Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Three-Component Ruthenium-Catalyzed Remote *C*-H Functionalization of 8-Aminoquinoline Amides

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1. General Remarks

Unless otherwise noted, all of these reactions were were carried out under an argon atmosphere. Solvent was freshly distilled prior to use unless otherwise noted. For column chromatography, silica gel (200-300 mesh) was employed. Analytical TLC was performed with silica gel GF254 plates. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Room temperature (r.t.) is 23-25°C.

Materials. Unless otherwise noted below, all other compounds have been reported in the literature or are commercially available. Commercial reagents were used without further purification. Extra dry PhCl was purchased from Energy and for the $[Ru(p\text{-}cymene)Cl_2]_2$, we used the cheaper brand Boka.

Instrumentation. Deuterated solvents were purchased from Cambridge Isotope Laboratories. ^{1}H NMR spectra were recorded on Bruker AVANCE III 400, 600 and INOVA instruments with 400, 300 and 600 MHz frequencies, and ^{13}C NMR spectra were recorded on Bruker AVANCE III 400 and 600 with 101 and 75 MHz frequencies. ^{19}F NMR spectra were recorded on a Bruker AVANCE III 400 spectrometer with a ^{19}F operating frequency of 376 MHz. Chemical shifts (δ) were reported in ppm relative to the residual solvent signal ($CDCl_3$ δ = 7.26 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR, CD_3OD δ = 3.31 for ^{1}H NMR and δ = 48.8 for ^{13}C NMR). Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet od triplet), td (triplet of doublets) or m (multiplet). HRMS was obtained using a Q-TOF instrument equipped with an ESI source. Data collection for crystal structure was performed at room temperature using Mo Kα radiation on a Bruker APEXII diffractometer.

2. Optimization of reaction conditions

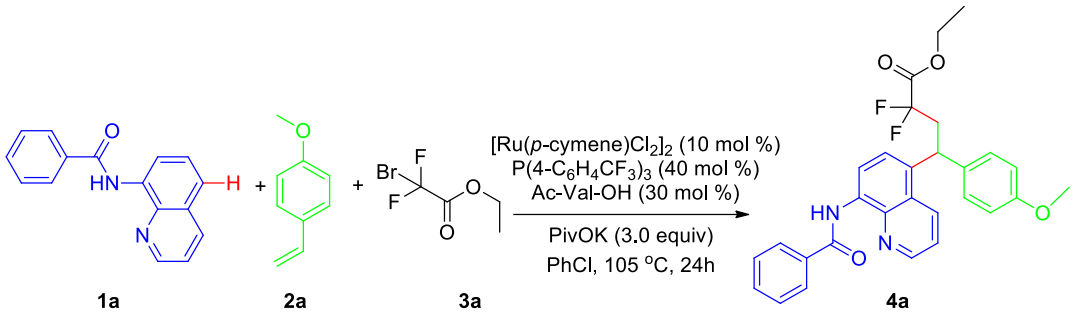


Table S1 Screening of base [a]

Entry	Ru	Ligand	Base	Solvent	Yield (%)
1	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	KOAc	DCE	20
2	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	K_2CO_3	DCE	0
3	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	t-BuOK	DCE	trace
4	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	K_3PO_4	DCE	0
5	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	DIPEA	DCE	trace
6	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PhCOONa	DCE	19
7	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	Li_2CO_3	DCE	0
8	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	NaOAc	DCE	22
9	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	DCE	25
10	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	none	DCE	0

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), **3a** (0.4 mmol) [Ru(p-cymene)Cl_2]$_2$ (10 mol %), PPh_3 (40 mol %), base (0.6 mmol), DCE (1.5 mL), 105 °C, 24 h. Ar. Isolated yields are given.

Table S2 Screening of solvents [b]

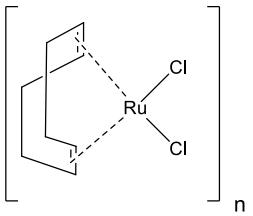
Entry	Ru	Ligand	Base	Solvent	Yield (%)
1	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	DCE	25
2	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	Dioxane	21
3	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	Toluene	37
4	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	MeCN	0
5	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	DME	0
6	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	DMF	0
7	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	THF	33
8	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	HFIP	0
9	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	PhCl	48

[b] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), **3a** (0.4 mmol) [Ru(p-cymene)Cl_2]$_2$ (10 mol %), PPh_3 (40 mol %), PivOK (0.6 mmol), solvent (1.5 mL), 105 °C, 24 h. Ar. Isolated yields are given.

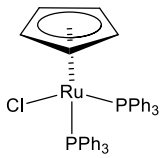
Table S3 Screening of catalysts [c]

Entry	Ru	Ligand	Base	Solvent	Yield (%)
1	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	PhCl	48
2	Ru(PPh_3)$_3Cl_2$	PPh_3	PivOK	PhCl	<10
3	Ru(cod)Cl_2	PPh_3	PivOK	PhCl	0
4	CpRu(PPh_3)Cl	PPh_3	PivOK	PhCl	0
5	[Ru(p-cymene)Cl_2]$_2$ [d]	PPh_3	PivOK	PhCl	16
6	[Ru(p-cymene)Cl_2]$_2$ [e]	PPh_3	PivOK	PhCl	<10
7	$FeCl_3$	PPh_3	PivOK	PhCl	0
8	Cu(OTf)$_2$	PPh_3	PivOK	PhCl	0
9	Cu(OAc)$_2$	PPh_3	PivOK	PhCl	0
10	CuTc	PPh_3	PivOK	PhCl	0
11	CuI	PPh_3	PivOK	PhCl	0
12	[Rh(Cp*)Cl_2]$_2$	PPh_3	PivOK	PhCl	0
13	[Rh(OAc)$_2$]$_2$	PPh_3	PivOK	PhCl	0
14	Rh(COD)$_2BF_4$	PPh_3	PivOK	PhCl	0
15	$NiBr_2$ • DME	PPh_3	PivOK	PhCl	0
16	$NiCl_2$ • DME	PPh_3	PivOK	PhCl	0
17	$NiCl_2$	PPh_3	PivOK	PhCl	0
18	Ni(OTf)$_2$	PPh_3	PivOK	PhCl	0
19	$CoBr_2$	PPh_3	PivOK	PhCl	0
20	Co(acac)$_2$	PPh_3	PivOK	PhCl	0
21	Co(PPh_3)$_3$Cl	PPh_3	PivOK	PhCl	trace
22	Cp*Co(CO)I_2	PPh_3	PivOK	PhCl	trace
23	Co(OAc)$_2$	PPh_3	PivOK	PhCl	0
24	none	PPh_3	PivOK	PhCl	0

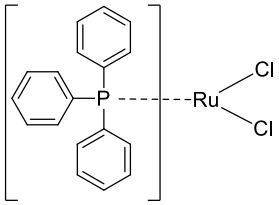
[c]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), **3a** (0.4 mmol) catalyst (10 mol %), PPH_3 (40 mol %), PivOK (0.6 mmol), PhCl (1.5 mL), 105 °C, 24 h. Ar. Isolated yields are given. [d]catalyst (7.5 mol %). [e]catalyst (5 mol %)



Ru(cod)Cl_2



CpRu(PPh_3)Cl



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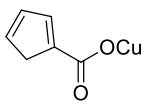

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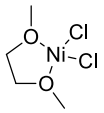
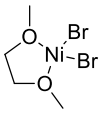


$NiCl_2$•DME

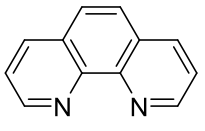


$NiBrBr_2$•DME

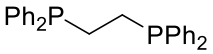
Table S4 Screening of ligands and additive [f]

Entry	Ru	Ligand/Additive	Base	Solvent	Yield (%)
1	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3	PivOK	PhCl	48
2	[Ru(*p*-cymene)Cl_2]$_2$	Phen	PivOK	PhCl	0
3	[Ru(*p*-cymene)Cl_2]$_2$	Dppe	PivOK	PhCl	0
4	[Ru(*p*-cymene)Cl_2]$_2$	Dcyphos	PivOK	PhCl	0
5	[Ru(*p*-cymene)Cl_2]$_2$	Ruphos	PivOK	PhCl	0
6	[Ru(*p*-cymene)Cl_2]$_2$	Pcy_3	PivOK	PhCl	0
7	[Ru(*p*-cymene)Cl_2]$_2$	TFP	PivOK	PhCl	43
8	[Ru(*p*-cymene)Cl_2]$_2$	P(4-C_6H_4OMe)$_3$	PivOK	PhCl	44
9	[Ru(*p*-cymene)Cl_2]$_2$	P(4-$C_6H_4CF_3$)$_3$	PivOK	PhCl	53
10	[Ru(*p*-cymene)Cl_2]$_2$	P(4-$C_6H_4CF_3$)$_3$/Ac-Val-OH	PivOK	PhCl	60
11	[Ru(*p*-cymene)Cl_2]$_2$	none	PivOK	PhCl	21

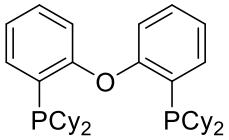
[f]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), **3a** (0.4 mmol) [Ru(p-cymene)Cl_2]$_2$ (10 mol %), ligand (40 mol %), additive (30 mol %, if have), PivOK (0.6 mmol), PhCl (1.5 mL), 105 °C, 24 h. Ar. Isolated yields are given.



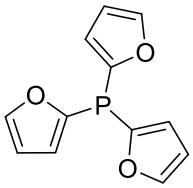
Phen



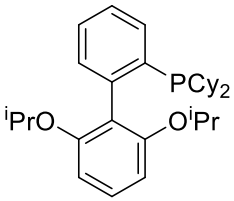
Dppe



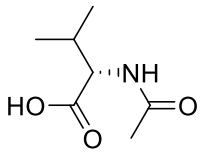
Dcyphos



TFP

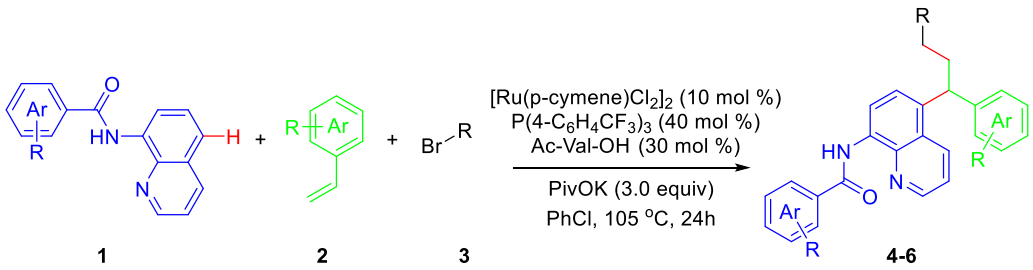


Ruphos



Ac-Val-OH

3. General Procedure

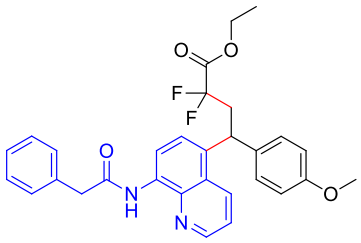


In an oven-dried 10 ml tube, starting amide **1** (0.2 mmol), PivOK (0.6 mmol, 84 mg), $[Ru(p\text{-cymene})Cl_2]_2$ (10 mol%, 12.2 mg), $P(4\text{-}C_6H_4CF_3)_3$ (40 mol%, 37.2 mg), Ac-Val-OH (30 mol%, 9.5mg) were added and charged with argon more than three times (The tube was sealed with tipping plug). PhCl (1.5 mL), olefin **2** (0.4 mmol) and alkyl bromides **3** (0.4mmol) was injected into the tube. It is worth noting that if the olefin is solid, it was added with other solids. The resulting suspension was stirred vigorously at 105 ℃ for 24 h. After the reaction was completed, the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel or preparative TLC (Petroleum ether/EtOAc = 10:1 - 5:1).

4. General Procedure for the Preparation of Starting amides[1]

All aromatic amides bearing an 8-aminoquinoline moiety were prepared by reacting the corresponding acid or the corresponding acid chlorides with 8-aminoquinoline.

5. Less successful and Unsuccessful Substrates



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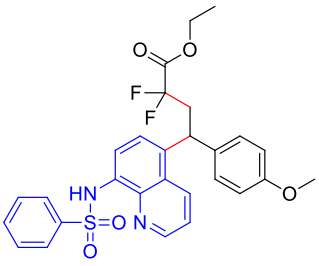

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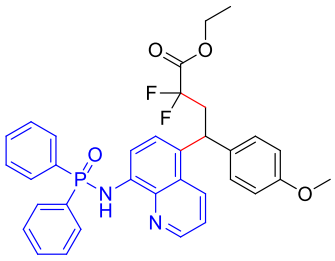

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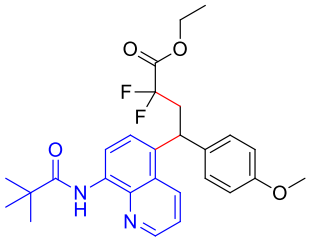

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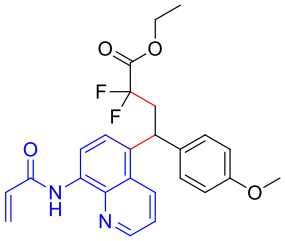

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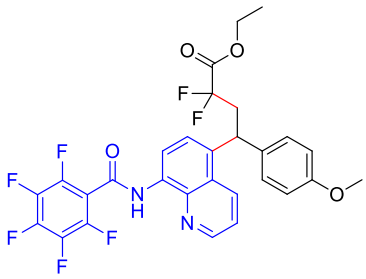

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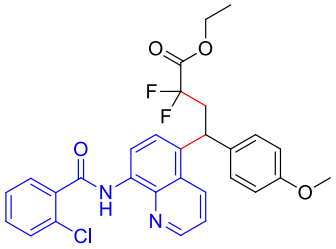

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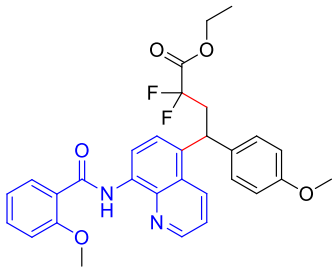

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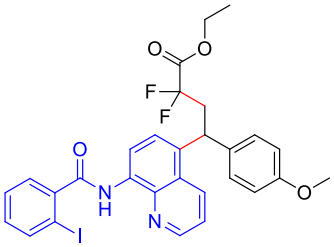

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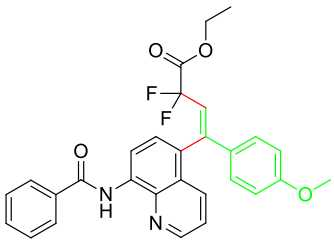

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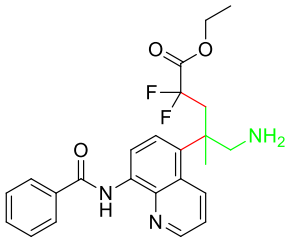

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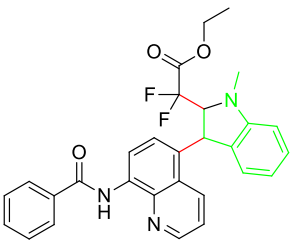

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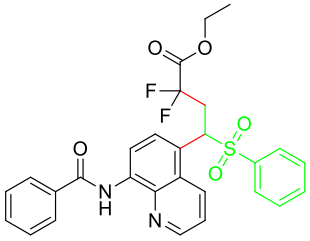

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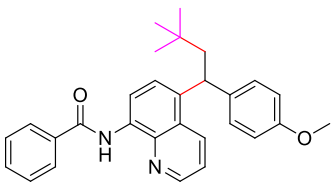

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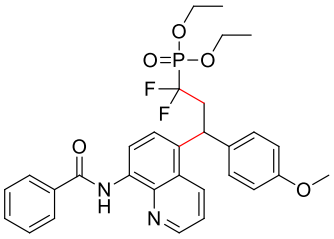

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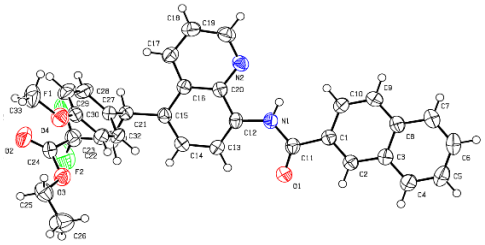
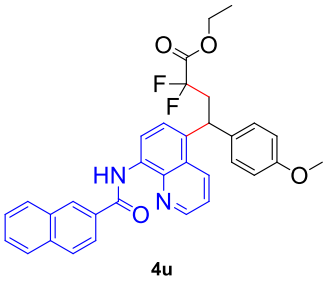
6. X-ray Single Crystal Diffraction Data of 4u





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Cell:	a=26.9151(4)	b=13.9396(2)	c=7.31714(13)
	alpha=90	beta=90	gamma=90
Temperature:	293 K		

	Calculated	Reported
Volume	2745.29(7)	2745.29(8)
Space group	P c a 21	P c a 21
Hall group	P 2c -2ac	P 2c -2ac
Moiety formula	C33 H28 F2 N2 O4	C33 H28 F2 N2 O4
Sum formula	C33 H28 F2 N2 O4	C33 H28 F2 N2 O4
Mr	554.57	554.57
Dx,g cm^{-3}	1.342	1.342
Z	4	4
Mu (mm-1)	0.808	0.808
F000	1160.0	1160.0
F000’	1163.84	
h,k,lmax	32, 16, 8	32, 16, 8
Nref	5171 [2806]	4341
Tmin,Tmax	0.934, 0.968	0.165, 1.000
Tmin’	0.893	

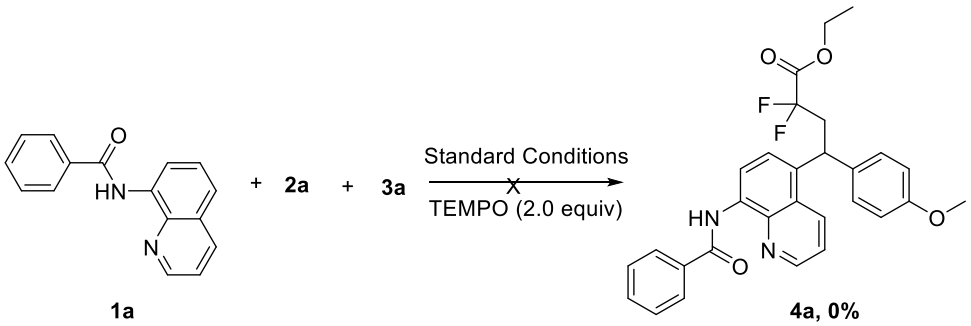
Correction method= # Reported T Limits: Tmin=0.165 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.55 / 0.84	Theta(max)= 69.756
R(reflections)= 0.0337 (4063)	wR2(reflections)= 0.0864 (4341)
S = 1.066	Npar= 373

Thermal ellipsoids are shown at 30% probability

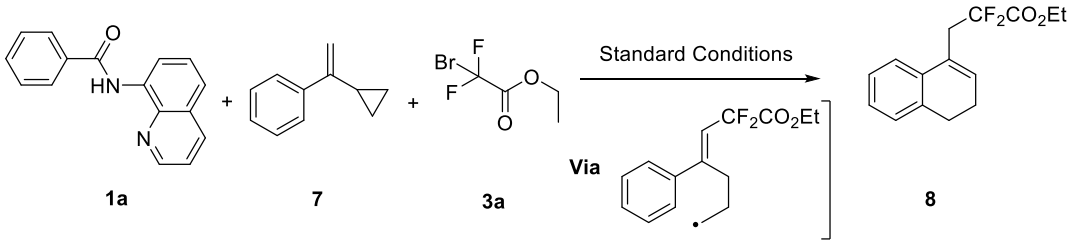
7. Preliminary Mechanism Research and Hydrolysis experiment

a) Radical scavenger



In an oven-dried 10 ml tube, starting amide **1a** (0.2 mmol), PivOK (0.6 mmol, 84 mg), $[Ru(p\text{-cymene})Cl_2]_2$ (10 mol%, 12.2 mg), $P(4\text{-}C_6H_4CF_3)_3$ (40 mol%, 37.2 mg), Ac-Val-OH (30 mol%, 9.5mg) and TEMPO (63mg, 0.4 mmol) were added and charged with argon more than three times (The tube was sealed with tipping plug). PhCl (1.5 mL), olefin **2a** (0.4 mmol) and alkyl bromides **3a** (0.4 mmol) was injected into the tube. The resulting suspension was stirred vigorously at 105 ℃ for 24 h. After the reaction was completed, the TLC was employed to observe the result, no desired product had been observed.

b) Radical clock experimenter



In an oven-dried 10 ml tube, starting amide **1a** (0.2 mmol), PivOK (0.6 mmol, 84 mg), $[Ru(p\text{-cymene})Cl_2]_2$ (10 mol%, 12.2 mg), $P(4\text{-}C_6H_4CF_3)_3$ (40 mol%, 37.2 mg), Ac-Val-OH (30 mol%, 9.5mg) were added and charged with argon more than three times (The tube was sealed with tipping plug). PhCl (1.5 mL), **7** (0.4 mmol) and alkyl bromides **3a** (0.4mmol) was injected into the tube. The resulting suspension was stirred vigorously at 105 ℃ for 24 h. After the reaction was completed, the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel to give the product **8** (14 mg, 26%) as a colorless oil.

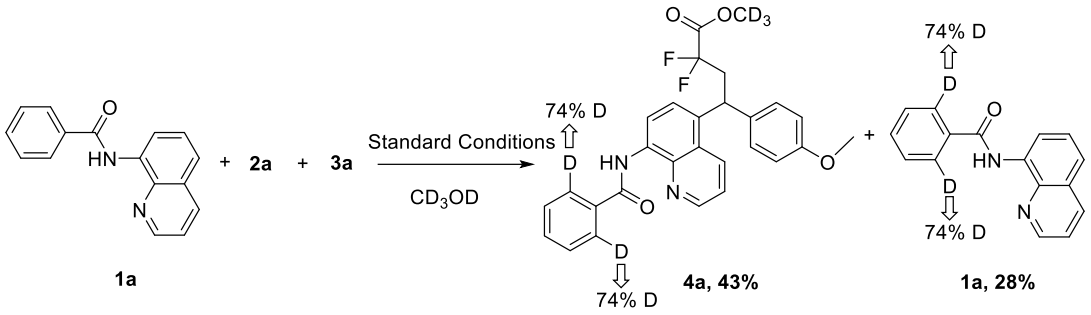
^{1}H NMR (400 MHz, Chloroform-d) δ 7.24 – 7.10 (m, 4H), 6.08 (t, J = 4.6 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.24 (t, J = 15.9 Hz, 2H), 2.74 (t, J = 8.0 Hz, 2H), 2.28 (td, J = 8.0, 4.7 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.2, 136.3, 133.9, 131.7, 127.6, 127.3, 127.2, 126.3, 122.8, 115.5, 62.7, 37.3 (t, *J* = 24.1 Hz), 28.0, 23.2, 13.8.

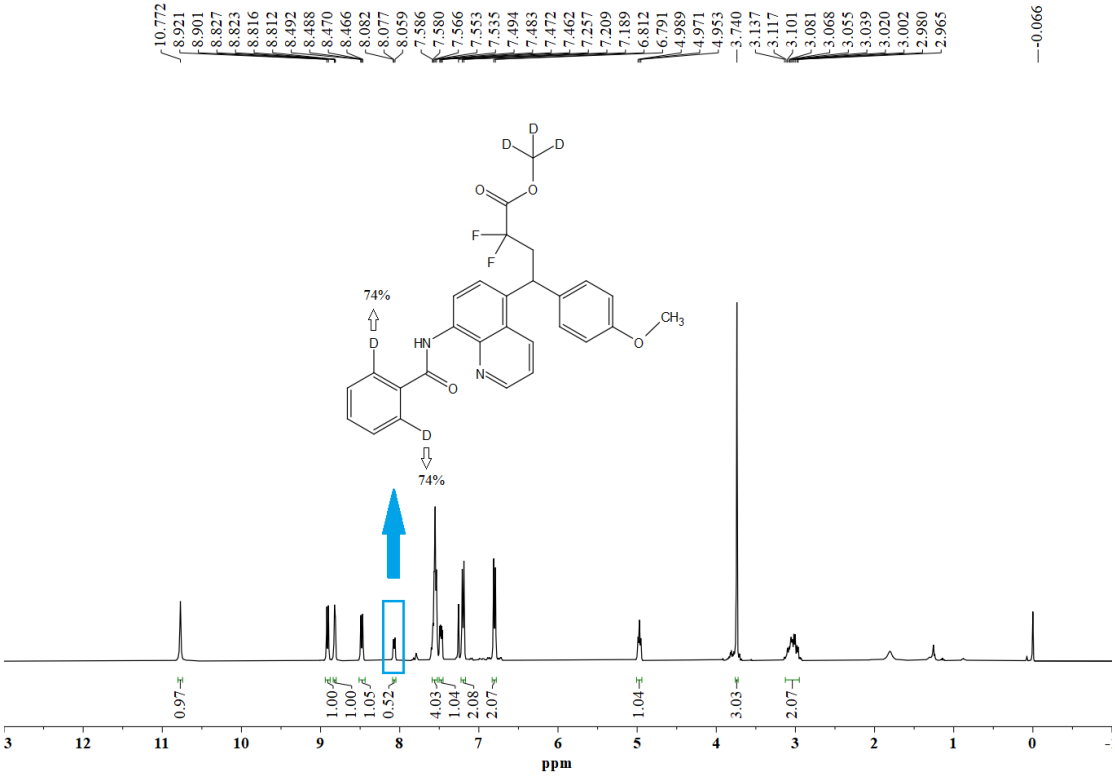
^{19}F NMR (376 MHz, Chloroform-*d*) δ -103.3.

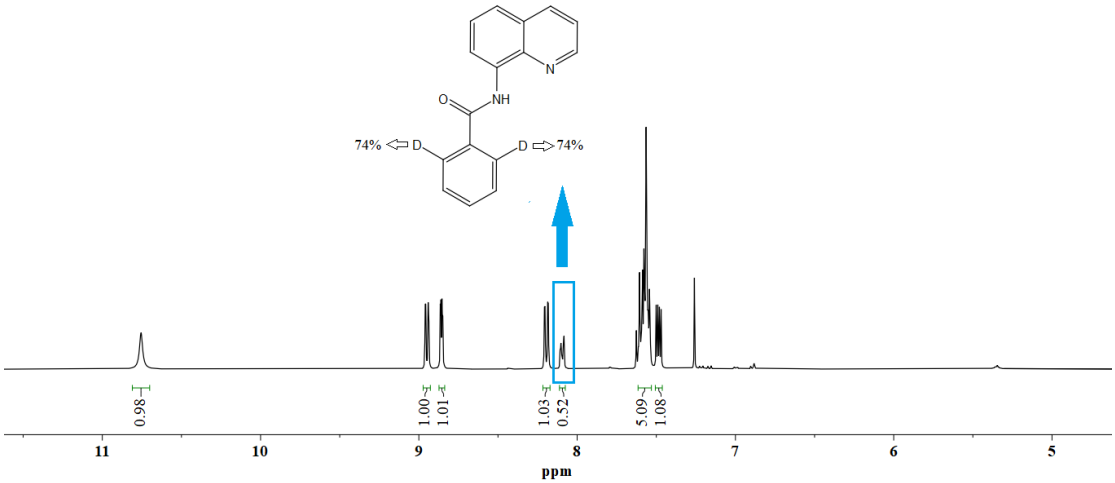
Spectra data was consist with the literature.[2]

c) H/D-Exchange study

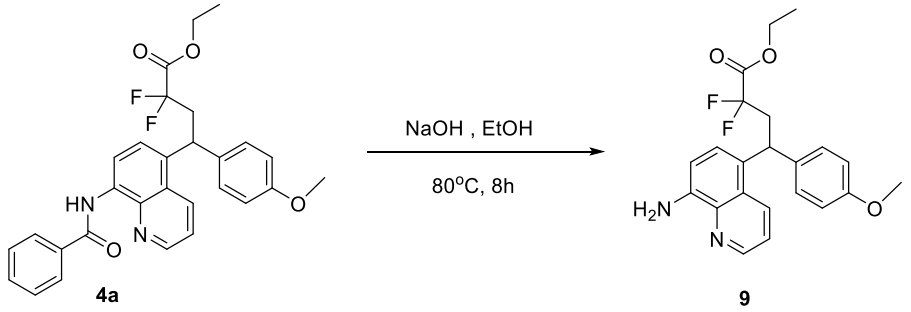


In an oven-dried 10 ml tube, starting amide **1a** (0.1 mmol), PivOK (0.3 mmol, 42 mg), $[Ru(p\text{-cymene})Cl_2]_2$ (10 mol%, 6.1 mg), $P(4\text{-}C_6H_4CF_3)_3$ (40 mol%, 18.6 mg), Ac-Val-OH (30 mol%, 4.8mg) were added and charged with argon more than three times (The tube was sealed with tipping plug). PhCl (0.6 mL), olefin **2a** (0.2 mmol), alkyl bromides **3a** (0.2 mmol) and CD_3OD (0.2 ml) was injected into the tube. The resulting suspension was stirred vigorously at 105 ℃ for 24 h. After the reaction was completed, the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel to give the product [Dn]-1a (7 mg, 28%) and [Dn]-4a (22 mg, 43%).





d) Hydrolysis experiment[3]



In an oven-dried 50 ml flask, **4a** (0.3 mmol, 150 mg) and NaOH (430 mg) were added and charged with argon more than three times. Then EtOH (4 mL) was added with a syringe. The reaction mixture was allowed to stir at 80 ℃ for 8 h. After completion of the reaction (TLC monitored), the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel to give the product **9** (81 mg, 68%) as a yellow solid.

^{1}H NMR (400 MHz, Methanol-d_4) δ 8.63 (dd, J = 4.2, 1.5 Hz, 1H), 8.50 (d, J = 10.3 Hz, 1H), 7.46 – 7.43 (m, 1H), 7.39 (dd, J = 8.6, 4.2 Hz, 1H), 7.19 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.0 Hz, 1H), 6.74 (d, J = 8.8 Hz, 2H), 4.94 (t, J = 6.9 Hz, 1H), 3.66 (s, 3H), 3.35 – 3.19 (m, 2H), 2.98 – 2.86 (m, 2H), 1.33 (t, J = 7.2 Hz, 3H).

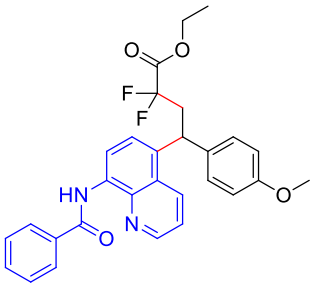
^{13}C NMR (101 MHz, Methanol-d_4) δ 159.4, 147.4, 142.9, 139.5, 137.3, 129.8, 129.1, 127.9, 127.1, 127.0, 122.1, 118.0, 114.6, 107.9, 55.4, 41.7 (t, J = 22.9 Hz), 39.8, 39.5, 14.2.

^{19}F NMR (376 MHz, Methanol-d_4) δ -103.2 – -105.0 (m).

8. References

1. (a)Y. Aihara and N. Chatani, *J. Am. Chem. Soc.*, 2013, **135**, 5308-5311; (b)C. Chen, R. Zeng, J. Zhang and Y. Zhao, *Eur. J. Org. Chem.*, 2017, **2017**, 6947-6950; (c)T. Kubo and N. Chatani, *Org. Lett.*, 2016, **18**, 1698-1701.
2. X. Nie, C. Cheng and G. Zhu, *Angew. Chem. Int. Ed.*, 2017, **56**, 1898-1902.
3. H. Sahoo, I. Ramakrishna and M. Baidya, *ChemistrySelect*, 2016, **1**, 1949-1953.

9. Characterization Data



Ethyl 4-(8-benzamidoquinolin-5-yl)-2, 2-difluoro-4-(4-methoxyphenyl)butanoate (**4a**)

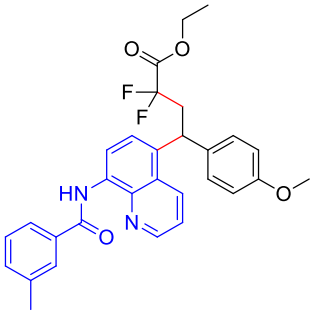
Yellow oil, 60% (60.1mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.91 (d, *J* = 8.1 Hz, 1H), 8.82 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.48 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 6.6 Hz, 2H), 7.59 – 7.53 (m, 4H), 7.48 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.98 (t, *J* = 7.2 Hz, 1H), 3.96 – 3.79 (m, 2H), 3.74 (s, 3H), 3.14 – 2.93 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.7 (t, *J* = 32.5 Hz), 158.4, 147.9, 139.2, 135.1, 134.1, 133.8, 133.0, 132.4, 131.9, 129.0, 128.8, 127.3, 126.1, 125.3, 121.8, 116.3, 115.9, 115.7 (t, *J* = 251.6 Hz), 114, 62.9, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.6 Hz), 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.3 – -105.7 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{27}F_2N_2O_4$ 505.1933; Found 505.1933.



Ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(8-(3-methylbenzamido)quinolin-5-yl)butanoate (**4b**)

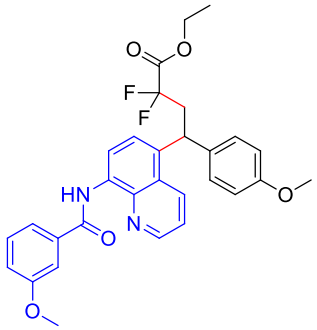
Yellow oil, 58% (60.1mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.74 (s, 1H), 8.91 (d, *J* = 8.1 Hz, 1H), 8.82 (d, *J* = 2.9 Hz, 1H), 8.48 (d, *J* = 8.6 Hz, 1H), 7.90 – 7.82 (m, 2H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.47 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.45 – 7.36 (m, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.98 (t, *J* = 6.8 Hz, 1H), 3.95 – 3.78 (m, 2H), 3.73 (s, 3H), 3.12 – 2.94 (m, 2H), 2.47 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.6, 163.6 (t, *J* = 32.6 Hz), 158.4, 147.8, 139.2, 138.6, 135.0, 134.1, 133.8, 132.9, 132.6, 132.3, 129.0, 128.6, 128.0, 126.0, 125.3, 124.1, 121.7, 115.8, 115.7(t, *J* = 252.0 Hz), 114.0, 62.8, 55.2, 40.6 (t, *J* = 23.2 Hz), 38.5 (t, *J* = 4.4 Hz), 21.4, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.6 – -105.2 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{29}F_2N_2O_4$ 519.2090; Found 519.2090.



Ethyl 2,2-difluoro-4-(8-(3-methoxybenzamido)quinolin-5-yl)-4-(4-methoxyphenyl)butanoate (**4c**)

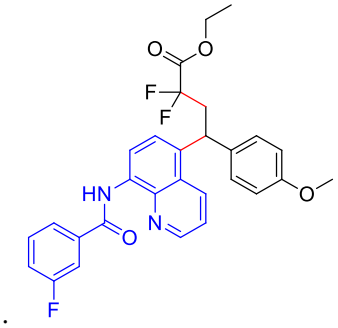
Yellow oil, 44% (46.9mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.76 (s, 1H), 8.90 (d, *J* = 8.1 Hz, 1H), 8.81 (d, *J* = 4.0 Hz, 1H), 8.48 (d, *J* = 8.5 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.50 – 7.42 (m, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.94 – 3.81 (m, 5H), 3.74 (s, 3H), 3.02 m, 2H), 1.14 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.2, 163.6 (t, *J* = 32.5 Hz), 160.0, 158.4, 147.8, 139.2, 136.6, 134.1, 133.7, 133.0, 132.3, 129.8, 129.0, 126.1, 125.3, 121.7, 119.0, 118.0, 115.8, 115.6 (t, *J* = 250.7 Hz), 114.0, 112.6, 62.8, 55.5, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.5 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.5 – -105.2 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{30}H_{29}F_2N_2O_5$ 535.2039; Found 535.2032.



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Ethyl 2,2-difluoro-4-(8-(3-fluorobenzamido)quinolin-5-yl)-4-(4-methoxyphenyl)butanoate (**4d**)

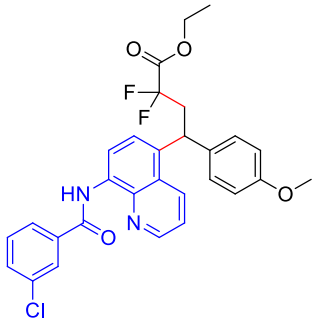
Yellow oil, 37% (39.1mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.76 (s, 1H), 8.88 (d, *J* = 8.1 Hz, 1H), 8.82 (d, *J* = 3.1 Hz, 1H), 8.49 (d, *J* = 8.4 Hz, 1H), 7.83 (s, 1H), 7.77 (d, *J* = 9.2 Hz, 1H), 7.57 – 7.47 (m, 3H), 7.31 – 7.26 (m, 1H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.98 (t, *J* = 7.0 Hz, 1H), 3.94 – 3.82 (m, 2H), 3.74 (s, 3H), 3.13 – 2.94 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.0 (d, *J* = 3.0 Hz), 163.6 (t, *J* = 32.8 Hz), 162.9(d, *J* = 248.5 Hz), 158.4, 147.9, 139.1, 137.3 (d, *J* = 6.8 Hz), 134.0, 133.4 (d, *J* = 6.6 Hz), 132.4, 130.4 (d, *J* = 7.9 Hz), 129.0, 126.1, 125.3, 122.7 (d, *J* = 3.0 Hz), 121.8, 118.9 (d, *J* = 21.3 Hz), 116.0, 115.6 (t, *J* = 252.0 Hz), 114.8, 114.5, 114.0, 62.8, 55.2, 40.6 (t, *J* = 23.2 Hz), 38.5 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -100.9 – -105.5 (m), -111.5.

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{29}H_{26}F_3N_2O_4$ 523.1839; Found 523.1839.



Ethyl 4-(8-(3-chlorobenzamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4e**)

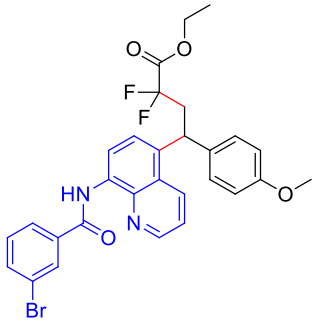
Brown oil, 61% (66.0mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.73 (s, 1H), 8.88 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.49 (d, *J* = 7.6 Hz, 1H), 8.05 (s, 1H), 7.93 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.94 – 3.82 (m, 2H), 3.74 (s, 3H), 3.11 – 2.95 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.9, 163.6 (t, *J* = 32.6 Hz), 158.4, 147.9, 139.1, 136.8, 135.0, 134.0, 133.4, 132.4, 131.8, 130.0, 128.9, 127.6, 126.0, 125.2, 125.2, 116.0, 115.6 (t, J = 252.0 Hz), 114.0, 62.8, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.6 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.1 – -105.8 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{26}ClF_2N_2O_4$ 539.1544; Found 539.1540.



Ethyl 4-(8-(3-bromobenzamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4f**)

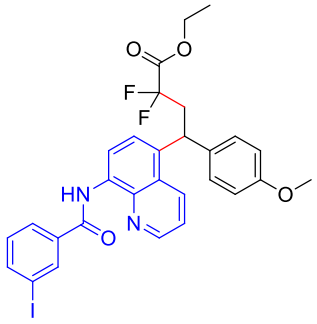
Brown oil, 53% (61.6mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.71 (s, 1H), 8.87 (d, *J* = 8.1 Hz, 1H), 8.83 (d, *J* = 4.1 Hz, 1H), 8.49 (d, *J* = 8.6 Hz, 1H), 8.20 (s, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.49 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.95 – 3.82 (m, 2H), 3.74 (s, 3H), 3.03 (m, 2H), 1.15 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.7, 163.6 (t, *J* = 32.5 Hz), 158.4, 147.9, 139.1, 137.0, 134.7, 134.0, 133.4, 133.4, 132.4, 130.6, 130.3, 128.9, 126.0, 125.6, 125.2, 123.0, 121.8, 116.0, 115.6 (t, J =252.0 Hz), 114.0, 62.8, 55.2, 40.5 (t, *J* = 23.2 Hz), 38.5 (t, *J* = 4.6 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.1 – -105.9 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{26}BrF_2N_2O_4$ 583.1039; Found 583.1036.



Ethyl 2,2-difluoro-4-(8-(3-iodobenzamido)quinolin-5-yl)-4-(4-methoxyphenyl)butanoate (**4g**)

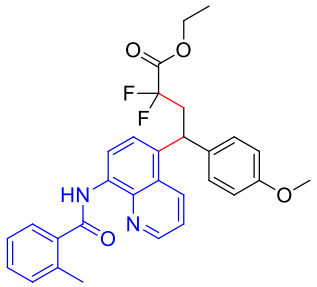
Yellow oil, 44% (55.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.69 (s, 1H), 8.87 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.49 (d, *J* = 7.4 Hz, 1H), 8.39 (t, *J* = 1.5 Hz, 1H), 8.00 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.49 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.94 – 3.82 (m, 2H), 3.74 (s, 3H), 3.10 – 2.96 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.7, 163.6 (t, *J* = 32.6 Hz), 158.4, 147.9, 140.7, 139.0, 136.9, 136.4, 133.9, 133.3, 132.3, 130.3, 128.9, 126.2, 126.0, 125.2, 121.8, 115.9, 115.6 (t, *J* = 251.5 Hz), 113.9, 94.5, 62.8, 55.2, 40.5 (t, *J* = 23.2 Hz), 38.5 (t, *J* = 4.2 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.6 – -105.2 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{26}IF_2N_2O_4$ 631.0900; Found 631.0894.



Ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(8-(2-methylbenzamido)quinolin-5-yl)butanoate (**4h**)

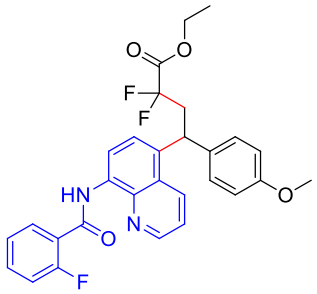
Yellow oil, 24% (23.0mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.23 (s, 1H), 8.91 (d, *J* = 8.1 Hz, 1H), 8.73 (d, *J* = 3.8 Hz, 1H), 8.47 (d, *J* = 8.6 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.45 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.40 (t, *J* = 7.0 Hz, 1H), 7.31 (t, *J* = 7.1 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.0 Hz, 1H), 3.96 – 3.84 (m, 2H), 3.74 (s, 3H), 3.11 – 2.95 (m, 2H), 2.59 (s, 3H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.1, 163.7 (t, *J* = 32.6 Hz), 158.4, 147.8, 139.1, 136.6, 136.6, 134.1, 133.9, 133.1, 132.3, 131.3, 130.3, 129.0, 127.2, 126.1, 126.0, 125.3, 121.7, 115.8, 115.6 (t, *J* = 251.2 Hz), 114.0, 62.8, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.4 Hz), 20.2, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.5 – -105.4 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{29}F_2N_2O_4$ 519.2090; Found 519.2094.



Ethyl 2,2-difluoro-4-(8-(2-fluorobenzamido)quinolin-5-yl)-4-(4-methoxyphenyl)butanoate (**4i**)

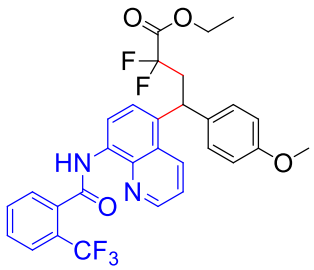
Yellow oil, 41% (42.1mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.18 (d, *J* = 12.2 Hz, 1H), 8.95 (d, *J* = 8.1 Hz, 1H), 8.84 (d, *J* = 5.6 Hz, 1H), 8.47 (d, *J* = 8.7 Hz, 1H), 8.21 (t, *J* = 8.7 Hz, 1H), 7.54 (dd, *J* = 8.2, 5.5 Hz, 2H), 7.47 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.23 (m, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.93 – 3.81 (m, 2H), 3.74 (s, 3H), 3.03 (m, 2H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.6 (t, *J* = 32.5 Hz), 161.5 (d, *J* = 3.2 Hz), 160.5 (d, *J* = 250.5Hz), 158.3, 148.0, 139.1, 133.9, 133.6, 133.5, 133.3, 132.2, 131.9 (d, *J* = 1.7 Hz), 129.0, 126.0, 125.1, 124.8 (d, *J* = 3.3 Hz), 121.9 (d, *J* = 11.6 Hz), 121.7, 116.5, 116.3 (d, *J* = 24.5 Hz), 115.6 (t, *J* = 252.0 Hz), 113.9, 62.8, 55.2, 40.5 (t, *J* = 23.2 Hz), 38.5 (t, *J* = 4.6 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.3 – -105.2 (m), -112.2.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{26}F_3N_2O_4$ 523.1839; Found 523.1833.



ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(8-(2-(trifluoromethyl)benzamido)quinolin-5-yl)butanoate (**4j**)

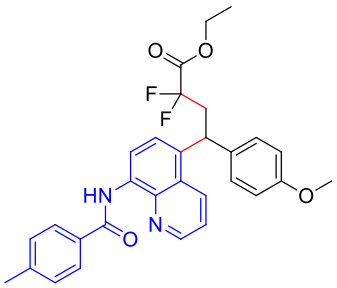
Yellow oil, 25% (28.7mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.18 (s, 1H), 8.89 (d, *J* = 8.1 Hz, 1H), 8.72 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.48 (dd, *J* = 8.7, 1.3 Hz, 1H), 7.79 (d, *J* = 6.6 Hz, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.45 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.94 – 3.83 (m, 2H), 3.74 (s, 3H), 3.11 – 2.96 (m, 2H), 1.14 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.8, 163.7 (t, *J* = 32.6 Hz), 158.5, 147.9, 138.9, 134.0, 133.7, 133.5, 132.5 (d, *J* = 10.4 Hz), 132.3, 132.2, 130.1, 128.9, 128.5, 127.6 (d, *J* = 32.1 Hz), 126.6 (q, *J* = 4.9 Hz), 126.0, 125.3, 123.6 (q, *J* = 273.7 Hz), 121.8, 116.2, 115.6 (t, *J* = 251.0 Hz), 114.0, 62.9, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.9, -101.6 – -105.2 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for 573.1807; Found 573.1821(2.4ppm<5ppm).



Ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(8-(4-methylbenzamido)quinolin-5-yl)butanoate (**4k**)

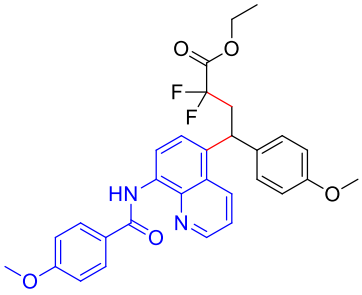
Yellow oil, 61% (52.4mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.75 (s, 1H), 8.91 (d, *J* = 8.1 Hz, 1H), 8.81 (d, *J* = 4.0 Hz, 1H), 8.47 (d, *J* = 8.5 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.46 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.97 (t, *J* = 7.0 Hz, 1H), 3.94 – 3.79 (m, 2H), 3.73 (s, 3H), 3.10 – 2.93 (m, 2H), 2.44 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.6 (t, *J* = 32.7 Hz), 158.4, 147.8, 142.3, 139.2, 134.1, 133.9, 132.8, 132.3, 132.2, 129.4, 129.0, 127.2, 126.0, 125.3, 121.7, 115.7, 115.6 (t, *J* = 252.0 Hz), 114.0, 62.8, 55.2, 40.6 (t, *J* = 23.0 Hz), 38.5 (t, *J* = 4.4 Hz), 21.5, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.5 – -105.1 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{29}F_2N_2O_4$ 519.2090; Found 519.2089.



Ethyl 2,2-difluoro-4-(8-(4-methoxybenzamido)quinolin-5-yl)-4-(4-methoxyphenyl)butanoate (**4l**)

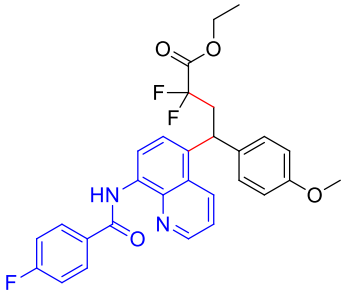
Yellow oil, 62% (66.3mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.71 (s, 1H), 8.89 (d, *J* = 8.1 Hz, 1H), 8.81 (d, *J* = 4.0 Hz, 1H), 8.47 (d, *J* = 8.6 Hz, 1H), 8.04 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.47 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.08 – 7.00 (m, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 4.97 (t, *J* = 7.2 Hz, 1H), 3.95 – 3.75 (m, 5H), 3.74 (s, 3H), 3.11 – 2.95 (m, 2H), 1.14 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.9, 163.7 (t, *J* = 32.6 Hz), 162.5, 158.4, 147.8, 139.2, 134.2, 134.0, 132.7, 132.4, 129.2, 129.0, 127.4, 126.1, 125.4, 121.7, 115.7(t, *J* = 251.4 Hz), 115.7, 114.0, 62.9, 55.5, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.5 Hz), 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.3 – -105.2 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{29}F_2N_2O_5$ 535.2039; Found 535.2039.



Ethyl 2,2-difluoro-4-(8-(4-fluorobenzamido)quinolin-5-yl)-4-(4-methoxyphenyl)butanoate (**4m**)

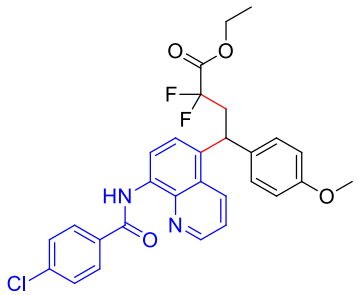
Yellow oil, 59% (61.1mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.73 (s, 1H), 8.88 (d, *J* = 8.1 Hz, 1H), 8.82 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.49 (d, *J* = 8.6 Hz, 1H), 8.08 (dd, *J* = 8.7, 5.3 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.49 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.25 – 7.19 (m, 4H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.96 – 3.78 (m, 2H), 3.74 (s, 3H), 3.12 – 2.93 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.0 (d, *J* = 253.5 Hz), 164.3, 163.7 (t, *J* = 32.7 Hz), 158.5, 147.9, 139.2, 134.1, 133.6, 133.2, 132.4, 131.3 (d, *J* = 3.0 Hz), 129.7 (d, *J* = 9.0 Hz), 129.0, 126.1, 125.3, 121.8, 116.0, 115.8 (d, *J* = 9.7 Hz), 115.7 (t, *J* = 251.5 Hz) 114.0, 62.9, 55.2, 40.6 (t, *J* = 23.2 Hz), 38.5 (t, *J* = 4.5 Hz), 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.4 – -105.3 (m), -107.6.

HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{29}H_{26}F_3N_2O_4$ 523.1839; Found 523.1839.



Ethyl 4-(8-(4-chlorobenzamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4n**)

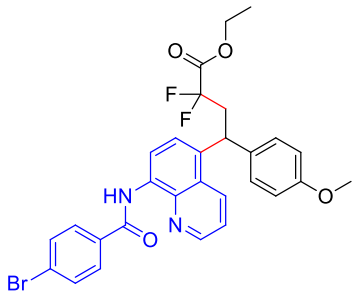
Yellow solid, 49% (52.4mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.75 (s, 1H), 8.88 (d, *J* = 8.1 Hz, 1H), 8.81 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.49 (d, *J* = 8.7 Hz, 1H), 8.00 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.54 – 7.44 (m, 3H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 4.98 (t, *J* = 7.2 Hz, 1H), 3.95 – 3.79 (m, 2H), 3.74 (s, 3H), 3.13 – 2.94 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.2, 163.6 (t, *J* = 32.6 Hz), 158.3, 147.8, 139.0, 138.1, 133.9, 133.4, 133.3, 133.2, 132.4, 129.0, 129.0, 128.6, 126.0, 125.1, 121.8, 115.8, 115.6 (t, *J* = 250.7 Hz), 113.9, 62.8, 55.2, 40.5 (t, *J* = 23.1 Hz), 38.4 (t, *J* = 4.3 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.5 – -105.3 (m).

HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{29}H_{26}ClF_2N_2O_4$ 539.1544; Found 539.1538.



Ethyl 4-(8-(4-bromobenzamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4o**)

Yellow oil, 54% (62.3mg).

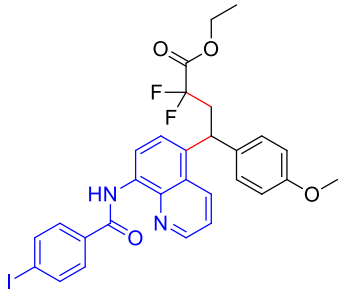
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.73 (s, 1H), 8.87 (d, *J* = 8.1 Hz, 1H), 8.81 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.48 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.1

Hz, 1H), 7.47 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.97 – 3.80 (m, 2H), 3.73 (s, 3H), 3.10 – 2.96 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.3, 163.6 (t, *J* = 32.5 Hz), 158.4, 147.9, 139.1, 134.0, 133.9, 133.5, 133.3, 132.4, 132.0, 129.0, 128.8, 126.6, 126.1, 125.3, 121.8, 115.9, 115.6 (t, *J* = 251.5 Hz), 114.0, 62.8, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -100.8 – -105.7 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{26}BrF_2N_2O_4$ 583.1039; Found 583.1040.



Ethyl 2,2-difluoro-4-(8-(4-iodobenzamido)quinolin-5-yl)-4-(4-methoxyphenyl)butanoate (**4p**)

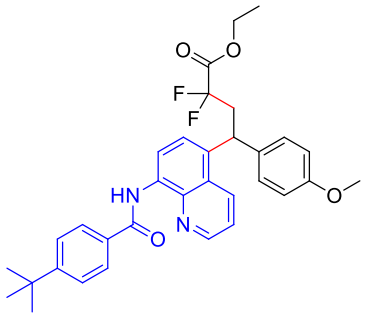
Yellow oil, 53% (66.4mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.73 (s, 1H), 8.87 (d, *J* = 8.1 Hz, 1H), 8.80 (d, *J* = 3.9 Hz, 1H), 8.48 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.47 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.98 (t, *J* = 7.0 Hz, 1H), 3.96 – 3.80 (m, 2H), 3.73 (s, 3H), 3.11 – 2.93 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 164.5, 163.6 (t, *J* = 32.5 Hz), 158.4, 147.9, 139.1, 138.0, 134.5, 134.0, 133.5, 133.3, 132.4, 129.0, 128.8, 126.1, 125.3, 121.8, 115.9, 115.6 (t, *J* = 250.9 Hz), 114.0, 98.9, 62.8, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.6 – -105.2 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{26}IF_2N_2O_4$ 631.0900; Found 631.0908.



Ethyl 4-(8-(4-(tert-butyl)benzamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4q**)

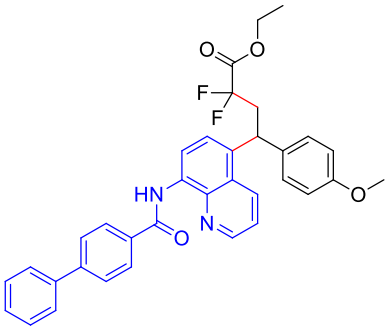
Yellow oil, 54% (60.8mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.75 (s, 1H), 8.91 (d, *J* = 8.1 Hz, 1H), 8.81 (d, *J* = 4.1 Hz, 1H), 8.47 (d, *J* = 8.7 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 2H), 7.56 (dd, *J* = 8.2, 6.7 Hz, 3H), 7.47 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.97 (t, *J* = 7.1 Hz, 1H), 3.93 – 3.81 (m, 2H), 3.74 (s, 3H), 3.09 – 2.96 (m, 2H), 1.38 (s, 9H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.6 (t, *J* = 32.6 Hz), 158.3, 155.3, 147.7, 139.1, 134.0, 133.8, 132.7, 132.3, 132.2, 128.9, 127.1, 126.0, 125.7, 125.2, 121.7, 115.7, 115.6 (t, *J* = 250.7 Hz), 113.9, 62.8, 55.2, 40.5 (t, *J* = 23.2 Hz), 38.4 (t, *J* = 4.5 Hz), 35.0, 31.1, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.6 – -105.1 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{33}H_{35}F_2N_2O_4$ 561.2559; Found 561.2554.



Ethyl 4-(8-([1,1'-biphenyl]-4-ylcarboxamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4r**)

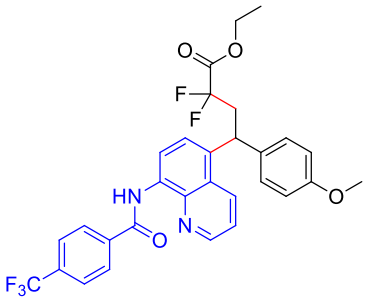
Yellow solid, 52% (60.5mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.82 (s, 1H), 8.93 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.48 (d, *J* = 7.6 Hz, 1H), 8.14 (d, *J* = 8.3 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.65 (d, *J* = 7.3 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.50 – 7.45 (m, 3H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.99 (t, *J* = 7.1 Hz, 1H), 3.94 – 3.82 (m, 2H), 3.74 (s, 3H), 3.11 – 2.97 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.0, 163.6 (t, *J* = 32.5 Hz), 158.3, 147.8, 144.5, 139.9, 139.1, 133.9, 133.7, 133.6, 132.9, 132.3, 129.0, 128.9, 128.0, 127.7, 127.4, 127.2, 126.0, 125.2, 121.7, 115.7, 115.6 (t, *J* = 251.5 Hz), 113.9, 62.8, 55.1, 40.5 (t, *J* = 23.2 Hz), 38.4 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.0 – -105.9 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{35}H_{31}F_2N_2O_4$ 581.2246; Found 581.2246.



Ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(8-(4-(trifluoromethyl)benzamido)quinolin-5-yl)butanoate (**4s**)

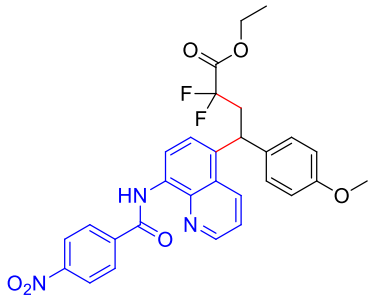
Yellow oil, 63% (72.0mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.81 (s, 1H), 8.89 (d, *J* = 8.1 Hz, 1H), 8.82 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.50 (dd, *J* = 8.7, 1.3 Hz, 1H), 8.17 (d, *J* = 8.1 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.49 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.99 (t, *J* = 7.1 Hz, 1H), 3.95 – 3.84 (m, 2H), 3.74 (s, 3H), 3.10 – 2.96 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.0, 163.6 (t, J = 32.3 Hz), 158.5, 148.0, 139.1, 138.3, 134.0, 133.6, 133.3, 132.5, 130.6, 129.0, 127.7, 126.1, 125.8 (q, *J* = 3.7 Hz), 125.3, 123.7 (q, *J* = 273.7 Hz), 121.8, 116.0, 115.6 (t, J = 251.5 Hz), 114.0, 113.0, 62.8, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, J = 4.0 Hz,), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.9, -100.1 – -106.3 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{26}F_5N_2O_4$ 573.1807; Found 573.1800.



Ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(8-(4-nitrobenzamido)quinolin-5-yl)butanoate (**4t**)

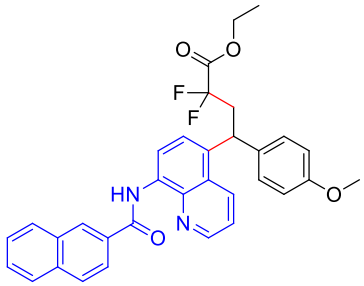
Yellow solid, 43% (46.6mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.85 (s, 1H), 8.88 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.51 (dd, *J* = 8.7, 1.4 Hz, 1H), 8.39 (d, *J* = 8.8 Hz, 2H), 8.22 (d, *J* = 8.9 Hz, 2H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.51 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 5.00 (t, *J* = 7.1 Hz, 1H), 3.96 – 3.84 (m, 2H), 3.74 (s, 3H), 3.11 – 2.96 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.6 (t, *J* = 32.4 Hz), 163.1, 158.5, 149.8, 148.0, 140.5, 139.1, 134.0, 133.9, 133.0, 132.5, 129.0, 128.4, 126.1, 125.2, 124.0, 121.9, 116.2, 115.6 (t, *J* = 252.0 Hz), 114.0, 62.8, 55.2, 40.5 (t, *J* = 23.0 Hz), 38.5 (t, *J* = 4.4 Hz), 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.4 – -105.4 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{29}H_{26}FN_3O_6$ 550.1784; Found 550.1788.



Ethyl 4-(8-(2-naphthamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4u**)

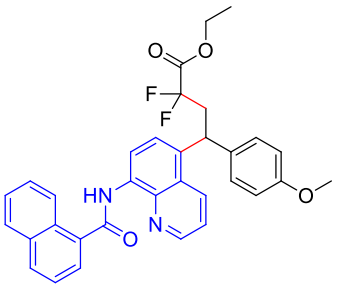
Yellow solid, 53% (59.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.92 (s, 1H), 8.97 (d, *J* = 8.1 Hz, 1H), 8.85 (d, *J* = 3.9 Hz, 1H), 8.58 (s, 1H), 8.49 (d, *J* = 8.6 Hz, 1H), 8.12 (d, *J* = 8.6 Hz, 1H), 8.01 (dd, *J* = 18.1, 8.4 Hz, 2H), 7.91 (d, *J* = 7.0 Hz, 1H), 7.58 (d, *J* = 6.7 Hz, 3H), 7.49 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.99 (t, *J* = 7.0 Hz, 1H), 3.94 – 3.81 (m, 2H), 3.74 (s, 3H), 3.12 – 2.96 (m, 2H), 1.15 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.5, 163.7 (t, *J* = 32.6 Hz), 158.5, 147.9, 139.3, 135.0, 134.1, 133.9, 133.1, 132.8, 132.4, 132.3, 129.2, 129.0, 128.7, 128.0, 127.9, 127.8, 126.8, 126.1, 125.4, 123.7, 121.8, 115.9, 115.7 (t, *J* = 251.5 Hz), 114.0, 62.9, 55.2, 40.7 (t, *J* = 22.9 Hz), 38.6 (t, *J* = 3.9 Hz), 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.5 – -105.2 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{33}H_{29}F_2N_2O_4$ 555.2090; Found 555.2088.



Ethyl 4-(8-(1-naphthamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4v**)

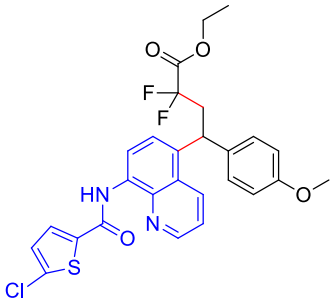
Yellow oil, 39% (43.1mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.45 (s, 1H), 9.03 (d, *J* = 8.1 Hz, 1H), 8.70 (d, *J* = 4.0 Hz, 1H), 8.49 (dd, *J* = 14.5, 8.2 Hz, 2H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.91 (t, *J* = 6.5 Hz, 2H), 7.62 – 7.54 (m, 4H), 7.44 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.00 (t, *J* = 7.1 Hz, 1H), 3.97 – 3.84 (m, 2H), 3.74 (s, 3H), 3.14 – 2.98 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.7, 163.7 (t, *J* = 32.7 Hz), 158.4, 147.9, 139.1, 134.6, 134.1, 134.0, 133.9, 133.3, 132.4, 131.2, 130.3, 129.1, 128.4, 127.4, 126.6, 126.1, 125.6, 125.5, 125.3, 124.9, 121.8, 116.0, 115.7 (t, *J* = 252.0 Hz), 114.0, 62.9, 55.3, 40.6 (t, *J* = 23.1 Hz), 38.6 (t, *J* = 4.2 Hz), 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.4 – -105.3 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{33}H_{29}F_2N_2O_4$ 555.2090; Found 555.2090.



Ethyl 4-(8-(5-chlorothiophene-2-carboxamido)quinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4w**)

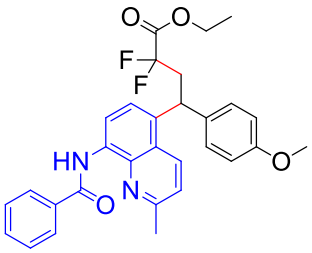
Yellow oil, 51% (55.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.53 (s, 1H), 8.80 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.75 (d, *J* = 8.1 Hz, 1H), 8.47 (dd, *J* = 8.7, 1.4 Hz, 1H), 7.58 (d, *J* = 4.0 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.47 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.98 (d, *J* = 4.0 Hz, 1H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.97 (t, *J* = 7.1 Hz, 1H), 3.94 – 3.81 (m, 2H), 3.73 (s, 3H), 3.10 – 2.94 (m, 2H), 1.14 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.6 (t, *J* = 32.5 Hz), 158.8, 158.4, 147.9, 138.8, 138.5, 136.1, 134.0, 133.3, 133.1, 132.4, 128.9, 127.6, 127.2, 126.0, 125.2, 121.8, 115.8, 115.6 (t, J = 252.0 Hz), 114.0, 62.8, 55.2, 40.5 (t, *J* = 23.2 Hz), 38.5 (t, *J* = 4.6 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.3 – -105.3 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{24}ClF_2N_2O_4S$ 545.1108; Found 545.1104.



Ethyl 4-(8-benzamido-2-methylquinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4x**)

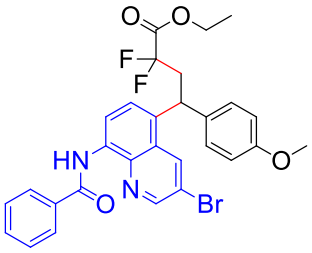
Yellow oil, 14% (14.3mg)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 10.84 (s, 1H), 8.86 (d, *J* = 8.1 Hz, 1H), 8.35 (d, *J* = 8.7 Hz, 1H), 8.07 (d, *J* = 7.1 Hz, 2H), 7.57 (m, 3H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.34 (d, *J* = 8.7 Hz, 1H), 7.19 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 4.95 (t, *J* = 7.0 Hz, 1H), 3.93 – 3.88 (m, 1H), 3.85 – 3.81 (m, 1H), 3.74 (s, 3H), 3.06 – 2.98 (m, 2H), 2.74 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.3, 163.7 (t, *J* = 32.7 Hz), 158.4, 156.8, 138.6, 135.3, 134.3, 133.1, 132.9, 132.5, 131.8, 129.0, 128.8, 127.2, 124.3, 124.2, 122.5, 115.8, 115.7 (t, *J* = 251.4Hz), 114.0, 62.8, 55.2, 40.6 (t, *J* = 23.1 Hz), 38.5 (t, *J* = 4.0 Hz), 25.2, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.8 – -105.0 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for 519.2090; Found 519.2102 (2.3ppm<5ppm).



Ethyl 4-(8-benzamido-3-bromoquinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4y**)

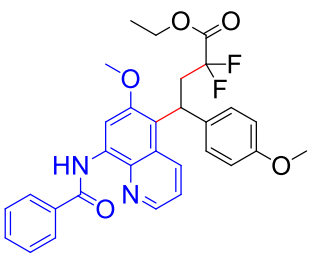
Brown oil, 21% (24.2mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.54 (s, 1H), 8.93 (d, *J* = 8.2 Hz, 1H), 8.81 (d, *J* = 2.1 Hz, 1H), 8.61 (d, *J* = 2.1 Hz, 1H), 8.04 (dd, *J* = 8.1, 1.4 Hz, 2H), 7.60 – 7.54 (m, 4H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.88 (t, *J* = 7.1 Hz, 1H), 3.97 – 3.88 (m, 2H), 3.75 (s, 3H), 3.08 – 2.94 (m, 2H), 1.18 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.6 (t, *J* = 32.4 Hz), 158.6, 148.9, 137.3, 134.9, 134.1, 134.0, 133.7, 132.3, 132.0, 128.9, 128.8, 127.2, 127.2, 126.6, 118.4, 116.3, 115.5 (t, *J* = 252.0 Hz), 114.1, 62.9, 55.2 (d, *J* = 8.0 Hz), 40.5 (t, *J* = 23.1 Hz), 38.5, 13.7 (d, *J* = 3.1 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -99.3 – -106.8 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for 583.1039; Found 583.1036.



Ethyl 4-(8-benzamido-6-methoxyquinolin-5-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate (**4z**)

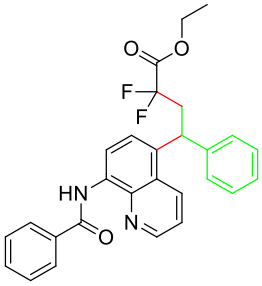
Brown oil, 68% (76.3mg)

1H NMR (400 MHz, Chloroform-d) δ 10.88 (s, 1H), 8.90 (s, 1H), 8.68 (d, J = 3.1 Hz, 1H), 8.40 (s, 1H), 8.08 (d, J = 6.7 Hz, 2H), 7.60 – 7.52 (m, 3H), 7.47 – 7.39 (m, 1H), 7.20 (d, J = 8.6 Hz, 2H), 6.78 (d, J = 8.7 Hz, 2H), 5.18 (s, 1H), 3.97 (s, 3H), 3.77 (m, 2H), 3.74 (s, 3H), 3.47 – 3.26 (m, 1H), 3.12 (qd, J = 15.0, 4.3 Hz, 1H), 1.03 (t, J = 7.1 Hz, 3H).

13C NMR (101 MHz, Chloroform-d) δ 165.4, 163.8 (t, J = 32.6 Hz), 157.8, 155.9, 145.4, 135.2, 134.8, 134.7, 134.7, 131.9, 128.8, 128.2, 127.4, 127.2, 122.1, 117.3, 116.3 (t, J = 251.5 Hz), 113.5, 104.9, 62.5, 56.3, 55.1, 37.7 (t, J = 22.6 Hz), 33.8, 13.5.

19F NMR (376 MHz, Chloroform-d) δ -105.9 (d, J = 259.9 Hz).

HRMS (ESI-TOF) m/z: [M + H]+ Calcd for 535.2039; Found 535.2055 (2.9ppm<5ppm).



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-phenylbutanoate (**5a**)

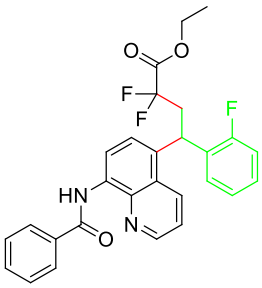
Yellow oil, 64% (60.4mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.77 (s, 1H), 8.93 (d, *J* = 8.1 Hz, 1H), 8.80 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.48 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.06 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.59 – 7.52 (m, 4H), 7.45 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.30 – 7.28 (m, 2H), 7.27 – 7.23 (m, 2H), 7.19 – 7.15 (m, 1H), 5.03 (t, *J* = 7.1 Hz, 1H), 3.91 – 3.78 (m, 2H), 3.15 – 2.97 (m, 2H), 1.12 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.6 (t, *J* = 32.6 Hz), 147.8, 142.1, 135.0, 133.8, 132.6, 132.3, 131.8, 128.7, 128.7, 128.6, 127.9, 127.2, 126.9, 126.1, 125.5, 121.7, 115.8, 115.5 (t, J= 252.0 Hz), 62.8, 40.4 (t, *J* = 23.3 Hz), 39.2 (t, *J* = 4.5 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.7 – -105.0 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{25}F_2N_2O_3$ 475.1828; Found 475.1828.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(2-fluorophenyl)butanoate (**5b**)

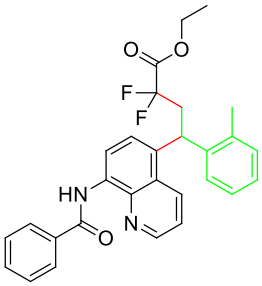
Yellow solid, 58% (57.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.82 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.56 (dd, *J* = 8.7, 1.5 Hz, 1H), 8.06 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.49 (m, 4H), 7.28 – 7.24 (m, 1H), 7.19 – 7.14 (m, 1H), 7.07 – 7.02 (m, 2H), 5.41 (t, *J* = 7.1 Hz, 1H), 4.00 – 3.90 (m, 2H), 3.12 – 3.00 (m, 2H), 1.18 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.6 (t, *J* = 32.5 Hz), 159.9 (d, *J* = 245.8 Hz), 147.9, 139.0, 135.0, 133.9, 132.0 (d, *J* = 2.4 Hz), 131.8, 131.8, 129.2 (d, *J* = 14.1 Hz), 129.0 (d, *J* = 3.7 Hz), 128.7, 128.7 (d, *J* = 5.9 Hz), 127.2, 126.1, 125.5, 124.4 (d, *J* = 3.5 Hz), 121.9, 115.8, 115.7 (d, *J* = 22.7 Hz), 115.4 (t, *J* = 251.5 Hz), 62.9, 39.5 (t, *J* = 23.4 Hz), 31.3, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -103.0 – -104.9 (m), -116.9.

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{28}H_{24}F_3N_2O_3$ 493.1734; Found 493.1738.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(o-tolyl)butanoate (**5c**)

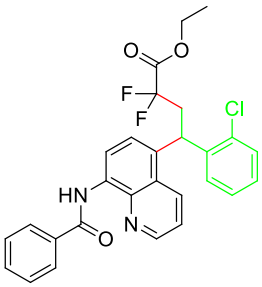
Yellow oil, 72% (70.3mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.77 (s, 1H), 8.87 – 8.81 (m, 2H), 8.49 (d, *J* = 8.1 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 2H), 7.57 – 7.51 (m, 4H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.26 (t, *J* = 5.5 Hz, 1H), 7.19 – 7.12 (m, 3H), 5.25 (t, *J* = 6.9 Hz, 1H), 3.89 – 3.80 (m, 2H), 3.01 – 2.88 (m, 2H), 2.33 (s, 3H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.7 (t, *J* = 32.2 Hz), 147.8, 139.7, 139.1, 135.7, 135.1, 133.7, 132.2, 131.9, 131.8, 131.0, 128.7, 127.2, 127.1, 127.0, 126.5, 126.2, 126.1, 121.9, 115.8, 115.4 (t, *J* = 251.3 Hz), 62.8, 39.8 (t, *J* = 23.5 Hz), 34.9 (t, *J* = 4.2 Hz), 19.7, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.1 – -104.7 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{29}H_{27}F_2N_2O_3$ 489.1984; Found 489.1985.



Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(2-chlorophenyl)-2,2-difluorobutanoate (**5d**)

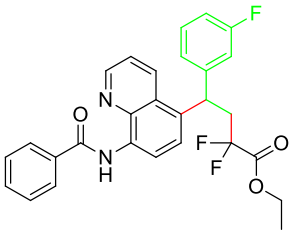
Yellow solid, 55% (55.6mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.79 (s, 1H), 8.91 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.54 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.09 – 8.05 (m, 2H), 7.57 – 7.51 (m, 5H), 7.38 (dd, *J* = 5.8, 1.8 Hz, 1H), 7.26 – 7.24 (m, 1H), 7.19 – 7.14 (m, 2H), 5.59 (t, *J* = 7.0 Hz, 1H), 4.02 – 3.94 (m, 2H), 3.08 – 2.87 (m, 2H), 1.18 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.7 (t, *J* = 32.5 Hz), 148.0, 139.7, 139.1, 135.0, 134.0, 133.4, 132.4, 131.8, 131.4, 130.0, 129.0, 128.8, 128.3, 127.2, 127.1, 126.4, 125.9, 122.0, 115.6, 115.2 (t, *J* = 252.1 Hz), 62.9, 39.3 (t, *J* = 23.4 Hz), 35.3 (t, *J* = 4.2 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.7 – -104.5 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{29}H_{24}ClF_2N_2O_3$ 509.1438; Found 509.1443.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(3-fluorophenyl)butanoate (**5e**)

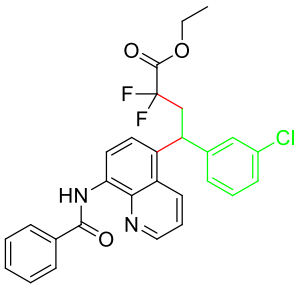
Yellow solid, 60% (59.3mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.79 (s, 1H), 8.93 (d, *J* = 8.1 Hz, 1H), 8.84 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.45 (dd, *J* = 8.7, 1.4 Hz, 1H), 8.07 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.59 – 7.53 (m, 4H), 7.50 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.24 (dd, *J* = 8.0, 6.0 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 6.98 (dt, *J* = 10.0, 2.2 Hz, 1H), 6.89 (m, 1H), 5.04 (t, *J* = 7.1 Hz, 1H), 3.99 – 3.87 (m, 2H), 3.11 – 3.00 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.5 (t, *J* = 32.3 Hz), 162.8 (d, *J* = 246.9 Hz), 147.9, 144.9 (d, *J* = 6.8 Hz), 135.0, 134.1, 132.1, 131.9, 130.2 (d, *J* = 8.1 Hz), 128.8, 127.2, 126.0, 125.6, 123.6 (d, *J* = 2.9 Hz), 121.8, 115.8, 115.4 (t, J = 252.0 Hz), 115.0, 114.8, 114.0, 113.8, 62.9, 40.2 (t, *J* = 23.3 Hz), 38.9, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -100.7 – -105.9 (m), -112.2.

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{28}H_{24}F_3N_2O_3$ 493.1734; Found 493.1737.



Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(3-chlorophenyl)-2,2-difluorobutanoate (**5f**)

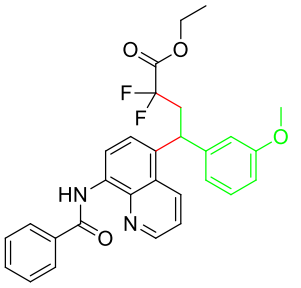
Yellow oil, 67% (68.0mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.94 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.43 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.07 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.59 – 7.54 (m, 4H), 7.49 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.27 (s, 1H), 7.22 – 7.17 (m, 3H), 5.02 (t, *J* = 7.1 Hz, 1H), 3.99 – 3.88 (m, 2H), 3.11 – 2.98 (m, 2H), 1.17 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.5 (t, *J* = 32.5 Hz), 148.0, 144.3, 139.2, 135.0, 134.5, 134.1, 132.1, 131.9, 131.7, 130.0, 128.8, 128.0, 127.2, 127.2, 126.2, 126.0, 125.7, 121.9, 115.8, 115.4 (t, *J* = 251.3 Hz), 63.0, 40.2 (t, *J* = 23.3 Hz), 38.9 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.1 – -104.8 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{24}ClF_2N_2O_3$ 509.1438; Found 509.1443.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(3-methoxyphenyl)butanoate (**5g**)

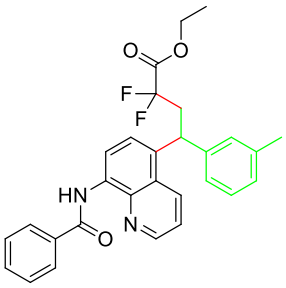
Yellow solid, 53% (53.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.93 (d, *J* = 8.1 Hz, 1H), 8.81 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.49 (d, *J* = 7.4 Hz, 1H), 8.07 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.61 – 7.52 (m, 4H), 7.46 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.82 (s, 1H), 6.71 (dd, *J* = 8.2, 2.3 Hz, 1H), 5.00 (t, *J* = 7.1 Hz, 1H), 3.94 – 3.81 (m, 2H), 3.73 (s, 3H), 3.12 – 2.99 (m, 2H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.6 (t, *J* = 32.6 Hz), 159.7, 147.8, 143.8, 139.1, 135.0, 133.8, 132.4, 132.3, 131.8, 129.7, 128.7, 127.2, 126.1, 125.5, 121.7, 120.2, 115.8, 115.5 (t, J = 251.5 Hz), 114.1, 111.8, 62.8, 55.1, 40.3 (t, *J* = 23.2 Hz), 39.2 (t, *J* = 4.5 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.8 – -104.9 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{27}F_2N_2O_4$ 505.1933; Found 505.1937.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(m-tolyl)butanoate (**5h**)

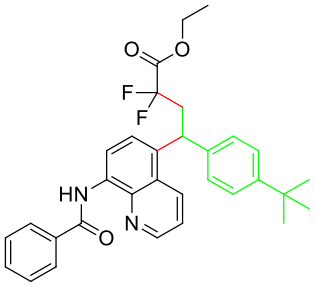
Yellow oil, 70% (68.1mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.83 (d, *J* = 1.7 Hz, 1H), 8.50 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 6.6 Hz, 2H), 7.59 – 7.53 (m, 4H), 7.48 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 12.5 Hz, 2H), 6.99 (d, *J* = 7.3 Hz, 1H), 4.99 (t, *J* = 7.1 Hz, 1H), 3.96 – 3.73 (m, 2H), 3.10 – 2.99 (m, 2H), 2.28 (s, 3H), 1.12 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.6 (t, *J* = 32.5 Hz), 147.8, 142.1, 139.1, 138.3, 135.0, 133.7, 132.7, 132.3, 131.8, 128.7, 128.5, 128.5, 127.7, 127.2, 126.1, 125.5, 124.9, 121.7, 115.8, 115.6 (t, *J* = 250.7 Hz), 62.7, 40.5 (t, *J* = 23.3 Hz), 39.1 (t, *J* = 4.6 Hz), 21.4, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.8 – -104.9 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{29}H_{27}F_2N_2O_3$ 489.1984; Found 489.1989.



Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(4-(tert-butyl)phenyl)-2,2-difluorobutanoate (**5i**)

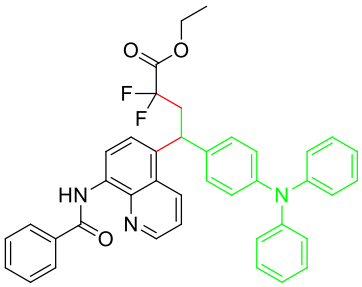
Yellow oil, 60% (63.4mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.77 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.82 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.52 (dd, *J* = 8.8, 1.6 Hz, 1H), 8.07 (d, *J* = 6.6 Hz, 2H), 7.61 – 7.52 (m, 4H), 7.49 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 4.99 (t, *J* = 7.2 Hz, 1H), 3.89 – 3.69 (m, 2H), 3.17 – 2.94 (m, 2H), 1.25 (s, 9H), 1.10 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.6 (t, *J* = 32.6 Hz), 149.8, 147.8, 139.1, 138.9, 135.1, 133.7, 133.0, 132.4, 131.8, 128.7, 127.5, 127.2, 126.1, 125.5, 125.4, 121.7, 115.9, 115.6 (t, *J* = 250.6 Hz), 62.7, 40.6 (t, *J* = 23.4 Hz), 38.7 (t, *J* = 4.5 Hz), 34.3, 31.2, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.3 – -105.3 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{32}H_{33}F_2N_2O_3$ 531.2454; Found 531.2454.



Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(4-(diphenylamino)phenyl)-2,2-difluorobutanoate (**5j**)

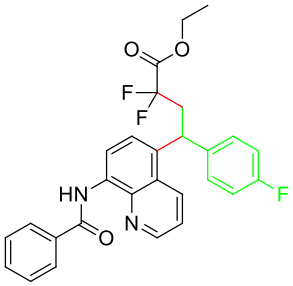
Yellow solid, 75% (96.3mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.84 (d, *J* = 4.0 Hz, 1H), 8.53 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 6.2 Hz, 2H), 7.61 – 7.50 (m, 5H), 7.22 (d, *J* = 8.1 Hz, 4H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 4H), 6.97 (dd, *J* = 8.0, 6.1 Hz, 4H), 4.99 (t, *J* = 7.2 Hz, 1H), 4.01 – 3.86 (m, 2H), 3.04 (dt, *J* = 15.4, 7.8 Hz, 2H), 1.17 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.6 (t, *J* = 32.5 Hz), 147.8, 147.5, 146.5, 139.1, 135.9, 135.0, 133.7, 132.9, 132.3, 131.8, 129.2, 128.7, 128.5, 127.2, 126.1, 125.5, 124.2, 123.6, 122.9, 121.7, 115.9, 115.6 (t, *J* = 251.1 Hz), 62.8, 40.5 (t, *J* = 22.9 Hz), 38.5 (t, *J* = 4.5 Hz), 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -100.3 – -106.3 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{40}H_{34}F_2N_3O_3$ 642.2563; Found 642.2565.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(4-fluorophenyl)butanoate (**5k**)

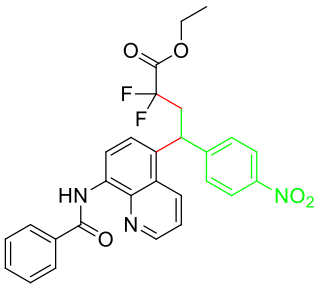
Yellow oil, 66% (65mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.93 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.44 (dd, *J* = 8.7, 1.3 Hz, 1H), 8.07 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.59 – 7.53 (m, 4H), 7.48 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.28 – 7.24 (m, 2H), 6.96 (t, *J* = 8.6 Hz, 2H), 5.03 (t, *J* = 7.1 Hz, 1H), 3.98 – 3.86 (m, 2H), 3.11 – 2.97 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.6 (t, *J* = 32.6 Hz), 161.6 (d, *J* = 246.2 Hz), 147.9, 139.2, 137.9 (d, *J* = 3.3 Hz), 135.0, 134.0, 132.4, 132.0 (d, *J* = 27.6 Hz), 129.5 (d, *J* = 8.1 Hz), 128.8, 127.2, 126.0, 125.4, 121.8, 115.8, 115.6, 115.5 (t, *J* = 251.2 Hz), 115.4, 62.9, 40.5 (t, *J* = 23.2 Hz), 38.6 (t, *J* = 4.5 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -100.6 – -106.1 (m), -114.9 – -115.9 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{28}H_{24}F_3N_2O_3$ 493.1734; Found 493.1736.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(4-nitrophenyl)butanoate (**5l**)

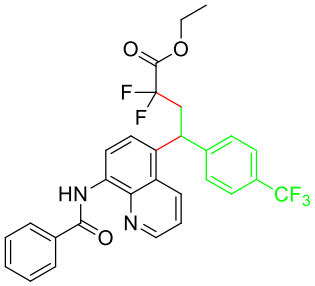
Yellow oil, 35% (36.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.79 (s, 1H), 8.95 (d, *J* = 8.1 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.3 Hz, 1H), 8.41 (dd, *J* = 8.7, 1.2 Hz, 1H), 8.13 (d, *J* = 8.8 Hz, 2H), 8.09 – 8.05 (m, 2H), 7.60 – 7.48 (m, 7H), 5.18 (t, *J* = 7.0 Hz, 1H), 4.07 – 3.97 (m, 2H), 3.09 (td, *J* = 15.8, 7.0 Hz, 2H), 1.19 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.4 (t, *J* = 32.3 Hz), 149.8, 148.1, 146.8, 139.2, 134.9, 134.5, 132.0, 131.8, 131.0, 128.8, 128.8, 127.2, 125.9, 125.9, 123.9, 122.0, 115.8, 115.2 (t, *J* = 252.0 Hz), 63.1, 39.9 (t, *J* = 23.2 Hz), 39.0 (t, *J* = 3.8 Hz), 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.7 – -104.6 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{24}F_2N_3O_5$ 520.1679; Found 520.1685.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(4-(trifluoromethyl)phenyl)butanoate (**5m**)

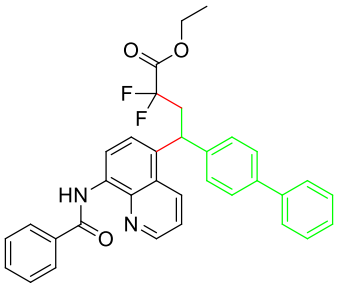
Yellow oil, 53% (57.5mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.79 (s, 1H), 8.94 (d, *J* = 8.1 Hz, 1H), 8.85 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.43 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.09 – 8.06 (m, 2H), 7.58 – 7.49 (m, 7H), 7.43 (d, *J* = 8.2 Hz, 2H), 5.11 (t, *J* = 7.1 Hz, 1H), 3.98 – 3.88 (m, 2H), 3.14 – 3.02 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.5 (t, *J* = 32.5 Hz), 148.0, 146.3, 139.2, 135.0, 134.2, 132.0, 131.9, 131.6, 128.8, 128.3, 127.2, 125.8 (d, *J* = 37.8 Hz), 125.7, 125.7, 125.6, 123.9 (d, *J* = 272.4 Hz), 121.9, 115.8, 115.3 (t, *J* = 251.4 Hz), 63.0, 40.2 (t, *J* = 23.3 Hz), 39.1 (t, *J* = 4.2 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.6, -100.9 – -105.7 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{24}F_5N_2O_3$ 543.1702; Found 543.1705.



Ethyl 4-([1,1'-biphenyl]-4-yl)-4-(8-benzamidoquinolin-5-yl)-2,2-difluorobutanoate (**5n**)

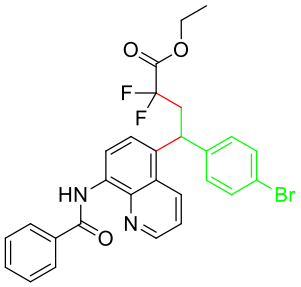
Yellow oil, 66% (75.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.79 (s, 1H), 8.95 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.53 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.08 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.58 – 7.49 (m, 9H), 7.41 – 7.33 (m, 5H), 5.08 (t, *J* = 7.1 Hz, 1H), 3.97 – 3.76 (m, 2H), 3.17 – 3.05 (m, 2H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.6 (t, *J* = 32.6 Hz), 147.9, 141.1, 140.3, 139.8, 139.2, 135.0, 133.9, 132.6, 132.3, 131.8, 128.8, 128.7, 128.3, 127.3, 127.2, 126.9, 126.9, 126.1, 125.5, 121.8, 115.8, 115.6 (t, *J* = 250.8 Hz), 62.8, 40.5 (t, *J* = 23.4 Hz), 38.9 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.5 – -105.1 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{34}H_{29}F_2N_2O_3$ 551.2141; Found 551.2146.



Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(4-bromophenyl)-2,2-difluorobutanoate (**5o**)

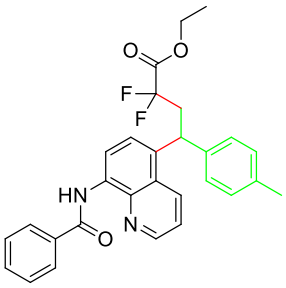
Yellow oil, 66% (72.8mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.93 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.41 (dd, *J* = 8.7, 1.5 Hz, 1H), 8.07 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.59 – 7.52 (m, 4H), 7.48 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 5.00 (t, *J* = 7.1 Hz, 1H), 3.99 – 3.85 (m, 2H), 3.09 – 2.97 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.5 (t, *J* = 32.5 Hz), 147.9, 141.3, 139.2, 135.0, 134.1, 132.1, 132.0, 131.9, 131.8, 129.6, 128.8, 127.2, 125.9, 125.5, 121.8, 120.9, 115.8, 115.4 (t, *J* = 251.3 Hz), 63.0, 40.2 (t, *J* = 23.3 Hz), 38.7 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.2 – -104.7 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{28}H_{24}BrF_2N_2O_3$ 553.0933 Found 553.0936.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(p-tolyl)butanoate (**5p**)

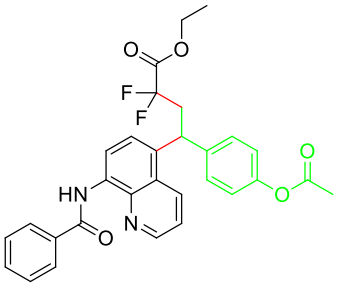
Yellow oil, 76% (74.5mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.77 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.80 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.49 (dd, *J* = 8.7, 1.3 Hz, 1H), 8.07 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.59 – 7.52 (m, 4H), 7.46 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 4.99 (t, *J* = 7.1 Hz, 1H), 3.92 – 3.78 (m, 2H), 3.12 – 2.98 (m, 2H), 2.26 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.6 (t, *J* = 32.5 Hz), 147.8, 139.2, 139.1, 136.6, 135.0, 133.7, 132.8, 132.3, 131.8, 129.3, 128.7, 127.8, 127.2, 126.1, 125.4, 121.7, 115.8, 115.6 (t, *J* = 250.9 Hz), 62.8, 40.5 (t, *J* = 23.2 Hz), 38.8 (t, *J* = 4.5 Hz), 20.9, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.8 – -104.9 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{29}H_{27}F_2N_2O_3$ 489.1984 Found 489.1988.



Ethyl 4-(4-acetoxyphenyl)-4-(8-benzamidoquinolin-5-yl)-2,2-difluorobutanoate (**5q**)

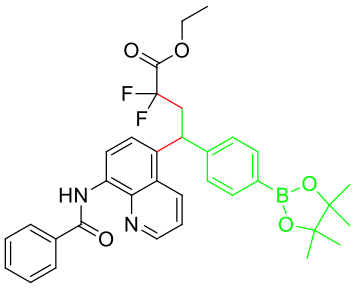
Yellow oil, 58% (62.1mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.8 (s, 1H), 8.9 (d, *J* = 8.1 Hz, 1H), 8.8 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.4 (d, *J* = 7.5 Hz, 1H), 8.1 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.6 – 7.5 (m, 4H), 7.5 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.3 (d, *J* = 8.6 Hz, 2H), 7.0 (d, *J* = 8.6 Hz, 2H), 5.0 (t, *J* = 7.1 Hz, 1H), 4.0 – 3.8 (m, 2H), 3.1 – 3.0 (m, 2H), 2.2 (s, 3H), 1.1 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.2, 165.3, 163.5 (t, *J* = 32.5 Hz), 149.5, 147.9, 139.5, 139.1, 135.0, 133.9, 132.3, 132.2, 131.8, 128.9, 128.7, 127.2, 126.0, 125.4, 121.8, 121.7, 115.8, 115.4 (t, J = 252.0 Hz), 62.9, 40.5 (t, *J* = 23.3 Hz), 38.7 (t, *J* = 4.5 Hz), 21.0, 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.3 – -105.3 (m).0

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{30}H_{27}F_2N_2O_5$ 533.1883 Found 533.1884.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butanoate (**5r**)

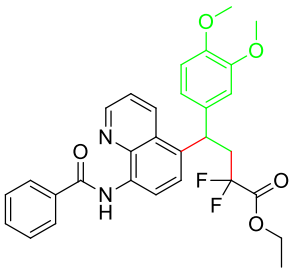
Yellow oil, 36% (43.6mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.81 (d, *J* = 3.0 Hz, 1H), 8.47 (d, *J* = 8.1 Hz, 1H), 8.07 (d, *J* = 6.6 Hz, 2H), 7.72 (d, *J* = 7.9 Hz, 2H), 7.56 (dt, *J* = 11.1, 6.0 Hz, 4H), 7.46 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 5.05 (t, *J* = 7.1 Hz, 1H), 3.94 – 3.81 (m, 2H), 3.07 (d, *J* = 7.1 Hz, 2H), 1.30 (s, 12H), 1.13 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.6 (t, *J* = 32.5 Hz), 147.8, 145.4, 139.2, 135.2, 135.1, 135.0, 133.9, 132.3, 132.3, 131.8, 128.7, 127.2 (d, *J* = 1.5 Hz), 126.1, 125.7, 125.5, 121.7, 115.8, 115.5 (t, *J* = 251.1 Hz), 83.8, 62.8, 40.2 (t, *J* = 23.0 Hz), 39.5 (t, *J* = 4.3 Hz), 24.8 (d, *J* = 2.5 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.2 – -104.6 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{34}H_{36}BF_2N_2O_5$ 601.2680 Found 601.2688.



Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(3,4-dimethoxyphenyl)-2,2-difluorobutanoate (**5s**)

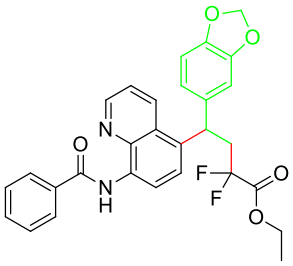
Brown oil, 60% (64.4mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.79 (s, 1H), 8.93 (d, *J* = 8.1 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.49 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.10 – 8.06 (m, 2H), 7.60 – 7.53 (m, 4H), 7.48 (dd, *J* = 8.6, 4.2 Hz, 1H), 6.84 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.78 – 6.74 (m, 2H), 4.97 (t, *J* = 7.1 Hz, 1H), 3.95 – 3.83 (m, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 3.12 – 2.96 (m, 2H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.6 (t, *J* = 32.7 Hz), 149.0, 147.9, 147.8, 139.2, 135.0, 134.6, 133.8, 132.7, 132.3, 131.8, 128.7, 127.2, 126.1, 125.3, 121.7, 120.0, 115.7, 115.6 (t, J =251.5 Hz), 111.2, 111.1, 62.8, 55.8, 55.8, 40.5 (t, *J* = 23.2 Hz), 39.0 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.4 – -105.1 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{29}F_2N_2O_5$ 535.2039 Found 535.2044.



Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(benzo[d][1,3]dioxol-5-yl)-2,2-difluorobutanoate (**5t**)

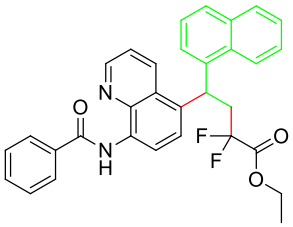
Yellow oil, 55% (57.4mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.77 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.81 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.46 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.07 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.58 – 7.51 (m, 4H), 7.47 (dd, *J* = 8.6, 4.2 Hz, 1H), 6.78 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.73 – 6.68 (m, 2H), 5.87 (d, *J* = 7.0 Hz, 2H), 4.95 (t, *J* = 7.1 Hz, 1H), 4.00 – 3.88 (m, 2H), 3.08 – 2.96 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.6 (t, *J* = 32.6 Hz), 147.9, 147.8, 146.4, 139.2, 136.1, 135.0, 133.9, 132.6, 132.3, 131.8, 128.7, 127.2, 126.1, 125.2, 121.7, 121.0, 115.8, 115.5 (t, *J* = 250.9 Hz), 108.3, 108.2, 101.0, 62.8, 40.5 (t, *J* = 23.3 Hz), 38.9 (t, *J* = 4.4 Hz), 13.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.9 – -104.9 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{29}H_{25}F_2N_2O_5$ 519.1726 Found 519.1730.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(naphthalen-1-yl)butanoate (**5u**)

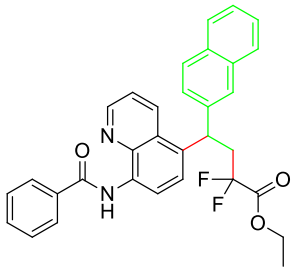
Yellow solid, 52% (54.3mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.79 (s, 1H), 8.90 (d, *J* = 8.1 Hz, 1H), 8.81 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.43 (d, *J* = 8.6 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.06 (s, 2H), 7.88 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.59 – 7.50 (m, 6H), 7.41 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.27 (d, *J* = 7.2 Hz, 1H), 5.91 (t, *J* = 6.9 Hz, 1H), 3.81 (m, 2H), 3.21 – 3.01 (m, 2H), 1.02 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.8 (t, *J* = 32.3 Hz), 147.9, 139.3, 137.9, 135.1, 134.2, 133.9, 132.1, 131.8, 131.8, 130.7, 129.2, 128.8, 127.9, 127.2, 126.9, 126.3, 126.2, 125.8, 125.4, 125.3, 122.4, 122.0, 115.7, 115.5 (t, *J* = 251.6 Hz), 62.9, 39.5 (t, *J* = 23.5 Hz), 34.4 (t, *J* = 3.9 Hz), 13.5.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -103.4 – -103.5 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{32}H_{27}F_2N_2O_3$ 525..1984 Found 525.1990.



Ethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoro-4-(naphthalen-2-yl)butanoate (**5v**)

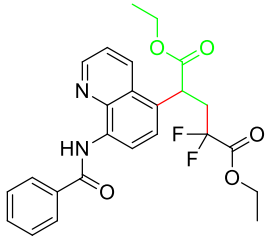
Yellow oil, 60% (62.5mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.95 (d, *J* = 8.1 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.54 (d, *J* = 8.1 Hz, 1H), 8.07 (d, *J* = 6.7 Hz, 2H), 7.74 (q, *J* = 9.7, 8.2 Hz, 4H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.48 – 7.39 (m, 3H), 7.37 (d, *J* = 8.7 Hz, 1H), 5.20 (t, *J* = 7.0 Hz, 1H), 3.79 – 3.61 (m, 2H), 3.26 – 3.06 (m, 2H), 1.02 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 163.6 (t, *J* = 32.4 Hz), 147.8, 139.5, 139.2, 135.0, 133.9, 133.2, 132.4, 132.3, 132.3, 131.8, 128.7, 128.5, 127.7, 127.5, 127.2, 126.4, 126.3, 126.2, 126.1, 126.0, 125.7, 121.7, 115.8, 115.6 (t, *J* = 251.0 Hz), 62.8, 40.3 (t, *J* = 23.4 Hz), 39.4 (t, *J* = 4.6 Hz), 13.5.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.3 – -105.0 (m).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{32}H_{27}F_2N_2O_3$ 525..1984 Found 525.1989.



Diethyl 4-(8-benzamidoquinolin-5-yl)-2,2-difluoropentanedioate (**5w**)

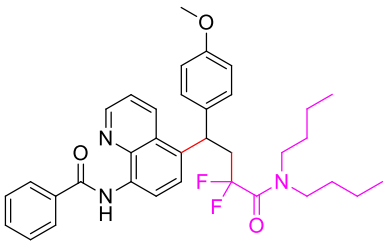
Yellow oil, 24% (22.7mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.81 (s, 1H), 8.93 – 8.88 (m, 2H), 8.54 (dd, *J* = 8.7, 1.5 Hz, 1H), 8.08 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.61 – 7.54 (m, 5H), 4.64 (dd, *J* = 8.6, 4.6 Hz, 1H), 4.22 – 4.08 (m, 4H), 3.34 – 3.23 (m, 1H), 2.65 – 2.49 (m, 1H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 165.4, 163.6 (t, *J* = 32.4 Hz), 148.1, 139.1, 135.0, 134.6, 132.1, 131.9, 128.8, 127.9, 127.3, 126.5, 126.0, 122.1, 116.1, 115.0 (t, *J* = 251.2 Hz), 63.1, 61.7, 39.7, 37.7 (t, *J* = 23.4 Hz), 13.9, 13.8.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -105.5 (d, *J* = 9.5 Hz).

HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{25}H_{25}F_2N_2O_5$ 471.1726 Found 471.1725.



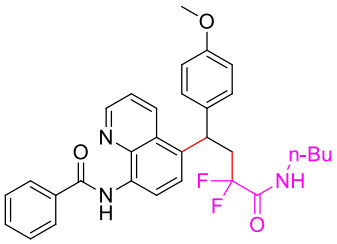
N-(5-(4-(dibutylamino)-3,3-difluoro-1-(4-methoxyphenyl)-4-oxobutyl)quinolin-8-yl)benzamide (**6a**)
Green oil, 37% (43.4mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.91 (d, *J* = 8.1 Hz, 1H), 8.80 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.54 (d, *J* = 8.7 Hz, 1H), 8.07 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.60 – 7.52 (m, 4H), 7.46 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 5.14 (t, *J* = 6.8 Hz, 1H), 3.74 (s, 3H), 3.34 – 3.23 (m, 4H), 3.15 – 3.05 (m, 2H), 1.50 – 1.42 (m, 4H), 1.34 – 1.27 (m, 2H), 1.25 – 1.21 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 162.8 (t, *J* = 28.8 Hz), 158.1, 147.6, 139.2, 135.6, 135.2, 134.2, 133.4, 132.7, 131.7, 128.8, 128.7, 127.2, 126.2, 125.7, 121.5, 119.1 (t, *J* = 256.1 Hz), 116.0, 113.9, 55.1, 47.4 (t, *J* = 5.8 Hz), 46.9, 40.7, 38.5, 30.9, 29.1, 20.1, 19.8, 13.8, 13.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -96.5 – -98.2 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{35}H_{40}F_2N_3O_3$ 588.3032 Found 588.3037.



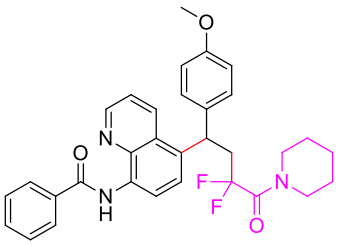
N-(5-(4-(butylamino)-3,3-difluoro-1-(4-methoxyphenyl)-4-oxobutyl)quinolin-8-yl)benzamide (**6b**)
Green oil, 70% (74.5mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.77 (s, 1H), 8.90 (d, *J* = 8.1 Hz, 1H), 8.82 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.50 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.07 (d, *J* = 6.4 Hz, 2H), 7.60 – 7.52 (m, 4H), 7.47 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 6.11 (s, 1H), 4.99 (t, *J* = 7.3 Hz, 1H), 3.75 (s, 3H), 3.16 – 3.10 (m, 2H), 3.09 – 2.99 (m, 2H), 1.38 – 1.32 (m, 2H), 1.28 – 1.23 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 163.8 (t, *J* = 28.3 Hz), 158.2, 147.7, 139.1, 135.0, 134.4, 133.5, 133.2, 132.4, 131.8, 128.8, 128.7, 127.2, 126.0, 125.7, 121.6, 117.6 (t, *J* = 253.9 Hz), 115.9, 113.9, 55.1, 39.5 (t, *J* = 22.5 Hz), 39.2, 38.8 (t, *J* = 3.6 Hz), 31.0, 19.8, 13.5.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.8 (d, *J* = 21.1 Hz).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{31}H_{32}F_2N_3O_3$ 532.2406 Found 532.2410.



N-(5-(3,3-difluoro-1-(4-methoxyphenyl)-4-oxo-4-(piperidin-1-yl)butyl)quinolin-8-yl)benzamide (**6c**)

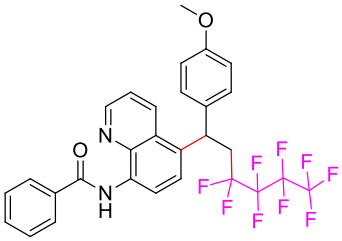
Brown oil, 72% (78.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.91 (d, *J* = 8.1 Hz, 1H), 8.80 (d, *J* = 2.9 Hz, 1H), 8.55 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 6.7 Hz, 2H), 7.60 – 7.52 (m, 4H), 7.46 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 5.14 (t, *J* = 6.8 Hz, 1H), 3.74 (s, 3H), 3.56 – 3.46 (m, 4H), 3.16 – 3.02 (m, 2H), 1.63 – 1.50 (m, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 161.5 (t, *J* = 28.7 Hz), 158.1, 147.6, 139.2, 135.5, 135.1, 134.2, 133.4, 132.6, 131.7, 128.8, 128.7, 127.2, 126.1, 125.6, 121.5, 116.4 (t, J =261.6 Hz), 115.9, 113.9, 55.1, 46.7 (t, *J* = 6.6 Hz), 44.3, 40.6 (t, *J* = 22.0 Hz), 38.4, 26.4, 25.5, 24.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -97.4 (d, *J* = 22.6 Hz).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{32}F_2N_3O_3$ 544.2406 Found 544.2410.



N-(5-(3,3,4,4,5,5,6,6,6-nonafluoro-1-(4-methoxyphenyl)hexyl)quinolin-8-yl)benzamide (**6d**)

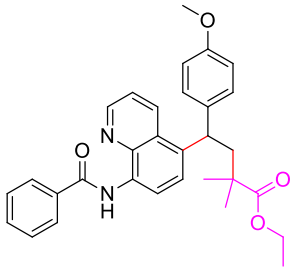
Green oil, 69% (82.8mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.95 (d, *J* = 8.1 Hz, 1H), 8.82 (d, *J* = 3.1 Hz, 1H), 8.47 (d, *J* = 8.2 Hz, 1H), 8.07 (d, *J* = 6.6 Hz, 2H), 7.54 (q, *J* = 7.2, 6.3 Hz, 4H), 7.47 (dd, *J* = 8.7, 4.1 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 5.15 (t, *J* = 6.9 Hz, 1H), 3.74 (s, 3H), 3.11 – 2.89 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.5, 158.5, 147.9, 139.3, 135.1, 134.5, 133.9, 132.8, 132.1, 131.9, 128.8, 128.7, 127.3, 126.0, 125.4, 121.8, 116.0, 114.2, 55.2, 37.3, 36.4 (t, *J* = 20.6 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (t, *J* = 9.6 Hz), -112.0 – -113.8 (m), -124.4 (d, *J* = 9.7 Hz), -125.8 – -125.9 (m).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{22}F_9N_2O_2$ 601.1532 Found 601.1536.



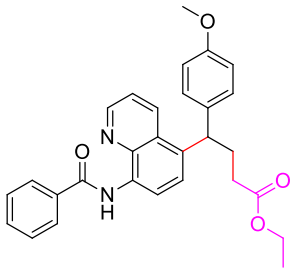
Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(4-methoxyphenyl)-2,2-dimethylbutanoate (**6e**)

Colorless oil, 33% (32.5mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.77 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.51 (d, *J* = 9.9 Hz, 1H), 8.07 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.58 – 7.52 (m, 3H), 7.45 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 4.72 (t, *J* = 6.7 Hz, 1H), 3.73 – 3.62 (m, 5H), 2.59 – 2.49 (m, 2H), 1.21 (s, 6H), 1.06 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.1, 165.3, 157.9, 147.6, 139.2, 136.5, 135.2, 135.2, 133.2, 132.5, 131.7, 128.9, 128.7, 127.2, 126.3, 125.4, 121.4, 116.0, 113.7, 60.3, 55.2, 46.5, 42.1, 41.3, 26.7, 25.7, 13.9.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{31}H_{33}N_2O_4$ 497.2435 Found 497.2439.



Ethyl 4-(8-benzamidoquinolin-5-yl)-4-(4-methoxyphenyl)butanoate (**6f**)

Yellow oil, 43% (40.1mg).

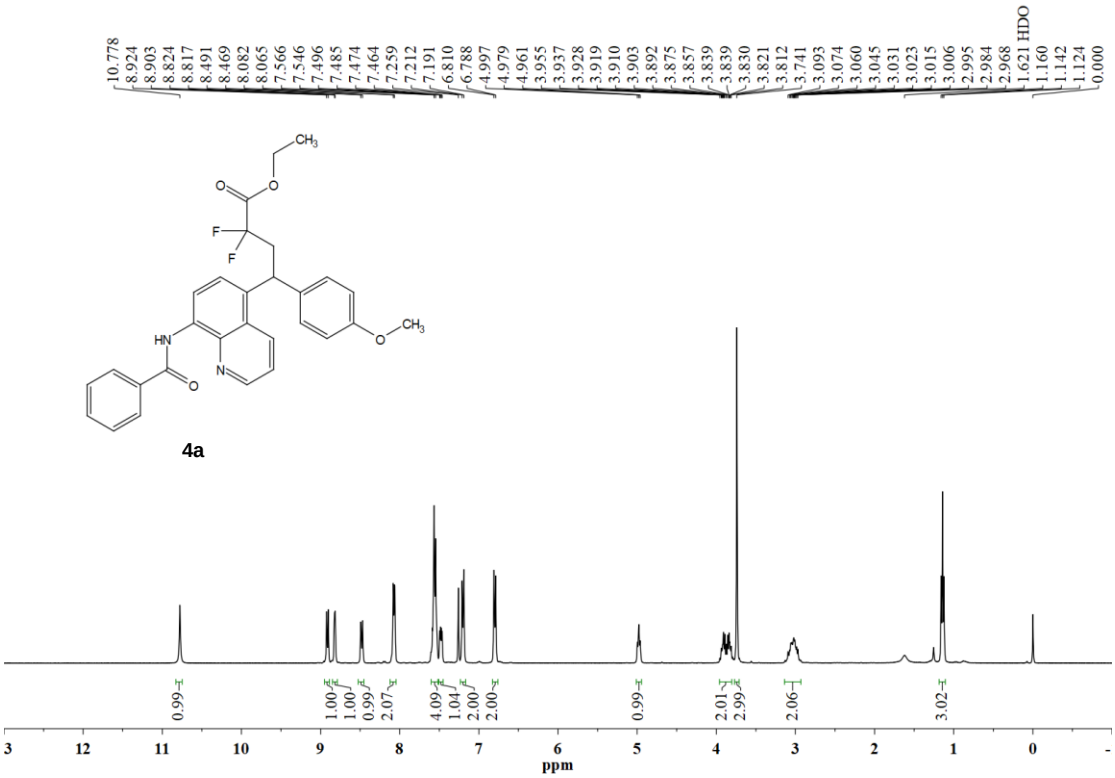
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.78 (s, 1H), 8.92 (d, *J* = 8.1 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.46 (dd, *J* = 8.7, 1.4 Hz, 1H), 8.08 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.61 – 7.52 (m, 4H), 7.42 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.17 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 4.62 (t, *J* = 7.3 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.74 (s, 3H), 2.54 – 2.41 (m, 2H), 2.40 – 2.32 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.4, 165.4, 158.1, 147.6, 139.3, 135.7, 135.2, 134.2, 133.4, 132.7, 131.7, 128.9, 128.7, 127.2, 126.7, 125.1, 121.4, 116.0, 114.0, 60.4, 55.2, 44.2, 32.5, 31.0, 14.2.

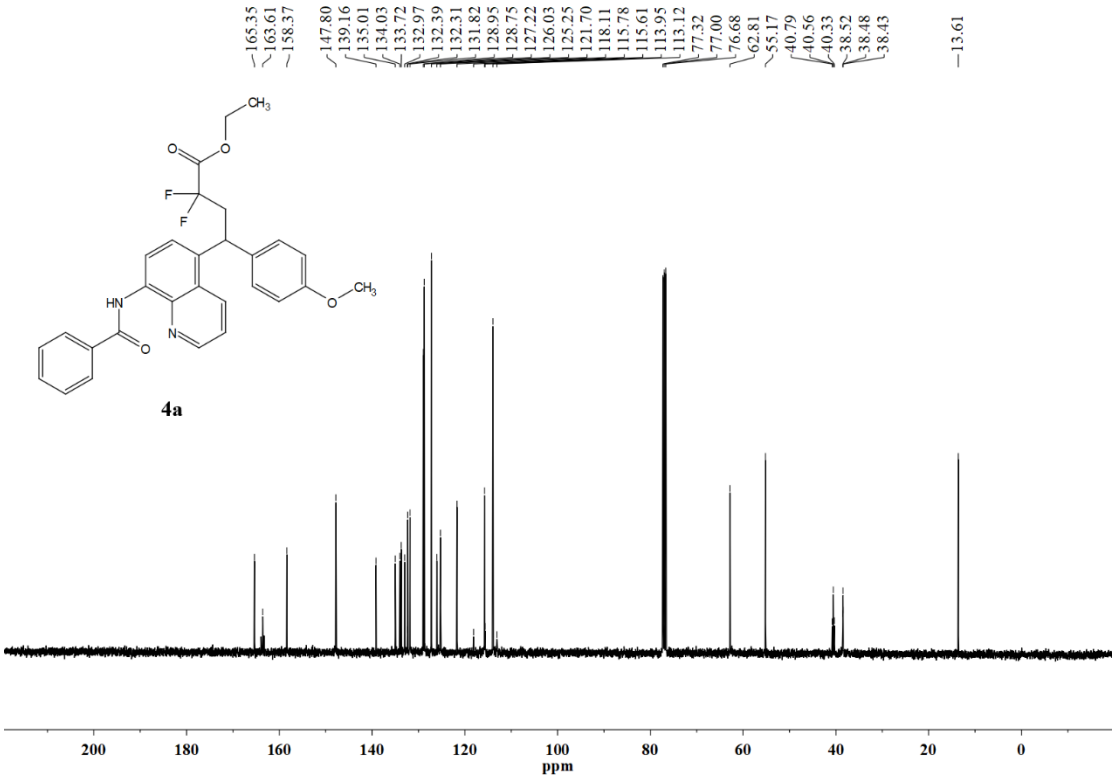
HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{29}N_2O_4$ 469.2122 Found 469.2127.

10. NMR Spectroscopic Data

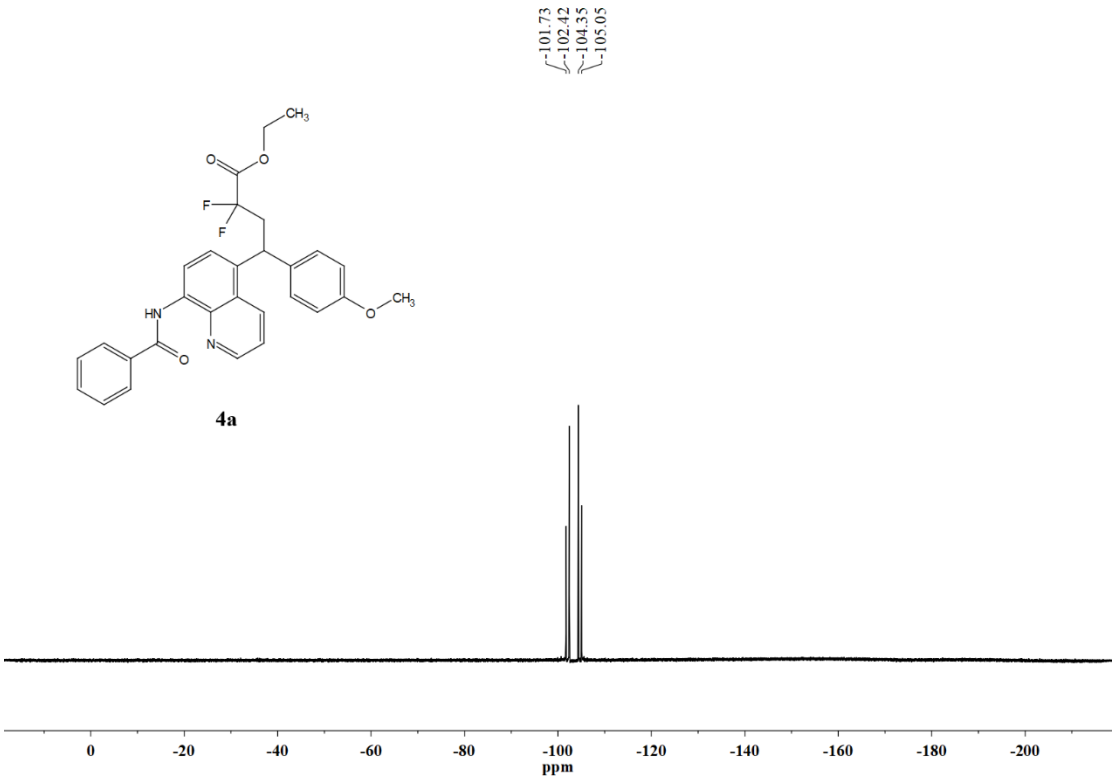
^{1}H NMR (400 MHz, Chloroform-*d*)



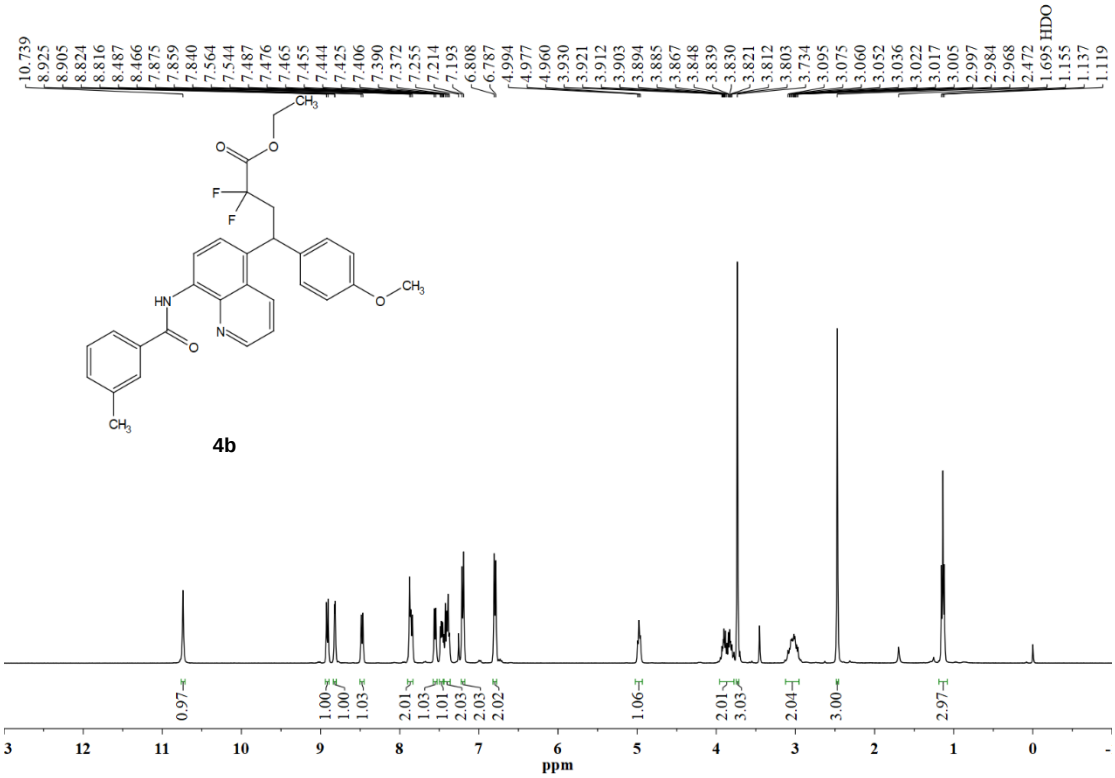
^{13}C NMR (101 MHz, Chloroform-*d*)



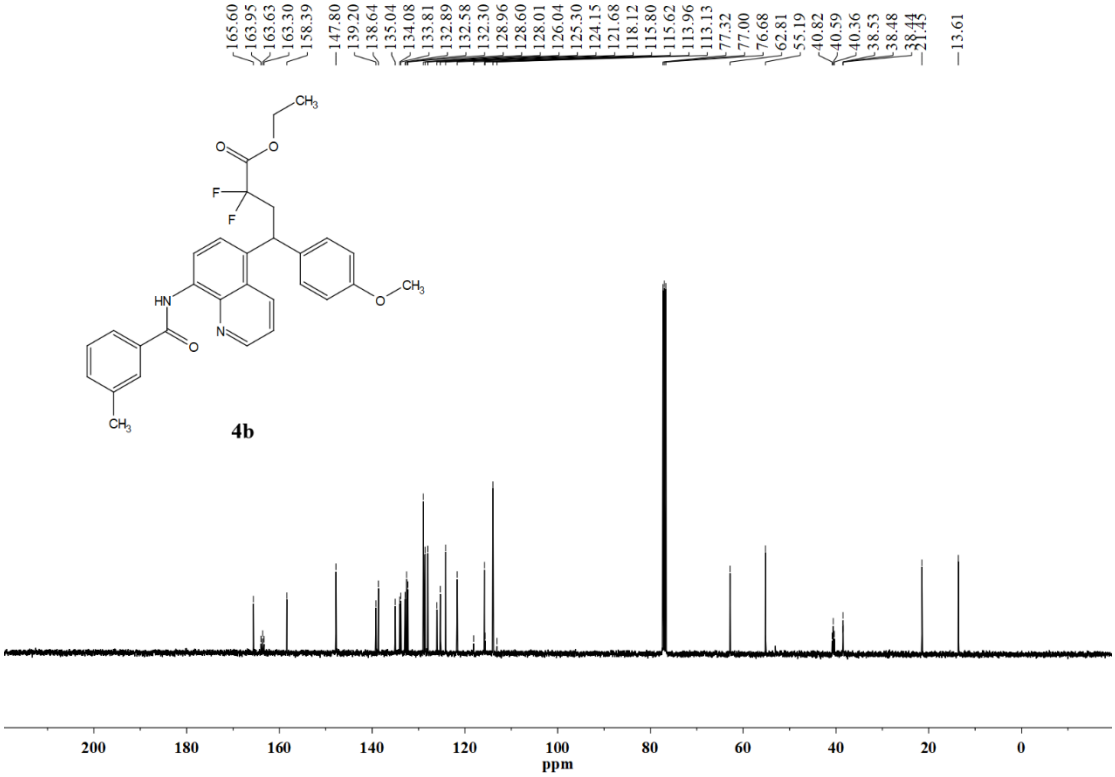
^{19}F NMR (376 MHz, Chloroform-*d*)



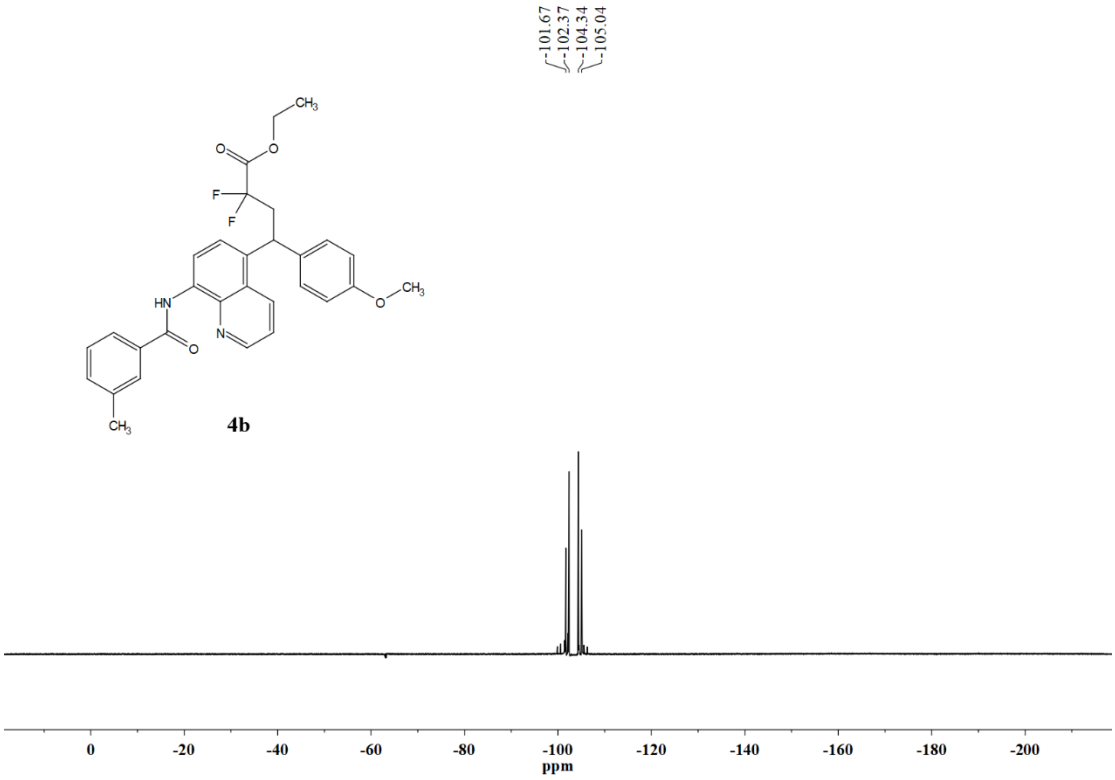
^{1}H NMR (400 MHz, Chloroform-*d*)



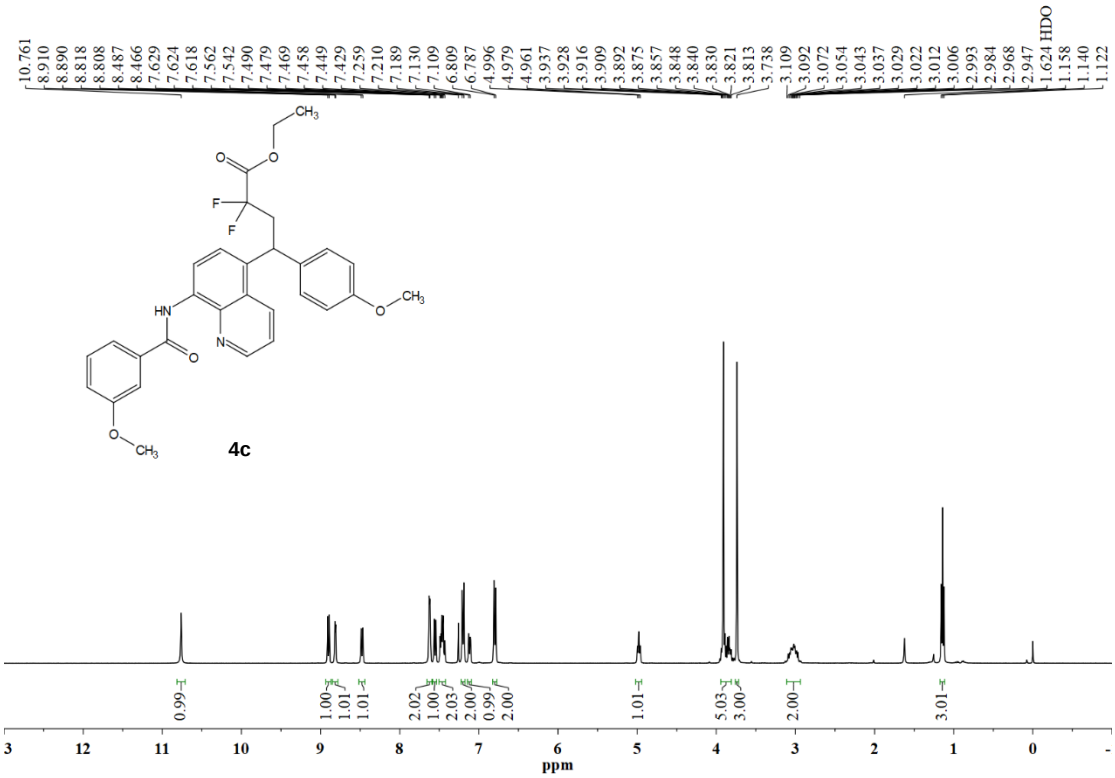
^{13}C NMR (101 MHz, Chloroform-*d*)



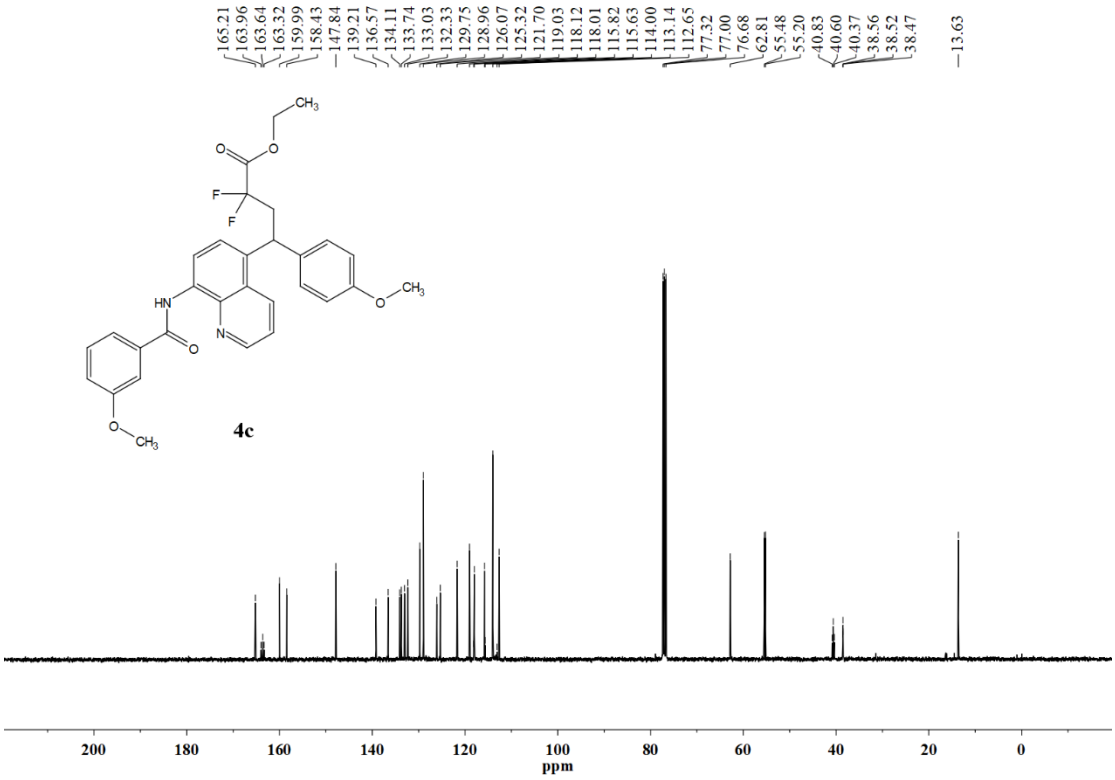
^{19}F NMR (376 MHz, Chloroform-*d*)



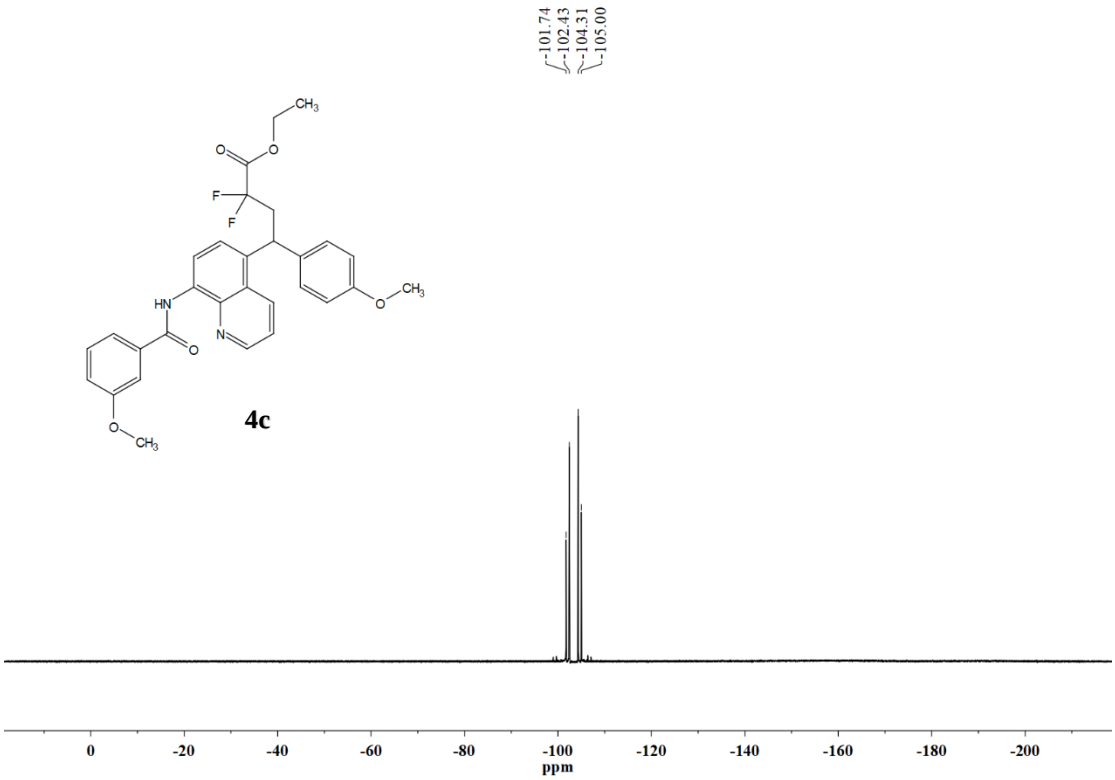
^{1}H NMR (400 MHz, Chloroform-*d*)



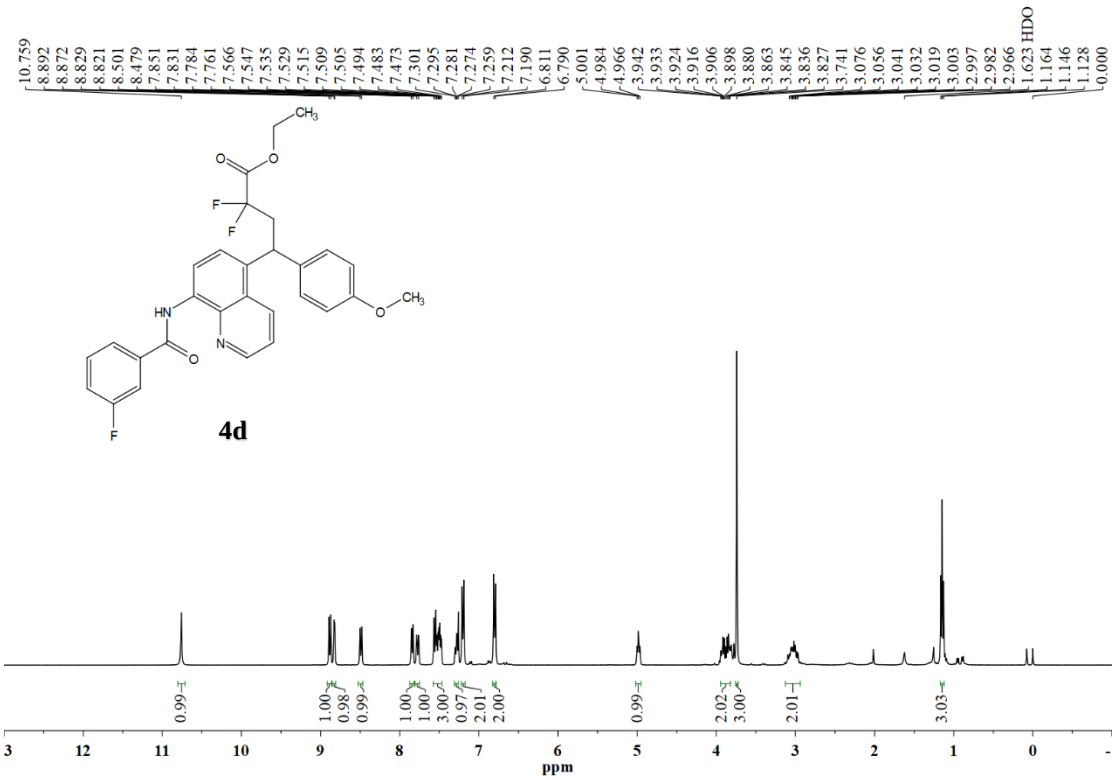
^{13}C NMR (101 MHz, Chloroform-*d*)



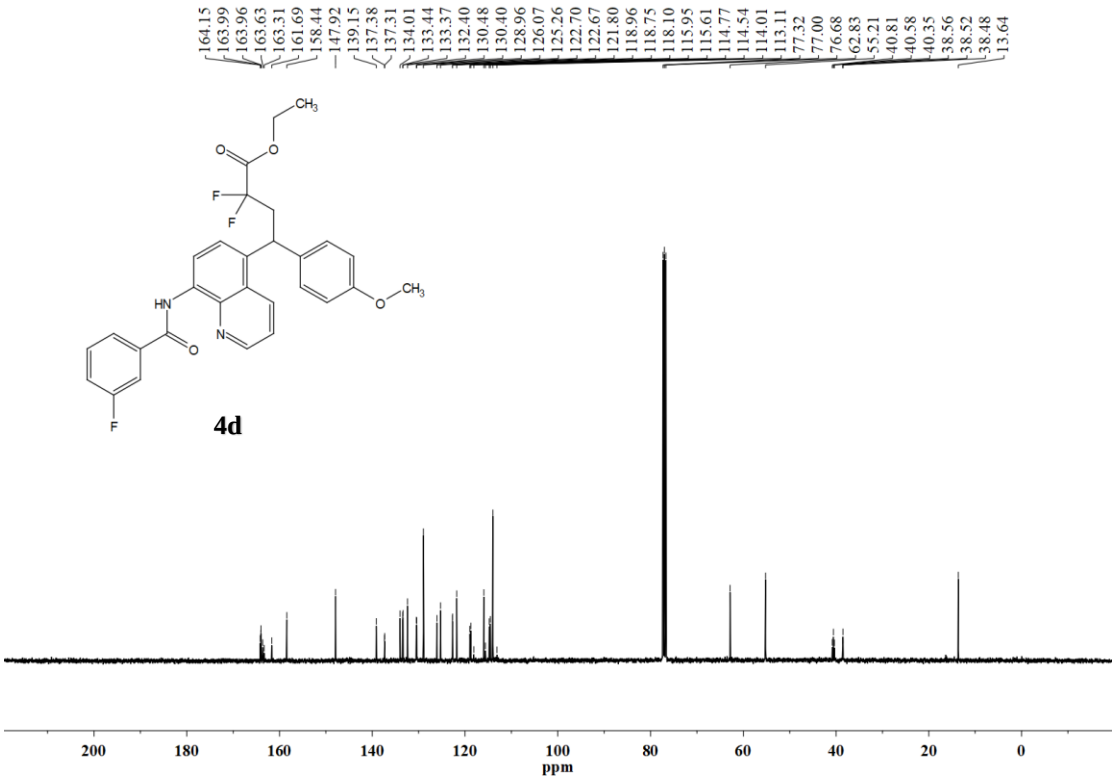
^{19}F NMR (376 MHz, Chloroform-*d*)



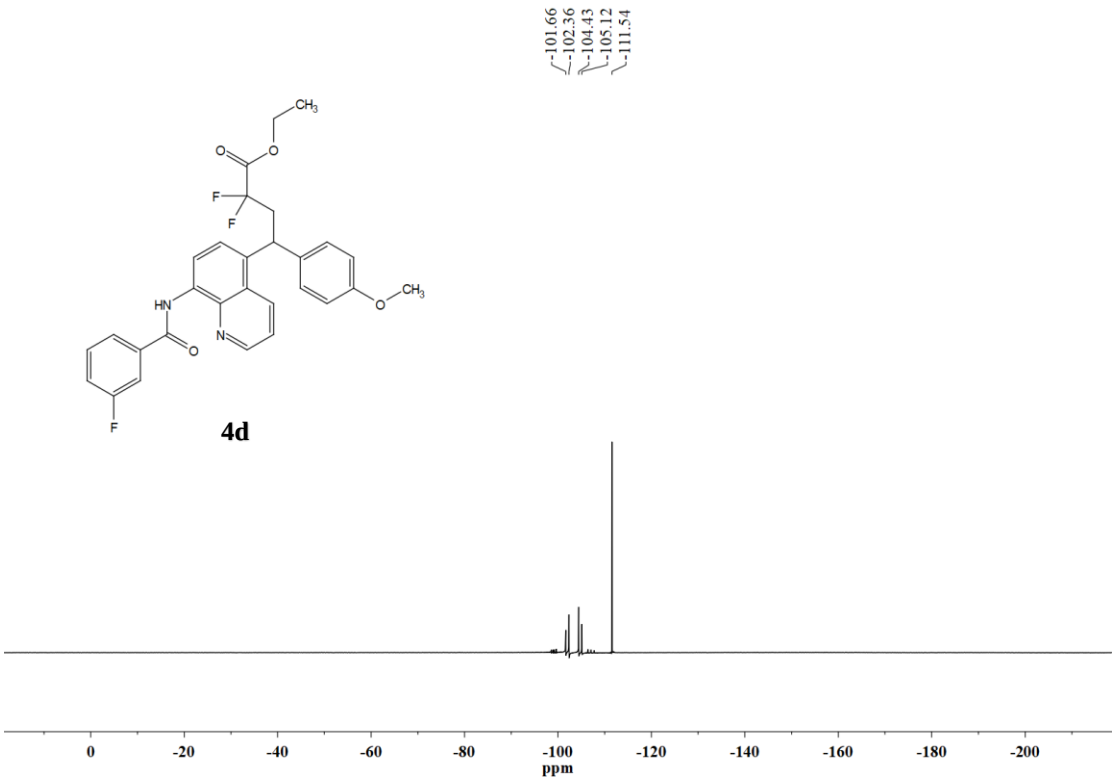
^{1}H NMR (400 MHz, Chloroform-*d*)



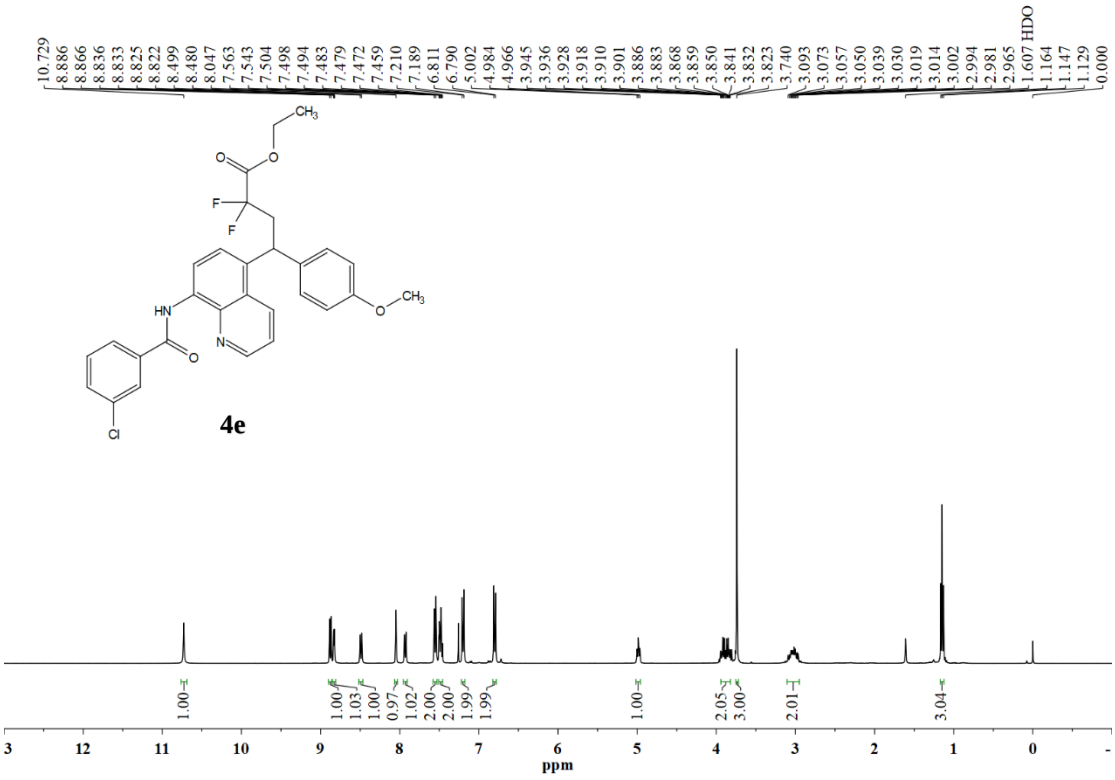
^{13}C NMR (101 MHz, Chloroform-*d*)



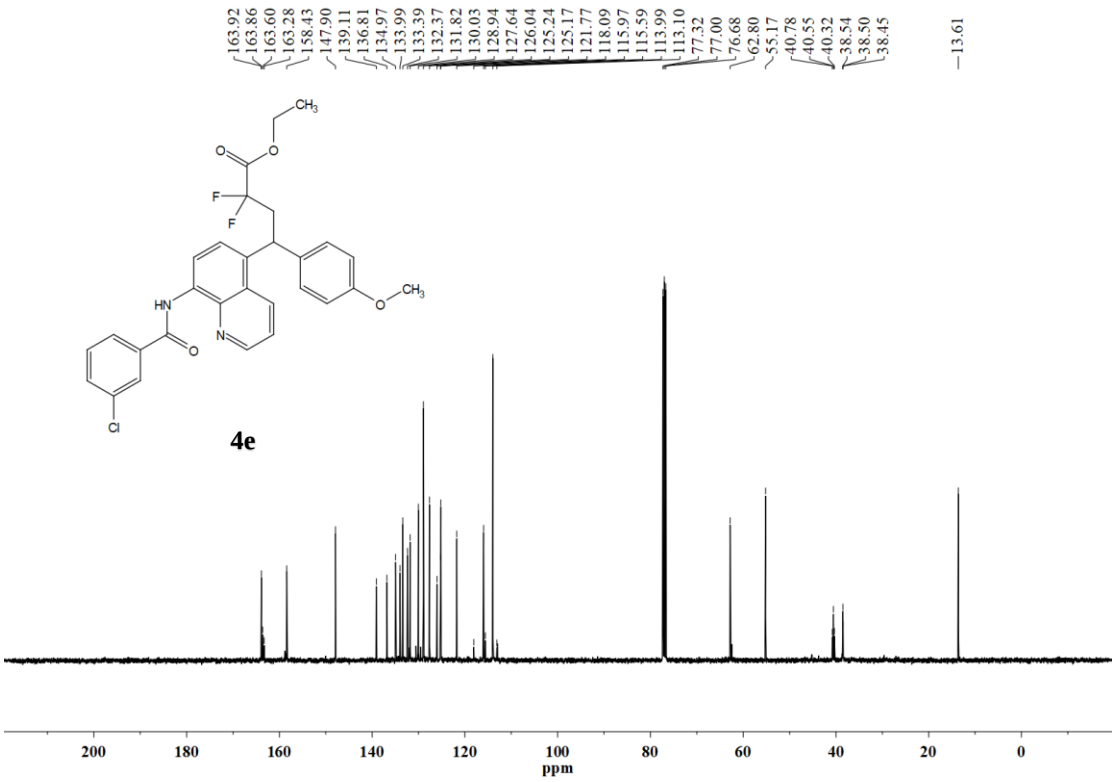
^{19}F NMR (376 MHz, Chloroform-*d*)



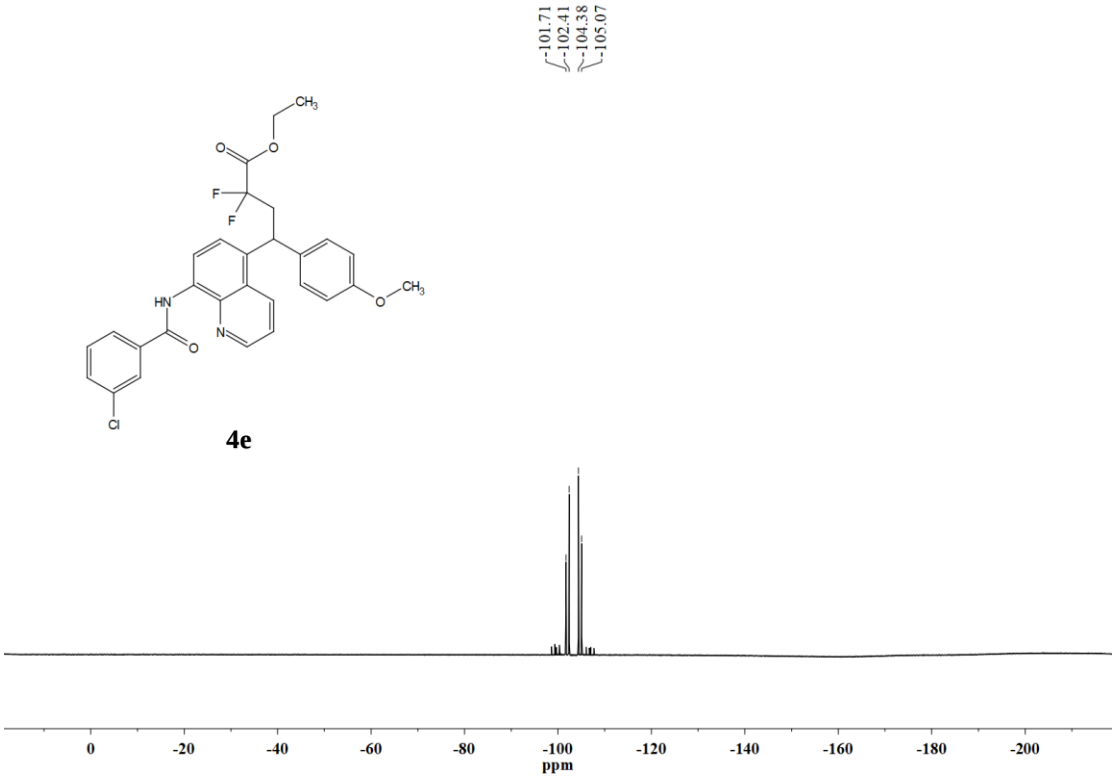
^{1}H NMR (400 MHz, Chloroform-*d*)



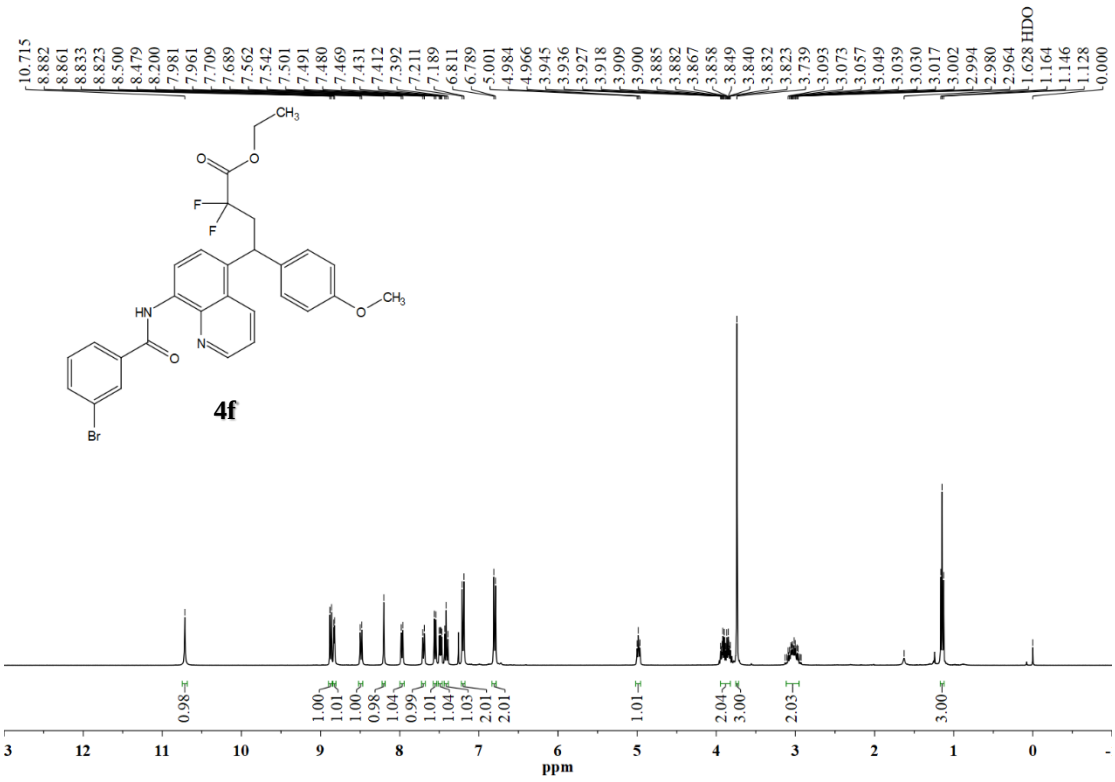
^{13}C NMR (101 MHz, Chloroform-*d*)



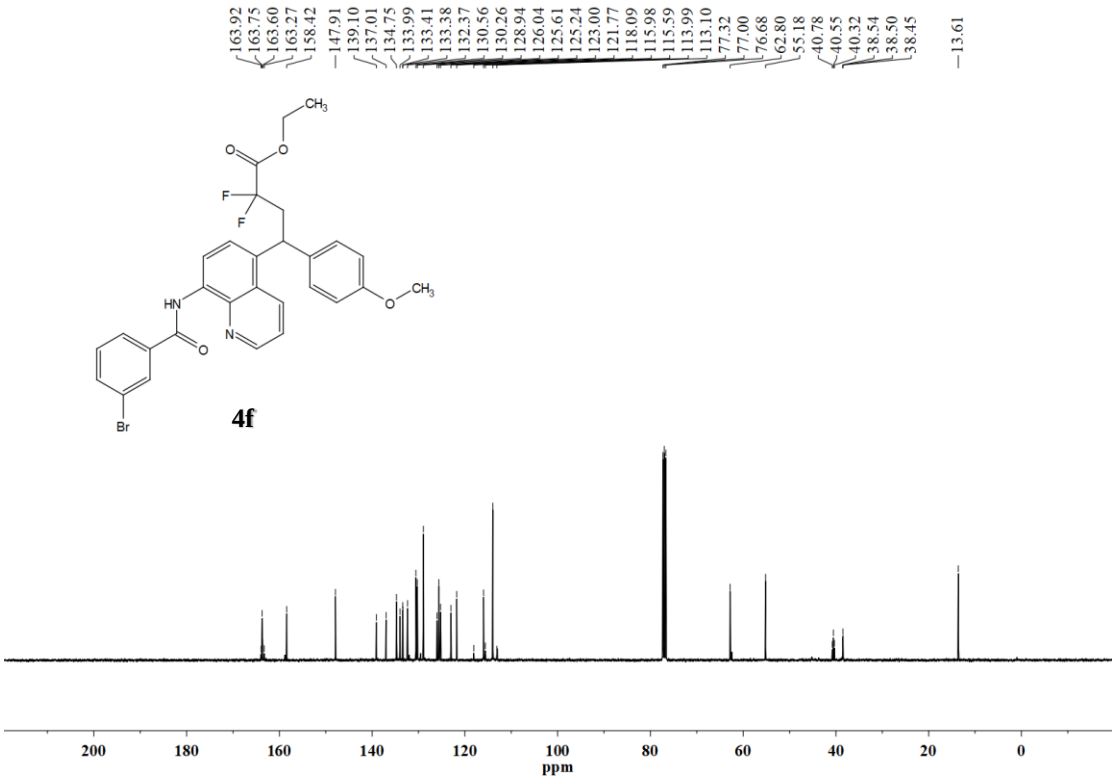
^{19}F NMR (376 MHz, Chloroform-*d*)



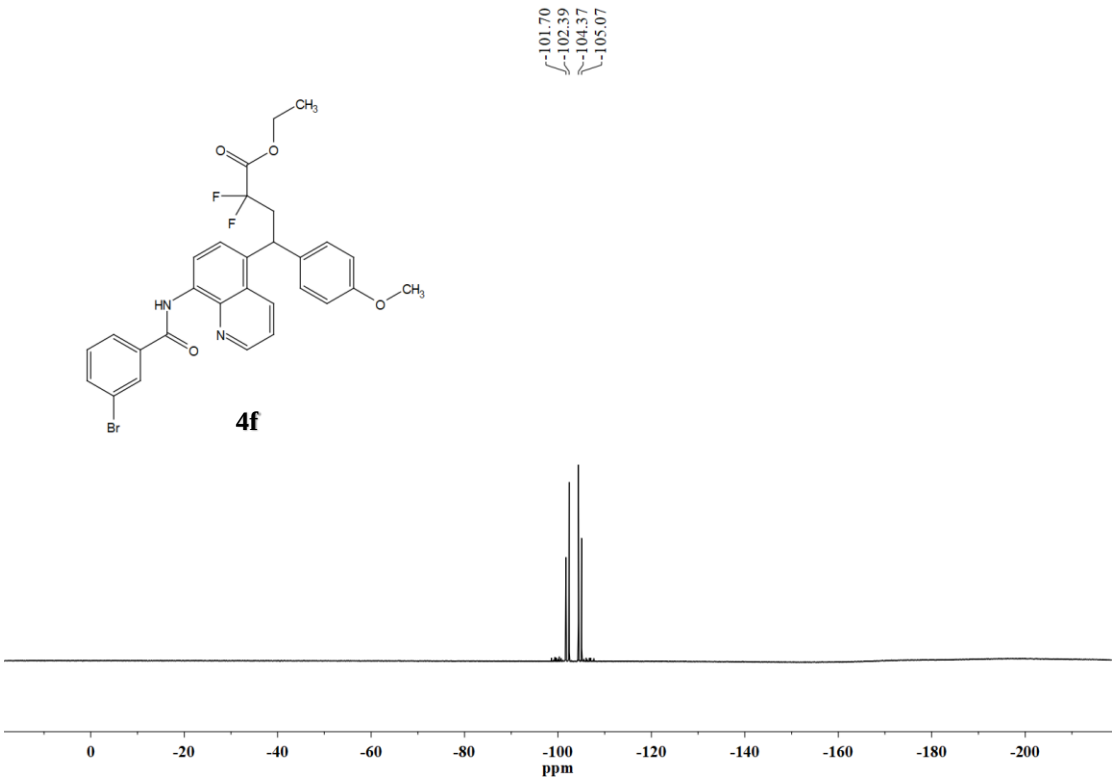
^{1}H NMR (400 MHz, Chloroform-*d*)



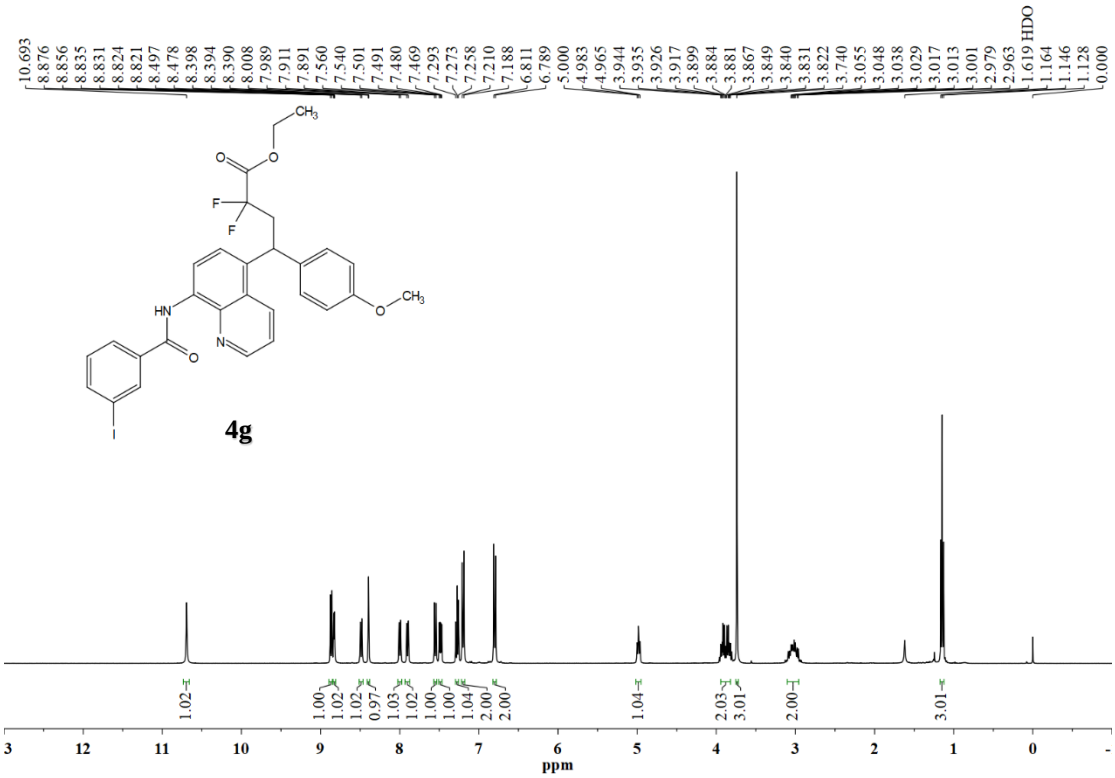
^{13}C NMR (101 MHz, Chloroform-*d*)



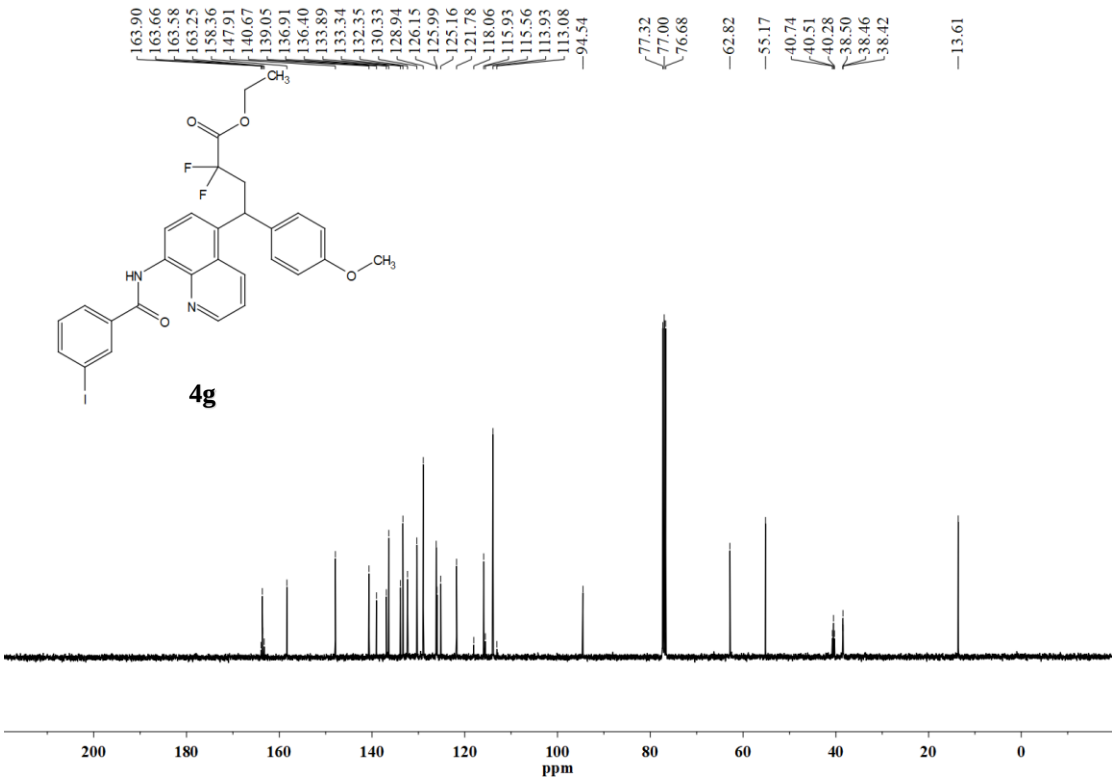
^{19}F NMR (376 MHz, Chloroform-*d*)



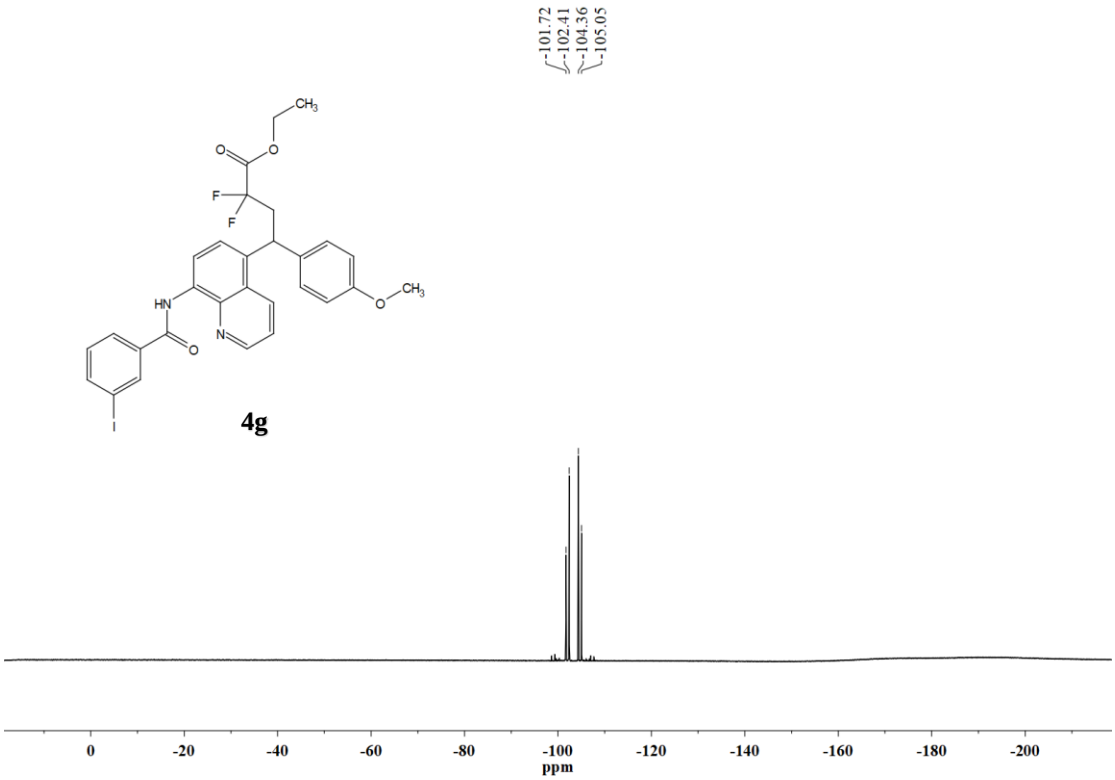
^{1}H NMR (400 MHz, Chloroform-*d*)



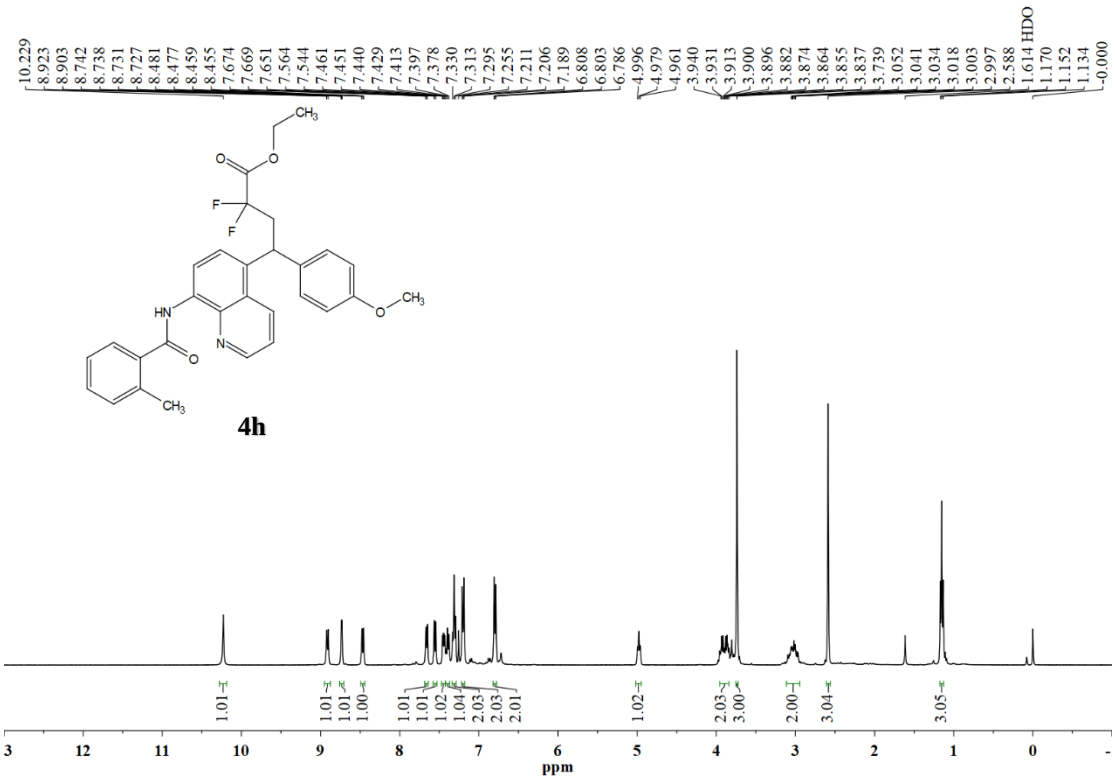
^{13}C NMR (101 MHz, Chloroform-*d*)



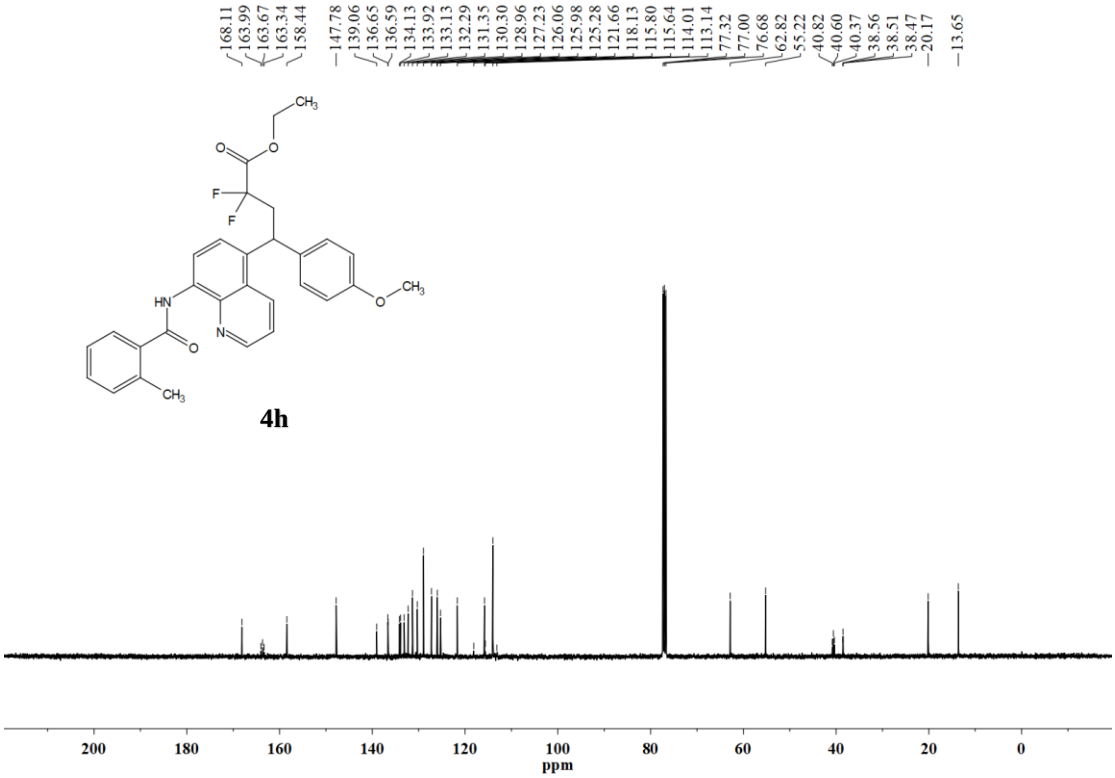
^{19}F NMR (376 MHz, Chloroform-*d*)



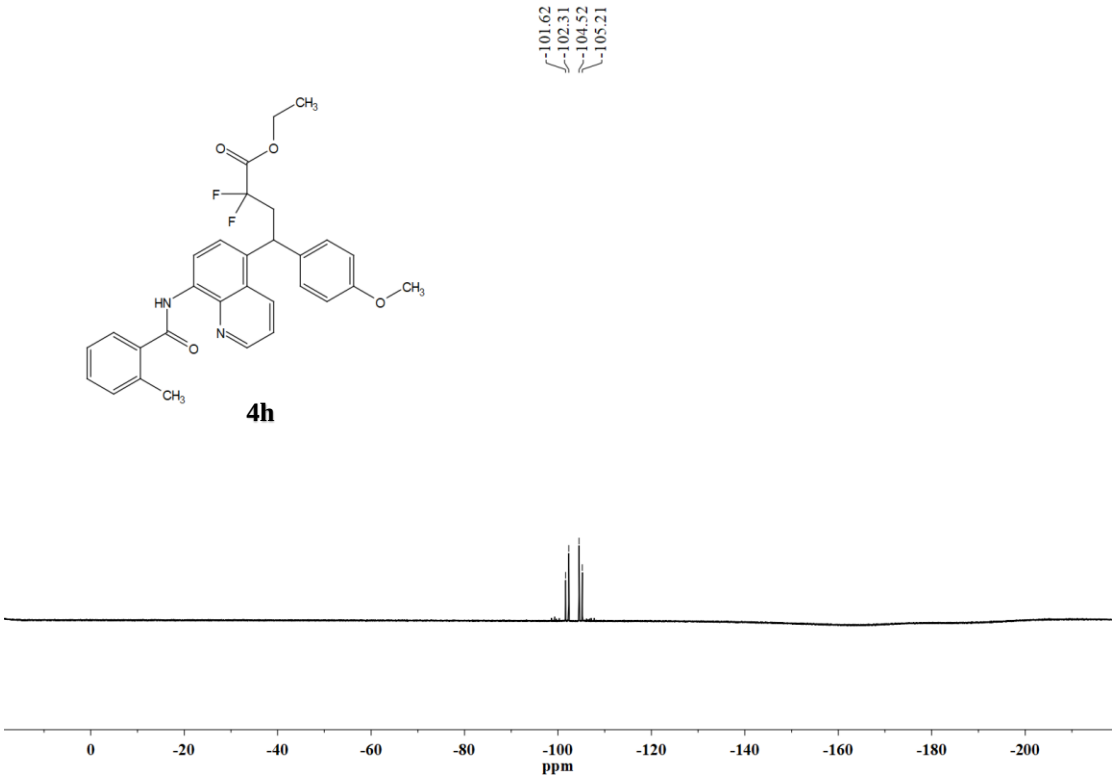
^{1}H NMR (400 MHz, Chloroform-*d*)



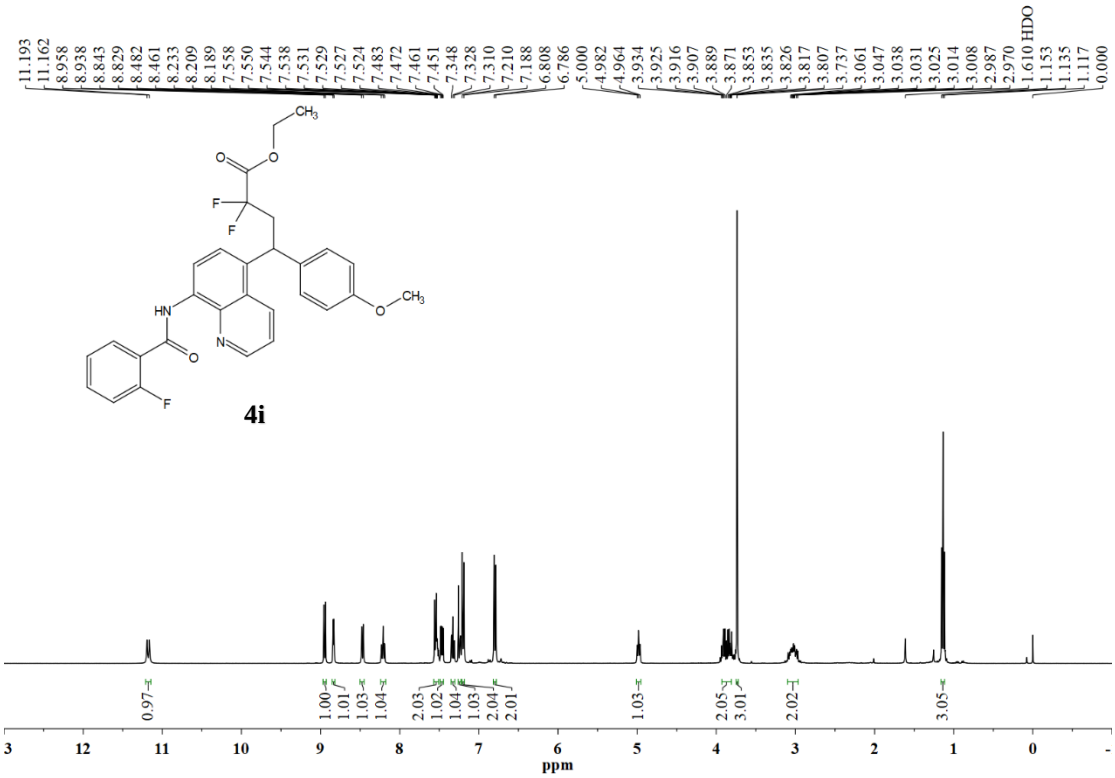
^{13}C NMR (101 MHz, Chloroform-*d*)



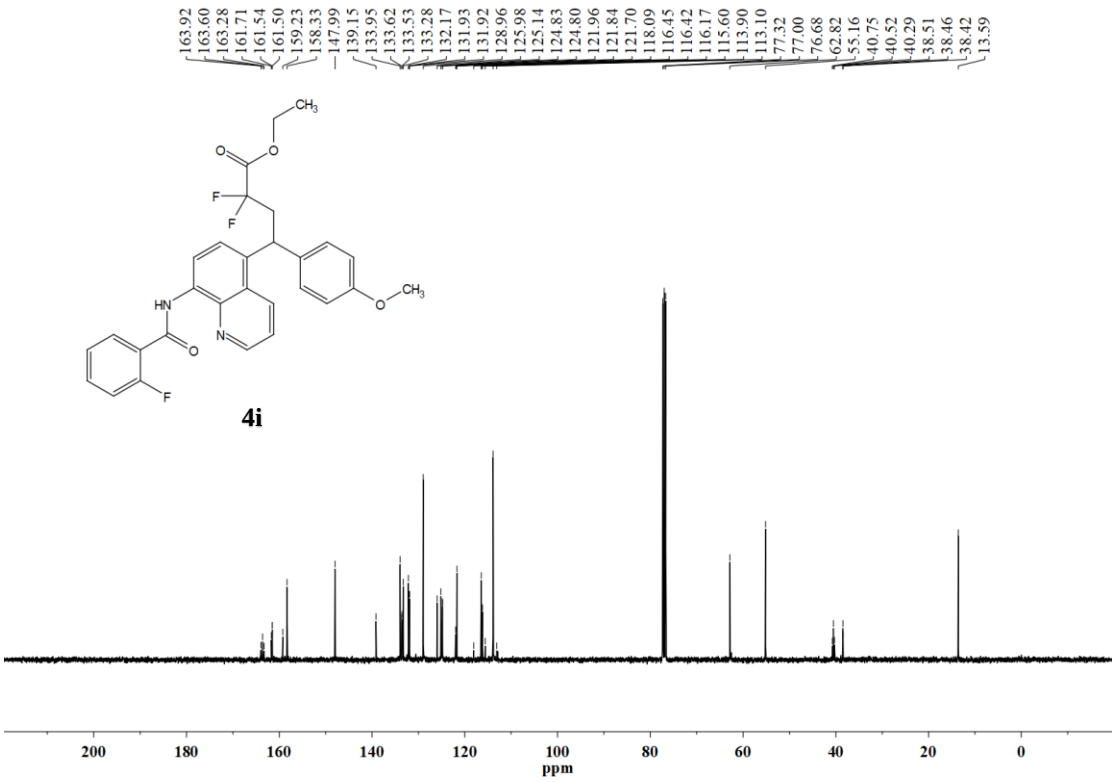
^{19}F NMR (376 MHz, Chloroform-*d*)



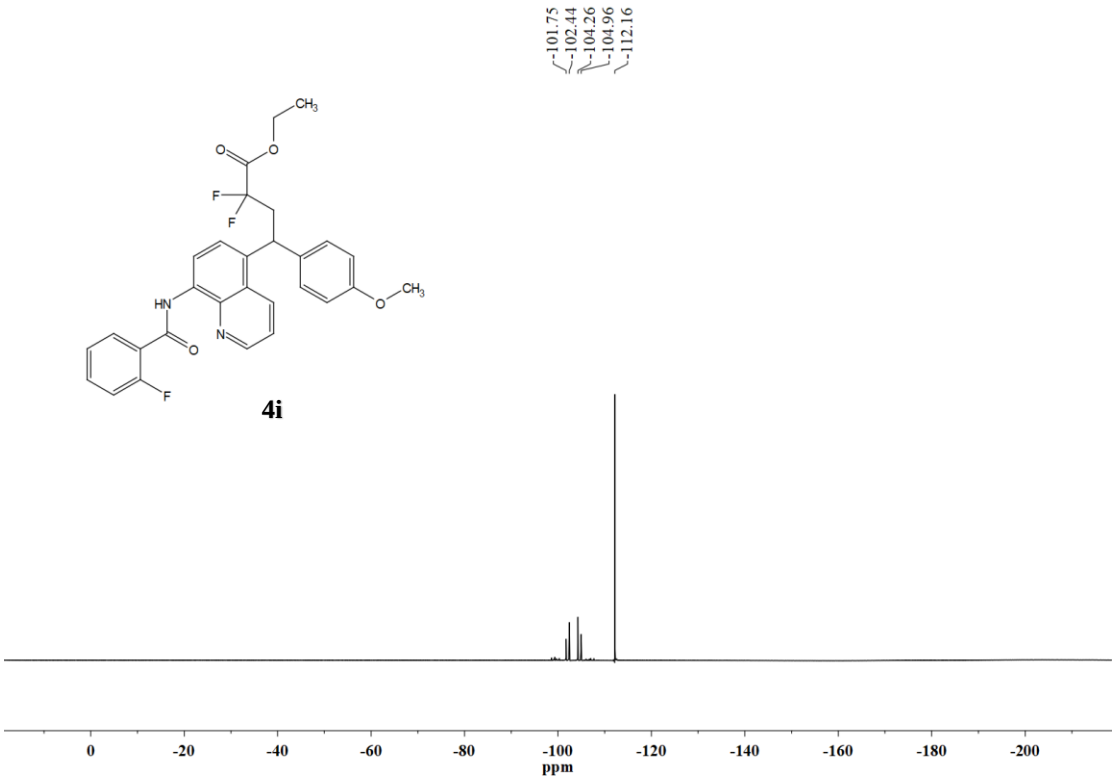
^{1}H NMR (400 MHz, Chloroform-*d*)



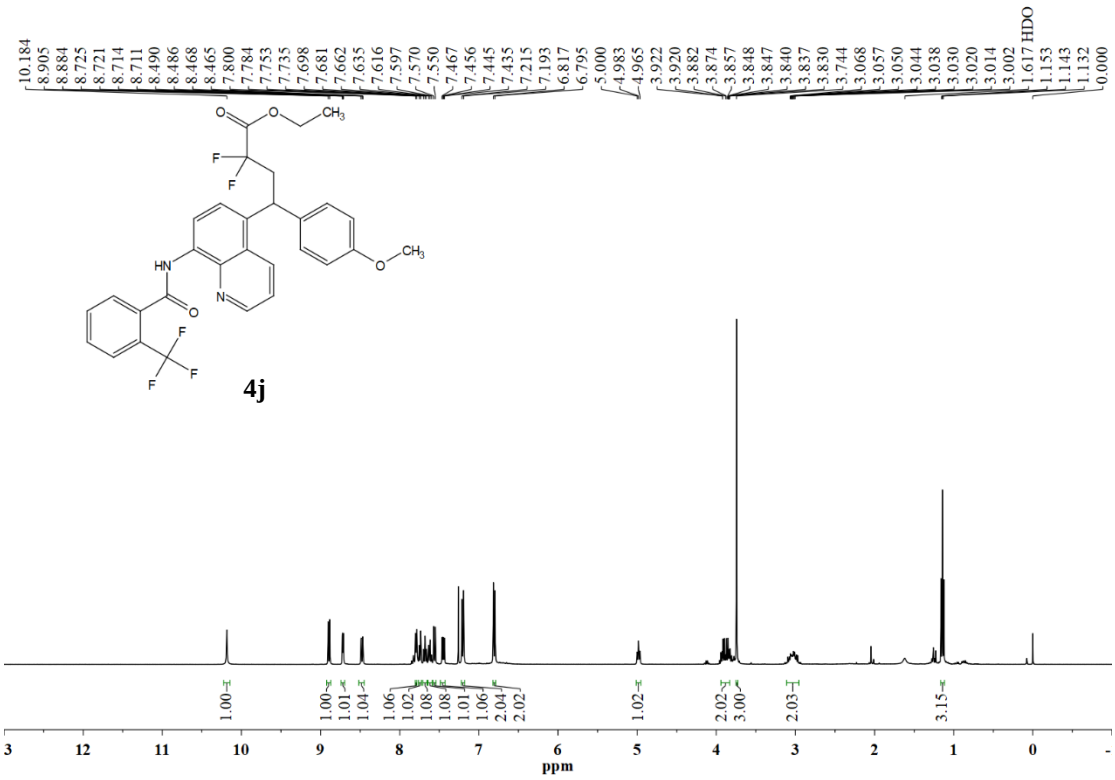
^{13}C NMR (101 MHz, Chloroform-*d*)



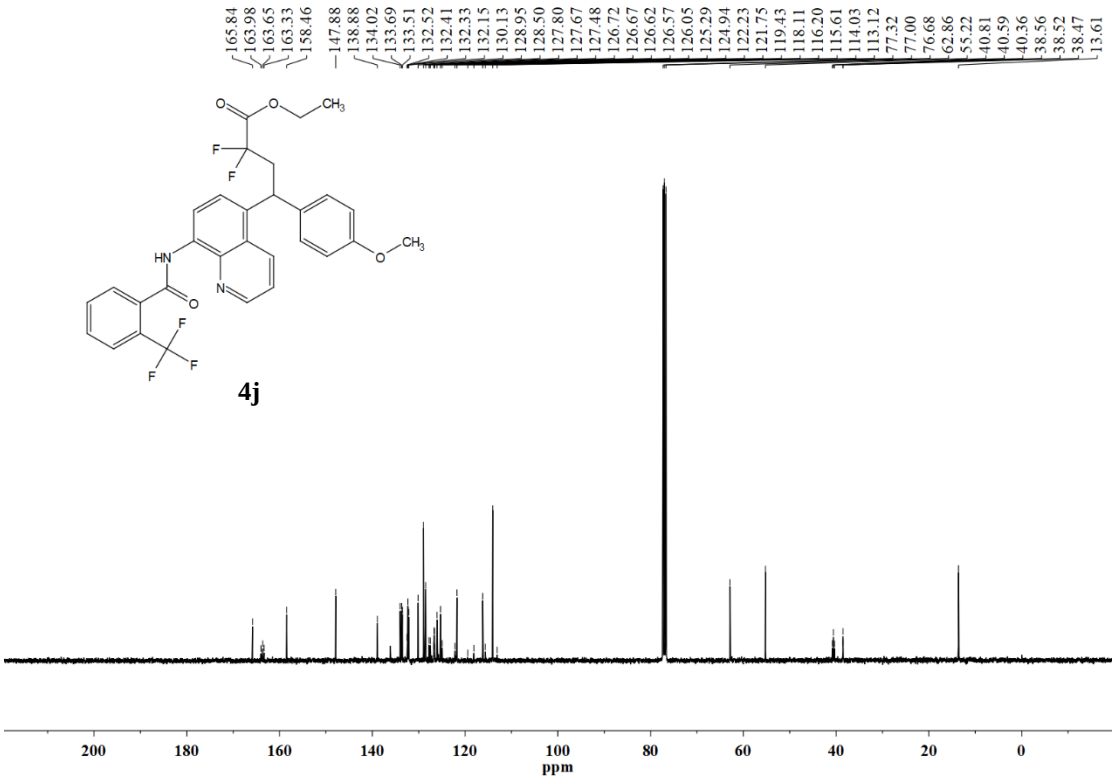
^{19}F NMR (376 MHz, Chloroform-*d*)



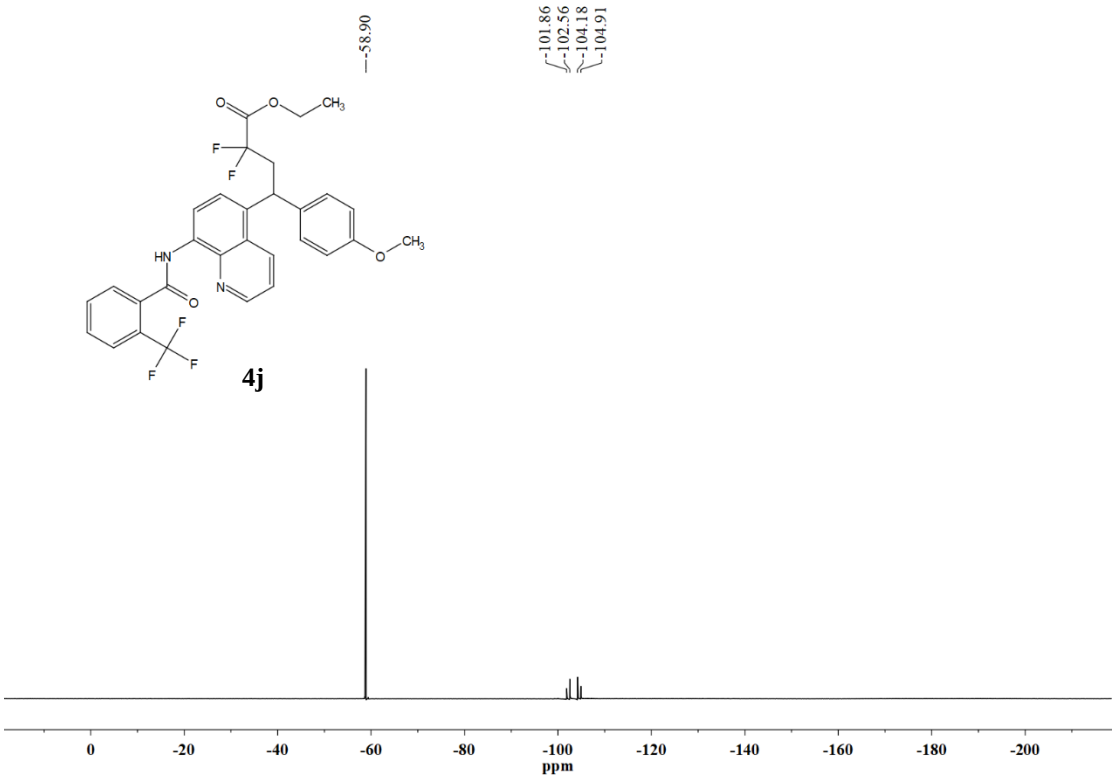
^{1}H NMR (400 MHz, Chloroform-*d*)



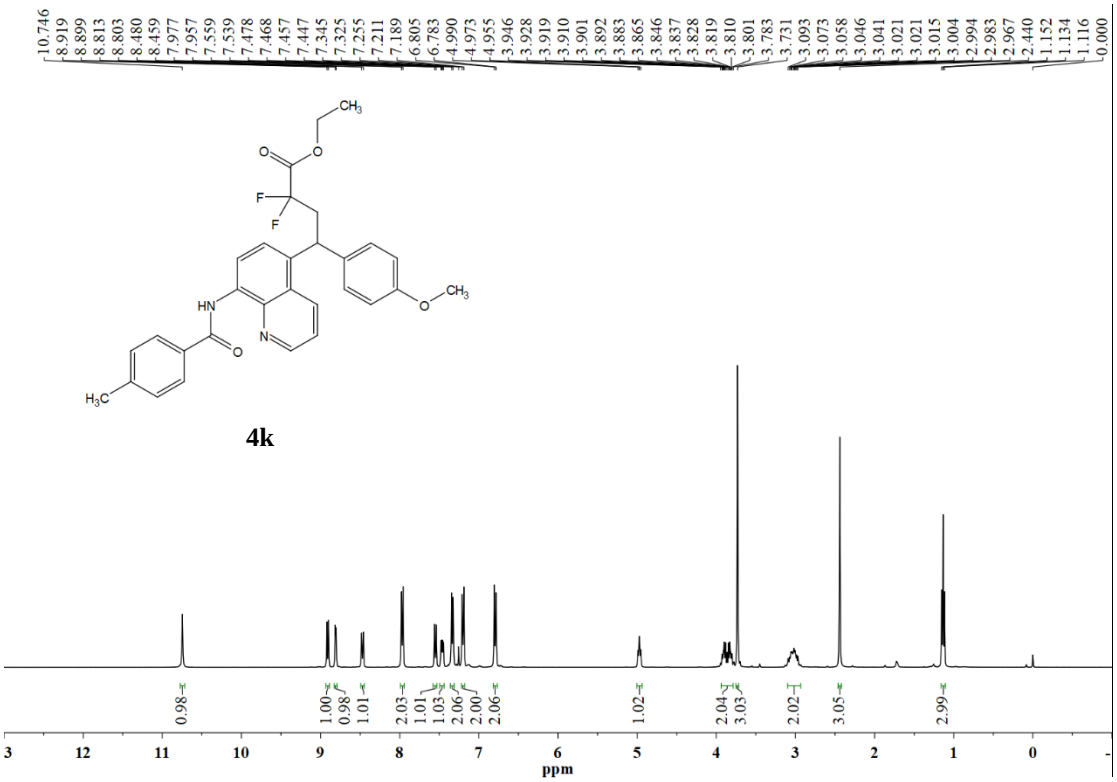
^{13}C NMR (101 MHz, Chloroform-*d*)



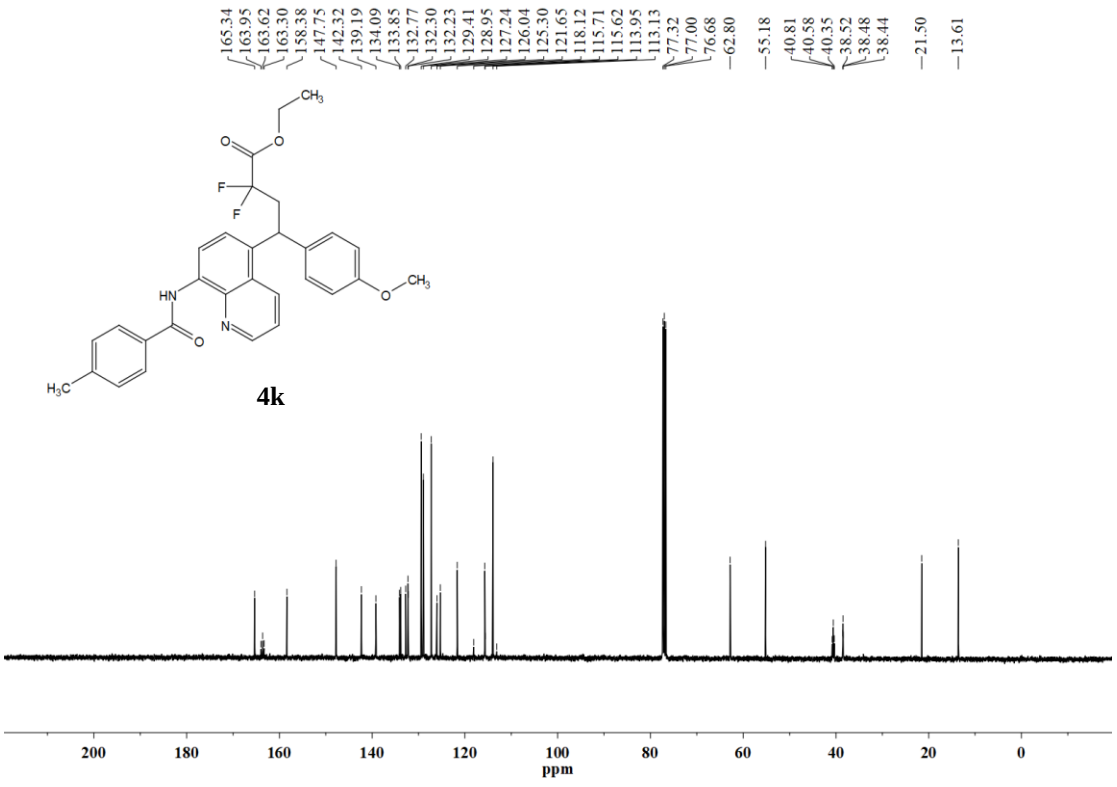
^{19}F NMR (376 MHz, Chloroform-*d*)



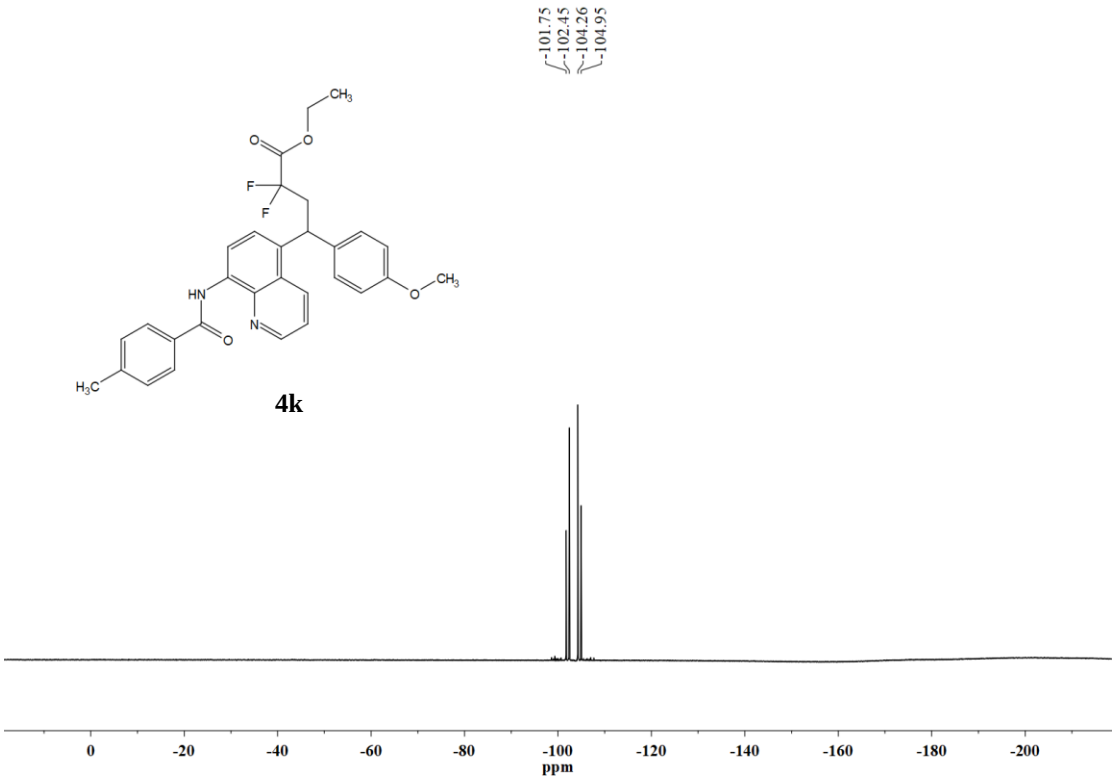
^{1}H NMR (400 MHz, Chloroform-*d*)



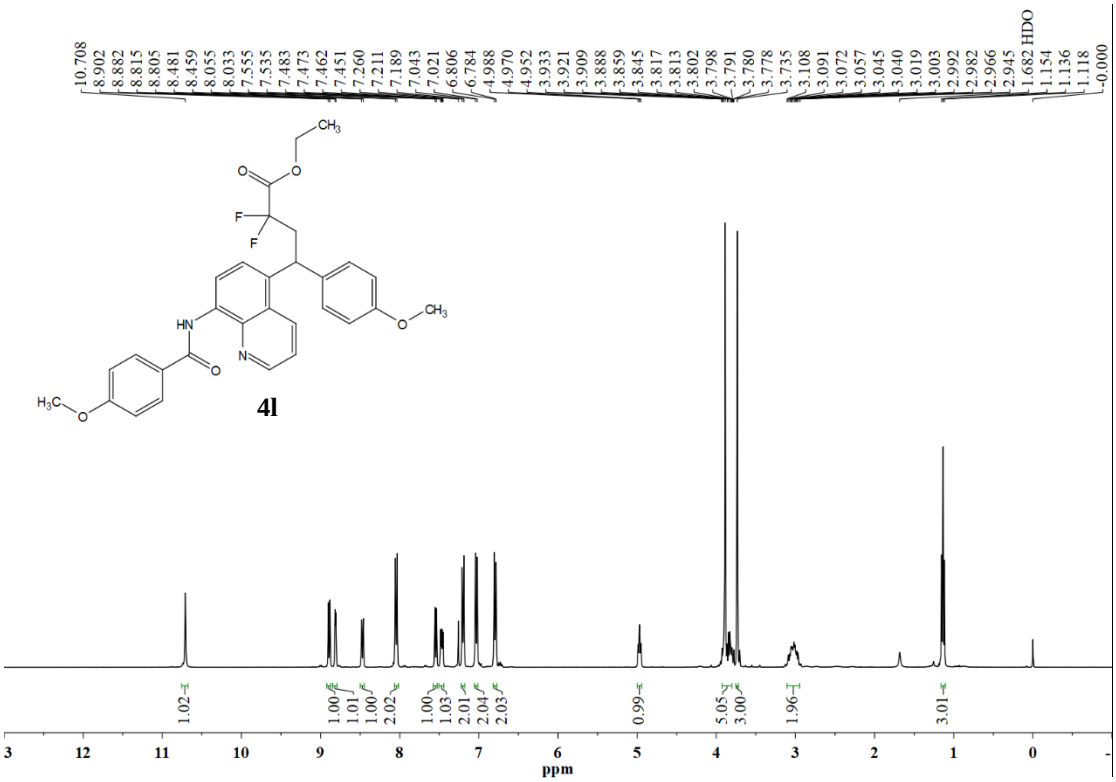
^{13}C NMR (101 MHz, Chloroform-*d*)



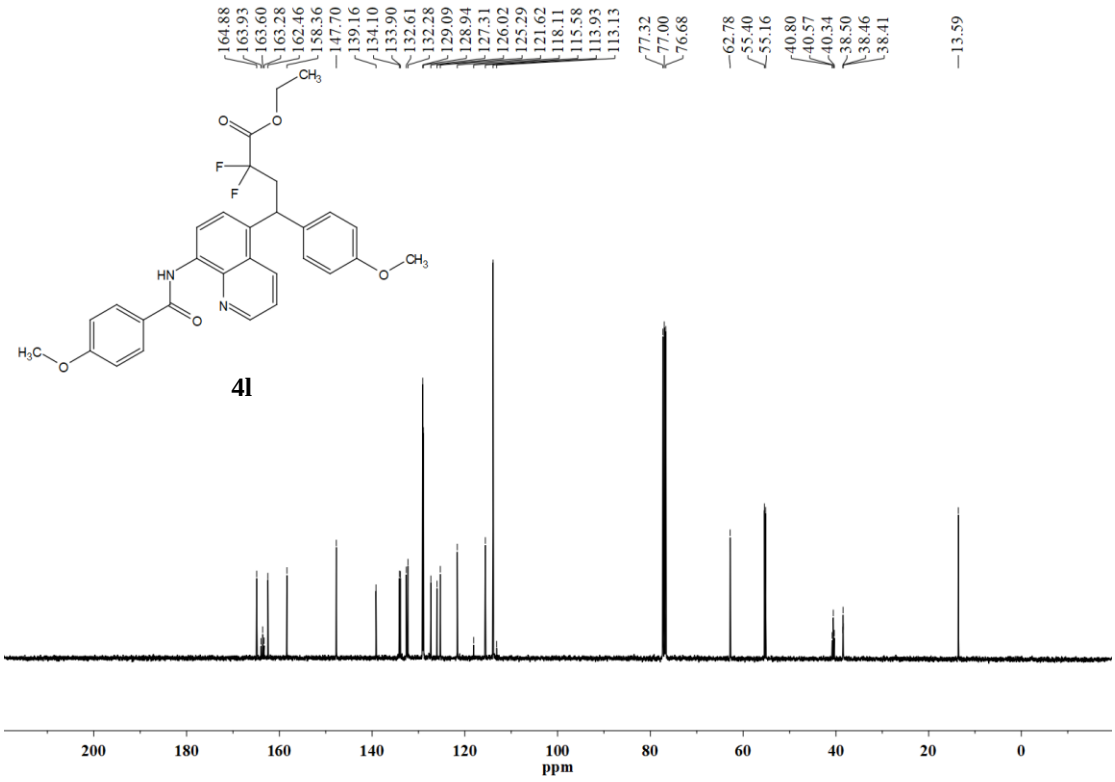
^{19}F NMR (376 MHz, Chloroform-*d*)



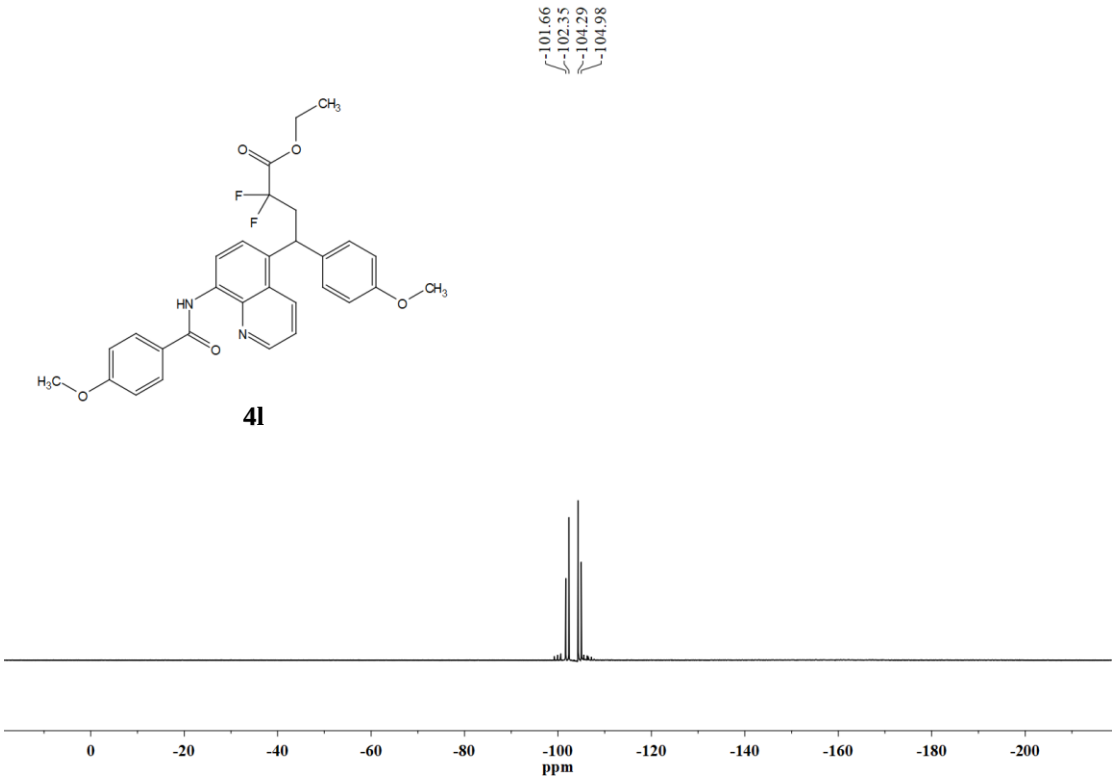
^{1}H NMR (400 MHz, Chloroform-*d*)



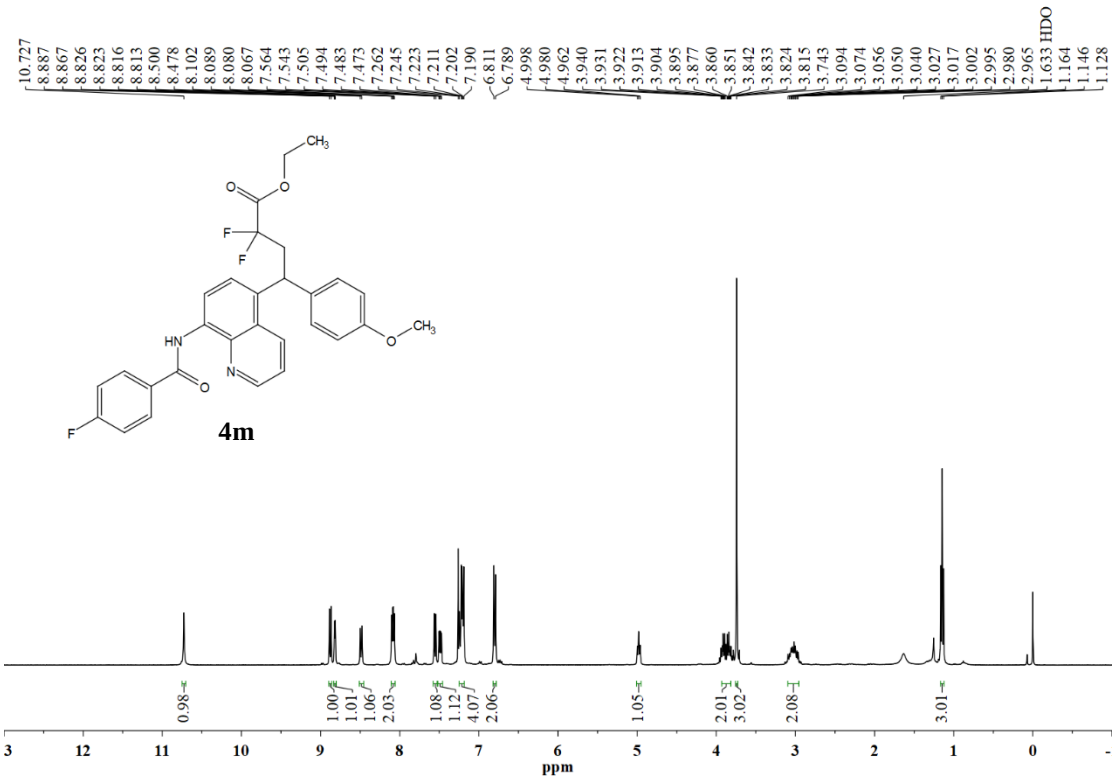
^{13}C NMR (101 MHz, Chloroform-*d*)



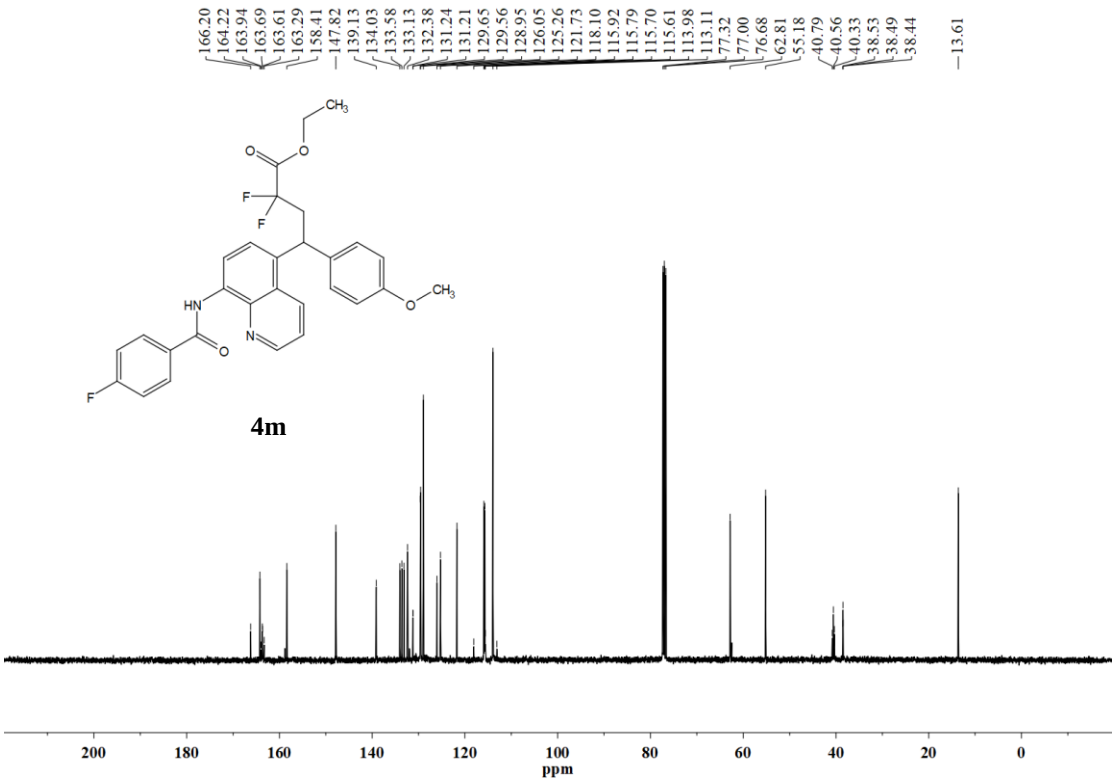
^{19}F NMR (376 MHz, Chloroform-*d*)



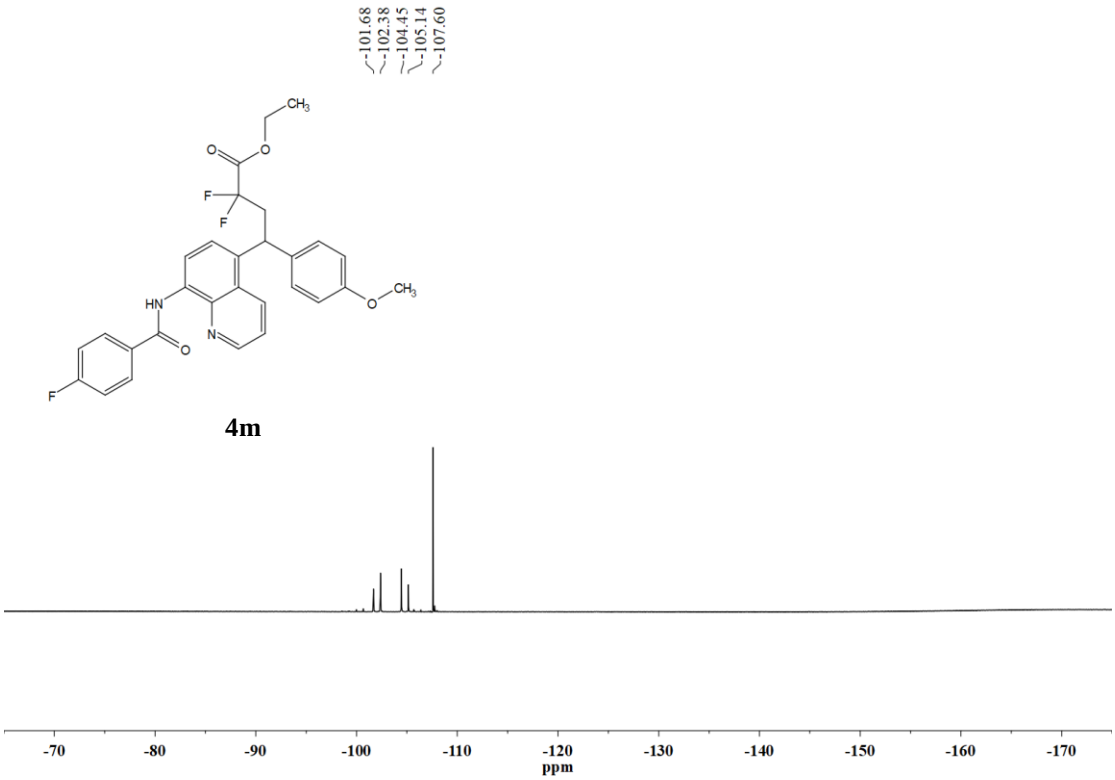
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

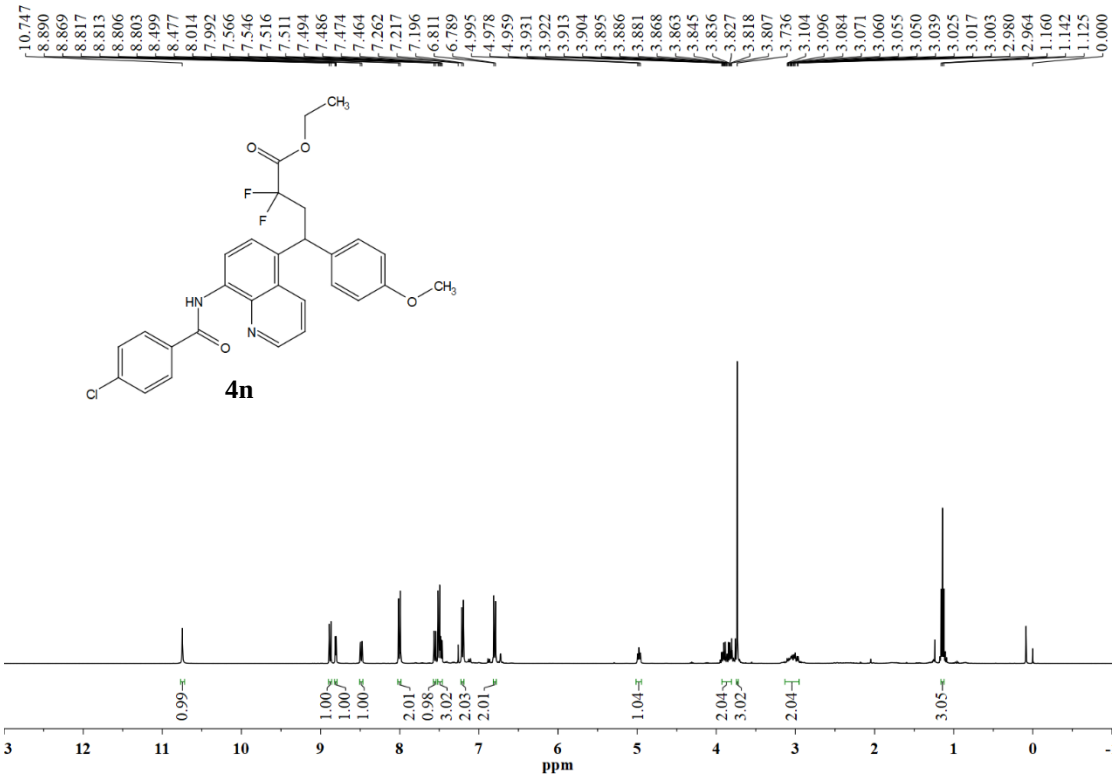


^{19}F NMR (376 MHz, Chloroform-*d*)



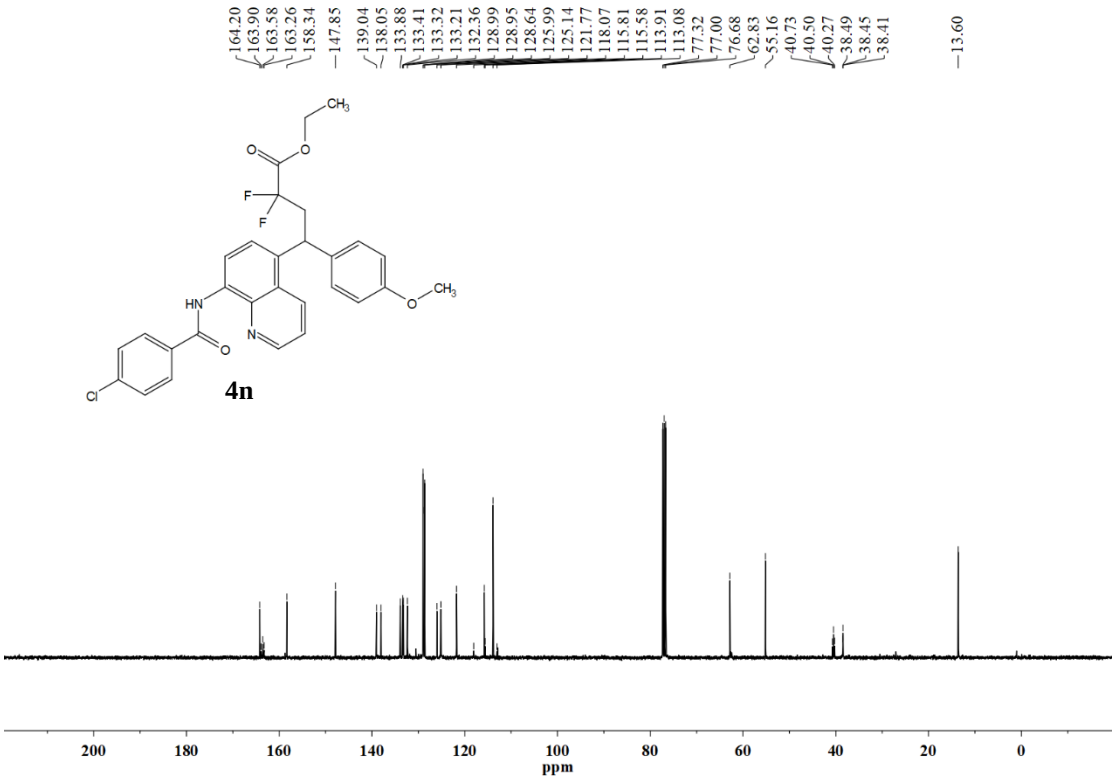
4m

^{1}H NMR (400 MHz, Chloroform-*d*)

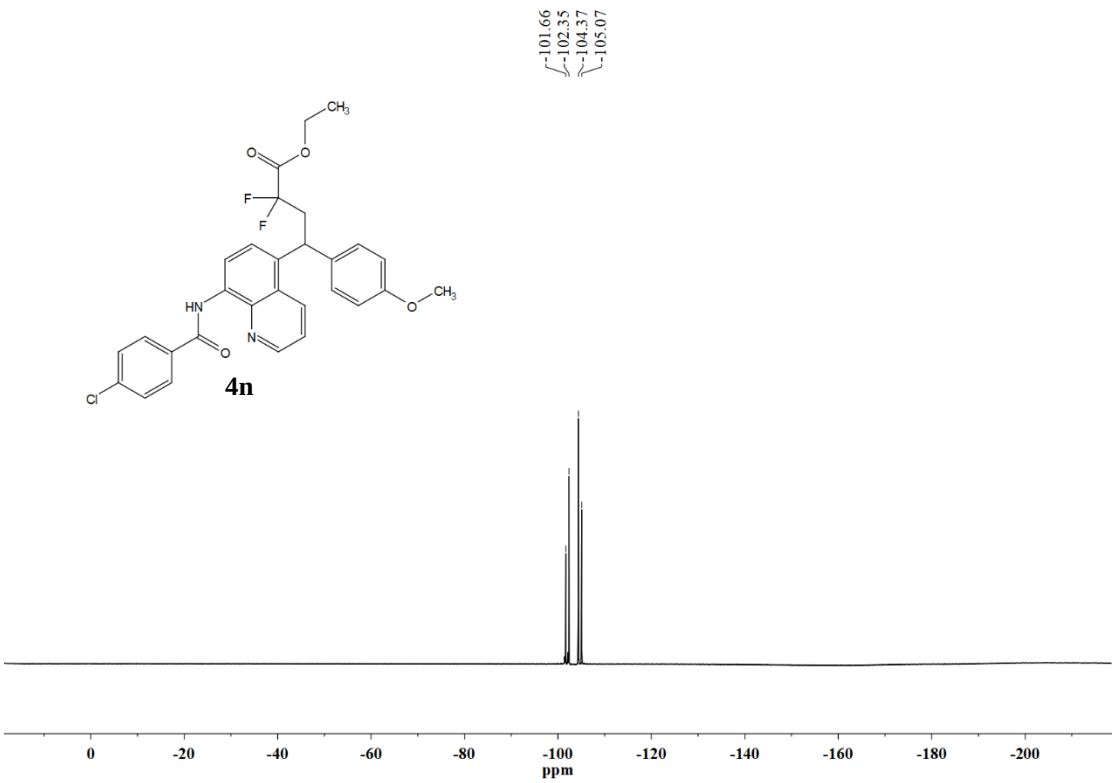


4n

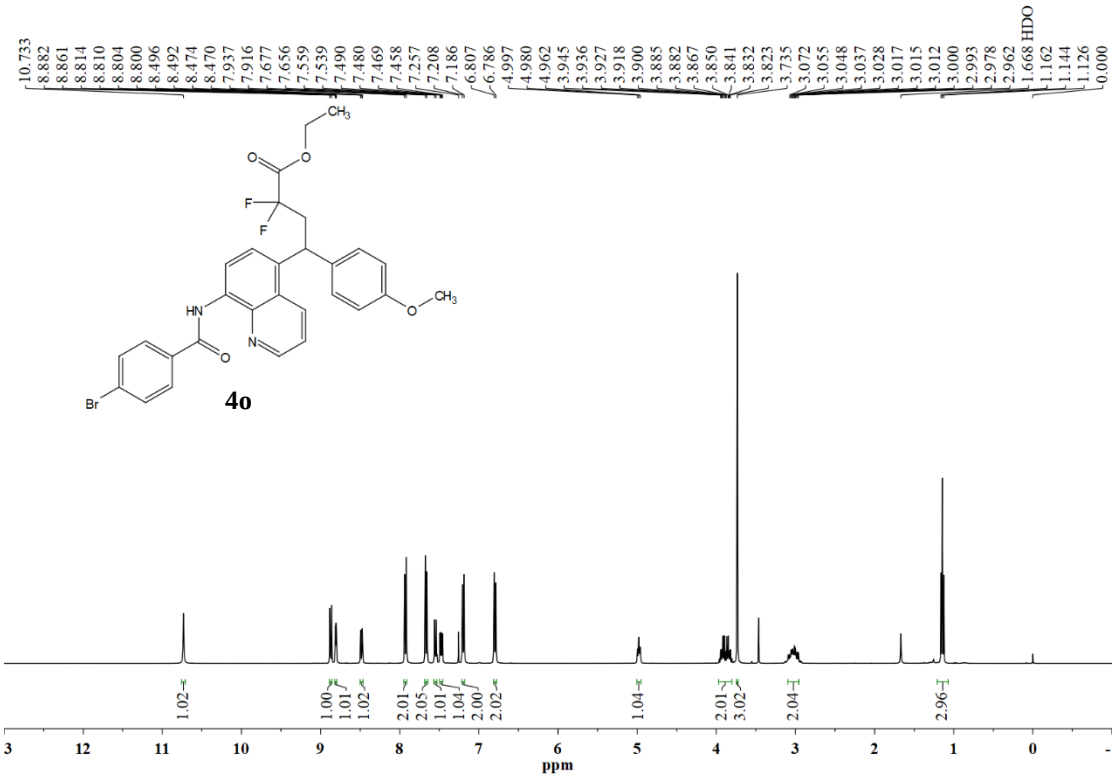
^{13}C NMR (101 MHz, Chloroform-*d*)



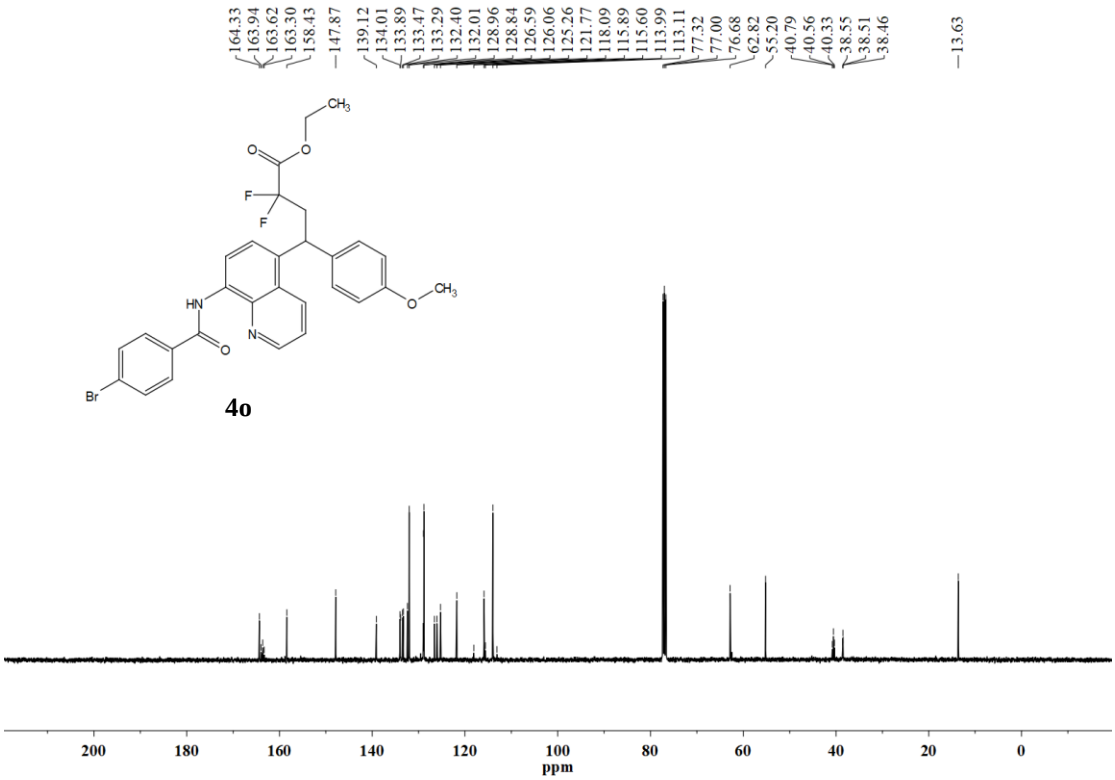
^{19}F NMR (376 MHz, Chloroform-*d*)



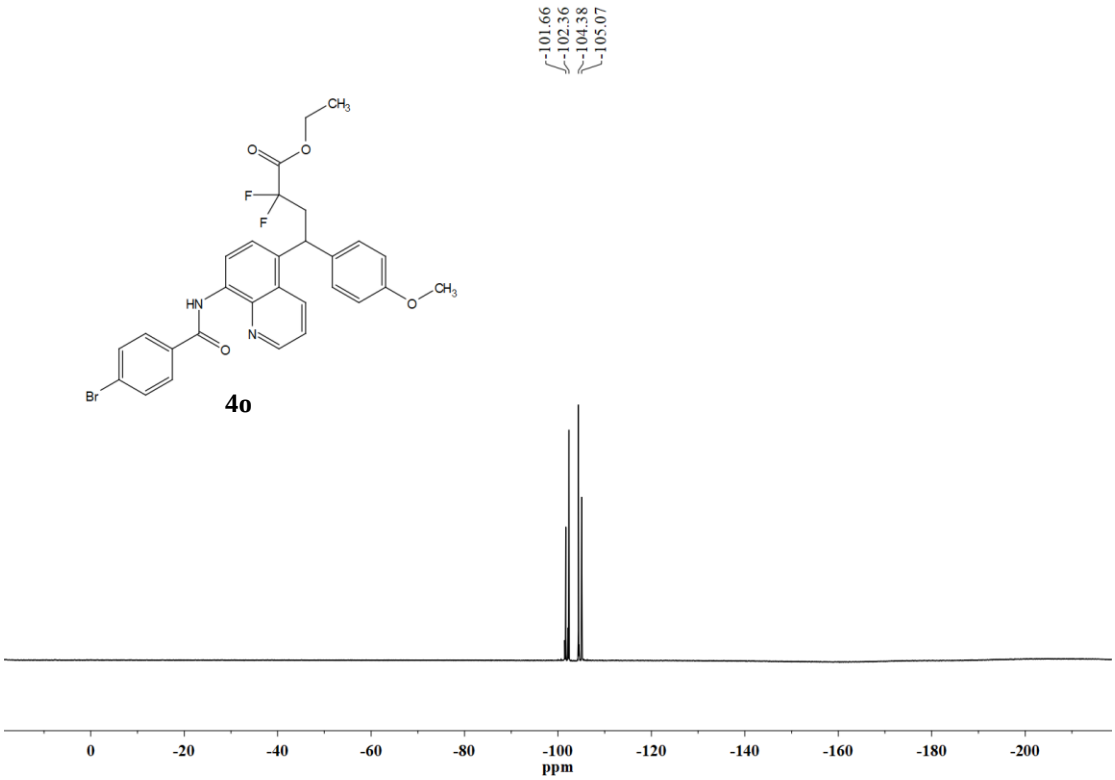
^{1}H NMR (400 MHz, Chloroform-*d*)



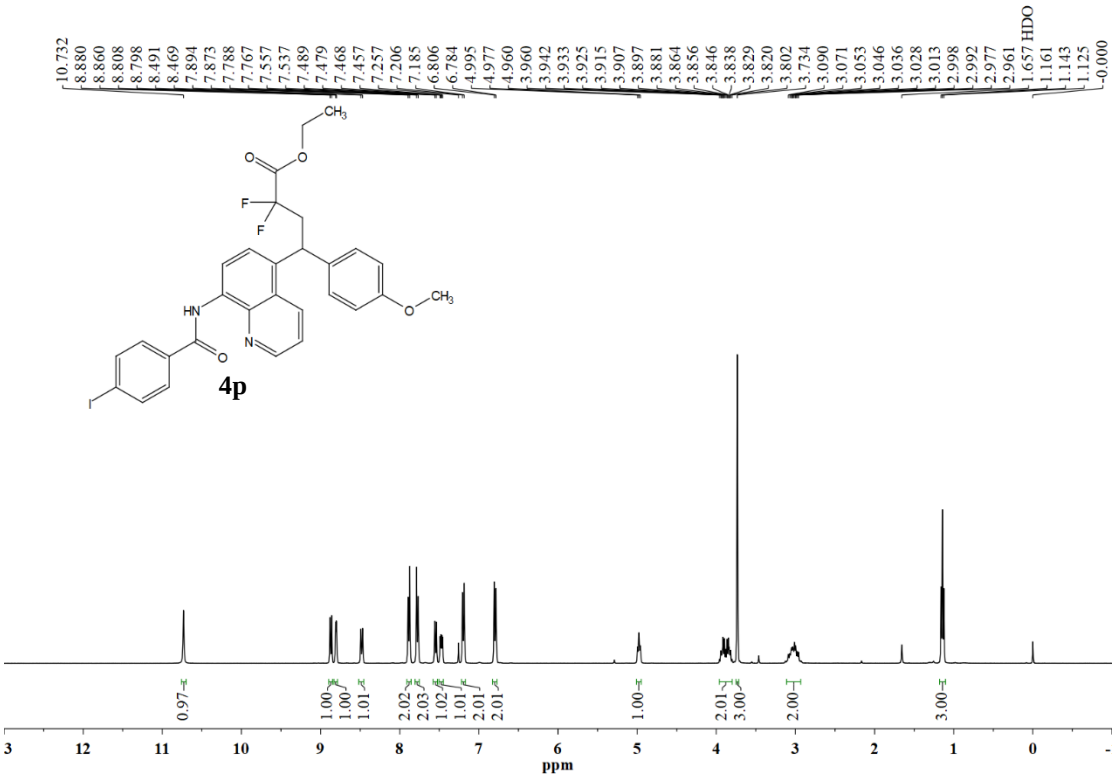
^{13}C NMR (101 MHz, Chloroform-*d*)



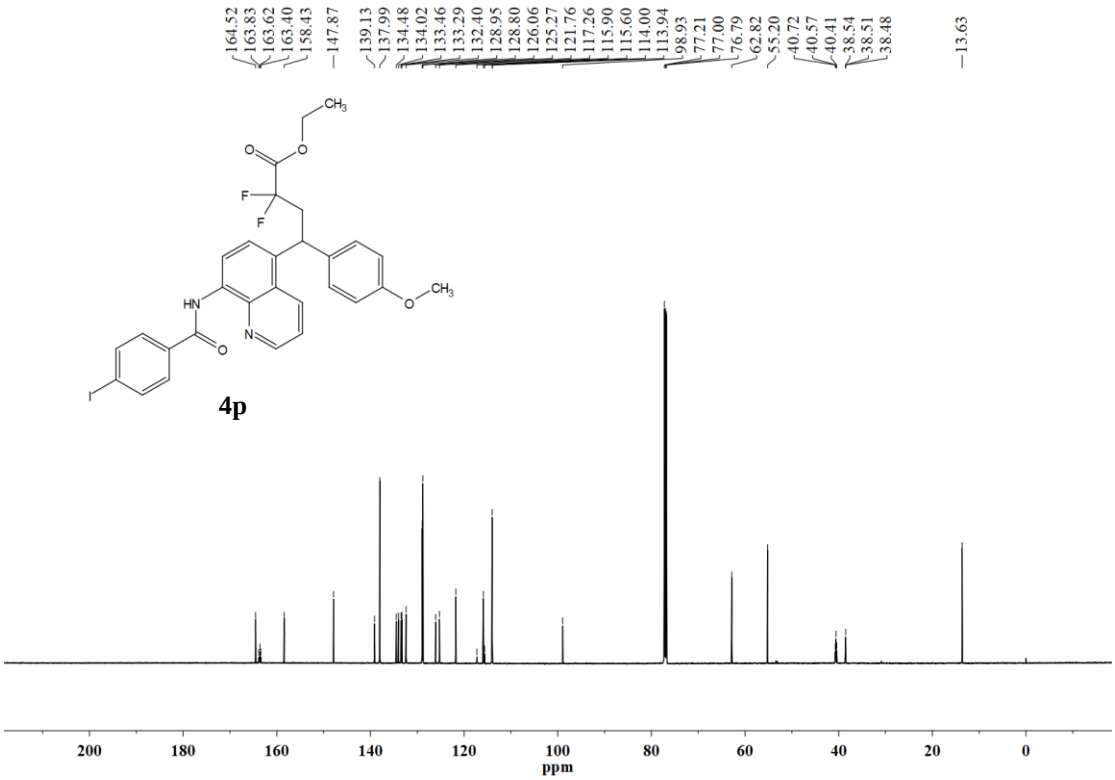
^{19}F NMR (376 MHz, Chloroform-*d*)



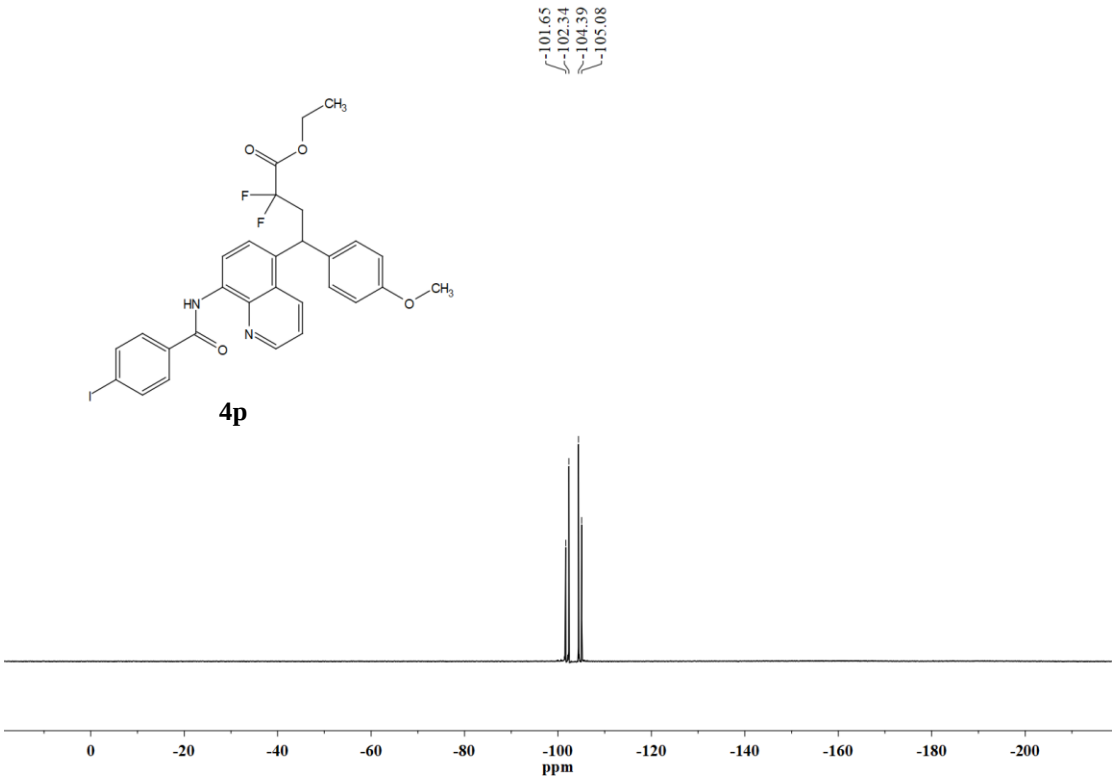
^{1}H NMR (400 MHz, Chloroform-*d*)



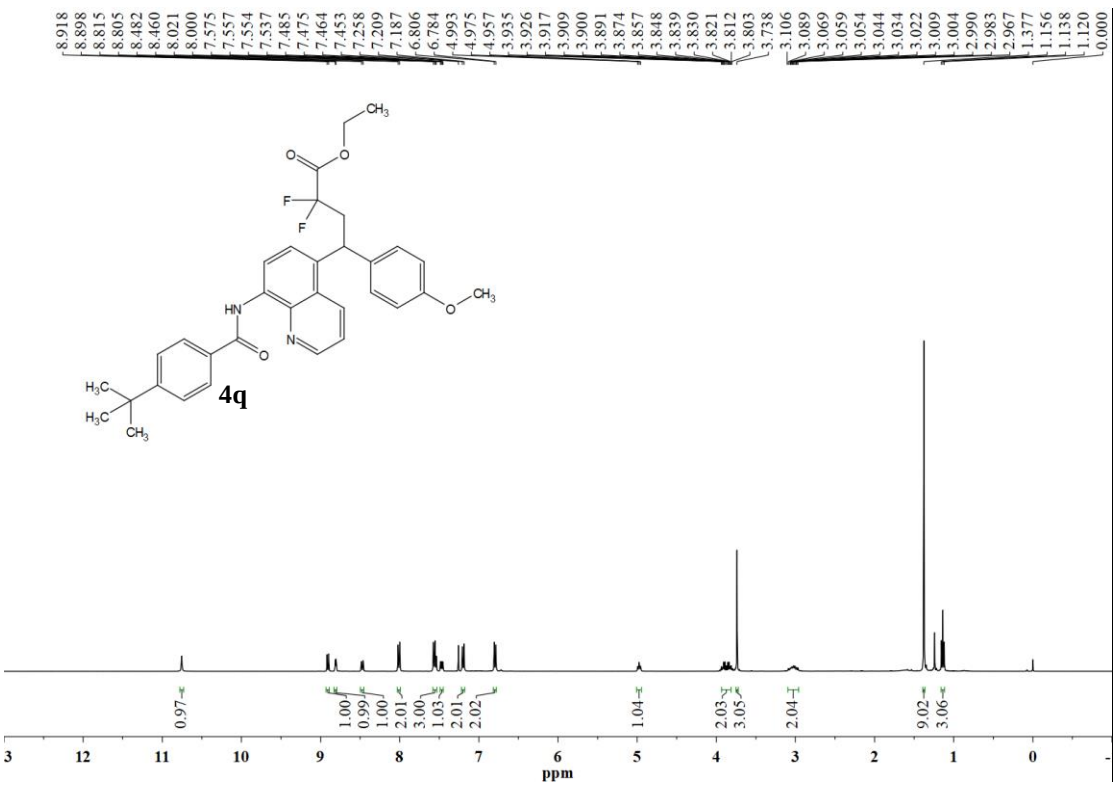
^{13}C NMR (151 MHz, Chloroform-*d*)



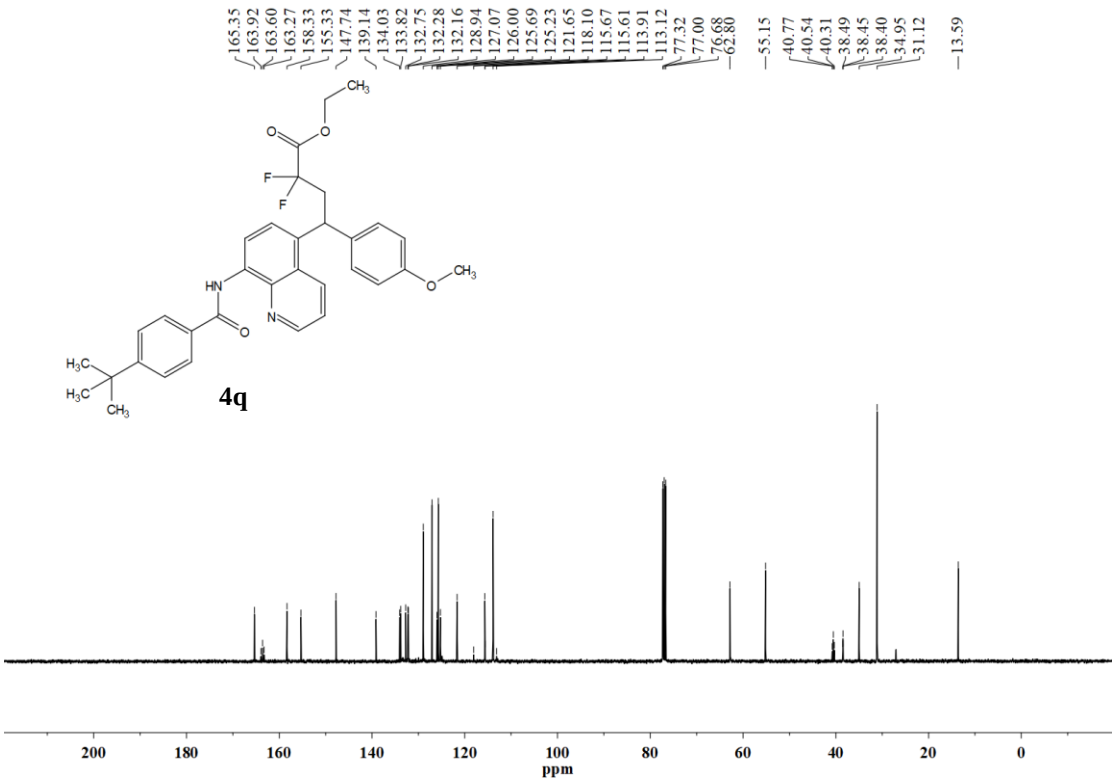
^{19}F NMR (376 MHz, Chloroform-*d*)



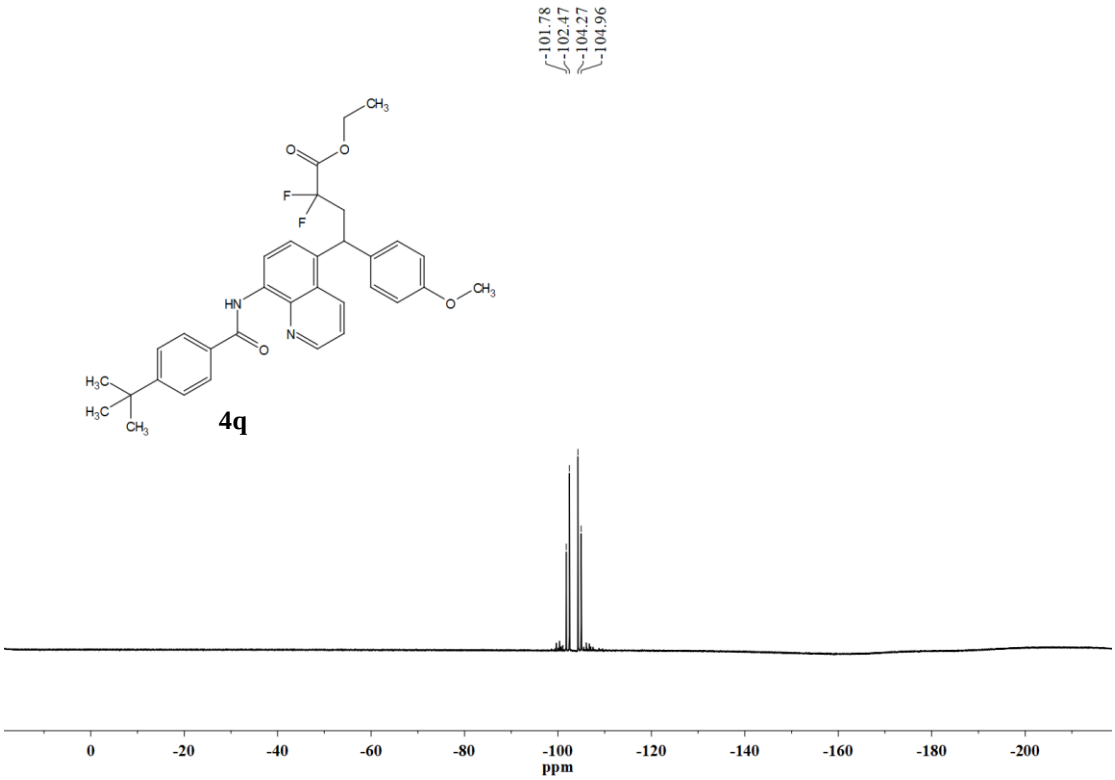
^{1}H NMR (400 MHz, Chloroform-*d*)



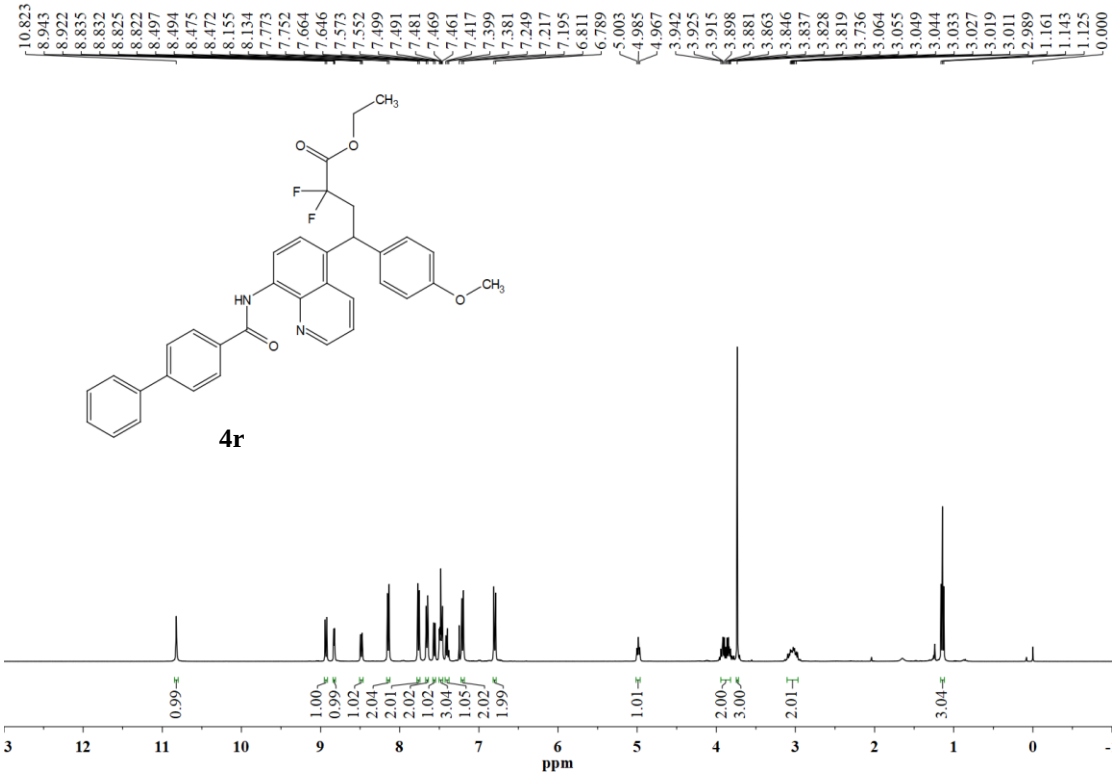
^{13}C NMR (101 MHz, Chloroform-*d*)



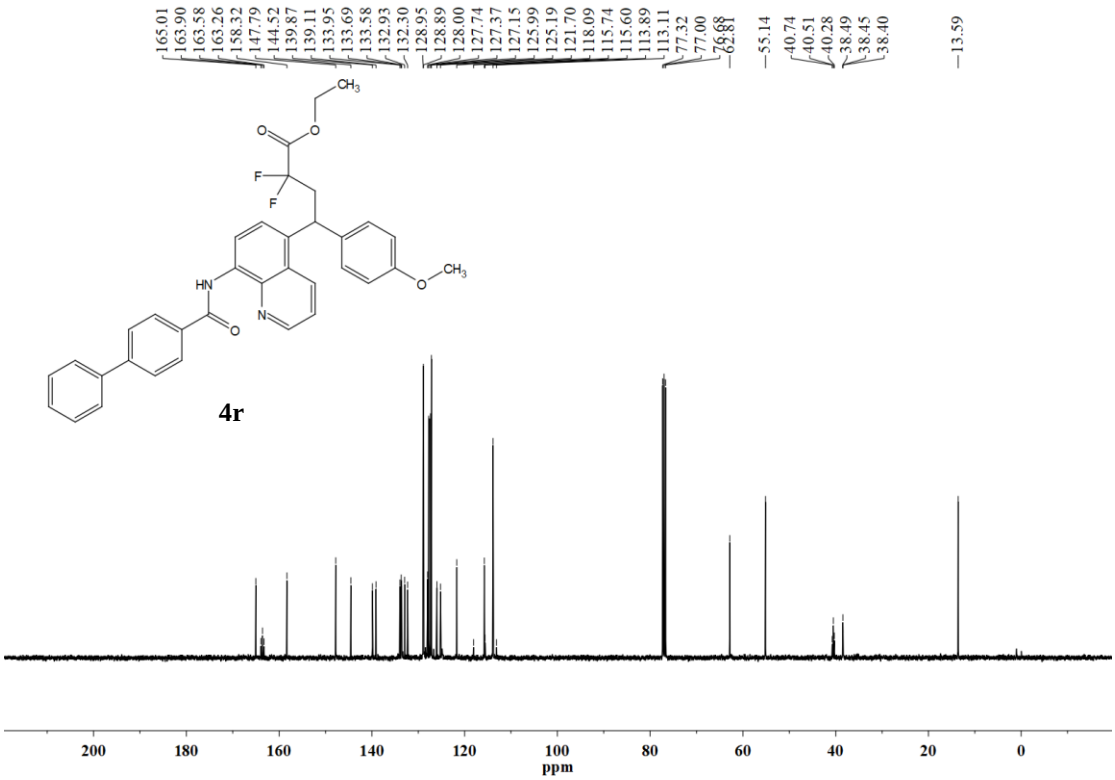
^{19}F NMR (376 MHz, Chloroform-*d*)



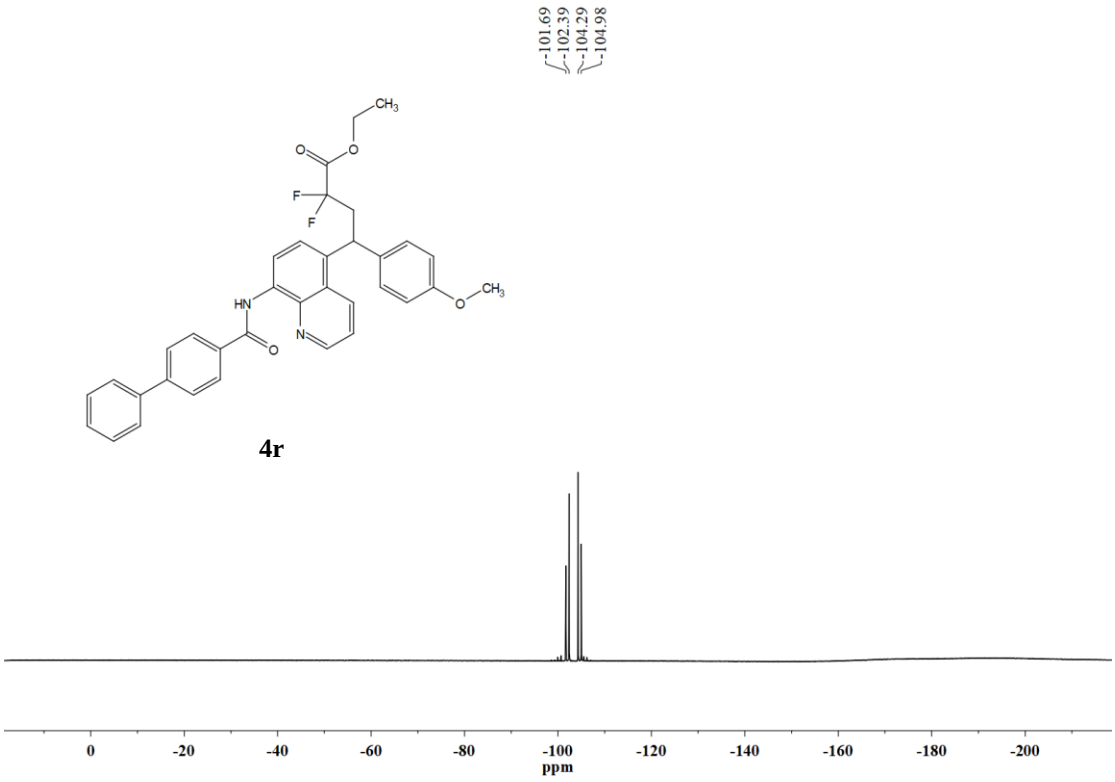
^{1}H NMR (400 MHz, Chloroform-*d*)



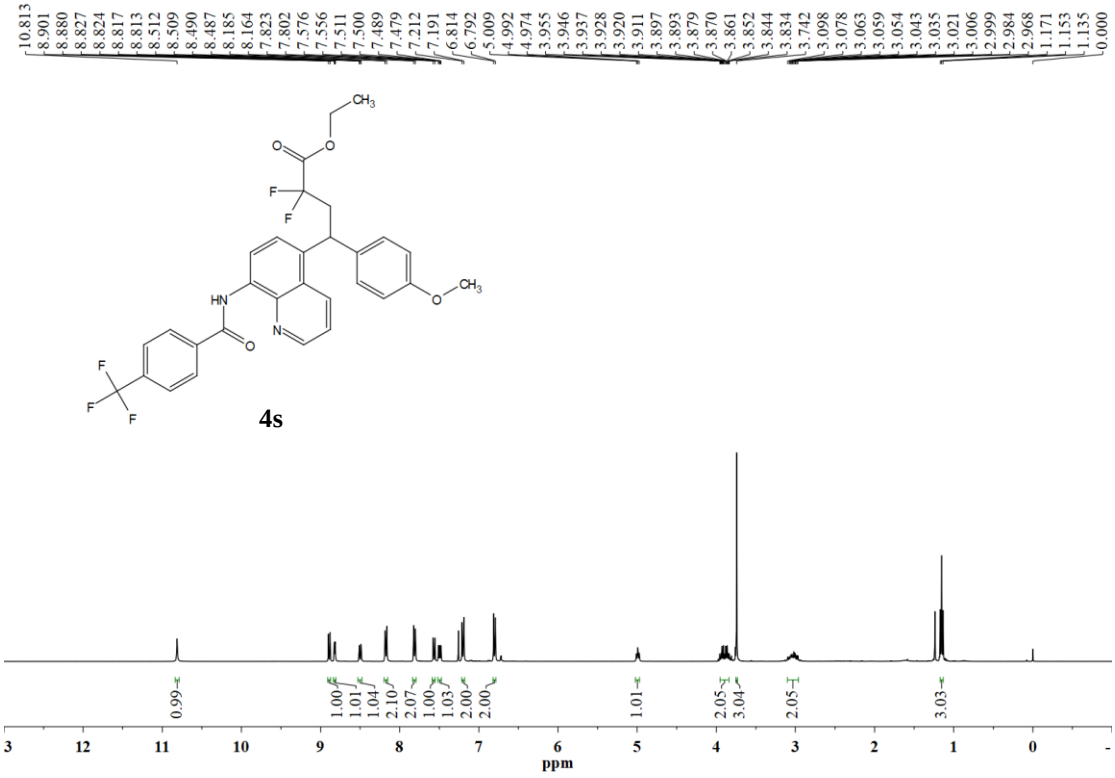
^{13}C NMR (101 MHz, Chloroform-*d*)



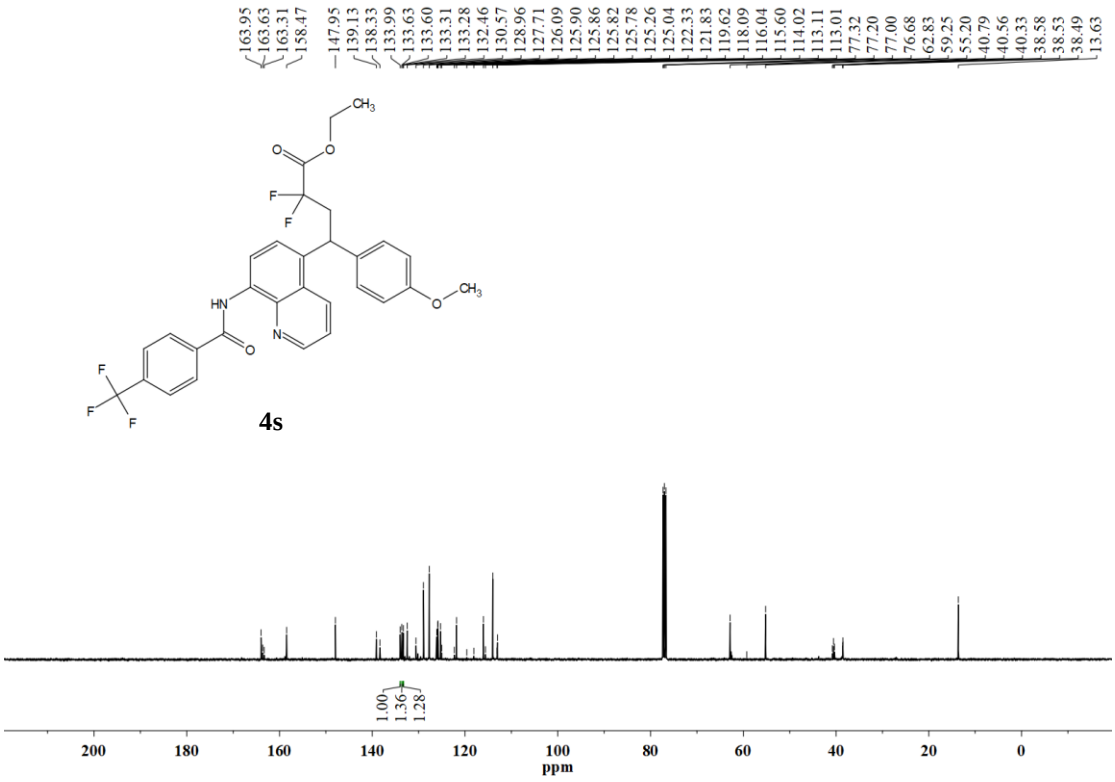
^{19}F NMR (376 MHz, Chloroform-*d*)



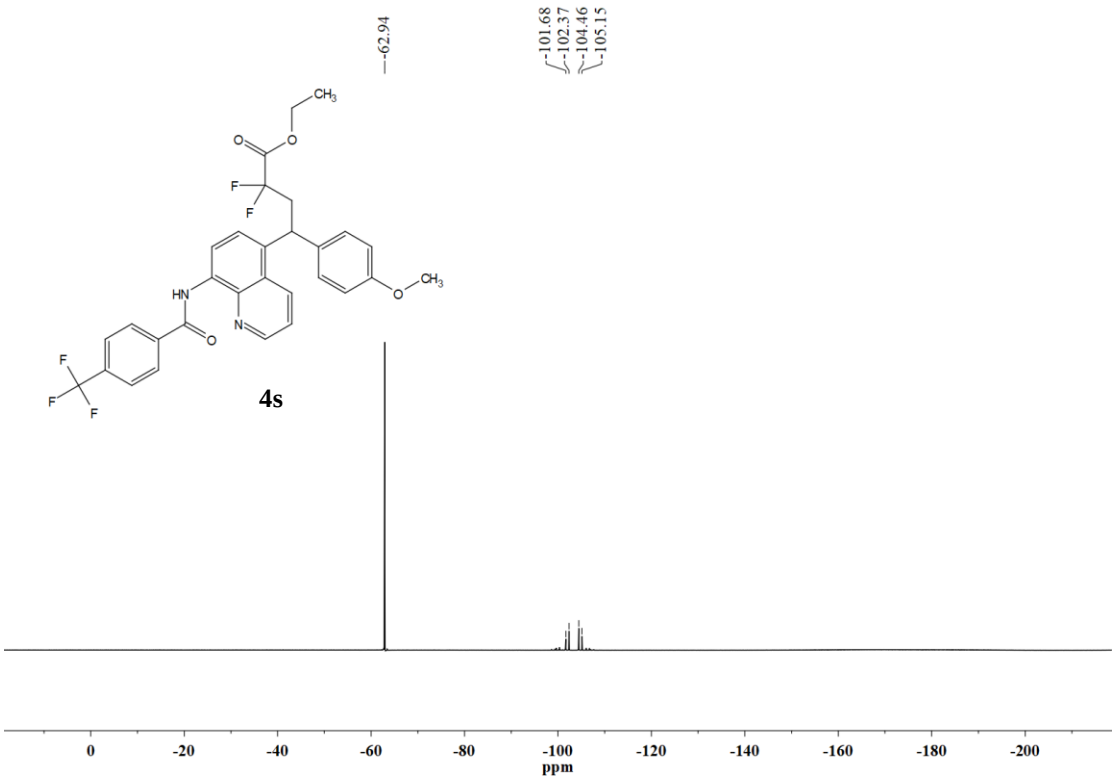
^{1}H NMR (400 MHz, Chloroform-*d*)



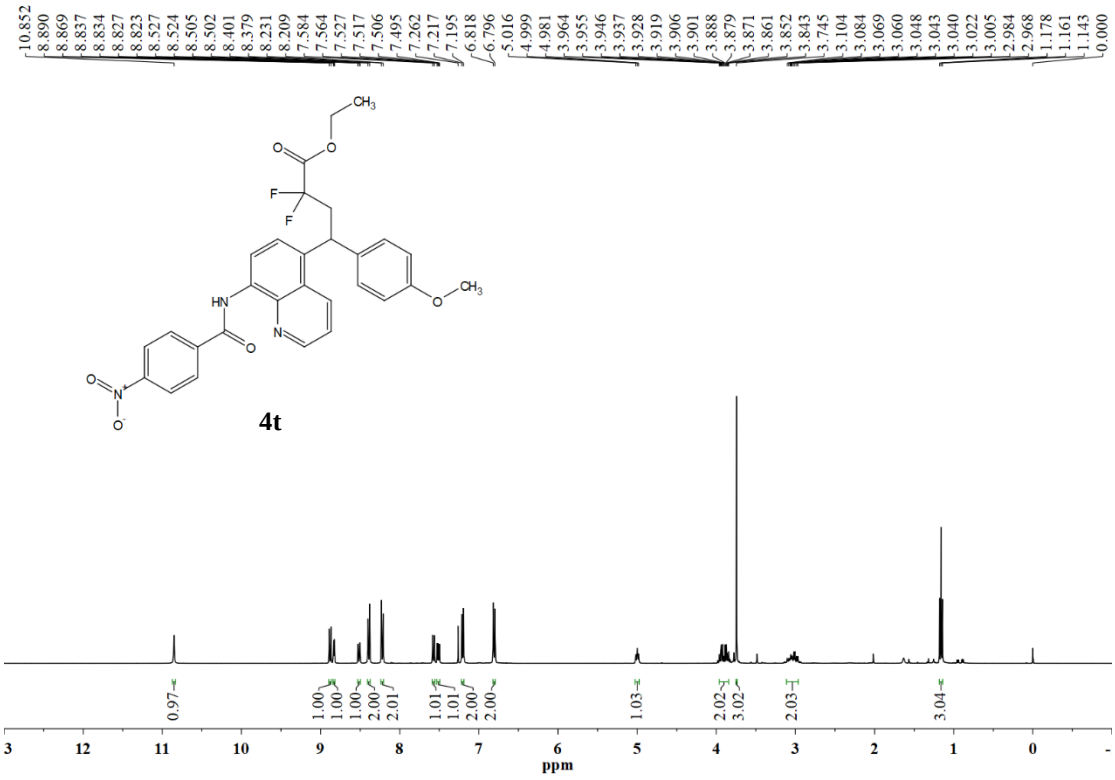
^{13}C NMR (101 MHz, Chloroform-*d*)



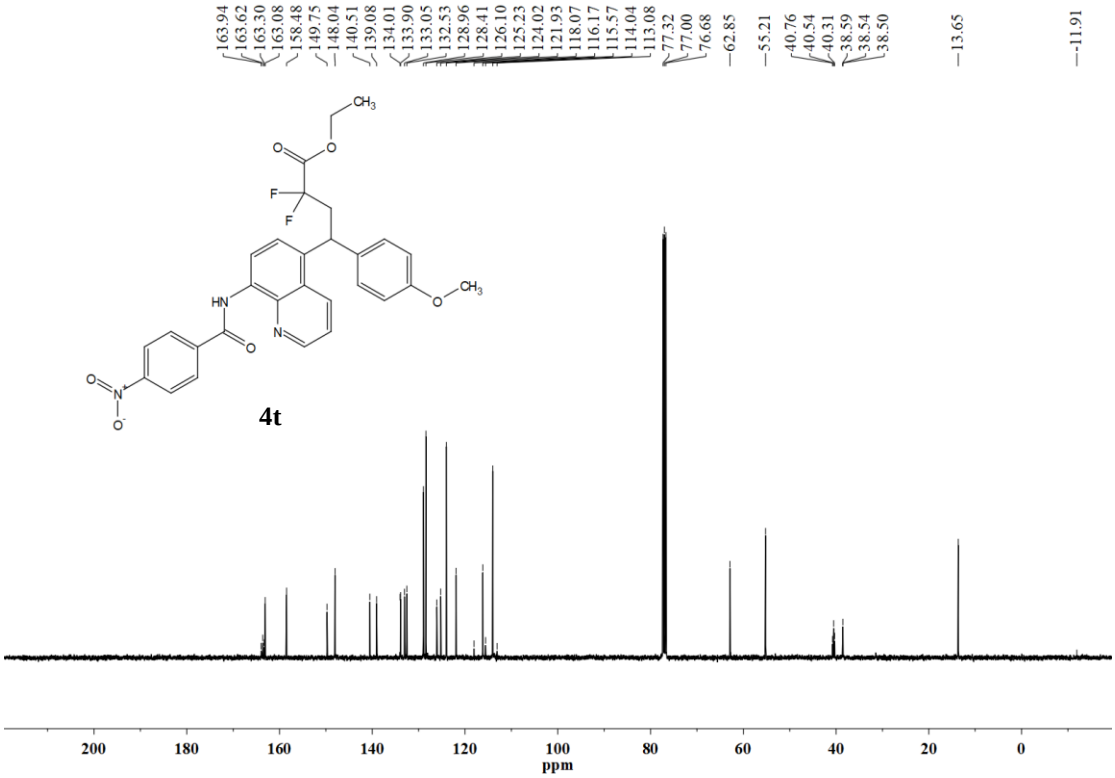
^{19}F NMR (376 MHz, Chloroform-*d*)



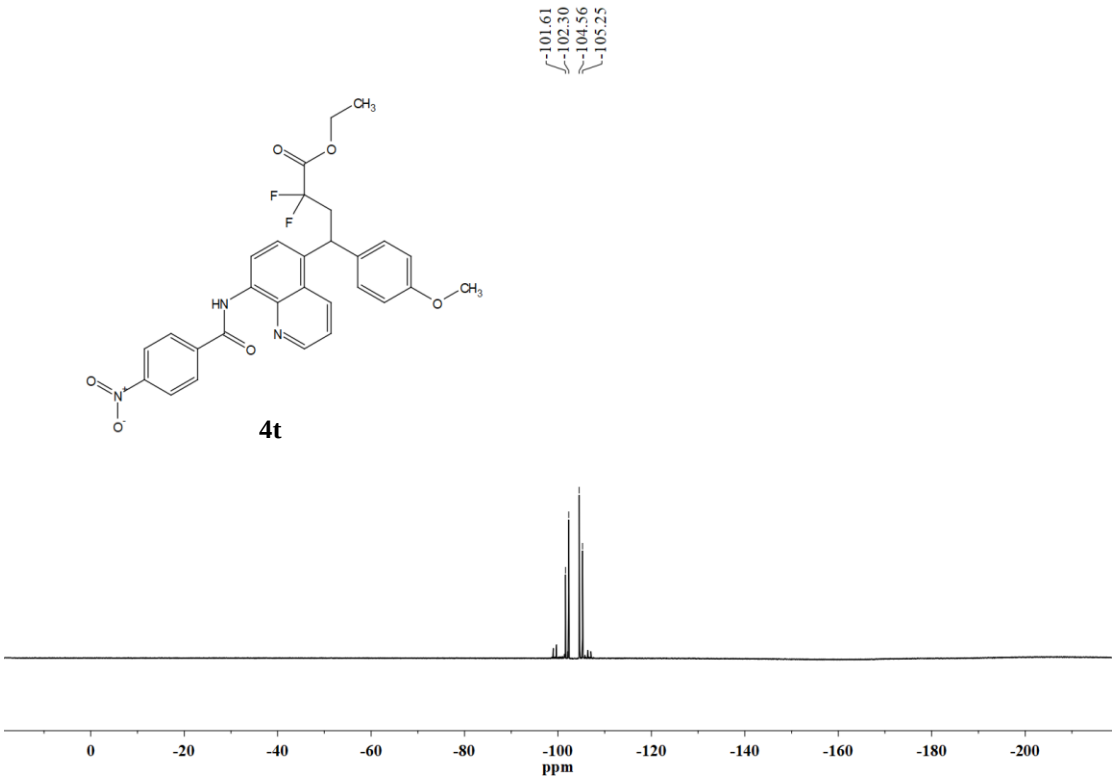
^{1}H NMR (400 MHz, Chloroform-*d*)



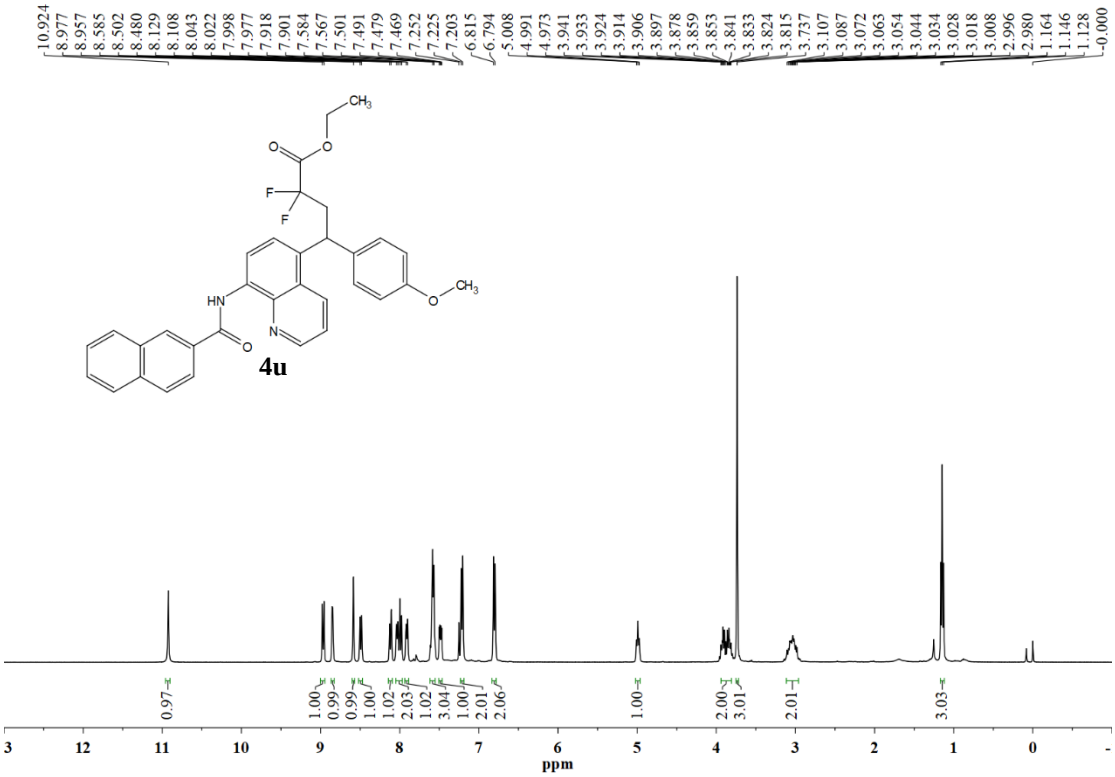
^{13}C NMR (101 MHz, Chloroform-*d*)



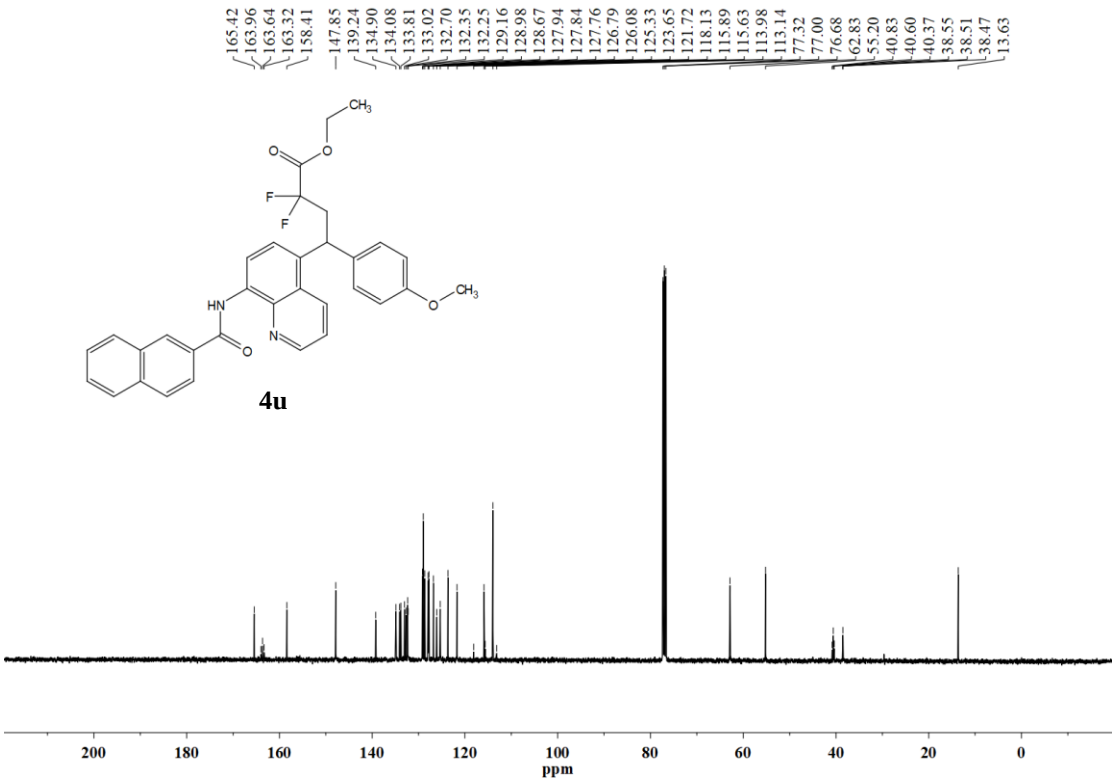
^{19}F NMR (376 MHz, Chloroform-*d*)



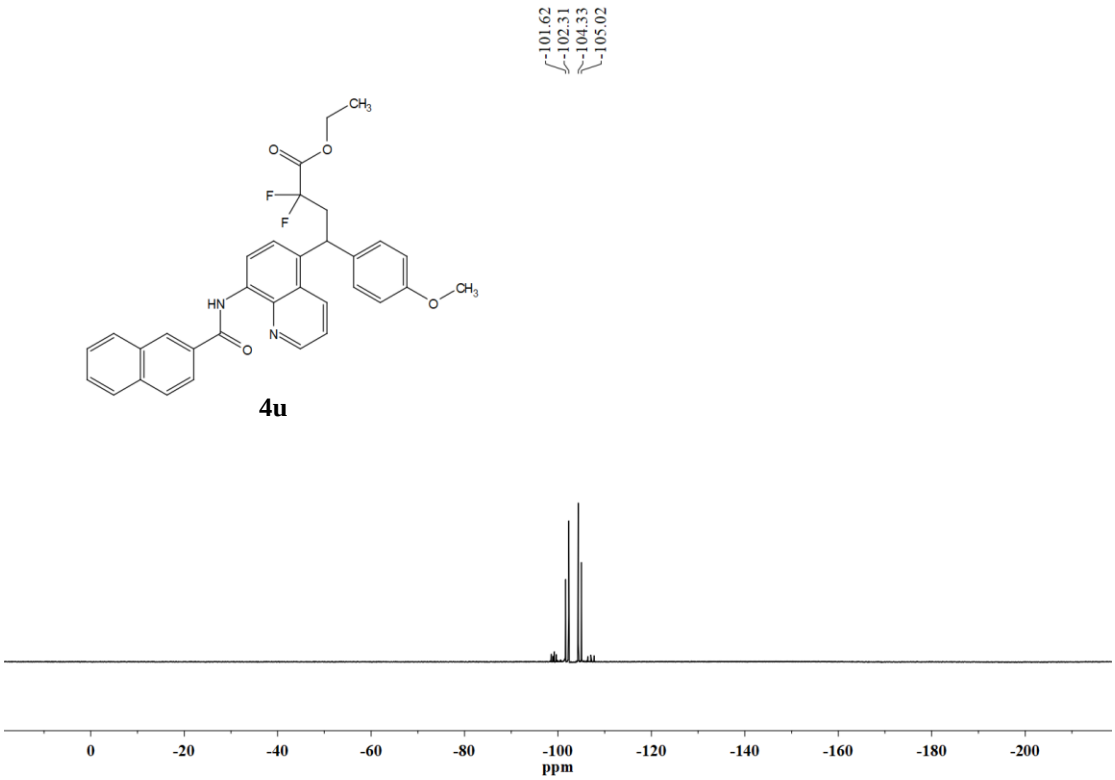
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

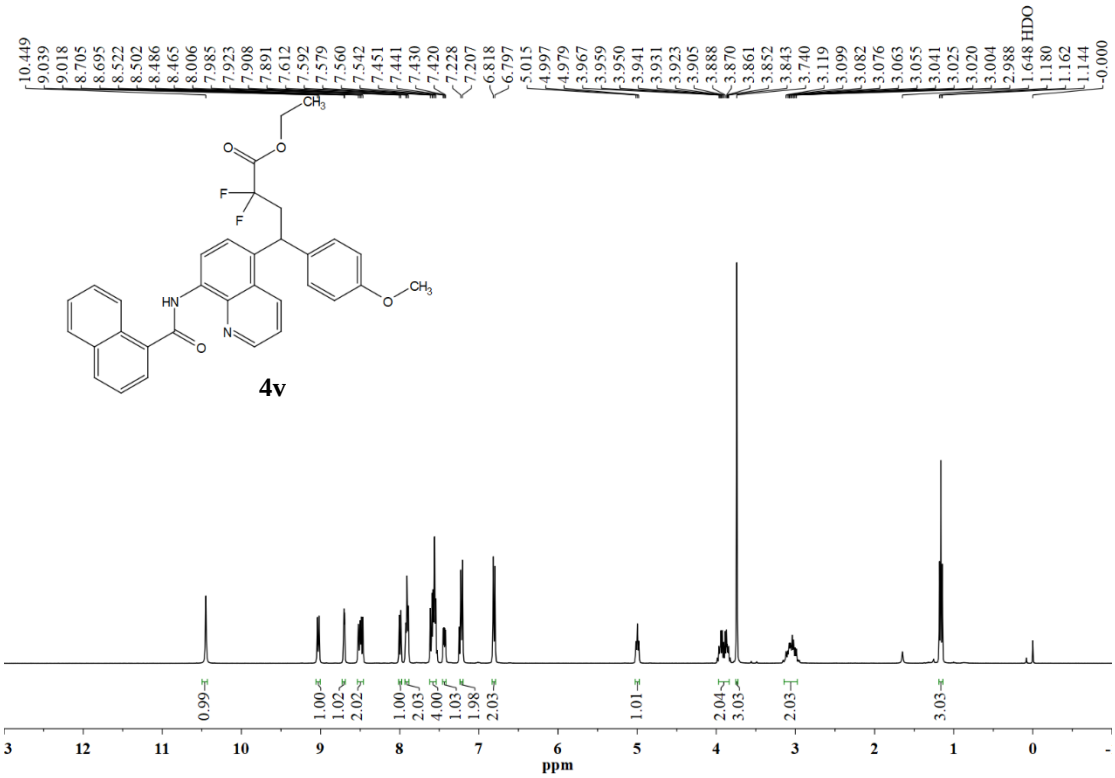


^{19}F NMR (376 MHz, Chloroform-*d*)



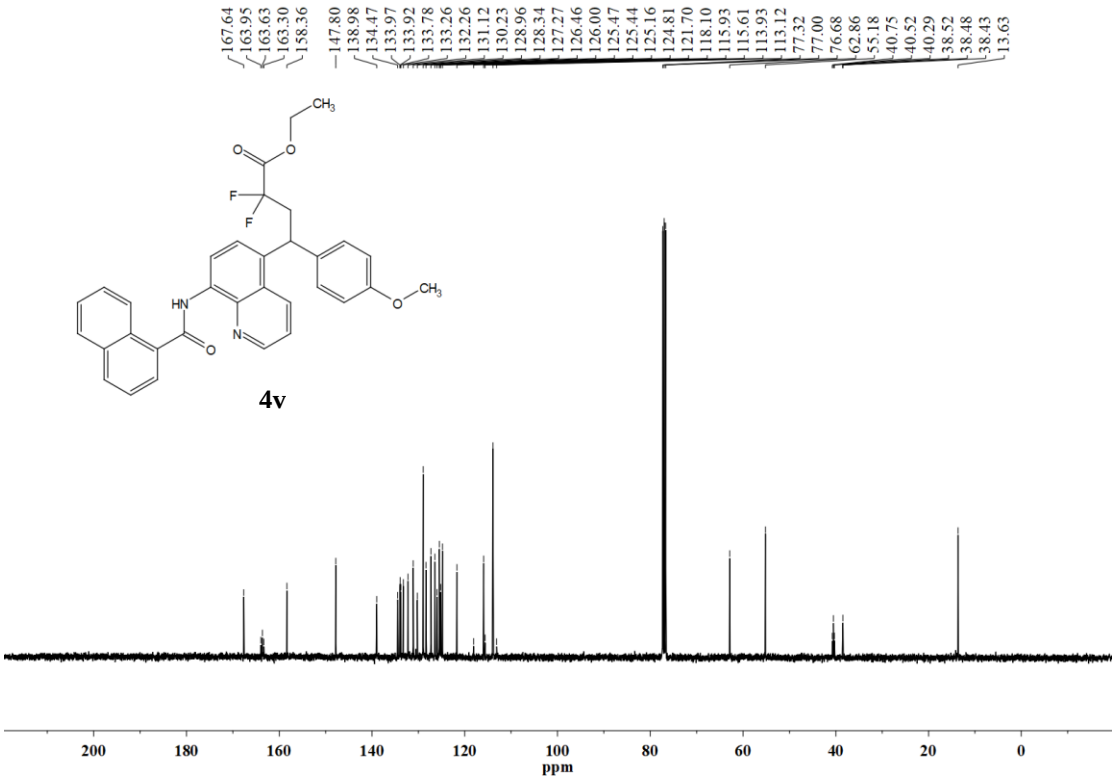
4u

^{1}H NMR (400 MHz, Chloroform-*d*)

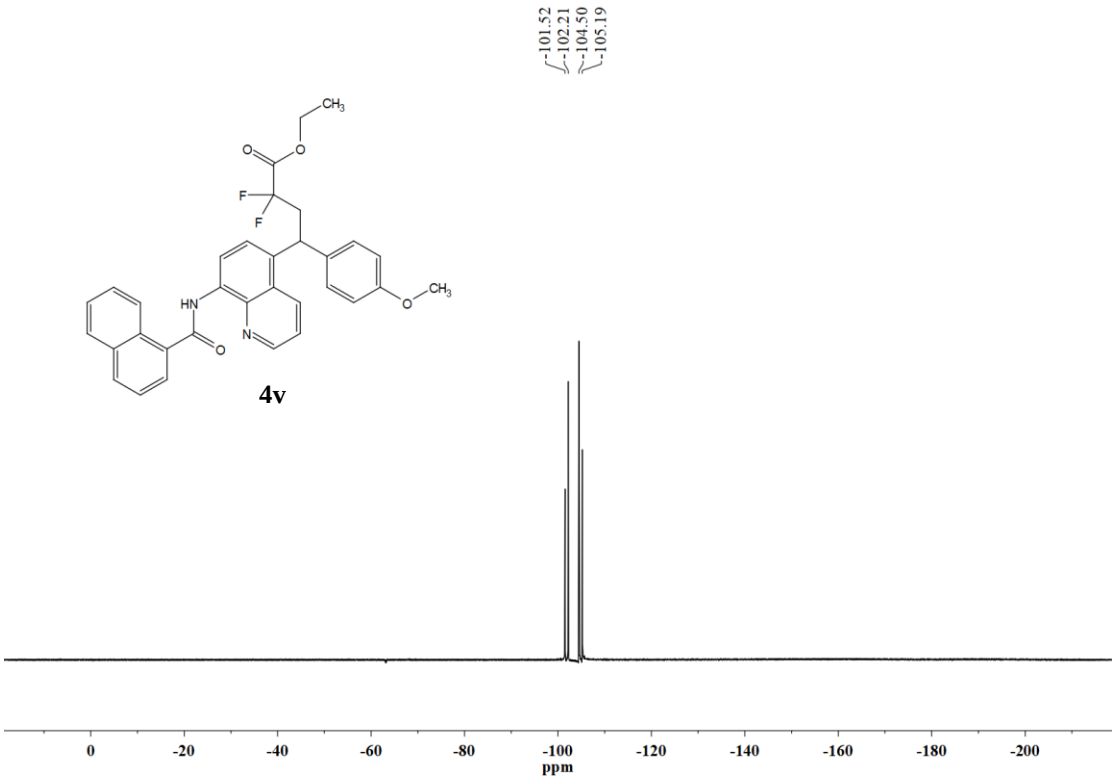


4v

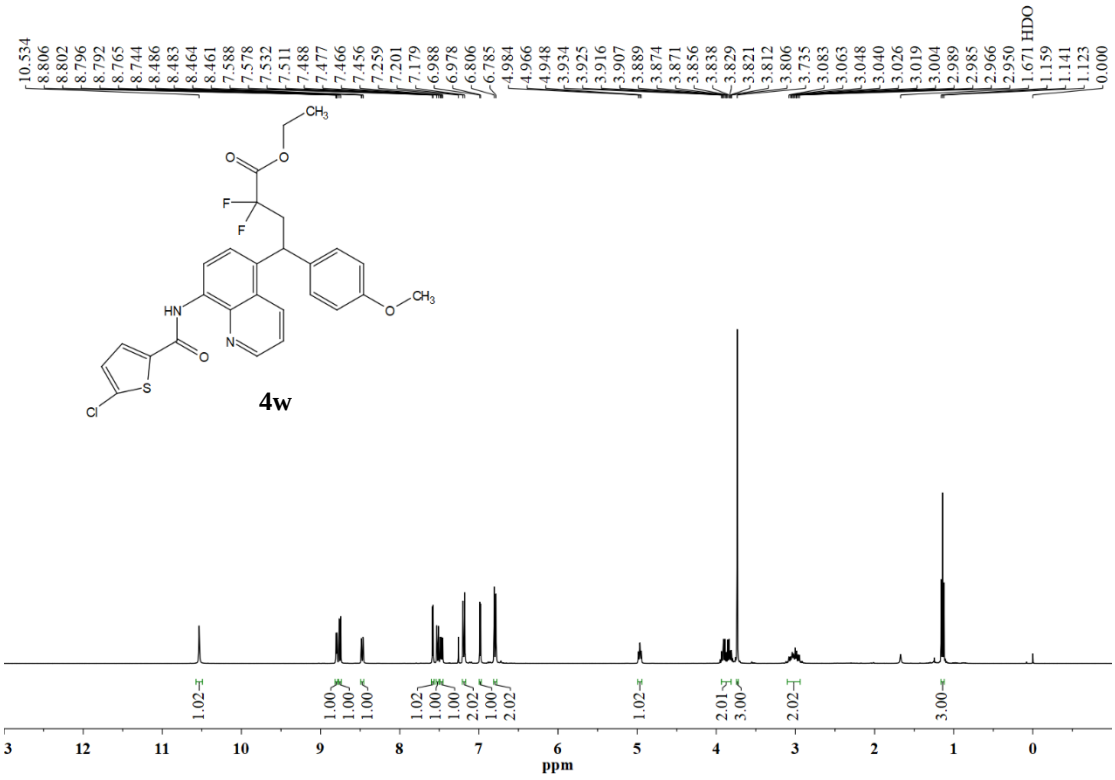
^{13}C NMR (101 MHz, Chloroform-*d*)



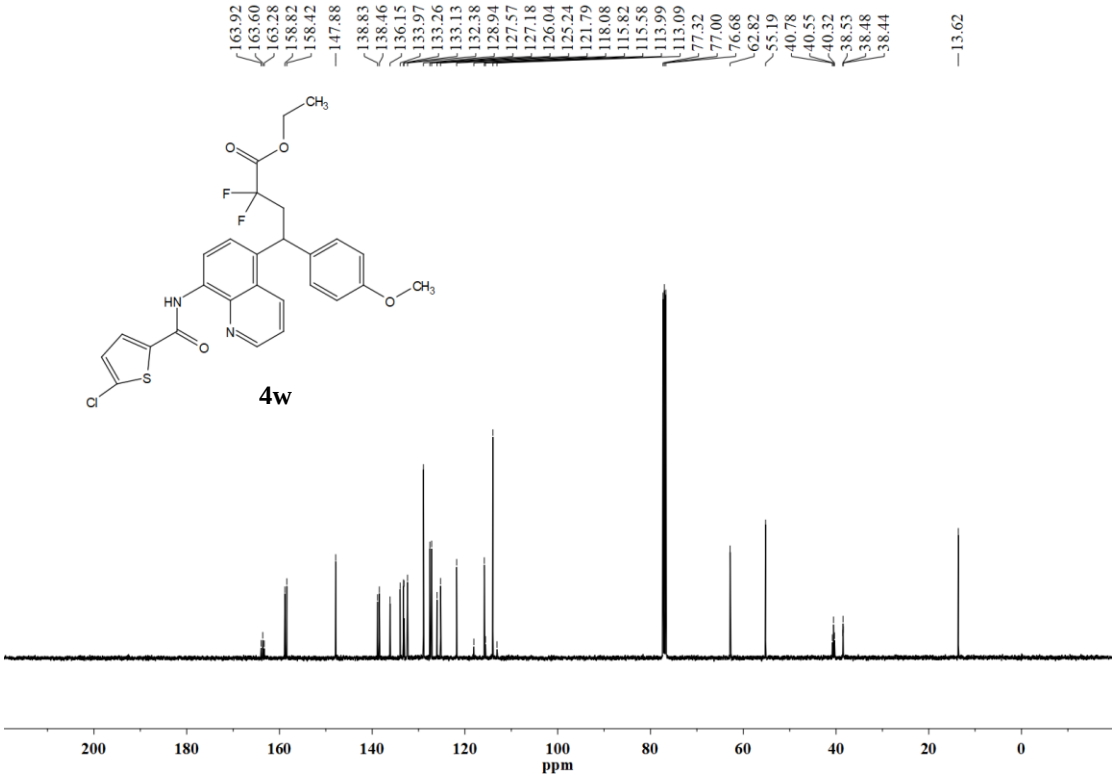
^{19}F NMR (376 MHz, Chloroform-*d*)



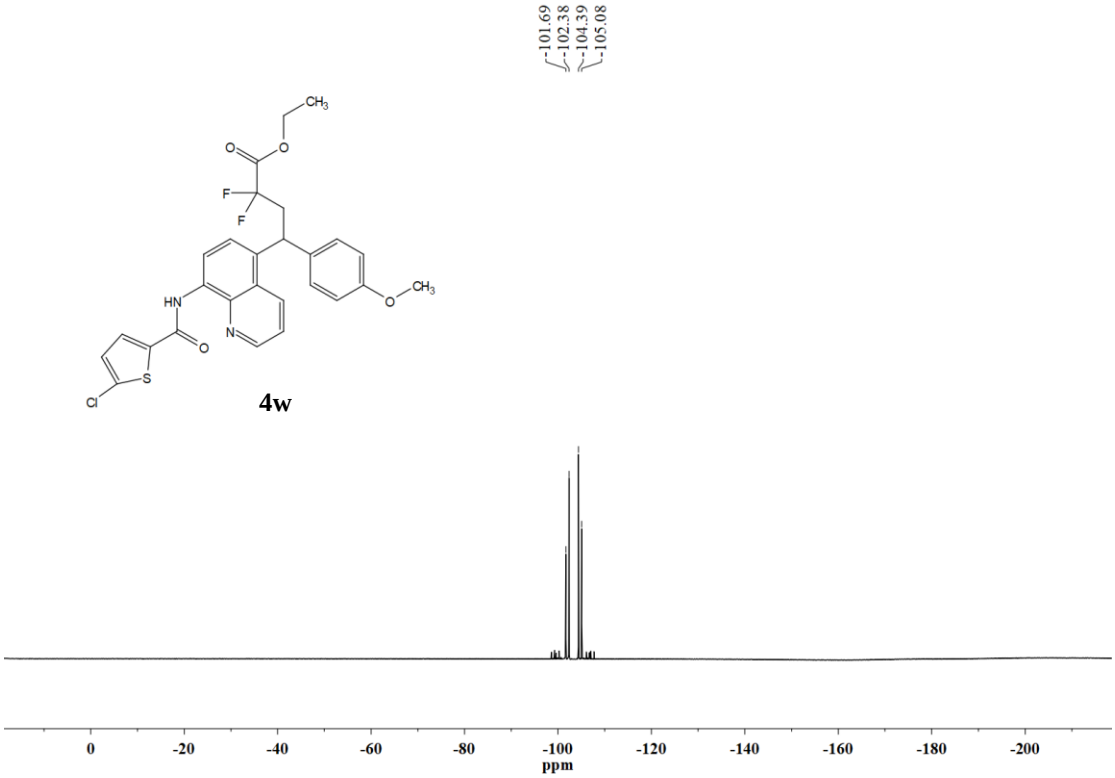
^{1}H NMR (400 MHz, Chloroform-*d*)



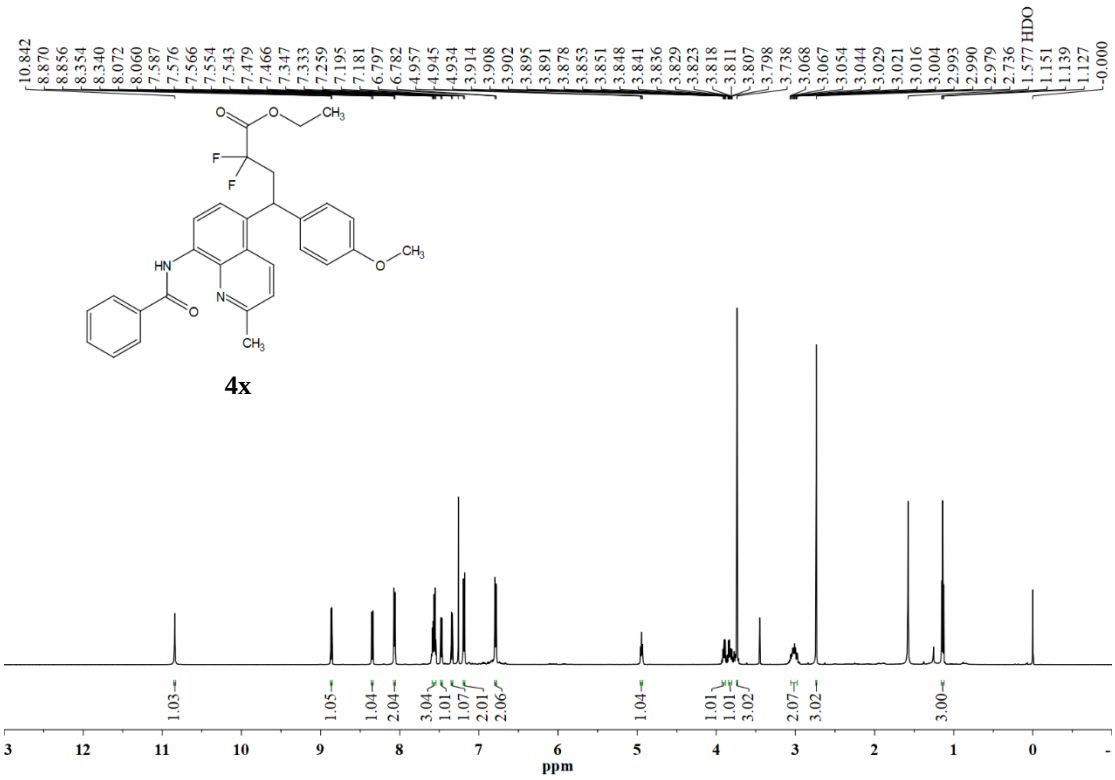
^{13}C NMR (101 MHz, Chloroform-*d*)



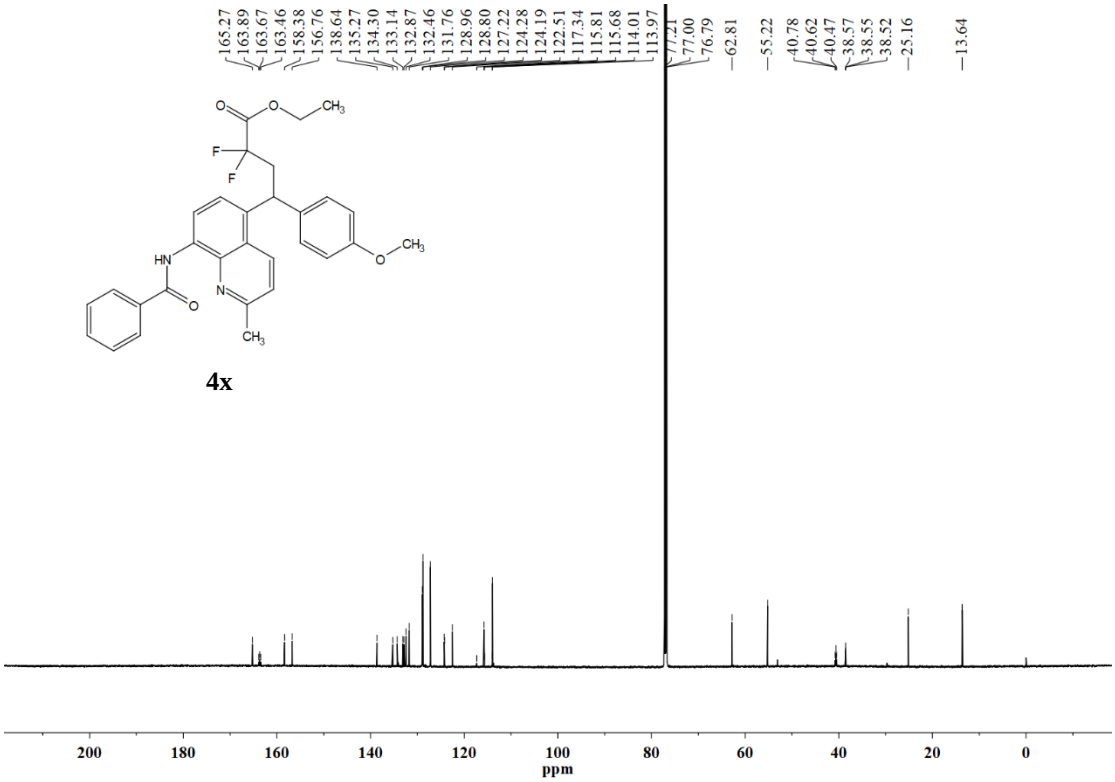
^{19}F NMR (376 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)

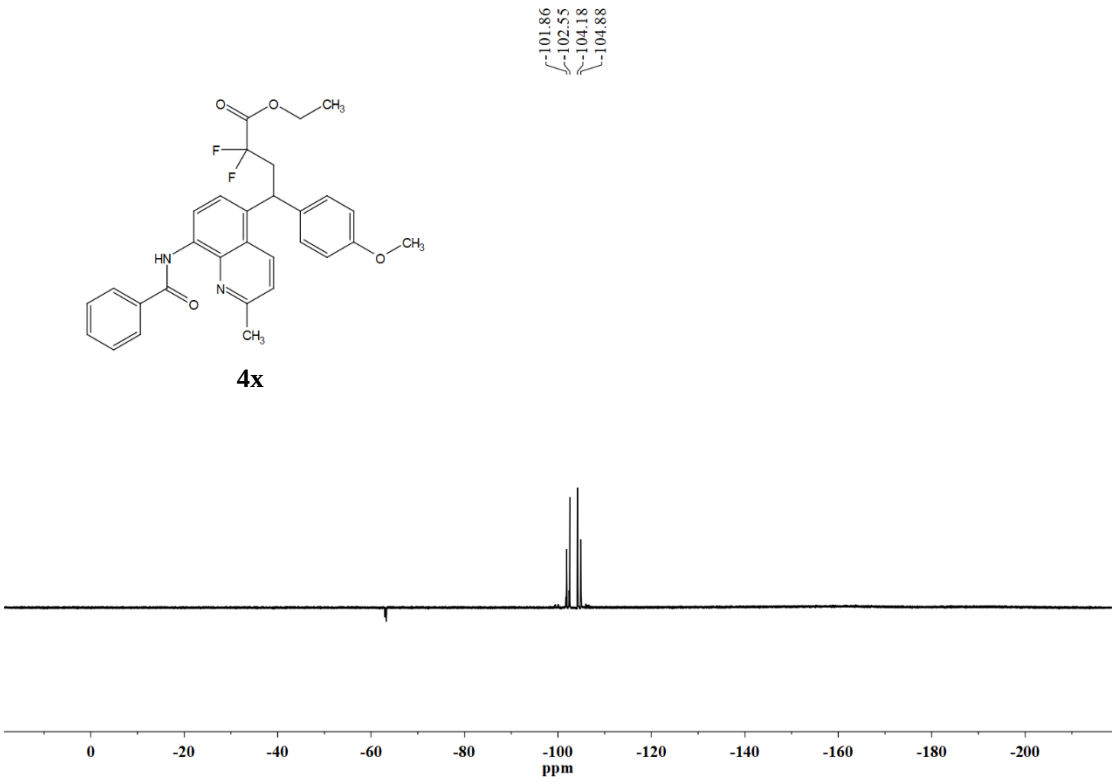


^{13}C NMR (101 MHz, Chloroform-*d*)



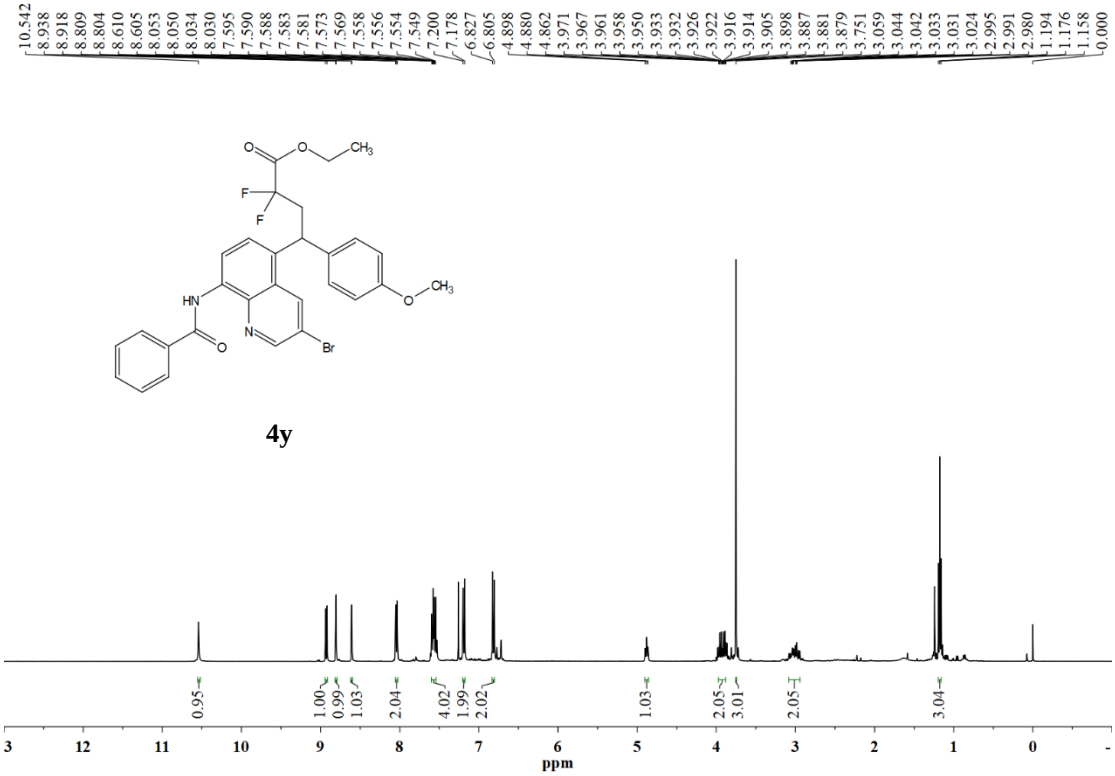
4x

^{19}F NMR (376 MHz, Chloroform-*d*)

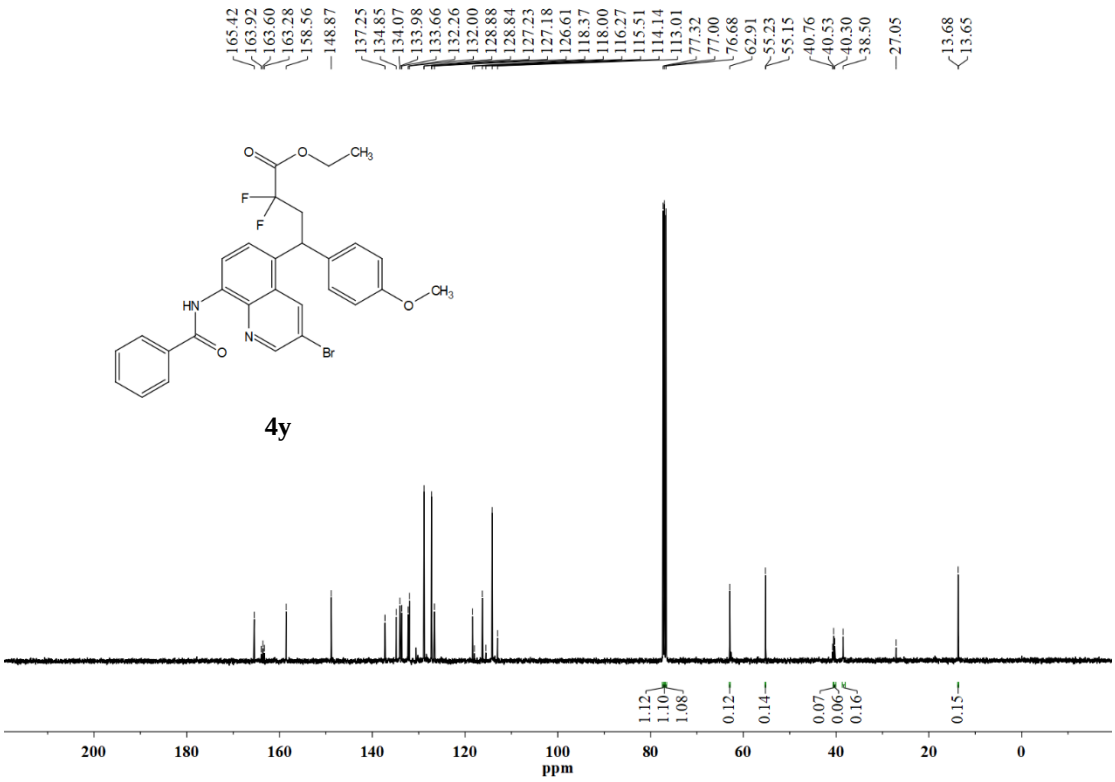


4x

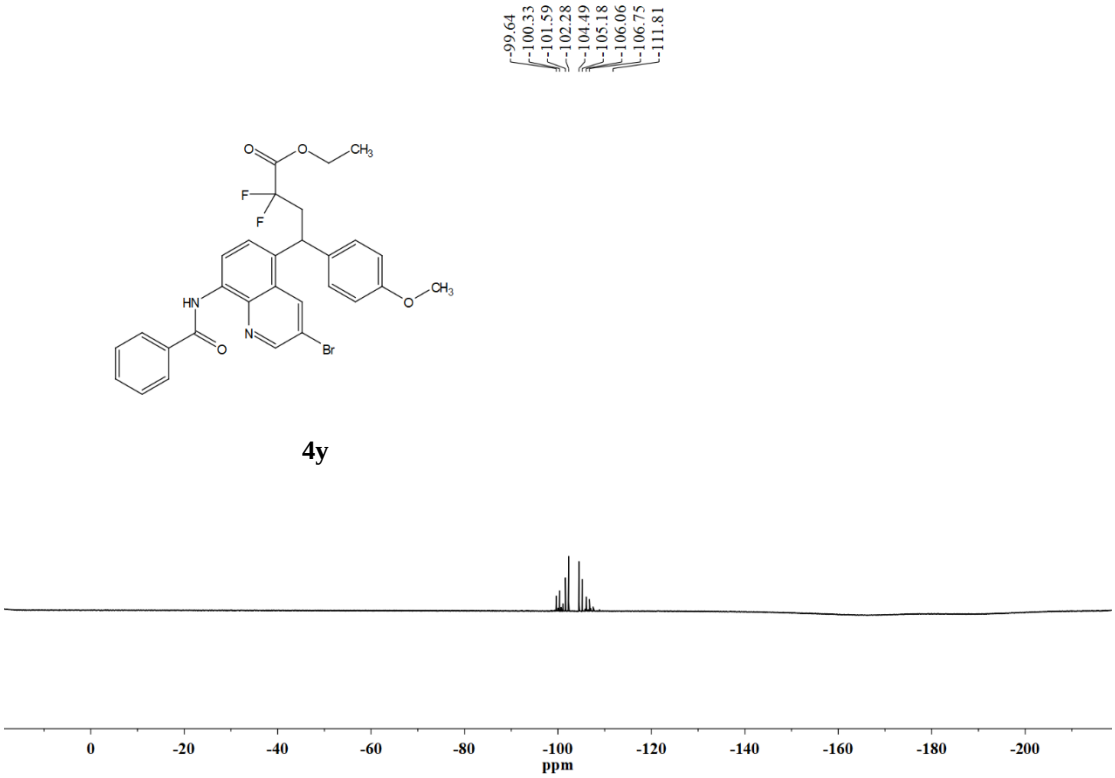
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

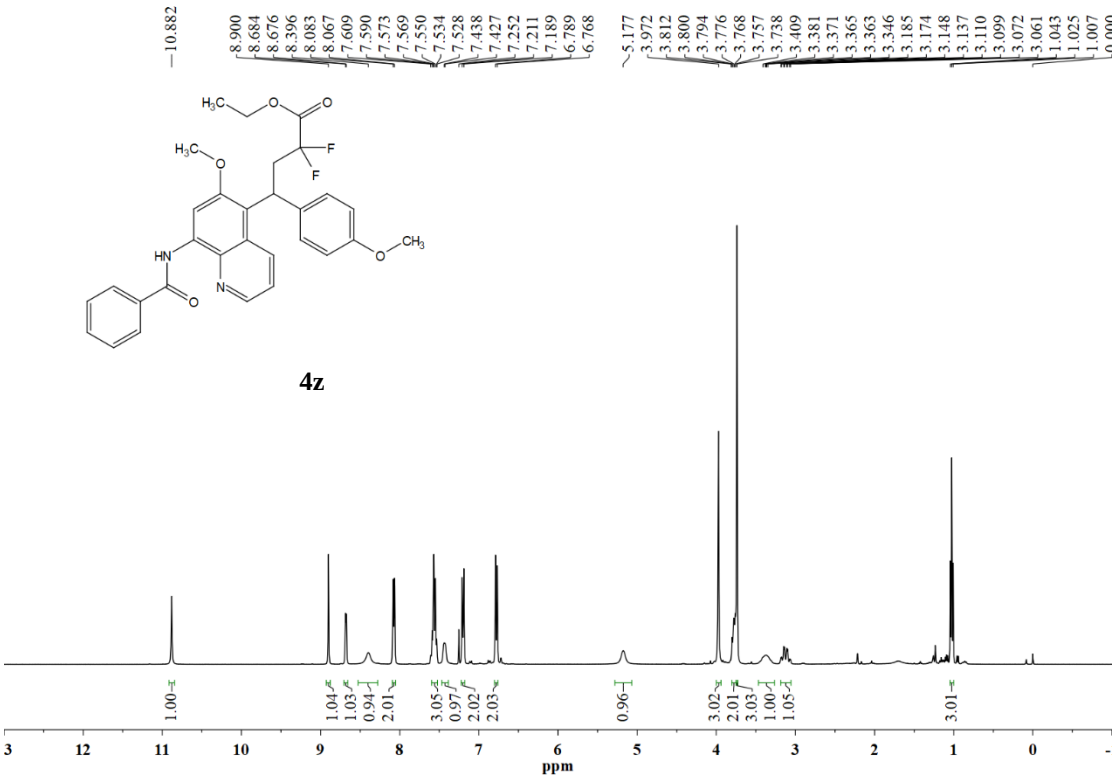


^{19}F NMR (376 MHz, Chloroform-*d*)



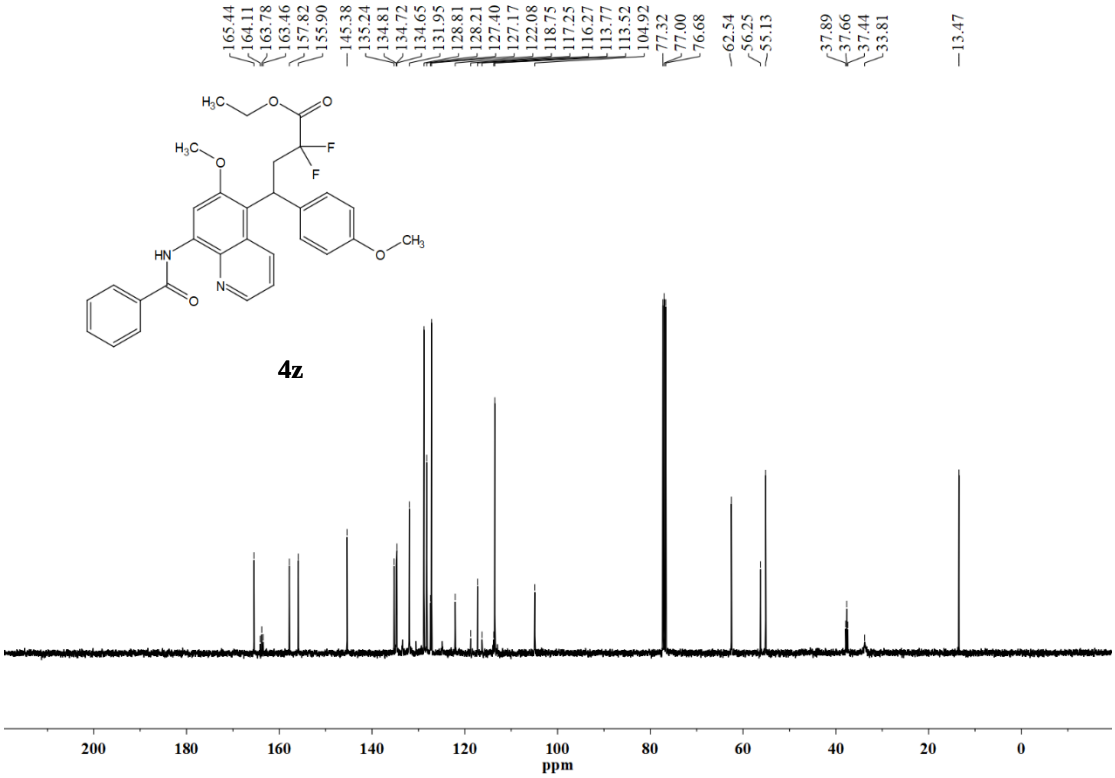
4y

^{1}H NMR (400 MHz, Chloroform-*d*)

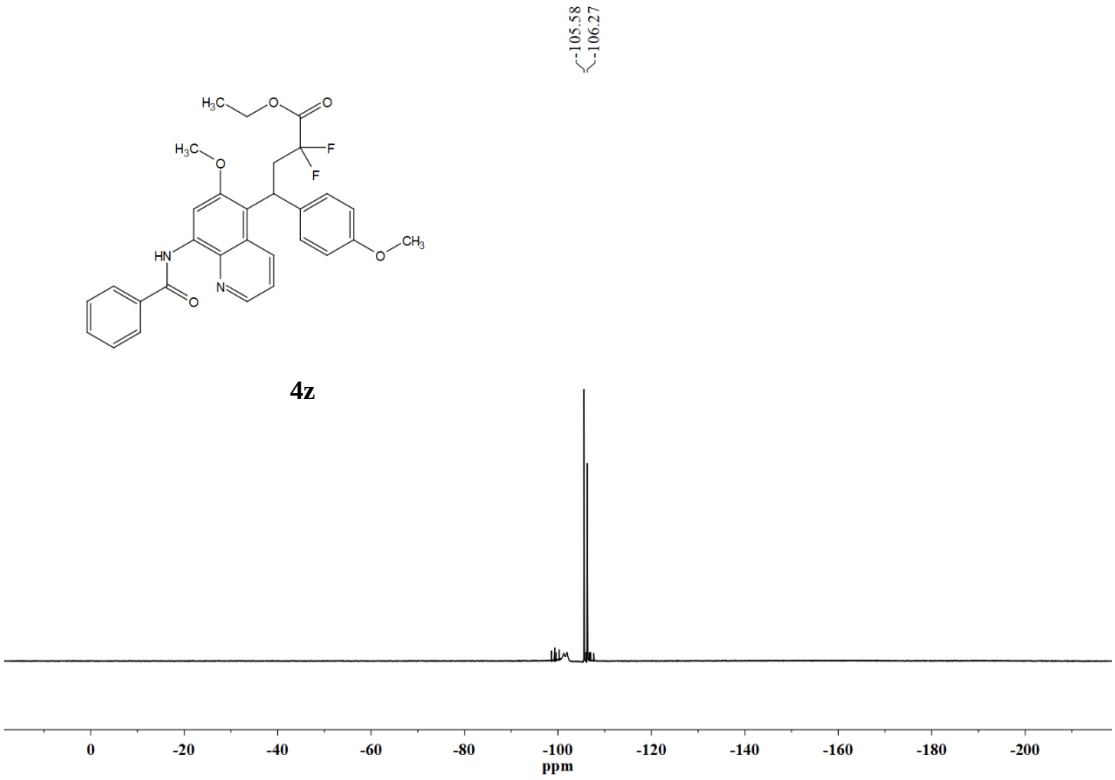


4z

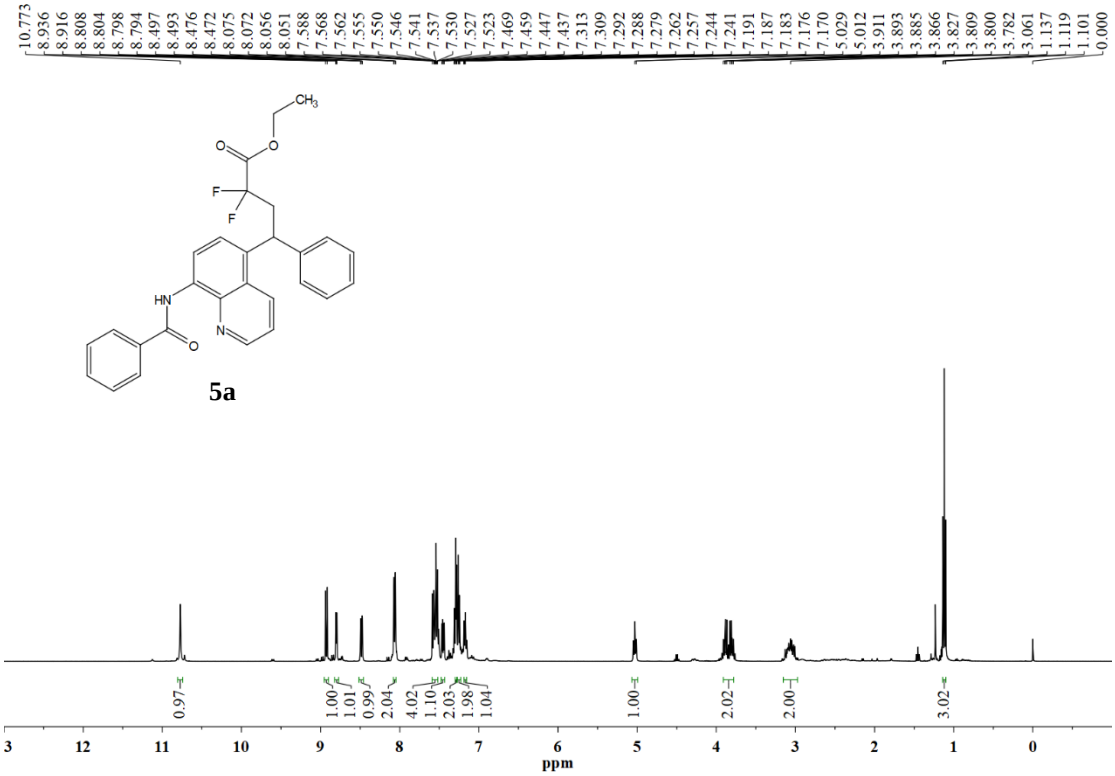
^{13}C NMR (101 MHz, Chloroform-*d*)



^{19}F NMR (376 MHz, Chloroform-*d*)

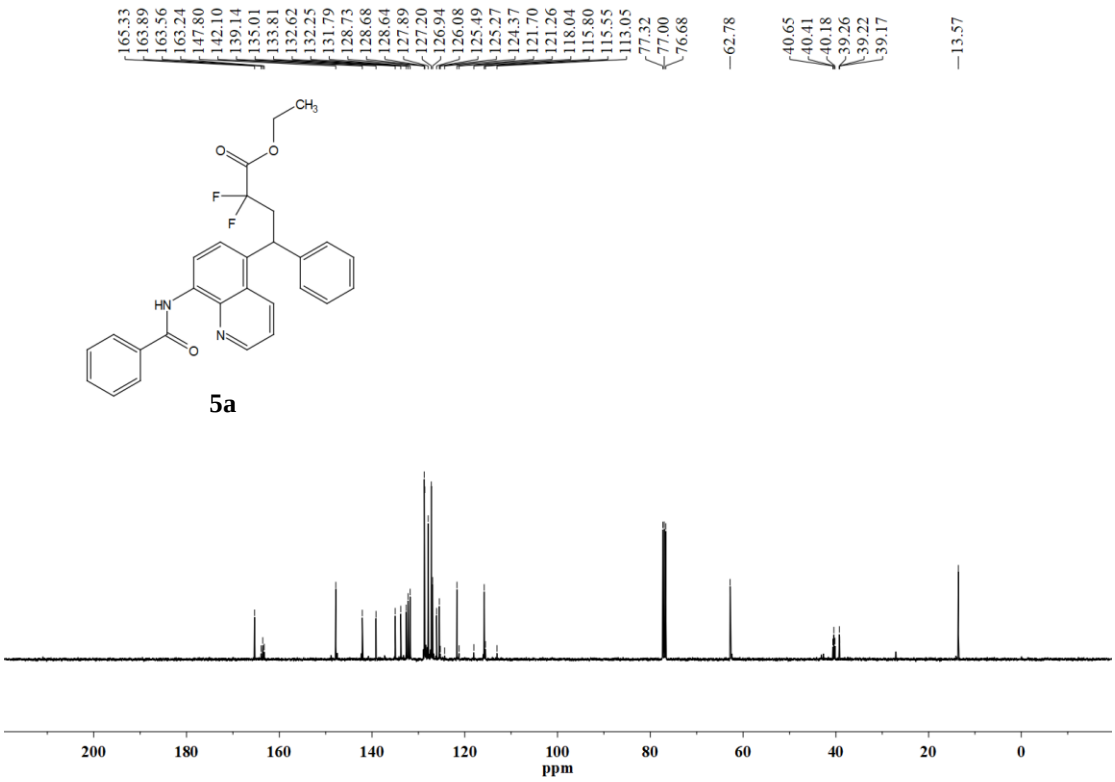


^{1}H NMR (400 MHz, Chloroform-*d*)



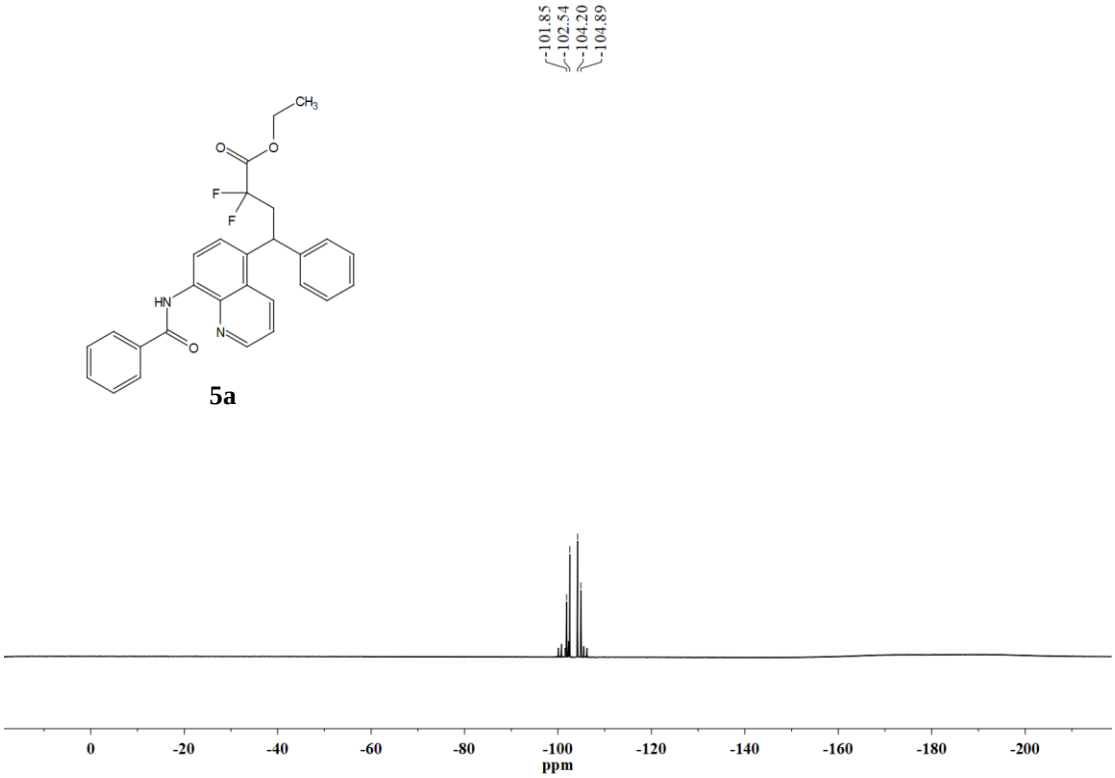
5a

^{13}C NMR (101 MHz, Chloroform-*d*)



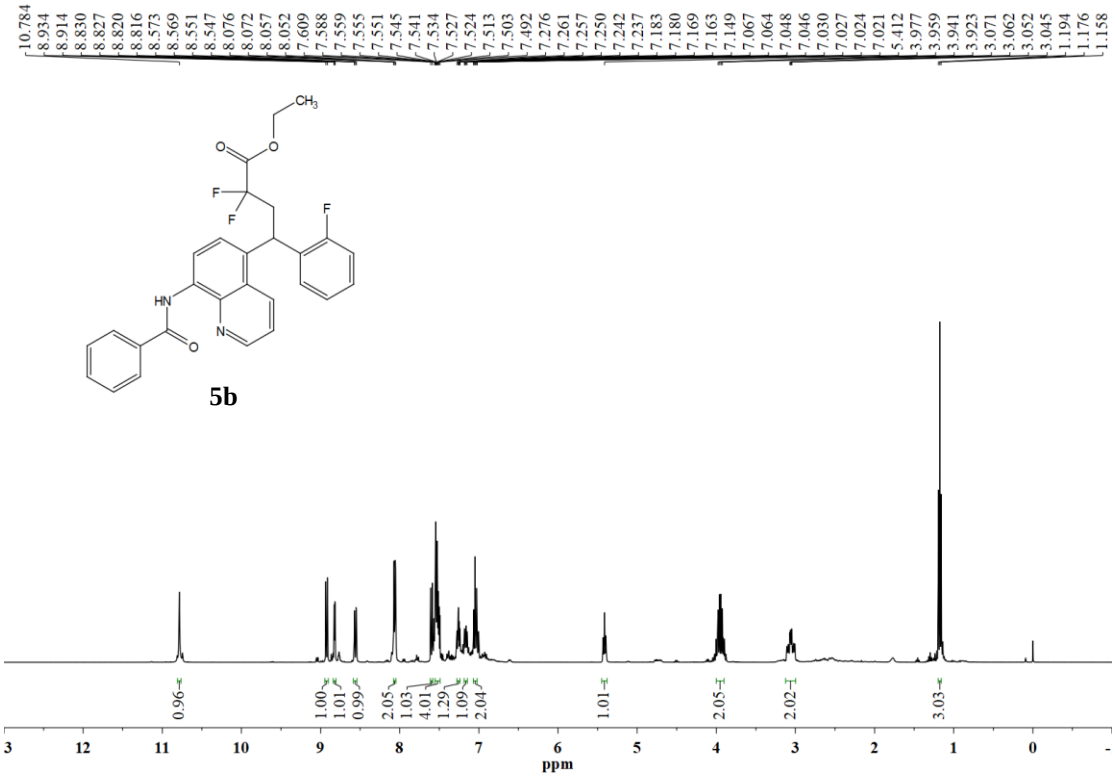
5a

^{19}F NMR (376 MHz, Chloroform-*d*)



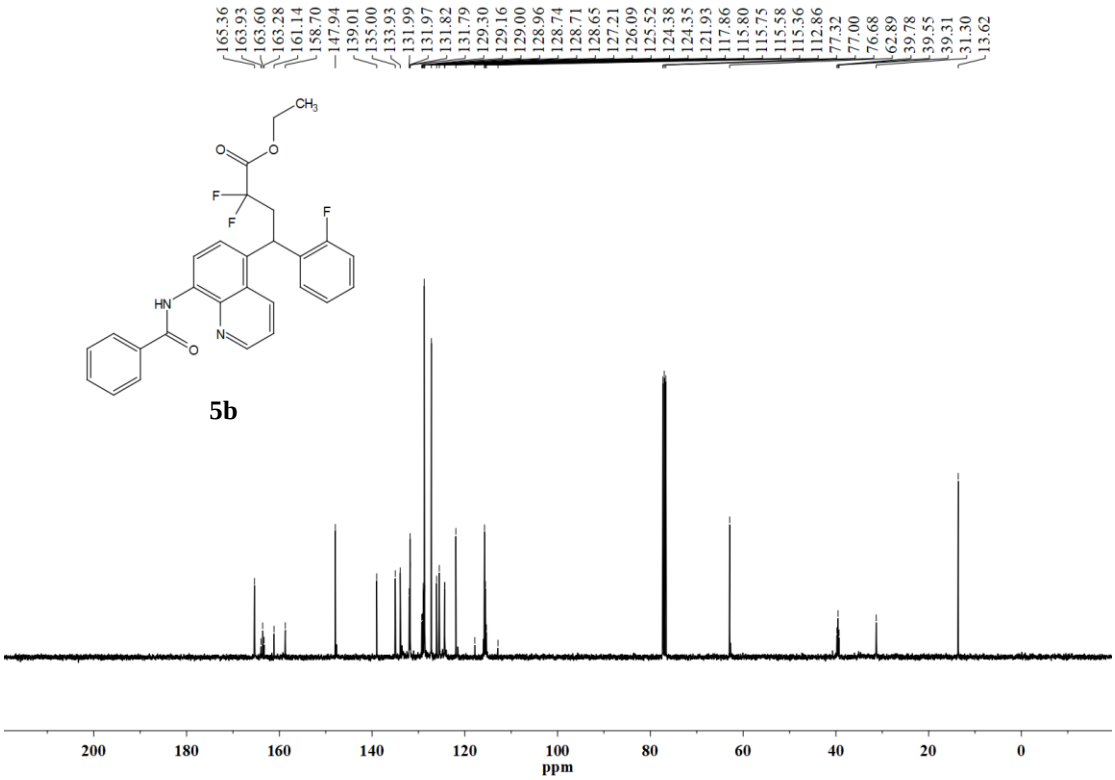
5a

^{1}H NMR (400 MHz, Chloroform-*d*)

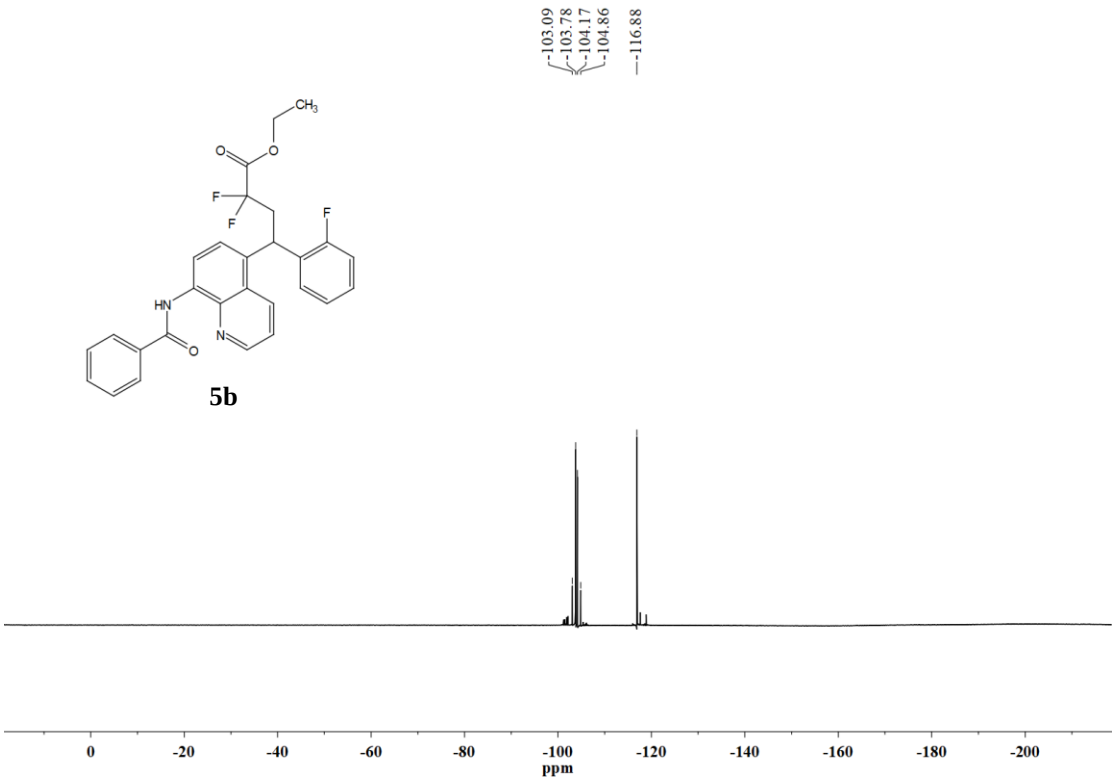


5b

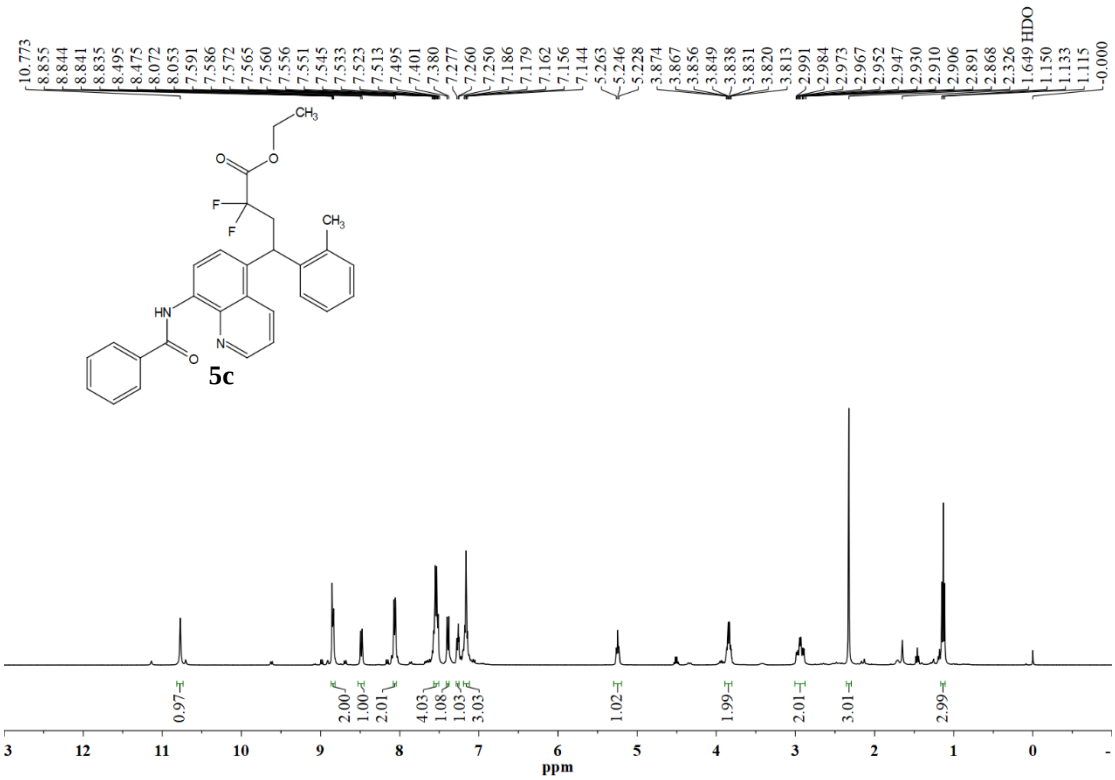
^{13}C NMR (101 MHz, Chloroform-*d*)



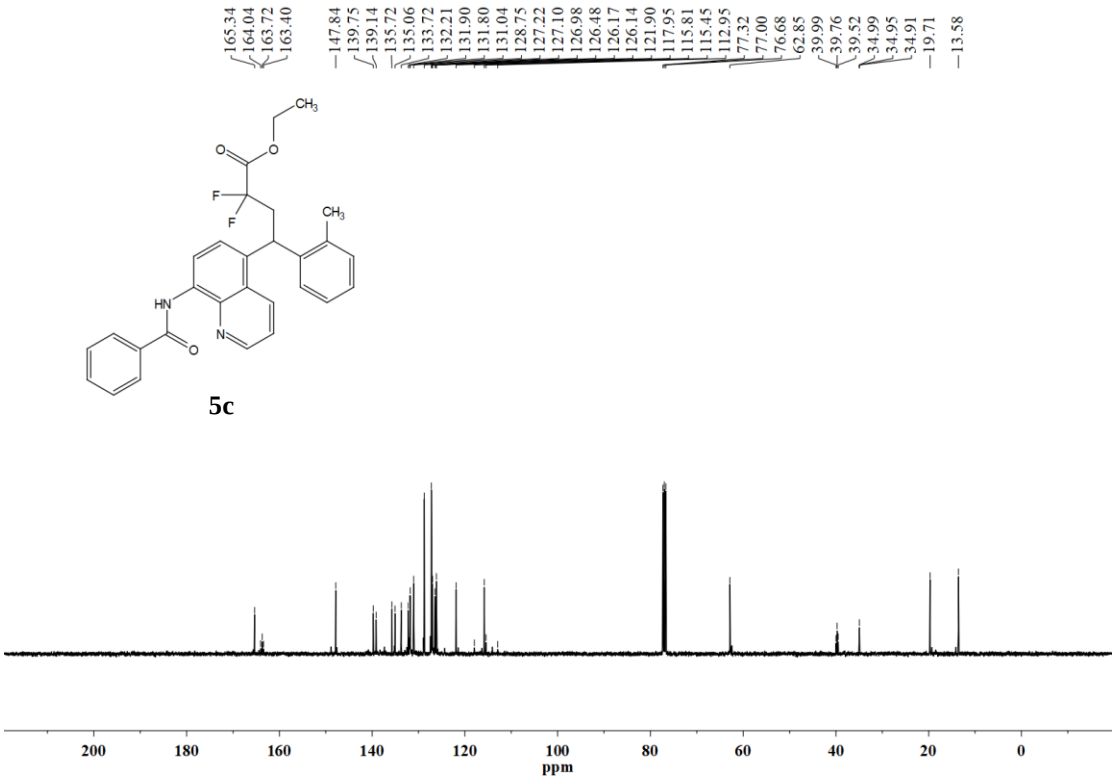
^{19}F NMR (376 MHz, Chloroform-*d*)



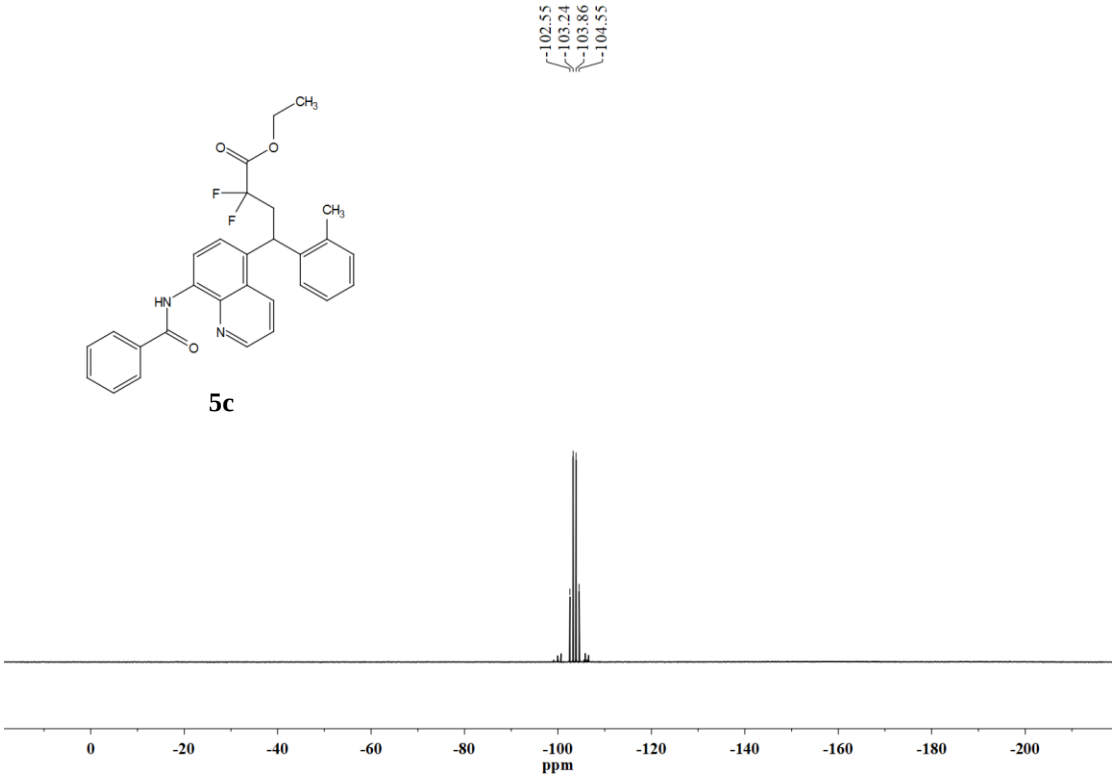
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

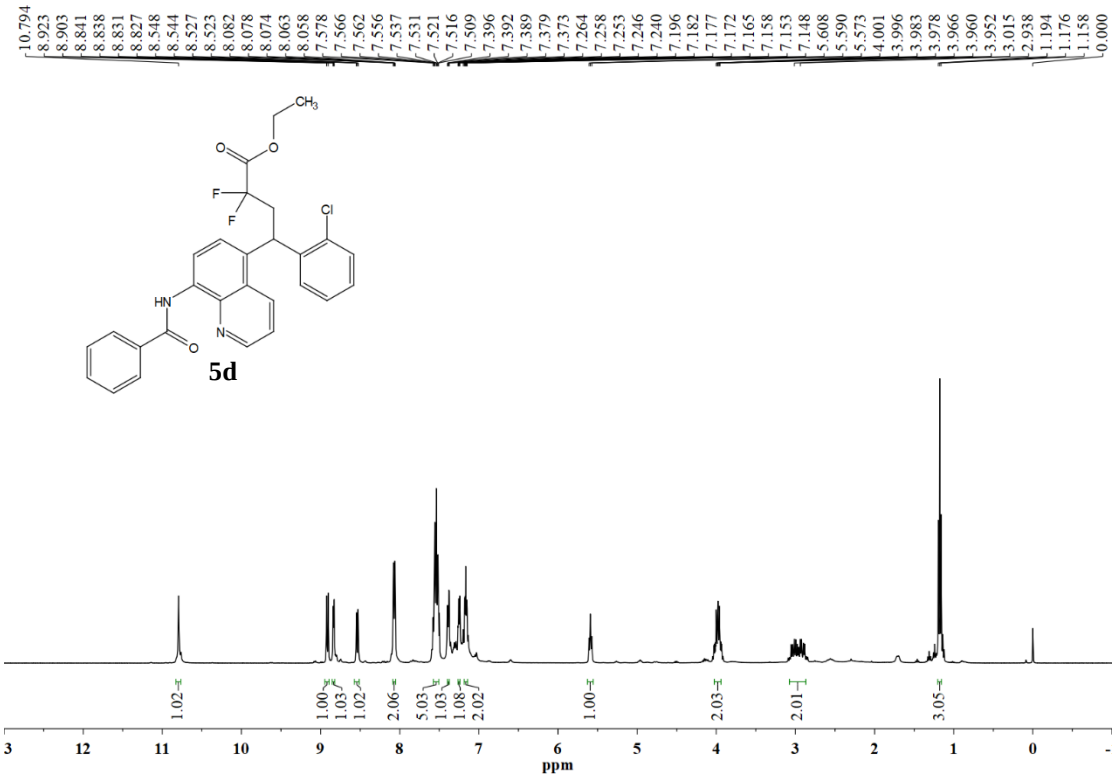


^{19}F NMR (376 MHz, Chloroform-*d*)



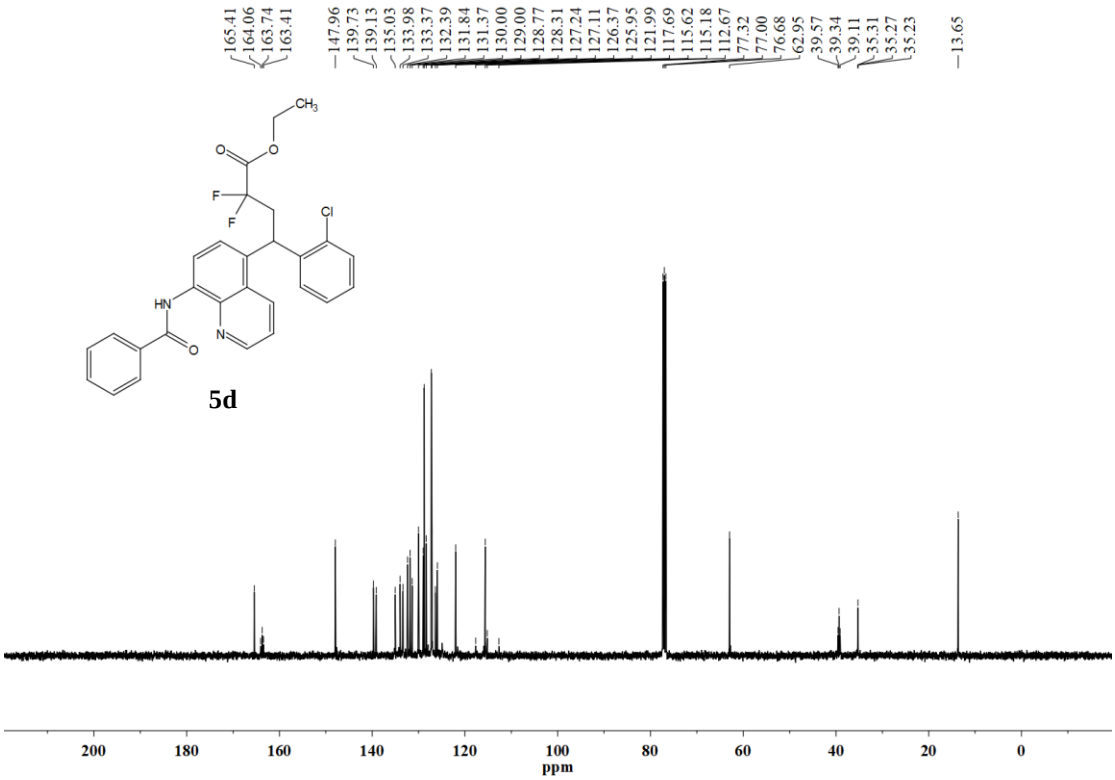
5c

^{1}H NMR (400 MHz, Chloroform-*d*)

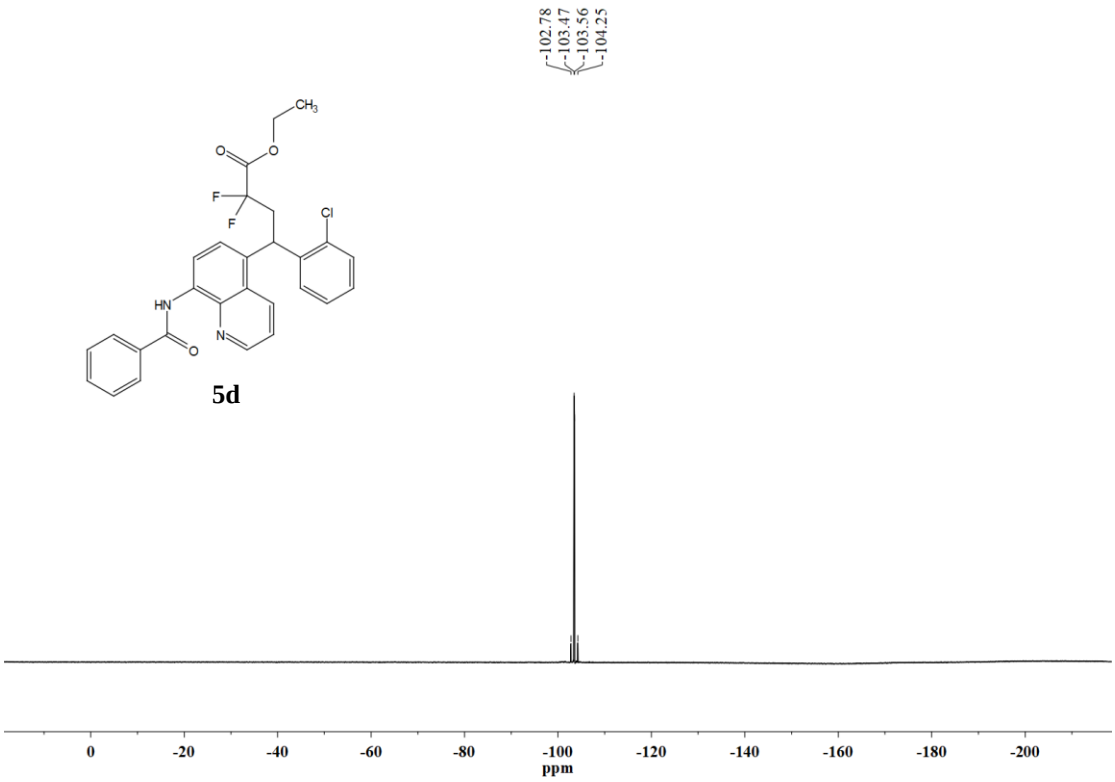


5d

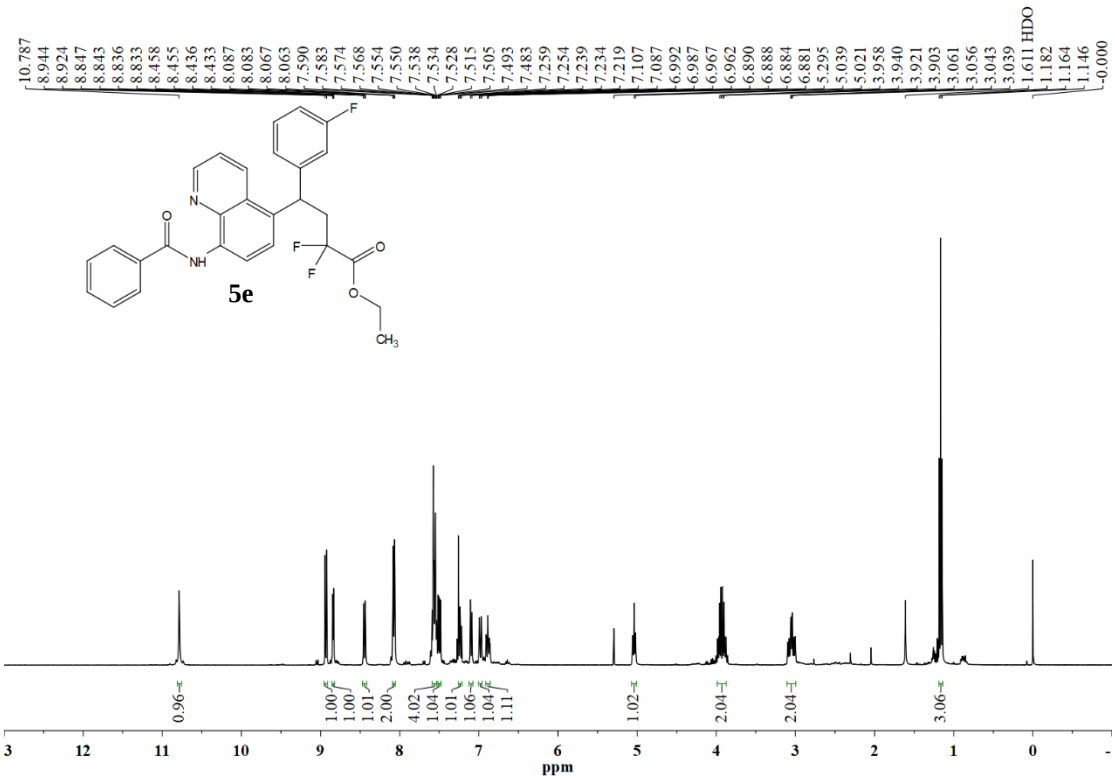
^{13}C NMR (101 MHz, Chloroform-*d*)



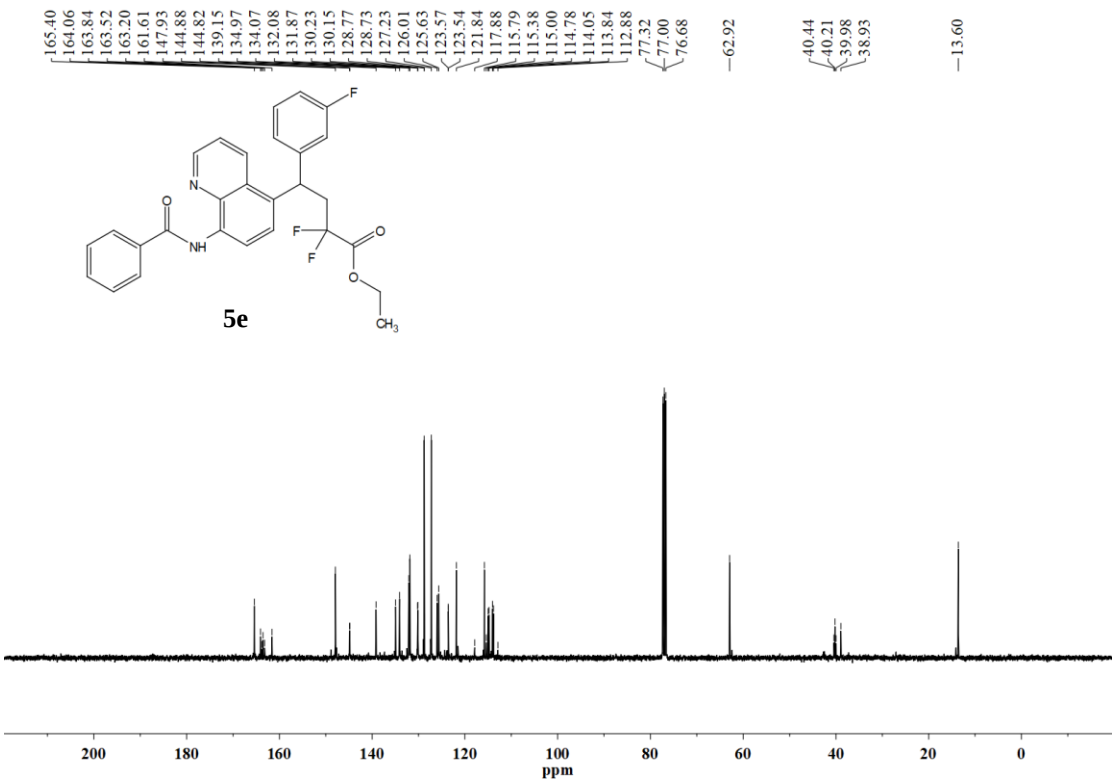
^{19}F NMR (376 MHz, Chloroform-*d*)



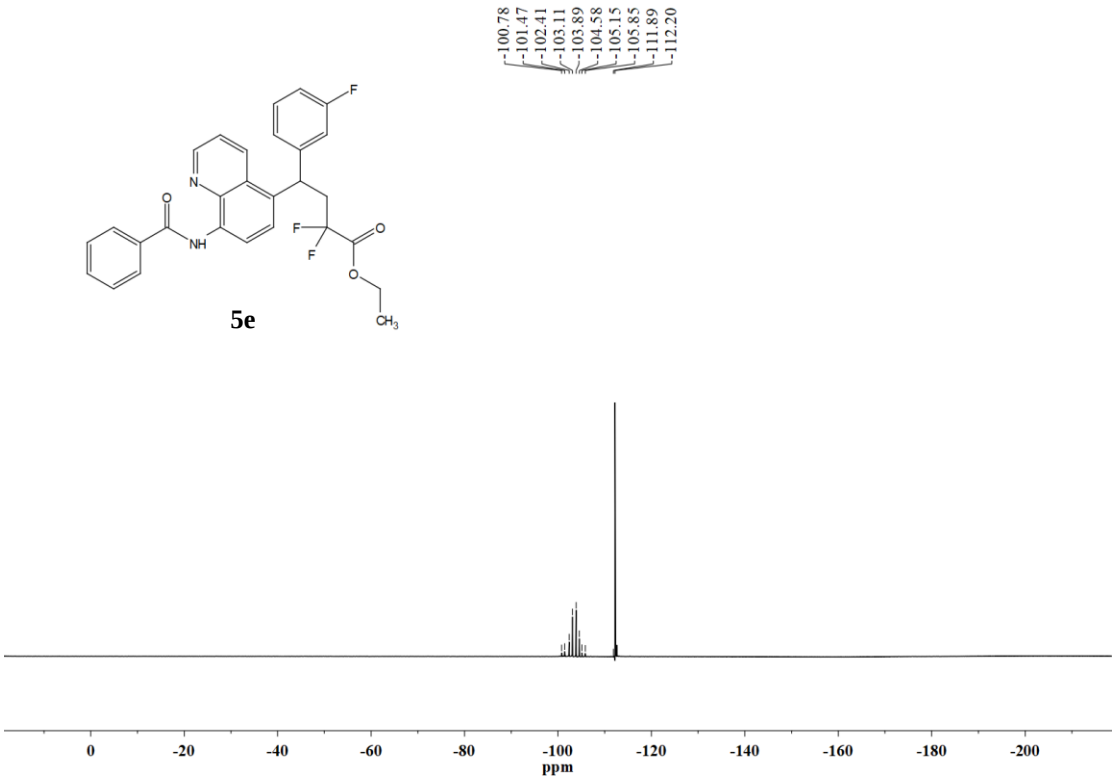
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

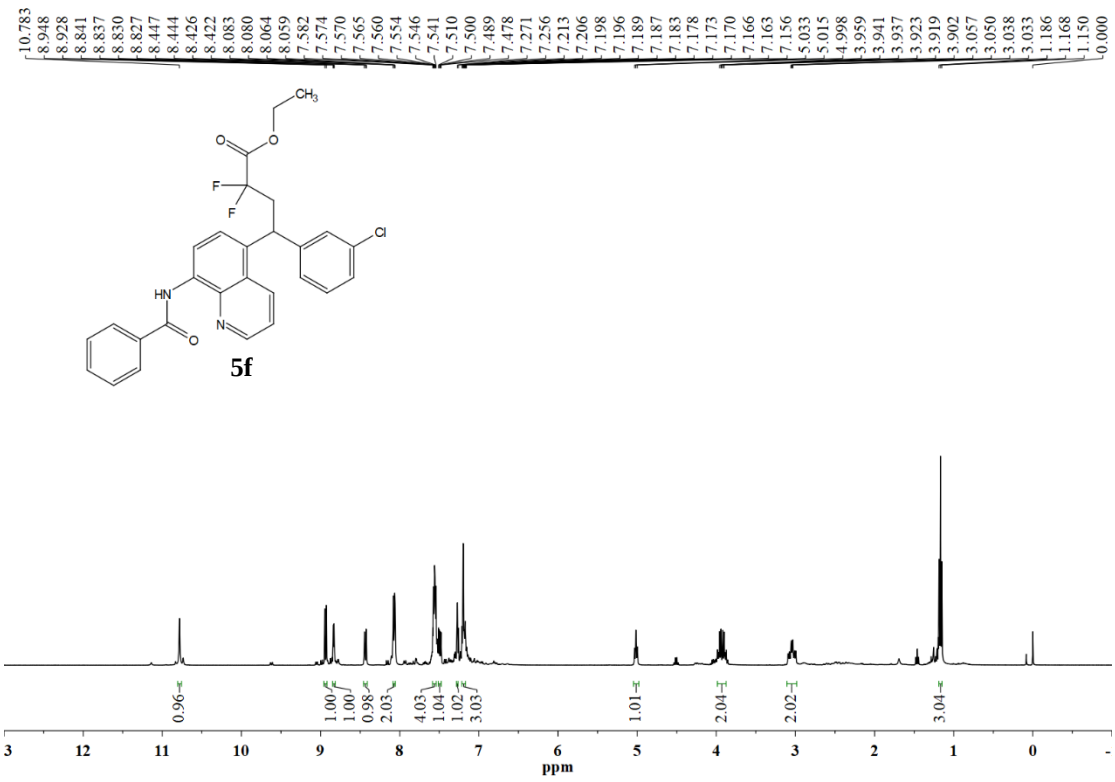


^{19}F NMR (376 MHz, Chloroform-*d*)



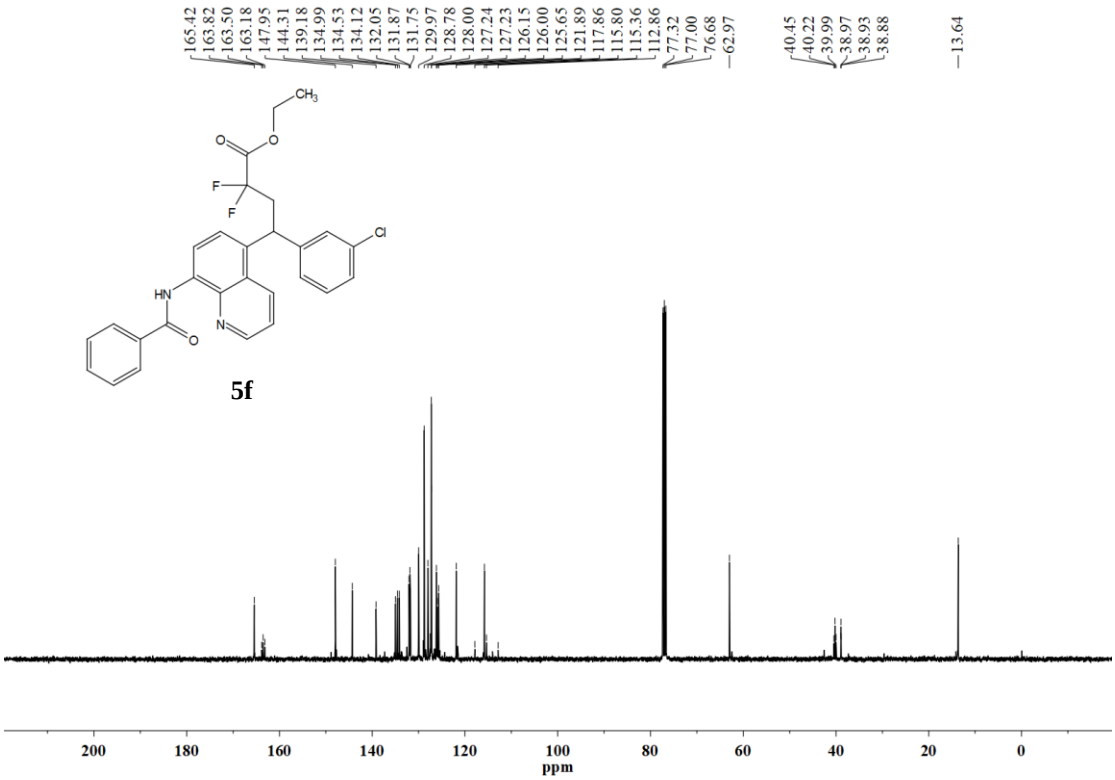
5e

^{1}H NMR (400 MHz, Chloroform-*d*)

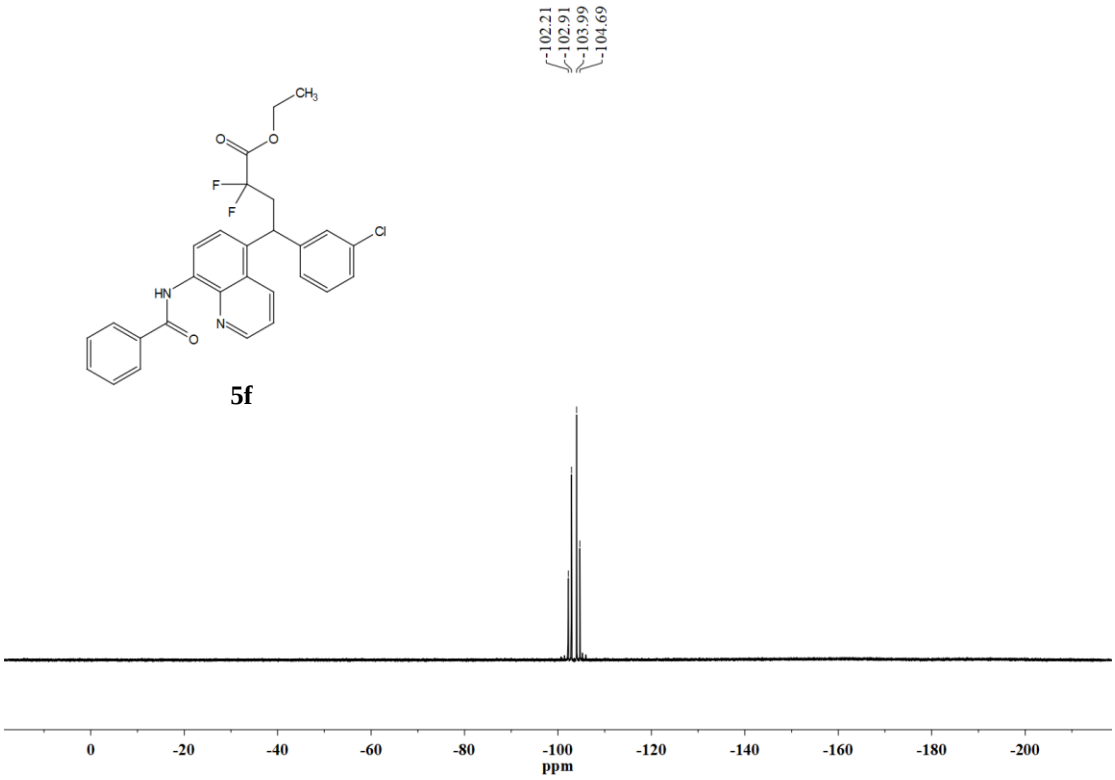


5f

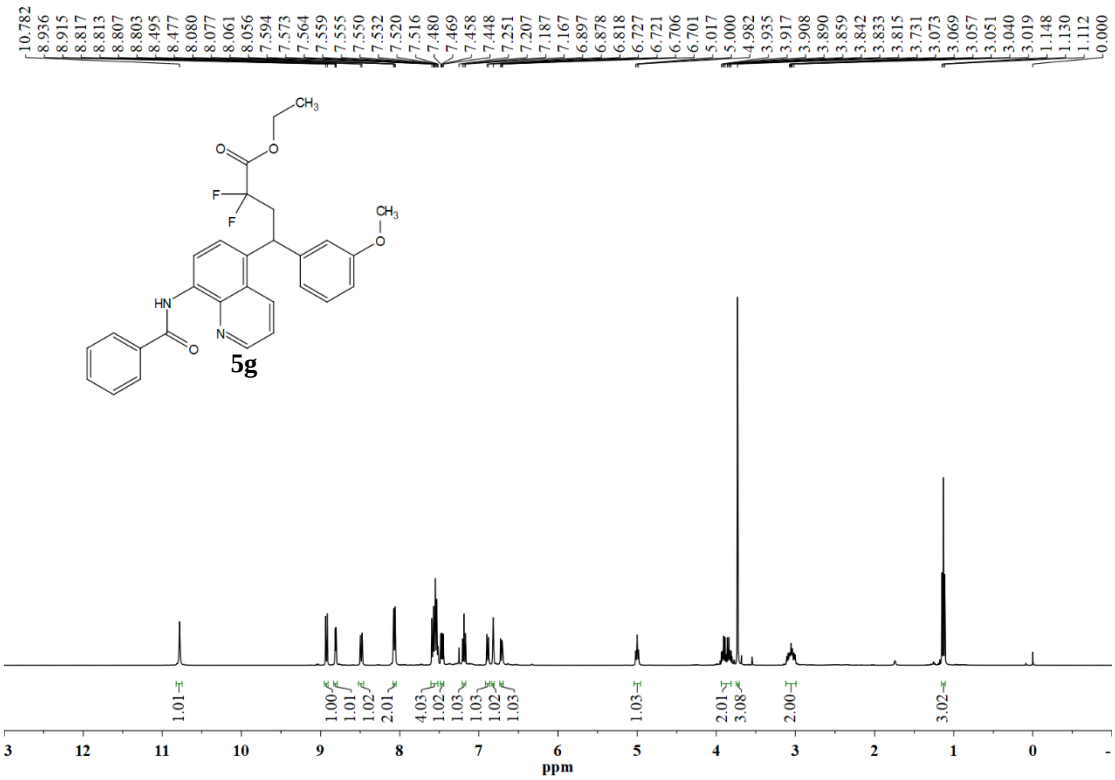
^{13}C NMR (101 MHz, Chloroform-*d*)



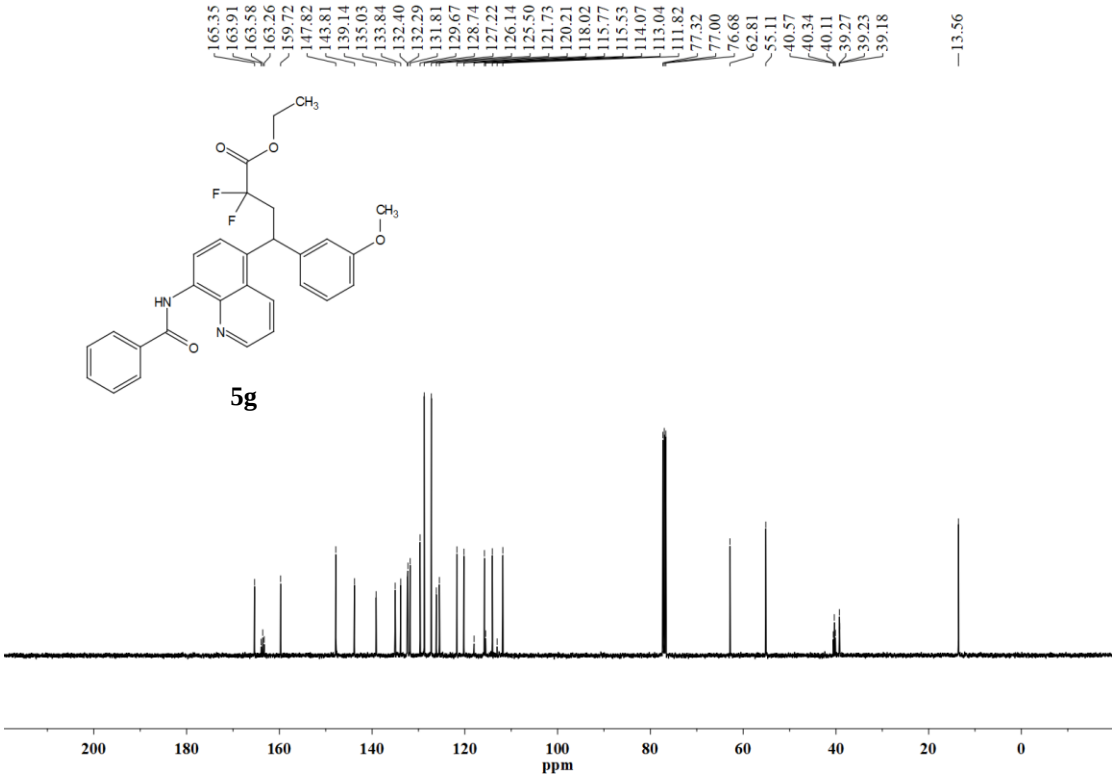
^{19}F NMR (376 MHz, Chloroform-*d*)



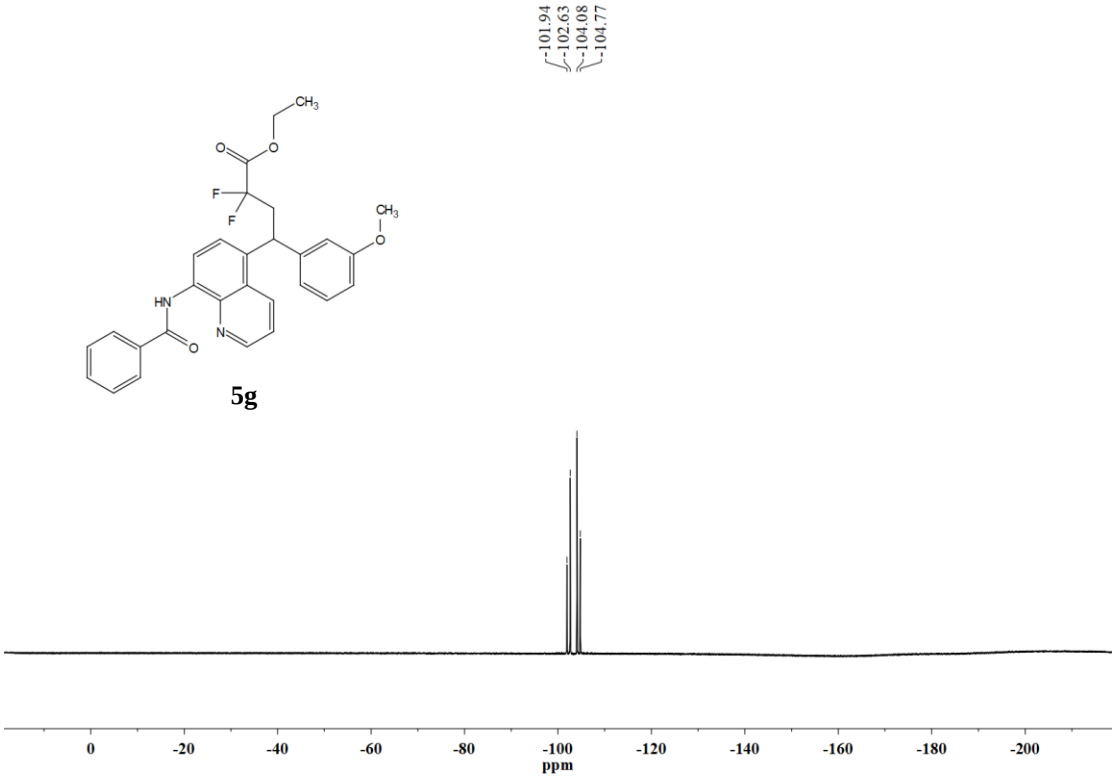
^{1}H NMR (400 MHz, Chloroform-*d*)



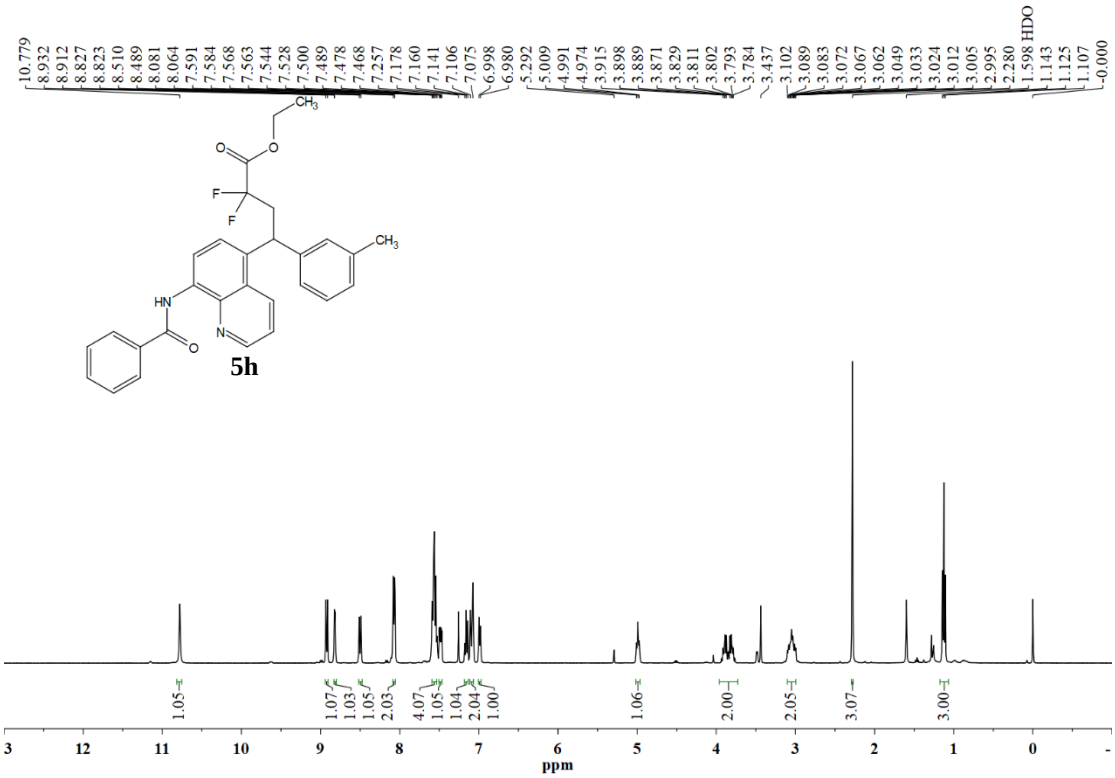
^{13}C NMR (101 MHz, Chloroform-*d*)



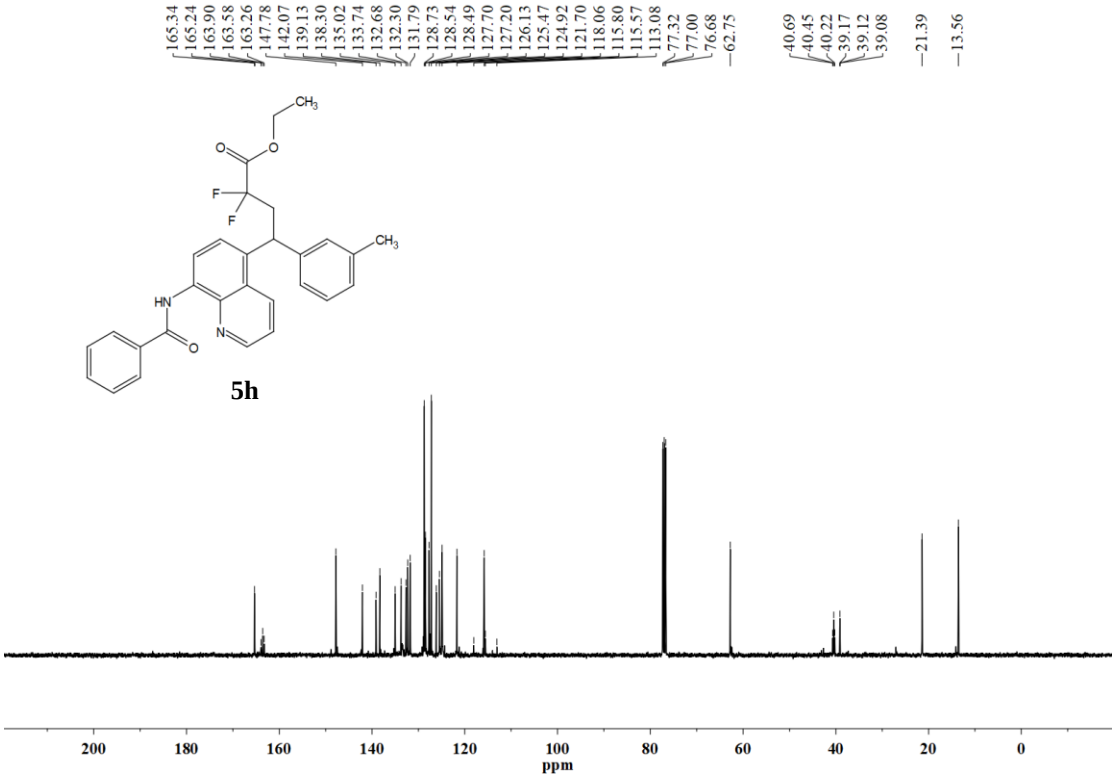
^{19}F NMR (376 MHz, Chloroform-*d*)



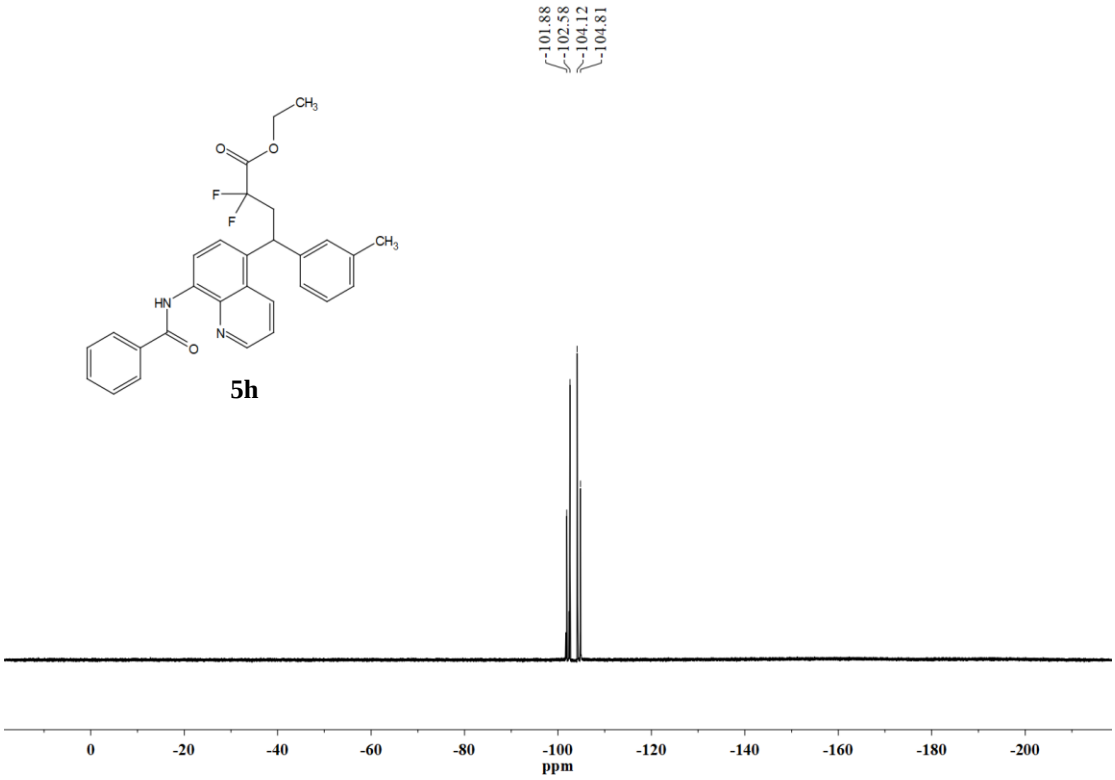
^{1}H NMR (400 MHz, Chloroform-*d*)



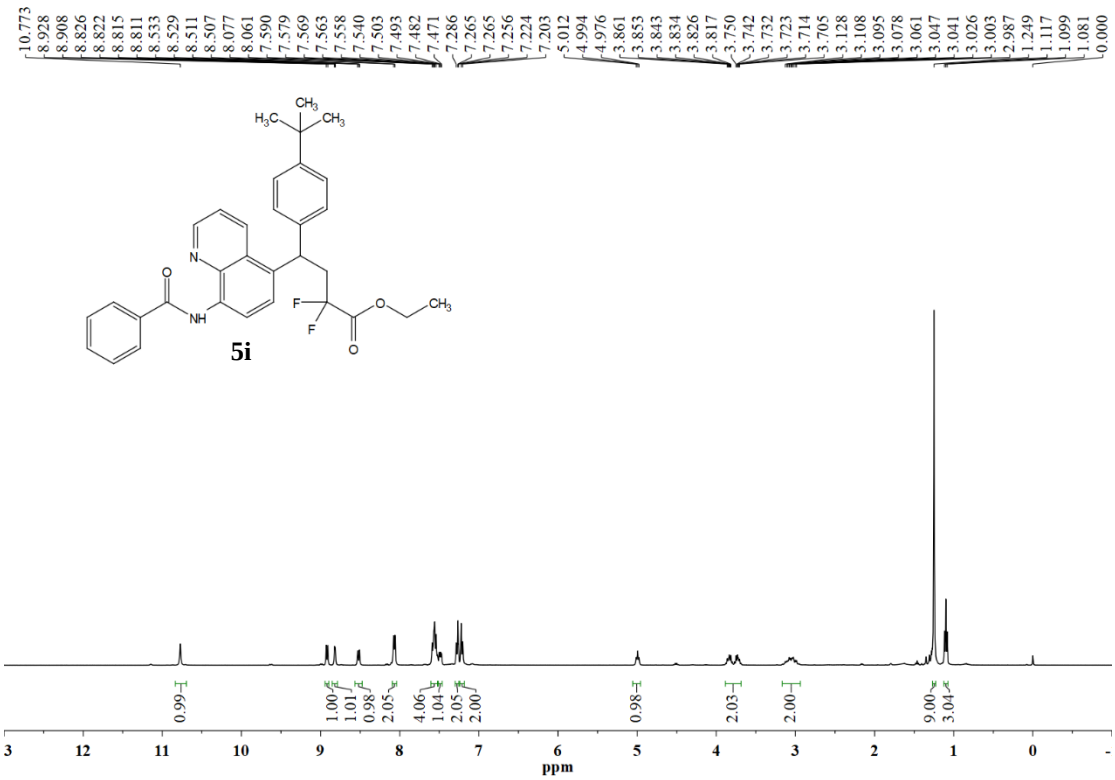
^{13}C NMR (101 MHz, Chloroform-*d*)



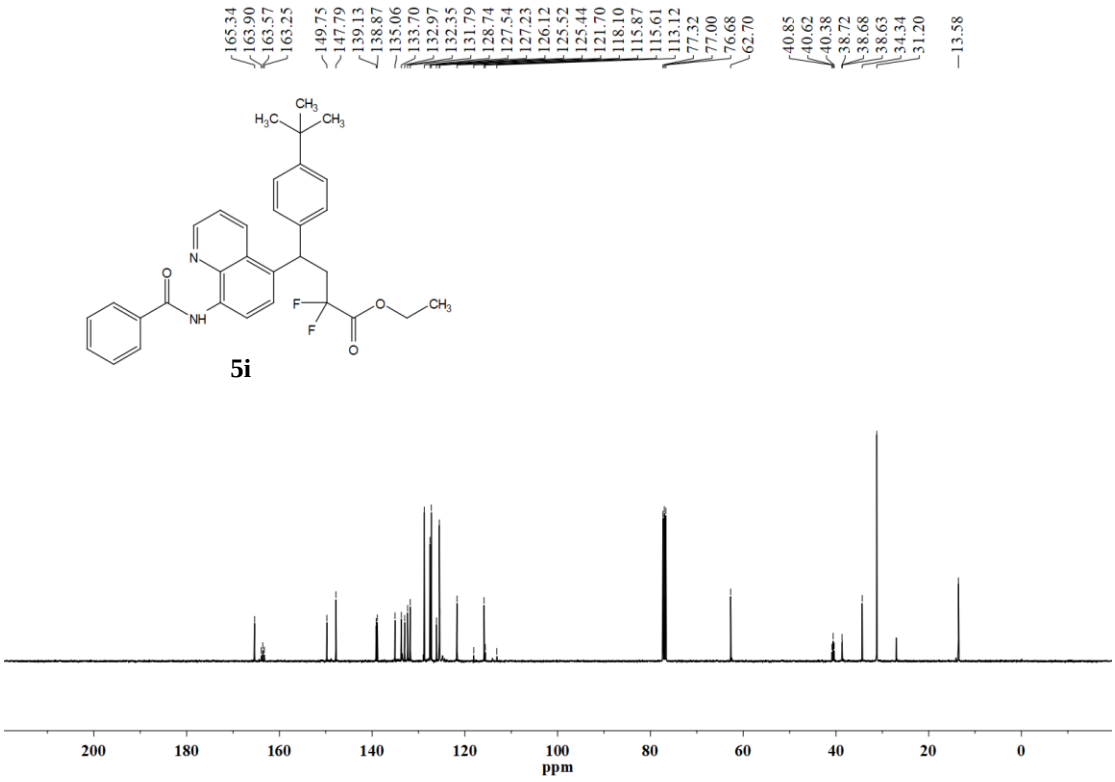
^{19}F NMR (376 MHz, Chloroform-*d*)



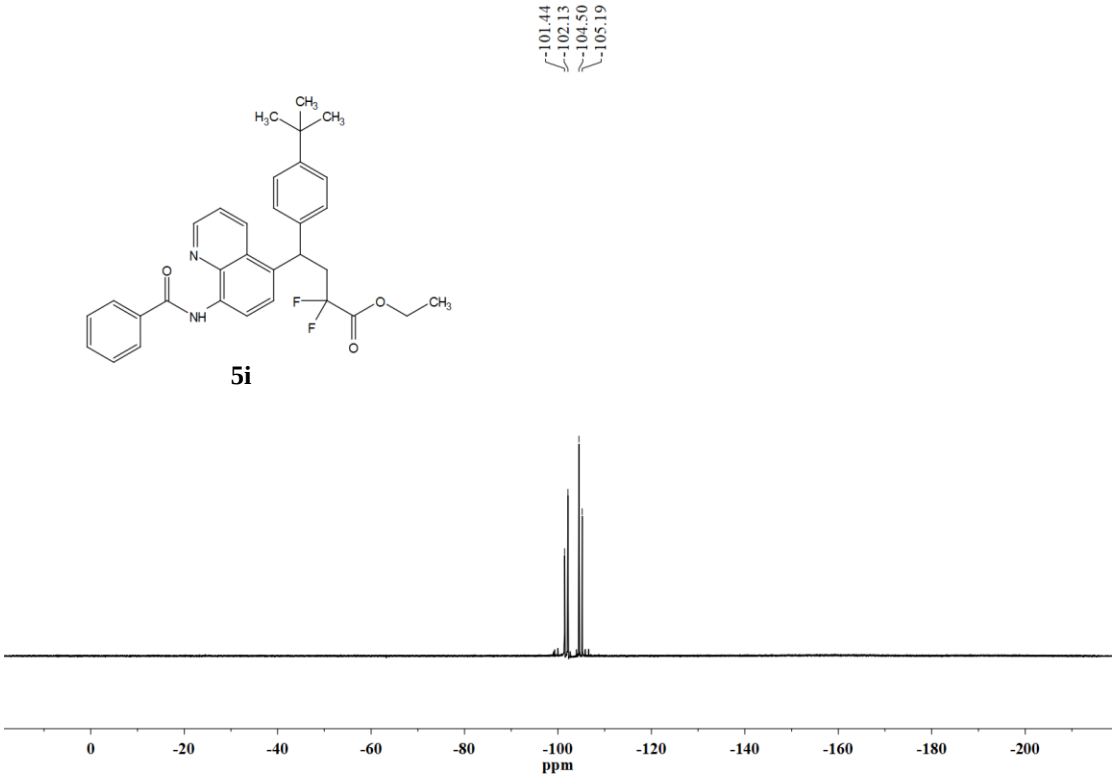
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



^{19}F NMR (376 MHz, Chloroform-*d*)



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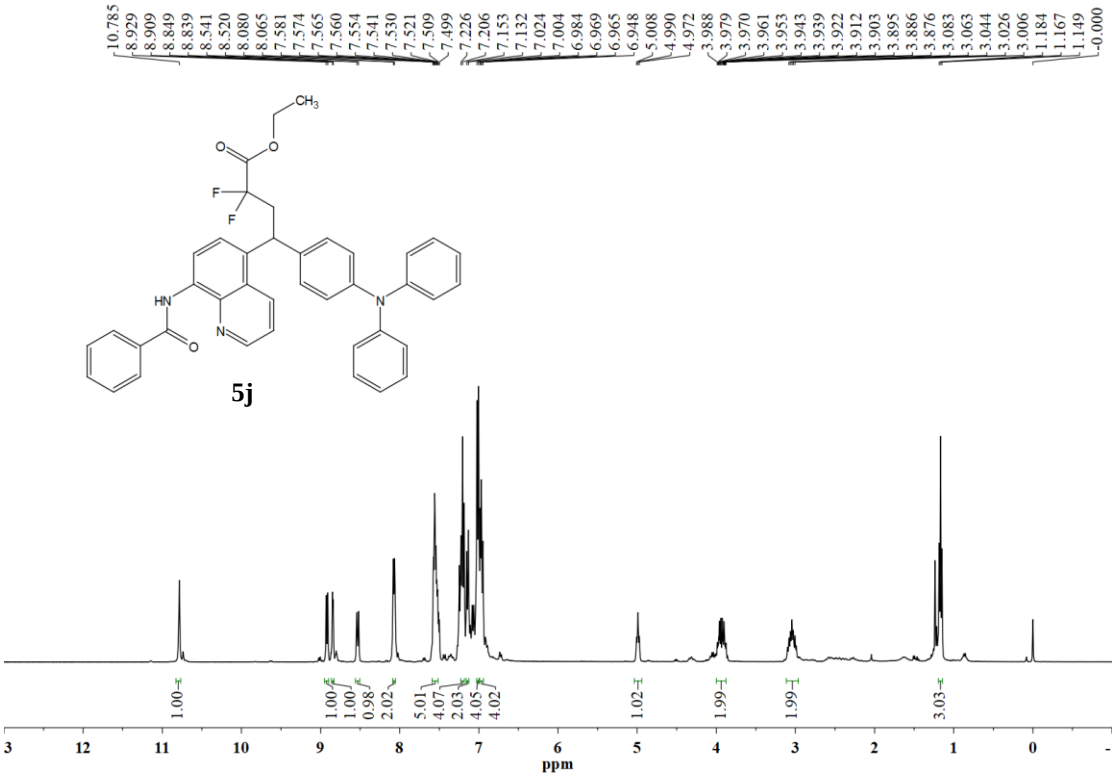
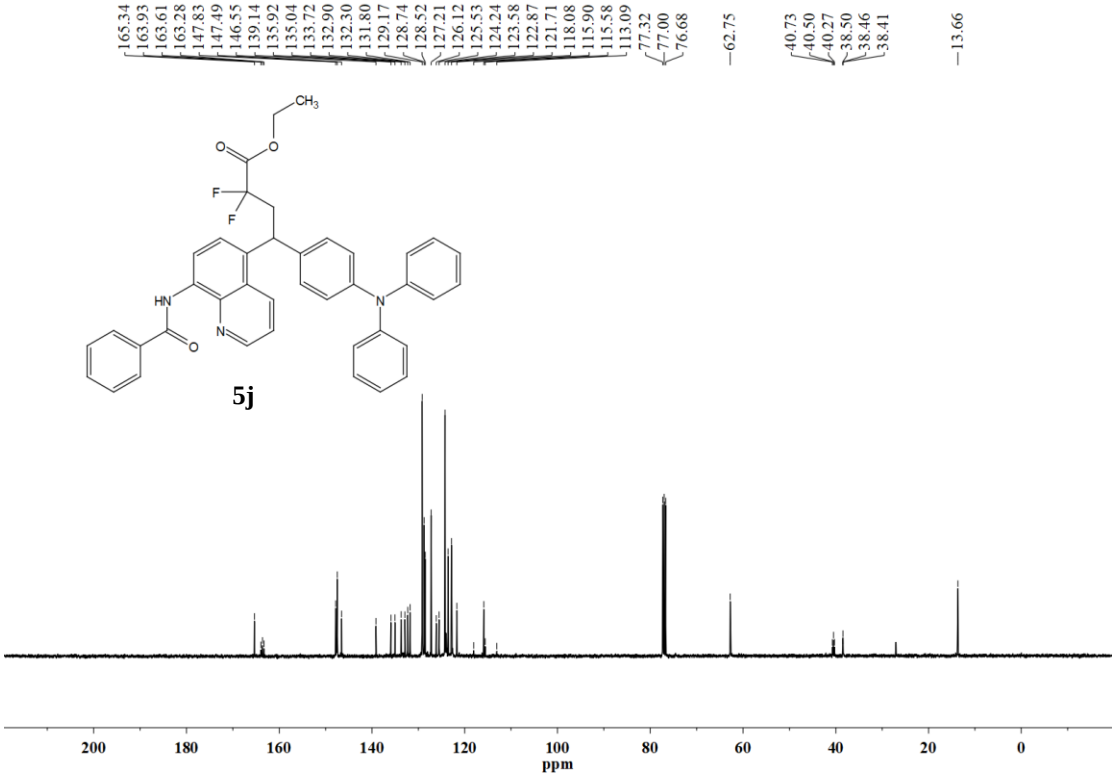


^{13}C NMR (101 MHz, Chloroform-*d*)



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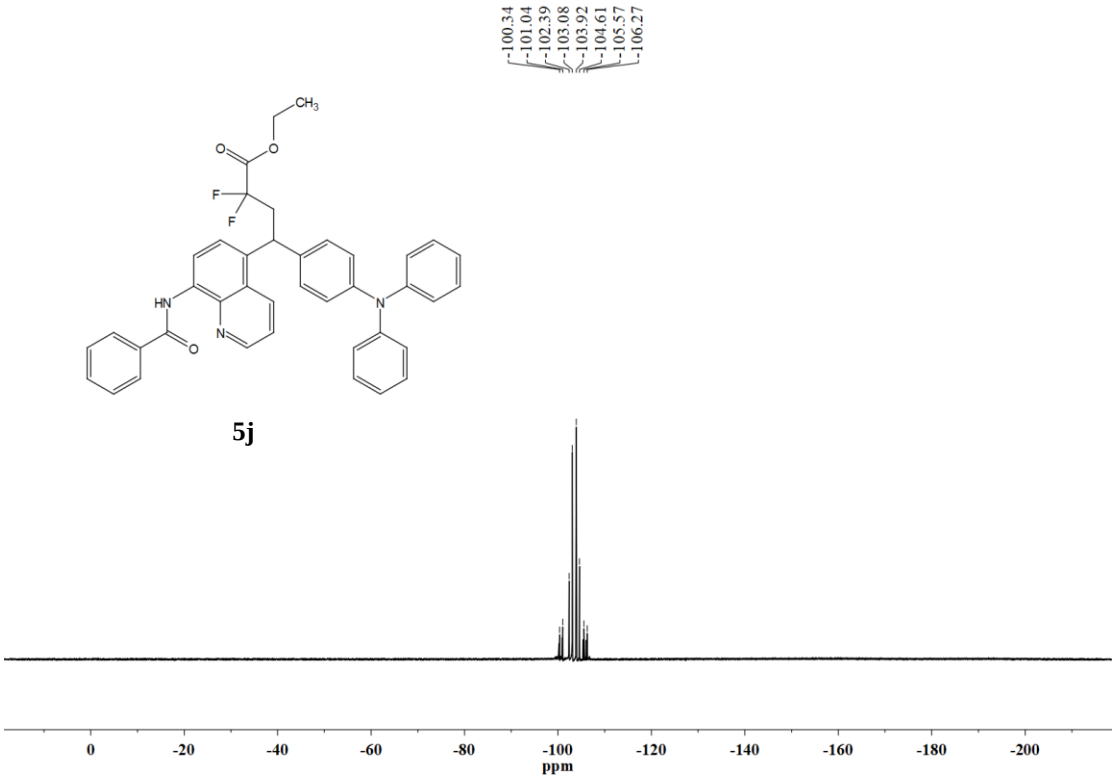

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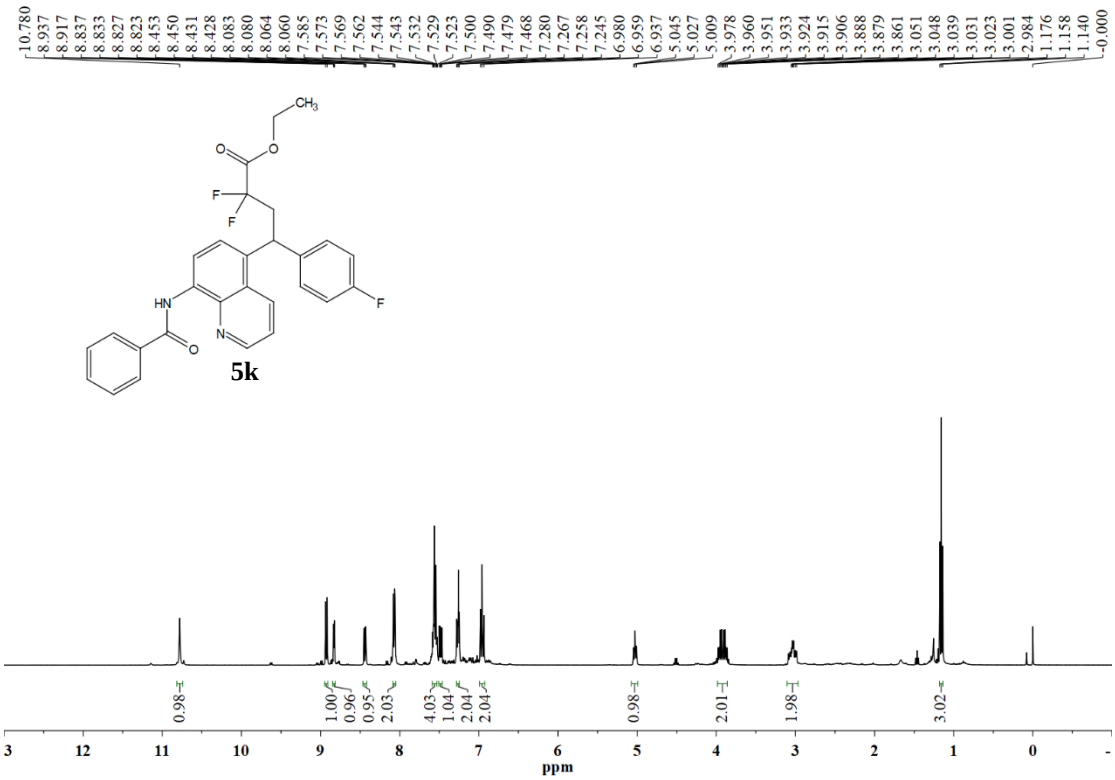

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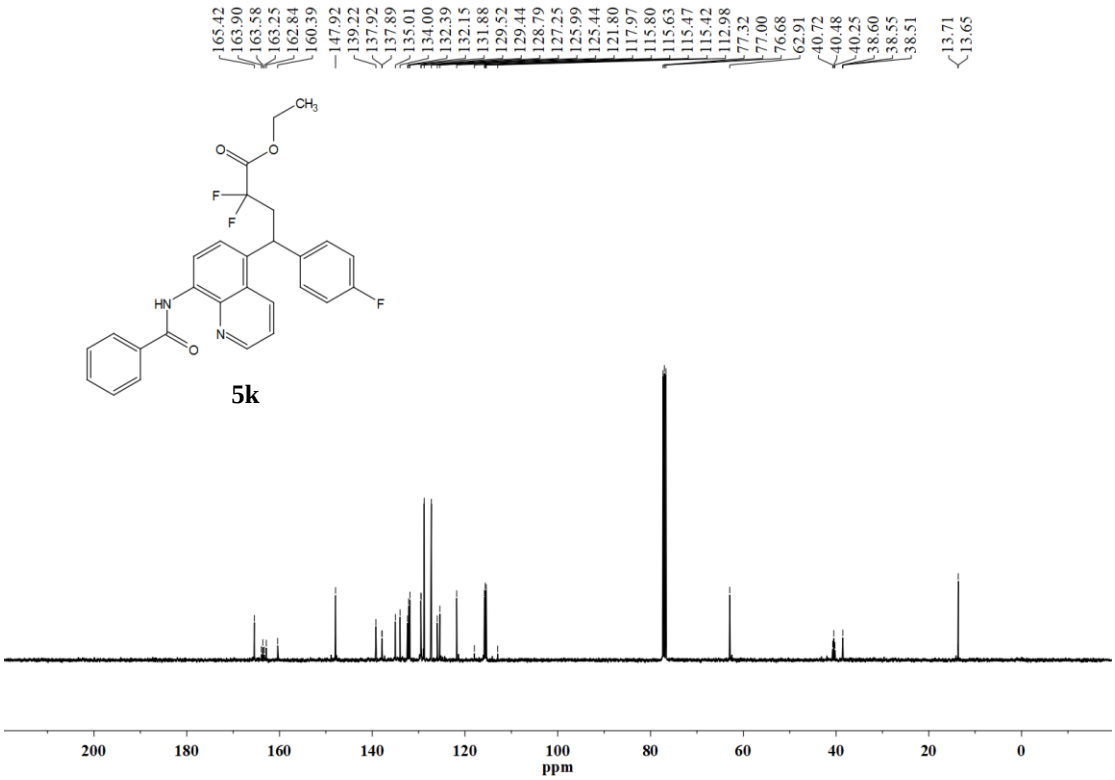

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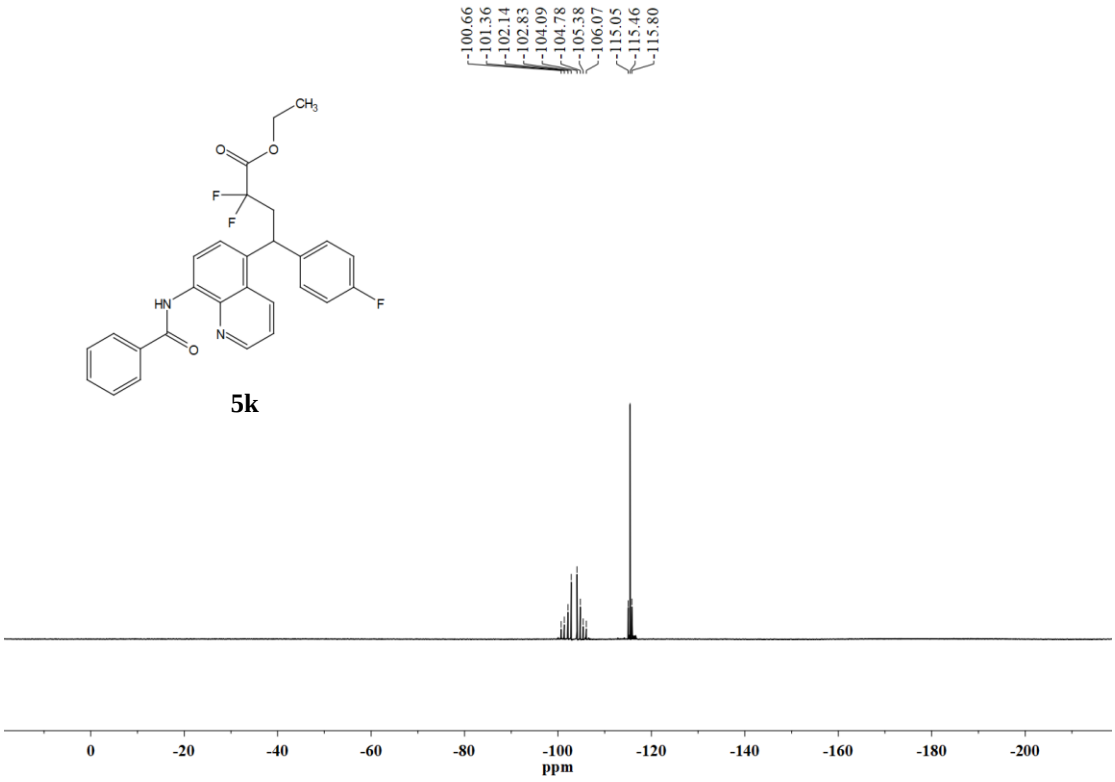

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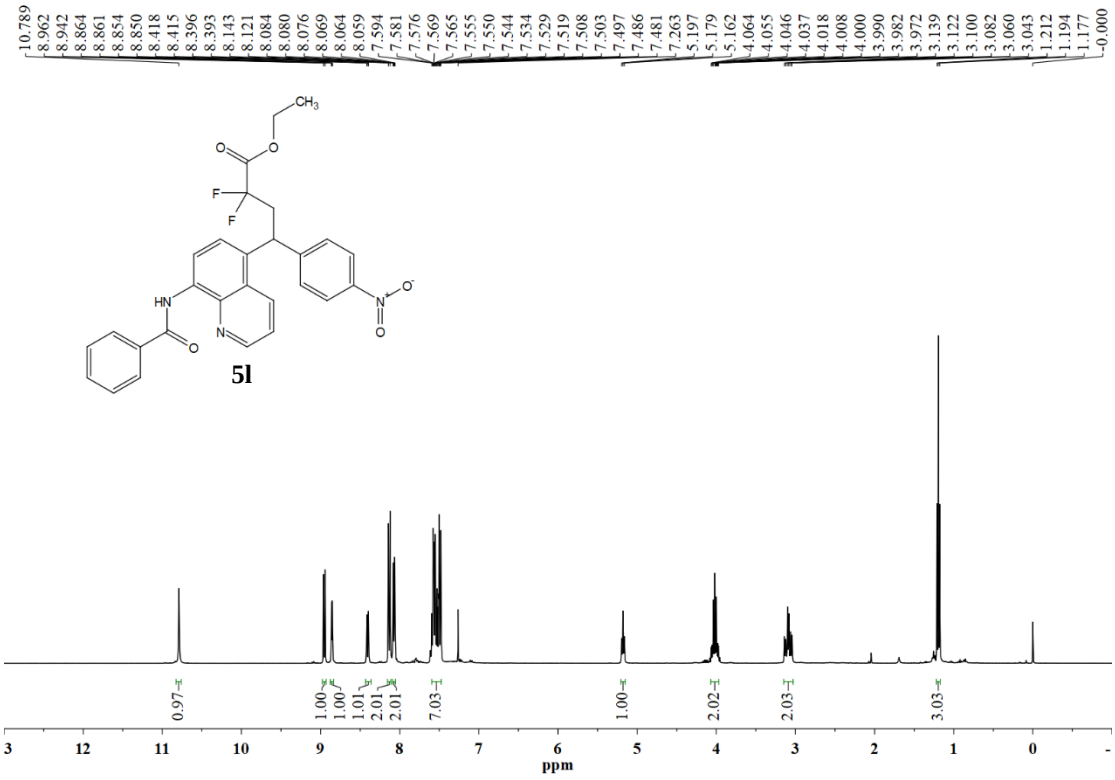

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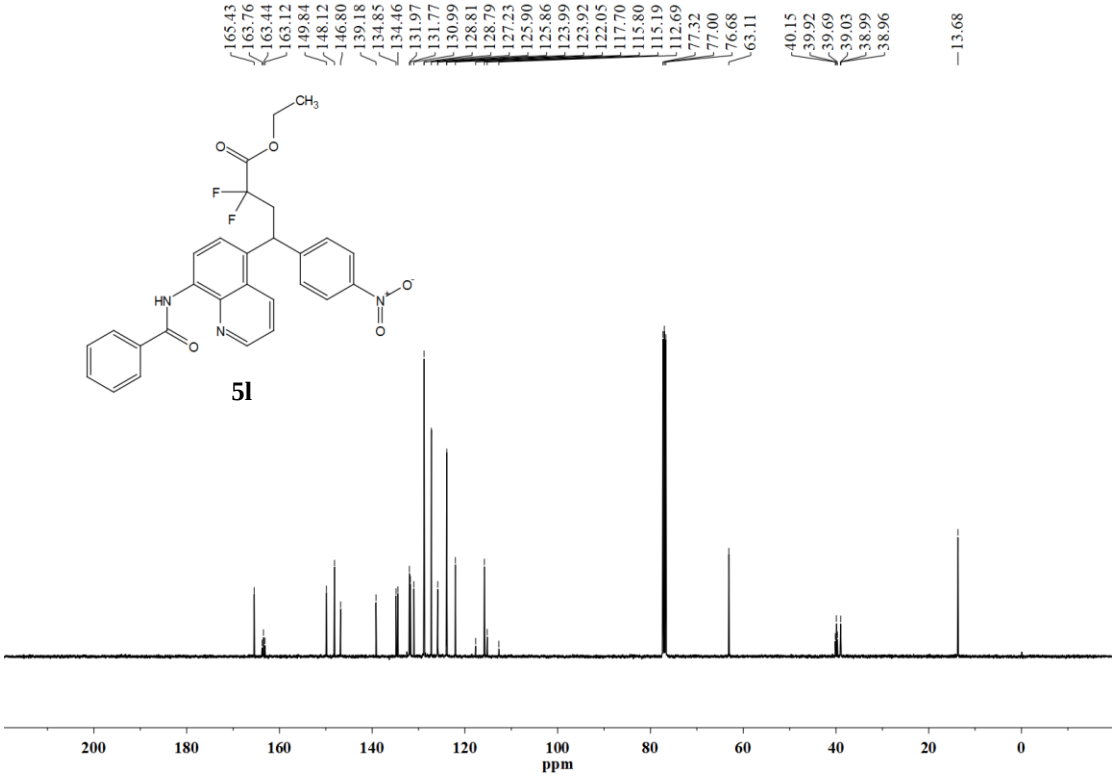

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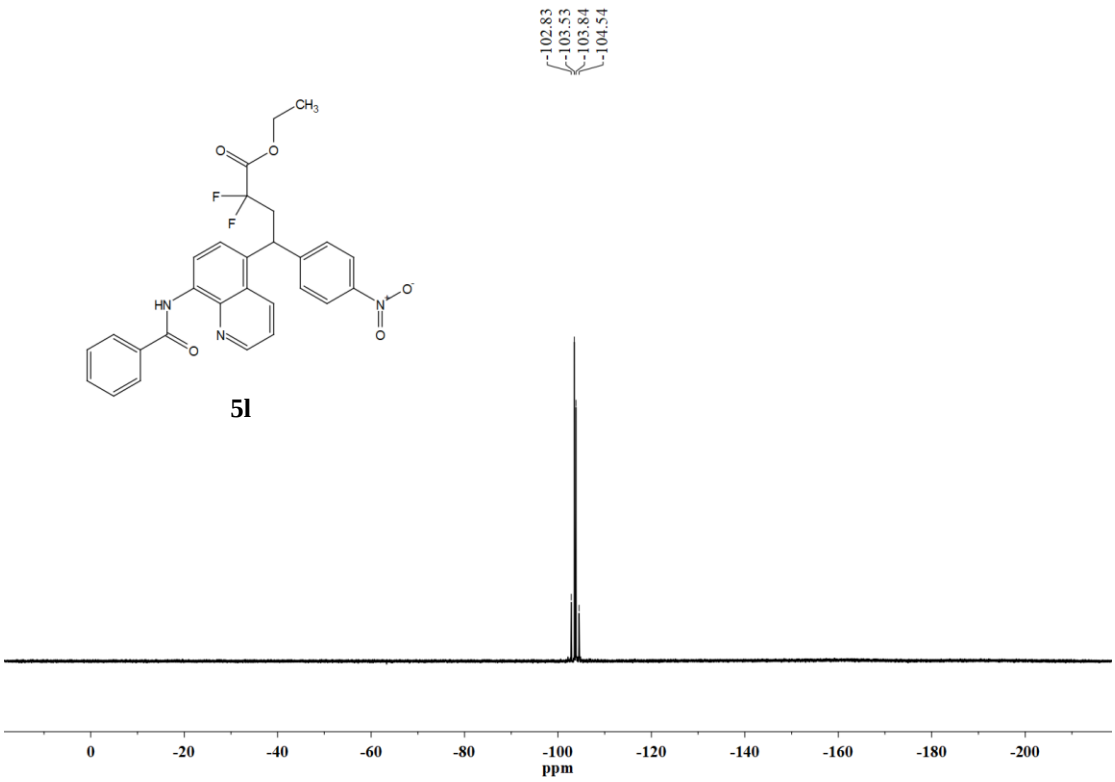

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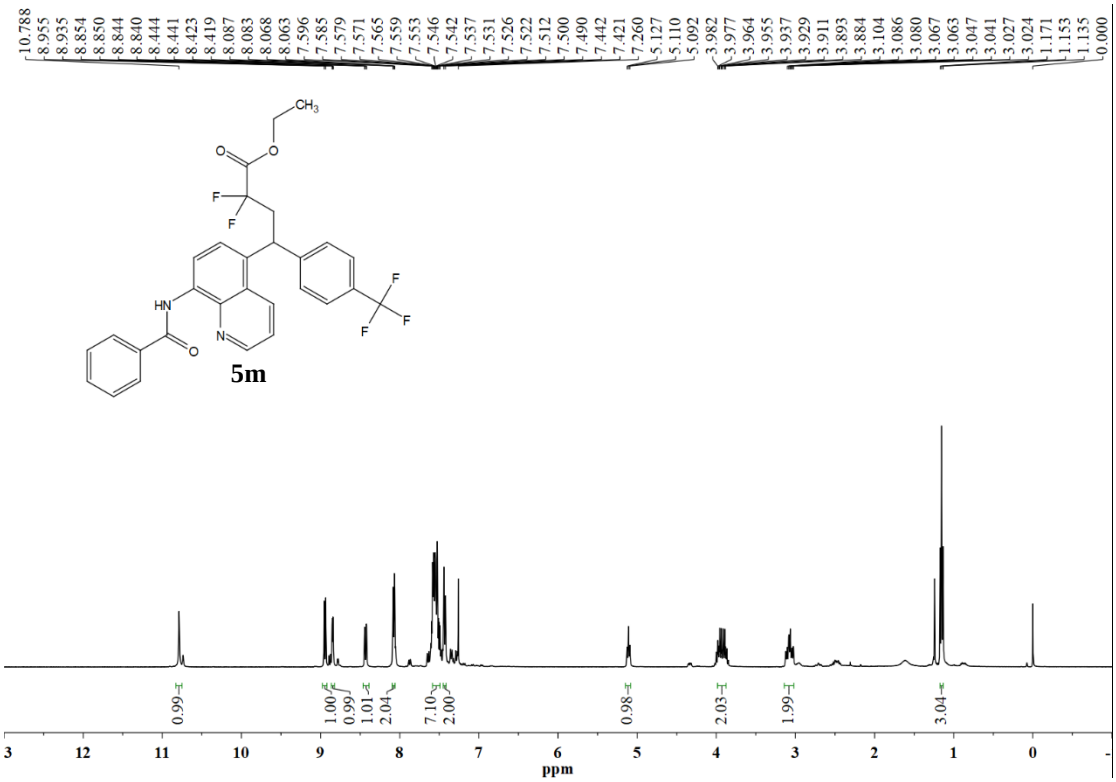

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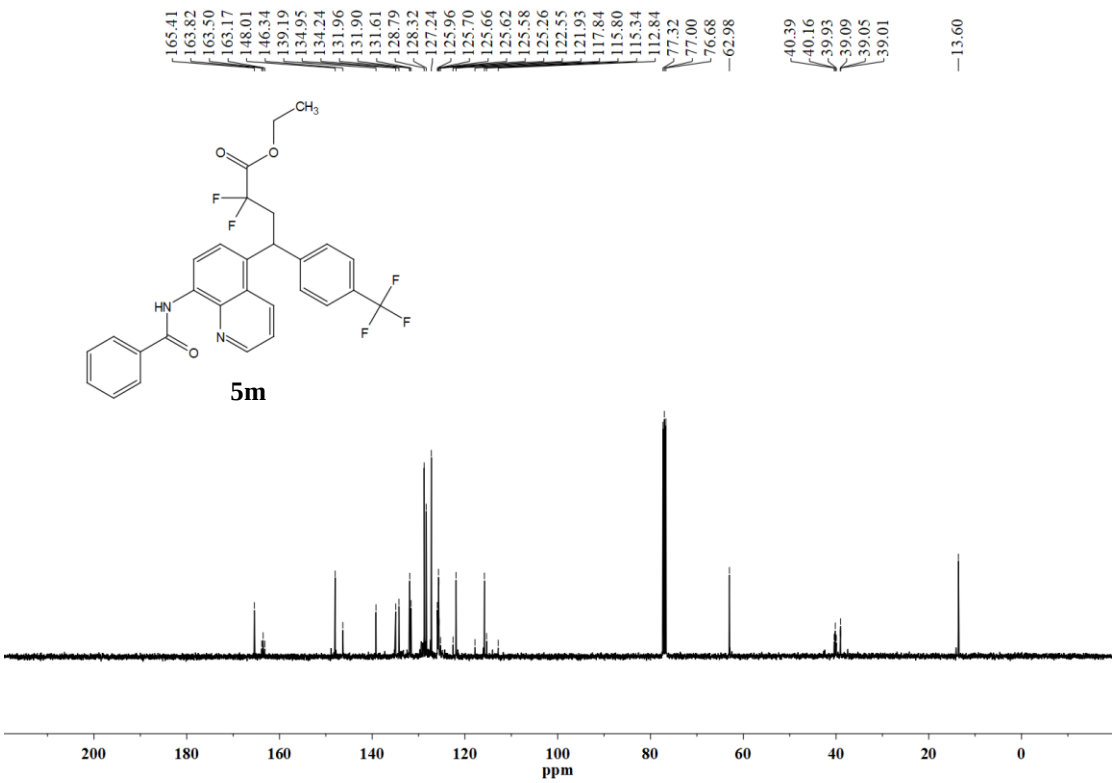

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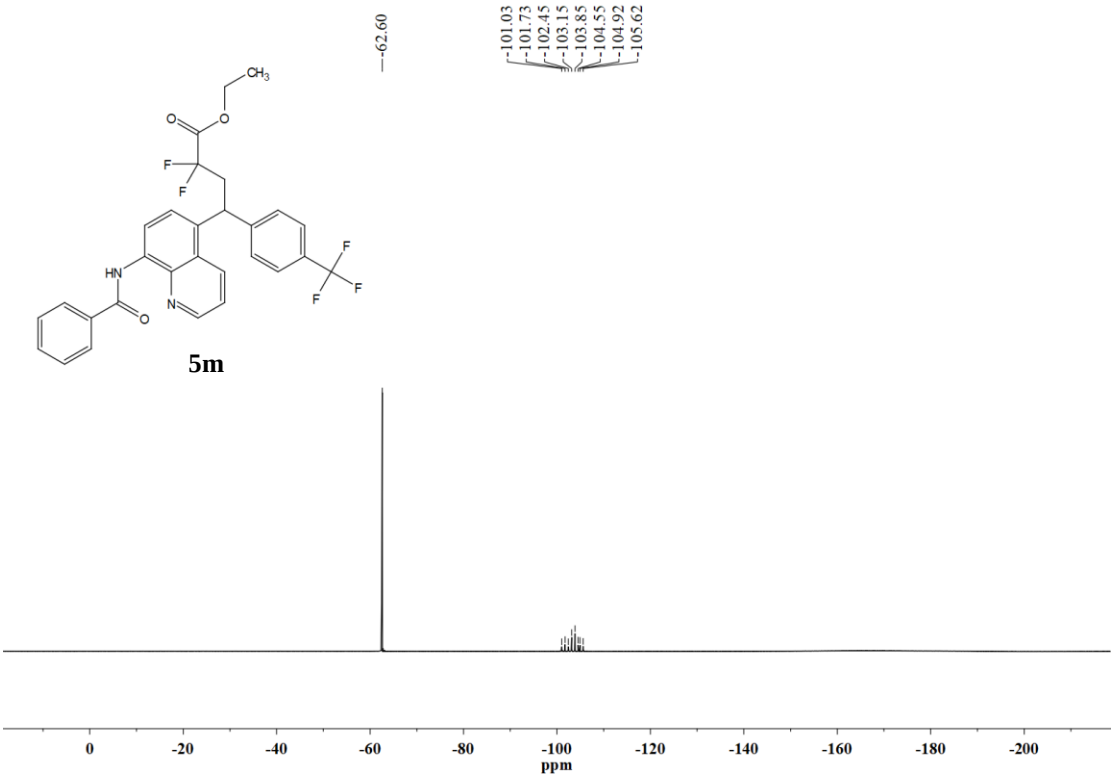

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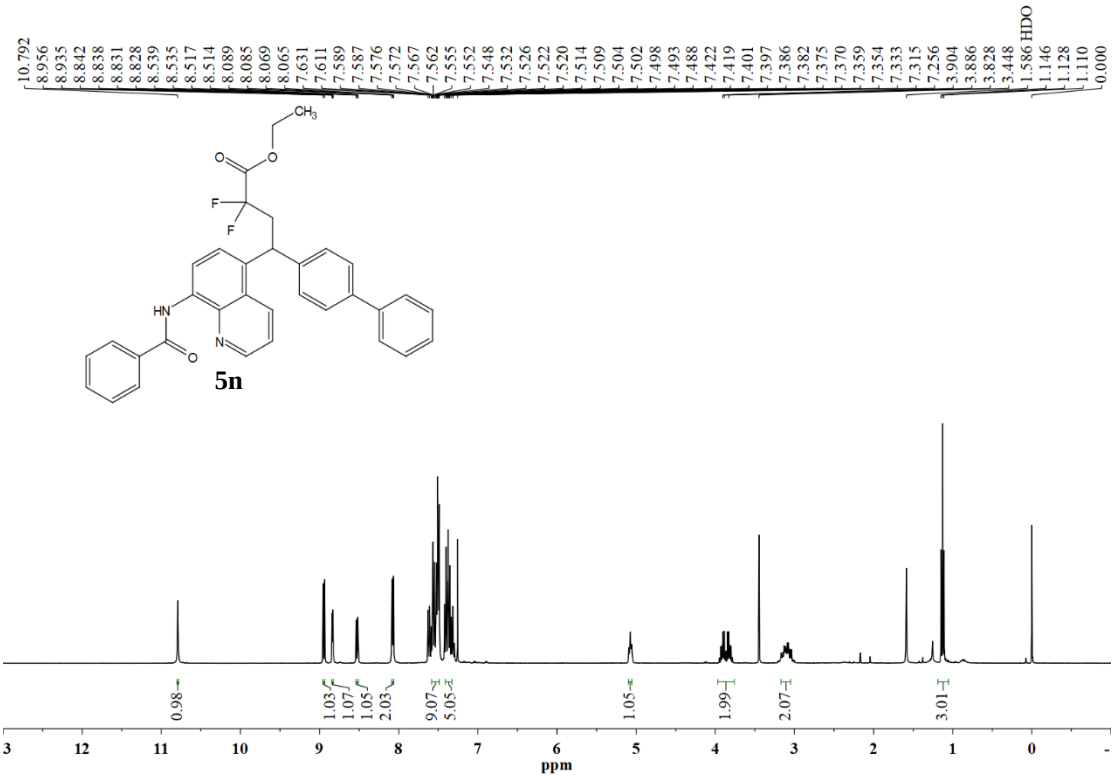

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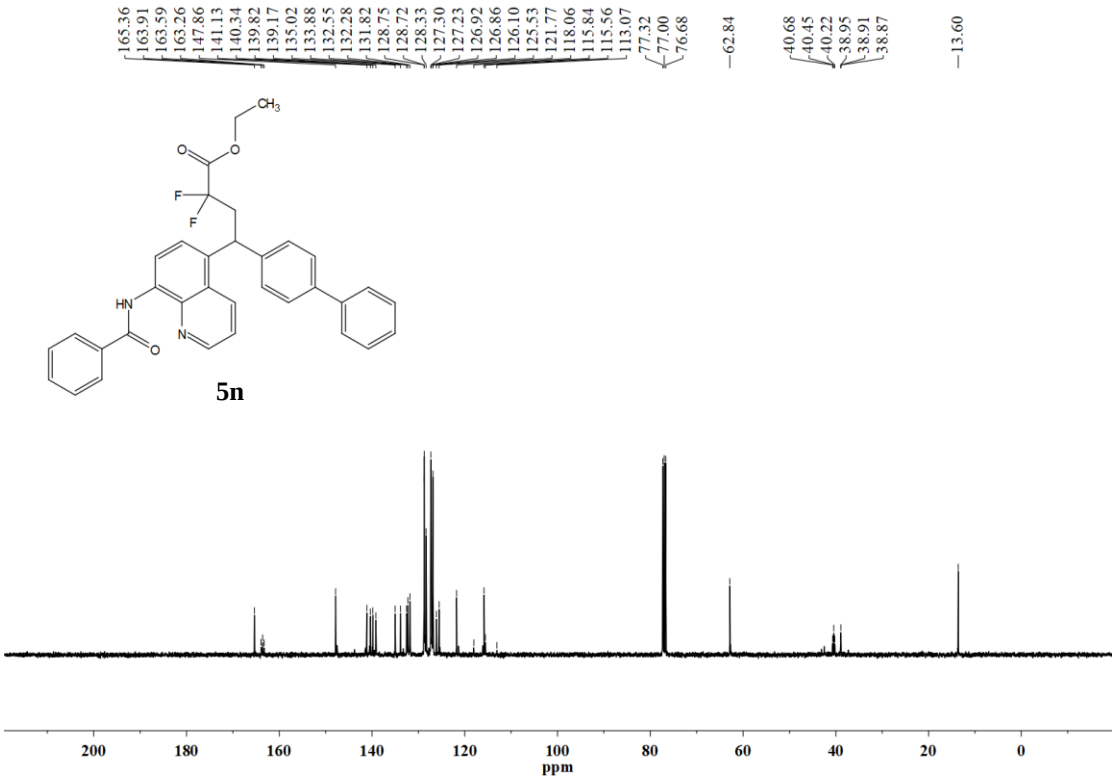
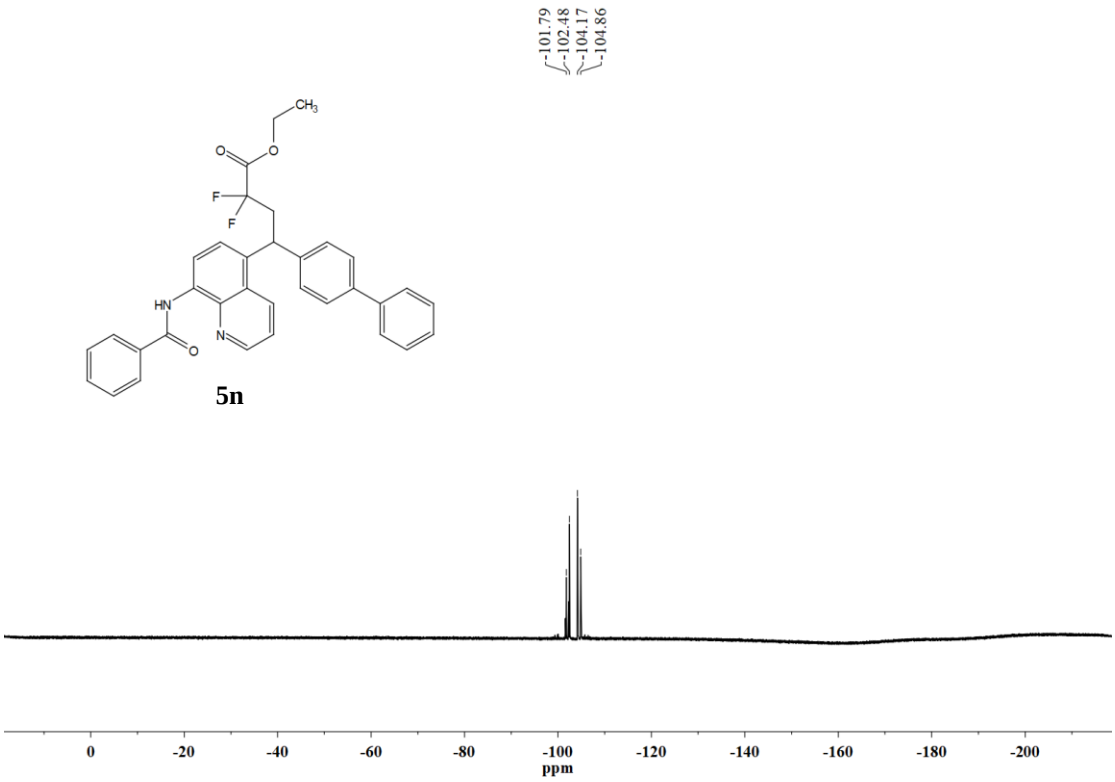


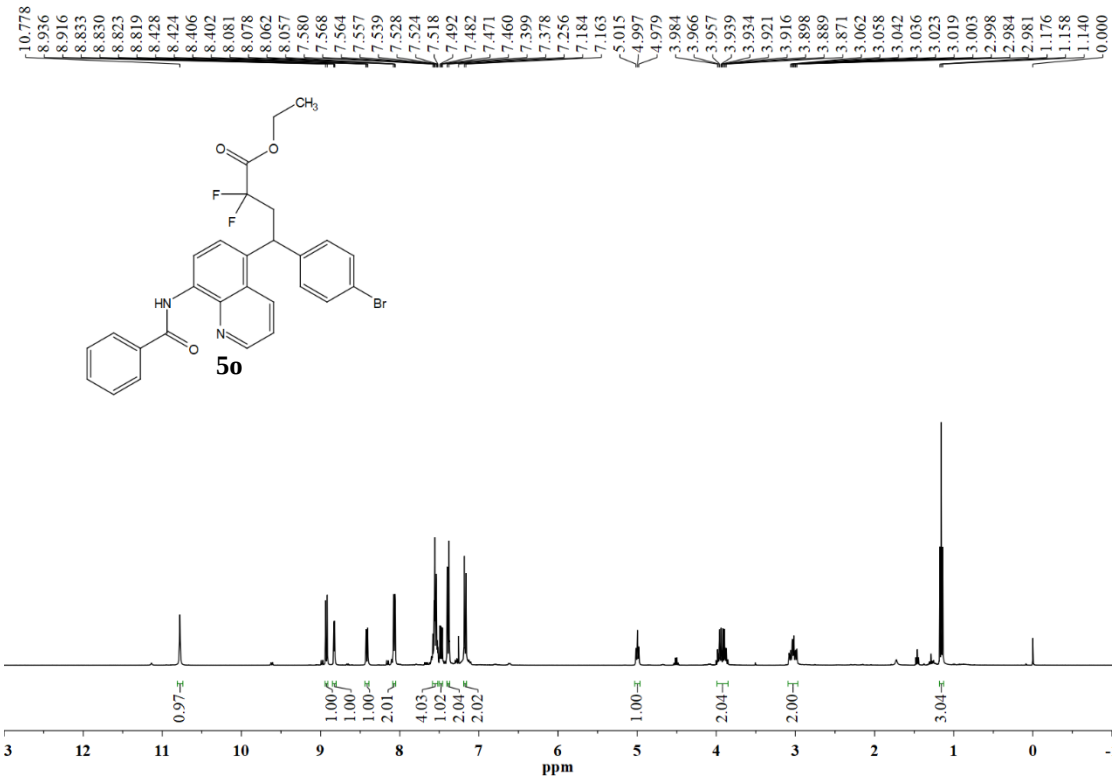
5n

^{19}F NMR (376 MHz, Chloroform-*d*)

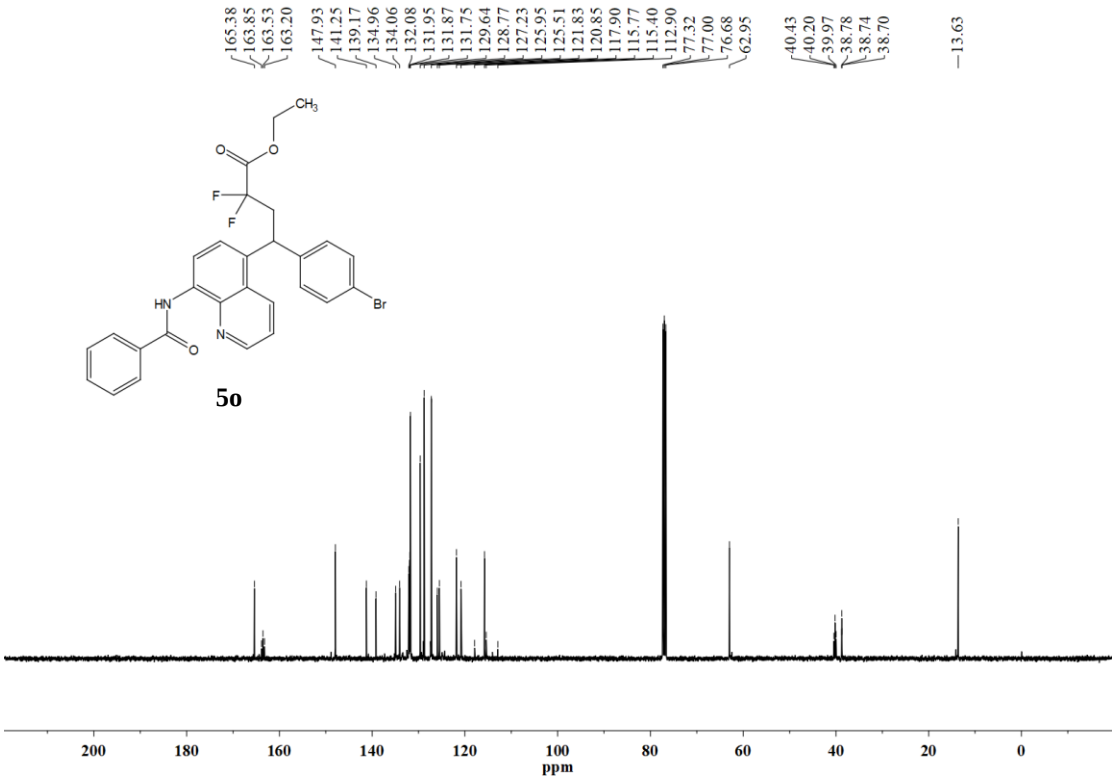


5n

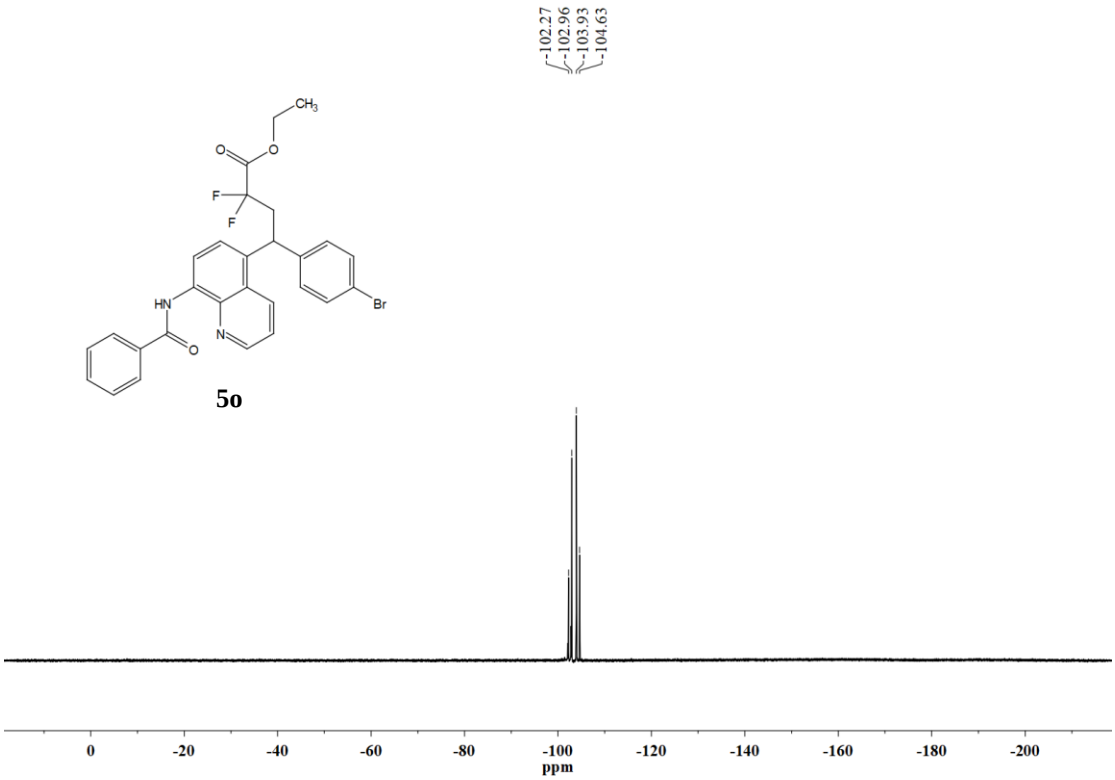
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



^{19}F NMR (376 MHz, Chloroform-*d*)



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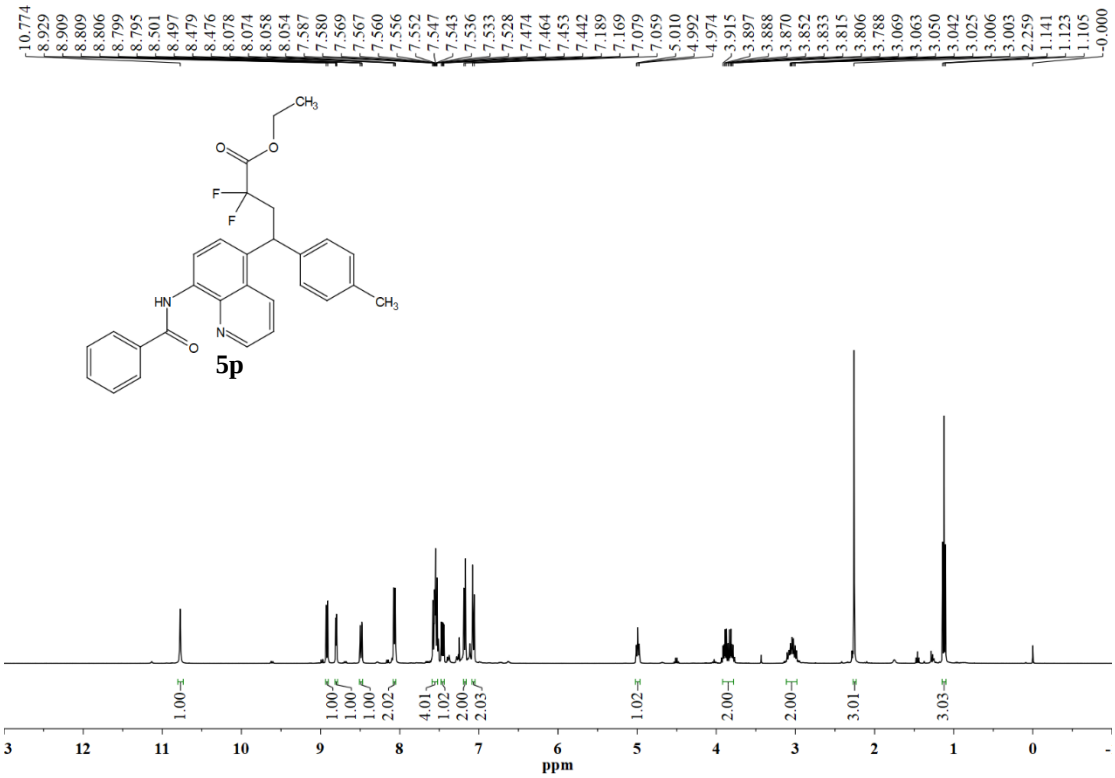

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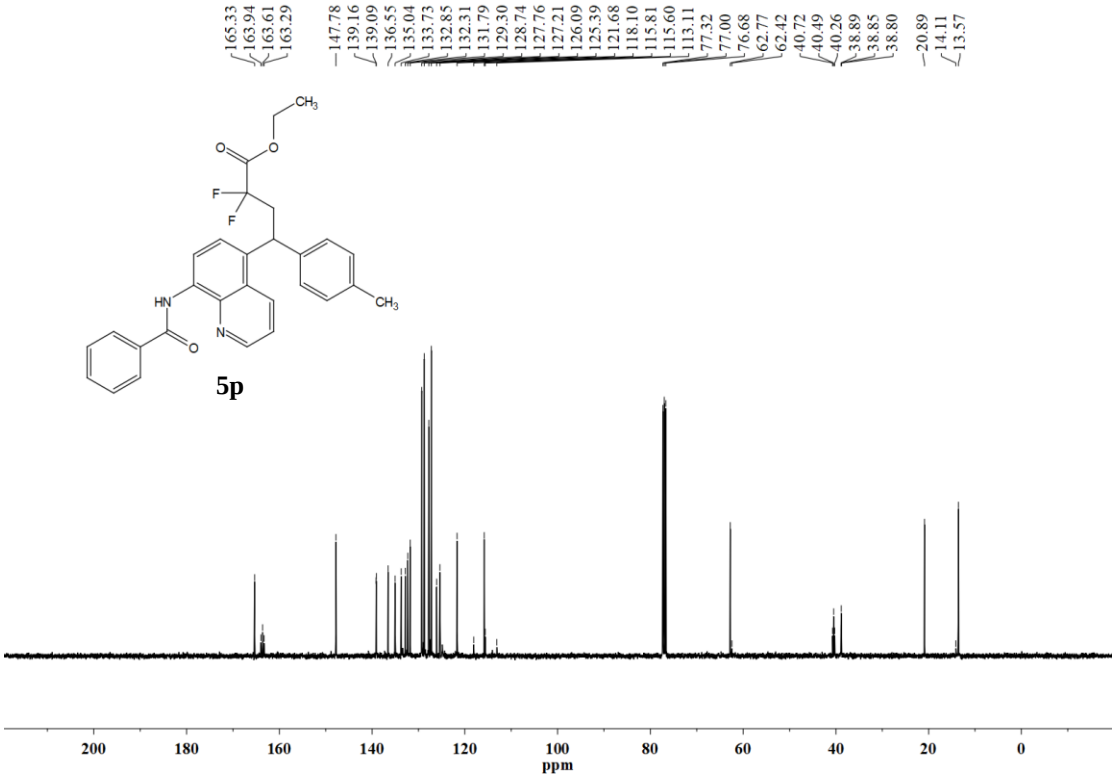

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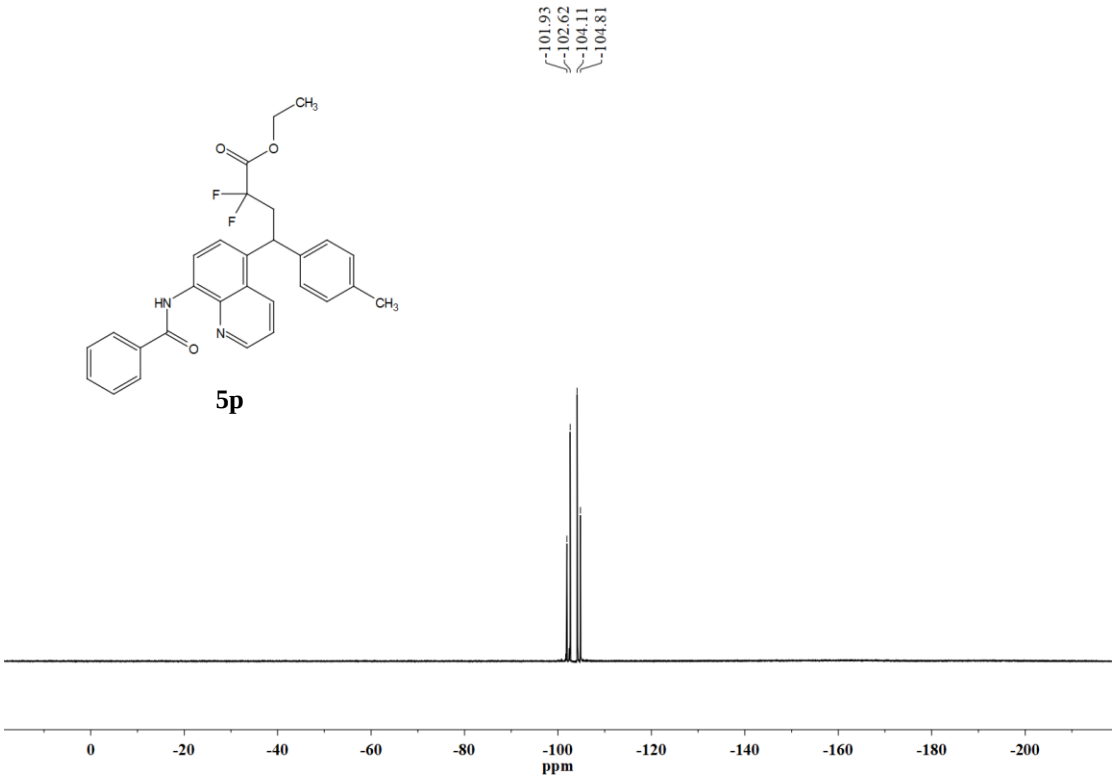

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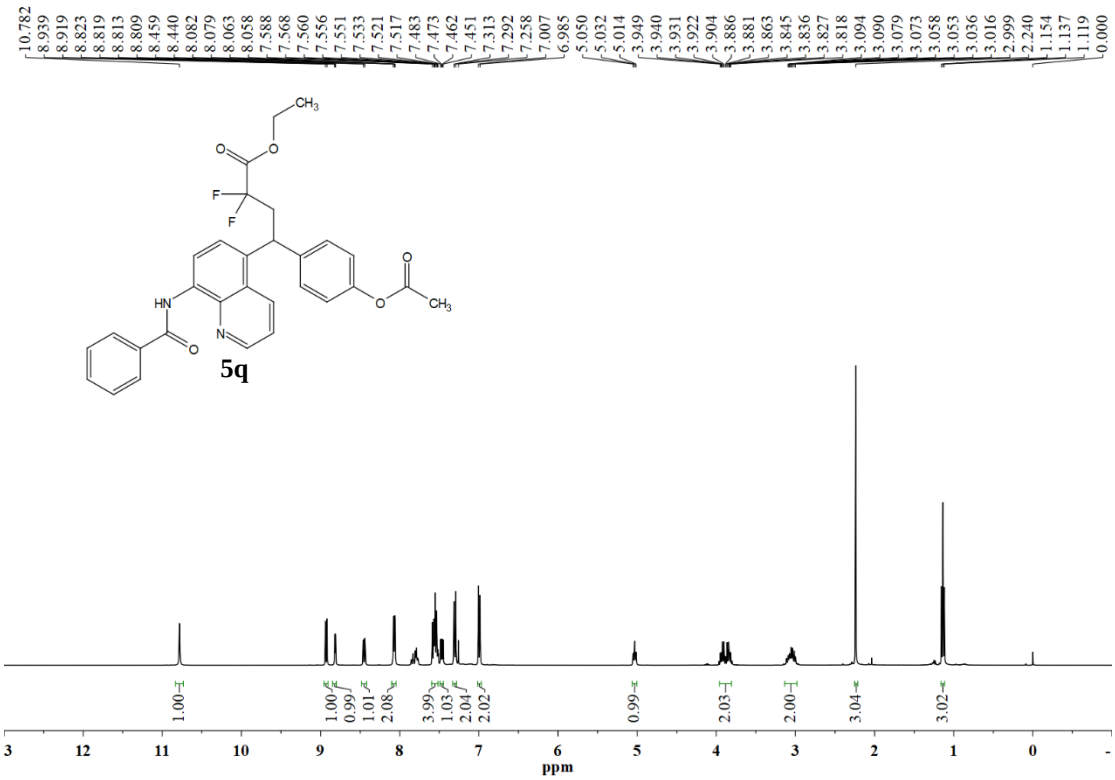

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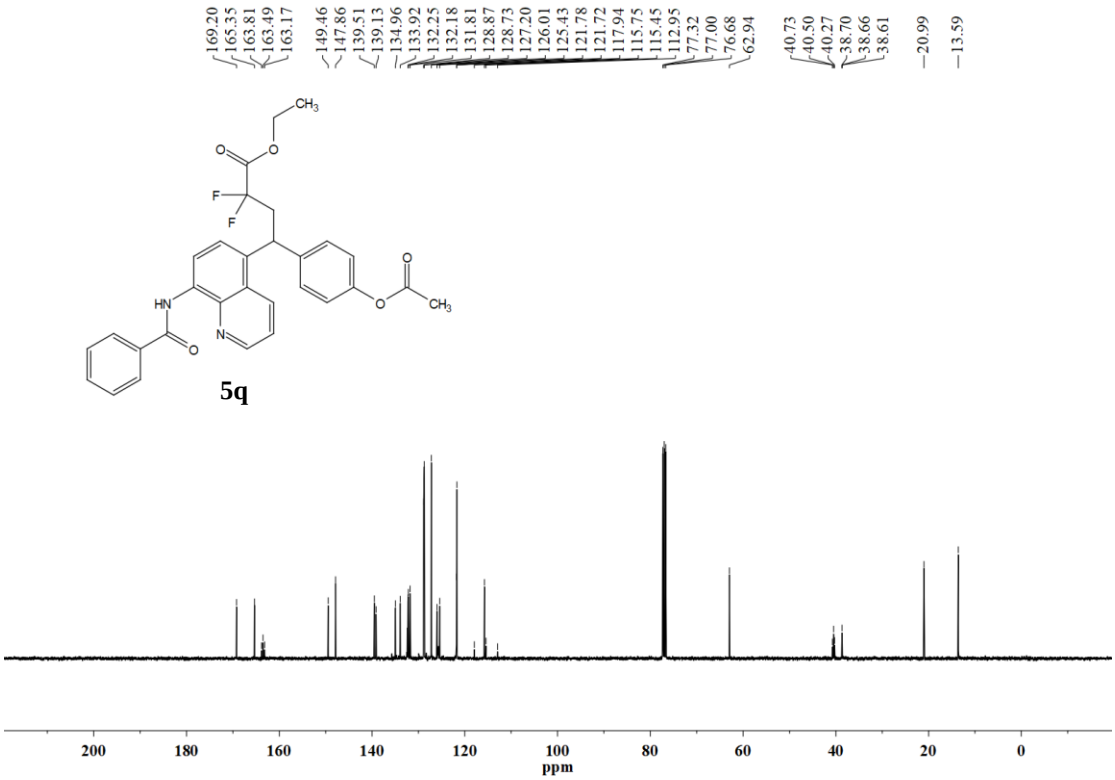

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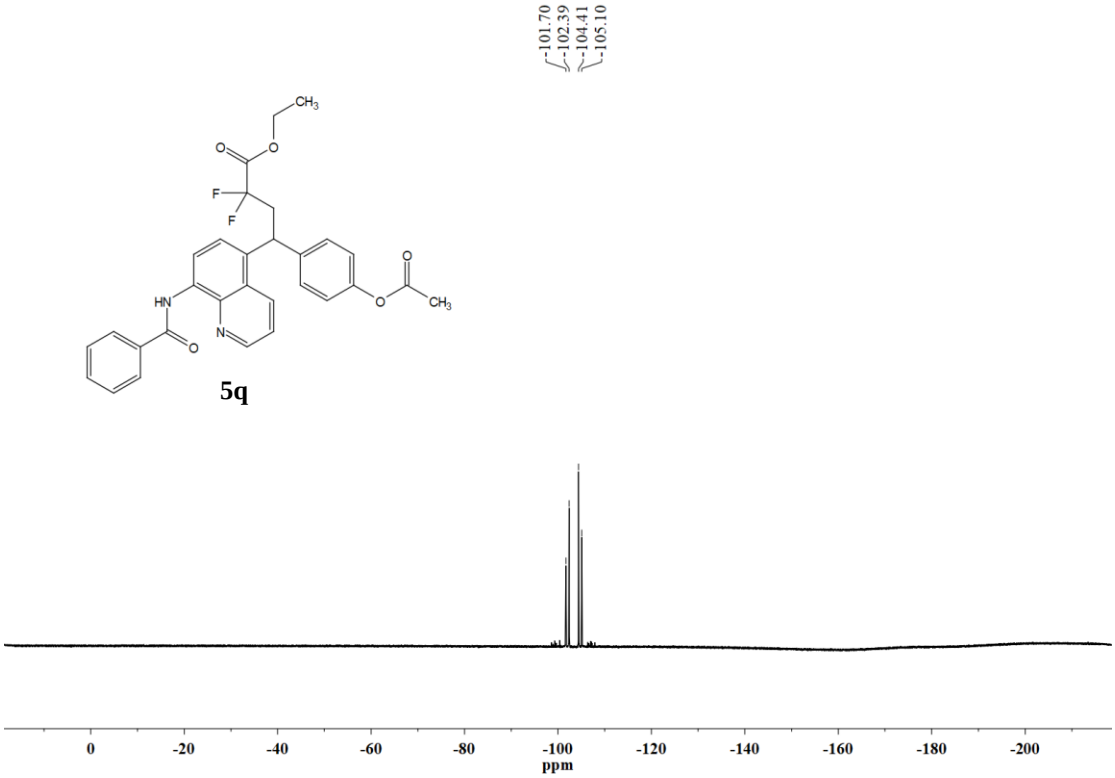

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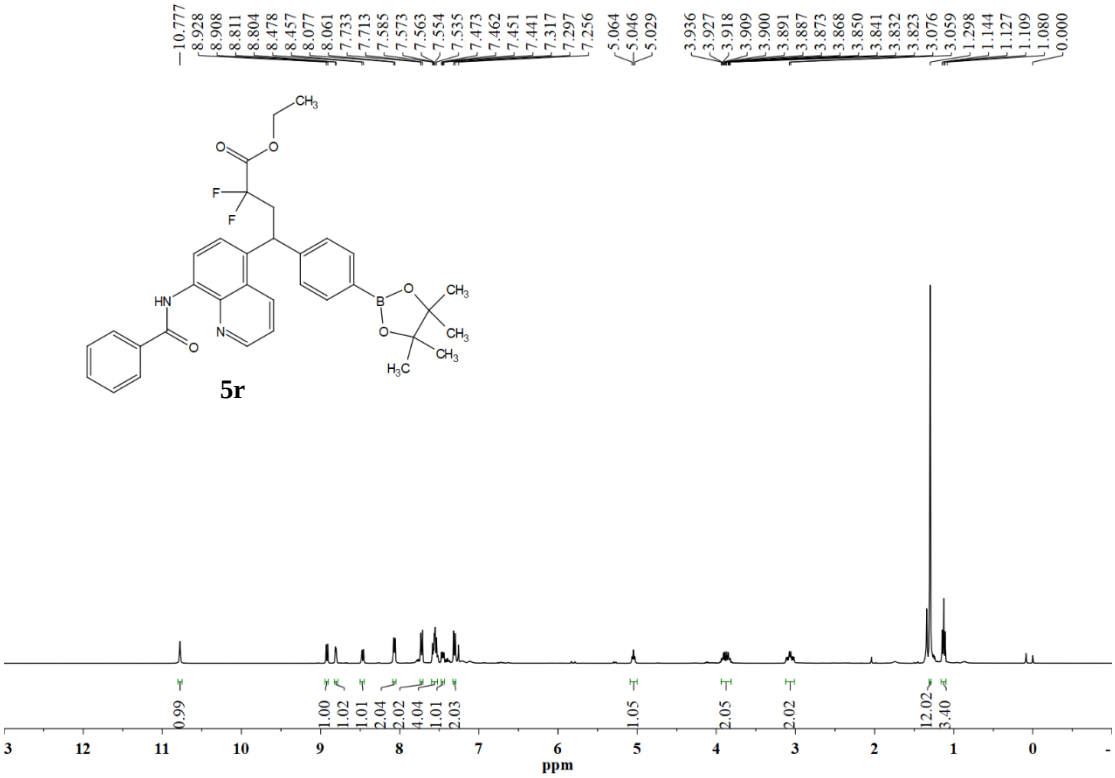

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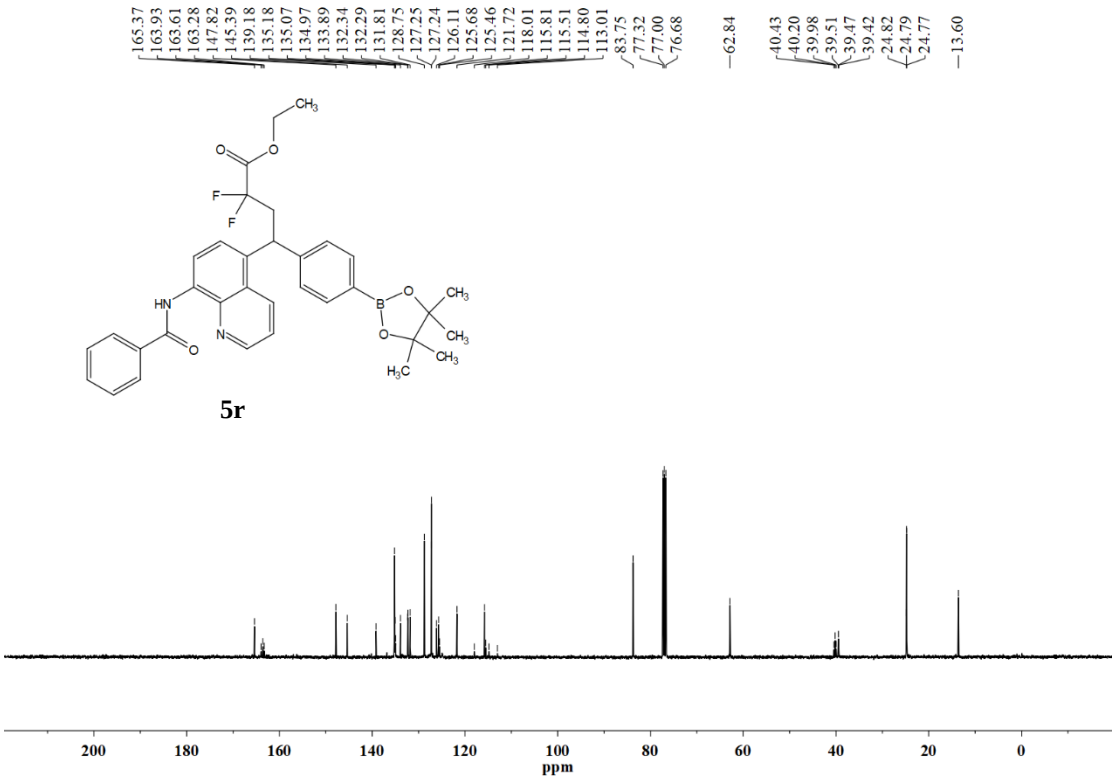

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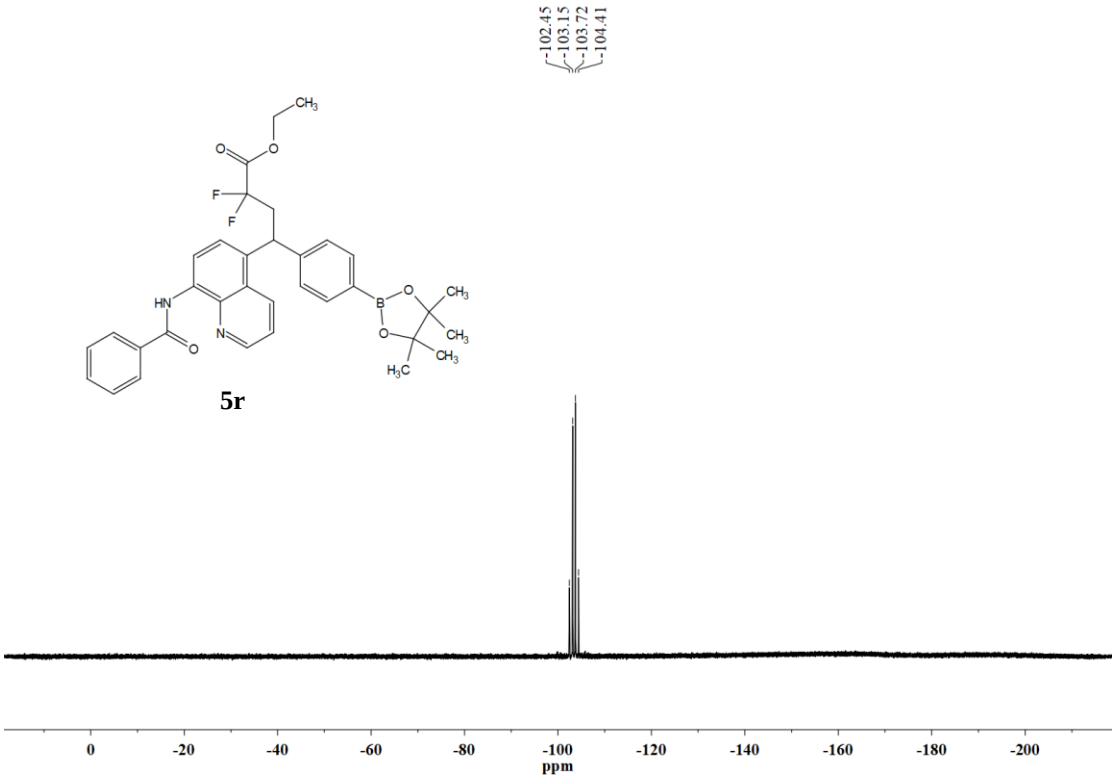

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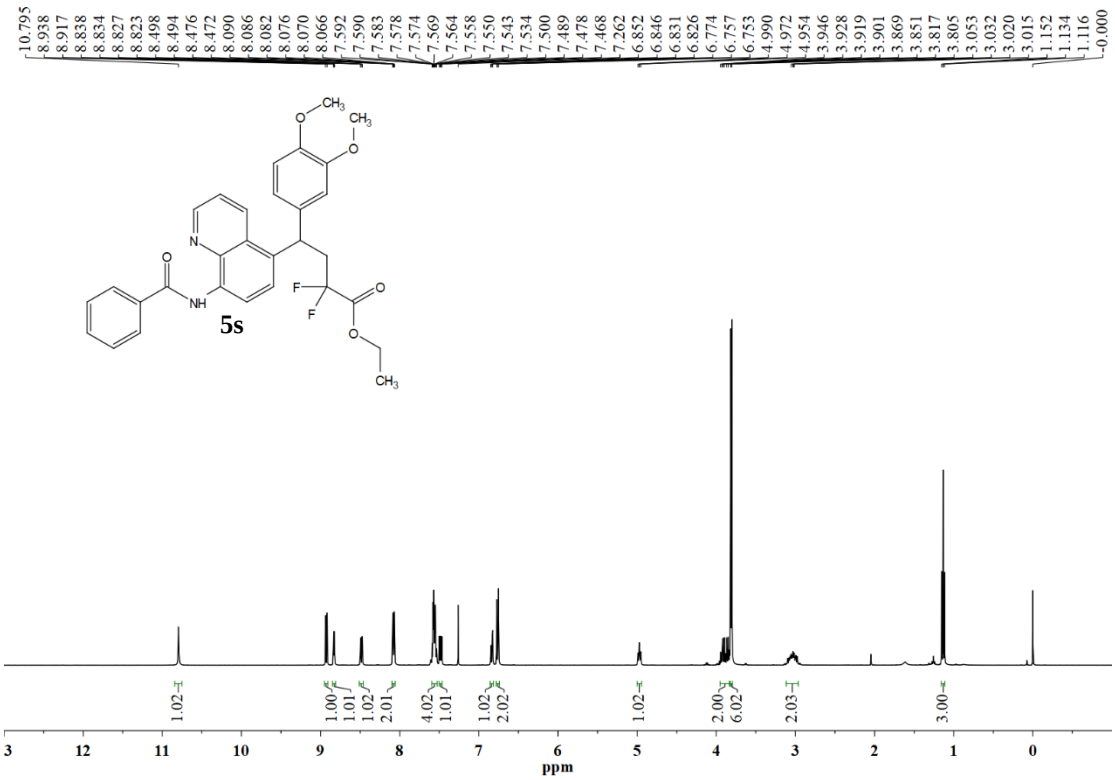

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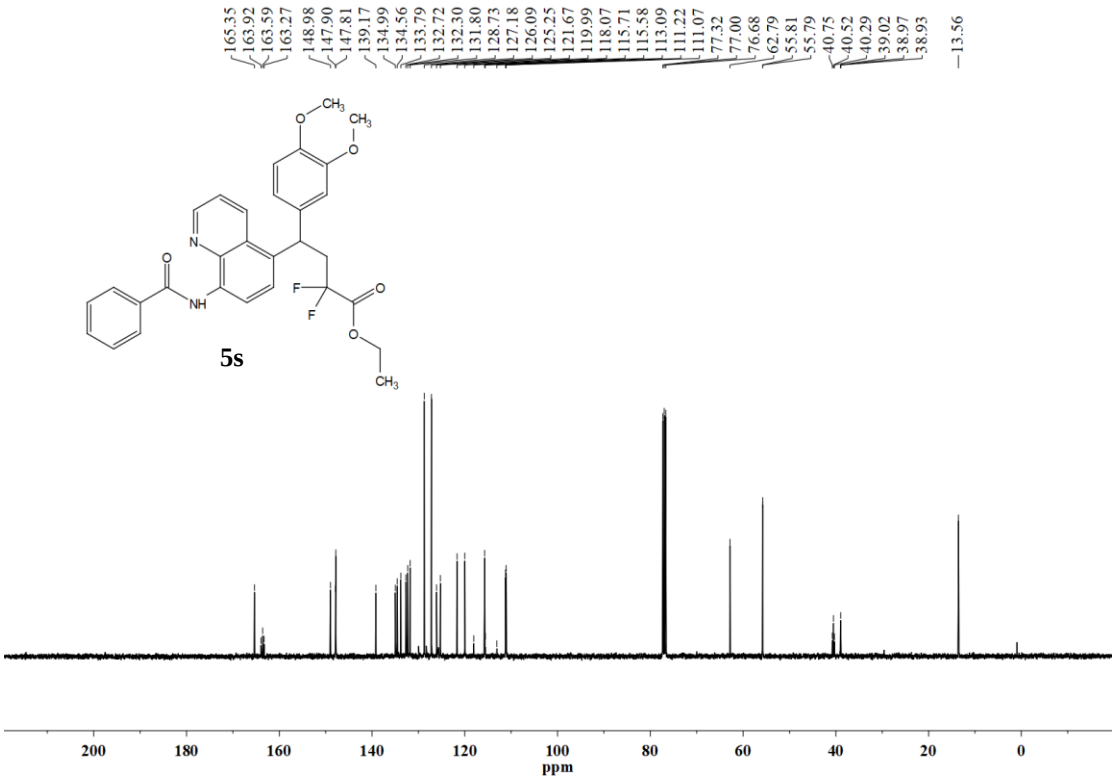
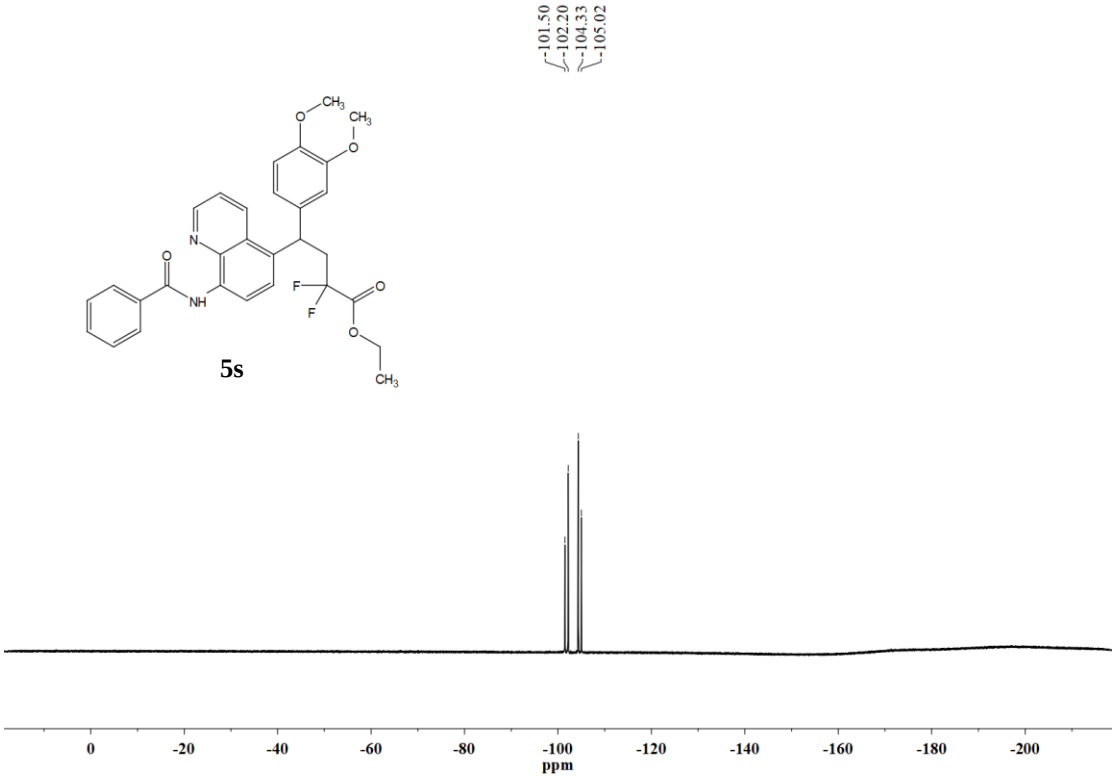


^{19}F NMR (376 MHz, Chloroform-*d*)



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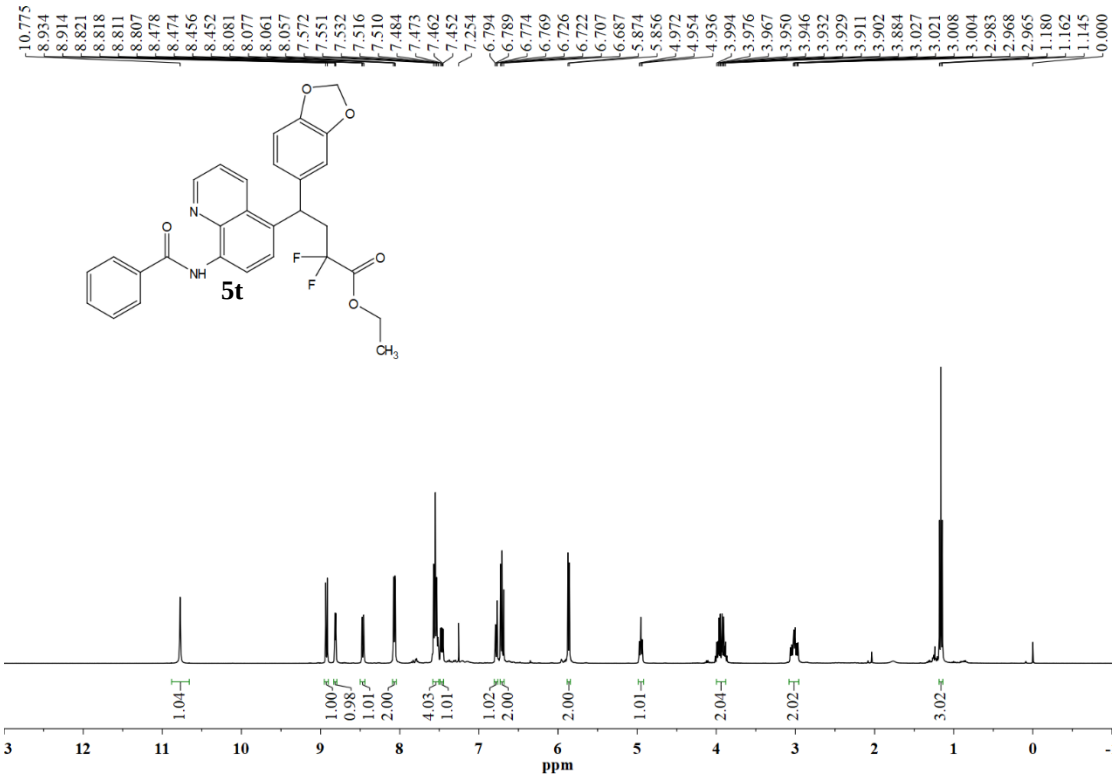
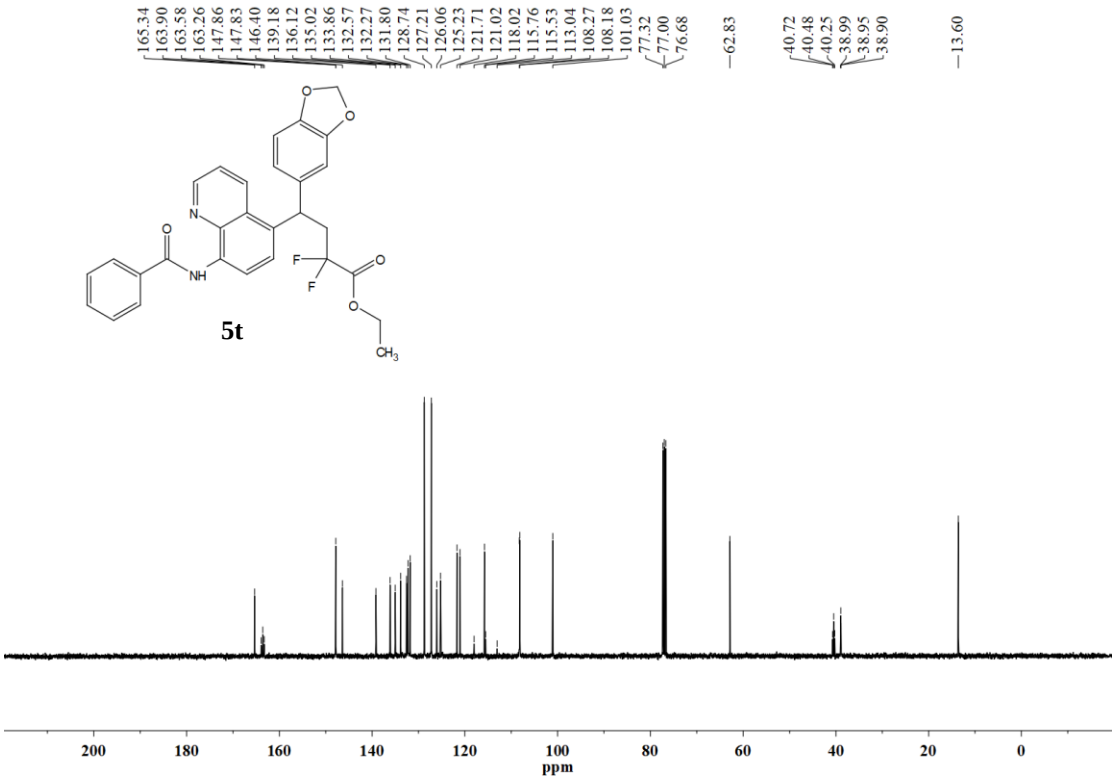
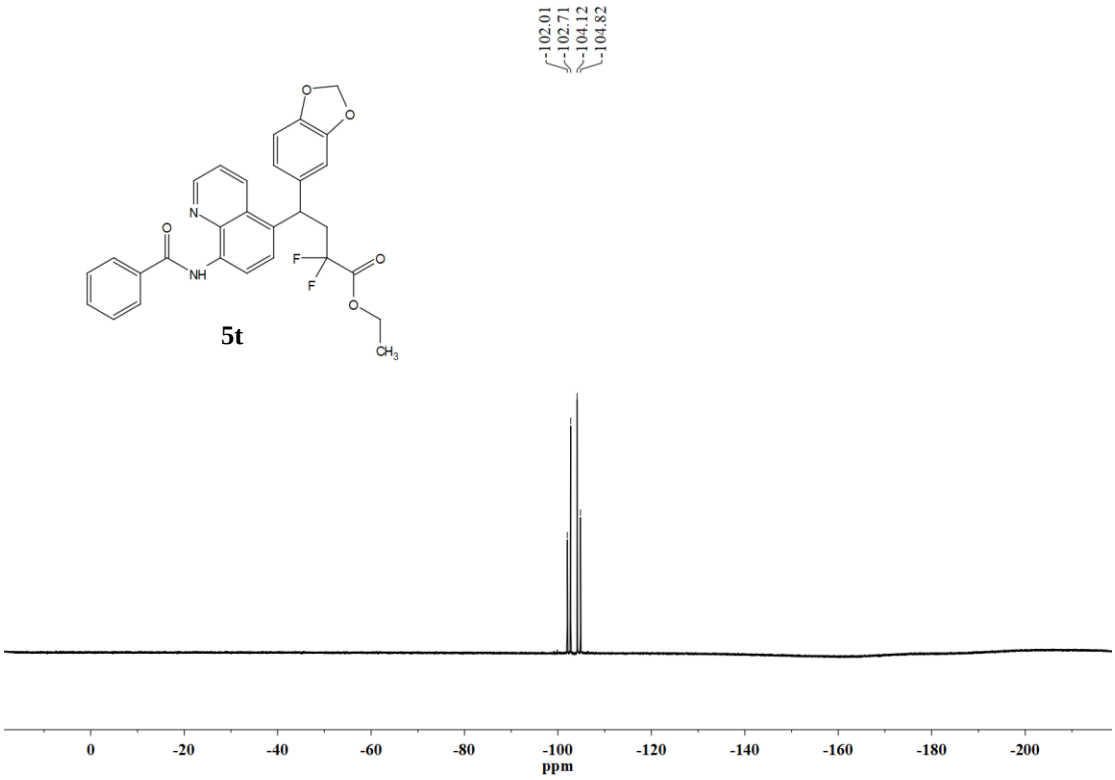


^{13}C NMR (101 MHz, Chloroform-*d*)



^{19}F NMR (376 MHz, Chloroform-*d*)



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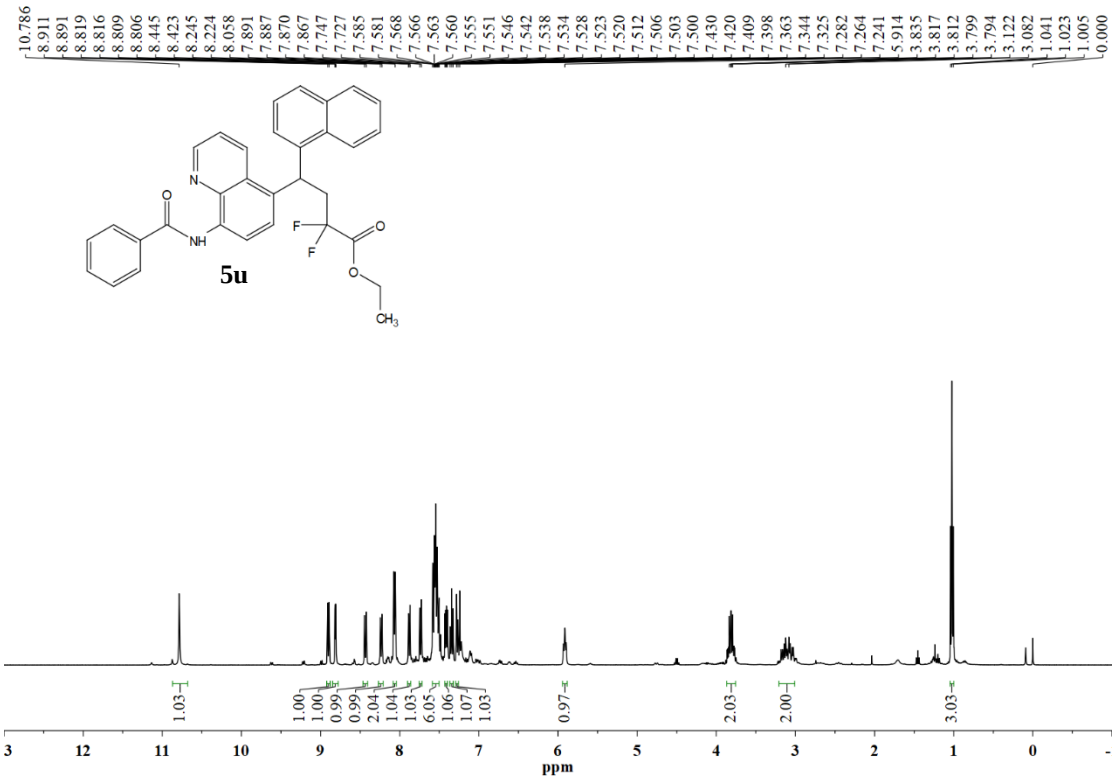

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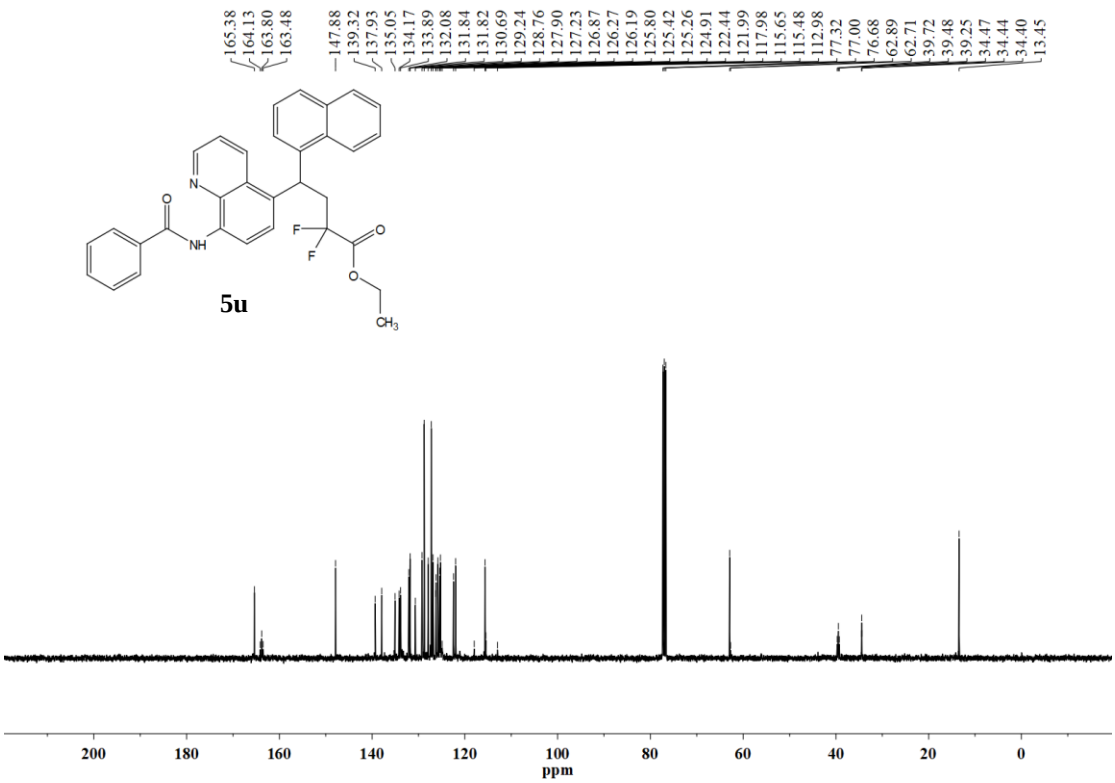

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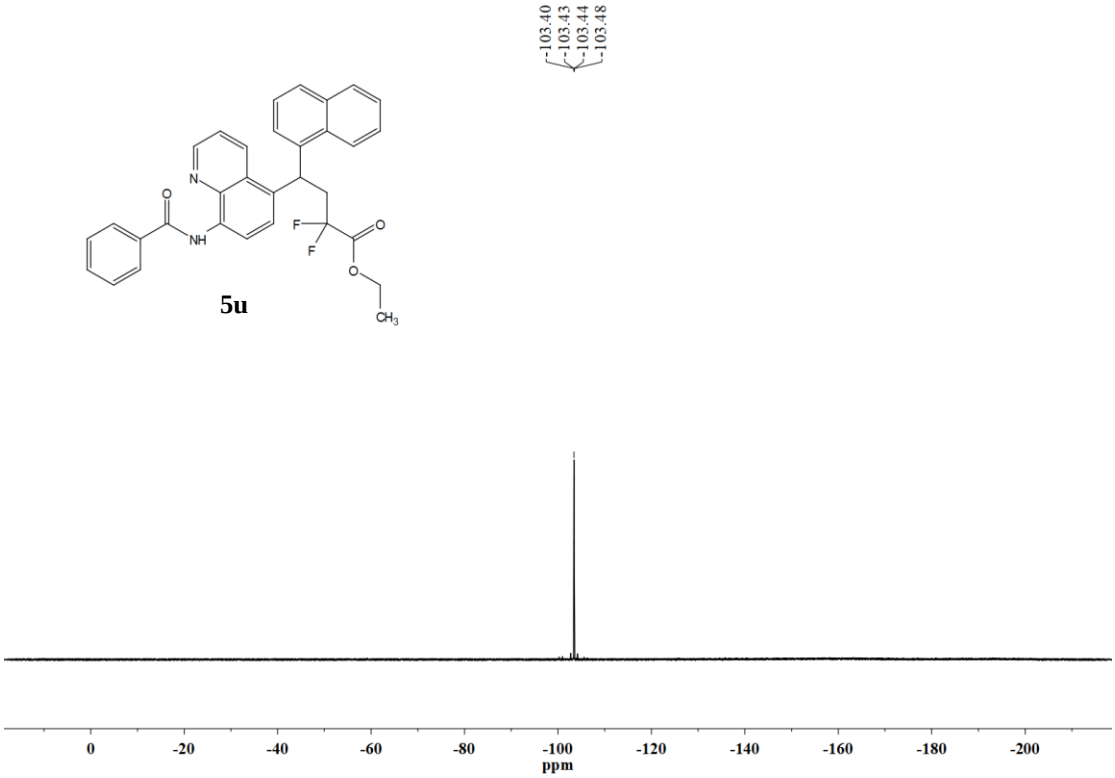

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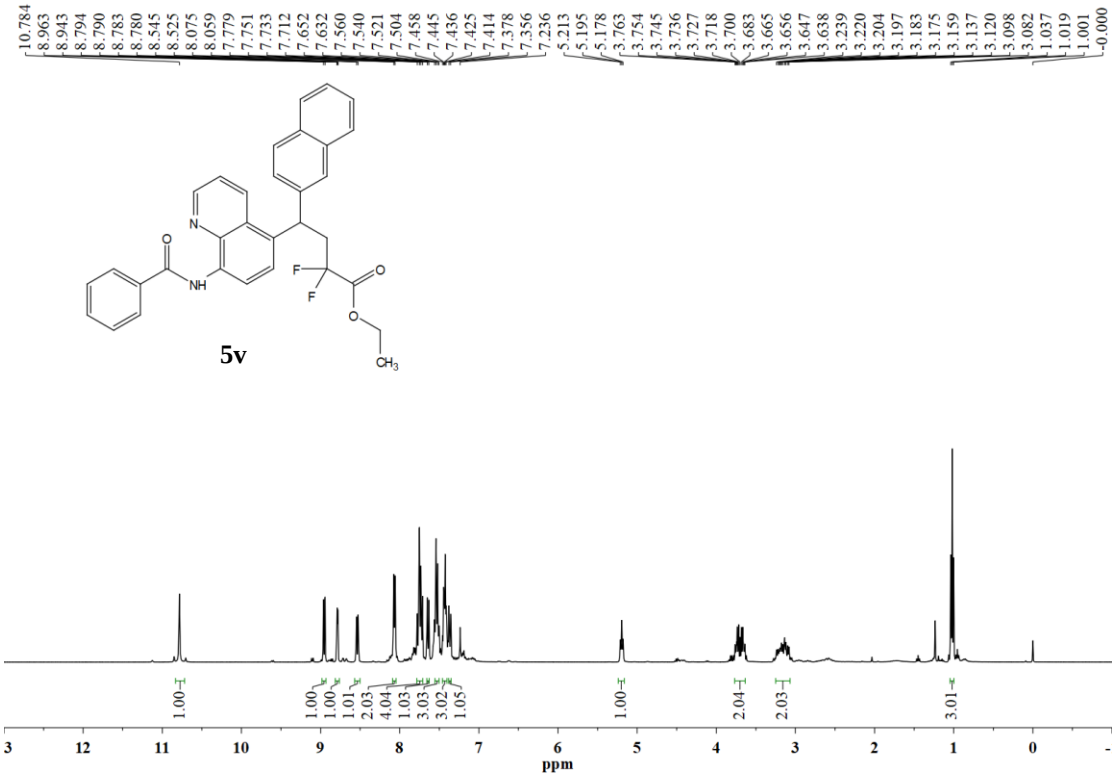

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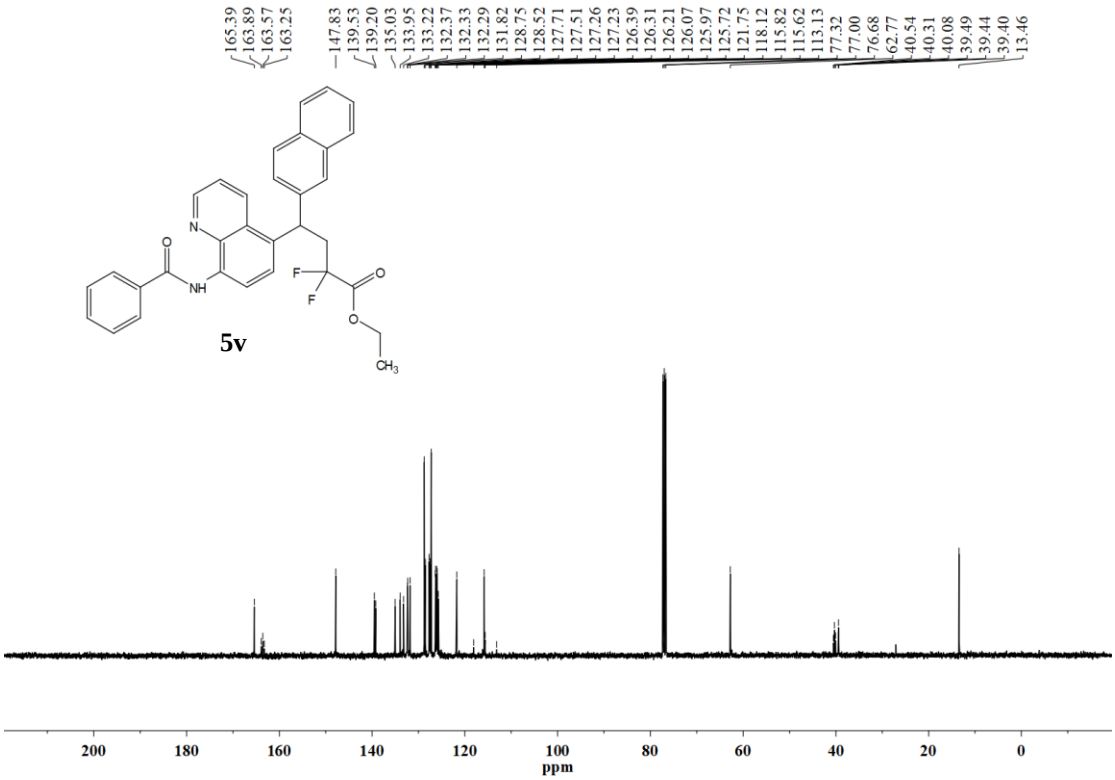

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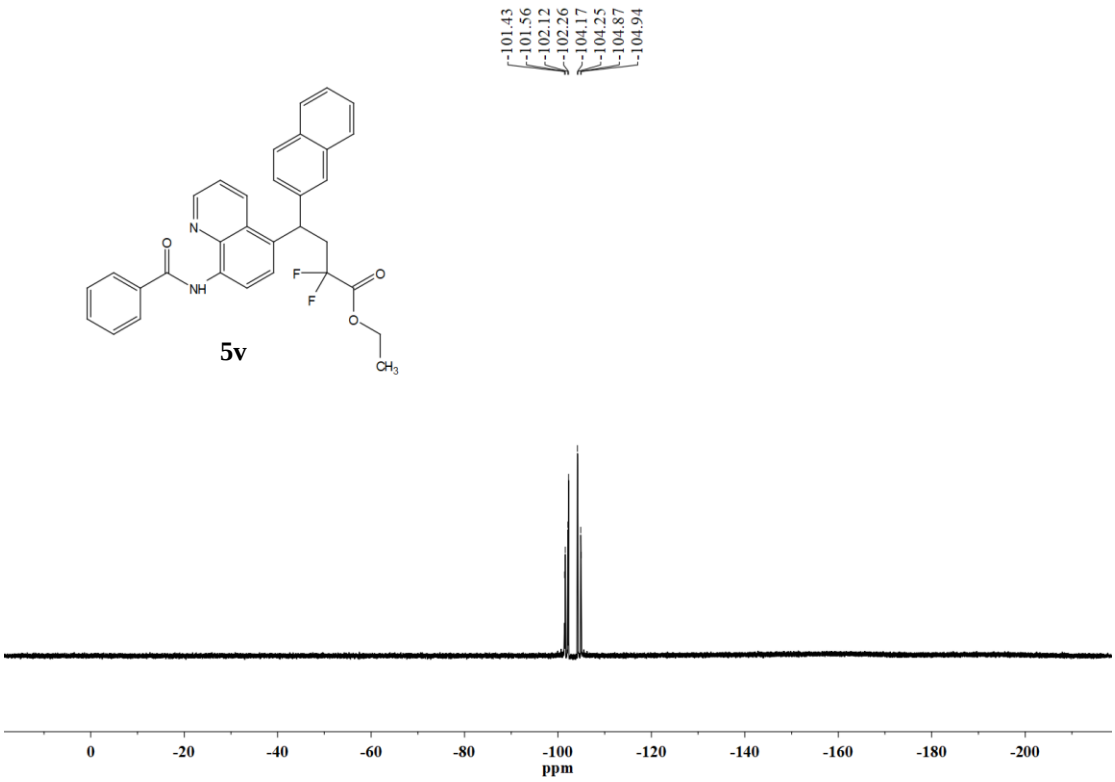

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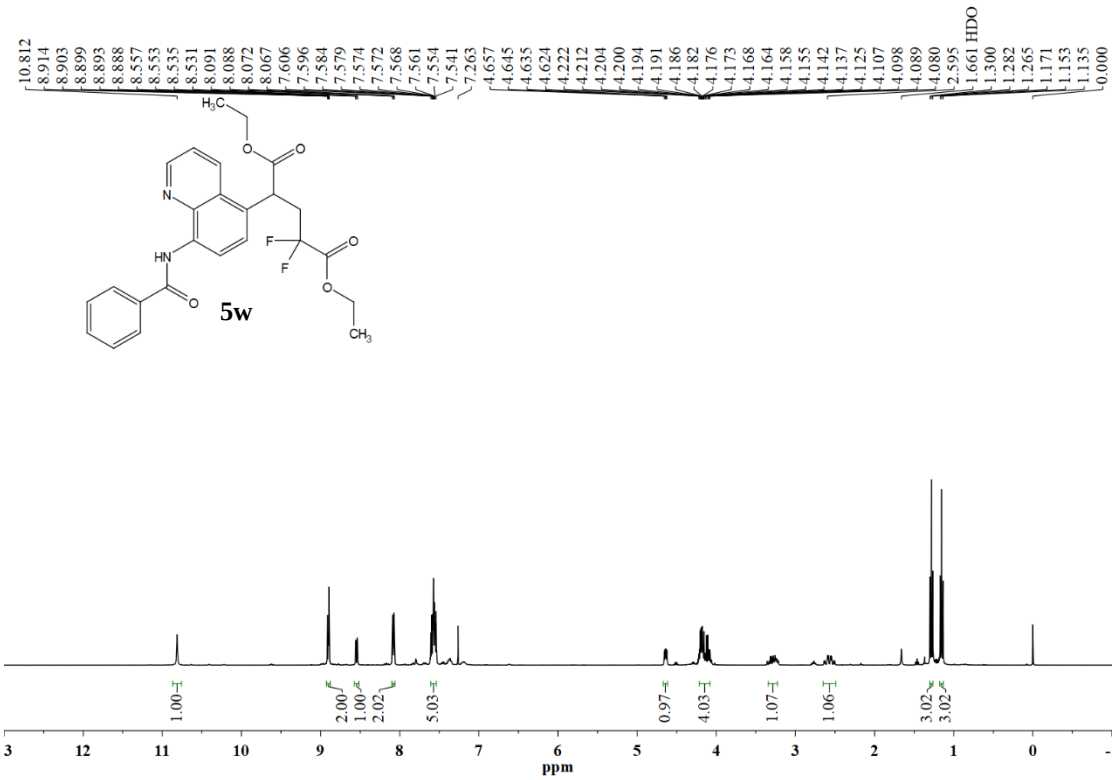
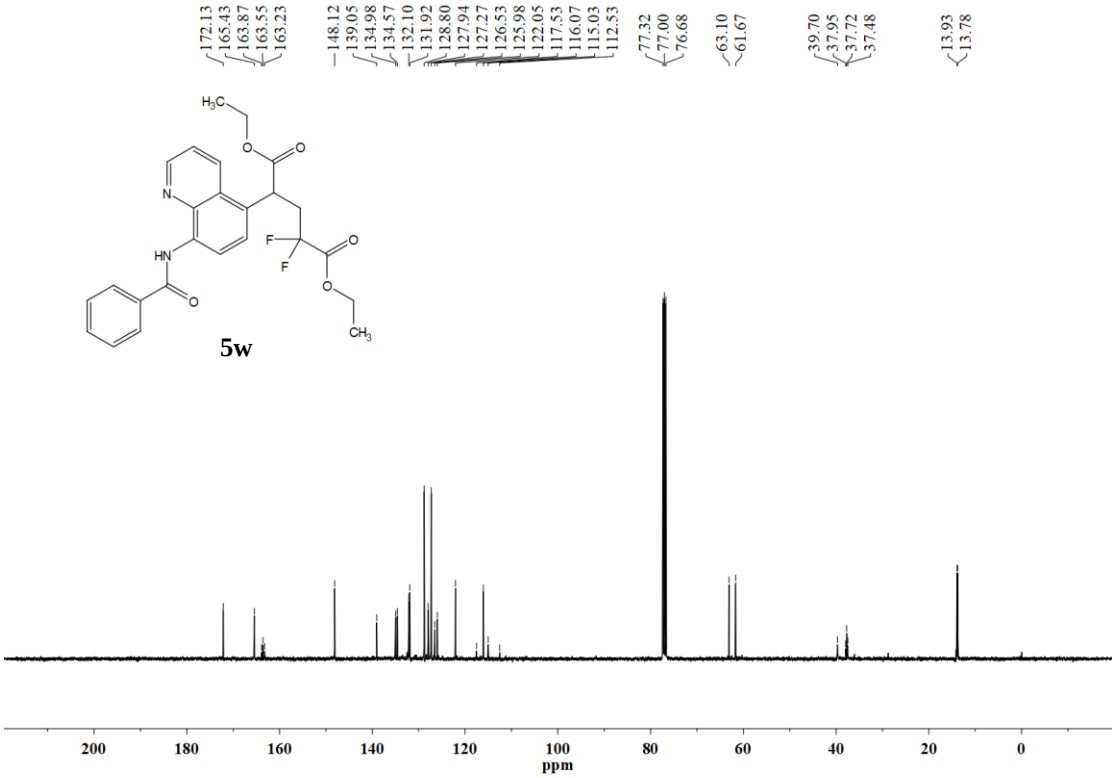


^{13}C NMR (101 MHz, Chloroform-*d*)



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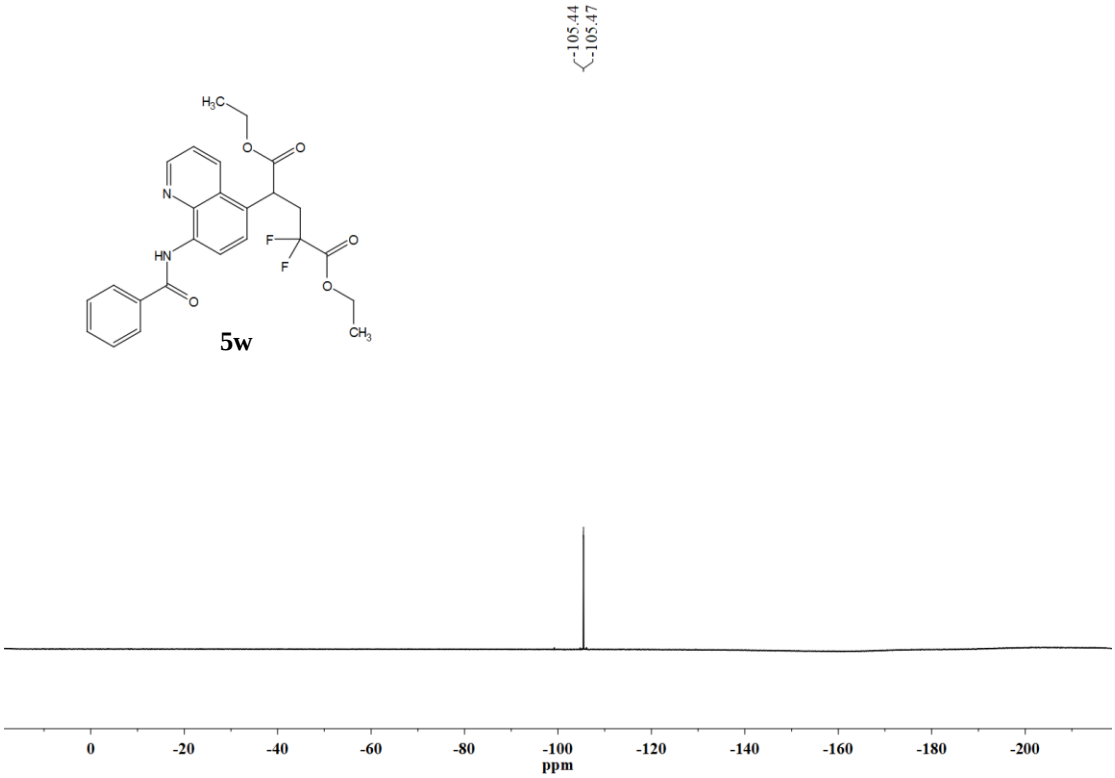

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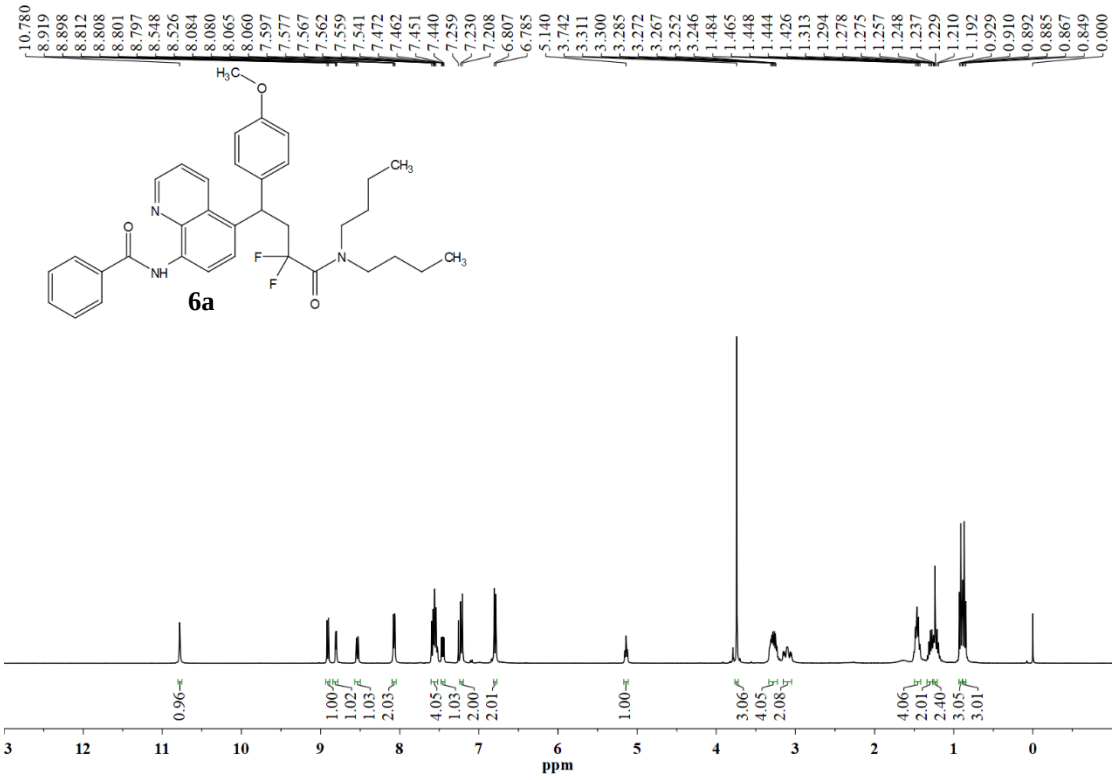

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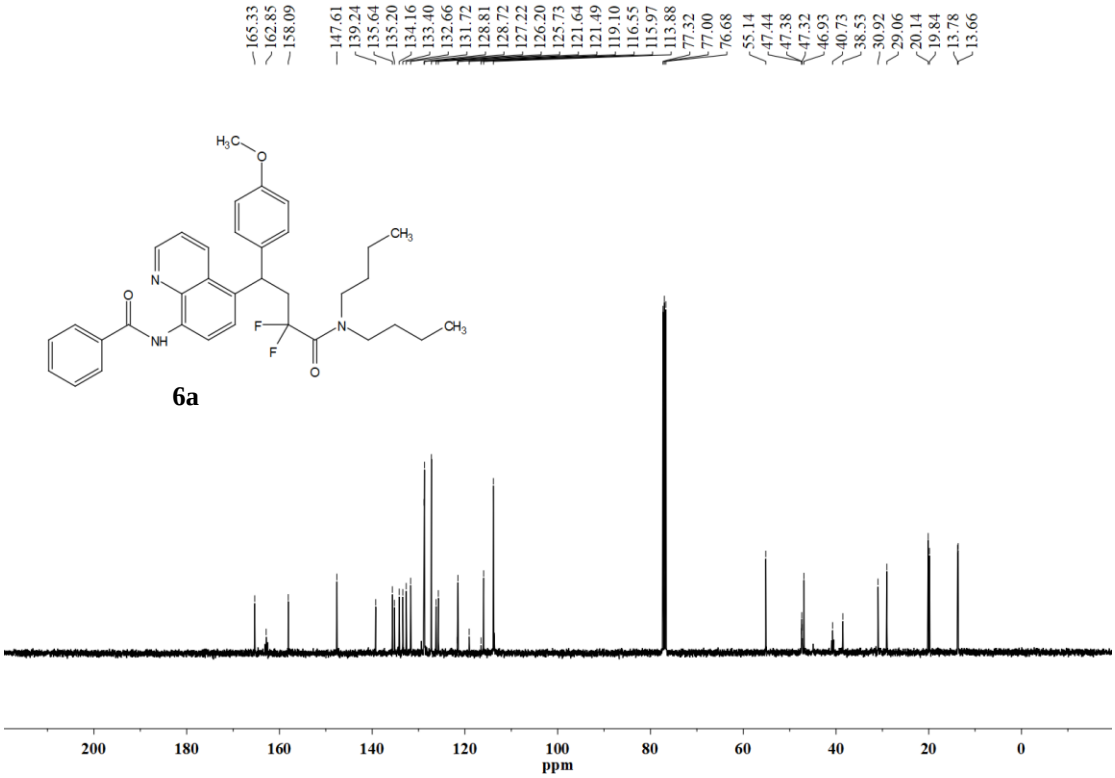

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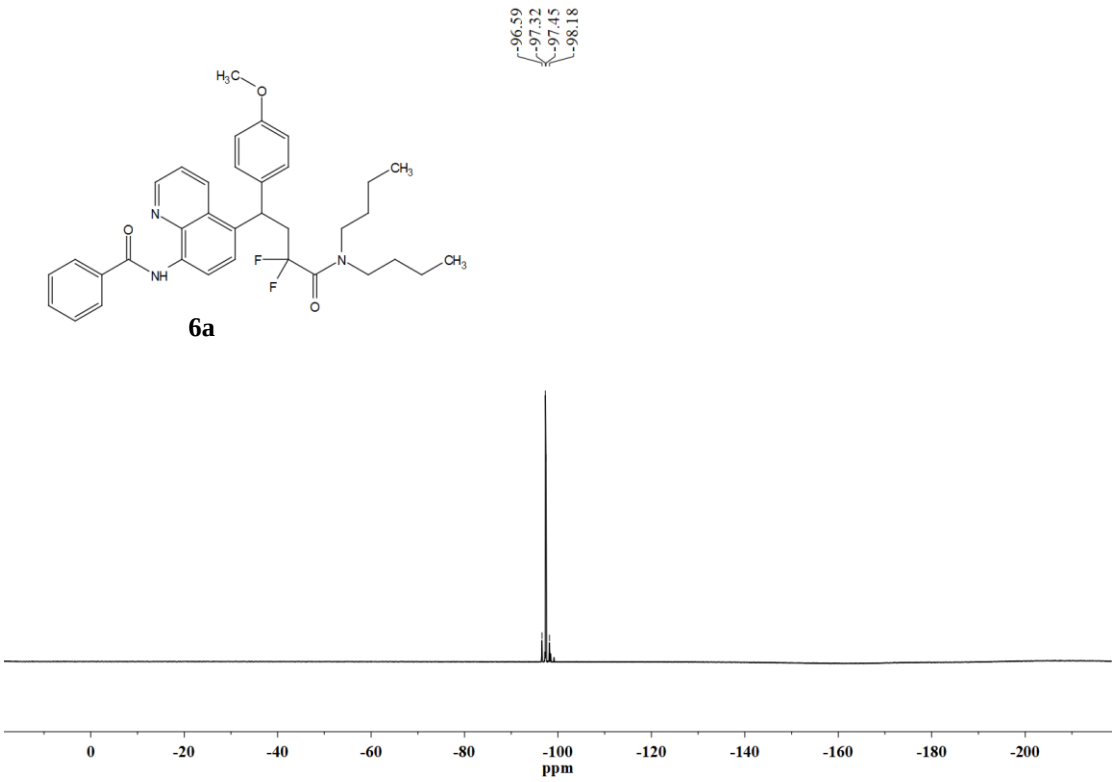
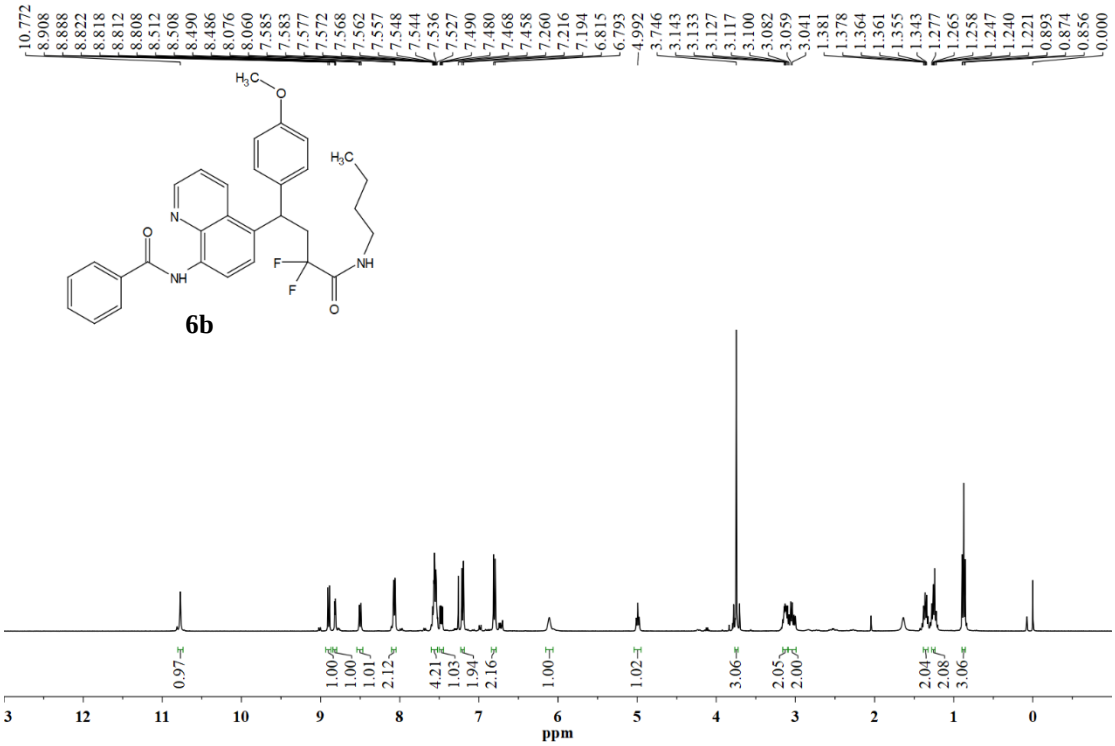
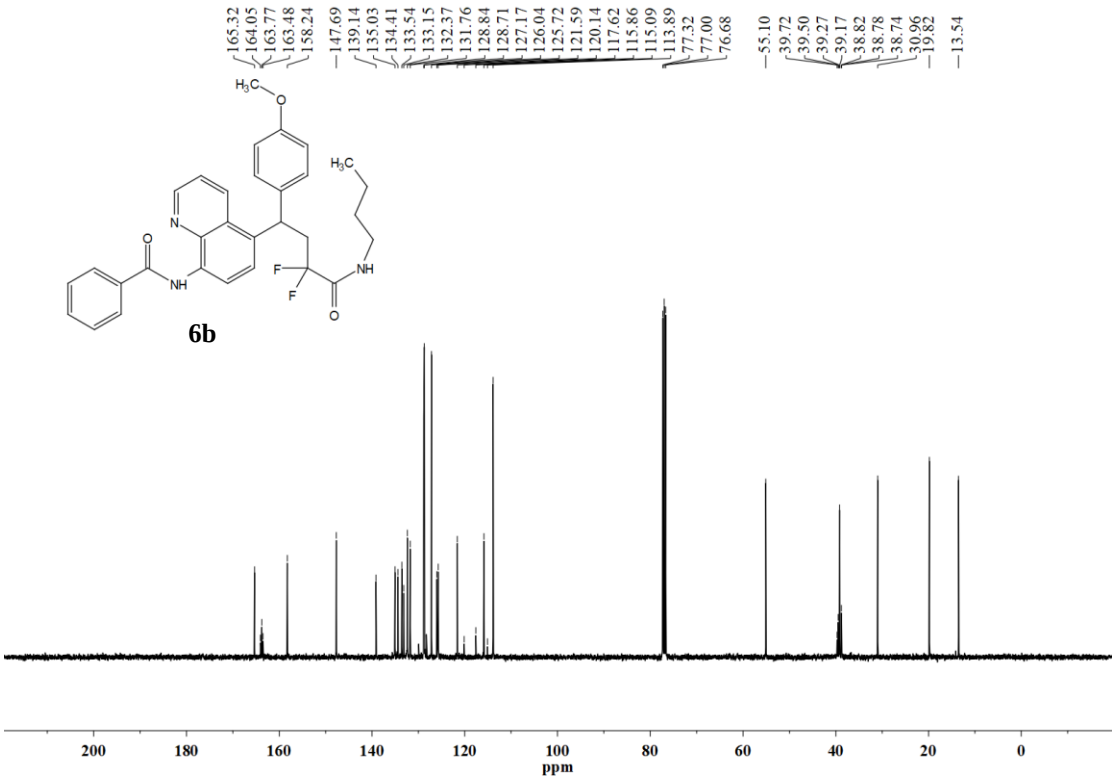


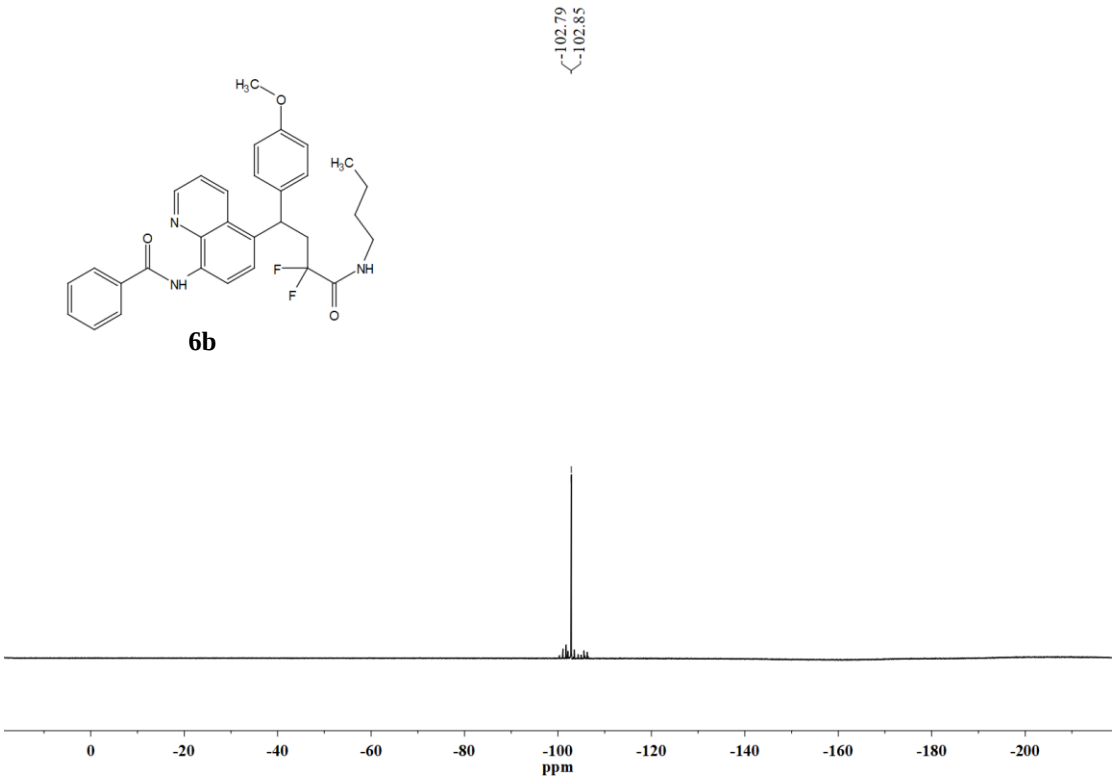
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

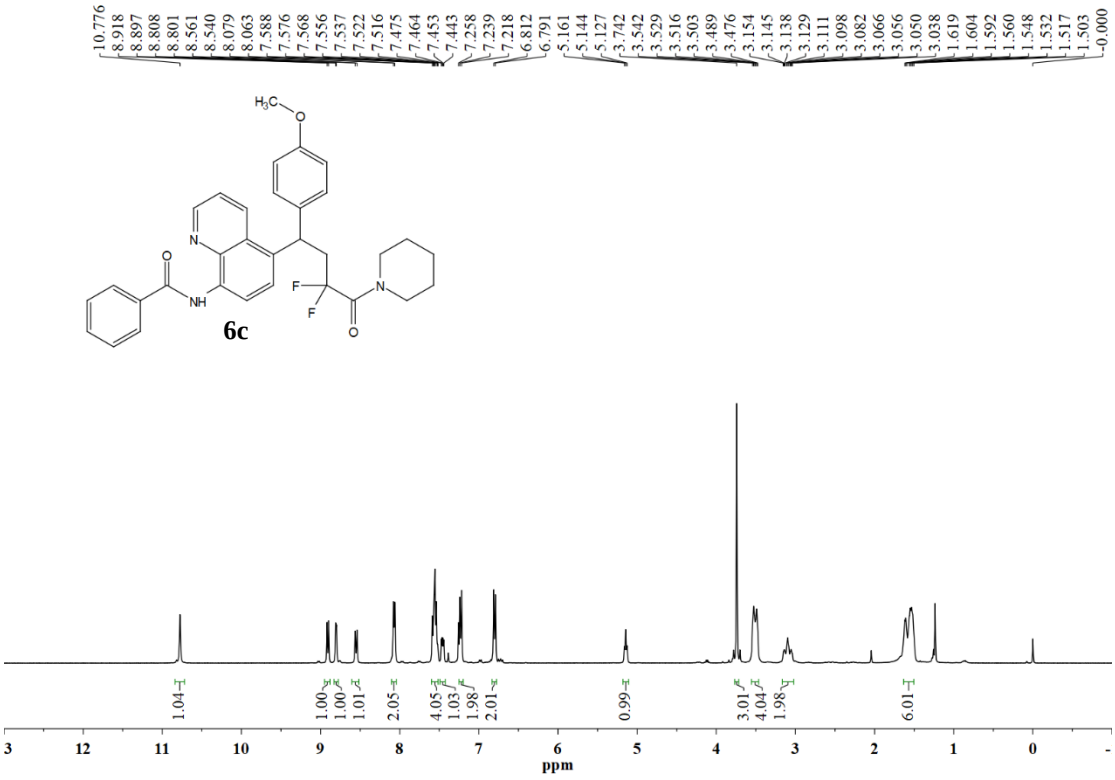


^{19}F NMR (376 MHz, Chloroform-*d*)



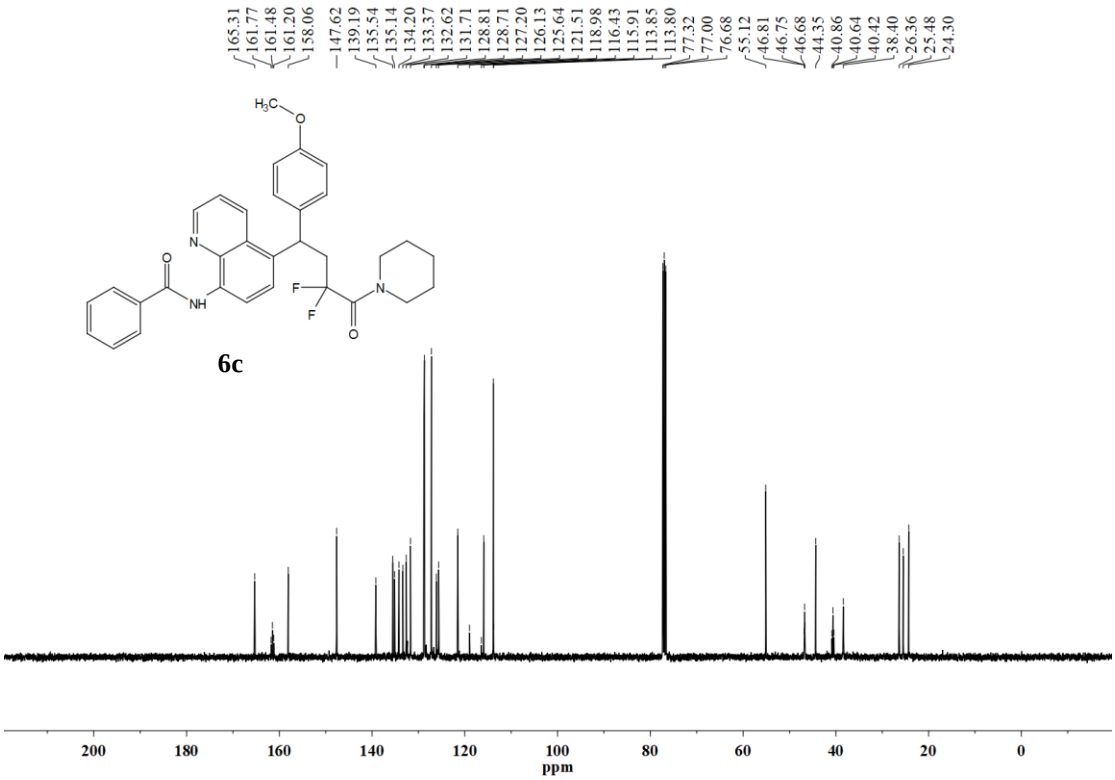
6b

^{1}H NMR (400 MHz, Chloroform-*d*)



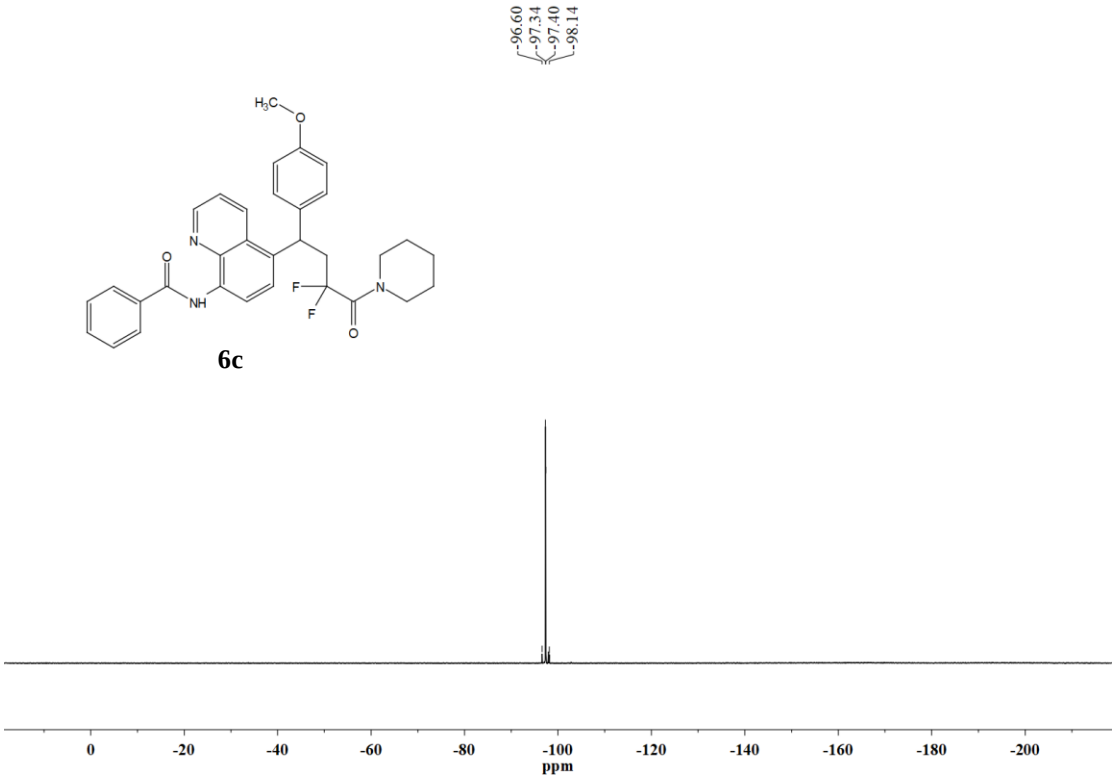
6c

^{13}C NMR (101 MHz, Chloroform-*d*)



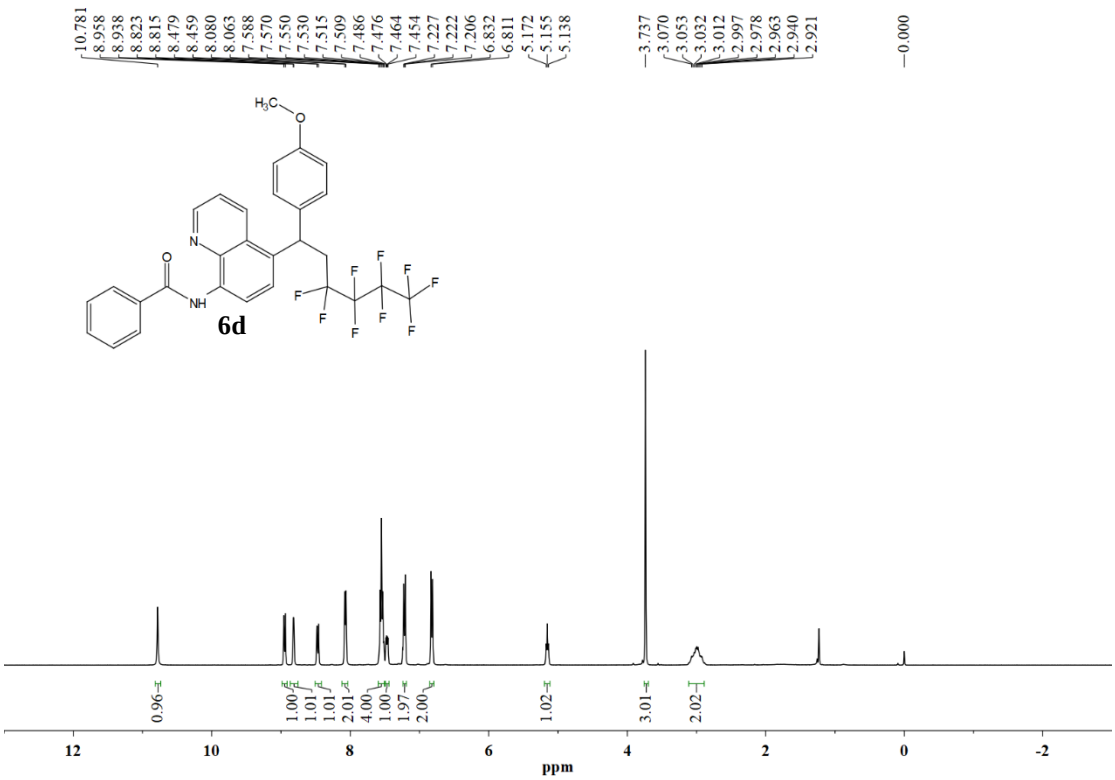
6c

^{19}F NMR (376 MHz, Chloroform-*d*)

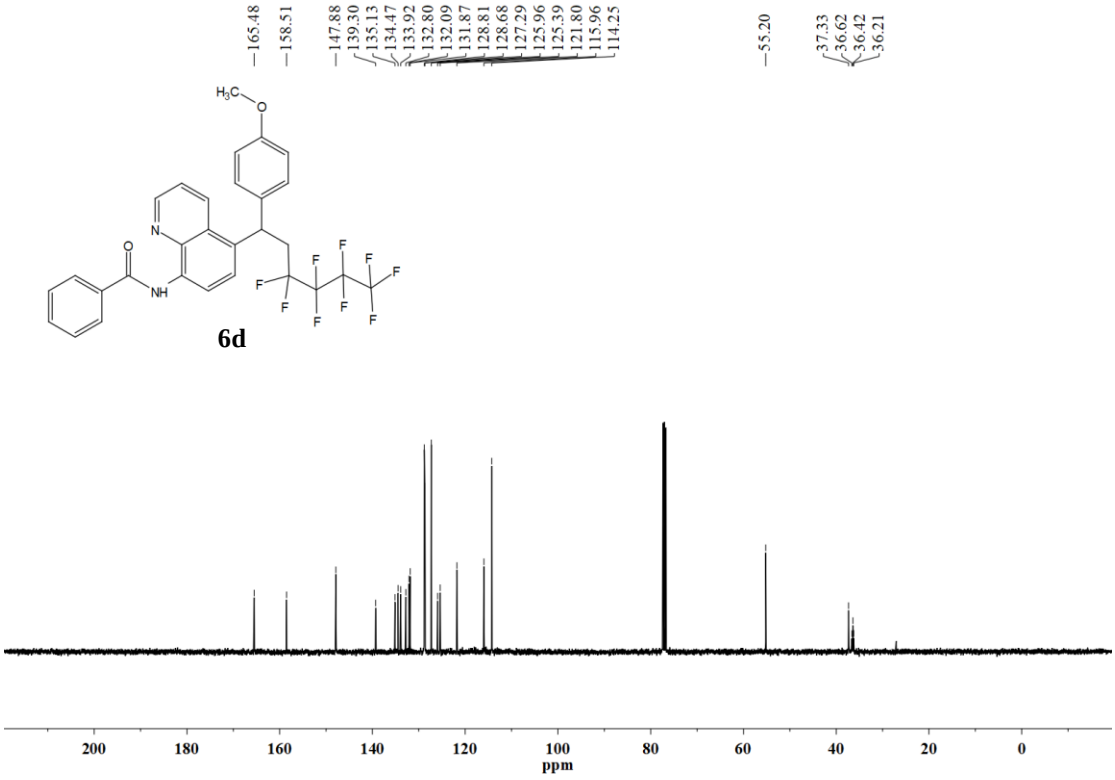


6c

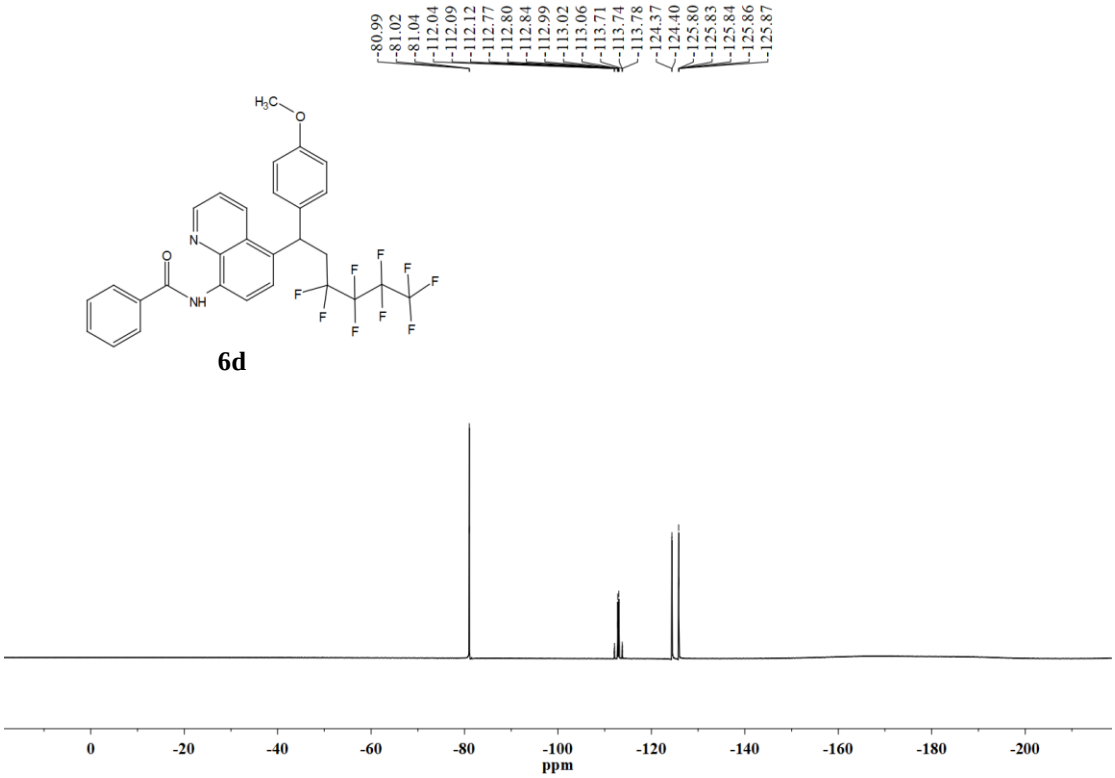
^{1}H NMR (400 MHz, Chloroform-*d*)



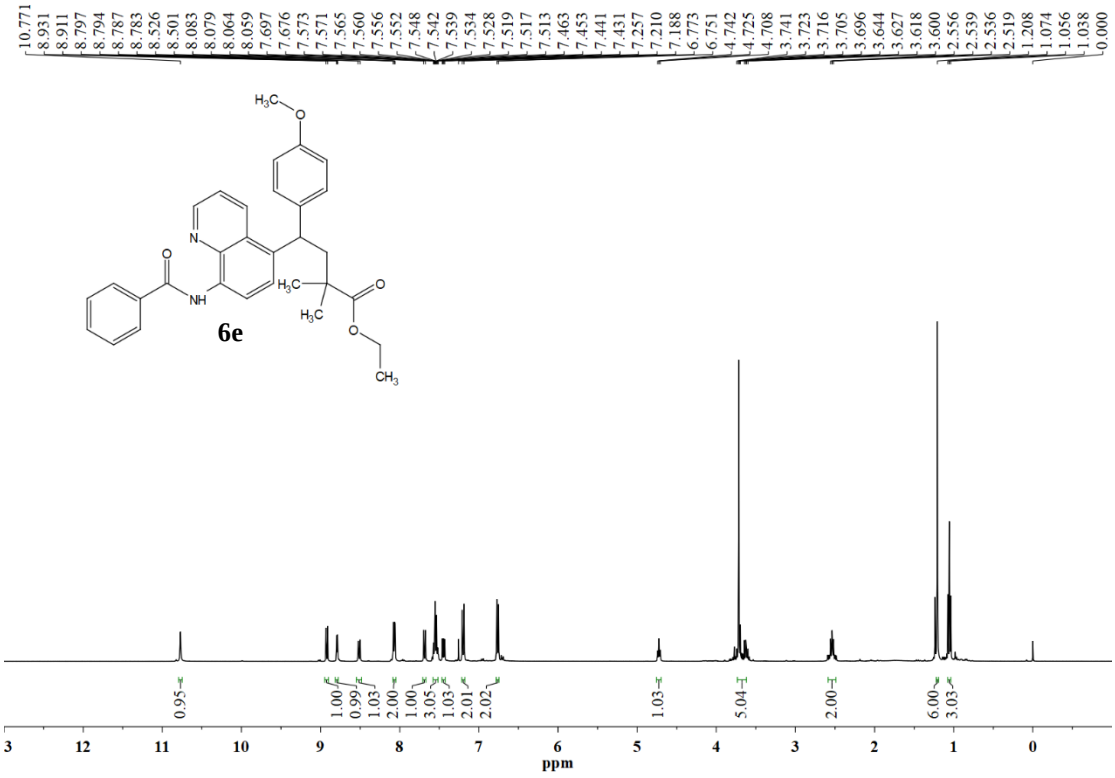
^{13}C NMR (101 MHz, Chloroform-*d*)



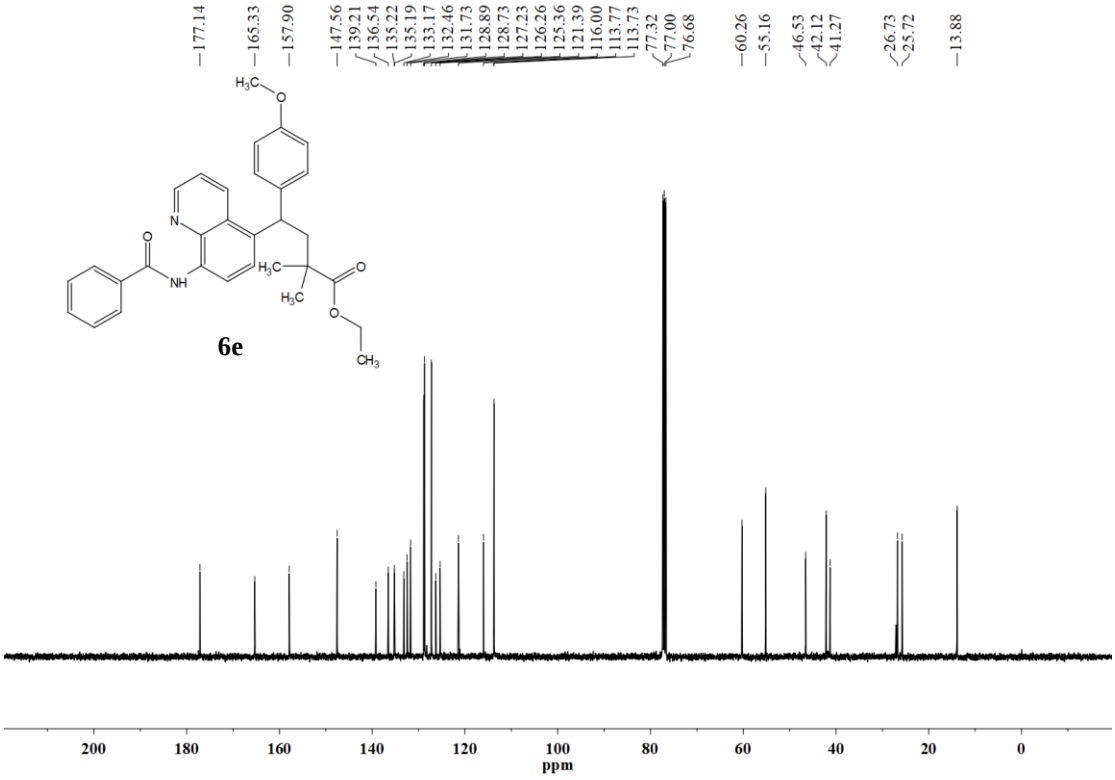
^{19}F NMR (376 MHz, Chloroform-*d*)



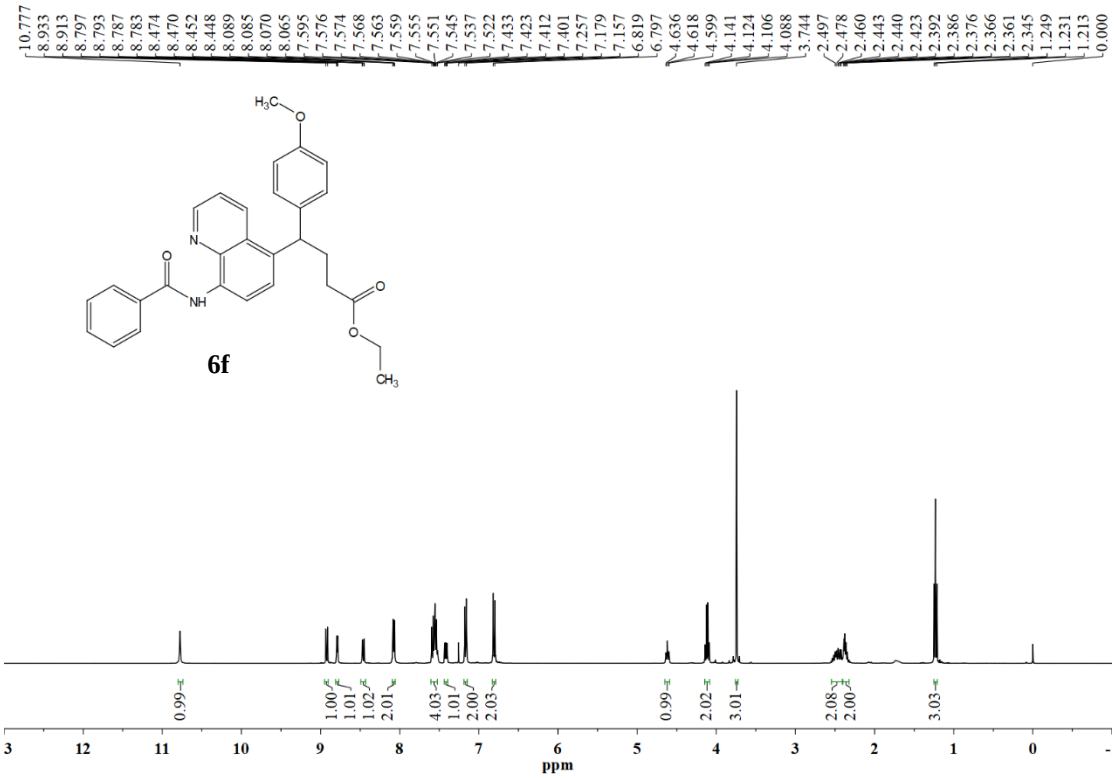
^{1}H NMR (400 MHz, Chloroform-*d*)



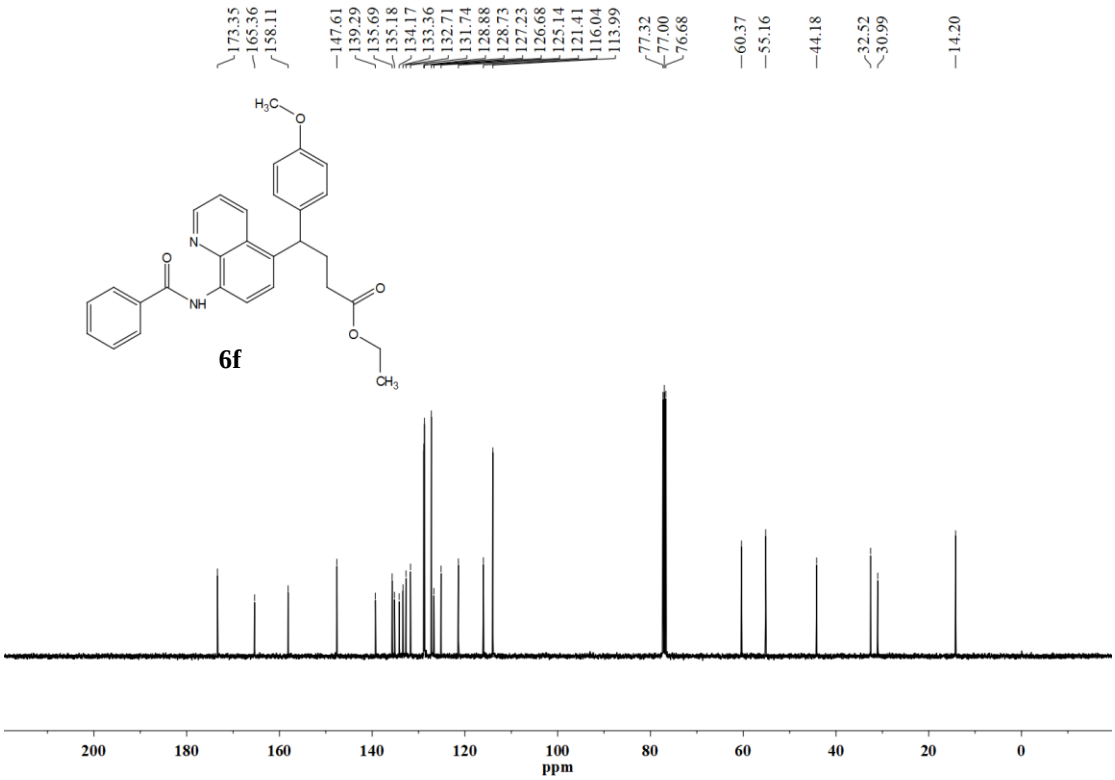
^{13}C NMR (101 MHz, Chloroform-*d*)



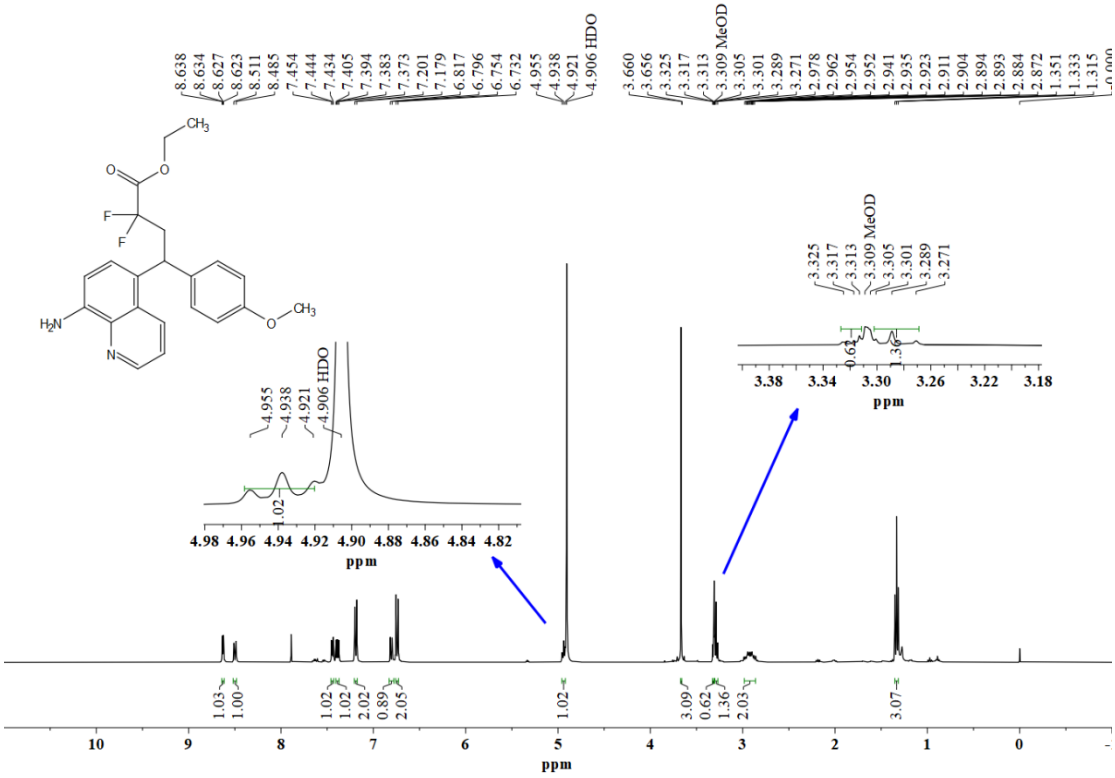
^{1}H NMR (400 MHz, Chloroform-*d*)



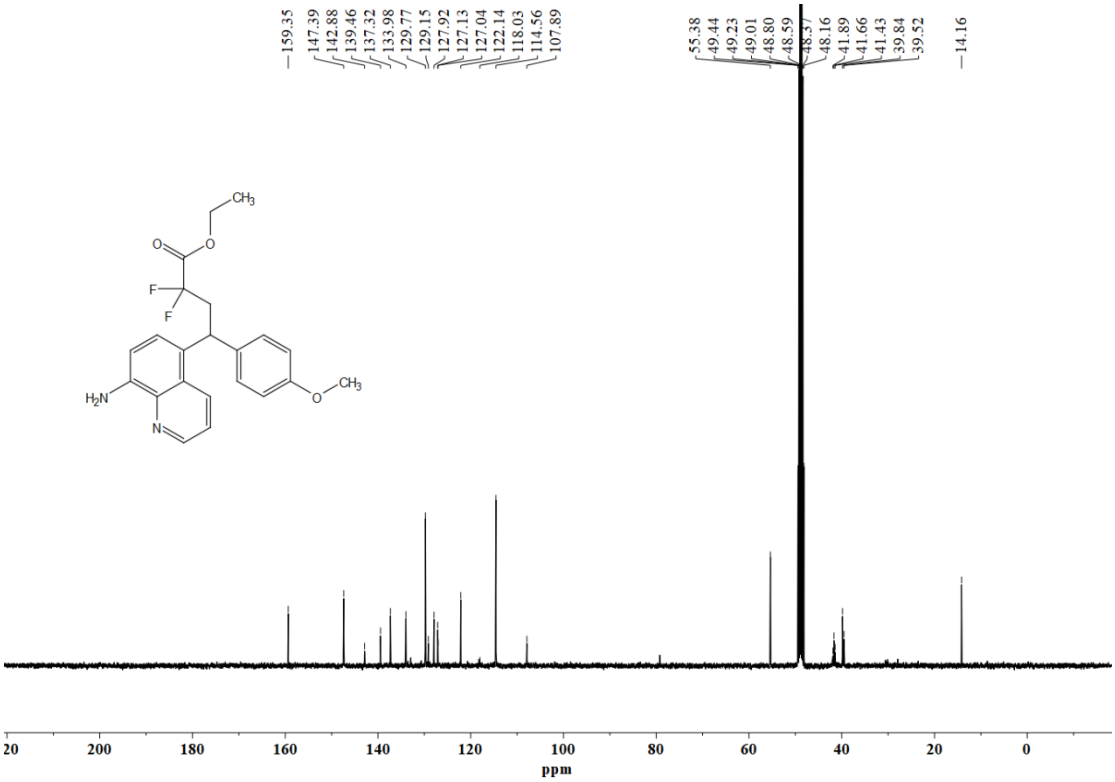
^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Methanol-d_4)



^{13}C NMR (101 MHz, Methanol-d_4)



^{19}F NMR (376 MHz, Methanol-d_4)