Supporting Information

Enantioselective Dearomatizing Formal (3+3) Cycloadditions of Bicyclobutanes with Aromatic Azomethine Imines: Access to Fused 2,3-Diazabicyclo[3.1.1]heptanes

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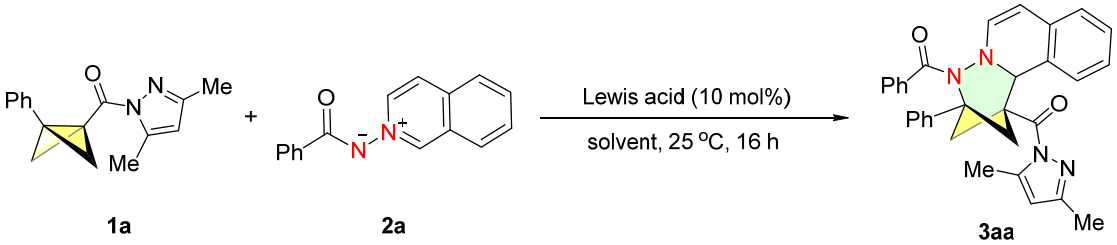
1 General Information

All reactions were performed in flame-dried glassware using conventional Schlenk techniques under a static pressure of nitrogen unless otherwise stated. Liquids and solutions were transferred with syringes. Bicyclo[1.1.0]butanes (BCBs)[1] and aromatic azomethine imines[2] were prepared according to reported procedures. $Zn(OTf)_2$ (98%, *Energy* Chemical Company) and other commercially available reagents were purchased from *Leyan*, *Energy Chemical* and *Bide* Chemical Company and used as received. The solvents (CH_2Cl_2, 1,2-dichloroethane, Et_2O, THF and toluene *etc*.) were dried and purified following standard procedures. PhCl and Ethyl acetate (EtOAc) were purchased from *Energy Chemical* (99%, Extra Dry) and used as received. Technical grade solvents for extraction or chromatography (Petroleum ether, CH_2Cl_2, and ethyl acetate) were distilled prior to use. Analytical thin layer chromatography (TLC) was performed on silica gel 60 F254 glass plates by *Merck*. Flash column chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) by *Grace* using the indicated solvents. ^1H, ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker AV400 or 600 instruments. Chemical shifts are reported in parts per million (ppm) and are referenced to the residual solvent resonance as the internal standard ($CDCl_3$: δ = 7.26 ppm for ^1H NMR and $CDCl_3$: δ = 77.0 ppm for ^{13}C NMR). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplett, q = quartet, m = multiplet), coupling constants (Hz), and integration. The full-scan mass spectra were taken on a hybrid quadrupole-orbitrap mass spectrometer equipped with a heated electrospray ionization source (ThermoFischer Scientific, Bremen, Germany). Chiral HPLC analysis was performed on a Shimadzu LC-20AD instrument using Daicel chiral columns at 35 ^oC and a mixture of HPLC-grade hexanes and isopropanol as eluent. Acknowledgement: the ^1H, ^{13}C NMR spectra, single crystal X-ray diffraction and HRMS (ESI) were performed at Analytical Instrumentation Center of Hunan University. The absolute configuration was determined by single crystal X-ray diffraction analysis on Rigaku XtaLAB PRO MM003-DS dual system with a Cu micro-focus source. Diffraction data was collected at 173 K on a Rigaku XtaLAB PRO MM003-DS dual System with a Cu micro-focus source.

2 Optimization Study

Table S1. Screening of Lewis acid and solvent for the (3+3) cycloaddition of BCB **1a** and azomethine imine **2a**[a]

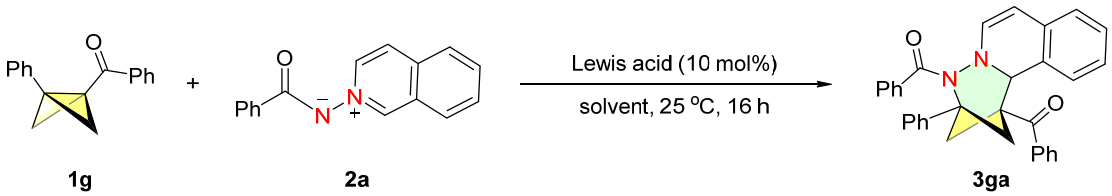


1a **2a** **3aa**

Entry	Lewis acid	solvent	Yield (%)[b]
1	$Fe(OTf)_2$	CH_2Cl_2	30
2	$Co(OTf)_2$	CH_2Cl_2	33
3	$Sc(OTf)_3$	CH_2Cl_2	25
4	$Zn(OTf)_2$	CH_2Cl_2	20
5	$Al(OTf)_3$	CH_2Cl_2	0
6	$Ni(OTf)_2$	CH_2Cl_2	35
7	$BF_3{\cdot}Et_2O$	CH_2Cl_2	0
8	$Ni(OTf)_2$	EtOAc	23
9	$Ni(OTf)_2$	toluene	25
10	$Ni(OTf)_2$	THF	11
11	$Ni(OTf)_2$	1,4-dioxane	22
12	$Ni(OTf)_2$	DCE	63
13	$Ni(OTf)_2$	CH_3CN	>99
14	$Ni(OTf)_2$	PhCl	19
15[c]	-	CH_3CN	*no reaction*

[a]The reactions were performed with **1a** (0.1 mmol), **2a** (0.12 mmol), Lewis acid catalyst (10 mol%) in solvent (2.0 mL) at room temperature for 16 h. [b]Determined by ^1H NMR analysis using CH_2Br_2 as an internal standard. Abbreviations: Tf = trifluoromethanesulfonyl; DCE = 1,2-dichloroethane. [c]Run at 80 °C

Table S2. Screening of Lewis acid and solvent for the (3+3) cycloaddition of BCB **1g** and azomethine imine **2a**[a]

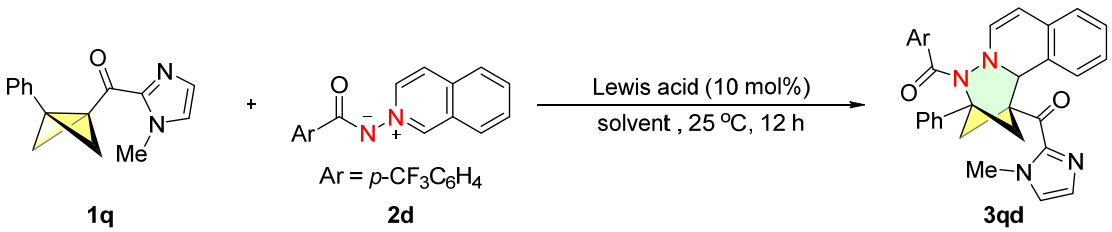


1g **2a** **3ga**

Entry	Lewis acid	Solvent	Yield (%)[b]
1	$Ni(OTf)_2$	MeCN	9
2	$Fe(OTf)_2$	CH_2Cl_2	29
3	$Co(OTf)_2$	CH_2Cl_2	15
4	$Sc(OTf)_3$	CH_2Cl_2	45
5	$Zn(OTf)_2$	CH_2Cl_2	22
6	AgOTf	CH_2Cl_2	0
7	$Eu(OTf)_3$	CH_2Cl_2	29
8	$BF_3{\cdot}Et_2O$	CH_2Cl_2	18
9	$Sc(OTf)_3$	EtOAc	34
10	$Sc(OTf)_3$	toluene	14
11	$Sc(OTf)_3$	THF	28
12	$Sc(OTf)_3$	1,4-dioxane	49
13	$Sc(OTf)_3$	DCE	41
14	$Sc(OTf)_3$	CH_3CN	84
15	$Sc(OTf)_3$	PhCl	32
16[c]	$Sc(OTf)_3$	CH_3CN	99

[a]The reactions were performed with **1g** (0.1 mmol), **2a** (0.12 mmol), Lewis acid catalyst (10 mol%) in solvent (2.0 mL) at 25 °C for 16 h. [b]Determined by ^1H NMR analysis using CH_2Br_2 as an internal standard. [c]Run at 50 °C. Abbreviations: Tf = trifluoromethanesulfonyl; DCE = 1,2-dichloroethane.

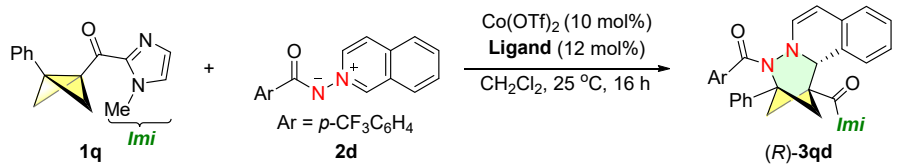
Table S3. Screening of Lewis acid and solvent for the (3+3) cycloaddition of BCB **1q** and azomethine imine **2d**[a]

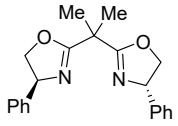


Entry	Lewis acid	Solvent	Yield (%)[b]
1	$Eu(OTf)_3$	CH_2Cl_2	62
2	$Ga(OTf)_3$	CH_2Cl_2	65
3	$Sc(OTf)_3$	CH_2Cl_2	80
4	$Zn(OTf)_2$	CH_2Cl_2	84
5	$Ni(OTf)_2$	CH_2Cl_2	86
6	$Cu(OTf)_2$	CH_2Cl_2	51
7	$Fe(OTf)_3$	CH_2Cl_2	84
8	$Fe(OTf)_2$	CH_2Cl_2	90
9	$Mg(OTf)_2$	CH_2Cl_2	15
10	$Yb(OTf)_3$	CH_2Cl_2	70
11	$Co(OTf)_2$	CH_2Cl_2	75
12	$BF_3{\cdot}Et_2O$	CH_2Cl_2	4
13	$B(C_6F_5)_3$	CH_2Cl_2	3
14	$Fe(OTf)_2$	EtOAc	73
15	$Fe(OTf)_2$	toluene	10
16	$Fe(OTf)_2$	THF	50
17	$Fe(OTf)_2$	1,4-dioxane	65
18	$Fe(OTf)_2$	DCE	32
19	$Fe(OTf)_2$	CH_3CN	18
20	$Fe(OTf)_2$	PhCl	5
21[c]	$Fe(OTf)_2$	CH_2Cl_2	92

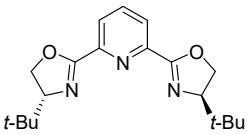
[a]The reactions were performed with **1q** (0.1 mmol), **2d** (0.12 mmol), Lewis acid catalyst (10 mol%) in solvent (2.0 mL) at room temperature for 12 h. [b]Determined by ^1H NMR analysis using CH_2Br_2 as an internal standard. [c]**2a** (Ar = Ph) was used. Abbreviations: Tf = trifluoromethanesulfonyl; BCF = tris(pentafluorophenyl)borane; DCE = 1,2-dichloroethane.

Table S4. Screening of chiral ligands for the enantioselective (3+3) cycloaddition of BCB **1q** and **2d**[a]

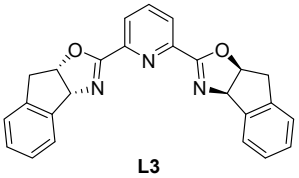




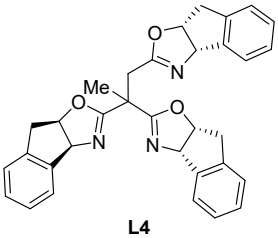
L1
79%, 6% *ee*



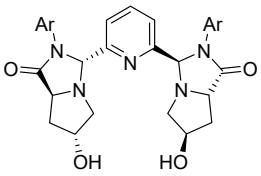
L2
68%, 22% *ee*



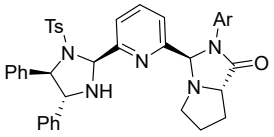
L3
18%, -17% *ee*



L4
87%, -1% ee



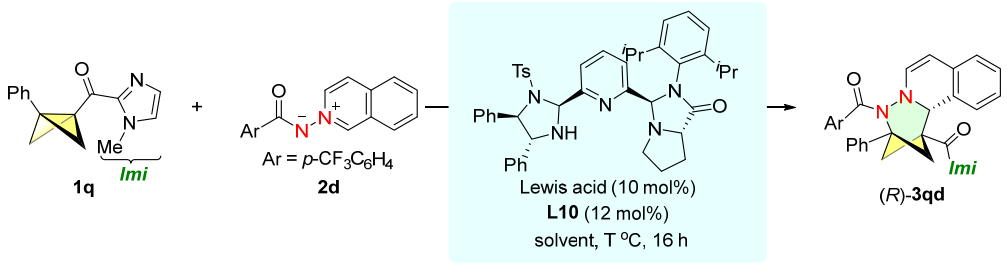
L5: Ar = Ph, 73%, 0% *ee*
L6: Ar = 2,6-$^{i}Pr_2C_6H_3$, 78%, 16% *ee*



L7: Ar = Ph, 81%, -13% *ee*
L8: Ar = 1-Naphthyl, 77%, 34% *ee*
L9: Ar = 2,6-$Et_2C_6H_3$, 85%, 64% *ee*
L10: Ar = 2,6-$^{i}Pr_2C_6H_3$, 85%, 70% *ee*

[a]Reaction conditions: **1q** (0.10 mmol), **2d** (0.12 mmol), $Co(OTf)_2$ (10 mol%) and Ligand (12 mol%), CH_2Cl_2 (2.0 mL), 25 °C, under N_2 for 16 h. The yields of (*R*)-**3qd** was determined by ^1H NMR with CH_2Br_2 as an internal standard. The *ee* value was determined by chiral HPLC with hexane/2-propanol.

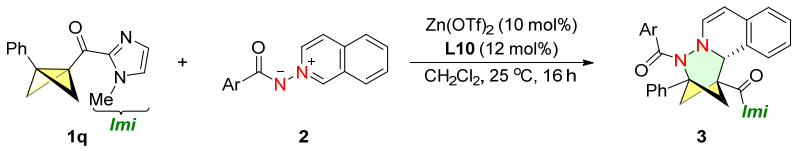
Table S5. Screening of Lewis acid, solvent and temperature for the enantioselective (3+3) cycloaddition of BCB **1q** and **2d** [a]

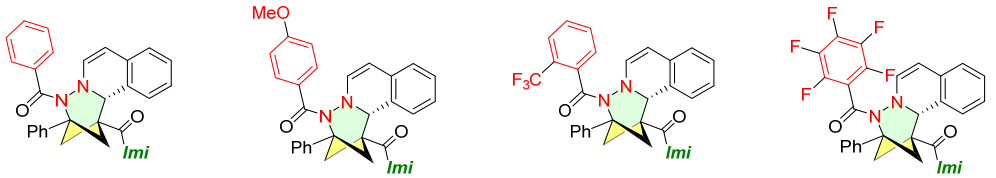


Entry	Lewis acid	Solvent	T (°C)	Yield (%)[b]	*ee* (%)[c]
1	$Co(OTf)_2$	CH_2Cl_2	25	85	70
2	$Ga(OTf)_3$	CH_2Cl_2	25	20	0
3	$Fe(OTf)_2$	CH_2Cl_2	25	65	88
4	$Mg(OTf)_2$	CH_2Cl_2	25	12	9
5	$Ni(OTf)_2$	CH_2Cl_2	25	83	28
6	$Sc(OTf)_3$	CH_2Cl_2	25	63	0
7	$Cu(OTf)_2$	CH_2Cl_2	25	67	3
8	$Zn(OTf)_2$	CH_2Cl_2	25	78	92
9[d]	$Zn(OTf)_2$	CH_2Cl_2	25	75	92
10	$Zn(OTf)_2$	EtOAc	25	64	90
11	$Zn(OTf)_2$	toluene	25	42	60
12	$Zn(OTf)_2$	THF	25	52	89
13	$Zn(OTf)_2$	1,4-dioxane	25	99	88
14	$Zn(OTf)_2$	DCE	25	74	88
15	$Zn(OTf)_2$	CH_3CN	25	24	12
16	$Zn(OTf)_2$	PhCl	25	70	89
17	$Zn(OTf)_2$	CH_2Cl_2/1,4-dioxane (v/v = 10:1)	25	86	90
18	$Zn(OTf)_2$	CH_2Cl_2/1,4-dioxane (v/v = 1:1)	25	90	88
19	$Zn(OTf)_2$	CH_2Cl_2	40	90	51
20	$Zn(OTf)_2$	CH_2Cl_2	10	58	85
21	$Zn(OTf)_2$	CH_2Cl_2	0	29	86
22	$Zn(OTf)_2$	CH_2Cl_2	-10	22	91
23	$Zn(OTf)_2$	CH_2Cl_2	-20	13	88

[a]Reaction conditions: **1q** (0.10 mmol), **2d** (0.12 mmol), Lewis acid (10 mol%), **L10** (12 mol%), in solvent (2.0 mL) under N_2 for 16 h. [b]The yields of (*R*)-**3qd** was determined by ^1H NMR using CH_2Br_2 as an internal standard. [c]The *ee* value was determined by chiral HPLC with hexane/2-propanol. [d]Under air.

Table S6. Investigate *N*-iminoisoquinolinium ylides **2** with different benzoyl protecting groups.[a]





(*R*)-**3qa**, 83% NMR yield, 88% *ee*

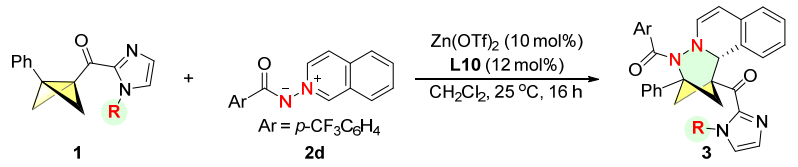
(*R*)-**3qe**, 80% NMR yield, 6% *ee*

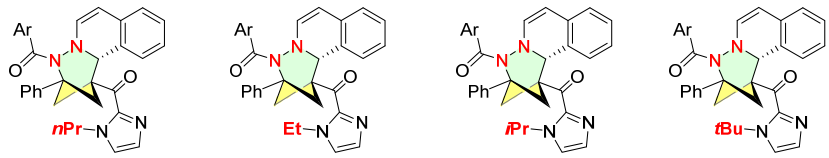
(*R*)-**3qf**, 92% NMR yield, 76% *ee*

(*R*)-**3qg**, 38% NMR yield, 54% *ee*

[a]Reaction conditions: **1q** (0.10 mmol, 1.0 equiv), **2** (0.12 mmol, 1.2 equiv), $Zn(OTf)_2$ (10 mol%) and **L10** (12 mol%), CH_2Cl_2 (2.0 mL), 25 °C, under N_2 for 16 h. The yields of **3** was determined by ^1H NMR with CH_2Br_2 as an internal standard. The *ee* value was determined by chiral HPLC with hexane/2-propanol.

Table S7. Investigate BCBs **1** with different acyl imidazole groups.[a]





(*R*)-**3aad**, 60%, 88% *ee*

(*R*)-**3ccd**, 46%, 84% *ee*

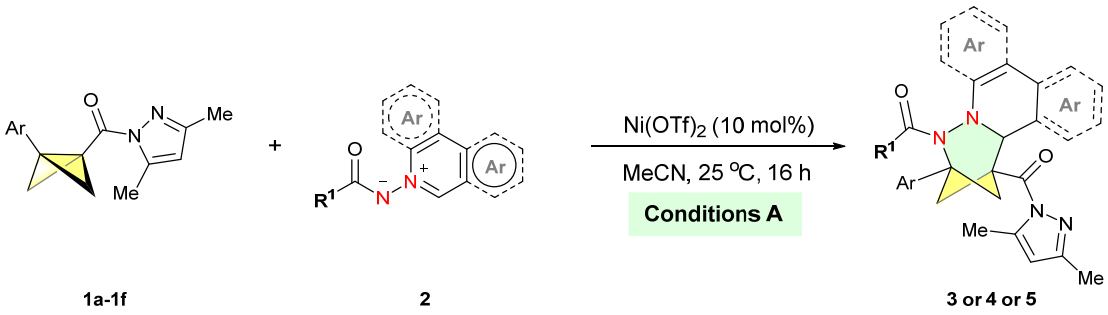
(*R*)-**3ddd**, 23%, 71% *ee*

(*R*)-**3eed**, trace

[a]Reaction conditions: **1** (0.10 mmol, 1.0 equiv), **2d** (0.12 mmol, 1.2 equiv), $Zn(OTf)_2$ (10 mol%) and **L10** (12 mol%), CH_2Cl_2 (2.0 mL), 25 °C, under N_2 for 16 h. The yields of **3** was determined by ^1H NMR with CH_2Br_2 as an internal standard. The *ee* value was determined by chiral HPLC with hexane/2-propanol.

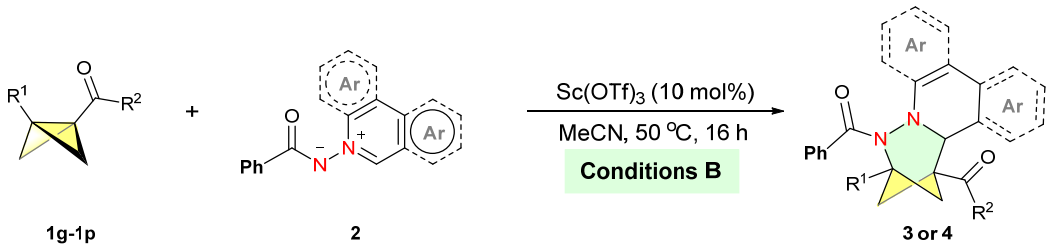
3 General Procedure for the (3+3) Cycloaddition Reactions

3.1 General procedure for (3+3) cycloadditions of pyrazole amide substituted BCBs **1a-1f** and azomethine imine **2** (**GP1**)



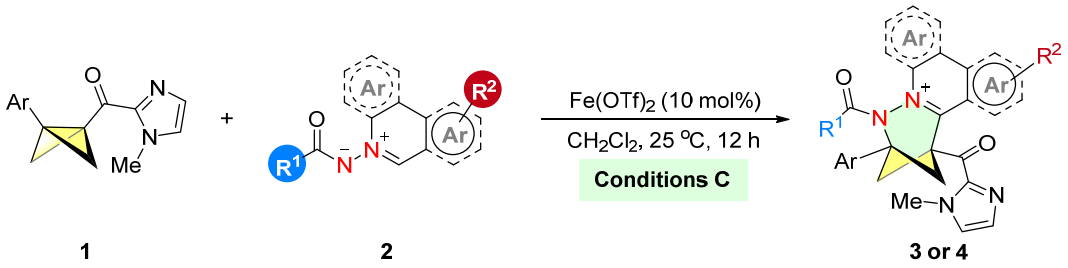
Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added the BCB **1** (0.20 mmol, 1.0 equiv), **2** (0.24 mmol, 1.2 equiv) and $Ni(OTf)_2$ (7.1 mg, 0.02 mmol) followed by 4.0 mL of anhydrous MeCN. The solution was stirred at 25 °C for 16 h till full conversion of BCB by TLC analysis. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification using PE/EtOAc (10:1, v/v) as the eluent, to afford the desired product **3 or 4 or 5**.

3.2 General procedure for (3+3) cycloadditions of BCB ketones **1g-1p** and azomethine imine **2** (**GP2**)



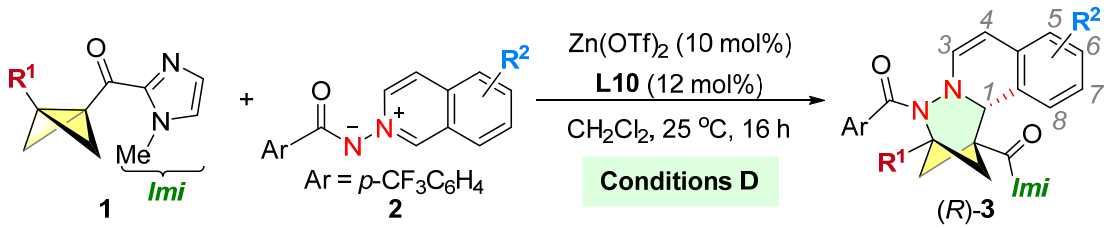
Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added the BCB **1** (0.20 mmol, 1.0 equiv), **2** (0.24 mmol, 1.2 equiv) and $Sc(OTf)_3$ (9.8 mg, 0.02 mmol) followed by 4.0 mL of anhydrous MeCN. The solution was stirred at 50 °C for 16 h till full conversion of BCBs by TLC analysis. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification using PE/EtOAc (10:1, v/v) as the eluent, to afford the desired product **3 or 4**.

3.3 General procedure for (3+3) cycloadditions of acyl imidazole substituted BCBs **1** and azomethine imines **2** (**GP3**)



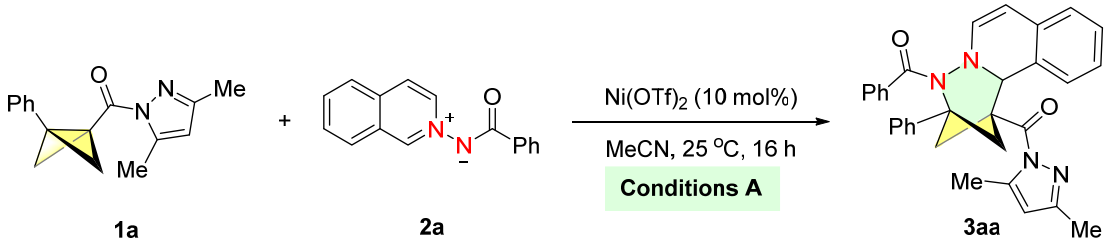
Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added the BCB **1** (0.20 mmol, 1.0 equiv), **2** (0.24 mmol, 1.2 equiv) and $Fe(OTf)_2$ (7.1 mg, 0.02 mmol) followed by 4.0 mL of anhydrous CH_2Cl_2. The solution was stirred at 25 °C for 12 h till full conversion of BCBs by TLC analysis. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification using PE/EtOAc (3:1, v/v) as the eluent, to afford the desired product **3 or 4**.

3.4 General procedure for the enantioselective (3+3) cycloadditions (**GP4**)

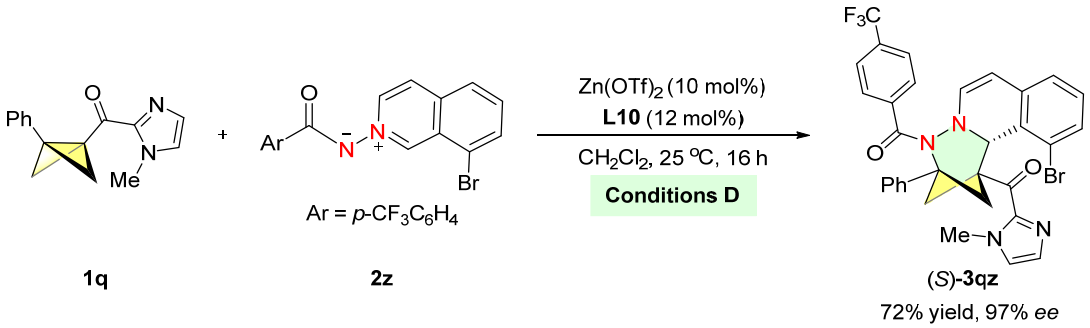


Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added $Zn(OTf)_2$ (7.3 mg, 0.02 mmol) and **L10** (17.8 mg, 0.024 mmol), followed by 4.0 mL of anhydrous CH_2Cl_2. The solution was stirred at 25 °C for 0.5 h, and then the BCBs **1** (0.20 mmol, 1.0 equiv) and **2** (0.24 mmol, 1.2 equiv) were added. Then the resulting mixture was stirred at room temperature for 16 h till full conversion of BCBs by TLC analysis. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification using PE/EtOAc (4:1, v/v) as the eluent, to afford the desired product **3**.

4 Scale-Up Experiment

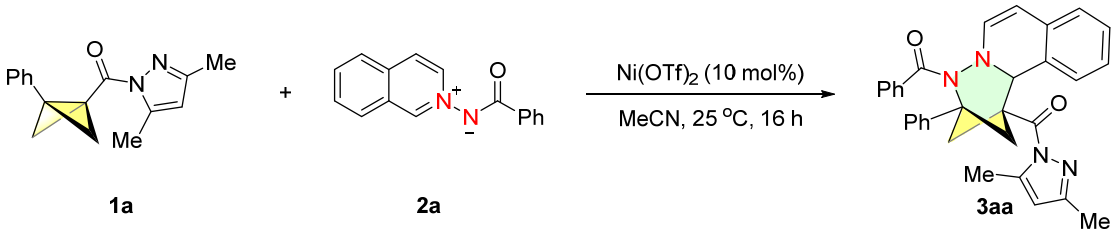


Under an atmosphere of N_2, to a 100 mL oven-dried Schlenk tube were added the BCB **1a** (252.3 mg, 1.0 mmol, 1.0 equiv), **2a** (297.9 mg, 1.2 mmol, 1.2 equiv) and $Ni(OTf)_2$ (35.7 mg, 0.1 mmol) followed by 20.0 mL of anhydrous MeCN. The solution was stirred at 25 °C for 16 h till full conversion of **1a** by TLC analysis. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification using PE/EtOAc (10:1, v/v) as the eluent, to afford the desired product **3aa** (492.0 mg, 98% yield).



Under an atmosphere of N_2, to a 100 mL oven-dried Schlenk tube were added $Zn(OTf)_2$ (36.4 mg, 0.10 mmol, 10 mol%) and **L10** (88.8 mg, 0.12 mmol, 12 mol%), followed by 25.0 mL of anhydrous CH_2Cl_2. The solution was stirred at 25 °C for 0.5 h, and then the BCB **1q** (238.3 mg, 1.0 mmol, 1.0 equiv) and **2z** (474.2 mg, 1.2 mmol, 1.2 equiv) were added. Then the resulting mixture was stirred at room temperature for 16 h till full conversion of **1q** by TLC analysis. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification using PE/EtOAc (4:1, v/v) as the eluent, to afford the desired product (*S*)-**3qz** (457.9 mg, 72% yield, 97% *ee*).

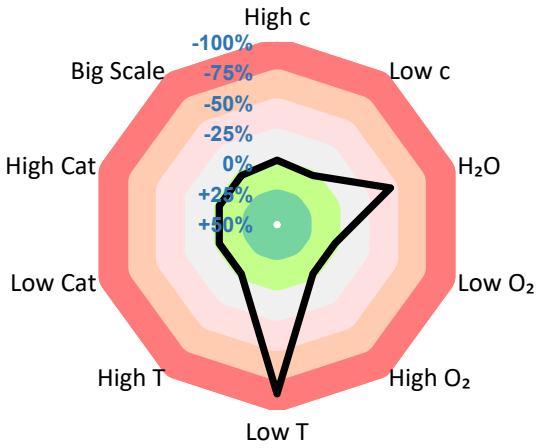
5 Sensitivity Assessment



Standard conditions: Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added the BCB **1a** (25.2 mg, 0.10 mmol, 1.0 equiv), the azomethine imine **2a** (29.8 mg, 0.12 mmol, 1.2 equiv), and $Ni(OTf)_2$ (3.6 mg, 0.01 mmol) followed by 2.0 mL of anhydrous MeCN. The solution was stirred at 25 °C for 16 h. After the solvent was removed under reduced pressure, CH_2Br_2 (0.10 mmol, 17.4 mg) was added as an internal standard, and the yield was determined by ^1H NMR analysis of the crude mixture.

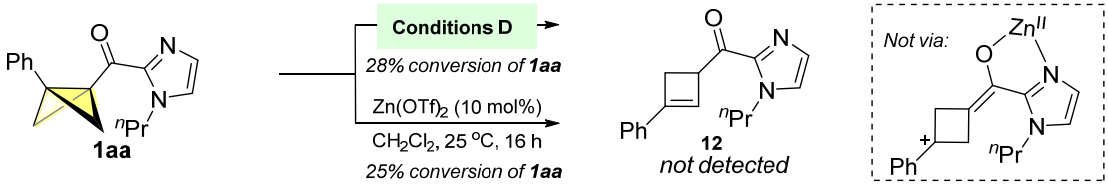
Table S8. Sensitivity assessment

Entry	Description	Deviation from Standard Condition	Yield (%)	Deviation (%)
1	control	-	99	-
2	high *c*	MeCN (1 mL)	96	-3
3	Low *c*	MeCN (4 mL)	99	0
4	high H_2O	+ H_2O (10 μL)	51	-48
5	low O_2	degassed solvent	99	0
6	high O_2	under air	99	0
7	low *T*	at 0 °C	10	-89
8	High *T*	at 50 °C	99	0
9	high *cat*	$Ni(OTf)_2$ (20 mol%)	99	0
10	low *cat*	$Ni(OTf)_2$ (5 mol%)	99	0
11	big scale	1.0 mmol scale	99	0



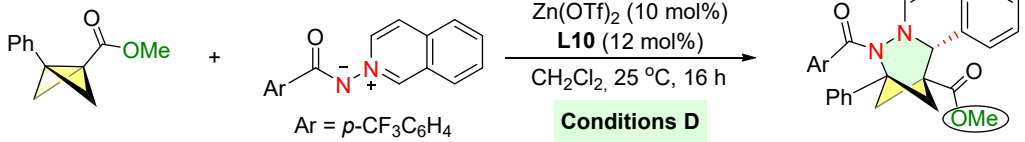
Comment: Condition-based sensitivity screening was performed,[3] revealing that low temperature inhibited the reaction. The reaction showed moderate sensitivity to moisture, with concentration, scale, catalyst loading, high temperature, and O_2 level having no significant impact on the reaction.

6 Unsuccessful Substrates and Control Experiments



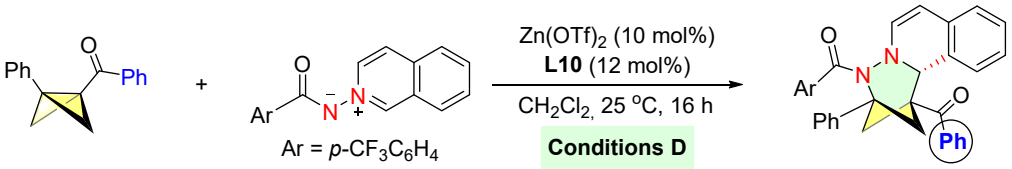
Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added $Zn(OTf)_2$ (3.6 mg, 0.010 mmol, 10 mol%) and L10 (8.9 mg, 0.012 mmol, 12 mol%), followed by 2 mL of anhydrous CH_2Cl_2. The solution was stirred at 25 °C for 0.5 h, and then the BCB **1aa** (26.6 mg, 0.1 mmol, 1.0 equiv) were added. Then the resulting mixture was stirred at room temperature for 16 h. The conversion of **1aa** and the yield of cyclobutene 12 was determined by ^1H NMR using CH_2Br_2 as an internal standard.

For the version without **L10**, the procedure remains the same, simply omitting the addition of L10 after the $Zn(OTf)_2$ addition.



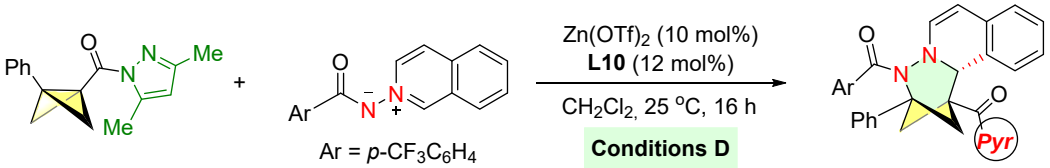
1ff (1.0 equiv) **2d** (1.2 equiv)

3ffd, 0% NMR yield
conversion of **1ff**: 0%



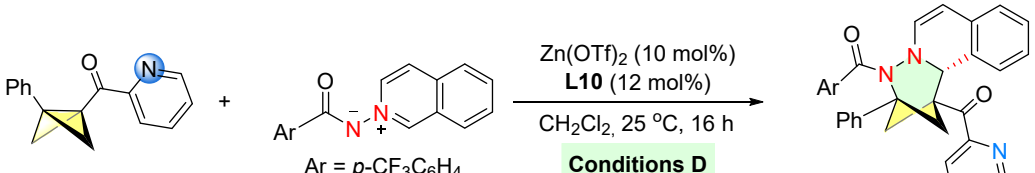
1g (1.0 equiv) **2d** (1.2 equiv)

3gd, 9% NMR yield
0% *ee*
conversion of **1g**: 9%



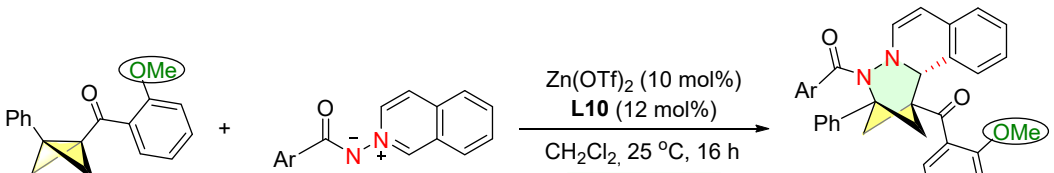
1a (1.0 equiv) **2d** (1.2 equiv)

3ad, 30% NMR yield
6% *ee*
conversion of BCB: 30%



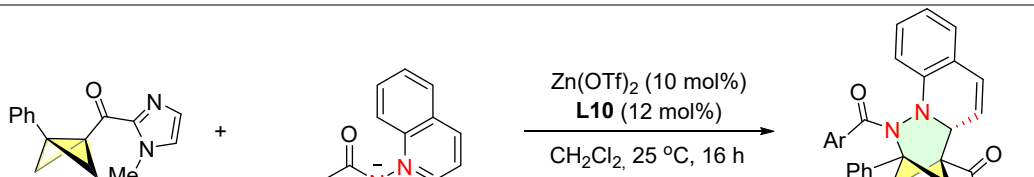
1o (1.0 equiv) **2d** (1.2 equiv)

3od, 97% NMR yield
0% *ee*
conversion of **1o**: 99%



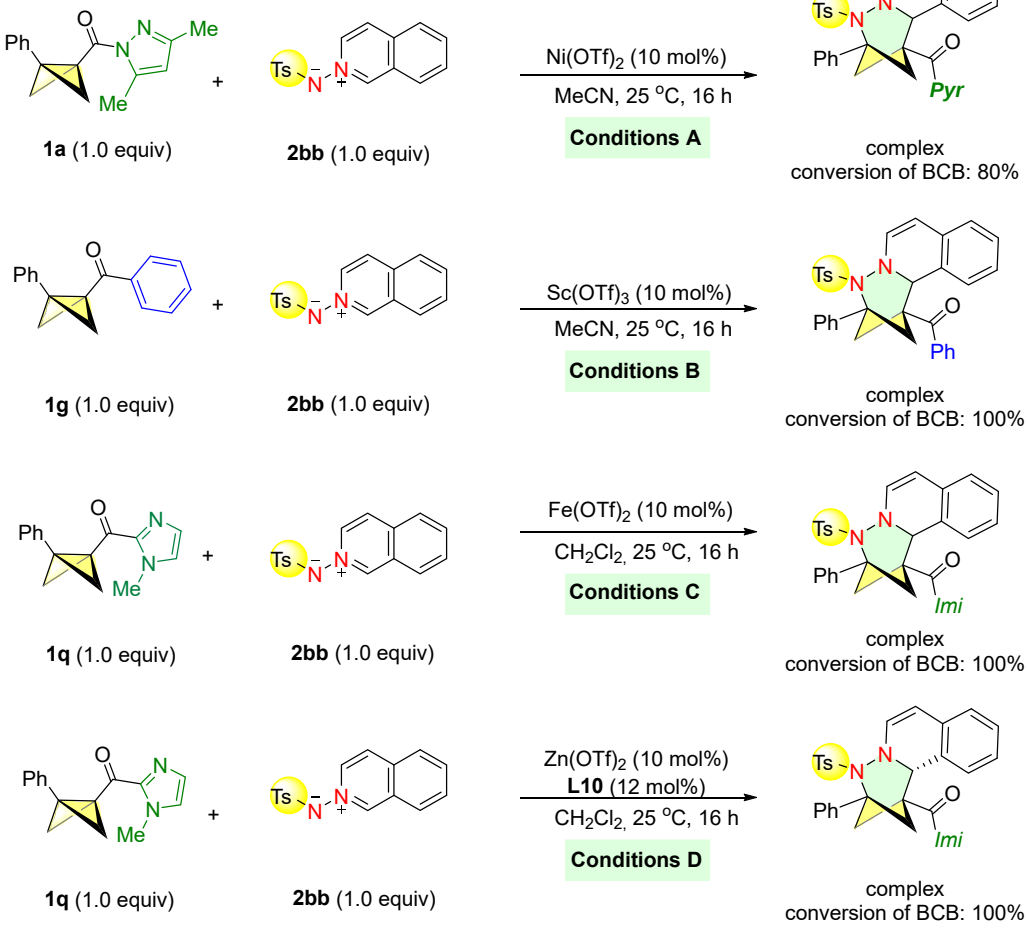
1bb (1.0 equiv) **2d** (1.2 equiv)

3bbd, 14% NMR yield
4% *ee*
conversion of **1bb**: 15%



1q (1.0 equiv) **2aa** (1.2 equiv)

(*R*)-**4qaa**, 54% NMR yield
41% *ee*


Ph
O
N
N
Me
Me
+
Ts
N
N
Ni(OTf)2 (10 mol%)
MeCN, 25 °C, 16 h
Conditions A
Ts
N
N
Ph
O
Pyr
complex
conversion of BCB: 80%
1a (1.0 equiv)
2bb (1.0 equiv)
Ph
O
+
Ts
N
N
Sc(OTf)3 (10 mol%)
MeCN, 25 °C, 16 h
Conditions B
Ts
N
N
Ph
O
Ph
complex
conversion of BCB: 100%
1g (1.0 equiv)
2bb (1.0 equiv)
Ph
O
N
N
Me
+
Ts
N
N
Fe(OTf)2 (10 mol%)
CH2Cl2, 25 °C, 16 h
Conditions C
Ts
N
N
Ph
O
Imi
complex
conversion of BCB: 100%
1q (1.0 equiv)
2bb (1.0 equiv)
Ph
O
N
N
Me
+
Ts
N
N
Zn(OTf)2 (10 mol%)
L10 (12 mol%)
CH2Cl2, 25 °C, 16 h
Conditions D
Ts
N
N
Ph
O
Imi
complex
conversion of BCB: 100%
1q (1.0 equiv)
2bb (1.0 equiv)

7 Non-Linear Effect Study

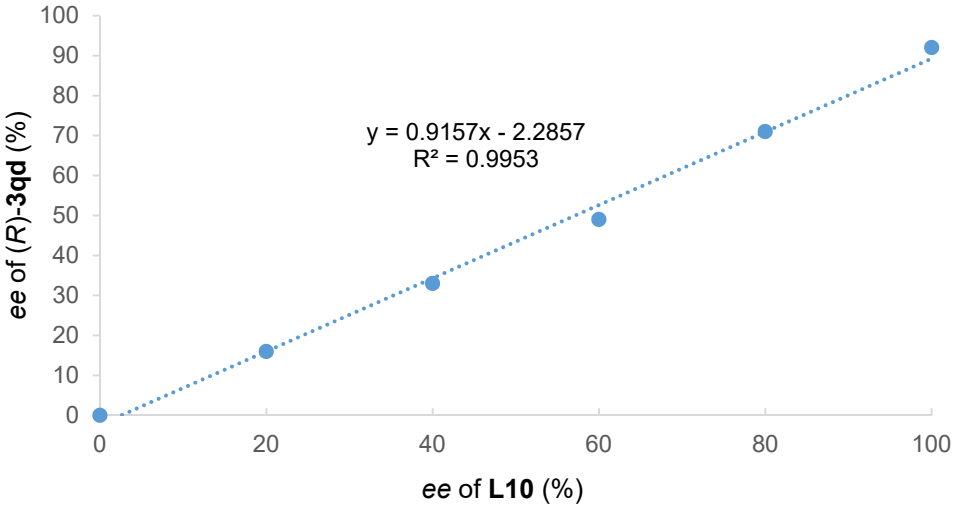
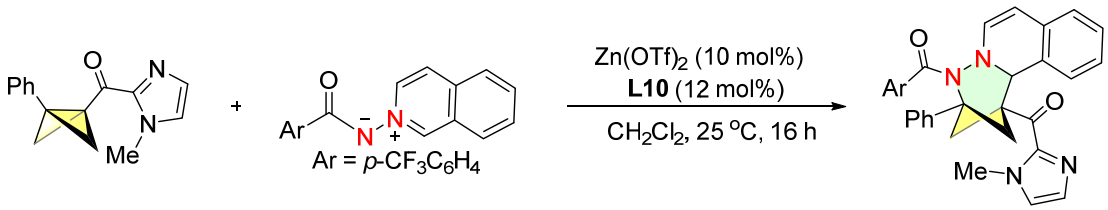


Figure S1. Non-linear effect study

Table S9. Tabulation of non-linear effects[a]

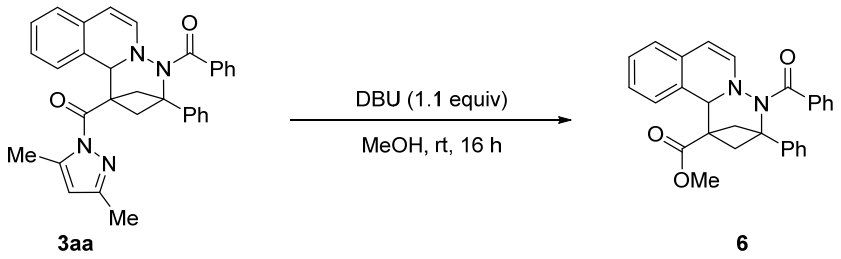


1q **2d** (*R*)-**3qd**

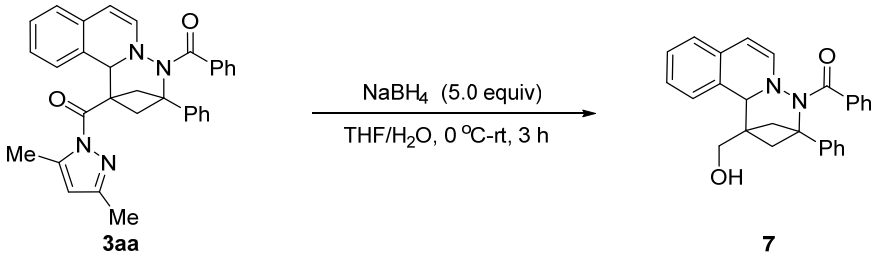
Entry	**L10** *ee* (%)[b]	(*R*)-**3qd** *ee* (%)[b]
1	20	16
2	40	33
3	60	49
4	80	71
5	100	92

[a]Reaction conditions: **1q** (0.10 mmol, 1.0 equiv), **2d** (0.12 mmol, 1.2 equiv), $Zn(OTf)_2$ (10 mol%) and **L10** (12 mol%), CH_2Cl_2 (2 mL), 25 °C, under N_2 for 16 h. [b]Determined by chiral HPLC with hexane/2-propanol.

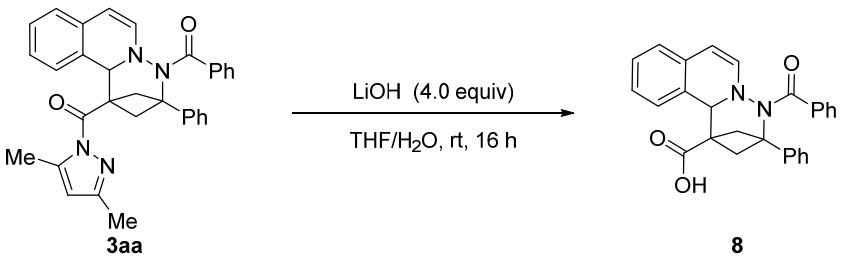
8 Synthetic Transformations



Synthesis of (6): To a solution of **3aa** (50.1 mg, 0.1 mmol, 1.0 equiv) in MeOH (2.0 mL) was added DBU (16.8 mg, 0.11 mmol, 1.1 equiv). The mixture was then stirred at room temperature for 16 h. Aqueous saturated NH_4Cl solution (2.0 mL) was added to quench the reaction. The mixture was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over anhydrous $MgSO_4$. Finally, the residue was directly subjected to a column chromatography purification (PE/EtOAc = 10:1) as the eluent to afford **6** (40.1 mg, 92% yield) as a white solid.

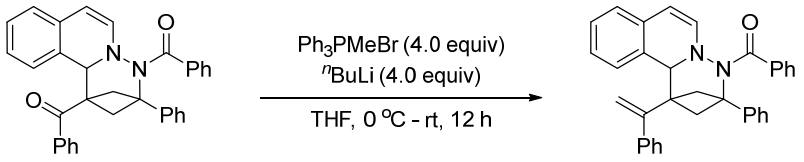


Synthesis of (7): To a solution of **3aa** (50.1 mg, 0.1 mmol, 1.0 equiv) in a mixed solvent of THF/H_2O (v/v = 4/1, 2.0 mL) at 0 °C was added $NaBH_4$ (18.9 mg, 0.5 mmol, 5.0 equiv) in one portion. The reaction mixture was gradually warmed up to room temperature and stirred for 3 h and then quenched by addition of 5 mL saturated aqueous $NaHCO_3$ solution. The mixture was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over anhydrous $MgSO_4$. Finally, the residue was directly subjected to a column chromatography purification (PE/EtOAc = 5:1) as the eluent to afford **7** (38.6 mg, 95% yield) as a white solid.



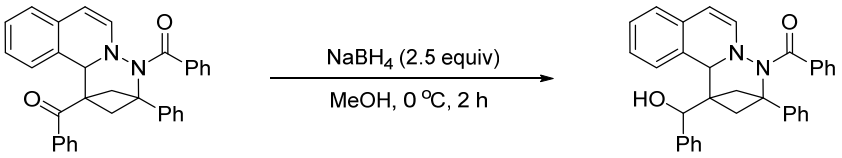
3aa **8**

Synthesis of (8): To a solution of **3aa** (50.1 mg, 0.1 mmol, 1.0 equiv) in a mixed solvent of THF/H_2O (v/v = 1/1, 2.0 mL) at room temperature was added lithium hydroxide (9.6 mg, 0.1 mmol, 4.0 equiv) in one portion. The mixture was stirred at room temperature for 16 h, then EtOAc (3 mL) was added to extract the reaction solution and the organic phase was removed. Acidified the aqueous phase with 1 N HCl to pH = 5~6, and extracted it with EtOAc (3 x 5 mL) and the combined organic phase was dried with $MgSO_4$. Finally, the residue was directly subjected to a column chromatography purification (PE/EtOAc = 1:1) as the eluent to afford **8** (39.8 mg, 94% yield) as a yellow solid.



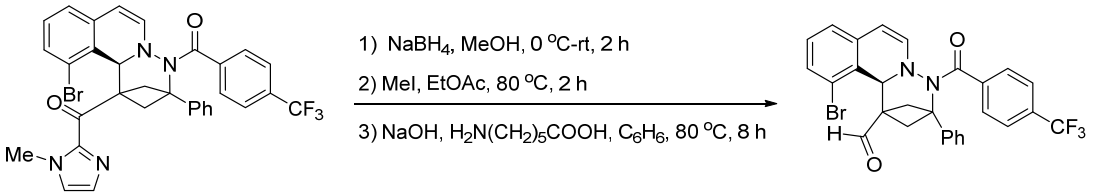
3ga **9**

Synthesis of (9): To a solution of methyl triphenylphosphonium bromide (0.40 mmol, 142.9 mg, 4.0 equiv) in anhydrous THF (1.0 mL) at 0 °C was added ^{n}BuLi (0.25 mL, 1.6 M in hexane, 0.4 mmol, 4.0 equiv) in one portion. The resulting yellow suspension was stirred at 0 °C for 45 min, then a solution of **3ga** (0.10 mmol, 48.3 mg, 1.0 equiv) in THF (1.0 mL) added dropwise. The mixture was stirred at room temperature for 16 h. The reaction mixture was quenched with water (5 mL), extracted with EtOAc (3 x 5 mL), and the combined organic phase was dried with $MgSO_4$. Finally, the residue was directly subjected to a column chromatography purification (PE/EtOAc = 10:1) as the eluent to afford **9** (44.8 mg, 93% yield) as a white solid.



3ga **10**

Synthesis of (10): To a solution of **3ga** (0.10 mmol, 48.3 mg, 1.0 equiv) in the MeOH (2.0 mL) was added $NaBH_4$ (9.5 mg, 0.25 mmol, 2.5 equiv) at 0 °C. and stirred 2 h. Then aqueous saturated NH_4Cl solution (5 mL) was added to quench the reaction. The aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic phases were washed by brine and dried over $MgSO_4$ and concentrated under reduced pressure after filtration. Finally, the residue was directly subjected to a column chromatography purification (PE/EtOAc = 5:1) as the eluent to afford **10** (45.1 mg, 93% yield (yields are combined isolated material), 5:1 *dr*) as a white solid.

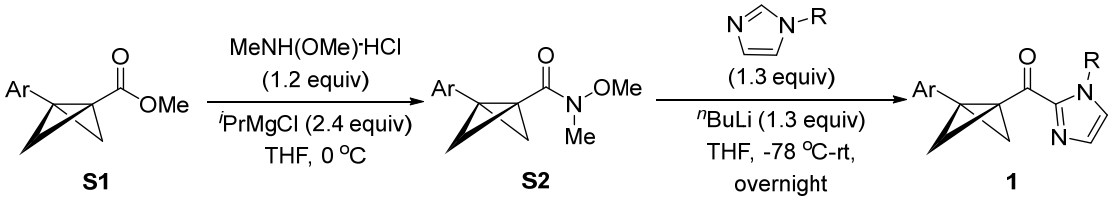


(*S*)-**3qz** **11**
97% *ee* 96% *ee*

Synthesis of (11): To a solution of (*S*)-**3qz** (0.20 mmol, 126.8 mg, 1.0 equiv) in the MeOH (4.0 mL) was added $NaBH_4$ (18.9 mg, 0.50 mmol, 2.5 equiv) at 0 °C, and stirred 2 h. Then aqueous saturated NH_4Cl solution (5 mL) was added to quench the reaction. The aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic phases were washed by brine and dried over $MgSO_4$ and concentrated under reduced pressure after filtration. The residue was directly subjected to a column chromatography purification to afford the intermediate. The intermediate in ethyl acetate (4.0 mL) was refluxed for 2 h in the presence of methyl iodide (0.2 mL, 3.2 mmol, 16.0 equiv), followed by evaporation of the volatile portion, to give a crystalline residue. And then 6-aminohexanoic acid (104 mg, 0.8 mmol, 4 equiv), 1 N NaOH (1 mL) and benzene (4 mL) were added. The two-layer solution was stirred at 80 °C for 8 h. The aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic

phases were washed by brine and dried over $MgSO_4$ and concentrated under reduced pressure after filtration. Finally, the residue was directly subjected to a column chromatography purification (PE/EtOAc = 8:1) as the eluent to afford **11** (70.8 g, 64% yield over 3 steps, 96% *ee*) as a white solid.

9 General Procedure for the Synthesis of New Bicyclobutanes (GP5)

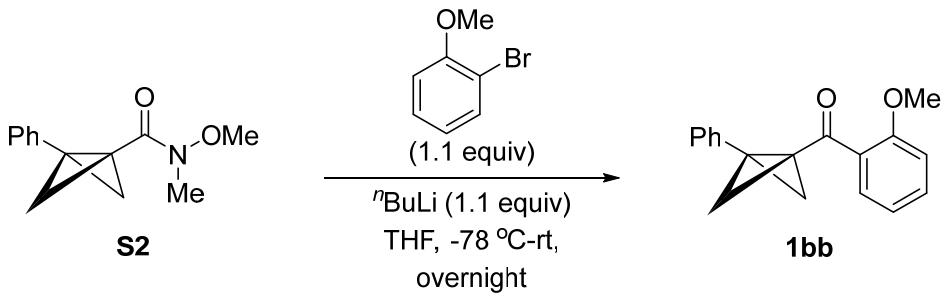


BCB esters **S1** were prepared according to literature procedures.[1] Weinreb amide derived BCBs **S2** were synthesized as following: An oven-dried 100 mL round bottom flask equipped with a stir bar was cooled under vacuum. After backfilled with N_2 (x 3) and capped with a septum, BCB esters **S1** (5.00 mmol, 1.00 equiv) and THF (25 mL) were added. The reaction was cooled to 0 °C. MeNH(OMe)·HCl (585 mg, 6 mmol, 1.2 equiv) and ^{i}PrMgCl (6.0 mL, 2.0 M in THF, 12.0 mmol, 2.4 equiv) were sequentially added to the solution. After stirred at the same temperature for 12 h, the reaction was quenched by saturated NH_4Cl solution (20 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (25 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The crude Weinreb amide derived BCBs **S2** was directly used in next reaction.

An oven-dried 100 mL round bottom flask equipped with a stir bar was cooled under vacuum. After backfilled with N_2 (x 3) and capped with a septum, *N*-substituted imidazole derivatives (6.5 mmol, 1.3 equiv) and THF (20 mL) were added. The reaction was cooled to -78 °C. ^{n}BuLi (2.6 mL, 2.5 M in THF, 6.5 mmol, 1.3 equiv) was added to the solution. After stirred at the same temperature for 20 min, **S2** dissolved in THF (5 mL) was added. Next, the reaction was warm to room temperature and stirred overnight. Then, the reaction was quenched by saturated NH_4Cl solution (20 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers

were washed with brine (25 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 5/1) to afford a new kind of BCB **1**.

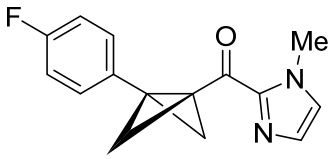
10 General Procedure for the Synthesis of New Bicyclobutanes Ketones (GP6)



S2 **1bb**

An oven-dried 100 mL round bottom flask equipped with a stir bar was cooled under vacuum. After backfilled with N_2 (x 3) and capped with a septum, aryl Bromides (5.5 mmol, 1.1 equiv) and THF (20 mL) were added. The reaction was cooled to -78 °C. ^{n}BuLi (2.6 mL, 2.5 M in THF, 5.5 mmol, 1.1 equiv) was added to the solution. After stirred at the same temperature for 30 min, purified S2 dissolved in THF (5 mL) was added. Next, the reaction was warm to room temperature and stirred overnight. Then, the reaction was quenched by saturated NH_4Cl solution (20 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (25 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 15/1) to afford a new kind of BCB ketones **1bb**.

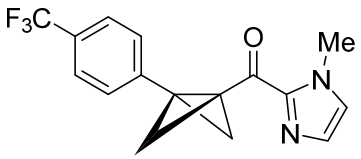
11 Characterization Data of New BCBs and Products



1u
$C_{15}H_{13}FN_2O$
M = 256.28 g/mol

(3-(4-fluorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone: (**1u**)
Prepared from methyl 3-(4- fluorophenyl)bicyclo[1.1.0]butane-1-carboxylate (1.03 g, 5 mmol, 1.0 equiv) according to the **GP5**. Purification by flash chromatography on silica gel afforded **1u** as a white solid (0.64 g, 50% yield over 2 steps).

1u: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 5/1). Mp: 109-111 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.27-7.23 (m, 2H), 7.07 (s, 1H), 6.94-6.88 (m, 3H), 3.68 (s, 3H), 3.61 (s, 2H), 1.89 (s, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 185.4, 162.1 (d, *J* = 244.9 Hz), 143.4, 129.2 (d, *J* = 3.0 Hz), 128.9, 127.6 (d, *J* = 8.0 Hz), 125.9, 115.3 (d, *J* = 21.6 Hz), 39.7, 38.1, 35.9, 32.5 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.96 ppm. **HRMS** (ESI) *m/z*: $[M+NH_4]^+$ calcd. for $C_{15}H_{17}N_3O$: 274.1350; found: 274.1358.

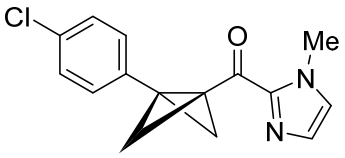


1v
$C_{16}H_{13}F_3N_2O$
M = 306.29 g/mol

(1-methyl-1H-imidazol-2-yl)(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1v**):
Prepared from methyl 3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butane-1-carboxylate (1.28 g, 5 mmol, 1.0 equiv) according to the **GP5**. Purification by flash chromatography on silica gel afforded **1v** as a white solid (0.55 g, 36% yield over 2 steps).

1v: $\mathbf{R_f}$ = 0.40 (petroleum ether/EtOAc = 5/1). Mp: 76-78 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.4 Hz, 2H) 7.30 (d, *J* = 8.0 Hz, 2H), 7.00 (s, 1H), 6.81 (s, 1H), 3.61-3.60 (m, 5H), 1.84 (s, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 184.8, 143.2, 138.1, 128.9, 128.8 (q, *J* = 32.3 Hz), 125.2 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 270.1 Hz), 126.2, 126.2,

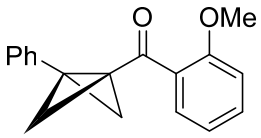
38.5, 38.1, 35.9, 33.5 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.48 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{16}H_{14}F_3N_2O$: 307.1053; found: 307.1046.



1y
$C_{15}H_{13}ClN_2O$
M = 272.73 g/mol

(3-(4-chlorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1H-imidazol-2-yl)methanone (**1y**): methyl 3-(4-chlorophenyl)bicyclo[1.1.0]butane-1-carboxylate (1.11 g, 5 mmol, 1.0 equiv) according to the **GP5**. Purification by flash chromatography on silica gel afforded **1y** as a white solid (0.69 g, 51% yield over 2 steps).

1y: $\mathbf{R_f}$ = 0.50 (petroleum ether/EtOAc = 5/1). Mp: 94-96 °C. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.22-7.20 (m, 2H), δ 7.18-7.16 (m, 2H), 7.06 (d, *J* = 0.6 Hz, 1H), 6.87 (s, 1H), 3.68 (s, 3H), 3.62 (s, 2H), 1.87 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 185.0, 143.2, 132.7, 132.1, 128.7, 128.35, 127.23, 125.94, 39.27, 37.98, 35.86, 32.90 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{15}H_{14}ClN_2O$: 273.0789; found: 273.0784.

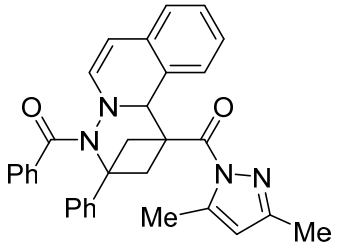


1bb
$C_{18}H_{16}O_2$
M = 264.32 g/mol

(2-methoxyphenyl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1bb**): Prepared from *N*-methoxy-*N*-methyl-3-phenylbicyclo[1.1.0]butane-1-carboxamide (1.09 g, 5 mmol, 1.0 equiv) according to the **GP6**. Purification by flash chromatography on silica gel afforded **1bb** as a white solid (0.75 g, 57%).

1bb: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 7/1). Mp: 109-111 °C.**^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.31-7.25 (m, 4H), 7.14-7.12 (m, 2H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.73 (t, *J* = 7.6 Hz, 1H), 6.52-6.50 (m, 1H), 3.69 (s, 3H), 2.97 (s, 2H), 1.81 (s, 2H) ppm. **^{13}C NMR**

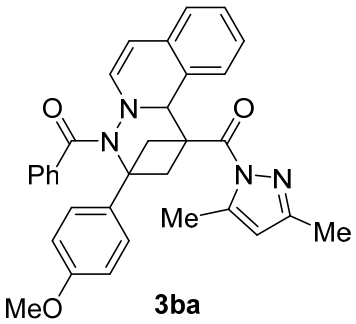
(100 MHz, $CDCl_3$): δ 197.8, 157.3, 133.1, 131.6, 129.0, 128.2, 127.9, 127.0, 125.8, 120.1, 110.9, 55.5, 39.9, 36.8, 34.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{17}O_2$: 265.1223; found: 265.1222.



3aa
$C_{32}H_{28}N_4O_2$
M = 500.60 g/mol

(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(3,5-dimethyl-1*H*-pyrazol-1-yl)methanone (3aa): Prepared from (3,5-dimethyl-1*H*-pyrazol-1-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 50.5 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3aa** as a white solid (99.1 mg, 99% yield).

3aa: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 10/1). Mp: 115-117 °C.^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 6.4 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.40-7.33 (m, 5H), 7.23-7.21 (m, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.79 (d, *J* = 7.2 Hz, 1H), 6.61 (t, *J* = 7.6 Hz, 1H), 5.95 (s, 1H), 5.79 (d, *J* = 7.6 Hz, 1H), 5.59 (s, 1H), 5.31 (d, *J* = 7.6 Hz, 1H), 3.74 (t, *J* = 10.0 Hz, 1H), 3.42 (d, *J* = 10.8 Hz, 1H), 3.25 (t, *J* = 10.0 Hz, 1H), 2.43 (d, *J* = 11.2 Hz, 1H), 2.30 (s, 3H), 2.26 (s, 3H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 175.0, 171.7, 152.8, 144.4, 142.0, 140.8, 135.6, 131.2, 130.7, 128.6, 128.2, 127.8, 126.9, 126.2, 125.4, 124.8, 124.5, 111.0, 100.7, 68.5, 68.3, 56.7, 48.7, 41.7, 14.0, 13.9 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{34}H_{28}N_4O_2Na$: 523.2104; found: 523.2108.



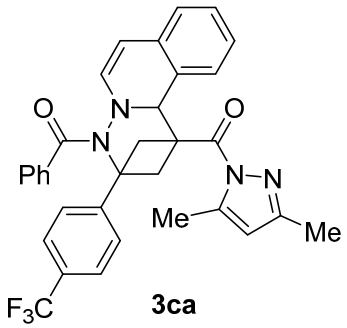
3ba

$C_{33}H_{30}N_4O_3$

M = 530.63 g/mol

(4-benzoyl-3-(4-methoxyphenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(3,5-dimethyl-1*H*-pyrazol-1-yl)methanone (3ba): Prepared from (3,5-dimethyl-1*H*-pyrazol-1-yl)(3-(4-methoxyphenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1b**, 56.5 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ba** as a white solid (105.1 mg, 99% yield).

3ba: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 5/1). Mp: 128-130 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 6.8 Hz, 2H), 7.42-7.34 (m, 3H), 7.30-7.25 (m, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 6.99-6.95 (m, 2H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.80-6.76 (m, 2H), 6.61 (t, *J* = 7.6 Hz, 1H), 5.95 (s, 1H), 5.78 (d, *J* = 5.6 Hz, 1H), 5.58 (s, 1H), 5.31 (d, *J* = 7.6 Hz, 1H), 3.81 (s, 3H), 3.71 (t, *J* = 10.0 Hz, 1H), 3.40 (d, *J* = 10.8 Hz, 1H), 3.22 (t, *J* = 10.0 Hz, 1H), 2.42 (d, *J* = 11.6 Hz, 1H), 2.30 (s, 3H), 2.27 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.0, 171.7, 159.6, 152.8, 144.4, 143.6, 140.7, 135.6, 131.2, 130.7, 129.3, 128.6, 128.2, 127.9, 126.2, 125.4, 124.5, 117.1, 111.8, 111.0, 100.7, 68.4, 68.3, 56.6, 55.2, 48.8, 41.8, 14.0, 13.9 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{33}H_{30}N_4O_3Na$: 553.2210; found: 553.2212.



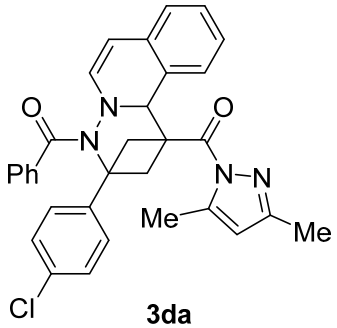
3ca

$C_{33}H_{27}F_3N_4O_2$

M = 568.60 g/mol

(4-benzoyl-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(3,5-dimethyl-1*H*-pyrazol-1-yl)methanone: (**3ca**) Prepared from (3,5-dimethyl-1*H*-pyrazol-1-yl)(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1c**, 64.0 mg, 0.2 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ca** as a yellow solid (88.2 mg, 78% yield).

3ca: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 244-246 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.72-7.70 (m, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.43-7.34 (m, 3H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.63 (t, *J* = 7.6 Hz, 1H), 5.95 (s, 1H), 5.80 (d, *J* = 8.0 Hz, 1H), 5.60 (s, 1H), 5.35 (d, *J* = 7.6 Hz, 1H), 3.76 (t, *J* = 10.6 Hz, 1H), 3.42 (d, *J* = 10.4 Hz, 1H), 3.24 (t, *J* = 10.0 Hz, 1H), 2.42 (d, *J* = 11.6 Hz, 1H), 2.30 (s, 3H), 2.26 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.1, 171.4, 153.0, 145.8, 144.5, 140.5, 135.1, 131.03, 130.96, 129.0 (q, *J* = 32 Hz), 128.7, 128.3, 128.1, 127.9, 126.2, 125.6, 125.3 (q, *J* = 4 Hz), 125.2, 124.6, 124.2 (q, *J* = 270 Hz), 111.1, 101.1, 68.3, 68.1, 56.6, 48.7, 41.5, 14.0, 13.9 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.35 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{28}F_3N_4O_2$: 569.2159; found: 569.2150.



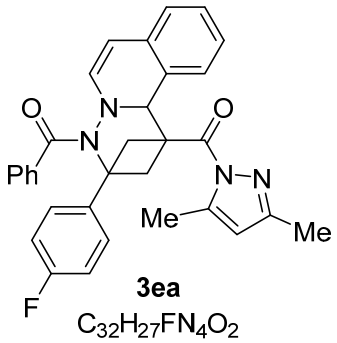
3da

$C_{32}H_{27}ClN_4O_2$

M = 535.04 g/mol

(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(3,5-dimethyl-1*H*-pyrazol-1-yl)methanone (3da): Prepared from (3-(4-chlorophenyl)bicyclo[1.1.0]butan-1-yl)(3,5-dimethyl-1*H*-pyrazol-1-yl)methanone (**1d**, 57.4 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3da** as a white solid (106.9 mg, 99% yield).

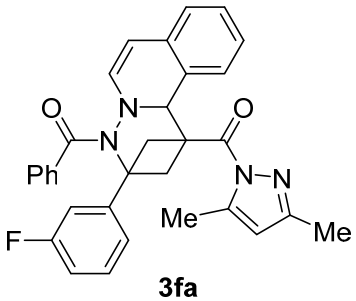
3da: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 10/1). Mp: 129-131 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 6.7 Hz, 2H), 7.41-7.30 (m, 7H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.84-6.79 (m, 2H), 6.62 (t, *J* = 7.6 Hz, 1H), 5.95 (s, 1H), 5.79 (s, 1H), 5.57 (s, 1H), 5.32 (d, *J* = 7.6 Hz, 1H), 3.73 (t, *J* = 10.0 Hz, 1H), 3.36 (d, *J* = 10.8 Hz, 1H), 3.23 (t, *J* = 9.6 Hz, 1H), 2.39 (d, *J* = 11.6 Hz, 1H), 2.30 (s, 3H), 2.26 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.1, 171.5, 152.9, 144.4, 140.6, 135.3, 132.6, 131.1, 130.8, 128.6, 128.4, 128.2, 128.1, 127.9, 126.3, 126.2, 125.5, 124.5, 111.0, 100.9, 68.2, 68.0, 56.6, 48.7, 41.6, 14.0, 13.9 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{27}ClN_4O_2Na$: 557.1715; found: 557.1724.



3ea
$C_{32}H_{27}FN_4O_2$
M = 518.59 g/mol

(4-benzoyl-3-(4-fluorophenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(3,5-dimethyl-1*H*-pyrazol-1-yl)methanone (3ea): Prepared from (3,5-dimethyl-1*H*-pyrazol-1-yl)(3-(4-fluorophenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1e**, 54.6 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ea** as a white solid (102.7 mg, 99% yield).

3ea: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 3/1). Mp: 134-136 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.2 Hz, 2H), 7.41-7.33 (m, 5H), 7.05-6.96 (m, 3H), 6.84-6.78 (m, 2H), 6.62 (t, *J* = 7.6 Hz, 1H), 5.95 (s, 1H), 5.79 (d, *J* = 7.6 Hz, 1H), 5.57 (s, 1H), 5.32 (d, *J* = 7.6 Hz, 1H), 3.74 (t, *J* = 10.0 Hz, 1H), 3.36 (d, *J* = 10.8 Hz, 1H), 3.25 (t, *J* = 10.0 Hz, 1H), 2.40 (d, *J* = 11.2 Hz, 1H), 2.30 (s, 3H), 2.26 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.2, 171.6, 161.7 (d, *J* = 243.8 Hz), 152.9, 144.4, 140.6, 137.9 (d, *J* = 3.2 Hz), 135.5, 131.1, 130.8, 128.6, 128.20, 128.15, 127.9, 126.6 (d, *J* = 8.1 Hz), 126.2, 125.5, 124.5, 115.0 (d, *J* = 21.4 Hz), 111.0, 100.8, 68.2, 68.0, 56.7, 48.8, 41.6, 14.0, 13.9 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.81 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{27}FN_4O_2Na$: 551.2010; found: 551.2010.



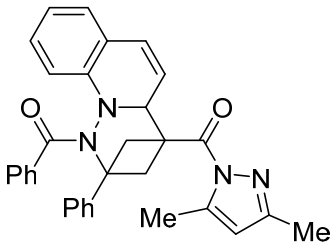
3fa

$C_{32}H_{27}FN_4O_2$

M = 518.59 g/mol

(4-benzoyl-3-(3-fluorophenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(3,5-dimethyl-1*H*-pyrazol-1-yl)methanone (3fa): Prepared from (3,5-dimethyl-1*H*-pyrazol-1-yl)(3-(3-fluorophenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1f**, 54.6 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3fa** as a white solid (72.6 mg, 70% yield).

3fa: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 10/1). Mp: 218-220 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 6.8 Hz, 2H), 7.43-7.28 (m, 4H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 10.0 Hz, 1H), 7.00-6.90 (m, 2H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.62 (t, *J* = 7.6 Hz, 1H), 5.95 (s, 1H), 5.80 (d, *J* = 7.6 Hz, 1H), 5.58 (s, 1H), 5.33 (d, *J* = 7.6 Hz, 1H), 3.73 (t, *J* = 10.0 Hz, 1H), 3.38 (d, *J* = 10.8 Hz, 1H), 3.22 (t, *J* = 9.6 Hz, 1H), 2.42 (d, *J* = 11.6 Hz, 1H), 2.30 (s, 3H), 2.26 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.1, 171.5, 162.9 (d, *J* = 243.9 Hz), 152.9, 144.6 (d, *J* = 7.2 Hz), 144.4, 140.6, 135.3, 131.1, 130.9, 129.8 (d, *J* = 8 Hz), 128.7, 128.3, 128.1, 127.9, 126.2, 125.5, 124.5, 120.3 (d, *J* = 2.8 Hz), 113.8 (d, *J* = 21.1 Hz), 111.9 (d, *J* = 22.1 Hz), 111.0, 100.9, 68.3, 68.0, 56.6, 48.7, 42.1, 14.0, 13.9 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.26 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{28}FN_4O_2$: 519.2191; found: 519.2191.



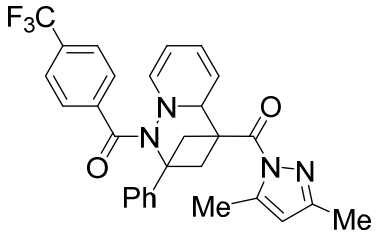
4ab

$C_{32}H_{28}N_4O_2$

M = 500.60 g/mol

(1-benzoyl-2-phenyl-2,3-dihydro-1*H*-2,4-methanopyridazino[1,6-*a*]quinolin-4(4a*H*)-yl)(3,5-dimethyl-1*H*-pyrazol-1-yl)methanone (4ab) : Prepared from (3,5-dimethyl-1*H*-pyrazol-1-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 50.5 mg, 0.2 mmol) and benzoyl(quinolin-1-ium-1-yl)amide (**2b**, 59.6 mg, 0.24 mmol) at room temperature for 16 h according to the **GP1**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **4ab** as a white solid (50.1 mg, 50% yield)

4ab: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 260-262 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.2 Hz, 2H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.39-7.34 (m, 4H), 7.29-7.24 (m, 4H), 6.88 (d, *J* = 7.2 Hz, 1H), 6.78 (t, *J* = 7.2 Hz, 1H), 6.25 (d, *J* = 10.0 Hz, 1H), 5.95 (s, 1H), 5.56 (d, *J* = 4.0 Hz, 1H), 5.01 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.25-3.16 (m, 2H), 2.98-2.93 (m, 1H), 2.51 (s, 3H), 2.39 (d, *J* = 11.2 Hz, 1H), 2.21 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.9, 171.3, 153.0, 146.3, 143.9, 142.2, 135.3, 130.7, 130.0, 128.1, 127.9, 127.8, 127.5, 127.4, 126.9, 126.0, 120.3, 120.1, 119.8, 111.7, 111.0, 68.5, 65.7, 57.0, 48.4, 39.3, 14.0, 13.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{29}N_4O_2$: 501.2285; found: 501.2282.



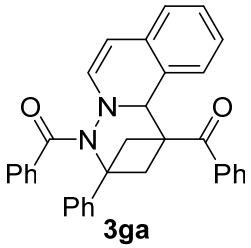
5ac

$C_{29}H_{25}F_3N_4O_2$

M = 518.54 g/mol

(3,5-dimethyl-1*H*-pyrazol-1-yl)(2-phenyl-1-(4-(trifluoromethyl)benzoyl)-2,3-dihydro-1*H*-2,4-methanopyrido[1,2-*b*]pyridazin-4(4a*H*)-yl)methanone (5ac): Prepared from (3,5-dimethyl-1*H*-pyrazol-1-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 50.5 mg, 0.20 mmol) and pyridin-1-ium-1-yl(4-(trifluoromethyl)benzoyl)amide (**2c**, 63.9 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **5ac** as a white solid (51.8 mg, 50% yield).

5ac: $\mathbf{R_f}$ = 0.25 (petroleum ether/EtOAc = 10/1). Mp: 97-99 °C.**^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.38-7.35 (m, 4H), 7.27-7.23 (m, 1H), 6.54 (d, *J* = 7.6 Hz, 1H), 5.94 (s, 1H), 5.73-5.69 (m 1H), 5.47 (d, *J* = 3.2 Hz, 1H), 4.69-4.61 (m, 2H), 3.45 (t, *J* = 10.4 Hz, 1H), 3.26 (d, *J* = 10.4 Hz, 1H), 3.01 (d, *J* = 9.6 Hz, 1H), 2.55 (d, *J* = 11.6 Hz, 1H), 2.51 (s, 3H), 2.21 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 174.3, 171.2, 152.9, 143.9, 141.7, 140.1, 139.6, 132.0 (q, *J* = 32.5 Hz), 128.3, 128.0, 127.1, 125.0 (q, *J* = 3.5 Hz), 124.8, 124.3, 123.8 (q, *J* = 267.6 Hz), 116.3, 111.0, 96.5, 68.1, 65.8, 56.6, 47.8, 40.7, 14.0, 13.9 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.86 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{26}F_3N_4O_2$: 519.2002; found: 519.1992.



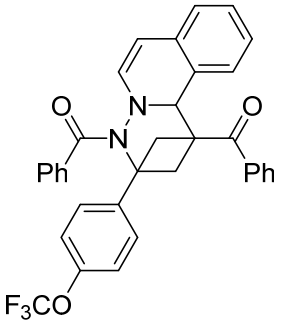
3ga

$C_{33}H_{26}N_2O_2$

M = 482.58 g/mol

(3-phenyl-2,3-dihydro-4*H*-1,3-methanopyridazino[6,1-a]isoquinoline-1,4(11b*H*)-diyl)bis(phenyl methanone) (3ga): Prepared from phenyl(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1g**, 46.9 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ga** as a yellow solid (95.3 mg, 99% yield).

3ga: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 144-146 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 6.8 Hz, 2H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.43-7.31 (m, 8H), 7.28-7.19 (m, 3H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.86 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.53 (t, *J* = 7.6, Hz, 1H), 6.45 (d, *J* = 7.6 Hz, 1H), 5.46 (s, 1H), 5.41 (d, *J* = 8.0 Hz, 1H), 3.87 (dd, *J* = 11.2, 8.8 Hz, 1H), 3.29 (d, *J* = 10.4 Hz, 1H), 3.06 (t, *J* = 10.0 Hz, 1H), 2.44 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 201.2, 175.3, 141.6, 141.0, 136.0, 135.5, 132.7, 130.84, 130.82, 128.7, 128.6, 128.3, 128.2, 128.1, 128.0, 127.9, 127.0, 125.8, 124.7, 124.5, 100.2, 69.7, 68.1, 58.4, 47.4, 43.6 ppm. **HRMS** (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{33}H_{26}N_2O_2K$: 521.1626; found: 521.1631.

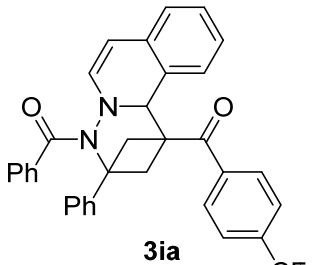


3ha
$C_{34}H_{25}F_3N_2O_3$
M = 566.58 g/mol

(3-(4-(trifluoromethoxy)phenyl)-2,3-dihydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinoline-1,4(11b*H*)-diyl)bis(phenylmethanone) (3ha): Prepared from phenyl(3-(4-(trifluoromethoxy)phenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1h**, 63.7 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ha** as a white solid (91.7 mg, 81% yield).

3ha: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 115-117 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 6.8 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.44-7.35 (m, 6H), 7.28-7.25 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.87 (t, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.54 (td, *J* = 7.4, 1.4 Hz, 1H), 6.45 (d, *J* = 7.6 Hz, 1H), 5.45 (s, 1H), 5.43 (d, *J* = 8.0 Hz, 1H), 3.87 (dd, *J* = 11.2, 8.8 Hz, 1H), 3.24 (d, *J* = 10.4 Hz, 1H), 3.06 (t, *J* = 9.2 Hz, 1H), 2.43 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$):

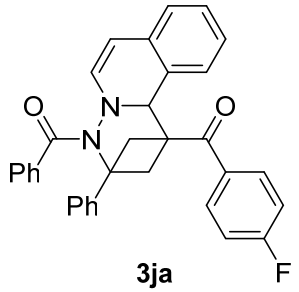
δ 201.0, 175.5, 148.0, 140.8, 140.4, 135.9, 135.1, 132.8, 131.0, 130.7, 128.8, 128.6, 128.2, 128.1, 128.0, 127.9, 126.4, 126.0, 124.6, 120.8, 120.4 (q, *J* = 255.6 Hz), 100.5, 69.7, 67.5, 58.3, 47.5, 43.5 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -57.81 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{26}F_3N_2O_3$: 567.1890; found: 567.1883.



3ia
$C_{34}H_{25}F_3N_2O_2$
M = 550.58 g/mol

(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(4-(trifluoromethyl)phenyl)methanone (3ia): Prepared from (3-phenylbicyclo[1.1.0]butan-1-yl)(4-(trifluoromethyl)phenyl)methanone (**1i**, 60.4 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ia** as a yellow solid (95.1 mg, 86% yield).

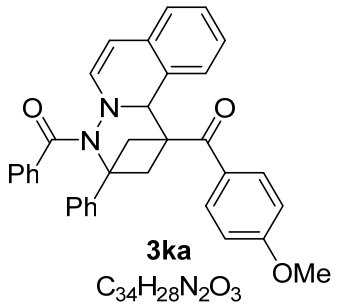
3ia: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 121-123 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.65 (m, *J* = 6.8 Hz, 4H) , 7.49 (d, *J* = 8.0 Hz, 2H), 7.43-7.41 (m, 3H), 7.38-7.32 (m, 4H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.89-6.81 (m, 2H), 6.54 (m, *J* = 7.6 Hz, 1H), 6.45 (d, *J* = 7.6 Hz, 1H), 5.44 (s, 1H), 5.42 (d, *J* = 8.0 Hz, 1H), 3.88 (dd, *J* = 10.8, 9.2 Hz, 1H), 3.28 (d, *J* = 10.4 Hz, 1H), 3.06 (t, *J* = 8.8 Hz, 1H), 2.42 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$):δ: 200.6, 175.3, 141.4, 141.1, 138.6, 135.3, 133.7 (q, *J* = 32.5 Hz), 130.9, 130.8, 128.9, 128.8, 128.3, 128.2, 128.1, 127.9, 127.8, 1271, 126.0, 125.1 (q, *J* = 3.7 Hz), 124.7, 123.4 (q, *J* = 278.4 Hz), 100.1, 69.7, 68.0, 58.4, 47.2, 43.6 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.22 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{34}H_{25}F_3N_2O_2Na$: 573.1760; found: 573.1749.



3ja
$C_{33}H_{25}FN_2O_2$
M = 500.57 g/mol

(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(4-fluorophenyl)methanone (3ja): Prepared from (4-fluorophenyl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1j**, 50.4 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ja** as a yellow solid (90.8 mg, 91% yield).

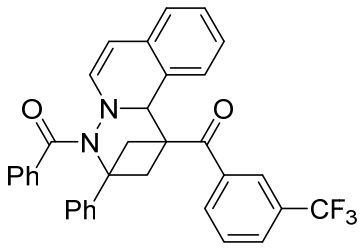
3ja: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 124-127 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69-7.66 (m, 2H), 7.64-7.61 (m, 2H), 7.43-7.32 (m, 7H), 7.22 (t, *J* = 7.2 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.93-6.85 (m, 3H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.53 (t, *J* = 7.6 Hz, 1H), 6.44 (d, *J* = 7.6 Hz, 1H), 5.41 (s, 1H), 5.40 (d, *J* = 7.6 Hz, 1H), 3.86 (dd, *J* = 11.2, 8.8 Hz, 1H), 3.28 (d, *J* = 10.0 Hz, 1H), 3.03 (t, *J* = 9.6 Hz, 1H), 2.44 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 199.7, 175.3, 165.1 (d, *J* = 254.1 Hz), 141.5, 141.1, 135.4, 132.5 (d, *J* = 3.1 Hz), 131.3 (d, *J* = 9.4 Hz), 130.9, 130.8, 128.8, 128.3, 128.2, 128.1, 127.93, 127.90, 127.0, 125.9, 124.7, 124.5, 115.3 (d, *J* = 21.7 Hz), 100.1, 69.7, 68.0, 58.3, 47.3, 43.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -104.83 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{26}FN_2O_2$: 501.1973; found: 501.1965.



3ka
$C_{34}H_{28}N_2O_3$
M = 512.61 g/mol

(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(4-methoxyphenyl)methanone (3ka): Prepared from (4-methoxyphenyl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1k**, 52.9 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ka** as a yellow solid (95.3 mg, 93% yield).

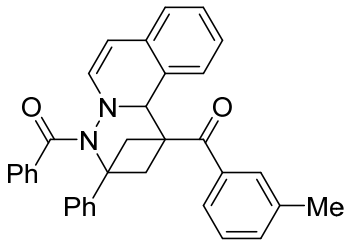
3ka: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 10/1). Mp: 116-118 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.4 Hz, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.43-7.31 (m, 7H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.87 (t, *J* = 7.6 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.54 (t, *J* = 7.6 Hz, 1H), 6.44 (d, *J* = 8.0 Hz, 1H), 5.42 (s, 1H), 5.39 (d, *J* = 8.0 Hz, 1H), 3.85 (t, *J* = 10.0 Hz, 1H), 3.78 (s, 3H), 3.29 (d, *J* = 10.4 Hz, 1H), 3.04 (t, *J* = 9.6 Hz, 1H), 2.44 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.3, 163.0, 141.7, 141.0, 135.5, 131.0, 130.8, 129.3, 128.6, 128.24, 128.17, 128.1, 128.0, 127.9, 126.9, 125.7, 124.7, 124.4, 113.4, 100.2, 69.7, 68.1, 58.2, 55.4, 47.4, 43.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{34}H_{29}N_2O_3$: 513.2173; found: 513.2177.



3la
$C_{34}H_{25}F_3N_2O_2$
M = 550.58 g/mol

(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(3-(trifluoromethyl)phenyl)methanone (3la): Prepared from (3-phenylbicyclo[1.1.0]butan-1-yl)(3-(trifluoromethyl)phenyl)methanone (**1l**, 60.5 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3la** as a yellow solid (89.5 mg, 81% yield).

3la: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 106-108 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79-7.78 (m, 2H), 7.68 (d, *J* = 7.2 Hz, 2H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.44-7.32 (m, 8H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.84-6.81 (m, 2H), 6.52-6.46 (m, 2H), 5.45 (d, *J* = 8.0 Hz, 1H), 5.40 (s, 1H), 3.92 (dd, *J* = 10.8, 8.8 Hz, 1H), 3.29 (d, *J* = 10.4 Hz, 1H), 3.04 (t, *J* = 9.6 Hz, 1H), 2.45 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 200.3, 175.4, 141.4, 141.3, 136.4, 135.4, 131.4, 130.91, 130.86, 130.5 (q, *J* = 32.7 Hz), 128.9 (q, *J* = 3.5 Hz), 128.84, 128.76, 128.3, 128.2, 127.99, 127.95, 127.8, 127.1, 126.0, 125.6 (q, *J* = 4.0 Hz), 124.9, 124.7, 123.4 (q, *J* = 270.9 Hz), 100.2, 69.8, 68.1, 58.3, 47.1, 43.9 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.94 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{34}H_{26}F_3N_2O_2Na$: 573.1760; found: 573.1749.

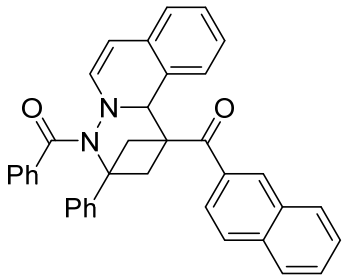


3ma
$C_{34}H_{28}N_2O_2$
M = 496.61 g/mol

(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(m-tolyl)methanone (3ma): Prepared from (3-phenylbicyclo[1.1.0]butan-1-yl)(*m*-tolyl)methanone (**1m**, 49.5 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ma** as a yellow solid (69.6 mg, 70% yield).

3ma: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 104-106 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.2 Hz, 2H), 7.42-7.31 (m, 9H), 7.23-7.19 (m, 2H), 7.14 (*t*, J = 7.6 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.86 (*t*, J = 7.6 Hz, 1H), 6.81 (*d*, J = 7.2 Hz, 1H), 6.54 (*t*, J = 7.6 Hz, 1H), 6.46 (d, *J* = 7.6 Hz, 1H), 5.44 (s, 1H), 5.41 (d, *J* = 7.6 Hz, 1H), 3.86 (dd, *J* = 10.8, 8.8 Hz, 1H), 3.28 (d, *J* = 10.4 Hz, 1H), 3.04 (t, *J* = 9.6 Hz, 1H), 2.42

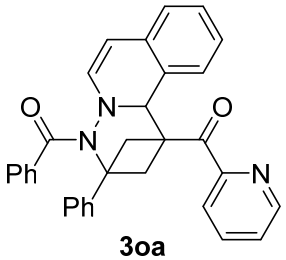
(d, *J* = 11.2 Hz, 1H), 2.26 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 201.5, 175.3, 141.6, 141.1, 137.9, 136.0, 135.5, 133.5, 130.9, 130.8, 129.3, 128.6, 128.25, 128.19, 128.14, 128.08, 128.0, 127.9, 127.0, 125.9, 125.8, 124.7, 124.4, 100.2, 69.8, 68.1, 58.5, 47.4, 43.8, 21.2 ppm. **HRMS** (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{34}H_{28}N_2O_2K$: 535.1783; found: 535.1767.



3na
$C_{37}H_{28}N_2O_2$
M = 532.64 g/mol

(1-(2-naphthoyl)-3-phenyl-1,2,3,11*b*-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(phenyl)methanone (3na): Prepared from naphthalen-2-yl(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1n**, 56.9 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3na** as a yellow solid (101.1 mg, 95% yield).

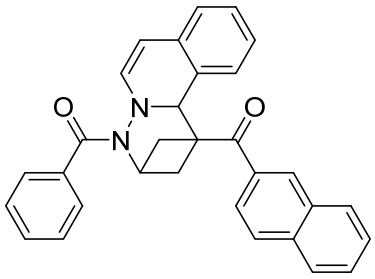
3na: **R_f** = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 108-110 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.78-7.76 (m, 2H), 7.72-7.70 (m, 4H), 7.55-7.48 (m, 2H), 7.44-7.31 (m, 7H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.79-6.72 (m, 2H), 6.46-6.42 (m, 2H), 5.52 (s, 1H), 5.47 (d, *J* = 7.6 Hz, 1H), 3.98 (t, *J* = 10.0 Hz, 1H), 3.36 (d, *J* = 10.4 Hz, 1H), 3.13 (t, *J* = 9.6 Hz, 1H), 2.49 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 201.1, 175.3, 141.6, 141.2, 135.5, 135.1, 133.4, 132.1, 130.9, 130.84, 130.79, 129.6, 128.7, 128.5, 128.3, 128.2, 128.12, 128.06, 128.0, 127.9, 127.6, 127.0, 126.6, 125.9, 124.7, 124.5, 124.0, 100.2, 69.9, 68.2, 58.6, 47.5, 43.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{37}H_{29}N_2O_2$: 533.2224; found: 533.2212.



3oa
$C_{32}H_{25}N_3O_2$
M = 483.57 g/mol

(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(pyridin-2-yl)methanone (3oa): Prepared from (3-phenylbicyclo[1.1.0]butan-1-yl)(pyridin-2-yl)methanone (**1o**, 47.6 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP2** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3oa** as a yellow solid (51.6 mg, 53% yield).

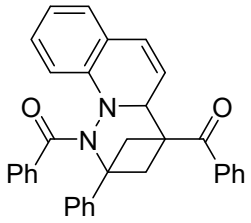
3oa: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 123-125 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.71 (d, *J* = 4.8 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.80-7.72 (m, 3H), 7.46-7.31 (m, 8H), 7.21 (t, *J* = 7.2 Hz, 1H), 6.91-6,87 (m, 2H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.48 (t, *J* = 7.6 Hz, 1H), 6.15 (d, *J* = 7.6 Hz, 1H), 5.88 (s, 1H), 5.33 (d, *J* = 7.6 Hz, 1H), 3.82 (dd, *J* = 11.2, 8.0 Hz, 1H), 3.27-3.18 (m, 2H), 2.37 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 200.3, 175.0, 153.1, 149.0, 142.1, 140.8, 136.8, 135.7, 131.2, 130.7, 128.7, 128.4, 128.3, 128.2, 127.8, 126.9, 126.8, 125.3, 124.8, 124.6, 122.8, 100.5, 69.1, 68.8, 59.0, 48.1, 42.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{26}N_3O_2$: 484.2020; found: 484.2012.



3pa
$C_{31}H_{24}N_2O_2$
M = 456.55 g/mol

(1-(2-naphthoyl)-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl) (phenyl)methanone (3pa) : Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1p**, 41.7 mg, 0.2 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) at room temperature for 16 h according to the **GP2**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3pa** as a yellow solid (32.0 mg, 35% yield)

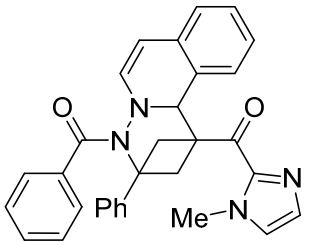
3pa: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 5/1). Mp: 207-209 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.78-7.67 (m, 6H), 7.55-7.46 (m, 2H), 7.42-7.37 (m, 3H), 6.76-6.70 (m, 2H), 6.56 (d, *J* = 7.6 Hz, 1H), 6.50-6.42 (m, 2H), 5.62 (s, 1H), 5.37 (d, *J* = 7.6 Hz, 1H), 4.94 (s, 1H), 3.50 (t, *J* = 9.2 Hz, 1H), 2.82 (dd, *J* = 10.0, 4.0 Hz, 1H), 2.72 (dd, *J* = 11.2, 4.8 Hz, 1H), 2.55 (t, *J* = 9.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 201.3, 172.4, 141.2, 135.0, 134.9, 133.3, 132.1, 130.8, 130.5, 129.5, 128.7, 128.5, 128.1, 128.02, 127.98, 127.9, 127.6, 126.6, 125.8, 124.5, 124.0, 100.4, 70.1, 61.6, 54.1, 48.1, 35.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{25}N_2O_2$: 457.1911; found: 457.1903.



4gb
$C_{33}H_{26}N_2O_2$
M = 482.58 g/mol

(2-phenyl-2,3-dihydro-1*H*-2,4-methanopyridazino[1,6-*a*]quinoline-1,4(4a*H*)-diyl)bis(phenyl methanone) (4gb) : Prepared from phenyl(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1g**, 46.9 mg, 0.2 mmol) and benzoyl(quinolin-1-ium-1-yl)amide (**2b**, 59.6 mg, 0.24 mmol) at room temperature for 16 h according to the **GP2**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **4gb** as a yellow solid (92.0 mg, 95% yield)

4gb: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 268-270 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.6 Hz, 2H), 7.77 (d, *J* = 7.6 Hz, 2H), 7.58-7.55 (m, 1H), 7.48-7.44 (m, 4H), 7.40-7.32 (m, 5H), 7.29-7.23 (m, 3H), 6.91 (d, *J* = 7.2 Hz, 1H), 6.83 (t, *J* = 6.8 Hz, 1H), 6.24 (d, *J* = 10.4 Hz, 1H), 5.30 (s, 1H), 5.05-5.03 (m, 1H), 3.26 (d, *J* = 9.6 Hz, 1H), 3.15-3.05 (m, 2H), 2.43 (d, *J* = 10.8 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 199.0, 175.8, 146.1, 141.8, 135.6, 134.9, 133.5, 131.0, 130.2, 128.9, 128.6, 128.12, 128.09, 127.9, 127.6, 127.4, 127.0, 125.9, 120.5, 119.5, 111.8, 68.4, 66.9, 59.6, 47.9, 40.3 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{27}N_2O_2$: 483.2067; found: 483.2066.



3qa
$C_{31}H_{26}N_4O_2$
M = 486.58 g/mol

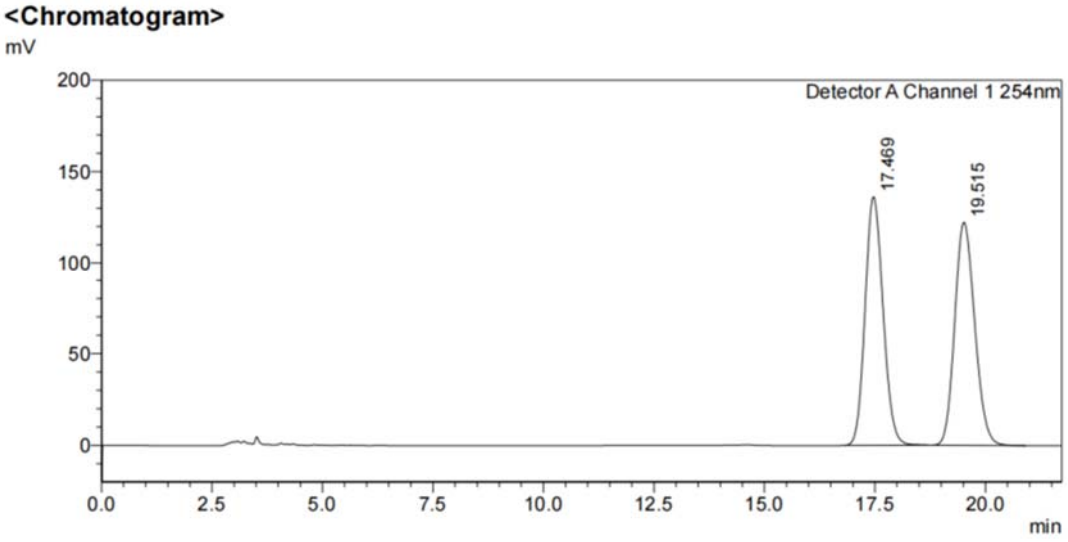
(4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qa): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qa** as a white solid (85.5 mg, 91% yield).

(*R*)-3qa: Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP4** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **(*R*)-3qa** as a white solid (77.7 mg, 80% yield).

3qa: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 257-259 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 6.0 Hz, 2H), 7.44 (d, *J* = 7.2 Hz, 2H), 7.37-7.32 (m, 5H), 7.23-

7.18 (m, 2H), 6.97 (s, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 7.2 Hz, 1H), 6.56 (t, *J* = 7.2 Hz, 1H), 5.88 (d, *J* = 7.6 Hz, 1H), 5.67 (s, 1H), 5.30 (d, *J* = 7.6 Hz, 1H), 3.76-3.71 (m, 1H), 3.71 (s, 3H), 3.38-3.28 (m, 2H), 2.40 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.9, 174.8, 142.7, 142.2, 141.0, 135.6, 131.3, 130.6, 129.8, 128.43, 128.38, 128.3, 128.1, 127.7, 126.7, 126.53, 126.46, 124.83, 124.82, 124.6, 100.5, 69.0, 68.6, 58.9, 48.3, 41.4, 35.6 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{27}N_4O_2$: 487.2129; found: 487.2126.

HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 17.28 min, tr (minor) = 19.41 min gave the isomeric composition of the product: 88% *ee*. $[\alpha]_D^{20}$ = -86.8 (*c* = 1.00, $CHCl_3$).



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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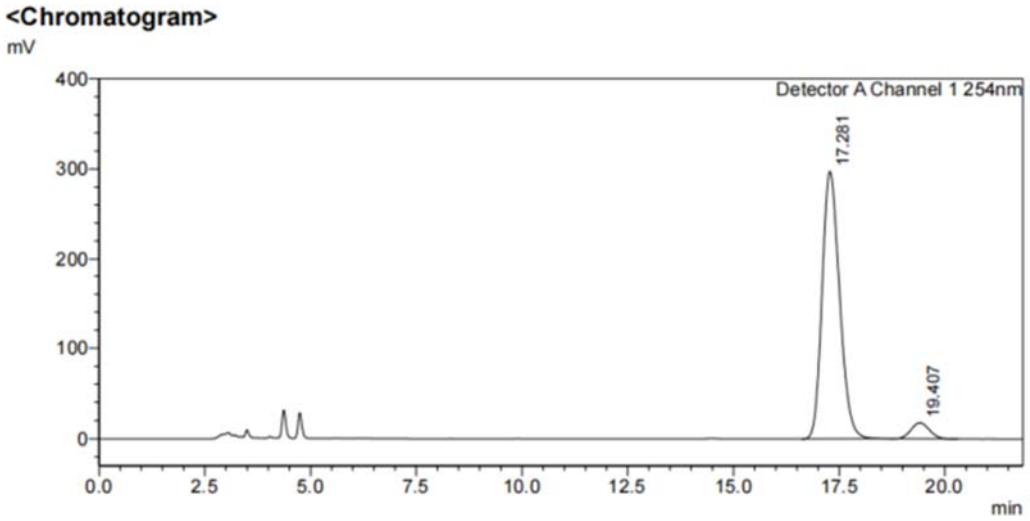
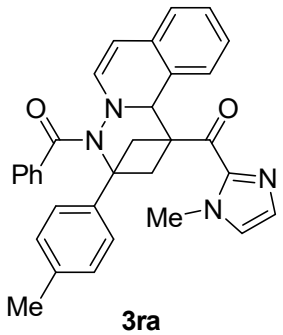
2	19.515	18.800	3839793	122279	49.929
Total			7690557	258443	100.000



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	17.281	16.617	8542135	297177	94.033
2	19.407	18.800	542071	17741	5.967
Total			9084206	314918	100.000



3ra

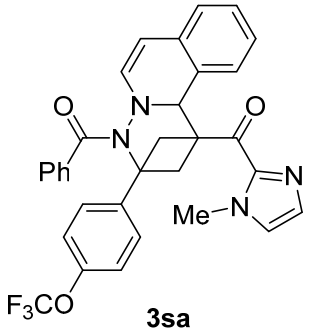
$C_{32}H_{28}N_4O_2$

M = 500.60 g/mol

(4-benzoyl-3-(p-tolyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ra): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-(*p*-tolyl)bicyclo[1.1.0]butan-1-yl)methanone (**1r**, 50.5 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**1a**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3ra** as a yellow solid (98.1 mg, 98% yield).

3ra: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 3/1). Mp: 147-149 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.39-7.32 (m, 5H), 7.25 (s, 1H), 7.19 (s, 1H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.98 (s, 1H), 6.93 (t, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.77

(d, *J* = 7.2 Hz, 1H), 6.56 (t, *J* = 8.4 Hz, 1H), 5.87 (d, *J* = 7.6 Hz, 1H), 5.65 (s, 1H), 5.30 (d, *J* = 7.6 Hz, 1H), 3.73 (s, 3H), 3.73-3.69 (m, 1H), 3.35-3.27 (m, 2H), 2.38 (d, *J* = 11.2 Hz, 1H), 2.31 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.0, 174.9, 142.8, 141.1, 139.4, 136.3, 135.8, 131.3, 130.5, 129.8, 128.9, 128.4, 128.3, 127.7, 126.50, 126.48, 124.82, 124.78, 124.6, 100.5, 69.0, 68.5, 58.9, 48.4, 41.4, 35.7, 21.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{29}N_4O_2$: 501.2285; found: 501.2277.

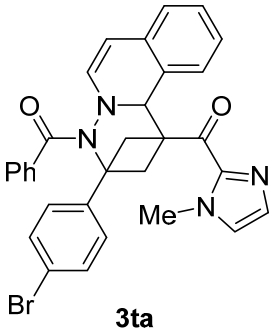


3sa
$C_{32}H_{25}F_3N_4O_3$
M = 570.57 g/mol

(4-benzoyl-3-(4-(trifluoromethoxy)phenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*] isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3sa): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-(4-(trifluoromethoxy)phenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1s**, 64.5 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3sa** as a yellow solid (111.8 mg, 98% yield).

3sa: **R_f** = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 214-216 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.2 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.39-7.32 (m, 3H), 7.19-7.17 (m, 3H), 6.99 (s, 1H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.57 (t, *J* = 7.6 Hz, 1H), 5.88 (d, *J* = 7.6 Hz, 1H), 5.65 (s, 1H), 5.32 (d, *J* = 7.6 Hz, 1H), 3.76-3.73 (m, 1H), 3.73 (s, 3H), 3.32-3.28 (m, 2H), 2.39 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.6, 175.1, 147.8, 142.6, 141.0, 140.8, 135.3, 131.2, 130.8, 129.8, 128.5, 128.3, 128.2, 127.8, 126.6, 126.5, 126.4, 125.0, 124.7, 120.6, 120.4 (q, *J* = 255.5 Hz), 100.8, 69.0, 68.0, 58.8, 48.3, 41.2, 35.6 ppm.

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.72 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{25}F_3N_4O_3Na$: 593.1771; found: 593.1761.



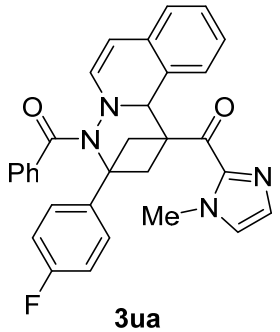
3ta

$C_{31}H_{25}BrN_4O_2$

M = 565.47 g/mol

(4-benzoyl-3-(3-bromophenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ta): Prepared from (3-(4-bromophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1t**, 63.4 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3ta** as a white solid (74.3 mg, 66% yield).

3ta: **R_f** = 0.35 (petroleum ether/EtOAc = 3/1). Mp: 232-234 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 6.8 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.38-7.33 (m, 5H), 7.19 (s, 1H), 6.98 (s, 1H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.57 (t, *J* = 7.6 Hz, 1H), 5.88 (d, *J* = 7.6 Hz, 1H), 5.65 (s, 1H), 5.31 (d, *J* = 7.6 Hz, 1H), 3.73 (s, 3H), 3.73-3.70 (m, 1H), 3.32-3.26 (m, 2H), 2.36 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.6, 175.0, 142.6, 141.3, 140.8, 135.3, 131.3, 131.2, 130.7, 129.8, 128.5, 128.28, 128.25, 127.8, 126.7, 126.6, 126.5, 124.9, 124.7, 120.6, 100.8, 69.0, 68.1, 58.8, 48.2, 41.2, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{26}BrN_4O_2$: 565.1234; found: 565.1225.



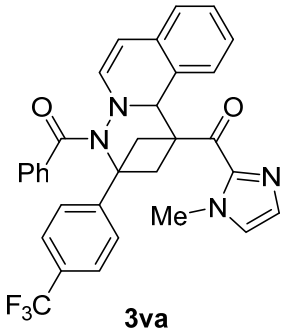
3ua

$C_{31}H_{25}FN_4O_2$

M = 504.57 g/mol

(4-benzoyl-3-(4-fluorophenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ua): Prepared from (3-(4-fluorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1u**, 51.3 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3ua** as a yellow solid (100.0 mg, 99% yield).

3ua: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 240-242 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.2 Hz, 2H), 7.41-7.32 (m, 5H), 7.25 (s, 1H), 7.19 (s, 1H), 7.04-6.99 (m, 3H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.57 (t, *J* = 7.6 Hz, 1H), 5.88 (d, *J* = 7.6 Hz, 1H), 5.65 (s, 1H), 5.31 (d, *J* = 8.0 Hz, 1H), 3.77-3.71 (m, 1H), 3.73 (s, 3H), 3.35-3.31 (m, 2H), 2.37 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.7, 175.1, 161.6 (d, *J* = 243.7 Hz), 142.7, 140.9, 138.2 (d, *J* = 3.2 Hz), 135.5, 131.2, 130.7, 129.8, 128.5, 128.31, 128.27, 127.8, 126.7 (d, *J* = 8.1 Hz), 126.6, 126.5, 124.9, 124.7, 114.9 (d, *J* = 21.4 Hz), 100.7, 69.0, 68.1, 58.9, 48.4, 41.3, 35.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.99 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{26}FN_4O_2$: 505.2034; found: 505.2039.



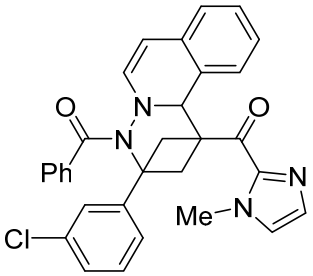
3va

$C_{32}H_{25}F_3N_4O_2$

M = 554.57 g/mol

(4-benzoyl-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3va): Prepared from ((1-methyl-1*H*-imidazol-2-yl)(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1v**, 61.3 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on Isilica gel using petroleum ether/EtOAc (3/1) afforded **3va** as a yellow solid (93.6 mg, 84% yield).

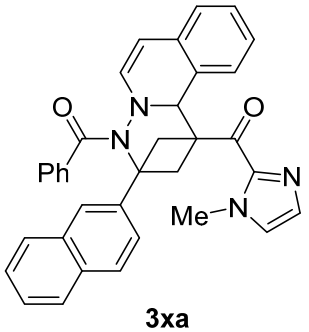
3va: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 257-259 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.42-7.33 (m, 3H), 7.20 (s, 1H), 7.01 (s, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.59 (t, *J* = 7.6 Hz, 1H), 5.89 (d, *J* = 8.0 Hz, 1H), 5.67 (s, 1H), 5.34 (d, *J* = 7.6 Hz, 1H), 3.78-3.73 (m, 1H), 3.75 (s, 3H), 3.39-3.28 (m, 2H), 2.39 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.5, 175.0, 146.1, 142.7, 140.8, 135.1, 131.2, 130.9, 129.9, 129.2 (q, *J* = 32.0 Hz), 128.6, 128.4, 128.2, 127.9, 126.7, 126.5, 125.3 (q, *J* = 3.3 Hz), 125.2, 125.0, 124.8, 124.2 (q, *J* = 270.2 Hz), 101.0, 69.1, 68.2, 58.8, 48.3, 41.2, 35.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.39 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{25}F_3N_4O_2Na$: 577.1822; found: 577.1825.



3wa
$C_{31}H_{25}ClN_4O_2$
M = 521.02 g/mol

(4-benzoyl-3-(3-chlorophenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3wa): Prepared from (3-(3-chlorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1w**, 54.6 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3wa** as a white solid (66.7 mg, 64% yield).

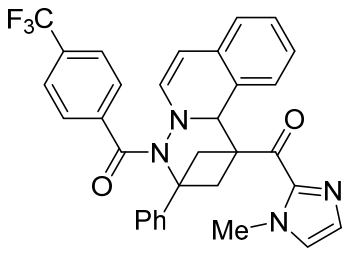
3wa: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 171-173 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 6.4 Hz, 2H), 7.39-7.25 (m, 7H), 7.19-7.18 (m, 2H), 7.00 (s, 1H), 6.95 (t, *J* = 7.4 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 6.8 Hz, 1H), 6.57 (t, *J* = 7.6 Hz, 1H), 5.89 (d, *J* = 7.6 Hz, 1H), 5.65 (s, 1H), 5.32 (d, *J* = 7.6 Hz, 1H), 3.74 (s, 3H), 3.72-3.69 (m, 1H), 3.34-3.25 (m, 2H), 2.38 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.6, 175.0, 144.3, 142.7, 140.9, 135.3, 134.1, 131.2, 130.8, 129.9, 129.5, 128.5, 128.4, 128.3, 127.8, 126.9, 126.6, 126.5, 125.2, 125.0, 124.7, 123.1, 100.8, 69.0, 68.1, 58.8, 48.3, 41.3, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{26}ClN_4O_2$: 521.1739; found: 521.1730.



3xa
$C_{35}H_{28}N_4O_2$
M = 536.64 g/mol

(4-benzoyl-3-(naphthalen-2-yl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3xa): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-(naphthalen-2-yl)bicyclo[1.1.0]butan-1-yl)methanone (**1x**, 57.7 mg, 0.20 mmol) and benzoyl(isoquinolin-2-ium-2-yl)amide (**2a**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3xa** as a yellow solid (106.0 mg, 99% yield).

3xa: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 173-175 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.85-7.78 (m, 4H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.45-7.31 (m, 5H), 7.24 (s, 1H), 7.20 (s, 1H), 6.98-6.93 (m, 3H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.58 (t, *J* = 7.6 Hz, 1H), 5.91 (d, *J* = 7.6 Hz, 1H), 5.72 (s, 1H), 5.35 (d, *J* = 7.6 Hz, 1H), 3.82 (t, *J* = 11.2 Hz, 1H), 3.73 (s, 3H), 3.50 (d, *J* = 10.4 Hz, 1H), 3.40 (t, *J* = 10.0 Hz, 1H), 2.45 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.9, 174.9, 142.8, 141.1, 139.7, 135.6, 133.2, 132.4, 131.3, 130.6, 129.8, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.6, 126.6, 126.5, 125.9, 125.6, 124.9, 124.7, 123.6, 123.3, 100.6, 69.1, 68.7, 58.9, 48.4, 41.5, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{35}H_{29}N_4O_2$: 537.2285; found: 537.2276.



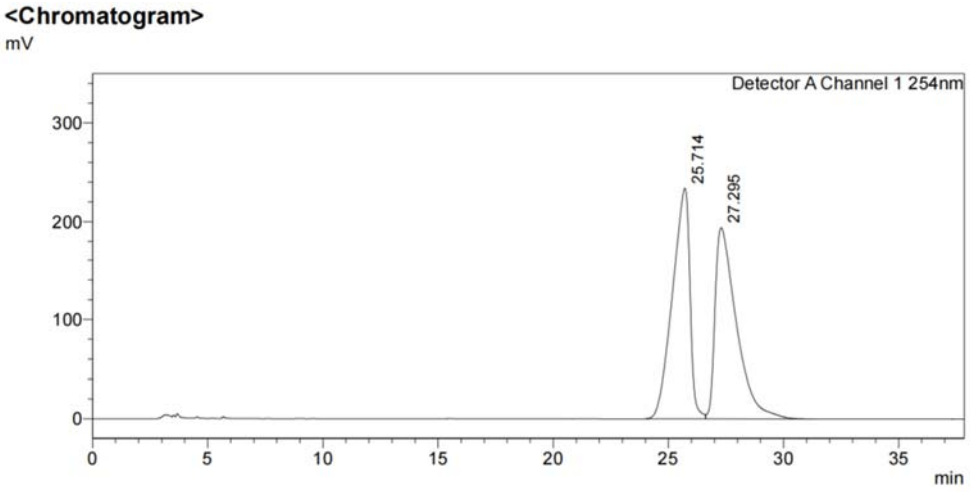
3qd
$C_{32}H_{25}F_3N_4O_2$
M = 554.57 g/mol

(1-methyl-1*H*-imidazol-2-yl)(3-phenyl-4-(4-(trifluoromethyl)benzoyl)-3,4-dihydro-2*H*-1,3-methano pyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone (3qd): Prepared from (1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.6 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qd** as a white solid (95.4 mg, 86% yield).

(*R*)-3qd: Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.6 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.8 mg, 0.24 mmol) according to the **GP4** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **(*R*)-3qd** as a yellow solid (80.9 mg, 73% yield).

3qd: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 123-125 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.25-7.20 (m, 2H), 7.01 (s, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.83-6.78 (m, 2H), 6.59 (t, *J* = 7.6 Hz, 1H), 5.89 (d, *J* = 7.6 Hz, 1H), 5.64 (s, 1H), 5.34 (d, *J* = 8.0 Hz, 1H), 3.77-3.72 (m, 1H), 3.74 (s, 3H), 3.37 (d, *J* = 10.4 Hz, 1H), 3.29 (t, *J* = 9.2 Hz, 1H), 2.42 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.6, 173.7, 142.7, 141.8, 140.4, 139.3, 132.1 (q, *J* = 32.4 Hz), 131.0, 129.9, 128.6, 128.4, 128.2, 127.0, 126.6, 126.5, 125.1, 124.90 (q, *J* = 3.7 Hz), 124.89, 124.8, 123.7(q, *J* = 270.9 Hz), 101.3, 69.1, 68.8, 58.8, 48.3, 41.2, 35.7 ppm.**^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.87 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{26}F_3N_4O_2$: 555.2002; found: 555.1993.

(*R*)-3qd: R_f = 0.36 (petroleum ether/EtOAc = 3/1). Mp: 120-122 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 24.62 min, tr (minor) = 26.57 min) gave the isomeric composition of the product: 92% *ee*. $[\alpha]_D^{20}$ = -133.6 (*c* = 1.10, $CHCl_3$).



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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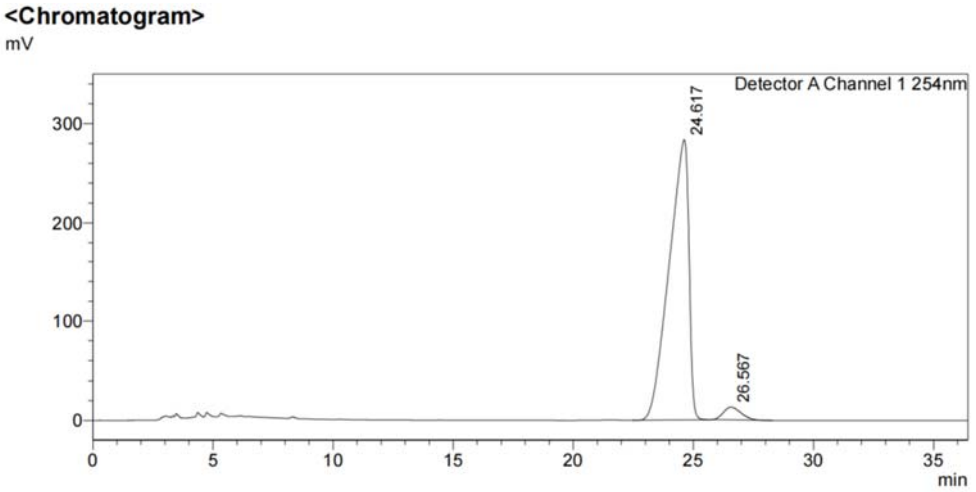
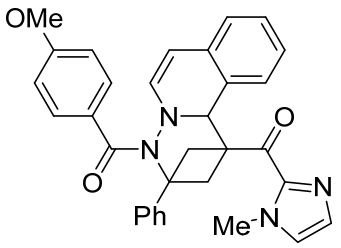
2	27.295	26.617	12507349	194259	50.315
Total			24858209	428458	100.000



Peak#	Ret. Time	Area	Peak Start	Height	Area%
1	24.617	16178025	22.458	283562	96.073
2	26.567	661205	25.783	12899	3.927
Total		16839229		296460	100.000



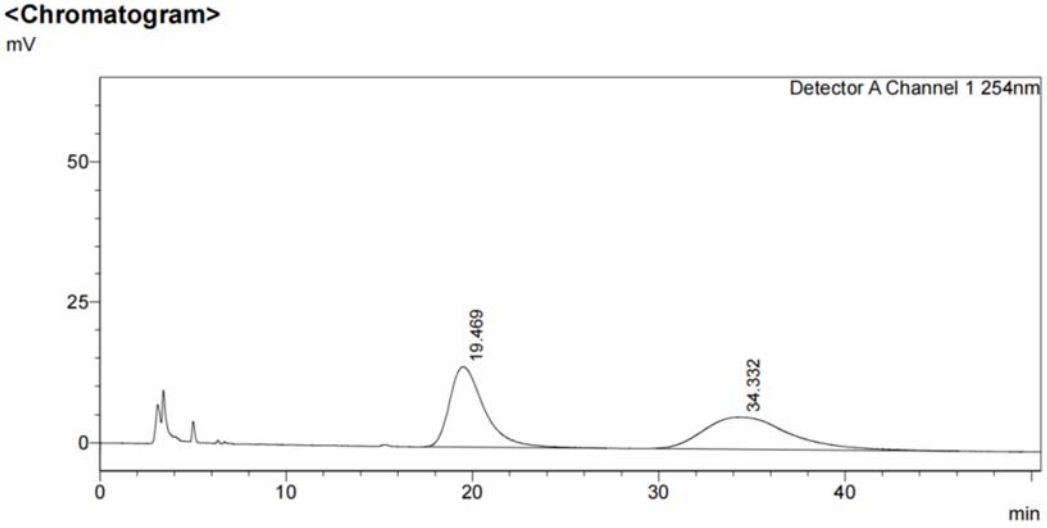
3qe
$C_{32}H_{28}N_4O_3$
M = 516.60 g/mol

(4-(4-methoxybenzoyl)-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qe): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-methoxybenzoyl)amide (**2e**, 66.8 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qe** as a yellow solid (102.3 mg, 99% yield).

(*R*)-3qe: Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-methoxybenzoyl)amide (**2e**, 66.8 mg, 0.24 mmol) according to the **GP4** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **(*R*)-3qe** as a yellow solid (80.3 mg, 78% yield).

3qe: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 3/1). Mp: 167-169 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 6.8 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.25 (s, 1H), 7.22-7.19 (m, 2H), 6.99 (s, 1H), 6.97-6.91 (m, 2H), 6.84-6.79 (m, 3H), 6.57 (t, *J* = 7.6 Hz, 1H), 5.88 (d, *J* = 7.6 Hz, 1H), 5.67 (s, 1H), 5.34 (d, *J* = 7.6 Hz, 1H), 3.78 (s, 3H), 3.75-7.70 (m, 4H), 3.37-3.27 (m, 2H), 2.39 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.0, 173.9, 161.6, 142.8, 142.5, 141.3, 131.4, 131.0, 129.8, 128.50, 128.45, 128.1, 127.4, 126.7, 126.5, 126.5, 124.9, 124.8, 124.6, 113.0, 100.5, 69.0, 68.7, 59.0, 55.2, 48.3, 41.5, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{29}N_4O_3$: 517.2234; found: 517.2227.

HPLC analysis (Chiralpak AS-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 19.91 min, tr (minor) = 35.23 min gave the isomeric composition of the product: 6% *ee*. $[\alpha]_D^{20}$ = -50.4 (*c* = 1.00, $CHCl_3$).



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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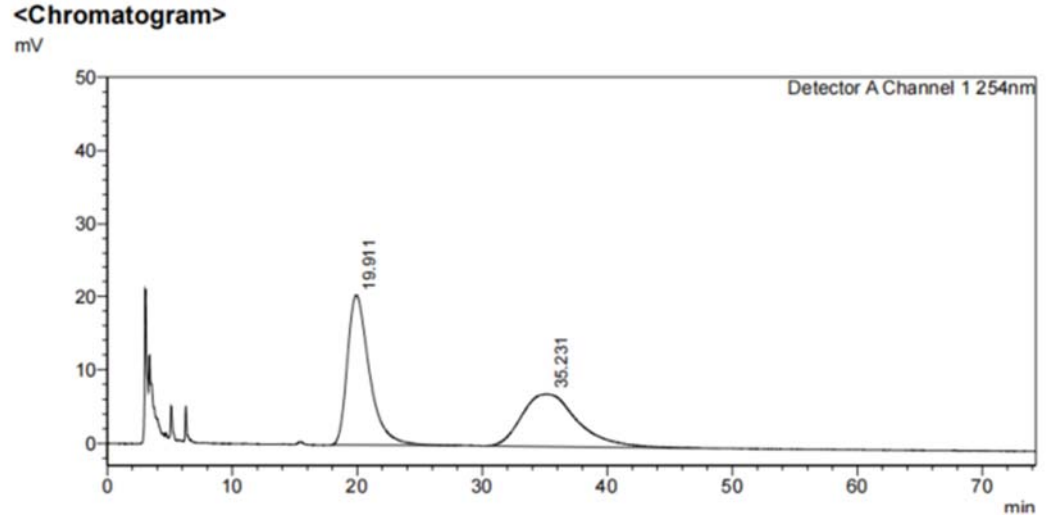
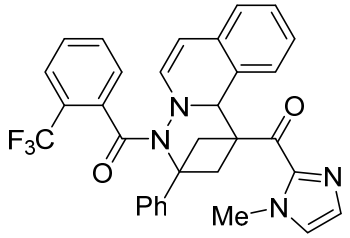
2	34.332	29.858	1823997	5693	49.817
Total			3661381	19878	100.000



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	19.911	17.950	2494200	20344	53.001
2	35.231	30.350	2211725	7148	46.999
Total			4705924	27491	100.000



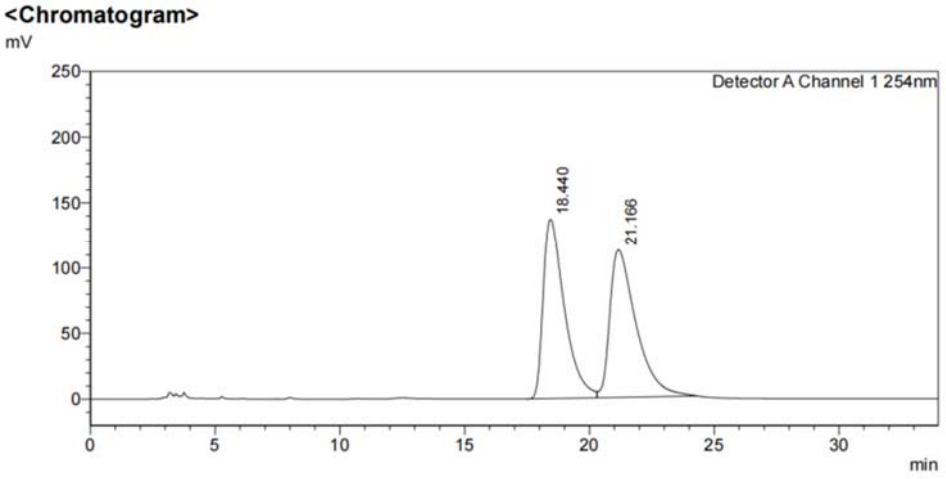
3qf
$C_{32}H_{25}F_3N_4O_2$
M = 554.57 g/mol

(1-methyl-1*H*-imidazol-2-yl)(3-phenyl-4-(2-(trifluoromethyl)benzoyl)-3,4-dihydro-2*H*-1,3-methano pyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone (3qf): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(2-(trifluoromethyl)benzoyl)amide (**2f**, 75.9 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qf** as a white solid (109.8 mg, 99% yield).

(*R*)-3qf: Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(2-(trifluoromethyl)benzoyl)amide (**2f**, 75.9 mg, 0.24 mmol) according to the **GP4** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **(*R*)-3qf** as a white solid (100.2 mg, 90% yield).

3qf: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 295-297 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.6 Hz, 1H), 7.54-7.47 (m, 2H), 7.44-7.40 (m, 3H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.22 (d, *J* = 13.2 Hz, 2H), 6.98 (s, 1H), 6.91 (t, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 7.6 Hz, 1H), 6.63 (d, *J* = 8 Hz, 1H), 6.59 (t, *J* = 7.6 Hz, 1H), 5.97 (d, *J* = 7.6 Hz, 1H), 5.83 (s, 1H), 5.17 (d, *J* = 7.6 Hz, 1H), 3.74 (s, 3H), 3.72-3.70 (m, 1H), 3.37-3.34 (m, 2H), 2.42 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.8, 172.3, 142.7, 141.5, 140.2, 135.9 (q, *J* = 2.5 Hz), 131.3, 131.1, 130.0, 129.0, 128.5, 128.4, 128.2, 126.9, 126.7 (q, *J* = 4.7 Hz), 126.53, 126.52, 124.9, 124.8, 124.6, 124.0 (q, *J* = 272.3 Hz), 101.1, 68.2, 68.0, 58.5, 47.5, 41.5, 35.6 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -57.72 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{26}F_3N_4O_2$: 555.2002; found: 555.1996.

HPLC analysis (Chiralpak OD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 17.98 min, tr (minor) = 20.94 min gave the isomeric composition of the product: 76% *ee*. $[\alpha]_D^{20}$ = -71.4 (*c* = 1.00, $CHCl_3$).



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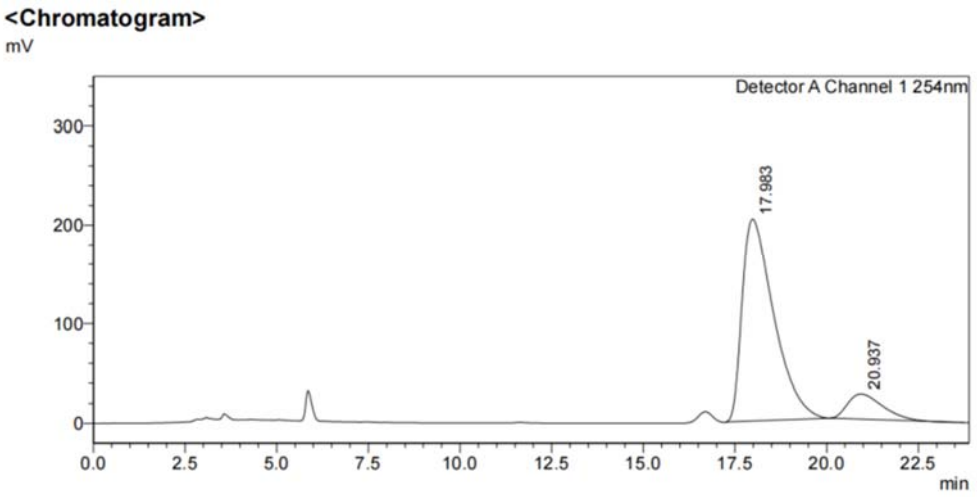
Total			16341136	249364	100.000



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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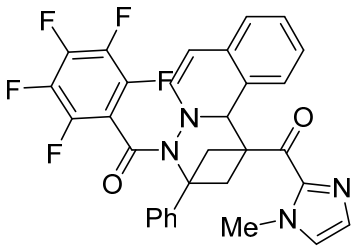
2	20.937	20.125	1694272	25334	12.170
Total			13921288	229152	100.000



3qg
$C_{31}H_{21}F_5N_4O_2$
M = 576.53 g/mol

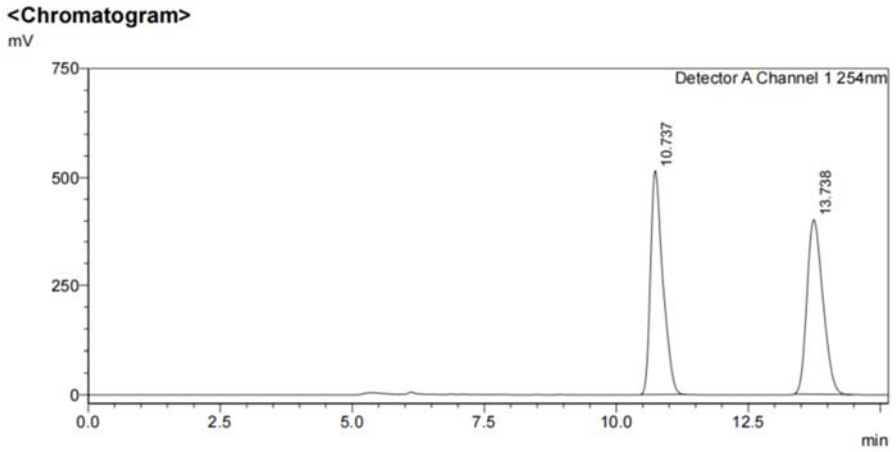
(1-methyl-1*H*-imidazol-2-yl)(4-(perfluorobenzoyl)-3-phenyl-3,4-dihydro-2*H*-1,3-methano pyridazino [6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone (3qg): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(perfluorobenzoyl)amide (**2g**, 81.2 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum CH_2Cl_2 afforded **3qg** as a white solid (49.6 mg, 43% yield).

(*R*)-3qg: Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(perfluorobenzoyl)amide (**2g**, 81.2 mg, 0.24 mmol) according to the **GP4** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum CH_2Cl_2 afforded **(*R*)-3qg** as a white solid (37.5 mg, 33% yield).

3qg: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 3/1). Mp: 231-233 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41-7.36 (m, 4H), 7.29-7.26 (m, 1H), 7.21 (s, 1H), 7.02 (s, 1H), 6.98 (t, *J* = 8.4 Hz, 1H), 6.78 (d, *J* = 76 Hz, 1H), 6.65 (t, *J* = 7.6 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 6.50 (d, *J* = 7.6 Hz, 1H), 5.82 (s, 1H), 5.27 (d, *J* = 8.0 Hz, 1H), 3.77 (s, 3H), 3.75 (t, *J* = 11.2 Hz, 1H), 3.38 (d, *J* = 10.4 Hz, 1H), 3.26 (t, *J* = 9.2 Hz, 1H), 2.44 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 190.3, 162.5, 144.6-144.4 (m), 143.1-142.78 (m), 142.6, 141.5-141.2 (m), 140.5, 139.1, 138.6-138.0 (m), 136.9-136.3 (m), 130.8, 130.1, 128.8, 128.4, 128.1, 127.3, 126.7, 126.7, 125.3, 124.94, 124.7, 113.1 (t, *J* = 23.7 Hz), 102.2, 76.8, 69.3, 69.0, 58.4, 48.7, 41.4, 35.6 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -141.48 (d, *J* = 22.2 Hz), -142.50 (d, *J* = 21.4 Hz), -152.82 (t, *J* = 20.7 Hz), -

159.88 (td, *J* = 22.2, 7.90 Hz), -160.96 (td, *J* = 22.6, 7.90 Hz) ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{22}F_5N_4O_2$: 577.1657 found: 577.1652.

HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 10.93 min, tr (minor) = 13.94 min gave the isomeric composition of the product: 54% *ee*. $[\alpha]_D^{20}$ = -31.0 (*c* =0.05, $CHCl_3$).



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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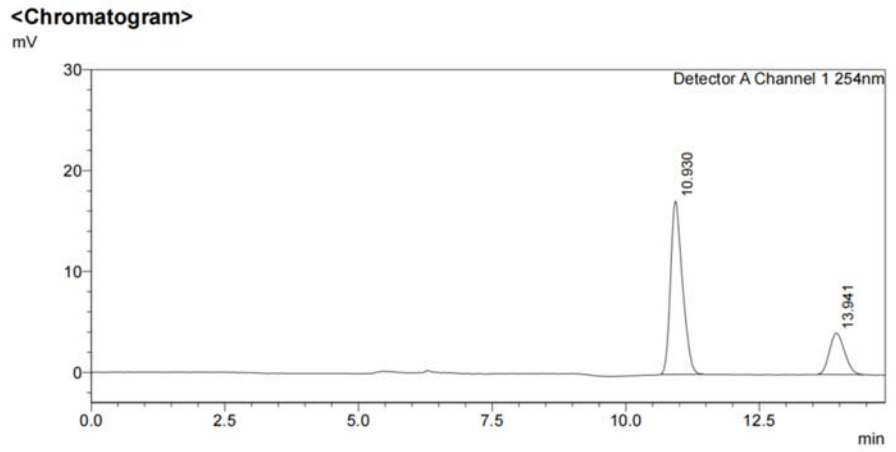
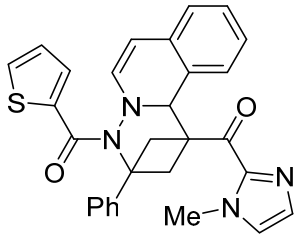
2	13.738	13.375	8367490	401547	49.939
Total			16755554	916499	100.000



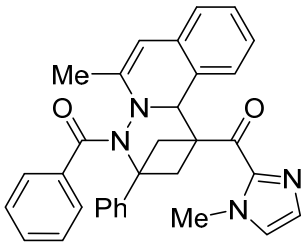
Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	10.930	10.650	266565	17168	76.790
2	13.941	13.583	80572	4098	23.210
Total			347137	21266	100.000



3qh
$C_{29}H_{24}N_4O_2S$
M = 492.60 g/mol

(1-methyl-1*H*-imidazol-2-yl)(3-phenyl-4-(thiophene-2-carbonyl)-3,4-dihydro-2*H*-1,3-methano pyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone (3qh): Prepared from (1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.6 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(thiophene-2-carbonyl)amide (**2h**, 61.0 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qh** as a yellow solid (78.8 mg, 80% yield).

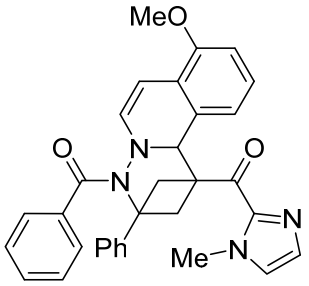
3qh: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 295-297 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98-7.97 (m, 1H), 7.43 (d, *J* = 4.4 Hz, 1H), 7.38-7.32 (m, 4H), 7.24-7.21 (m, 1H), 7.17 (s, 1H), 7.05-7.01 (m, 3H), 6.90 (d, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 7.6 Hz, 1H), 6.65 (t, *J* = 7.2 Hz, 1H), 5.99-5.96 (m, 2H), 5.49 (d, *J* = 7.6 Hz, 1H), 3.77 (s, 3H), 3.72 (t, *J* = 11.2 Hz, 1H), 3.36 (d, *J* = 10.4 Hz, 1H), 3.23 (t, *J* = 10.4 Hz, 1H), 2.38 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.6, 165.7, 142.7, 142.4, 140.1, 135.8, 133.8, 133.5, 131.2, 129.8, 128.7, 128.4, 128.3, 126.8, 126.6, 125.2, 125.0, 124.5, 102.0, 69.0, 68.4, 58.7, 48.7, 41.1, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{29}H_{24}N_4O_2SNa$: 515.1512; found: 515.1516.



3qi
$C_{32}H_{28}N_4O_2$
M = 500.60 g/mol

(4-benzoyl-6-methyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qi): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(3-methylisoquinolin-2-ium-2-yl)amide (**2i**, 63.0 mg, 0.24 mmol) in 40 °C according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qi** as a white solid (47.0 mg, 47% yield).

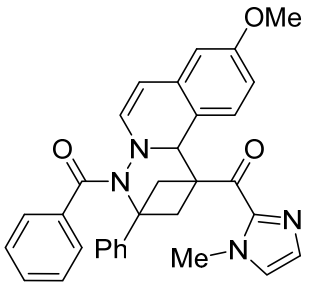
3qi: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 207-209 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 6.8 Hz, 2H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.39-7.30 (m, 5H), 7.25-7.21 (m, 1H), 7.18 (s, 1H), 6.99 (s, 1H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 6.55 (t, *J* = 7.6 Hz, 1H), 5.95 (d, *J* = 7.6 Hz, 1H), 5.85 (s, 1H), 5.14 (s, 1H), 3.74 (s, 3H), 3.47-3.31 (m, 3H), 2.43 (d, *J* = 11.2 Hz, 1H), 2.24 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.2, 173.5, 145.1, 142.8, 142.0, 135.6, 132.6, 130.3, 129.8, 128.4, 128.2, 128.1, 127.9, 127.7, 126.7, 126.5, 126.0, 125.2, 123.8, 123.7, 99.7, 70.8, 69.7, 58.4, 50.1, 40.8, 35.7, 19.5 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{29}N_4O_2$: 501.2285; found: 501.2279.



3qj
$C_{32}H_{28}N_4O_3$
M = 516.60 g/mol

(4-benzoyl-8-methoxy-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qj): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(5-methoxyisoquinolin-2-ium-2-yl)amide (**2j**, 66.8 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qj** as a white solid (96.1 mg, 93% yield).

3qj: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 3/1). Mp: 267-269 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.2 Hz, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.38-7.30 (m, 5H), 7.23-7.19 (m, 2H), 6.98 (s, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.54 (t, *J* = 8.0 Hz, 1H), 6.49 (d, *J* = 8.4 Hz, 1H), 5.68 (d, *J* = 8.0 Hz, 1H), 5.65 (s, 1H), 5.48 (d, *J* = 7.6 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H),3.73-3.69 (m, 1H), 3.38-3.28 (m, 2H), 2.37 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.7, 174.8, 153.2, 142.8, 142.2, 140.3, 135.6, 130.5, 129.7, 129.4, 128.4, 128.1, 127.7, 126.7, 126.5, 125.6, 124.8, 120.6, 118.9, 110.2, 94.5, 68.9, 68.6, 59.0, 55.3, 48.4, 41.4, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{29}N_4O_3$: 517.2234; found: 517.2225.

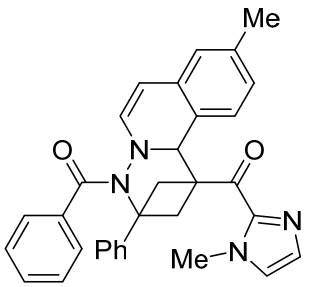


3qk
$C_{32}H_{28}N_4O_3$
M = 516.60 g/mol

(4-benzoyl-9-methoxy-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1H-imidazol-2-yl)methanone (3qk): Prepared from (1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(6-methoxyisoquinolin-2-ium-2-yl)amide (**2k**, 66.8 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qk** as a white solid (100.2 mg, 97% yield).

3qk: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 3/1). Mp: 259-261 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.2 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.40 -7.32 (m, 5H), 7.23-7.20 (m, 2H), 6.99 (s, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.32 (s, 1H), 6.11 (d, *J* = 8.4 Hz, 1H), 5.78 (d, *J* = 8.4 Hz, 1H), 5.65 (s, 1H), 5.27 (d, *J* = 8.0 Hz, 1H), 3.75 (s, 3H), 3.69-3.66 (m, 1H), 3.64 (s, 3H), 3.36-3.27 (m, 2H), 2.37 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.0, 174.8, 159.5, 142.7, 142.2, 141.5, 135.7, 132.5, 130.6, 129.8, 128.3, 128.1, 127.8, 127.6, 126.7, 126.5, 124.8, 120.7, 110.7, 109.4, 100.4,

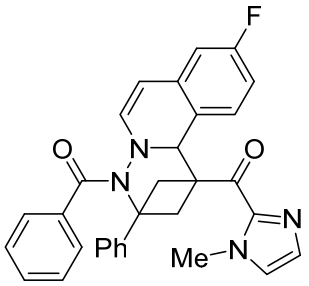
68.71, 68.65, 58.9, 55.0, 48.2, 41.1, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{29}N_4O_3$: 517.2234; found: 517.2230.



3pl
$C_{32}H_{28}N_4O_2$
M = 500.60 g/mol

(4-benzoyl-9-methyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ql): Prepared from (1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(6-methylisoquinolin-2-ium-2-yl)amide (**2l**, 62.9 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3ql** as a white solid (72.1 mg, 72% yield).

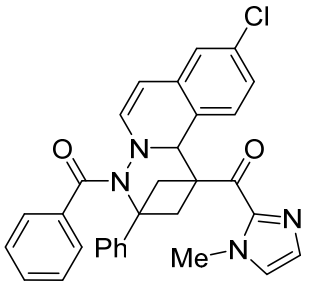
3ql: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 287-289 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 6.8 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.39-7.32 (m, 5H), 7.23-7.19 (m 2H), 7.00 (s, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.61 (s, 1H), 6.39 (d, *J* = 8.0 Hz, 1H), 5.76 (d, *J* = 8.0 Hz, 1H), 5.66 (s, 1H), 5.27 (d, *J* = 8.0 Hz, 1H), 3.76 (s, 3H), 3.69 (dd, *J* = 10.8, 8.4 Hz, 1H), 3.36-3.28 (m, 2H), 2.37 (d, *J* = 11.6 Hz, 1H), 2.11 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.0, 174.9, 142.8, 142.2, 141.0, 138.1, 135.7, 131.0, 130.5, 129.8, 128.3, 128.1, 127.7, 126.7, 126.5, 126.4, 125.6, 125.5, 124.8, 100.5, 68.8, 68.6, 58.9, 48.3, 41.1, 35.7, 20.9 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{28}N_4O_2Na$: 523.2104; found: 523.2105.



3qm
$C_{31}H_{25}FN_4O_2$
M = 504.57 g/mol

(4-benzoyl-9-fluoro-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qm): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(6-fluoroisoquinolin-2-ium-2-yl)amide (**2m**, 63.9 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qm** as a white solid (93.9 mg, 93% yield).

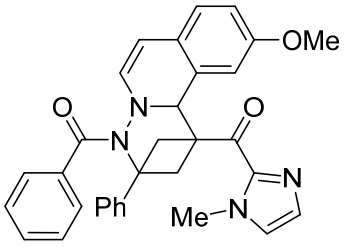
3qm: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 277-279 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 6.4 Hz, 2H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.39-7.32 (m, 5H), 7.24-7.19 (m, 2H), 6.99 (s, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.47 (dd, *J* = 9.6, 2.8 Hz, 1H), 6.24 (td, *J* = 8.4, 2.4 Hz, 1H), 5.88 (dd, *J* = 8.8, 6.0 Hz, 1H), 5.67 (s, 1H), 5.25 (d, *J* = 7.6 Hz, 1H), 3.76 (s, 3H), 3.67 (dd, *J* =11.6, 8.4 Hz, 1H), 3.36-3.26 (m, 2H), 2.41 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.8, 174.8, 162.6 (d, *J* = 244.9 Hz), 142.6, 142.0 (d, *J* = 2.5 Hz), 135.6, 133.7 (d, *J* = 8.7 Hz), 130.7, 129.9, 128.3, 128.2, 128.1, 128.0, 127.8, 126.8, 126.7, 124.8, 124.0 (d, *J* = 3.1 Hz), 111.3 (d, *J* = 4.2 Hz), 111.0 (d, *J* = 3.6 Hz), 99.7 (d, *J* = 2.3 Hz), 68.7, 58.8, 48.2, 41.5, 35.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -114.10 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{26}FN_4O_2$: 505.2034; found: 505.2025.



3qn
$C_{31}H_{25}ClN_4O_2$
M = 521.02 g/mol

(4-benzoyl-9-chloro-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qn): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(6-chloroisoquinolin-2-ium-2-yl)amide (**2n**, 67.8 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qn** as a white solid (70.9 mg, 68% yield).

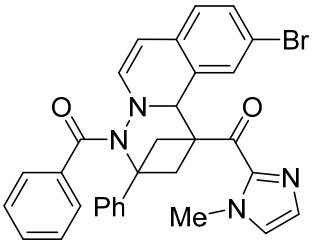
3qn: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 266-268 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.2 Hz, 2H), 7.43-7.34 (m, 7H), 7.24-7.20 (m, 2H), 7.01 (s, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.75 (s, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 5.84 (d, *J* = 8.0 Hz, 1H), 5.66 (s, 1H), 5.24 (d, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.66 (dd, *J* = 10.8, 8.8 Hz, 1H), 3.35-3.25 (m, 2H), 2.41 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$):δ 190.7, 174.8, 142.6, 142.2, 142.0, 135.5, 134.2, 133.2, 130.7, 129.9, 128.3, 128.2, 127.8, 127.8, 126.9, 126.7, 124.8, 124.5, 124.4, 99.4, 68.6, 58.9, 48.3, 41.5, 35.8 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{31}H_{25}ClN_4O_2Na$: 543.1558; found: 543.1555.



3qo
$C_{32}H_{28}N_4O_3$
M = 516.60 g/mol

(4-benzoyl-10-methoxy-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qo): Prepared from (1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(7-methoxyisoquinolin-2-ium-2-yl)amide (**2o**, 66.8 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qo** as a yellow solid (102.3 mg, 99% yield).

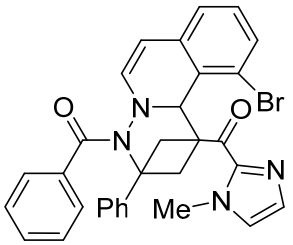
3qo: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 3/1). Mp: 156-159 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.2 Hz, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.38-7.32 (m, 5H), 7.25-7.19 (m, 2H), 7.00 (s, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 5.65 (s, 1H), 5.58 (s, 1H), 5.29 (d, *J* = 7.6 Hz, 1H), 3.76 (s, 3H), 3.72 (t, *J* = 10.0 Hz, 1H), 3.34 (t, *J* = 10.4 Hz, 2H), 3.29 (s, 3H), 2.36 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.6, 174.9, 157.2, 142.9, 142.2, 139.0, 135.7, 130.6, 129.9, 129.7, 128.3, 128.1, 127.7, 126.7, 126.5, 125.8, 124.8, 124.1, 114.3, 112.1, 100.2, 69.1, 68.5, 58.9, 54.7, 48.3, 40.9, 35.6 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{29}N_4O_3$: 517.2234; found: 517.2227.



3qp
$C_{31}H_{25}BrN_4O_2$
M = 565.47 g/mol

(4-benzoyl-10-bromo-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qp): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(7-bromoisoquinolin-2-ium-2-yl)amide (**2p**, 78.5 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qp** as a white solid (106.3 mg, 94% yield).

3qp: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 240-242 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.2 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.39-7.32 (m, 5H), 7.24-7.21 (m, 2H), 7.04-7.02 (m, 2H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 5.83 (s, 1H), 5.57 (s, 1H), 5.24 (d, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.65 (t, *J* = 10.0 Hz, 1H), 3.40 (d, *J* = 10.4 Hz, 1H), 3.32 (t, *J* = 10.0 Hz, 1H), 2.43 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.5, 174.9, 142.7, 142.0, 141.4, 135.5, 131.2, 130.7, 130.3, 130.2, 130.0, 129.6, 128.2, 127.8, 127.1, 126.8, 125.9, 124.8, 117.8, 99.6, 68.7, 68.5, 58.9, 48.3, 41.1, 35.8 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{26}BrN_4O_2$: 565.1234; found: 565.1228.

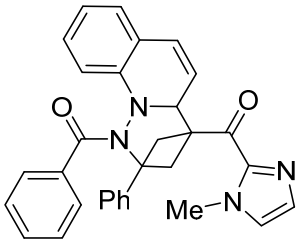


3qq
$C_{31}H_{25}BrN_4O_2$
M = 565.47 g/mol

(4-benzoyl-11-bromo-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (3qq): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(8-bromoisoquinolin-2-ium-2-yl)amide (**2q**, 78.5 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **3qq** as a white solid (96.1 mg, 85% yield).

3qq: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 3/1). Mp: 275-277 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 7.4 Hz, 2H), 7.47 (d, J = 7.2 Hz, 2H), 7.41-7.34 (m, 5H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.79 (s, 1H), 6.72 (s, 1H), 6.70-6.65 (m, 2H), 5.51 (s, 1H), 5.40 (d, *J* = 8.0 Hz, 1H), 4.14 (t, *J* = 10.0 Hz, 1H), 3.79 (s, 3H), 3.61 (d, *J* = 10.8 Hz, 1H), 2.99 (t, *J* = 10.0 Hz, 1H), 2.49 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.2, 174.9, 142.7, 140.0, 141.8, 135.5, 135.3, 130.7, 129.4, 129.22, 129.18, 128.3, 128.2, 128.1, 127.9, 126.8, 125.7, 125.0,

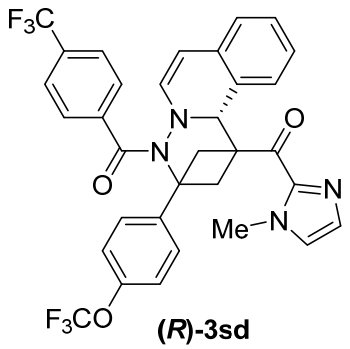
123.4, 122.4, 101.1, 69.2, 68.4, 57.9, 46.1, 45.2, 35.9 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{31}H_{25}BrN_4O_2Na$: 587.1053; found: 587.1052.



4qb
$C_{31}H_{26}N_4O_2$
M = 486.58 g/mol

(1-benzoyl-2-phenyl-2,3-dihydro-1*H*-2,4-methanopyridazino[1,6-*a*]quinolin-4(4a*H*)-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (4qb): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and benzoyl(quinolin-1-ium-1-yl)amide (**2d**, 59.6 mg, 0.24 mmol) according to the **GP3** at rt for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **4qd** as a white solid (84.8 mg, 87% yield).

4qd: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 284-286 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.2 Hz, 2H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.39-7.34 (m, 4H), 7.28-7.21 (m, 4H), 7.16 (s, 1H), 7.02 (s, 1H), 6.86 (d, *J* = 6.8 Hz, 1H), 6.77 (t, *J* = 6.8 Hz, 1H), 6.20 (d, *J* = 10.0 Hz, 1H), 5.74 (d, *J* = 3.6 Hz, 1H), 5.07 (dd, *J* = 10.0, 4.4 Hz, 1H), 3.97 (s, 3H), 3.21 (t, *J* = 9.6 Hz, 1H), 3.12 (d, *J* = 10.0 Hz, 1H), 2.89 (d, *J* = 10.8 Hz, 1H), 2.36 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.1, 175.7, 146.5, 142.4, 141.6, 135.2, 130.7, 129.98, 129.95, 128.0, 127.8, 127.7, 127.6, 127.0, 126.9, 126.8, 126.0, 121.1, 120.1, 119.8, 111.8, 68.4, 66.2, 60.0, 48.5, 38.4, 35.9 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{31}H_{26}N_4O_2Na$: 509.1936; found: 509.1948.



(*R*)-3sd

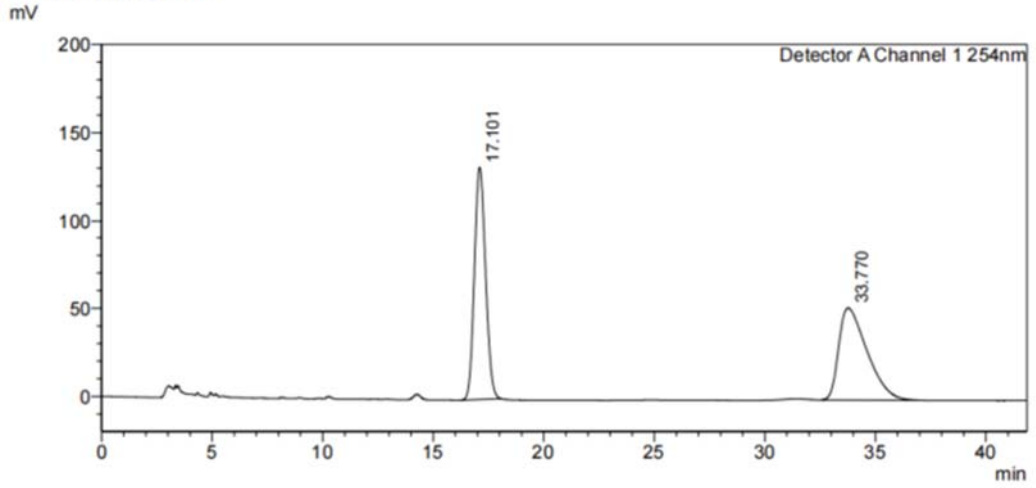
$C_{33}H_{24}F_6N_4O_3$

M = 638.57 g/mol

(*R*)-(1-methyl-1*H*-imidazol-2-yl)(3-(4-(trifluoromethoxy)phenyl)-4-(4-(trifluoromethyl)benzoyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone ((*R*)-3sd) : Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-(4-(trifluoromethoxy)phenyl) bicyclo[1.1.0]butan-1-yl)methanone (**1s**, 64.5 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **(*R*)-3sd** as a yellow solid (106.2 mg, 83% yield).

(*R*)-3sd: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 120-122 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 16.36 min, tr (minor) = 33.75 min) gave the isomeric composition of the product: 95% *ee*. $[\alpha]_D^{20}$ = -106.4 (*c* = 2.60, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.11-7.10 (m, 3H), 6.91 (s, 1H), 6.87 (t, *J* = 7.2 Hz, 1H), 6.72-6.70 (m, 2H), 6.51 (t, *J* = 7.6 Hz, 1H), 5.80 (d, *J* = 7.6 Hz, 1H), 5.55 (s, 1H), 5.26 (d, *J* = 8.0 Hz, 1H), 3.68-3.65 (m, 1H), 3.64 (s, 3H), 3.27-3.19 (m, 2H), 2.32 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): 190.3, 173.9, 148.0 (q, *J* = 1.9 Hz), 142.6, 140.5, 140.2, 138.9, 132.2 (q, *J* = 32.4 Hz), 130.9, 129.9, 128.7, 128.4, 128.1, 126.7, 126.52, 126.49, 125.2, 124.94 (q, *J* = 3.7 Hz), 124.89, 123.7 (q, *J* = 270.7 Hz), 120.7, 120.4 (q, *J* = 255.4 Hz), 101.6, 69.0, 68.2, 58.7, 48.4, 41.0, 35.6 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -57.74, -62.89 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{25}F_6N_4O_3$: 639.1825; found: 639.1826.

<Chromatogram>



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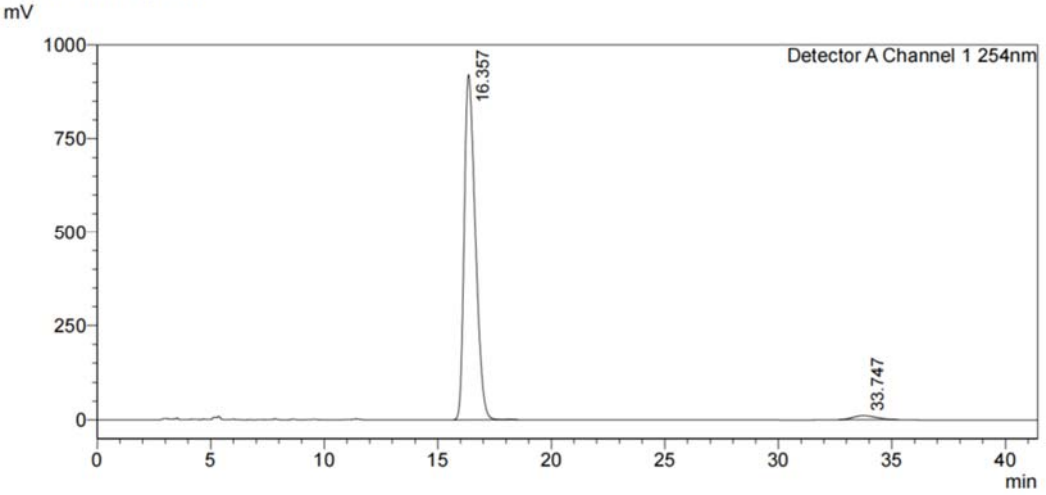

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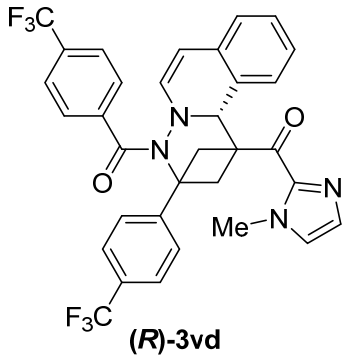
2	33.747	32.700	779934	10577	2.428
Total			32121007	931066	100.000



(*R*)-3vd

$C_{33}H_{24}F_6N_4O_2$

M = 622.57 g/mol

(*R*)-(1-methyl-1*H*-imidazol-2-yl)(4-(4-(trifluoromethyl)benzoyl)-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone ((*R*)-3vd) : Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1v**, 61.3 mg, 0.2 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **(*R*)-3vd** as a yellow solid (104.6 mg, 84% yield)

(*R*)-3vd: $\mathbf{R_f}$ = 0.25 (petroleum ether/EtOAc = 3/1). Mp: 131-133 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 16.96 min, tr (minor) = 52.68 min) gave the isomeric composition of the product: 96% *ee*. $[\alpha]_D^{20}$ = -113.9 (*c* = 1.18, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 4H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.21 (s, 1H), 7.02 (s, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.83-6.80 (m, 2H), 6.61 (t, *J* = 7.6 Hz, 1H), 5.90 (d, *J* = 8.0 Hz, 1H), 5.65 (s, 1H), 5.37 (d, *J* = 7.6 Hz, 1H), 3.79-3.74 (m, 1H), 3.75 (s, 3H), 3.38 (d, *J* = 10.8 Hz, 1H), 3.30 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.2, 173.8, 145.6, 142.6, 140.2, 138.7, 132.3 (q, *J* = 32.4 Hz), 130.9, 129.9, 129.1 (q, *J* = 32.2 Hz), 128.7, 128.4, 128.1, 126.8, 126.5, 125.4 (q, *J* = 3.8 Hz), 125.3, 125.01, 125.0, 124.1 (q, *J* = 270.3 Hz), 123.7 (q, *J* = 270.8 Hz), 101.7, 69.1, 68.4, 58.7, 48.3, 41.0, 35.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.40, -62.92 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{33}H_{24}F_6N_4O_2Na$: 645.1696; found: 645.1694.

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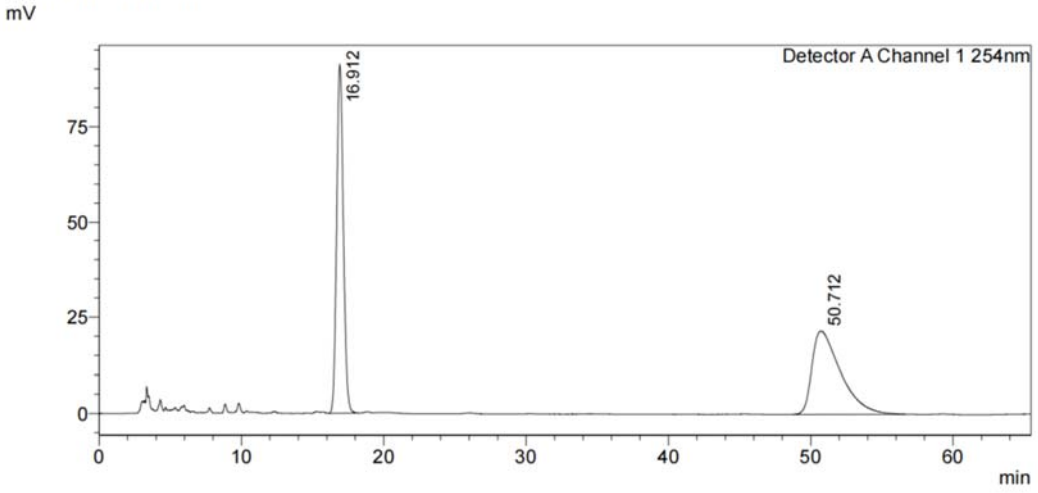

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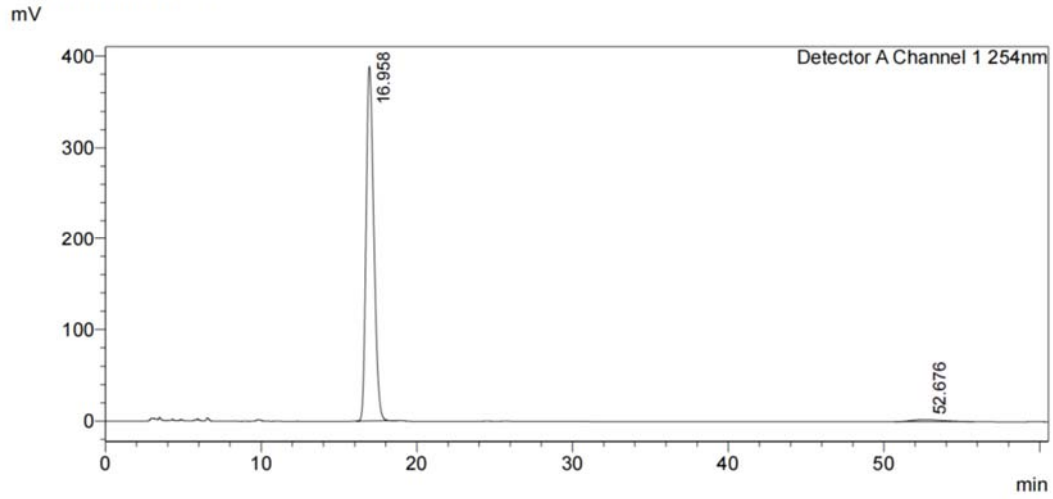

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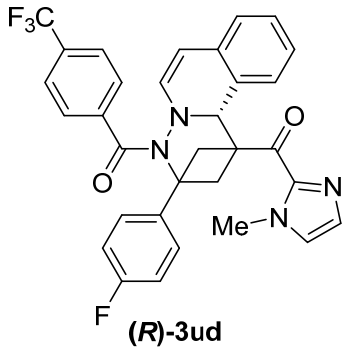

(*R*)-3ud

$C_{32}H_{24}F_4N_4O_2$

M = 572.56 g/mol

(*R*)-(3-(4-fluorophenyl)-1-(1-methyl-1*H*-imidazole-2-carbonyl)-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3ud) : Prepared from (3-(4-fluorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1u**, 51.3 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3ud** as a yellow solid (95.0 mg, 83% yield).

(*R*)-**3ud**: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 145-147 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 25.11 min, tr (minor) = 38.97 min) gave the isomeric composition of the product: 94% *ee*. $[\alpha]_D^{20}$ = -116.4 (*c* = 2.40, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.42-7.38 (m, 2H), 7.20 (s, 1H), 7.03 (t, *J* = 8.8 Hz, 3H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.79 (d, *J* = 7.2 Hz, 2H), 6.59 (t, *J* = 7.6 Hz, 1H), 5.89 (d, *J* = 7.6 Hz, 1H), 5.63 (s, 1H), 5.34 (d, *J* = 7.6 Hz, 1H), 3.76-3.72 (m, 1H), 3.74 (s, 3H), 3.34-3.27 (m, 2H), 2.39 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.4, 173.9, 161.7 (d, *J* = 244.0 Hz), 142.6, 140.3, 139.1, 137.7 (d, *J* = 3.1 Hz), 132.1 (q, *J* = 32.3 Hz), 130.9, 129.9, 128.7, 128.3, 128.1, 126.8, 126.7 (d, *J* = 5.8 Hz), 126.5, 125.2, 124.93 (q, *J* = 3.8 Hz), 124.87, 123.7 (q, *J* = 270.7 Hz), 115.1 (d, *J* = 21.4 Hz), 101.4, 69.0, 68.3, 58.7, 48.5, 41.1, 35.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.88, -115.53 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{25}F_4N_4O_2$: 573.1988; found: 573.1898.

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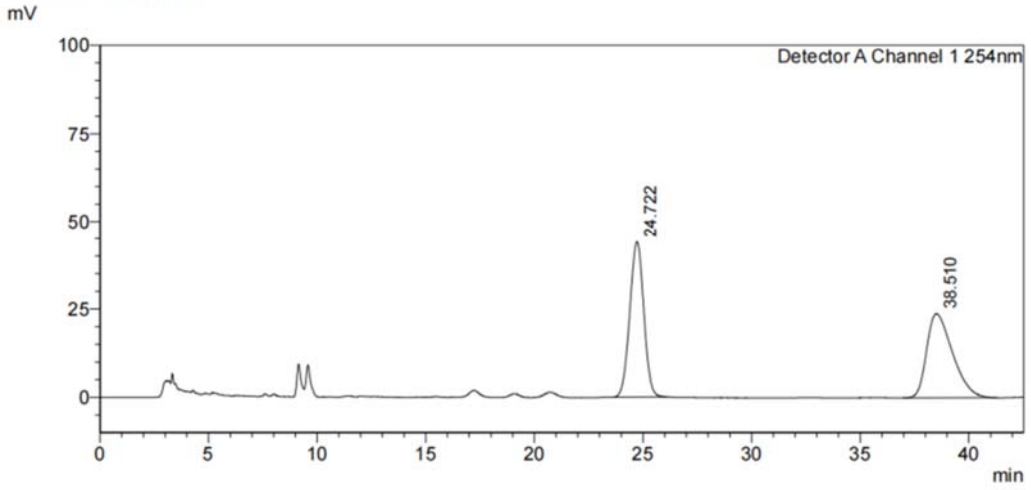

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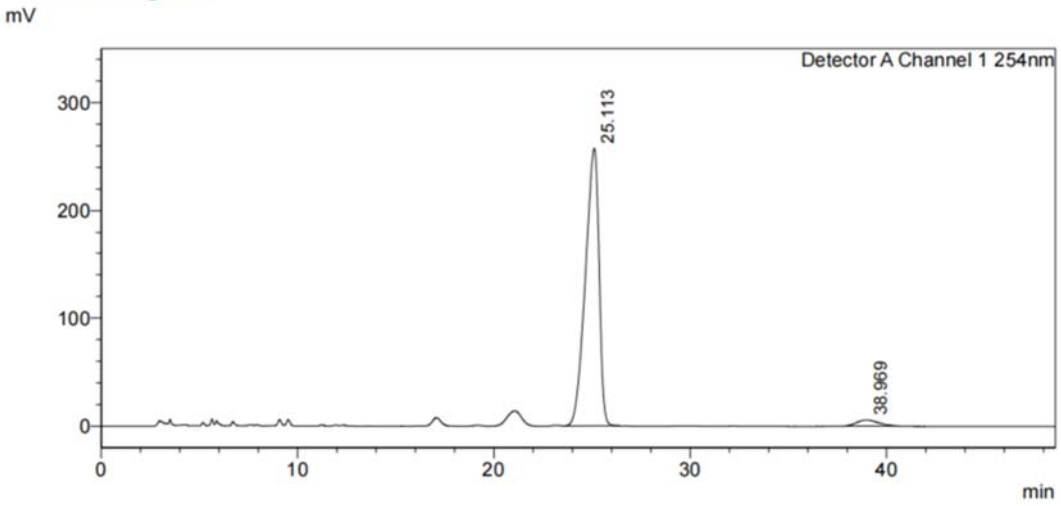

Peak#	Ret. Time	Peak Start	Area	Height	Area%
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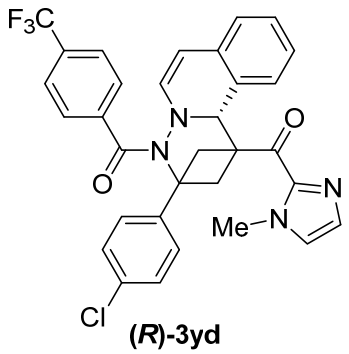

(*R*)-3yd

$C_{32}H_{24}ClF_3N_4O_2$

M = 589.02 g/mol

(*R*)-(3-(4-chlorophenyl)-1-(1-methyl-1*H*-imidazole-2-carbonyl)-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3yd) : Prepared from (3-(4-chlorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1y**, 54.5 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature in **CH_2Cl_2/MeCN (10/1)** for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3yd** as a white solid (94.2 mg, 80% yield).

(*R*)-**3yd**: **R_f** = 0.25 (petroleum ether/EtOAc = 3/1). Mp: 150-152 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 18.39 min, tr (minor) = 37.06 min) gave the isomeric composition of the product: 95% *ee*. $[\alpha]_D^{20}$ = -164.4 (*c* = 1.15, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.8 Hz, 2H), 7.20 (s, 1H), 7.01 (s, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 2H), 6.60 (t, *J* = 7.6 Hz, 1H), 5.89 (d, *J* = 7.6 Hz, 1H), 5.63 (s, 1H), 5.34 (d, *J* = 8.0 Hz, 1H), 3.78-3.71 (m, 1H), 3.75 (s, 3H), 3.33-3.25 (m, *J* = 8.0 Hz, 2H), 2.39 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.4, 173.8, 142.6, 140.4, 140.3, 139.0, 132.8, 132.2 (q, *J* = 32.4 Hz), 130.9, 129.9, 128.7, 128.4, 128.4, 128.1, 126.7, 126.5, 125.2, 125.0 (q, *J* = 3.7 Hz), 124.9, 123.7 (q, *J* = 270.9 Hz), 101.5, 69.0, 68.3, 58.7, 48.3, 41.0, 35.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.89 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{24}ClF_3N_4O_2Na$: 611.1432; found: 611.1427.

*Note：In CH_2Cl_2 under standard conditions, (R)-**3xb** was obtained with a 90% yield and 89% ee.*

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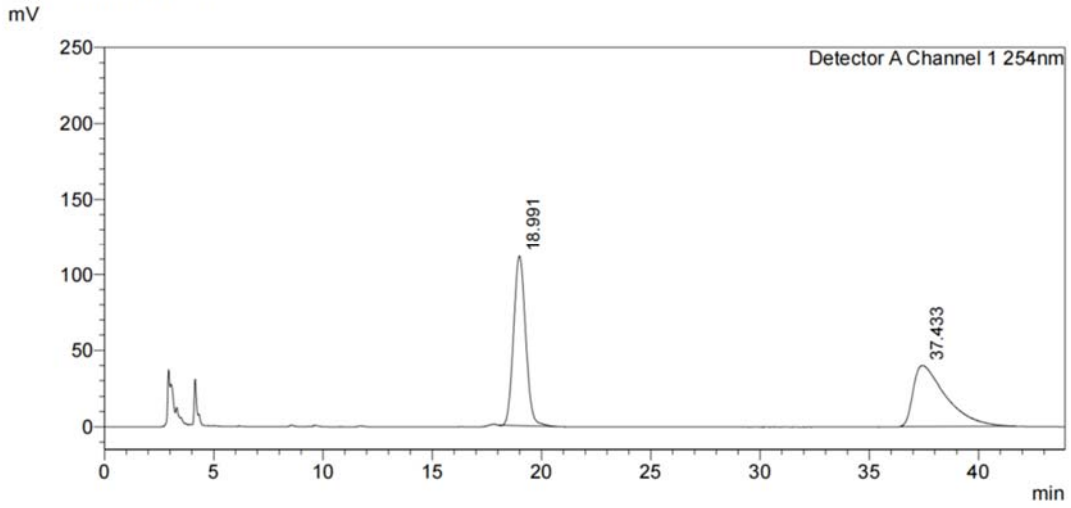

Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	18.991	18.000	4269930	111403	50.619
2	37.433	36.342	4165548	39854	49.381
Total			8435478	151257	100.000

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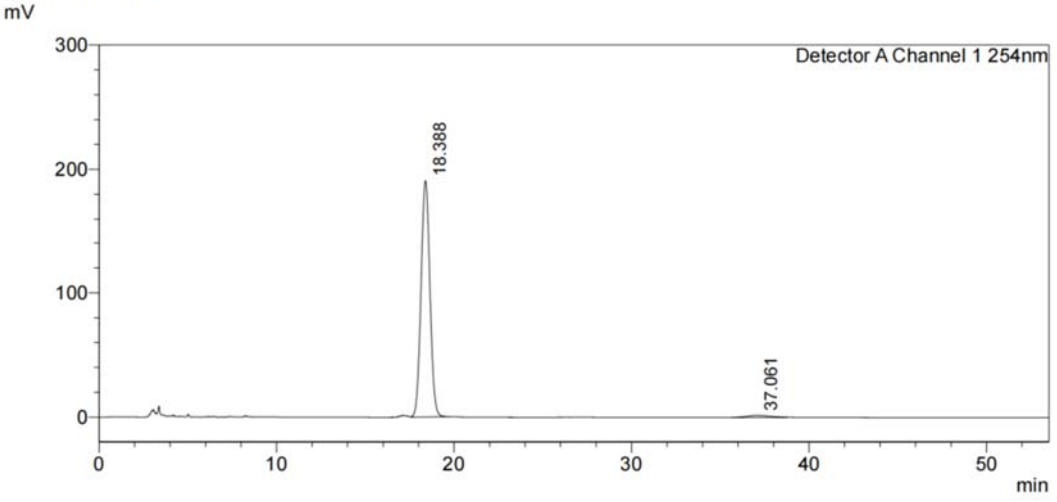
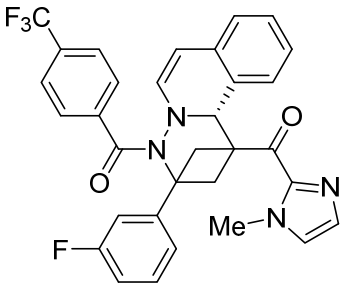


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	18.388	17.550	6613248	190806	97.480
2	37.061	35.625	170971	1723	2.520
Total			6784219	192530	100.000



(*R*)-3zd
$C_{32}H_{24}F_4N_4O_2$
M = 572.56 g/mol

(*R*)-(3-(3-fluorophenyl)-1-(1-methyl-1*H*-imidazole-2-carbonyl)-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3zd) : Prepared from (3-(3-fluorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1z**, 51.3 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3zd** as a yellow solid (89.3 mg, 78% yield).

(*R*)-**3zd**: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 129-131 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 19.18 min, tr (minor) = 26.43 min) gave the isomeric composition of the product: 94% *ee*. $[\alpha]_D^{20}$ = -113.5 (*c* = 2.13, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.31 (q, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 6.8 Hz, 2H), 7.12 (d, *J* = 9.6 Hz, 1H), 7.00 (s, 1H), 6.98-6.91 (m, 2H), 6.80 (t, *J* = 7.2 Hz, 2H), 6.60 (t, *J* = 7.6 Hz, 1H), 5.89 (d, *J* = 6.0 Hz, 1H), 5.64 (s, 1H), 5.35 (d, *J* = 7.2 Hz, 1H), 3.74-3.70 (m, 1H), 3.74 (s, 3H), 3.34 (d, *J* = 10.8 Hz, 1H), 3.27 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.3, 173.7, 162.8 (d, *J* = 244.1 Hz), 144.4 (d, *J* = 7.2 Hz), 142.6, 140.2, 138.9, 132.2 (q, *J* = 32.4 Hz), 130.9, 129.9, 129.8, 128.7, 128.4, 128.1, 126.7, 126.5, 125.2, 124.93 (q, *J* = 3.8 Hz), 124.87, 123.7 (q, *J* = 270.8 Hz), 120.4 (d, *J* = 2.8 Hz), 113.9 (d, *J* = 21.0 Hz), 112.0 (d, *J* = 22.1 Hz), 101.5, 69.0, 68.3, 58.6, 48.3, 41.2, 35.6 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.85, -113.10 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{24}F_4N_4O_2Na$: 595.1728; found: 595.1731.

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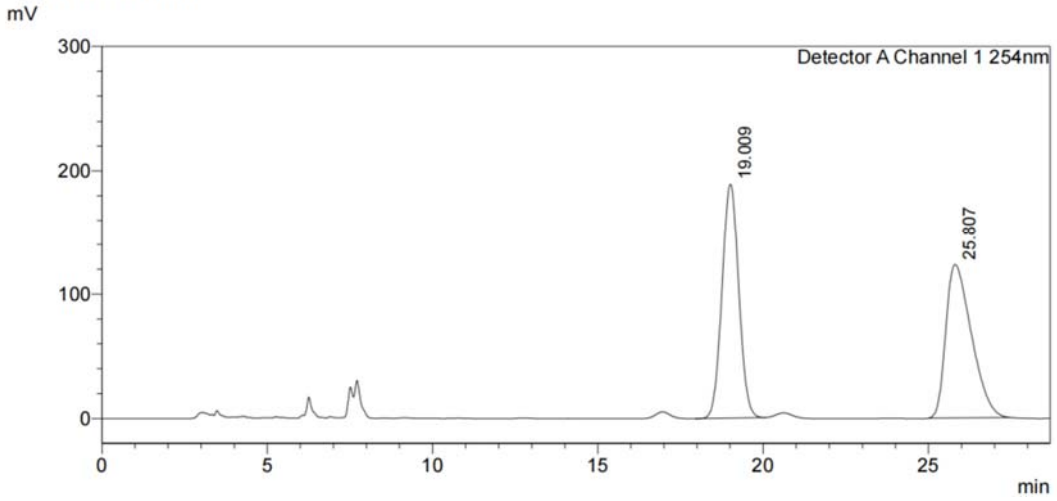

Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	19.009	17.950	6668948	188873	50.070
2	25.807	25.008	6650205	123333	49.930
Total			13319153	312206	100.000

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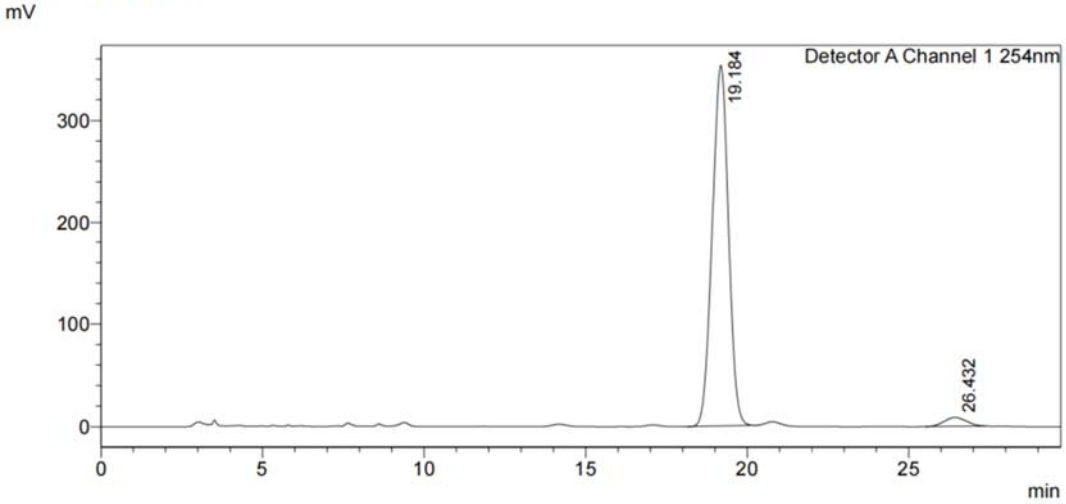
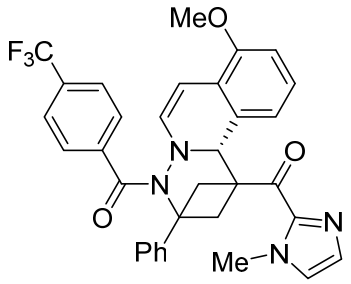


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	19.184	18.158	12349719	352960	96.753
2	26.432	25.517	414452	8597	3.247
Total			12764171	361557	100.000



(*R*)-3qr
$C_{33}H_{27}F_3N_4O_3$
M = 584.60 g/mol

(*R*)-(8-methoxy-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3qr) : Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and (5-methoxyisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2r**, 83.1 mg, 0.24 mmol) at room temperature in **CH_2Cl_2/MeCN** (10/1) for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3qr** as a yellow solid (102.8 mg, 88% yield).

(*R*)-**3qr**: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 3/1). Mp: 217-219 °C. HPLC analysis (Chiralpak IC, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 26.73 min, tr (minor) = 20.28 min) gave the isomeric composition of the product: 93% *ee*. $[\alpha]_D^{20}$ = -148.7 (*c* = 1.28, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.21 (d, *J* = 13.6 Hz, 2H), 6.99 (s, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.57 (t, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 9.4 Hz, 1H), 5.72 (d, *J* = 8.0 Hz, 1H), 5.63 (s, 1H), 5.49 (d, *J* = 7.6 Hz, 1H), 3.77-3.75 (m, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.37 (d, *J* = 10.4 Hz, 1H), 3.30 (t, *J* = 9.2 Hz, 1H), 2.39 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.3, 173.6, 153.3, 142.7, 141.8, 139.6, 139.2, 131.9 (q, *J* = 32.3 Hz), 129.7, 129.2, 128.4, 128.2, 126.9, 126.6, 125.9, 124.85, 124.82 (q, *J* = 3.6 Hz), 123.7 (q, *J* = 270.8 Hz), 120.3, 118.8, 110.3, 95.3, 68.8, 68.7, 58.8, 55.2, 48.5, 41.2, 35.6 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.81 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{33}H_{27}F_3N_4O_3Na$: 607.1927; found: 607.1932.

*Note：In CH_2Cl_2 under standard conditions, (R)-**3pq** was obtained with a 71% yield and 88% ee.*

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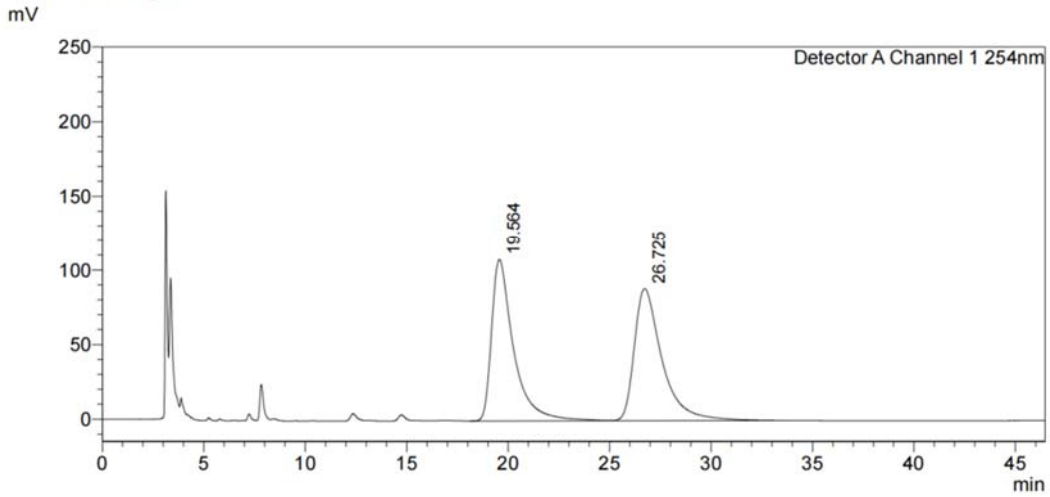

Peak#	Ret. Time	Peak Start	Area	Height	Area%
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2	26.725	25.100	8419996	88514	50.751
Total			16590838	196742	100.000

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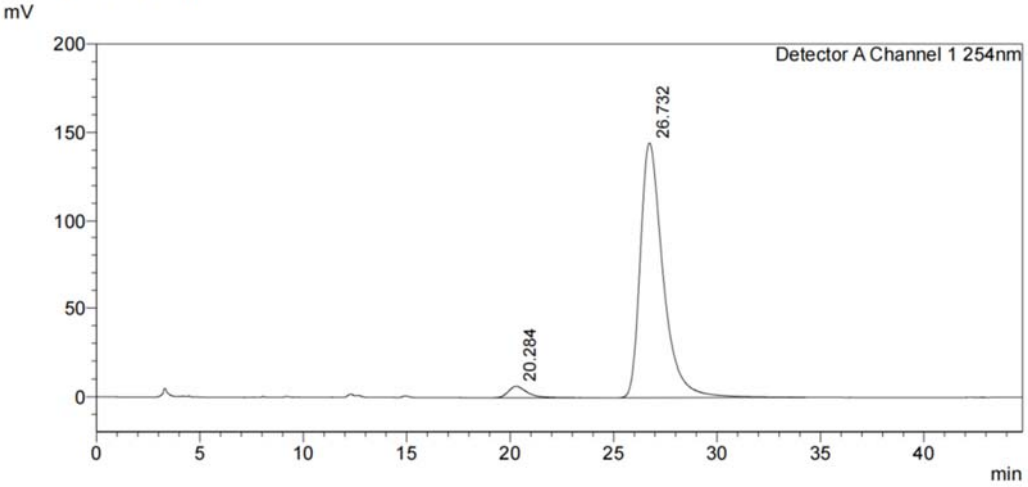
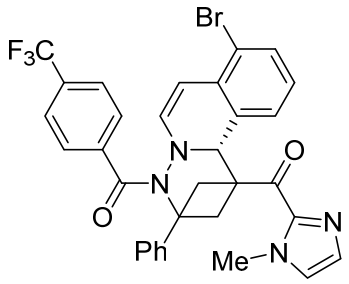


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	20.284	19.158	417241	6504	3.632
2	26.732	25.200	11070052	144696	96.368
Total			11487293	151200	100.000



(*R*)-3qs
$C_{32}H_{24}BrF_3N_4O_2$
M = 633.47 g/mol

(*R*)-(8-bromo-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3qs): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and (5-bromoisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2s**, 94.8 mg, 0.24 mmol) at room temperature in **CH_2Cl_2/MeCN** (10/1) for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3qs** as a white solid (96.0 mg, 76% yield).

(*R*)-**3qs** R_f = 0.35 (petroleum ether/EtOAc = 3/1). Mp: 148-150 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 18.96 min, tr (minor) = 26.04 min) gave the isomeric composition of the product: 91% *ee*. $[\alpha]_D^{20}$ = -83.0 (*c* = 1.13, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.25-7.17 (m, 3H), 7.01 (s, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.42 (t, *J* = 8.0 Hz, 1H), 5.89 (d, *J* = 7.6 Hz, 1H), 5.71 (d, *J* = 8.0 Hz, 1H), 5.61 (s, 1H), 3.76 (s, 3H), 3.72 (t, *J* = 9.2 Hz, 1H), 3.36 (d, *J* = 10.4 Hz, 1H), 3.27 (t, *J* = 9.2 Hz, 1H), 2.45 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.3, 173.6, 142.6, 141.5, 139.0, 132.8, 132.2 (q, *J* = 32.3 Hz), 130.9, 130.1, 129.9, 128.4, 128.3, 127.1, 126.7, 125.9, 125.8, 124.9, 125.0 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 271.0 Hz), 120.3, 99.8, 69.1, 68.9, 58.8, 48.4, 41.6, 35.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.89 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{25}BrF_3N_4O_2$: 633.1107; found: 633.1100.

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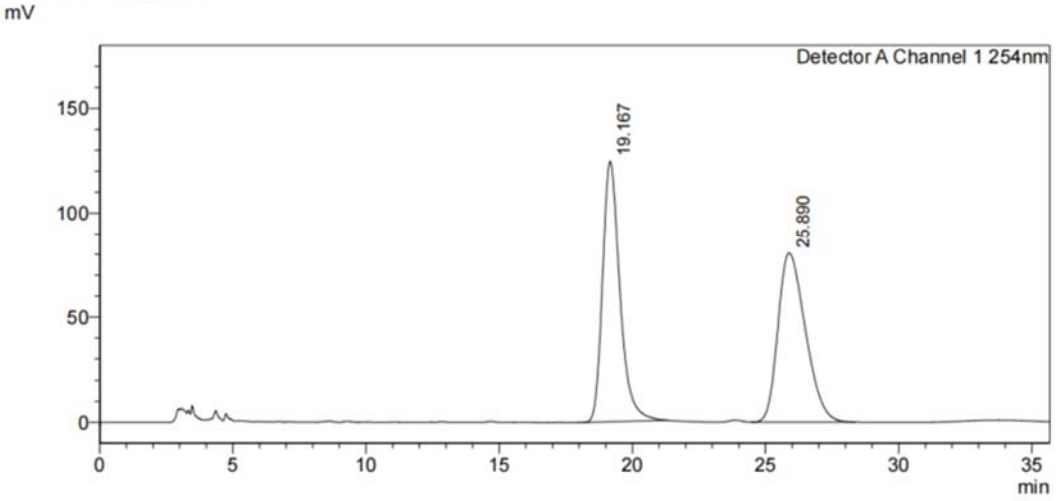

Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	19.167	17.925	5632241	124573	49.375
2	25.890	24.467	5774894	80610	50.625
Total			11407135	205183	100.000

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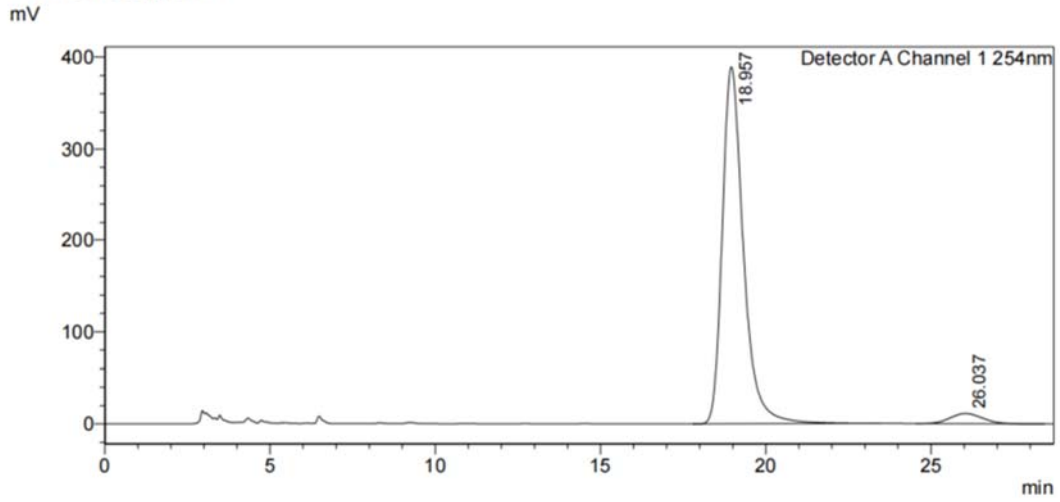
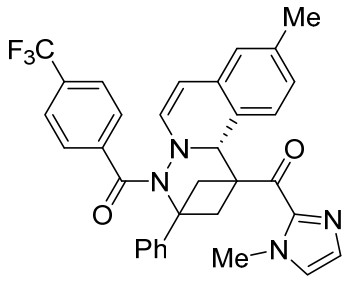


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	18.957	17.800	17318932	389363	95.733
2	26.037	24.542	771891	11128	4.267
Total			18090822	400491	100.000



(*R*)-3qt
$C_{33}H_{27}F_3N_4O_2$
M = 568.60 g/mol

(*R*)-(9-methyl-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3qt): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and (6-methylisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2t**, 79.3 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3qt** as a yellow solid (74.9 mg, 66% yield).

(*R*)-**3qt**: $\mathbf{R_f}$ = 0.25 (petroleum ether/EtOAc = 3/1). Mp: 227-229 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 12.90 min, tr (minor) = 24.23 min) gave the isomeric composition of the product: 91% *ee*. $[\alpha]_D^{20}$ = -113.6 (*c* = 0.25, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.00 (s, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.62 (s, 1H), 6.41 (d, *J* = 7.6 Hz, 1H), 5.77 (d, *J* = 8.0 Hz, 1H), 5.65 (s, 1H), 5.29 (d, *J* = 8.0 Hz, 1H), 3.74 (s, 3H), 3.73-3.68 (m, 1H), 3.36 (d, *J* = 10.8 Hz, 1H), 3.30 (d, *J* = 8.4 Hz, 1H), 2.39 (d, *J* = 11.2 Hz, 1H), 2.10 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.6, 173.7, 142.6, 141.8, 140.4, 139.3, 138.3, 131.9 (q, *J* = 32.4 Hz), 130.7, 129.8, 128.3, 128.2, 126.9, 126.6, 126.4, 125.8, 125.6, 125.3, 124.85, 124.83 (q, *J* = 3.2 Hz), 123.7 (q, *J* = 270.8 Hz), 101.3, 68.83, 68.78, 58.7, 48.3, 40.9, 35.6, 20.8 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.81 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{33}H_{27}F_3N_4O_2Na$: 591.1978; found: 591.1978.

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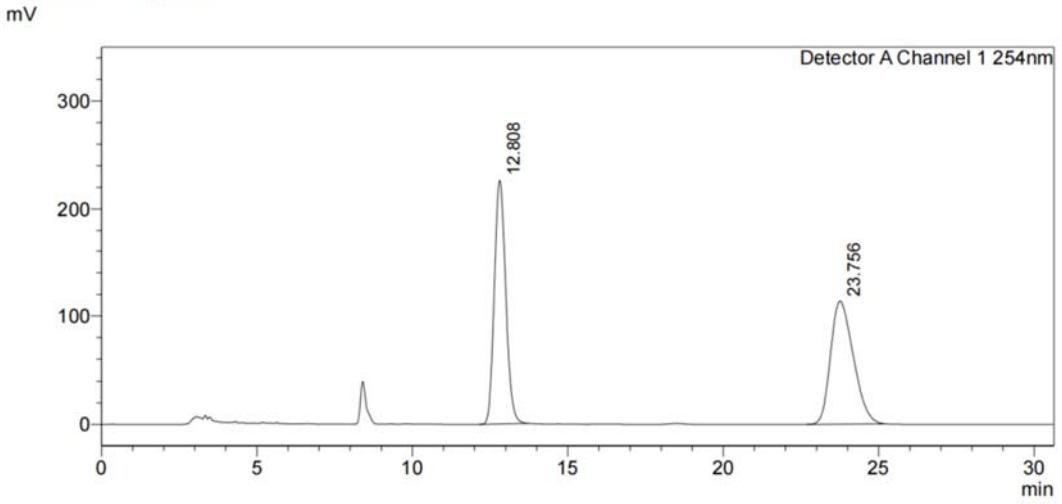

Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	12.808	12.150	5735894	226258	49.808
2	23.756	22.692	5780037	113527	50.192
Total			11515931	339785	100.000

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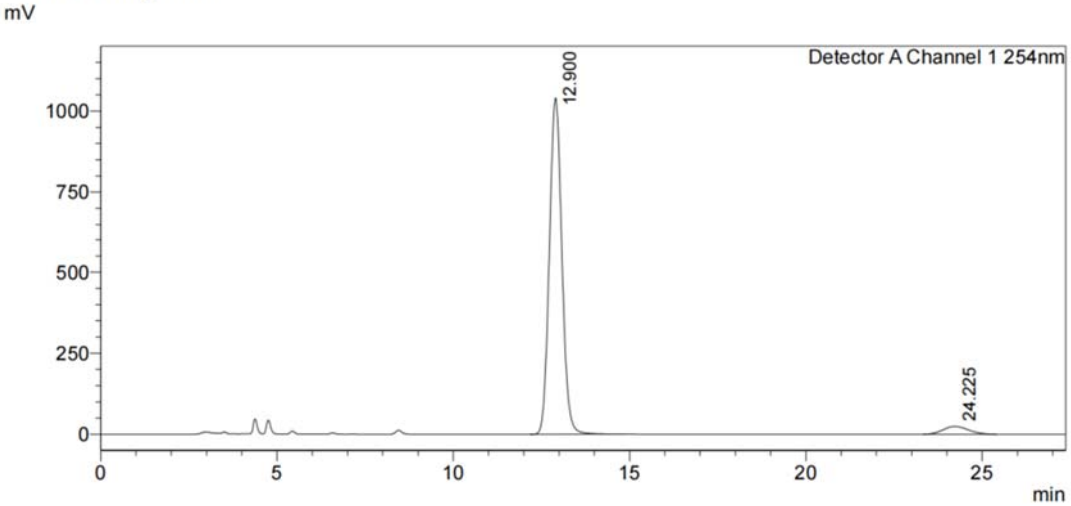
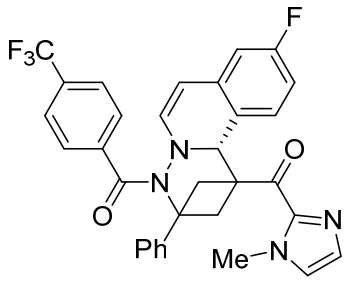


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	12.900	12.183	25657646	1040395	95.521
2	24.225	23.325	1203150	24199	4.479
Total			26860796	1064593	100.000

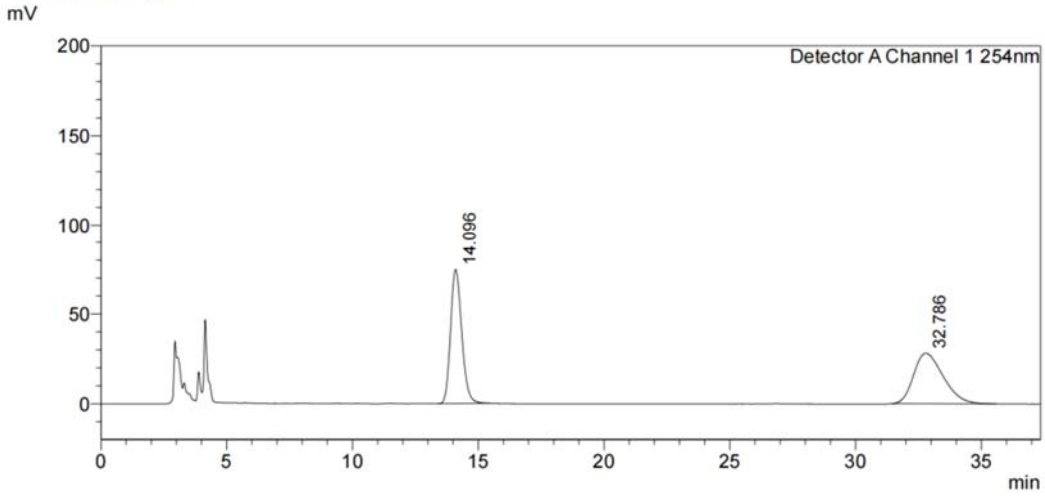


(*R*)-3pu
$C_{32}H_{24}F_4N_4O_2$
M = 572.56 g/mol

(*R*)-(9-fluoro-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3qu): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and (6-fluoroisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2u**, 80.2mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3qu** as a yellow solid (94.6 mg, 83% yield).

(*R*)-**3qu**: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 3/1). Mp: 123-125 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 13.98 min, tr (minor) = 33.06 min) gave the isomeric composition of the product: 93% *ee*. $[\alpha]_D^{20}$ = -114.7. (*c* = 2.18, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.24-7.21 (m, 2H), 7.02 (s, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.48 (d, *J* = 9.2 Hz, 1H), 6.27 (t, *J* = 8.4 Hz, 1H), 5.89 (t, *J* = 7.6 Hz, 1H), 5.65 (s, 3H), 5.28 (d, *J* = 8.0 Hz, 1H), 3.78 (s, 3H), 3.68 (t, *J* = 11.2 Hz, 1H), 3.35 (d, *J* = 10.8 Hz, 1H), 3.27 (t, *J* = 9.2 Hz, 1H), 2.42 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.5, 173.6, 162.7 (d, *J* = 245.2 Hz), 142.5, 141.6, 141.5, 139.1, 133.4 (d, *J* = 8.6 Hz), 132.2 (q, *J* = 32.3 Hz), 130.0, 128.4, 128.3, 128.1 (d, *J* = 8.4 Hz), 127.1, 126.8, 125.0 (q, *J* = 3.8 Hz), 124.9, 123.9 (d, *J* = 3.2 Hz), 123.7 (q, *J* = 271.0 Hz), 111.6 (d, *J* = 4.0 Hz), 111.3 (d, *J* = 4.6 Hz), 100.5 (d, *J* = 2.2 Hz), 68.9, 68.7, 58.7, 48.3, 41.3, 35.8 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.89, -113.80 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{24}F_4N_4O_2Na$: 595.1728; found: 595.1721

<Chromatogram>



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	14.096	13.408	2307361	74728	50.126
2	32.786	31.467	2295799	28063	49.874
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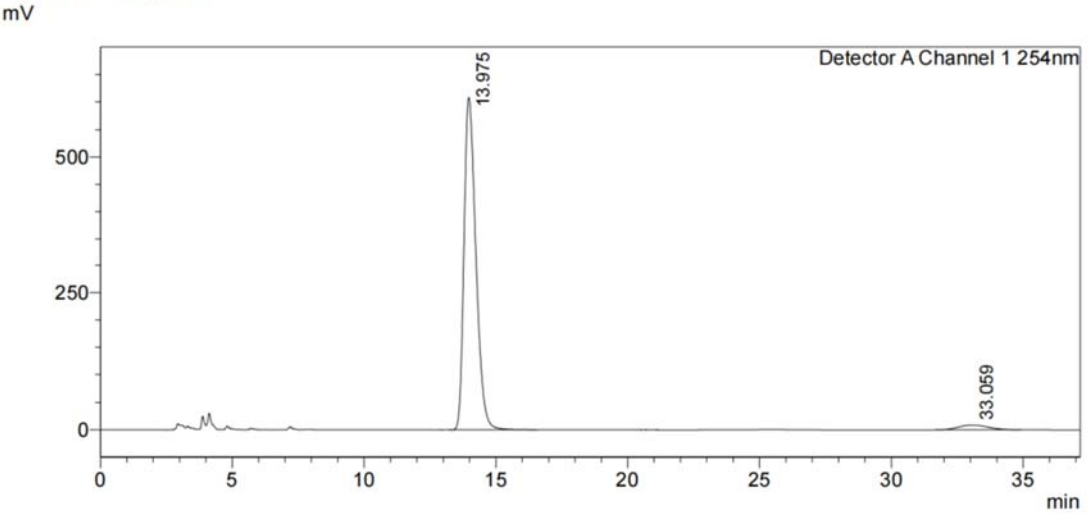
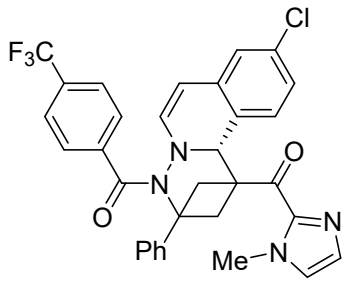


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	13.975	13.217	19019220	607908	96.498
2	33.059	31.700	690238	8757	3.502
Total			19709458	616665	100.000



(*R*)-3qv
$C_{32}H_{24}ClF_3N_4O_2$
M = 589.02 g/mol

(*R*)-(9-chloro-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3qv) : Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and (6-chloroisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2v**, 84.2mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3qv** as a yellow solid (84.8 mg, 72% yield).

(*R*)-**3qv**: $\mathbf{R_f}$ = 0.25 (petroleum ether/EtOAc = 3/1). Mp: 220-222 °C. HPLC analysis (Chiralpak OD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 24.38 min, tr (minor) = 18.65 min) gave the isomeric composition of the product: 95% *ee*. $[\alpha]_D^{20}$ = -118.6 (*c* = 1.23, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 12.0 Hz, 2H), 7.03 (s, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.77 (s, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 5.85 (d, *J* = 8.0 Hz, 1H), 5.64 (s, 1H), 5.27 (d, *J* = 8.0 Hz, 1H), 3.79 (s, 3H), 3.67 (dd, *J* = 11.6, 9.2 Hz, 1H), 3.35 (d, *J* = 10.4 Hz, 1H), 3.26 (t, *J* = 9.2 Hz, 1H), 2.42 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.3, 173.6, 142.5, 141.5, 139.1, 134.4, 132.9, 132.2 (q, *J* = 32.4 Hz), 130.0, 128.33, 128.28, 127.8, 127.1, 126.8, 126.5, 125.0 (q, *J* = 3.7 Hz), 124.9, 124.8, 124.6, 123.7 (q, *J* = 270.8 Hz), 100.2, 68.9, 68.6, 58.7, 48.4, 41.3, 35.8 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.89 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{25}ClF_3N_4O_2$: 589.1613; found: 589.1614.

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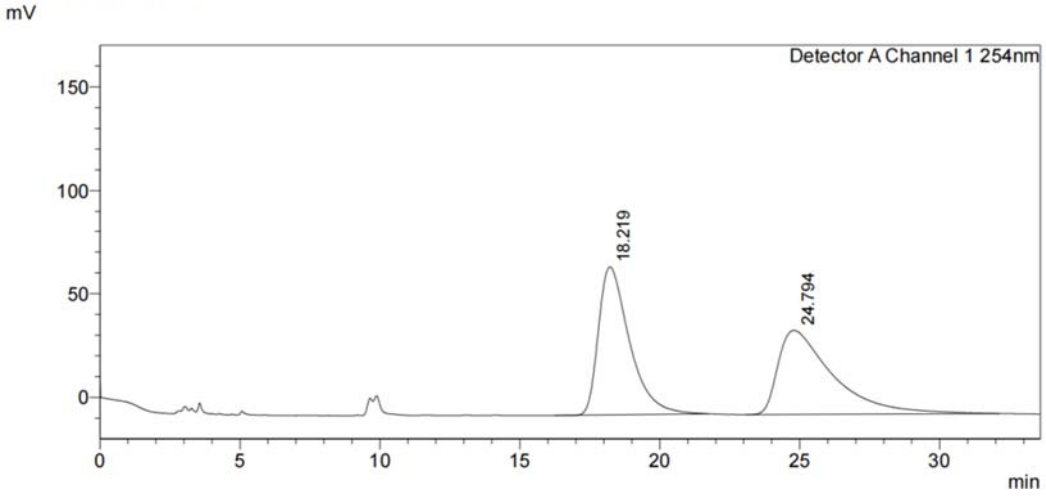

Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	18.219	16.267	5501595	71229	49.965
2	24.794	23.075	5509235	40458	50.035
Total			11010830	111688	100.000

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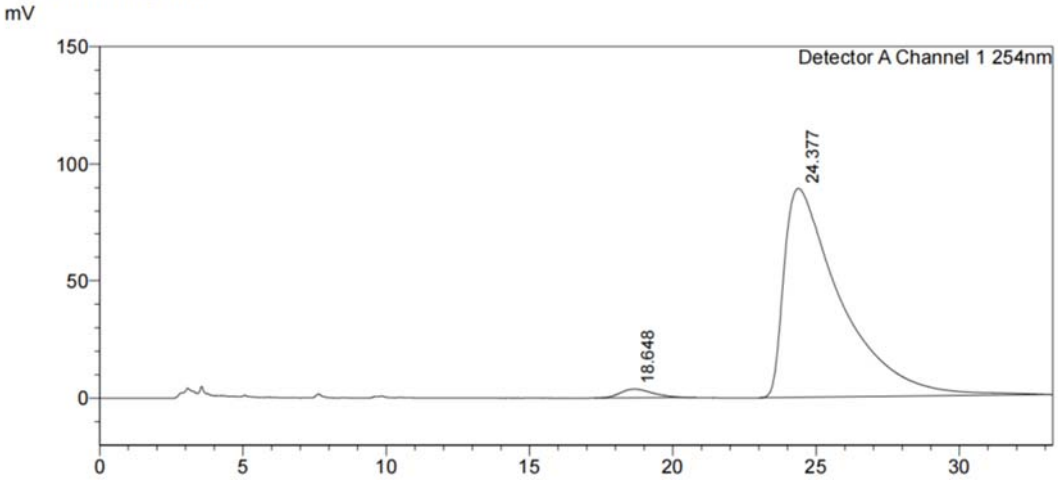
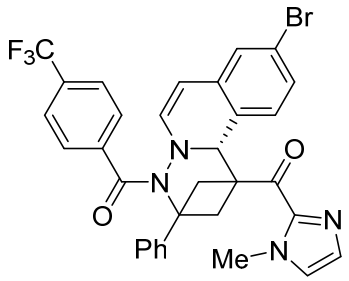


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	18.648	17.258	298409	3743	2.365
2	24.377	23.042	12319093	89281	97.635
Total			12617502	93024	100.000



(*R*)-3qw
$C_{32}H_{24}BrF_3N_4O_2$
M = 633.47 g/mol

(*R*)-(9-bromo-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3qw): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and (6-bromoisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2w**, 94.8 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3qw** as a yellow solid (78.5 mg, 62% yield).

(*R*)-**3qw**: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 3/1). Mp: 238-240 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 15.95 min, tr (minor) = 51.82 min) gave the isomeric composition of the product: 93% *ee*. $[\alpha]_D^{20}$ = -137.2 (*c* =1.03, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.24-7.20 (m, 2H), 7.01 (s, 1H), 6.91 (d, *J* = 1.2 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.69 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.79 (d, *J* = 8.0 Hz, 1H), 5.64 (s, 1H), 5.25 (d, *J* = 7.6 Hz, 1H), 3.77 (s, 3H), 3.66 (dd, *J* = 11.2, 8.8 Hz, 1H), 3.35 (d, *J* = 10.8 Hz, 1H), 3.27 (t, *J* = 8.8 Hz, 1H), 2.42 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.2, 173.6, 142.4, 141.5, 139.1, 133.2, 132.6 (q, *J* = 32.4 Hz), 129.9, 128.3, 128.2, 128.0, 127.7, 127.4, 127.1, 127.0, 126.8, 124.9 (q, *J* = 3.7 Hz), 124.8, 123.7 (q, *J* = 270.9 Hz), 122.6, 100.0, 68.9, 68.6, 58.6, 48.3, 41.2, 35.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.82 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{25}BrF_3N_4O_2$: 633.1107; found: 633.1105.

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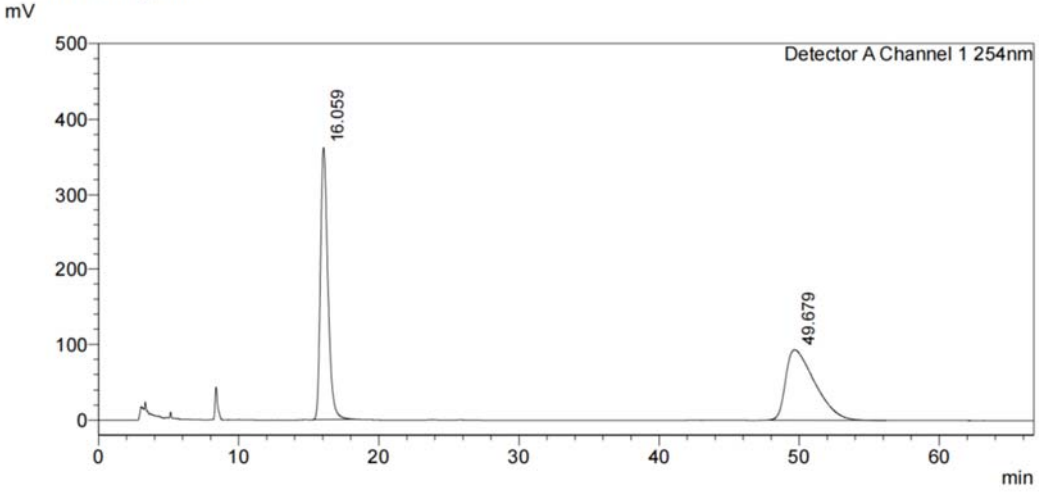

Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	16.059	15.317	13288574	361866	49.822
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Total			26672199	454541	100.000

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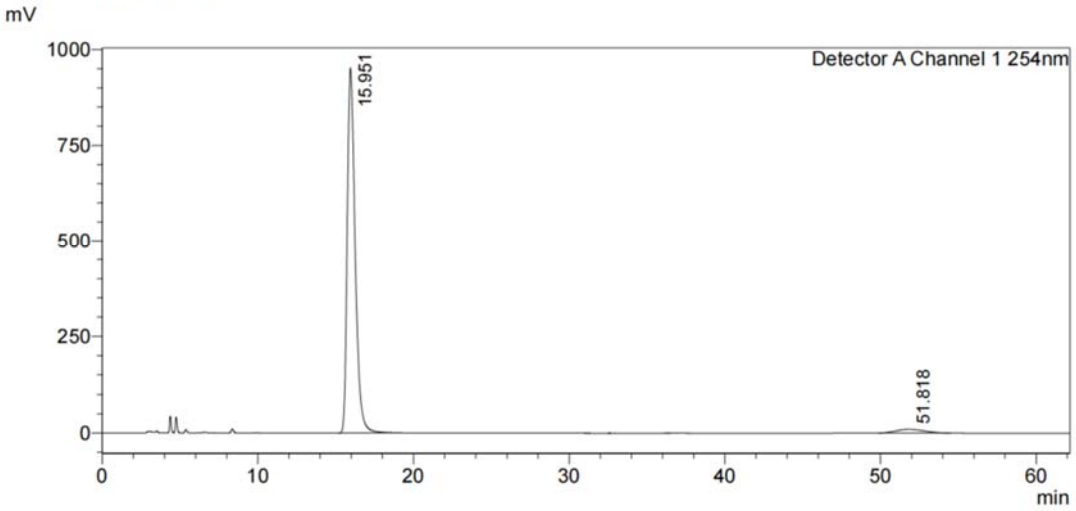
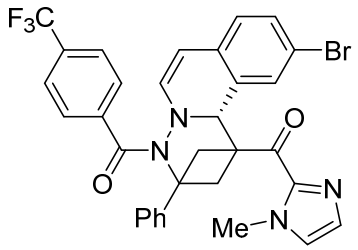


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	15.951	15.192	33524026	951070	96.553
2	51.818	49.892	1196951	9636	3.447
Total			34720977	960706	100.000



(*R*)-3qx
$C_{32}H_{24}BrF_3N_4O_2$
M = 633.47 g/mol

(*R*)-(10-bromo-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetra hydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl) phenyl)methanone ((*R*)-3qx) : Prepared from (1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and (7-bromoisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2x**, 94.8 mg, 0.24 mmol) at room temperature in CH_2Cl_2/MeCN (10/1) for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3qx** as a yellow solid (102.0 mg, 81% yield).

(*R*)-**3qx**: $\mathbf{R_f}$ = 0.5 (petroleum ether/EtOAc = 3/1). Mp: 144-147 °C. HPLC analysis (Chiralpak IC, ^{i}PrOH/hexane = 5/95, 1.0 mL/min, 254 nm; tr (major) = 30.69 min, tr (minor) = 24.61 min) gave the isomeric composition of the product: 95% *ee*. $[\alpha]_D^{20}$ = -147.2 (*c* = 0.63, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.24 (d, *J* = 6.8 Hz, 2H), 7.56 (d, *J* = 6.4 Hz, 2H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 5.84 (s, 1H), 5.55 (s, 1H), 5.27 (d, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 3.67 (t, *J* = 9.6 Hz, 1H), 3.41 (d, *J* = 10.4 Hz, 1H), 3.31 (t, *J* = 8.8 Hz, 1H), 2.45 (d, *J* = 11.6 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.2, 173.7, 142.6, 141.6, 140.8, 139.1, 132.1 (q, *J* = 32.4 Hz), 131.3, 130.08, 130.07, 130.0, 129.7, 128.3, 127.2, 127.1, 126.1, 124.94 (q, *J* = 3.7 Hz), 124.87, 123.7 (q, *J* = 270.8 Hz), 118.1, 100.3, 68.9, 68.5, 58.8, 48.3, 40.9, 35.8 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.86 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{25}BrF_3N_4O_2$: 633.1107; found: 633.1101.

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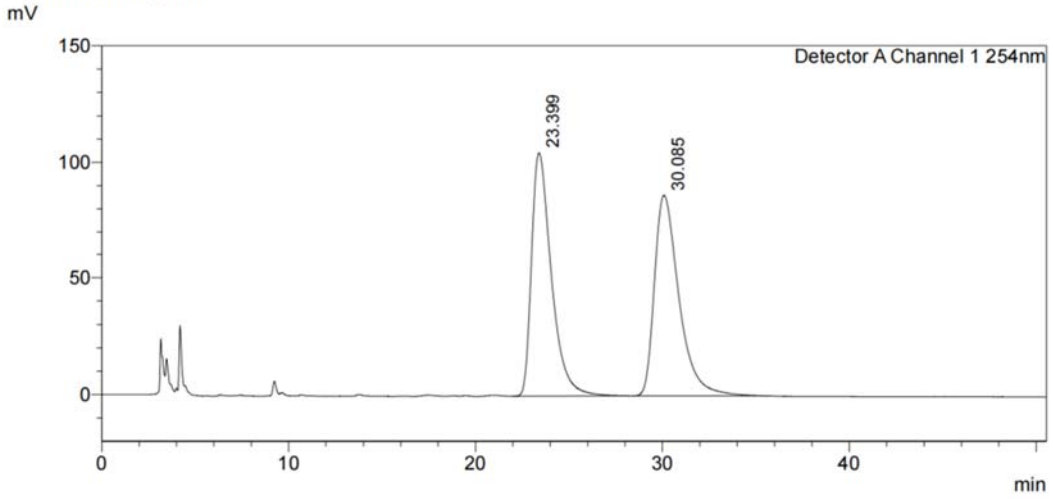

Peak#	Ret. Time	Peak End	Area	Height	Area%
1	23.399	28.250	7718403	104822	49.524
2	30.085	35.758	7866848	86374	50.476
Total			15585251	191196	100.000

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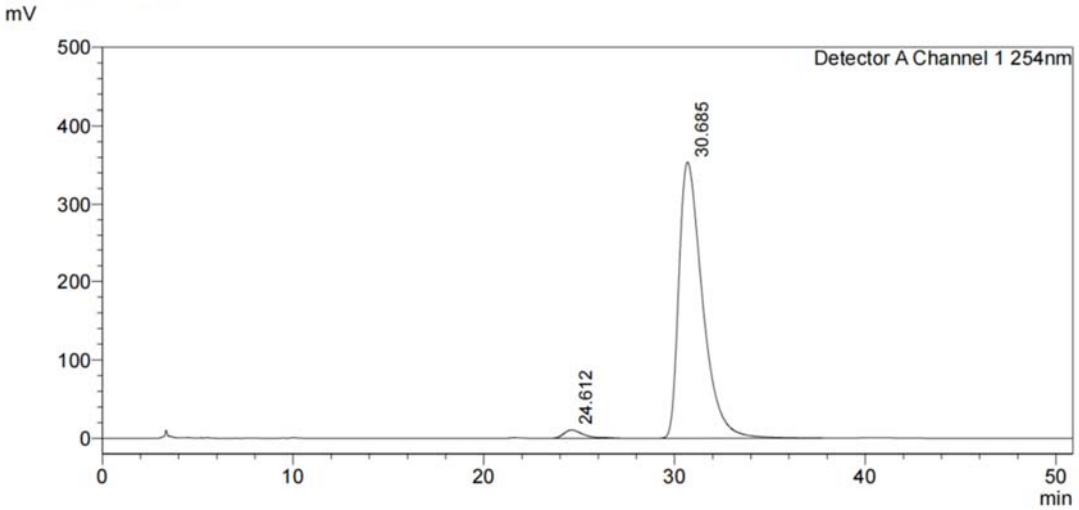
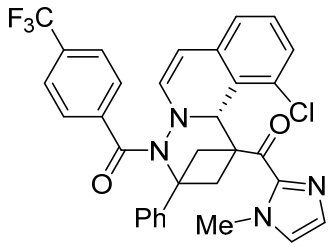


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	24.612	23.317	764263	10589	2.458
2	30.685	29.133	30326136	353497	97.542
Total			31090399	364086	100.000

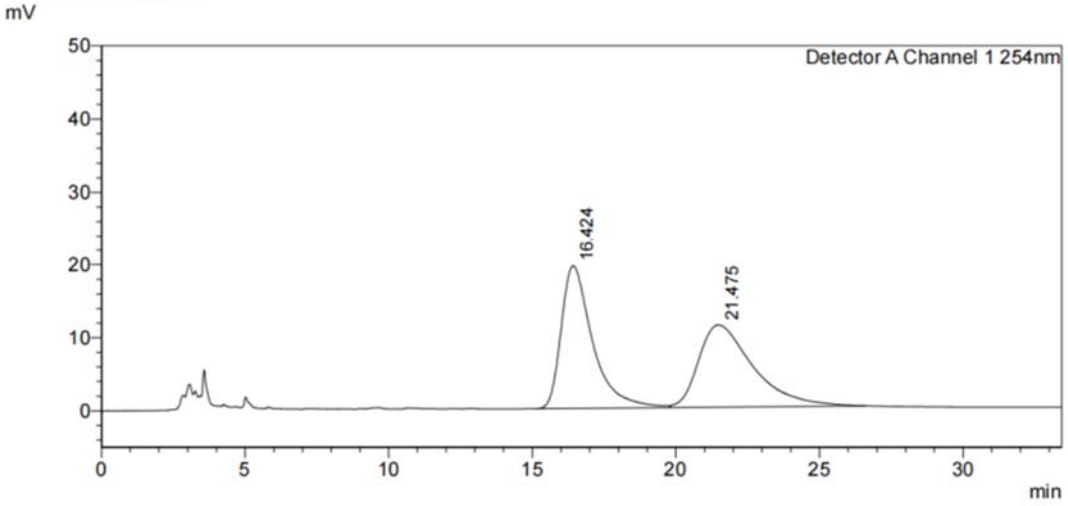


(*S*)-3qy
$C_{32}H_{24}ClF_3N_4O_2$
M = 589.02 g/mol

(*S*)-(11-chloro-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*S*)-3qy) : Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and (8-chloroisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2y**, 84.2mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*S*)-**3qy** as a yellow solid (97.5 mg, 83% yield).

(*S*)-**3qy**: $\mathbf{R_f}$ = 0.25 (petroleum ether/EtOAc = 3/1). Mp: 233-235 °C. HPLC analysis (Chiralpak OD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 19.39 min, tr (minor) = 16.71 min) gave the isomeric composition of the product: 93% *ee*. $[\alpha]_D^{20}$ = 9.4 (*c* = 2.00, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.82-6.79 (m, 2H), 6.75 (s, 1H), 6.67-6.64 (m, 2H), 5.51 (s, 1H), 5.45 (d, *J* = 7.6 Hz, 1H), 4.14 (dd, *J* = 10.8, 9.6 Hz, 1H), 3.79 (s, 3H), 3.60 (d, *J* = 11.2 Hz, 1H), 3.00 (t, *J* = 10.0 Hz, 1H), 2.50 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.0, 173.7, 142.6, 141.5, 141.2, 139.0, 134.5, 132.2 (d, *J* = 32.6 Hz), 131.9, 129.31, 129.26, 128.4, 128.3, 127.1, 126.4, 126.1, 125.8, 125.04, 124.99 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 269.7 Hz), 122.9, 101.6, 68.6, 67.0, 57.8, 45.7, 45.5, 35.8 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.89 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{25}ClF_3N_4O_2$: 589.1613; found:589.1602.

<Chromatogram>



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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2	21.475	19.800	1486423	11263	49.961
Total			2975196	30803	100.000

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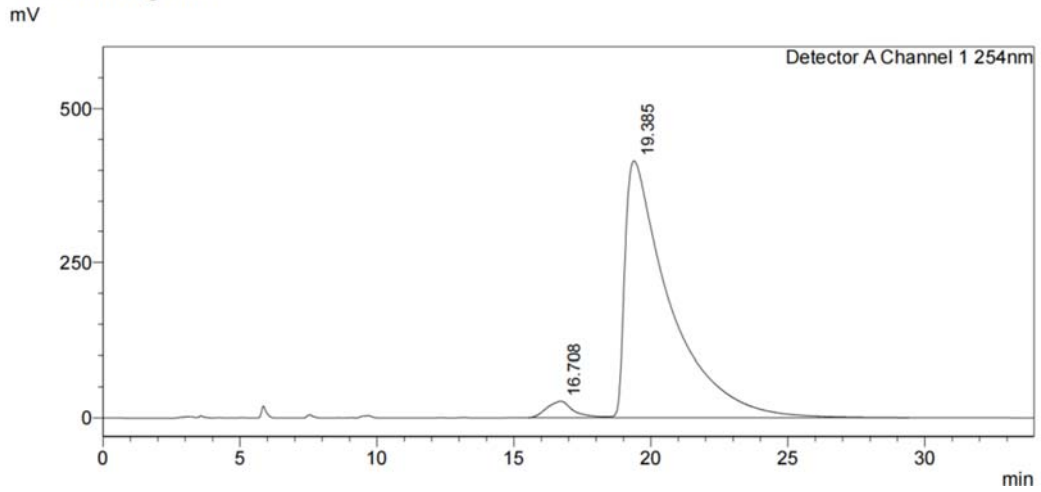
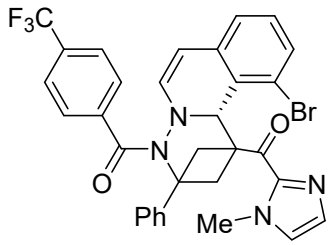


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	16.708	15.517	1753803	26544	3.587
2	19.385	18.300	47142976	415019	96.413
Total			48896779	441563	100.000

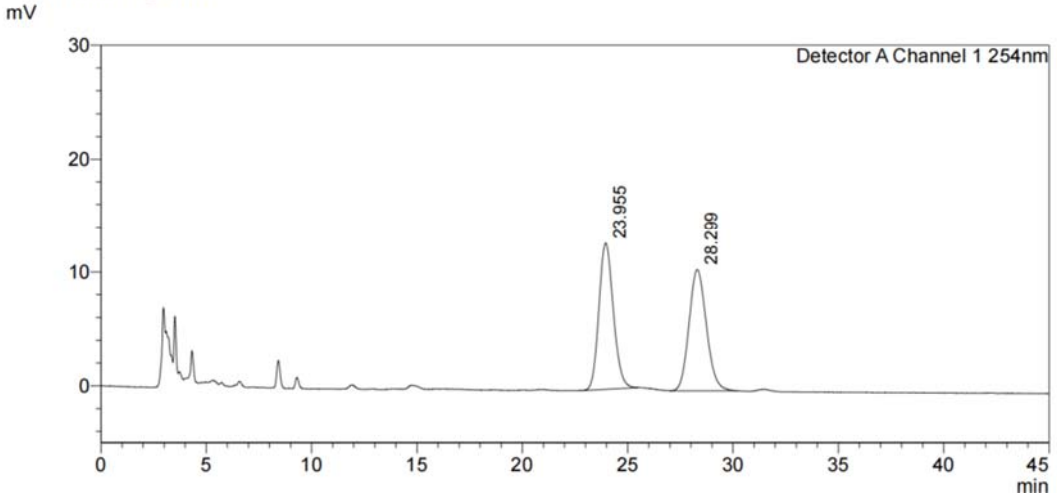


(*S*)-3qz
$C_{32}H_{24}BrF_3N_4O_2$
M = 633.47 g/mol

(*S*)-(11-bromo-1-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3qz): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q** 47.7 mg, 0.20 mmol) and (8-bromoisoquinolin-2-ium-2-yl)(4-(trifluoromethyl)benzoyl)amide (**2z,** 94.8mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*S*)-**3qz** as a white solid (88.7 mg, 70% yield).

(*S*)-**3qz**: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 210-212 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 26.81 min, tr (minor) = 23.47 min) gave the isomeric composition of the product: 97% *ee*. $[\alpha]_D^{20}$ = +12.0 (*c* = 0.88, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.80 (s, 1H), 6.73-6.67 (m, 3H), 5.48 (m, 1H), 5.43 (d, *J* = 7.6 Hz, 1H), 4.16 (dd, *J* = 11.6, 9.6 Hz, 1H), 3.80 (s, 1H), 3.62 (d, *J* = 10.8 Hz, 1H), 2.98 (t, *J* = 9.6 Hz, 2H), 2.50 (d, *J* = 11.6 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 189.9, 173.7, 142.6, 141.5, 141.2, 139.0, 135.0, 132.2 (q, *J* = 32.5 Hz), 129.54, 129.45, 129.3, 128.4, 128.2, 128.0, 127.1, 125.8, 125.04, 125.0 (q, *J* = 3.9 Hz), 123.7 (q, *J* = 270.5 Hz,), 123.5, 122.4, 101.8, 69.2, 68.6, 57.8, 46.0, 45.4, 35.9 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.87 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{32}H_{25}BrF_3N_4O_2$: 633.1107; found: 633.1102.

<Chromatogram>



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2	28.299	27.008	610140	10636	49.948
Total			1221553	23481	100.000

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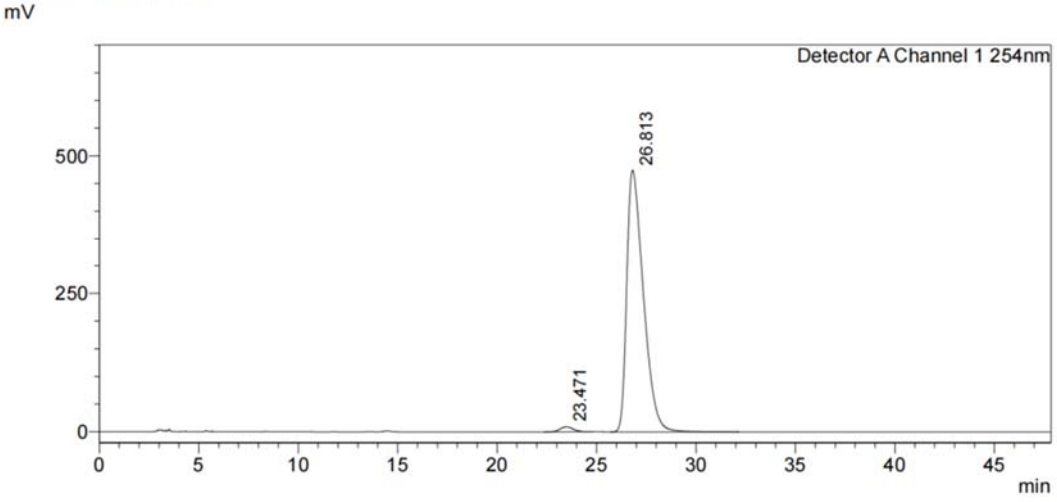
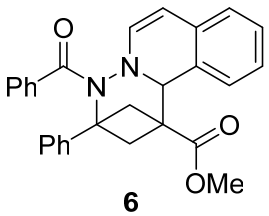


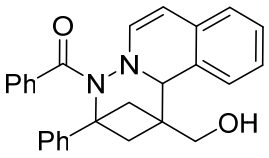
Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	23.471	22.367	424018	9133	1.519
2	26.813	25.700	27498640	474178	98.481
Total			27922658	483311	100.000



6

$C_{28}H_{24}N_2O_3$
M = 436.51 g/mol

Methyl-4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*] isoquinoline-1(11*bH*)-carboxylate (6): R_f = 0.5 (petroleum ether/EtOAc = 5/1). Mp: 209-211 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 7.2 Hz, 2H), 7.42-7.32 (m, 7H), 7.25-7.22 (m, 1H), 7.09 (t, *J* = 7.2 Hz, 1H) , 6.92 (t, *J* = 7.6 Hz, 1H), 6.86-6.84 (m, 2H), 6.77 (d, *J* = 7.6 Hz, 1H), 5.32 (d, *J* = 7.6 Hz, 1H), 5.16 (s, 1H), 3.56 (d, *J* = 11.2, 9.2 Hz, 1H), 3.41 (s, 3H), 3.23 (d, *J* = 10.4 Hz, 1H), 2.82 (d, *J* = 10.0 Hz, 1H), 2.33 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.2, 171.9, 141.6, 140.6, 135.4, 130.9, 130.8, 128.8, 128.3, 128.1, 128.0, 127.9, 127.2, 127.0, 125.6, 124.7, 124.5, 100.5, 68.2, 67.8, 53.6, 51.7, 45.7, 41.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{25}N_2O_3$: 437.1860; found: 437.1864.

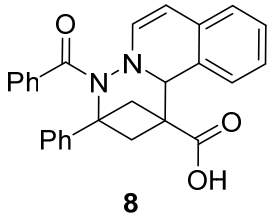


7

$C_{27}H_{24}N_2O_2$
M = 408.50 g/mol

(1-(hydroxymethyl)-3-phenyl-1,2,3,11*b*-tetrahydro-4*H*-1,3-methanopyridazino [6,1-*a*]isoquinolin-4-yl)(phenyl)methanone (7): R_f = 0.35 (petroleum ether/EtOAc = 5/1). Mp: 193-195 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 7.2 Hz, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.40-7.30 (m, 5H), 7.24-7.21 (m, 1H), 7.13-7.09 (m, 1H), 6.98-6.97 (m, 2H), 6.84 (d, *J* = 7.6 Hz, 2H), 5.27 (d, *J* = 7.6 Hz, 1H), 4.93 (s, 1H), 3.43 (d, *J* = 11.2 Hz, 1H), 3.34 (d, *J* = 11.6 Hz, 1H), 3.25 (t, *J* = 9.2 Hz, 1H), 3.00 (d, *J* = 10.0 Hz, 1H), 2.46 (t, *J* = 9.6 Hz, 1H), 2.03 (d, *J* = 10.8 Hz, 1H), 1.20 (s, br, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.2, 142.6, 141.7, 135.8, 131.5, 130.6, 128.6, 128.2, 128.1, 128.0,

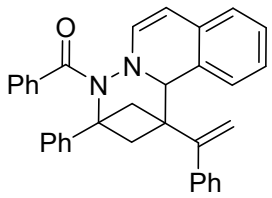
127.99, 127.8, 126.8, 125.6, 124.8, 124.3, 100.0, 69.7, 68.8, 64.5, 48.5, 43.9, 40.8 ppm. **HRMS** (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{27}H_{24}N_2O_2K$: 447.1469; found:447.1463.



8

$C_{27}H_{22}N_2O_3$
M = 422.48 g/mol

4-benzoyl-3-phenyl-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinoline-1(11b*H*)-carboxylic acid (8): R_f = 0.3 (petroleum ether/EtOAc = 1/2). Mp: 145-147 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.2 Hz, 2H), 7.41-7.33 (m, 7H), 7.24-7.22 (m, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.84-6.77 (m, 3H), 5.31 (d, *J* = 7.6 Hz, 1H), 5.19 (s, 1H), 3.54 (t, *J* = 10.4 Hz, 1H), 3.22 (d, *J* = 10.4 Hz, 1H), 2.81 (t, *J* = 9.6 Hz, 1H), 2.33 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 176.9, 175.3, 141.5, 140.5, 135.3, 130.9, 130.8, 128.8, 128.3, 128.1, 127.9, 127.7, 127.0, 125.8, 124.8, 124.4, 100.6, 68.0, 67.6, 53.5, 46.0, 41.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{27}H_{23}N_2O_3$: 423.1703; found: 423.1701.

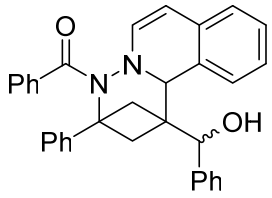


9

$C_{34}H_{28}N_2O$
M = 480.61 g/mol

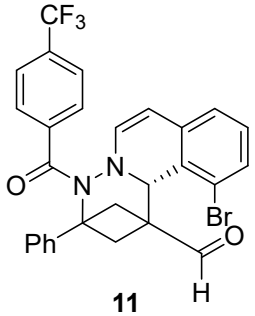
phenyl(3-phenyl-1-(1-phenylvinyl)-1,2,3,11b-tetrahydro-4*H*-1,3-methano pyridazino[6,1-*a*]isoquinolin-4-yl)methanone (9): R_f = 0.7 (petroleum ether/EtOAc = 5/1). Mp: 182-184 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.2 Hz, 2H), 7.41-7.30 (m, 7H), 7.22-7.14(m, 6H), 6.96-6.90 (m, 2H), 6.78 (d, *J* = 7.2 Hz, 1H), 6.69-6.61 (m, 2H), 5.35 (s, 1H), 5.34 (s, 1H), 5.21 (s, 1H), 4.76 (s, 1H), 3.70 (t, *J* = 10.0 Hz, 1H), 3.09 (d, *J* = 10.0 Hz, 1H), 2.96 (d, *J* = 9.6 Hz, 1H), 2.14 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C**

NMR (100 MHz, $CDCl_3$): δ 175.1, 150.0, 142.2, 141.2, 139.2, 135.6, 131.1, 130.7, 129.5, 128.9, 128.3, 128.14, 128.09, 128.06, 127.8, 127.3, 126.7, 126.5, 125.0, 124.8, 123.7, 115.6, 100.1, 71.7, 68.2, 53.5, 48.8, 45.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{34}H_{29}N_2O$: 481.2274; found:484.2267.



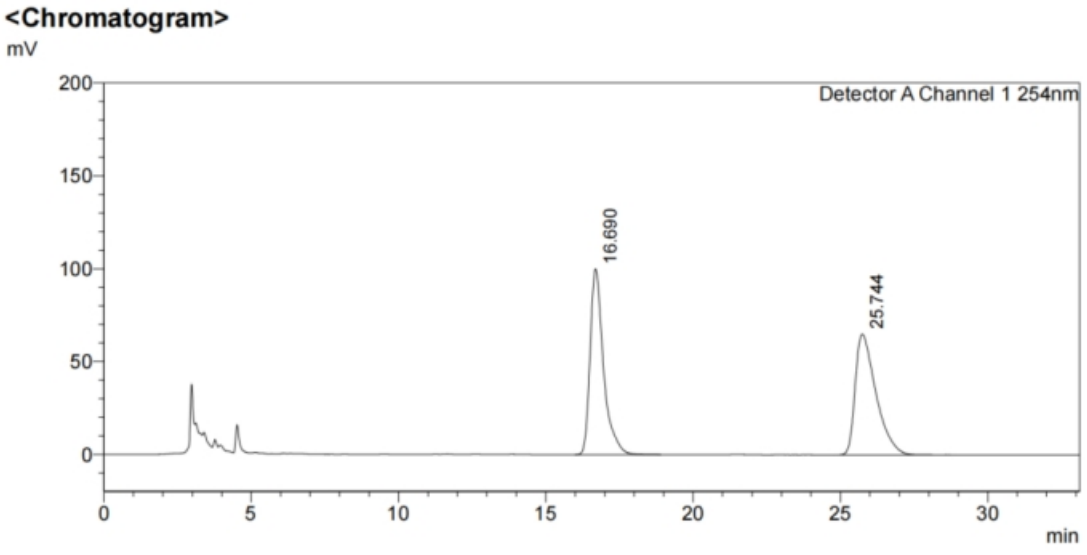
10
$C_{33}H_{28}N_2O_2$
M = 484.60 g/mol
d.r. = 5:1

(1-(hydroxy(phenyl)methyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methano pyridazino[6,1-*a*]isoquinolin-4-yl)(phenyl)methanone (10): R_f (major)= 0.5 (petroleum ether/EtOAc = 5/1). Mp: 258-260 °C. **^{1}H NMR for the major isomer** (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.2 Hz, 2H), 7.40-7.29 (m, 6H), 7.25-7.23 (m, 2H), 7.21-7.13 (m, 6H), 7.01-6.97 (m, 2H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 5.38 (d, *J* = 7.6 Hz, 1H), 4.93 (s, 1H), 4.74 (s, 1H), 3.36-3.27 (m, 1H), 2.34 (d, *J* = 4.0 Hz, 2H), 2.10 (d, J = 11.2 Hz, 1H), 1.58 (br s, 1H) ppm. **^{13}C NMR for the major isomer** (100 MHz, $CDCl_3$): δ 175.0, 142.5, 142.2, 139.6, 135.6, 132.1, 130.7, 129.1, 128.3, 128.2, 128.1, 127.82, 127.76, 127.1, 126.6, 126.0, 124.6, 124.3, 100.3, 72.4, 70.7, 68.9, 51.8, 45.0, 38.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{29}N_2O_2$: 485.2224; found: 485.2216.



11
$C_{28}H_{20}BrF_3N_2O_2$
M = 553.38 g/mol

(*S*)-11-bromo-3-phenyl-4-(4-(trifluoromethyl)benzoyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinoline-1(11b*H*)-carbaldehyde (11): R_f = 0.5 (petroleum ether/EtOAc = 5/1). Mp: 67-69 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 16.62 min, tr (minor) = 26.05 min gave the isomeric composition of the product: 96% *ee*. $[\alpha]_D^{20}$ = +10.3 (*c* = 0.40, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.33 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.21-7.17 (m, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.79 (t, *J* = 8.4 Hz, 2H), 5.27 (s, 1H), 5.25 (s, 1H), 3.52 (t, *J* = 9.6 Hz, 1H), 3.44 (d, *J* = 10.4 Hz, 1H), 2.45 (t, *J* = 9.2 Hz, 1H), 2.02 (d, *J* = 10.8 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 198.0, 173.7, 141.3, 141.0, 138.7, 134.0, 132.5 (q, *J* = 32.5 Hz), 130.6, 130.5, 128.41, 128.40, 127.4, 125.9, 125.1 (q, *J* = 3.7 Hz), 124.8, 124.2, 123.7, 123.6 (q, *J* = 271.0 Hz), 100.9, 69.1, 67.5, 54.8, 43.6, 41.2 ppm. **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -62.90 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{28}H_{20}BrF_3N_2O_2Na$: 575.0550; found:575.0531.



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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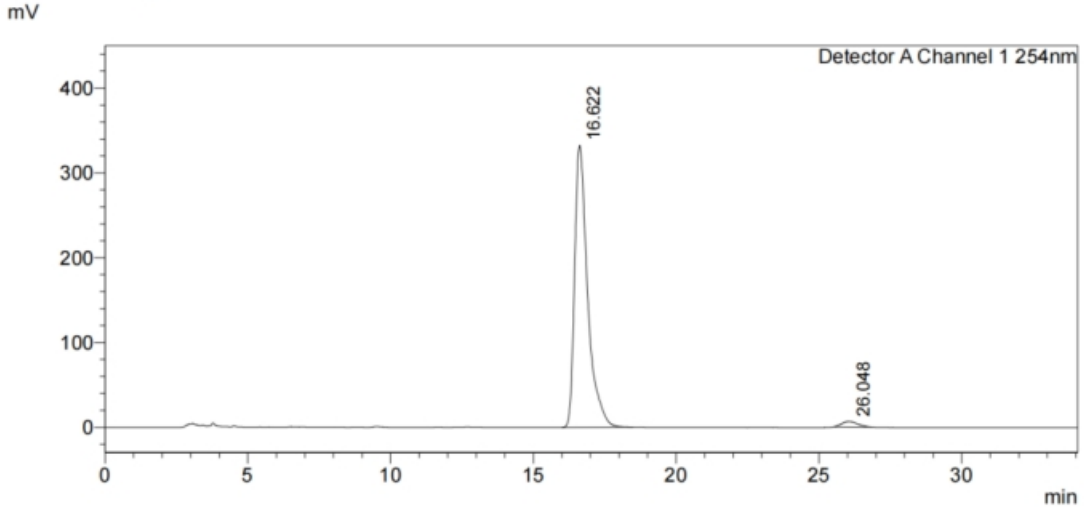
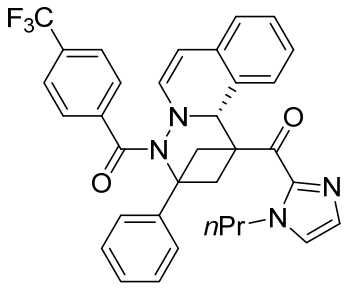
2	25.744	24.842	3188156	64975	50.122
Total			6360752	165019	100.000

<Chromatogram>



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	16.622	16.008	10509619	332491	97.785
2	26.048	25.533	238104	6252	2.215
Total			10747723	338743	100.000

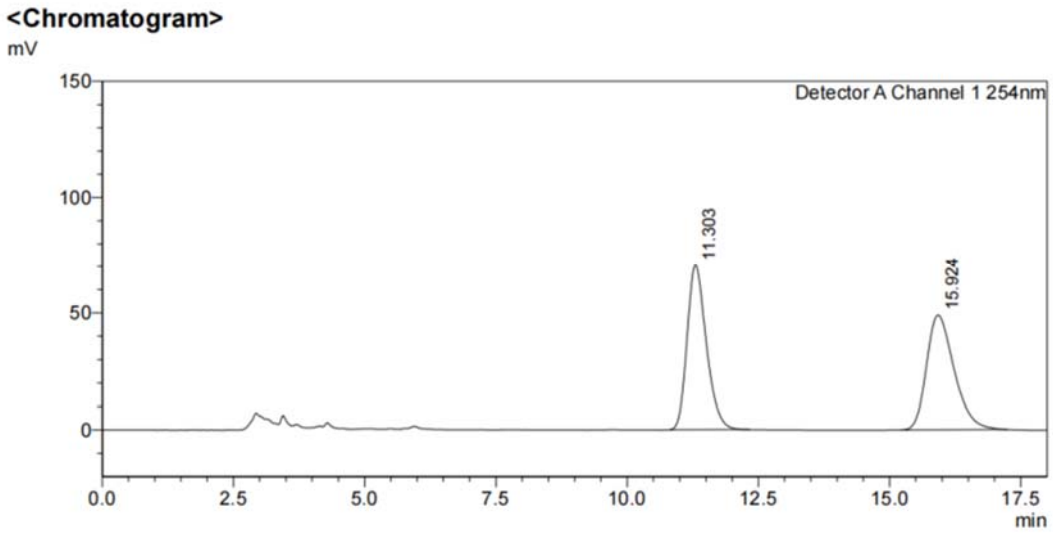


(*R*)-3aad
$C_{34}H_{29}F_3N_4O_2$
M = 582.63 g/mol

(*R*)-(3-phenyl-1-(1-propyl-1*H*-imidazole-2-carbonyl)-1,2,3,11b-tetrahydro-4*H*-1,3-methano pyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3aad) : Prepared from (3-phenylbicyclo[1.1.0]butan-1-yl)(1-propyl-1*H*-imidazol-2-yl)methanone (**1aa**, 53.3 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3aad** as a white solid (66.4 mg, 57% yield).

(*R*)-**3aad**: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 238-240 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 11.20 min,

tr (minor) = 15.84 min) gave the isomeric composition of the product: 88% *ee*. $[\alpha]_D^{20}$ = -121.5 (*c* = 1.00, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$):δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.25-7.21 (m , 2H), 7.05 (s, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.80 (dd, *J* = 11.2, 7.6 Hz, 2H), 6.56 (d, *J* = 7.6 Hz, 1H), 5.97 (d, *J* = 7.6 Hz, 1H), 5.71 (s, 1H), 5.33 (d, *J* = 7.6 Hz, 1H), 4.29-4.22 (m, 1H), 4.00-3.93(m , 1H), 3.73 (dd, *J* = 11.2, 8.4 Hz, 1H), 3.37-3.28 (m, 2H), 2.39 (d, *J* = 11.6 Hz, 1H), 1.62-1.53 (m, 2H), 0.82 (t, *J* = 7.2 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.3, 173.6, 142.0, 141.8, 140.4, 132.0 (q, *J* = 32.4 Hz), 139.3, 129.8, 128.5, 128.4, 128.3, 128.2, 127.0, 126.7, 126.0, 125.3, 124.89, 124.86 (q, *J* = 3.6 Hz), 124.8, 123.7 (q, *J* = 271.5 Hz), 101.3, 69.1, 68.8, 59.0, 50.0, 48.6, 41.2, 23.8, 11.0 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.86 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{34}H_{29}F_3N_4O_2Na$: 605.2135; found: 605.2137.



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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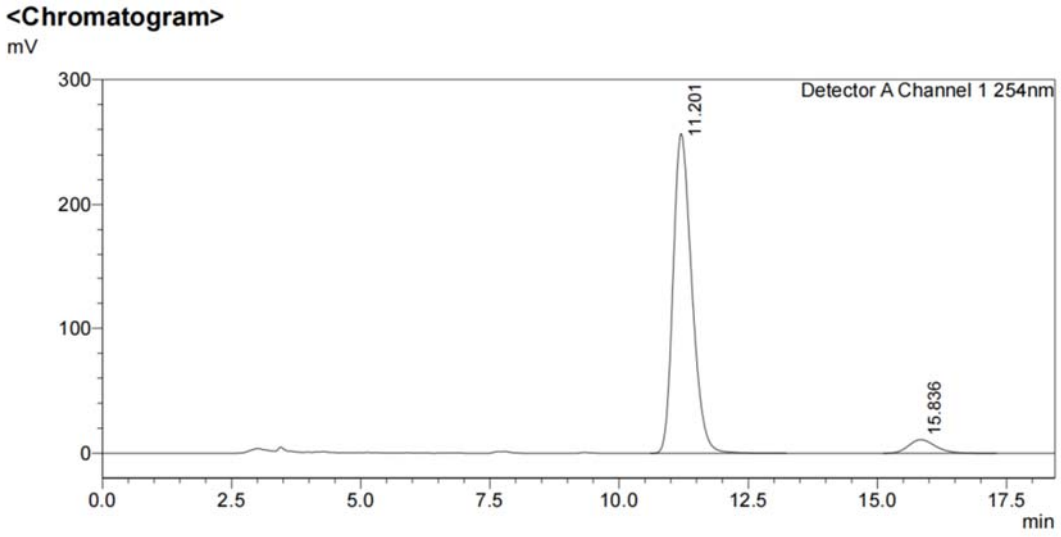
2	15.924	15.200	1794378	48957	50.000
Total			3588737	119397	100.000



Peak#	Ret. Time	Peak Start	Area	Height	Area%
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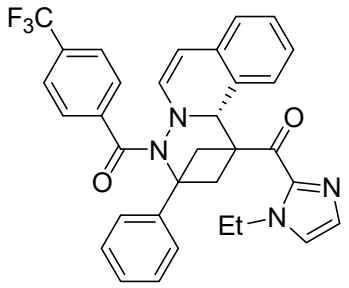
2	15.836	15.117	397492	10842	5.807
Total			6844979	267443	100.000

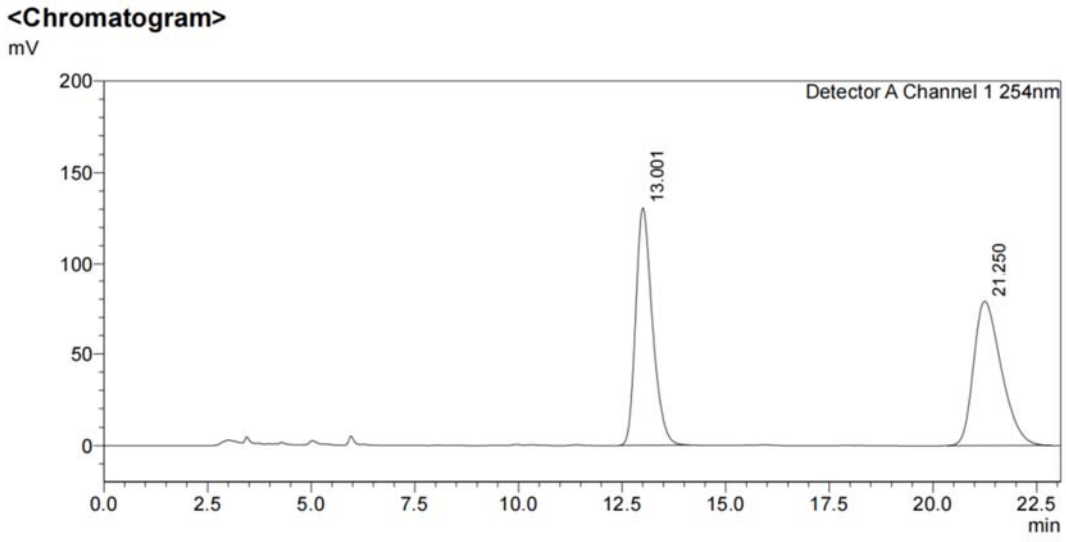


(*R*)-3ccd
$C_{33}H_{27}F_3N_4O_2$
M = 568.60 g/mol

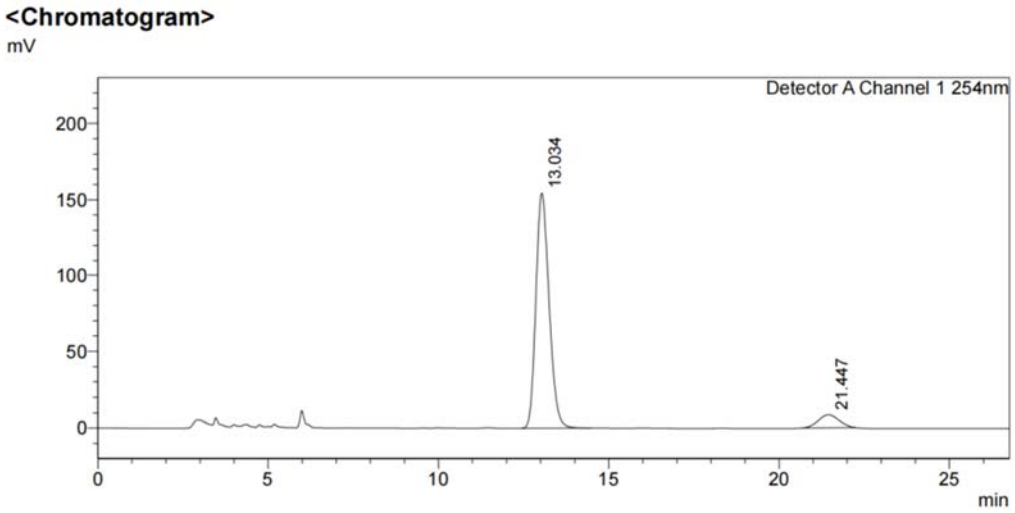
(*R*)-(1-ethyl-1H-imidazol-2-yl)(3-phenyl-4-(4-(trifluoromethyl)benzoyl)-3,4-dihydro-2*H*-1,3-methano pyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone ((*R*)-3ccd) : Prepared from (1-ethyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1cc**, 50.5 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3ccd** as a white solid (51.4 mg, 45% yield).

(*R*)-**3ccd**: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 220-222 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 13.03 min,

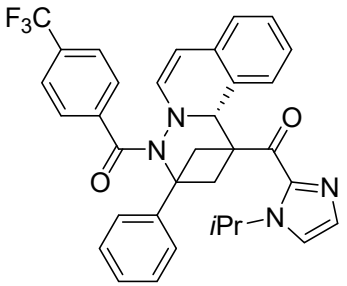
tr (minor) = 21.45 min) gave the isomeric composition of the product: 84% *ee*. $[\alpha]_D^{20}$ = -69.1 (*c* = 1.00, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.35 (d, *J* = 7.2 Hz, 2H), 7.24-7.22 (m, 2H), 7.07 (s, 1H), 6.94 (d, *J* = 7.2 Hz, 1H), 6.80 (dd, *J* = 12.0, 7.6 Hz, 2H), 6.56 (t, *J* = 7.2 Hz, 1H), 5.94 (d, *J* = 7.6 Hz, 1H), 5.70 (s, 1H), 5.33 (d, *J* = 8.0 Hz, 1H), 4.36-4.27 (m, 1H), 4.12-4.03 (m, 1H), 3.74 (dd, *J* = 11.2, 8.8Hz, 1H), 3.38-3.28 (m, 1H), 2.40 (d, *J* = 11.2, 2H), 1.21 (t, *J* = 7.2 Hz, 3H) ppm.**^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.3, 173.6, 142.0, 141.8, 140.5, 139.3, 132.1 (q, *J* = 32.5 Hz), 131.0, 130.1, 128.5, 128.4, 128.3, 128.2, 127.0, 126.7, 125.3, 125.1, 124.90, 124.89 (q, *J* =3.6 Hz), 124.8, 123.7 (q, *J* =270.6 Hz), 101.3, 69.1, 68.9, 59.0, 48.6, 43.5, 41.2, 16.1. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.87 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{33}H_{27}F_3N_4O_2Na$: 591.1978; found: 591.1982.



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	13.001	12.442	3649910	130514	49.870
2	21.250	20.350	3668973	78883	50.130
Total			7318883	209397	100.000



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	13.034	12.450	4151647	154383	91.997
2	21.447	20.683	361149	8559	8.003
Total			4512796	162941	100.000

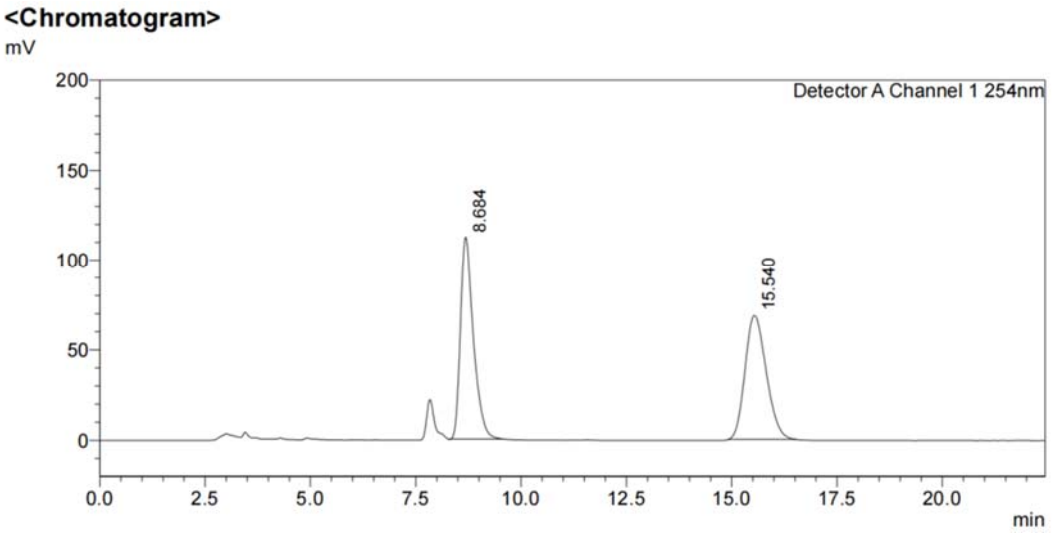


(*R*)-3ddd
$C_{34}H_{29}F_3N_4O_2$
M = 582.63 g/mol

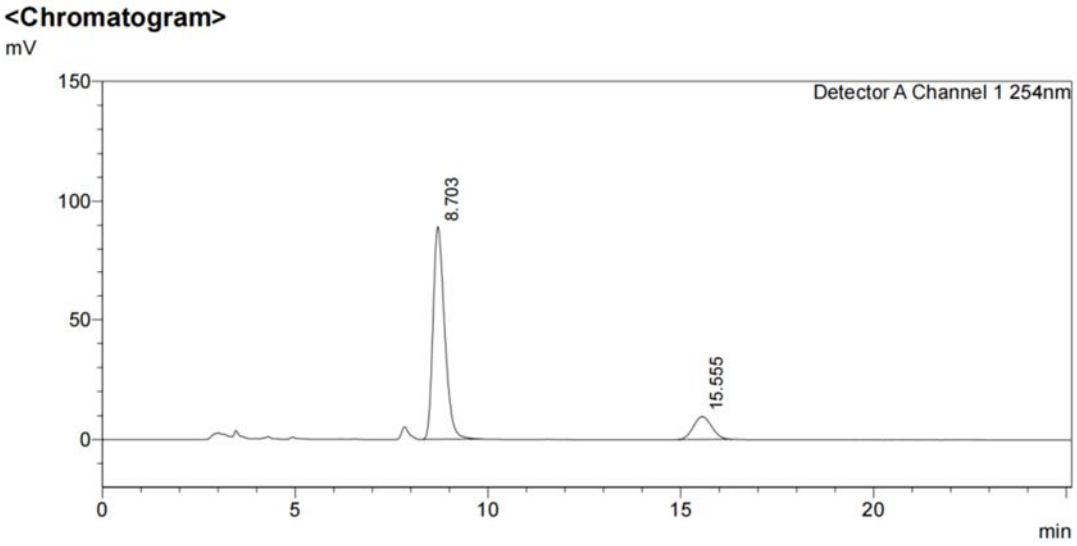
(*R*)-(1-isopropyl-1*H*-imidazol-2-yl)(3-phenyl-4-(4-(trifluoromethyl)benzoyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone ((*R*)-3ddd) : Prepared from (1-isopropyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1dd**, 53.3 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded (*R*)-**3ddd** as a white solid (25.5 mg, 22% yield).

(*R*)-**3ddd**: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 210-212 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 8.70 min, tr

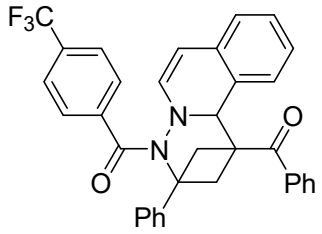
(minor) = 15.56 min) gave the isomeric composition of the product: 71% *ee*. $[\alpha]_D^{20}$ = -90.0 (*c* =0.80, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.26-7.22 (m, 3H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.80 (dd, *J* = 12.0, 8.0 Hz, 2H), 6.55, (t, *J* = 7.6 Hz, 1H), 5.93 (d, *J* = 7.6 Hz, 1H), 5.71 (s, 1H), 5.33 (d, *J* = 7.6 Hz, 1H), 5.28-5.20 (m, 1H), 3.73 (dd, *J* = 10.4, 9.2 Hz, 1H), 3.38-3.29 (m, 2H), 2.40 (d, *J* = 11.6 Hz, 1H), 1.39 (d, *J* = 6.4 Hz, 3H), 1.22 (d, *J* = 6.4 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.7, 173.6, 141.8, 140.5, 139.3, 132.0 (q, *J* = 32.5 Hz), 131.0, 130.4, 128.5, 128.4, 128.2, 127.0, 126.8, 125.3, 124.90 (q, *J* = 3.5 Hz), 124.89, 124.8, 123.7 (q, *J* = 270.8 Hz), 121.0, 101.3, 69.1, 68.9, 59.3, 49.0, 48.7, 41.2, 23.5, 23.1 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.88 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{34}H_{29}F_3N_4O_2Na$: 605.2135; found: 605.2127.



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	8.684	8.267	2388719	112206	49.880
2	15.540	14.925	2400196	68502	50.120
Total			4788916	180708	100.000



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	8.703	8.308	1864704	89211	85.497
2	15.555	14.933	316315	9573	14.503
Total			2181019	98784	100.000

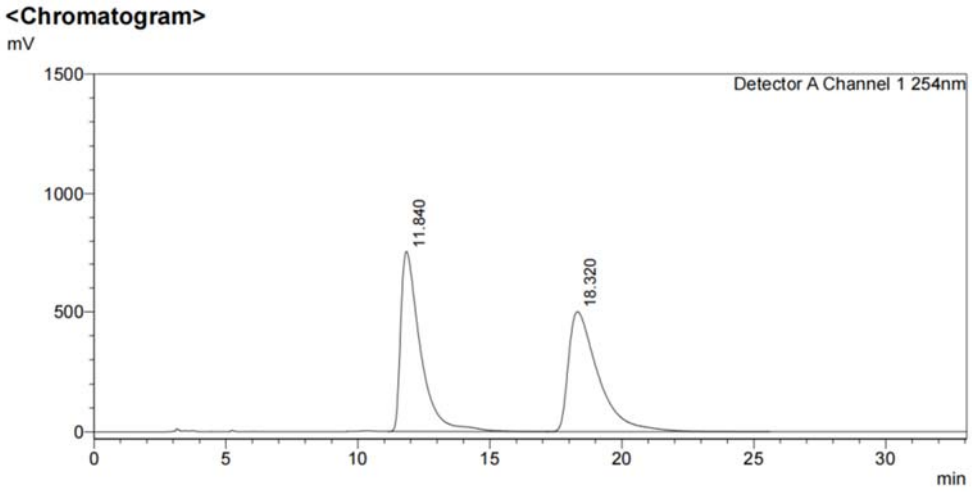


3gd
$C_{34}H_{25}F_3N_2O_2$
M = 550.58 g/mol

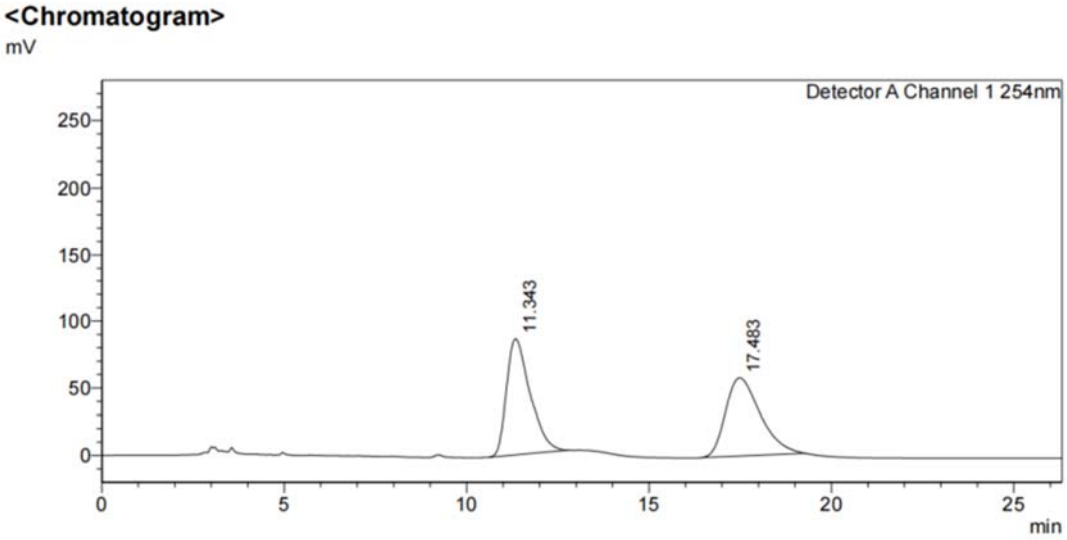
(1-benzoyl-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone (3gd): Prepared from (phenyl(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1g**, 46.9 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3gd** as a yellow solid (8.0 mg, 8% yield).

3gd: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). Mp: 120-122 °C. HPLC analysis (Chiralpak OD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 11.34 min,

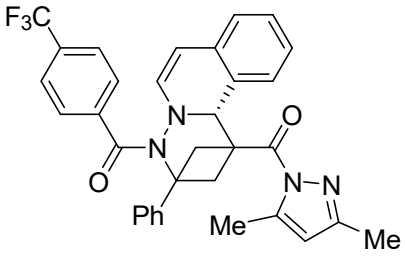
tr (minor) = 17.48 min) gave the isomeric composition of the product: 0% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.63-7.58 (m, 4H), 7.42-7.32 (m, 5H), 7.27-7.21 (m, 3H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.89-6.80 (m, 2H), 6.54 (t, *J* = 7.6 Hz, 1H), 6.47 (d, *J* = 7.6 Hz, 1H), 5.44-5.43 (m, 2H), 3.89 (t, *J* =9 .6 Hz, 1H), 3.29 (d, *J* = 10.4 Hz, 1H), 3.04 (t, *J* = 9.2 Hz, 1H), 2.59 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 201.0, 174.0, 141.2, 140.4, 139.0, 135.9, 132.7, 132.3 (q, *J* = 32.5 Hz), 130.5, 128.8, 128.6, 128.3, 128.23, 128.2, 128.1, 127.8, 127.2, 126.1, 125.0 (q, *J* = 3.5 Hz), 124.8, 124.6, 123.7 (q, *J* = 271.1 Hz), 101.0, 69.8, 68.3, 58.2, 47.4, 43.4 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.85 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{34}H_{25}F_3N_2O_2Na$: 573.1765; found: 573.1760.



Peak#	Ret. Time	Peak Start	Area	Height	Height%
1	11.840	11.125	38977237	751335	60.078
2	18.320	17.167	39149688	499266	39.922
Total			78126925	1250601	100.000



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	11.343	10.608	3874538	86163	50.200
2	17.483	16.442	3843672	57937	49.800
Total			7718210	144100	100.000

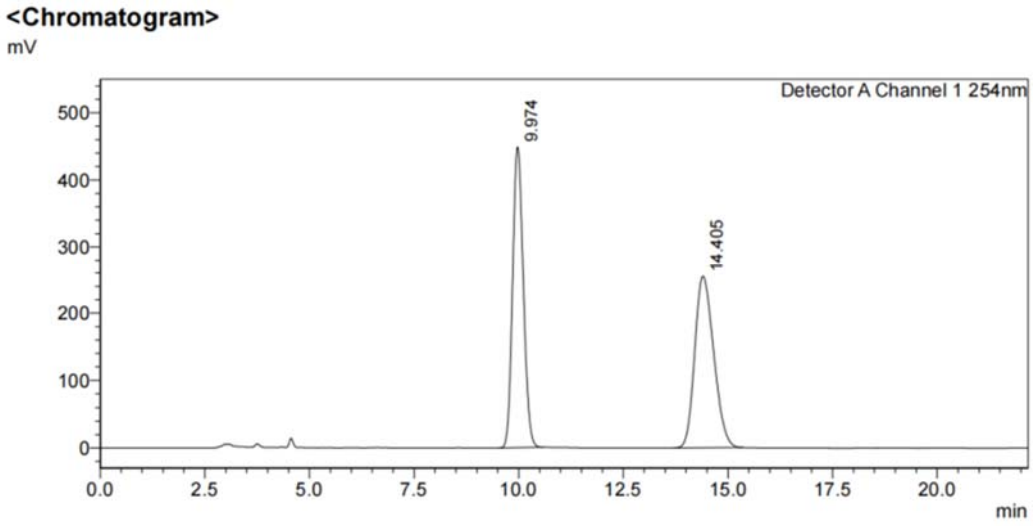


(*R*)-3ad
$C_{33}H_{27}F_3N_4O_2$
M = 568.60 g/mol

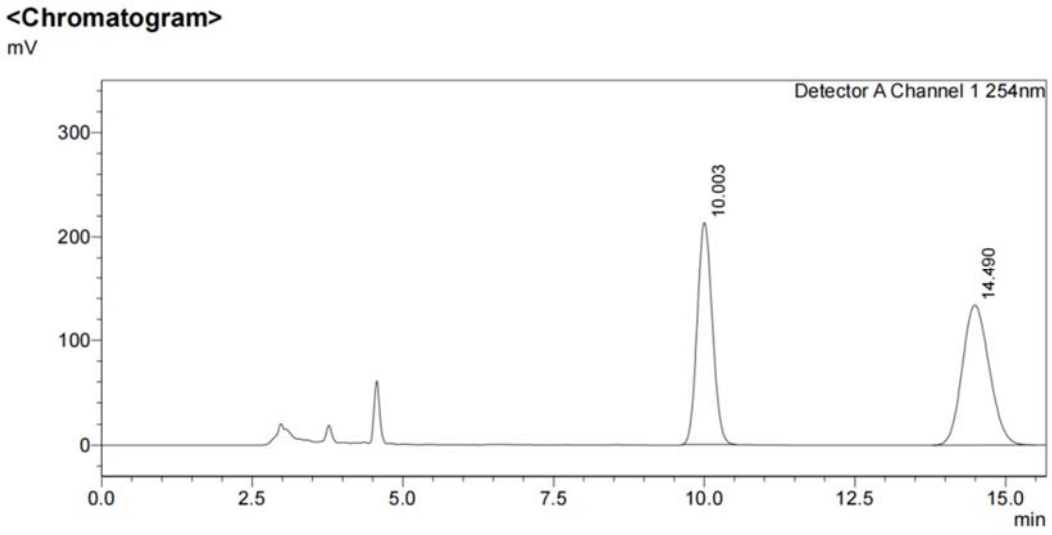
(*R*)-(3,5-dimethyl-1H-pyrazol-1-yl)(3-phenyl-4-(4-(trifluoromethyl)benzoyl)-3,4-dihydro-2*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-1(11b*H*)-yl)methanone ((*R*)-3ad): (3,5-dimethyl-1H-pyrazol-1-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 50.5 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **(*R*)-3ad** as a white solid (31.8 mg, 28% yield).

(*R*)-3ad: $\mathbf{R}_f$ = 0.4 (petroleum ether/EtOAc = 10/1). Mp: 210-212 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 14.49 min,

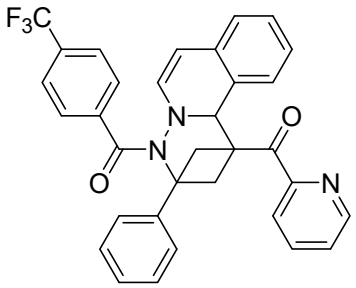
tr (minor) = 10.00 min) gave the isomeric composition of the product: 6% *ee*. $[\alpha]_D^{20}$ = -9.4 (*c* = 1.00, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.27-7.24 (m, 1H), 6.99 (t, *J* = 7.2 Hz, 1H), 6.81 (d, *J* = 6.4 Hz, 2H), 6.64 (t, *J* = 7.2 Hz, 1H), 5.96 (s, 1H), 5.80 (s, 1H), 5.56 (s, 1H), 5.34 (d, *J* = 8.0 Hz, 1H), 3.76 (t, *J* = 10.4 Hz, 1H), 3.42 (d, *J* = 10.8 Hz, 1H), 3.23 (t, *J* = 9.2 Hz, 1H), 2.45 (d, *J* = 11.6 Hz, 1H), 2.30 (s, 3H), 2.27 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 173.8, 171.5, 152.9, 144.5, 141.5, 140.2, 139.2, 132.2 (q, *J* = 32.4 Hz), 130.9, 128.7, 128.30, 128.28, 128.1, 127.1, 126.2, 125.7, 125.0 (q, *J* = 3.8 Hz), 124.8, 124.6, 123.7 (q, *J* = 270.7 Hz), 111.0, 101.4, 68.7, 68.3, 56.6, 48.7, 41.6, 13.9, 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.89 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{33}H_{27}F_3N_4O_2Na$: 591.1978; found:591.1976.



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	9.974	9.508	7966208	448431	49.765
2	14.405	13.692	8041344	254766	50.235
Total			16007552	703197	100.000



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	10.003	9.642	3705739	212856	47.139
2	14.490	13.800	4155572	133598	52.861
Total			7861311	346454	100.000



3od

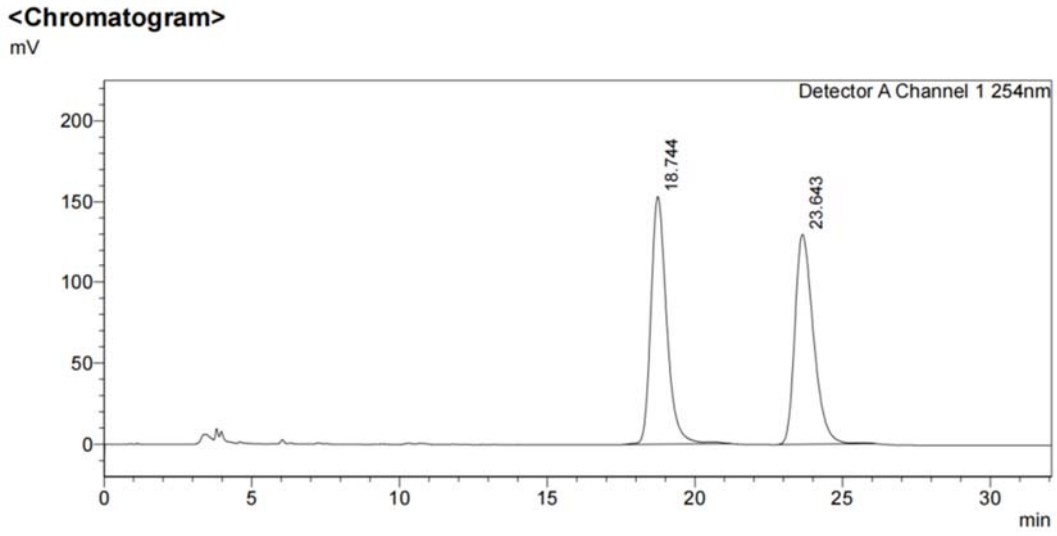
$C_{33}H_{24}F_3N_3O$

M = 551.57 g/mol

(3-phenyl-1-picolinoyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*]isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone (3od) : Prepared from (3-phenylbicyclo[1.1.0]butan-1-yl)(pyridin-2-yl)methanone (**1o**, 47.1 mg, 0.2 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2d**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3od** as a yellow solid (97.2 mg, 88% yield)

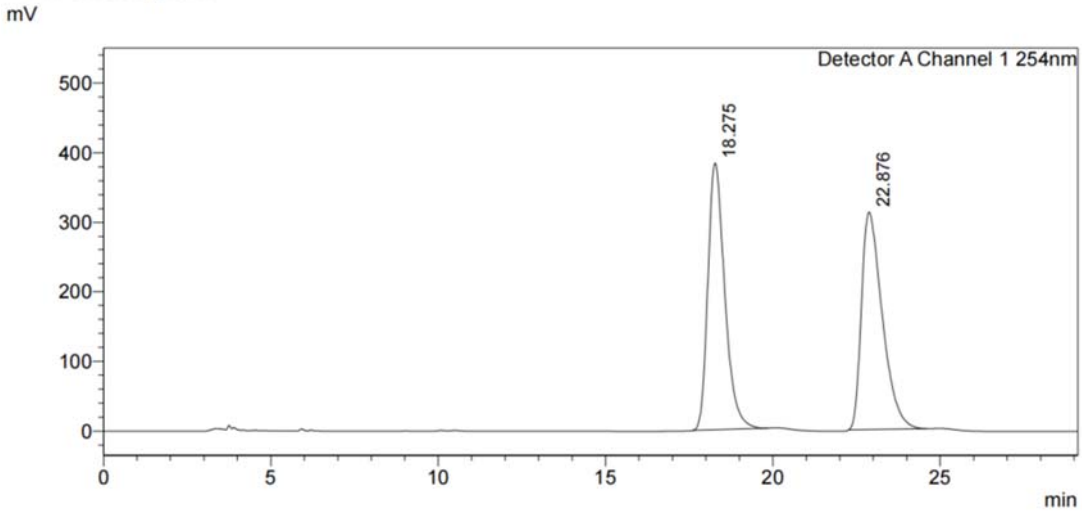
3od: $\mathbf{R_f}$ = 0.25 (petroleum ether/EtOAc = 3/1). Mp: 110-112 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 18.28 min,

tr (minor) = 22.88 min) gave the isomeric composition of the product: 0% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.71 (d, *J* = 4.0 Hz, 1H), 7.85-7.76 (m, 4H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.45-7.40 (m, 3H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.25-7.23 (m, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.50 (t, *J* = 7.6 Hz, 1H), 6.16 (d, *J* = 7.6 Hz, 1H), 5.84 (s, 1H), 5.35 (d, *J* = 7.6 Hz, 1H), 3.86-3.82 (m, 1H), 3.25-3.19 (m, 2H), 2.39 (d, *J* = 11.6 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 200.0, 173.8, 153.1, 149.0, 141.7, 140.2, 139.3, 136.9, 132.1 (q, *J* = 32.4 Hz), 130.9, 128.5, 128.3, 127.01, 126.98, 126.9, 125.6, 125.0 (q, *J* = 3.7 Hz), 124.8, 124.8, 123.7 (q, *J* = 270.8 Hz), 122.9, 101.3, 69.1, 69.0, 58.9, 48.1, 42.0 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.88 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{25}F_3N_3O$: 552.1893; found: 552.1887.

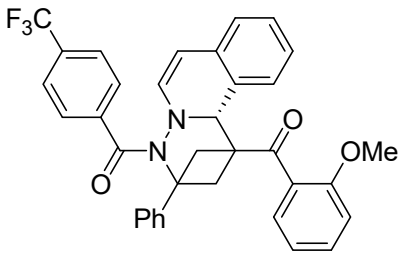


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	18.744	17.542	5693996	153356	50.086
2	23.643	22.842	5674554	129957	49.914
Total			11368550	283312	100.000

<Chromatogram>



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	18.275	17.608	13460154	383511	49.879
2	22.876	22.267	13525711	313019	50.121
Total			26985865	696530	100.000

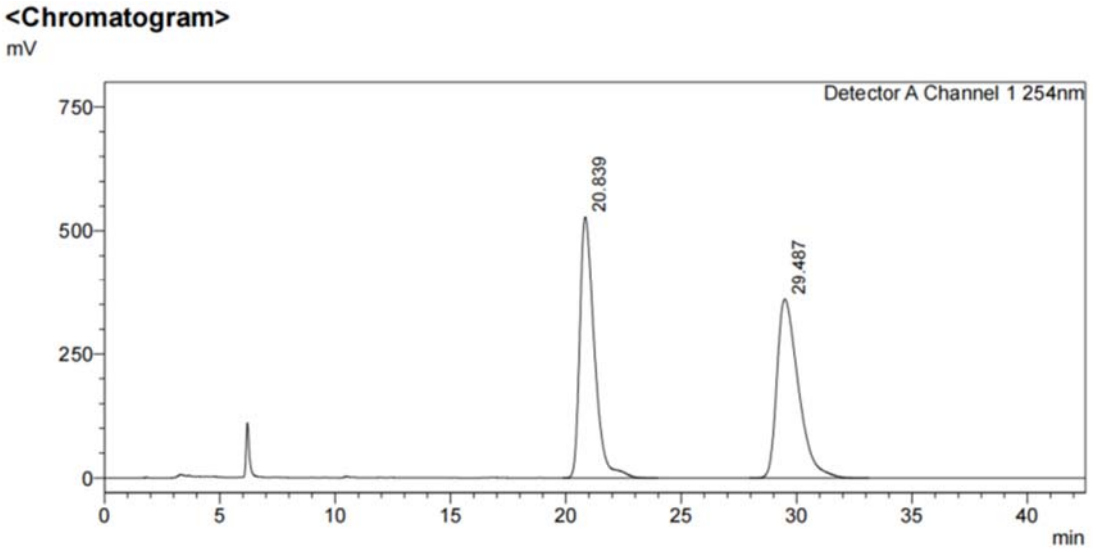


(*R*)-3bbd
$C_{35}H_{27}F_3N_2O_3$
M = 580.61 g/mol

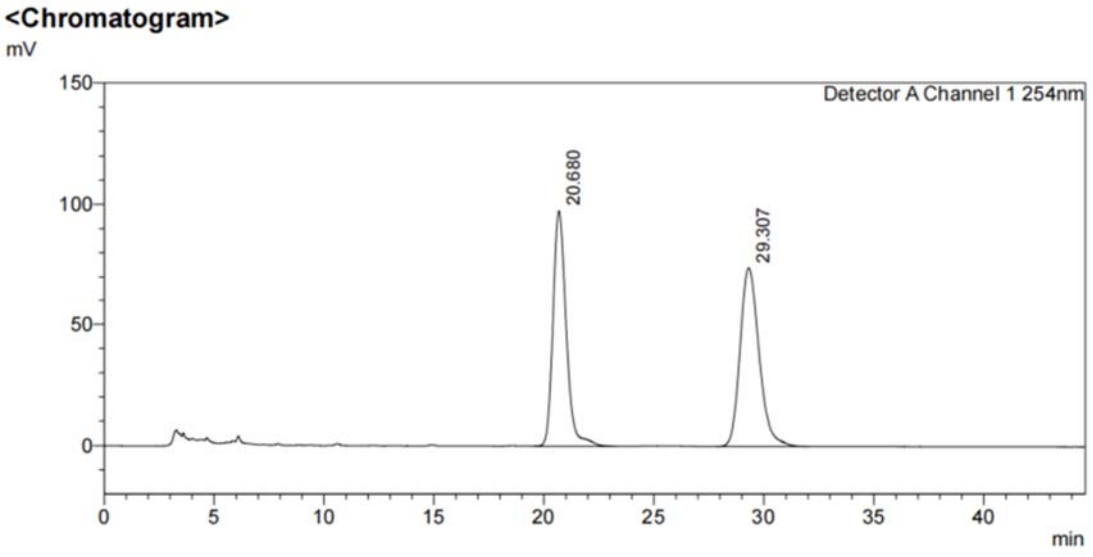
(*R*)-(1-(2-methoxybenzoyl)-3-phenyl-1,2,3,11b-tetrahydro-4*H*-1,3-methanopyridazino[6,1-*a*] isoquinolin-4-yl)(4-(trifluoromethyl)phenyl)methanone ((*R*)-3bbd) : Prepared from (2-methoxyphenyl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1bb**, 52.9 mg, 0.20 mmol) and isoquinolin-2-ium-2-yl(4-(trifluoromethyl)benzoyl)amide (**2b**, 75.9 mg, 0.24 mmol) at room temperature for 16 h according to the **GP4**. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded (*R*)-**3bbd** as a yellow solid (12.8 mg, 11% yield).

(*R*)-**3bbd**: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 5/1). Mp: 117-119 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 29.31 min,

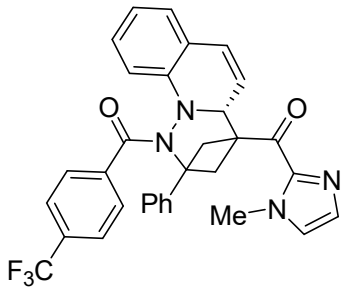
tr (minor) = 20.68 min) gave the isomeric composition of the product: 4% *ee*. $[\alpha]_D^{20}$ = -0.4 (*c* = 0.75, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.43-7.39 (m, 1H), 7.37-7.27 (m, 5H), 7.23-7.19 (m, 1H), 7.02-6.99 (m, 1H), 6.93-6.75 (m, 6H), 5.57 (s, 1H), 5.39 (d, *J* = 7.6 Hz, 1H), 3.82 (s, 3H), 3.76-3.71 (m, 1H), 3.08 (d, *J* = 10.4 Hz, 1H), 2.91 (t, *J* = 9.2 Hz, 1H), 2.17 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.3, 174.1, 157.3, 141.5, 140.0, 139.3, 133.7, 132.2 (q, *J* = 32.5 Hz), 130.9, 130.7, 128.9, 128.4, 128.2, 128.1, 127.1, 127.0, 126.0, 125.0 (q, *J* = 3.9 Hz), 124.8, 124.3, 123.7 (q, *J* = 270.3 Hz), 120.9, 111.0, 68.7, 68.0, 59.2, 55.0, 46.2, 42.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.89 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{35}H_{28}F_3N_2O_3$: 581.2047; found: 581.2038.



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	20.839	19.867	23194874	528320	49.822
2	29.487	27.967	23360475	361191	50.178
Total			46555349	889511	100.000



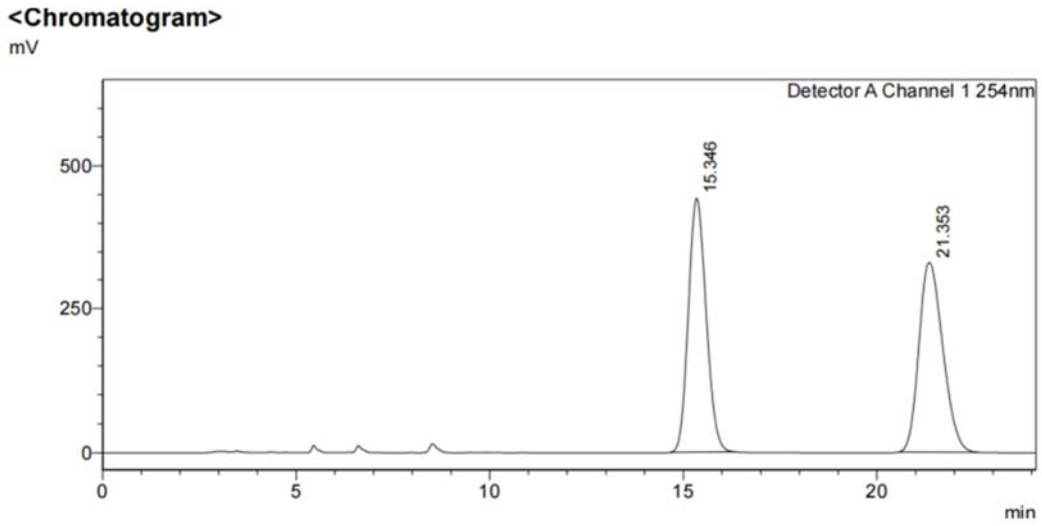
Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	20.680	19.608	4061854	97530	47.790
2	29.307	27.817	4437512	74085	52.210
Total			8499366	171615	100.000



(*R*)-4qaa
$C_{32}H_{25}F_3N_4O_2$
M = 554.57 g/mol

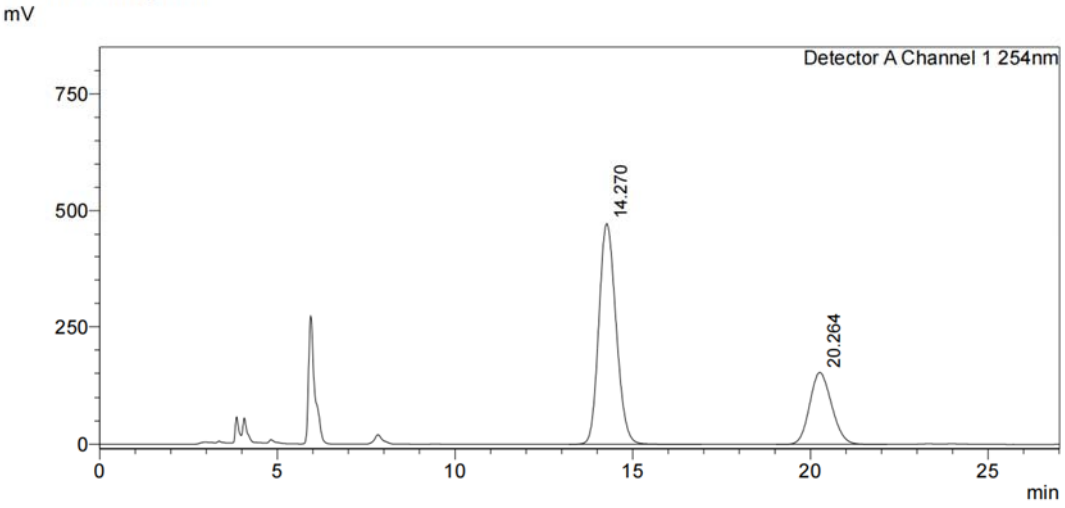
(*R*)-(1-methyl-1*H*-imidazol-2-yl)(2-phenyl-1-(4-(trifluoromethyl)benzoyl)-2,3-dihydro-1*H*-2,4-methanopyridazino[1,6-*a*]quinolin-4(4a*H*)-yl)methanone ((*R*)-4qaa): Prepared from (1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1q**, 47.7 mg, 0.20 mmol) and quinolin-1-ium-1-yl(4-(trifluoromethyl)benzoyl)amide (**2aa** 75.9 mg, 0.24 mmol) according to the **GP4** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) afforded **(*R*)-4qaa** as a yellow solid (55.4 mg, 50% yield).

(*R*)-4qaa: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). Mp: 271-273 °C. HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 14.27 min, tr (minor) = 20.26 min) gave the isomeric composition of the product: 41% *ee*. $[\alpha]_D^{20}$ = -49.8 (*c* = 1.00, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.33-7.23 (m, 3H), 7.17 (s, 1H), 7.03 (s, 1H), 6.88 (d, *J* = 7.2 Hz, 1H), 6.80 (t, *J* = 7.2 Hz, 1H), 6.21 (d, *J* = 10.0 Hz, 1H), 5.71 (d, *J* = 4.4 Hz, 1H), 5.08 (dd, *J* = 10.0, 4.4 Hz, 1H), 3.98 (s, 3H), 3.22-3.11 (m, 2H), 2.90 (dd, *J* = 11.6, 8.8 Hz, 1H), 2.38 (d, *J* = 11.2 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 189.7, 174.6, 146.1, 141.9, 141.5, 138.8, 132.1 (q, *J* = 32.3 Hz)， 130.01, 129.98, 128.1, 128.0, 127.6, 127.0, 126.0, 124.8 (q, *J* = 3.8 Hz), 123.8 (q, *J* = 270.9 Hz), 120.9, 120.5, 119.8, 111.5, 68.5, 66.3, 59.8, 48.5, 38.2, 35.8 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.90 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{32}H_{25}F_3N_4O_2Na$: 577.1822; found: 577.1813.



Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	15.346	14.675	14116863	442282	49.963
2	21.353	20.567	14137848	330806	50.037
Total			28254711	773088	100.000

<Chromatogram>

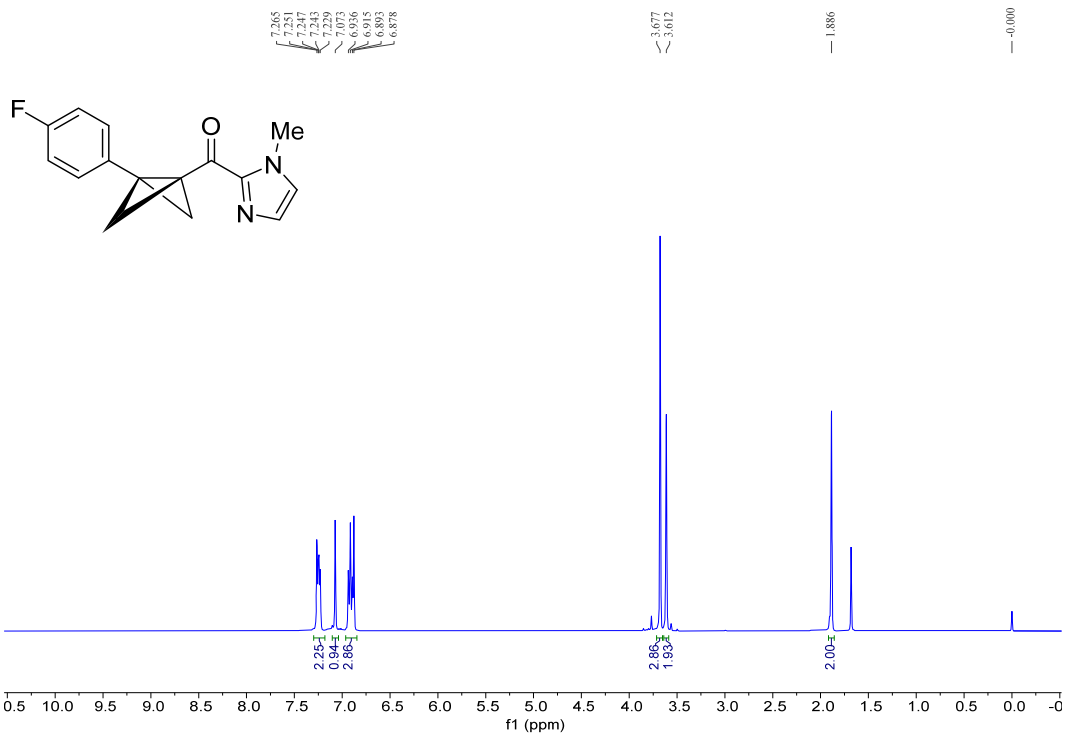


Peak#	Ret. Time	Peak Start	Area	Height	Area%
1	14.270	13.217	15904508	472676	70.643
2	20.264	19.042	6609565	152424	29.357
Total			22514073	625100	100.000

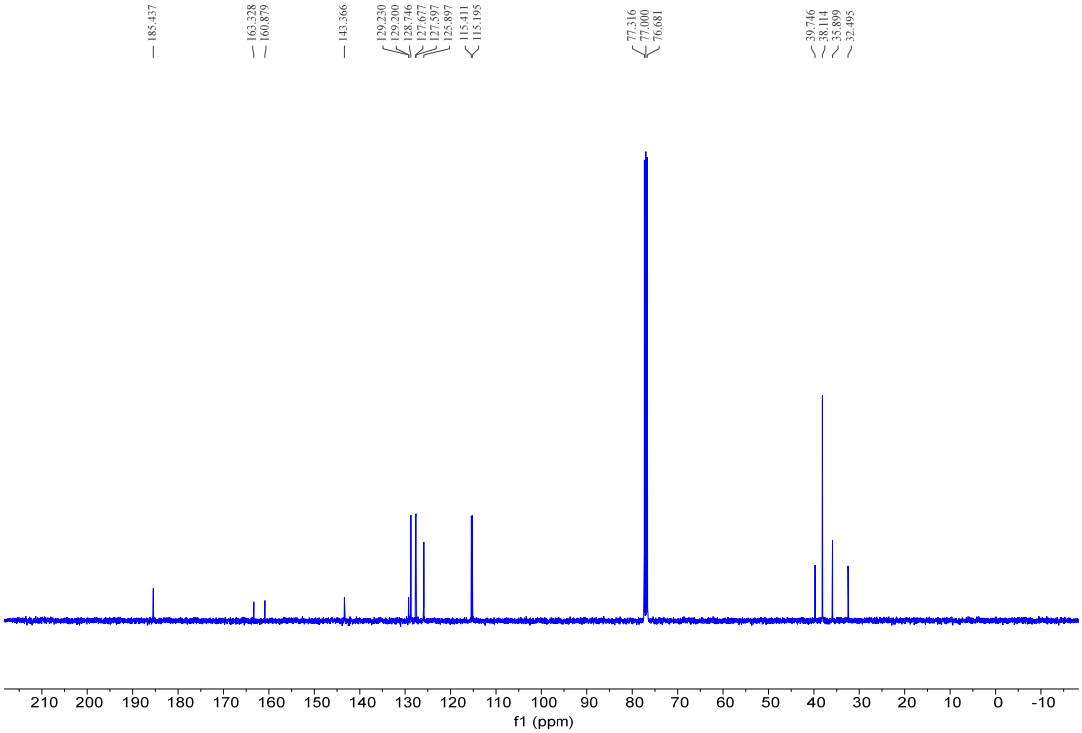
12 NMR Spectra

H, ^{13}C and ^{19}F NMR Spectra for Compound 1u:

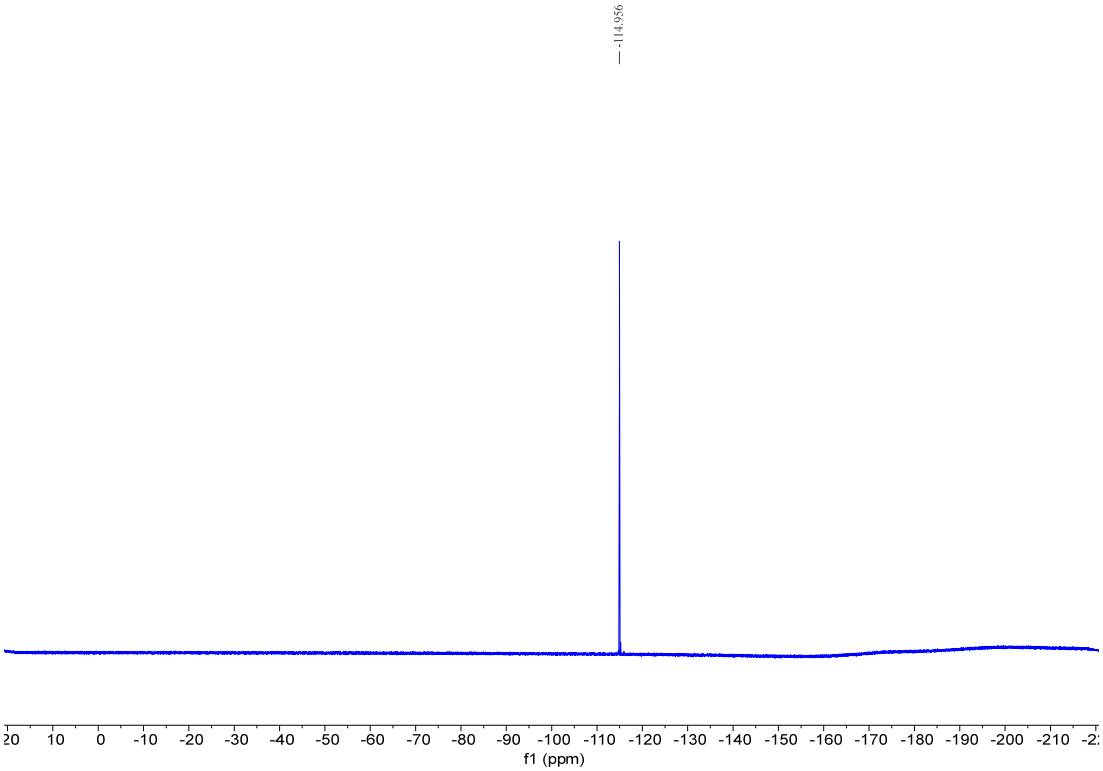
^{1}H NMR (400 MHz, $CDCl_3$)



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

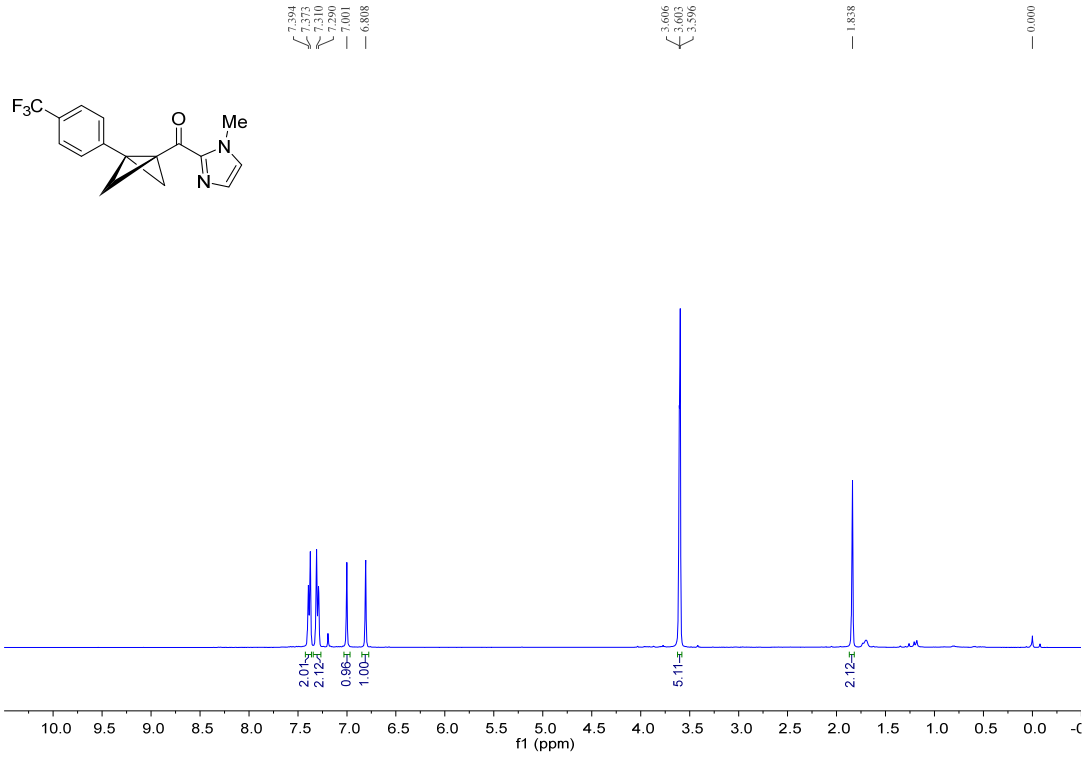


^{19}F NMR (376 MHz, $CDCl_3$)

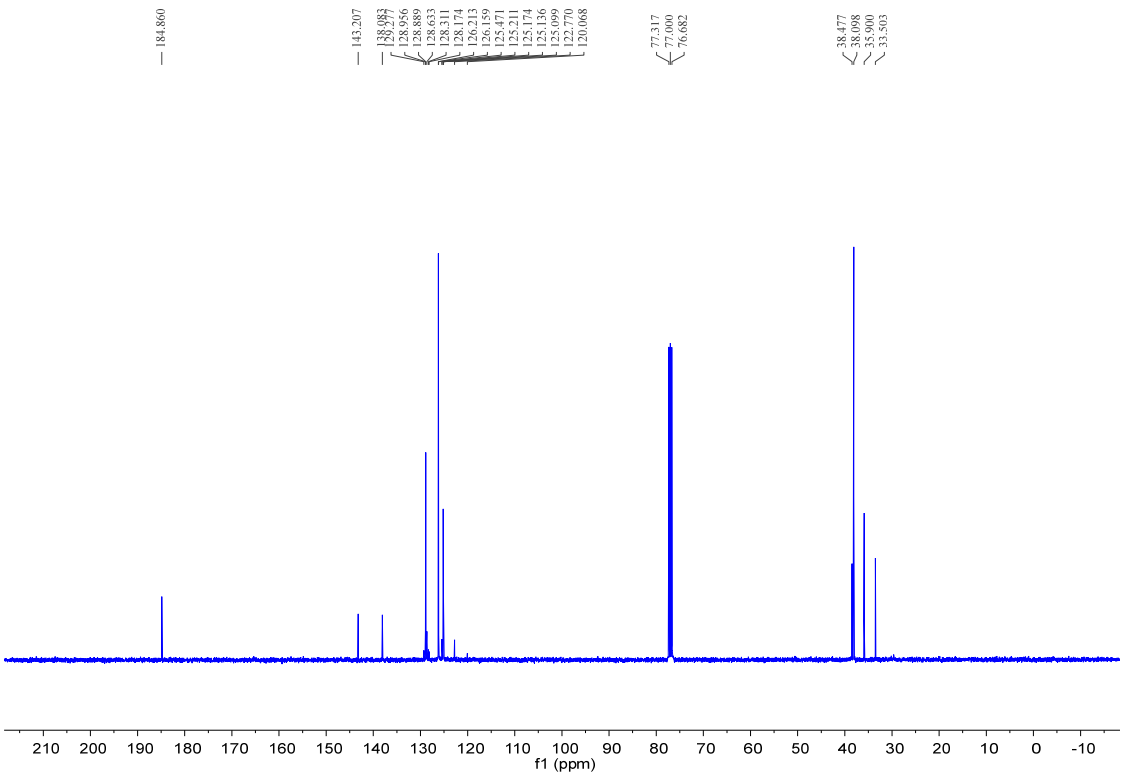


H, ^{13}C and ^{19}F NMR Spectra for Compound 1v:

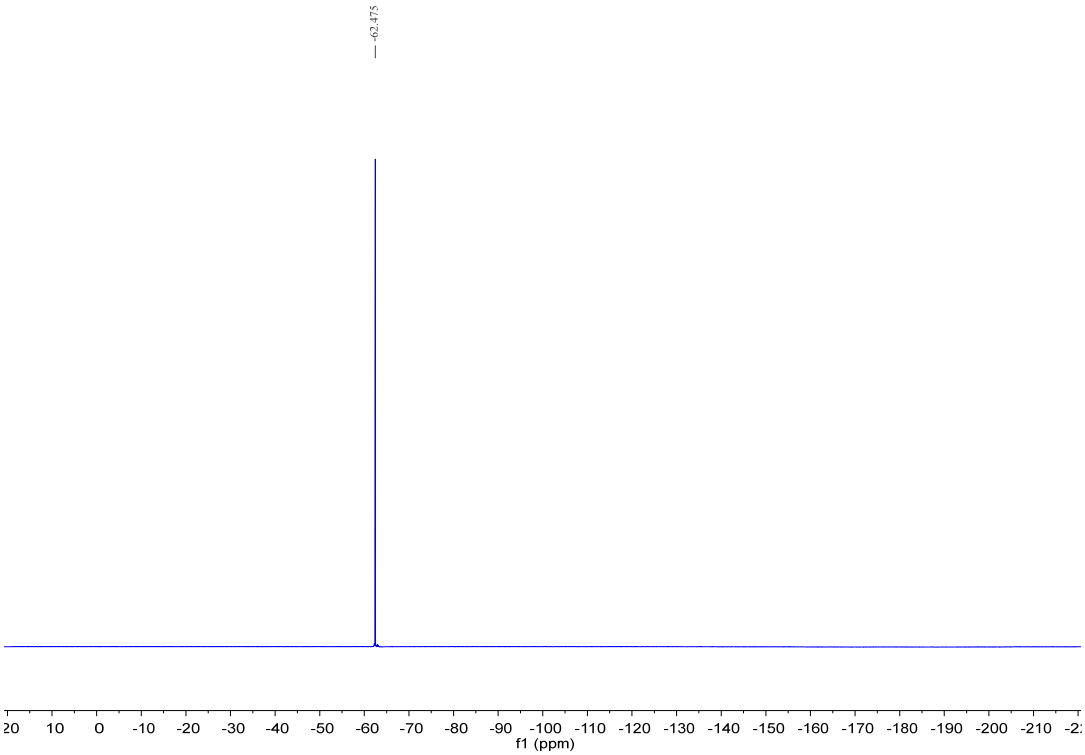
^{1}H NMR (400 MHz, $CDCl_3$)



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

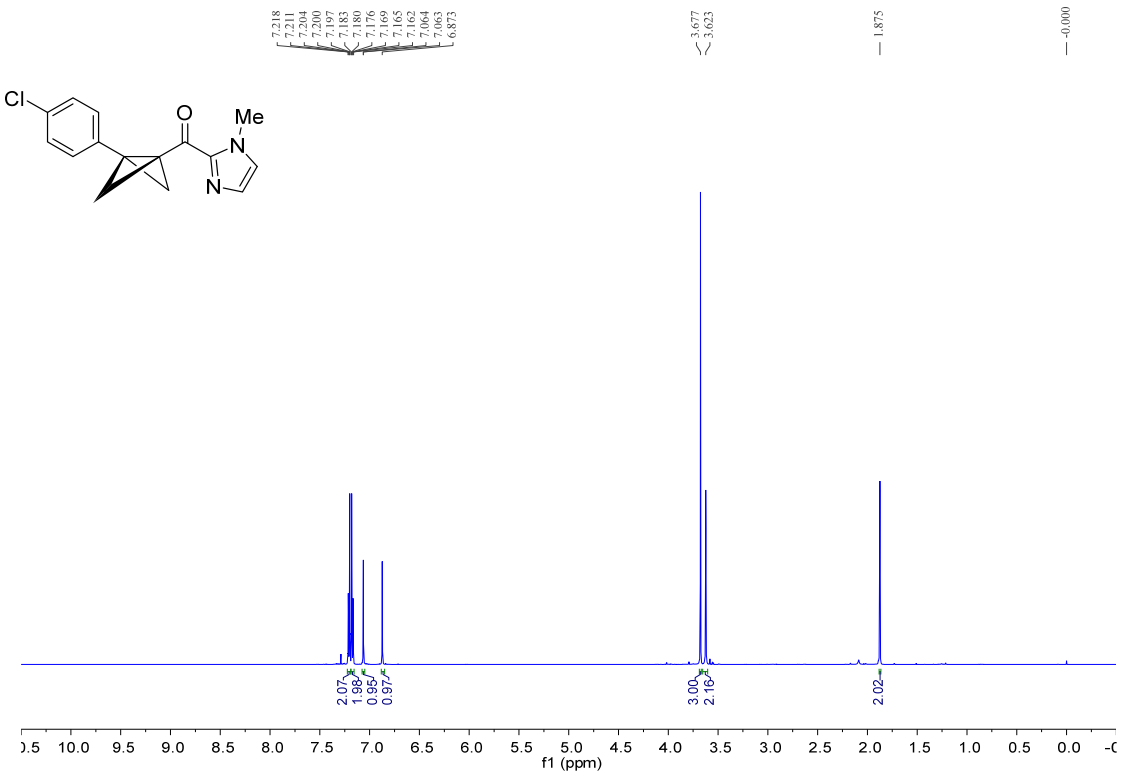


^{19}F NMR (376 MHz, $CDCl_3$)

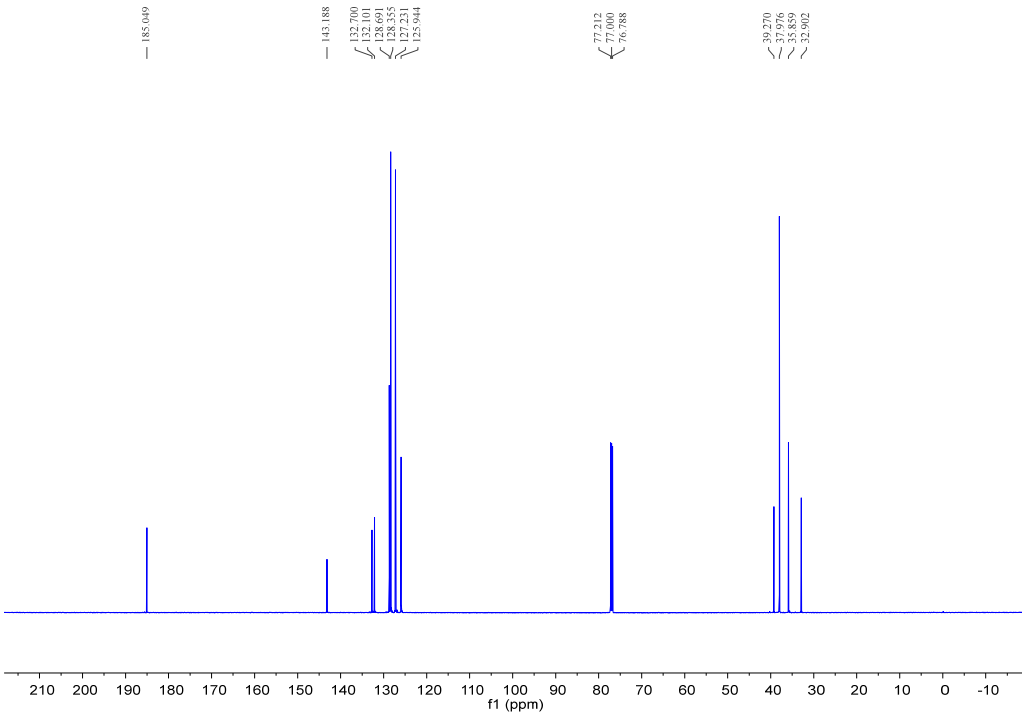


^{1}H and ^{13}C NMR Spectra for Compound 1y:

^{1}H NMR (600 MHz, $CDCl_3$)

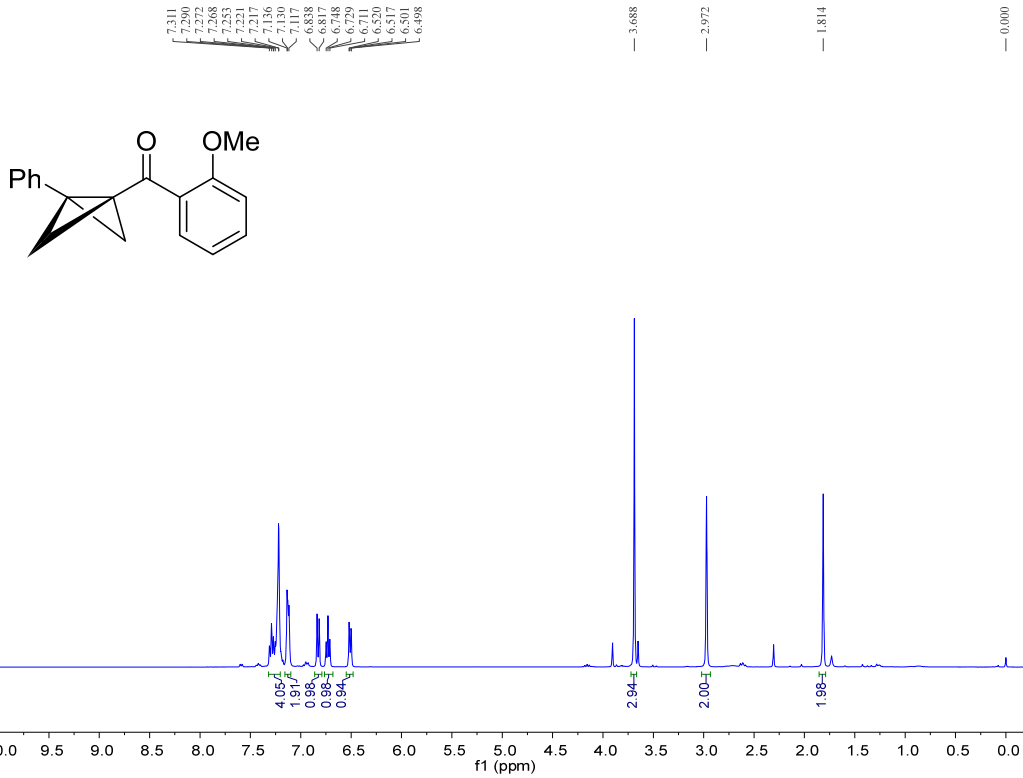


^{13}C NMR (150 MHz, $CDCl_3$)

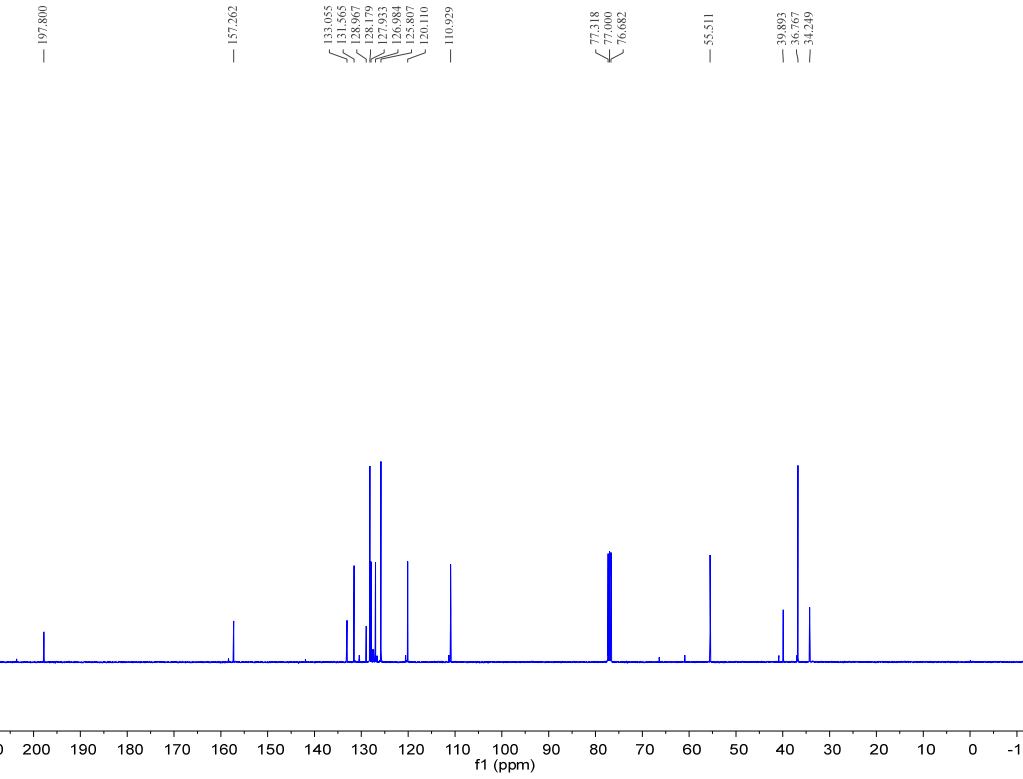


^{1}H and ^{13}C NMR Spectra for Compound 1bb

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

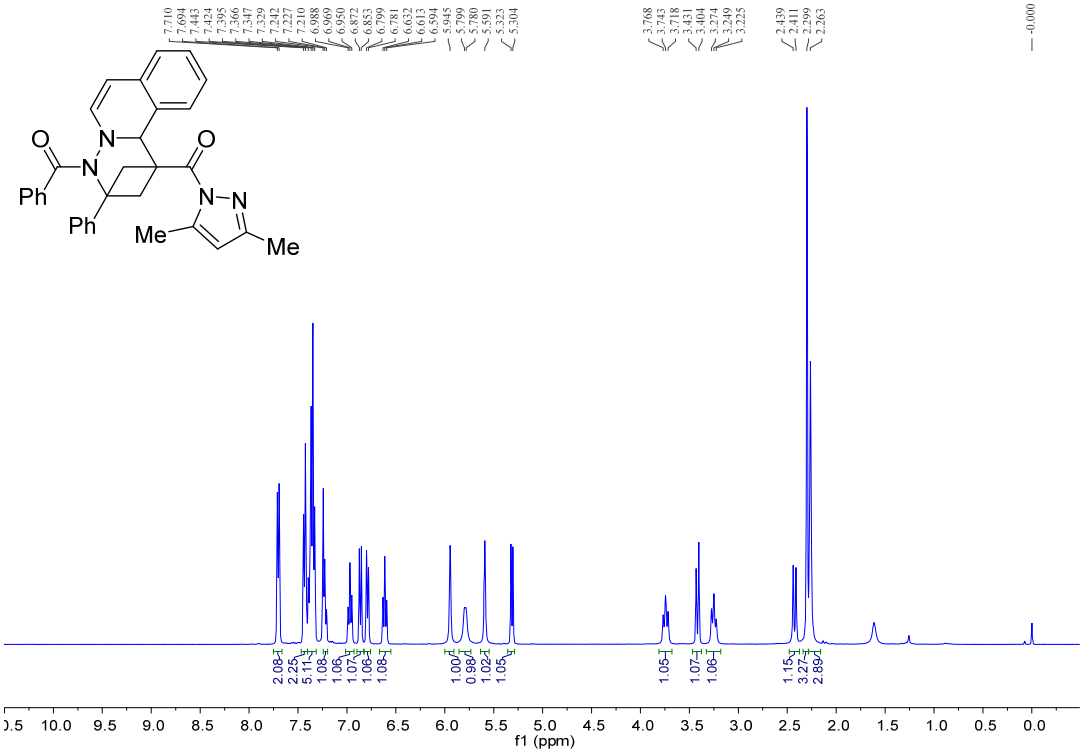


^{13}C NMR (100 MHz, $CDCl_3$)

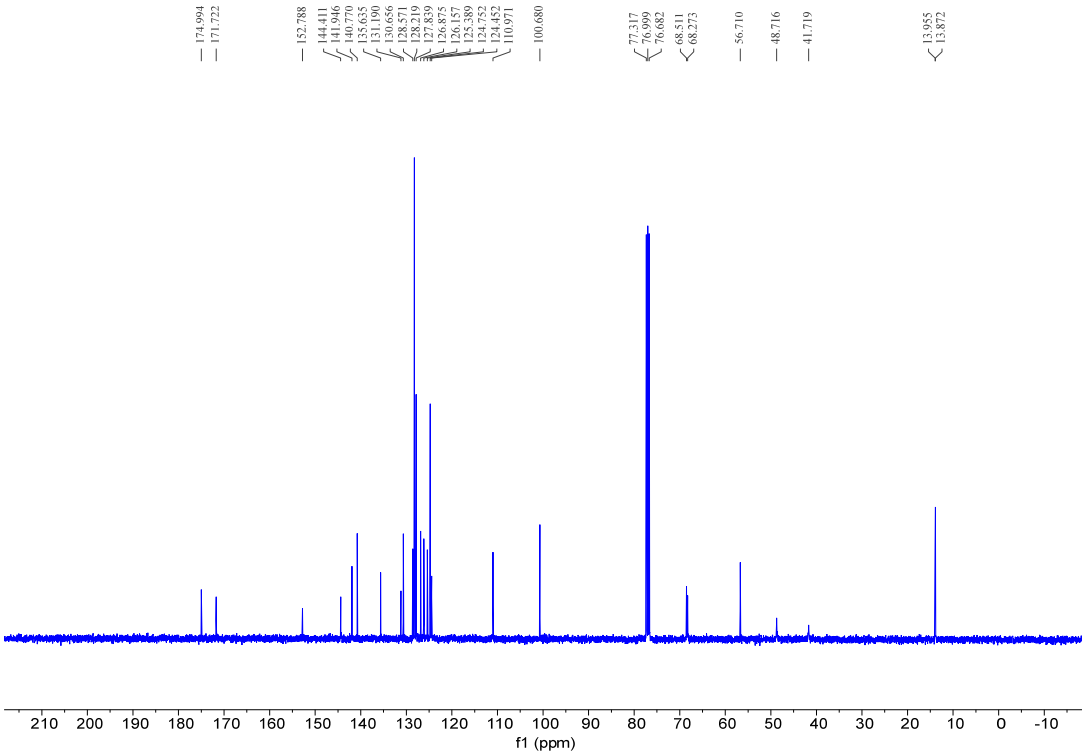


^{1}H and ^{13}C NMR Spectra for Compound 3aa:

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

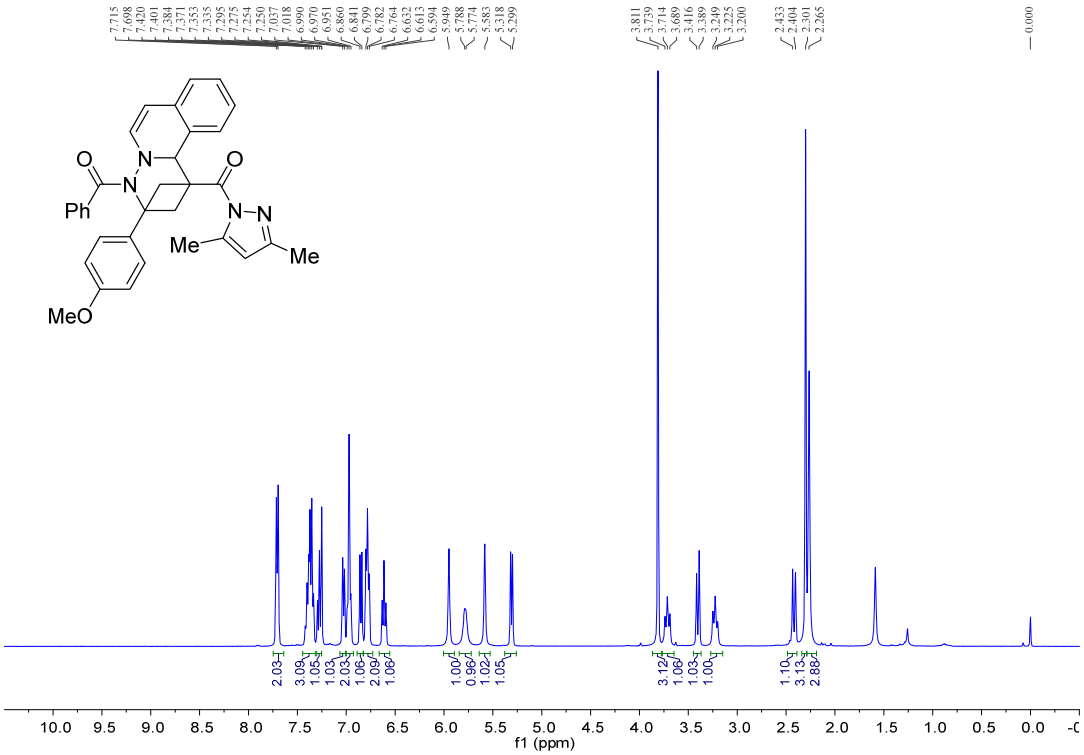


^{13}C NMR (100 MHz, $CDCl_3$)

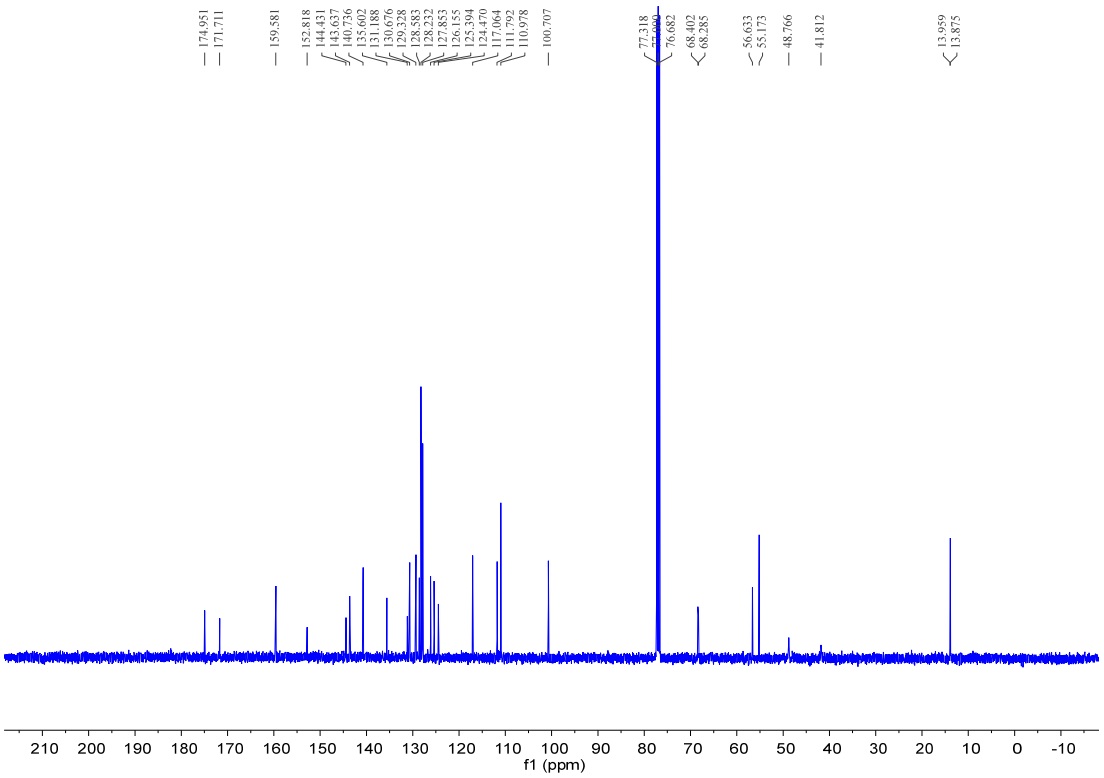


^{1}H and ^{13}C NMR Spectra for Compound 3ba:

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

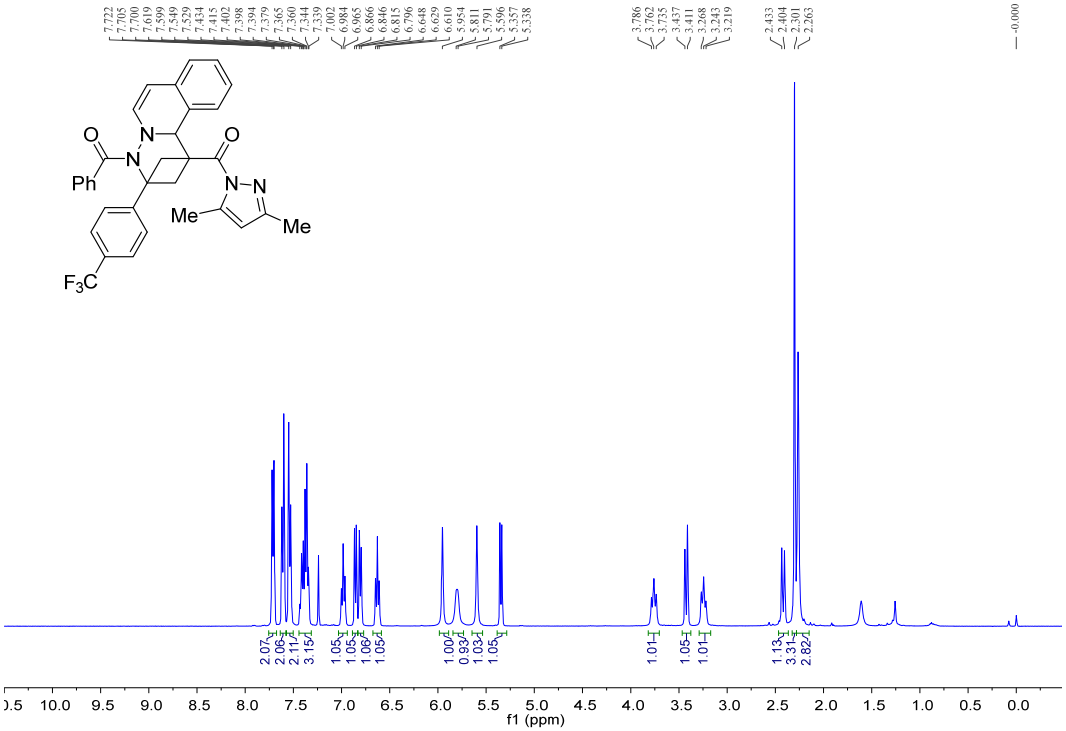


^{13}C NMR (100 MHz, $CDCl_3$)

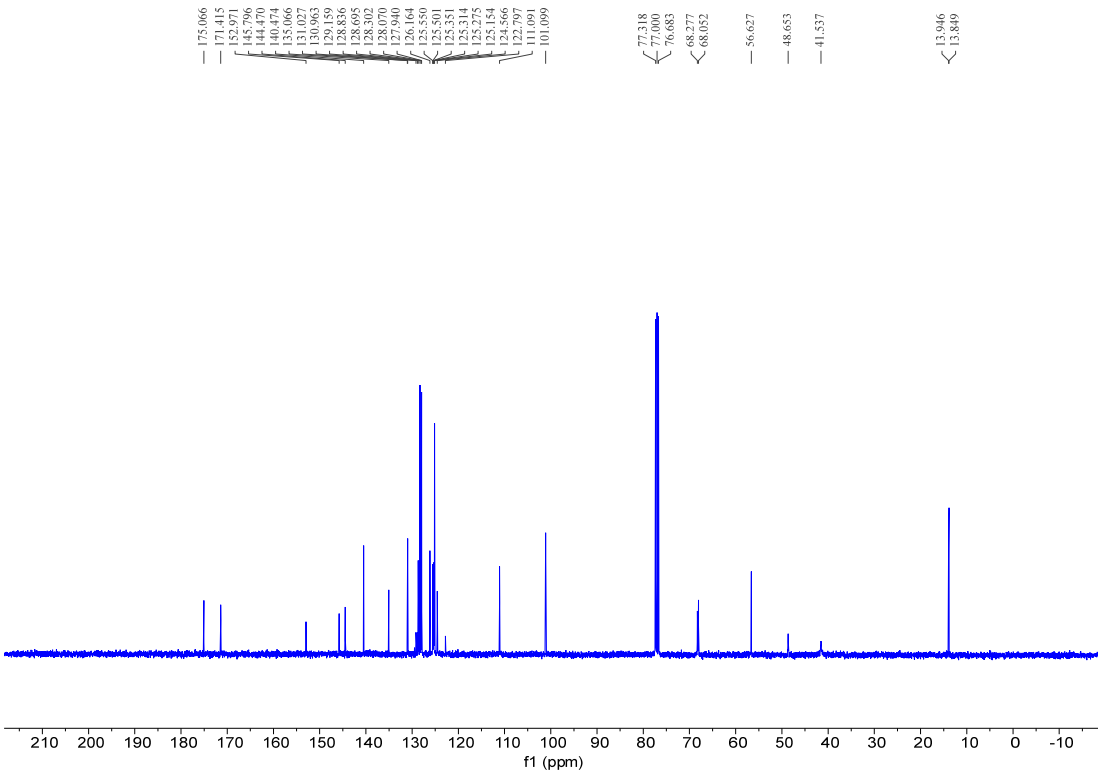


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3ca:

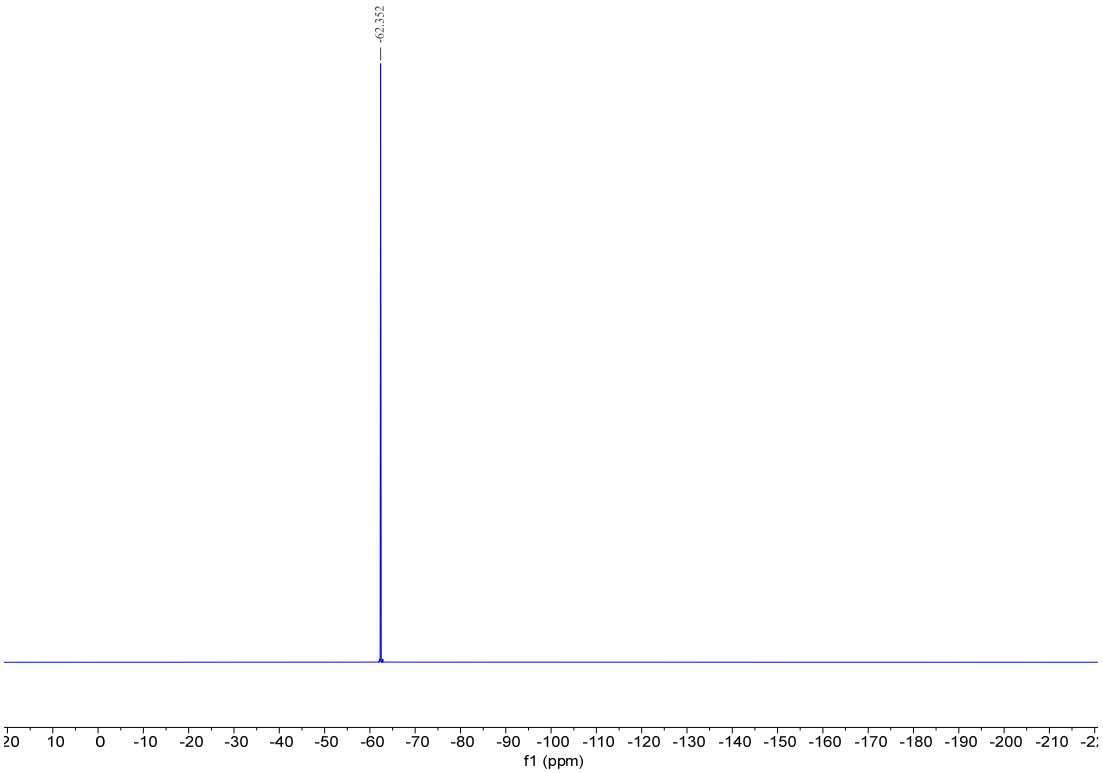
^{1}H NMR (400 MHz, $CDCl_3$)



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

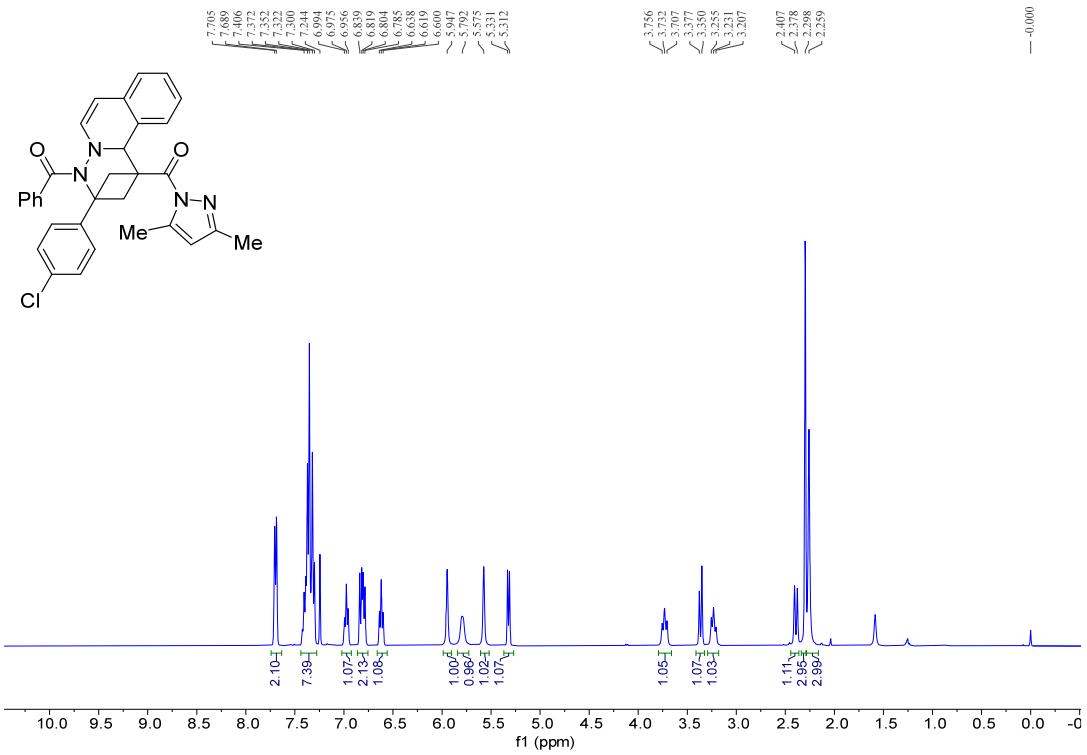


^{19}F NMR (376 MHz, $CDCl_3$)

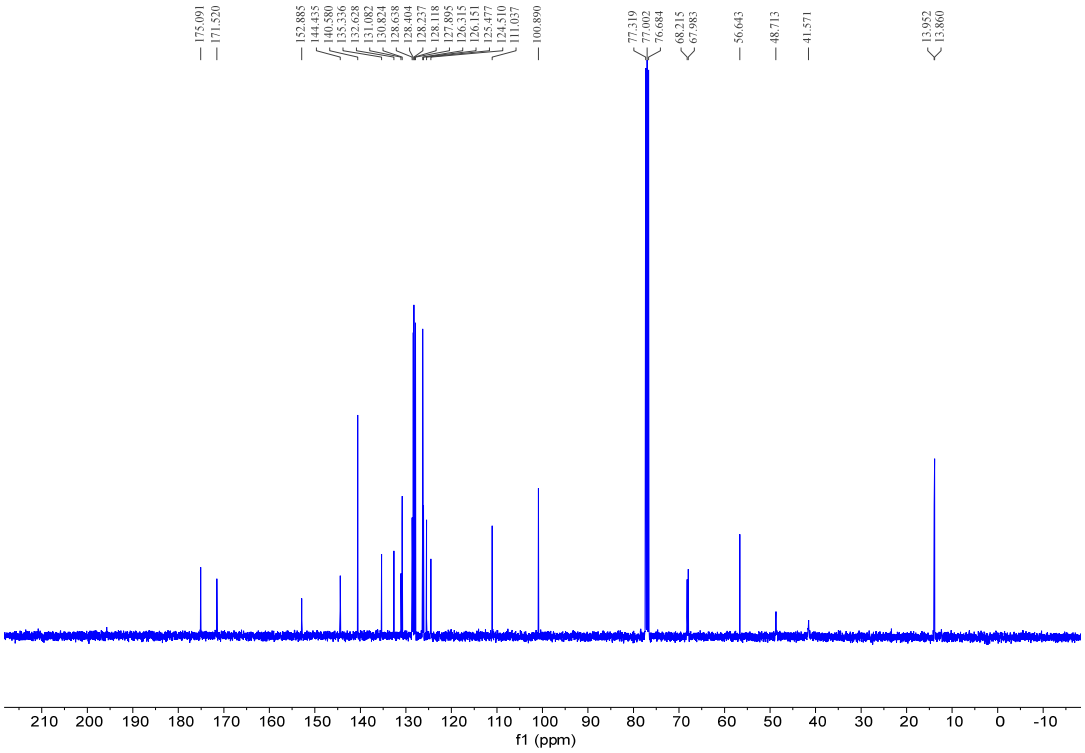


^{1}H and ^{13}C NMR Spectra for Compound 3da:

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

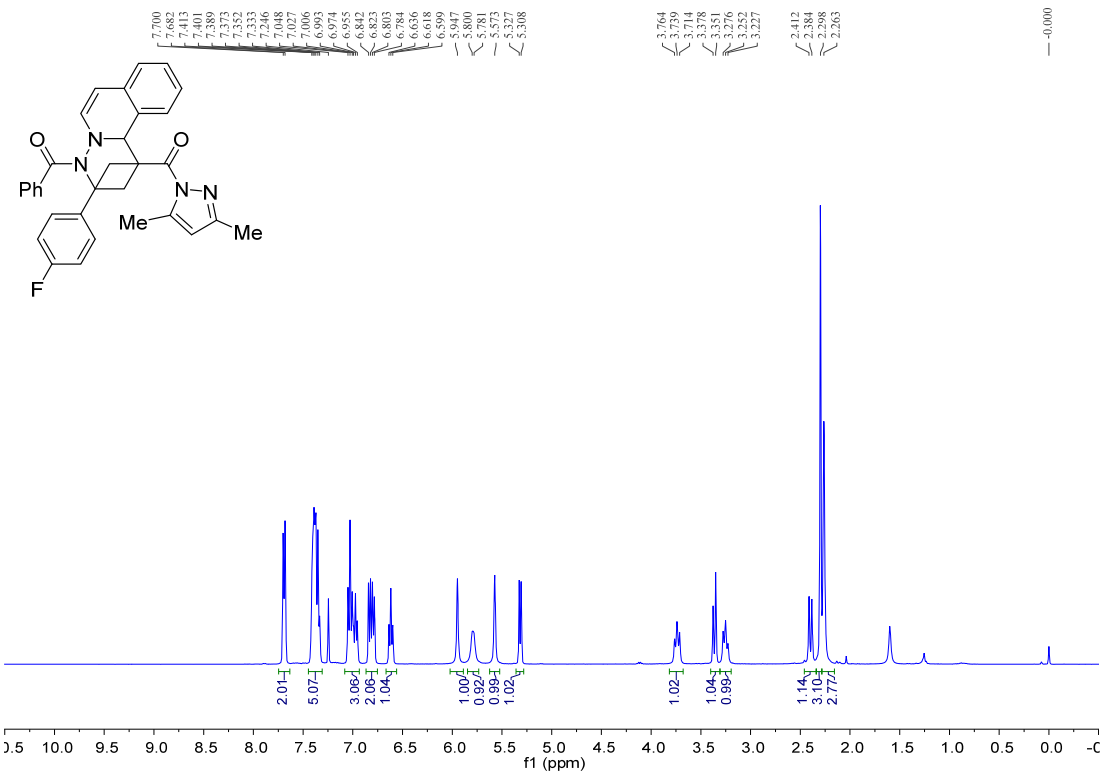


^{13}C NMR (100 MHz, $CDCl_3$)

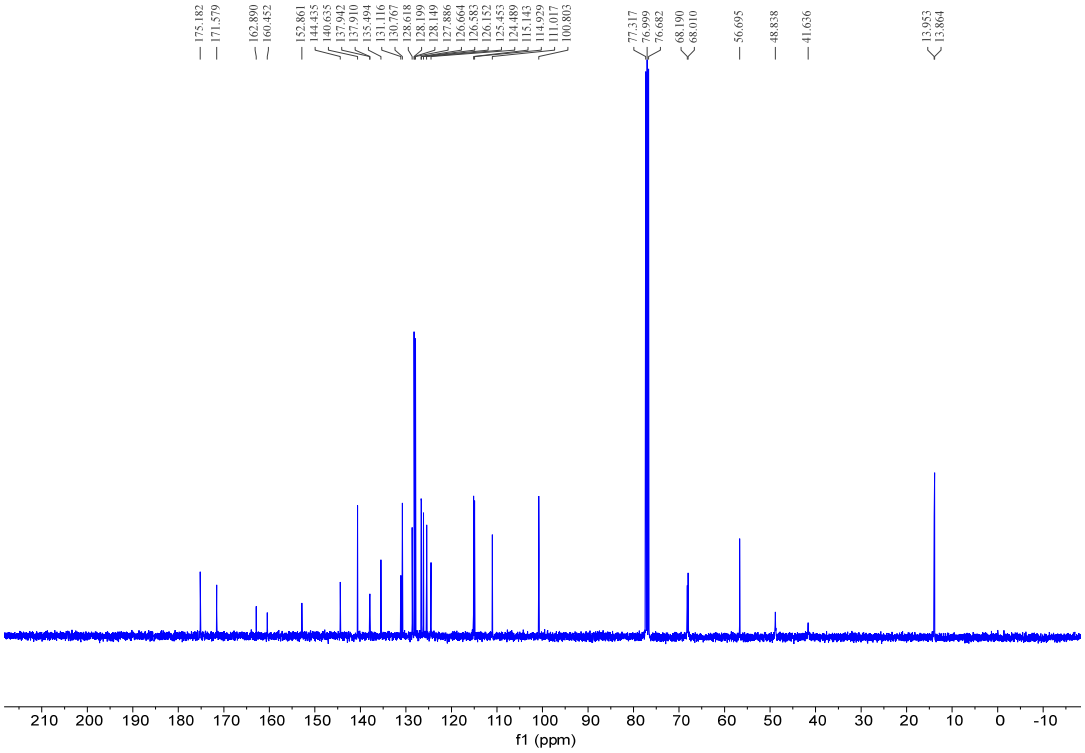


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3ea:

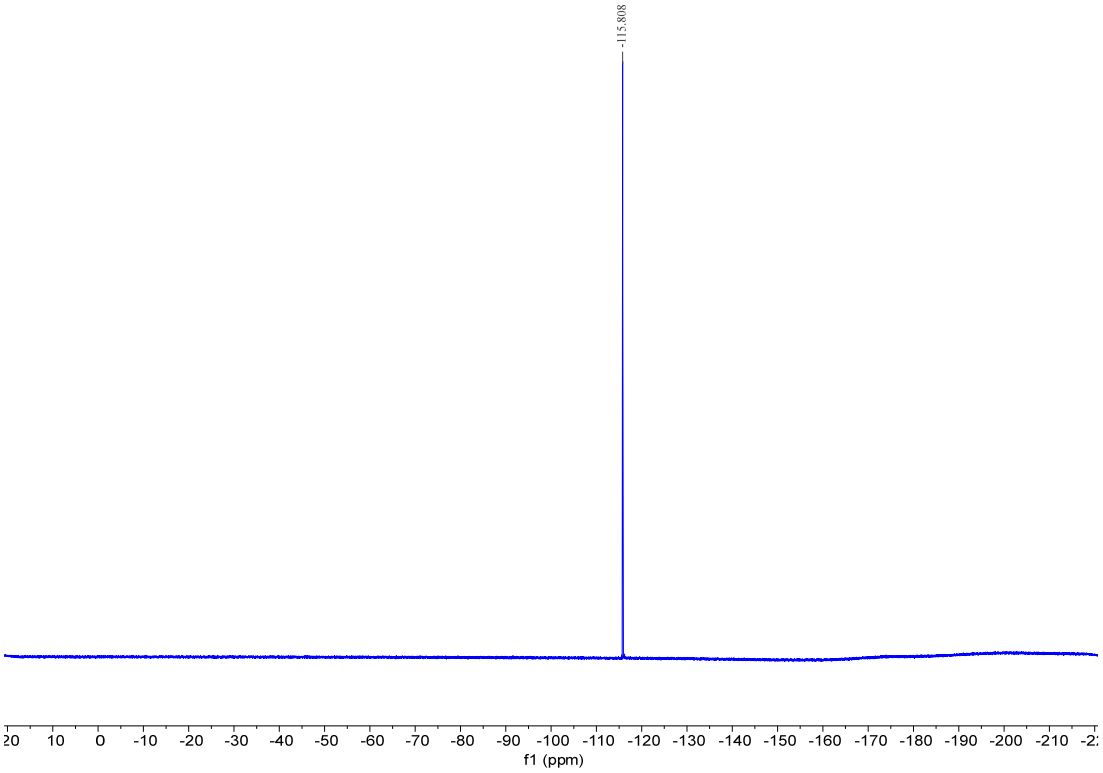
^{1}H NMR (400 MHz, $CDCl_3$)



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

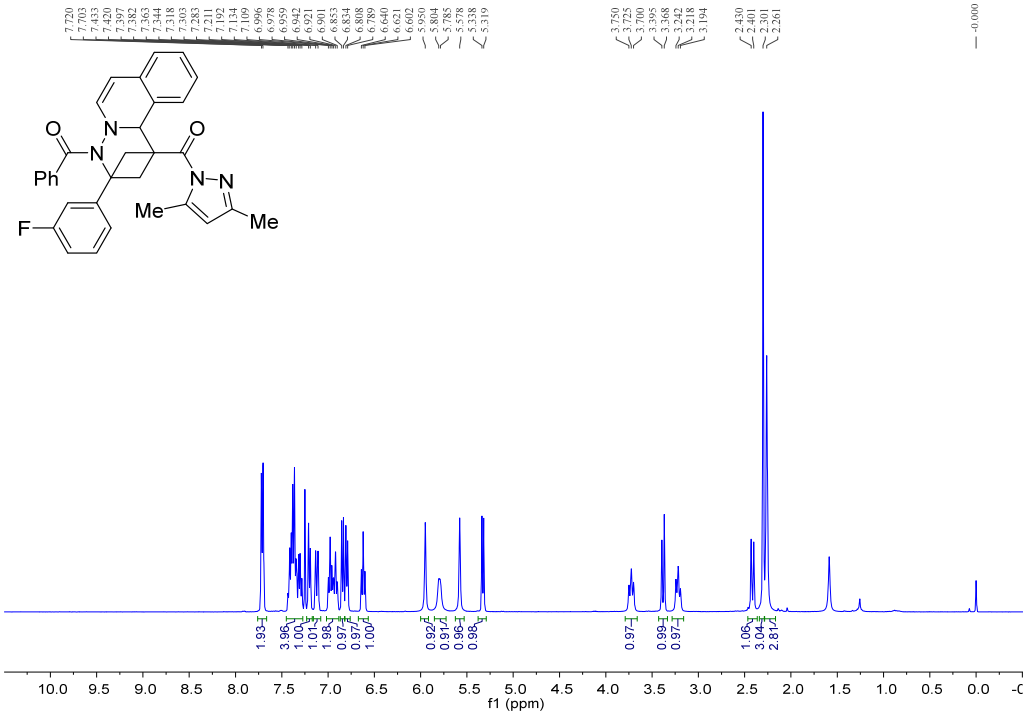


^{19}F NMR (376 MHz, $CDCl_3$)

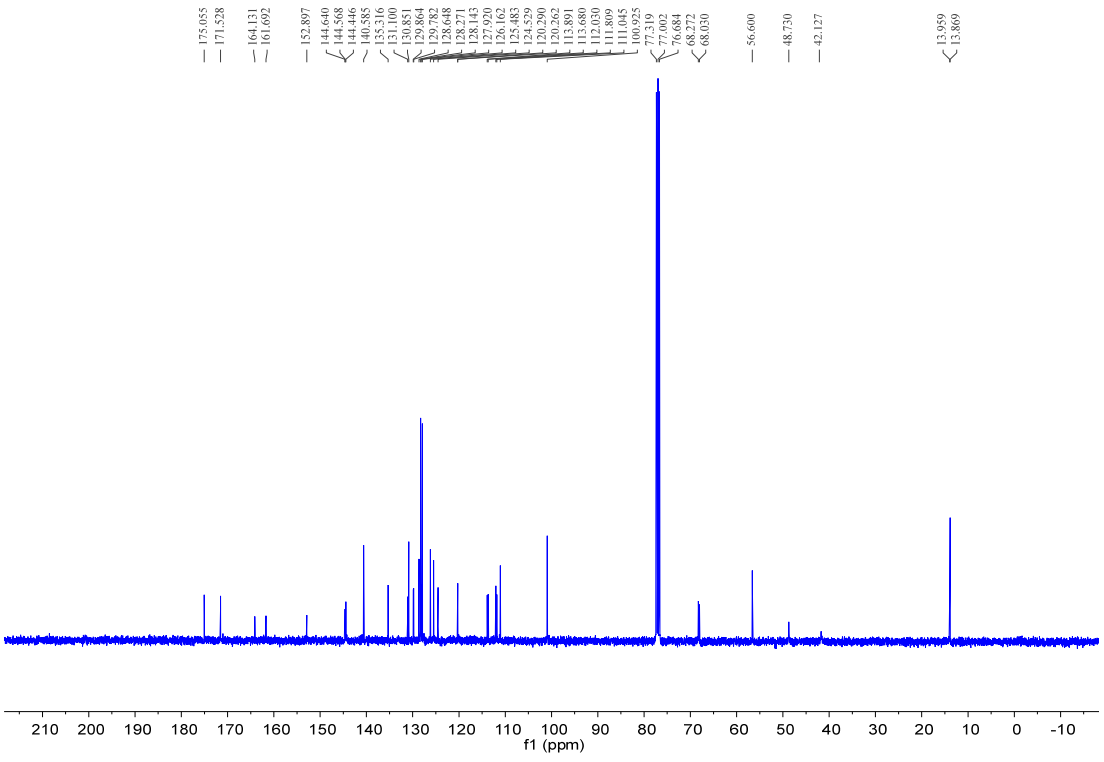


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3fa:

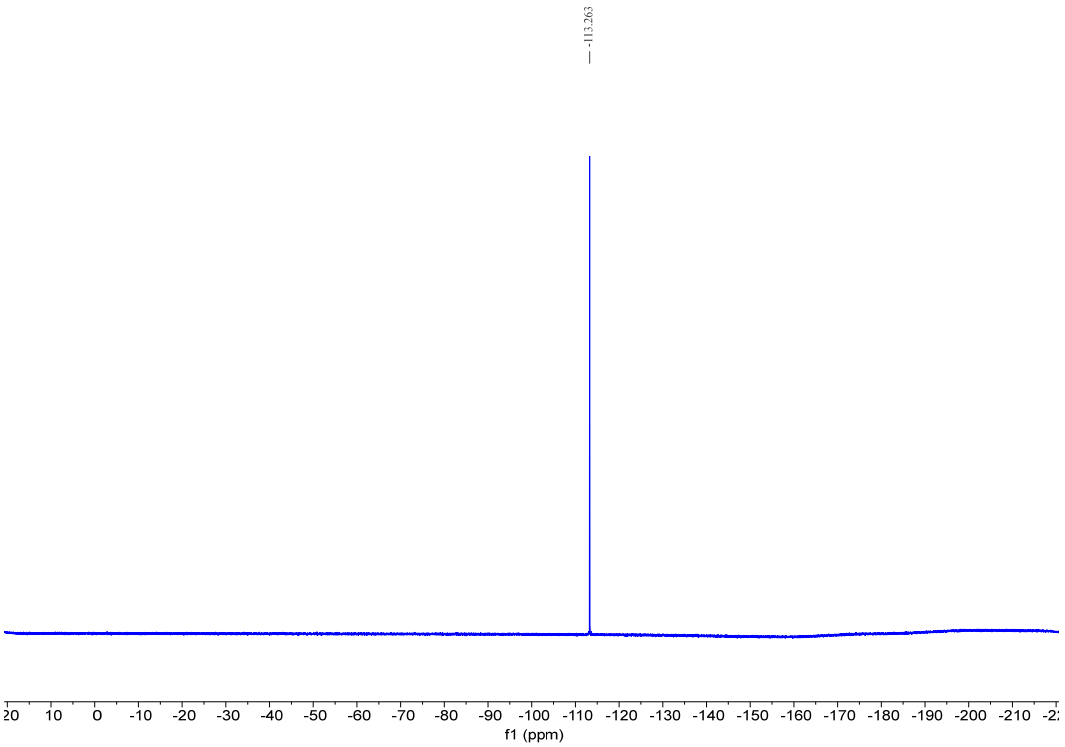
^{1}H NMR (400 MHz, $CDCl_3$)



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

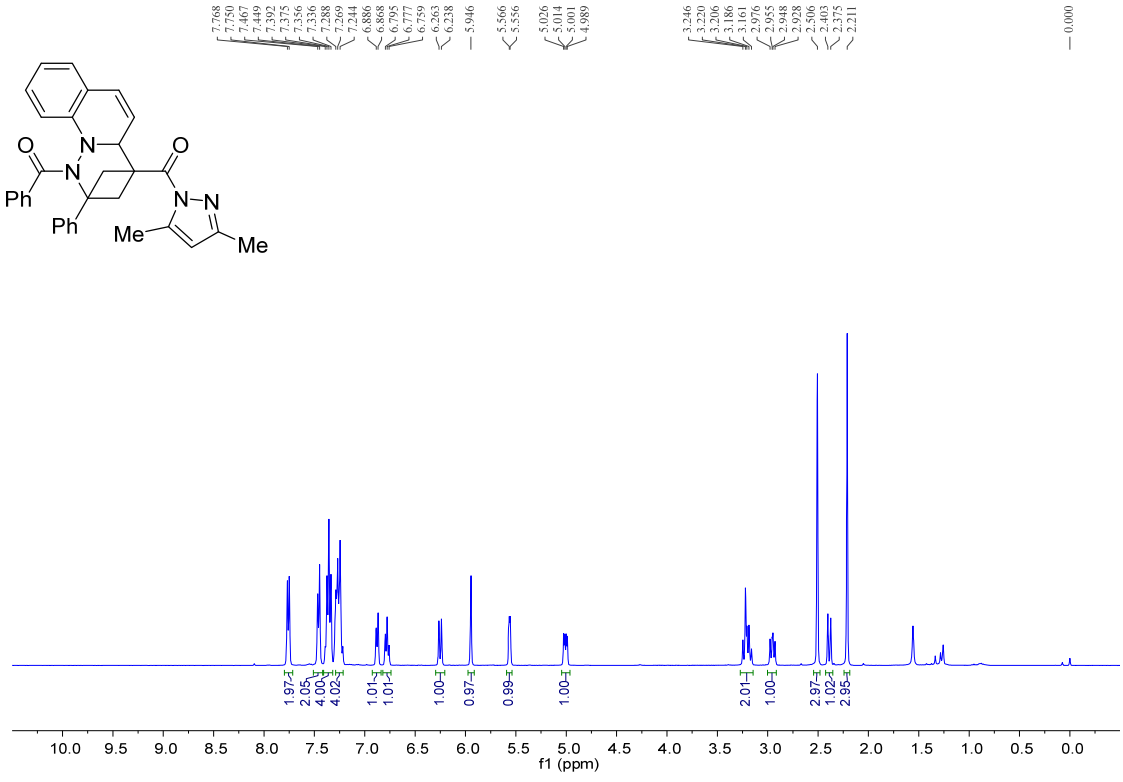


^{19}F NMR (376 MHz, $CDCl_3$)

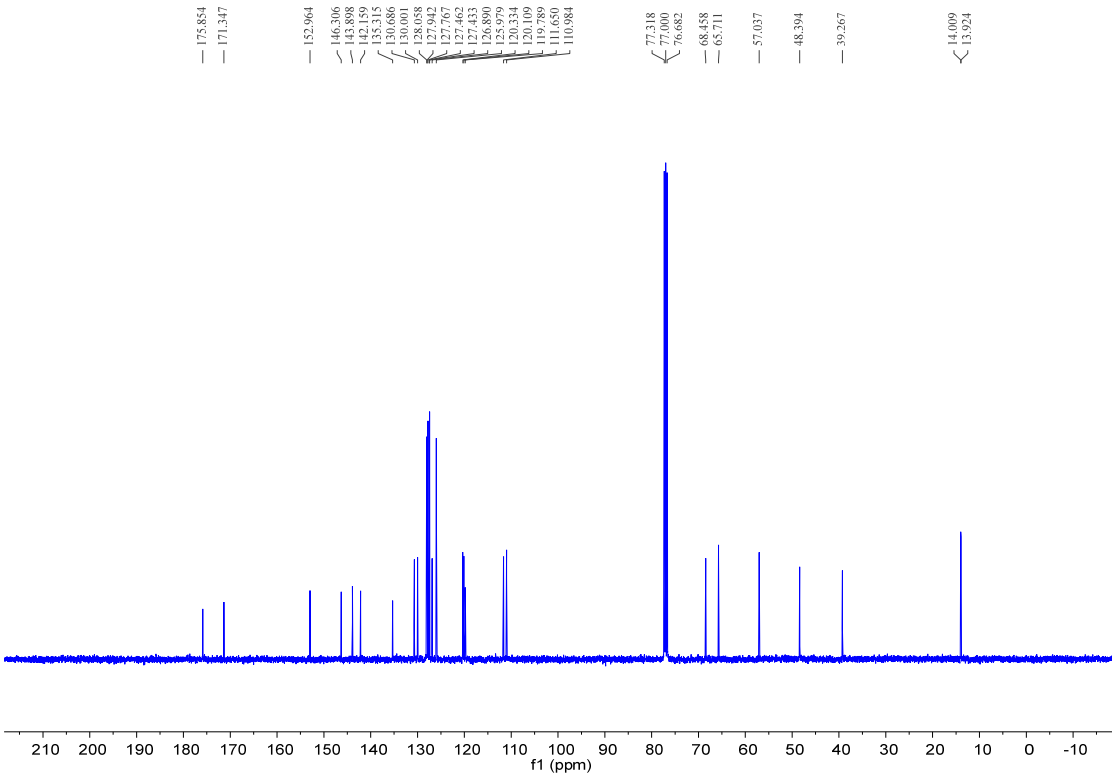


^{1}H and ^{13}C NMR Spectra for Compound 4ab:

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

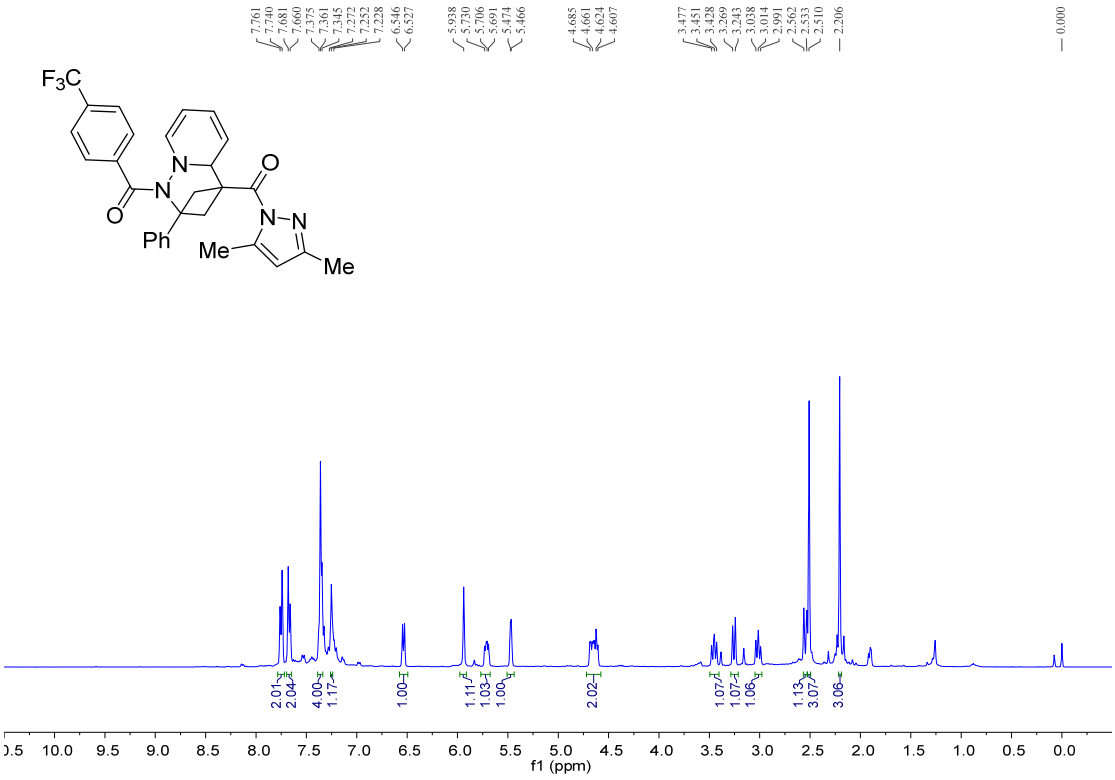


^{13}C NMR (100 MHz, $CDCl_3$)

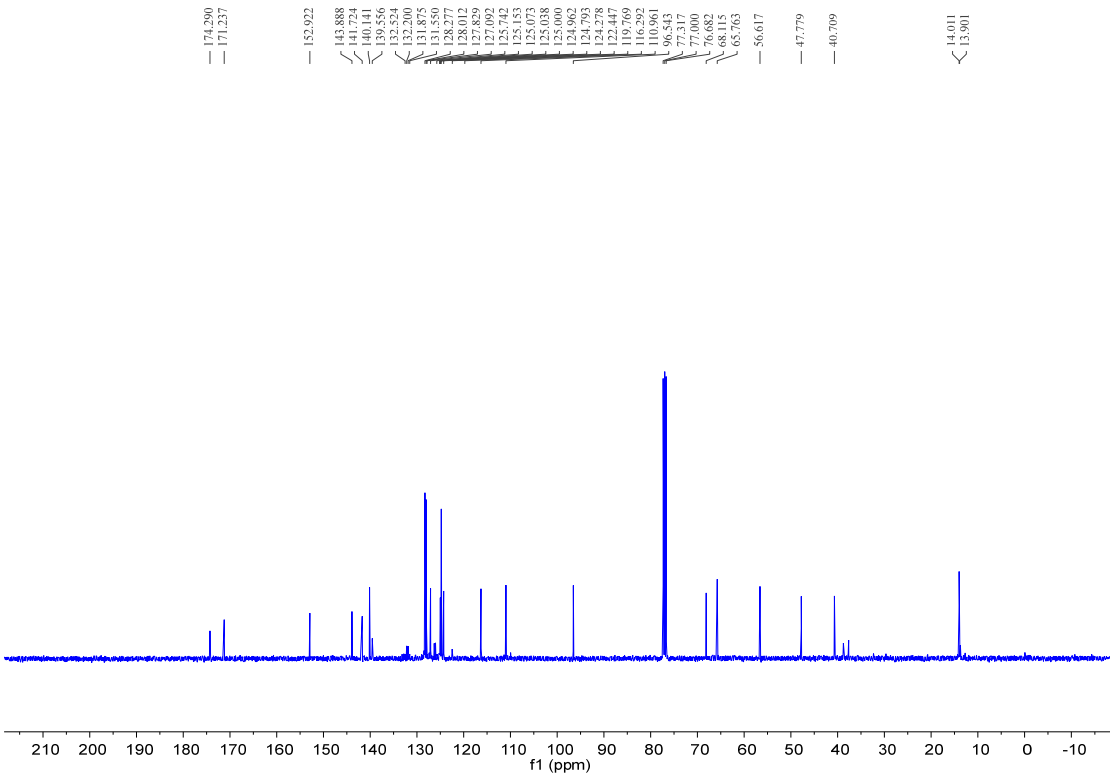


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 5ac:

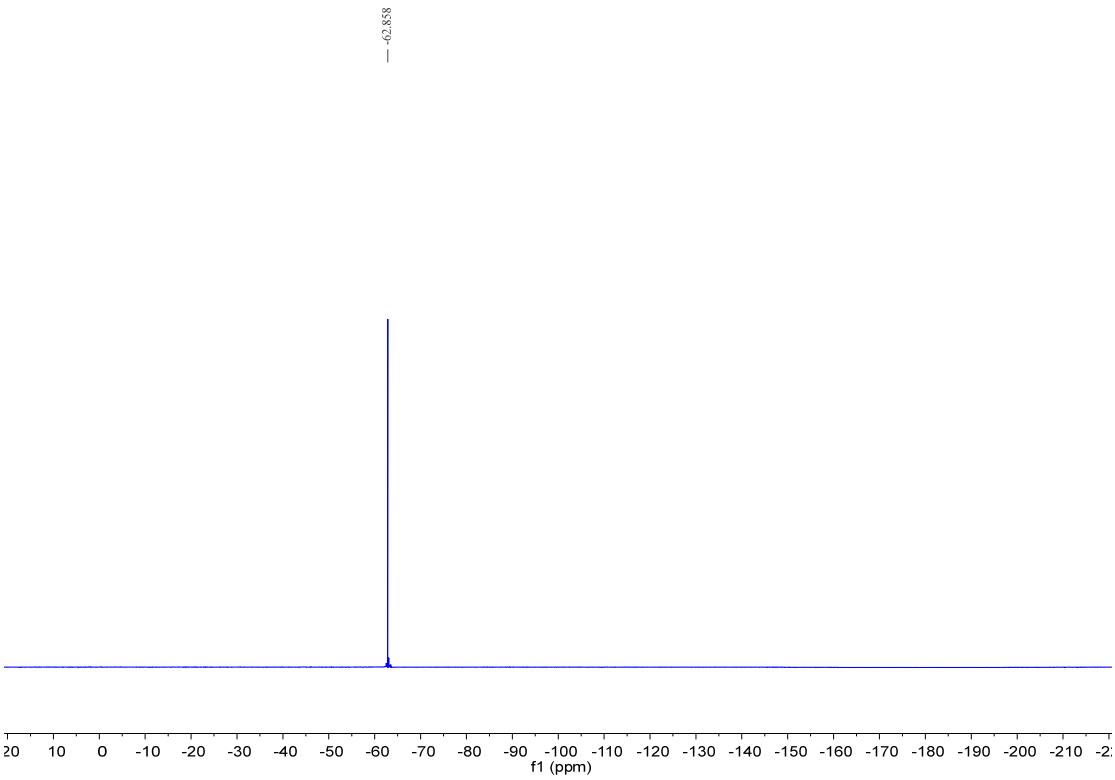
^{1}H NMR (400 MHz, $CDCl_3$)



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

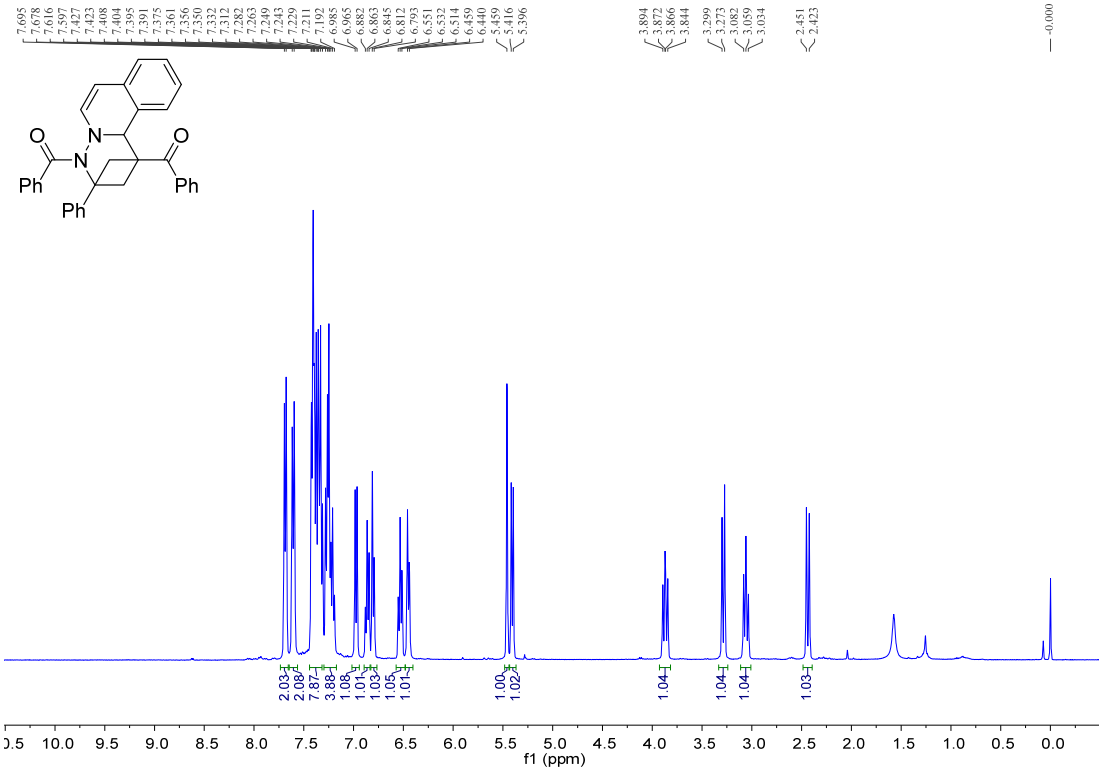


^{19}F NMR (376 MHz, $CDCl_3$)

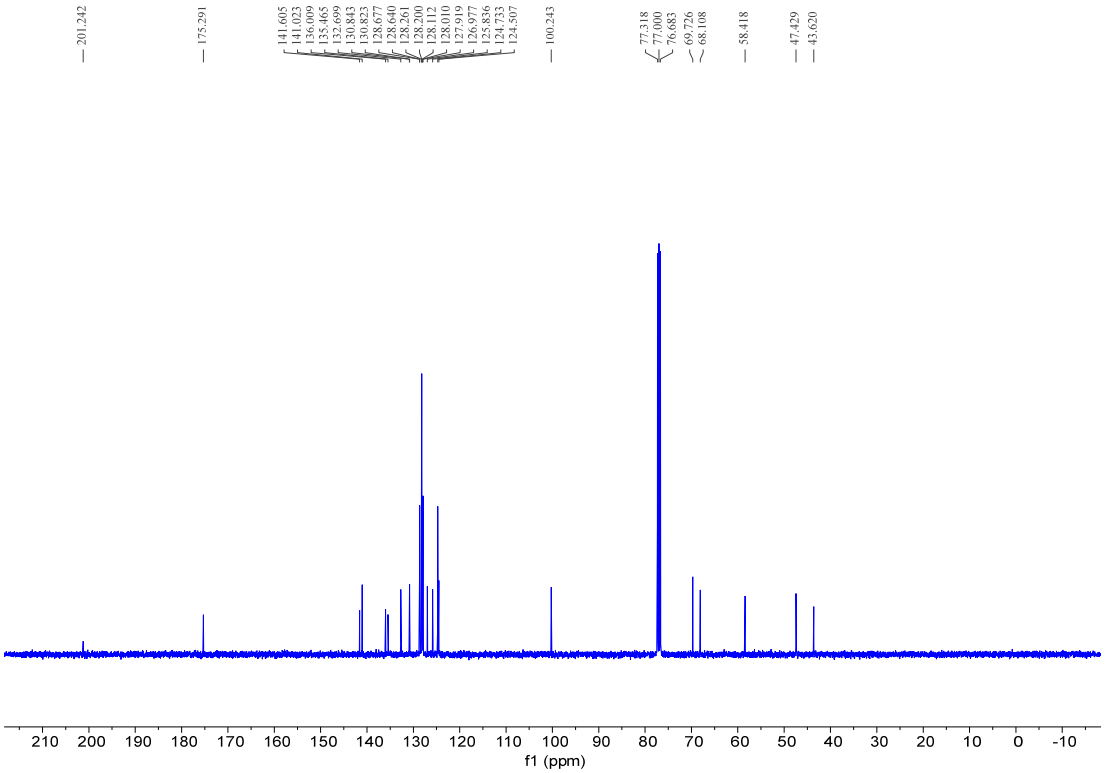


^{1}H and ^{13}C NMR Spectra for Compound 3ga:

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

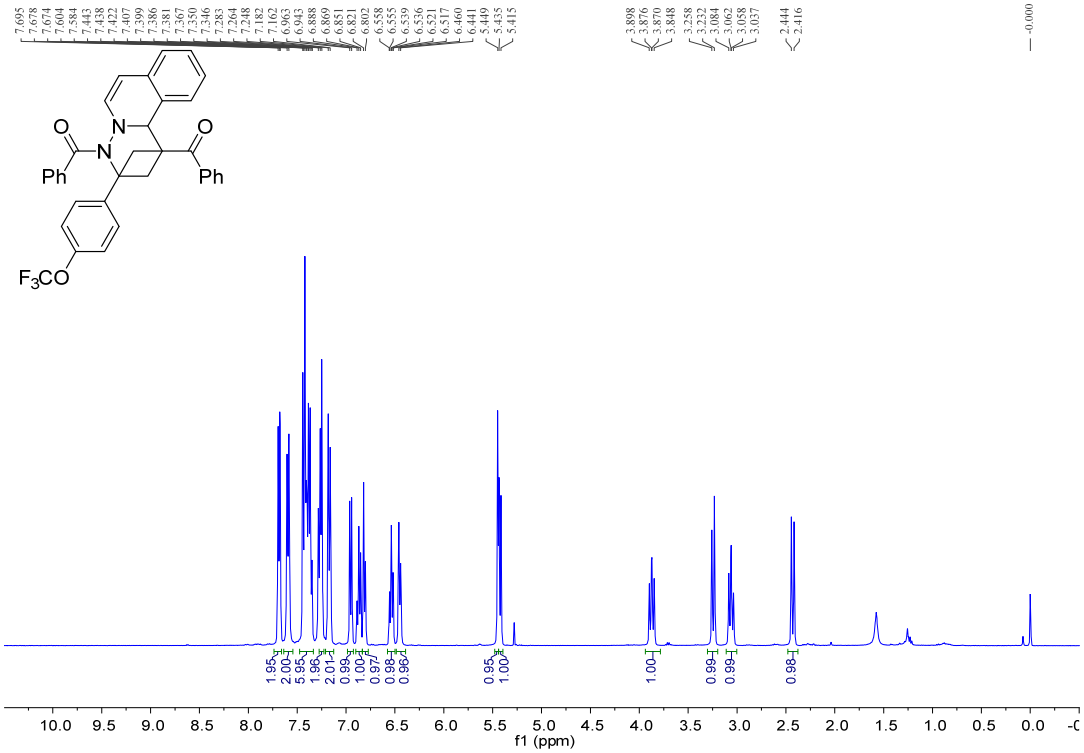


^{13}C NMR (100 MHz, $CDCl_3$)

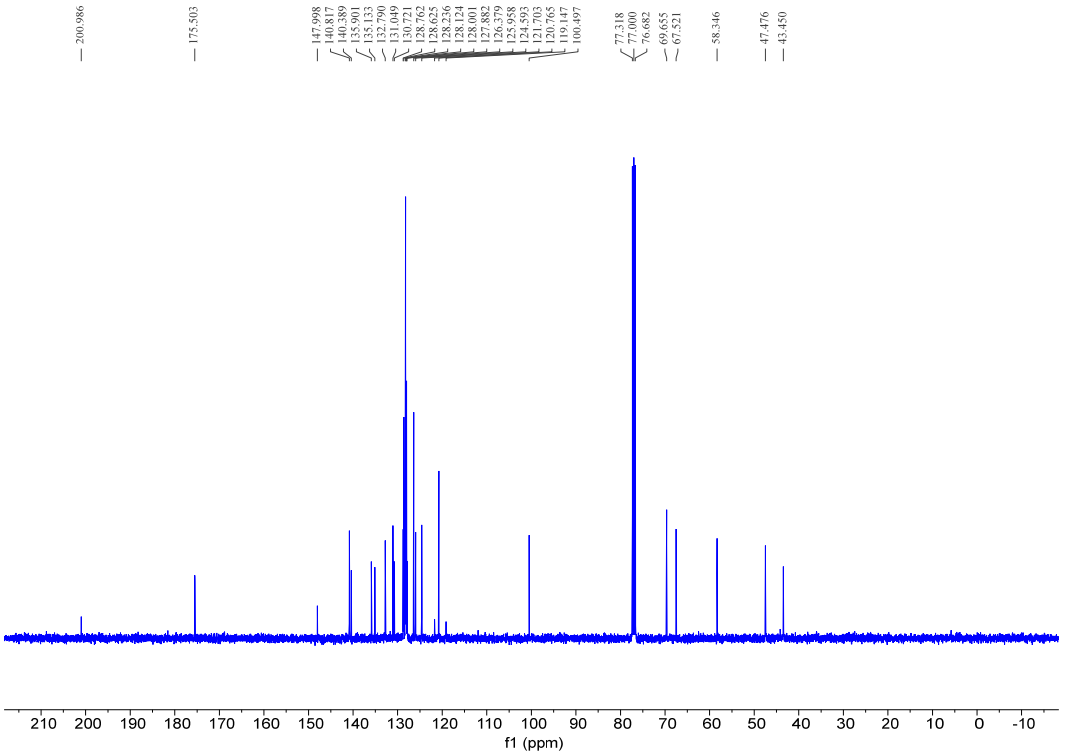


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3ha:

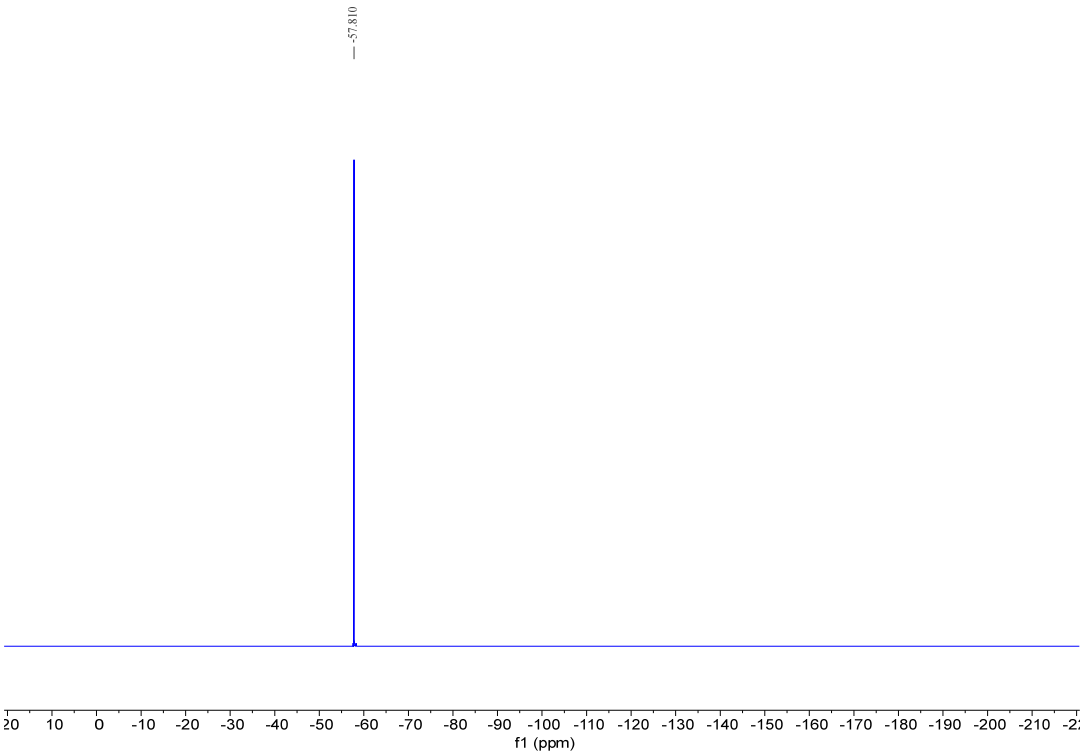
^{1}H NMR (400 MHz, $CDCl_3$)



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

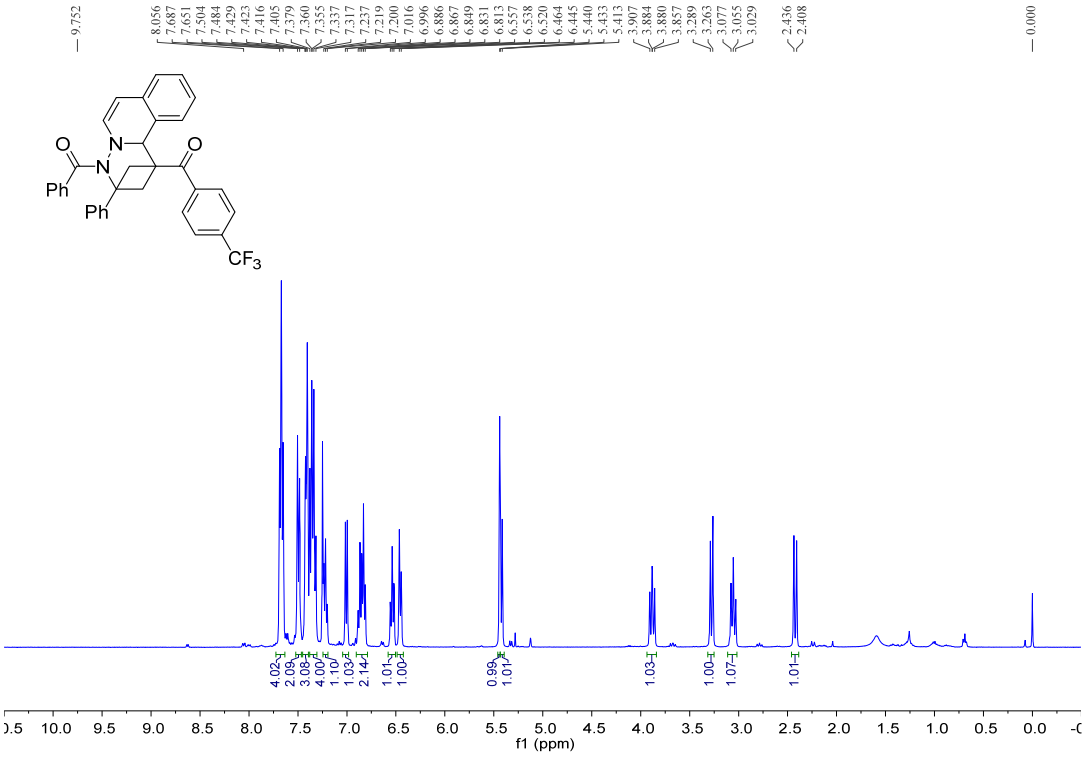


^{19}F NMR (376 MHz, $CDCl_3$)

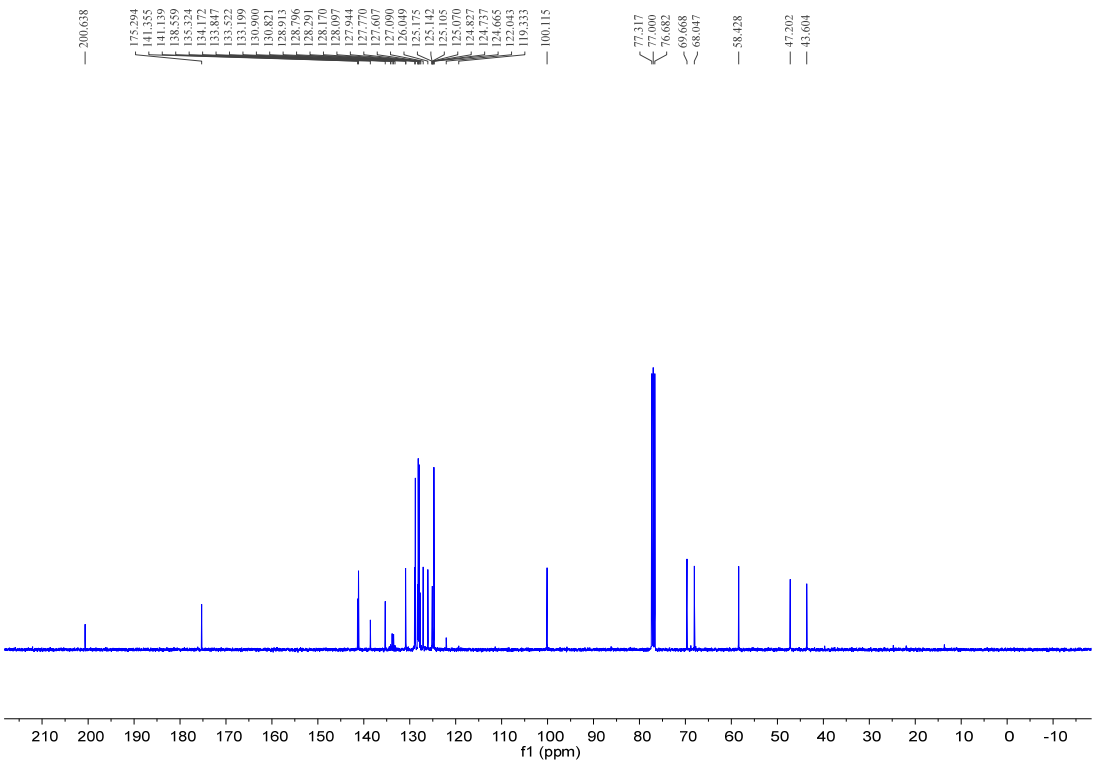


^{1}H and ^{13}C NMR Spectra for Compound 3ia:

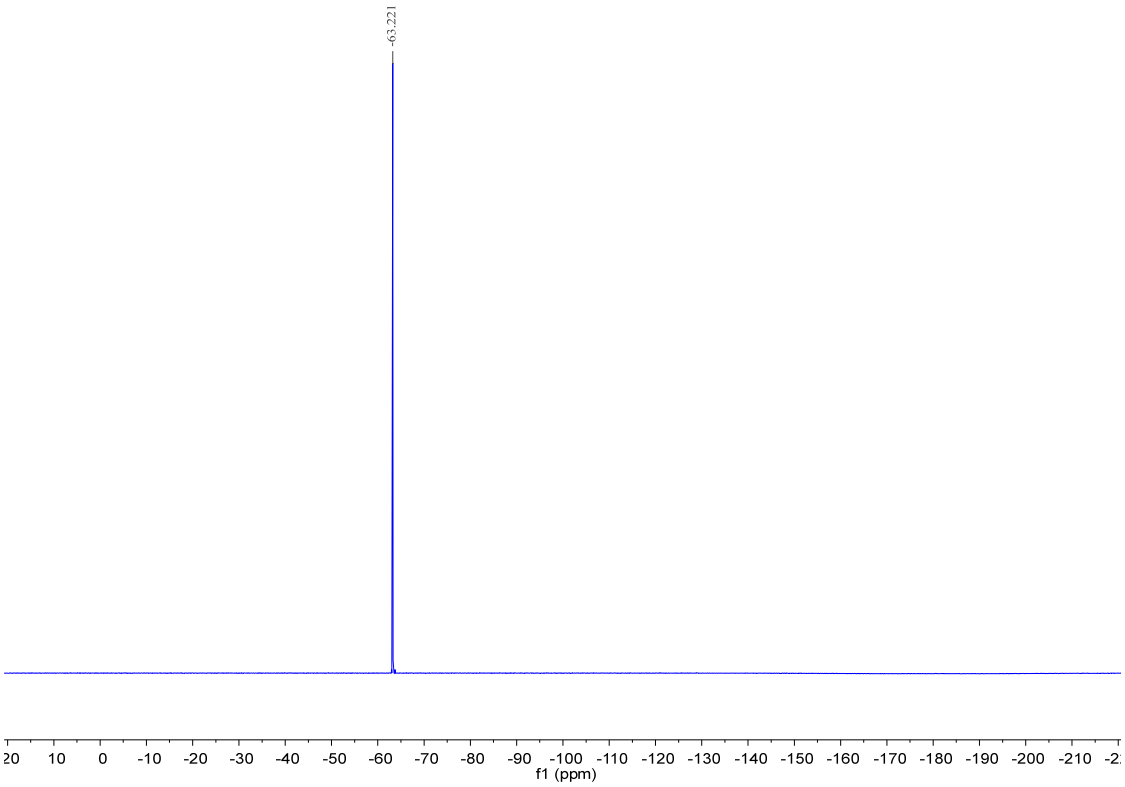
^{1}H NMR (400 MHz, $CDCl_3$)



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

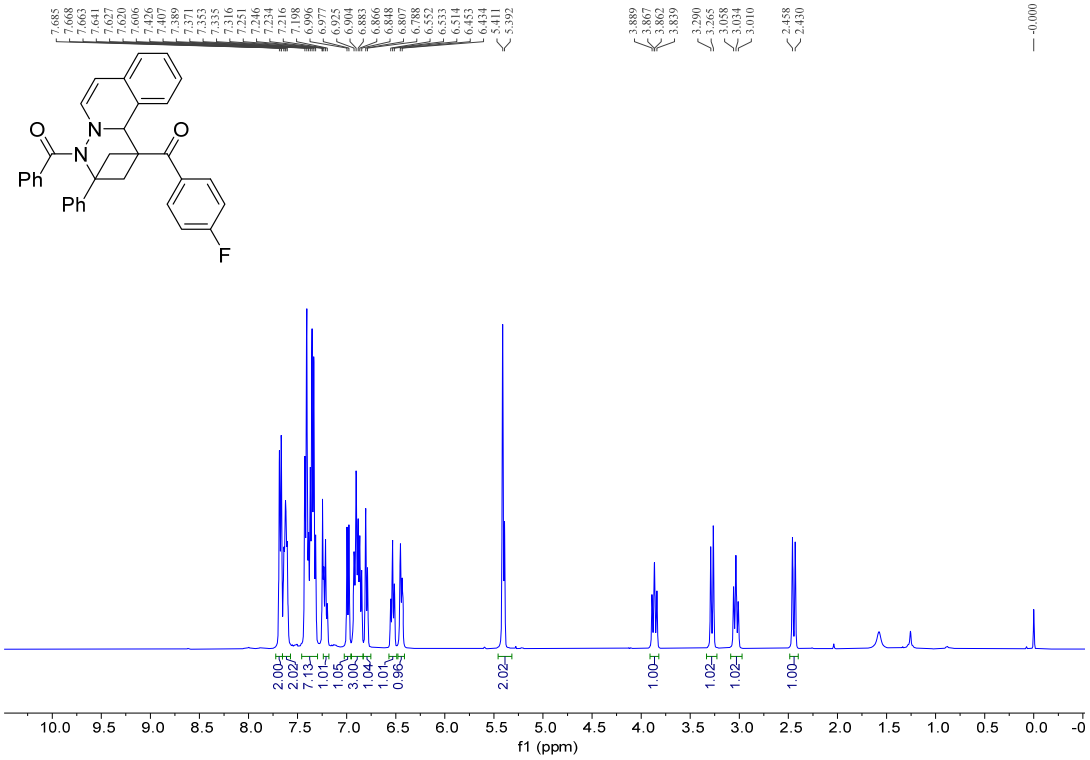


^{19}F NMR (376 MHz, $CDCl_3$)

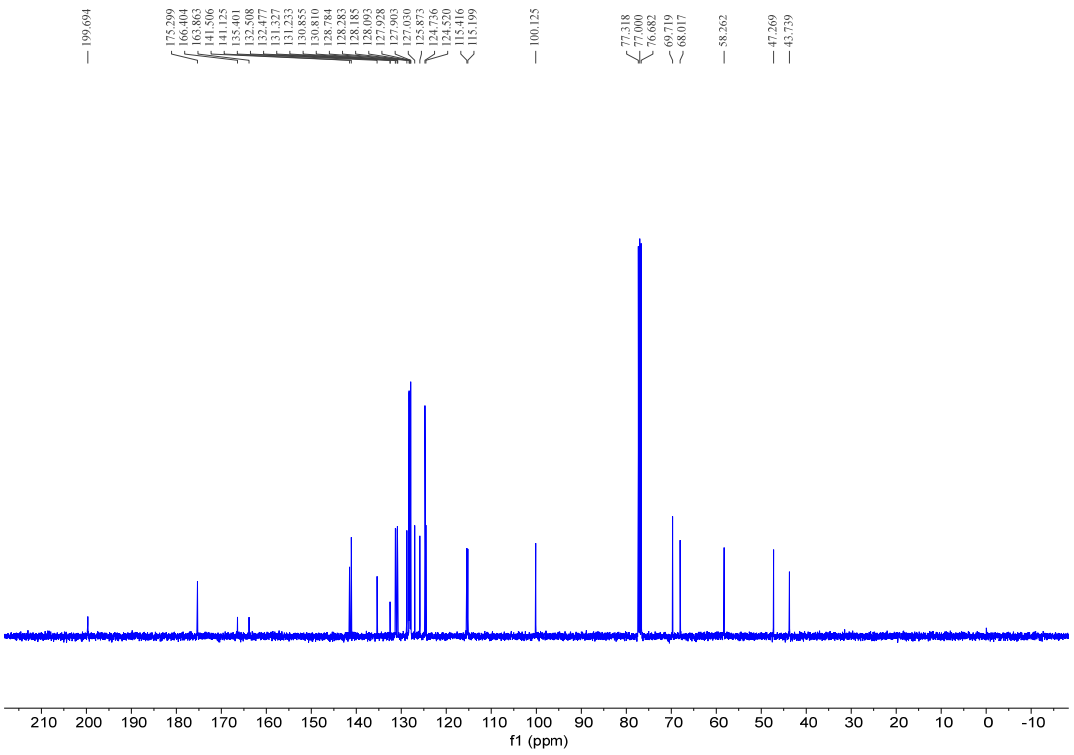


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3ja:

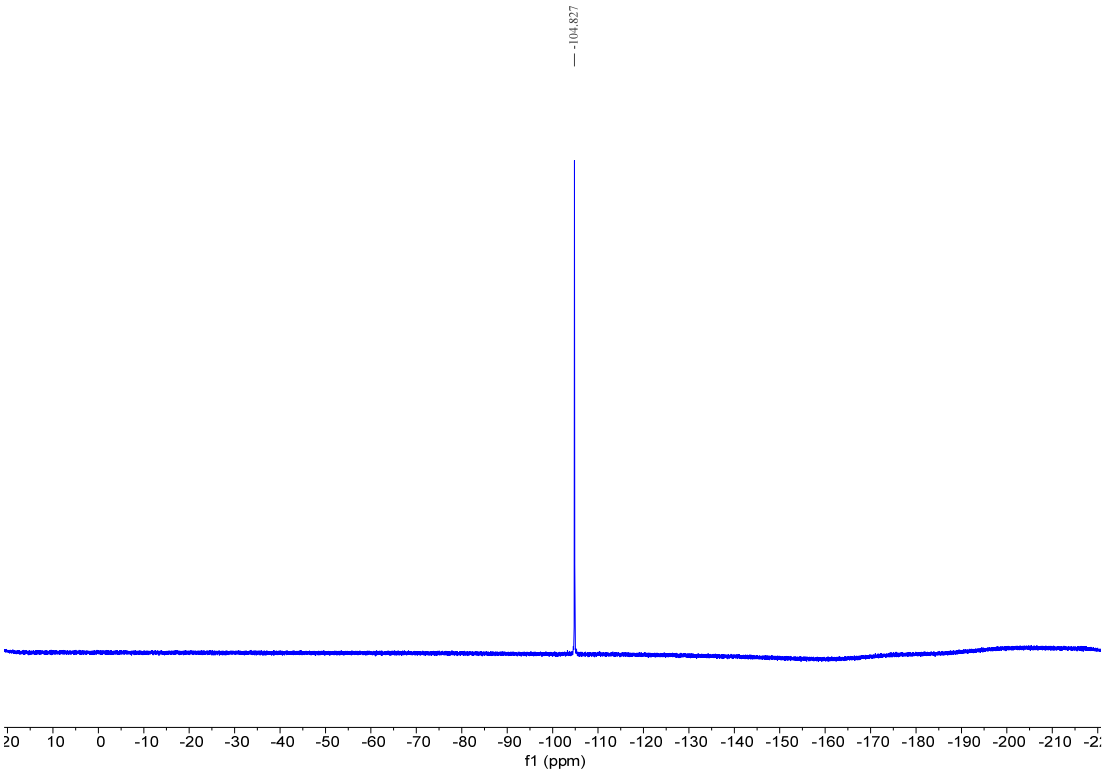
^{1}H NMR (400 MHz, $CDCl_3$)



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

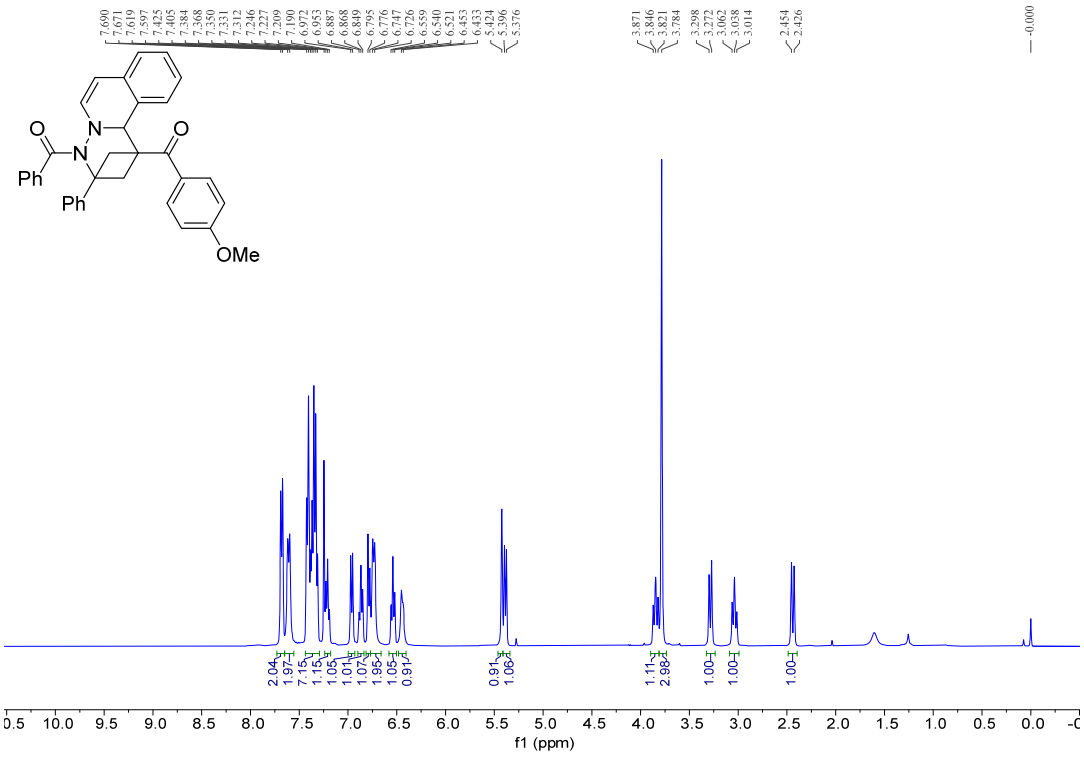


^{19}F NMR (376 MHz, $CDCl_3$)

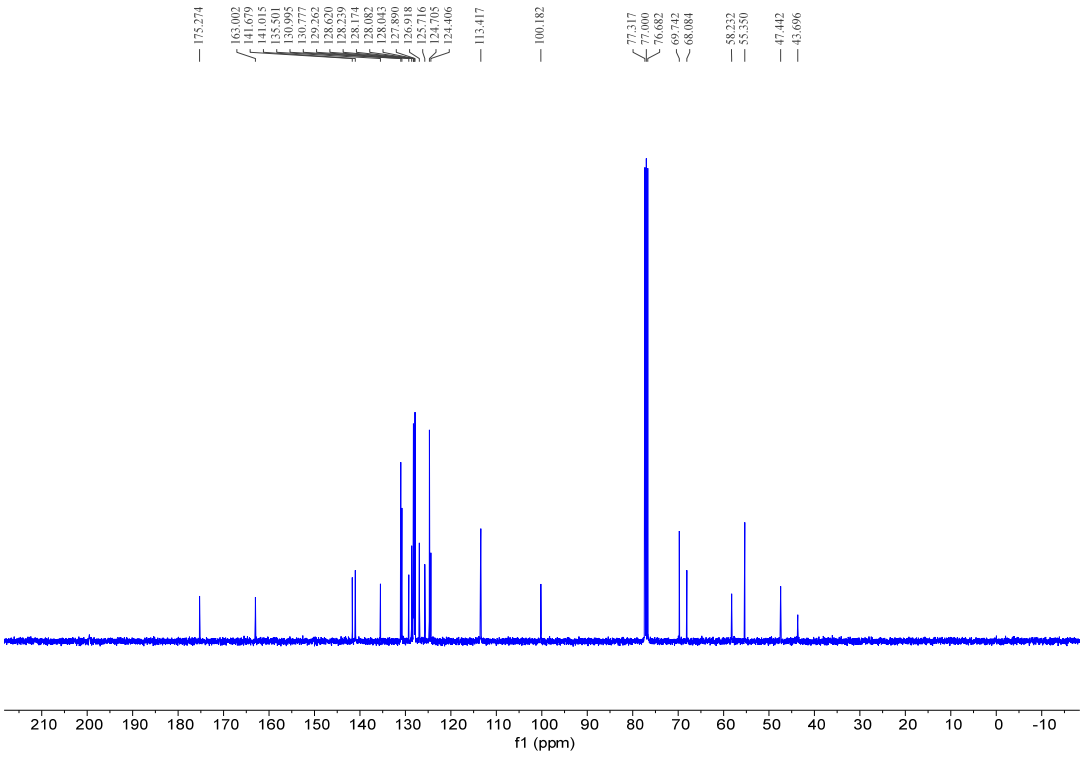


^{1}H and ^{13}C NMR Spectra for Compound 3ka:

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

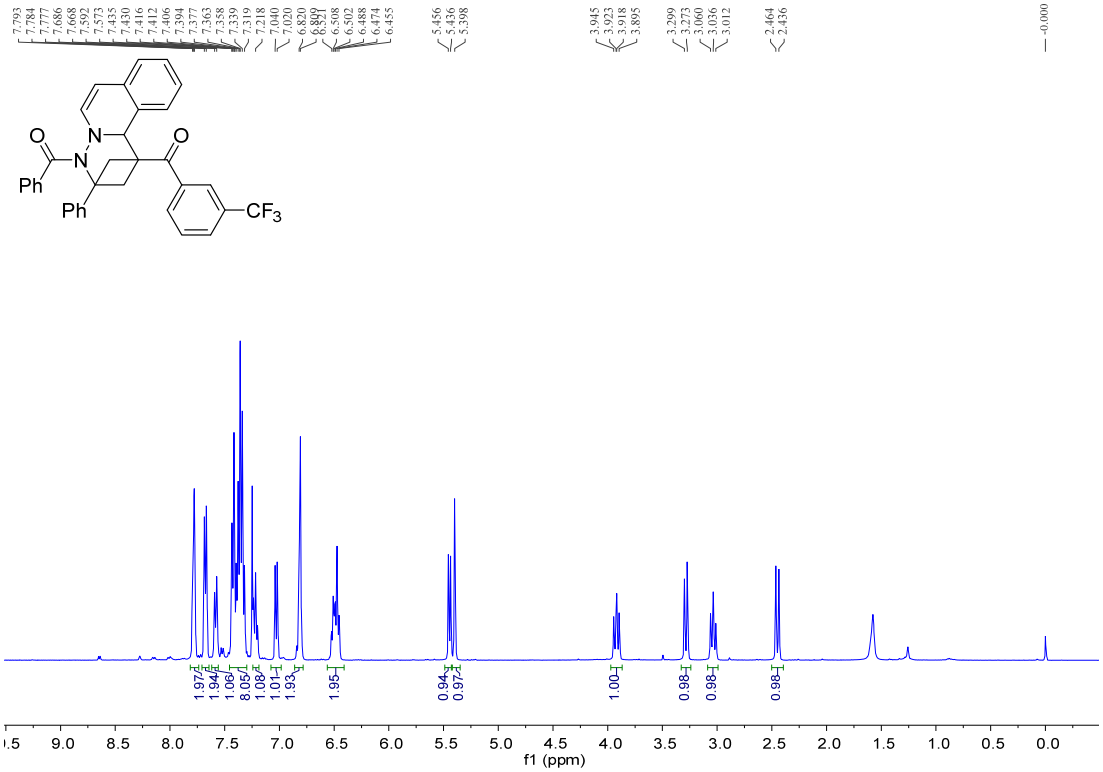


^{13}C NMR (100 MHz, $CDCl_3$)

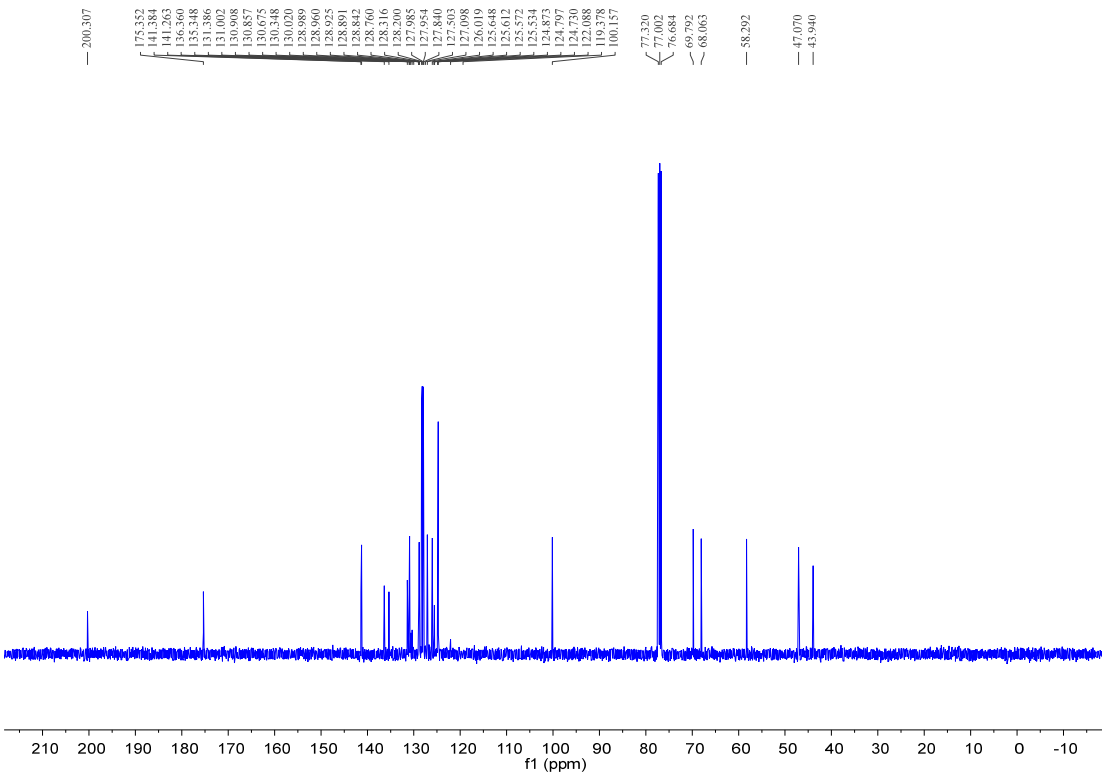


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3la:

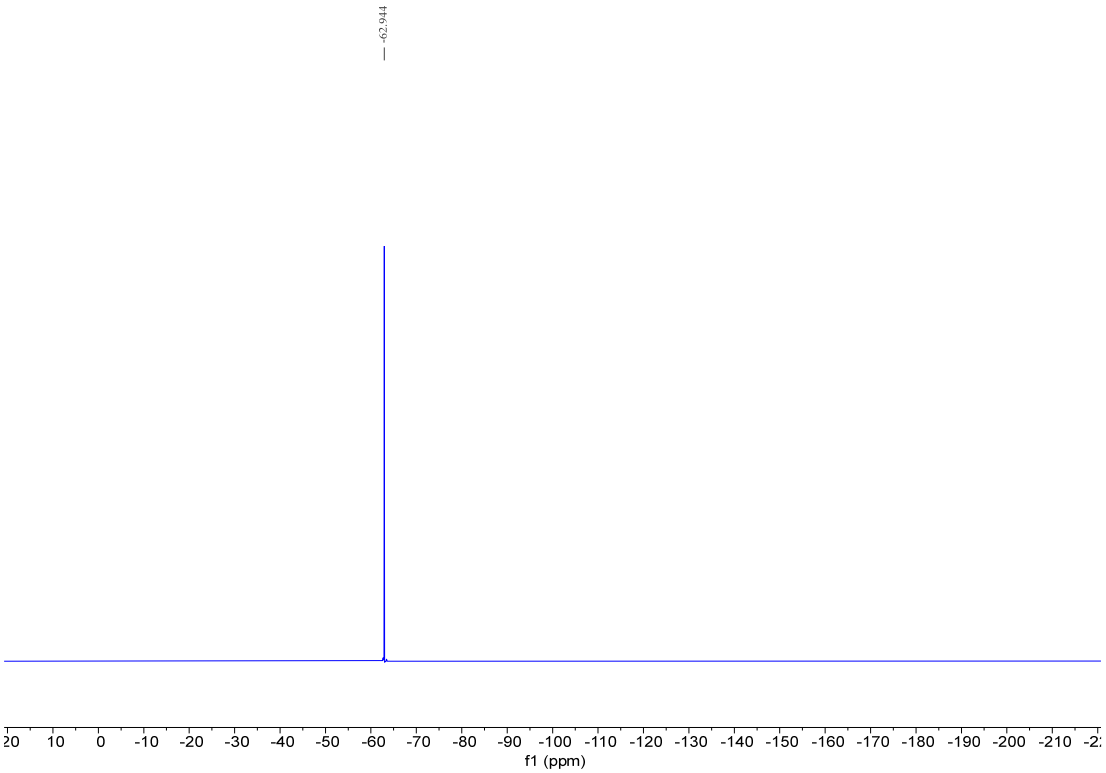
^{1}H NMR (400 MHz, $CDCl_3$)



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

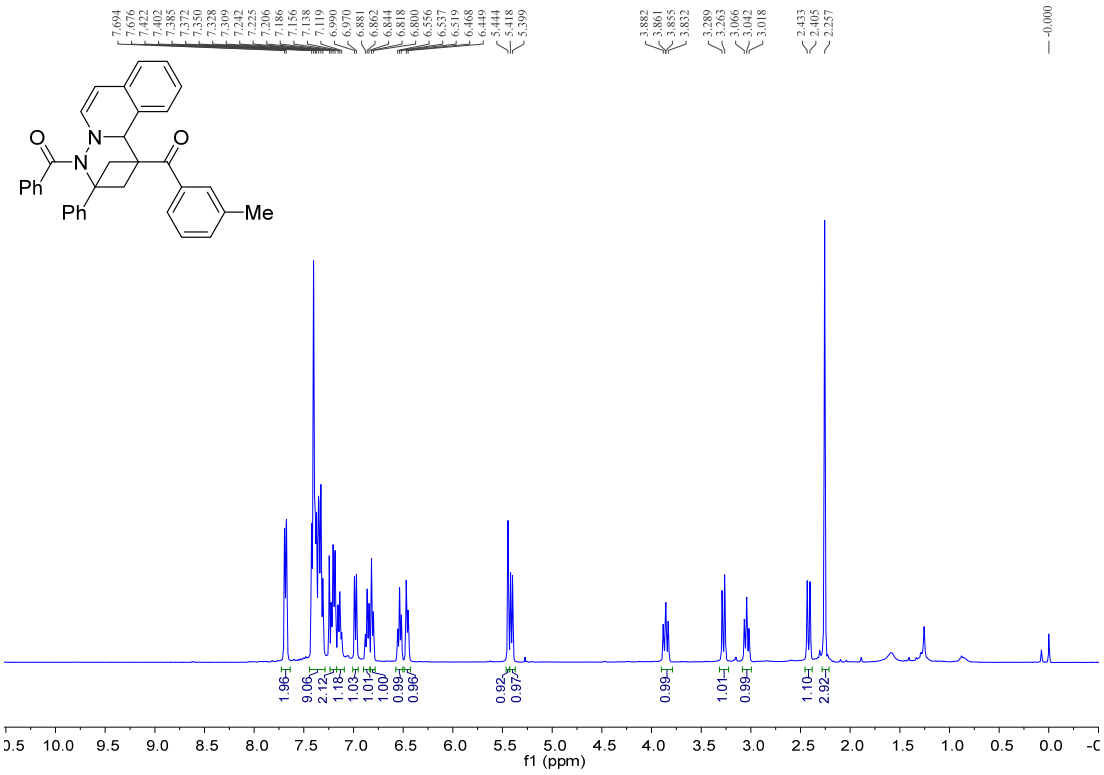


^{19}F NMR (376 MHz, $CDCl_3$)

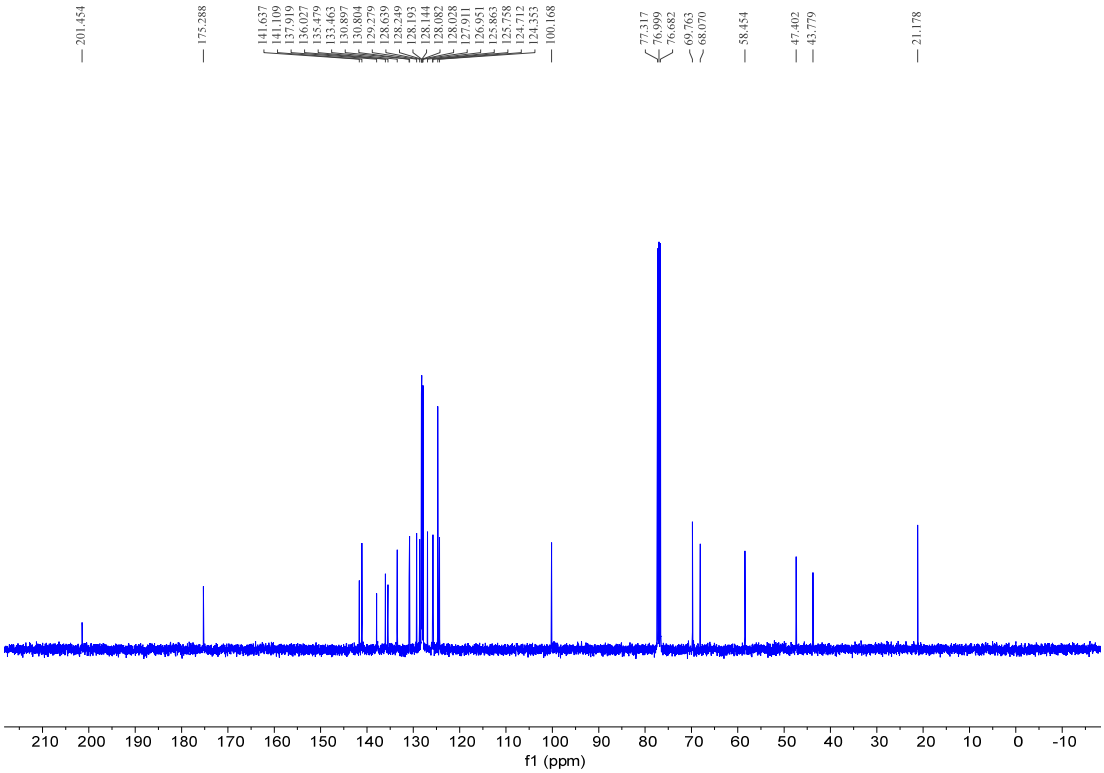


^{1}H and ^{13}C NMR Spectra for Compound 3ma:

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

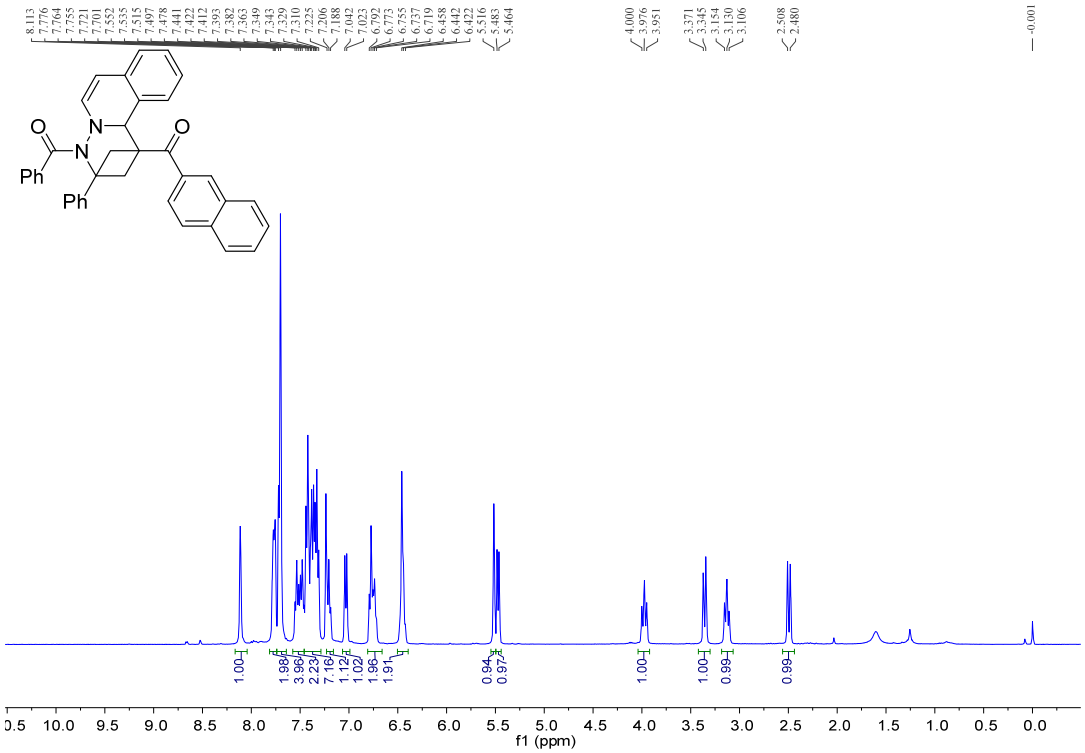


^{13}C NMR (100 MHz, $CDCl_3$)

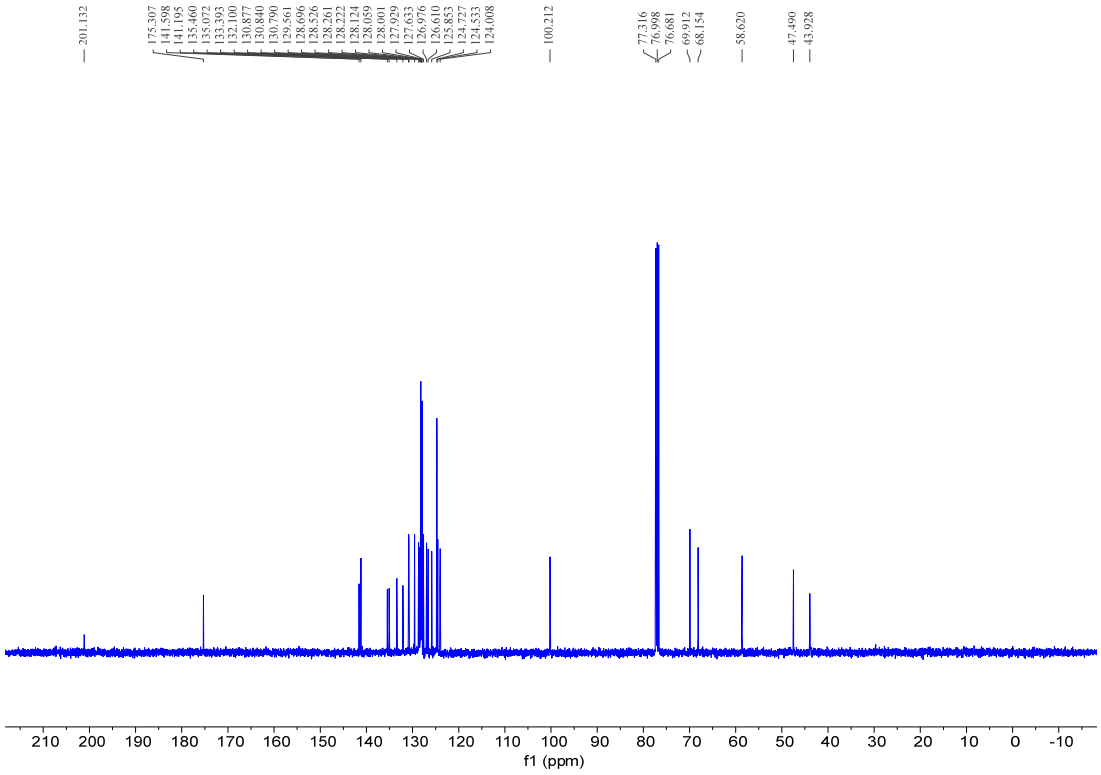


^{1}H and ^{13}C NMR Spectra for Compound 3na:

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

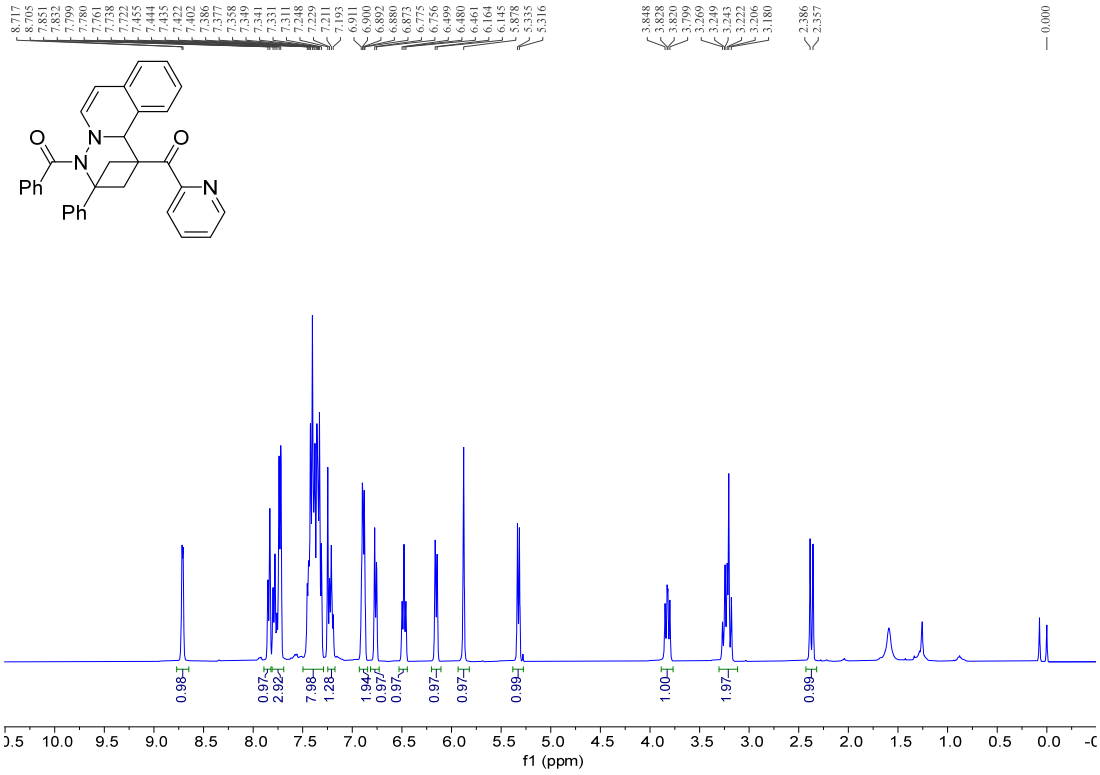


^{13}C NMR (100 MHz, $CDCl_3$)

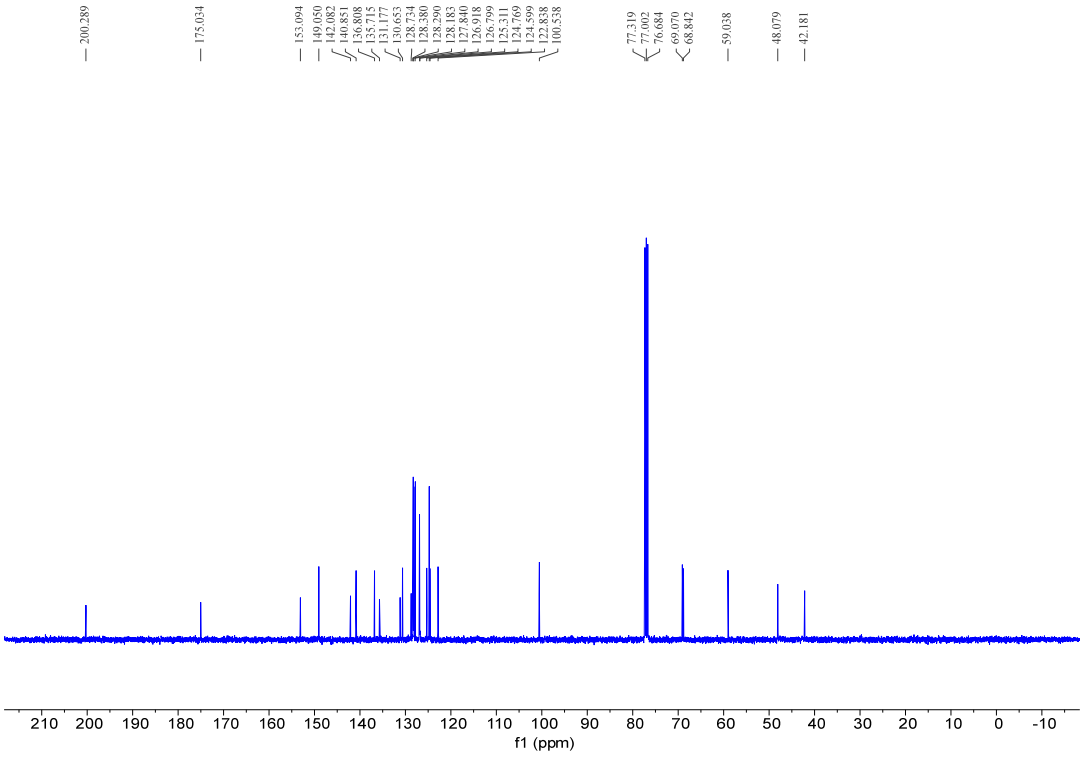


^{1}H and ^{13}C NMR Spectra for Compound 3oa:

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

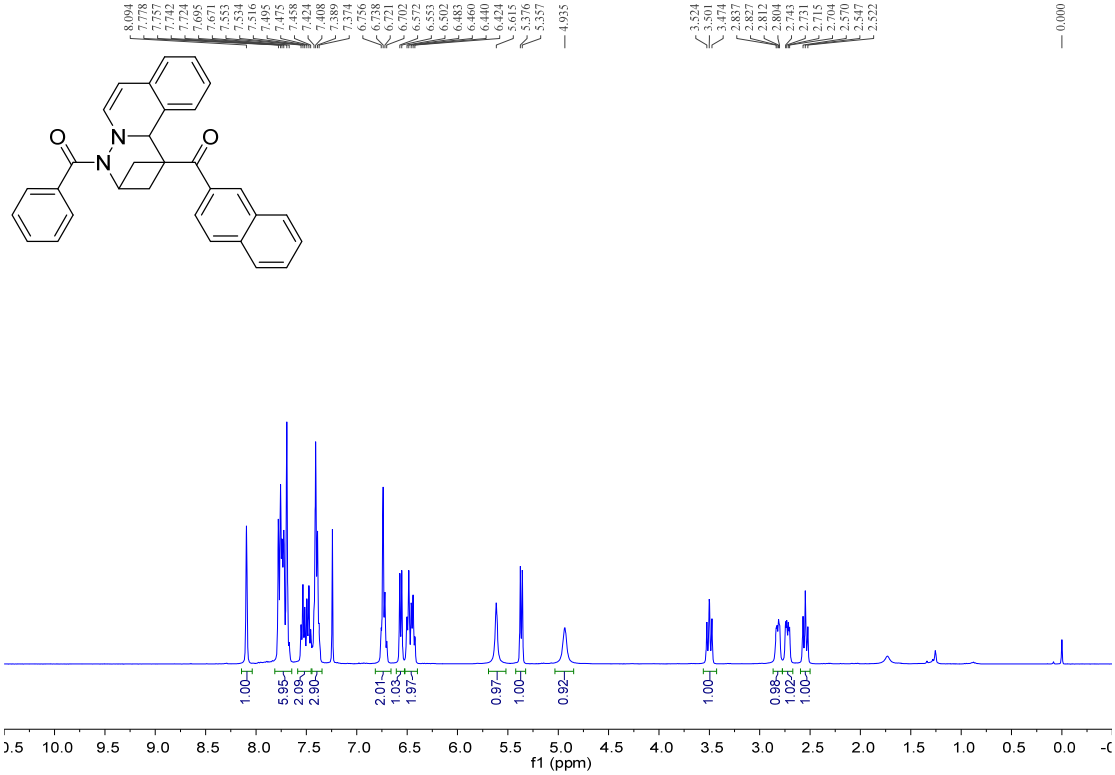


^{13}C NMR (100 MHz, $CDCl_3$)

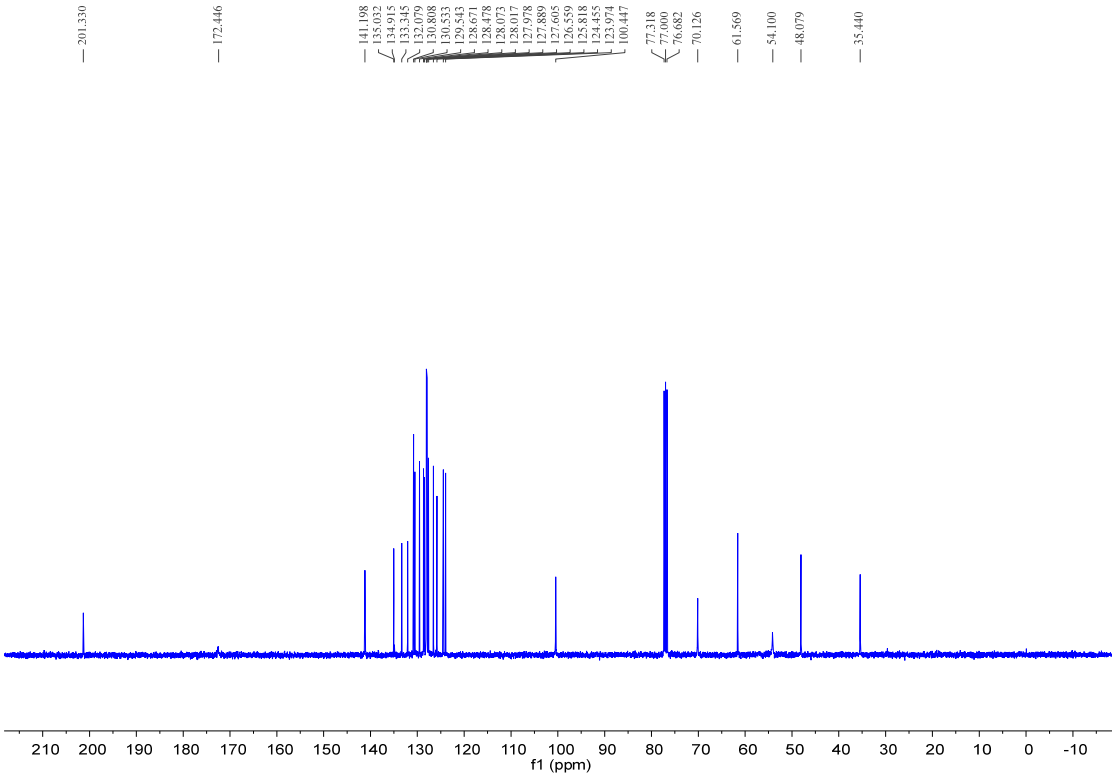


^{1}H and ^{13}C Spectra for Compound 3pa:

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

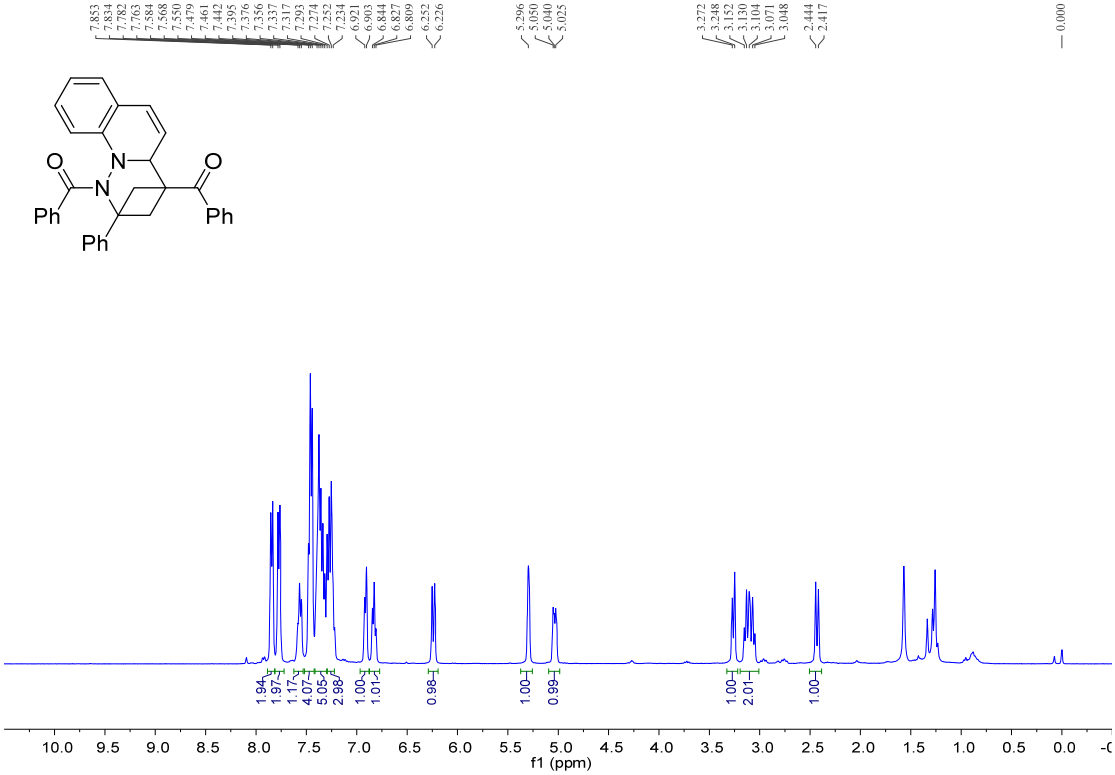


^{13}C NMR (100 MHz, $CDCl_3$)

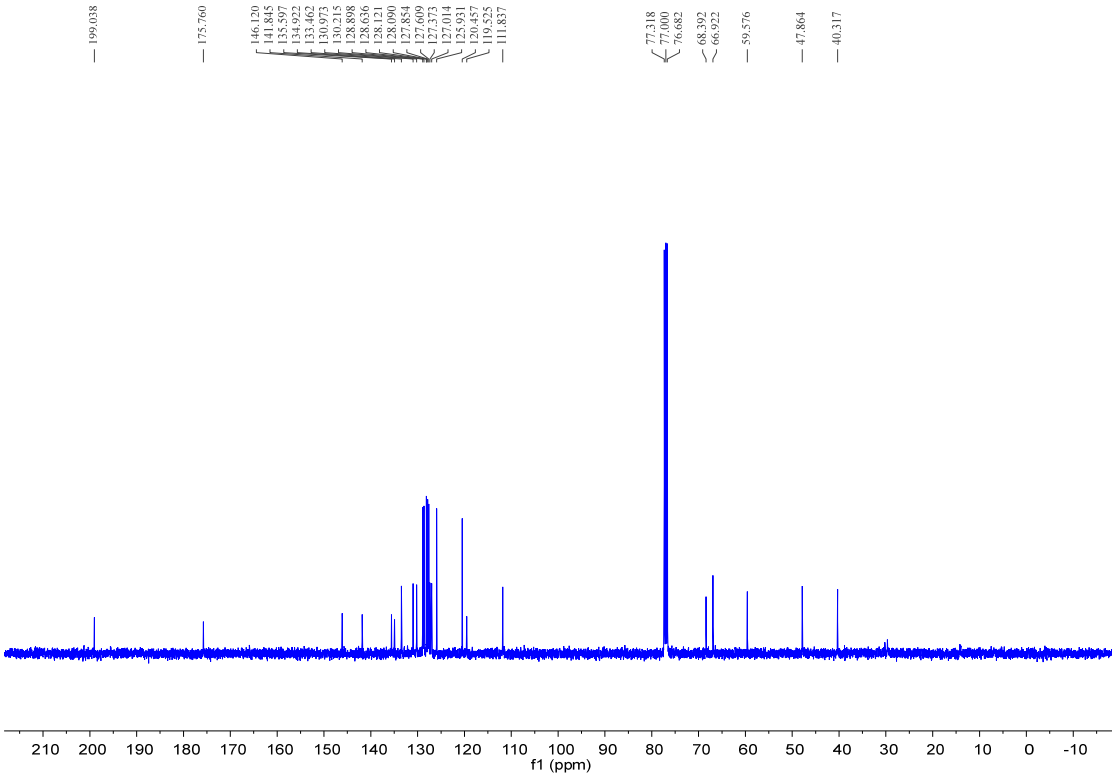


^{1}H and ^{13}C NMR Spectra for Compound 4gb:

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

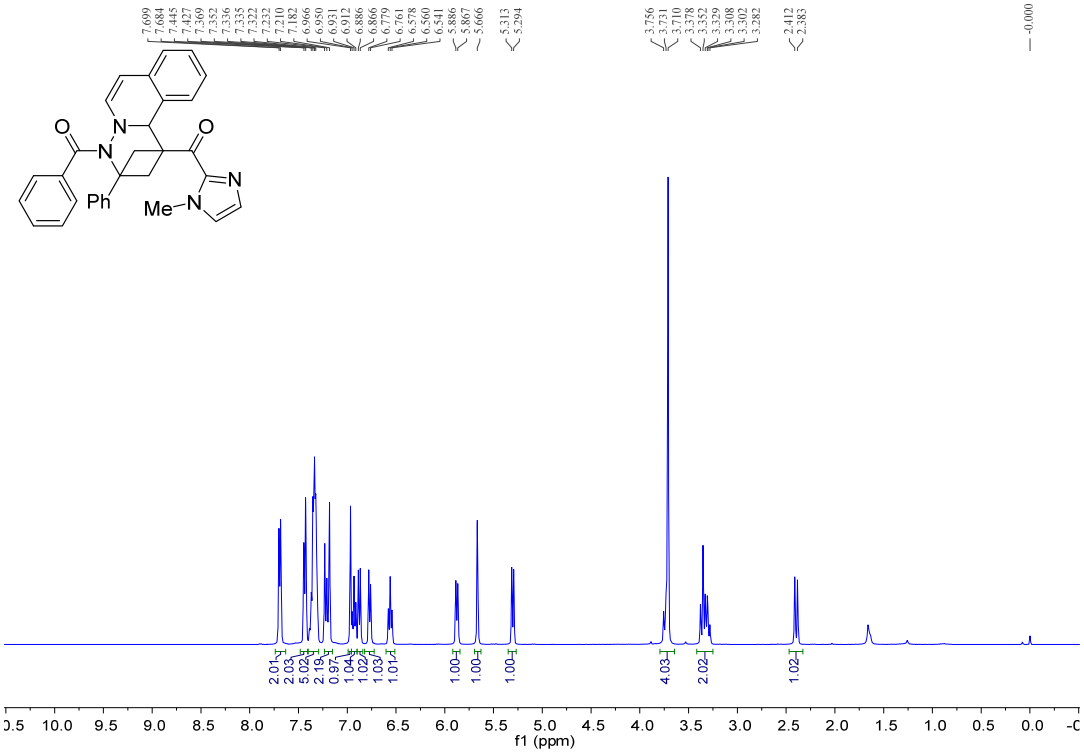


^{13}C NMR (100 MHz, $CDCl_3$)

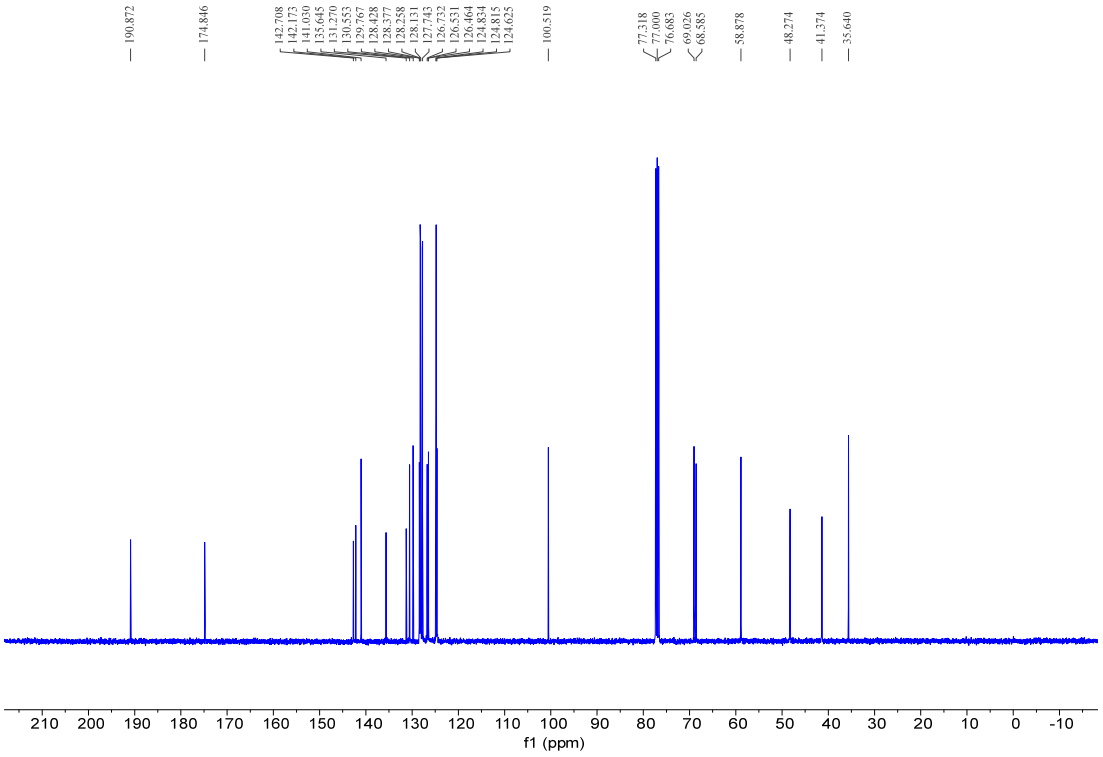


^{1}H and ^{13}C NMR Spectra for Compound 3qa:

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

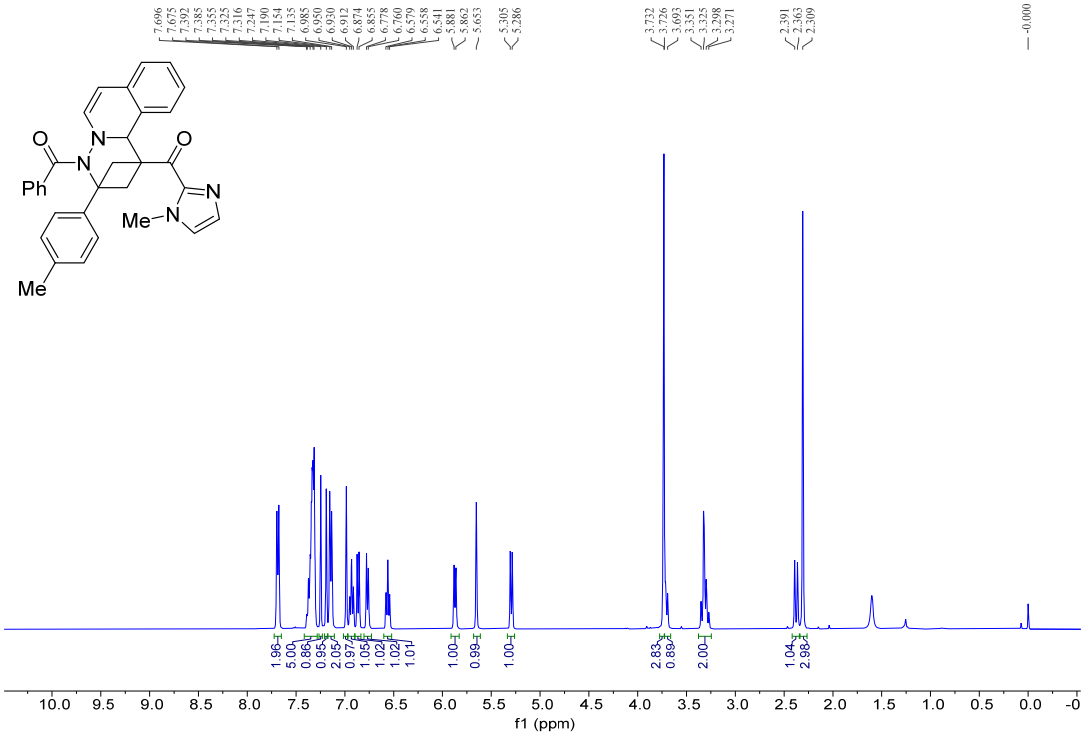


^{13}C NMR (100 MHz, $CDCl_3$)

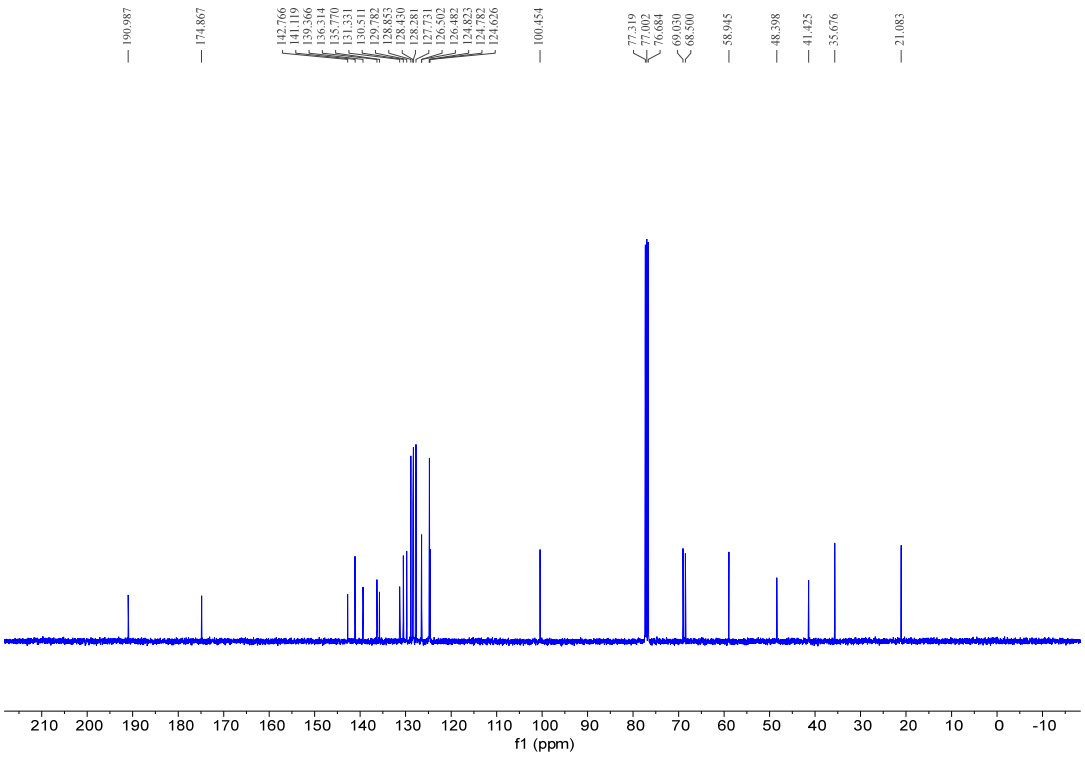


^{1}H and ^{13}C NMR Spectra for Compound 3ra:

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

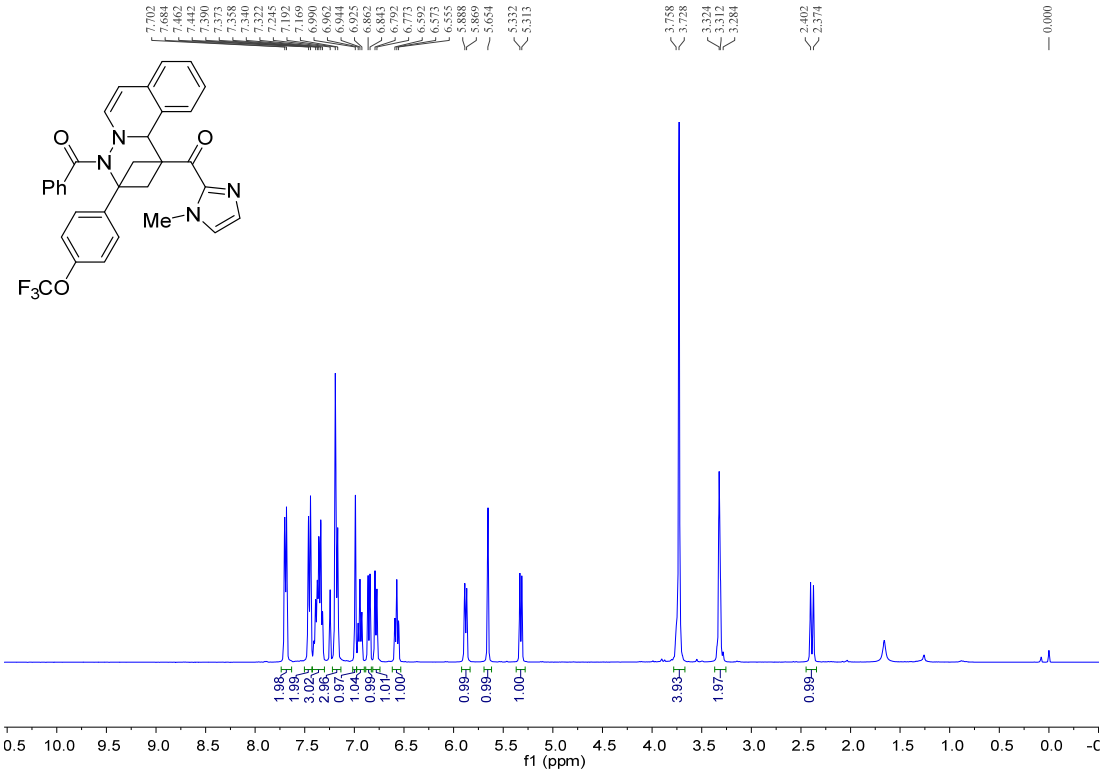


^{13}C NMR (100 MHz, $CDCl_3$)

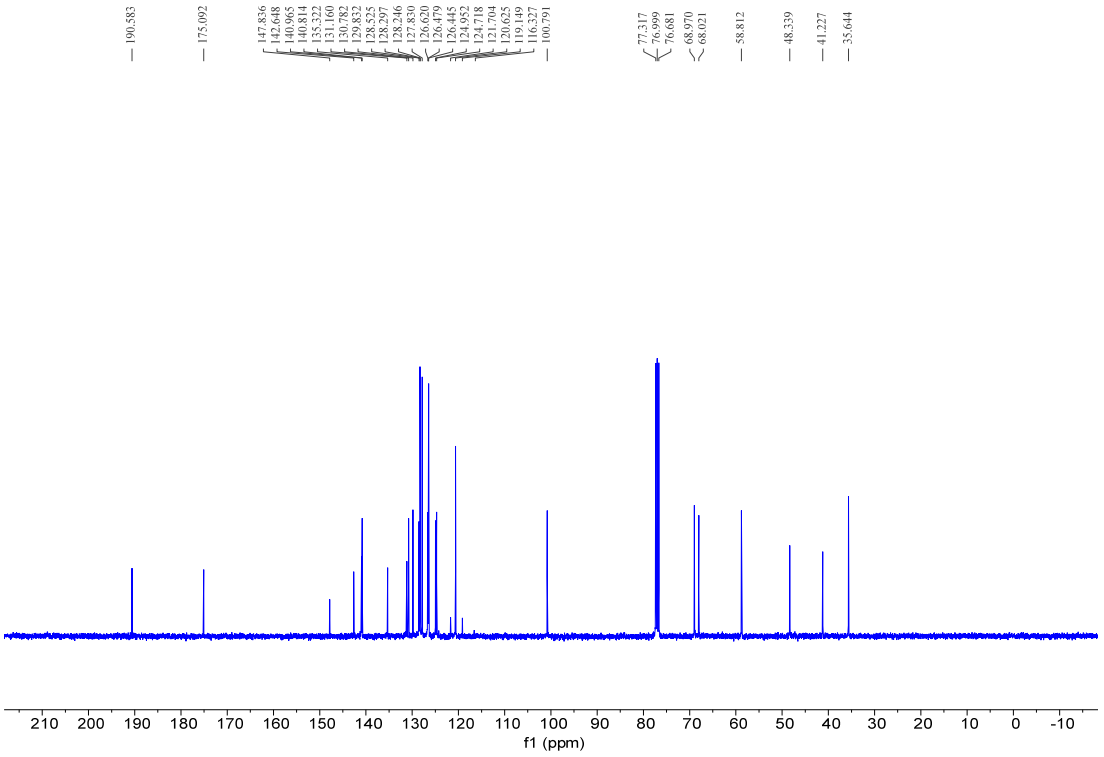


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3sa:

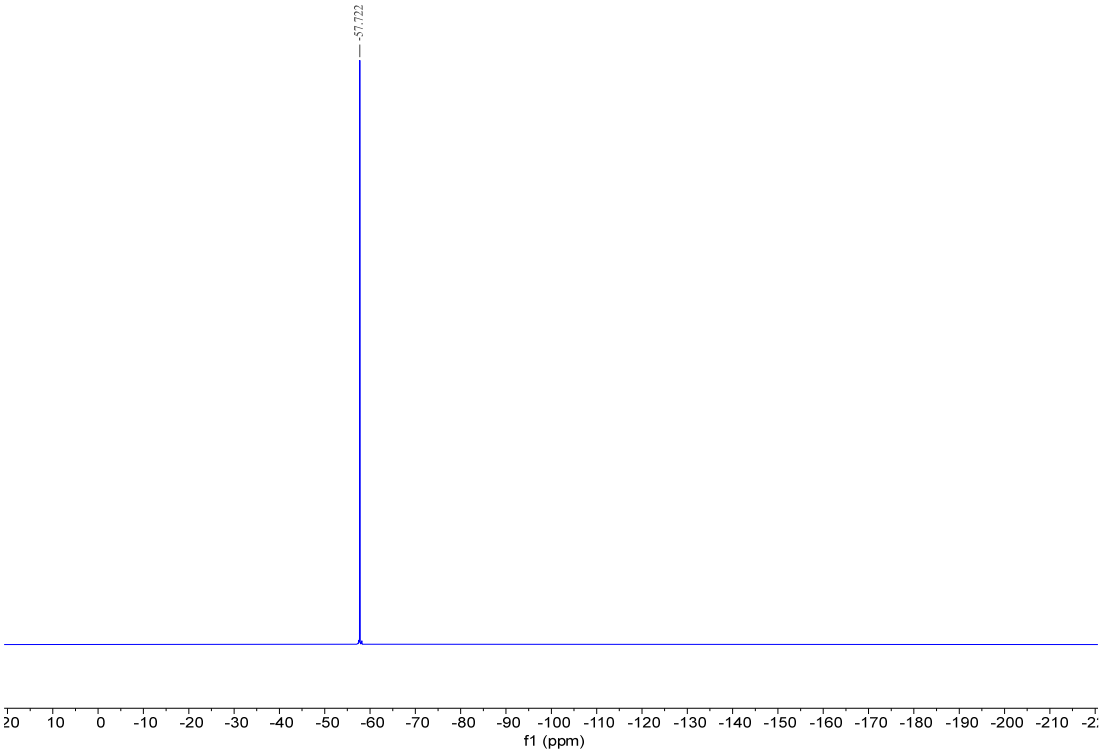
^{1}H NMR (400 MHz, $CDCl_3$)



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

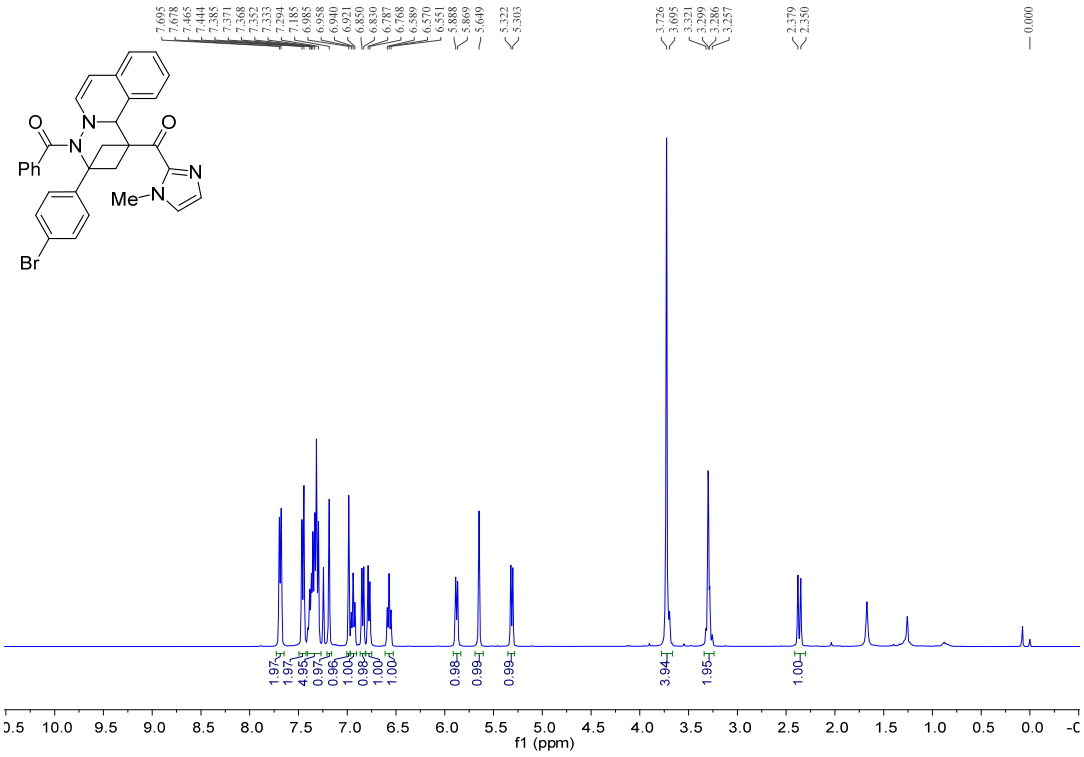


^{19}F NMR (376 MHz, $CDCl_3$)

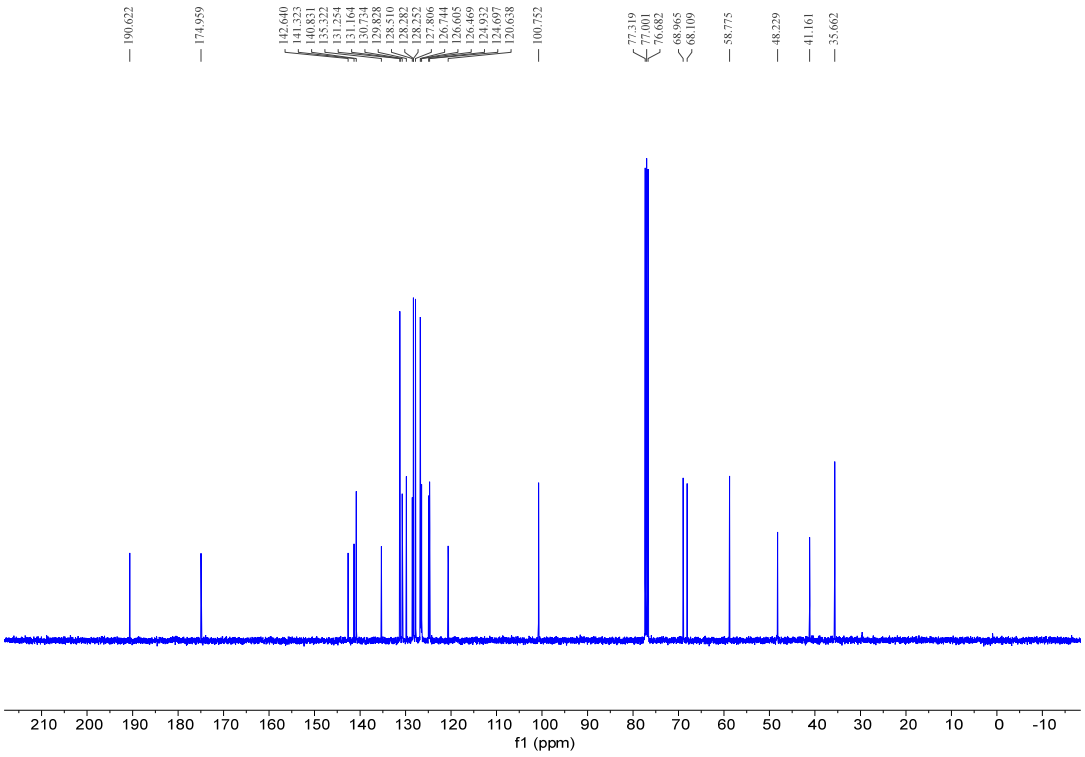


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3ta:

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

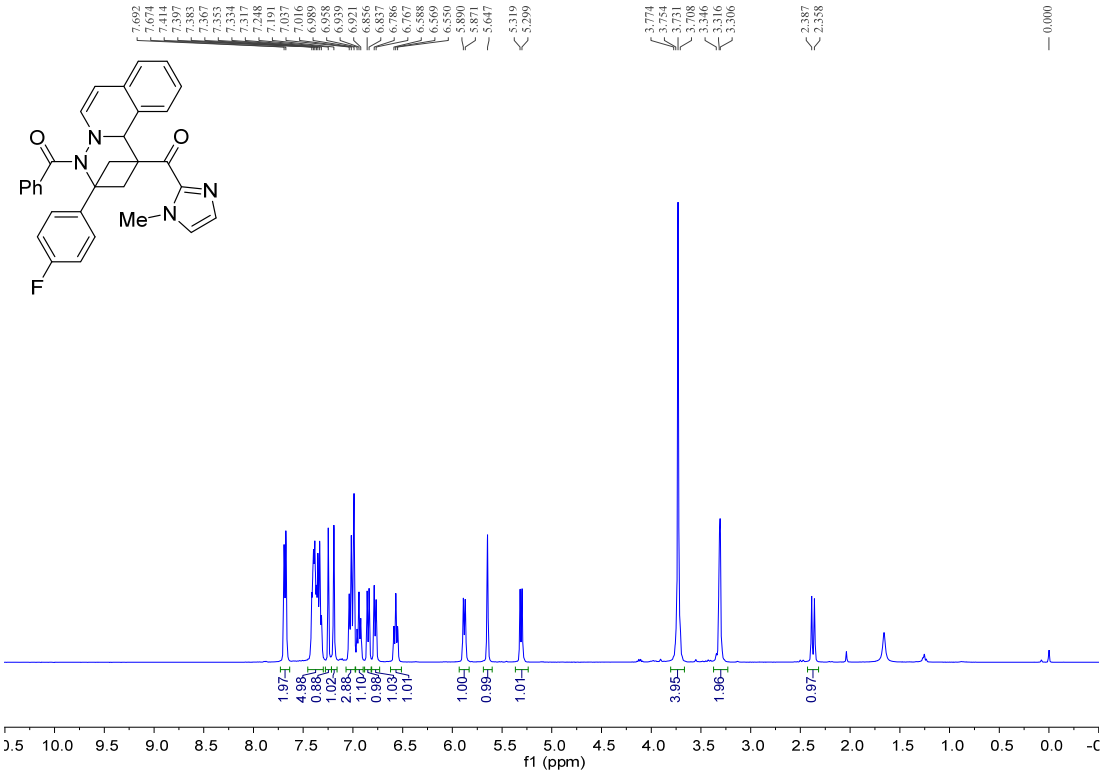


^{13}C NMR (100 MHz, $CDCl_3$)

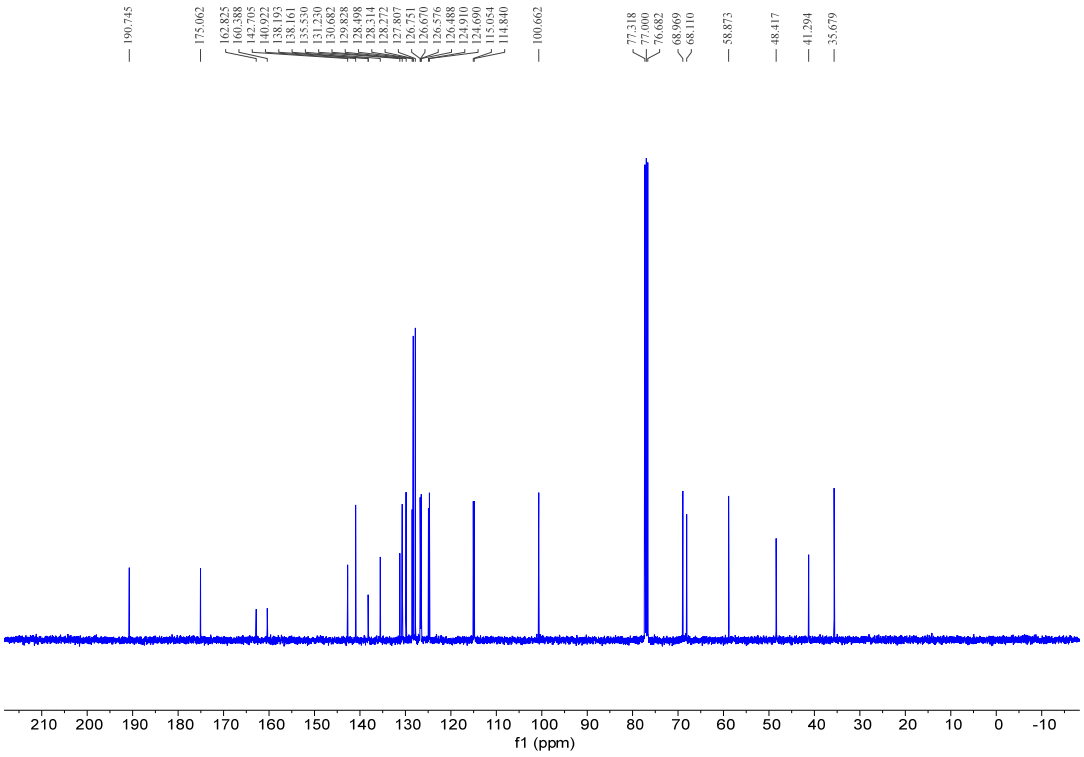


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3ua:

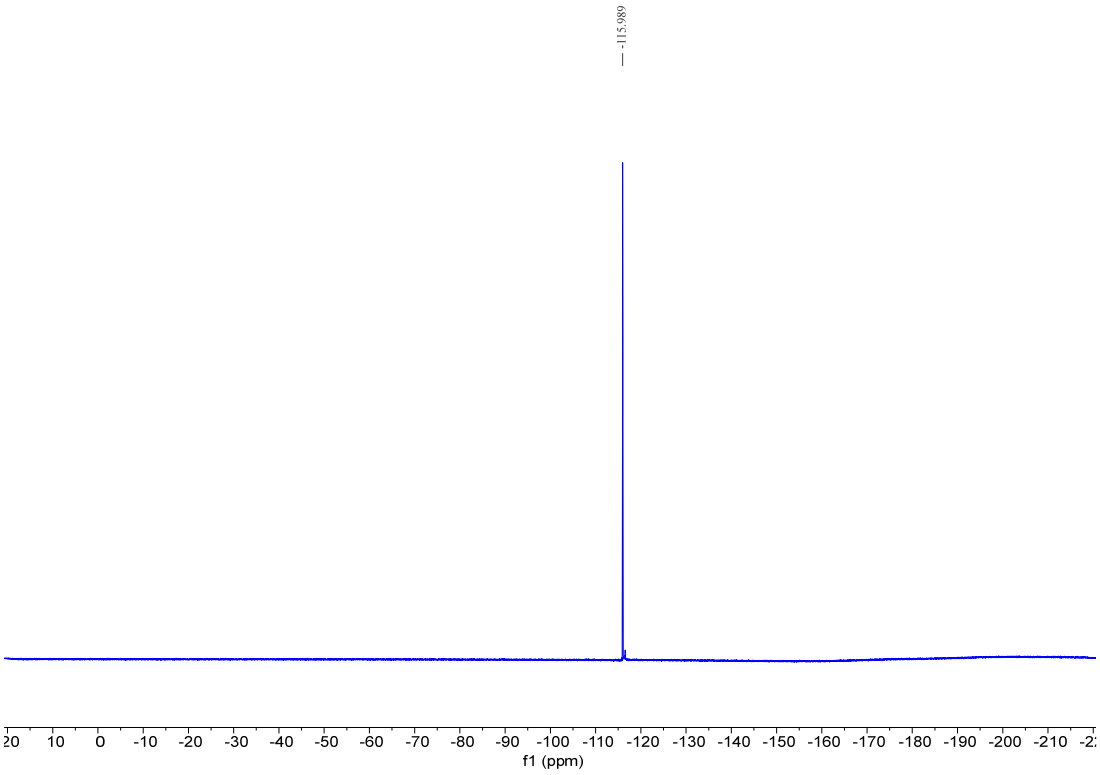
^{1}H NMR (400 MHz, $CDCl_3$)



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

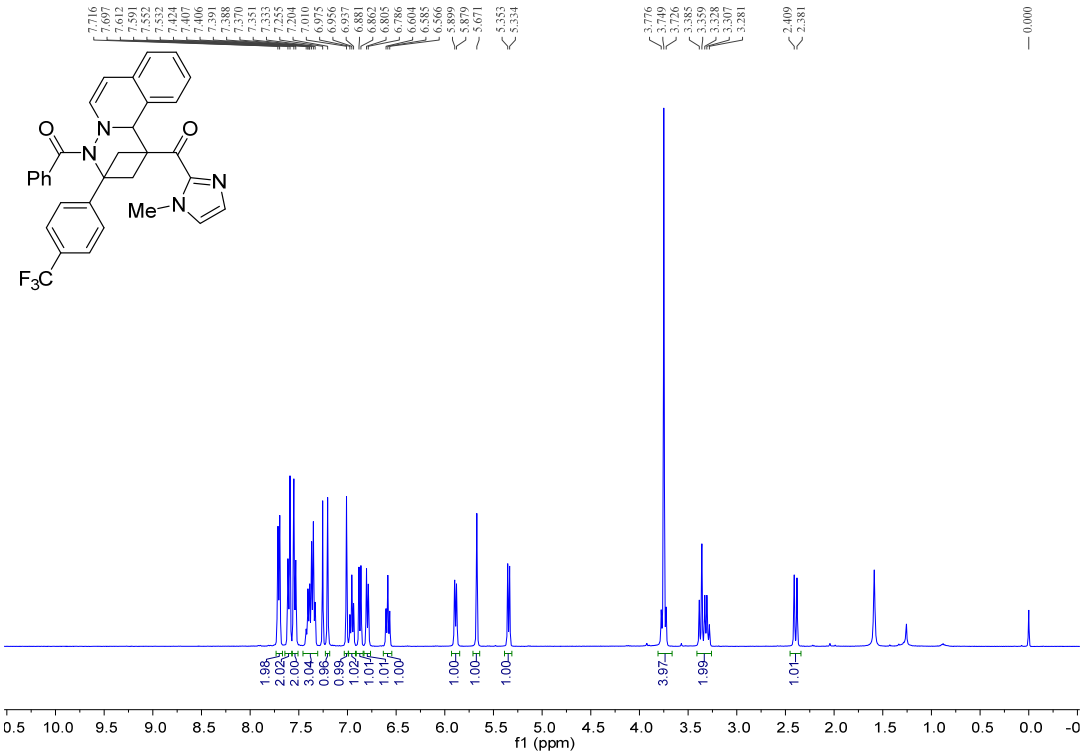


^{19}F NMR (376 MHz, $CDCl_3$)

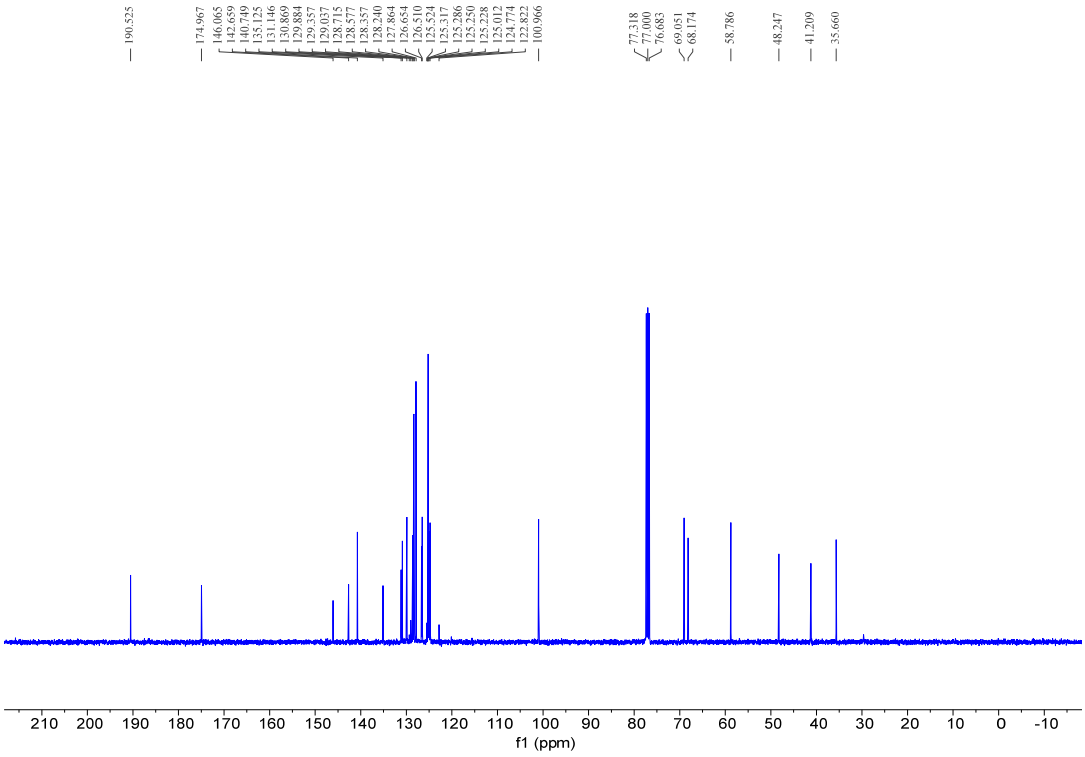


^{1}H and ^{13}C NMR Spectra for Compound 3va:

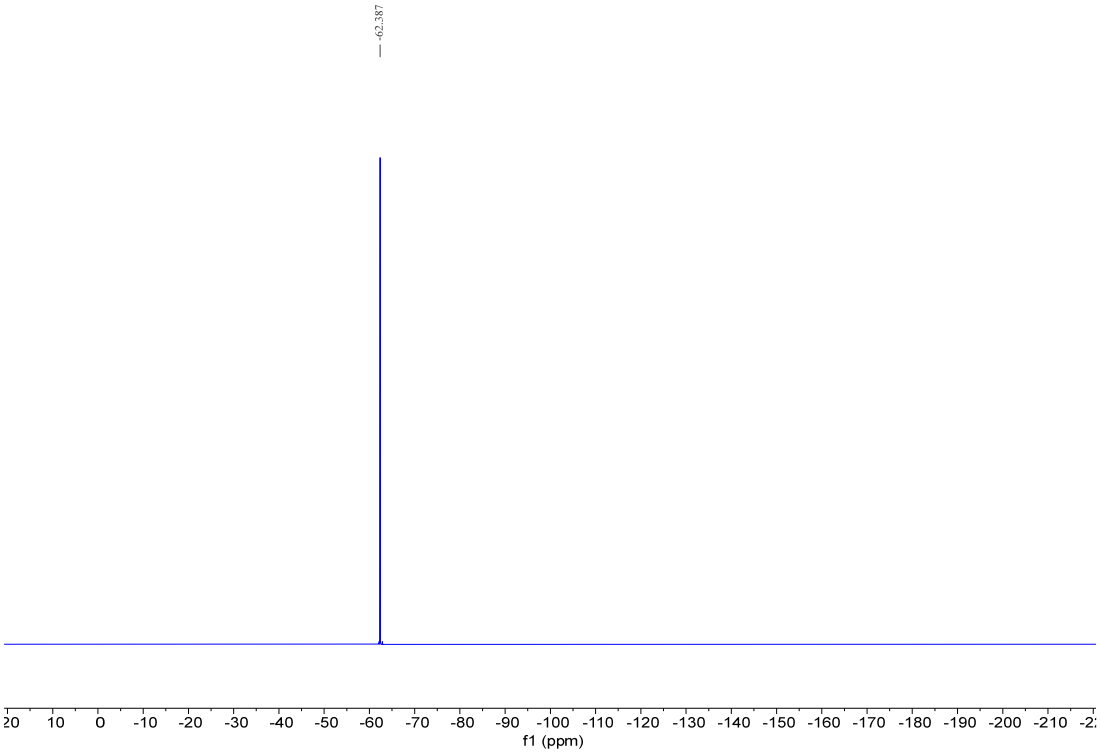
^{1}H NMR (400 MHz, $CDCl_3$)



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

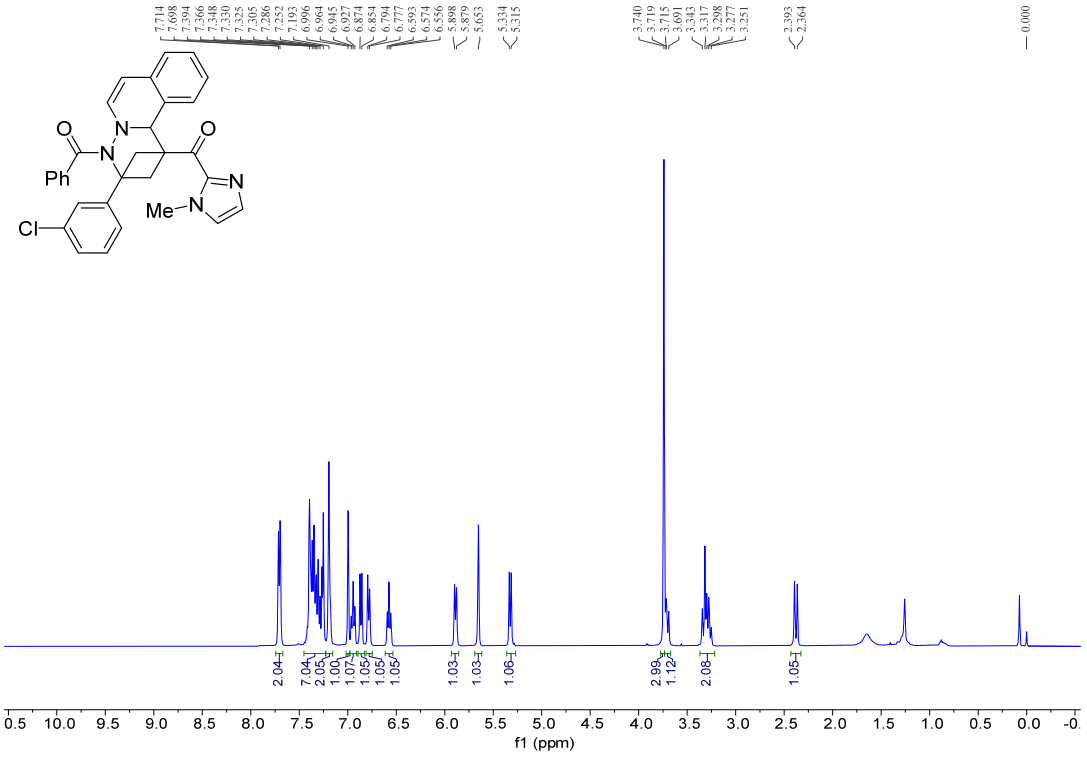


^{19}F NMR (376 MHz, $CDCl_3$)

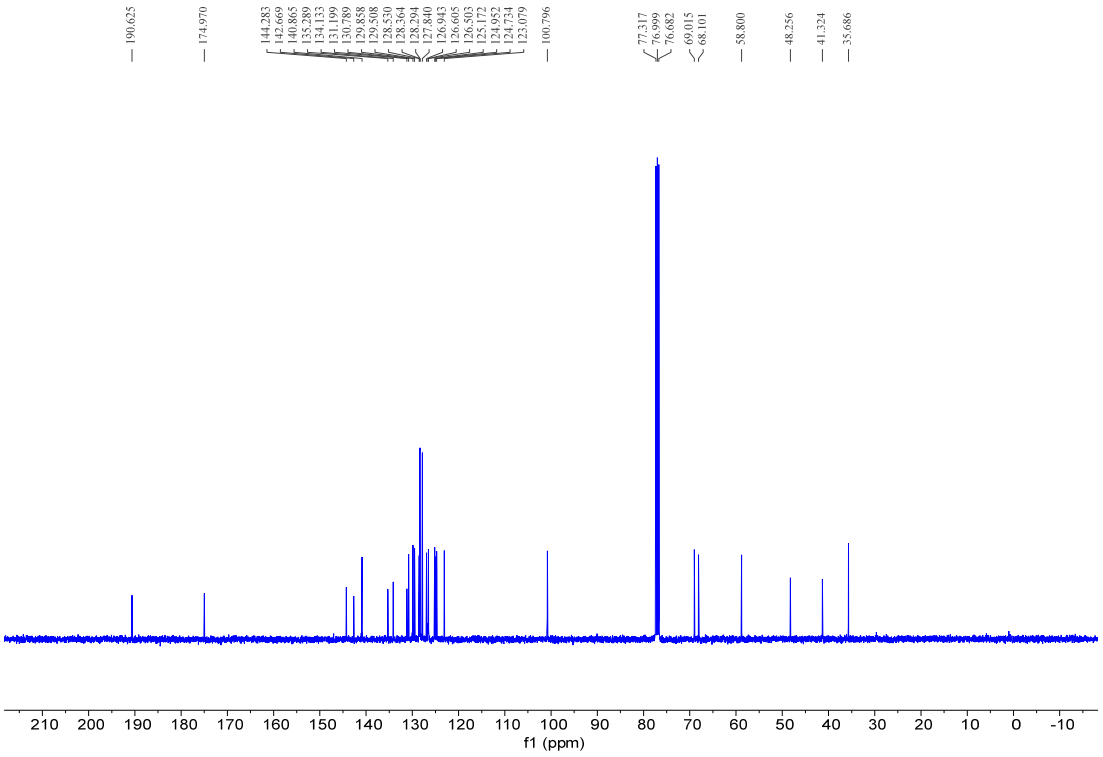


^{1}H and ^{13}C NMR Spectra for Compound 3wa:

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

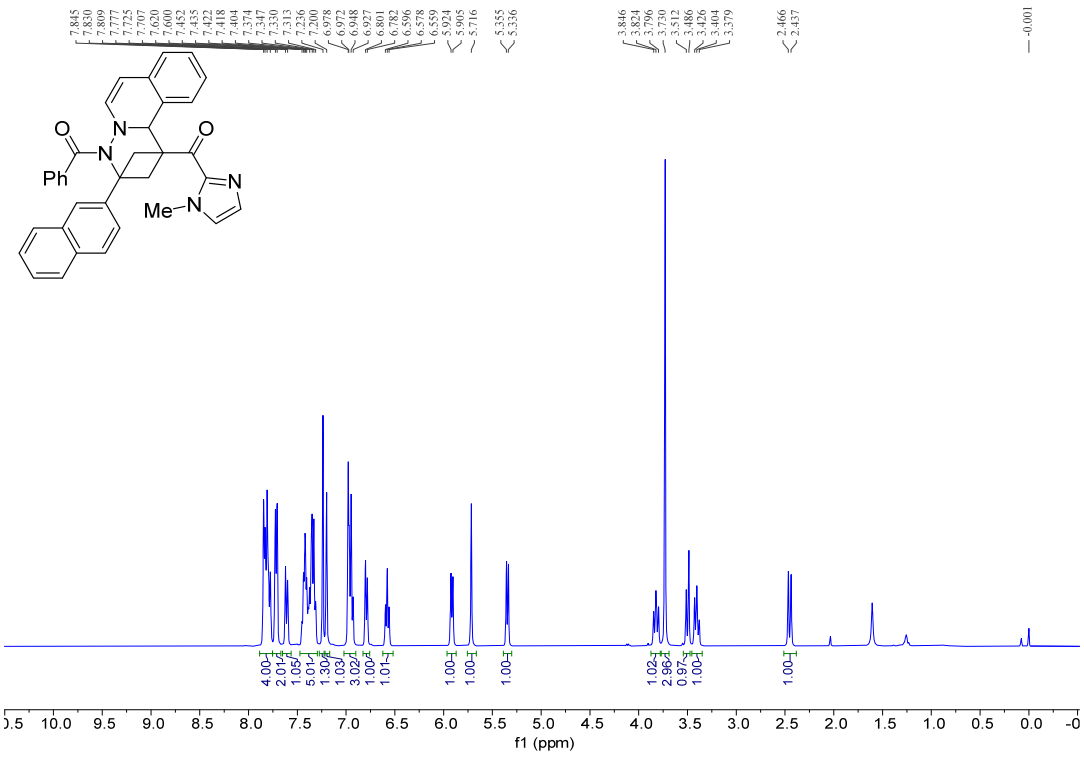


^{13}C NMR (100 MHz, $CDCl_3$)

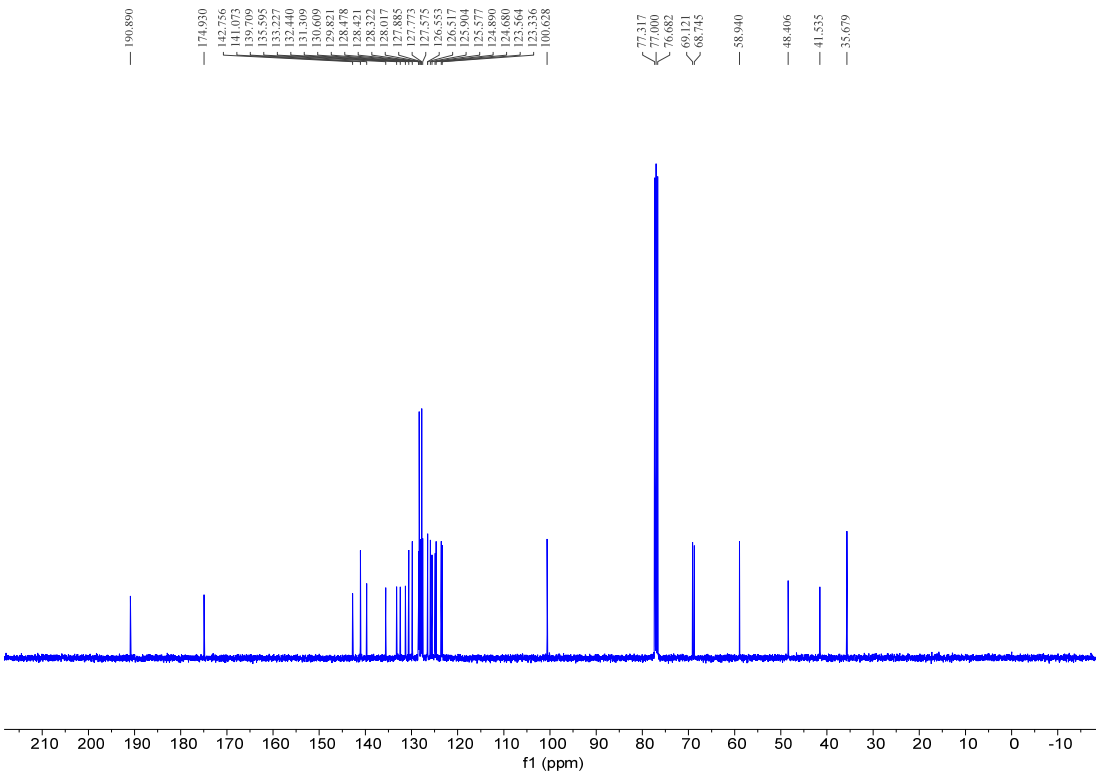


^{1}H and ^{13}C NMR Spectra for Compound 3xa:

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

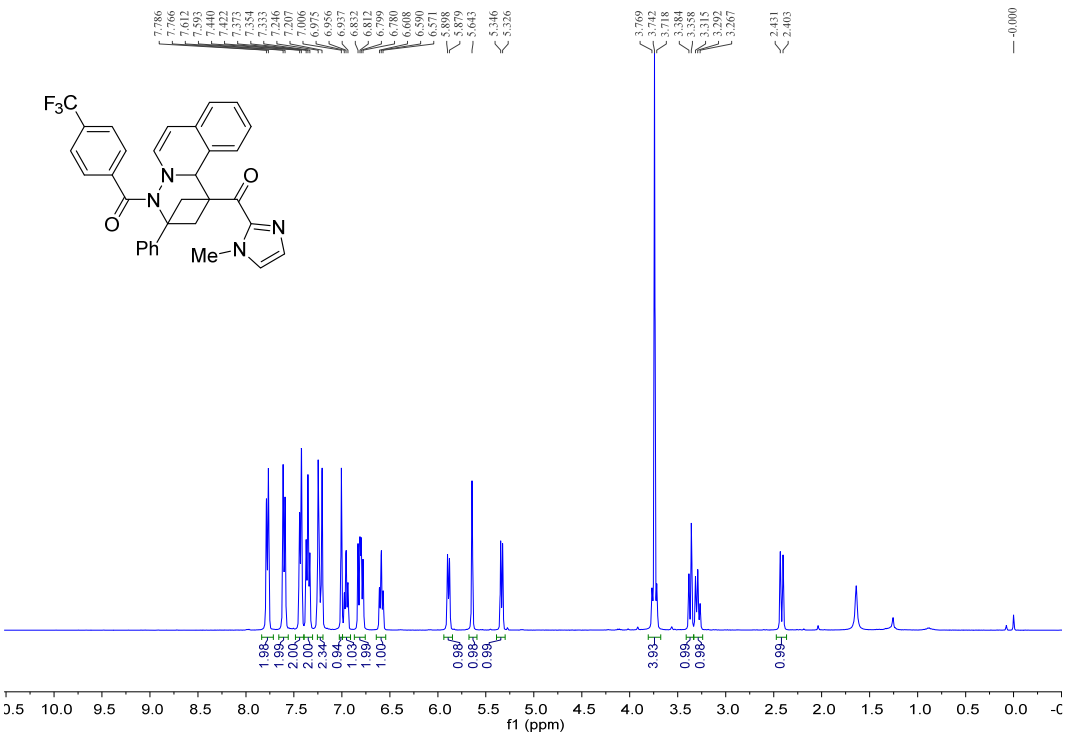


^{13}C NMR (100 MHz, $CDCl_3$)

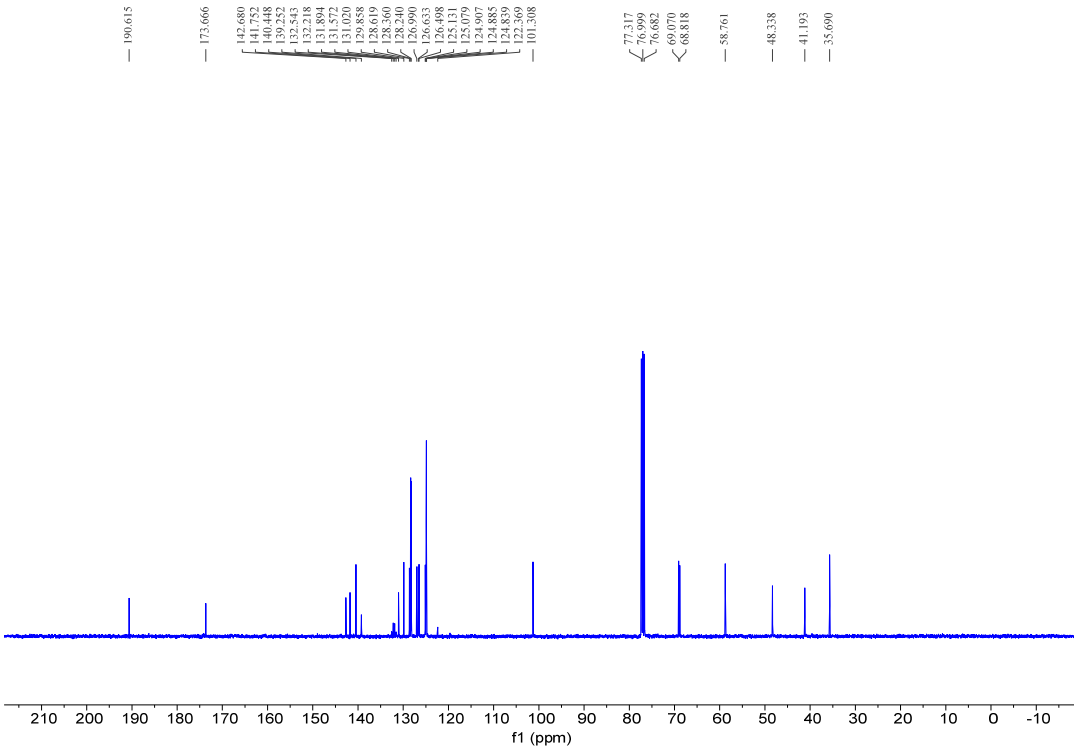


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3qd:

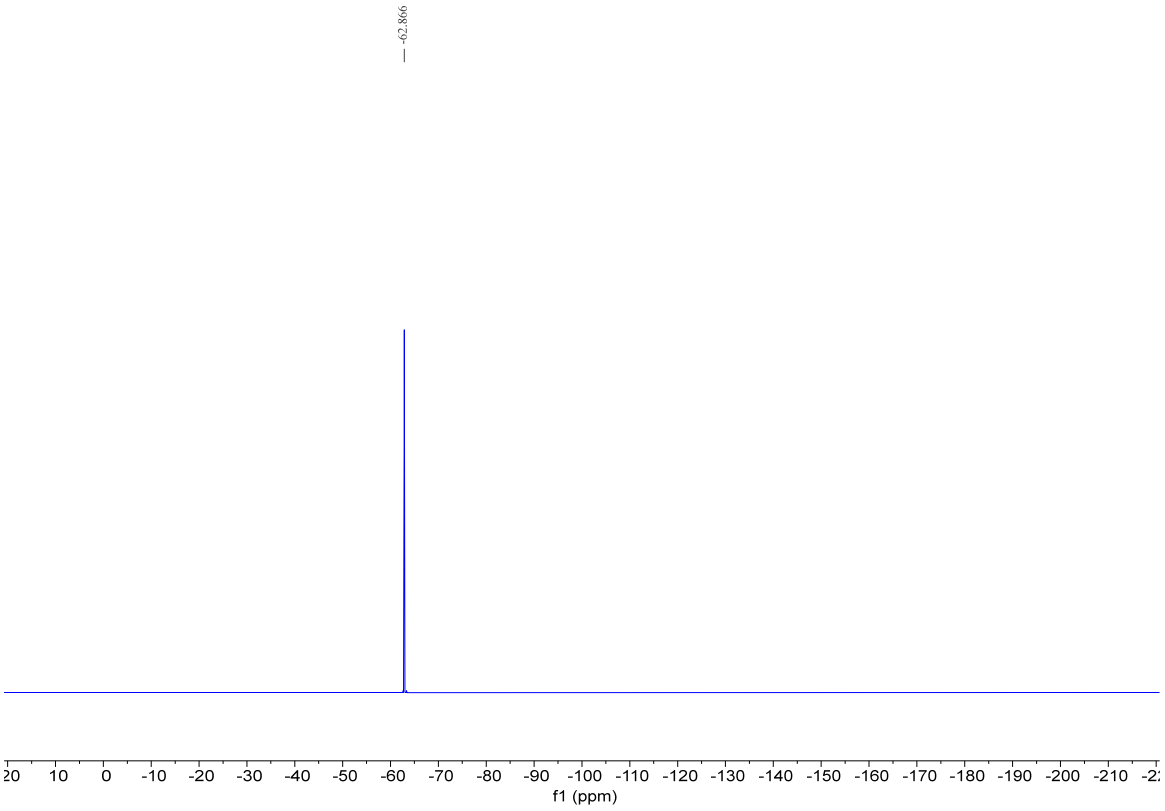
^{1}H NMR (400 MHz, $CDCl_3$)



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

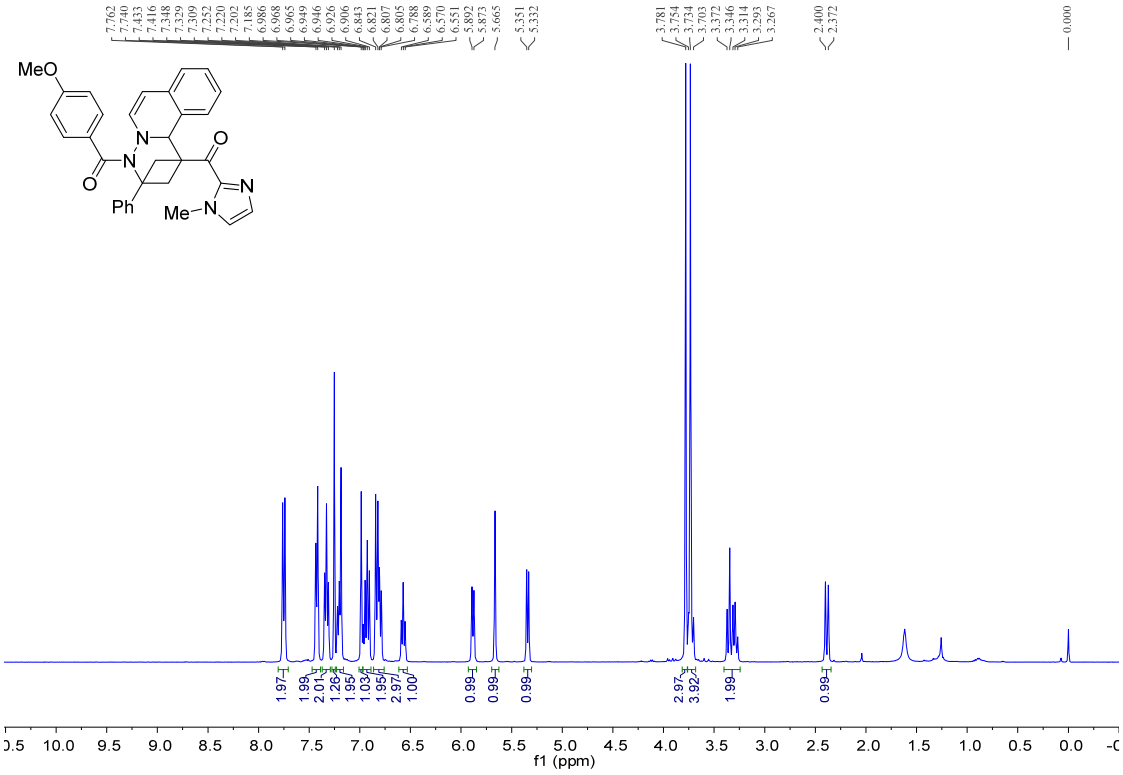


^{19}F NMR (376 MHz, $CDCl_3$)

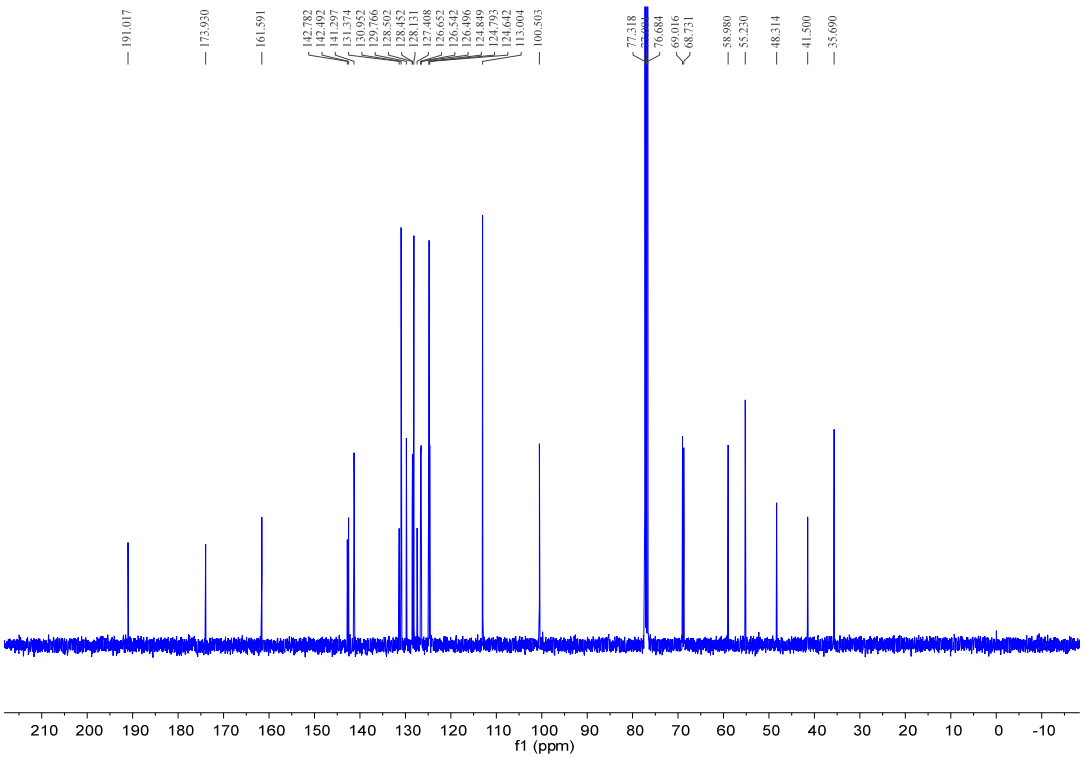


^{1}H and ^{13}C NMR Spectra for Compound 3qe:

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

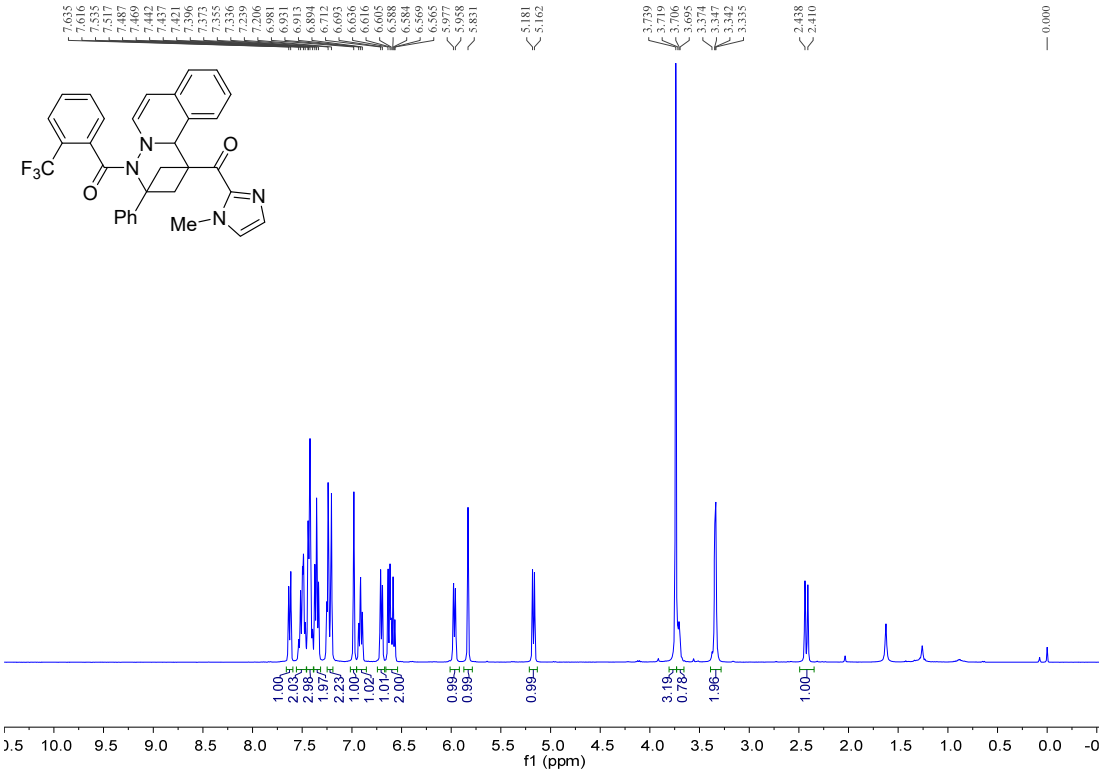


^{13}C NMR (100 MHz, $CDCl_3$)

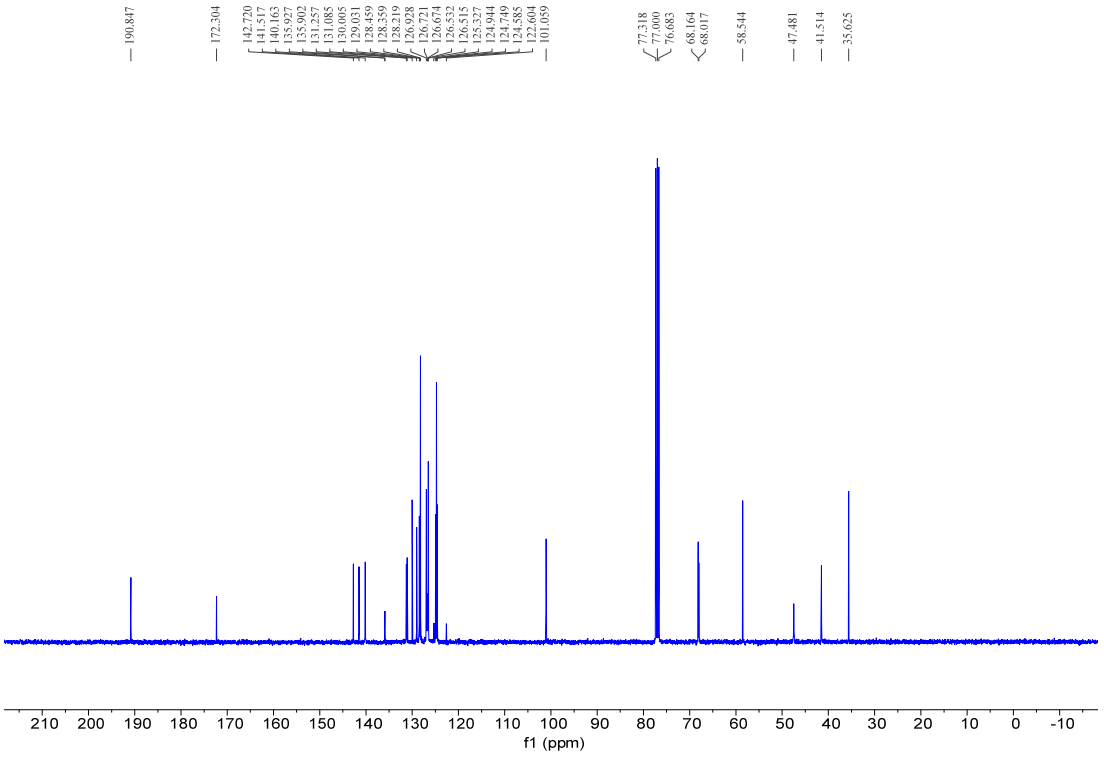


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3qf:

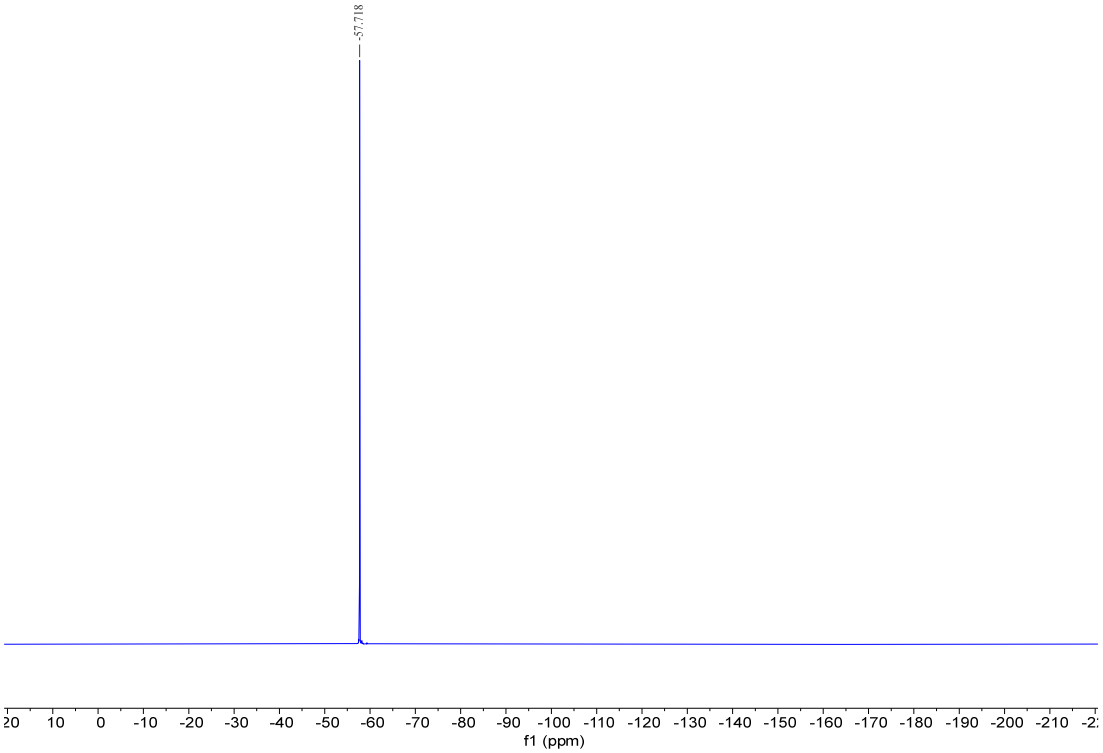
^{1}H NMR (400 MHz, $CDCl_3$)



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

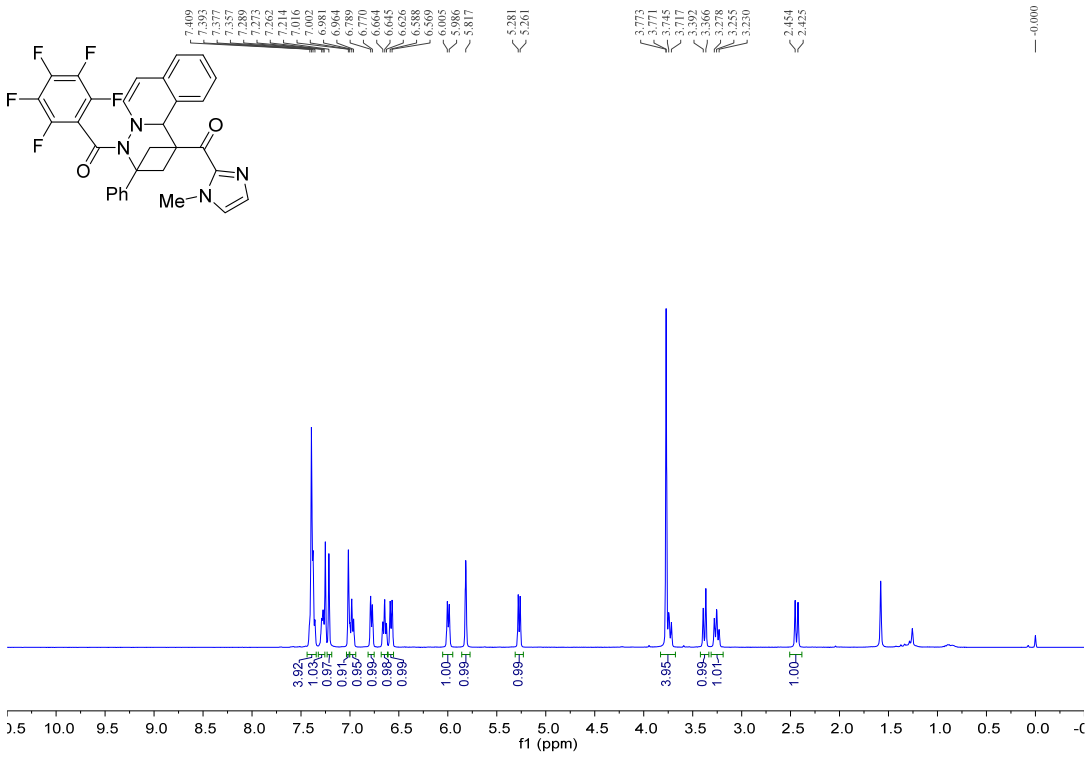


^{19}F NMR (376 MHz, $CDCl_3$)

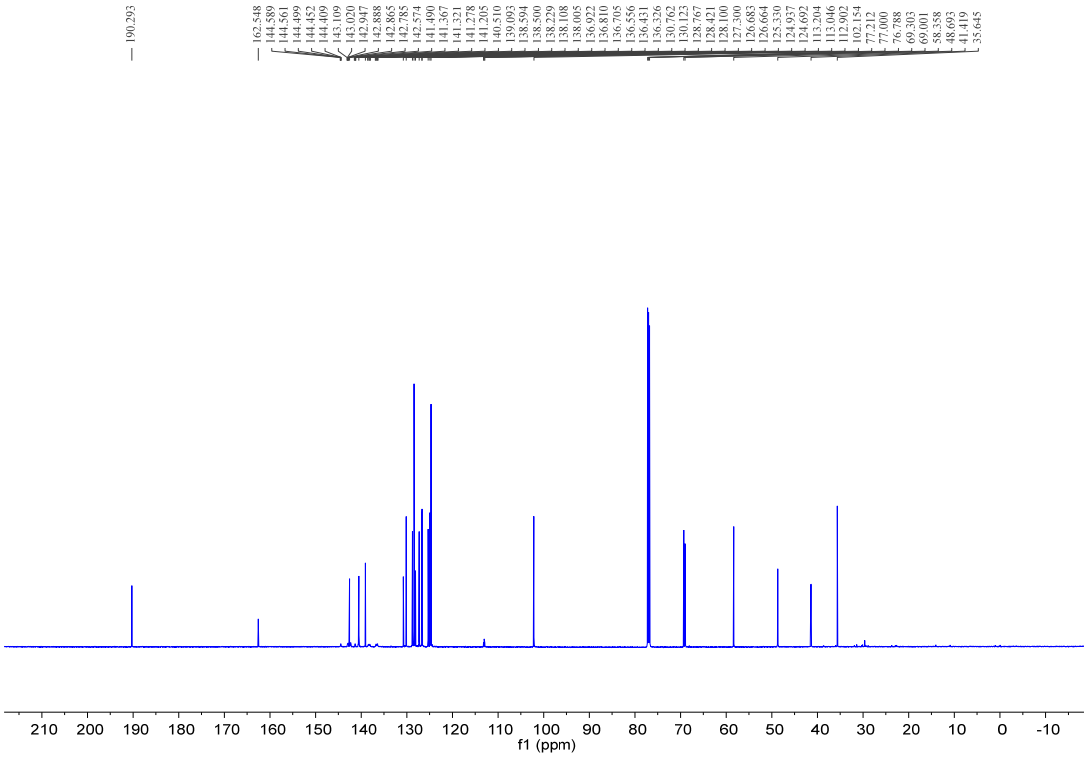


^{1}H and ^{13}C NMR Spectra for Compound 3qg:

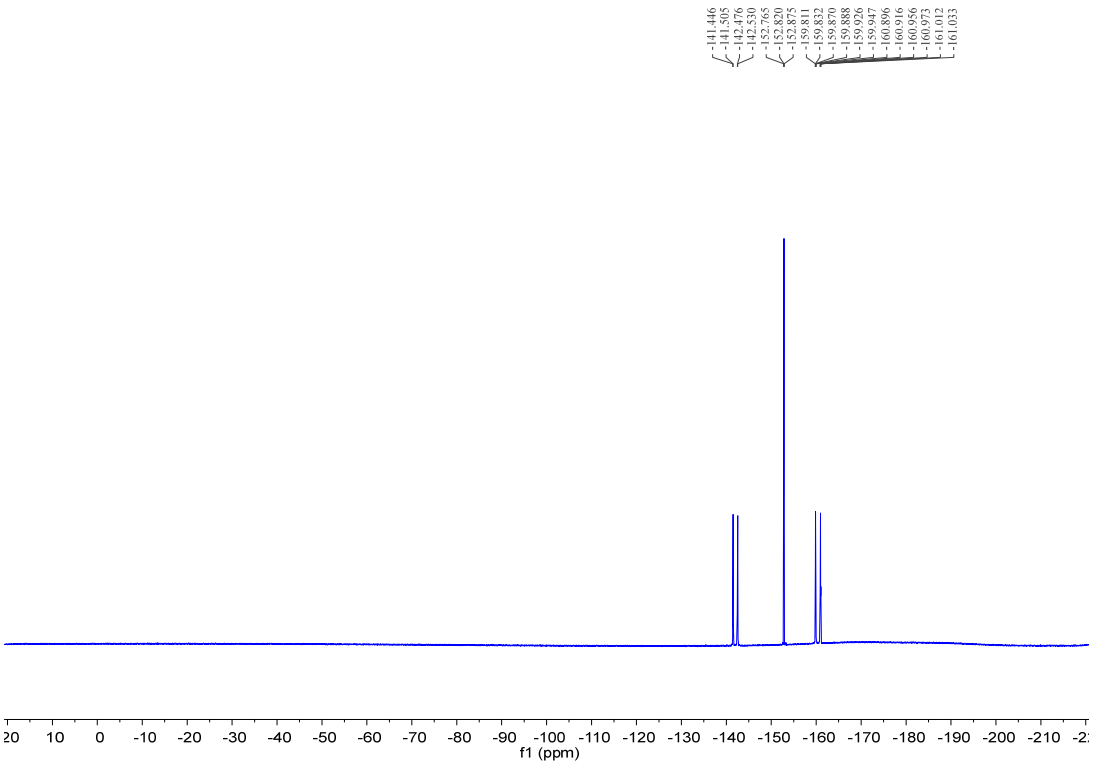
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)

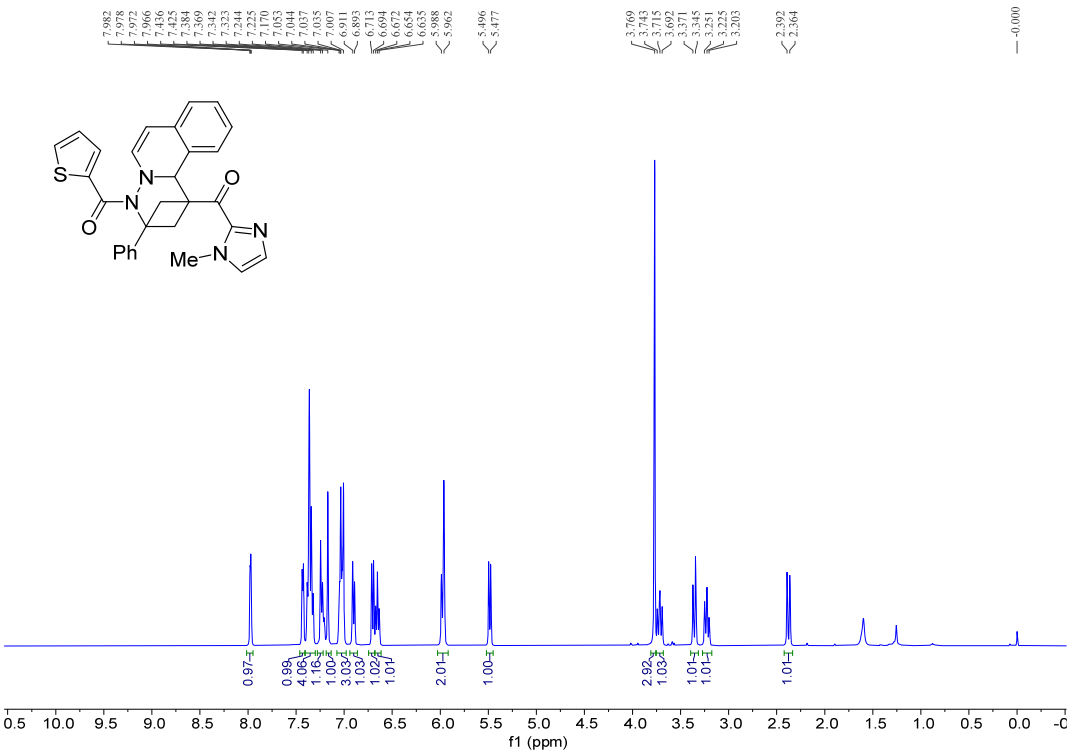


^{19}F NMR (376 MHz, $CDCl_3$)

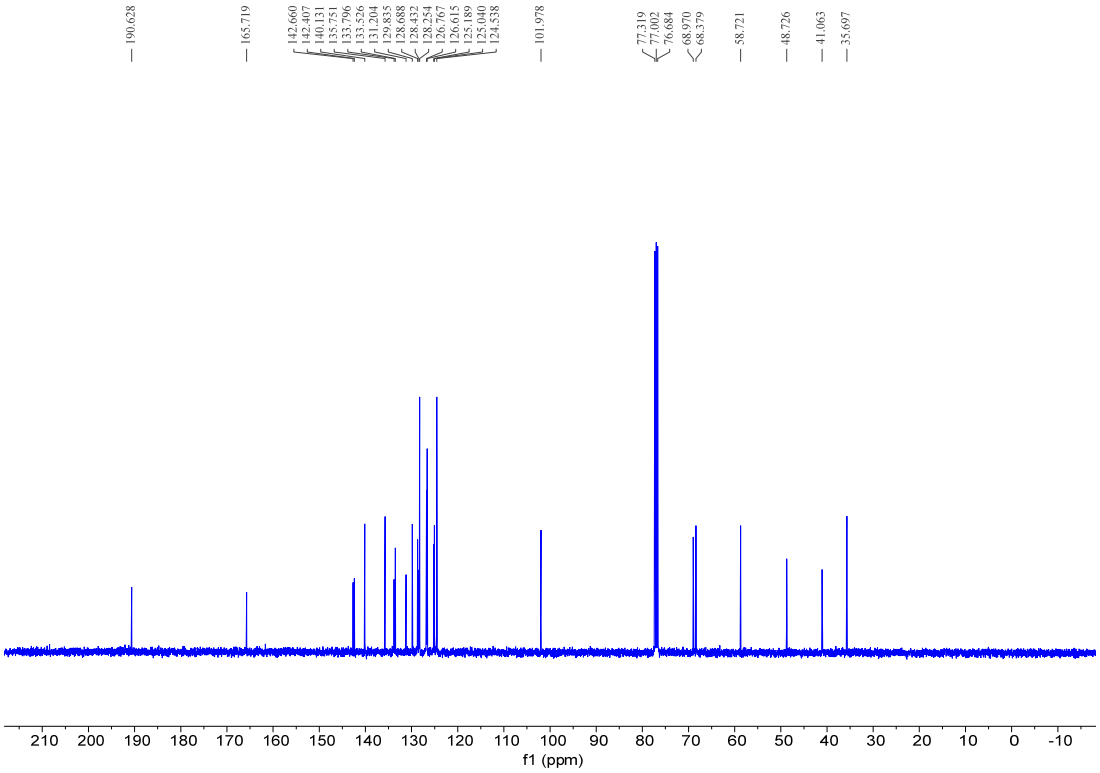


^{1}H and ^{13}C NMR Spectra for Compound 3qh:

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

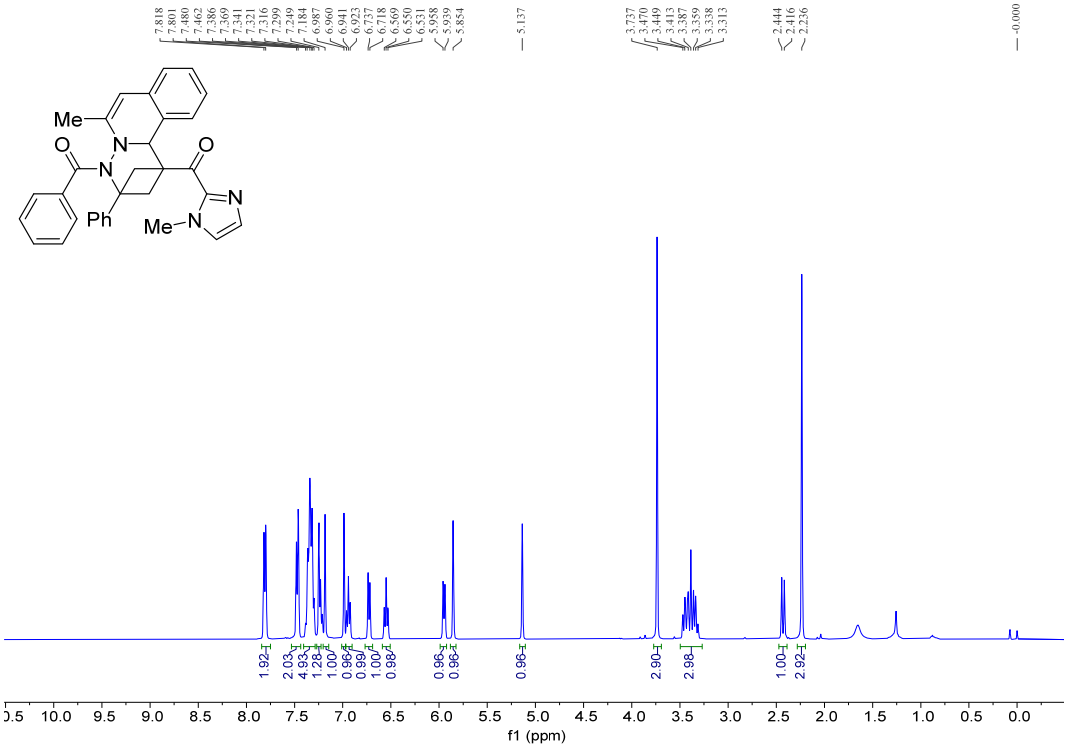


^{13}C NMR (100 MHz, $CDCl_3$)

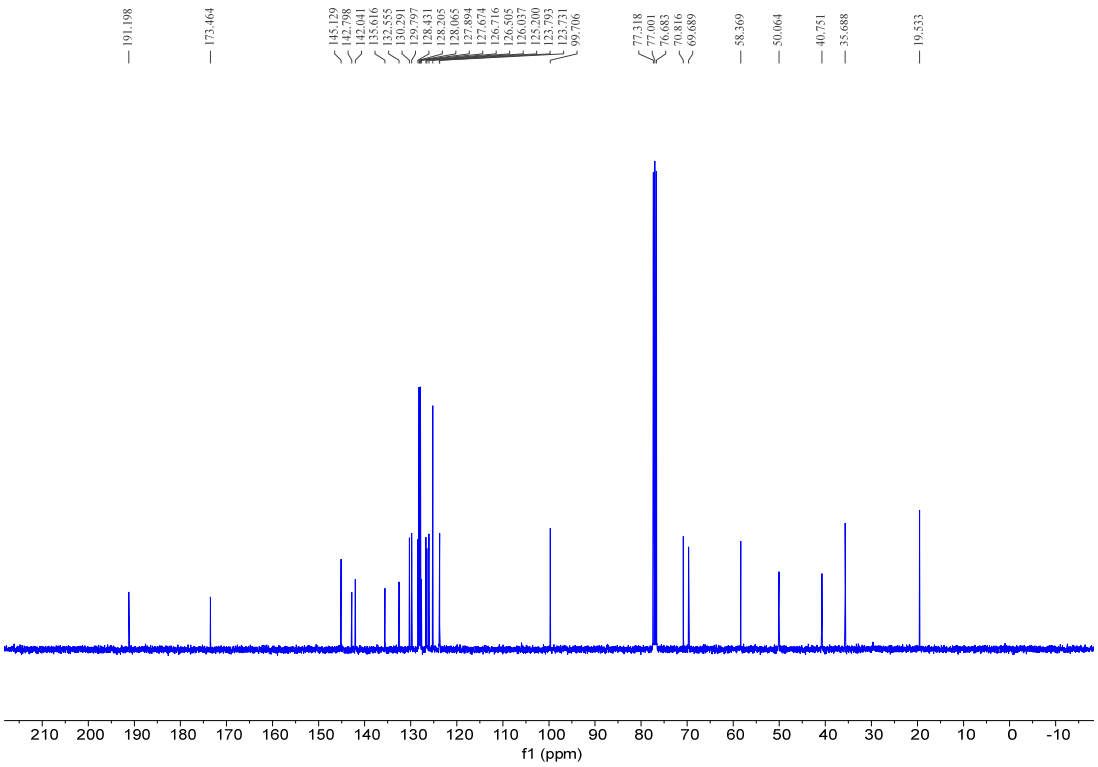


^{1}H and ^{13}C NMR Spectra for Compound 3qi:

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

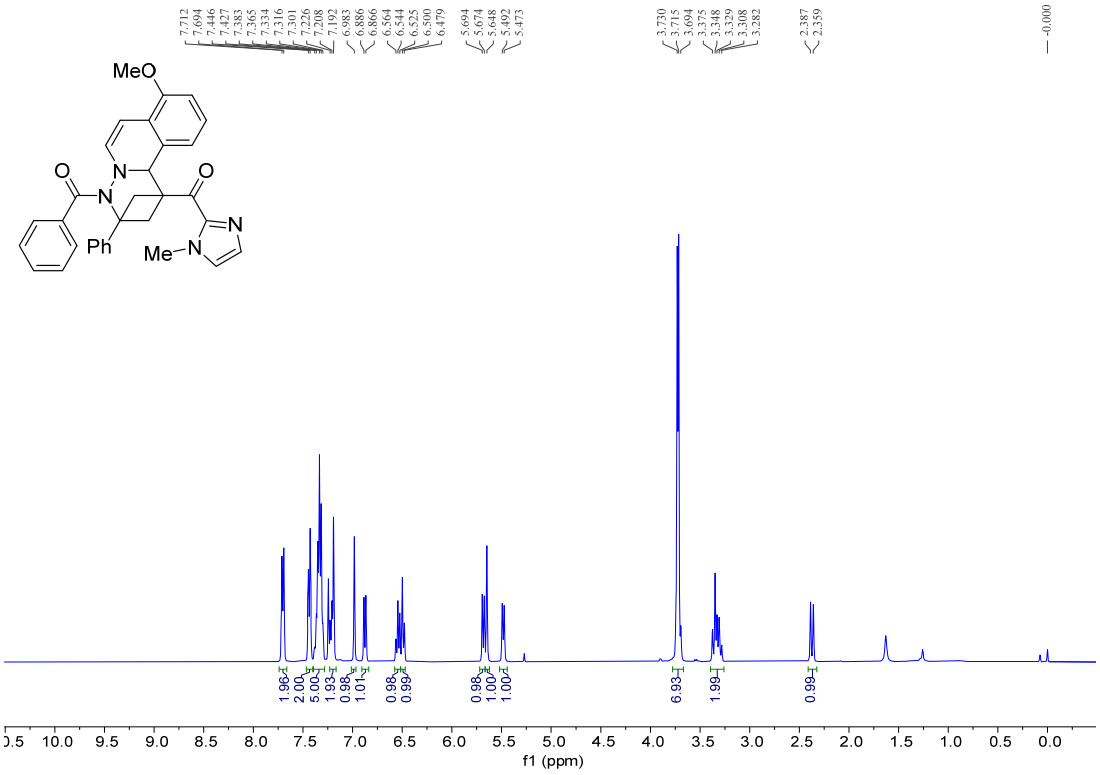


^{13}C NMR (100 MHz, $CDCl_3$)

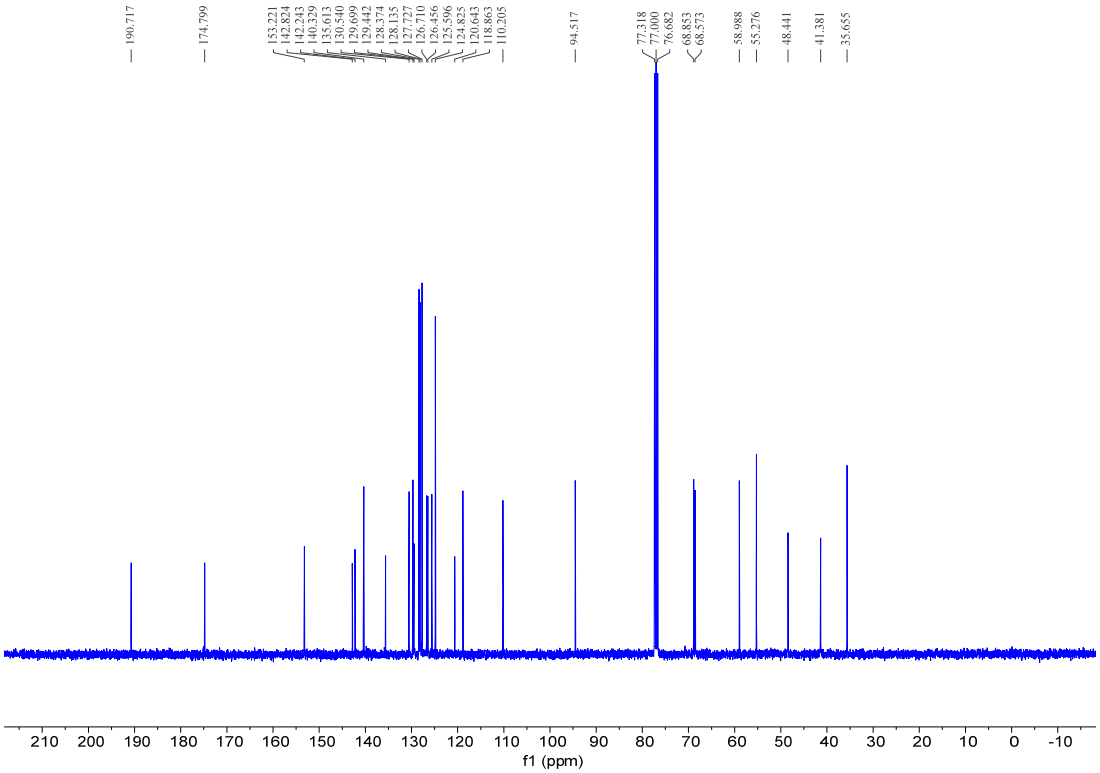


^{1}H and ^{13}C NMR Spectra for Compound 3qj:

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

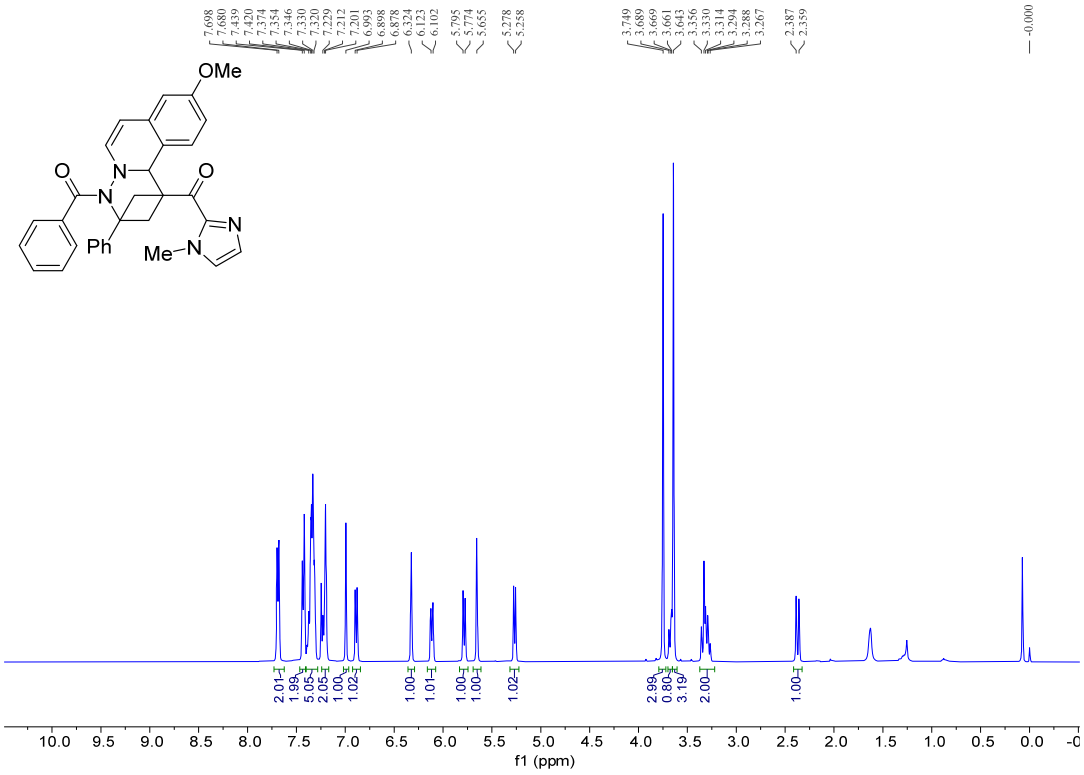


^{13}C NMR (100 MHz, $CDCl_3$)

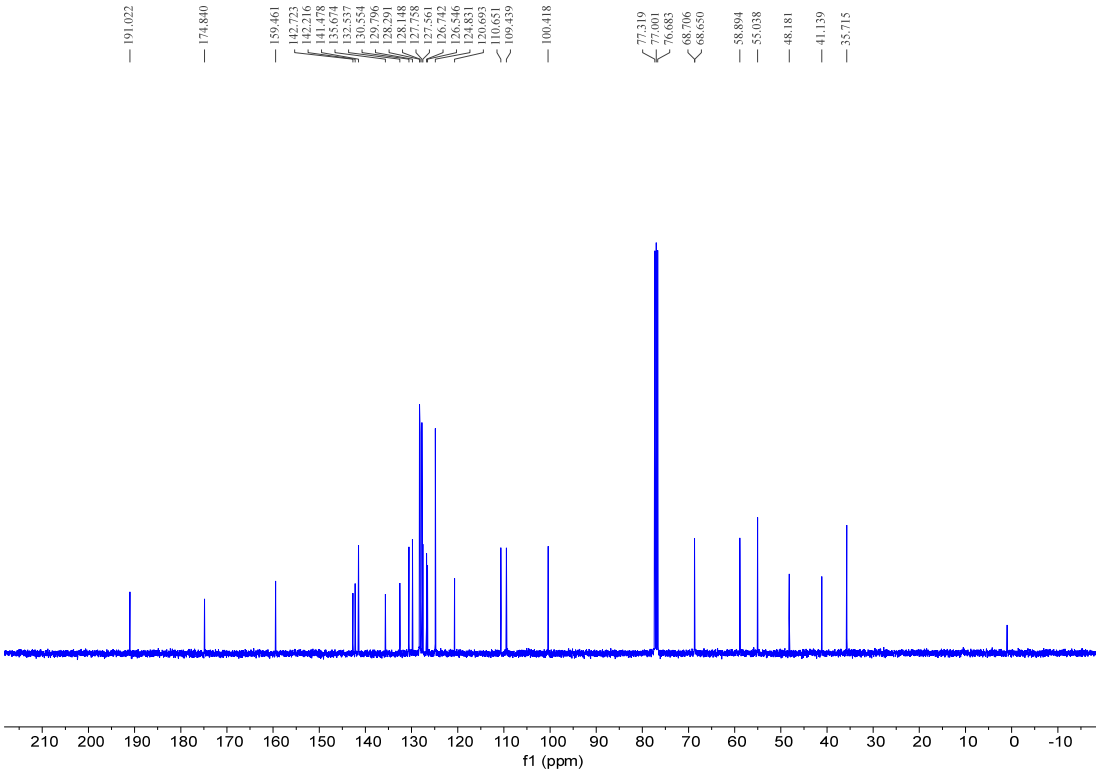


^{1}H and ^{13}C NMR Spectra for Compound 3qk:

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

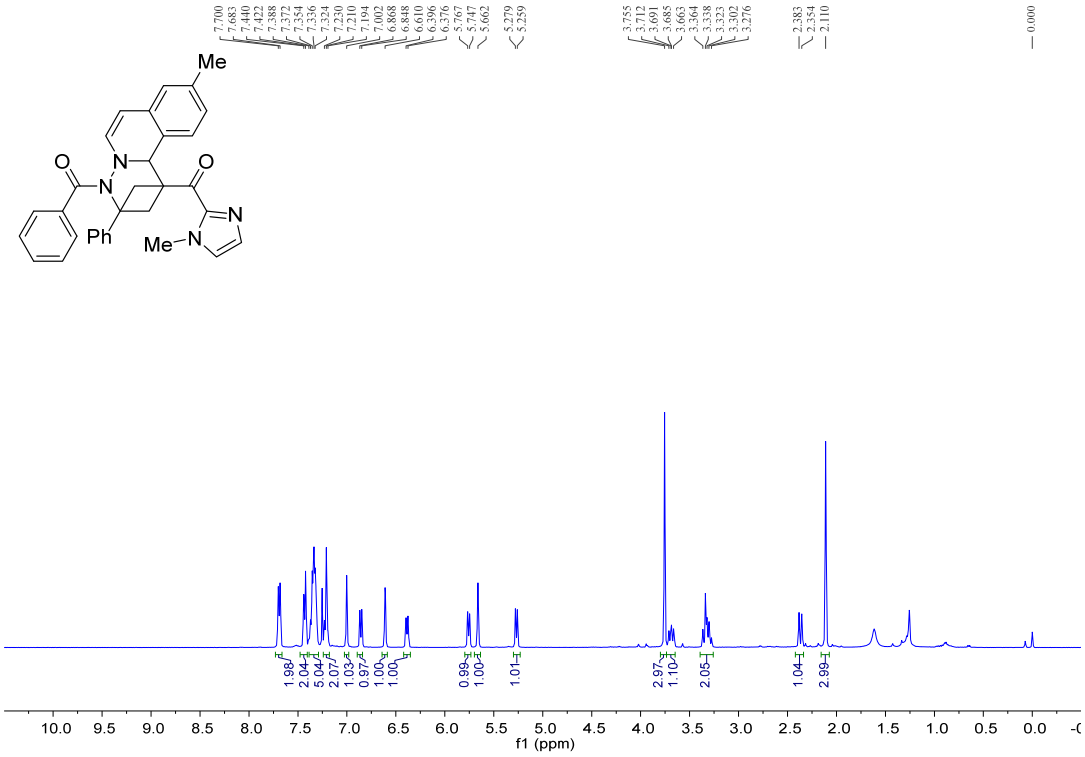


^{13}C NMR (100 MHz, $CDCl_3$)

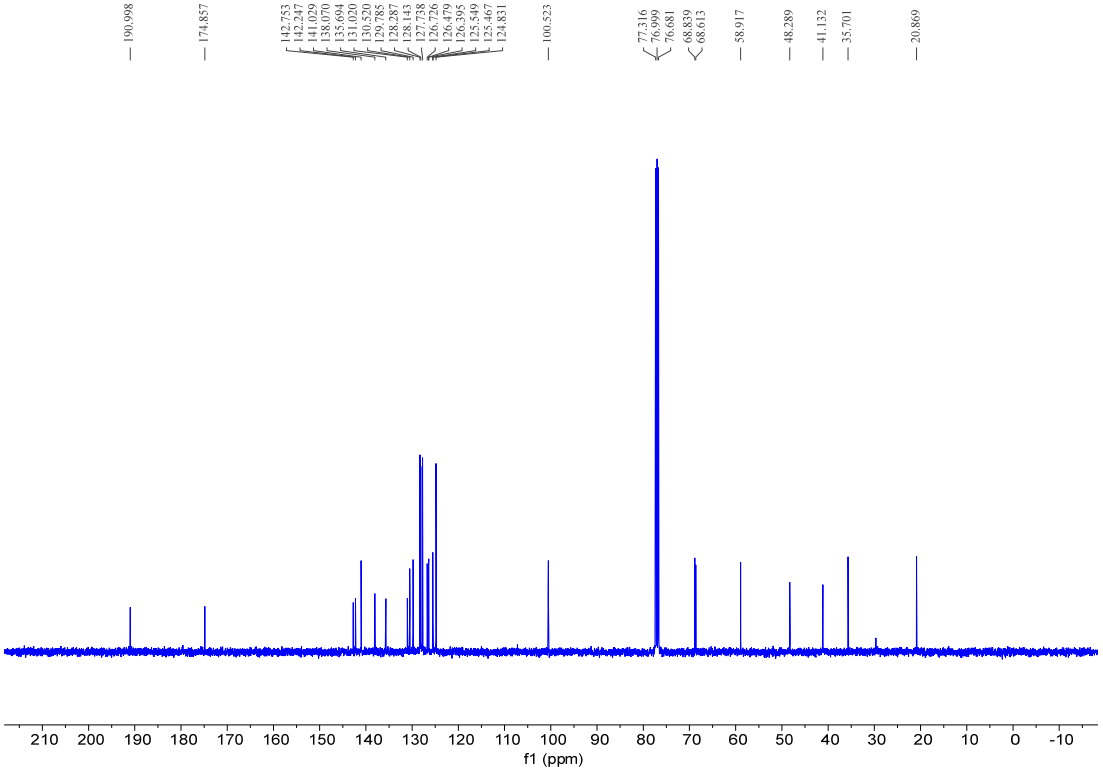


^{1}H and ^{13}C NMR Spectra for Compound 3ql:

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

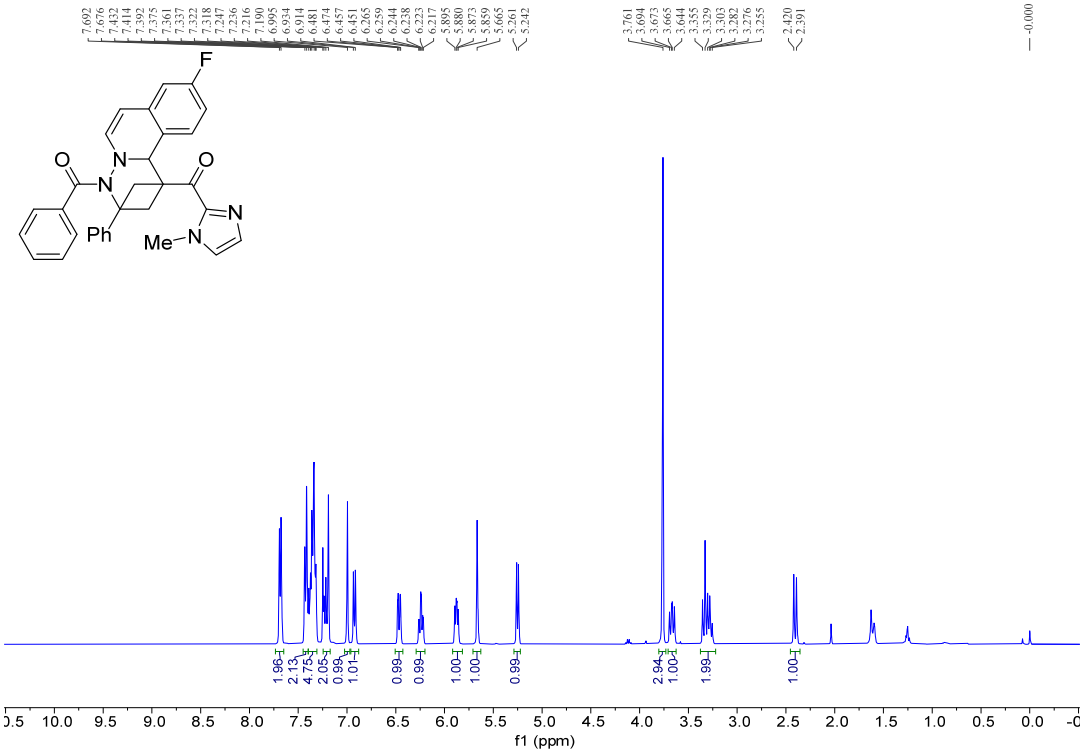


^{13}C NMR (100 MHz, $CDCl_3$)

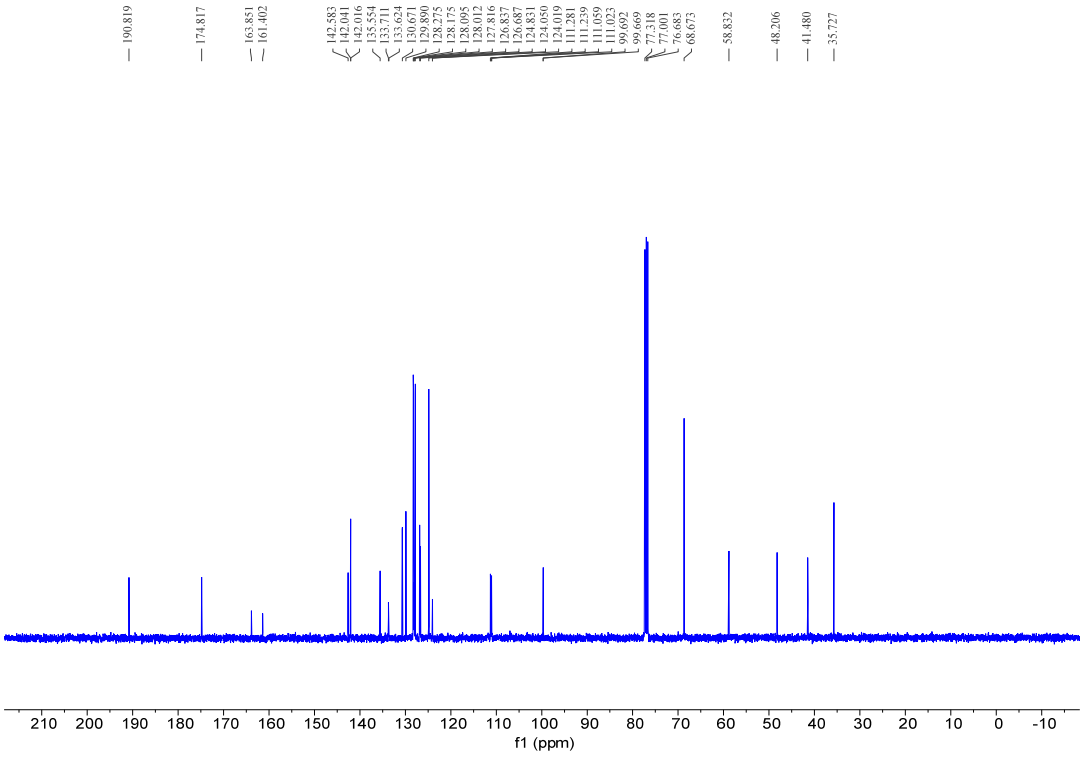


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3qm:

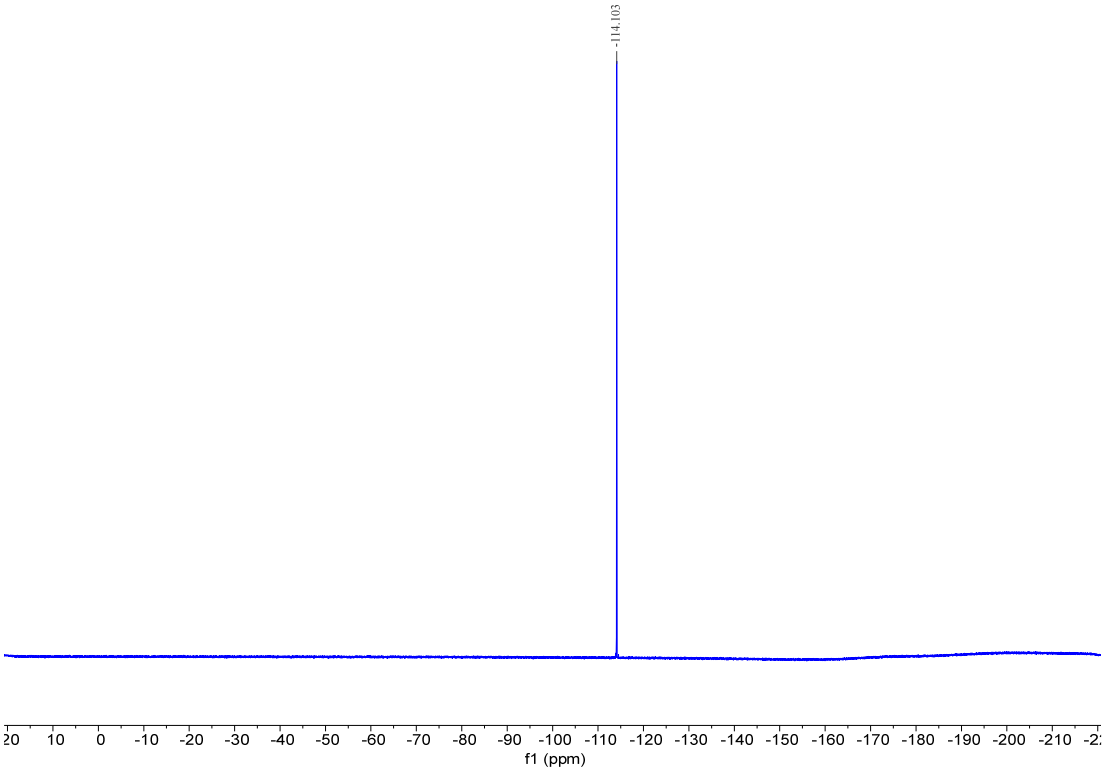
^{1}H NMR (400 MHz, $CDCl_3$)



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

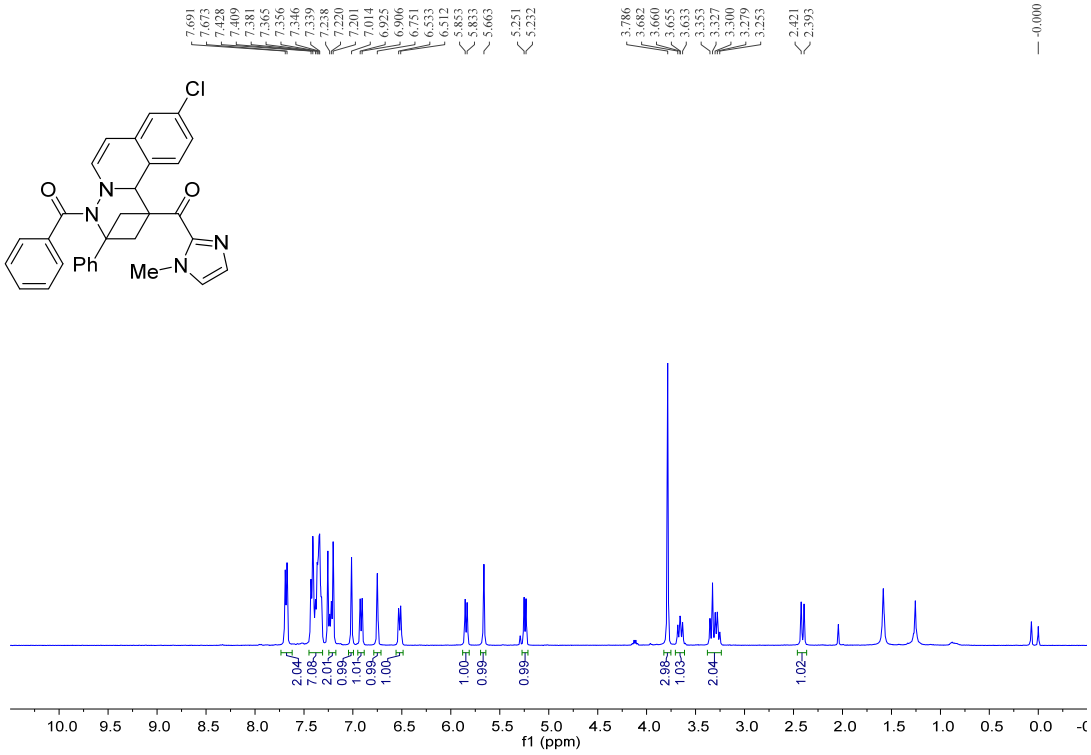


^{19}F NMR (376 MHz, $CDCl_3$)

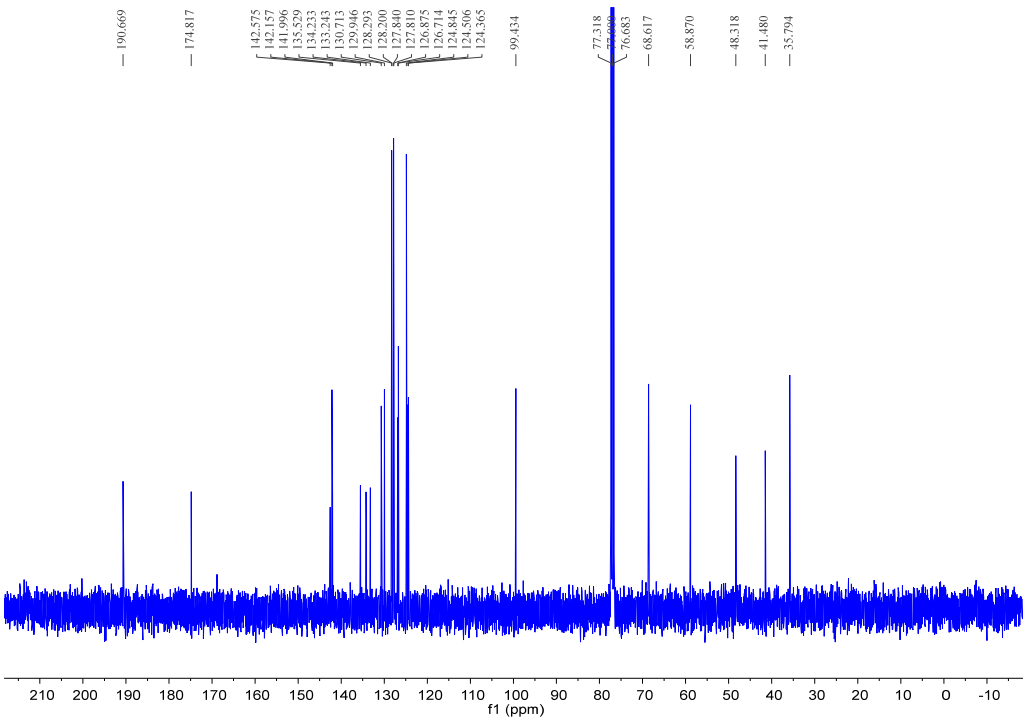


^{1}H and ^{13}C NMR Spectra for Compound 3qn:

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

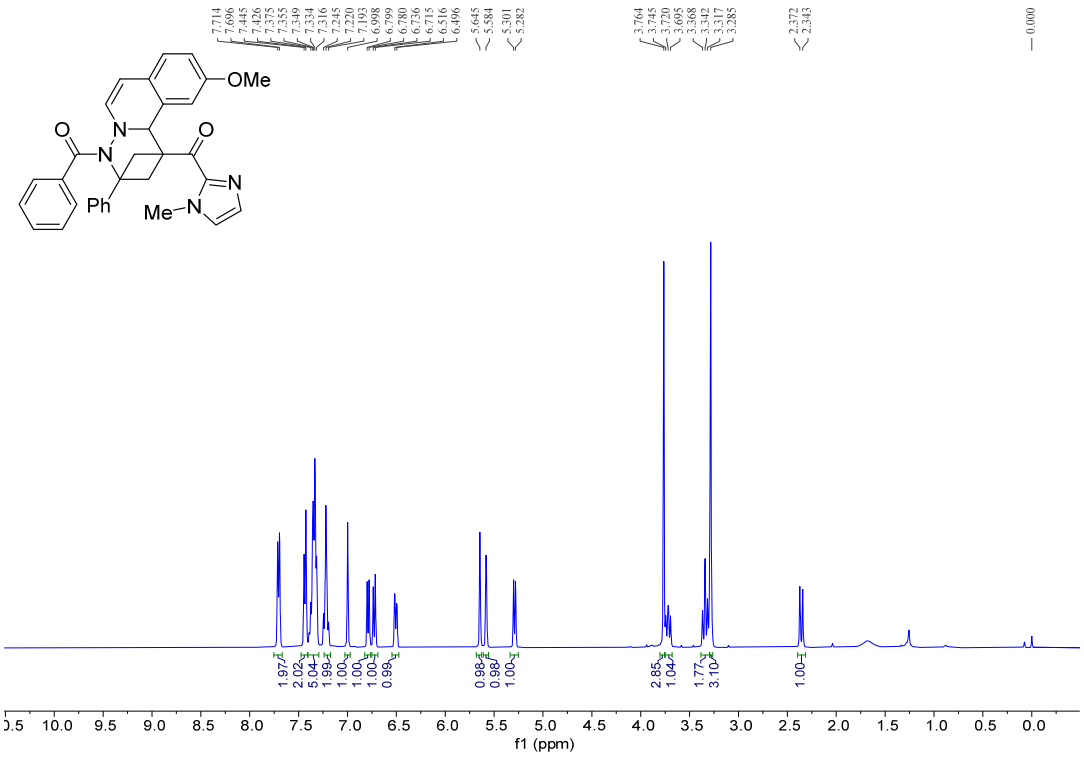


^{13}C NMR (100 MHz, $CDCl_3$)

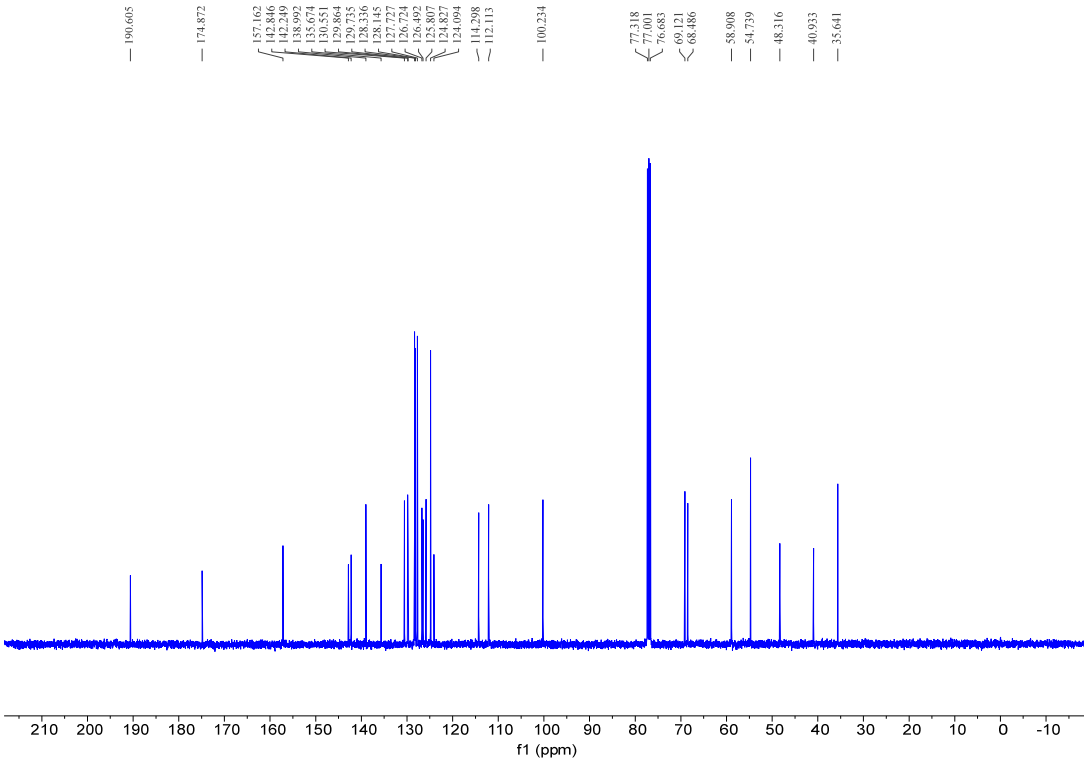


^{1}H and ^{13}C NMR Spectra for Compound 3qo:

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

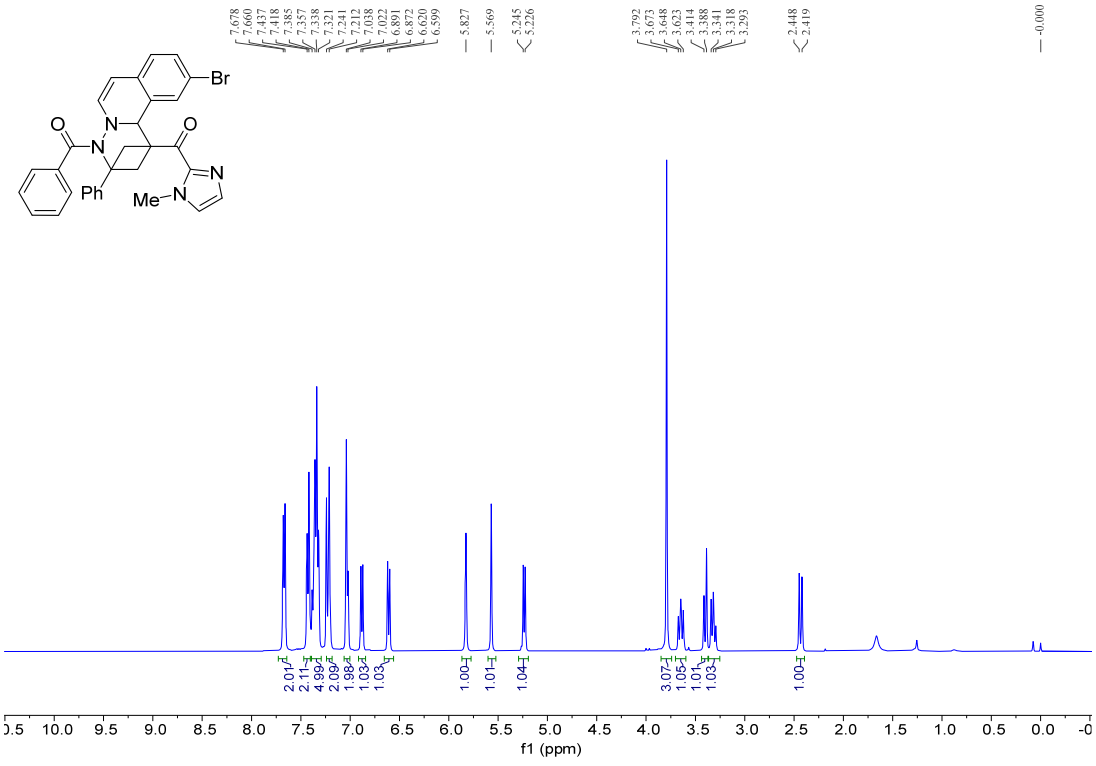


^{13}C NMR (100 MHz, $CDCl_3$)

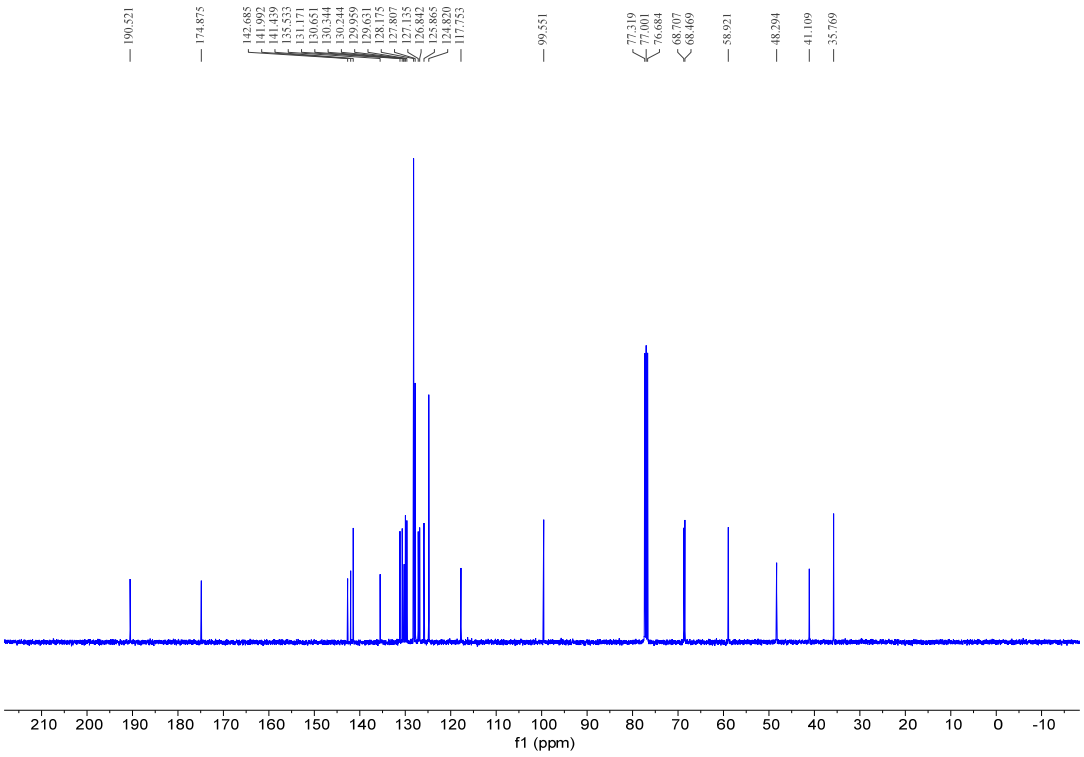


^{1}H and ^{13}C NMR Spectra for Compound 3qp:

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

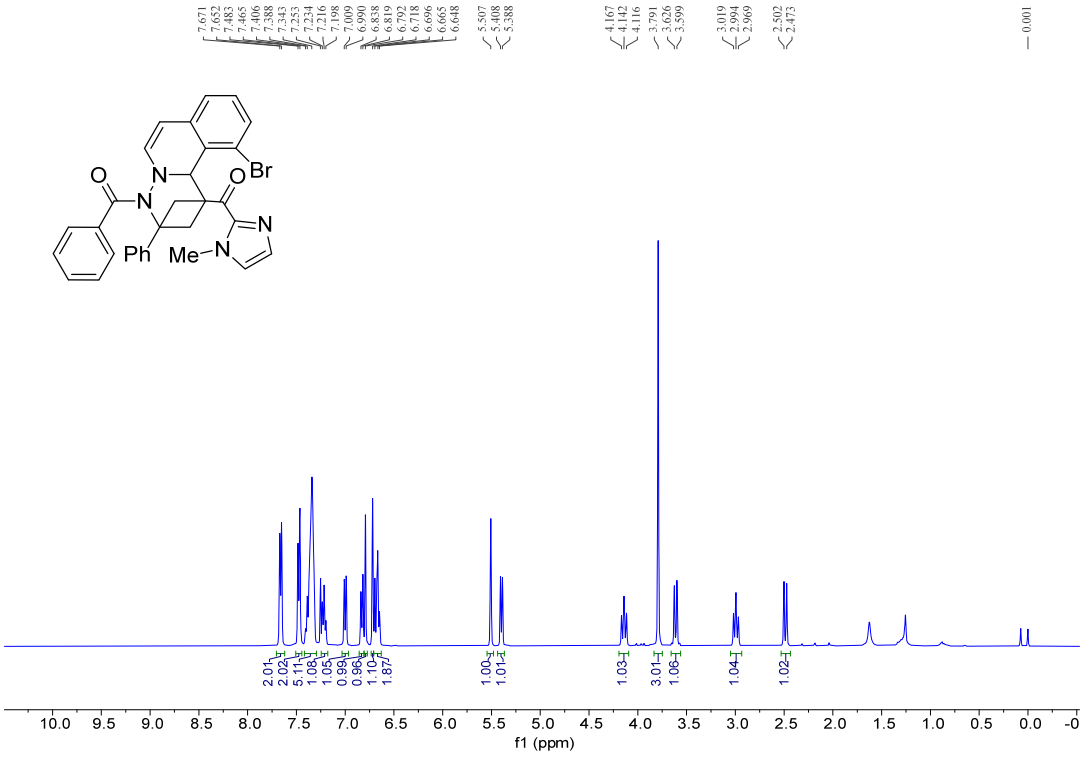


^{13}C NMR (100 MHz, $CDCl_3$)

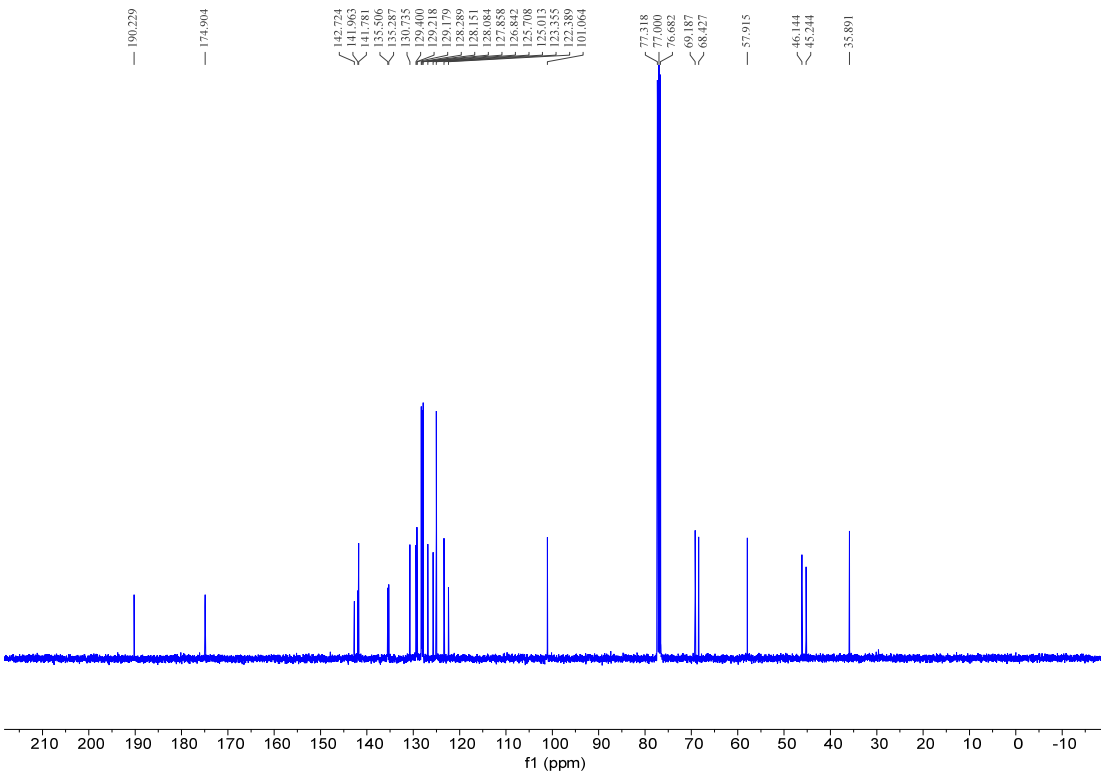


^{1}H and ^{13}C NMR Spectra for Compound 3qq:

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

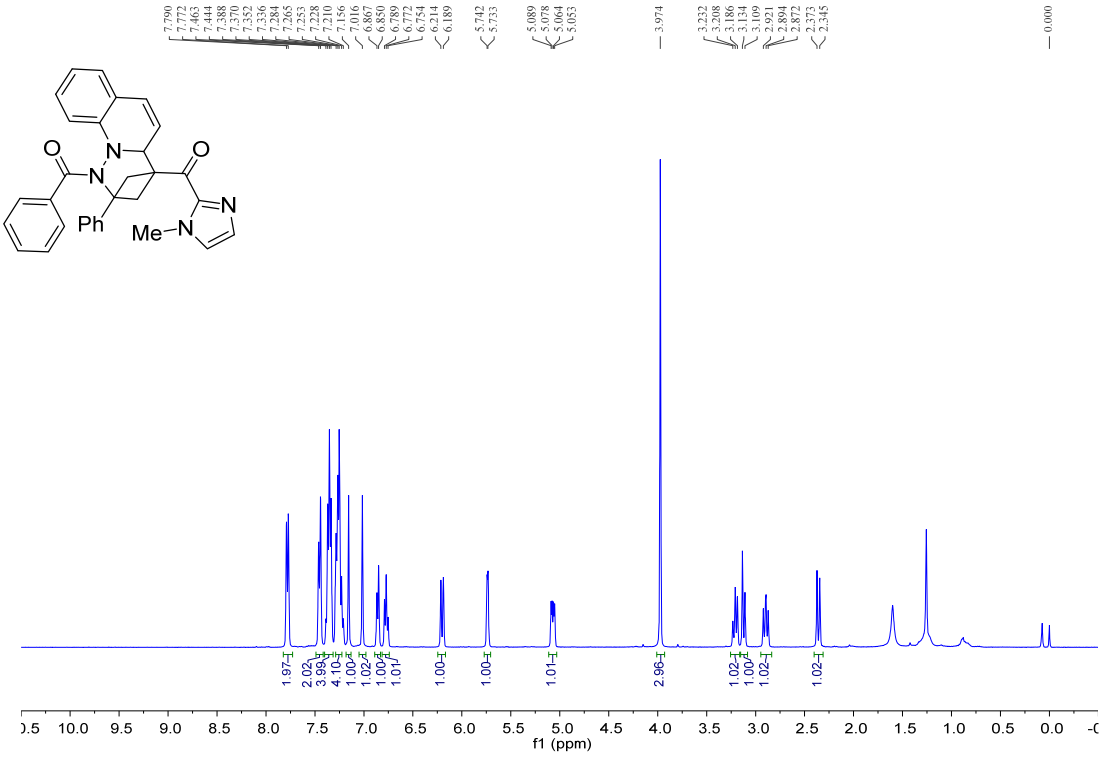


^{13}C NMR (100 MHz, $CDCl_3$)

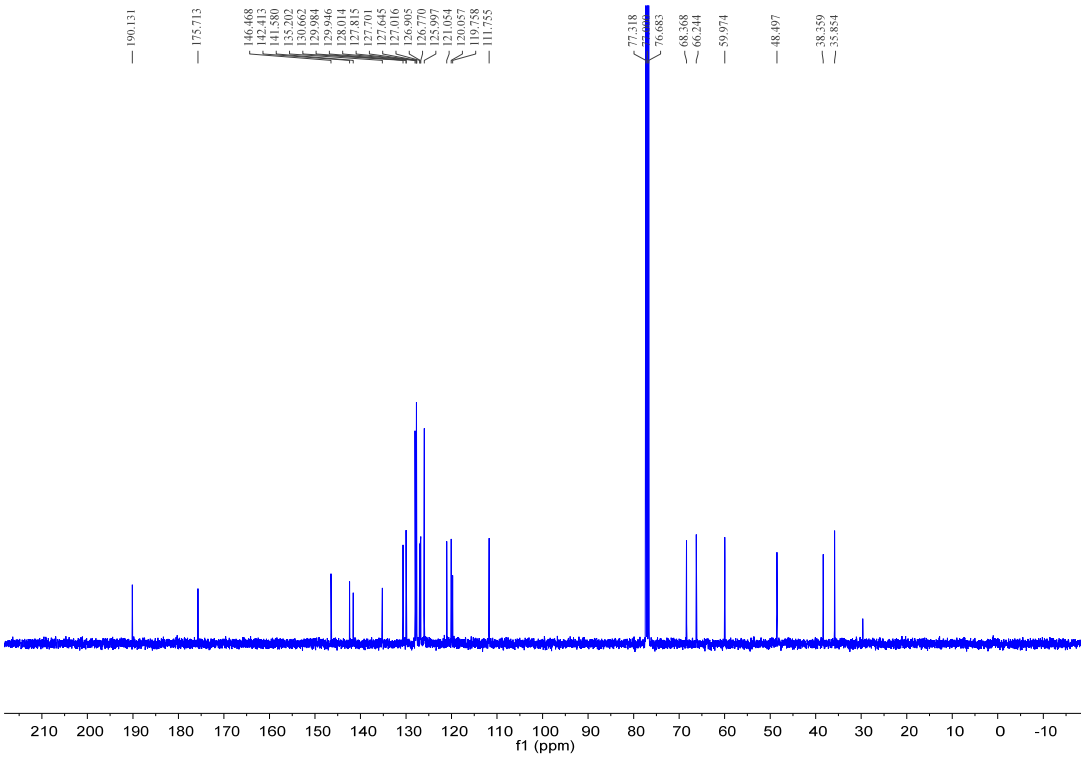


^{1}H and ^{13}C NMR Spectra for Compound 4qb:

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

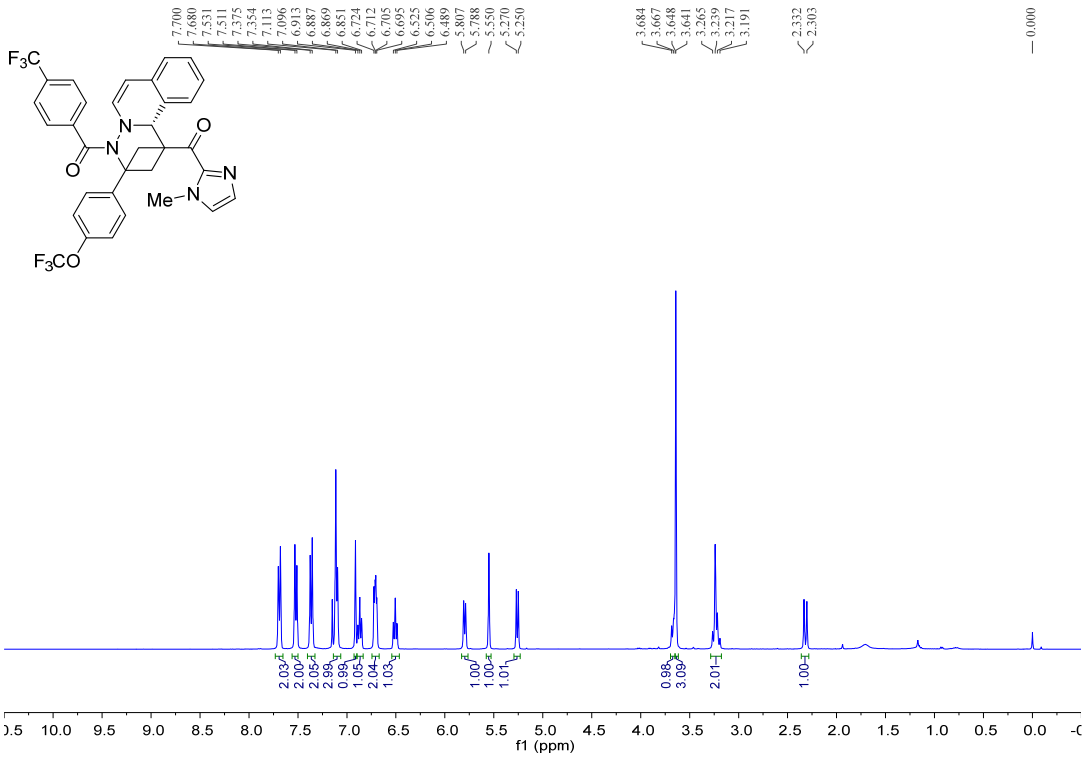


^{13}C NMR (100 MHz, $CDCl_3$)

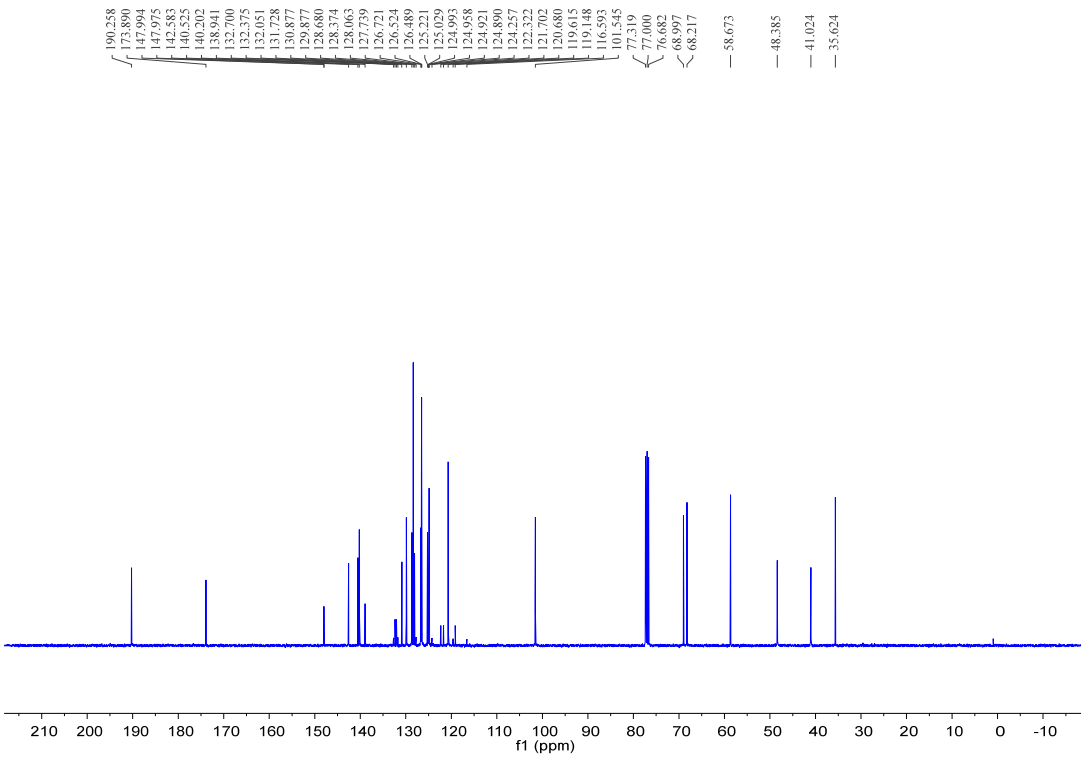


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3sd:

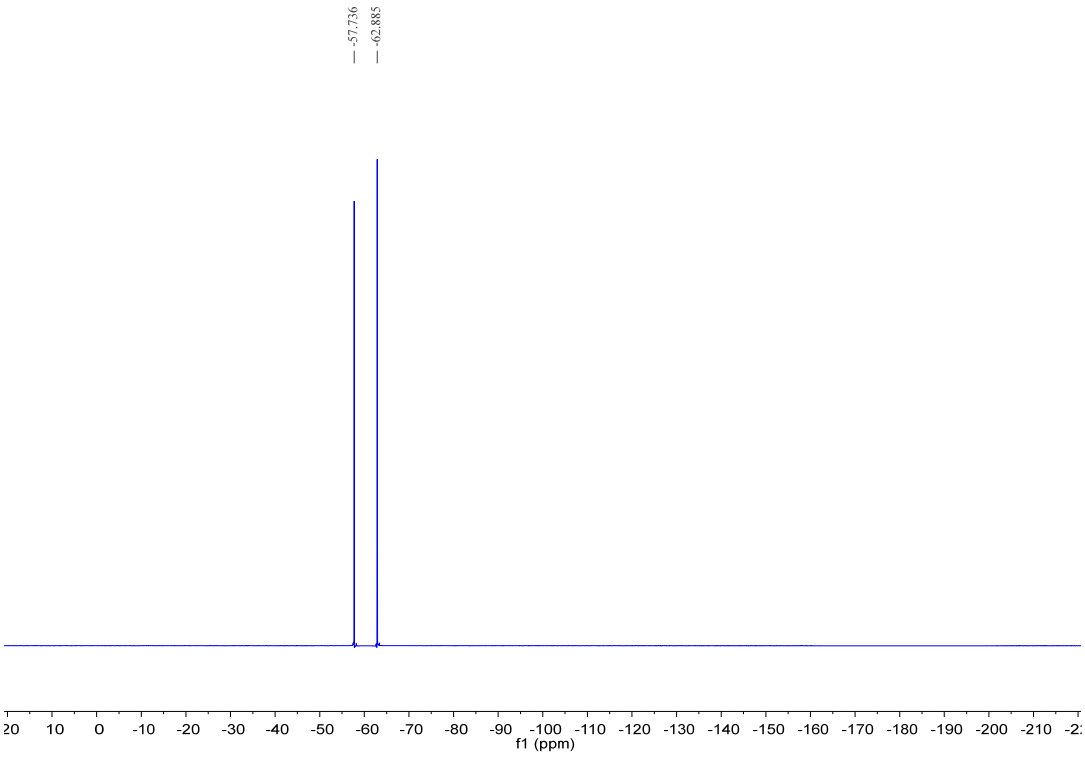
^{1}H NMR (400 MHz, $CDCl_3$)



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

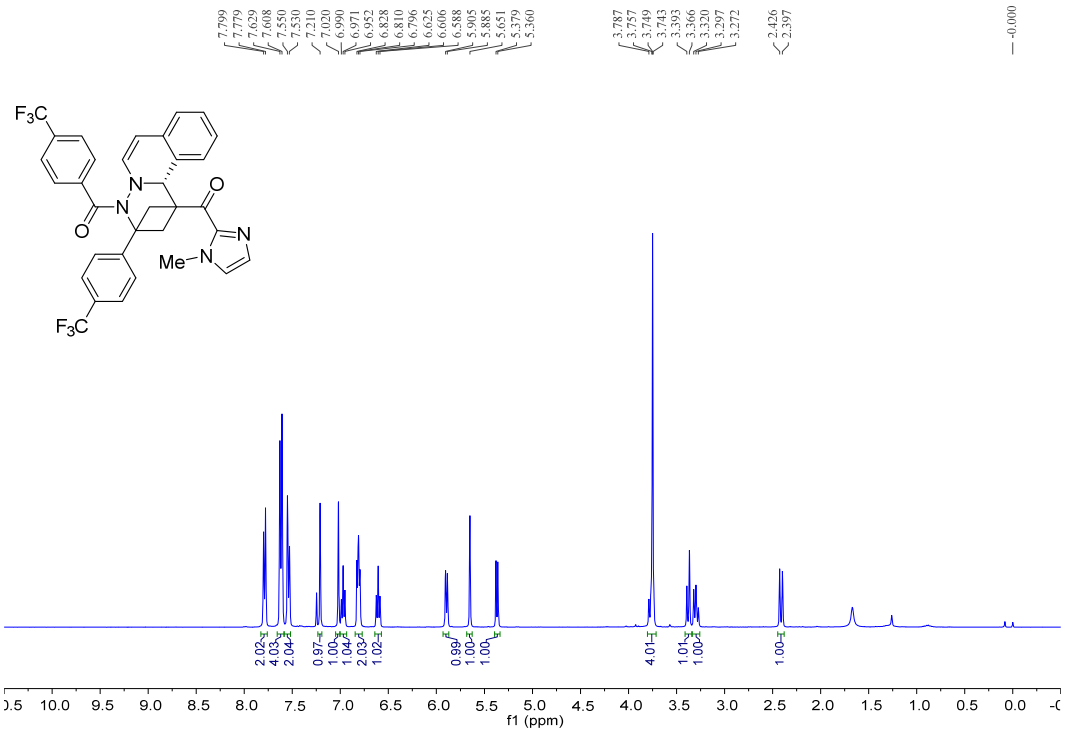


^{19}F NMR (376 MHz, $CDCl_3$)

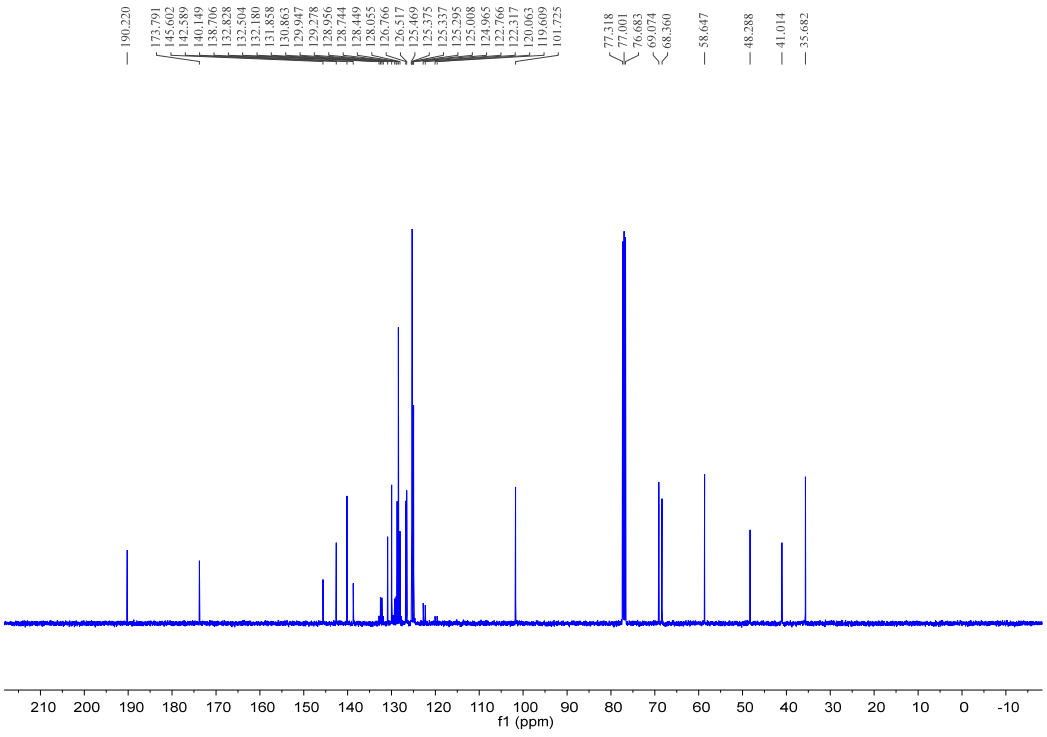


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3vd:

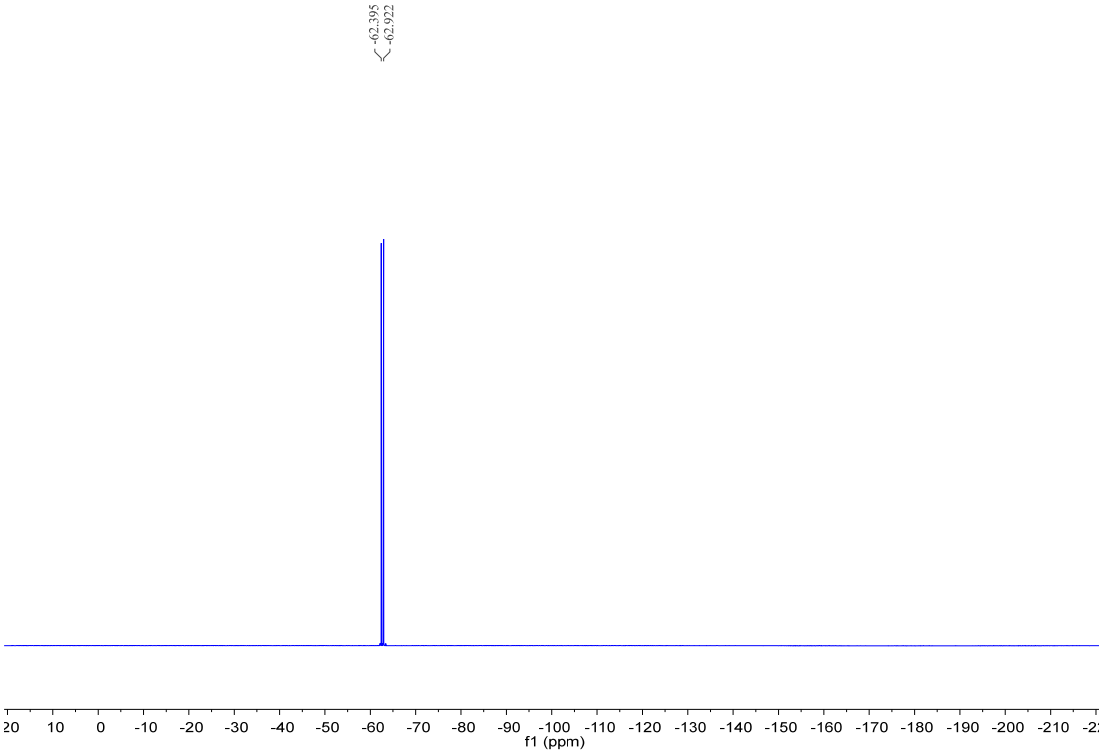
^{1}H NMR (400 MHz, $CDCl_3$)



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

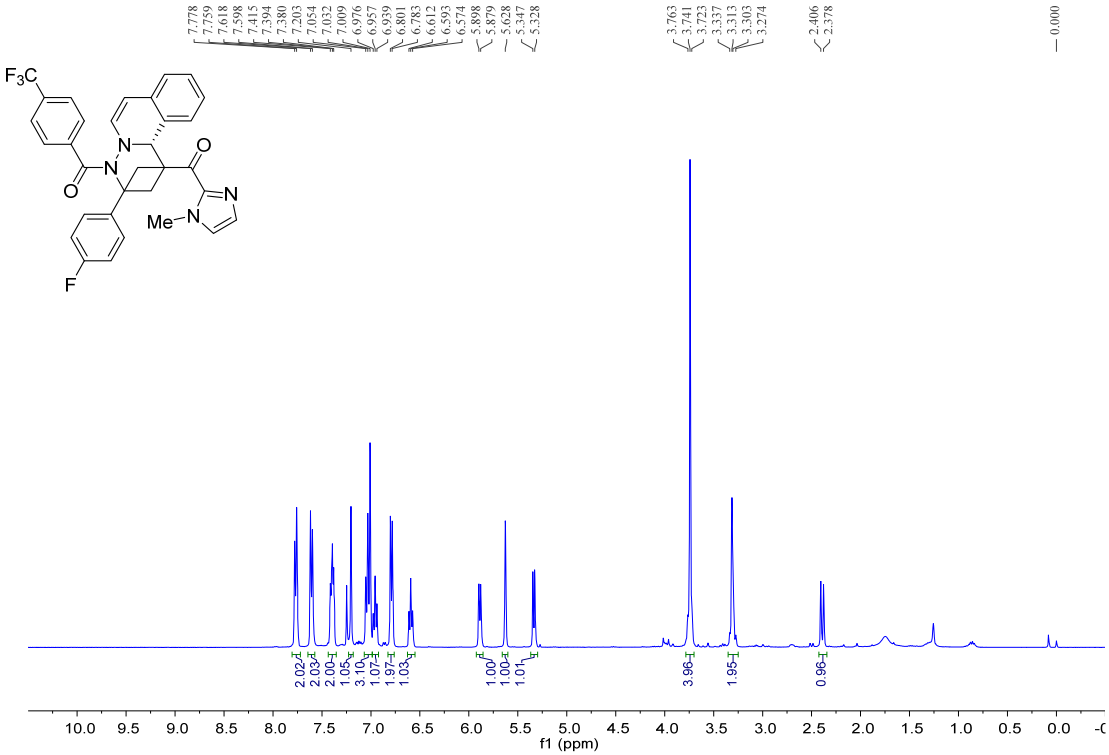


^{19}F NMR (376 MHz, $CDCl_3$)

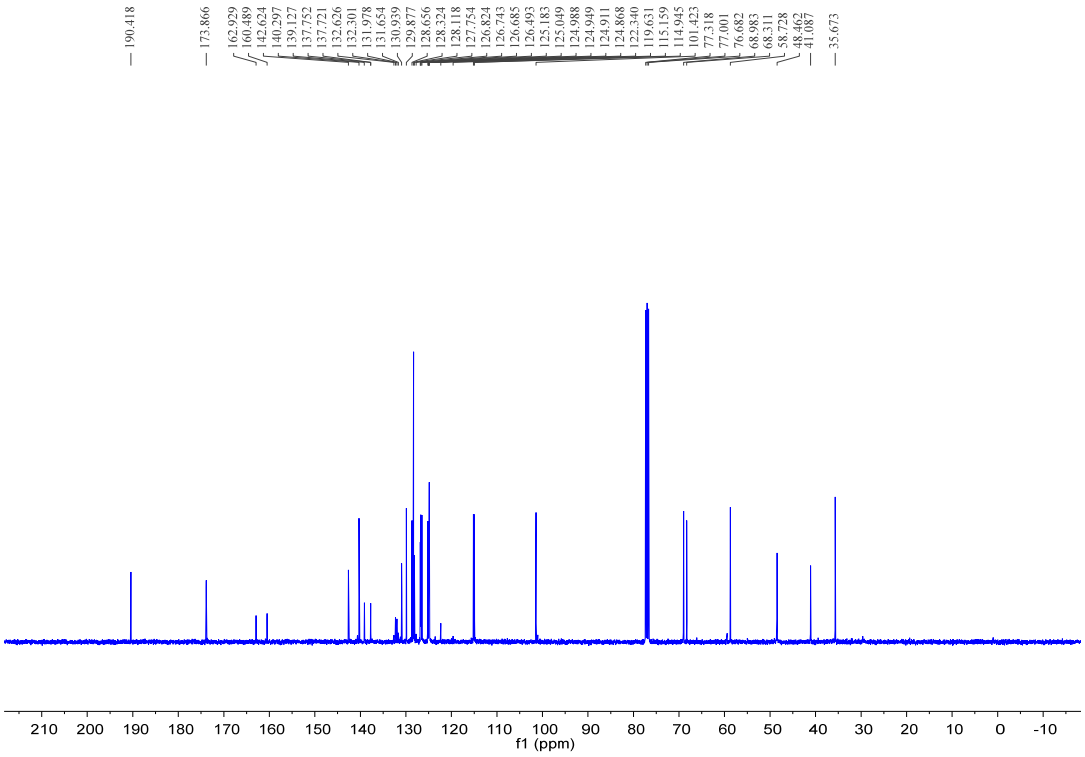


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3ud:

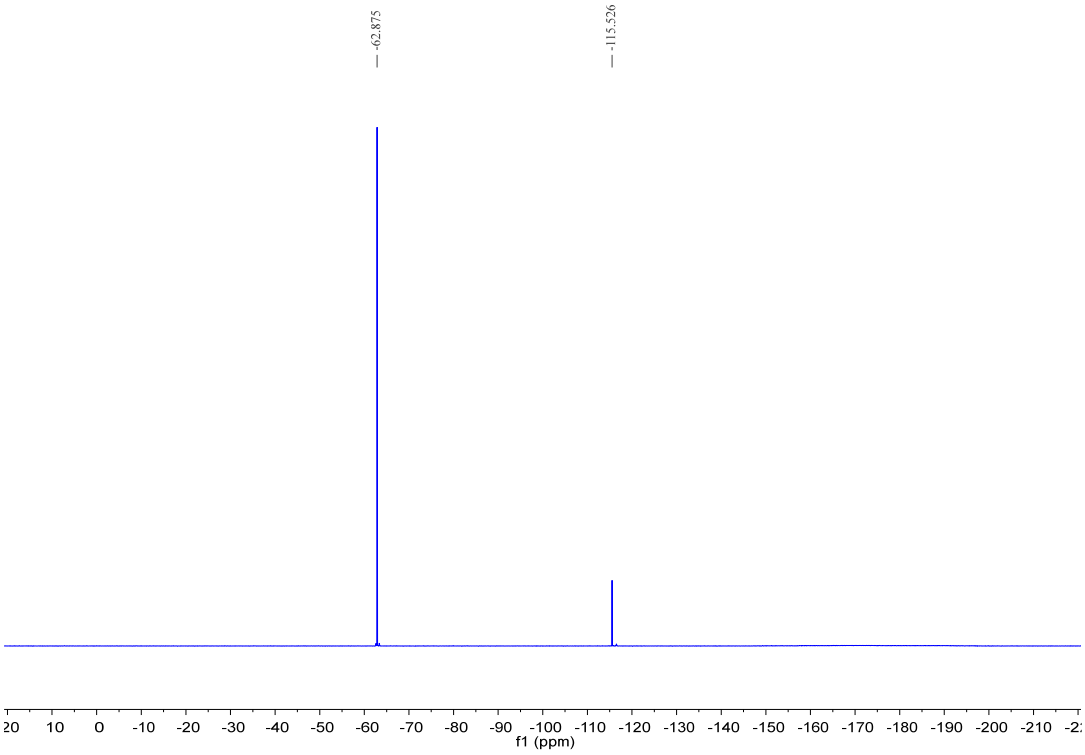
^{1}H NMR (400 MHz, $CDCl_3$)



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

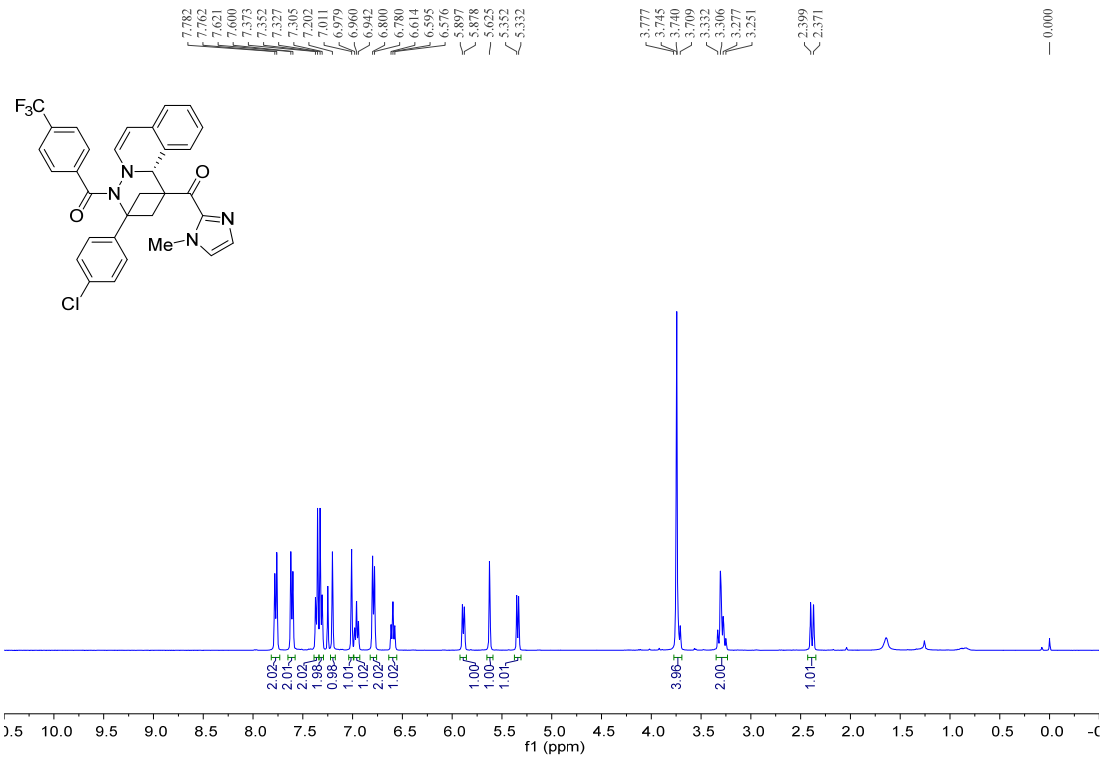


^{19}F NMR (376 MHz, $CDCl_3$)

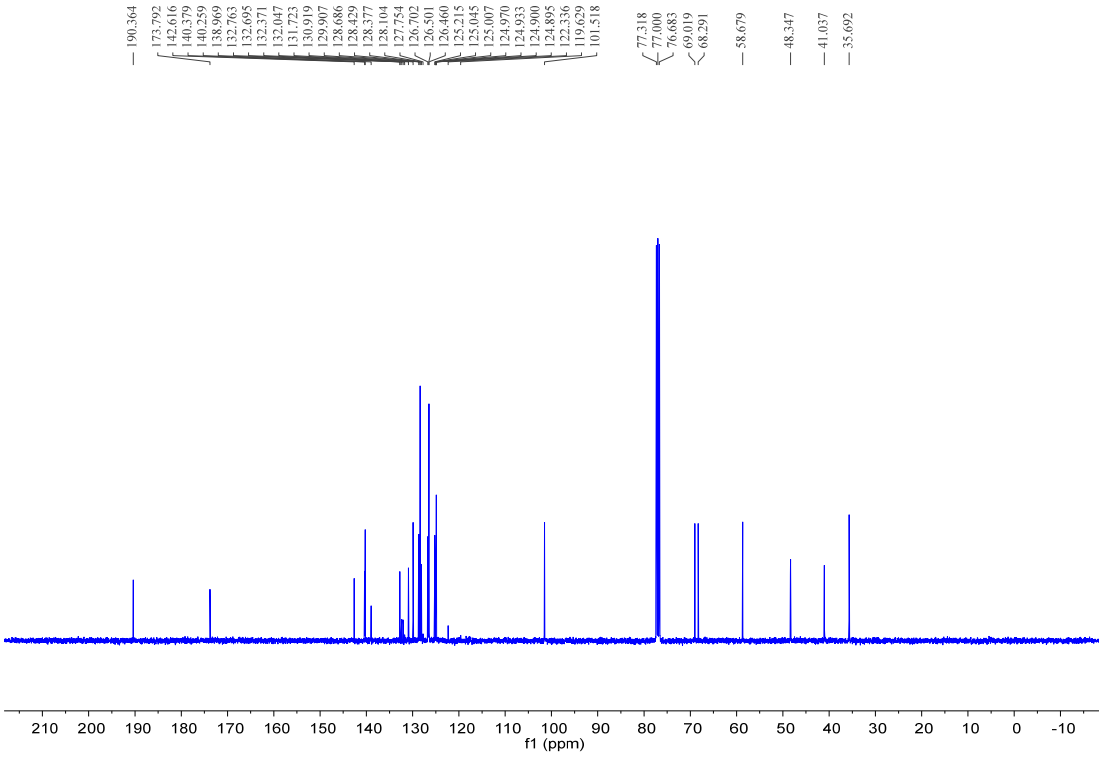


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3yd:

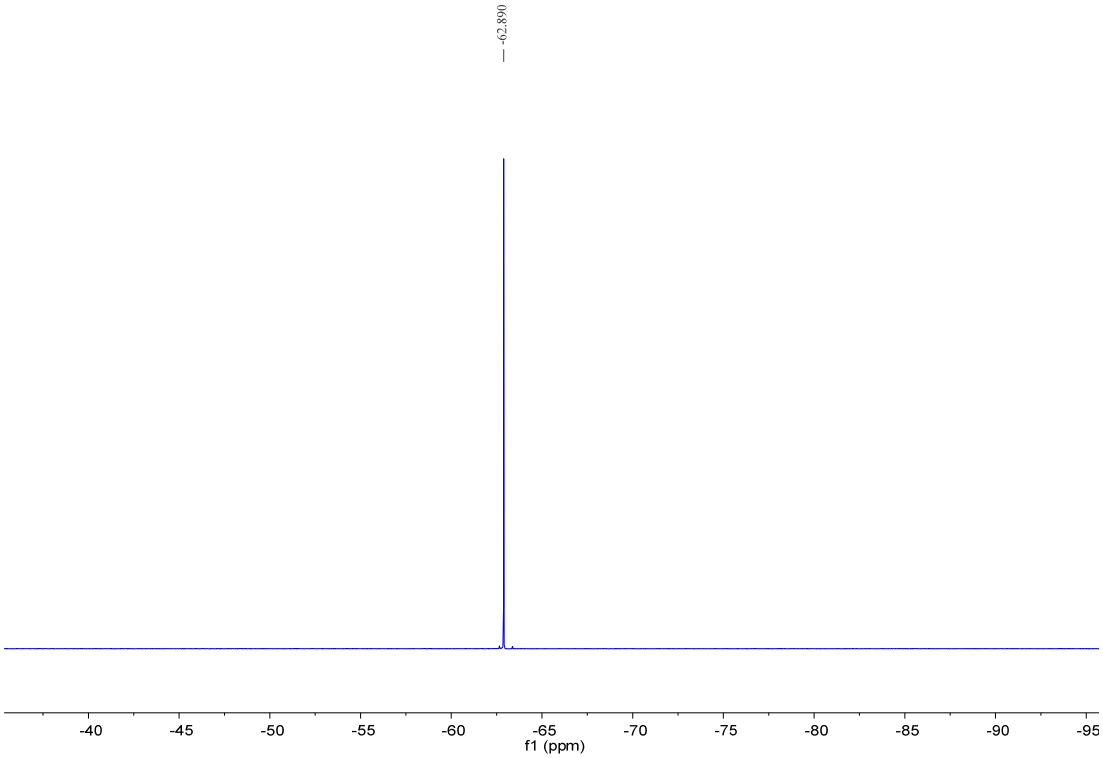
^{1}H NMR (400 MHz, $CDCl_3$)



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

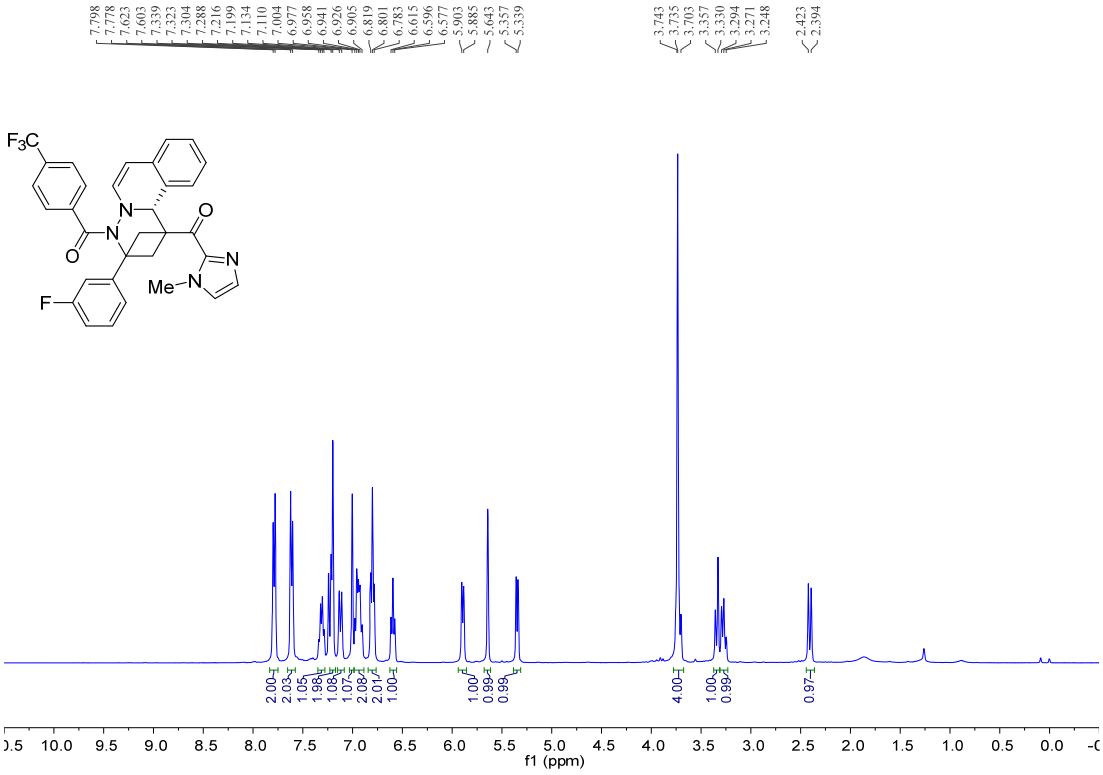


^{19}F NMR (376 MHz, $CDCl_3$)

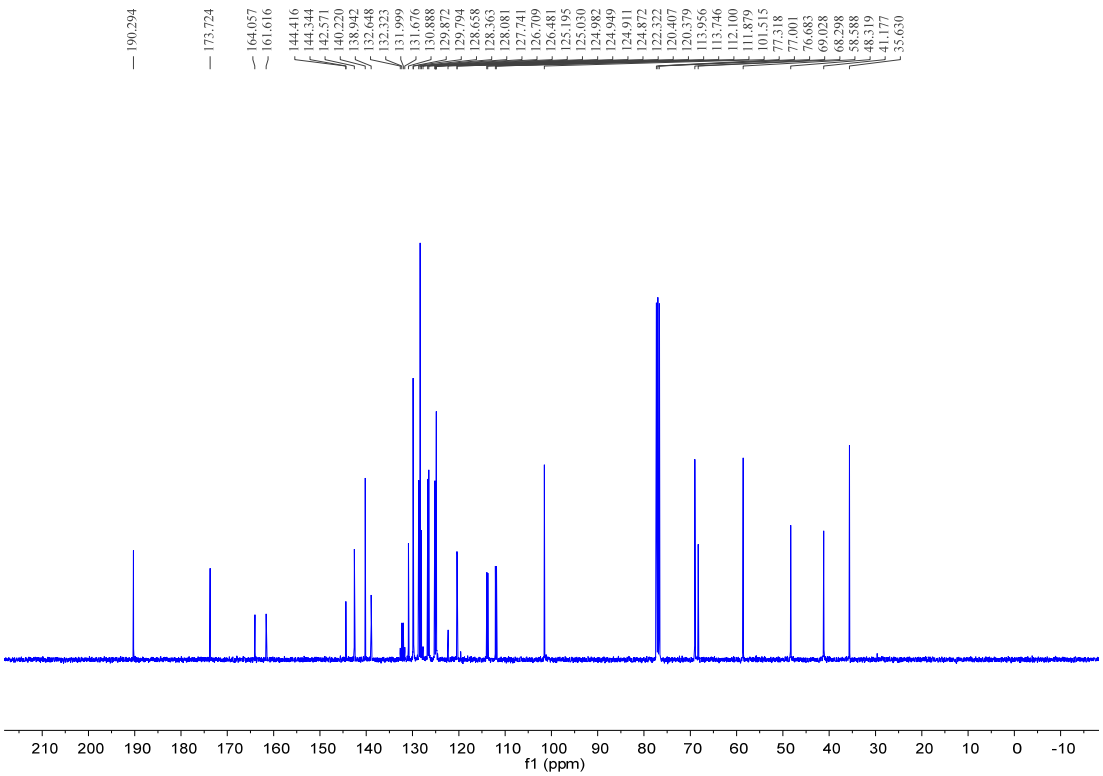


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3zd:

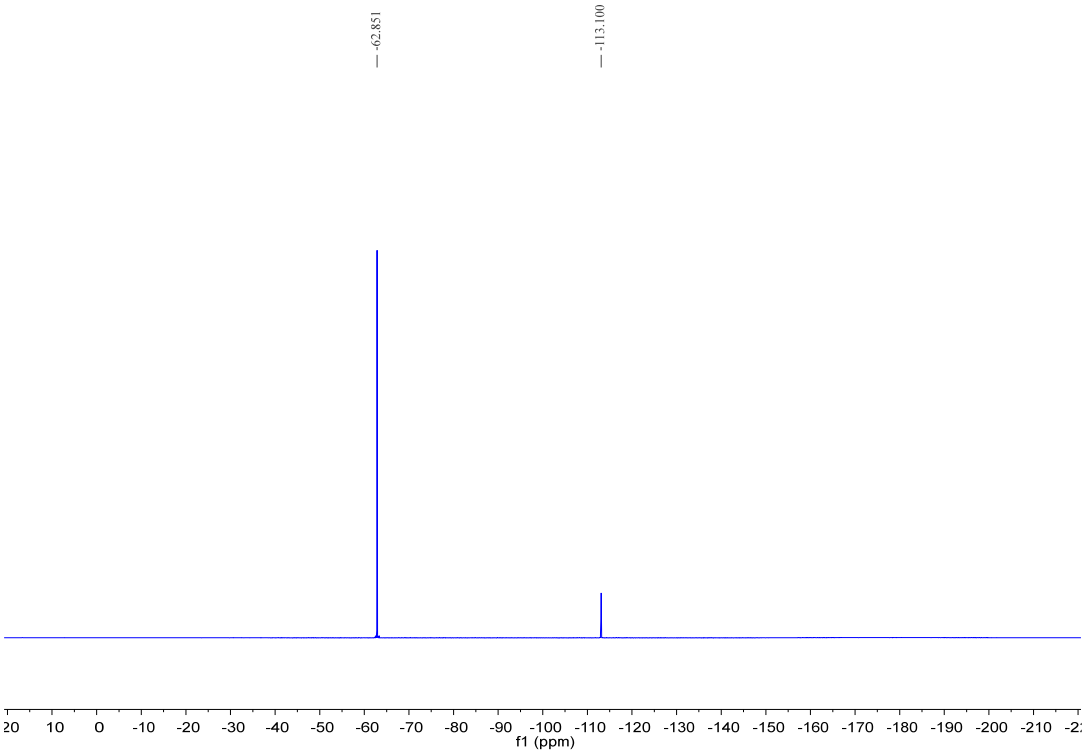
^{1}H NMR (400 MHz, $CDCl_3$)



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

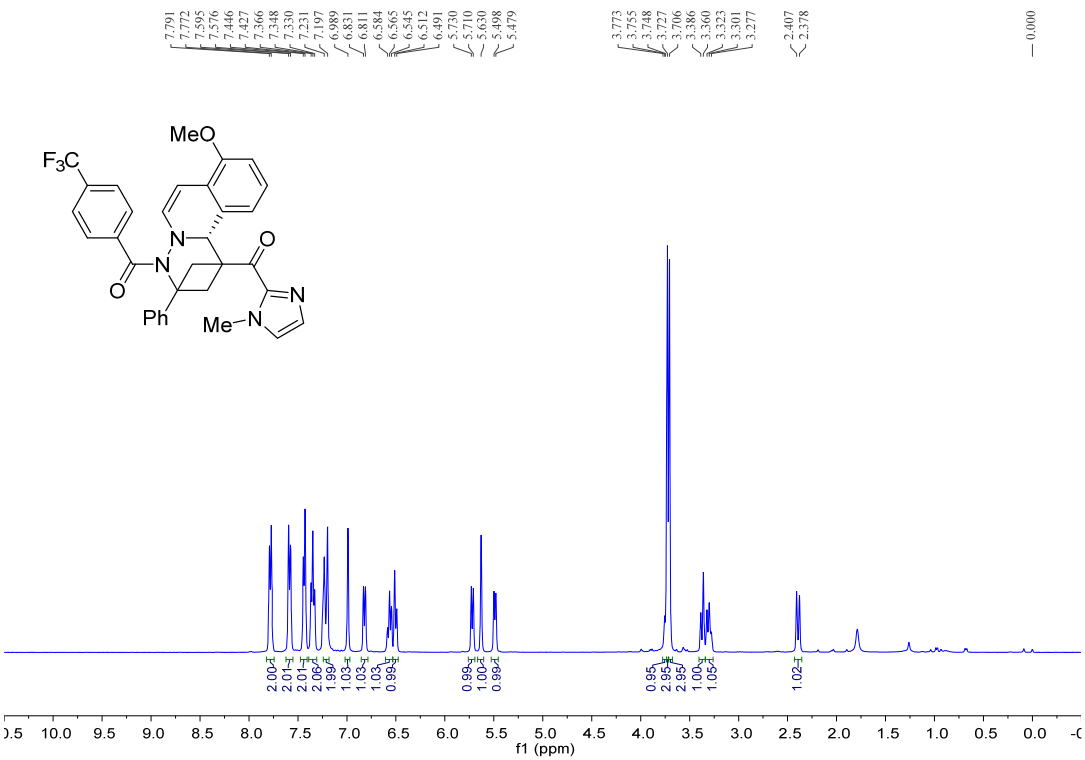


^{19}F NMR (376 MHz, $CDCl_3$)

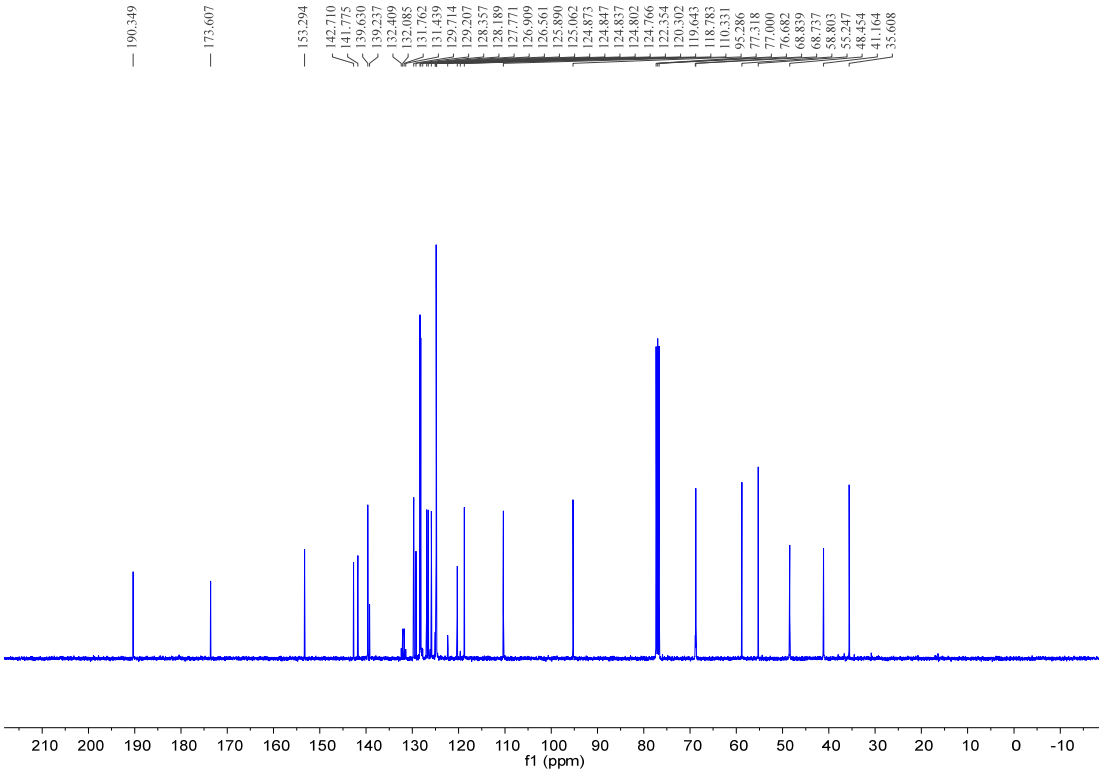


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3qr:

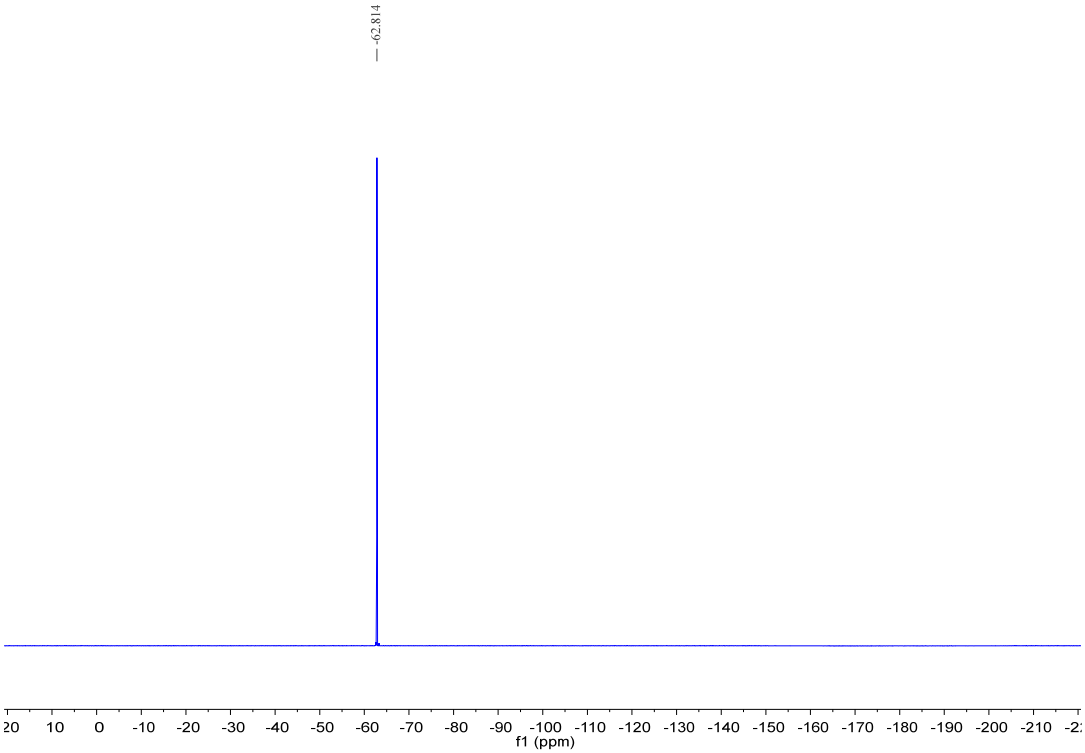
^{1}H NMR (400 MHz, $CDCl_3$)



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

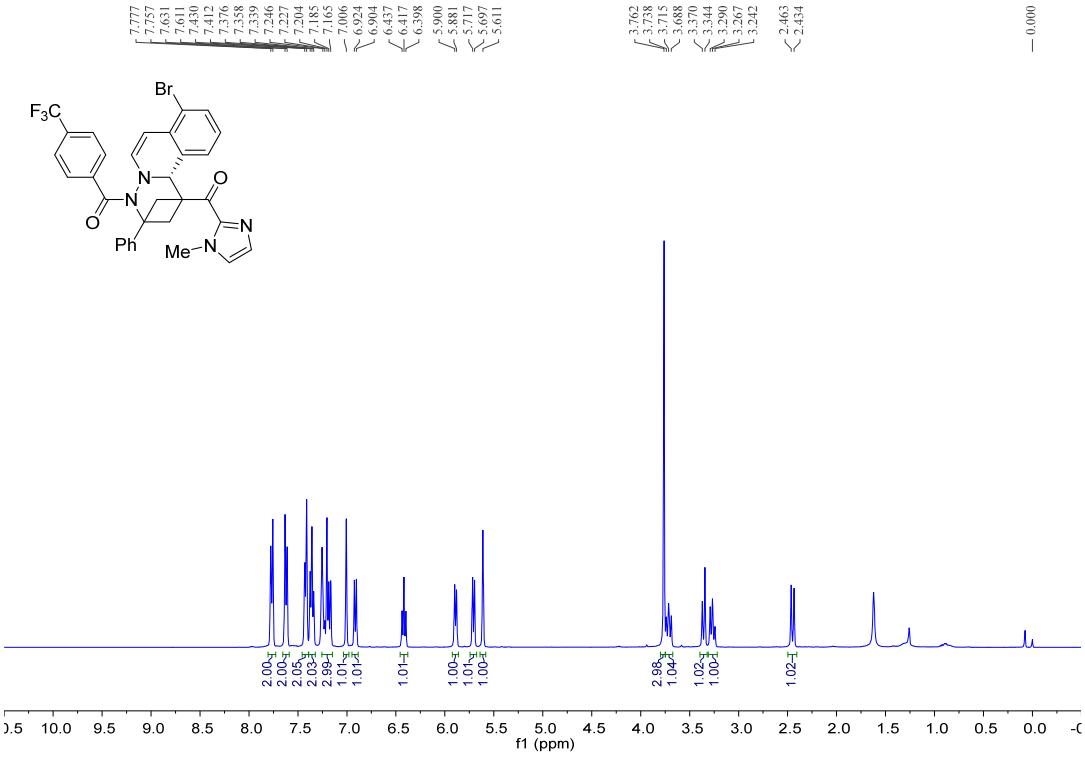


^{19}F NMR (376 MHz, $CDCl_3$)

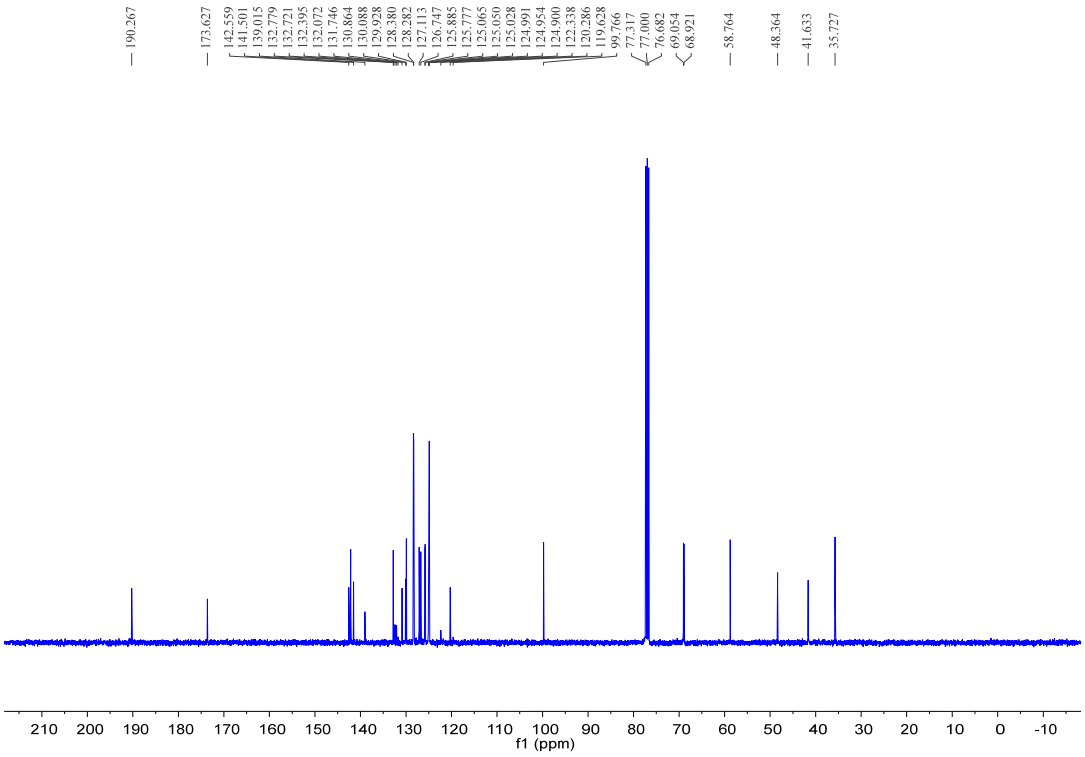


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3qs:

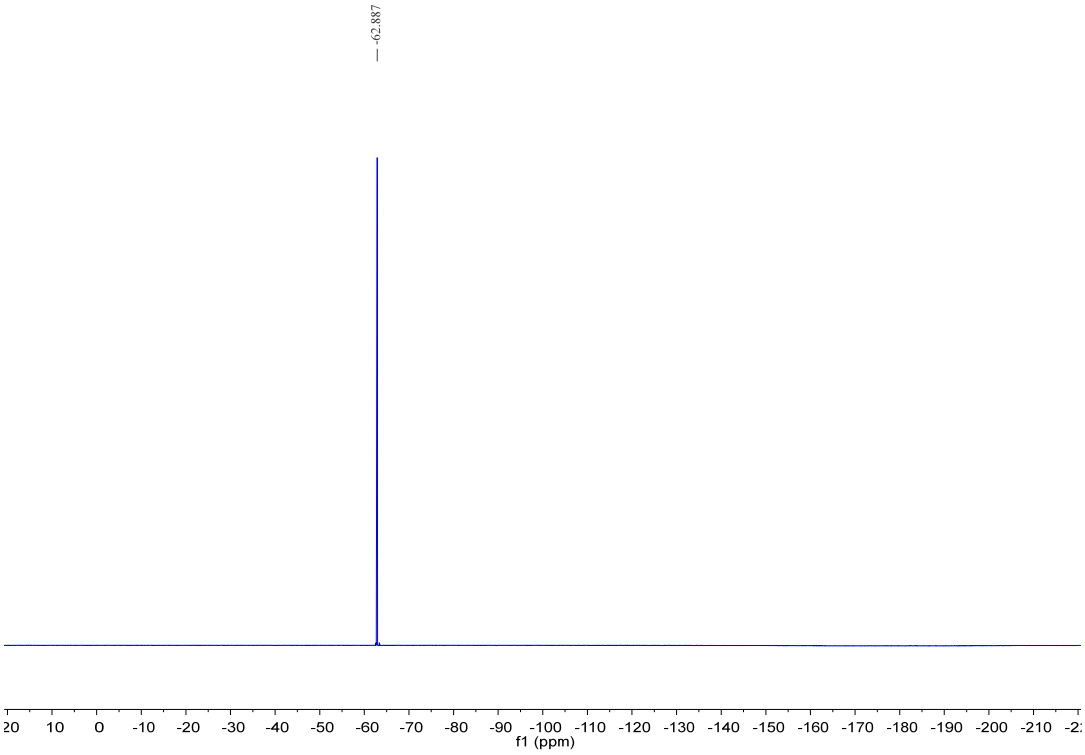
^{1}H NMR (400 MHz, $CDCl_3$)



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

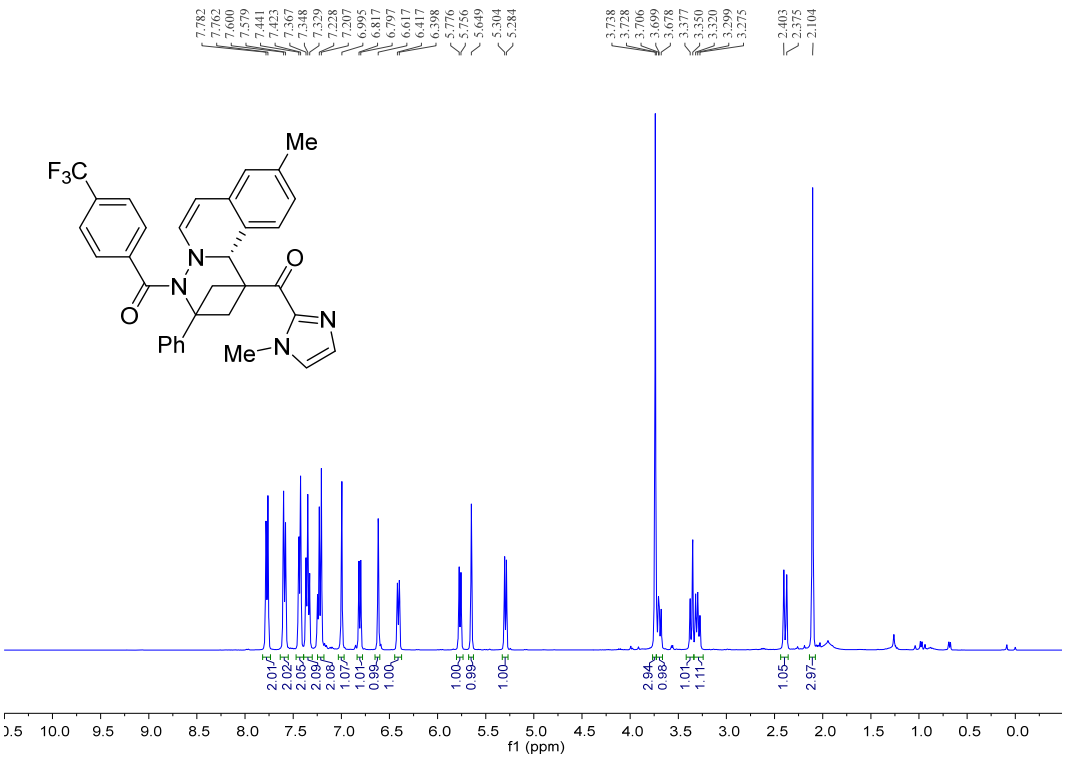


^{19}F NMR (376 MHz, $CDCl_3$)

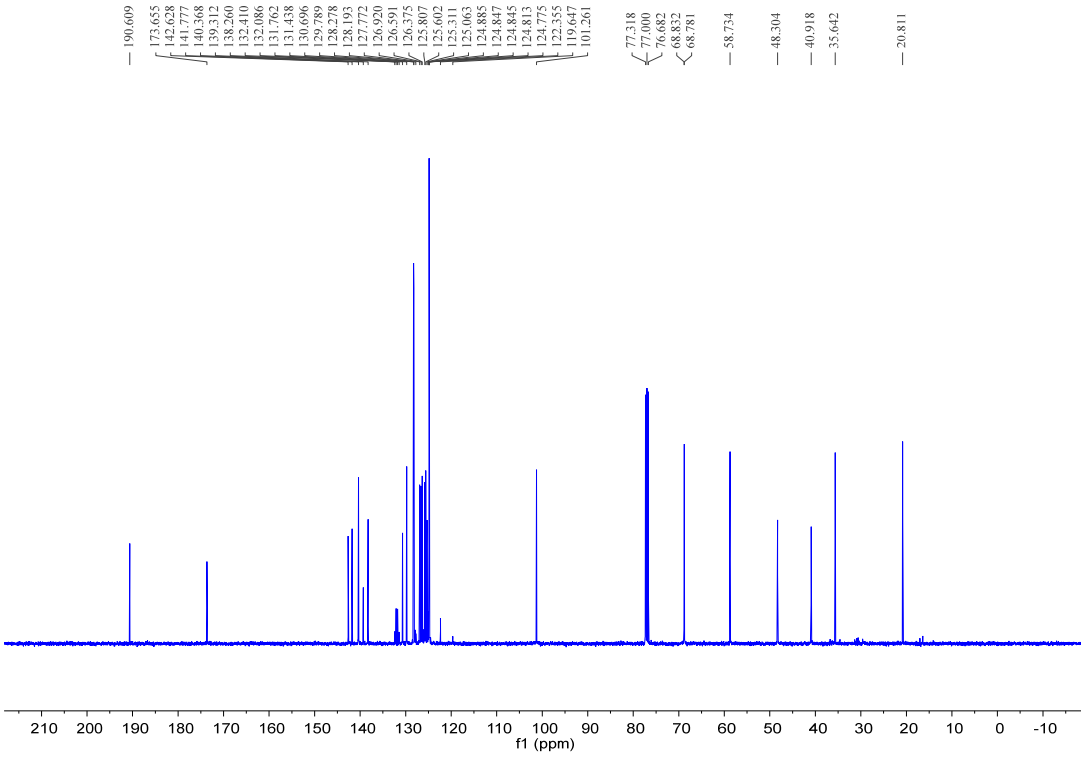


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3qt:

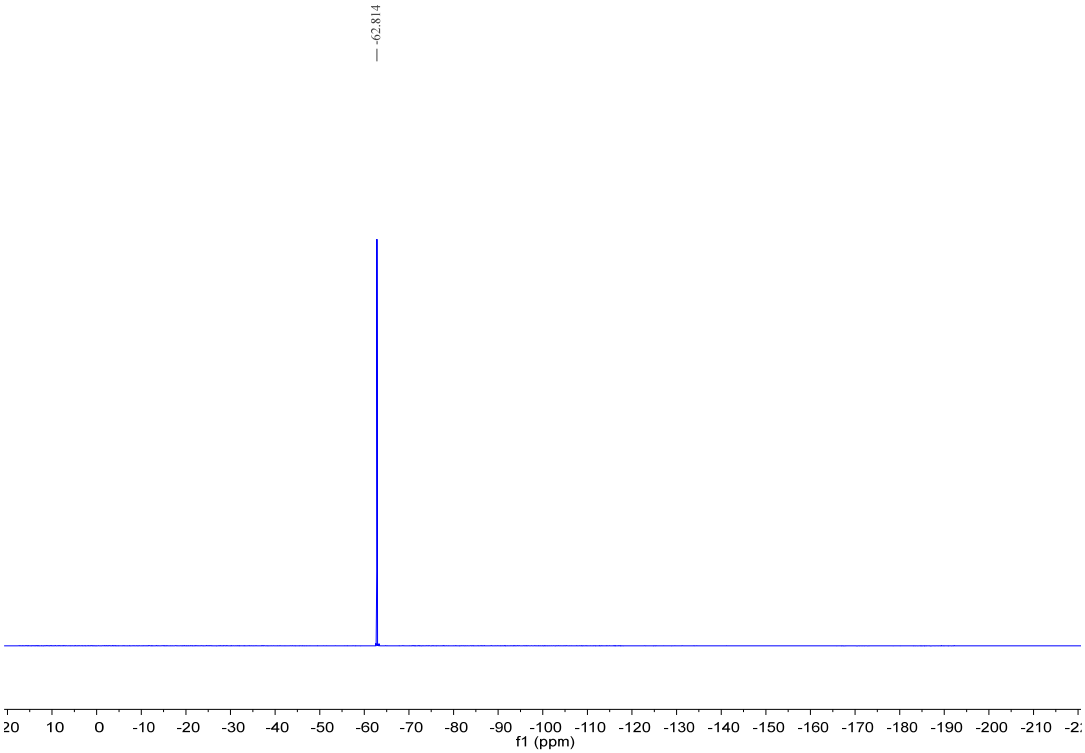
^{1}H NMR (400 MHz, $CDCl_3$)



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

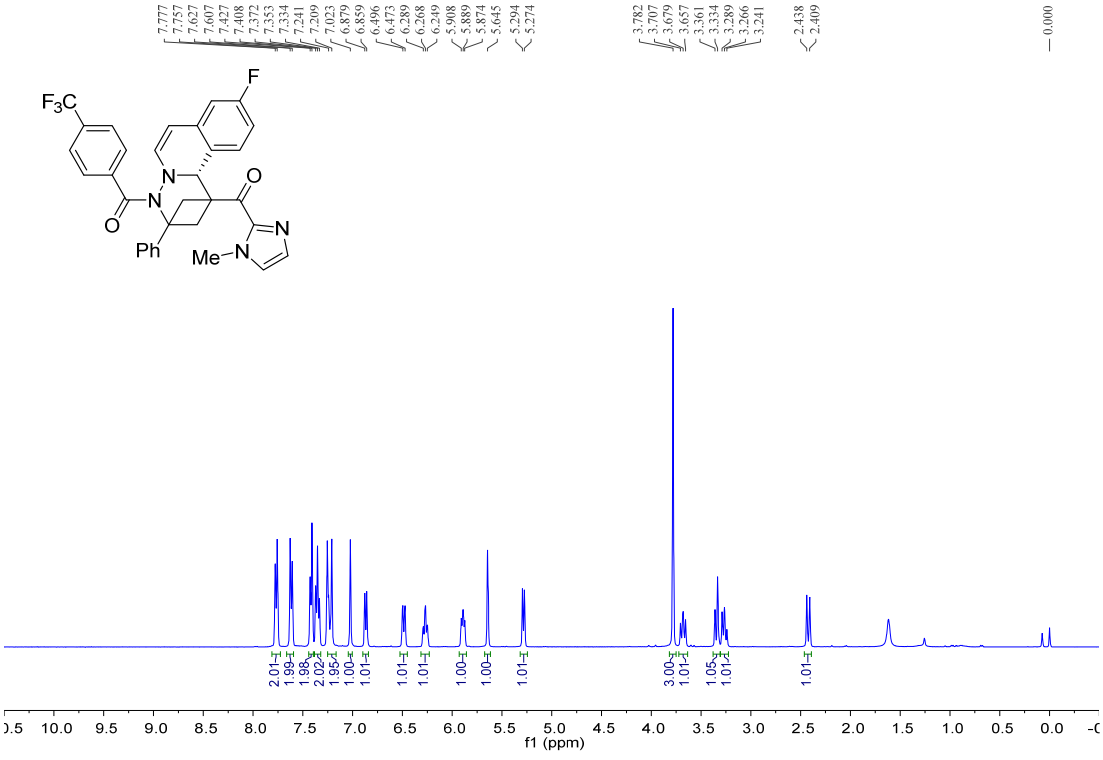


^{19}F NMR (376 MHz, $CDCl_3$)

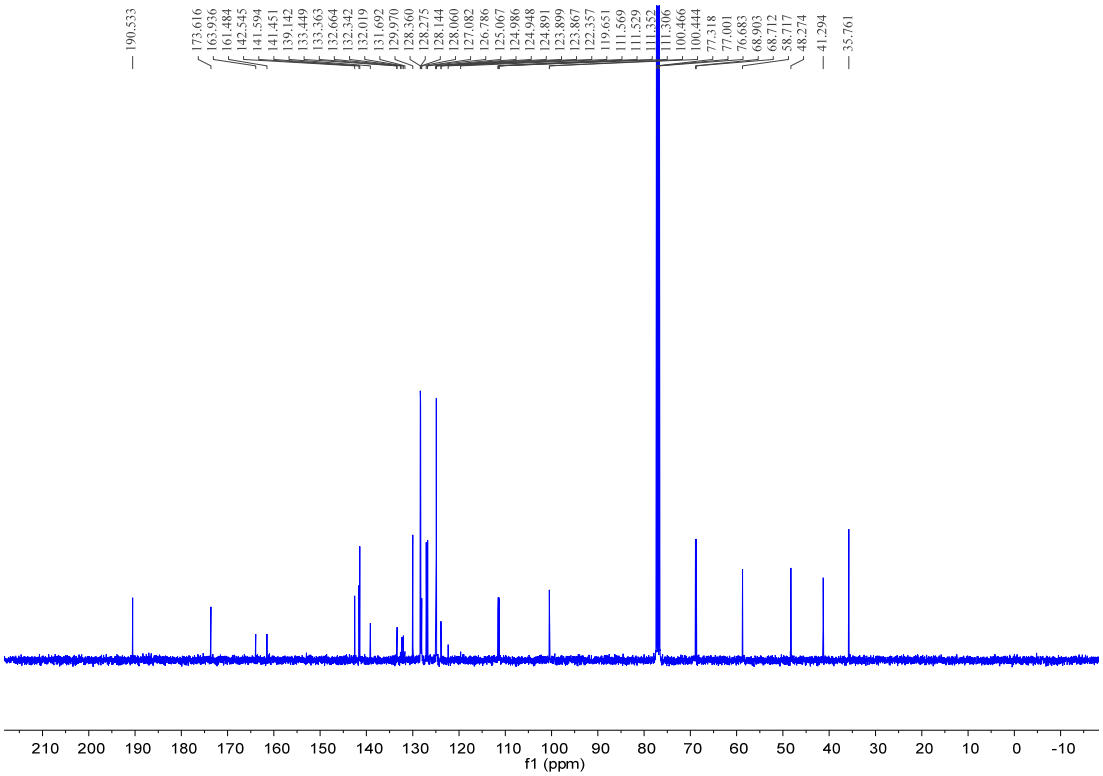


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3qu:

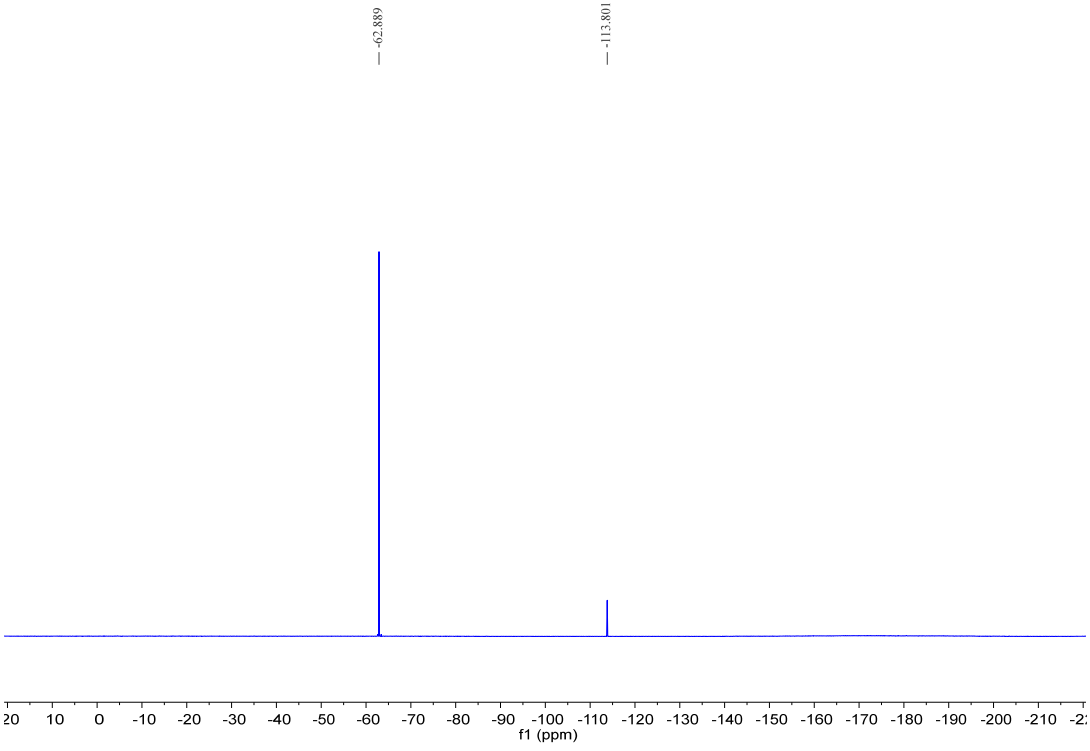
^{1}H NMR (400 MHz, $CDCl_3$)



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

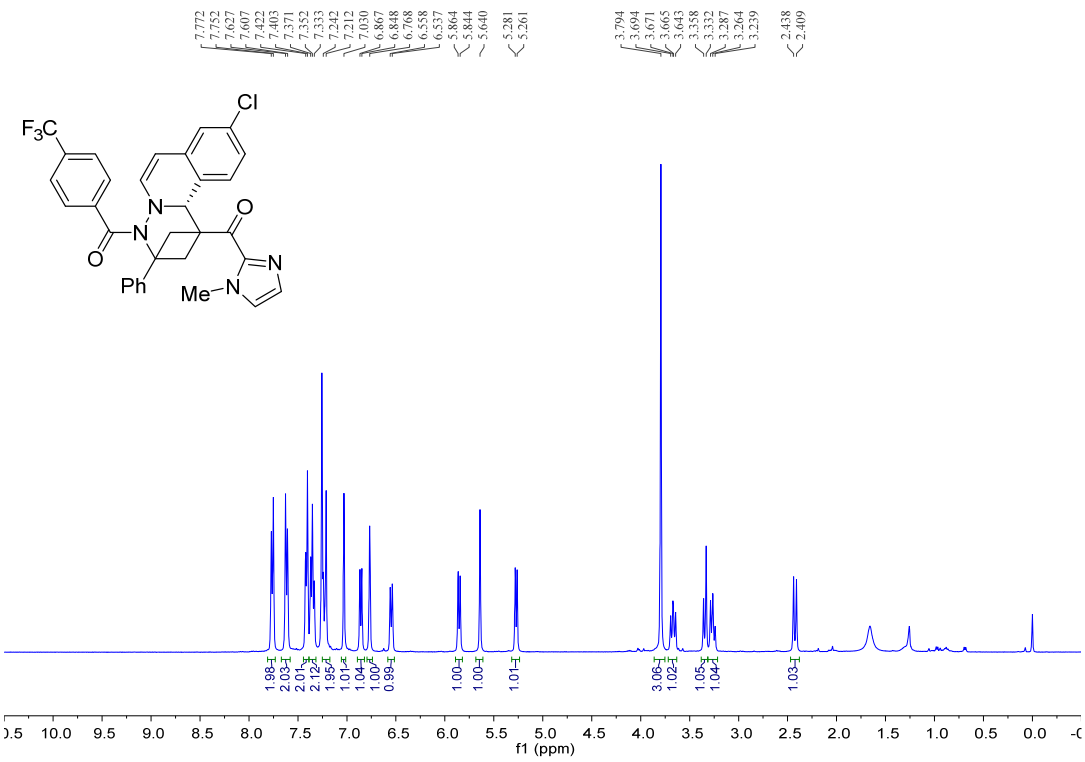


^{19}F NMR (376 MHz, $CDCl_3$)

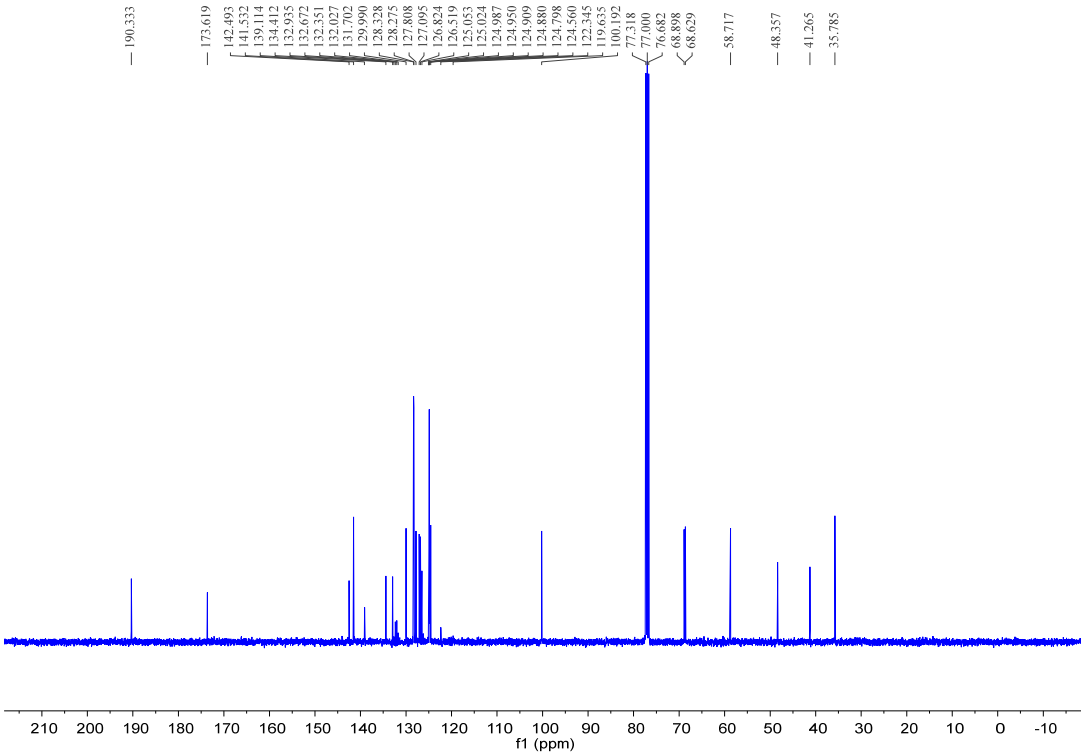


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3qv:

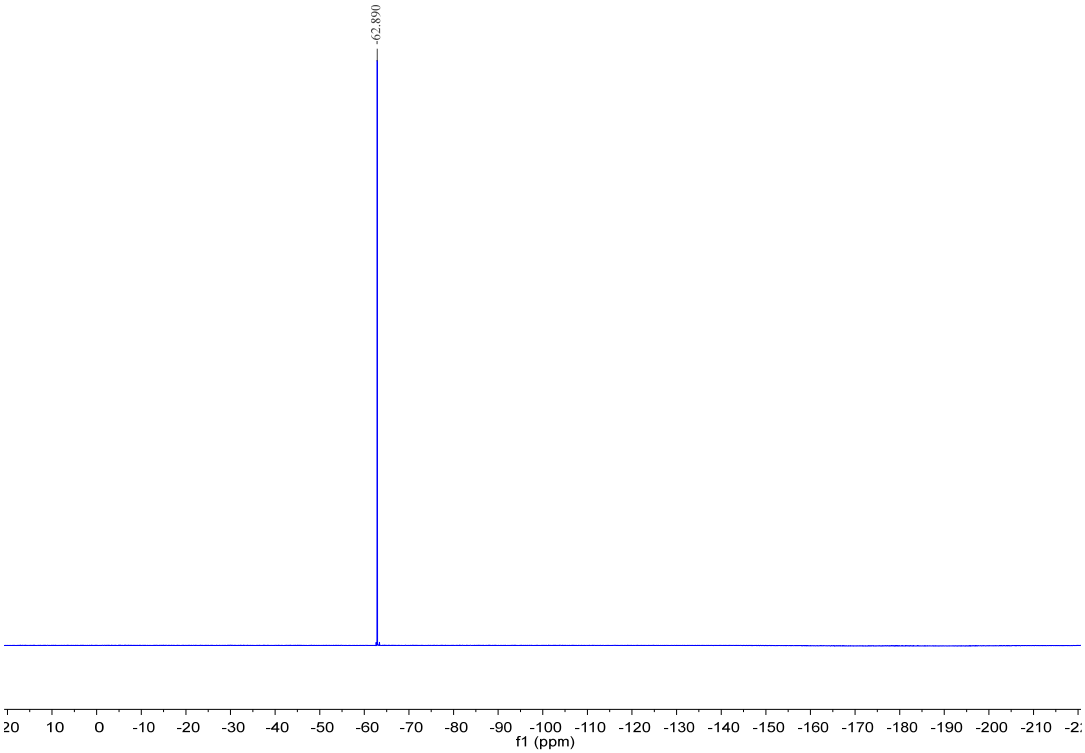
^{1}H NMR (400 MHz, $CDCl_3$)



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

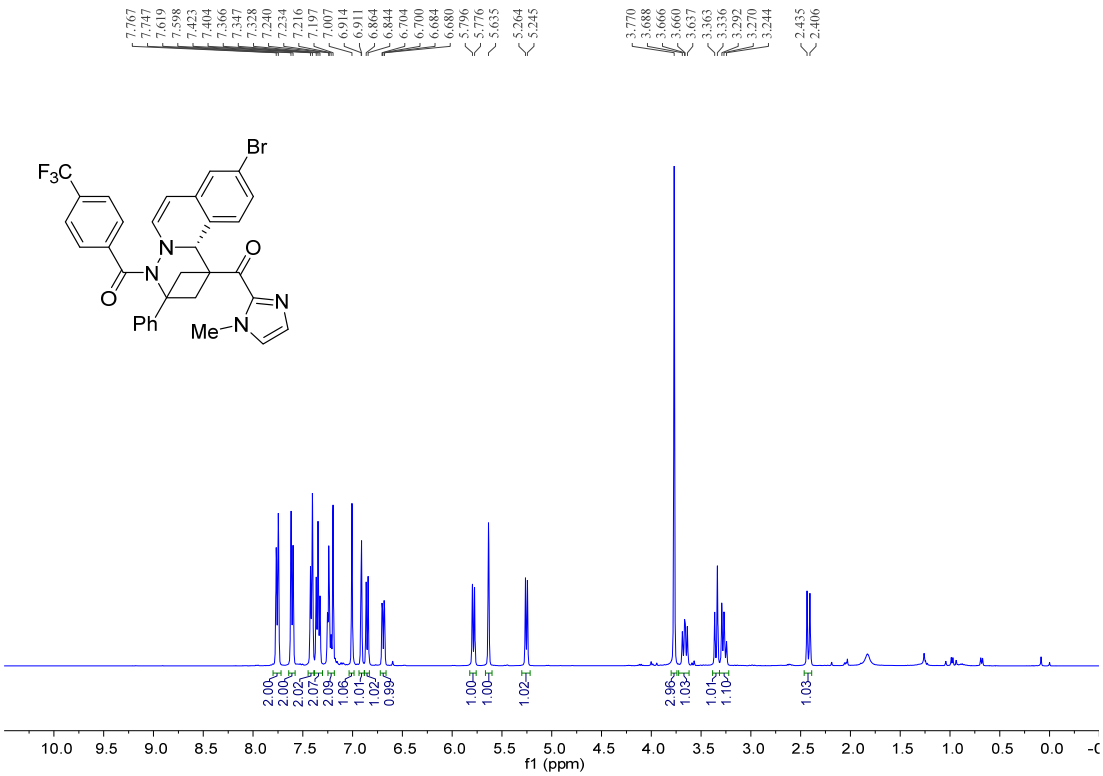


^{19}F NMR (376 MHz, $CDCl_3$)

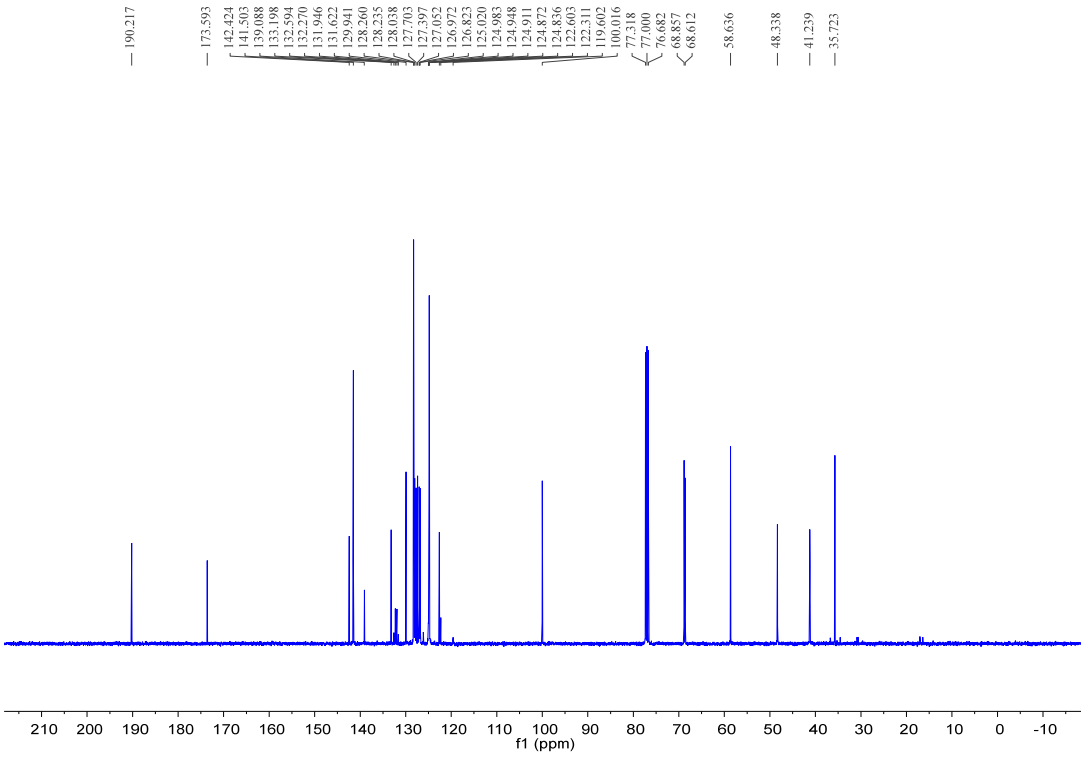


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3qw:

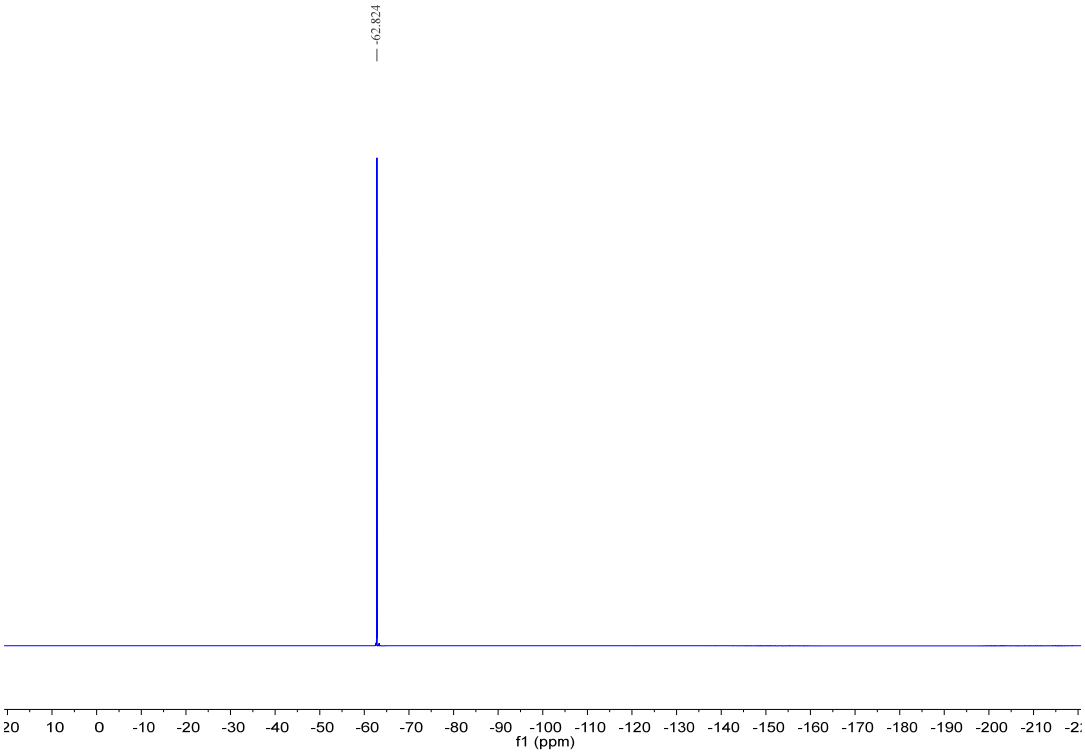
^{1}H NMR (400 MHz, $CDCl_3$)



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

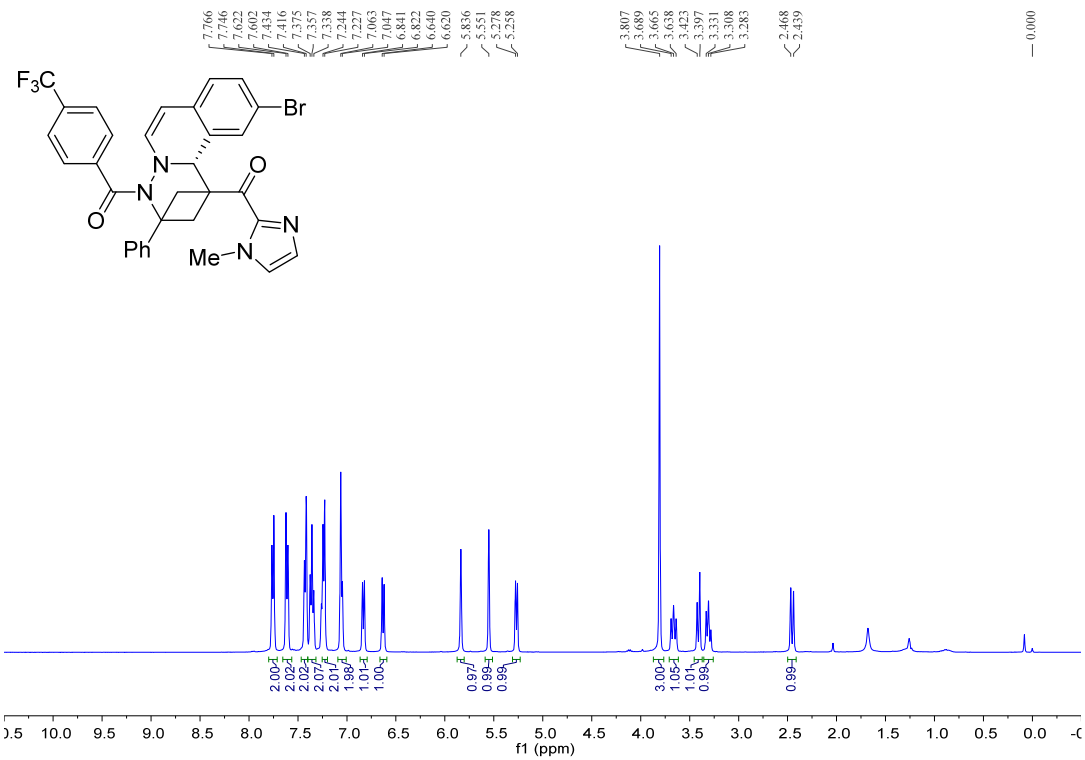


^{19}F NMR (376 MHz, $CDCl_3$)

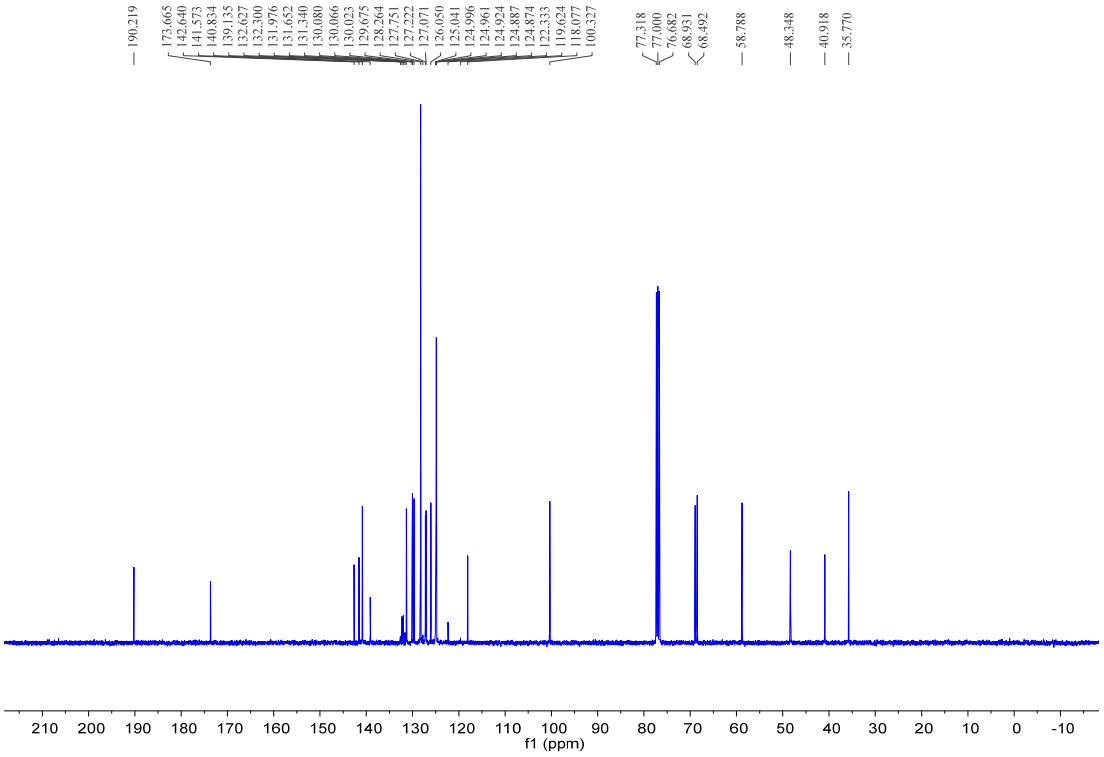


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3qx:

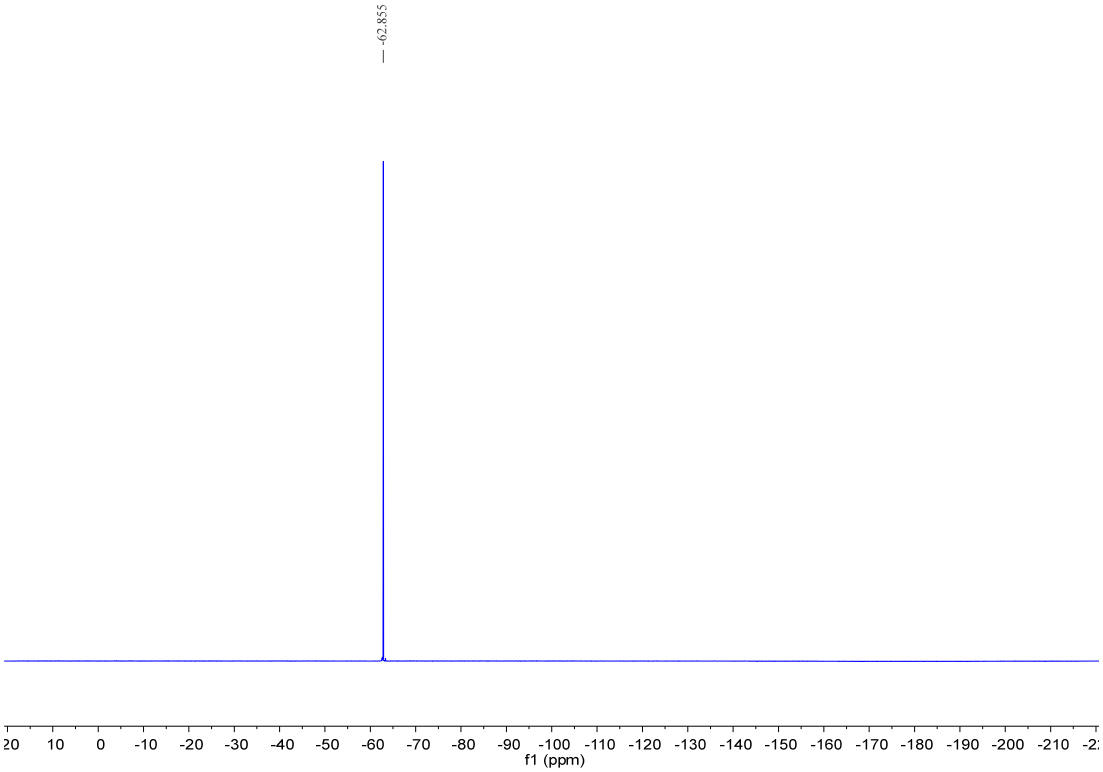
^{1}H NMR (400 MHz, $CDCl_3$)



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

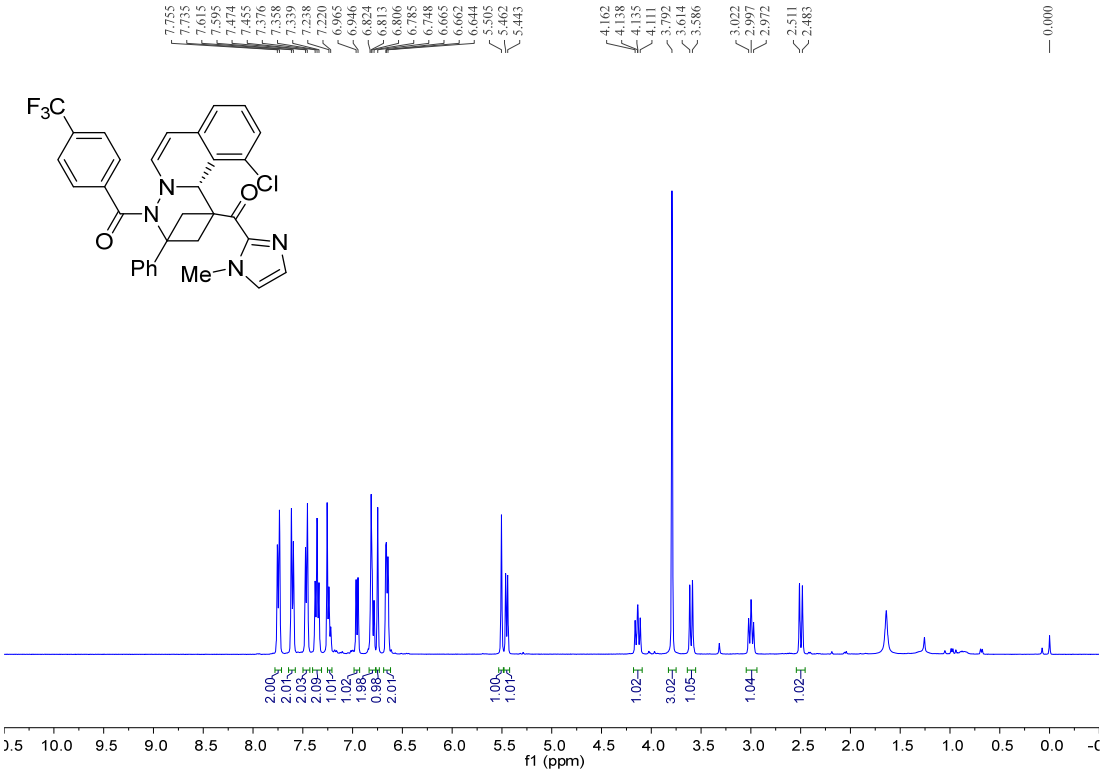


^{19}F NMR (376 MHz, $CDCl_3$)

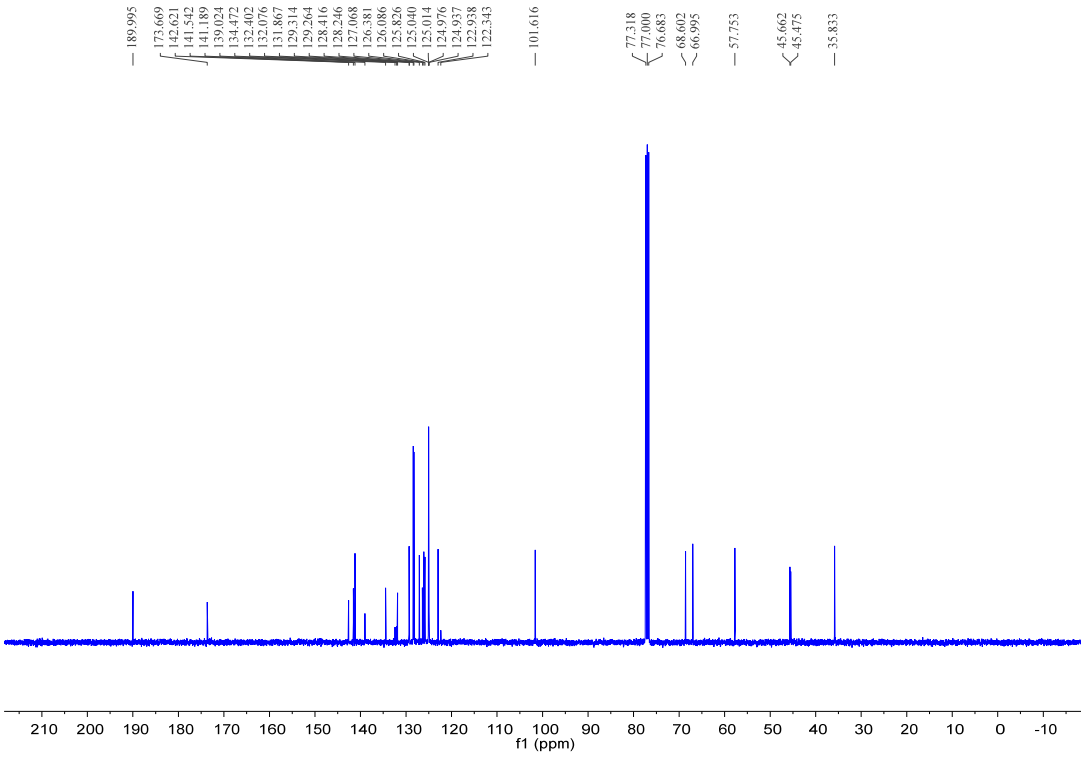


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*S*)-3qy:

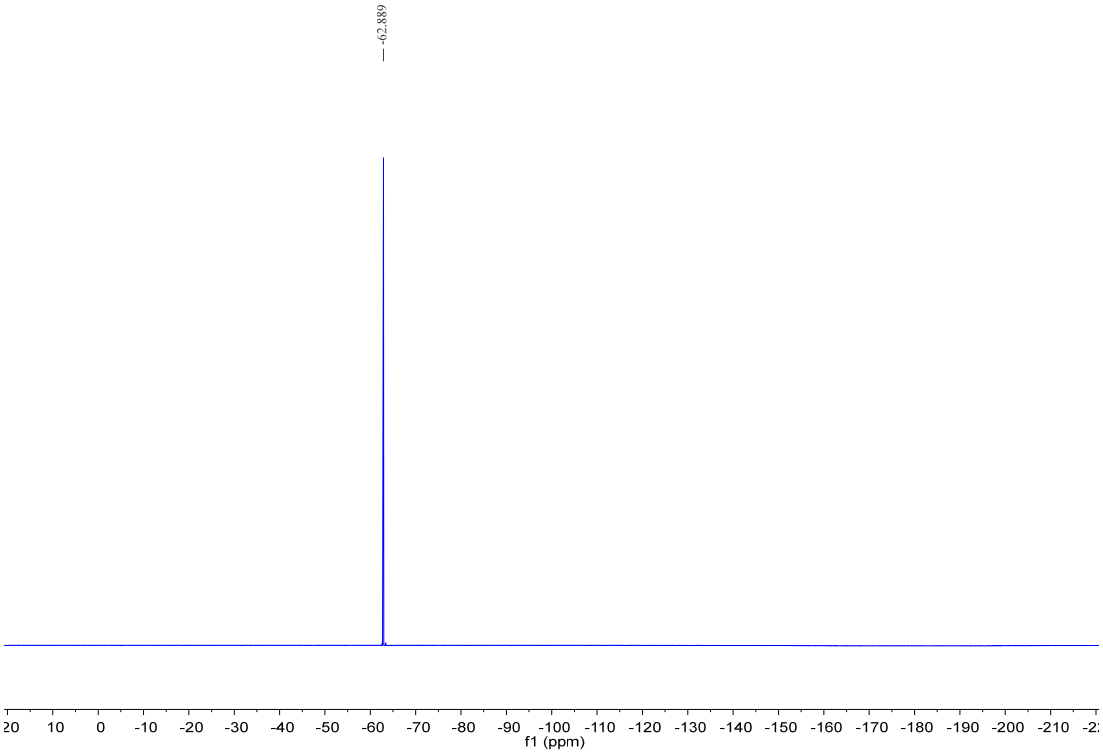
^{1}H NMR (400 MHz, $CDCl_3$)



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

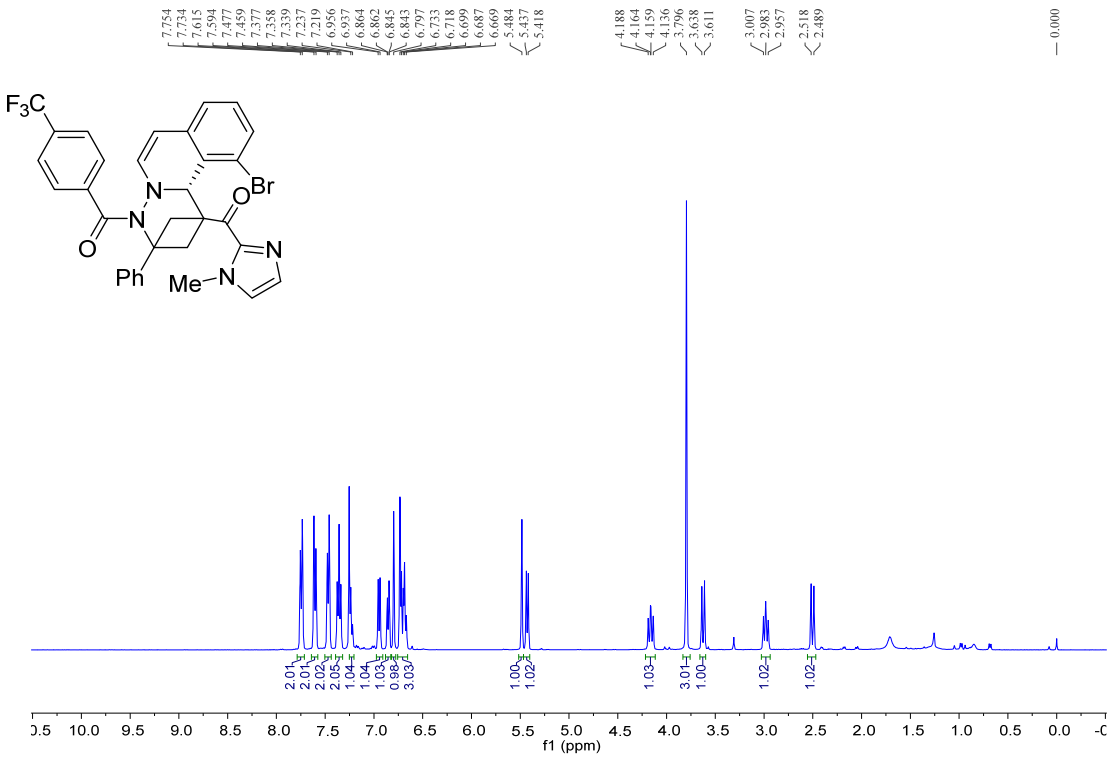


^{19}F NMR (376 MHz, $CDCl_3$)

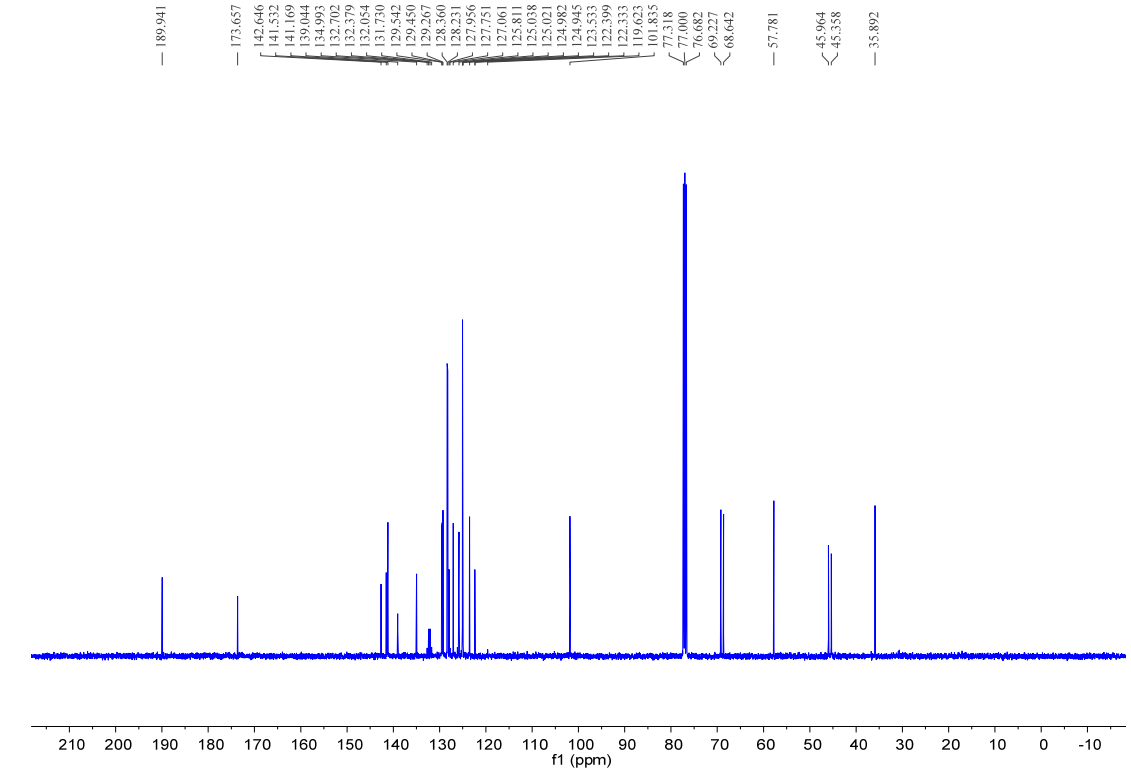


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*S*)-3qz:

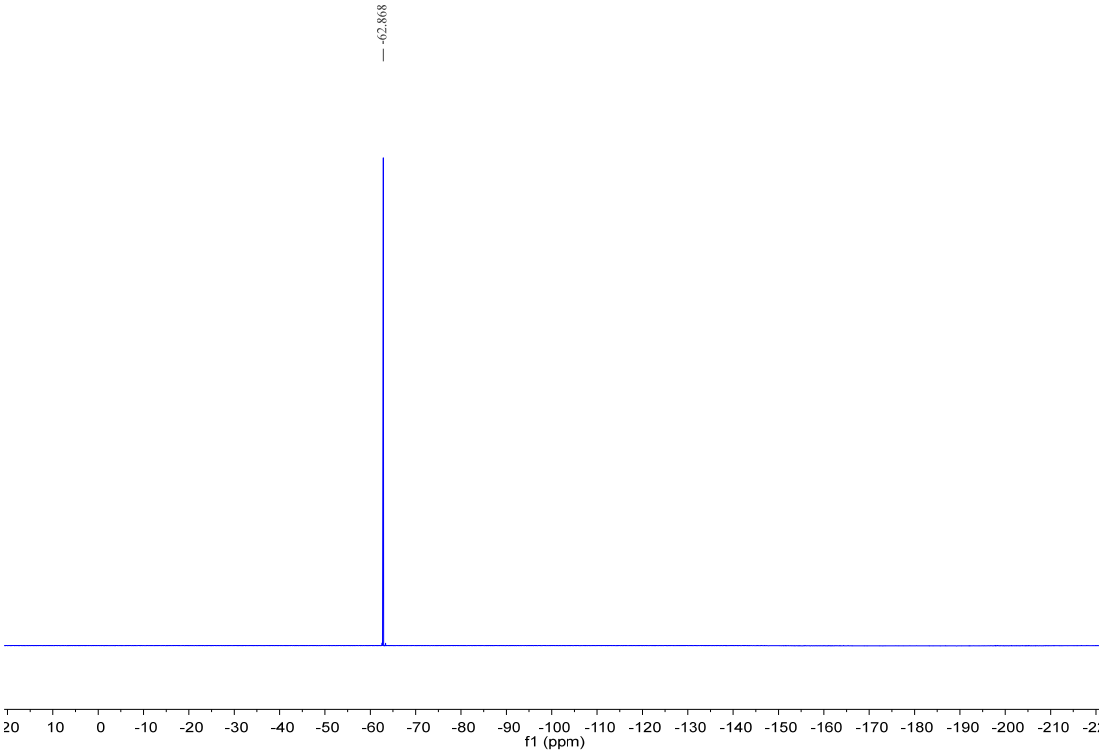
^{1}H NMR (400 MHz, $CDCl_3$)



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

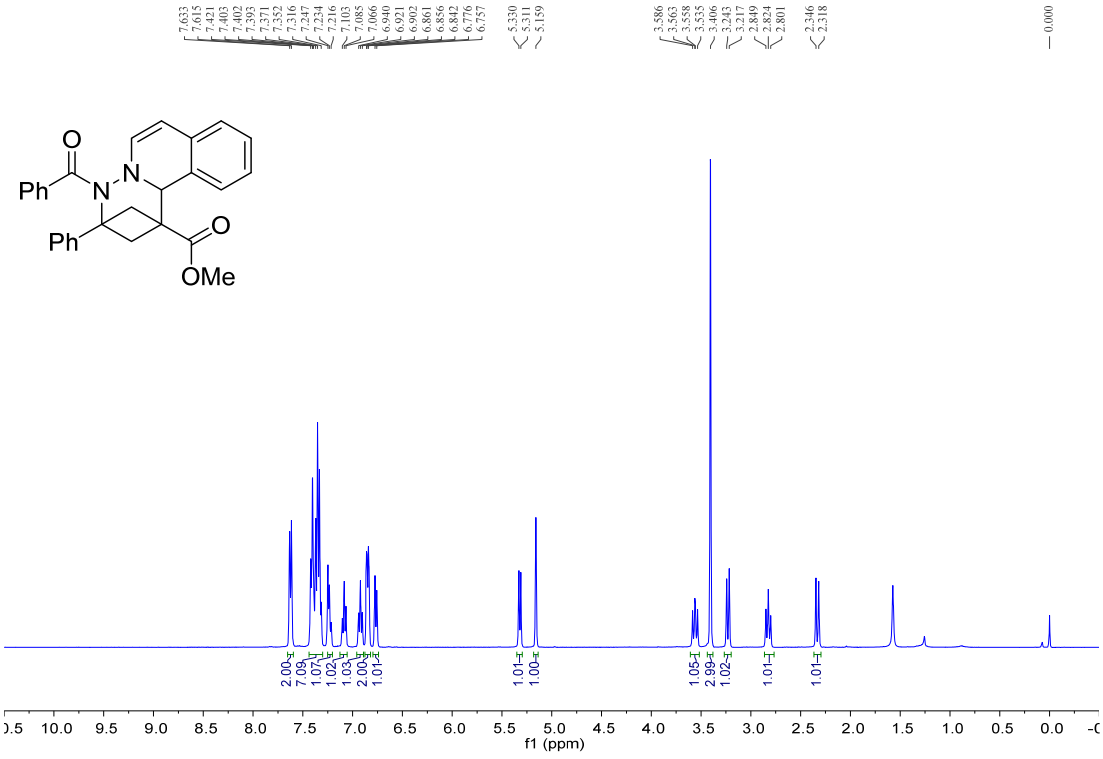


^{19}F NMR (376 MHz, $CDCl_3$)

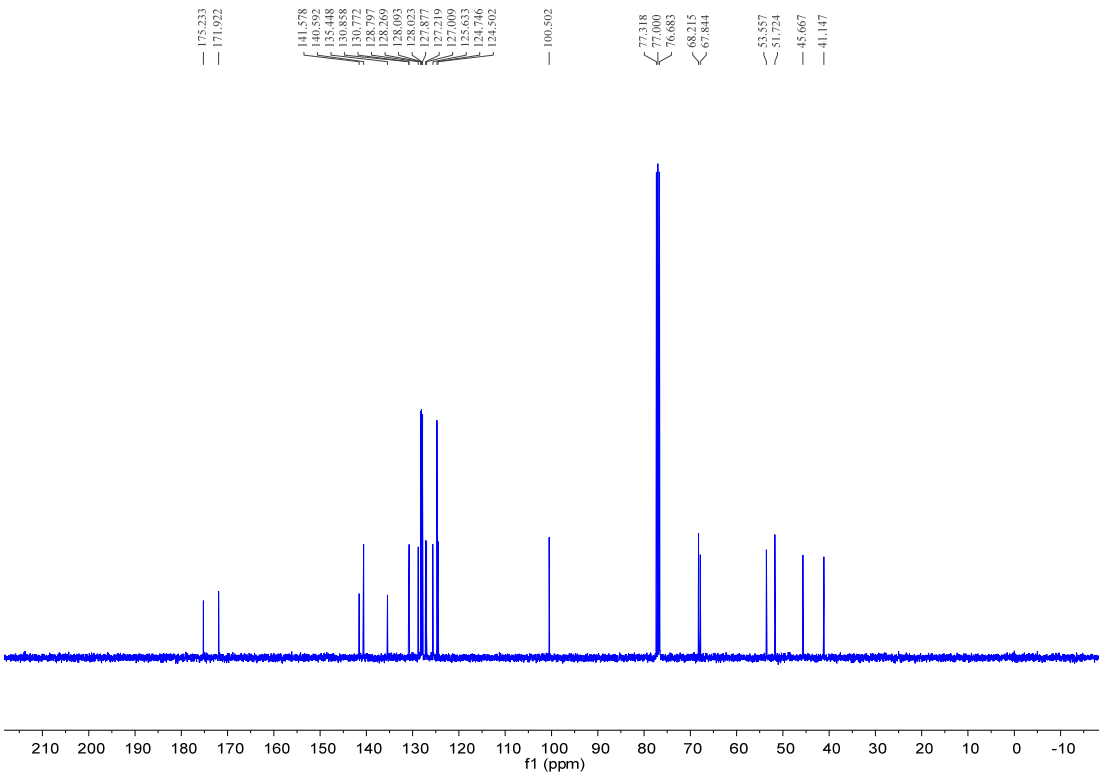


^{1}H and ^{13}C NMR Spectra for Compound 6:

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

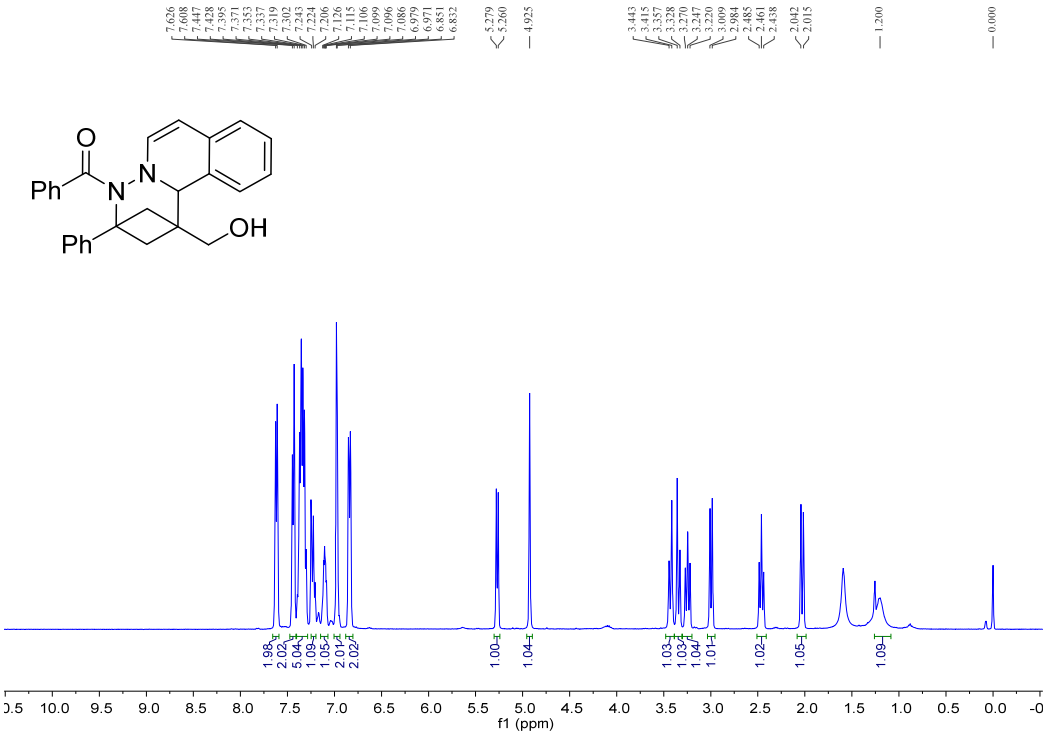


^{13}C NMR (100 MHz, $CDCl_3$)

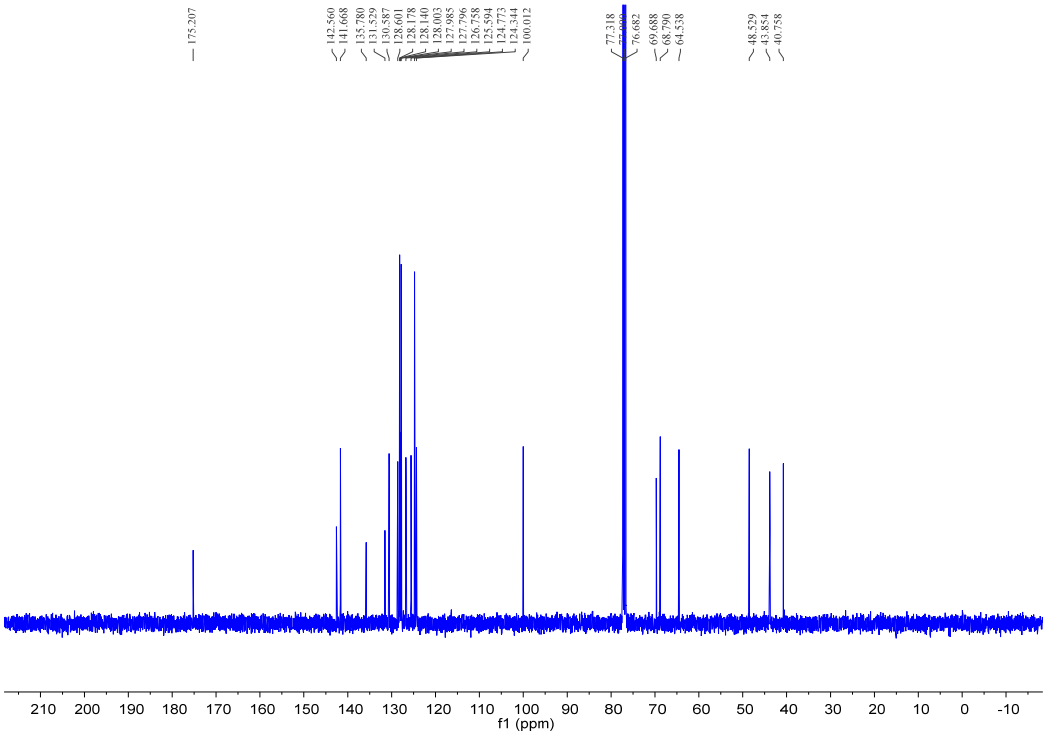


^{1}H and ^{13}C NMR Spectra for Compound 7:

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

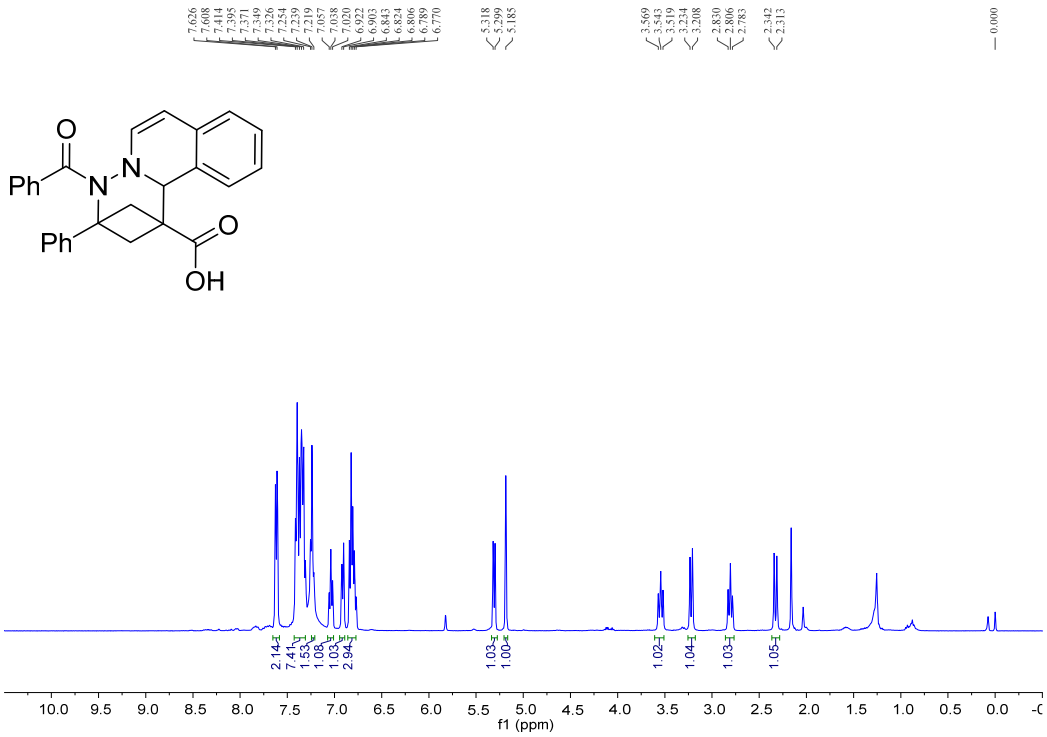


^{13}C NMR (100 MHz, $CDCl_3$)

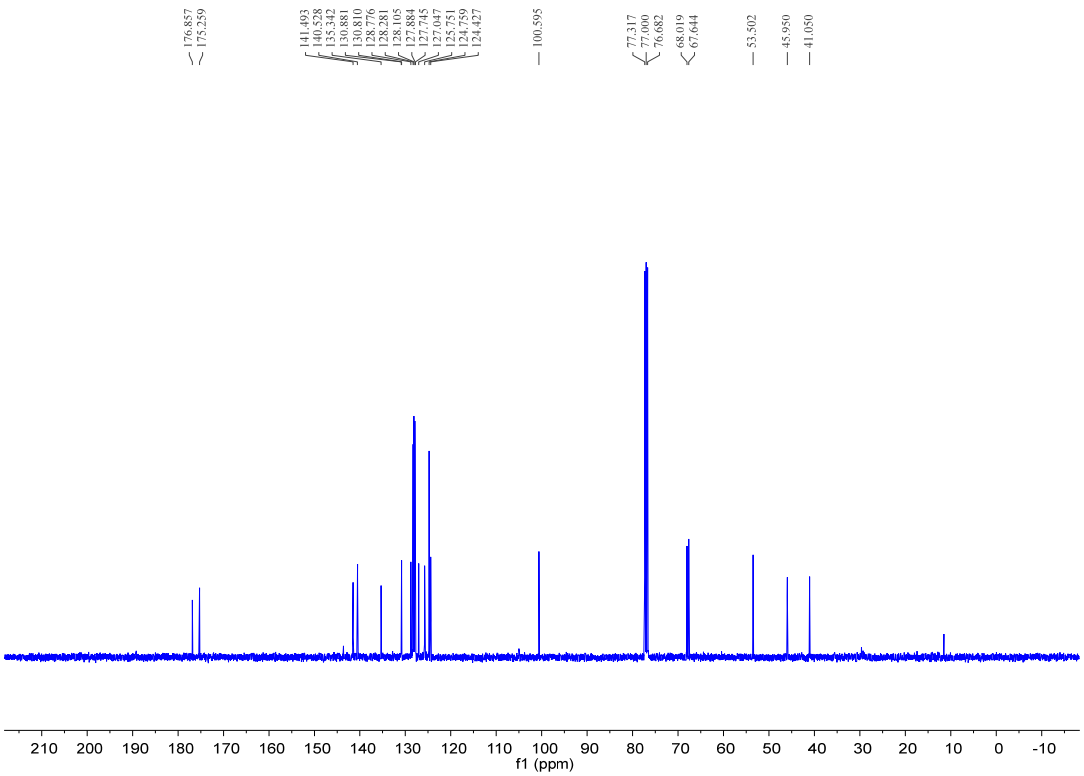


^{1}H and ^{13}C NMR Spectra for Compound 8:

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

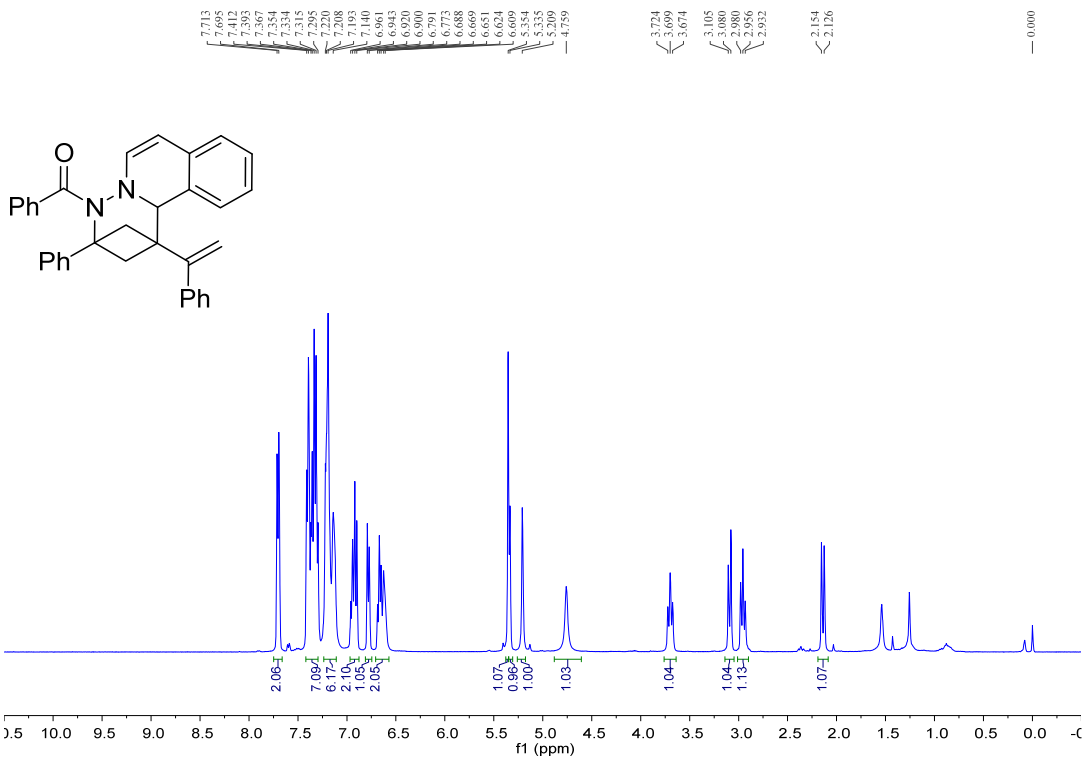


^{13}C NMR (100 MHz, $CDCl_3$)

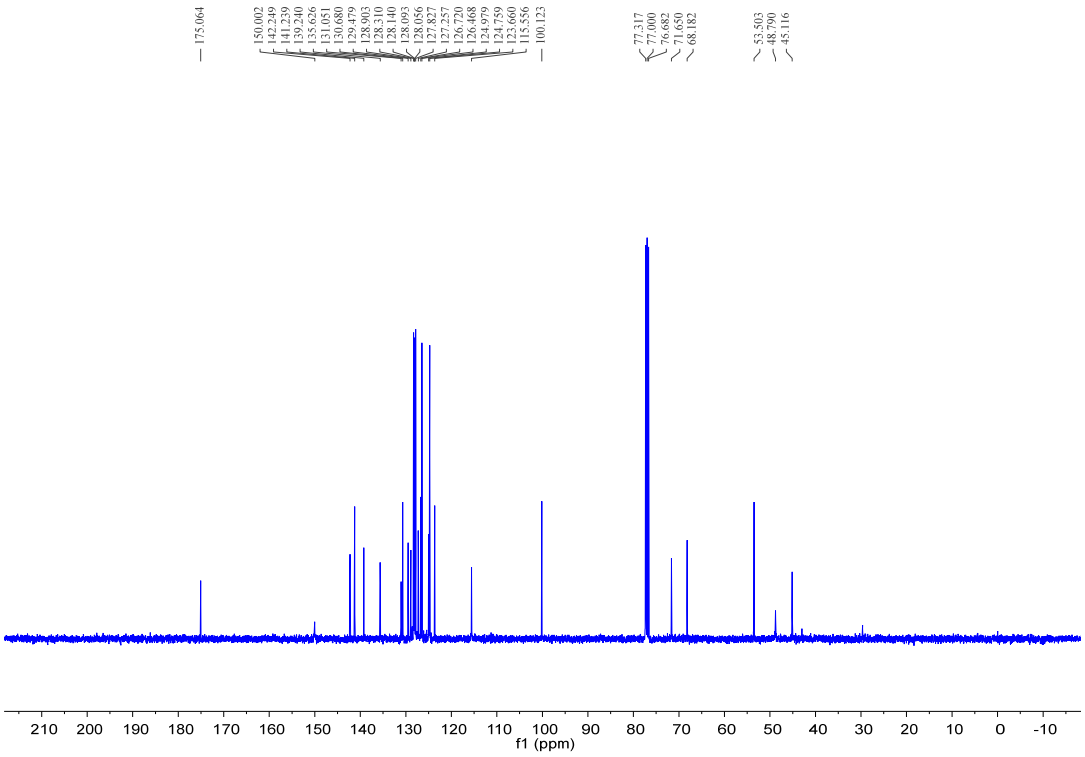


^{1}H and ^{13}C NMR Spectra for Compound 9:

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

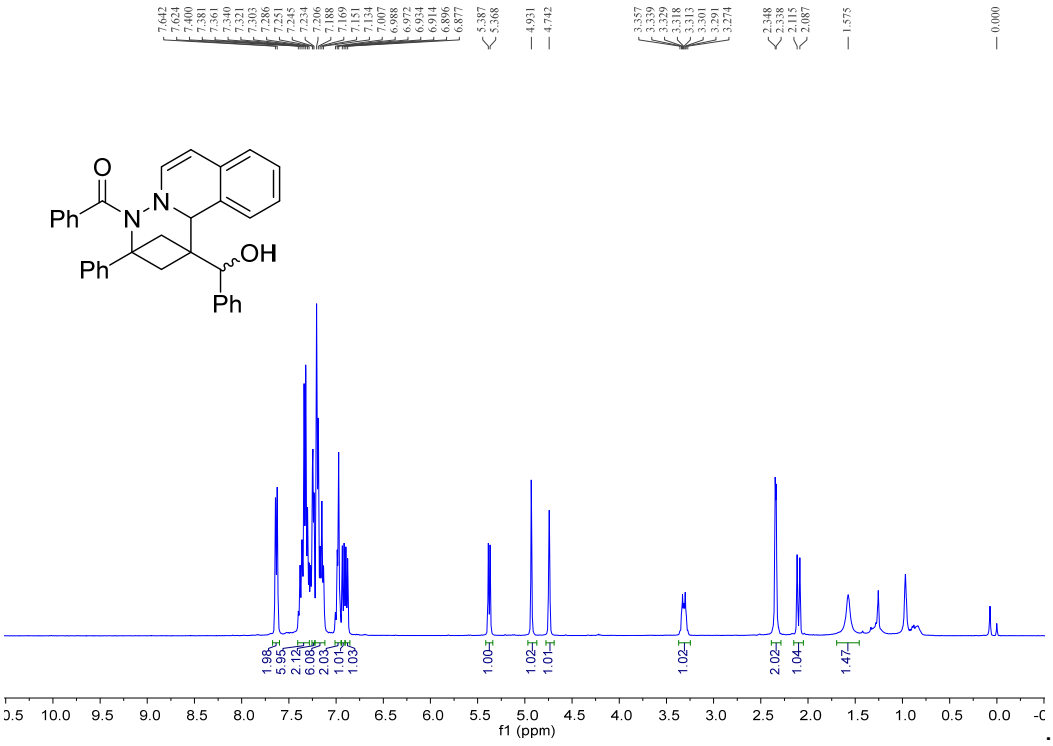


^{13}C NMR (100 MHz, $CDCl_3$)

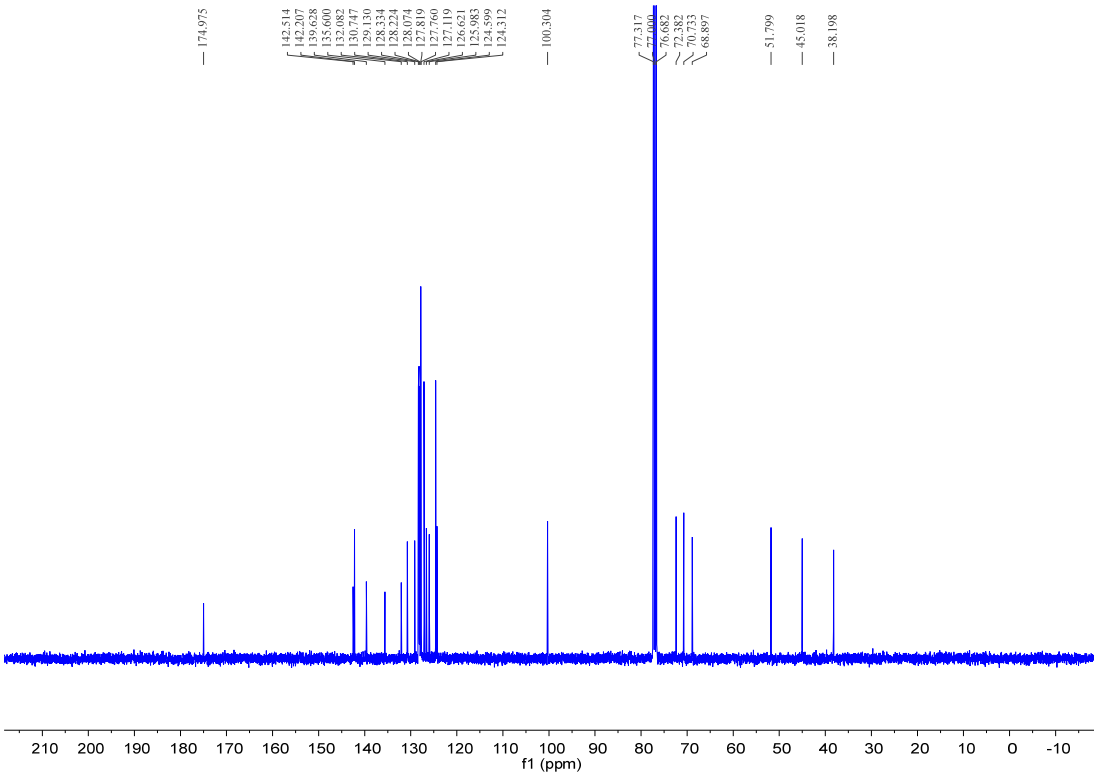


^{1}H and ^{13}C NMR Spectra for Compound 10 (the major isomer):

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

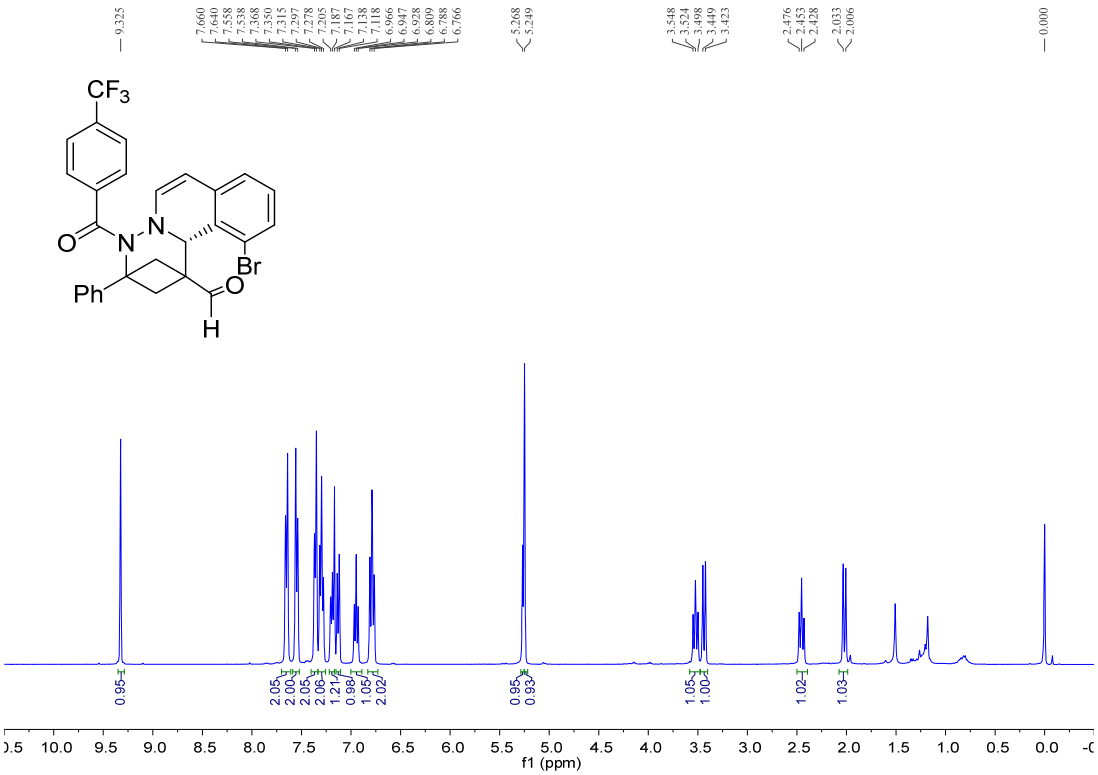


^{13}C NMR (100 MHz, $CDCl_3$)

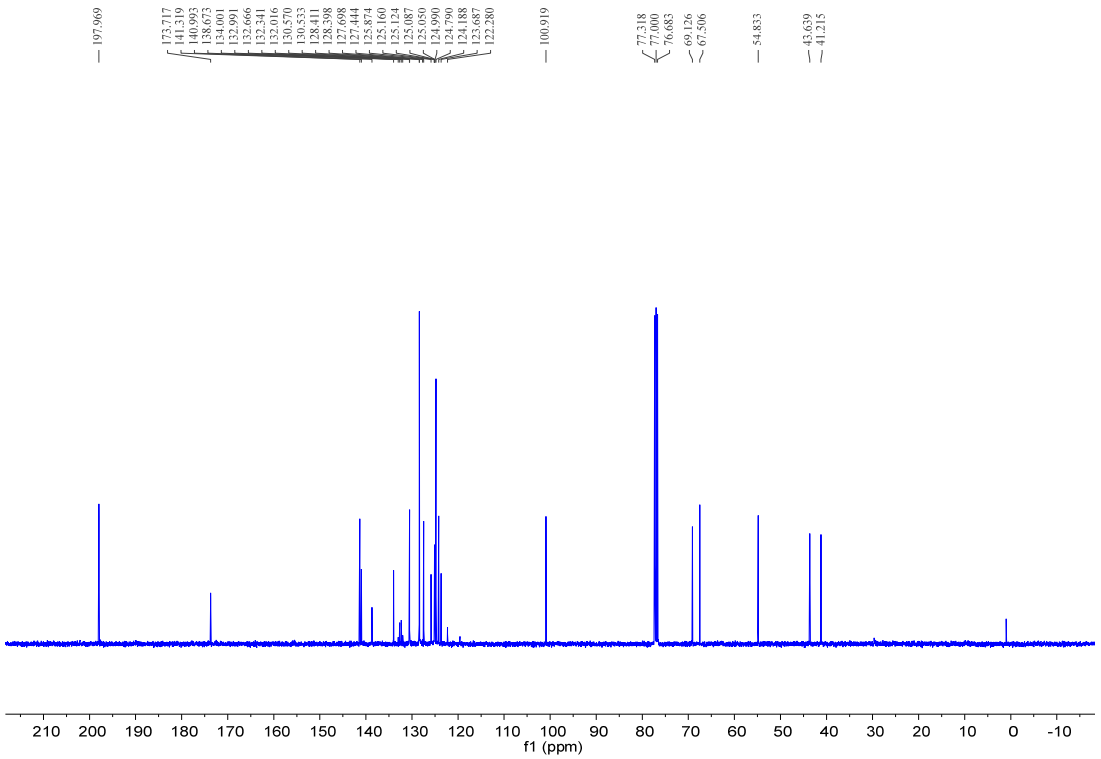


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 11:

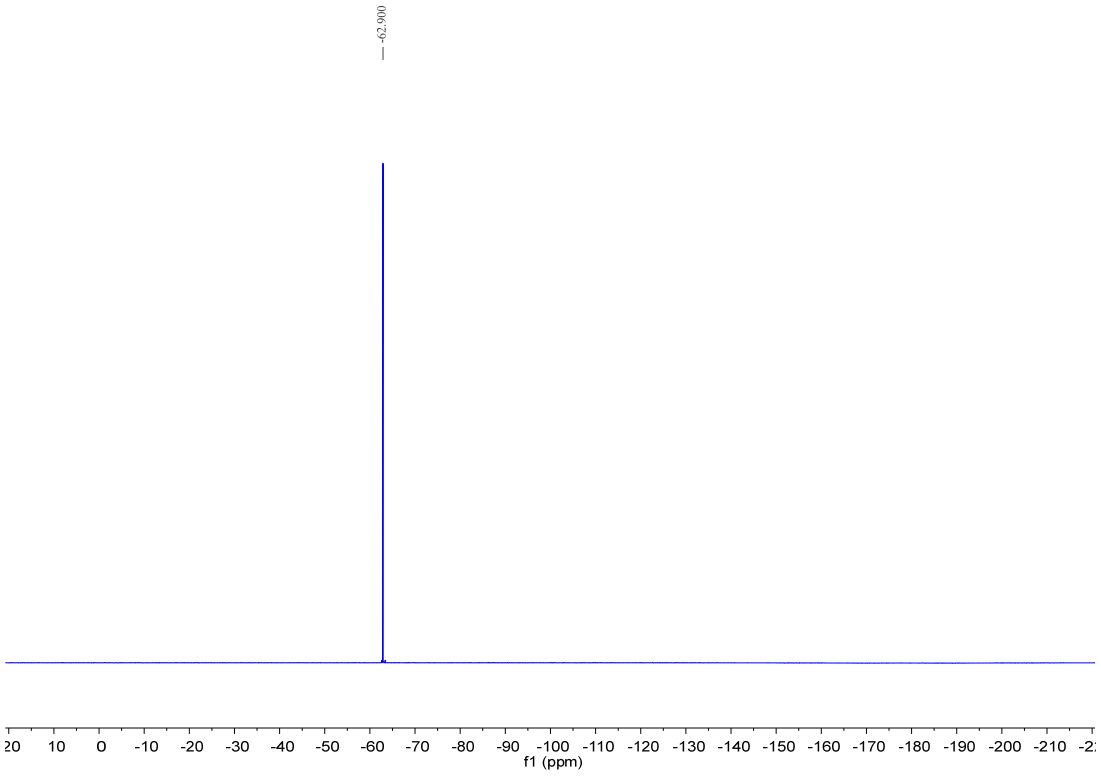
^{1}H NMR (400 MHz, $CDCl_3$)



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

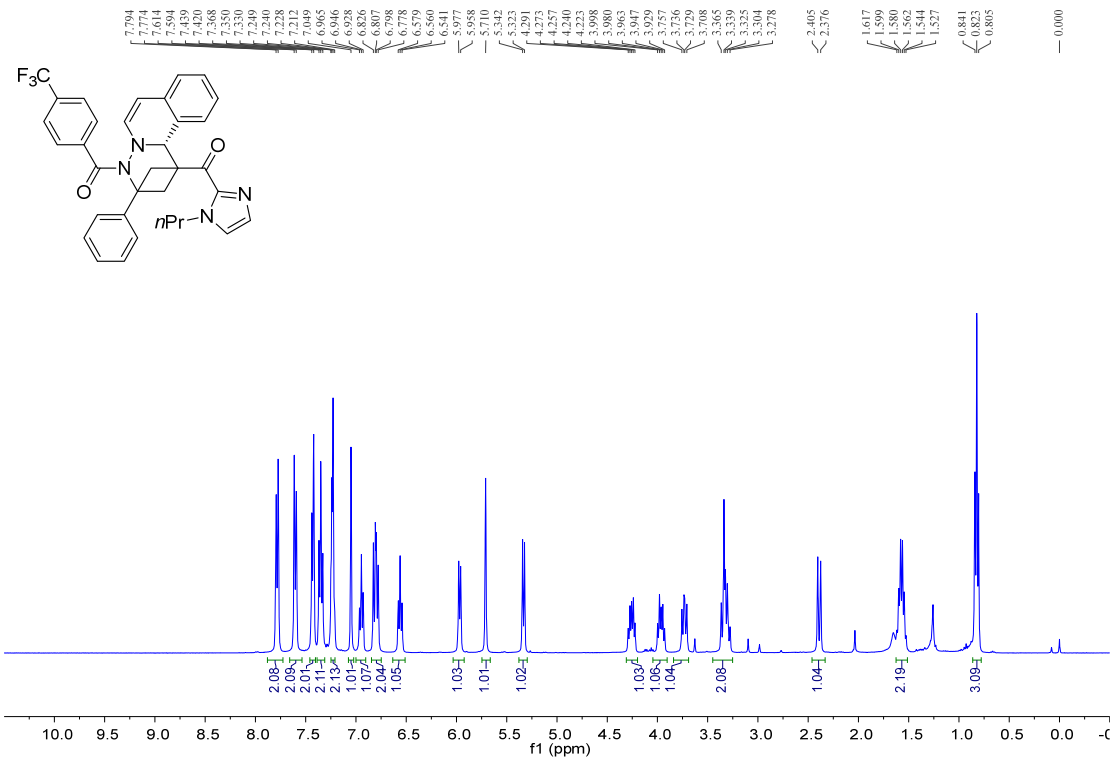


^{19}F NMR (376 MHz, $CDCl_3$)

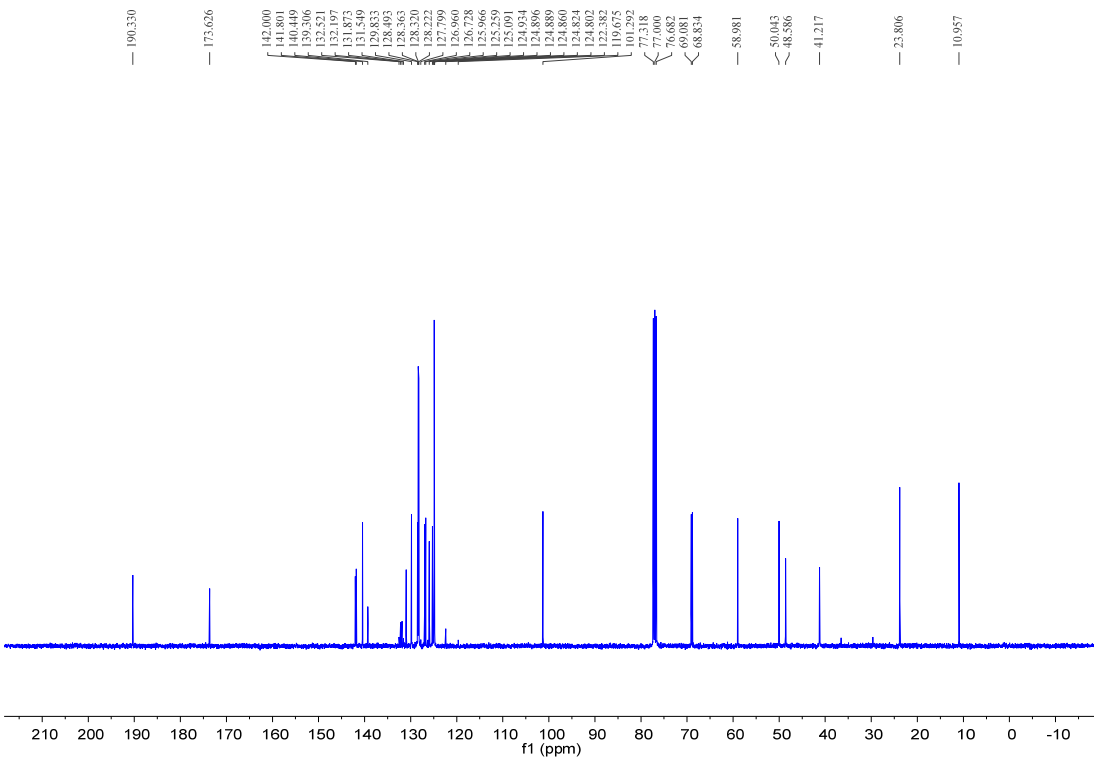


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3aad:

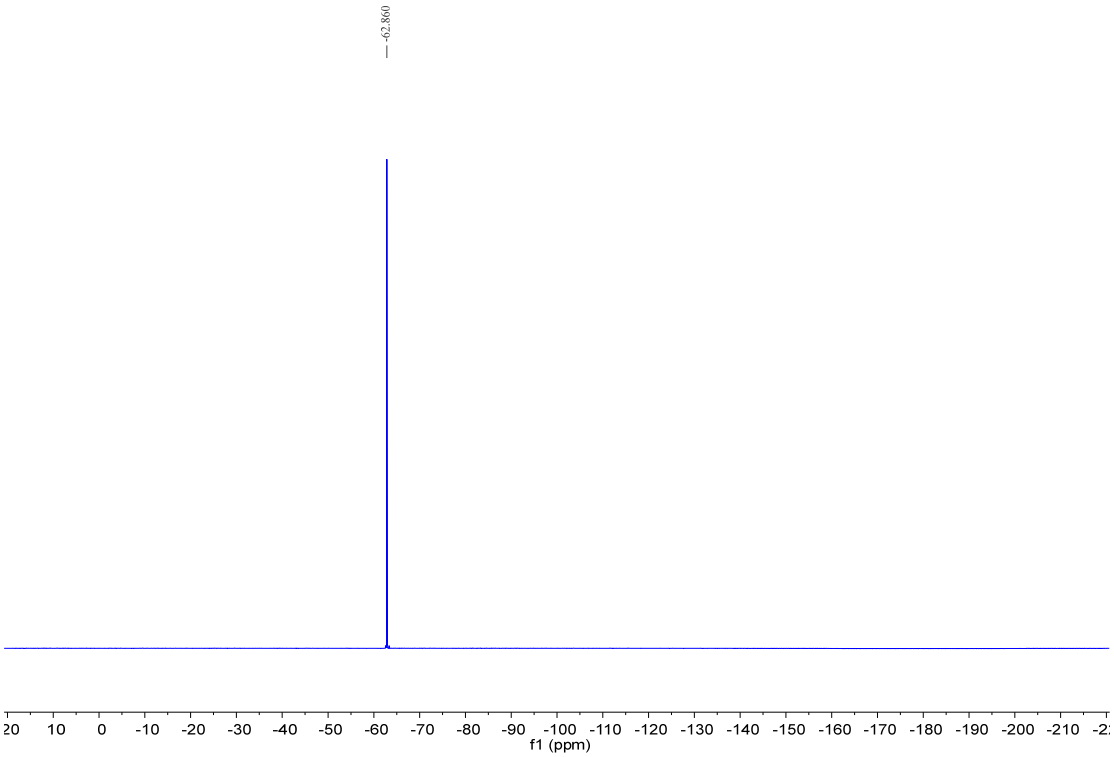
^{1}H NMR (400 MHz, $CDCl_3$)



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

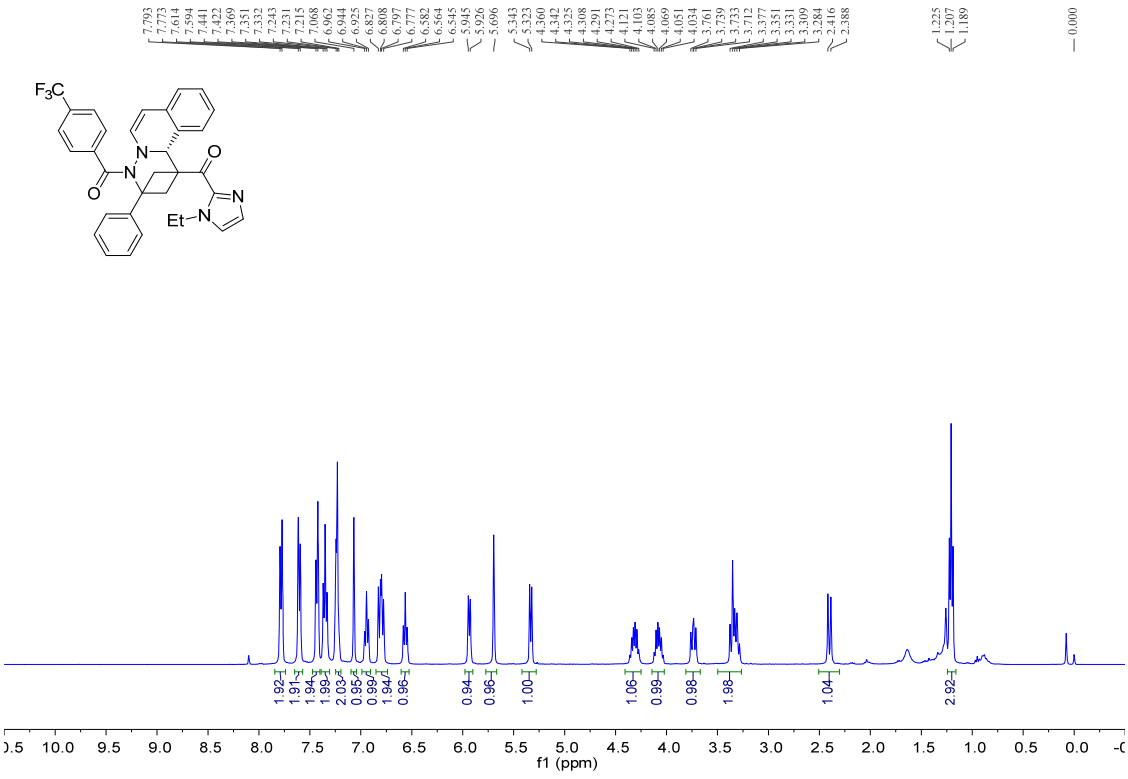


^{19}F NMR (376 MHz, $CDCl_3$)

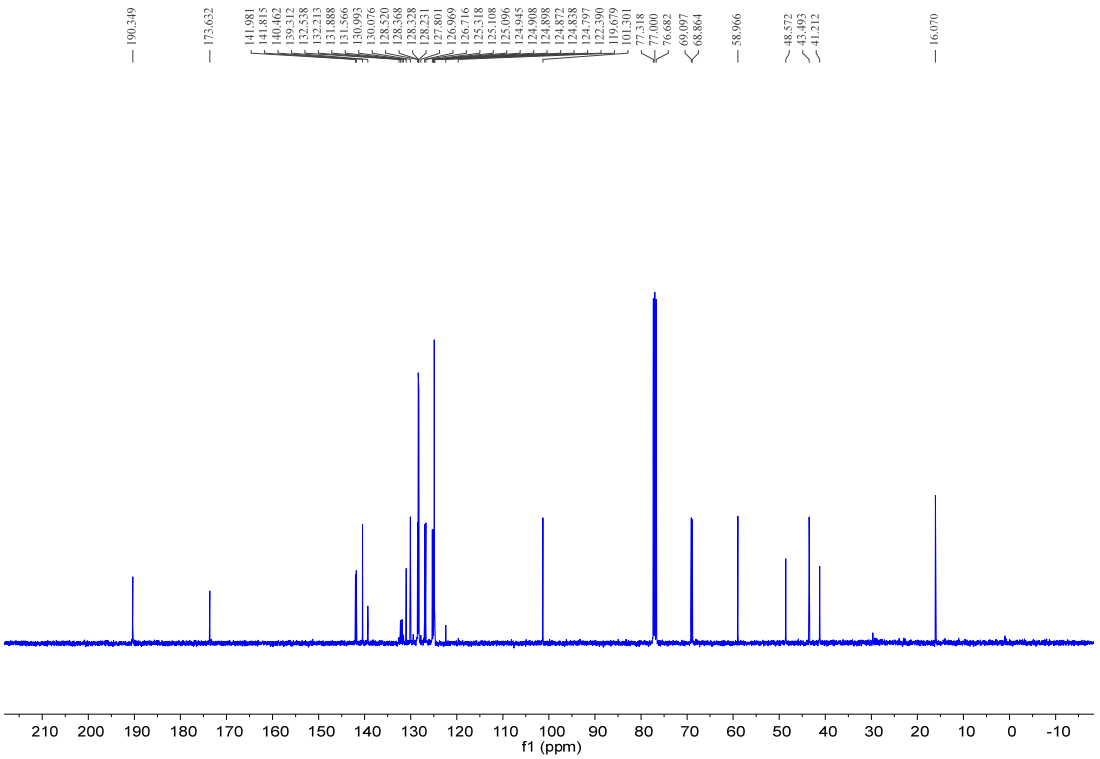


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3ccd:

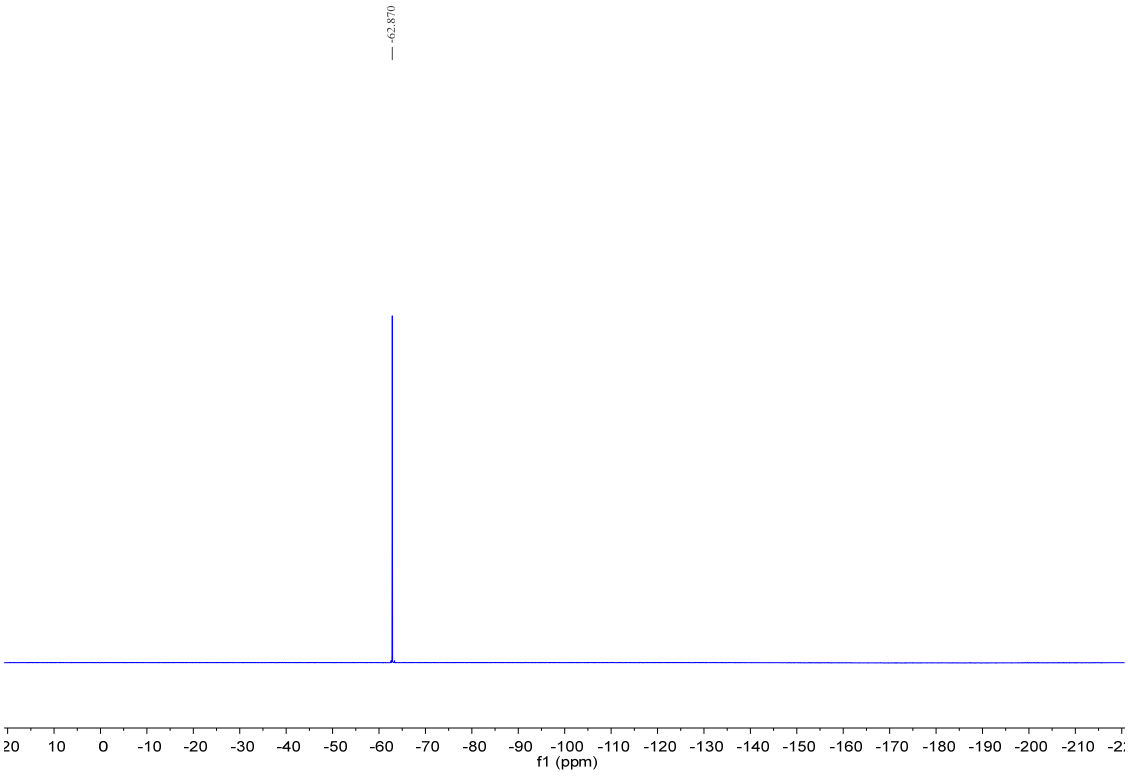
^{1}H NMR (400 MHz, $CDCl_3$)



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

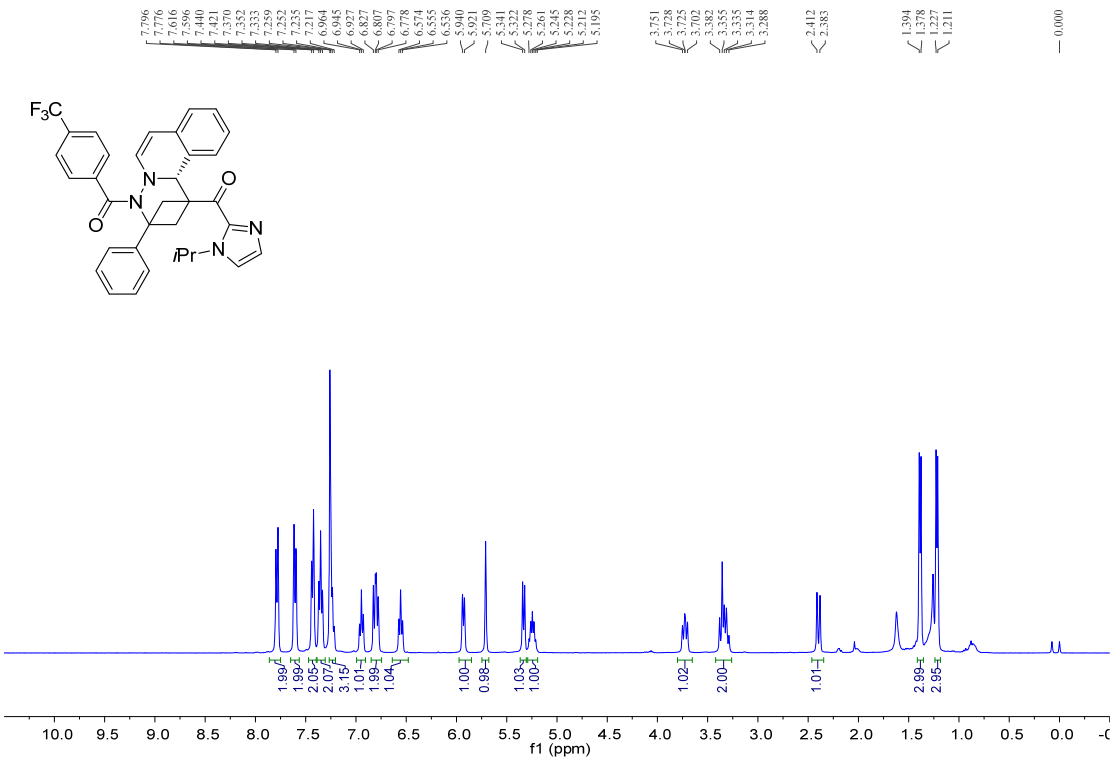


^{19}F NMR (376 MHz, $CDCl_3$)

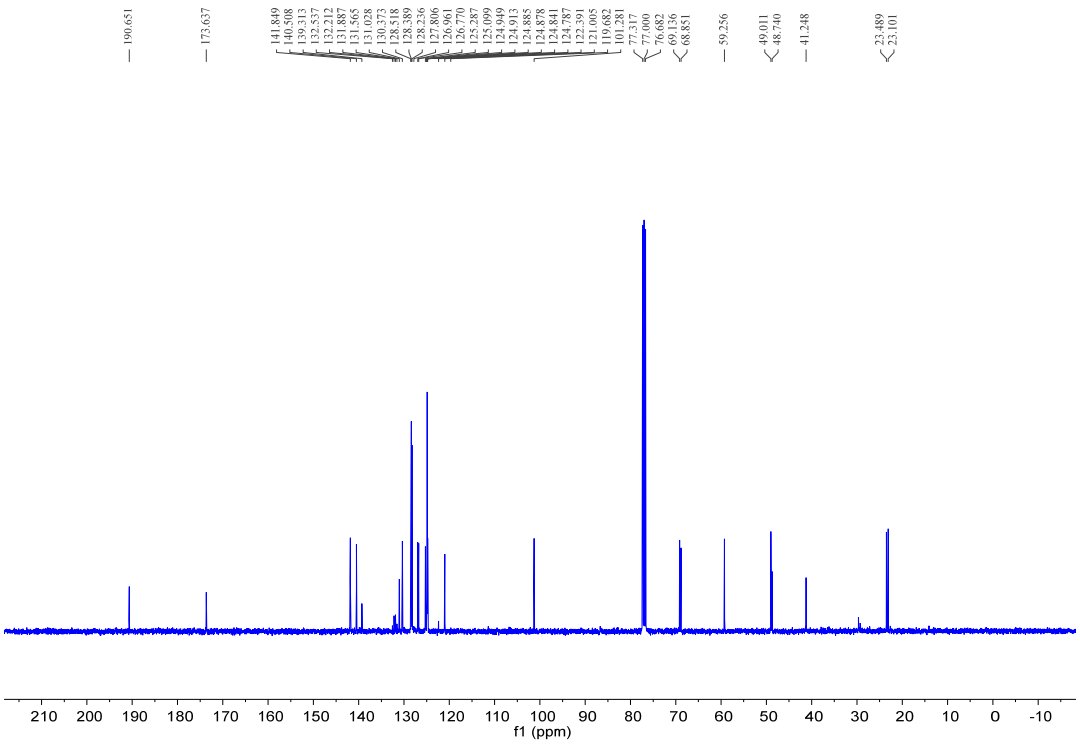


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3ddd:

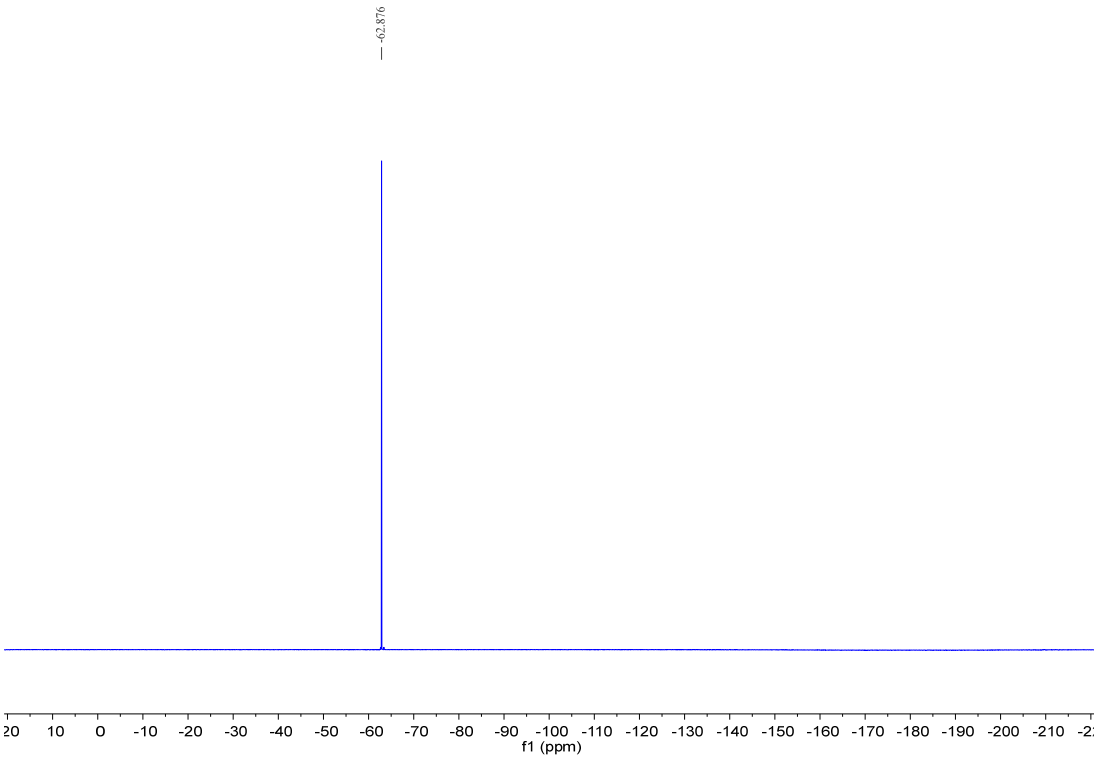
^{1}H NMR (400 MHz, $CDCl_3$)



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

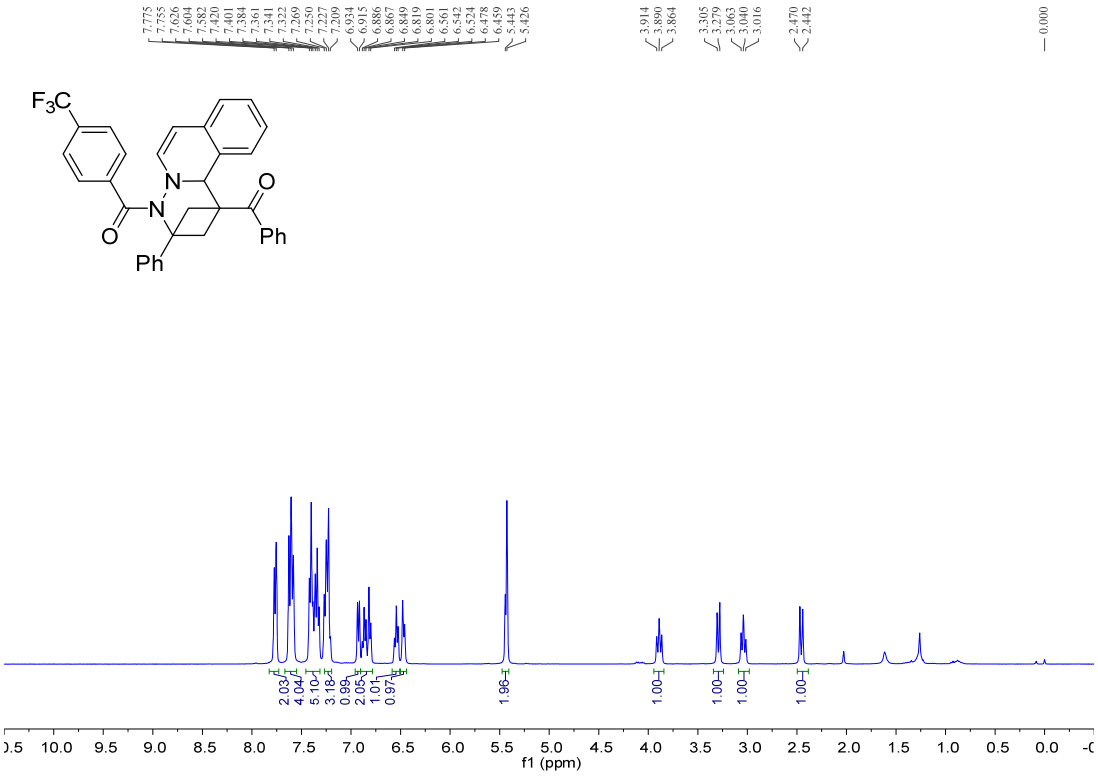


^{19}F NMR (376 MHz, $CDCl_3$)

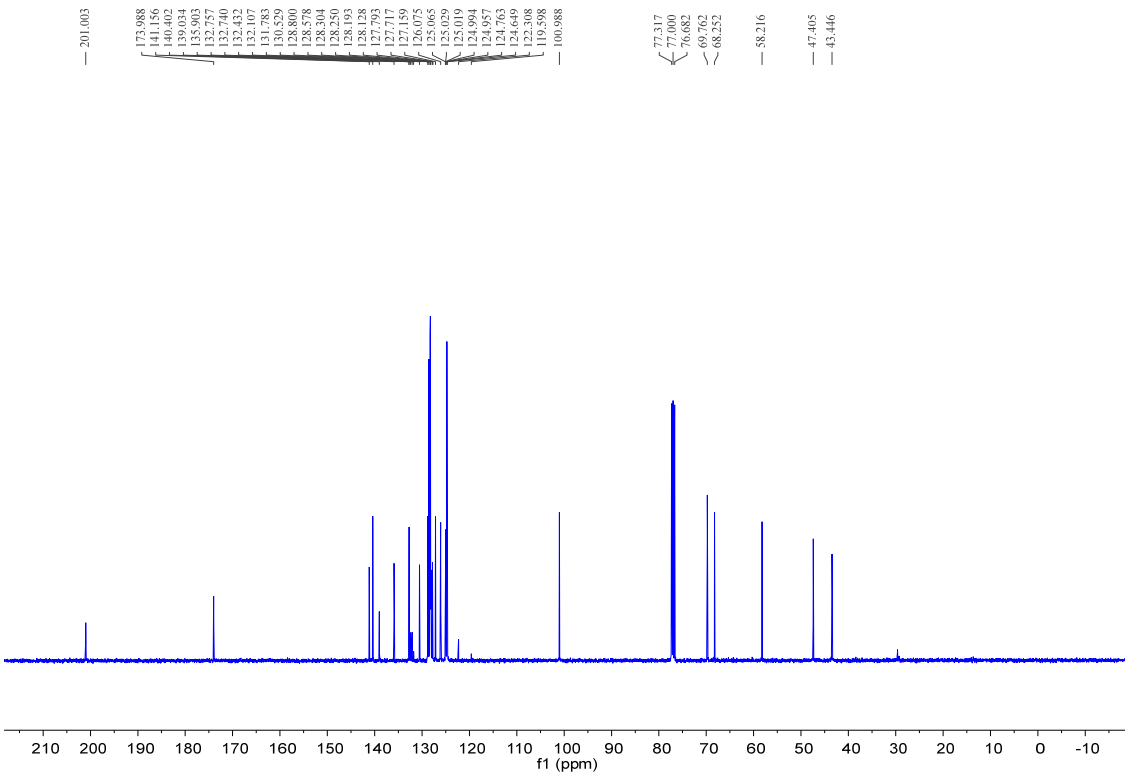


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3gd:

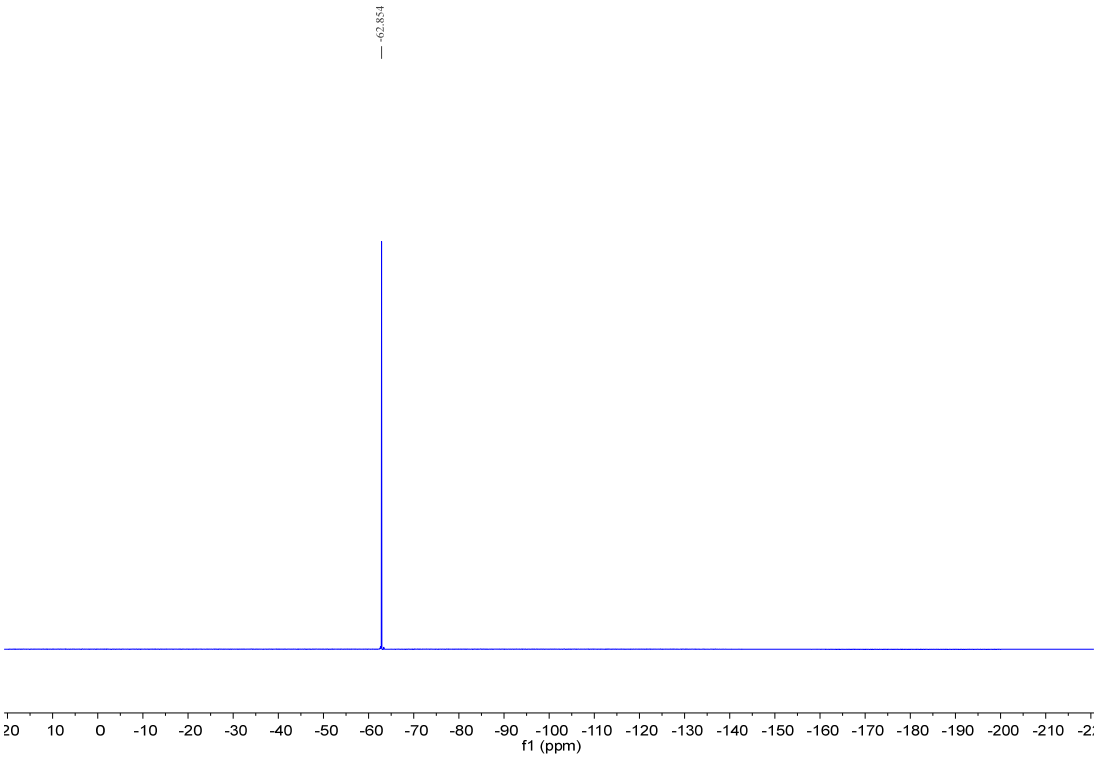
^{1}H NMR (400 MHz, $CDCl_3$)



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

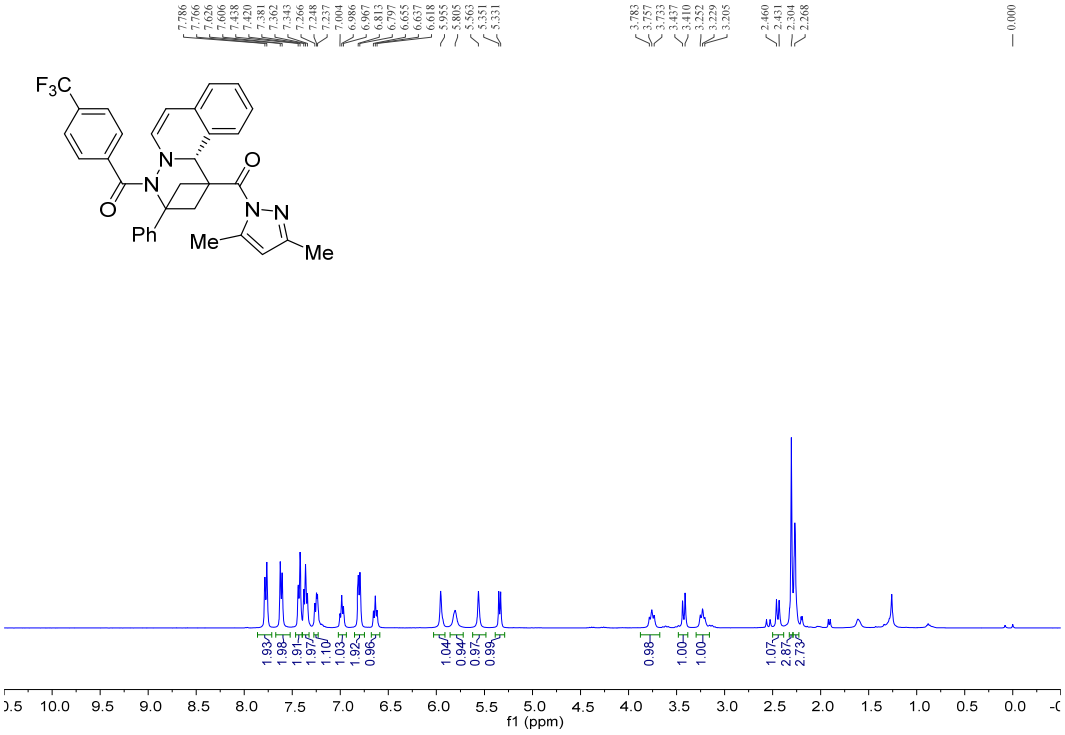


^{19}F NMR (376 MHz, $CDCl_3$)

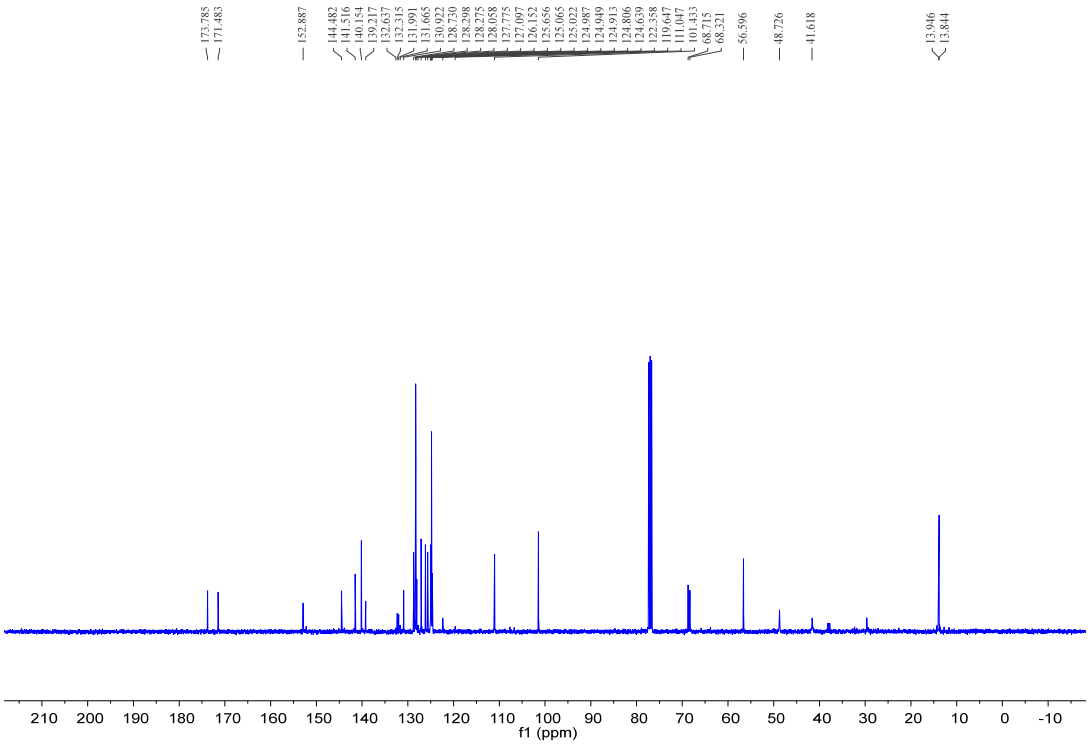


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3ad:

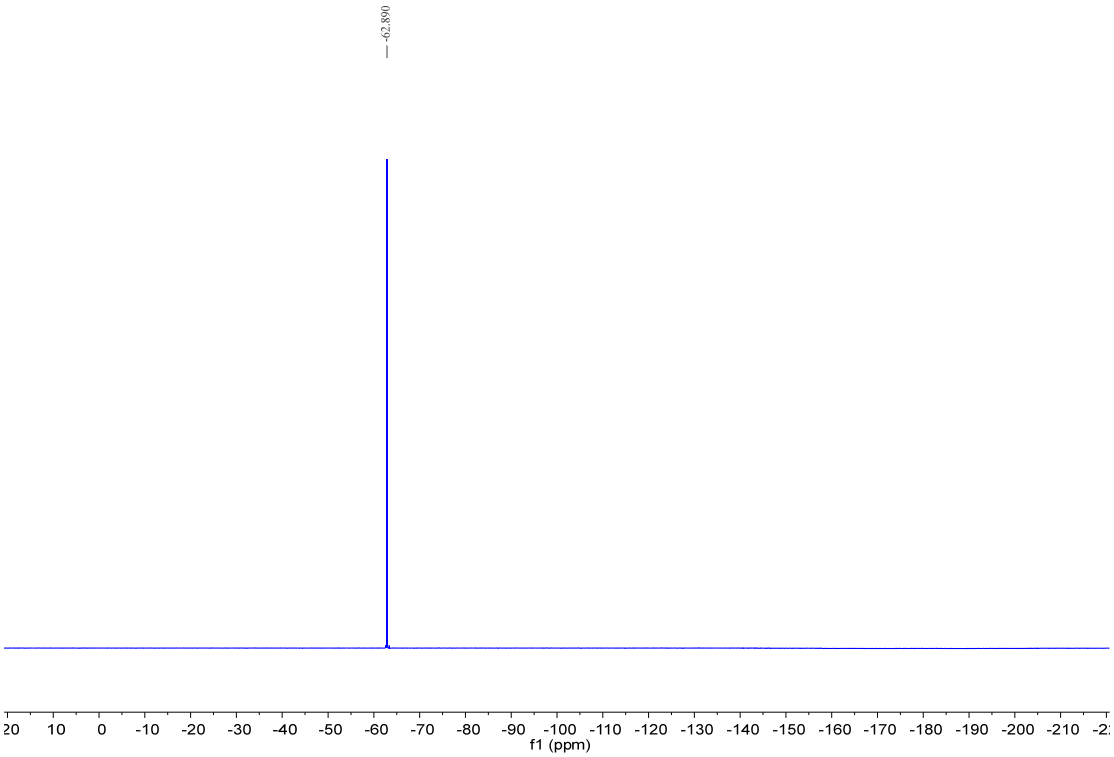
^{1}H NMR (400 MHz, $CDCl_3$)



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

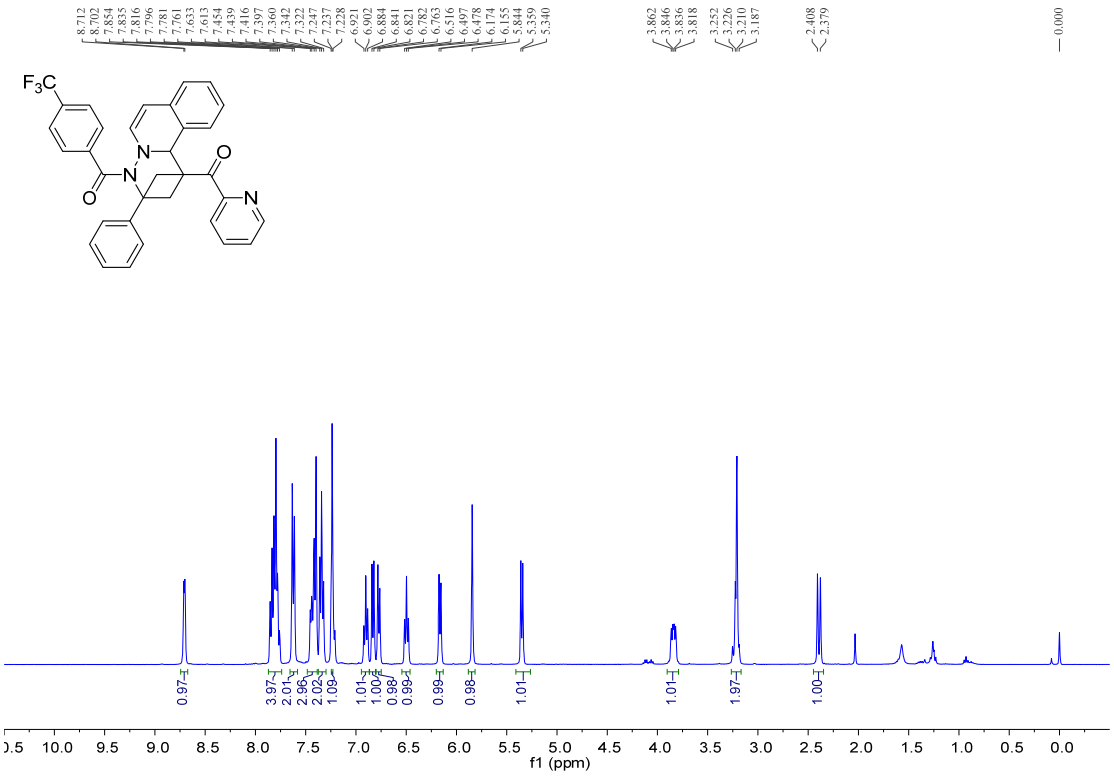


^{19}F NMR (376 MHz, $CDCl_3$)

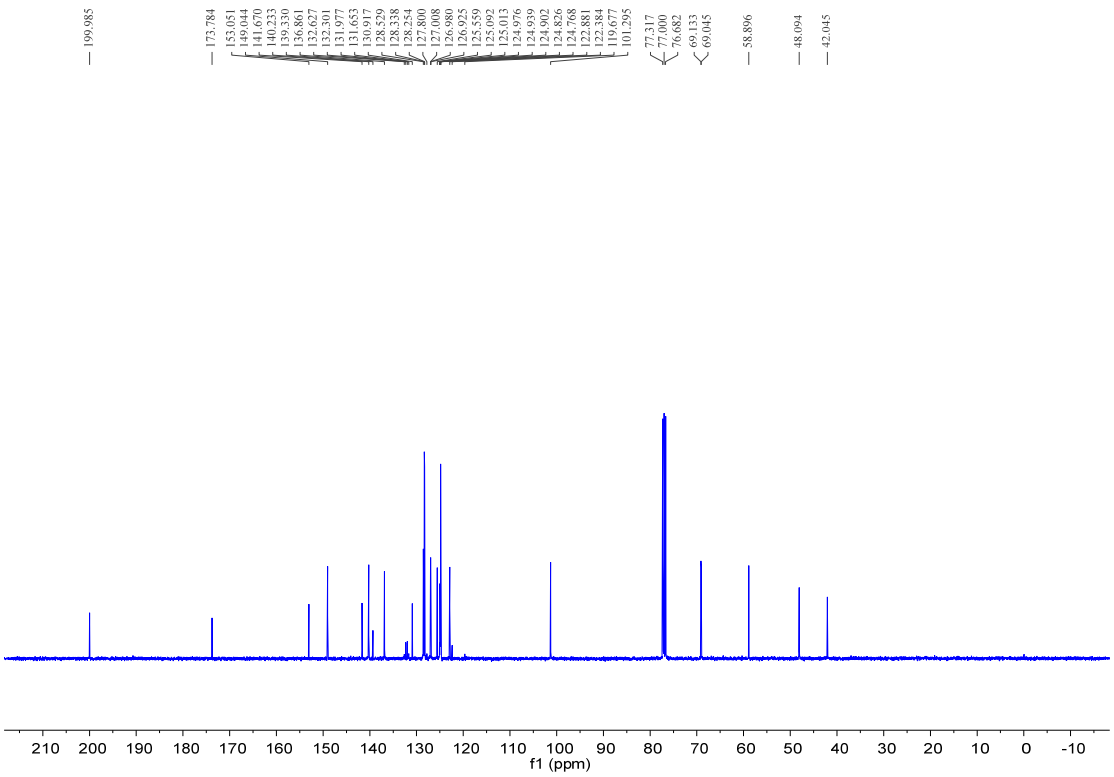


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound 3od:

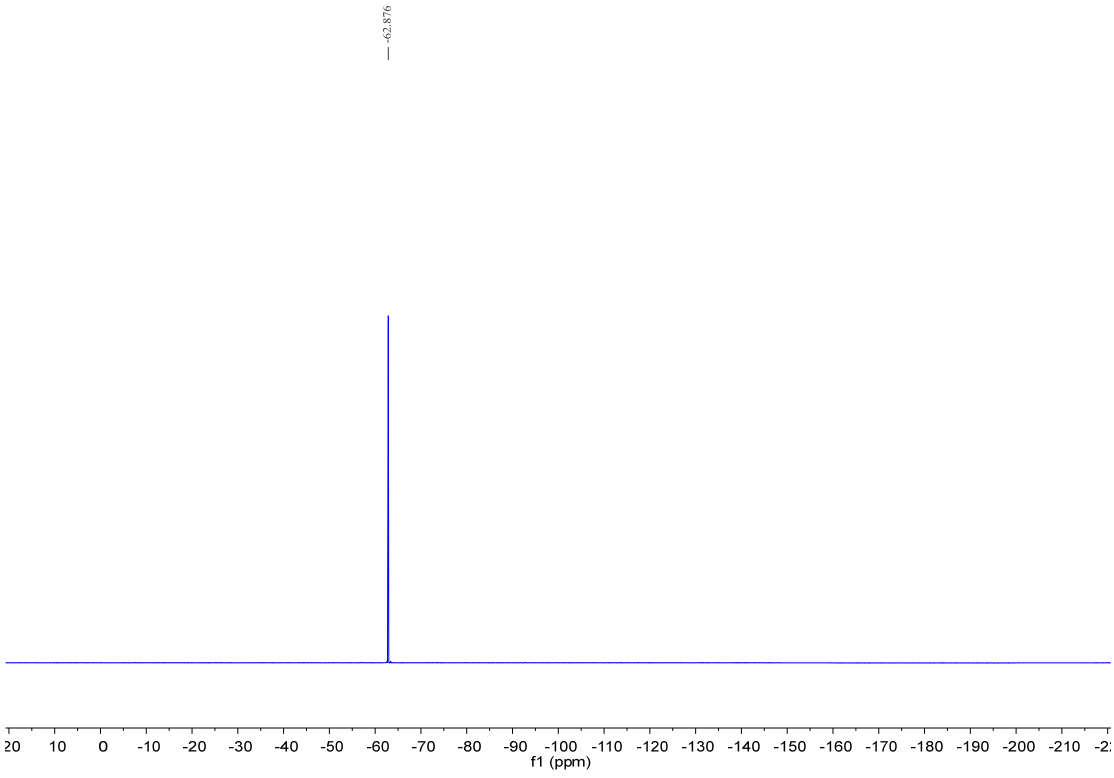
^{1}H NMR (400 MHz, $CDCl_3$)



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

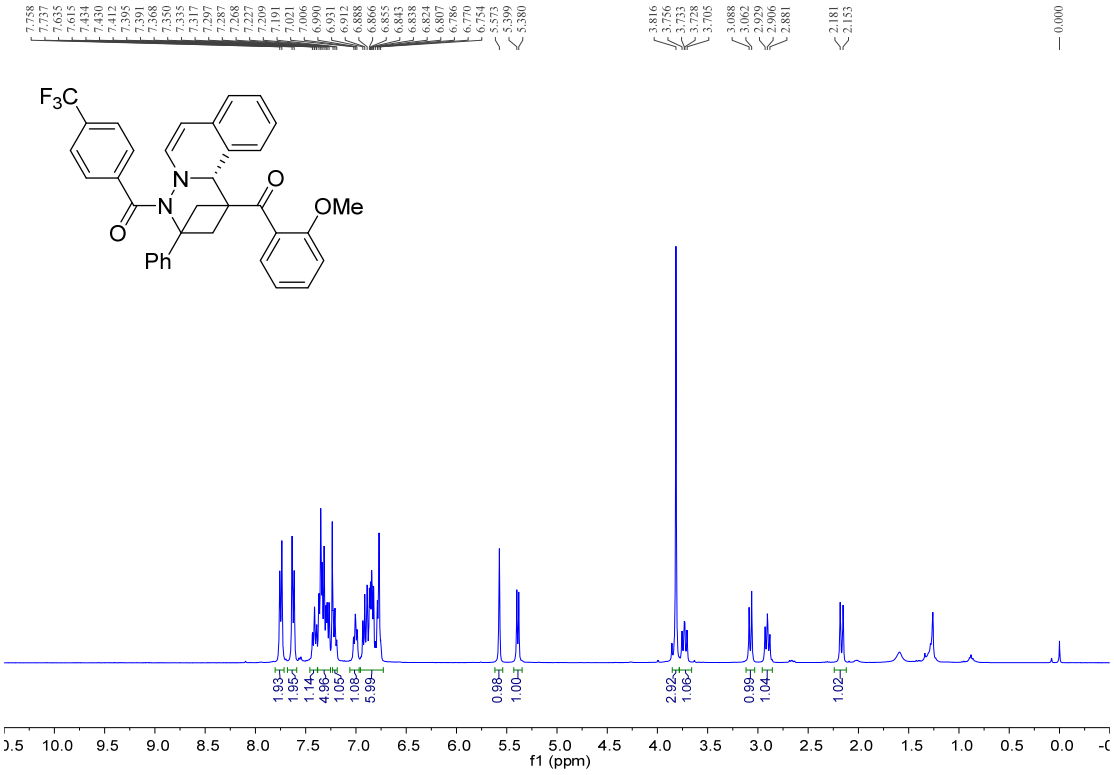


^{19}F NMR (376 MHz, $CDCl_3$)

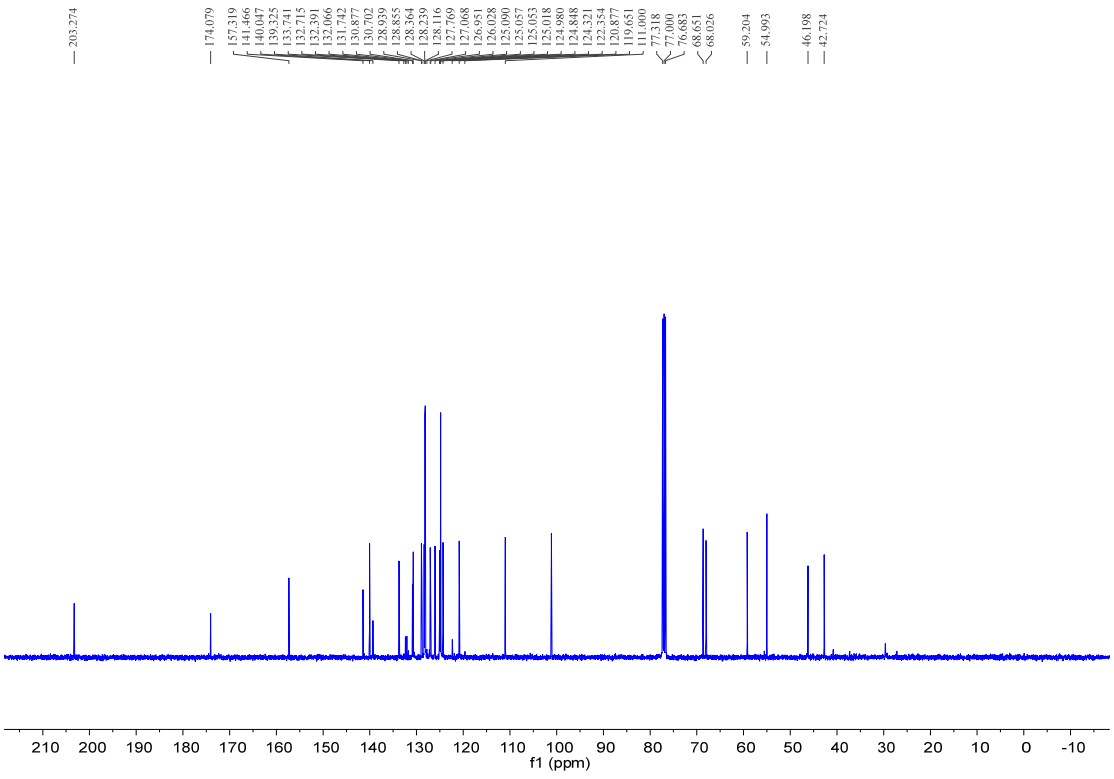


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-3bbd:

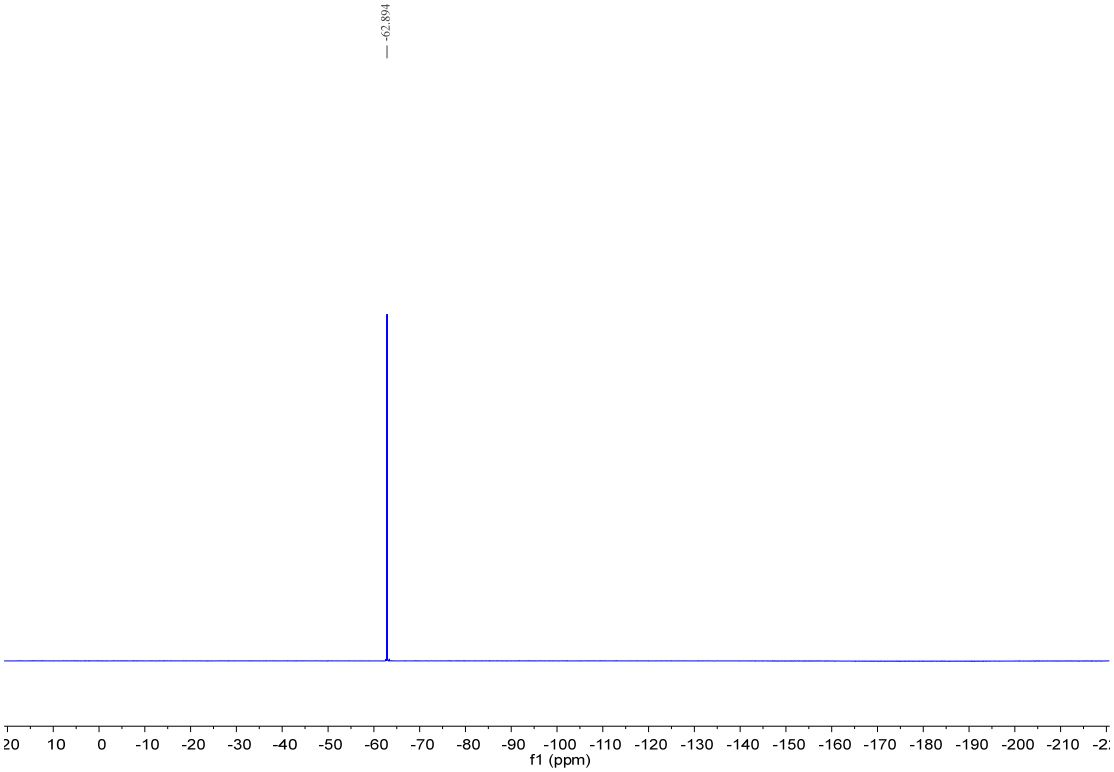
^{1}H NMR (400 MHz, $CDCl_3$)



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

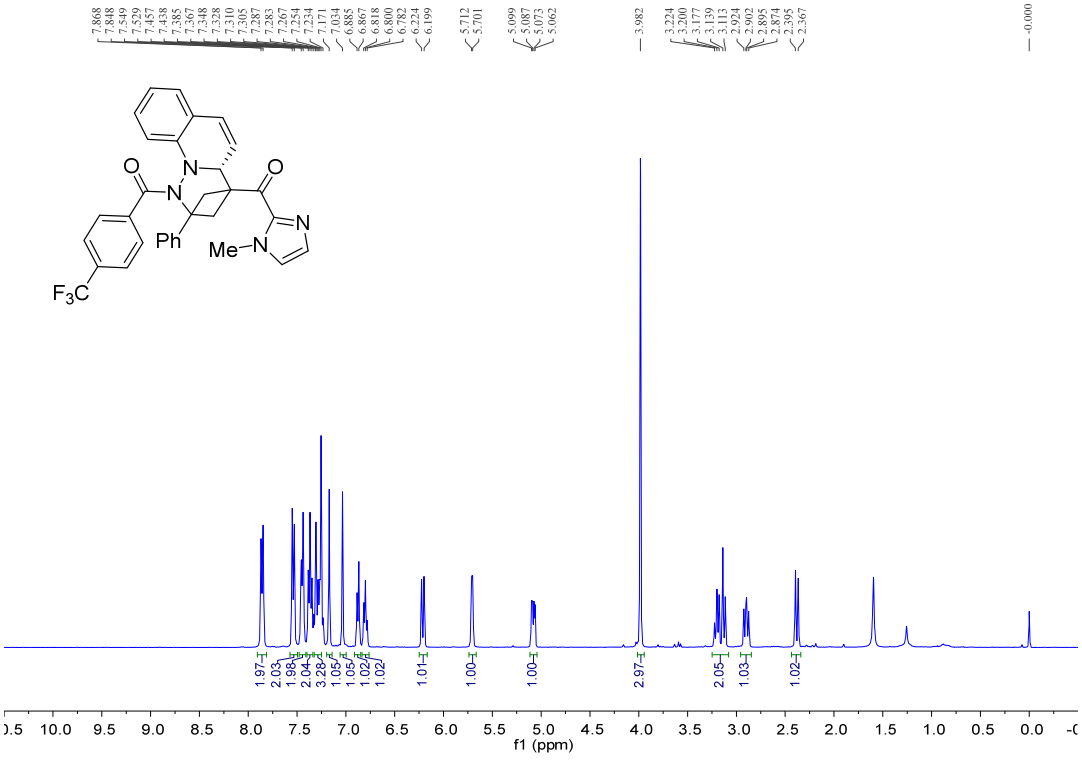


^{19}F NMR (376 MHz, $CDCl_3$)

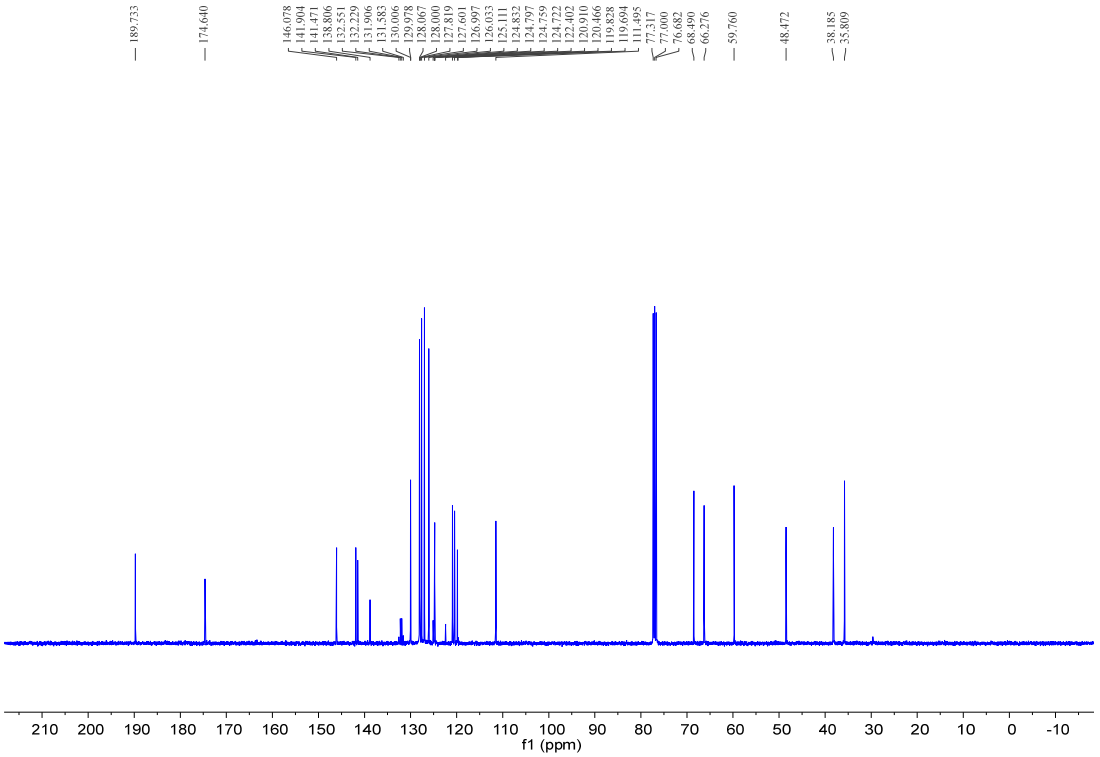


^{1}H ,^{13}C and ^{19}F NMR Spectra for Compound (*R*)-4qaa:

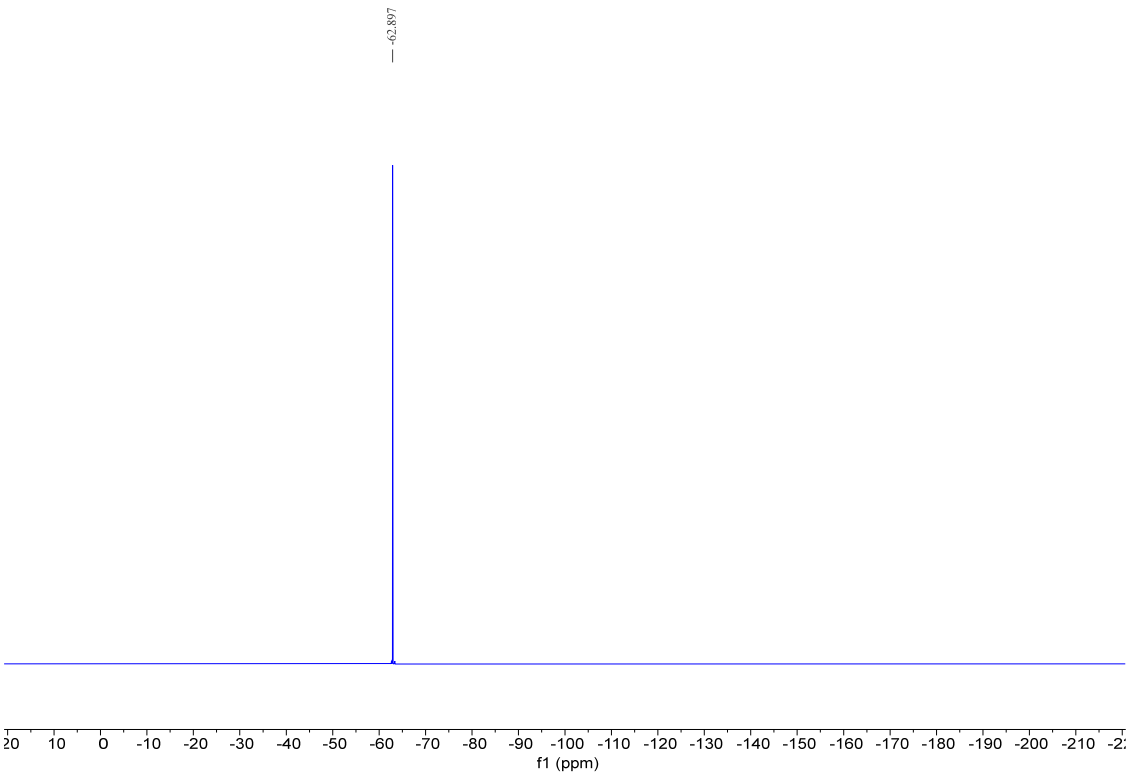
^{1}H NMR (400 MHz, $CDCl_3$)



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

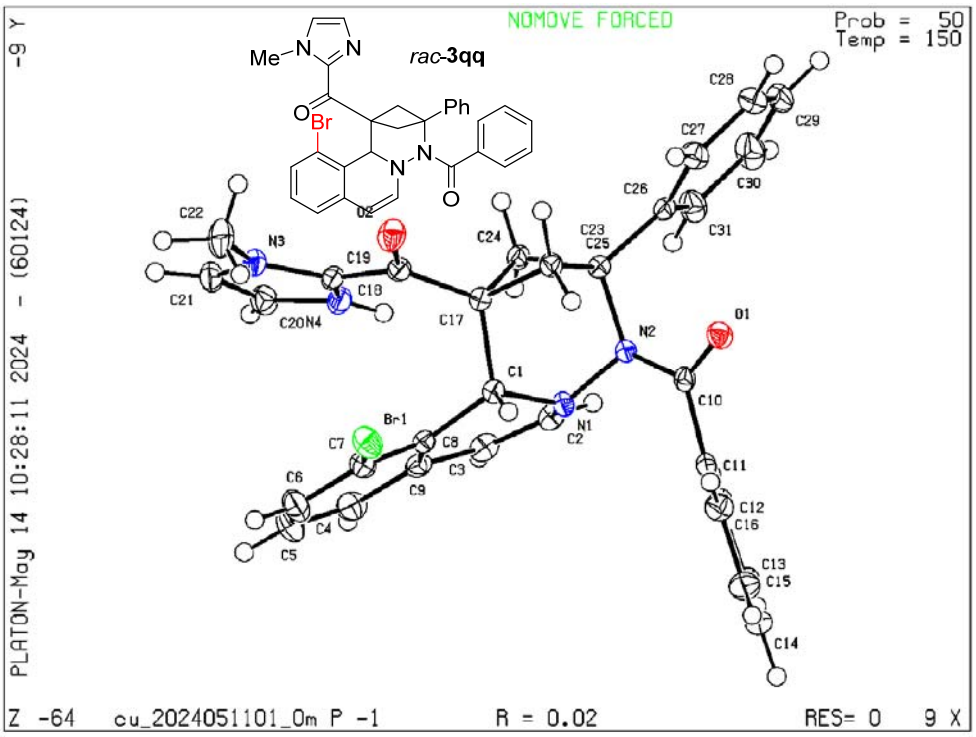


^{19}F NMR (376 MHz, $CDCl_3$)



13 Crystal Structure of 3qq and (*R*)-3qw

The crystals are grown by slow solvent (CH_2Cl_2/Et_2O/*n*-Hexane) evaporation at room temperature. CCDC number of ***rac*-3qq** is 2375376. The thermal ellipsoids are 50% probability level.



Datablock: cu_2024051101_0m

Bond precision: C-C = 0.0025 A Wavelength=1.54178

Cell: a=9.8157(2) b=11.2682(3) c=14.0489(4)
alpha=102.996(1) beta=101.657(1) gamma=114.452(1)
Temperature: 150 K

	Calculated	Reported
Volume	1299.74(6)	1299.74(6)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C31 H26 Br N4 O2	C31 H26 Br N4 O2
Sum formula	C31 H26 Br N4 O2	C31 H25 Br N4 O2
Mr	566.46	565.46
Dx,g cm-3	1.447	1.445
Z	2	2
Mu (mm-1)	2.447	2.447
F000	582.0	580.0
F000'	582.11	
h,k,lmax	11,13,16	11,13,16
Nref	4762	4746
Tmin,Tmax	0.756,0.891	0.073,0.894
Tmin'	0.686	

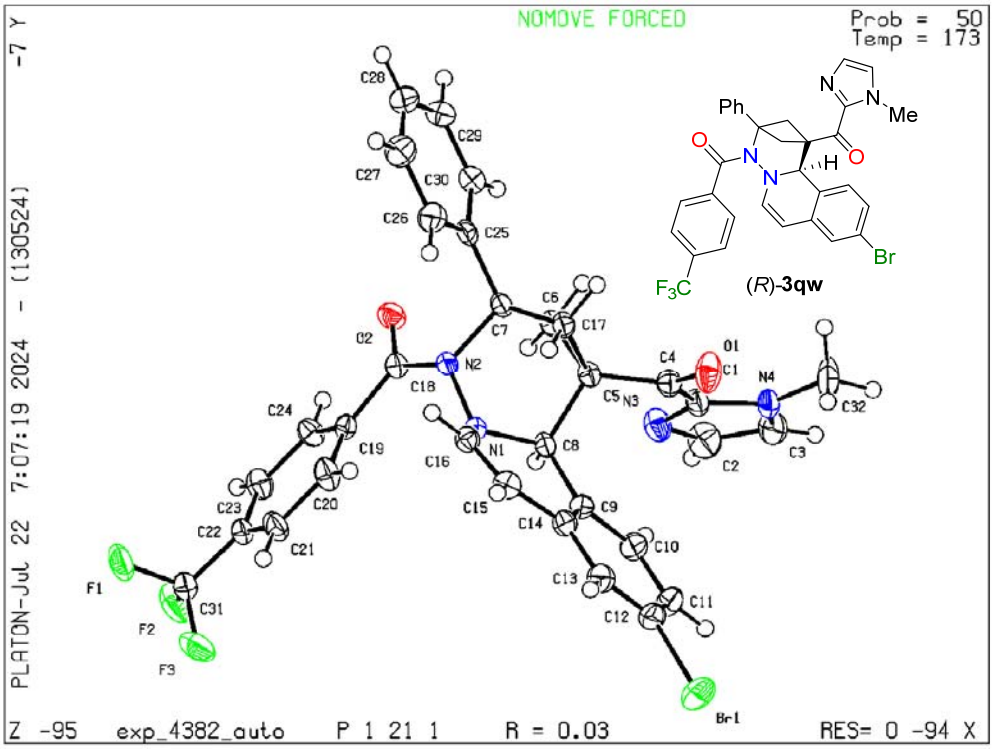
Correction method= # Reported T Limits: Tmin=0.073 Tmax=0.894
AbsCorr = MULTI-SCAN

Data completeness= 0.997 Theta(max)= 68.224

R(reflections)= 0.0242(4670) wR2(reflections)= 0.0626(4746)

S = 1.053 Npar= 344

Note: After one recrystallization (CH_2Cl_2/*n*-Hexane), the *ee* value of (*R*)-**3qw** increased to 96%. CCDC number of (*R*)-**3qw** (96% *ee*) is 2375377.



Datablock: exp_4382_auto

```
Bond precision:   C-C = 0.0049 A          Wavelength=1.54184

Cell:             a=10.8729(2)     b=12.8772(1)      c=10.9786(2)
                  alpha=90         beta=112.161(2)   gamma=90
Temperature:      173 K

                  Calculated                  Reported
Volume            1423.59(4)                  1423.59(4)
Space group       P 21                        P 1 21 1
Hall group        P 2yb                       P 2yb
Moiety formula    C32 H24 Br F3 N4 O2         C32 H24 Br F3 N4 O2
Sum formula       C32 H24 Br F3 N4 O2         C32 H24 Br F3 N4 O2
Mr                633.45                      633.46
Dx,g cm-3         1.478                       1.478
Z                 2                           2
Mu (mm-1)         2.457                       2.457
F000              644.0                       644.0
F000'             644.58
h,k,lmax          12,15,13                    12,15,13
Nref              5077[ 2662]                 5058
Tmin,Tmax         0.488,0.582                 0.539,1.000
Tmin'             0.434

Correction method= # Reported T Limits: Tmin=0.539 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.90/1.00        Theta(max)= 67.069

R(reflections)= 0.0322( 4895)                wR2(reflections)=
                                             0.0842( 5058)
S = 1.088                  Npar= 380
```

The detailed crystal data and structure refinement for (*R*)-3qw are presented below (the Flack parameter is -0.032(8)

Identification code	exp_4382_auto
Empirical formula	$C_{32}H_{24}BrF_3N_4O_2$
Formula weight	633.46
Temperature/K	172.99(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	10.8729(2)
b/Å	12.87720(10)
c/Å	10.9786(2)
α/°	90
β/°	112.161(2)
γ/°	90
Volume/Å^3	1423.59(4)
Z	2
ρ_{calc}g/cm^3	1.478
μ/mm^{-1}	2.457
F(000)	644.0
Crystal size/mm^3	0.32 × 0.26 × 0.22
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.696 to 134.138
Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 15, -13 ≤ l ≤ 13
Reflections collected	32191
Independent reflections	5058 [R_{int} = 0.0775, R_{sigma} = 0.0378]
Data/restraints/parameters	5058/1/380
Goodness-of-fit on F^2	1.088
Final R indexes [I>=2σ (I)]	R_1 = 0.0322, wR_2 = 0.0822
Final R indexes [all data]	R_1 = 0.0334, wR_2 = 0.0842
Largest diff. peak/hole / e Å^{-3}	0.21/-0.54
Flack parameter	-0.032(8)

14 References

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