Supporting Information

Construction of Axially Chiral 2-Arylpyrroles by Catalytic Asymmetric Suzuki-Miyaura Cross-Coupling: An Efficient Approach to Esaxerenone

Ling Jia,[a] Bing Li,[a] Xi Wang,[a] Jinfeng Zhao,[b] Jingping Qu[c] and Yuhan Zhou*[a]

[a.] State Key Laboratory of Fine Chemicals, Department of Pharmaceutical Engineering, School of Chemical Engineering, Dalian University of Technology, 2 Linggong road, Dalian 116024, China.

[b.] Instrumental Analysis Center, Dalian University of Technology, 2 Linggong road, Dalian 116024, China.

[c.] State Key Laboratory of Fine Chemicals, School of Chemical Engineering, Dalian University of Technology, 2 Linggong road, Dalian 116024, China.

E-mail: zhouyh@dlut.edu.cn (Y. Zhou)

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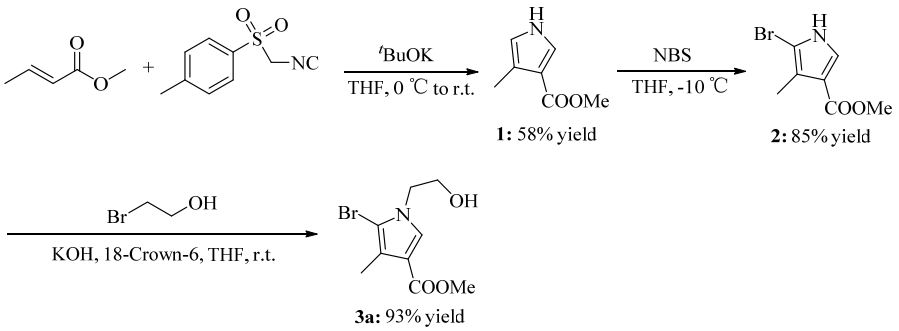
1. Synthesis of methyl 5-bromo-1-(2-hydroxyethyl)-4-methyl-1*H*-pyrrole-3-carboxylate (3a)

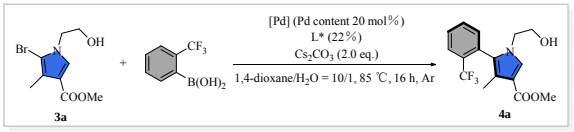
Compound **3a** was obtained by a three-step reaction. Trans-methyl crotonate and tosylmethyl isocyanide were used as starting materials, and **3a** was obtained by cyclization, bromination and *N*-hydroxylation reaction in sequence.

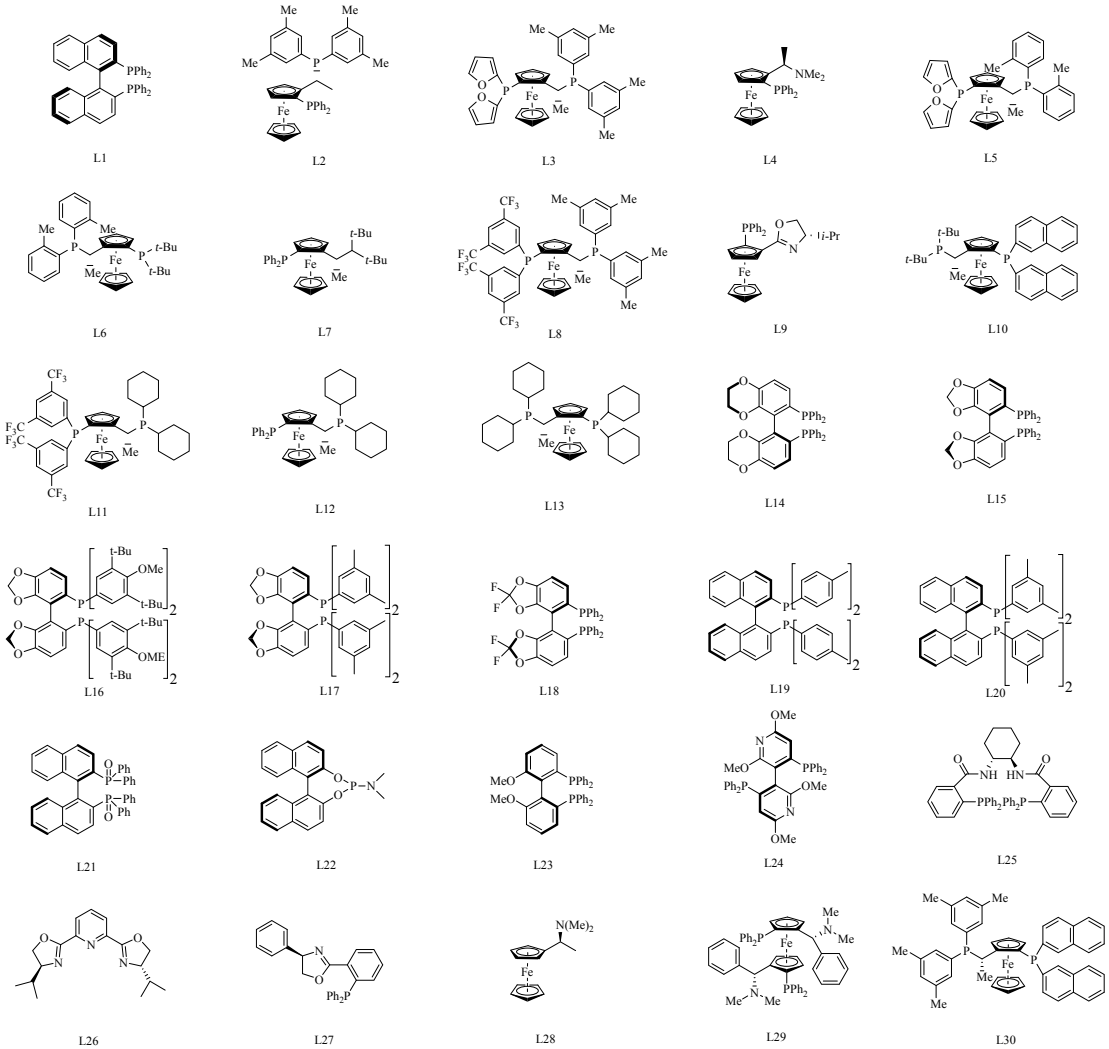


2. Additional optimization

To ensure that optimal conditions were not missed, the ligands were further screened using 1,4-dioxane/H_2O as solvent. The metal sources of $Pd(OAc)_2$ and $[Pd(C_3H_5)Cl]_2$ were carefully screened, respectively (Table S1).

Table S1 Optimization of the ligand in 1,4-dioxane/H_2O.[a]





Entry	Catalyst	Ligand	Yield[%][b]	ee[%][c]
1	$Pd(OAc)_2$	**L1**	85[d]	51
2	$Pd(OAc)_2$	**L14**	73	29
3	$Pd(OAc)_2$	**L15**	78	0
4	$Pd(OAc)_2$	**L17**	91	9
5	$Pd(OAc)_2$	**L18**	6	57
6	$Pd(OAc)_2$	**L19**	70	52
7	$Pd(OAc)_2$	**L20**	74	54
8	$Pd(OAc)_2$	**L23**	76	23
9	$Pd(OAc)_2$	**L24**	69	25
10	$Pd(OAc)_2$	**L29**	62	48
11	$Pd(OAc)_2$	**L30**	5	88
12	$Pd(OAc)_2$	**L16**	NR	
13	$Pd(OAc)_2$	**L21**	NR	

14	$Pd(OAc)_2$	**L22**		NR	
15	$Pd(OAc)_2$	**L25**		NR	
16	$Pd(OAc)_2$	**L26**		NR	
17	$Pd(OAc)_2$	**L28**		NR	
18	$Pd(OAc)_2$	**L7**		NR	
19	$Pd(OAc)_2$	**L8**		NR	
20	$Pd(OAc)_2$	**L9**		NR	
21	$Pd(OAc)_2$	**L2**		NR	
22	$Pd(OAc)_2$	**L3**		NR	
23	$[Pd(C_3H_5)Cl]_2$	**L1**	6		82
24	$[Pd(C_3H_5)Cl]_2$	**L17**	23		95
25	$[Pd(C_3H_5)Cl]_2$	**L18**	43		49
26	$[Pd(C_3H_5)Cl]_2$	**L19**	8		52
27	$[Pd(C_3H_5)Cl]_2$	**L20**	44		64
28	$[Pd(C_3H_5)Cl]_2$	**L27**	10		53
29	$[Pd(C_3H_5)Cl]_2$	**L8**	9		98
30	$[Pd(C_3H_5)Cl]_2$	**L9**	36		34
31	$[Pd(C_3H_5)Cl]_2$	**L2**	49		88
32	$[Pd(C_3H_5)Cl]_2$	**L3**	18		97
33	$[Pd(C_3H_5)Cl]_2$	**L30**	13		77
34	$[Pd(C_3H_5)Cl]_2$	**L14**		NR	
35	$[Pd(C_3H_5)Cl]_2$	**L16**		NR	
36	$[Pd(C_3H_5)Cl]_2$	**L21**		NR	
37	$[Pd(C_3H_5)Cl]_2$	**L26**		NR	
38	$[Pd(C_3H_5)Cl]_2$	**L28**		NR	
39	$[Pd(C_3H_5)Cl]_2$	**L7**		NR	
40	$[Pd(C_3H_5)Cl]_2$	**L4**		NR	
41	$[Pd(C_3H_5)Cl]_2$	**L5**		NR	
42	$[Pd(C_3H_5)Cl]_2$	**L10**		NR	
43	$[Pd(C_3H_5)Cl]_2$	**L11**		NR	
44	$[Pd(C_3H_5)Cl]_2$	**L12**		NR	
45	$[Pd(C_3H_5)Cl]_2$	**L13**		NR	

[a] Reaction conditions: Under argon atmosphere, **3a** (0.100 mmol), (2-(trifluoromethyl)phenyl)boronic acid (0.200 mmol), catalyst (Pd content 0.020 mmol), Ligand (0.022 mmol) and the Cs_2CO_3 (0.200 mmol) in the solvent 1,4-dioxane/H_2O = 10/1 (3.000 mL) at 85 °C for 16 h. [b] The yields were determined by ^1H NMR of the crude materials using *o*-phenanthroline as an internal standard. [c] Determined by HPLC analysis on a chiral stationary phase. [d] Isolated yields after chromatography.

Table S2 Optimization of the solvent.[a]

Entry	Solvent	Yield[%][b]	ee[%][c]
1	1,4-Dioxane:H_2O=10:1	49[d]	88
2	Et_2O:H_2O=10:1	88[d]	89
3	MeOH:H_2O=10:1	7	96
4	THF:H_2O=10:1	19	98
5	EA:H_2O=10:1	3	89
6	IPA:H_2O=10:1	4	96
7	MeCN:H_2O=10:1	26	78
8	Tol.:H_2O=10:1	49	95
9	Xylene:H_2O=10:1	47	96
10	Benzotrifluoride:H_2O=10:1	42	93
11	EG:H_2O=10:1	NR	
12	DME:H_2O=10:1	NR	
13	Diethylene glycol:H_2O=10:1	NR	
14	EDC:H_2O=10:1	NR	
15	Tol.	NR	
16	DMF	NR	
17	Anhydrous Et_2O	88[d]	84
18	Et_2O (with 1 eq of H_2O)	85[d]	89
19	Et_2O (with 2 eq of H_2O)	89[d]	92
20	Et_2O:H_2O=20:1	87[d]	92
21	Et_2O:H_2O=5:1	81[d]	89

[a] Reaction conditions: Under argon atmosphere, compound 3a (0.100 mmol), (2-(trifluoromethyl)phenyl)boronic acid (0.200 mmol), $[Pd(C_3H_5)Cl]_2$ (0.010 mmol), L3 (0.022 mmol) and the Cs_2CO_3 (0.200 mmol) at 85 °C for 16 h (react in heavy-wall pressure bottle). [b] The yields were determined by ^{1}H NMR of the crude materials using *o*-phenanthroline as an internal standard. [c] Determined by HPLC analysis on a chiral stationary phase. [d] Isolated yields after chromatography.

Table S3 Optimization of the base.[a]

Entry	Base	Yield[%][b]	ee[%][c]
1	KOH	57[d]	89
2	NaOH	83[d]	88
3	K_3PO_4	17	73
4	^{t}BuOK	28	92
5	Cs_2CO_3	89[d]	92
6	Et_3N	NR	
7	Pyridine	NR	

[a] Reaction conditions: Under argon atmosphere, compound 3a (0.1 mmol), (2-(trifluoromethyl)phenyl)boronic acid (0.2 mmol), $[Pd(C_3H_5)Cl]_2$ (0.01 mmol) and the L3 (0.022 mmol) in the solvent Et_2O (0.2 mmol H_2O) (3.0

mL) at 85 °C for 16 h (react in heavy-wall pressure bottle). [b] The yields were determined by ^{1}H NMR of the crude materials using *o*-phenanthroline as an internal standard. [c] Determined by HPLC analysis on a chiral stationary phase. [d] Isolated yields after chromatography.

Table S4 Optimization of the temperature.[a]

Entry	Temp.[℃]	Yield[%][b]	ee[%][c]
1	30	NR	
2	60	45	87
3	80	81	92
4	85	89[d]	92
5	90	90	87
6	100	90	82

[a] Reaction conditions: Under argon atmosphere, compound 3a (0.1 mmol), (2-(trifluoromethyl)phenyl)boronic acid (0.2 mmol), $[Pd(C_3H_5)Cl]_2$ (0.01 mmol) and the L3 (0.022 mmol) and the Cs_2CO_3 (0.200 mmol) in the solvent Et_2O (0.2 mmol H_2O) (3.0 mL) for 16 h (react in heavy-wall pressure bottle). [b] The yields were determined by ^{1}H NMR of the crude materials using *o*-phenanthroline as an internal standard. [c] Determined by HPLC analysis on a chiral stationary phase. [d] Isolated yields after chromatography.

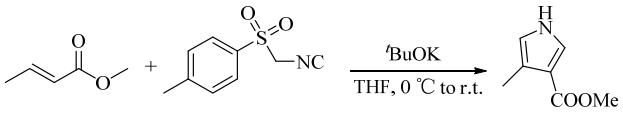
3. Materials and methods

3.1 Instruments and materials

Unless otherwise noted, all reagents were purchased from commercial sources and no purification in the further procedure is required. All solvents used were treated prior to use according to the standard methods. Column chromatography was performed on silica gel (200-300 mesh) using petroleum ether/ethyl acetate as eluent. The nuclear magnetic resonance (NMR) spectra (^{1}H NMR, ^{19}F NMR and ^{13}C NMR) were recorded on a Bruker Avance II 400 MHz, Varian DLG 400, Bruker AVANCE Ⅲ 500 and Bruker Avance NEO 600M NMR spectrometer, using chloroform-d or dimethyl sulfoxide-d6 as the solvent and tetramethylsilane (TMS) as an internal standard. The melting points were obtained by the Novel X-4 spectrometer. HRMS (ESI) were recorded on a Waters Synapt G2 *Si*. The enantiomeric excess was determined by chiral HPLC with *n*-hexane and *i*-propanol as eluents.

3.2 Experimental procedure

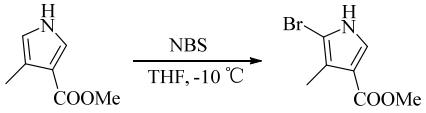
Procedure for synthesis of 1 (methyl 4-methyl-1*H*-pyrrole-3-carboxylate)[1-2]



1

Trans-methyl crotonate (20 mmol) and tosylmethyl isocyanide (20 mmol) was dissolved in THF solution (20 mL) in a reaction flask. Mixture 1 was obtained after stirring at 0 °C for 1 h. Potassium *tert*-butoxide and THF are added to the reaction flask, placed at 0 °C, and mixture 1 was slowly dripped in. It was then left to react at room temperature for 16 h. After the reaction was complete (TLC monitoring), the mixture was poured into saturated salt water, extracted three times with ethyl acetate, and washed three times with saturated salt water, and then the organic phase was dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and **1** was obtained in 58% yield.

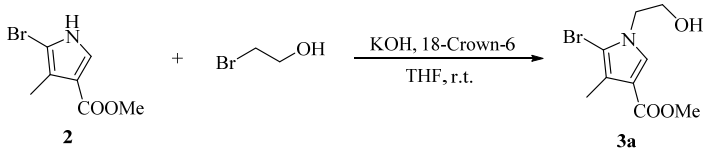
Procedure for synthesis of 2 (methyl 5-bromo-4-methyl-1*H*-pyrrole-3-carboxylate)[3]



1 **2**

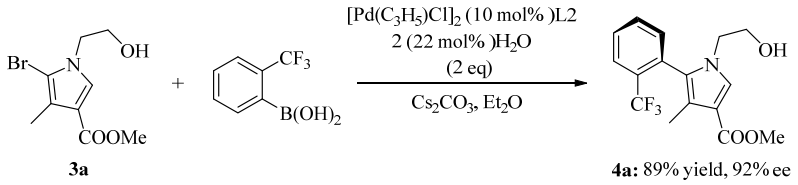
1 (10 mmol) and 20 mL of THF were sequentially added to a three-necked flask and stirred at -10 °C for 0.5 h. Subsequently, *N*-bromosuccinimide (10 mmol) was added to the system and stirred for 36 h. The reaction was quenched by saturated salt water. The system was extracted three times with ethyl acetate, washed three times with saturated salt water, and the organic phase was dried over anhydrous Na_2SO_4. Compound **2** was obtained in 85% yield after the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel and eluted with ethyl acetate and petroleum ether (1:15).

Procedure for synthesis of 3a (methyl 5-bromo-1-(2-hydroxyethyl)-4-methyl-1*H*-pyrrole-3-carboxylate)[4-5]



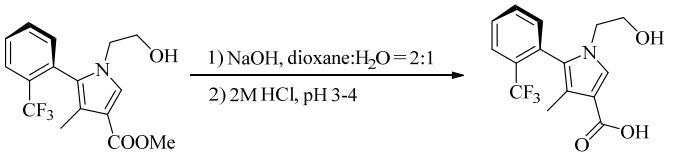
Compound **2** (5 mmol), 2-bromoethanol (10 mmol), 18-crown-6 (1 mmol) and KOH (20 mmol) were placed in a solvent (THF:H_2O = 500:1) and stirred at room temperature for 24 h. After the reaction was complete (TLC monitoring), the mixture was poured into saturated salt water, extracted three times with ethyl acetate, and washed three times with saturated salt water, and then the organic phase was dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel and eluted with ethyl acetate and petroleum ether (1:3) with a yield of 93% to obtain compound **3a**.

Procedure for synthesis of 4a ((*S*)-methyl 1-(2-hydroxyethyl)-4-methyl-5-(2-(trifluoromethyl) phenyl)-1*H*-pyrrole-3-carboxylate)



3a (0.1 mmol), (2-(trifluoromethyl)phenyl)boronic acid (0.2 mmol), $[Pd(C_3H_5)Cl]_2$ (0.01 mmol), **L22** (0.022 mmol), Cs_2CO_3 (0.2 mmol), H_2O (0.2 mmol) were added to 15 mL heavy-wall pressure bottle under argon, followed by ether (3 mL). The reaction was stirred at room temperature for 15 min and then at 85 °C for 16 h. After the reaction was complete (TLC monitoring), the mixture was poured into saturated salt water, extracted three times with ethyl acetate, and washed three times with saturated salt water, and then the organic phase was dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel and eluted with ethyl acetate and petroleum ether (1:3) to obtain compound **4a** (89% yield, 92% ee). Compound 4 was observed to exhibit a significant self-disproportionation of enantiomers (SDE) phenomenon, and in order to ensure the accuracy of enantiomer selectivity, it is necessary to collect all products when conventional silica gel columns are used for separation.[6-9]

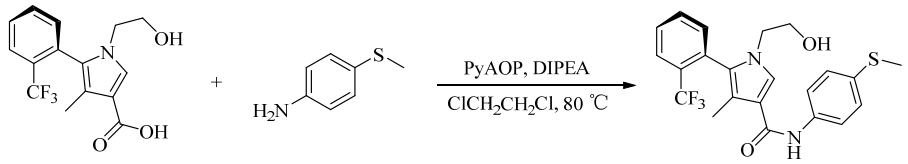
Procedure for synthesis of 5a ((*S*)-1-(2-hydroxyethyl)-4-methyl-5-(2-(trifluoromethyl) phenyl)-1*H*-pyrrole-3-carboxylic acid)



4a **5a:** 79% yield, 92% ee

Compound **4a** (1.0 mmol), NaOH (2.0 mmol) and 5 mL of solvent (1,4-dioxane:H_2O = 2:1) were sequentially added to a three-necked flask. The reaction was carried out under reflux for 2 h at 90 °C, the mixture was cooled to room temperature, and diluted hydrochloric acid was used to adjust the pH to 3-4, and the mixture was stirred for another hour. The mixture was poured into saturated salt water, extracted three times with ethyl acetate, and washed three times with saturated salt water, and then the organic phase was dried over anhydrous Na_2SO_4. Compound **5a** (79% yield, 92% ee) was obtained after the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel and eluted with methanol and dichloromethane (1:30).

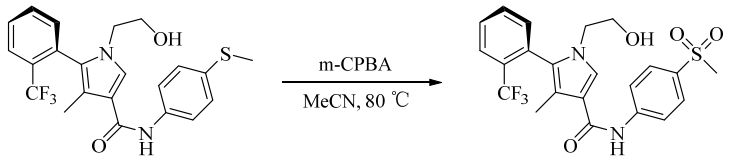
Procedure for synthesis of 6a ((*S*)-1-(2-hydroxyethyl)-4-methyl-*N*-(4-(methylthio)phenyl)-5-(2-(trifluoromethyl)phenyl)-1*H*-pyrrole-3-carboxamide)



5a **6a:** 87% yield, 92% ee

The compound **5a** (0.5 mmol), 4-(methylmercapto)aniline (0.6 mmol), PyAOP (0.75 mmol), DIPEA (2.0 mmol), 1,2-dichloroethane (5 mL) were added to 25 ml reaction bottles respectively. The reaction was placed at 80 °C and stirred for 36 h. After the reaction was complete (TLC monitoring), the mixture was poured into saturated salt water, extracted three times with ethyl acetate, and washed three times with saturated salt water, and then the organic phase was dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel and eluted with ethyl acetate and petroleum ether (1:3) to obtain compound **6a** (87% yield, 92% ee).

Procedure for synthesis of esaxerenone

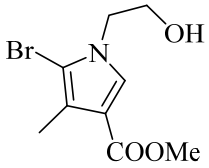


6a **Esaxerenone:** 69% yield, 92% ee

Compound **6a** (0.1 mmol), 3-chloroperoxybenzoic acid (0.3 mmol), and 3 mL of acetonitrile were sequentially added into a 10 mL reaction flask and stirred at room temperature for 16 h. After the reaction was complete (TLC monitoring), the mixture was poured into saturated salt water, extracted three times with ethyl acetate, and washed three times with $NaHCO_3$ solution, and then the organic phase was dried with anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel and eluted with methanol and dichloromethane (1:30) to obtain esaxerenone (69% yield, 92% ee).

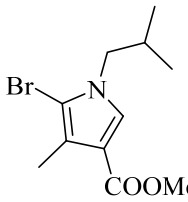
4. Experimental characterization data

Methyl 5-bromo-1-(2-hydroxyethyl)-4-methyl-1H-pyrrole-3-carboxylate (3a)



White solid; m.p. 101.2-101.5 °C; 93% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.43 (s, 1H,), 4.06 (t, *J* = 5.3 Hz, 2H), 3.89 - 3.86 (m, 2H), 3.77 (s, 3H), 2.22 (s, 3H), 1.95 (t, *J* = 5.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 127.9, 121.2, 114.4, 103.4, 61.6, 51.1, 50.9, 11.7; HRMS (ESI) *m/z*: calcd for $C_9H_{13}BrNO_3$ ($[M+H]^+$) 262.0079, found 262.0074.

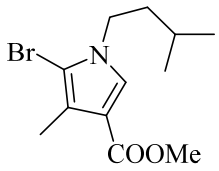
Methyl 5-bromo-1-isobutyl-4-methyl-1H-pyrrole-3-carboxylate (3b)



Light yellow oily liquid; 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31 (s, 1H), 3.78 (s, 3H), 3.67 (d, *J* = 7.3 Hz, 2H), 2.24 (s, 3H), 2.11 – 2.03 (m, 1H), 0.90 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.9, 127.4, 120.6, 113.9, 103.9, 56.3, 50.8, 29.5, 19.8, 11.8; HRMS

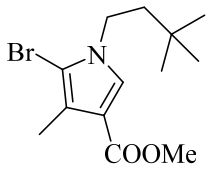
(ESI) *m/z*: calcd for $C_{11}H_{17}BrNO_2$ ($[M+H]^+$) 274.0443, found 274.0439.

Methyl 5-bromo-1-isopentyl-4-methyl-1H-pyrrole-3-carboxylate (3c)



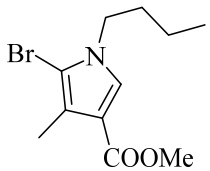
Light yellow oily liquid; 87% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.34 (s, 1H), 3.88 (t, *J* = 7.3 Hz, 2H), 3.78 (s, 3H), 2.23 (s, 3H), 1.67 - 1.55 (m, 3H), 0.95 (d, *J* = 5.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 126.5, 120.7, 114.2, 103.6, 50.8, 47.3, 39.5, 25.5, 22.4, 11.8; HRMS (ESI) *m/z*: calcd for $C_{12}H_{19}BrNO_2$ ($[M+H]^+$) 288.0599, found 288.0595.

Methyl 5-bromo-1-(3,3-dimethylbutyl)-4-methyl-1H-pyrrole-3-carboxylate (3d)



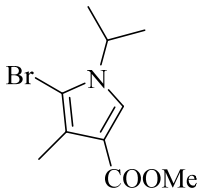
Light yellow oily liquid; 84% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.35 (s, 1H), 3.87 (t, *J* = 8.5 Hz, 2H), 3.78 (s, 3H), 2.23 (s, 3H), 1.62 (t, *J* = 8.5 Hz, 2H), 0.98 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.8, 126.4, 120.7, 114.2, 103.5, 50.8, 45.8, 44.7, 29.9, 29.2, 11.7; HRMS (ESI) *m/z*: calcd for $C_{13}H_{21}BrNO_2$ ($[M+H]^+$) 302.0756, found 302.0750.

Methyl 5-bromo-1-butyl-4-methyl-1H-pyrrole-3-carboxylate (3e)



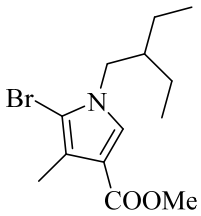
Light yellow oily liquid; 79% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.33 (s, 1H), 3.87 (t, *J* = 7.2 Hz, 2H), 3.78 (s, 3H), 2.24 (s, 3H), 1.74 - 1.68 (m, 2H), 1.36 - 1.29 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 126.7, 120.6, 114.1, 103.6, 50.8, 48.7, 32.6, 19.6, 13.6, 11.7; HRMS (ESI) *m/z*: calcd for $C_{11}H_{17}BrNO_2$ ($[M+H]^+$) 274.0443, found 274.0434.

Methyl 5-bromo-1-isopropyl-4-methyl-1H-pyrrole-3-carboxylate (3f)



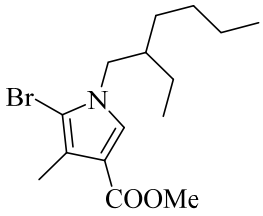
Light yellow oily liquid; 95% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44 (s, 1H), 4.47 (hept, *J* = 6.8 Hz, 1H), 3.78 (d, *J* = 1.7 Hz, 3H), 2.25 (s, 3H), 1.41 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 122.8, 120.3, 114.3, 103.4, 50.7, 49.7, 23.0, 11.6; HRMS (ESI) *m/z*: calcd for $C_{10}H_{15}BrNO_2$ ($[M+H]^+$) 260.0286, found 260.0282.

Methyl 5-bromo-1-(2-ethylbutyl)-4-methyl-1H-pyrrole-3-carboxylate (3g)



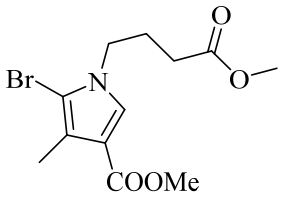
Light yellow oily liquid; 89% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31 (s, 1H), 3.78 (s, 3H), 3.75 (d, *J* = 7.5 Hz, 2H), 2.24 (s, 3H), 1.77 - 1.70 (m, 1H), 1.35 - 1.24 (m, 4H), 0.89 (t, *J* = 7.5 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 127.4, 120.6, 114.0, 104.0, 52.4, 50.7, 41.4, 23.0, 11.8, 10.5; HRMS (ESI) *m/z*: calcd for $C_{13}H_{21}BrNO_2$ ($[M+H]^+$) 302.0756, found 302.0745.

Methyl 5-bromo-1-(2-ethylhexyl)-4-methyl-1H-pyrrole-3-carboxylate (3h)



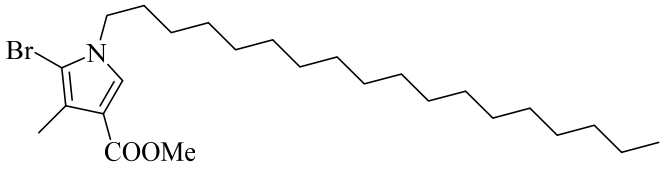
Light yellow oily liquid; 83% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.30 (s, 1H), 3.79 (s, 3H), 3.78 - 3.71 (m, 2H), 2.24 (s, 3H), 1.82 - 1.77 (m, 1H), 1.33 - 1.21 (m, 8H), 0.90 - 0.87 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.0, 127.5, 120.6, 114.0, 104.0, 52.8, 50.8, 40.0, 30.2, 28.4, 23.5, 22.9, 14.0, 11.8, 10.5; HRMS (ESI) *m/z*: calcd for $C_{15}H_{25}BrNO_2$ ($[M+H^+]$) 330.1069, found 330.1060.

Methyl 5-bromo-1-(4-methoxy-4-oxobutyl)-4-methyl-1H-pyrrole-3-carboxylate (3i)



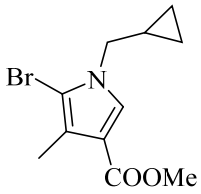
Light yellow oily liquid; 79% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.34 (s, 1H), 3.97 (t, *J* = 7.0 Hz, 2H), 3.79 (s, 3H), 3.69 (s, 3H), 2.31 (t, *J* = 7.2 Hz, 2H), 2.23 (s, 3H), 2.09 - 2.04 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 172.9, 164.8, 126.9, 121.0, 114.5, 103.6, 51.8, 50.9, 47.9, 30.4, 25.7, 11.8; HRMS (ESI) *m/z*: calcd for $C_{12}H_{16}BrNO_4Na$ ($[M+Na]^+$) 340.0160, found 340.0152.

Methyl 5-bromo-4-methyl-1-octadecyl-1H-pyrrole-3-carboxylate (3j)



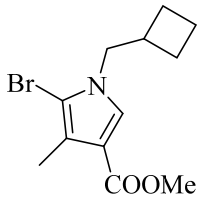
Light yellow oily liquid; 81% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.25 (s, 1H), 3.77 (t, *J* = 7.3 Hz, 2H), 3.70 (s, 3H), 2.16 (s, 3H), 1.66 - 1.62 (m, 2H), 1.18 (s, 30H), 0.80 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm, three carbons missing): 163.9, 125.7, 119.6, 113.1, 102.6, 49.7, 48.0, 30.9, 29.6, 28.7, 28.7, 28.65, 28.62, 28.5, 28.43, 28.37, 28.1, 25.4, 21.7, 13.1, 10.9, 10.8; HRMS (ESI) *m/z*: calcd for $C_{25}H_{45}BrNO_2$ ($[M+H]^+$) 470.2634, found 470.2623.

Methyl 5-bromo-1-(cyclopropylmethyl)-4-methyl-1H-pyrrole-3-carboxylate (3k)



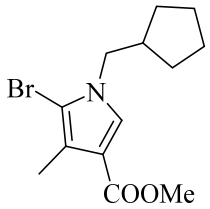
Light yellow oily liquid; 87% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.46 (s, 1H), 3.79 (s, 3H), 3.73 (d, *J* = 7.1 Hz, 2H), 2.25 (s, 3H), 1.25 - 1.18 (m, 1H), 0.66 - 0.62 (m, 2H), 0.38 - 0.35 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 126.4, 120.6, 114.2, 103.5, 53.3, 50.8, 11.8, 11.2, 4.0; HRMS (ESI) *m/z*: calcd for $C_{11}H_{15}BrNO_2$ ($[M+H]^+$) 272.0286, found 272.0283.

Methyl 5-bromo-1-(cyclobutylmethyl)-4-methyl-1H-pyrrole-3-carboxylate (3l)



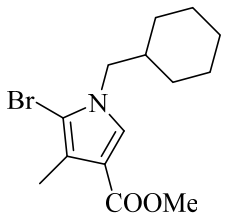
Light yellow oily liquid; 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31 (s, 1H), 3.88 (d, *J* = 7.3 Hz, 2H), 3.78 (s, 3H), 2.78 - 2.67 (m, 1H), 2.23 (s, 3H), 2.09 - 2.02 (m, 2H), 1.95 - 1.83 (m, 2H), 1.80 - 1.71 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 165.0, 126.6, 120.5, 114.1, 103.7, 53.8, 50.8, 35.7, 25.9, 18.2, 11.8; HRMS (ESI) *m/z*: calcd for $C_{12}H_{17}BrNO_2$ ($[M+H]^+$) 286.0443, found 286.0435.

Methyl 5-bromo-1-(cyclopentylmethyl)-4-methyl-1H-pyrrole-3-carboxylate (3m)



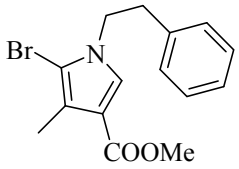
Light yellow oily liquid; 95% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.34 (s, 1H), 3.90 - 3.78 (m, 2H), 3.78 (s, 3H), 2.36 - 2.28 (m, 1H), 2.24 (s, 3H), 1.76 - 1.64 (m, 4H), 1.57 (d, *J* = 7.5 Hz, 2H), 1.27 - 1.21 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 127.0, 120.5, 114.0, 103.8, 53.6, 50.8, 40.8, 30.1, 24.8, 11.8; HRMS (ESI) *m/z*: calcd for $C_{13}H_{19}BrNO_2$ ($[M+H]^+$) 300.0599, found 300.0595.

Methyl 5-bromo-1-(cyclohexylmethyl)-4-methyl-1H-pyrrole-3-carboxylate (3n)



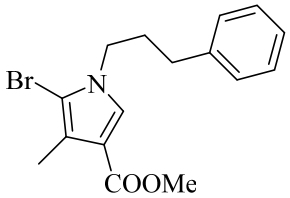
Light yellow oily liquid; 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.29 (s, 1H), 3.78 (s, 3H), 3.69 (d, *J* = 7.3 Hz, 2H), 2.24 (s, 3H), 1.74 - 1.58 (m, 6H), 1.23 - 1.13 (m, 3H), 0.98 - 0.90 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 127.5, 120.5, 113.9, 104.0, 55.2, 50.8, 38.7, 30.5, 26.2, 25.6, 11.8; HRMS (ESI) *m/z*: calcd for $C_{14}H_{21}BrNO_2$ ($[M+H]^+$) 314.0756, found 314.0752.

Methyl 5-bromo-4-methyl-1-phenethyl-1H-pyrrole-3-carboxylate (3o)



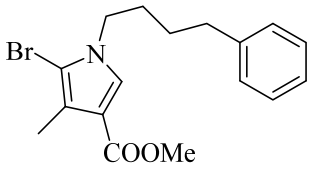
Light yellow oily liquid; 82% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.28 (t, *J* = 7.2 Hz, 2H), 7.25 - 7.19 (m, 2H), 7.15 - 7.03 (m, 2H), 4.07 (t, *J* = 7.6 Hz, 2H), 3.75 (s, 3H), 2.99 (t, *J* = 7.6 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.8, 137.4, 128.8, 128.7, 127.0, 126.9, 121.0, 114.2, 103.4, 50.8, 50.5, 37.3, 11.8; HRMS (ESI) *m/z*: calcd for $C_{15}H_{17}BrNO_2$ ($[M+H]^+$) 322.0443, found 322.0434.

Methyl 5-bromo-4-methyl-1-(3-phenylpropyl)-1H-pyrrole-3-carboxylate (3p)



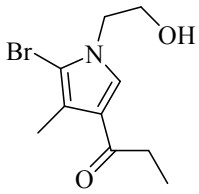
Light yellow oily liquid; 83% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.33 (s, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.22 - 7.15 (m, 3H), 3.89 (t, *J* = 7.3 Hz, 2H), 3.78 (s, 3H), 2.62 (t, *J* = 7.7 Hz, 2H), 2.24 (s, 3H), 2.11 - 2.05 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 140.5, 128.6, 128.3, 126.8, 126.3, 120.9, 114.3, 103.6, 50.9, 48.4, 32.6, 31.9, 11.8; HRMS (ESI) *m/z*: calcd for $C_{16}H_{19}BrNO_2$ ($[M+H]^+$) 336.0599, found 336.0592.

Methyl 5-bromo-4-methyl-1-(4-phenylbutyl)-1H-pyrrole-3-carboxylate (3q)



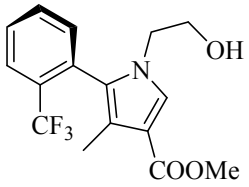
Light yellow oily liquid; 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31 - 7.25 (m, 3H), 7.20 - 7.13 (m, 3H), 3.87 (t, *J* = 7.1 Hz, 2H), 3.77 (s, 3H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.23 (s, 3H), 1.80 - 1.73 (m, 2H), 1.66 - 1.59 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 141.6, 128.43, 128.40, 126.7, 126.0, 120.8, 114.2, 103.6, 50.8, 48.9, 35.3, 30.1, 28.1, 11.8; HRMS (ESI) *m/z*: calcd for $C_{17}H_{21}BrNO_2$ ($[M+H]^+$) 350.0756, found 350.0747.

1-(5-Bromo-1-(2-hydroxyethyl)-4-methyl-1H-pyrrol-3-yl)propan-1-one (3v)

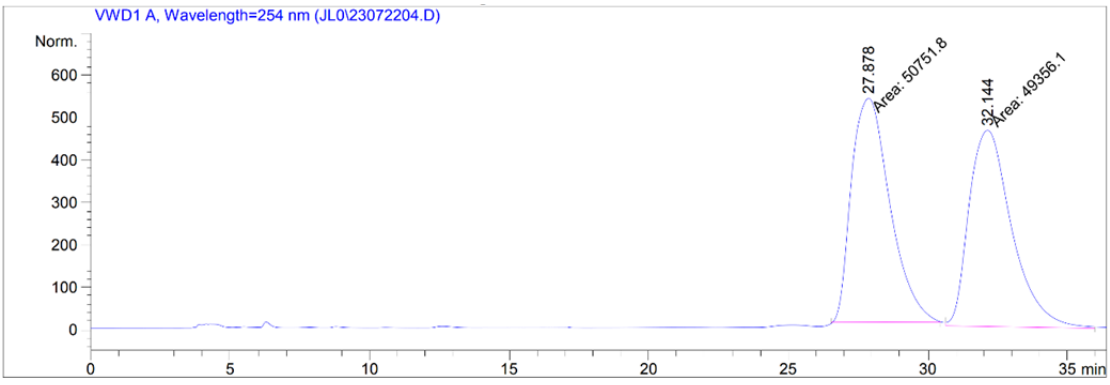


White solid; m.p. 108.9-109.3 °C; 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.42 (s, 1H), 4.10 - 4.07 (m, 2H), 3.90 (t, *J* = 5.2 Hz, 2H), 2.70 (q, *J* = 7.4 Hz, 2H), 2.26 (s, 3H), 1.15 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 196.6, 128.1, 123.0, 120.9, 104.9, 61.5, 51.3, 32.3, 12.3, 8.7; HRMS (ESI) *m/z*: calcd for $C_{10}H_{14}BrNNaO_2$ ($[M+Na]^+$) 282.0106, found 282.0098.

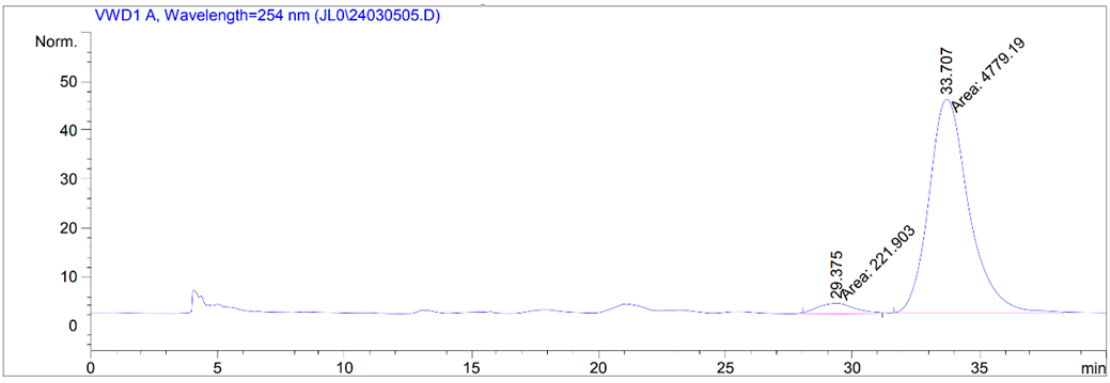
(S)-Methyl 1-(2-hydroxyethyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4a)



White solid; m.p. 108.7-109.1 °C; 89% yield; 92% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.79 (d, *J* = 7.8 Hz, 1H), 7.63 - 7.55 (m, 2H), 7.47 (s, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 3.80 (s, 3H), 3.77-3.61 (m, 4H), 2.00 (s, 3H), 1.26 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 165.9, 134.5, 131.6 (q, *J* = 29.3 Hz), 131.7, 130.3 (q, *J* = 2.0 Hz), 129.3, 128.1, 126.7, 126.4 (q, *J* = 5.1 Hz), 123.6 (q, *J* = 274.7 Hz), 120.7, 113.8, 61.9, 50.7, 49.5, 11.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.0; HRMS (ESI) *m/z*: calcd for $C_{16}H_{17}F_3NO_3$ ($[M+H]^+$) 328.1161, found 328.1151; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 29.375 min, t_{minor} = 33.707 min.

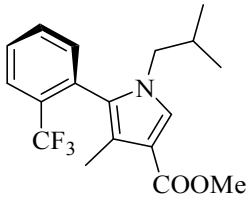


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	27.878	MM	1.6023	5.07518e4	527.88940	50.6971
2	32.144	MM	1.7790	4.93561e4	462.38864	49.3029

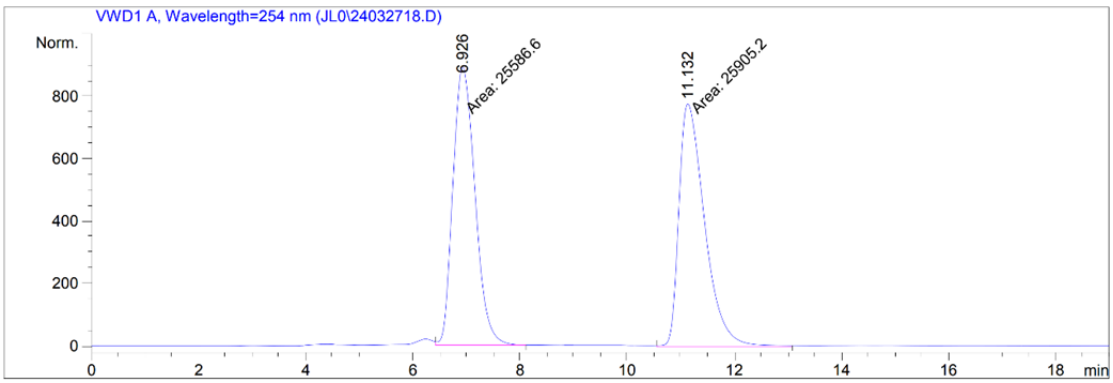


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	29.375	MM	1.7125	221.90266	2.15969	4.4371
2	33.707	MM	1.8226	4779.19287	43.70218	95.5629

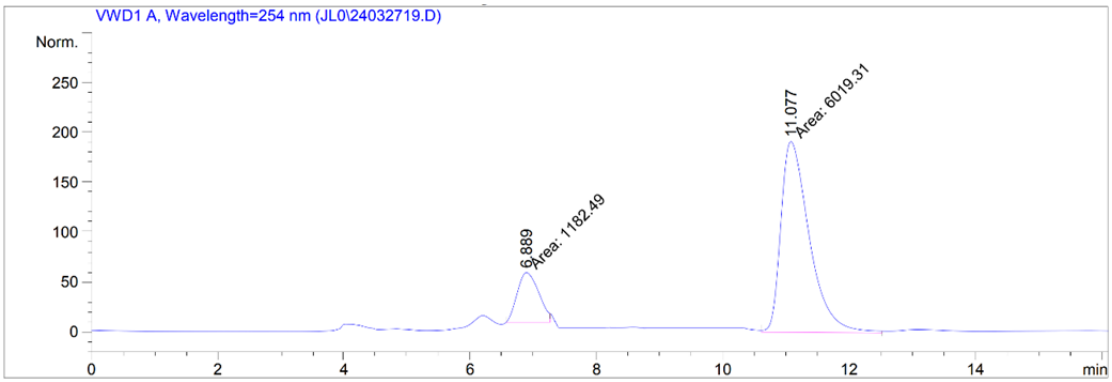
(S)-Methyl 1-isobutyl-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4b)



Light yellow oily liquid; 93% yield; 67% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.72 - 7.70 (m, 1H), 7.59 - 7.43 (m, 2H), 7.32 - 7.20 (m, 2H), 3.73 (s, 3H), 3.34 (dd, *J* = 13.9, 8.0 Hz, 1H), 3.11 (dd, *J* = 13.9, 8.0 Hz, 1H), 1.92 (s, 3H), 1.82 - 1.71 (m, 1H), 0.74 (d, *J* = 6.7 Hz, 3H), 0.64 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 165.9, 134.6, 131.6 (q, *J* = 29.3 Hz), 131.5, 130.7 (q, *J* = 2.0 Hz), 129.1, 128.3, 126.4 (q, *J* = 5.1 Hz), 126.3, 123.6 (q, *J* = 274.7 Hz), 120.2, 113.3, 55.2, 50.6, 29.5, 19.9, 11.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{18}H_{21}F_3NO_2$ ($[M+H]^+$) 340.1524, found 340.1523; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 6.889 min, t_{minor} = 11.077 min.

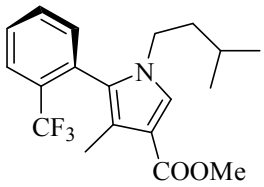


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.926	MM	0.4780	2.55866e4	892.07086	49.6906
2	11.132	MM	0.5555	2.59052e4	777.23480	50.3094

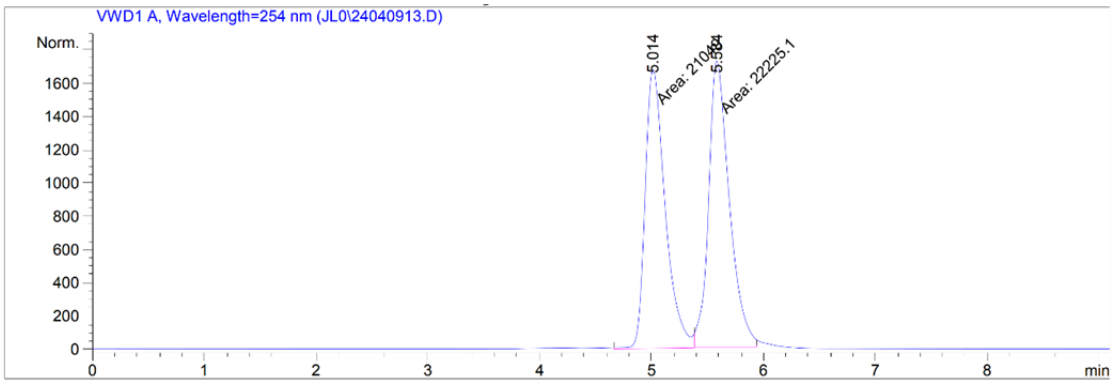


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.889	MM	0.3942	1182.48926	49.99250	16.4194
2	11.077	MM	0.5235	6019.30615	191.65340	83.5806

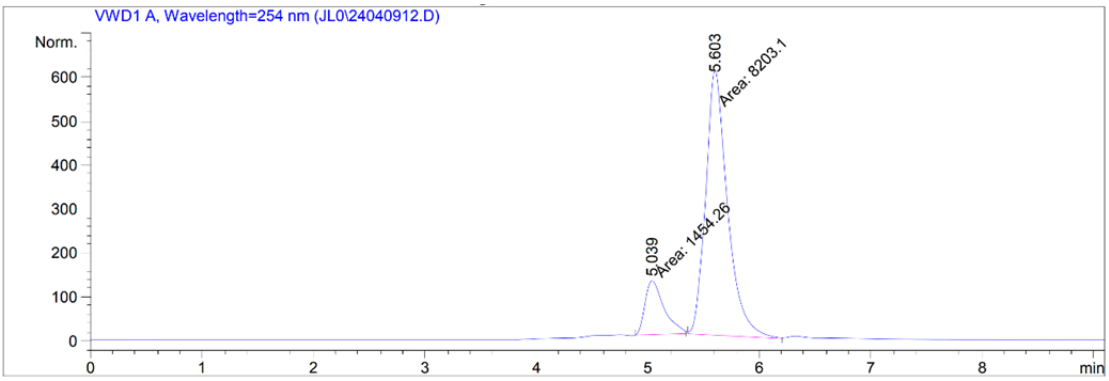
(S)-Methyl 1-isopentyl-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4c)



Light yellow oily liquid; 92% yield; 70% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.73 - 7.70 (m, 1H), 7.57 - 7.46 (m, 2H), 7.29 (s, 1H), 7.25 (d, *J* = 7.4 Hz, 1H), 3.73 (s, 3H), 3.54 - 3.45 (m, 1H), 3.38 - 3.31 (m, 1H), 1.92 (s, 3H), 1.44 - 1.32 (m, 3H), 0.69 (d, *J* = 6.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.8, 133.3, 130.6 (q, *J* = 29.3 Hz), 130.6, 129.6 (q, *J* = 2.0 Hz), 128.1, 126.9, 125.4 (q, *J* = 5.1 Hz), 124.7, 122.6 (q, *J* = 274.7 Hz), 119.1, 112.4, 49.6, 44.7, 38.7, 24.4, 21.21, 21.18, 10.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.0; HRMS (ESI) *m/z*: calcd for $C_{19}H_{23}F_3NO_2$ ($[M+H]^+$) 354.1681, found 354.1679; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 8/2, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 5.039 min, t_{minor} = 5.603 min.

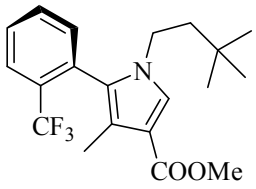


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.014	MM	0.2086	2.10490e4	1681.42261	48.6410
2	5.584	MM	0.2149	2.22251e4	1723.30432	51.3590

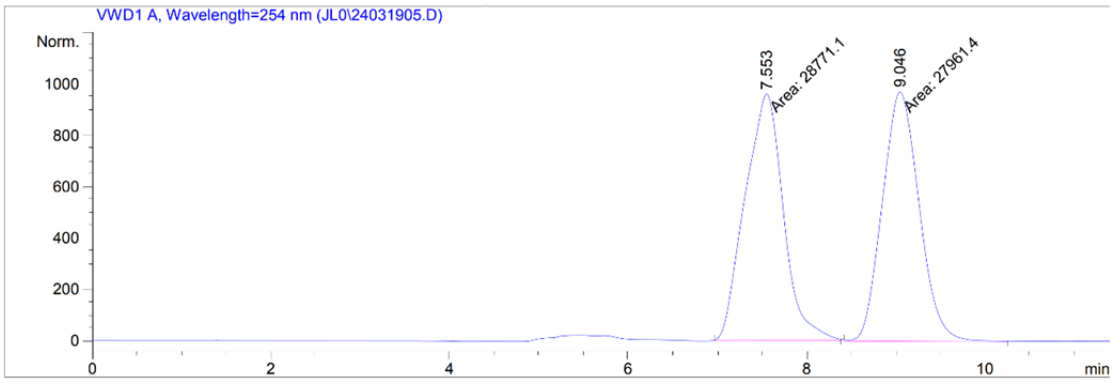


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.039	MM	0.1978	1454.26257	122.52046	15.0586
2	5.603	MM	0.2267	8203.10352	602.97595	84.9414

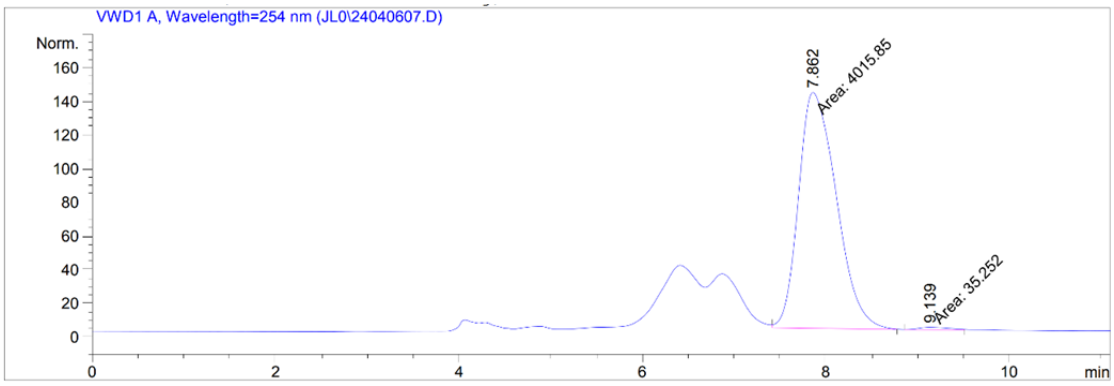
(S)-Methyl 1-(3,3-dimethylbutyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4d)



Light yellow oily liquid; 84% yield; 98% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.72 (d, *J* = 7.8 Hz, 1H), 7.56 - 7.53 (m, 1H), 7.50 - 7.47 (m, 1H), 7.29 (s, 1H), 7.26 (d, *J* = 7.4 Hz, 1H), 3.73 (s, 3H), 3.51 - 3.45 (m, 1H), 3.36 - 3.30 (m, 1H), 1.93 (s, 3H), 1.52 - 1.36 (m, 2H), 0.66 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.8, 133.3, 130.6 (q, *J* = 29.3 Hz), 130.5, 129.6 (q, *J* = 2.0 Hz), 128.1, 126.9, 125.4 (q, *J* = 5.1 Hz), 124.7, 122.6 (q, *J* = 274.7 Hz), 119.1, 112.5, 49.6, 43.8, 43.0, 28.6, 27.9, 10.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.0; HRMS (ESI) *m/z*: calcd for $C_{20}H_{25}F_3NO_2$ ($[M+H]^+$) 368.1837, found 368.1825; HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.862 min, t_{minor} = 9.133 min.

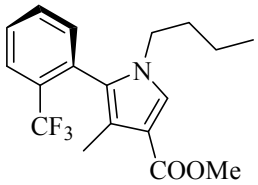


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.553	MM	0.4988	2.87711e4	961.35565	50.7137
2	9.046	MM	0.4792	2.79614e4	972.52527	49.2863



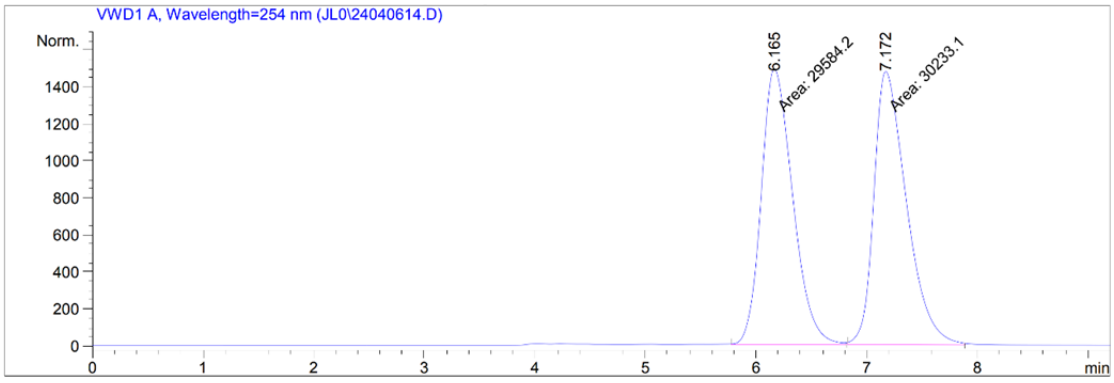
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.862	MM	0.4777	4015.84961	140.11859	99.1298
2	9.139	MM	0.4037	35.25204	1.45547	0.8702

(S)-Methyl 1-butyl-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4e)

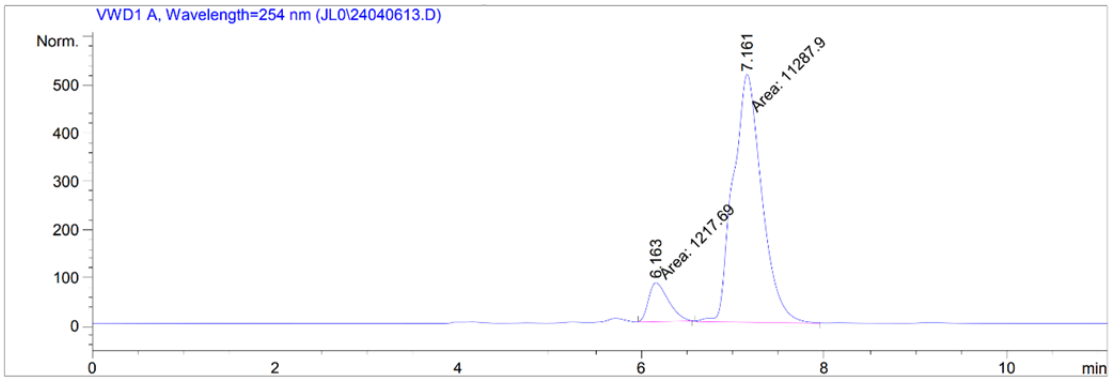


Light yellow oily liquid; 90% yield; 80% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.71 (d, *J* = 7.7 Hz, 1H), 7.54 - 7.47 (m, 2H), 7.29 (s, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 3.73 (s, 3H), 3.52 - 3.46 (m, 1H), 3.37 - 3.31 (m, 1H), 1.92 (s, 3H), 1.52 - 1.46 (m, 2H), 1.15 - 1.08 (m, 2H), 0.73 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.8, 133.3, 130.6 (q, *J* = 29.0 Hz), 130.6, 129.7 (q, *J* = 1.3 Hz), 128.1, 127.0, 125.4 (q, *J* = 5.0 Hz), 124.7, 122.6 (q, *J* = 274.7 Hz), 119.1, 112.3, 49.6, 46.2, 31.7, 18.7, 12.5, 10.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{18}H_{21}F_3NO_2$ ($[M+H]^+$) 340.1524, found 340.1514; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 9/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 6.163 min,

t_{minor} = 7.161 min.

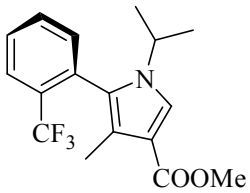


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.165	MM	0.3304	2.95842e4	1492.28284	49.4576
2	7.172	MM	0.3410	3.02331e4	1477.79321	50.5424



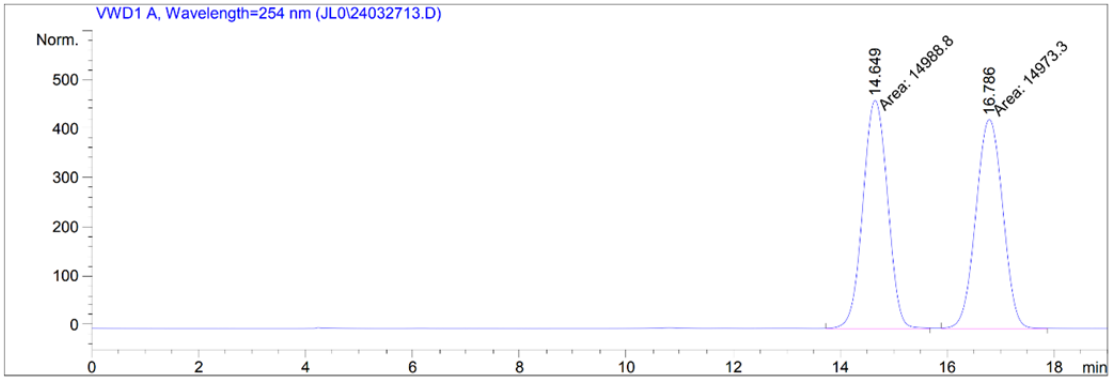
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.163	MM	0.2514	1217.69373	80.73673	9.7372
2	7.161	MM	0.3653	1.12879e4	514.95129	90.2628

(S)-Methyl 1-isopropyl-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4f)

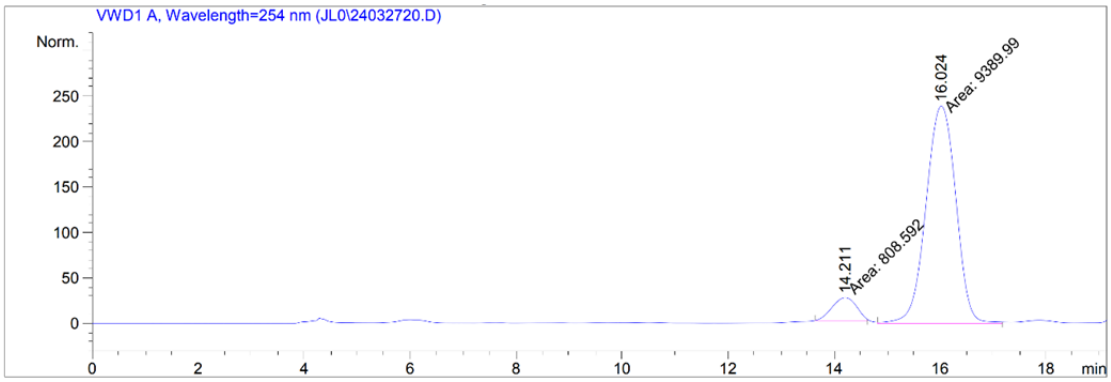


Light yellow oily liquid; 89% yield; 84% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.80 (d, *J* = 8.3 Hz, 1H), 7.63 - 7.60 (m, 1H), 7.58 - 7.55 (m, 1H), 7.45 (s, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 3.81 (s, 3H), 3.75 - 3.70 (m, 1H), 1.98 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 3H), 1.22 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.9, 134.2, 131.7, 131.6 (q, *J* = 29.0 Hz), 130.9 (q, *J* = 2.5 Hz), 129.1, 127.6, 126.4 (q, *J* = 5.0 Hz), 123.6 (q, *J* = 274.7 Hz), 122.1, 119.6, 113.7, 50.6, 48.3, 25.0, 22.3, 11.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.0; HRMS (ESI) *m/z*: calcd for $C_{17}H_{19}F_3NO_2$ ($[M+H]^+$)

326.1368, found 326.1364; HPLC analysis: Daicel CHIRALPAK IG, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 14.211 min, t_{minor} = 16.024 min.

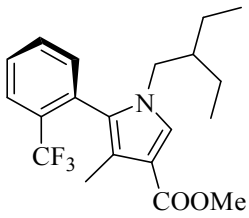


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.649	MM	0.5365	1.49888e4	465.62558	50.0259
2	16.786	MM	0.5850	1.49733e4	426.62582	49.9741



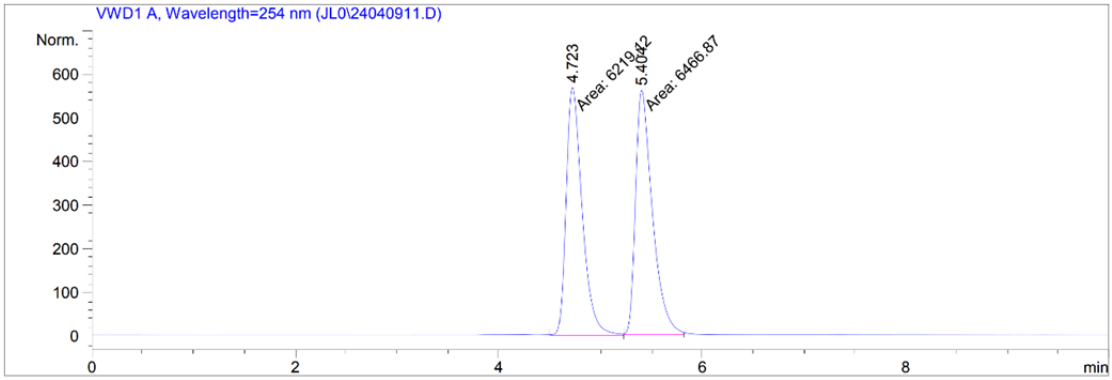
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.211	MM	0.5315	808.59174	25.35479	7.9285
2	16.024	MM	0.6541	9389.98633	239.26376	92.0715

(S)-Methyl 1-(2-ethylbutyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4g)

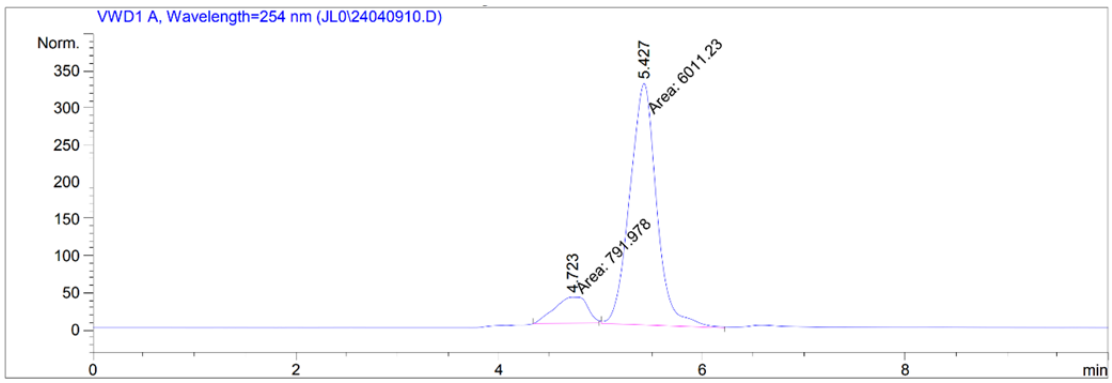


Light yellow oily liquid; 86% yield; 77% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.72 - 7.70 (m, 1H), 7.55 - 7.52 (m, 1H), 7.49 - 7.46 (m, 1H), 7.25 - 7.24 (m, 2H), 3.73 (s, 3H), 3.42 (dd, *J* = 14.0, 7.1 Hz, 1H), 3.22 (dd, *J* = 14.0, 7.1 Hz, 1H), 1.93 (s, 3H), 1.38 - 1.30 (m, 1H), 1.18 - 1.09 (m, 2H), 1.06 -

0.97 (m, 2H), 0.67 (t, J = 7.5 Hz, 3H), 0.53 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 133.6, 130.5 (q, J = 29.3 Hz), 130.5, 129.6 (q, J = 2.0 Hz), 128.0, 127.3, 125.6, 125.4 (q, J = 5.1 Hz), 122.6 (q, J = 274.7 Hz), 119.2, 112.2, 50.1, 49.6, 40.7, 22.2, 22.0, 10.1, 9.5, 9.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.0; HRMS (ESI) *m/z*: calcd for $C_{20}H_{25}F_3NO_2$ ($[M+H]^+$) 368.1837, found 368.1835; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 8/2, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 4.723 min, t_{minor} = 5.427 min.

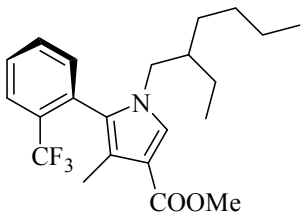


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.723	MM	0.1823	6219.11768	568.50317	49.0235
2	5.404	MM	0.1924	6466.87012	560.23627	50.9765

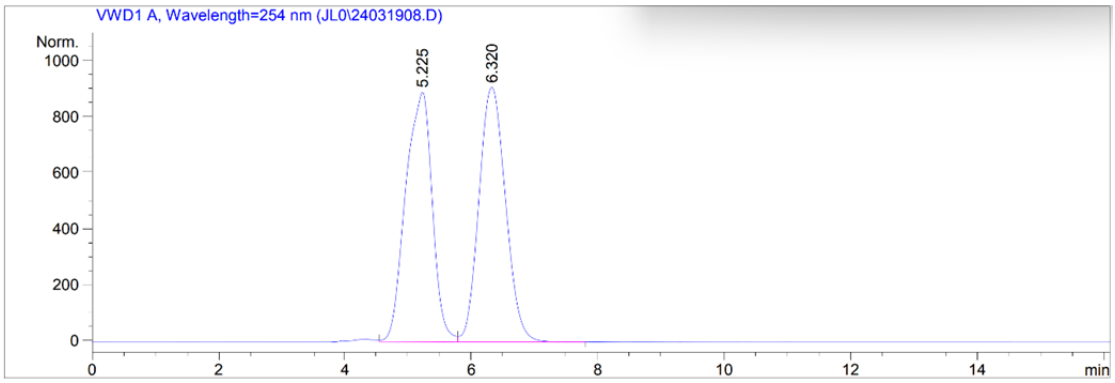


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.723	MM	0.3736	791.97791	35.33341	11.6412
2	5.427	MM	0.3068	6011.22900	326.55435	88.3588

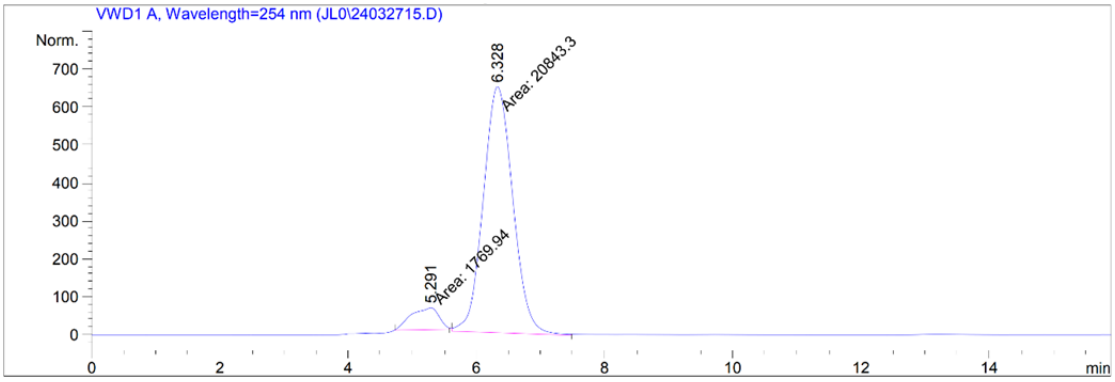
(S)-Methyl 1-(2-ethylhexyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4h)



Light yellow oily liquid; 89% yield; 84% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.78 (d, *J* = 7.7 Hz, 1H), 7.63 - 7.53 (m, 2H), 7.34 - 7.28 (m, 2H), 3.81 (s, 3H), 3.54 - 3.43 (m, 1H), 3.35 - 3.24 (m, 1H), 2.00 (s, 3H), 1.49 - 1.43 (m, 1H), 1.30 - 0.99 (m, 8H), 0.85 - 0.59 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 165.9, 134.7, 131.6 (q, *J* = 29.3 Hz), 131.5, 130.7 (q, *J* = 2.0 Hz), 129.1, 128.3, 126.8, 126.5 (q, *J* = 4.0 Hz), 123.7 (q, *J* = 274.7 Hz), 120.3, 113.2, 51.5, 50.6, 40.2, 30.4, 28.6, 23.7, 22.8, 14.0, 11.1, 10.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.0; HRMS (ESI) *m/z*: calcd for $C_{22}H_{29}F_3NO_2$ ($[M+H]^+$) 396.2150, found 396.2144; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 5.291 min, t_{minor} = 6.328 min.

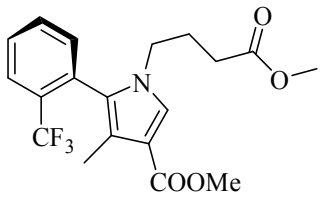


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.225	VV	0.4019	2.61869e4	892.81036	49.4982
2	6.320	VB	0.4604	2.67179e4	910.23907	50.5018

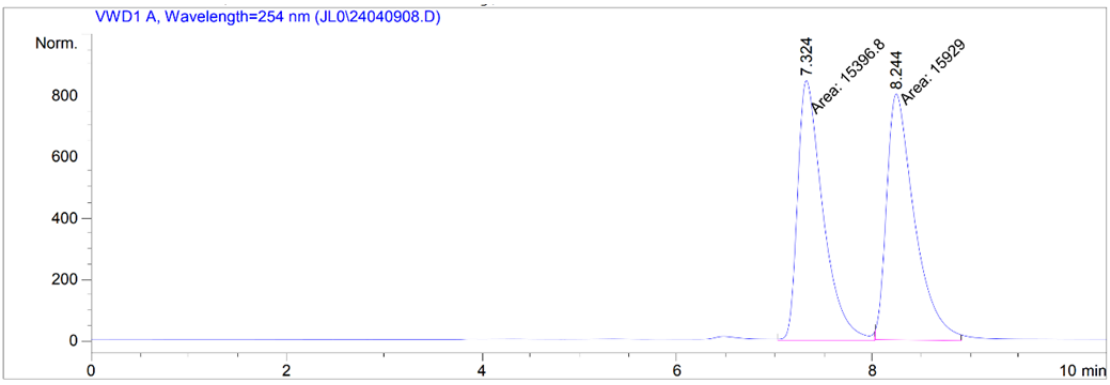


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.291	MM	0.5075	1769.94189	58.12447	7.8270
2	6.328	MM	0.5356	2.08433e4	648.61115	92.1730

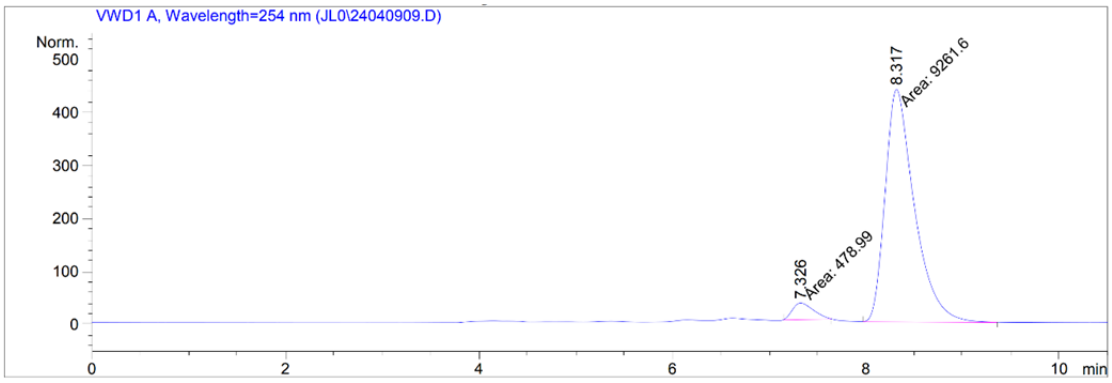
(S)-Methyl 1-(4-methoxy-4-oxobutyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4i)



Light yellow oily liquid; 87% yield; 90% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.80 - 7.78 (m, 1H), 7.65 - 7.54 (m, 2H), 7.36 (s, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 3.81 (s, 3H), 3.69 - 3.63 (m, 1H), 3.61 (s, 3H), 3.53 - 3.47 (m, 1H), 2.20 (t, *J* = 7.3 Hz, 2H), 1.99 (s, 3H), 1.93 -1.85 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 172.8, 165.7, 134.3, 131.7, 131.6 (q, *J* = 29.0 Hz), 130.4 (q, *J* = 2.5 Hz), 129.2, 128.0, 126.5 (q, *J* = 5.0 Hz), 125.8, 123.6 (q, *J* = 273.4 Hz), 120.5, 113.8, 51.7, 50.7, 46.5, 30.6, 25.7, 11.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{19}H_{20}F_3NO_4Na$ ($[M+H]^+$) 406.1242, found 406.1233; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 8/2, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.326 min, t_{minor} = 8.317 min.

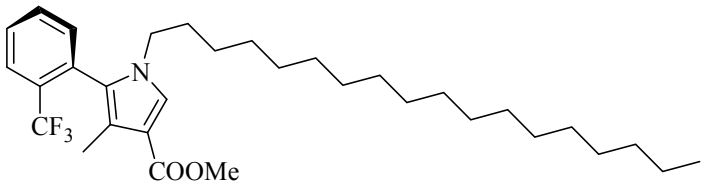


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.324	MM	0.3024	1.53968e4	848.70972	49.1505
2	8.244	MM	0.3309	1.59290e4	802.27435	50.8495

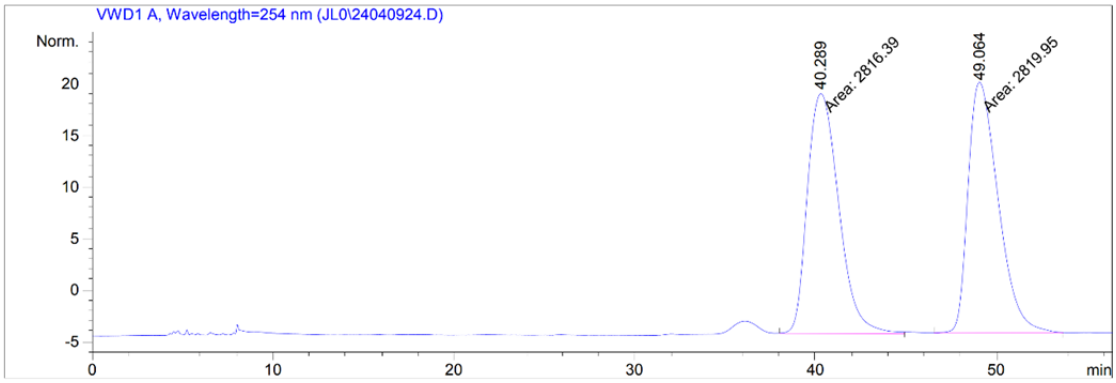


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.326	MM	0.2526	478.98990	31.60016	4.9175
2	8.317	MM	0.3514	9261.60156	439.29535	95.0825

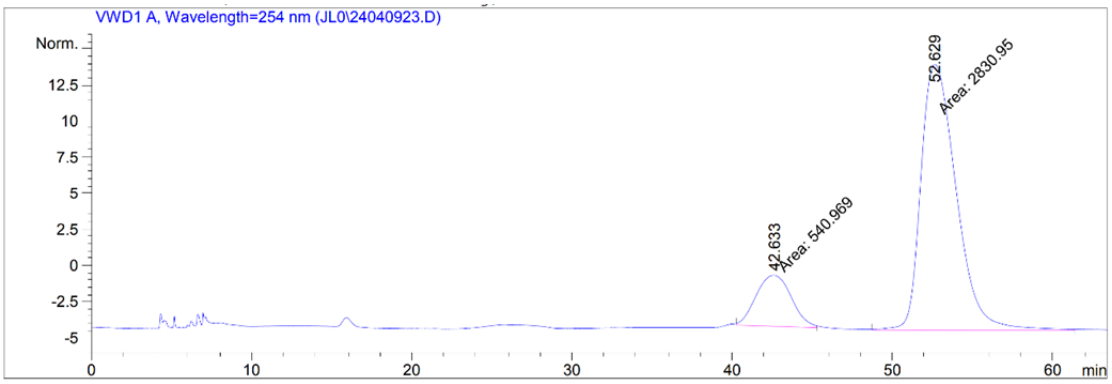
(S)-Methyl 4-methyl-1-octadecyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4j)



Light yellow oily liquid; 79% yield; 78% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.72 - 7.70 (m, 1H), 7.56 - 7.44 (m, 2H), 7.28 (s, 1H), 7.24 (d, *J* = 7.4 Hz, 1H), 3.73 (s, 3H), 3.50 - 3.45 (m, 1H), 3.35 - 3.29 (m, 1H), 1.92 (s, 3H), 1.52 - 1.47 (m, 2H), 1.24 -1.14 (m, 24H), 1.10 - 1.08 (m, 6H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm, four carbons missing): 164.8, 133.3, 130.6 (q, *J* = 29.3 Hz), 130.5, 129.7 (q, *J* = 3.0 Hz), 128.0, 127.0, 125.4 (q, *J* = 5.1 Hz), 124.7, 122.6 (q, *J* = 274.7 Hz), 119.1, 112.3, 49.6, 46.5, 30.9, 29.6, 28.69, 28.65, 28.63, 28.58, 28.5, 28.35, 28.32, 28.0, 25.5, 21.7, 13.1, 10.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{32}H_{49}F_3NO_2$ ($[M+H]^+$) 536.3715, found 536.3706; HPLC analysis: Daicel CHIRALPAK IG, *n*-hexane/*i*-PrOH = 500/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 42.633 min, t_{minor} = 52.629 min.

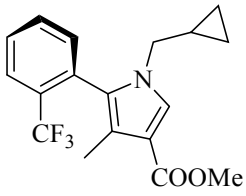


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	40.289	MM	2.0184	2816.38916	23.25548	49.9684
2	49.064	MM	1.9340	2819.95361	24.30108	50.0316



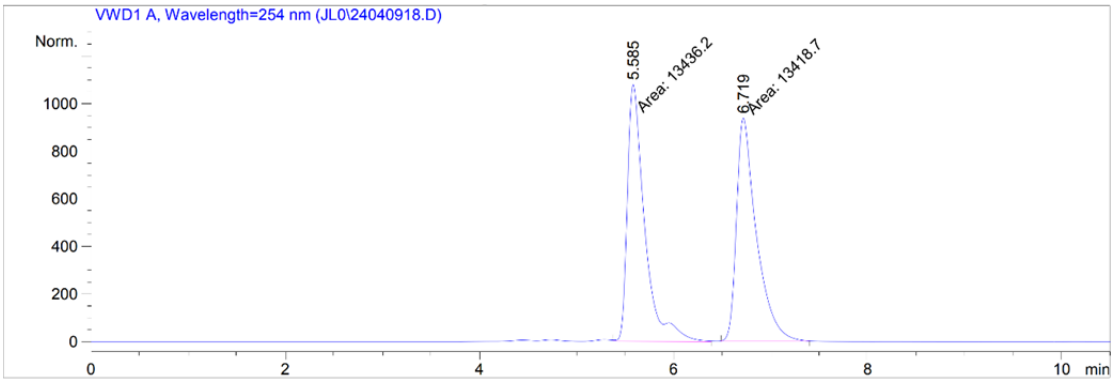
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	42.633	MM	2.5476	540.96918	3.53901	16.0434
2	52.629	MM	2.5638	2830.94800	18.40368	83.9566

(S)-Methyl 1-(cyclopropylmethyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4k)

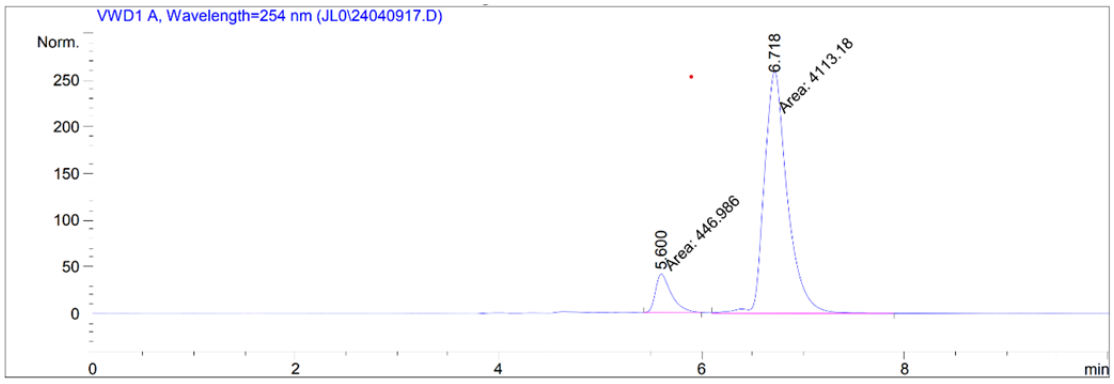


Light yellow oily liquid; 92% yield; 80% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.74 - 7.68 (m, 1H), 7.57 -7.47 (m, 2H), 7.47 (s, 1H), 7.29 - 7.24 (m, 1H), 3.74 (s, 3H), 3.29 - 3.20 (m, 2H), 1.93 (s, 3H), 0.99 - 0.88 (m, 1H), 0.53 - 0.44 (m, 2H), 0.13 - 0.03 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.8, 133.3, 130.62 (q, J = 30.3 Hz), 130.61, 129.8 (q, J = 2.0 Hz), 128.1, 126.8, 125.3 (q, J = 5.1 Hz), 124.6, 122.6 (q, J = 274.7 Hz), 119.2, 112.3, 51.2, 49.6, 10.12, 10.05, 3.2, 3.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{18}H_{19}F_3NO_2$ ($[M+H]^+$) 338.1368,

found 338.1359; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 8/2, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 5.600 min, t_{minor} = 6.718 min.

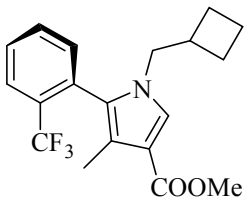


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.585	MM	0.2073	1.34362e4	1080.01672	50.0327
2	6.719	MM	0.2381	1.34187e4	939.42688	49.9673



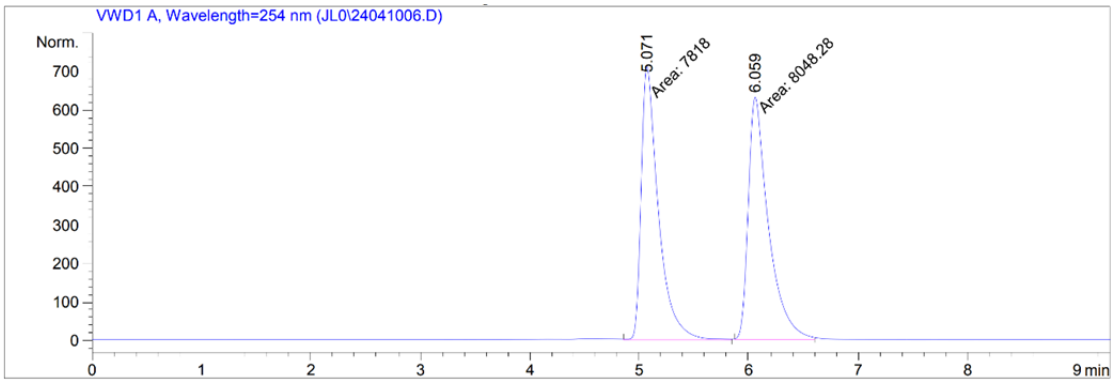
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.600	MM	0.1806	446.98627	41.24826	9.8020
2	6.718	MM	0.2645	4113.17969	259.20743	90.1980

(S)-Methyl 1-(cyclobutylmethyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4l)

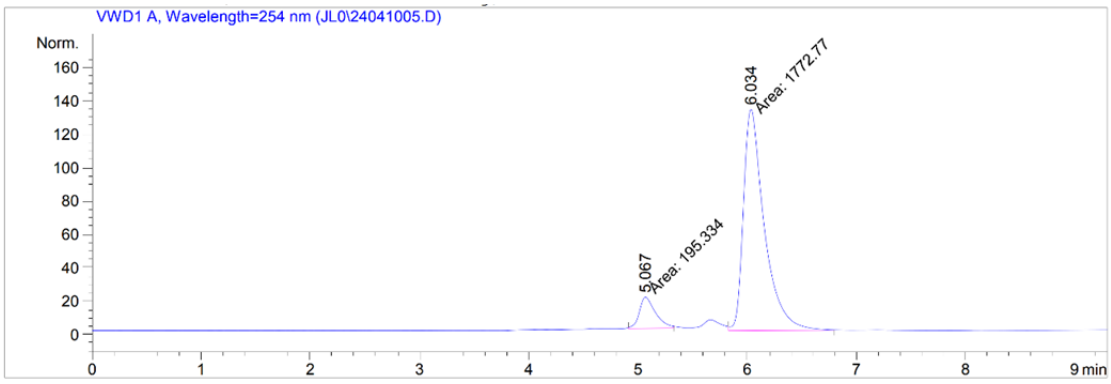


Light yellow oily liquid; 90% yield; 80% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.73 - 7.71 (m, 1H), 7.58 - 7.43 (m, 2H), 7.30 - 7.20 (m, 2H), 3.72 (s, 3H), 3.47 (dd, *J* = 13.9, 7.5 Hz, 1H), 3.35 (dd, *J* = 13.9, 7.5 Hz, 1H), 2.53 - 2.43 (m, 1H), 1.99 - 1.86 (m, 5H), 1.82 - 1.65 (m, 2H), 1.60 - 1.45 (m, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.8, 133.4, 130.59 (q, *J* = 30.2 Hz), 130.58, 129.7 (q, *J* = 2.5 Hz), 128.1, 126.9, 125.4 (q, *J* = 5.0 Hz), 124.6, 122.6 (q, *J* = 273.4 Hz), 119.1, 112.3, 51.8, 49.6, 34.5, 25.3, 25.2, 17.1, 10.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{19}H_{21}F_3NO_2$ ($[M+H]^+$) 352.1524, found 352.1519; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 7/3, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 5.067 min, t_{minor} = 6.034 min.

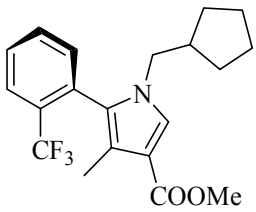


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.071	MM	0.1833	7817.99902	710.68219	49.2743
2	6.059	MM	0.2129	8048.27539	630.17822	50.7257

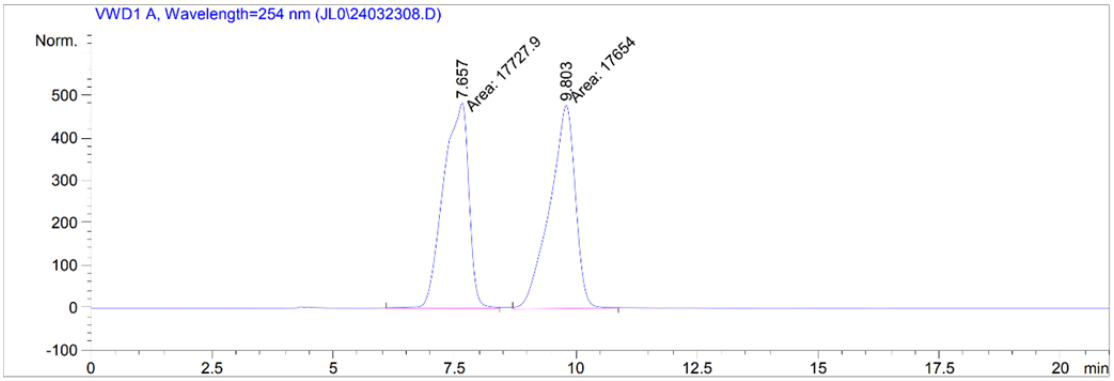


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.067	MM	0.1723	195.33429	18.89714	9.9250
2	6.034	MM	0.2230	1772.76855	132.49469	90.0750

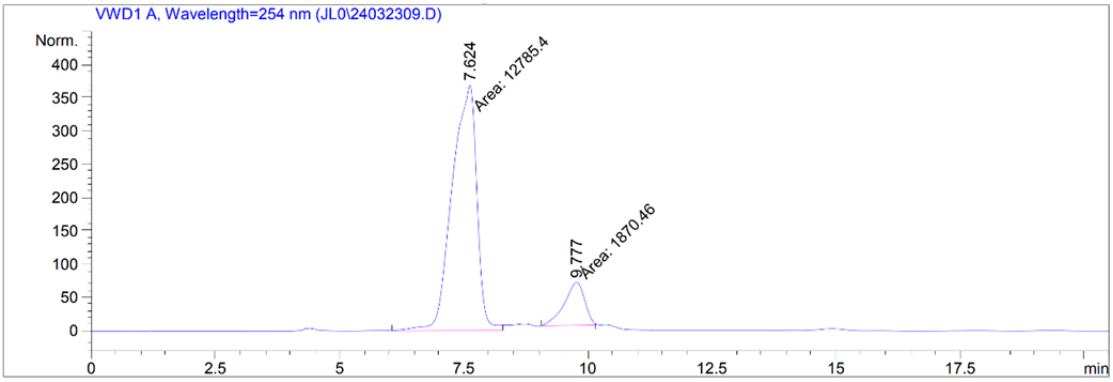
(S)-Methyl 1-(cyclopentylmethyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4m)



Light yellow oily liquid; 91% yield; 74% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.71 (d, *J* = 7.7 Hz, 1H), 7.55 - 7.52 (m, 1H), 7.50 - 7.47 (m, 1H), 7.31 (s, 1H), 7.25 (d, *J* = 7.4 Hz, 1H), 3.73 (s, 3H), 3.43 (dd, *J* = 13.9, 8.0 Hz, 1H), 3.24 (dd, *J* = 13.9, 8.0 Hz, 1H), 2.08 - 2.02 (m, 1H), 1.92 (s, 3H), 1.62 - 1.57 (m, 1H), 1.53 - 1.46 (m, 2H), 1.46 - 1.39 (m, 3H), 1.07 - 0.89 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.9, 133.5, 130.6 (q, *J* = 29.3 Hz), 130.5, 129.7 (q, *J* = 2.0 Hz), 128.0, 127.1, 125.4 (q, *J* = 5.1 Hz), 125.0, 122.6 (q, *J* = 274.7 Hz), 119.1, 112.2, 51.4, 49.6, 39.6, 29.34, 29.30, 23.8, 23.7, 10.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{20}H_{23}F_3NO_2$ ([M+H] $^{+}$) 366.1691, found 366.1678; HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.624 min, t_{minor} = 9.777 min.

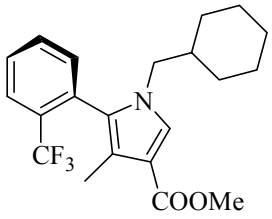


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.657	MM	0.6104	1.77279e4	484.02072	50.1045
2	9.803	MM	0.6148	1.76540e4	478.56396	49.8955

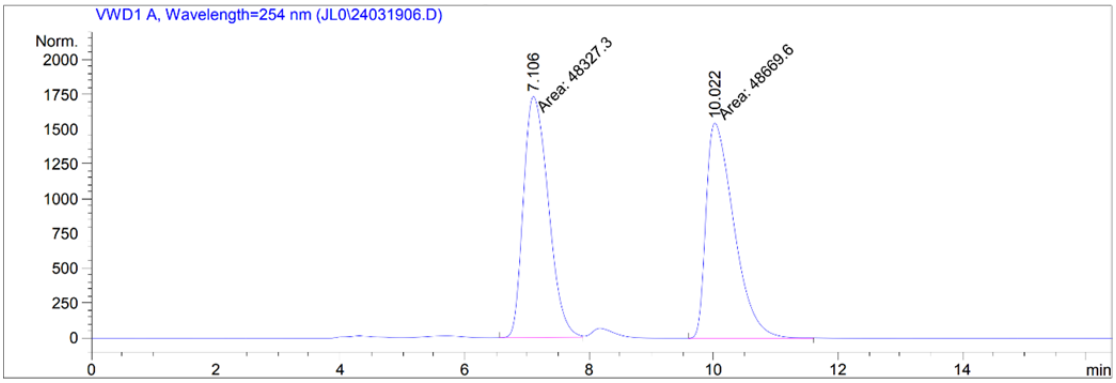


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.624	MM	0.5772	1.27854e4	369.20117	87.2374
2	9.777	MM	0.4804	1870.46326	64.88753	12.7626

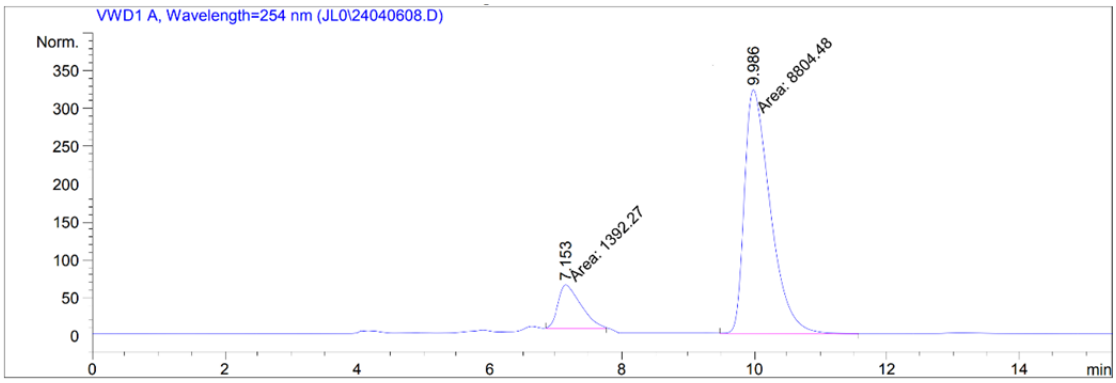
(S)-Methyl 1-(cyclohexylmethyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4n)



Light yellow oily liquid; 85% yield; 73% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.71 (d, *J* = 7.8 Hz, 1H), 7.55 - 7.47 (m, 2H), 7.25 - 7.23 (m, 2H), 3.73 (s, 3H), 3.37 (dd, *J* = 13.9, 8.0 Hz, 1H), 3.12 (dd, *J* = 13.9, 8.0 Hz, 1H), 1.92 (s, 3H), 1.58 - 1.33 (m, 6H), 1.10 - 0.96 (m, 3H), 0.74 - 0.56 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 163.4, 132.1, 129.0 (q, *J* = 30.0 Hz), 128.9, 128.1, 126.5, 125.8, 123.9, 123.8, 121.1 (q, *J* = 274.7 Hz), 117.5, 110.7, 51.5, 48.1, 36.3, 28.12, 28.08, 23.7, 23.2, 23.1, 8.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{21}H_{25}F_3NO_2$ ($[M+H]^+$) 380.1837, found 380.1826; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.153 min, t_{minor} = 9.986 min.

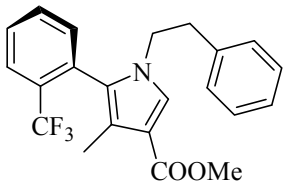


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.106	MM	0.4643	4.83273e4	1734.90149	49.8236
2	10.022	MM	0.5226	4.86696e4	1552.21045	50.1764

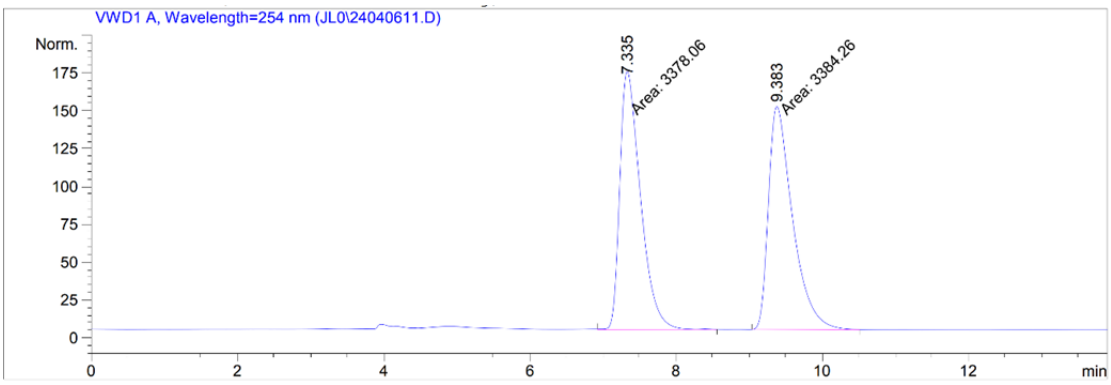


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.153	MM	0.4039	1392.27295	57.44848	13.6541
2	9.986	MM	0.4558	8804.47754	321.94016	86.3459

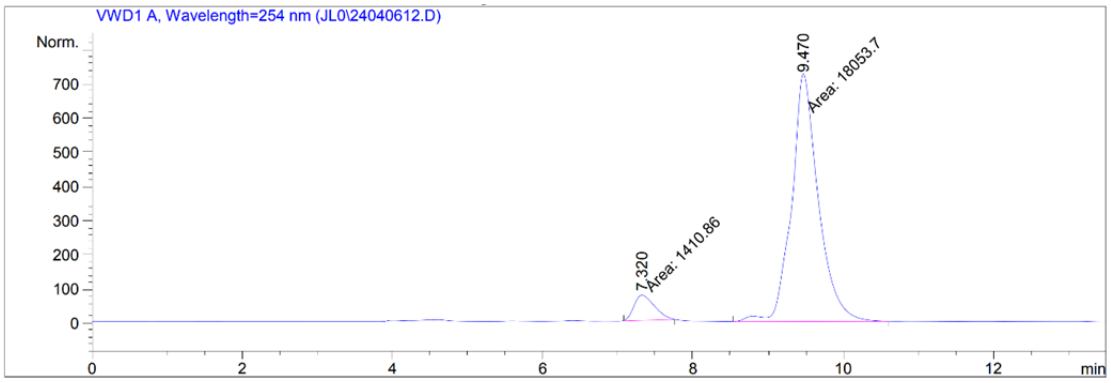
(S)-Methyl 4-methyl-1-phenethyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4o)



Light yellow oily liquid; 87% yield; 86% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.70 - 7.68 (m, 1H), 7.48 - 7.39 (m, 2H), 7.31 (s, 1H), 7.17 - 7.13 (m, 3H), 6.82 - 6.79 (m, 3H), 3.79 - 3.74 (m, 4H), 3.53 - 3.47 (m, 1H), 2.86 - 2.75 (m, 2H), 1.90 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.8, 136.7, 133.4, 130.53, 130.47 (q, J = 30.2 Hz), 129.3 (q, J = 2.5 Hz), 128.0, 127.7, 127.6, 127.1, 125.7, 125.2 (q, J = 5.0 Hz), 124.5, 122.6 (q, J = 273.4 Hz), 119.1, 112.7, 49.7, 47.9, 36.6, 10.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.1; HRMS (ESI) *m/z*: calcd for $C_{22}H_{21}F_3NO_2$ ($[M+H]^+$) 388.1524, found 388.1519; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 9/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.320 min, t_{minor} = 9.470 min.

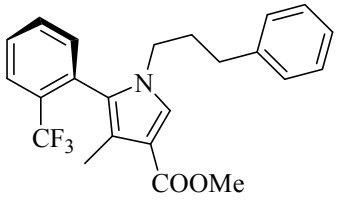


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.335	MM	0.3294	3378.05518	170.89644	49.9541
2	9.383	MM	0.3828	3384.26221	147.35121	50.0459

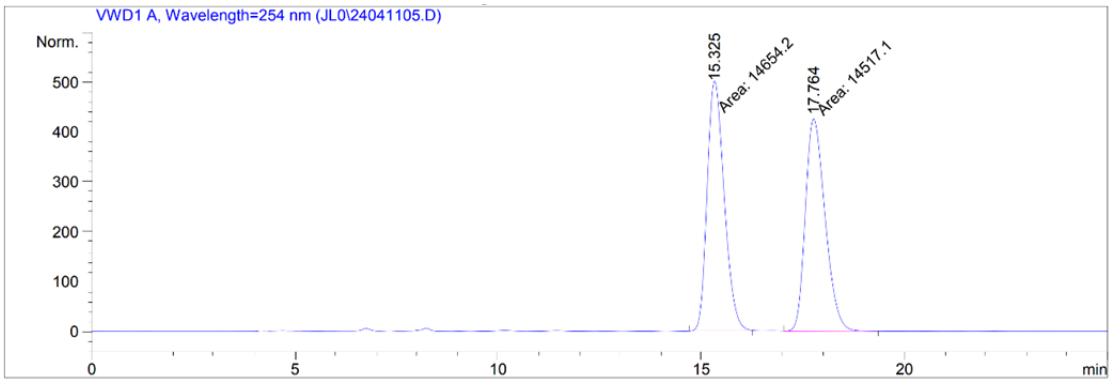


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.320	MM	0.3167	1410.86377	74.25980	7.2484
2	9.470	MM	0.4152	1.80537e4	724.72791	92.7516

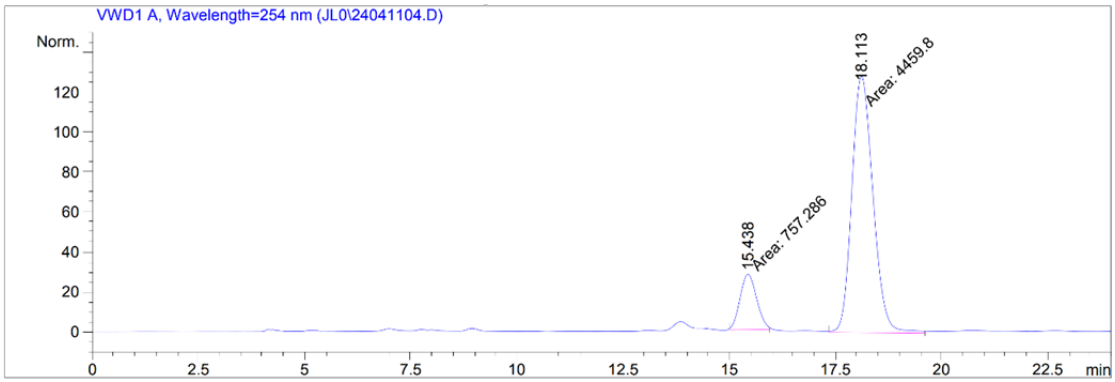
(S)-Methyl 4-methyl-1-(3-phenylpropyl)-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4p)



Light yellow oily liquid; 89% yield; 71% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.69 (d, *J* = 7.5 Hz, 1H), 7.51 - 7.44 (m, 2H), 7.24 - 7.11 (m, 4H), 7.07 (t, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 7.4 Hz, 2H), 3.72 (s, 3H), 3.55 - 3.49 (m, 1H), 3.41 - 3.35 (m, 1H), 2.40 (t, *J* = 7.7 Hz, 2H), 1.92 (s, 3H), 1.86 - 1.72 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.8, 139.5, 133.3, 130.6, 130.5 (q, *J* = 30.2 Hz), 129.5 (q, *J* = 2.5 Hz), 128.1, 127.4, 127.4, 127.1, 127.1, 127.0, 125.4 (q, *J* = 5.0 Hz), 125.1, 124.8, 122.6 (q, *J* = 274.7 Hz), 119.3, 112.5, 49.6, 46.0, 31.6, 31.0, 10.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.0; HRMS (ESI) *m/z*: calcd for $C_{23}H_{23}F_3NO_2$ ($[M+H]^+$) 402.1681, found 402.1673; HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 15.438 min, t_{minor} = 18.113 min.

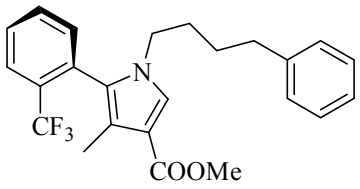


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.325	MM	0.4870	1.46542e4	501.48343	50.2350
2	17.764	MM	0.5670	1.45171e4	426.74701	49.7650



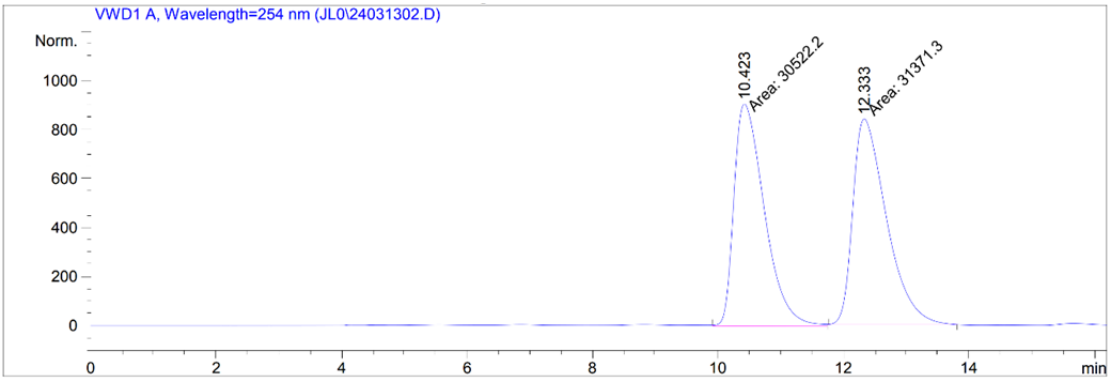
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.438	MM	0.4535	757.28632	27.83315	14.5155
2	18.113	MM	0.5784	4459.80371	128.51349	85.4845

(S)-Methyl 4-methyl-1-(4-phenylbutyl)-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (4q)

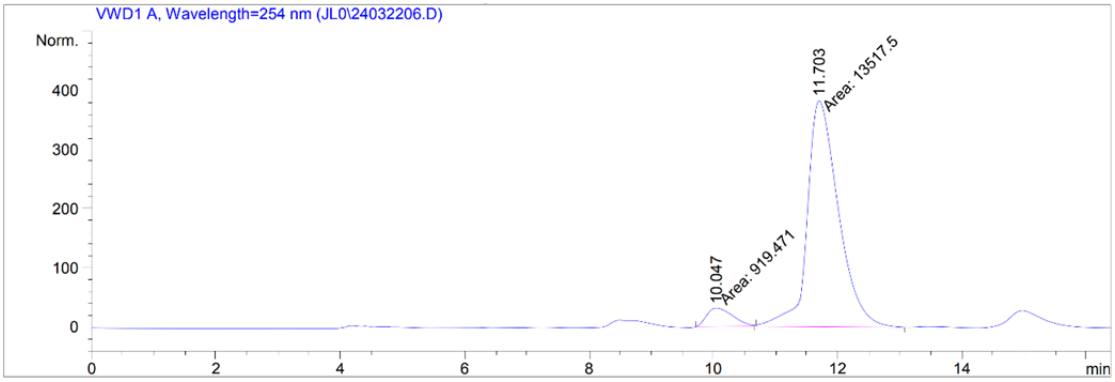


Light yellow oily liquid; 88% yield; 87% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.70 - 7.69 (m, 1H), 7.49 - 7.44 (m, 2H), 7.24 - 6.86 (m, 7H), 3.72 (s, 3H), 3.52 - 3.47 (m, 1H), 3.38 - 3.32 (m, 1H), 2.48 - 2.38 (m, 2H), 1.91 (s, 3H), 1.54 - 1.49 (m, 2H), 1.44 - 1.38 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.8, 141.6, 134.3, 131.63, 131.59 (q, J = 30.0 Hz), 130.6 (q, J = 2.5 Hz), 129.1, 128.4, 128.3, 128.0, 126.4 (q, J = 5.0 Hz), 125.92, 125.86, 123.6 (q, J = 274.7 Hz), 120.4, 113.4, 50.6, 47.4, 35.2, 30.0, 28.1, 11.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -61.0; HRMS (ESI) *m/z*: calcd for

$C_{24}H_{25}F_3NO_2$ ([M+H]$^+$) 416.1837, found 416.1835; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 10.047 min, t_{minor} = 11.703 min.

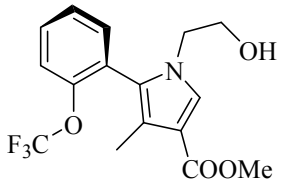


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.423	MM	0.5612	3.05222e4	906.44415	49.3141
2	12.333	MM	0.6221	3.13713e4	840.47162	50.6859



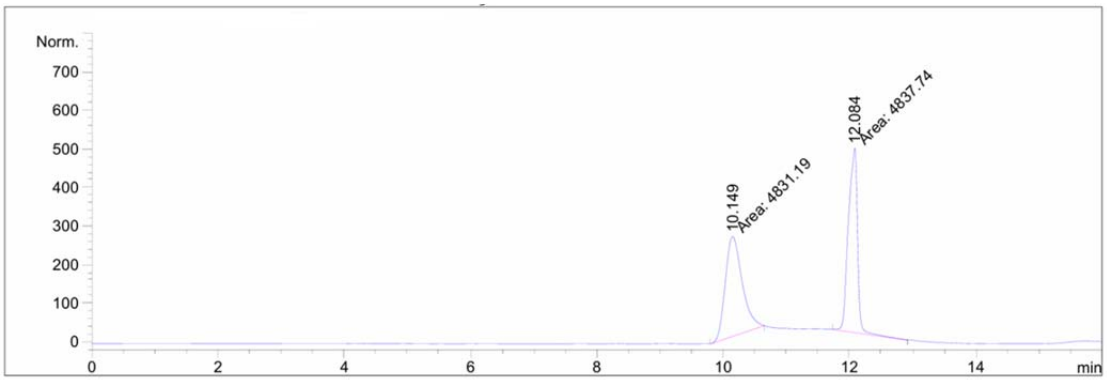
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.047	MM	0.4888	919.47095	31.35111	6.3689
2	11.703	MM	0.5894	1.35175e4	382.25873	93.6311

(S)-Methyl 1-(2-hydroxyethyl)-4-methyl-5-(2-(trifluoromethoxy)phenyl)-1H-pyrrole-3-carboxylate (4r)

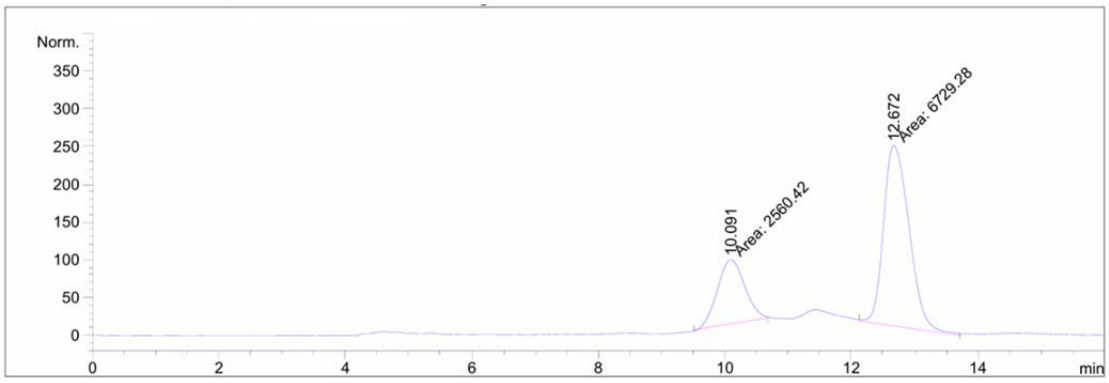


Light yellow oily liquid; 91% yield; 45% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.49 - 7.48 (m, 1H), 7.40 - 7.30 (m, 3H), 7.26 (s, 1H), 3.87 - 3.77 (m, 5H), 3.76 - 3.53 (m, 2H), 2.09 (s, 3H), 1.74 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 165.8, 148.0, 133.9, 130.2, 127.3, 127.0, 126.5,

125.1, 121.1, 121.0, 120.3 (q, J = 259.6 Hz), 114.0, 62.0, 50.7, 49.7, 10.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): -57.41; HRMS (ESI) *m/z*: calcd for $C_{16}H_{17}F_3NO_4$ ($[M+H]^+$) 344.1110, found 344.1109; HPLC analysis: Daicel CHIRALPAK AS-H, *n*-hexane/*i*-PrOH = 9/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 10.091 min, t_{minor} = 12.672 min.

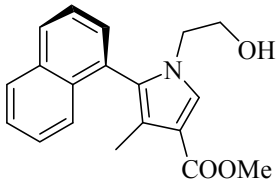


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.149	MM	0.3101	4831.19385	259.65042	49.9662
2	12.084	MM	0.1684	4837.73584	478.90143	50.0338



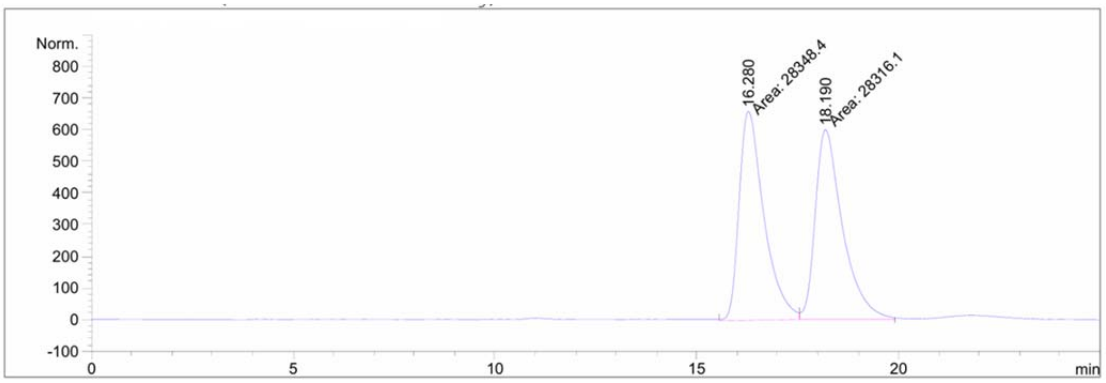
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.091	MM	0.5014	2560.41919	85.11072	27.5619
2	12.672	MM	0.4682	6729.28076	239.53938	72.4381

(S)-Methyl 1-(2-hydroxyethyl)-4-methyl-5-(naphthalen-1-yl)-1H-pyrrole-3-carboxylate (4s)

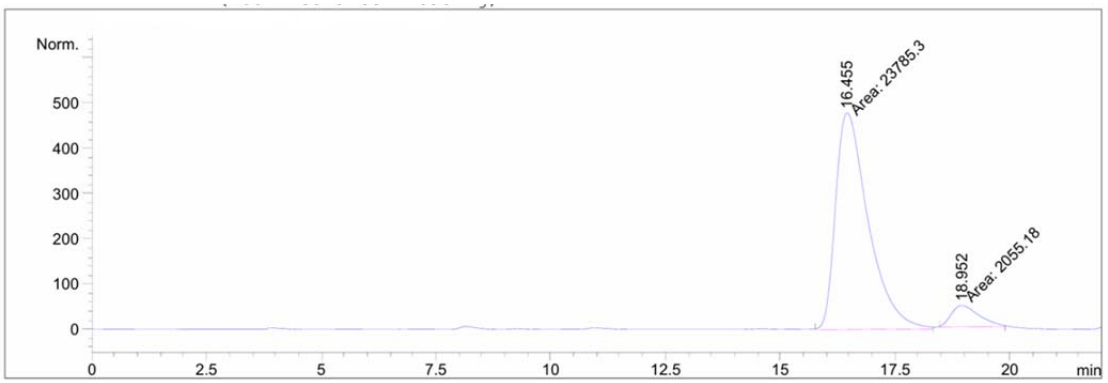


Light yellow oily liquid; 79% yield; 84% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.93 - 7.90 (m, 2H), 7.66 - 7.33 (m, 6H), 3.84 - 3.81 (m, 3H), 3.80 - 3.76 (m, 2H), 3.51 - 3.49 (m, 2H), 2.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 166.0, 133.7, 133.5, 130.0, 129.9, 129.12, 129.06, 128.4, 127.2, 126.8, 126.2, 125.5, 125.3, 120.8, 113.9, 62.2, 50.8, 49.9, 11.1; HRMS (ESI) *m/z*:

calcd for $C_{19}H_{20}NO_3$ ([M+H]$^+$) 310.1443, found 310.1438; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 9/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 16.455 min, t_{minor} = 18.952 min.

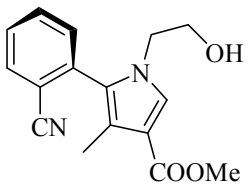


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.280	MM	0.7148	2.83484e4	660.95563	50.0285
2	18.190	MM	0.7860	2.83161e4	600.46399	49.9715



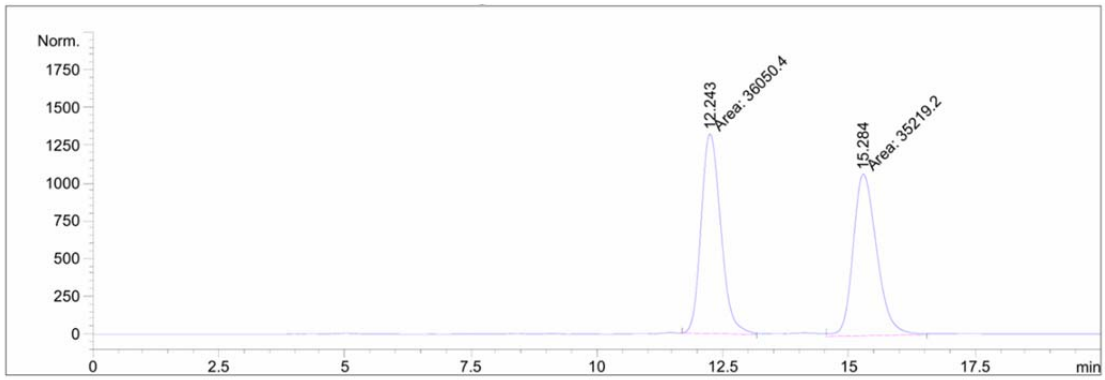
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.455	MM	0.8271	2.37853e4	479.27597	92.0467
2	18.952	MM	0.7177	2055.17578	47.72520	7.9533

S)-Methyl 5-(2-cyanophenyl)-1-(2-hydroxyethyl)-4-methyl-1H-pyrrole-3-carboxylate (4t)

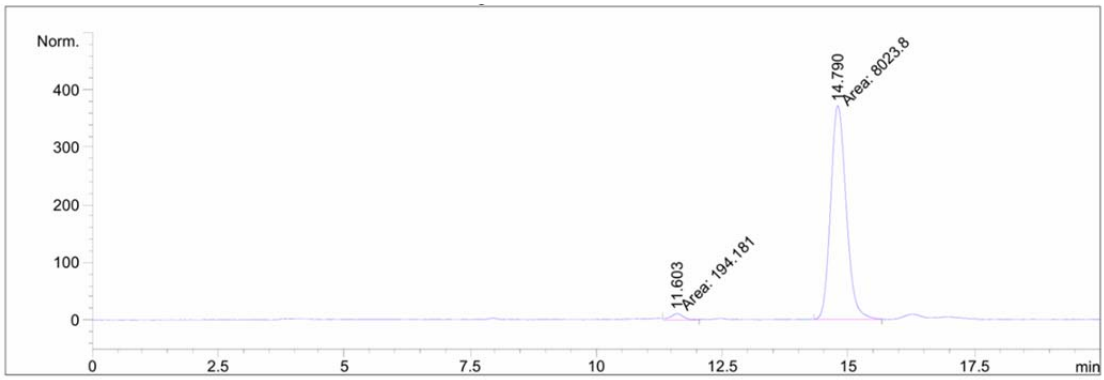


Light yellow oily liquid; 31% yield; 95% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.74 - 7.70 (m, 1H), 7.63 - 7.58 (m, 1H), 7.47 - 7.43 (m, 2H), 7.36 -7.33 (m, 1H), 3.88 - 3.77 (m, 2H), 3.74 (s, 3H), 3.66 - 3.57 (m, 2H), 2.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 164.5, 134.5, 132.2, 131.7, 131.6, 131.0, 127.8, 127.6, 127.0, 126.3, 120.9, 114.1, 61.1, 49.8, 48.8, 10.2; HRMS (ESI) *m/z*: calcd for $C_{16}H_{16}N_2NaO_3$ ([M+Na$^+$) 307.1059, found 307.1056; HPLC analysis: Daicel

CHIRALPAK IC-H, *n*-hexane/*i*-PrOH = 5/4, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 11.603 min, t_{minor} = 14.790 min.

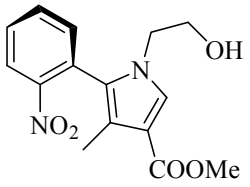


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.243	MM	0.4536	3.60504e4	1324.47913	50.5831
2	15.284	MM	0.5476	3.52192e4	1071.94849	49.4169



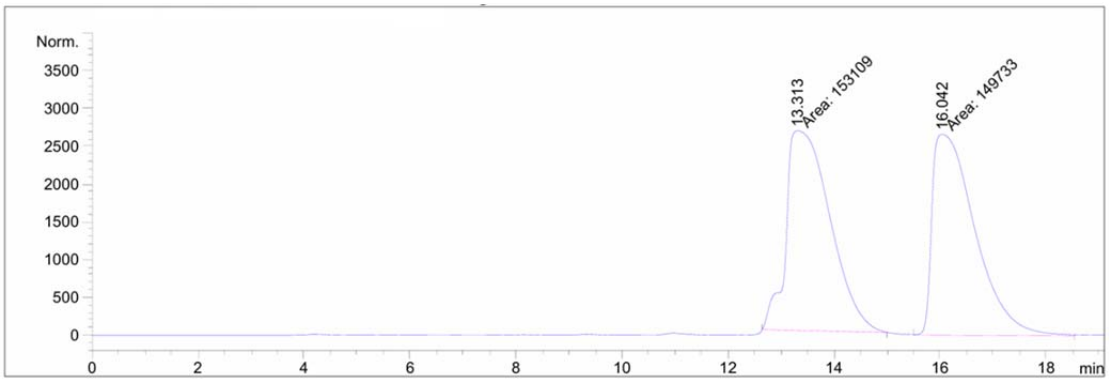
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.603	MM	0.3034	194.18121	10.66536	2.3629
2	14.790	MM	0.3593	8023.80469	372.16510	97.6371

(S)-Methyl 1-(2-hydroxyethyl)-4-methyl-5-(2-nitrophenyl)-1H-pyrrole-3-carboxylate (4u)

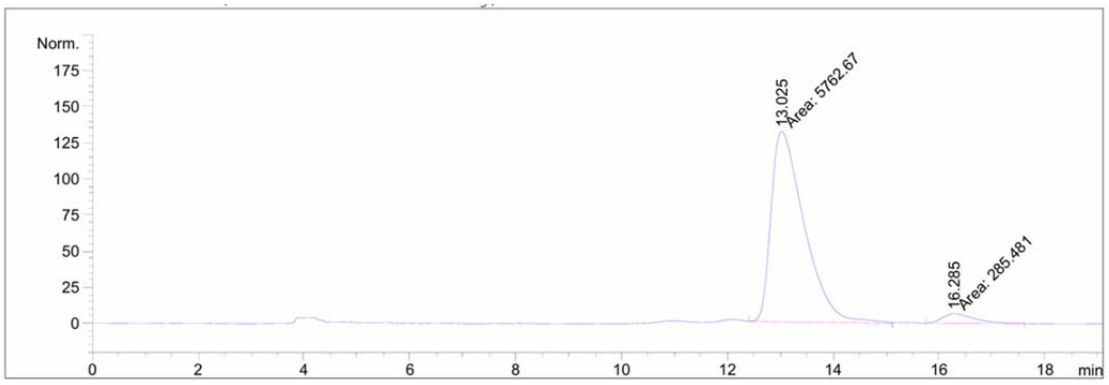


Light yellow oily liquid; 78% yield; 91% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.99 -7.98 (m, 1H), 7.70 - 7.67 (m, 1H), 7.61 - 7.58 (m, 1H), 7.48 (s, 1H), 7.42 - 7.40 (m, 1H), 3.93 - 3.81 (m, 2H), 3.78 (s, 3H), 3.72 - 3.63 (m, 2H), 1.99 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 165.6, 150.7, 134.2, 132.8, 129.9, 127.8, 126.3, 126.1, 124.5, 120.6, 114.1, 61.8, 50.8, 50.1, 10.8; HRMS (ESI) *m/z*: calcd for $C_{15}H_{17}N_2O_5$ ($[M+H]^+$) 305.1137, found 305.1132; HPLC analysis: Daicel CHIRALPAK IG-H, *n*-hexane/*i*-PrOH = 6/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time:

t_{major} = 13.025 min, t_{minor} = 16.285 min.

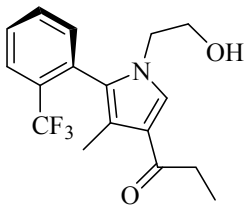


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.313	MM	0.9651	1.53109e5	2644.11182	50.5574
2	16.042	MM	0.9381	1.49733e5	2660.16846	49.4426



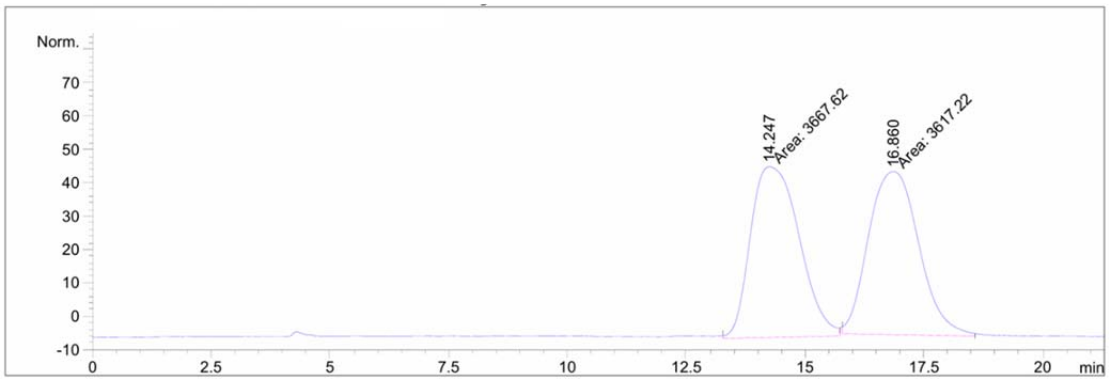
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.025	MM	0.7268	5762.67383	132.15210	95.2799
2	16.285	MM	0.7101	285.48080	6.70023	4.7201

(S)-1-(1-(2-Hydroxyethyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrol-3-yl)propan-1-one (4v)

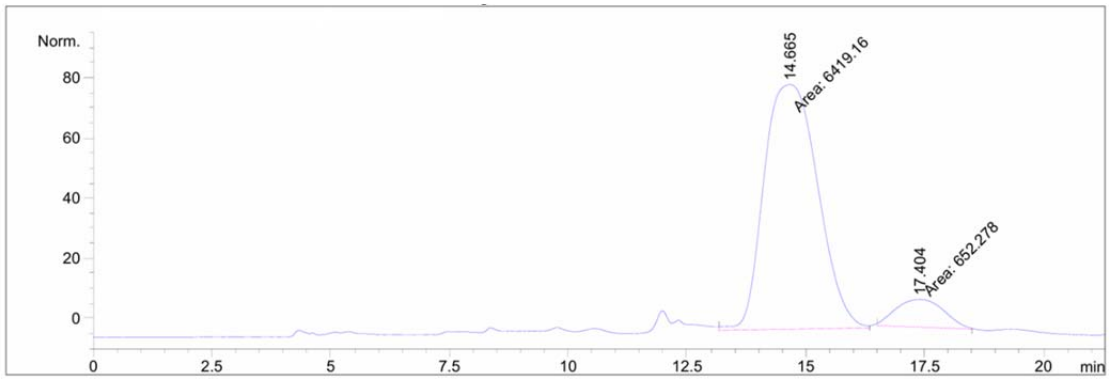


Light yellow oily liquid; 88% yield; 82% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.79 - 7.78 (m, 1H), 7.63 - 7.54 (m, 2H), 7.47 (s, 1H), 7.35 - 7.33 (m, 1H), 3.79 - 3.63 m, 4H), 2.80 - 2.74 (m, 2H), 2.01 (s, 3H), 1.22 - 1.09 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 197.6, 134.4, 131.8, 131.5 (q, J = 29.3 Hz), 130.2 (q, J = 3.0 Hz), 129.3, 128.7, 127.1, 126.5 (q, J = 5.1 Hz), 123.6 (q, J = 274.7 Hz), 122.8, 120.4, 61.9, 49.6, 32.9, 11.7, 8.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): -61.04; HRMS (ESI) *m/z*: calcd for $C_{17}H_{19}F_3NO_2$ ($[M+H]^+$) 326.1368, found 326.1360; HPLC analysis:

Daicel CHIRALPAK AS-H, *n*-hexane/*i*-PrOH = 9/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 14.665 min, t_{minor} = 17.404 min.

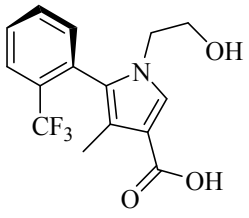


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.247	MM	1.1915	3667.61694	51.30151	50.3459
2	16.860	MM	1.2311	3617.22461	48.96938	49.6541



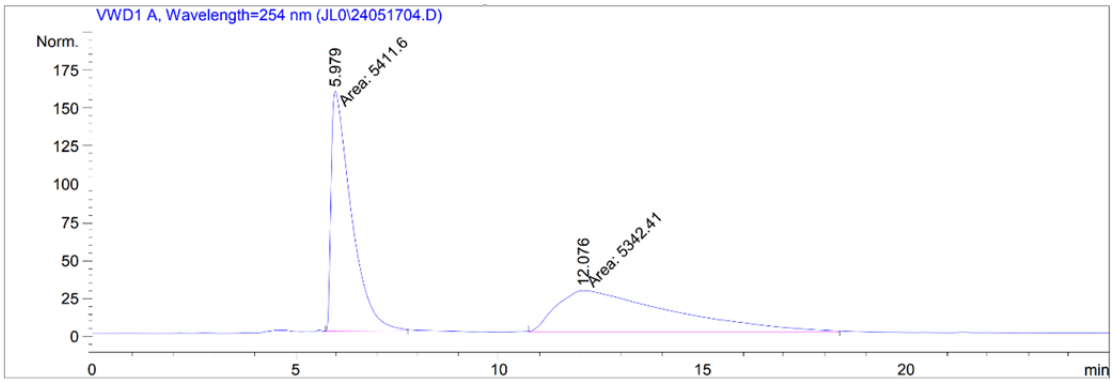
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.665	MM	1.3166	6419.15967	81.26168	90.7759
2	17.404	MM	1.1788	652.27771	9.22245	9.2241

(S)-1-(2-Hydroxyethyl)-4-methyl-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylic acid (5a)

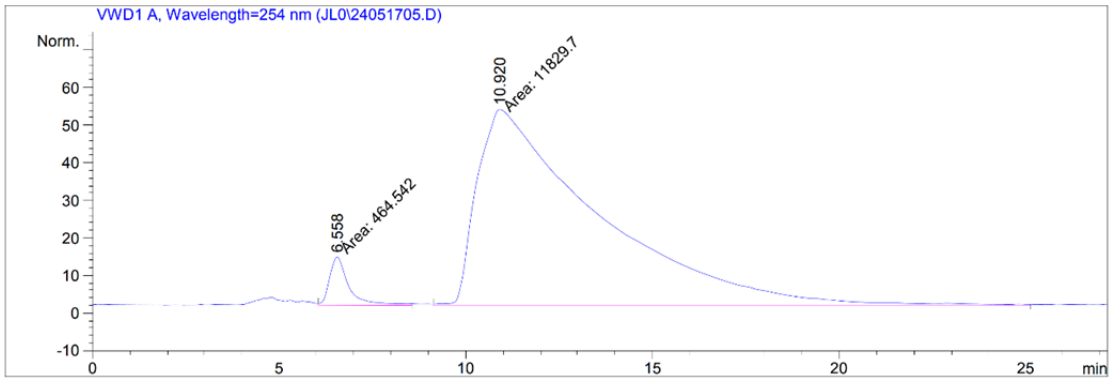


White solid; m.p. 172.3-172.7 °C; 75% yield; 92% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 11.65 (s, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.80 - 7.76 (m, 1H), 7.73 - 7.69 (m, 1H), 7.51 (s, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 4.87 (s, 1H), 3.51 - 3.42 (m, 4H), 1.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 135.3, 132.9, 130.44 (q, *J* = 2.0 Hz), 130.40 (q, *J* = 29.3 Hz), 130.1, 128.0, 127.6, 126.7 (q, *J* = 5.1

Hz), 124.2 (q, J = 274.7 Hz), 119.1, 113.7, 60.8, 49.7, 11.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ (ppm): -59.63; HRMS (ESI) *m/z*: calcd for $C_{15}H_{15}F_3NO_3$ ($[M+H]^+$) 314.1004, found 314.1002; HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 1/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 6.558 min, t_{minor} = 10.920 min.

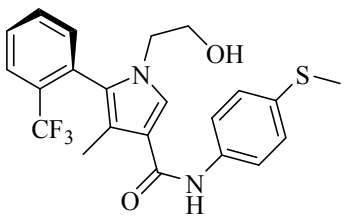


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.979	MM	0.5723	5411.59961	157.60480	50.3217
2	12.076	MM	3.2693	5342.40723	27.23508	49.6783

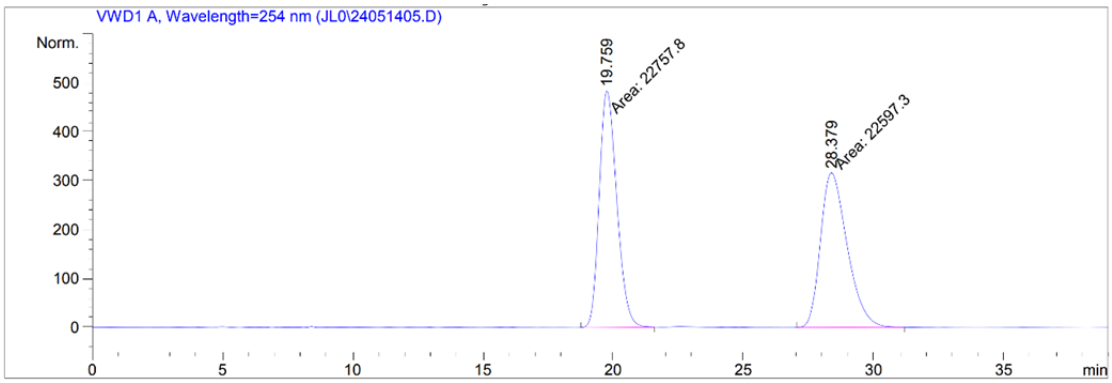


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.558	MM	0.6015	464.54175	12.87145	3.7785
2	10.920	MM	3.7688	1.18297e4	52.31427	96.2215

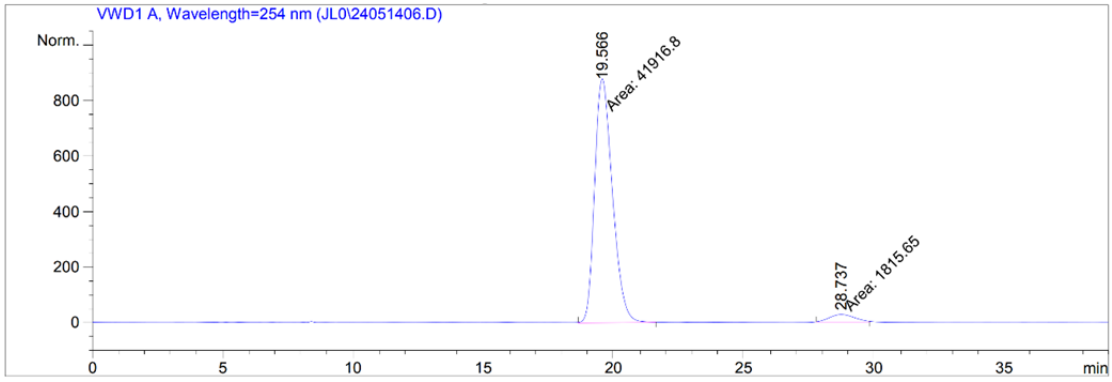
(S)-1-(2-Hydroxyethyl)-4-methyl-N-(4-(methylthio)phenyl)-5-(2-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxamide (6a)



White solid; m.p. 200.9-201.3 °C; 80% yield; 92% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 9.56 (s, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.80 - 7.77 (m, 1H), 7.75 - 7.64 (m, 4H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 4.91 (s, 1H), 3.70 - 3.65 (m, 1H), 3.56 - 3.53 (m, 1H), 3.49 - 3.45 (m, 2H), 2.46 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 163.9, 138.0, 135.3, 133.0, 131.2, 130.6 (q, *J* = 2.0 Hz), 130.4 (q, *J* = 29.3 Hz), 130.1, 128.1, 127.6, 126.7 (q, *J* = 6.1 Hz), 124.3 (q, *J* = 274.7 Hz), 124.2, 120.8, 119.0, 117.1, 60.9, 49.8, 16.2, 11.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -59.52; HRMS (ESI) *m/z*: calcd for $C_{22}H_{22}F_3N_2O_2S$ ($[M+H]^+$) 435.1354, found 435.1346; HPLC analysis: Daicel CHIRALPAK IG, *n*-hexane/*i*-PrOH = 7/3, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 19.566 min, t_{minor} = 28.737 min.

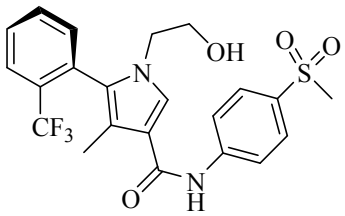


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.759	MM	0.7842	2.27578e4	483.69830	50.1770
2	28.379	MM	1.1924	2.25972e4	315.84601	49.8230

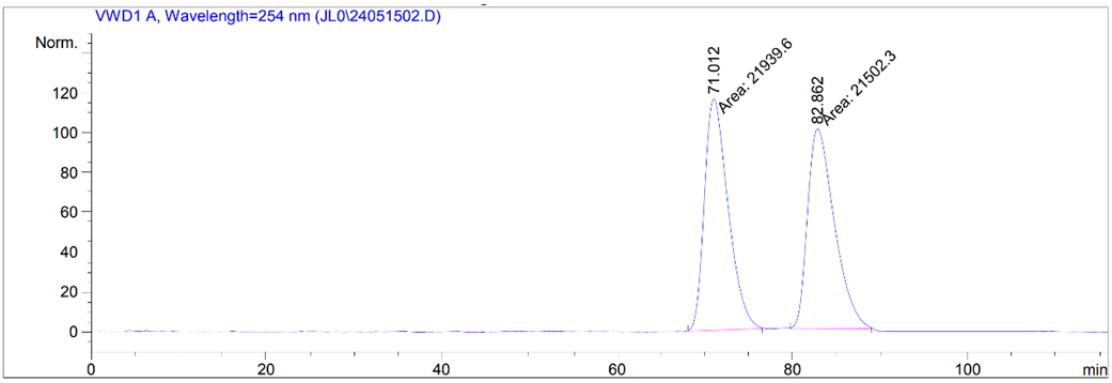


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.566	MM	0.7936	4.19168e4	880.28687	95.8483
2	28.737	MM	1.1094	1815.65210	27.27722	4.1517

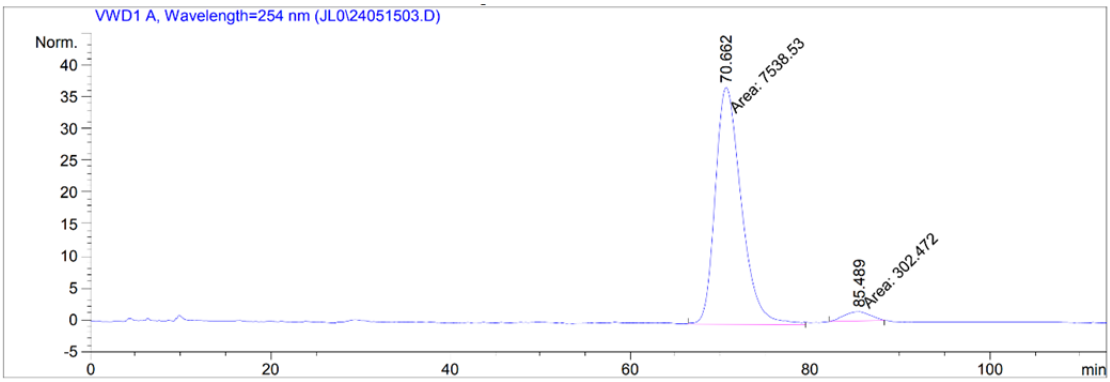
Esaxerenone



White solid; m.p. 160.2-160.4 °C; 69% yield; 92% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.39 (s, 1H), 7.79 - 7.73 (m, 3H), 7.62 - 7.50 (m, 4H), 7.32 (d, *J* = 7.4 Hz, 1H), 3.70 - 3.56 (m, 4H), 2.67 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.4, 142.0, 138.4, 134.5, 131.9, 131.4 (q, *J* = 30.2 Hz), 130.2, 129.4, 128.7, 126.4 (q, *J* = 6.3 Hz), 124.7, 124.0, 123.7 (q, *J* = 277.2 Hz), 120.6, 119.1, 117.3, 61.5, 49.6, 43.5, 11.2; ^{19}F NMR (470 MHz, $CDCl_3$) δ (ppm): -60.9; HRMS (ESI) *m/z*: calcd for $C_{22}H_{22}F_3N_2O_4S$ ($[M+H]^+$) 467.1525, found 467.1517; HPLC analysis: Daicel CHIRALPAK IG, *n*-hexane/*i*-PrOH = 7/2, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 70.662 min, t_{minor} = 85.489 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	71.012	MM	3.1374	2.19396e4	116.54932	50.5034
2	82.862	MM	3.5557	2.15023e4	100.78790	49.4966



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	70.662	MM	3.3759	7538.53320	37.21762	96.1424
2	85.489	MM	3.4221	302.47229	1.47312	3.8576

5. References

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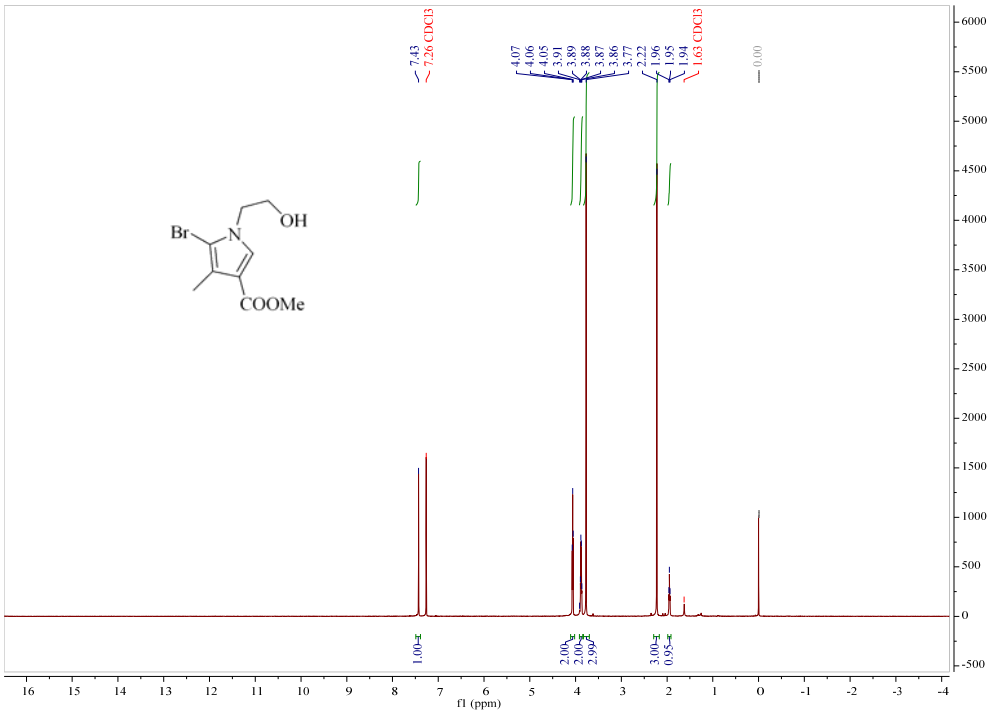
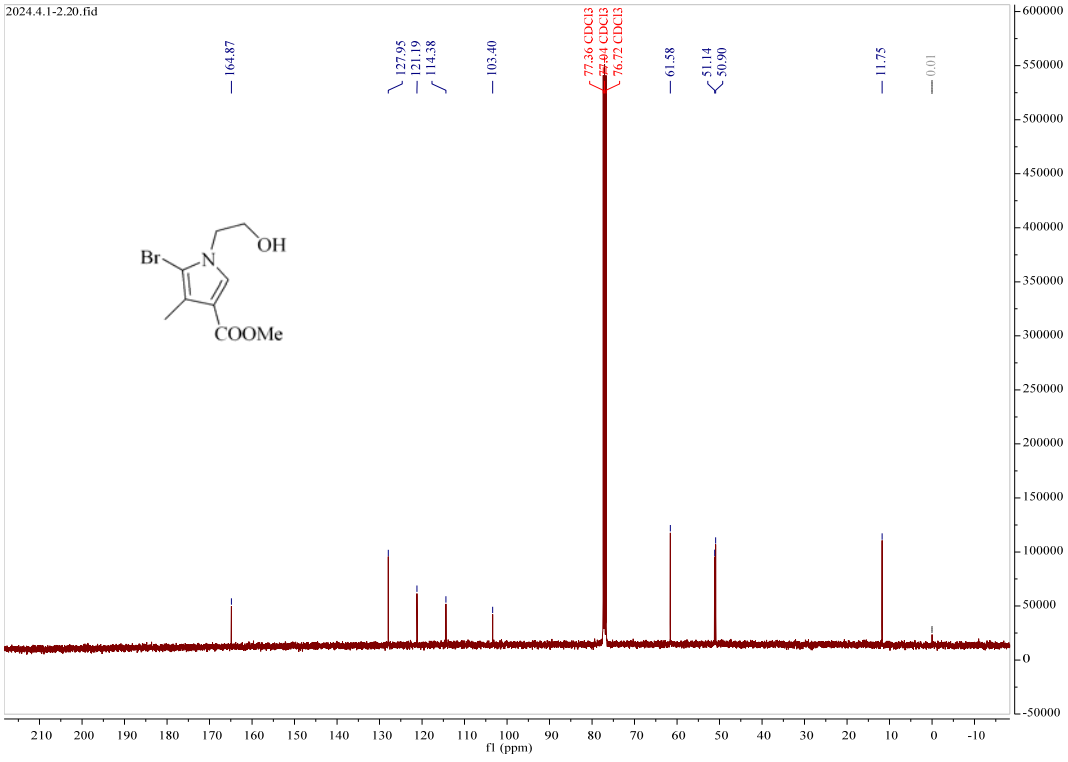
6. Copy of NMR spectra for the products

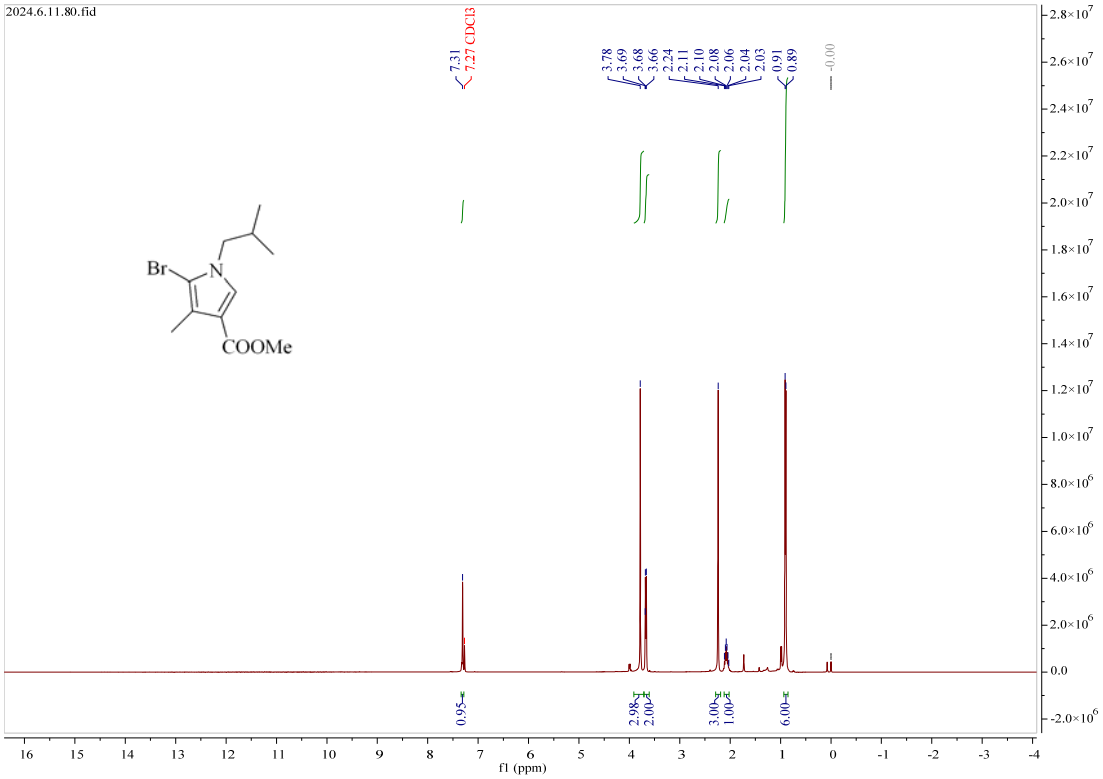
^{1}H NMR (500 MHz, $CDCl_3$) (3a)



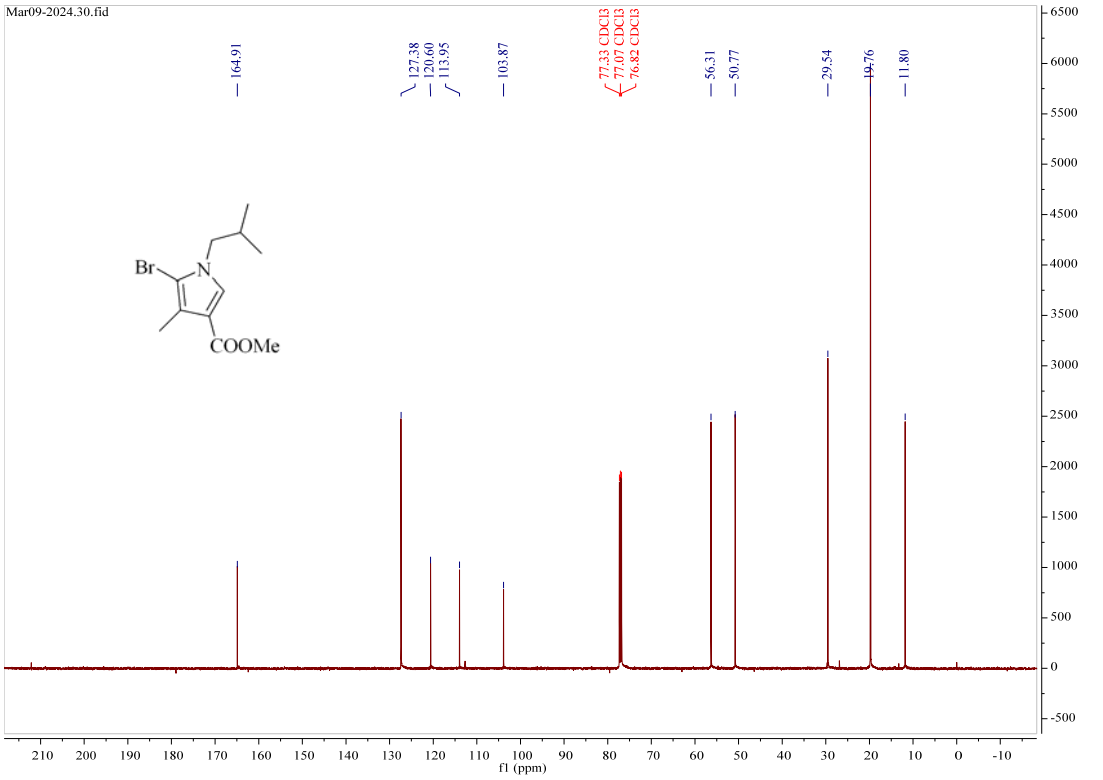
^{13}C NMR (101 MHz, $CDCl_3$) (3a)



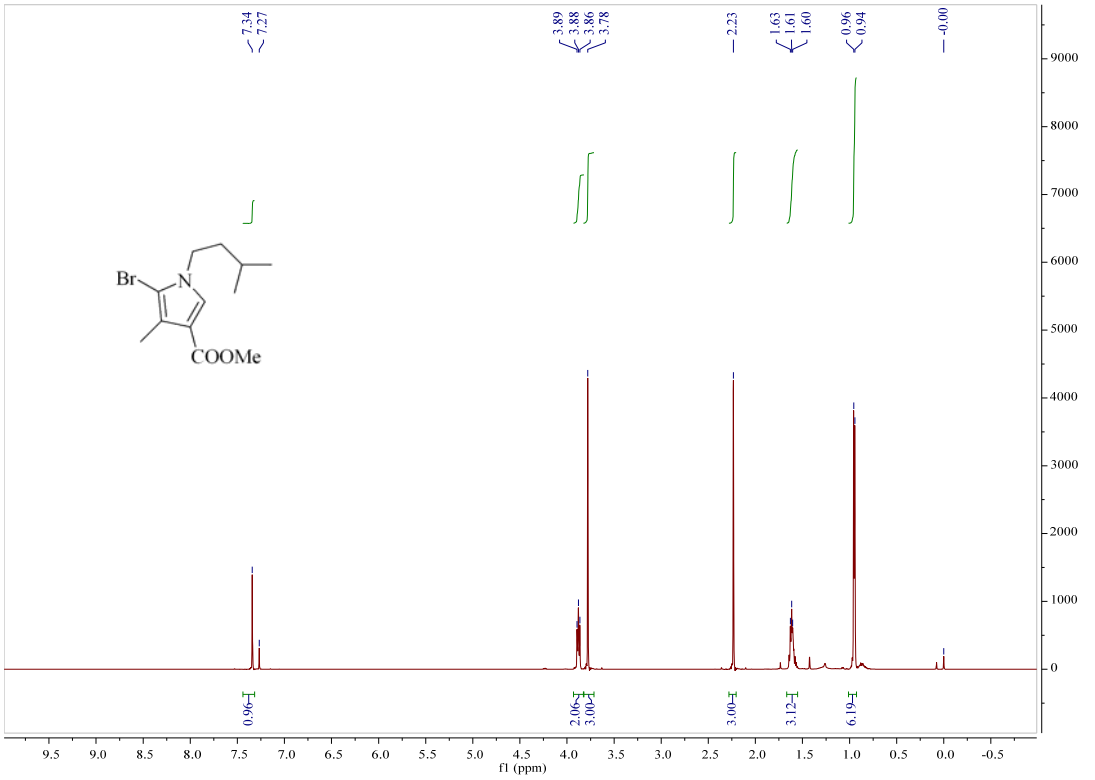
^{1}H NMR (400 MHz, $CDCl_3$) (3b)



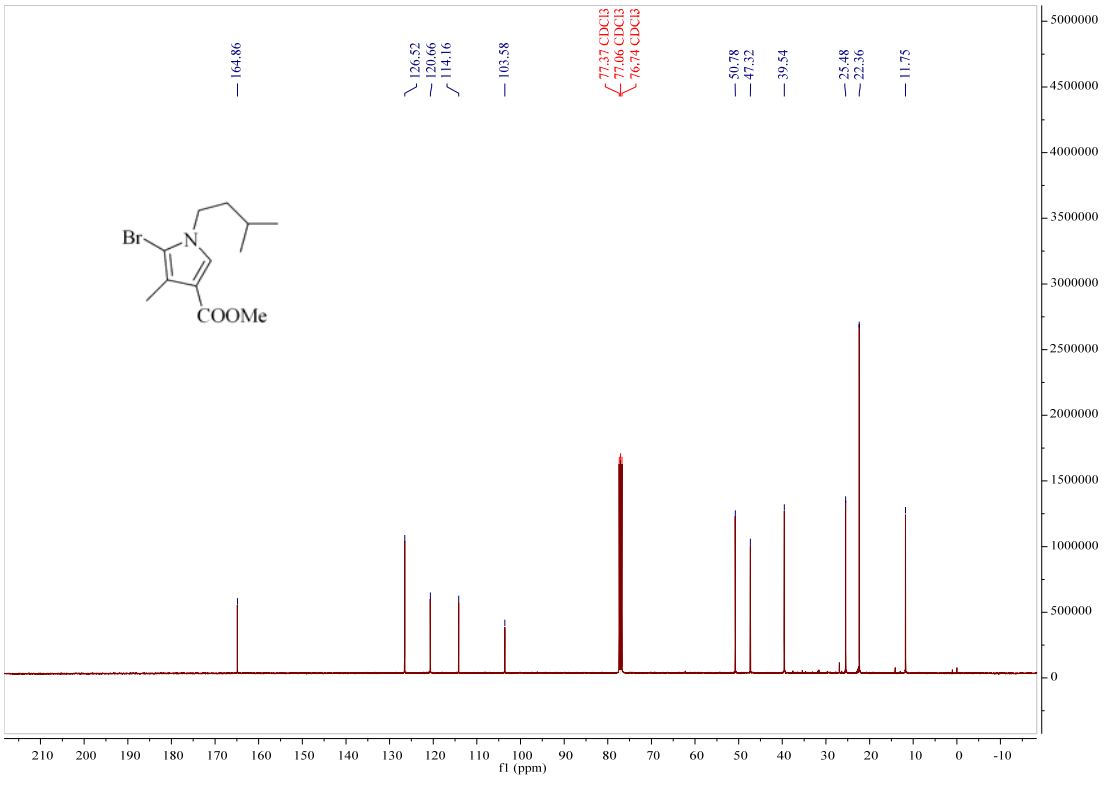
^{13}C NMR (126 MHz, $CDCl_3$) (3b)



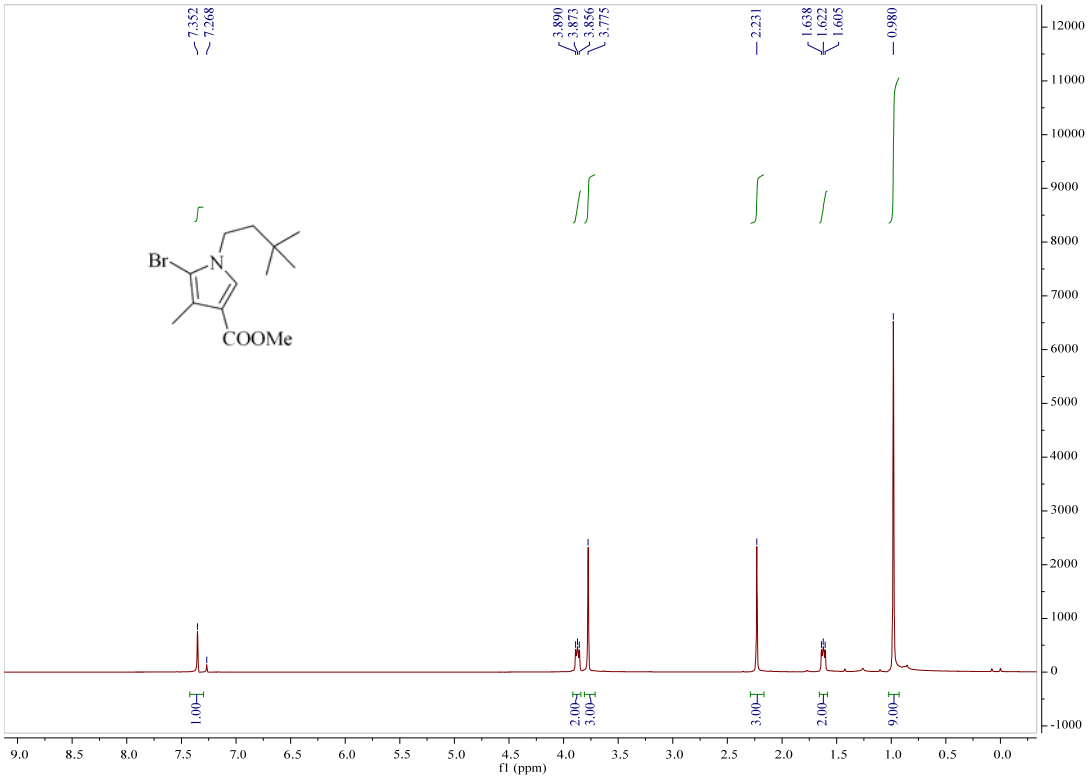
^{1}H NMR (500 MHz, $CDCl_3$) (3c)



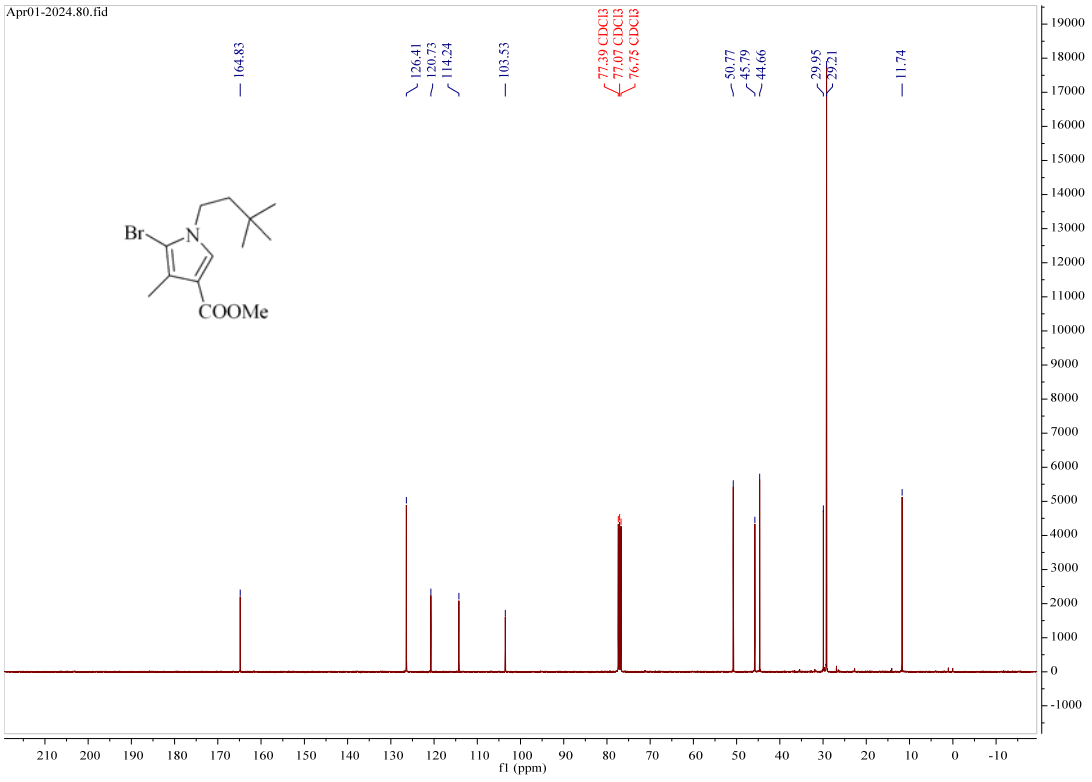
^{13}C NMR (101 MHz, $CDCl_3$) (3c)



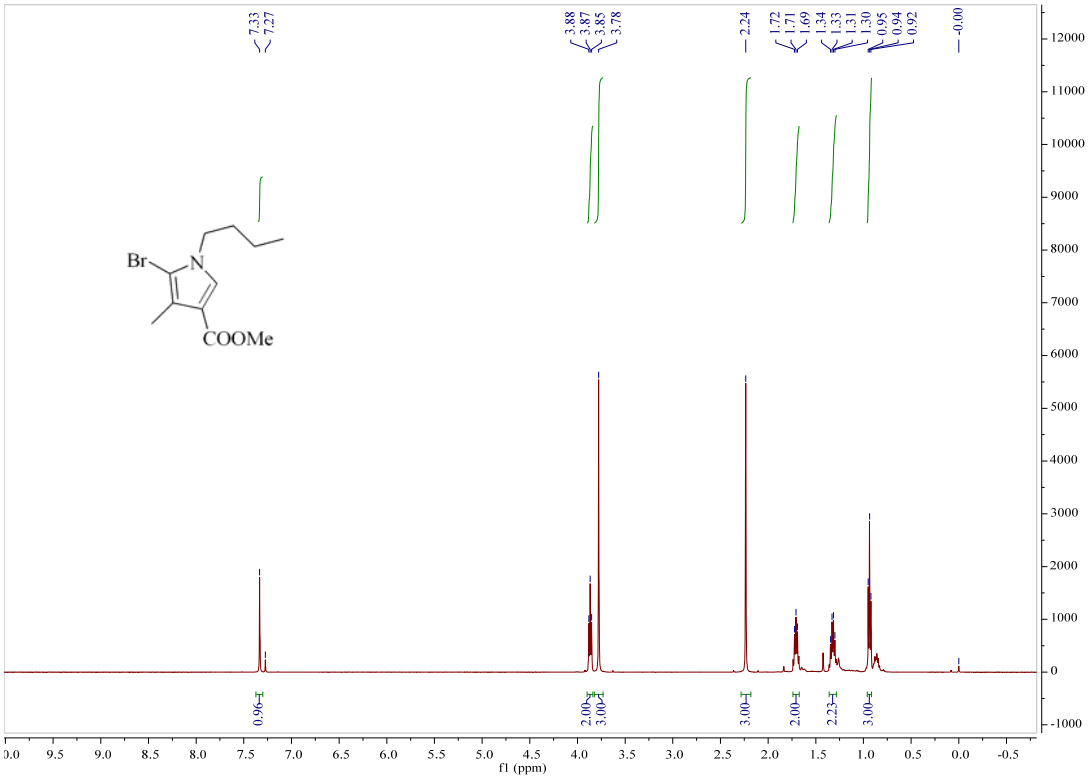
^{1}H NMR (500 MHz, $CDCl_3$) (3d)



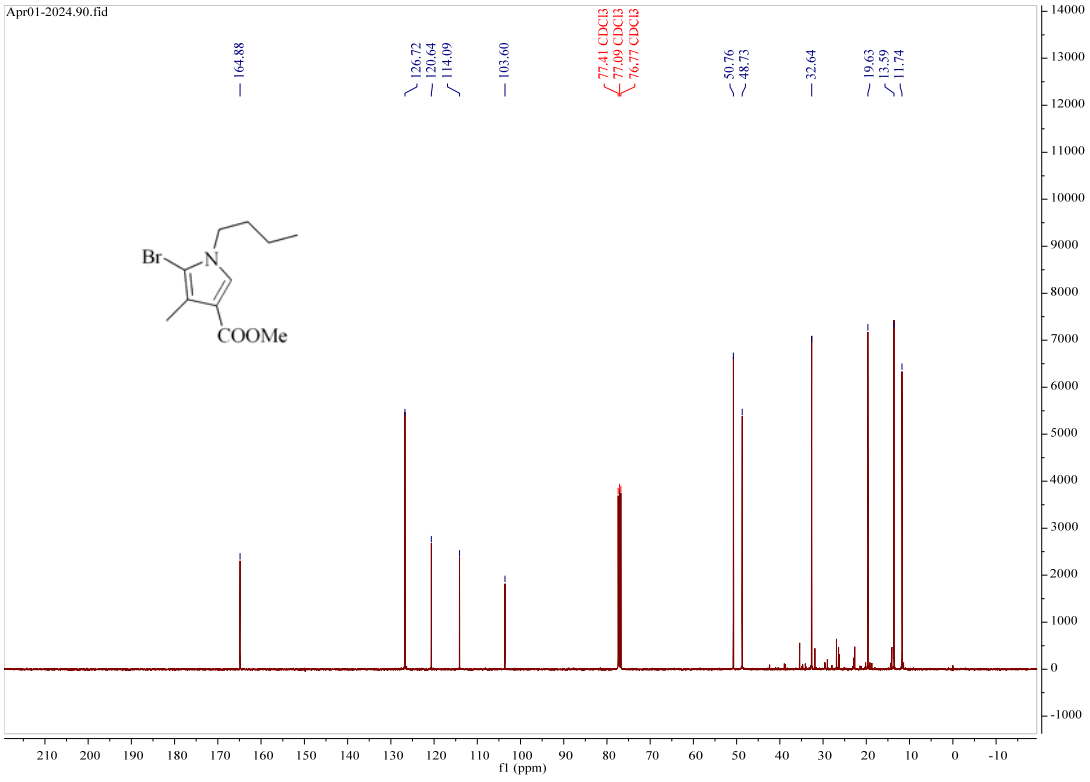
^{13}C NMR (101 MHz, $CDCl_3$) (3d)



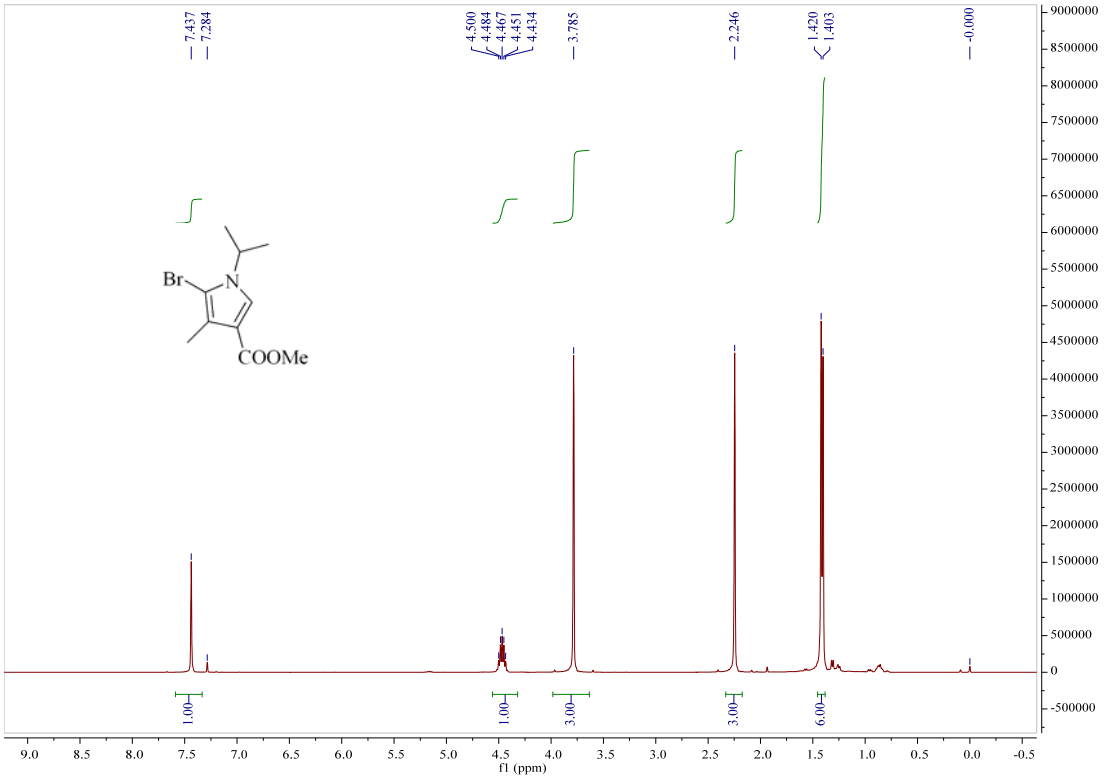
^{1}H NMR (500 MHz, $CDCl_3$) (3e)



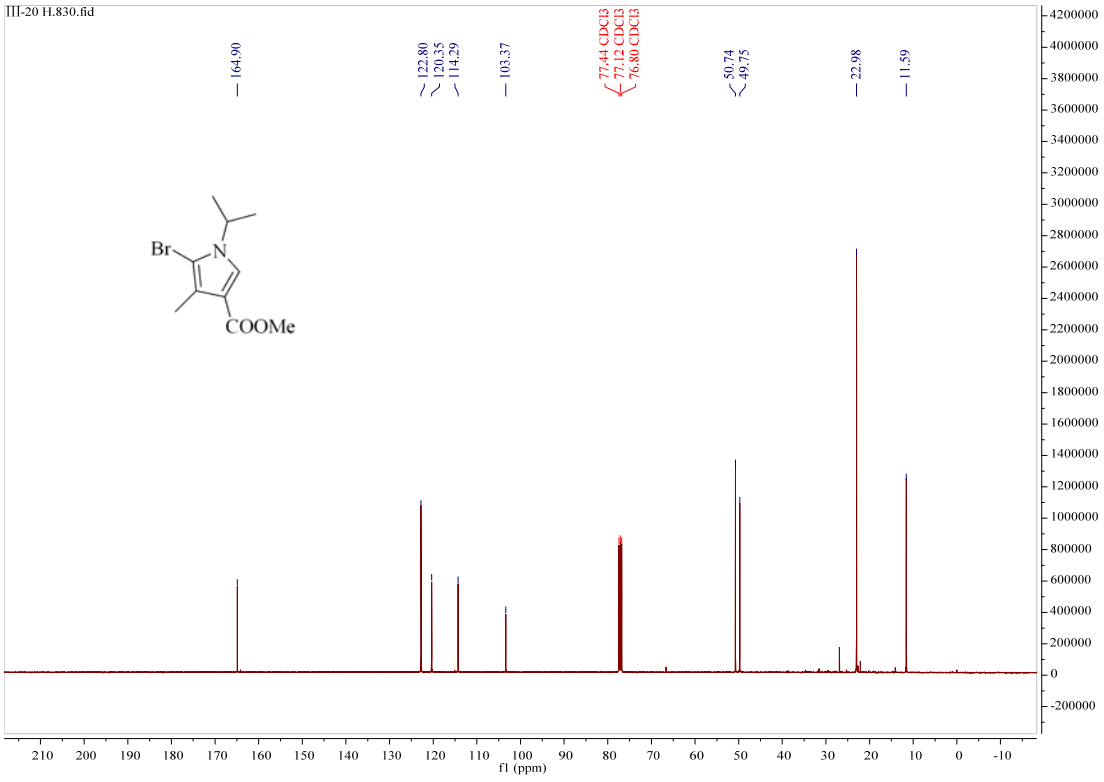
^{13}C NMR (101 MHz, $CDCl_3$) (3e)



^{1}H NMR (400 MHz, $CDCl_3$) (3f)



^{13}C NMR (101 MHz, $CDCl_3$) (3f)



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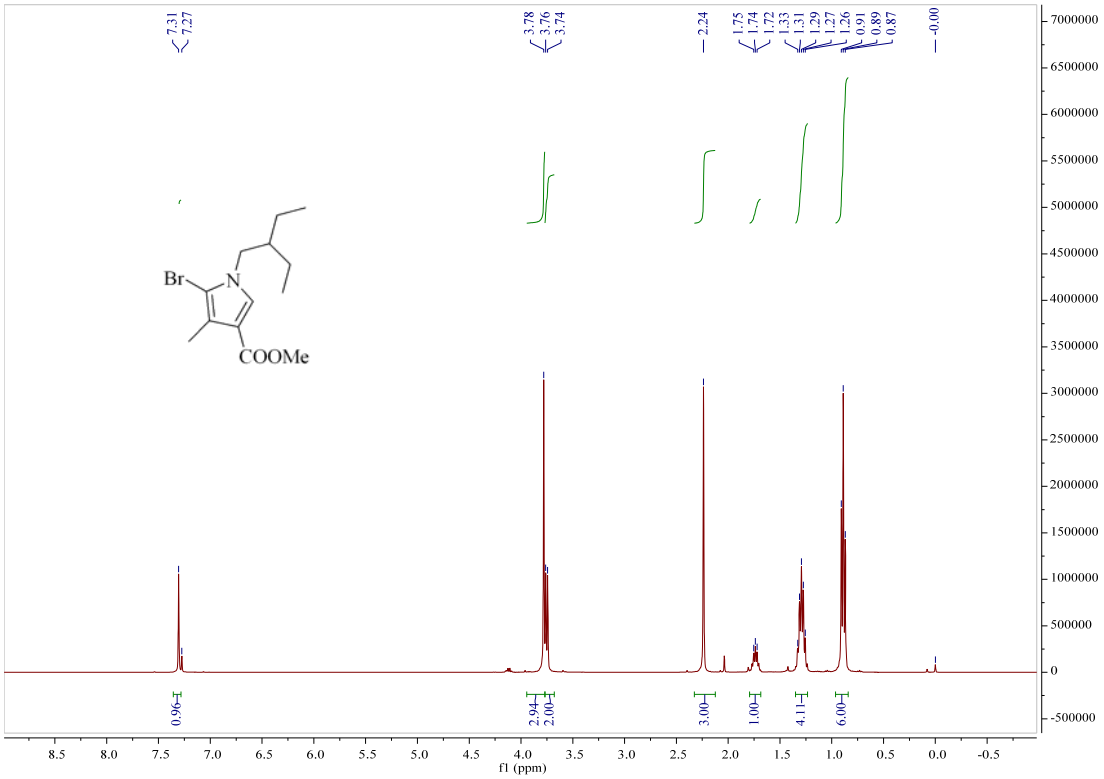
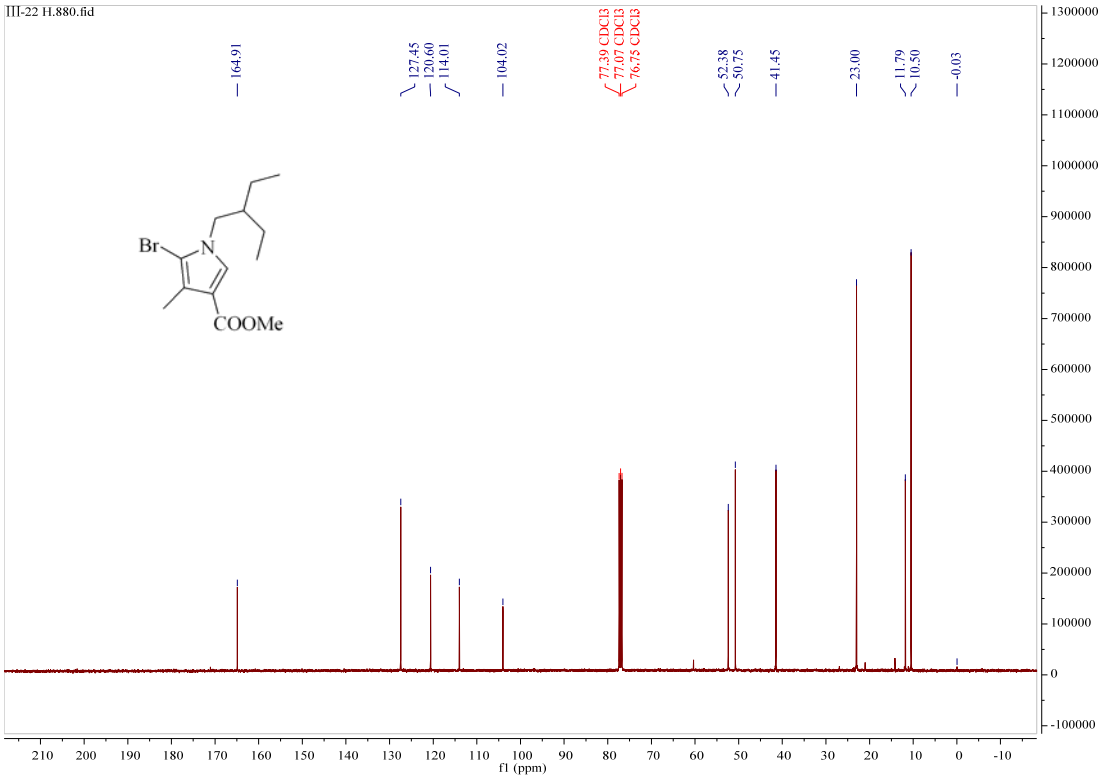
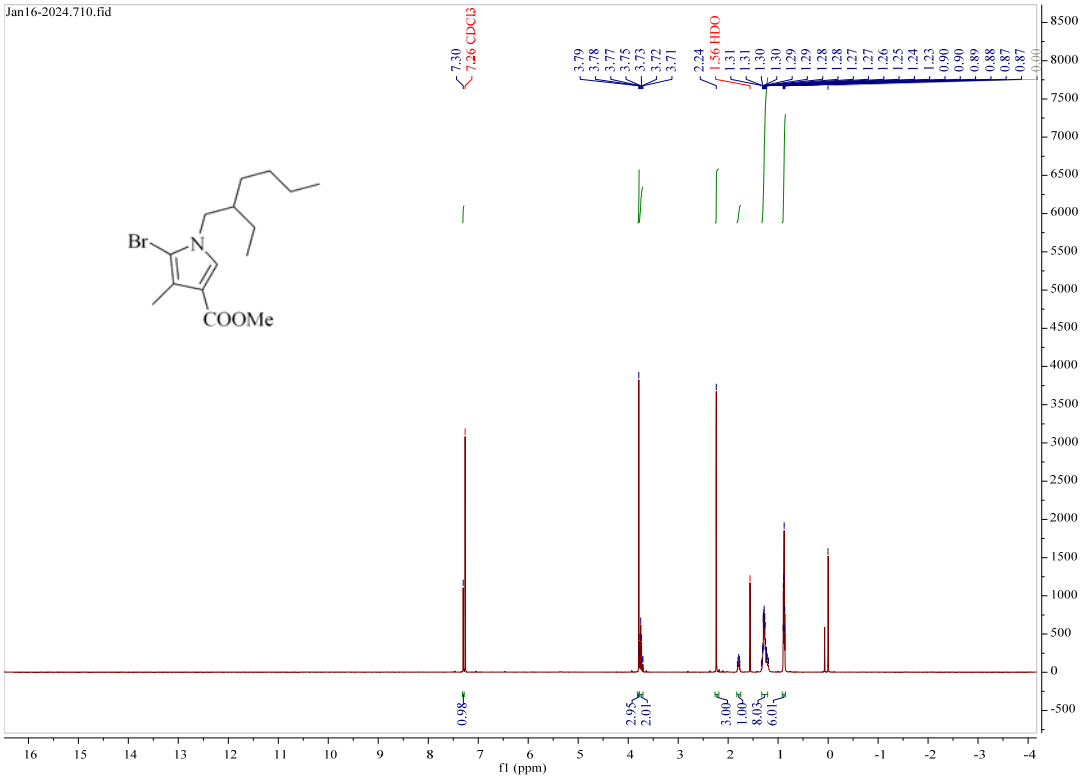


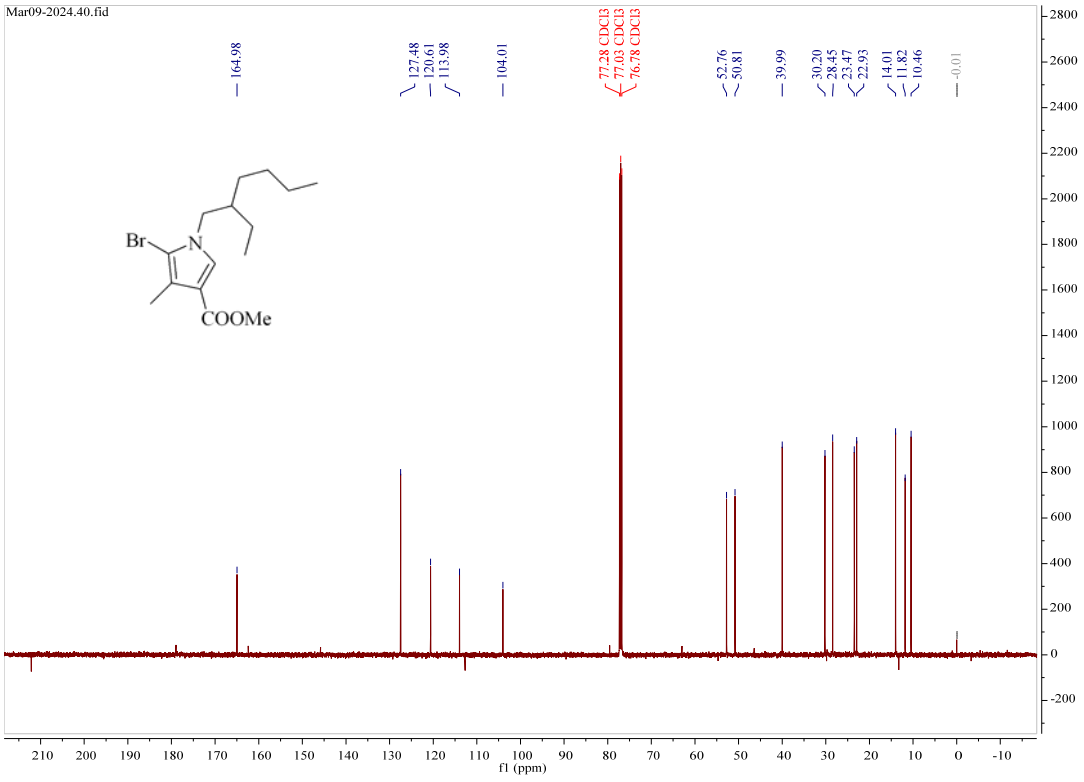
^{13}C NMR (101 MHz, $CDCl_3$) (3g)



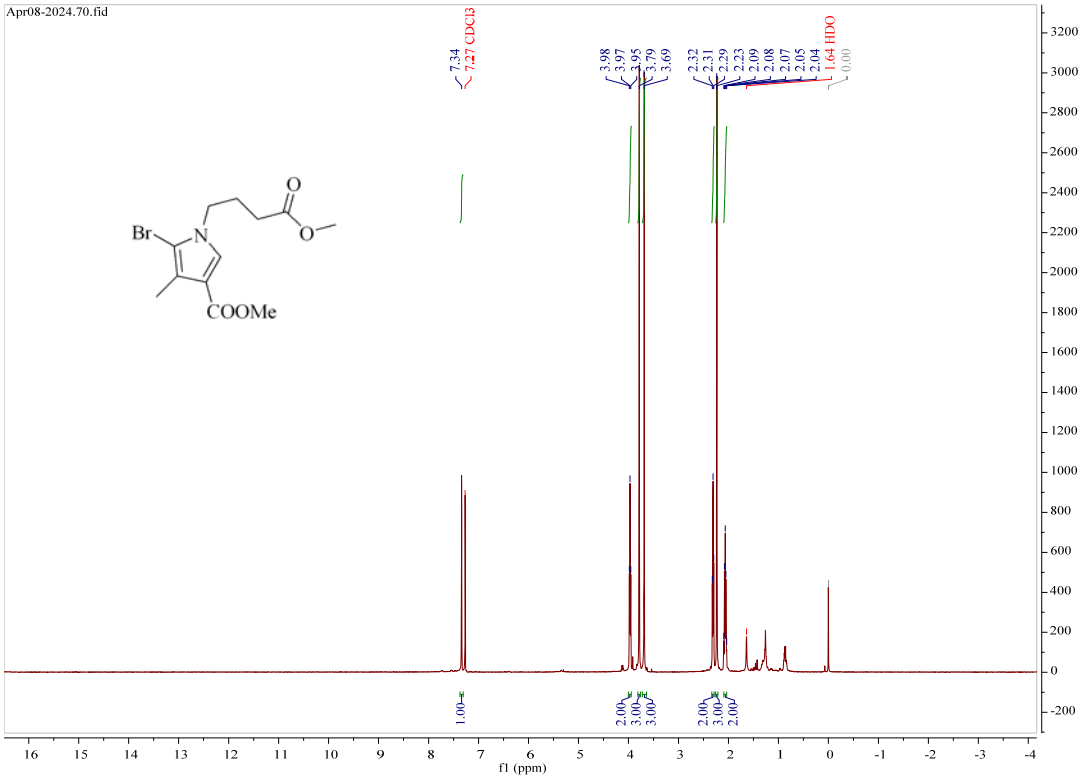
^{1}H NMR (500 MHz, $CDCl_3$) (3h)



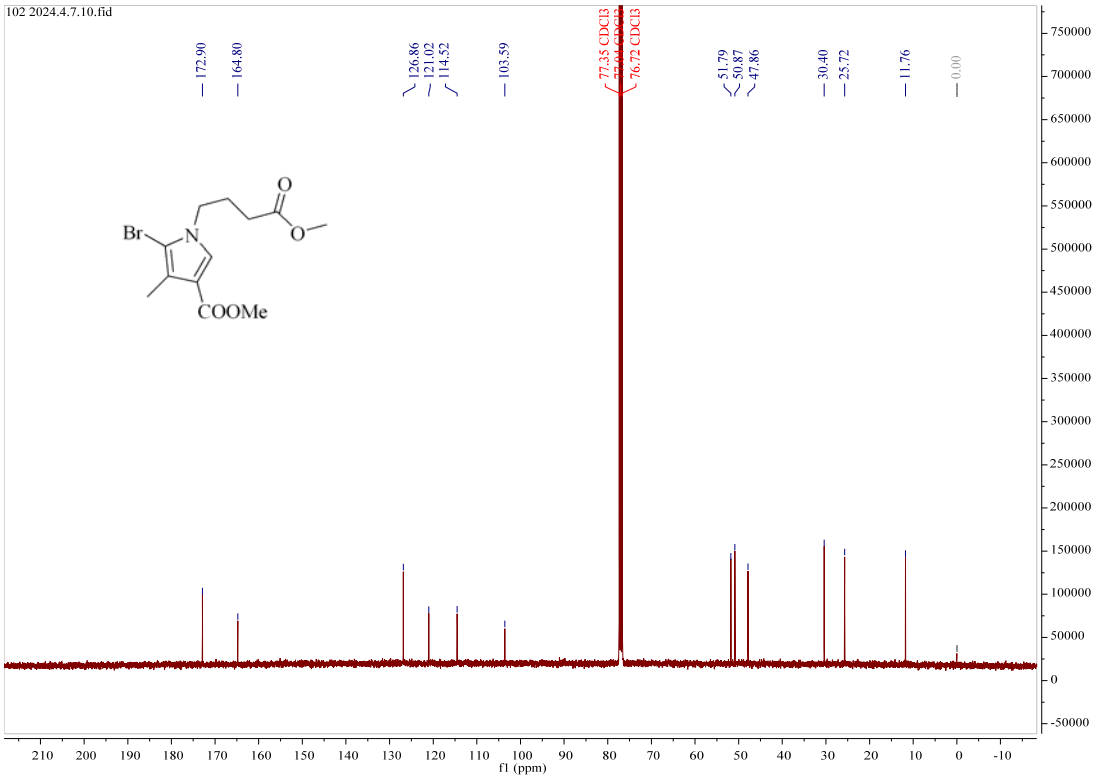
^{13}C NMR (126 MHz, $CDCl_3$) (3h)



^{1}H NMR (500 MHz, $CDCl_3$) (3i)



^{13}C NMR (101 MHz, $CDCl_3$) (3i)



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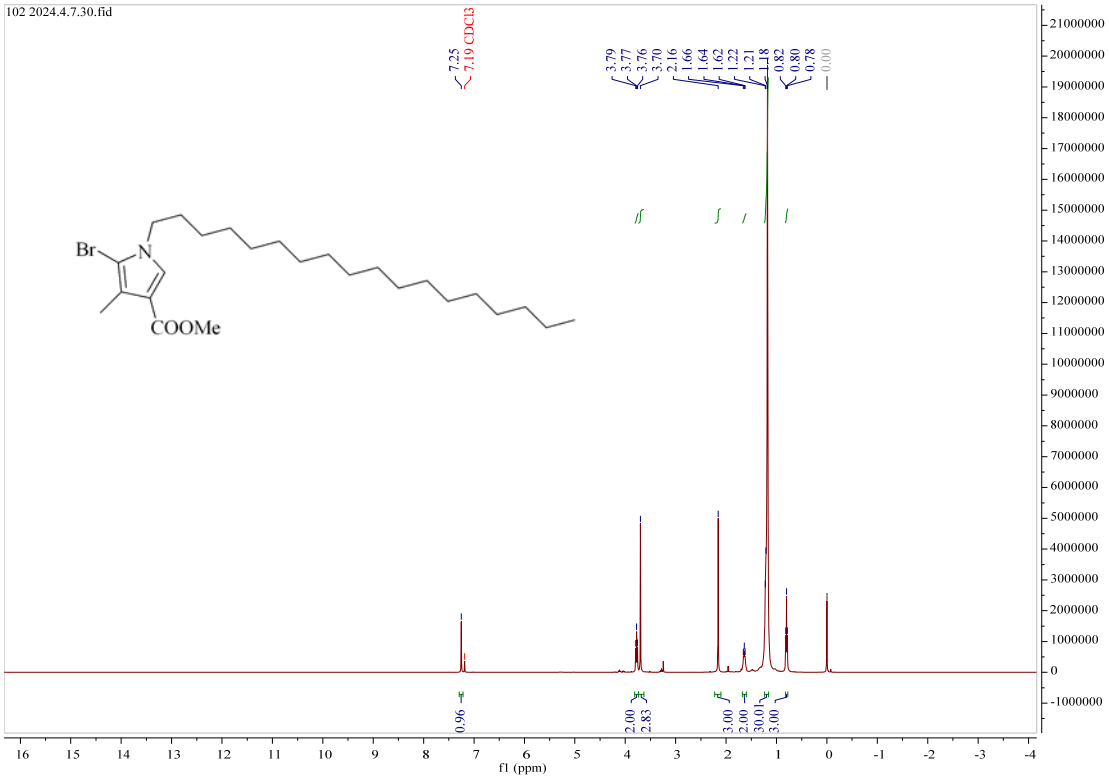

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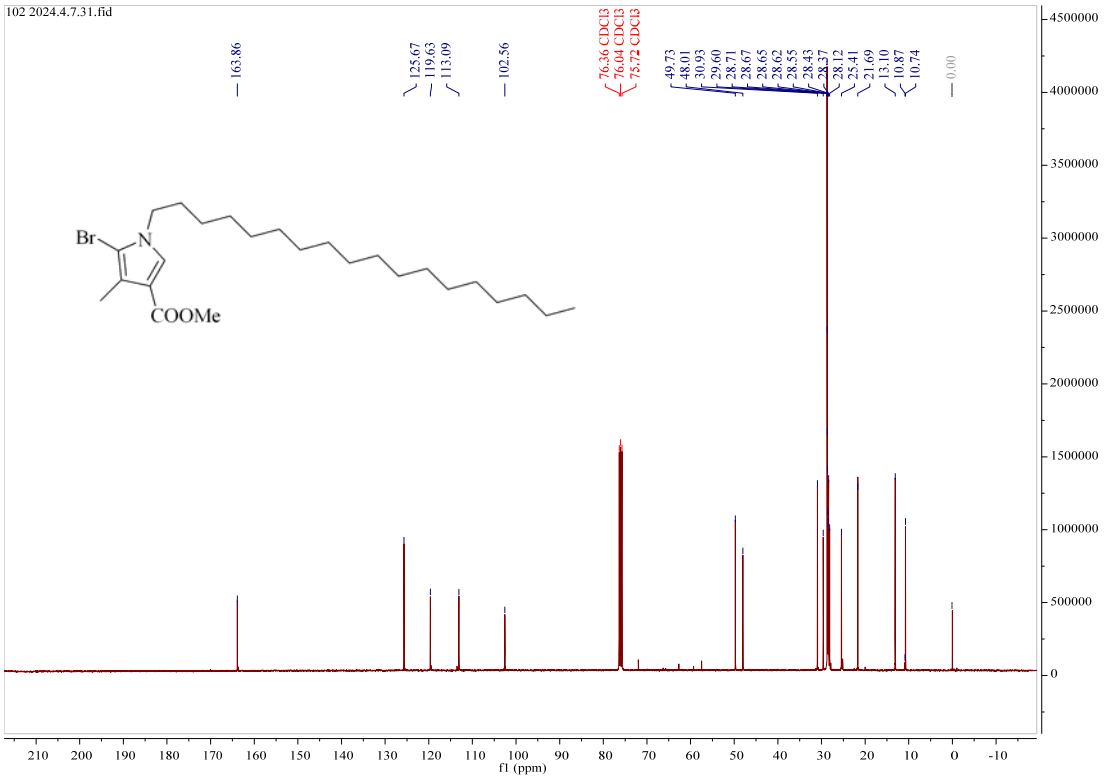

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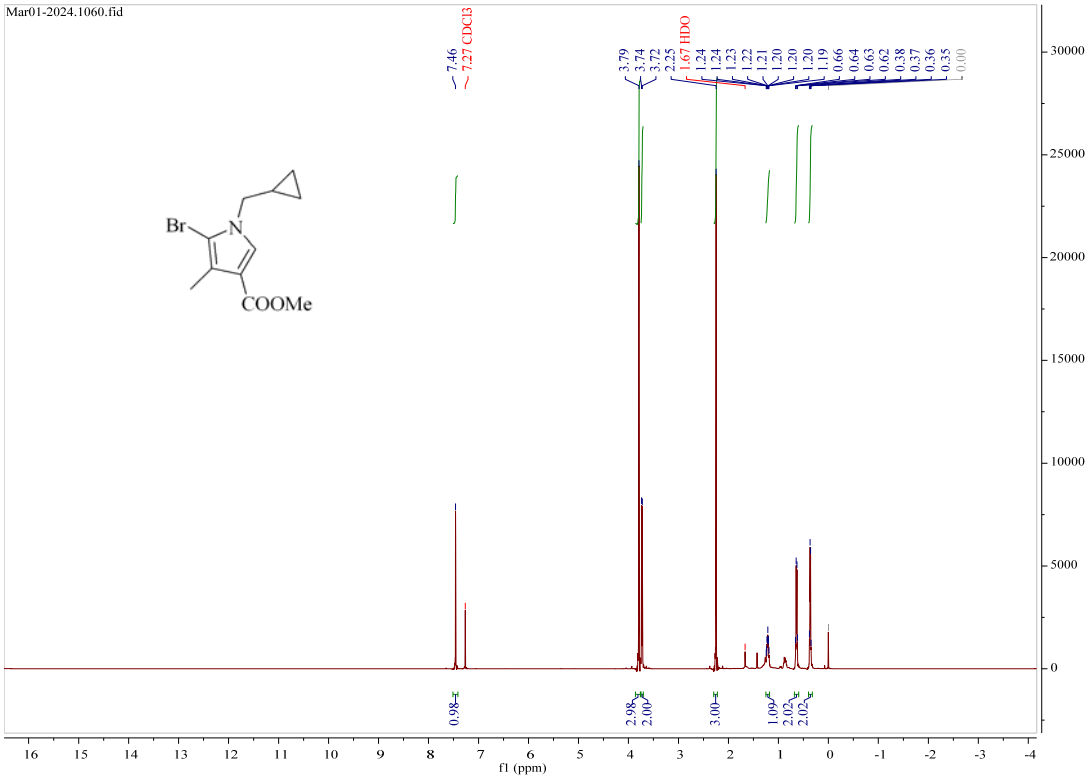

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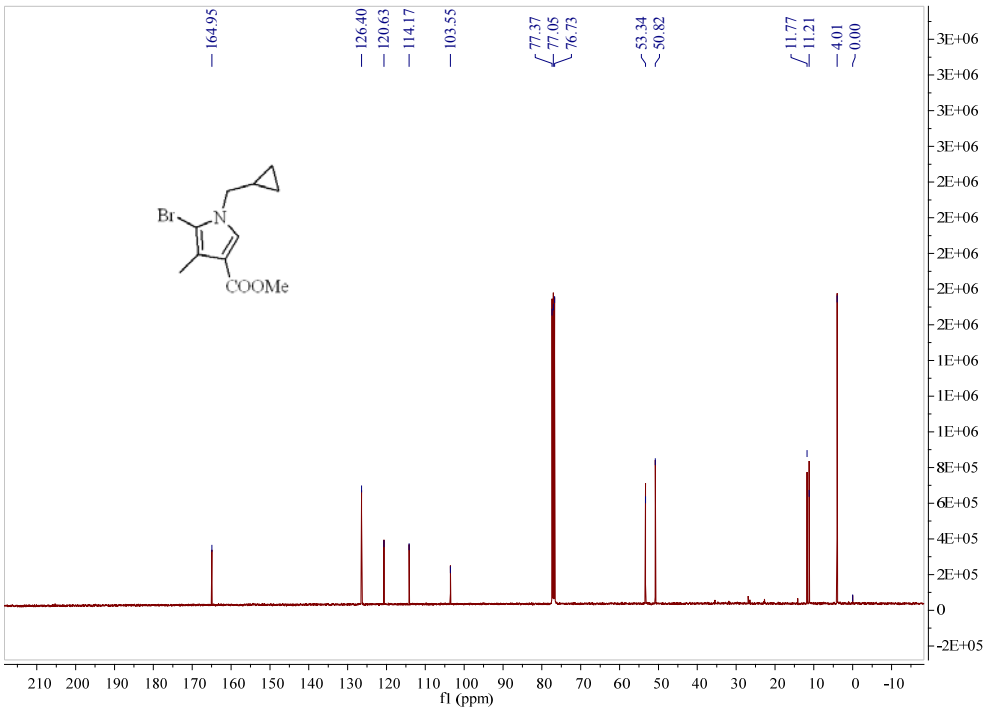

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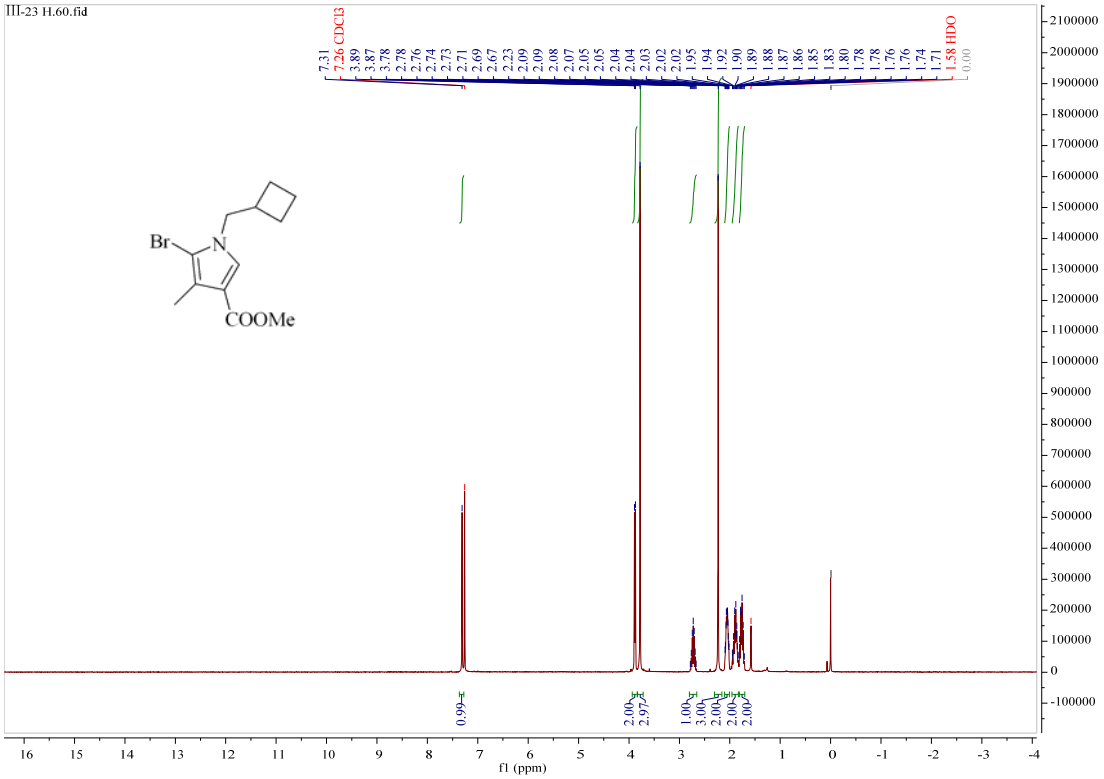

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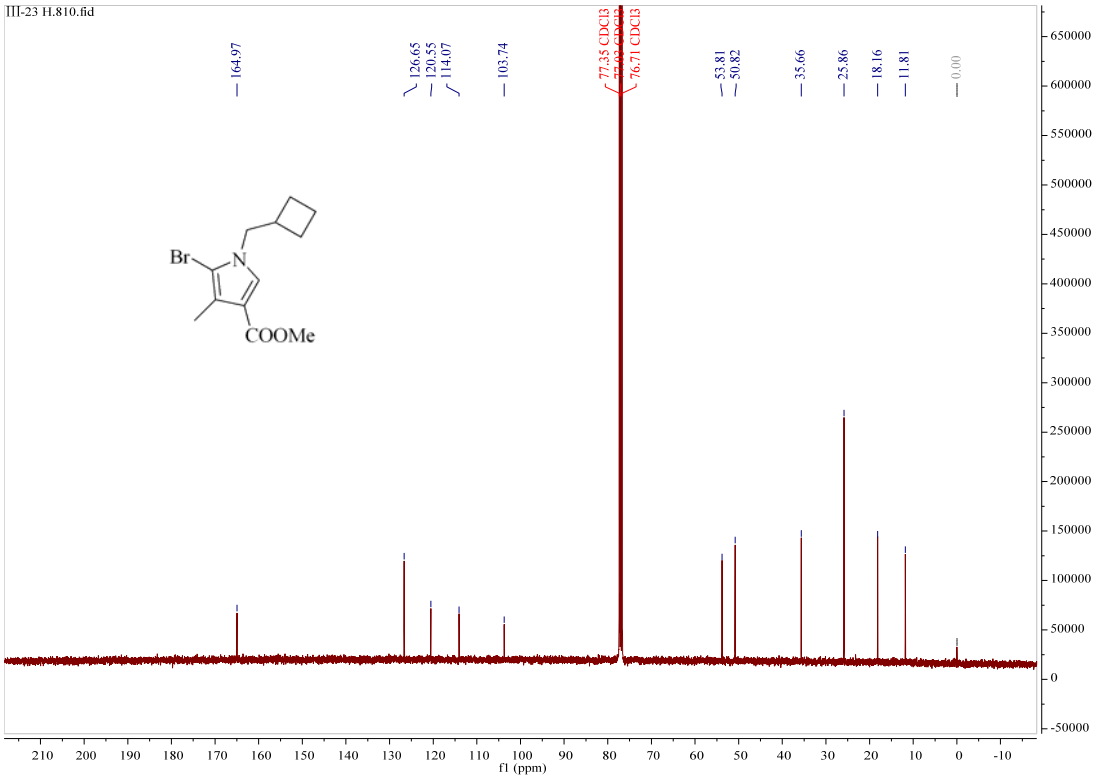

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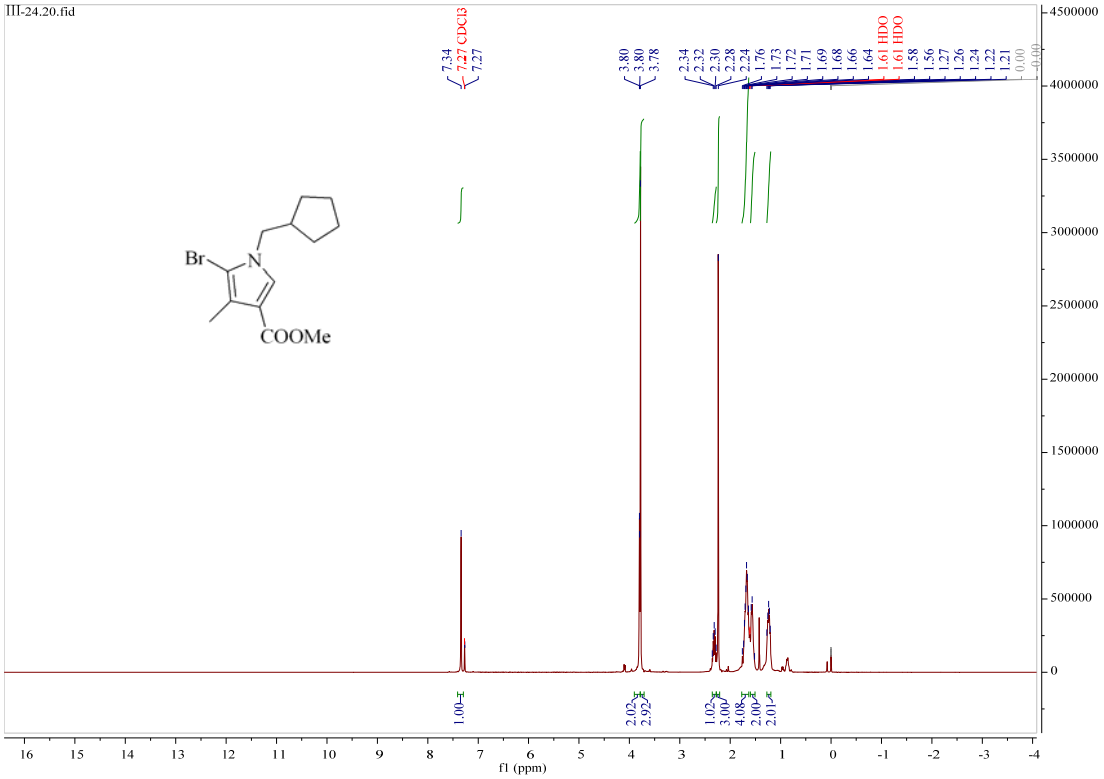

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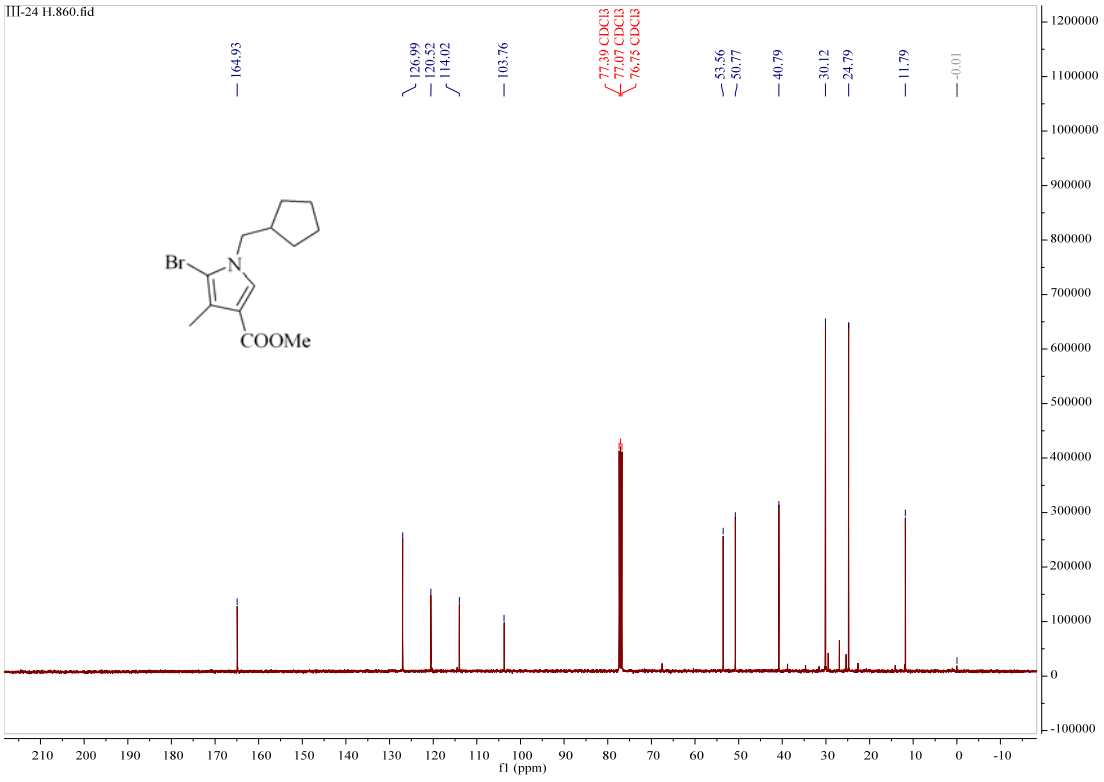

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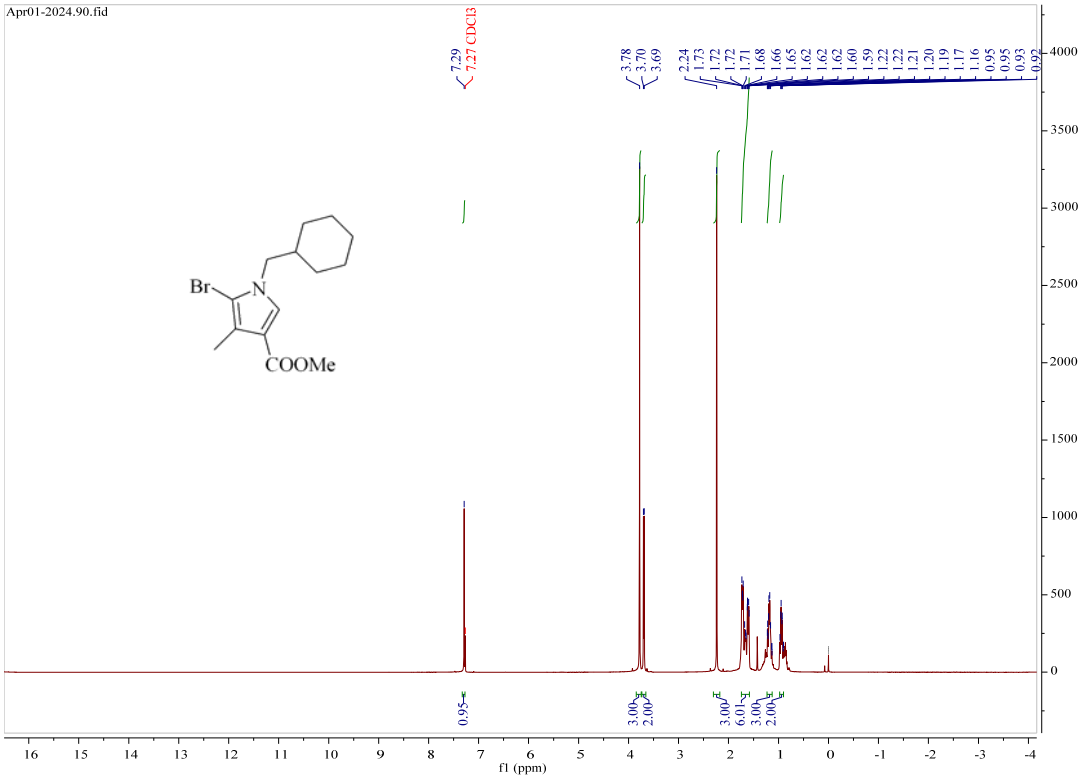
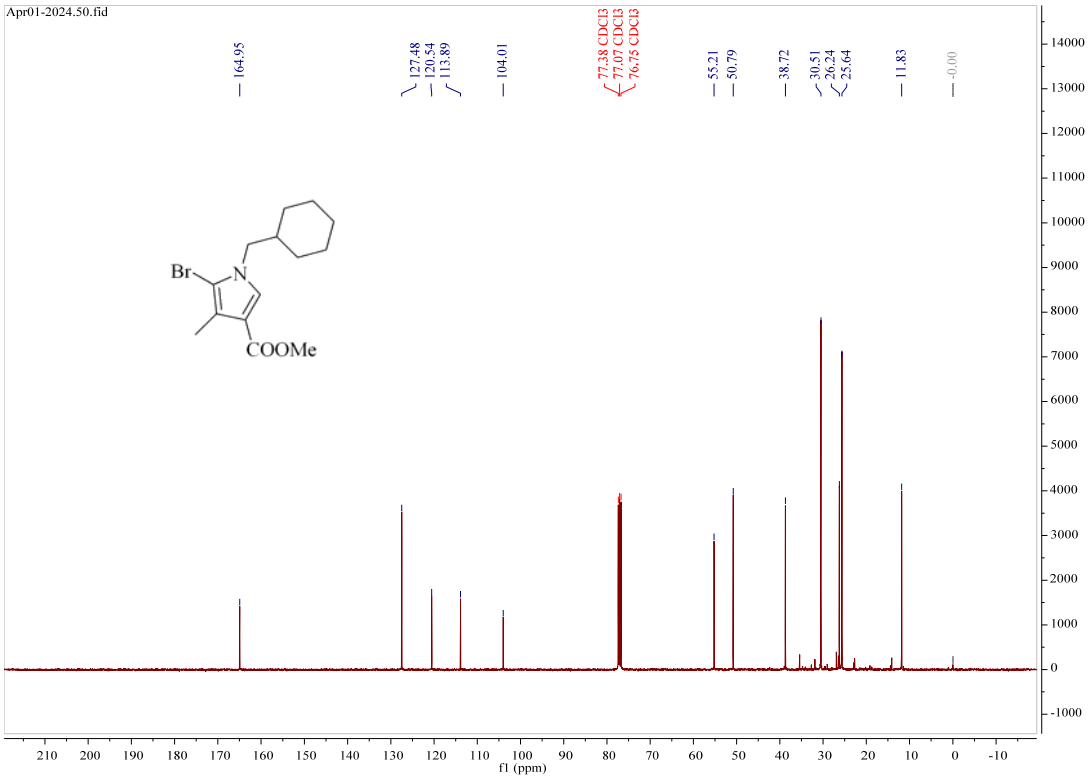
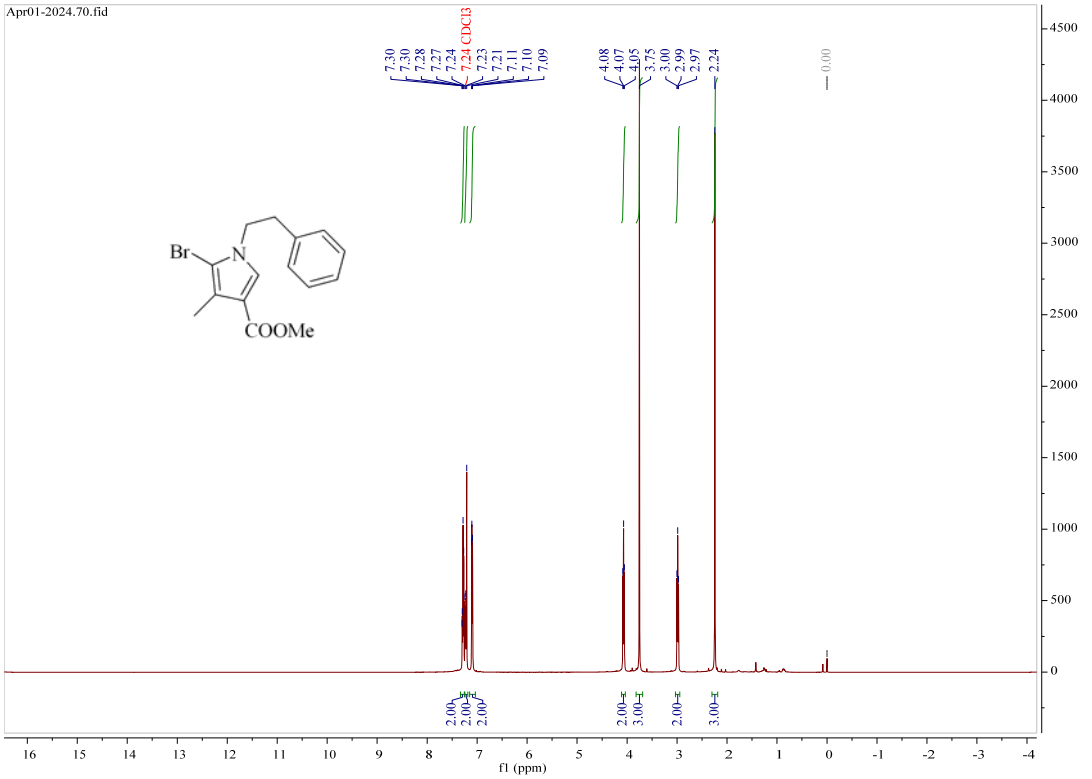


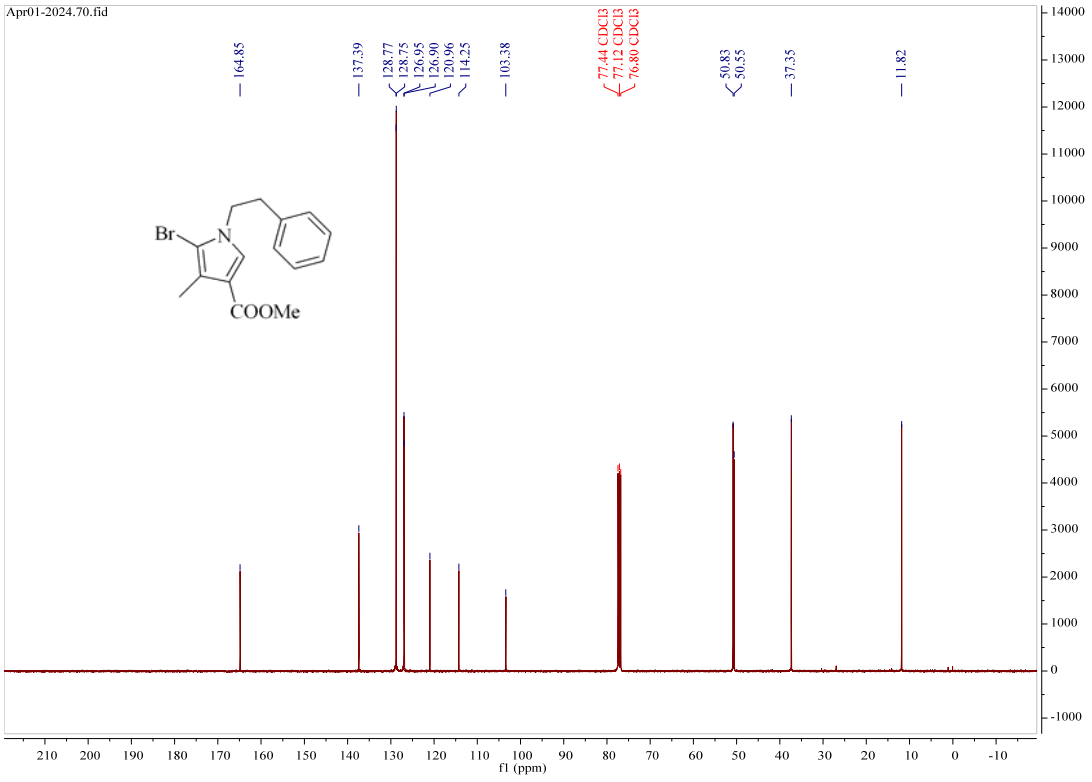
^{13}C NMR (101 MHz, $CDCl_3$) (3n)



^{1}H NMR (500 MHz, $CDCl_3$) (3o)



^{13}C NMR (101 MHz, $CDCl_3$) (3o)



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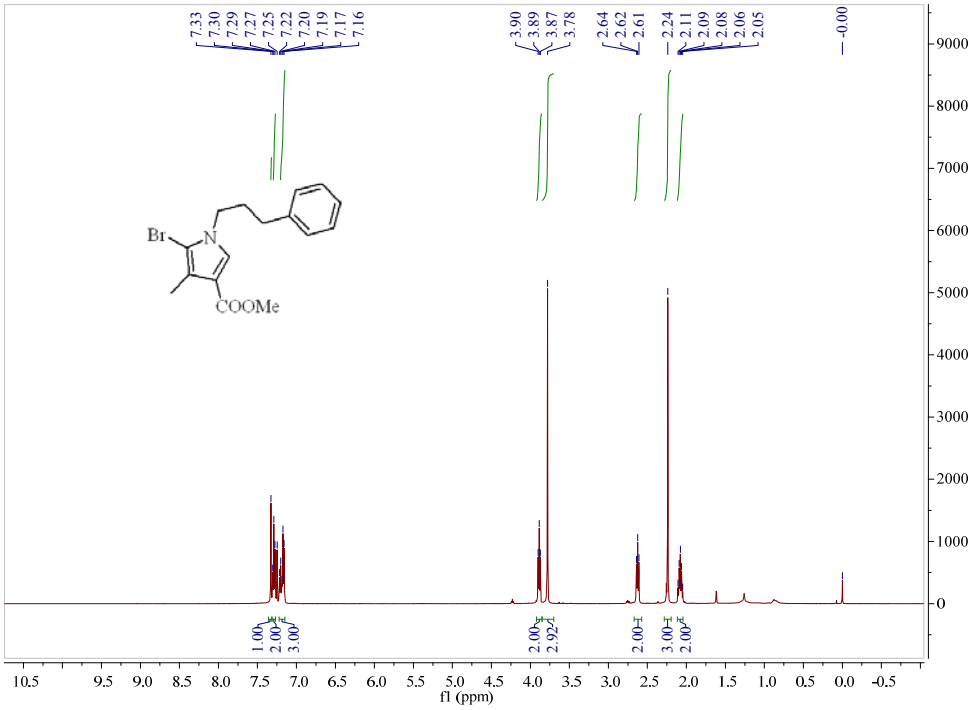
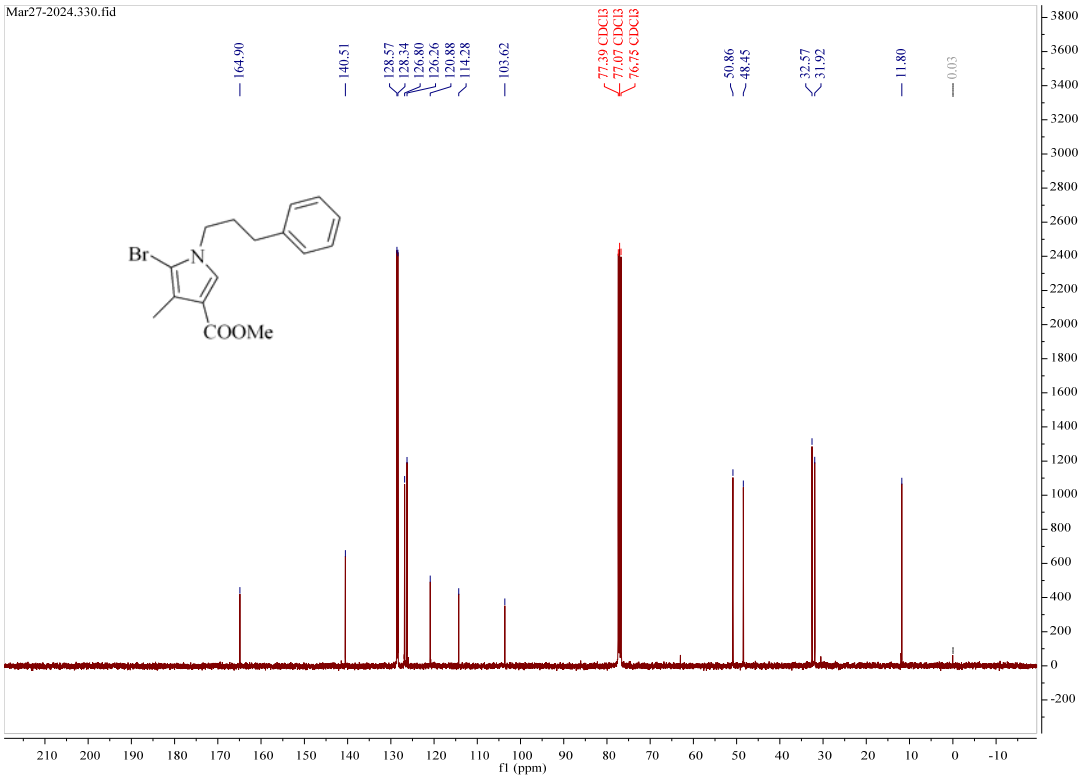


^{13}C NMR (101 MHz, $CDCl_3$) (3p)



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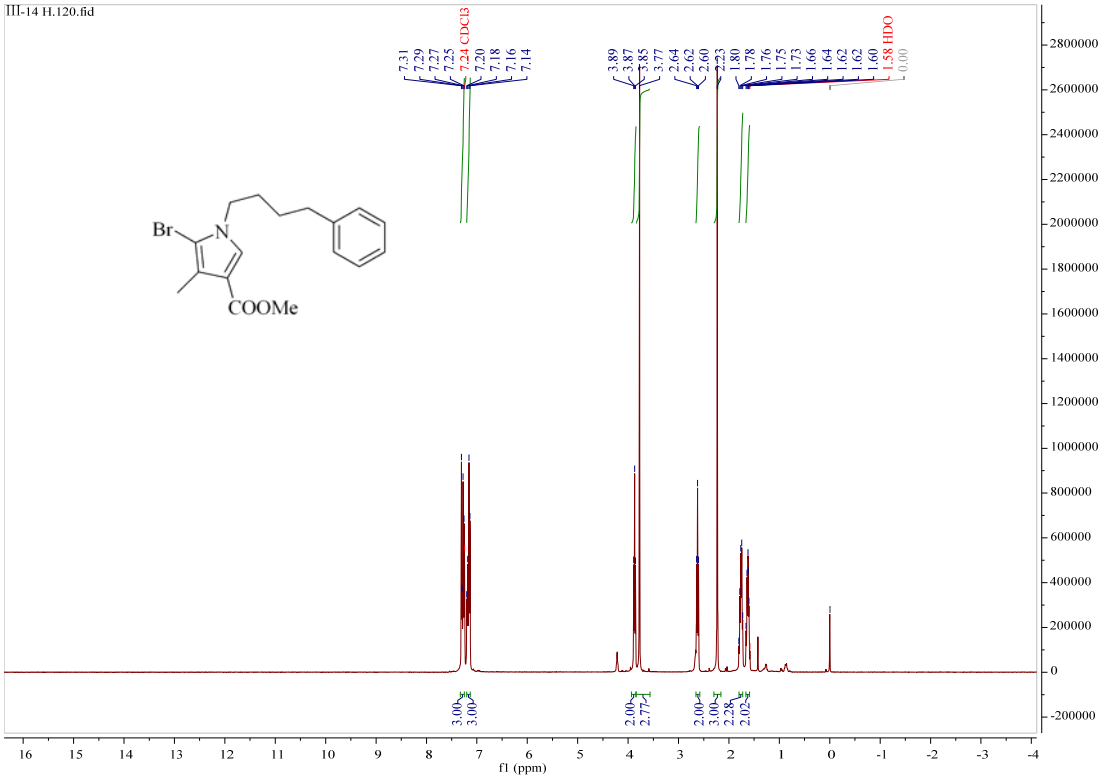

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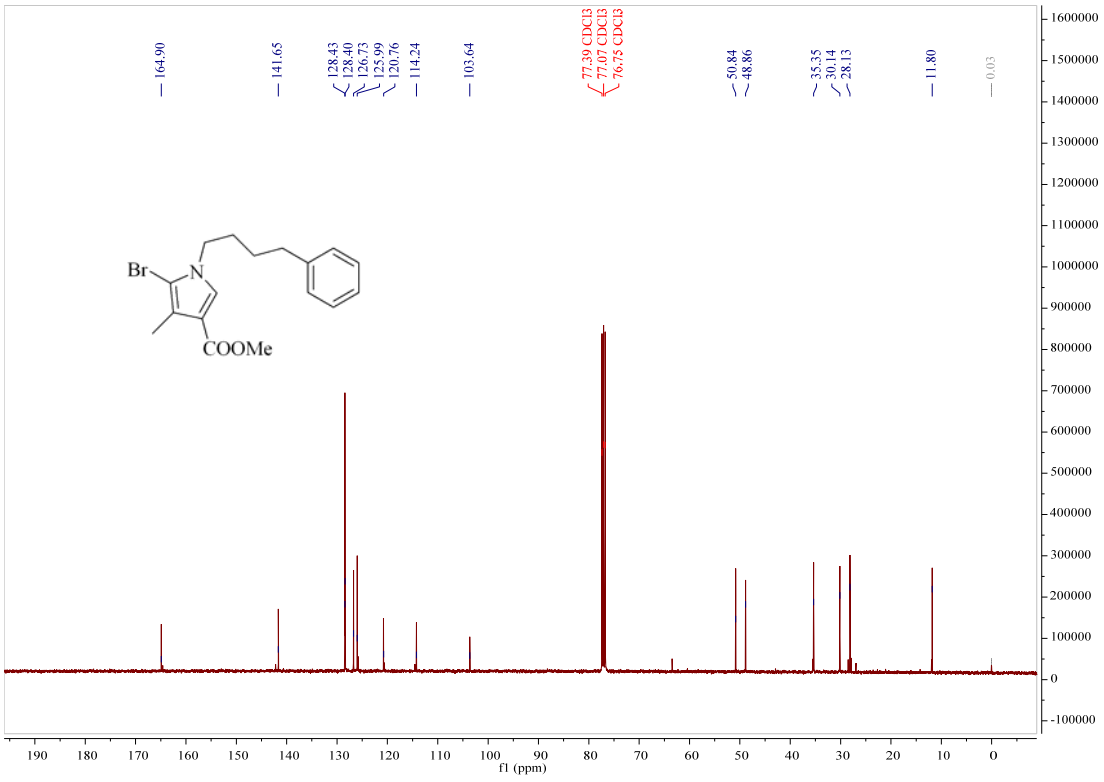
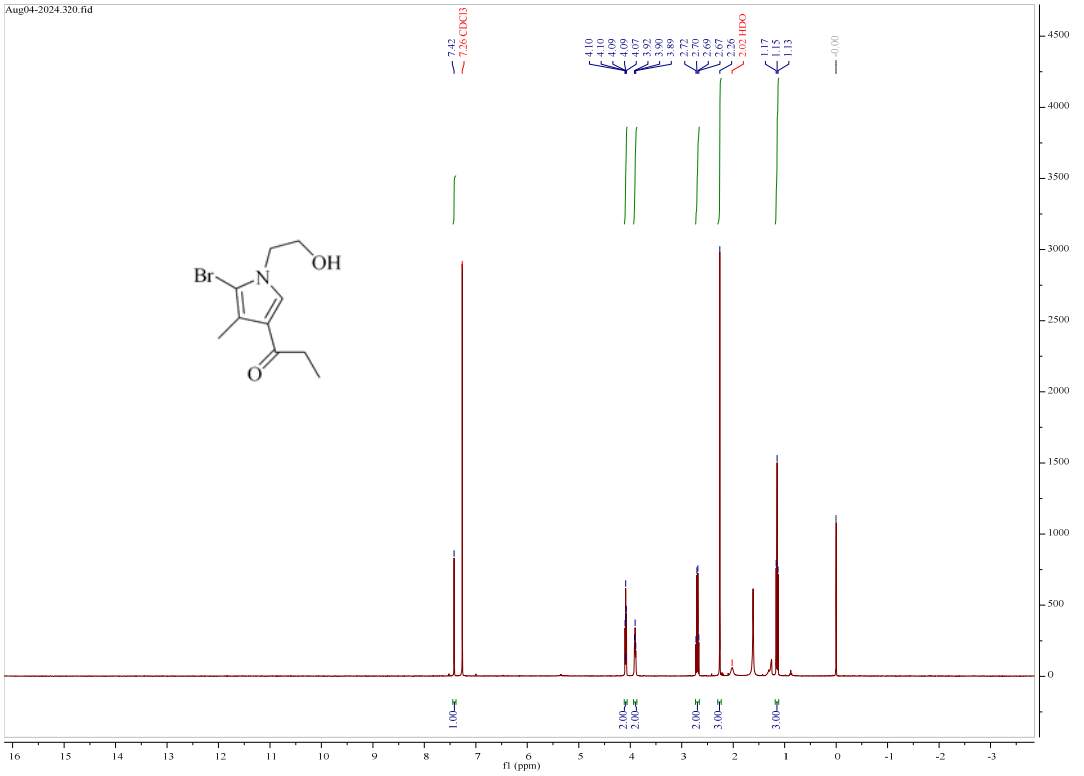


^{1}H NMR (400 MHz, $CDCl_3$) (3v)



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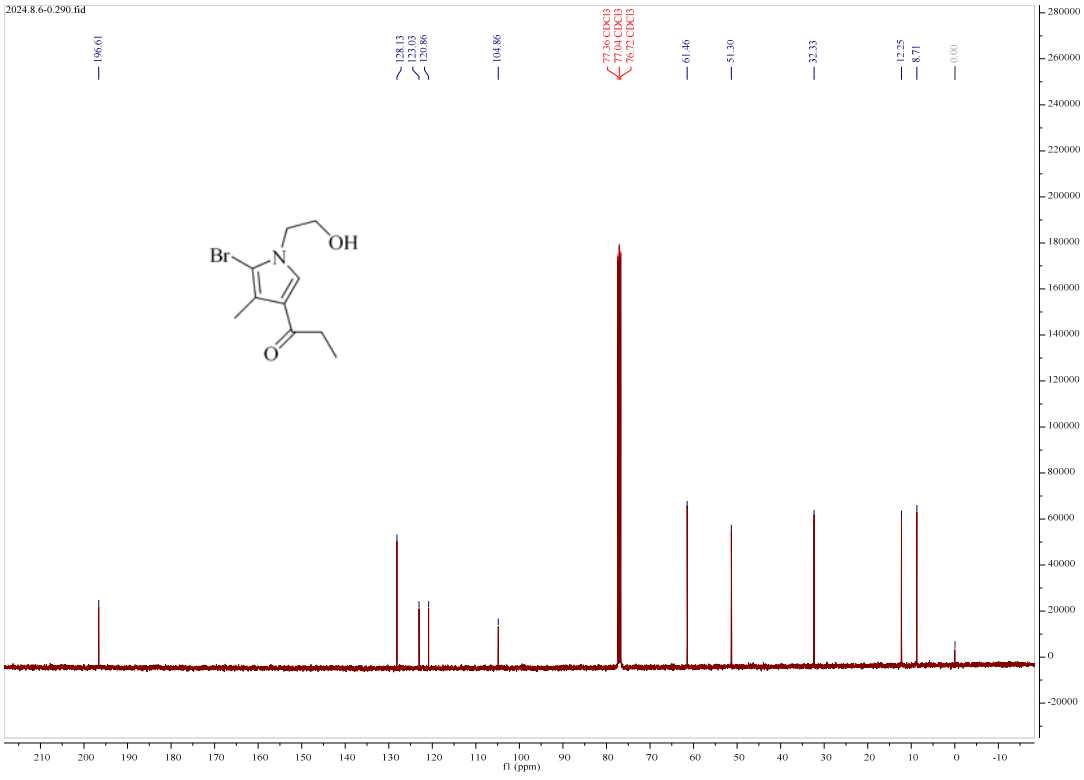
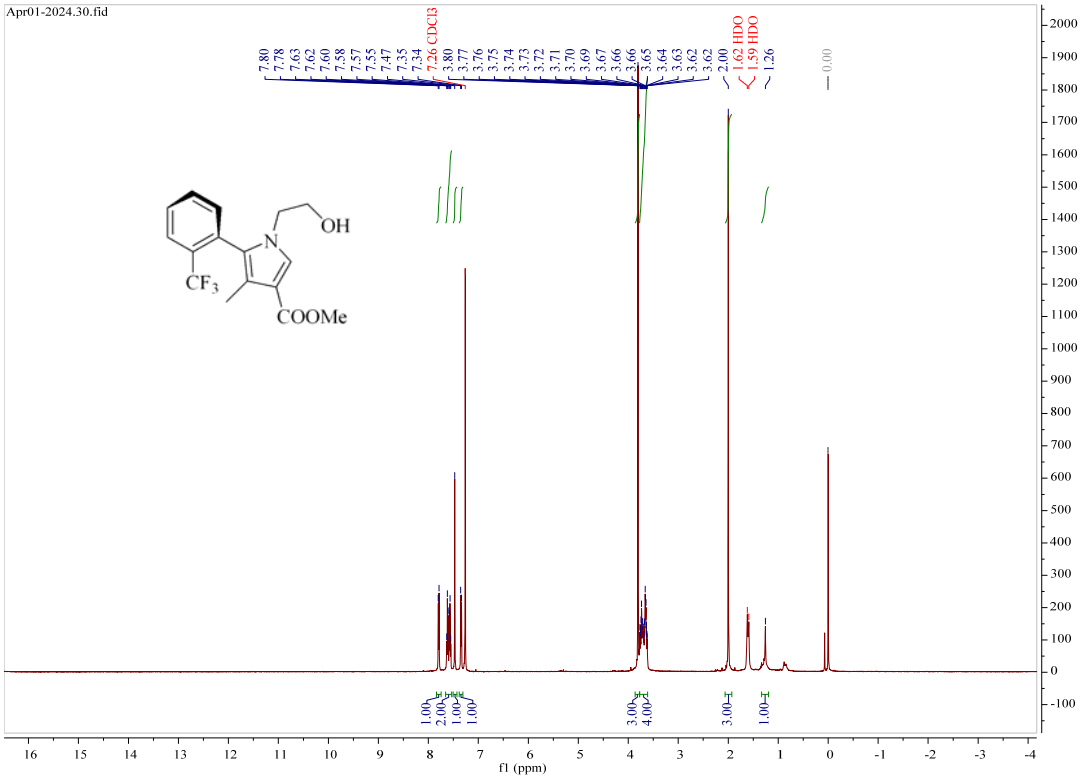
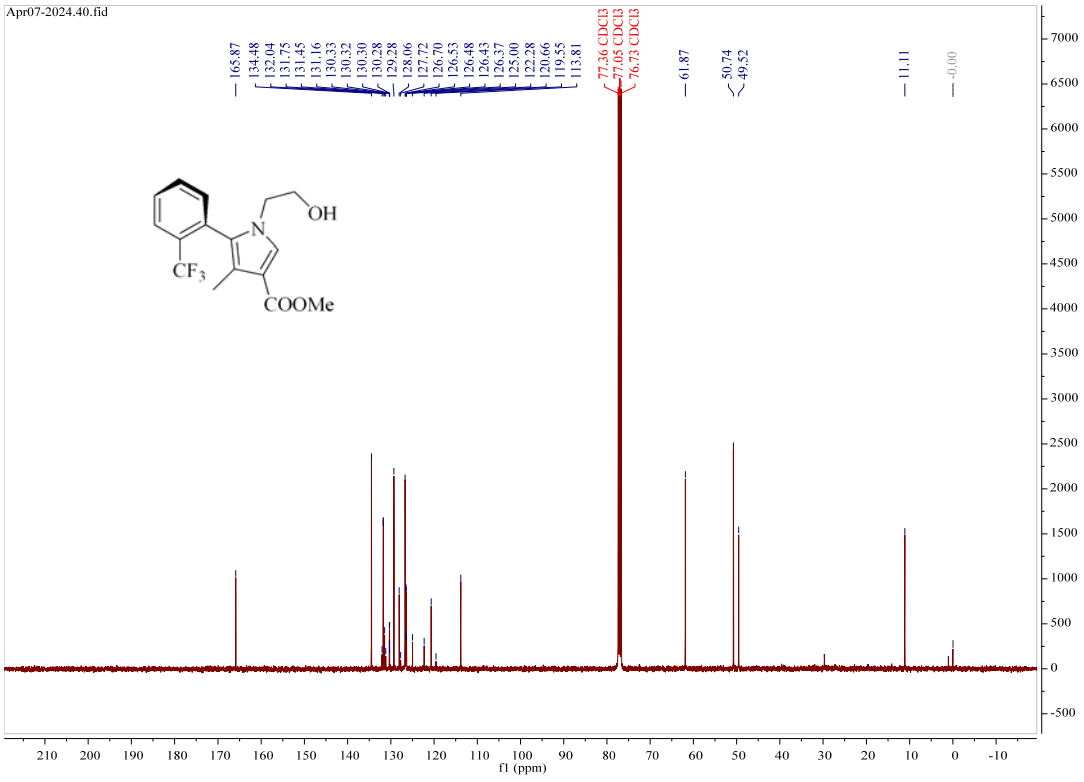


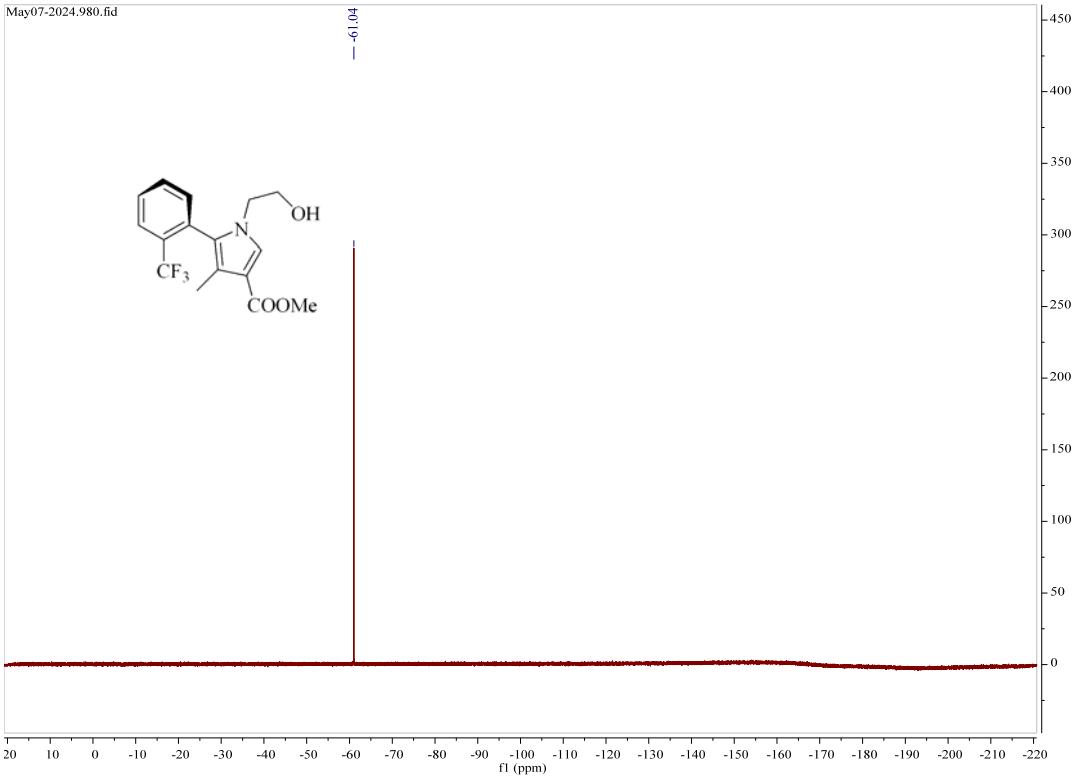
^{1}H NMR (500 MHz, $CDCl_3$) (4a)



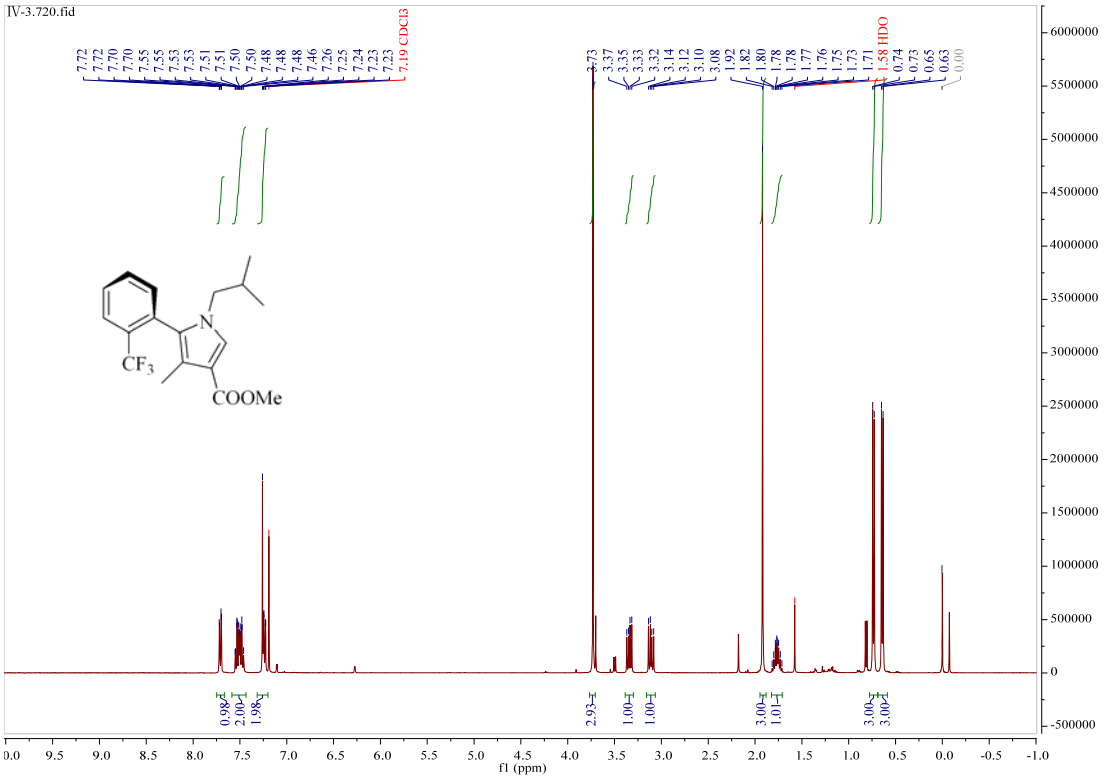
^{13}C NMR (101 MHz, $CDCl_3$) (4a)



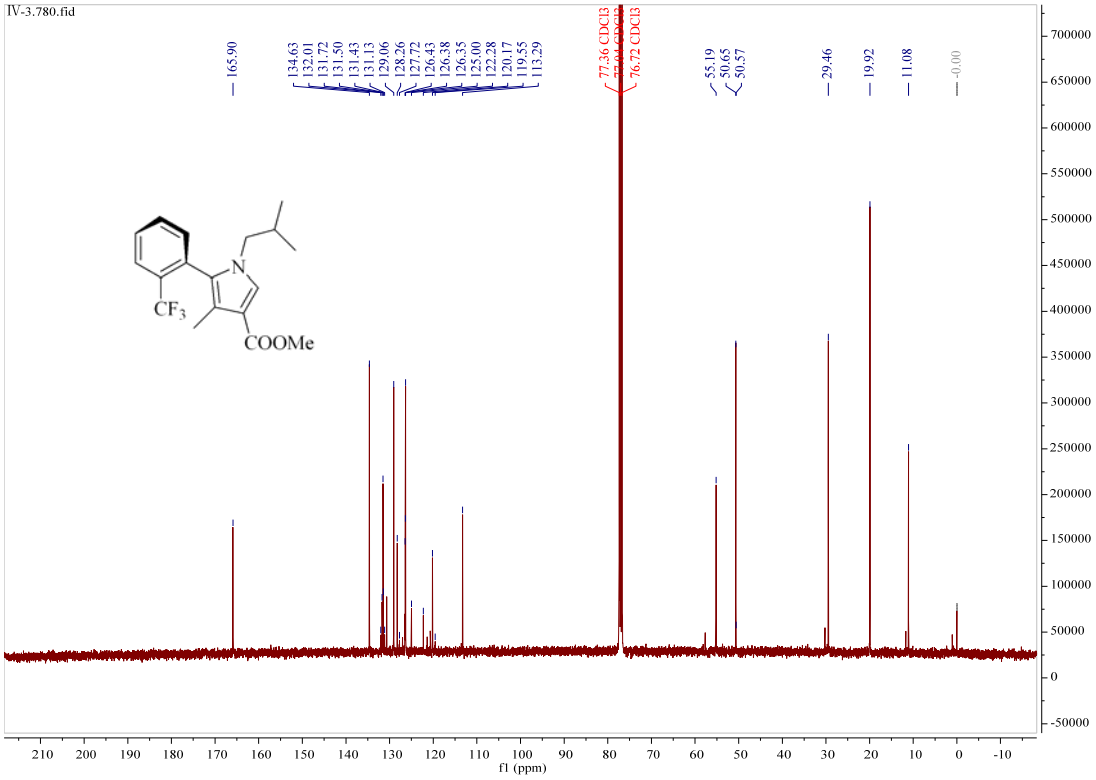
^{19}F NMR (470 MHz, $CDCl_3$) (4a)



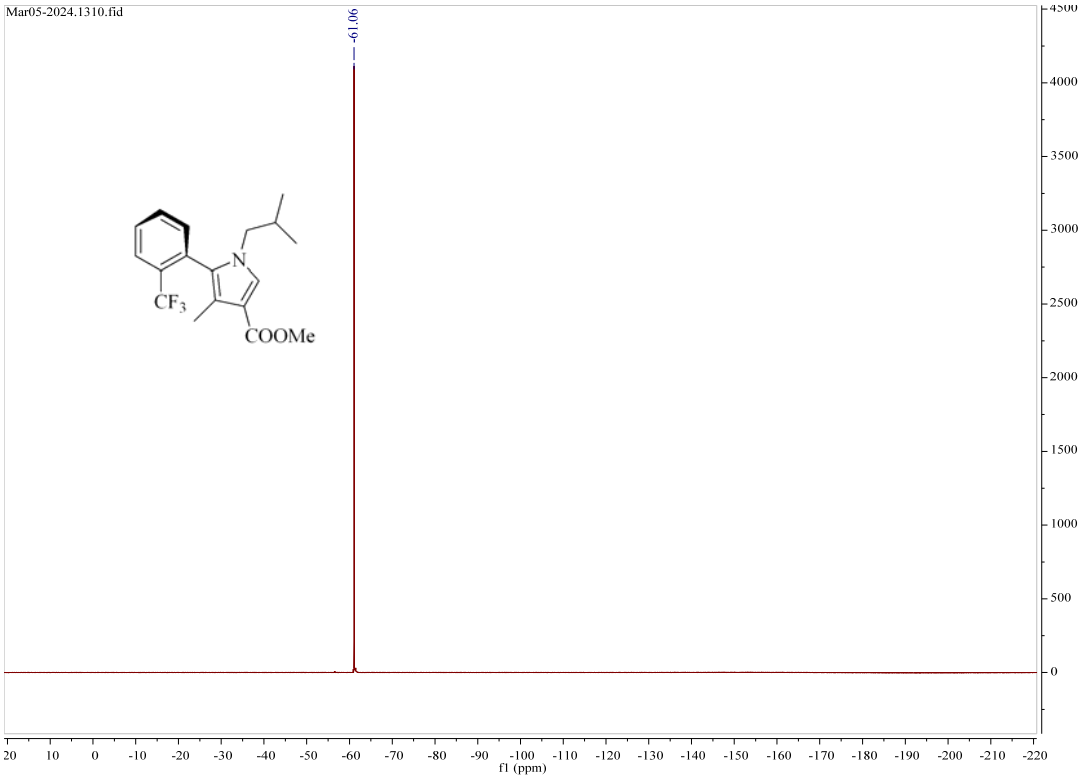
^{1}H NMR (400 MHz, $CDCl_3$) (4b)



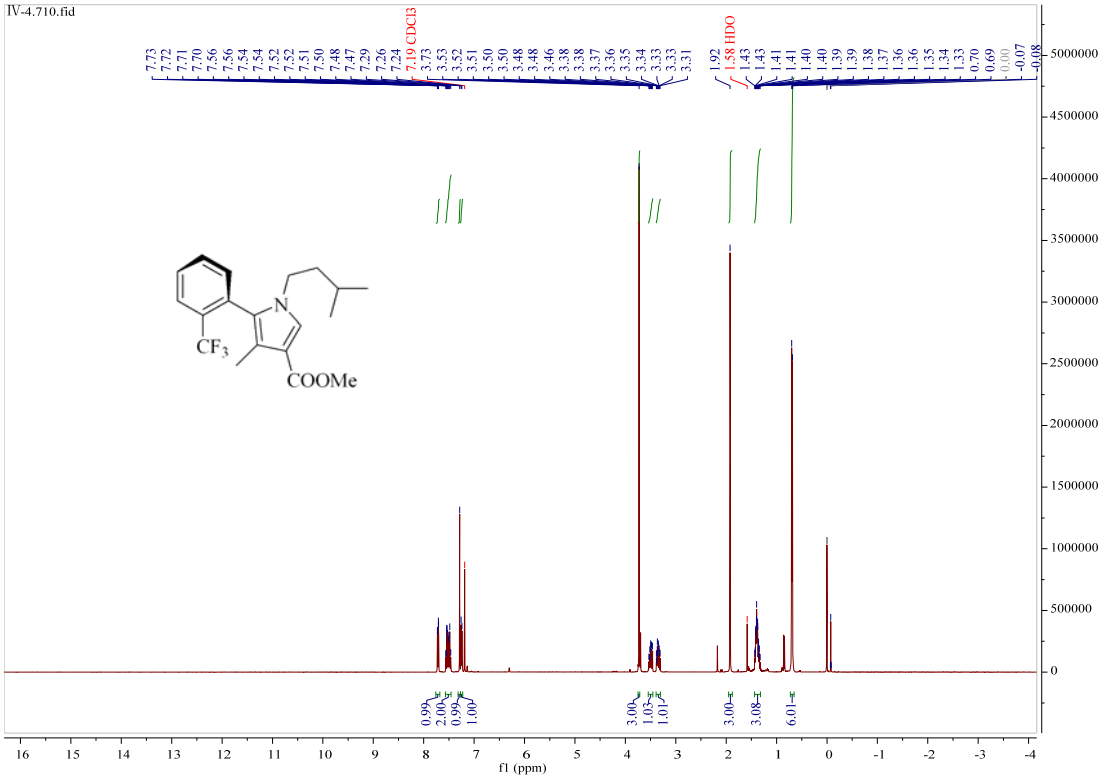
^{13}C NMR (101 MHz, $CDCl_3$) (4b)



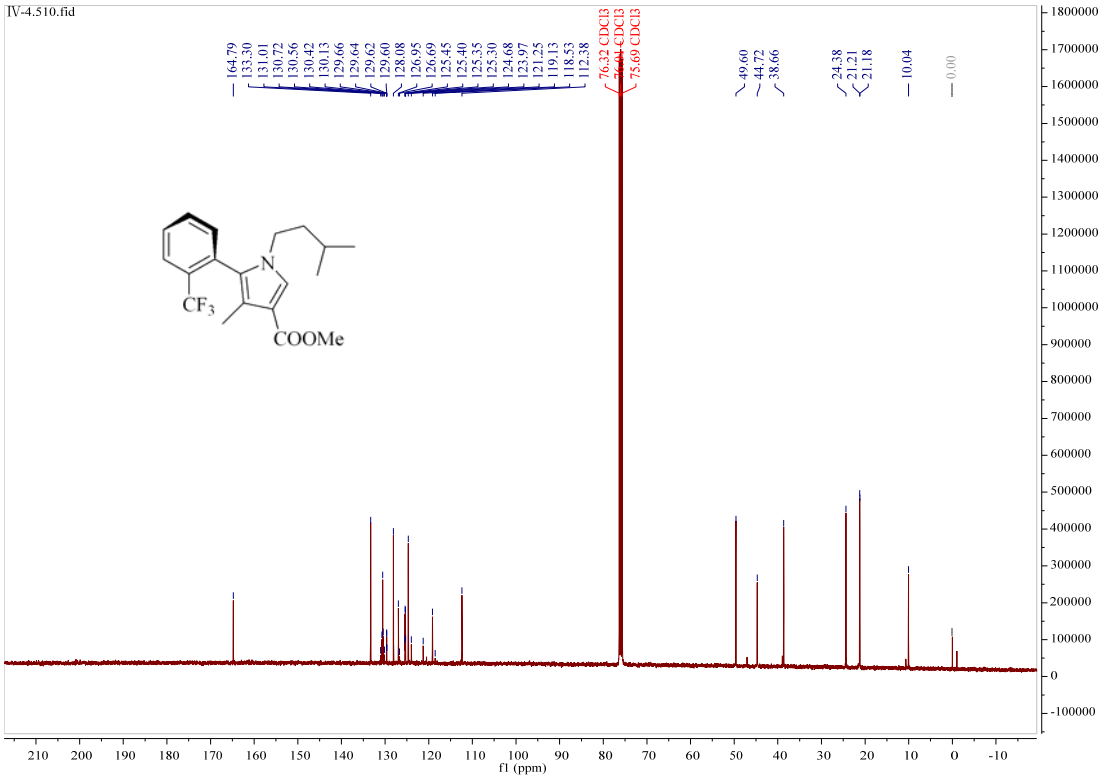
^{19}F NMR (470 MHz, $CDCl_3$) (4b)



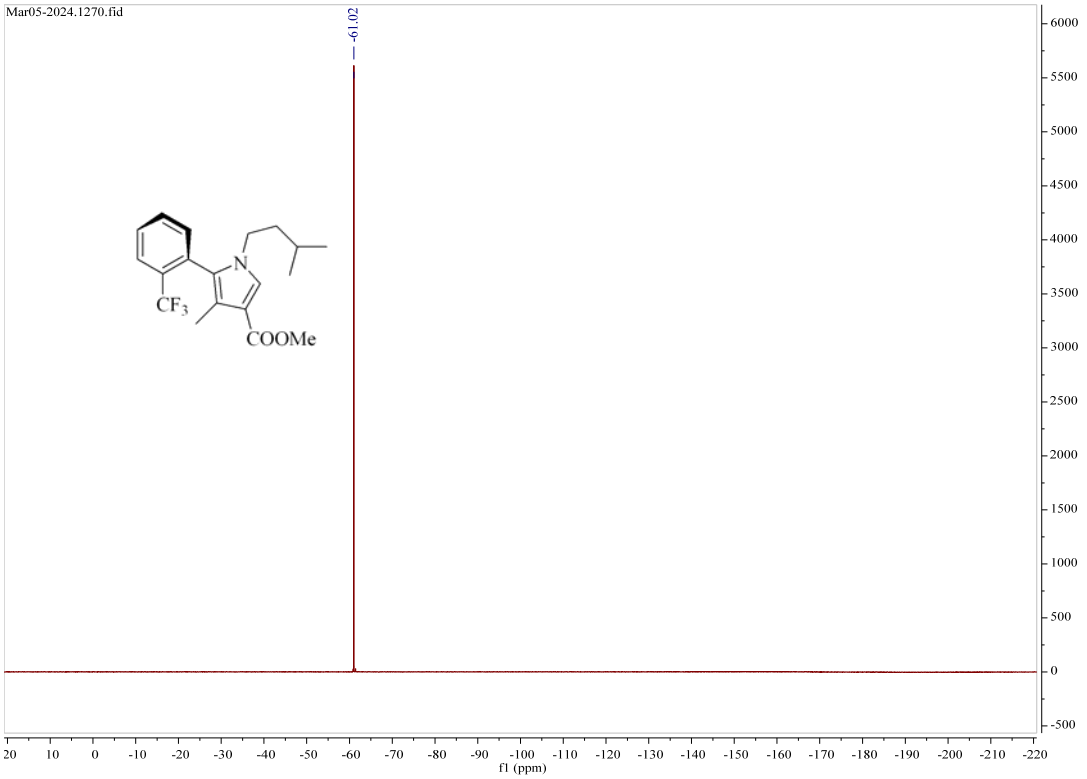
^{1}H NMR (400 MHz, $CDCl_3$) (4c)



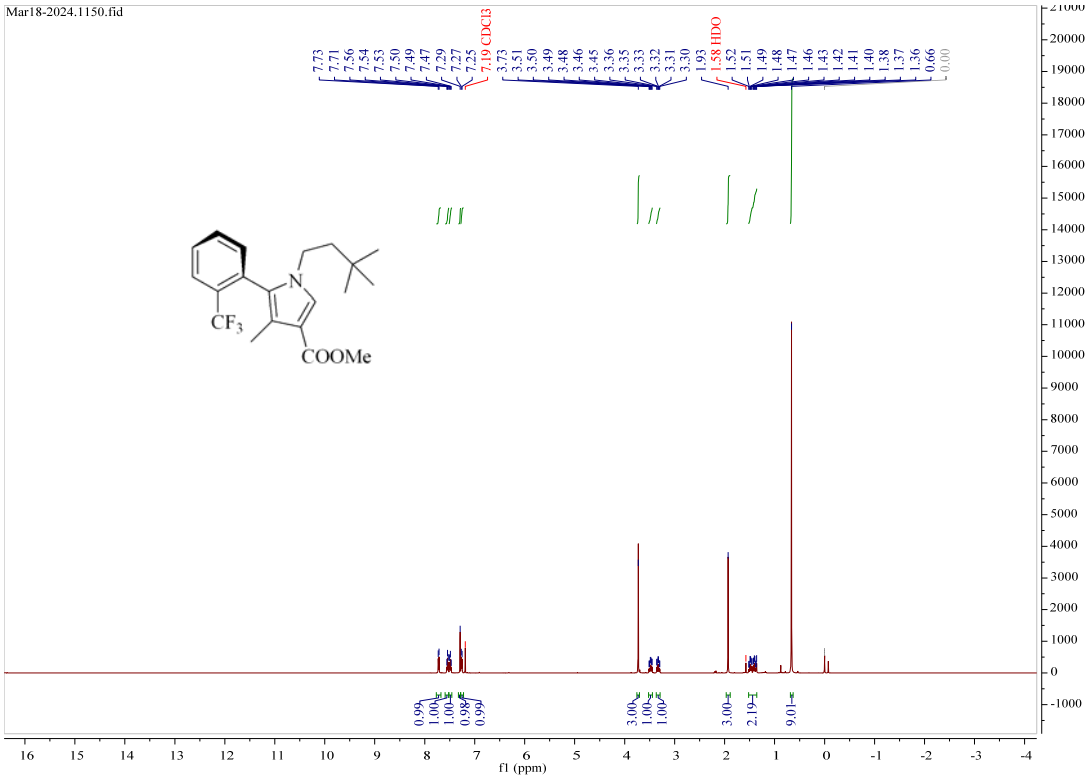
^{13}C NMR (101 MHz, $CDCl_3$) (4c)



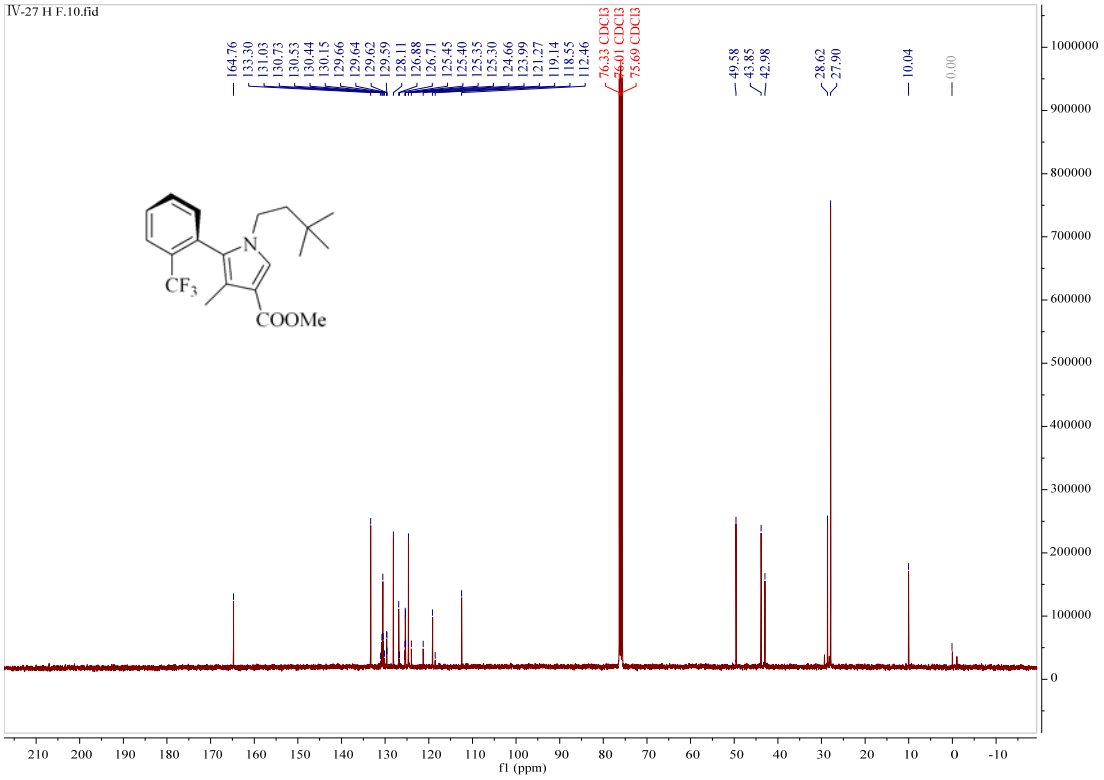
^{19}F NMR (470 MHz, $CDCl_3$) (4c)



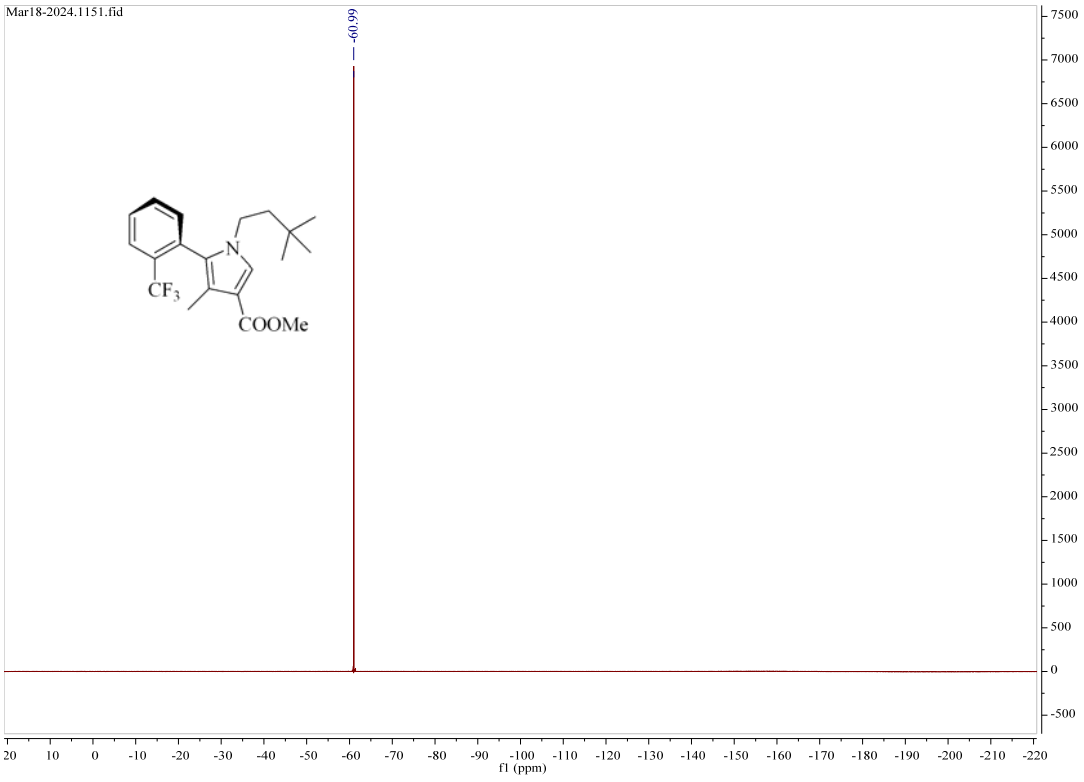
^{1}H NMR (500 MHz, $CDCl_3$) (4d)



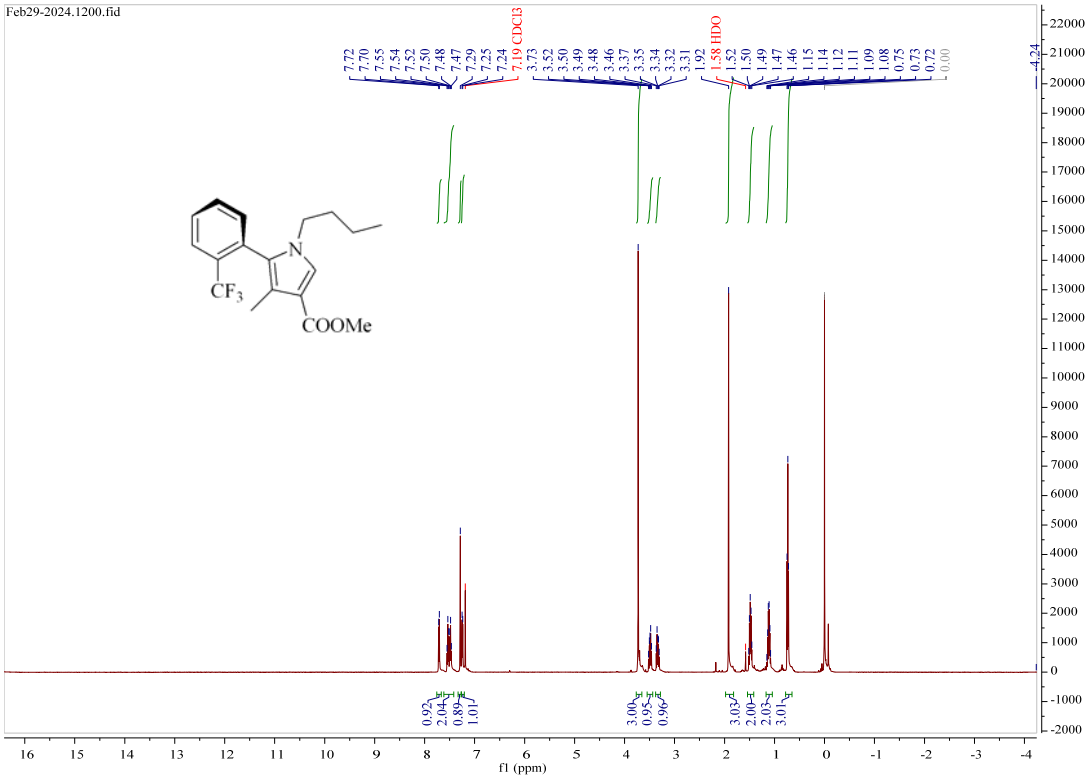
^{13}C NMR (101 MHz, $CDCl_3$) (4d)



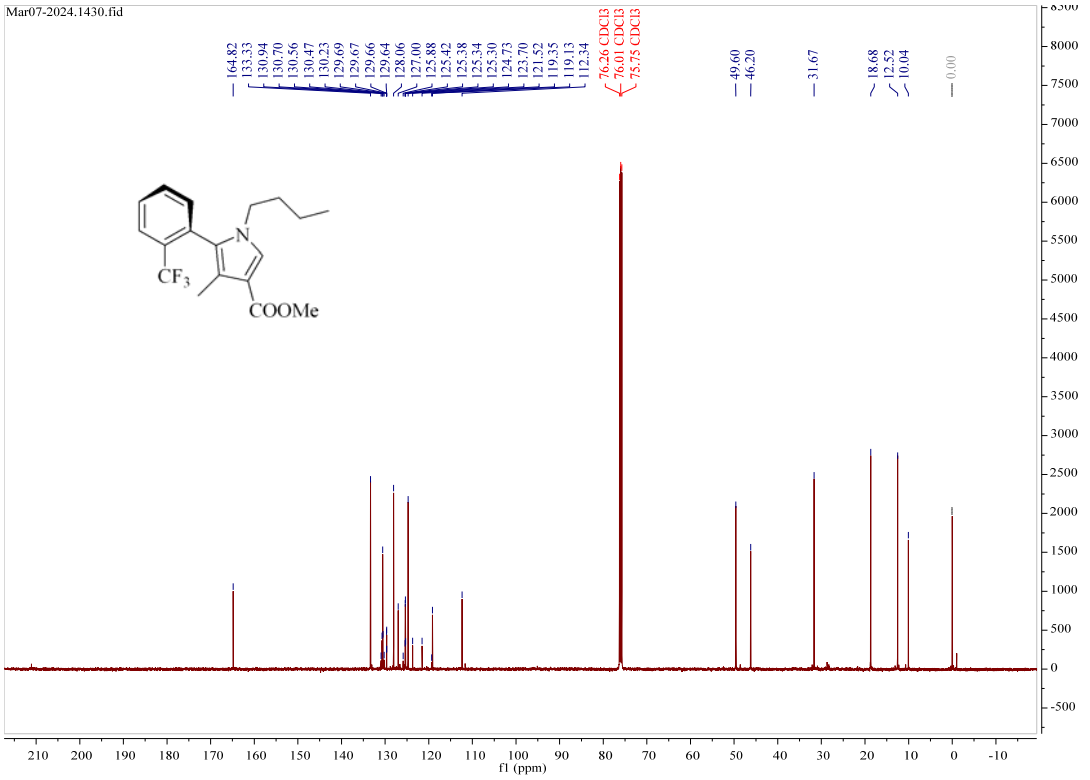
^{19}F NMR (470 MHz, $CDCl_3$) (4d)



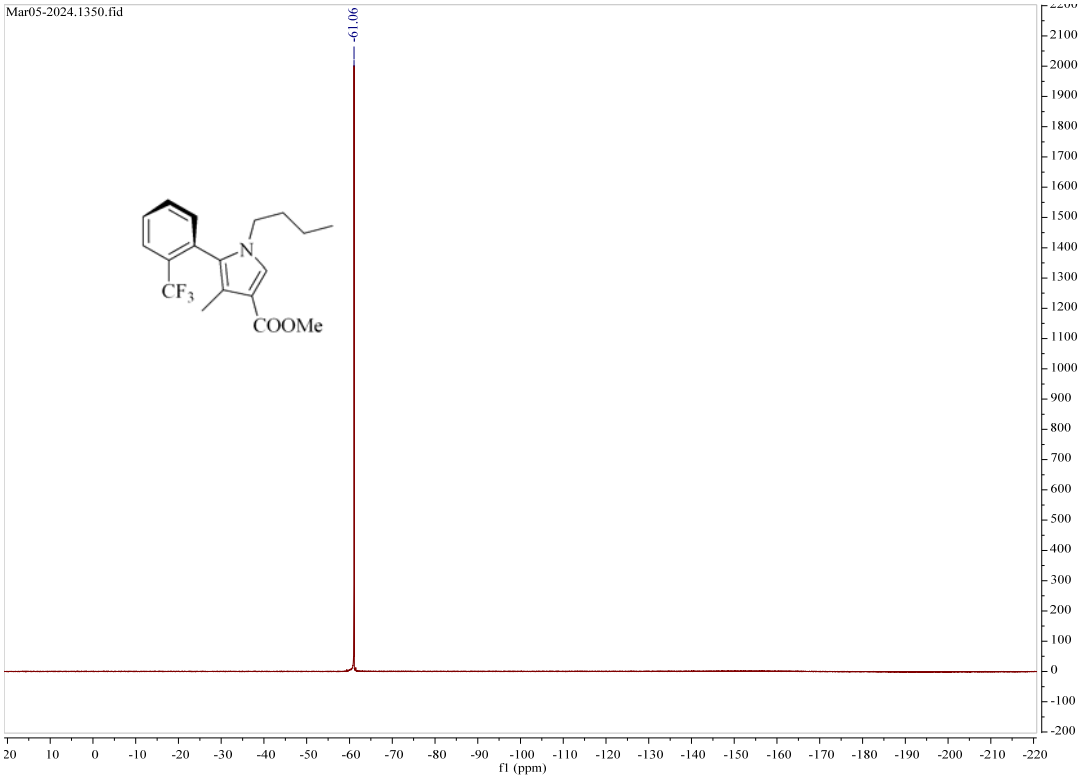
^{1}H NMR (500 MHz, $CDCl_3$) (4e)



^{13}C NMR (126 MHz, $CDCl_3$) (4e)



^{19}F NMR (470 MHz, $CDCl_3$) (4e)



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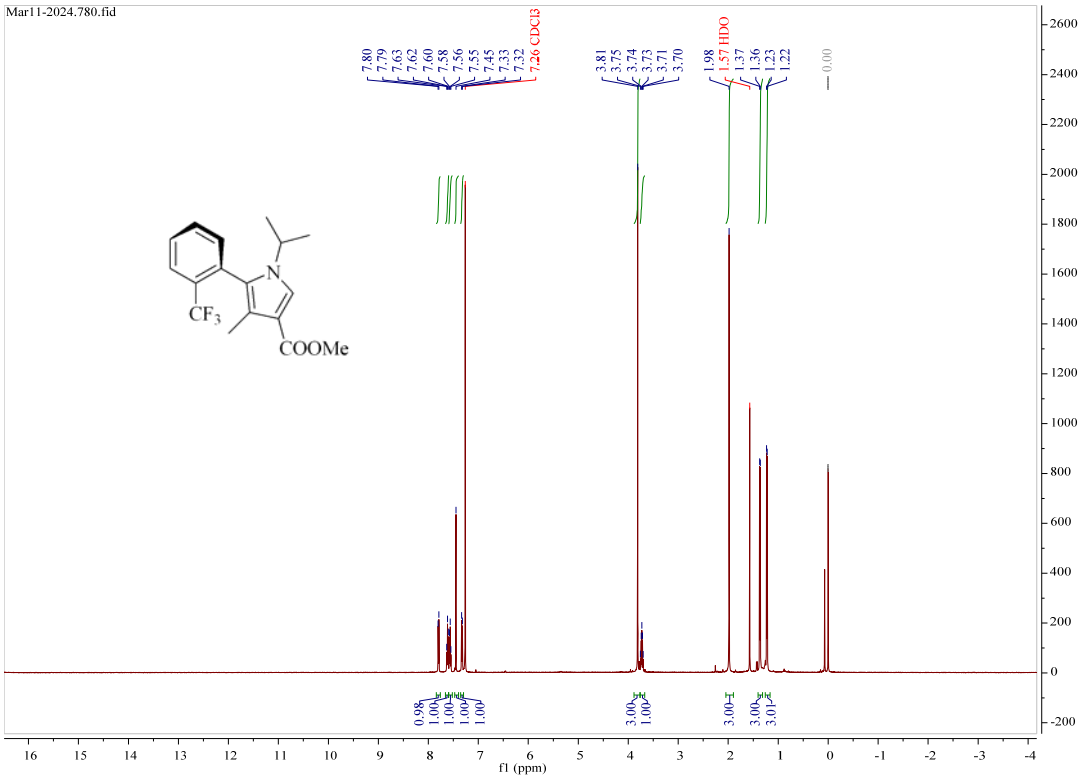
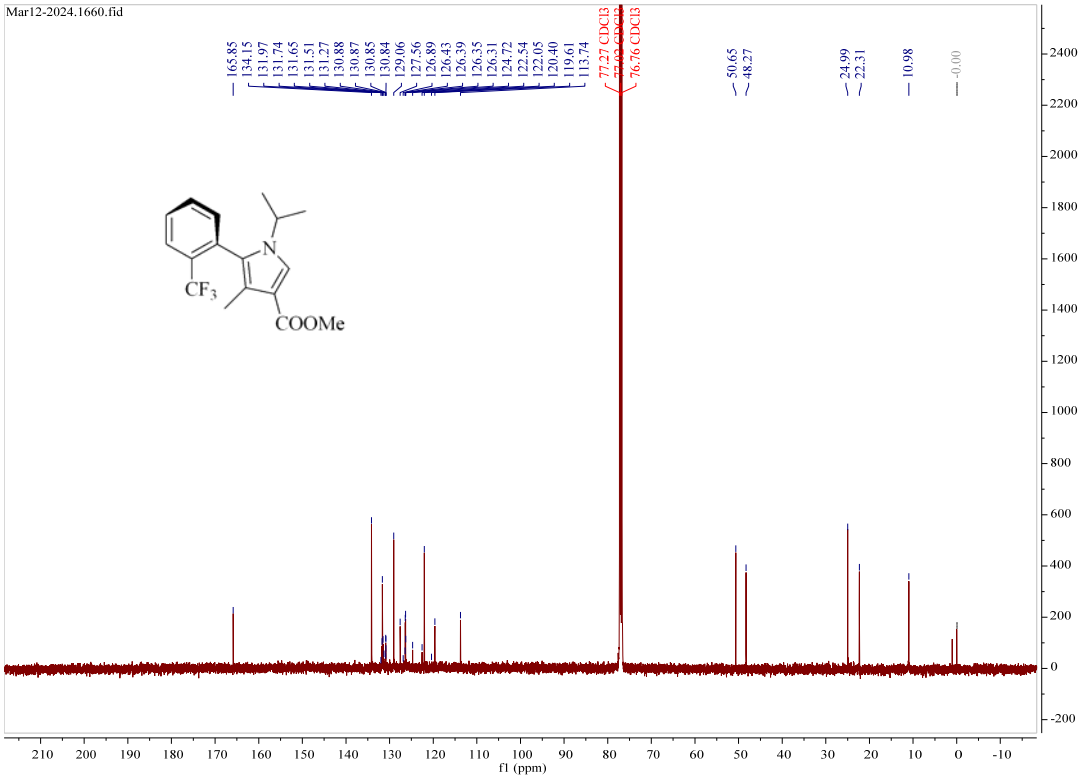
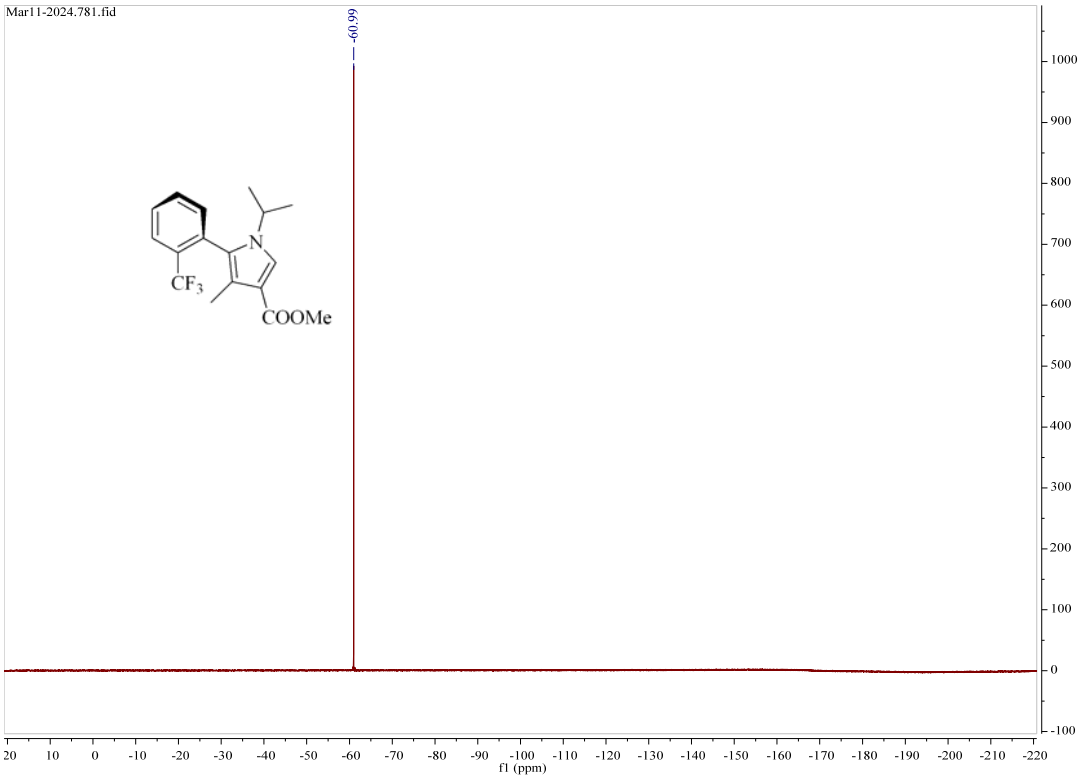


^{13}C NMR (126 MHz, $CDCl_3$) (4f)



^{19}F NMR (470 MHz, $CDCl_3$) (4f)



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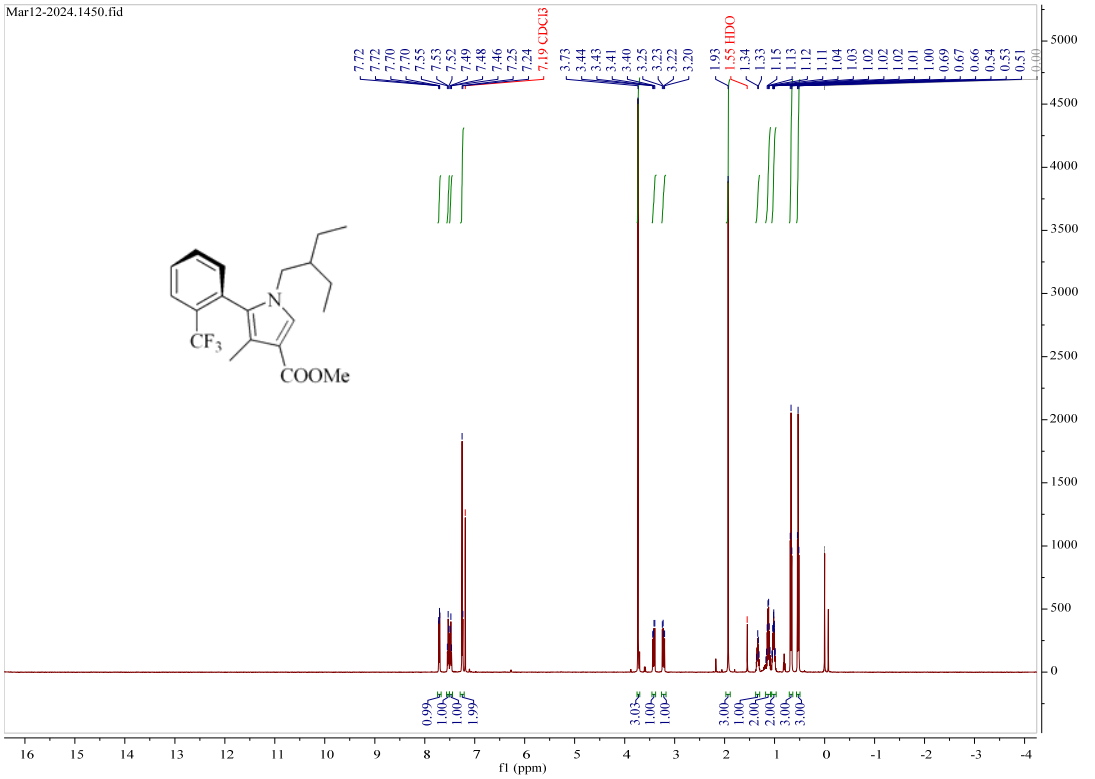
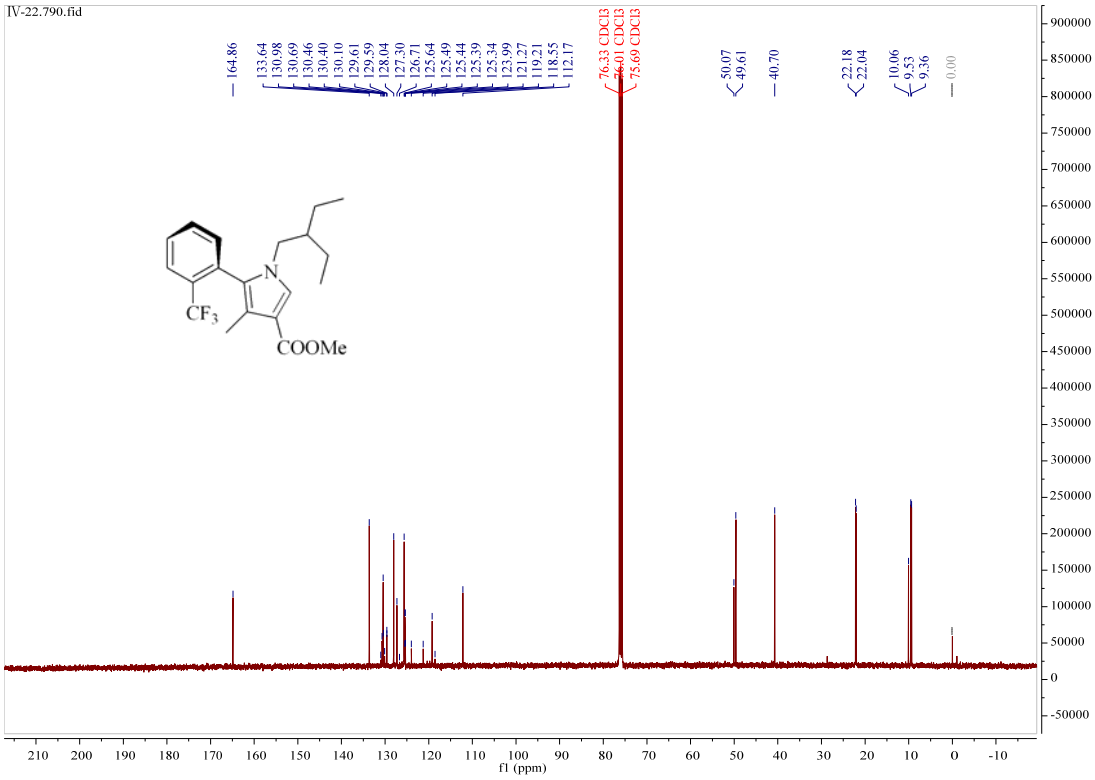
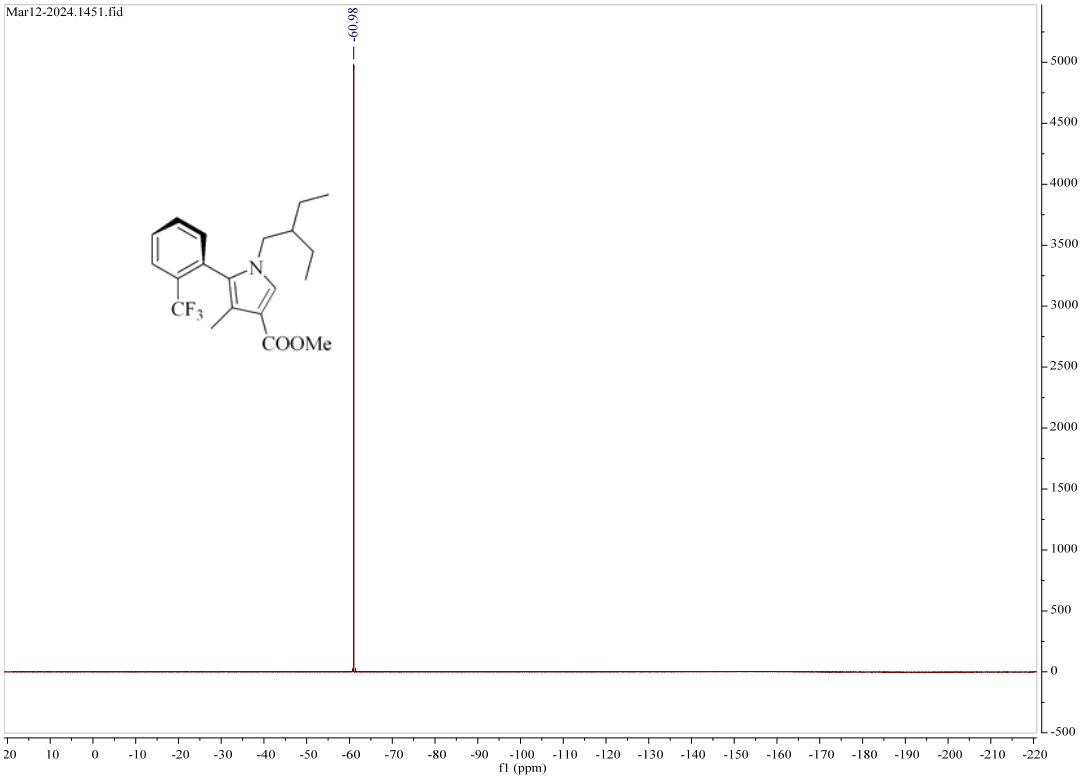


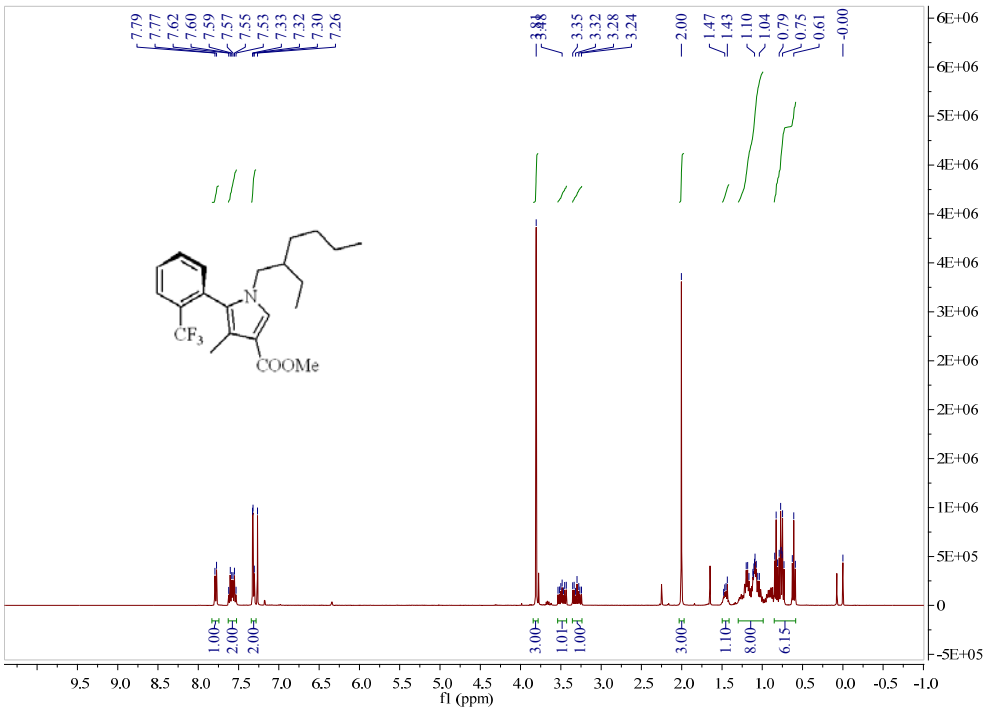
^{13}C NMR (101 MHz, $CDCl_3$) (4g)



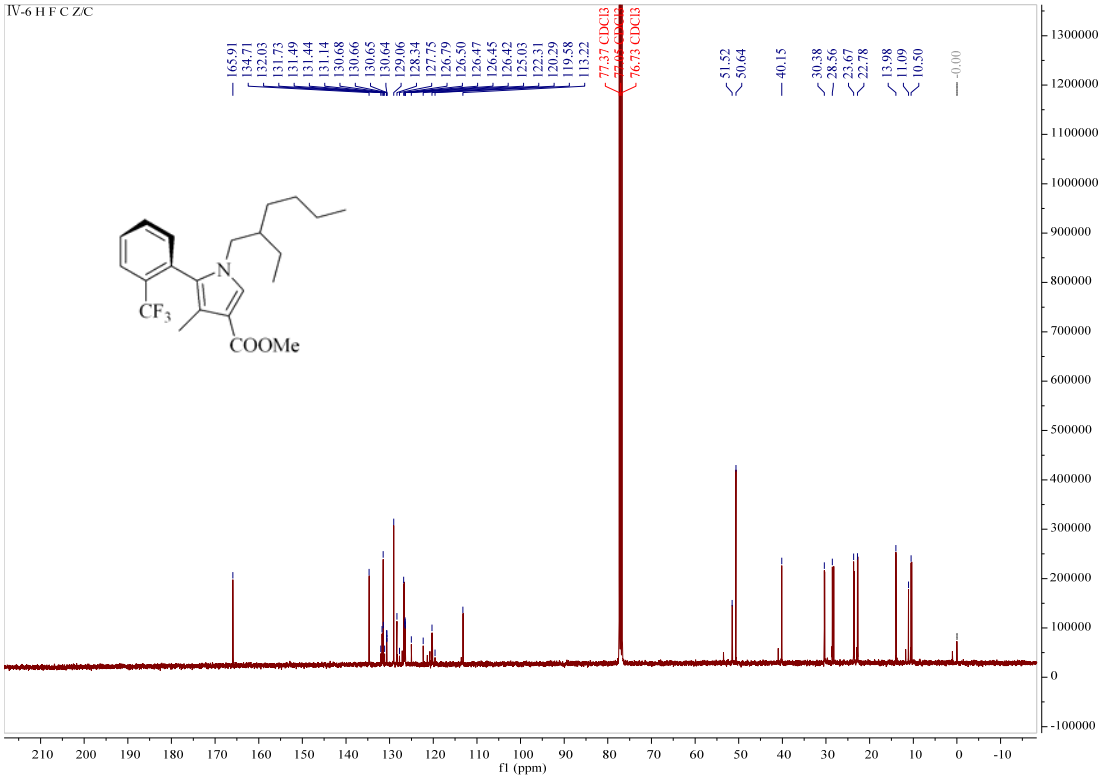
^{19}F NMR (470 MHz, $CDCl_3$) (4g)



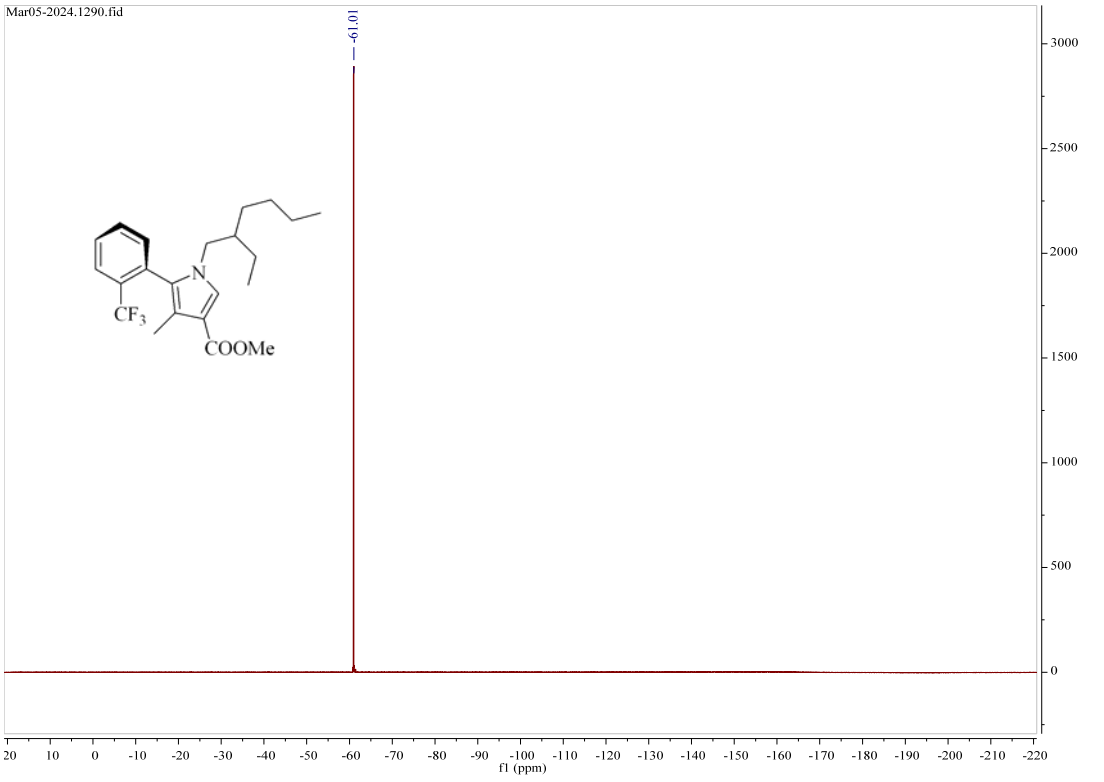
^{1}H NMR (400 MHz, $CDCl_3$) (4h)



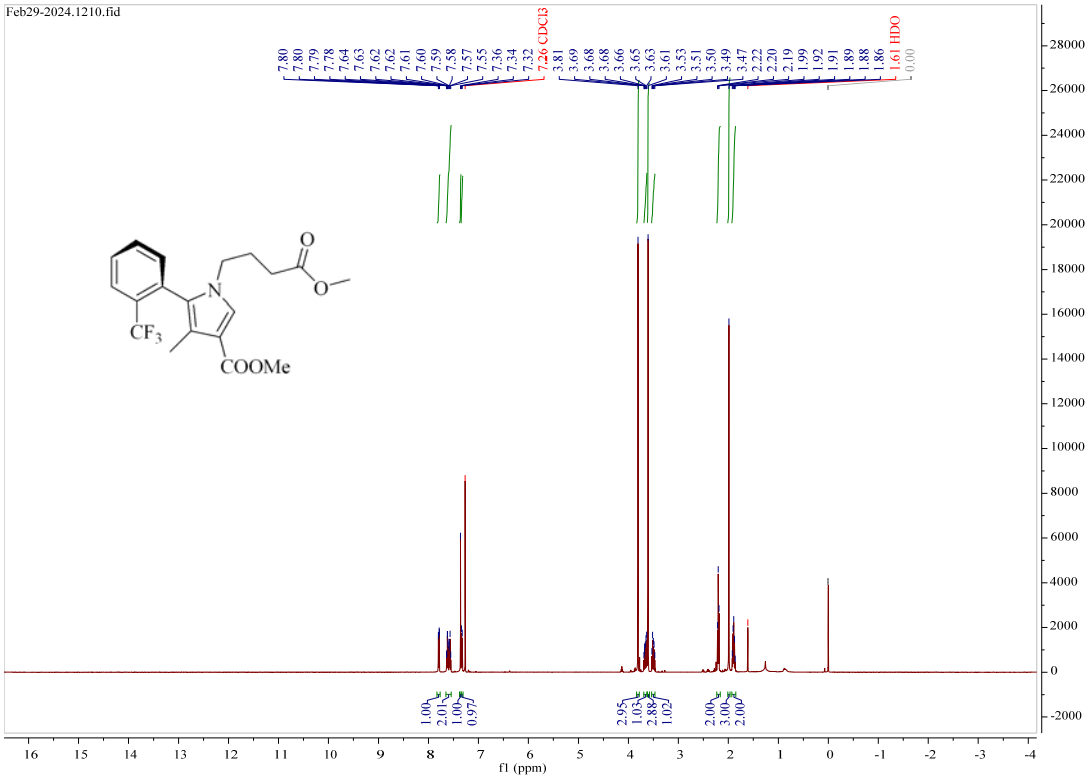
^{13}C NMR (101 MHz, $CDCl_3$) (4h)



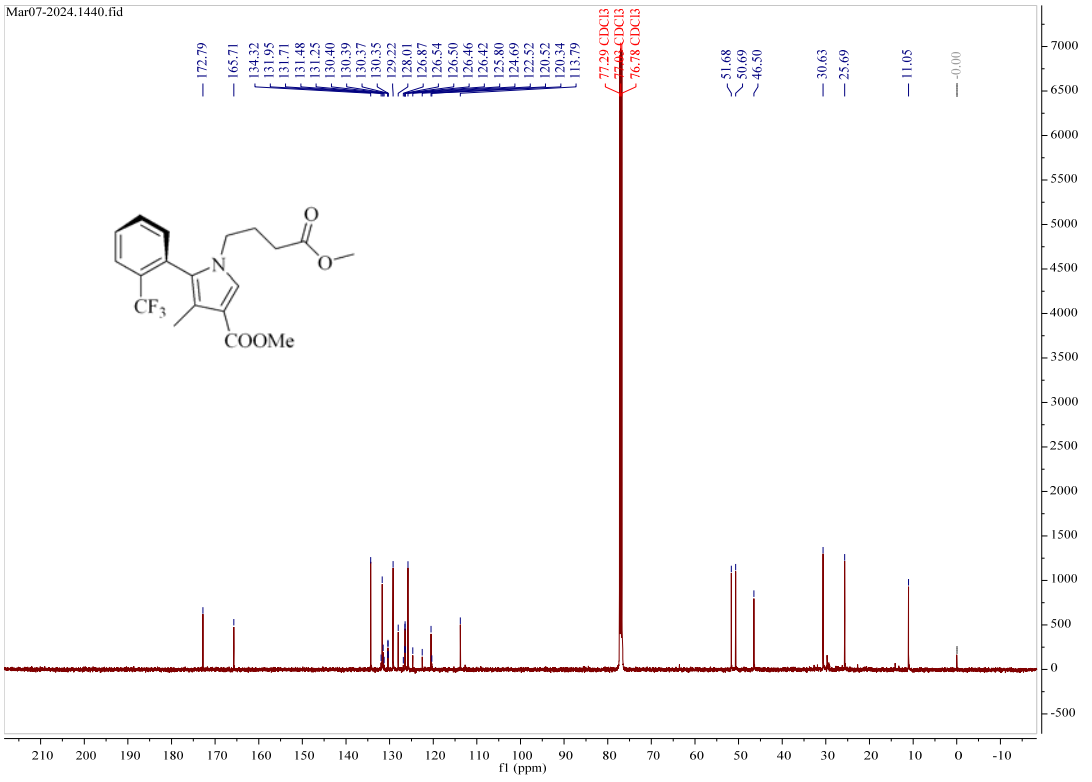
^{19}F NMR (470 MHz, $CDCl_3$) (4h)



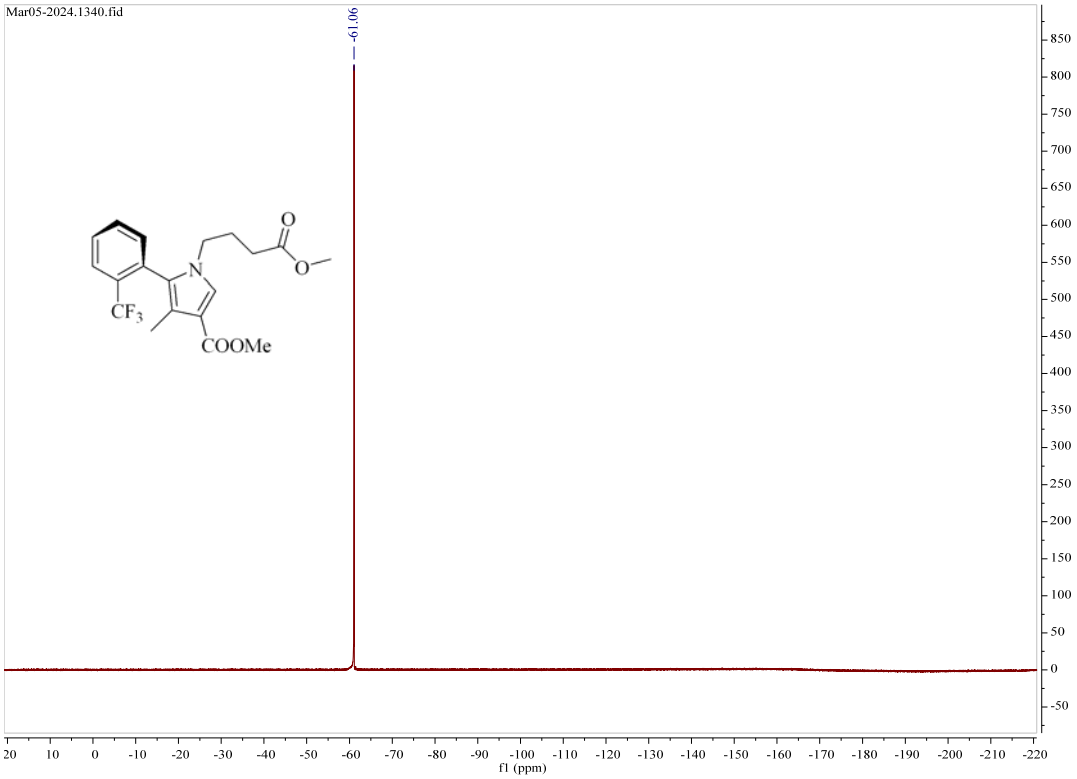
^{1}H NMR (500 MHz, $CDCl_3$) (4i)



^{13}C NMR (126 MHz, $CDCl_3$) (4i)



^{19}F NMR (470 MHz, $CDCl_3$) (4i)



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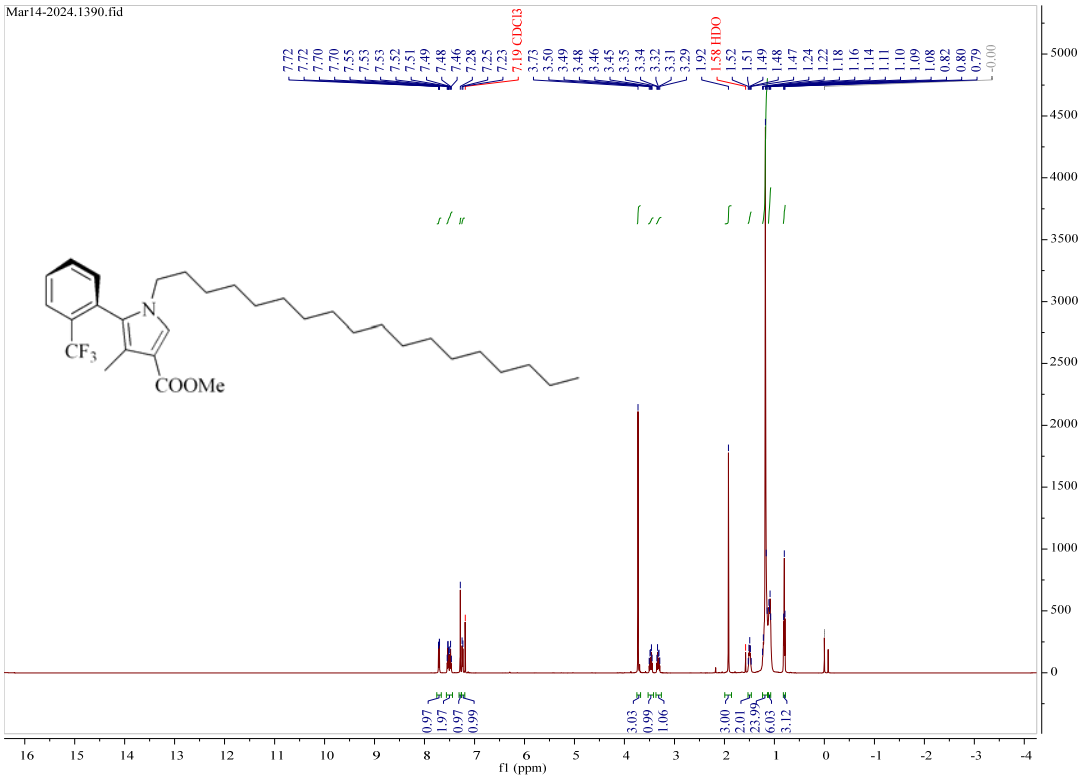
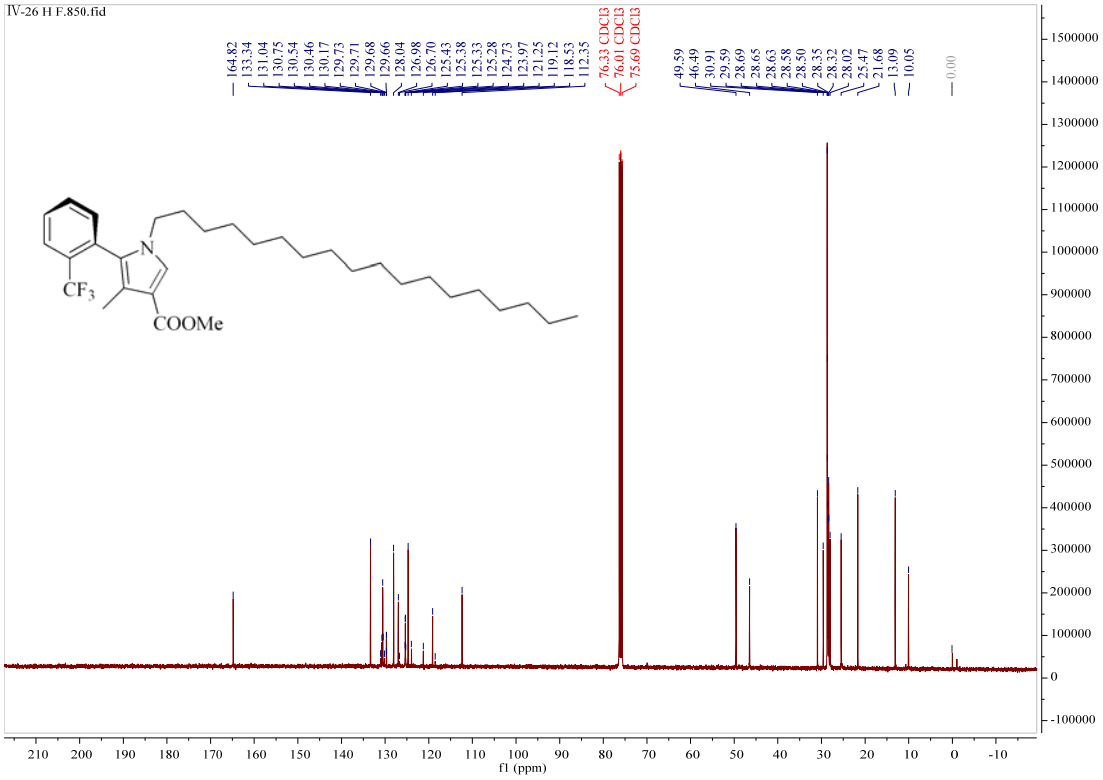
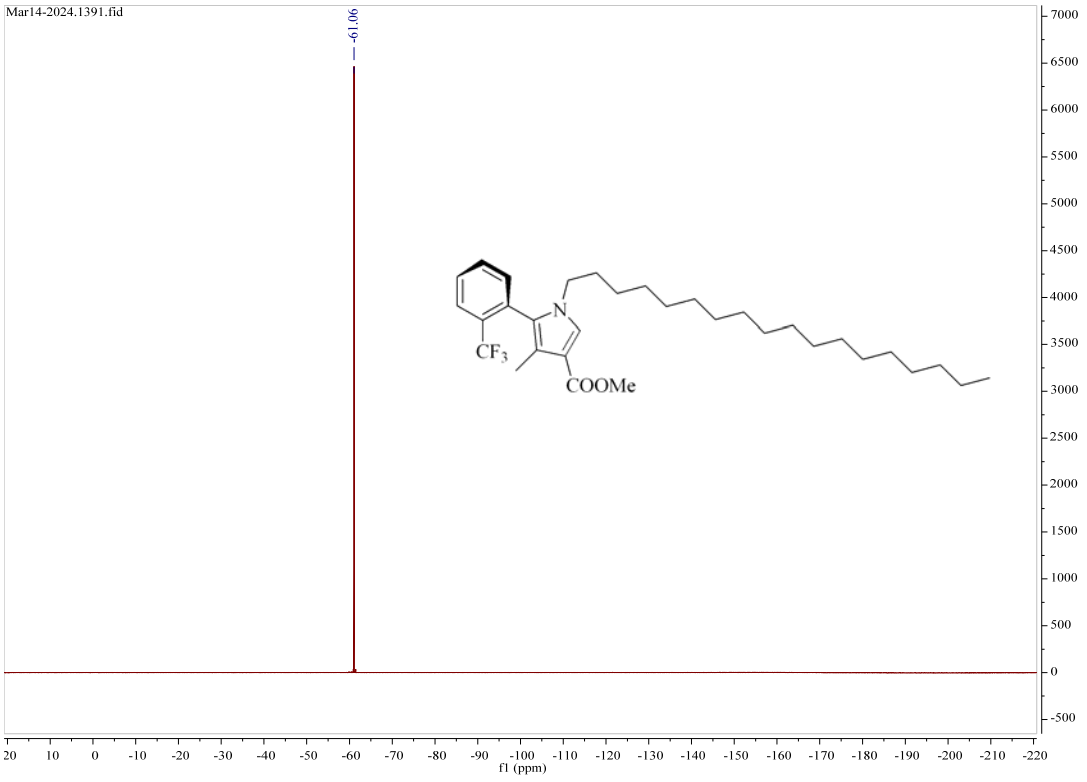


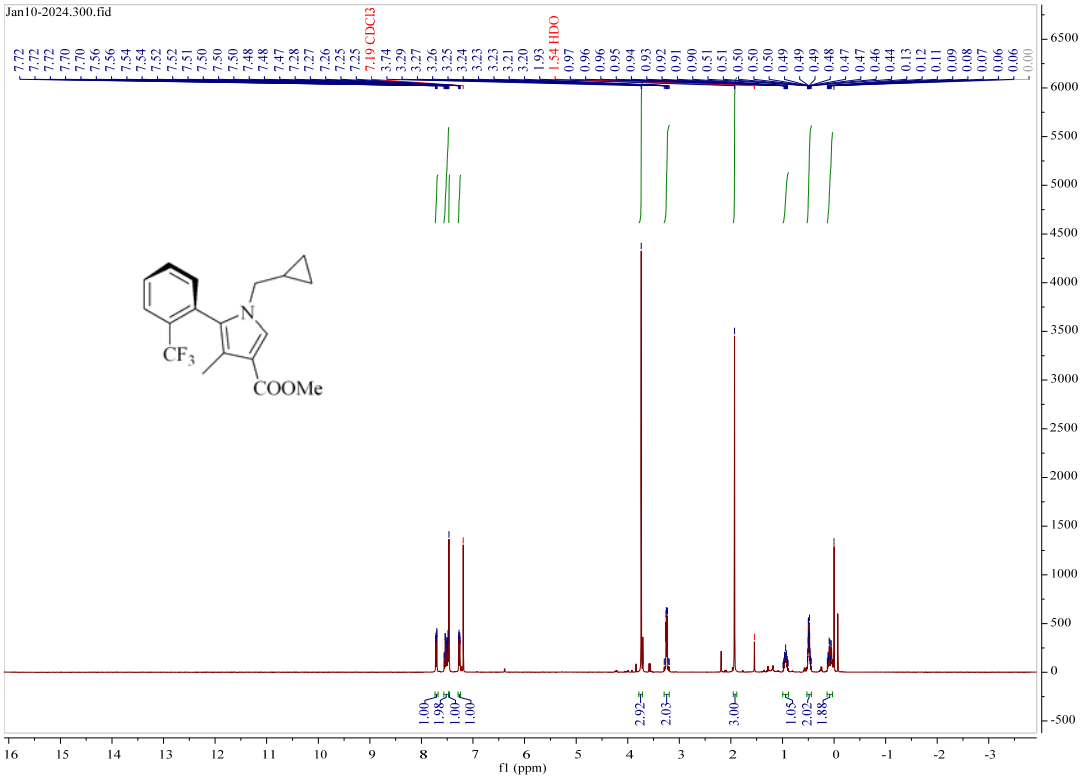
^{13}C NMR (101 MHz, $CDCl_3$) (4j)



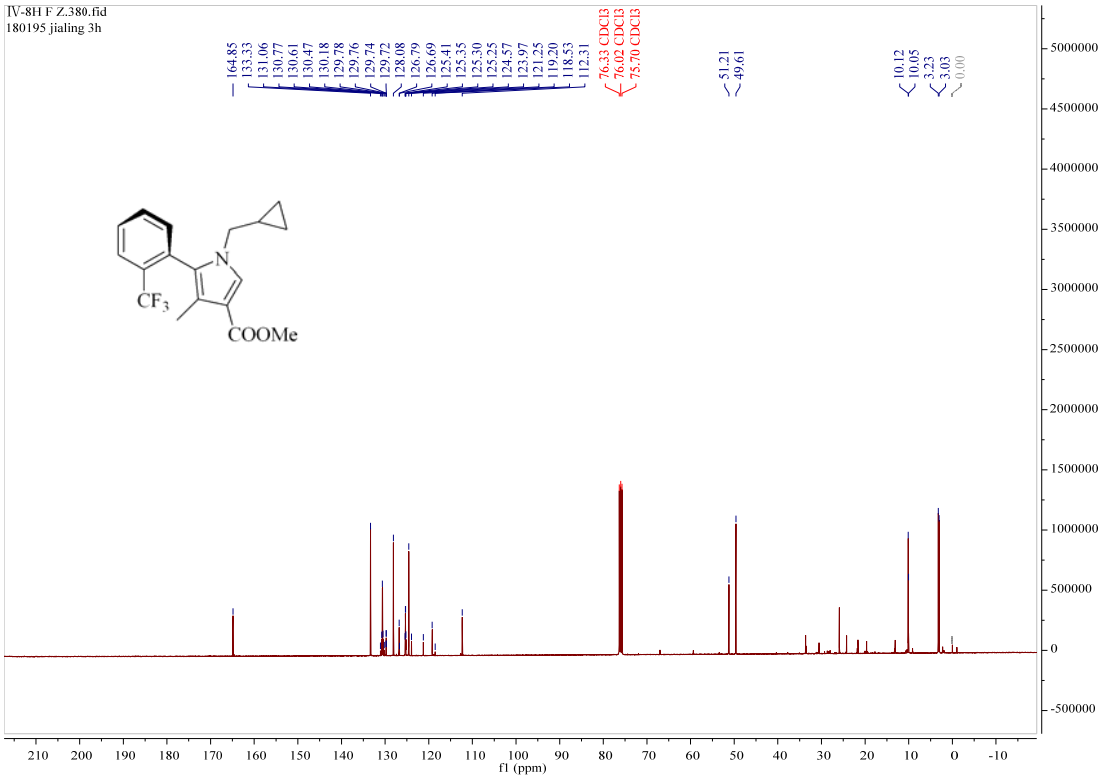
^{19}F NMR (470 MHz, $CDCl_3$) (4j)



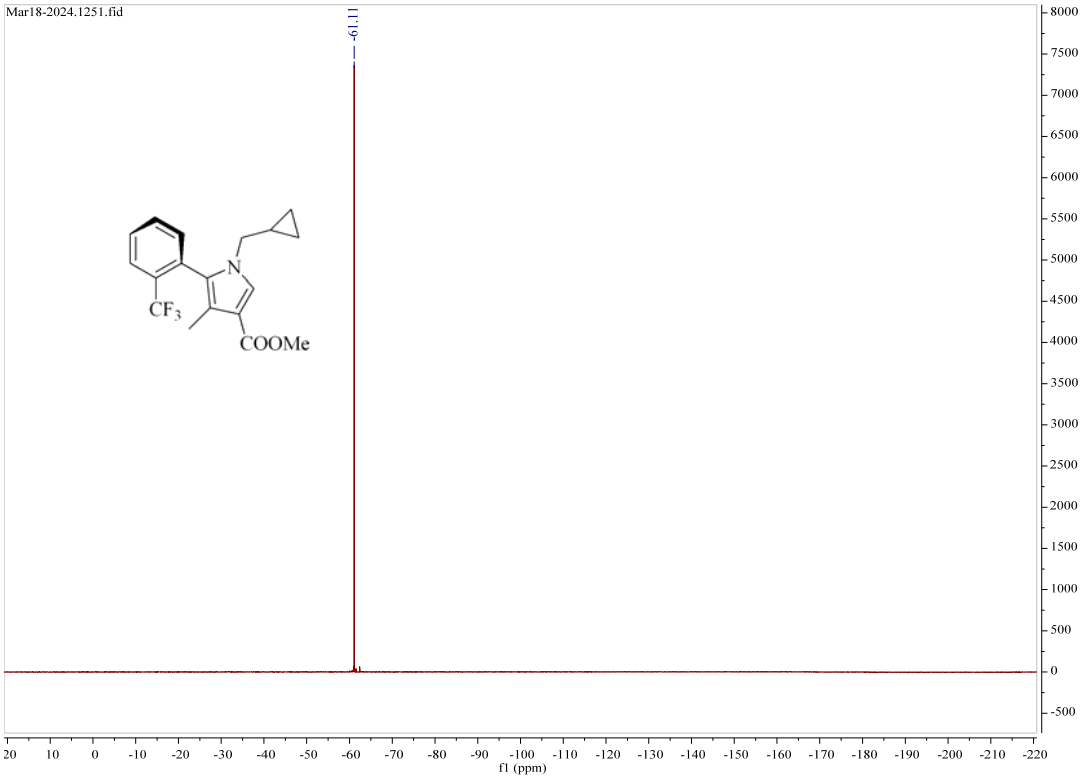
^{1}H NMR (400 MHz, $CDCl_3$) (4k)



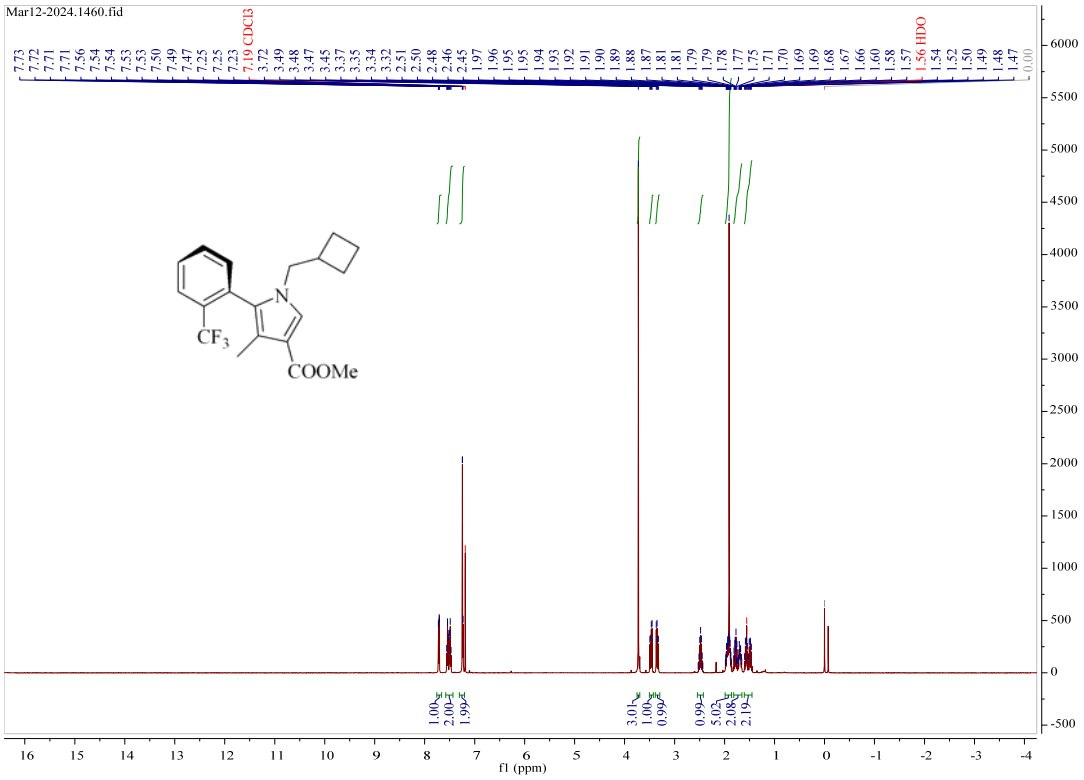
^{13}C NMR (101 MHz, $CDCl_3$) (4k)



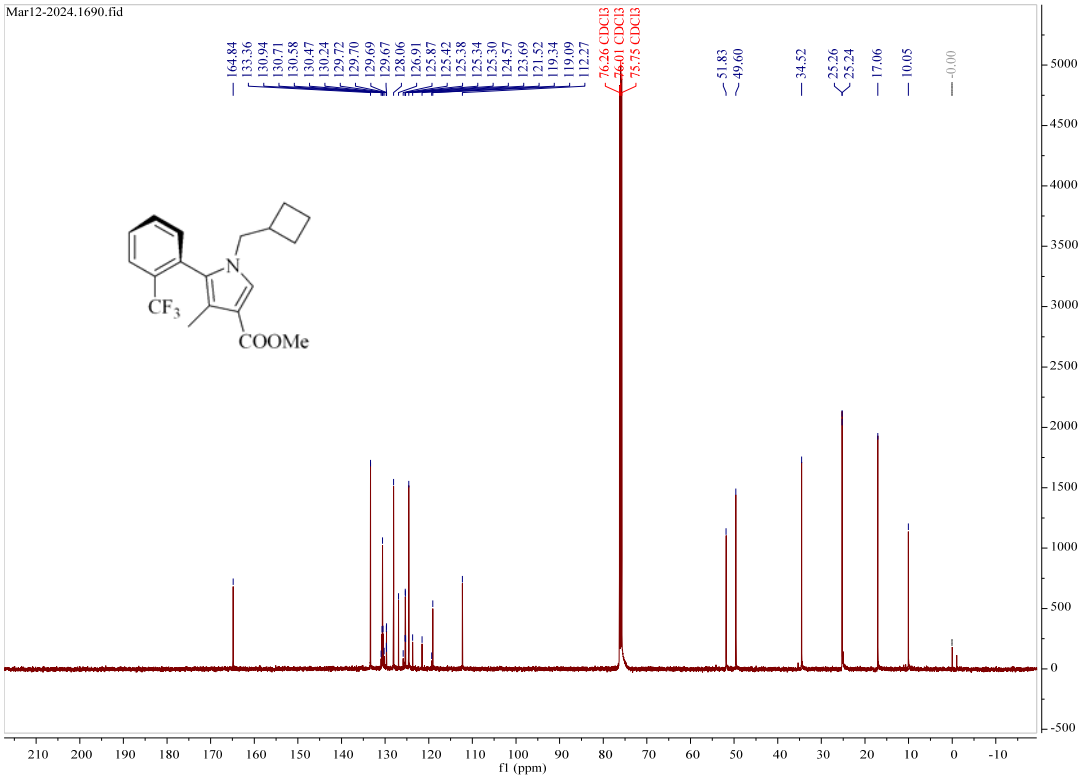
^{19}F NMR (470 MHz, $CDCl_3$) (4k)



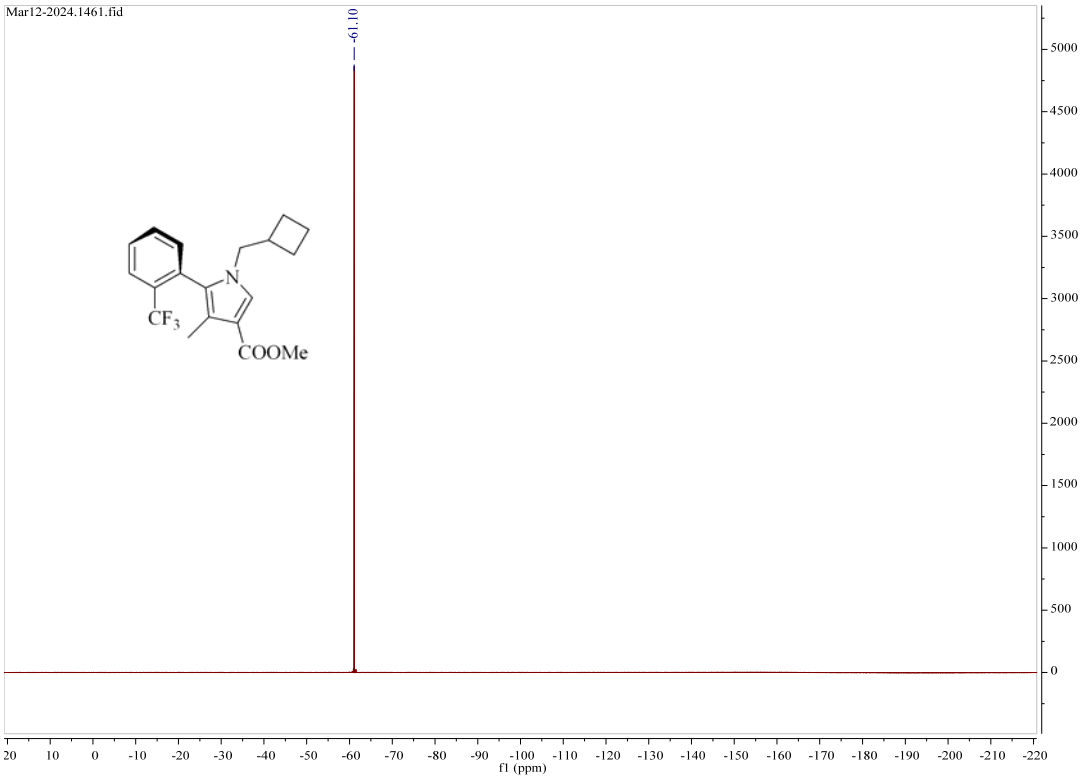
^{1}H NMR (500 MHz, $CDCl_3$) (4l)



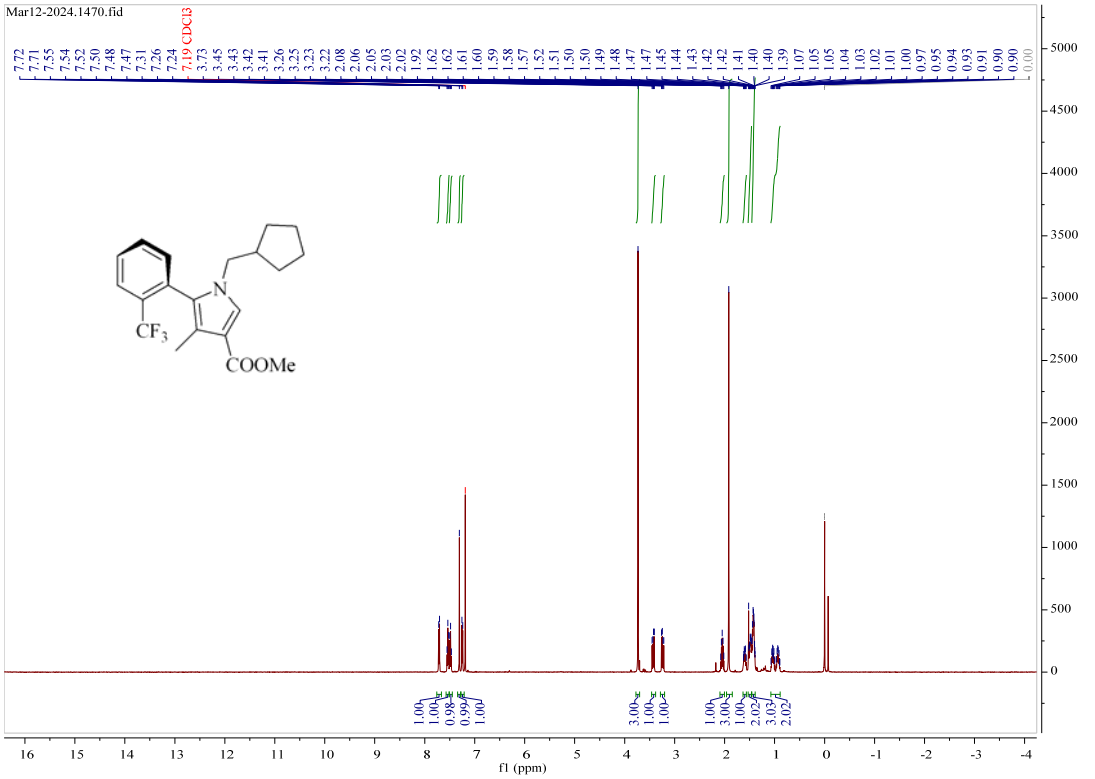
^{13}C NMR (126 MHz, $CDCl_3$) (4l)



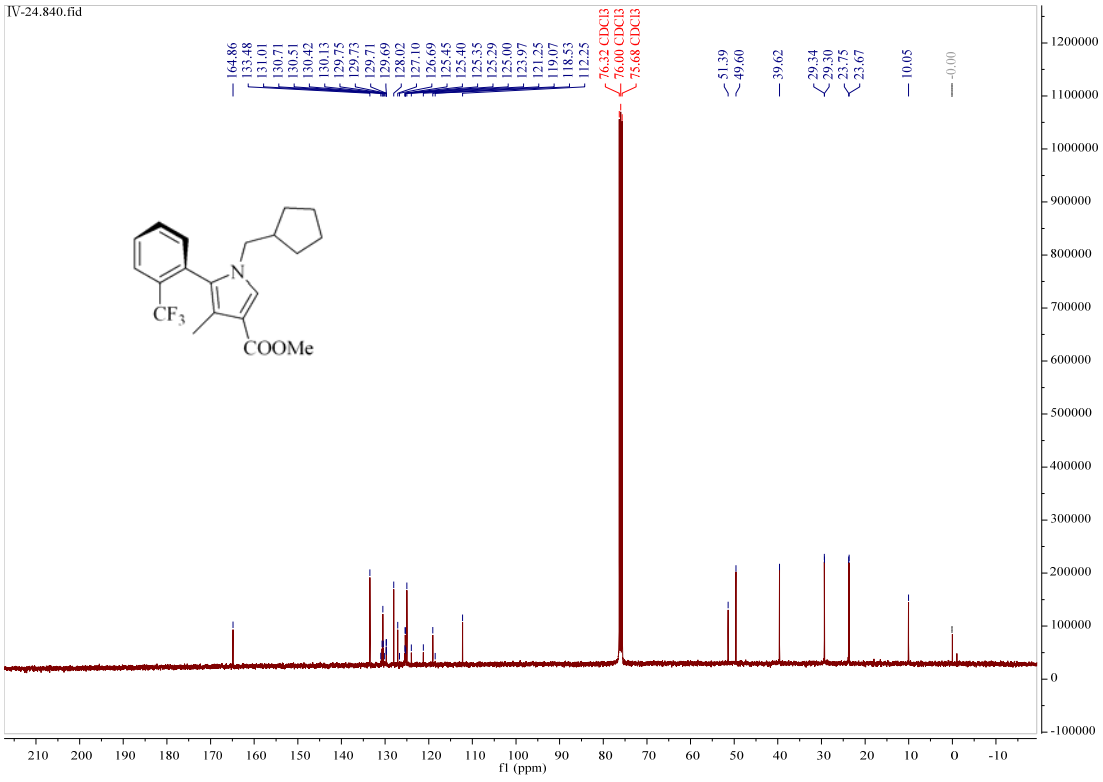
^{19}F NMR (470 MHz, $CDCl_3$) (4l)



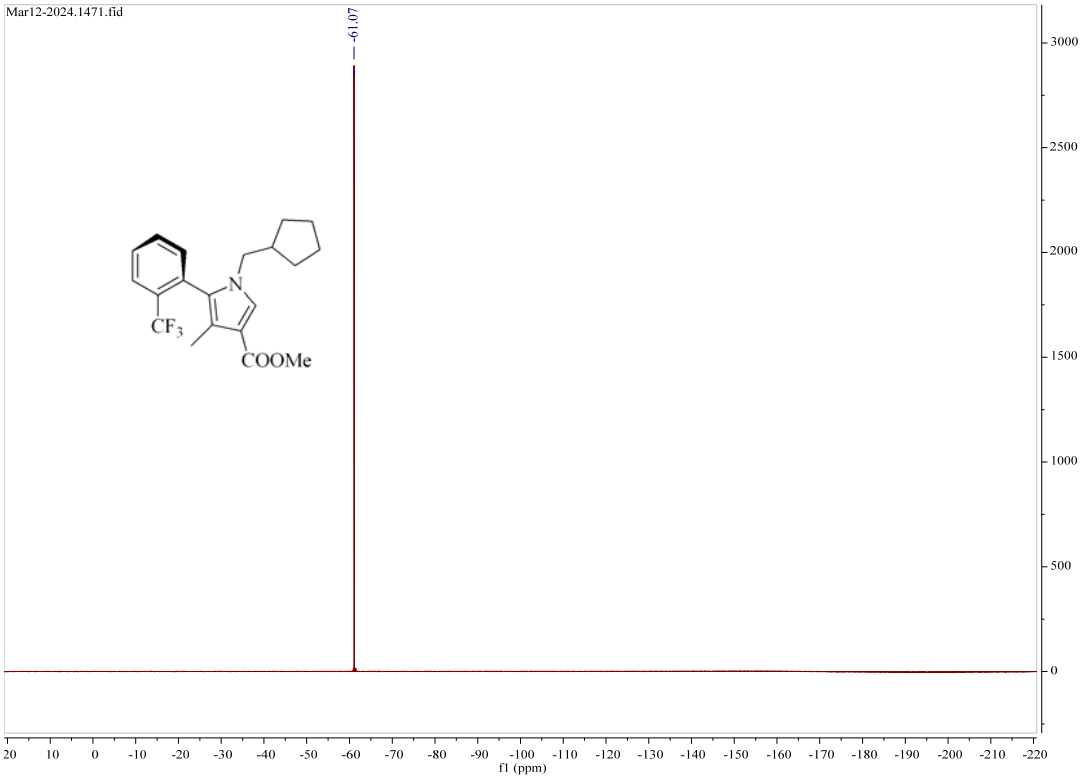
^{1}H NMR (500 MHz, $CDCl_3$) (4m)



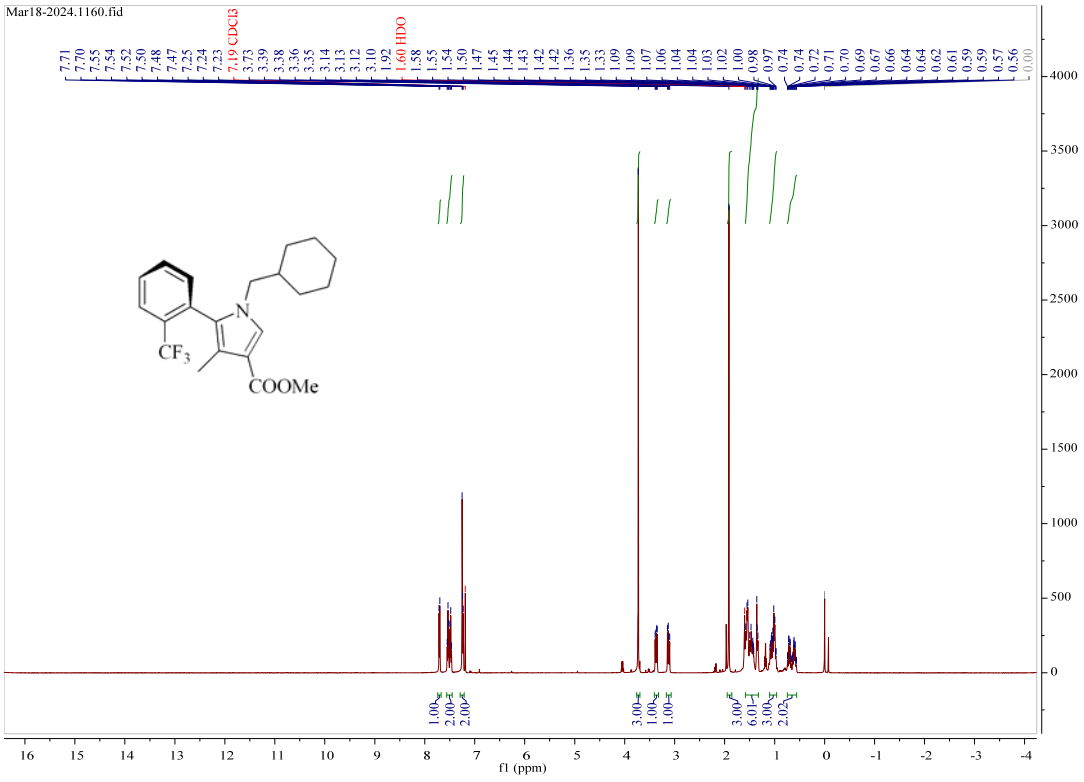
^{13}C NMR (101 MHz, $CDCl_3$) (4m)



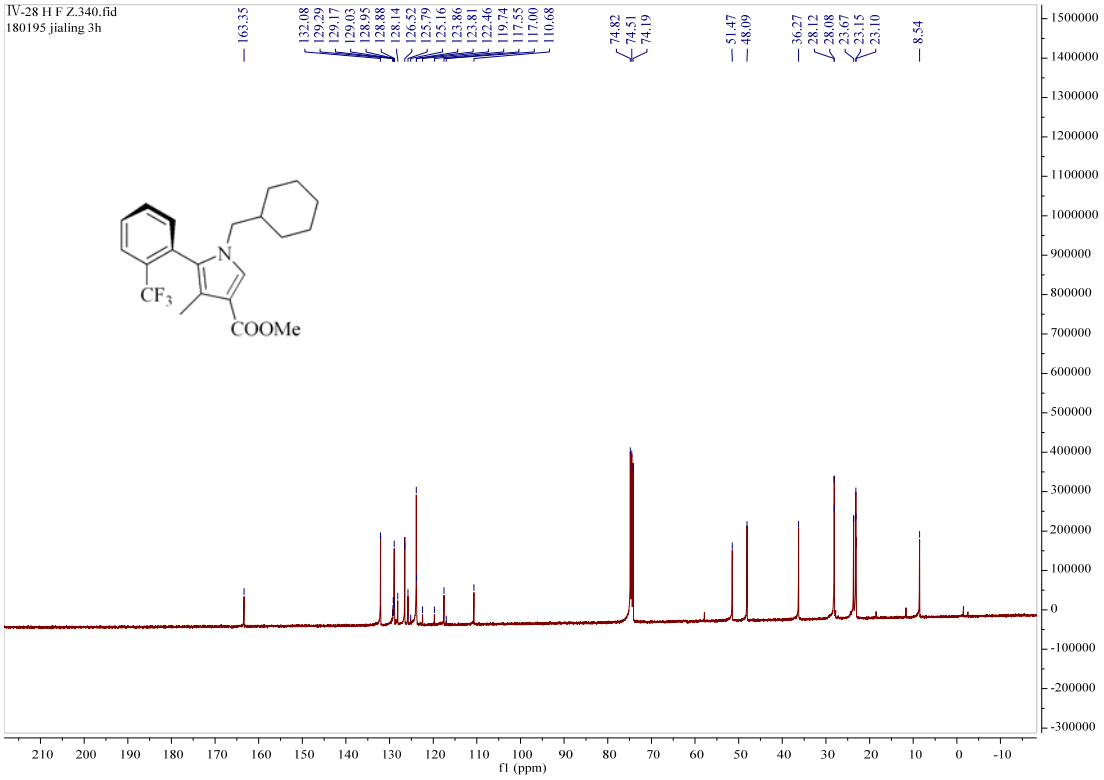
^{19}F NMR (470 MHz, $CDCl_3$) (4m)



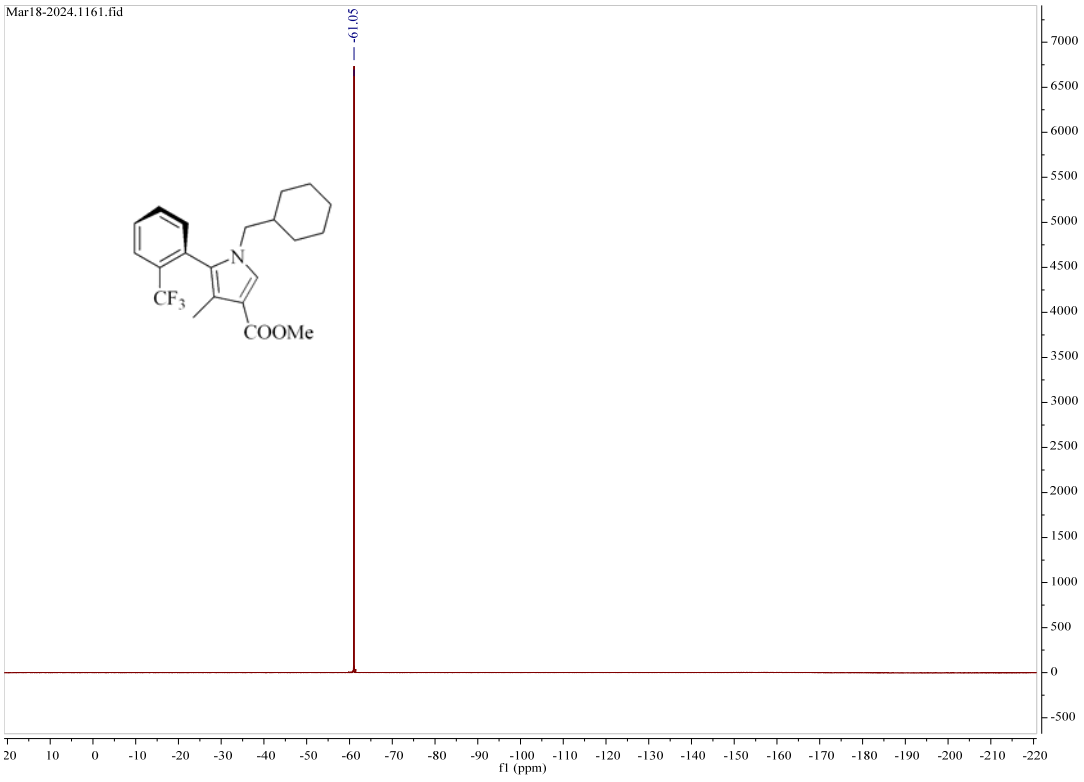
^{1}H NMR (500 MHz, $CDCl_3$) (4n)



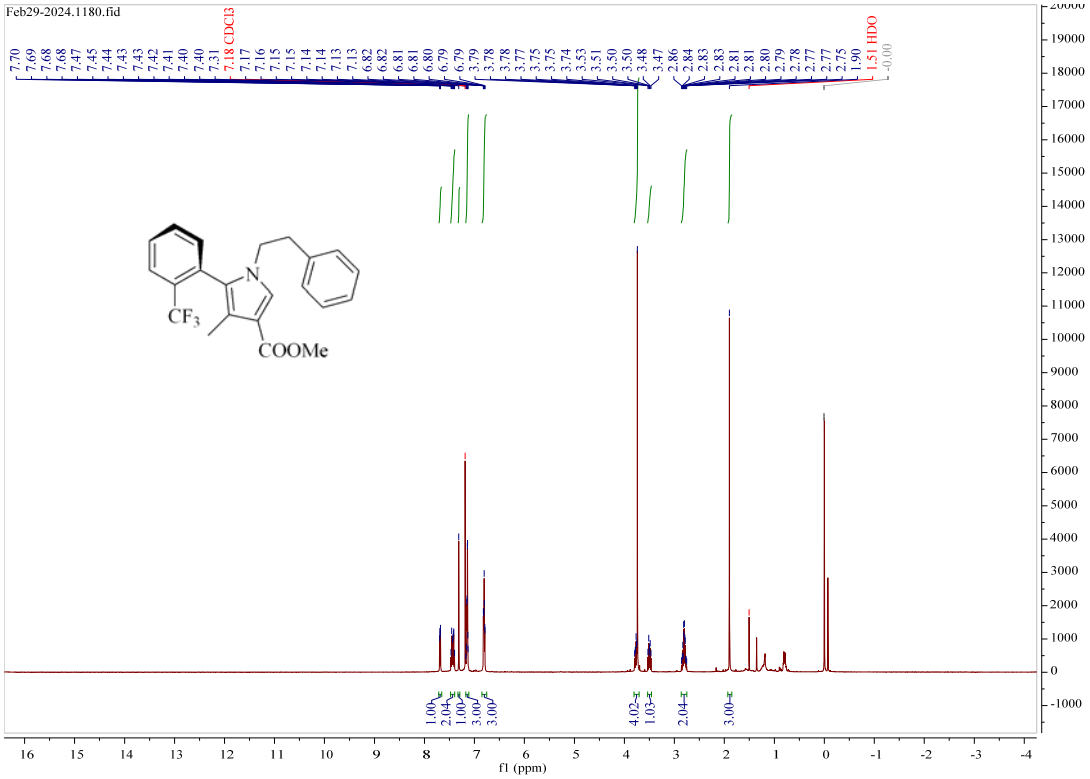
^{13}C NMR (101 MHz, $CDCl_3$) (4n)



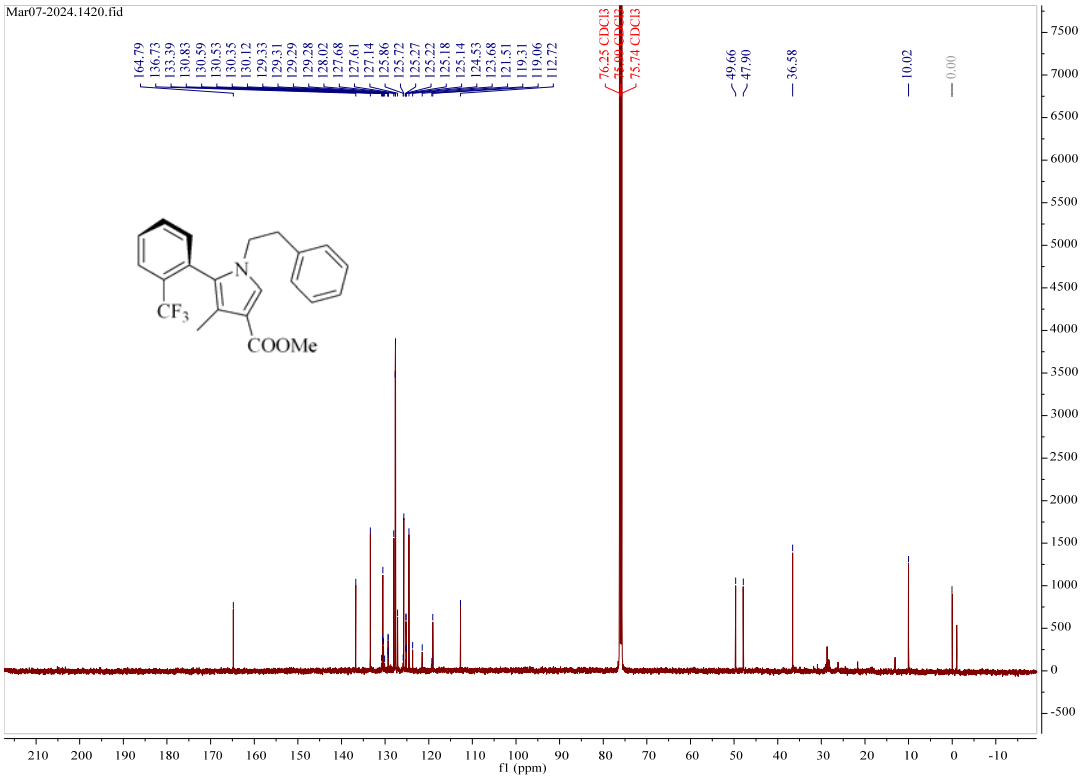
^{19}F NMR (470 MHz, $CDCl_3$) (4n)



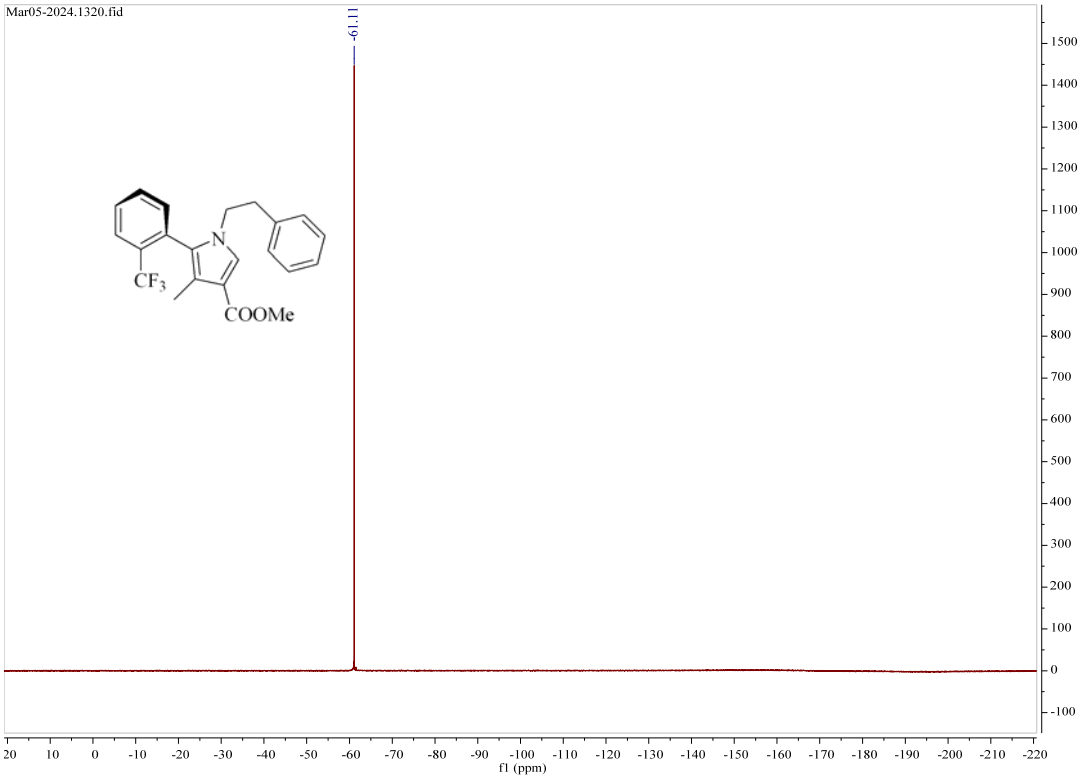
^{1}H NMR (500 MHz, $CDCl_3$) (4o)



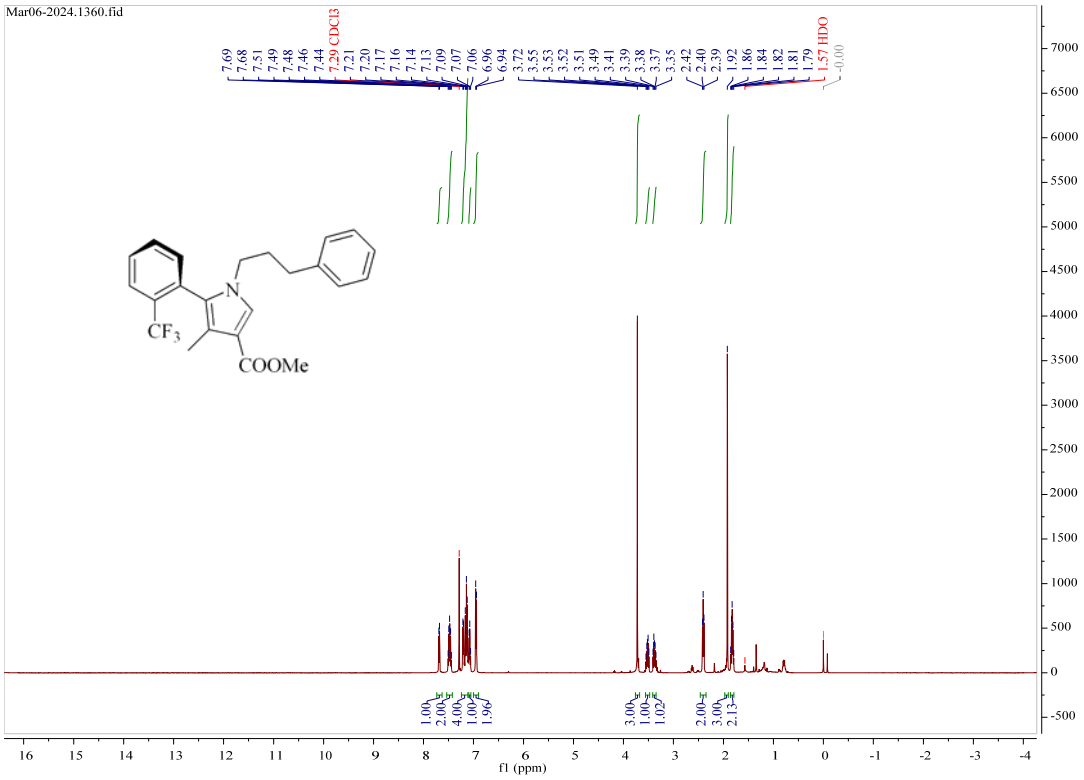
^{13}C NMR (126 MHz, $CDCl_3$) (4o)



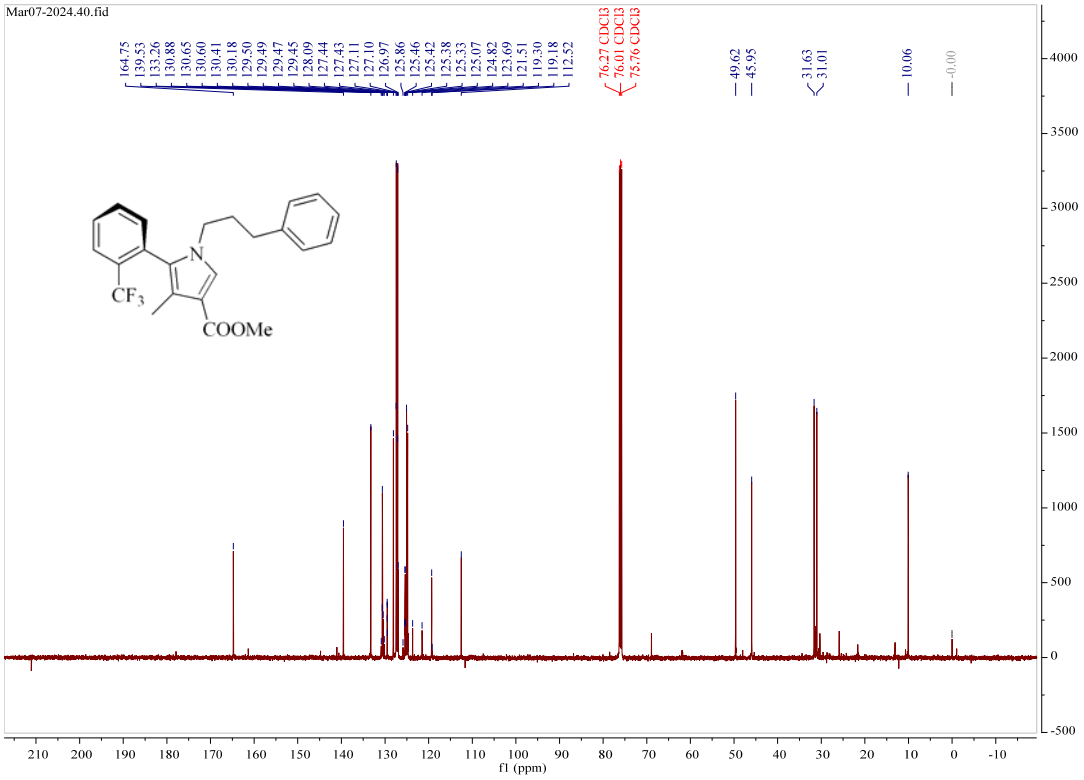
^{19}F NMR (470 MHz, $CDCl_3$) (4o)



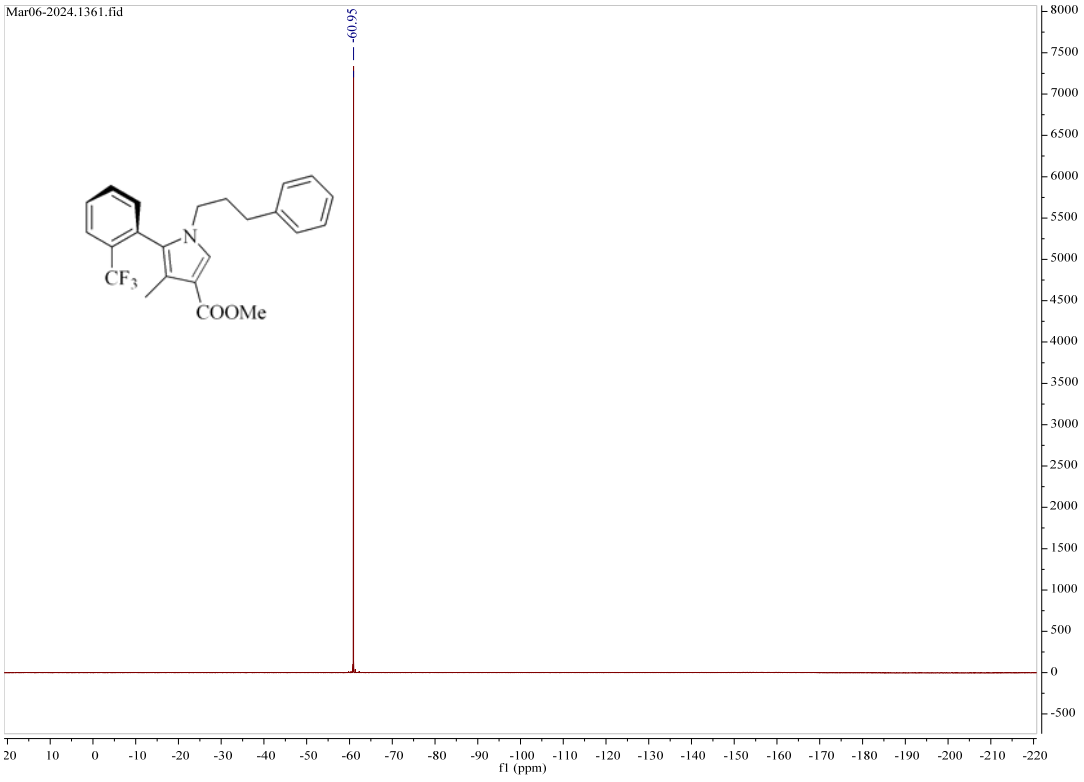
^{1}H NMR (500 MHz, $CDCl_3$) (4p)



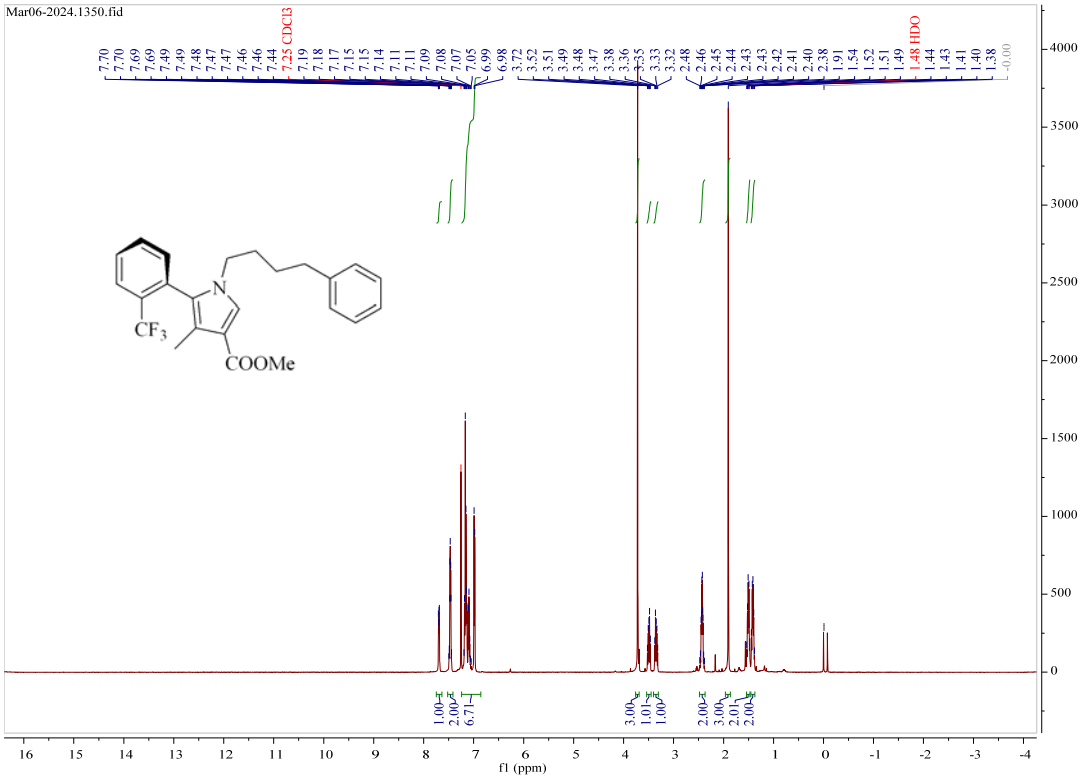
^{13}C NMR (126 MHz, $CDCl_3$) (4p)



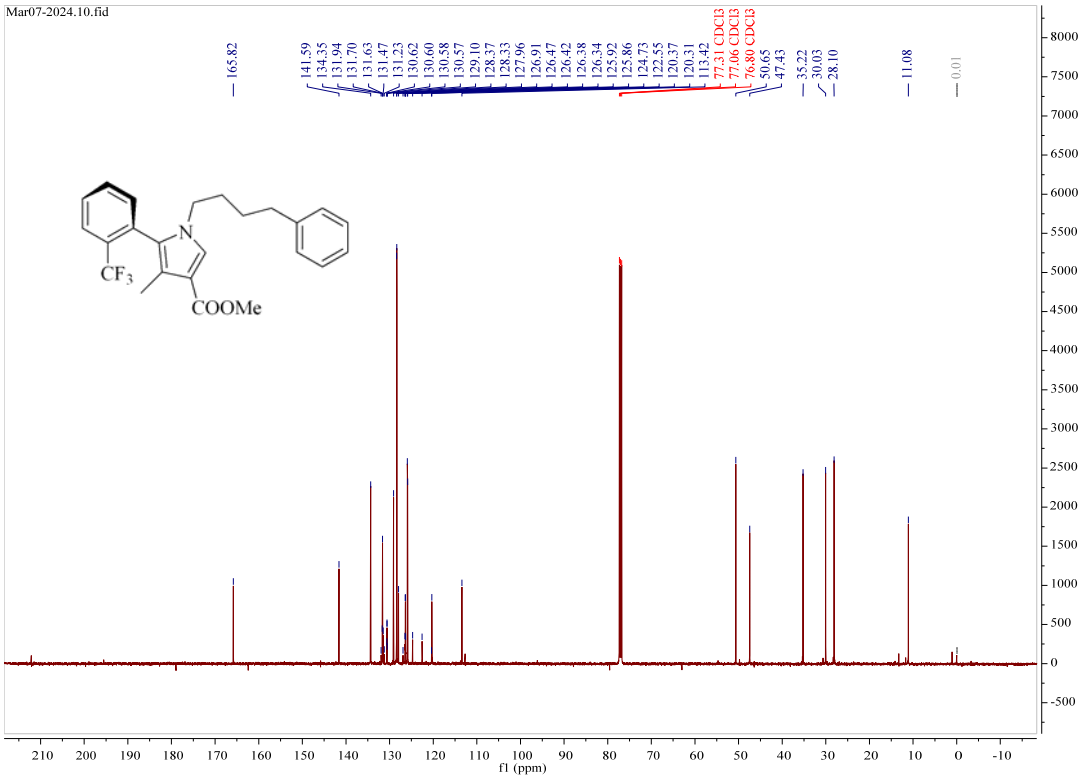
^{19}F NMR (470 MHz, $CDCl_3$) (4p)



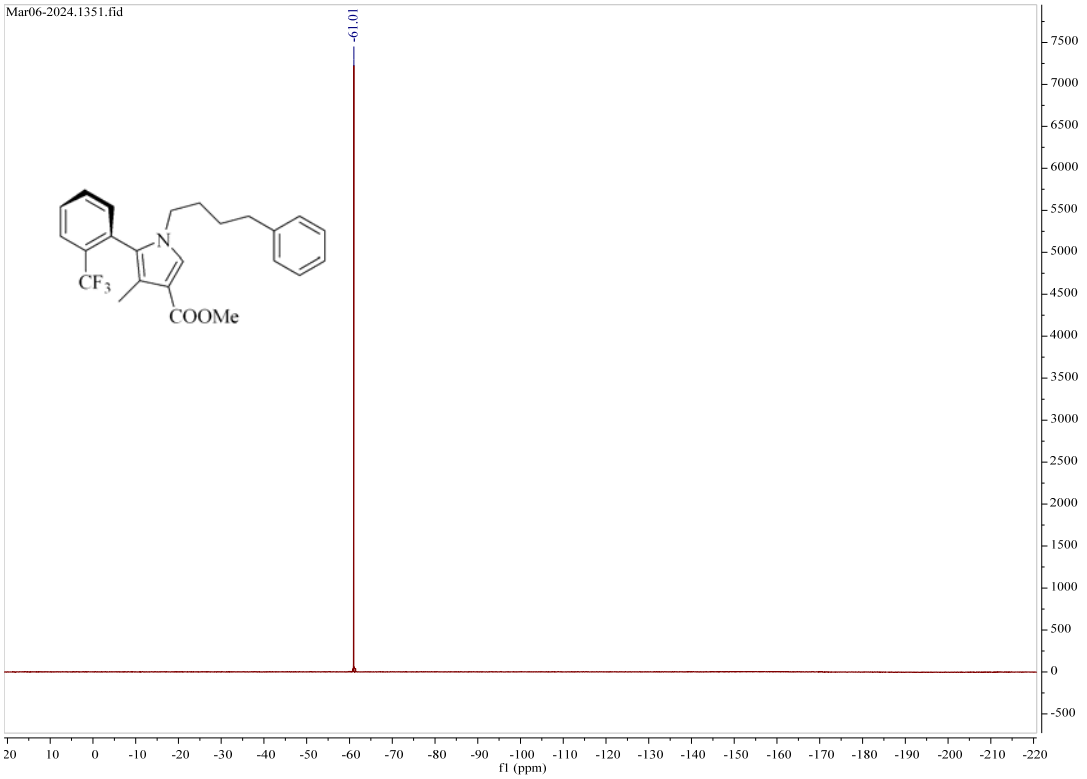
^{1}H NMR (500 MHz, $CDCl_3$) (4q)



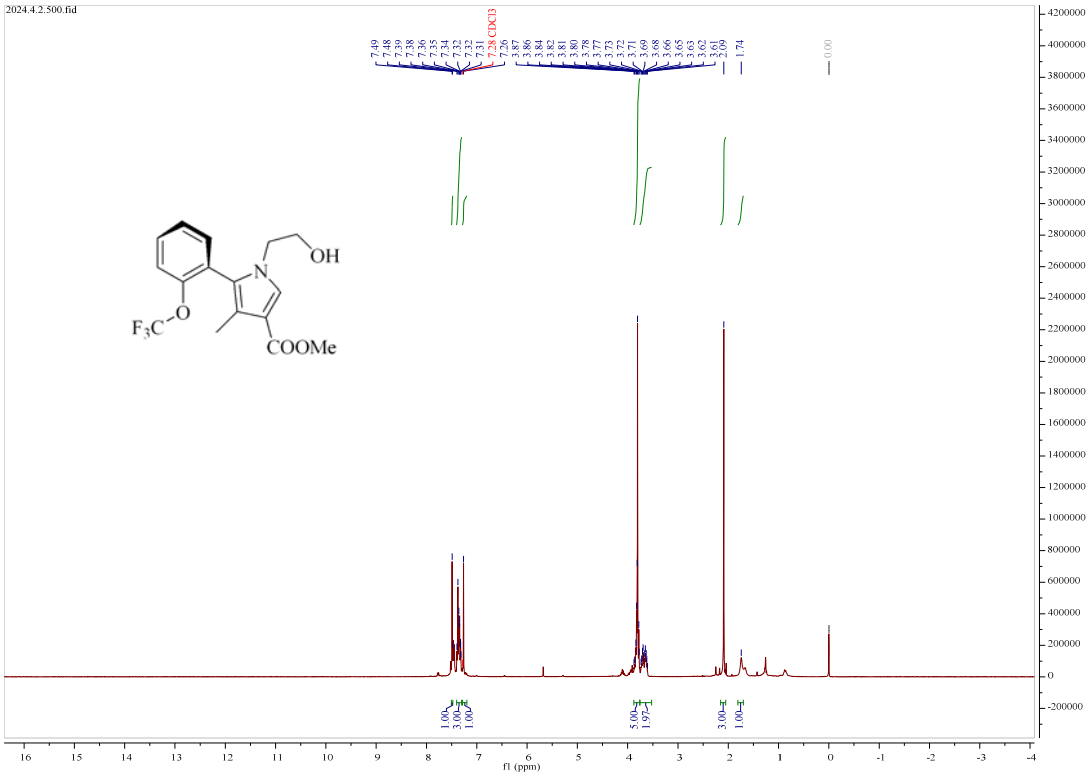
^{13}C NMR (126 MHz, $CDCl_3$) (4q)



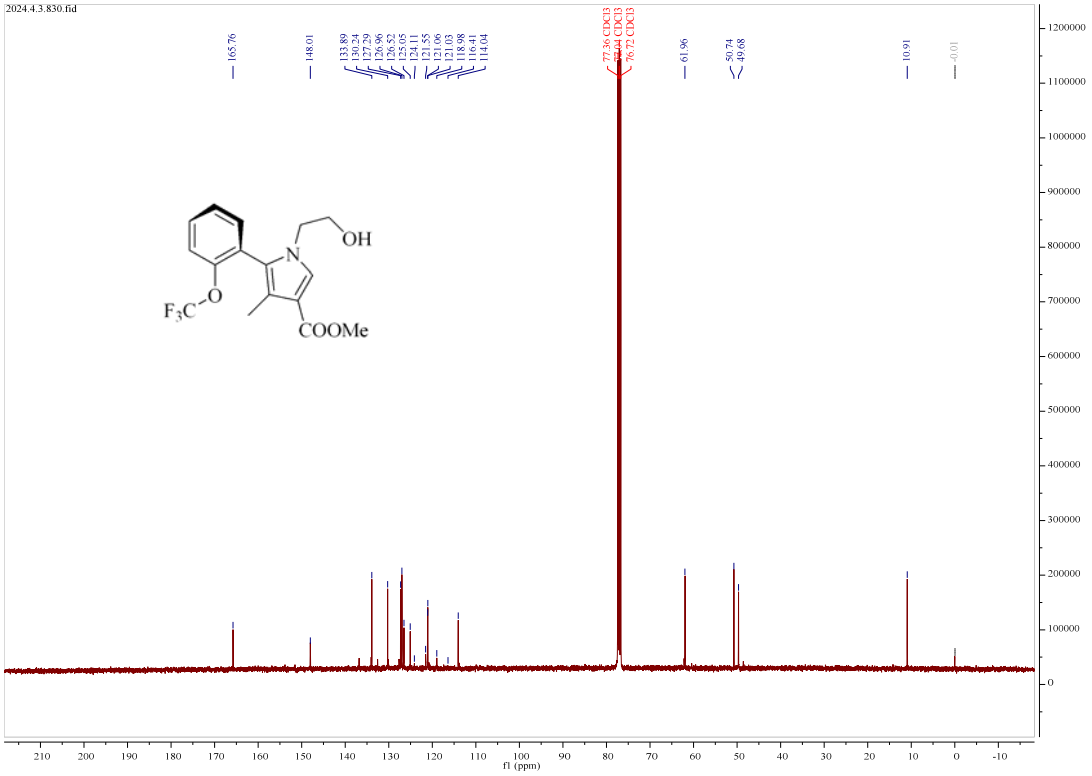
^{19}F NMR (470 MHz, $CDCl_3$) (4q)



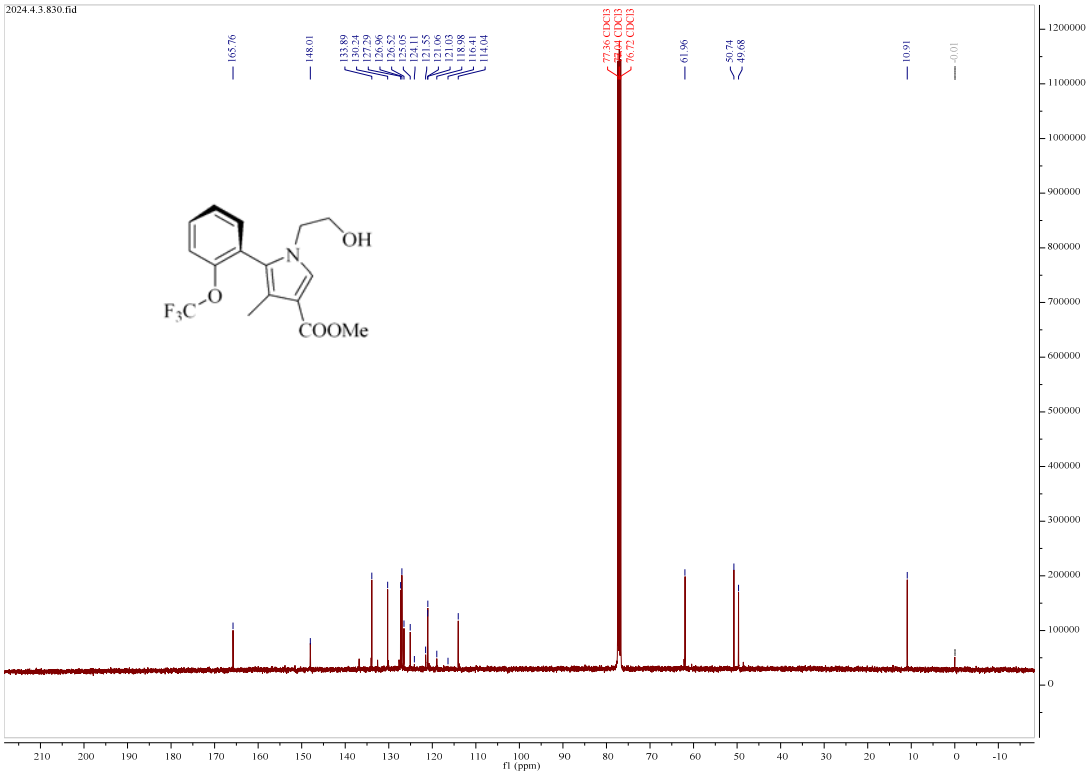
^{1}H NMR (400 MHz, $CDCl_3$) (4r)



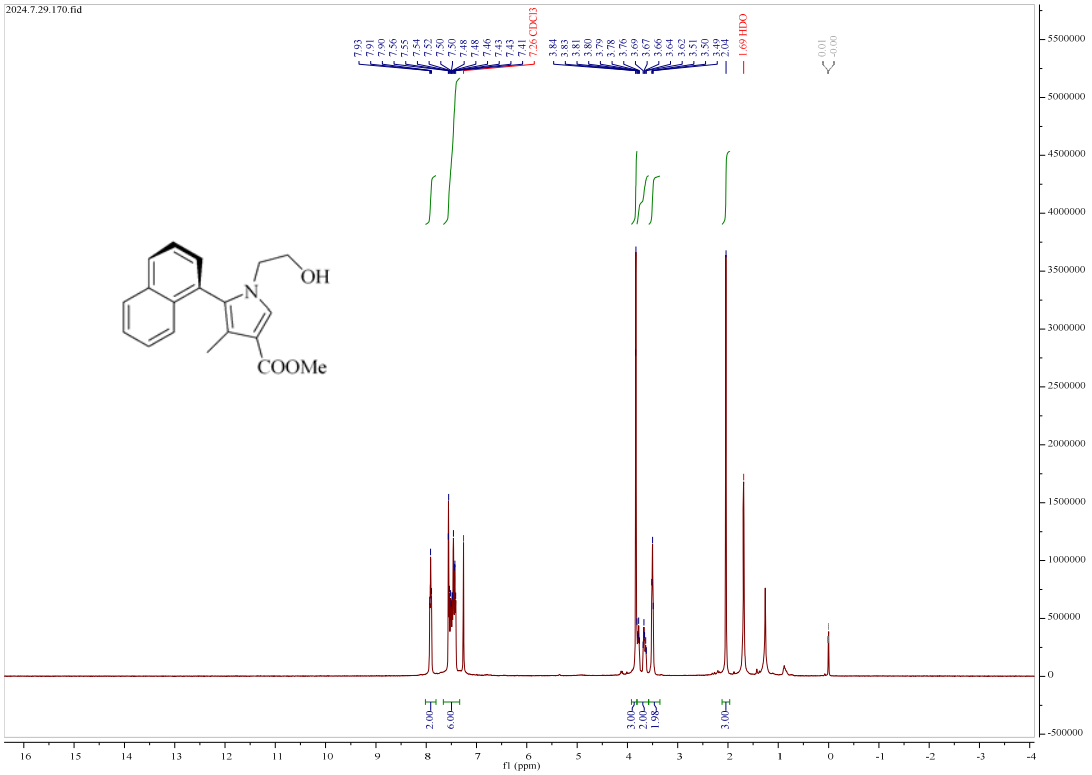
^{13}C NMR (101 MHz, $CDCl_3$) (4r)



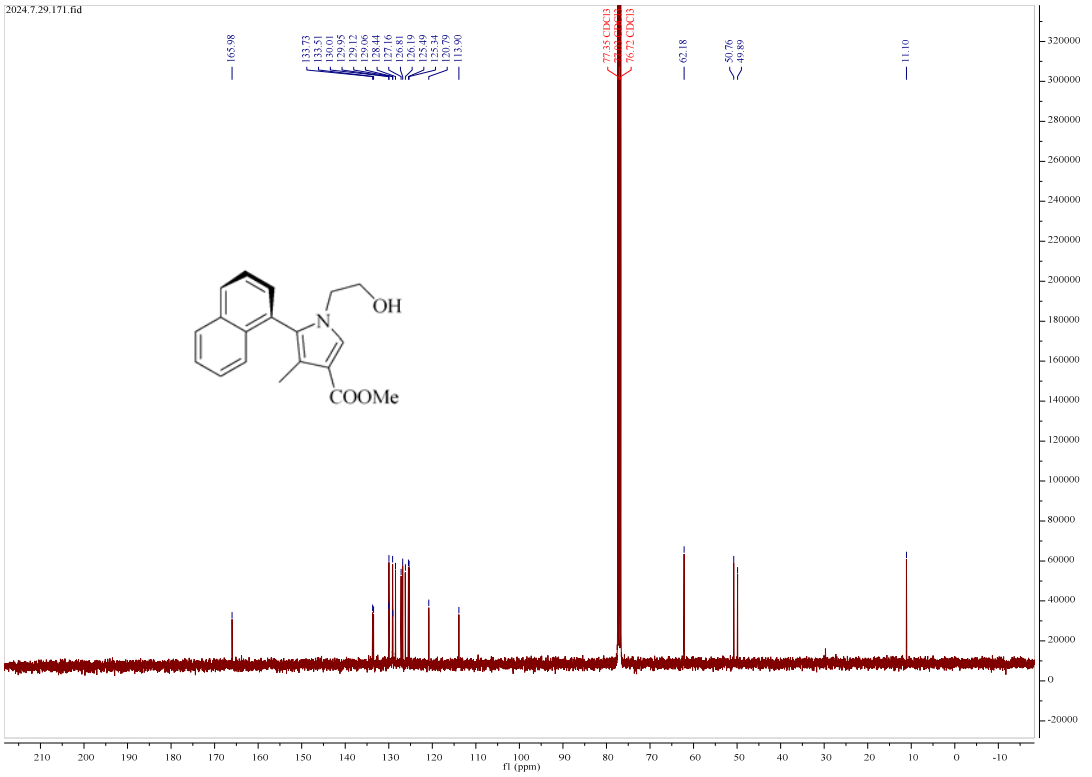
^{19}F NMR (376 MHz, $CDCl_3$) (4r)



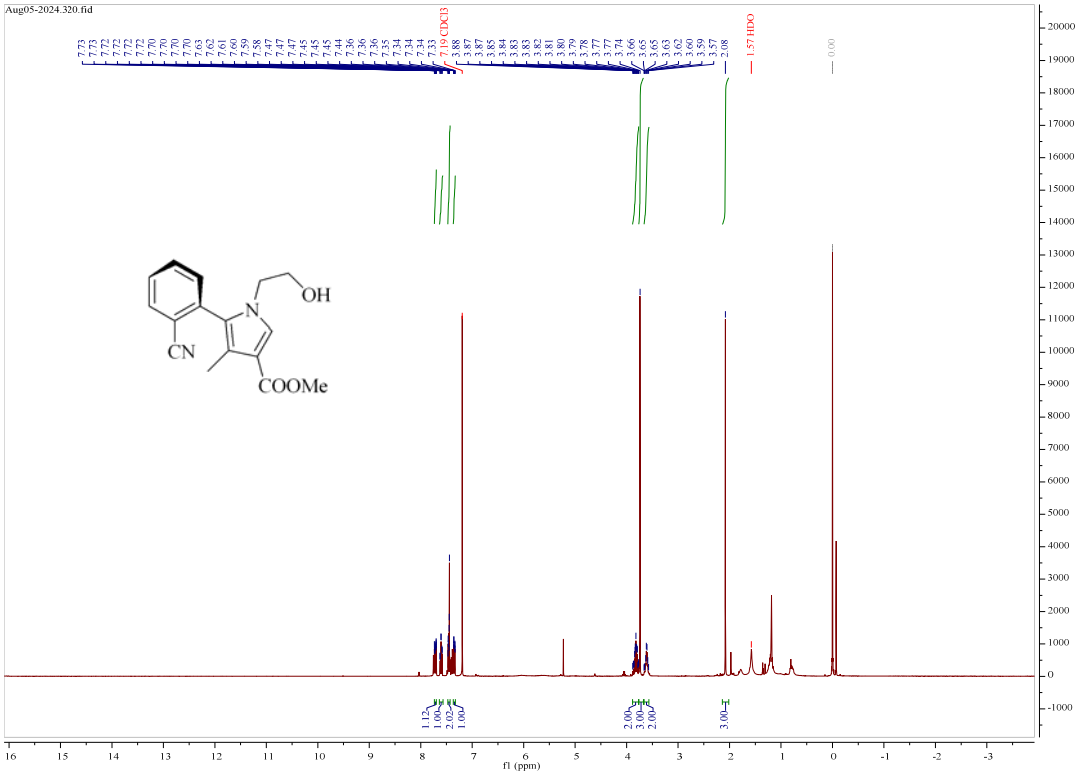
^{1}H NMR (400 MHz, $CDCl_3$) (4s)



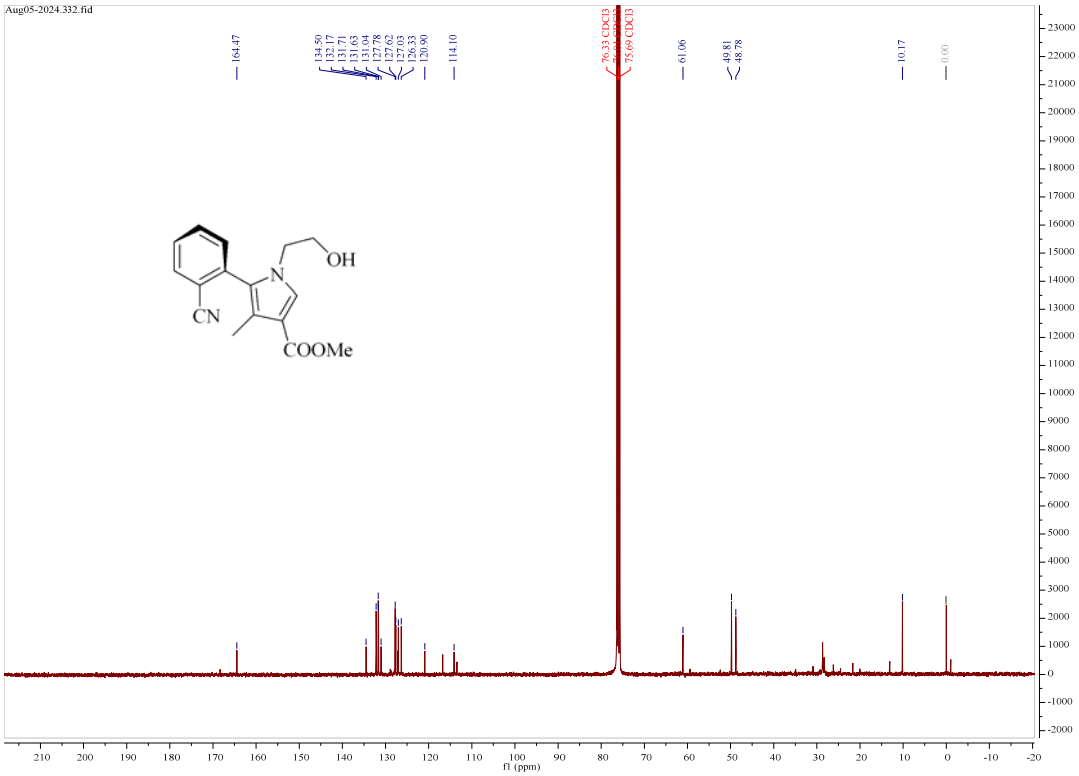
^{13}C NMR (101 MHz, $CDCl_3$) (4s)



^{1}H NMR (400 MHz, $CDCl_3$) (4t)



^{13}C NMR (101 MHz, $CDCl_3$) (4t)



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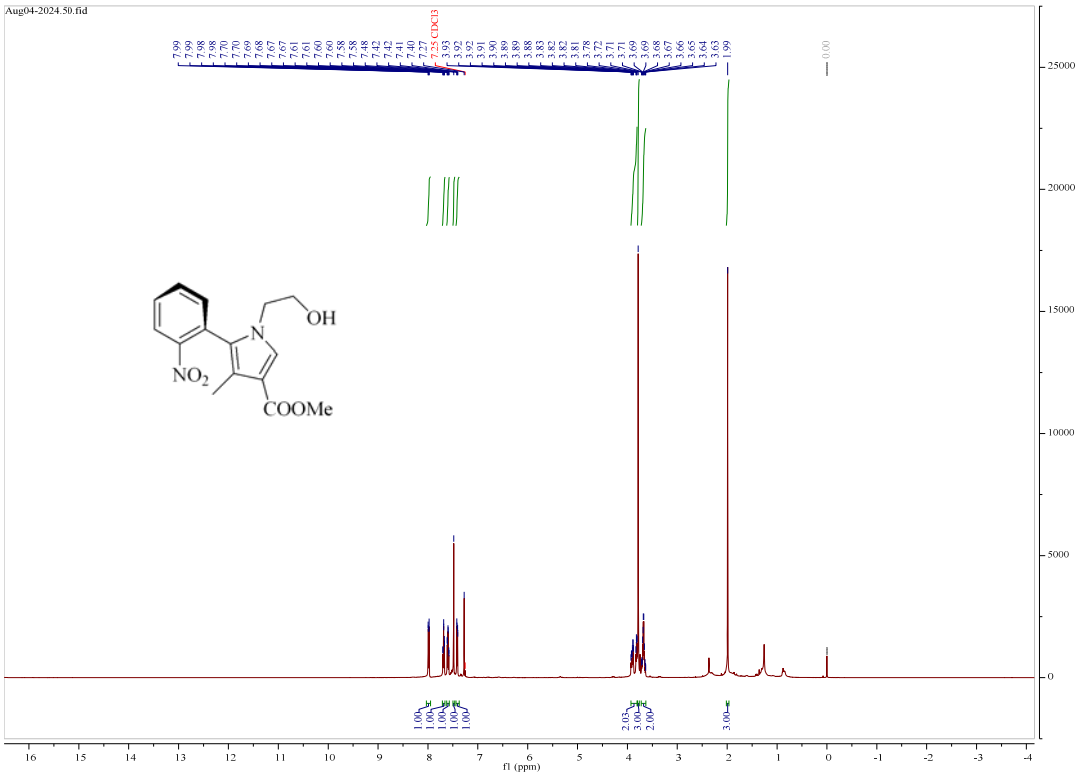
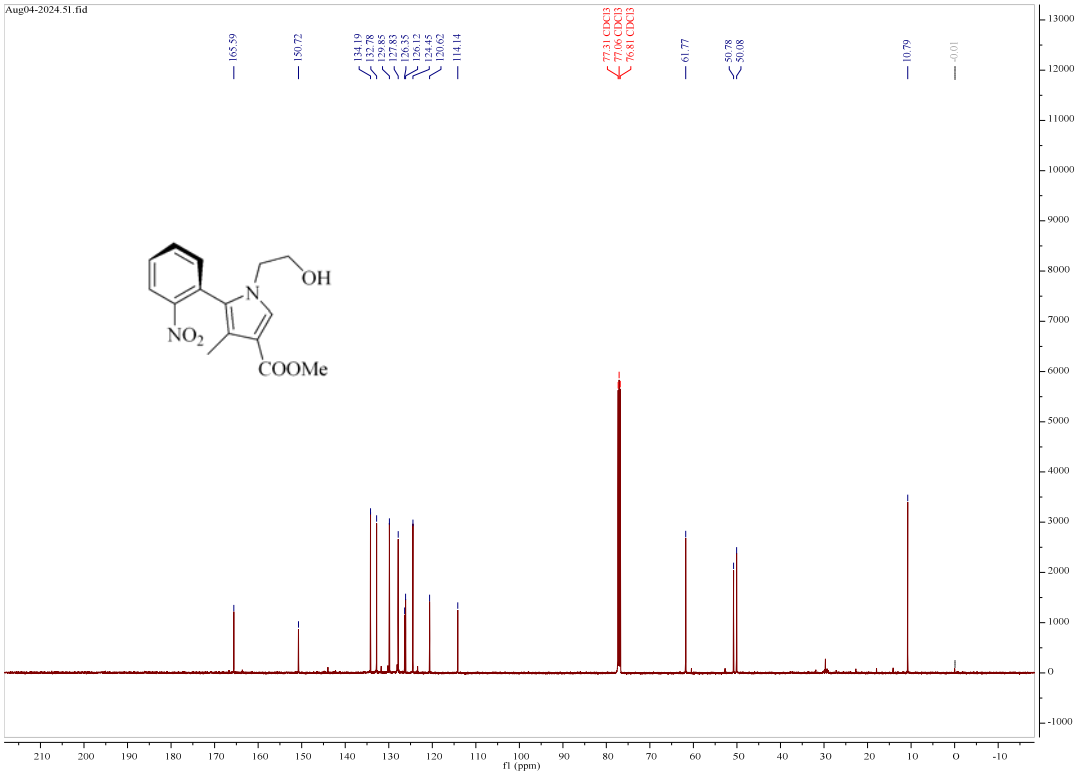
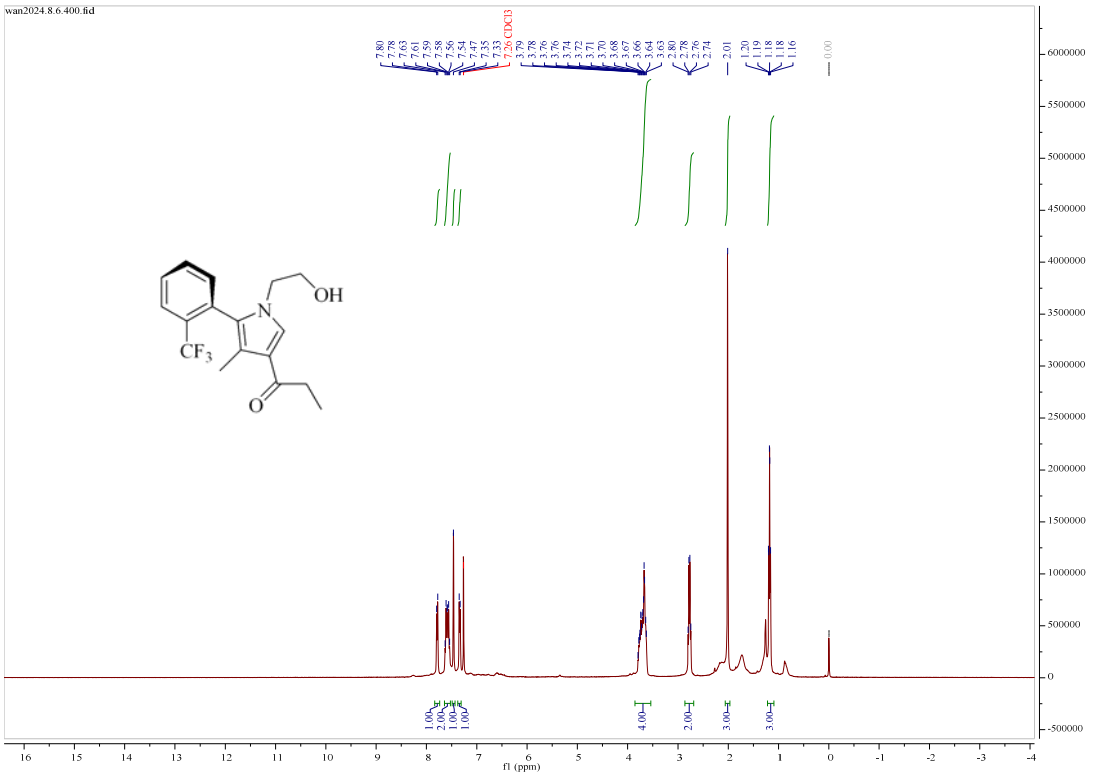


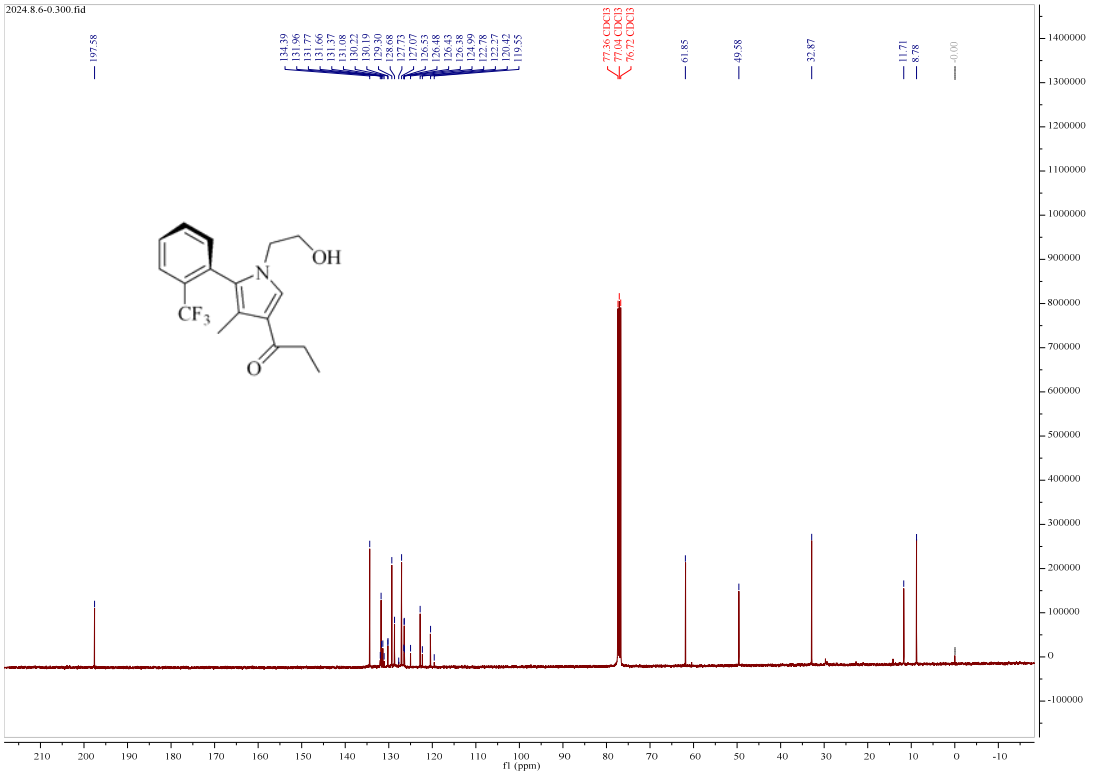
^{13}C NMR (101 MHz, $CDCl_3$) (4u)



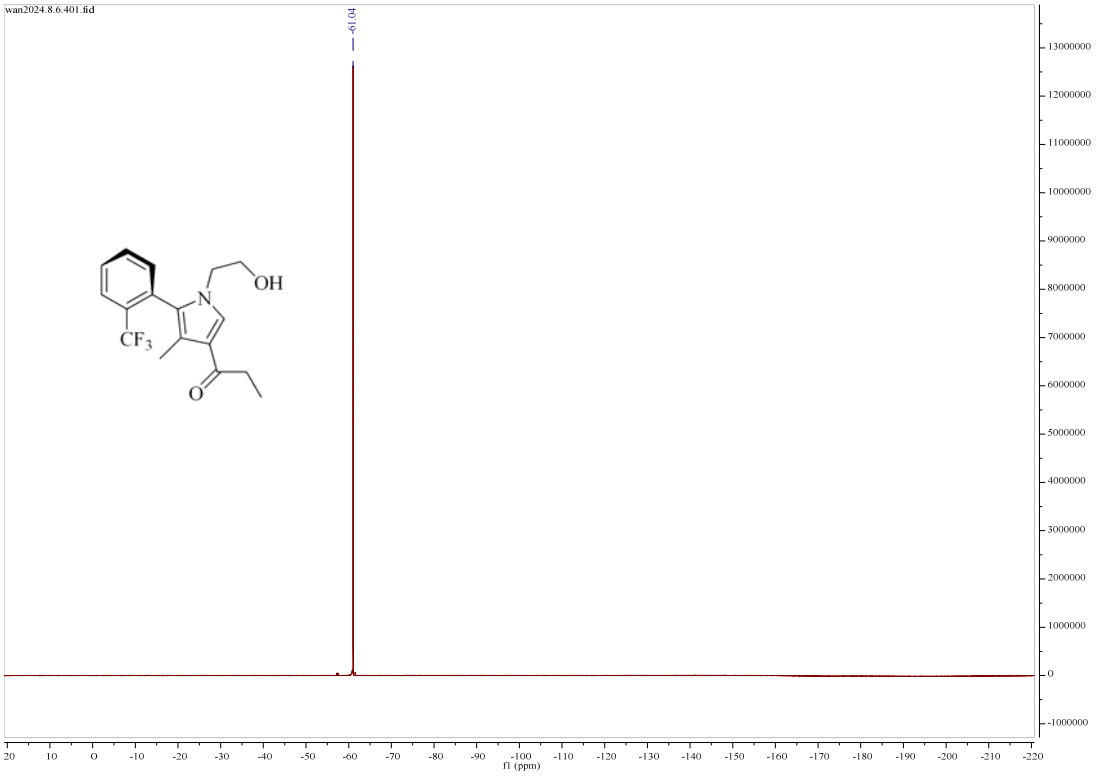
^{1}H NMR (400 MHz, $CDCl_3$) (4v)



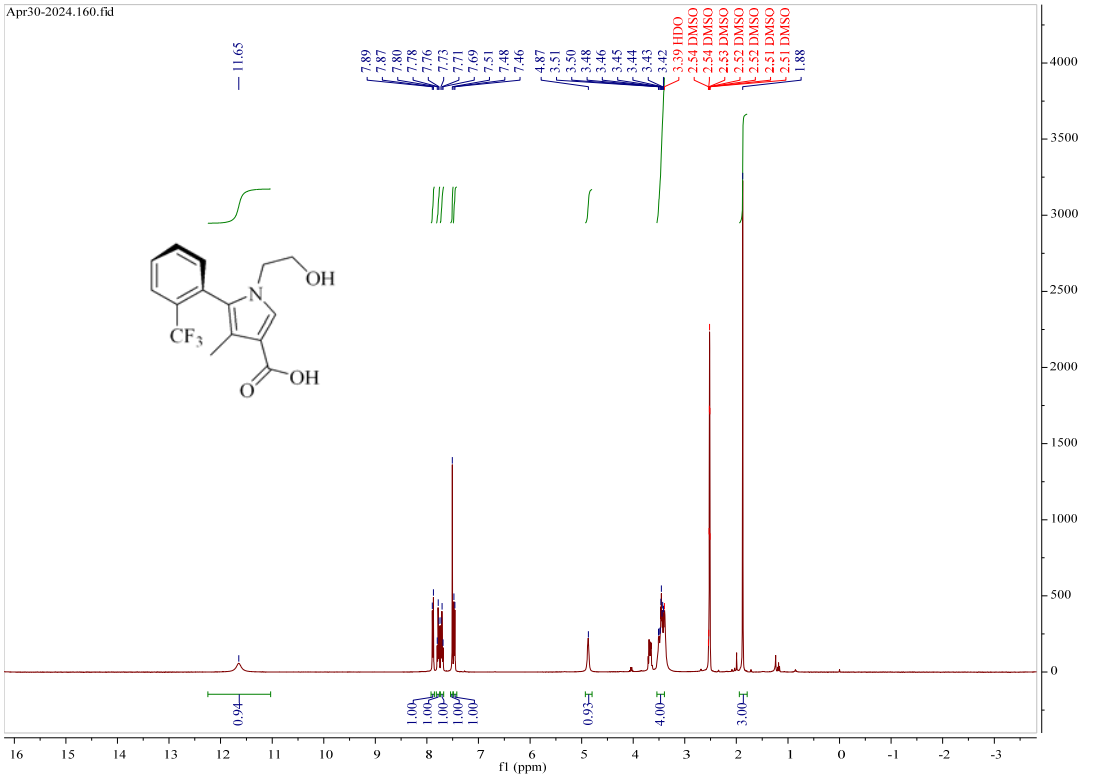
^{13}C NMR (101 MHz, $CDCl_3$) (4v)



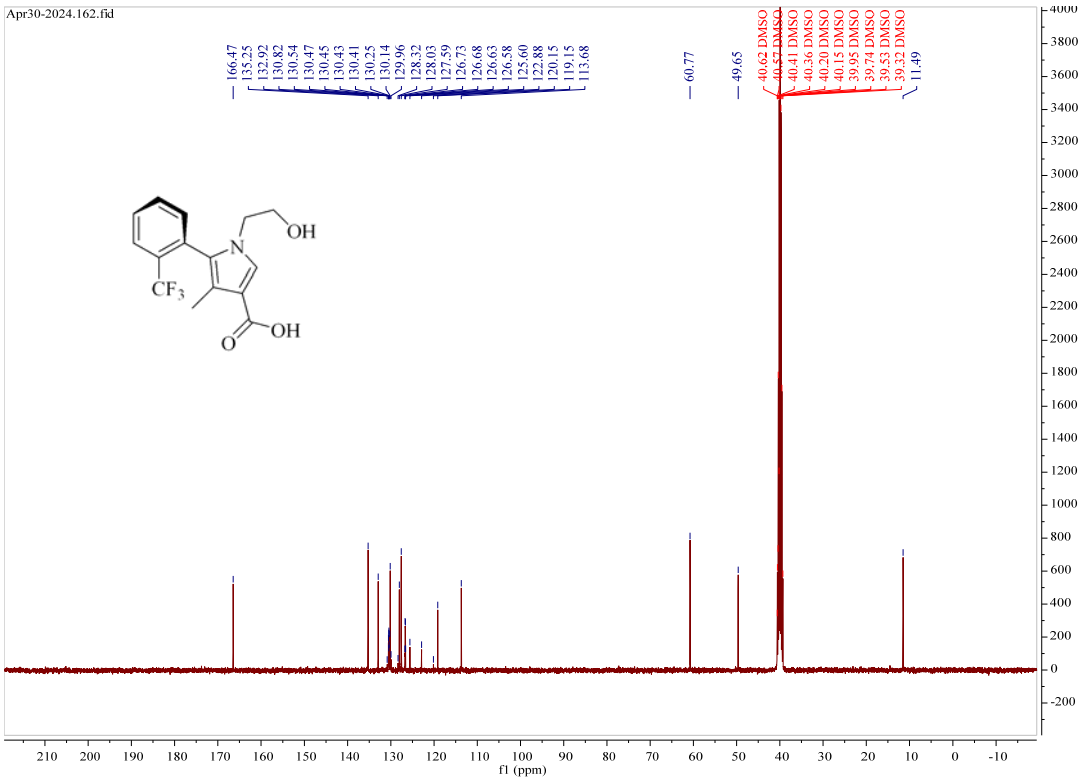
^{19}F NMR (376 MHz, $CDCl_3$) (4v)



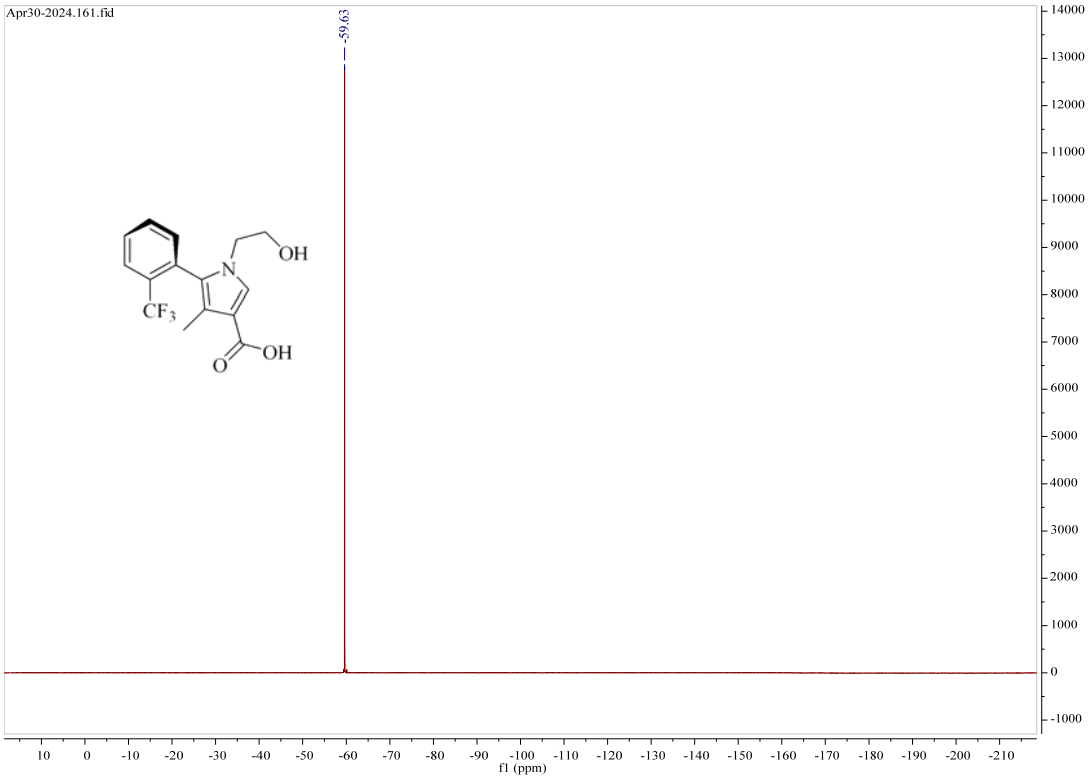
^{1}H NMR (400 MHz, $CDCl_3$) (5a)



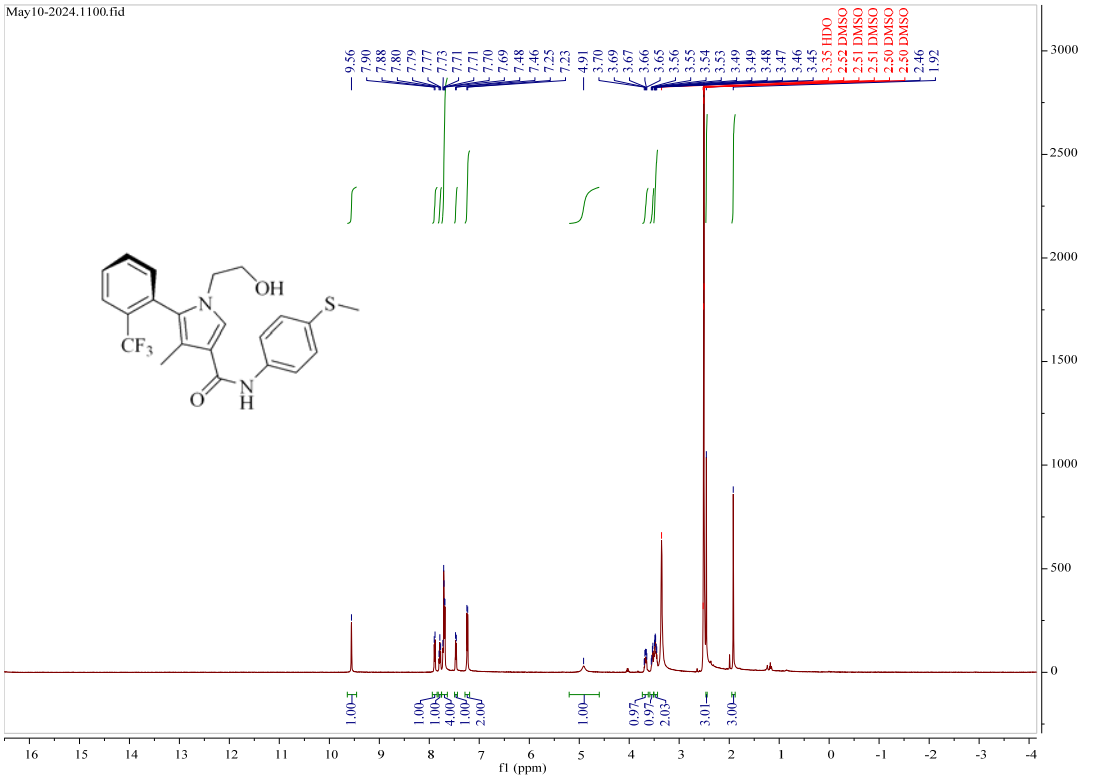
^{13}C NMR (101 MHz, $CDCl_3$) (5a)



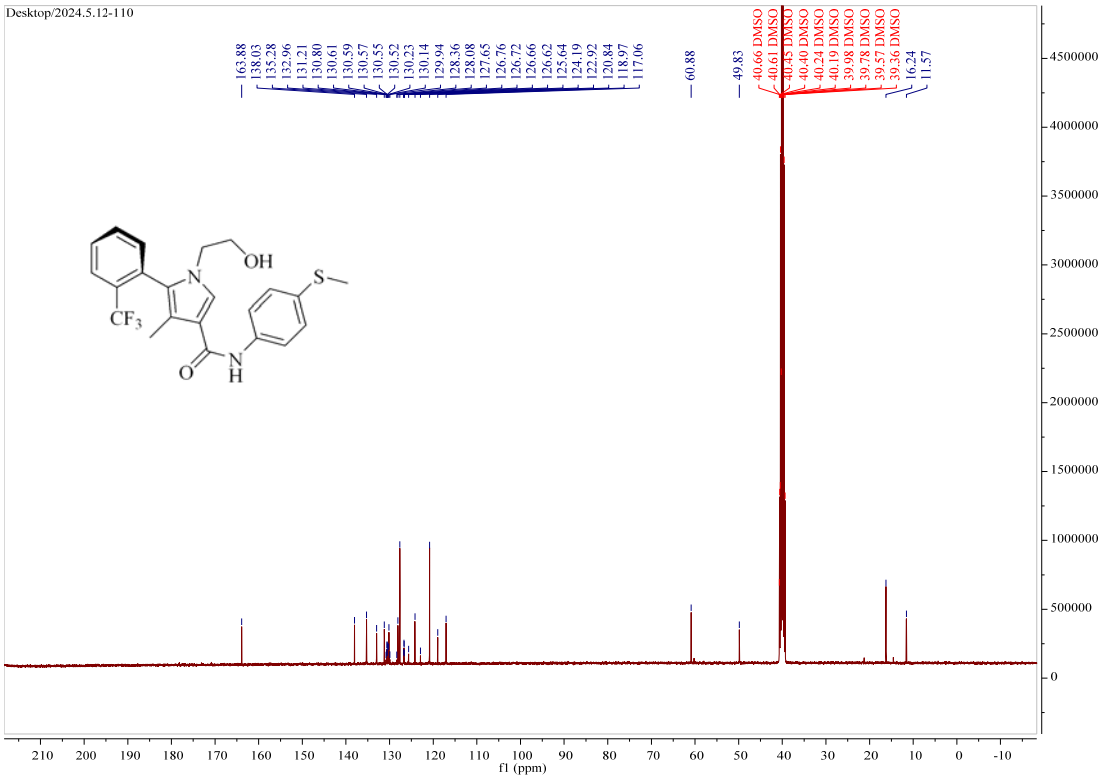
^{19}F NMR (377 MHz, $CDCl_3$) (5a)



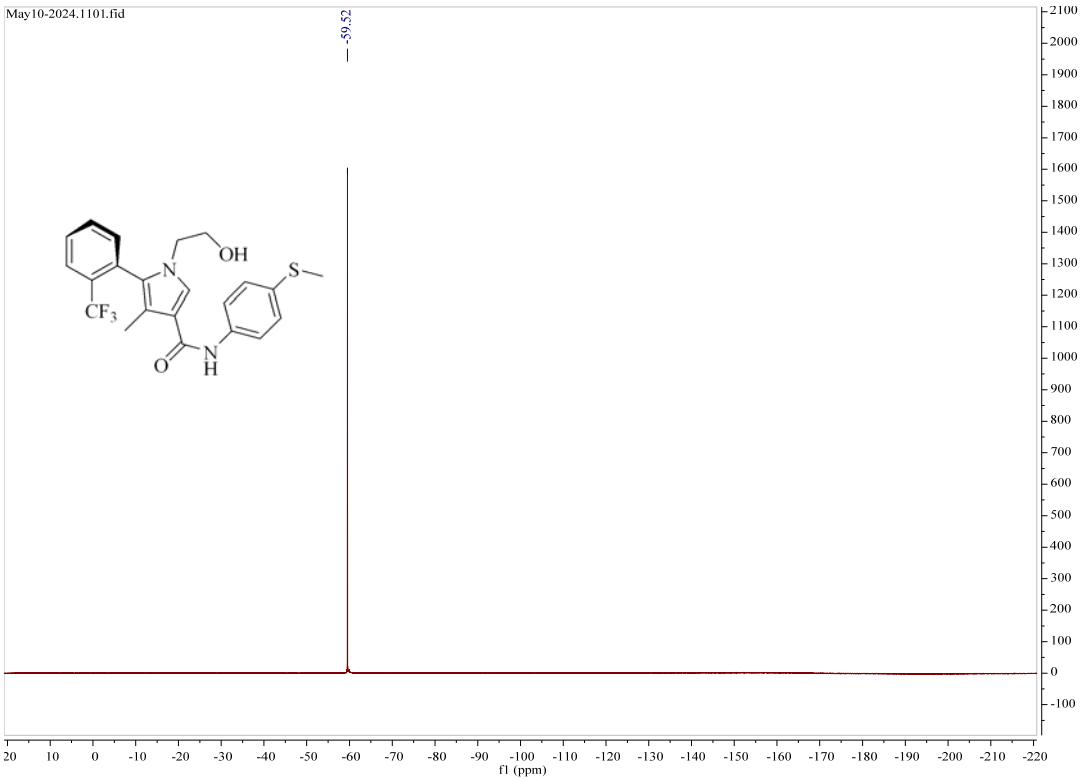
^{1}H NMR (500 MHz, $CDCl_3$) (6a)



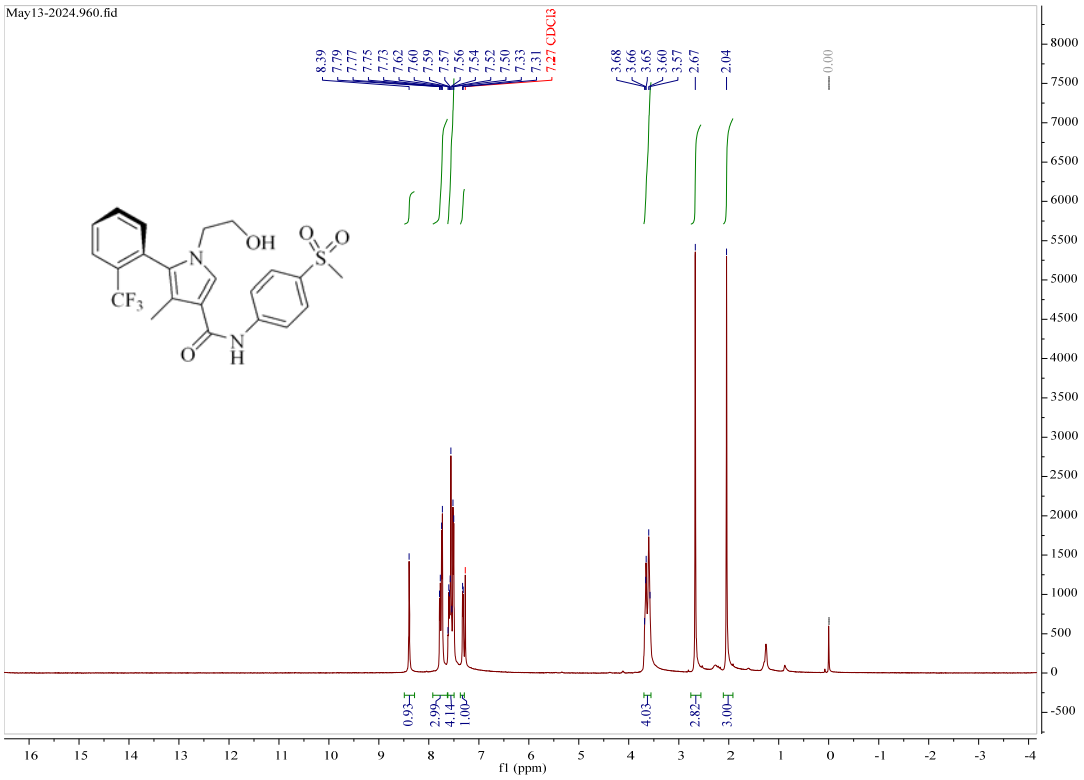
^{13}C NMR (101 MHz, $CDCl_3$) (6a)



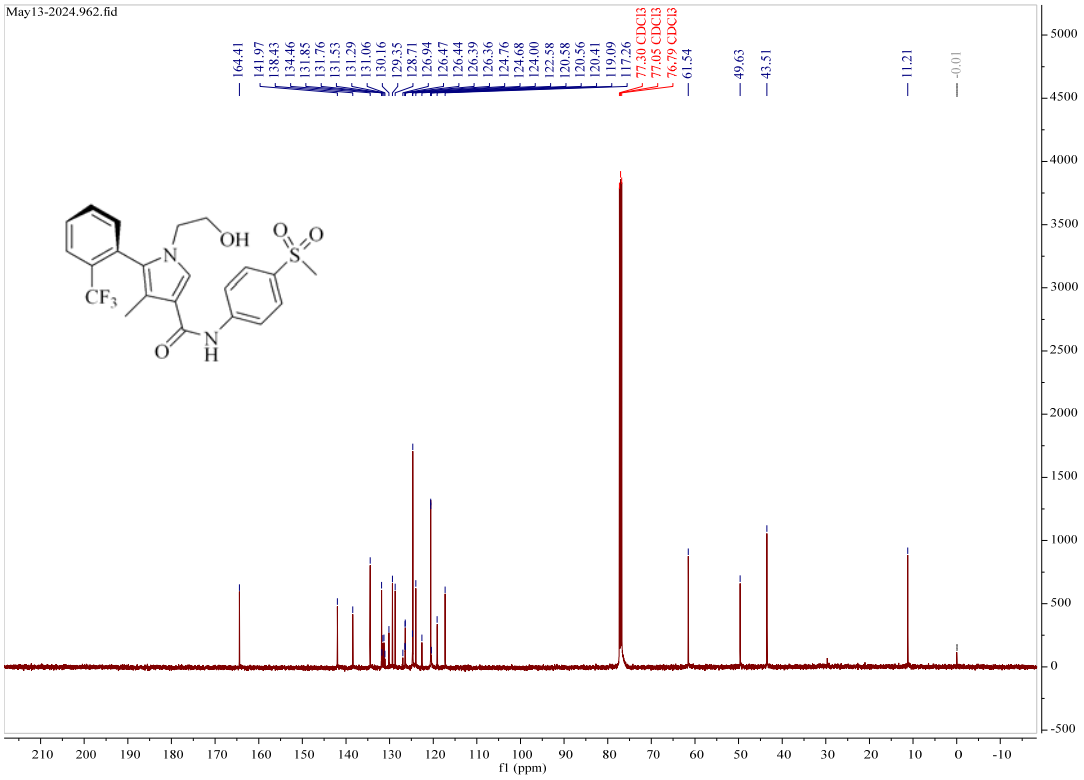
^{19}F NMR (470 MHz, $CDCl_3$) (6a)



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



^{13}C NMR (126 MHz, $CDCl_3$) (esaxerenone)



^{19}F NMR (470 MHz, $CDCl_3$) (esaxerenone)