

Photoredox/Copper Catalyzed Enantioselective Synthesis of Chiral β - Difluoroalkyl Nitriles Involving CF₃ Group Activation

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1. General Information

Methods: All data were collected on Bruker ASCENDTM operating at 400 MHz for ¹H NMR, 101 MHz for ¹³C{¹H} NMR, and 376 MHz for ¹⁹F{¹H} NMR (with complete proton decoupling). Chemical shifts are reported in parts per million (ppm). ¹H NMR spectra data were assigned CDCl₃ resonance as 7.26 ppm and reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad), coupling constant (*J* values) in Hz, and integration. Chemical shifts for ¹³C NMR spectra were recorded in ppm with the central peak of residue CDCl₃ (77.16 ppm) as the internal standard. Visualization of the developed chromatogram was performed by UV absorbance (254 nm). All datas were acquired on Waters G2-S Qtof spectrometer (electrospray ionization: ESI). X-ray crystallography studies were carried out on Rigaku ROD, Synergy Custom DW system using Cu-K_α radiation ($\lambda = 1.54184$ Å). Enantiomeric ratio (ee) values were determined by chiral HPLC with chiral AS-H, AD-H, OJ-H, IC, IA, IB columns with *n*-hexane and *i*-PrOH as solvents. Optical rotations were measured on a PerkinElmer 343 polarimeter. UV-Vis absorption spectra were recorded on a UH5700 spectrophotometer S2 (Hitachi). Stern-Volmer quenching experiments were carried by Agilent Technologies F-4600 spectrofluorometer. Photocatalytic reaction was carried out using photoreactor from WATTCAS (<https://www.wattcas.com>). The light source used in gram scale reaction is purple lamp (20 W, 410 nm), which is bought from Xuzhou Ai Jia electronic technology Co. LTD.

Materials: Unless otherwise noted, all reagents obtained from commercial suppliers were used without further purification. Commercially available chemicals were obtained from Infinity Heowns, Admas, J&K, Leyan, Bide Pharmatech. Flash chromatography was performed using 200-300 mesh silica gel (Yantai Xinnuo Chemicals) with the indicated eluents according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on glass-backed silica gel plates (Yantai Xinnuo Chemicals or Energy Chemical).



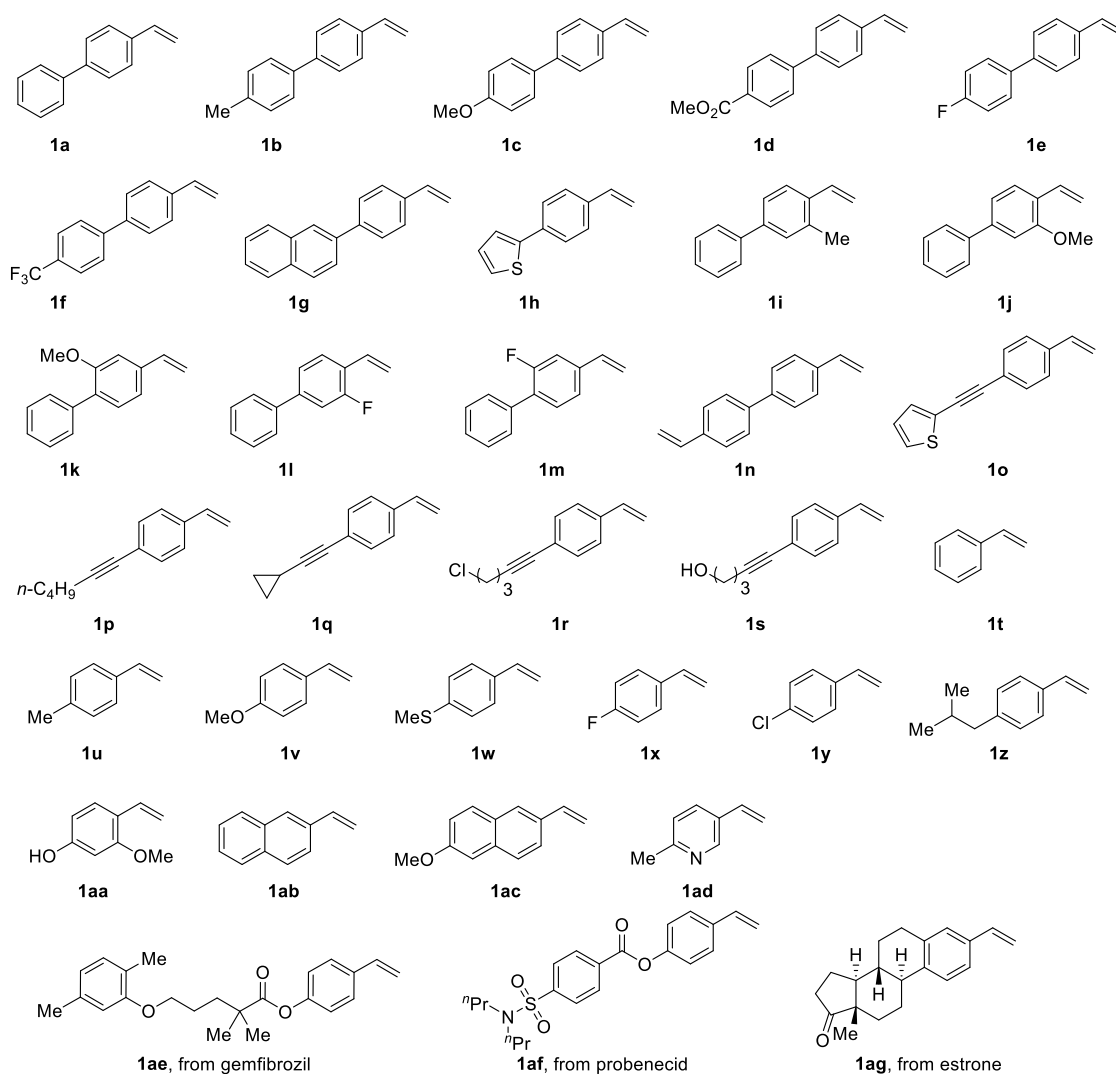
photoreactor



quartz tube

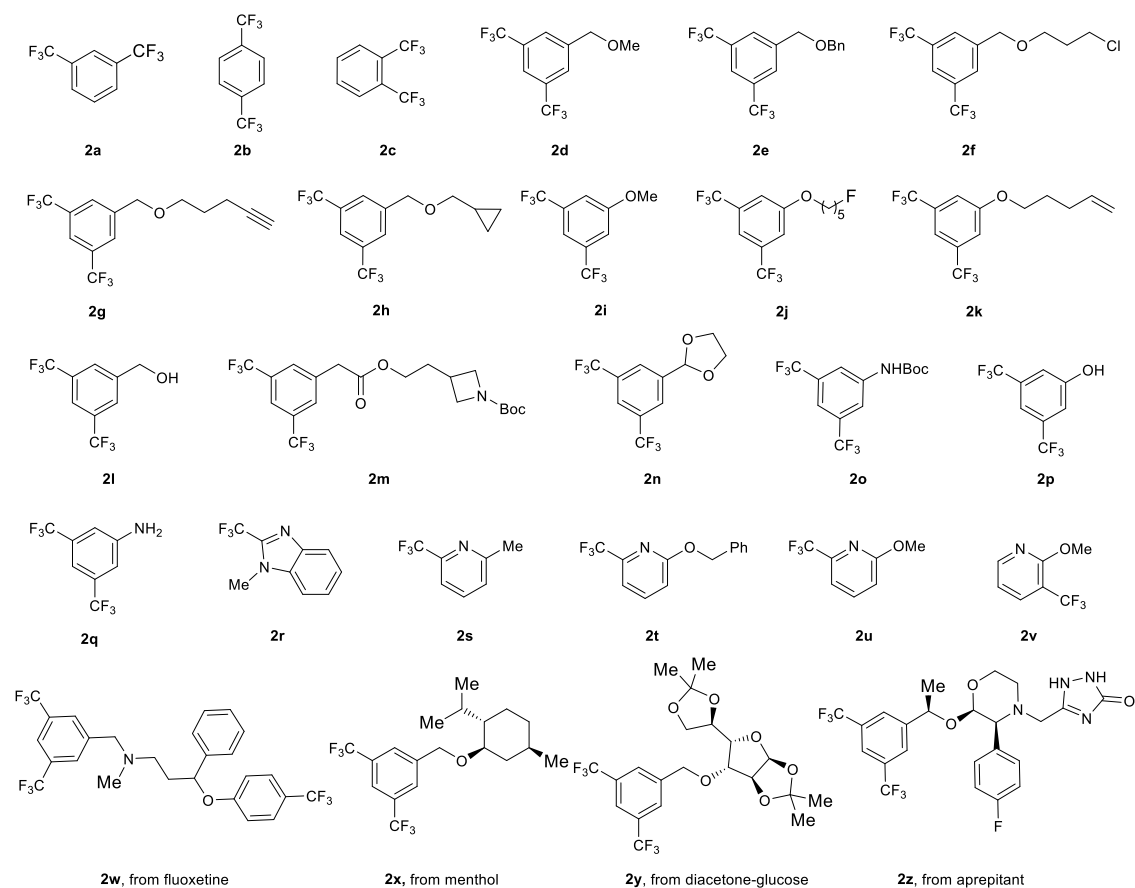
2. Synthesis of Substrates

2.1 Preparation of alkene substrates



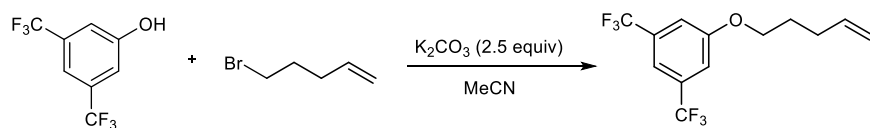
Unless otherwise stated, all starting materials were commercially available. The starting compounds **1b-1m**^[1-4], **1n**^[5], **1o-1s**^[6], **1z-1ac**^[7,8], **1ae**^[9], **1af**^[10] and **1ag**^[11] were prepared according to the literature procedure.

2.2 Preparation of trifluoromethylarene substrates



Unless otherwise stated, all starting materials were commercially available. The starting compounds **2f**^[12], **2g**^[13], **2h**^[14], **2i**^[12], **2j**^[14], **2n**^[13], **2o**^[12], **2r**^[15] and **2w-2z**^[13] were prepared according to the literature procedure.

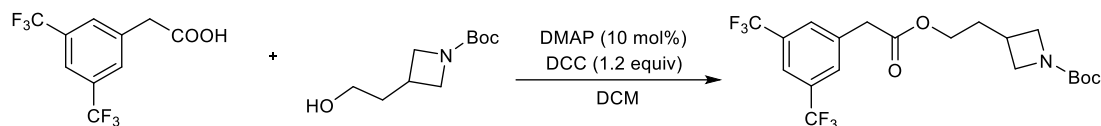
Synthesis of 1-(pent-4-en-1-yloxy)-3,5-bis(trifluoromethyl)benzene (**2k**)



To a 25 mL oven-dried round-bottom flask equipped with a Teflon-coated magnetic stir bar was added 3,5-bis(trifluoromethyl)phenol (1.0 g, 4.3 mmol, 1.0 equiv), CH₃CN (20.0 mL), and K₂CO₃ (1.5 g, 10.8 mmol, 2.5 equiv). 5-bromopent-1-ene (1.281 g, 8.6 mmol, 2.0 equiv) was then added, and the resulting mixture was refluxed for 12 h. Upon completion, the solvent was removed under vacuum. The residue was diluted with water and extracted with Et₂O (20.0 mL×3). The combined organic phases were washed with 20.0 mL water and 40.0 mL brine, dried over anhydrous Na₂SO₄, and concentrated

in vacuo. The crude product was purified by silica gel chromatography (petroleum ether: ethyl acetate = 20:1, R_f = 0.3) to give the title compound **2k** as a colorless oil (0.846 g, 66% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.45 (s, 1H), 7.30 (s, 2H), 5.86 (m, 1H), 5.14 – 5.00 (m, 2H), 4.05 (t, J = 6.4 Hz, 2H), 2.27 (q, J = 7.2 Hz, 2H), 1.94 (p, J = 6.8 Hz, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 159.8, 137.4, 132.9 (q, J = 33.2 Hz), 123.4 (q, J = 272.7 Hz), 115.8, 115.0 (q, J = 3.9 Hz), 114.3 – 114.2 (m), 68.1, 30.1, 28.3. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -63.12; HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{13}\text{H}_{11}\text{F}_6\text{O}$: 297.0714; found 297.0709.

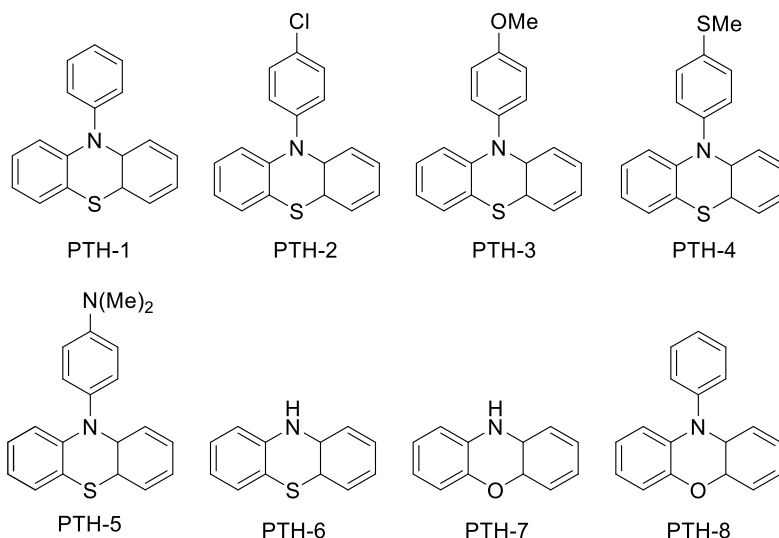
Synthesis of *tert*-butyl 3-(2-(2-(3-(trifluoromethyl)phenyl)acetoxy)ethyl)azetidine-1-carboxylate (**2m**)



To a 50 mL round-bottom flask was added 2-(3,5-bis(trifluoromethyl)phenyl)acetic acid (1.36 g, 5.0 mmol, 1.0 equiv) and *tert*-butyl 3-(2-hydroxyethyl)azetidine-1-carboxylate (1.106 g, 5.5 mmol, 1.1 equiv) in dichloromethane (10 mL). The mixture was stirred at room temperature for 30 min. Then, a solution of *N,N*-dicyclohexylcarbodiimide (1.24 g, 6.0 mmol, 1.2 equiv) and 4-dimethylaminopyridine (61 mg, 0.50 mmol, 10 mol%) in dichloromethane (10 mL) was added slowly under ice-cooling. The reaction mixture was allowed to warm to room temperature and stirred. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether: ethyl acetate = 20:1, R_f = 0.3) afforded the compound **2m** as a pale-yellow oil. (2.11 g, 93 %). ^1H NMR (400 MHz, CDCl_3) δ 7.81 (s, 1H), 7.74 (s, 2H), 4.11 (dt, J = 6.3, 3.9 Hz, 2H), 4.05 – 3.94 (m, 2H), 3.79 – 3.70 (m, 2H), 3.57 (td, J = 5.8, 2.8 Hz, 2H), 2.60 – 2.48 (m, 1H), 1.95 (t, J = 7.2 Hz, 2H), 1.43 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 170.0, 156.4, 136.2, 132.0 (q, J = 33.6 Hz), 129.8 (d, J = 4.0 Hz), 123.3 (q, J = 273.8 Hz), 121.8 – 121.2 (m), 79.6, 63.6, 40.7, 33.2, 28.5, 26.3. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.88; HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd.

for C₂₀H₂₂F₆NO₄: 454.1453; found 454.1462.

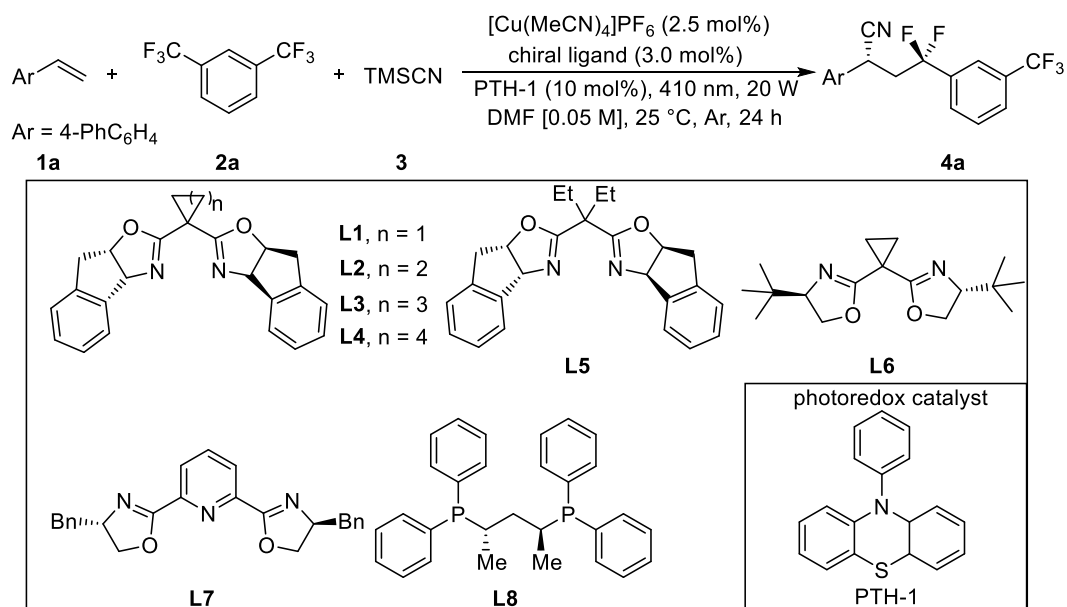
2.3 Preparation of photoredox catalysts



Unless otherwise stated, all starting materials were commercially available. The starting compounds PTH-2^[16], PTH-3^[17], PTH-4^[17], PTH-5^[17], PTH-8^[18] prepared according to the literature procedure.

3. Detailed Optimization of Reaction Conditions

Table S1. Screening of different ligands.^a



Entry	Ligand	Conv. (1a %)	Yield (4a %) ^b (ee %) ^c
1	L1	>99	52 (92)
2	L2	>99	38 (46)

3	L3	>99	37 (15)
4	L4	>99	47 (n.d.)
5	L5	90	39 (2)
6	L6	92	38 (n.d.)
7	L7	>99	33 (n.d.)
8	L8	>99	36 (n.d.)

^a Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol, 2.0 equiv), **3** (0.15 mmol, 1.5 equiv), PTH-1 (10 mol%), [Cu(MeCN)₄]PF₆ (2.5 mol%), and chiral ligand (3.0 mol%) in DMF [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. ^b Yields were detected by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard. ^c Determined by HPLC analysis on a chiral stationary phase. Note: n.d. = not detected.

Table S2. Optimization of the copper salts.^a

Ar = 4-PhC₆H₄

1a **2a** **3** **4a**

Entry	Cu salt	Conv. (1a %)	Yield (4a %) ^b (ee %) ^c
1	[Cu(MeCN) ₄]PF ₆	>99	52 (92)
2	CuTc	61	16 (88)
3	CuOAc	>99	46 (90)
4	[Cu(MeCN) ₄]BF ₄	>99	47 (90)
5	CuBr	>99	42 (90)
6	CuCN	>99	45 (86)
8	CuSCN	>99	40 (84)
9	Cu(OTf)·Toluene	70	19 (86)
10	CuDPP	>99	21 (63)
11	Cu(OTf) ₂	84	17 (87)

^a Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol, 2.0 equiv), **3** (0.15 mmol, 1.5 equiv), PTH-1 (10 mol%), **Cu salt** (2.5 mol%), and **L1** (3.0 mol%) in DMF [0.05 M] were stirred, irradiation with 20 W 410

nm violet LEDs at room temperature for 24 h under argon atmosphere. ^b Yields were detected by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard. ^c Determined by HPLC analysis on a chiral stationary phase. Note: CuDPP (Cu(I) diphenylphosphinate).

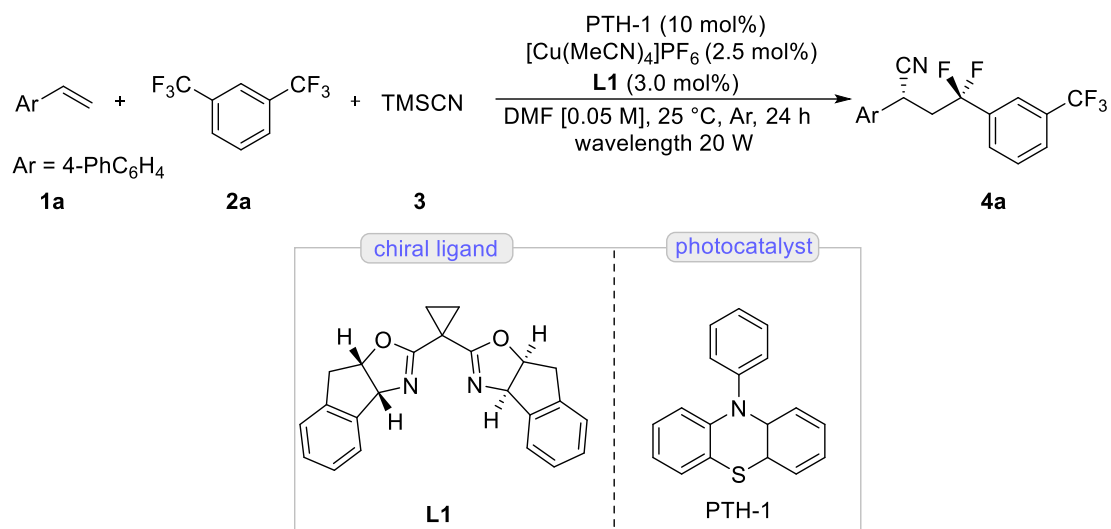
Table S3. Screening of the photoredox catalysts.^a

chiral ligand byproducts photocatalyst					
Entry	PC	Conv. (1a %)	Yield (B-1 %)	Yield (B-2 %)	Yield (4a %) ^b (ee %) ^c
1	<i>fac</i> -Ir(ppy) ₃	80	45	n.d.	n.d.
2	4-CzIPN	60	50	n.d.	n.d.
3	[Ir(dtbbpy)(ppy) ₂] ⁺ PF ₆ ⁻	<5	trace	n.d.	n.d.
4	[Mes-Acr] ⁺ BF ₄ ⁻	42	28	n.d.	n.d.
5	Thioxanthone	<5	trace	n.d.	n.d.
6	PTH-1	>99	<5	<5	52 (92)
7	PTH-2	>99	<5	<5	32 (92)
8	PTH-3	>99	<5	<5	40 (92)
9	PTH-4	>99	<5	<5	41 (94)
10	PTH-5	>99	<5	n.d.	43 (90)
11	PTH-6	>99	<5	12	38 (93)
12	PTH-7	16	<5	n.d.	trace
13	PTH-8	21	n.d.	n.d.	trace

^a Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol, 2.0 equiv), **3** (0.15 mmol, 1.5 equiv), PC (10 mol%), [Cu(MeCN)₄]⁺PF₆⁻ (2.5 mol%), and **L1** (3.0 mol%) in DMF [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. ^b Yields were detected by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard. ^c Determined by HPLC

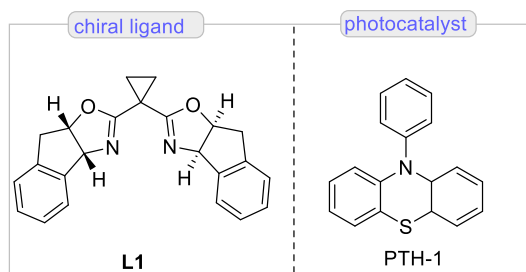
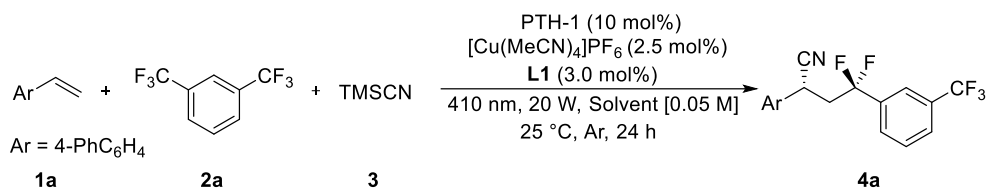
analysis on a chiral stationary phase. Note: n.d. = not detected.

Table S4. Screening of the light source wavelengths.^a



Entry	Wavelengths	Conv. (1a %)	Yield (4a %) ^b (ee %) ^c
1	365 nm	>99	28 (92)
2	390 nm	>99	37 (91)
3	410 nm	>99	52 (92)
4	430 nm	46	21 (91)
5	450 nm	<5	n.d.
6 ^d	410 nm	>99	19 (92)

^a Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol, 2.0 equiv), **3** (0.15 mmol, 1.5 equiv), PTH-1 (10 mol%), [Cu(MeCN)₄]PF₆ (2.5 mol%) and **L1** (3.0 mol%) in DMF [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. ^b Yields were detected by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard. ^c Determined by HPLC analysis on a chiral stationary phase. ^d [0.1 M] instead of [0.05 M]. Note: n.d. = not detected.

Table S5. Screening of the solvents.^a

Entry	Solvent	Conv. (1a %)	Yield (4a %) ^b (ee %) ^c
1	DMF	>99	52 (92)
2	DMAc	95	35 (91)
3	MeCN	19	11 (90)
4	DMSO	35	18 (89)
5	NMP	>99	13 (90)
6	EA	<5	n.d.
7	MTBE	83	n.d.
8	MeCN: DMF = 3:1	>99	73 (92)
9	DMA: DMF = 3:1	>99	55 (90)
10	NMP: DMF = 3:1	>99	43 (90)
11	Toluene: DMF = 3:1	95	32 (91)

^a Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol, 2.0 equiv), **3** (0.15 mmol, 1.5 equiv), PTH-1 (10 mol%), [Cu(MeCN)₄]PF₆ (2.5 mol%), and **L1** (3.0 mol%) in **solvent** [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. ^b Yields were detected by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard. ^c Determined by HPLC analysis on a chiral stationary phase. Note: n.d. = not detected.

Table S6. Screening of additives.^a

$ \begin{array}{c} \text{Ar-CH=CH}_2 + \text{F}_3\text{C-C}_6\text{H}_4\text{-CF}_3 + \text{TMSCN} \xrightarrow[\text{additive (20 mol\%)}]{\begin{array}{c} \text{PTH-1 (10 mol\%)} \\ \text{Cu(MeCN)}_4\text{PF}_6 \text{ (2.5 mol\%)} \\ \text{L1 (3.0 mol\%)} \\ \text{MeCN: DMF = 3:1 [0.05 M]} \\ 410 \text{ nm, 20 W, 25 }^\circ\text{C, Ar, 24 h} \end{array}} \text{Ar-CH(CN)-CH}_2\text{-CF}_2\text{-C}_6\text{H}_4\text{-CF}_3 \\ \text{Ar = 4-PhC}_6\text{H}_4 \\ \textbf{1a} \qquad \qquad \textbf{2a} \qquad \qquad \textbf{3} \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \textbf{4a} \end{array} $			
Entry	Additive	Conv. (1a %)	Yield (4a %) ^b (ee %) ^c
1	Zn(OAc) ₂	>99	37 (88)
2	Zn(OTf) ₂	>99	39 (90)
3	Sc(OTf) ₃	>99	70 (80)
4	Yb(OTf) ₃	>99	71 (85)
5	B(C ₆ F ₅) ₃	>99	73 (77)
6	TMSOTf	>99	53 (88)

^a Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol, 2.0 equiv), **3** (0.15 mmol, 1.5 equiv), PTH-1 (10 mol%), [Cu(MeCN)₄]PF₆ (2.5 mol%), and **L1** (3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. ^b Yields were detected by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard. ^c Determined by HPLC analysis on a chiral stationary phase.

Table S7. Control experiments.^a

Ar = 4-PhC₆H₄ **1a** **2a** **3** **4a**

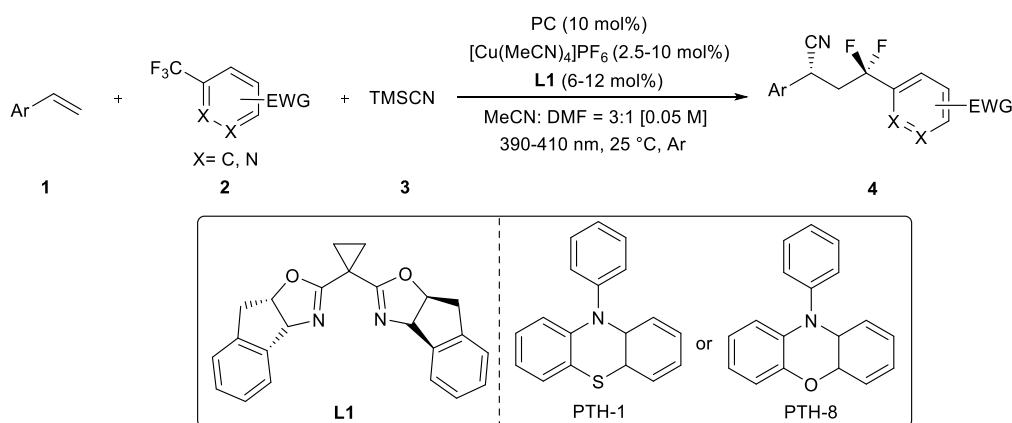
Entry	Variation from above conditions	Conv. (1a %)	Yield (4a %) ^b	ee (%) ^c
1	none	>99	73 (65) ^d	92
2	no Cu	>99	n.d.	n.d.
3	no L1	>99	32	n.d.
4	no PC	<5	n.d.	n.d.
5	in dark	<5	n.d.	n.d.
6	blue LED	<5	n.d.	n.d.

^a Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol, 2.0 equiv), **3** (0.15 mmol, 1.5 equiv), PTH-1 (10 mol%),

[Cu(MeCN)₄]PF₆ (2.5 mol%), and **L1** (3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere.^b Yields were detected by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard.^c Determined by HPLC analysis on a chiral stationary phase.^d Isolated yield. Note: n.d. = not detected.

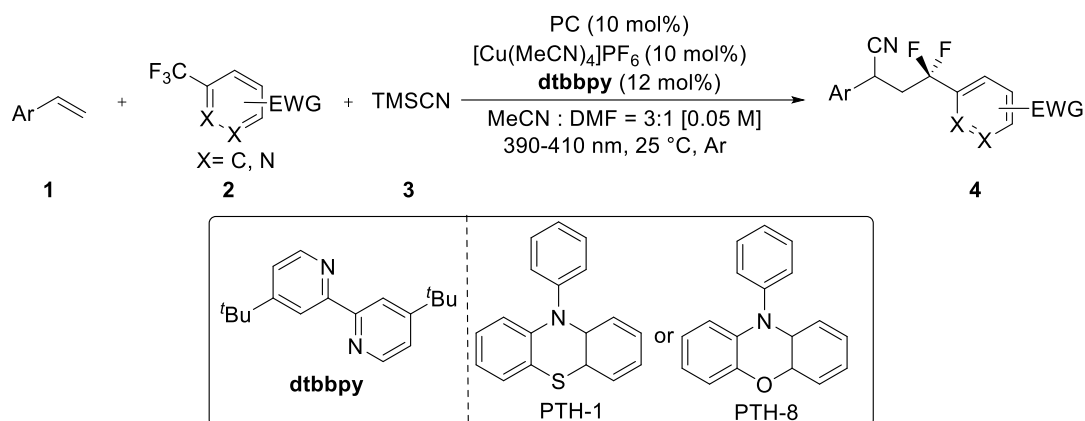
4. General Procedure and Experiment Details

4.1 General procedure A for the synthesis of chiral products



In a flame-dried 10.0 mL Schlenk quartz tube equipped with a magnetic stir bar was charged sequentially with Cu(MeCN)₄PF₆ and **L1** under Ar atmosphere, followed by the addition of super dry *N,N*-dimethylformamide (1.0 mL). The mixture was stirred at room temperature for 30 min. To the resulting mixture was added PTH-1 or PTH-8 (0.02 mmol, 10 mol%), alkene **1** (0.2 mmol, 1.0 equiv), trifluoromethylarenes **2** (0.4 mmol, 2.0 equiv), **3** (0.3 mmol, 1.5 equiv) and super dry acetonitrile (3.0 mL) under Ar. The reaction mixture was stirred at a distance of 2~3 cm from a 390-410 nm LEDs at 25 °C for about 10-48 h until the reaction was completed, as monitored by TLC analysis. The mixture was then diluted with water (10 mL) and extracted with ethyl acetate (10 mL×3), dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give the product.

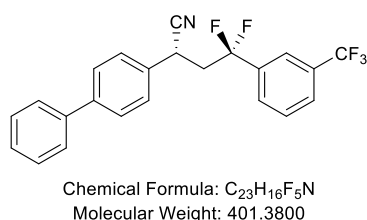
4.2 General procedure for preparation of racemic products



In a flame-dried 10.0 mL Schlenk quartz tube equipped with a magnetic stir bar was sequentially charged with $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (7.5 mg, 20 μmol) and **dtbbpy** (6.4 mg, 24 μmol) under Ar atmosphere, followed by the addition of super dry *N,N*-Dimethylformamide (1.0 mL). The mixture was stirred at room temperature for 30 min. To the resulting mixture was then added PTH-1 or PTH-8 (0.02 mmol, 0.1 equiv), alkene **1** (0.20 mmol, 1.0 equiv), trifluoromethylarenes **2** (0.4 mmol, 2.0 equiv), TMSCN (0.30 mmol, 1.5 equiv) and super dry acetonitrile (3.0 mL) under Ar. The mixture was stirred at a distance of 2~3 cm from a 390-410 nm LEDs at room temperature for about 10-48 h until the reaction was completed, as monitored by TLC analysis. The mixture was diluted with water (10 mL) and then extracted with ethyl acetate (10 mL $\times$ 3), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give the product.

4.3 Characterization Data of Products

(R)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(trifluoromethyl)phenyl)butanenitrile (4a)



The compound **4a** was prepared according to the general procedure employing **1a** (36.1

mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 51.9 mg, 65% isolated yield, white solid, mp: 48 – 50 °C, (petroleum ether: ethyl acetate = 12:1, R_f = 0.3, [α]_D²⁵ = 7.7 (c = 1.0 in CHCl₃); 92% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 14.07 min, t_R (minor) = 11.91 min.

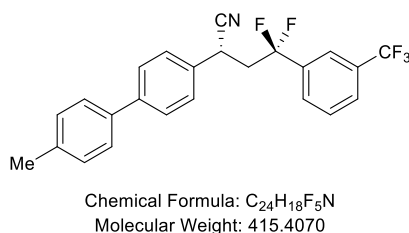
¹H NMR (400 MHz, CDCl₃) δ 7.79 (s, 1H), 7.74 (t, *J* = 8.0 Hz, 2H), 7.65 – 7.54 (m, 5H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.45 – 7.37 (m, 3H), 4.20 (dd, *J* = 9.7, 4.3 Hz, 1H), 3.03 – 2.84 (m, 1H), 2.70 – 2.57 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 141.8, 140.1, 136.9 (t, *J* = 26.5 Hz), 133.6, 131.5 (q, *J* = 33.1 Hz), 129.7, 128.0, 128.5 (t, *J* = 6.2 Hz), 128.2, 127.9, 127.8, 127.5 – 127.4 (m), 127.2, 123.9 (q, *J* = 273.8 Hz), 122.2 – 122.0 (m), 120.3 (t, *J* = 244.0), 119.7, 45.1 (t, *J* = 27.5 Hz), 31.1 (t, *J* = 3.4 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.76 (s), -96.05 (d, *J* = 249.4 Hz), -97.30 (d, *J* = 249.4 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₃H₁₅F₅N: 400.1125; found 400.1128.

(*R*)-4,4-difluoro-2-(4'-methyl-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4b**)**



The compound **4b** was prepared according to the general procedure employing **1b** (38.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 56.5 mg, 68%

isolated yield, white solid, mp: 86 – 88 °C, (petroleum ether: ethyl acetate = 12:1, R_f = 0.2, $[\alpha]_D^{25}$ = 8.1 (c = 1.0 in CHCl_3); 92% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 12.53 min, t_R (minor) = 13.60 min.

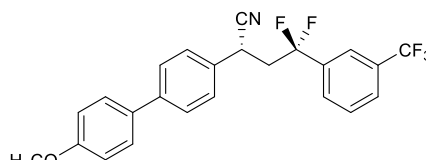
^1H NMR (400 MHz, CDCl_3) δ 7.68 (s, 1H), 7.64 (t, J = 8.1 Hz, 2H), 7.49 (d, J = 8.1 Hz, 3H), 7.38 (s, 2H), 7.30 (d, J = 7.9 Hz, 2H), 7.17 (d, J = 7.8 Hz, 2H), 4.09 (dd, J = 9.7, 4.3 Hz, 1H), 2.90 – 2.76 (m, 1H), 2.59 – 2.46 (m, 1H), 2.31 (s, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 141.8, 137.8, 137.2, 136.9 (t, J = 26.5 Hz), 133.3, 131.5 (q, J = 33.1 Hz), 129.8, 129.7, 128.5 (t, J = 6.1 Hz), 128.0, 127.8, 127.6 – 127.4 (m), 127.0, 123.7 (q, J = 274.6 Hz), 122.4 – 122.0 (m), 120.3 (t, J = 246.5 Hz), 119.7, 45.1 (t, J = 27.6 Hz), 31.1 (t, J = 3.4 Hz), 21.2.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.78, -96.01 (d, J = 249.5 Hz), -97.28 (d, J = 249.6 Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{24}\text{H}_{17}\text{F}_5\text{N}$: 414.1281; found 414.1289.

(*R*)-4,4-difluoro-2-(4'-methoxy-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4c)



Chemical Formula: $\text{C}_{24}\text{H}_{18}\text{F}_5\text{NO}$
Molecular Weight: 431.4060

The compound **4c** was prepared according to the general procedure employing **1c** (42.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 57.8 mg, 67% isolated yield, white solid, mp: 94 – 96 °C, (petroleum ether: ethyl acetate = 6:1, R_f = 0.3, $[\alpha]_D^{25}$ = 6.9 (c = 1.0 in CHCl_3); 90% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 20.08 min, t_R (minor) = 16.84 min.

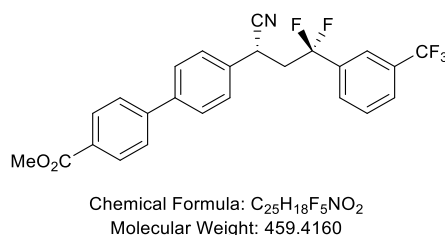
¹H NMR (400 MHz, CDCl₃) δ 7.77 (s, 1H), 7.73 (t, *J* = 8.2 Hz, 2H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.52 – 7.47 (m, 2H), 7.40 – 7.37 (m, 2H), 7.02 – 6.95 (m, 2H), 4.17 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.86 (s, 3H), 3.00 – 2.85 (m, 1H), 2.69 – 2.53 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 159.7, 141.4, 136.9 (t, *J* = 26.6 Hz), 133.0, 132.6, 131.5 (q, *J* = 33.1 Hz), 129.7, 128.5 (t, *J* = 6.1 Hz), 128.3, 127.8, 127.7, 127.5 – 127.4 (m), 123.7 (q, *J* = 273.7 Hz), 122.2 – 121.9 (m), 120.4 (t, *J* = 246.4 Hz), 119.7, 114.5, 55.5, 45.1 (t, *J* = 27.6 Hz), 31.1 (t, *J* = 3.4 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.80, -96.03 (d, *J* = 250.0 Hz), -97.26 (d, *J* = 249.8 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₄H₁₇F₅NO: 430.1230; found 430.1233.

methyl (R)-4'-(1-cyano-3,3-difluoro-3-(3-(trifluoromethyl)phenyl)propyl)-[1,1'-biphenyl]-4-carboxylate (4d)



The compound **4d** was prepared according to the general procedure employing **1d** (47.2 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 28.5 mg, 31% isolated yield, white solid, mp: 106 – 108 °C, (petroleum ether: ethyl acetate = 6:1, *R_f* = 0.2, [α]_D²⁵ = 6.4 (c = 1.0 in CHCl₃); 89% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 80:20 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major) = 13.05 min, *t_R* (minor) = 11.37 min.

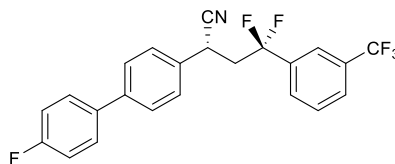
¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, *J* = 8.1 Hz, 2H), 7.74 (dd, *J* = 14.5, 6.8 Hz, 3H), 7.66 – 7.58 (m, 5H), 7.45 (d, *J* = 7.9 Hz, 2H), 4.21 (dd, *J* = 9.7, 4.4 Hz, 1H), 3.94 (s, 3H), 2.93 (m, 1H), 2.63 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 166.9, 144.4, 140.6, 136.8 (t, $J = 26.5$ Hz), 134.6, 131.6 (q, $J = 32.4$ Hz), 130.3, 129.7, 129.5, 128.5 (t, $J = 5.6$ Hz), 128.4, 128.0, 127.6 – 127.4 (m), 127.4, 122.1, 123.6 (q, $J = 273.5$ Hz), 122.2 – 122.0 (m), 120.3 (t, $J = 246.5$ Hz), 52.3, 45.0 (t, $J = 27.5$ Hz), 31.2 (t, $J = 3.5$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.80, -96.09 (d, $J = 249.7$ Hz), -97.18 (d, $J = 249.8$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{25}\text{H}_{17}\text{F}_5\text{NO}_2$: 458.1179; found 458.1187.

(*R*)-4,4-difluoro-2-(4'-fluoro-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4e)



Chemical Formula: $\text{C}_{23}\text{H}_{15}\text{F}_6\text{N}$
Molecular Weight: 419.3704

The compound **4e** was prepared according to the general procedure employing **1e** (39.6 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $\text{V}_{\text{MeCN}}: \text{V}_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 48.6 mg, 58% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.3$, $[\alpha]_D^{25} = -2.0$ ($c = 1.0$ in CHCl_3); 92% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 15.47 min, t_R (minor) = 13.40 min.

^1H NMR (400 MHz, CDCl_3) δ 7.80 – 7.68 (m, 3H), 7.60 (t, $J = 7.8$ Hz, 1H), 7.58 – 7.47 (m, 4H), 7.42 (s, 1H), 7.40 (s, 1H), 7.14 (t, $J = 8.6$ Hz, 2H), 4.19 (dd, $J = 9.5, 4.5$ Hz, 1H), 3.00 – 2.86 (m, 1H), 2.69 – 2.56 (m, 1H).

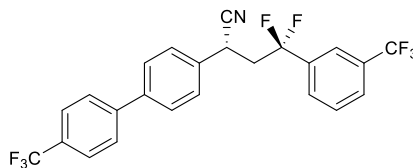
$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 162.9 (d, $J = 247.3$ Hz), 140.9, 136.9 (t, $J = 26.6$ Hz), 136.2 (d, $J = 3.1$ Hz), 133.7, 131.59 (q, $J = 33.1$ Hz), 129.7, 128.8 (d, $J = 8.2$ Hz), 128.5 (t, $J = 6.0$ Hz), 128.1, 127.9, 127.7 – 127.4 (m), 123.7 (q, $J = 273.6$ Hz), 122.22 – 122.0 (m), 120.3 (t, $J = 246.4$ Hz), 116.0 (d, $J = 21.4$ Hz), 45.1 (t, $J = 27.6$ Hz), 31.1

(t, $J = 3.4$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.81, -96.08 (d, $J = 249.5$ Hz), -97.23 (d, $J = 249.7$ Hz), -114.80.

HRMS-ESI (m/z): $[\text{M-H}]^-$ calcd. for $\text{C}_{23}\text{H}_{14}\text{F}_6\text{N}$: 418.1030; found 418.1034.

(*R*)-4,4-difluoro-2-(4'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4f)



Chemical Formula: $\text{C}_{24}\text{H}_{15}\text{F}_8\text{N}$
Molecular Weight: 469.3782

The compound **4f** was prepared according to the general procedure employing **1f** (49.6 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 33.8 mg, 36% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.3$, $[\alpha]_D^{25} = 7.3$ ($c = 1.0$ in CHCl_3); 90% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 14.93 min, t_R (minor) = 13.13 min.

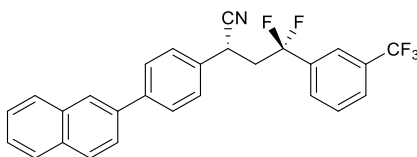
^1H NMR (400 MHz, CDCl_3) δ 7.78 – 7.69 (m, 5H), 7.68 – 7.65 (m, 2H), 7.63 – 7.59 (m, 3H), 7.46 (d, $J = 8.3$ Hz, 2H), 4.21 (dd, $J = 9.4, 4.6$ Hz, 1H), 3.00 – 2.87 (m, 1H), 2.70 – 2.54 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 143.6, 140.4, 136.8 (t, $J = 26.4$ Hz), 134.7, 131.59 (q, $J = 33.4$ Hz), 131.59 (q, $J = 32.7$ Hz), 129.7, 128.5 (t, $J = 5.7$ Hz), 128.4, 128.1, 127.5, 126.00 (q, $J = 3.8$ Hz), 126.00 (q, $J = 273.1$ Hz), 123.7 (q, $J = 273.8$ Hz), 122.1 – 122.0 (m), 120.3 (t, $J = 246.4$ Hz), 119.5, 45.0 (t, $J = 27.6$ Hz), 31.2 (t, $J = 3.5$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.50, -62.82, -96.15 (d, $J = 249.5$ Hz), -97.23 (d, $J = 249.3$ Hz).

HRMS-ESI (m/z): $[\text{M-H}]^-$ calcd. for $\text{C}_{24}\text{H}_{14}\text{F}_8\text{N}$: 468.0999; found 468.1002.

(*R*)-4,4-difluoro-2-(4-(naphthalen-2-yl)phenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4g**)**



Chemical Formula: C₂₇H₁₈F₅N
Molecular Weight: 451.4400

The compound **4g** was prepared according to the general procedure employing **1g** (46.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 55.1 mg, 61% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, R_f = 0.2, [α]_D²⁵ = 10.3 (c = 1.0 in CHCl₃); 94% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 15.70 min, t_R (minor) = 14.34 min.

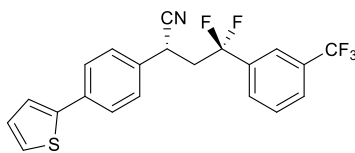
¹H NMR (400 MHz, CDCl₃) δ 8.02 (s, 1H), 7.91 (q, *J* = 10.3, 9.4 Hz, 3H), 7.79 (s, 1H), 7.77 – 7.67 (m, 5H), 7.61 (t, *J* = 8.4 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.46 (d, *J* = 6.8 Hz, 2H), 4.22 (dd, *J* = 9.3, 4.2 Hz, 1H), 3.04 – 2.86 (m, 1H), 2.71 – 2.58 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 141.8, 137.4, 136.9 (t, *J* = 26.5 Hz), 133.7, 132.9, 131.6 (q, *J* = 33.2 Hz), 129.7, 128.8, 128.5, 128.4, 127.9, 127.8, 127.7 – 127.3 (m), 126.6, 126.4, 126.1, 125.3, 123.7 (q, *J* = 273.3 Hz), 122.3 – 121.9 (m), 120.4 (t, *J* = 246.2 Hz), 119.7, 45.1 (t, *J* = 27.5 Hz), 31.2 (t, *J* = 3.5 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.76, -96.03 (d, *J* = 249.4 Hz), -97.21 (d, *J* = 249.6 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₇H₁₇F₅N: 450.1287; found 450.1284.

(*R*)-4,4-difluoro-2-(4-(thiophen-2-yl)phenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4h)



Chemical Formula: C₂₁H₁₄F₅NS
Molecular Weight: 407.4020

The compound **4h** was prepared according to the general procedure employing **1h** (37.2 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 40.7 mg, 50% isolated yield, yellow solid, mp: 74 – 76 °C, (petroleum ether: ethyl acetate = 10:1, R_f = 0.3, [α]_D²⁵ = 12.5 (c = 1.0 in CHCl₃); 94% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 210 nm, 25 °C), *t*_R (major) = 13.29 min, *t*_R (minor) = 11.61 min.

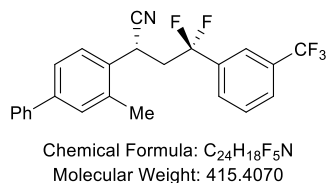
¹H NMR (400 MHz, CDCl₃) δ 7.77 – 7.70 (m, 3H), 7.62 – 7.58 (m, 3H), 7.34 – 7.31 (m, 4H), 7.09 (t, *J* = 4.4 Hz, 1H), 4.16 (dd, *J* = 9.6, 4.5 Hz, 1H), 2.97 – 2.83 (m, 1H), 2.66 – 2.53 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 143.1, 136.9 (t, *J* = 26.5 Hz), 135.1, 133.7, 131.6 (q, *J* = 32.6 Hz), 129.7, 128.5 (t, *J* = 5.9 Hz), 128.3, 128.0, 127.6 – 127.5 (m), 126.9, 125.7, 123.9, 123.7 (q, *J* = 273.6 Hz), 122.2 – 121.9 (m), 120.3 (t, *J* = 246.3 Hz), 119.5, 45.0 (t, *J* = 27.5 Hz), 31.1 (t, *J* = 3.7 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.80, -96.12 (d, *J* = 249.5 Hz), -97.21 (d, *J* = 249.6 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₁H₁₃F₅NS: 406.0689; found 406.0692.

(*R*)-4,4-difluoro-2-(3-methyl-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4i**)**



The compound **4i** was prepared according to the general procedure employing **1i** (38.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 55.7 mg, 67% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, R_f = 0.3, [α]_D²⁵ = 35.7 (c = 1.0 in CHCl₃); 94% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 12.11 min, t_R (minor) = 11.64 min.

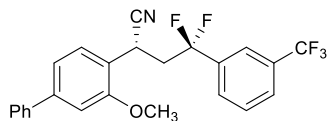
¹H NMR (400 MHz, CDCl₃) δ 7.79 (s, 1H), 7.75 (t, *J* = 6.3 Hz, 2H), 7.62 (t, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 2H), 7.52 – 7.43 (m, 5H), 7.38 (t, *J* = 7.4 Hz, 1H), 4.36 (dd, *J* = 10.1, 3.5 Hz, 1H), 2.99 – 2.85 (m, 1H), 2.60 – 2.48 (m, 1H), 2.41 (s, 3H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 141.9, 140.2, 136.9 (t, *J* = 26.5 Hz), 135.3, 132.1, 131.6 (d, *J* = 32.9 Hz), 130.2, 129.7, 129.0, 128.5 (t, *J* = 6.0 Hz), 128.0, 127.8, 127.7 – 127.3 (m), 127.2, 126.0, 123.7 (q, *J* = 273.4 Hz), 122.4 – 121.7 (m), 120.4 (t, *J* = 246.0 Hz), 120.0, 43.9 (t, *J* = 27.6 Hz), 27.9 (t, *J* = 3.4 Hz), 19.3.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.78, -96.53 (d, *J* = 249.2 Hz), -97.98 (d, *J* = 249.2 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₄H₁₇F₅N: 414.1281; found 414.1278.

(R)-4,4-difluoro-2-(3-methoxy-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4j)



Chemical Formula: C₂₄H₁₈F₅NO
Molecular Weight: 431.4060

The compound **4j** was prepared according to the general procedure employing **1j** (42.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 62.1 mg, 72% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, R_f = 0.2, [α]_D²⁵ = 1.8 (c = 1.0 in CHCl₃); 90% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 0.5 mL/min, λ = 254 nm, 25 °C), t_R (major) = 19.73 min, t_R (minor) = 18.55 min.

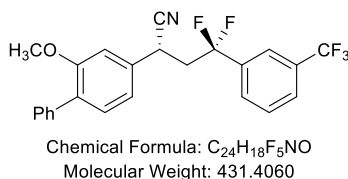
¹H NMR (400 MHz, CDCl₃) δ 7.77 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 2H), 7.48 – 7.42 (m, 3H), 7.40 – 7.37 (m, 1H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.05 (s, 1H), 4.39 (dd, *J* = 9.7, 4.0 Hz, 1H), 3.90 (s, 3H), 2.94 – 2.80 (m, 1H), 2.75 – 2.62 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 156.3, 143.7, 140.5, 137.0 (t, *J* = 26.5 Hz), 131.4 (q, *J* = 32.9 Hz), 129.5, 129.0, 128.6 (t, *J* = 6.1 Hz), 128.0, 127.3 – 127.2 (m), 123.8 (q, *J* = 273.7 Hz), 122.4 – 122.2 (m), 121.6, 120.7 (t, *J* = 246.1 Hz), 120.0, 119.8, 110.0, 55.7, 42.4 (t, *J* = 27.7 Hz), 26.4 (t, *J* = 4.2 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.71, -93.32 (d, *J* = 250.8 Hz), -98.38 (d, *J* = 250.7 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₄H₁₇F₅NO: 430.1230; found 430.1234.

(R)-4,4-difluoro-2-(2-methoxy-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4k)



The compound **4k** was prepared according to the general procedure employing **1k** (42.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 51.4 mg, 60% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 8:1, *R_f* = 0.2, [α]_D²⁵ = 6.7 (c = 1.0 in CHCl₃); 95% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major) = 9.83 min, *t_R* (minor) = 8.83 min.

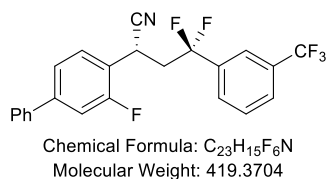
¹H NMR (400 MHz, CDCl₃) δ 7.79 (s, 1H), 7.75 (t, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.50 – 7.48 (m, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.37 – 7.31 (m, 2H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.93 (s, 1H), 4.18 (dd, *J* = 9.8, 4.2 Hz, 1H), 3.83 (s, 3H), 3.02 – 2.88 (m, 1H), 2.72 – 2.59 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 157.2, 137.6, 136.9 (t, *J* = 26.6 Hz), 135.1, 131.8, 131.4, 131.3 (q, *J* = 33.0 Hz), 129.7, 129.5, 128.5 (t, *J* = 5.9 Hz), 128.2, 127.6 – 127.5 (m), 123.5 (q, *J* = 273.7 Hz), 122.3 – 122.0 (m), 120.4 (t, *J* = 246.3 Hz), 119.7, 110.2, 55.9, 45.1 (t, *J* = 27.6 Hz), 31.5 (t, *J* = 3.5 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.78, -95.97 (d, *J* = 249.7 Hz), -97.35 (d, *J* = 249.7 Hz).

HRMS-ESI (*m/z*): [M-H][−]calcd. for C₂₄H₁₇F₅NO: 430.1230; found 430.1237.

(R)-4,4-difluoro-2-(3-fluoro-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4l)



The compound **4l** was prepared according to the general procedure employing **1l** (39.6 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 34.4 mg, 41% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, R_f = 0.3, [α]_D²⁵ = 19.6 (c = 1.0 in CHCl₃); 93% ee, determined by HPLC analysis AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 10.36 min, t_R (minor) = 9.35 min.

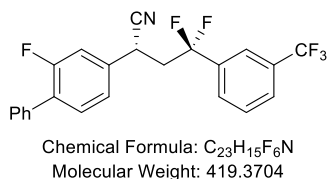
¹H NMR (400 MHz, CDCl₃) δ 7.76 (s, 1H), 7.71 (d, *J* = 5.9 Hz, 2H), 7.61 – 7.57 (m, 1H), 7.52 (t, *J* = 8.9 Hz, 3H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 11.6 Hz, 1H), 4.43 (dd, *J* = 9.3, 4.6 Hz, 1H), 2.99 – 2.85 (m, 1H), 2.75 – 2.62 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 156.0 (d, *J* = 248.9 Hz), 144.5 (d, *J* = 8.1 Hz), 138.9, 136.7 (t, *J* = 27.7 Hz), 131.6 (q, *J* = 32.9 Hz), 129.7, 129.5 (d, *J* = 3.4 Hz), 129.2, 128.6, 128.6 (t, *J* = 4.7 Hz), 127.6 – 127.4 (m), 127.1, 123.7 (d, *J* = 3.3 Hz), 123.7 (q, *J* = 274.2 Hz), 122.2 – 122.0 (m), 120.4 (d, *J* = 14.2 Hz), 120.3 (t, *J* = 246.5 Hz), 118.7, 114.8 (d, *J* = 21.7 Hz), 43.1 (t, *J* = 27.7 Hz), 25.7 (q, *J* = 3.6 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.82, -95.33 (d, *J* = 250.2 Hz), -98.08 (d, *J* = 250.1 Hz), -117.21.

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₃H₁₄F₆N: 418.1030; found 418.1037.

(R)-4,4-difluoro-2-(2-fluoro-[1,1'-biphenyl]-4-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4m)



The compound **4m** was prepared according to the general procedure employing **1m** (39.6 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 43.6 mg, 52% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, R_f = 0.2, [α]_D²⁵ = 4.4 (c = 1.0 in CHCl₃); 91% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 13.96 min, t_R (minor) = 13.18 min.

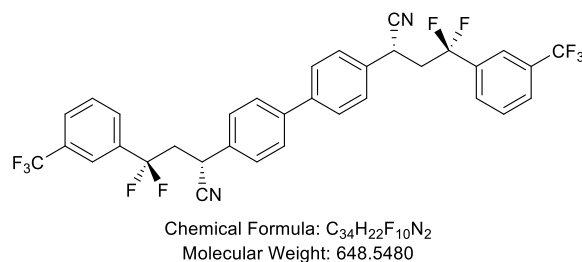
¹H NMR (400 MHz, CDCl₃) δ 7.80 – 7.69 (m, 3H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.58 – 7.51 (m, 1H), 7.51 – 7.43 (m, 4H), 7.43 – 7.35 (m, 1H), 7.25 – 7.13 (m, 2H), 4.20 (dd, *J* = 9.4, 4.5 Hz, 1H), 3.00 – 2.86 (m, 1H), 2.70 – 2.57 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 160.0 (d, *J* = 250.7 Hz), 136.8 (t, *J* = 26.4 Hz), 135.7 (d, *J* = 7.7 Hz), 134.8, 131.9 (d, *J* = 3.9 Hz), 131.3 (q, *J* = 33.2 Hz), 129.8, 129.7, 129.0 (d, *J* = 2.9 Hz), 128.7, 128.5 (t, *J* = 6.1 Hz), 128.3, 127.7 – 127.5 (m), 123.5 (q, *J* = 273.5 Hz), 123.4 (d, *J* = 3.3 Hz), 122.2 – 122.0 (m), 120.3 (t, *J* = 249.2 Hz), 119.2, 115.5 (d, *J* = 25 Hz), 44.9 (t, *J* = 27.6 Hz), 30.9 (t, *J* = 3.5 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.80, -96.18 (d, *J* = 249.5 Hz), -97.30 (d, *J* = 249.9 Hz), -115.55.

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₃H₁₄F₆N: 418.1030; found 418.1039.

(2*R*,2'*R*)-2,2'-([1,1'-biphenyl]-4,4'-diyl)bis(4,4-difluoro-4-(3-(trifluoromethyl)phenyl)butanenitrile) (4n)



The compound **4n** was prepared according to the general procedure employing **1n** (41.2 mg, 0.2 mmol), **2a** (171.2 mg, 0.8 mmol, 4.0 equiv), **3** (59.6 mg, 0.6 mmol, 3.0 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (3.7 mg, 5.0 mol%), and **L1** (4.2 mg, 6.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 34 h under argon atmosphere. 69.9 mg, 54% isolated yield, white solid, mp: 128 – 130 °C, (petroleum ether: ethyl acetate = 5:1, *R_f* = 0.3, [α]_D²⁵ = 2.7 (c = 1.0 in CHCl₃); 99% ee, 7:1 dr. determined by HPLC analysis (IA, hexane/*i*-PrOH, 70:30 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major) = 16.38 min, *t_R* (minor) = 8.99 min, *t_R* (*meso*-**4n**) = 11.05 min.

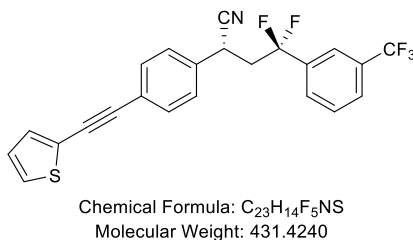
¹H NMR (400 MHz, CDCl₃) δ 7.78 – 7.68 (m, 6H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.58 – 7.56 (m, 4H), 7.46 – 7.39 (m, 4H), 4.20 (dd, *J* = 9.5, 4.5 Hz, 2H), 3.0 – 2.86 (m, 2H), 2.68 – 2.55 (m, 2H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 139.8, 136.8 (t, *J* = 26.6 Hz), 131.5 (q, *J* = 33.0 Hz), 131.2, 129.7, 128.4 (t, *J* = 6.2 Hz), 127.8, 127.6 – 127.4 (m), 127.1, 123.6 (q, *J* = 273.7 Hz), 122.2 – 122.0 (m), 120.3 (t, *J* = 245.4 Hz), 119.6, 45.0 (t, *J* = 27.6 Hz), 30.9 (t, *J* = 3.4 Hz), 15.6.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.80, -96.17 (d, *J* = 249.3 Hz), -97.27 (d, *J* = 249.4 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₃₄H₂₁F₁₀N₂: 647.1545; found 647.1553.

(*R*)-4,4-difluoro-2-(4-(thiophen-2-ylethynyl)phenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4o)



The compound **4o** was prepared according to the general procedure employing **1o** (42.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 34 h under argon atmosphere. 31.7 mg, 37% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 8:1, *R_f* = 0.3, [α]_D²⁵ = -5.9 (c = 1.0 in CHCl₃); 90% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major) = 15.06 min, *t_R* (minor) = 13.13 min.

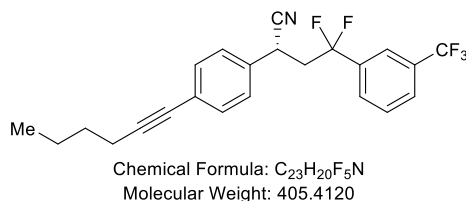
¹H NMR (400 MHz, CDCl₃) δ 7.71 – 7.70 (m, 3H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 7.9 Hz, 2H), 7.35 – 7.30 (m, 4H), 7.02 (t, *J* = 4.4 Hz, 1H), 4.15 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.00 – 2.82 (m, 1H), 2.64 – 2.51 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 136.8 (t, *J* = 26.7 Hz), 134.7, 132.5, 132.4, 131.6 (q, *J* = 32.4 Hz), 129.7, 128.5 (t, *J* = 5.7 Hz), 127.9, 127.7 – 127.6 (m), 127.5, 127.3, 123.8, 123.6 (q, *J* = 272.6 Hz), 122.9, 122.2 – 122.0 (m), 120.3 (t, *J* = 246.7 Hz), 119.1, 91.2, 84.1, 44.95 (t, *J* = 27.5 Hz), 31.3 (t, *J* = 3.3 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.82, -96.34 (d, *J* = 249.5 Hz), -97.27 (d, *J* = 249.5 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₃H₁₃F₅NS: 430.0689; found 430.0697.

(*R*)-4,4-difluoro-2-(4-(hex-1-yn-1-yl)phenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4p)



The compound **4p** was prepared according to the general procedure employing **1p** (36.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 34 h under argon atmosphere. 33.3 mg, 41% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 12:1, R_f = 0.2, [α]_D²⁵ = 4.4 (c = 1.0 in CHCl₃); 94% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 98:2 v/v, flow rate 0.5 mL/min, λ = 254 nm, 25 °C), t_R (major) = 19.69 min, t_R (minor) = 18.30 min.

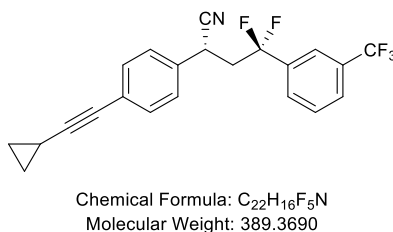
¹H NMR (400 MHz, CDCl₃) δ 7.67 (d, *J* = 5.1 Hz, 2H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 4.04 (dd, *J* = 9.6, 4.4 Hz, 1H), 2.86 – 2.72 (m, 1H), 2.53 – 2.70 (m, 1H), 2.33 (t, *J* = 7.0 Hz, 2H), 1.55 – 1.50 (m, 2H), 1.44 – 1.35 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 136.8 (t, *J* = 26.5 Hz), 133.7, 132.6, 131.6 (q, *J* = 33.1 Hz), 129.7, 128.4 (t, *J* = 5.9 Hz), 127.7 – 127.4 (m), 127.2, 124.9, 123.6 (q, *J* = 273.5 Hz), 122.2 – 121.9 (m), 120.3 (t, *J* = 246.3 Hz), 119.4, 92.1, 79.7, 45.0 (t, *J* = 27.5 Hz), 31.2 (t, *J* = 3.2 Hz), 30.8, 22.2, 19.2, 13.8.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.84, -96.31 (d, *J* = 249.6 Hz), -97.25 (d, *J* = 249.4 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₃H₁₉F₅N: 404.1438; found 404.1445.

(R)-2-(4-(cyclopropylethynyl)phenyl)-4,4-difluoro-4-(3-(trifluoromethyl)phenyl)butanenitrile (4q)



The compound **4q** was prepared according to the general procedure employing **1q** (33.6 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 34 h under argon atmosphere. 34.3 mg, 44% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, R_f = 0.3, [α]_D²⁵ = 14.1 (c = 1.0 in CHCl₃); 93% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t*_R (major) = 9.87min, *t*_R (minor) = 10.60 min.

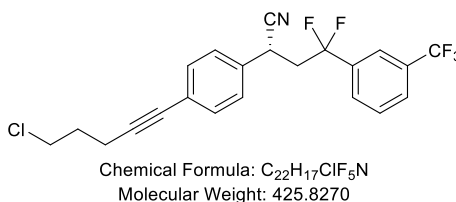
¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J* = 5.0 Hz, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.52 (t, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 5.6 Hz, 2H), 4.00 (dd, *J* = 9.7, 4.3 Hz, 1H), 2.85 – 2.71 (m, 1H), 2.52 – 2.39 (m, 1H), 1.26 (td, *J* = 8.3, 4.2 Hz, 1H), 0.83 – 0.78 (m, 2H), 0.75 – 0.71 (q, *J* = 3.5, 2.8 Hz, 2H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 136.8 (t, *J* = 26.5 Hz), 133.7, 132.7, 131.3 (q, *J* = 33.2 Hz), 129.7, 128.5 (t, *J* = 6.1 Hz), 127.6 – 127.5 (m), 127.3, 124.8, 123.5 (q, *J* = 273.6 Hz), 122.3 – 122.0 (m), 120.3 (t, *J* = 246.2 Hz), 119.4, 95.1, 74.9, 45.0 (t, *J* = 27.6 Hz), 31.3 (t, *J* = 3.4 Hz), 8.8, 0.3.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.83, -96.32 (d, *J* = 249.5 Hz), -97.28 (d, *J* = 249.5 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₂H₁₅F₅N: 388.1125; found 388.1130.

(*R*)-2-(4-(5-chloropent-1-yn-1-yl)phenyl)-4,4-difluoro-4-(3-(trifluoromethyl)phenyl)butanenitrile (4r)



The compound **4r** was prepared according to the general procedure employing **1r** (40.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0

mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 34 h under argon atmosphere. 44.3 mg, 52% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.2$, $[\alpha]_D^{25} = 16.1$ ($c = 1.0$ in CHCl_3); 91% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 12.26 min, t_R (minor) = 13.52 min.

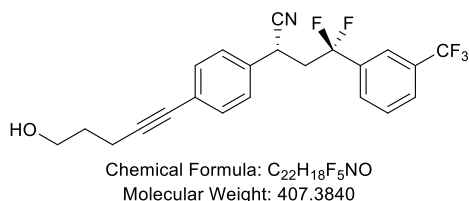
^1H NMR (400 MHz, CDCl_3) δ 7.70 – 7.65 (m, 2H), 7.64 – 7.59 (m, 1H), 7.53 (t, $J = 8.0$ Hz, 1H), 7.37 – 7.29 (m, 2H), 7.21 (d, $J = 1.9$ Hz, 2H), 4.05 (dd, $J = 9.5, 4.5$ Hz, 1H), 3.63 (t, $J = 6.4$ Hz, 2H), 2.86 – 2.73 (m, 1H), 2.54 (t, $J = 6.8$ Hz, 2H), 2.52 – 2.38 (m, 1H), 1.99 (p, $J = 6.6$ Hz, 2H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 136.8 (t, $J = 26.5$ Hz), 134.1, 132.7, 131.6 (q, $J = 34.3$ Hz), 129.7, 128.4 (t, $J = 6.0$ Hz), 127.6 – 127.5 (m), 127.3, 124.4, 123.6 (q, $J = 273.4$ Hz), 122.2 – 121.9 (m), 120.3 (t, $J = 248.8$ Hz), 117.8, 89.7, 80.6, 45.0 (t, $J = 27.5$ Hz), 43.8, 31.4, 31.3 (t, $J = 3.3$ Hz), 17.0.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.83, -96.32 (d, $J = 249.5$ Hz), -97.25 (d, $J = 249.5$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{22}\text{H}_{16}\text{ClF}_5\text{N}$: 424.0897; found 424.0891.

(*R*)-4,4-difluoro-2-(4-(5-hydroxypent-1-yn-1-yl)phenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4s)



The compound **4s** was prepared according to the general procedure employing **1s** (37.2 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 34 h under argon atmosphere. 31.1 mg, 38% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 3:1, $R_f = 0.3$, $[\alpha]_D^{25} = -2.8$

(*c* = 1.0 in CHCl₃); 89% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 85:15 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t*_R (major) = 13.65 min, *t*_R (minor) = 15.23 min.

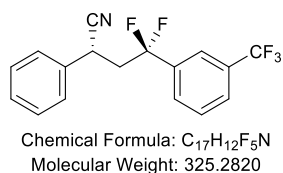
¹H NMR (400 MHz, CDCl₃) δ 7.69 – 7.64 (m, 2H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 4.05 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.73 (t, *J* = 6.2 Hz, 2H), 2.90 – 2.69 (m, 1H), 2.54 – 2.38 (m, 3H), 1.79 (p, *J* = 6.6 Hz, 2H), 1.59 (s, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 136.8 (t, *J* = 26.6 Hz), 133.9, 132.6, 131.6 (q, *J* = 33.0 Hz), 129.7, 128.4 (t, *J* = 5.9 Hz), 127.6 – 127.5 (m), 127.3, 124.6, 123.6 (q, *J* = 273.7 Hz), 122.1 – 121.9 (m), 120.3 (t, *J* = 244.2 Hz), 119.4, 91.0, 80.2, 61.8, 44.9 (t, *J* = 27.5 Hz), 31.4, 31.2 (t, *J* = 3.3 Hz), 16.1.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.82, -96.27 (d, *J* = 254.3 Hz), -97.25 (d, *J* = 249.6 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₂H₁₇F₅NO: 406.1230; found 406.1232.

(*R*)-4,4-difluoro-2-phenyl-4-(3-(trifluoromethyl)phenyl)butanenitrile (4t)



The compound **4t** was prepared according to the general procedure employing **1t** (20.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (3.7 mg, 5.0 mol%), and **L1** (4.3 mg, 6.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 32.6 mg, 50% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 15:1, *R*_f = 0.3, [α]_D²⁵ = 12.9 (*c* = 1.0 in CHCl₃); 91% ee, determined by HPLC analysis (AS-H, hexane/*i*-PrOH, 98:2 v/v, flow rate 0.8 mL/min, λ = 210 nm, 25 °C), *t*_R (major) = 24.14 min, *t*_R (minor) = 23.24 min.

¹H NMR (400 MHz, CDCl₃) δ 7.77 – 7.68 (m, 3H), 7.66 – 7.54 (m, 1H), 7.41 – 7.38 (m, 1H), 7.37 (d, *J* = 0.8 Hz, 1H), 7.37 – 7.32 (m, 3H), 4.14 (dd, *J* = 9.7, 4.4 Hz, 1H),

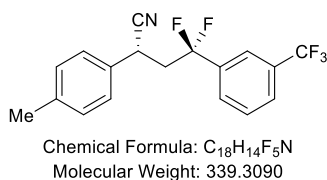
2.96 – 2.82 (m, 1H), 2.67 – 2.50 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 136.9 (t, $J = 26.6$ Hz), 134.8, 131.5 (q, $J = 33.1$ Hz), 129.7, 129.6, 128.8, 128.5 (t, $J = 5.9$ Hz), 127.6 – 127.3 (m), 127.4, 123.6 (q, $J = 273.6$ Hz), 122.3 – 122.0 (m), 120.3 (t, $J = 246.4$ Hz), 119.7, 45.1 (t, $J = 27.5$ Hz), 31.4 (t, $J = 3.3$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.80, -96.19 (d, $J = 249.3$ Hz), -97.39 (d, $J = 249.3$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{17}\text{H}_{11}\text{F}_5\text{N}$: 324.0812; found 324.0812.

(*R*)-4,4-difluoro-2-(*p*-tolyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4u**)**



The compound **4u** was prepared according to the general procedure employing **1u** (23.6 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (3.7 mg, 5.0 mol%), and **L1** (4.3 mg, 6.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 33.6 mg, 50% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 15:1, $R_f = 0.3$, $[\alpha]_D^{25} = 18.9$ ($c = 1.0$ in CHCl_3); 93% ee, determined by HPLC analysis (OJ-H, hexane/*i*-PrOH, 98:2 v/v, flow rate 0.8 mL/min, $\lambda = 210$ nm, 25 °C), t_R (major) = 22.1 min, t_R (minor) = 25.98 min.

^1H NMR (400 MHz, CDCl_3) δ 7.77 – 7.68 (m, 3H), 7.59 (t, $J = 8.0$ Hz, 1H), 7.20 (q, $J = 8.1$ Hz, 4H), 4.09 (dd, $J = 9.6, 4.4$ Hz, 1H), 2.94 – 2.80 (m, 1H), 2.62 – 2.50 (m, 1H), 2.34 (s, 3H).

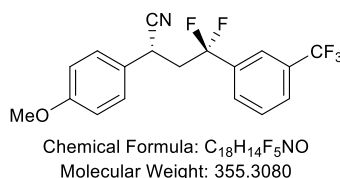
$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 138.7, 137.0 (t, $J = 26.9$ Hz), 131.8, 131.5 (q, $J = 33.1$ Hz), 130.2, 129.7, 128.5 (t, $J = 6.1$ Hz), 127.5 – 127.4 (m), 127.22, 123.7 (q, $J = 273.5$ Hz), 122.3 – 122.0 (m), 120.4 (t, $J = 246.3$ Hz), 119.9, 45.1 (t, $J = 27.5$ Hz), 31.0 (t, $J = 3.5$ Hz), 21.2.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.82, -96.02 (d, $J = 249.5$ Hz), -97.30 (d, $J =$

249.6 Hz).

HRMS-ESI (m/z): $[M-H]^-$ calcd. for $C_{18}H_{13}F_5N$: 338.0968; found 338.0970.

(*R*)-4,4-difluoro-2-(4-methoxyphenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4v)



The compound **4v** was prepared according to the general procedure employing **1v** (26.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[Cu(MeCN)_4]PF_6$ (3.7 mg, 5.0 mol%), and **L1** (4.3 mg, 6.0 mol%) in $V_{MeCN}: V_{DMF} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 34.1 mg, 48% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.3$, $[\alpha]_D^{25} = 7.7$ ($c = 1.0$ in $CHCl_3$); 91% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 97:3 v/v, flow rate 0.8 mL/min, $\lambda = 210$ nm, 25 °C), t_R (major) = 16.85 min, t_R (minor) = 18.00 min.

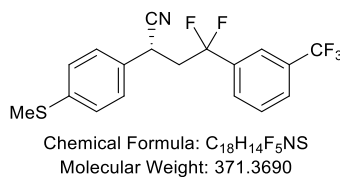
1H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.57 (m, 3H), 7.51 (t, $J = 8.0$ Hz, 1H), 7.15 (d, $J = 8.4$ Hz, 2H), 6.80 (d, $J = 8.3$ Hz, 2H), 4.00 (dd, $J = 9.6, 4.6$ Hz, 1H), 3.71 (s, 3H), 2.87 – 2.70 (m, 1H), 2.55 – 2.40 (m, 1H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.8, 136.9 (t, $J = 26.5$ Hz), 131.5 (q, $J = 32.9$ Hz), 129.7, 128.5, 128.5 (t, $J = 6.9$ Hz), 127.5 – 127.4 (m), 126.6, 123.7 (q, $J = 273.5$ Hz), 122.1 – 120.0 (m), 120.4 (t, $J = 246.3$ Hz), 120.0, 114.8, 55.5, 45.1 (t, $J = 27.5$ Hz), 30.6 (t, $J = 3.4$ Hz).

$^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -62.82, -95.88 (d, $J = 249.4$ Hz), -97.32 (d, $J = 249.9$ Hz).

HRMS-ESI (m/z): $[M-H]^-$ calcd. for $C_{18}H_{13}F_5NO$: 354.0917; found 354.0919.

(*R*)-4,4-difluoro-2-(4-(methylthio)phenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4w)



The compound **4w** was prepared according to the general procedure employing **1w** (30.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (3.7 mg, 5.0 mol%), and **L1** (4.3 mg, 6.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 41.6 mg, 56% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, R_f = 0.3, [α]_D²⁵ = -4.0 (c = 1.0 in CHCl₃); 93% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 98:2 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 16.10 min, t_R (minor) = 15.40 min.

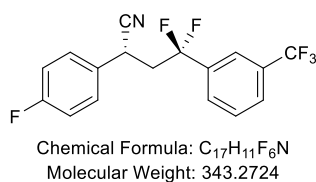
¹H NMR (400 MHz, CDCl₃) δ 7.69 – 7.58 (m, 3H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.19 – 7.14 (m, 4H), 4.02 (dd, *J* = 9.5, 4.5 Hz, 1H), 2.86 – 2.72 (m, 1H), 2.57 – 2.42 (m, 1H), 2.39 (s, 3H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 139.9, 136.8 (t, *J* = 26.6 Hz), 131.5 (q, *J* = 33.1 Hz), 131.2, 129.7, 128.4 (t, *J* = 6.0 Hz), 127.8, 127.5 – 127.4 (m), 127.1, 131.5 (q, *J* = 273.6 Hz), 122.4 – 121.9 (m), 120.3 (t, *J* = 246.5 Hz), 119.6, 44.9 (d, *J* = 27.6 Hz), 30.9 (t, *J* = 3.4 Hz), 15.6.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.80, -96.17 (d, *J* = 249.3 Hz), -97.27 (d, *J* = 249.4 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₁₈H₁₃F₅NS: 370.0689; found 370.0689.

(*R*)-4,4-difluoro-2-(4-fluorophenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile
(4x)



The compound **4x** was prepared according to the general procedure employing **1x** (24.4

mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (3.7 mg, 5.0 mol%), and **L1** (4.3 mg, 6.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 24.6 mg, 36% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 15:1, R_f = 0.3, [α]_D²⁵ = 4.0 (c = 1.0 in CHCl₃); 92% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 98:2 v/v, flow rate 0.8 mL/min, λ = 210 nm, 25 °C), t_R (major) = 15.50 min, t_R (minor) = 16.79 min.

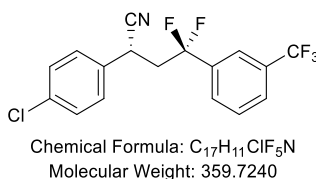
¹H NMR (400 MHz, CDCl₃) δ 7.70 – 7.59 (m, 3H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.29 – 7.21 (m, 2H), 7.00 (t, *J* = 8.4 Hz, 2H), 4.06 (dd, *J* = 9.4, 4.7 Hz, 1H), 2.87 – 2.73 (m, 1H), 2.55 – 2.42 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 162.8 (d, *J* = 248.6 Hz), 136.8 (t, *J* = 26.5 Hz), 131.6 (q, *J* = 33.0 Hz), 130.6 (d, *J* = 3.4 Hz), 129.7, 129.2 (d, *J* = 8.5 Hz), 128.4 (t, *J* = 6.0 Hz), 127.9 – 126.9 (m), 123.6 (q, *J* = 273.6 Hz), 122.2 – 121.9 (m), 120.3 (t, *J* = 246.5 Hz), 119.5, 116.5 (d, *J* = 21.9 Hz), 45.1 (t, *J* = 27.5 Hz), 30.8 (t, *J* = 3.5 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.85, -96.20 (d, *J* = 249.7 Hz), -97.32 (d, *J* = 249.9 Hz), -112.63.

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₁₇H₁₀F₆N: 342.0717; found 342.0725.

(*R*)-2-(4-chlorophenyl)-4,4-difluoro-4-(3-(trifluoromethyl)phenyl)butanenitrile
(4y)



The compound **4y** was prepared according to the general procedure employing **1y** (27.6 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (3.7 mg, 5.0 mol%), and **L1** (4.3 mg, 6.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 24.5 mg, 34% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 15:1, R_f = 0.3, [α]_D²⁵ = 9.2

($c = 1.0$ in CHCl_3); 92% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 26.60 min, t_R (minor) = 23.69 min.

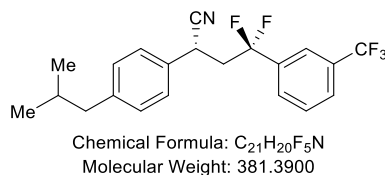
^1H NMR (400 MHz, CDCl_3) δ 7.78 – 7.66 (m, 3H), 7.60 (t, $J = 7.8$ Hz, 1H), 7.38 (d, $J = 8.2$ Hz, 2H), 7.29 (d, $J = 8.2$ Hz, 2H), 4.14 (dd, $J = 9.4, 4.6$ Hz, 1H), 2.96 – 2.80 (m, 1H), 2.64 – 2.46 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 136.8 (t, $J = 26.9$ Hz), 135.0, 133.3, 131.6 (q, $J = 33.5$ Hz), 129.8, 129.8, 128.8, 128.4 (t, $J = 6.0$ Hz), 127.7 – 127.5 (m), 123.6 (q, $J = 273.9$ Hz), 122.2 – 122.0 (m), 120.2 (t, $J = 246.4$ Hz), 119.3, 45.0 (t, $J = 27.6$ Hz), 31.0 (t, $J = 3.5$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.83, -96.34 (d, $J = 249.6$ Hz), -97.27 (d, $J = 249.8$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{17}\text{H}_{10}\text{ClF}_5\text{N}$: 358.0422; found 358.0427.

(*R*)-4,4-difluoro-2-(4-isobutylphenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4z)



The compound **4z** was prepared according to the general procedure employing **1z** (32.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (3.7 mg, 5.0 mol%), and **L1** (4.3 mg, 6.0 mol%) in $\text{V}_{\text{MeCN}}: \text{V}_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 33.6 mg, 44% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 15:1, $R_f = 0.3$, $[\alpha]_D^{25} = 6.8$ ($c = 1.0$ in CHCl_3); 91% ee, determined by HPLC analysis (OJ-H, hexane/*i*-PrOH, 98:2 v/v, flow rate 0.8 mL/min, $\lambda = 210$ nm, 25 °C), t_R (major) = 12.75 min, t_R (minor) = 14.21 min.

^1H NMR (400 MHz, CDCl_3) δ 7.78 (s, 1H), 7.75 (t, $J = 8.8$ Hz, 2H), 7.62 (t, $J = 7.8$ Hz, 1H), 7.26 (d, $J = 7.9$ Hz, 2H), 7.18 (d, $J = 7.9$ Hz, 2H), 4.13 (dd, $J = 9.8, 4.2$ Hz,

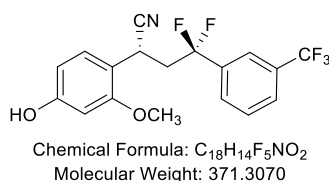
1H), 2.98 – 2.84 (m, 1H), 2.66 – 2.53 (m, 1H), 2.49 (d, $J = 7.2$ Hz, 2H), 1.92 – 1.81 (m, 1H), 0.92 (d, $J = 6.6$ Hz, 6H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 142.5, 137.0 (t, $J = 26.5$ Hz), 132.0, 131.5 (q, $J = 32.8$ Hz), 130.2, 129.7, 128.5 (t, $J = 6.0$ Hz), 127.6 – 127.3 (m), 127.1, 123.9 (q, $J = 273.5$ Hz), 122.2 – 122.0 (m), 120.4 (t, $J = 246.3$ Hz), 119.9, 45.2 (t, $J = 27.5$ Hz), 45.0, 31.1 (t, $J = 3.5$ Hz), 30.3, 22.4.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.82, -96.04 (d, $J = 249.6$ Hz), -97.43 (d, $J = 249.6$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{21}\text{H}_{19}\text{F}_5\text{N}$: 380.1438; found 380.1447.

(*R*)-4,4-difluoro-2-(4-hydroxy-2-methoxyphenyl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4aa)



The compound **4aa** was prepared according to the general procedure employing **1aa** (30.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 30.5 mg, 41% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 5:1, $R_f = 0.3$, $[\alpha]_D^{25} = 3.1$ ($c = 1.0$ in CHCl_3); 92% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 98:2 v/v, flow rate 0.8 mL/min, $\lambda = 210$ nm, 25 °C), t_R (major) = 15.50 min, t_R (minor) = 16.79 min.

^1H NMR (400 MHz, CDCl_3) δ 7.82 – 7.66 (m, 3H), 7.59 (t, $J = 8.0$ Hz, 1H), 6.89 (d, $J = 8.7$ Hz, 1H), 6.80 (d, $J = 1.9$ Hz, 2H), 5.67 (s, 1H), 4.06 (dd, $J = 9.7, 4.5$ Hz, 1H), 3.90 (s, 3H), 2.96 – 2.80 (m, 1H), 2.62 – 2.49 (m 1H).

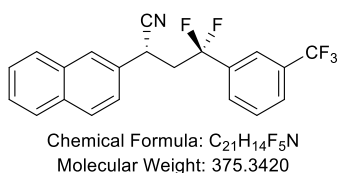
$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 147.2, 146.0, 136.9 (t, $J = 26.8$ Hz), 131.5 (q, $J = 32.9$ Hz), 129.7, 128.5 (t, $J = 6.1$ Hz), 127.5 – 127.4 (m), 126.4, 123.7 (q, $J = 273.4$

Hz), 122.1 – 121.8 (m), 120.5, 120.3 (t, $J = 245.3$ Hz), 120.0, 115.2, 109.6, 56.2, 45.3 (t, $J = 27.4$ Hz), 31.1 (t, $J = 3.5$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.81, -95.93 (d, $J = 249.1$ Hz), -97.43 (d, $J = 249.5$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{18}\text{H}_{13}\text{F}_5\text{NO}_2$: 370.0866; found 370.0870.

(*R*)-4,4-difluoro-2-(naphthalen-2-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4ab)



The compound **4ab** was prepared according to the general procedure employing **1ab** (30.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $\text{V}_{\text{MeCN}}: \text{V}_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 40.2 mg, 54% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.3$, $[\alpha]_D^{25} = 19.6$ ($c = 1.0$ in CHCl_3); 93% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 98:2 v/v, flow rate 1.0 mL/min, $\lambda = 210$ nm, 25 °C), t_R (major) = 16.81 min, t_R (minor) = 18.11 min.

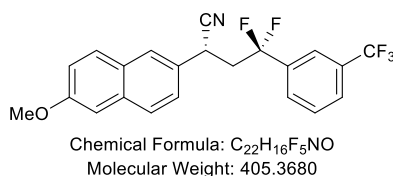
^1H NMR (400 MHz, CDCl_3) δ 7.88 (d, $J = 8.6$ Hz, 1H), 7.86 – 7.80 (m, 3H), 7.78 (s, 1H), 7.72 (d, $J = 7.9$ Hz, 2H), 7.58 (t, $J = 7.6$ Hz, 1H), 7.56 – 7.50 (m, 2H), 7.40 (dd, $J = 8.5, 2.0$ Hz, 1H), 4.31 (dd, $J = 9.6, 4.3$ Hz, 1H), 3.04 – 2.90 (m, 1H), 2.74 – 2.61 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 136.8 (t, $J = 26.7$ Hz), 133.3, 133.0, 131.9, 131.5 (q, $J = 33.0$ Hz), 129.7, 129.6, 128.5 (t, $J = 5.9$ Hz), 128.0, 127.8, 127.6 – 127.3 (m), 127.1, 127.0, 126.7, 124.5, 123.6 (q, $J = 273.6$ Hz), 122.2 – 122.0 (m), 120.4 (t, $J = 246.1$ Hz), 119.7, 45.0 (t, $J = 27.6$ Hz), 31.6 (t, $J = 3.4$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.77, -96.04 (d, $J = 249.4$ Hz), -97.20 (d, $J = 251.0$ Hz).

HRMS-ESI (m/z): $[M-H]^-$ calcd. for $C_{21}H_{13}F_5N$: 374.0968; found 374.0973.

(*R*)-4,4-difluoro-2-(6-methoxynaphthalen-2-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4ac)



The compound **4ac** was prepared according to the general procedure employing **1ac** (36.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[Cu(MeCN)_4]PF_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{MeCN}: V_{DMF} = 3:1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere. 51.8 mg, 64% isolated yield, yellow solid, mp: 74 – 76 °C, (petroleum ether: ethyl acetate = 8:1, $R_f = 0.3$, $[\alpha]_D^{25} = 19.6$ ($c = 1.0$ in $CHCl_3$); 92% ee, determined by HPLC analysis (OB-H, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 10.79 min, t_R (minor) = 9.25 min.

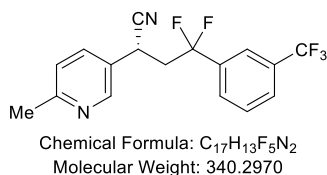
1H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.67 (m, 6H), 7.57 (t, $J = 7.9$ Hz, 1H), 7.35 (d, $J = 8.5$ Hz, 1H), 7.19 (d, $J = 9.0$ Hz, 1H), 7.13 (s, 1H), 4.26 (dd, $J = 9.7, 4.3$ Hz, 1H), 3.92 (s, 3H), 3.02 – 2.88 (m, 1H), 2.72 – 2.59 (m, 1H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.5, 136.9 (t, $J = 26.5$ Hz), 134.4, 131.5 (q, $J = 33.0$ Hz), 129.6, 129.5, 129.4, 128.8, 128.5 (t, $J = 5.05$ Hz), 128.4, 127.5 – 126.5 (m), 126.5, 125.0, 123.9 (q, $J = 273.5$ Hz), 122.2 – 122.0 (m), 120.4 (t, $J = 246.1$ Hz), 120.0, 119.9, 105.8, 55.5, 45.0 (t, $J = 27.6$ Hz), 31.4 (t, $J = 3.4$ Hz).

$^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -62.79, -95.88 (d, $J = 249.7$ Hz), -97.16 (d, $J = 249.7$ Hz).

HRMS-ESI (m/z): $[M-H]^-$ calcd. for $C_{22}H_{15}F_5NO$: 404.1074; found 404.1073.

(*R*)-4,4-difluoro-2-(6-methylpyridin-3-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4ad)



The compound **4ad** was prepared according to the general procedure employing **1ad** (23.8 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (3.7 mg, 5.0 mol%), and **L1** (4.3 mg, 6.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 24.5 mg, 36% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 3:1, R_f = 0.2, [α]_D²⁵ = 20.5 (c = 1.0 in CHCl₃); 78% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 12.62 min, t_R (minor) = 11.86 min.

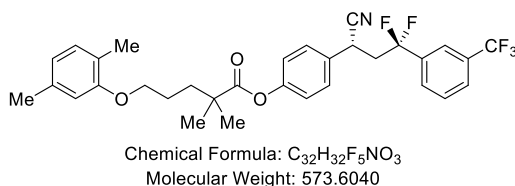
¹H NMR (400 MHz, CDCl₃) δ 8.46 (s, 1H), 7.78 – 7.66 (m, 3H), 7.65 – 7.56 (m, 2H), 7.20 (d, *J* = 8.1 Hz, 1H), 4.17 (dd, *J* = 9.2, 5.0 Hz, 1H), 2.96 – 2.82 (m, 1H), 2.63– 2.51 (m, 4H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 159.4, 148.1, 136.6 (t, *J* = 26.5 Hz), 135.2, 131.6 (q, *J* = 33.1 Hz), 129.8, 128.4 (t, *J* = 6.1 Hz), 127.7, 127.7 – 127.6 (m), 123.8, 123.6 (q, *J* = 273.3 Hz), 122.1 – 122.0 (m), 120.2 (t, *J* = 246.4 Hz), 119.0, 44.7 (t, *J* = 27.6 Hz), 28.9 (t, *J* = 3.5 Hz), 24.3.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.84, -96.34 (d, *J* = 249.5 Hz), -97.21 (d, *J* = 249.8 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₁₇H₁₂F₅N₂: 339.0921; found 339.0919.

(R)-4-(1-cyano-3,3-difluoro-3-(3-(trifluoromethyl)phenyl)propyl)phenyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (4ae)



The compound **4ae** was prepared according to the general procedure employing **1ae**

(70.4 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 48 h under argon atmosphere. 51.6 mg, 45% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 5:1, R_f = 0.3, [α]_D²⁵ = 5.8 (c = 1.0 in CHCl₃); 88% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, λ = 210 nm, 25 °C), t_R (major) = 8.49 min, t_R (minor) = 7.14 min.

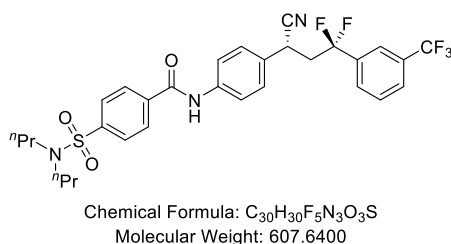
¹H NMR (400 MHz, CDCl₃) δ 7.76 – 7.72 (m, 2H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 2H), 7.08 – 7.01 (m, 3H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.64 (s, 1H), 4.16 (dd, *J* = 9.8, 4.2 Hz, 1H), 4.00 (t, *J* = 5.5 Hz, 2H), 2.98 – 2.82 (m, 1H), 2.65 – 2.49 (m, 1H), 2.32 (s, 3H), 2.18 (s, 3H), 1.89 (s, 4H), 1.38 (d, *J* = 2.3 Hz, 6H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 176.2, 156.9, 151.3, 136.8 (t, *J* = 26.4 Hz), 136.6, 132.1, 131.5 (q, *J* = 33.2 Hz), 130.5, 129.7, 128.5, 128.4, 128.4, 127.6 – 127.5 (m), 123.7, 123.6 (q, *J* = 273.5 Hz), 122.8, 122.2 – 122.0 (m), 120.9, 120.3 (t, *J* = 246.3 Hz), 119.5, 112.0, 67.8 45.1 (t, *J* = 27.5 Hz), 42.6, 37.2, 30.9 (t, *J* = 3.4 Hz), 25.4, 25.2, 21.5, 15.9.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.78, -96.35 (d, *J* = 249.6 Hz), -97.25 (d, *J* = 249.5 Hz).

HRMS-ESI (*m/z*): [M+Na]⁺ calcd. for C₃₂H₃₂F₅NO₃Na: 596.2200; found 596.2200.

(*R*)-*N*-(4-(1-cyano-3,3-difluoro-3-(3-(trifluoromethyl)phenyl)propyl)phenyl)-4-(*N,N*-dipropylsulfamoyl)benzamide (4af)



The compound **4af** was prepared according to the general procedure employing **1af** (77.4 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5

equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 48 h under argon atmosphere. 51.5 mg, 42% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 3:1, R_f = 0.3, [α]_D²⁵ = 15.4 (c = 1.0 in CHCl₃); 92% ee, determined by HPLC analysis (IC, hexane/*i*-PrOH, 70:30 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t*_R (major) = 20.24 min, *t*_R (minor) = 12.69 min.

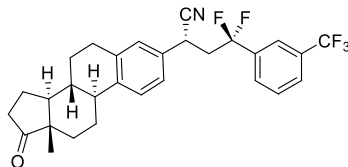
¹H NMR (400 MHz, CDCl₃) δ 8.67 (d, *J* = 7.4 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 2H), 7.79 – 7.67 (m, 7H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 4.15 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.07 (t, *J* = 7.2 Hz, 4H), 2.98 – 2.79 (m, 1H), 2.65 – 2.52 (m, 1H), 1.51 (h, *J* = 7.5 Hz, 4H), 0.86 (t, *J* = 7.4 Hz, 6H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.0, 142.8, 138.7, 138.5, 136.8 (t, *J* = 26.5 Hz), 131.5 (q, *J* = 32.9 Hz), 130.7, 129.7, 128.5 (t, *J* = 6.2 Hz), 128.2, 128.1, 127.6 – 127.5 (m), 127.3, 123.6 (q, *J* = 273.7 Hz), 122.2 – 121.9 (m), 121.2, 120.3 (t, *J* = 246.0 Hz), 119.8, 50.1, 44.9 (t, *J* = 27.4 Hz), 30.9 (t, *J* = 3.4 Hz), 22.0, 11.3.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.78, -96.20 (d, *J* = 249.3 Hz), -97.20 (d, *J* = 249.3 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₃₀H₂₉F₅N₃O₃S: 606.1850; found 606.1853.

(*R*)-4,4-difluoro-2-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)-4-(3-(trifluoromethyl)phenyl)butanenitrile (4ag**)**



Chemical Formula: C₂₉H₂₈F₅NO
Molecular Weight: 501.5410

The compound **4ag** was prepared according to the general procedure employing **1ag** (56.0 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410

nm violet LEDs at room temperature for 48 h under argon atmosphere. 45.1 mg, 45% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 4:1, R_f = 0.3, $[\alpha]_D^{25}$ = 83.8 (c = 1.0 in CHCl_3); 88% ee, >20:1 dr. determined by HPLC analysis (IA, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 26.52 min, t_R (minor) = 25.37 min.

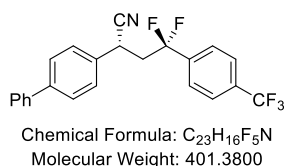
^1H NMR (400 MHz, CDCl_3) δ 7.78 – 7.71 (m, 3H), 7.61 (t, J = 7.9 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.08 (s, 1H), 4.08 (dd, J = 9.8, 4.3 Hz, 1H), 2.98 – 2.84 (m, 3H), 2.66 – 2.57 (m, 1H), 2.53 (dd, J = 18.7, 8.6 Hz, 1H), 2.45 – 2.40 (m, 1H), 2.29 (t, J = 7.5 Hz, 1H), 2.21 – 2.01 (m, 3H), 1.98 (d, J = 8.1 Hz, 1H), 1.71 – 1.40 (m, 6H), 0.93 (s, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 220.6, 140.5, 137.9, 136.9 (t, J = 26.5 Hz), 132.1, 131.4 (q, J = 32.9 Hz), 129.6, 128.4 (t, J = 6.0 Hz), 127.8, 127.4 – 127.3 (m), 126.5, 124.6, 123.6 (q, J = 273.6 Hz), 122.1 – 121.9 (m), 120.3 (t, J = 246.1 Hz), 119.8, 50.5, 48.0, 44.9 (t, J = 27.5 Hz), 44.3, 38.0, 35.9, 31.6, 30.9 (t, J = 3.2 Hz), 29.4, 26.3, 25.7, 21.6, 13.9.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.74, -95.96 (d, J = 249.6 Hz), -97.30 (d, J = 249.6 Hz).

HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{29}\text{H}_{29}\text{F}_5\text{NO}$: 502.2169; found 502.2165.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(4-(trifluoromethyl)phenyl)butanenitrile (4ah)



The compound **4ah** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2b** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-8 (5.2 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 44.3 mg, 54% isolated yield, white solid, mp: 120 – 122 °C, (petroleum ether: ethyl acetate = 10:1, R_f

= 0.3, $[\alpha]_D^{25} = 17.4$ ($c = 1.0$ in CHCl_3); 96% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 98:2 v/v, flow rate 1.0 mL/min, $\lambda = 210$ nm, 25 °C), t_R (major) = 27.32 min, t_R (minor) = 29.15 min.

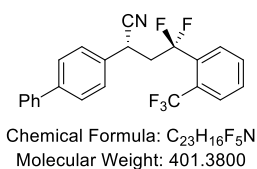
^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 8.3$ Hz, 2H), 7.66 (d, $J = 7.8$ Hz, 2H), 7.62 – 7.56 (m, 4H), 7.45 (t, $J = 7.6$ Hz, 2H), 7.42 – 7.38 (m, 3H), 4.17 (dd, $J = 9.7, 4.4$ Hz, 1H), 3.00 – 2.84 (m, 1H), 2.68 – 2.55 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 141.9, 140.1, 139.4 (t, $J = 26.3$ Hz), 133.7, 133.0 (q, $J = 32.4$ Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 126.0 (q, $J = 3.8$ Hz), 125.7 (t, $J = 6.2$ Hz), 123.7 (q, $J = 273.7$ Hz), 120.4 (t, $J = 246.3$ Hz), 119.7, 45.1 (t, $J = 27.5$ Hz), 31.1 (t, $J = 3.5$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.94, -96.13 (d, $J = 249.8$ Hz), -97.70 (d, $J = 249.8$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{23}\text{H}_{15}\text{F}_5\text{N}$: 400.1125; found 400.1132.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(2-(trifluoromethyl)phenyl)butanenitrile (4ai)



The compound **4ai** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2c** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-8 (5.2 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN} : $\text{V}_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 48.9 mg, 61% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.3$, $[\alpha]_D^{25} = -4.8$ ($c = 1.0$ in CHCl_3); 93% ee, determined by HPLC analysis (IB hexane/*i*-PrOH, 98:2 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 19.10 min, t_R (minor) = 20.67 min.

^1H NMR (400 MHz, CDCl_3) δ 7.83 (d, $J = 8.0$ Hz, 1H), 7.75 (d, $J = 8.1$ Hz, 1H), 7.68 (d, $J = 8.0$ Hz, 1H), 7.60 – 7.57 (m, 5H), 7.45 (d, $J = 7.9$ Hz, 4H), 7.38 (t, $J = 7.5$ Hz,

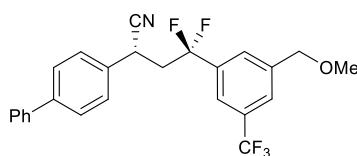
1H), 4.28 (d, $J = 8.8$ Hz, 1H), 3.01 – 2.86 (m, 1H), 2.76 – 2.63 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 141.7, 140.2, 134.4 (t, $J = 28.0$ Hz), 133.9, 132.4, 130.8, 129.0, 128.2, 128.1 (t, $J = 9.4$ Hz), 128.0 (q, $J = 6.0$ Hz), 127.9, 127.8, 127.2, 123.6 (q, $J = 274.4$ Hz), 120.5 (t, $J = 248.0$ Hz), 119.8, 45.7 (t, $J = 26.6$ Hz), 31.0 (t, $J = 3.2$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -57.65 (t, $J = 14.3$ Hz, 1H), -92.87 (dq, $J = 252.6$, 13.9 Hz), -94.39 (dq, $J = 252.7$, 17.4 Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{23}\text{H}_{15}\text{F}_5\text{N}$: 400.1125; found 400.1130.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(methoxymethyl)-5-(trifluoromethyl)phenyl)butanenitrile (4aj)



Chemical Formula: $\text{C}_{25}\text{H}_{20}\text{F}_5\text{NO}$
Molecular Weight: 445.4330

The compound **4aj** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2d** (103.2 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $\text{V}_{\text{MeCN}}: \text{V}_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 55.2 mg, 62% isolated yield, white solid, mp: 50 – 52 °C, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.3$, $[\alpha]_D^{25} = 4.7$ ($c = 1.0$ in CHCl_3); 90% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 11.04 min, t_R (minor) = 9.14 min.

^1H NMR (400 MHz, CDCl_3) δ 7.70 (s, 1H), 7.68 (s, 2H), 7.60 (d, $J = 8.2$ Hz, 2H), 7.56 (d, $J = 7.5$ Hz, 2H), 7.46 (t, $J = 7.5$ Hz, 2H), 7.40 (dd, $J = 11.0$, 7.7 Hz, 3H), 4.53 (s, 2H), 4.20 (dd, $J = 9.6$, 4.4 Hz, 1H), 3.45 (s, 3H), 3.00 – 2.86 (m, 1H), 2.69 – 2.56 (m, 1H).

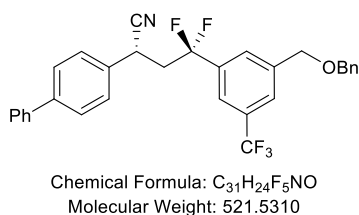
$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 141.9, 141.0, 140.1, 137.1 (t, $J = 26.6$ Hz), 133.7, 131.7 (q, $J = 33.1$ Hz), 129.1, 128.2, 127.9, 127.8, 127.3, 127.1 (t, $J = 5.8$ Hz), 126.2 –

126.1 (m), 123.6 (q, $J = 273.8$ Hz), 121.3 – 121.1 (m), 120.3 (t, $J = 246.3$ Hz), 119.7, 73.4, 58.8, 45.1 (t, $J = 27.5$ Hz), 31.1 (t, $J = 3.5$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.72, -95.98 (d, $J = 249.2$ Hz), -97.30 (d, $J = 249.3$ Hz).

HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{25}\text{H}_{20}\text{F}_5\text{NONa}$: 468.1363; found 468.1353.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4-(3-((benzyloxy)methyl)-5-(trifluoromethyl)phenyl)-4,4-difluorobutanenitrile (4ak)



The compound **4ak** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2e** (133.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 49.8 mg, 48% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.3$, $[\alpha]_D^{25} = 8.3$ ($c = 1.0$ in CHCl_3); 91% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 14.02 min, t_R (minor) = 11.85 min.

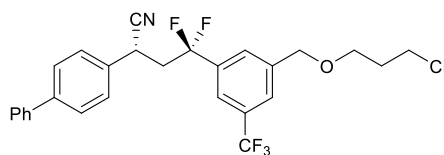
^1H NMR (400 MHz, CDCl_3) δ 7.72 (s, 1H), 7.69 (s, 2H), 7.61 – 7.56 (m, 4H), 7.46 (t, $J = 7.5$ Hz, 2H), 7.41 – 7.36 (m, 7H), 7.35 – 7.31 (m, 1H), 4.62 (d, $J = 4.3$ Hz, 4H), 4.19 (dd, $J = 9.6, 4.4$ Hz, 1H), 2.99 – 2.85 (m, 1H), 2.68 – 2.55 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 141.8, 141.0, 140.1, 137.5, 137.1 (t, $J = 26.5$ Hz), 133.6, 131.7 (q, $J = 33.0$ Hz), 129.0, 128.7, 128.2, 128.2, 128.0, 127.9, 127.8, 127.2, 126.3 – 126.2 (m), 123.6 (q, $J = 273.9$ Hz), 121.3 – 121.1 (m), 120.3 (t, $J = 246.7$ Hz), 119.7, 73.1, 70.8, 45.0 (t, $J = 27.4$ Hz), 31.1 (t, $J = 3.3$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.69, -95.83 (dd, $J = 249.3, 3.3$ Hz), -97.25 (d, $J = 249.4$ Hz).

HRMS-ESI (m/z): $[M+Na]^+$ calcd. for $C_{31}H_{24}F_5NONa$: 544.1676; found 544.1677.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4-(3-((3-chloropropoxy)methyl)-5-(trifluoromethyl)phenyl)-4,4-difluorobutanenitrile (4al)



Chemical Formula: $C_{27}H_{23}ClF_5NO$
Molecular Weight: 507.9290

The compound **4al** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2f** (128.0 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[Cu(MeCN)_4]PF_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{MeCN}: V_{DMF} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 53.8 mg, 53% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, $R_f = 0.3$, $[\alpha]_D^{25} = -0.8$ ($c = 1.0$ in $CHCl_3$); 88% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 13.75 min, t_R (minor) = 11.40 min.

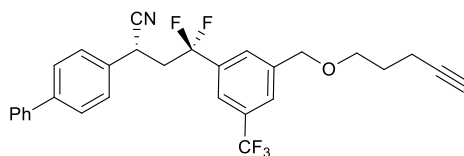
1H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.67 (m, 3H), 7.63 – 7.58 (m, 2H), 7.56 (d, $J = 7.6$ Hz, 2H), 7.48 – 7.38 (m, 5H), 4.60 (s, 2H), 4.20 (dd, $J = 9.7, 4.4$ Hz, 1H), 3.68 (q, $J = 7.1$ Hz, 4H), 3.00 – 2.86 (m, 1H), 2.69 – 2.56 (m, 1H), 2.09 (p, $J = 6.1$ Hz, 2H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 141.8, 141.0, 140.1, 137.1 (t, $J = 26.6$ Hz), 133.6, 131.7 (q, $J = 33.1$ Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 127.0 (t, $J = 6.1$ Hz), 126.2 – 125.9 (m), 123.6 (q, $J = 273.8$ Hz), 121.3 – 121.1 (m), 120.3 (t, $J = 246.3$ Hz), 119.7, 71.5, 67.4, 45.0 (t, $J = 27.4$ Hz), 41.9, 32.6, 31.1 (t, $J = 3.2$ Hz).

$^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -62.67, -95.91 (d, $J = 249.2$ Hz), -97.25 (d, $J = 249.3$ Hz).

HRMS-ESI (m/z): $[M+Na]^+$ calcd. for $C_{27}H_{23}ClF_5NONa$: 530.1286; found 530.1283.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-((pent-4-yn-1-yloxy)methyl)-5-(trifluoromethyl)phenyl)butanenitrile (4am)



Chemical Formula: C₂₉H₂₄F₅NO
Molecular Weight: 497.5090

The compound **4am** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2g** (124.0 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 64.7 mg, 65% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 12:1, R_f = 0.3, [α]_D²⁵ = 6.6 (c = 1.0 in CHCl₃); 91% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 12.32 min, t_R (minor) = 10.40 min.

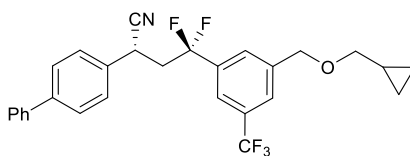
¹H NMR (400 MHz, CDCl₃) δ 7.71 (s, 1H), 7.68 (s, 2H), 7.62 – 7.56 (m, 4H), 7.48 – 7.36 (m, 5H), 4.59 (s, 2H), 4.20 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.64 (t, *J* = 6.1 Hz, 2H), 3.00 – 2.87 (m, 1H), 2.70 – 2.57 (m, 1H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.95 (s, 1H), 1.87 (p, *J* = 6.6 Hz, 2H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 141.8, 141.2, 140.1, 137.0 (t, *J* = 26.5 Hz), 133.6, 131.6 (q, *J* = 33.2 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 127.0 (t, *J* = 5.9 Hz), 126.3 – 125.9 (m), 123.6 (q, *J* = 273.7 Hz), 121.4 – 120.8 (m), 120.3 (t, *J* = 246.3 Hz), 119.7, 83.7, 71.7, 69.4, 68.9, 45.0 (t, *J* = 27.4 Hz), 31.1 (t, *J* = 3.3 Hz), 28.5, 15.4.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.68, -95.82 (d, *J* = 253.3 Hz), -97.30 (d, *J* = 249.3 Hz).

HRMS-ESI (*m/z*): [M+Na]⁺ calcd. for C₂₉H₂₄F₅NONa: 520.1676; found 520.1678.

(R)-2-([1,1'-biphenyl]-4-yl)-4-(3-((cyclopropylmethoxy)methyl)-5-(trifluoromethyl)phenyl)-4,4-difluorobutanenitrile (4an)



Chemical Formula: C₂₈H₂₄F₅NO
Molecular Weight: 485.4980

The compound **4an** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2h** (119.2 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 36.9 mg, 38% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 4:1, R_f = 0.3, [α]_D²⁵ = 11.0 (c = 1.0 in CHCl₃); 94% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 11.13 min, t_R (minor) = 10.03 min.

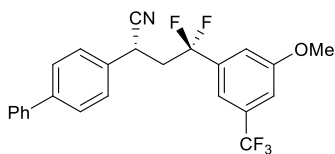
¹H NMR (400 MHz, CDCl₃) δ 7.72 (s, 1H), 7.68 (d, *J* = 9.5 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 7.0 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.43 – 7.37 (m, 3H), 4.61 (s, 2H), 4.20 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.38 (d, *J* = 6.9 Hz, 2H), 3.01 – 2.85 (m, 1H), 2.69 – 2.56 (m, 1H), 1.17 – 1.06 (m, 1H), 0.59 (dt, *J* = 8.0, 5.2 Hz, 2H), 0.24 (dt, *J* = 6.0, 4.6 Hz, 2H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 141.9, 141.4, 140.1, 137.1 (t, *J* = 26.5 Hz), 133.7, 131.7 (q, *J* = 33.2 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 126.3 – 126.2 (m), 123.7 (q, *J* = 273.6 Hz), 121.2 – 120.3 (m), 120.4 (t, *J* = 245.8 Hz), 119.7, 75.9, 71.3, 45.1 (t, *J* = 27.5 Hz), 31.1 (t, *J* = 3.4 Hz), 10.7, 3.3.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.70, -95.90 (d, *J* = 249.1 Hz), -97.32 (d, *J* = 249.1 Hz).

HRMS-ESI (*m/z*): [M+Na]⁺ calcd. for C₂₈H₂₄F₅NONa: 508.1676; found 508.1673.

(R)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-methoxy-5-(trifluoromethyl)phenyl)butanenitrile (4ao)



Chemical Formula: C₂₄H₁₈F₅NO
Molecular Weight: 431.4060

The compound **4ao** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2i** (97.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 49.1 mg, 57% isolated yield, white solid, mp: 60 – 62 °C, (petroleum ether: ethyl acetate = 8:1, R_f = 0.3, [α]_D²⁵ = 4.9 (c = 1.0 in CHCl₃); 90% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 12.81 min, t_R (minor) = 10.29 min.

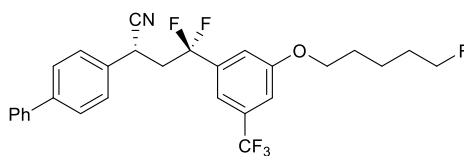
¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, *J* = 7.9 Hz, 2H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.42 – 7.36 (m, 3H), 7.32 (s, 1H), 7.20 (s, 2H), 4.17 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.88 (s, 3H), 2.98 – 2.84 (m, 1H), 2.67 – 2.54 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 160.3, 141.9, 140.1, 138.3 (t, *J* = 26.6 Hz), 133.7, 132.9 (q, *J* = 33.1 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 123.5 (q, *J* = 273.8 Hz), 120.2 (t, *J* = 246.4 Hz), 119.7, 114.4 (t, *J* = 6.2 Hz), 114.1 – 113.9 (m), 113.1 – 112.9 (m), 56.0, 45.0 (t, *J* = 27.6 Hz), 31.2 (t, *J* = 3.4 Hz), 29.9.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.87, -95.82 (d, *J* = 248.7 Hz), -97.42 (d, *J* = 248.6 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₄H₁₇F₅NO: 430.1230; found 430.1232.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-((5-fluoropentyl)oxy)-5-(trifluoromethyl)phenyl)butanenitrile (4ap)



Chemical Formula: C₂₈H₂₅F₆NO
Molecular Weight: 505.5044

The compound **4ap** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2j** (127.2 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 64.5 mg, 64% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, R_f = 0.3, [α]_D²⁵ = 7.5 (c = 1.0 in CHCl₃); 91% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 13.71 min, t_R (minor) = 11.46 min.

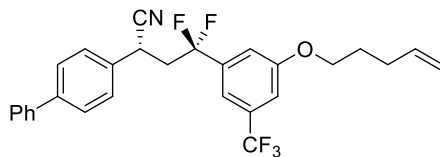
¹H NMR (400 MHz, CDCl₃) δ 7.64 – 7.55 (m, 4H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.43 – 7.36 (m, 3H), 7.33 (s, 1H), 7.20 (s, 2H), 4.55 (t, *J* = 6.0 Hz, 1H), 4.43 (t, *J* = 5.9 Hz, 1H), 4.17 (dd, *J* = 9.5, 4.4 Hz, 1H), 4.03 (t, *J* = 6.3 Hz, 2H), 3.01 – 2.83 (m, 1H), 2.61 (m, 1H), 1.91 – 1.71 (m, 4H), 1.56 – 1.50 (m, 2H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 159.8, 141.8, 140.1, 138.3 (t, *J* = 26.5 Hz), 133.7, 132.8 (q, *J* = 33.0 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 123.5 (q, *J* = 273.7 Hz), 120.2 (t, *J* = 246.5 Hz), 119.7, 114.8 (t, *J* = 6.5 Hz), 114.0 – 113.8 (m), 113.4 – 113.3 (m), 84.0 (d, *J* = 165.2 Hz), 68.5, 45.0 (t, *J* = 27.6 Hz), 31.2 (t, *J* = 3.4 Hz), 30.2 (d, *J* = 19.6 Hz), 28.8, 22.1 (d, *J* = 5.1 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.84, -95.62 (d, *J* = 249.0 Hz), -97.41 (d, *J* = 248.7 Hz), -218.57 (m).

HRMS-ESI (*m/z*): [M+Na]⁺ calcd. for C₂₈H₂₅F₆NONa: 528.1738; found 528.1735.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(pent-4-en-1-yloxy)-5-(trifluoromethyl)phenyl)butanenitrile (4aq**)**



Chemical Formula: C₂₈H₂₄F₅NO
Molecular Weight: 485.4980

The compound **4aq** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2k** (159.2 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 57.8 mg, 60% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 15:1, R_f = 0.3, [α]_D²⁵ = 9.2 (c = 1.0 in CHCl₃); 91% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t*_R (major) = 8.79 min, *t*_R (minor) = 7.64 min.

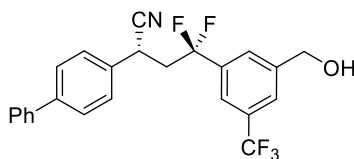
¹H NMR (400 MHz, CDCl₃) δ 7.62 – 7.56 (m, 4H), 7.48 – 7.36 (m, 5H), 7.32 (s, 1H), 7.21 (s, 2H), 5.91 – 5.81 (m, 1H), 5.09 (d, *J* = 17.0 Hz, 1H), 5.04 (d, *J* = 10.3 Hz, 1H), 4.18 (dd, *J* = 9.7, 4.4 Hz, 1H), 4.03 (t, *J* = 6.3 Hz, 2H), 2.99 – 2.85 (m, 1H), 2.68 – 2.55 (m, 1H), 2.26 (q, *J* = 7.3 Hz, 2H), 1.92 (p, *J* = 6.9 Hz, 2H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 159.8, 141.8, 140.1, 138.3 (t, *J* = 26.5 Hz), 137.5, 133.7, 132.8 (q, *J* = 32.9 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 123.5 (q, *J* = 273.8 Hz), 120.2 (t, *J* = 246.7 Hz), 119.7, 115.7, 114.8 (t, *J* = 6.2 Hz), 114.0 – 113.7 (m), 113.5 – 113.3 (m), 68.0, 45.0 (t, *J* = 27.6 Hz), 31.2 (t, *J* = 3.6 Hz), 30.0, 28.3.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.83, -95.64 (d, *J* = 248.6 Hz), -97.44 (d, *J* = 248.5 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₈H₂₃F₅NO: 484.1700; found 484.1706.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(hydroxymethyl)-5-(trifluoromethyl)phenyl)butanenitrile (4ar)



Chemical Formula: C₂₄H₁₈F₅NO
Molecular Weight: 431.4060

The compound **4ar** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2l** (97.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 53.3 mg, 62% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 4:1, R_f = 0.3, [α]_D²⁵ = 8.5 (c = 1.0 in CHCl₃); 89% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 16.91 min, t_R (minor) = 15.21 min.

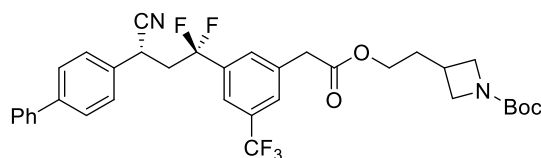
¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, *J* = 7.9 Hz, 2H), 7.68 (s, 1H), 7.59 (d, *J* = 7.9 Hz, 2H), 7.56 (d, *J* = 7.5 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.47 – 7.36 (m, 3H), 4.80 (s, 2H), 4.19 (dd, *J* = 9.7, 4.3 Hz, 1H), 3.00 – 2.86 (m, 1H), 2.70 – 2.60 (m, 1H), 2.13 (s, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 143.2, 141.9, 140.1, 137.1 (t, *J* = 26.5 Hz), 133.6, 131.8 (q, *J* = 32.8 Hz), 129.1, 128.2, 128.0, 127.8, 127.2, 126.6 (t, *J* = 5.6 Hz), 125.6 – 125.5 (m), 123.6 (q, *J* = 273.8 Hz), 121.2 – 120.7 (m), 120.3 (t, *J* = 246.4 Hz), 119.7, 64.0, 45.0 (t, *J* = 27.6 Hz), 31.1 (t, *J* = 3.6 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.72, -95.64 (d, *J* = 246.3 Hz), -97.44 (d, *J* = 246.3 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₄H₁₇F₅NO: 430.1230; found 430.1239.

***tert*-butyl (*R*)-3-(2-(2-(3-(3-([1,1'-biphenyl]-4-yl)-3-cyano-1,1-difluoropropyl)-5-(trifluoromethyl)phenyl)acetoxy)ethyl)azetidine-1-carboxylate (4as)**



Chemical Formula: $C_{35}H_{35}F_5N_2O_4$
Molecular Weight: 642.6670

The compound **4as** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2m** (182.1 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[Cu(MeCN)_4]PF_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{MeCN}: V_{DMF} = 3:1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 52.4 mg, 41% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 5:1, $R_f = 0.3$, $[\alpha]_D^{25} = 5.1$ ($c = 1.0$ in $CHCl_3$); 90% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 18.49 min, t_R (minor) = 15.01 min.

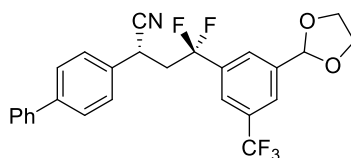
1H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.64 (d, $J = 4.7$ Hz, 2H), 7.61 – 7.55 (m, 4H), 7.48 – 7.39 (m, 4H), 7.39 – 7.34 (m, 1H), 4.19 (dd, $J = 9.6, 4.4$ Hz, 1H), 4.11 (t, $J = 6.4$ Hz, 2H), 4.00 (t, $J = 8.4$ Hz, 2H), 3.71 (s, 2H), 3.57 (dd, $J = 8.6, 5.5$ Hz, 2H), 3.00 – 2.86 (m, 1H), 2.71 – 2.50 (m, 2H), 1.93 (q, $J = 6.7$ Hz, 2H), 1.43 (s, 9H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.2, 156.4, 141.9, 140.1, 137.3 (t, $J = 26.4$ Hz), 136.0, 133.6, 131.9 (q, $J = 33.0$ Hz), 129.5 (t, $J = 6.1$ Hz), 129.0, 128.5 – 128.3 (m), 128.2, 127.9, 127.8, 127.2, 123.5 (q, $J = 271.2$ Hz), 121.2 – 120.9 (m), 120.2 (t, $J = 246.6$ Hz), 119.6, 79.5, 63.5, 54.4, 45.0 (t, $J = 27.5$ Hz), 40.7, 33.2, 31.1 (t, $J = 3.3$ Hz), 28.2, 26.3.

$^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -62.70, -95.53 (d, $J = 4.2$ Hz), -97.22 (d, $J = 249.6$ Hz).

HRMS-ESI (m/z): $[M+Na]^+$ calcd. for $C_{35}H_{35}F_5N_2O_4Na$: 665.2415; found 665.2416.

(*R*)-4-(3-(1,3-dioxolan-2-yl)-5-(trifluoromethyl)phenyl)-2-([1,1'-biphenyl]-4-yl)-4,4-difluorobutanenitrile (4at**)**



Chemical Formula: $C_{26}H_{20}F_5NO_2$
Molecular Weight: 473.4430

The compound **4at** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2n** (114.4 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[Cu(MeCN)_4]PF_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{MeCN}: V_{DMF} = 3:1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 37.8 mg, 40% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 4:1, $R_f = 0.3$, $[\alpha]_D^{25} = 9.2$ ($c = 1.0$ in $CHCl_3$); 90% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 13.13 min, t_R (minor) = 9.79 min.

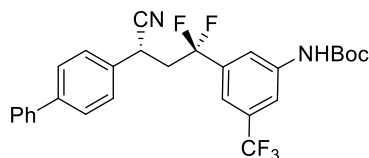
1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, $J = 11.9$ Hz, 2H), 7.76 (s, 1H), 7.62 – 7.56 (m, 4H), 7.48 – 7.36 (m, 5H), 5.87 (s, 1H), 4.21 (dd, $J = 9.7, 4.3$ Hz, 1H), 4.18 – 4.03 (m, 4H), 3.00 – 2.86 (m, 1H), 2.69 – 2.55 (m, 1H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 141.9, 140.7, 140.1, 137.2 (t, $J = 26.8$ Hz), 133.6, 131.8 (q, 33.4 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 126.6 (t, $J = 7.0$ Hz), 125.8 – 125.7 (m), 123.5 (q, $J = 275.7$ Hz), 122.8 – 122.6 (m), 120.2 (t, $J = 246.6$), 119.7, 102.20, 65.6, 45.0 (t, $J = 27.3$ Hz), 31.0 (t, $J = 3.1$ Hz).

$^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -62.70, -96.02 (d, $J = 249.4$ Hz), -97.55 (d, $J = 249.4$ Hz).

HRMS-ESI (m/z): $[M+H]^+$ calcd. for $C_{26}H_{21}F_5NO_2$: 474.1492; found 474.1490.

***tert*-butyl (R)-(3-(3-([1,1'-biphenyl]-4-yl)-3-cyano-1,1-difluoropropyl)-5-(trifluoromethyl)phenyl)carbamate (4au)**



Chemical Formula: $C_{28}H_{25}F_5N_2O_2$
Molecular Weight: 516.5120

The compound **4au** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2o** (131.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 68.1 mg, 66% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 2:1, R_f = 0.2, [α]_D²⁵ = 3.9 (c = 1.0 in CHCl₃); 90% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 8.24 min, t_R (minor) = 7.04 min.

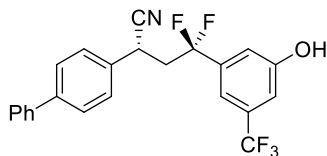
¹H NMR (400 MHz, CDCl₃) δ 7.76 (s, 2H), 7.60 – 7.55 (m, 4H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.41 – 7.36 (m, 4H), 6.84 (s, 1H), 4.17 (dd, *J* = 9.8, 4.3 Hz, 1H), 2.98 – 2.84 (m, 1H), 2.68 – 2.55 (m, 1H), 1.53 (s, 9H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 152.3, 141.8, 140.1, 140.0, 137.7 (t, *J* = 26.7 Hz), 133.6, 132.3 (q, *J* = 32.9 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 123.4 (q, *J* = 274.1 Hz), 120.2 (t, *J* = 246.2 Hz), 119.7, 117.8 (t, *J* = 8.2 Hz), 117.1 – 116.8 (m), 116.1 – 115.8 (m), 81.9, 44.9 (t, *J* = 27.3 Hz), 31.1 (d, *J* = 3.4 Hz), 28.3.

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.89, -95.69 (d, *J* = 248.8 Hz), -97.57 (d, *J* = 248.7 Hz).

HRMS-ESI (*m/z*): [M+Na]⁺ calcd. for C₂₈H₂₅F₅N₂O₂Na: 539.1734; found 539.1733.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-hydroxy-5-(trifluoromethyl)phenyl)butanenitrile (4av)



Chemical Formula: C₂₃H₁₆F₅NO
Molecular Weight: 417.3790

The compound **4av** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2p** (92.0 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410

nm violet LEDs at room temperature for 40 h under argon atmosphere. 38.4 mg, 46% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 3:1, R_f = 0.3, $[\alpha]_D^{25}$ = 6.2 (c = 1.0 in CHCl_3); 91% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 97:3 v/v, flow rate 0.8 mL/min, λ = 254 nm, 25 °C), t_R (major) = 37.00 min, t_R (minor) = 35.24 min.

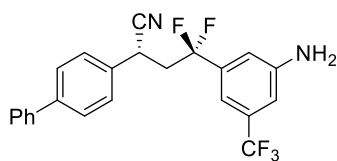
^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 7.1 Hz, 2H), 7.46 (dd, J = 8.4, 6.6 Hz, 2H), 7.40 (dd, J = 7.7, 5.8 Hz, 3H), 7.29 (s, 1H), 7.19 (d, J = 7.2 Hz, 2H), 6.34 (s, 1H), 4.20 (dd, J = 9.9, 4.2 Hz, 1H), 2.97 – 2.84 (m, 1H), 2.67 – 2.54 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 156.9, 142.0, 140.1, 138.4 (t, J = 26.6 Hz), 133.3, 133.0 (q, J = 33.2 Hz), 129.1, 128.3, 128.0, 127.8, 127.2, 123.4 (q, J = 273.7 Hz), 120.1 (t, J = 246.6 Hz), 119.8, 115.6 (t, J = 6.0 Hz), 114.9 – 114.8 (m), 114.0 – 113.8 (m), 44.9 (t, J = 27.6 Hz), 31.1 (t, J = 3.4 Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.92, -96.02 (d, J = 248.3 Hz), -97.44 (d, J = 248.5 Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{23}\text{H}_{15}\text{F}_5\text{NO}$: 416.1074; found 416.1081.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4-(3-amino-5-(trifluoromethyl)phenyl)-4,4-difluorobutanenitrile (4aw)



Chemical Formula: $\text{C}_{23}\text{H}_{17}\text{F}_5\text{N}_2$
Molecular Weight: 416.3950

The compound **4aw** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2q** (91.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 40 h under argon atmosphere. 40.8 mg, 49% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 3:1, R_f = 0.3, $[\alpha]_D^{25}$ = 15.5 (c = 1.0 in CHCl_3); 92% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 80:20

v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 14.67 min, t_R (minor) = 12.12 min.

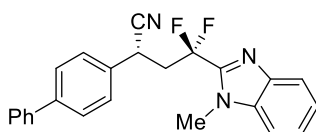
^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 7.9 Hz, 2H), 7.57 (d, J = 8.3 Hz, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.40 (d, J = 7.6 Hz, 3H), 7.09 (s, 1H), 6.97 (s, 2H), 4.14 (dd, J = 9.8, 4.3 Hz, 1H), 3.80 (brs, 2H), 2.96 – 2.82 (m, 1H), 2.64 – 2.51 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 147.3, 141.8, 140.1, 137.9 (t, J = 26.4 Hz), 133.7, 132.6 (q, J = 32.8 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 123.7 (q, J = 274.2 Hz), 120.4 (t, J = 246.2 Hz), 119.8, 114.2 (t, J = 6.2 Hz), 113.4 – 113.2 (m), 111.6 – 111.3 (m), 45.0 (t, J = 27.7 Hz), 31.2 (t, J = 3.4 Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -63.06, -95.85 (d, J = 247.5 Hz), -97.86 (d, J = 247.7 Hz).

HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{23}\text{H}_{18}\text{F}_5\text{N}_2$: 417.1390; found 417.1391.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(1-methyl-1H-benzo[d]imidazol-2-yl)butanenitrile (4ax)



Chemical Formula: $\text{C}_{24}\text{H}_{19}\text{F}_2\text{N}_3$
Molecular Weight: 387.4338

The compound **4ax** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2r** (80.0 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (7.5 mg, 10 mol%), and **L1** (8.6 mg, 12 mol%) in $V_{\text{MeCN}}:V_{\text{DMF}} = 3:1$ [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 25.6 mg, 33% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 3:1, R_f = 0.3, $[\alpha]_D^{25} = -35.77$ (c = 1.0 in CHCl_3); 83% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 23.51 min, t_R (minor) = 21.81 min.

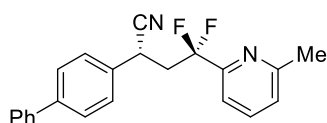
^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, J = 8.0 Hz, 1H), 7.66 (s, 1H), 7.65 (d, J = 2.1 Hz, 1H), 7.60 (d, J = 1.9 Hz, 2H), 7.59 (dt, J = 3.2, 1.8 Hz, 2H), 7.49 – 7.44 (m, 4H), 7.41 – 7.34 (m, 2H), 4.66 (dd, J = 8.2, 6.2 Hz, 1H), 4.01 (s, 3H), 3.35 – 3.25 (m, 2H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 145.3 (t, $J = 30.4$ Hz), 141.7, 141.1, 140.3, 136.4, 134.1, 129.0, 128.2, 128.0, 127.8, 127.3, 125.0, 123.4, 121.0, 120.1, 117.9 (t, $J = 240.6$ Hz), 110.2, 41.7 (t, $J = 23.0$ Hz), 31.3 (t, $J = 3.9$ Hz), 31.2 (t, $J = 3.9$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -90.22 (d, $J = 284.3$ Hz), -94.44 (d, $J = 284.3$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{24}\text{H}_{18}\text{F}_2\text{N}_3$: 386.1469; found 386.1472.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(6-methylpyridin-2-yl)butanenitrile (4ay)



Chemical Formula: $\text{C}_{22}\text{H}_{18}\text{F}_2\text{N}_2$
Molecular Weight: 348.3968

The compound **4ay** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2s** (64.4 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (7.5 mg, 10 mol%), and **L1** (8.6 mg, 12 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 23.0 mg, 33% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 4:1, $R_f = 0.3$, $[\alpha]_D^{25} = -3.5$ ($c = 1.0$ in CHCl_3); 87% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 10.53 min, t_R (minor) = 8.77 min.

^1H NMR (400 MHz, CDCl_3) δ 7.71 (t, $J = 8.1$ Hz, 1H), 7.61 – 7.58 (m, 4H), 7.52 (d, $J = 7.9$ Hz, 1H), 7.48 – 7.44 (m, 4H), 7.39 – 7.35 (m, 1H), 7.24 (d, $J = 7.5$ Hz, 1H), 4.24 (dd, $J = 9.9, 4.7$ Hz, 1H), 3.17 – 3.05 (m, 1H), 3.03 – 2.88 (m, 1H), 2.58 (s, 3H).

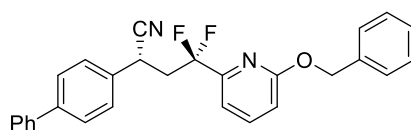
$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 158.8, 152.7 (t, $J = 28.5$ Hz), 141.5, 140.3, 137.6, 134.3, 129.0, 128.0, 127.9, 127.8, 127.2, 125.1, 120.1, 119.8 (t, $J = 243.8$ Hz), 117.3 (t, $J = 4.4$ Hz), 41.9 (t, $J = 25.7$ Hz), 31.2 (d, $J = 4.8$ Hz), 24.5.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -96.59 (d, $J = 259.0$ Hz), -97.90 (d, $J = 259.0$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{22}\text{H}_{17}\text{F}_2\text{N}_2$: 347.1360; found 347.1367.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4-(6-(benzyloxy)pyridin-2-yl)-4,4-

difluorobutanenitrile (**4az**)



Chemical Formula: C₂₈H₂₂F₂N₂O

Molecular Weight: 440.4938

The compound **4az** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2t** (70.8 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (7.5 mg, 10 mol%), and **L1** (8.6 mg, 12 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 34.2 mg, 39% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 3:1, R_f = 0.3, [α]_D²⁵ = -16.5 (c = 1.0 in CHCl₃); 92% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 210 nm, 25 °C), t_R (major) = 17.05 min, t_R (minor) = 14.45 min.

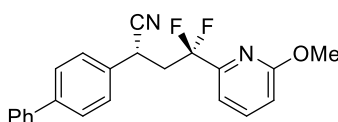
¹H NMR (400 MHz, CDCl₃) δ 7.67 (t, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 4H), 7.48 – 7.39 (m, 4H), 7.39 – 7.26 (m, 6H), 7.24 (s, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 5.36 (s, 2H), 4.09 (dd, *J* = 9.5, 4.9 Hz, 1H), 3.11 – 2.92 (m, 1H), 2.87 – 2.76 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 163.2, 150.4 (t, *J* = 28.9 Hz), 141.6, 140.23, 139.8, 137.1, 134.1, 129.0, 128.7, 128.1, 128.0, 127.9, 127.9, 127.2, 120.0, 119.5 (t, *J* = 244.2 Hz), 113.6, 113.2 (t, *J* = 4.8 Hz), 68.1, 41.7 (t, *J* = 26.1 Hz), 31.1 (t, *J* = 4.3 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -96.91 (d, *J* = 256.5 Hz), -98.69 (d, *J* = 256.6 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₈H₂₁F₂N₂O: 439.1622; found 439.1612.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(6-methoxypyridin-2-yl)butanenitrile (**4ba**)



Chemical Formula: C₂₂H₁₈F₂N₂O

Molecular Weight: 364.3958

The compound **4ba** was prepared according to the general procedure employing **1a**

(36.1 mg, 0.2 mmol), **2u** (101.2 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (7.5 mg, 10 mol%), and **L1** (8.6 mg, 12 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 29.5 mg, 41% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 10:1, *R_f* = 0.3, [α]_D²⁵ = -23.5 (c = 1.0 in CHCl₃); 90% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 93:7 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major) = 13.23 min, *t_R* (minor) = 10.80 min.

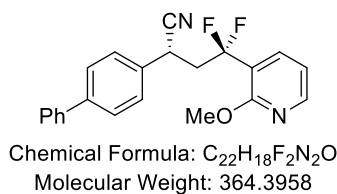
¹H NMR (400 MHz, CDCl₃) δ 7.68 (t, *J* = 7.9 Hz, 1H), 7.58 (t, *J* = 8.4 Hz, 4H), 7.48 – 7.39 (m, 4H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.29 (d, *J* = 7.3 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 4.18 (dd, *J* = 9.5, 4.8 Hz, 1H), 3.95 (s, 3H), 3.19 – 3.08 (m, 1H), 2.99 – 2.86 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 163.9, 150.5 (t, *J* = 28.9 Hz), 141.6, 140.3, 139.7, 134.2, 129.0, 128.1, 127.9, 127.9, 127.2, 120.0, 119.6 (t, *J* = 244.2 Hz), 113.3, 113.0 (t, *J* = 4.9 Hz), 53.8, 41.7 (t, *J* = 25.9 Hz), 31.2 (t, *J* = 4.4 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -96.42 (d, *J* = 257.8 Hz), -98.29 (d, *J* = 257.6 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₂H₁₇F₂N₂O: 363.1309; found 363.1311.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(2-methoxypyridin-3-yl)butanenitrile (4bb)



The compound **4bb** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2v** (70.8 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (7.5 mg, 10 mol%), and **L1** (8.6 mg, 12 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. 31.8 mg, 44% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 3:1, *R_f* = 0.3, [α]_D²⁵ = -5.6 (c = 1.0 in CHCl₃); 89% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major) = 12.21 min, *t_R* (minor)

= 10.66 min.

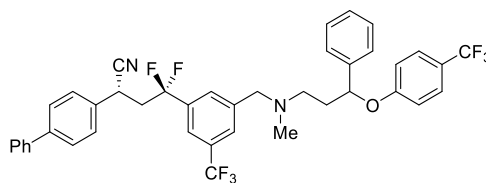
¹H NMR (400 MHz, CDCl₃) δ 8.25 (dd, *J* = 5.0, 1.7 Hz, 1H), 7.85 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.58 – 7.55 (m, 4H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.40 – 7.34 (m, 3H), 6.97 (dd, *J* = 7.5, 5.0 Hz, 1H), 4.05 (dd, *J* = 9.5, 4.9 Hz, 1H), 4.01 (s, 3H), 3.18 – 3.04 (m, 1H), 3.00 – 2.88 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 160.5, 149.3, 141.4, 140.2, 136.1 (t, *J* = 8.2 Hz), 133.8, 129.0, 128.0, 127.9, 127.8, 127.2, 119.9, 119.7 (t, *J* = 245.3 Hz), 117.7 (t, *J* = 26.7 Hz), 116.7, 54.0, 42.2 (t, *J* = 27.1 Hz), 31.4 (t, *J* = 4.3 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -94.90 (d, *J* = 253.5 Hz), -96.03 (d, *J* = 253.7 Hz).

HRMS-ESI (*m/z*): [M-H][−] calcd. for C₂₂H₁₇F₂N₂O: 363.1309; found 363.1303.

(2*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-((methyl(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)amino)methyl)-5-(trifluoromethyl)phenyl)butanenitrile (4bc)



Chemical Formula: C₄₁H₃₄F₈N₂O
Molecular Weight: 722.7232

The compound **4bc** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2w** (214.1 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 48 h under argon atmosphere. 78 mg, 54% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 4:1, *R_f* = 0.3, [*α*]_D²⁵ = -1.6 (c = 1.0 in CHCl₃); 84% ee, 1:1 dr. determined by HPLC analysis (IA, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major-1) = 10.18 min, *t_R* (minor-1) = 9.68 min; *t_R* (major-2) = 11.48 min, *t_R* (minor-2) = 8.78 min.

¹H NMR (400 MHz, CDCl₃) δ 7.57 (s, 1H), 7.55 (s, 1H), 7.50 (d, *J* = 8.2 Hz, 3H), 7.48 – 7.44 (m, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.33 – 7.27 (m, 5H), 7.21 (d, *J* = 5.6 Hz, 4H), 7.18 – 7.13 (m, 1H), 6.75 (d, *J* = 6.4 Hz, 2H), 5.16 (dd, *J* = 10.8, 4.6 Hz, 1H), 4.08 (dt,

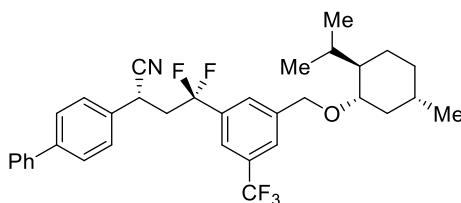
$J = 9.6, 4.0$ Hz, 1H), 3.47 (t, $J = 3.0$ Hz, 2H), 2.89 – 2.70 (m, 1H), 2.61 – 2.40 (m, 3H), 2.14 – 2.01 (m, 4H), 1.98 – 1.90 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 160.6, 141.9, 141.1, 140.1, 136.9 (t, $J = 26.3$ Hz), 133.7, 131.6 (q, $J = 32.8$ Hz), 129.0, 128.9, 128.8 – 128.6 (m), 128.2, 128.0, 127.8, 127.7, 127.2, 126.9 (q, $J = 3.7$ Hz), 125.9, 124.5 (q, $J = 275.2$ Hz), 123.7 (q, $J = 272.3$ Hz), 122.9 (q, $J = 33.2$ Hz), 120.9 – 120.7 (m), 120.4 (t, $J = 246.1$ Hz), 119.7 (d, $J = 2.5$ Hz), 115.7, 78.2, 61.8, 53.7, 45.1 (t, $J = 27.6$ Hz), 42.4, 36.7, 31.1.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -61.51, -62.57, -95.96 (dd, $J = 249.2, 53.8$ Hz), -96.91 (dd, $J = 249.3, 31.1$ Hz).

HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{41}\text{H}_{35}\text{F}_8\text{N}_2\text{O}$: 723.2622; found 723.2625.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-((((1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl)oxy)methyl)-5-(trifluoromethyl)phenyl)butanenitrile (4bd)



Chemical Formula: $\text{C}_{34}\text{H}_{36}\text{F}_5\text{NO}$
Molecular Weight: 569.6600

The compound **4bd** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2x** (152.9 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $\text{V}_{\text{MeCN}}: \text{V}_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 48 h under argon atmosphere. 58.1 mg, 51% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 5:1, $R_f = 0.3$, $[\alpha]_D^{25} = -33.1$ ($c = 1.0$ in CHCl_3); 92% ee, >20:1 dr. determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 5.53 min, t_R (minor) = 4.72 min.

^1H NMR (400 MHz, CDCl_3) δ 7.75 (s, 1H), 7.70 (d, $J = 7.3$ Hz, 2H), 7.61 (m, 4H), 7.45 (m, 5H), 4.77 (d, $J = 12.4$ Hz, 1H), 4.51 (d, $J = 12.4$ Hz, 1H), 4.22 (dd, $J = 9.7, 4.4$ Hz, 1H), 3.24 (td, $J = 10.6, 4.1$ Hz, 1H), 2.95 (m, 1H), 2.65 (m, 1H), 2.34 – 2.24

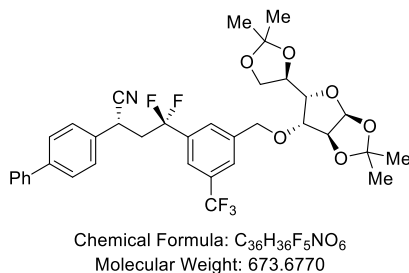
(m, 1H), 2.20 (d, J = 12.2 Hz, 1H), 1.70 (t, J = 10.0 Hz, 2H), 1.45 – 1.33 (m, 2H), 1.09 – 0.85 (m, 9H), 0.78 (d, J = 6.9 Hz, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 141.9, 141.4, 140.1, 136.9 (t, J = 26.4 Hz), 133.7, 131.6 (q, J = 32.8 Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 126.5 – 125.8 (m), 123.7 (q, J = 273.8 Hz), 121.1 – 120.7 (m), 120.4 (t, J = 246.0 Hz), 119.7, 79.8, 69.1, 48.4, 45.0 (t, J = 27.4 Hz), 40.4, 34.6, 31.7, 31.1 (t, J = 3.4 Hz), 25.9, 23.5, 22.5, 21.1, 16.3.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.70, -95.70 (d, J = 249.2 Hz), -97.52 (d, J = 249.0 Hz).

HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{34}\text{H}_{36}\text{F}_5\text{NONa}$: 592.2615; found 592.2614.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4-(3-((((3*aS*,5*S*,6*R*,6*aS*)-5-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl)oxy)methyl)-5-(trifluoromethyl)phenyl)-4,4-difluorobutanenitrile (4be)



The compound **4be** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol), **2y** (194.5 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 48 h under argon atmosphere. 75.4 mg, 56% isolated yield, colorless oil, (petroleum ether: ethyl acetate = 1:1, R_f = 0.3, $[\alpha]_D^{25} = -15.0$ (c = 1.0 in CHCl_3); 91% ee, >20:1 dr. determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 90:10 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 11.16 min, t_R (minor) = 9.73 min.

^1H NMR (400 MHz, CDCl_3) δ 7.78 (s, 1H), 7.69 (s, 2H), 7.60 (d, J = 7.8 Hz, 2H), 7.56 (d, J = 7.0 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.42 – 7.36 (m, 3H), 5.92 (d, J = 3.6 Hz, 1H), 4.81 (d, J = 12.8 Hz, 1H), 4.72 (d, J = 12.8 Hz, 1H), 4.64 (d, J = 3.7 Hz, 1H), 4.37

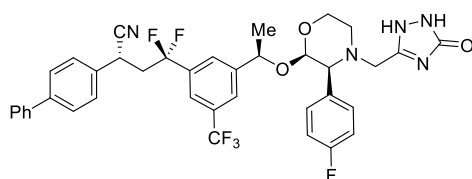
(dd, $J = 10.2, 5.7$ Hz, 1H), 4.19 (dd, $J = 9.6, 4.4$ Hz, 1H), 4.15 – 4.10 (m, 2H), 4.06 – 4.02 (m, 2H), 3.00 – 2.86 (m, 1H), 2.69 – 2.56 (m, 1H), 1.51 (s, 3H), 1.43 (s, 3H), 1.36 (s, 3H), 1.33 (s, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 141.9, 140.3, 140.0, 137.1 (t, $J = 26.5$ Hz), 133.6, 131.8 (q, $J = 33.3$ Hz), 129.0, 128.2, 127.9, 127.8, 127.2, 127.1 (t, $J = 5.6$ Hz), 126.3 – 126.2 (m), 123.6 (q, $J = 273.7$ Hz), 121.5 – 121.3 (m), 120.3 (t, $J = 246.2$ Hz), 119.6, 112.1, 109.5, 105.4, 82.5, 82.4, 81.4, 72.4, 71.0, 67.7, 45.0 (t, $J = 27.5$ Hz), 31.1 (t, $J = 3.4$), 27.0, 26.9, 26.3, 25.3.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.62, -95.69 (d, $J = 249.8$ Hz), -97.23 (d, $J = 249.4$ Hz).

HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{36}\text{H}_{36}\text{F}_5\text{NO}_6\text{Na}$: 696.2360; found 696.2363.

(*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(((*R*)-1-(((2*R*,3*S*)-3-(4-fluorophenyl)-4-((5-oxo-2,5-dihydro-1*H*-1,2,4-triazol-3-yl)methyl)morpholin-2-yl)oxy)ethyl)-5-(trifluoromethyl)phenyl)butanenitrile (4bf)



Chemical Formula: $\text{C}_{38}\text{H}_{33}\text{F}_6\text{N}_5\text{O}_3$
Molecular Weight: 721.7044

The compound **4bf** was prepared according to the general procedure employing **1a** (36.1 mg, 0.2 mmol, 2.0 equiv), **2z** (53.4 mg, 0.1 mmol), **3** (14.9 mg, 0.15 mmol, 1.5 equiv), PTH-1 (2.8 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (0.9 mg, 2.5 mol%), and **L1** (1.1 mg, 3.0 mol%) in $\text{V}_{\text{MeCN}}: \text{V}_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 48 h under argon atmosphere. 33.2 mg, 46% isolated yield, white solid, mp: 182 – 184 °C, (dichloromethane: methanol = 20:1, $R_f = 0.3$, $[\alpha]_D^{25} = 41.8$ ($c = 1.0$ in CHCl_3); 82% ee, >20:1 dr. determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 80:20 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 17.10 min, t_R (minor) = 11.50 min.

^1H NMR (400 MHz, CDCl_3) δ 10.84 (s, 1H), 10.53 (s, 1H), 7.65 – 7.56 (m, 4H), 7.53 (s, 1H), 7.51 – 7.35 (m, 7H), 7.16 (s, 1H), 7.05 (d, $J = 8.9$ Hz, 3H), 4.87 (q, $J = 6.6$ Hz,

1H), 4.37 (s, 1H), 4.30 (t, $J = 11.0$ Hz, 1H), 4.15 (dd, $J = 9.4, 4.4$ Hz, 1H), 3.68 (d, $J = 10.5$ Hz, 1H), 3.59 (d, $J = 14.5$ Hz, 1H), 3.47 (s, 1H), 2.95 (d, $J = 13.5$ Hz, 2H), 2.86 – 2.72 (m, 1H), 2.57 (t, $J = 11.8$ Hz, 1H), 2.51 – 2.42 (m, 1H), 1.47 (d, $J = 6.5$ Hz, 3H).

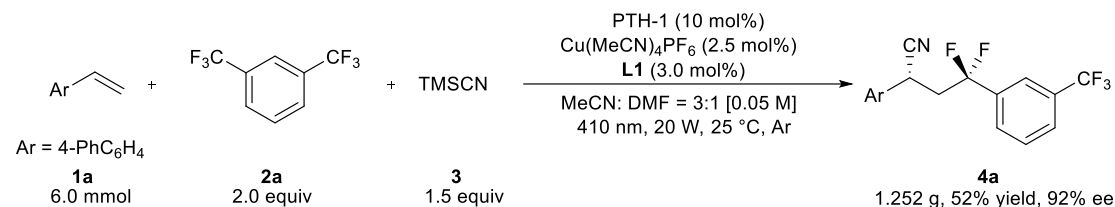
$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 163.8 (d, $J = 248.4$ Hz), 157.4, 145.3 (d, $J = 4.8$ Hz), 141.8, 140.0, 136.9 (t, $J = 26.4$ Hz), 133.6, 132.4 (d, $J = 3.2$ Hz), 131.7 (q, $J = 33.2$ Hz), 131.1 (d, $J = 7.9$ Hz), 129.0, 128.2, 128.0, 127.9, 127.2, 126.2 (t, $J = 4.0$ Hz), 125.0 (m), 123.3 (q, $J = 273.9$ Hz), 121.5 – 120.9 (m), 120.1 (t, $J = 246.7$ Hz), 119.6, 115.6 (d, $J = 21.5$ Hz), 95.5, 72.8, 69.0, 59.4, 52.4, 51.0, 44.7 (t, $J = 27.6$ Hz), 31.0 (t, $J = 3.5$ Hz), 24.5.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.73, -95.50 (d, $J = 250.1$ Hz), -97.15 (d, $J = 249.8$ Hz), -113.41.

HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{38}\text{H}_{34}\text{F}_6\text{N}_5\text{O}_3$: 722.2566; found 722.2568.

5. Product Derivatization

5.1 Gram-scale reaction (4a)

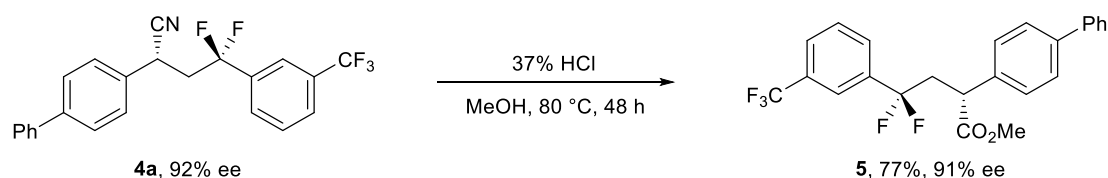


In a flame-dried 250.0 mL Schlenk quartz tube equipped with a magnetic stir bar was sequentially charged with $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (55.9 mg, 2.5 mol%) and **L1** (64.2 mg, 3 mol%) under Ar atmosphere, followed by the addition of super dry *N,N*-Dimethylformamide (30 mL). The mixture was stirred at room temperature for 30 min. To the resulting mixture was then added PTH-1 (165.2 mg, 0.6 mmol, 10 mol%), **1a** (1.08 g, 6.0 mmol), **2a** (2.568 g, 12 mmol, 2.0 equiv), **3** (892.9 mg, 9.0 mmol, 1.5 equiv) and super dry acetonitrile (90 mL) under Ar. The mixture was stirred at a distance of 2~3 cm from a 410 nm LEDs at 25 °C until the reaction was completed, as monitored by TLC analysis. The mixture was diluted with water (100 mL) and then extracted with ethyl acetate (50 mL×3), Combine organic phase and wash saturated NaCl (100 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The residue

was purified by flash chromatography on silica gel (petroleum ether: ethyl acetate = 12:1) to give the product **4a** with 52 % yield and 92% ee.

5.2 General procedure for synthesis of 5-14

Synthesis of methyl (*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(trifluoromethyl)phenyl)butanoate (**5**)^[19]



To a solution of **4a** (80.3 mg, 0.2 mmol) in methanol (2.0 mL) was added 37% HCl (2.0 mL), the reaction was heated to 80 °C in a sealed tube and stirred 48 h under argon atmosphere. After cooling to room temperature, the reaction was quenched with cold water and extracted with ethyl acetate (10 mL×3). The combined organic phase was dried over Na₂SO₄, filtered and concentrated under vacuum. The product was purified by silica gel column chromatography (petroleum ether: ethyl acetate = 15:1, *R_f* = 0.3) to give **5** as a colorless oil. (66.9 mg, 77% yield, [α]_D²⁵ = -43.5 (c = 1.0 in CHCl₃); 91% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major) = 6.90 min, *t_R* (minor) = 5.70 min)

¹H NMR (400 MHz, CDCl₃) δ 7.66 (s, 1H), 7.61 (t, *J* = 7.9 Hz, 2H), 7.57 – 7.52 (m, 5H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.37 – 7.33 (m, 3H), 3.94 (dd, *J* = 9.5, 3.9 Hz, 1H), 3.56 (s, 3H), 3.33 – 3.16 (m, 1H), 2.60 – 2.47 (m, 1H).

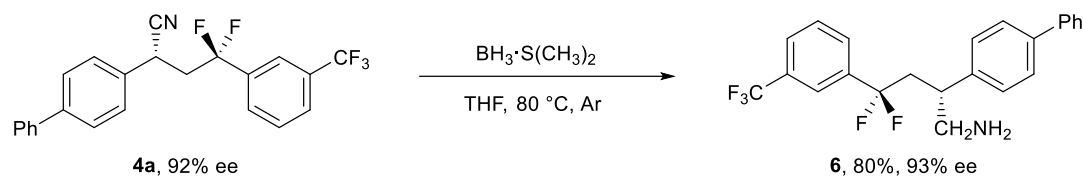
¹³C{¹H} NMR (101 MHz, CDCl₃) δ 173.3, 140.9, 140.6, 137.8 (t, *J* = 27.0 Hz), 137.0, 131.2 (q, *J* = 32.8 Hz), 129.3, 128.9, 128.7 (t, *J* = 6.8 Hz), 128.2, 127.8, 127.6, 127.2, 127.1 – 126.7 (m), 123.8 (q, *J* = 273.9 Hz), 122.3 – 122.2 (m), 121.4 (t, *J* = 245.3 Hz), 52.6, 45.2 (t, *J* = 3.3 Hz), 42.7 (t, *J* = 27.0 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.75, -96.34 (d, *J* = 247.8 Hz), -96.39 (d, *J* = 247.8 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₄H₁₈F₅O₂: 433.1227; found 433.1227.

Synthesis of (*R*)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(trifluoromethyl)phen

yl)butan-1-amine (6)^[20]



BH₃·SMe₂ (0.3 mmol) was added to a solution of **4a** (80.3 mg, 0.2 mmol) in dry THF (2 mL) at room temperature under an Ar atmosphere, and then refluxed for 18 h. The reaction was quenched by the dropwise addition of 6 M aqueous HCl (1 mL). After refluxing for a further 2 h, the solution was made basic with 6 M aqueous NaOH, then extracted three times with CH₂Cl₂. The combined extracts were dried over Na₂SO₄ and the solvent was removed in vacuo. The product was purified by silica gel column chromatography (dichloromethane: methanol = 10/1, R_f = 0.3) to give **6** as a colorless oil. (64.8 mg, 80% yield, [α]_D²⁵ = -2.2 (c = 1.0 in CHCl₃); 93% ee, determined by HPLC analysis (IC, hexane/*i*-PrOH, 80:20 v/v, flow rate 0.5 mL/min, λ = 254 nm, 25 °C), *t*_R (major) = 14.07 min, *t*_R (minor) = 13.05 min)

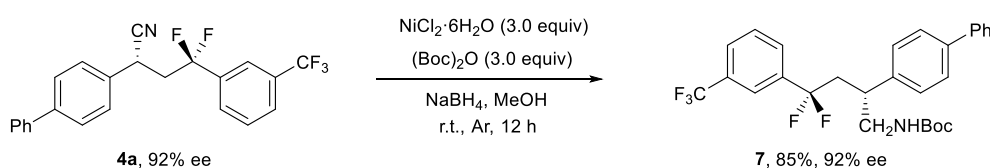
¹H NMR (400 MHz, CDCl₃) δ 7.67 – 7.59 (m, 2H), 7.58 – 7.55 (m, 3H), 7.50 – 7.40 (m, 5H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 3.03 – 2.90 (m, 3H), 2.65 – 2.49 (m, 2H), 1.37 (s, 2H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 141.1, 140.8, 139.9, 138.3 (t, *J* = 27.3 Hz), 131.0 (q, *J* = 32.8 Hz), 129.1, 128.9, 128.6 (t, *J* = 5.9 Hz), 128.3, 127.5, 127.4, 127.1, 126.6 – 126.5 (m), 123.8 (q, *J* = 272.9 Hz), 122.4 – 122.1 (m), 122.2 (t, *J* = 244.9 Hz), 48.3, 43.5 (t, *J* = 2.9 Hz), 42.8 (t, *J* = 26.6 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.74, -90.81 (d, *J* = 247.3 Hz), -96.35 (d, *J* = 247.3 Hz).

HRMS-ESI (*m/z*): [M+H]⁺ calcd. for C₂₃H₂₁F₅N: 406.1594; found 406.1597.

Synthesis of *tert*-butyl (*R*)-(2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(trifluoromethyl)phenyl)butyl)carbamate (7)^[21]



CH₂Cl₂. The combined organic layers were dried over MgSO₄ and concentrated in vacuo. The residue was purified by silica column chromatography (petroleum ether: ethyl acetate = 15:1, *R_f* = 0.3) to give **8** as a colorless oil. (28.5mg, 70%)

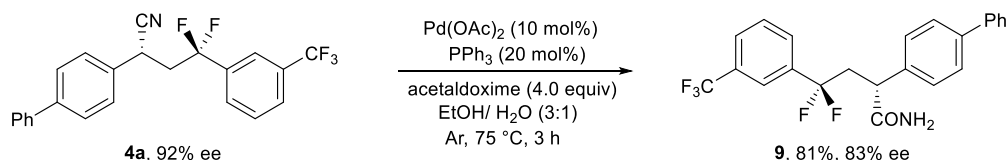
¹H NMR (400 MHz, CDCl₃) δ 9.67 (s, 1H), 7.71 (s, 1H), 7.69 – 7.64 (m, 2H), 7.58 – 7.51 (m, 5H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.21 (d, *J* = 8.3 Hz, 2H), 4.03 (t, *J* = 6.3 Hz, 1H), 3.32 – 3.18 (m, 1H), 2.60 – 2.41 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 197.4, 141.2, 140.4, 137.9 (t, *J* = 27.1 Hz), 133.9, 131.2 (q, *J* = 32.8 Hz), 129.4, 129.4, 129.0, 128.6 (t, *J* = 6.0 Hz), 128.2, 127.8, 127.2, 127.0 – 126.9 (m), 123.8 (q, *J* = 272.9 Hz), 122.3 – 122.1 (m), 121.7 (t, *J* = 245.0 Hz), 52.8 (t, *J* = 2.2 Hz), 38.8 (t, *J* = 27.1 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -62.77, -93.73 (d, *J* = 247.8 Hz), -96.30 (d, *J* = 247.9 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₂₃H₁₆F₅O: 403.1121; found 403.1128.

Synthesis of (R)-2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-4-(3-(trifluoromethyl)phenyl)butanamide (**9**)^[21]



A mixture of **4a** (80.3 mg, 0.2 mmol), acetaldoxime (47.3 mg, 0.8 mmol), Pd(OAc)₂ (4.5 mg, 0.02 mmol) and PPh₃ (10.5 mg, 0.04 mmol) in aqueous EtOH (EtOH/H₂O = 3/1, 4 mL) was heated to 75 °C in a 25 mL round-bottomed flask for 3 hours under argon atmosphere. The reaction mixture was filtered through a pad of Celite and washed with DCM. The combined organic layers were concentrated under vacuum. The product was purified by silica gel column chromatography (petroleum ether: ethyl acetate = 2:1, *R_f* = 0.3) to give **9** as a white solid, mp: 146 – 148 °C. (67.9 mg, 81% yield, [α]_D²⁵ = -51.8 (c = 1.0 in CHCl₃); 83% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 80:20 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), *t_R* (major) = 7.56 min, *t_R* (minor) = 8.34 min)

¹H NMR (400 MHz, CDCl₃) δ 7.73 (s, 1H), 7.68 (t, *J* = 6.3 Hz, 2H), 7.60 – 7.51 (m,

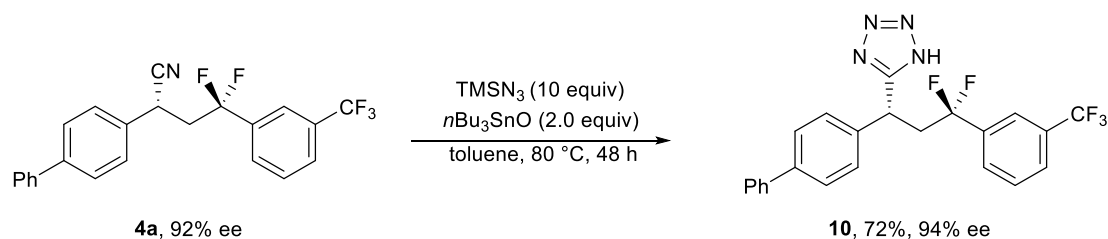
5H), 7.46 (t, $J = 7.5$ Hz, 2H), 7.40 – 7.35 (m, 3H), 5.50 (s, 2H), 3.87 (t, $J = 6.4$ Hz, 1H), 3.45 – 3.30 (m, 1H), 2.63 – 2.49 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 174.3, 140.8, 140.5, 138.1, 138.0 (t, $J = 27.1$ Hz), 131.1 (q, $J = 32.6$ Hz), 129.3, 128.9, 128.6 (t, $J = 6.1$ Hz), 128.3, 127.9, 127.6, 127.1, 127.0 – 126.6 (m), 123.8 (q, $J = 273.5$ Hz), 122.3 – 122.0 (m), 121.8 (t, $J = 244.7$ Hz), 46.2 (t, $J = 2.6$ Hz), 42.1 (t, $J = 26.6$ Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.73, -95.35 (d, $J = 247.1$ Hz), -96.34 (d, $J = 246.9$ Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{23}\text{H}_{17}\text{F}_5\text{NO}$: 418.1230; found 418.1223.

Synthesis of (R)-5-(1-([1,1'-biphenyl]-4-yl)-3,3-difluoro-3-(3-(trifluoromethyl)phenyl)propyl)-1H-tetrazole (**10**)^[22]



To a solution of **4a** (40.1 mg, 0.1 mmol) in toluene (2.0 mL) was added trimethylsilylazide (115 mg, 1.0 mmol) and tributyltin oxide (61.5 mg, 0.2 mmol). The reaction mixture was stirred at 80 °C for 48 h. The reaction mixture was concentrated under vacuum, the product was purified by silica gel column chromatography (dichloromethane: methanol = 20:1, $R_f = 0.3$) to give **10** as a colorless oil. (32.0 mg, 72% yield, $[\alpha]_D^{25} = -3.3$ ($c = 1.0$ in CHCl_3); 94% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 85:15 v/v, flow rate 1.0 mL/min, $\lambda = 254$ nm, 25 °C), t_R (major) = 8.19 min, t_R (minor) = 5.74 min)

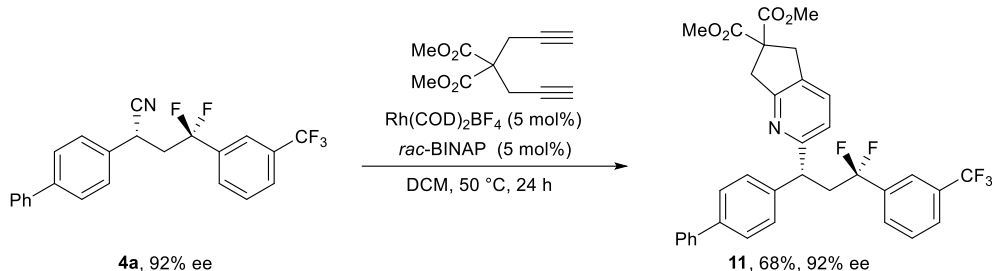
^1H NMR (400 MHz, CDCl_3) δ 15.12 (s, 1H), 7.67 (s, 1H), 7.61 – 7.57 (m, 2H), 7.48 – 7.42 (m, 4H), 7.42 – 7.38 (m, 3H), 7.35 (t, $J = 7.5$ Hz, 2H), 7.33 – 7.28 (m, 1H), 5.06 (t, $J = 2.0$ Hz, 1H), 3.64 – 3.50 (m, 1H), 3.08 – 2.94 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 141.2, 140.1, 137.3 (t, $J = 26.8$ Hz), 131.1 (q, $J = 32.8$ Hz), 129.4, 128.9, 128.5 (t, $J = 5.4$ Hz), 128.2, 128.0, 127.7, 127.1, 123.6 (q, $J = 273.3$ Hz), 122.1 – 122.0 (m), 121.3 (t, $J = 245.2$ Hz), 43.9 (t, $J = 26.9$ Hz), 35.7.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.79 (d, J = 4.7 Hz), -94.71 (d, J = 247.6 Hz), -96.78 (d, J = 247.4 Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{23}\text{H}_{16}\text{F}_5\text{N}_4$: 443.1295; found 443.1302.

Synthesis of dimethyl (*R*)-2-(1-([1,1'-biphenyl]-4-yl)-3,3-difluoro-3-(3-(trifluoromethyl)phenyl)propyl)-5,7-dihydro-6*H*-cyclopenta[*b*]pyridine-6,6-dicarboxylate (11**)^[23]**



rac-BINAP (5 mol%) and $[\text{Rh}(\text{COD})_2]\text{BF}_4$ (5 mol%) were dissolved in DCM (1.0 mL), and the mixture was stirred at room temperature for 20 min. To this mixture was added **4a** (40.1 mg, 0.1 mmol) and dimethyl 2,2-di(prop-2-yn-1-yl) malonate (31.5 mg, 0.15 mmol). The reaction was stirred at 50 °C for 24 hours. The reaction mixture was filtered through a pad of Celite and washed with DCM. The combined organic layers were concentrated under vacuum. The product was purified by silica gel column chromatography (petroleum ether: ethyl acetate = 3:1, R_f = 0.3) to give **11** as a colorless oil. (41.2 mg, 68% yield, $[\alpha]_D^{25}$ = -5.9 (c = 1.0 in CHCl_3); 92% ee, determined by HPLC analysis (AD-H, hexane/*i*-PrOH, 85:15 v/v, flow rate 1.0 mL/min, λ = 254 nm, 25 °C), t_R (major) = 11.59 min, t_R (minor) = 9.89 min)

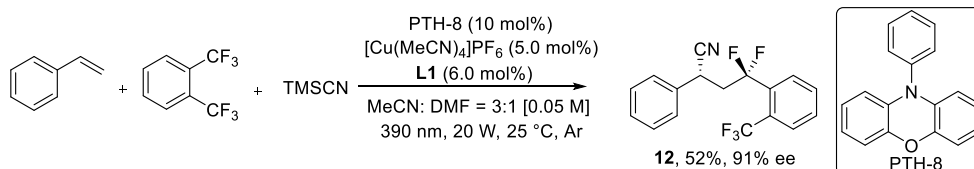
^1H NMR (400 MHz, CDCl_3) δ 8.33 (s, 1H), 7.61 (s, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.41 (t, J = 7.7 Hz, 3H), 7.38 – 7.29 (m, 3H), 6.92 (s, 1H), 4.35 (t, J = 6.8 Hz, 1H), 3.77 (s, 3H), 3.72 (s, 3H), 3.61 – 3.42 (m, 5H), 3.01 – 2.82 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 171.6, 160.2, 150.6, 144.9, 142.1, 140.9, 139.8, 138.2 (t, J = 26.9 Hz), 134.2, 130.7 (q, J = 32.9 Hz), 129.0, 128.8 (t, J = 6.1 Hz), 128.3, 128.8, 127.5, 127.3, 127.1, 126.6 – 126.2 (m), 123.8 (q, J = 272.0 Hz), 122.6 – 122.3 (m), 122.2 (t, J = 244.7 Hz), 119.2, 60.1, 53.3, 47.3, 43.9 (t, J = 27.0 Hz), 40.3, 38.1.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.72, -92.39 (d, J = 247.3 Hz), -95.79 (d, J = 247.1 Hz).

HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{34}\text{H}_{29}\text{F}_5\text{NO}_4$: 610.2017; found 610.2017.

(*R*)-4,4-difluoro-2-phenyl-4-(2-(trifluoromethyl)phenyl)butanenitrile (12**)**



The compound **12** was prepared according to the general procedure employing **1t** (20.8 mg, 0.2 mmol), **2c** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-8 (5.2 mg, 10 mol%), $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (3.7 mg, 5 mol%), and **L1** (4.3 mg, 6 mol%) in $V_{\text{MeCN}}: V_{\text{DMF}} = 3: 1$ [0.05 M] were stirred, irradiation with 20 W 390 nm violet LEDs at room temperature for 10 h under argon atmosphere. (33.8 mg, 52% isolated yield, colorless oil, petroleum ether: ethyl acetate = 10:1, R_f = 0.3, $[\alpha]_D^{25} = 16.1$ (c = 1.0 in CHCl_3); 91% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 98:2 v/v, flow rate 1.0 mL/min, λ = 210 nm, 25 °C), t_R (major) = 9.87 min, t_R (minor) = 10.70 min)

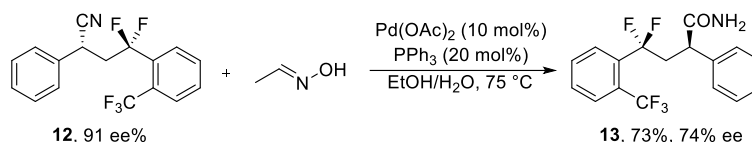
^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, J = 7.8 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.42 – 7.32 (m, 5H), 4.2 (dd, J = 10.2, 4.0 Hz, 1H), 3.0 – 2.8 (m, 1H), 2.7 – 2.5 (m, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 135.0, 134.4 (t, J = 26.9 Hz), 132.4, 130.8, 129.5, 128.7, 128.0 (t, J = 9.1 Hz), 127.7 (q, J = 6.4 Hz), 127.3, 123.6 (q, J = 274.2 Hz), 120.5 (t, J = 246.4 Hz), 119.8, 45.7 (tq, J = 26.9, 2.8 Hz), 31.3 (t, J = 3.3 Hz).

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -57.7 (dd, J = 18.0, 13.9 Hz), -93.0 (dq, J = 252.5, 14.3 Hz), -94.5 (dq, J = 252.7, 14.3 Hz).

HRMS-ESI (m/z): $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{17}\text{H}_{11}\text{F}_5\text{N}$: 324.0812; found 324.0811.

(*R*)-4,4-difluoro-2-phenyl-4-(2-(trifluoromethyl)phenyl)butanamide (13**)^[21]**



A mixture of **12** (65.1 mg, 0.2 mmol), acetaldoxime (47.3 mg, 0.8 mmol), Pd(OAc)₂ (4.5 mg, 0.02 mmol) and PPh₃ (10.5 mg, 0.04 mmol) in aqueous EtOH (EtOH/H₂O = 3/1, 4 mL) was heated to 75 °C in a 25 mL round-bottomed flask for 3 hours under argon atmosphere. The reaction mixture was filtered through a pad of Celite and washed with DCM. The combined organic layers were concentrated under vacuum. The product was purified by silica gel column chromatography (petroleum ether: ethyl acetate = 3:1, *R_f* = 0.2) to give **13** as a yellow solid, mp: 114 – 116 °C. (49.8 mg, 73% isolated yield, [α]_D²⁵ = -15.9 (c = 1.0 in CHCl₃); 74% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 80:20 v/v, flow rate 1.0 mL/min, λ = 210 nm, 25 °C), *t_R* (major) = 5.75 min, *t_R* (minor) = 9.65 min)

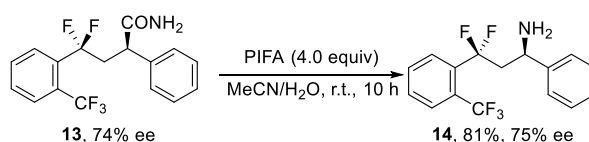
¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.60 – 7.51 (m, 2H), 7.32 – 7.28 (m, 5H), 5.5 (s, 2H), 3.94 (dd, *J* = 7.5, 5.4 Hz, 1H), 3.35 – 3.21 (m, 1H), 2.63 – 2.47 (m, 1H).

¹³C{¹H} NMR (101 MHz, CDCl₃) δ 174.4, 139.4, 135.8 (t, *J* = 27.4 Hz), 132.0, 130.2, 129.1, 128.2 (t, *J* = 9.0 Hz), 127.9, 127.8, 127.5 (q, *J* = 6.4 Hz), 123.6 (q, *J* = 274.7 Hz), 122.0 (t, *J* = 246.4 Hz), 46.4 (t, *J* = 3.0 Hz), 42.8 (t, *J* = 24.2 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -57.7 (dd, *J* = 19.5, 13.5 Hz), -93.1 (dq, *J* = 250.1, 13.9 Hz), -94.1 (dq, *J* = 250.1, 13.9 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₁₇H₁₃F₅NO: 342.0917; found 342.0923.

(*R*)-3,3-difluoro-1-phenyl-3-(2-(trifluoromethyl)phenyl)propan-1-amine (14**)**^[24]



[Bis(trifluoroacetoxy)iodo]benzene (51.6 mg, 0.12 mmol) and H₂O (0.2 mL) were added sequentially to a stirred solution of **13** (34.3 mg, 0.1 mmol) in MeCN (1.0 mL) at rt. After 10 h the reaction mixture was acidified with 6 M aq HCl (0.1 mL) and washed with Et₂O (2×5 mL). The resultant aqueous solution was then basified (to pH

14) using 2.0 M aq NaOH and extracted with CH₂Cl₂ (2×10 mL). The combined organic layers were concentrated under vacuum. The product was purified by silica gel column chromatography (dichloromethane: methanol = 10:1, *R_f* = 0.3) to give **14** as a colorless oil. (25.6 mg, 81% isolated yield, $[\alpha]_D^{25} = -5.9$ (*c* = 1.0 in CHCl₃); 75% ee, determined by HPLC analysis (IB, hexane/*i*-PrOH, 85:15 v/v, flow rate 1.0 mL/min, λ = 210 nm, 25 °C), *t_R* (major) = 5.45 min, *t_R* (minor) = 6.25 min).

¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.37 – 7.30 (m, 4H), 7.26 – 7.22 (m, 1H), 4.5 (dd, *J* = 8.1, 4.2 Hz, 1H), 2.6 – 2.4 (m, 2H), 1.8 (s, 2H).

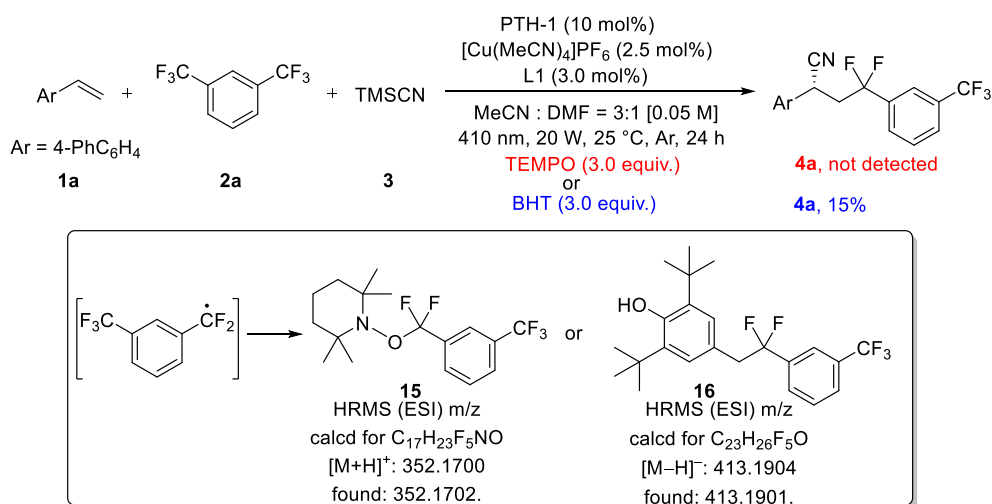
¹³C{¹H} NMR (101 MHz, CDCl₃) δ 145.3, 136.2 (t, *J* = 26.3 Hz), 132.0, 130.1, 128.8, 127.9 (t, *J* = 9.1 Hz), 127.7 (q, *J* = 6.6 Hz), 127.5, 126.4, 123.7 (q, *J* = 273.7 Hz), 122.4 (t, *J* = 246.4 Hz), 51.1, 49.3 (t, *J* = 25.3 Hz).

¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -57.6 (t, *J* = 15.0 Hz), -91.6 (dq, *J* = 250.0, 15.8 Hz), -94.2 (dq, *J* = 249.7, 15.8 Hz).

HRMS-ESI (*m/z*): [M-H]⁻ calcd. for C₁₆H₁₃F₅N: 314.0968; found 314.0961.

6. Mechanistic Studies

6.1 Radical trapping experiments



In a flame-dried 10.0 mL Schlenk quartz tube equipped with a magnetic stir bar was charged sequentially with Cu(MeCN)₄PF₆ (1.9 mg, 2.5 mol%) and **L1** (2.1 mg, 3.0 mol%) under Ar atmosphere, followed by the addition of super dry *N,N*-

Dimethylformamide (3.0 mL). Then the mixture was stirred at room temperature for 30 min. To the resulting mixture were added PTH-1 (5.5 mg, 0.02 mmol, 10 mol%), **1a** (36.1 mg, 0.20 mmol, 1.0 equiv), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), TMSCN (29.8 mg, 0.3 mmol, 1.5 equiv), super dry acetonitrile (3.0 mL) and TEMPO or BHT (0.60 mmol 3.0 equiv) under Ar. The mixture was stirred at a distance of 2~3 cm from a 410 nm LEDs at rt for about 24 h as monitored by TLC analysis. The corresponding trapping product **15** and **16** were detected by HRMS.

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

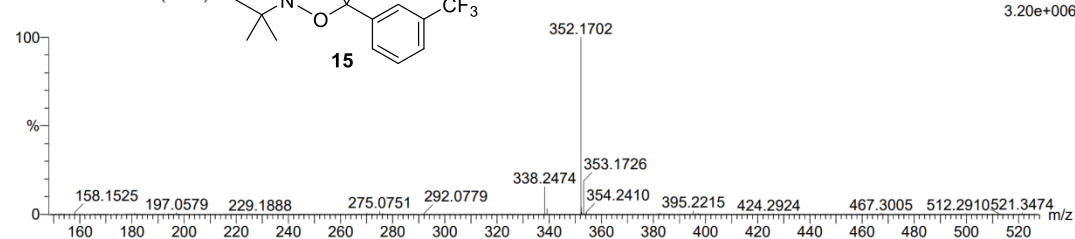
288 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 17-17 H: 23-23 N: 0-10 O: 0-50 F: 5-5 Na: 0-1

45

251016-13-CFX11 15 (0.104)



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
352.1702	352.1700	0.2	0.6	4.5	1051.6	n/a	n/a	C17 H23 N O F5

Figure S1: Image for HRMS analysis of **15**

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

456 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 23-23 H: 26-26 N: 0-100 O: 0-100 F: 5-6

49--N

260208-3-CF-F-2895-----n 10 (0.111)

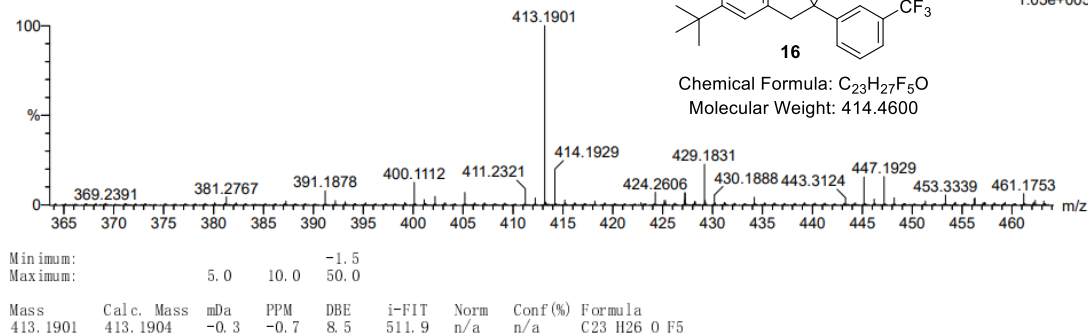
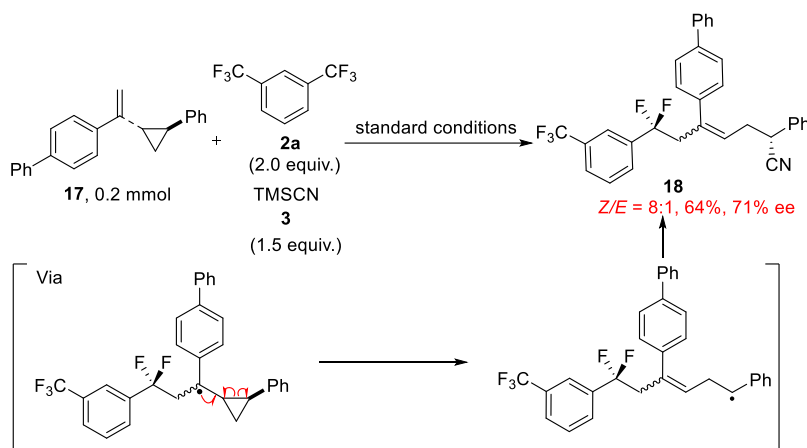


Figure S2: Image for HRMS analysis of 16

6.2 Radical clock experiment



The compound **17** as synthesized according to literature procedures^[25]. This reaction was conducted according to the general procedure employing **17** (59.3 mg, 0.2 mmol), **2a** (85.6 mg, 0.4 mmol, 2.0 equiv), **3** (29.8 mg, 0.3 mmol, 1.5 equiv), PTH-1 (5.5 mg, 10 mol%), [Cu(MeCN)₄]PF₆ (1.9 mg, 2.5 mol%), and **L1** (2.1 mg, 3.0 mol%) in V_{MeCN}: V_{DMF} = 3: 1 [0.05 M] were stirred, irradiation with 20 W 410 nm violet LEDs at room temperature for 24 h under argon atmosphere.

(R)-5-([1,1'-biphenyl]-4-yl)-7,7-difluoro-2-phenyl-7-(3-(trifluoromethyl)phenyl)hept-4-enitrile (18); 64% isolated yield, colorless oil, Z/E = 8:1, petroleum ether: ethyl acetate = 10:1, R_f = 0.3, [α]_D²⁵ = 14.2 (c = 1.0 in CHCl₃); 71% ee, determined by HPLC analysis (IA, hexane/*i*-PrOH, 95:5 v/v, flow rate 1.0

mL/min, $\lambda = 254$ nm, 25 °C), t_R (major-1) = 10.27 min, t_R (minor-1) = 8.94 min; t_R (major-2) = 15.27 min, t_R (minor-2) = 19.52 min.

^1H NMR (400 MHz, CDCl_3) δ 7.50 – 7.42 (m, 5H), 7.36 – 7.31 (m, 5H), 7.30 – 7.21 (m, 4H), 7.14 – 7.01 (m, 2H), 6.76 (d, $J = 7.9$ Hz, 2H), 5.58 (t, $J = 7.4$ Hz, 1H), 3.67 (t, $J = 7.0$ Hz, 1H), 3.18 (t, $J = 15.4$ Hz, 2H), 2.50 (t, $J = 7.2$ Hz, 2H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 140.6, 140.2, 137.8, 136.4 (t, $J = 27.1$ Hz), 136.4 (t, $J = 4.1$ Hz), 134.9, 130.8 (q, $J = 32.7$ Hz), 129.3, 129.2, 129.1, 128.9, 128.8 (t, $J = 5.6$ Hz), 128.6, 128.6, 128.3, 127.5, 127.5, 127.1, 127.0, 126.7 – 126.4 (m), 123.8 (q, $J = 270.2$ Hz), 122.5 – 122.4 (m), 121.2 (t, $J = 246.2$ Hz), 120.3, 48.3 (t, $J = 27.8$ Hz), 37.4, 35.2.

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -62.69, -93.48 (d, $J = 39.9$ Hz).

HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{32}\text{H}_{24}\text{F}_5\text{NNa}$: 540.1727; found 540.1730.

6.3 UV-Vis absorption spectra

UV-Vis spectra of the individual component were recorded, including substrate **1a**, **2a**, PTH-1, copper salts $\text{Cu}(\text{MeCN})_4\text{PF}_6$, and copper complexes $\text{Cu}(\text{MeCN})_4\text{PF}_6/\text{L1}$ (generated *in situ* by stirring a 1:1.2 mixture of $\text{Cu}(\text{MeCN})_4\text{PF}_6$ and chiral ligand **L1**). All of the samples were prepared as a 1.0 mM solution in DMF (super dry) and used freshly for the measurement.

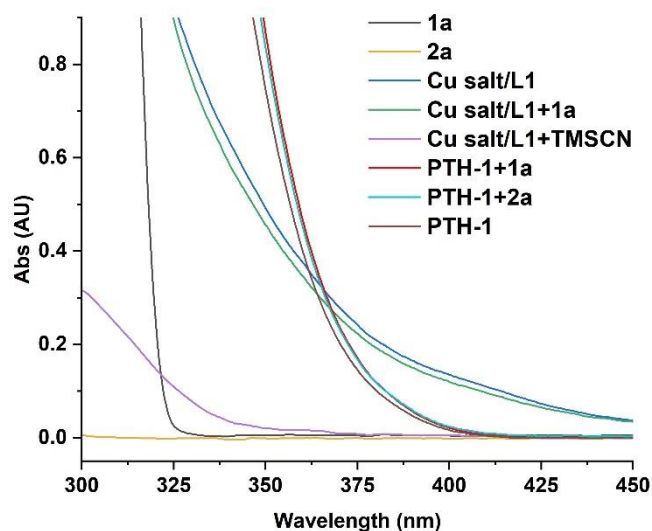


Figure S3. UV/Vis absorption spectra of the related components recorded in DMF.

6.4 Stern-Volmer luminescence quenching studies

Stern-Volmer quenching experiments were carried by Agilent Technologies F-4600 spectrofluorometer, using a 2×10^{-4} M solution of photoredox catalyst PTH-1 variable concentrations (2×10^{-3} , 4×10^{-3} , 6×10^{-3} , 8×10^{-3} M) of 1,3-bis(trifluoromethyl)-benzene, $\text{Cu}(\text{MeCN})_4\text{PF}_6$ and $\text{Cu}(\text{MeCN})_4\text{PF}_6/\text{L1}$, 1,3-bis(trifluoromethyl)-benzene (4×10^{-3} , 0.8×10^{-3} , 1.2×10^{-3} , 1.6×10^{-3} , 4×10^{-3} M) in super dry DMF. The samples were prepared in 4 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside Ar filled glove-box. The solution was irradiated at 350 nm and the fluorescence was measured from 370 nm to 600 nm. The intensity of the emission peak at 445.6 nm expressed as the ratio I_0/I , where I_0 is the emission intensity of photoredox catalyst at 445.6 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured. Stern-Volmer plots for each component were given in **Figures S4-S6** below.

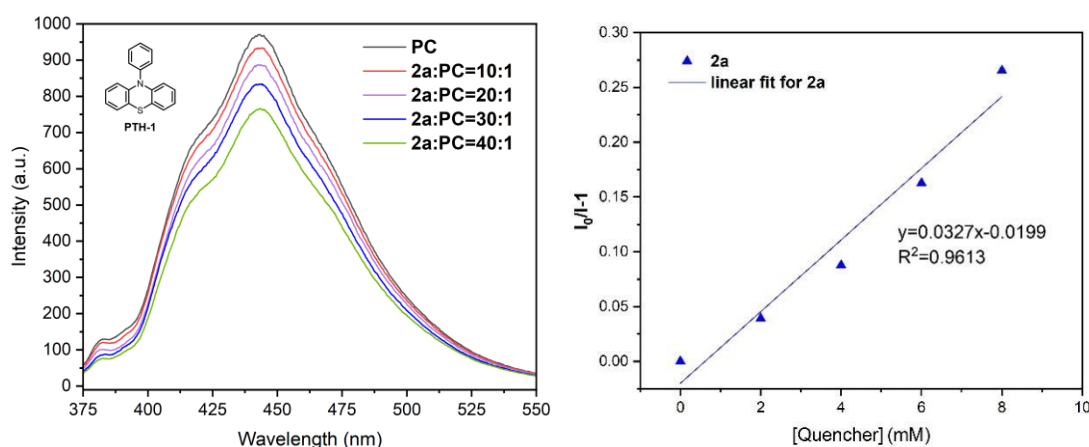


Figure S4. Photoredox catalyst emission quenching by 2a.

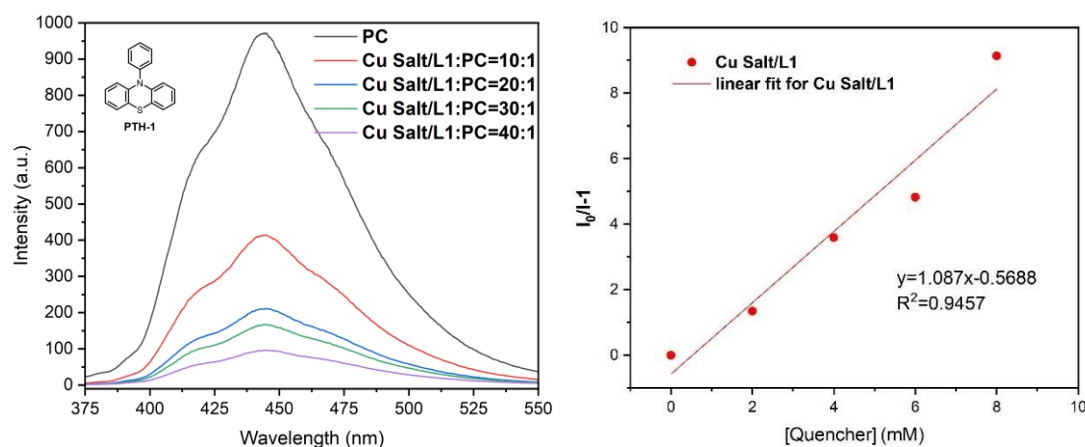


Figure S5. Photoredox catalyst emission quenching by **Cu salt/L1**.

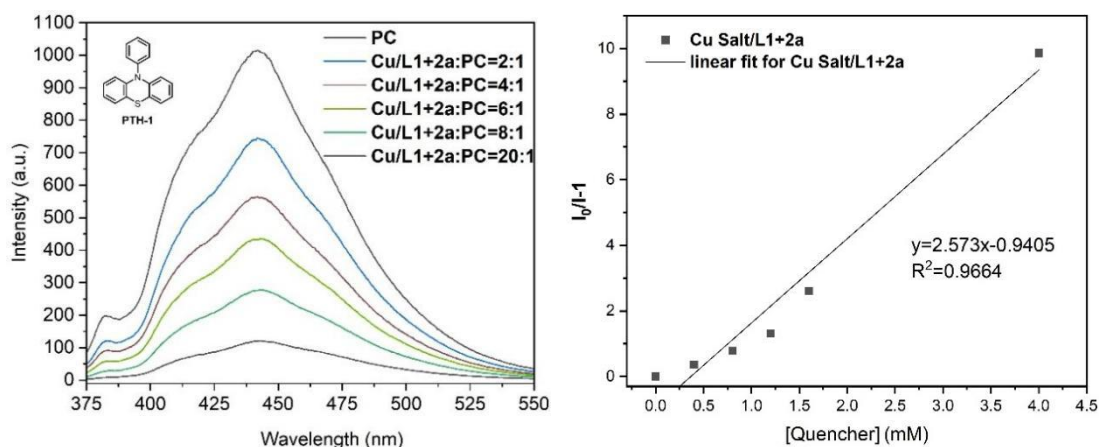


Figure S6. Photoredox catalyst emission quenching by **Cu salt/L1+2a**.

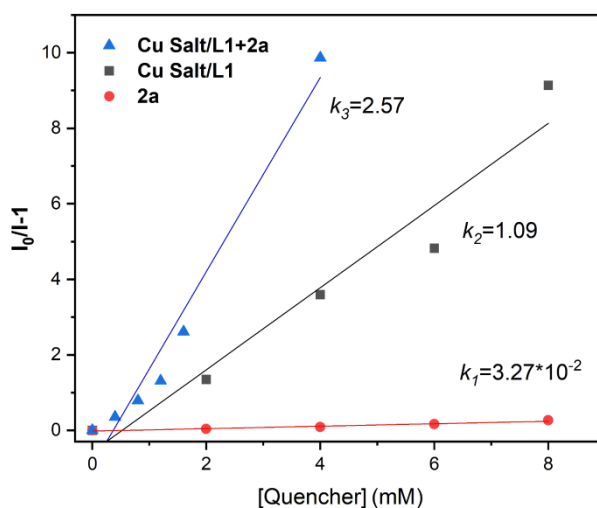
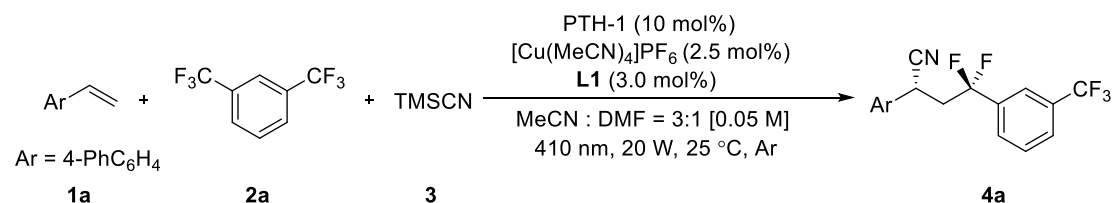


Figure S7. Stern-Volmer fluorescence quenching studies of photoredox catalyst with different concentrations of quencher. (**2a**, **Cu salt/L1**, **Cu salt/L1+2a**)

6.5 Light on/off experiments



In a flame-dried 10.0 mL Schlenk quartz tube equipped with a magnetic stir bar was charged sequentially with Cu(MeCN)₄PF₆ (0.9 mg, 2.5 μmol) and **L1** (1.1 mg, 3.0 μmol) under Ar atmosphere, followed by the addition of super dry *N,N*-Dimethylformamide (0.5 mL). Then the mixture was stirred at room temperature for 30 min. To the resulting mixture was added PTH-1 (0.01 mmol, 10 mol%), **1a** (0.1 mmol, 1.0 equiv), **2a** (0.2

mmol, 2.0 equiv), TMSCN (0.15 mmol, 1.5 equiv) and super dry acetonitrile (1.5 mL) under Ar. The mixture was stirred at a distance of 2~3 cm from a 410 nm LEDs at 25 °C for 2 h and then stirred in the dark for 2 h. This procedure was repeated alternatively for 10 h, and the yield of the product was determined by ^1H NMR with 1,3,5-trimethoxybenzene as an internal standard at each point the light was turned off or on. The results are shown in **Figure S8** below. This result shows that constant light irradiation is needed to progress the reaction.

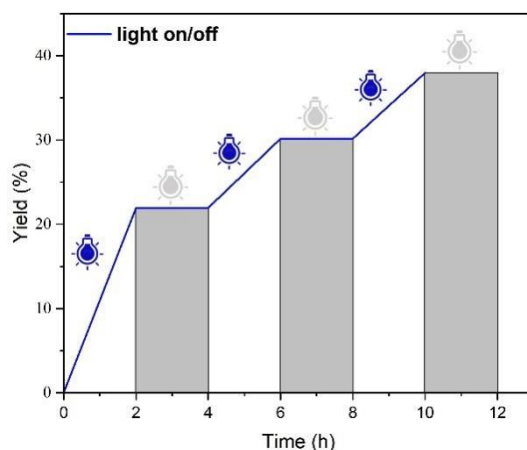
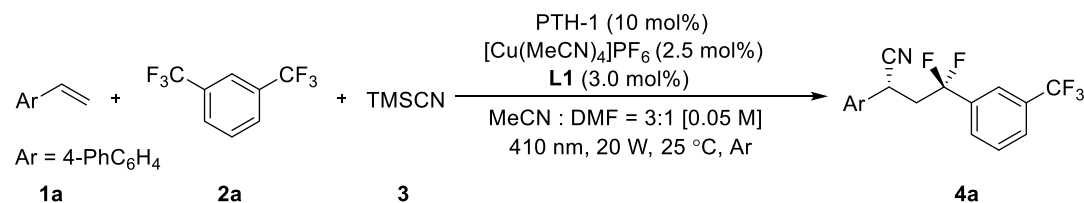


Figure S8. Light-on/light-off experiments.

6.6 Quantum yield calculation



In a flame-dried 10.0 mL Schlenk quartz tube equipped with a magnetic stir bar was charged sequentially with Cu(MeCN)₄PF₆ (0.9 mg, 2.5 μmol) and **L1** (1.1 mg, 3.0 μmol) under Ar atmosphere, followed by the addition of super dry *N,N*-Dimethylformamide (0.5 mL). Then the mixture was stirred at room temperature for 30 min. To the resulting mixture was added PTH-1 (0.01 mmol, 10 mol%), **1a** (0.1 mmol, 1.0 equiv), **2a** (0.2 mmol, 2.0 equiv), TMSCN (0.15 mmol, 1.5 equiv) and super dry acetonitrile (1.5 mL) under Ar. The sample was irradiated ($\lambda = 410$ nm with intensity of 1.782 W/cm²) for 7200s. After irradiation, the yield of product was determined by ^1H NMR with 1,3,5-trimethoxybenzene as an internal standard. The quantum yield was determined as

follows: [26]

$$M = 0.1 \text{ mmol} \times 21.9\% = 0.0219 \text{ mmol} = 2.19 \times 10^{-5} \text{ mol}$$

The light intensity of purple LED strip light ($\lambda = 410 \text{ nm}$, 20 W) was 1.782 W/cm^2

$$\eta = \frac{N_e}{N_p} \times 100\% = \frac{\frac{2 \times M \times N_A}{S \times P \times t}}{\frac{h \times c}{\lambda}} \times 100\% = \frac{2 \times M \times N_A \times h \times c}{S \times P \times t \times \lambda} \times 100\%$$

$$= \frac{2 \times (2.19 \times 10^{-5}) \times (6.022 \times 10^{23}) \times (6.63 \times 10^{-34}) \times (3 \times 10^8)}{1.766 \times 1.782 \times 7200 \times (410 \times 10^{-9})} \times 100\% = 0.06\%$$

Where, M represents the amount of formed product (mol), N_A is the Avogadro constant ($6.022 \times 10^{23} \text{ mol}^{-1}$), h is the Planck constant ($6.63 \times 10^{-34} \text{ J}\cdot\text{s}$), c is the light speed ($3 \times 10^8 \text{ m}\cdot\text{s}^{-1}$), S is the irradiation area ($r_{\text{quartz tube}} = 0.75 \text{ cm}$, $S = \pi r^2 = 1.766 \text{ cm}^2$), P is the light intensity ($1.782 \text{ W}\cdot\text{cm}^{-2}$), t is irradiation time (7200 s), λ is the wavelength of light (m). Therefore, the low quantum yield ($\phi = 0.06\%$) indicates that a radical chain process did not appear to be involved.

6.7 Non-linear effect experiments

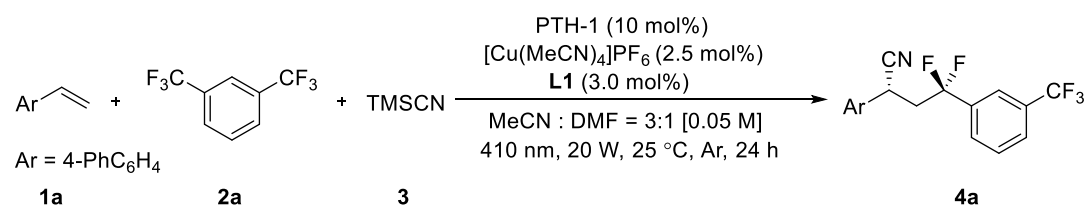


Table S8. The ee values of product catalyzed by ligand in different ee value

Entry	L1 (ee %)	Product 4a (ee %)
1	100	92
2	50	41
3	0	0
4	-50	-41
5	-100	-92

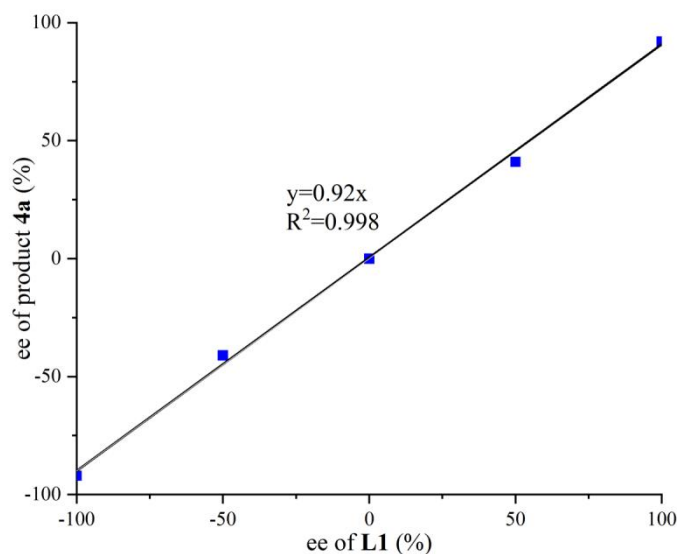


Figure S9. Relationship between ee values of ligand **L1** and product **4a**.

In a flame-dried 10.0 mL Schlenk quartz tube equipped with a magnetic stir bar was charged sequentially with $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (0.9 mg, 2.5 μmol) and **L1** (1.1 mg, 3.0 μmol) under Ar atmosphere, followed by the addition of super dry *N,N*-Dimethylformamide (0.5 mL). Then the mixture was stirred at room temperature for 30 min. To the resulting mixture was added PTH-1 (0.01 mmol, 10 mol%), **1a** (0.1 mmol, 1.0 equiv), **2a** (0.2 mmol, 2.0 equiv), TMSCN (0.15 mmol, 1.5 equiv) and super dry acetonitrile (1.5 mL) under Ar. The mixture was stirred at a distance of 2~3 cm from a 410 nm LEDs at room temperature for about 24 h until the reaction completed, as monitored by TLC analysis. The concentrated reaction residue was purified by flash column chromatography on silica gel with petroleum ether/ethyl acetate (10:1) as eluent to give corresponding product. The purified product **4a** was analyzed by chiral HPLC.

7. DFT calculation

DFT calculations were performed with the Gaussian 16 software package.^[27] All geometry optimizations of compounds were achieved using M06-2X functional and the Def2-TZVP basis set. Frequency calculations were also conducted at the same level of theory to obtain vibrational frequencies and thermal corrections to enthalpy at 298 K. The carbon–halogen bond dissociation energies (BDEs) of a series of difluoroalkyl halides (F, Cl, Br and I) were obtained: 119.2 kcal mol⁻¹ (C–F, PhCF_2F), 78.4 kcal mol⁻¹ (C–Cl, PhCF_2Cl), 62.3 kcal mol⁻¹ (C–Br, PhCF_2Br), and 44.7 kcal mol⁻¹ [C–I, PhCF_2I].

PhCF₃

C	-0.96100281	0.30638046	0.00401074
C	-1.67115081	-0.88854454	0.00410674
C	-3.05544681	-0.87010154	0.00404074
C	-3.72548081	0.34770346	0.00407474
C	-3.02399581	1.54246546	0.00402574
C	-1.63539881	1.51773746	0.00405574
H	0.12105919	0.29082946	0.00403174
H	-1.14493581	-1.83370454	0.00422174
H	-3.61934381	-1.79438254	0.00401174
H	-3.55771181	2.48260746	0.00405374
H	-1.08222881	2.44742746	0.00413374
C	-5.22766181	0.33261346	0.00426574
F	-5.75187081	1.56141346	0.00423674
F	-5.71429881	-0.30528954	-1.06989326
F	-5.71453881	-0.30568054	1.07759474

Zero-point correction= 0.106441 (Hartree/Particle)

Thermal correction to Energy= 0.114275

Thermal correction to Enthalpy= 0.115219

Thermal correction to Gibbs Free Energy= 0.070879

Sum of electronic and zero-point Energies= -569.211720

Sum of electronic and thermal Energies= -569.203886

Sum of electronic and thermal Enthalpies= -569.202942

Sum of electronic and thermal Free Energies= -569.247283

PhCF₂Cl

C	-0.26462396	0.54317548	0.00000000
C	0.42130104	-0.65968152	0.09926300
C	1.79351304	-0.66344452	0.29728500
C	2.47197704	0.54311748	0.39871700

C	1.79355504	1.74968948	0.29733600
C	0.42132204	1.74598948	0.09931100
H	-1.33572496	0.54315648	-0.15401000
H	-0.11275496	-1.59748652	0.02394700
H	2.33622404	-1.59583052	0.37759500
H	2.33627004	2.68207348	0.37766500
H	-0.11265696	2.68384048	0.02404200
C	3.96103904	0.54313048	0.58931400
F	4.36956904	1.62122848	1.27342500
F	4.36957704	-0.53504952	1.27330800
Cl	4.82271204	0.54319448	-0.97440900
Zero-point correction=			0.104554 (Hartree/Particle)
Thermal correction to Energy=			0.112753
Thermal correction to Enthalpy=			0.113697
Thermal correction to Gibbs Free Energy=			0.069890
Sum of electronic and zero-point Energies=			-929.545855
Sum of electronic and thermal Energies=			-929.537655
Sum of electronic and thermal Enthalpies=			-929.536711
Sum of electronic and thermal Free Energies=			-929.580519\
PhCF ₂ Br			
C	-2.18662957	0.59883454	0.00783917
C	-2.84835357	1.80182154	0.21325917
C	-4.17186857	1.80606354	0.62550217
C	-4.82573957	0.59937254	0.83450217
C	-4.17191957	-0.60758846	0.62691017
C	-2.84840457	-0.60388346	0.21466217
H	-1.15327857	0.59862554	-0.31324083
H	-2.33292157	2.73954954	0.05415517
H	-4.69545657	2.73854154	0.78872717
H	-4.69554657	-1.53985346	0.79122317

H	-2.33301157	-1.54181746	0.05665017
C	-6.25889257	0.59965054	1.27017317
F	-6.55393157	-0.47797146	2.00781917
F	-6.55393157	1.67819654	2.00646417
Br	-7.47711257	0.59867554	-0.27226683
Zero-point correction=			0.103857 (Hartree/Particle)
Thermal correction to Energy=			0.112343
Thermal correction to Enthalpy=			0.113287
Thermal correction to Gibbs Free Energy=			0.067975
Sum of electronic and zero-point Energies=			-3043.538281
Sum of electronic and thermal Energies=			-3043.529794
Sum of electronic and thermal Enthalpies=			-3043.528850
Sum of electronic and thermal Free Energies=			-3043.574163
PhCF ₂ I			
C	-1.82451257	0.02785277	0.00036461
C	-2.45795157	0.30996077	-1.20242639
C	-3.72487157	0.87227477	-1.20649139
C	-4.35155957	1.15470577	0.00039261
C	-3.72487857	0.87219977	1.20726361
C	-2.45795957	0.30988177	1.20317061
H	-0.83579057	-0.41184223	0.00035361
H	-1.96449157	0.09271577	-2.14033339
H	-4.22594557	1.09450377	-2.13921139
H	-4.22595757	1.09436877	2.13999461
H	-1.96450657	0.09257677	2.14106661
C	-5.72409957	1.74943677	0.00040761
F	-5.93373257	2.51641677	1.07987961
F	-5.93373257	2.51647677	-1.07902239
I	-7.26263757	0.20510677	0.00036761
Zero-point correction=			0.103424 (Hartree/Particle)

Thermal correction to Energy=	0.112078
Thermal correction to Enthalpy=	0.113022
Thermal correction to Gibbs Free Energy=	0.066878
Sum of electronic and zero-point Energies=	-766.971787
Sum of electronic and thermal Energies=	-766.963133
Sum of electronic and thermal Enthalpies=	-766.962189
Sum of electronic and thermal Free Energies=	-767.008333
PhCF ₂ (Free radical)	
C	-0.09749304 -1.00269969 -0.01312606
C	0.60439696 0.20222431 -0.01313306
C	1.98117196 0.21850631 -0.01312206
C	2.70034496 -1.00269869 -0.01310306
C	1.98117196 -2.22390569 -0.01309706
C	0.60439796 -2.20762469 -0.01310906
H	-1.17867204 -1.00270069 -0.01313406
H	0.06375496 1.13979331 -0.01315006
H	2.52304196 1.15411831 -0.01312806
H	2.52304396 -3.15951669 -0.01308406
H	0.06375396 -3.14519269 -0.01310606
C	4.08703196 -1.00270069 -0.01306906
F	4.82577396 -2.08914169 -0.01312206
F	4.82577296 0.08374331 -0.01313506
Zero-point correction=	0.100337 (Hartree/Particle)
Thermal correction to Energy=	0.107855
Thermal correction to Enthalpy=	0.108800
Thermal correction to Gibbs Free Energy=	0.067218
Sum of electronic and zero-point Energies=	-469.290040
Sum of electronic and thermal Energies=	-469.282521
Sum of electronic and thermal Enthalpies=	-469.281577
Sum of electronic and thermal Free Energies=	-469.323159

F (Free radical)

F	0.00000000	0.00000000	0.00000000
Zero-point correction=			0.000000 (Hartree/Particle)
Thermal correction to Energy=			0.001416
Thermal correction to Enthalpy=			0.002360
Thermal correction to Gibbs Free Energy=			-0.014813
Sum of electronic and zero-point Energies=			-99.733728
Sum of electronic and thermal Energies=			-99.732311
Sum of electronic and thermal Enthalpies=			-99.731367
Sum of electronic and thermal Free Energies=			-99.748541

Cl (Free radical)

Cl	0.00000000	0.00000000	0.00000000
Zero-point correction=			0.000000 (Hartree/Particle)
Thermal correction to Energy=			0.001416
Thermal correction to Enthalpy=			0.002360
Thermal correction to Gibbs Free Energy=			-0.015677
Sum of electronic and zero-point Energies=			-460.132584
Sum of electronic and thermal Energies=			-460.131168
Sum of electronic and thermal Enthalpies=			-460.130223
Sum of electronic and thermal Free Energies=			-460.148261

Br (Free radical)

Br	-0.66852369	0.30640668	0.00000000
Zero-point correction=			0.000000 (Hartree/Particle)
Thermal correction to Energy=			0.001416
Thermal correction to Enthalpy=			0.002360
Thermal correction to Gibbs Free Energy=			-0.016830
Sum of electronic and zero-point Energies=			-2574.150304
Sum of electronic and thermal Energies=			-2574.148888
Sum of electronic and thermal Enthalpies=			-2574.147944
Sum of electronic and thermal Free Energies=			-2574.167134

I (Free radical)

I	2.11699169	1.74079807	-0.02278830
Zero-point correction=			0.000000 (Hartree/Particle)
Thermal correction to Energy=			0.001416
Thermal correction to Enthalpy=			0.002360
Thermal correction to Gibbs Free Energy=			-0.017503
Sum of electronic and zero-point Energies=			-297.611788
Sum of electronic and thermal Energies=			-297.610372
Sum of electronic and thermal Enthalpies=			-297.609428
Sum of electronic and thermal Free Energies=			-297.629291

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9. Crystallographic Data of 4a (CCDC 2533995)

The crystal of **4a** was obtained through slow evaporation of a CH₂Cl₂/hexane solution of **4a** at room temperature. The molecular structure of **4a** was then determined by X-ray crystallography.

Data for the single-crystal structure determination were collected with Rigaku ROD, Synergy Custom DW system using Cu-K α radiation ($\lambda = 1.54184$ Å). Software packages used: Olex 2 for structure solution and refinement, and Mercury for graphics.

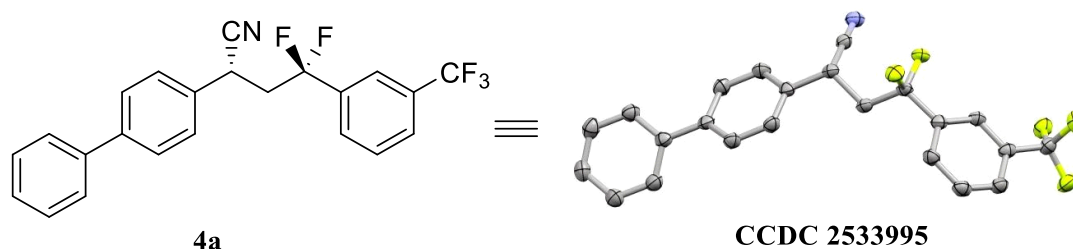


Figure S10. Molecular structure of **4a**. Thermal ellipsoids at 50% probability level, H atoms omitted for clarity.

Empirical formula	C ₂₃ H ₁₆ F ₅ N
Formula weight	401.37
Temperature/K	100.00(10)
Crystal system	triclinic
Space group	<i>P</i> 1
<i>a</i> /Å	6.6933(3)
<i>b</i> /Å	8.0103(3)
<i>c</i> /Å	17.6619(6)
α /°	95.624(3)
β /°	97.569(3)
γ /°	94.704(3)
Volume/Å ³	929.85(6)
<i>Z</i>	2

$\rho_{\text{calc}}/\text{cm}^3$	1.434
μ/mm^{-1}	1.020
F(000)	412.0
Crystal size/ mm^3	$0.06 \times 0.04 \times 0.03$
Radiation	$\text{CuK}\alpha$ ($\lambda = 1.54184$)
2Θ range for data collection/ $^\circ$	10.166 to 152.274
Index ranges	$-7 \leq h \leq 8, -9 \leq k \leq 10, -22 \leq l \leq 22$
Reflections collected	15188
Independent reflections	6607 [$R_{\text{int}} = 0.0465, R_{\text{sigma}} = 0.0436$]
Data/restraints/parameters	6607/3/523
Goodness-of-fit on F^2	1.080
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0535, wR_2 = 0.1527$
Final R indexes [all data]	$R_1 = 0.0559, wR_2 = 0.1547$
Largest diff. peak/hole / $\text{e } \text{\AA}^{-3}$	0.37/-0.31
Flack parameter	0.01(7)

10. NMR Spectra of Starting Materials and Products

Figure S11. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **2k**.

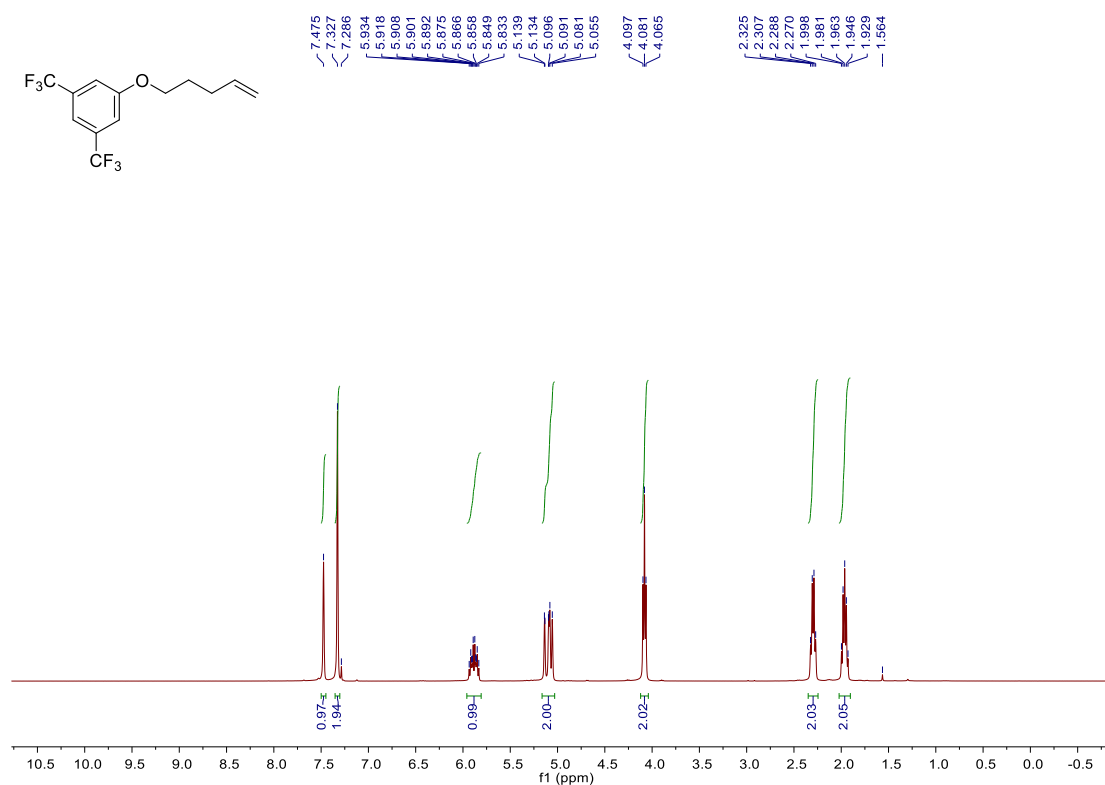


Figure S12. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **2k**.

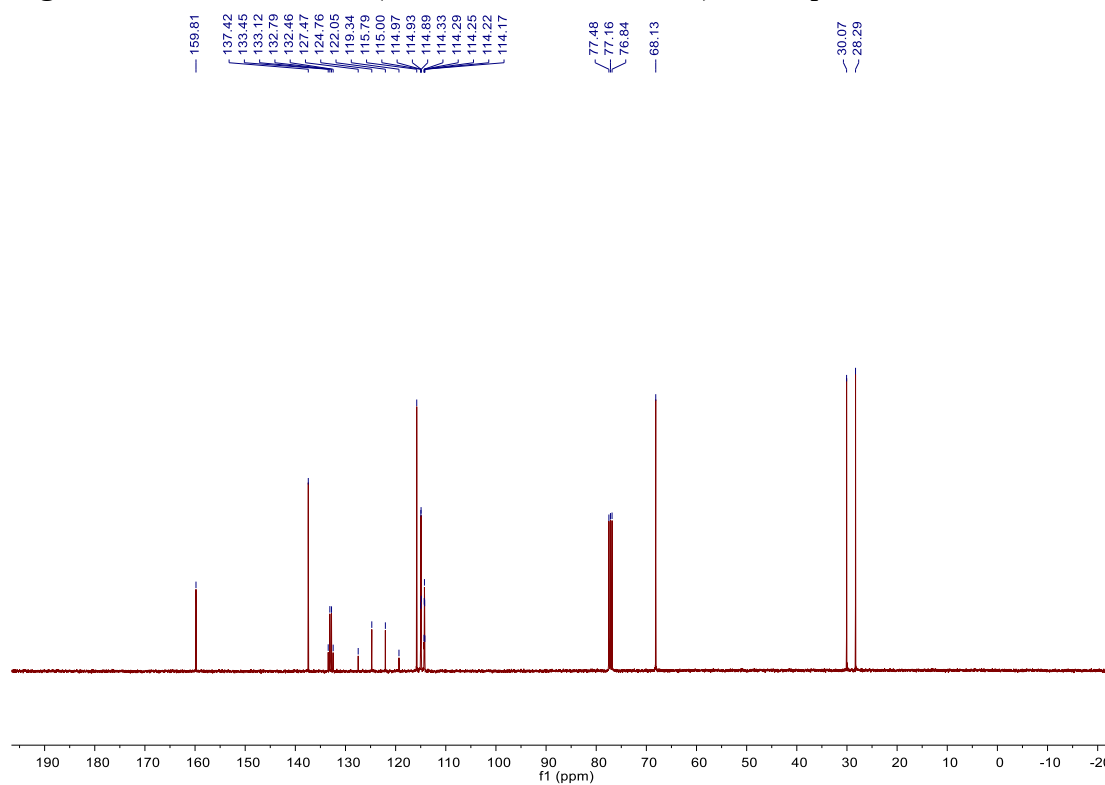


Figure S13. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **2k**.

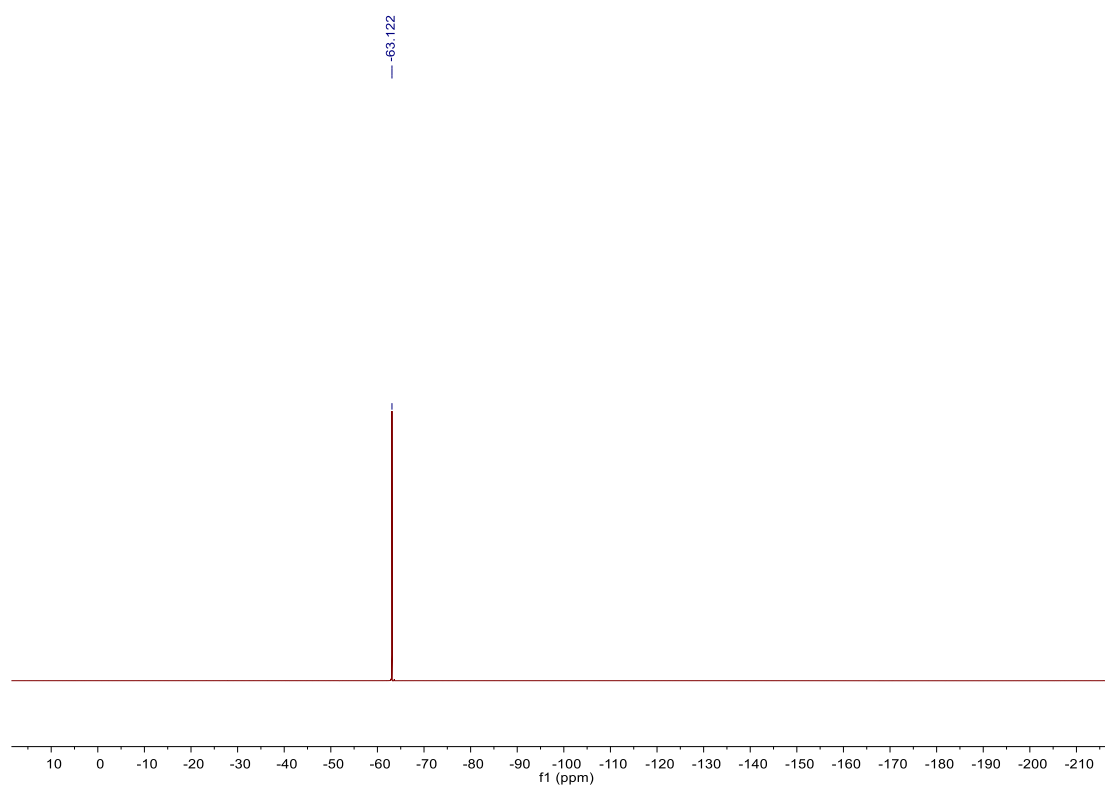


Figure S14. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **2m**.

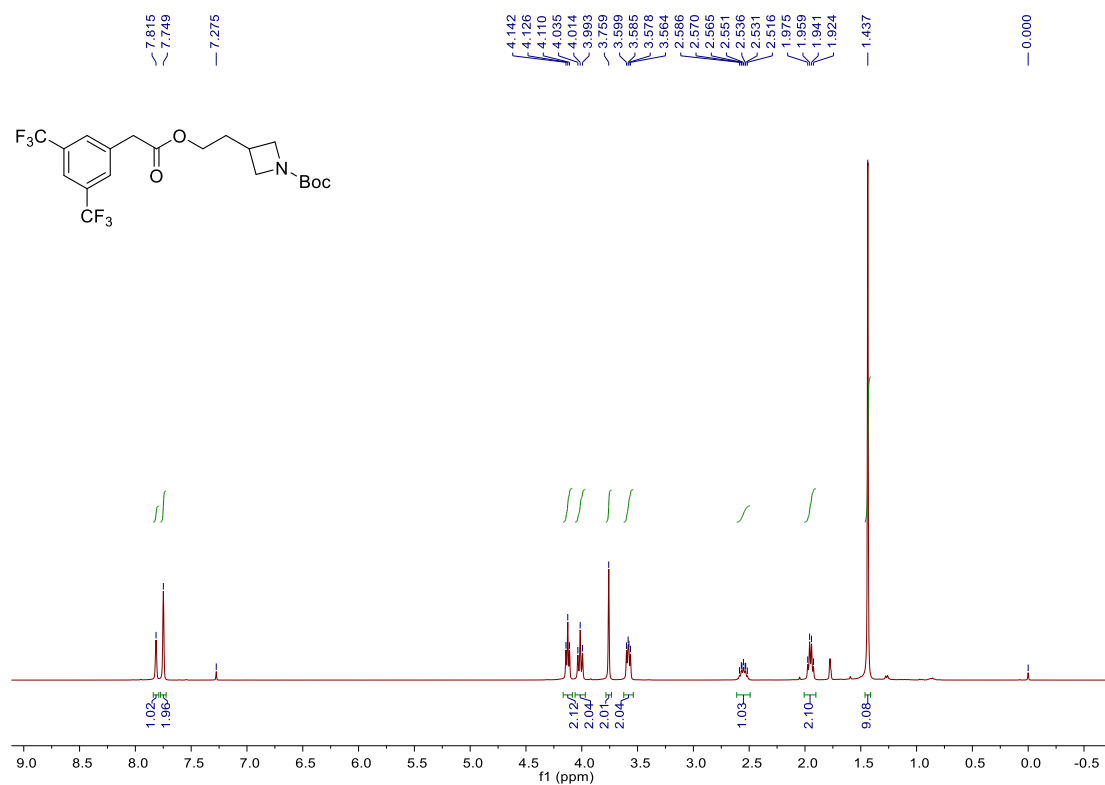


Figure S15. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **2m**.

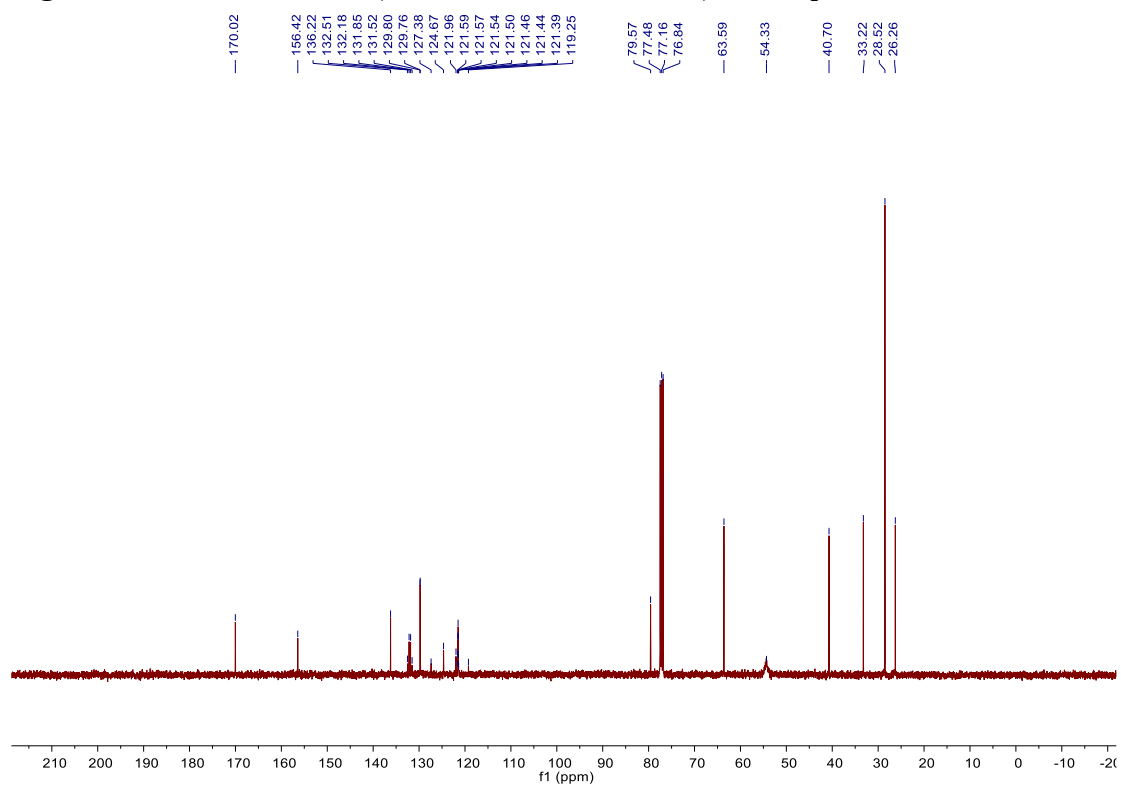


Figure S16. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **2m**.

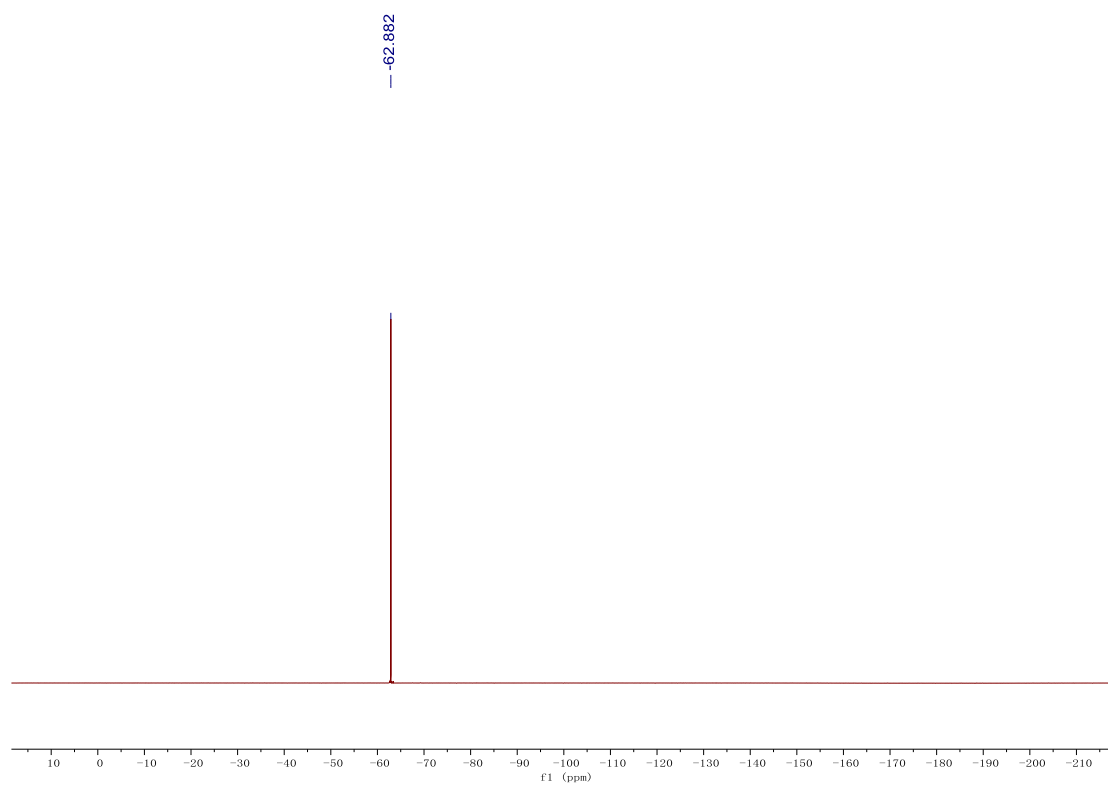


Figure S17. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4a**.

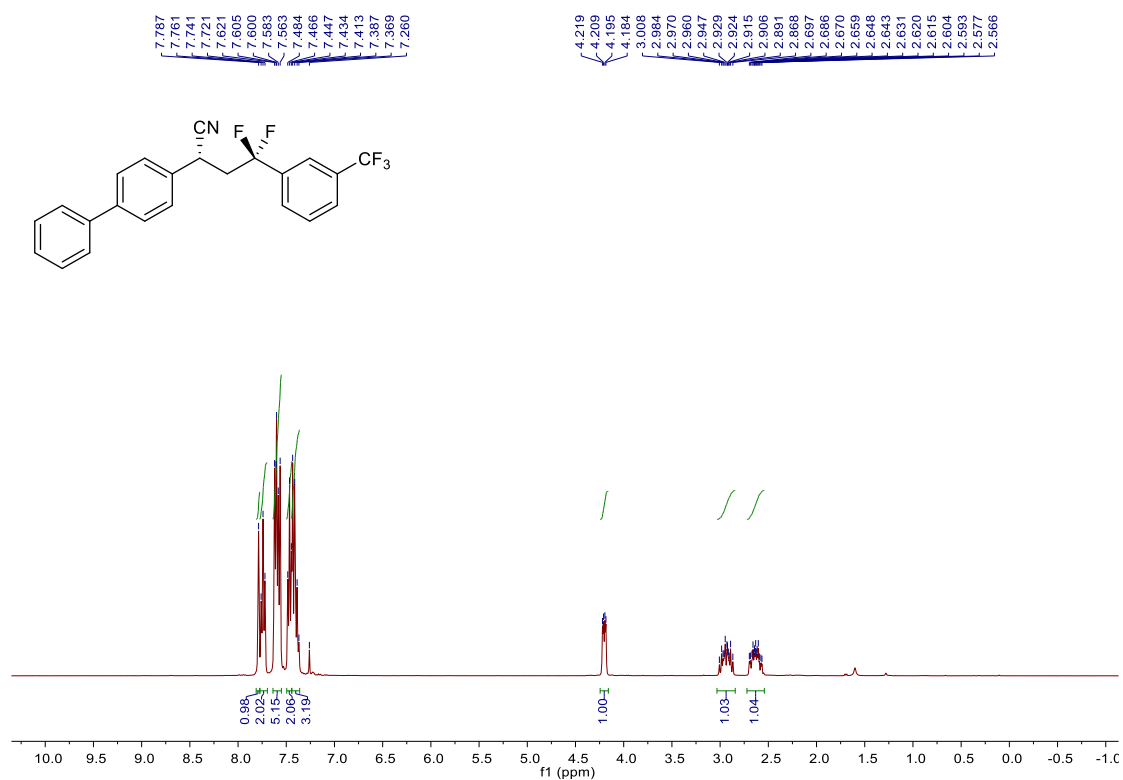


Figure S18. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4a**.

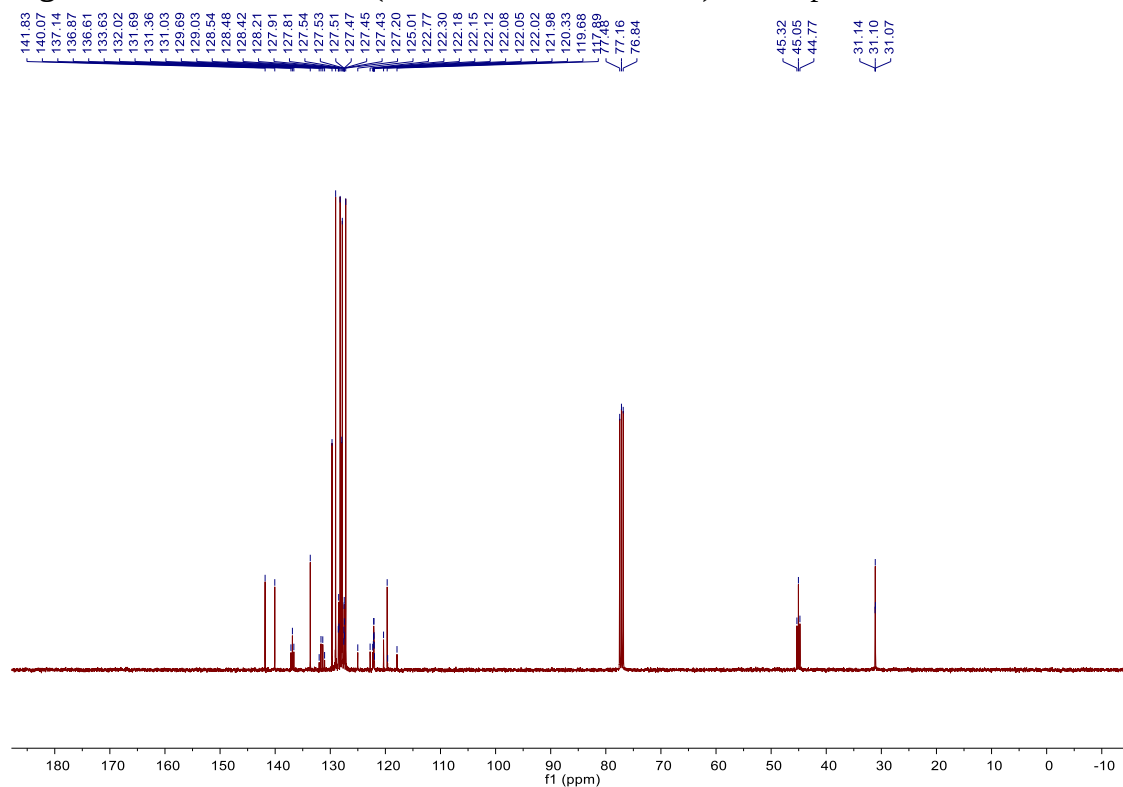


Figure S19. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4a**.

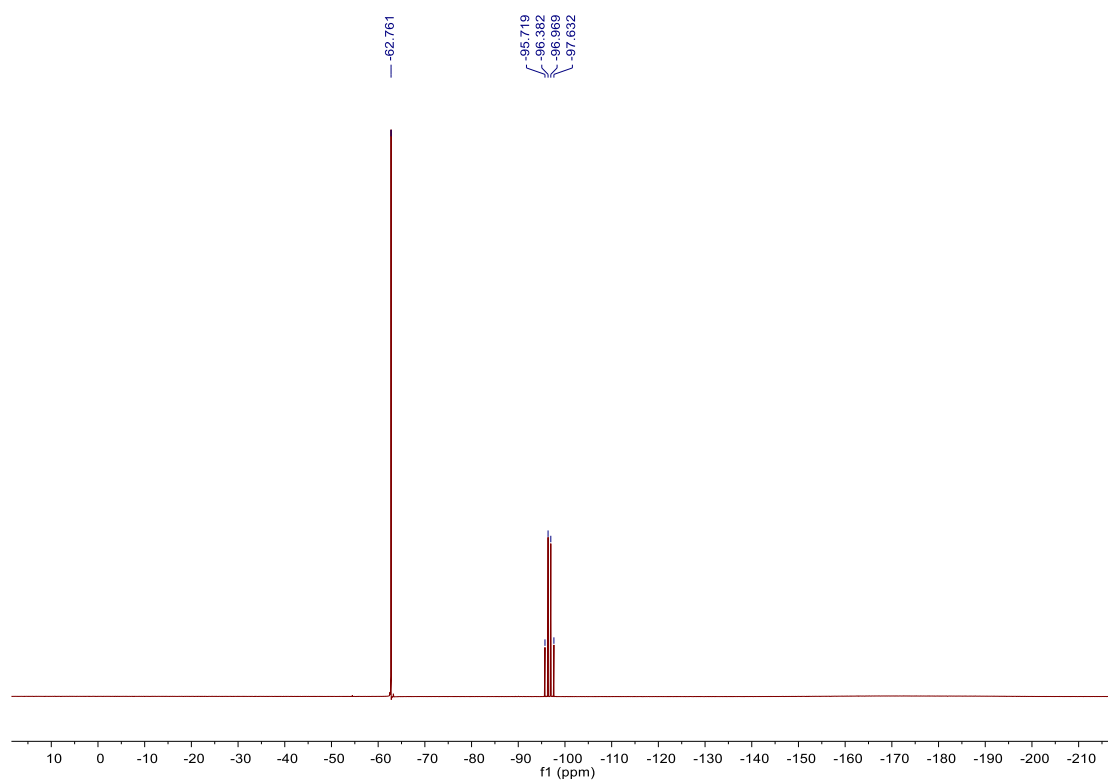


Figure S20. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4b**.

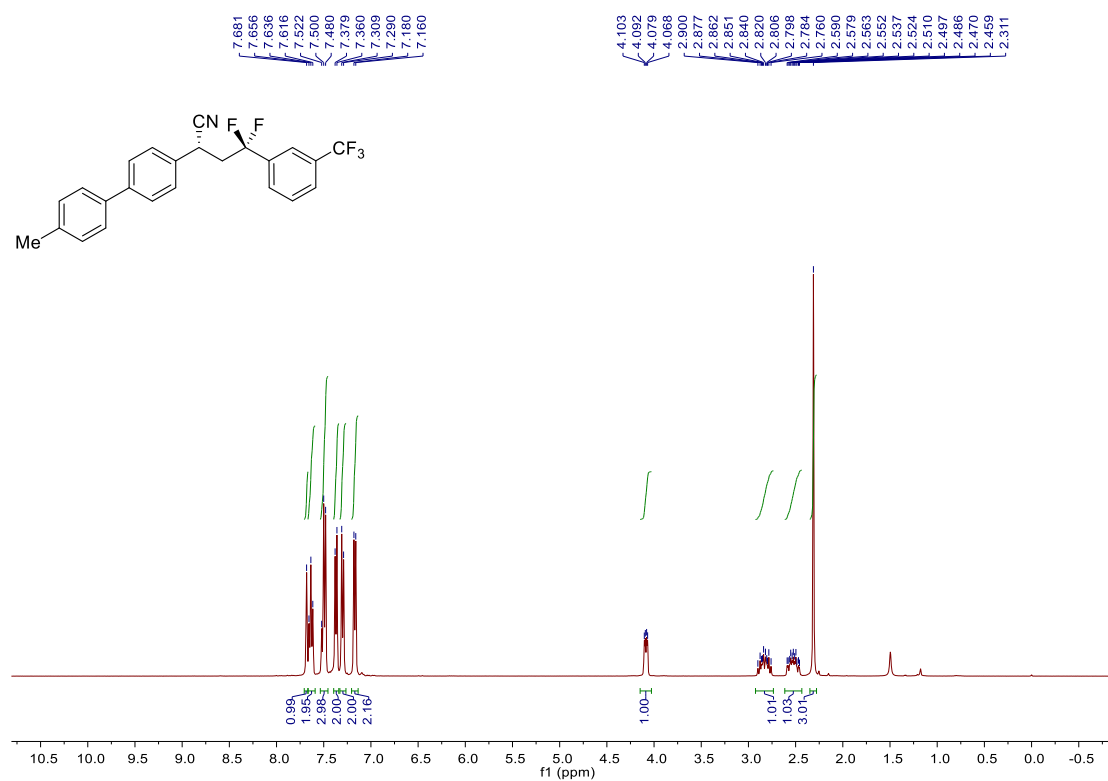


Figure S21. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4b**.

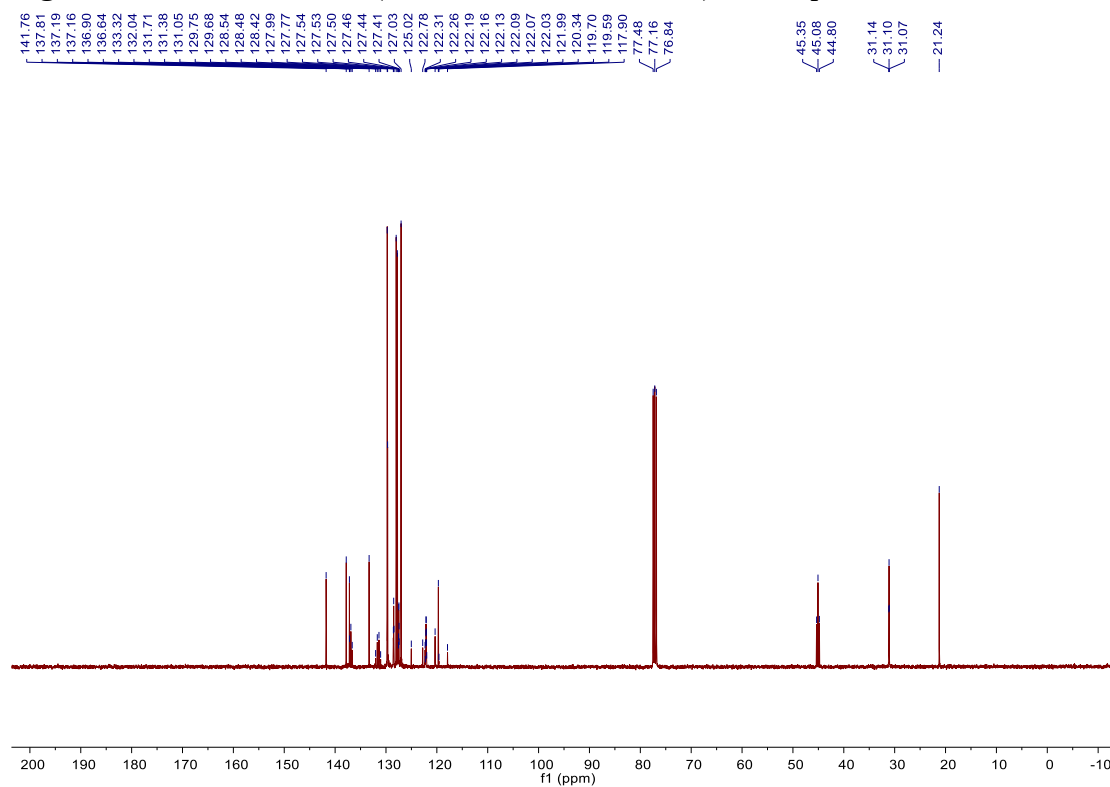


Figure S22. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4b**.

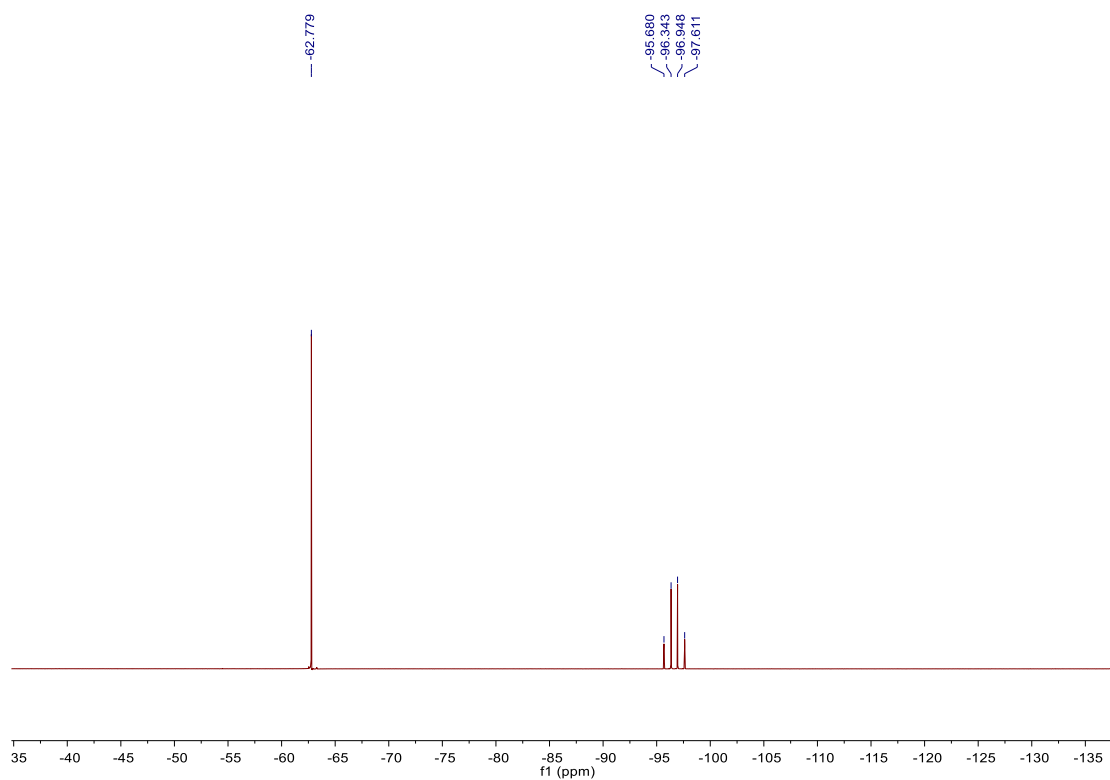


Figure S23. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound 4c.

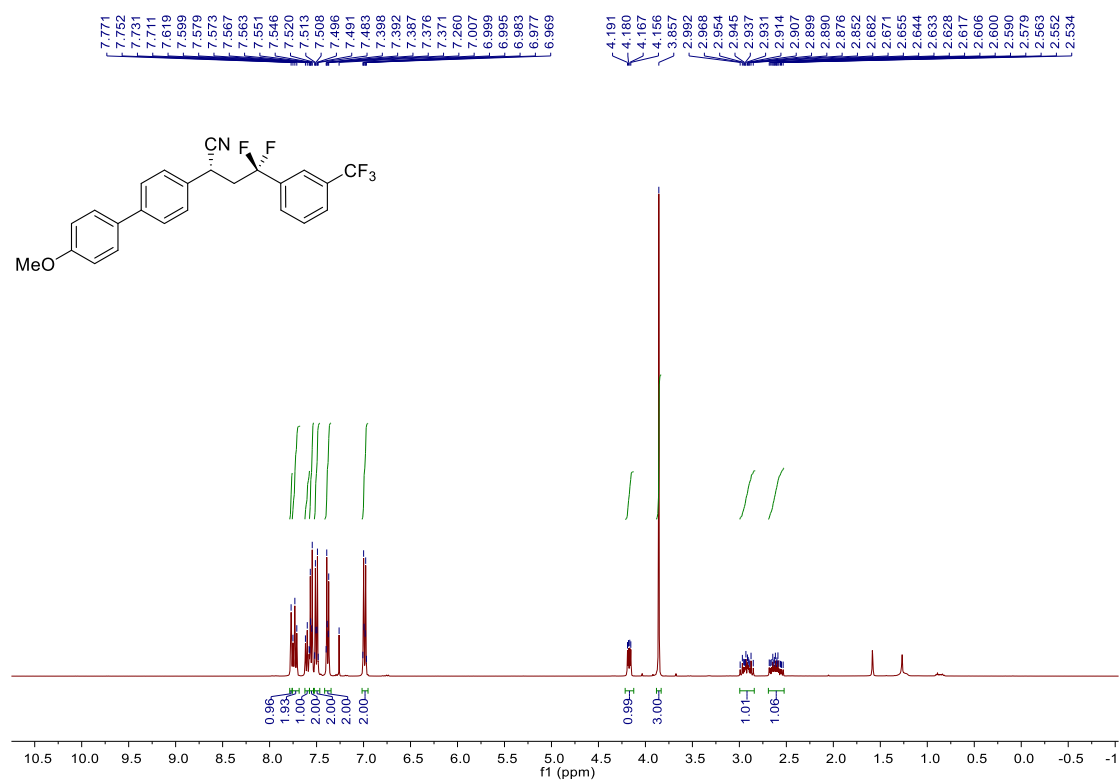


Figure S24. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound 4c.

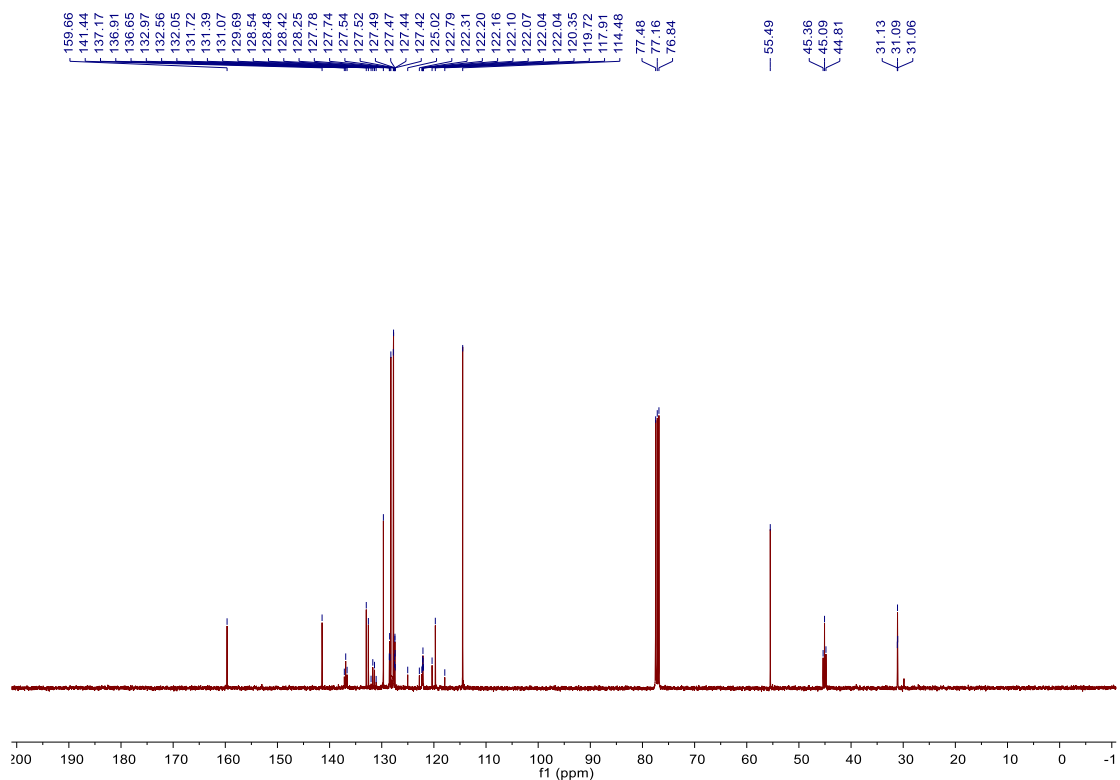


Figure S25. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4c**.

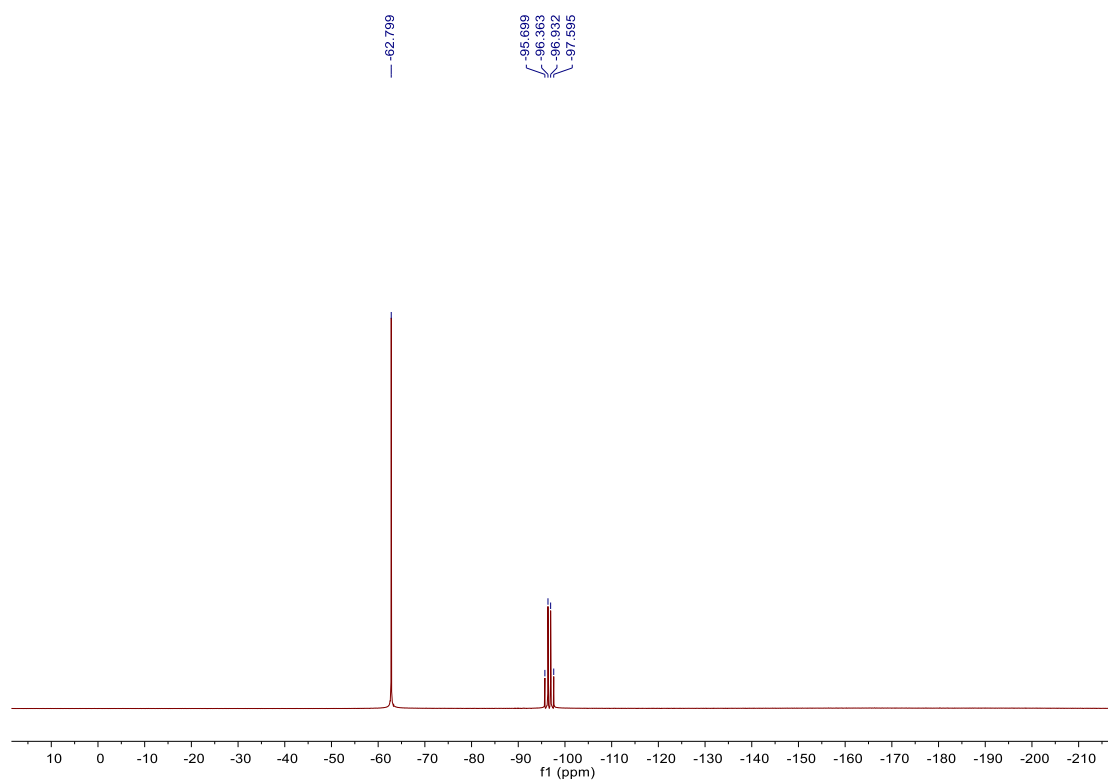


Figure S26. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4d**.

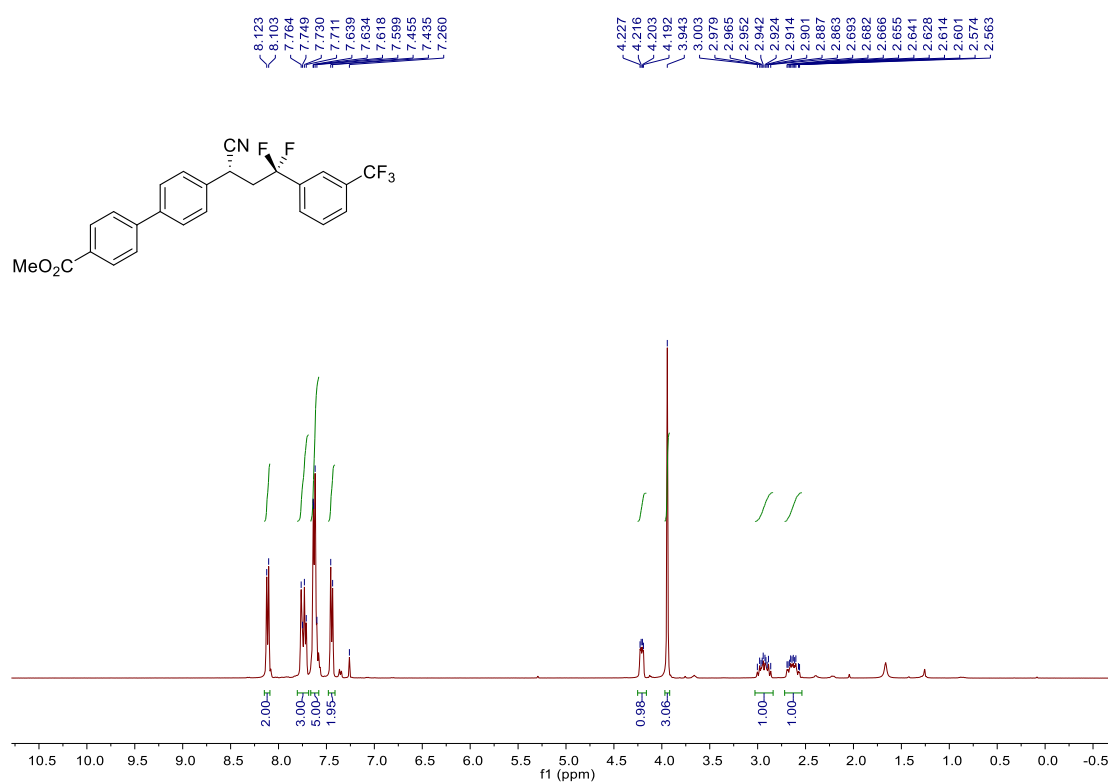


Figure S27. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4d**.

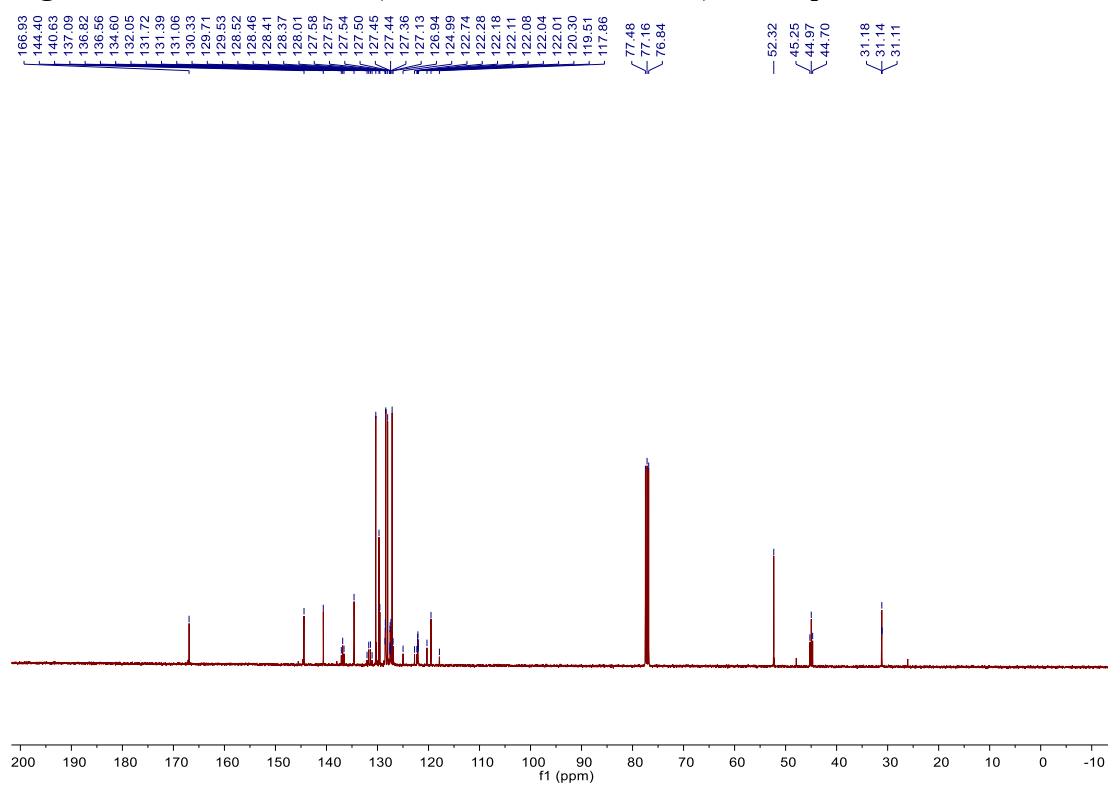


Figure S28. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4d**.

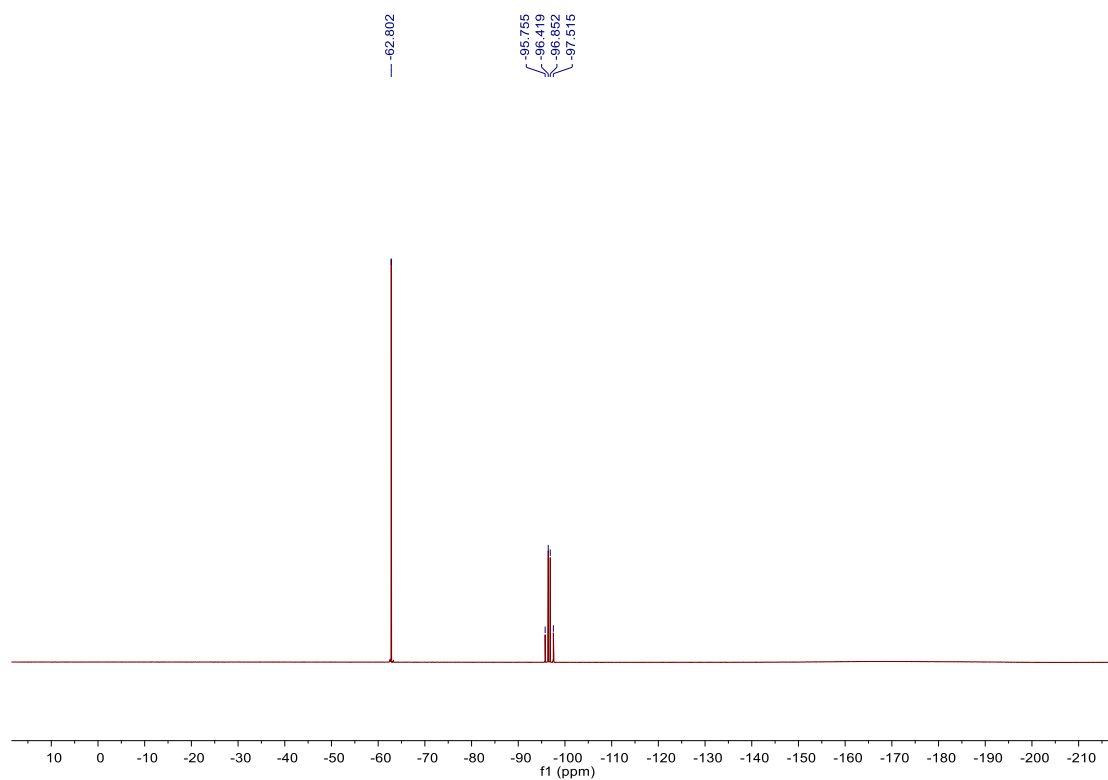


Figure S29. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4e**.

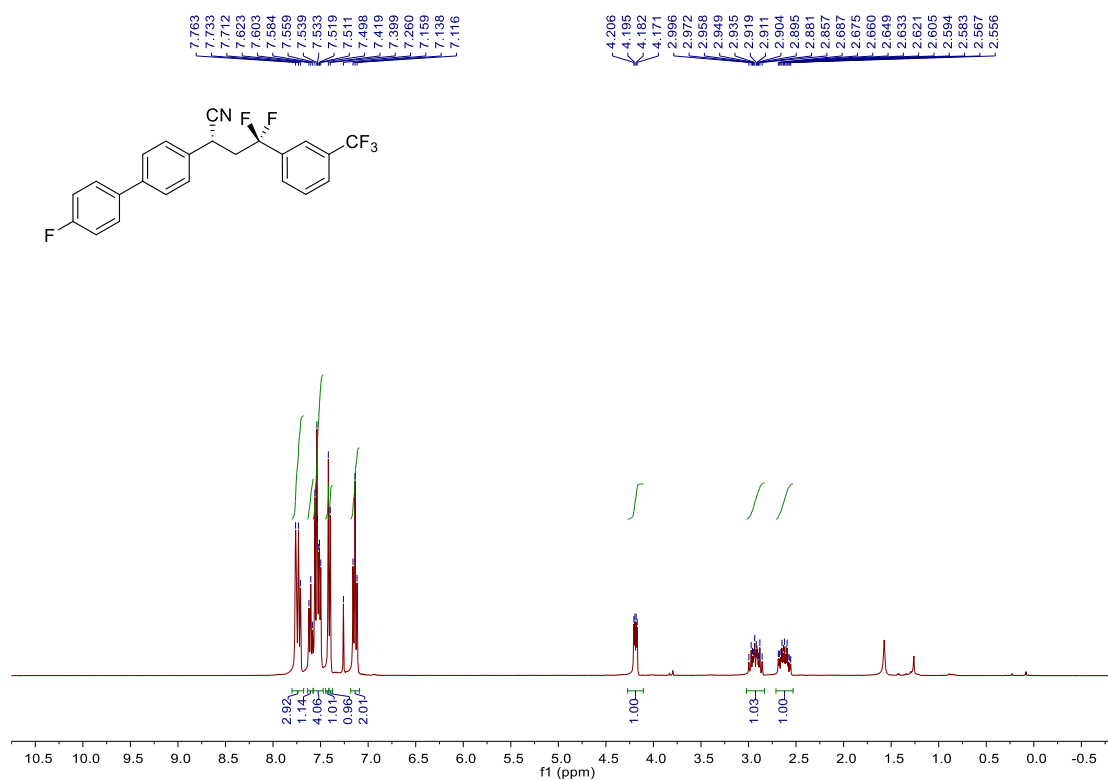


Figure S30. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4e**.

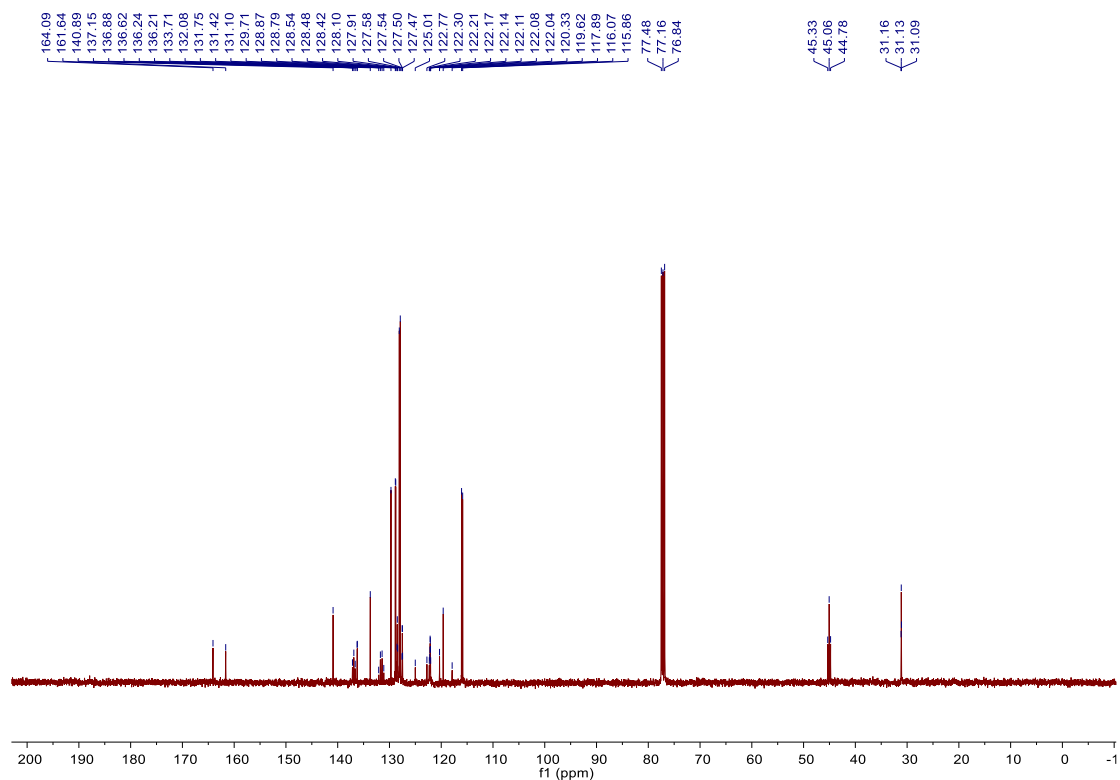


Figure S31. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4e**.

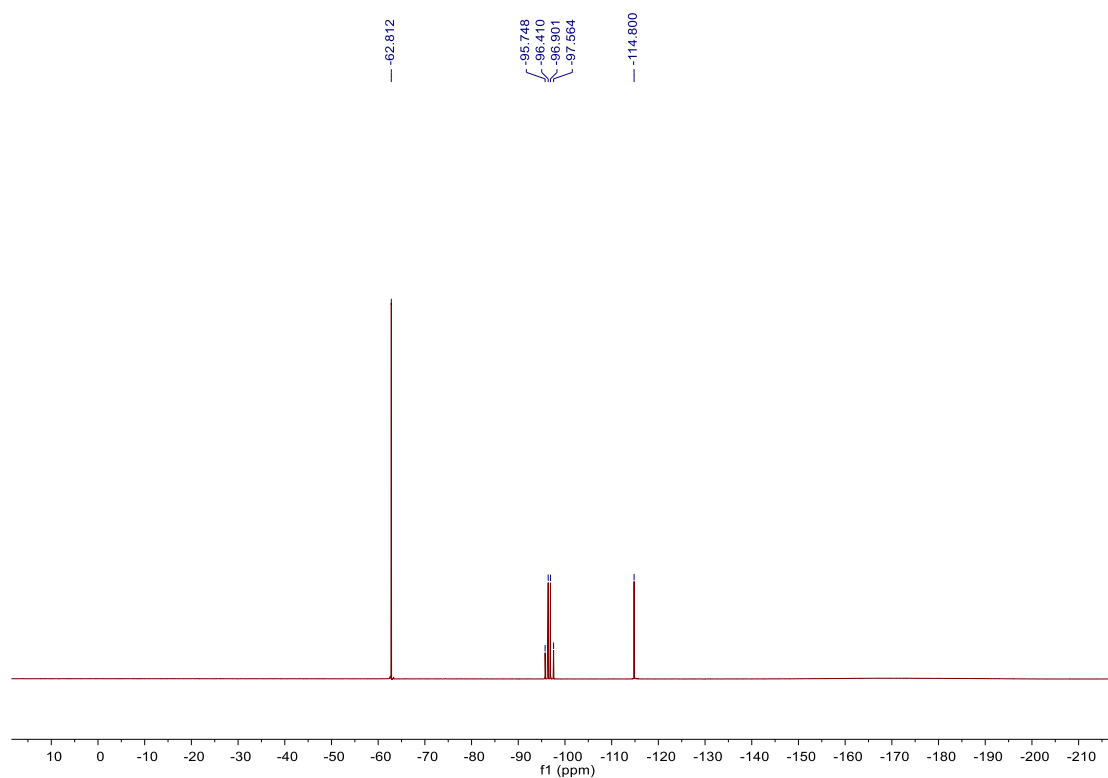


Figure S32. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4f**.

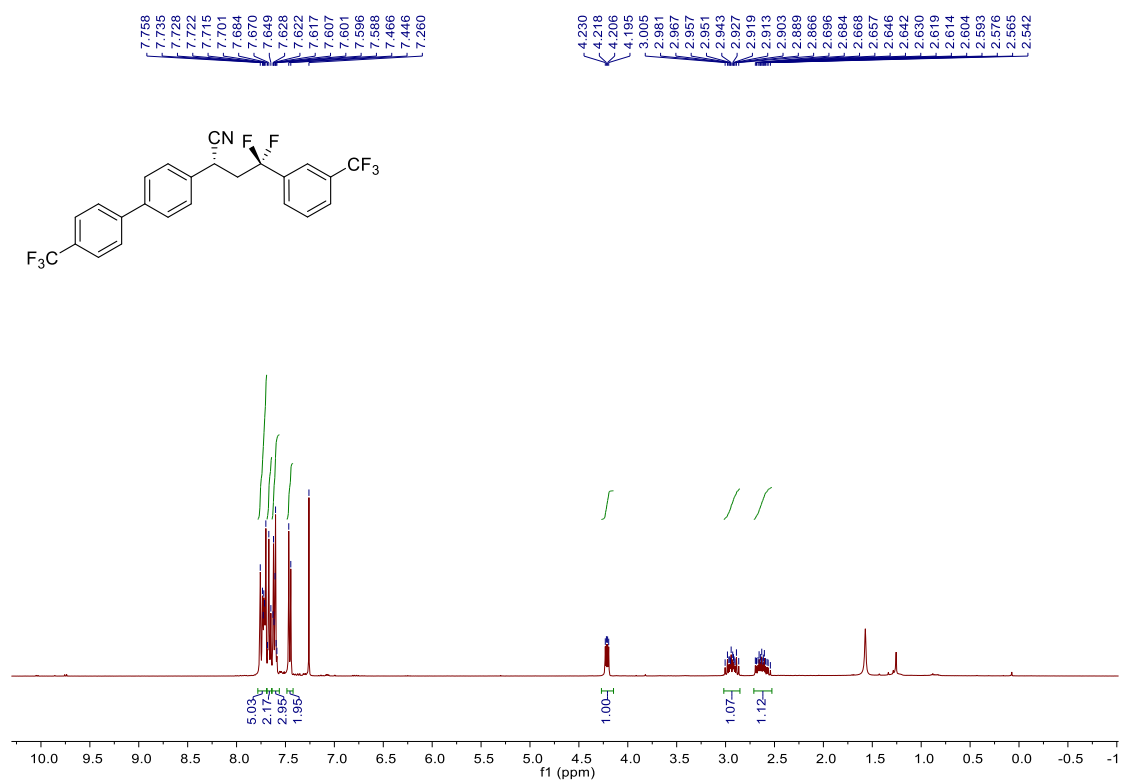


Figure S33. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4f**.

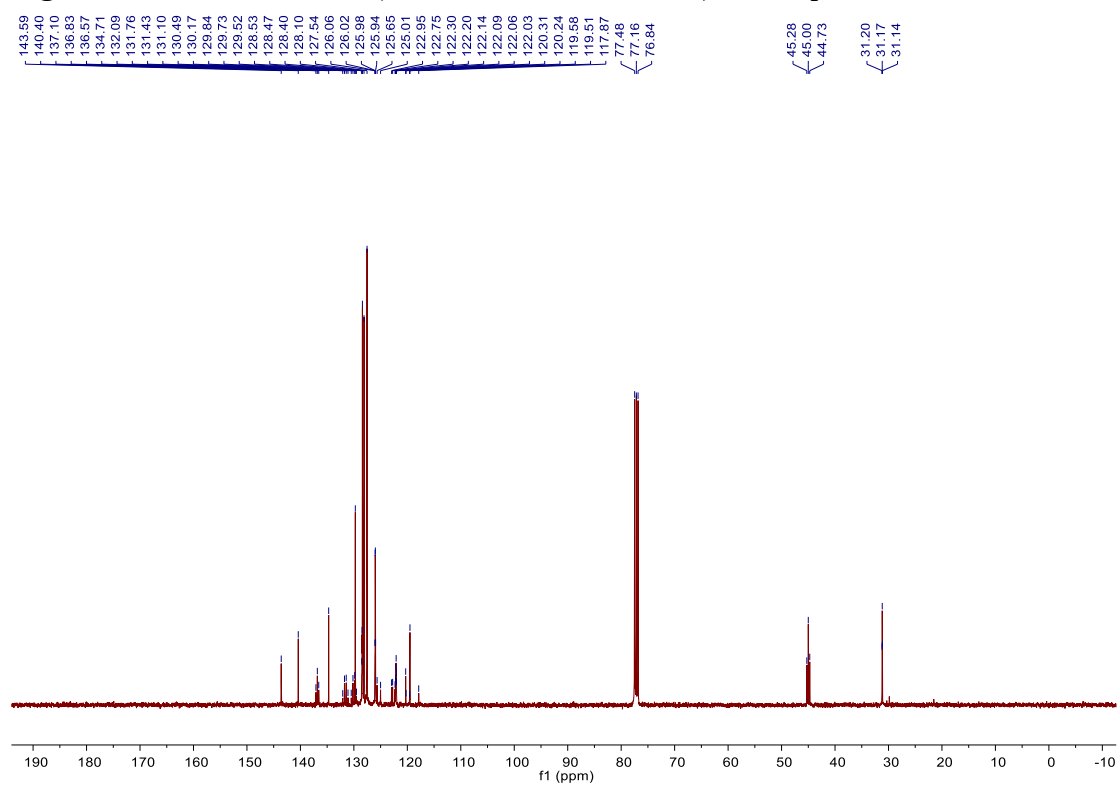


Figure S34. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4f**.

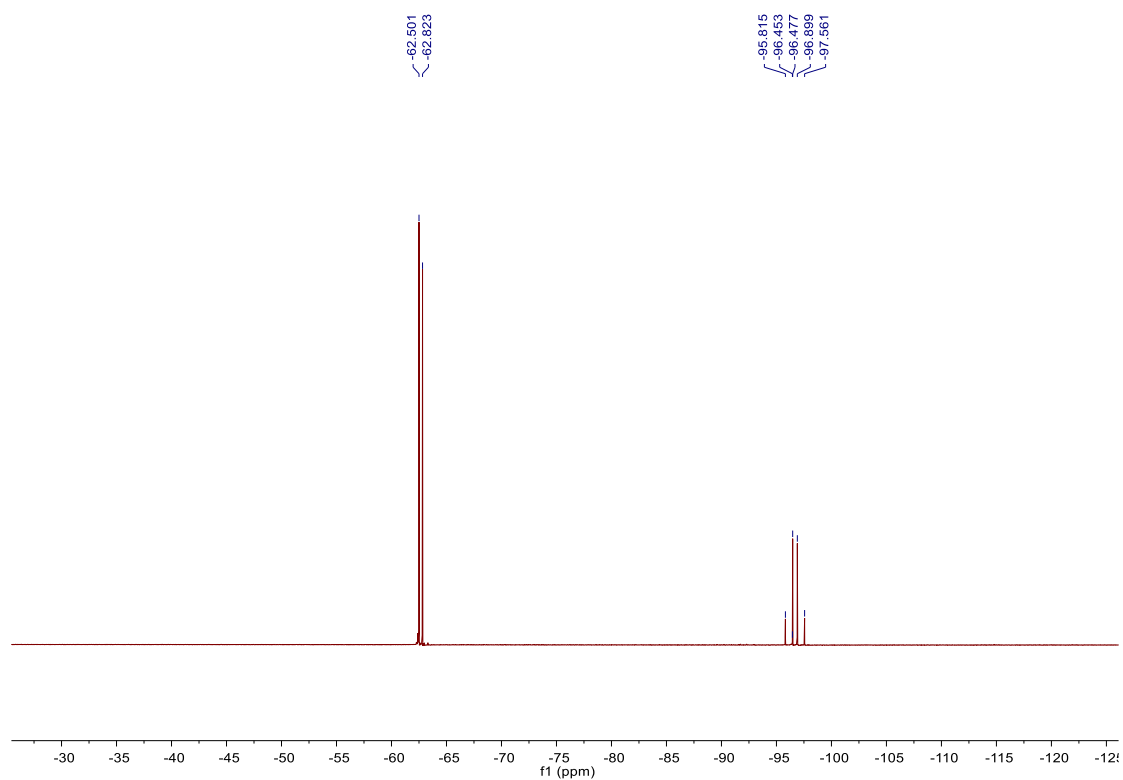


Figure S35. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4g**.

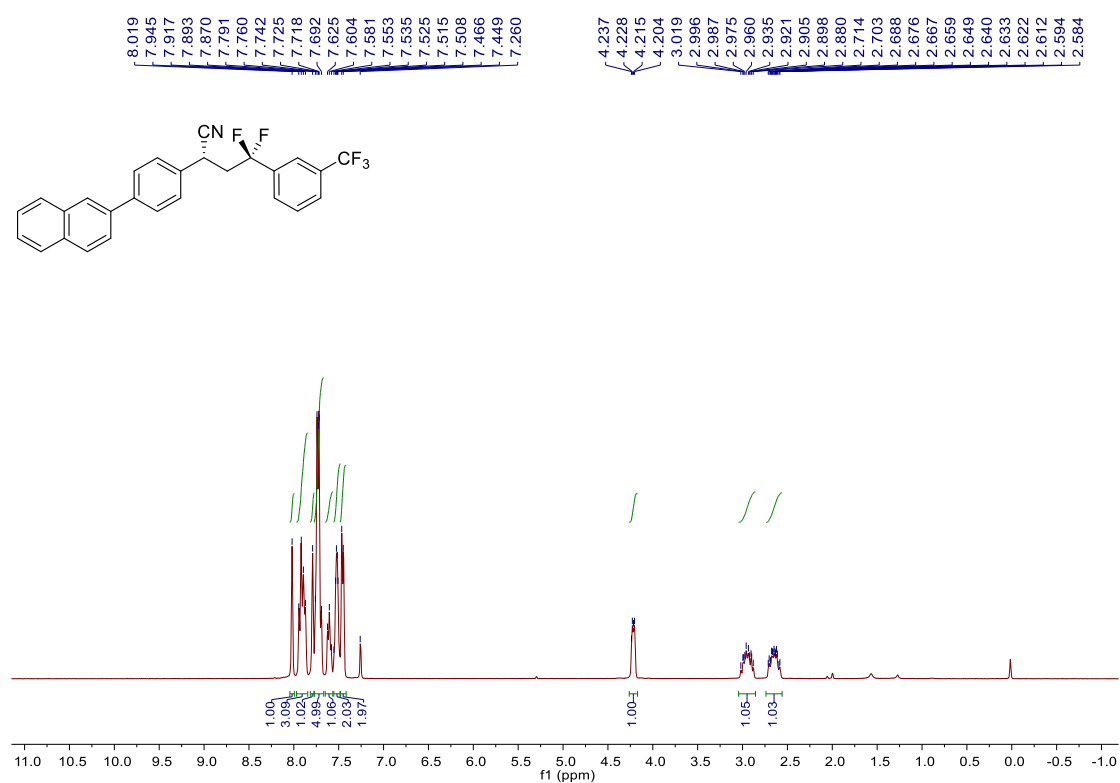


Figure S36. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4g**.

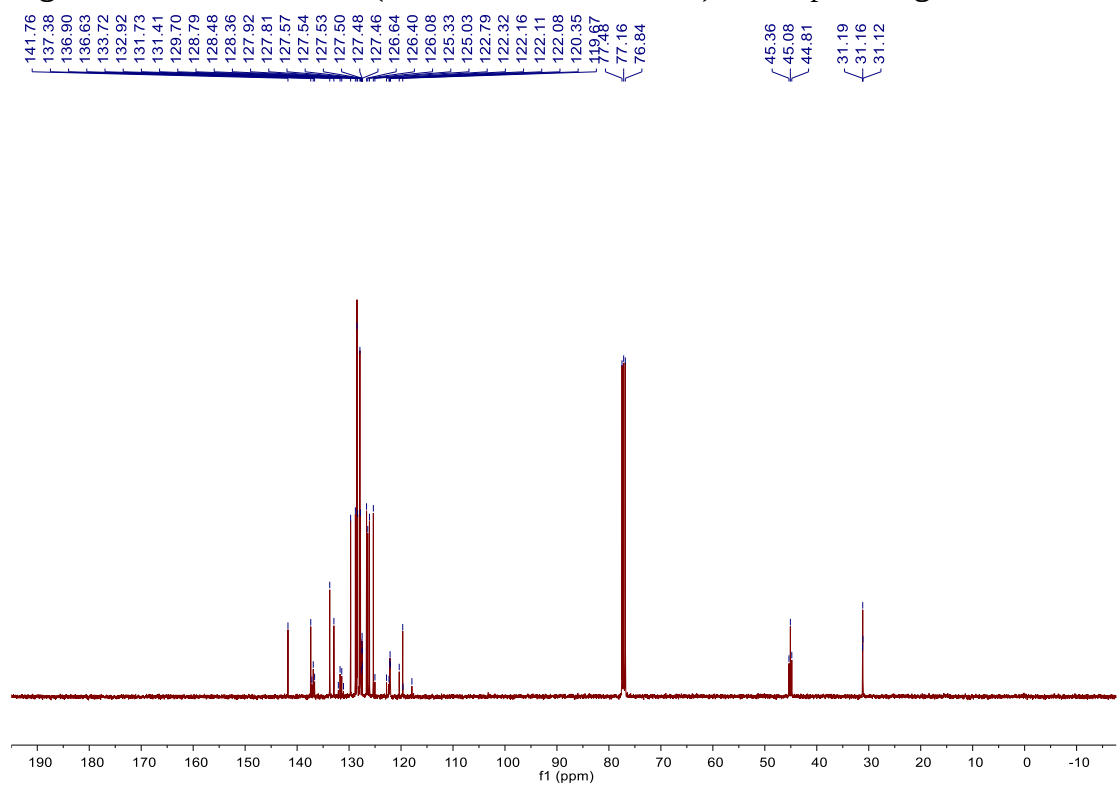


Figure S37. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4g**.

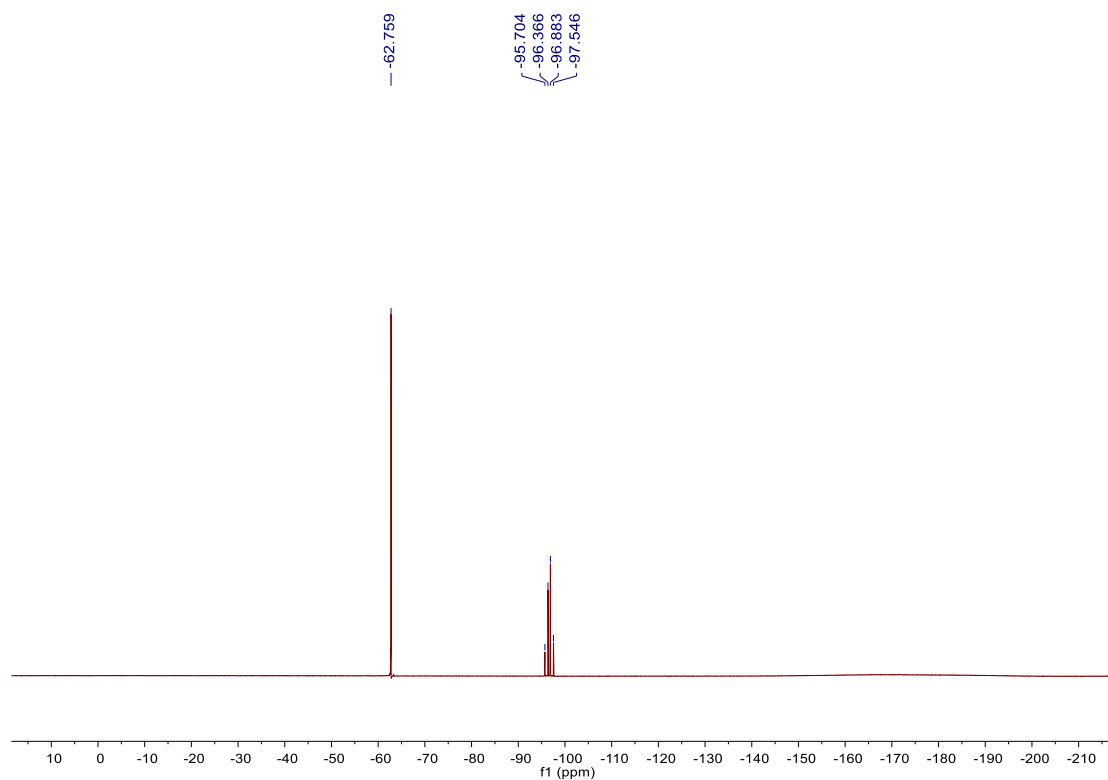


Figure S38. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4h**.

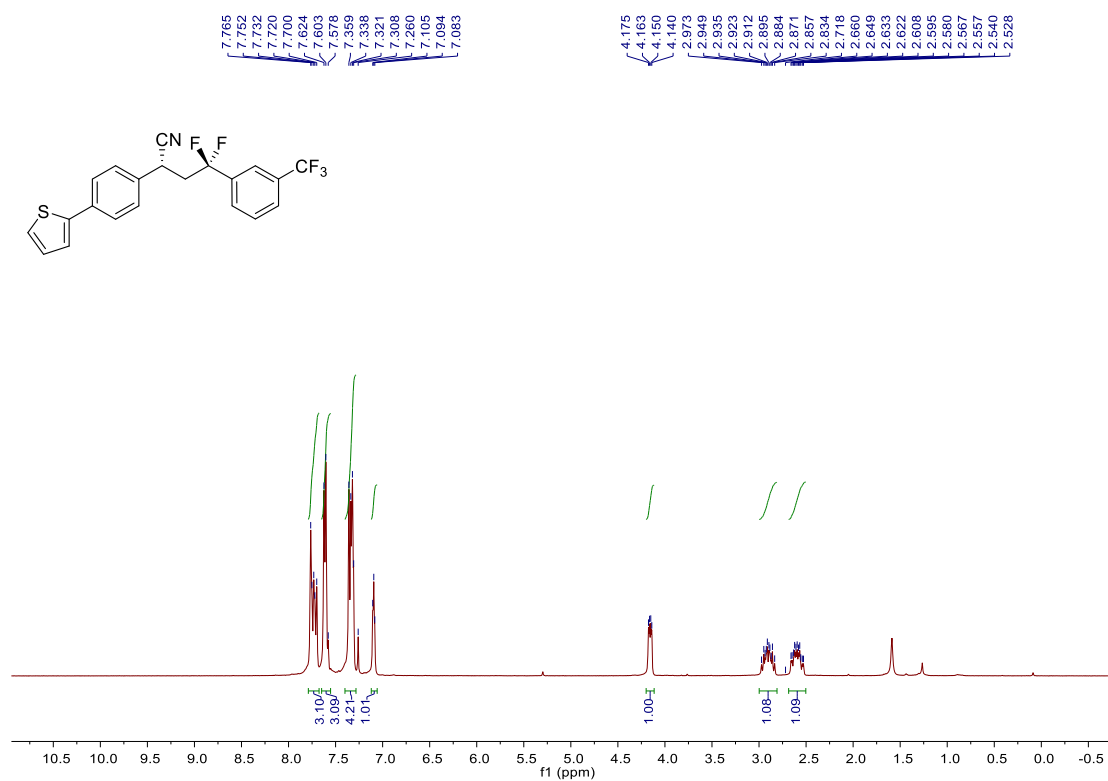


Figure S39. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4h**.

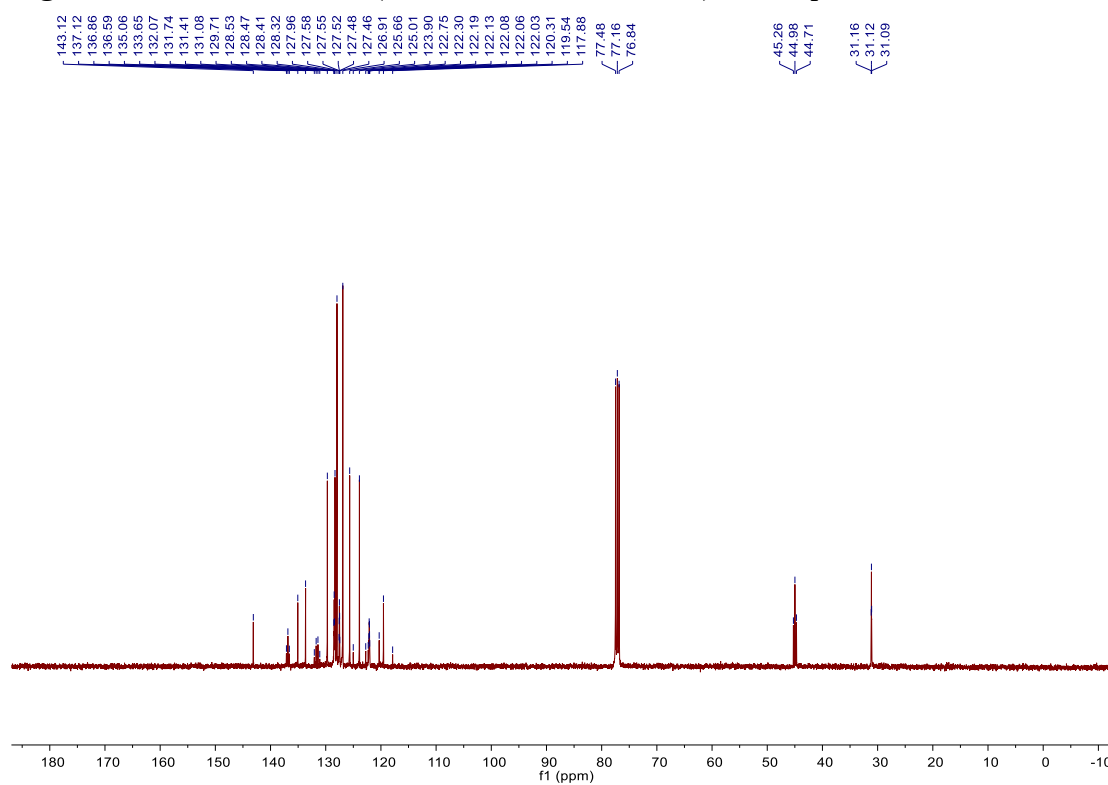


Figure S40. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4h**.

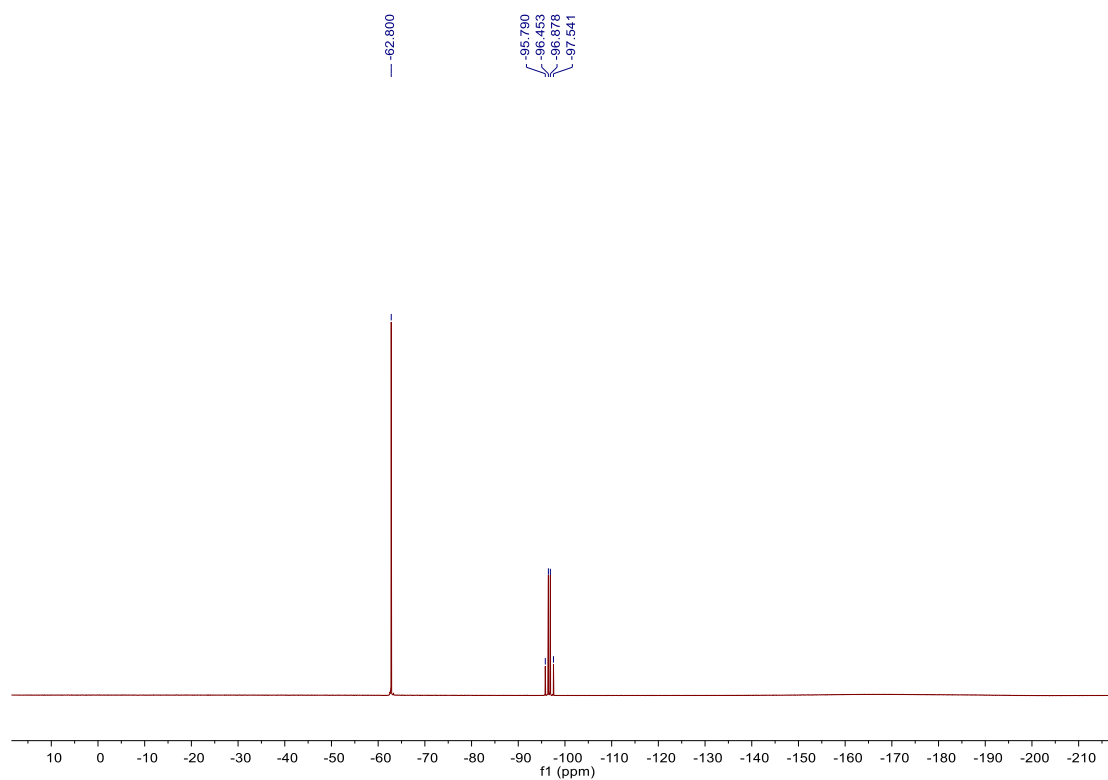


Figure S41. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4i**.

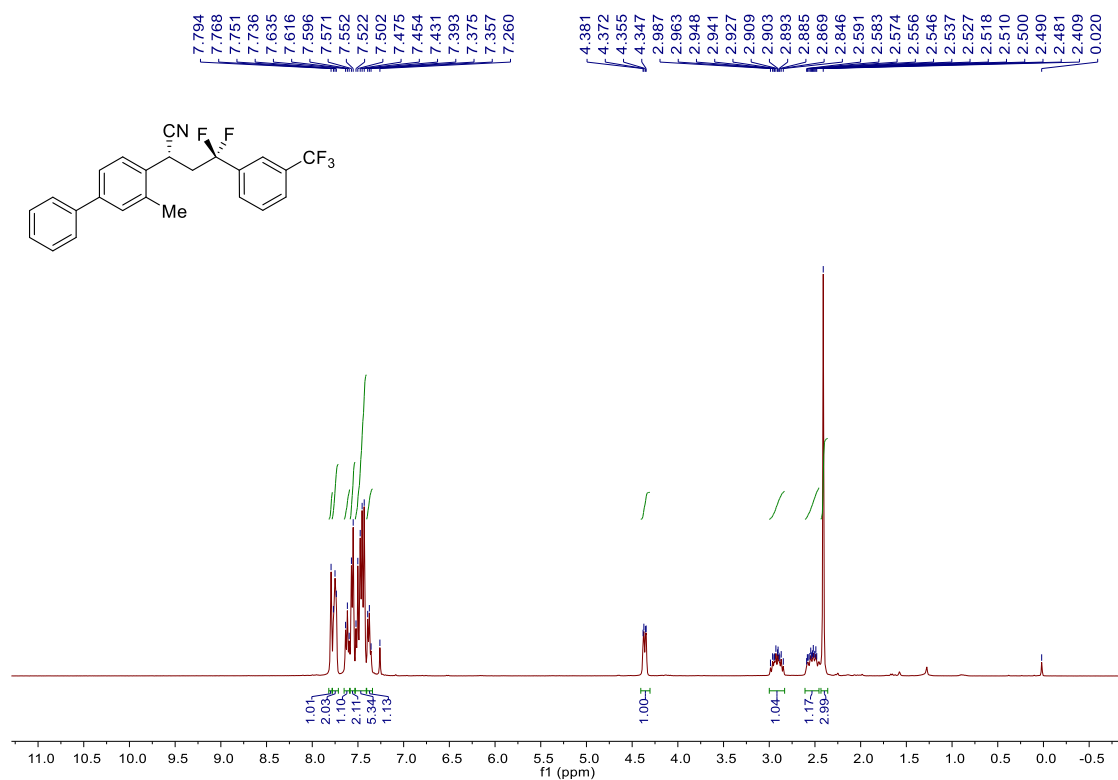


Figure S42. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4i**.

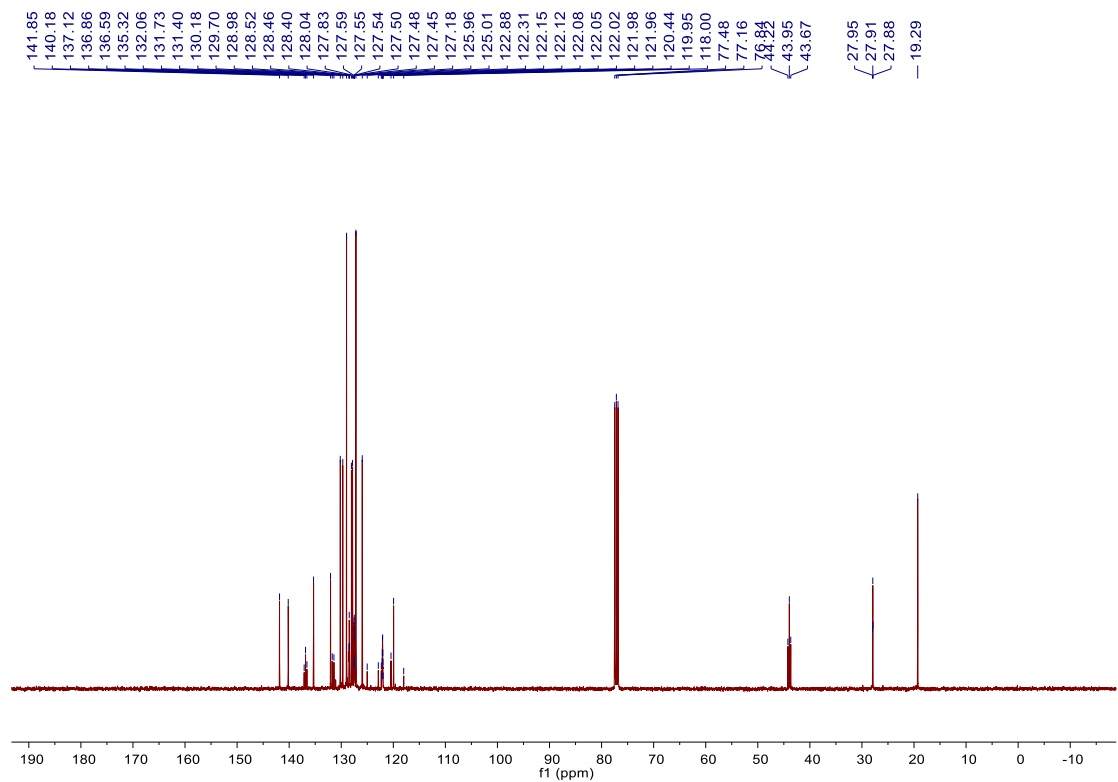


Figure S43. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4i**.

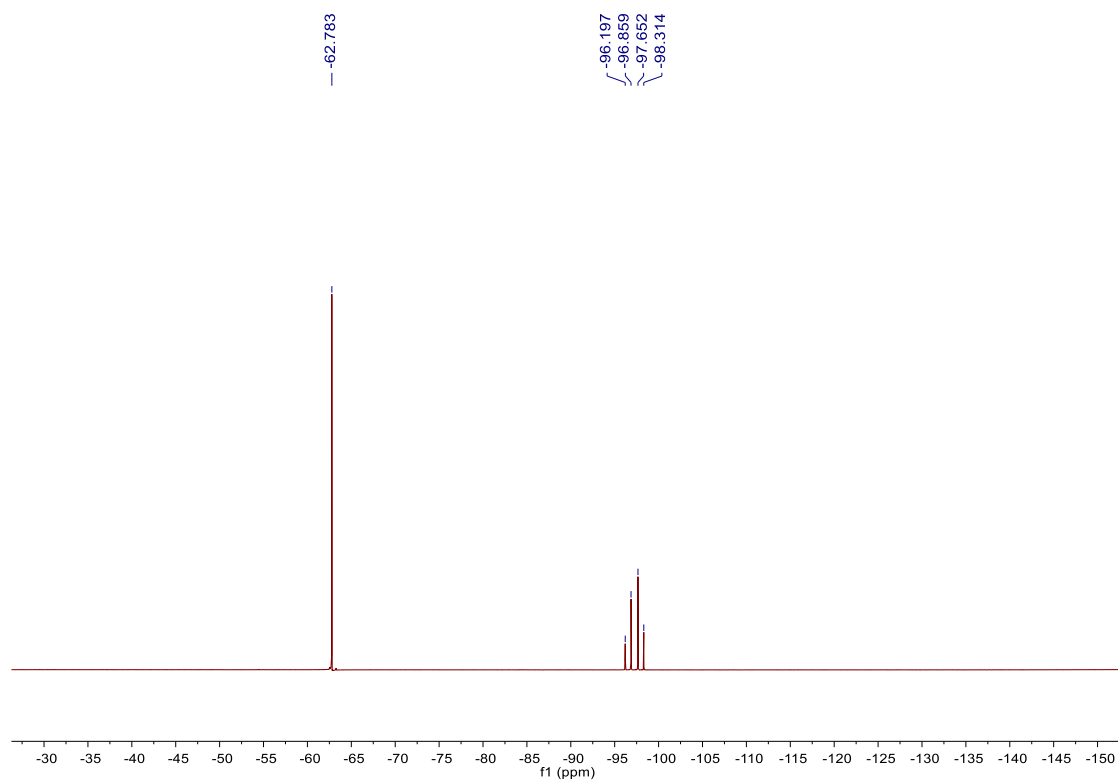


Figure S44. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4j**.

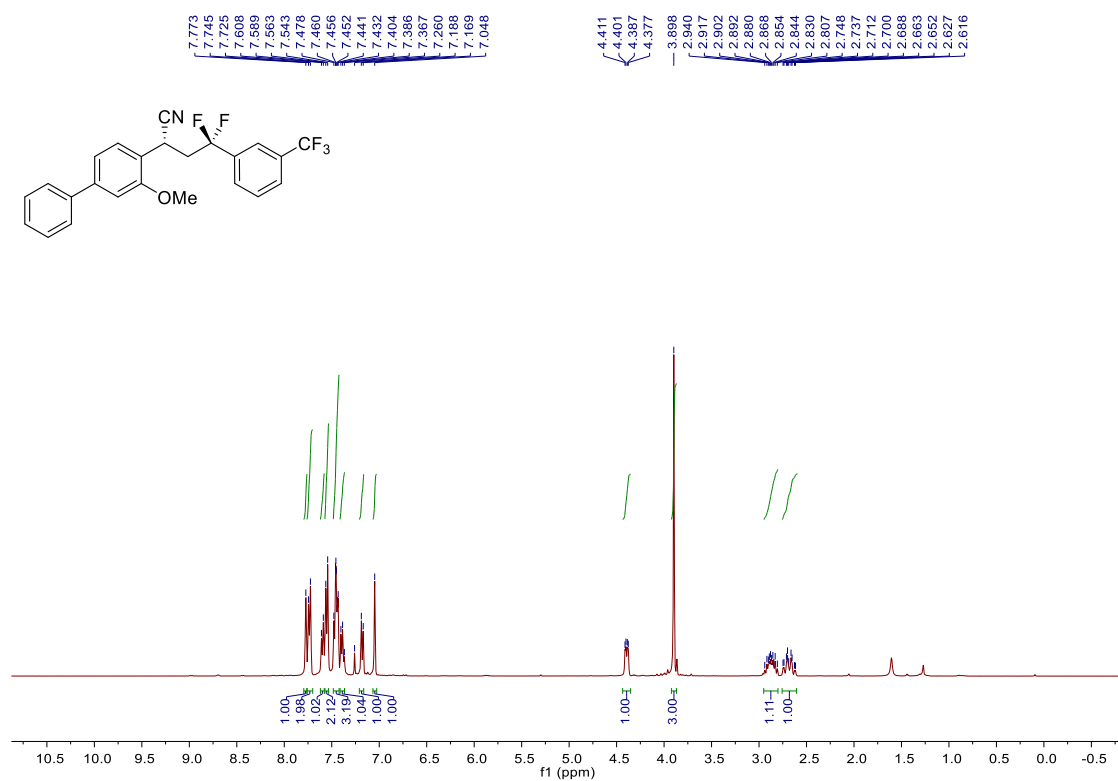


Figure S45. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4j**.

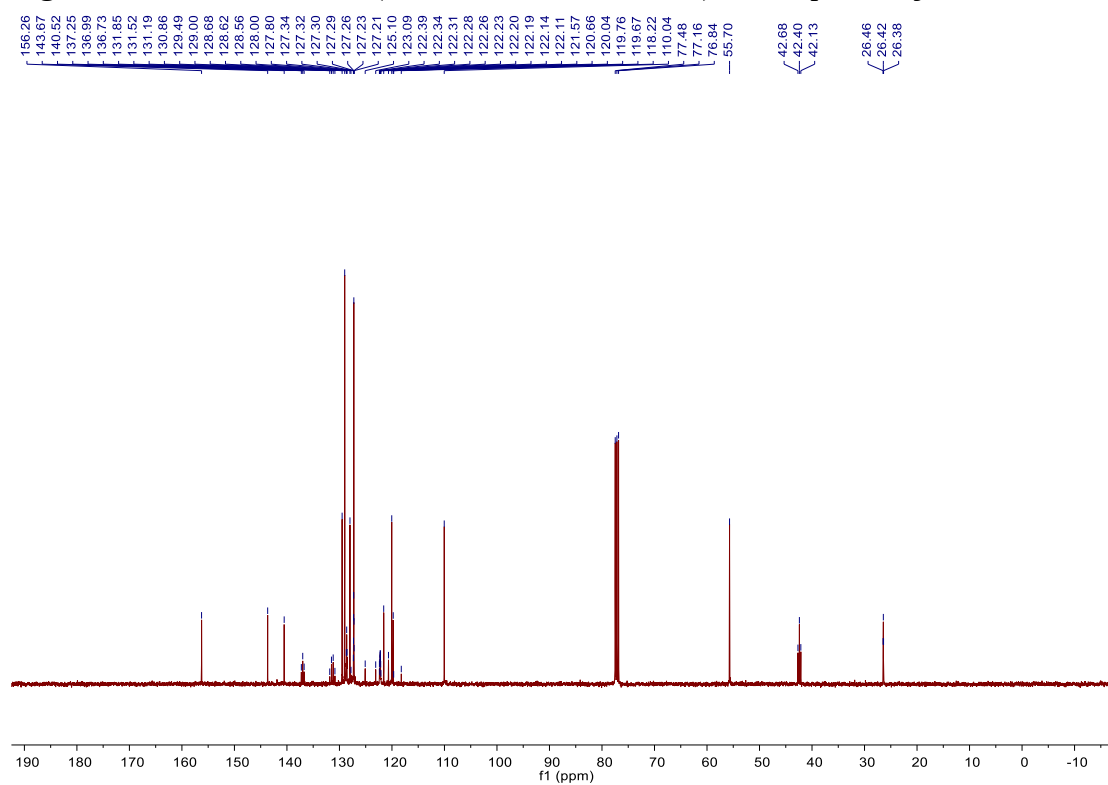


Figure S46. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4j**.

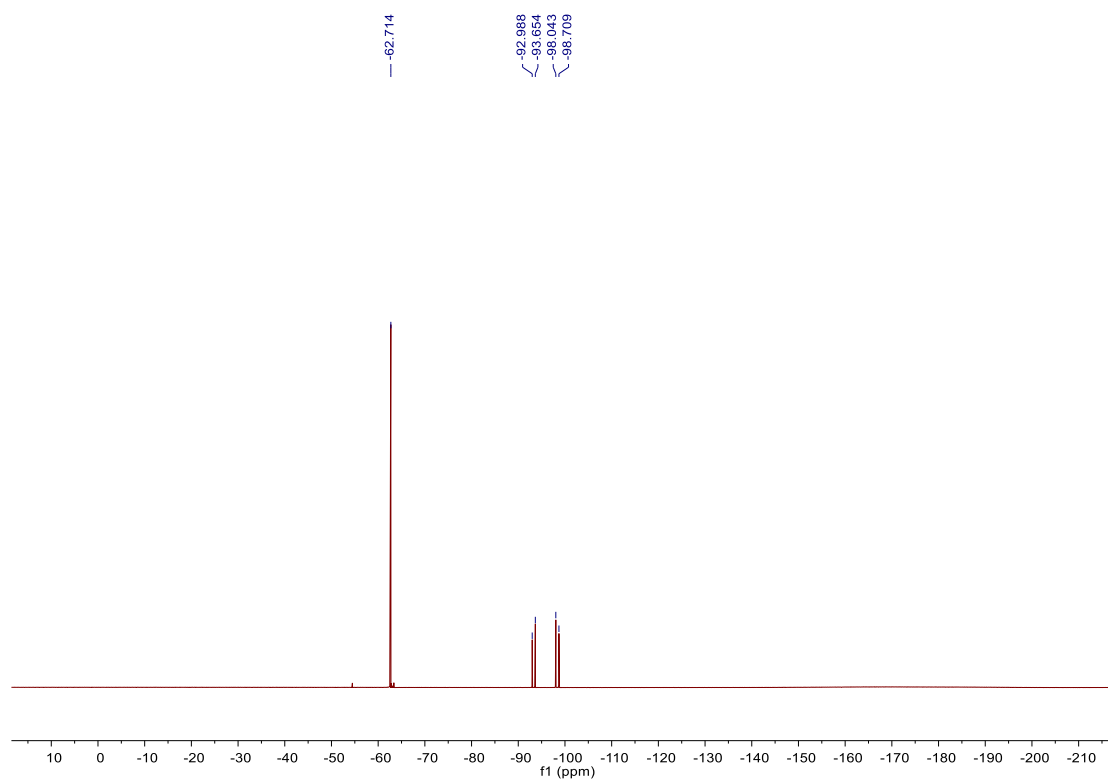


Figure S47. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4k**.

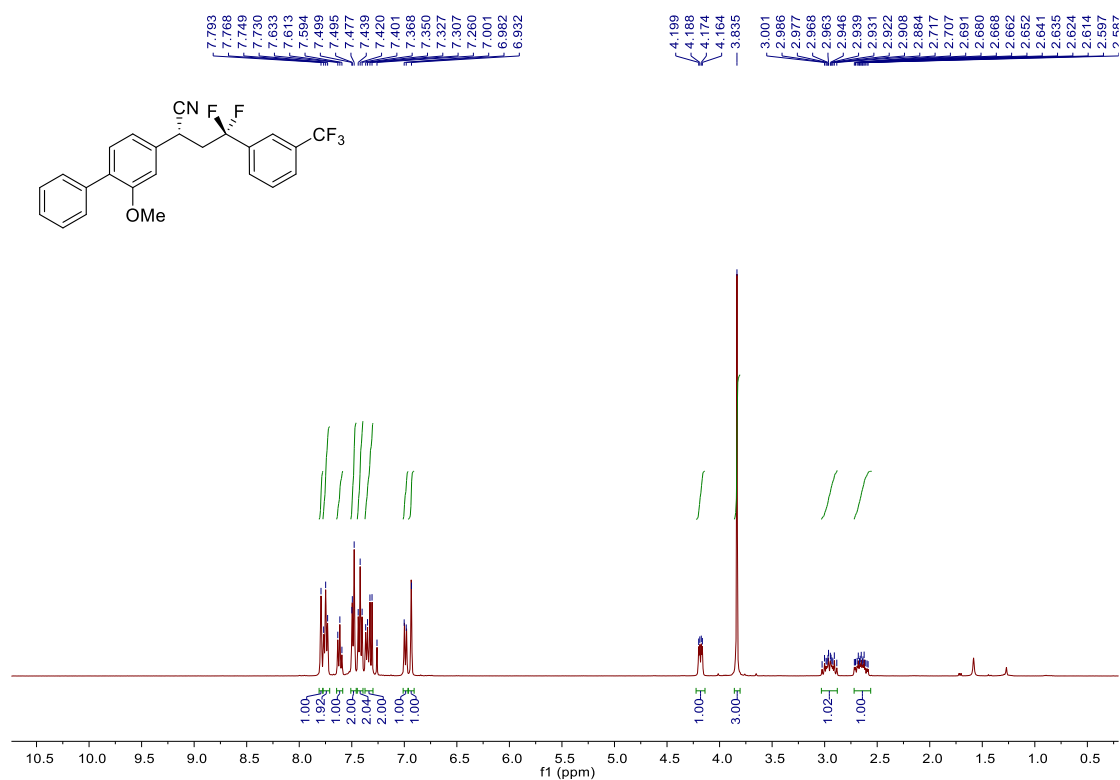


Figure S48. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4k**.

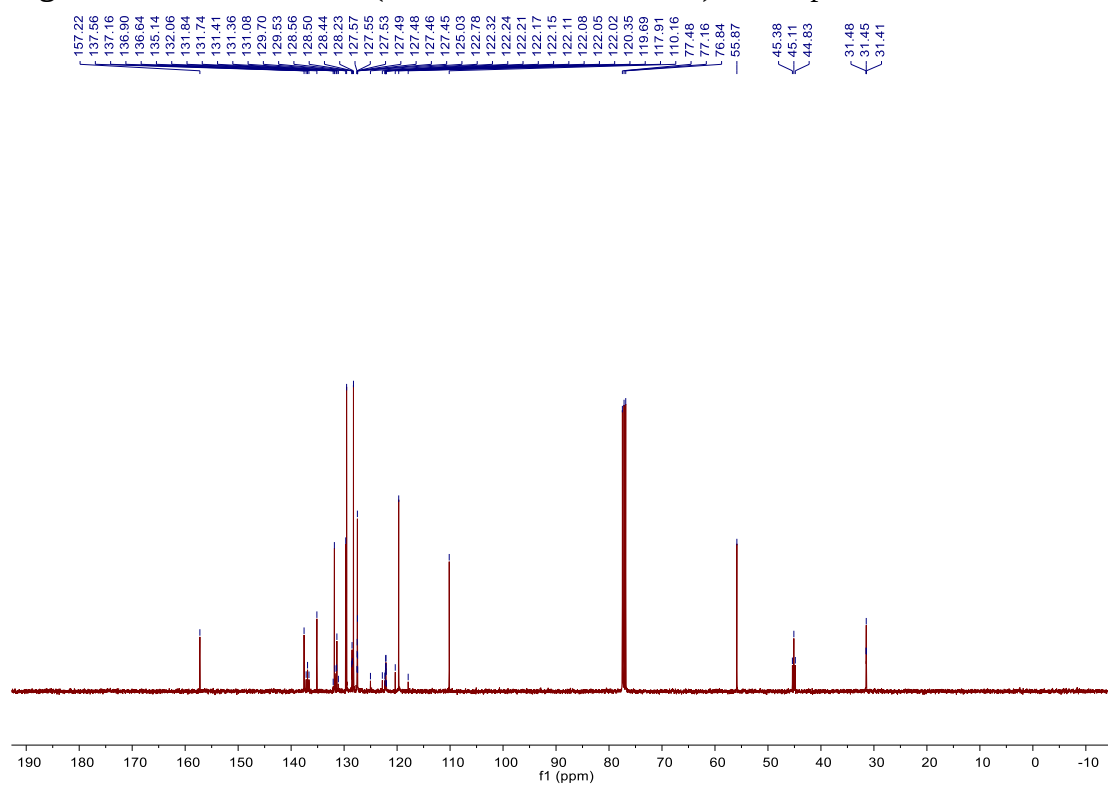


Figure S49. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4k**.

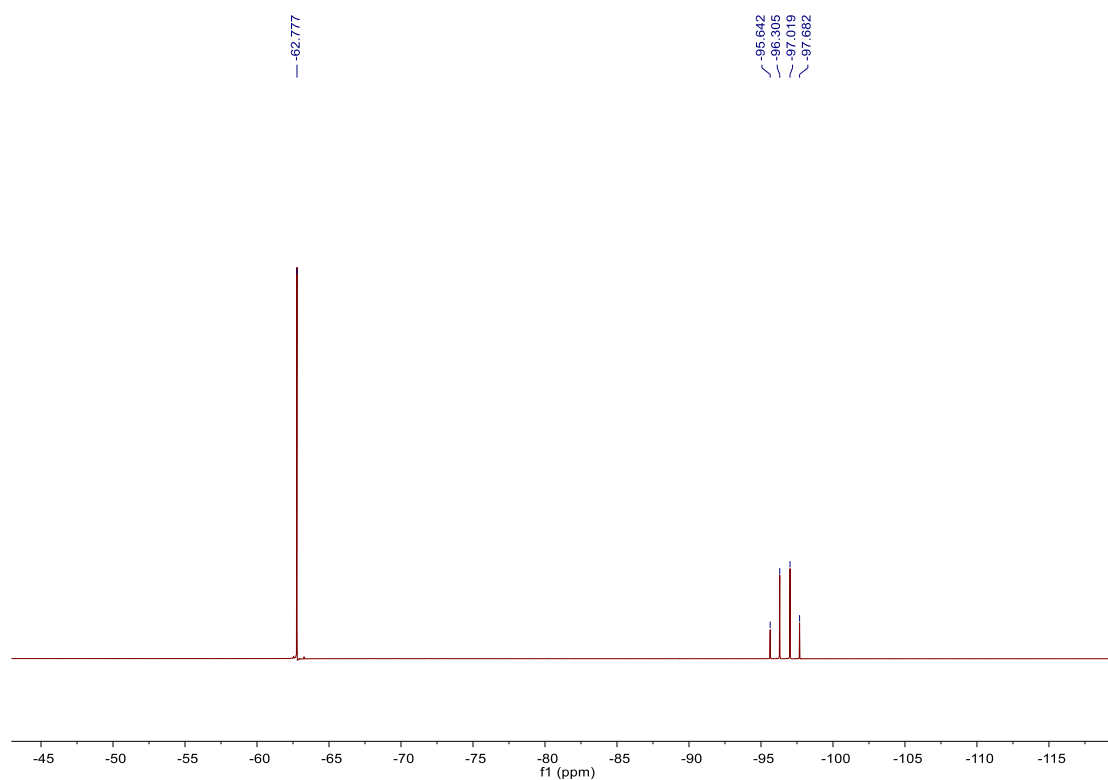


Figure S50. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4l**.

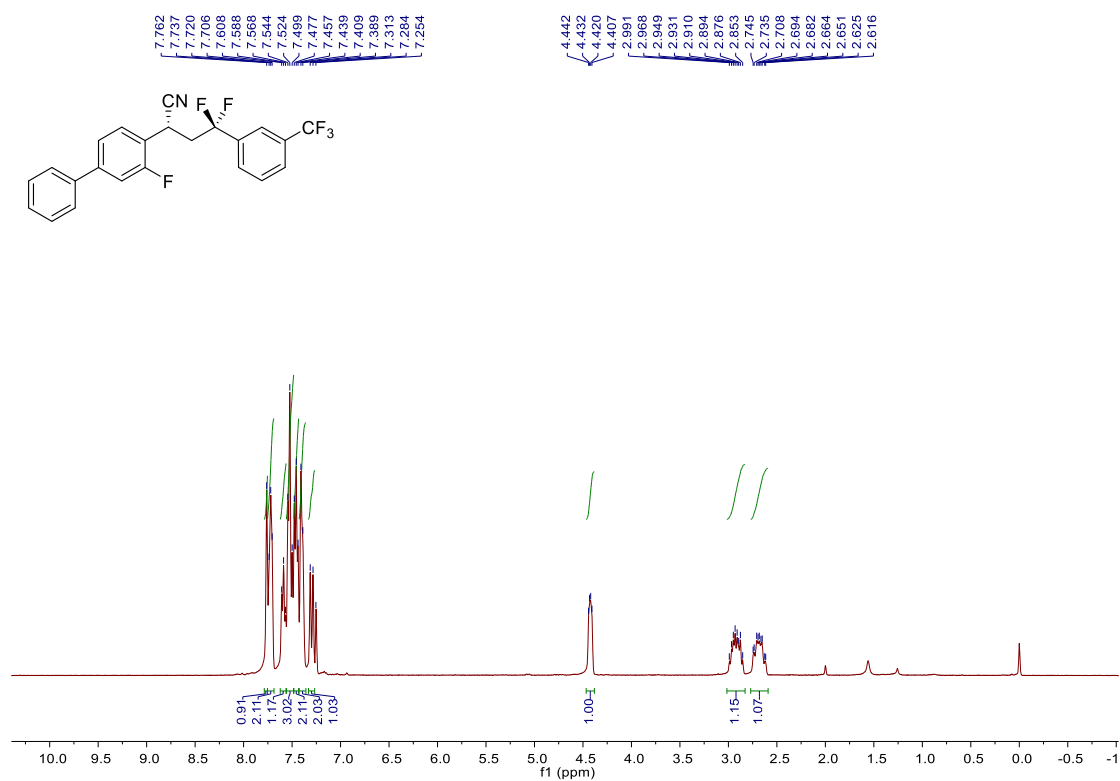


Figure S51. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4l**.

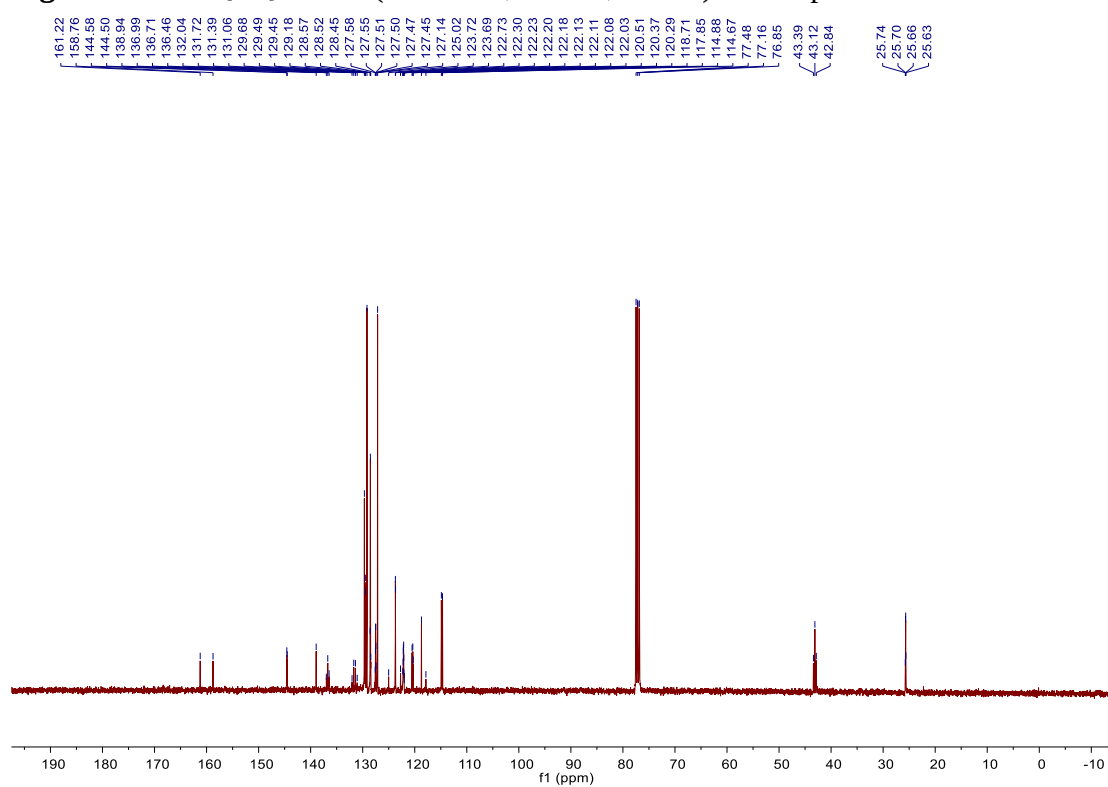


Figure S52. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4l**.

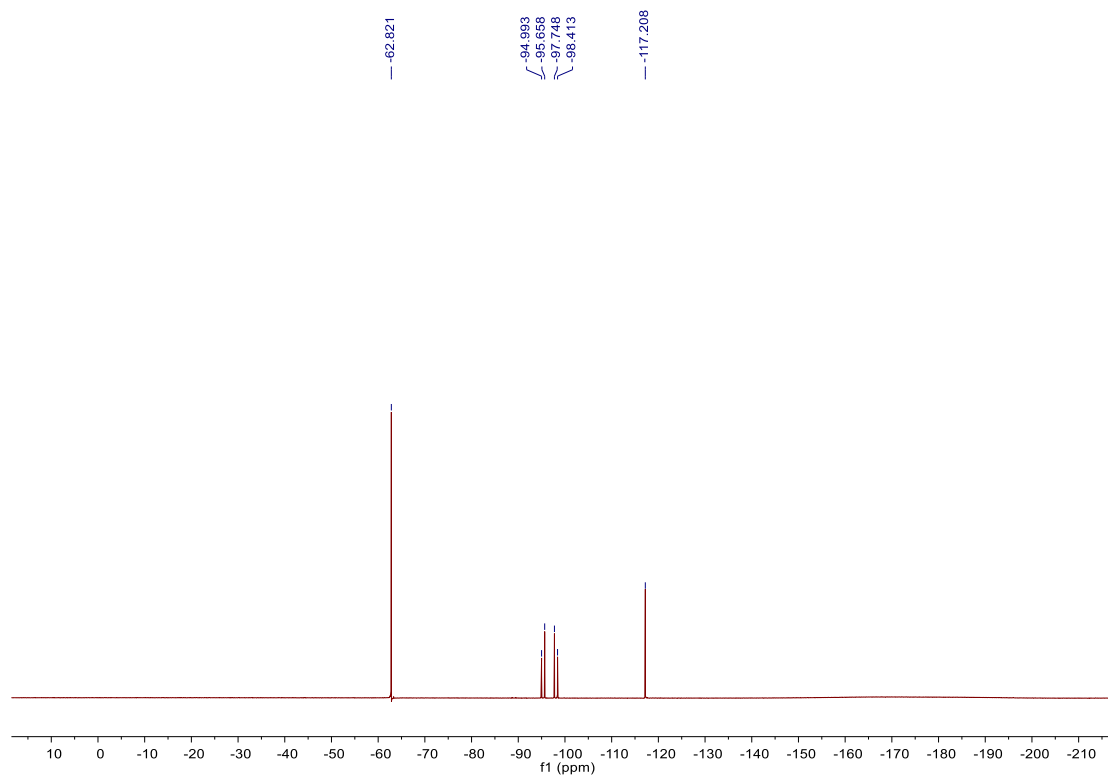


Figure S53. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4m**.

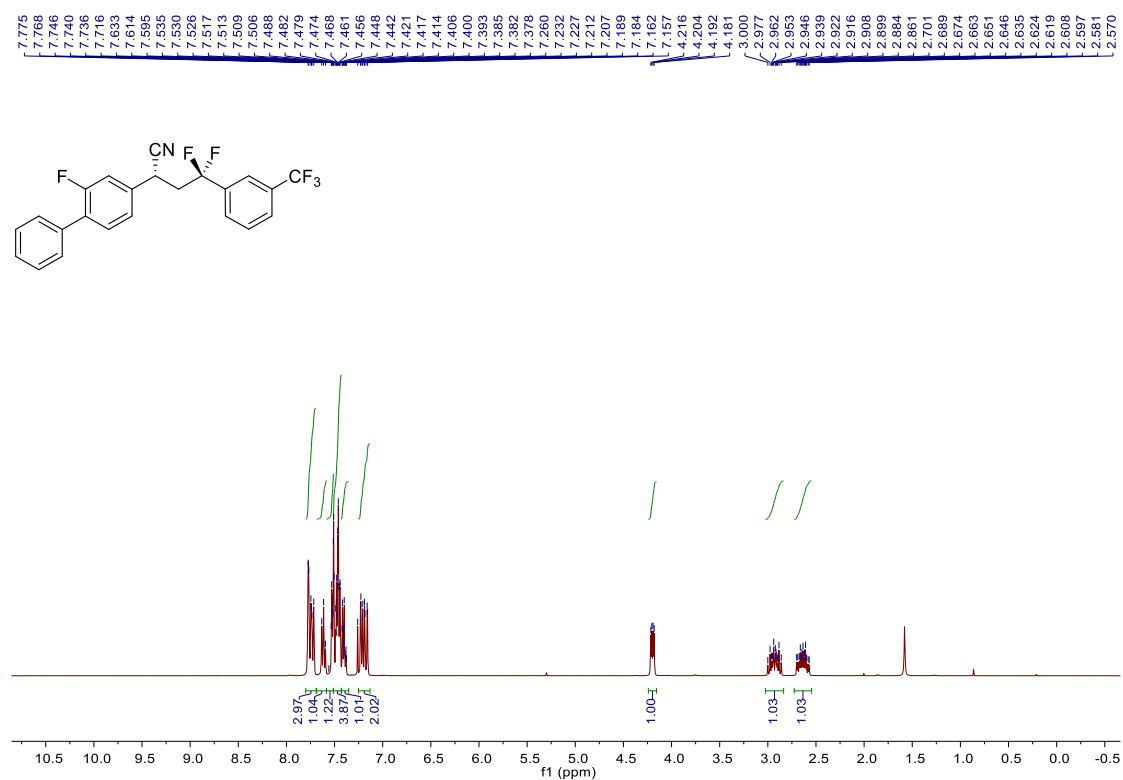


Figure S54. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4m**.

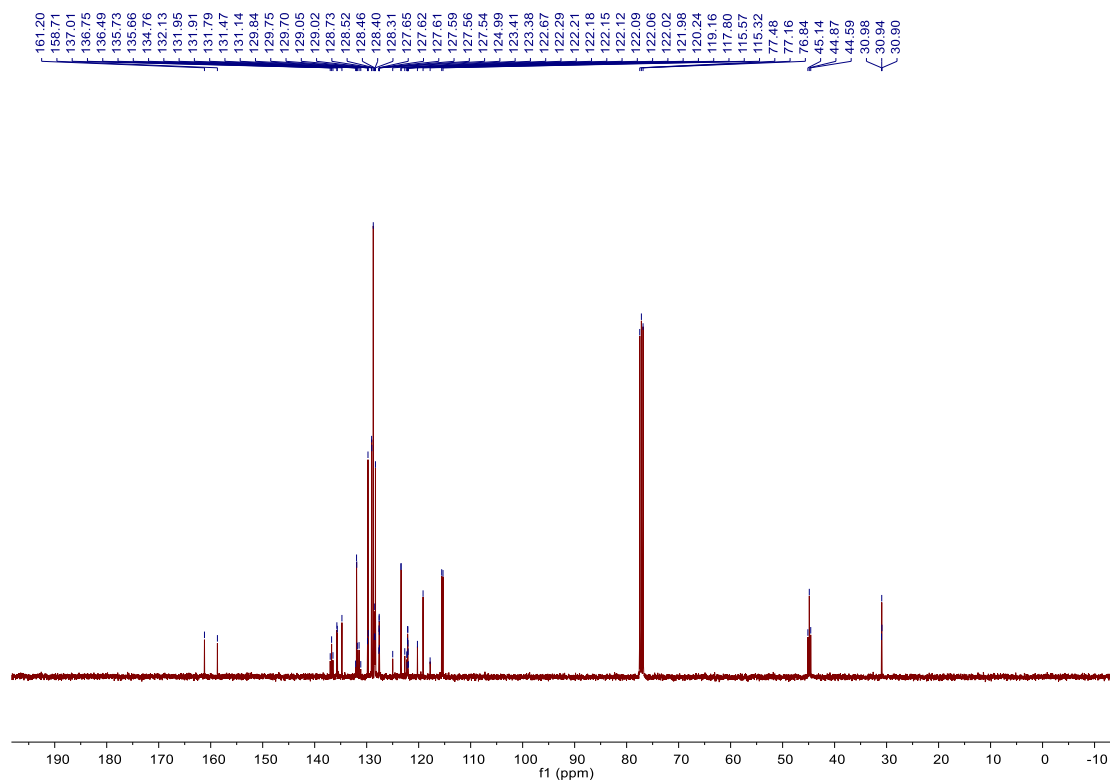


Figure S55. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4m**.

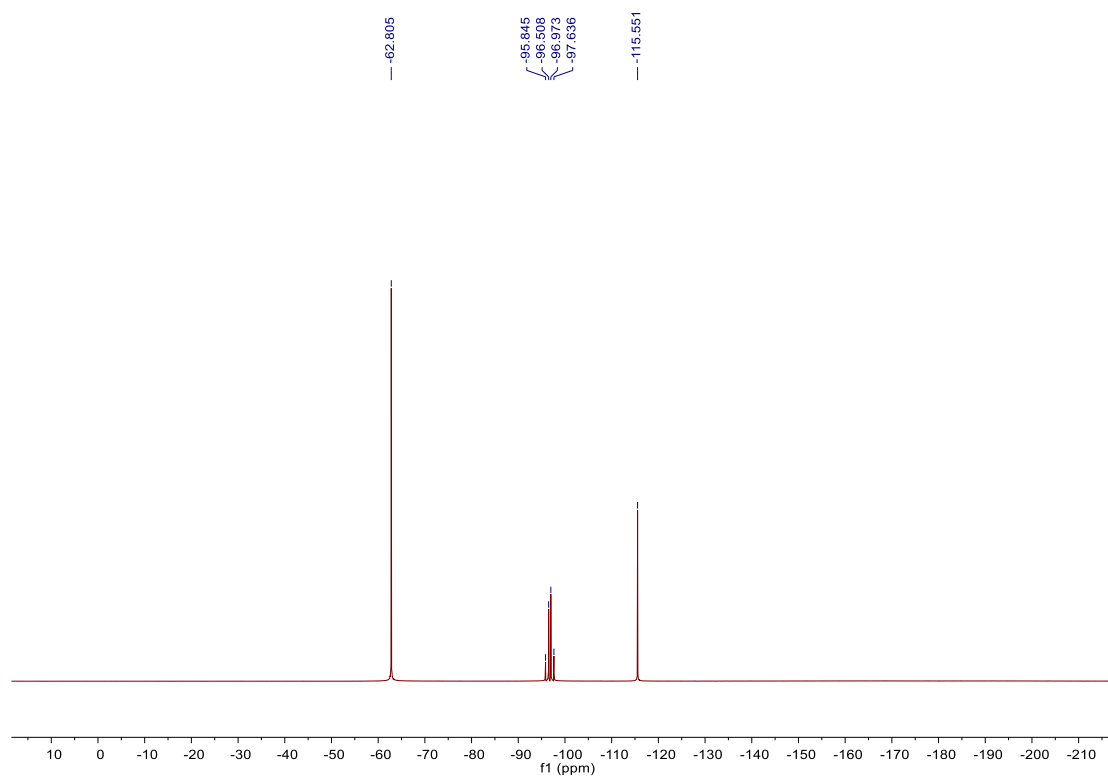


Figure S56. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4n**.

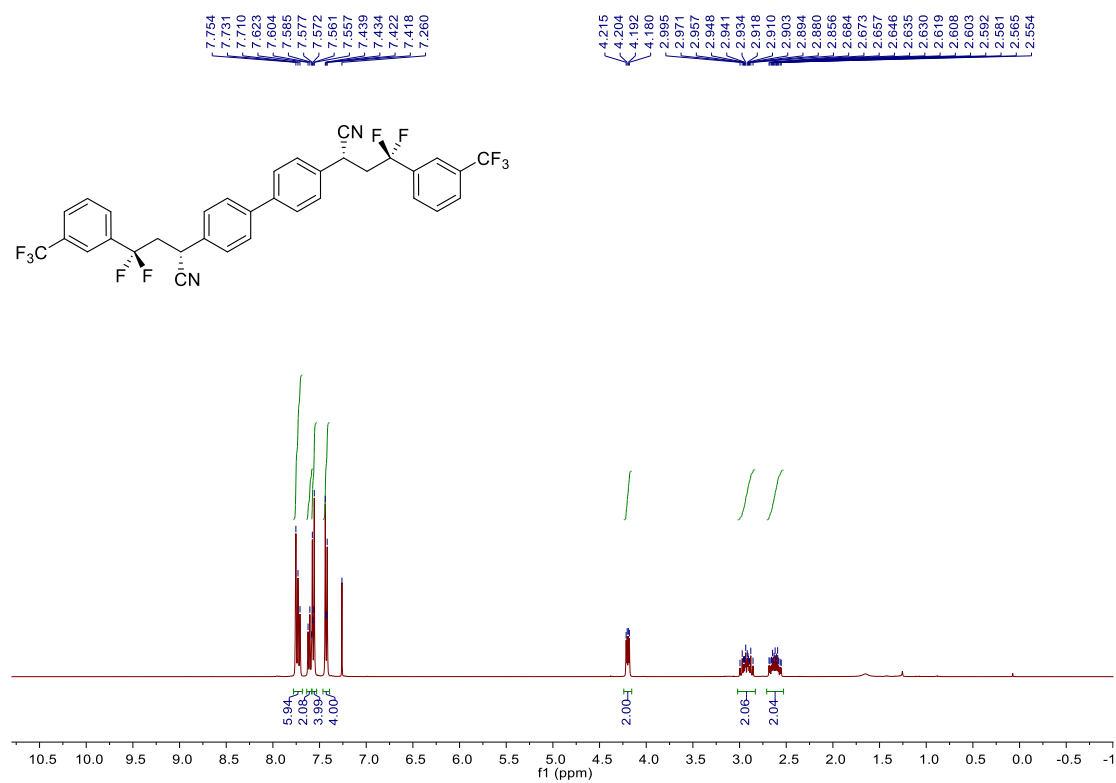


Figure S57. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4n**

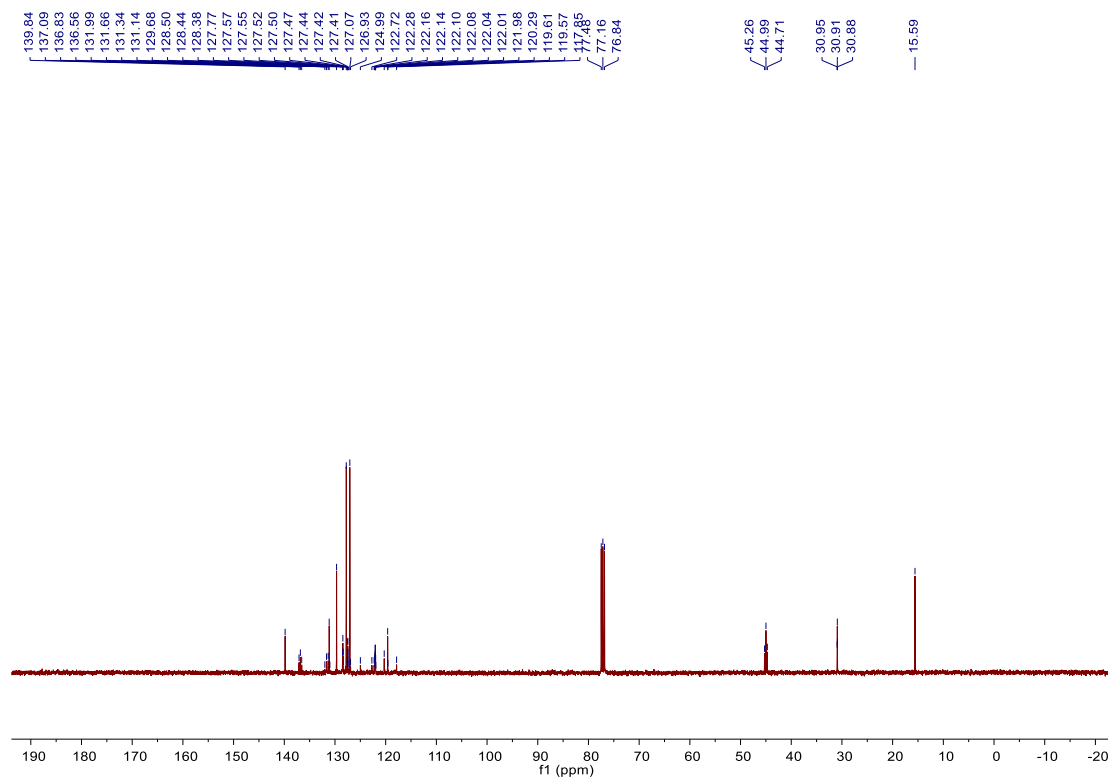


Figure S58. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4n**.

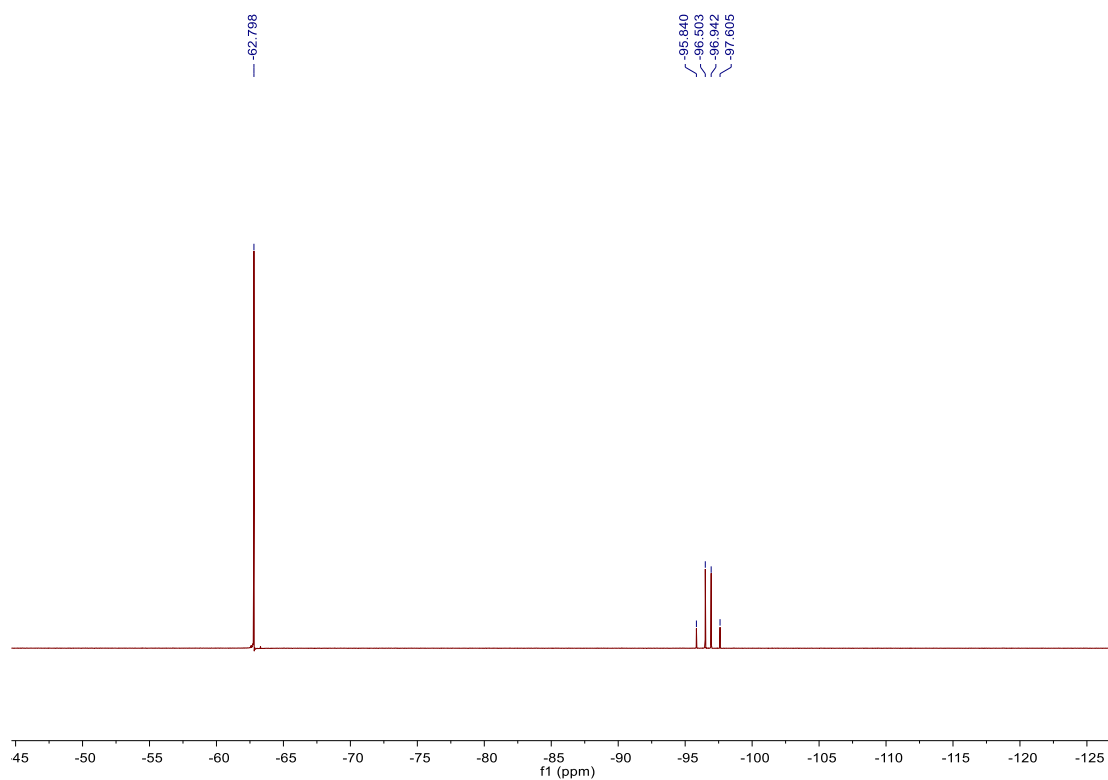


Figure S59. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4o**.

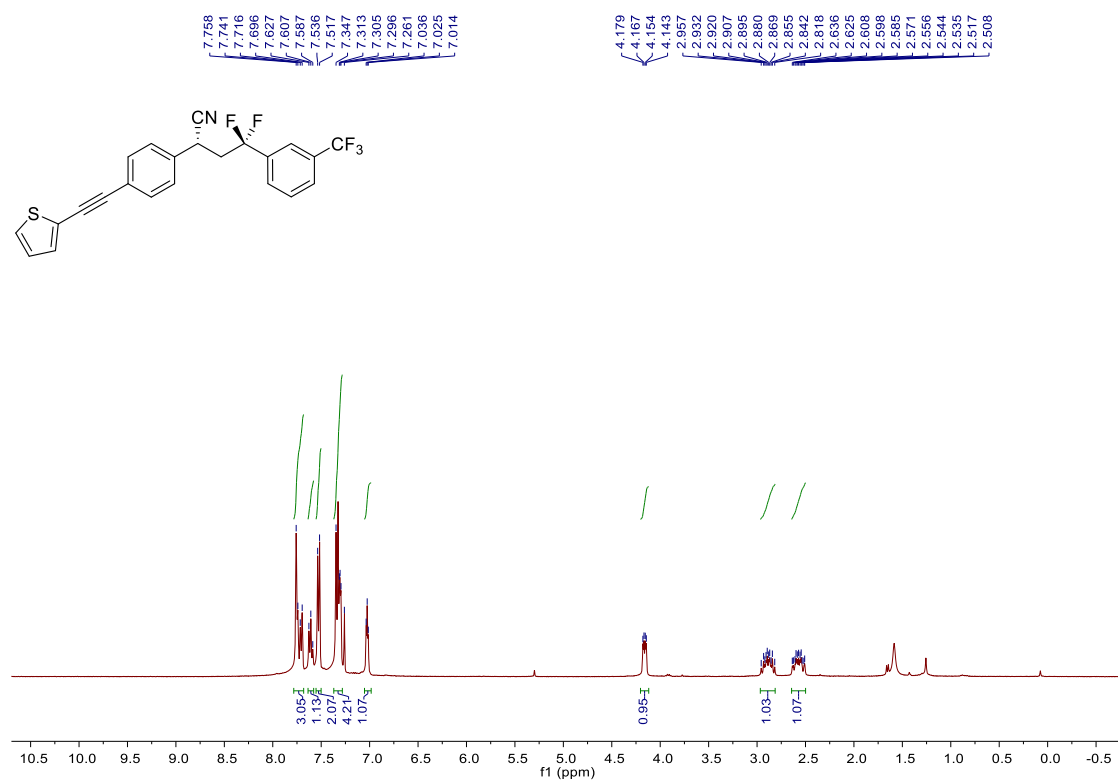


Figure S60. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4o**.

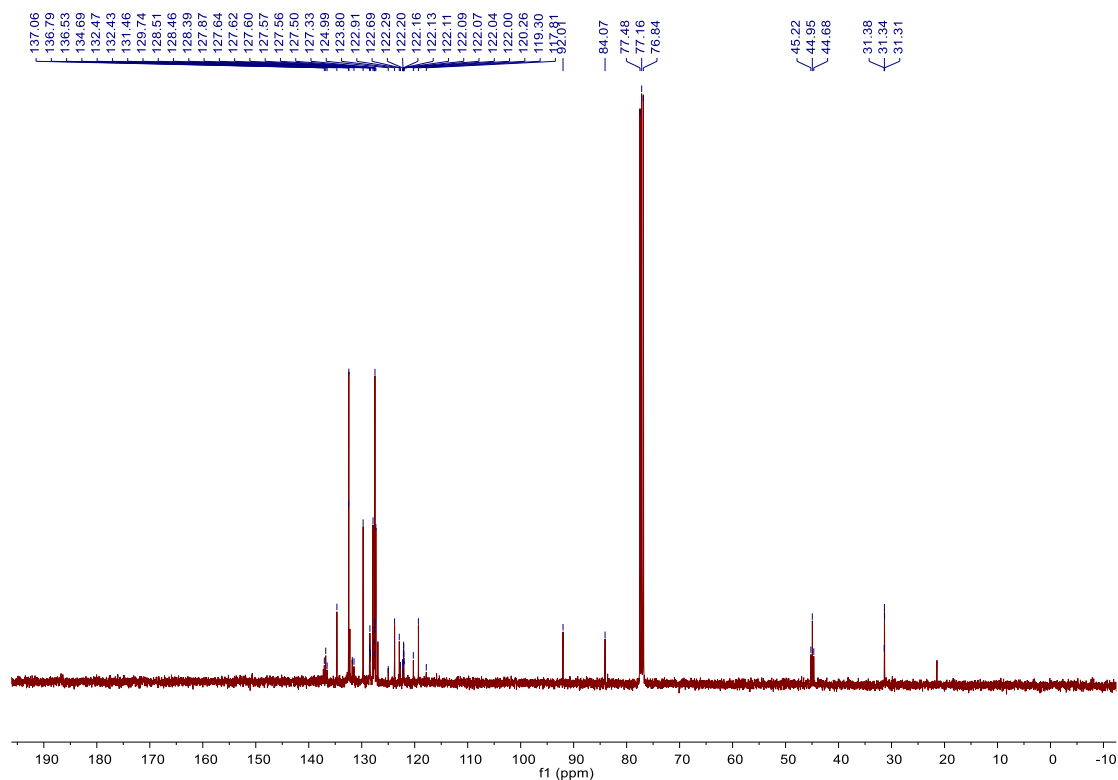


Figure S61. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4o**.

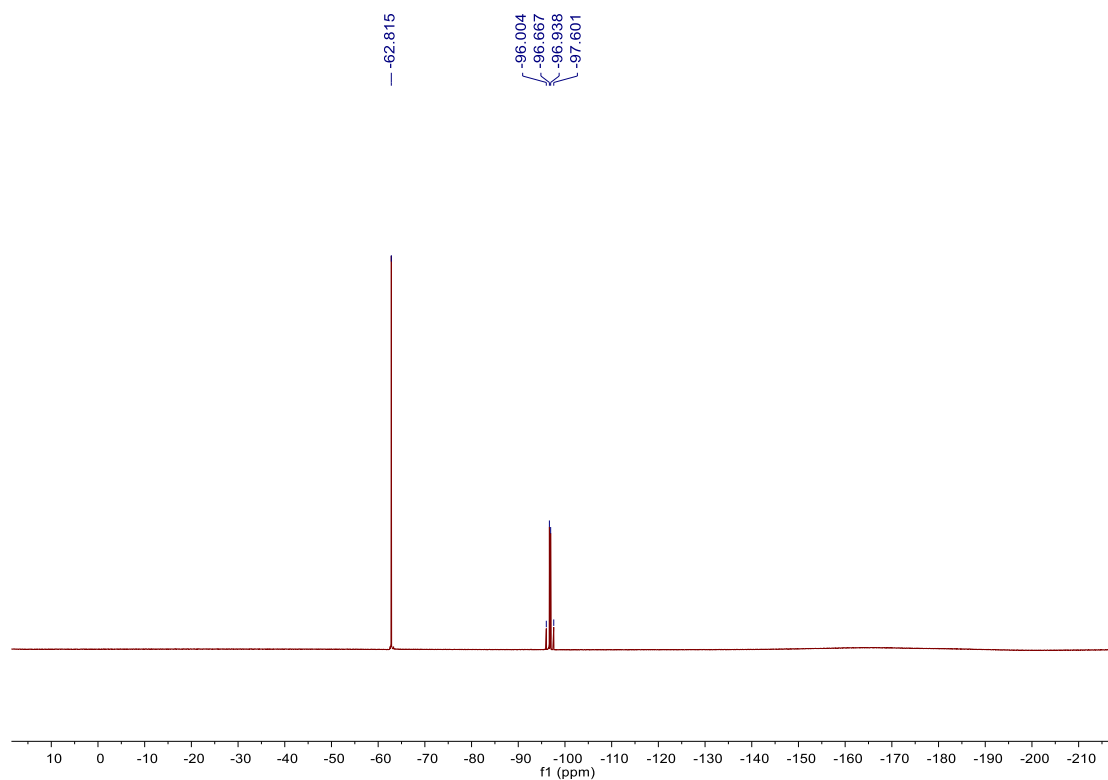


Figure S62. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4p**.

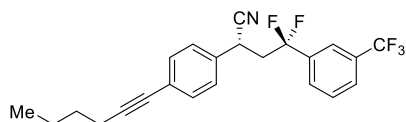
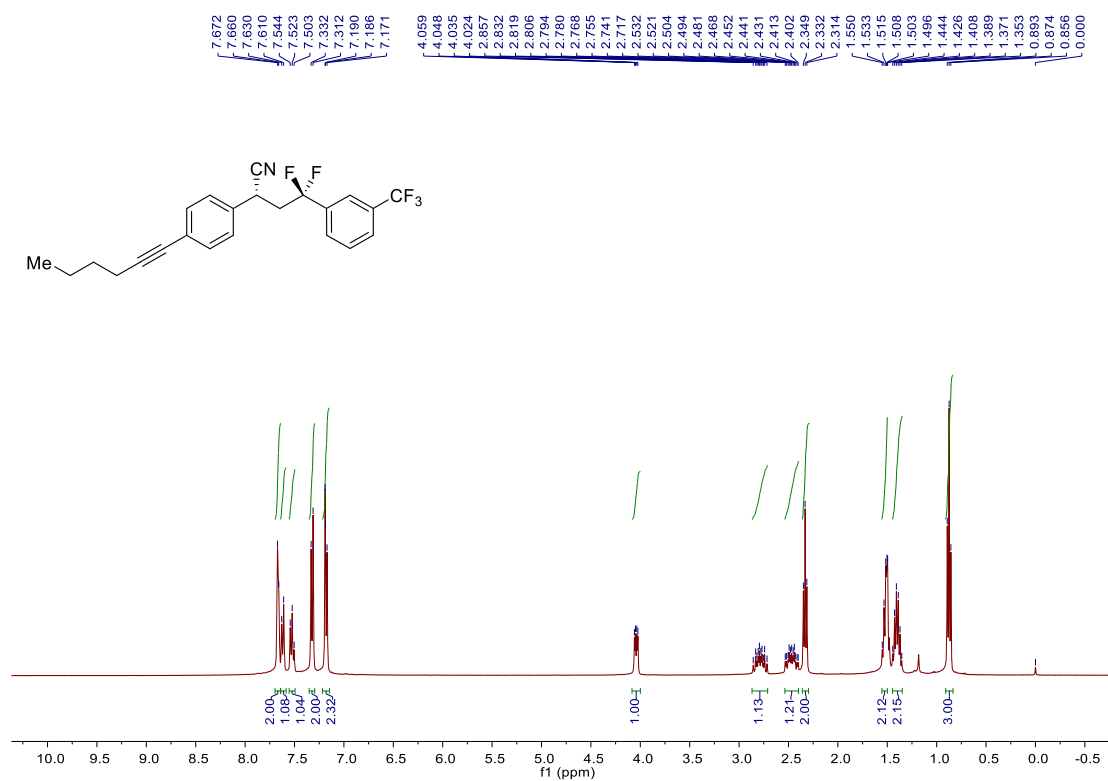


Figure S63. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4p**.

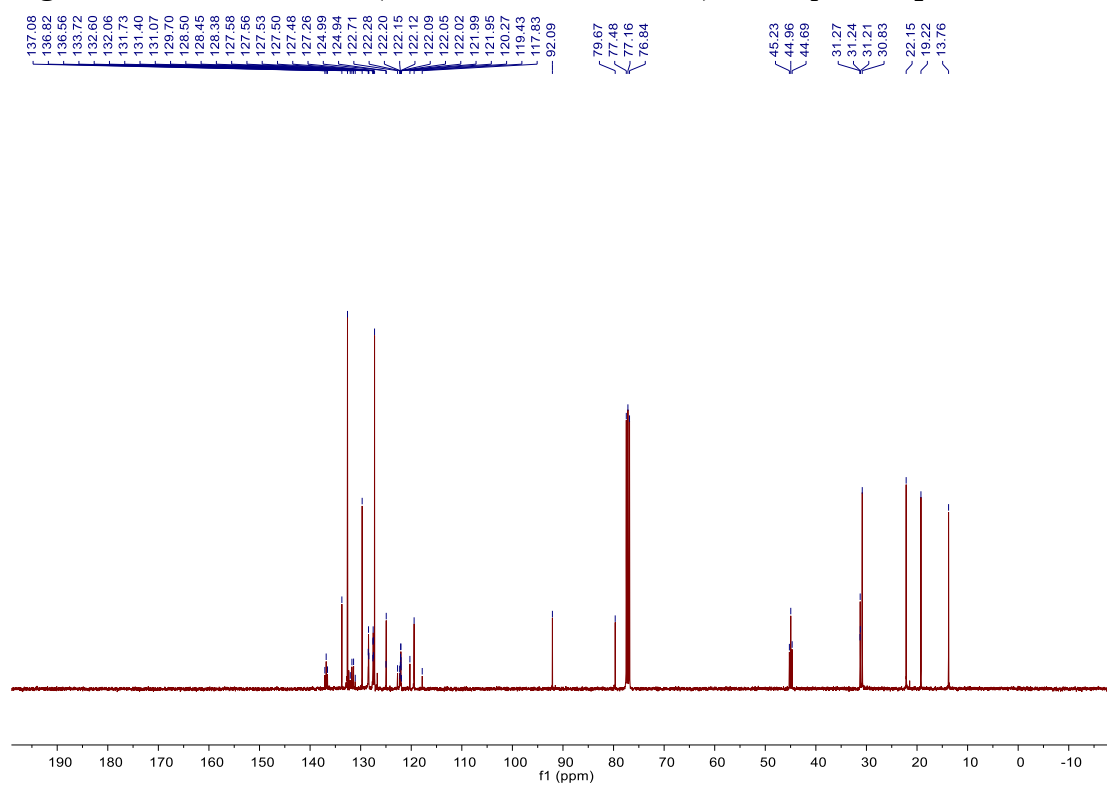


Figure S64. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4p**.

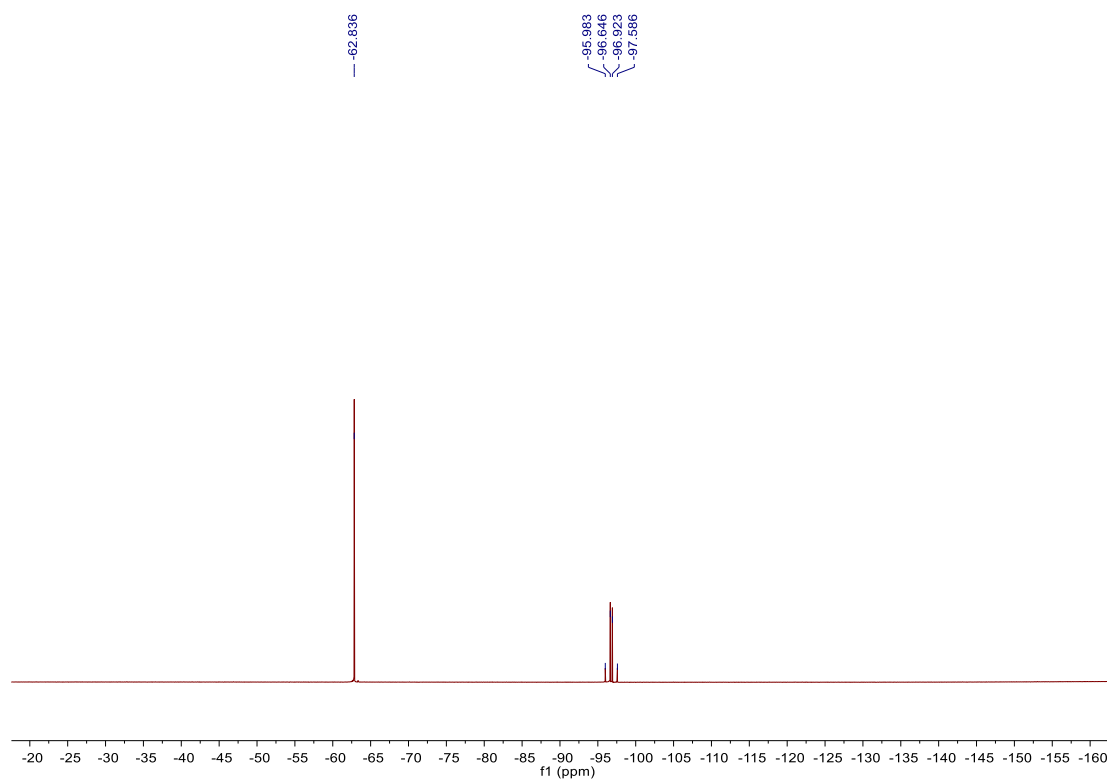


Figure S65. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4q**.

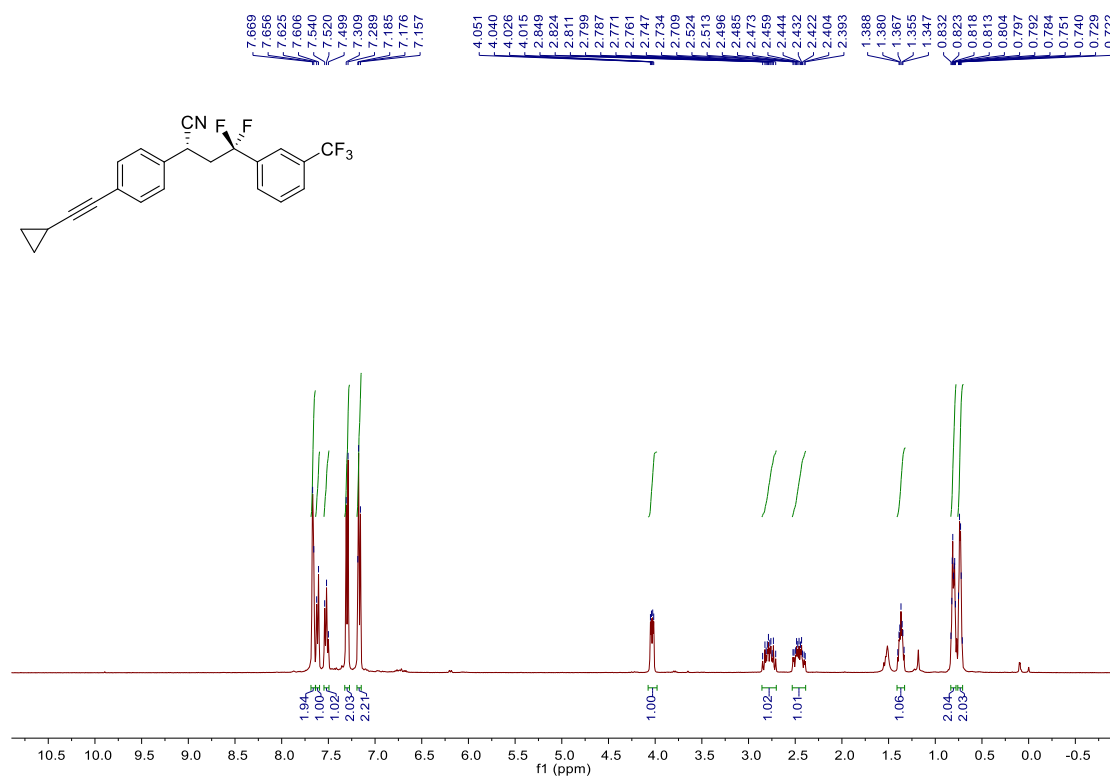


Figure S66. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4q**.

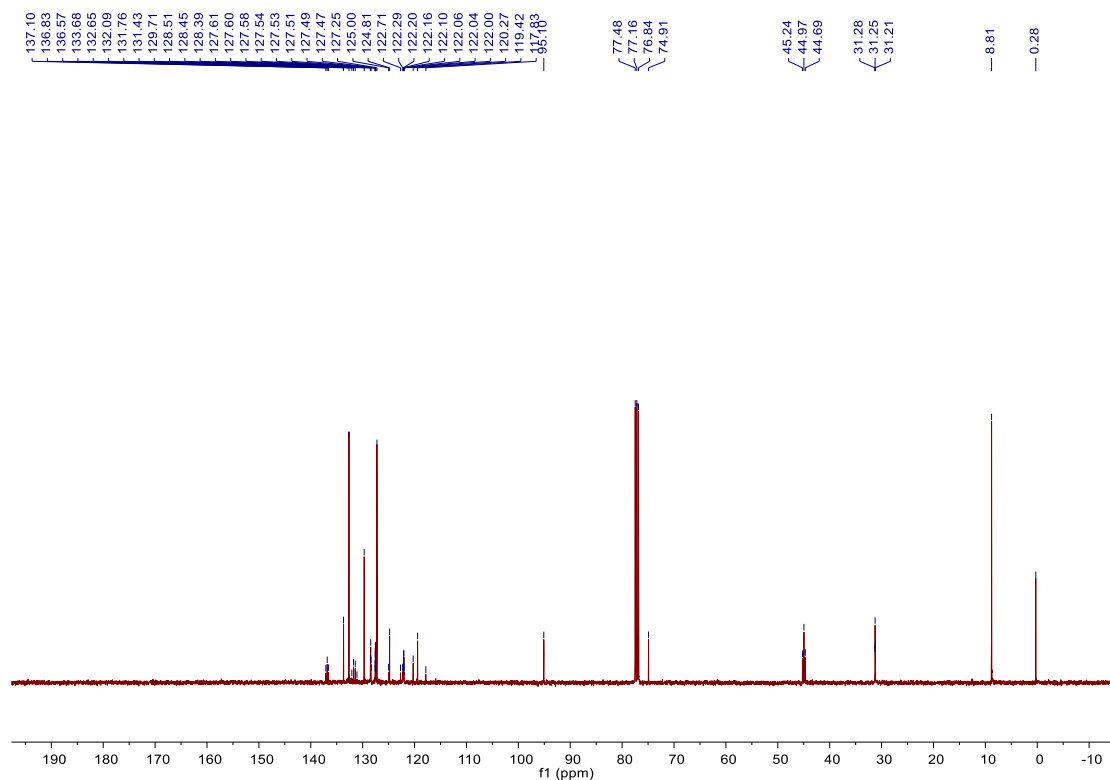


Figure S67. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4q**.

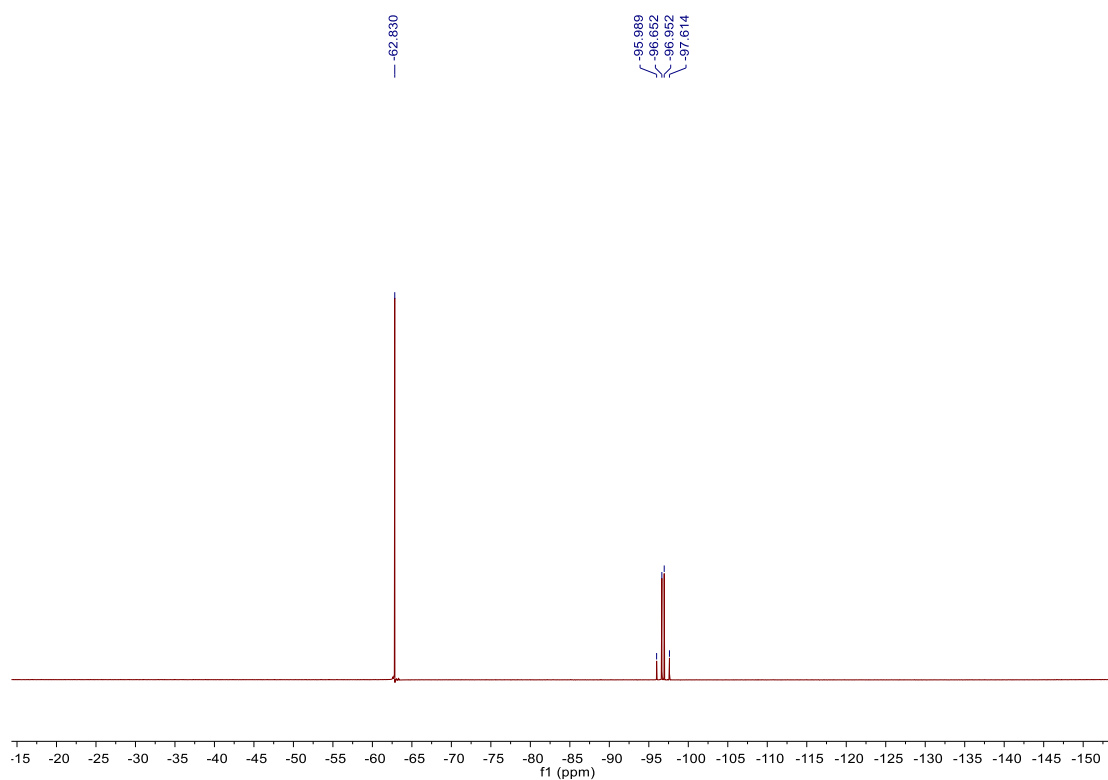


Figure S68. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4r**.

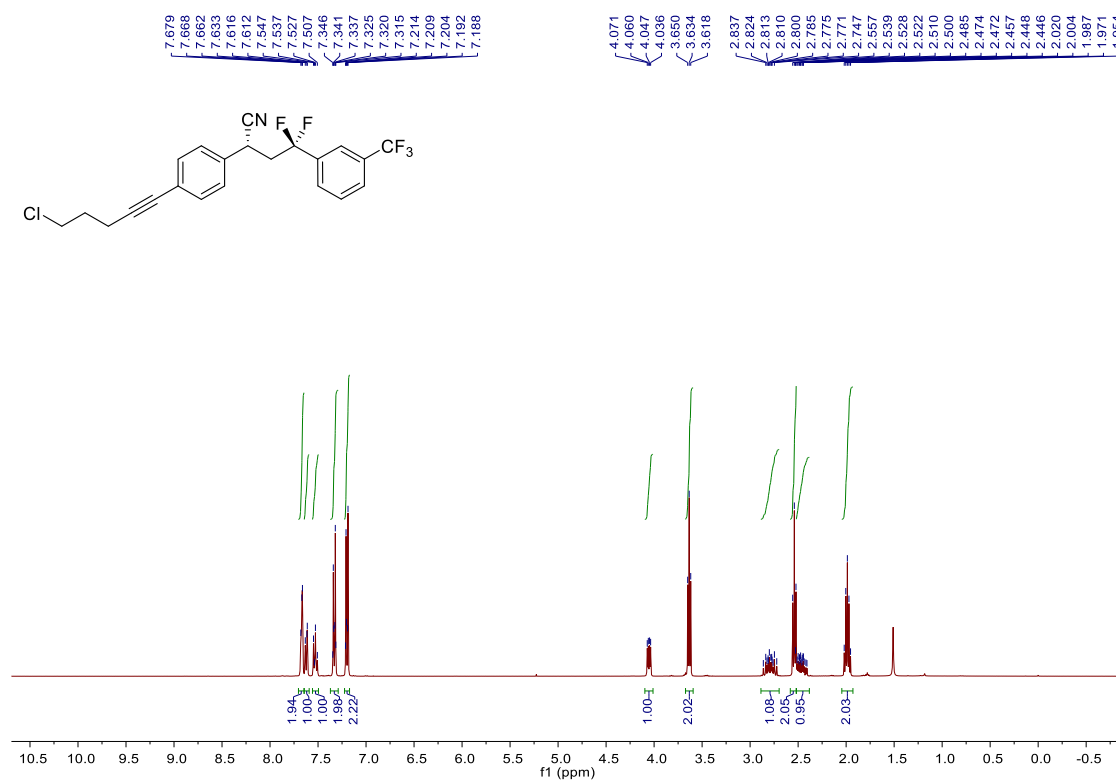


Figure S69. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4r**.

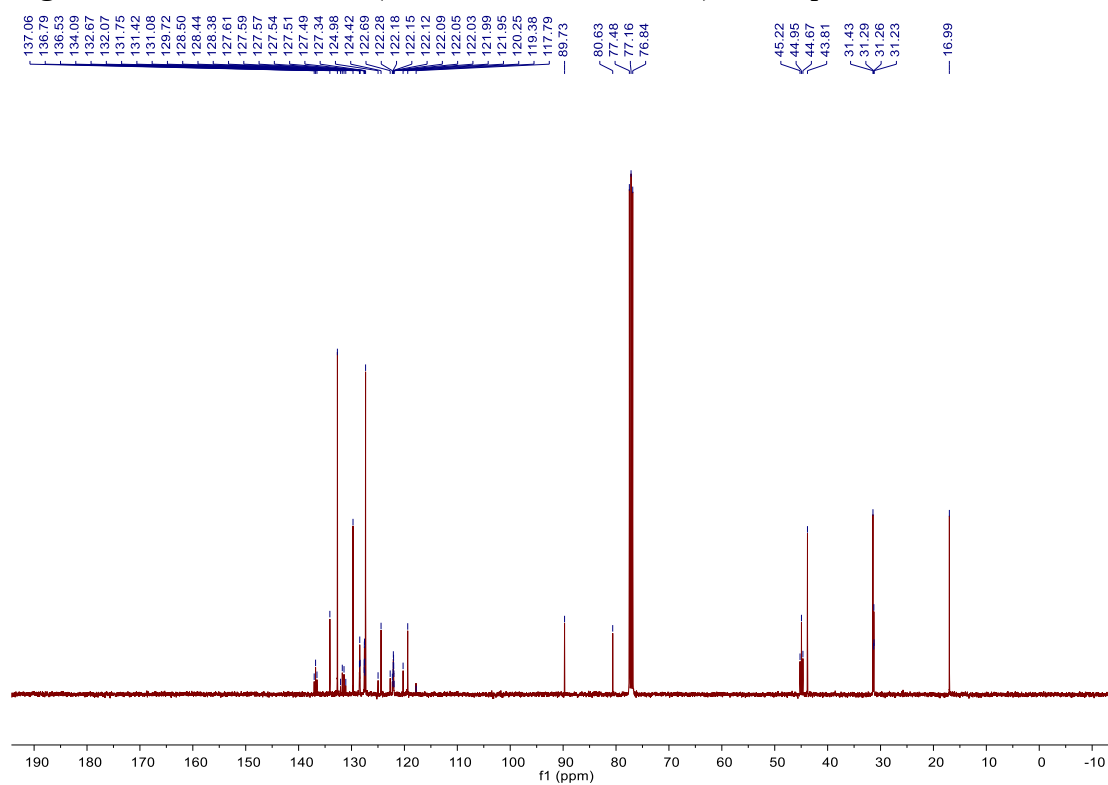
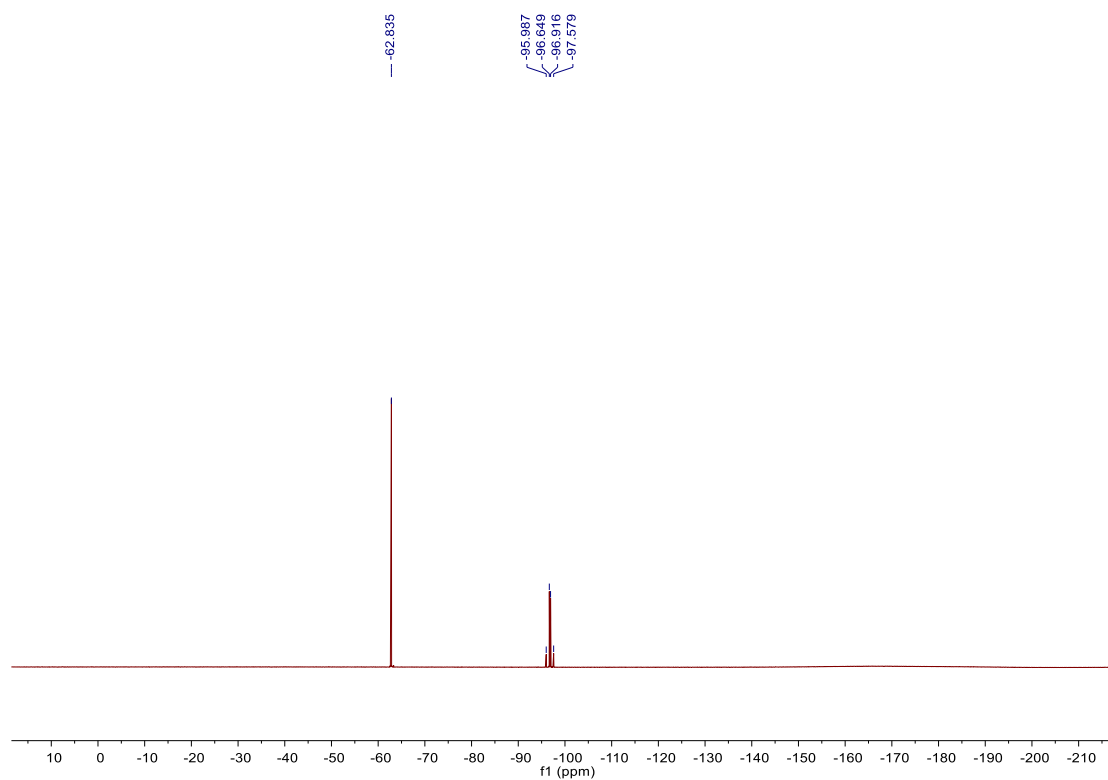


Figure S70. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4r**.



OC#CCc1ccc(cc1)C(F)(F)Cc2ccc(cc2)C(F)(F)F

Chemical structure: OC#CCc1ccc(cc1)C(F)(F)Cc2ccc(cc2)C(F)(F)F

¹H NMR spectrum (ppm):

- 7.672, 7.665, 7.656, 7.628, 7.608, 7.541, 7.521, 7.505, 7.531, 7.310, 7.196, 7.176 (Aromatic protons, multiplet)
- 4.064, 4.053, 4.040, 4.029 (CH₂ protons, multiplet)
- 3.750, 3.734, 3.719 (CH₂ protons, multiplet)
- 2.832, 2.819, 2.805, 2.794, 2.779, 2.770, 2.765, 2.754, 2.741, 2.717, 2.532, 2.521, 2.505, 2.494, 2.482, 2.465, 2.447, 2.430, 2.413, 1.899, 1.889, 1.802, 1.786, 1.769, 1.753, 1.503 (Aliphatic protons, multiplet)

Integration values (from left to right): 1.82, 0.92, 1.00, 2.05, 2.21, 0.92, 2.12, 1.02, 3.13, 2.12, 1.04.

137.05
136.79
136.53
133.94
132.61
132.55
131.72
131.30
131.07
129.70
128.49
128.44
128.38
127.60
127.57
127.55
127.52
127.50
127.46
127.30
124.98
124.58
122.69
122.27
122.18
122.14
122.10
122.08
122.04
122.01
121.97
121.94
120.25
119.55
119.39
117.81
91.00
80.20
77.48
77.16
76.84
61.80
45.17
44.90
44.63
31.40
31.26
31.23
31.20
16.09

f1 (ppm)

Figure S73. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4s**.

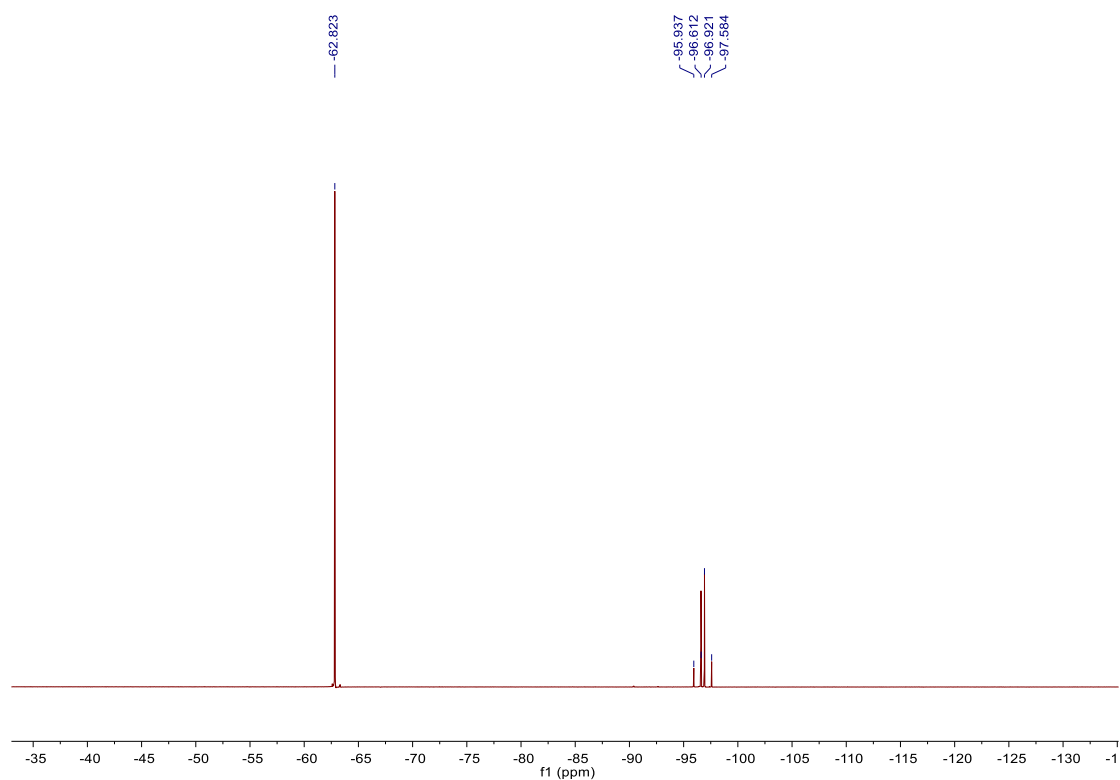


Figure S74. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4t**.

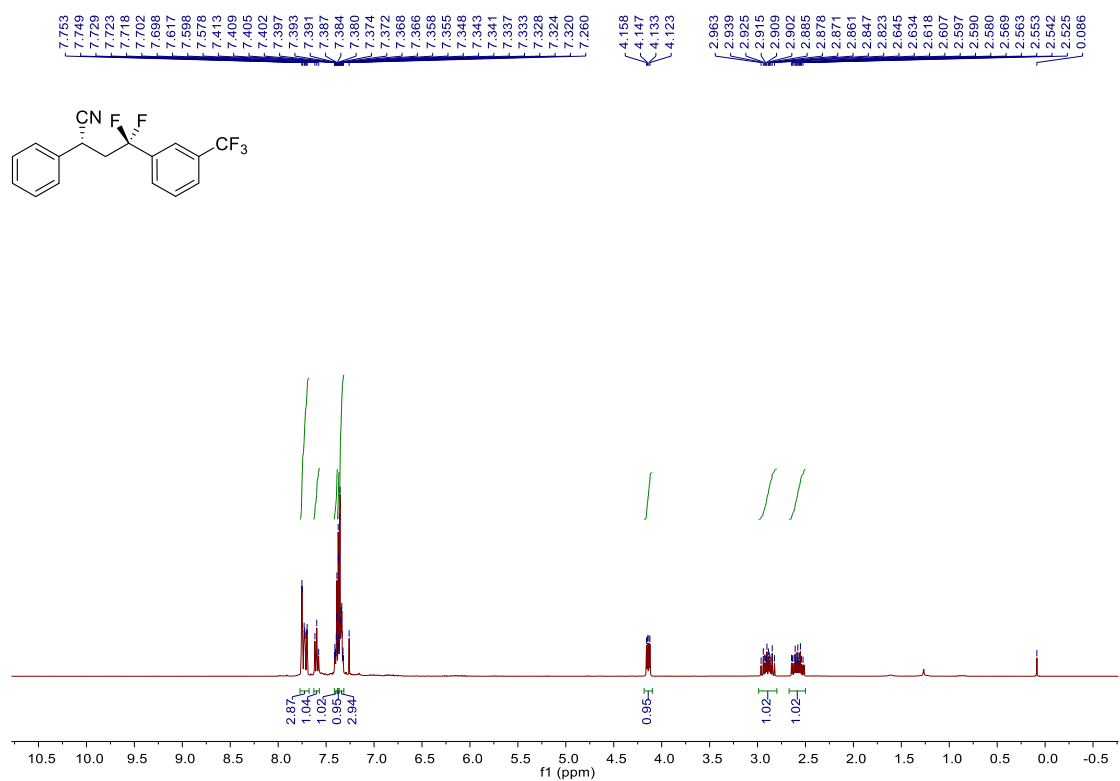


Figure S75. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4t**.

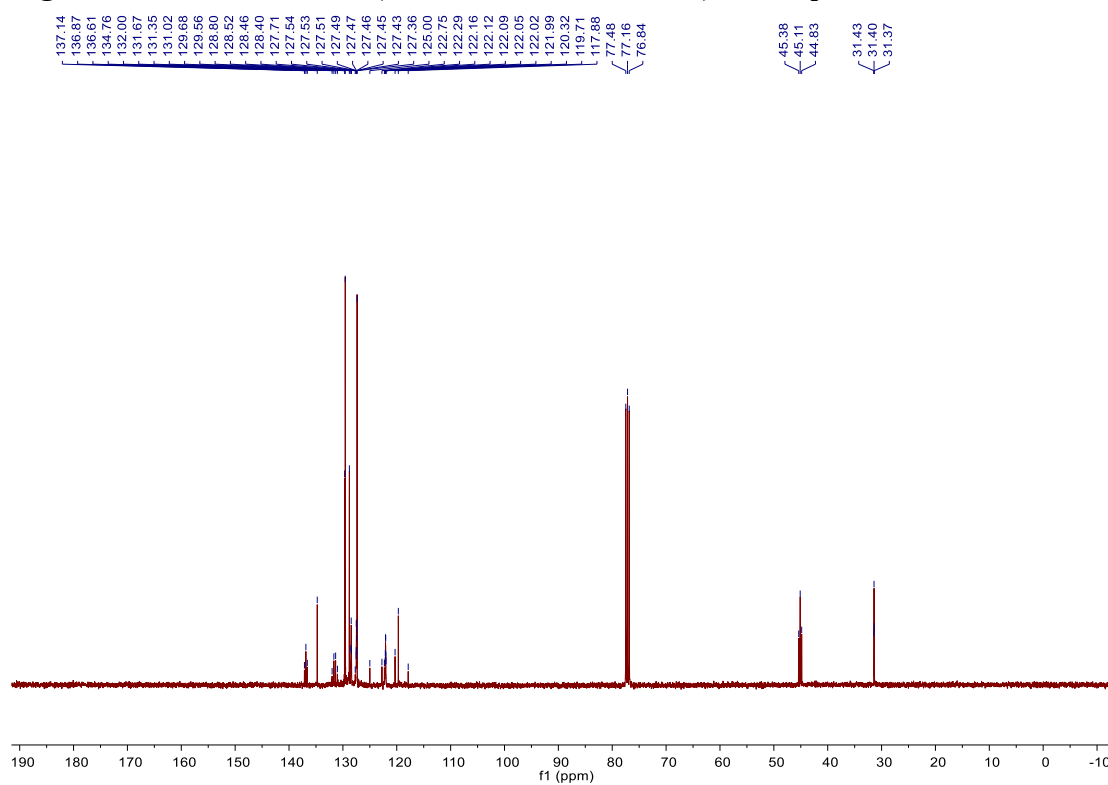


Figure S76. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4t**.

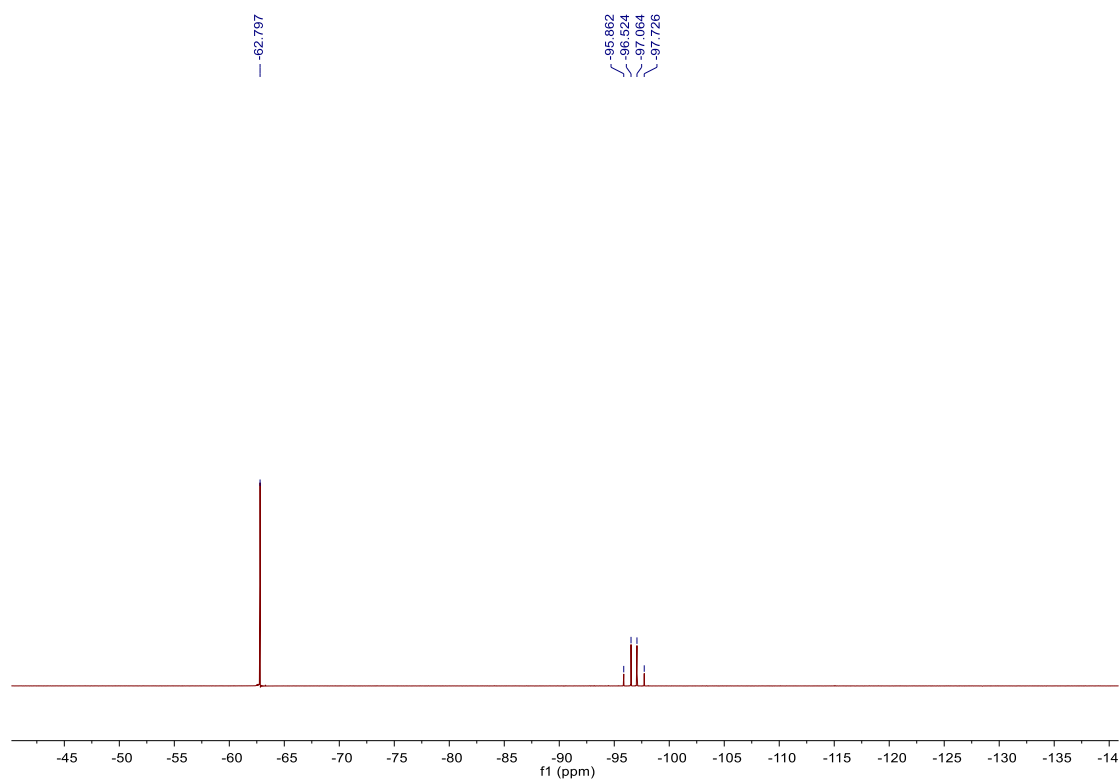


Figure S77. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4u**.

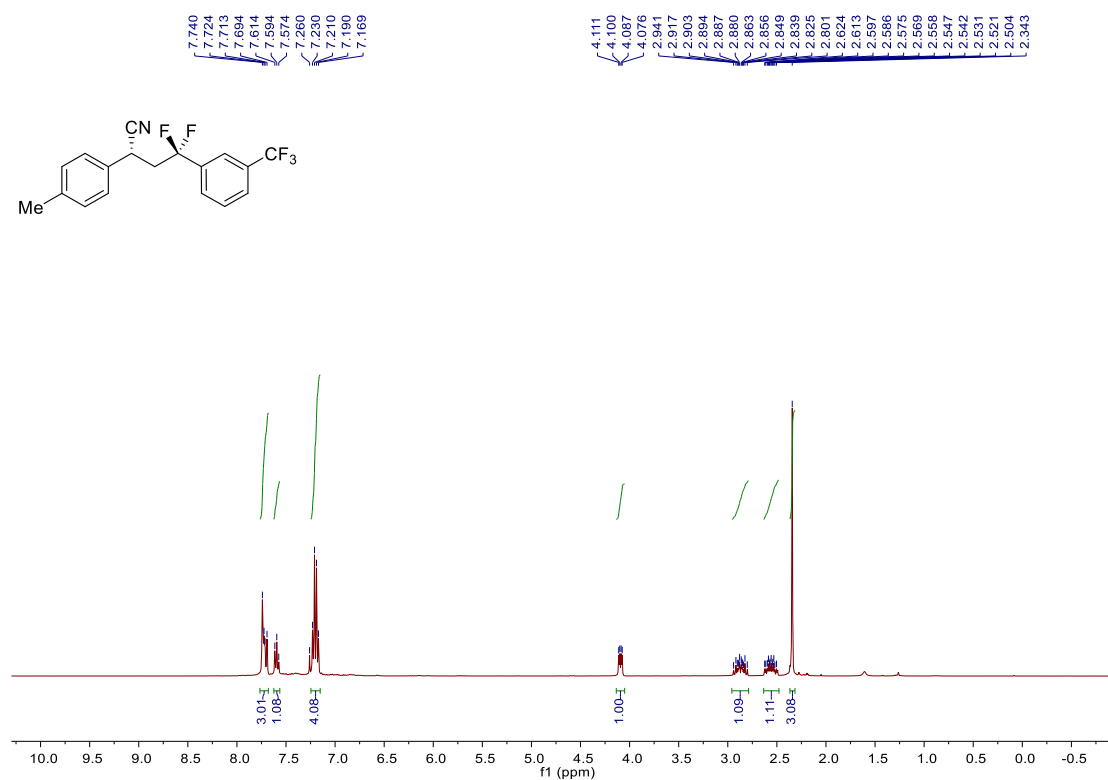


Figure S78. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4u**.

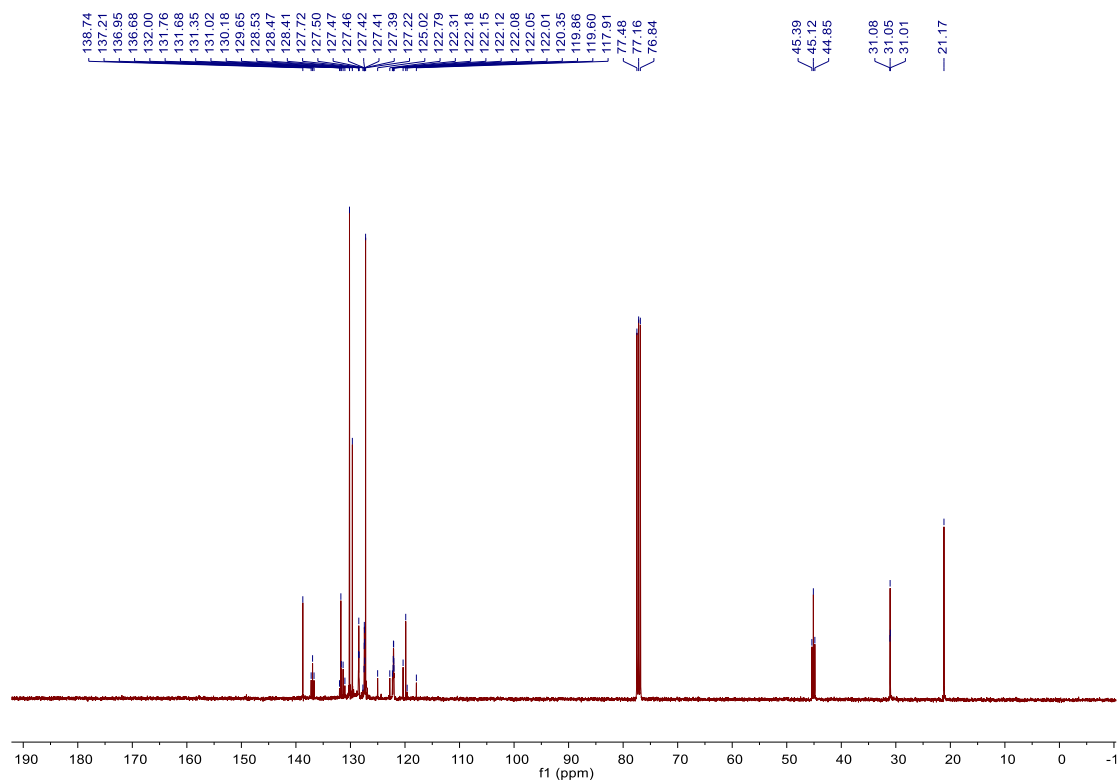


Figure S79. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4u**.

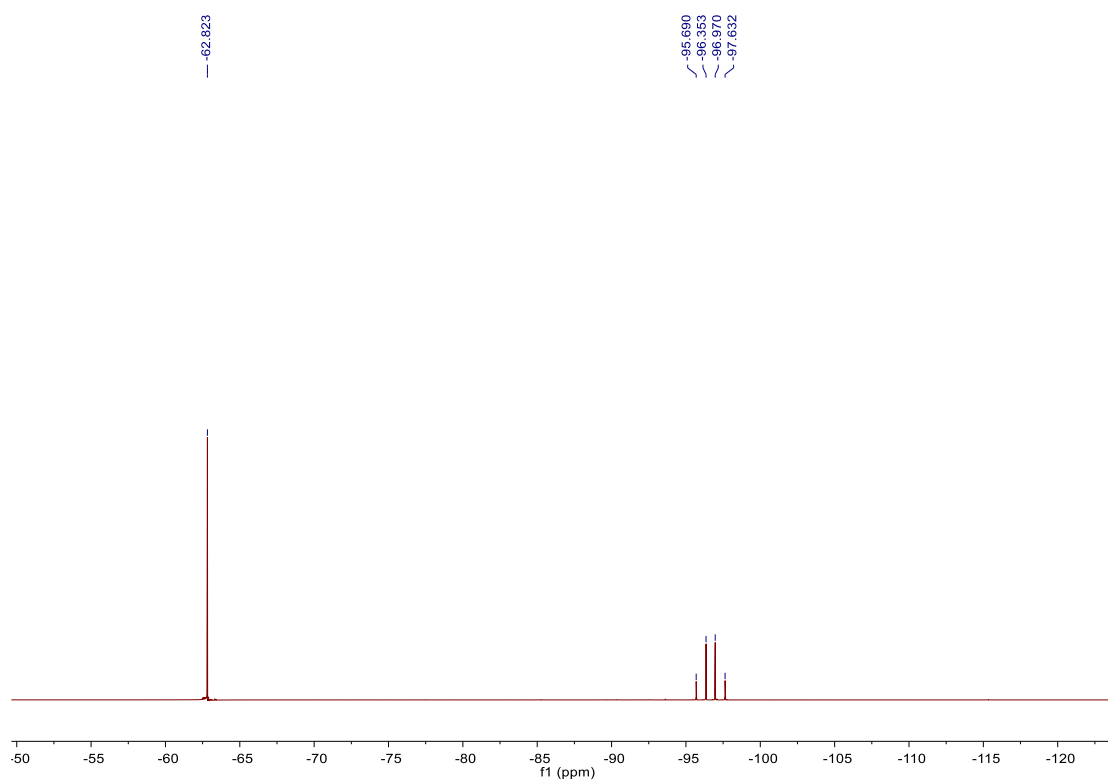


Figure S80. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4v**.

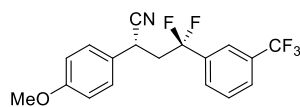
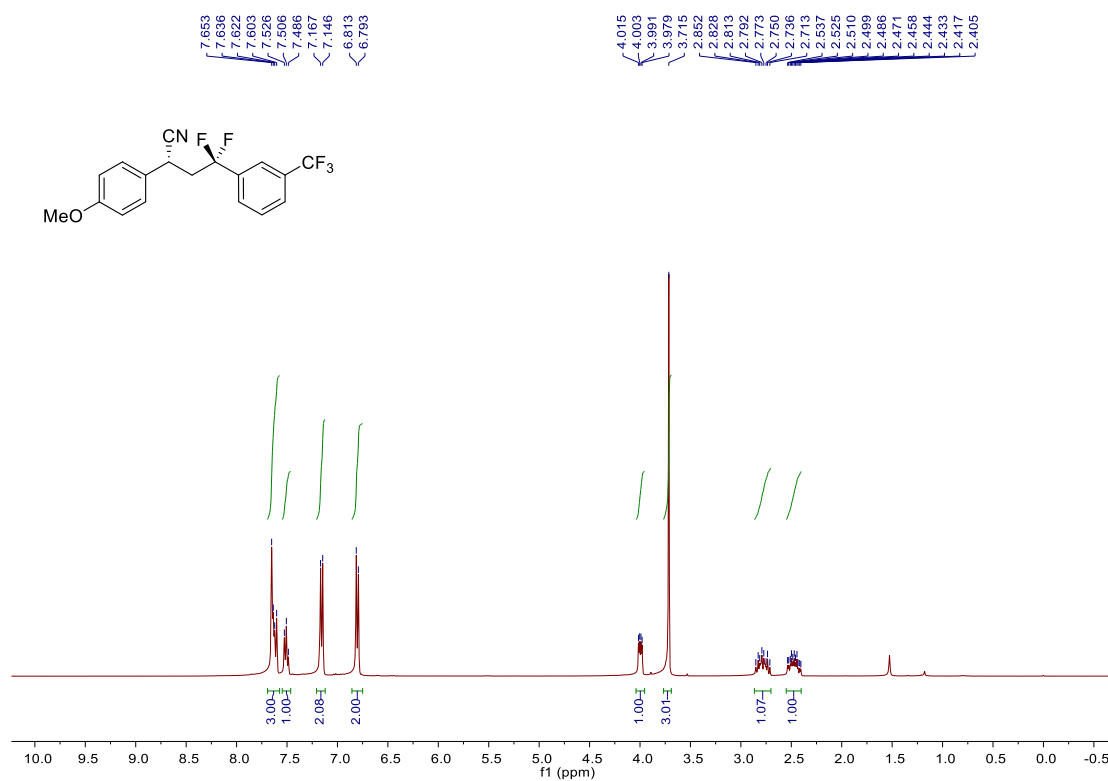


Figure S81. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4v**.

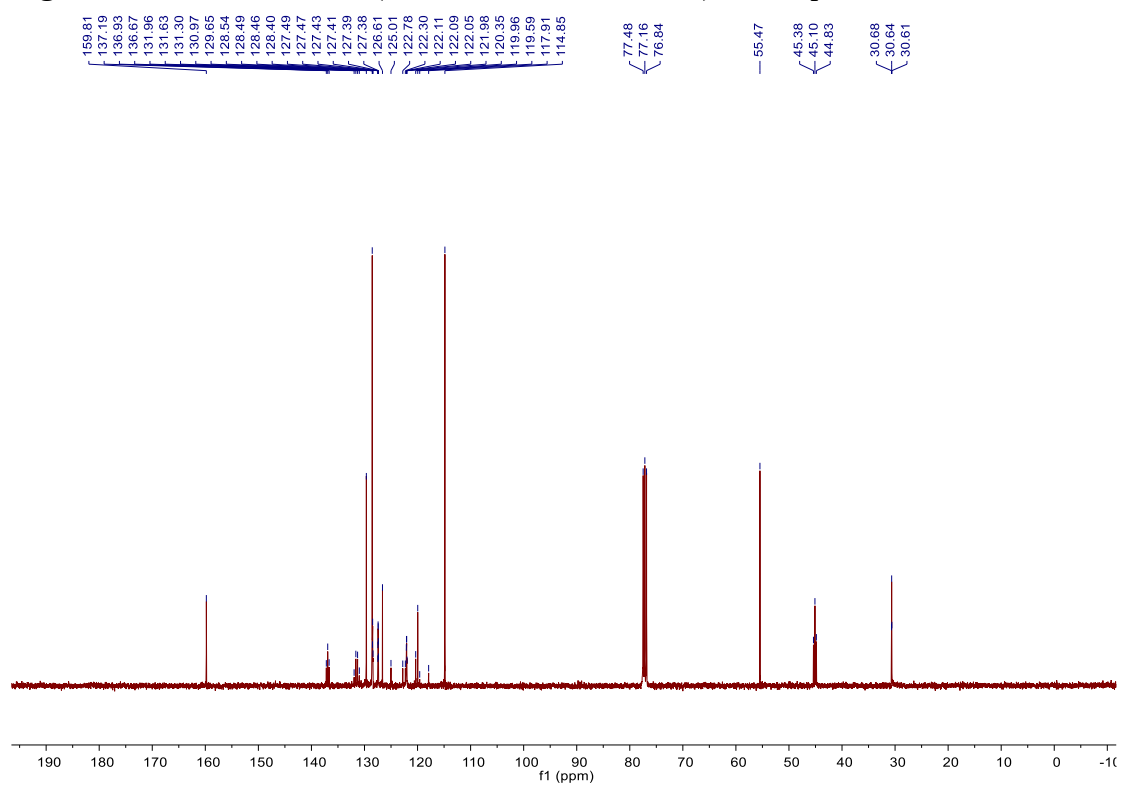


Figure S82. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4v**.

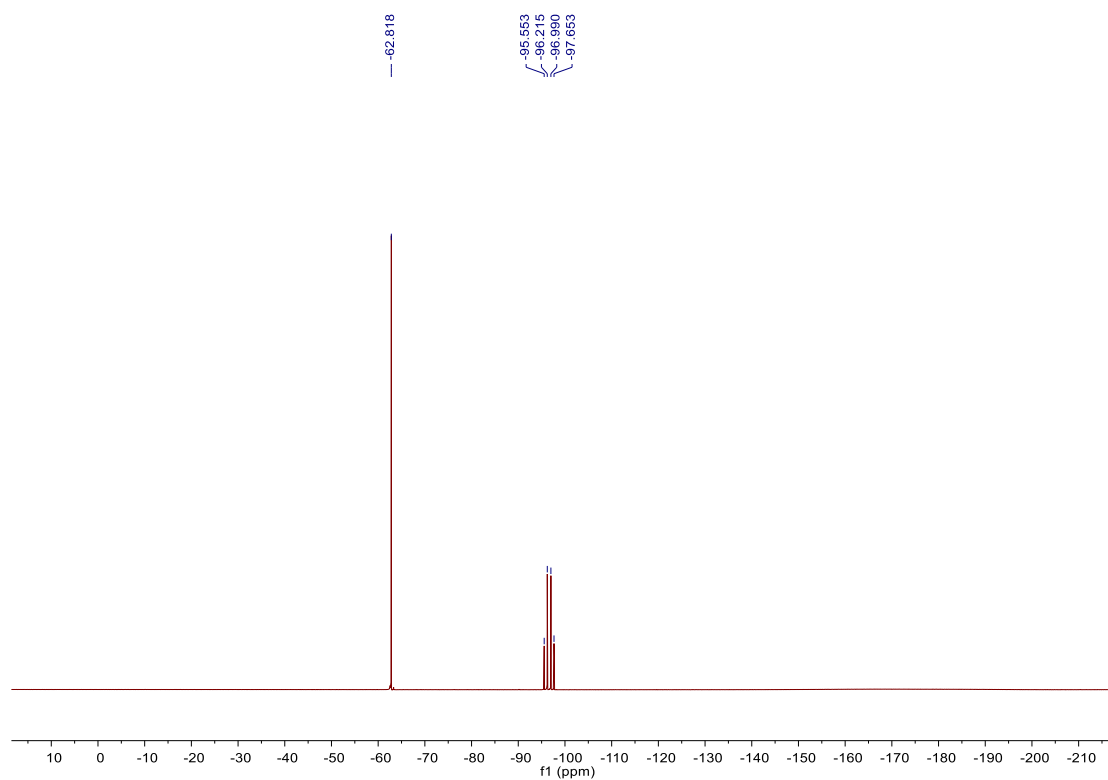


Figure S83. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4w**.

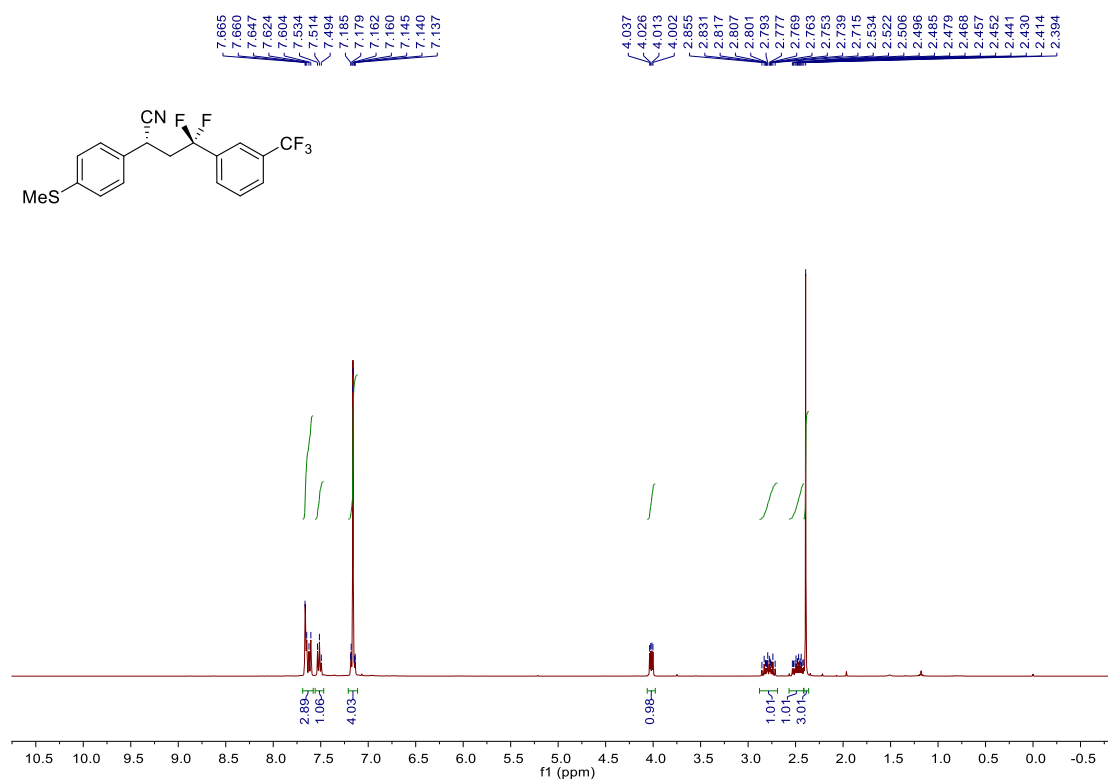


Figure S84. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4w**.

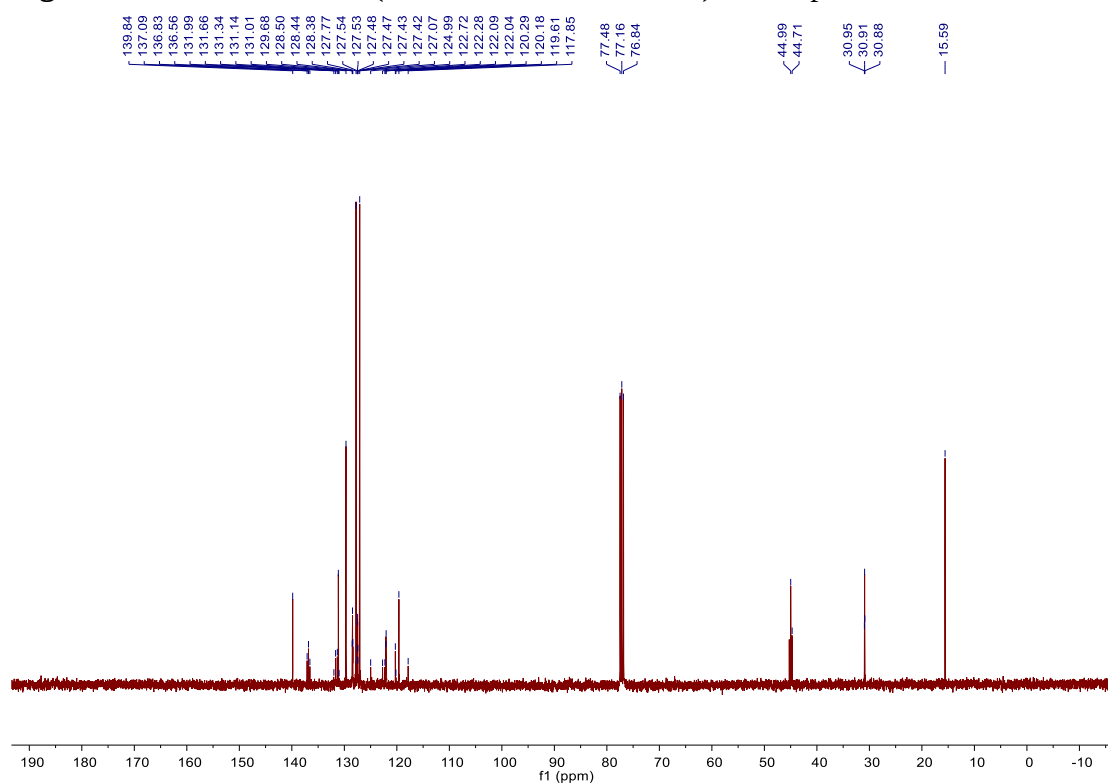


Figure S85. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4w**.

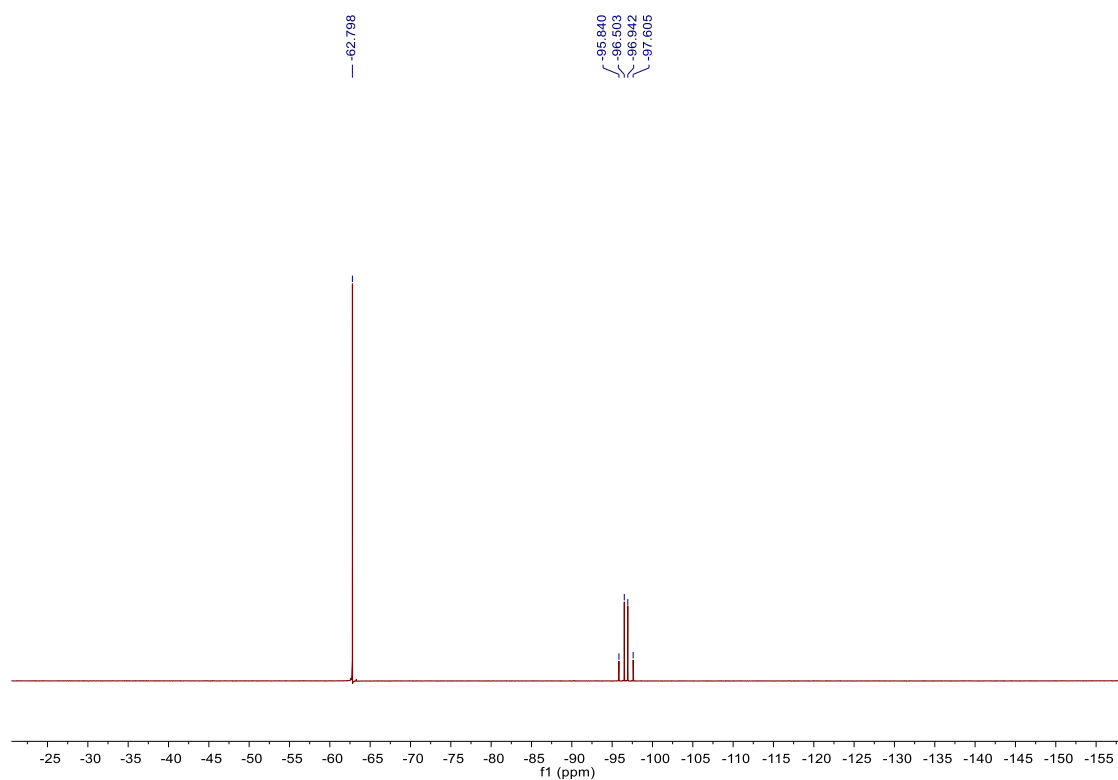


Figure S86. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4x**.

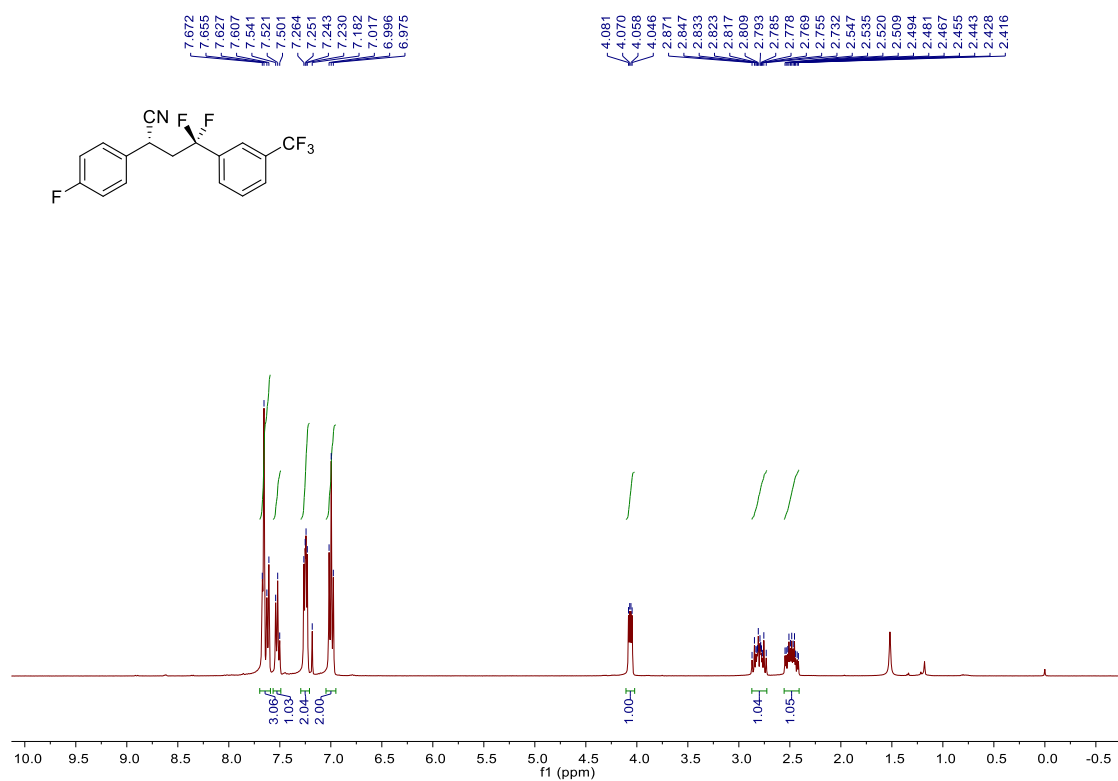


Figure S87. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4x**.

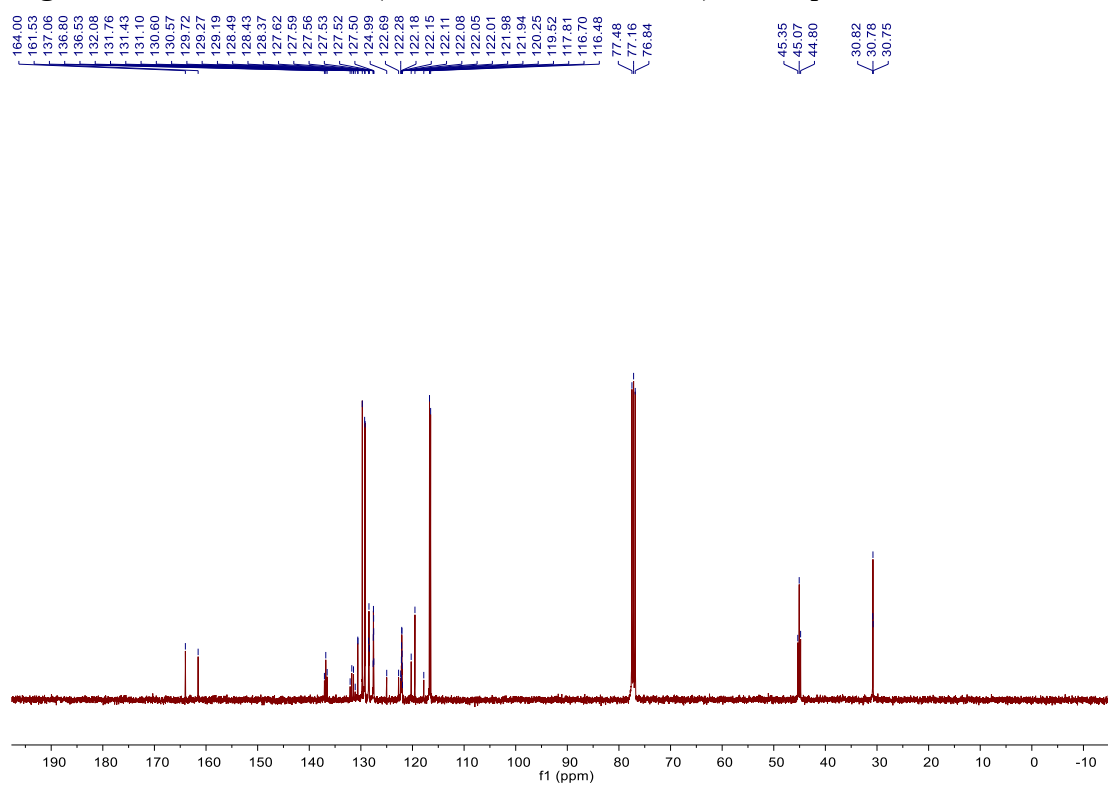
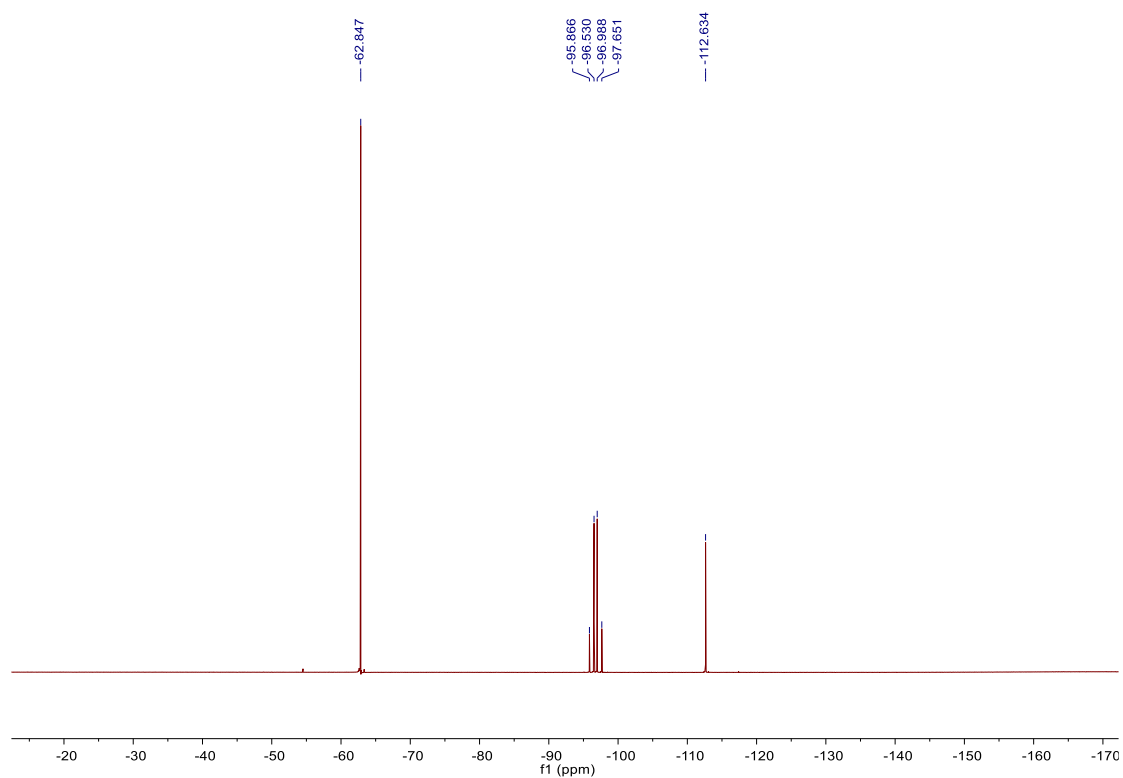


Figure S88. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4x**.



Chemical structure: Clc1ccc(cc1)[C@H](C(F)(F)F)c2cc(C(F)(F)F)ccc2

¹H NMR spectrum (ppm):

- 7.756, 7.735, 7.703, 7.683, 7.622, 7.603, 7.583, 7.568, 7.501, 7.480, 7.280
- 4.155, 4.144, 4.132, 4.120
- 2.958, 2.942, 2.917, 2.904, 2.891, 2.880, 2.865, 2.853, 2.840, 2.827, 2.802, 2.616, 2.605, 2.588, 2.576, 2.569, 2.551, 2.538, 2.525, 2.514, 2.497, 2.486

Integration values: 3.06, 1.06, 2.03, 1.99, 1.00, 1.13, 1.06

137.02
136.75
136.48
136.21
133.25
132.14
131.80
131.47
129.79
131.15
129.75
128.81
128.49
128.43
128.37
127.70
127.67
127.64
127.61
127.58
127.56
127.53
127.51
124.99
122.66
122.27
122.16
122.15
122.12
122.09
122.06
122.03
122.00
121.96
120.22
119.27
77.48
77.16
76.84
45.26
44.99
44.71
30.98
30.95
30.91

Figure S91. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4y**.

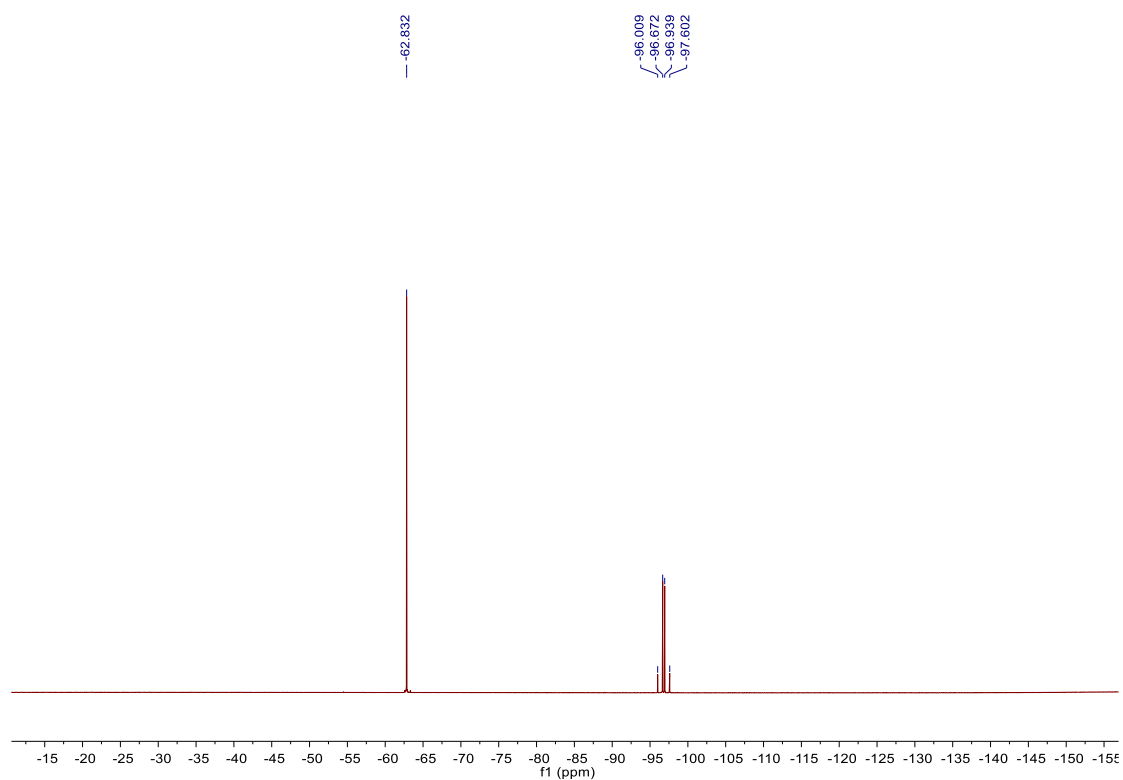


Figure S92. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4z**.

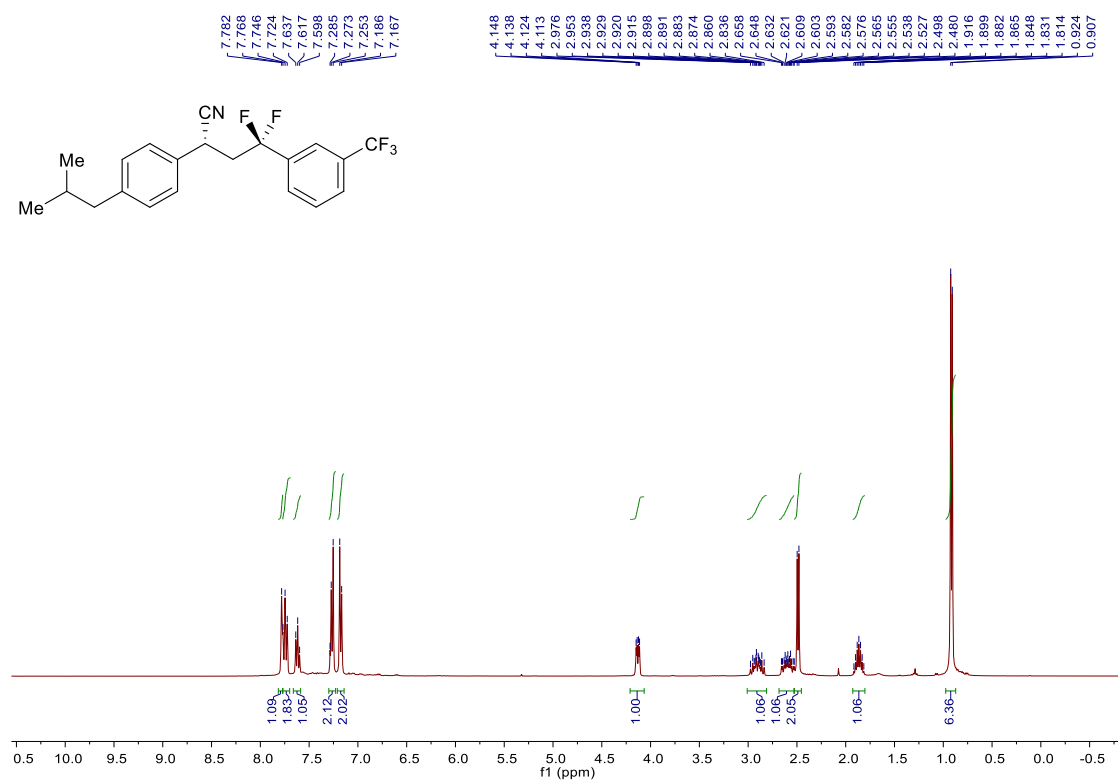


Figure S93. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4z**.

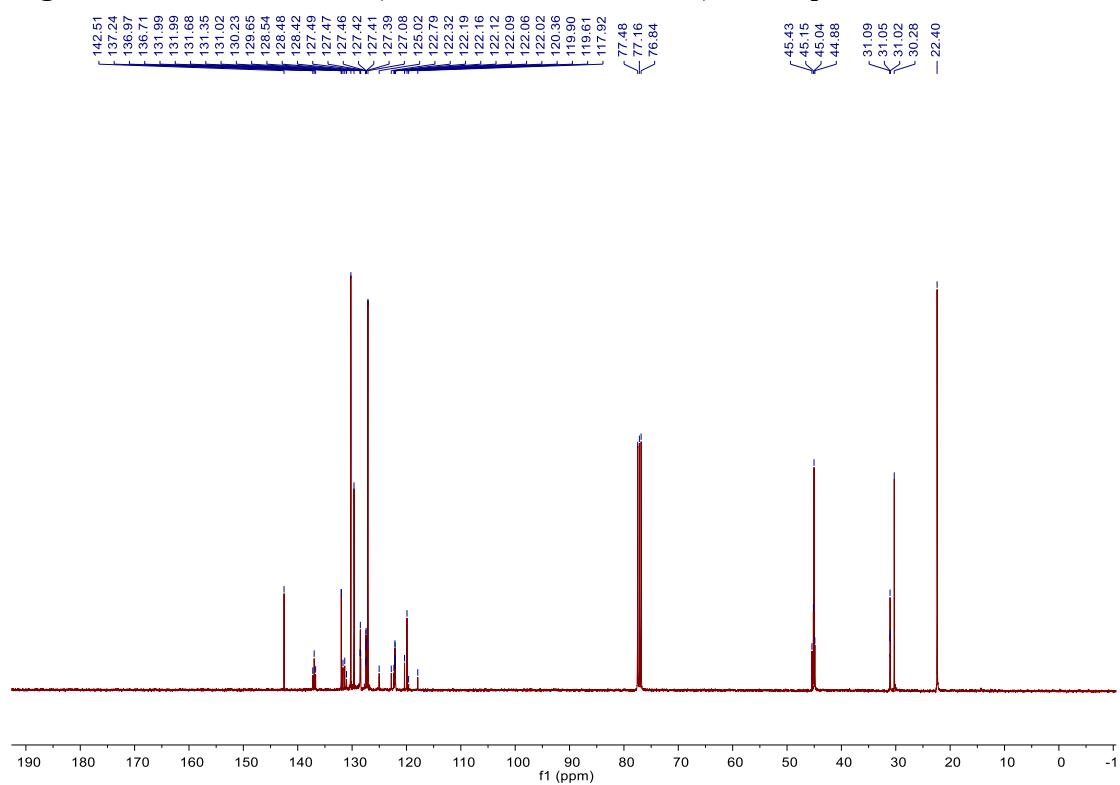
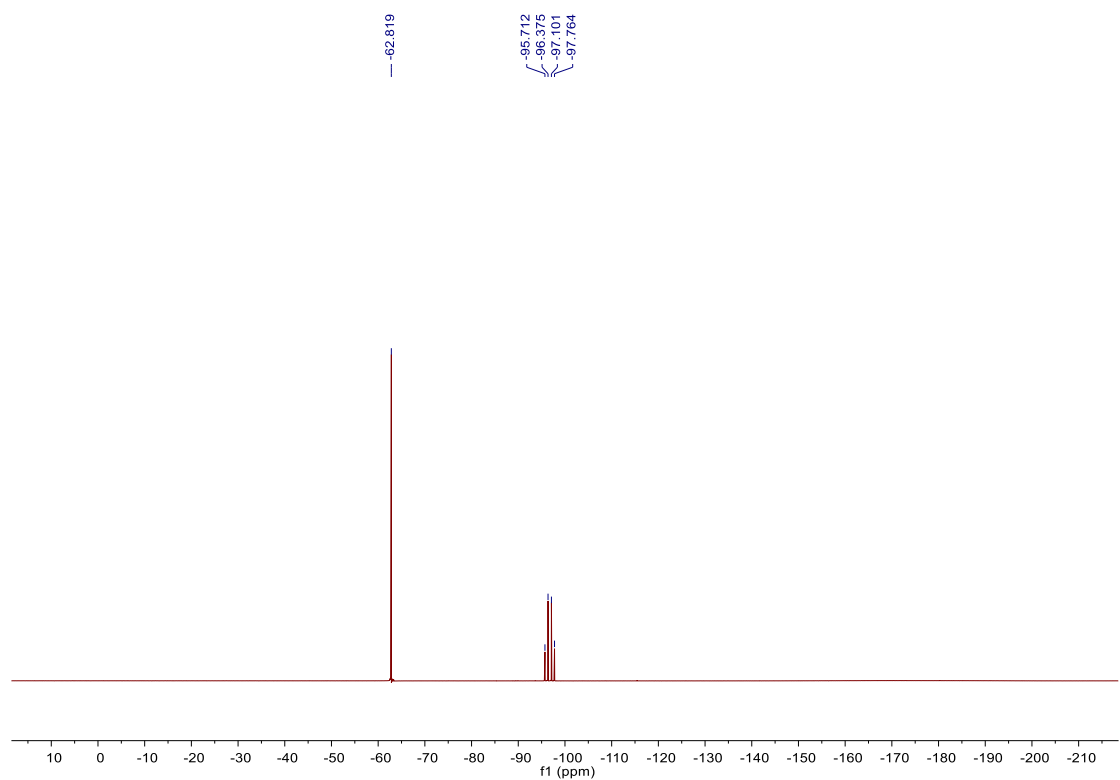


Figure S94. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4z**.



Chemical structure: COc1cc(C#N)ccc1C(F)(F)Cc2ccc(C(F)(F)F)cc2

¹H NMR spectrum (ppm):

- 7.742, 7.726, 7.708, 7.688, 7.614, 7.594, 7.574, 7.260, 6.889, 6.878, 6.806, 6.801, 6.789
- 5.673
- 4.075, 4.064, 4.051, 4.040, 3.904
- 2.962, 2.941, 2.918, 2.903, 2.894, 2.888, 2.880, 2.862, 2.857, 2.848, 2.839, 2.825, 2.801, 2.623, 2.612, 2.596, 2.585, 2.573, 2.566, 2.577, 2.547, 2.541, 2.530, 2.519, 2.507

Integration values (from left to right): 3.00, 0.99, 1.01, 1.91, 0.91, 1.02, 3.00, 1.15, 1.02.

147.16
146.02
137.19
136.82
136.66
132.00
131.68
131.35
131.02
129.66
128.53
128.47
128.41
127.54
127.52
127.48
127.45
127.43
127.40
126.41
125.01
122.77
122.30
122.10
122.06
122.03
120.46
120.34
119.98
117.91
115.16
109.86
77.45
77.16
76.84
— 56.18
45.52
45.25
44.98
31.15
31.12
31.06

270 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -10 -20 -30 -40 -50 -60 -70

f1 (ppm)

Figure S97. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4aa**.

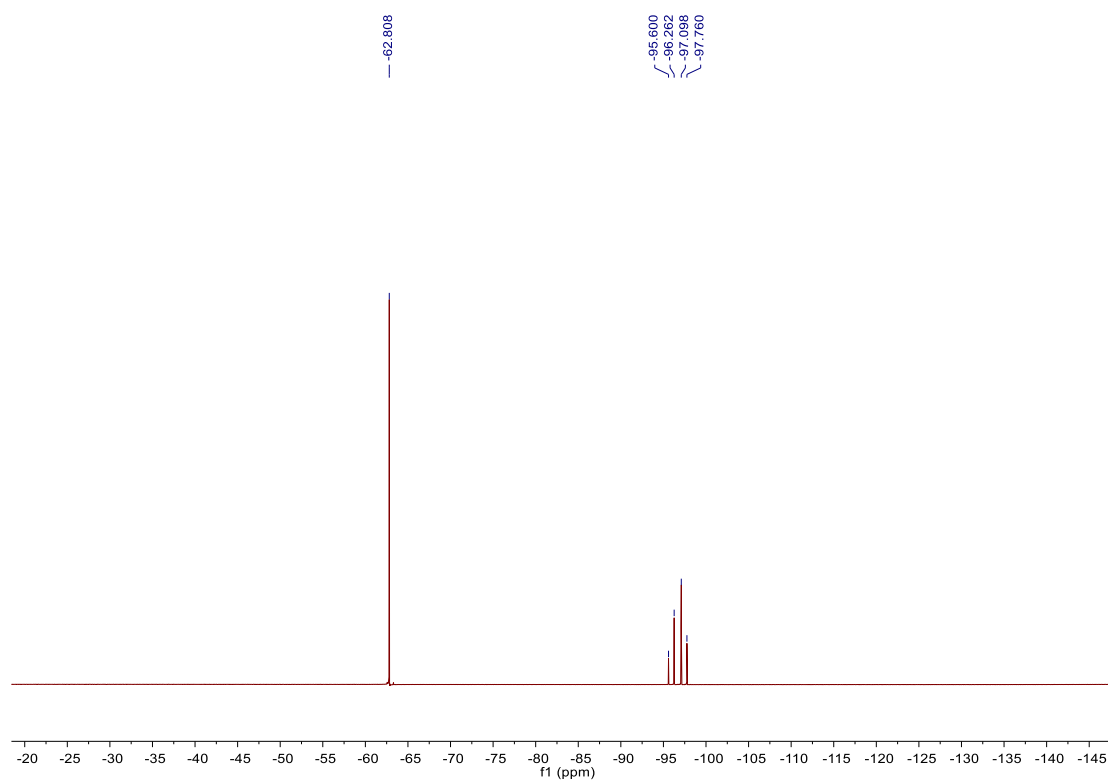


Figure S98. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ab**.

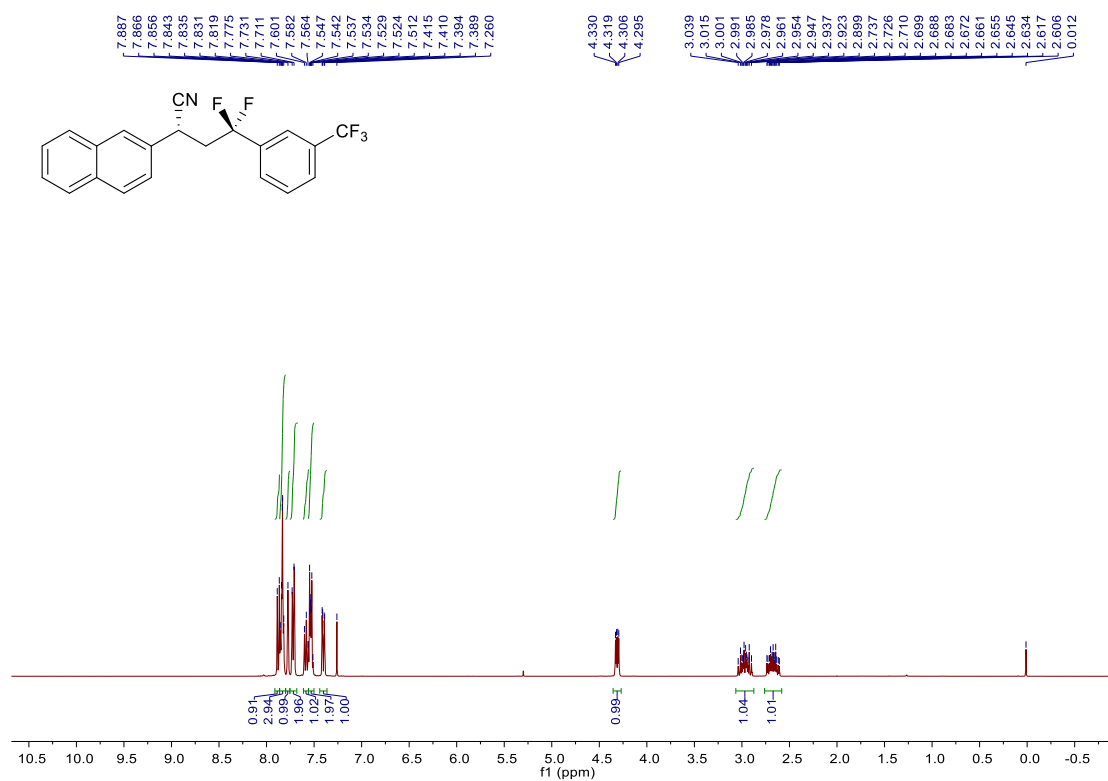


Figure S99. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ab**.

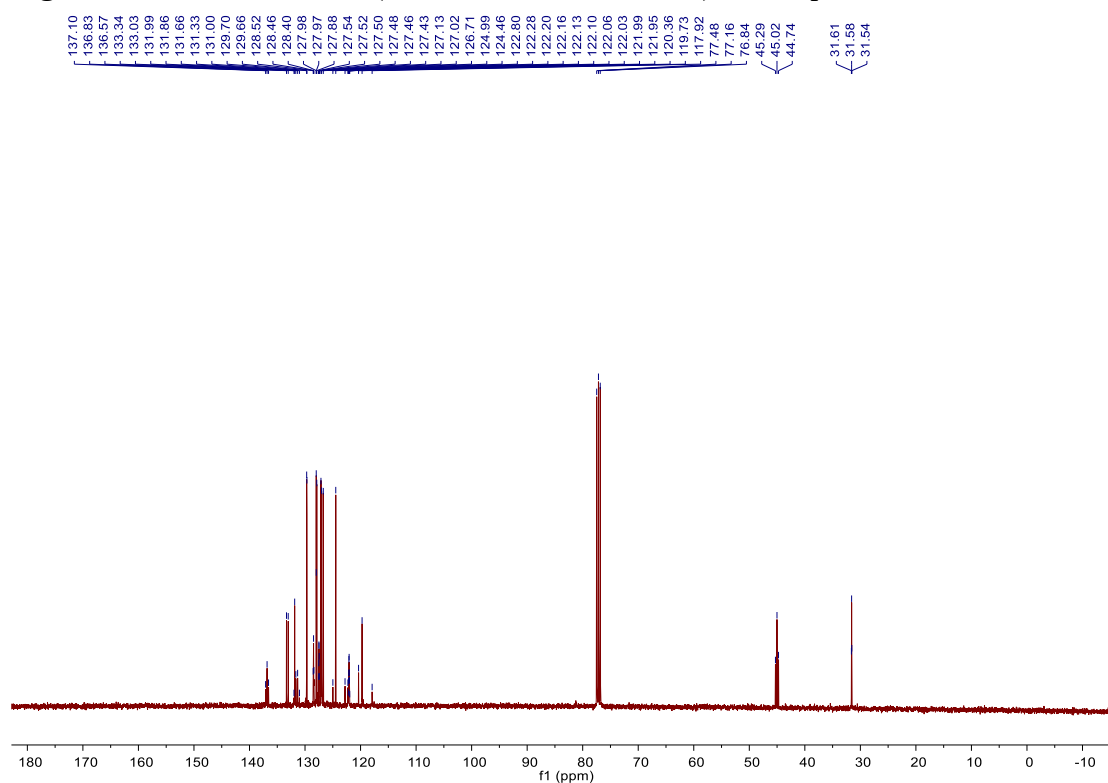


Figure 100. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ab**.

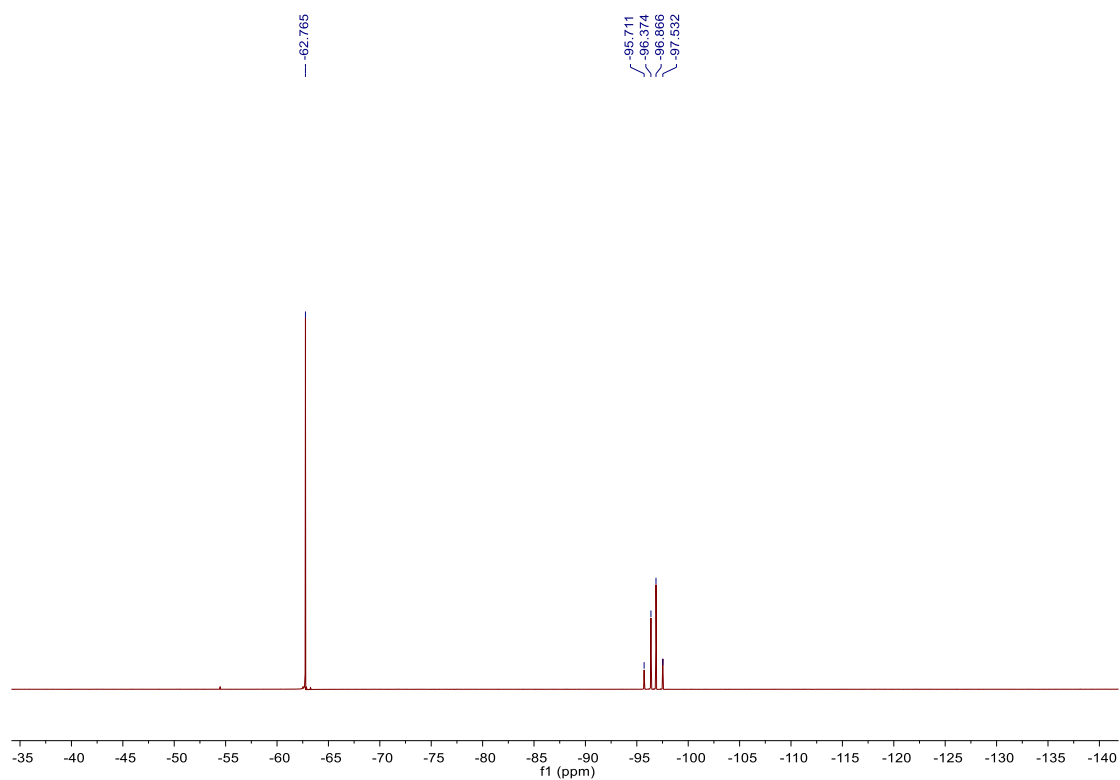


Figure S101. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ac**.

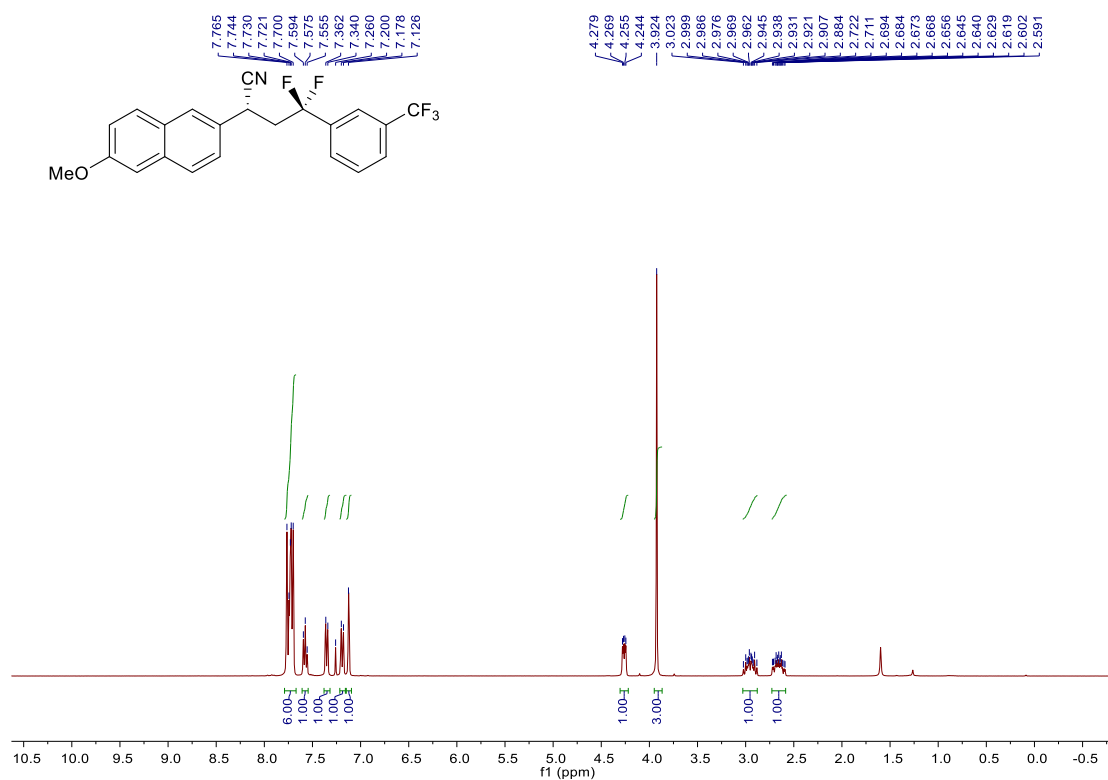


Figure S102. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ac**.

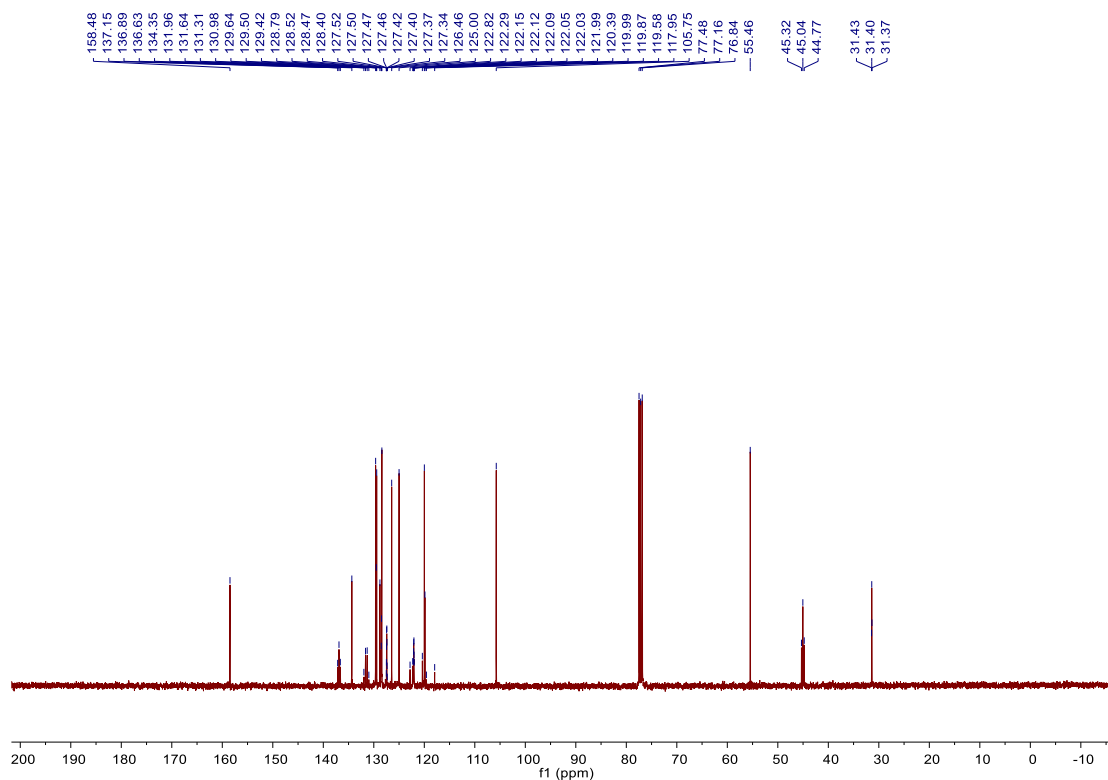


Figure S103. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ac**.

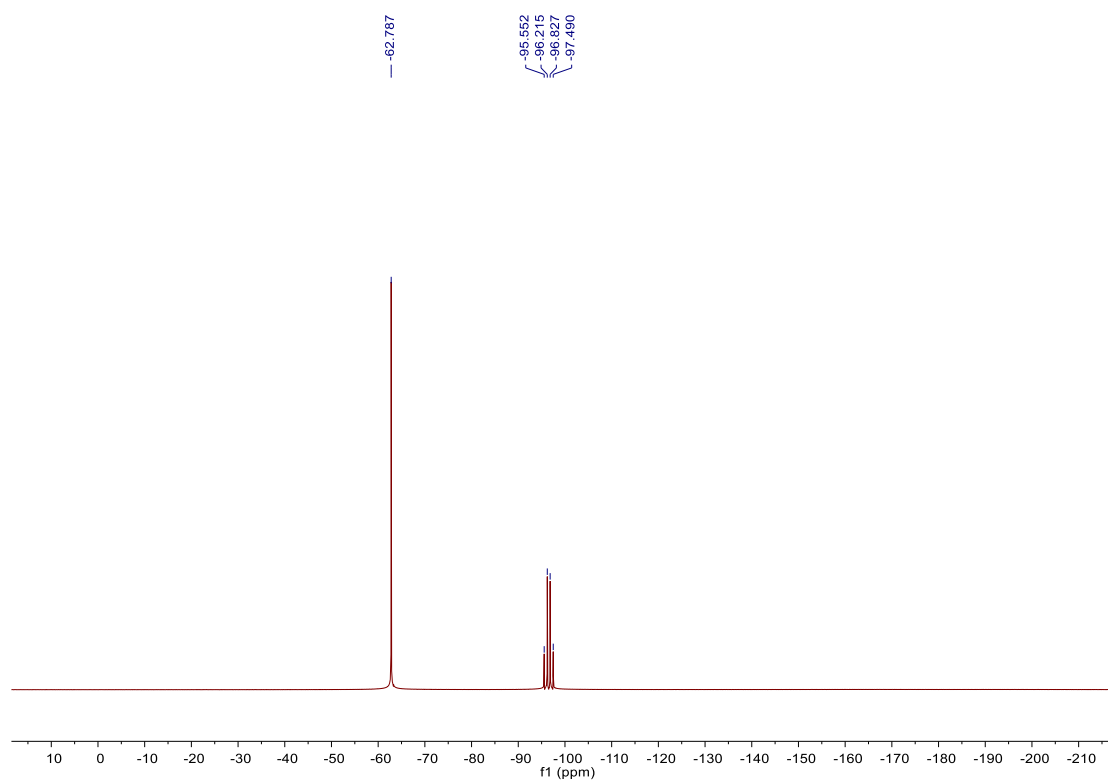


Figure S104. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ad**.

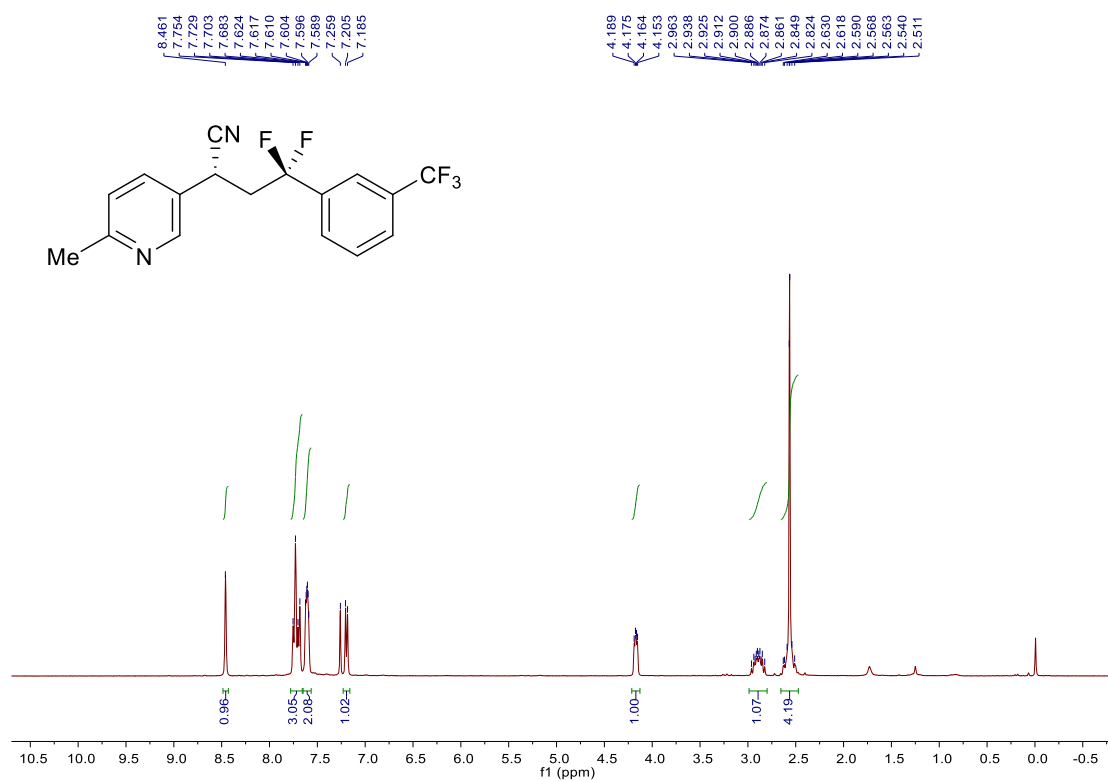


Figure S105. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ad**.

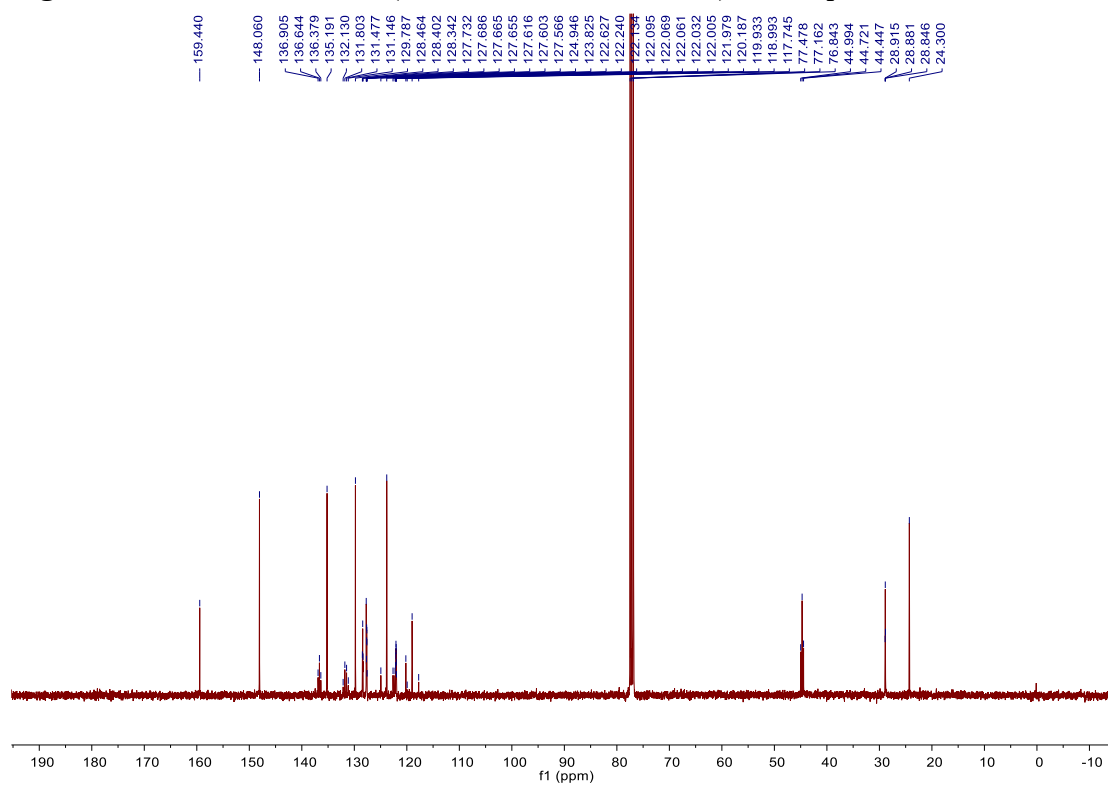


Figure S106. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ad**.

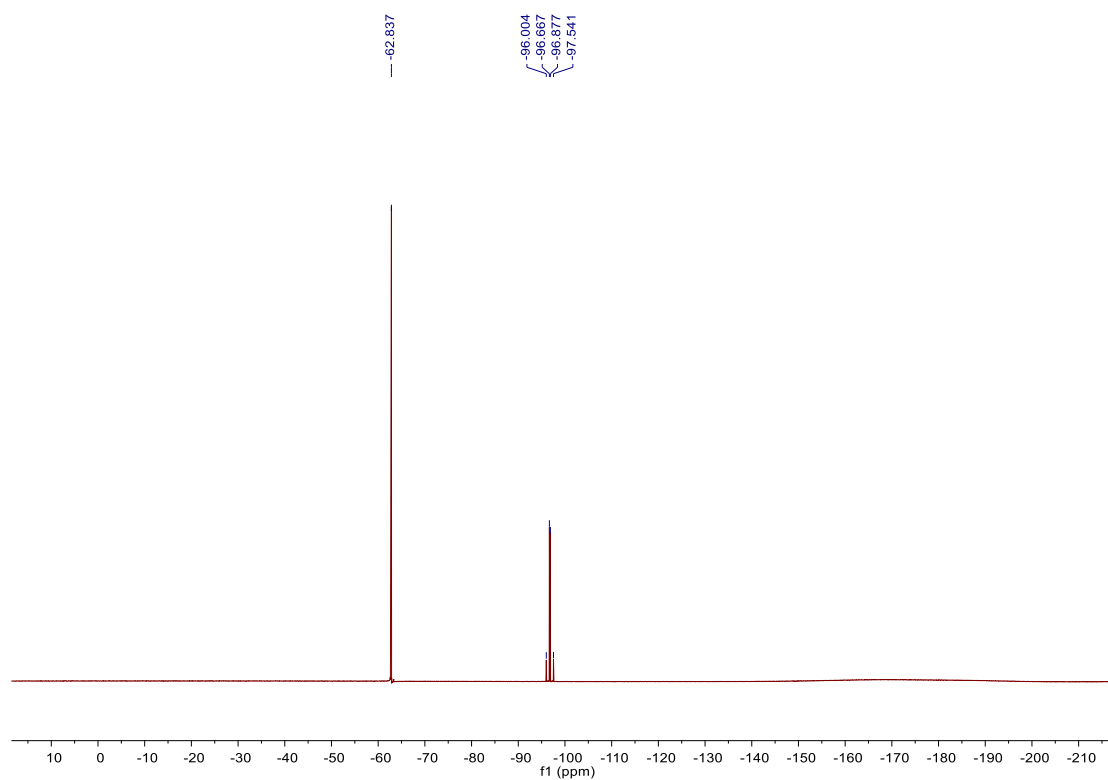


Figure S107. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ae**.

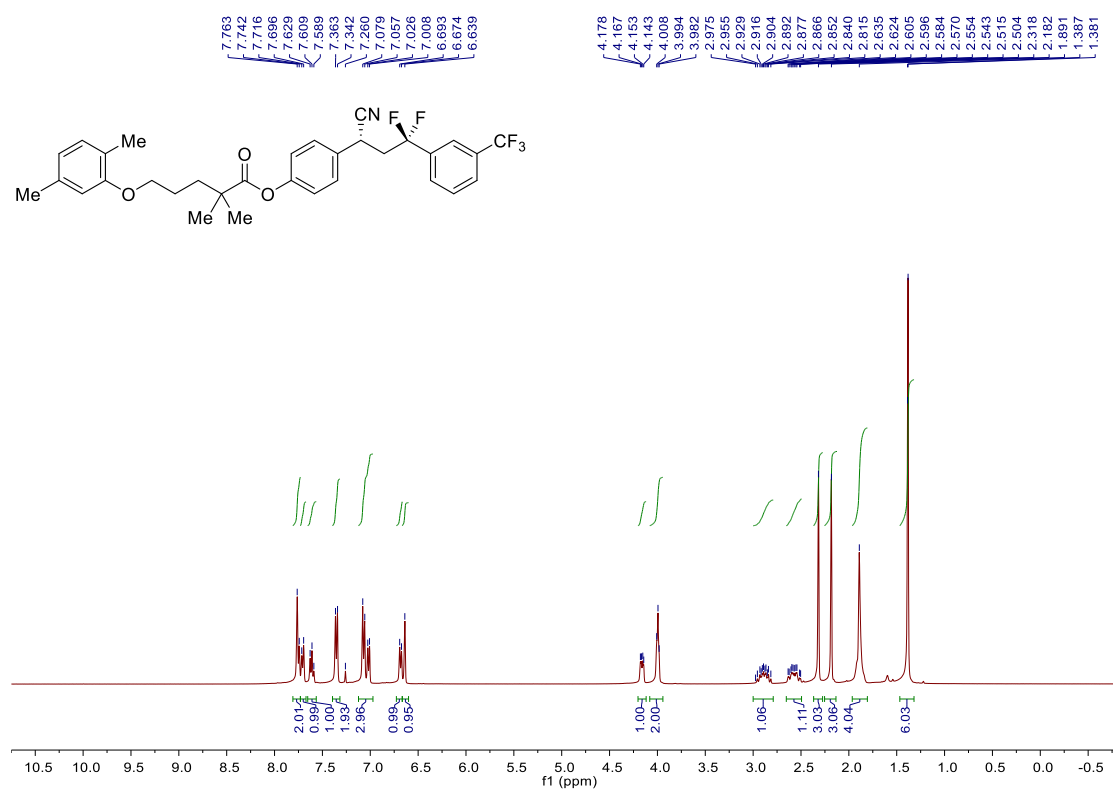


Figure S108. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ae**.

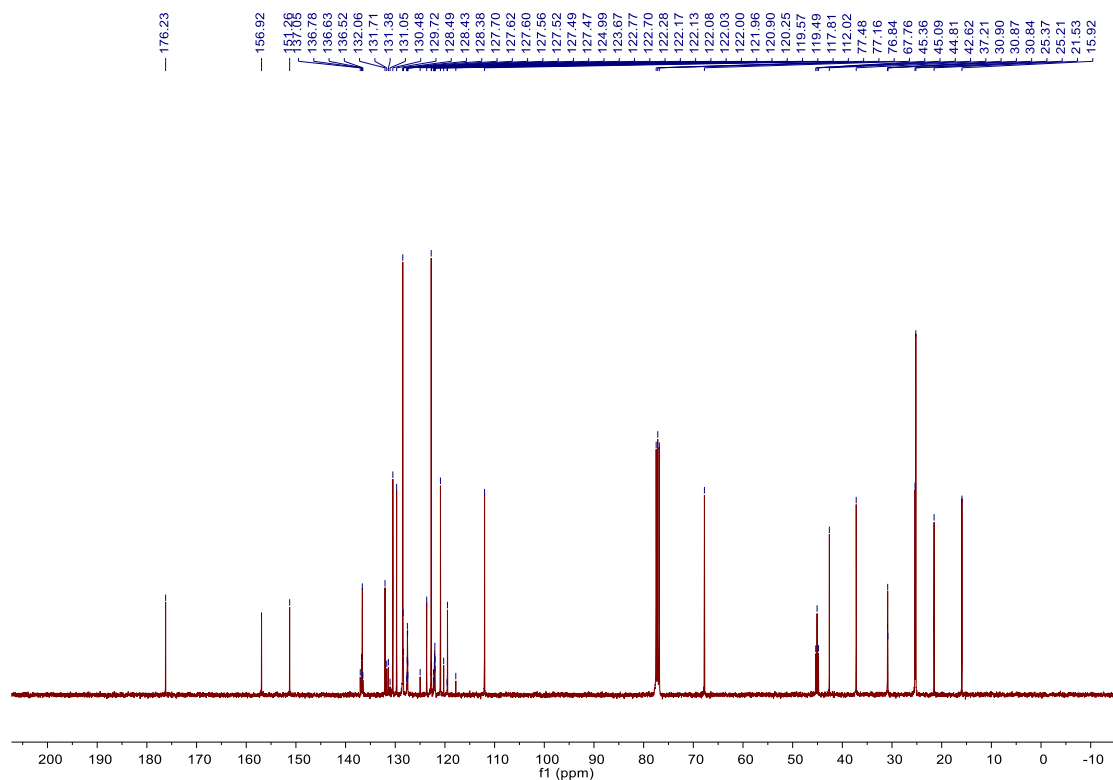


Figure S109. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ae**.

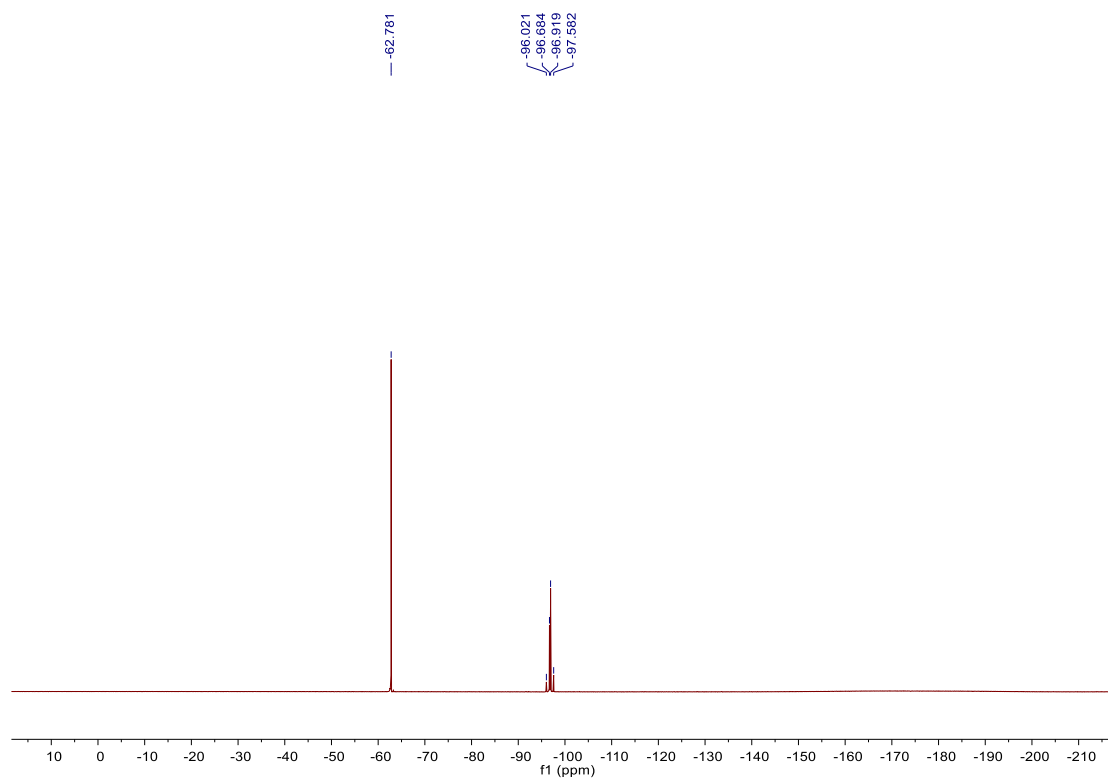


Figure S110. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4af**.

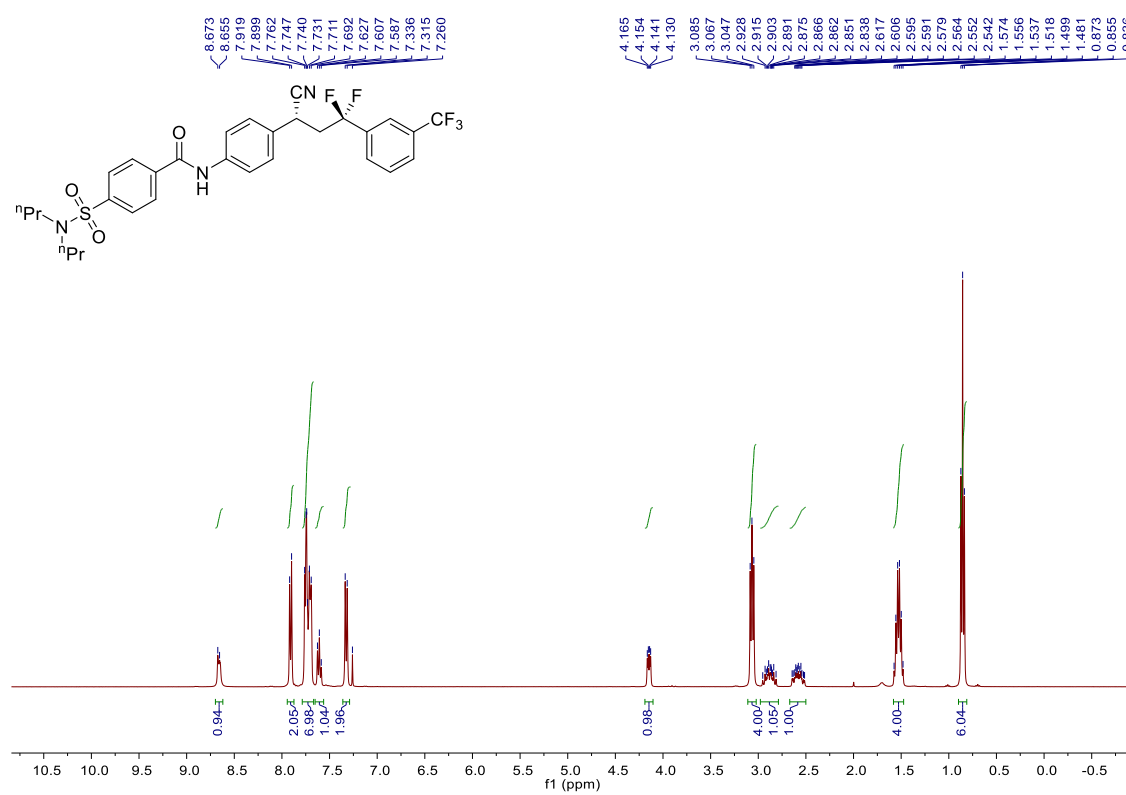


Figure S111. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4af**.

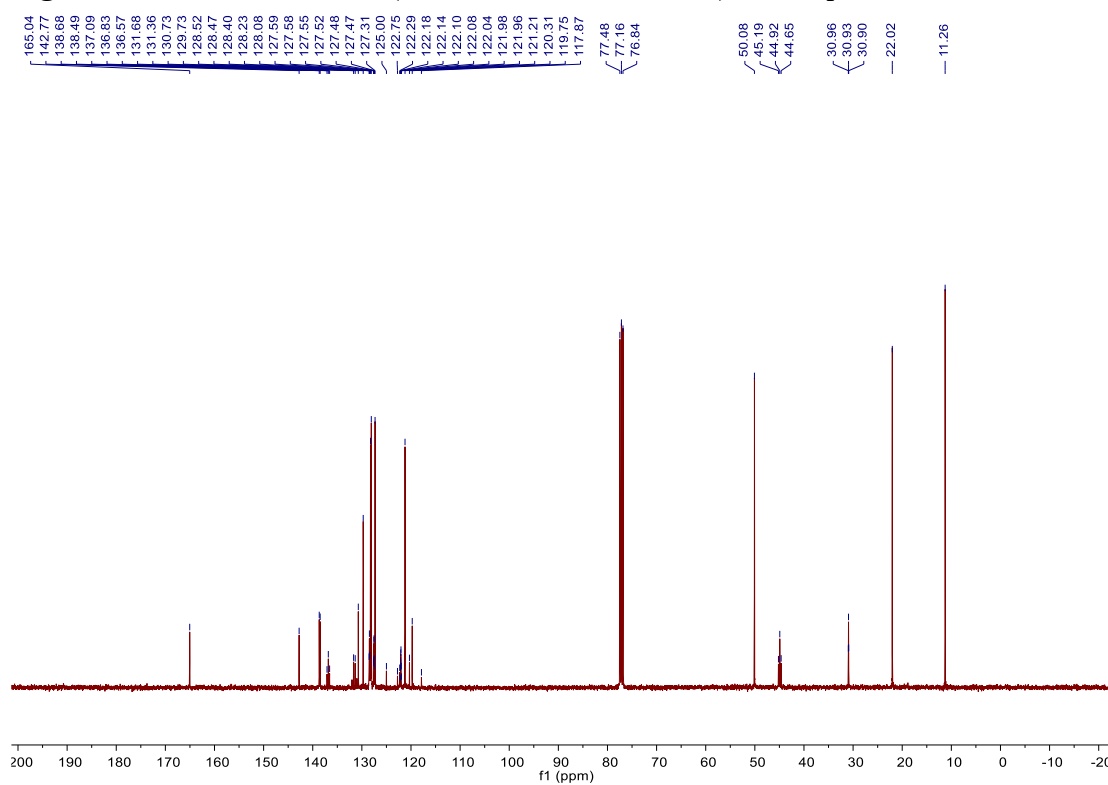


Figure S112. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4af**.

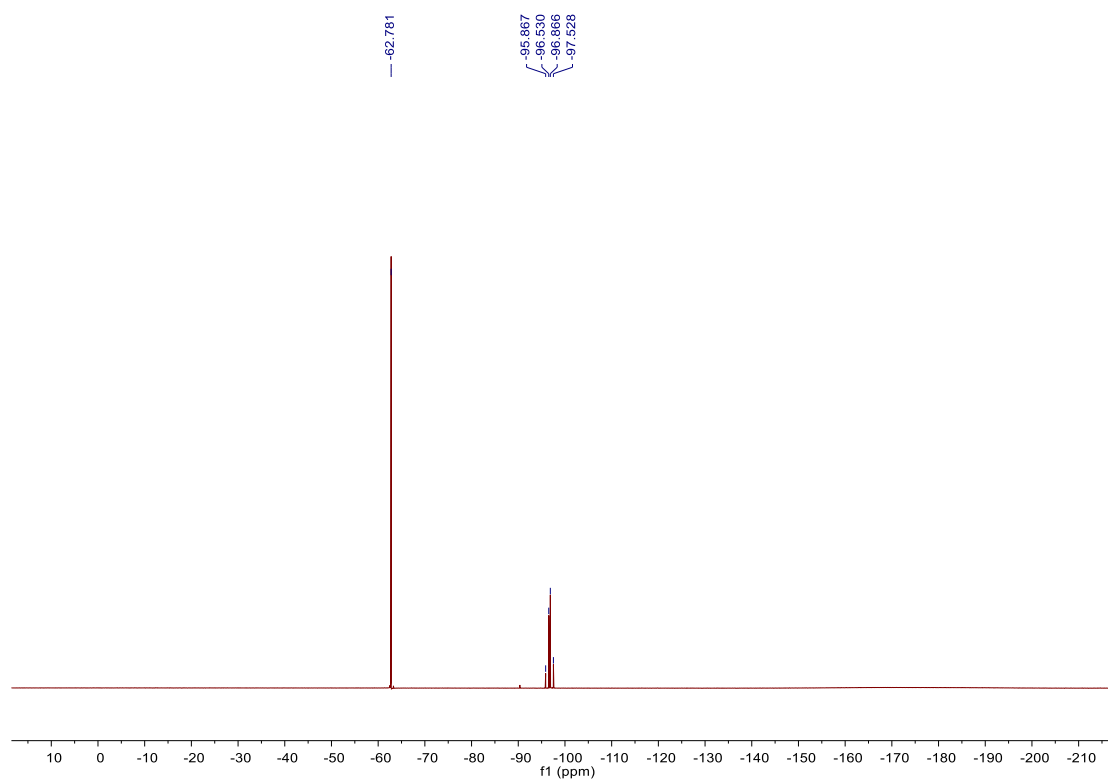


Figure S113. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ag**.

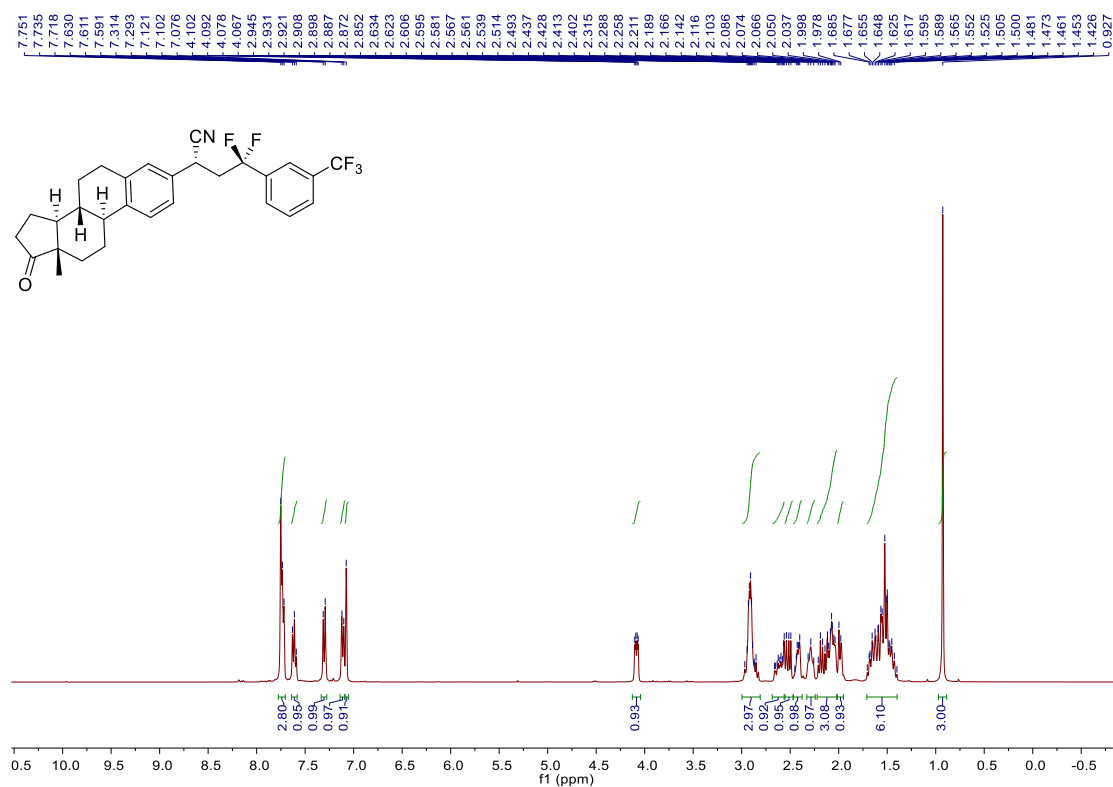


Figure S114. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ag**.

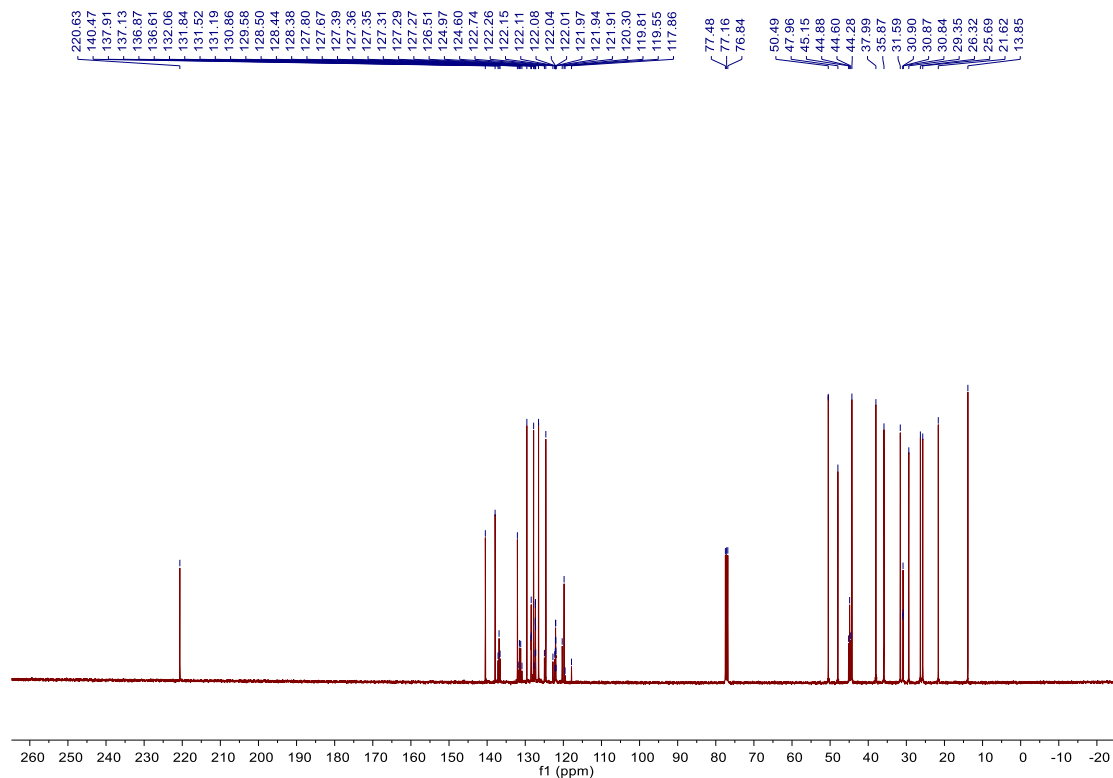


Figure S115. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ag**.

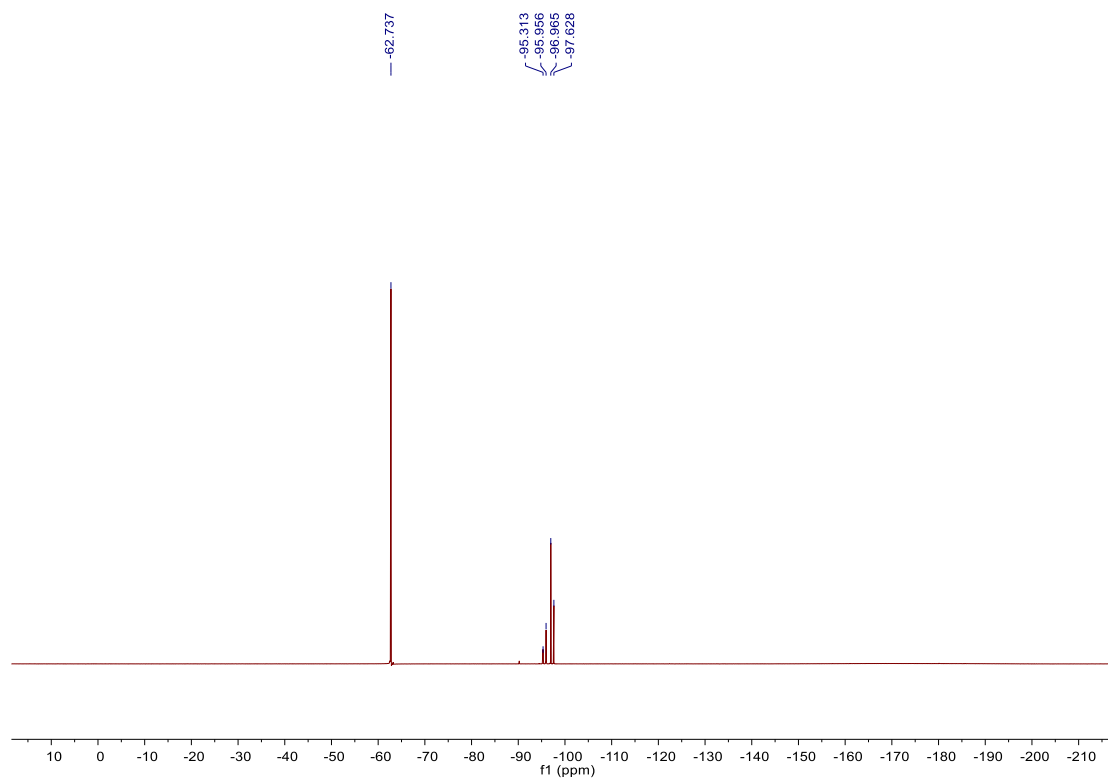


Figure S116. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ah**.

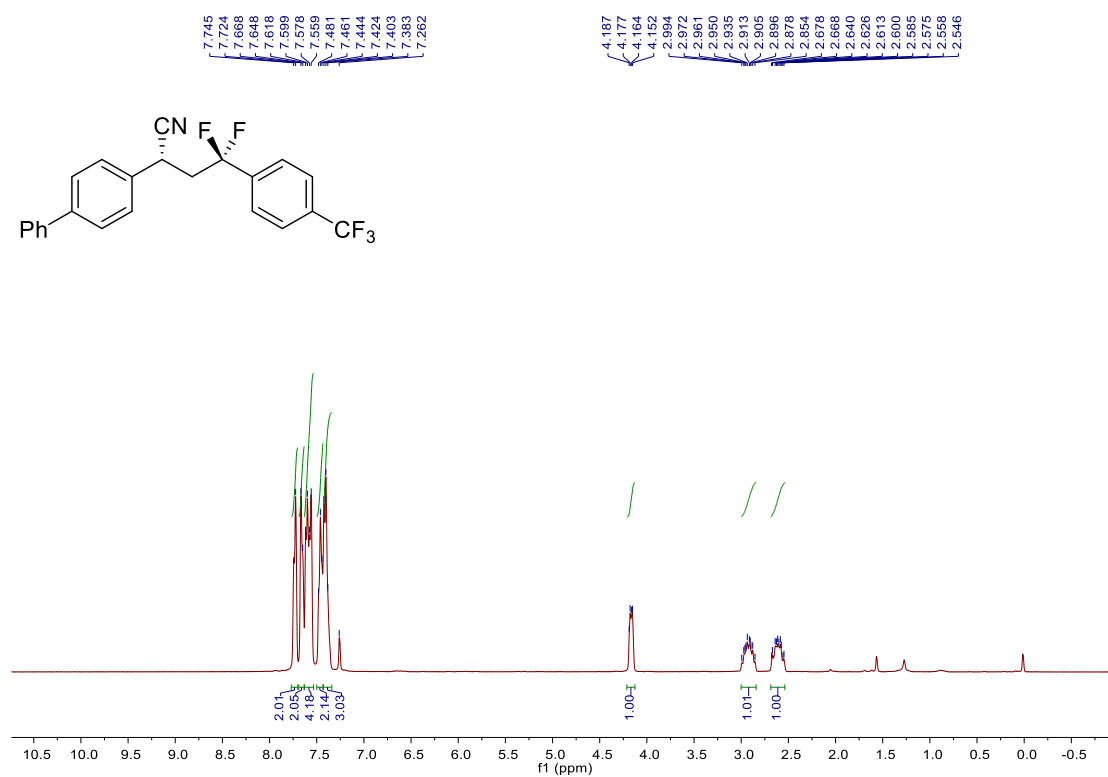


Figure S117. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ah**.

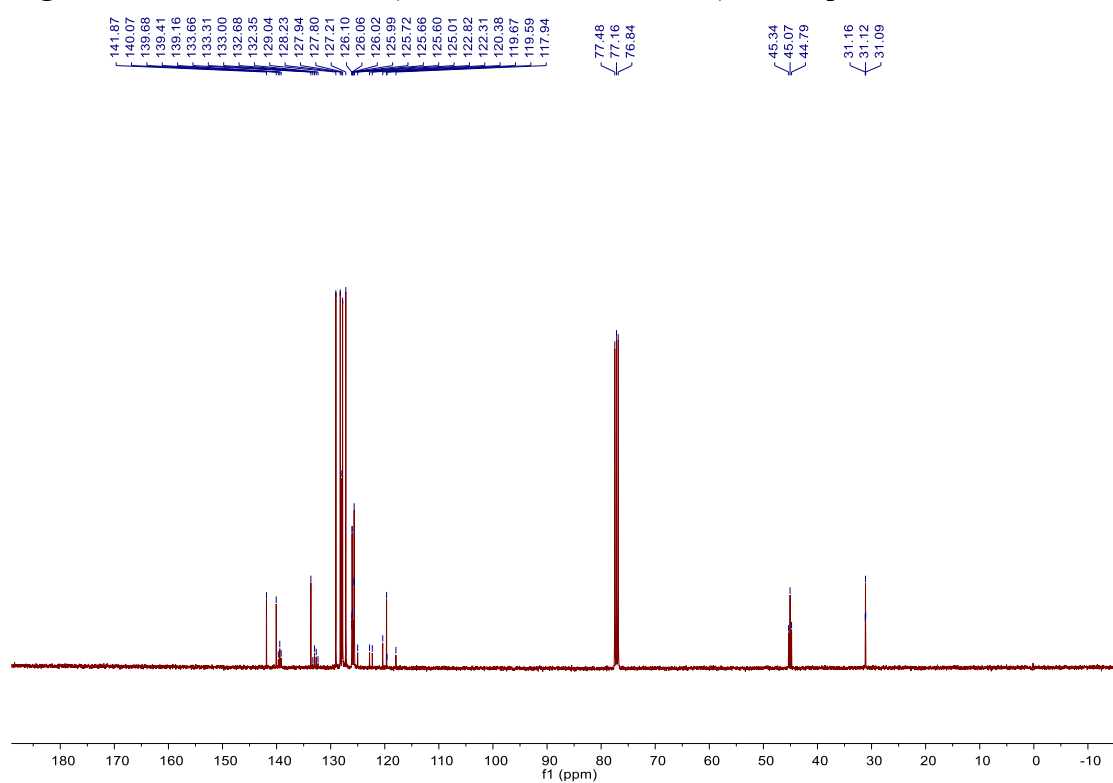


Figure S118. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ah**.

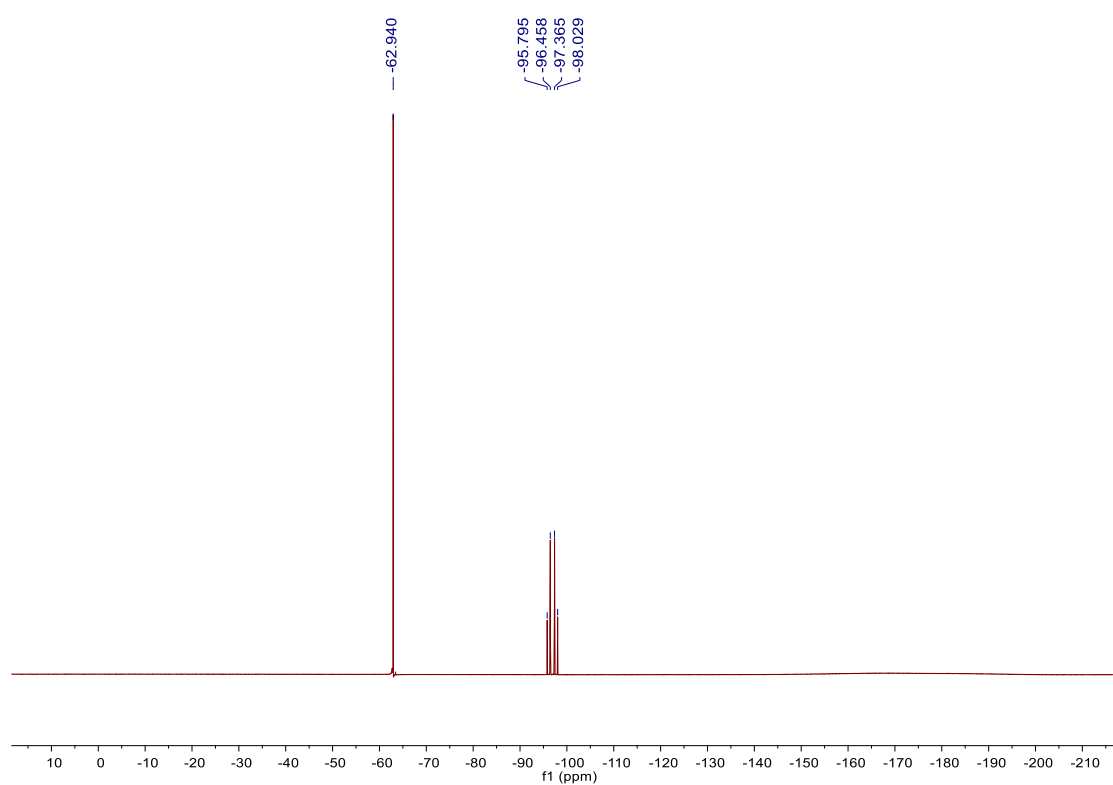


Figure S119. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ai**.

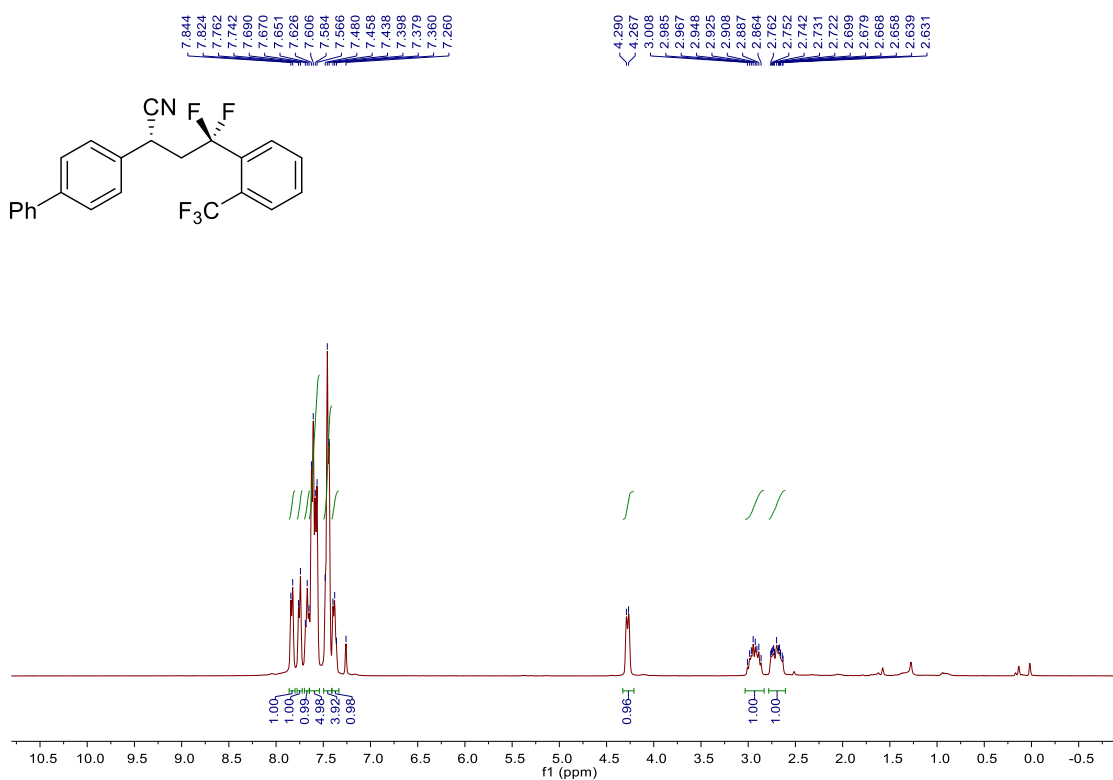


Figure S120. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ai**.

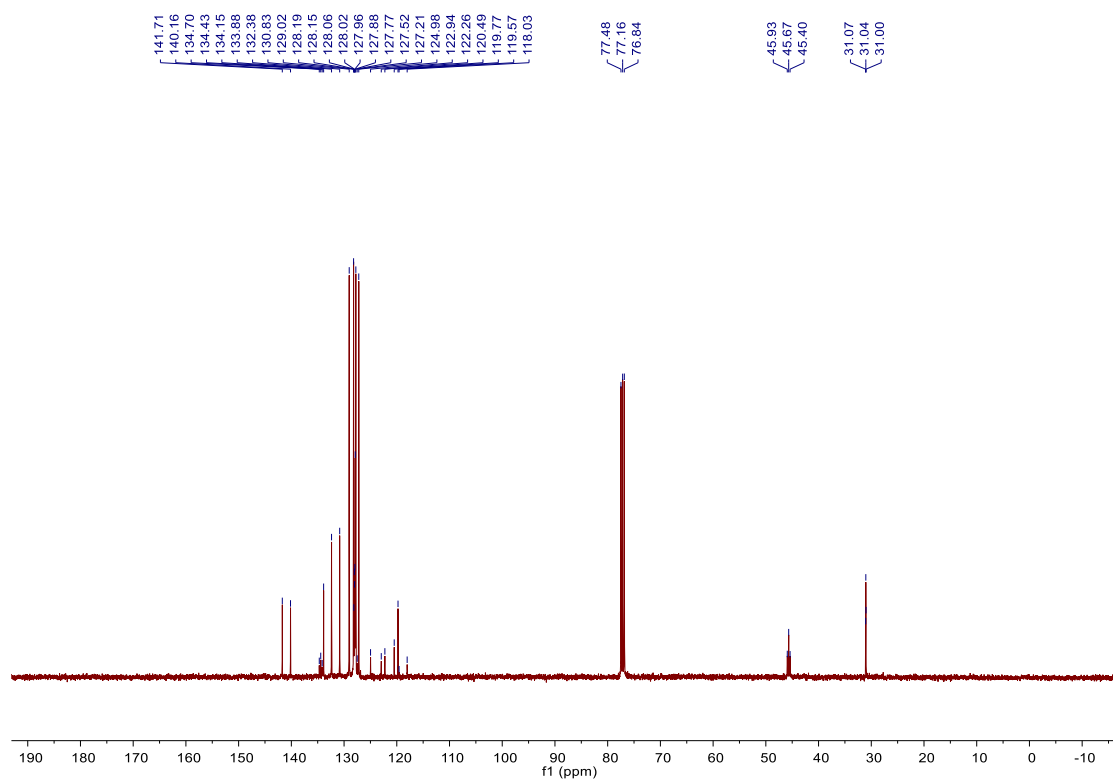


Figure S121. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ai**.

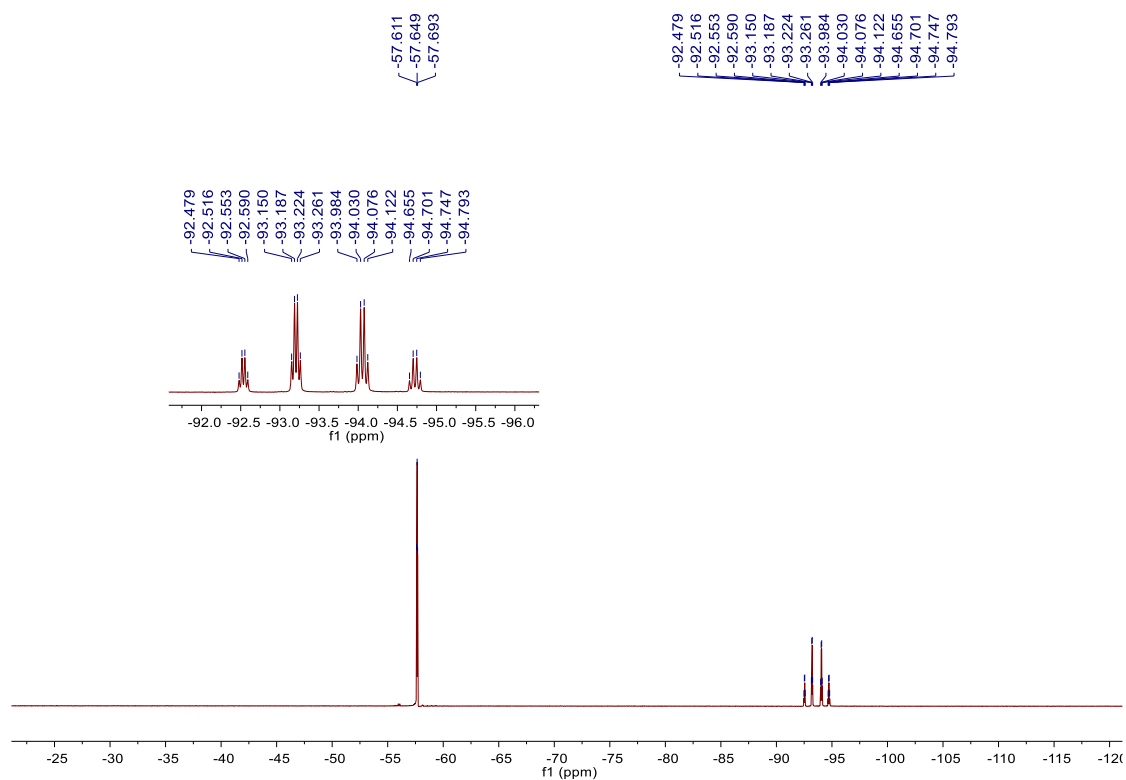


Figure S122. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4aj**.

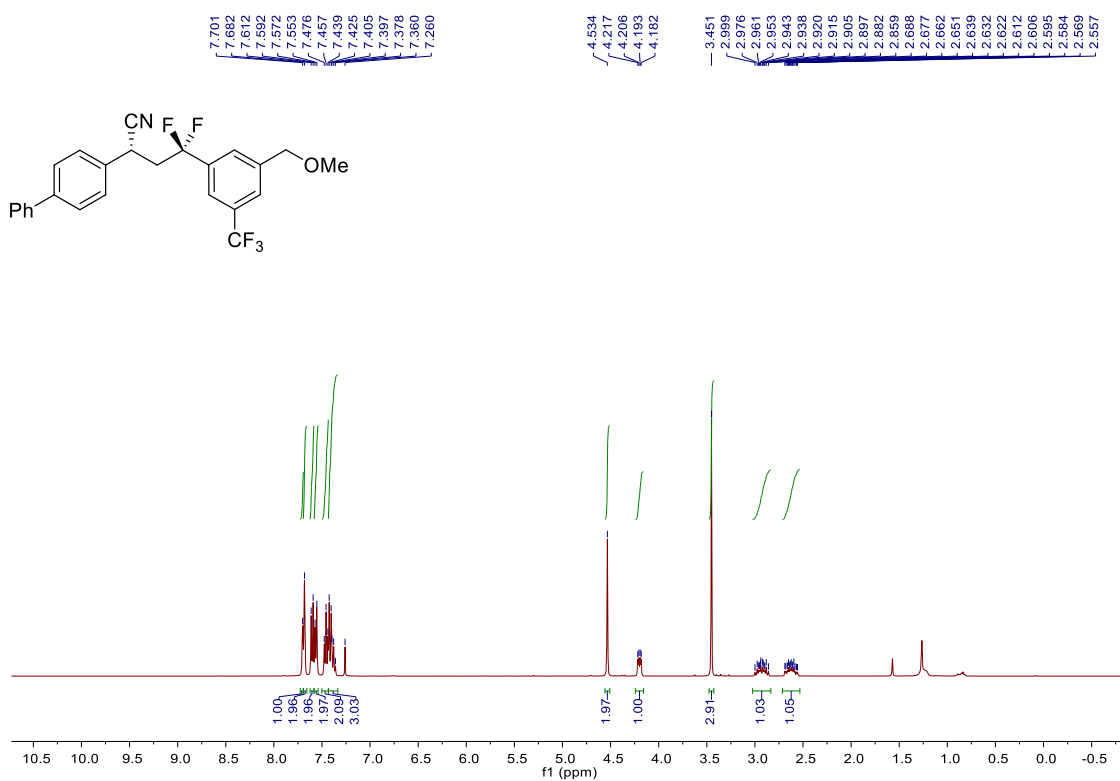


Figure S123. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4aj**.

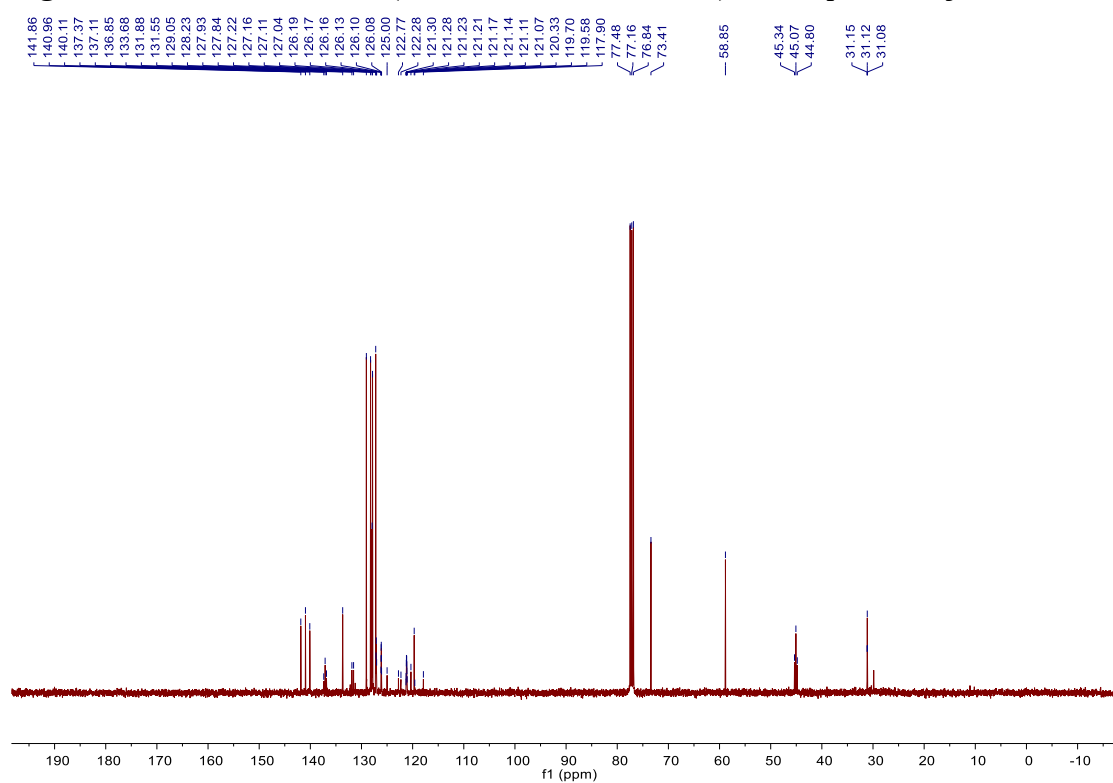


Figure S124. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4aj**.

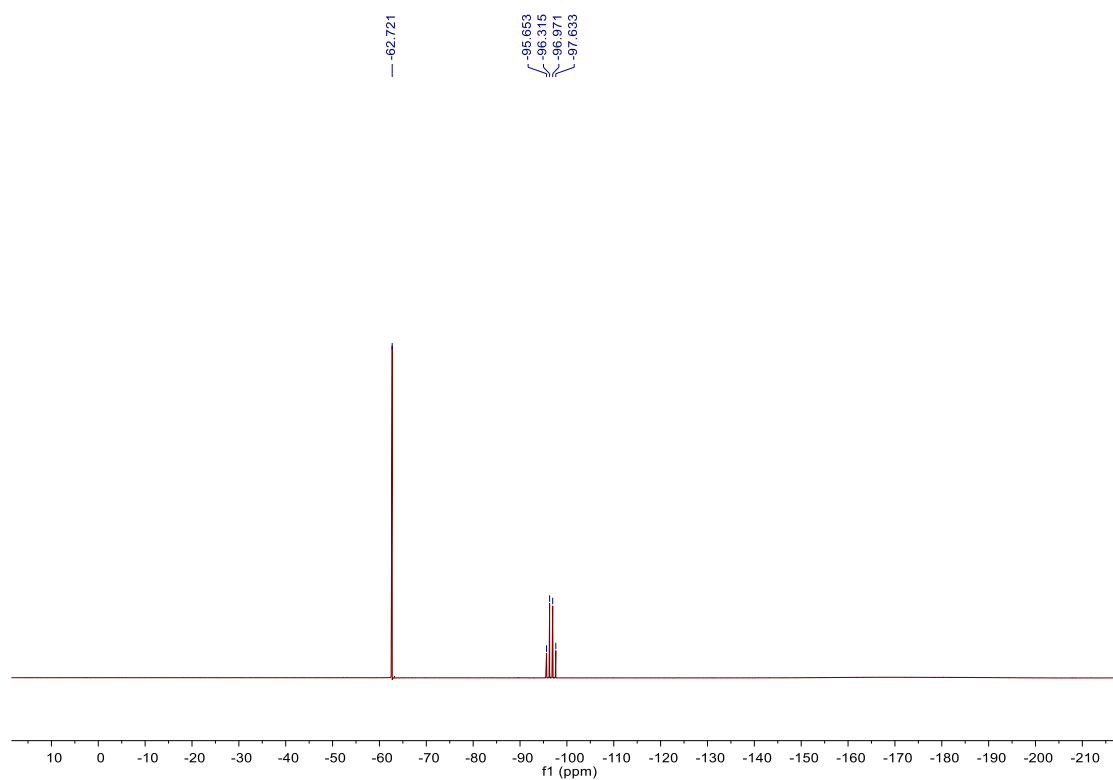


Figure S125. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ak**.

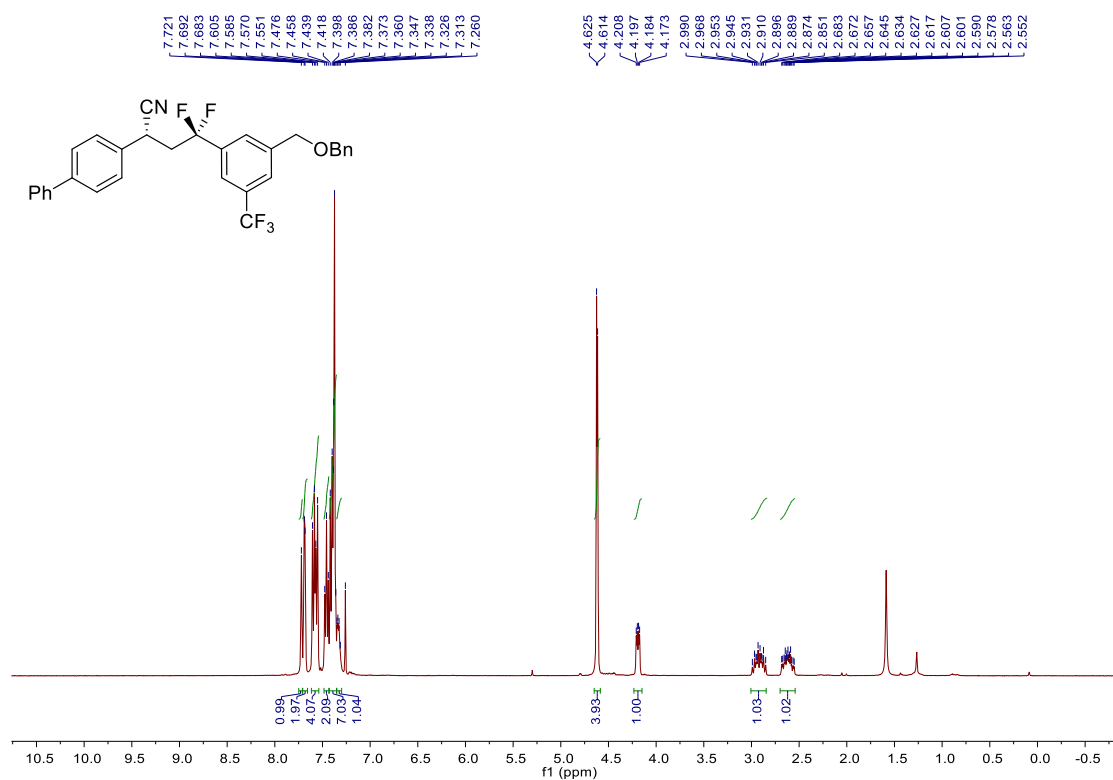


Figure S126. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ak**.

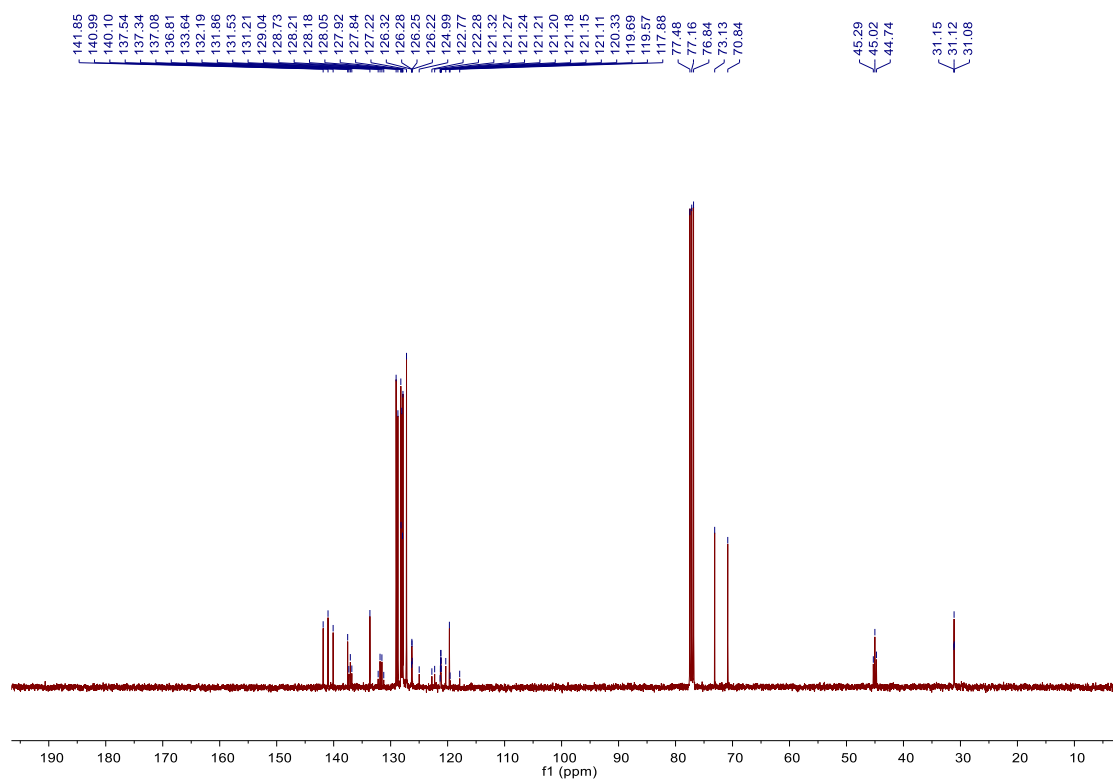


Figure S127. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ak**.

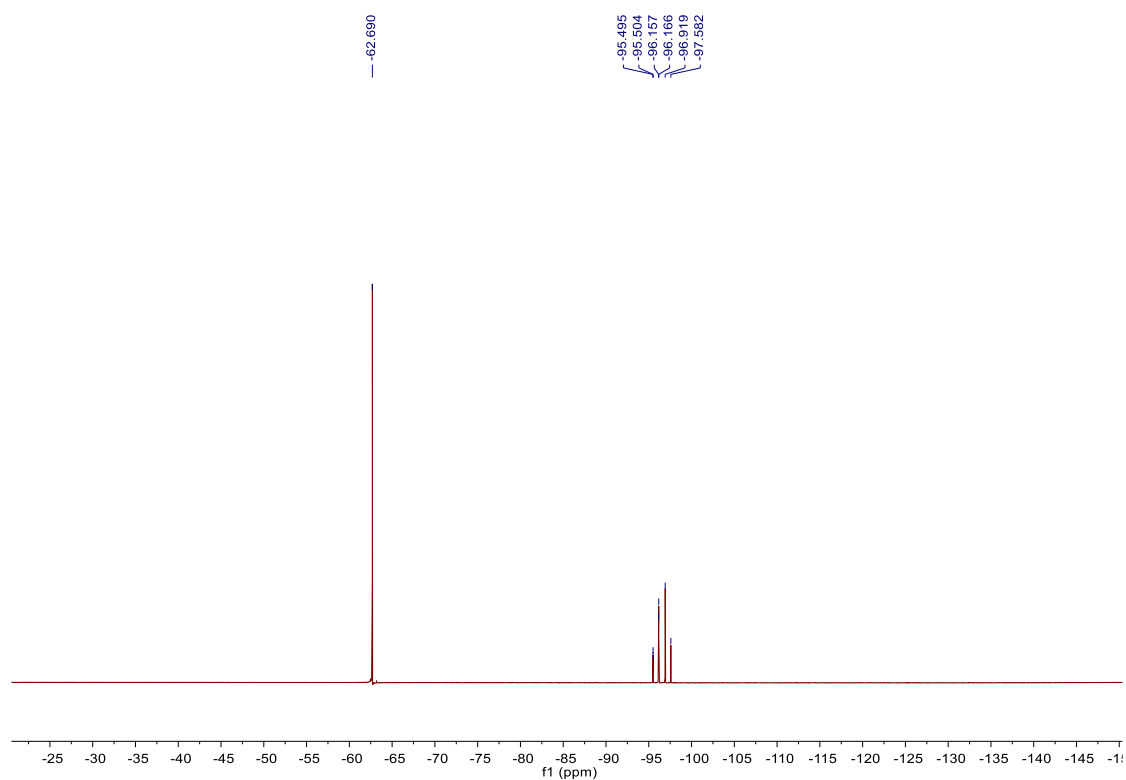


Figure S128. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4al**.

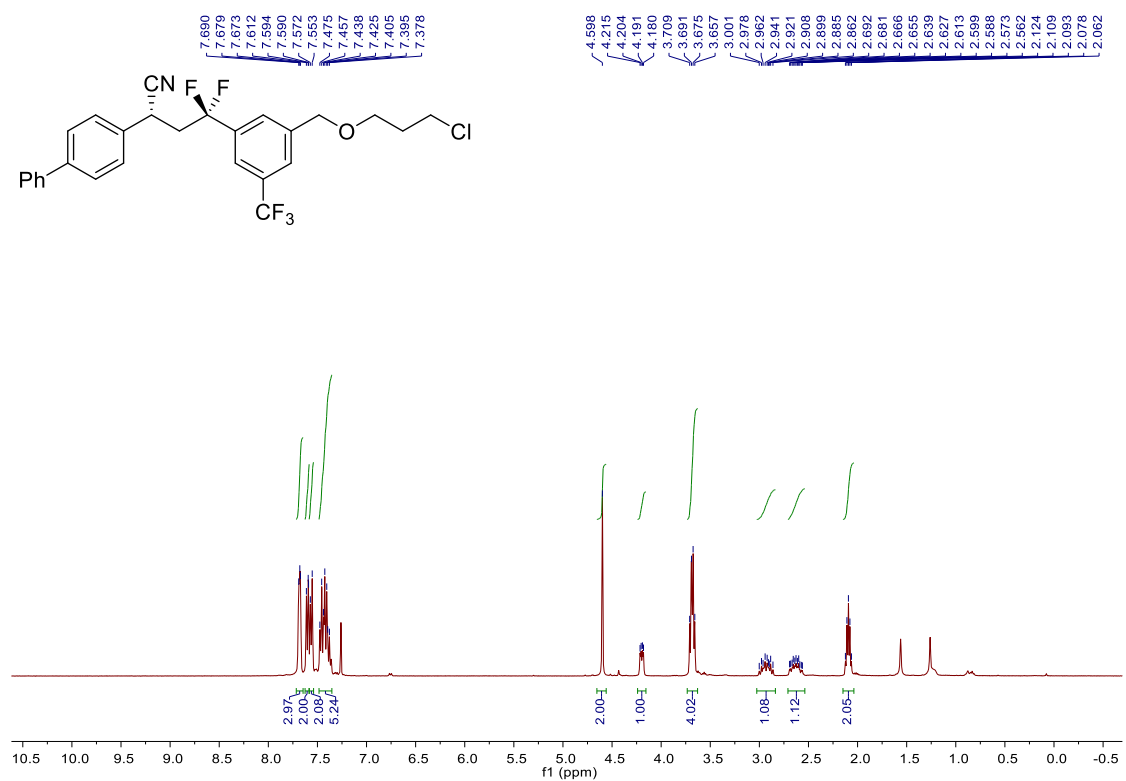


Figure S129. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4al**.

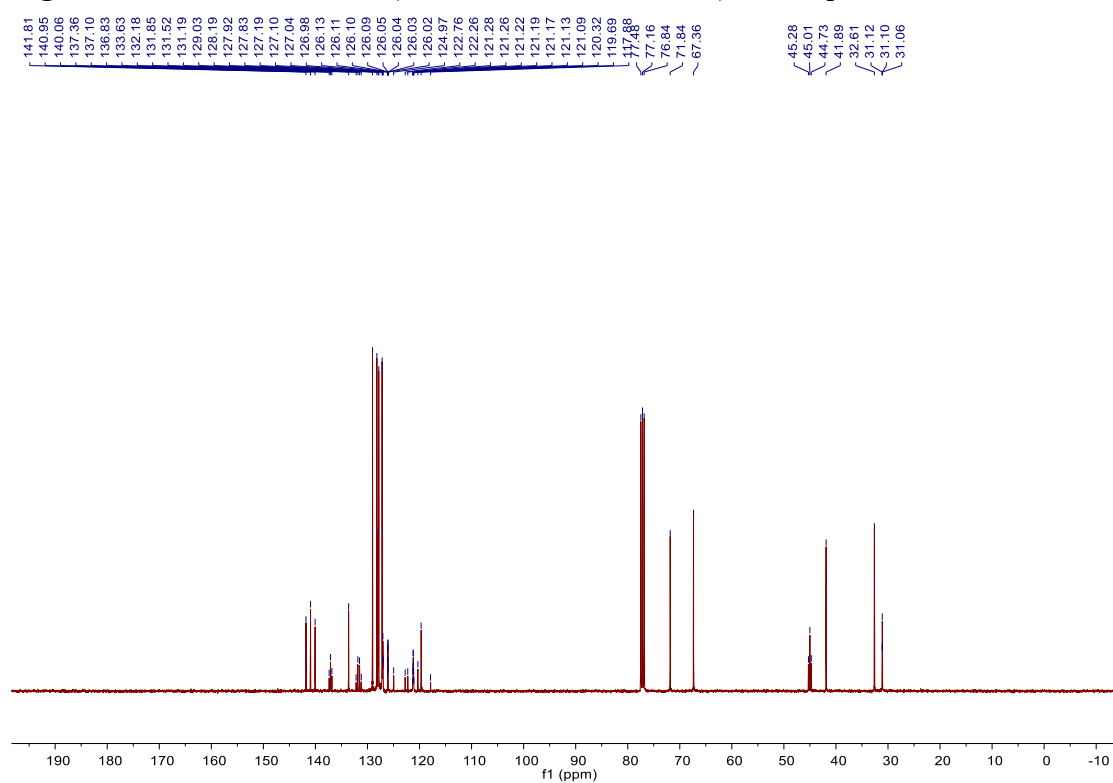


Figure S130. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4al**.

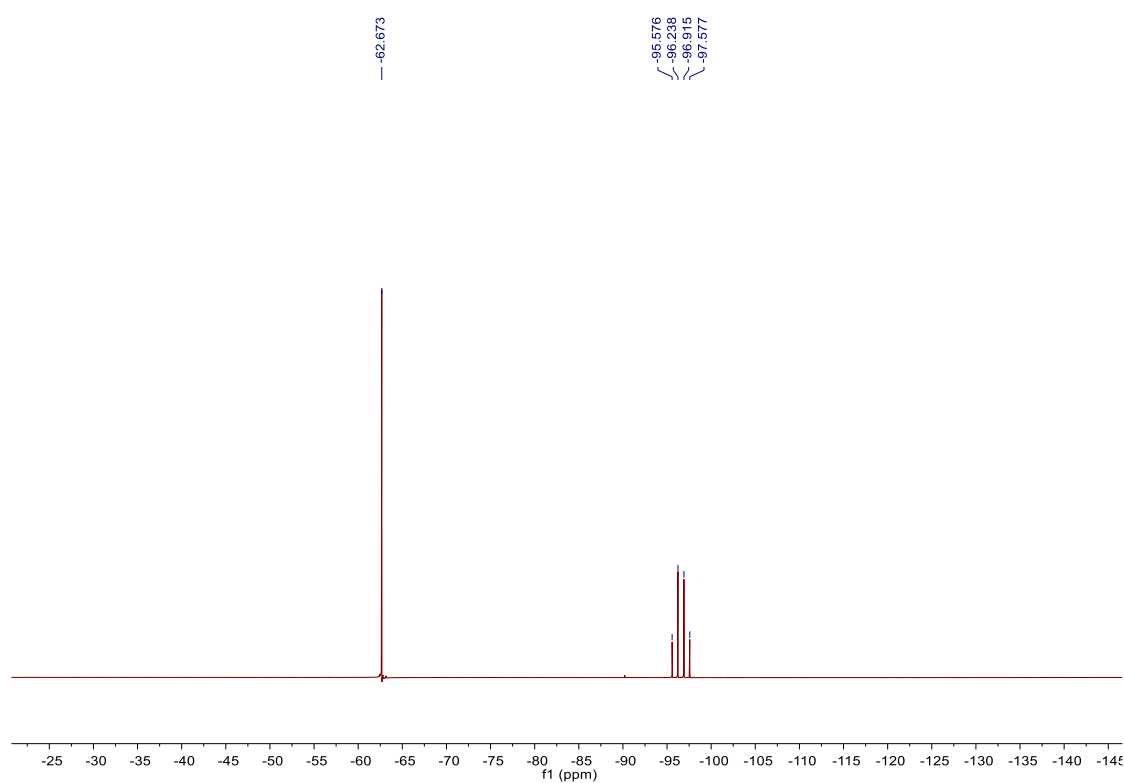


Figure S131. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4am**.

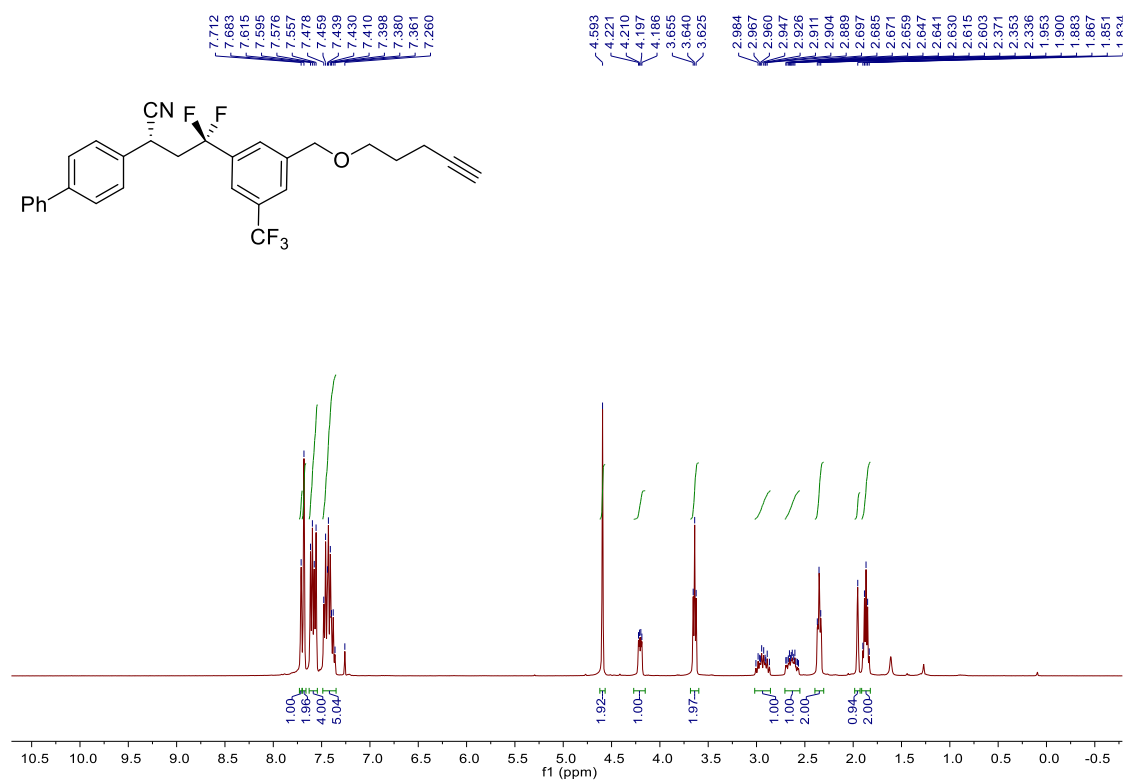


Figure S132. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4am**.

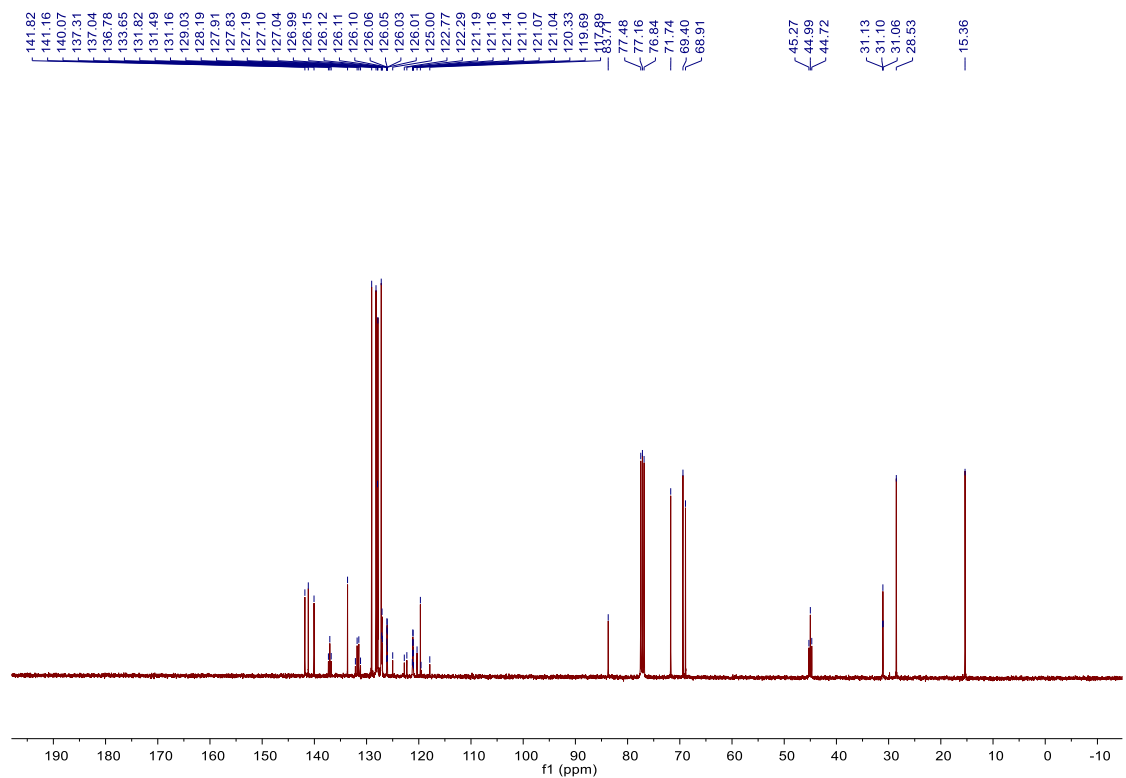


Figure S133. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4am**.

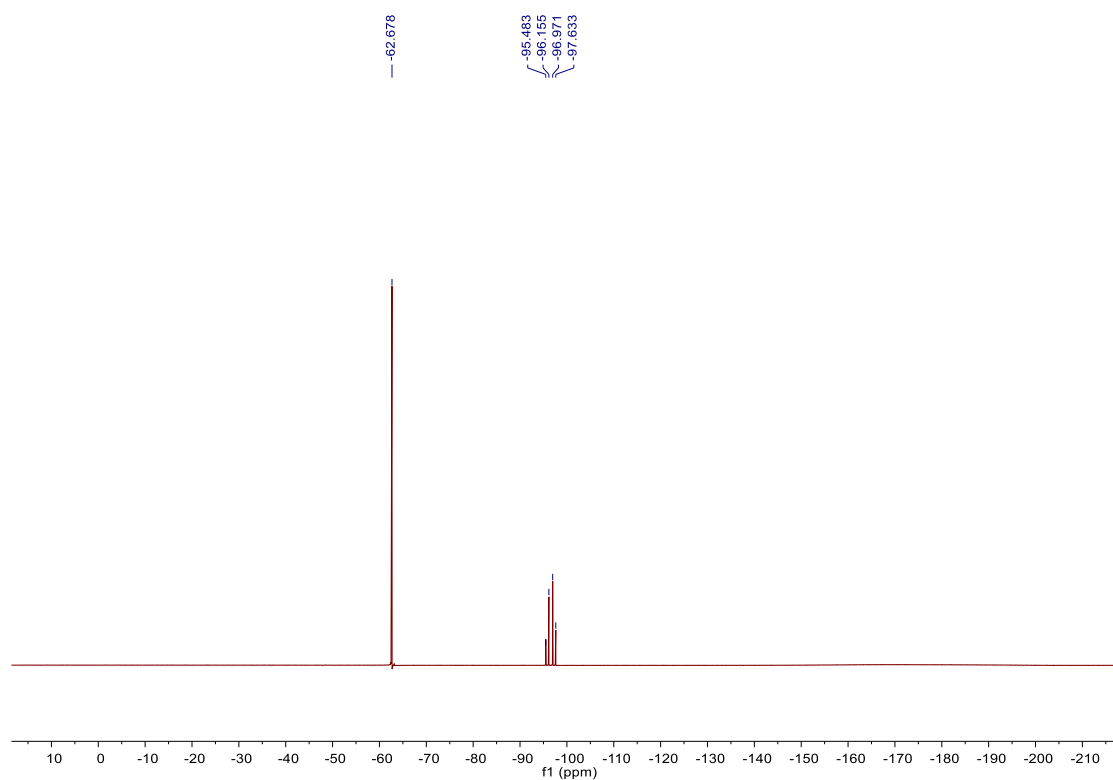


Figure S134. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4an**.

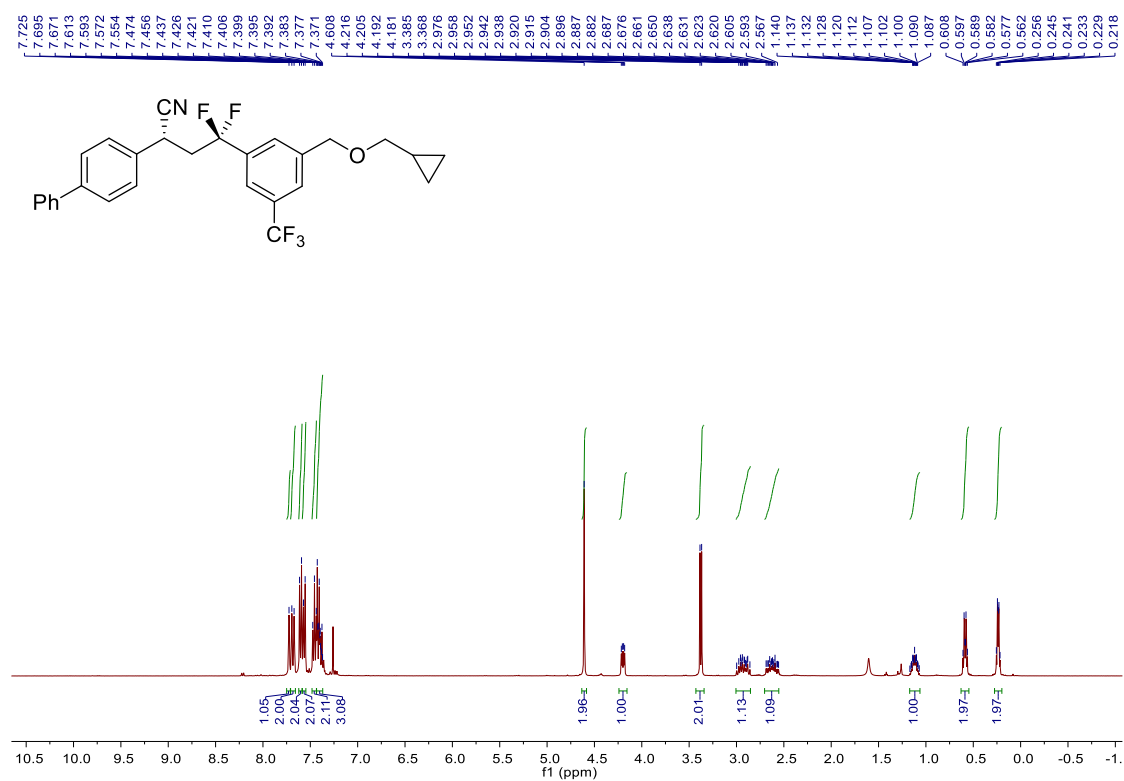


Figure S135. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4an**.

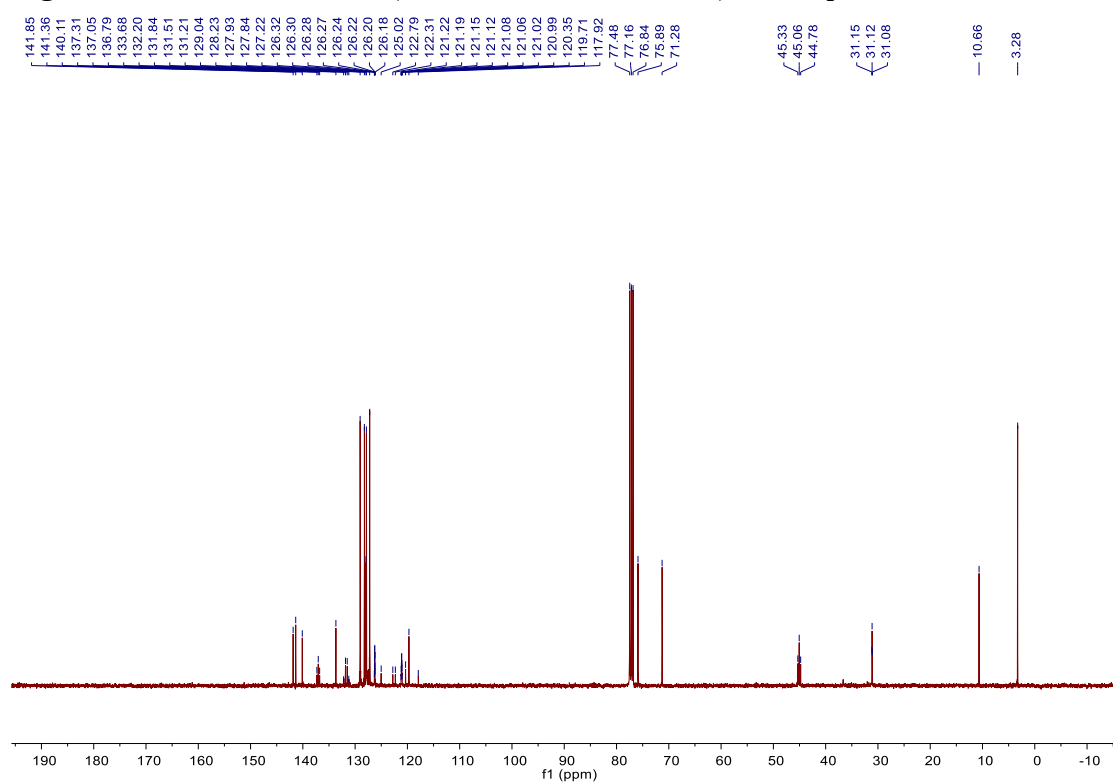


Figure S136. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4an**.

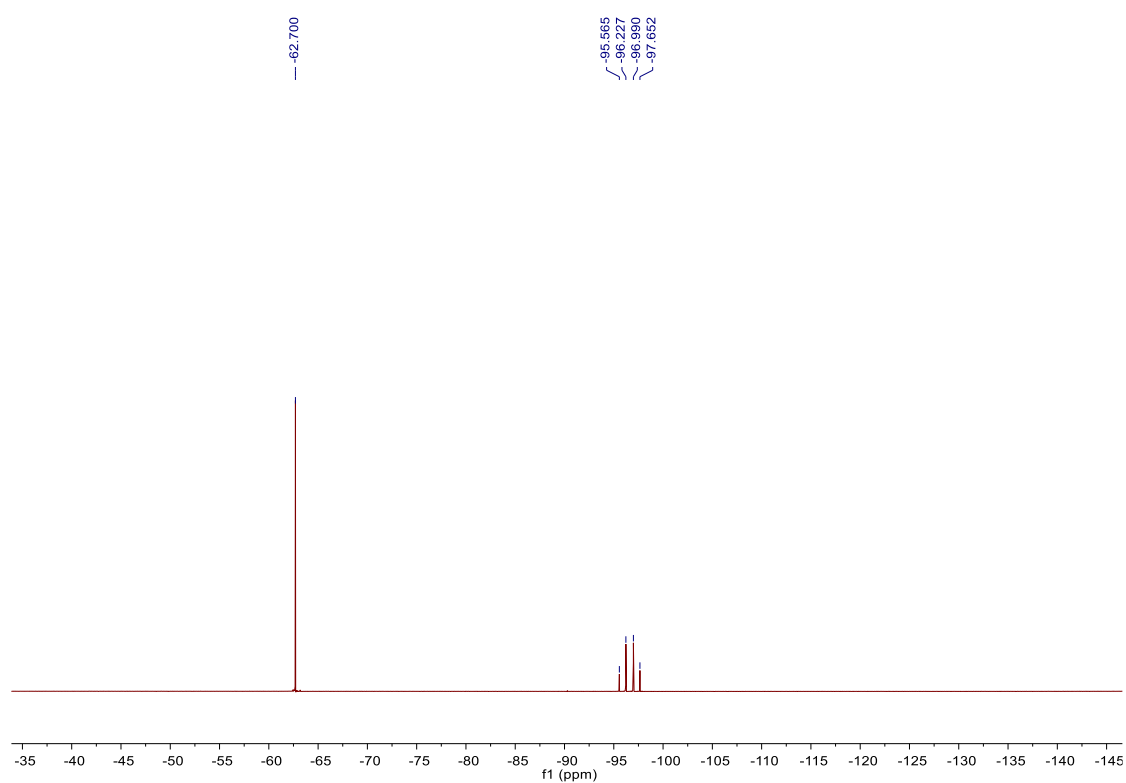


Figure S137. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ao**.

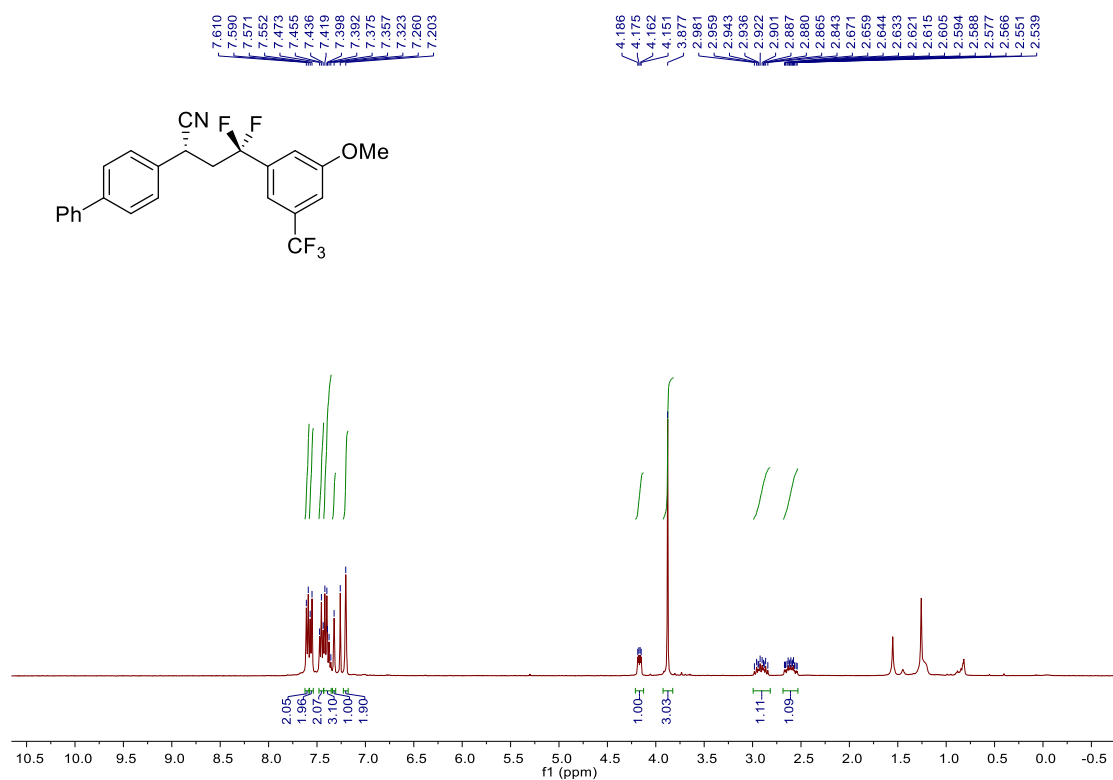


Figure S138. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ao**.

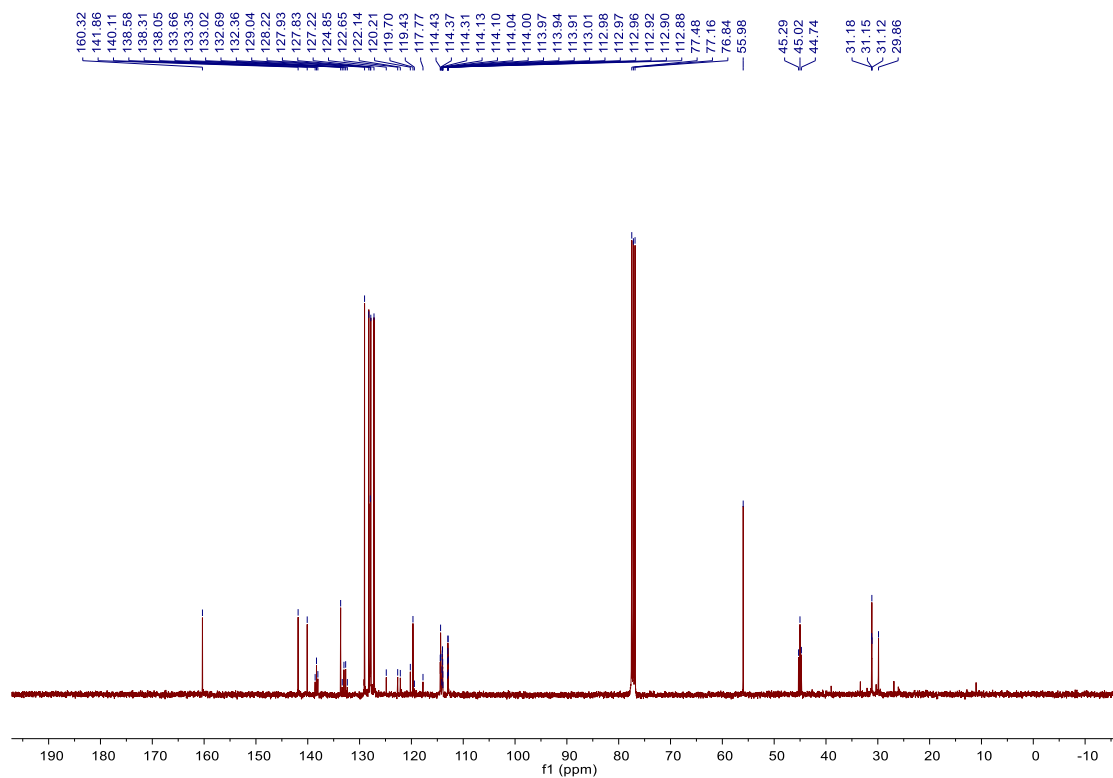


Figure S139. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ao**.

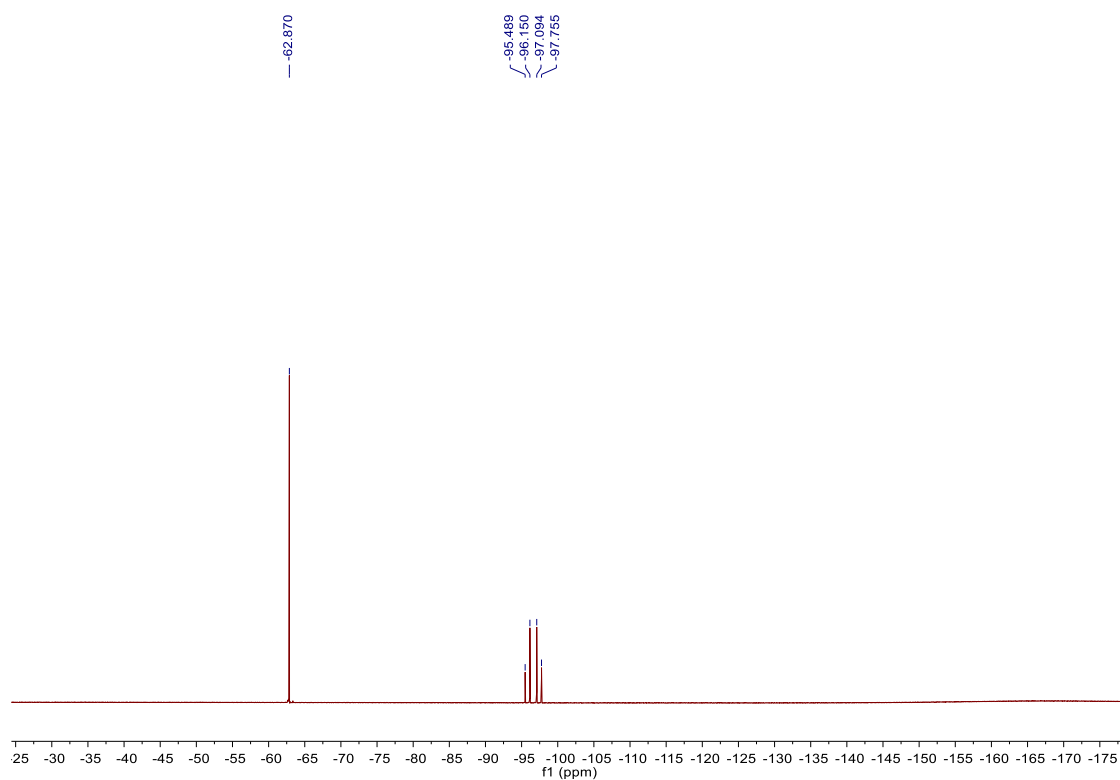


Figure S140. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ap**.

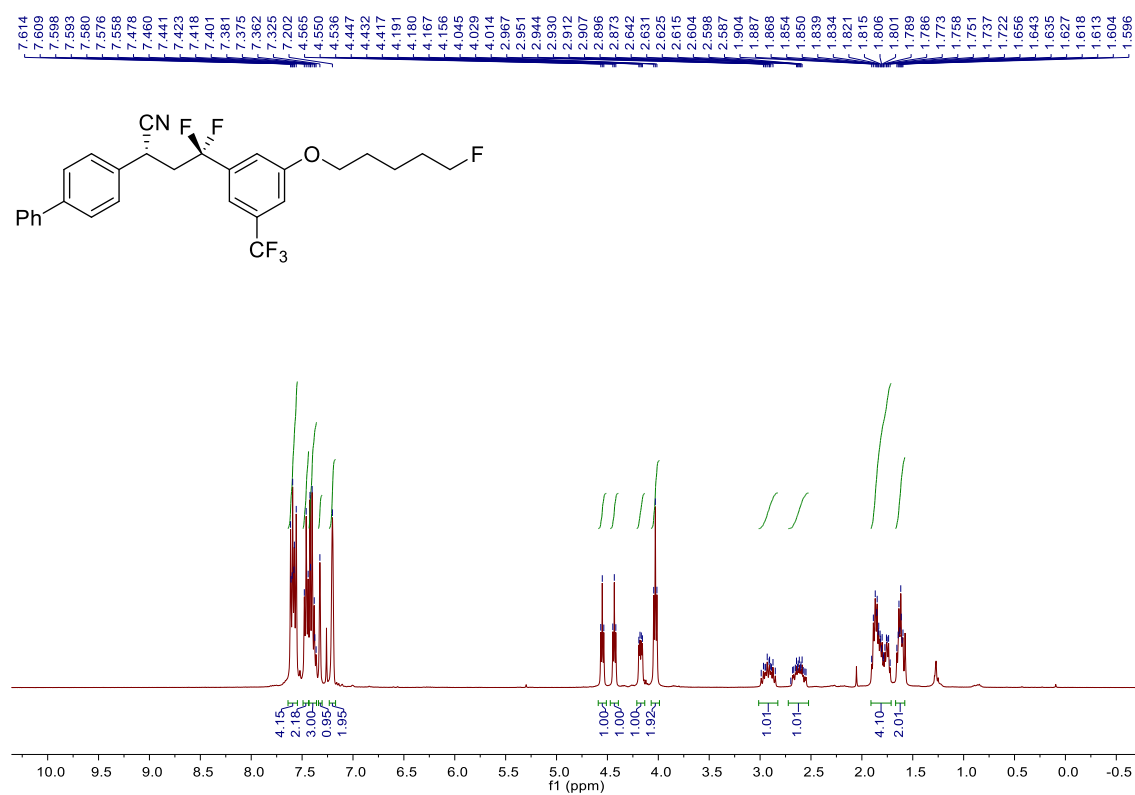


Figure S141. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ap**.

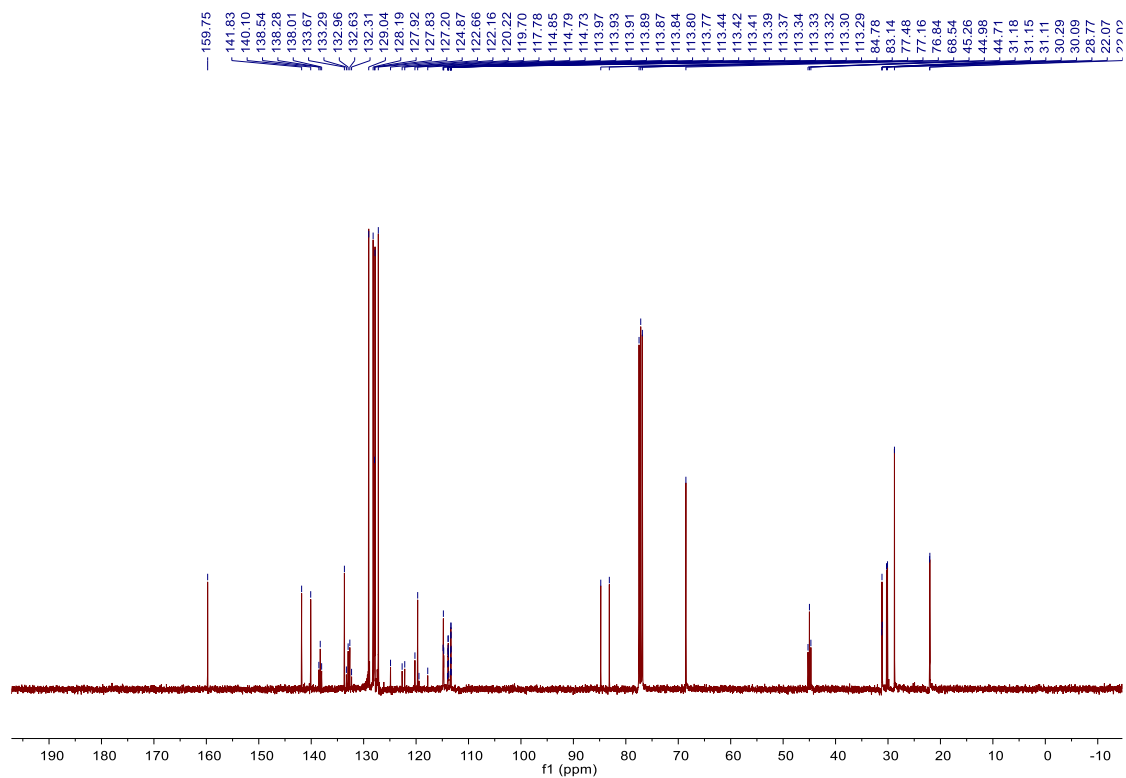
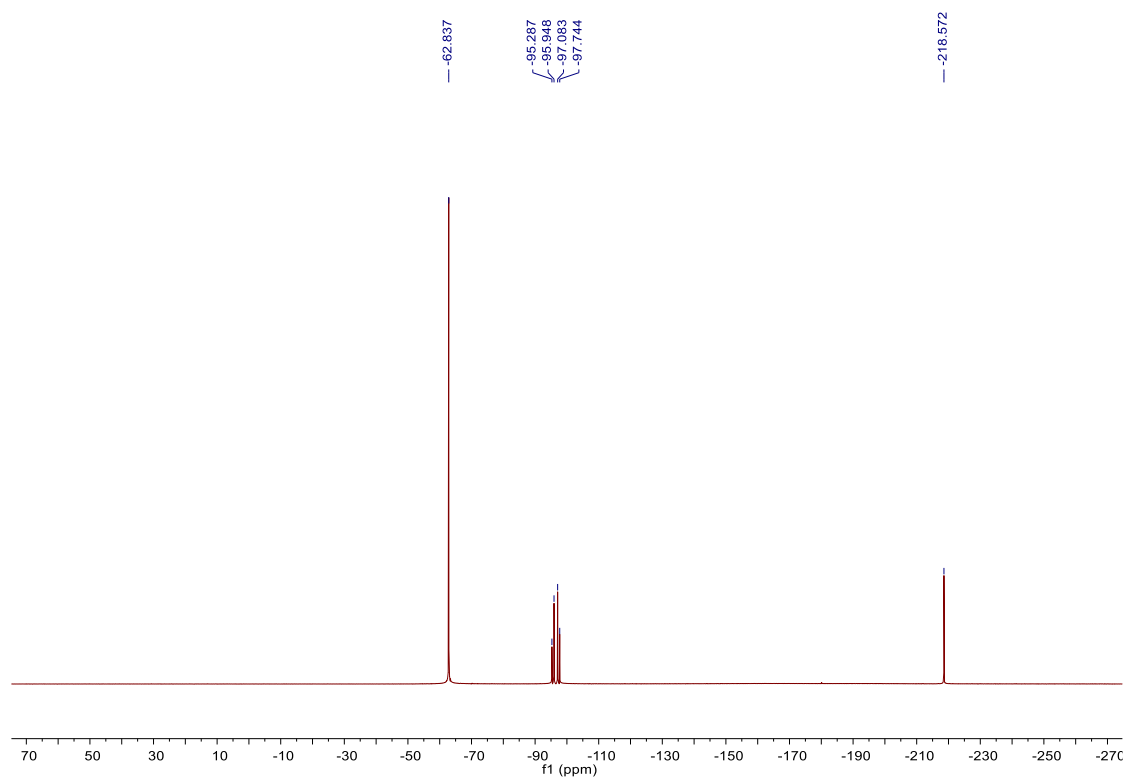


Figure S142. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ap**.



C=CCCOc1ccc(C(F)(F)F)cc1C[C@H](c2ccc(cc2)C#N)C(F)(F)F

Chemical structure: C=CCCOc1ccc(C(F)(F)F)cc1C[C@H](c2ccc(cc2)C#N)C(F)(F)F

¹H NMR spectrum (ppm):

- 7.615, 7.595, 7.580, 7.576, 7.559, 7.479, 7.461, 7.442, 7.424, 7.403, 7.382, 7.364, 7.322, 7.261, 7.206, 5.907, 5.889, 5.890, 5.872, 5.862, 5.864, 5.847, 5.837, 5.829, 5.821, 5.805, 5.111, 5.068, 5.054, 5.029, 4.184, 4.182, 4.168, 4.158, 4.043, 4.027, 4.011, 2.968, 2.951, 2.945, 2.931, 2.910, 2.894, 2.889, 2.874, 2.851, 2.680, 2.669, 2.654, 2.643, 2.626, 2.614, 2.599, 2.587, 2.576, 2.285, 2.286, 2.280, 2.230, 1.953, 1.936, 1.918, 1.901, 1.884

Integration values (from left to right): 4.09, 5.20, 0.98, 1.97, 1.00, 1.00, 0.97, 1.00, 2.03, 1.05, 1.02, 2.04, 2.05

159.80
141.84
140.11
138.53
138.26
138.00
137.46
133.68
133.27
132.95
132.63
132.30
129.04
128.20
127.92
127.63
127.11
124.83
122.67
122.18
120.23
119.70
117.79
115.73
114.88
114.82
114.75
113.98
113.94
113.87
113.86
113.84
113.78
113.73
113.46
113.44
113.43
113.41
113.38
113.35
113.34
113.33
77.48
77.16
76.84
68.01
45.28
45.00
44.73
31.19
31.15
31.12
30.04
28.29

Figure S145. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4aq**.

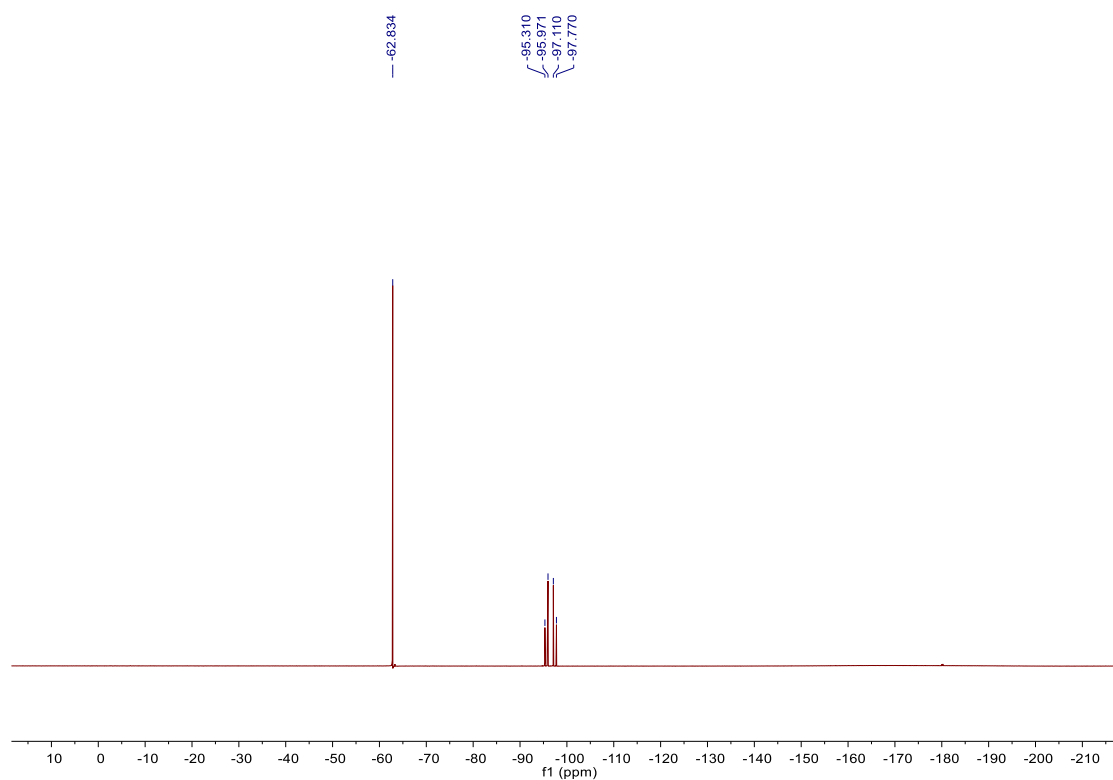


Figure S146. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ar**.

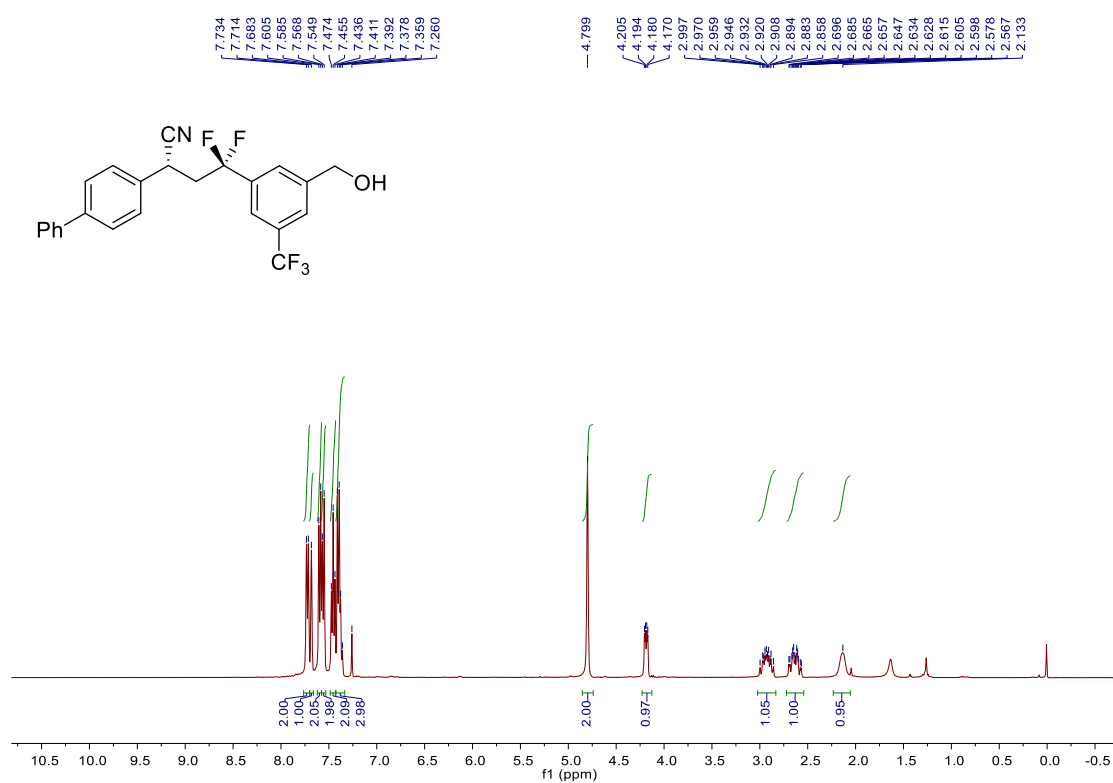


Figure S147. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ar**.

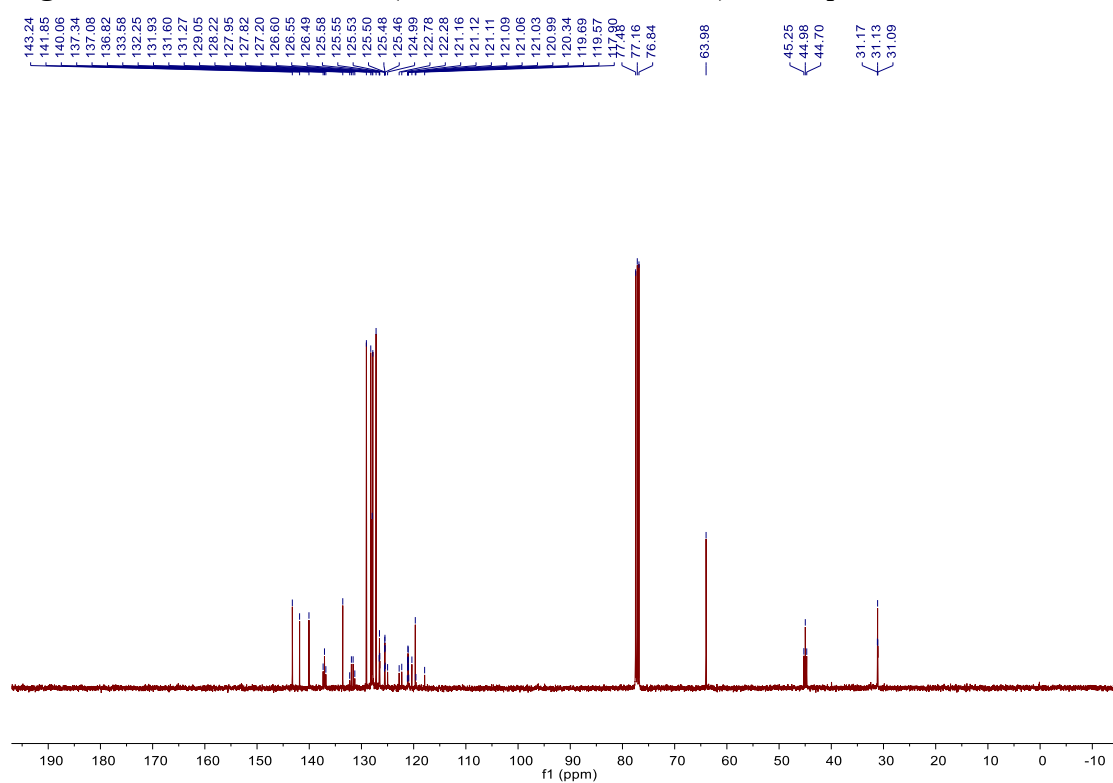


Figure S148. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ar**.

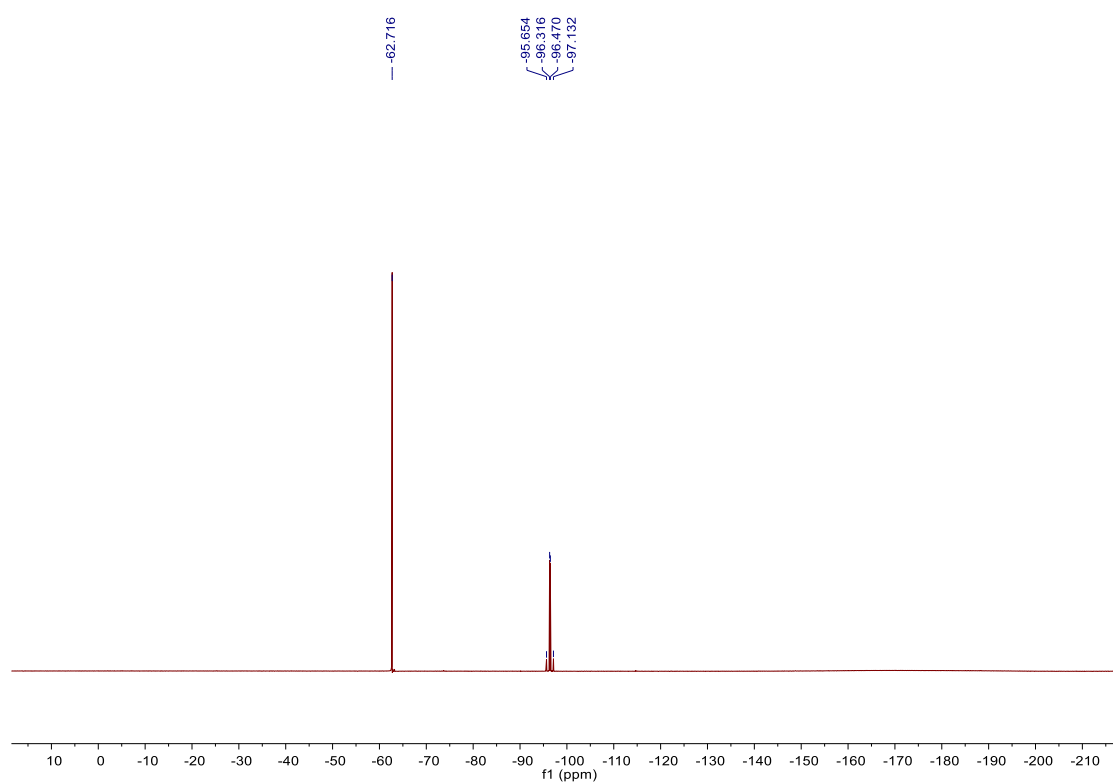


Figure S149. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4as**.

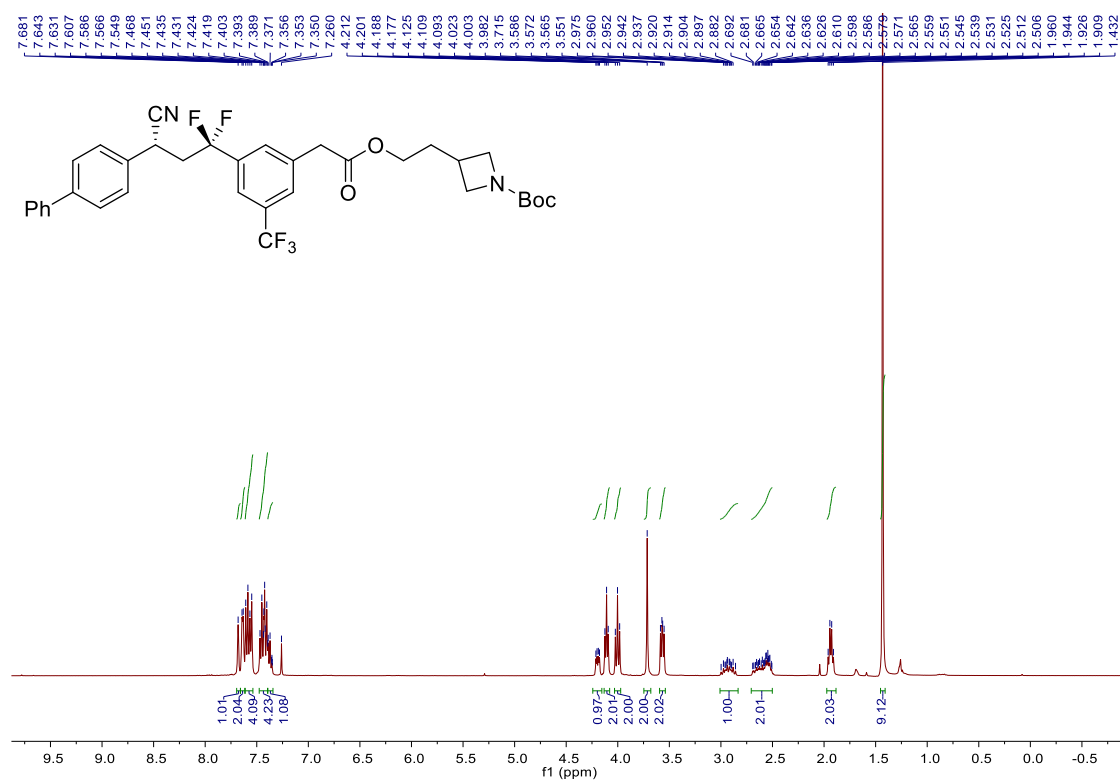


Figure S150. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4as**.

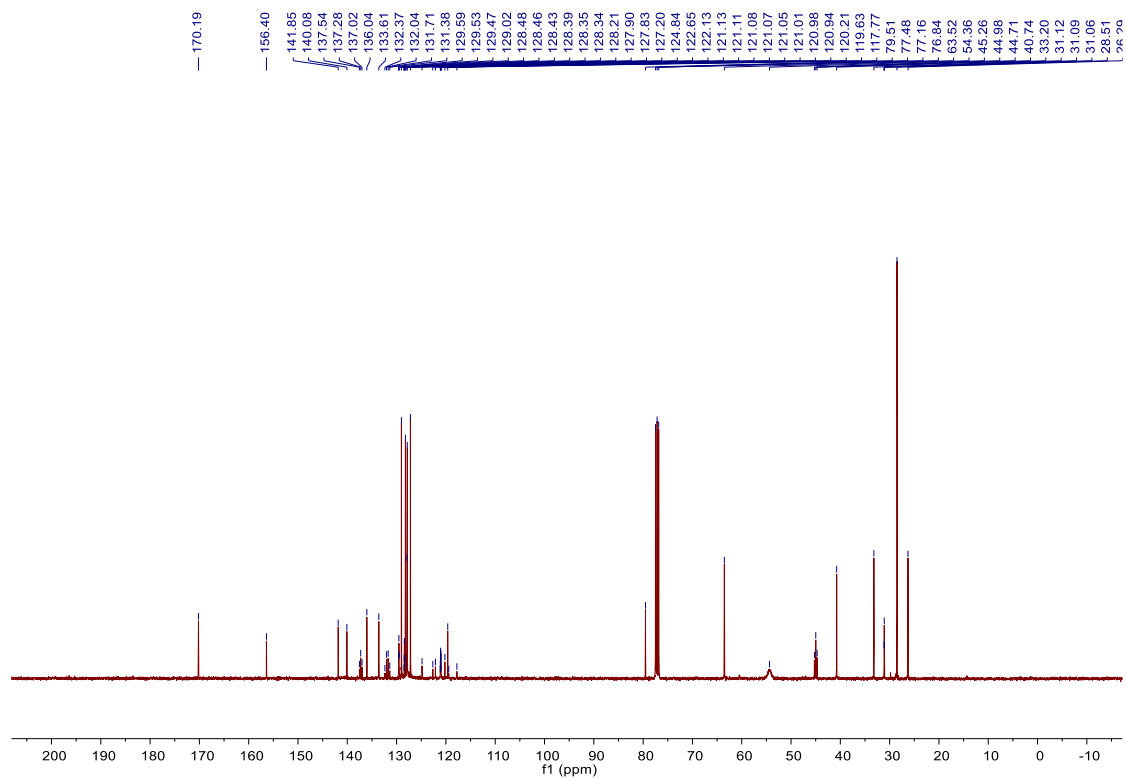


Figure S151. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4as**.

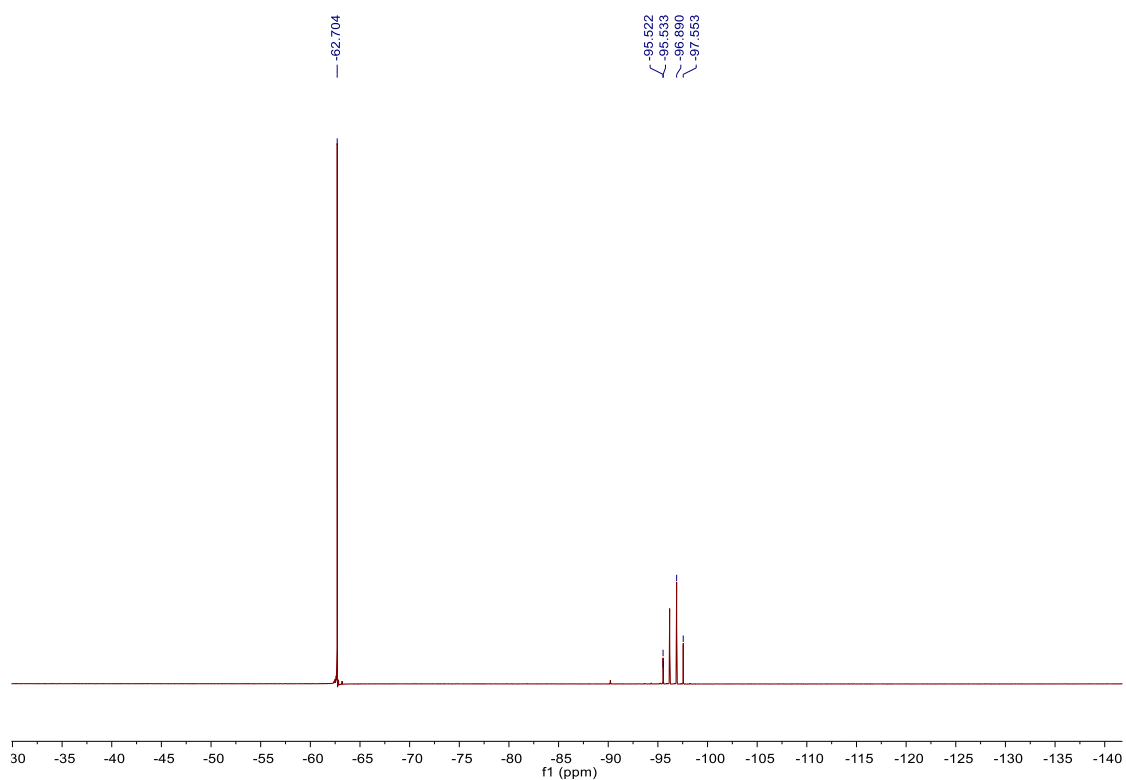


Figure S152. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4at**.

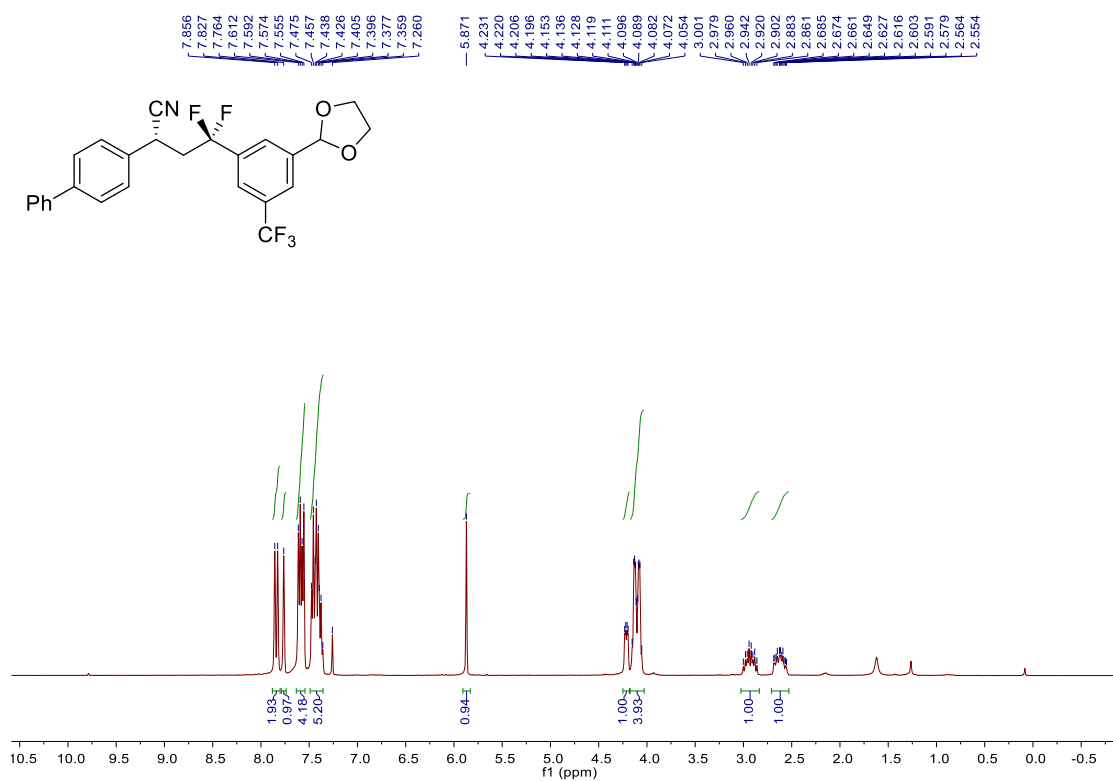


Figure S153. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4at**.

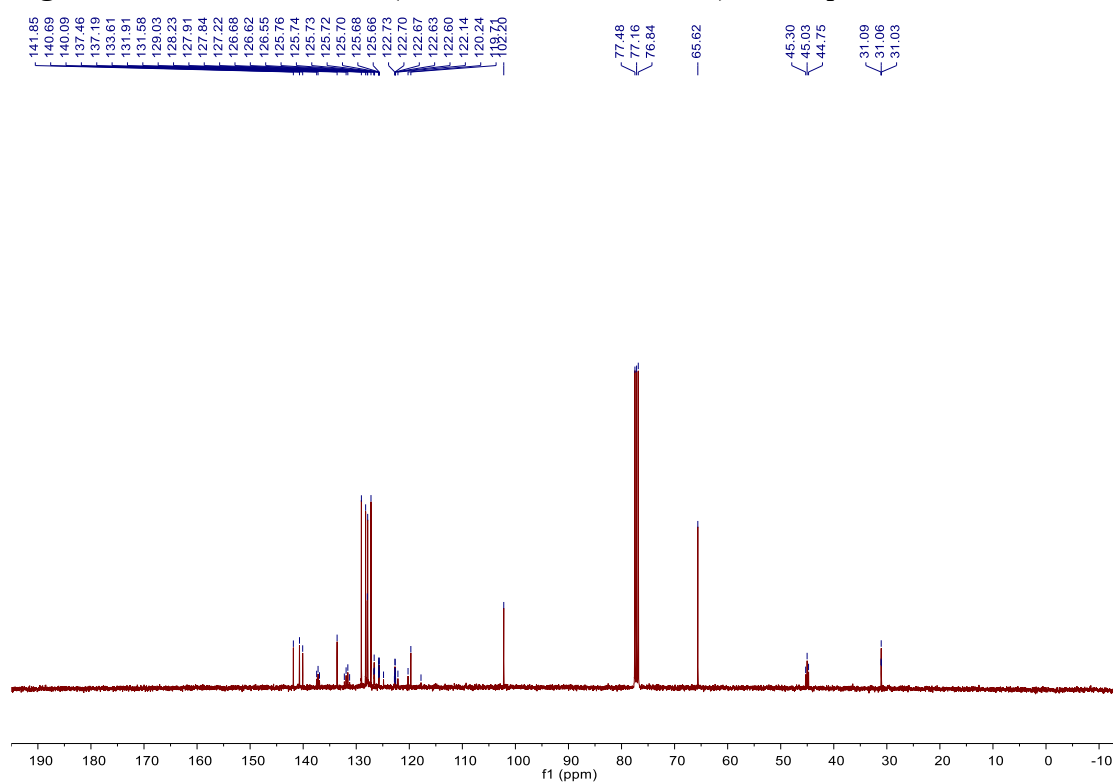


Figure S154. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4at**.

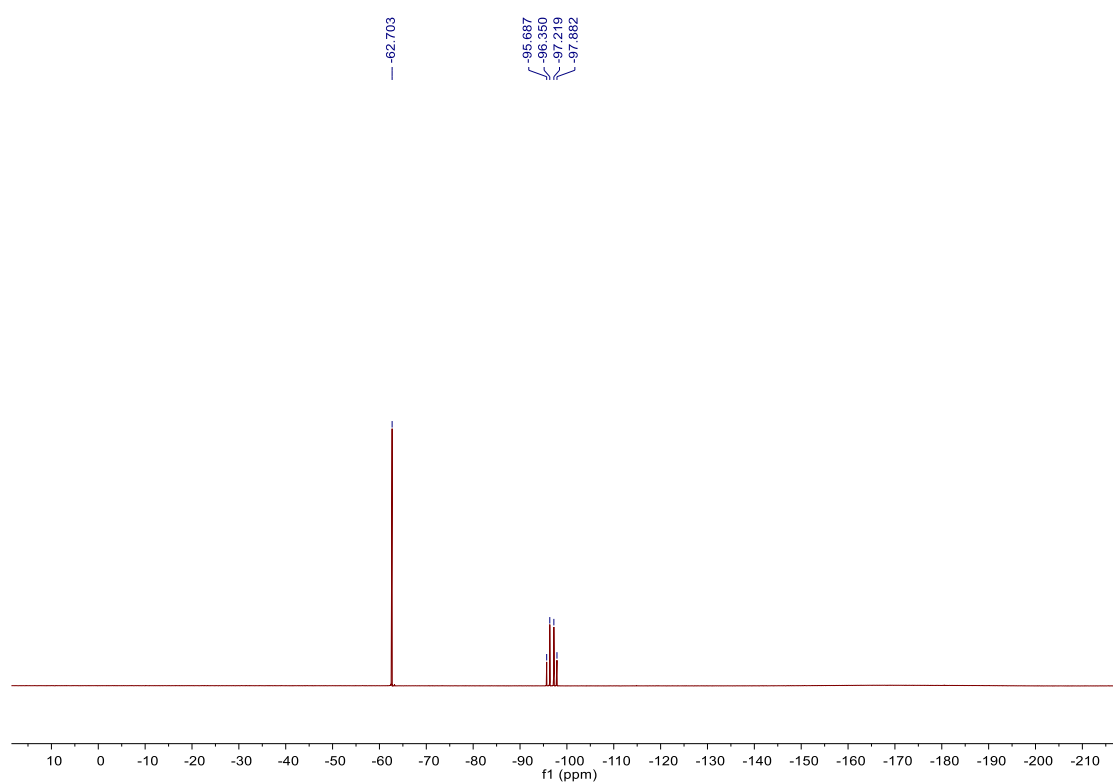


Figure S155. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4au**.

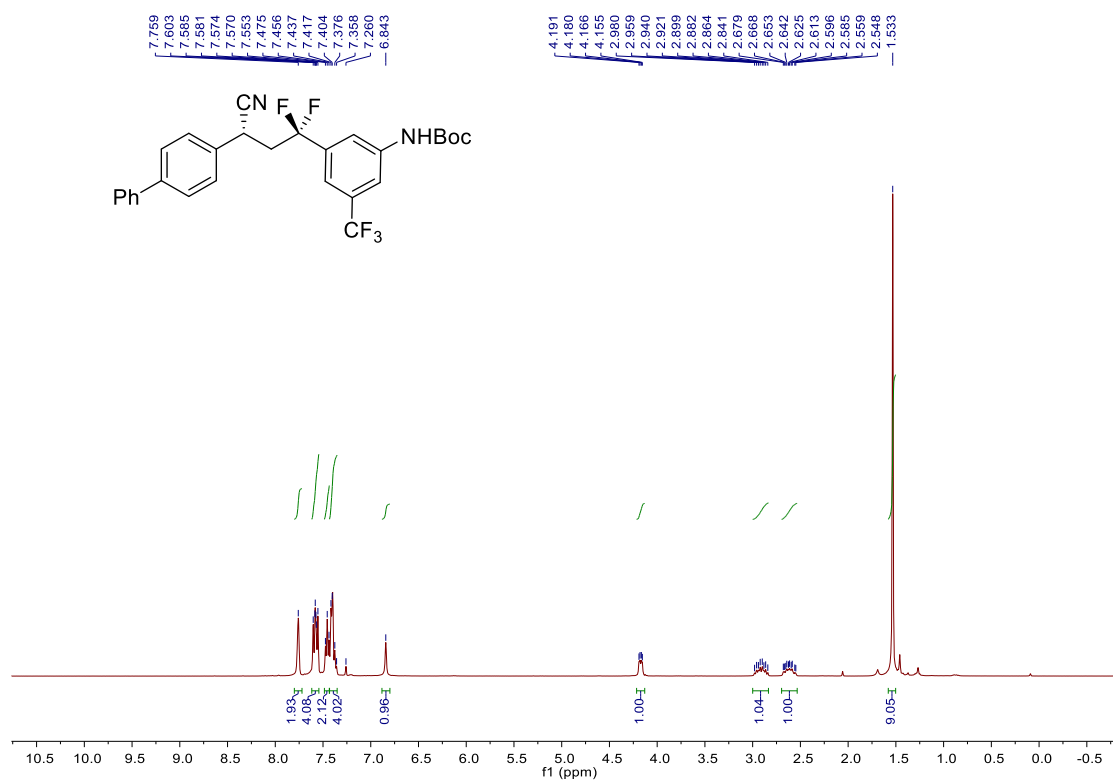


Figure S156. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4au**.

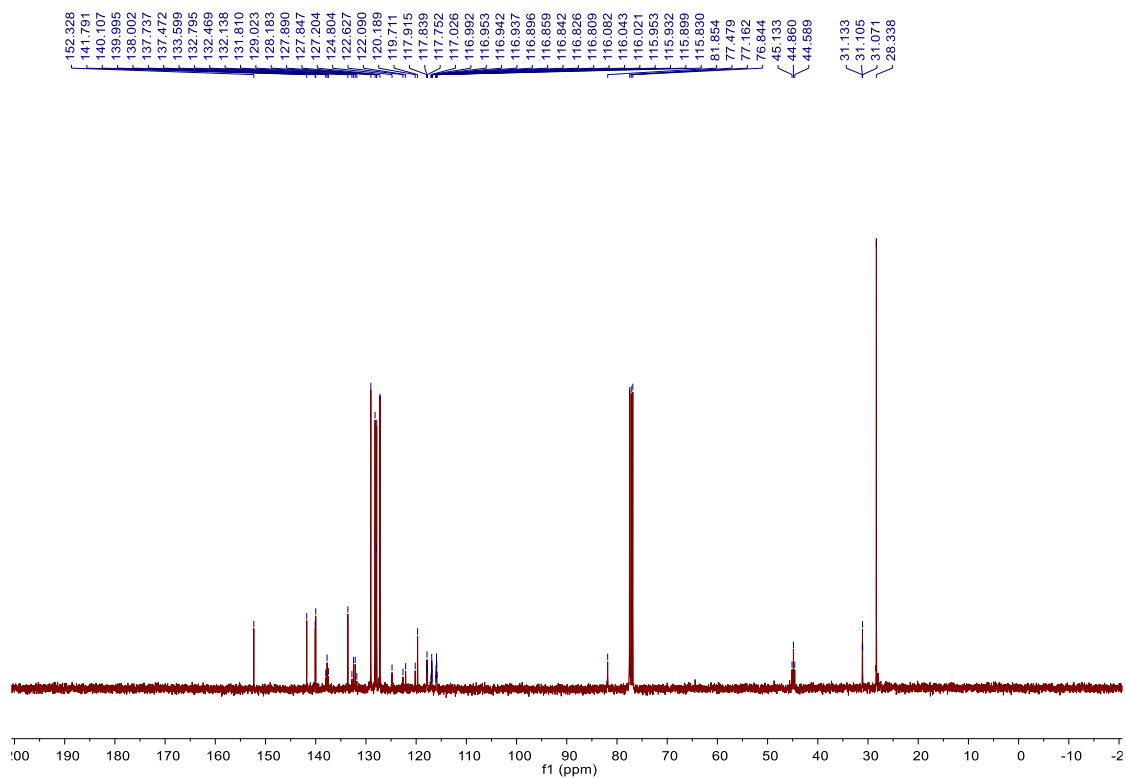


Figure S157. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4au**.

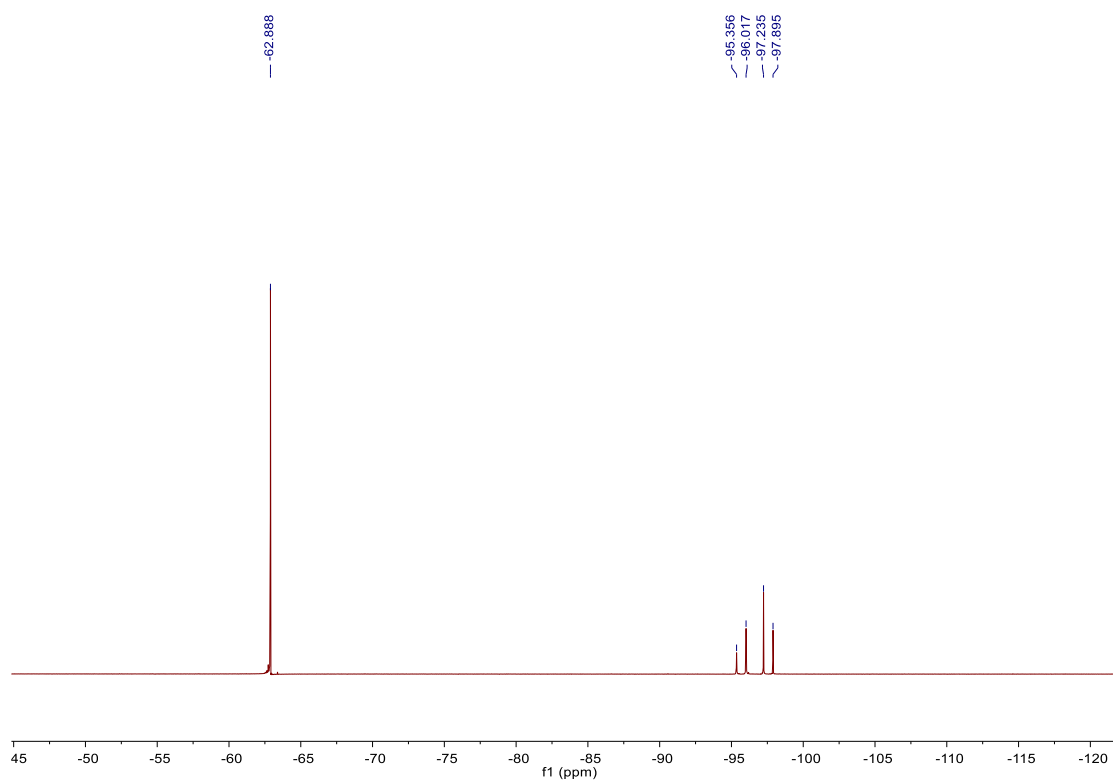


Figure S158. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4av**.

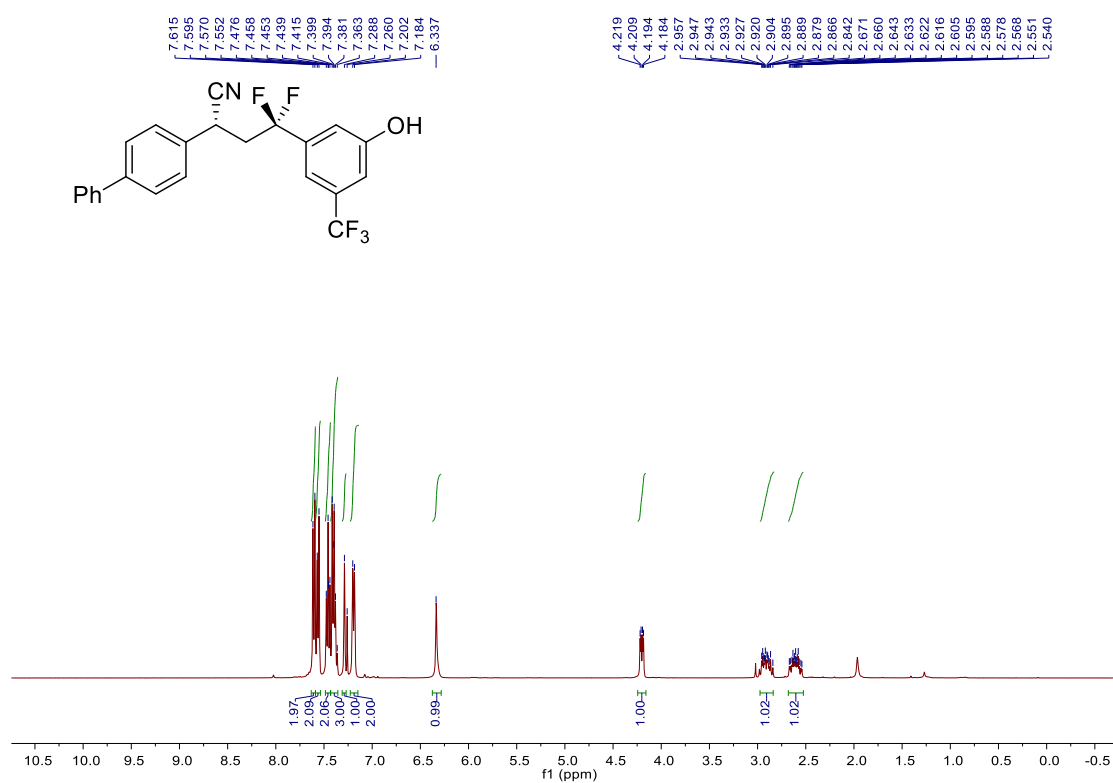


Figure S159. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4av**.

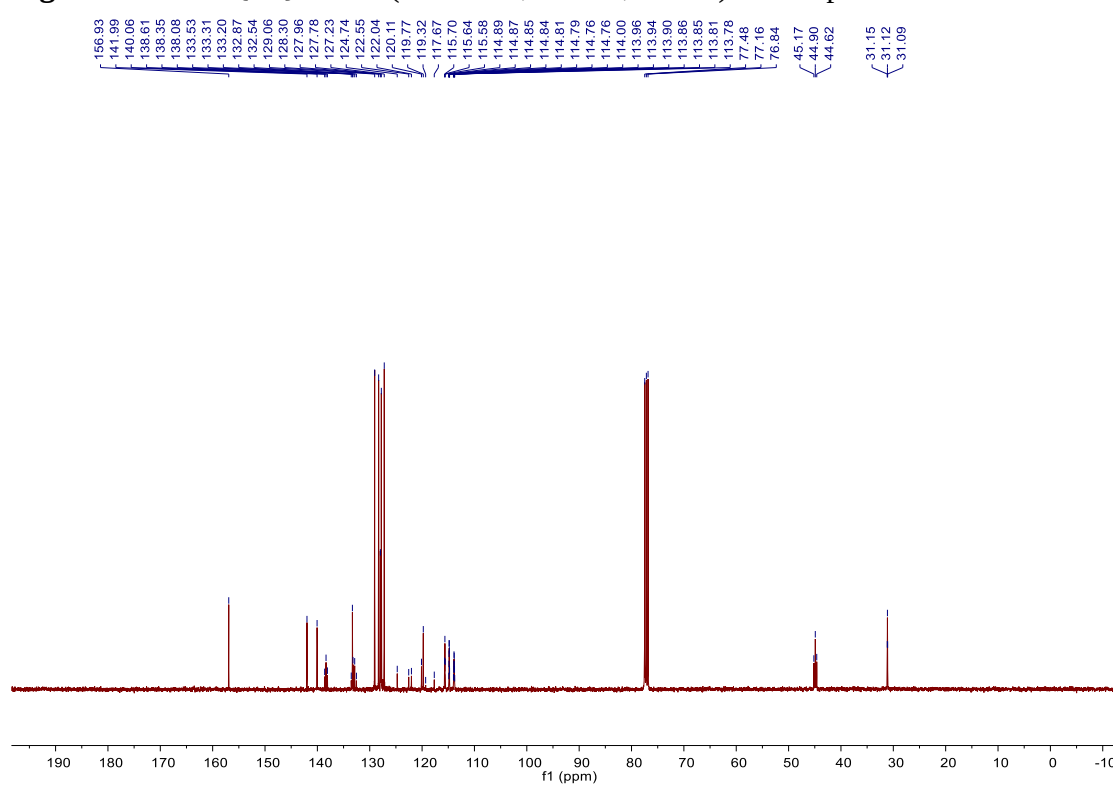


Figure S160. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4av**.

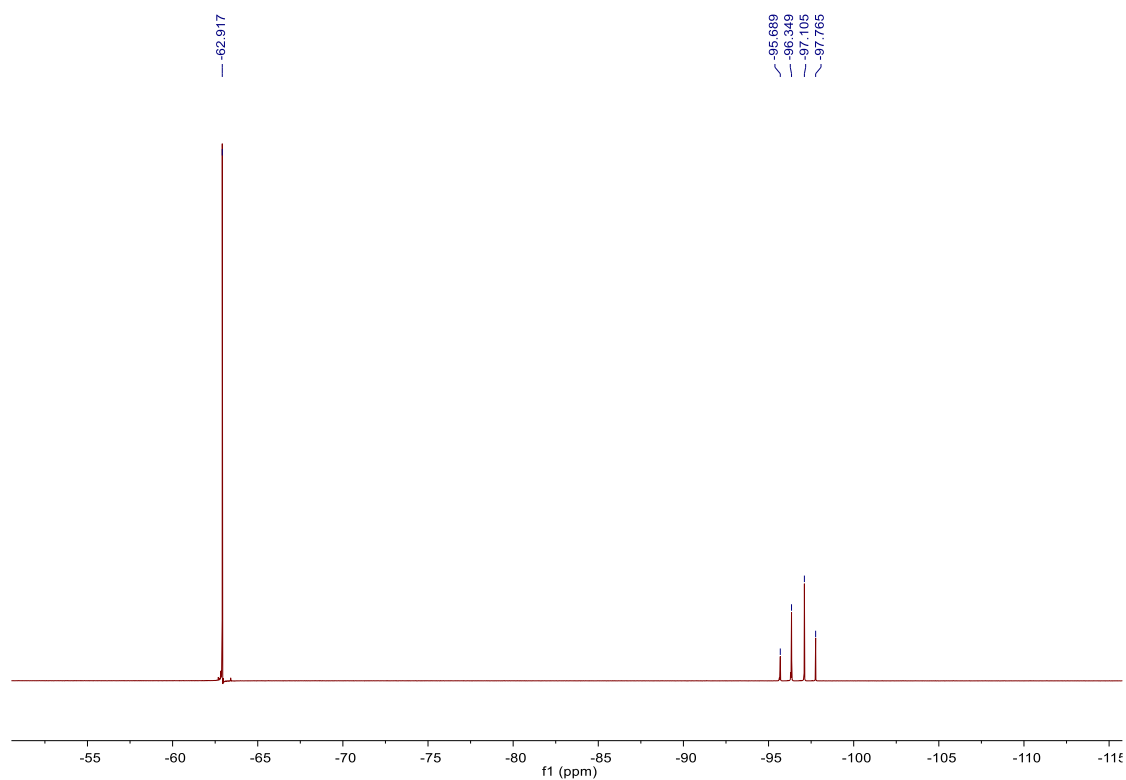


Figure S161. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4aw**.

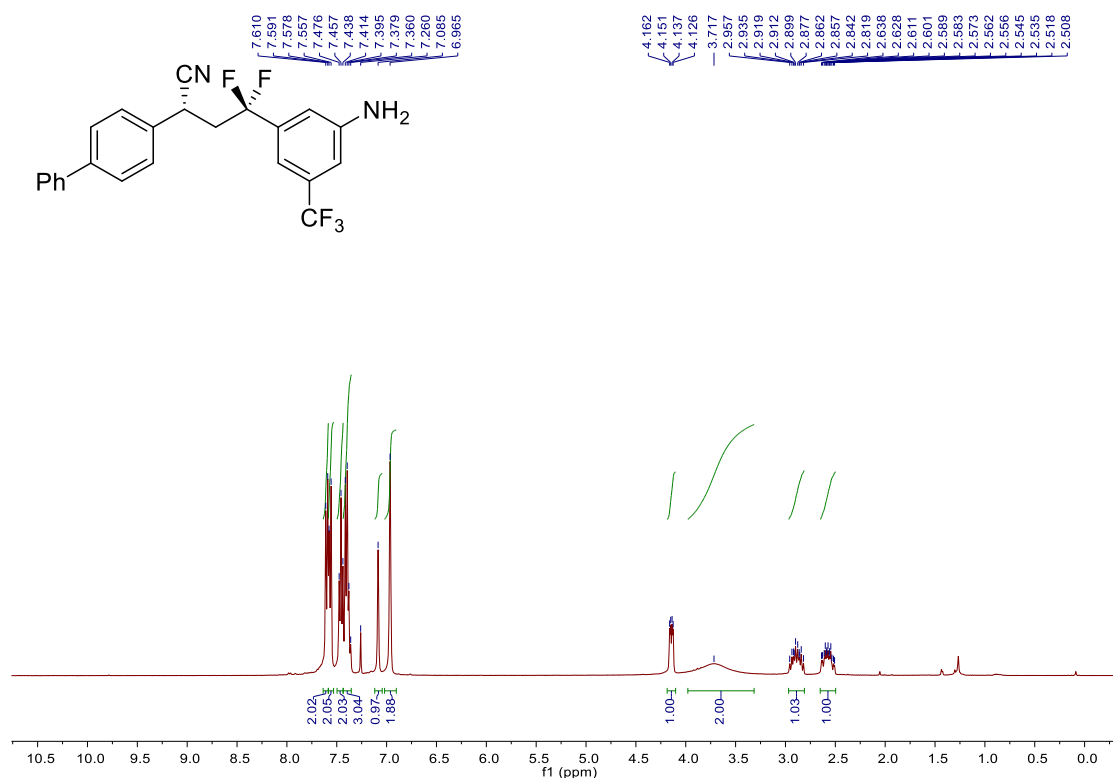


Figure S162. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4aw**.

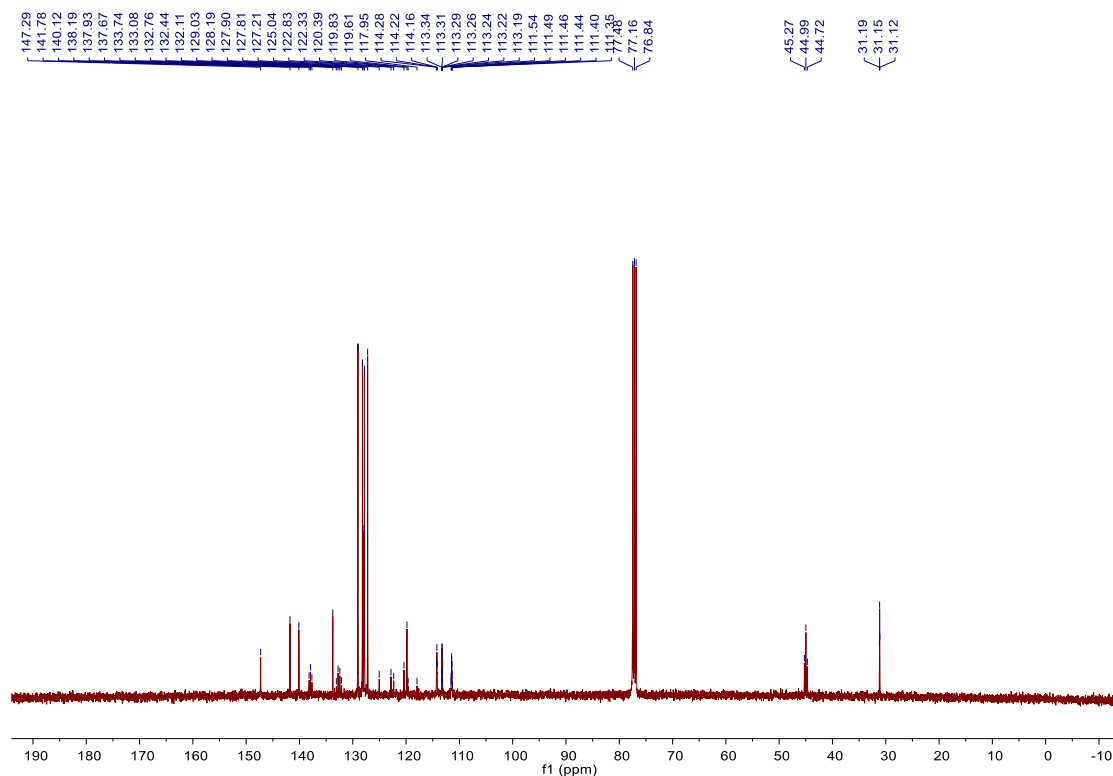


Figure S163. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4aw**.

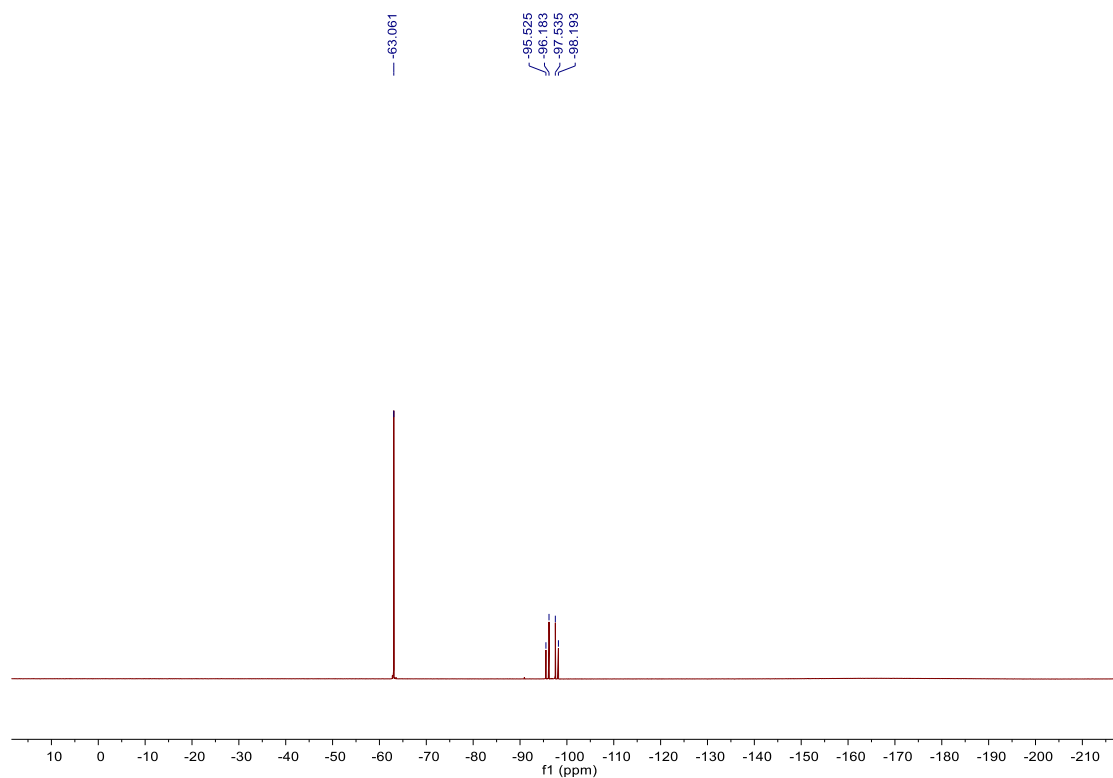


Figure S164. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ax**.

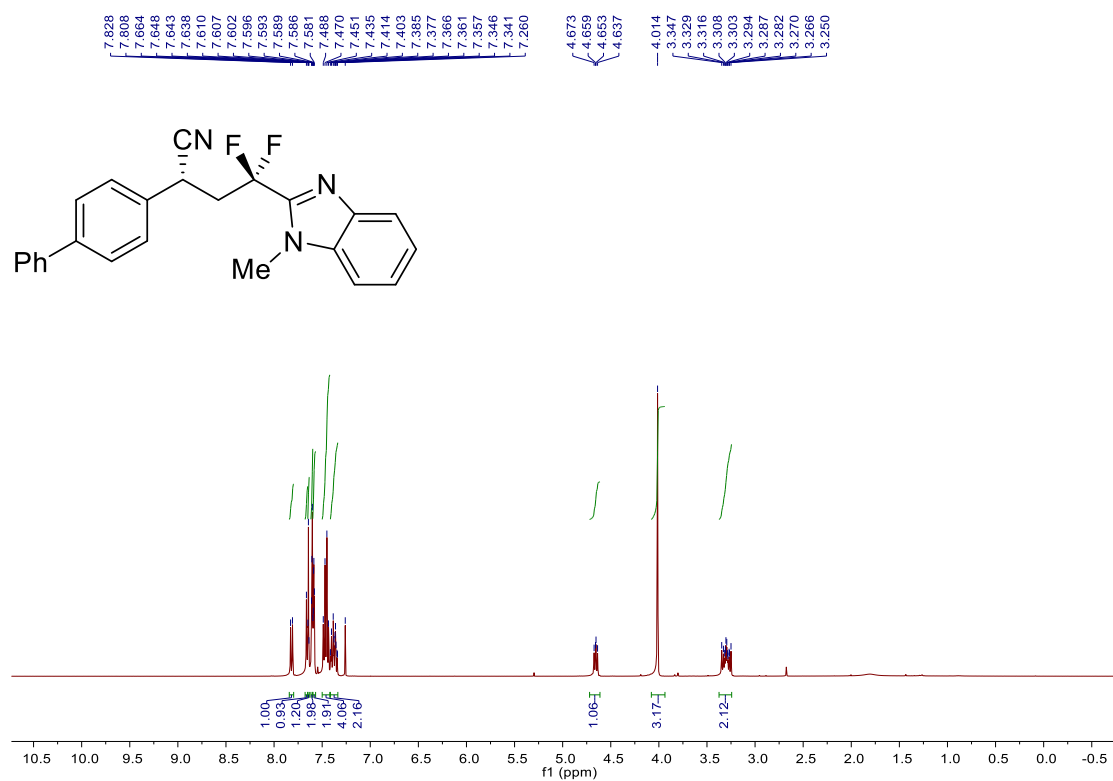


Figure S165. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ax**.

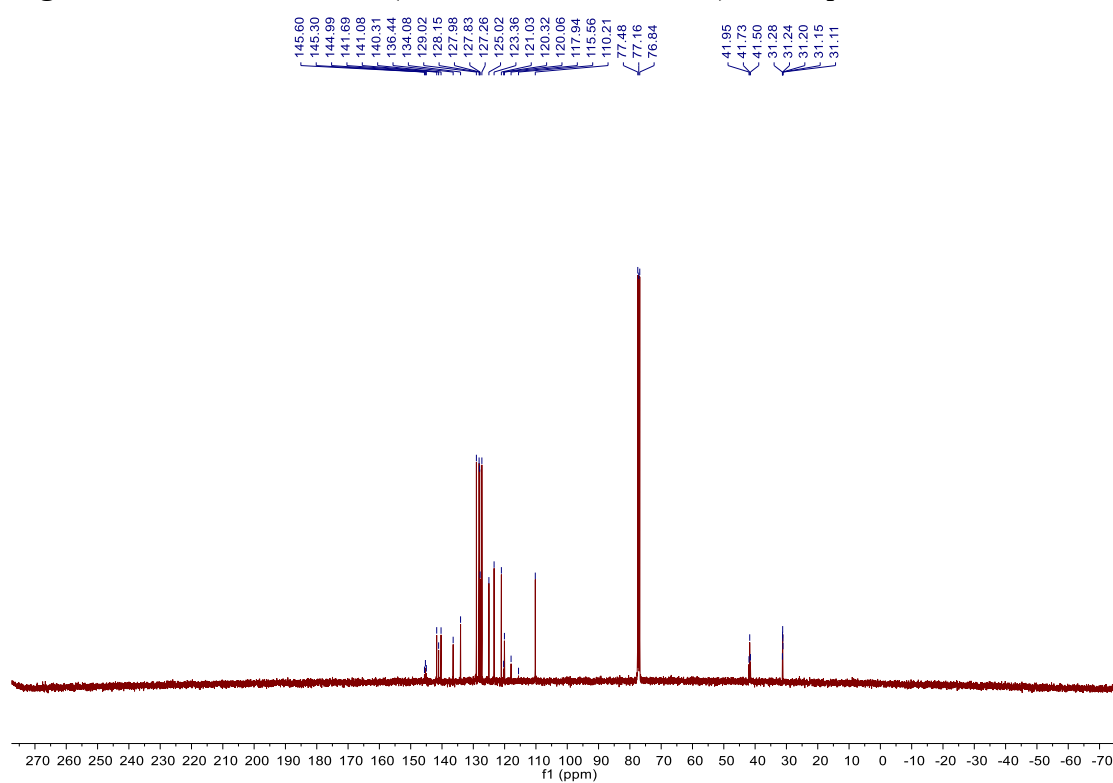


Figure S166. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ax**.

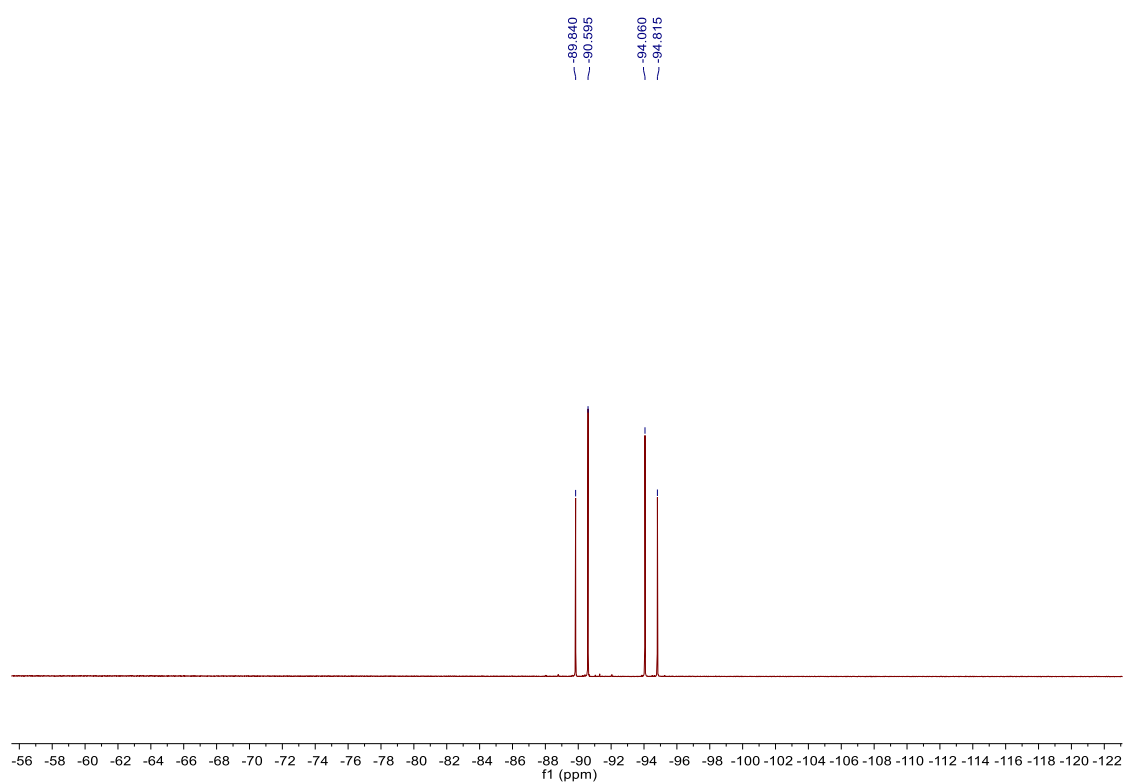


Figure S167. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ay**.

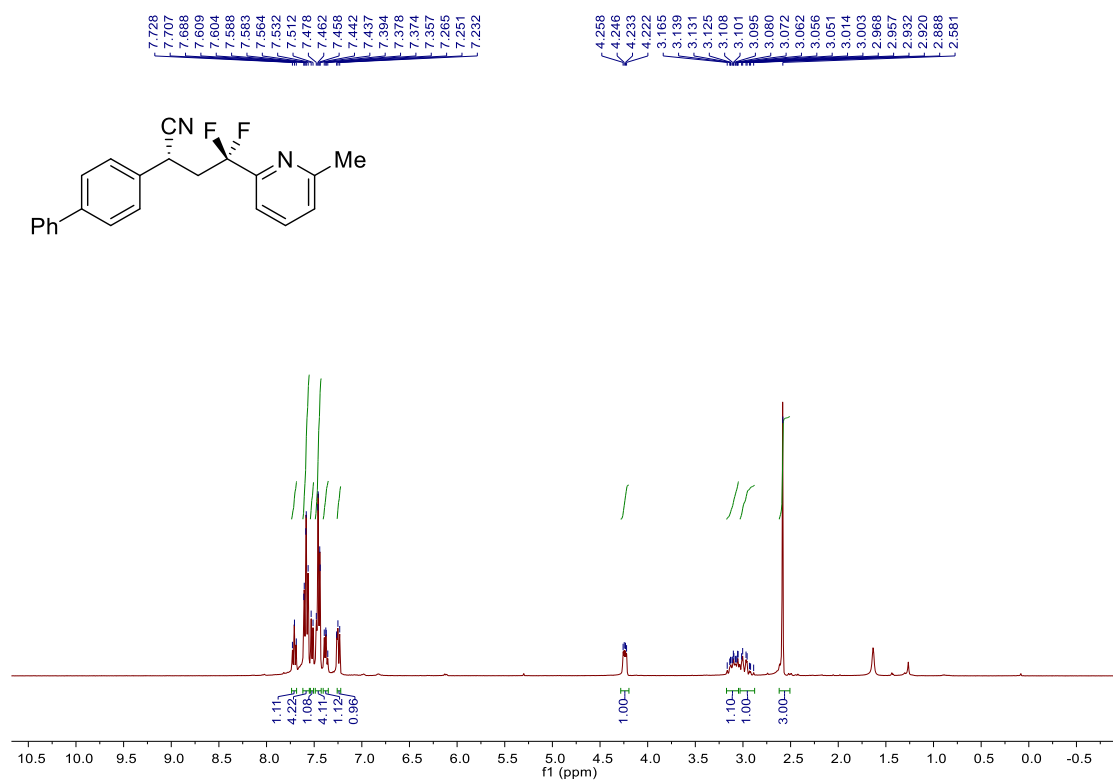


Figure S168. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ay**.

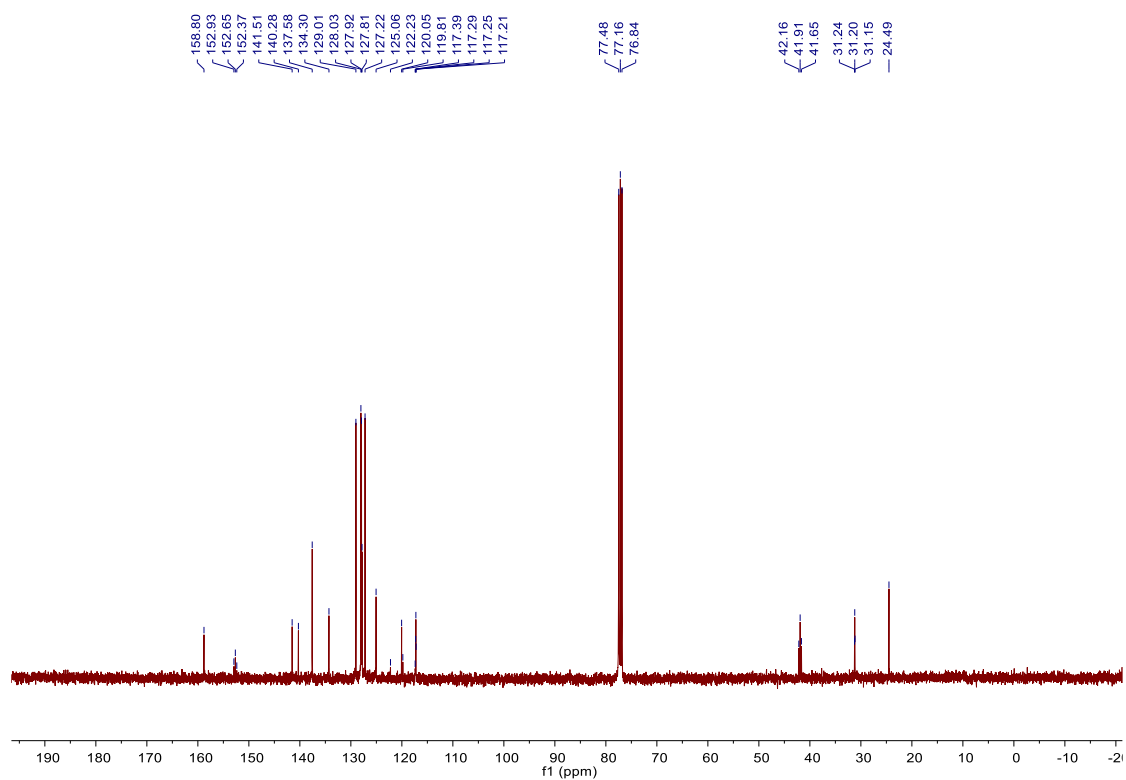


Figure S169. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ay**.

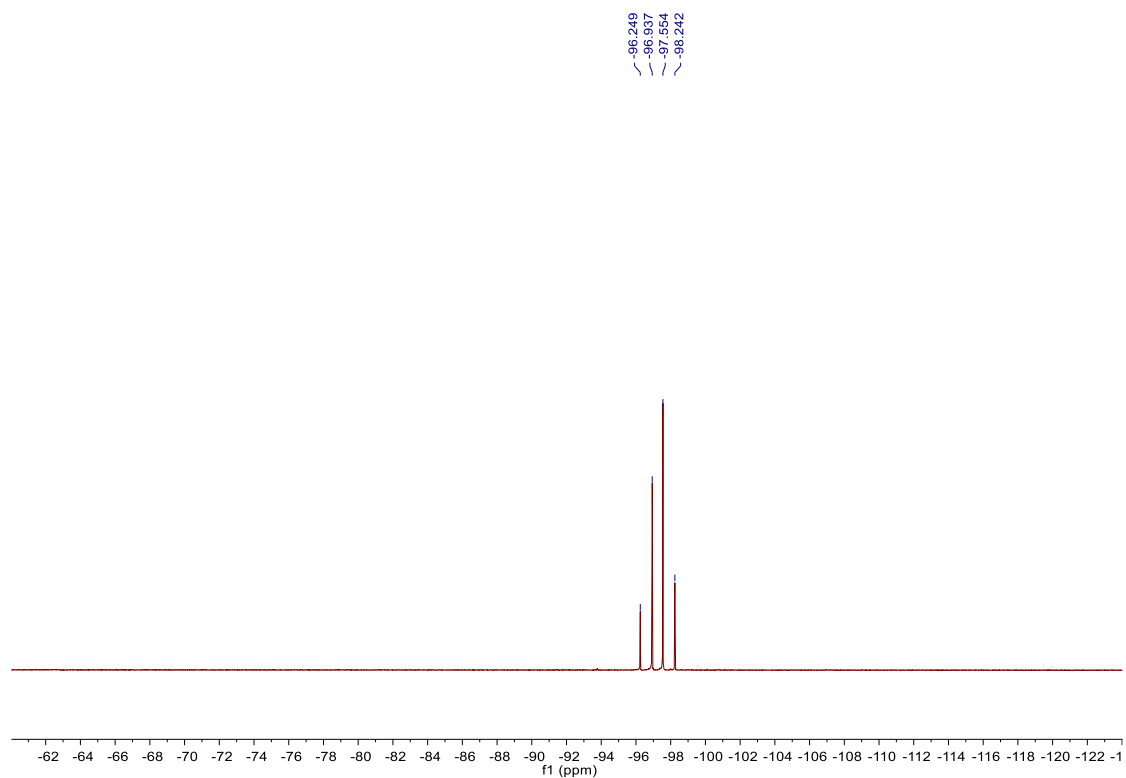


Figure S170. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4az**.

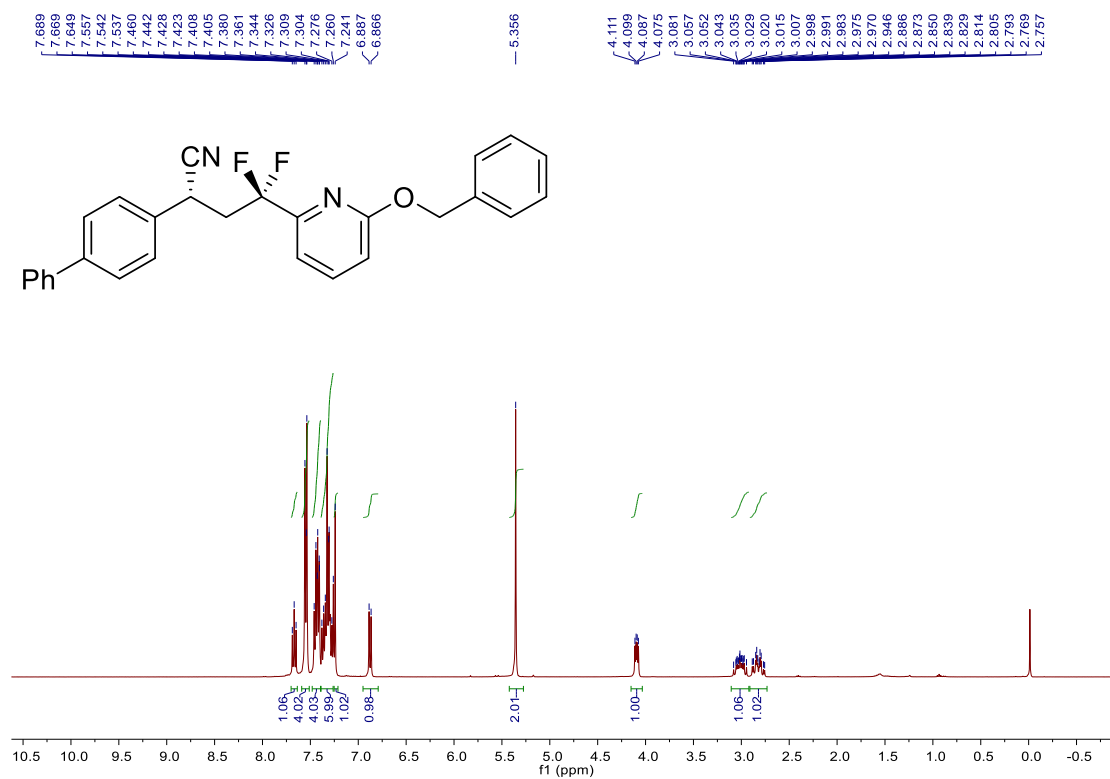


Figure S171. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4az**.

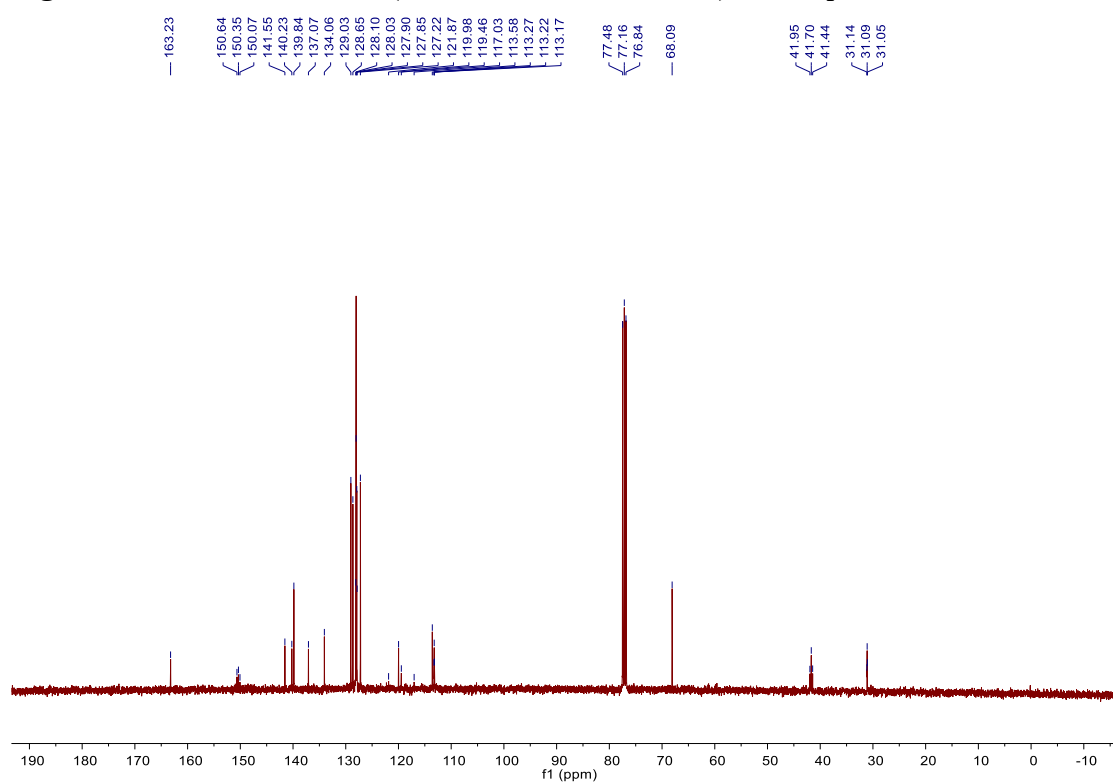


Figure S172. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4az**.

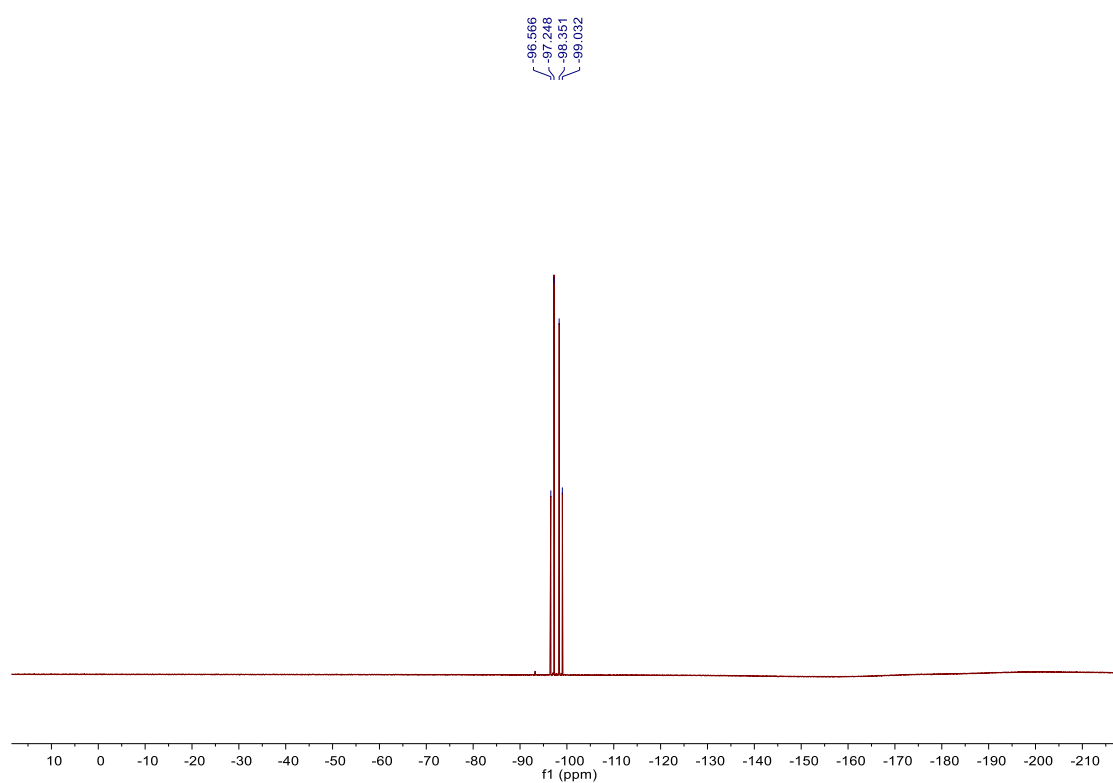


Figure S173. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4ba**.

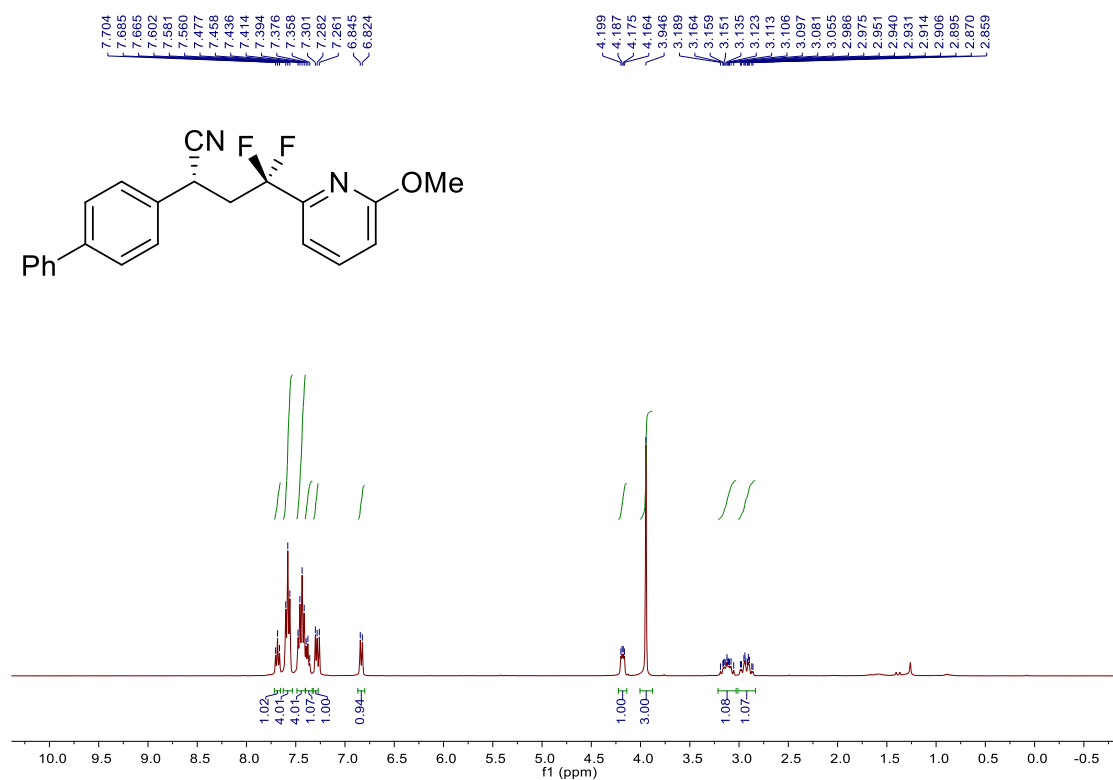


Figure S174. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4ba**.

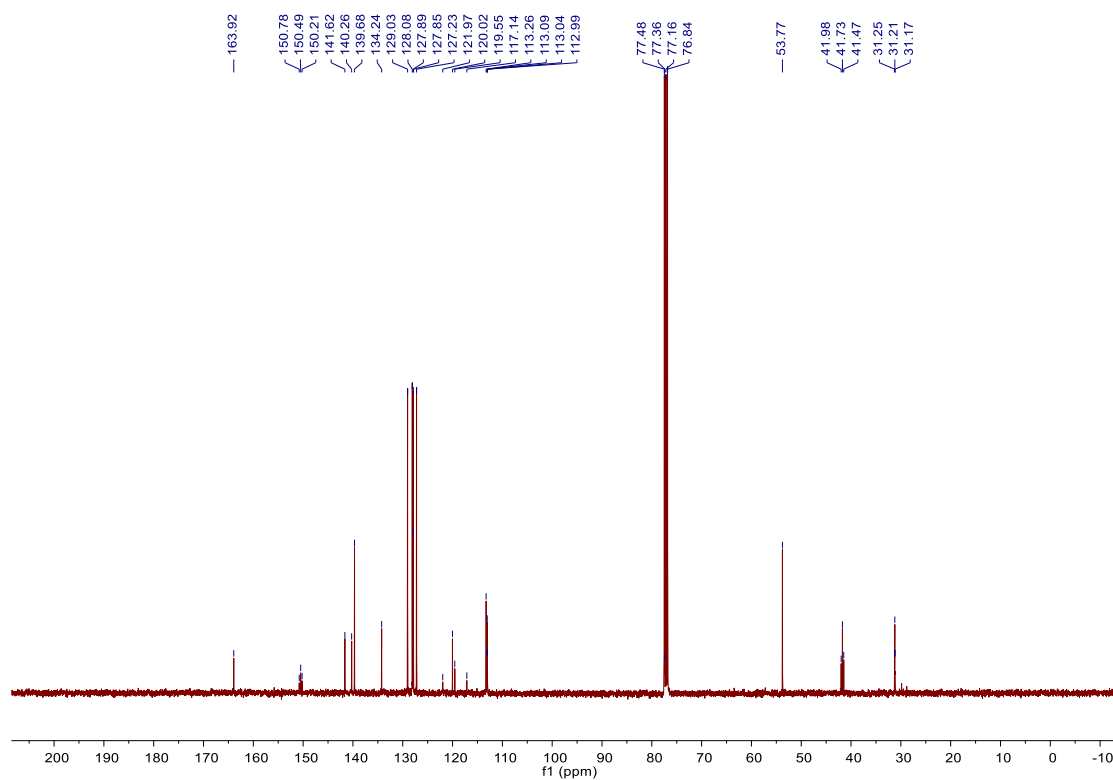


Figure S175. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4ba**.

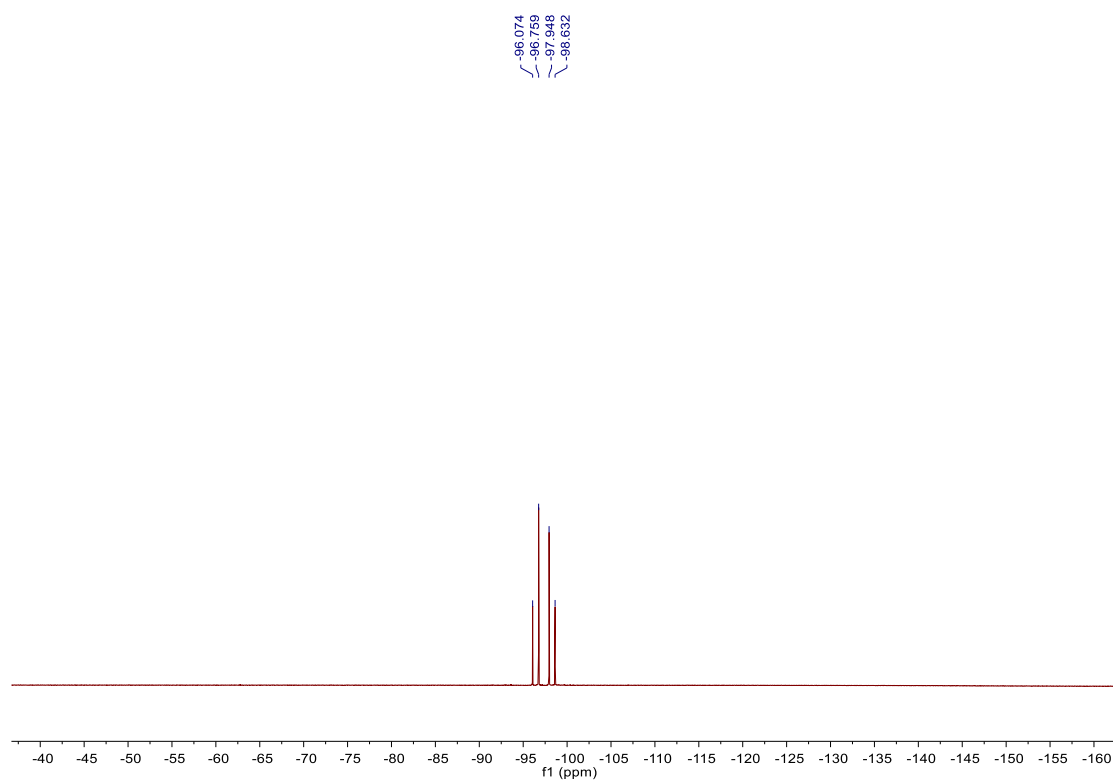


Figure S176. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4bb**.

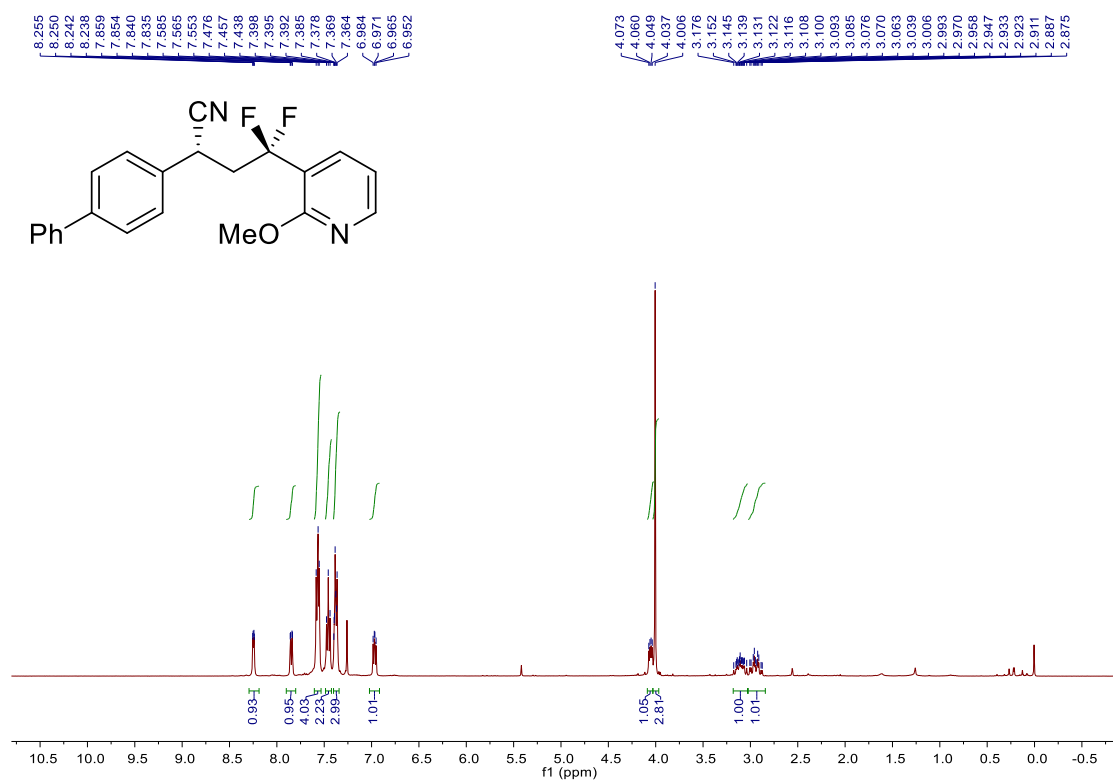


Figure S177. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4bb**.

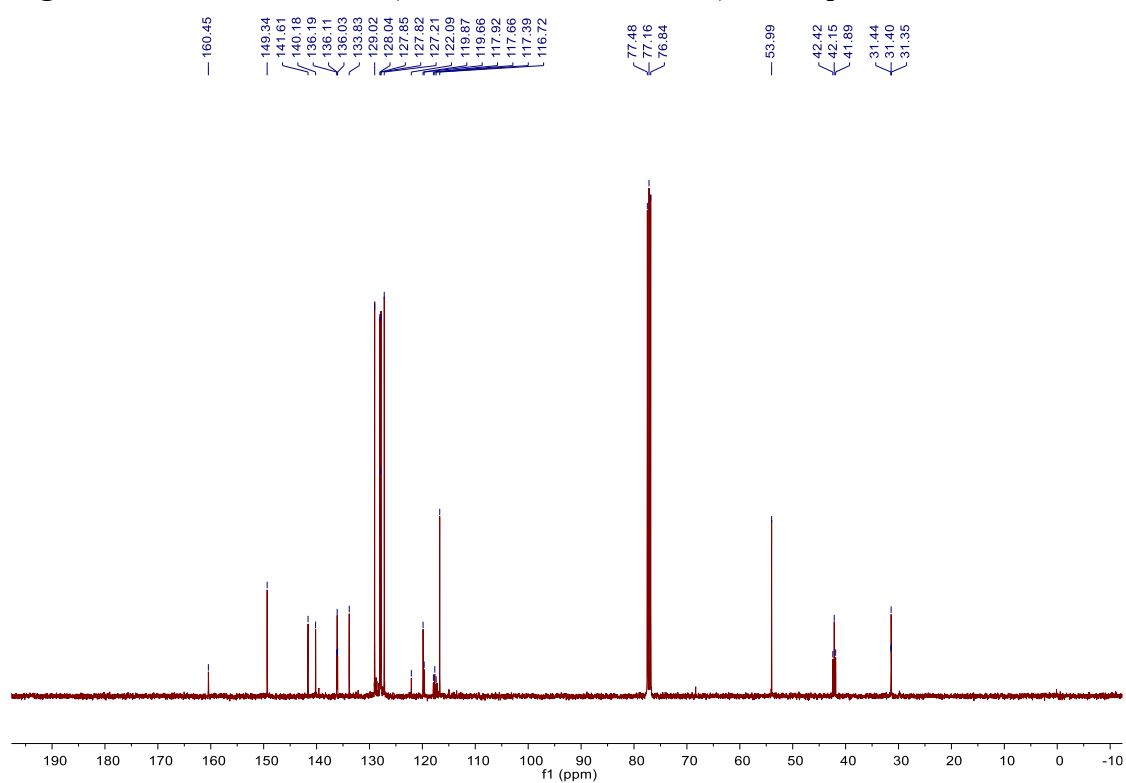


Figure S178. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4bb**.

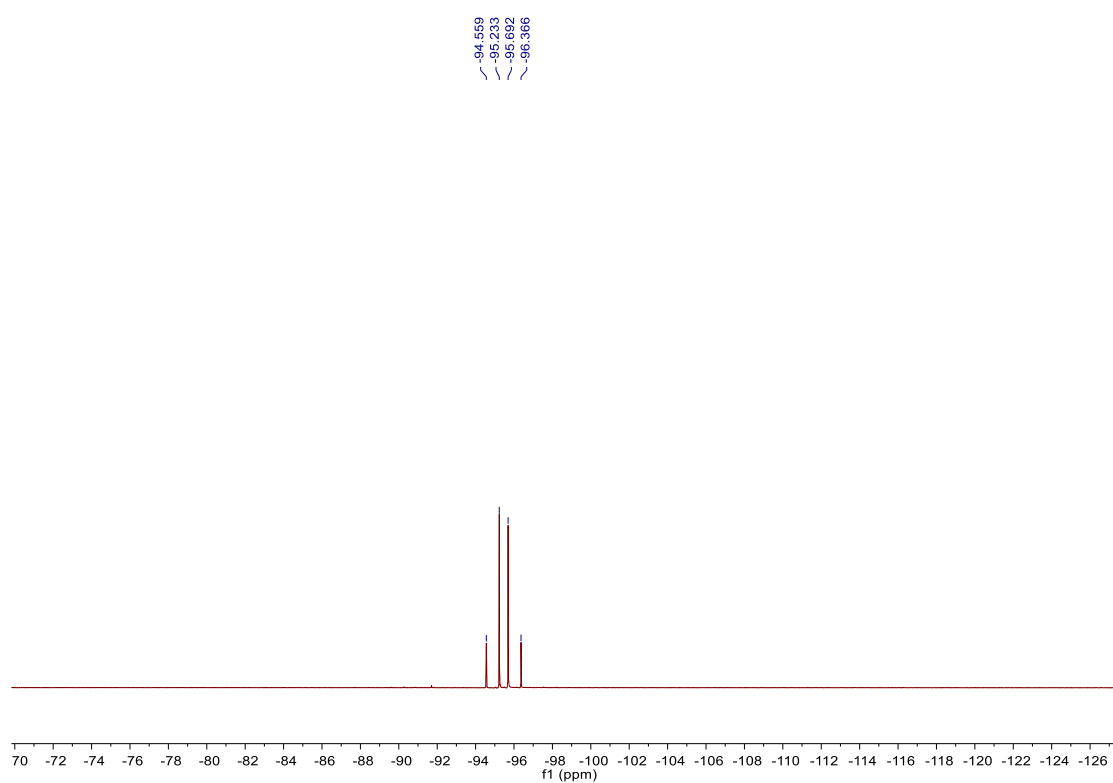


Figure S179. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4bc**.

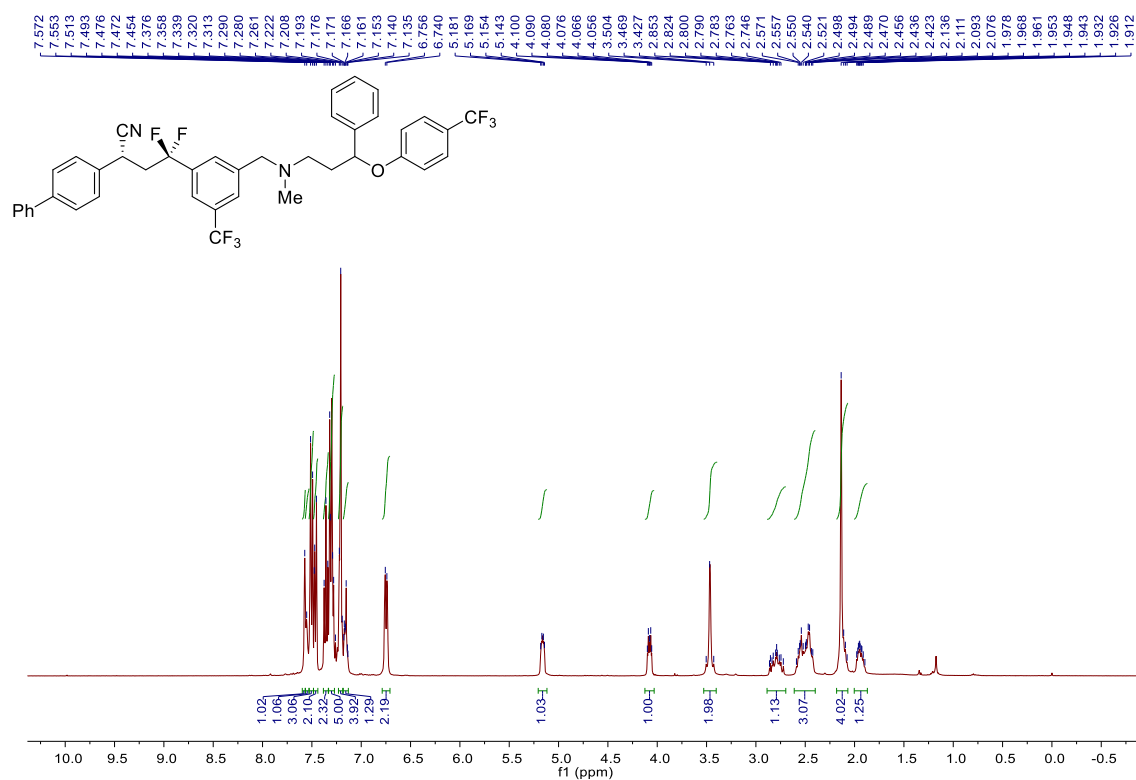


Figure S180. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4bc**.

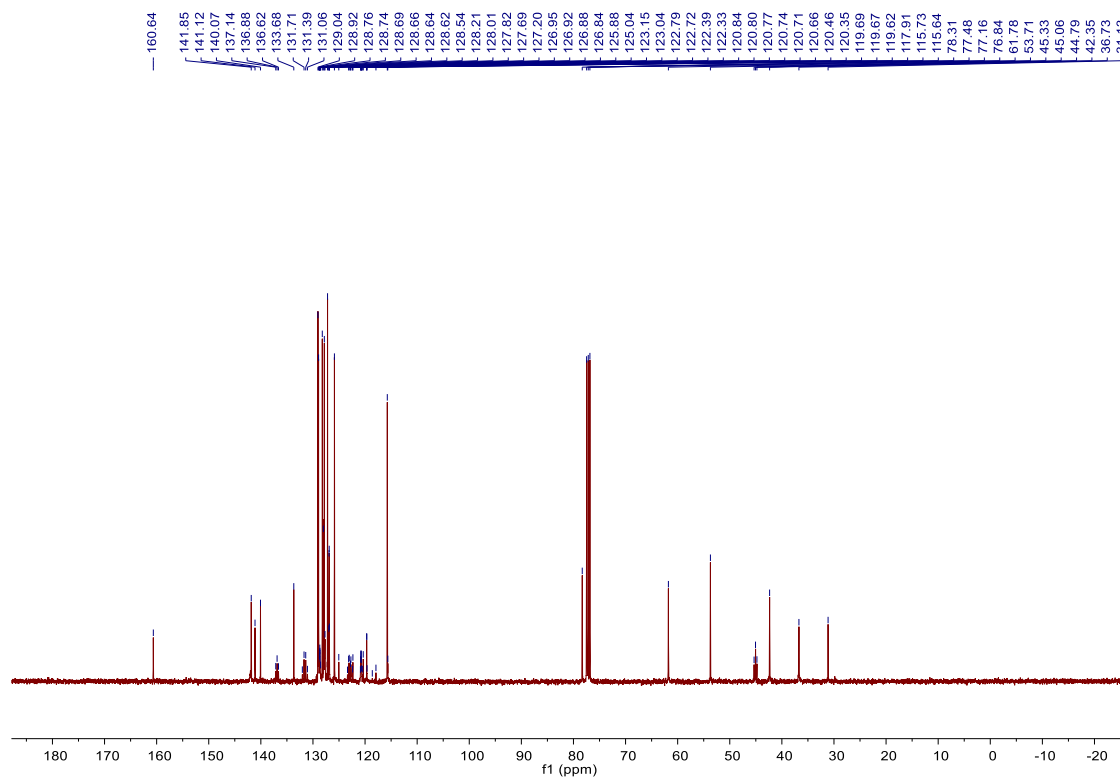


Figure S181. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4bc**.

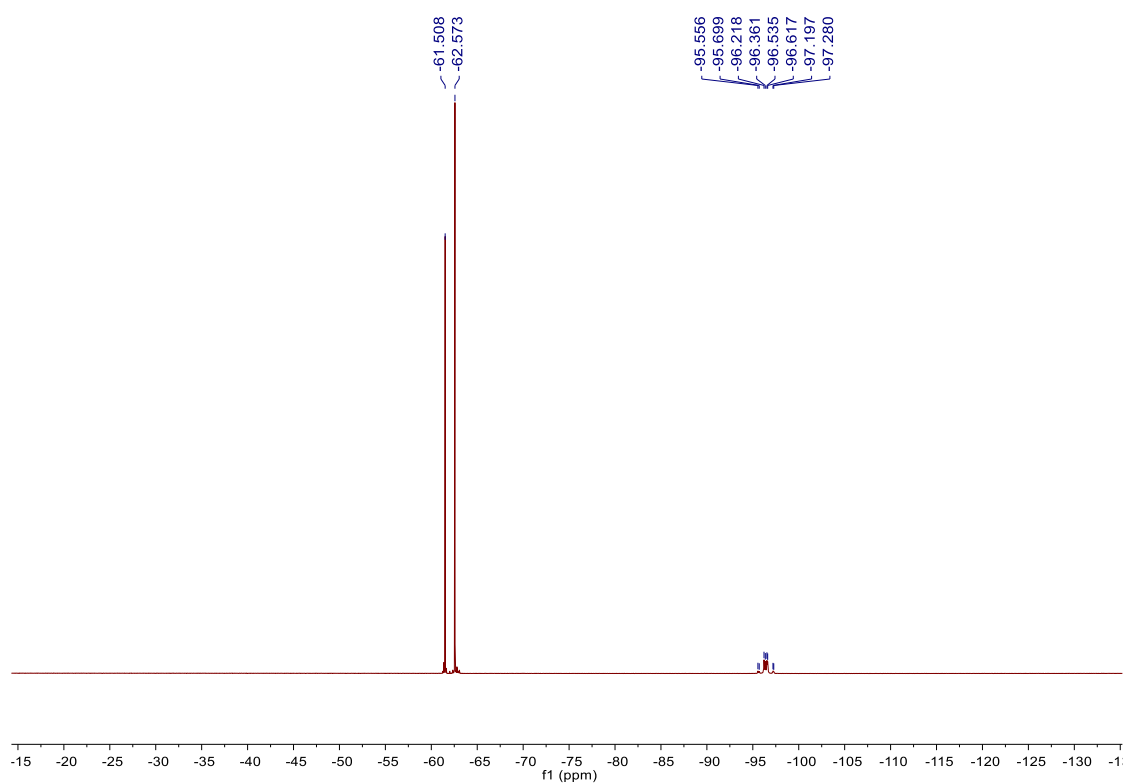


Figure S182. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4bd**.

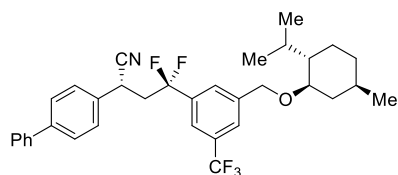
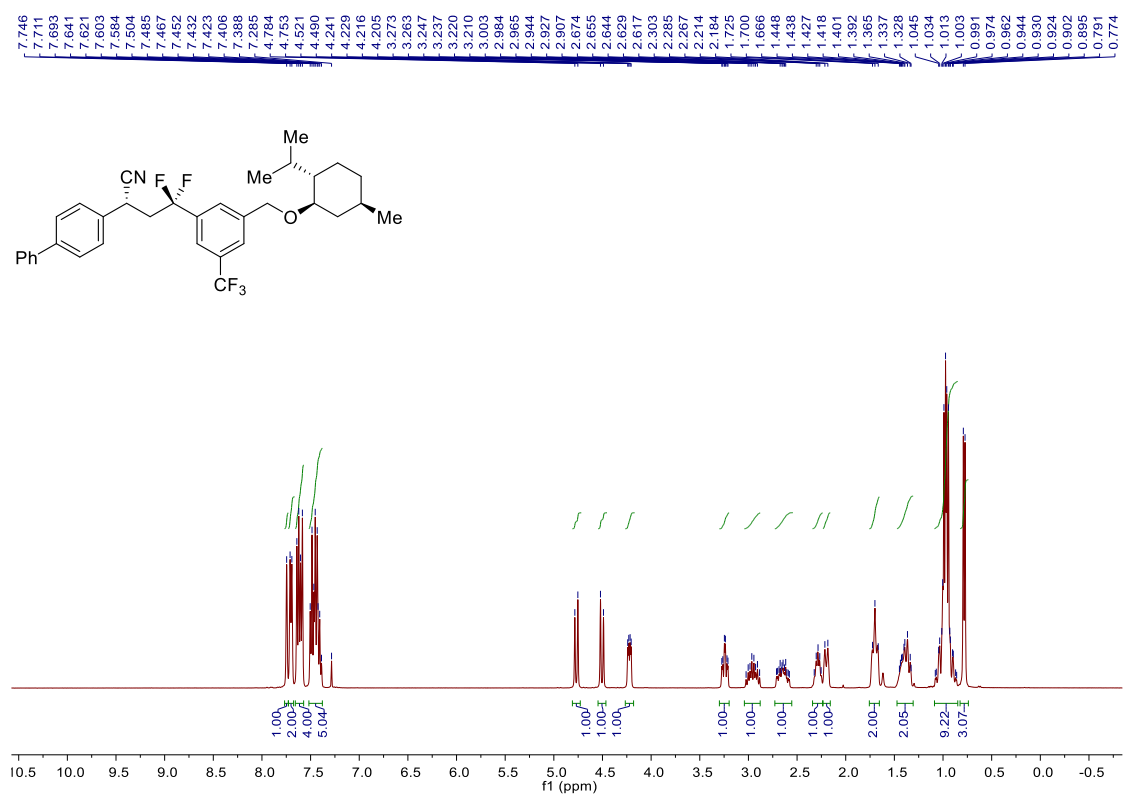


Figure S183. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4bd**.

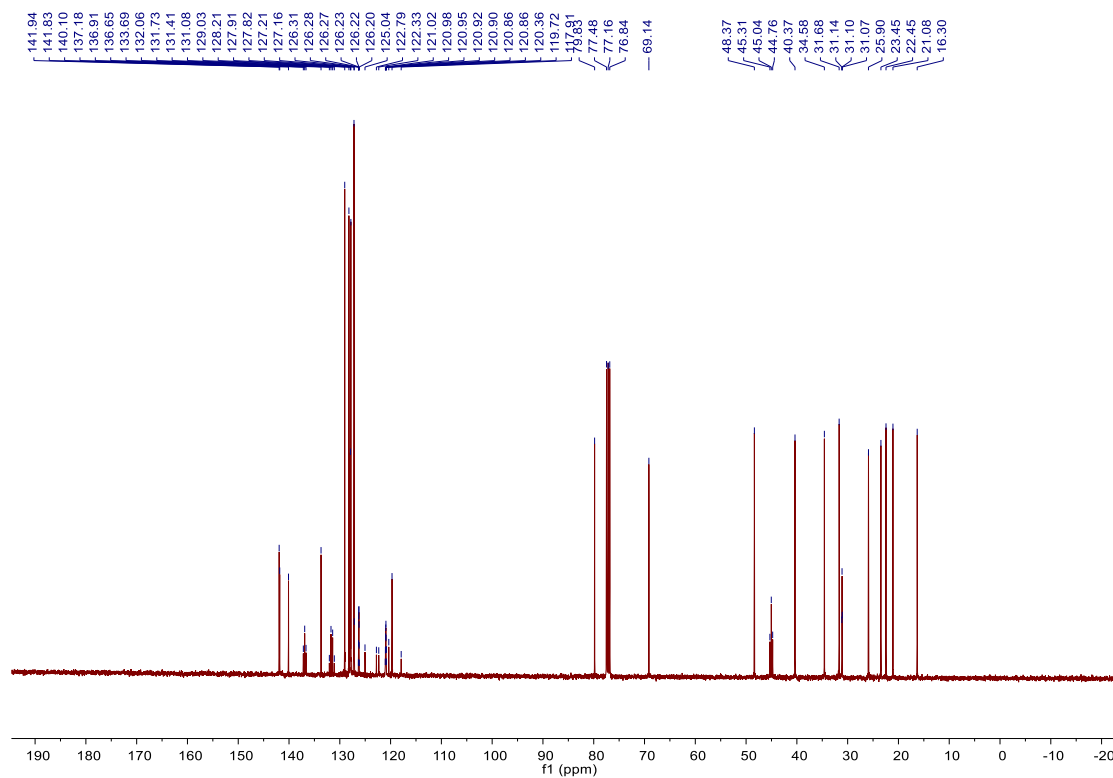
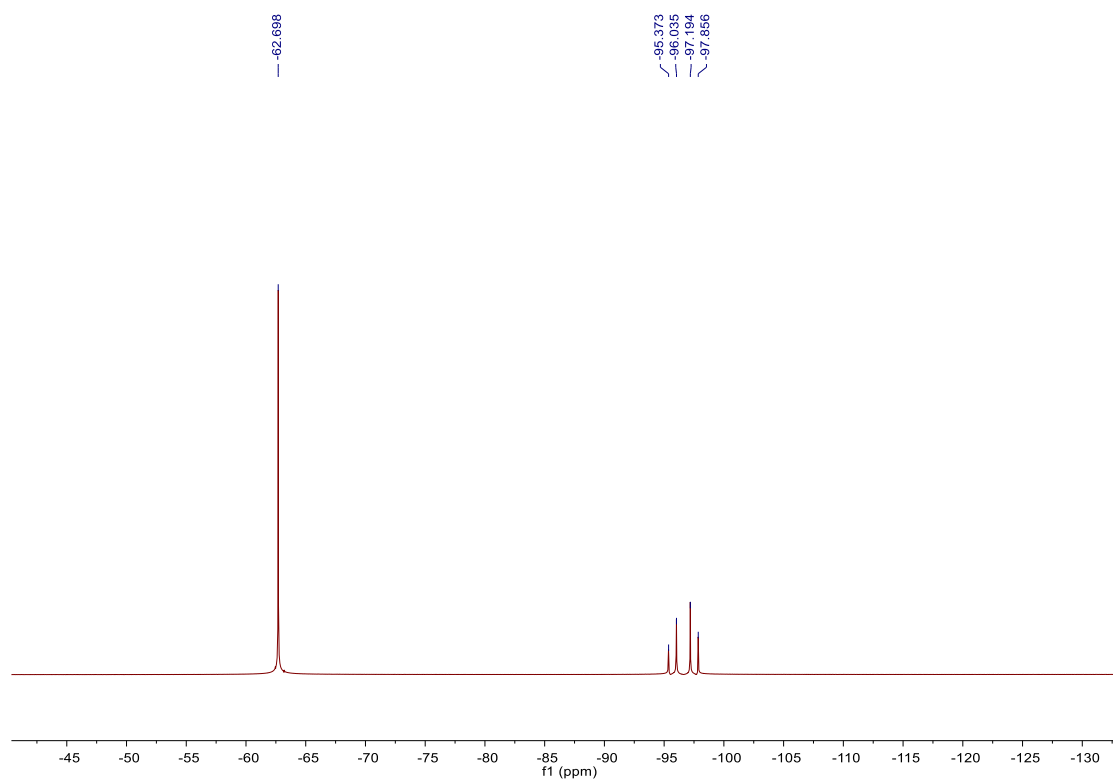


Figure S184. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4bd**.



Chemical structure of compound 10: CC1(C)OC2C(C1)OC(C2)OC(C3=CC=C(C=C3)C(F)(F)F)C(F)(F)C(C#N)C4=CC=CC=C4

¹H NMR spectrum (CDCl₃) of compound 10. The x-axis represents the chemical shift in ppm, ranging from -0.5 to 10.5. The spectrum shows several peaks corresponding to the protons in the molecule. The peaks are labeled with their chemical shifts (ppm) and integration values.

Peak list (ppm): 7.776, 7.687, 7.609, 7.589, 7.567, 7.549, 7.474, 7.455, 7.436, 7.419, 7.398, 7.377, 7.358, 7.260, 5.928, 5.919, 4.823, 4.791, 4.736, 4.704, 4.644, 4.635, 4.393, 4.379, 4.356, 4.344, 4.210, 4.199, 4.186, 4.175, 4.154, 4.137, 4.131, 4.123, 4.116, 4.108, 4.102, 4.102, 4.056, 4.043, 4.035, 4.021, 4.021, 2.976, 2.960, 2.953, 2.940, 2.919, 2.904, 2.883, 2.869, 2.657, 2.640, 2.628, 2.613, 2.601, 1.507, 1.434, 1.365, 1.328.

Integration values (from left to right): 1.00, 2.00, 2.03, 2.06, 3.11, 1.00, 1.01, 1.04, 1.00, 1.00, 2.06, 2.00, 1.00, 1.00, 3.20, 3.10, 3.05, 3.14.

141.86
140.27
139.54
137.97
137.11
136.84
133.56
132.28
131.95
131.62
129.03
128.20
128.20
127.93
127.81
127.18
127.13
127.08
126.34
126.31
126.28
126.26
126.24
126.22
124.94
122.71
122.20
121.50
121.45
121.41
121.39
121.35
120.27
119.63
112.08
109.51
105.37
82.36
81.39
77.48
77.16
76.84
72.35
71.00
67.71

45.25
44.98
44.71

31.14
31.10
31.07
26.98
26.90
26.32
25.27

Figure S187. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4be**.

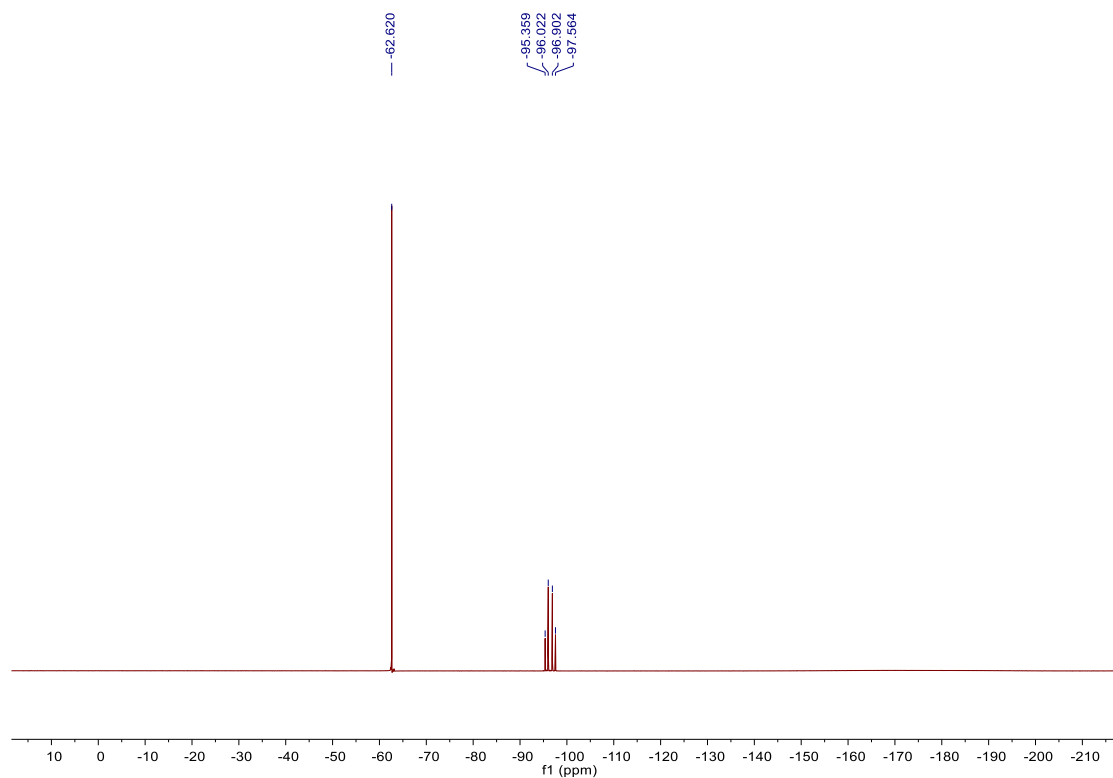


Figure S188. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **4bf**.

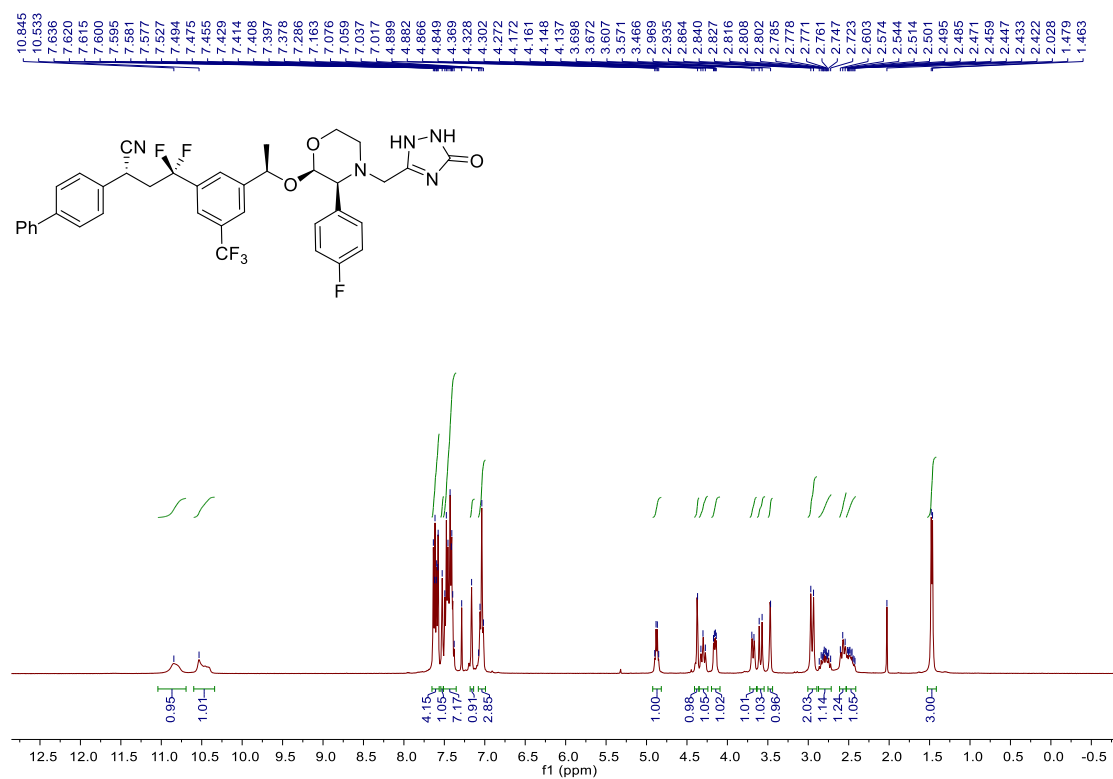


Figure S189. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **4bf**.

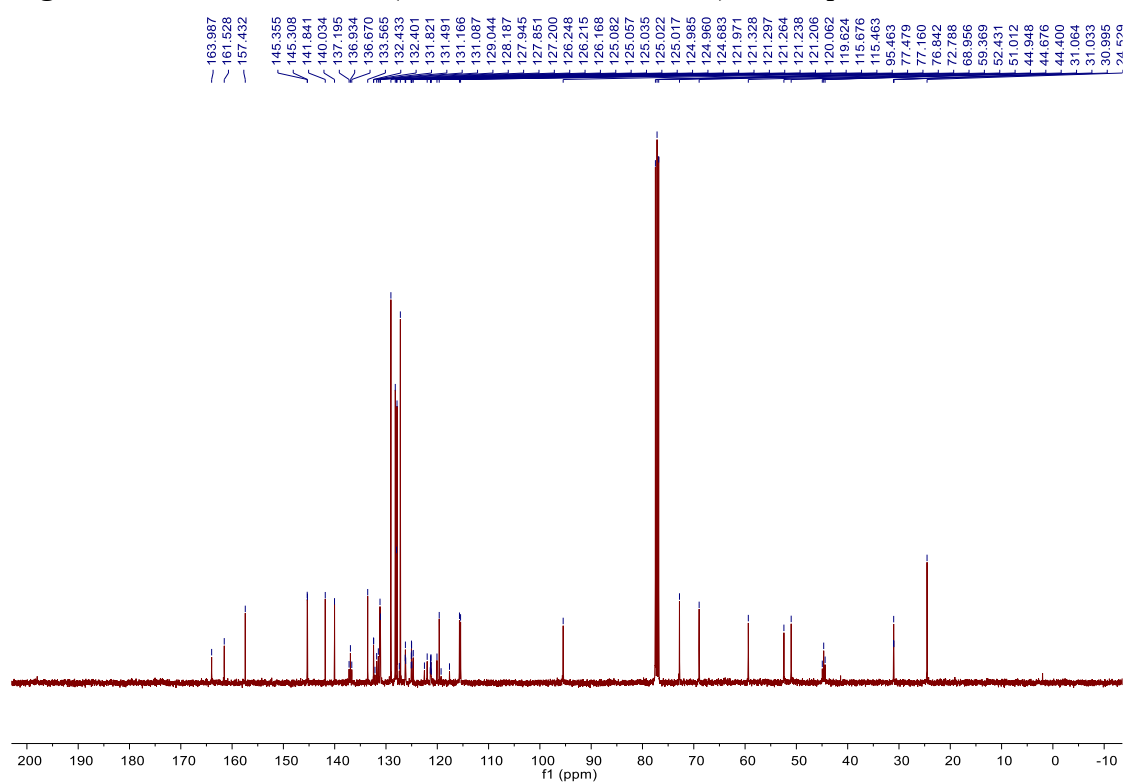


Figure S190. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **4bf**.

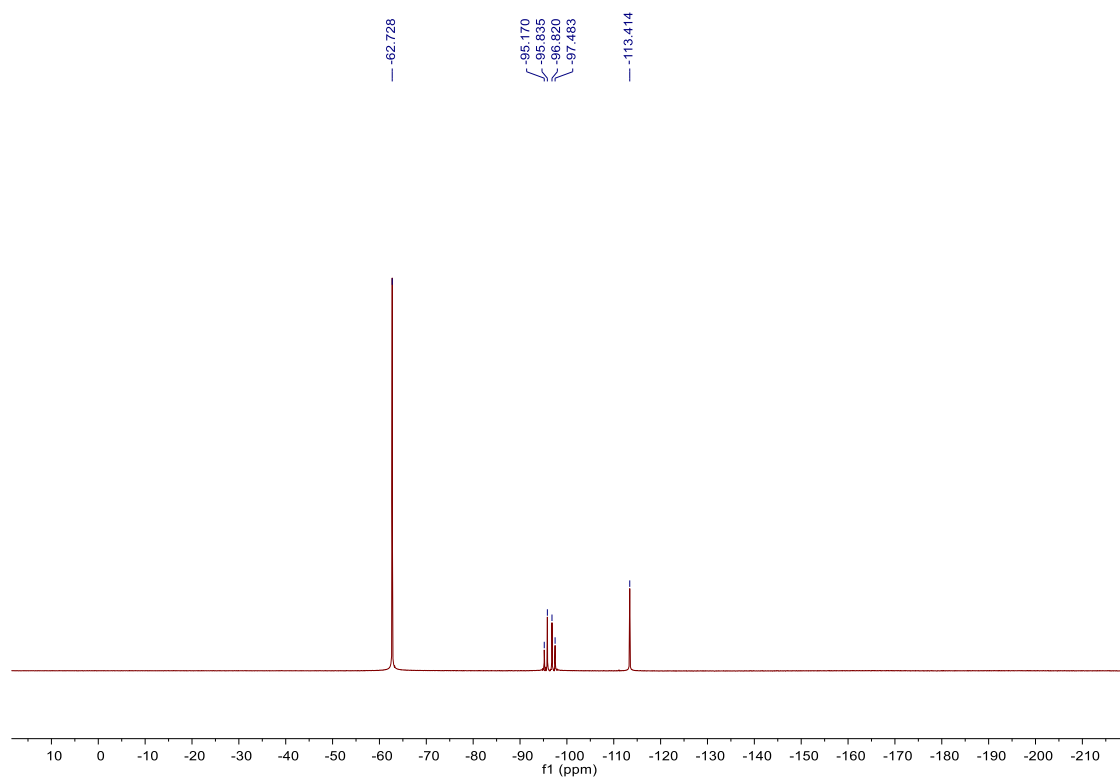


Figure S191. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **5**.

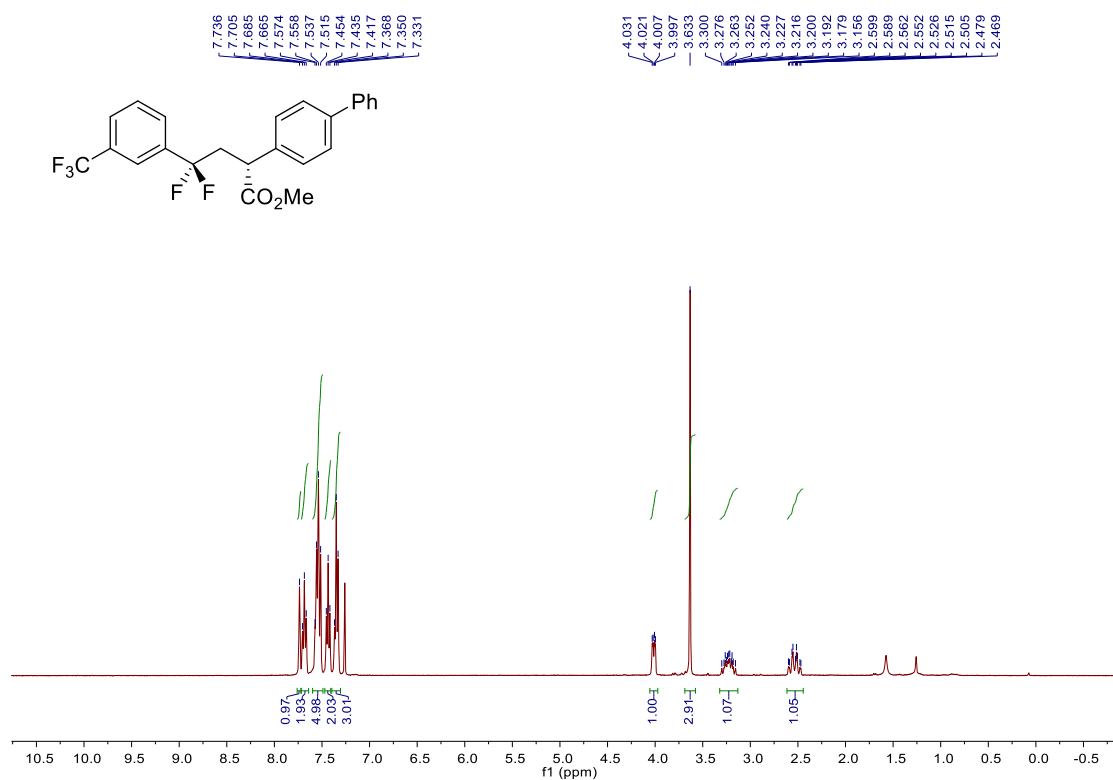


Figure S192. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **5**.

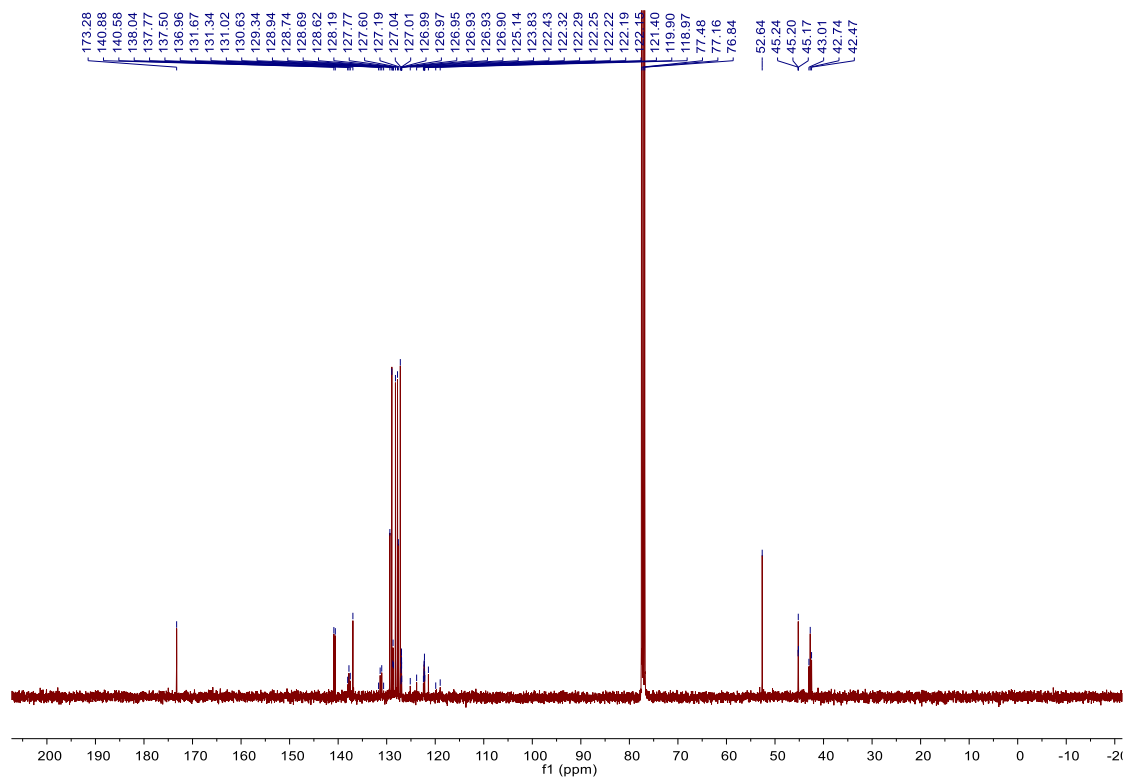


Figure S193. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **5**.

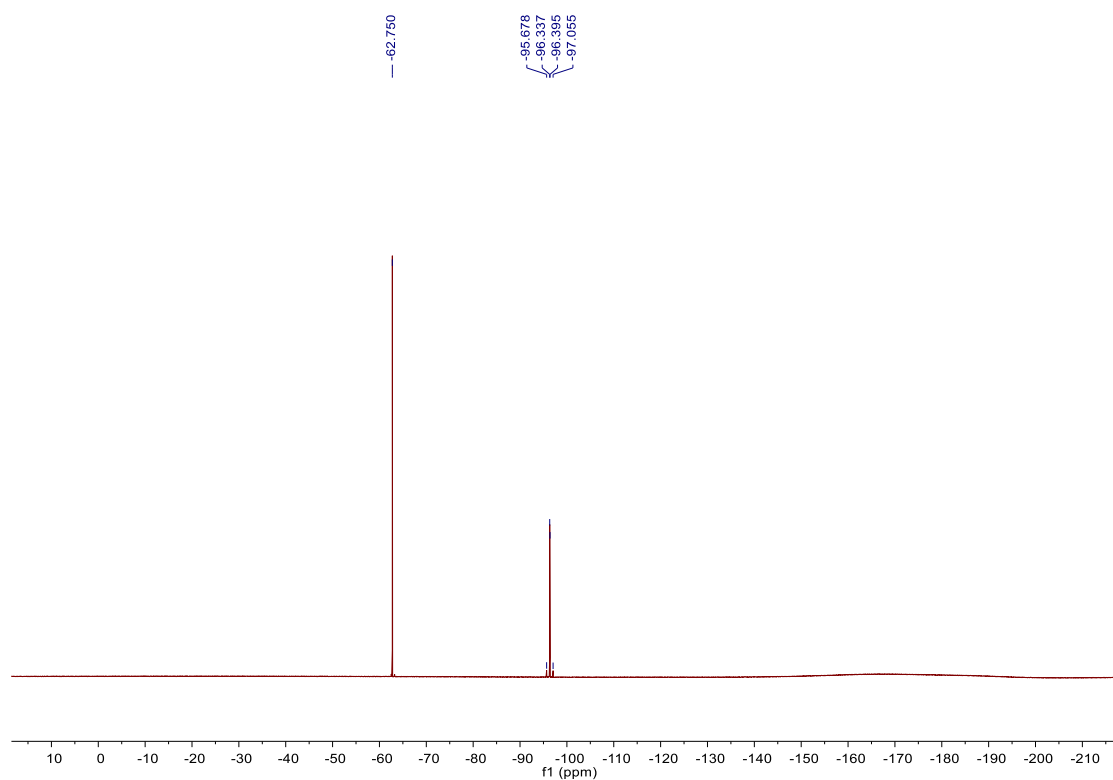


Figure S194. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **6**.

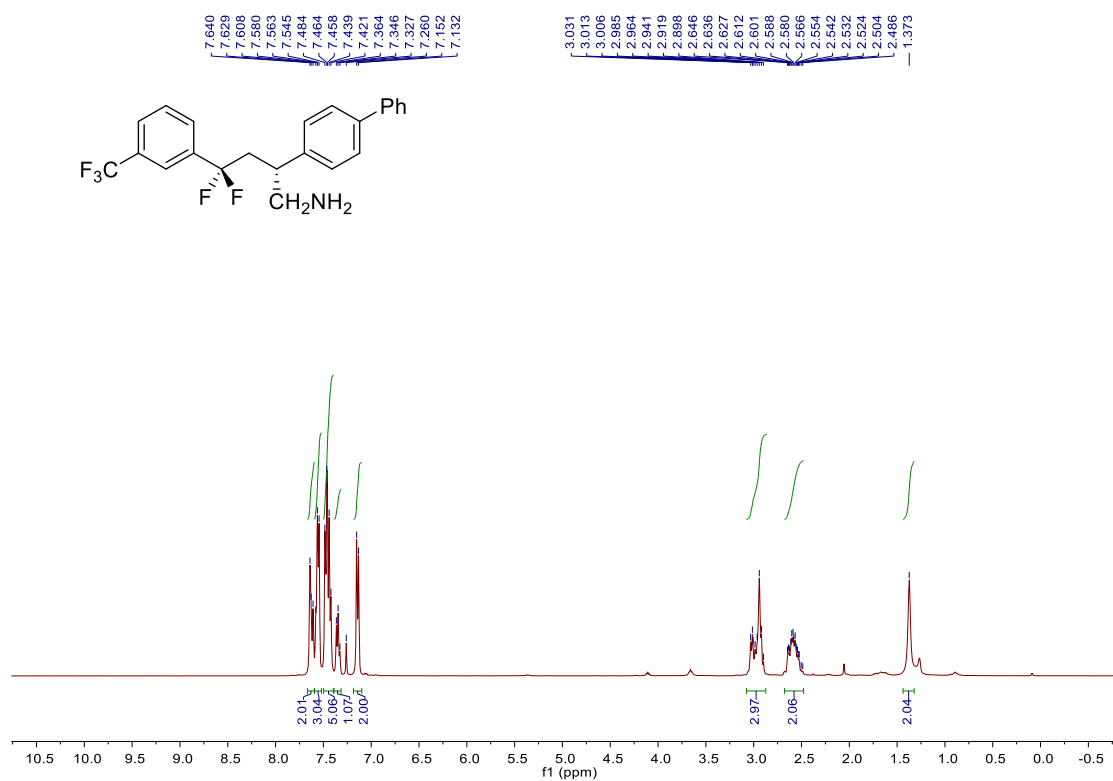


Figure S195. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **6**.

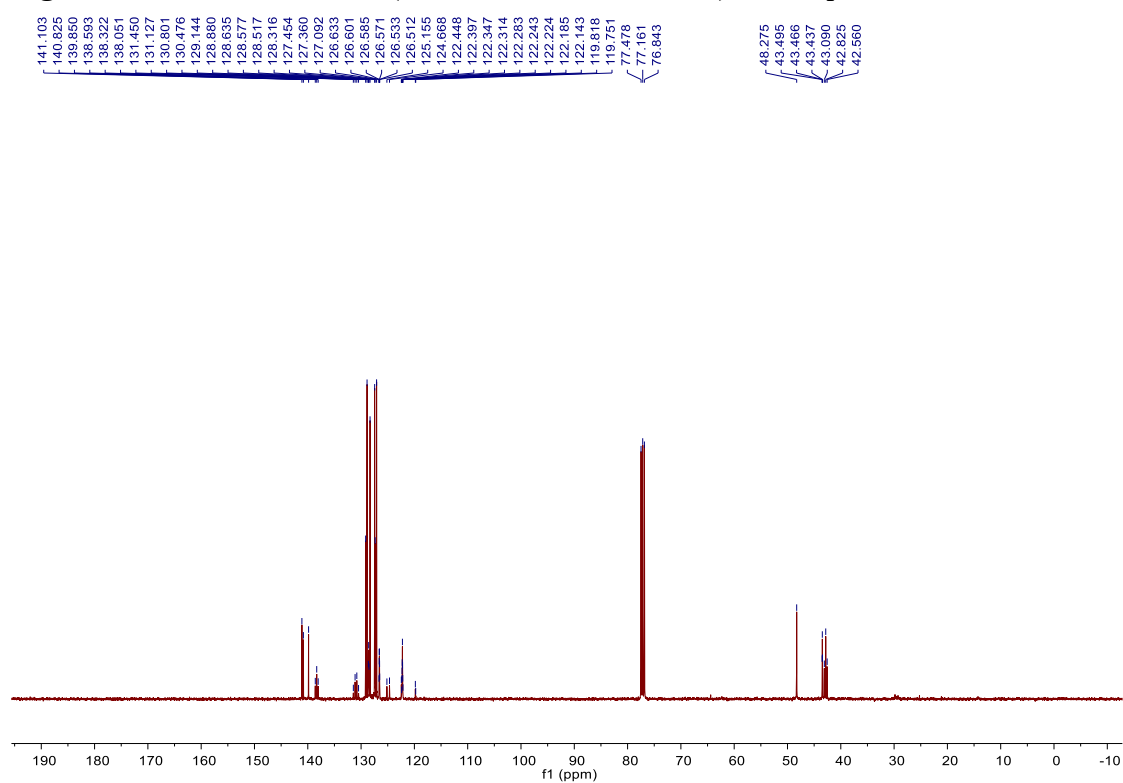


Figure S196. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **6**.

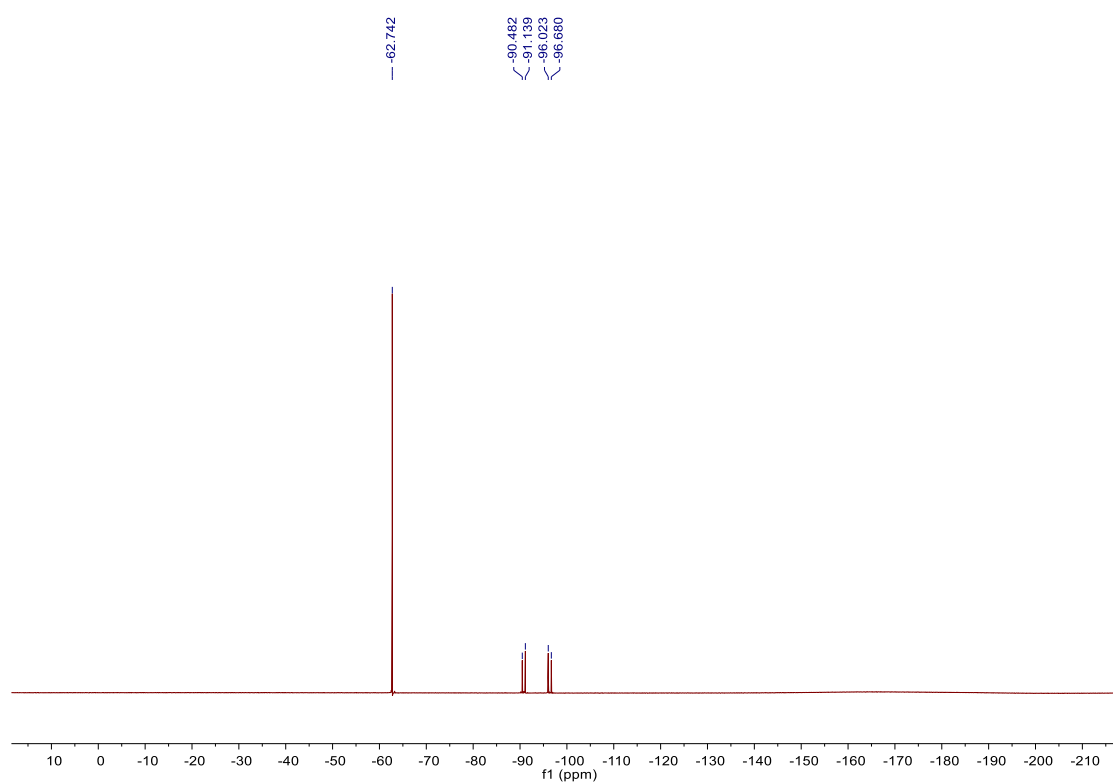


Figure S197. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound 7.

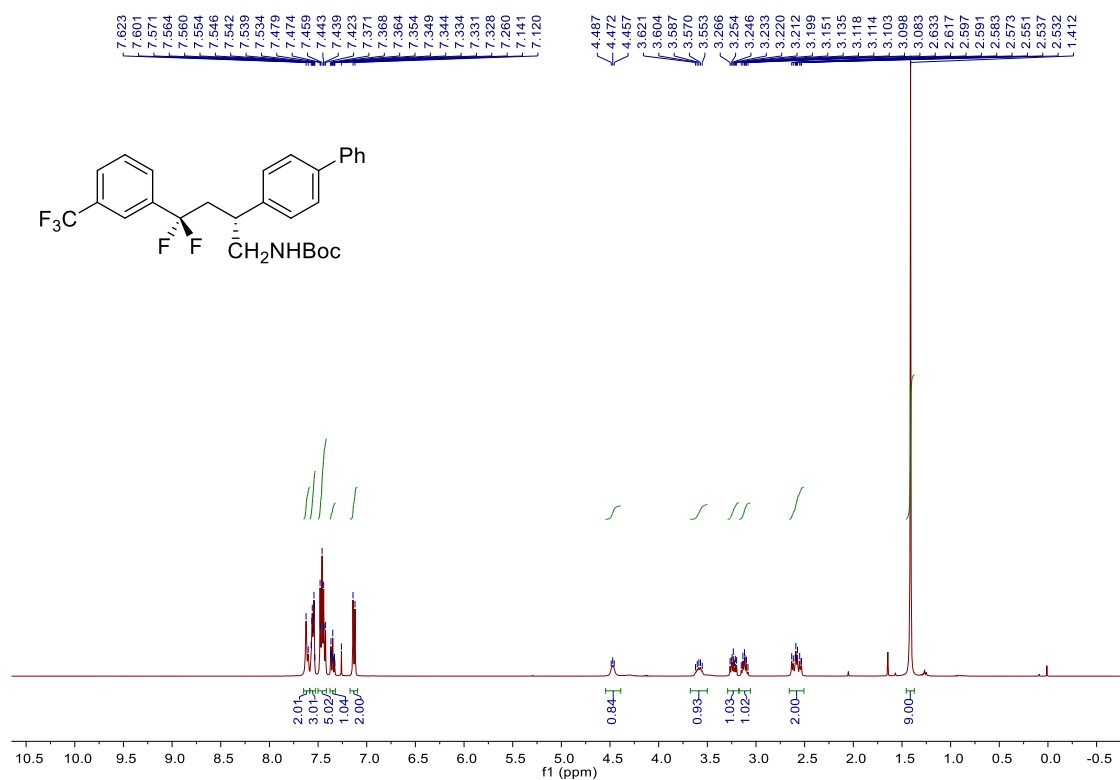


Figure S198. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound 7.

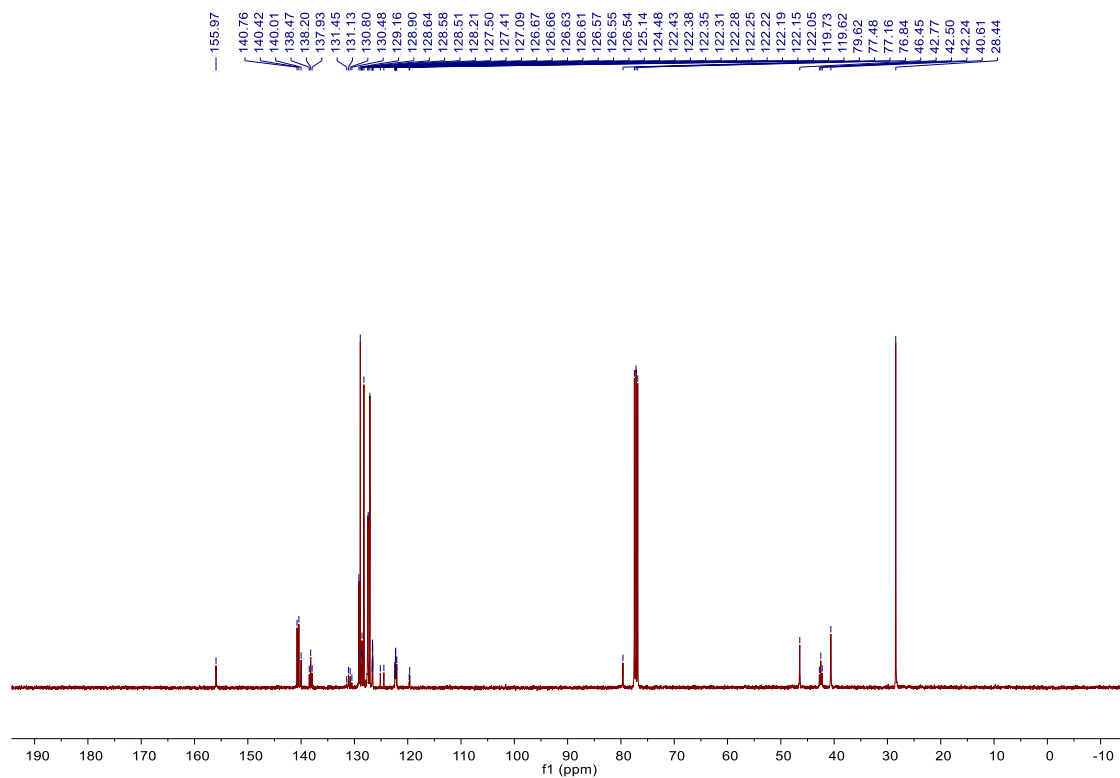


Figure S199. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **7**.

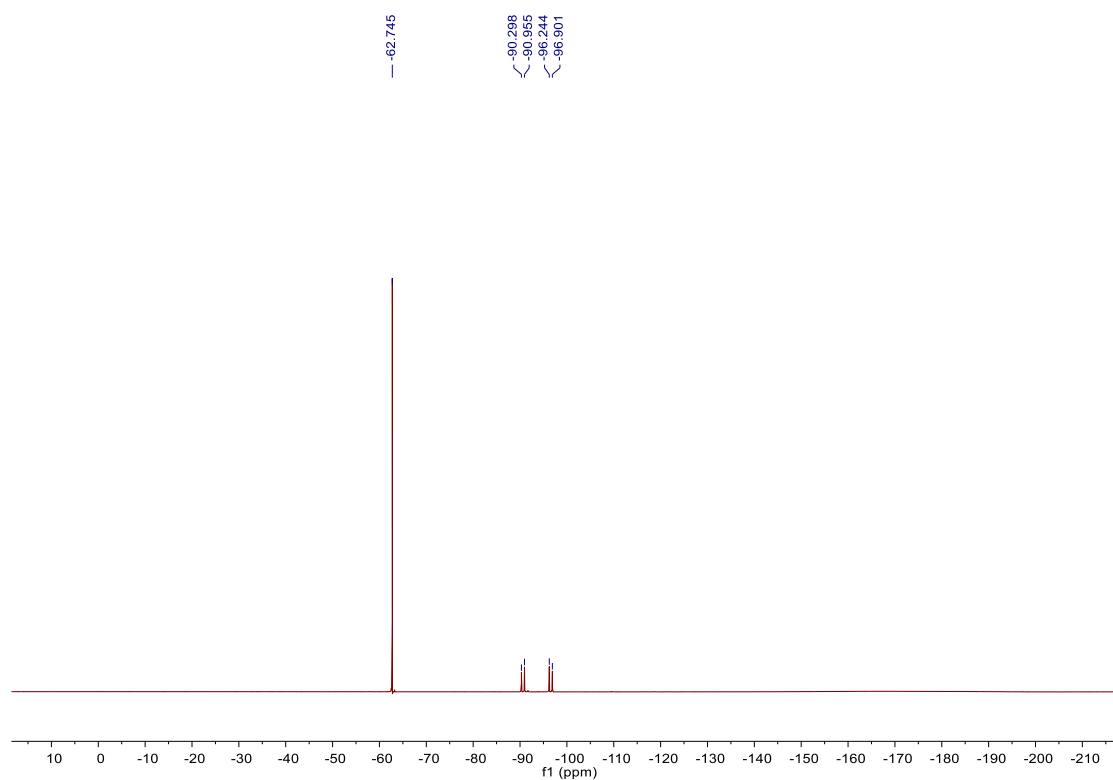


Figure S200. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **8**.

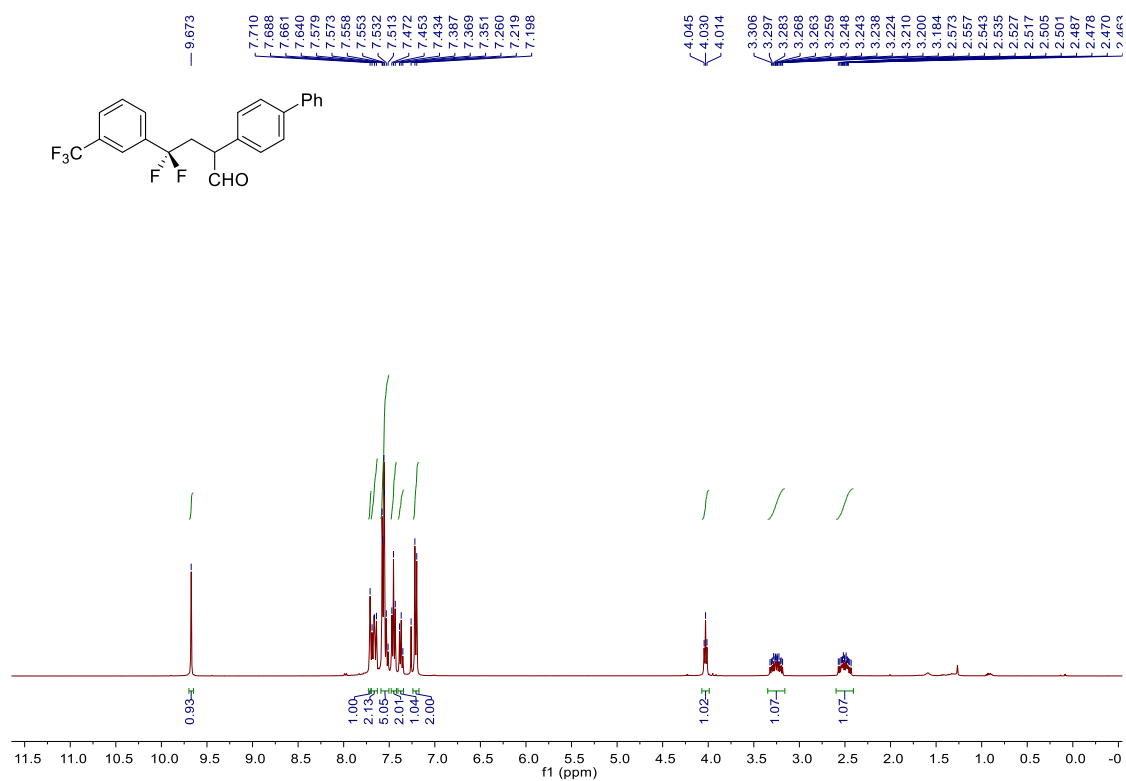


Figure S201. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **8**.

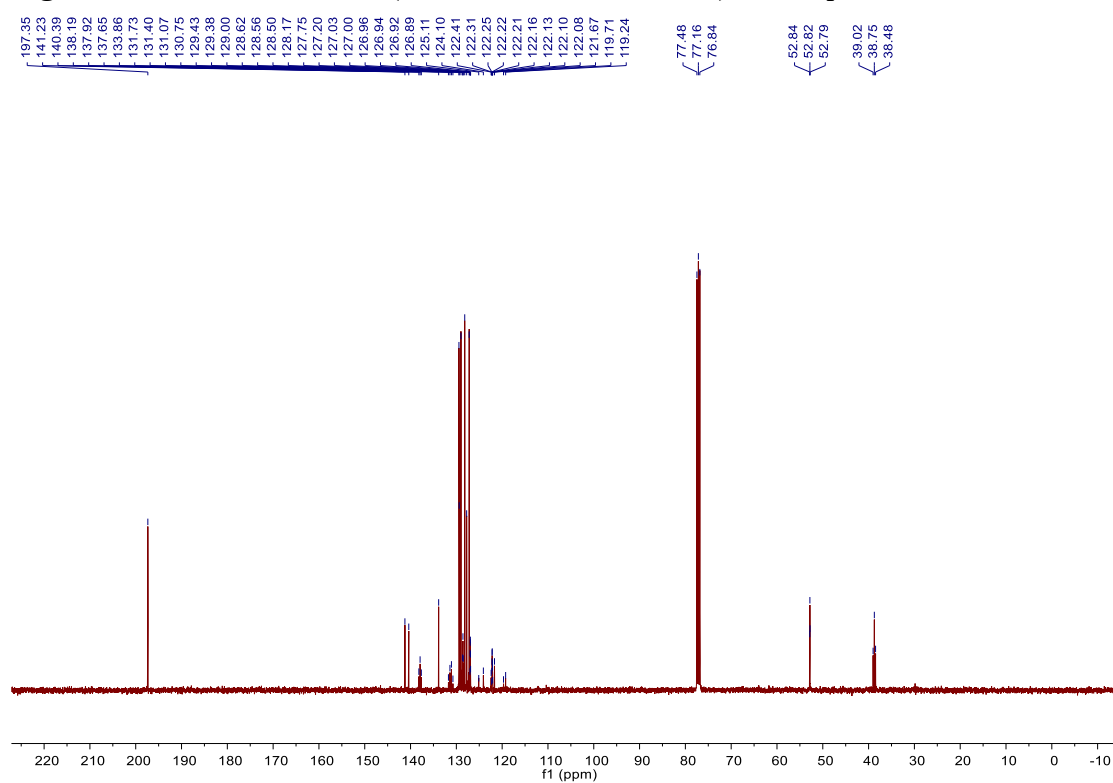


Figure S202. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **8**.

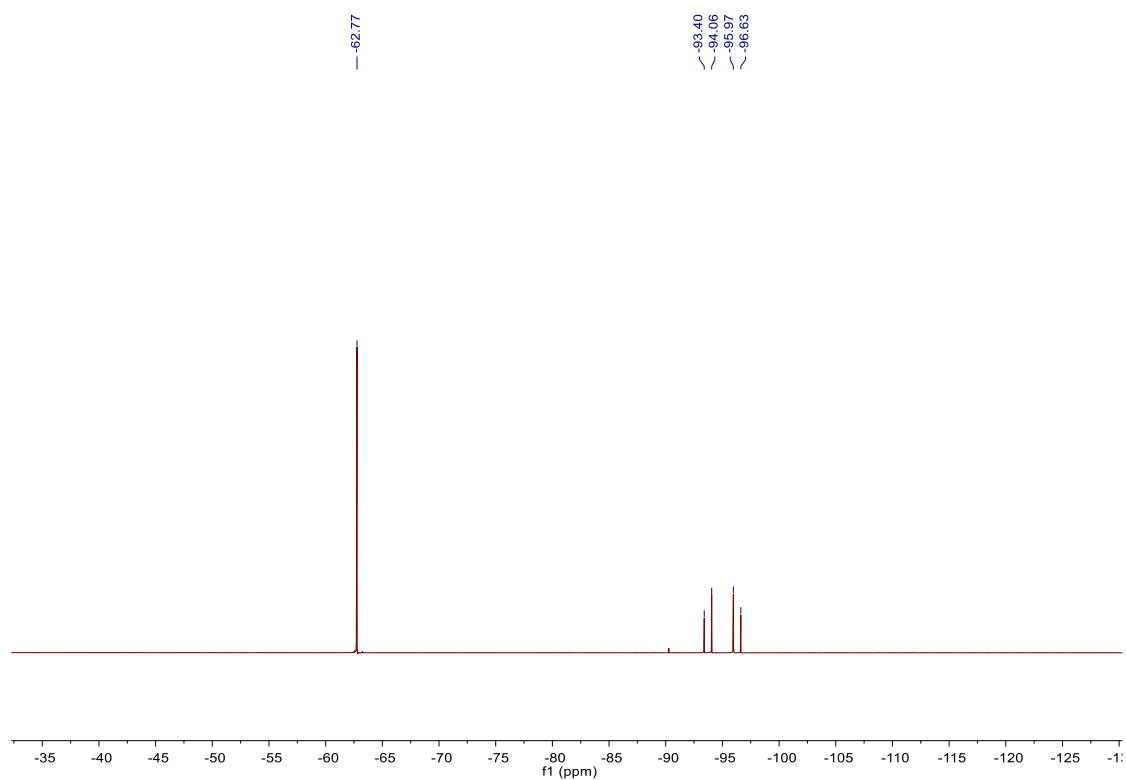


Figure S203. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **9**.

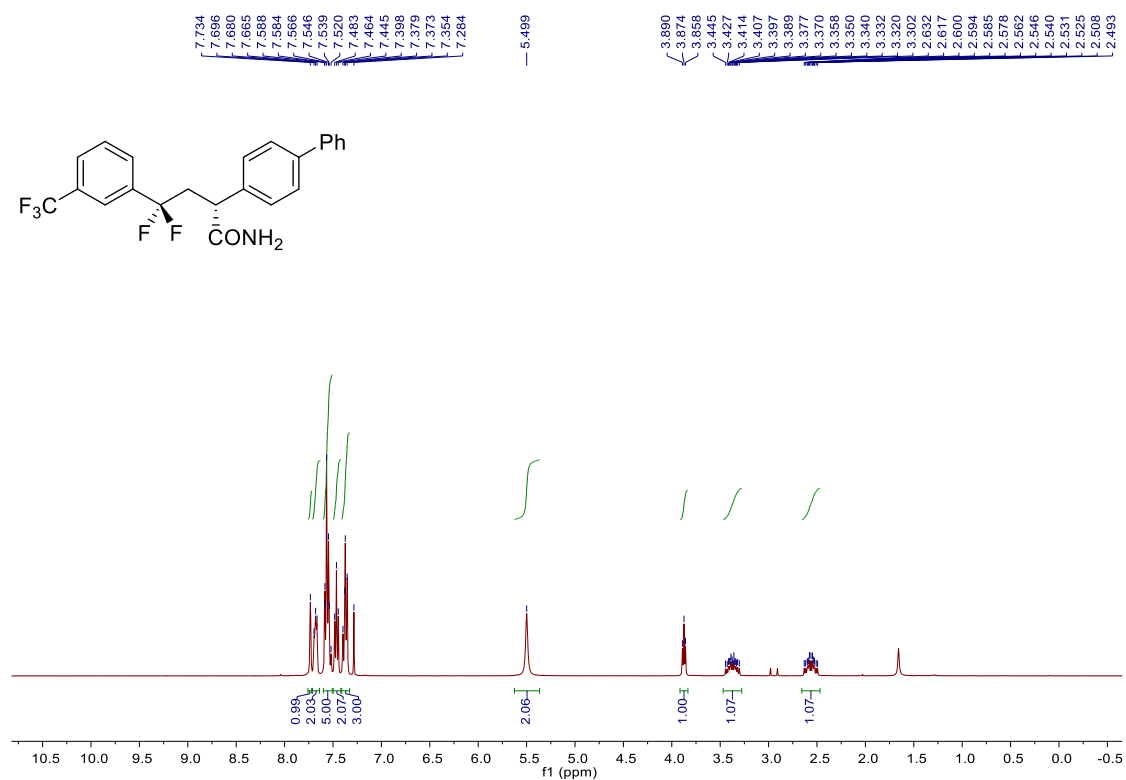


Figure S204. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **9**.

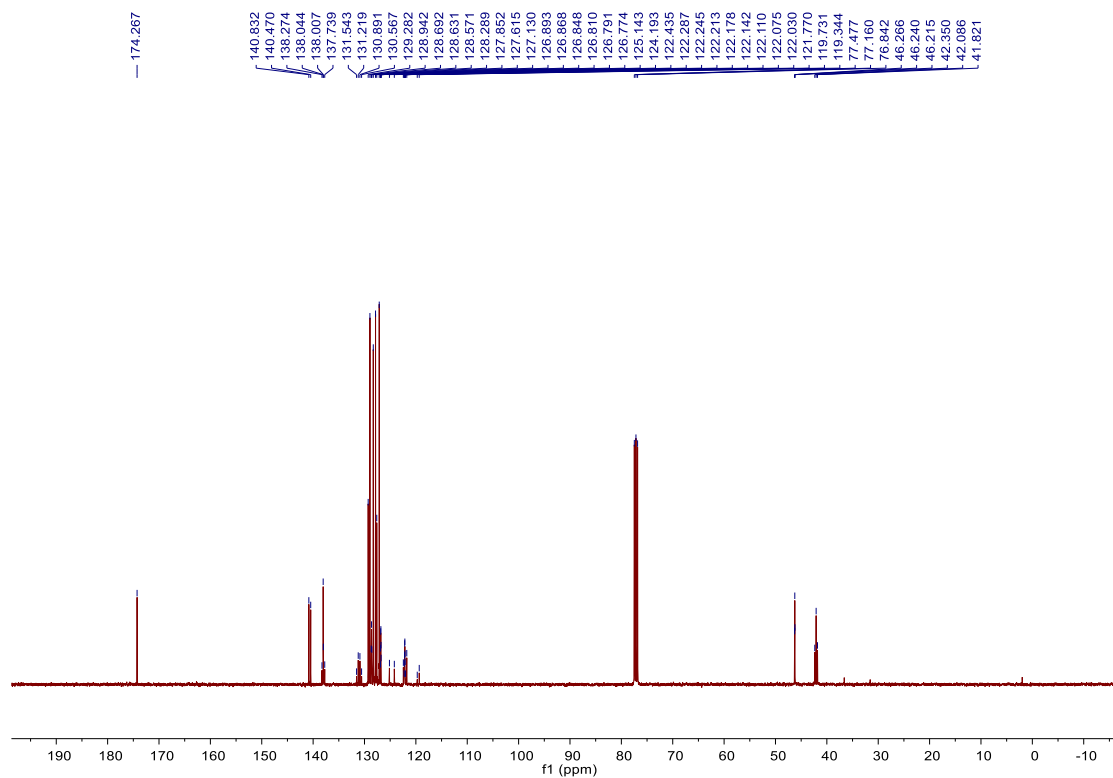


Figure S205. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **9**.

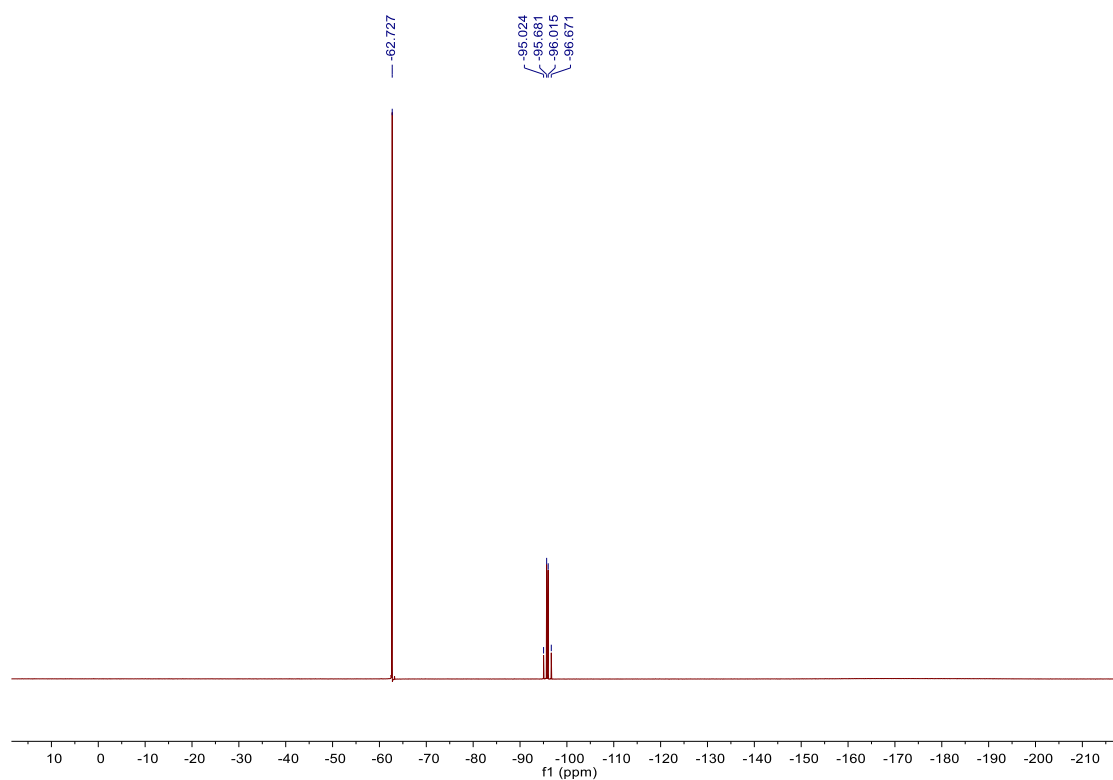


Figure S206. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **10**.

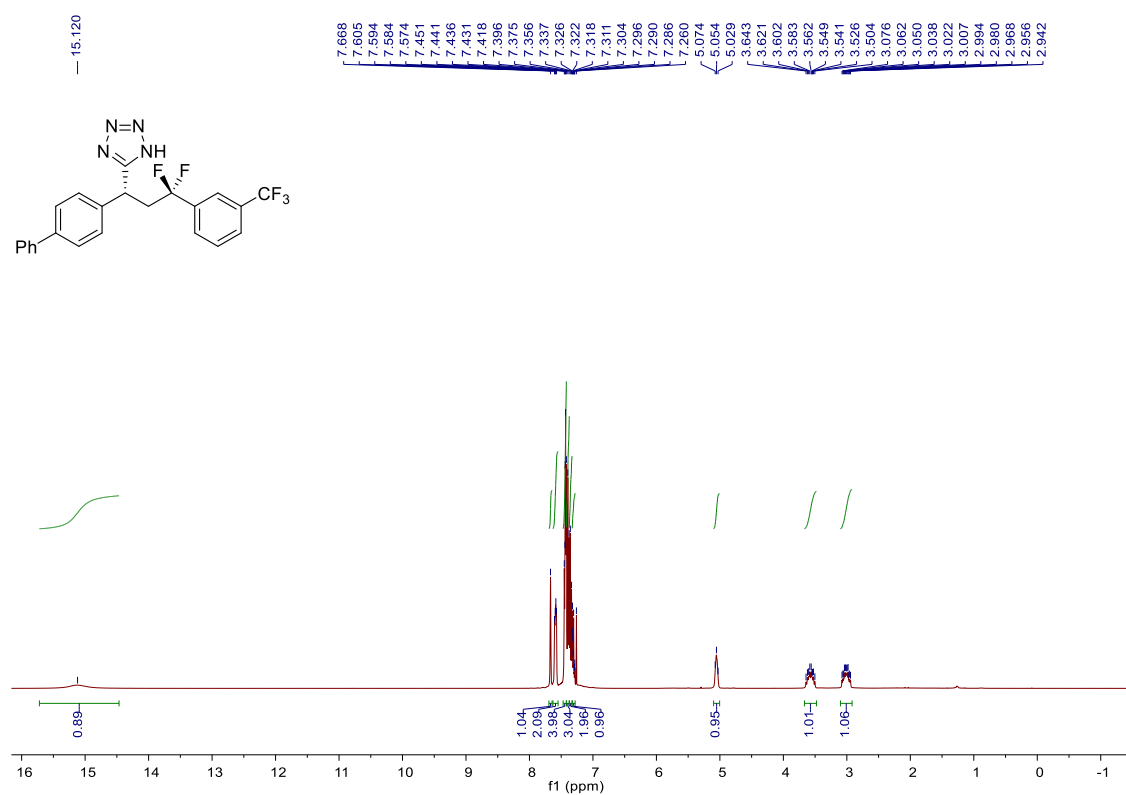


Figure S207. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **10**.

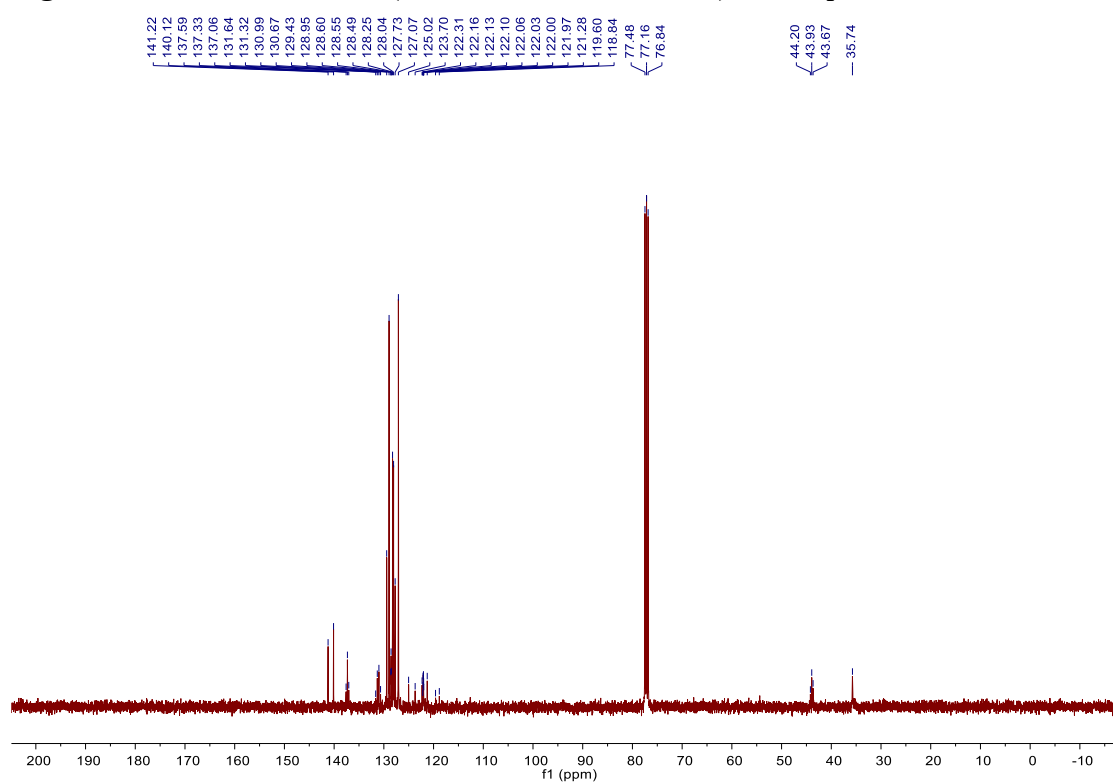


Figure S208. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **10**.

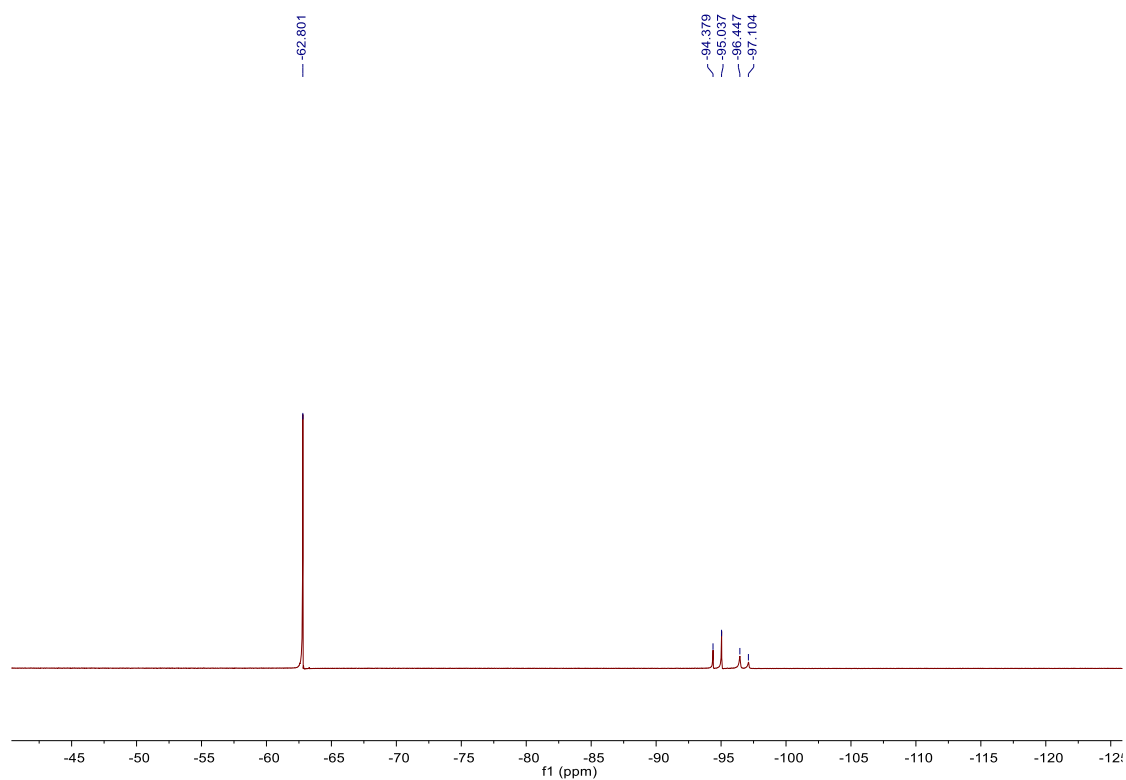


Figure S209. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **11**.

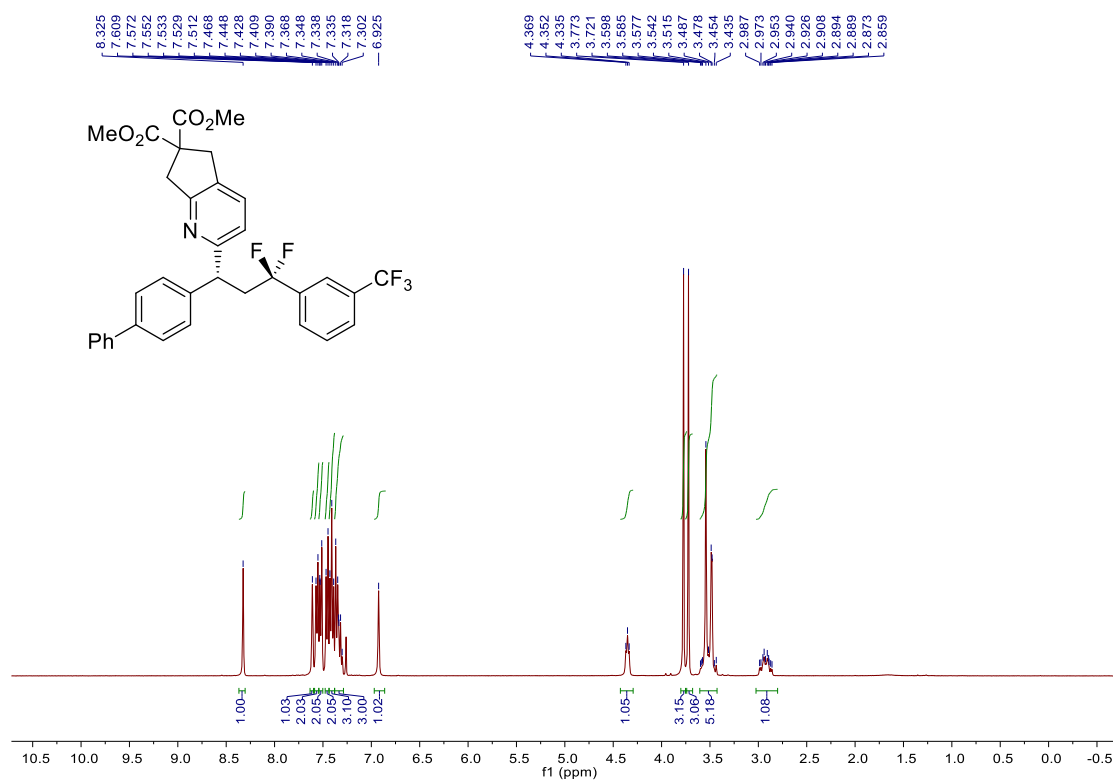


Figure S210. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **11**.

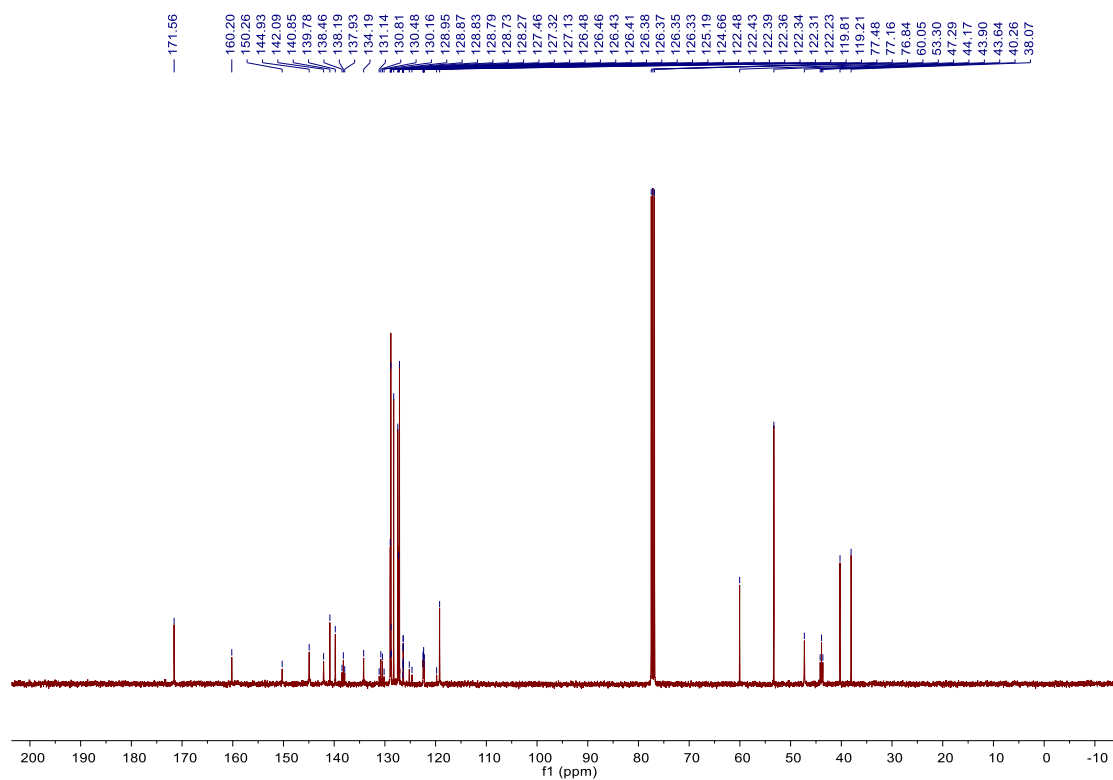


Figure S211. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **11**.

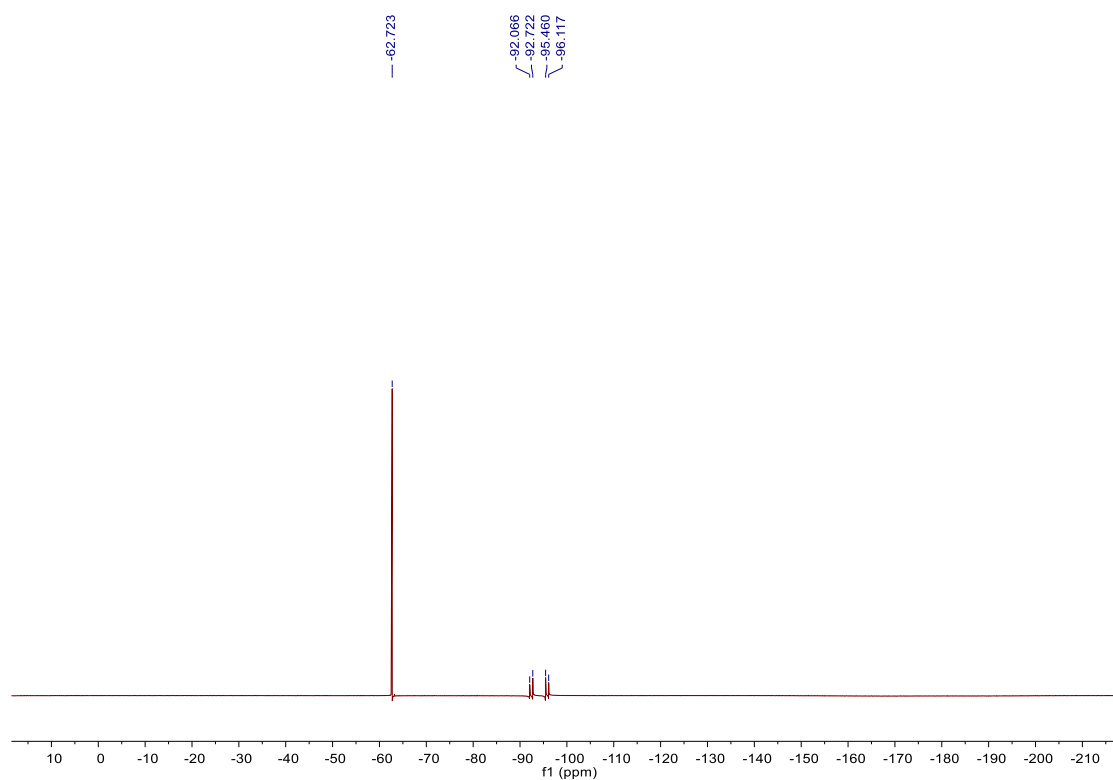


Figure S212. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **12**.

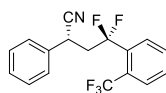
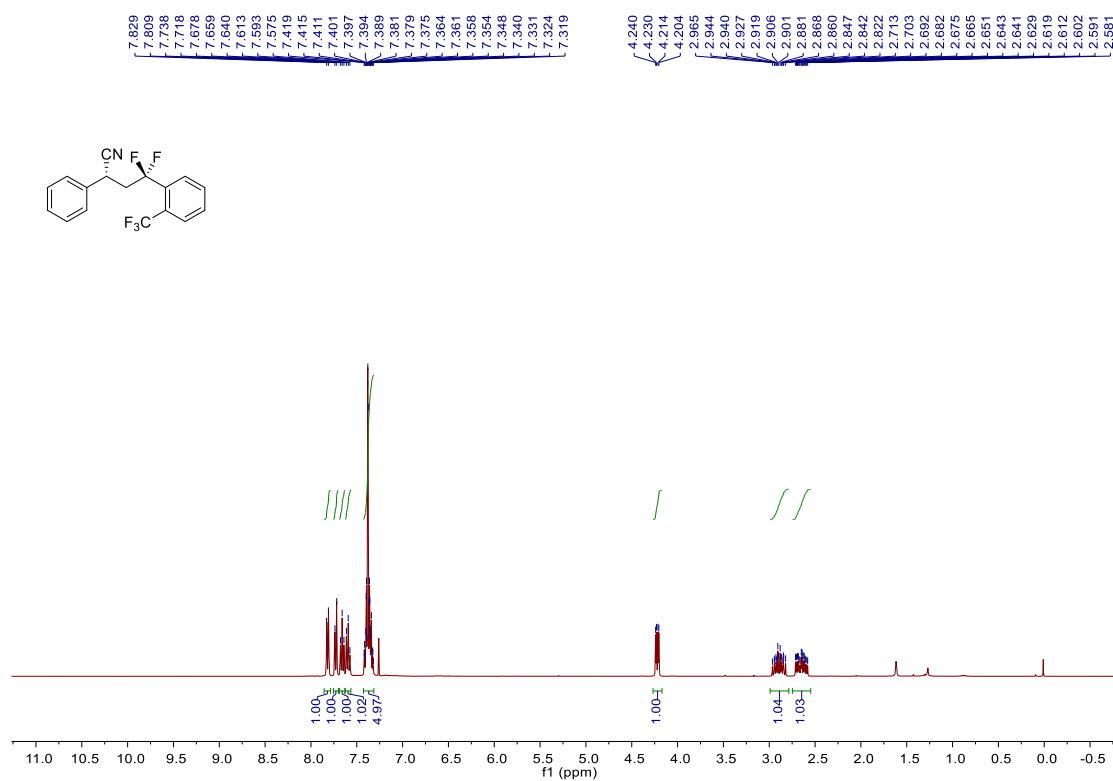


Figure S213. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **12**.

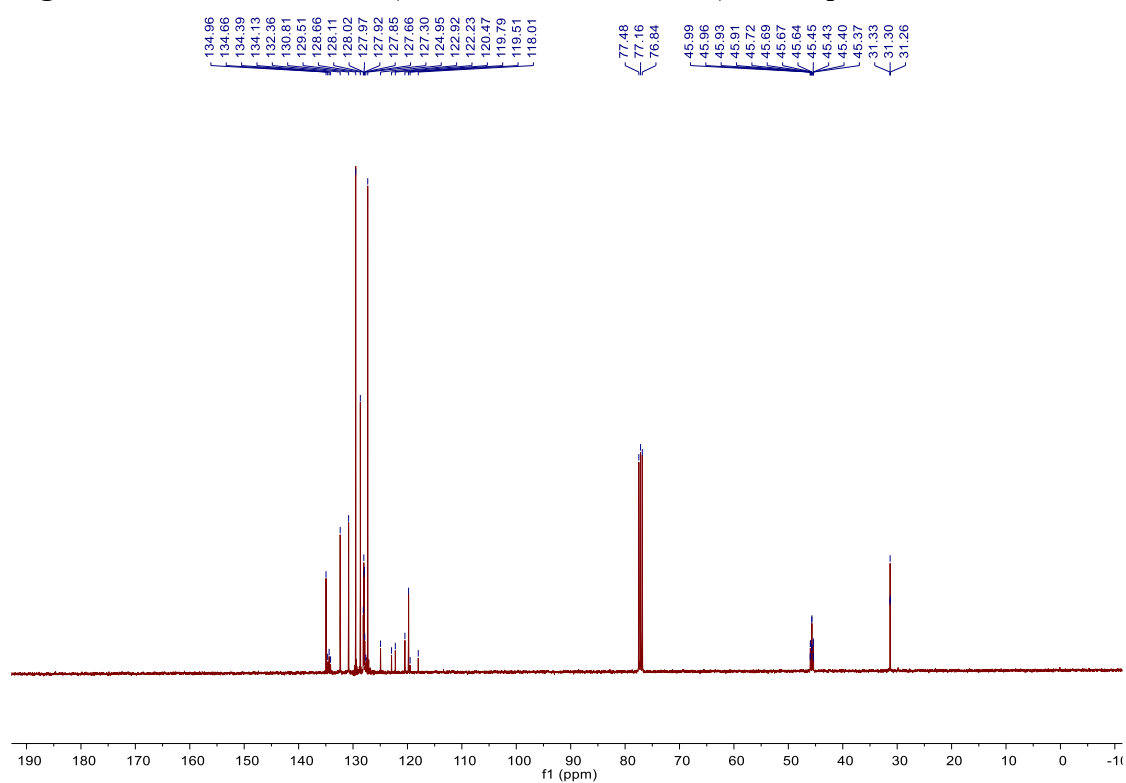


Figure S214. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **12**.

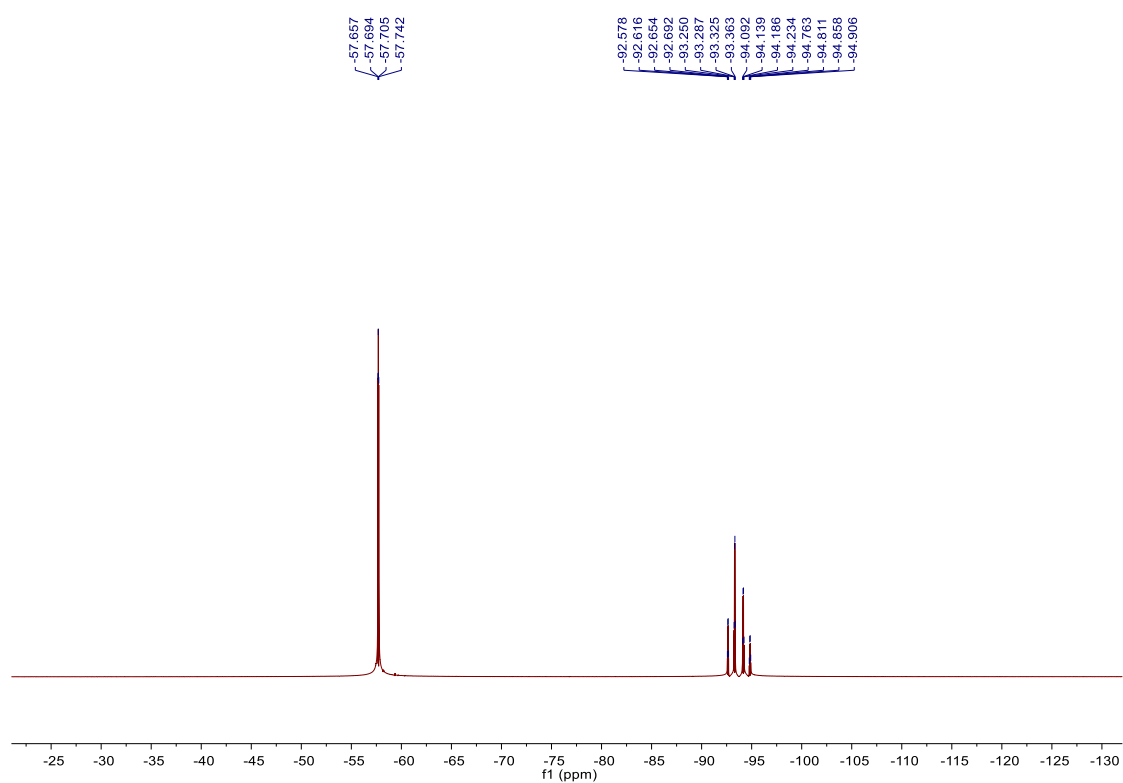


Figure S215. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound 13.

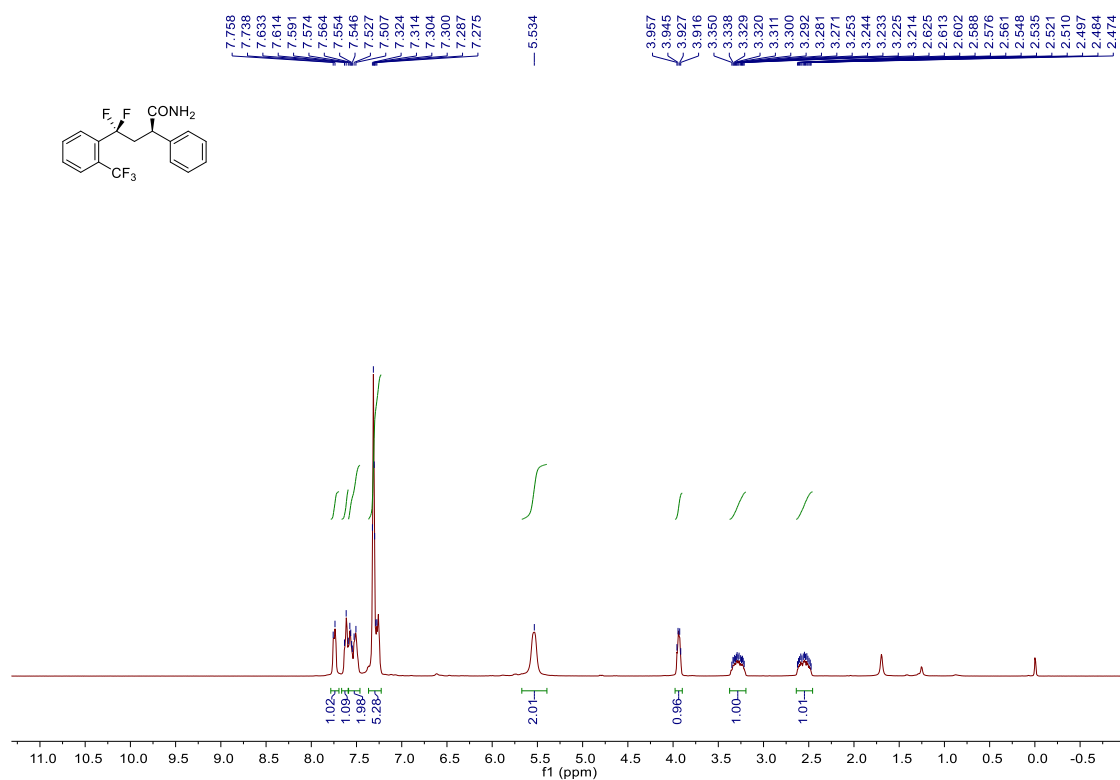


Figure S216. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound 13.

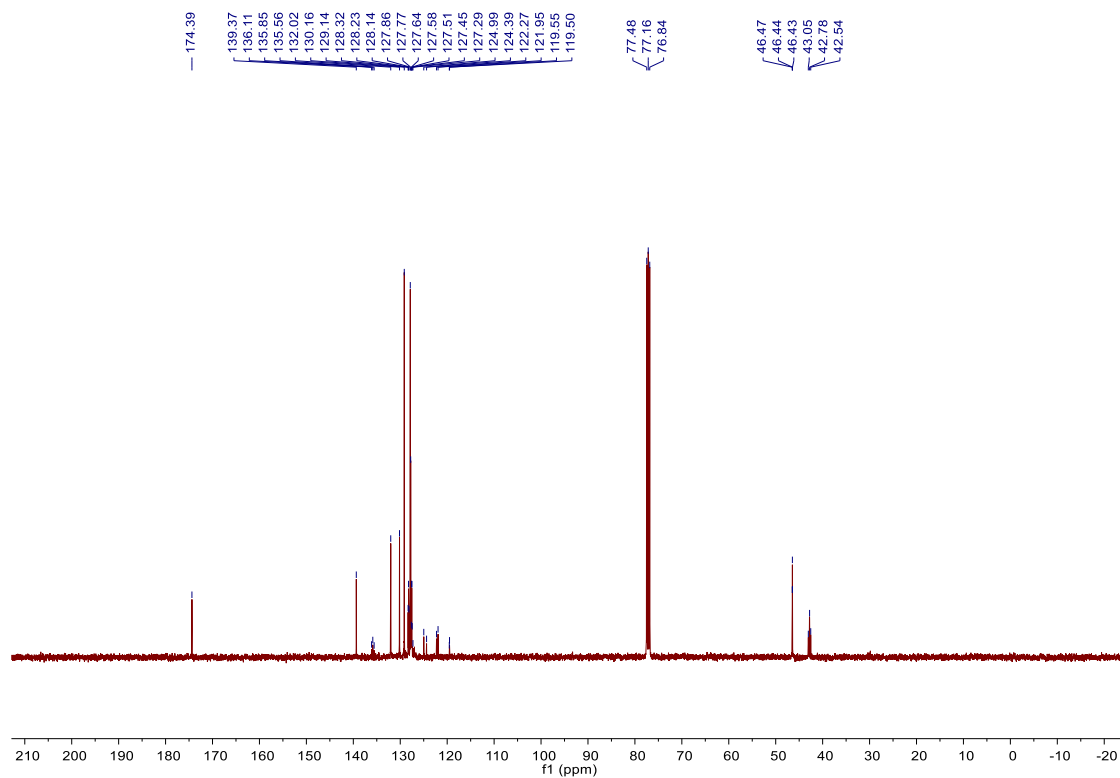


Figure S217. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **13**.

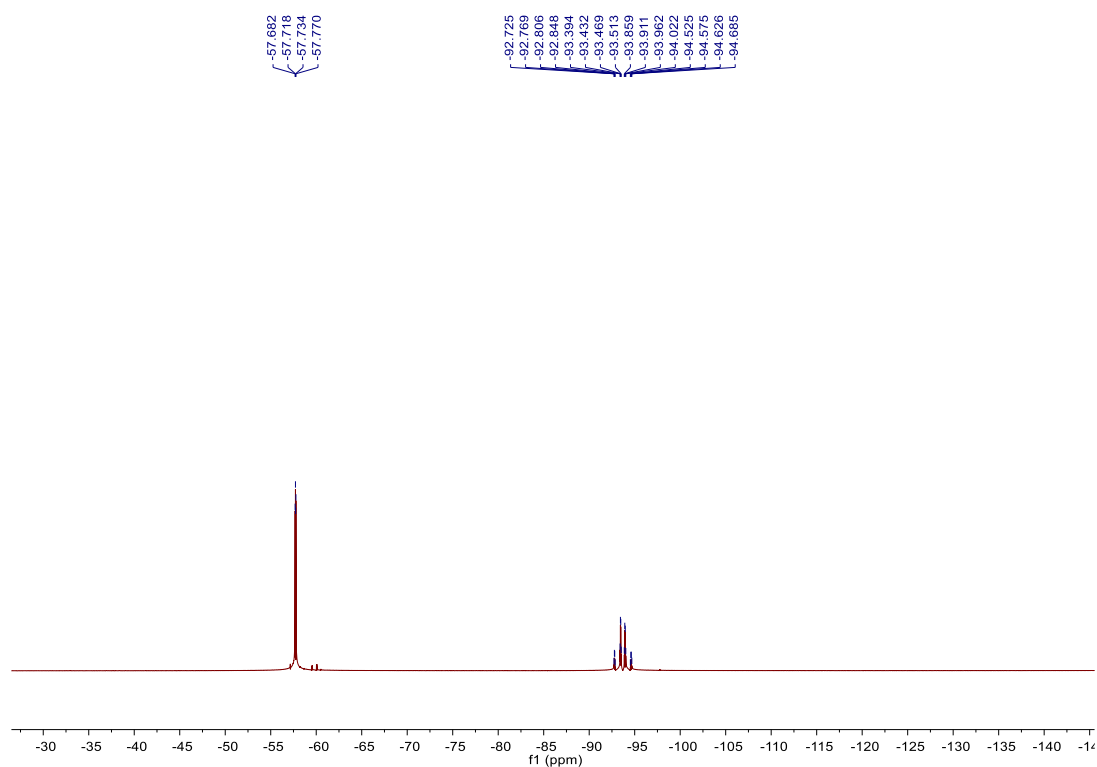


Figure S218. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **14**.

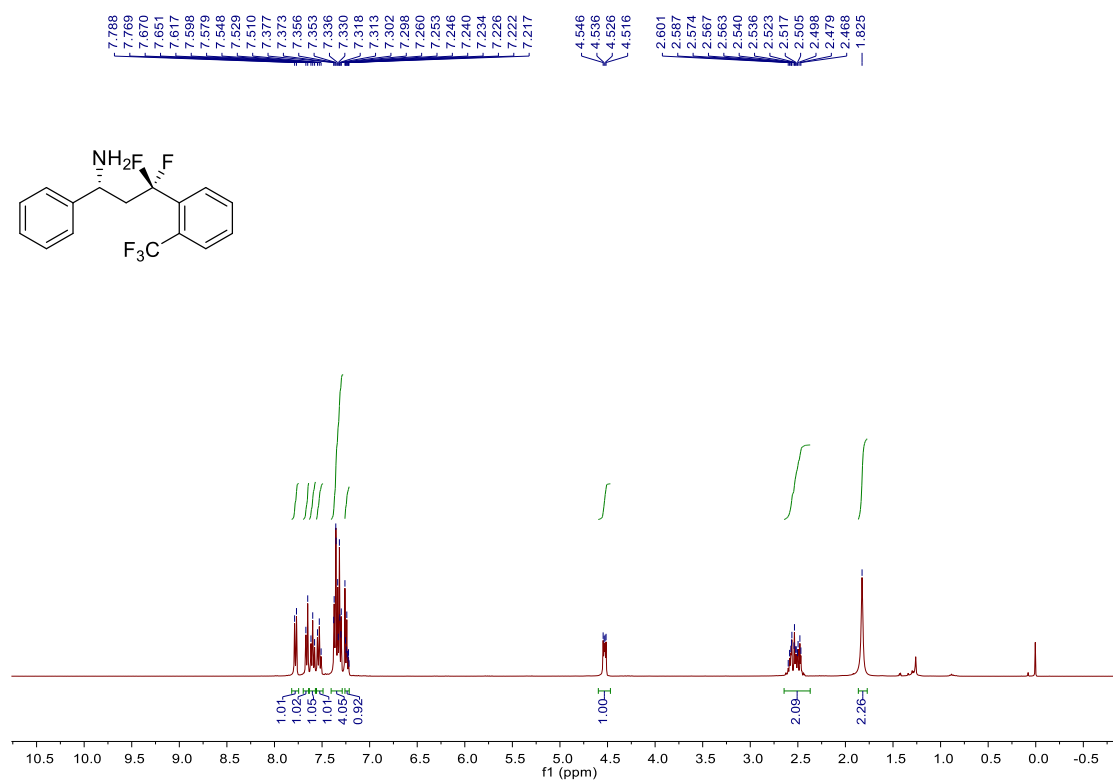


Figure S219. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **14**.

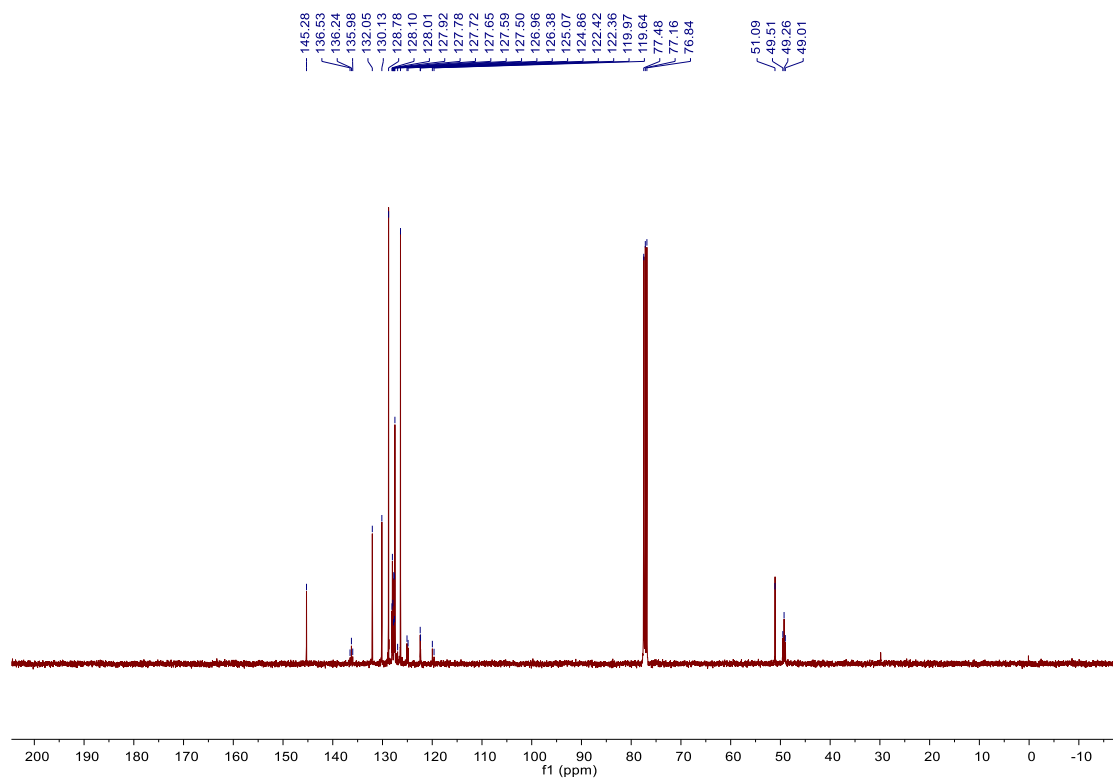


Figure S220. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **14**.

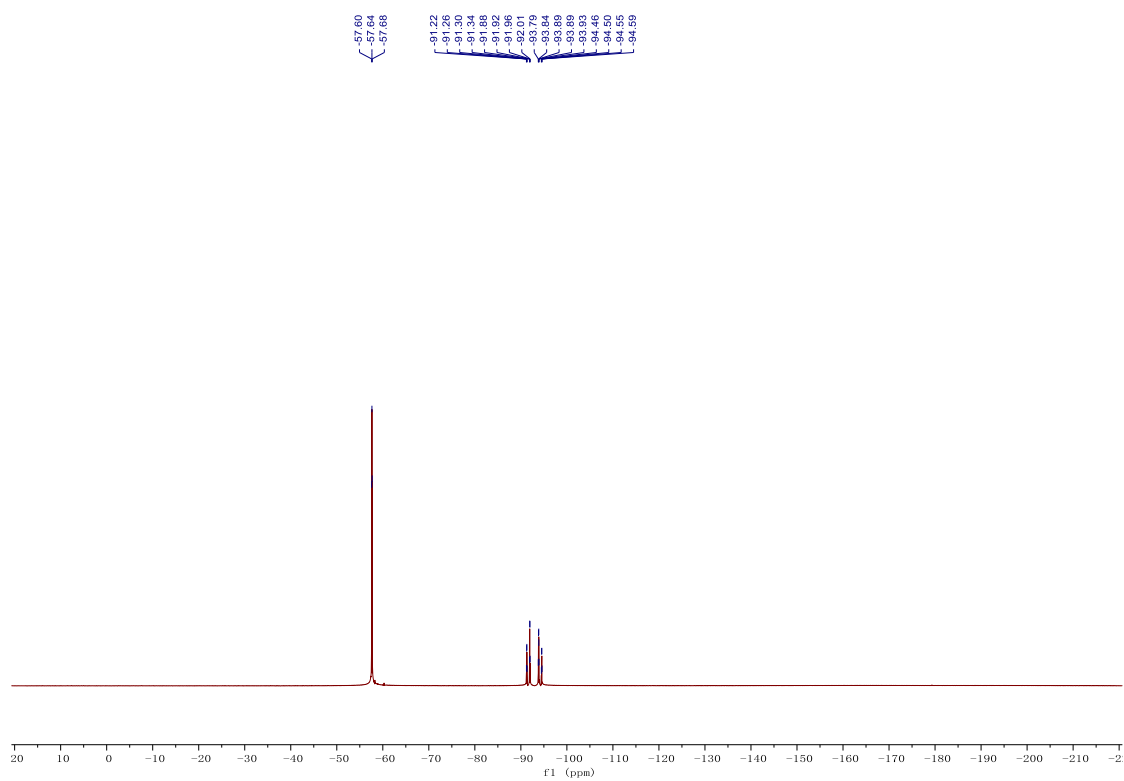


Figure S221. ^1H NMR (400 MHz, CDCl_3 , 298 K) of compound **18**.

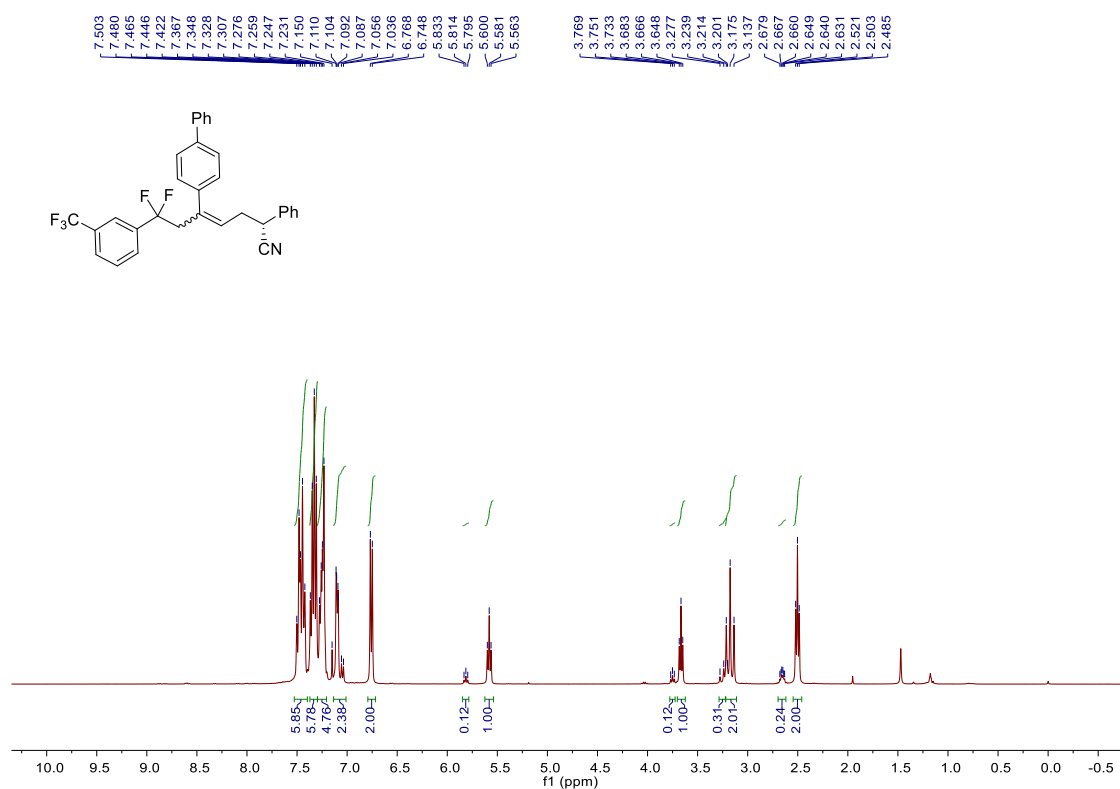


Figure S222. $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 298 K) of compound **18**.

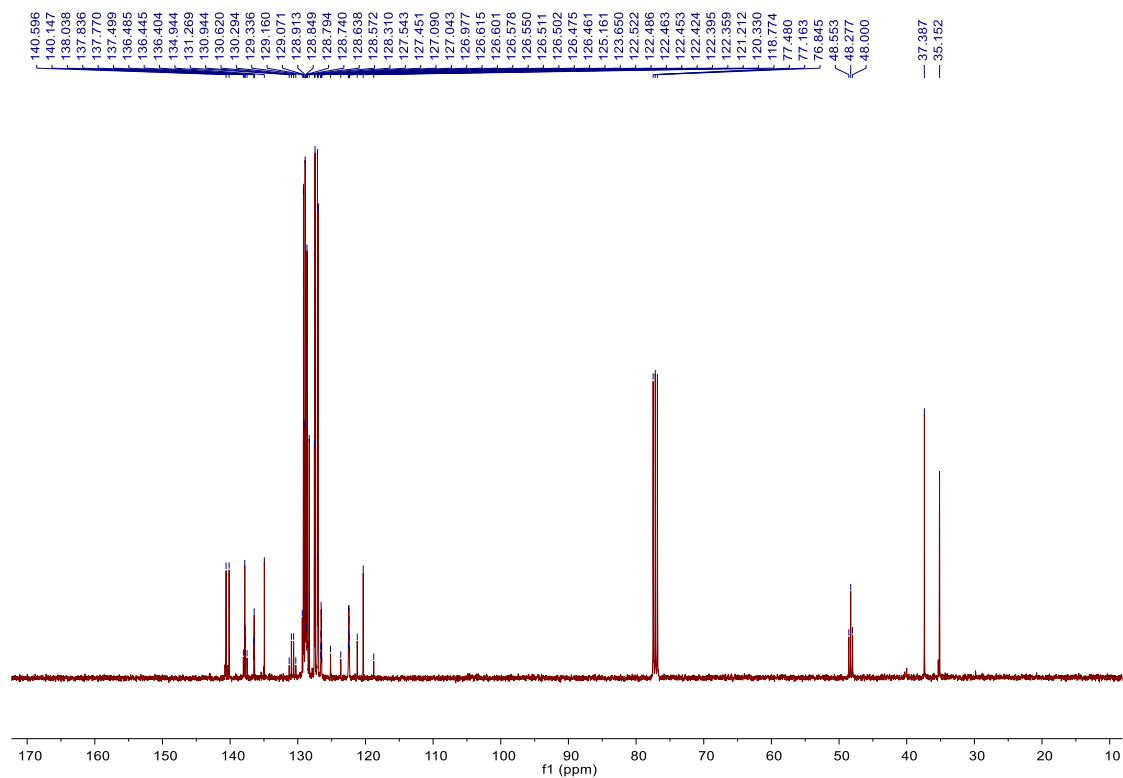


Figure S223. $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3 , 298 K) of compound **18**.

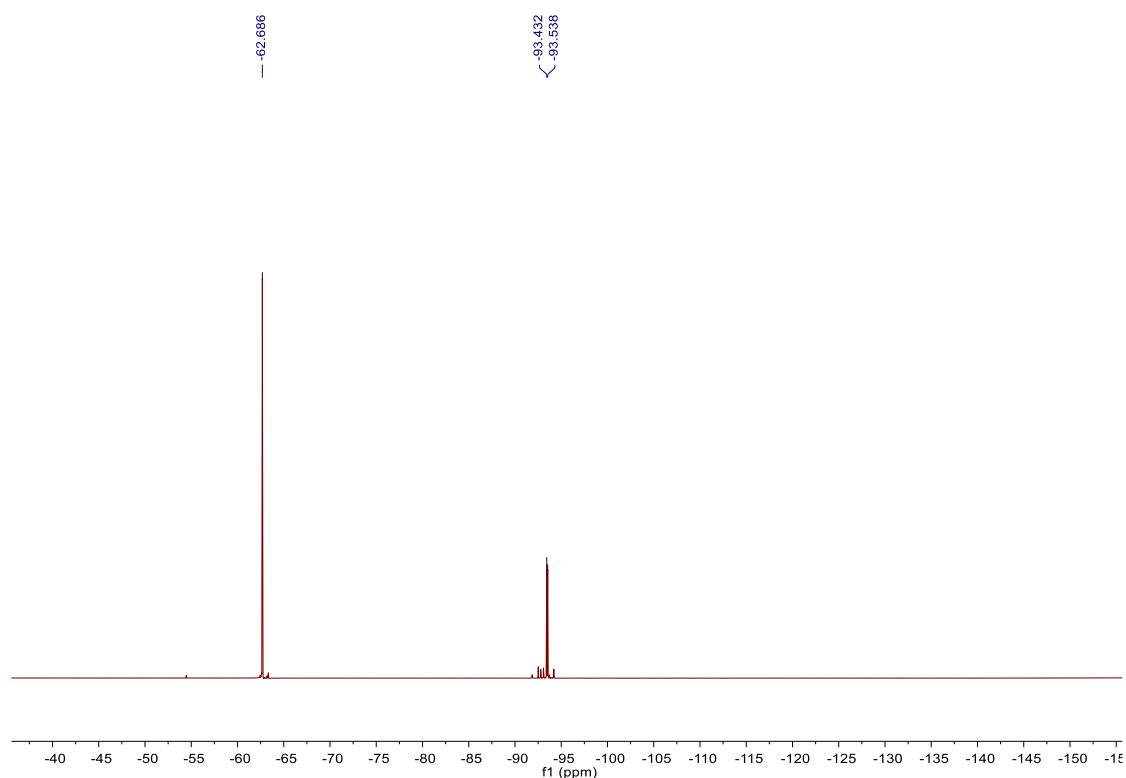
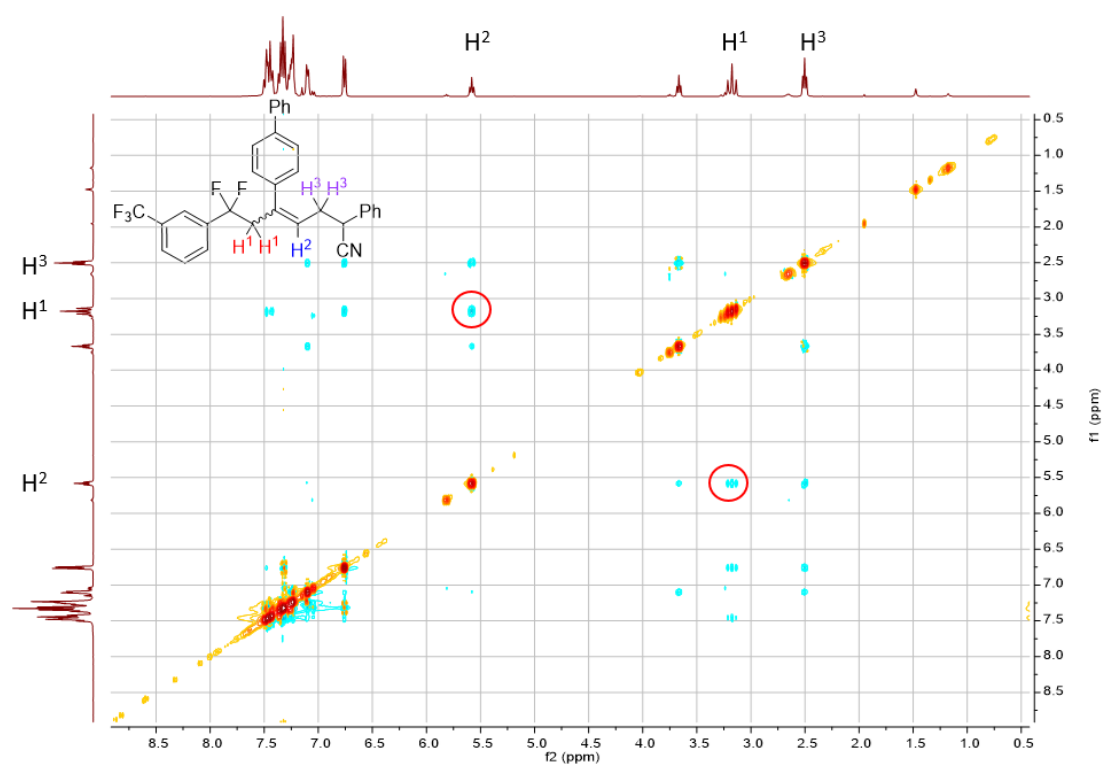
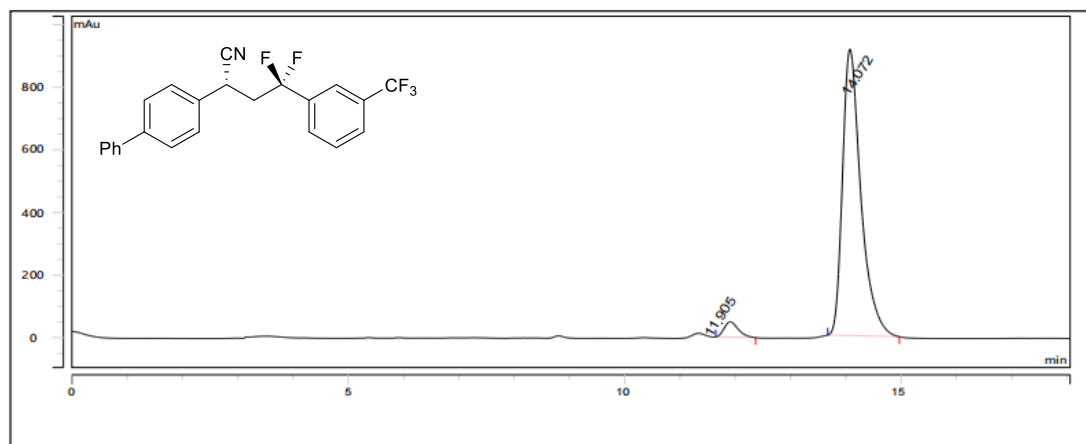


Figure S224. ^1H -NOESY NMR (400 MHz, CDCl_3 , 298 K) of compound **18**.



11.HPLC Analysis of Products

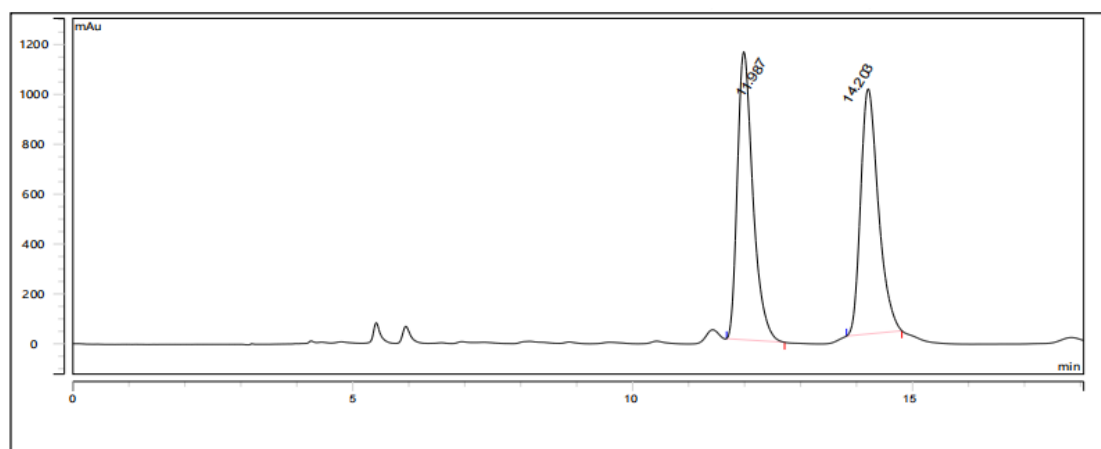
Chiral HPLC spectrum of chiral **4a**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.905	871.17750	0.465	49.282	3.959
2	14.072	21134.69831	0.576	916.911	96.041
3		22005.87581	0.520	966.193	100.000

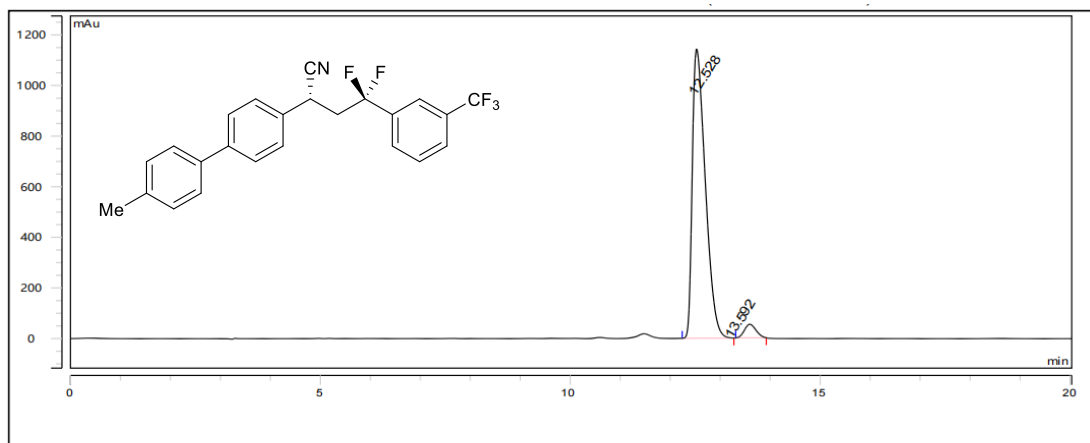
Chiral HPLC spectrum of racemic **4a**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.987	22313.03435	0.492	1157.771	50.746
2	14.203	21657.39658	0.568	984.563	49.254
3		43970.43093	0.530	2142.334	100.000

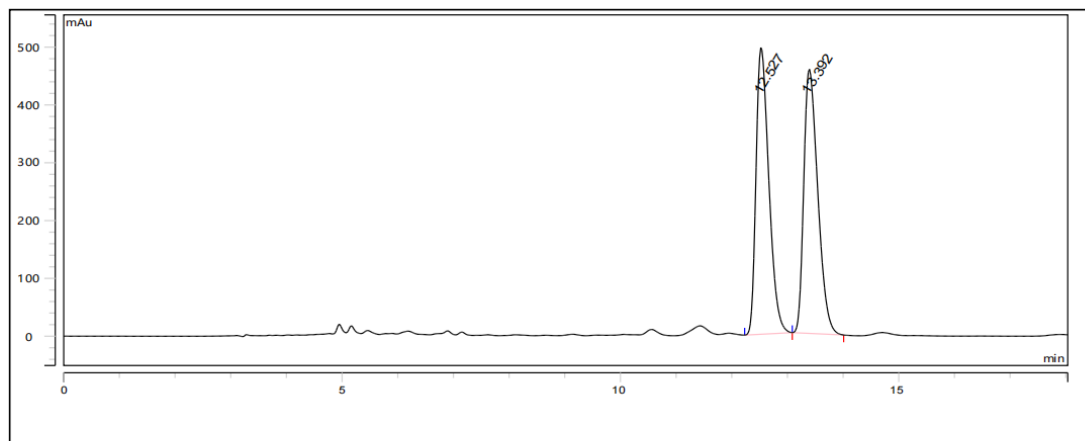
Chiral HPLC spectrum of chiral **4b**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.528	20687.42746	0.479	1145.605	95.968
2	13.592	869.12480	0.434	54.008	4.032
3		21556.55225	0.457	1199.613	100.000

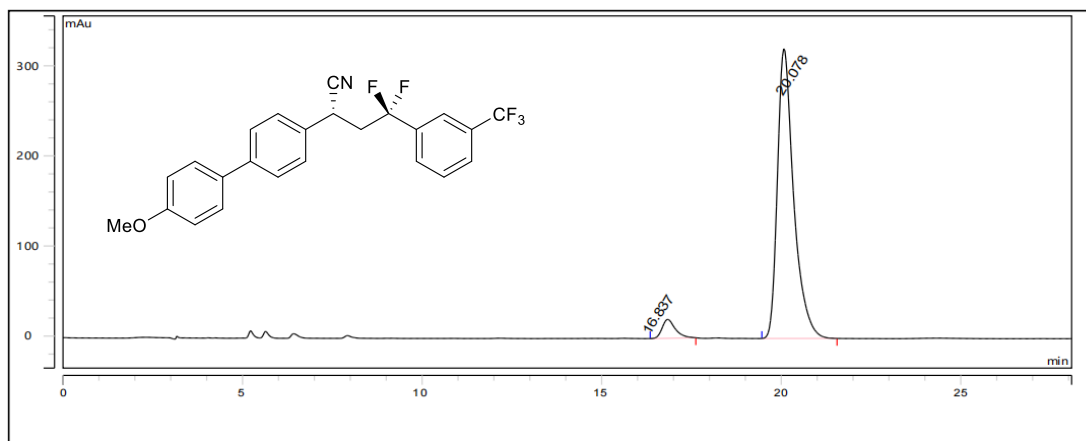
Chiral HPLC spectrum of racemic **4b**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.527	7940.21755	0.421	496.659	49.904
2	13.392	7970.72691	0.461	457.218	50.096
3		15910.94446	0.441	953.878	100.000

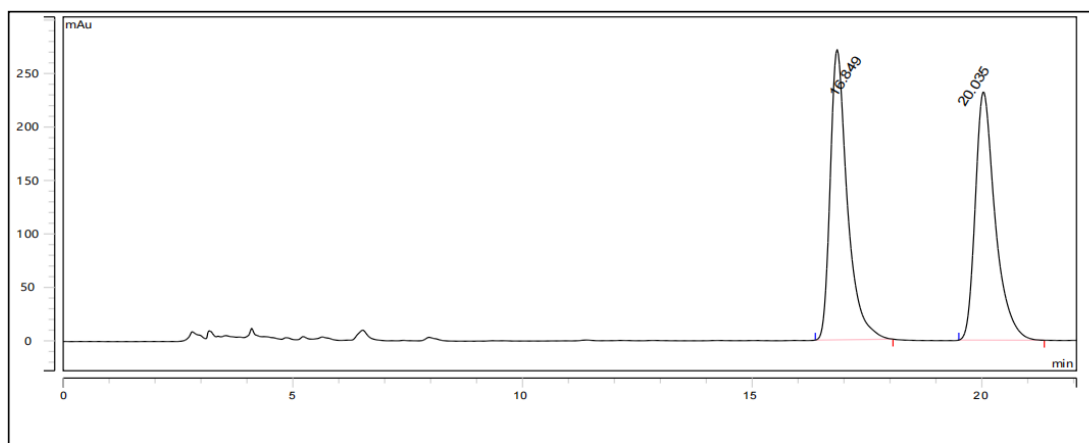
Chiral HPLC spectrum of chiral **4c**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	16.837	529.60105	0.635	21.005	4.967
2	20.078	10131.97847	0.781	322.096	95.033
3		10661.57953	0.708	343.102	100.000

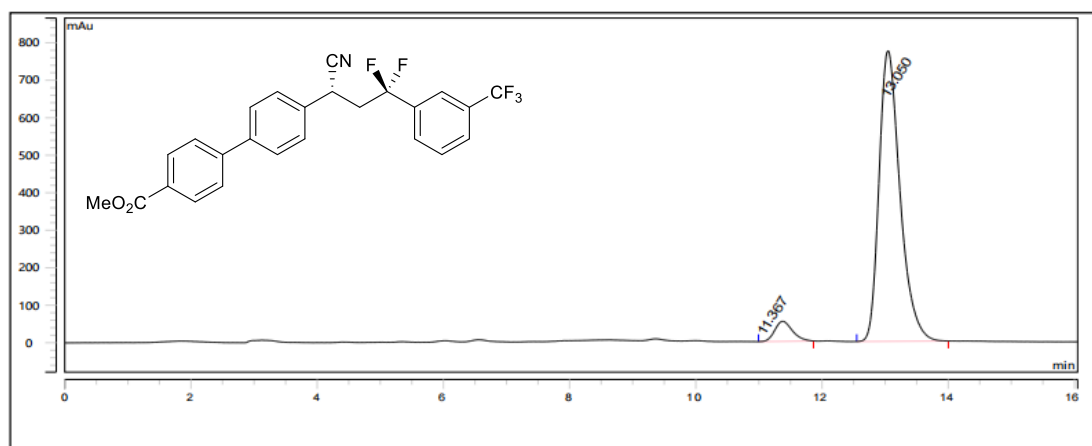
Chiral HPLC spectrum of racemic **4c**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	16.849	7047.99623	0.633	271.668	50.230
2	20.035	6983.39925	0.746	232.510	49.770
3		14031.39548	0.689	504.178	100.000

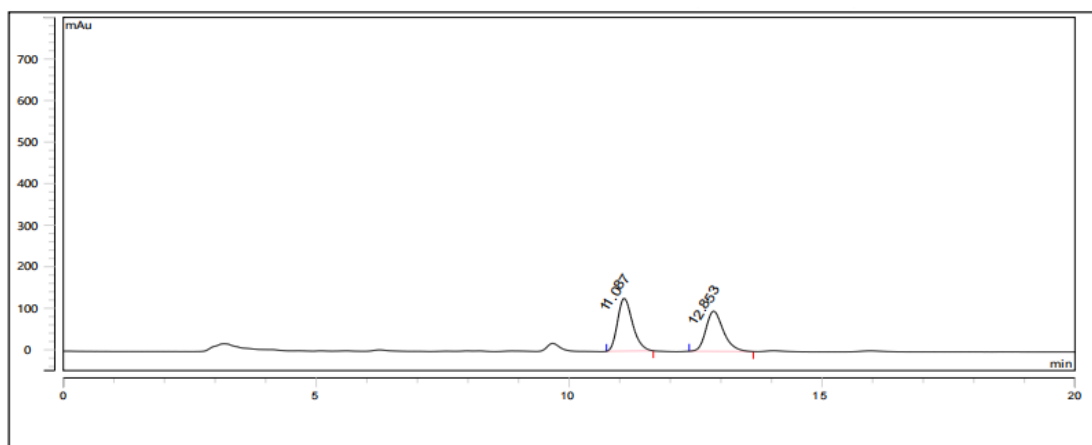
Chiral HPLC spectrum of chiral **4d**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.367	1038.26816	0.505	53.727	5.476
2	13.050	17921.23937	0.592	775.483	94.524
3		18959.50753	0.548	829.210	100.000

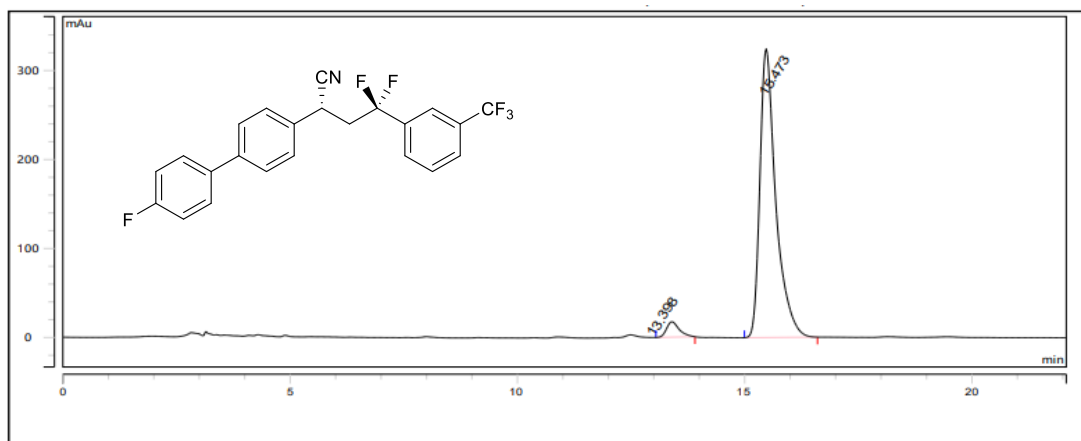
Chiral HPLC spectrum of racemic **4d**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.087	2620.70230	0.538	127.164	53.088
2	12.853	2315.85246	0.612	96.886	46.912
3		4936.55476	0.575	224.051	100.000

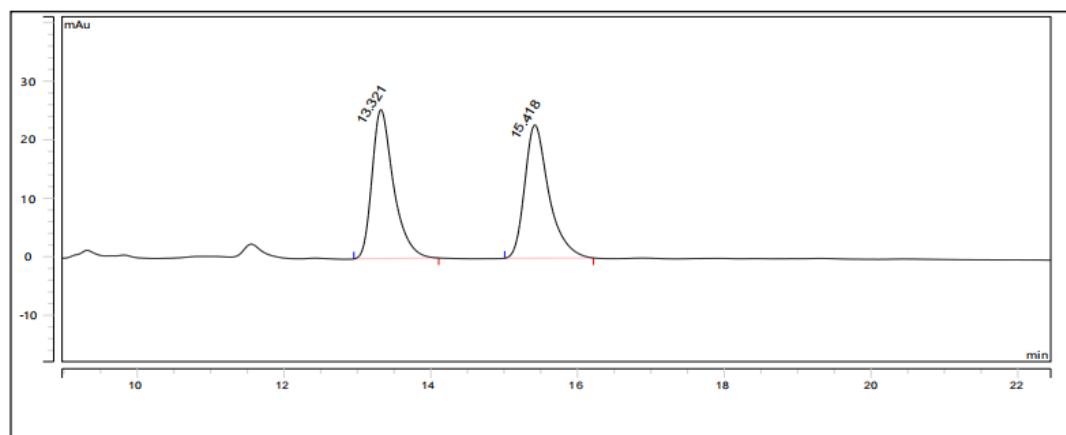
Chiral HPLC spectrum of chiral **4e**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.398	333.06810	0.483	17.416	4.051
2	15.473	7889.72813	0.587	324.580	95.949
3		8222.79623	0.535	341.996	100.000

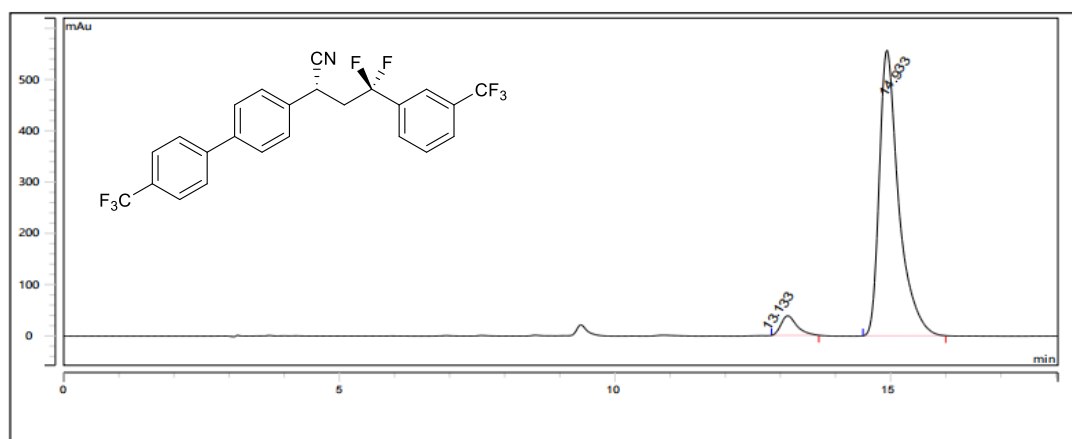
Chiral HPLC spectrum of racemic **4e**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.321	520.07225	0.511	25.460	49.942
2	15.418	521.27663	0.569	22.780	50.058
3		1041.34888	0.540	48.240	100.000

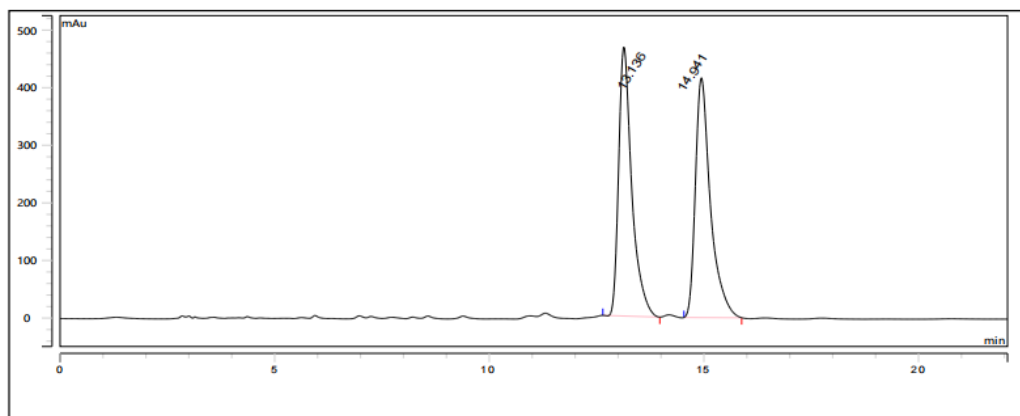
Chiral HPLC spectrum of chiral **4f**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.133	757.11875	0.502	38.145	5.248
2	14.933	13670.86635	0.593	557.547	94.752
3		14427.98511	0.548	595.692	100.000

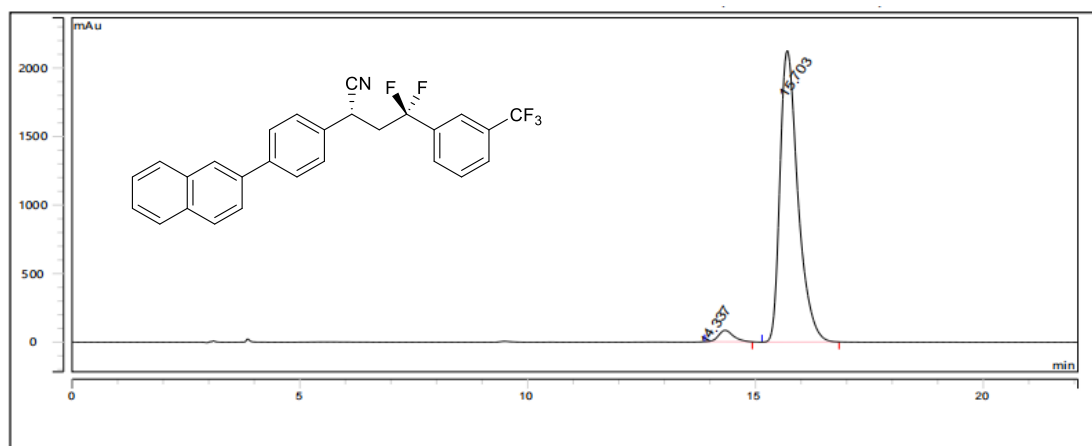
Chiral HPLC spectrum of racemic **4f**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.136	9929.36985	0.517	468.855	49.455
2	14.941	10148.32821	0.590	417.333	50.545
3		20077.69806	0.553	886.188	100.000

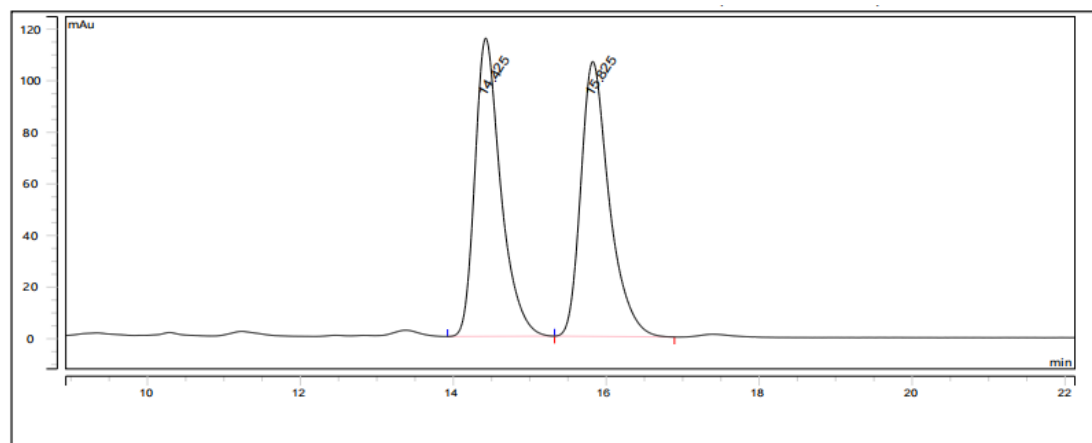
Chiral HPLC spectrum of chiral **4g**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	14.337	1903.49510	0.574	84.218	3.160
2	15.703	58339.12967	0.696	2129.036	96.840
3		60242.62477	0.635	2213.254	100.000

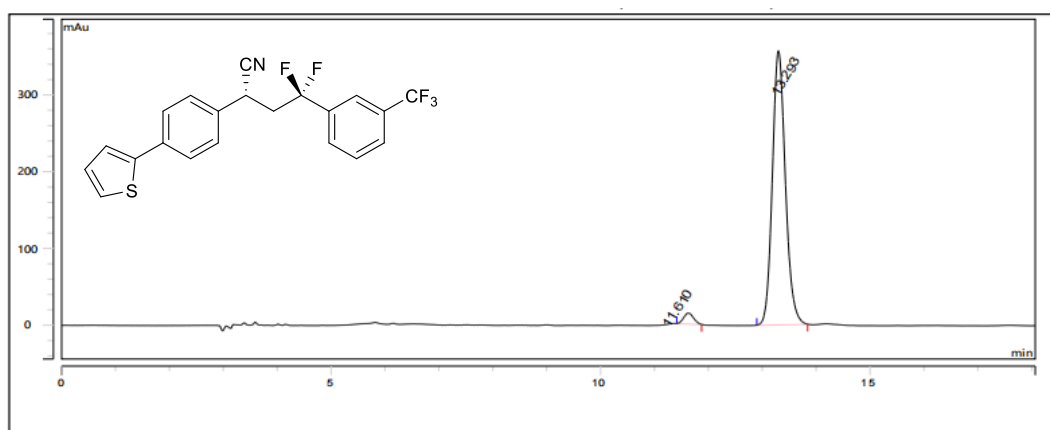
Chiral HPLC spectrum of racemic **4g**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	14.425	2719.29040	0.591	115.716	49.682
2	15.825	2754.09105	0.649	106.638	50.318
3		5473.38145	0.620	222.354	100.000

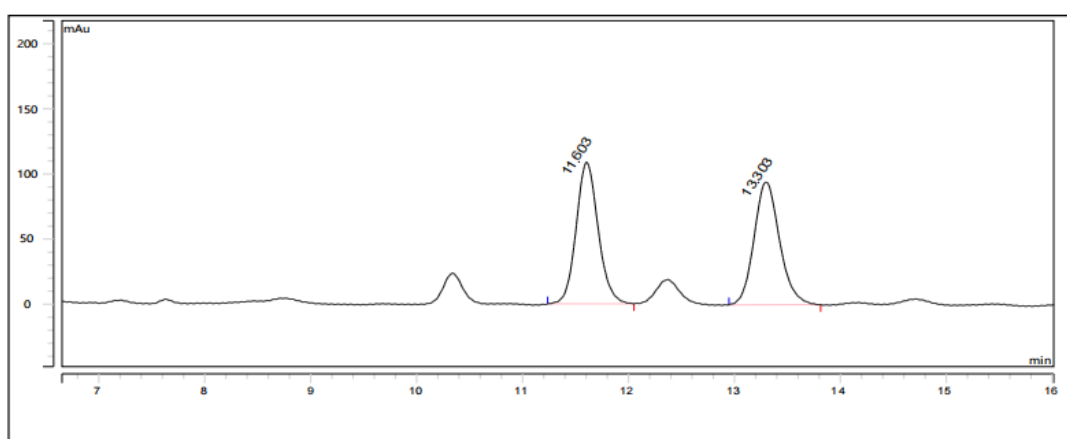
Chiral HPLC spectrum of chiral **4h**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.610	186.07910	0.349	14.430	3.006
2	13.293	6004.73734	0.432	357.745	96.994
3		6190.81644	0.390	372.175	100.000

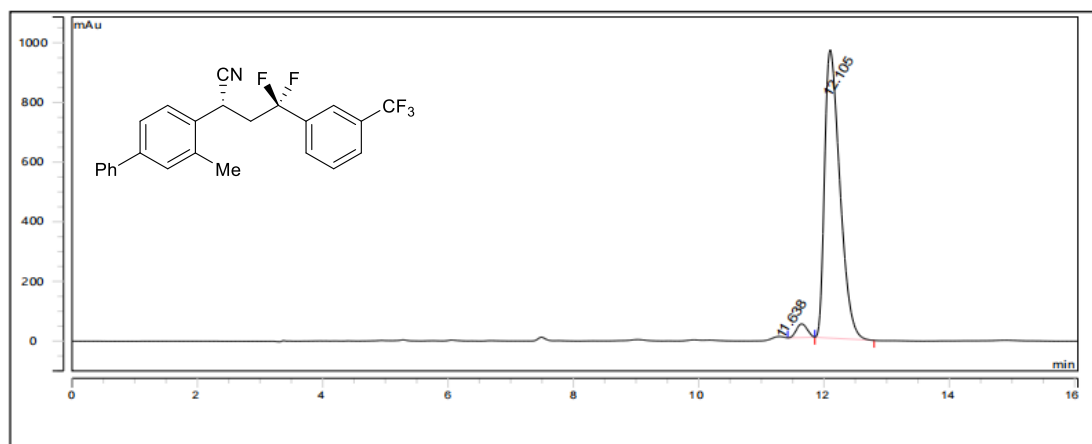
Chiral HPLC spectrum of racemic **4h**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.603	1572.67330	0.372	109.254	49.888
2	13.303	1579.76116	0.432	94.213	50.112
3		3152.43446	0.402	203.467	100.000

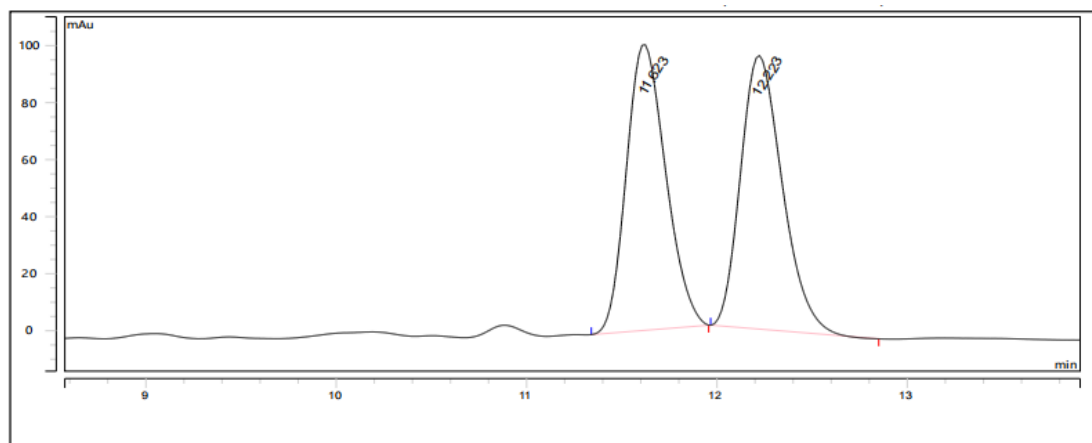
Chiral HPLC spectrum of chiral **4i**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.638	549.02410	0.331	46.165	3.241
2	12.105	16391.47947	0.448	967.539	96.759
3		16940.50357	0.389	1013.704	100.000

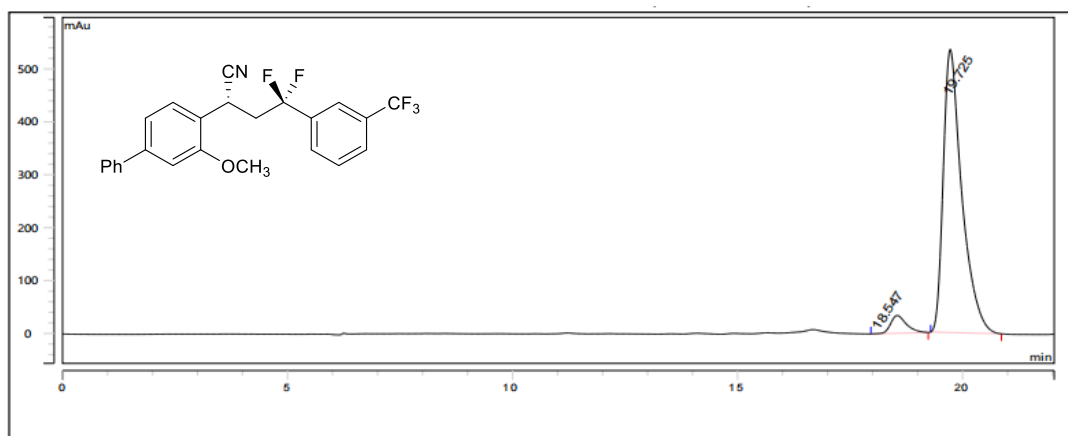
Chiral HPLC spectrum of racemic **4i**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.623	1439.99485	0.383	100.217	49.638
2	12.223	1460.97820	0.402	95.969	50.362
3		2900.97305	0.392	196.186	100.000

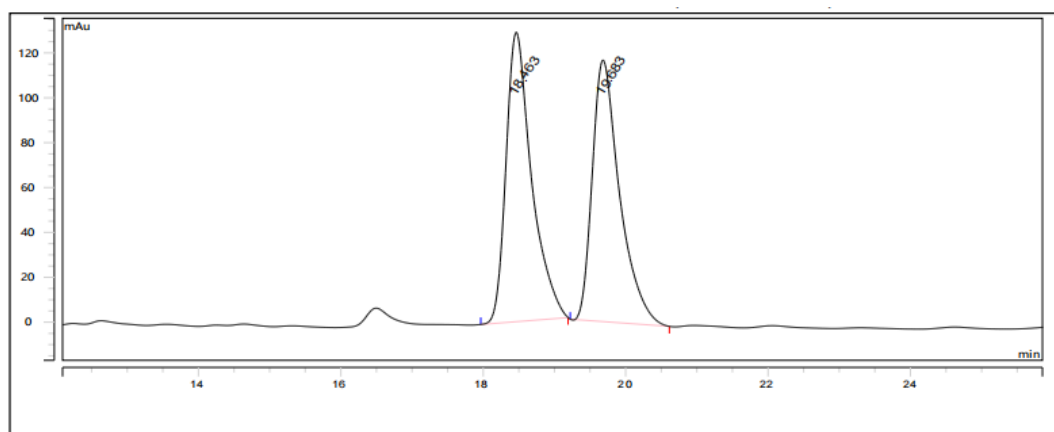
Chiral HPLC spectrum of chiral **4j**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	18.547	813.41508	0.610	33.791	5.029
2	19.725	15362.65081	0.713	535.631	94.971
3		16176.06589	0.662	569.422	100.000

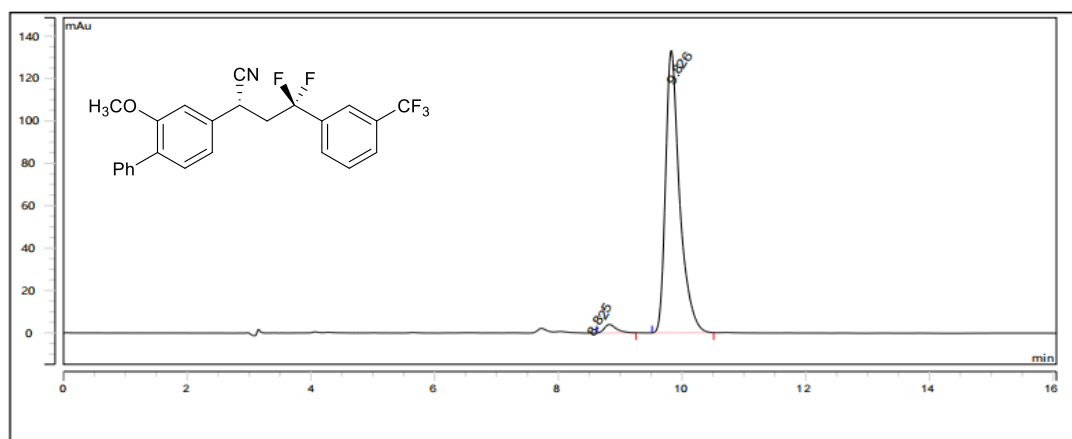
Chiral HPLC spectrum of racemic **4j**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	18.463	3217.45530	0.619	129.016	50.869
2	19.683	3107.53430	0.668	116.599	49.131
3		6324.98960	0.644	245.615	100.000

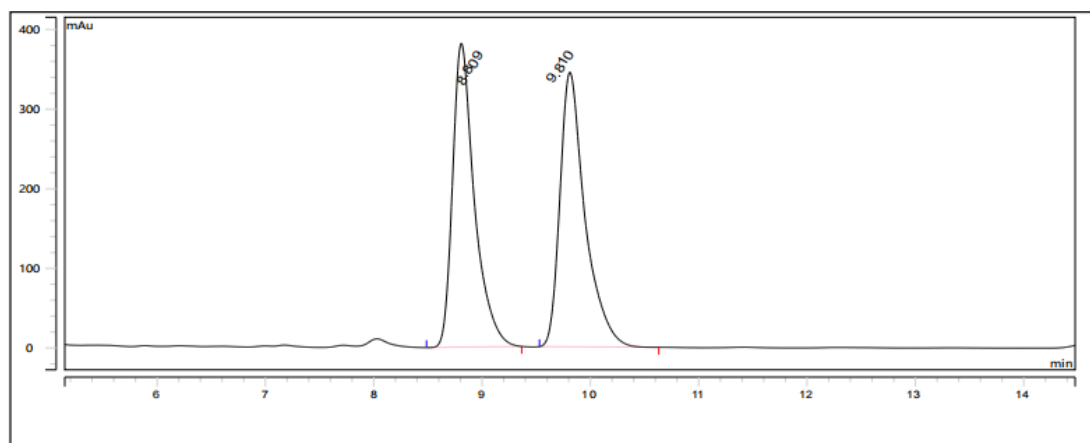
Chiral HPLC spectrum of chiral **4k**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.825	53.55125	0.336	4.027	2.480
2	9.826	2105.97480	0.386	133.638	97.520
3		2159.52605	0.361	137.665	100.000

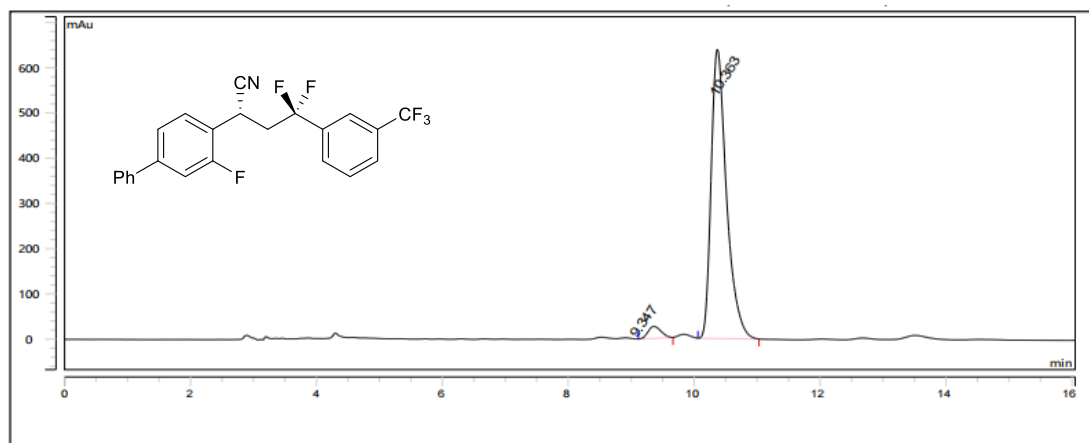
Chiral HPLC spectrum of racemic **4k**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.809	5341.25865	0.344	381.947	49.083
2	9.810	5540.88378	0.391	345.247	50.917
3		10882.14243	0.367	727.195	100.000

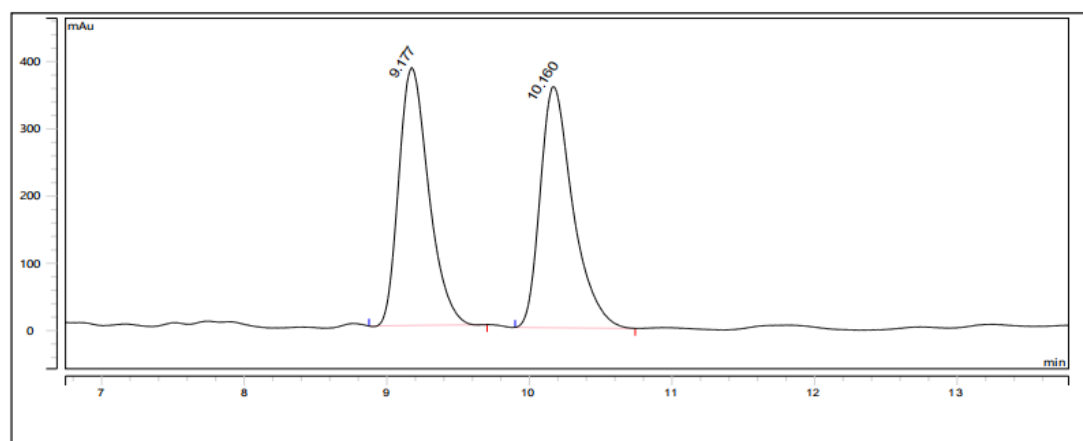
Chiral HPLC spectrum of chiral **4I**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.347	378.94570	0.383	26.635	3.377
2	10.363	10842.14352	0.428	639.811	96.623
3		11221.08922	0.406	666.446	100.000

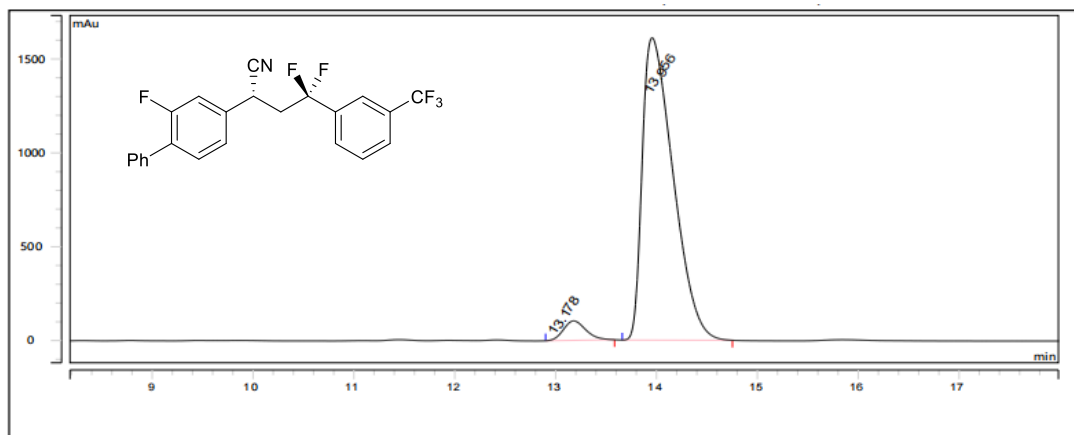
Chiral HPLC spectrum of racemic **4I**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.177	5593.51809	0.380	384.440	49.433
2	10.160	5721.93826	0.404	358.703	50.567
3		11315.45635	0.392	743.142	100.000

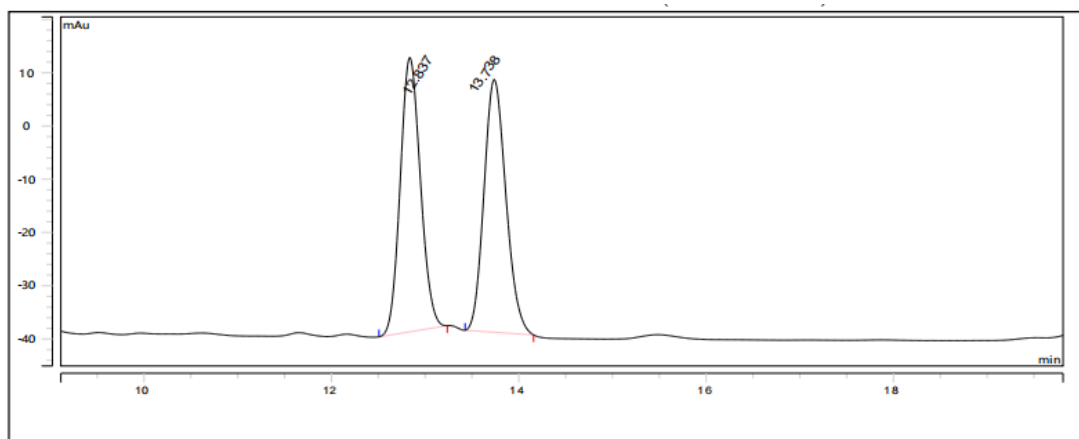
Chiral HPLC spectrum of chiral **4m**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.178	1593.69155	0.404	103.644	4.442
2	13.956	34287.06908	0.569	1611.070	95.558
3		35880.76063	0.487	1714.714	100.000

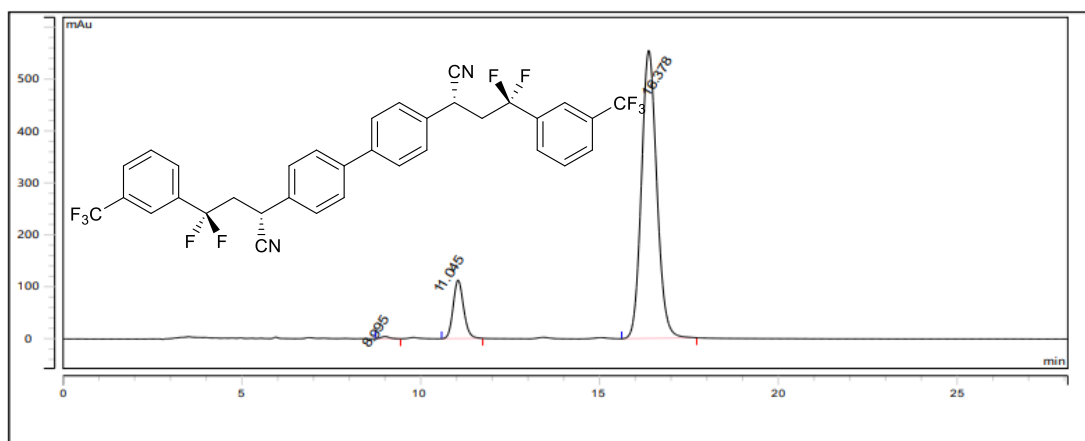
Chiral HPLC spectrum of racemic **4m**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.837	769.81870	0.396	51.544	49.927
2	13.738	772.05636	0.429	47.497	50.073
3		1541.87506	0.413	99.040	100.000

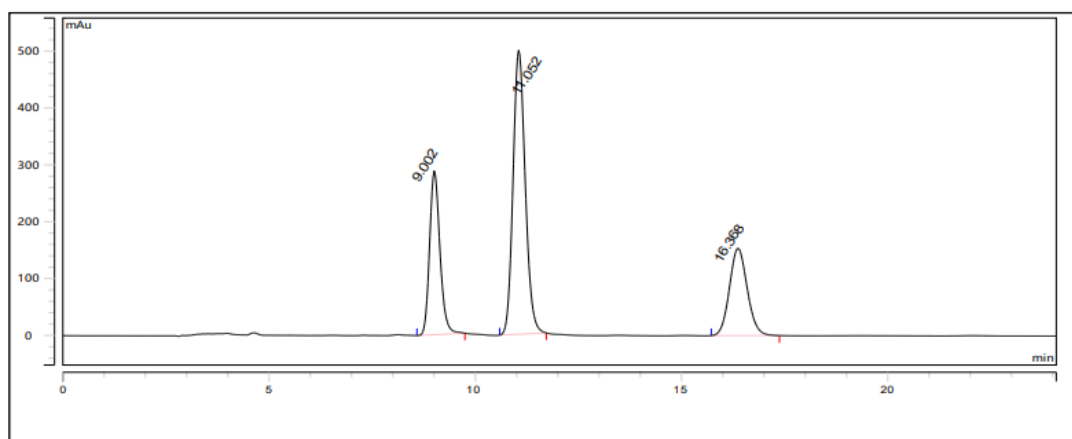
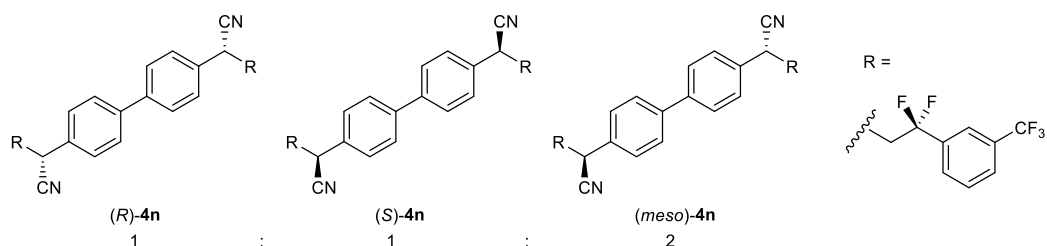
Chiral HPLC spectrum of chiral **4n**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.995	71.59790	0.428	4.400	0.377
2	11.045	2289.93085	0.525	113.437	12.061
3	16.378	16625.39276	0.777	556.359	87.562
4		18986.92152	0.577	674.197	100.000

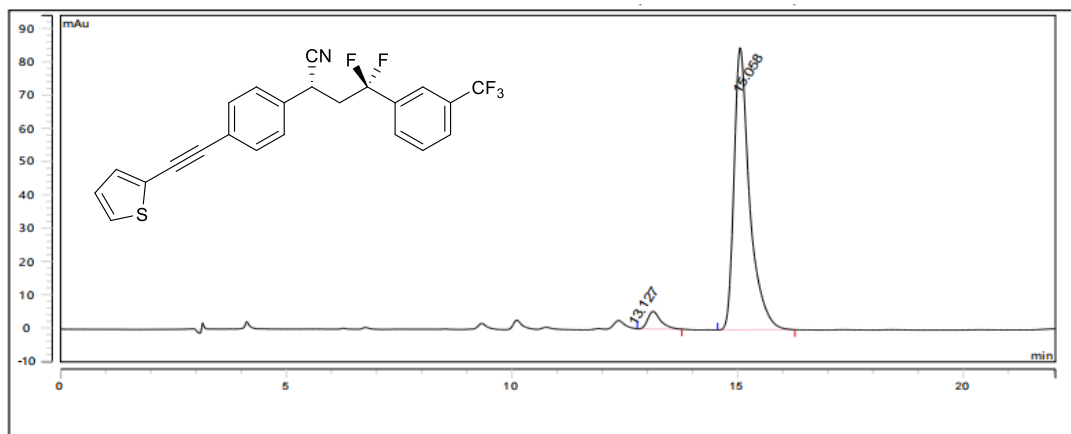
Chiral HPLC spectrum of racemic **4n**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.002	5007.99305	0.446	288.747	25.259
2	11.052	10226.08350	0.534	499.973	51.577
3	16.368	4592.75090	0.783	153.698	23.164
4		19826.82745	0.587	942.419	100.000

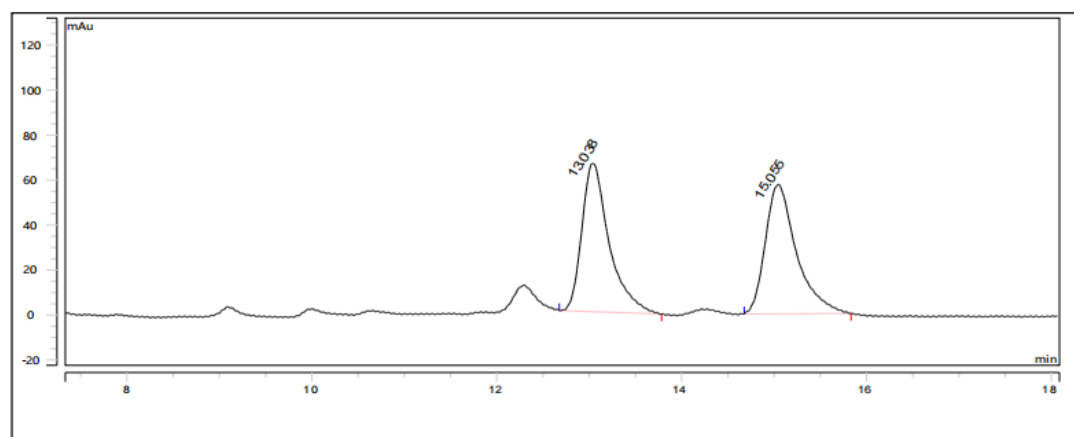
Chiral HPLC spectrum of chiral **4o**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.127	103.34525	0.484	5.294	4.837
2	15.058	2033.07554	0.572	84.967	95.163
3		2136.42079	0.528	90.261	100.000

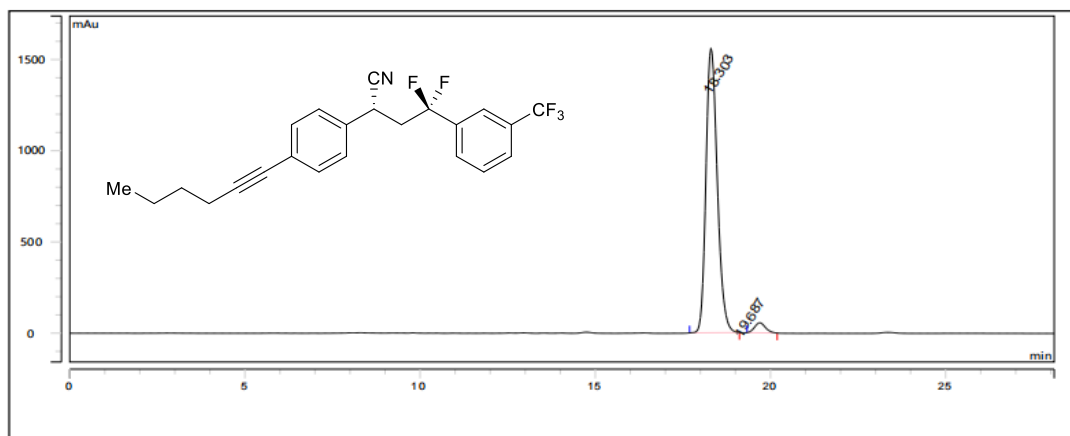
Chiral HPLC spectrum of racemic **4o**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.038	1353.57920	0.499	65.933	50.097
2	15.055	1348.35370	0.575	57.652	49.903
3		2701.93290	0.537	123.585	100.000

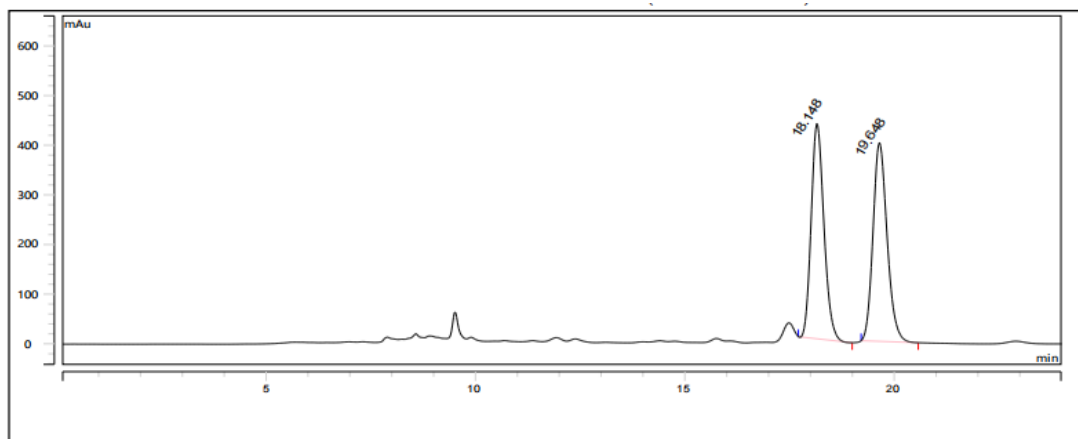
Chiral HPLC spectrum of chiral **4p**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	18.303	35102.76196	0.586	1561.806	96.756
2	19.687	1176.81610	0.568	55.106	3.244
3		36279.57806	0.577	1616.912	100.000

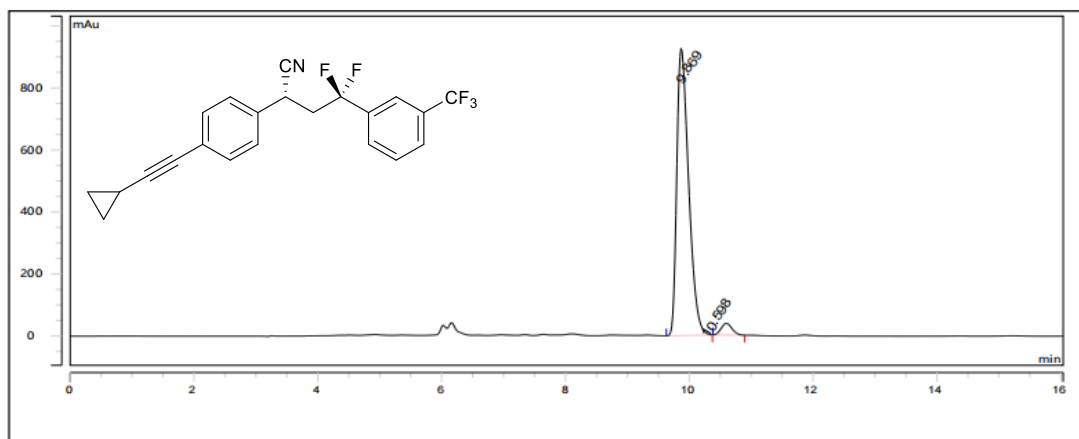
Chiral HPLC spectrum of racemic **4p**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	18.148	9156.55268	0.553	433.422	49.418
2	19.648	9372.21026	0.606	400.940	50.582
3		18528.76294	0.579	834.362	100.000

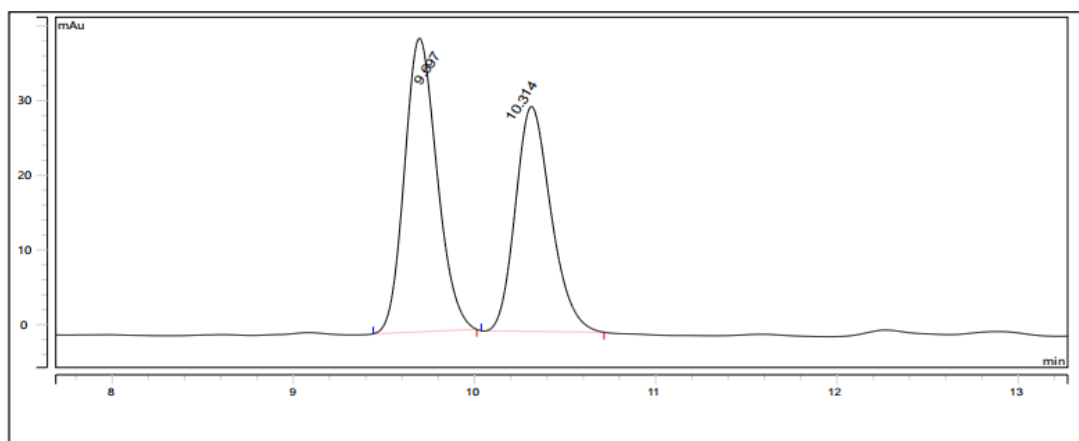
Chiral HPLC spectrum of chiral **4q**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.869	12298.49353	0.349	926.606	96.402
2	10.598	459.03620	0.325	37.868	3.598
3		12757.52973	0.337	964.474	100.000

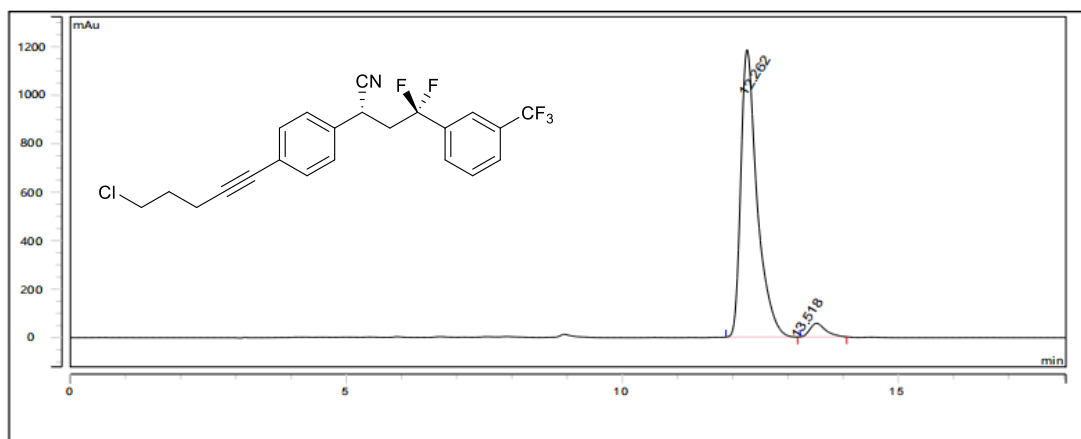
Chiral HPLC spectrum of racemic **4q**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.697	491.51370	0.329	39.322	54.408
2	10.314	411.86320	0.357	30.137	45.592
3		903.37690	0.343	69.459	100.000

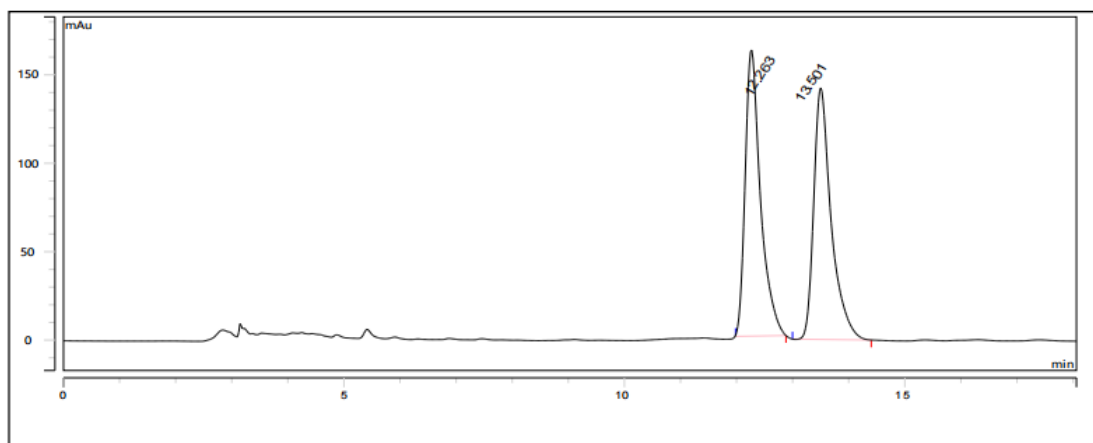
Chiral HPLC spectrum of chiral **4r**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.262	24396.36694	0.499	1188.475	95.638
2	13.518	1112.71555	0.502	56.175	4.362
3		25509.08249	0.500	1244.649	100.000

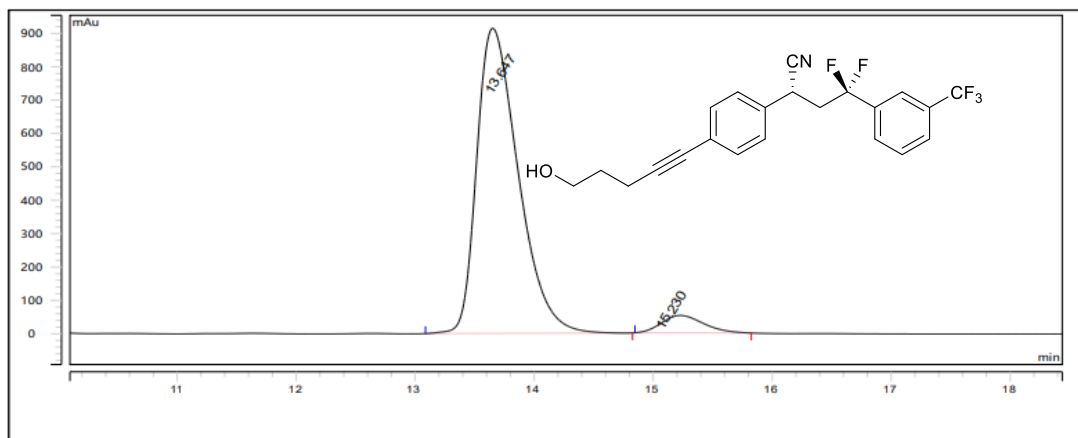
Chiral HPLC spectrum of racemic **4r**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.263	3067.59320	0.465	162.172	49.984
2	13.501	3069.57895	0.524	142.263	50.016
3		6137.17215	0.494	304.435	100.000

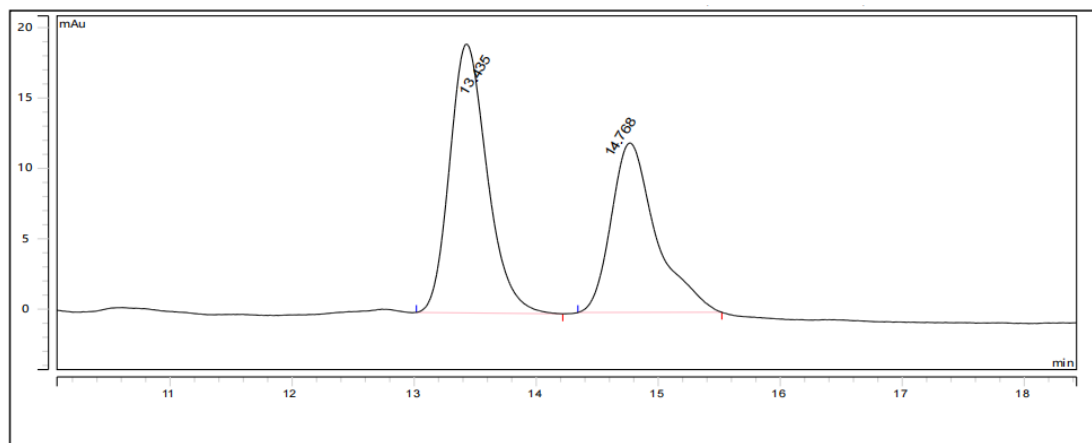
Chiral HPLC spectrum of chiral **4s**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.647	22128.01998	0.631	914.824	94.551
2	15.230	1275.16240	0.650	52.219	5.449
3		23403.18238	0.641	967.043	100.000

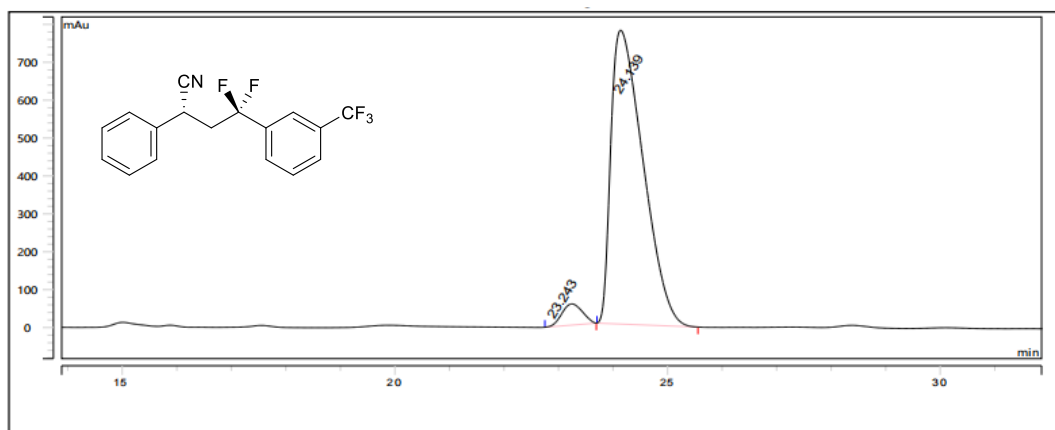
Chiral HPLC spectrum of racemic **4s**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.435	409.29665	0.554	19.106	57.020
2	14.768	308.51300	0.612	12.054	42.980
3		717.80965	0.583	31.161	100.000

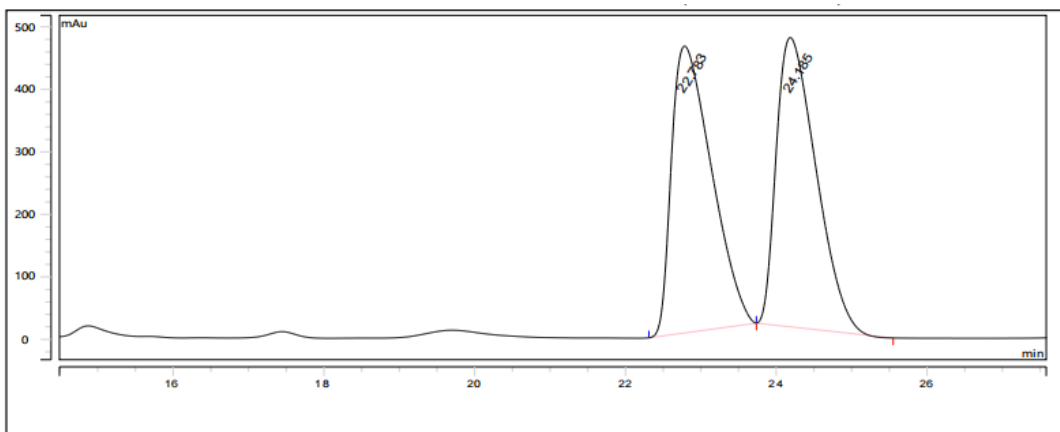
Chiral HPLC spectrum of chiral **4t**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	23.243	1460.72230	0.727	55.978	4.389
2	24.139	31824.00862	1.117	775.750	95.611
3		33284.73092	0.922	831.728	100.000

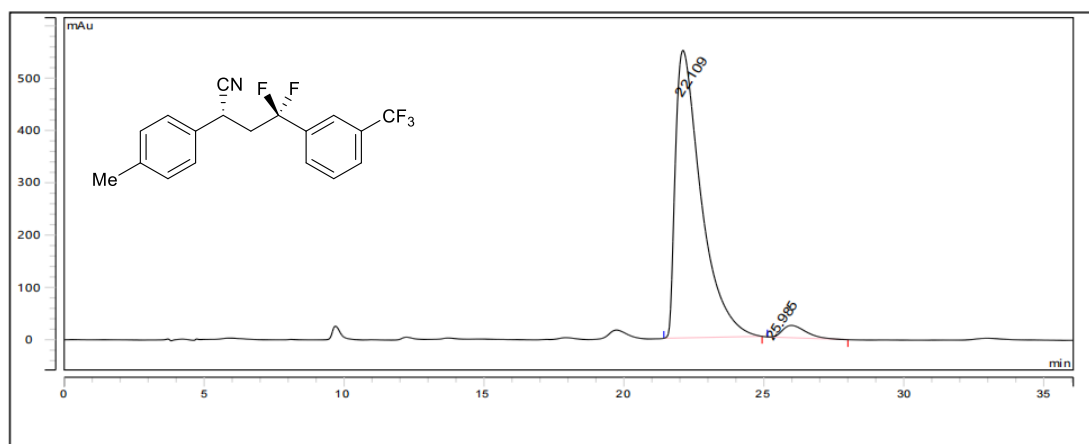
Chiral HPLC spectrum of racemic **4t**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	22.783	16899.74326	1.008	459.063	49.927
2	24.185	16949.44921	0.994	462.981	50.073
3		33849.19247	1.001	922.044	100.000

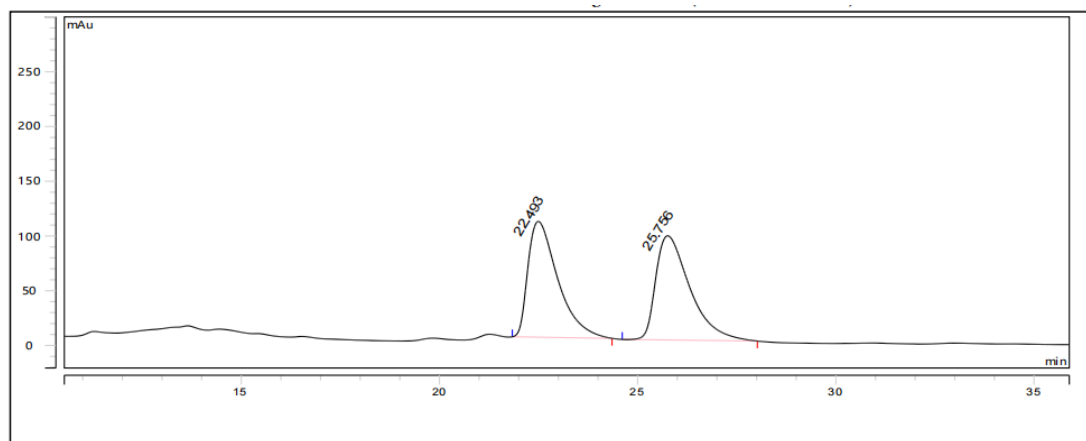
Chiral HPLC spectrum of chiral **4u**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	22.109	35099.52894	1.598	550.352	96.262
2	25.985	1362.93403	1.524	23.544	3.738
3		36462.46297	1.561	573.896	100.000

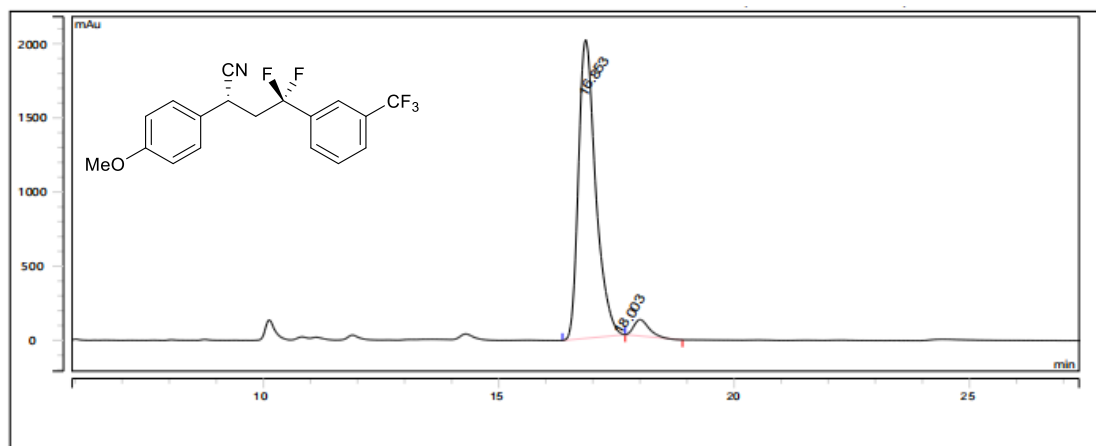
Chiral HPLC spectrum of racemic **4u**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	22.493	5549.12187	1.346	105.818	49.280
2	25.756	5711.23731	1.527	95.242	50.720
3		11260.35918	1.436	201.060	100.000

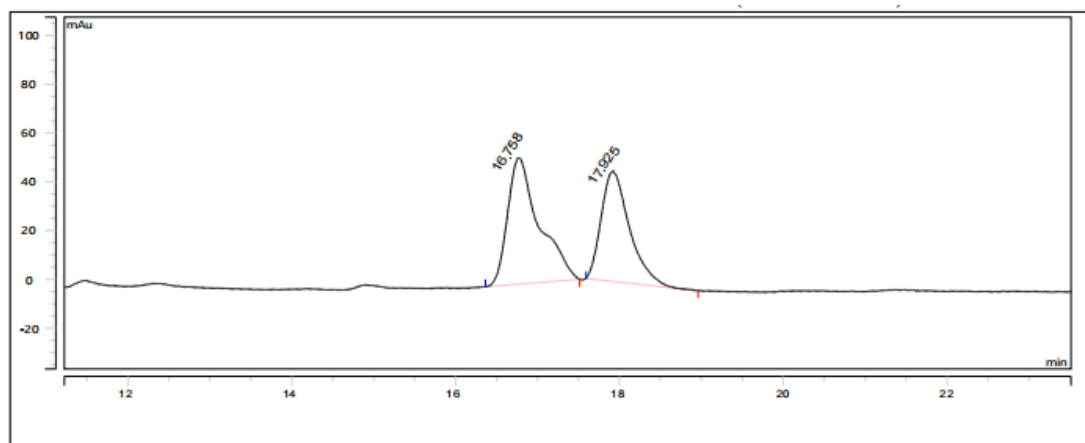
Chiral HPLC spectrum of chiral **4v**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	16.853	51225.99298	0.643	2013.605	95.495
2	18.003	2416.67094	0.579	110.521	4.505
3		53642.66392	0.611	2124.126	100.000

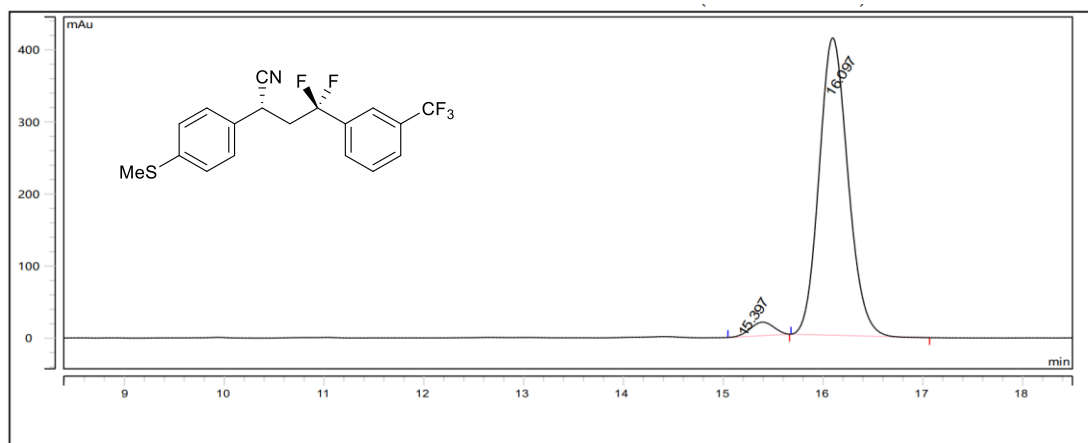
Chiral HPLC spectrum of racemic **4v**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	16.758	1386.35830	0.594	51.896	56.043
2	17.925	1087.38010	0.613	45.442	43.957
3		2473.73840	0.604	97.338	100.000

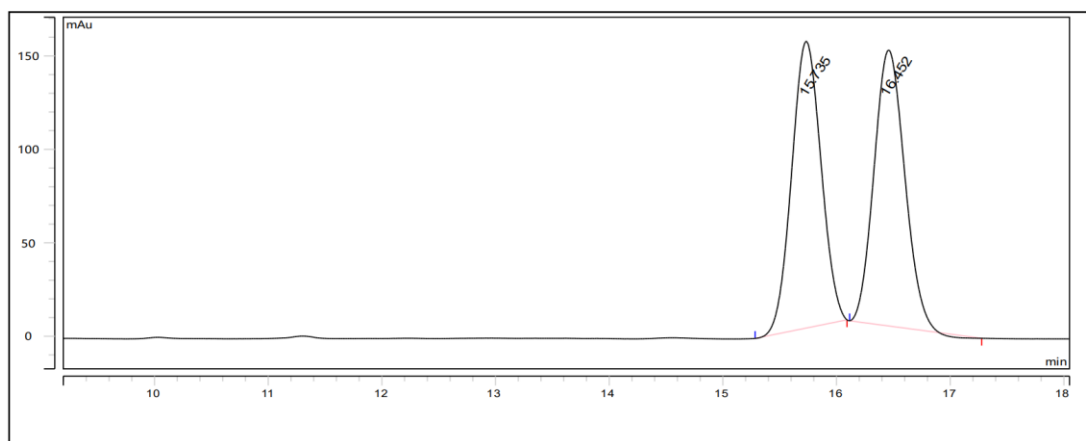
Chiral HPLC spectrum of chiral **4w**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.397	305.29215	0.450	18.660	3.557
2	16.097	8277.05709	0.526	413.262	96.443
3		8582.34925	0.488	431.922	100.000

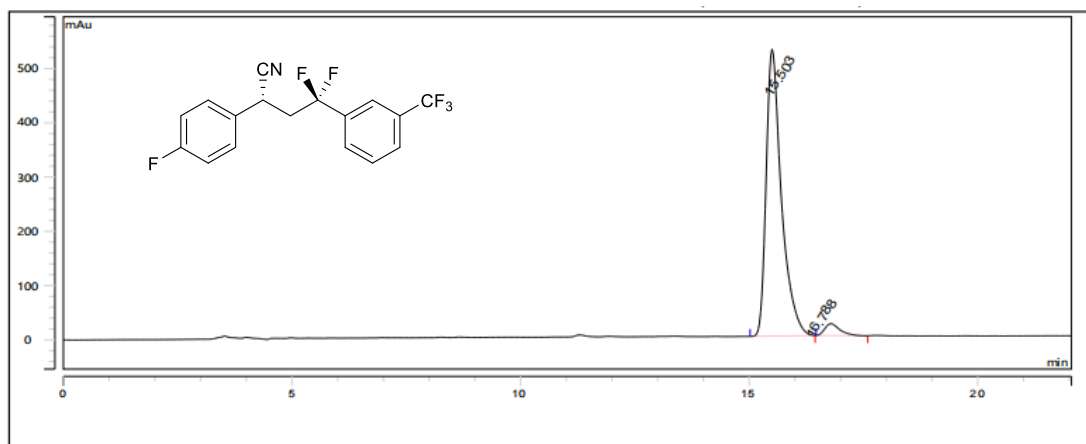
Chiral HPLC spectrum of racemic **4w**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.735	2750.00279	0.480	153.661	49.968
2	16.452	2753.54320	0.502	147.553	50.032
3		5503.54599	0.491	301.214	100.000

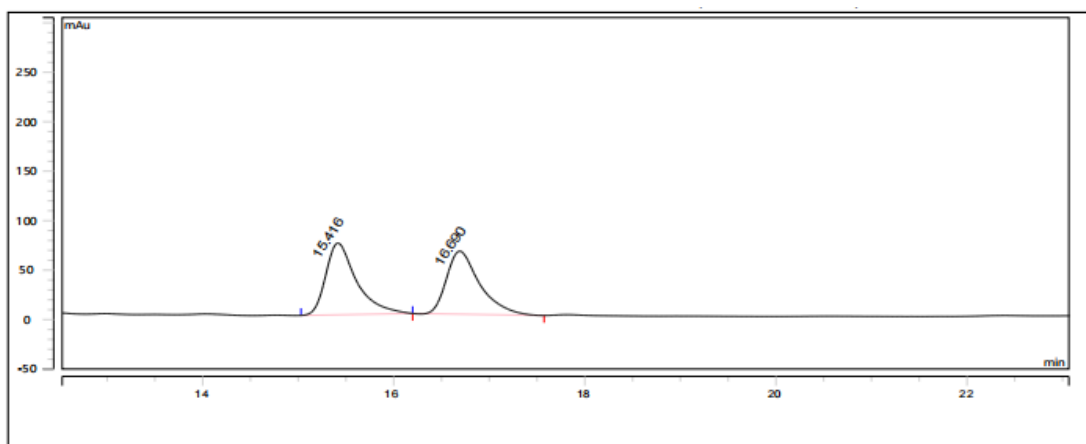
Chiral HPLC spectrum of chiral **4x**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.503	12265.38011	0.568	529.047	96.090
2	16.788	499.15385	0.579	21.958	3.910
3		12764.53395	0.574	551.005	100.000

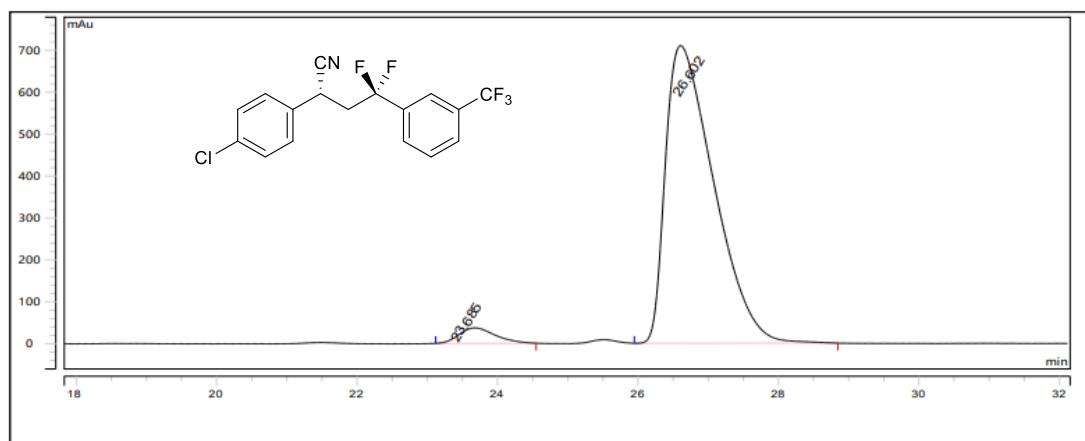
Chiral HPLC spectrum of racemic **4x**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.416	1617.91675	0.543	72.524	51.310
2	16.690	1535.31510	0.601	63.763	48.690
3		3153.23185	0.572	136.287	100.000

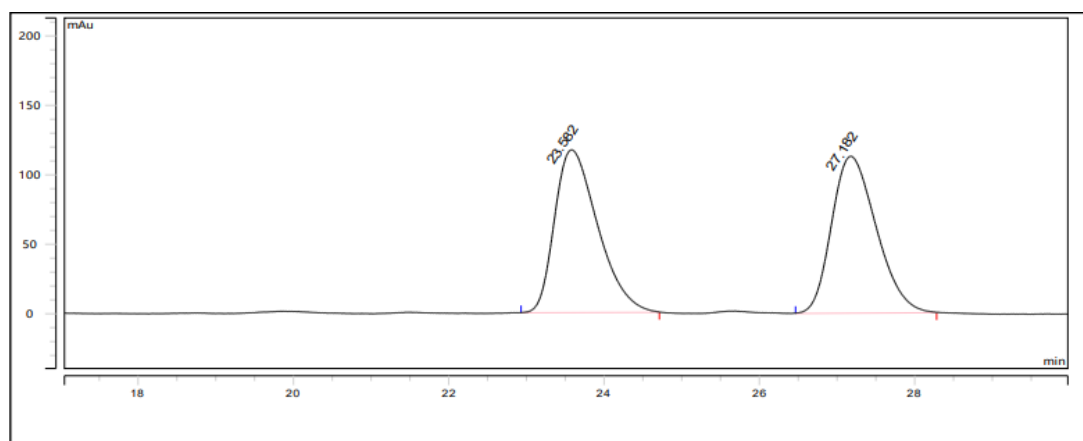
Chiral HPLC spectrum of chiral **4y**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	23.685	1328.63505	0.937	37.131	3.766
2	26.602	33951.76583	1.275	710.402	96.234
3		35280.40089	1.106	747.533	100.000

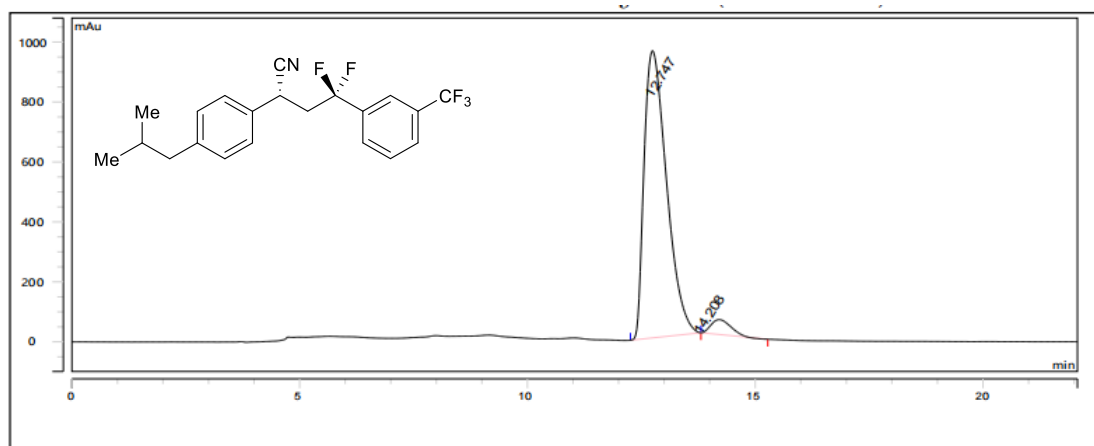
Chiral HPLC spectrum of racemic **4y**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	23.582	4527.68499	1.019	117.310	50.055
2	27.182	4517.65745	1.063	113.000	49.945
3		9045.34244	1.041	230.310	100.000

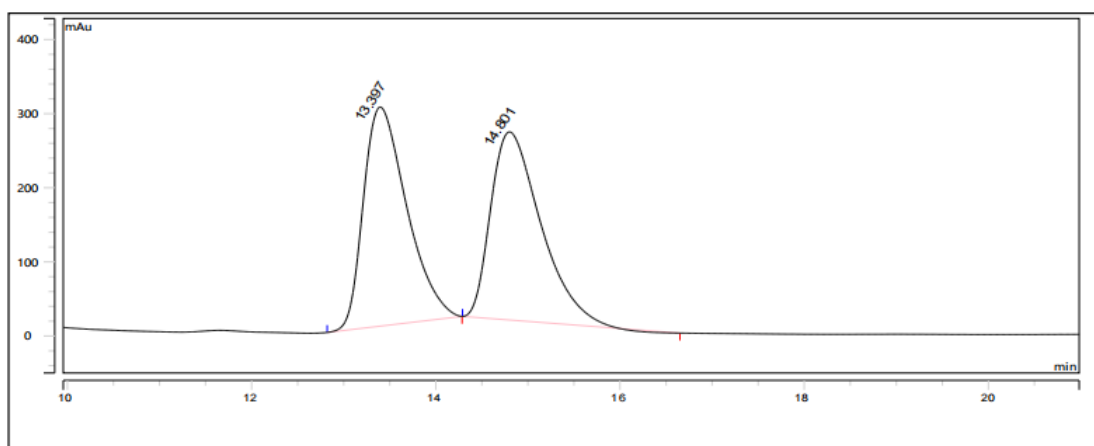
Chiral HPLC spectrum of chiral **4z**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.747	32819.64335	0.919	958.494	95.624
2	14.208	1501.84498	0.845	49.859	4.376
3		34321.48833	0.882	1008.353	100.000

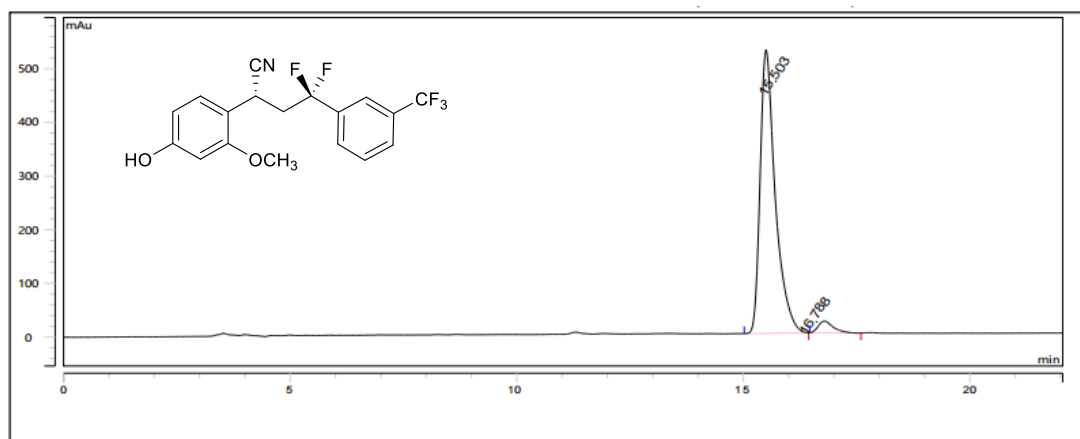
Chiral HPLC spectrum of racemic **4z**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.397	9657.62699	0.862	295.680	50.179
2	14.801	9588.71283	0.992	253.890	49.821
3		19246.33982	0.927	549.570	100.000

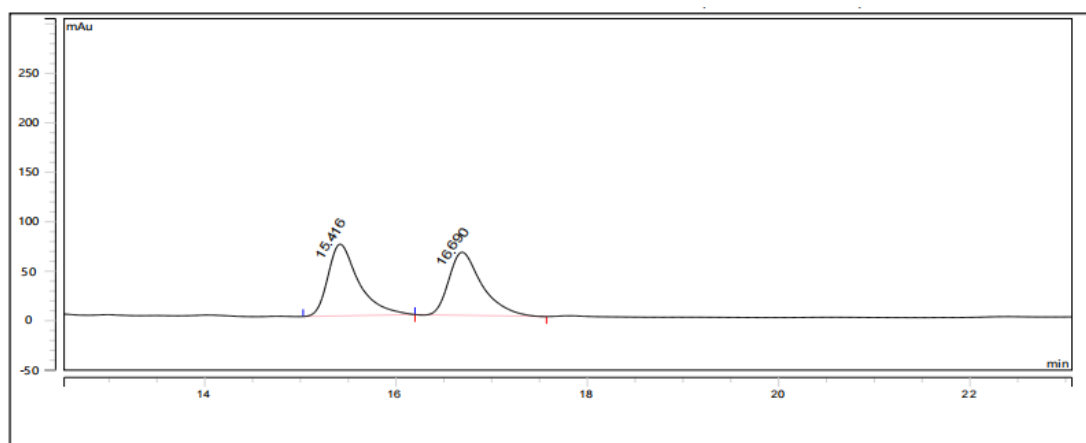
Chiral HPLC spectrum of chiral **4aa**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.503	12265.38011	0.568	529.047	96.090
2	16.788	499.15385	0.579	21.958	3.910
3		12764.53395	0.574	551.005	100.000

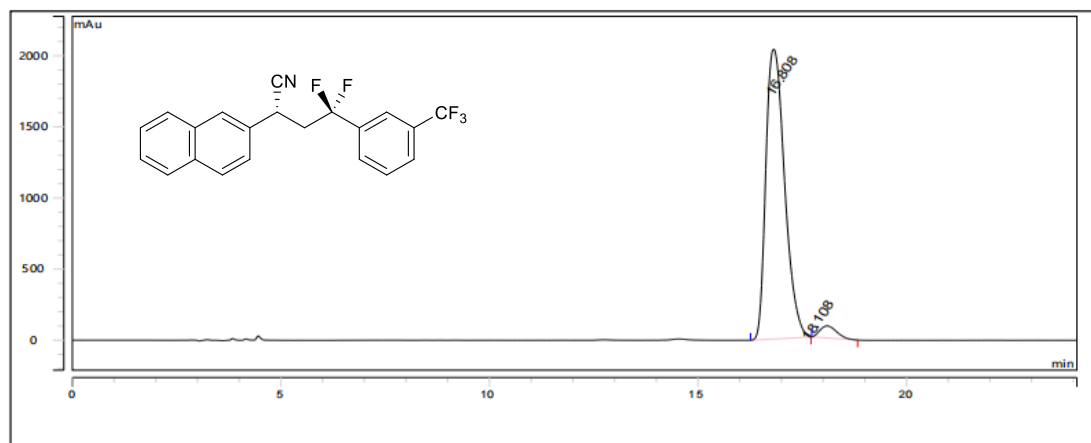
Chiral HPLC spectrum of racemic **4aa**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.416	1617.91675	0.543	72.524	51.310
2	16.690	1535.31510	0.601	63.763	48.690
3		3153.23185	0.572	136.287	100.000

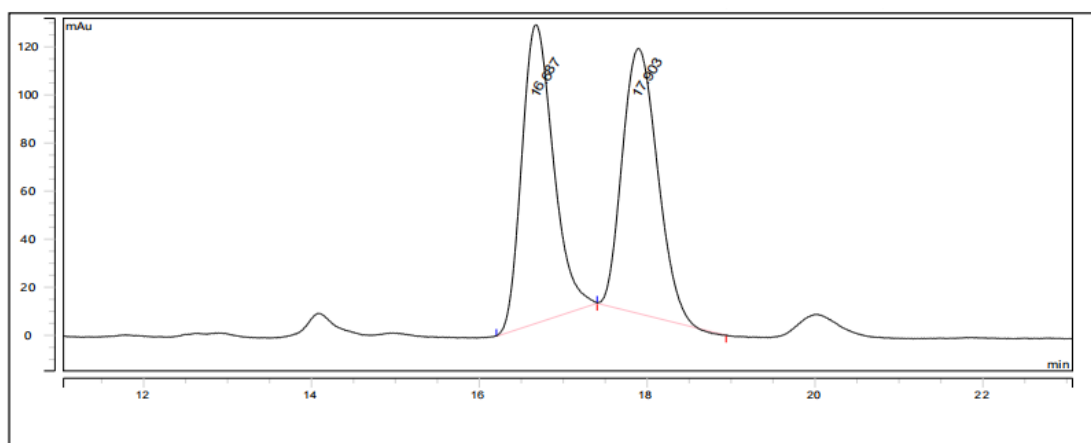
Chiral HPLC spectrum of chiral **4ab**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	16.808	63756.12984	0.827	2039.959	96.418
2	18.108	2368.44863	0.760	85.260	3.582
3		66124.57847	0.794	2125.220	100.000

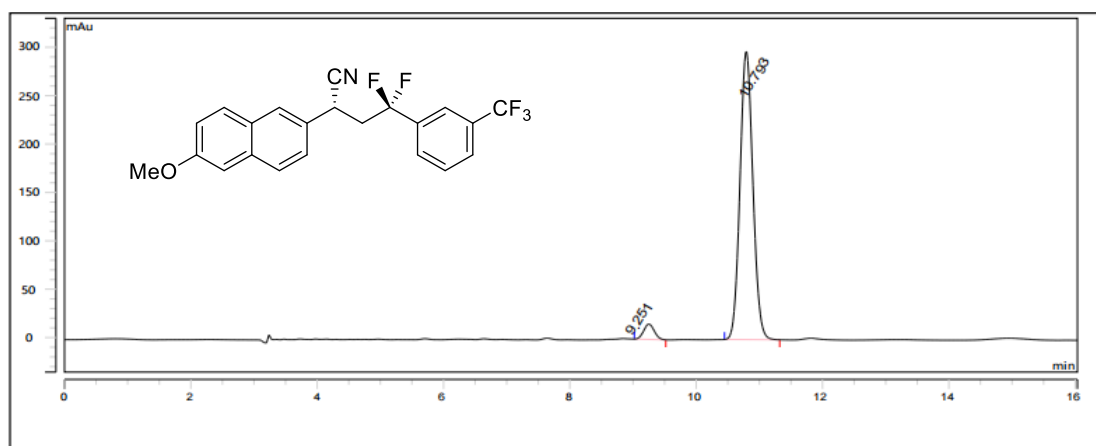
Chiral HPLC spectrum of racemic **4ab**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	16.687	3262.24726	0.687	124.046	50.290
2	17.903	3224.67700	0.790	110.345	49.710
3		6486.92426	0.739	234.392	100.000

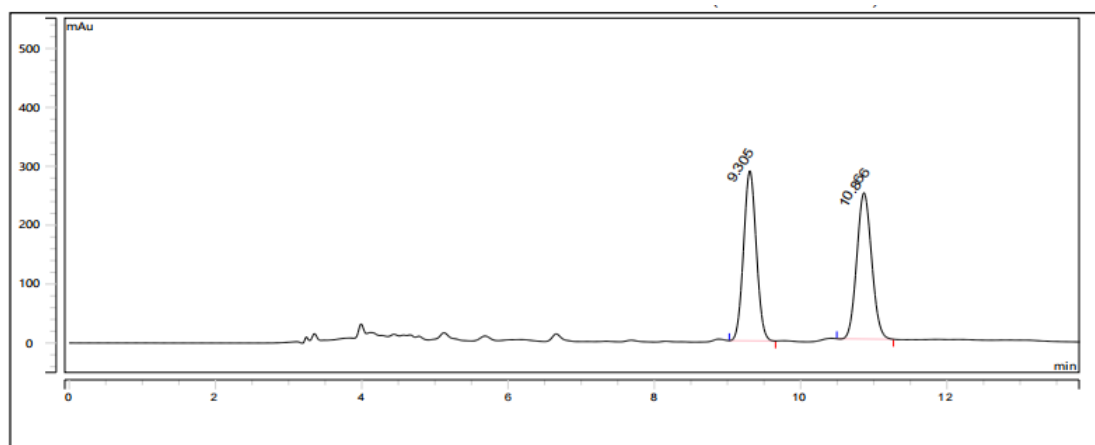
Chiral HPLC spectrum of chiral **4ac**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.251	184.16465	0.310	15.901	4.181
2	10.793	4220.45992	0.372	298.492	95.819
3		4404.62457	0.341	314.394	100.000

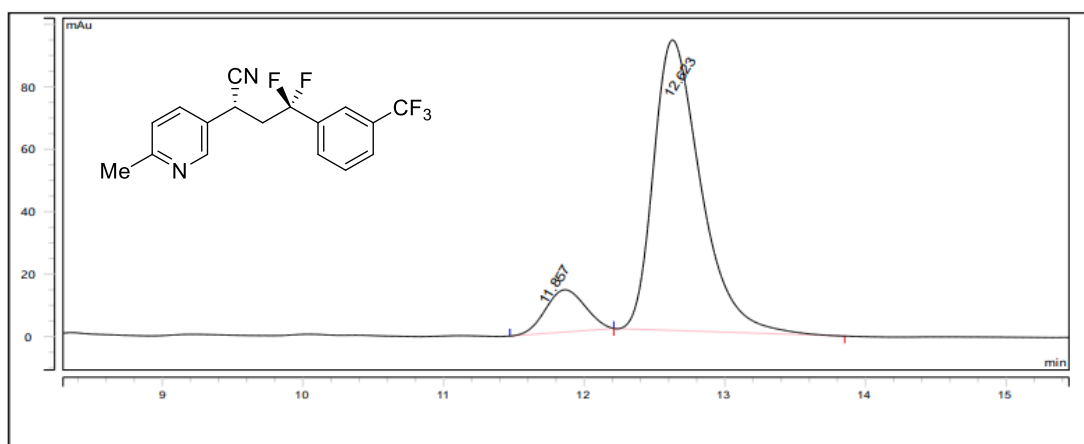
Chiral HPLC spectrum of racemic **4ac**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.305	3476.83631	0.318	289.357	49.855
2	10.866	3497.05699	0.372	248.536	50.145
3		6973.89330	0.345	537.893	100.000

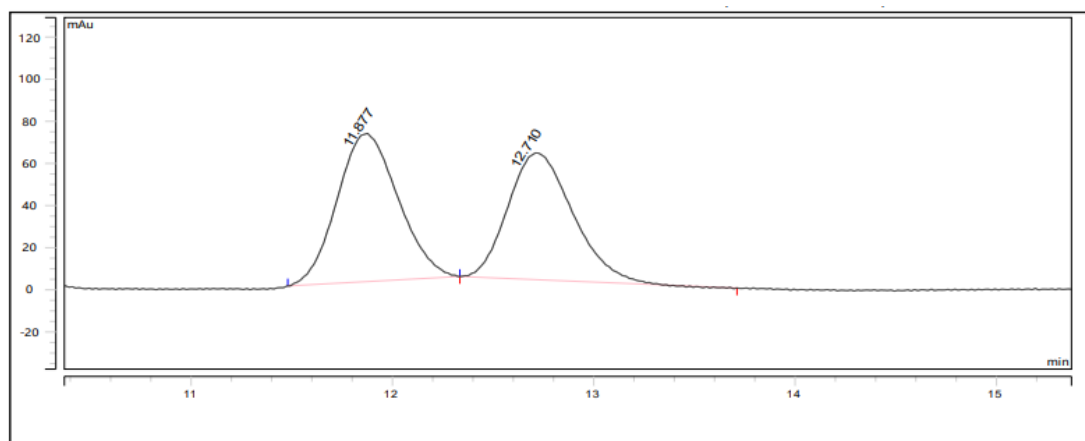
Chiral HPLC spectrum of chiral **4ad**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.857	263.69030	0.532	13.555	10.800
2	12.623	2177.77370	0.595	93.070	89.200
3		2441.46400	0.564	106.625	100.000

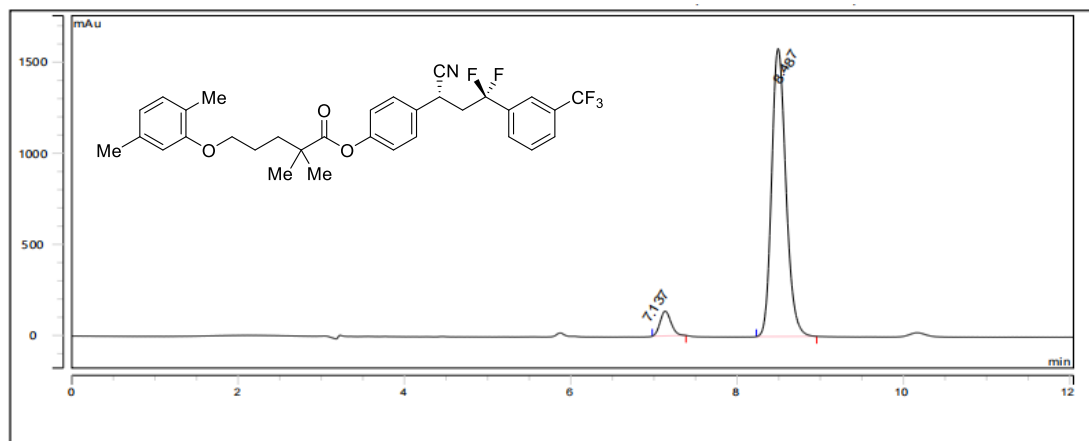
Chiral HPLC spectrum of racemic **4ad**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.877	1483.06000	0.565	70.395	52.453
2	12.710	1344.32485	0.593	60.153	47.547
3		2827.38485	0.579	130.548	100.000

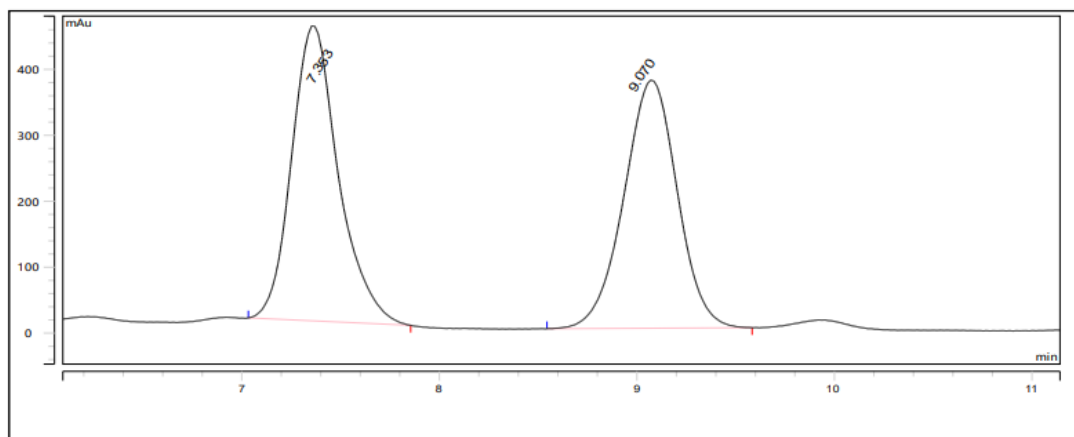
Chiral HPLC spectrum of chiral **4ae**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	7.137	1236.35120	0.239	136.764	6.149
2	8.487	18870.96631	0.309	1583.135	93.851
3		20107.31751	0.274	1719.900	100.000

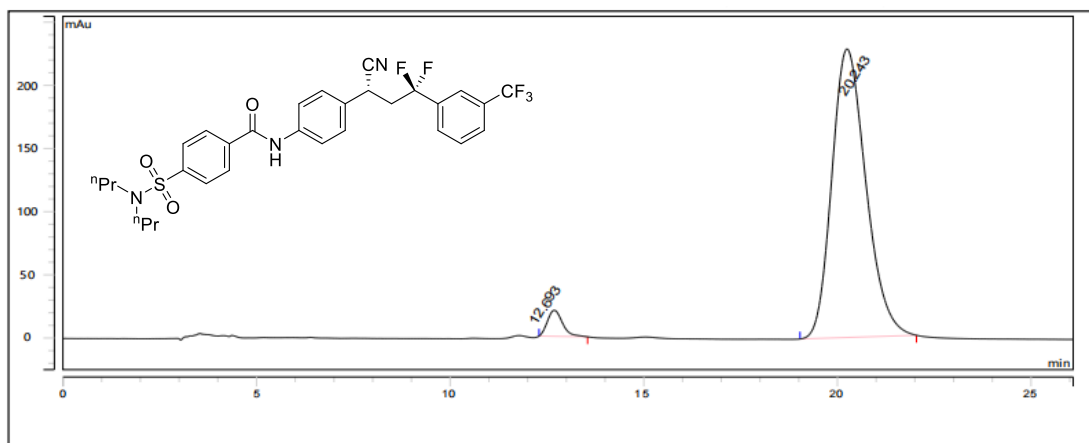
Chiral HPLC spectrum of racemic **4ae**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	7.353	7362.28928	0.416	447.121	50.994
2	9.070	7075.34963	0.491	376.385	49.006
3		14437.63891	0.453	823.506	100.000

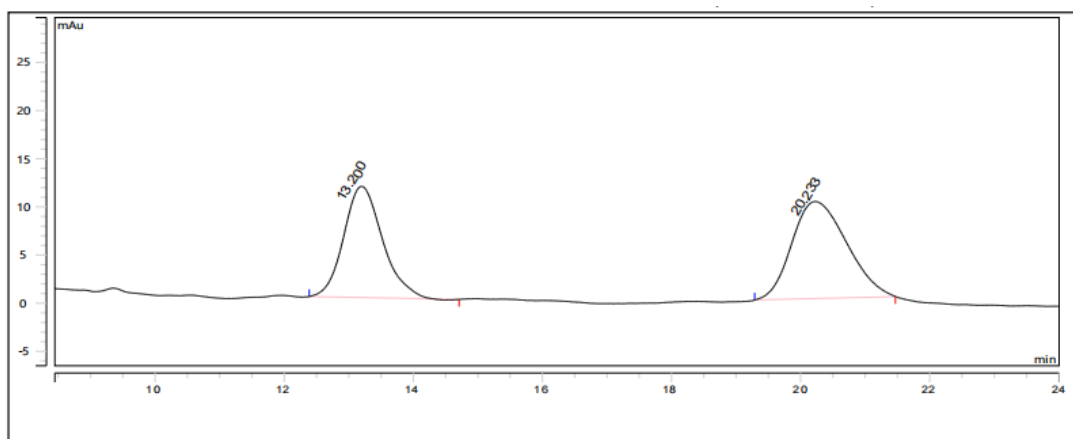
Chiral HPLC spectrum of chiral **4af**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.693	556.60150	0.701	20.703	3.833
2	20.243	13962.81016	1.602	228.502	96.167
3		14519.41166	1.152	249.205	100.000

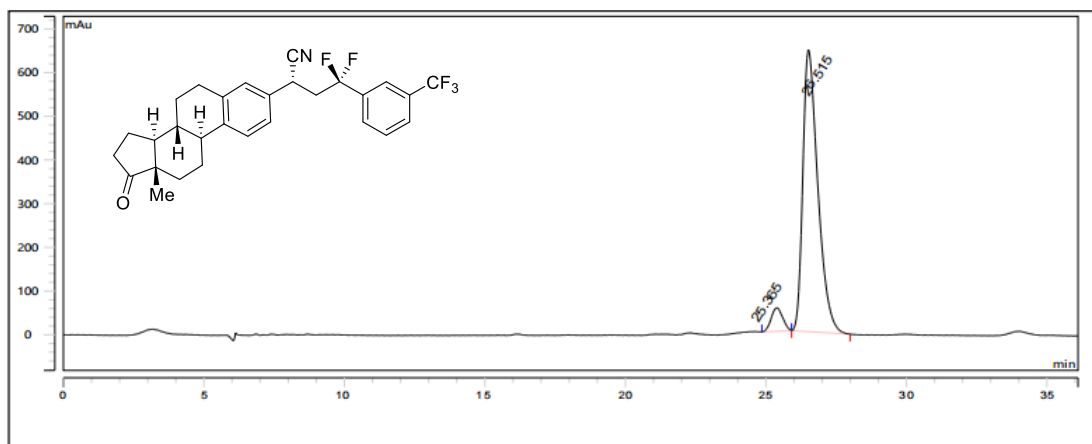
Chiral HPLC spectrum of racemic **4af**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.200	482.53940	1.078	11.545	44.822
2	20.233	594.01980	1.597	10.084	55.178
3		1076.55920	1.337	21.629	100.000

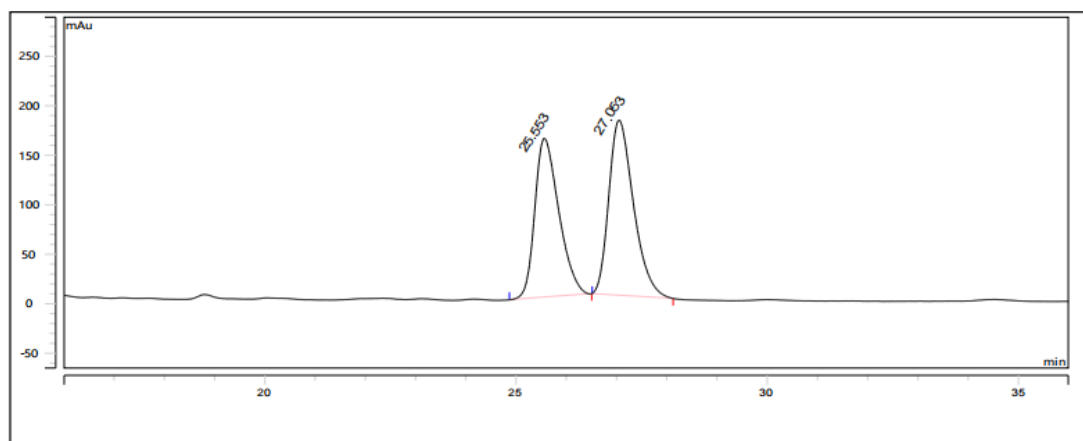
Chiral HPLC spectrum of chiral **4ag**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	25.365	1518.30125	0.768	54.010	5.973
2	26.515	23901.36561	0.951	647.332	94.027
3		25419.66686	0.859	701.342	100.000

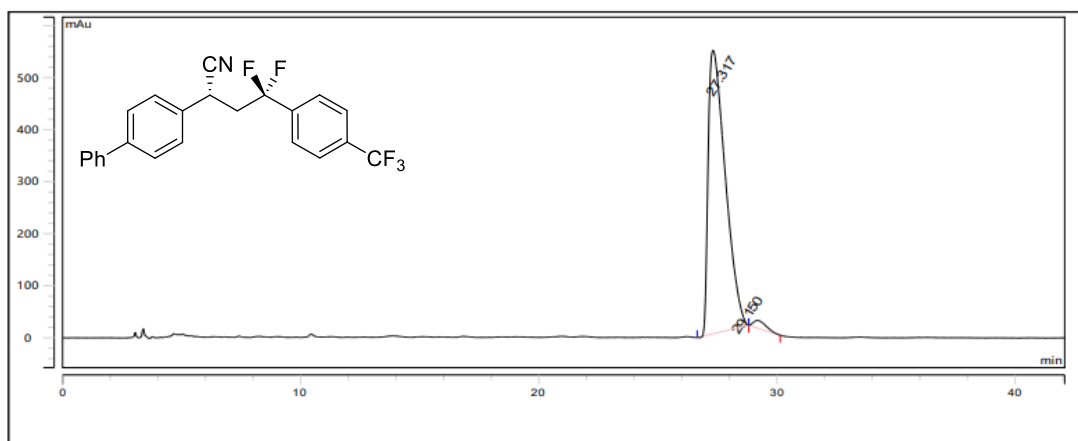
Chiral HPLC spectrum of racemic **4ag**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	25.553	5298.74281	0.869	160.591	46.757
2	27.053	6033.74588	0.887	176.704	53.243
3		11332.48869	0.878	337.295	100.000

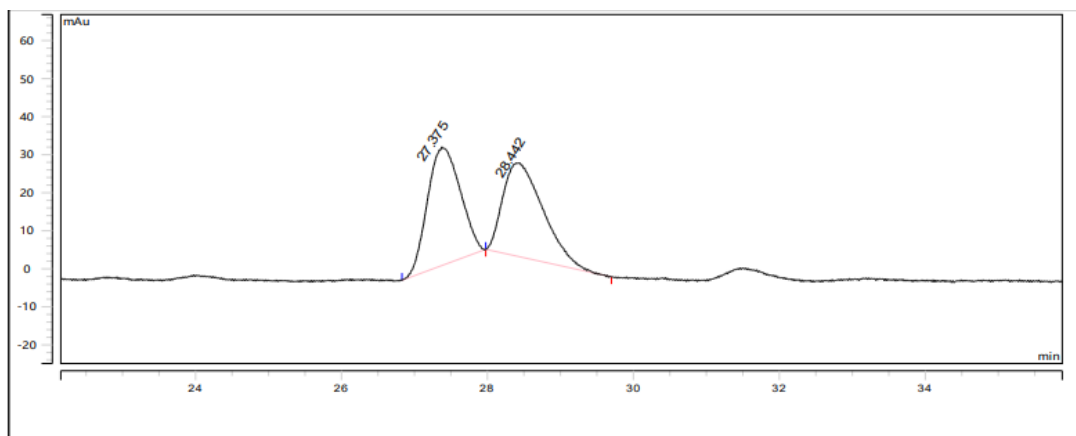
Chiral HPLC spectrum of chiral **4ah**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	27.317	27210.86783	1.346	546.496	97.955
2	29.150	568.13475	1.080	14.500	2.045
3		27779.00258	1.213	560.995	100.000

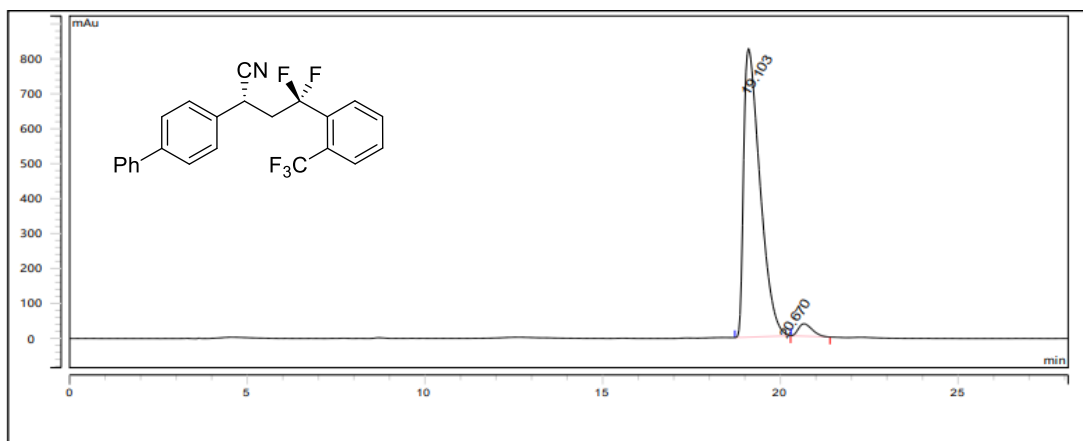
Chiral HPLC spectrum of racemic **4ah**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	27.375	968.01430	0.858	31.224	50.518
2	28.442	948.15670	1.033	24.701	49.482
3		1916.17100	0.945	55.924	100.000

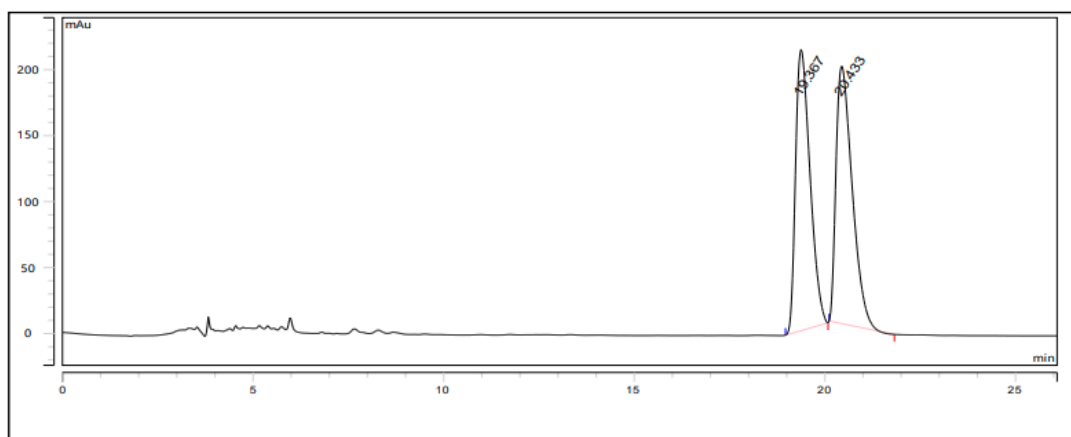
Chiral HPLC spectrum of chiral **4ai**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	19.103	26454.76362	0.844	827.197	96.502
2	20.670	959.04710	0.725	35.675	3.498
3		27413.81072	0.785	862.872	100.000

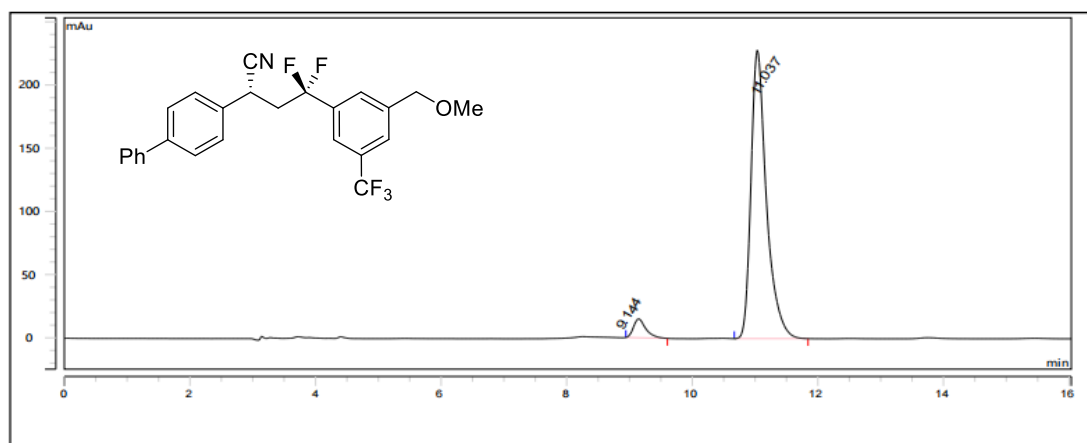
Chiral HPLC spectrum of racemic **4ai**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	19.367	5617.49961	0.706	213.078	49.362
2	20.433	5762.64119	0.785	195.105	50.638
3		11380.14080	0.745	408.183	100.000

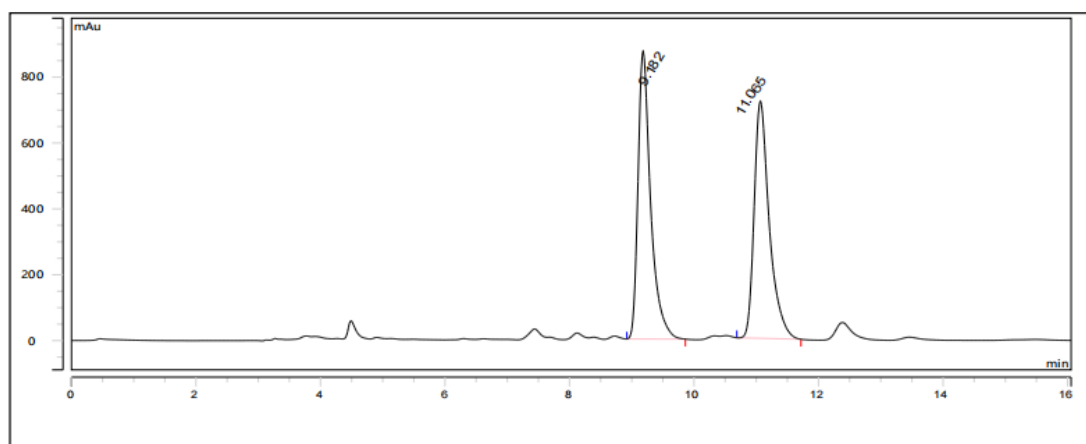
Chiral HPLC spectrum of chiral **4aj**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.144	203.06577	0.340	14.957	4.951
2	11.037	3898.09839	0.420	228.270	95.049
3		4101.16416	0.380	243.227	100.000

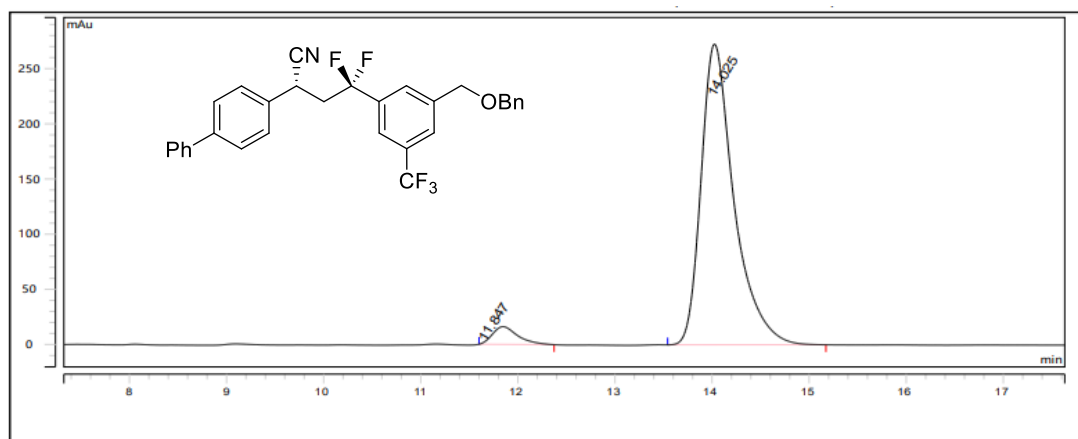
Chiral HPLC spectrum of racemic **4aj**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.182	12327.95320	0.342	875.992	50.352
2	11.065	12155.72683	0.416	721.281	49.648
3		24483.68003	0.379	1597.273	100.000

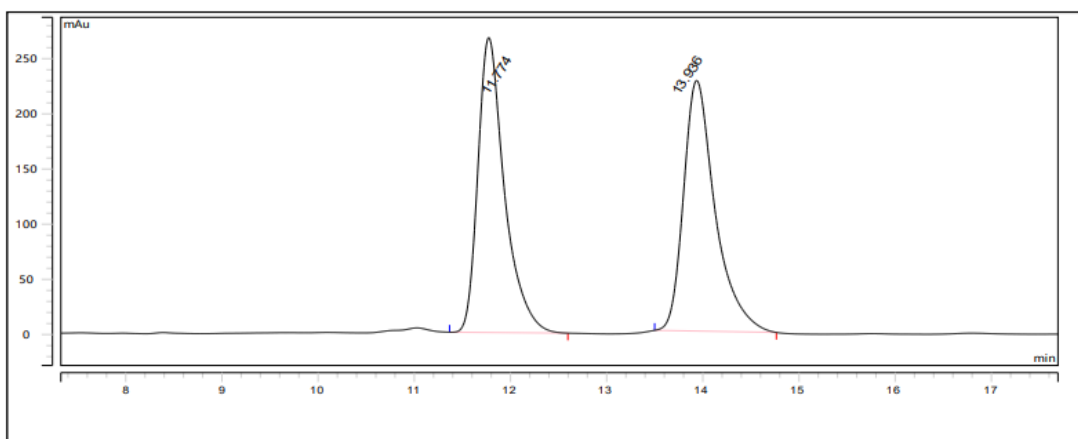
Chiral HPLC spectrum of chiral **4ak**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.847	290.12002	0.461	16.061	4.319
2	14.025	6426.64063	0.579	272.567	95.681
3		6716.76066	0.520	288.628	100.000

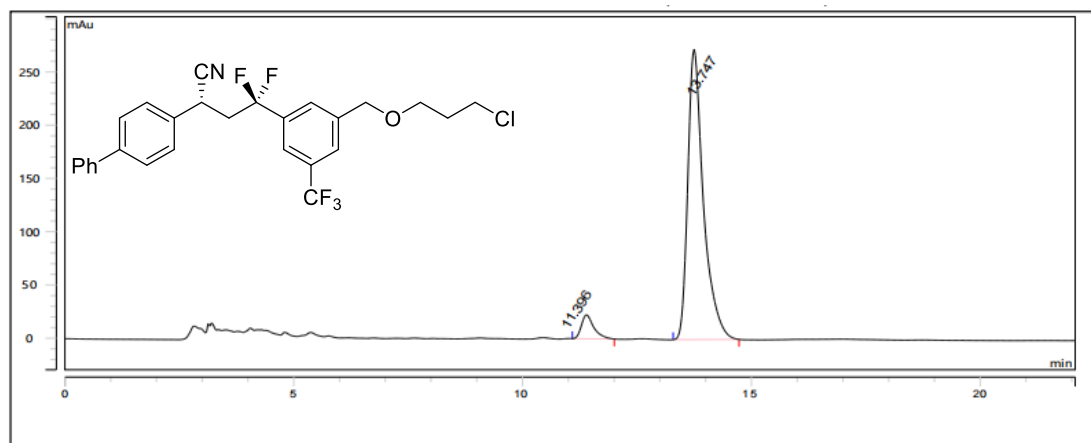
Chiral HPLC spectrum of racemic **4ak**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.774	5134.16545	0.474	267.397	49.748
2	13.936	5186.14550	0.563	227.147	50.252
3		10320.31094	0.519	494.543	100.000

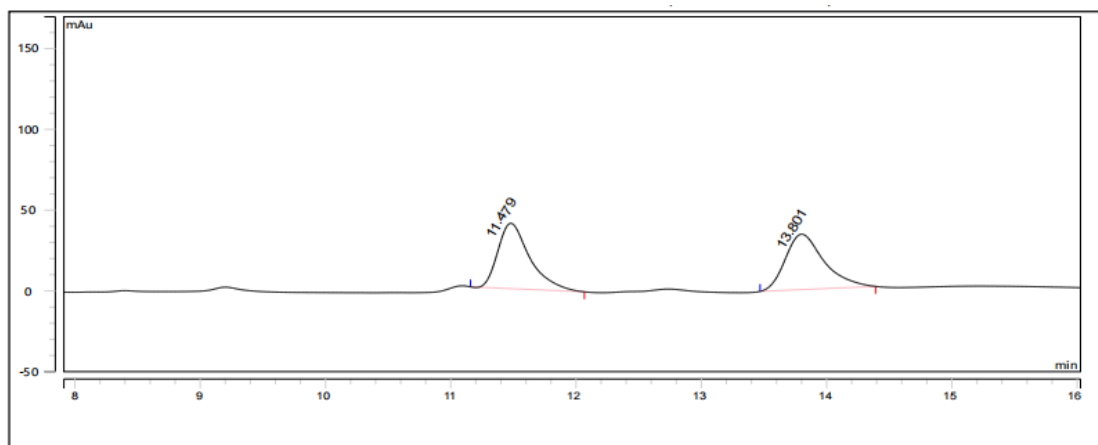
Chiral HPLC spectrum of chiral **4al**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.396	419.59744	0.461	22.506	6.087
2	13.747	6474.20577	0.577	272.689	93.913
3		6893.80322	0.519	295.195	100.000

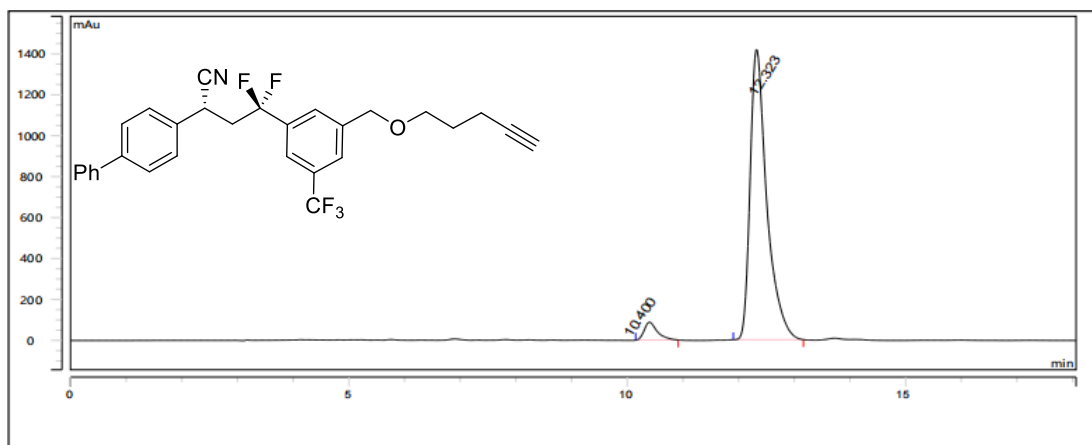
Chiral HPLC spectrum of racemic **4al**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.479	716.11365	0.442	40.502	49.335
2	13.801	735.41295	0.543	34.330	50.665
3		1451.52659	0.492	74.832	100.000

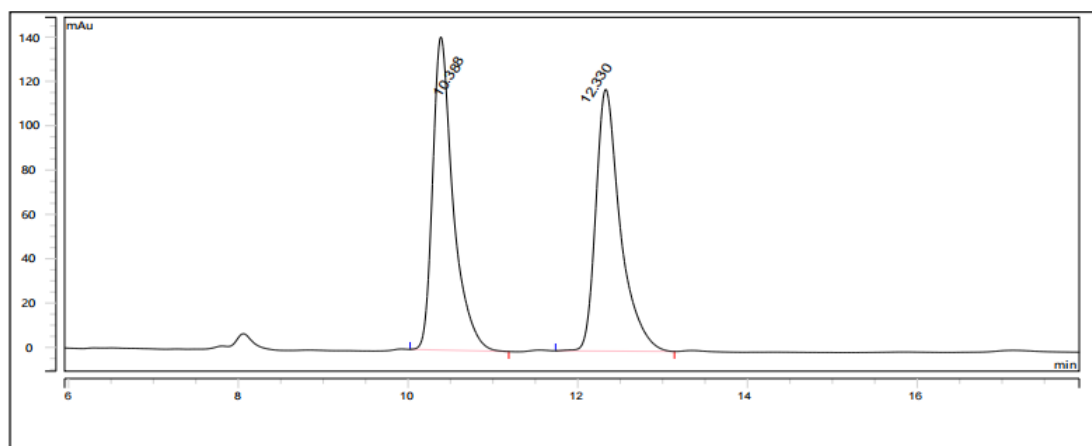
Chiral HPLC spectrum of chiral **4am**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.400	1428.98628	0.401	87.897	4.618
2	12.323	29512.37300	0.506	1421.403	95.382
3		30941.35927	0.454	1509.299	100.000

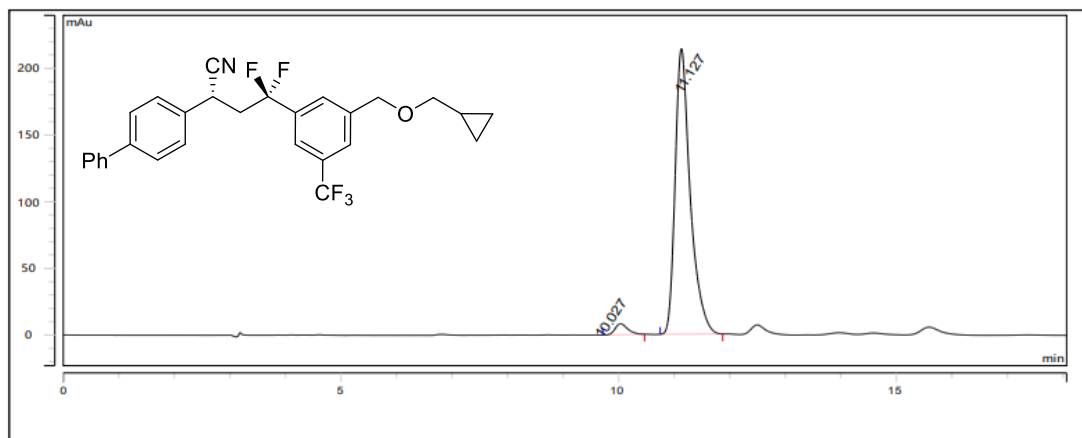
Chiral HPLC spectrum of racemic **4am**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.388	2366.75535	0.405	141.346	49.967
2	12.330	2369.88228	0.487	118.194	50.033
3		4736.63762	0.446	259.540	100.000

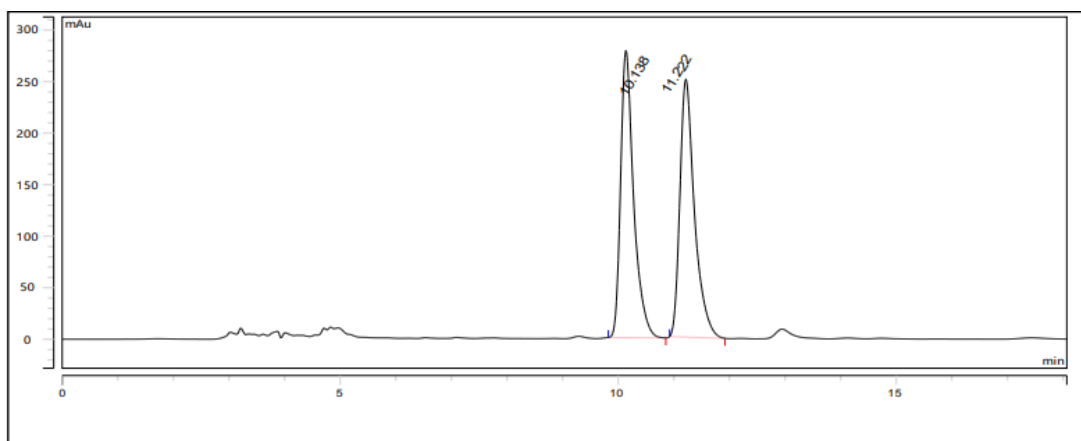
Chiral HPLC spectrum of chiral **4an**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.027	128.73045	0.400	8.299	3.081
2	11.127	4049.12665	0.466	214.995	96.919
3		4177.85710	0.433	223.294	100.000

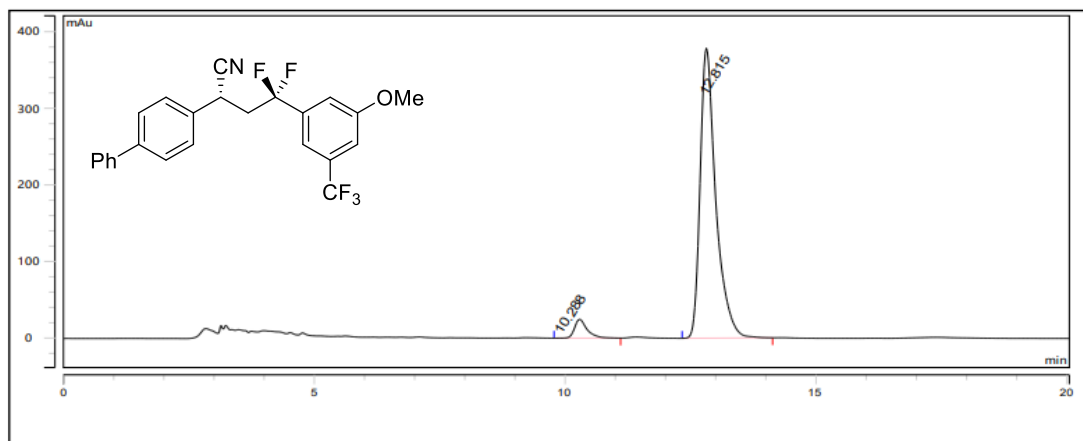
Chiral HPLC spectrum of racemic **4an**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.138	4524.94940	0.399	279.805	49.860
2	11.222	4550.41035	0.449	250.714	50.140
3		9075.35975	0.424	530.518	100.000

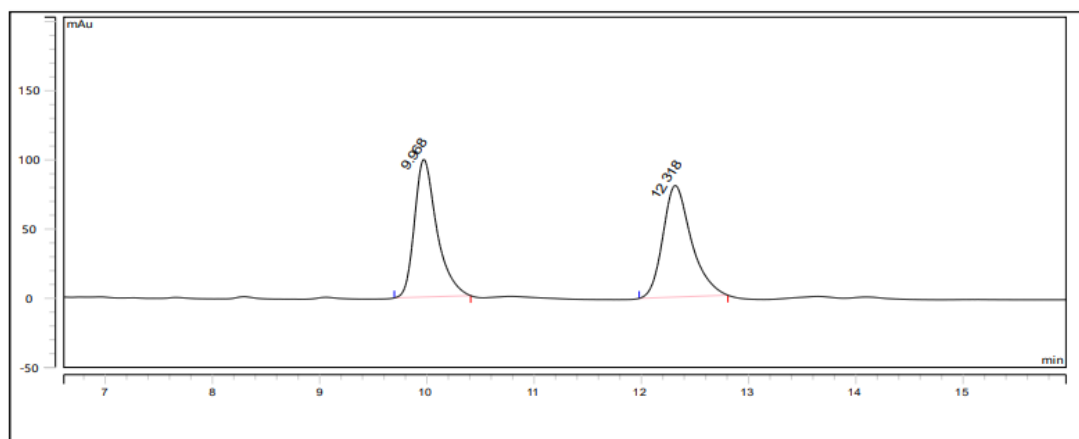
Chiral HPLC spectrum of chiral **4ao**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.288	425.83733	0.417	24.614	4.931
2	12.815	8209.73341	0.528	378.696	95.069
3		8635.57075	0.472	403.310	100.000

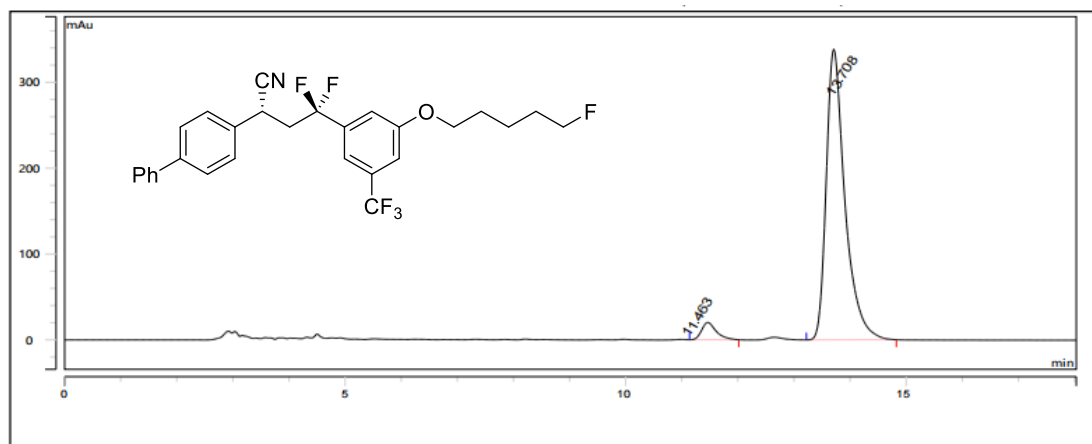
Chiral HPLC spectrum of racemic **4ao**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.968	1440.86810	0.361	99.739	49.190
2	12.318	1488.30155	0.467	80.786	50.810
3		2929.16965	0.414	180.525	100.000

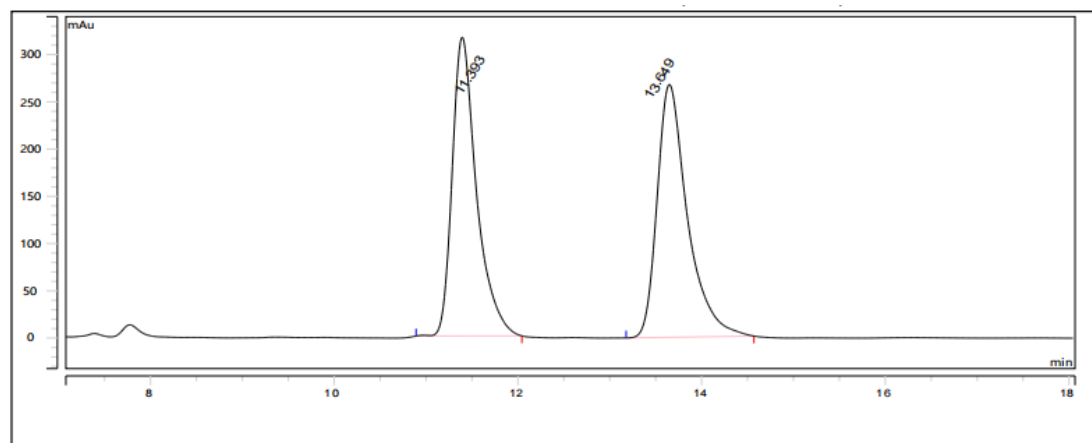
Chiral HPLC spectrum of chiral **4ap**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.463	362.75090	0.449	20.203	4.427
2	13.708	7831.72254	0.568	338.712	95.573
3		8194.47344	0.508	358.915	100.000

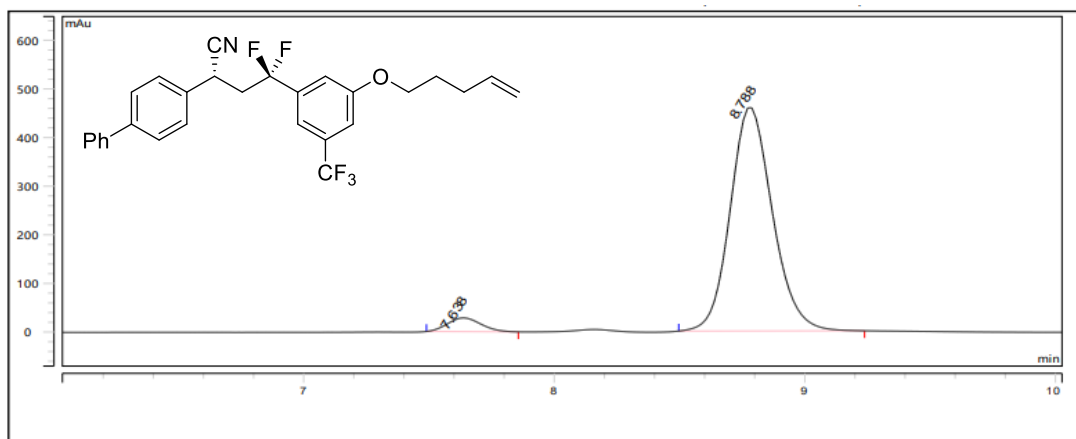
Chiral HPLC spectrum of racemic **4ap**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.393	5813.61847	0.454	316.388	48.711
2	13.649	6121.34834	0.560	267.655	51.289
3		11934.96681	0.507	584.043	100.000

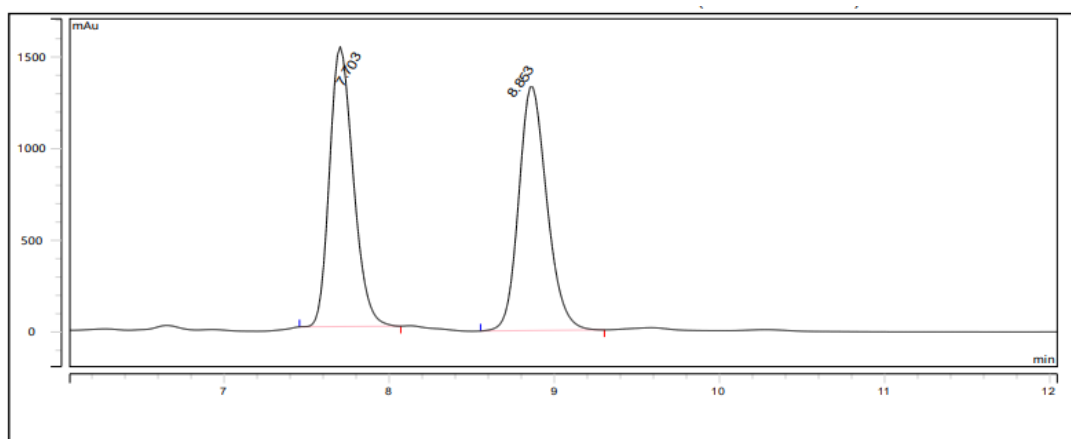
Chiral HPLC spectrum of chiral **4aq**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	7.638	259.14265	0.247	28.303	4.587
2	8.788	5390.39780	0.304	459.020	95.413
3		5649.54045	0.275	487.323	100.000

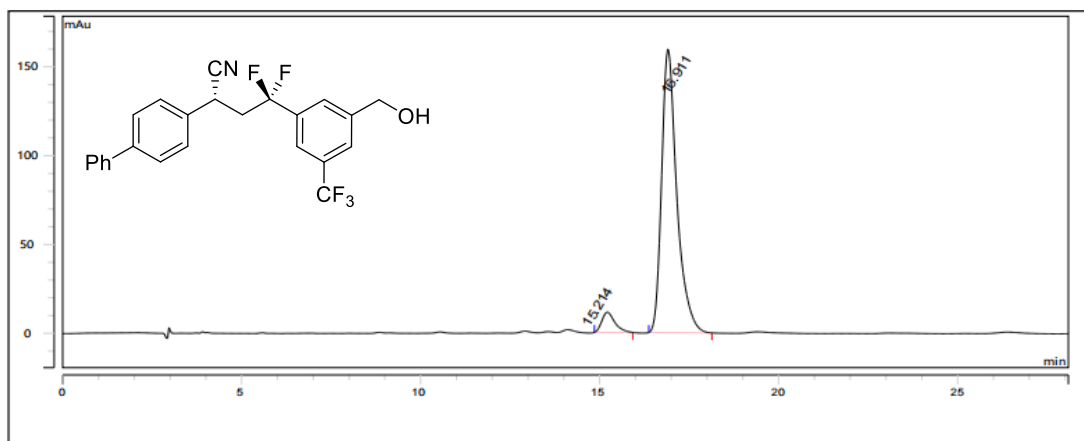
Chiral HPLC spectrum of racemic **4aq**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	7.703	15305.74673	0.262	1526.674	49.222
2	8.853	15789.58262	0.308	1328.781	50.778
3		31095.32936	0.285	2855.456	100.000

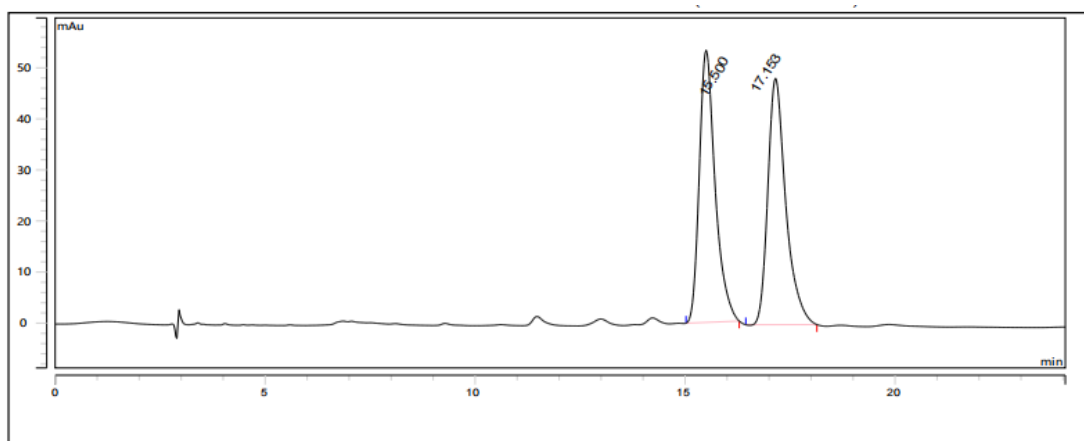
Chiral HPLC spectrum of chiral **4ar**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.214	285.79830	0.636	11.458	5.726
2	16.911	4705.40775	0.728	159.925	94.274
3		4991.20605	0.682	171.383	100.000

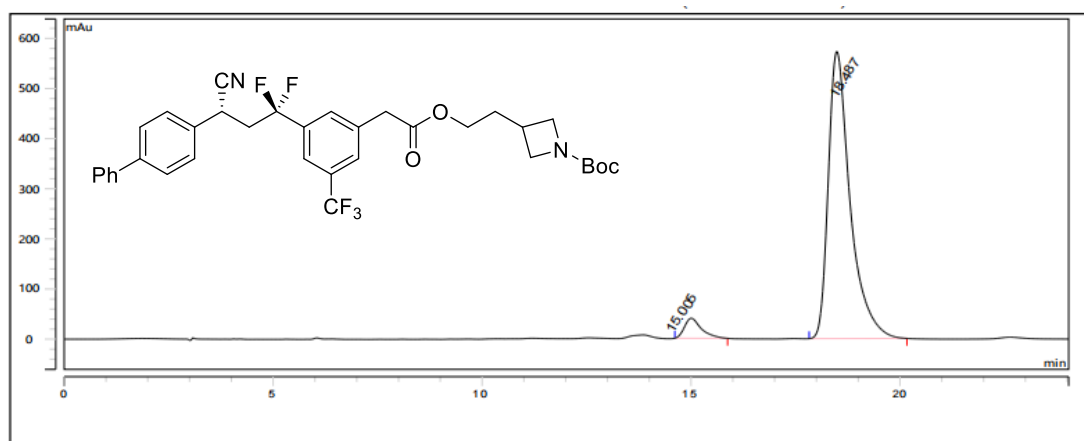
Chiral HPLC spectrum of racemic **4ar**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.500	1400.45500	0.662	53.323	49.419
2	17.153	1433.35965	0.740	48.275	50.581
3		2833.81465	0.701	101.598	100.000

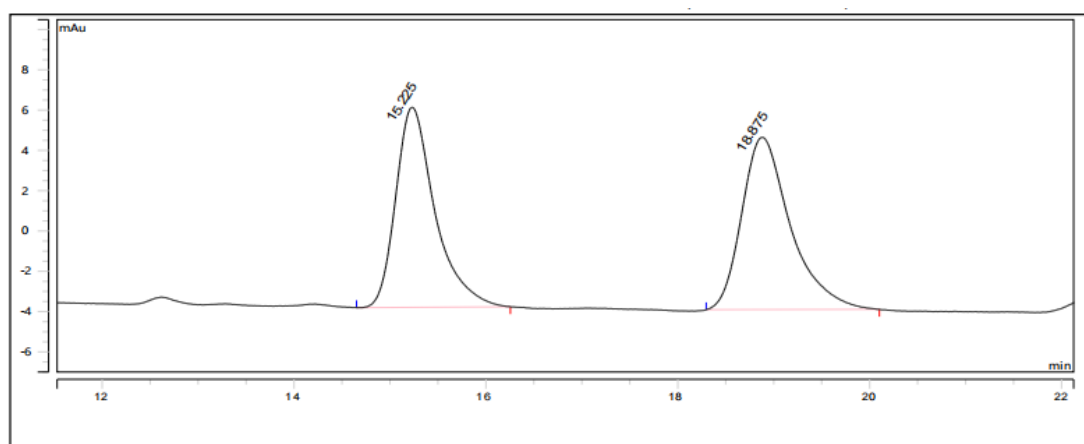
Chiral HPLC spectrum of chiral **4as**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.005	1122.31195	0.694	40.021	5.116
2	18.487	20814.42588	0.886	573.441	94.884
3		21936.73782	0.790	613.462	100.000

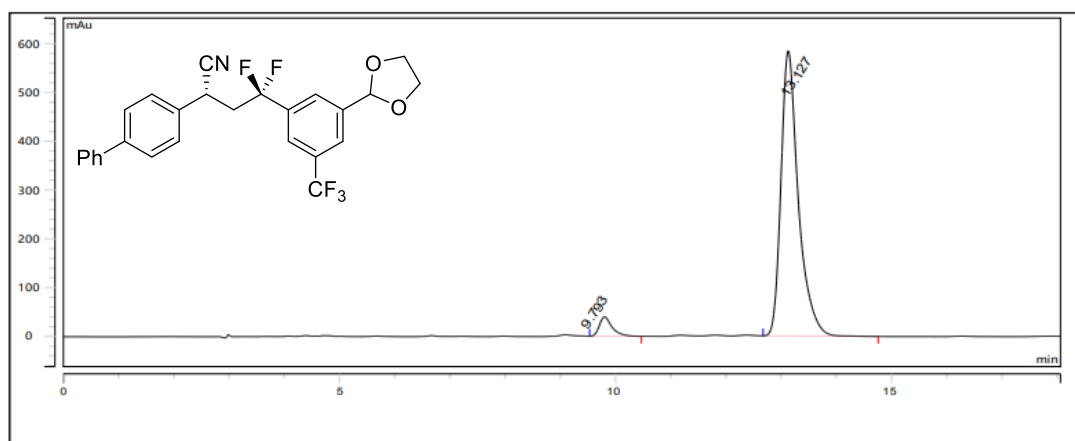
Chiral HPLC spectrum of racemic **4as**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	15.225	282.28320	0.701	9.927	48.353
2	18.875	301.51830	0.880	8.549	51.647
3		583.80150	0.790	18.476	100.000

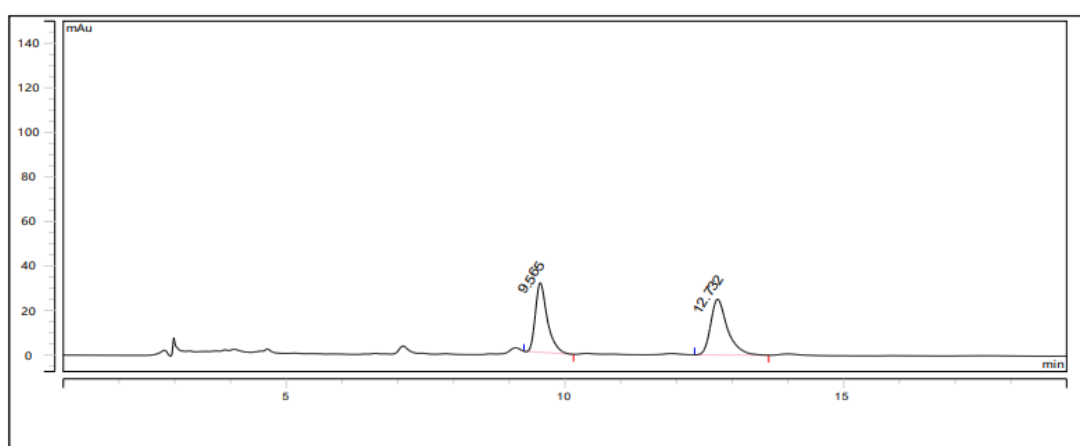
Chiral HPLC spectrum of chiral **4at**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.793	634.67982	0.390	39.843	4.741
2	13.127	12751.18525	0.534	586.083	95.259
3		13385.86506	0.462	625.926	100.000

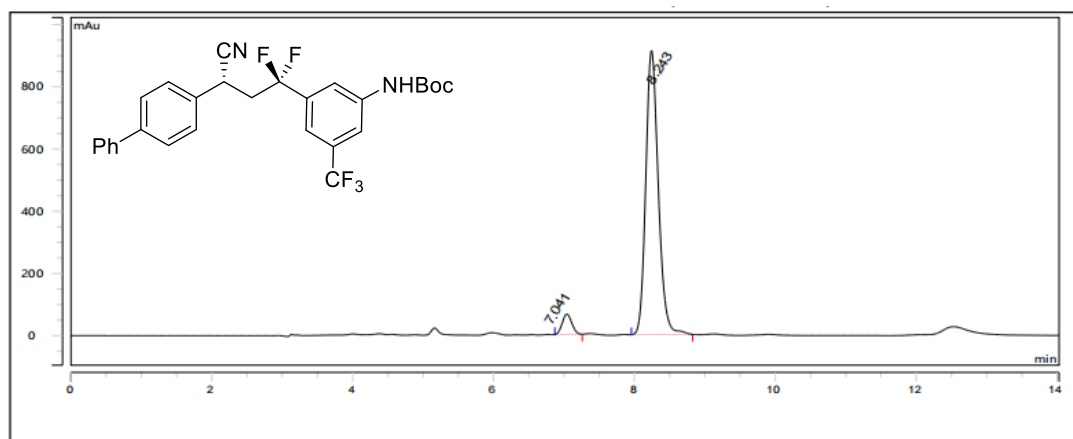
Chiral HPLC spectrum of racemic **4at**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.565	463.67770	0.370	31.197	46.881
2	12.732	525.38010	0.514	25.091	53.119
3		989.05780	0.442	56.288	100.000

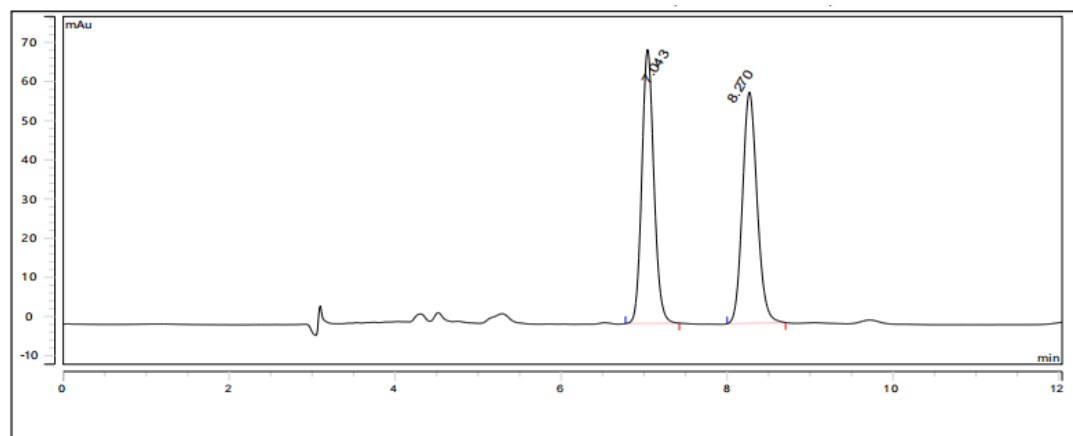
Chiral HPLC spectrum of chiral **4au**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	7.041	617.24010	0.251	65.975	5.190
2	8.243	11276.62822	0.316	916.973	94.810
3		11893.86832	0.284	982.948	100.000

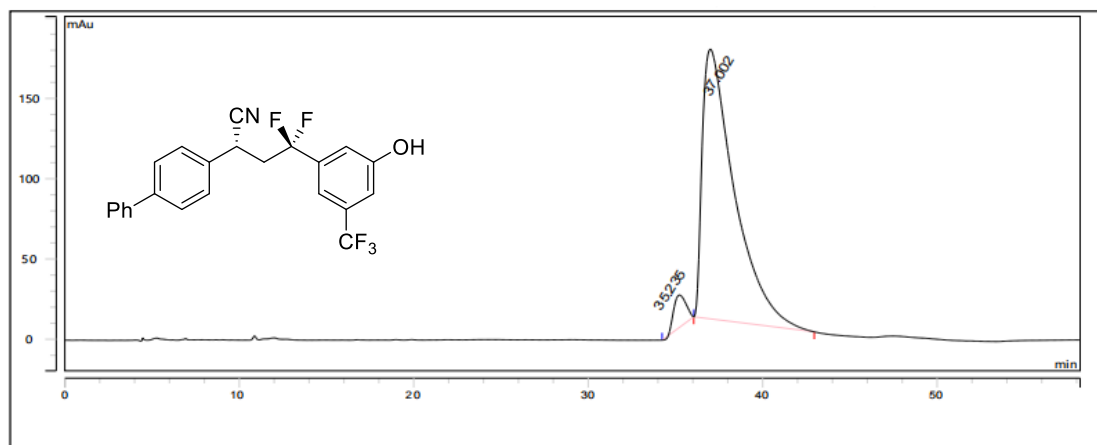
Chiral HPLC spectrum of racemic **4au**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	7.043	706.81773	0.261	70.173	49.413
2	8.270	723.60810	0.317	59.163	50.587
3		1430.42583	0.289	129.336	100.000

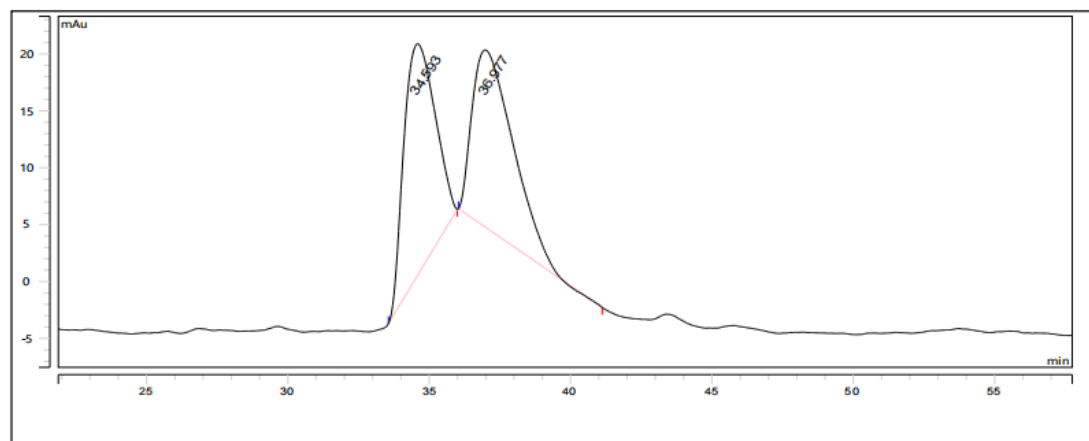
Chiral HPLC spectrum of chiral **4av**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	35.235	972.62489	1.400	20.173	4.328
2	37.002	21499.01089	3.163	168.130	95.672
3		22471.63578	2.281	188.303	100.000

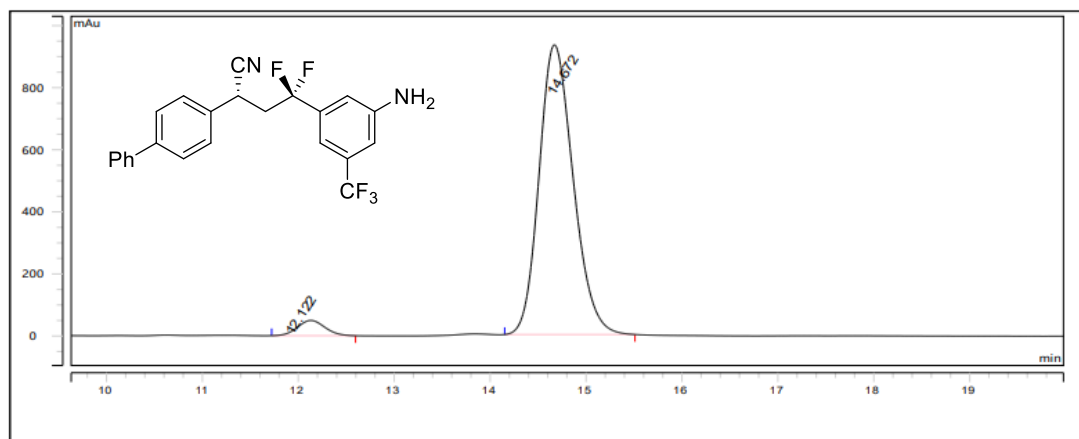
Chiral HPLC spectrum of racemic **4av**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	34.593	1561.36320	2.178	20.341	49.420
2	36.977	1598.04363	2.811	15.582	50.580
3		3159.40683	2.494	35.923	100.000

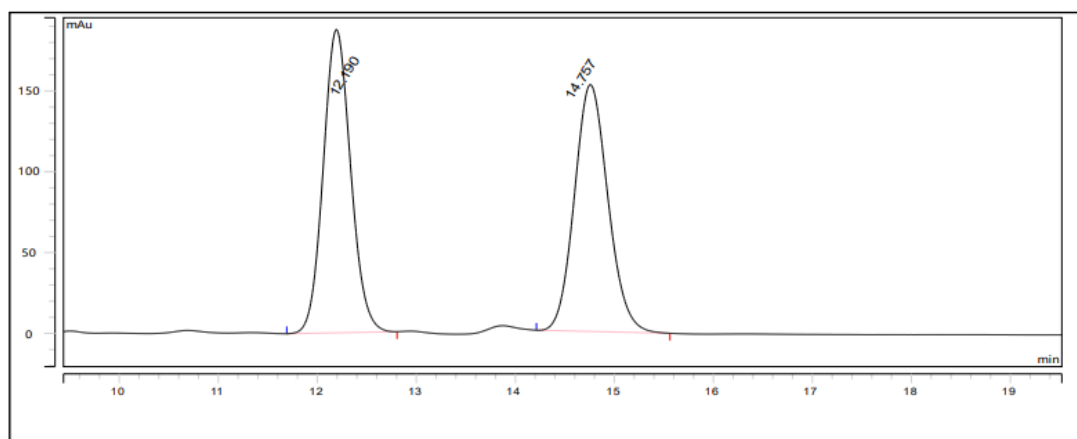
Chiral HPLC spectrum of chiral **4aw**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.122	974.49820	0.525	49.142	4.050
2	14.672	23088.70987	0.647	934.190	95.950
3		24063.20807	0.586	983.333	100.000

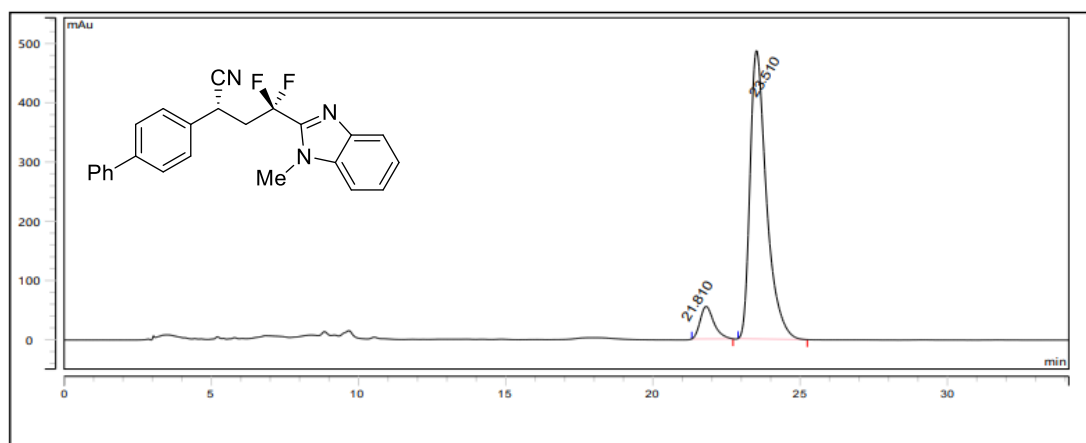
Chiral HPLC spectrum of racemic **4aw**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.190	3614.16157	0.504	187.910	50.089
2	14.757	3601.34440	0.618	152.900	49.911
3		7215.50597	0.561	340.810	100.000

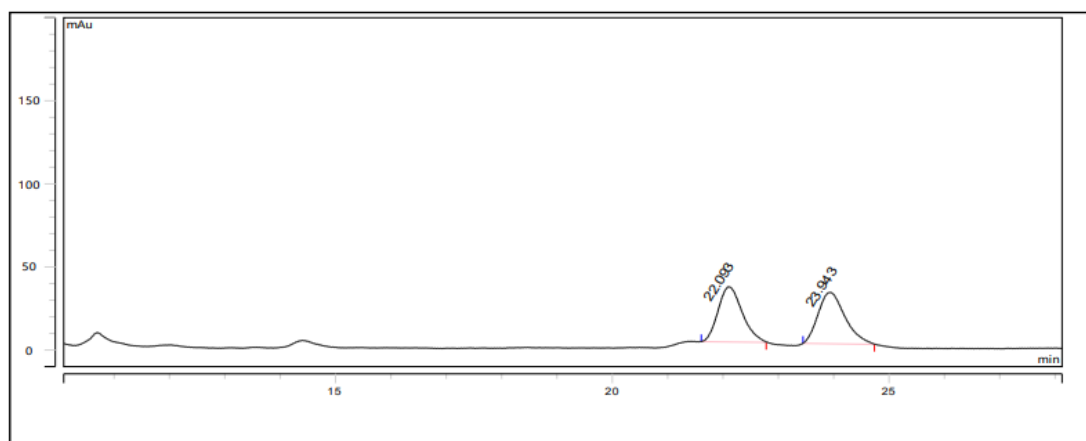
Chiral HPLC spectrum of chiral **4ax**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	21.810	1768.21160	0.823	55.099	8.557
2	23.510	18896.79419	0.968	487.725	91.443
3		20665.00579	0.895	542.825	100.000

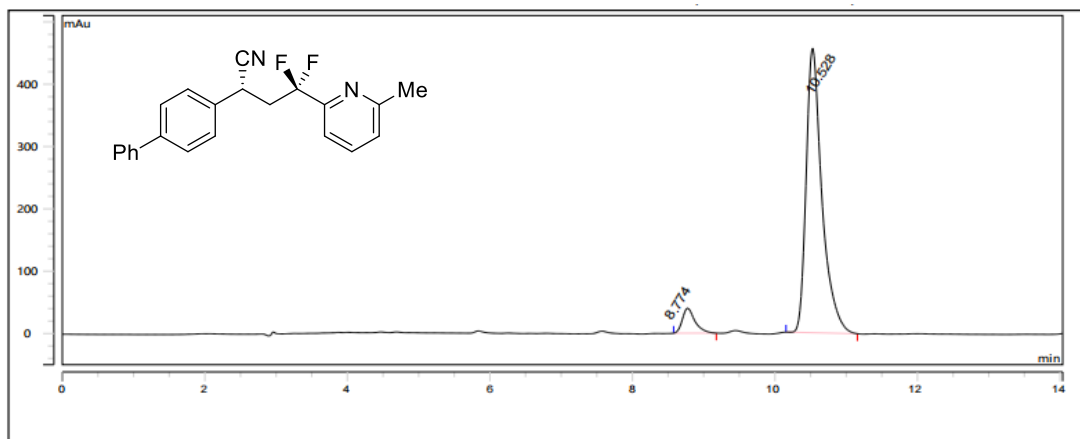
Chiral HPLC spectrum of racemic **4ax**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	22.093	1006.79405	0.797	33.452	49.019
2	23.943	1047.09744	0.891	31.059	50.981
3		2053.89149	0.844	64.511	100.000

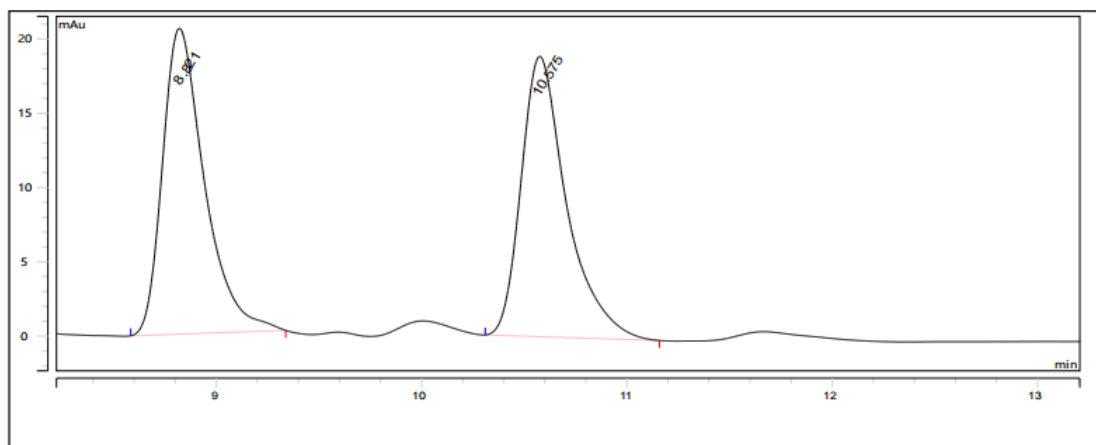
Chiral HPLC spectrum of chiral **4ay**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.774	488.97100	0.303	40.159	6.506
2	10.528	7026.93929	0.376	457.545	93.494
3		7515.91029	0.339	497.704	100.000

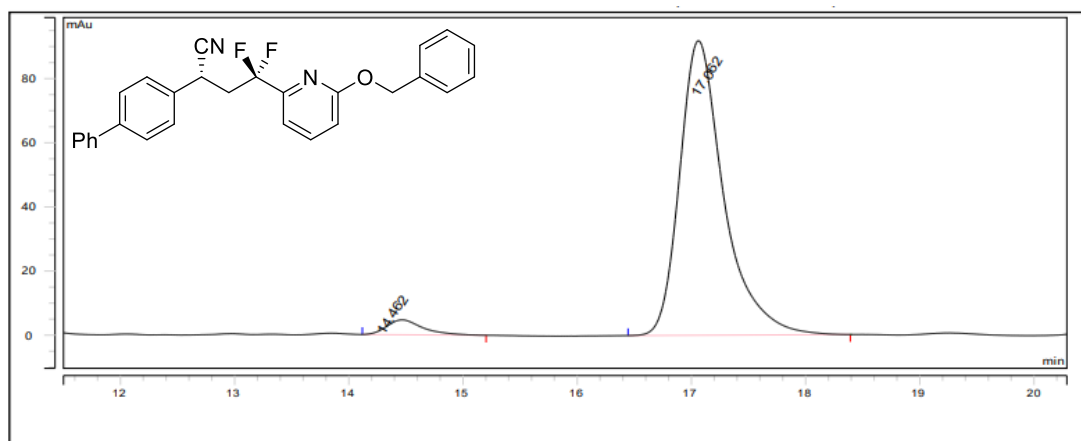
Chiral HPLC spectrum of racemic **4ay**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.821	292.32155	0.357	20.589	50.198
2	10.575	290.01141	0.378	18.875	49.802
3		582.33296	0.368	39.464	100.000

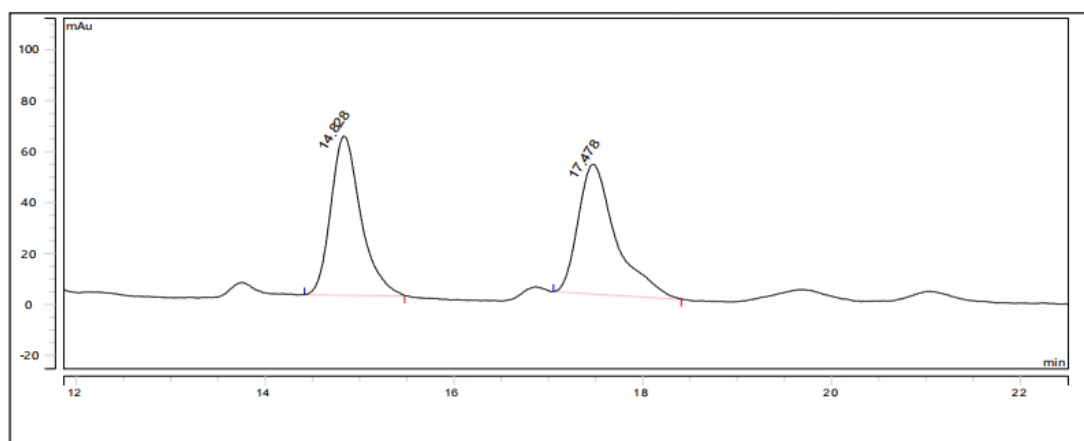
Chiral HPLC spectrum of chiral **4az**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	14.462	101.43982	0.548	4.637	3.949
2	17.062	2467.47431	0.657	91.990	96.051
3		2568.91413	0.602	96.627	100.000

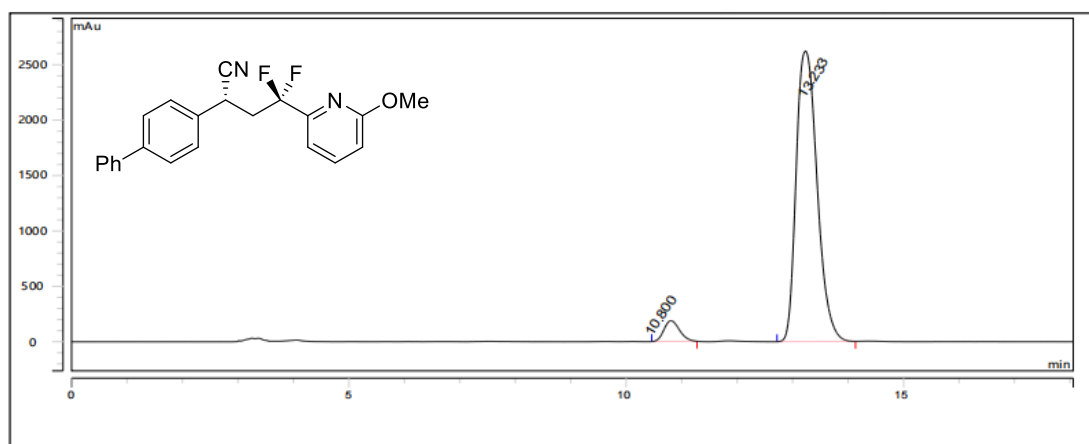
Chiral HPLC spectrum of racemic **4az**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	14.828	1384.45140	0.556	62.693	49.413
2	17.478	1417.35210	0.658	50.907	50.587
3		2801.80350	0.607	113.600	100.000

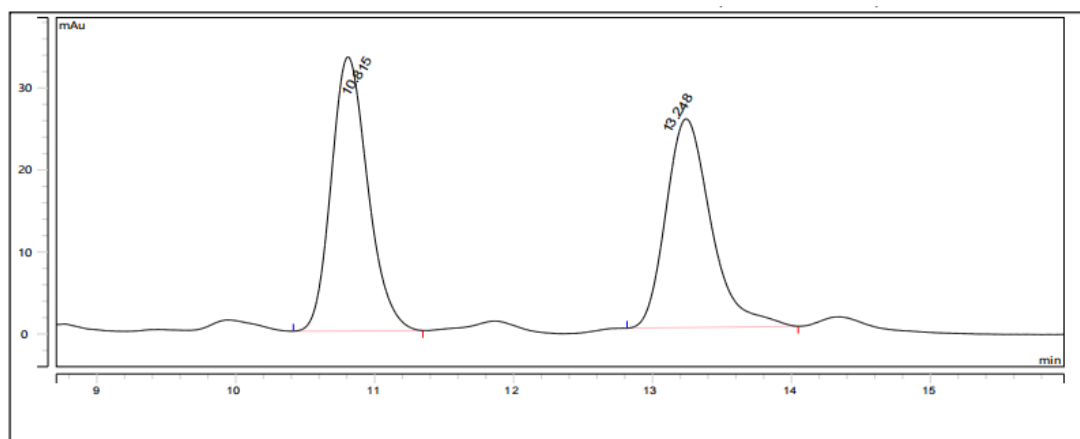
Chiral HPLC spectrum of chiral **4ba**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.800	3638.82950	0.517	187.199	5.020
2	13.233	68848.85220	0.696	2625.454	94.980
3		72487.68170	0.607	2812.653	100.000

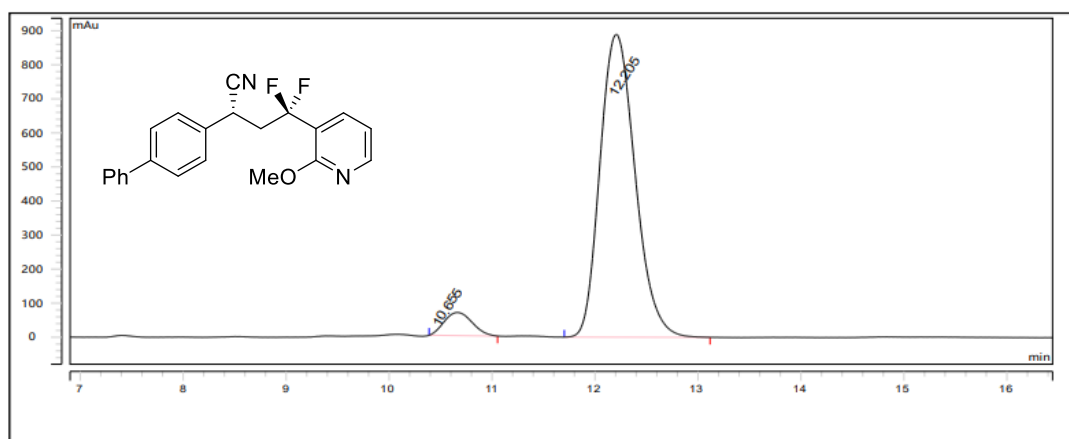
Chiral HPLC spectrum of racemic **4ba**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.815	611.17167	0.477	33.418	51.608
2	13.248	573.08184	0.573	25.438	48.392
3		1184.25351	0.525	58.857	100.000

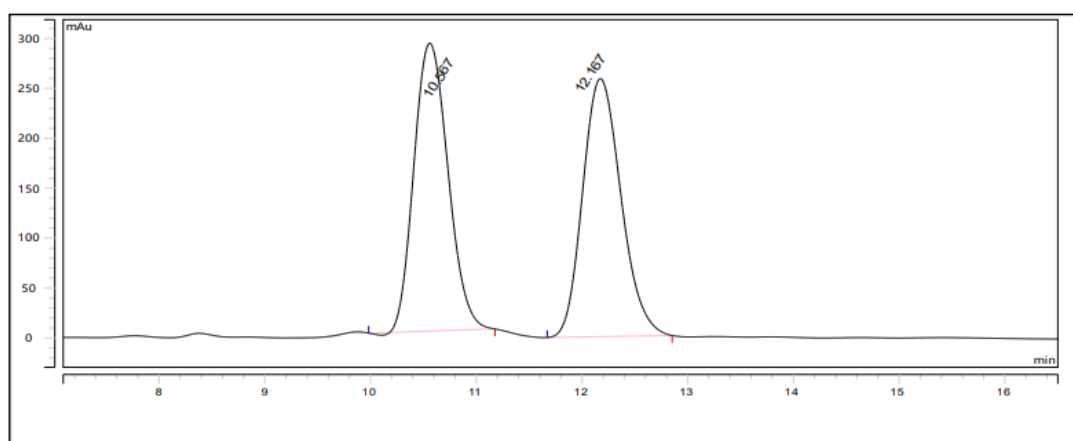
Chiral HPLC spectrum of chiral **4bb**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.655	1280.36700	0.522	67.966	5.720
2	12.205	21103.72570	0.628	889.723	94.280
3		22384.09269	0.575	957.689	100.000

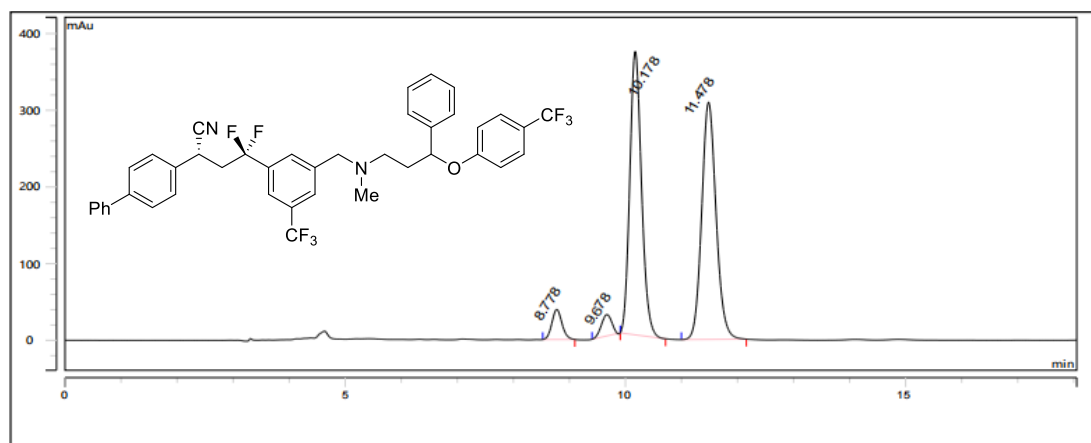
Chiral HPLC spectrum of racemic **4bb**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	10.567	6456.09185	0.603	288.494	49.781
2	12.167	6512.76740	0.667	258.499	50.219
3		12968.85926	0.635	546.993	100.000

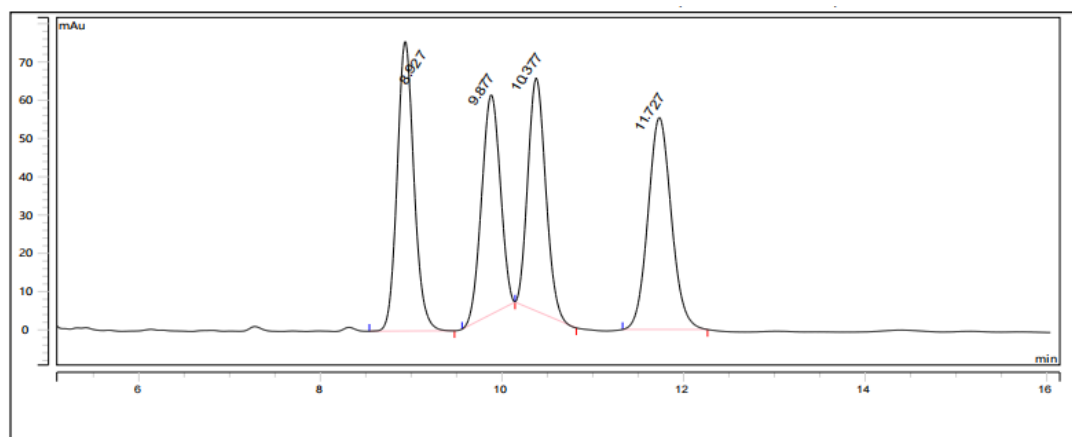
Chiral HPLC spectrum of chiral **4bc**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.778	490.95970	0.325	39.496	4.186
2	9.678	355.13440	0.354	27.843	3.028
3	10.178	5367.32021	0.377	371.863	45.764
4	11.478	5514.80203	0.460	310.025	47.022
5		11728.21634	0.379	749.226	100.000

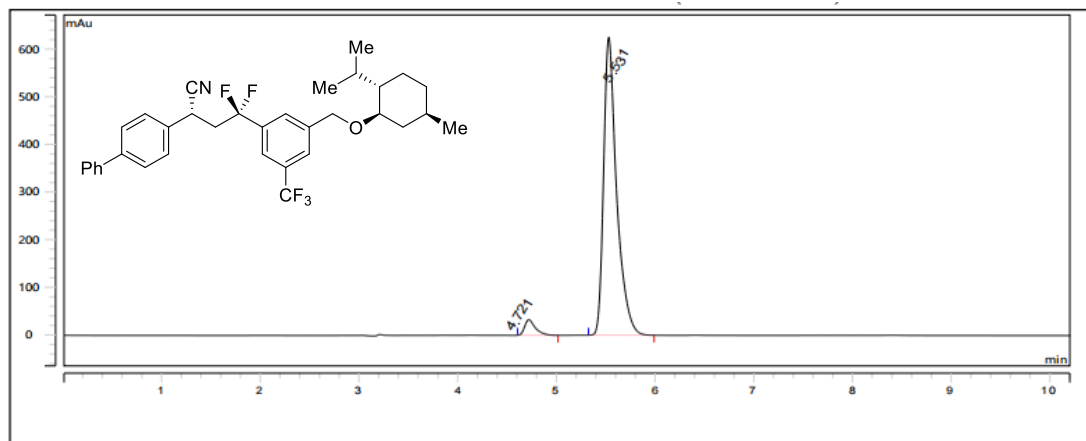
Chiral HPLC spectrum of racemic **4bc**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.927	977.92665	0.333	75.705	27.013
2	9.877	818.75715	0.386	57.472	22.616
3	10.377	831.78510	0.364	61.027	22.976
4	11.727	991.79520	0.466	55.396	27.396
5		3620.26410	0.387	249.599	100.000

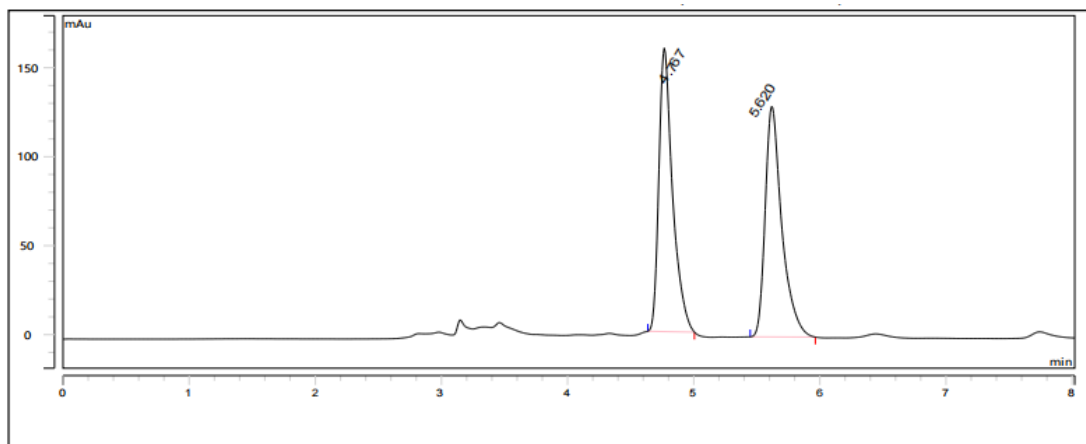
Chiral HPLC spectrum of chiral **4bd**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	4.721	244.79460	0.183	32.951	4.100
2	5.531	5725.31460	0.224	626.124	95.900
3		5970.10920	0.203	659.075	100.000

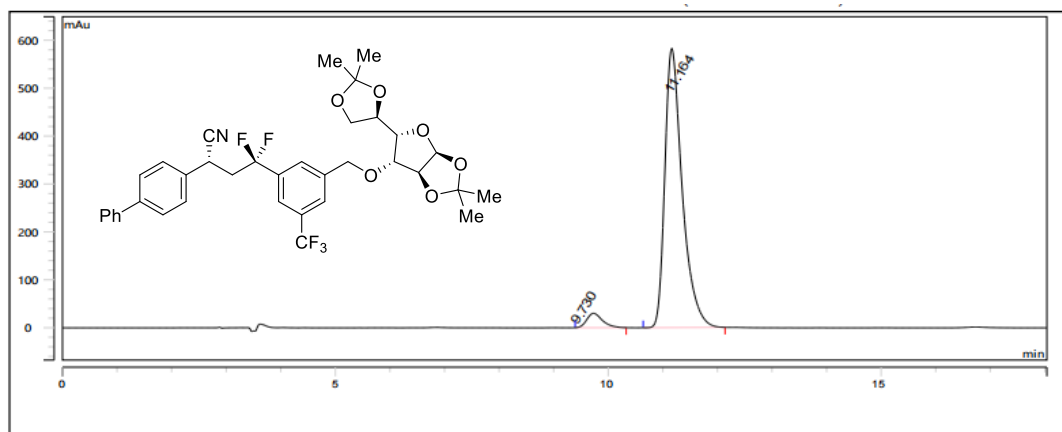
Chiral HPLC spectrum of racemic **4bd**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	4.767	1199.94205	0.186	159.379	50.283
2	5.620	1186.41260	0.225	129.683	49.717
3		2386.35465	0.206	289.062	100.000

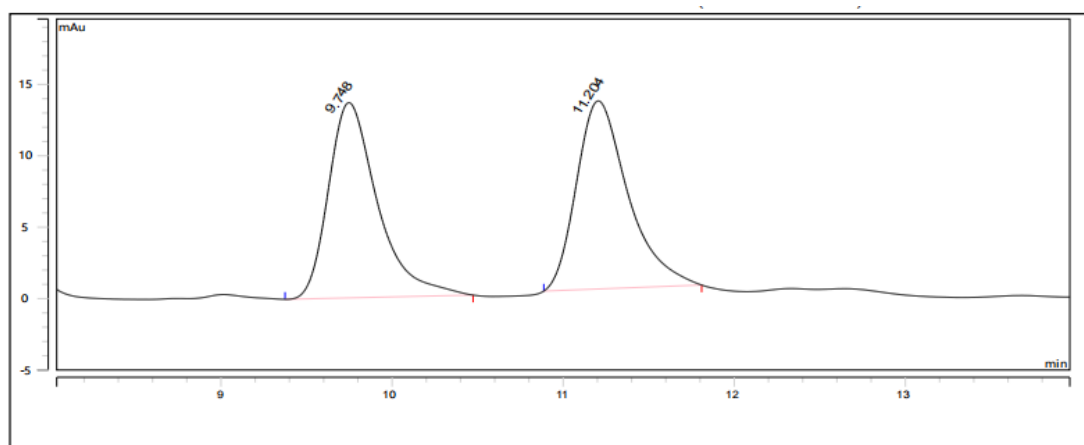
Chiral HPLC spectrum of chiral **4be**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.730	595.60608	0.508	30.119	4.414
2	11.164	12897.10078	0.554	583.215	95.586
3		13492.70685	0.531	613.334	100.000

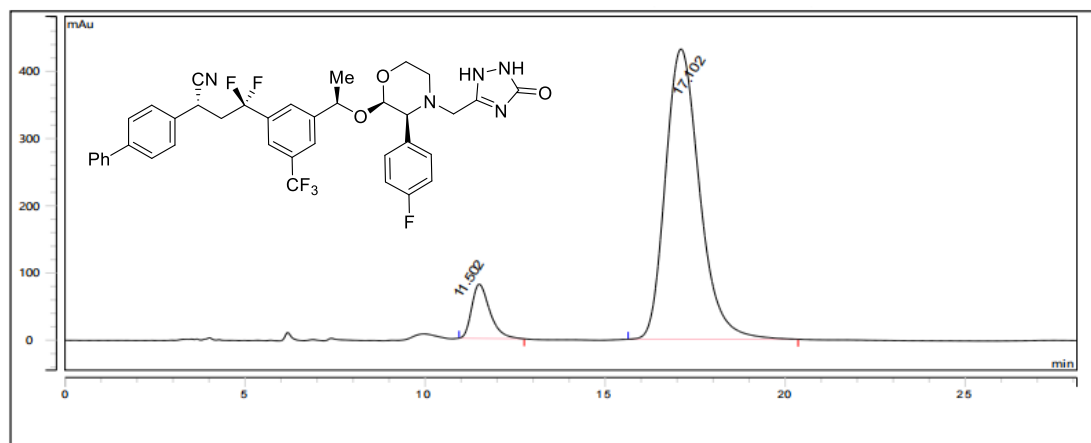
Chiral HPLC spectrum of racemic **4be**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.748	272.78375	0.497	13.672	49.678
2	11.204	276.32445	0.533	13.171	50.322
3		549.10820	0.515	26.843	100.000

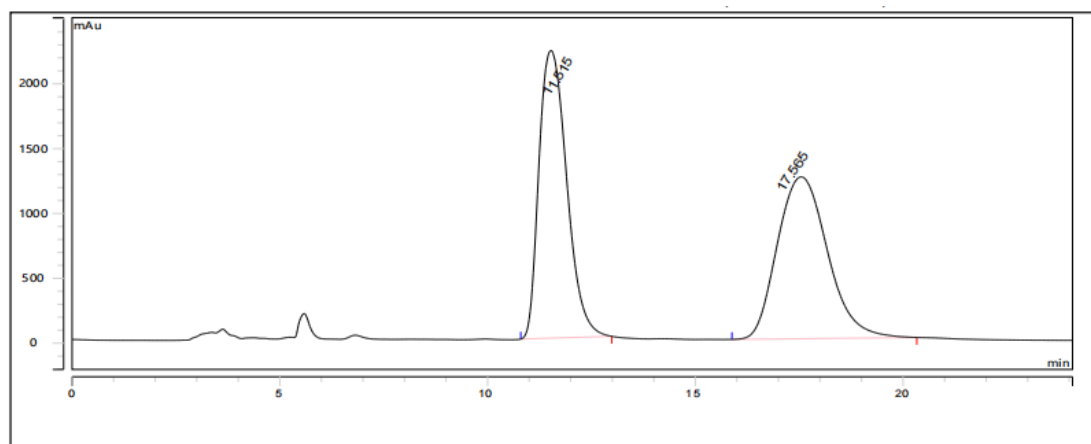
Chiral HPLC spectrum of chiral **4bf**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.502	2819.60011	0.893	80.763	9.008
2	17.102	28479.99712	1.701	432.150	90.992
3		31299.59723	1.297	512.913	100.000

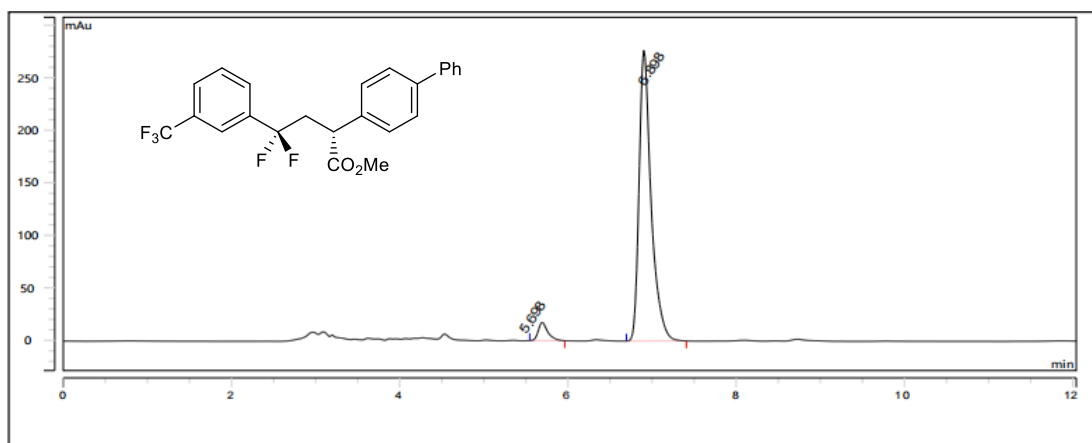
Chiral HPLC spectrum of racemic **4bf**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	11.515	103198.66511	1.246	2222.414	49.601
2	17.565	104859.87938	2.234	1248.726	50.399
3		208058.54449	1.740	3471.139	100.000

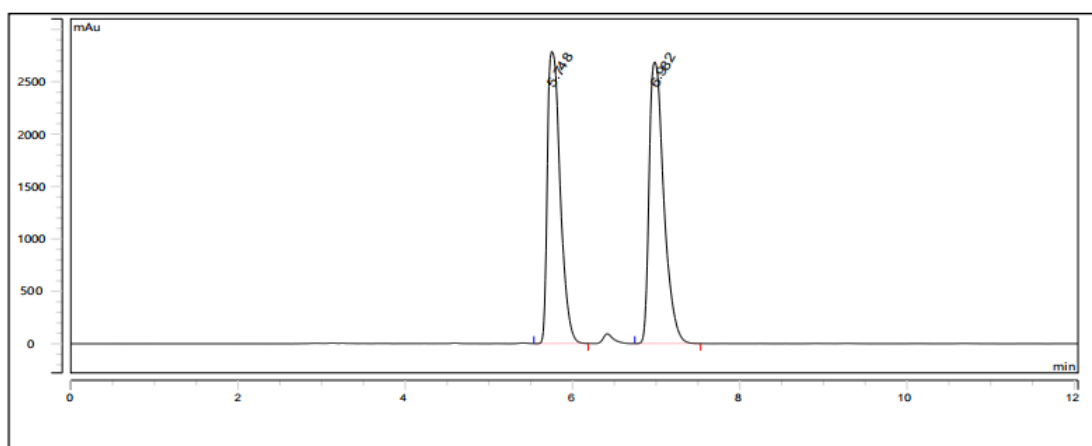
Chiral HPLC spectrum of chiral **5**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	5.698	136.30470	0.194	17.365	4.725
2	6.898	2748.51900	0.243	277.259	95.275
3		2884.82370	0.218	294.624	100.000

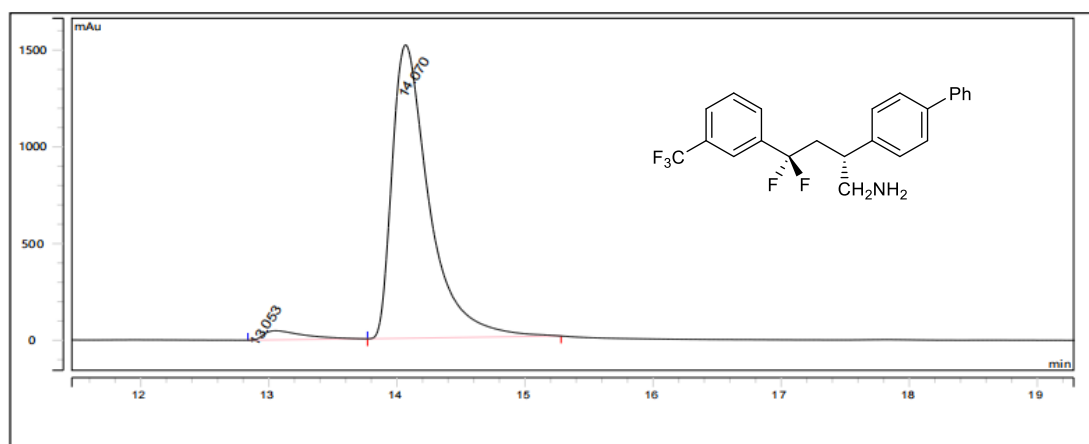
Chiral HPLC spectrum of racemic **5**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	5.748	29656.10116	0.278	2787.354	47.496
2	6.982	32783.53184	0.312	2690.544	52.504
3		62439.63301	0.295	5477.898	100.000

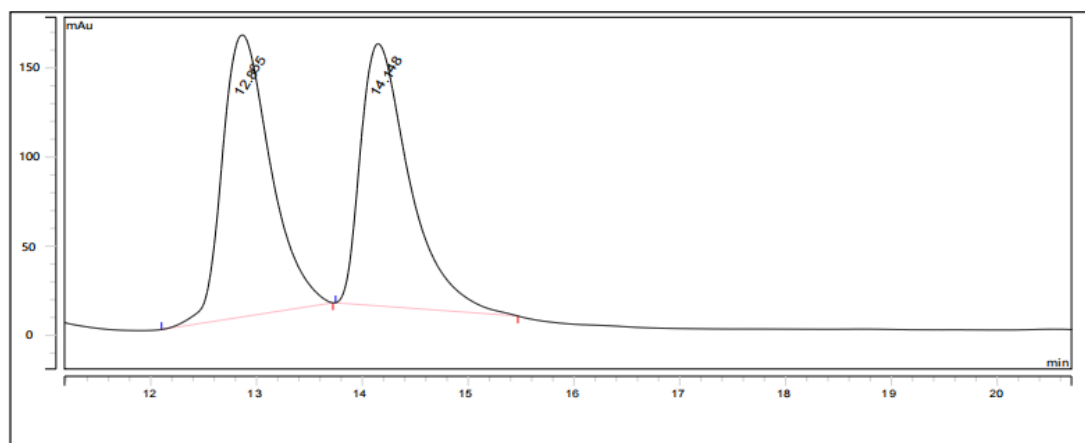
Chiral HPLC spectrum of chiral **6**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	13.053	1030.10700	0.547	47.432	3.262
2	14.070	30552.28188	0.488	1519.504	96.738
3		31582.38887	0.517	1566.935	100.000

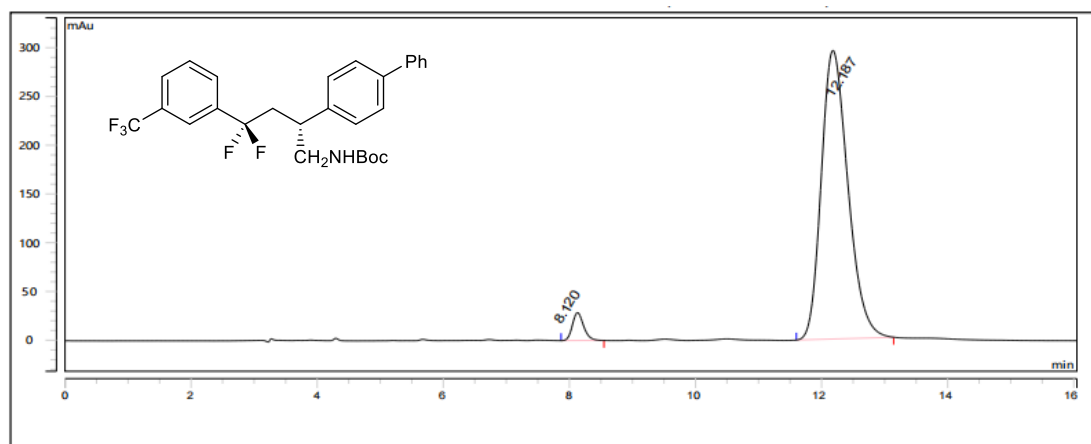
Chiral HPLC spectrum of racemic **6**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	12.865	5034.75363	0.822	158.218	51.456
2	14.148	4749.80241	0.810	147.214	48.544
3		9784.55605	0.816	305.432	100.000

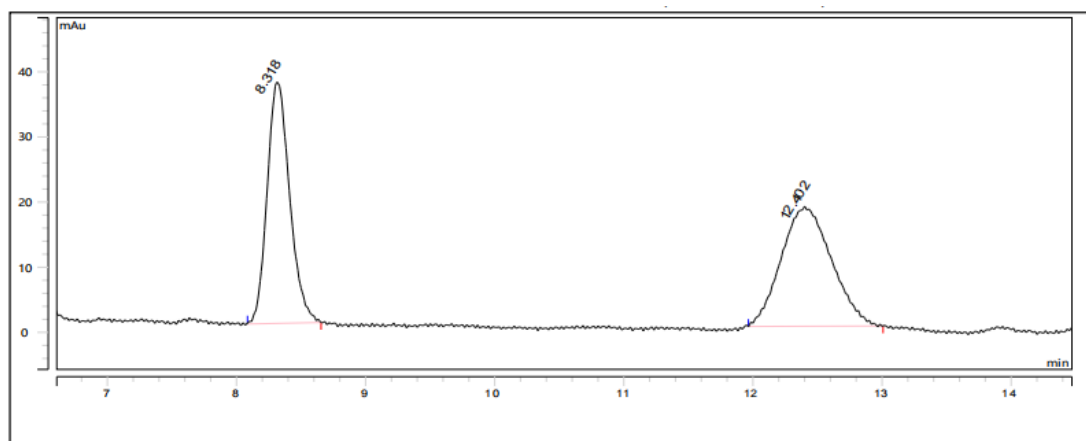
Chiral HPLC spectrum of chiral **7**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.120	353.59189	0.319	28.658	3.910
2	12.187	8690.62786	0.769	296.120	96.090
3		9044.21974	0.544	324.778	100.000

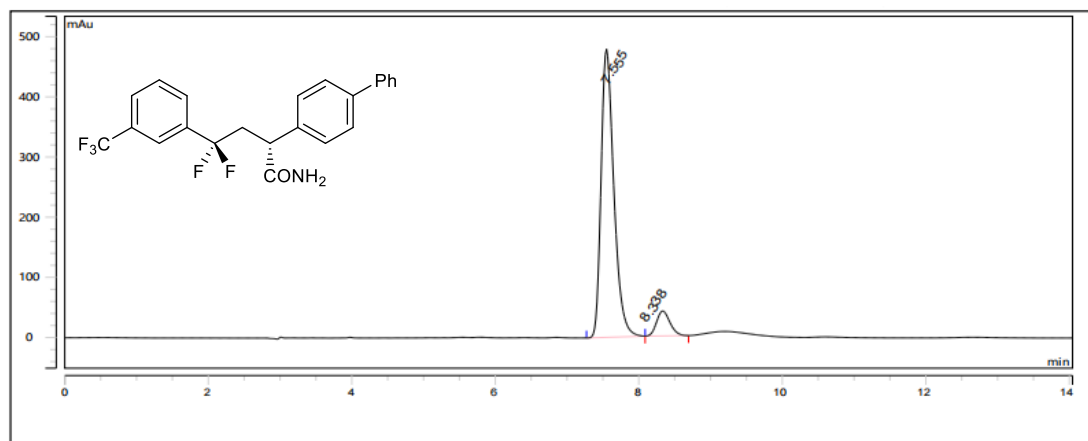
Chiral HPLC spectrum of racemic **7**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.318	449.66435	0.314	37.062	47.583
2	12.402	495.34515	0.725	18.475	52.417
3		945.00950	0.520	55.537	100.000

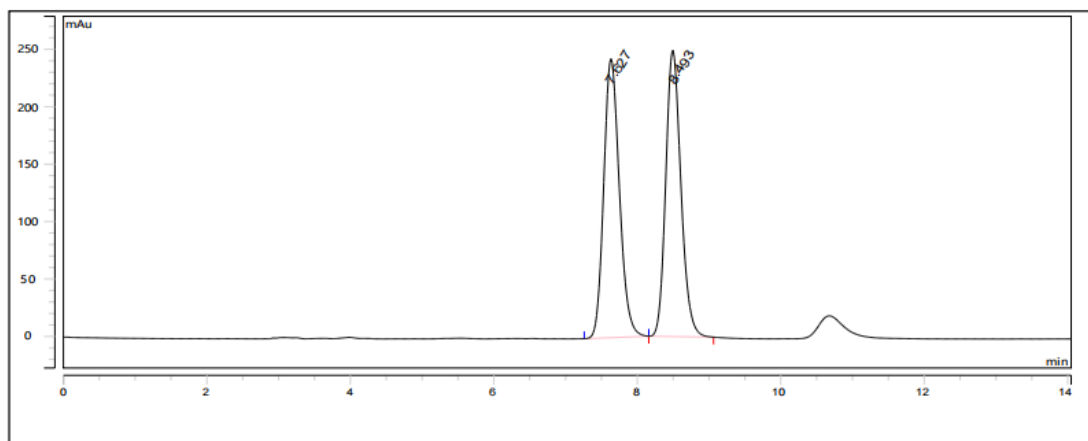
Chiral HPLC spectrum of chiral **9**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	7.555	5918.40379	0.317	479.871	91.729
2	8.338	533.63650	0.338	41.685	8.271
3		6452.04030	0.328	521.556	100.000

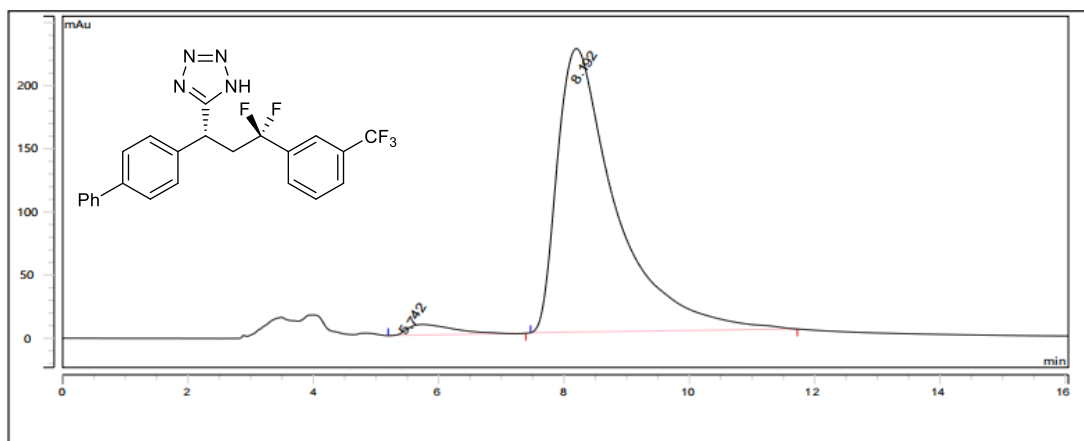
Chiral HPLC spectrum of racemic **9**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	7.627	3672.42580	0.394	243.365	50.088
2	8.493	3659.52211	0.380	250.711	49.912
3		7331.94790	0.387	494.077	100.000

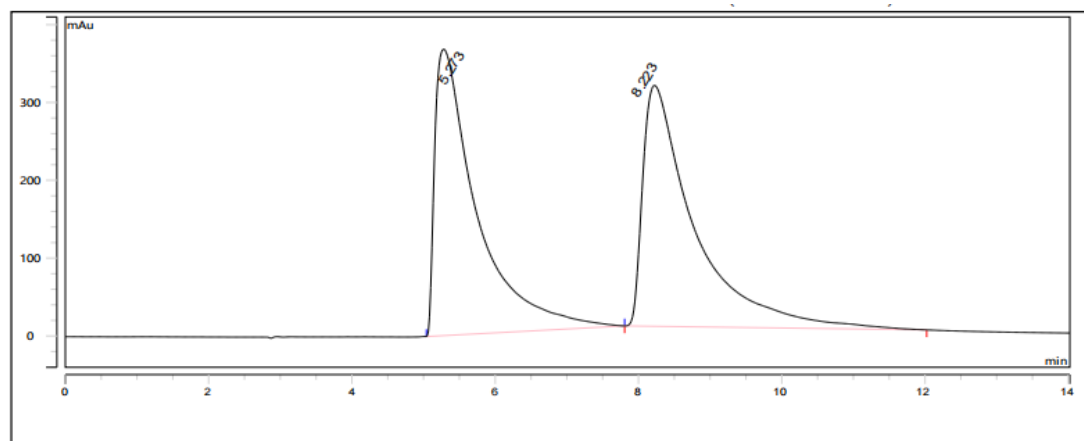
Chiral HPLC spectrum of chiral **10**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	5.742	419.67971	1.337	8.385	2.787
2	8.192	14640.41704	1.517	224.715	97.213
3		15060.09675	1.427	233.100	100.000

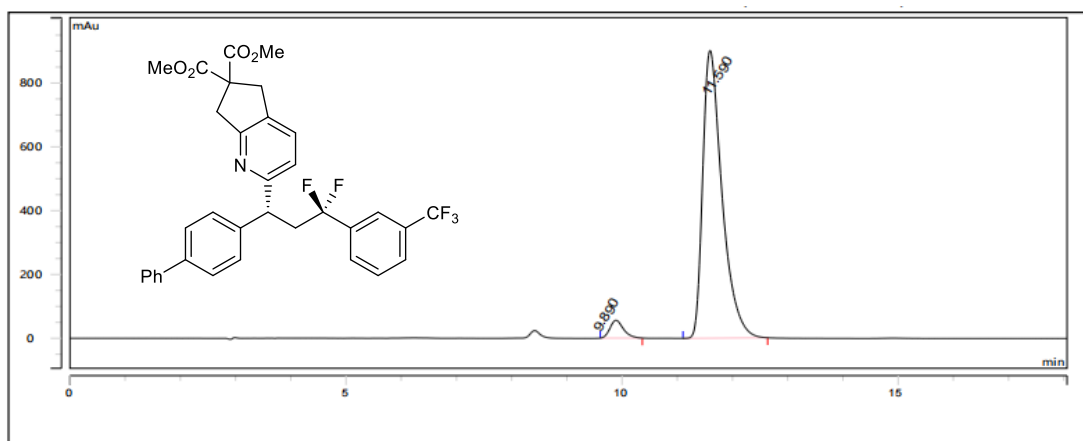
Chiral HPLC spectrum of racemic **10**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	5.273	14988.82617	0.902	368.123	49.238
2	8.223	15452.95667	1.082	309.811	50.762
3		30441.78283	0.992	677.934	100.000

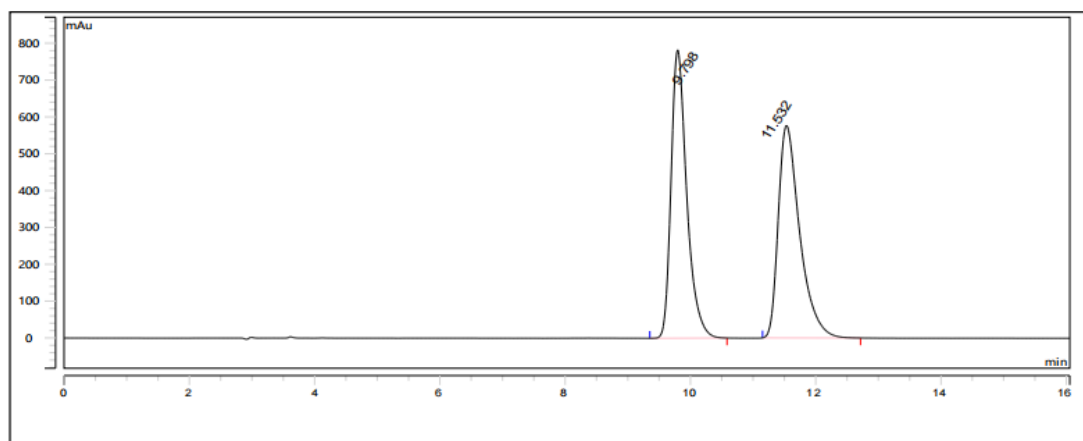
Chiral HPLC spectrum of chiral **11**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.890	943.83760	0.434	56.043	4.134
2	11.590	21889.74810	0.614	903.721	95.866
3		22833.58570	0.524	959.764	100.000

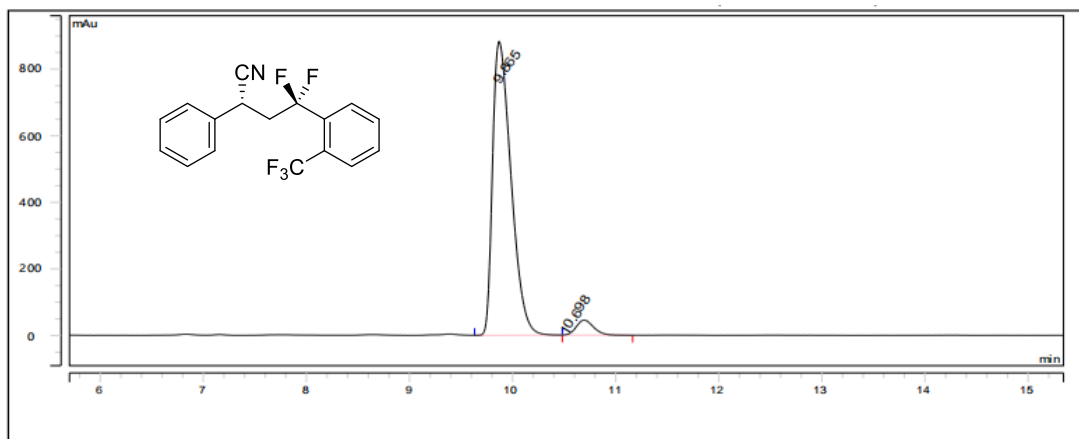
Chiral HPLC spectrum of racemic **11**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.798	13586.97119	0.438	783.865	49.824
2	11.532	13682.83792	0.598	577.173	50.176
3		27269.80912	0.518	1361.039	100.000

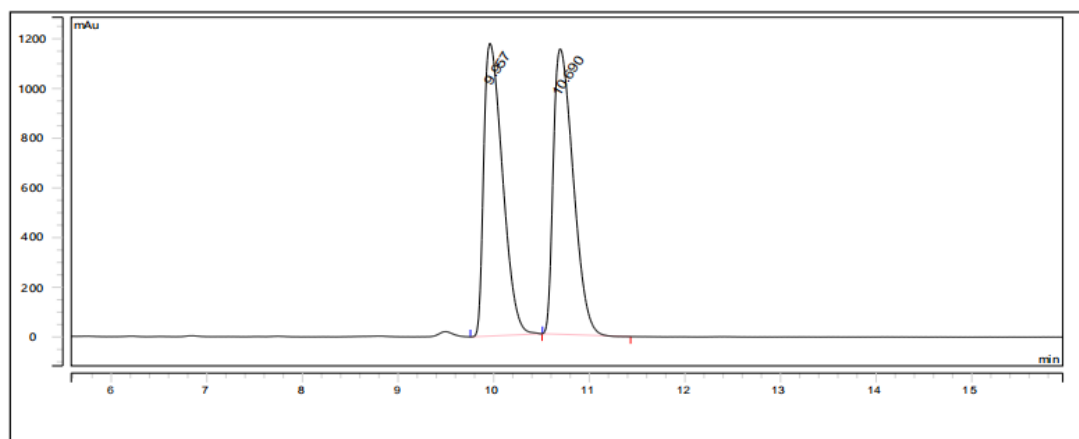
Chiral HPLC spectrum of chiral **12**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.865	10967.21209	0.329	884.424	95.433
2	10.698	524.81140	0.305	45.085	4.567
3		11492.02349	0.317	929.508	100.000

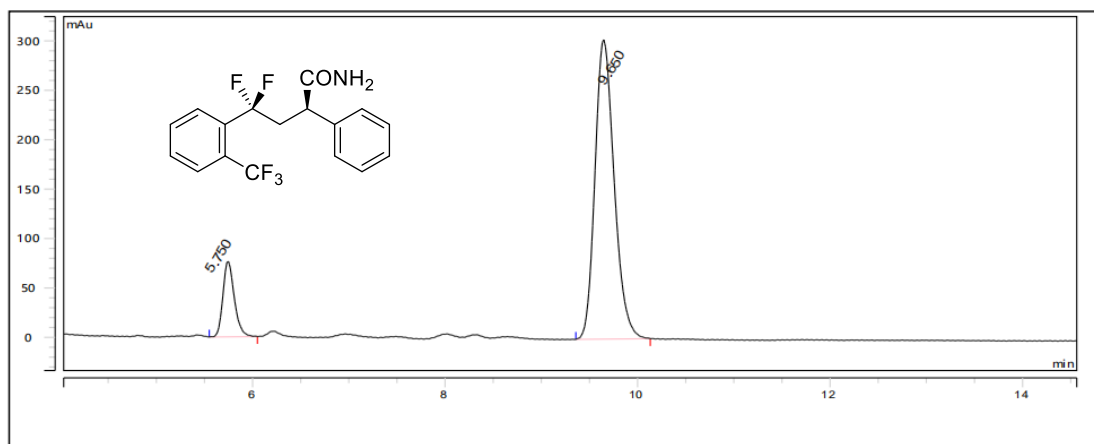
Chiral HPLC spectrum of racemic **12**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.957	16096.25850	0.367	1178.909	49.270
2	10.690	16573.08378	0.389	1149.106	50.730
3		32669.34228	0.378	2328.014	100.000

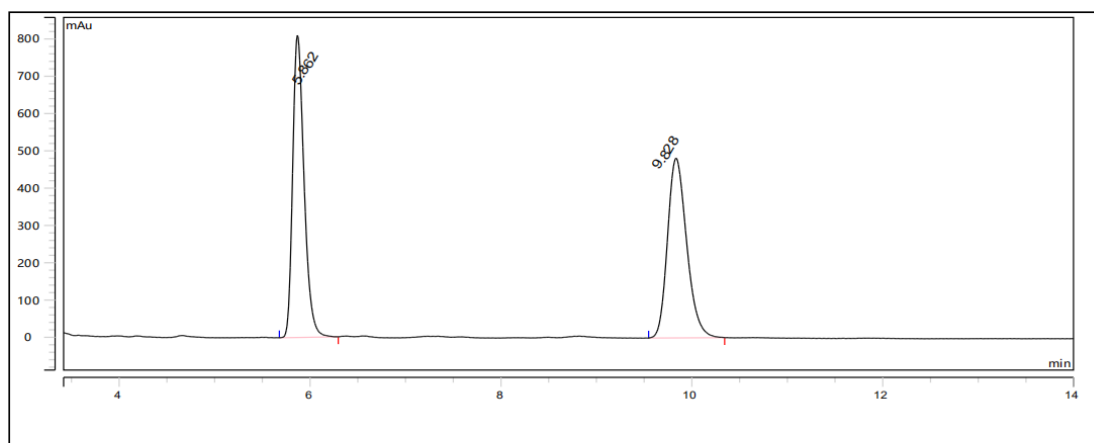
Chiral HPLC spectrum of chiral **13**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	5.750	631.32165	0.212	76.318	13.063
2	9.650	4201.44688	0.360	303.027	86.937
3		4832.76853	0.286	379.345	100.000

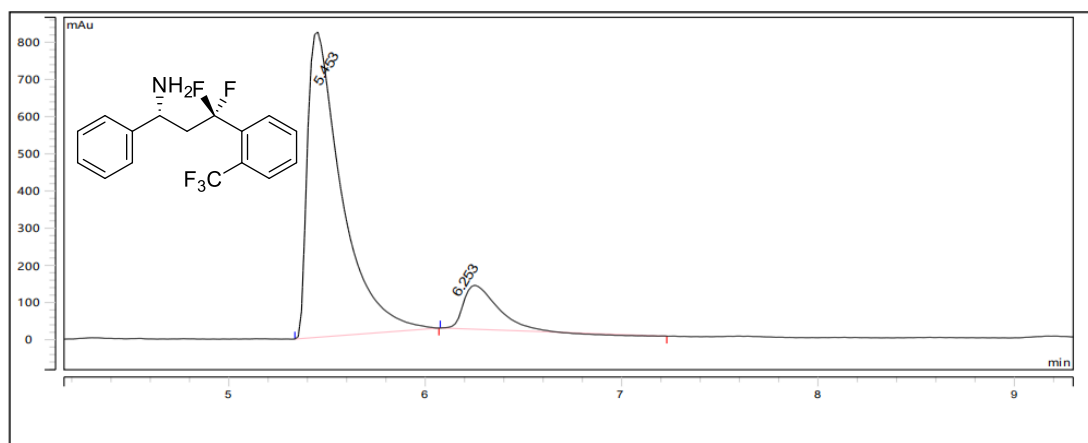
Chiral HPLC spectrum of racemic **13**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	5.862	6735.18119	0.214	812.667	50.040
2	9.828	6724.44267	0.363	482.683	49.960
3		13459.62386	0.288	1295.349	100.000

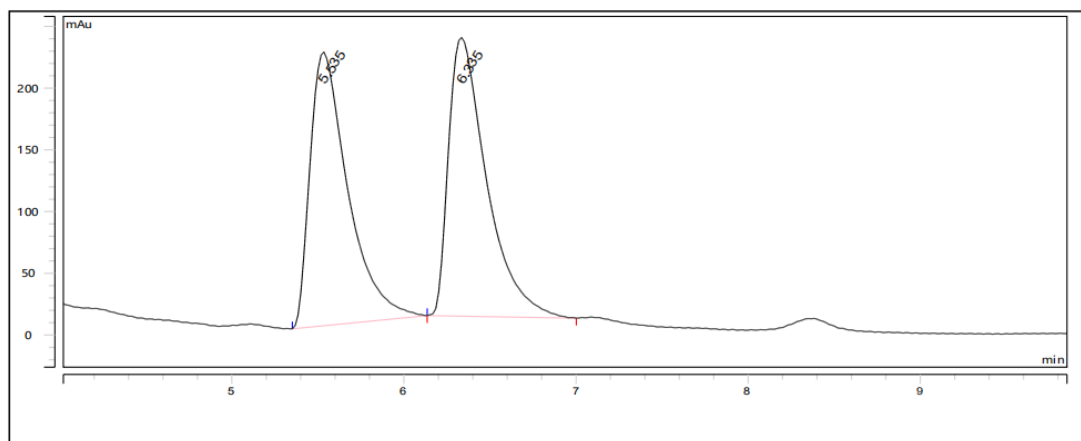
Chiral HPLC spectrum of chiral **14**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	5.453	9960.99551	0.292	821.369	87.727
2	6.253	1393.58316	0.311	118.409	12.273
3		11354.57867	0.301	939.779	100.000

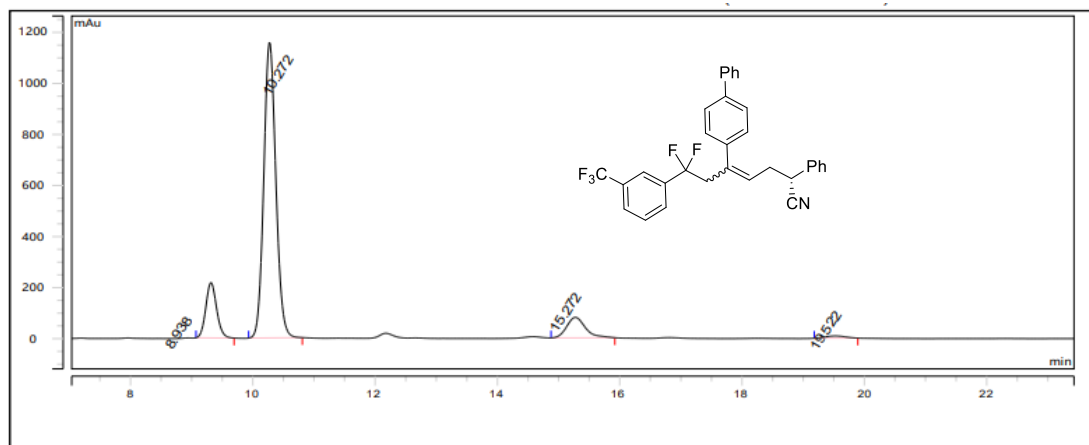
Chiral HPLC spectrum of racemic **14**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	5.535	3388.60070	0.385	221.764	49.446
2	6.335	3464.52585	0.387	225.767	50.554
3		6853.12655	0.386	447.532	100.000

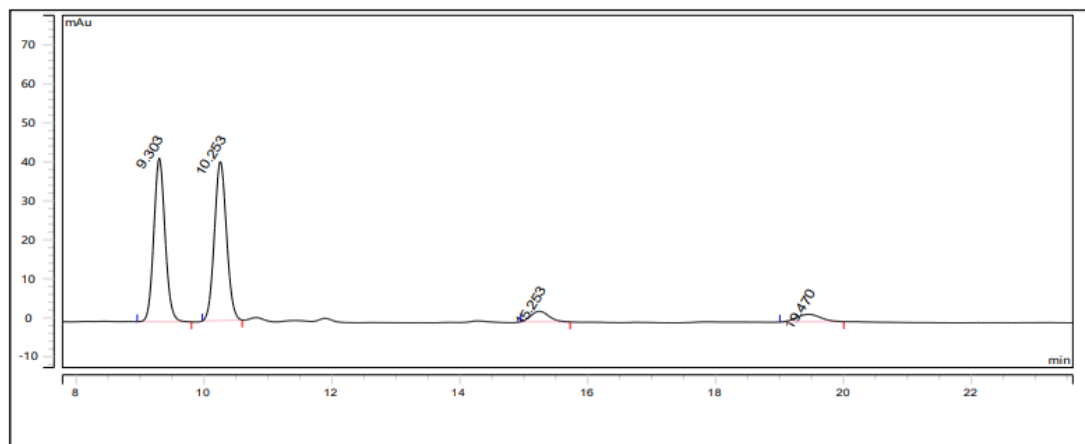
Chiral HPLC spectrum of chiral **18**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	8.938	2656.82360	1.018	0.802	13.001
2	10.272	15878.53577	0.356	1165.564	77.700
3	15.272	1705.29530	0.536	80.571	8.345
4	19.522	195.15070	0.623	8.753	0.955
5		20435.80537	0.633	1255.690	100.000

Chiral HPLC spectrum of racemic **18**



Peak list

No	Retention time	PeakArea(mAu*s)	Peak width	Peak height	Area Ratio(%)
1	9.303	514.55380	0.317	42.121	44.569
2	10.253	536.95030	0.345	40.973	46.508
3	15.253	52.89440	0.524	2.704	4.581
4	19.470	50.12385	0.688	1.949	4.342
5		1154.52235	0.469	87.746	100.000