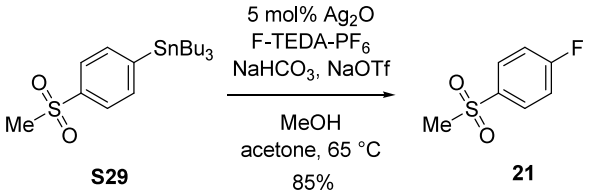
S26 **18**

To rifamycin S derivative (**S26**) (32.7 mg, 0.0300 mmol, 1.00 equiv) in acetone (0.6 mL) at 23 ºC was added silver triflate (1.54 mg, 0.00600 mmol, 20.0 mol%), sodium bicarbonate (5.04 mg, 0.0600 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (10.3 mg, 0.0600 mmol, 2.00 equiv), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (21.1 mg, 0.0450 mmol, 1.50 equiv) and MeOH (12 μL, 0.15 mmol, 5.0 equiv). The reaction mixture was stirred for 3 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2. The filtrate was concentrated in vacuo and the residue was purified by preparative TLC, eluting with hexane/EtOAc 2:1 (v/v), to afford 15.9 mg of the title compound as a yellow solid (65% yield, ^{19}F NMR yield: 70%). (Note: The fluorinated rifamycin S derivative was not stable to silca gel and also slowly decomposed in $CDCl_3$ at 23 ºC.)

R_f = 0.20 (hexane/EtOAc 2:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.31 (dd, *J* = 8.5 Hz, 5.0 Hz, 2H, H-40, H-44), 8.23 (s, 1H, NH), 7.80 (s, 1H, H-7), 7.26–7.22 (m, 2H, H-41, H-43), 6.25–6.17 (m, 3H, H-14, H-13, H-25), 5.89 (dd, *J* = 15.5 Hz, 6.5 Hz, 1H, H-15), 5.13 (dd, *J* = 12.5 Hz, 7.5 Hz, 1H, H-24), 4.64 (d, *J* = 10.5 Hz, 1H, H-21), 3.70 (d, *J* = 4.5 Hz, 1H, OH-19), 3.59 (d, *J* = 10.0 Hz, 1H, H-17), 3.38–3.37 (m, 2H, H-23, OH-17), 3.12 (s, 3H, H-36), 3.05–3.02 (m, 1H, H-19), 2.34 (s, 3H, H-28), 2.32–2.29 (m, 1H, H-16), 2.04 (s, 3H, H-33), 2.03–1.98 (m, 1H, H-22), 1.97 (s, 3H, H-29), 1.81–1.80 (m, 1H, H-18), 1.77 (s, 3H, H-37), 1.69–1.67 (m, 1H, H-20), 1.08 (d, *J* = 7.0 Hz, 3H, H-31), 0.84 (d, *J* = 7.0 Hz, 3H, H-30), 0.68 (d, *J* = 7.0 Hz, 3H, H-32), 0.18 (d, *J* = 7.0 Hz, 3H, H-35). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 192.37 (C-27), 182.00 (C-9), 177.77 (C-6), 173.28 (C-3), 173.11 (C-34), 169.29 (C-11), 166.54 (d, *J* = 255 Hz, C-42), 163.22 (C-38), 155.61 (C-1),

144.76 (C-25), 141.89 (C-15), 139.94 (C-8), 133.51 (d, J = 9.1 Hz, C-40, C-44), 133.51 (C-13), 132.22 (C-5), 130.78 (C-12), 124.67 (C-39), 124.01 (C-14), 118.47 (C-2), 116.14 (C-24), 115.88 (d, J = 20 Hz, C-41, C-43), 115.80 (C-7), 114.81 (C-4), 108.83 (C-26), 81.53 (C-23), 77.25 (C-19), 73.48 (C-21), 73.14 (C-17), 56.89 (C-36), 39.02 (C-16), 37.38 (C-20), 37.27 (C-22), 32.76 (C-18), 22.03 (C-37), 21.06 (C-33), 19.99 (C-29), 16.93 (C-30), 11.75 (C-35), 11.18 (C-31), 8.84 (C-32), 8.79 (C-28). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –106.55. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + H]^+$,818.3183. Found, 818.3164. The proton and carbon NMR resonances were assigned by COSY, HSQC and HMBC experiments.

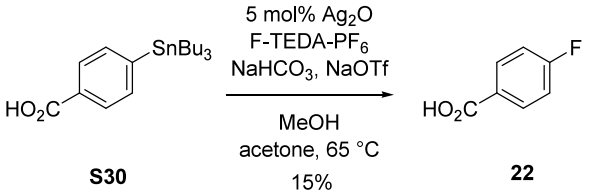
4-Fluorophenylmethylsulfone[28] (21)



To (4-methylsulfonylphenyl)tributylstannane (**S29**) (44.6 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv) and MeOH (20 μL, 0.50 mmol, 5.0 equiv). The reaction mixture was stirred for 4 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 1:1 (v/v), to afford 14.8 mg of the title compound as a colorless solid (85% yield).

R_f = 0.30 (hexanes/EtOAc 1:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.00–7.97 (m, 2H), 7.29–7.25 (m, 2H), 3.07 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 165.77 (d, J = 255 Hz), 136.66, 130.27 (d, J = 10 Hz), 116.66 (d, J = 23 Hz), 44.66. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –103.9. These spectroscopic data correspond to previously reported data.[28]

4-Fluorobenzoic acid (22)



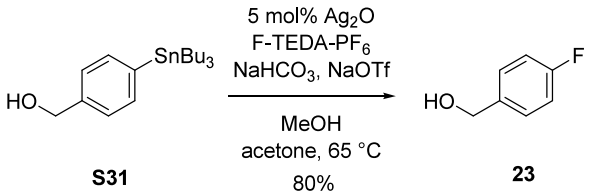
To 4-(tributylstannyl)benzoic acid (**S30**) (41.2 mg, 0.100 mmol, 1.00 equiv) in acetone (2

[28] M. Peyronneau, *et al*, *Eur. J. Org. Chem.* **22**, 4636 (2004).

mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv) and MeOH (20 μL, 0.50 mmol, 5.0 equiv). The reaction mixture was stirred for 4 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 1:2 (v/v), to afford 2.1 mg of the title compound as a colorless solid (15% yield).

R_f = 0.25 (hexanes/EtOAc 1:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 11.68 (s, 1H), 8.15–8.13 (m, 2H), 7.17–7.14 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 170.39, 166.35 (d, J = 254 Hz), 132.89 (d, J = 10 Hz), 125.41, 115.75 (d, J = 22 Hz). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –104.4. These spectroscopic data correspond to those of authentic sample purchased from Alfa Aesar.

4-Fluorobenzylalcohol[29] (23)

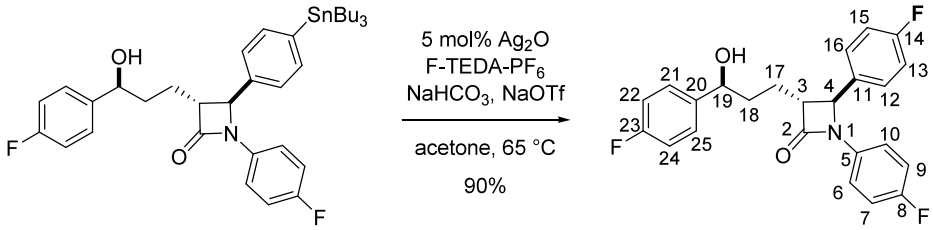


To 4-(Tributylstannyl)benzyl alcohol (**S31**) (39.8 mg, 0.100 mmol, 1.00 equiv) in acetone (2 mL) at 23 ºC was added silver oxide (1.16 mg, 0.00500 mmol, 5.00 mol%), sodium bicarbonate (16.8 mg, 0.200 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (17.2 mg, 0.100 mmol, 1.00 equiv), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (70.5 mg, 0.150 mmol, 1.50 equiv) and MeOH (20 μL, 0.50 mmol, 5.0 equiv). The reaction mixture was stirred for 4 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 3:1 (v/v), to afford 10.1 mg of the title compound as a colorless oil (80% yield).

R_f = 0.60 (hexanes/EtOAc 2:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.34–7.32 (m, 2H), 7.06–7.03 (m, 2H), 4.66 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 162.29 (d, J = 244 Hz), 136.55, 128.73 (d, J = 8.3 Hz), 115.36 (d, J = 22 Hz), 64.64. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –115.3. These spectroscopic data correspond to previously reported data.[29]

[29] T. Furuya., H. M. Kaiser, T. Ritter, *Angew. Chem., Int. Ed.* **47**, 5993 (2008).

(14-Fluoro)ezetimibe (26)

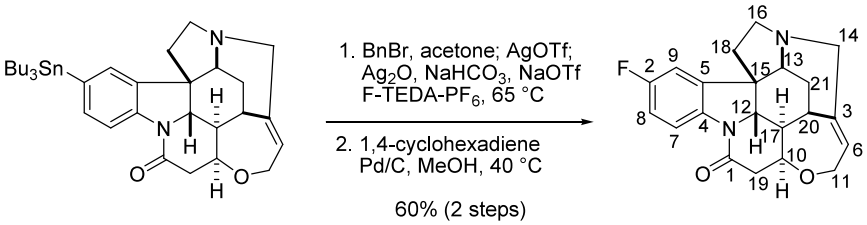


25 **26**

To (Tributylstannyl)ezetimibe (**25**) (19.8 mg, 0.0290 mmol, 1.00 equiv) in acetone (0.6 mL) at 23 ºC was added silver oxide (0.34 mg, 0.0015 mmol, 5.0 mol%), sodium bicarbonate (4.87 mg, 0.0580 mmol, 2.00 equiv), sodium trifluoromethanesulfonate (4.96 mg, 0.0290 mmol, 1.00 equiv) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (20.5 mg, 0.0436 mmol, 1.50 equiv). The reaction mixture was stirred for 5 hr at 65 ºC in a sealed vial. After cooling to 23 ºC, the reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC, eluting with hexane/EtOAc 2:1 (v/v), to afford 10.7 mg of the title compound as a colorless solid (90% yield).

R_f = 0.30 (hexane/EtOAc 2:1 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.31–7.28 (m, 4H, H-12, H-16, H-21, H-25), 7.22–7.20 (m, 2H, H-6, H-10), 7.08–7.00 (m, 4H, H-13, H-15, H-22, H-24), 6.95–6.92 (m, 2H, H-7, H-9), 4.72 (m, 1H, H-19), 4.61 (d, *J* = 2.0 Hz, 1H, H-2), 3.07–3.05 (m, 1H, H-3), 2.17 (br s, 1H, OH), 2.03–1.89 (m, 4H, H-17, H-18). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 167.25 (C-4), 162.75 (d, *J* = 246 Hz, C-23), 162.23 (d, *J* = 244 Hz, C-14), 159.04 (d, *J* = 241 Hz, C-8), 139.97 (C-11), 133.66 (C-5), 133.30 (C-20), 127.55 (d, *J* = 8.7 Hz, C-12, C-16), 127.36 (d, *J* = 7.4 Hz, C-21, C-25), 118.32 (d, *J* = 7.4 Hz, C-6, C-10), 116.32 (d, *J* = 22 Hz, C-22, C-24), 115.89 (d, *J* = 23 Hz, C-7, C-9), 115.38 (d, *J* = 21 Hz, C-13, C-15), 73.16 (C-19), 60.77 (C-2), 60.48 (C-3), 36.56 (C-18), 25.07 (C-17). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –115.71, –118.20, –120.62. Mass Spectrometry: HRMS-FIA (m/z): Calcd for $[M + Na]^+$, 434.1338. Found, 434.1344. The proton and carbon NMR resonances were assigned by COSY, HSQC and HMBC experiments.

2-Fluorostrychnine (30)



29 **30**

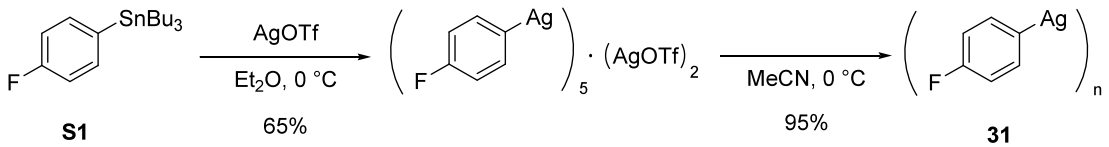
To 2-tributylstannylstrychnine (**29**) (62.3 mg, 0.100 mmol, 1.00 equiv) in acetone (1 mL) at

23 ºC was added benzyl bromide (11.9 μL, 0.100 mmol, 1.00 equiv). The reaction mixture was stirred for 12 hr at 23 ºC and cooled to –78 ºC. To the reaction mixture was added AgOTf (25.7 mg, 0.100 mmol, 1.00 equiv) in acetone (1.0 mL) dropwise over 2 min and the reaction mixture was warmed to 23 ºC. To the reaction mixture was added Ag_2O (1.2 mg, 0.0050 mmol, 5.0 mol%), $NaHCO_3$ (16.8 mg, 0.200 mmol, 2.00 equiv), NaOTf (17.2 mg, 0.100 mmol, 1.00 equiv), and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluoro-phosphate) (70.5 mg, 0.150 mmol, 1.50 equiv). The reaction mixture was heated to 65 ºC and stirred for 2 hr before cooled to 23 ºC. The reaction mixture was filtered through a pad of celite, eluting with CH_2Cl_2 and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC on SiO_2, eluting with CH_2Cl_2/MeOH 9:1 (v/v), to afford a mixture of fluorination and hydrodestannylation products (ca. 4:1) as a colorless solid. This material was used in the next step without further purification.

To the crude *N*-benzyl-2-fluorostrychnine (<0.100 mmol) in MeOH (1 mL) at 23 ºC was added 10% Pd/C (11 mg) and 1,4-cyclohexadiene (468 μL, 5.00 mmol). The reaction mixture was heated to 40 ºC and stirred for 4 hr. The reaction mixture was filtered through a pad of celite, eluting with MeOH and the filtrate was concentrated in vacuo. The residue was purified by preparative TLC on Al_2O_3, eluting with acetone/benzene 2:3 (v/v), to afford 21.5 mg of the title compound as a colorless solid (60% over 2 steps).

R_f = 0.55 (Al_2O_3, acetone/benzene 2:3 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.05 (dd, *J* = 9.0 Hz, 4.5 Hz, 1H, H-7), 6.93 (ddd, *J* = 9.0 Hz, 9.0 Hz, 3.0 Hz, 1H, H-8), 6.84 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H, H-9), 5.92–5.86 (m, 1H, H-6), 4.30–4.26 (m, 1H, H-10), 4,14 (dd, *J* = 14 Hz, 7.0 Hz, 1H, H-11b), 4.05 (dd, *J* = 14 Hz, 7.0 Hz, 1H, H-11a), 3.90–3.86 (m, 2H, H-12, H-13), 3.69 (d, *J* = 15 Hz, 1H, H-14b), 3.20 (dd, *J* = 10 Hz, 7.0 Hz, 1H, H-16b), 3.18–3.09 (m, 2H, H-20, H-19b), 2.90–2.83 (m, 1H, H-16a), 2.71 (d, *J* = 15 Hz, 1H, H-14a), 2.65 (dd, *J* = 17 Hz, 3.0 Hz, 1H, H-19a), 2.40–2.33 (m, 1H, H-21b), 1.94–1.83 (m, 2H, H-18a, H-18b), 1.45 (d, *J* = 14 Hz, 1H, H-21a), 1.29–1.23 (m, 1H, H-17). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 169.14 (C-1), 159.87 (d, *J* = 243 Hz, C-2), 140.36 (C-3), 138.32 (C-4), 134.96 (C-5), 127.31 (C-6), 117.11 (d, *J* = 8.3 Hz, C-7), 114.90 (d, *J* = 22.9 Hz, C-8), 109.53 (d, *J* = 23.8 Hz, C-9), 77.61 (C-10), 64.60 (C-11), 60.48 (C-12), 60.26 (C-13), 52.61 (C-14), 51.91 (C-15), 50.31 (C-16), 48.18 (C-17), 42.73 (C-18), 42.33 (C-19), 31.53 (C-20), 26.87 (C-21). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –118.7. Mass Spectrometry: HRMS-FIA (m/z): Calcd for [M + H], 353.16598. Found, 353.16524. The proton and carbon NMR resonances were assigned by COSY, HSQC and HMBC experiments.

(4-Fluorophenyl)silver[3] (31)



S1 **31**

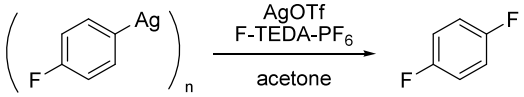
To silver triflate (514 mg, 2.00 mmol, 2.00 equiv) in Et_2O (10 mL) at 0 ºC was added (4-fluorophenyl)tributylstannane (**S1**) (385 mg, 1.00 mmol, 1.00 equiv). The reaction mixture was stirred for 1 hr at 0 ºC and the solvent was decanted. The residue was washed

with Et_2O (3 ×10 mL) and dried in vacuo at 0 ºC to afford 200 mg of the (4-fluorophenyl)silver-silver triflate as a yellow solid (65% yield).

To (4-fluorophenyl)silver-silver triflate 5:2 complex (153 mg, 0.500 mmol, 1.00 equiv) was added MeCN (2.5 mL) at 0 ºC. The reaction mixture was stirred for 1 min at 0 ºC and the suspension was filtered off and washed with MeCN (2.5 mL) at 0 ºC to afford 96.0 mg of the (4-Fluorophenyl)silver as an off-white solid (95% yield).

NMR Spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, –10 ºC, δ): 7.76 (dd, J = 7.6 Hz, 7.6 Hz, 2H), 7.00 (dd, J = 7.6 Hz, 7.6 Hz, 2H). ^{19}F NMR (375 MHz, $CDCl_3$, –10 ºC, δ): –107.75 (s br). Due to the low solubility and the thermal instability, the title compound was not amenable to further characterization.

Fluorination of (4-fluorophenyl)silver with various amount of AgOTf



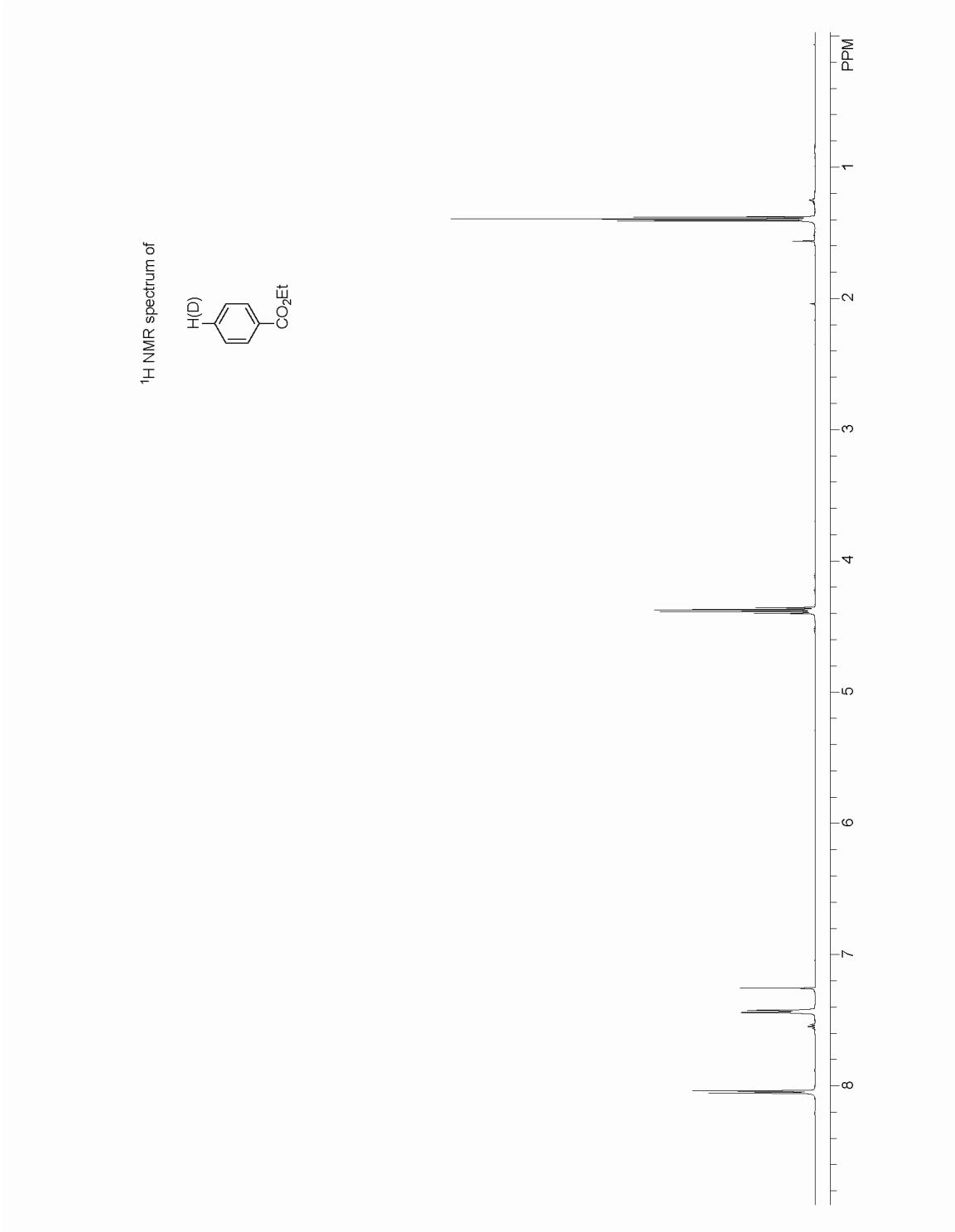
31 **32**

To (4-fluorophenyl)silver (**31**) (10.2 mg, 0.0500 mmol, 1.00 equiv) in acetone (1.0 mL) at 23 ºC was added 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (28.3 mg, 0.120 mmol, 1.20 equiv) and various amount of silver triflate. The reaction mixture was stirred for 20 min at 23 ºC. To the reaction mixture was added 3-nitrofluorobenzene (5.0 μL, 0.047 mmol). The yield was determined by comparing the integration of the ^{19}F NMR (375 MHz, acetone-*d6*, 23 ºC) resonance of 1,4-difluorobenzene (–121.6 ppm) and that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S13.

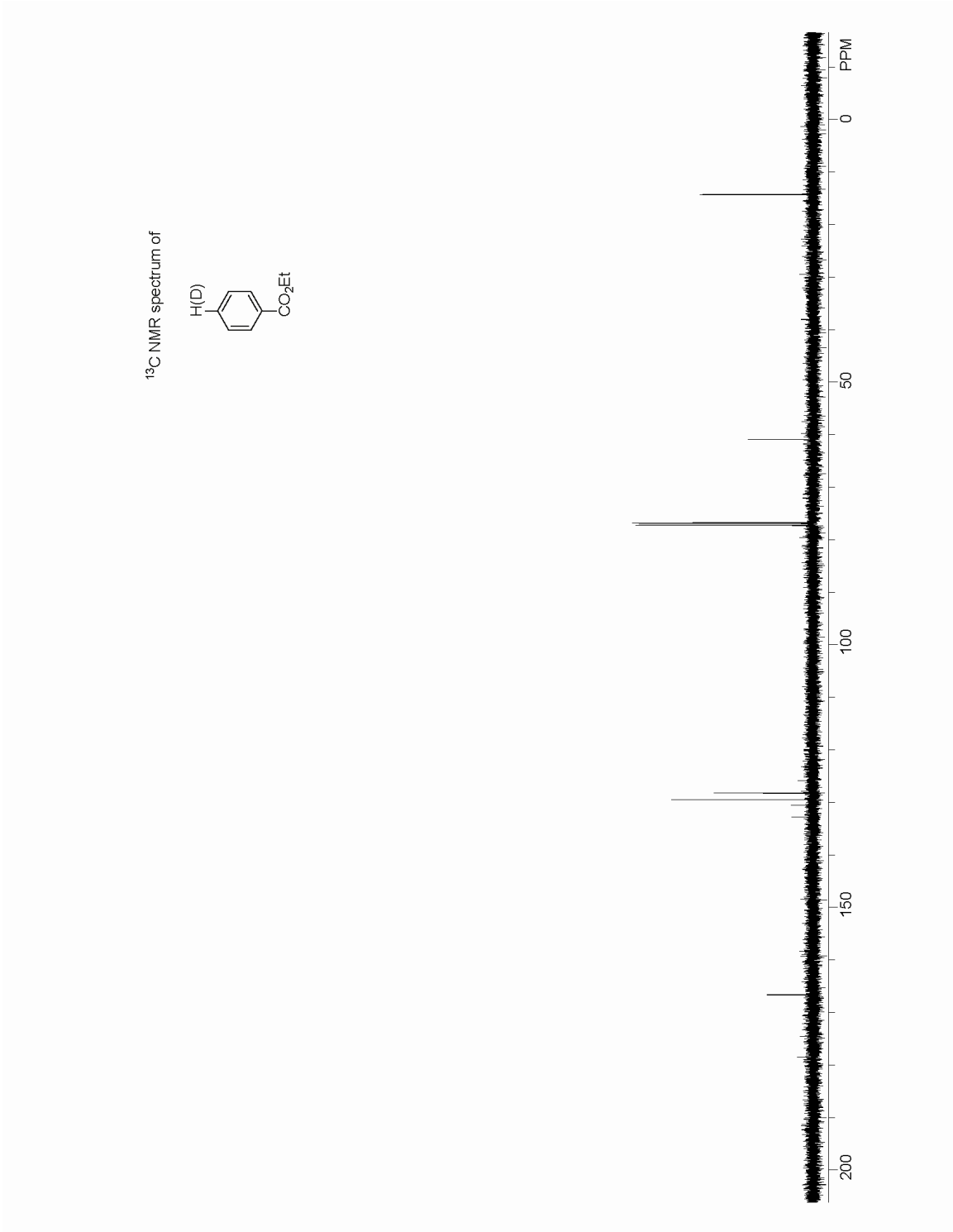
Table S13: Fluorination of (4-fluorophenyl)silver with various amount of AgOTf

AgOTf	Yield [%] (^{19}F NMR)
None	47
1.0 equiv	84
2.0 equiv	81

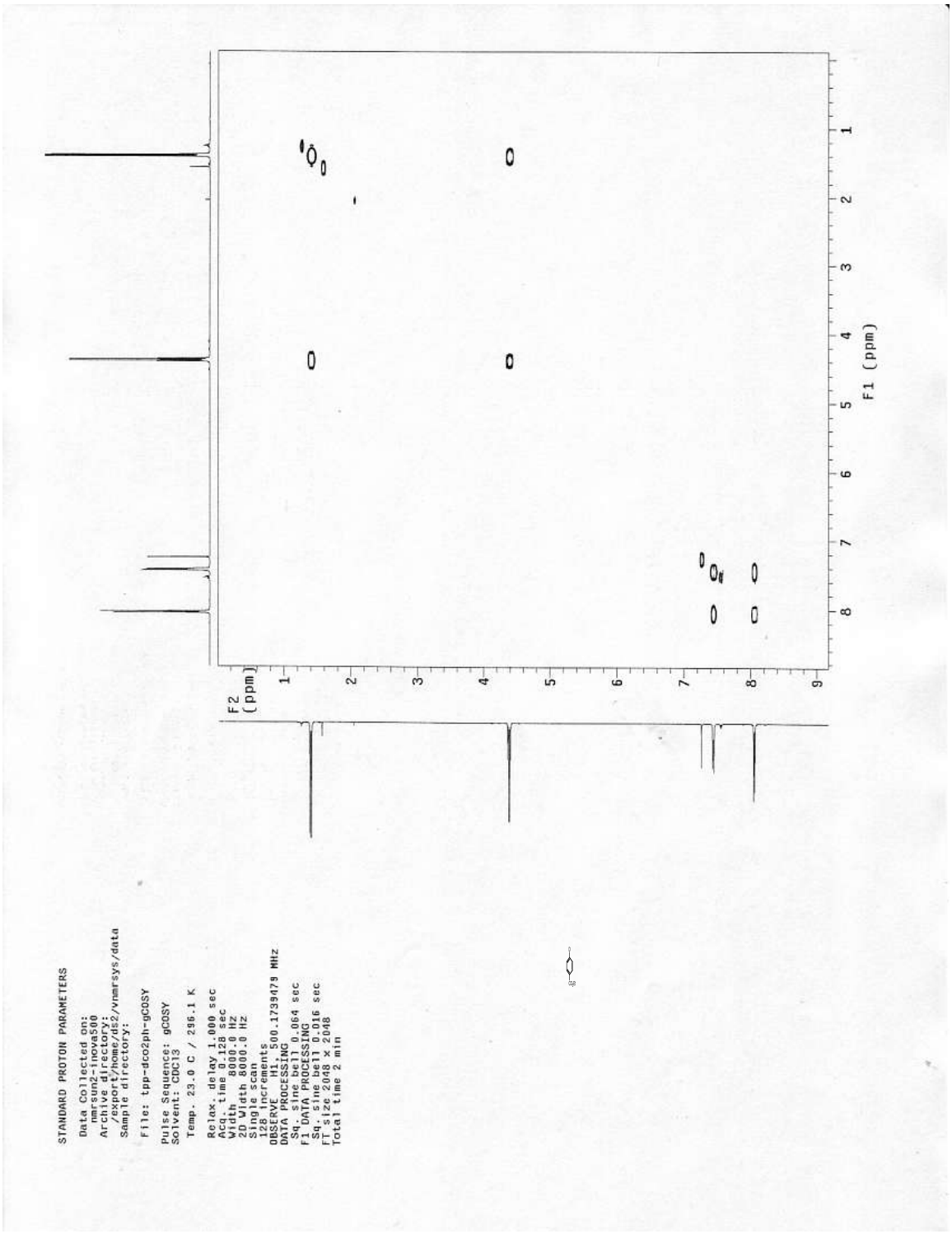
Spectroscopic Data



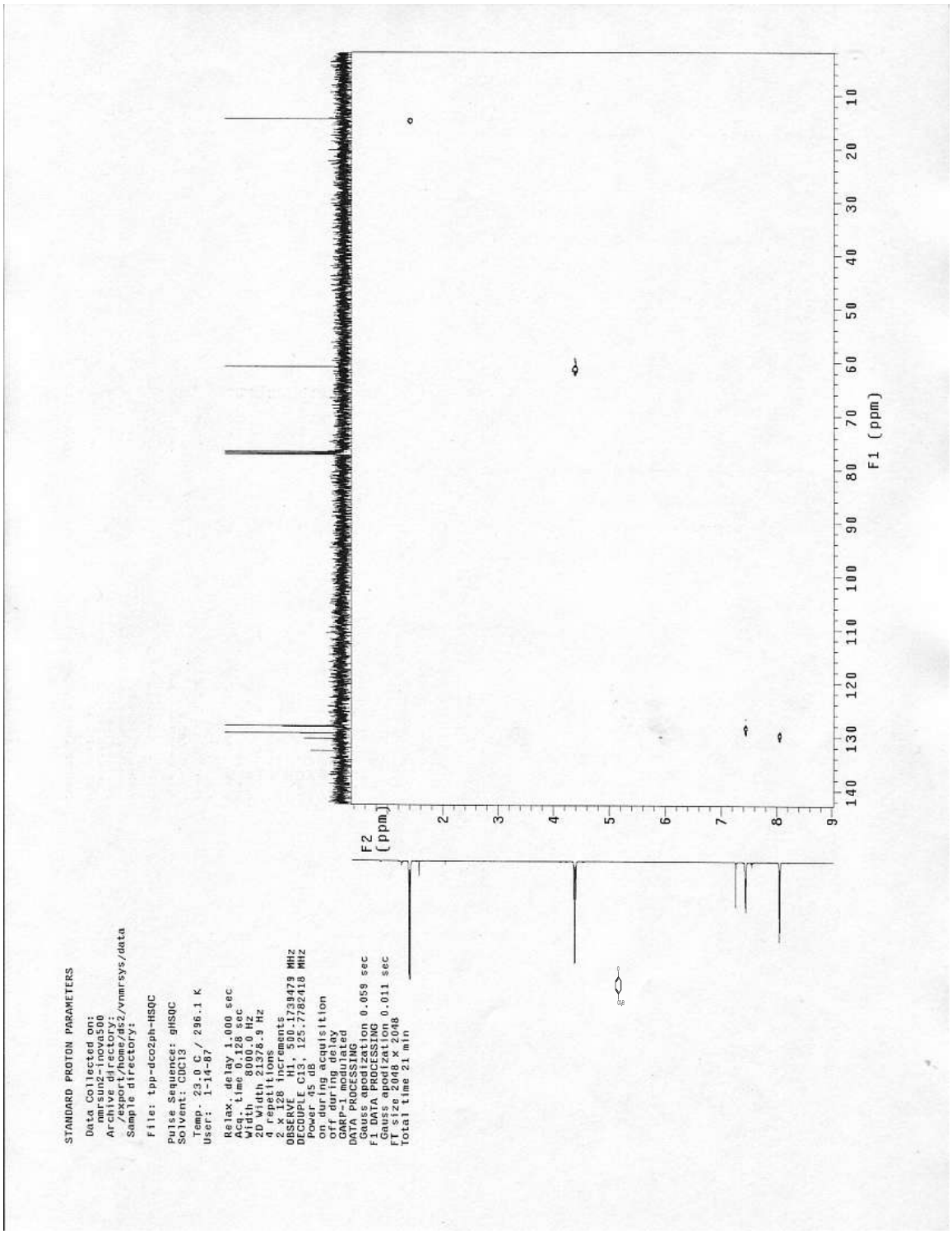
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of 4-deutero-ethyl benzoate **2a**



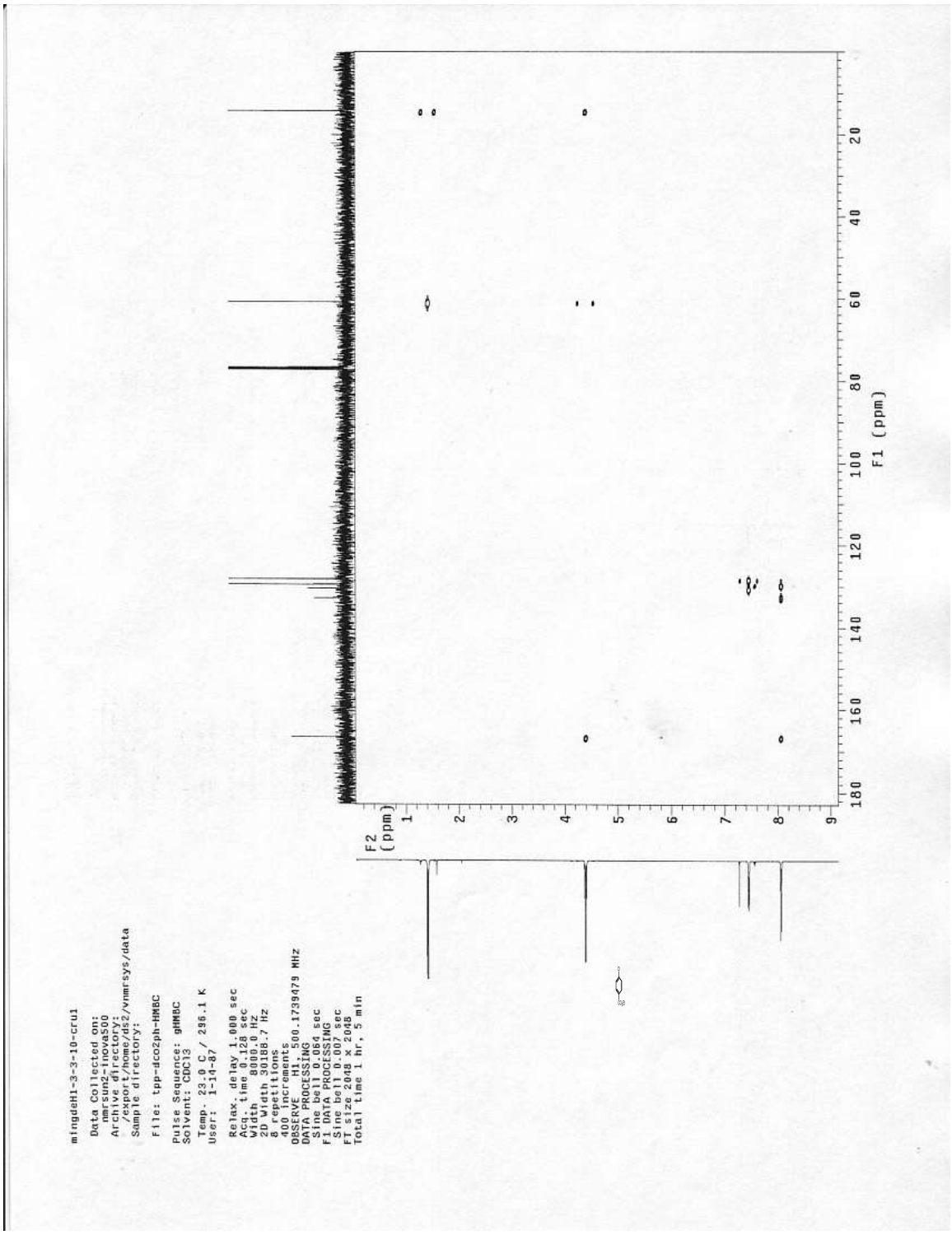
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of 4-deutero-ethyl benzoate **2a**



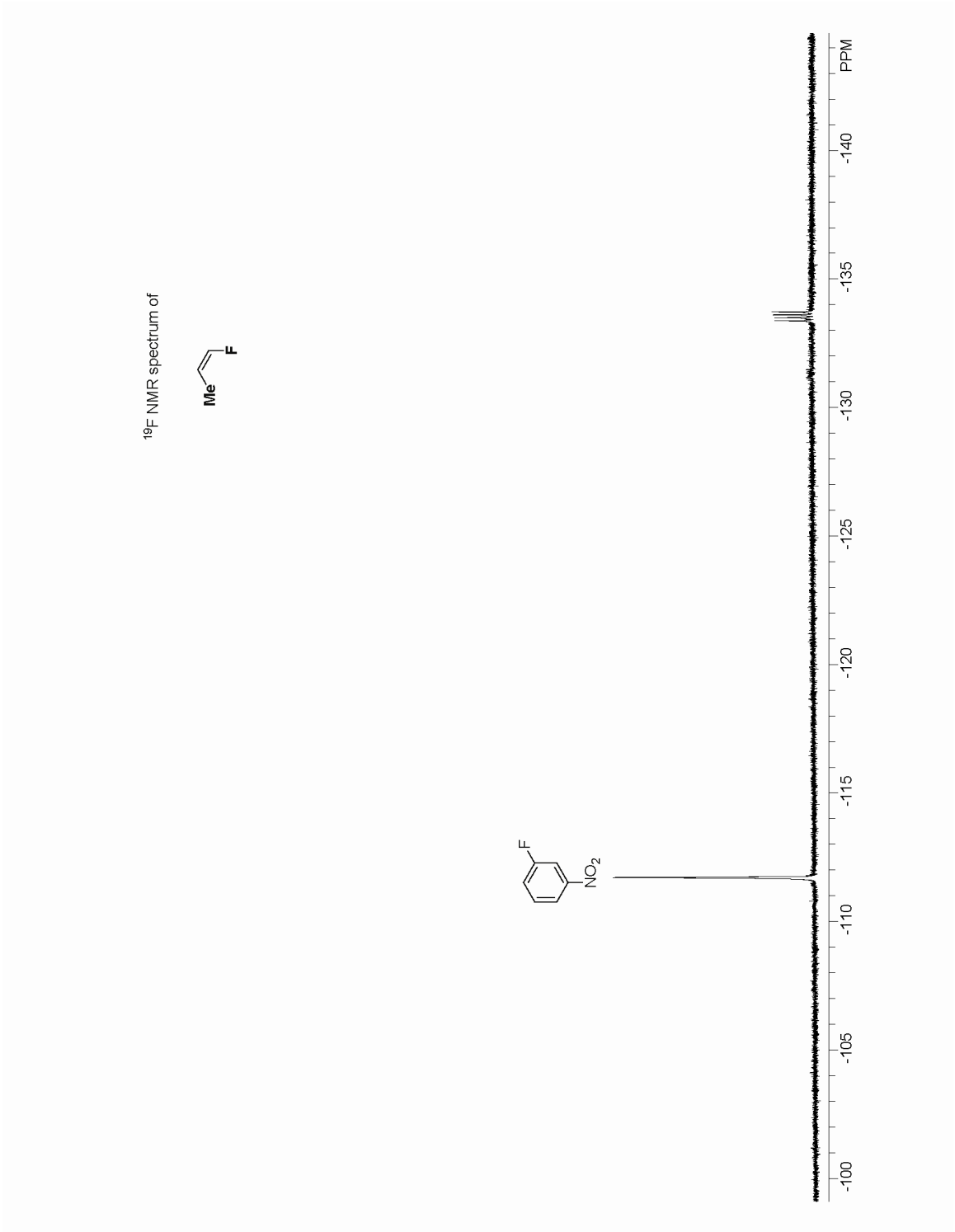
^{1}H-^{1}H COSY spectrum (500 MHz, $CDCl_3$, 23 ºC) of **2a**



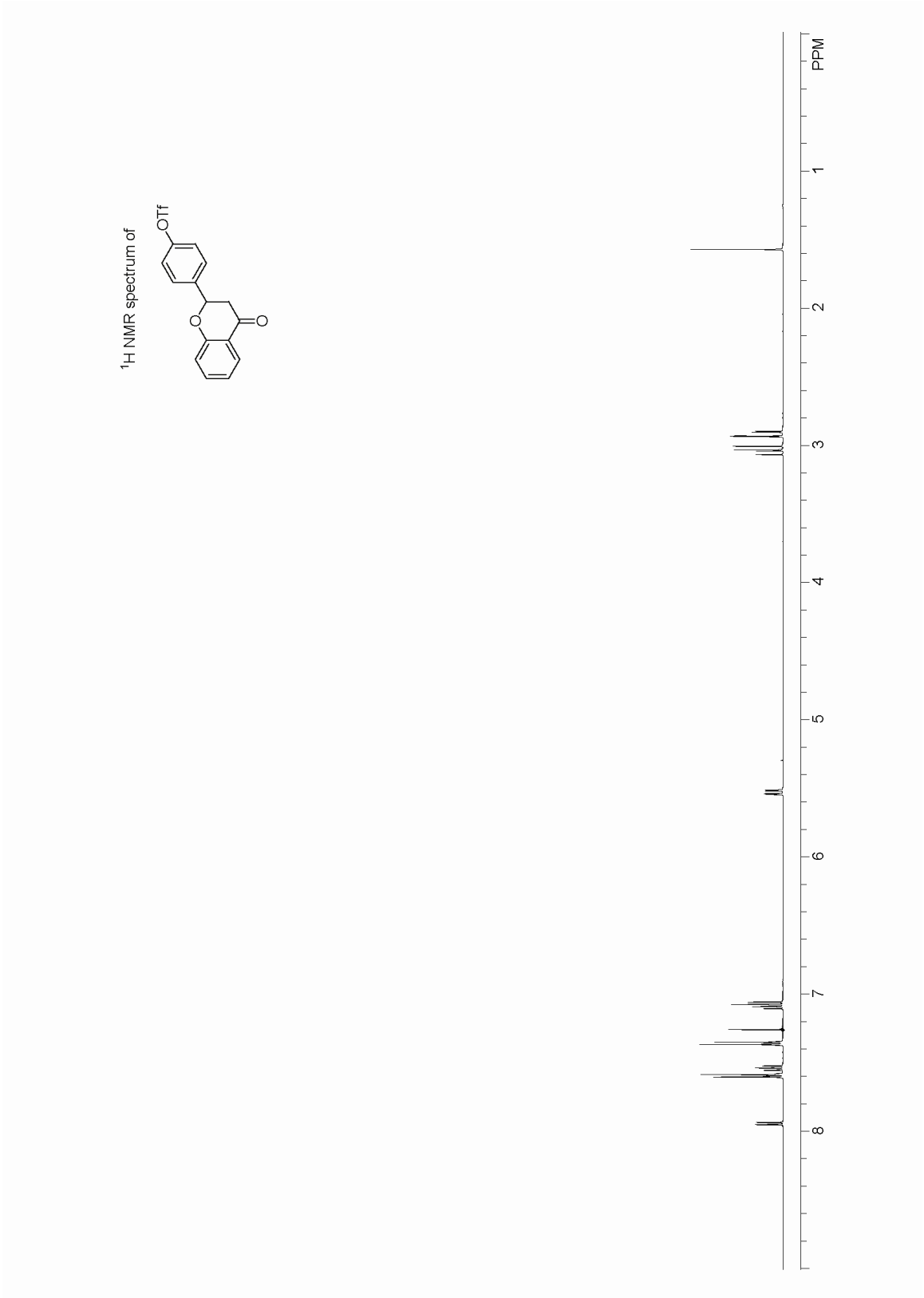
HSQC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **2a**



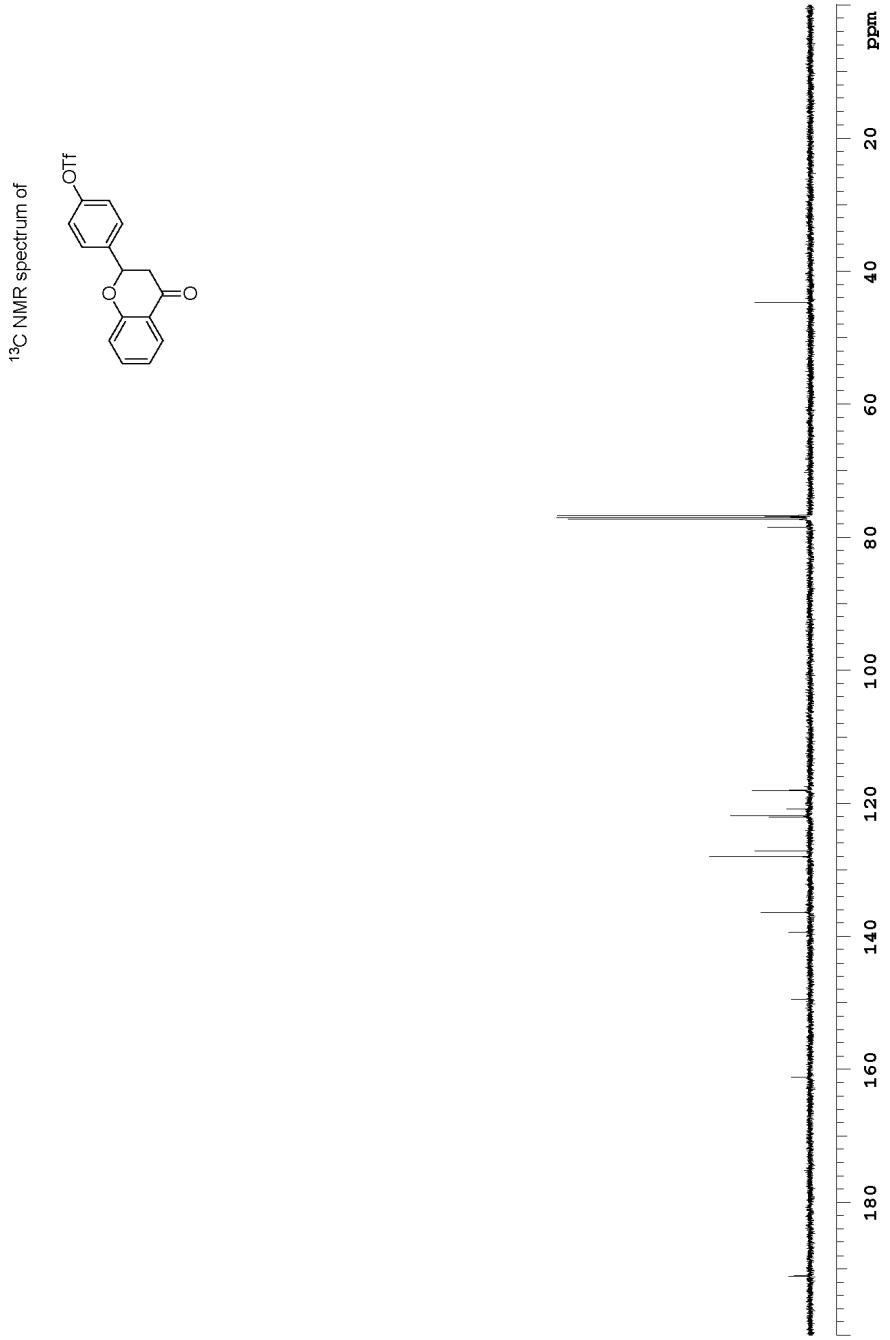
HMBC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **2a**



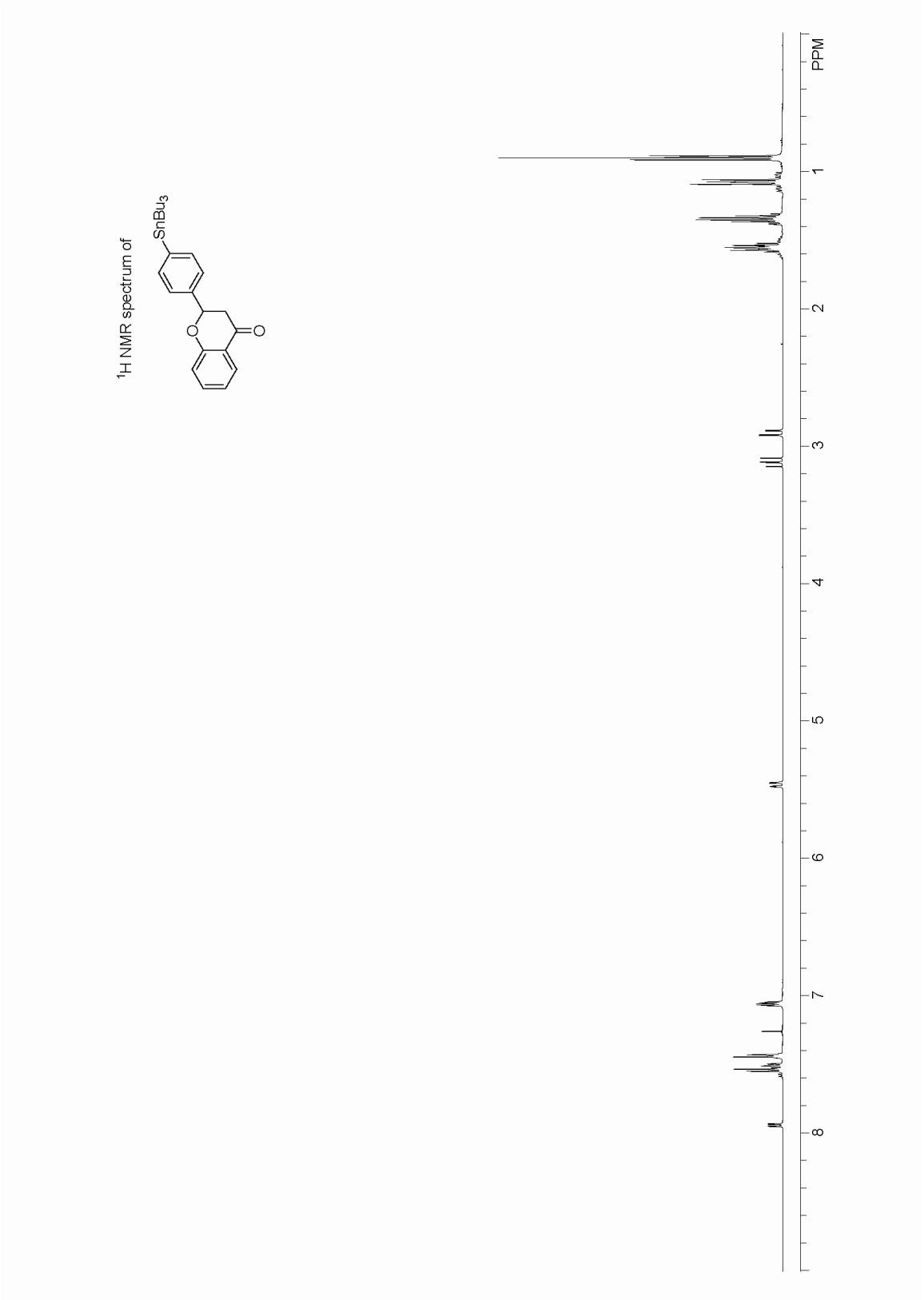
^{19}F NMR spectrum (375 MHz, acetone-d_6, 23 ºC) of (*Z*)-β-fluoropropene



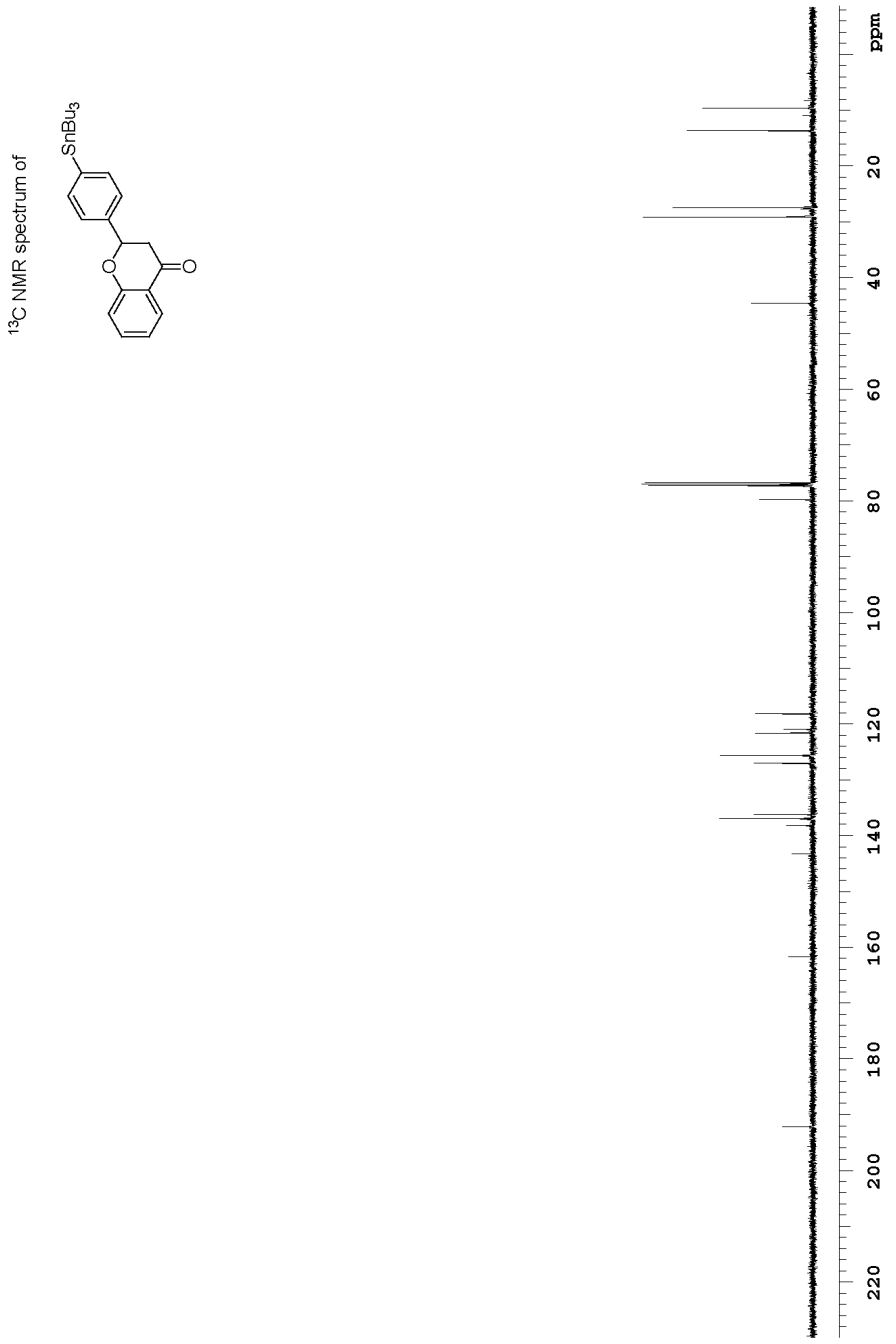
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S7**



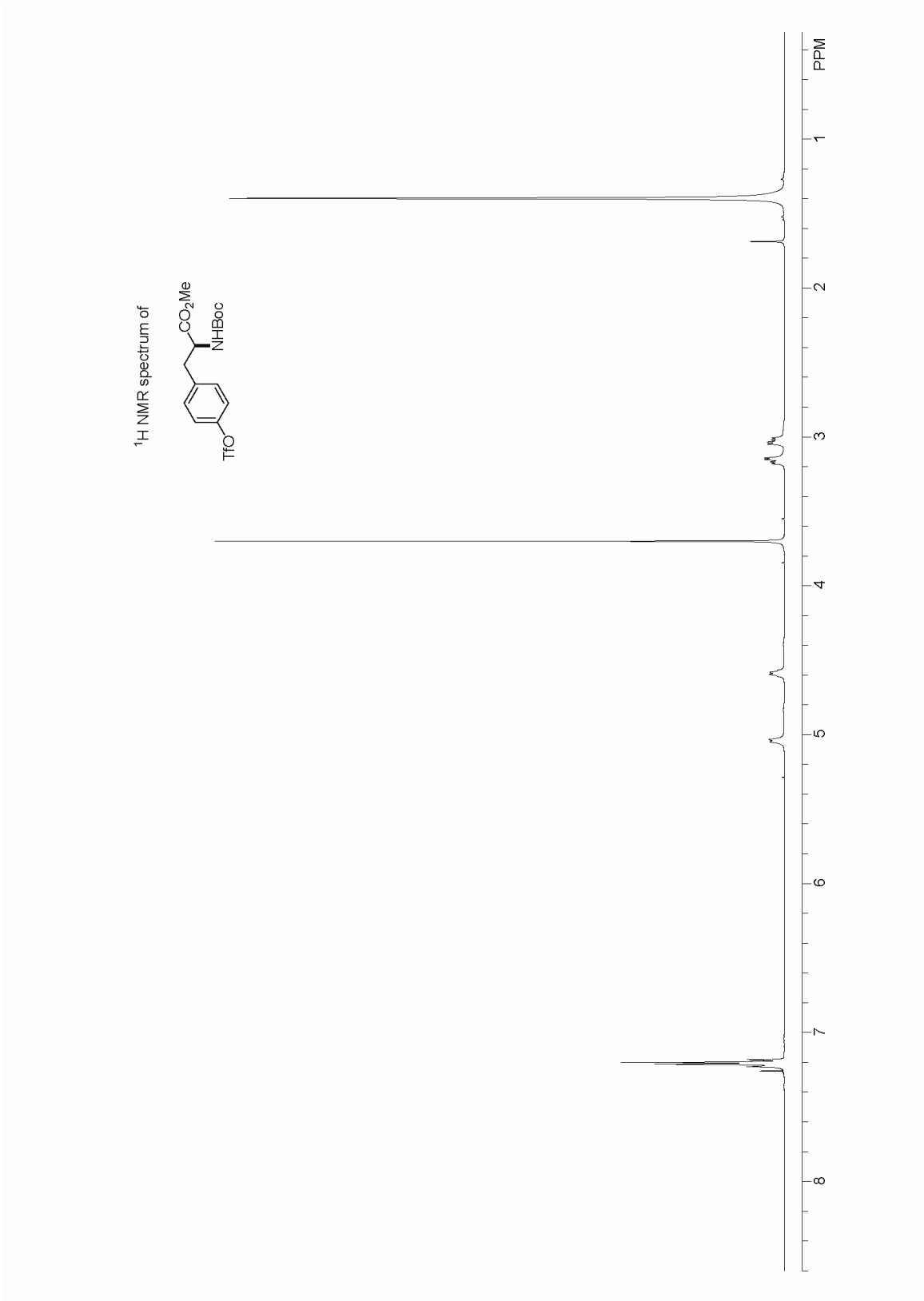
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S7**



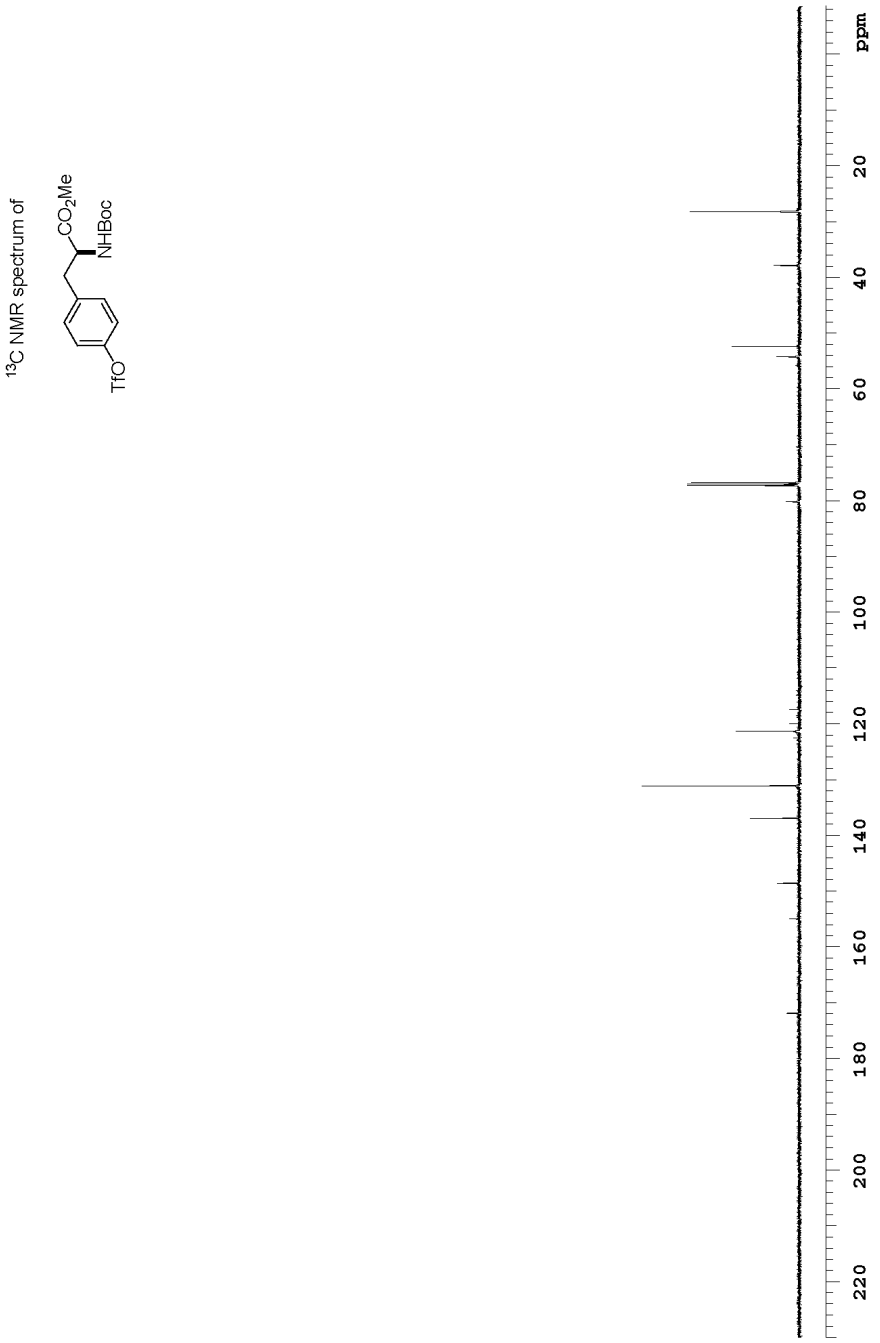
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S8**



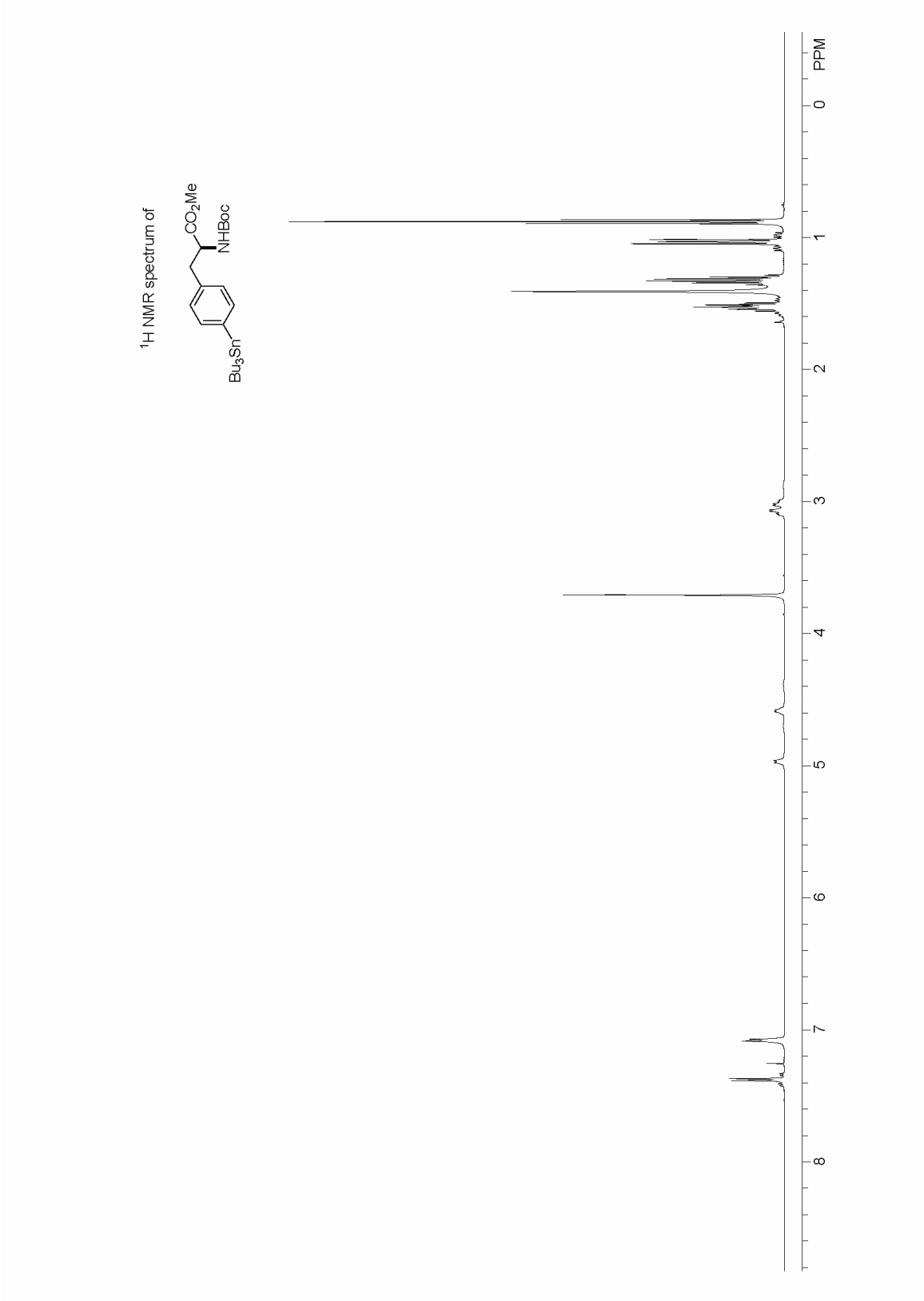
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S8**



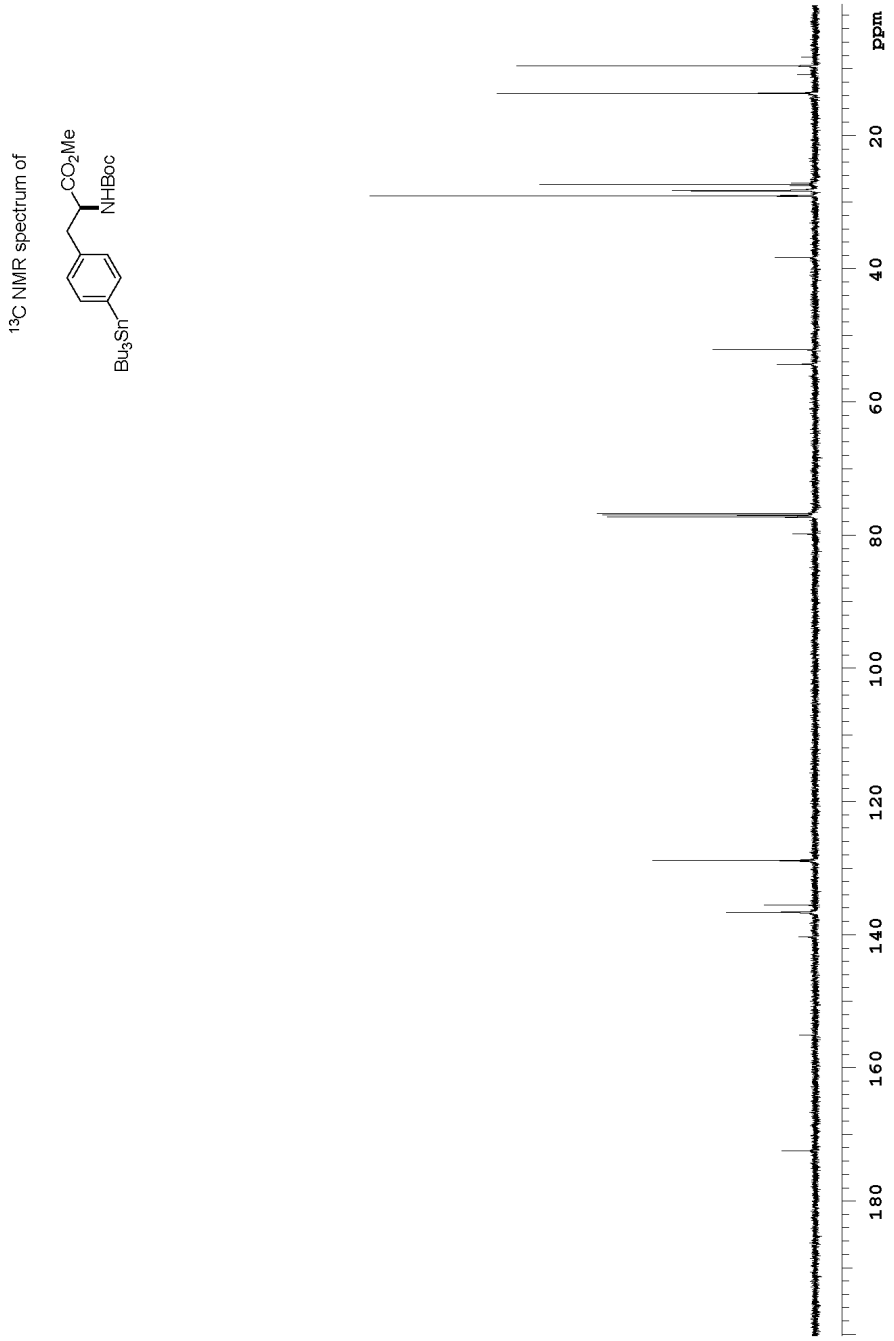
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S9**



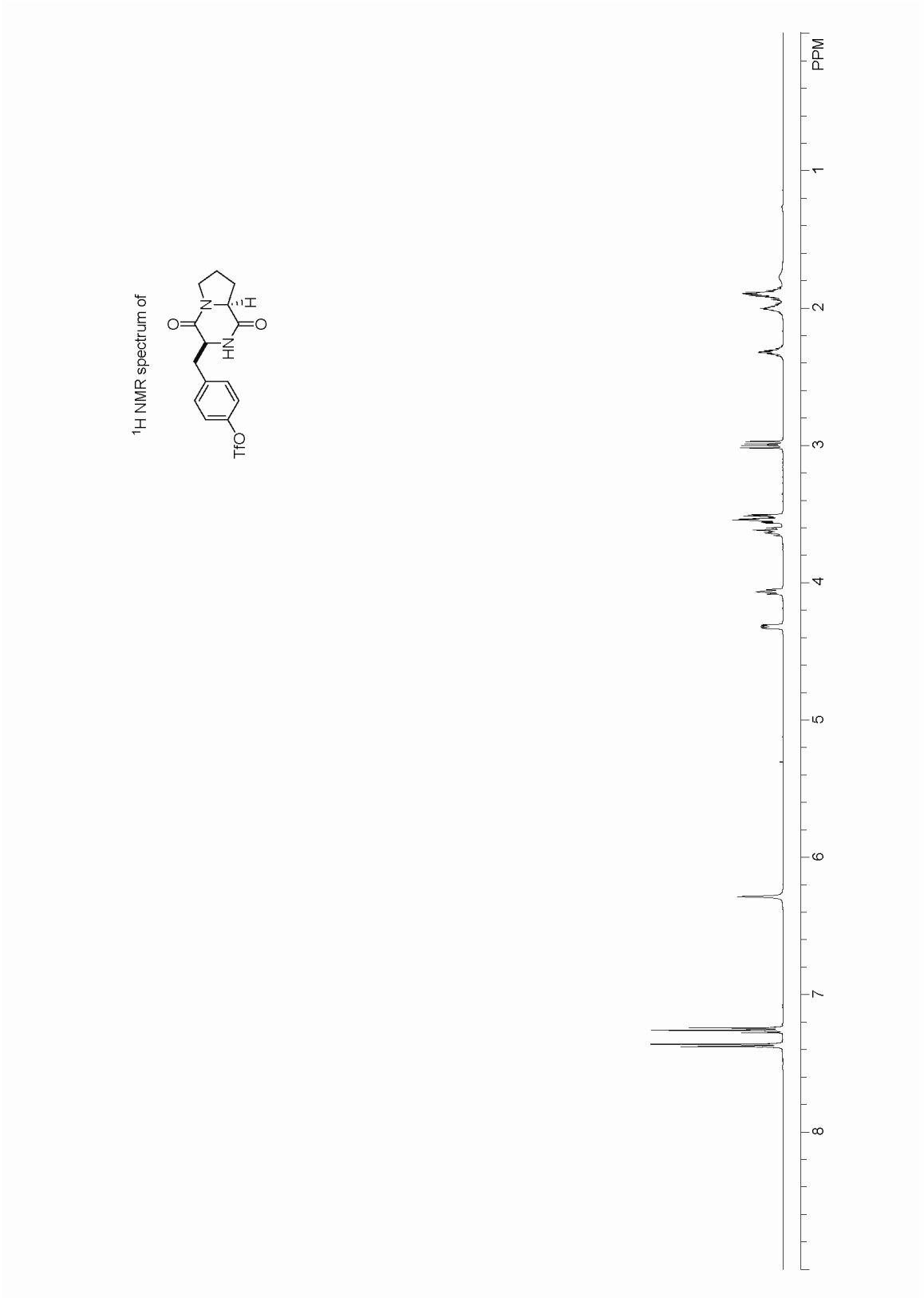
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S9**



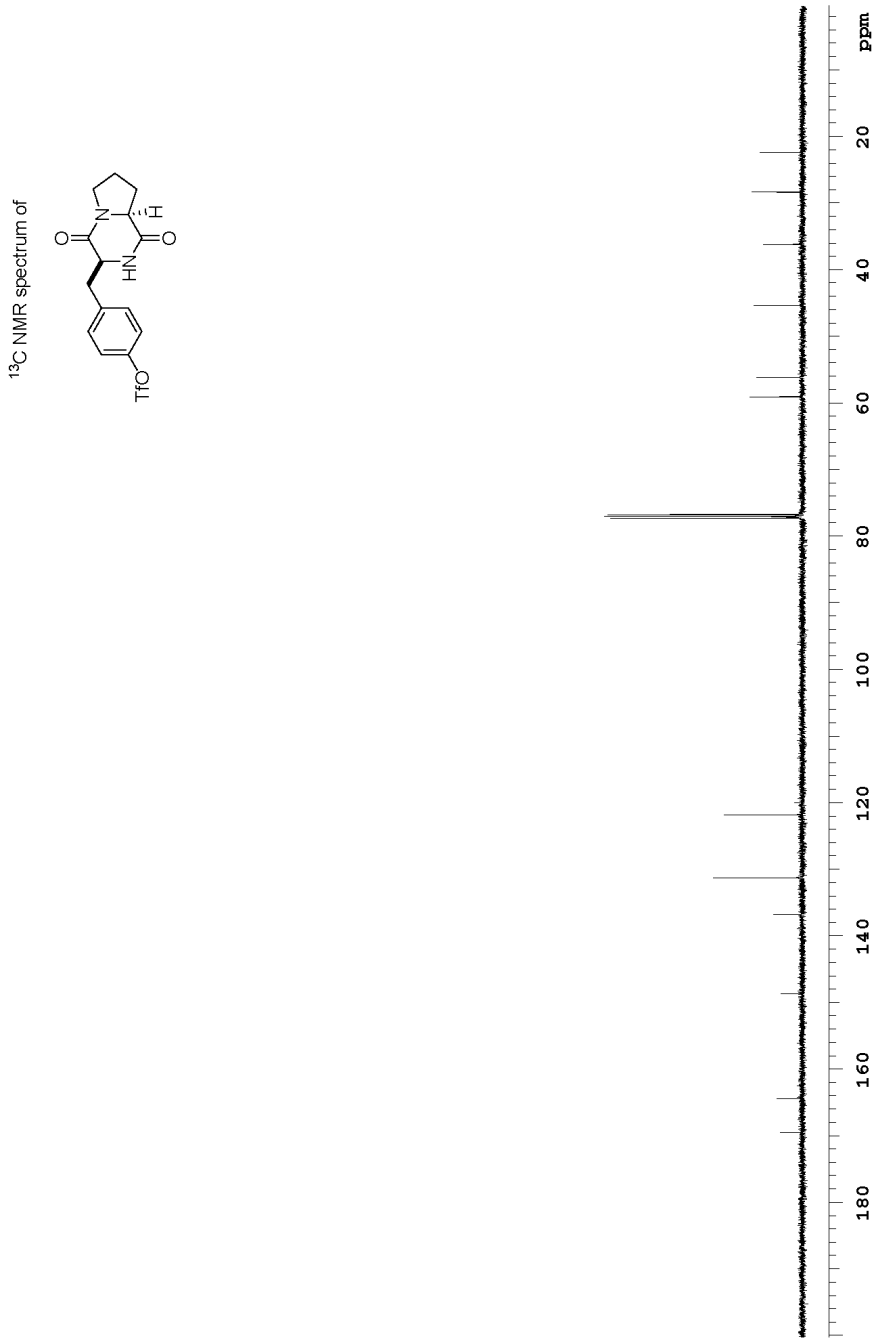
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S10**



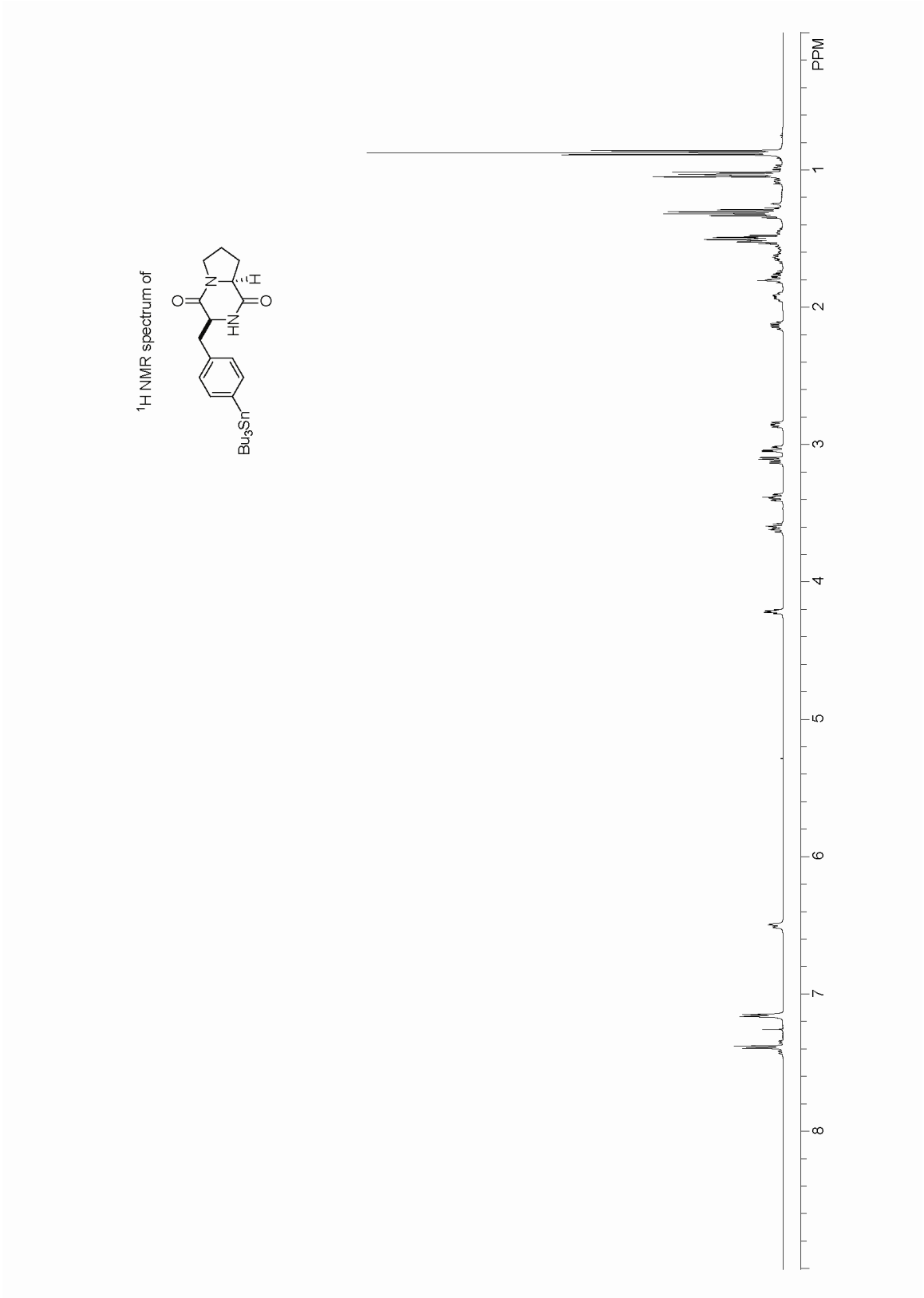
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S10**



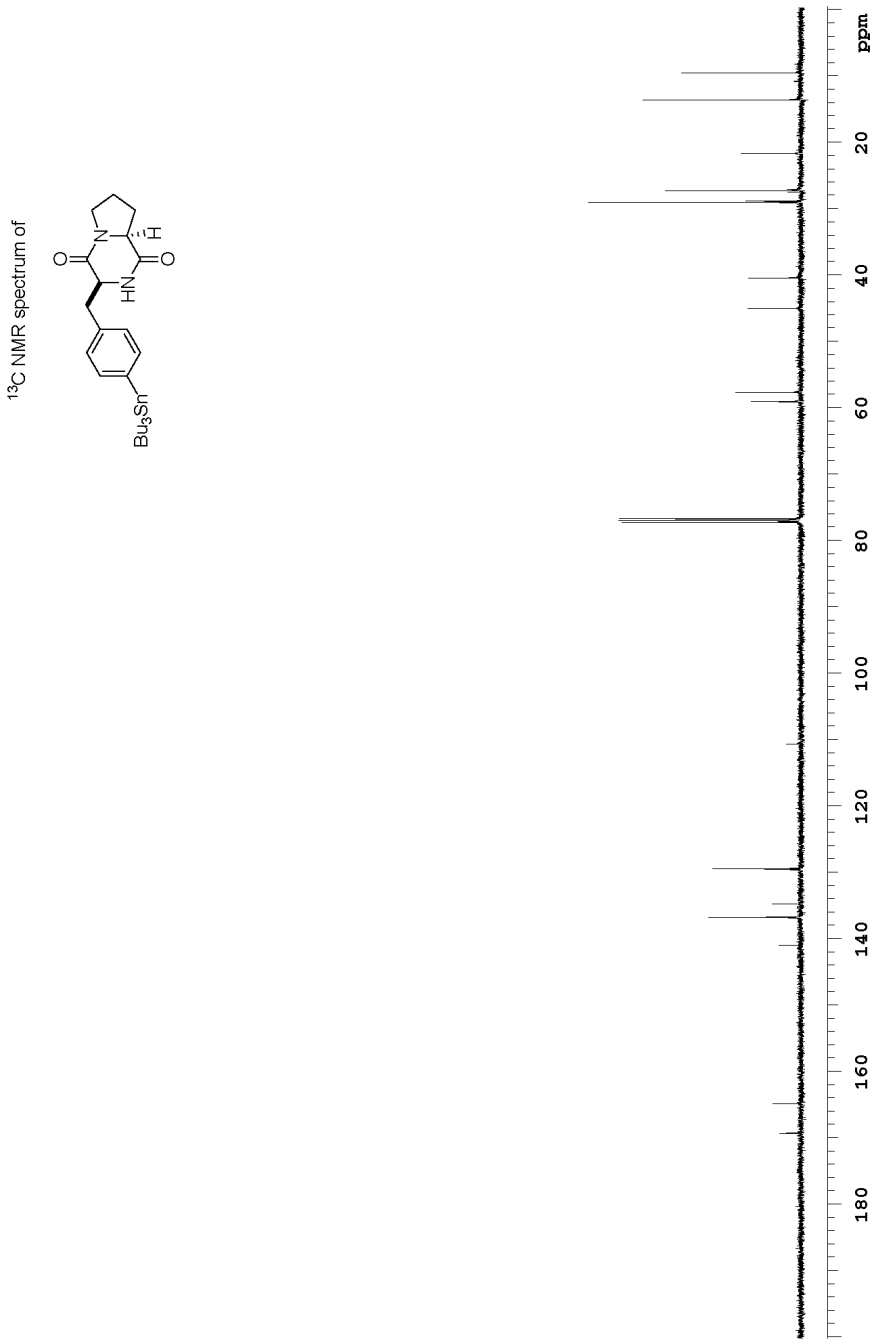
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S11**



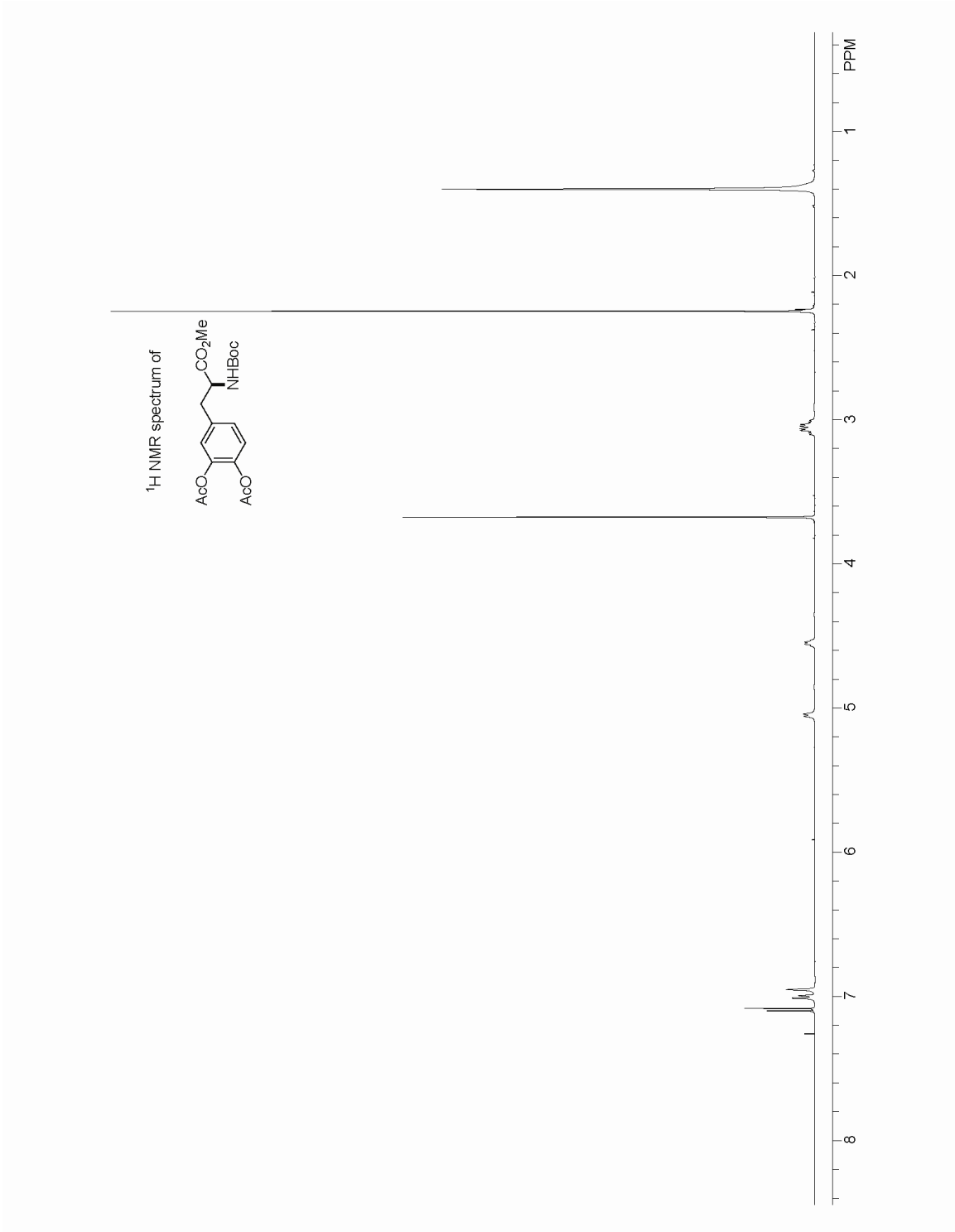
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S11**



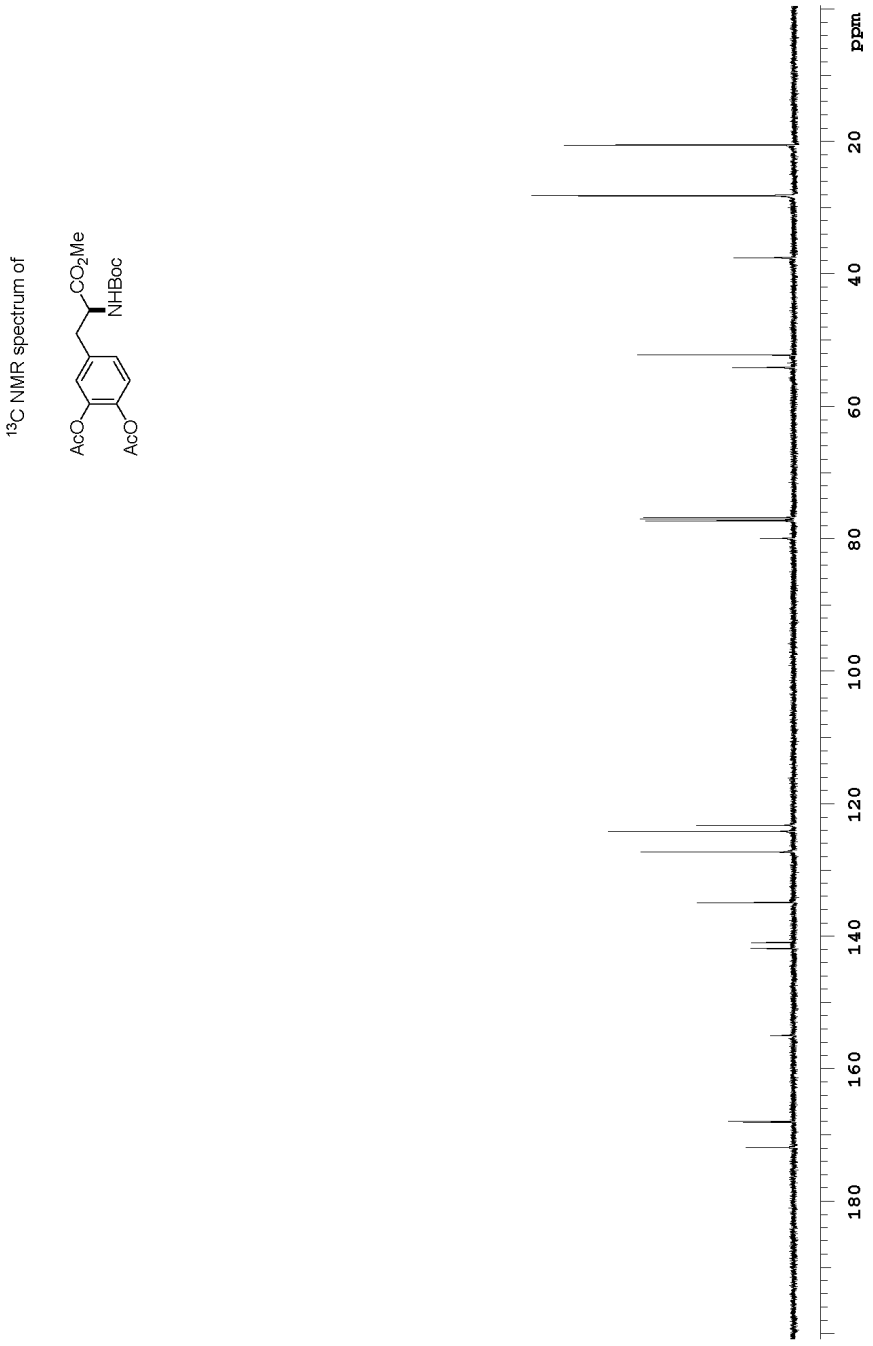
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S12**



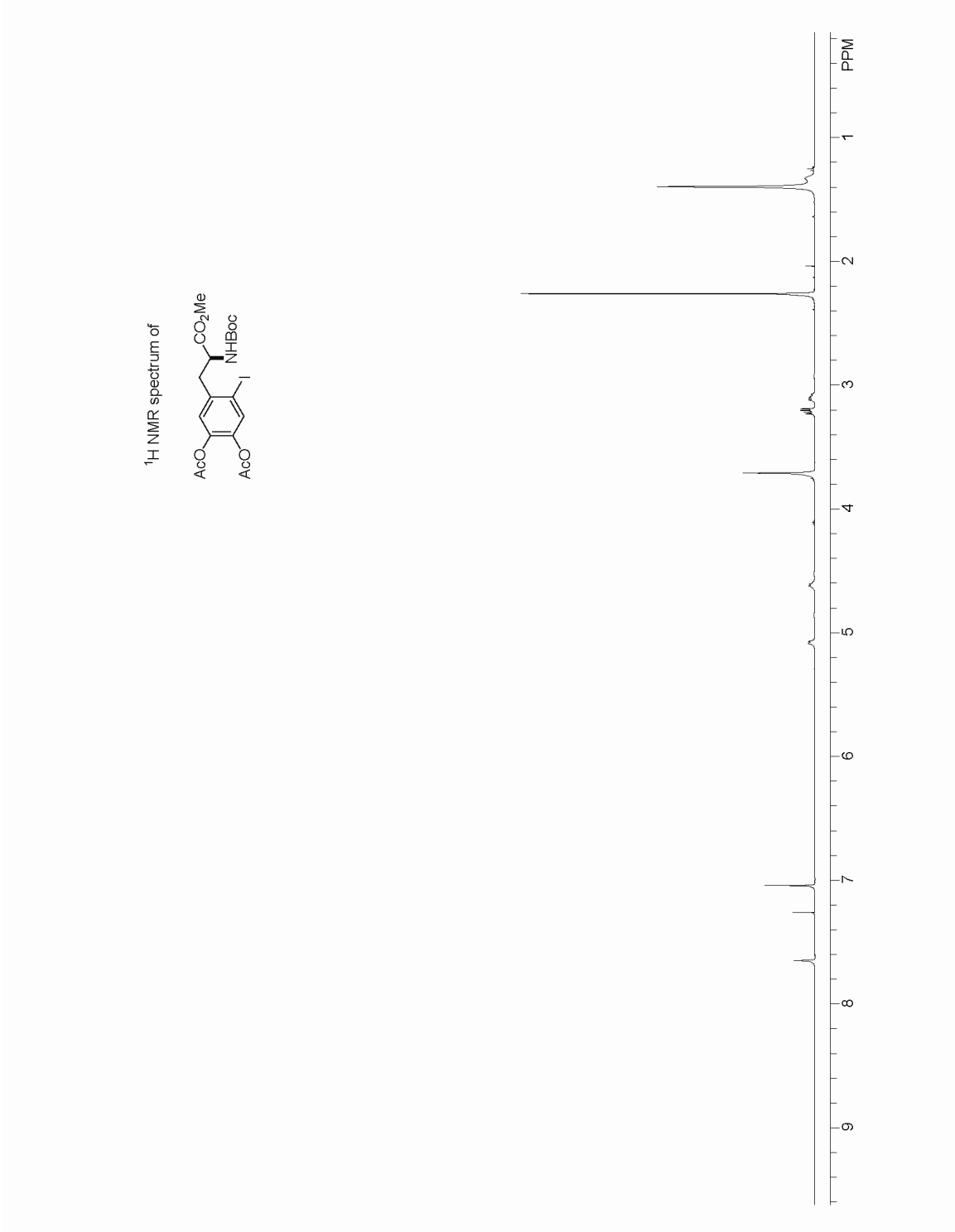
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S12**



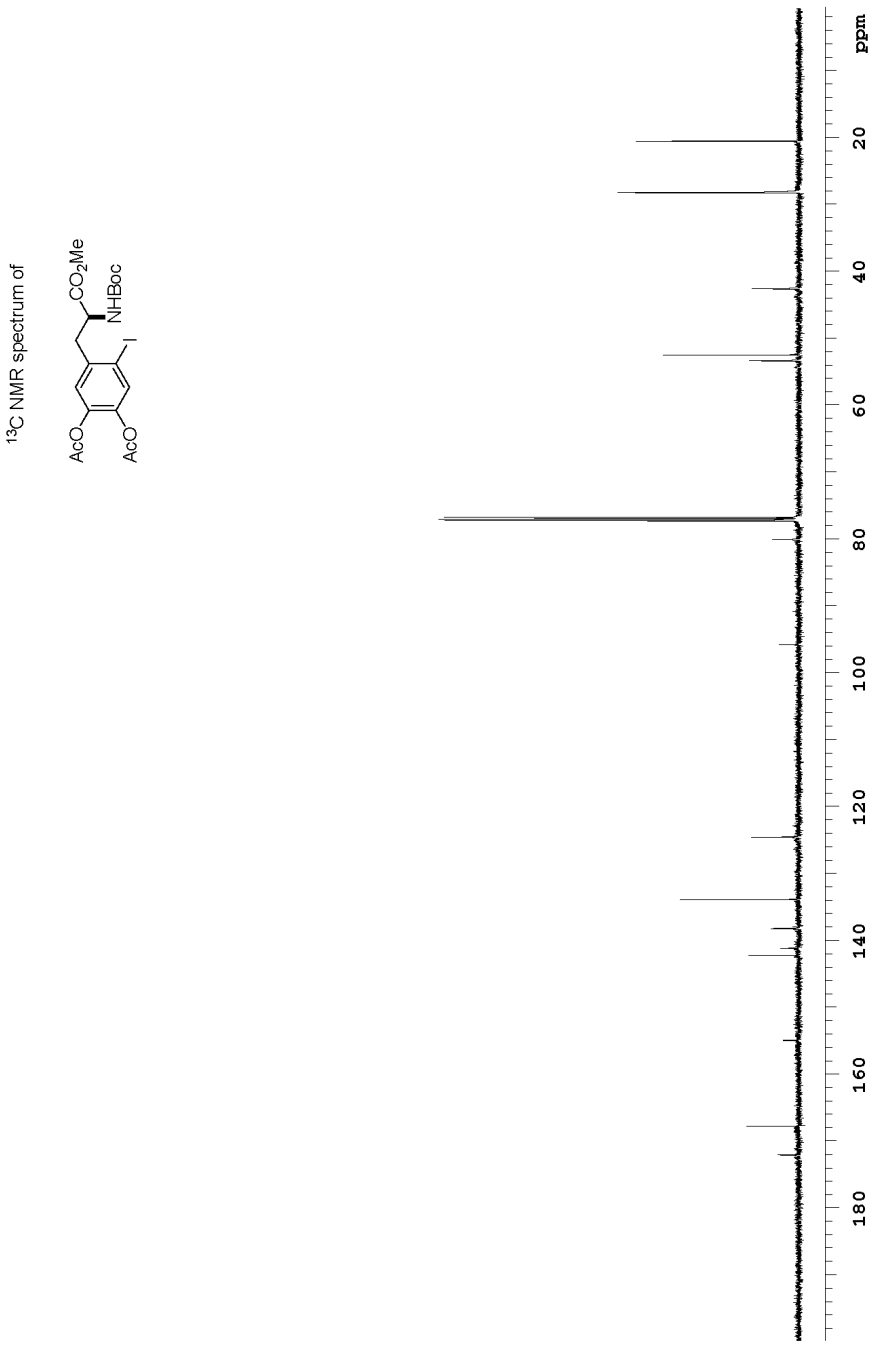
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S14**



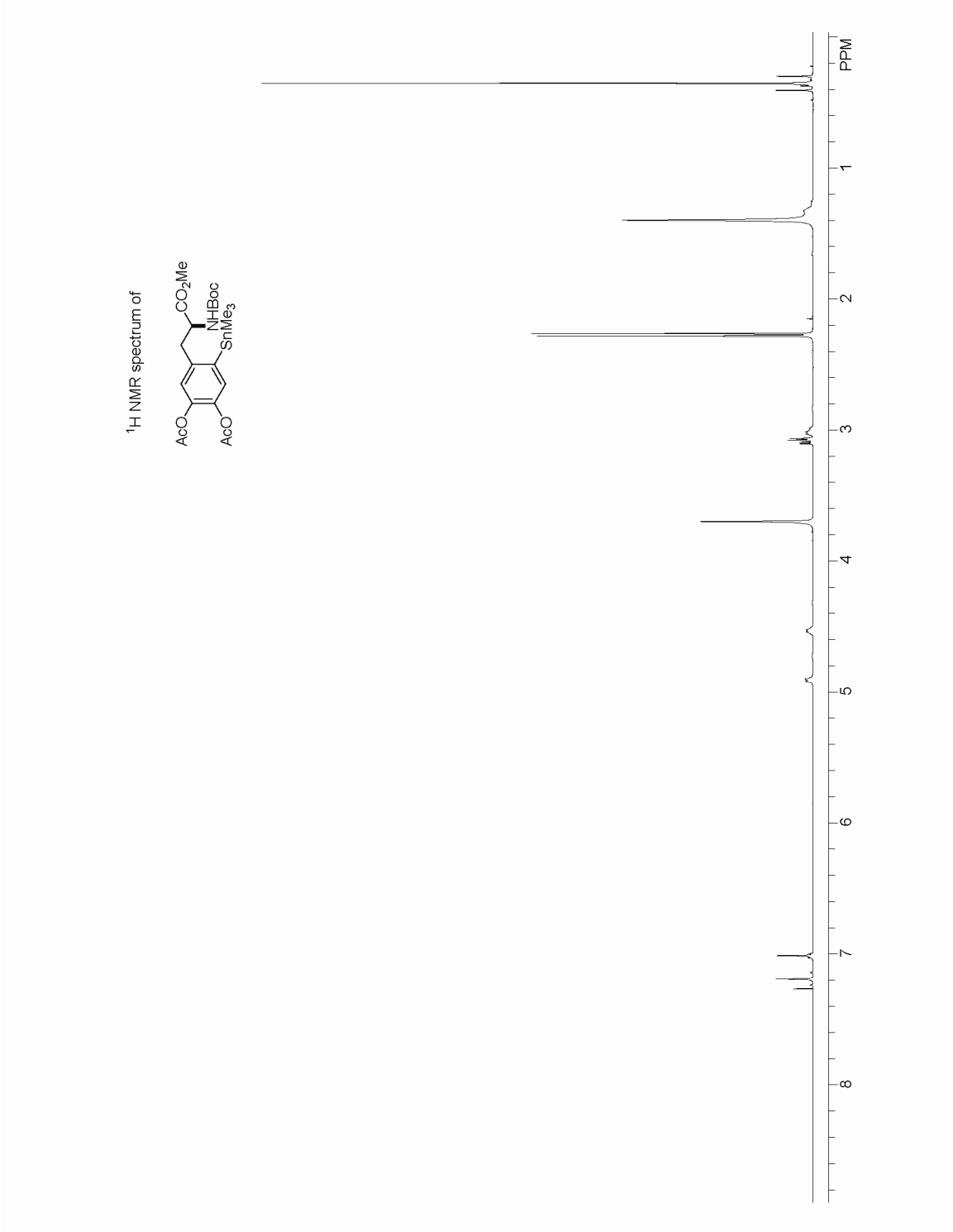
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S14**



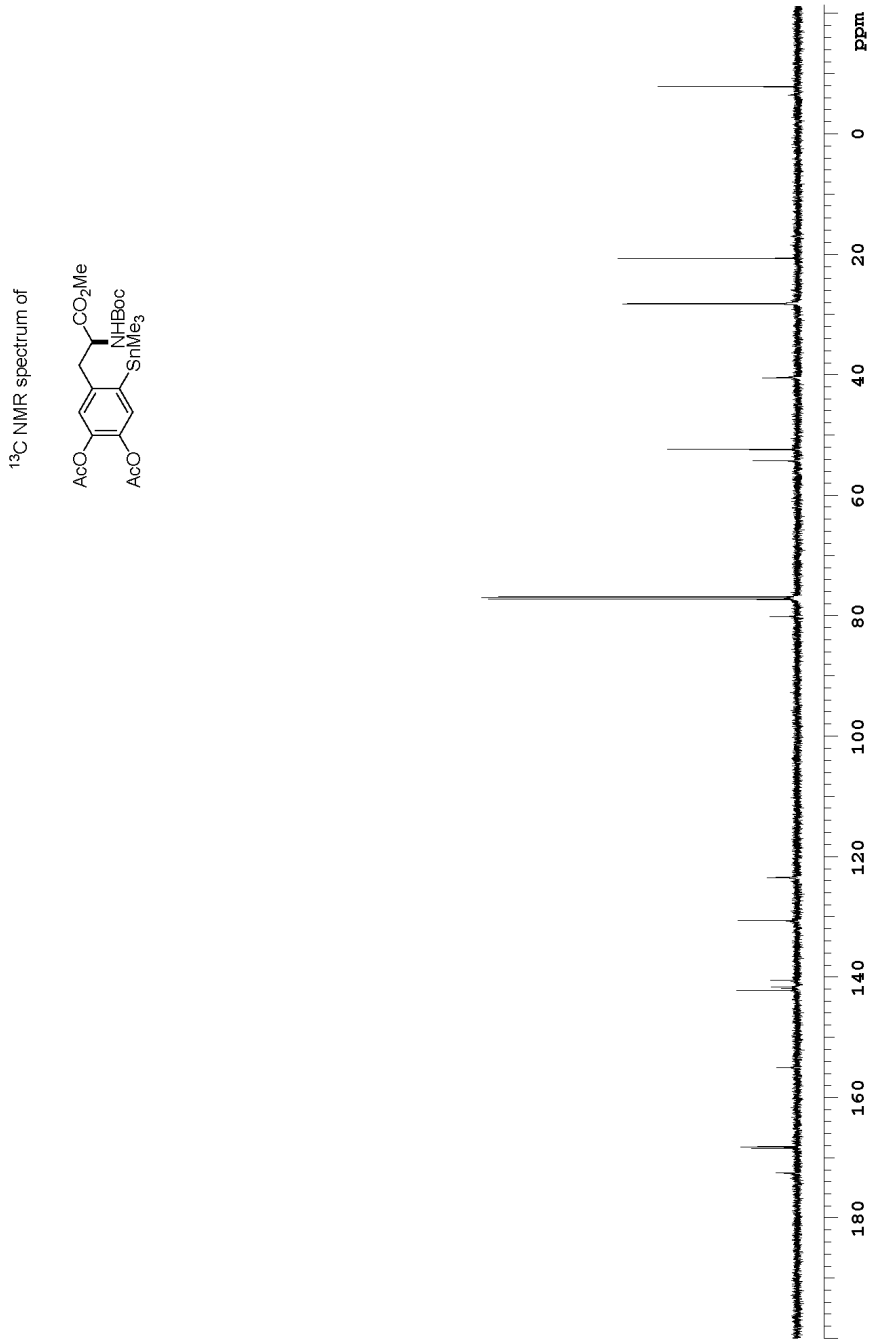
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S15**



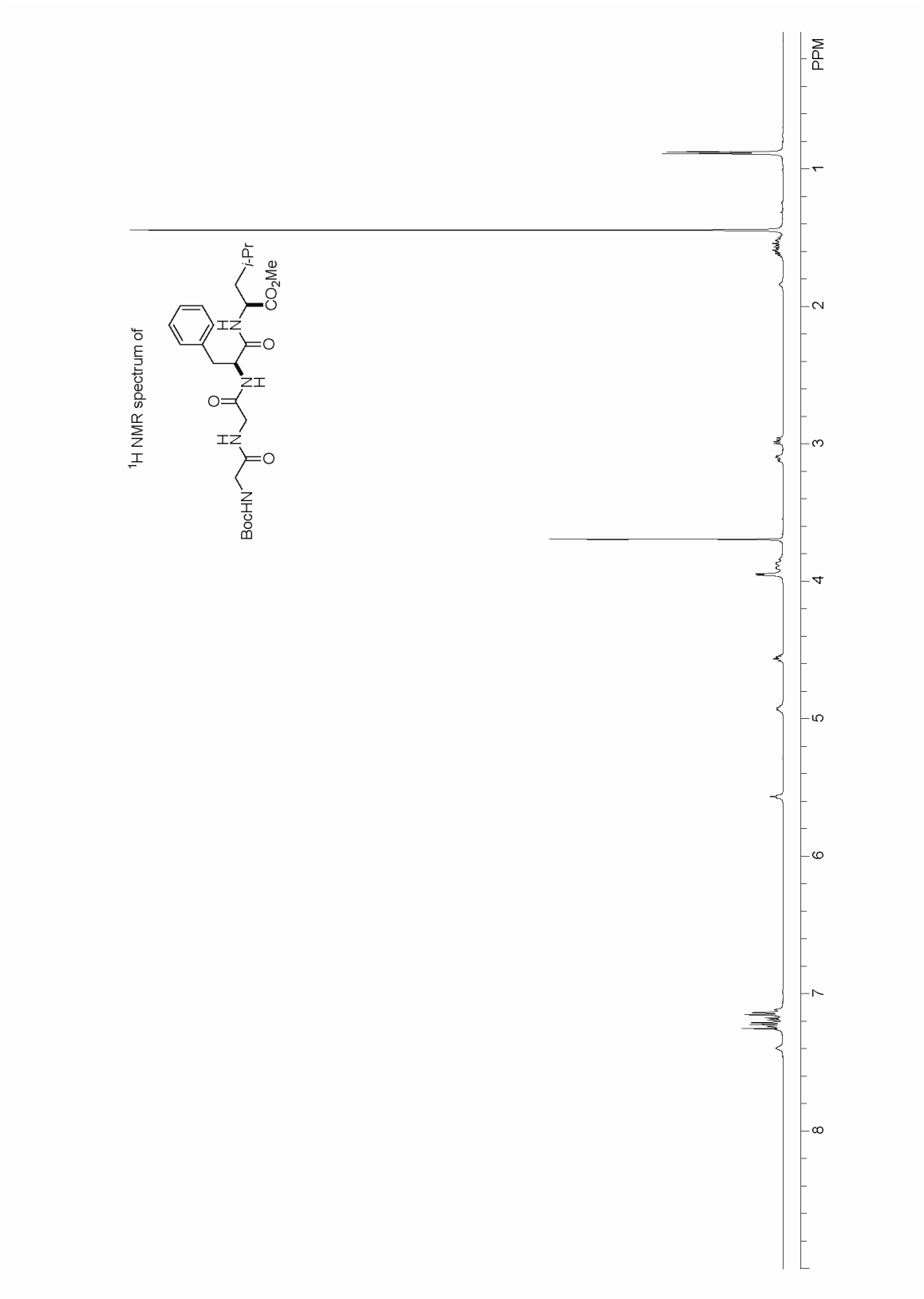
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S15**



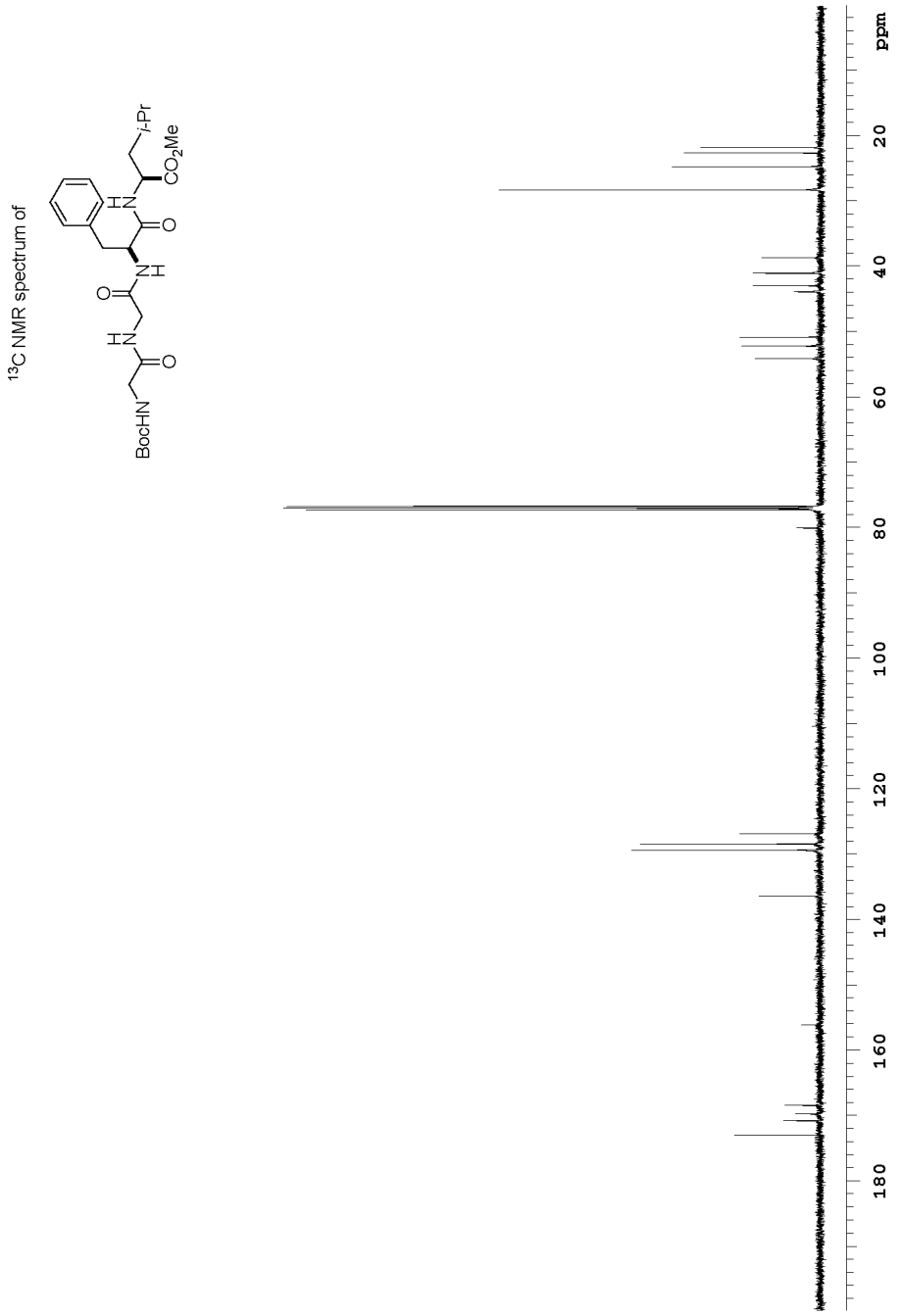
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S16**



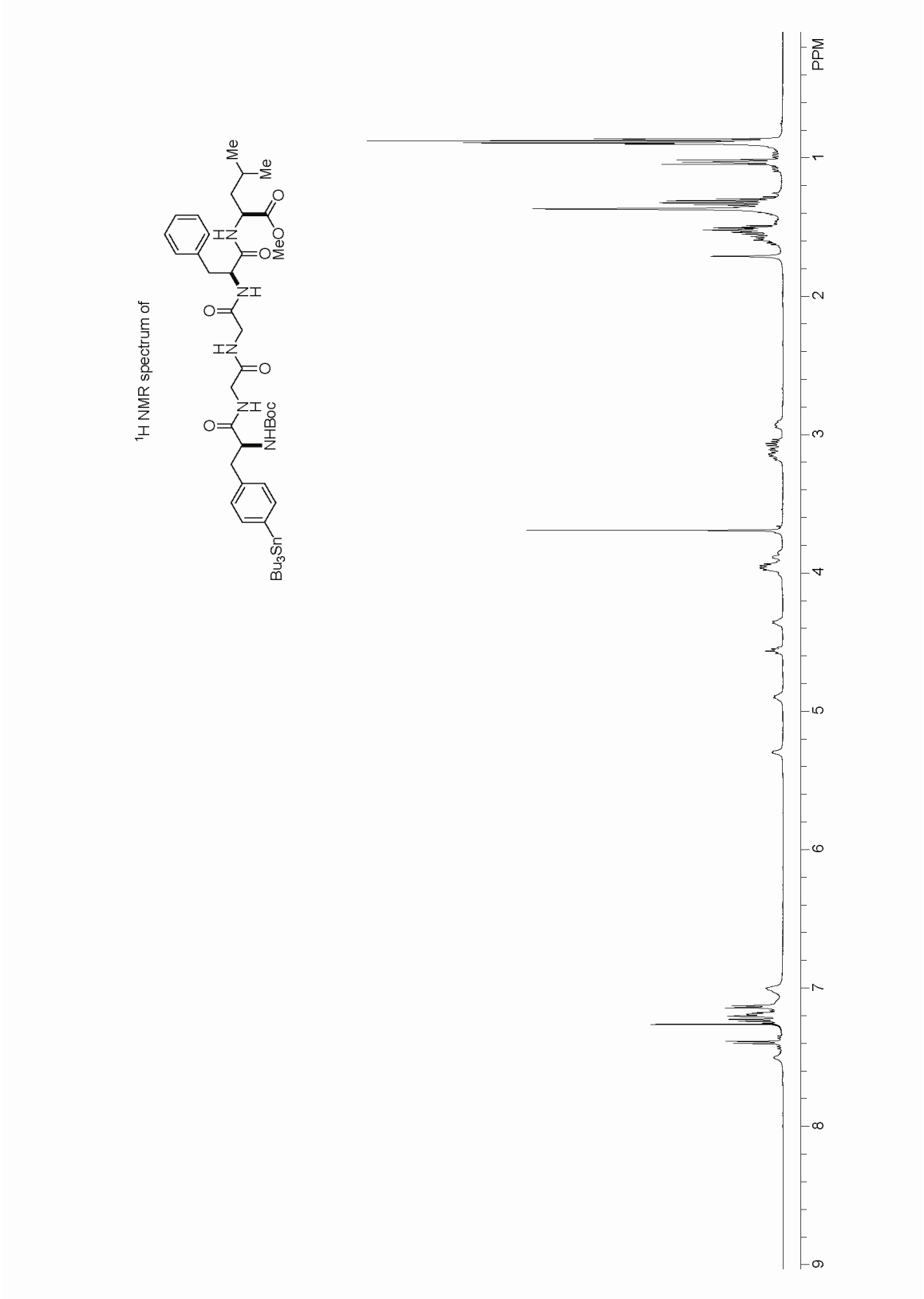
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S16**



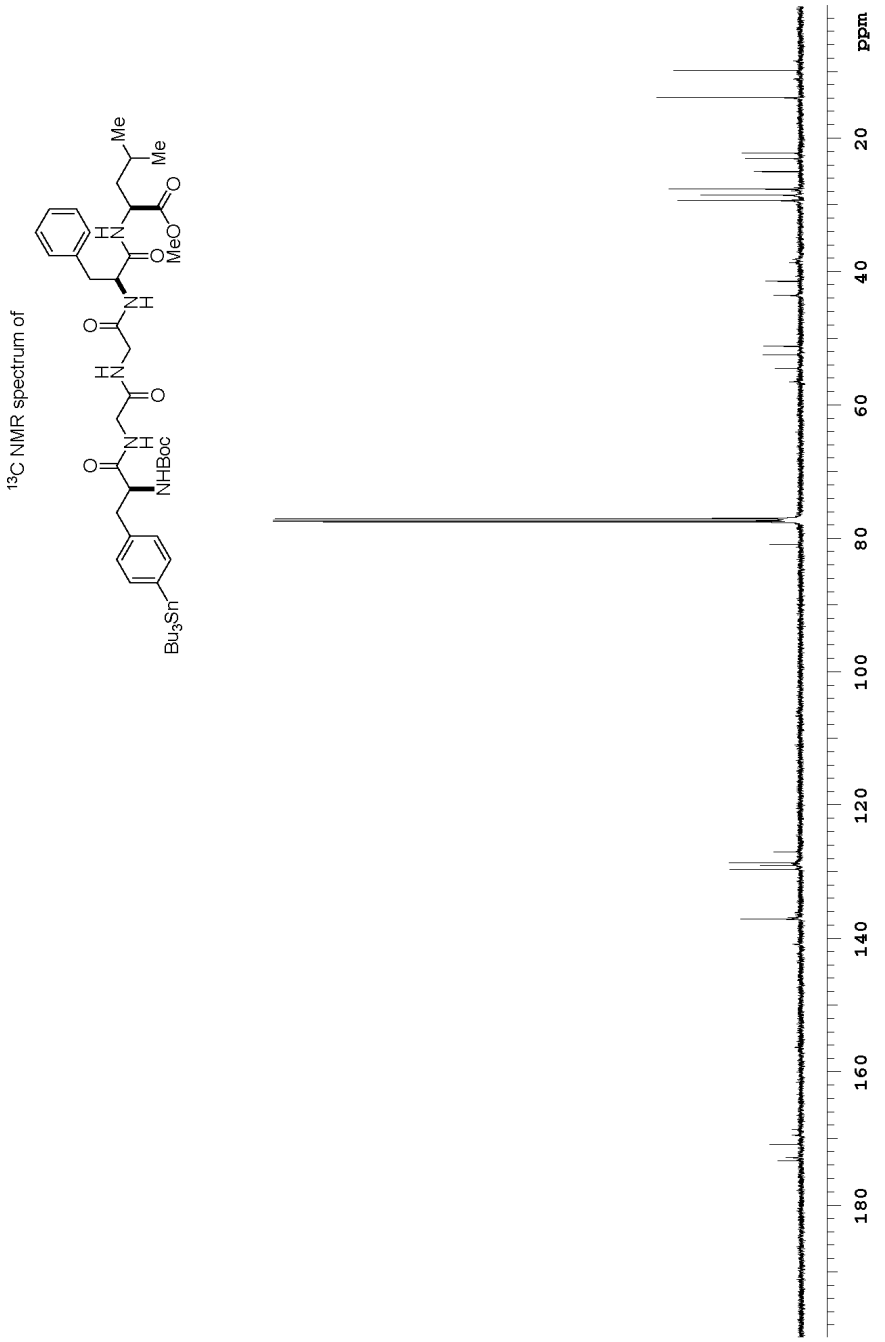
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S19**



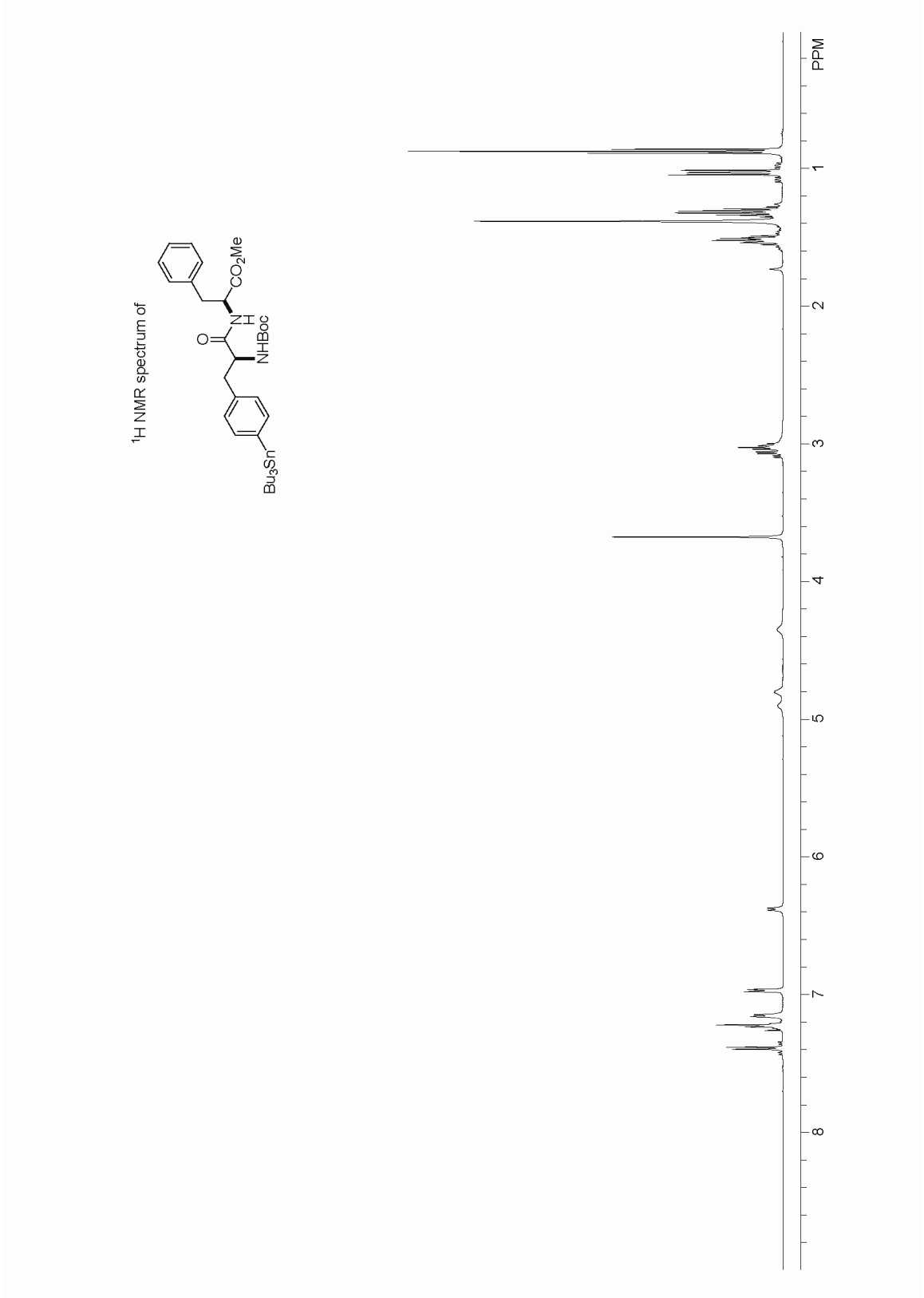
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S19**



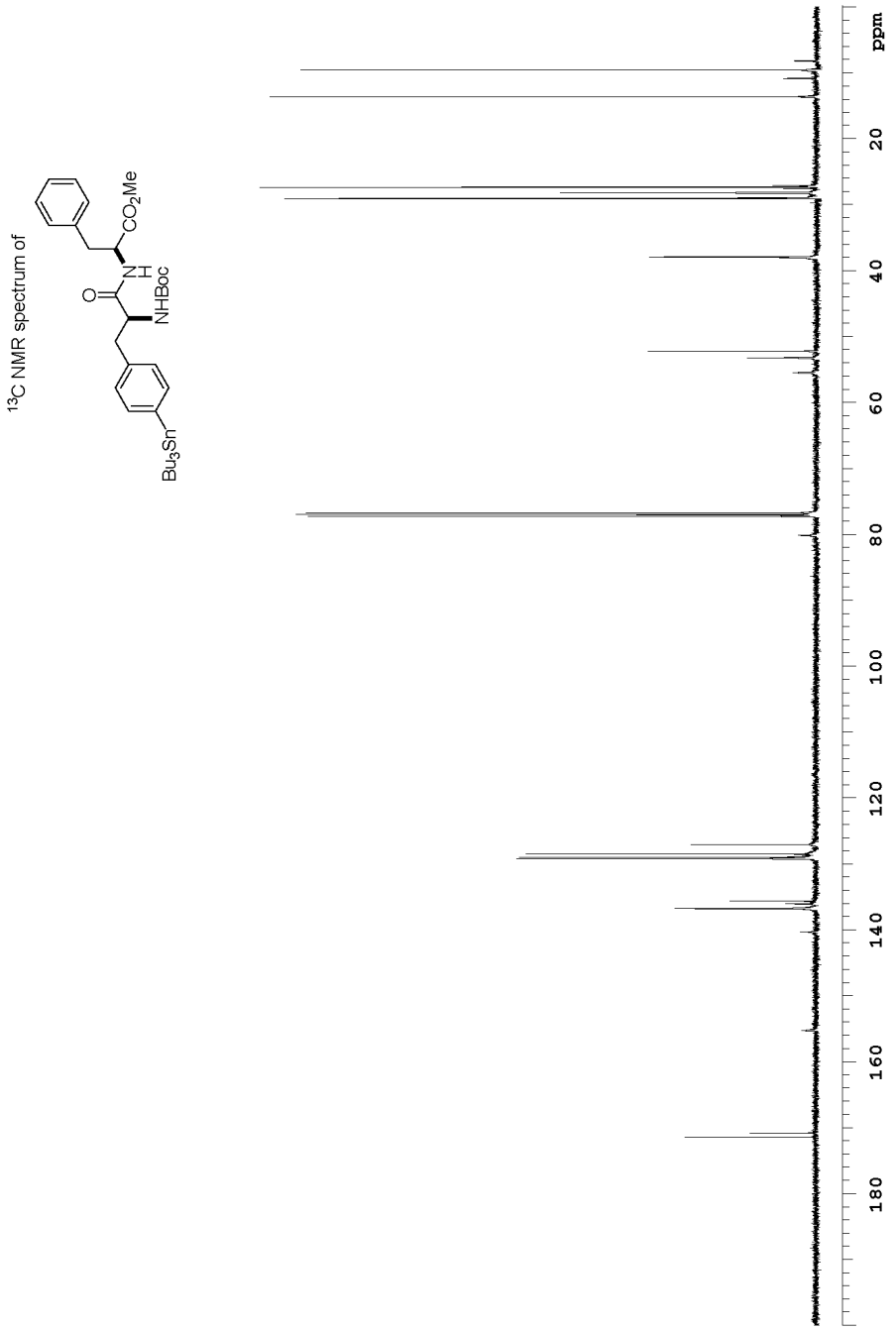
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S20**



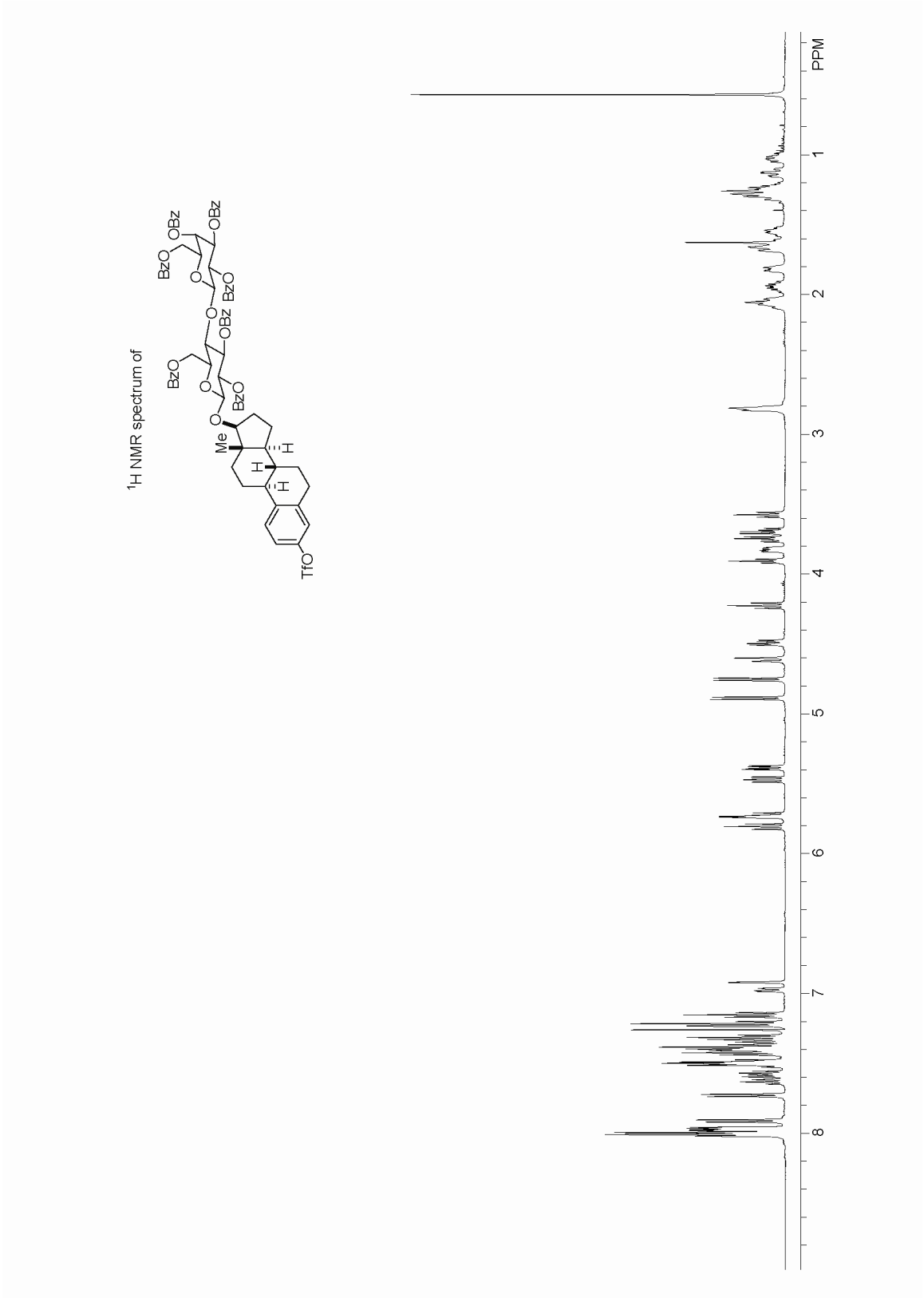
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S20**



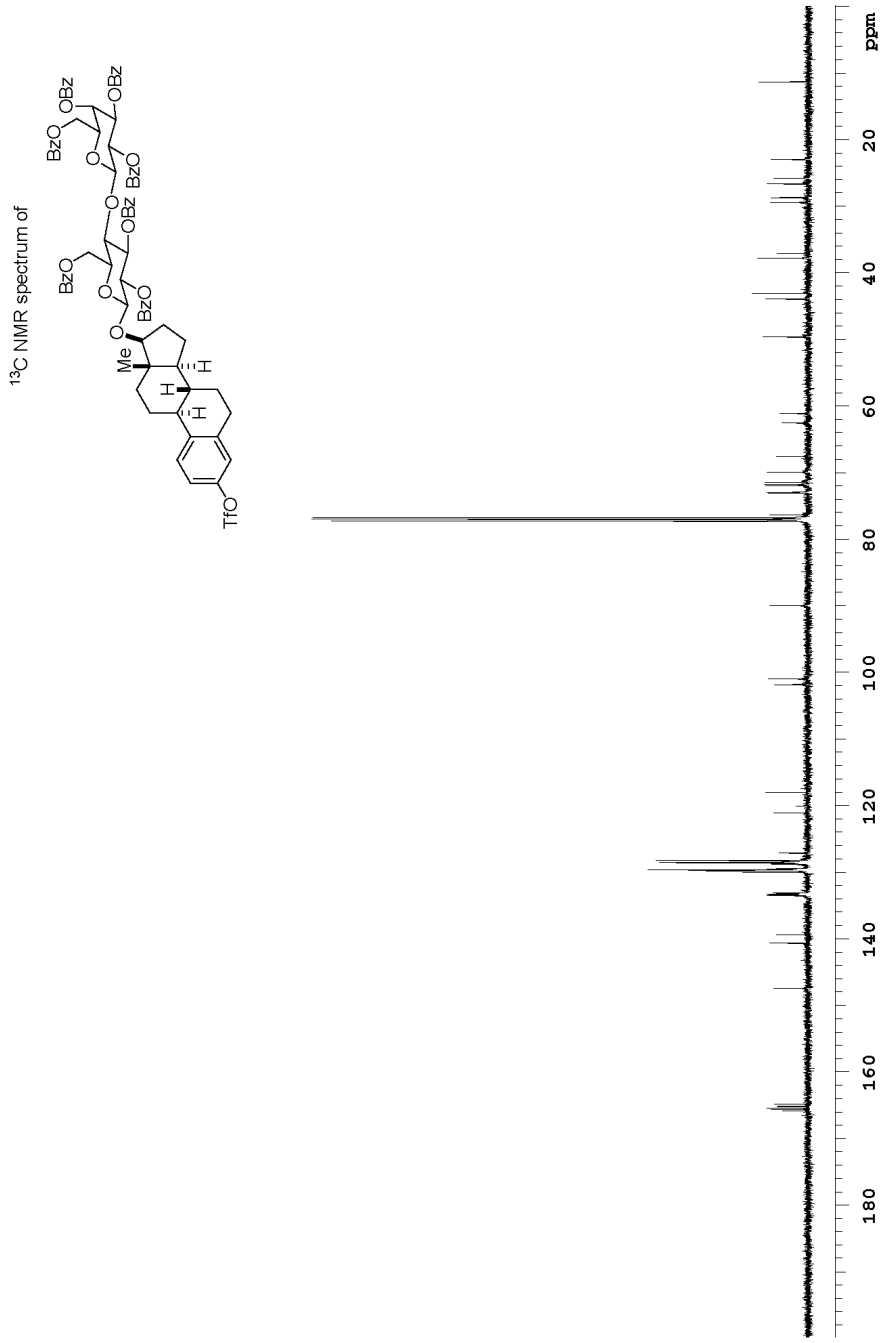
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S21**



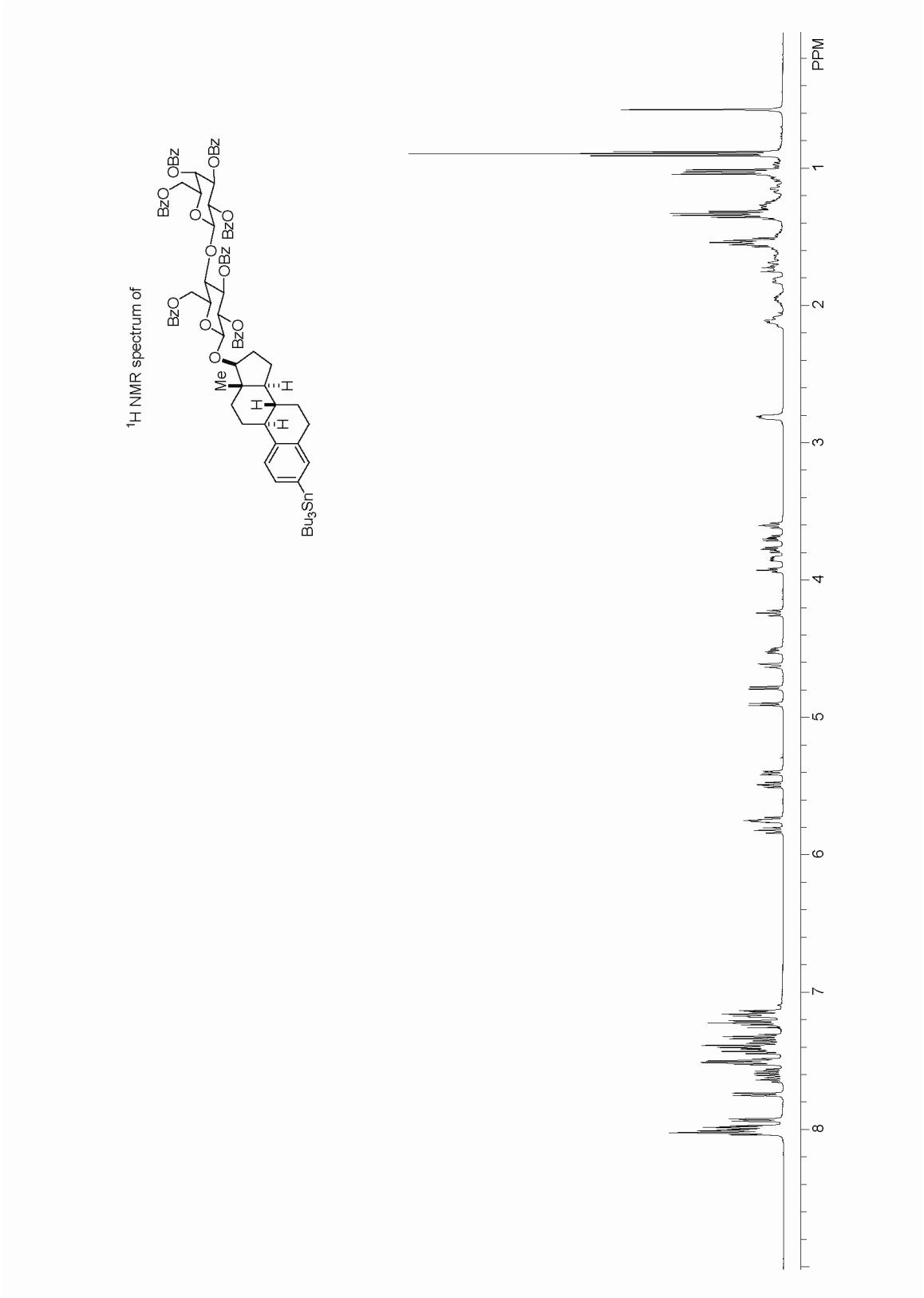
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S21**



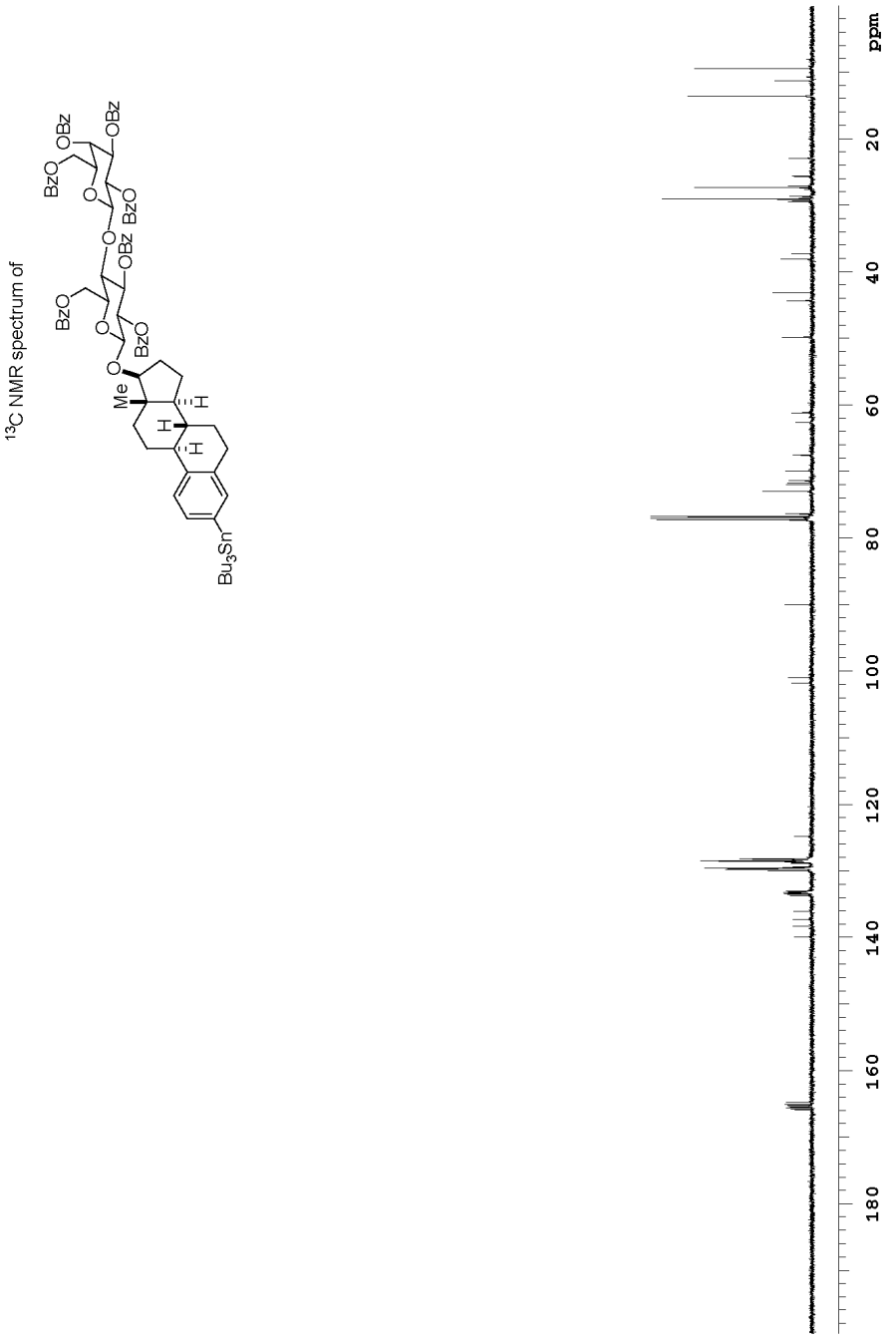
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S23**



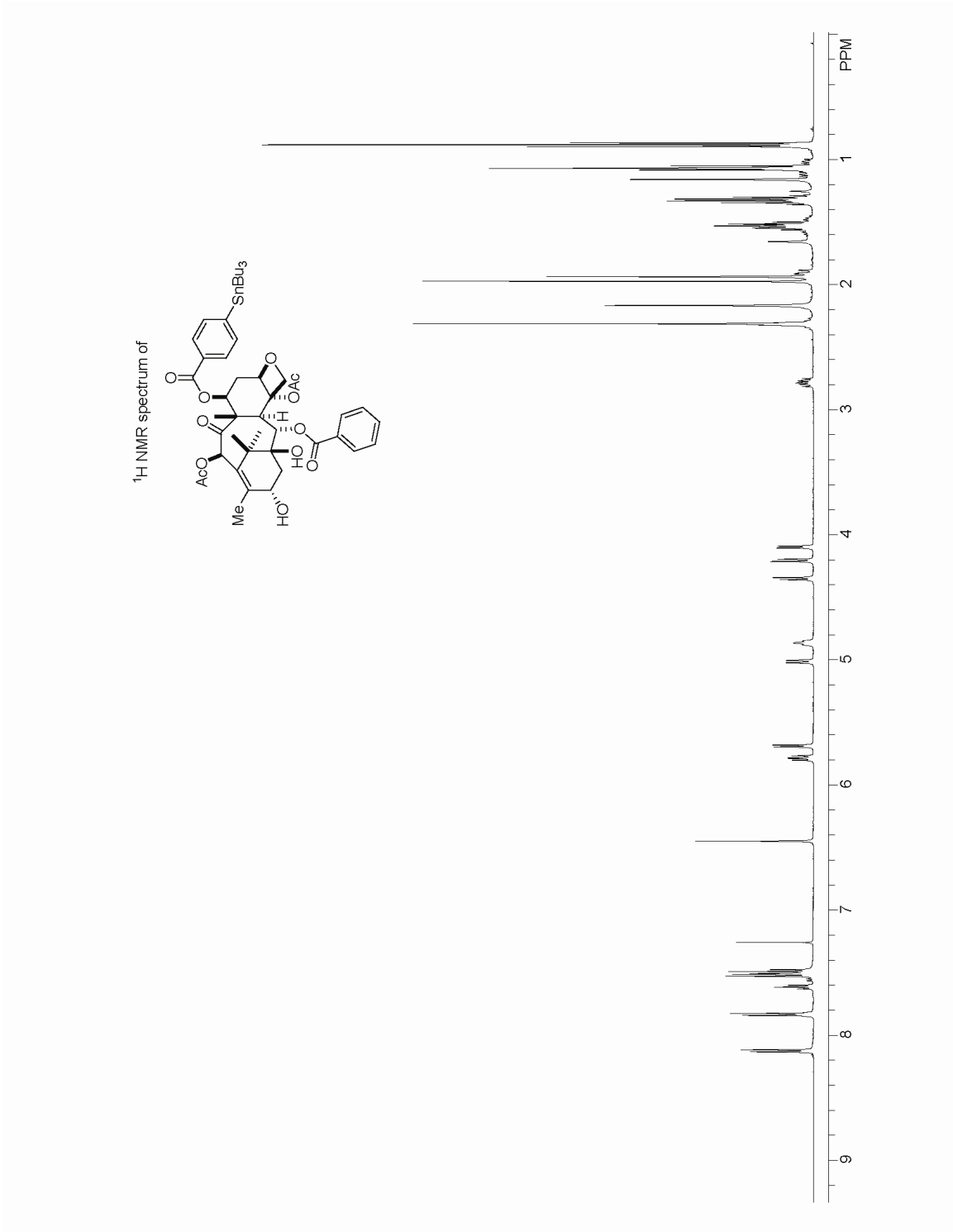
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S23**



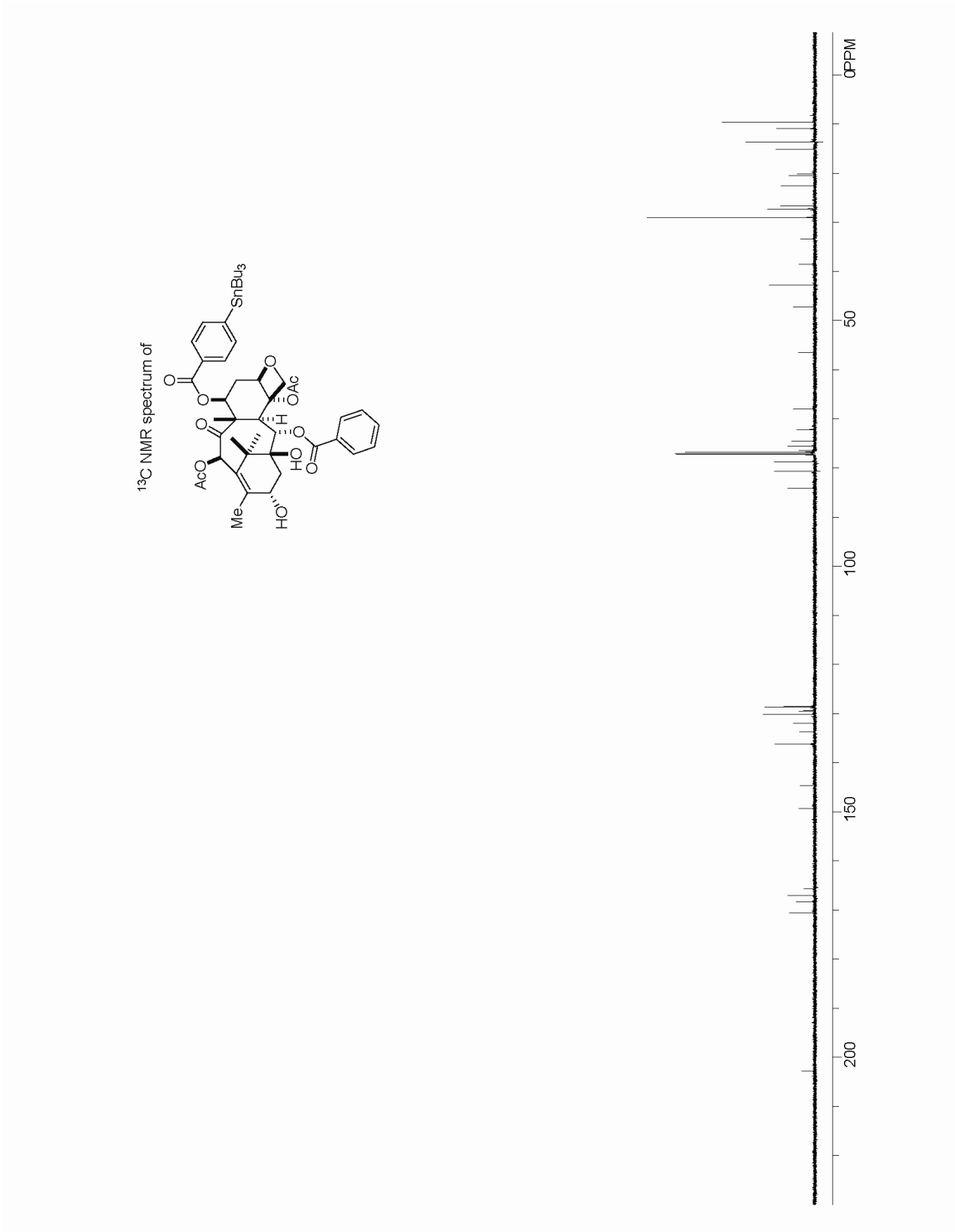
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S24**



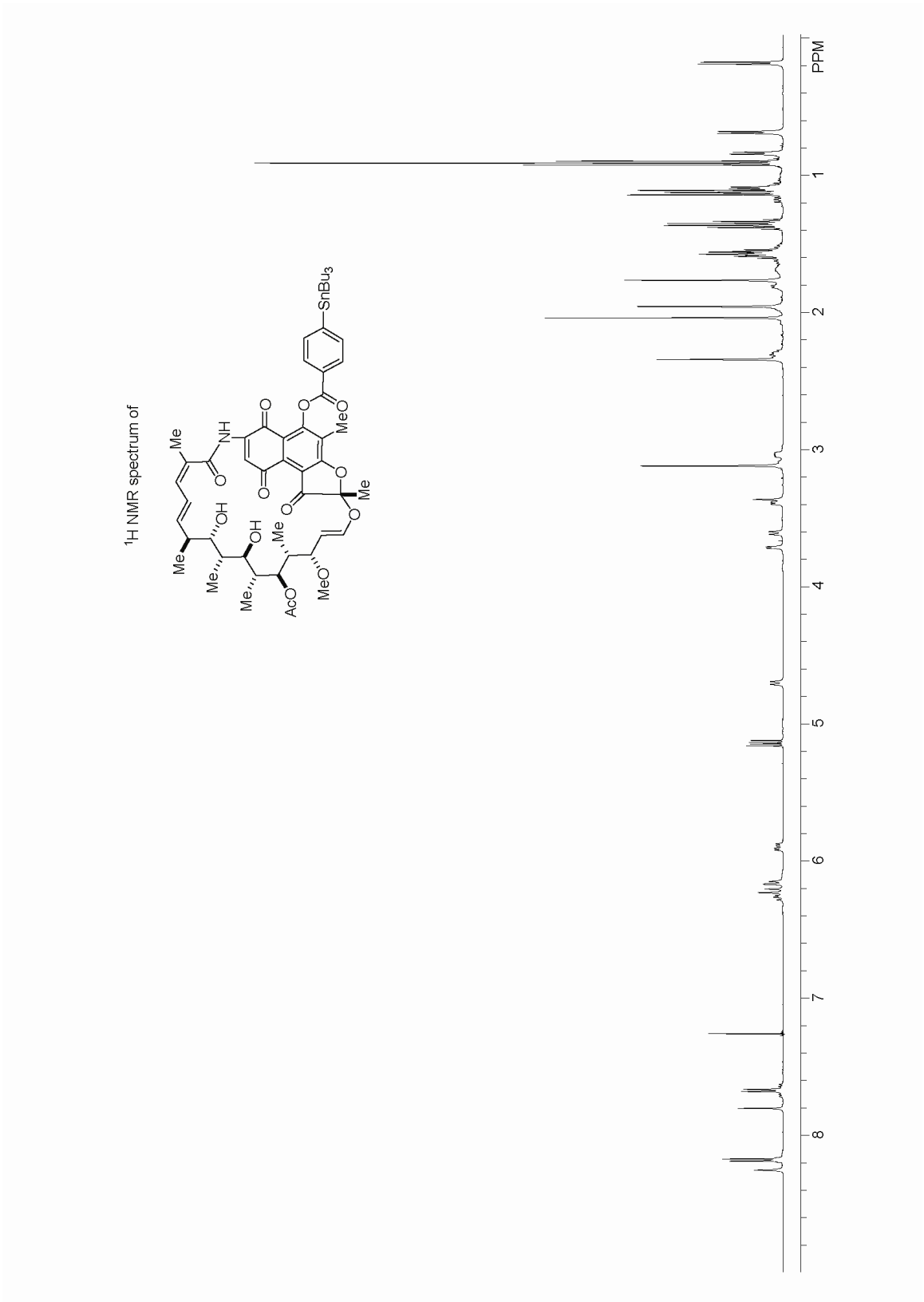
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S24**



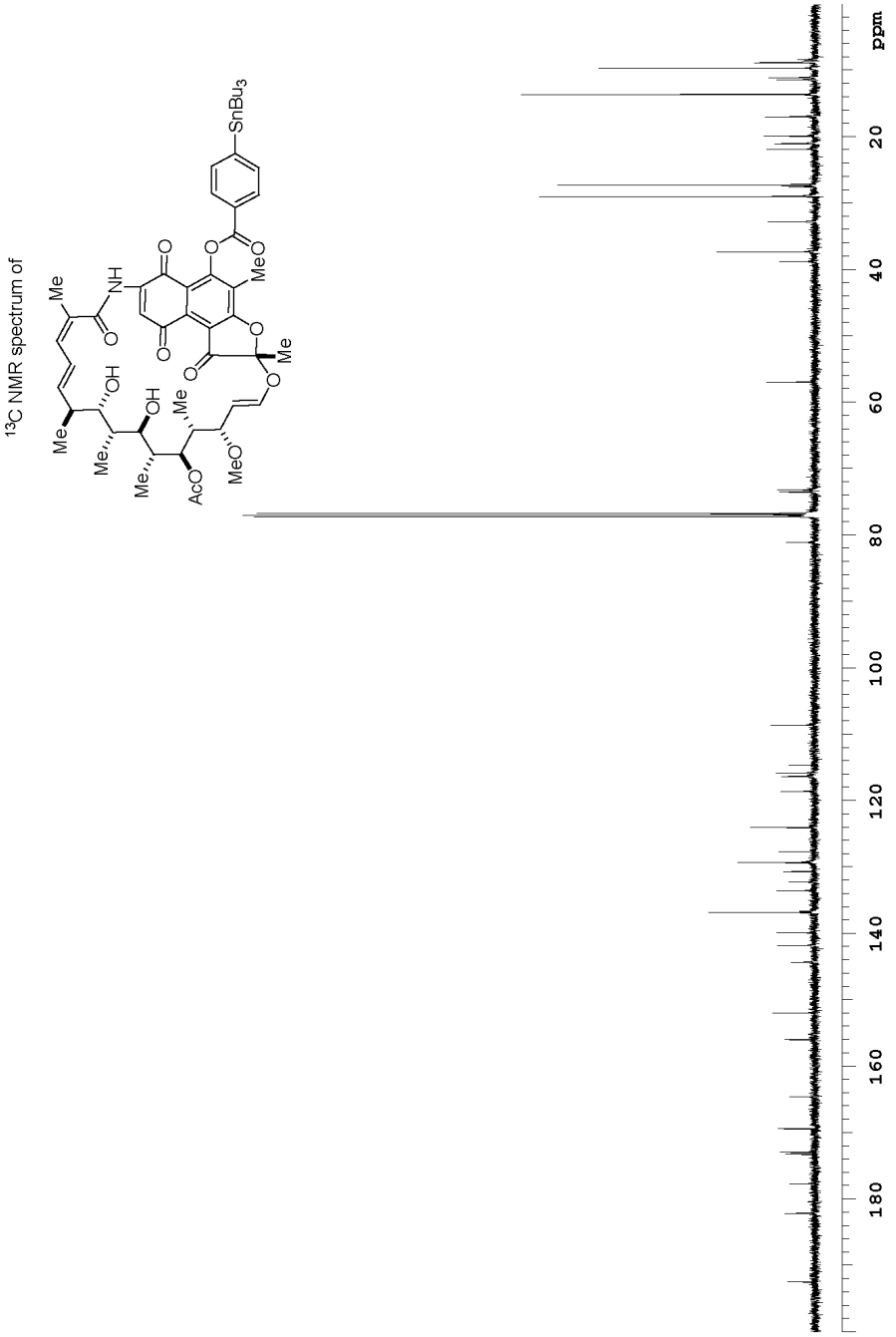
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S25**



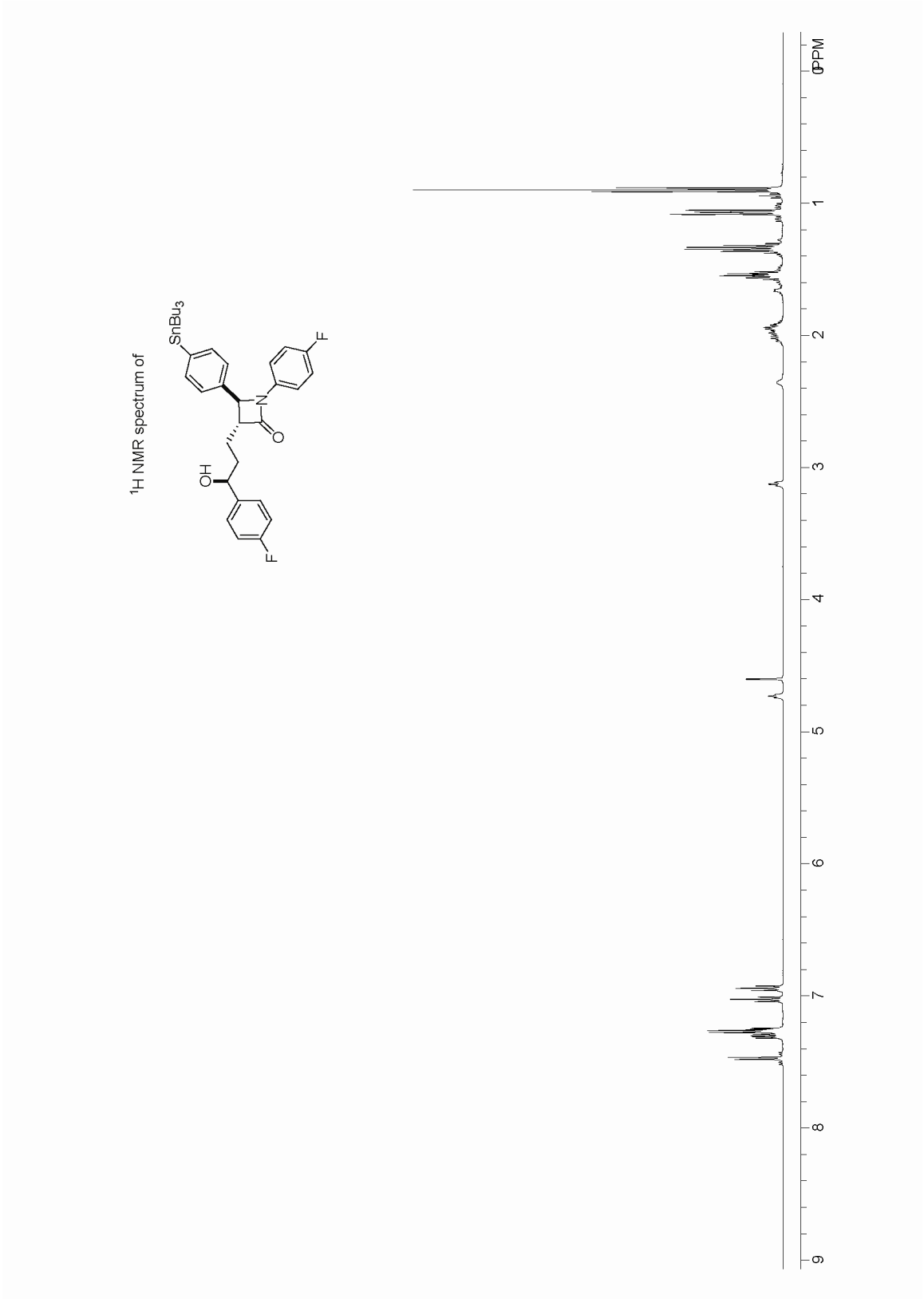
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S25**



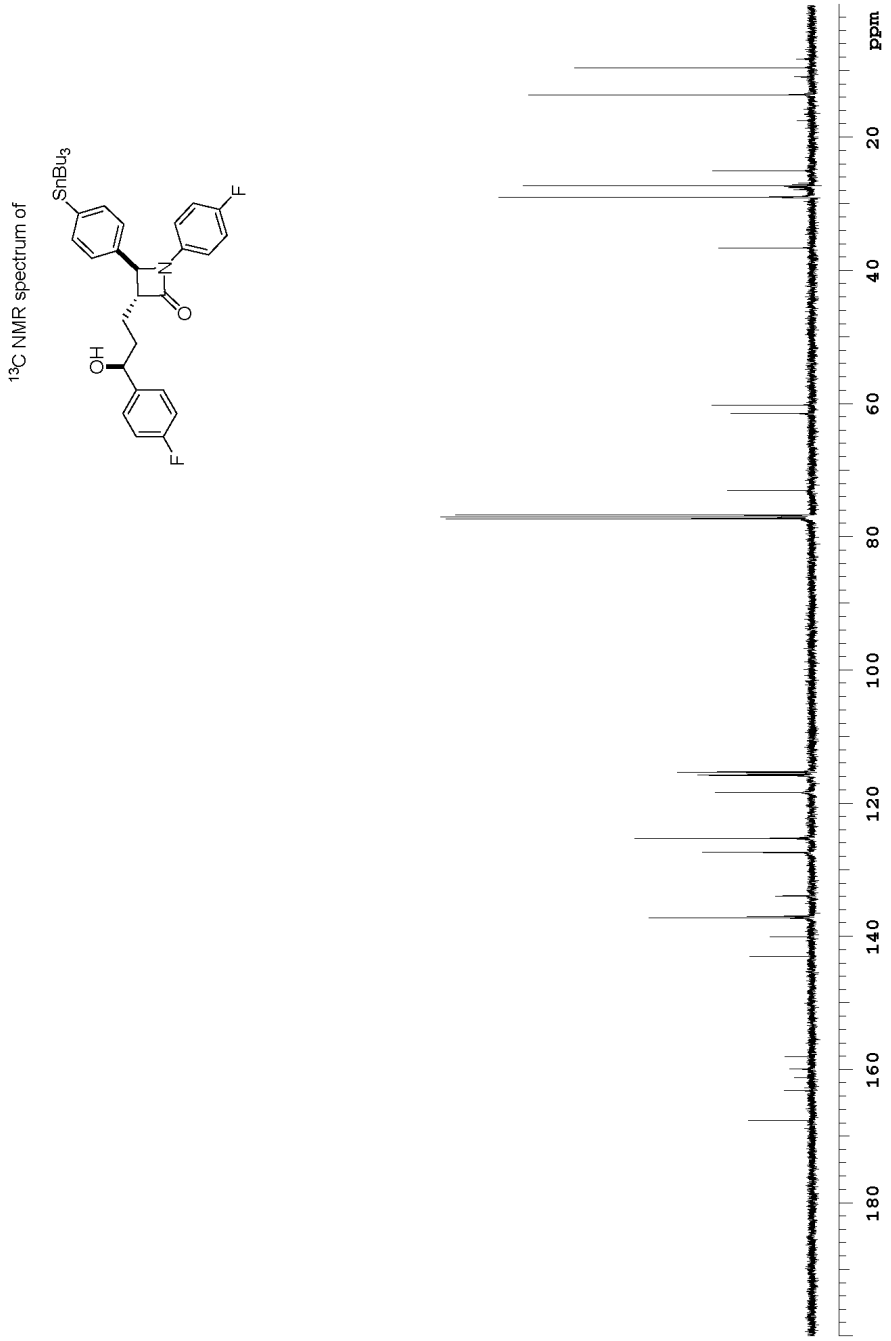
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S26**



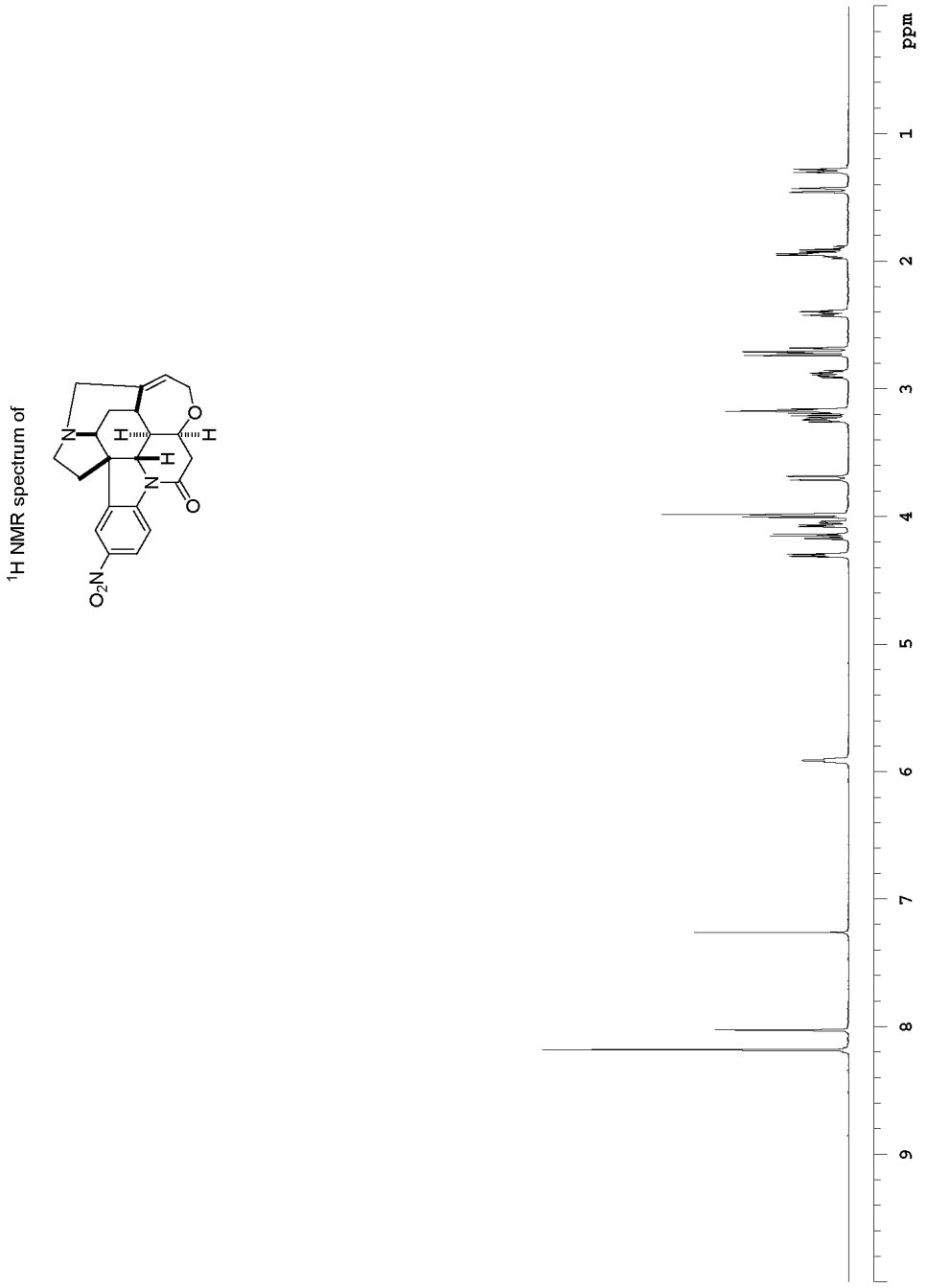
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S26**



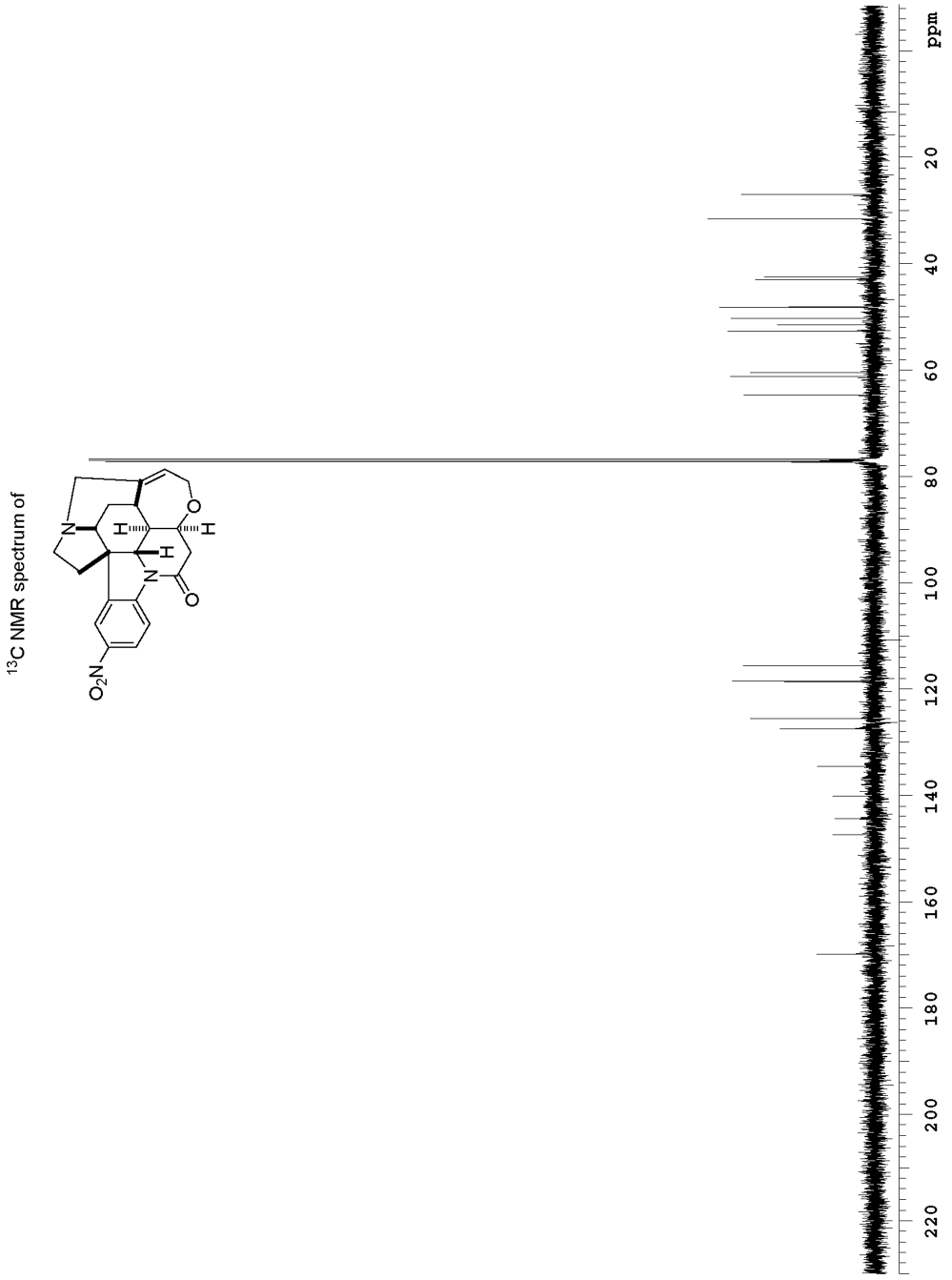
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **25**



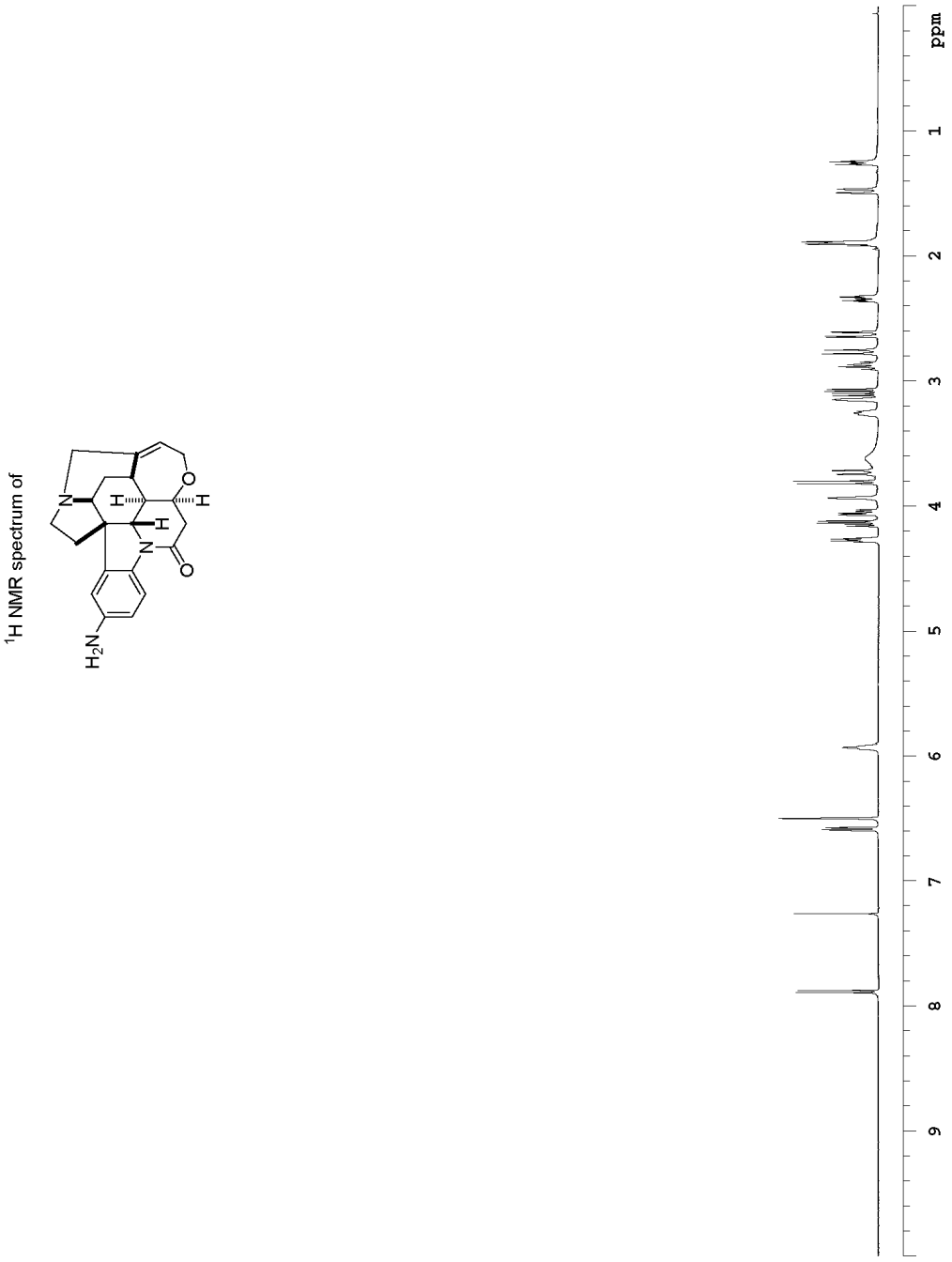
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **25**



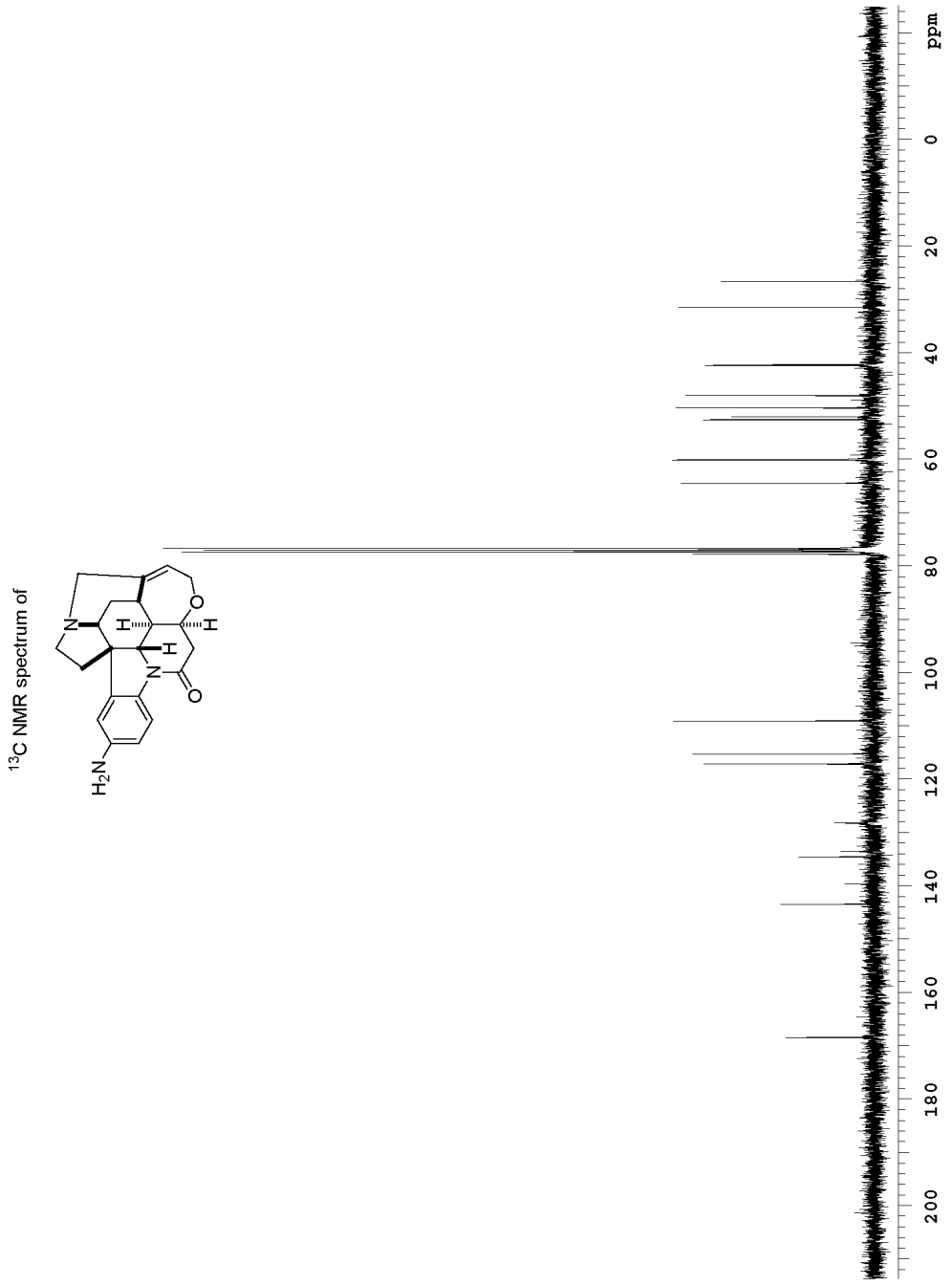
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S33**



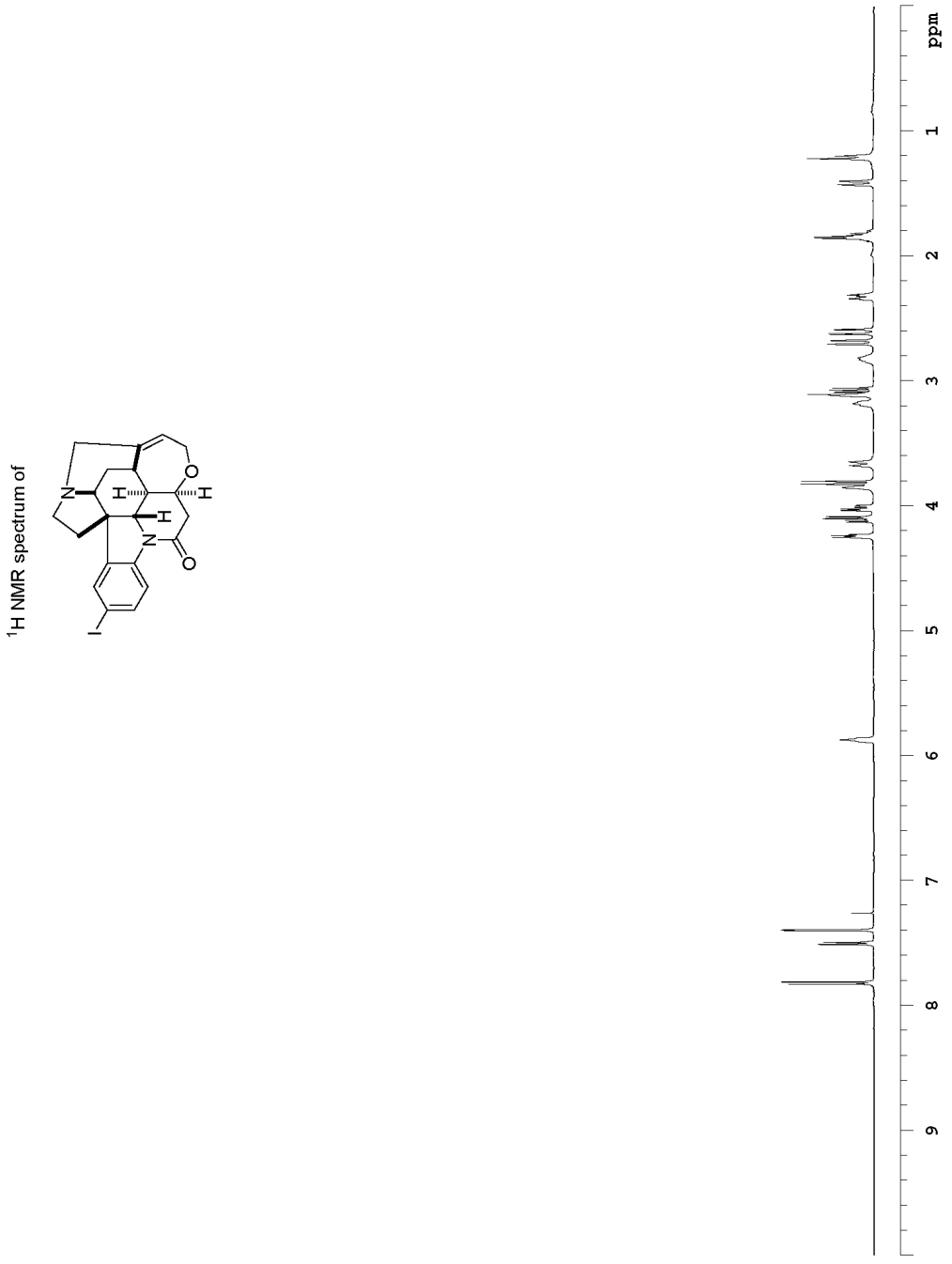
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S33**



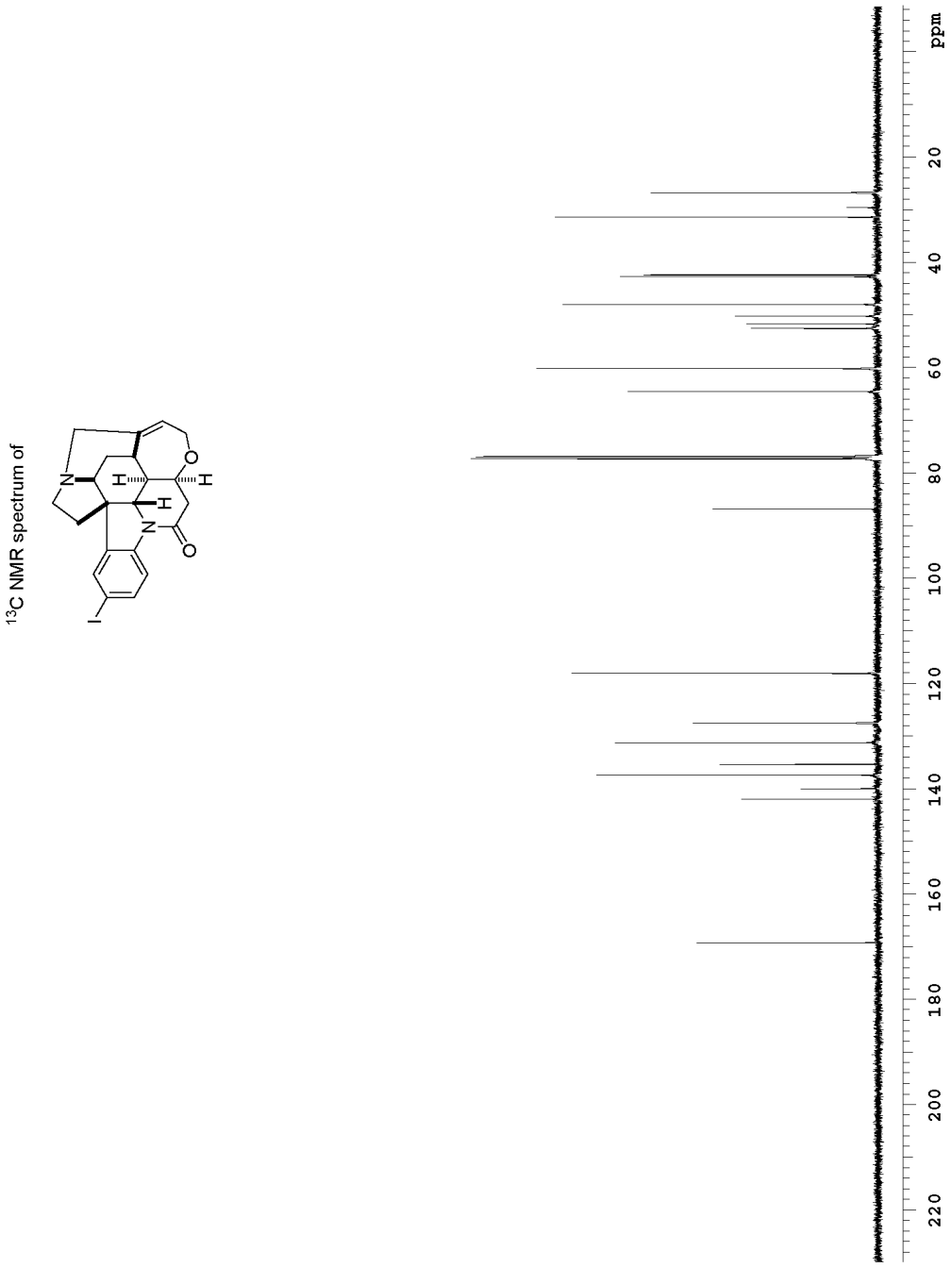
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **S34**



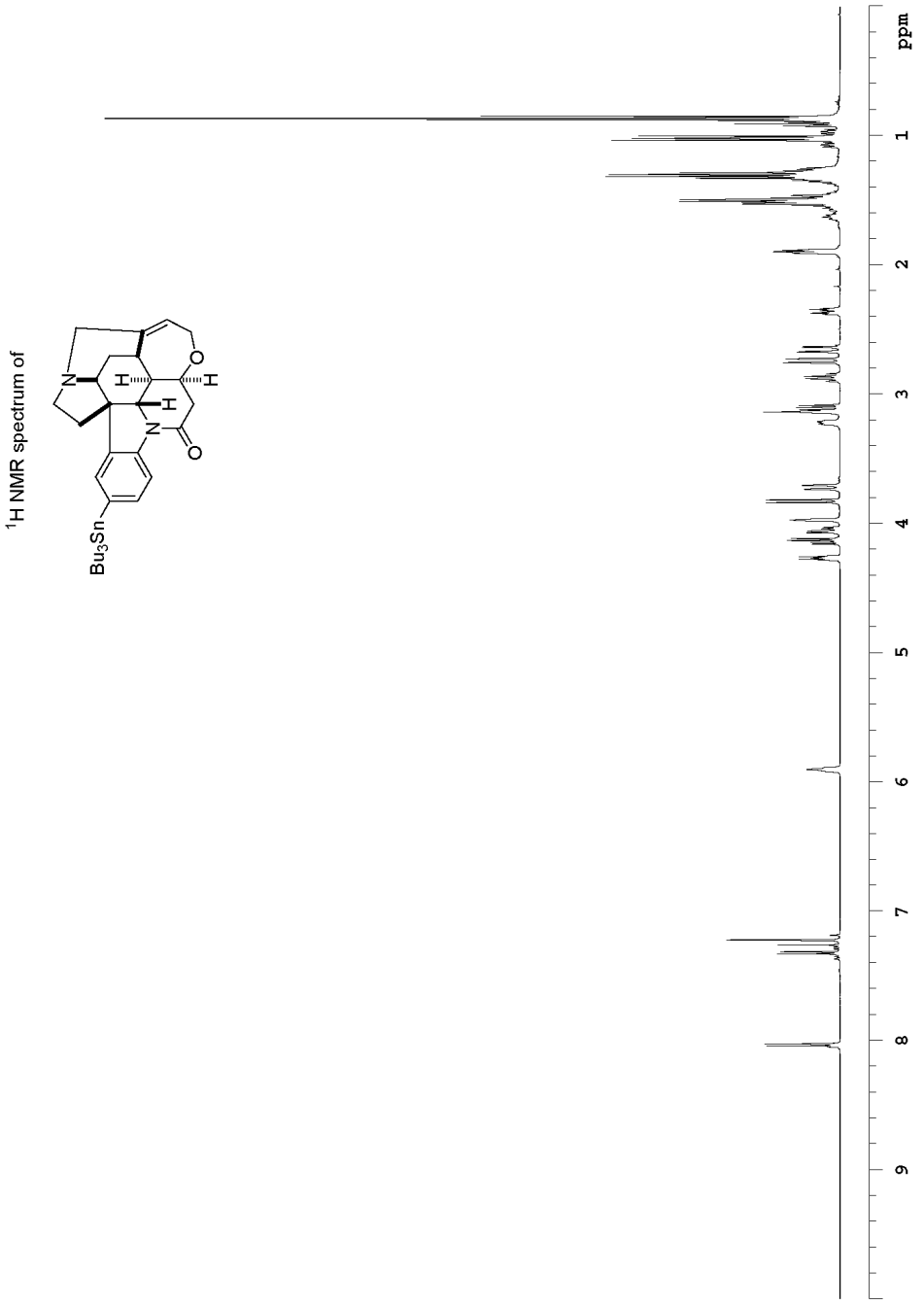
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **S34**



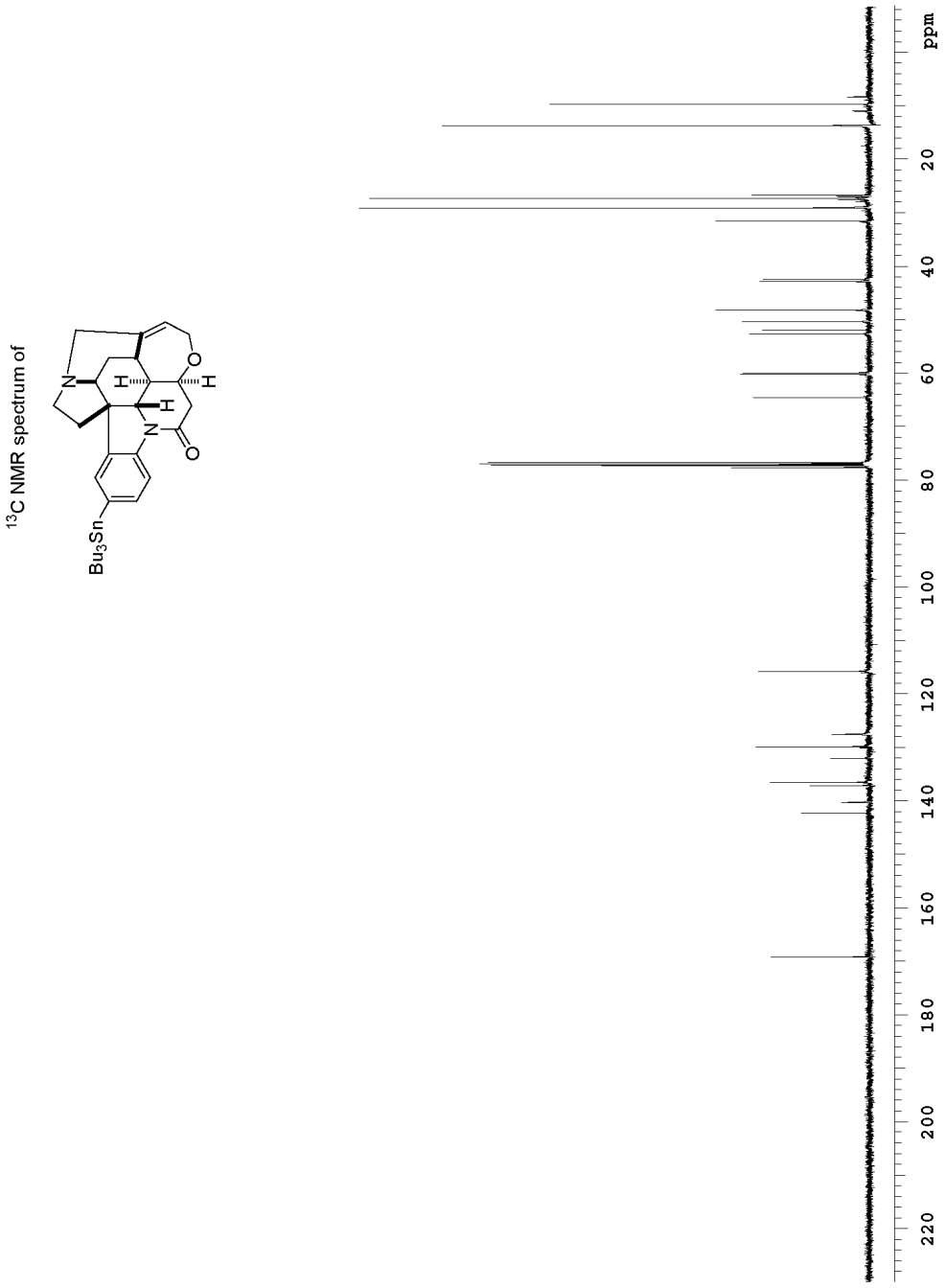
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **28**



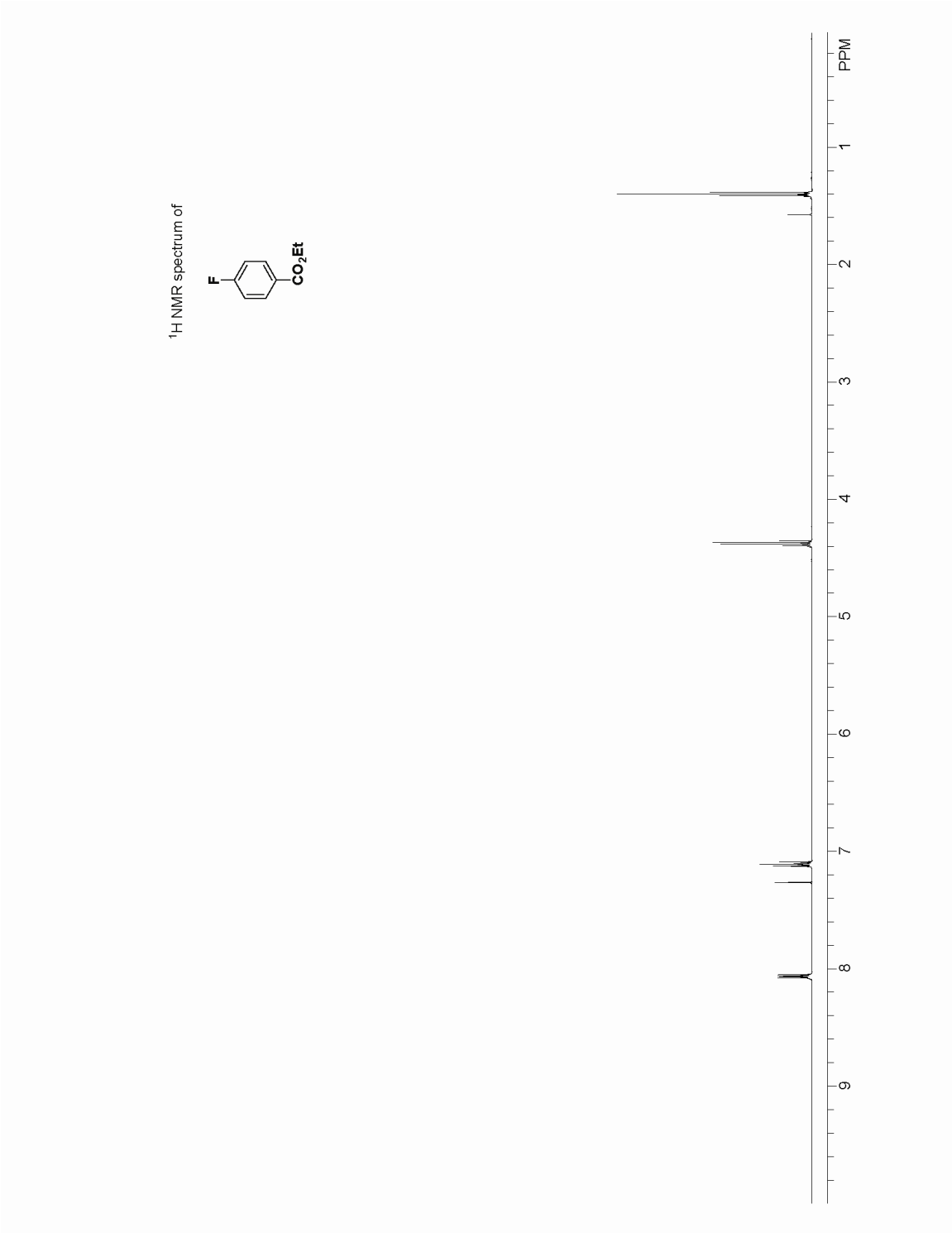
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **28**



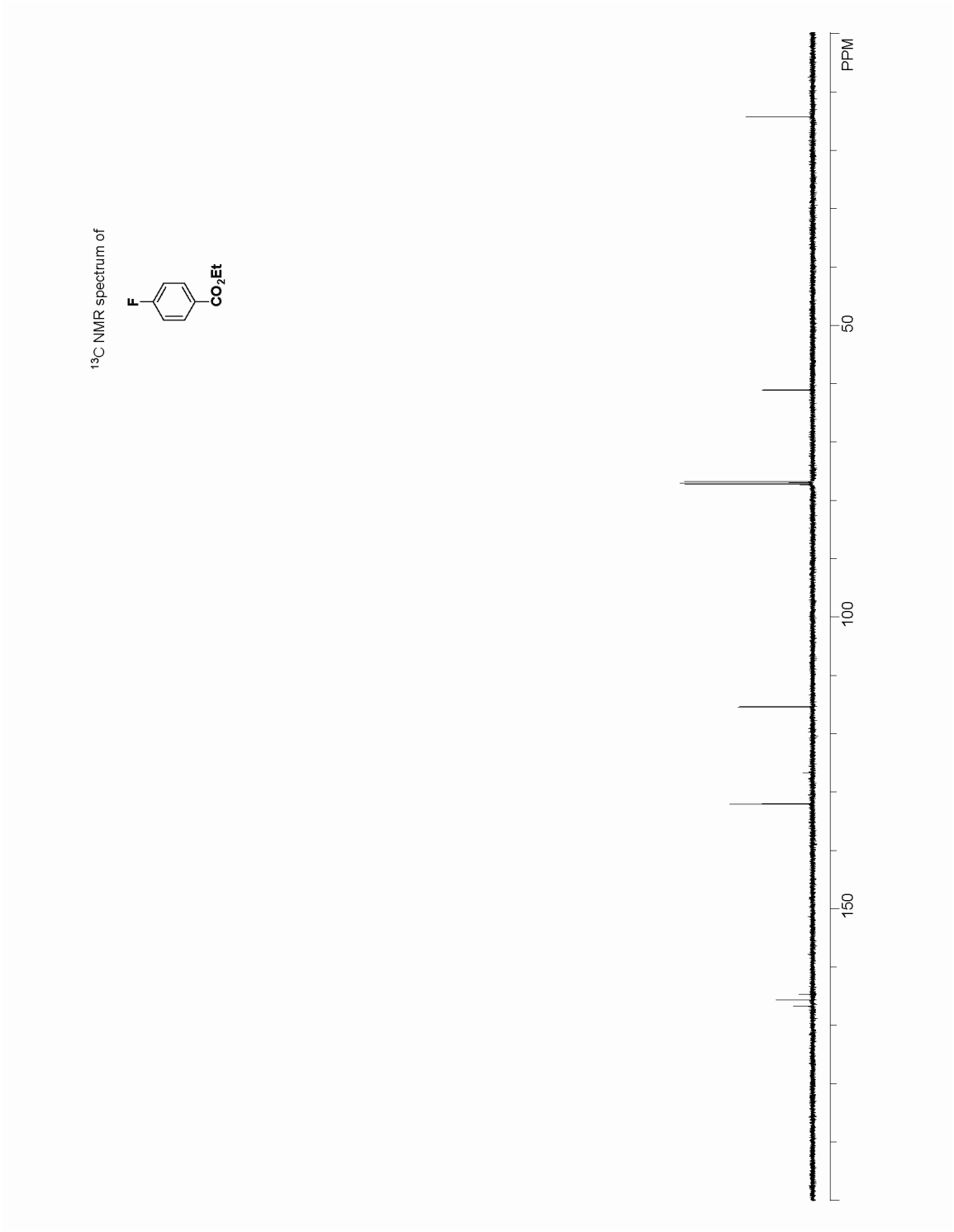
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **29**



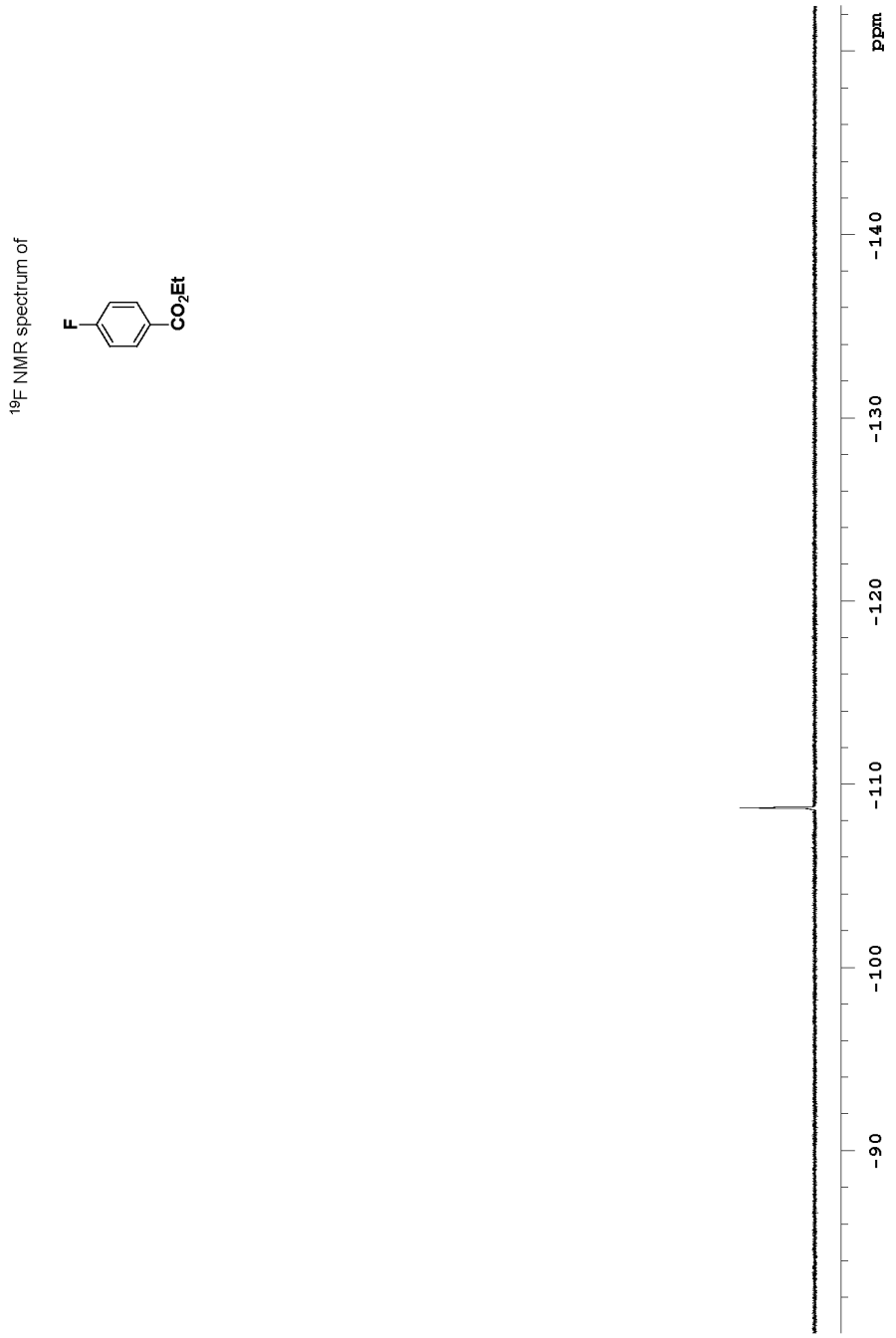
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **29**



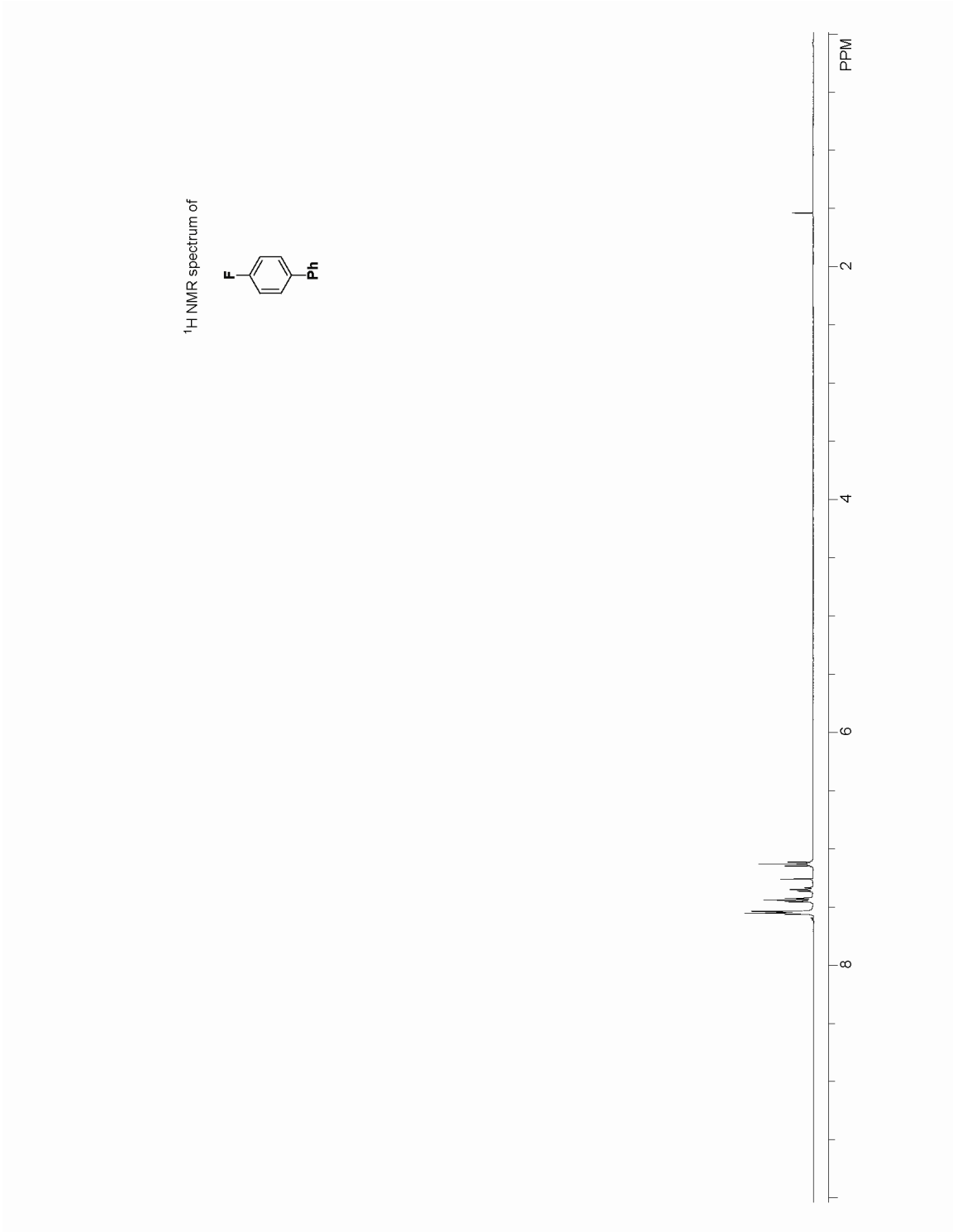
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **2**



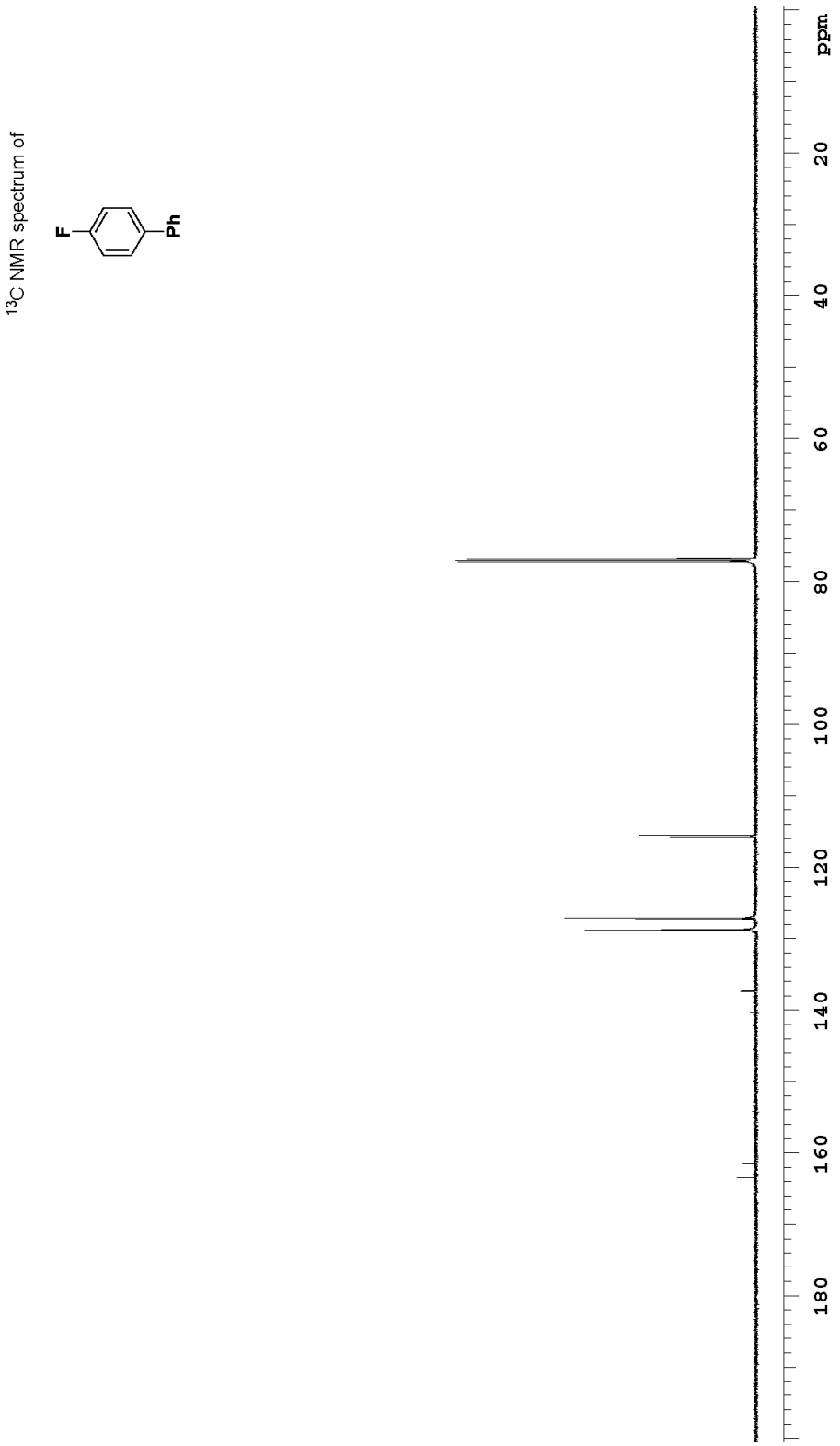
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **2**



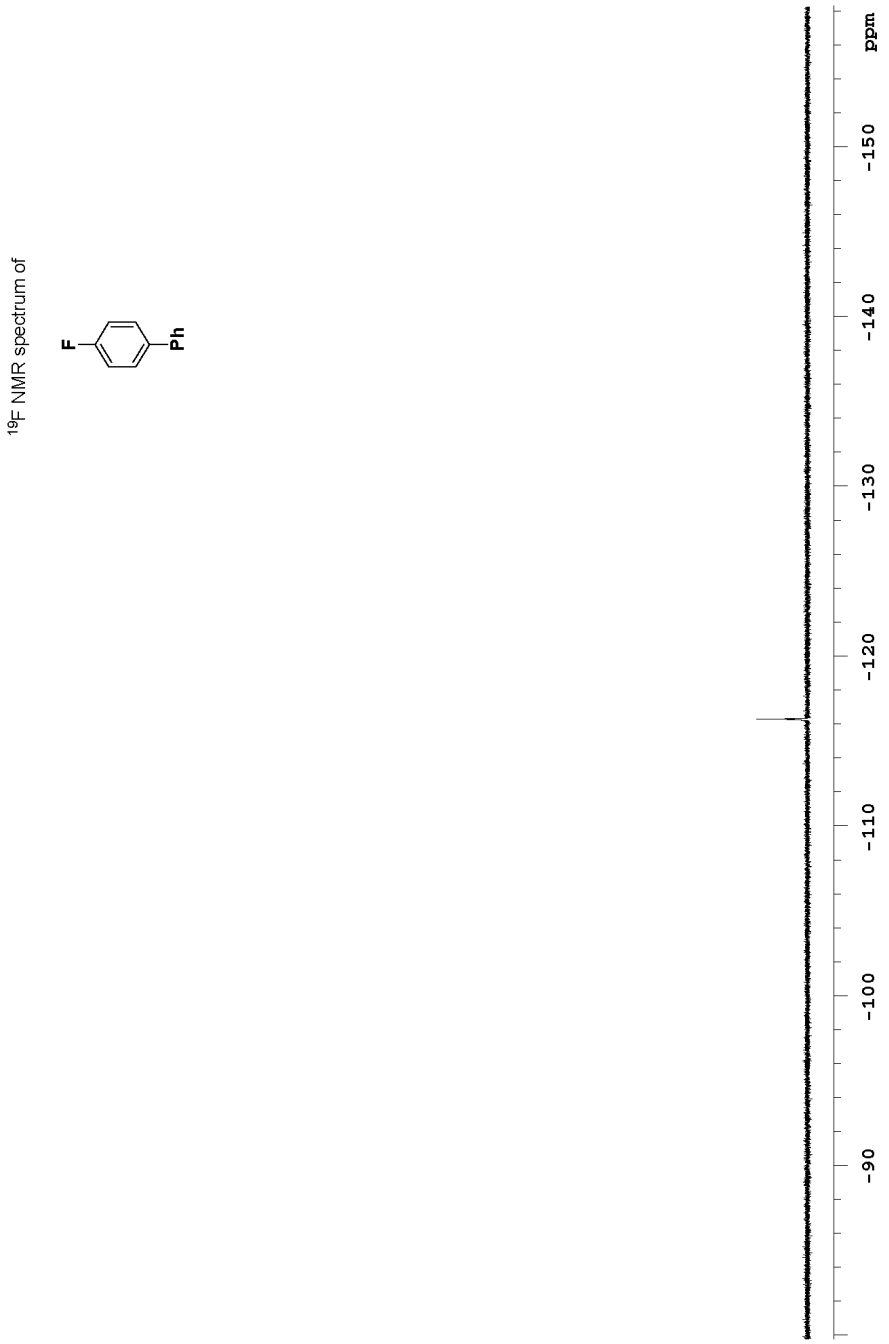
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **2**



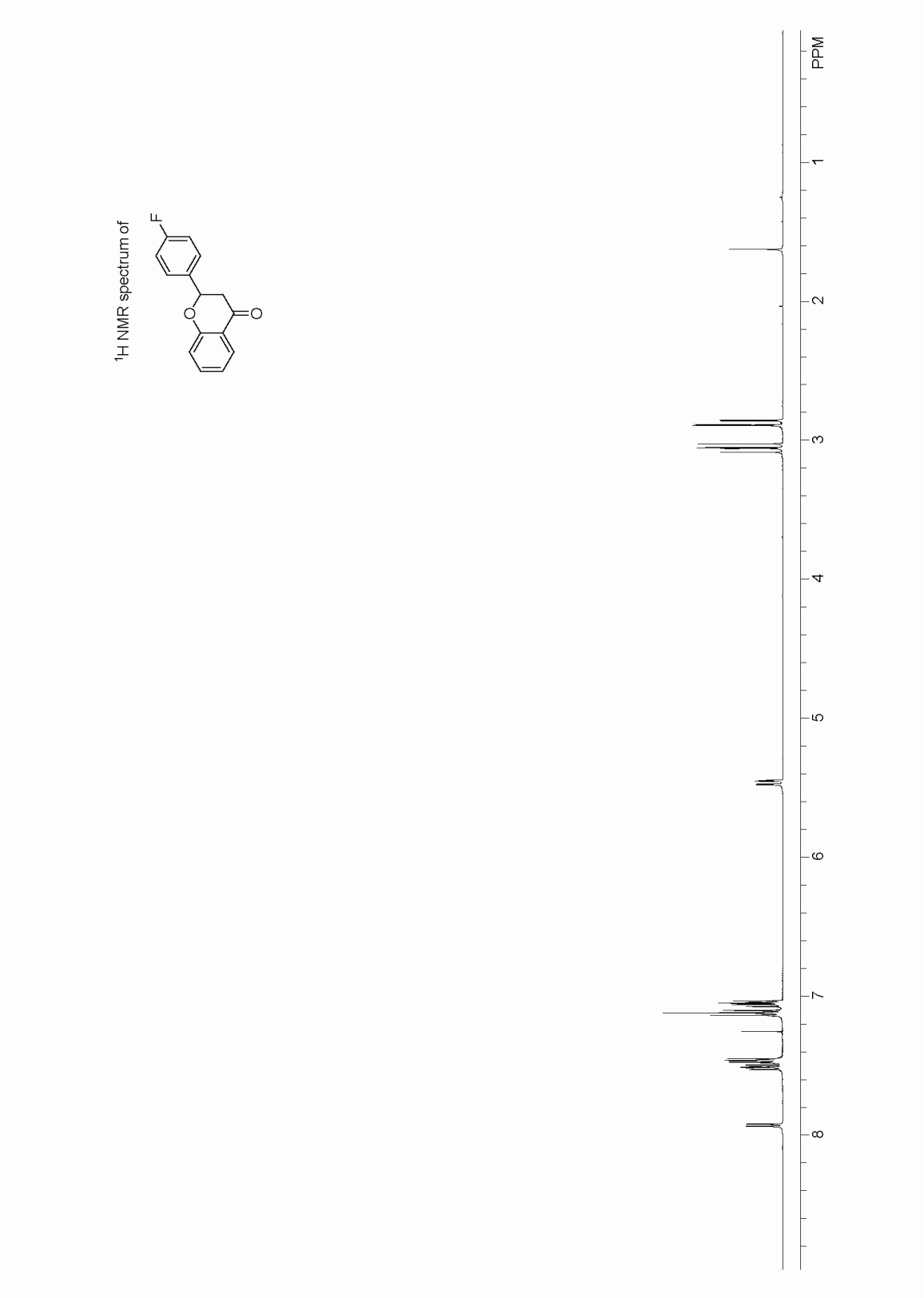
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **3**



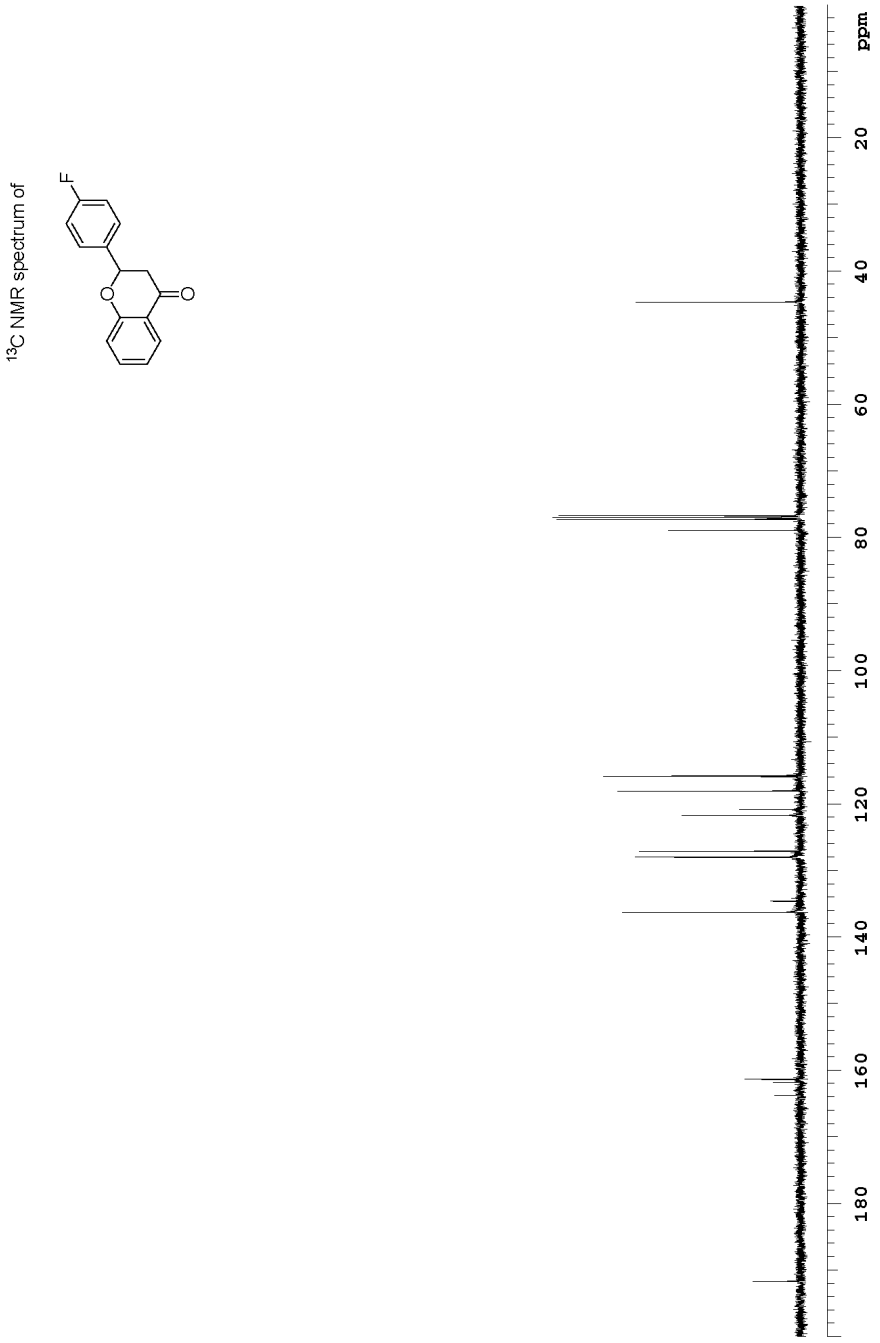
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **3**



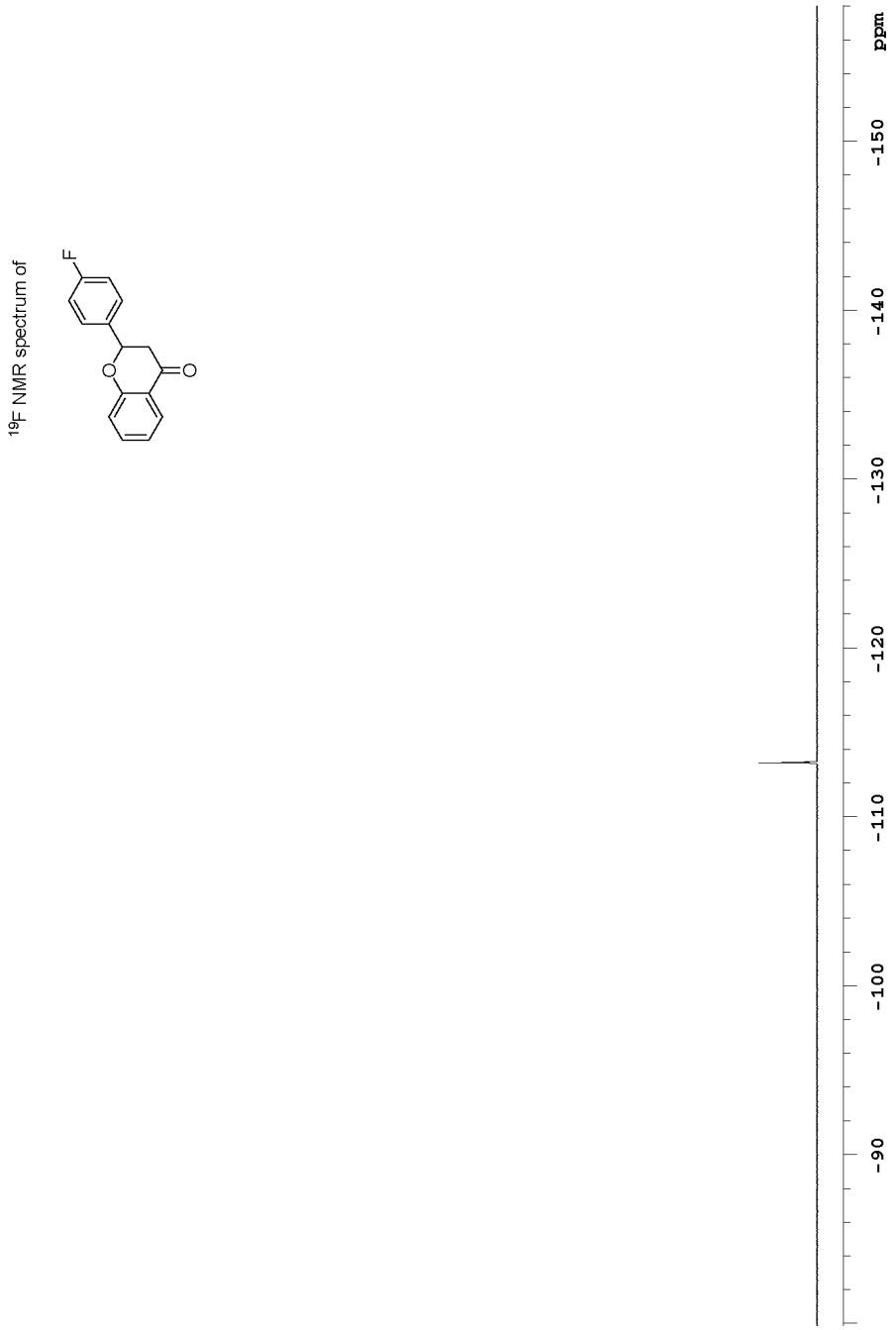
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **3**



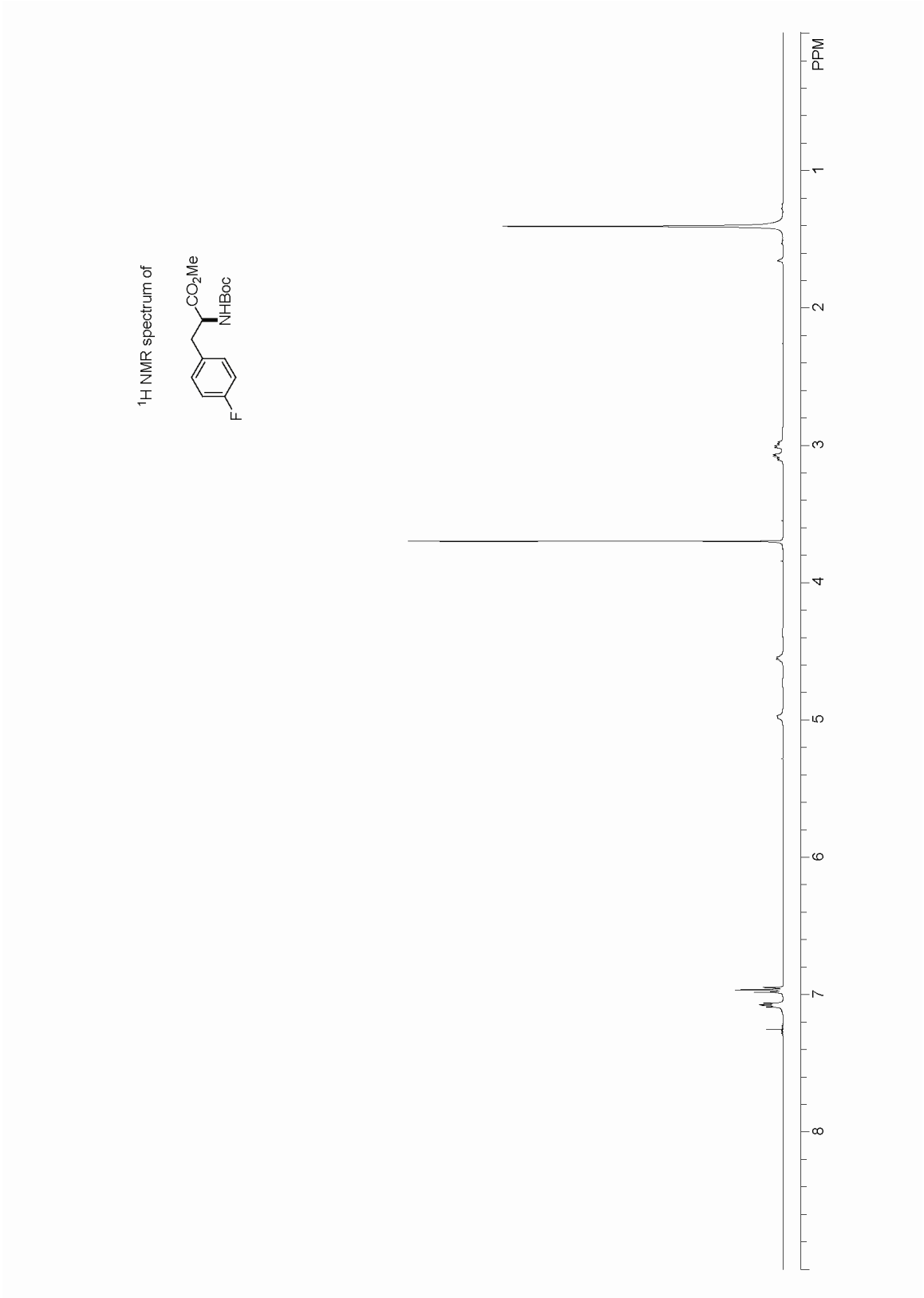
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **8**



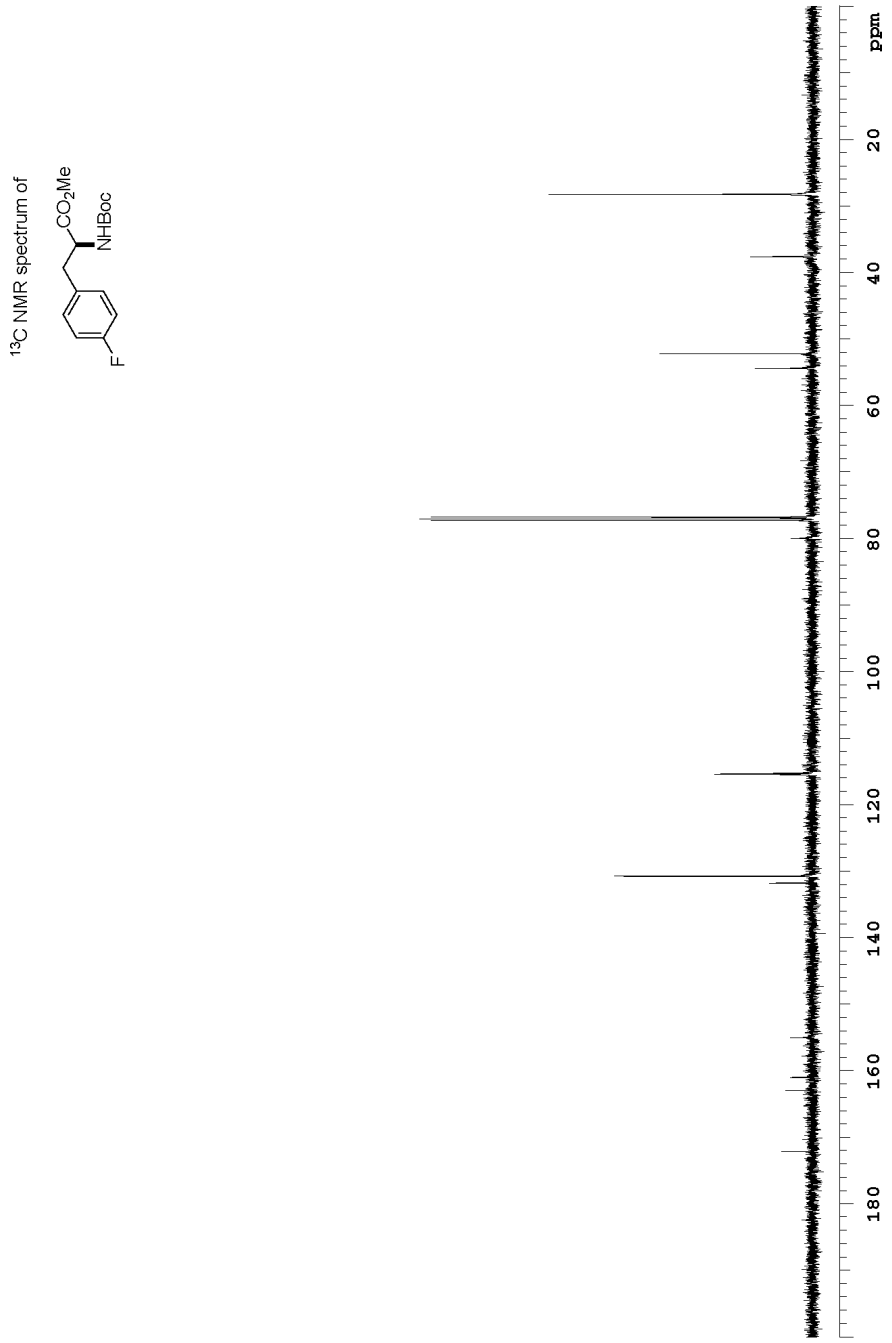
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **8**



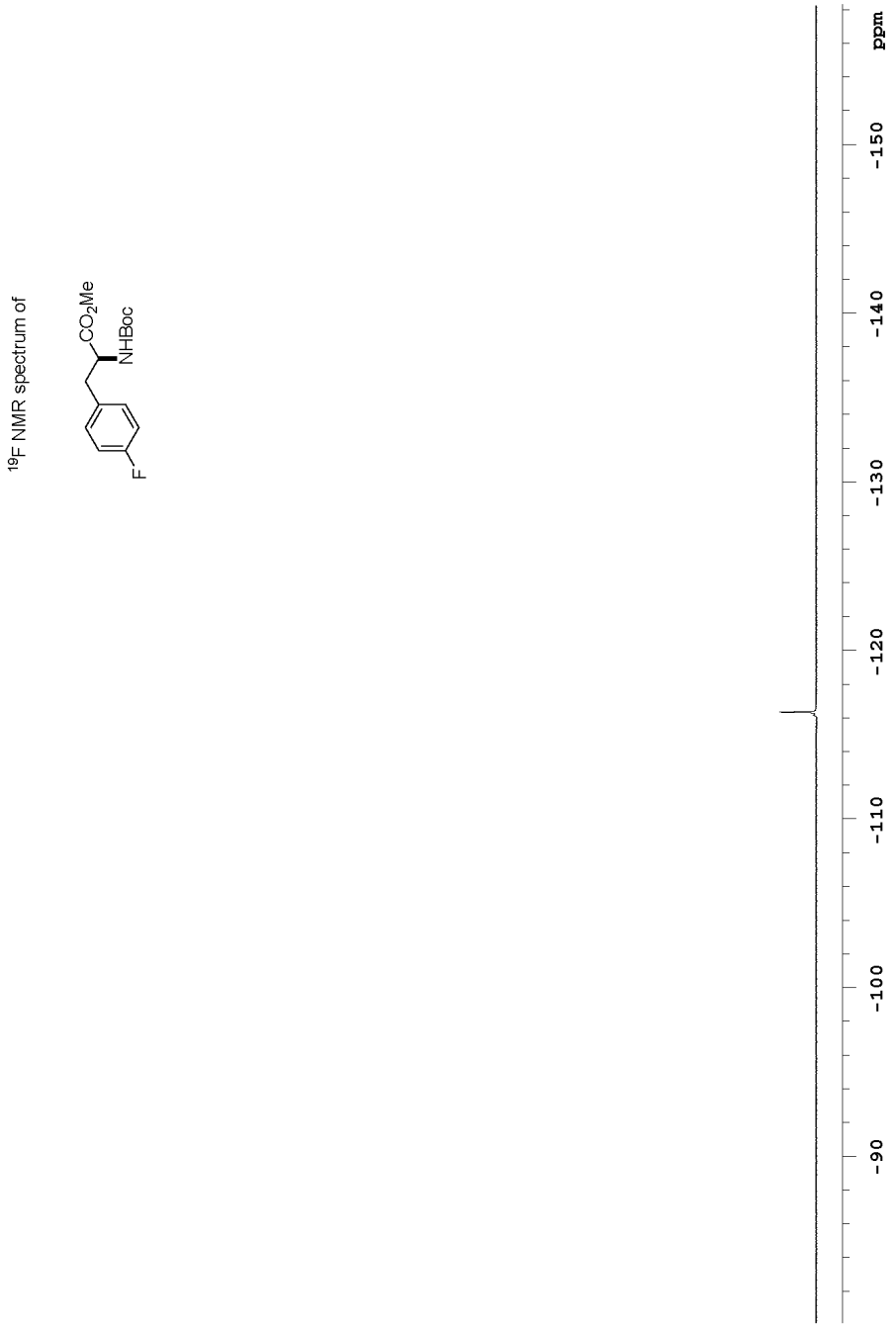
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **8**



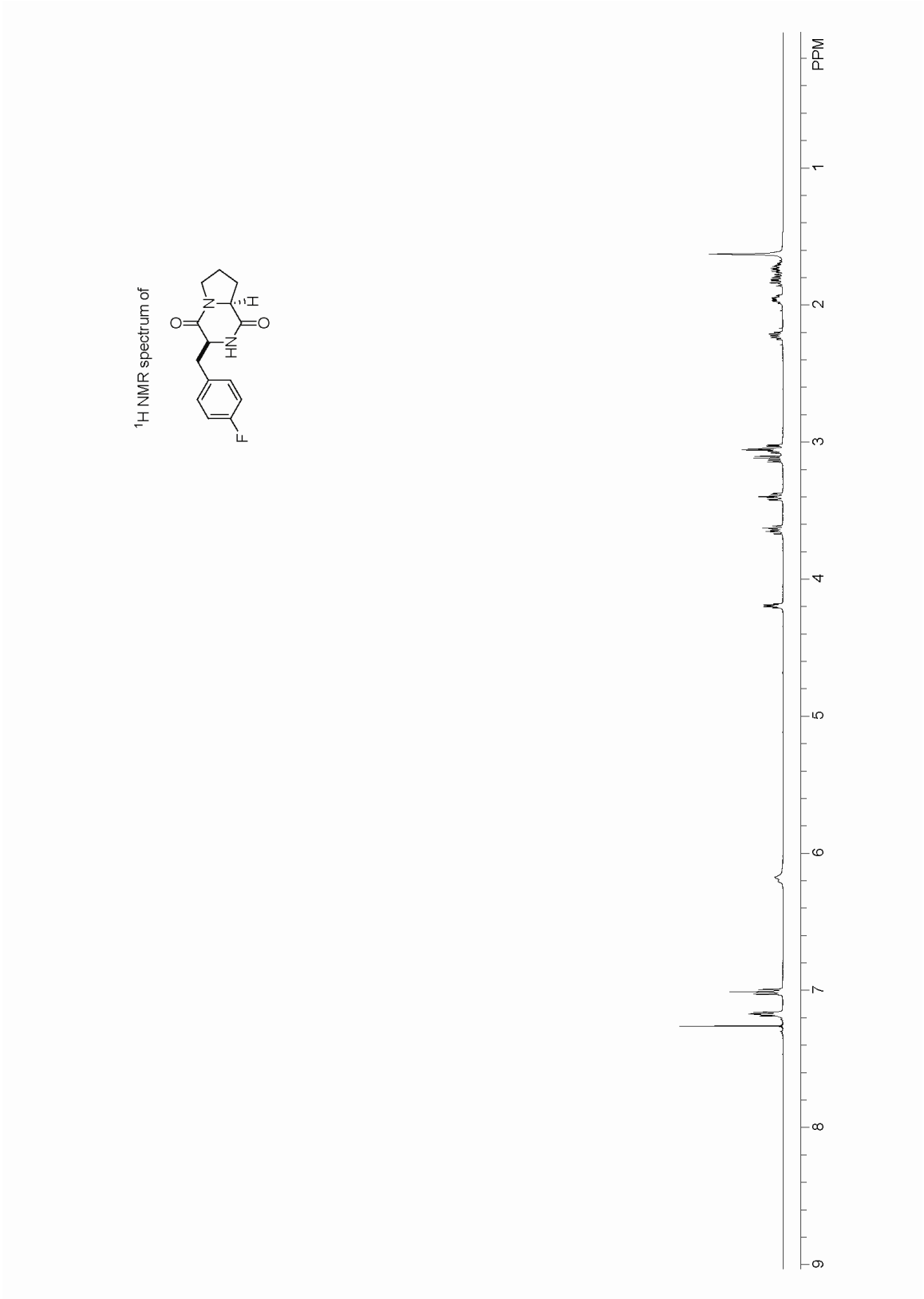
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **9**



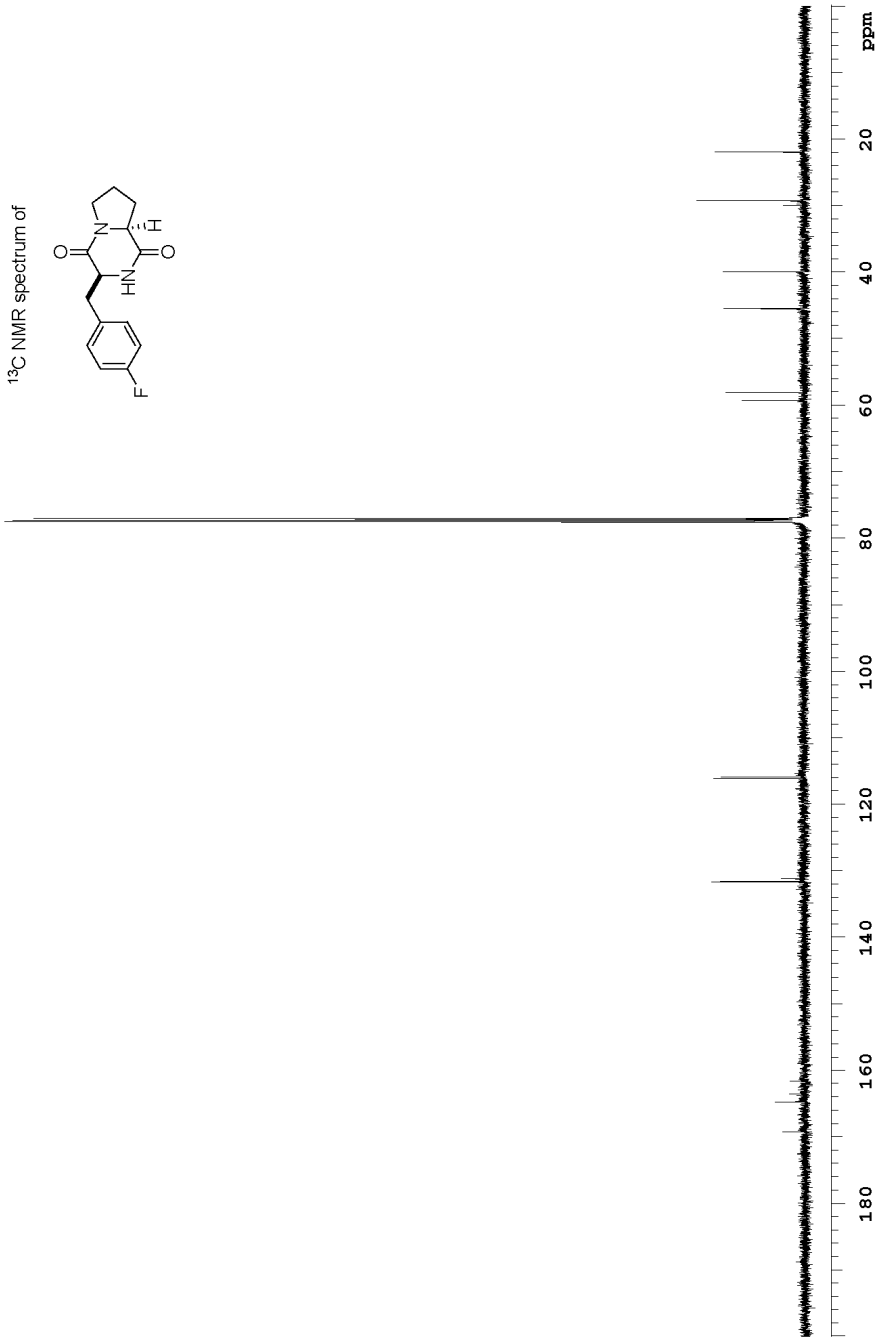
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **9**



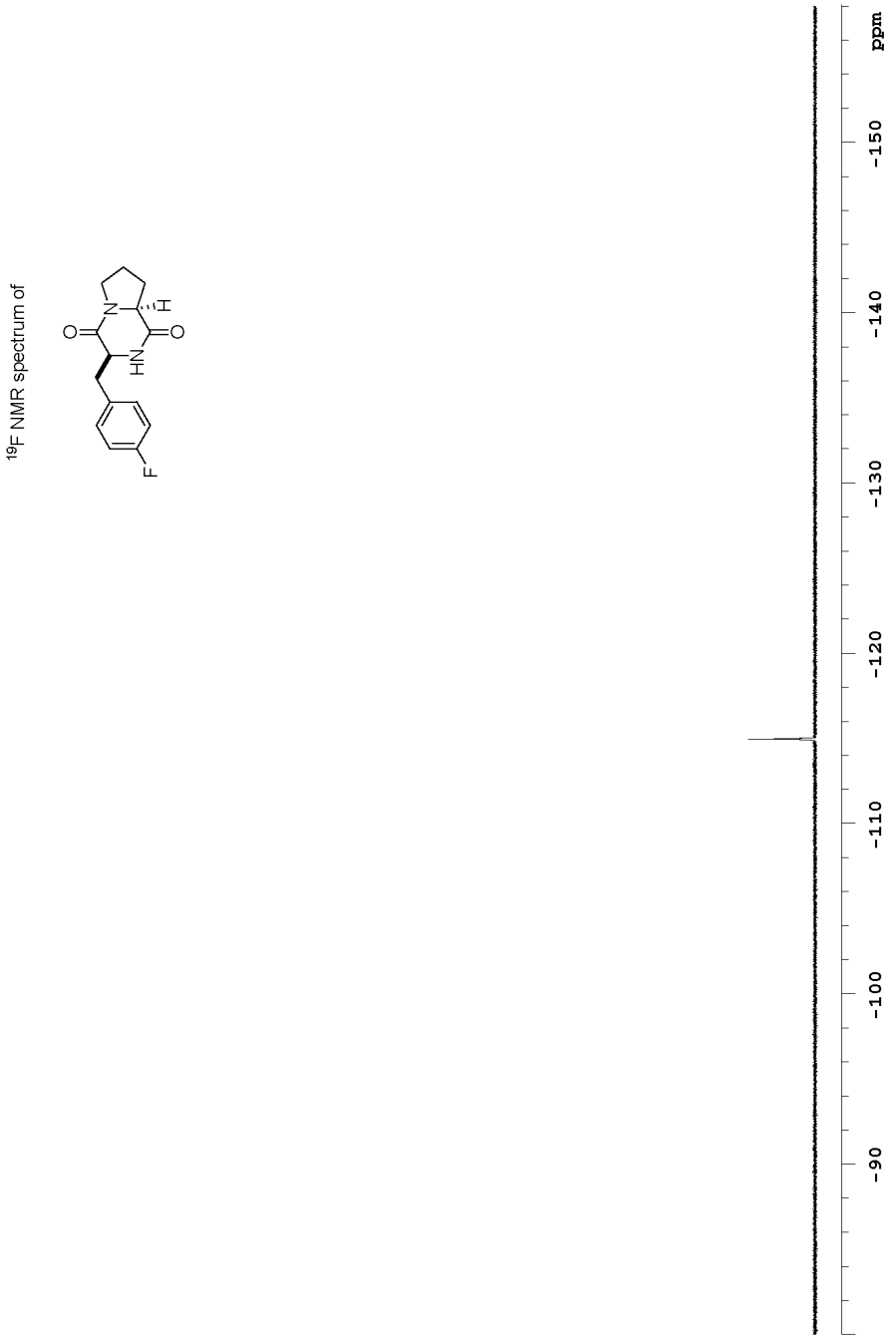
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **9**



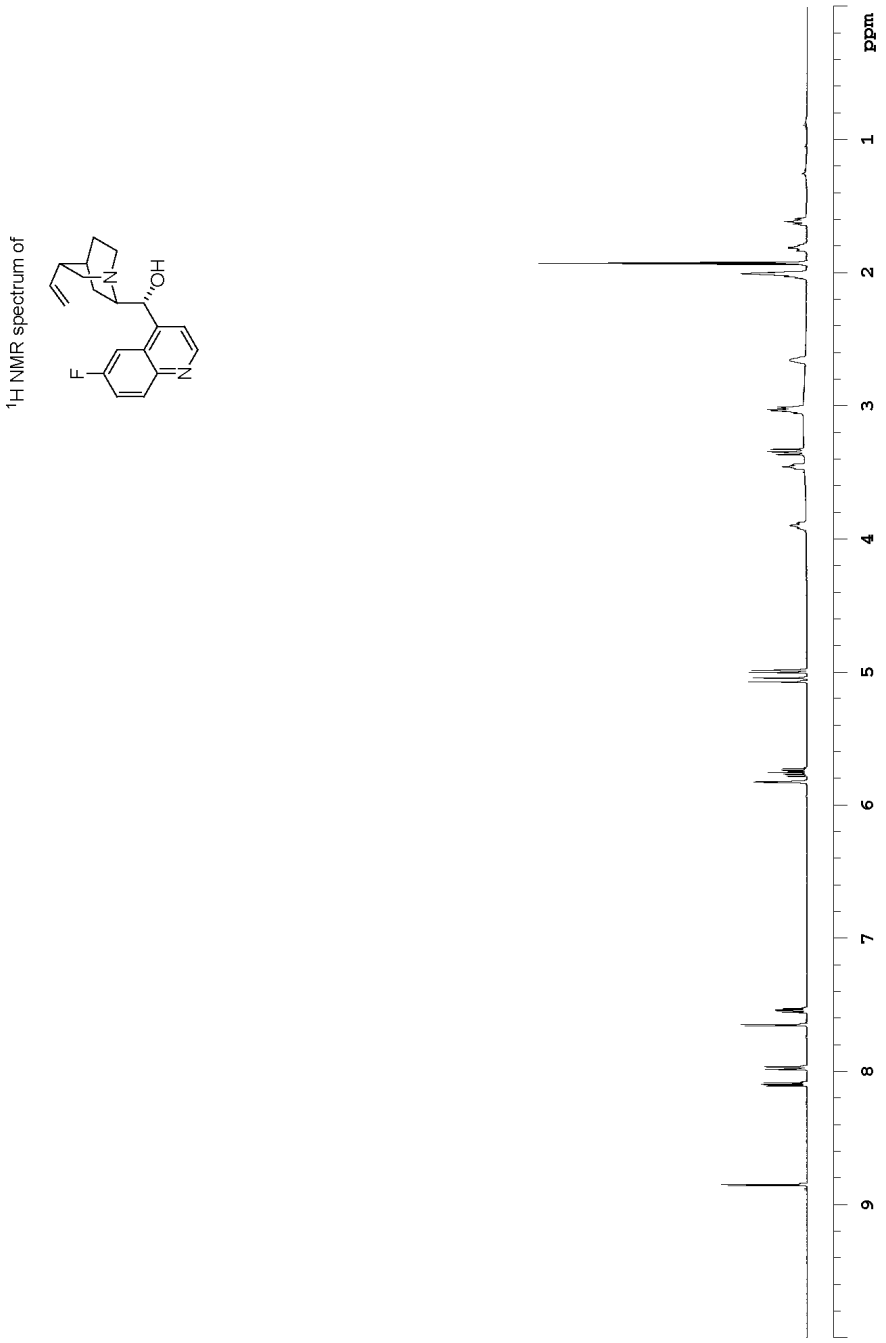
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **10**



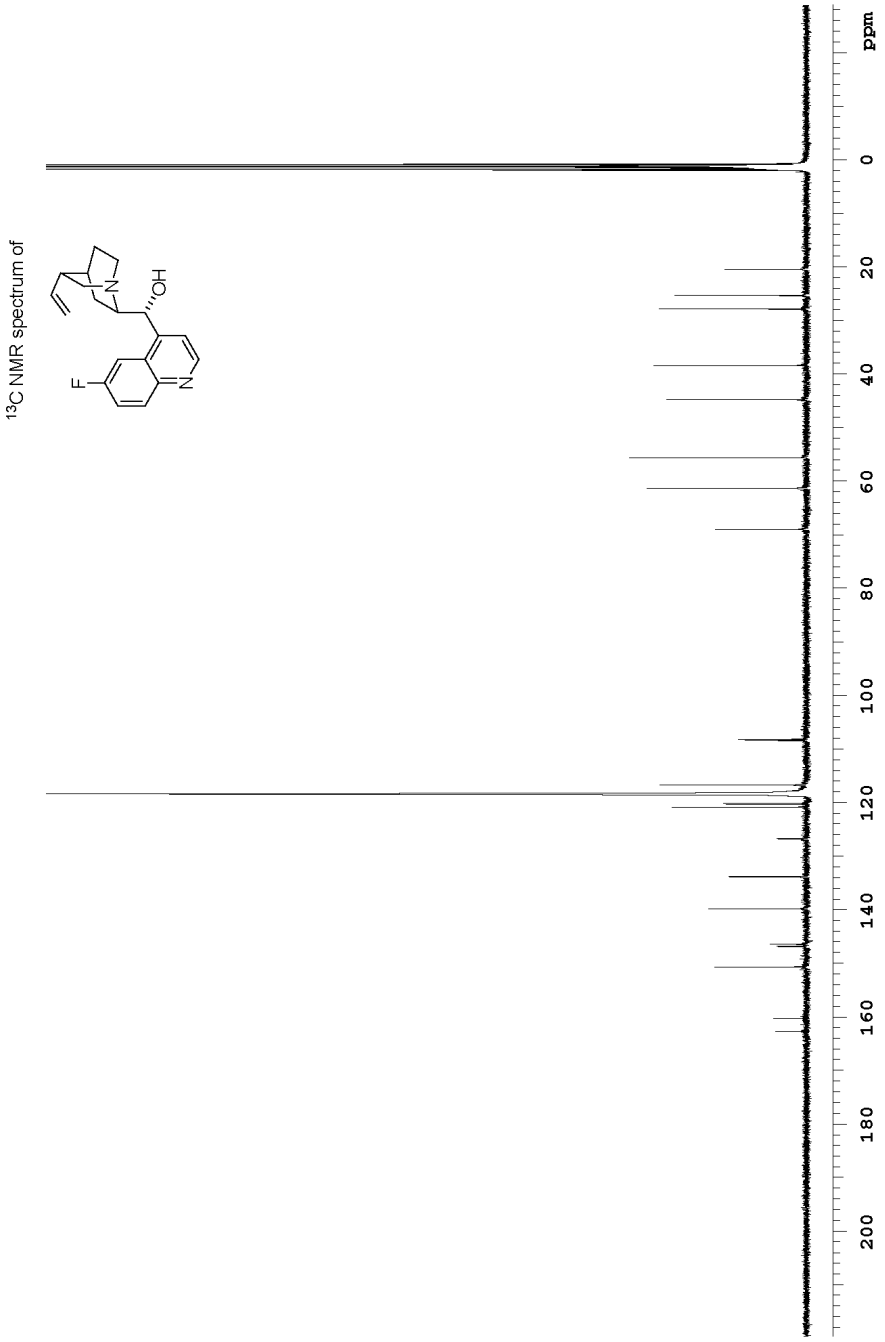
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **10**



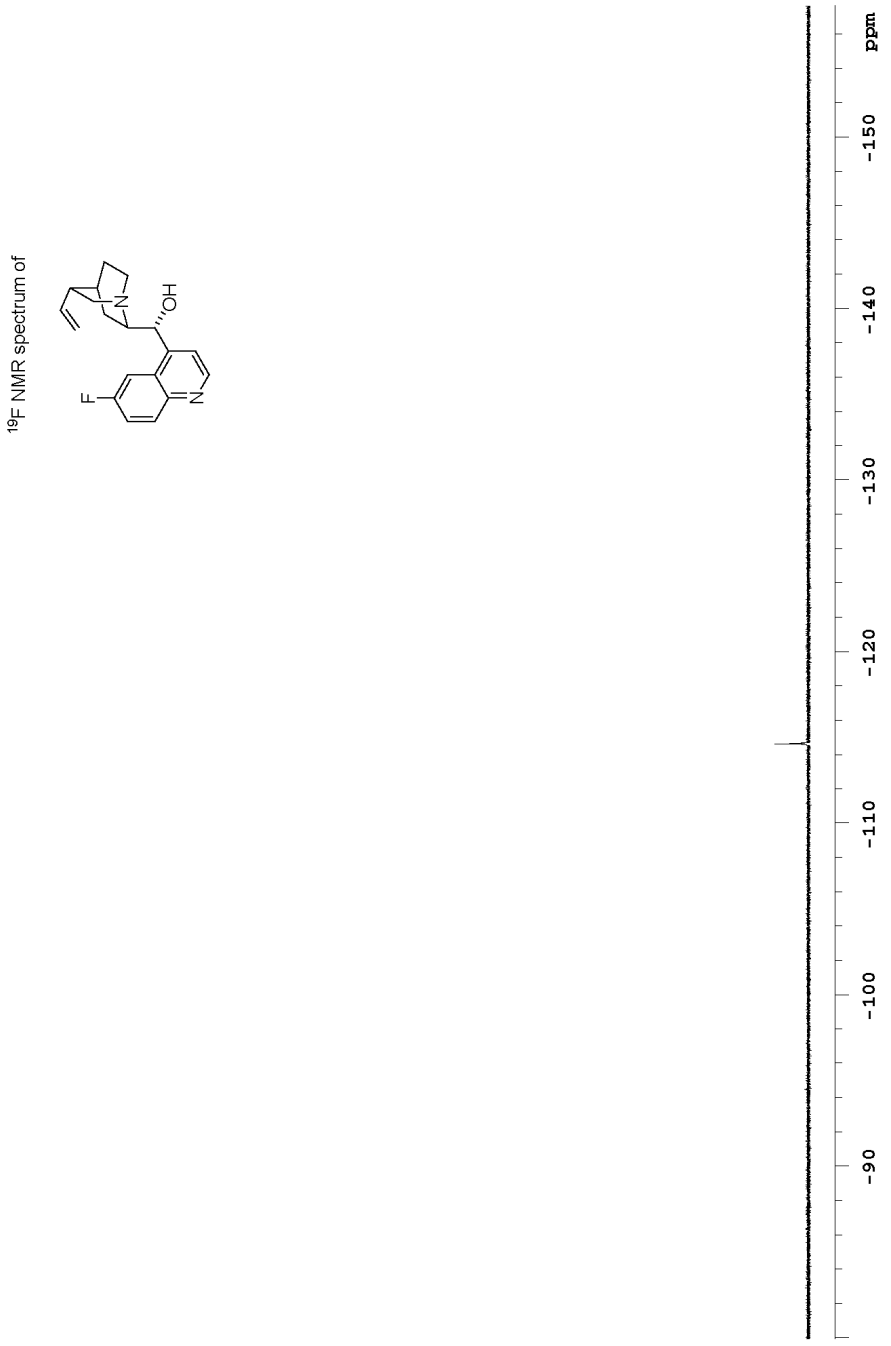
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **10**



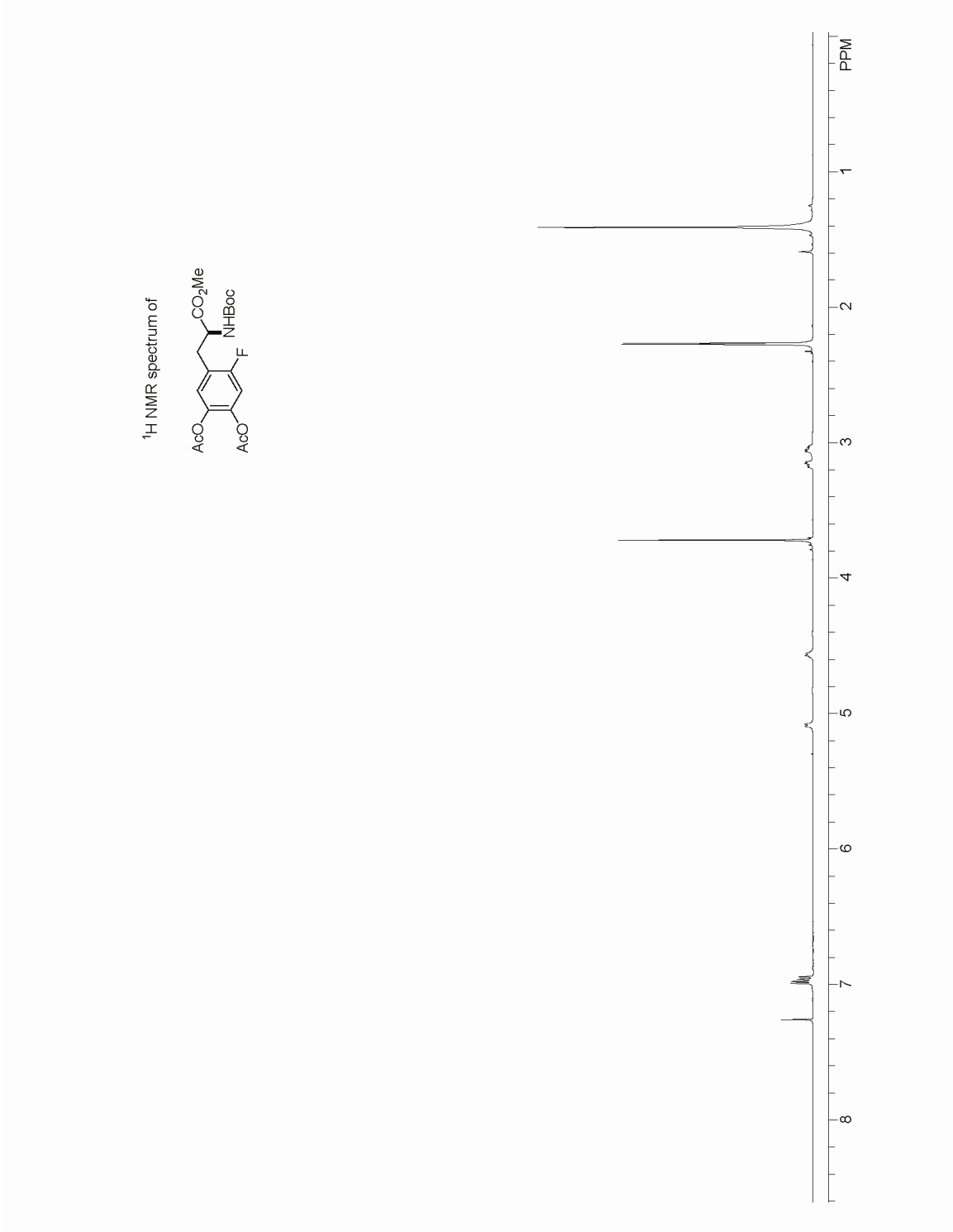
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **11**



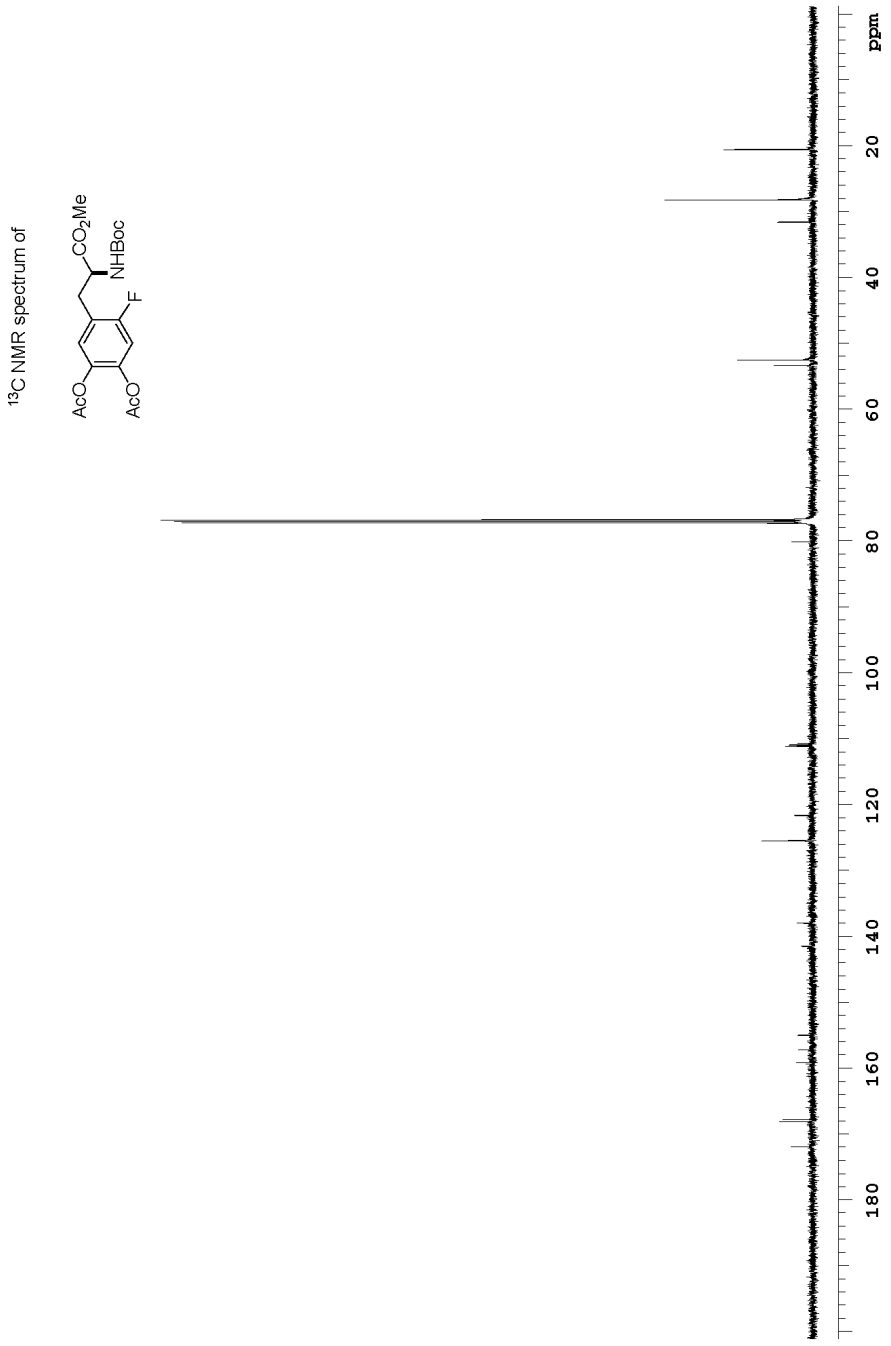
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **11**



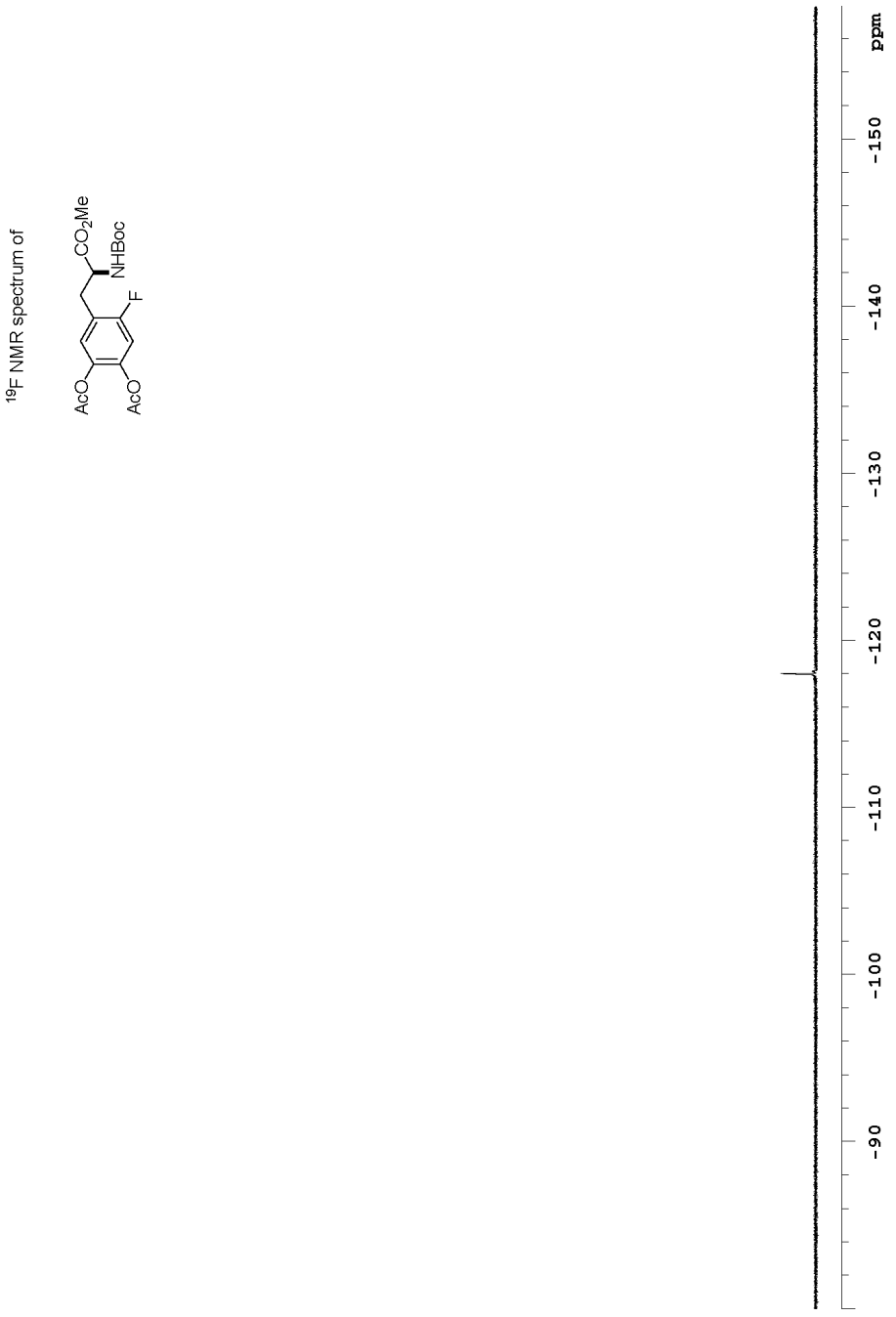
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **11**



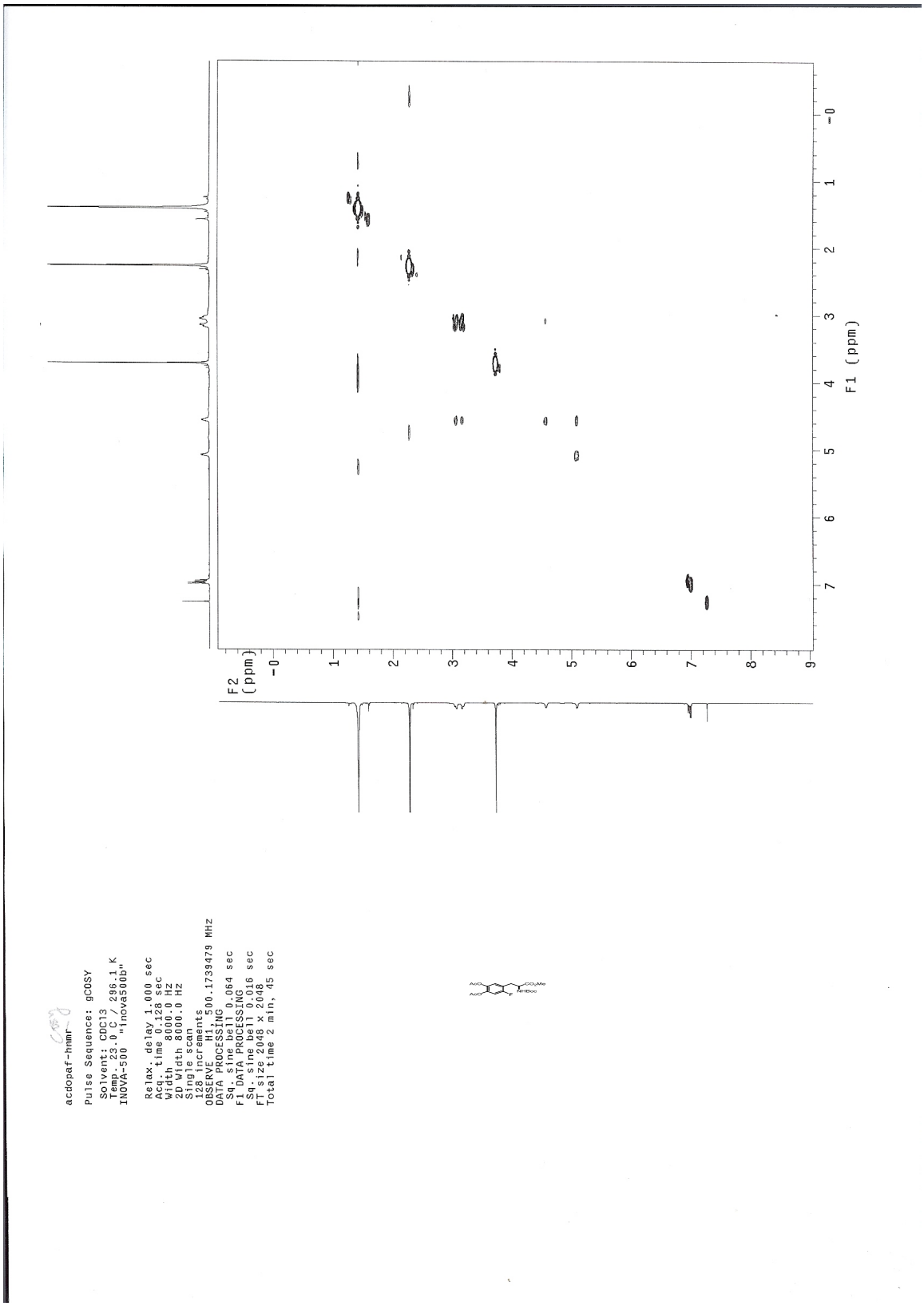
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **12**



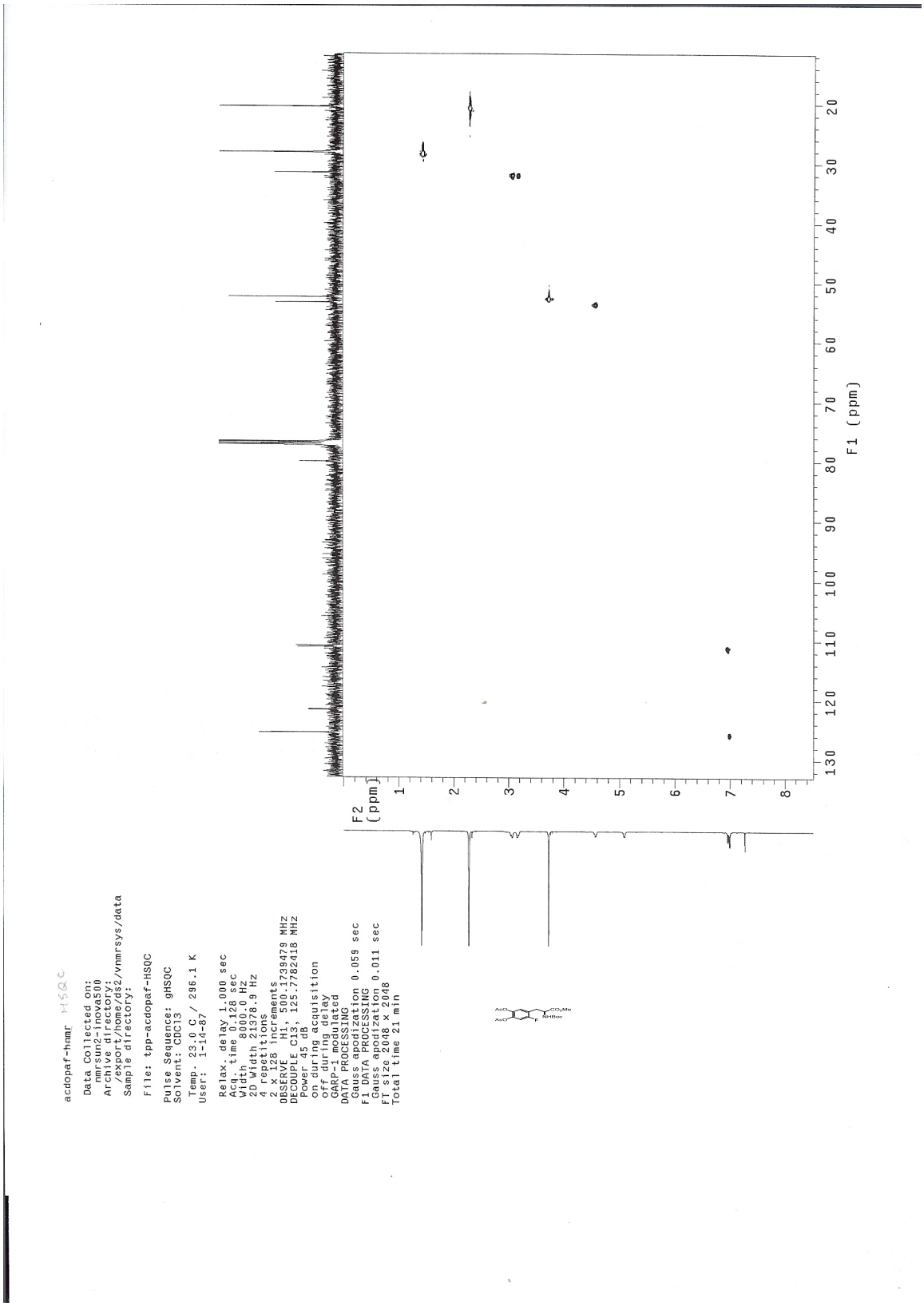
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **12**



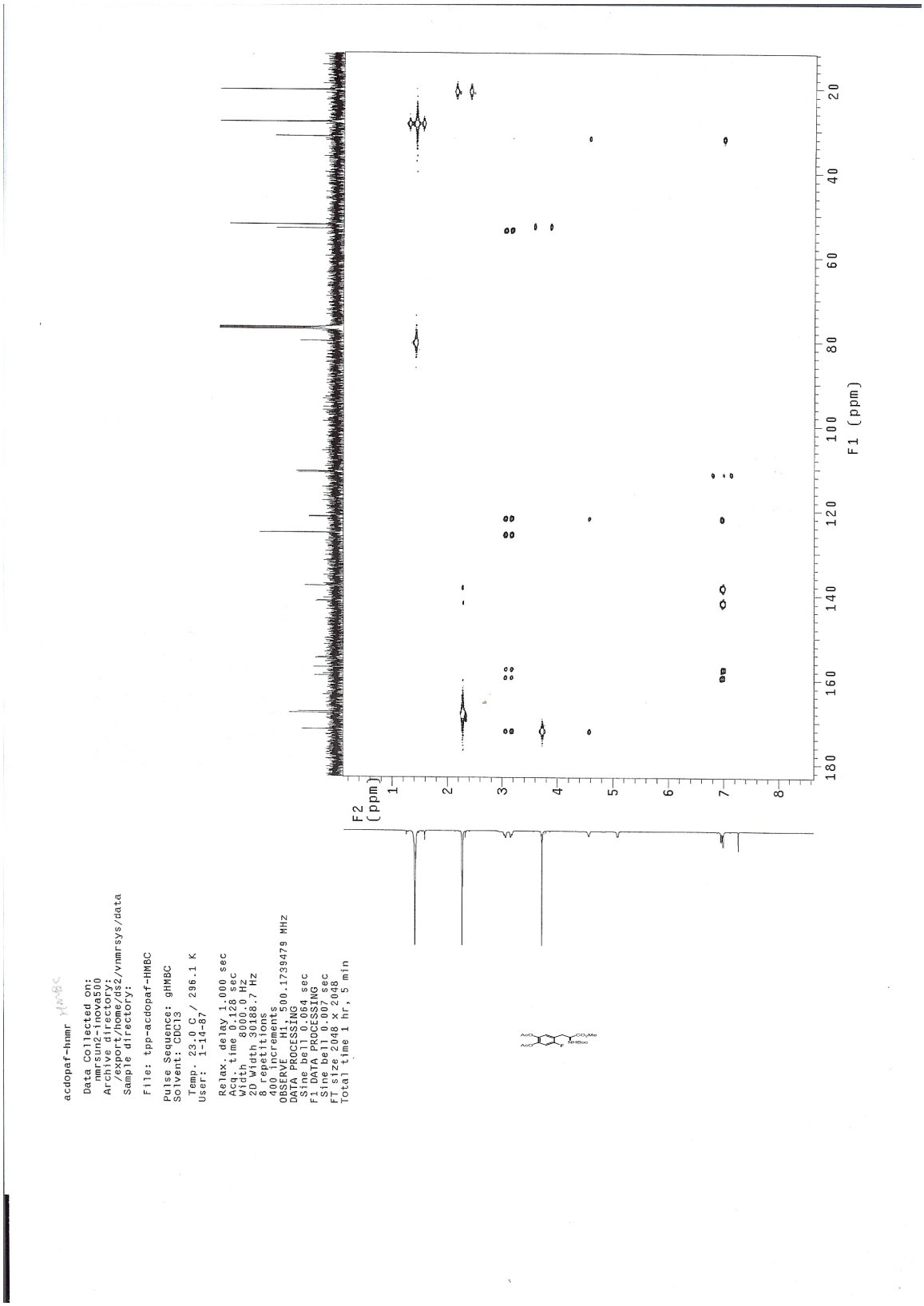
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **12**



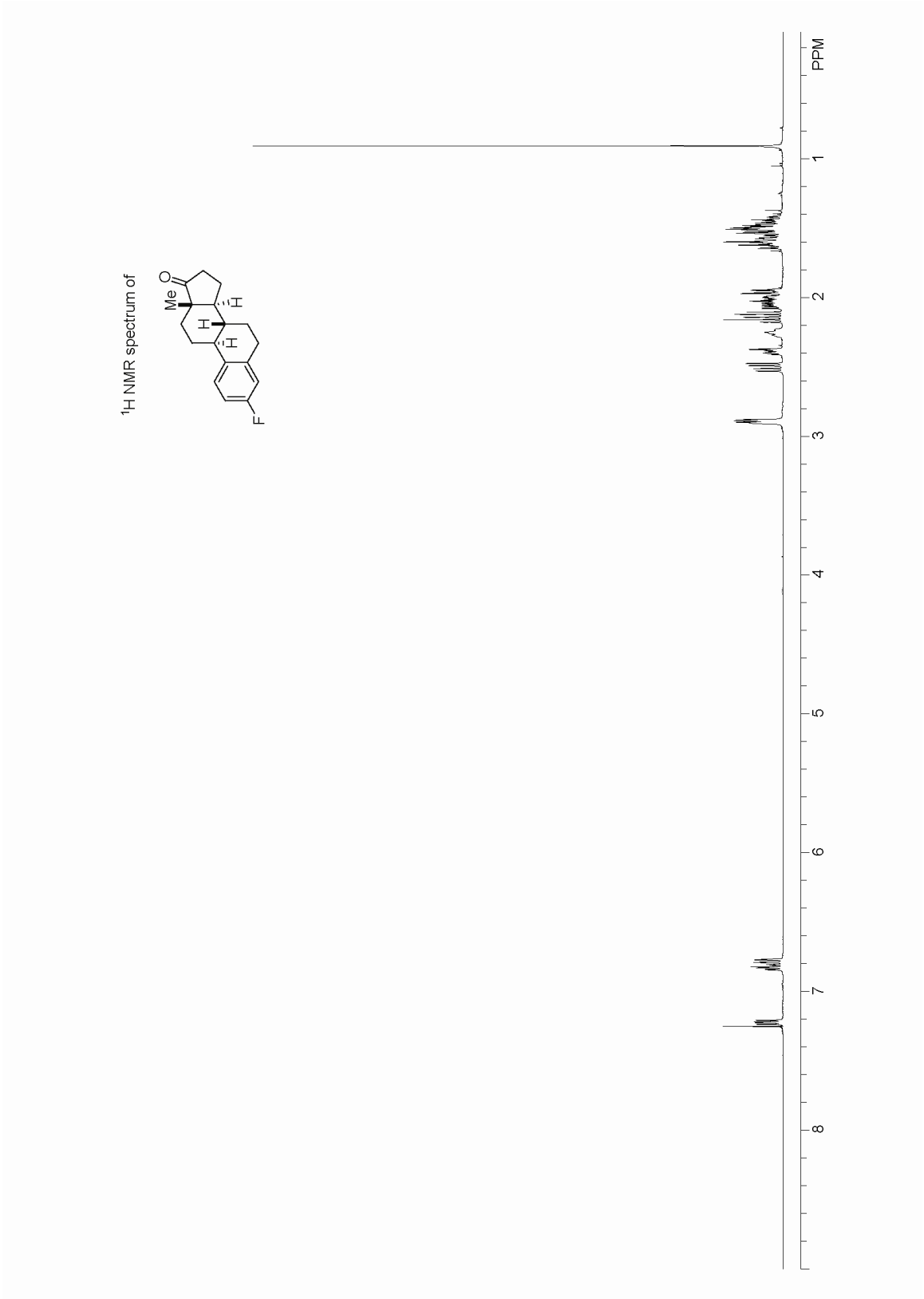
^{1}H-^{1}H COSY spectrum (500 MHz, $CDCl_3$, 23 ºC) of **12**



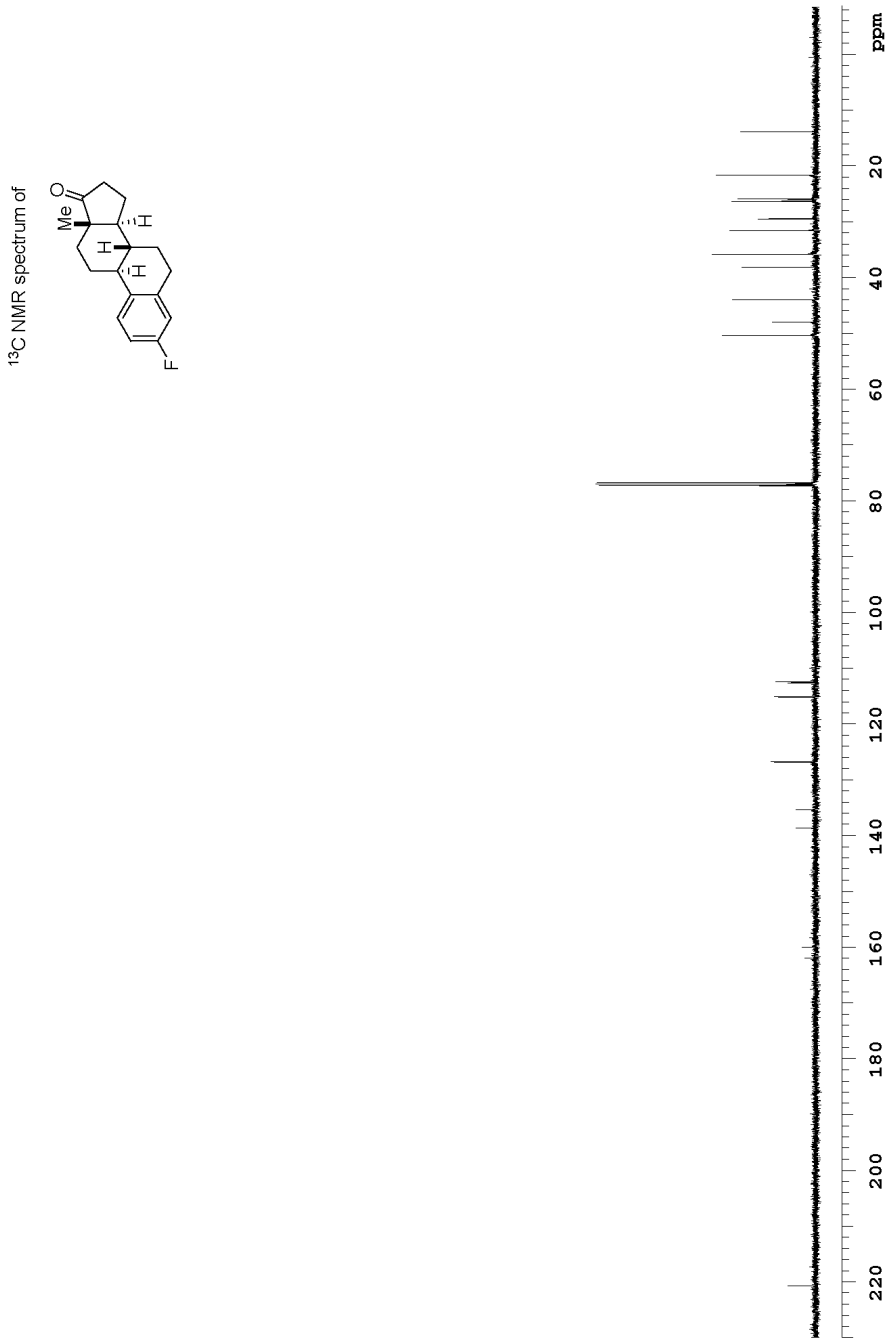
HSQC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **12**



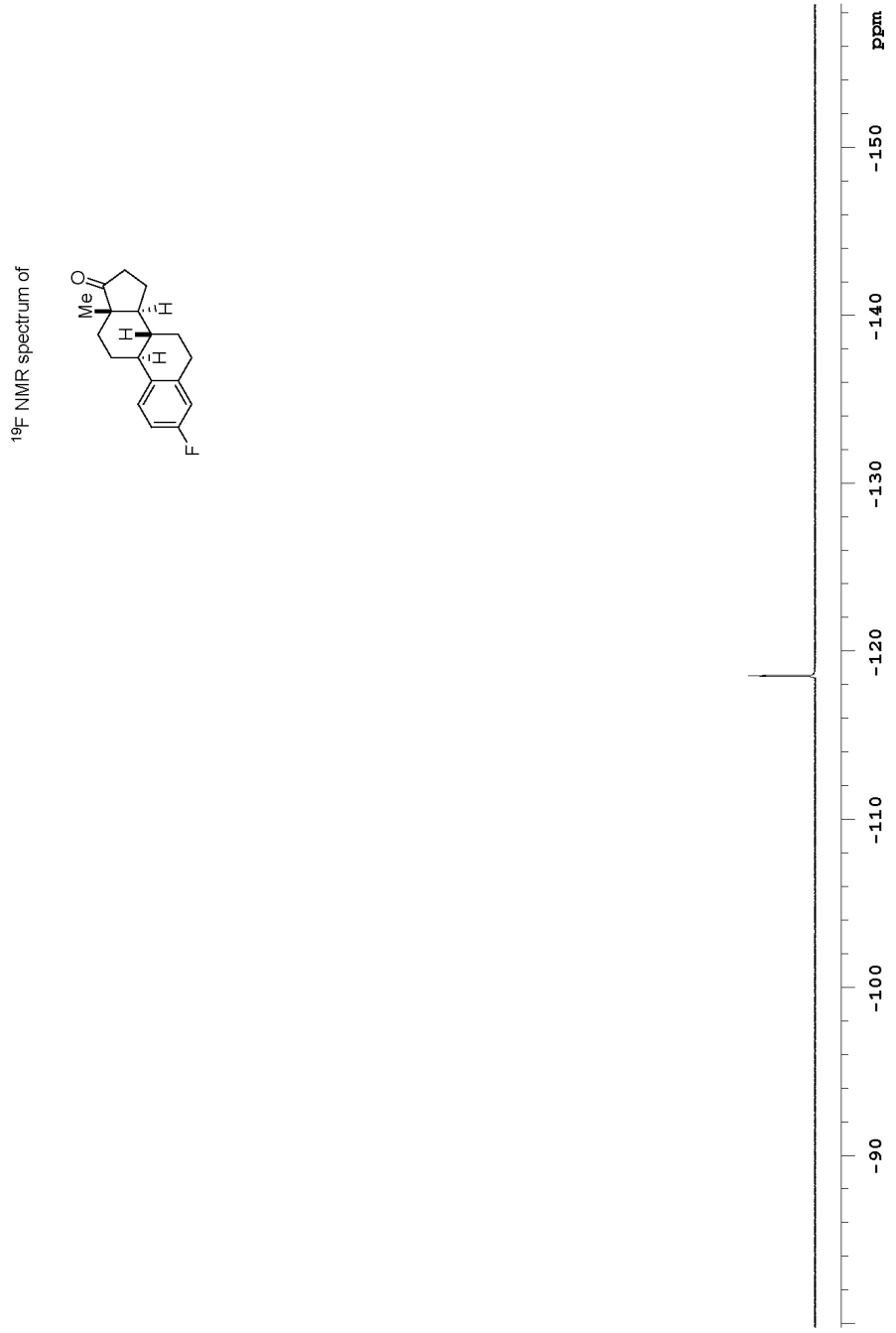
HMBC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **12**



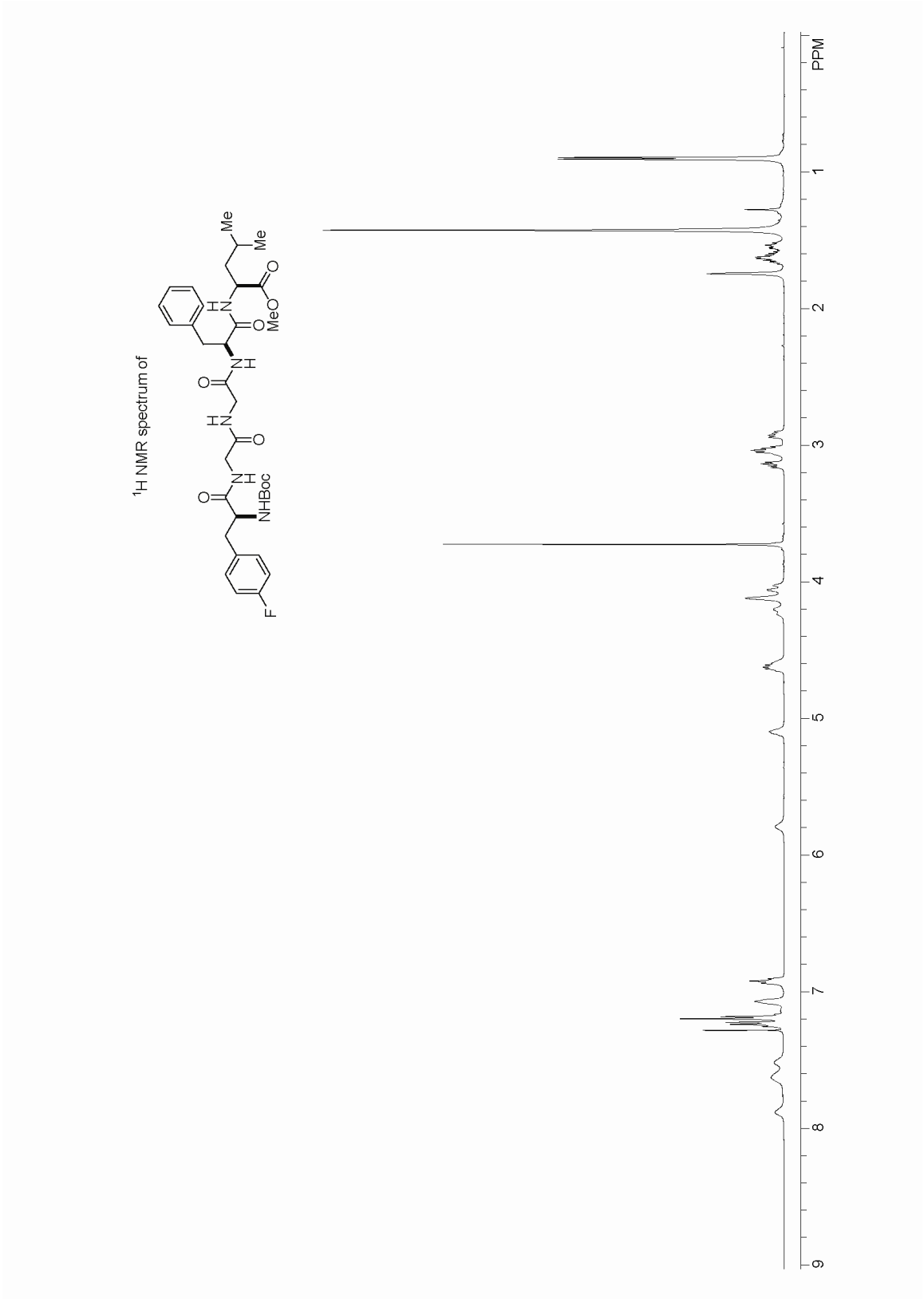
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **13**



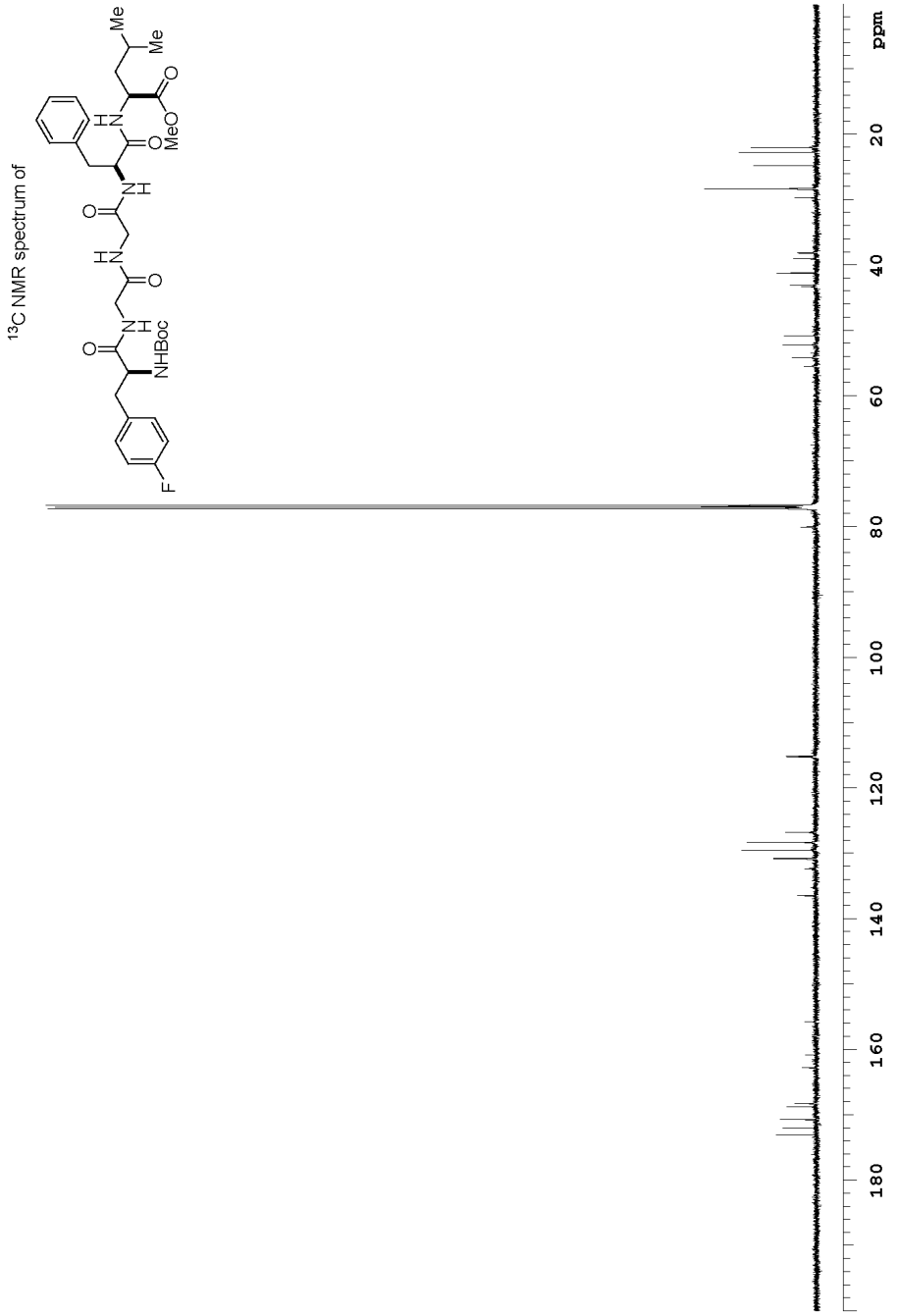
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **13**



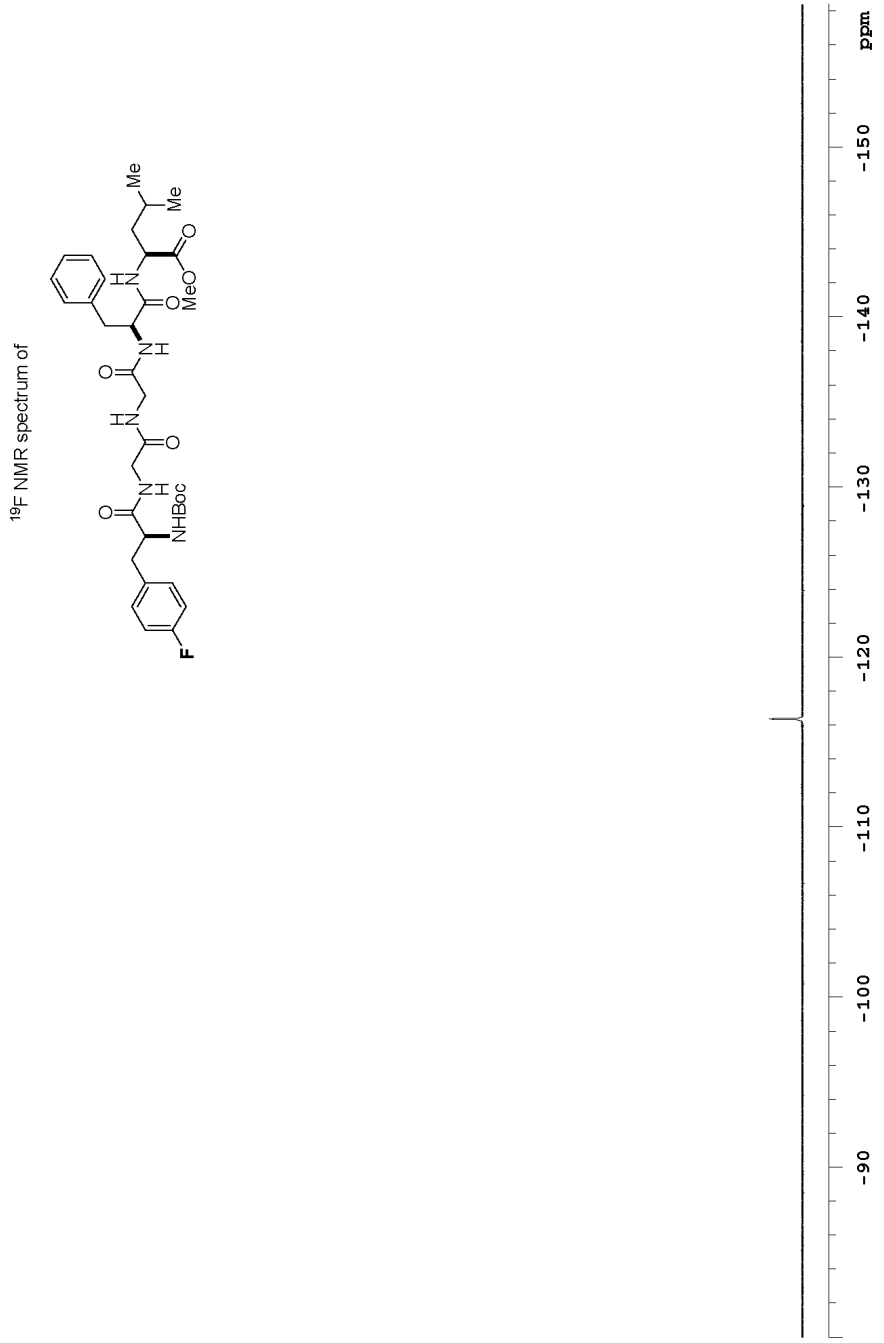
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **13**



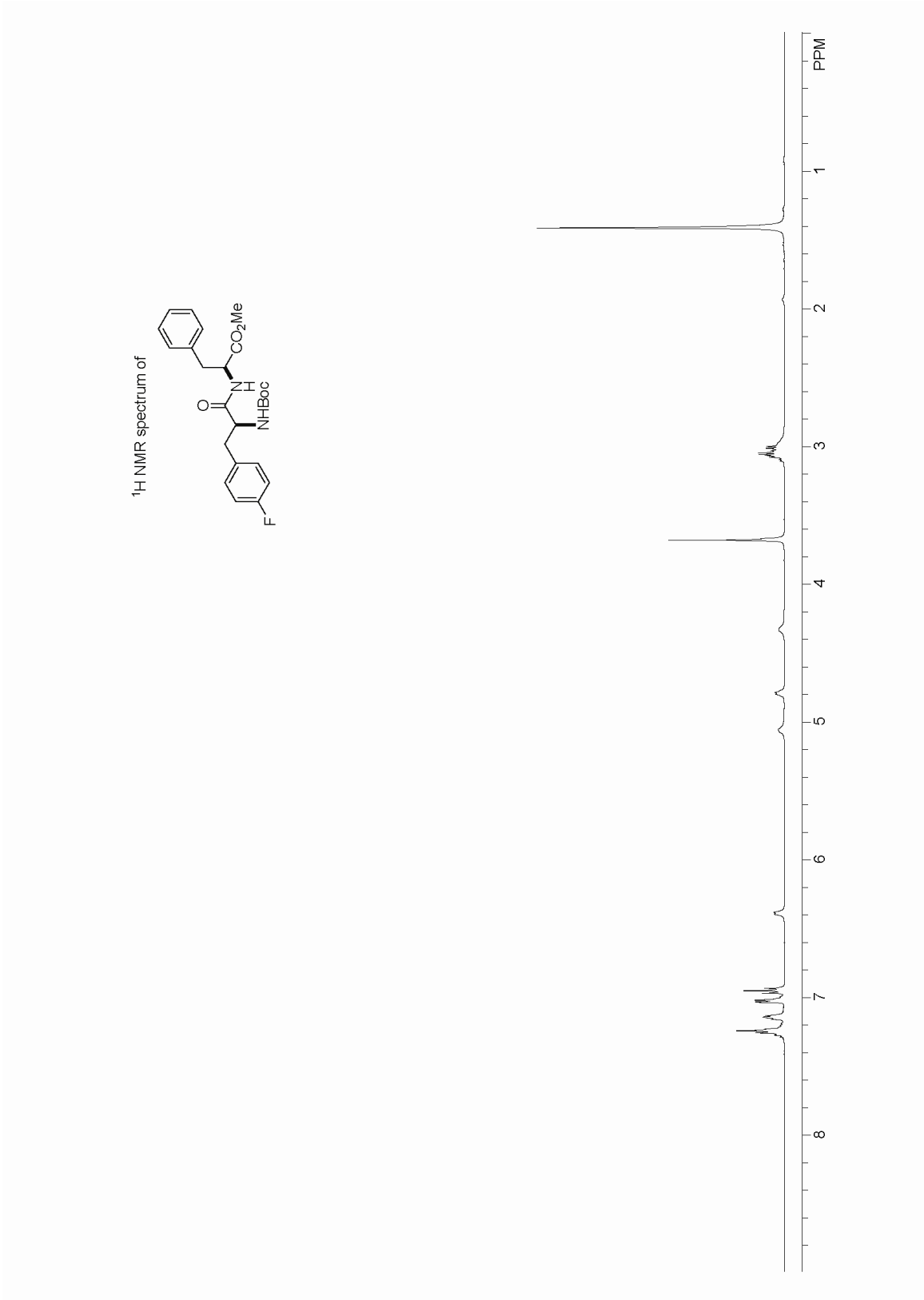
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **14**



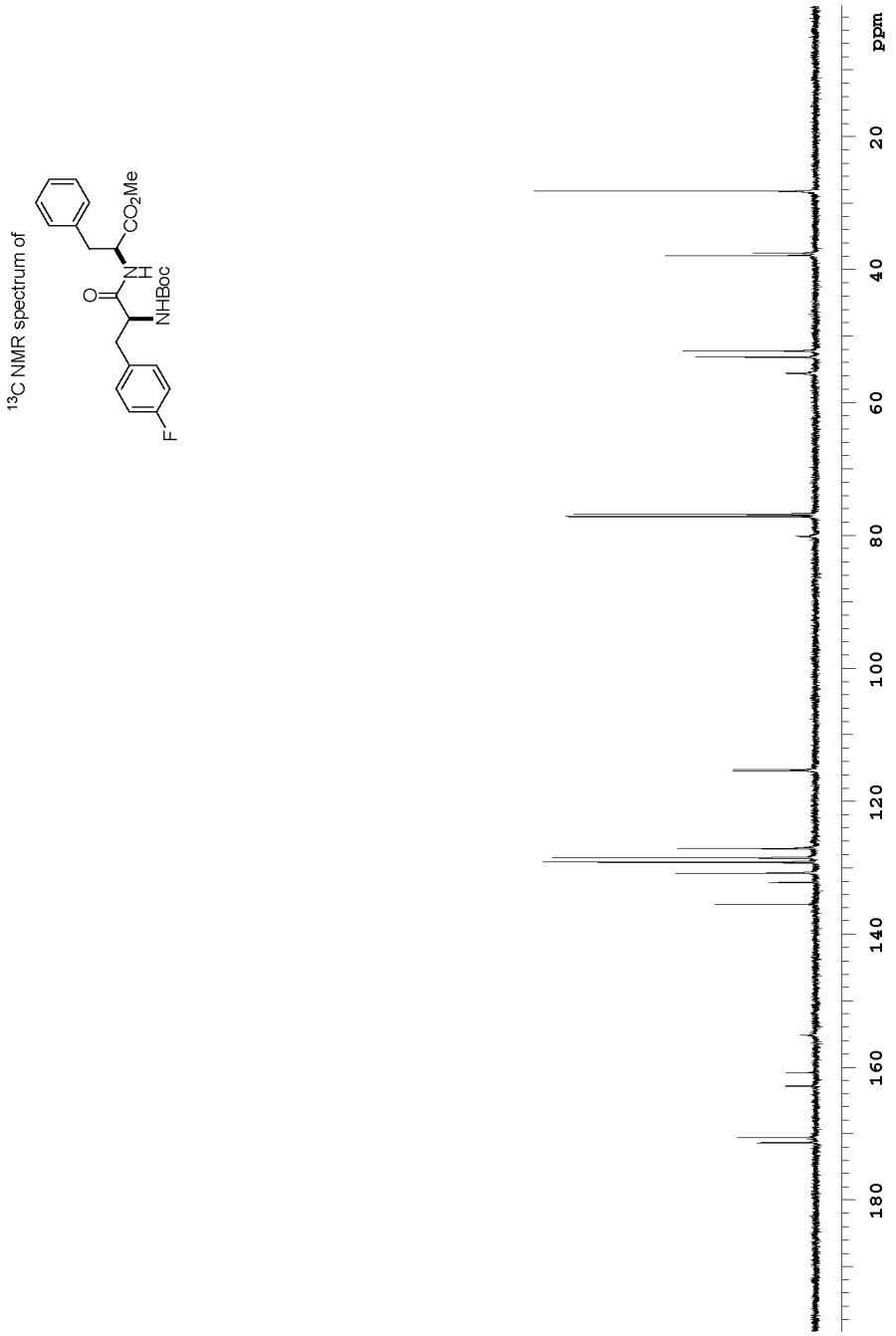
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **14**



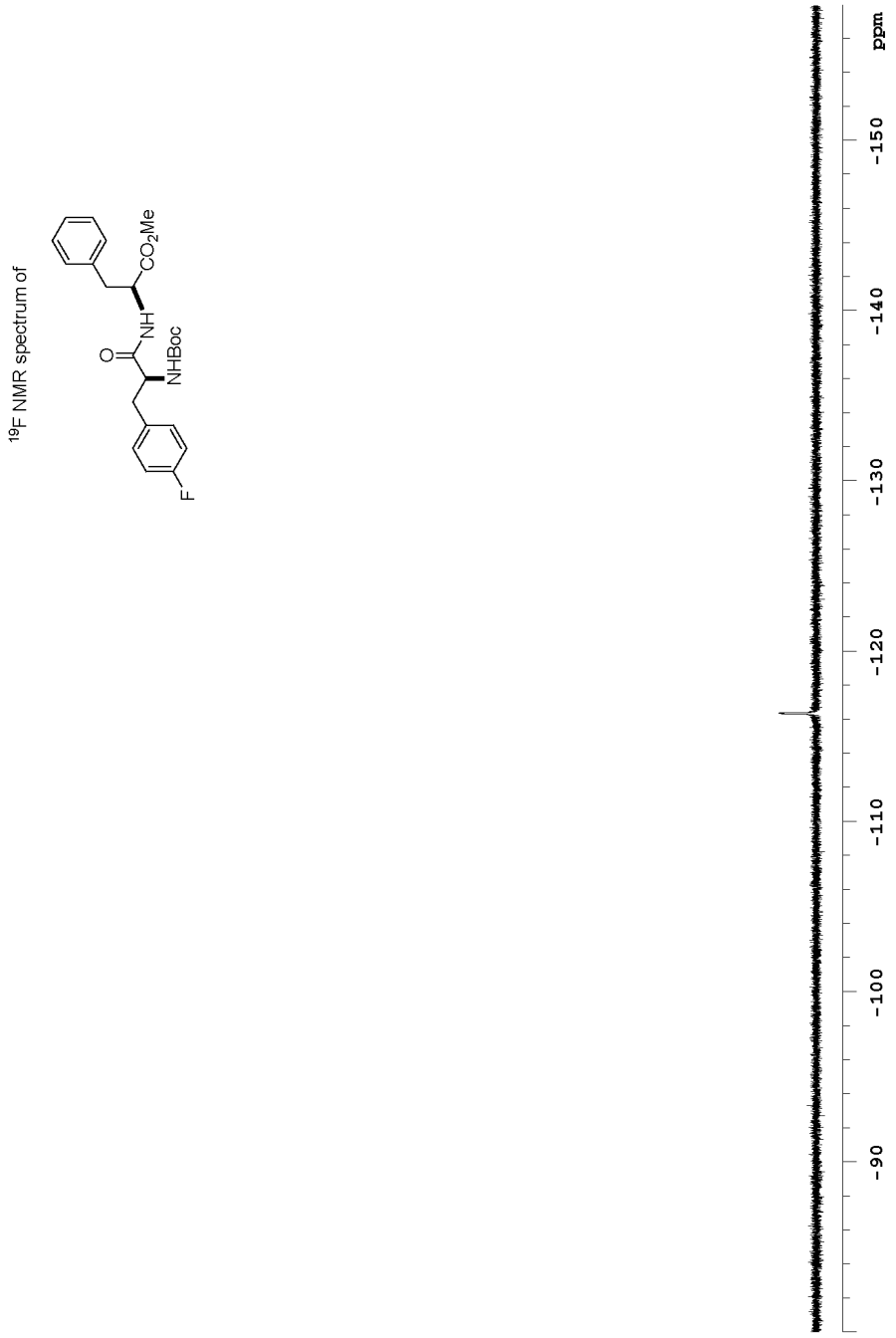
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **14**



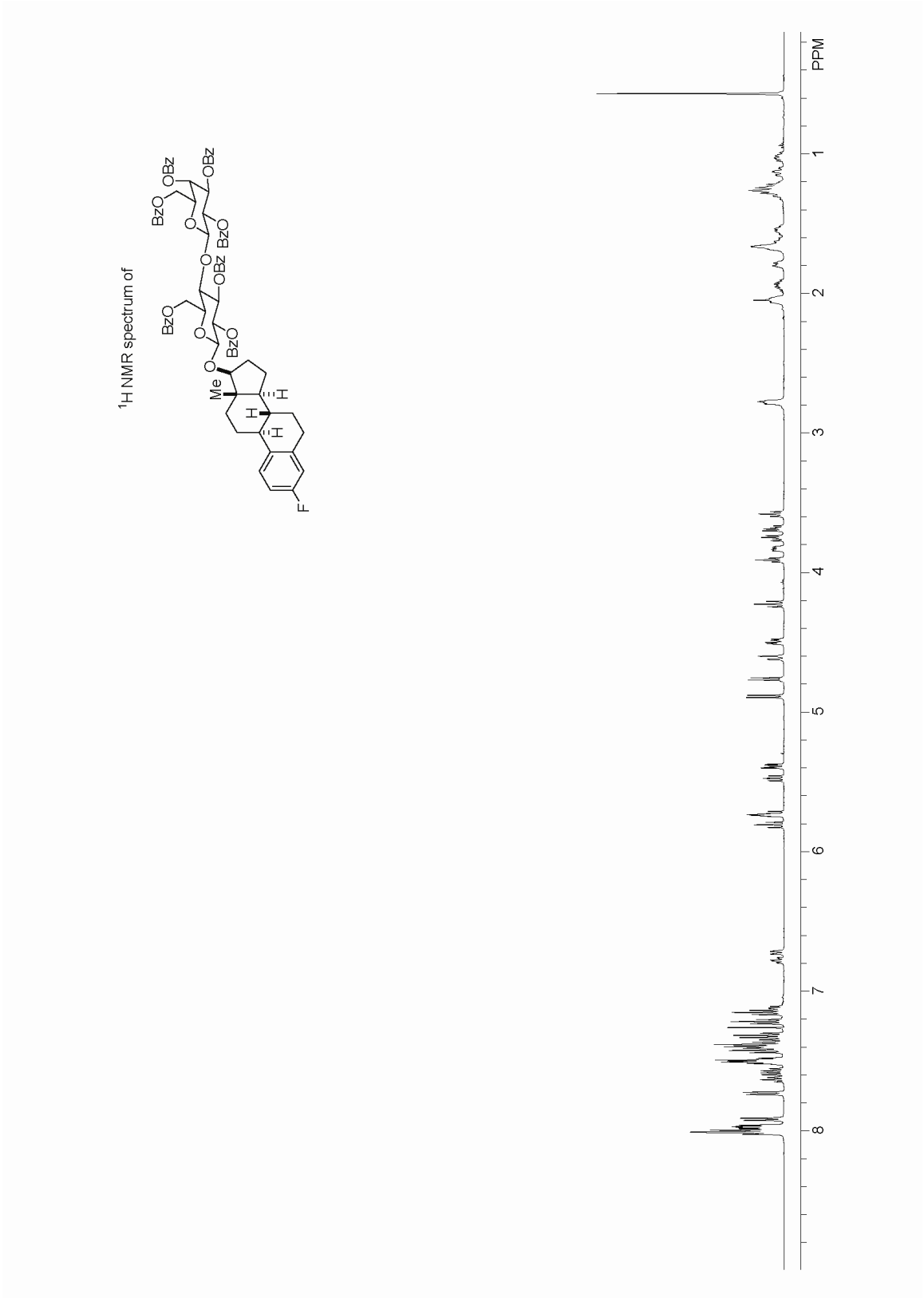
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **15**



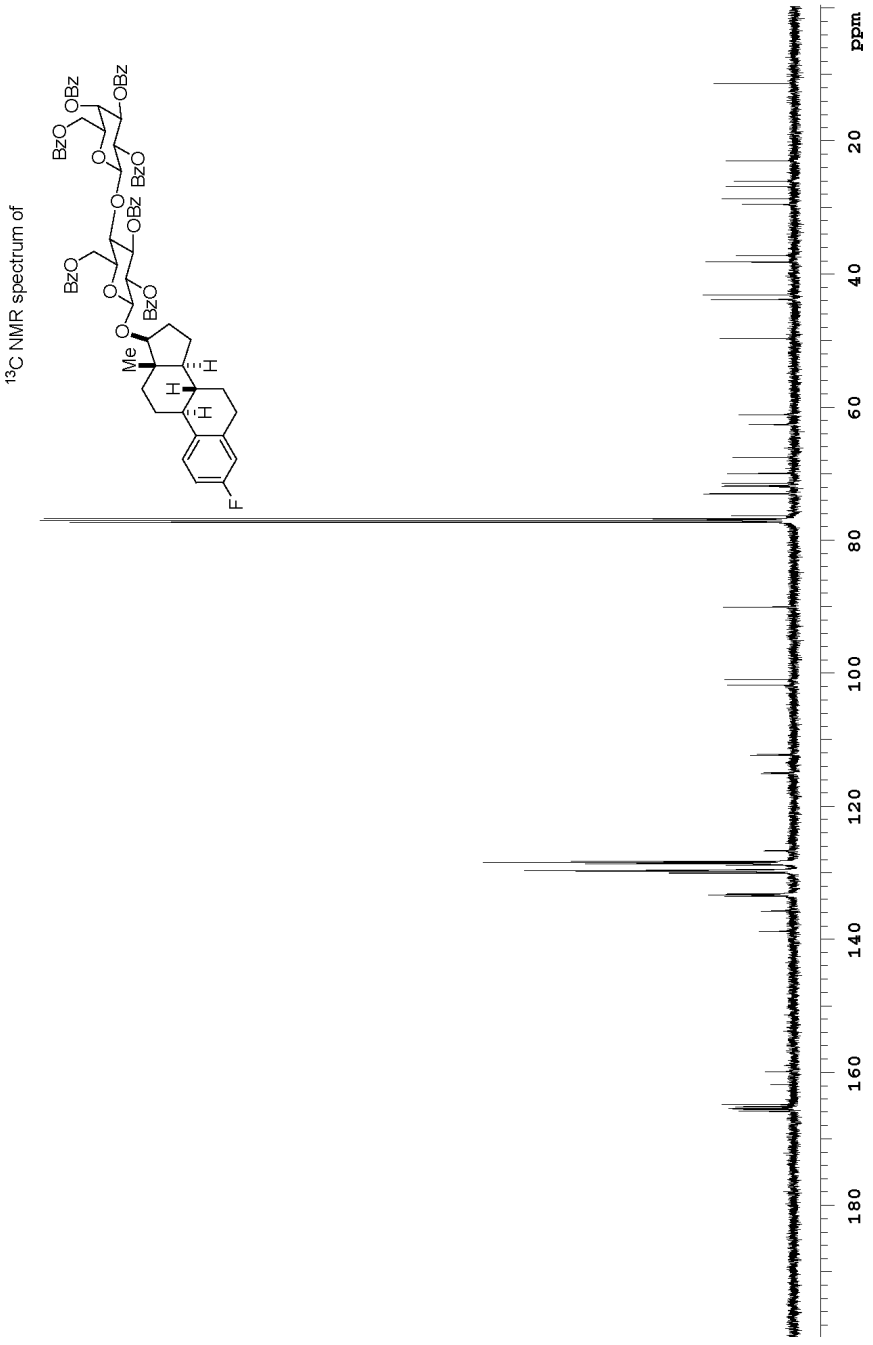
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **15**



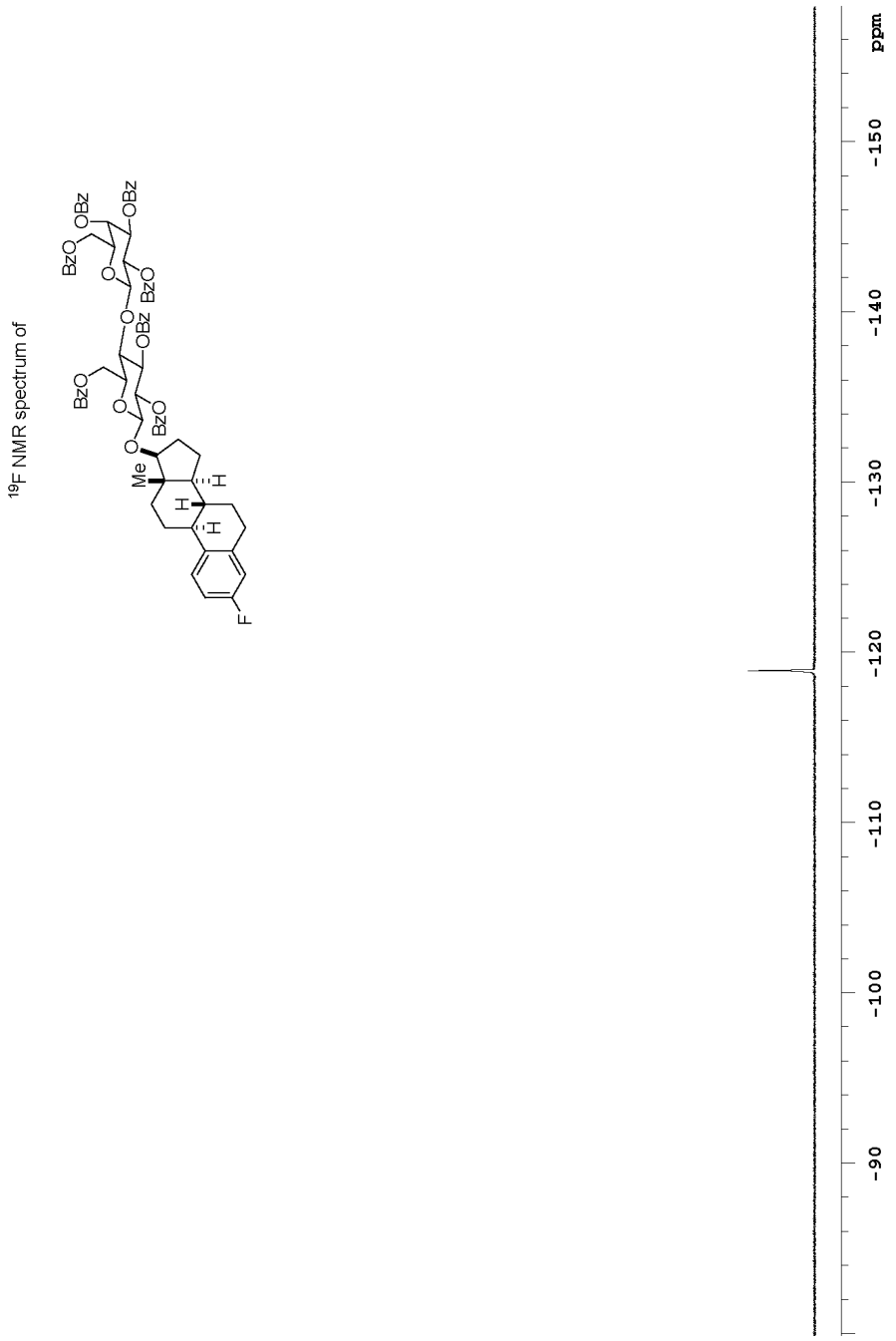
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **15**



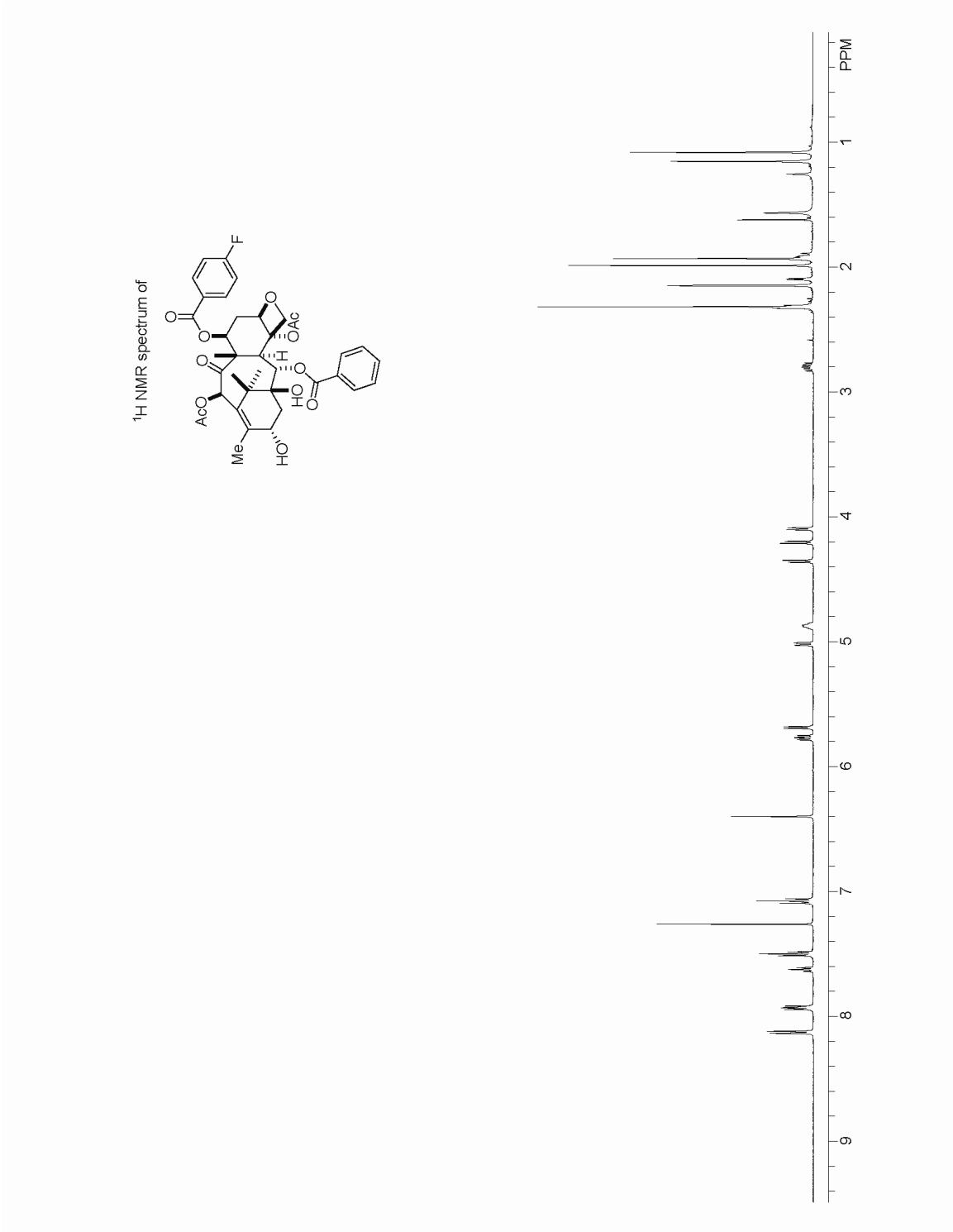
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **16**



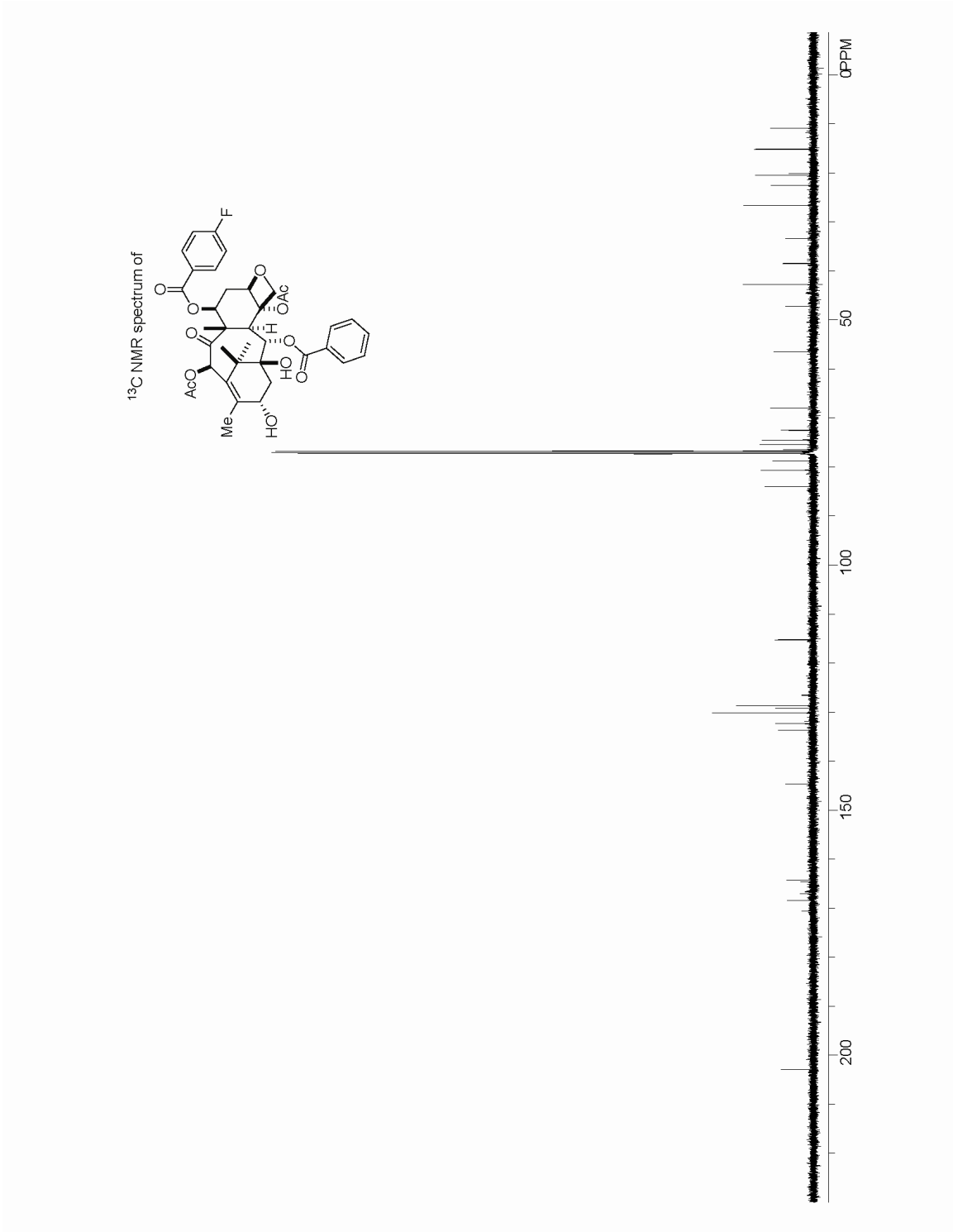
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **16**



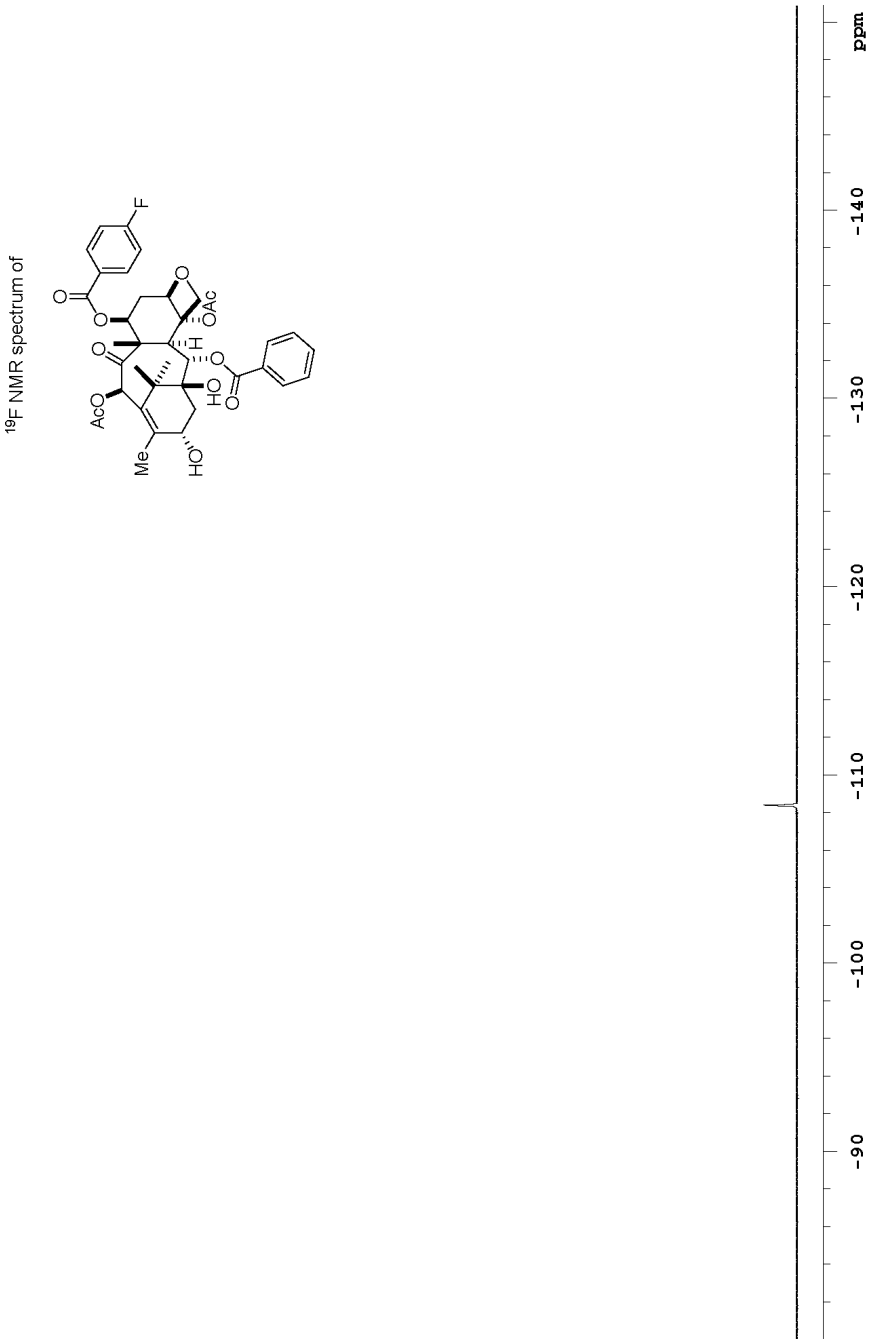
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **16**



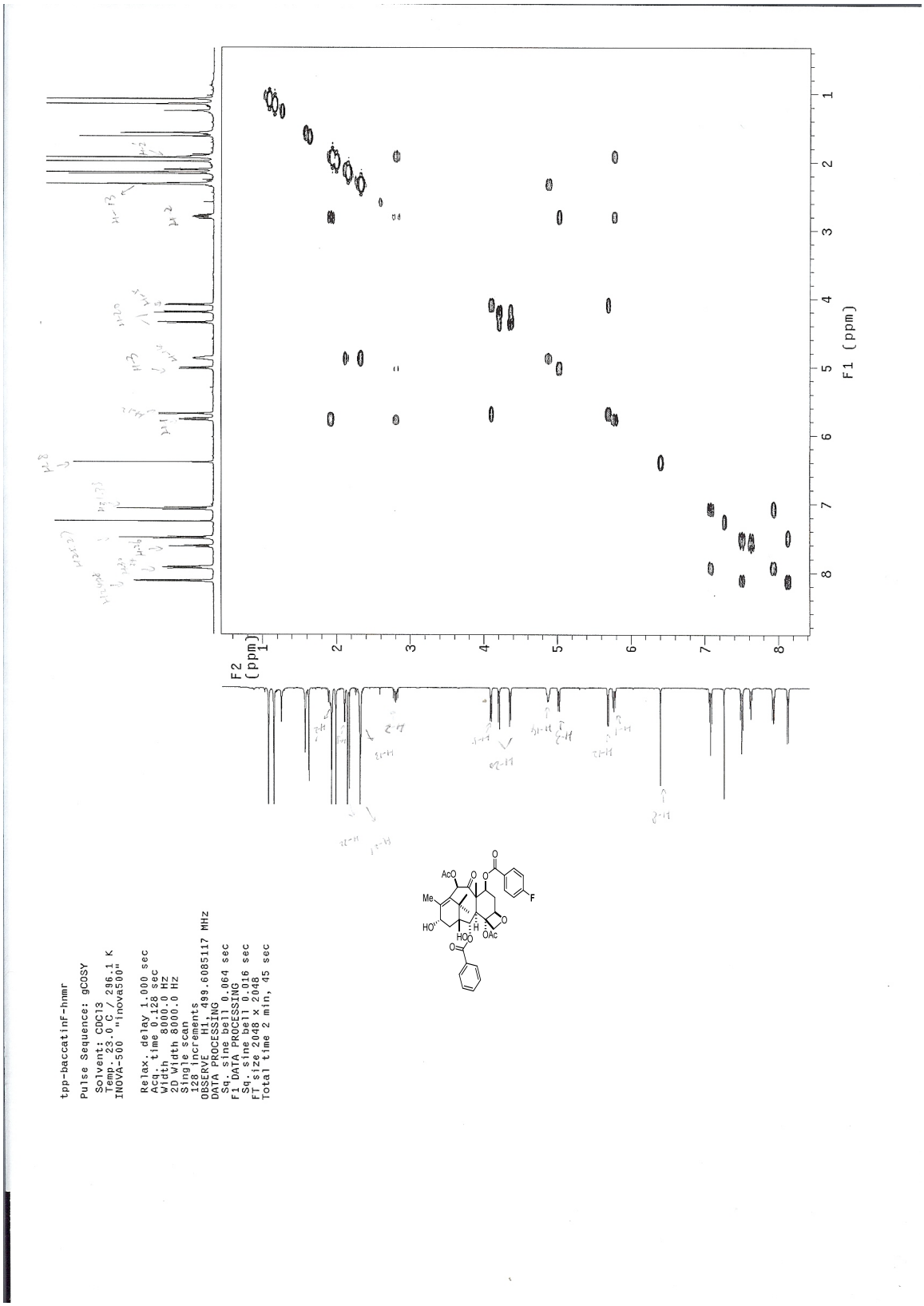
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **17**



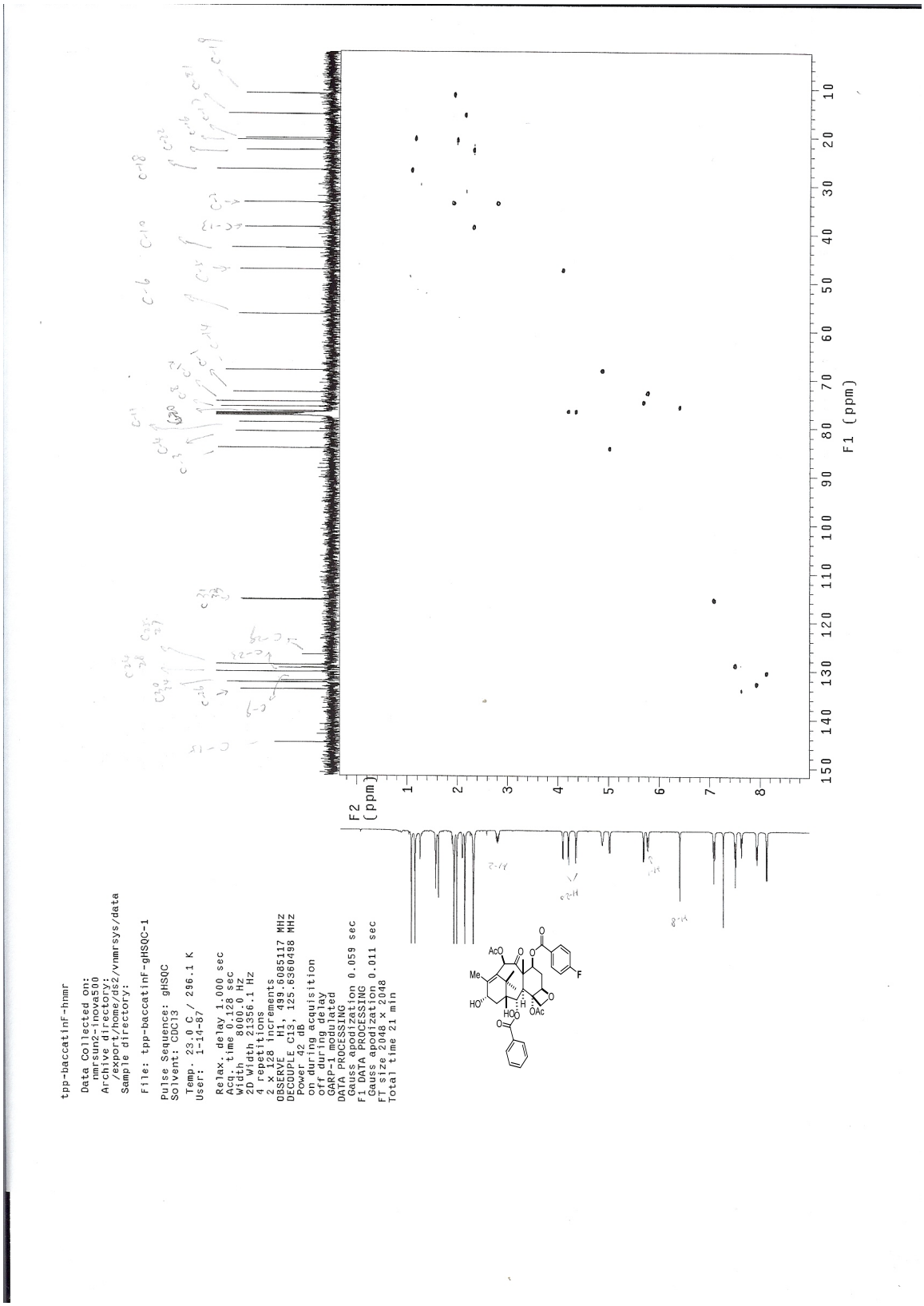
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **17**



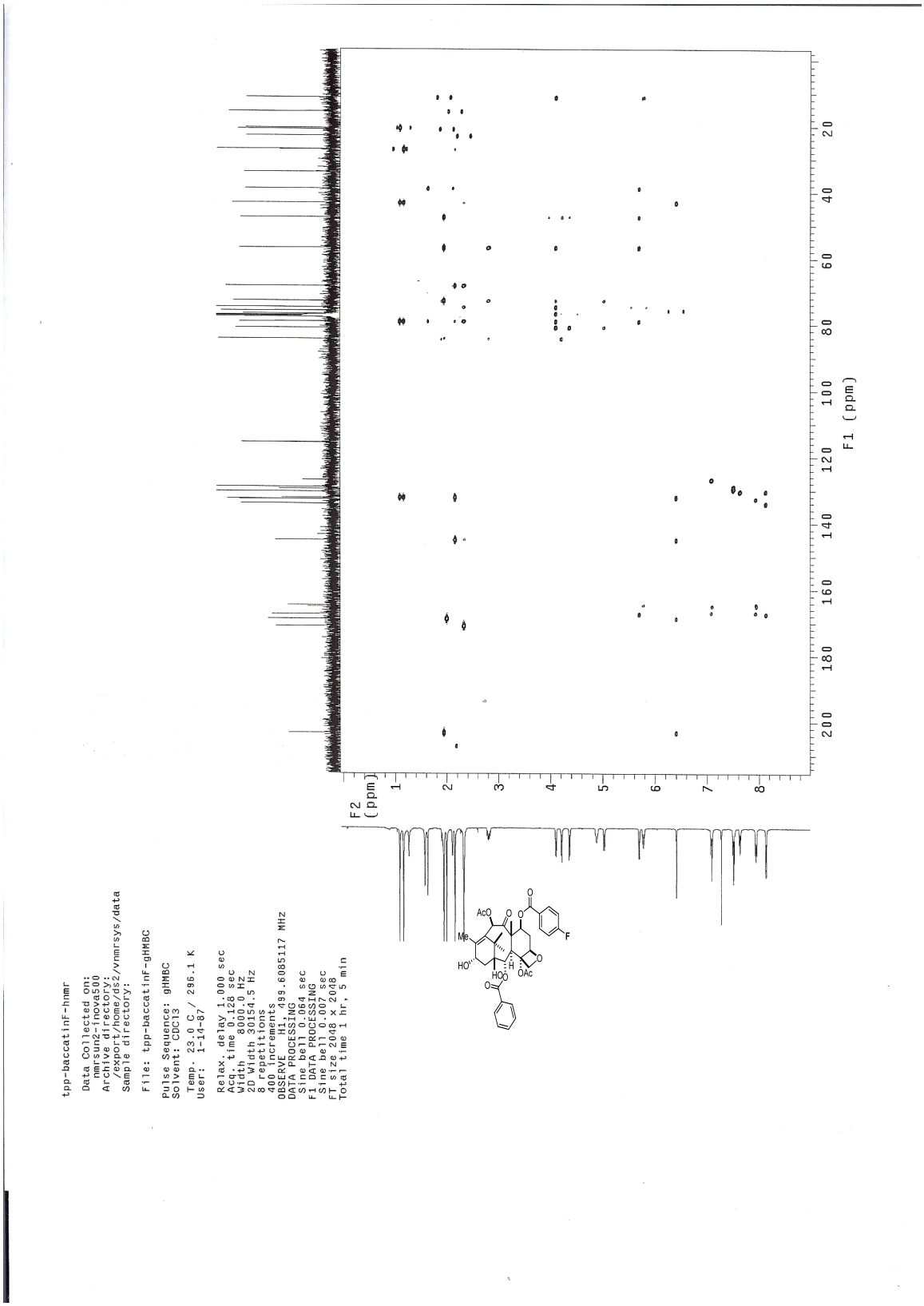
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **17**



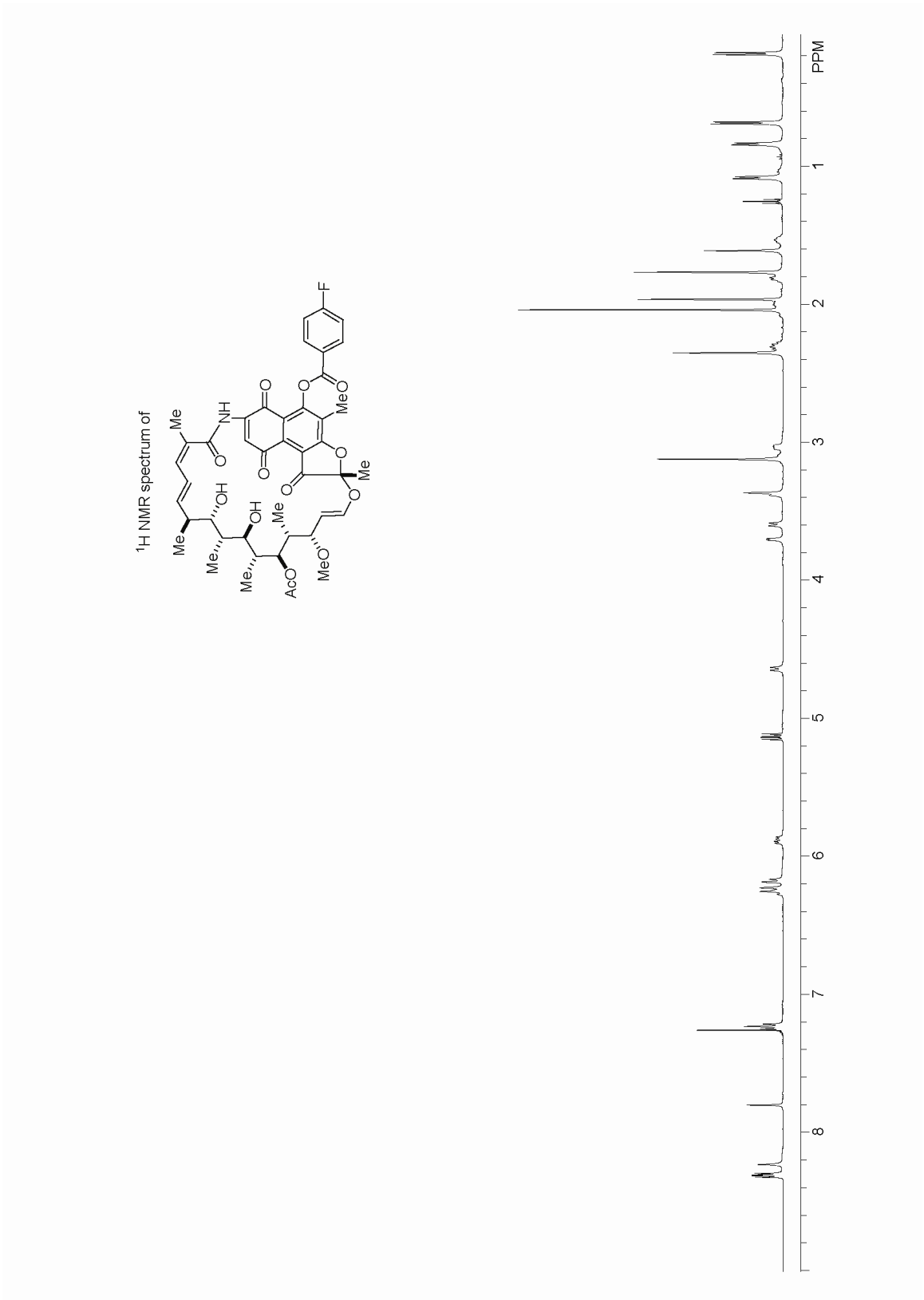
^{1}H-^{1}H COSY spectrum (500 MHz, $CDCl_3$, 23 ºC) of **17**



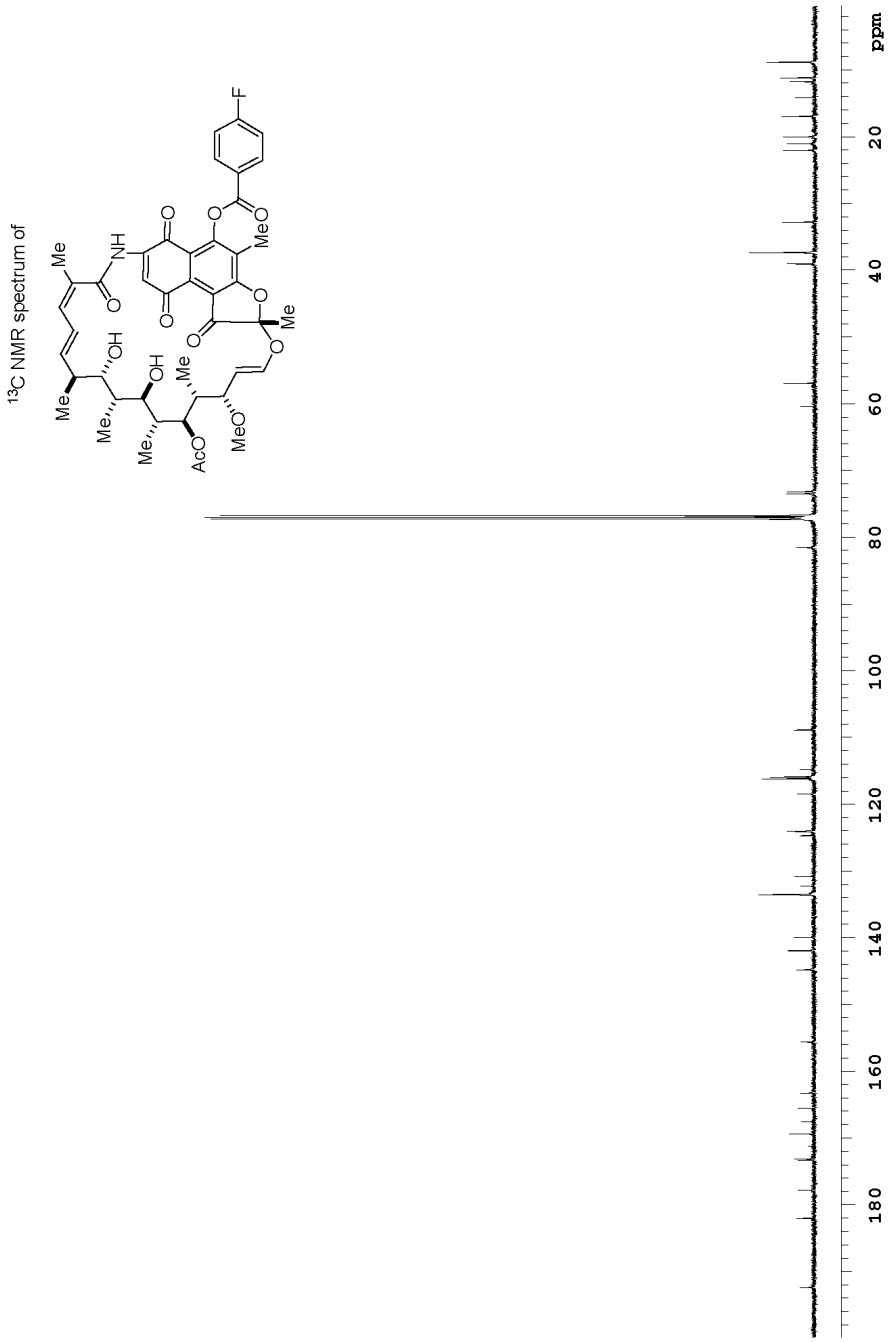
HSQC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **17**



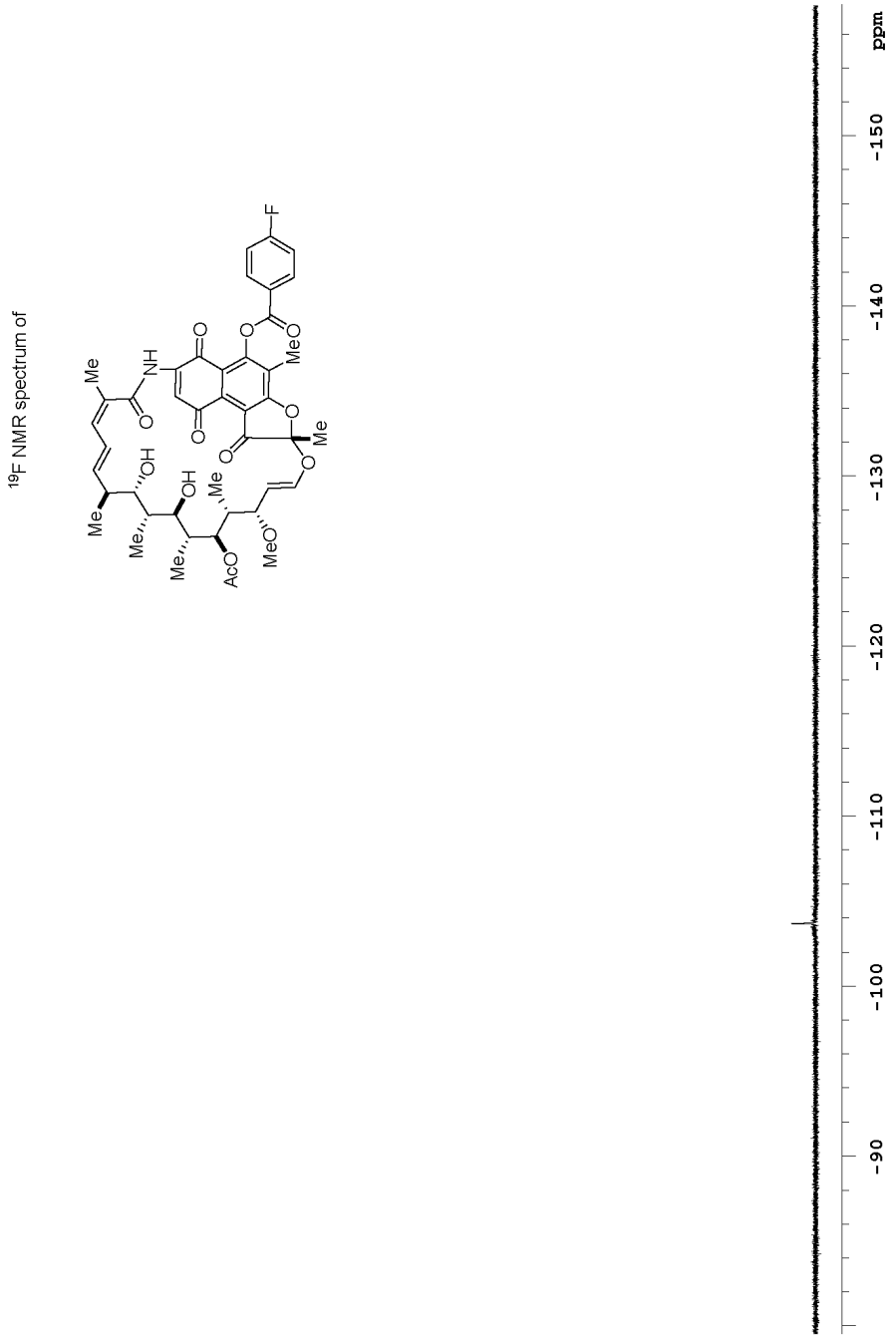
HMBC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **17**



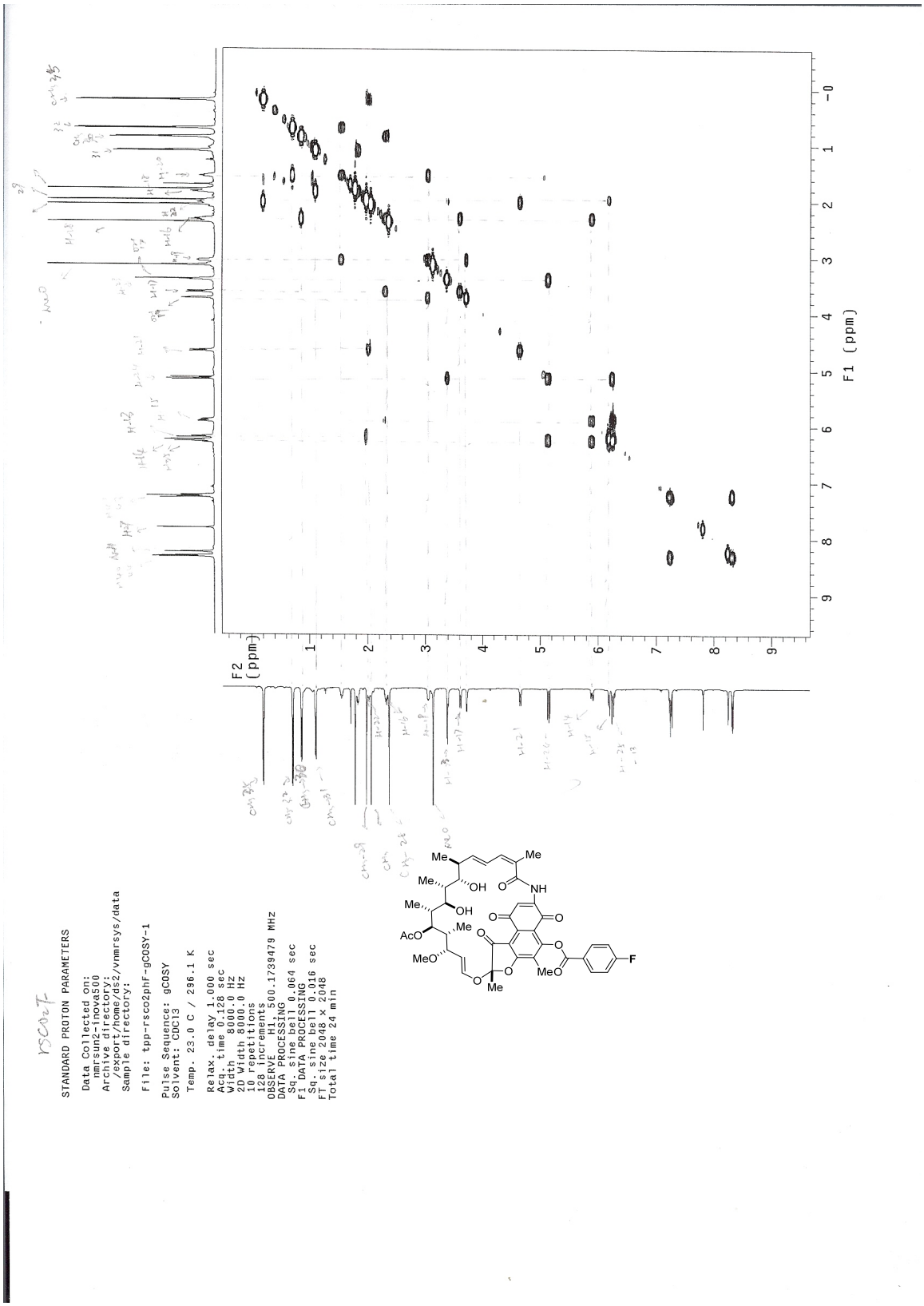
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **18**



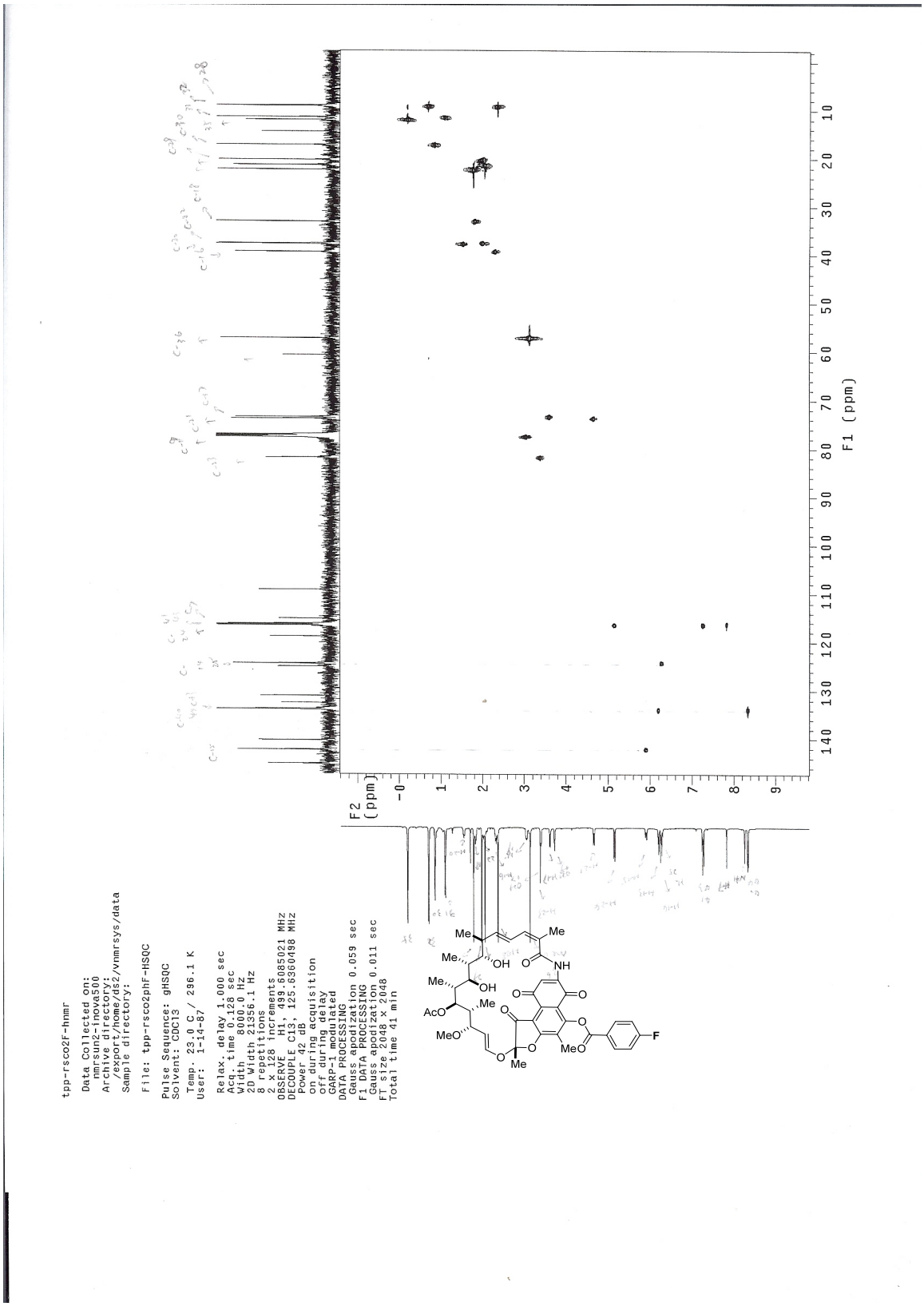
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **18**



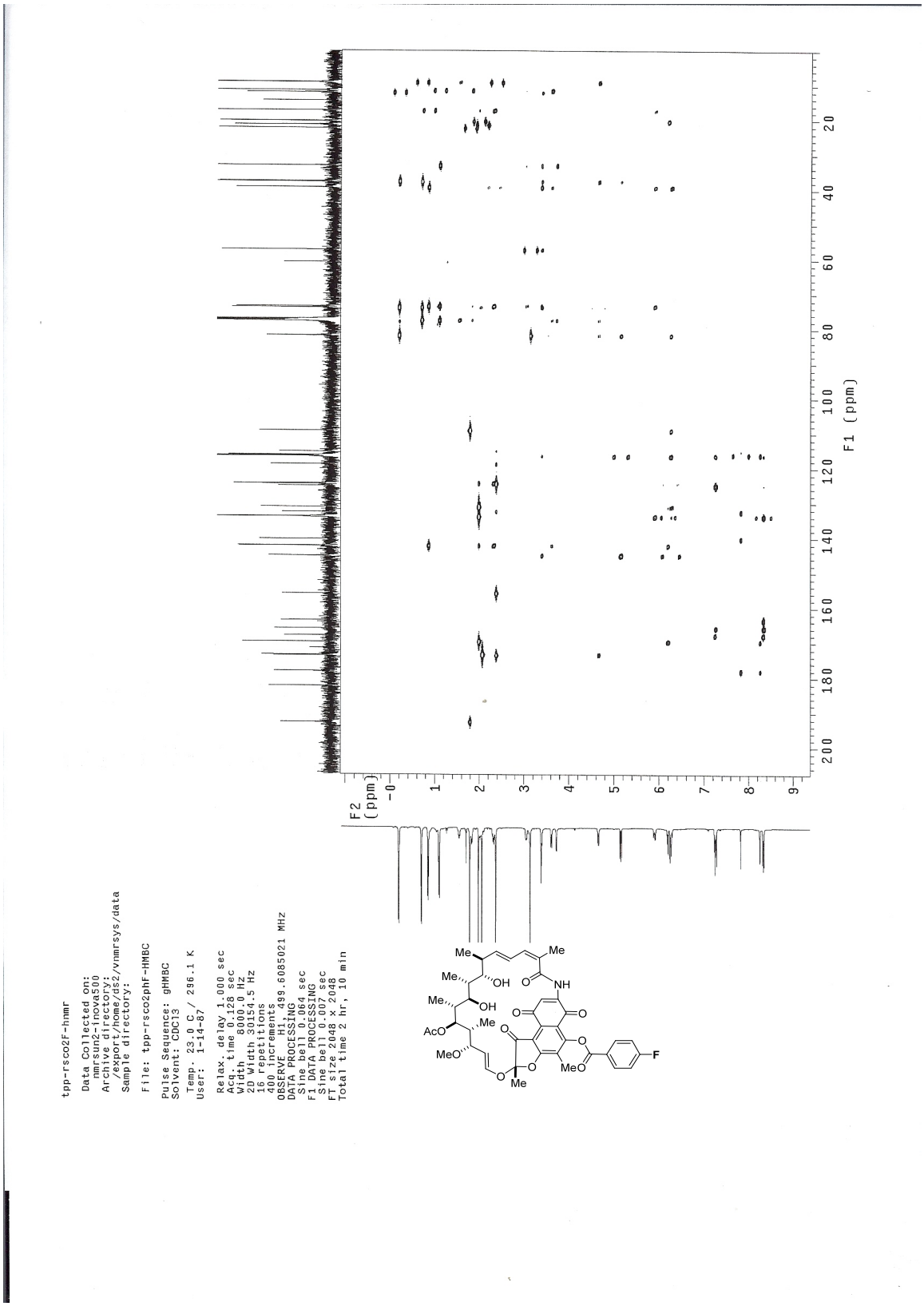
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **18**



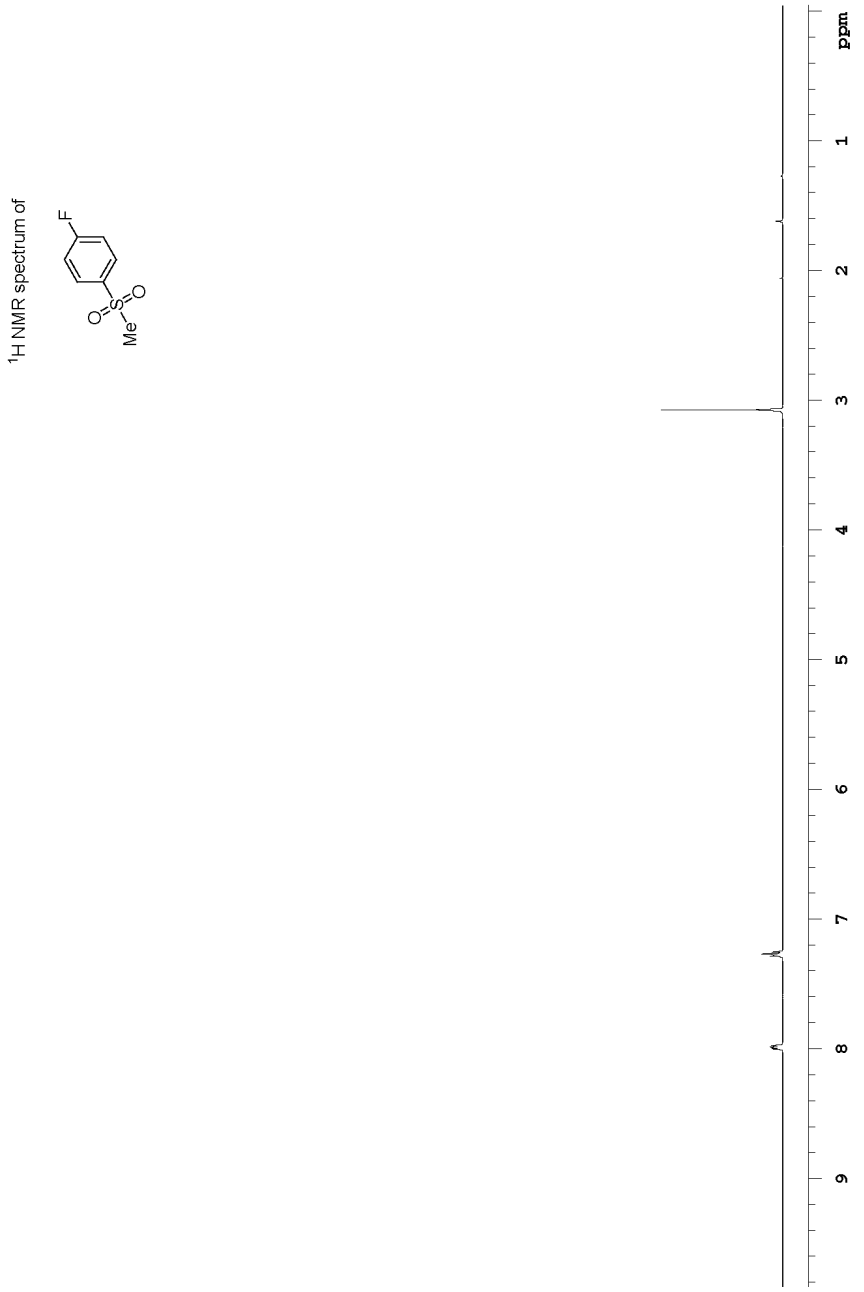
^{1}H-^{1}H COSY spectrum (500 MHz, $CDCl_3$, 23 ºC) of **18**



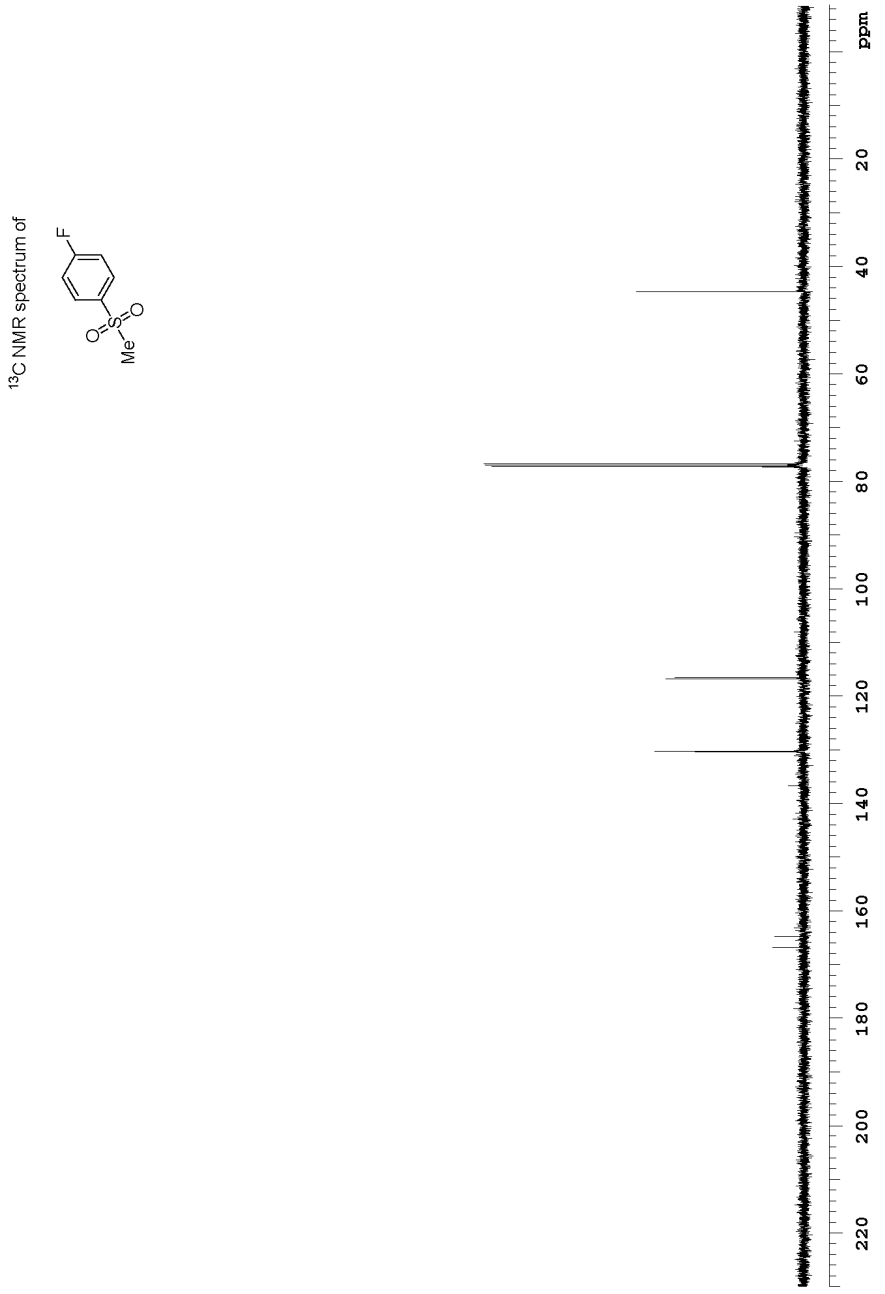
HSQC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **18**



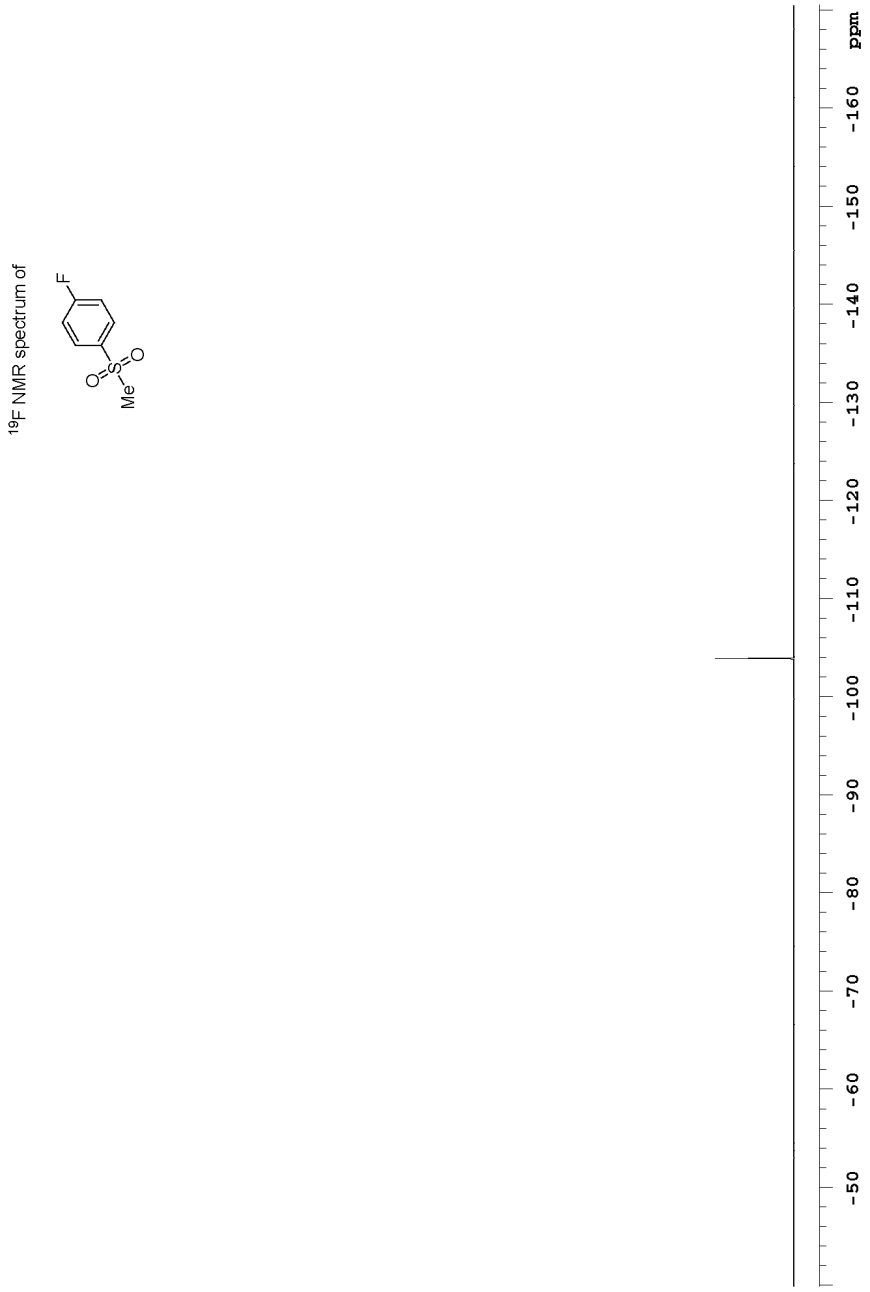
HMBC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **18**



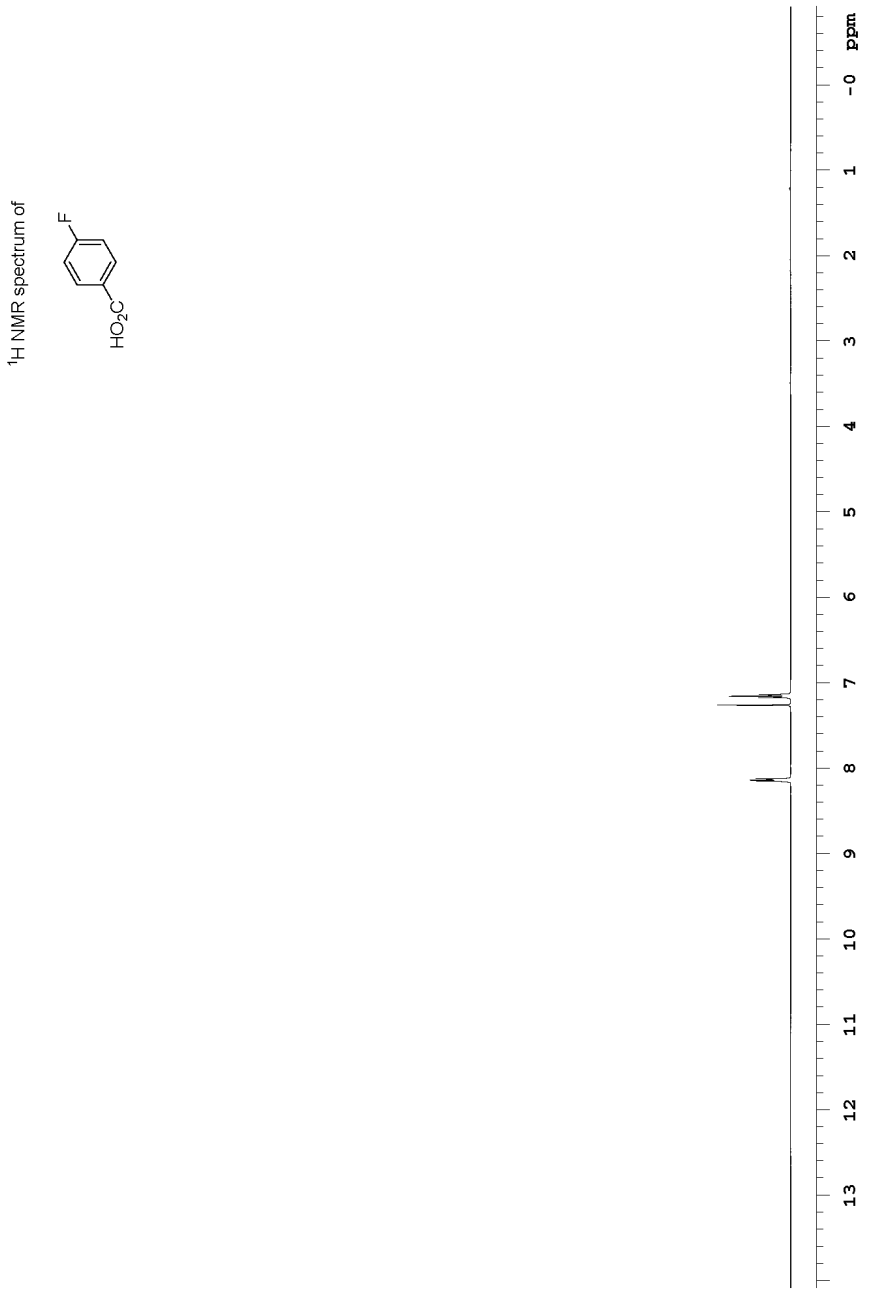
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **21**



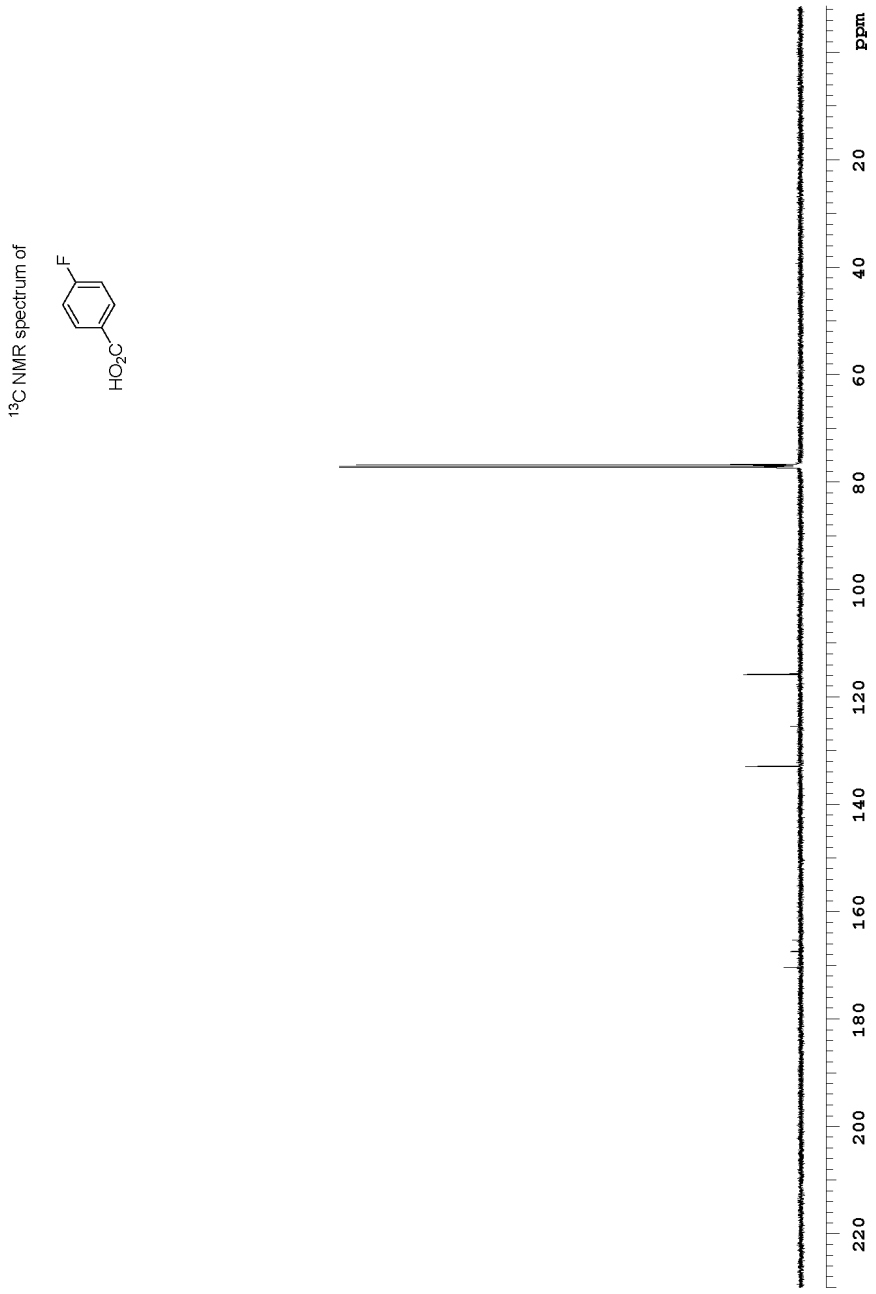
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **21**



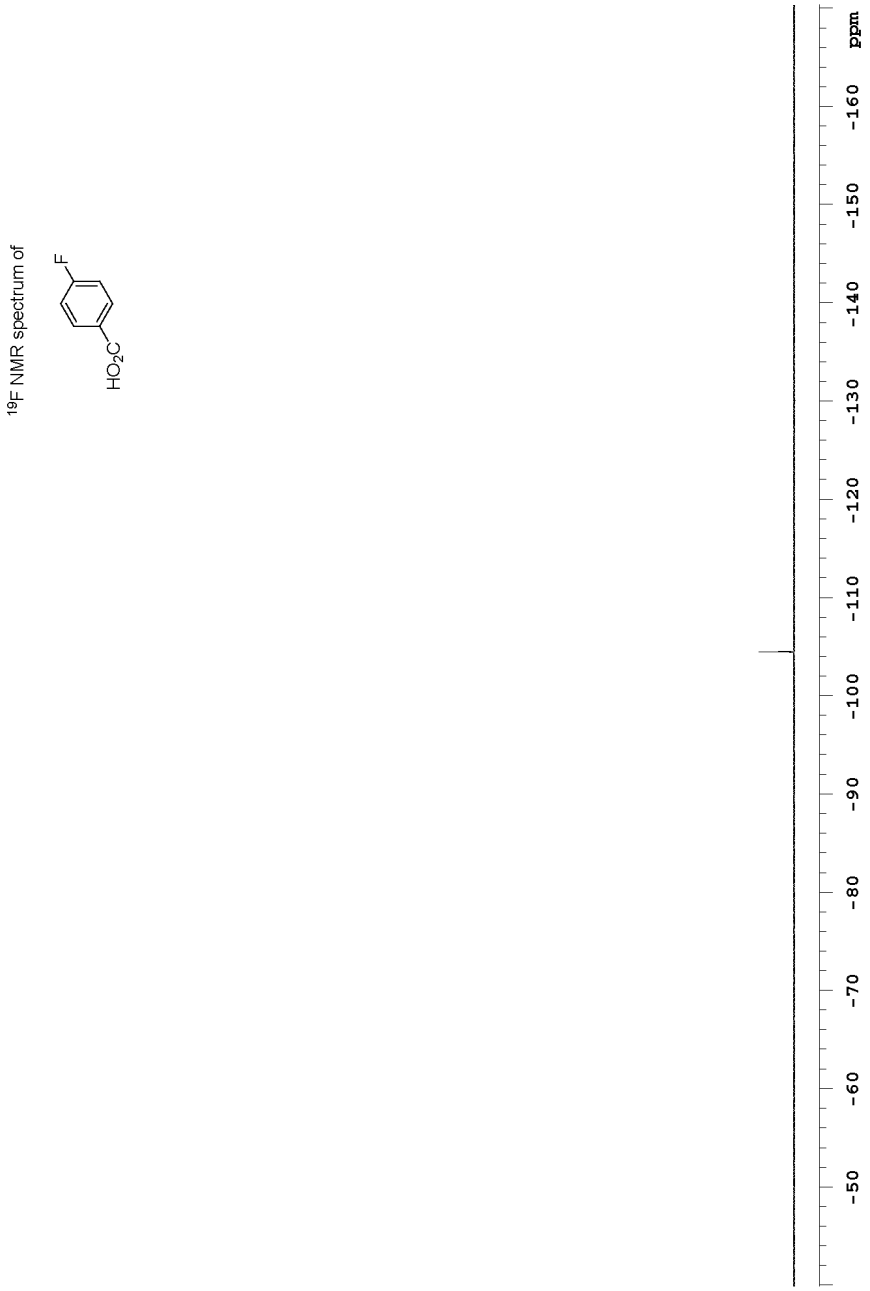
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **21**



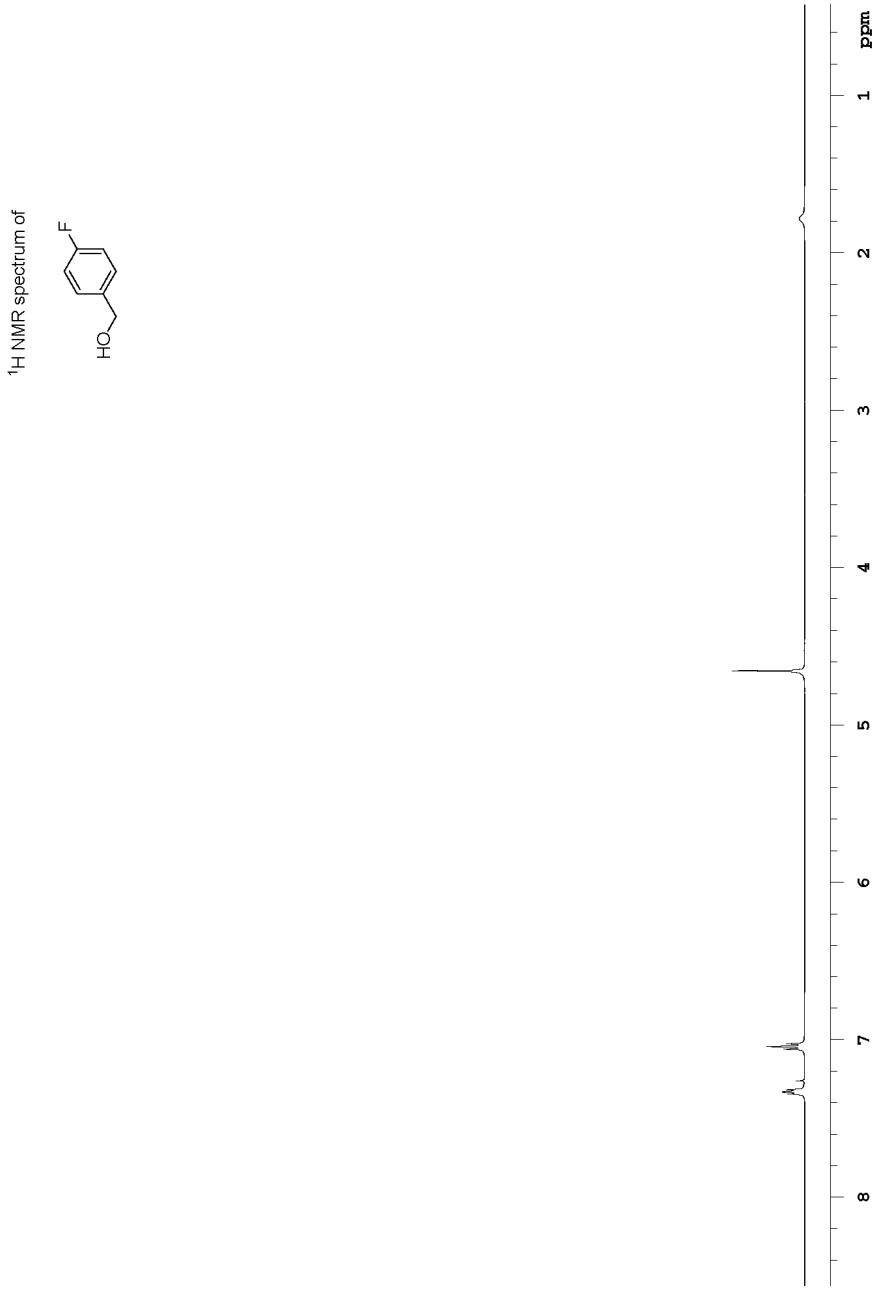
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **22**



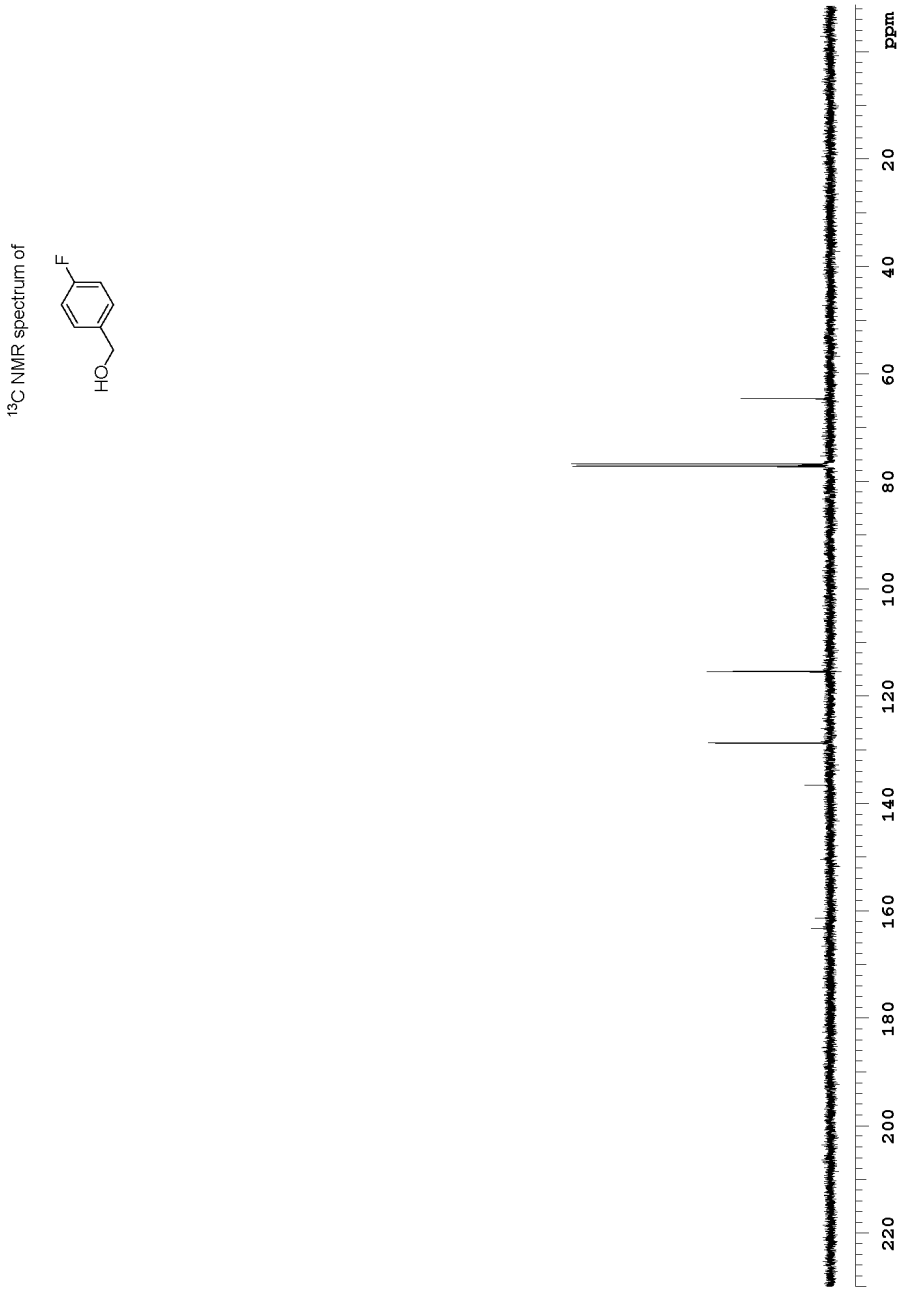
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **22**



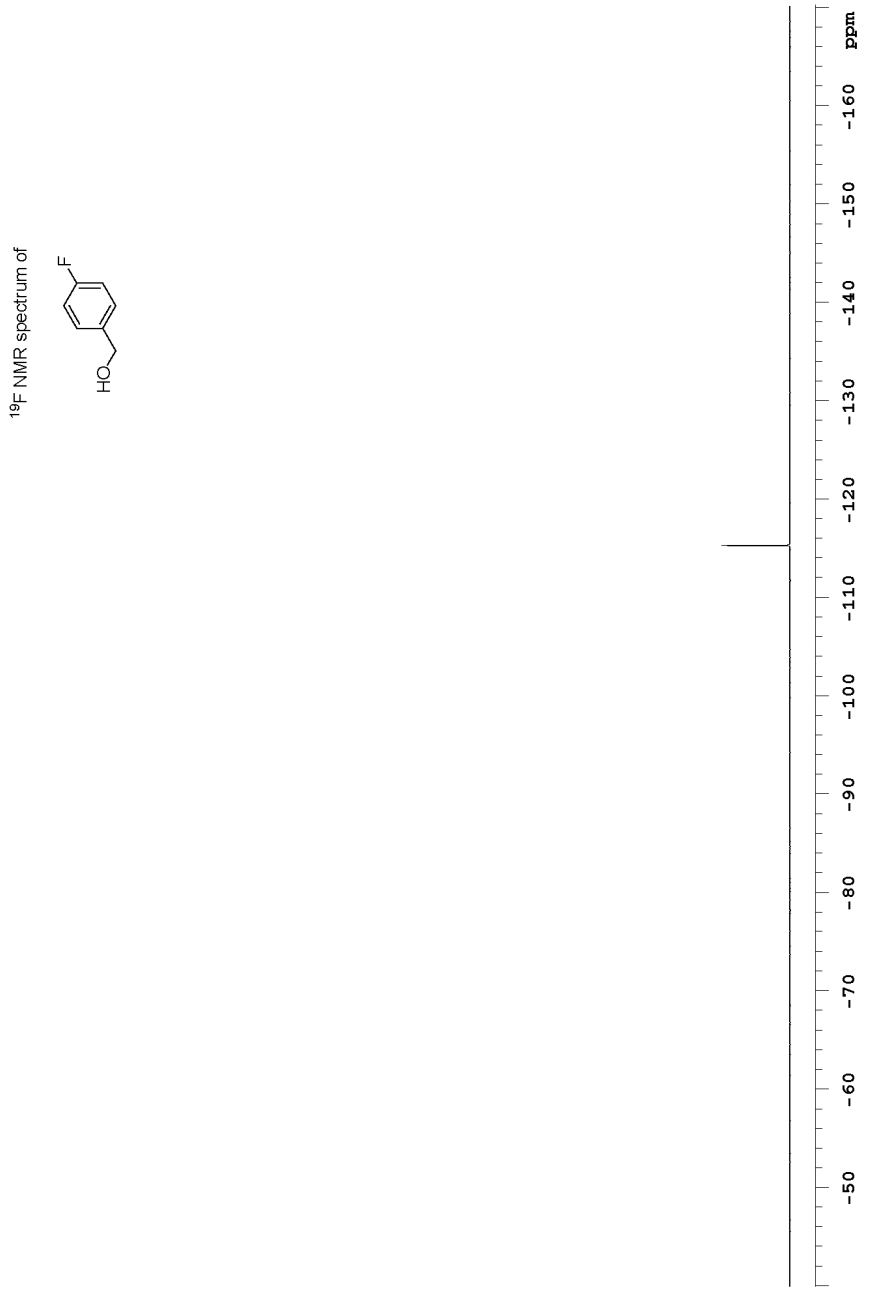
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **22**



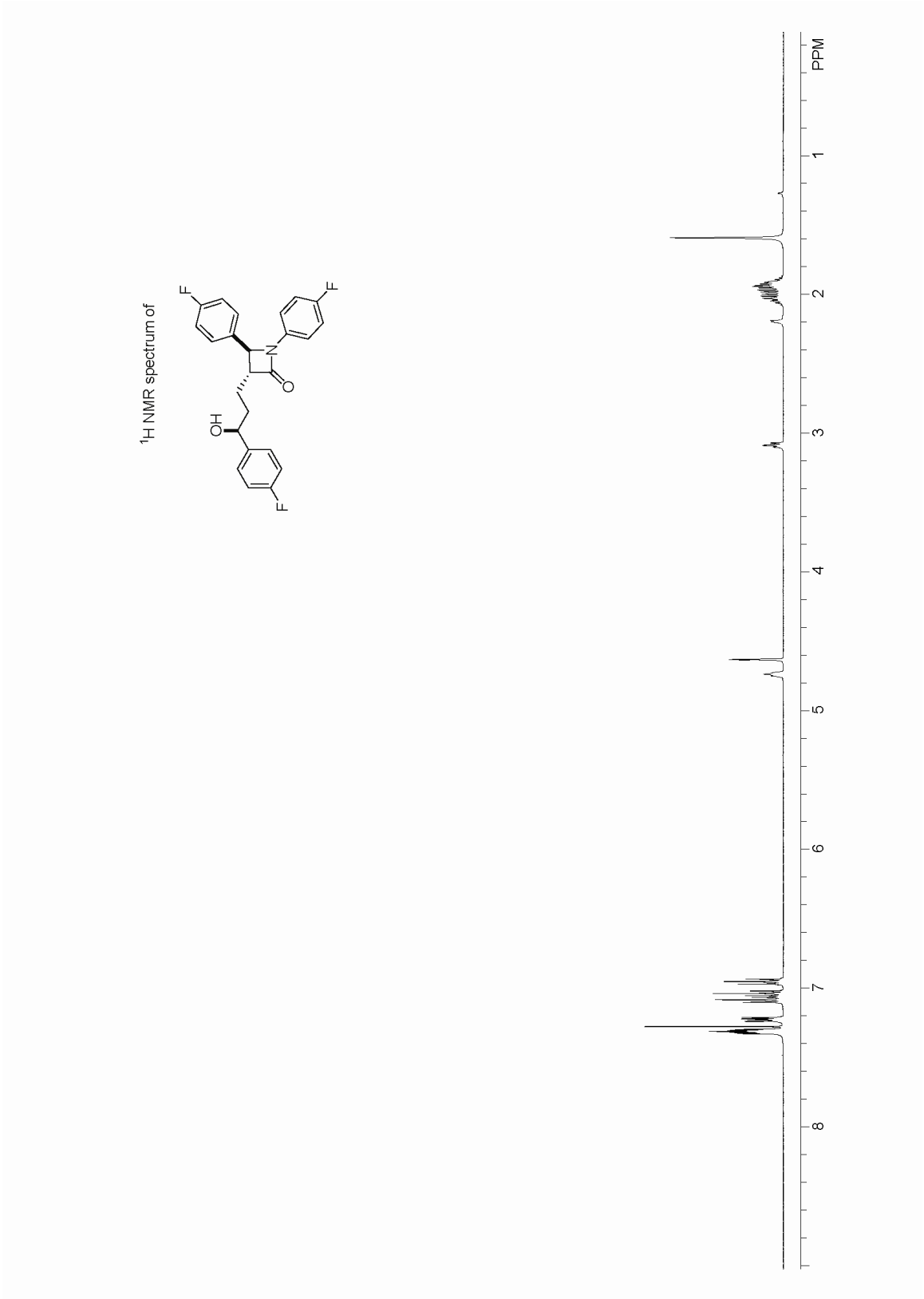
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **23**



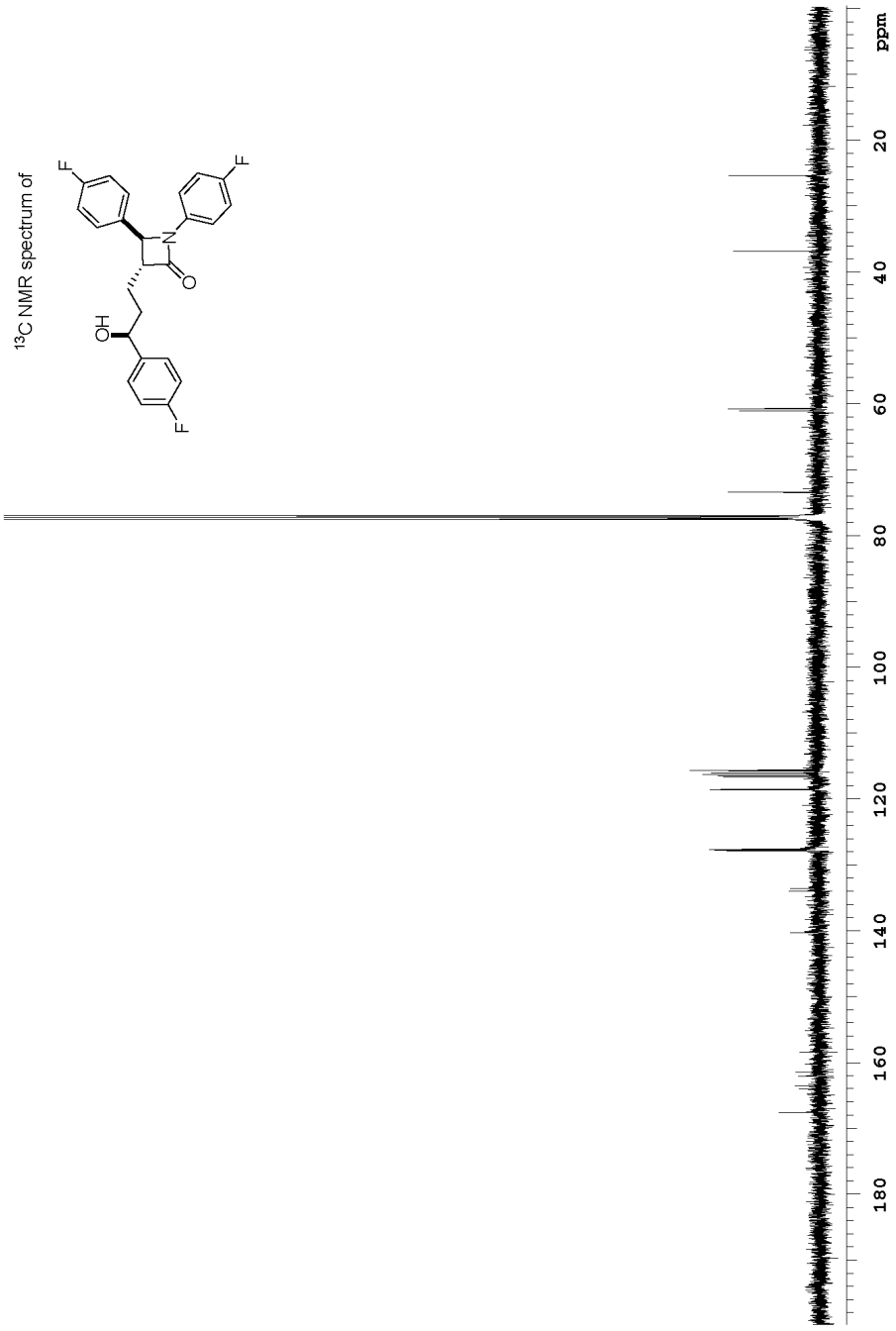
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **23**



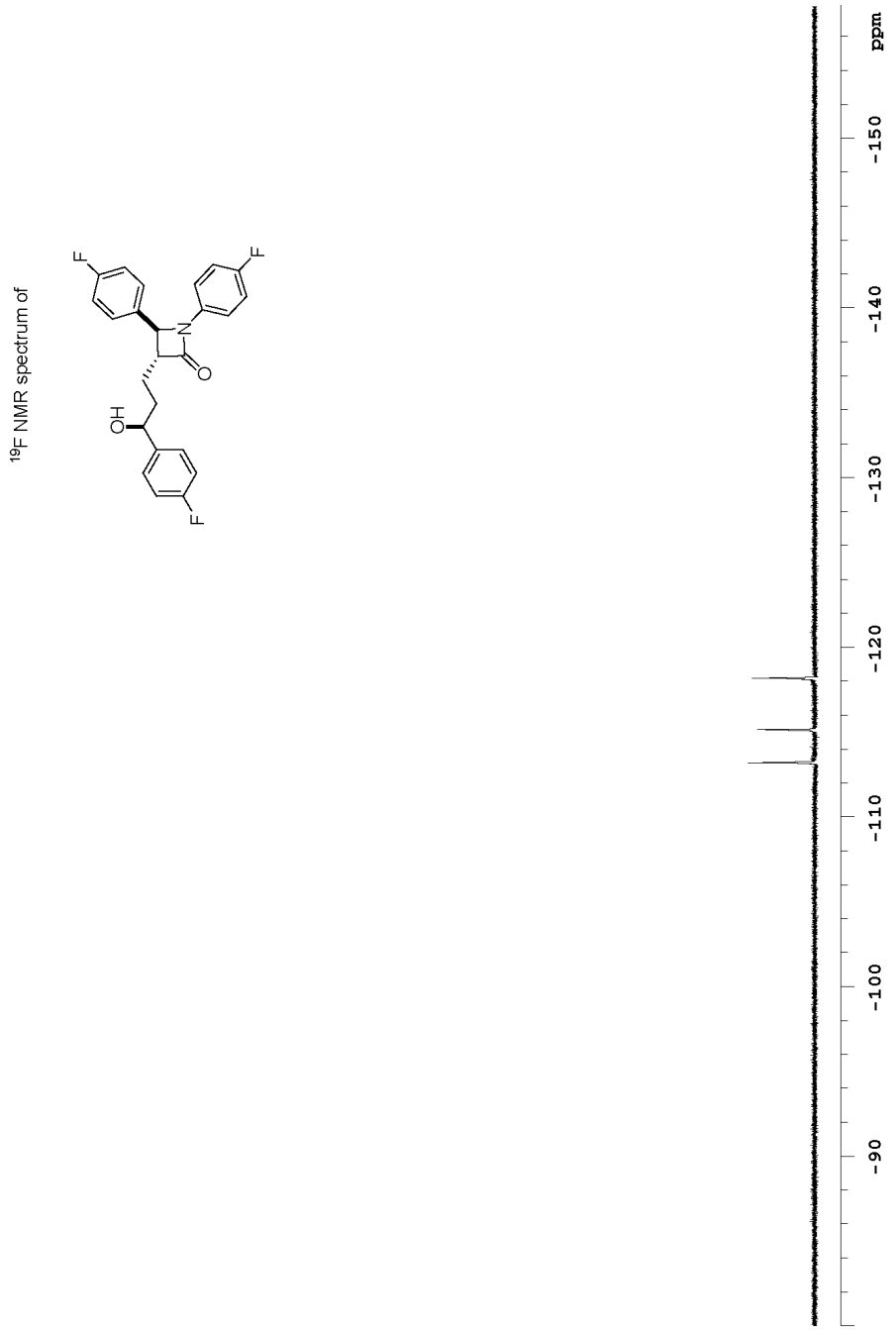
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **23**



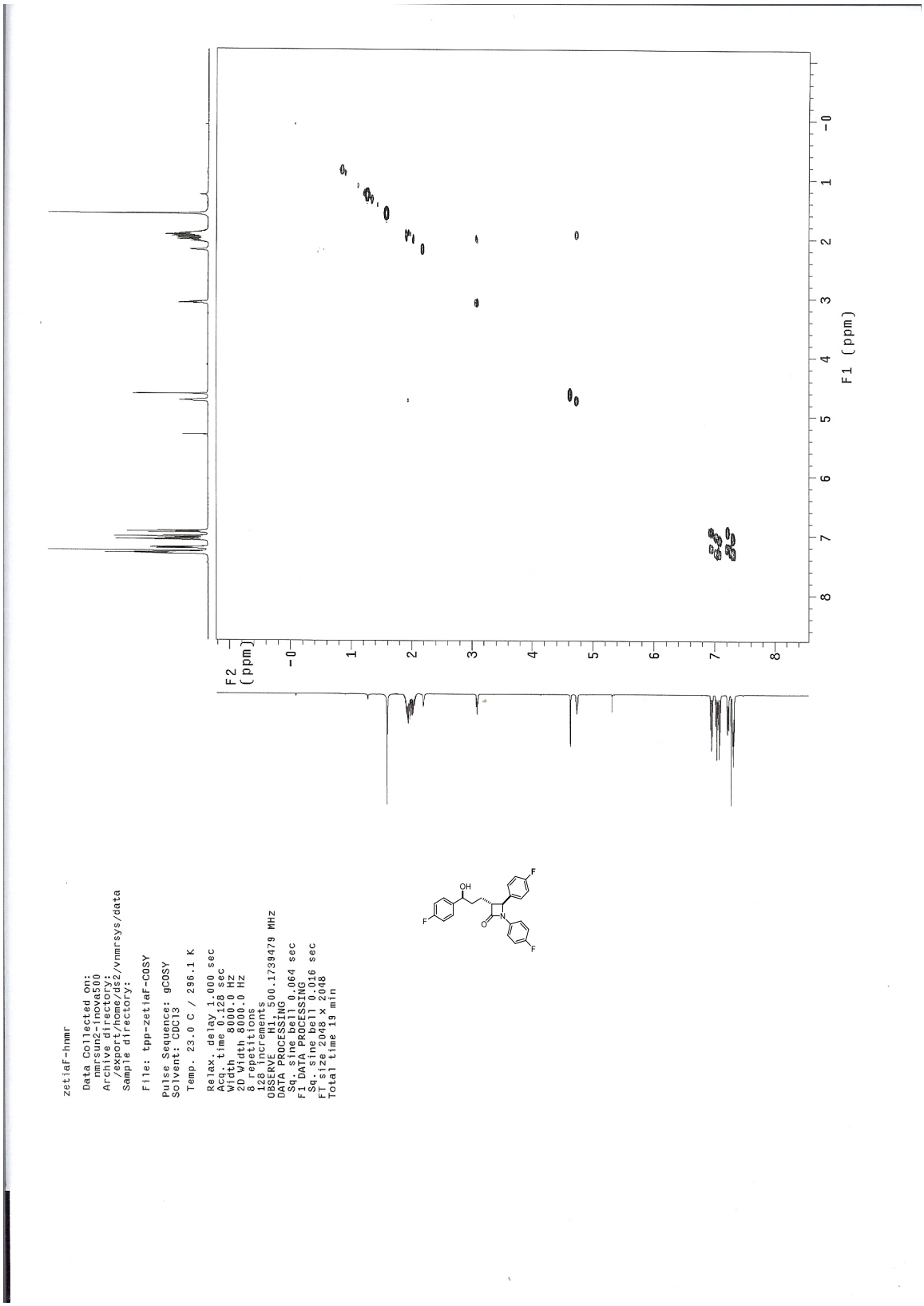
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **26**



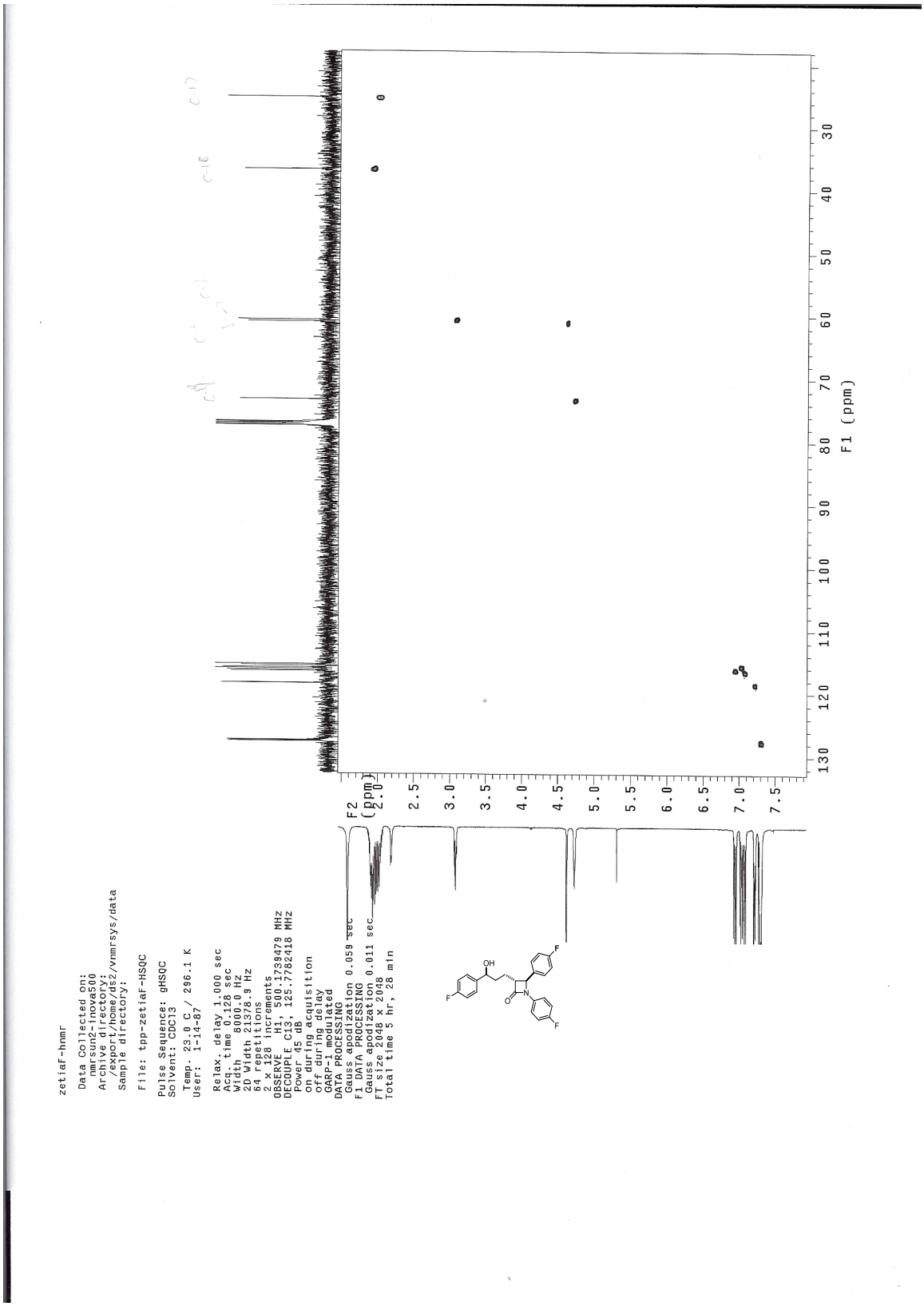
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **26**



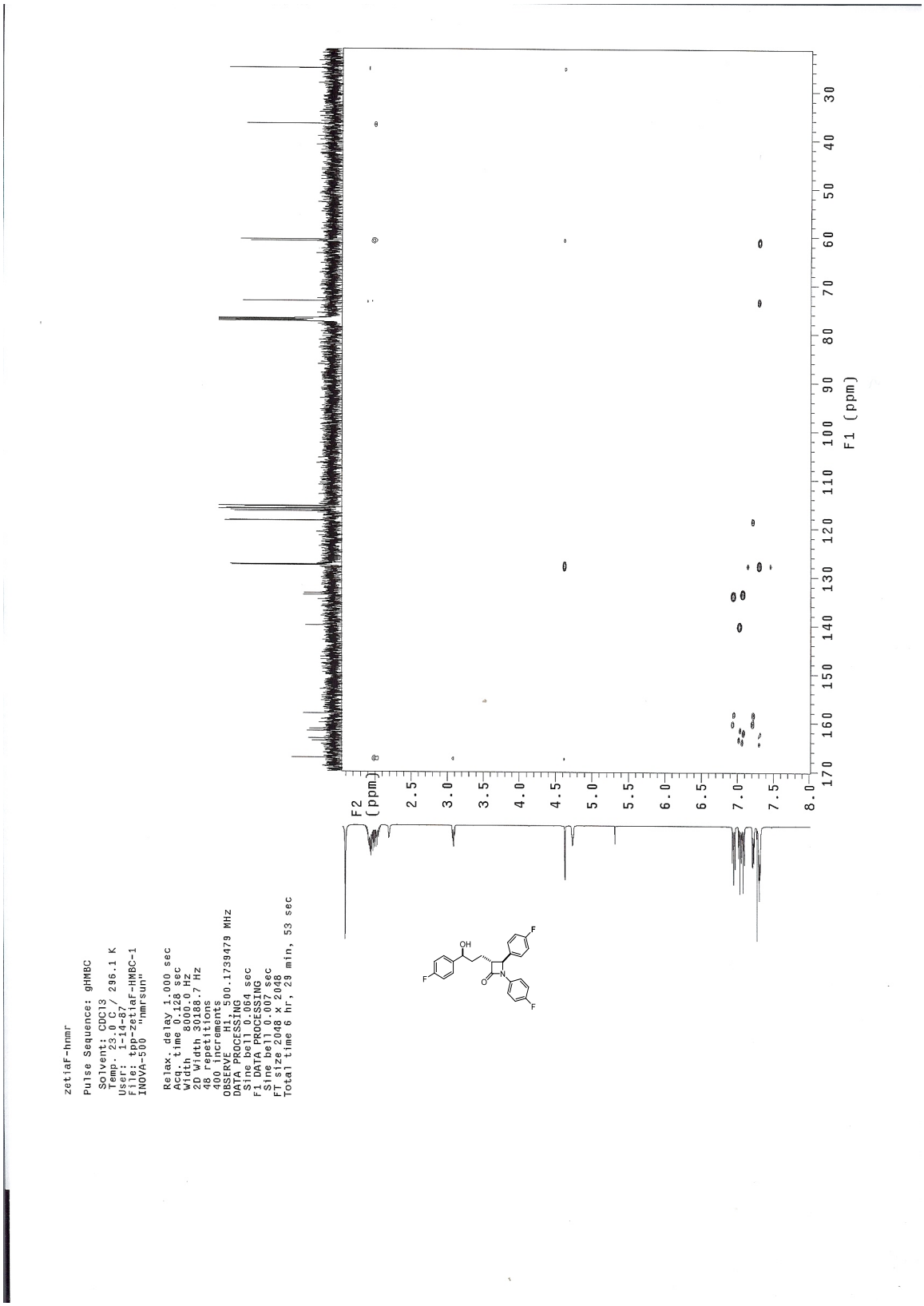
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **26**



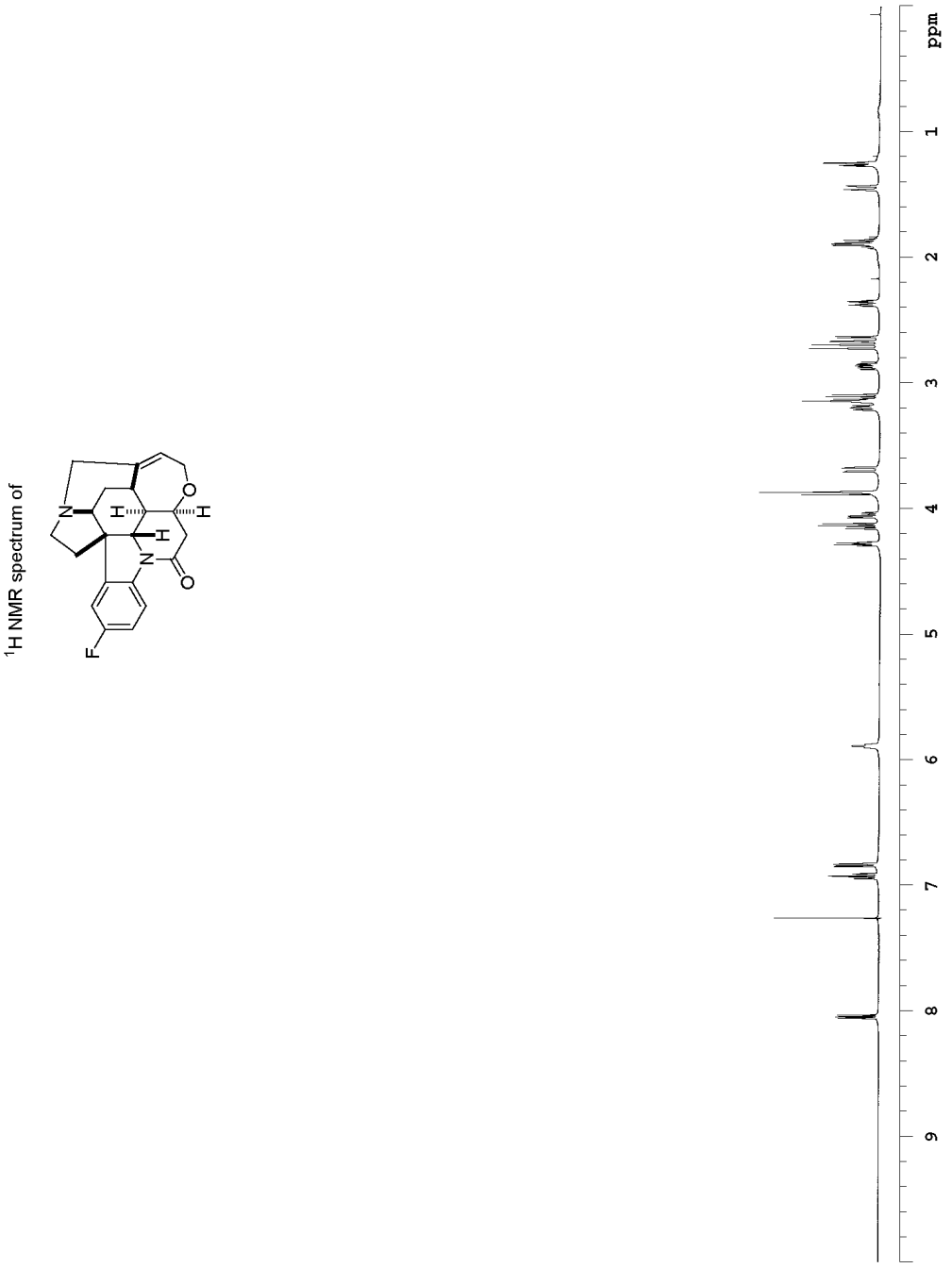
^{1}H-^{1}H COSY spectrum (500 MHz, $CDCl_3$, 23 ºC) of **26**



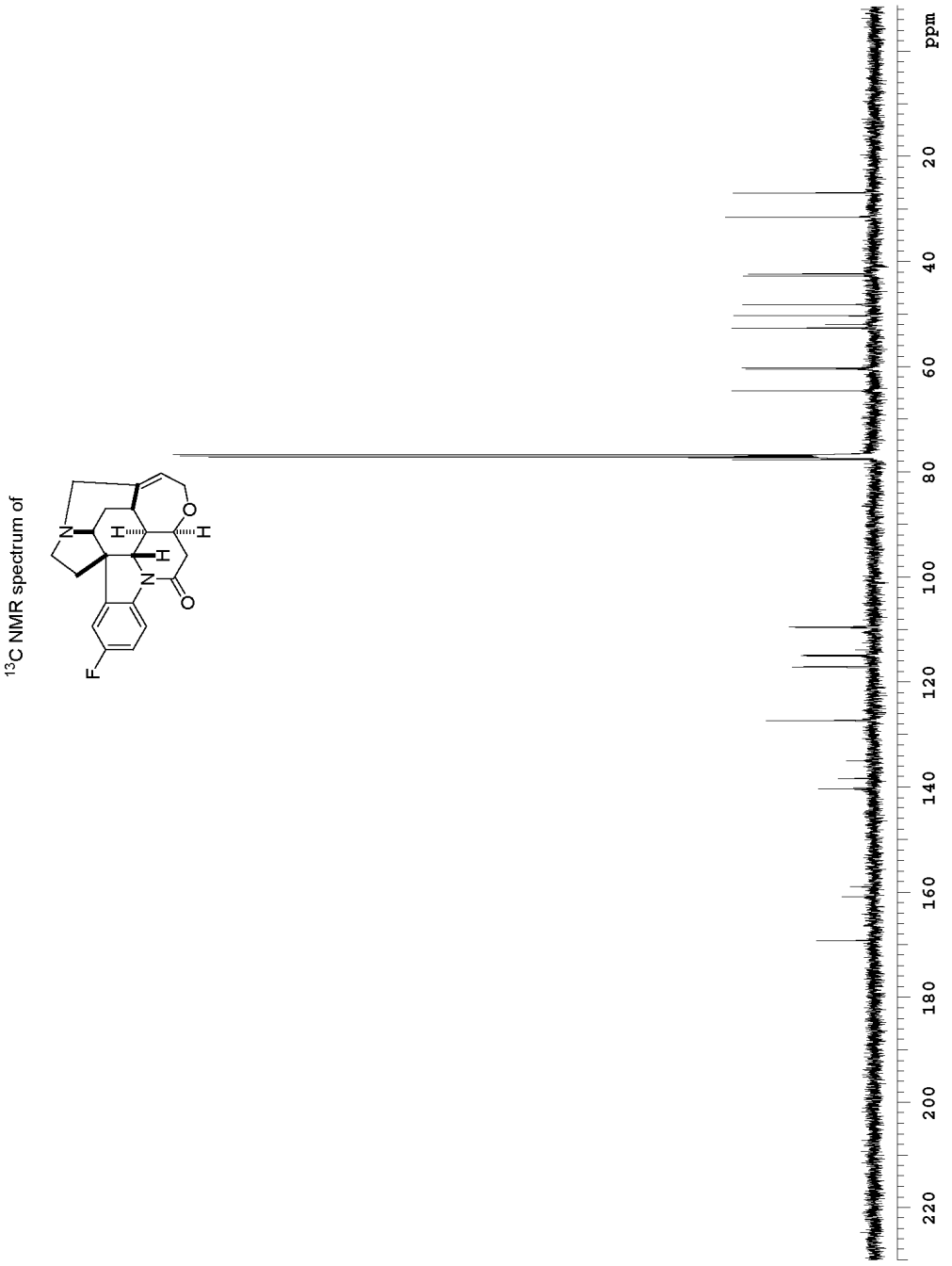
HSQC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **26**



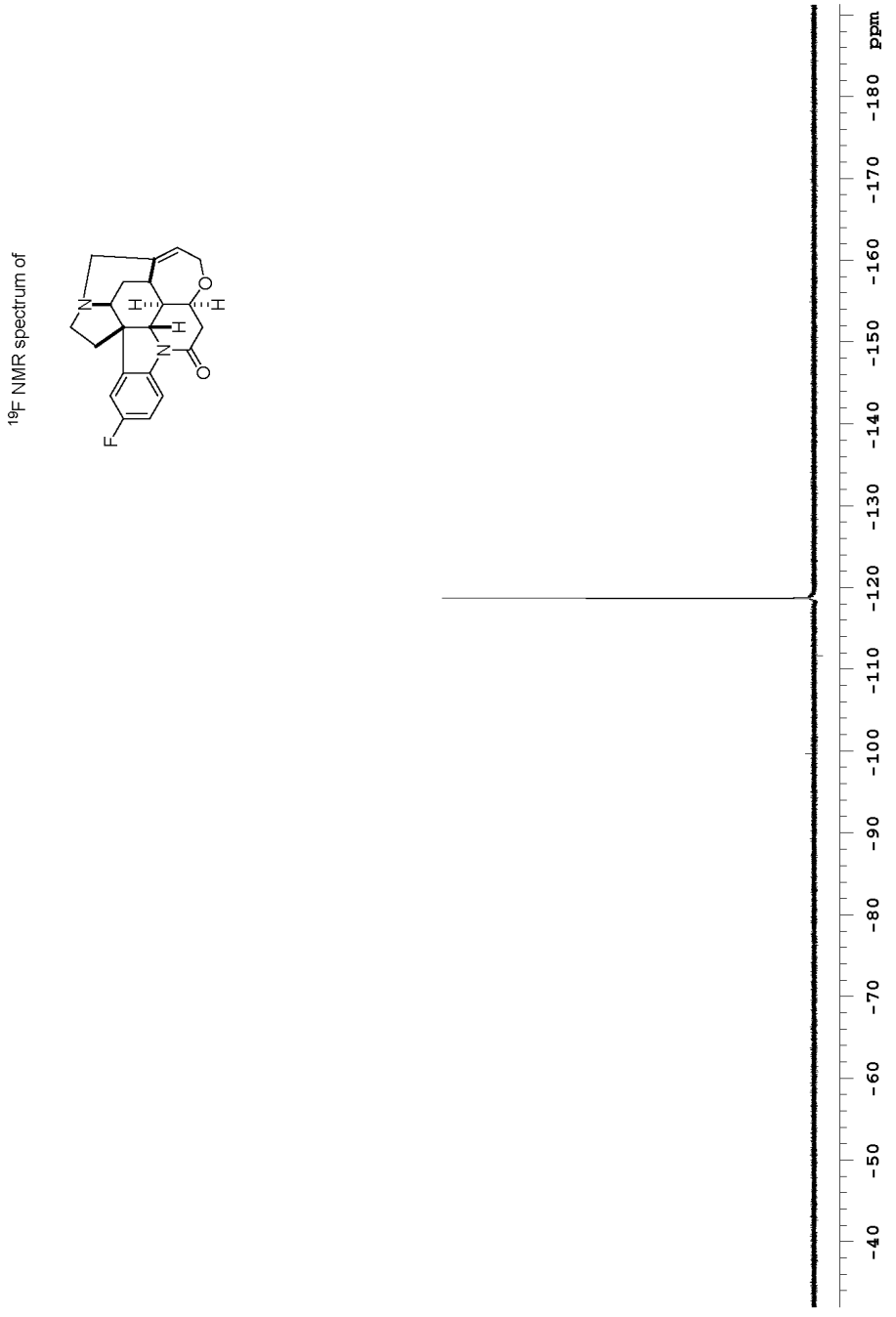
HMBC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **26**



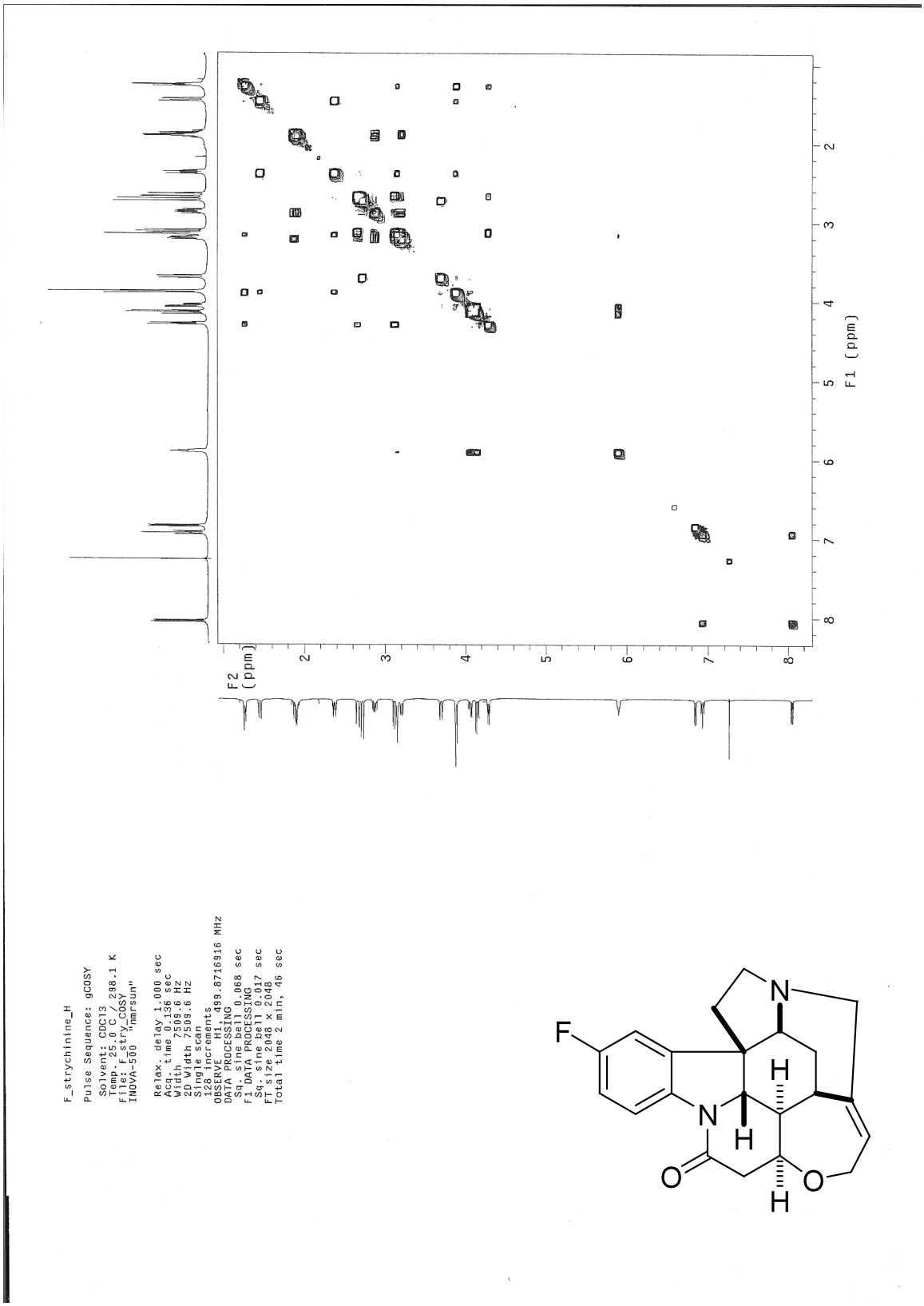
^{1}H NMR spectrum (500 MHz, $CDCl_3$, 23 ºC) of **30**



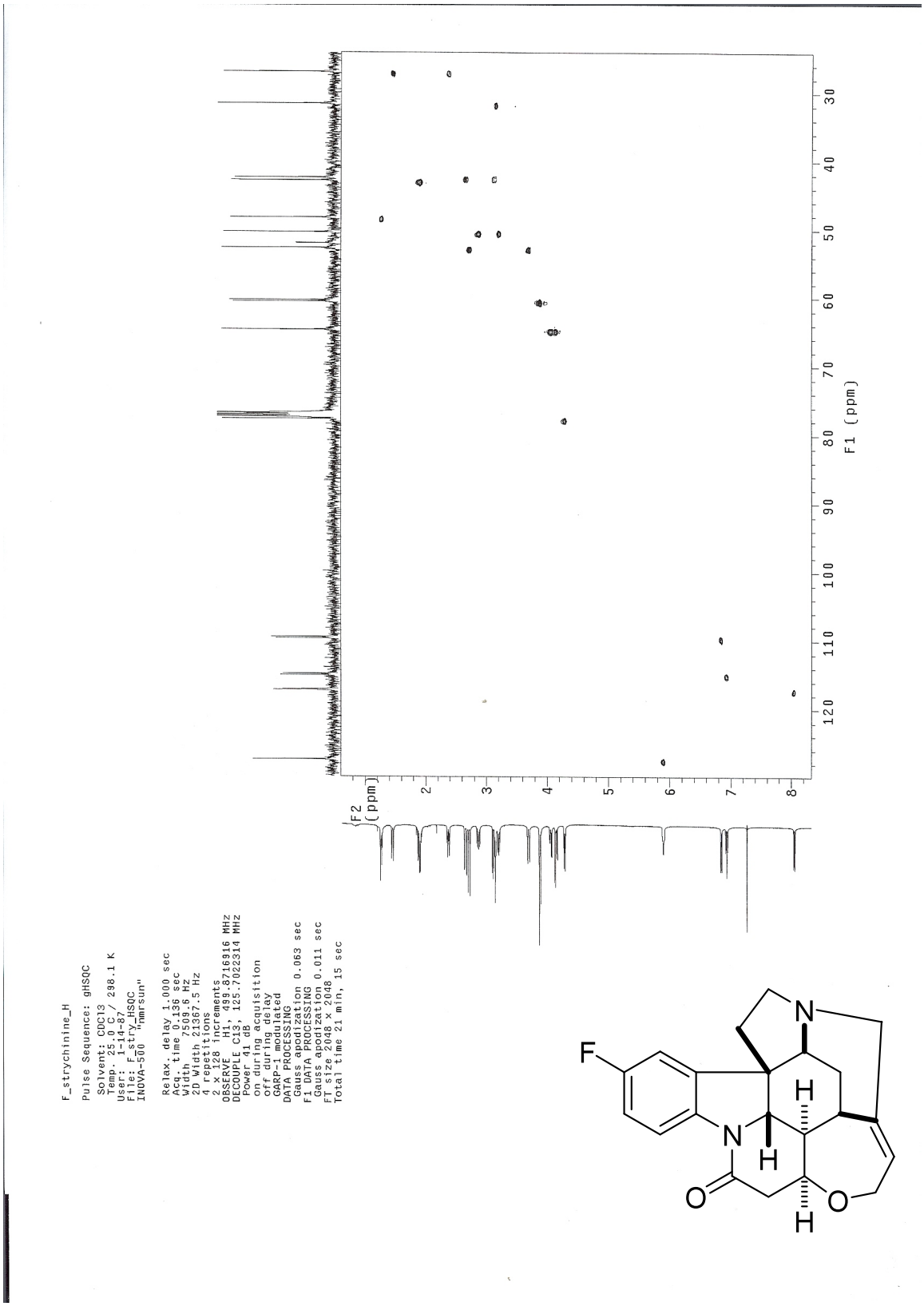
^{13}C NMR spectrum (125 MHz, $CDCl_3$, 23 ºC) of **30**



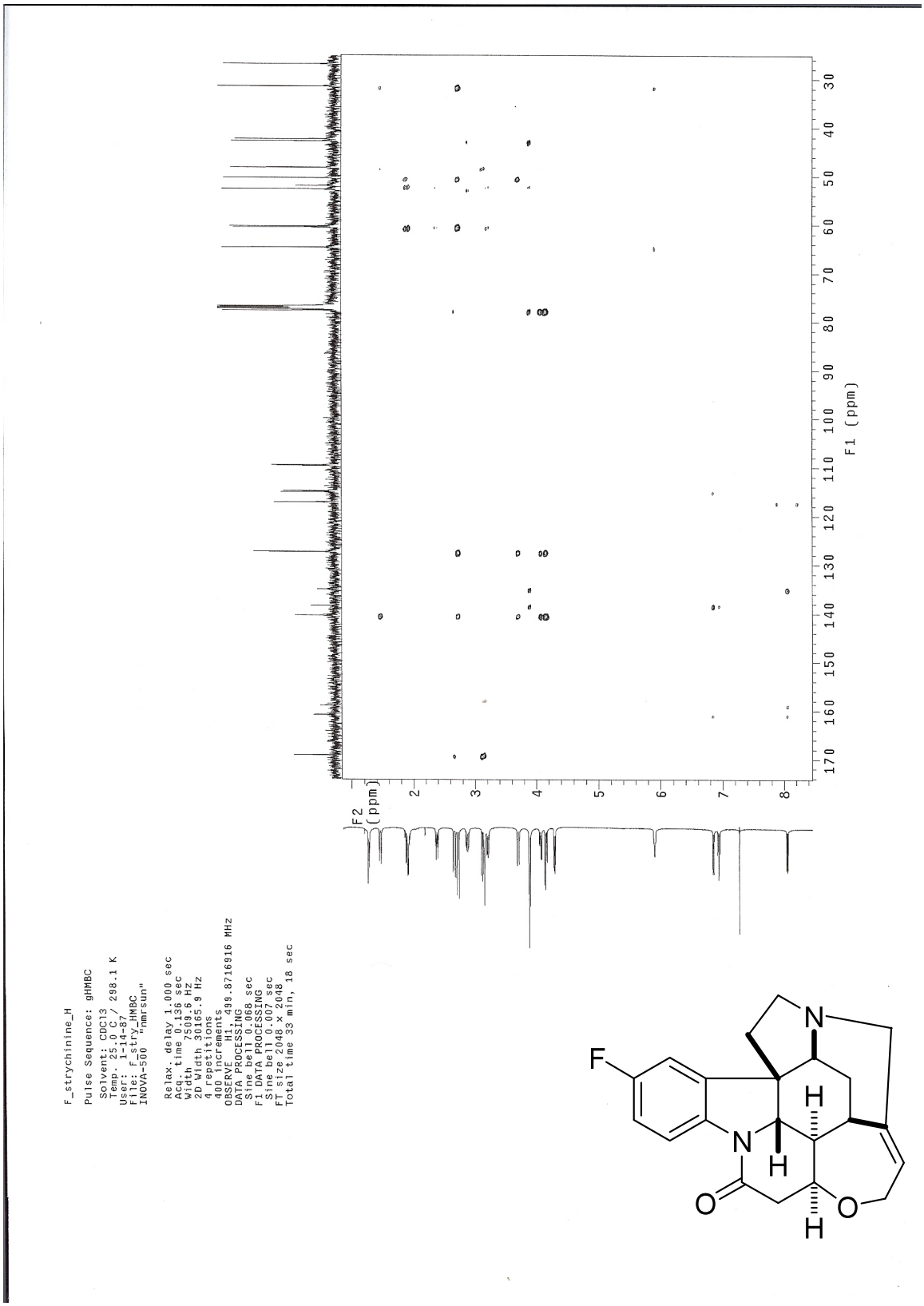
^{19}F NMR spectrum (375 MHz, $CDCl_3$, 23 ºC) of **30**



^{1}H-^{1}H COSY spectrum (500 MHz, $CDCl_3$, 23 ºC) of **30**



HSQC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **30**



HMBC spectrum (500 MHz, $CDCl_3$, 23 ºC) of **30**