Supporting information for

An efficient direct electrolysis method for the synthesis of 1,1,1,3,3,3-hexafluoroisopropyxy substituted imidazo[1,2-*a*]pyridines

Yanyan Kong,*[a,b] Ming Gong,[b] Xuemei Xu,[a] Yangjie Wu[b] and Xingmao Jiang*[a]

[a]Key Laboratory of Green Chemical Process of Ministry of Education, Hubei Key Laboratory of Novel Chemical Reactor and Green Chemical Technology, School of Chemical Engineering & Pharmacy, Wuhan Institute of Technology, Wuhan 430073, P.R. China. E-mail: kongyanyan@wit.edu.cn, jxm@wit.edu.cn

[b]Henan Key Laboratory of Chemical Biology and Organic Chemistry, Key Laboratory of Applied Chemistry of Henan Universities, College of Chemistry, Zhengzhou University, Zhengzhou 450052, P.R. China.

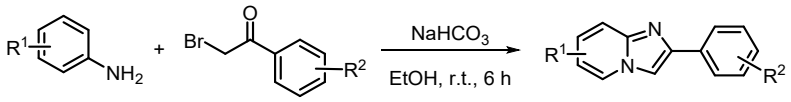
Table of contents

1. General Information

All reagents were used in analytical grades and were obtained from commercial sources and were not degassed. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminum plates with F-254 indicator, visualized by irradiation with UV light. Flash chromatography columns were packed with 200-300 mesh silica gel and silica gel was purchased from Qing Dao Hai Yang Chemical Industry. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer in $CDCl_3$. All chemical shifts (δ) were reported in ppm and coupling constants (J) in Hz relative to tetramethylsilane as internal standard (δ = 0 ppm). For the ^{19}F spectra, α-trifluorotoluene served as external standard (δ = -63.9 ppm). High resolution mass spectra (HRMS) were obtained on an Agilent LC-MSD-Trap-XCT spectrometer with micromass MS software using electrospray ionization (ESI). The Cyclic voltammetry (CV) was recorded in CH_3CN by CHI660E. The LCD Digital Hotplate Magnetic Stirrer MS-H-Pro^{+} and Digital Single Channel Adjustable Automatic Electronic Pipette Micropipette dPettee^{+} were purchased from Dragon Laboratory Instruments Limited. Electrolysis was conducted using a IKA Electra 2.0 at constant voltage mode.

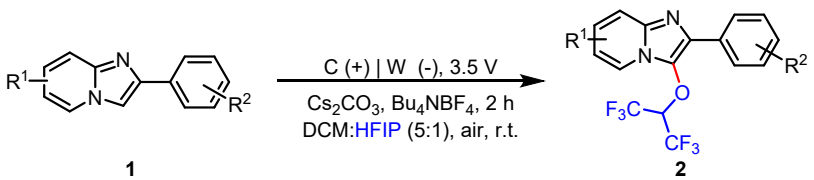
2. Experimental Procedures

General procedure for the synthesis of 2-arylimidazo[1,2-*a*]pyridine[1]



A dried round-bottom flask equipped with a magnetic stirring bar was charged with 2-aminopyridine (1.2 mmol, 1.2 equiv), 2-bromoacetophenone (1.0 mmol, 1.0 equiv) and $NaHCO_3$ (131 mg, 1.56 mmol, 1.56 equiv) under a nitrogen atmosphere. EtOH (0.8 mL) was then added, and the resulting solution was stirred at room temperature for 6 h. After completion of the reaction, the resulting mixture was diluted with water (15 mL) and extract with ether (3 ×20 mL). The combined organic layer was washed with brine (25 mL), dried with anhydrous Na_2SO4, The product was purified by silica gel column with petroleum ether/EtOAc as the eluent.

General procedure for the electrochemical cross-dehydrogenative coupling of 1,1,1,3,3,3-hexafluoroisopropyxy and imidazo[1,2-*a*]pyridine

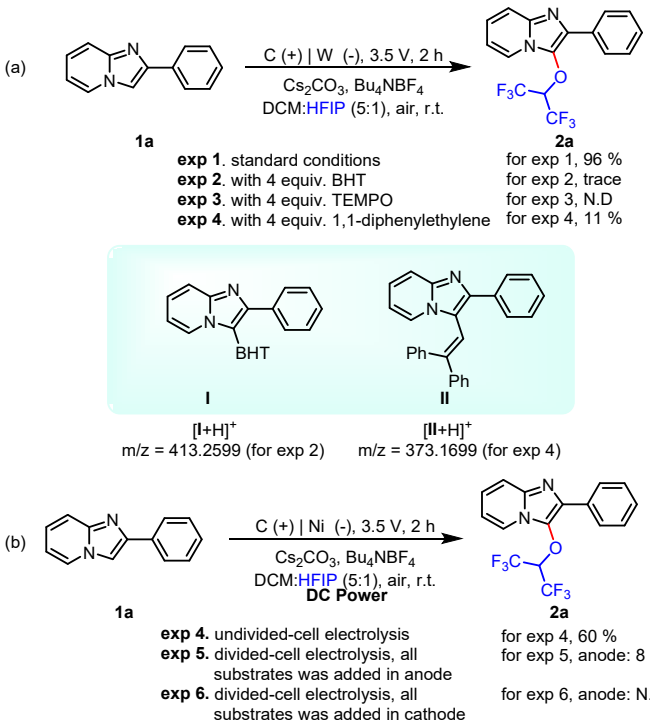


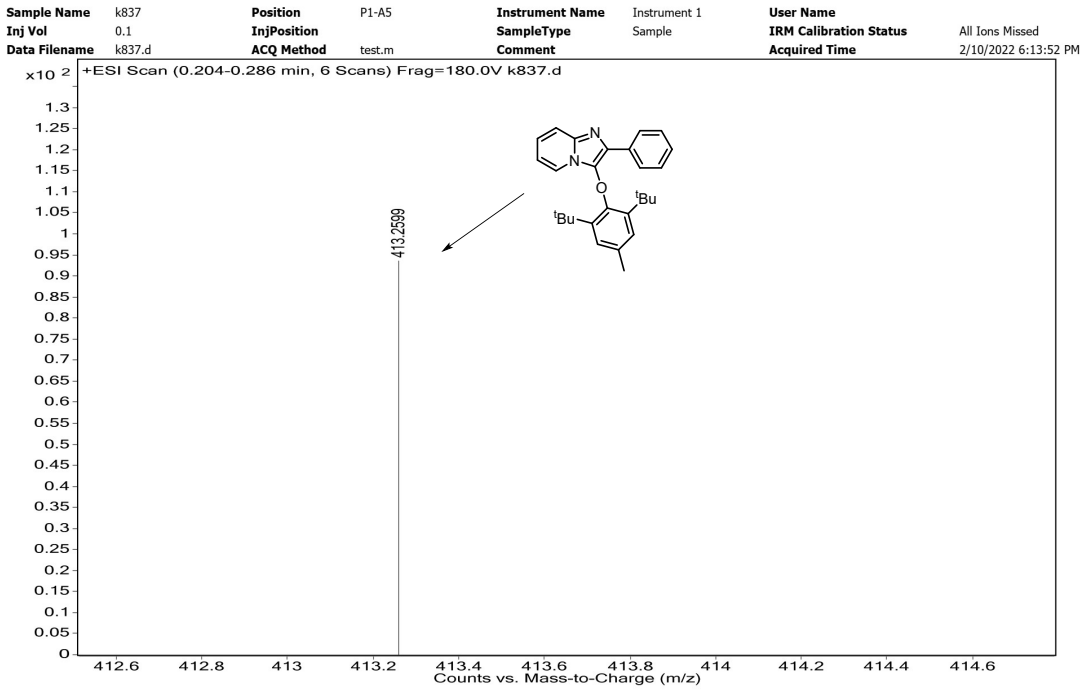
1 2

The Electrasyn vial cap was connected to the Electrasyn 2.0 and the reaction mixture was electrolyzed under a constant voltage of 3.5 V. Graphite plate was used as the anode, and

solvents were not degassed. After the reaction, the ElectraSyn vial cap was removed, and electrodes were rinsed with DCM (3 mL), which was combined with crude mixture. The product was purified by column chromatography on silica gel (ethylacetate/petroleum ether = 1:5 or 1:20, v/v) to give the desired product. Finally, the gram-scale synthesis was carried out by applying DC power and graphite rod was used as the anode.

3. Contorl Experiments





4. Cyclic Voltammetry Experiments

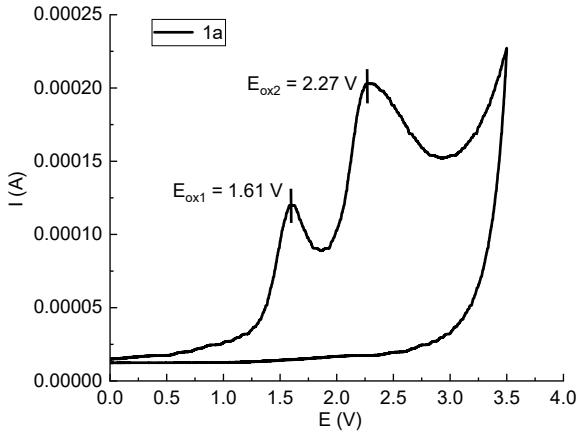


Figure S1. Cyclic voltammetry experiments of **1a** in DCM:HFIP (5:1) with 0.1 M Bu_4NBF_4, the scan rate is 0.1 V/s. The working electrode was a glassy carbon electrode, the counter electrode was a platinum wire, and the reference electrode was a Ag/AgCl electrode.

The electrochemical reaction could not proceed without current. When chemical oxidants (such as TBHP and K_2S2O_8) were applied instead of current, the substrate **1a** could not be converted to any other compounds. As for bromine-derivatives 6-bromo-2-phenylimidazo[1,2-*a*]pyridine (**1o**) and 8-bromo-2-phenylimidazo[1,2-*a*]pyridine (**1v**), we could not observe any evidence of dehalogenation. CV plots were shown as below. Their oxidant potentials were higher than **1a**.

And then, the electrochemical reactions were conducted at 4.5V, but the higher cell potential did not increase the yields of **2o** and **2v**. Therefore, we speculate that the electrochemical properties of bromine-derivatives might be unreactive.

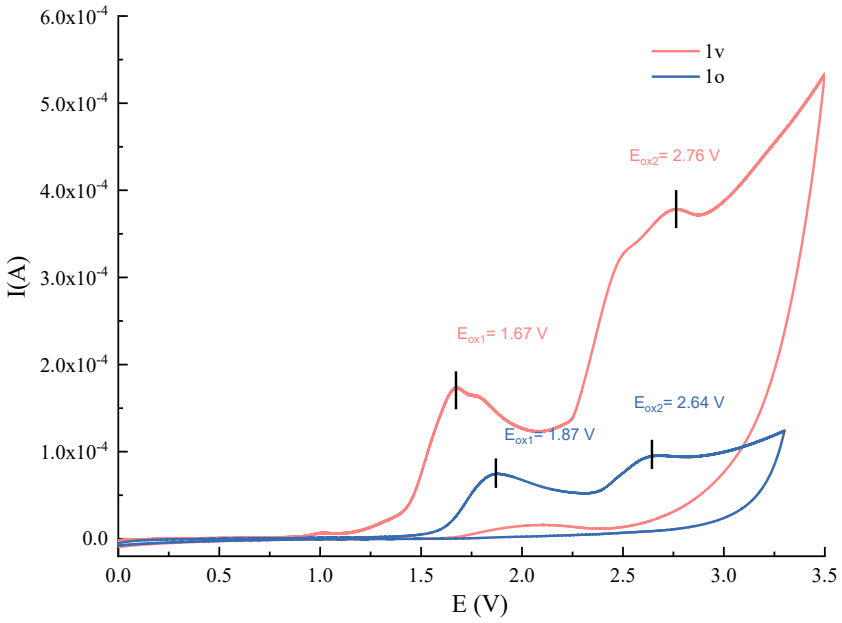


Figure S2. Cyclic voltammetry experiments of **1o** and **1v** in DCM:HFIP (5:1) with 0.1 M Bu_4NBF_4, the scan rate is 0.1 V/s. The working electrode was a glassy carbon electrode, the counter electrode was a platinum wire, and the reference electrode was a Ag/AgCl electrode.

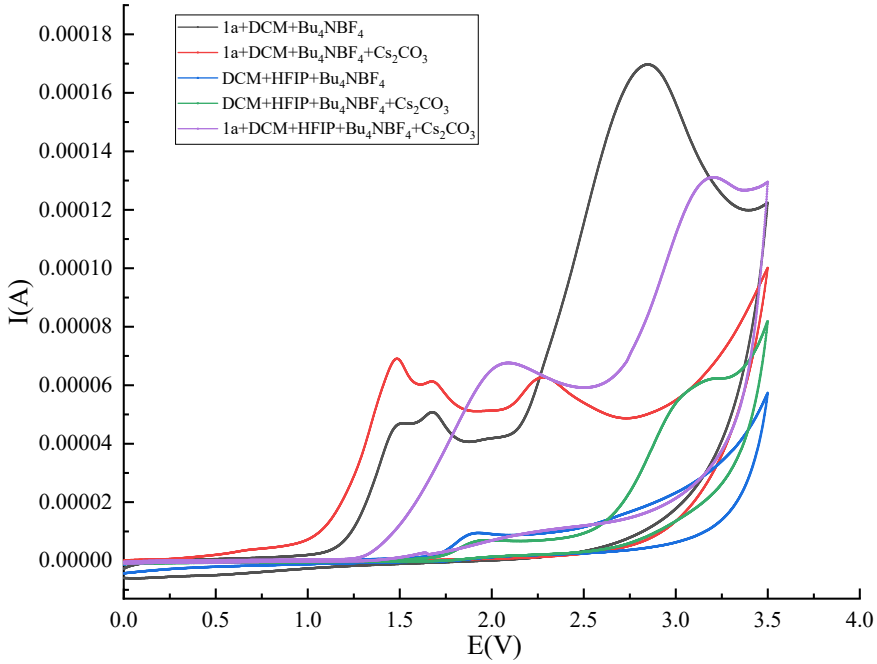


Figure S3. Cyclic voltammetry experiments. The working electrode was a glassy carbon electrode, the counter electrode was a platinum wire, and the reference electrode was a Ag/AgCl electrode. (a) **1a**+DCM+Bu_4NBF_4; (b) **1a**+DCM+Bu_4NBF_4+Cs_2CO_3; (c) DCM+HFIP+Bu_4NBF_4; (d) DCM+HFIP+Bu_4NBF_4+Cs_2CO_3; (e) **1a**+DCM+HFIP+Bu_4NBF_4+Cs_2CO_3.

According to the results, it found that: 1) the base could promote the oxidation of compound **1a**; 2) when HFIP was added, the oxidant potential of **1a** was changed; 3) solvent could be oxidized when there are no compound which is easier to be oxidized; 4) the reductive peak of HFIP was not measured.

5. Computational Details

All the calculations were conducted by using the Gaussian 16 program package.[2] The B3LYP[3] functional together with Becke-Johnson damping corrections[4] (abbreviated as B3LYP-D3BJ) and the 6-311+G(d,p) basis sets[5] were used for all the calculations. The polarizable continuum model (PCM)[6] was employed to consider the solvent effect of DCM:HFIP. The intrinsic reaction coordinate (IRC)[6] analysis was carried out to confirm that all the saddle point connected the correct reactant and product on the potential energy surface. With the help of Multiwfn 3.7-dew[7] and VMD VERSION 1.9.3 program[8], we drawn these structures**.**

1a

Sum of electronic and zero-point Energies= -610.614779
Sum of electronic and thermal Energies= -610.604189
Sum of electronic and thermal Enthalpies= -610.603245
Sum of electronic and thermal Free Energies= -610.652264

N	-1.83953700	0.69537000	-0.02604300
N	-0.48197400	-1.08284600	0.04472400
C	-3.04383700	1.35381800	-0.05485900
H	-2.99944500	2.43292300	-0.09785800
C	-4.19245100	0.63127600	-0.02789800
H	-5.14045800	1.14986900	-0.05055100
C	-4.14440200	-0.79253500	0.02961400
H	-5.07004800	-1.35304800	0.05139900
C	-2.94759400	-1.44600300	0.05727200
H	-2.87372800	-2.52416500	0.10075100
C	-1.74605700	-0.69445700	0.02813500
C	-0.55437200	1.17922500	-0.04293800
C	0.25896600	0.06514300	0.00261300
C	1.73008500	0.02856500	0.00294300
C	2.48481600	1.20426200	0.06785800
H	1.98752600	2.16576400	0.12833200
C	3.87273800	1.15268400	0.06264300
H	4.44433400	2.07170000	0.11425200
C	4.52828300	-0.07423800	-0.00486800
H	5.61092100	-0.11340200	-0.00804900
C	3.78384100	-1.24859900	-0.06633700
H	4.28649800	-2.20717000	-0.11833600

C	2.39495900	-1.19893200	-0.06230500
H	1.80682300	-2.10669300	-0.11007400
H	-0.35170000	2.23529700	-0.09188300

2a

Sum of electronic and zero-point Energies= -1399.157798
Sum of electronic and thermal Energies= -1399.138056
Sum of electronic and thermal Enthalpies= -1399.137112
Sum of electronic and thermal Free Energies= -1399.207948

F	-3.04176300	-1.55014900	-0.97047400
F	-2.56607600	-3.12053400	0.42892500
F	-1.43475400	-2.91802000	-1.39834300
F	-0.38296000	-2.84245800	1.91867700
F	0.80356000	-2.72119200	0.11904000
F	0.87161600	-1.12455900	1.56632700
O	-0.57800200	-0.44675400	-0.73499100
N	-1.22895800	1.77622900	-0.19166700
N	0.75253600	2.76317300	0.15767100
C	-2.59605700	1.70246700	-0.31625400
H	-3.00412900	0.75099100	-0.62613800
C	-3.33118100	2.81554600	-0.06764400
H	-4.40635100	2.76599500	-0.16507900
C	-2.69104400	4.03431800	0.30420700
H	-3.29591100	4.91022800	0.49915200
C	-1.33279400	4.10527000	0.40517200
H	-0.81470600	5.01580000	0.67418500
C	-0.55652000	2.94873900	0.14603300
C	-0.25266600	0.82531300	-0.37353500
C	0.95821100	1.45238300	-0.17066500
C	2.30751600	0.88012100	-0.27420700
C	2.54523400	-0.30232400	-0.98221100
H	1.72689100	-0.80991300	-1.47780700
C	3.82958200	-0.82673500	-1.05676300
H	4.00193400	-1.74423100	-1.60664200
C	4.89138400	-0.17410600	-0.43651800
H	5.89225100	-0.58436300	-0.49711900
C	4.66171900	1.01030700	0.25825000
H	5.48438500	1.52499400	0.74024500
C	3.37821600	1.53555200	0.33942900
H	3.18845400	2.45586100	0.87748000
C	-1.08072400	-1.28992100	0.28276000
H	-1.64172100	-0.74072000	1.04487400
C	-2.03995100	-2.24523300	-0.42422000
C	0.07261900	-2.01406400	0.97906100

3

Sum of electronic and zero-point Energies= -789.281489
Sum of electronic and thermal Energies= -789.272816
Sum of electronic and thermal Enthalpies= -789.271872
Sum of electronic and thermal Free Energies= -789.316359

C	-0.00035100	0.66876600	-0.49365000
H	0.00026700	0.52558700	-1.60151900
C	1.25855200	-0.10236700	-0.04008200
C	-1.25639100	-0.10513100	-0.03943400
O	-0.00712200	1.92021500	-0.05512100
F	1.35256900	-0.22706600	1.29497900
F	2.36320100	0.54677400	-0.44332700
F	1.35621300	-1.35200700	-0.54630900
F	-1.29647200	-1.39519100	-0.44187400
F	-2.35749200	0.47525400	-0.54818000
F	-1.41292400	-0.12053300	1.29376500

4

Sum of electronic and zero-point Energies= -789.049435
Sum of electronic and thermal Energies= -789.040788
Sum of electronic and thermal Enthalpies= -789.039844
Sum of electronic and thermal Free Energies= -789.085224

C	-0.00027500	0.56693100	-0.55678000
H	0.00010300	0.49496800	-1.64973600
C	1.27468400	-0.11995600	-0.03313700
C	-1.27498300	-0.11956600	-0.03297500
O	0.00110500	1.85699600	-0.08059500
F	1.31176500	-0.16831000	1.29309900
F	2.33741800	0.56568200	-0.45204600
F	1.36355800	-1.35935300	-0.50566300
F	-1.32590800	-1.38422400	-0.44076900
F	-2.33891700	0.52022000	-0.51644700
F	-1.34852700	-0.09794700	1.29203100

5

Sum of electronic and zero-point Energies= -610.390694
Sum of electronic and thermal Energies= -610.380066
Sum of electronic and thermal Enthalpies= -610.379122
Sum of electronic and thermal Free Energies= -610.428404

N	1.84312400	0.68517000	-0.01996700
N	0.45848000	-1.10222100	0.02850300
C	3.03596200	1.36520500	-0.03873800
H	2.97810100	2.44367200	-0.06879000

C	4.18946500	0.64141500	-0.01765500
H	5.13812900	1.15727200	-0.03143200
C	4.13393900	-0.76908600	0.02210700
H	5.05763000	-1.33268900	0.03956200
C	2.92480600	-1.44610000	0.03919000
H	2.86234100	-2.52439900	0.06930600
C	1.75626500	-0.70212700	0.01678800
C	0.56986800	1.16501000	-0.03028300
C	-0.27728200	-0.00820100	0.00367800
C	-1.72963200	-0.00003900	0.00249500
C	-2.44242100	1.20598400	0.04692700
H	-1.92285000	2.15544200	0.08988600
C	-3.82902600	1.18984100	0.04445200
H	-4.37898700	2.12133200	0.08018600
C	-4.50946700	-0.02388300	-0.00299900
H	-5.59254100	-0.03393200	-0.00658100
C	-3.80408800	-1.22753200	-0.04551200
H	-4.33878100	-2.16806500	-0.08243100
C	-2.42045100	-1.21996700	-0.04184700
H	-1.85667600	-2.14353800	-0.07547300
H	0.35477200	2.22114600	-0.06559400

6

Sum of electronic and zero-point Energies= -609.703235
Sum of electronic and thermal Energies= -609.692453
Sum of electronic and thermal Enthalpies= -609.691509
Sum of electronic and thermal Free Energies= -609.740681

N	-1.80491400	0.68862800	0.00000000
N	-0.45587600	-1.14190900	-0.00002000
C	-2.98699700	1.39415500	0.00000400
H	-2.88493900	2.47048800	0.00002200
C	-4.15991700	0.70317000	-0.00001300
H	-5.10097400	1.23211500	-0.00000900
C	-4.12229900	-0.70733600	-0.00003600
H	-5.05868100	-1.25241100	-0.00005000
C	-2.92870400	-1.42745200	-0.00004000
H	-2.90522300	-2.50743300	-0.00005700
C	-1.75431300	-0.71106300	-0.00002100
C	-0.56306200	1.25273300	0.00001500
C	0.27136700	-0.05923200	0.00000000
C	1.70150900	-0.02353600	0.00000900
C	2.37233200	1.21643600	0.00003600
H	1.79799000	2.13330200	0.00004900
C	3.75705900	1.24465400	0.00004500

H	4.28004100	2.19187600	0.00006600
C	4.47270800	0.05014800	0.00002800
H	5.55580700	0.07527500	0.00003500
C	3.81307100	-1.18639500	0.00000200
H	4.38705000	-2.10382600	-0.00001200
C	2.43609800	-1.22894900	-0.00000800
H	1.90135400	-2.17041200	-0.00002800

7

Sum of electronic and zero-point Energies= -609.927700
Sum of electronic and thermal Energies= -609.917064
Sum of electronic and thermal Enthalpies= -609.916120
Sum of electronic and thermal Free Energies= -609.966055

N	1.84677700	-0.71789000	-0.00002600
N	0.49763100	1.07653300	0.00004300
C	3.04488600	-1.39306500	-0.00005300
H	2.98678700	-2.47201700	-0.00009300
C	4.19560000	-0.67551800	-0.00002900
H	5.14049100	-1.20016600	-0.00005100
C	4.15841100	0.75108200	0.00002500
H	5.08914700	1.30325400	0.00004500
C	2.96892000	1.41756600	0.00005300
H	2.90518000	2.49750300	0.00009400
C	1.76010900	0.67798900	0.00002600
C	0.55768000	-1.15435200	-0.00003700
C	-0.27084100	-0.05922300	0.00000100
C	-1.73664300	-0.03039800	0.00000100
C	-2.46885400	-1.22137700	-0.00002000
H	-1.94449800	-2.17177100	-0.00003300
C	-3.85674000	-1.19184300	-0.00002100
H	-4.41485500	-2.12046300	-0.00003700
C	-4.53022800	0.02789700	-0.00000200
H	-5.61332300	0.05041800	-0.00000300
C	-3.80555600	1.21617600	0.00001800
H	-4.32428900	2.16745900	0.00003300
C	-2.41575400	1.18964500	0.00002000
H	-1.84144400	2.10780000	0.00003600

9

Sum of electronic and zero-point Energies= -150.424778
Sum of electronic and thermal Energies= -150.422406
Sum of electronic and thermal Enthalpies= -150.421462
Sum of electronic and thermal Free Energies= -150.444532

O	0.00000000	0.00000000	0.65956700

O	0.00000000	0.00000000	-0.65956700

10

Sum of electronic and zero-point Energies=			-151.023832
Sum of electronic and thermal Energies=			-151.020934
Sum of electronic and thermal Enthalpies=			-151.019990
Sum of electronic and thermal Free Energies=			-151.045544
O	0.05517600	-0.67930700	0.00000000
H	-0.88281800	-0.88766200	0.00000000
O	0.05517600	0.79026400	0.00000000

11

Sum of electronic and zero-point Energies=			-150.875621
Sum of electronic and thermal Energies=			-150.872771
Sum of electronic and thermal Enthalpies=			-150.871827
Sum of electronic and thermal Free Energies=			-150.897758
O	0.05489400	-0.59768200	0.00000000
H	-0.87829900	-0.87505100	0.00000000
O	0.05489400	0.70706300	0.00000000

14

Sum of electronic and zero-point Energies=			-1399.713893
Sum of electronic and thermal Energies=			-1399.693651
Sum of electronic and thermal Enthalpies=			-1399.692707
Sum of electronic and thermal Free Energies=			-1399.765637
F	2.82723800	0.14163500	1.01297400
F	3.54973700	-1.80166300	0.41607800
F	2.05757600	-1.63204400	1.96680400
F	1.80665800	-3.44170200	-0.80113700
F	0.17923700	-3.05853900	0.56456300
F	-0.02578200	-2.55424600	-1.52107800
O	0.30945900	-0.38342700	0.20039700
N	0.66277300	1.86003500	-0.60013000
N	-1.27754600	2.45239000	0.39819600
C	1.90912500	2.07981400	-1.11828000
H	2.34932400	1.28552800	-1.70569200
C	2.52795600	3.26737500	-0.89675900
H	3.51119000	3.44005400	-1.30900000
C	1.86625500	4.27211300	-0.12703600
H	2.36835300	5.21294200	0.05838700
C	0.60346500	4.06673100	0.35690600
H	0.06661900	4.81916000	0.91823100
C	-0.04076000	2.83873300	0.10220500
C	-0.15803500	0.66939800	-0.67149600

C	-1.43745400	1.21090800	-0.08270800
C	-2.66663100	0.46684000	0.00802000
C	-2.77761200	-0.83511800	-0.51205100
H	-1.92476000	-1.30634900	-0.98387500
C	-3.97532200	-1.53039900	-0.42298400
H	-4.04193600	-2.53269300	-0.82944000
C	-5.08418000	-0.95099400	0.18916300
H	-6.01629200	-1.49801800	0.26043900
C	-4.98416200	0.33950800	0.71154500
H	-5.84269900	0.79687300	1.18930700
C	-3.79472800	1.04293000	0.62422500
H	-3.71178800	2.04494200	1.02619000
C	1.36695300	-1.17598500	-0.25207700
H	1.79870300	-0.83639500	-1.19840600
C	2.46702600	-1.12560900	0.80506400
C	0.83253400	-2.58624100	-0.49170900
H	-0.20752100	0.27341100	-1.69179000

15

Sum of electronic and zero-point Energies= -1399.554898
Sum of electronic and thermal Energies= -1399.535023
Sum of electronic and thermal Enthalpies= -1399.534078
Sum of electronic and thermal Free Energies= -1399.605190

F	-3.23703400	-0.33215500	-0.90631900
F	-3.36916000	-2.36965600	-0.19800300
F	-2.03384200	-1.86928100	-1.81848000
F	-1.43964900	-3.18983200	1.50208200
F	-0.15891100	-3.04817300	-0.23048200
F	0.35300300	-1.98547000	1.57544300
O	-0.56002500	-0.24278200	-0.30549900
N	-0.71328800	2.05893300	0.30948100
N	1.46824600	2.49461700	-0.15919200
C	-2.02699700	2.30422100	0.45167700
H	-2.67742800	1.46717900	0.66026600
C	-2.47444700	3.59823900	0.31511400
H	-3.52854500	3.80696000	0.42234600
C	-1.55478500	4.61607300	0.04279800
H	-1.90309000	5.63610000	-0.05629300
C	-0.20486700	4.33574800	-0.11217600
H	0.53090400	5.09430800	-0.33621000
C	0.19610500	3.01888000	0.01433400
C	0.00493900	0.76822000	0.45217900
C	1.40186300	1.21821500	0.00235200
C	2.55872300	0.34033200	-0.12327700

C	2.42867000	-0.99764000	-0.51232000
H	1.45875000	-1.40832400	-0.74859500
C	3.56232200	-1.78601200	-0.65375200
H	3.46072600	-2.81725200	-0.96684200
C	4.82108900	-1.25022500	-0.40095800
H	5.70232800	-1.87127200	-0.50554100
C	4.95452800	0.08466200	-0.02047500
H	5.93570900	0.49928700	0.17275100
C	3.83075700	0.88295200	0.10987700
H	3.91670700	1.92144500	0.40372300
C	-1.43890400	-1.13474900	0.34712000
H	-1.90569900	-0.70172400	1.23705300
C	-2.53875600	-1.44546000	-0.66737200
C	-0.66492300	-2.37486600	0.80026400
H	0.04356700	0.52026300	1.51883700

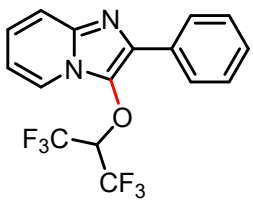
18

Sum of electronic and zero-point Energies=			-75.897490
Sum of electronic and thermal Energies=			-75.895130
Sum of electronic and thermal Enthalpies=			-75.894186
Sum of electronic and thermal Free Energies=			-75.913735
O	0.00000000	0.00000000	0.10676500
H	0.00000000	0.00000000	-0.85411700

19

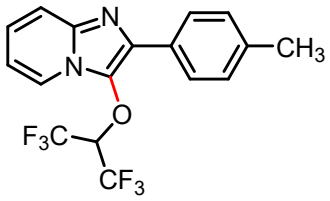
Sum of electronic and zero-point Energies=			-76.397283
Sum of electronic and thermal Energies=			-76.394448
Sum of electronic and thermal Enthalpies=			-76.393504
Sum of electronic and thermal Free Energies=			-76.414926
O	0.00000000	0.00000000	0.11872900
H	0.00000000	0.75487800	-0.47491600
H	0.00000000	-0.75487800	-0.47491600

6. Characterization Data

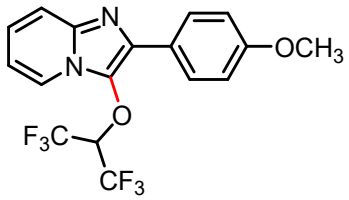


3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-phenylimidazo[1,2-*a*]pyridine (2a): Yellow solid (103.7 mg, 96%). mp. 155.0-159.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07-7.99 (m, 1H), 7.95-7.85 (m, 2H), 7.62-7.55 (m, 1H), 7.54-7.47 (m, 2H), 7.45-7.37

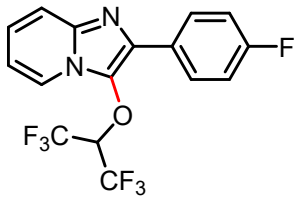
(m, 1H), 7.25-7.17 (m, 1H), 6.89 (t, J = 6.7 Hz, 1H), 4.74-4.63 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 132.3, 131.9, 129.1, 129.0, 128.6, 127.7, 124.7, 121.5, 120.6 (d, J = 284.6 Hz), 117.9, 112.7, 76.3-75.6 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{16}H_{11}F_6N_2O$ $(M+H)^+$: 361.0770; found: 361.0768.



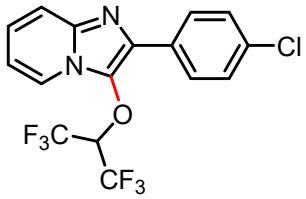
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-(p-tolyl)imidazo[1,2-*a*]pyridine(2b): Yellow solid (110.0 mg, 98%). mp. 133.6-137.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 6.9 Hz, 1H), 7.81-7.75 (m, 2H), 7.69-7.53 (m, 1H), 7.34-7.29 (m, 2H), 7.23-7.17 (m, 1H), 6.91-6.85 (m, 1H), 4.76-4.65 (m, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 138.6, 132.0, 129.7, 129.1, 129.0, 127.6, 124.6, 121.5, 120.7 (d, J = 284.6 Hz), 117.8, 112.6, 77.3-75.2 (m), 21.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O$ $(M+H)^+$: 375.0927; found: 375.0931.



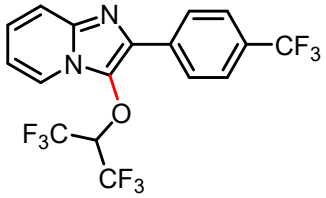
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (2c): Yellow solid (110.0 mg, 94%). mp. 110.5-112.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 6.9 Hz, 1H), 7.85-7.79 (m, 2H), 7.58-7.52 (m, 1H), 7.22-7.16 (m, 1H), 7.06-7.00 (m, 2H), 6.88 (t, J = 6.9 Hz, 1H), 4.74-4.64 (m, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 139.3, 131.7, 129.1, 124.5, 124.3, 121.5, 120.6 (d, J = 183.9 Hz), 117.7, 114.4, 112.6, 77.2-75.4 (m), 55.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O_2$ $(M+H)^+$: 391.0876; found: 391.0879.



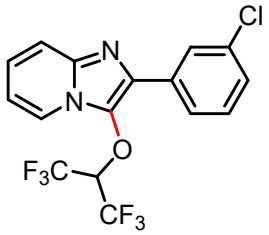
2-(4-fluorophenyl)-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)imidazo[1,2-*a*]pyridine (2d): Yellow solid (96.4 mg, 85%). mp. 152.9-154.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 6.7 Hz, 1H), 7.03-7.82 (m, 2H), 7.60-7.53 (m, 1H), 7.25-7.15 (m, 3H), 6.91 (t, J = 6.7 Hz, 1H), 4.68-4.57 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9 (d, J = 248.7 Hz), 139.4, 132.1, 129.5 (d, J = 8.1 Hz), 128.5, 128.0 (d, J = 2.9 Hz), 124.9, 121.5, 120.6 (d, J = 284.6 Hz), 117.0 (d, J = 179.0 Hz), 115.9, 112.9, 77.2-75.8 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7, -112.6. HRMS (ESI) calculated for $C_{16}H_{10}F_7N_2O$ $(M+H)^+$: 379.0676; found: 379.0680.



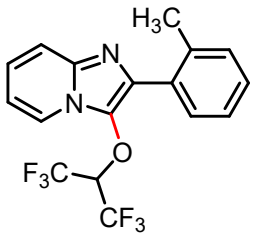
2-(4-chlorophenyl)-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)imidazo[1,2-*a*]pyridine (2e): Yellow solid (89.8 mg, 76%). mp. 143.2-144.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 6.9 Hz, 1H), 7.89-7.80 (m, 2H), 7.60-7.54 (m, 1H), 7.51-7.45 (m, 2H), 7.25-7.20 (m, 1H), 6.94-6.87 (m, 1H), 4.70-4.60 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.5, 134.6, 132.3, 130.4, 129.2, 128.9, 128.4, 125.0, 121.5, 120.6 (d, J = 284.6 Hz), 118.0, 113.0, 77.2-75.8 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.6. HRMS (ESI) calculated for $C_{16}H_{10}ClF_6N_2O$ $(M+H)^+$: 395.0380; found: 395.0379.



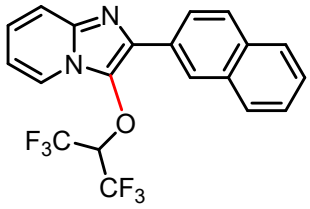
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine (2f): Yellow solid (52.7 mg, 41%). mp. 114.2-115.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09-7.99 (m, 3H), 7.79-7.72 (m, 2H), 7.63-7.57 (m, 1H), 7.29-7.23 (m, 1H), 6.97-6.89 (m, 1H), 4.68-4.59 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.7, 135.5, 132.8, 130.4 (dd, J_1 = 32.3 Hz, J_2 = 33.0 Hz), 128.1, 127.8, 126.0-125.8 (m), 125.3, 122.7, 120.5 (d, J = 281.7 Hz), 120.0, 117.2, 113.2, 77.2-76.0 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.6, -72.5. HRMS (ESI) calculated for $C_{17}H_{10}F_9N_2O$ $(M+H)^+$: 429.0649; found: 429.0645.



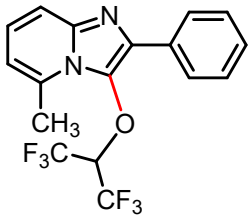
2-(3-chlorophenyl)-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)imidazo[1,2-*a*]pyridine (2g): Brown solid (91.0 mg, 77%). mp. 136.8-138.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06-8.01 (m, 1H), 7.95-7.91 (m, 1H), 7.81-7.75 (m, 1H), 7.61-7.55 (m, 1H), 7.47-7.36 (m, 2H), 7.25-7.21 (m, 1H), 6.95-6.89 (m, 1H), 4.71-4.61 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.5, 135.1, 133.7, 132.6, 130.2, 128.6, 128.0, 127.7, 125.6, 125.1, 121.6, 120.6 (d, J = 256.0 Hz), 118.0, 113.1, 77.2-76.2 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.6. HRMS (ESI) calculated for $C_{16}H_{10}ClF_6N_2O$ $(M+H)^+$: 395.0380; found: 395.0378.



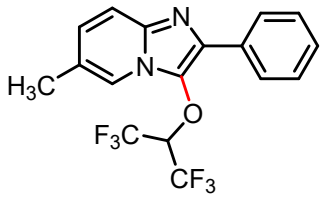
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-(o-tolyl)imidazo[1,2-*a*]pyridine(2h): Yellow solid (102.1 mg, 91%). mp. 102.0-104.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 7.0 Hz, 1H), 7.59-7.53 (m, 1H), 7.47-7.42 (m, 1H), 7.39-7.31 (m, 2H), 7.31-7.27 (m, 1H), 7.24-7.17 (m, 1H), 6.89 (dt, J_1 = 1.0 Hz, J_2 = 6.9 Hz, 1H), 4.48-4.40 (m, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9, 137.8, 133.1, 130.8, 130.6, 130.4, 129.2, 128.8, 126.0, 124.7, 124.3, 121.4, 120.5 (d, J = 283.9 Hz), 118.9, 112.6, 77.6-76.3 (m), 19.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ -73.5. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O$ $(M+H)^+$: 375.0927; found: 375.0927.



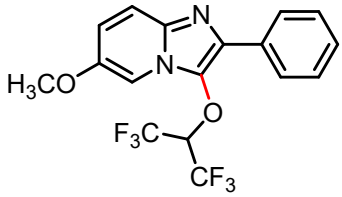
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-(naphthalen-2-yl)imidazo[1,2-*a*]pyridine (2i): Brown solid (73.8 mg, 60%). mp. 146.4-147.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 8.11-8.03 (m, 2H), 8.02-7.96 (m, 1H), 7.95-7.85 (m, 2H), 7.65-7.58 (m, 1H), 7.58-7.49 (m, 2H), 7.25-7.20 (m, 1H), 6.95-6.88 (m, 1H), 4.80-4.69 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.6, 133.5, 133.2, 132.5, 129.3, 129.0, 128.8, 128.3, 127.8, 126.8, 126.6, 126.6, 125.1, 124.8, 121.6, 120.6 (d, J = 286.8 Hz), 117.9, 112.8, 77.2-75.8 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.6. HRMS (ESI) calculated for $C_{20}H_{13}F_6N_2O$ $(M+H)^+$: 411.0927; found: 411.0927.



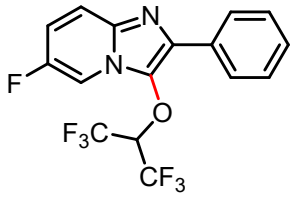
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-5-methyl-2-phenylimidazo[1,2-*a*]pyridine (2j): Yellow oil (49.4 mg, 44%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.78 (m, 2H), 7.55-7.48 (m, 2H), 7.45-7.37 (m, 2H), 7.12-7.05 (m, 1H), 6.54 (d, J = 6.9 Hz, 1H), 4.81-4.70 (m, 1H), 2.81 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 135.1, 134.3, 132.2, 129.1, 128.8, 128.7, 128.2, 125.1, 120.5 (d, J = 284.6 Hz), 115.7, 113.7, 77.2-75.1 (m), 18.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.0. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O$ $(M+H)^+$: 375.0927; found: 375.0932.



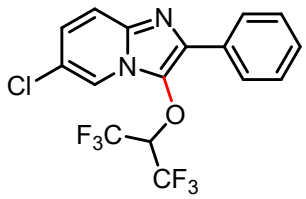
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-6-methyl-2-phenylimidazo[1,2-a]pyridine (2k): Yellow solid (110.0 mg, 98%). mp. 129.1-131.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91-7.85 (m, 2H), 7.78 (s, 1H), 7.53-7.45 (m, 3H), 7.43-7.36 (m, 1H), 7.09-7.03 (m, 1H), 4.73-4.64 (m, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 132.1, 132.1, 129.0, 128.9, 128.4, 127.9, 127.6, 122.6, 120.7 (d, J = 283.9 Hz), 119.0, 117.2, 77.3-75.5 (m), 18.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O$ $(M+H)^+$: 375.0927; found: 375.0930.



3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-6-methoxy-2-phenylimidazo[1,2-a]pyridine (2l): Brown solid (71.4 mg, 61%). mp. 108.4-112.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90-7.84 (m, 2H), 7.52-7.48 (m, 2H), 7.26-7.45 (m, 2H), 7.42-7.36 (m, 1H), 7.00 (dd, J_1 =2.3 Hz, J_2 = 7.5 Hz, 1H), 4.72-4.63 (m, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.6, 136.6, 130.0, 130.1, 129.2, 129.0, 128.4, 127.5, 120.7 (d, J = 281.7 Hz), 120.3, 118.2, 102.8, 77.2-75.9 (m), 50.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O_2$ $(M+H)^+$: 391.0876; found: 391.0879.

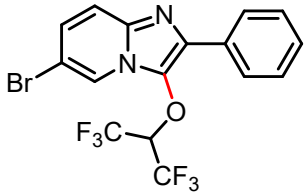


6-fluoro-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-phenylimidazo[1,2-*a*]pyridine (2m): Brown solid (82.8 mg, 73%). mp. 142.8-143.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97-7.93 (m, 1H), 7.89-7.84 (m, 2H), 7.59-7.48 (m, 3H), 7.45-7.40 (m, 1H), 7.18-7.10 (m, 1H), 4.73-4.63 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.6 (d, J = 238.4 Hz), 137.0, 133.2, 131.6, 130.7, 129.1, 128.8, 127.6, 120.6 (d, J = 287.6 Hz), 118.6 (d, J = 8.8 Hz), 117.0 (d, J = 25.7 Hz), 108.4 (d, J = 41.8 Hz), 77.3-75.5 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -77.7, -138.3. HRMS (ESI) calculated for $C_{16}H_{10}F_7N_2O$ $(M+H)^+$: 379.0676; found: 379.0676.

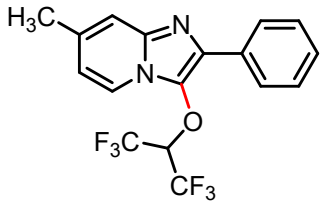


6-chloro-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-phenylimidazo[1,2-*a*]pyridine (2n): Yellow solid (86.3 mg, 73%). mp. 150.5-151.3 °C. ^{1}H NMR (400

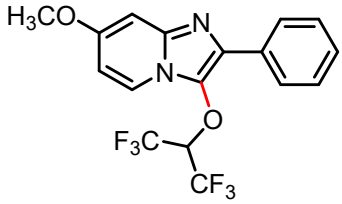
MHz, $CDCl_3$): δ 8.08-8.03 (m, 1H), 7.90-7.83 (m, 2H), 7.55-7.47 (m, 3H), 7.46-7.39 (m, 1H), 7.20-7.14 (m, 1H), 4.74-4.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 132.3, 131.5, 130.2, 129.1, 128.9, 127.7, 126.2, 121.4, 120.5 (d, J = 282.4 Hz), 119.4, 118.4, 77.3-75.8 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{16}H_{10}ClF_6N_2O$ $(M+H)^+$: 395.0380; found: 395.0383.



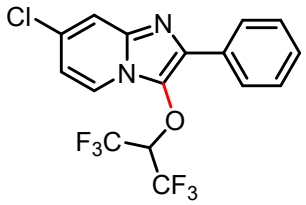
6-bromo-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-phenylimidazo[1,2-*a*]pyridine (2o): Yellow solid (35.5 mg, 27%). mp. 144.9-147.7 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.17-8.13 (m, 1H), 7.90-7.83 (m, 2H), 7.54-7.46 (m, 3H), 7.45-7.40 (m, 1H), 7.29 (d, J = 1.8 Hz, 1H), 4.73-4.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 132.1, 131.3, 129.9, 129.1, 128.9, 128.3, 127.7, 121.6, 120.5 (m, J = 287.6 Hz), 118.6, 107.8, 77.2-75.5 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.6. HRMS (ESI) calculated for $C_{16}H_{10}BrF_6N_2O$ $(M+H)^+$: 438.9875; found: 438.9878.



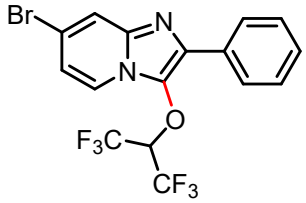
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-2-phenylimidazo[1,2-*a*]pyridine (2p): Yellow solid (72.9 mg, 65%). mp. 110.2-113.7 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.06-7.85 (m, 3H), 7.55-7.45 (m, 2H), 7.45-7.36 (m, 1H), 7.31 (s, 1H), 6.90-6.70 (m, 1H), 4.70-4.18 (m, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.9, 138.7, 135.7, 132.1, 129.1, 128.9, 128.4, 127.6, 120.8, 117.0, 116.2, 115.4, 77.3-75.0 (m), 21.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O$ $(M+H)^+$: 375.0927; found: 375.0925.



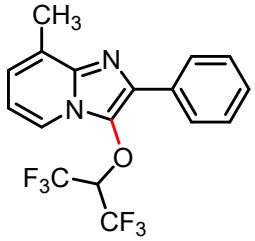
3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methoxy-2-phenylimidazo[1,2-*a*]pyridine (2q): Yellow solid (67.9 mg, 58%). mp. 150.9-154.9 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.90-7.80 (m, 3H), 7.53-7.45 (m, 2H), 7.43-7.35 (m, 1H), 6.82 (d, J = 2.1 Hz, 1H), 6.65-6.57 (m, 1H), 4.69-4.59 (m, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.2, 141.1, 131.9, 129.8 (d, J = 58.7 Hz), 129.0, 128.5, 127.9, 127.6, 122.2, 108.3, 94.7, 73.3-75.8 (m), 55.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O_2^+$ $(M+H)^+$: 391.0876; found: 391.0880.



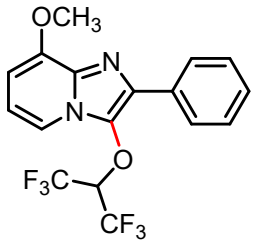
7-chloro-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-phenylimidazo[1,2-*a*]pyridine (2r): Yellow solid (42.6 mg, 36%). mp. 134.0-135.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98-7.92 (m, 1H), 7.91-7.82 (m, 2H), 7.59-7.55 (m, 1H), 7.54-7.47 (m, 2H), 7.46-7.39 (m, 1H), 6.88 (dd, J_1 = 2.0 Hz, J_2 = 5.4 Hz, 1H), 4.73-4.62 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 132.4, 131.4, 131.3, 139.8, 129.1, 128.9, 127.7, 121.9, 119.1, 116.7, 114.5, 77.2-75.6 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{16}H_{10}ClF_6N_2O$ $(M+H)^+$: 395.0380; found: 395.0378.



7-bromo-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-phenylimidazo[1,2-a]pyridine (2s): Yellow solid (80.2 mg, 61%). mp. 124.0-127.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13-8.03 (m, 1H), 7.91-7.84 (m, 2H), 7.83-7.73 (m, 1H), 7.55-7.46 (m, 2H), 7.45-7.37 (m, 1H), 7.07-6.96 (m, 1H), 4.73-4.62 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 131.3, 129.6, 129.1, 128.9, 127.9, 127.7, 124.3, 121.8, 120.1, 118.6, 116.8, 77.2-15.6 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{16}H_{10}BrF_6N_2O$ $(M+H)^+$: 438.9875; found: 438.9872.

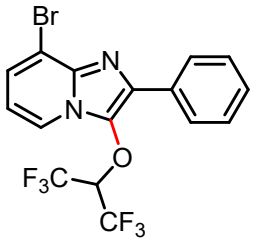


3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-8-methyl-2-phenylimidazo[1,2-a]pyridine (2t): Yellow oil (69.6 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.85 (m, 3H), 7.54-7.46 (m, 2H), 7.43-7.38 (m, 1H), 7.03-6.96 (m, 1H), 6.79 (t, J = 6.9 Hz, 1H), 4.71-4.62 (m, 1H), 2.63 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4, 139.7, 132.6, 132.2, 131.8, 128.9, 128.4, 127.9, 123.3, 120.9 (d, J = 214.9 Hz), 119.4, 112.8, 77.2-75.5 (m), 16.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O$ $(M+H)^+$: 375.0927; found: 375.0930.



3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-8-methoxy-2-phenylimidazo[1,2-

***a*]pyridine (2u):** Yellow solid (69.0 mg, 59%). mp. 158.5-159.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97-7.90 (m, 2H), 7.67 (d, J = 6.7 Hz, 1H), 7.52-7.44 (m, 2H), 7.42-7.35 (m, 1H), 6.79 (t, J = 7.2 Hz, 1H), 6.52-6.45 (m, 1H), 4.75-4.63 (m, 1H), 4.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 133.9, 133.0, 131.8, 128.8, 128.4, 127.8, 120.6 (d, J = 278.0 Hz), 114.5, 112.8, 100.5, 77.3-75.4 (m), 55.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{17}H_{13}F_6N_2O_2$ $(M+H)^+$: 391.0876; found: 391.0879.



8-bromo-3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-phenylimidazo[1,2-a]pyridine (2v): Yellow solid (43.4 mg, 33%). mp. 106.5-108.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (m, 1H), 7.95-7.87 (m, 2H), 7.56-7.47 (m, 3H), 7.46-7.38 (m, 1H), 6.78 (t, J = 7.0 Hz, 1H), 4.74-4.63 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 133.2, 131.4, 130.0, 129.0, 128.9, 128.1, 127.0, 120.9, 120.5 (d, J = 286.8 Hz), 112.8, 112.2, 77.2-75.5 (m). ^{19}F NMR (376 MHz, $CDCl_3$): δ -72.7. HRMS (ESI) calculated for $C_{16}H_{10}BrF_6N_2O$ $(M+H)^+$: 438.9875; found: 438.9876.

7. References

[1]. B. S. Santanielli, M. J. Price and J. K. M. Jr. *J. Chem. Educ*., 2017, **94**, 388-391.

[2] Gaussian 16, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman and D. J. Fox, Gaussian, Inc., Wallingford CT, 2019.

[3] (a) A. D. Becke, *J. Chem. Phys*., 1993, **98**, 5648-5652; (b) P. J. Stephens, F. J. Devlin, C. F. Chabalowski and M. J. Frisch, *J. Phys. Chem*., 1994, **98**, 11623-11627; (c) C. Lee, W. Yang and R. G. Parr, Phys. *Rev. B*, 1988, **37**, 785-789.

[4] S. Grimme, S. Ehrlich and L. Goerigk, *J. Comput. Chem*., 2011, **32**, 1456-1465.

[5] R. Krishnan, J. S. Binkley, R. Seeger and J. A. Pople, *J. Chem. Phys*., 1980, **72**, 650-654.

[6] M. Cossi, V. Barone, R. Cammi and J. Tomasi, *Chem. Phys. Lett*., 1996, **255**, 327-335.

[7] (a) T. Lu and F. Chen, *J. Comput. Chem*., 2012, **33**, 580-592; (b) E. R. Johnson, S. Keinan,

P. Mori-Sánchez, J. Contreras-García, A. J. Cohen and W. Yang, *J. Am. Chem. Soc*., 2010, **132**, 6498-6506.
[8] W. Humphrey, A. Dalke and K. Schluten, *J. Molec. Graphics*, 1996, **14**, 33-38.

8. ^{1}H, ^{13}C and ^{19}F NMR Spectra

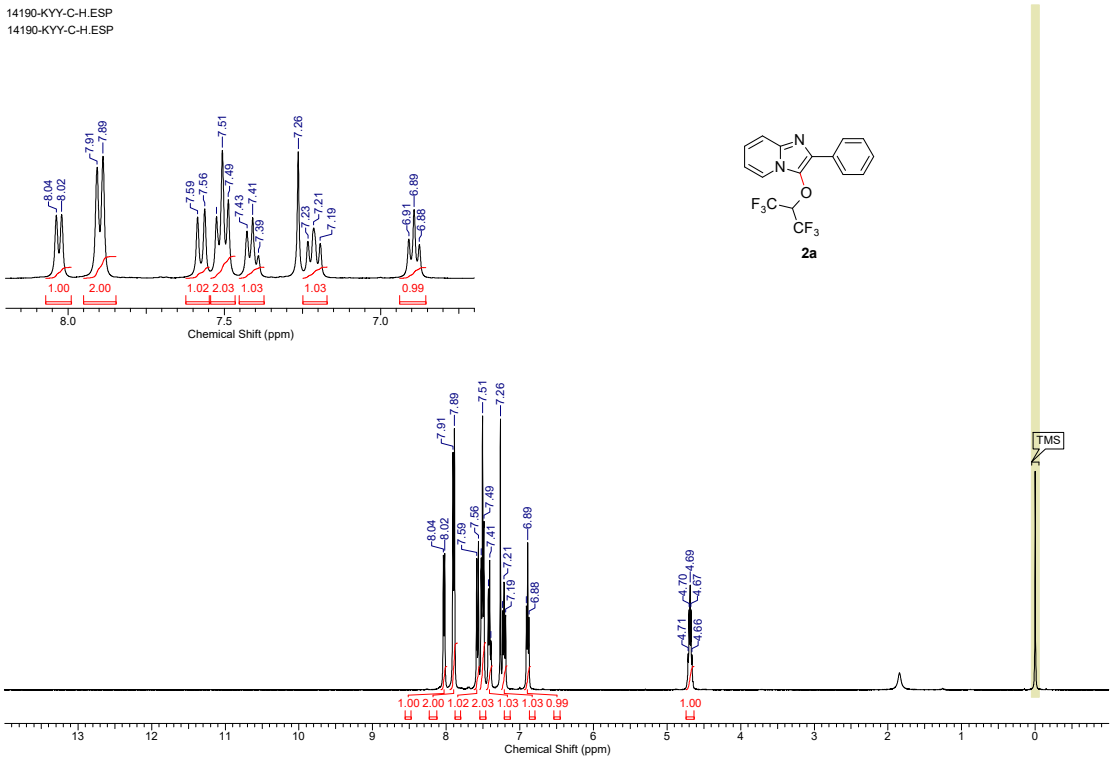


Figure S2. ^{1}H NMR spectrum of compound **2a**

13391-KYY-C-F.ESP

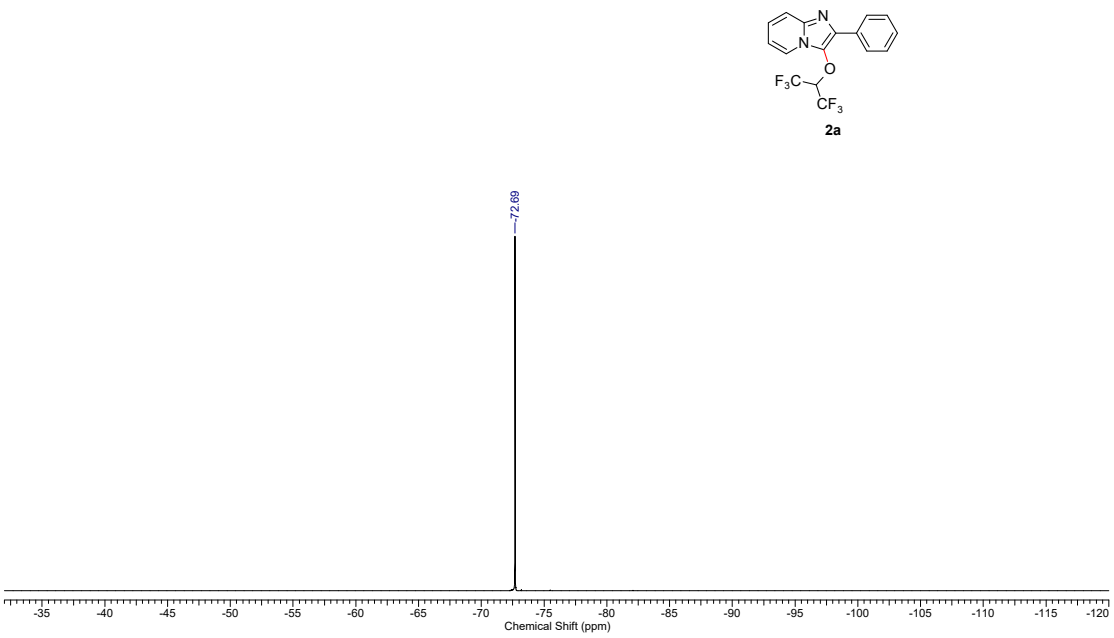


Figure S3. ^{19}F NMR spectrum of compound **2a**

13392-KYY-C-C.ESP

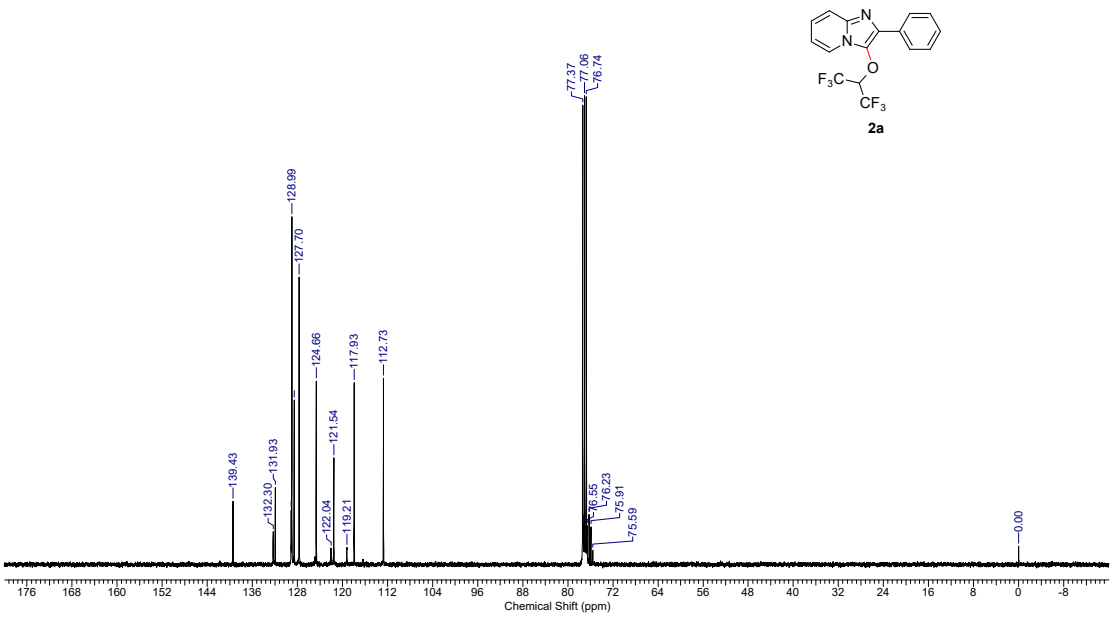


Figure S4. ^{13}C NMR spectrum of compound **2a**

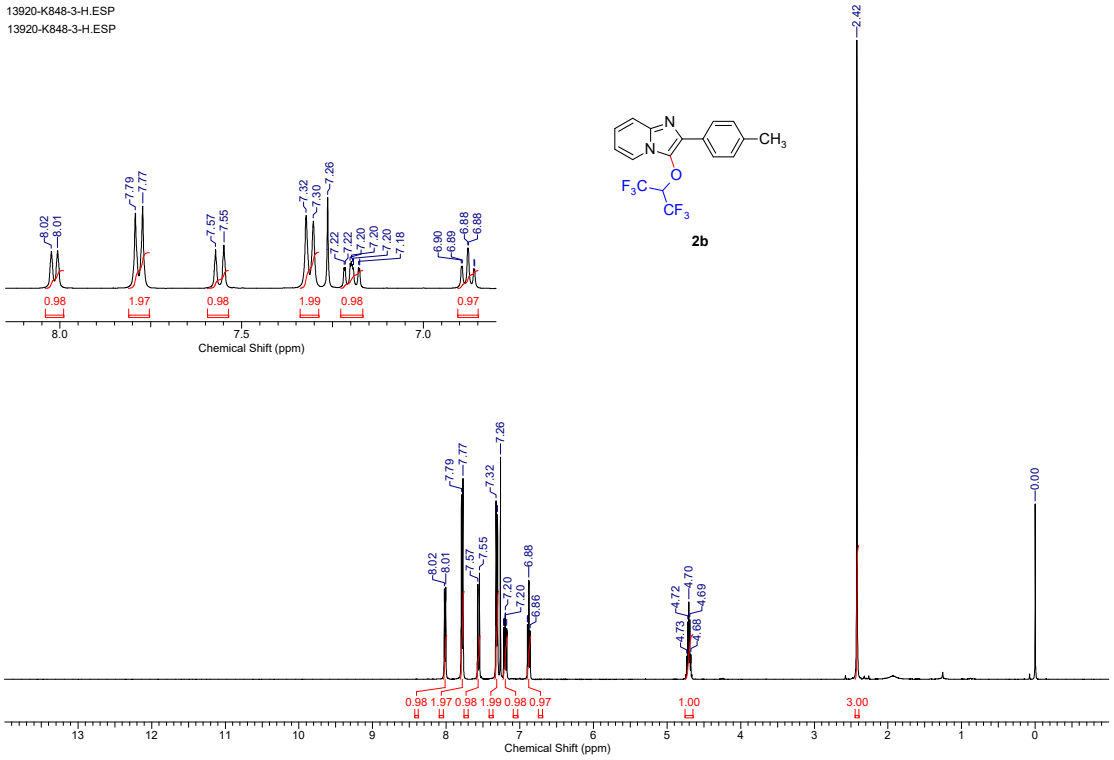


Figure S5. ^{1}H NMR spectrum of compound **2b**

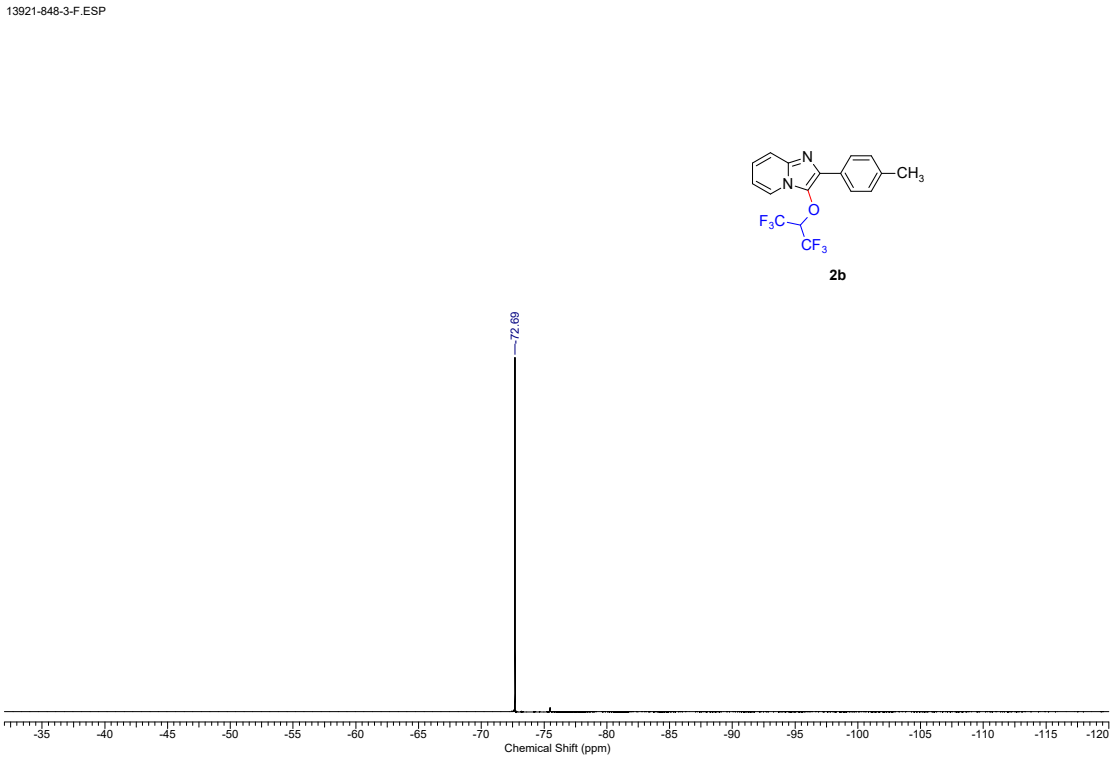


Figure S6. ^{19}F NMR spectrum of compound **2b**

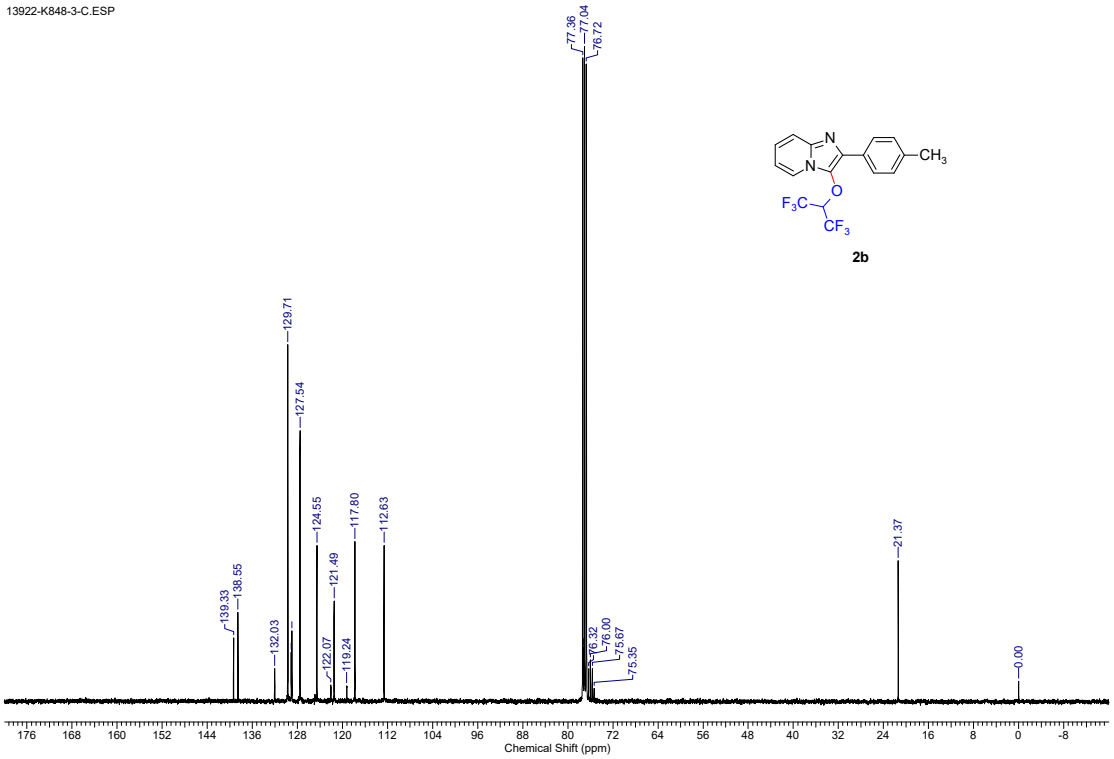


Figure S7. ^{13}C NMR spectrum of compound **2b**

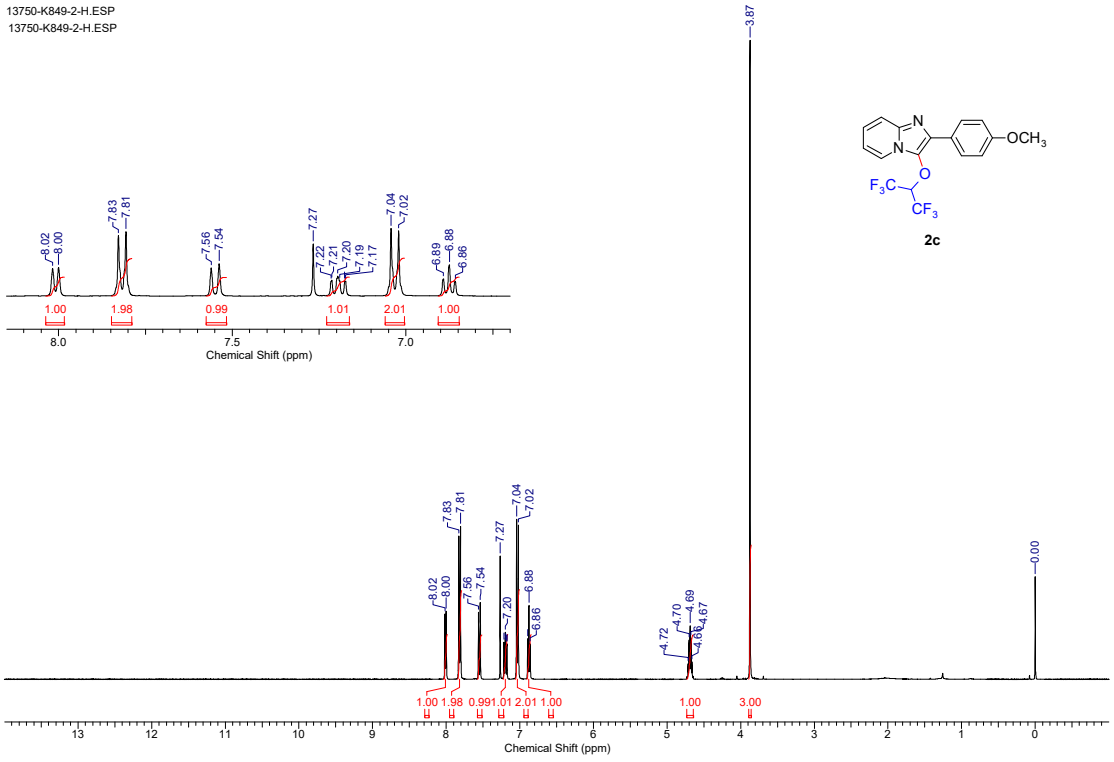


Figure S8. ^{1}H NMR spectrum of compound **2c**

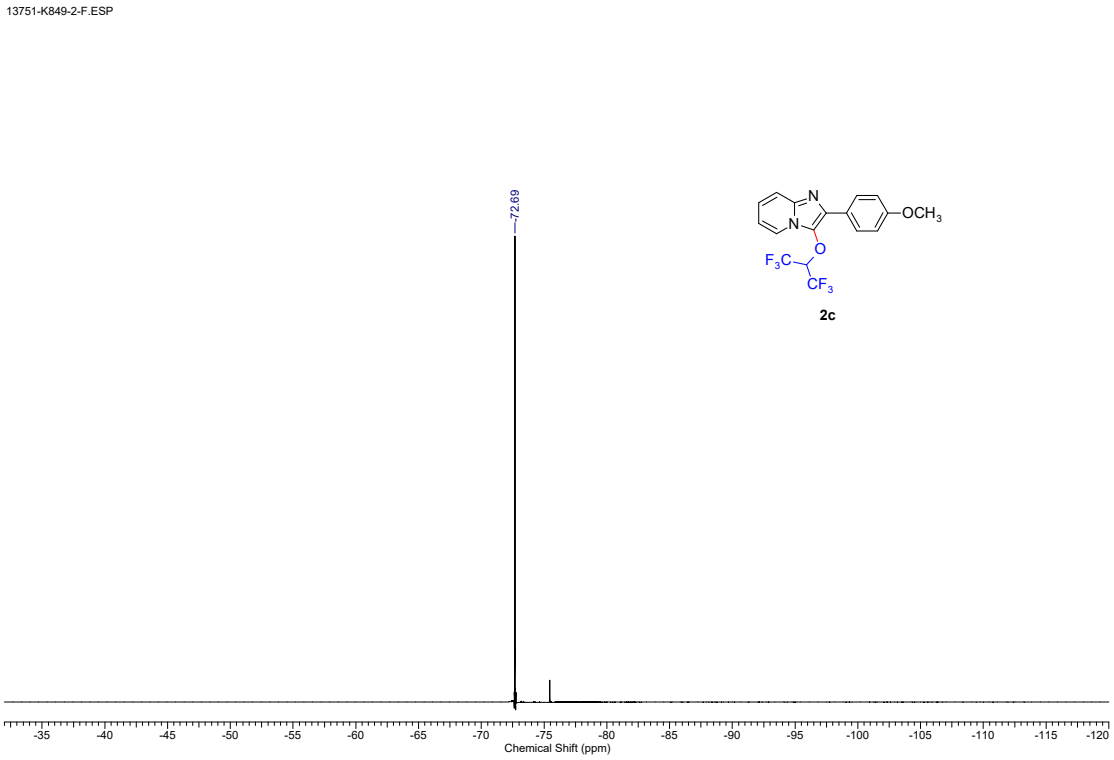


Figure S9. ^{19}F NMR spectrum of compound **2c**

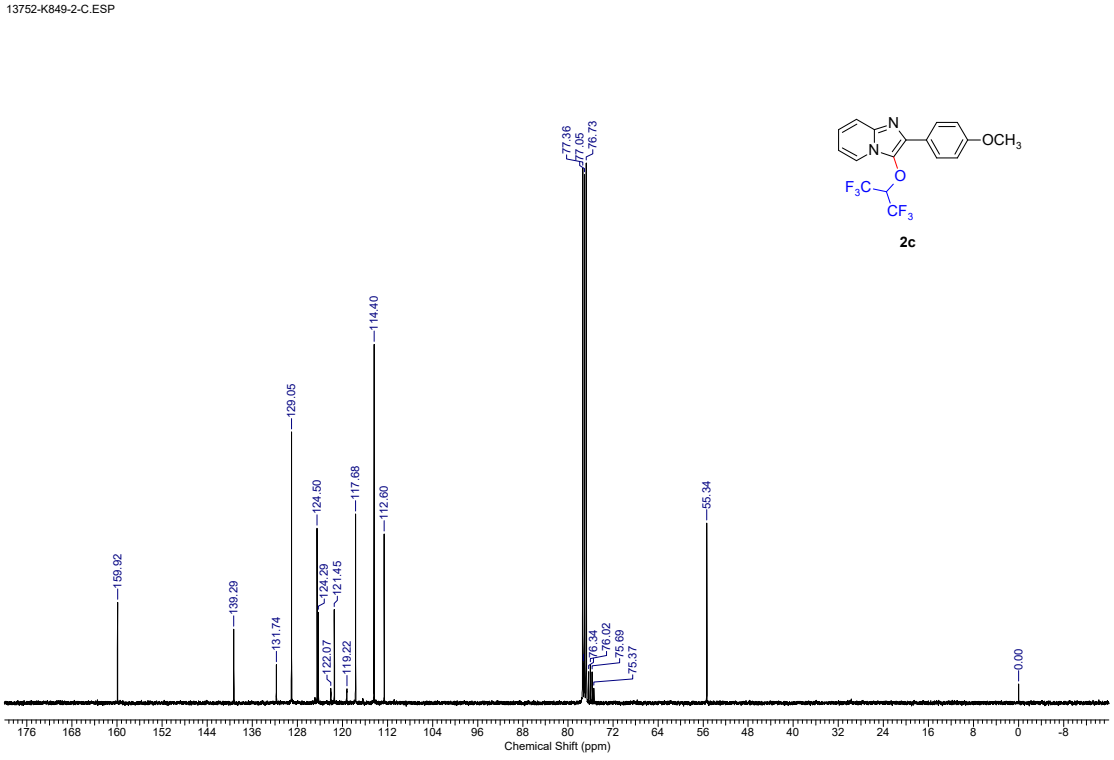


Figure S10. ^{13}C NMR spectrum of compound **2c**

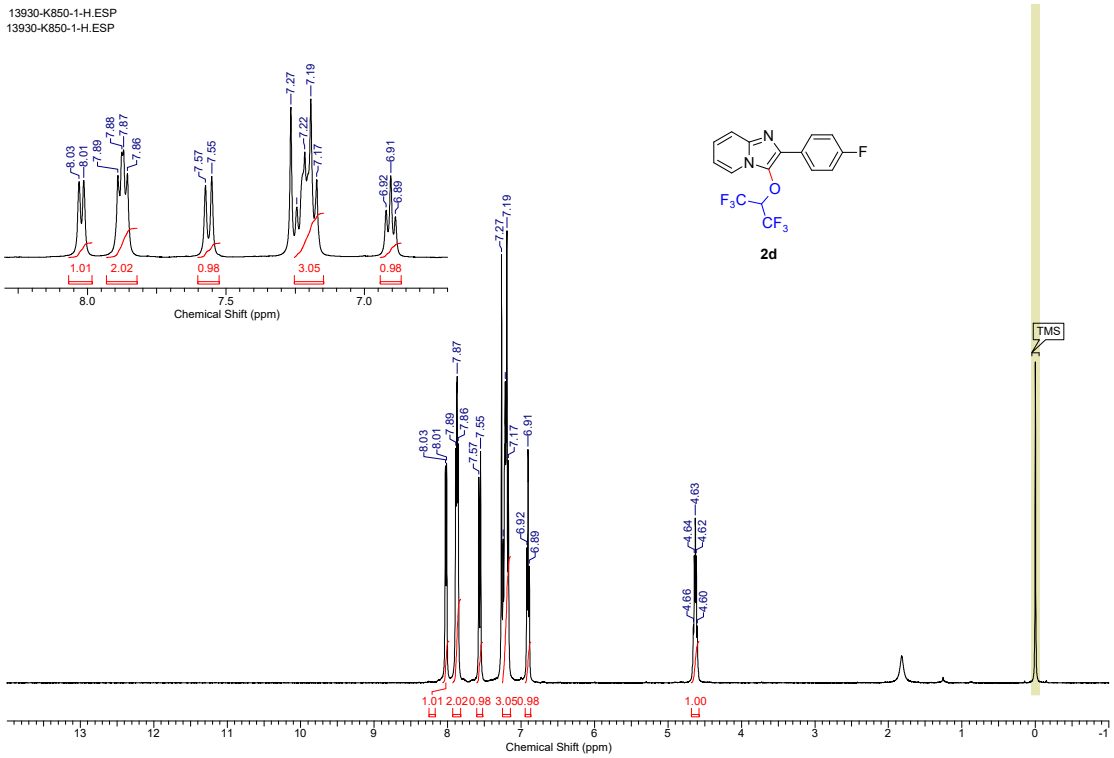


Figure S11. ^{1}H NMR spectrum of compound **2d**

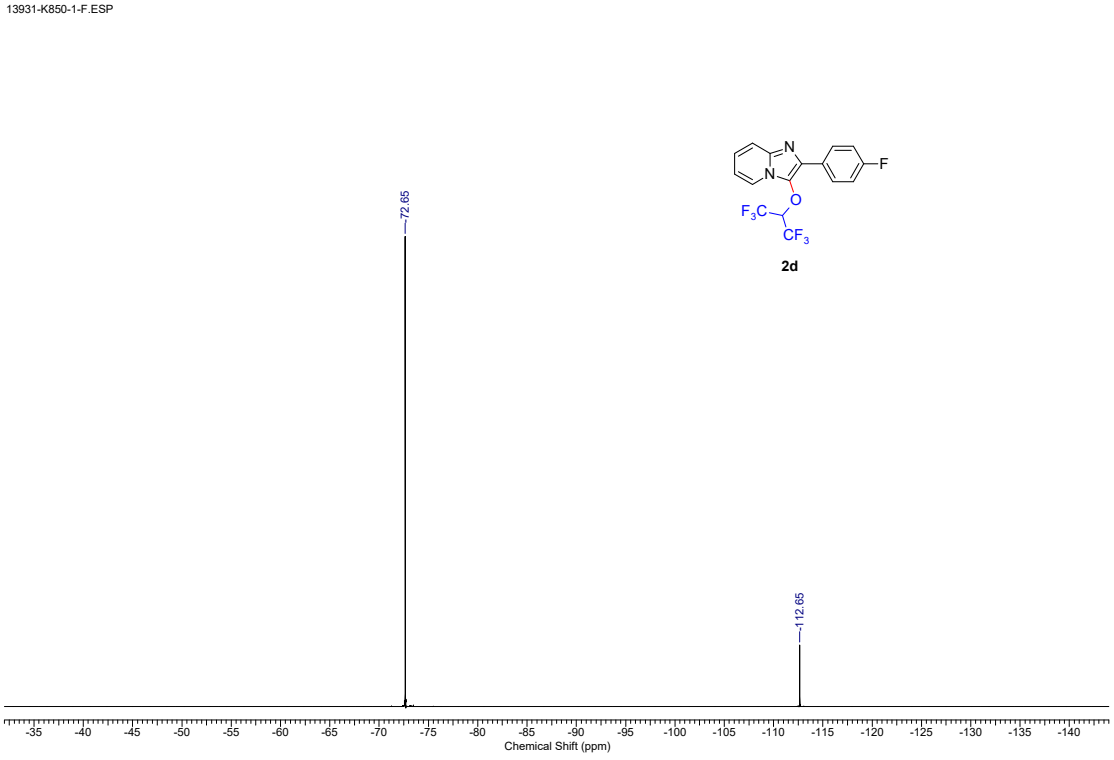


Figure S12. ^{19}F NMR spectrum of compound **2d**

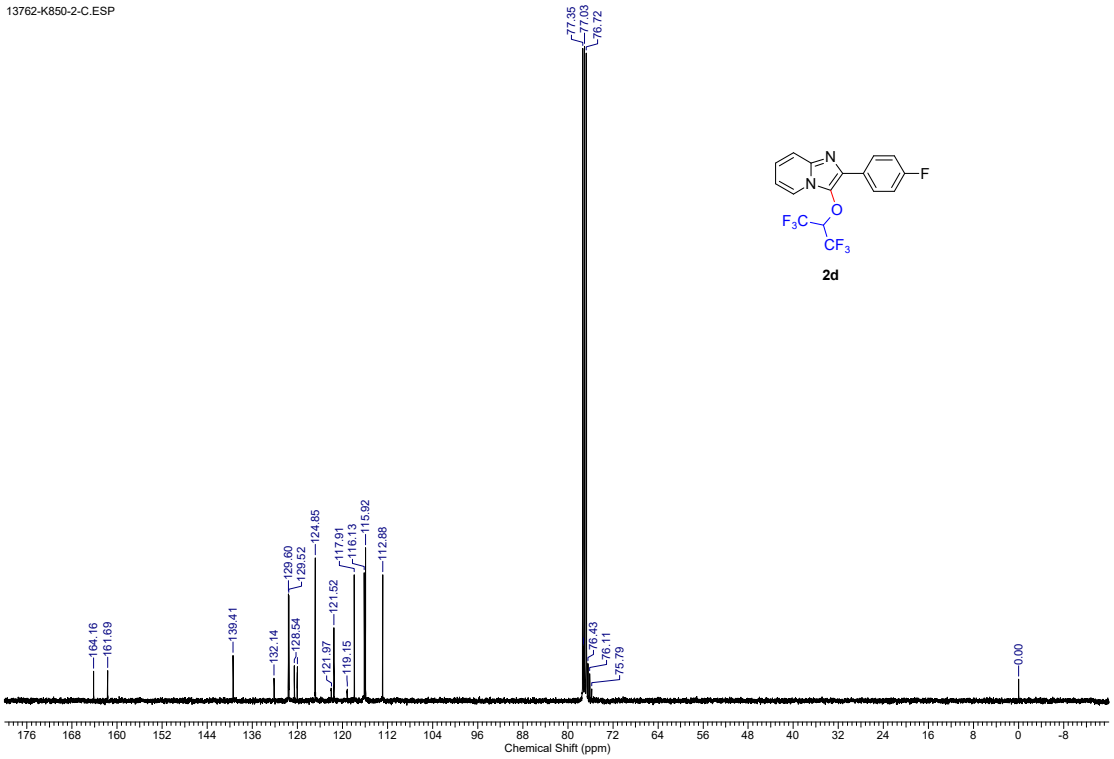


Figure S13. ^{13}C NMR spectrum of compound **2d**

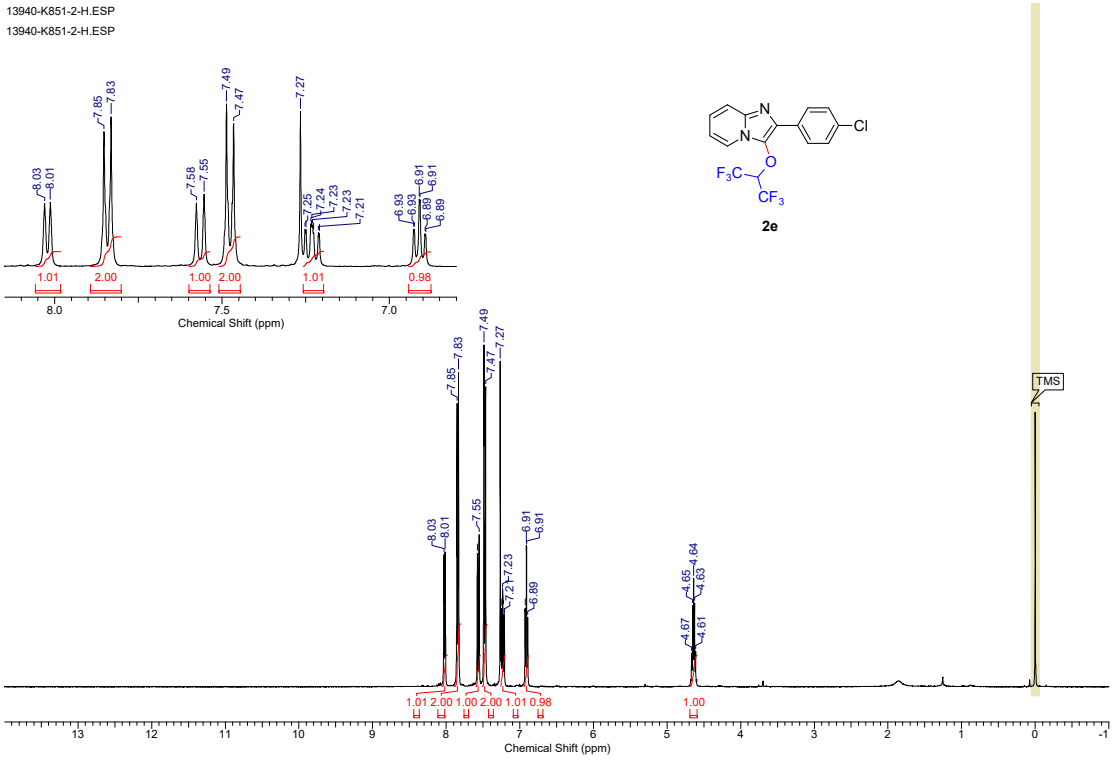


Figure S14. ^{1}H NMR spectrum of compound **2e**

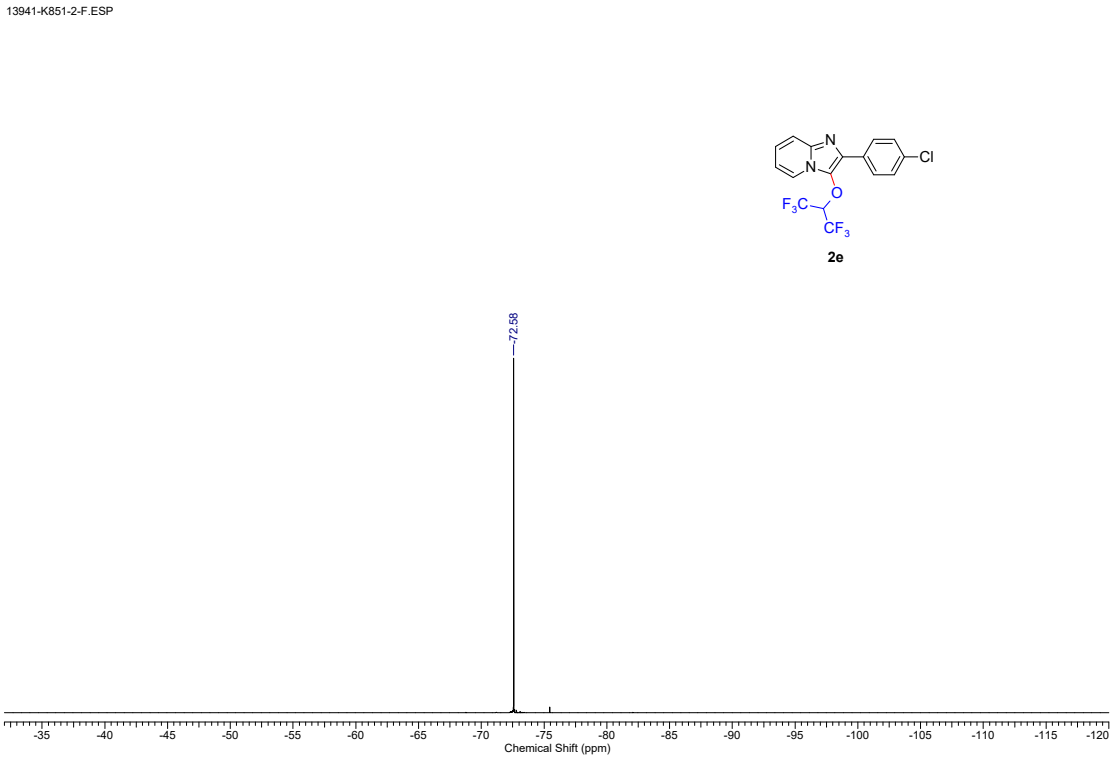


Figure S15. ^{19}F NMR spectrum of compound **2e**

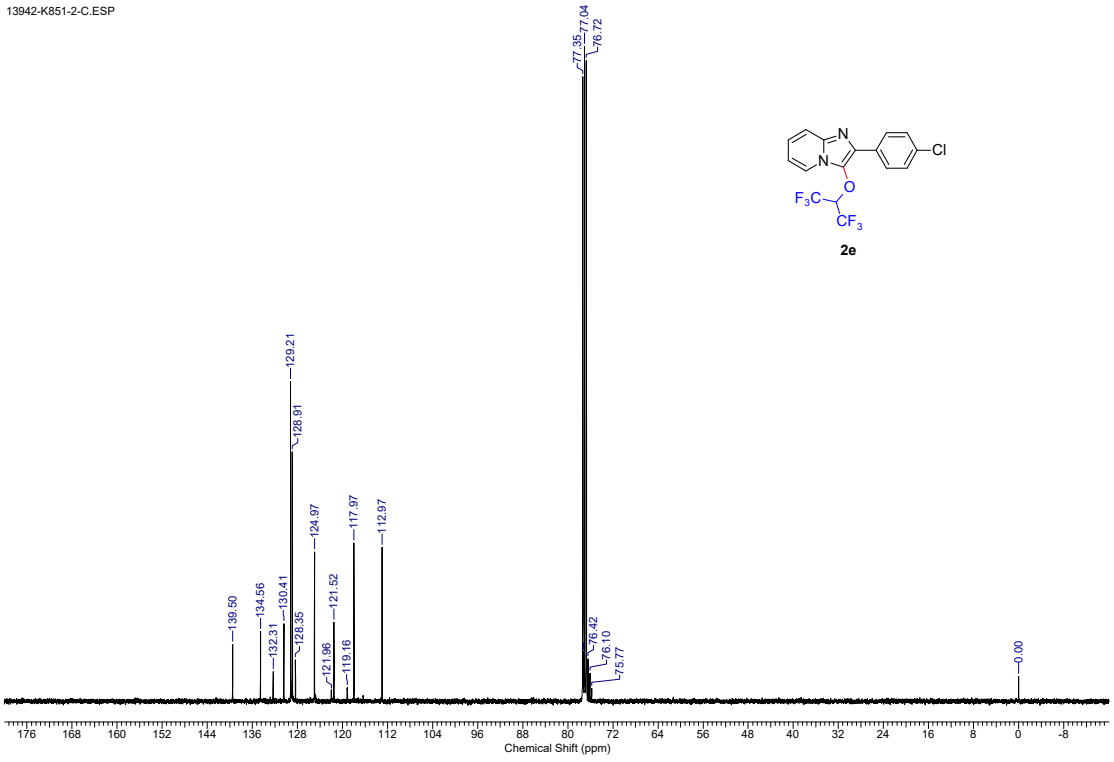


Figure S16. ^{13}C NMR spectrum of compound **2e**

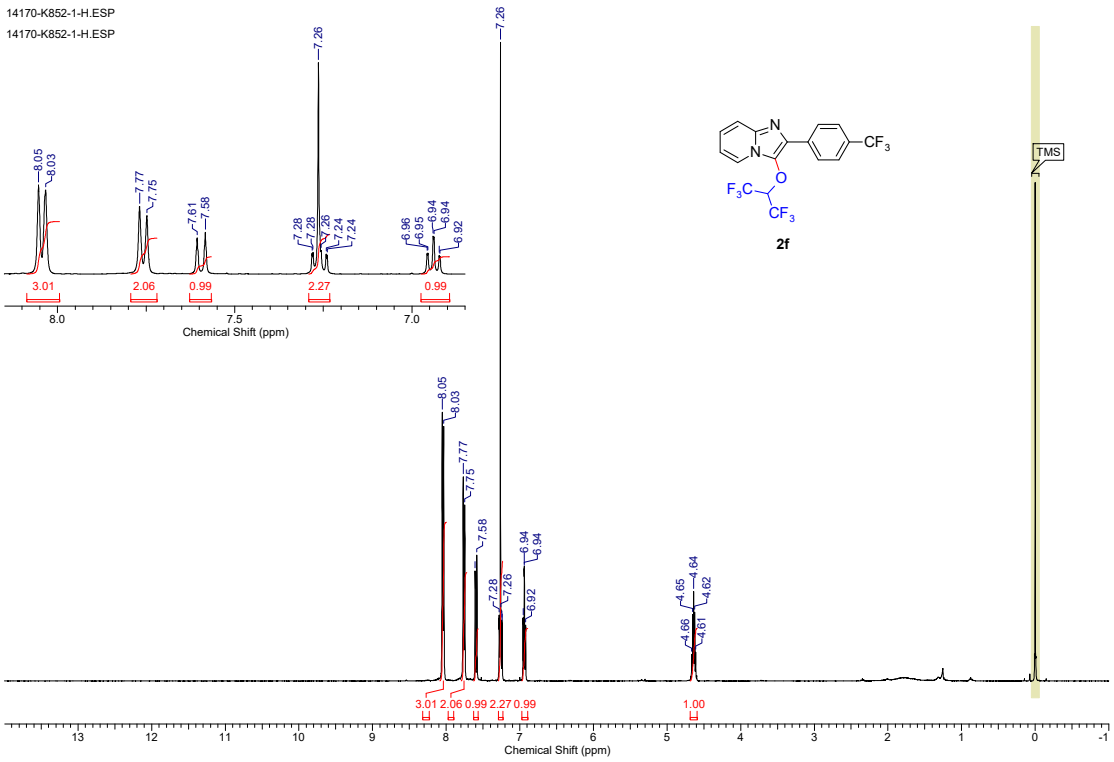


Figure S17. ^{1}H NMR spectrum of compound **2f**

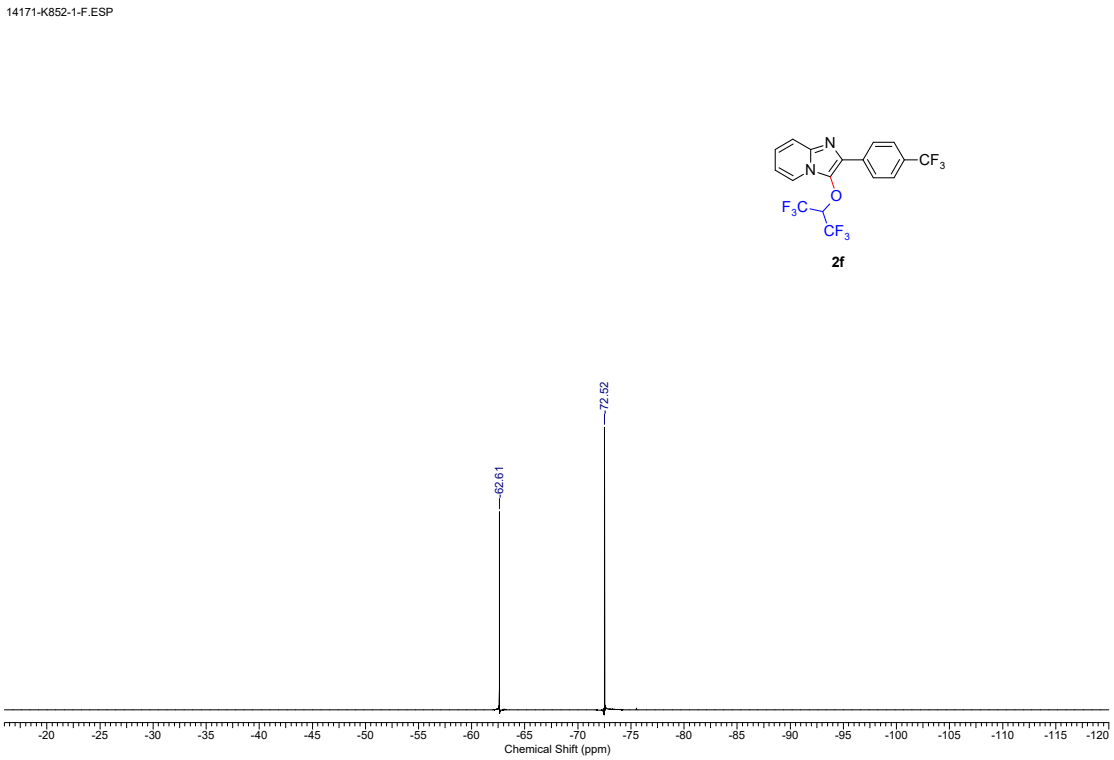


Figure S18. ^{19}F NMR spectrum of compound **2f**

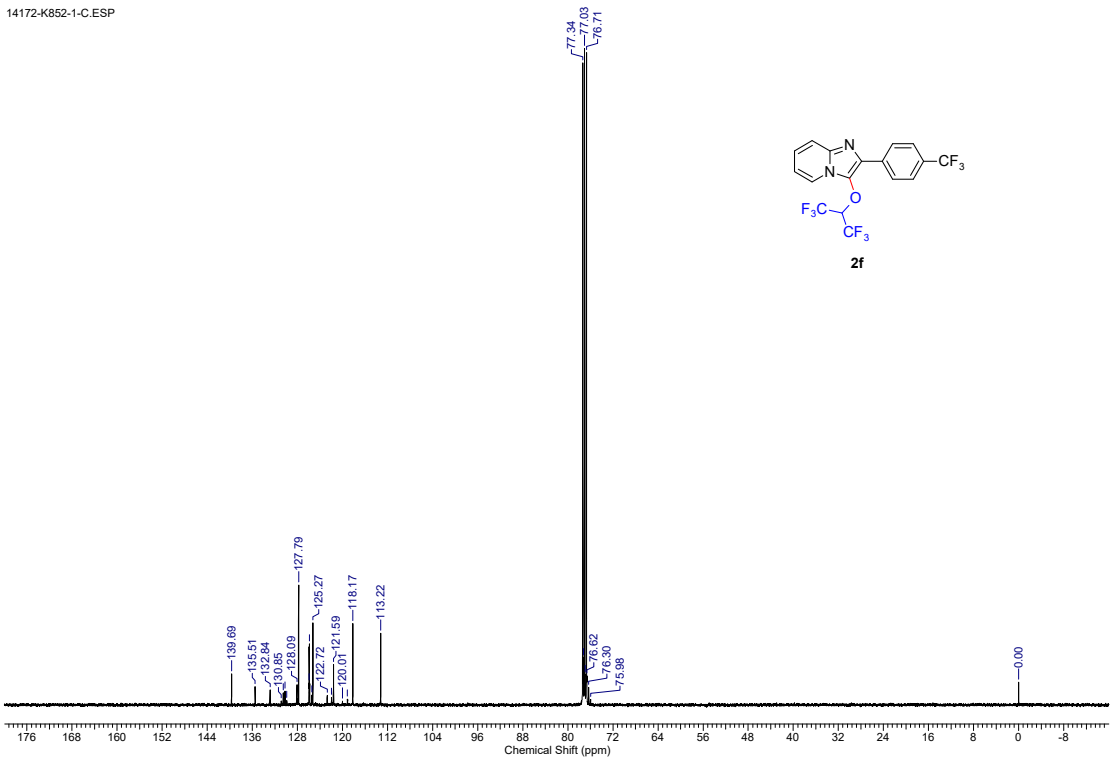


Figure S19. ^{13}C NMR spectrum of compound **2f**

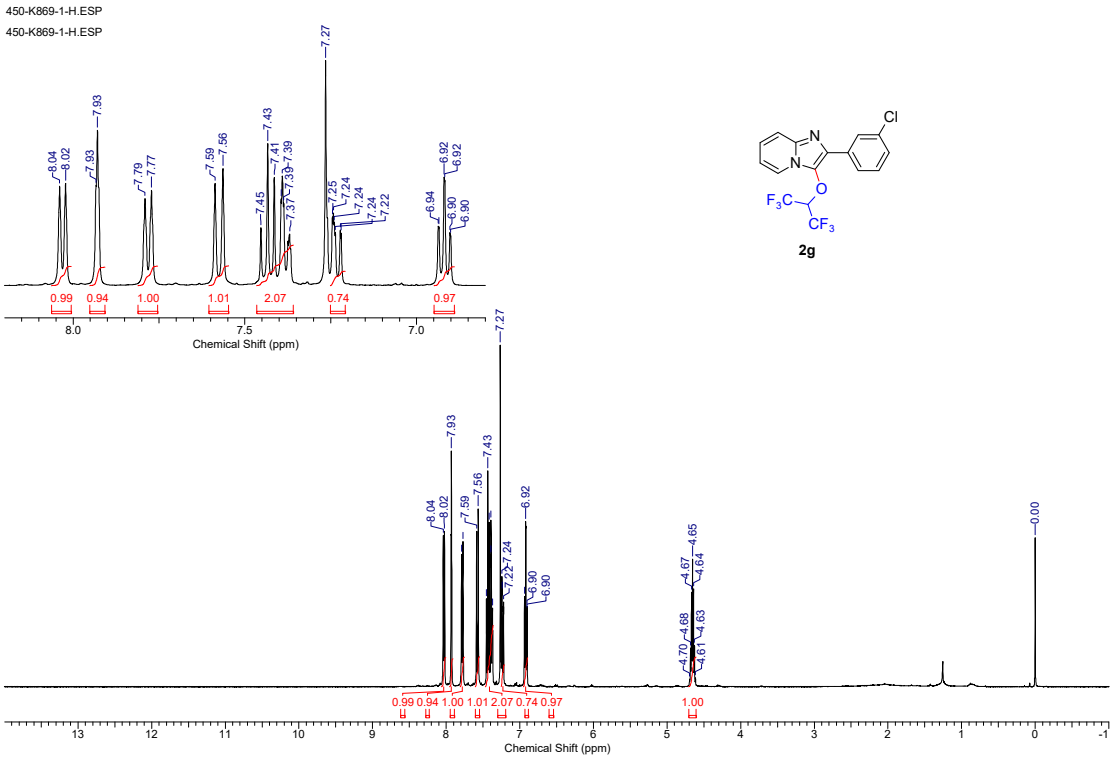


Figure S20. ^{1}H NMR spectrum of compound **2g**

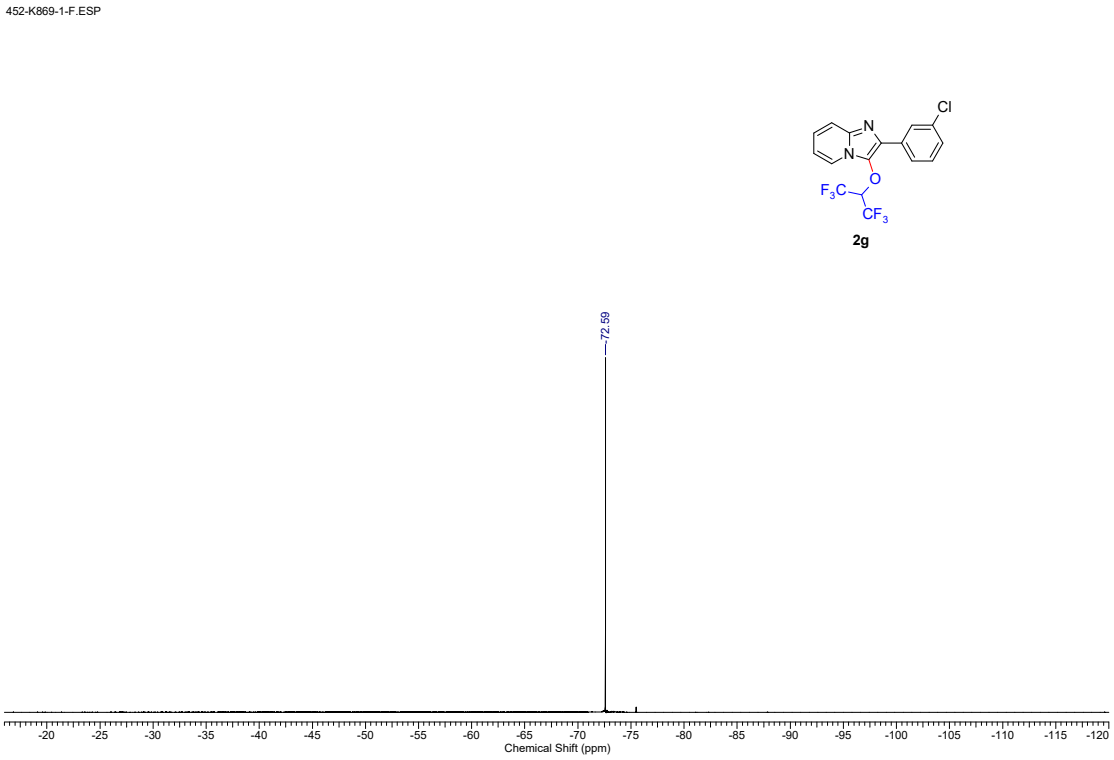


Figure S21. ^{19}F NMR spectrum of compound **2g**

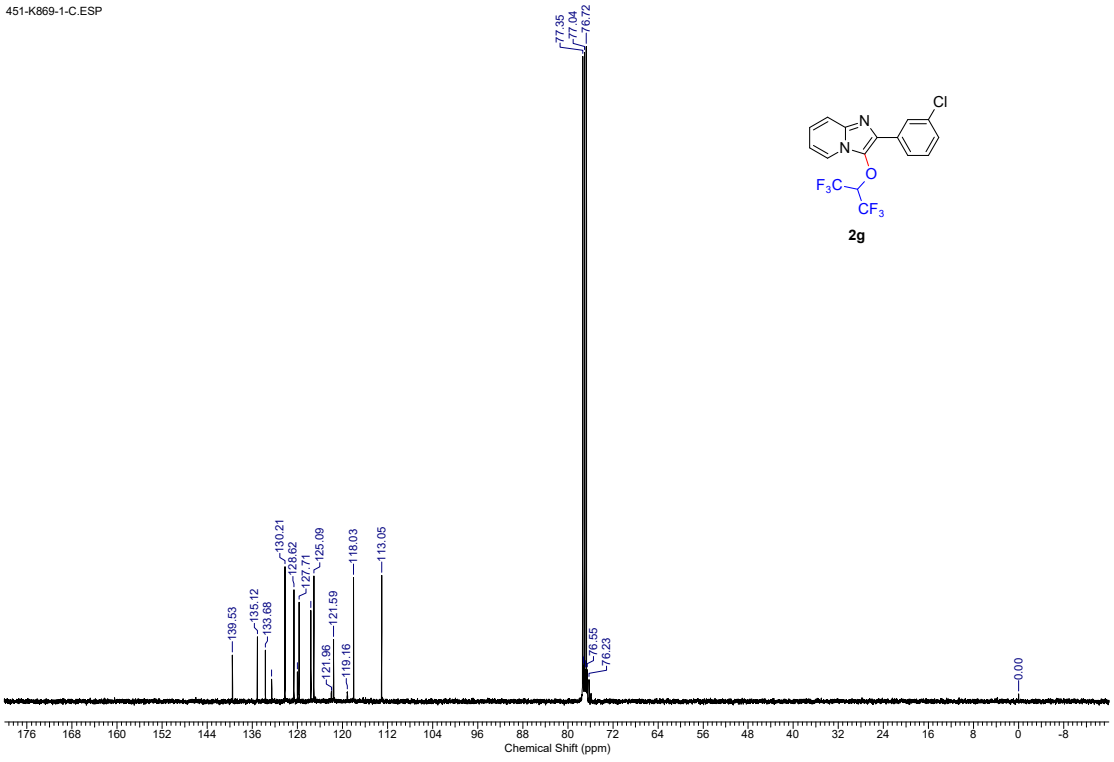


Figure S22. ^{13}C NMR spectrum of compound **2g**

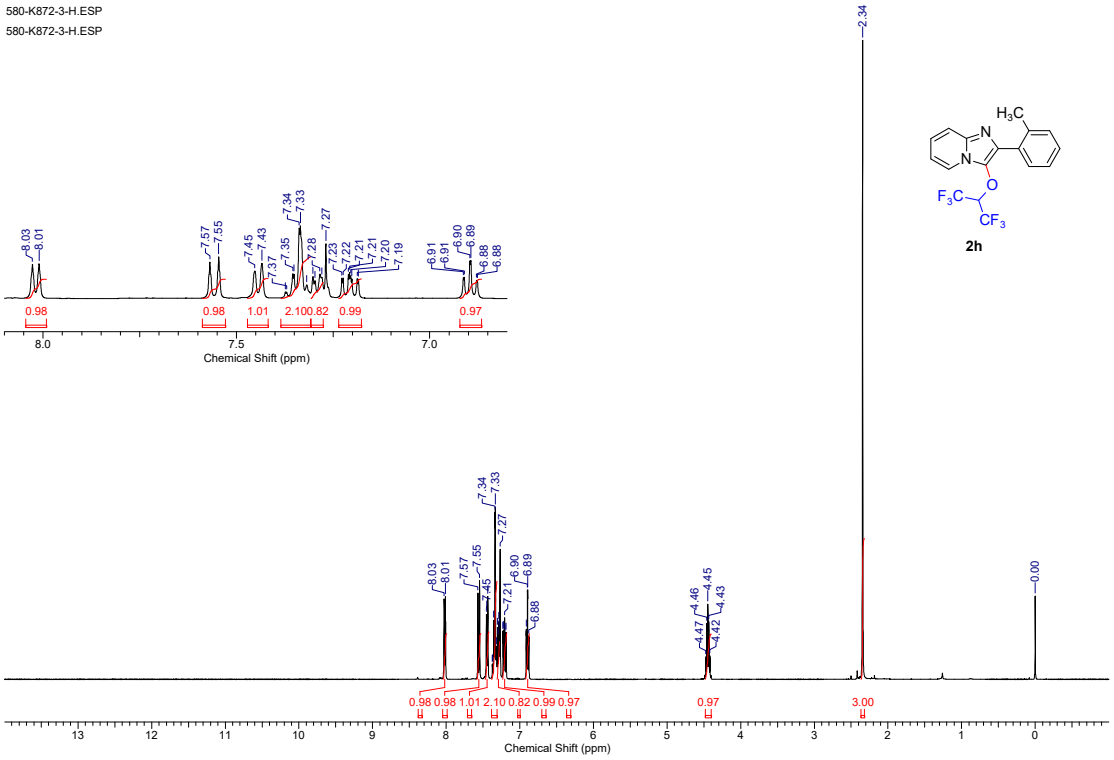


Figure S23. ^{1}H NMR spectrum of compound **2h**

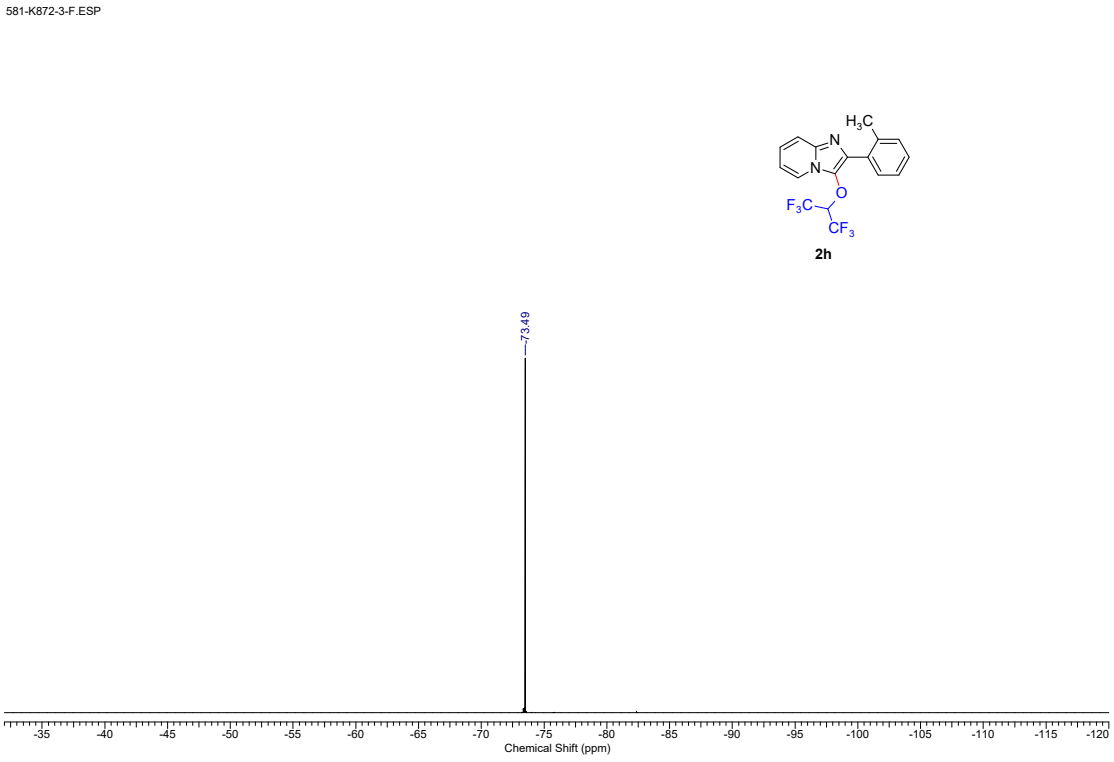


Figure S24. ^{19}F NMR spectrum of compound **2h**

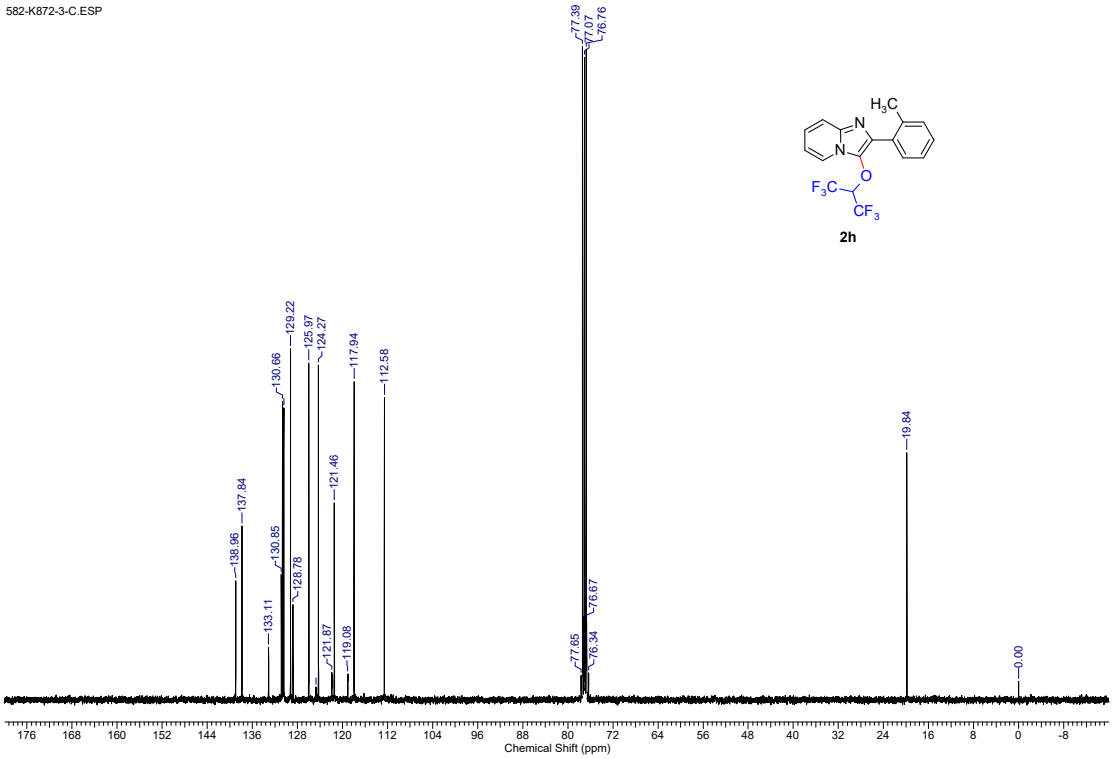


Figure S25. ^{13}C NMR spectrum of compound **2h**

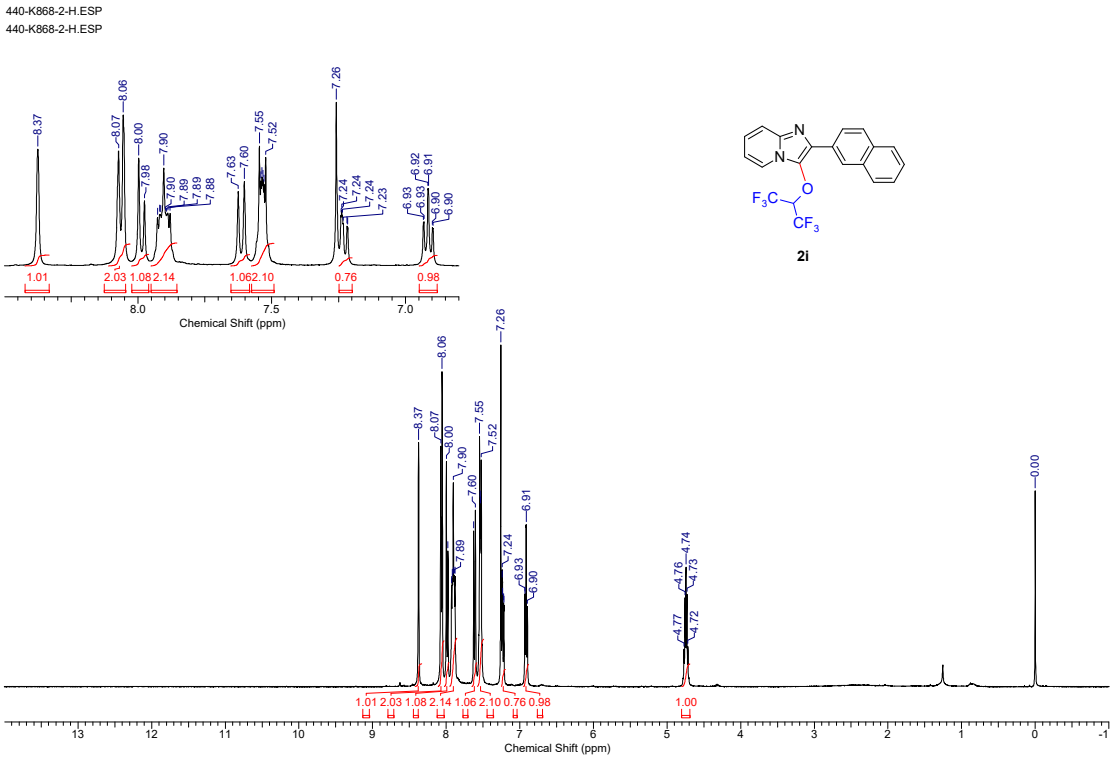


Figure S26. ^{1}H NMR spectrum of compound **2i**

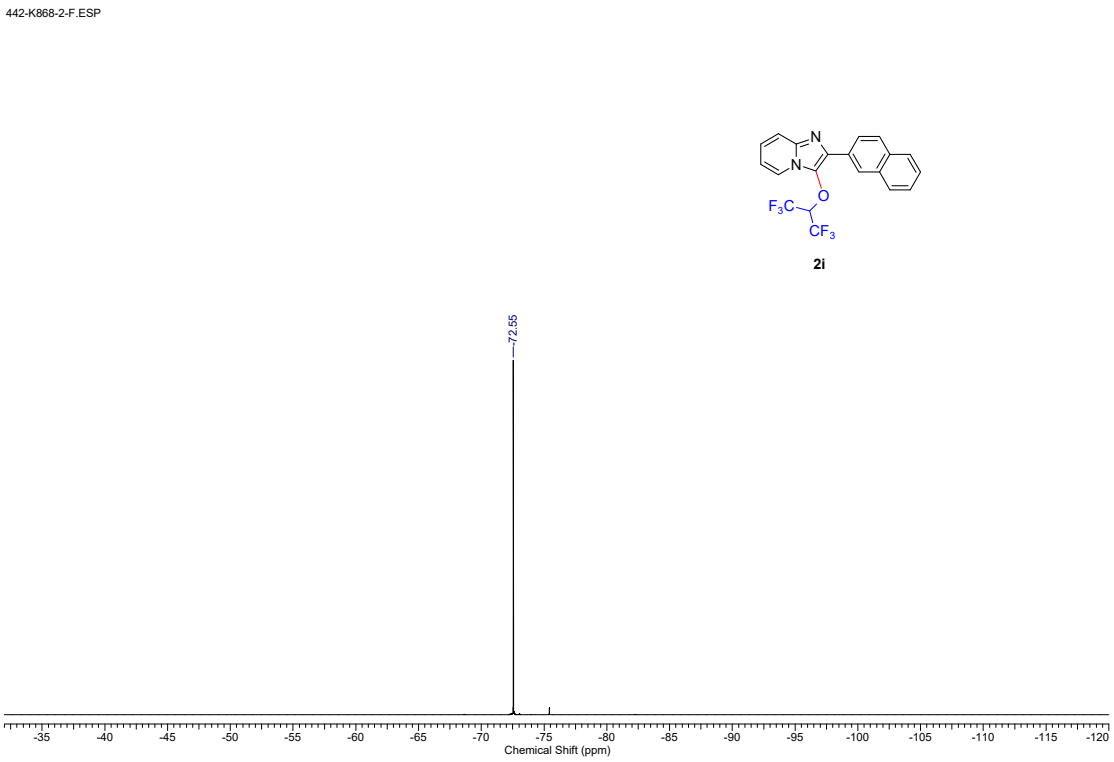


Figure S27. ^{19}F NMR spectrum of compound **2i**

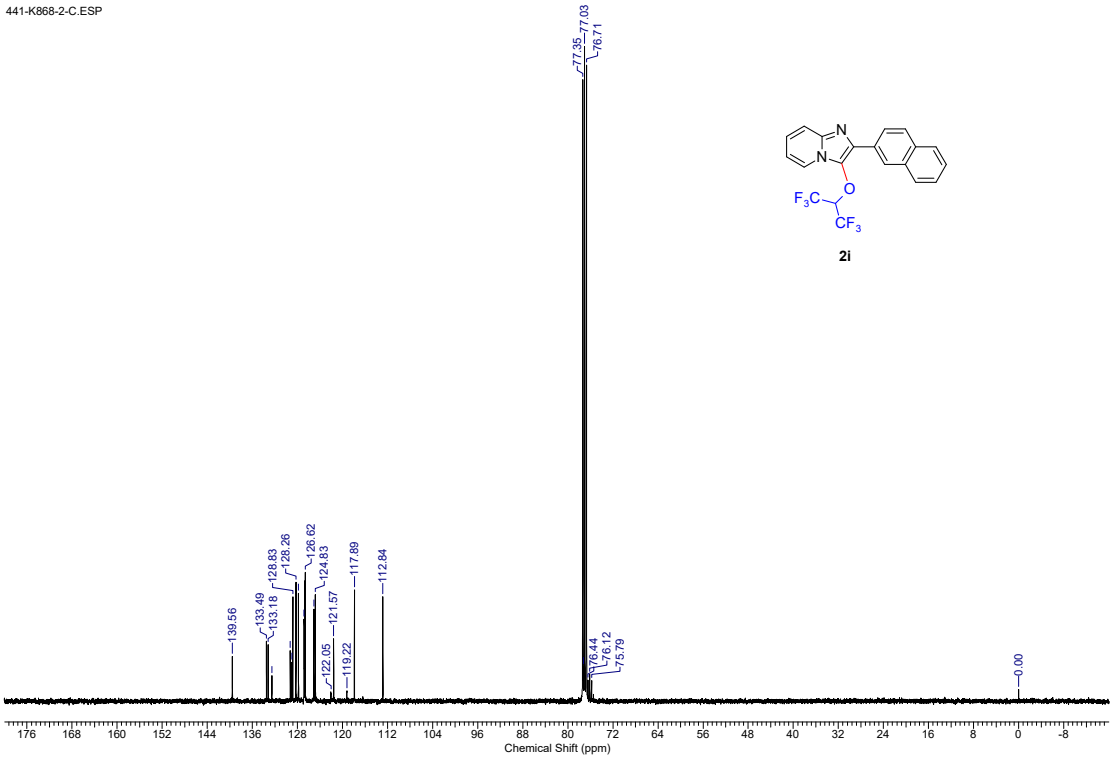


Figure S28. ^{13}C NMR spectrum of compound **2i**

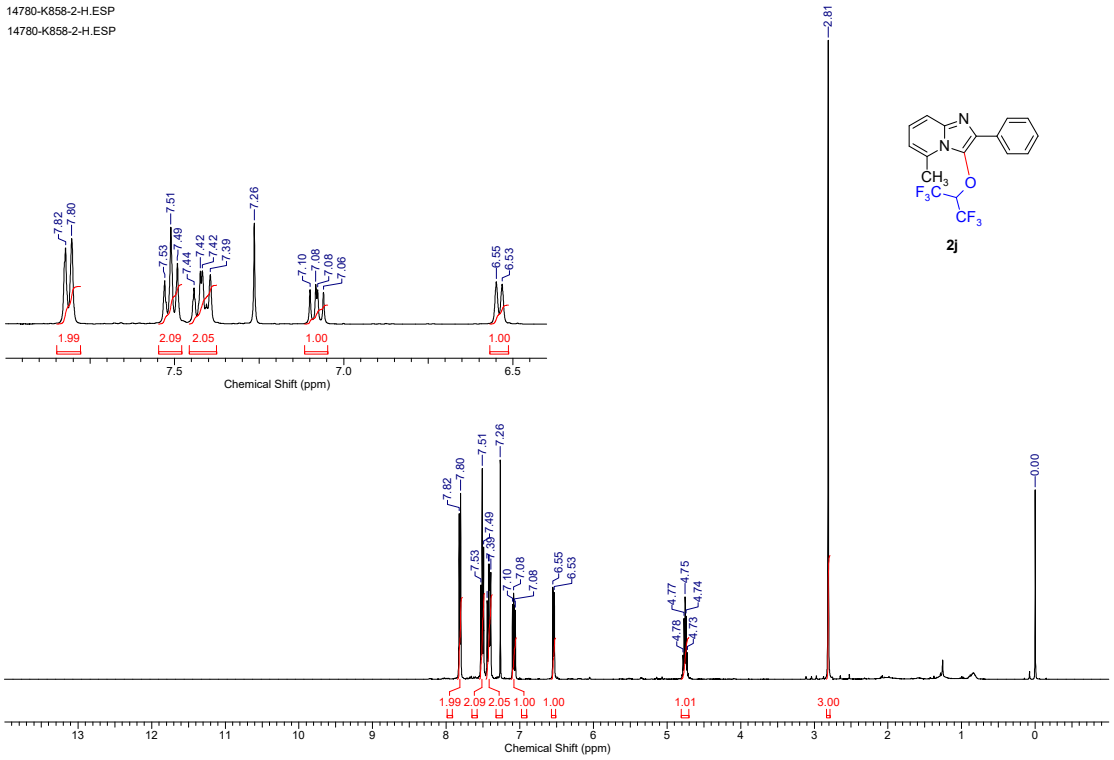


Figure S29. ^{1}H NMR spectrum of compound **2j**

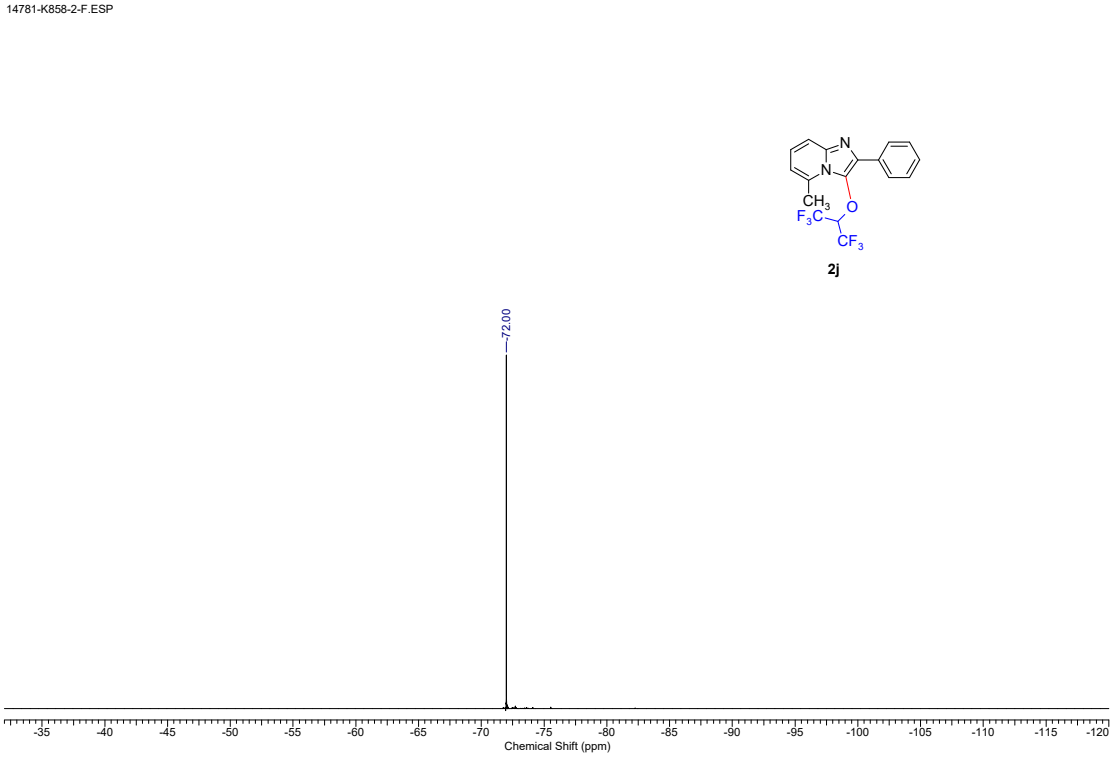


Figure S30. ^{19}F NMR spectrum of compound **2j**

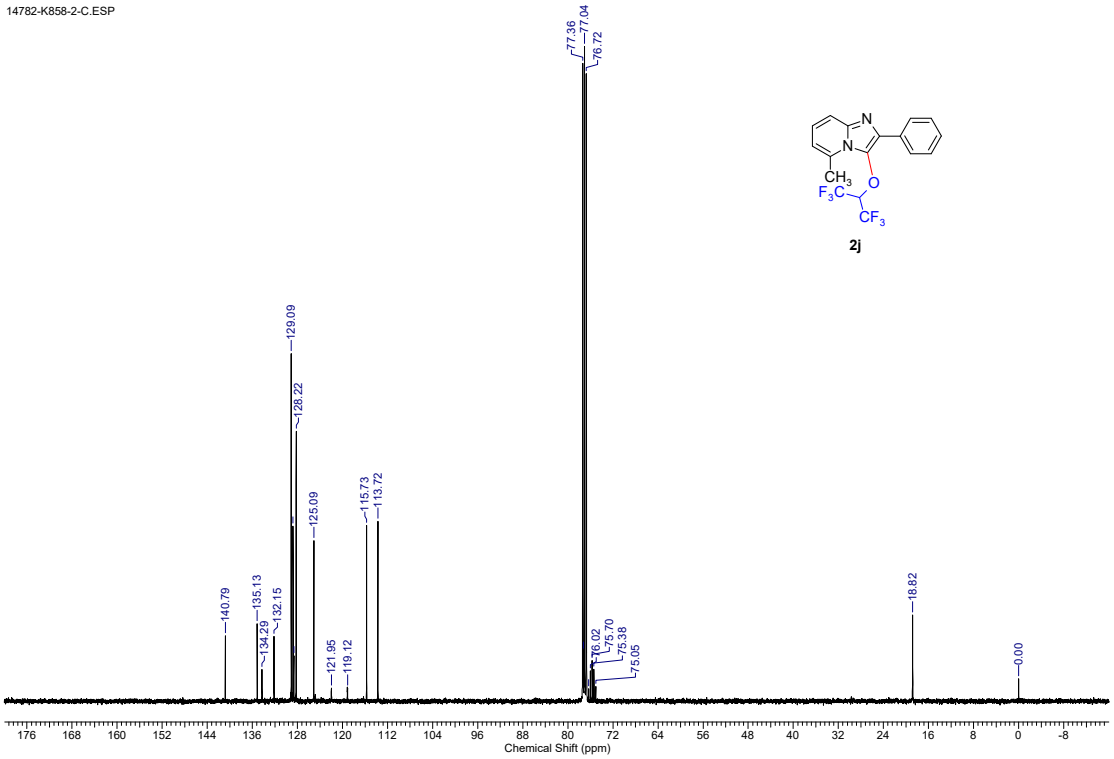


Figure S31. ^{13}C NMR spectrum of compound **2j**

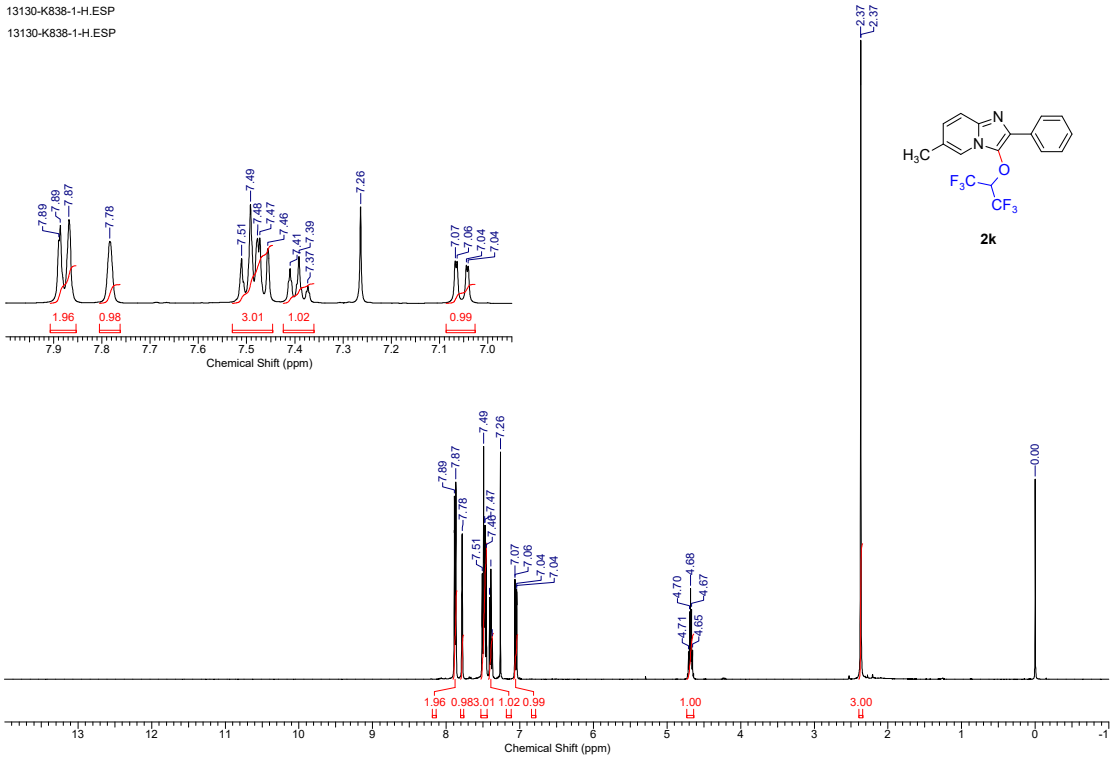


Figure S32. ^{1}H NMR spectrum of compound **2k**

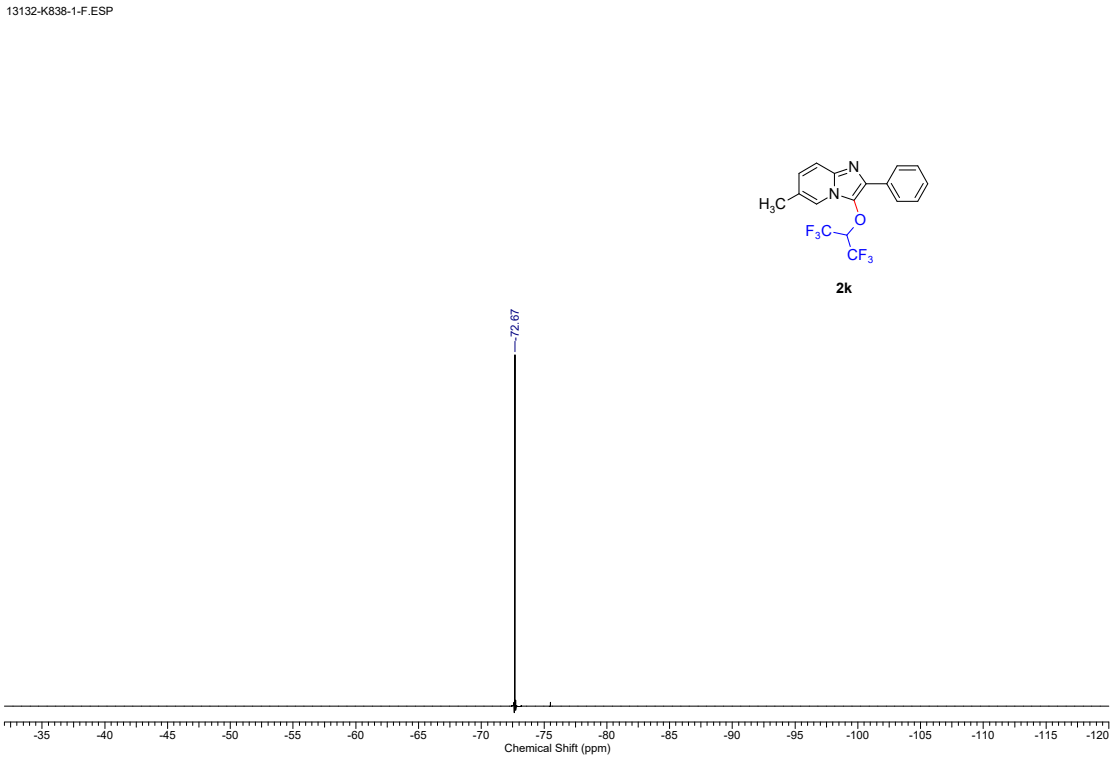


Figure S33. ^{19}F NMR spectrum of compound **2k**

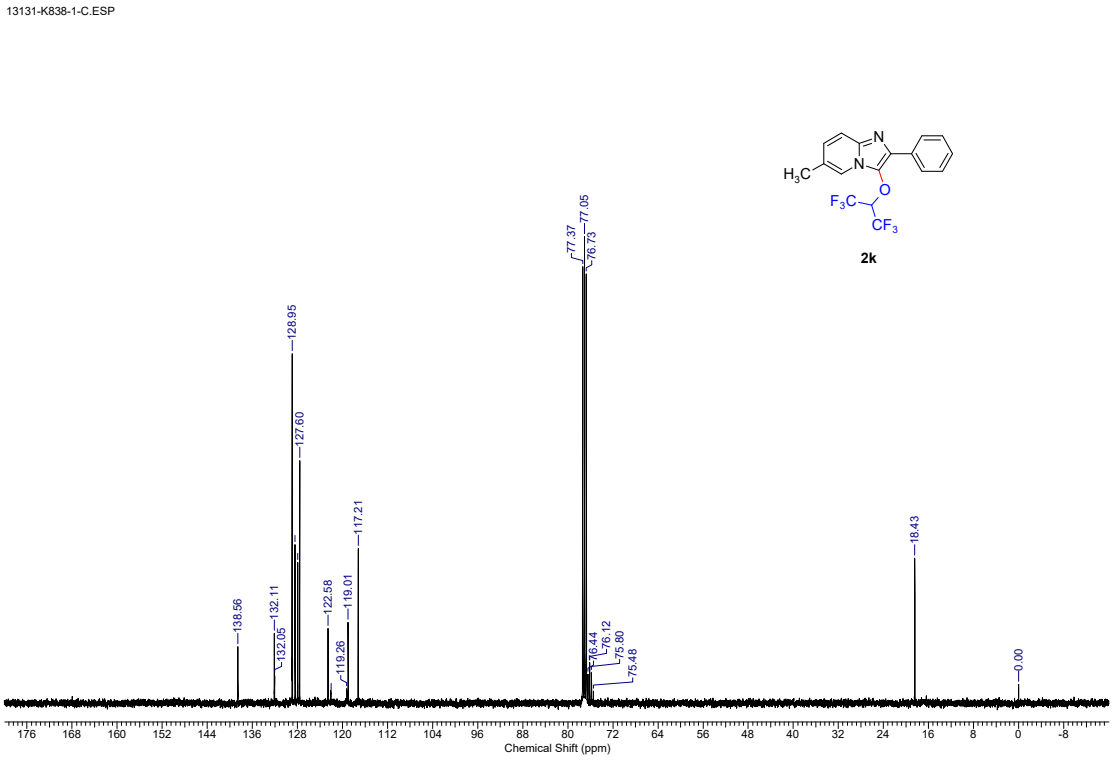


Figure S34. ^{13}C NMR spectrum of compound **2k**

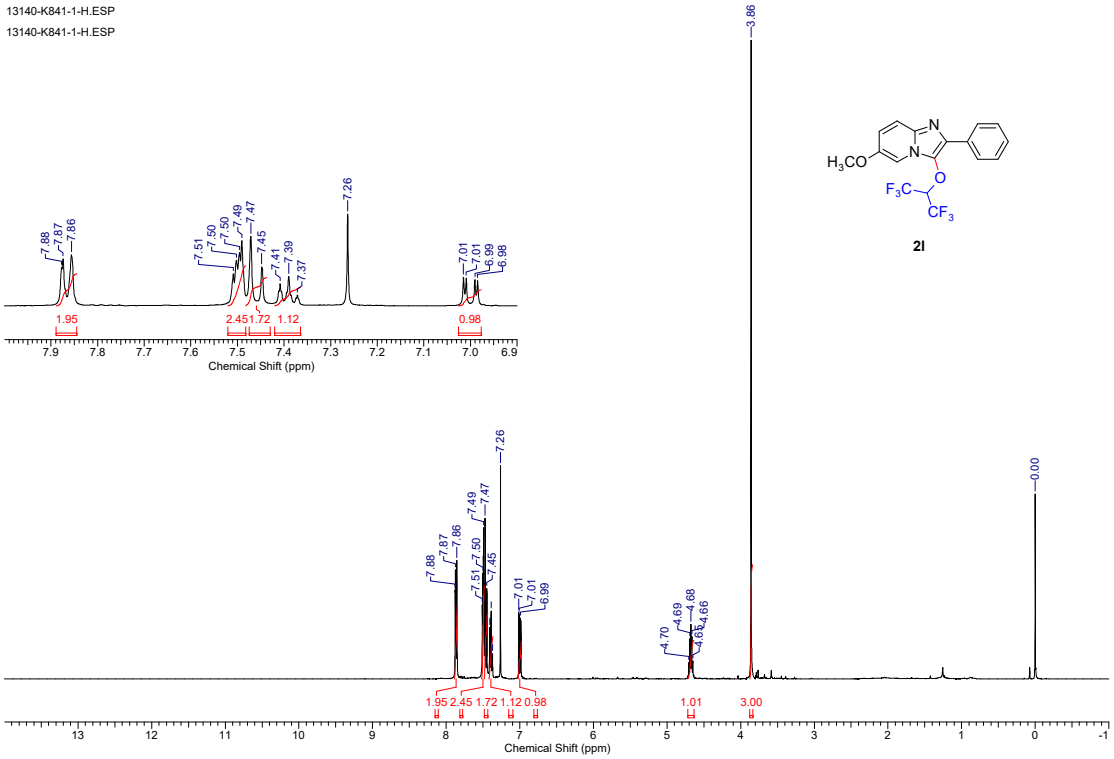


Figure S35. ^{1}H NMR spectrum of compound **2l**

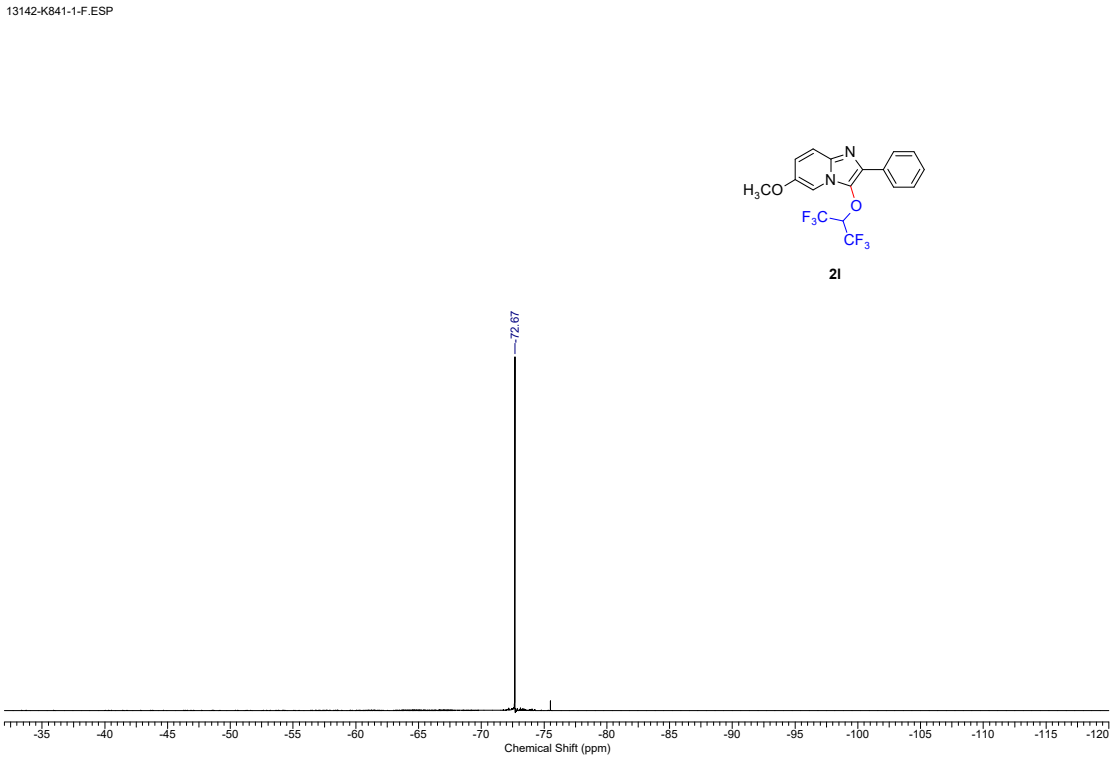


Figure S36. ^{19}F NMR spectrum of compound **2l**

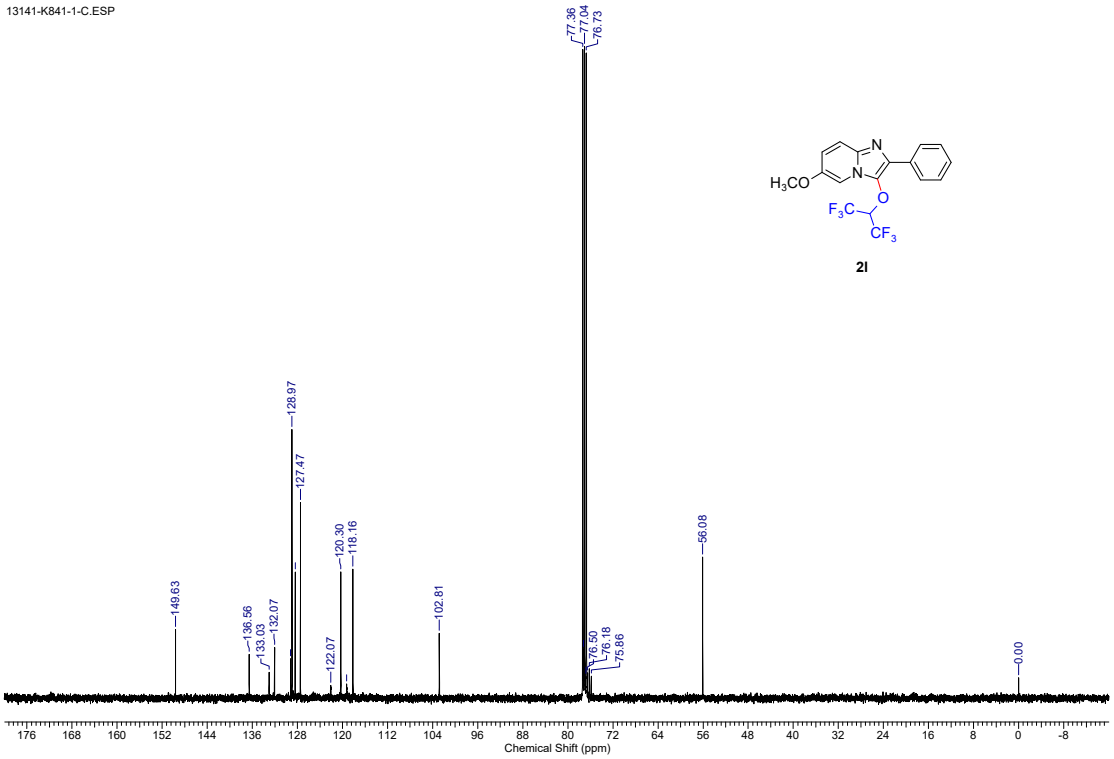


Figure S37. ^{13}C NMR spectrum of compound **2l**

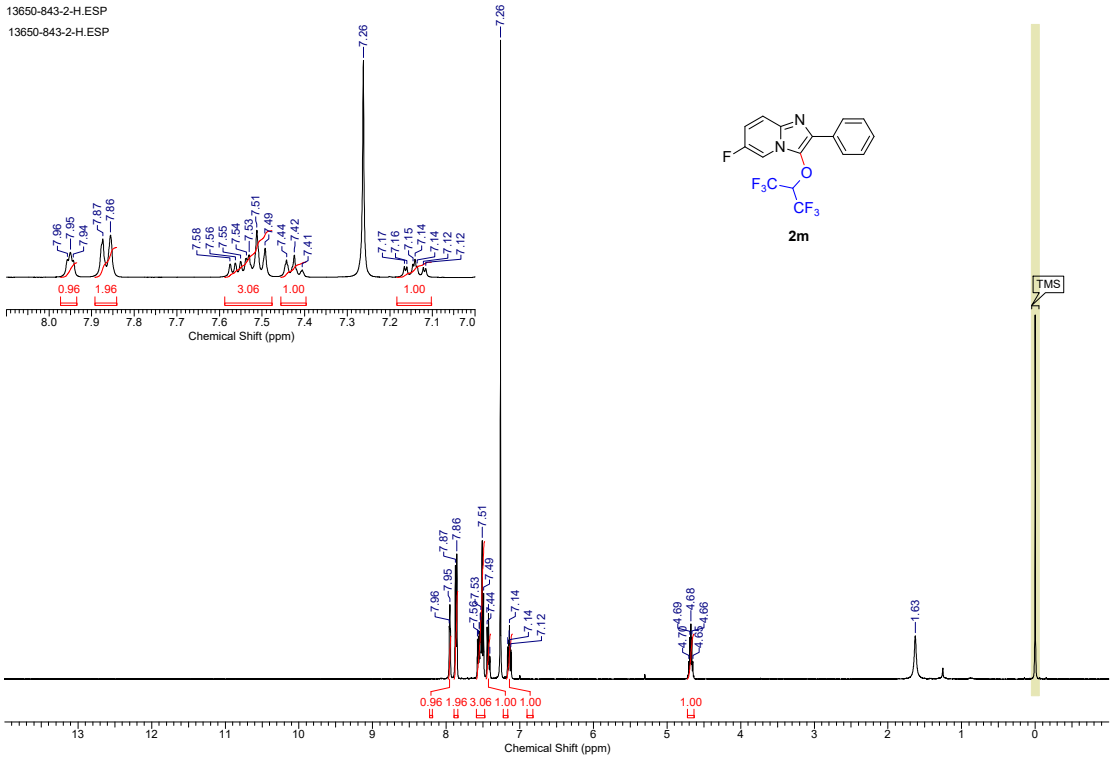


Figure S38. ^{1}H NMR spectrum of compound **2m**

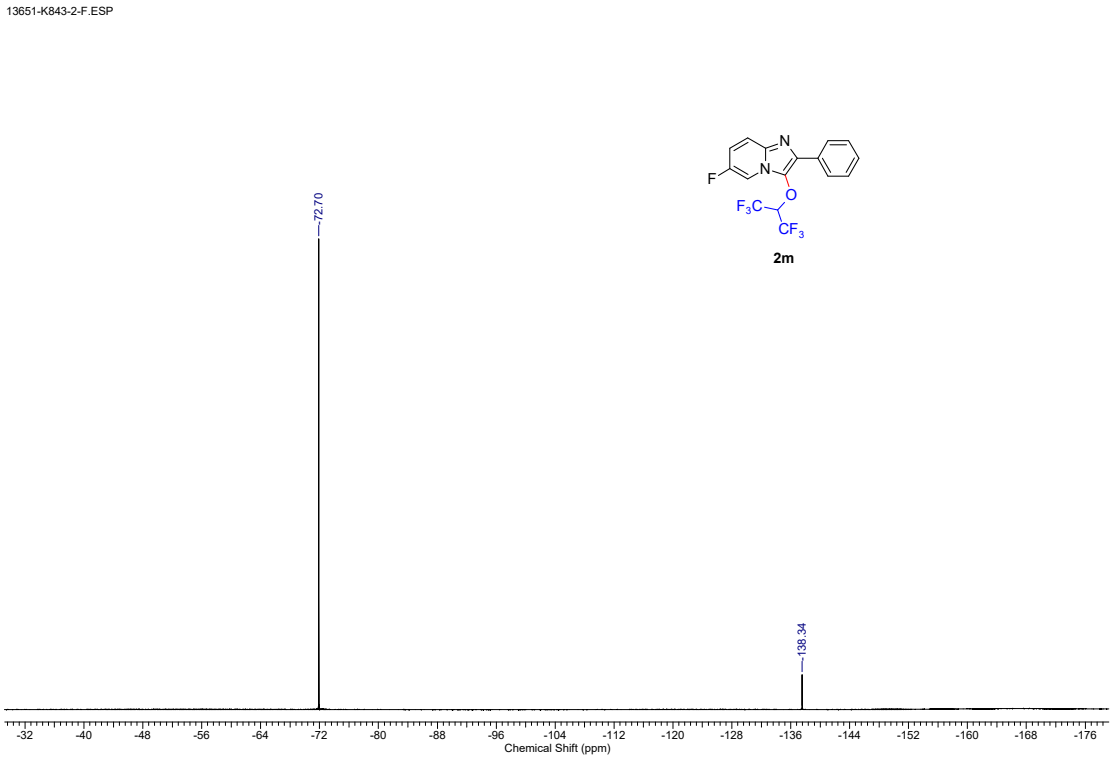


Figure S39. ^{19}F NMR spectrum of compound **2m**

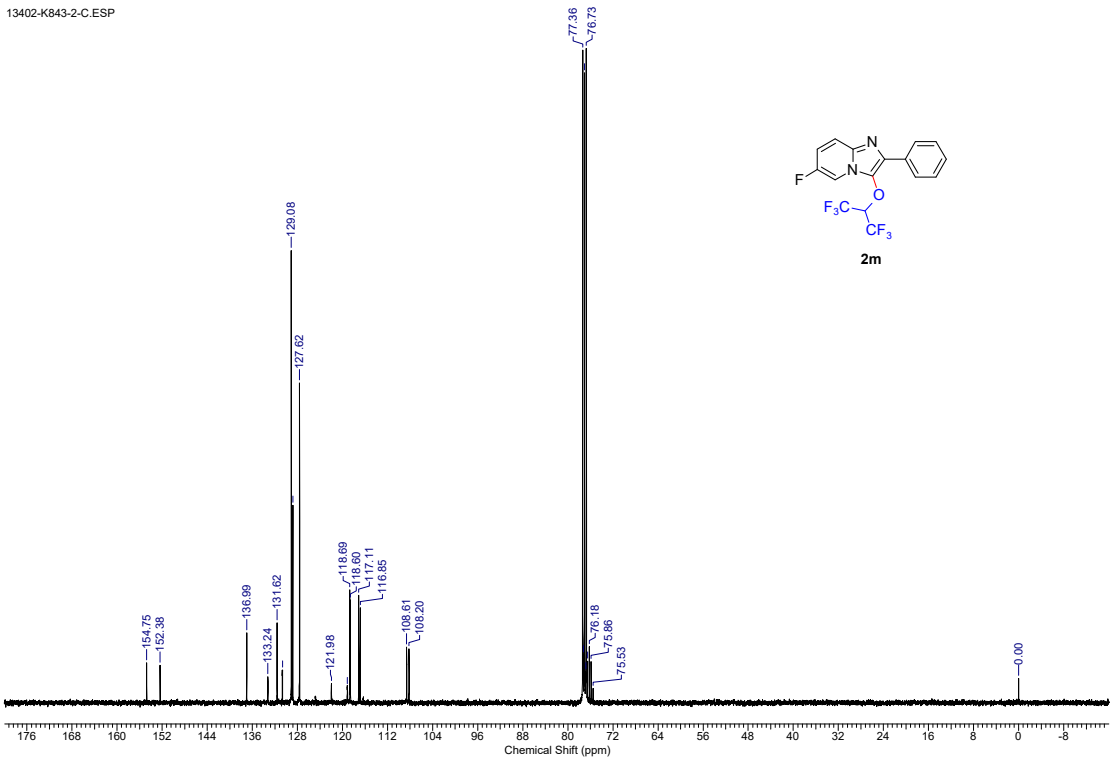


Figure S40. ^{13}C NMR spectrum of compound **2m**

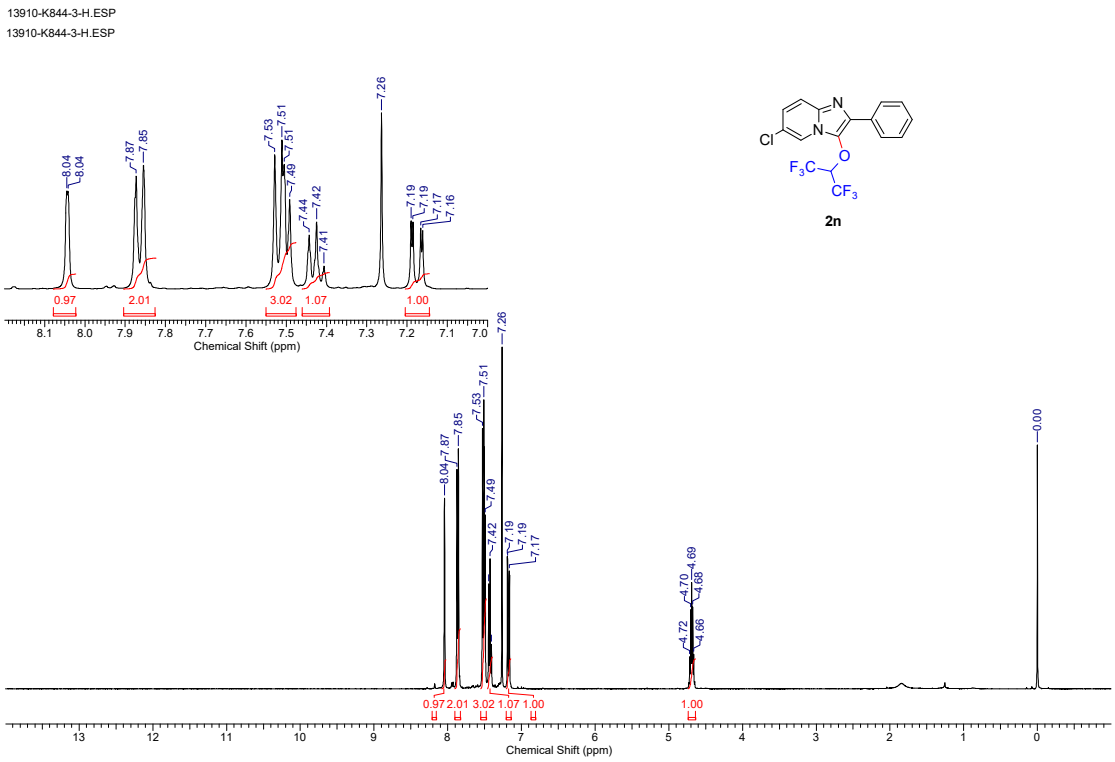


Figure S41. ^{1}H NMR spectrum of compound **2n**

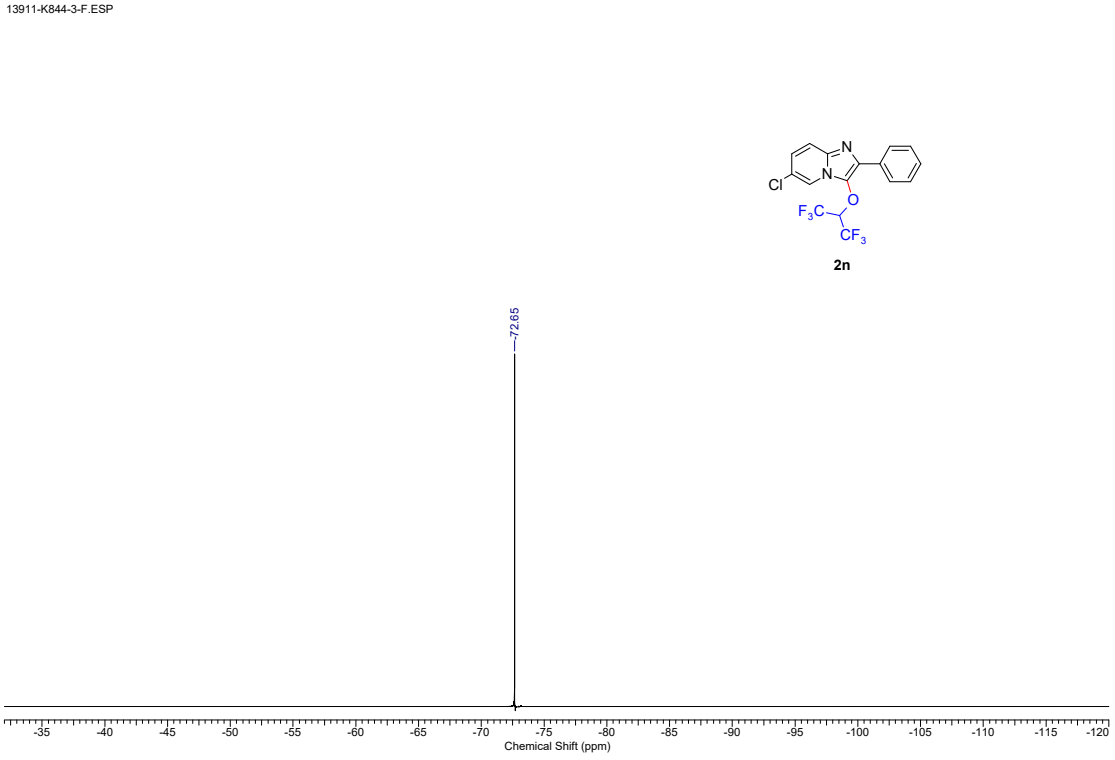


Figure S42. ^{19}F NMR spectrum of compound **2n**

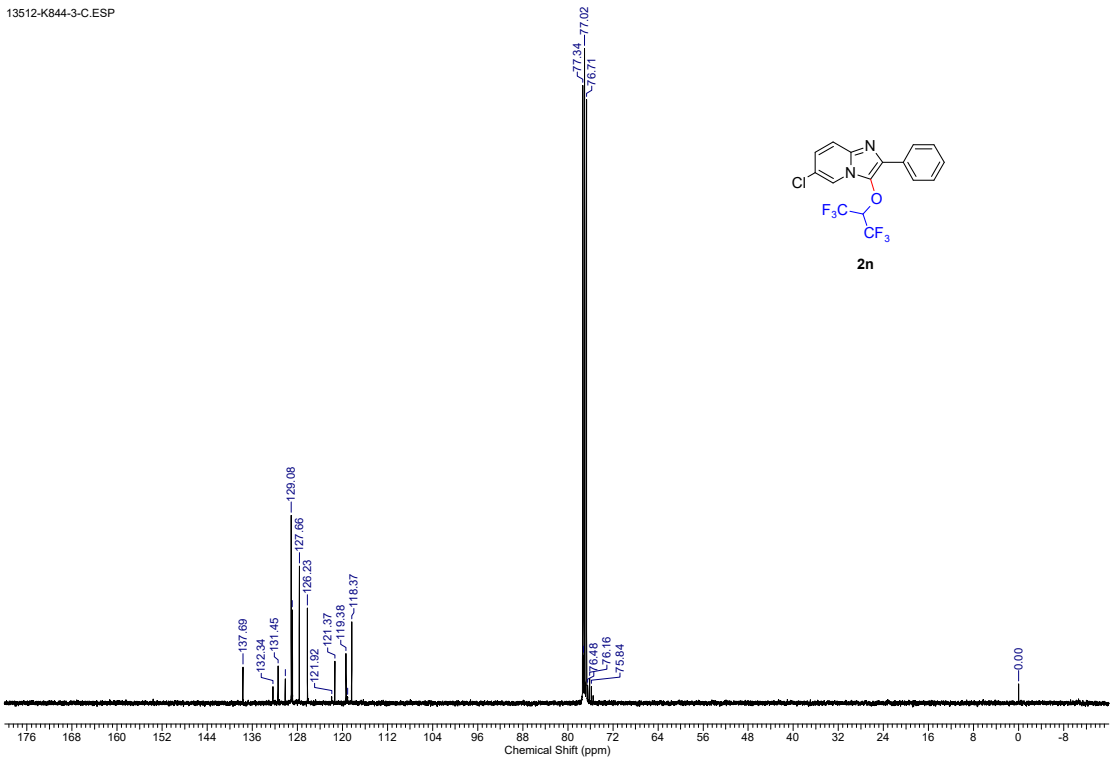


Figure S43. ^{13}C NMR spectrum of compound **2n**

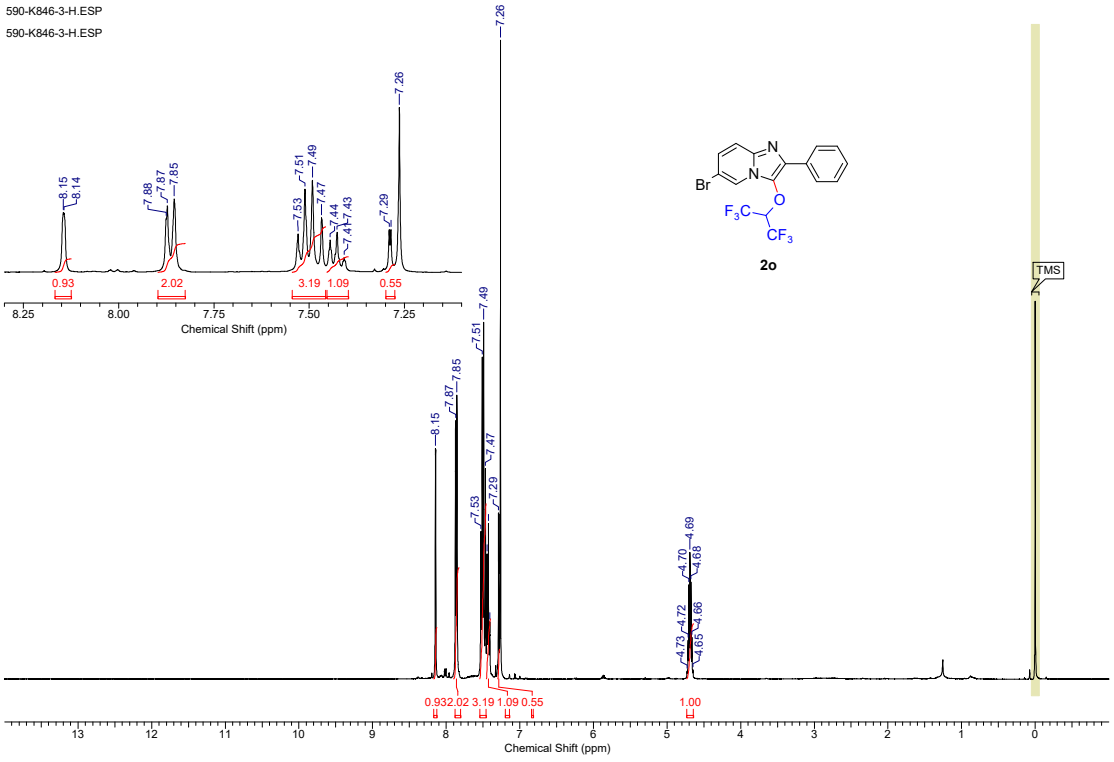


Figure S44. ^{1}H NMR spectrum of compound **2o**

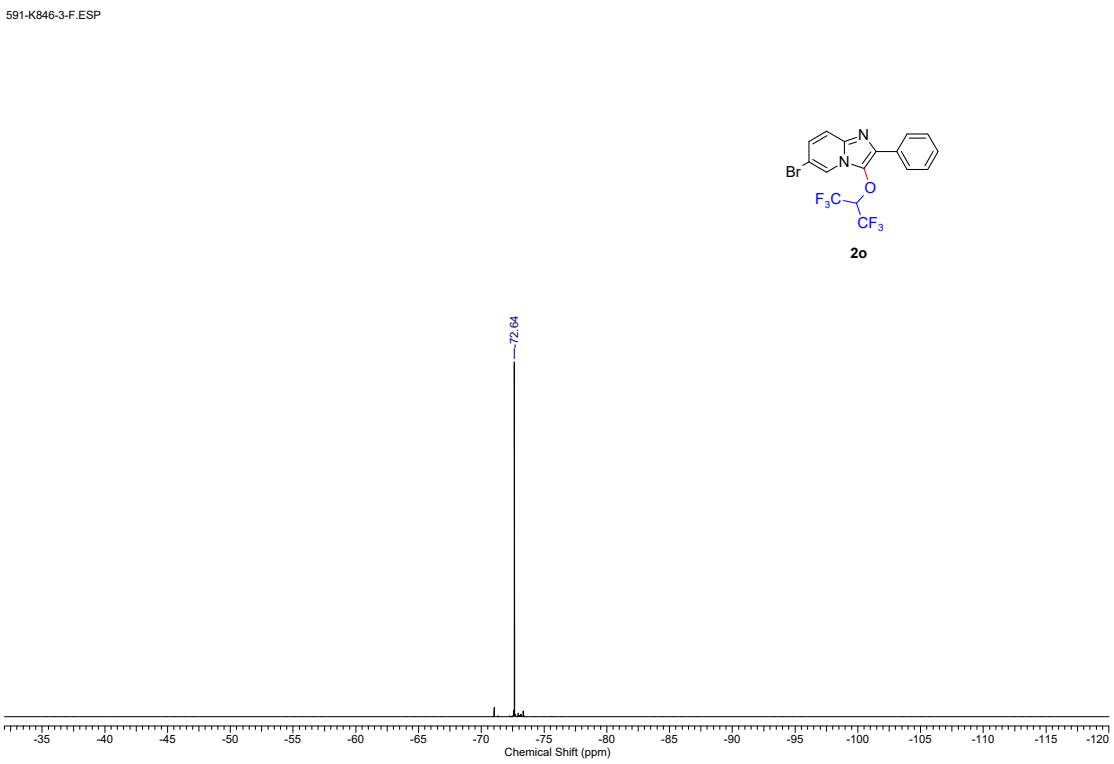


Figure S45. ^{19}F NMR spectrum of compound **2o**

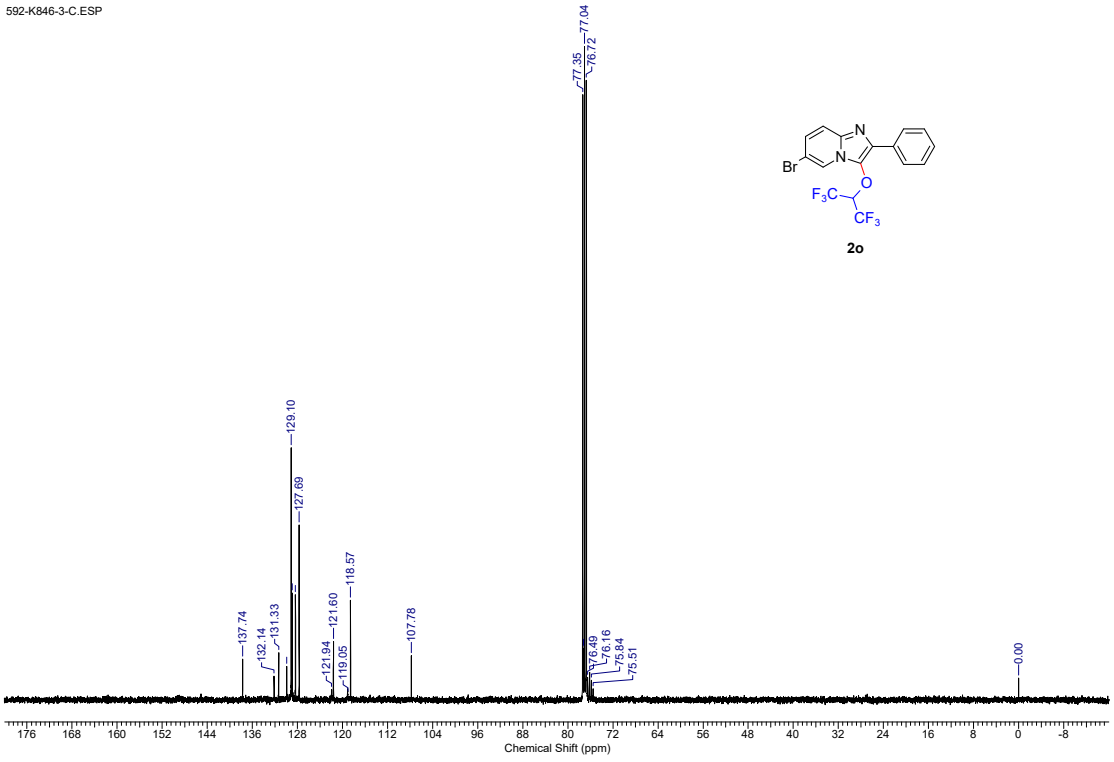


Figure S46. ^{13}C NMR spectrum of compound **2o**

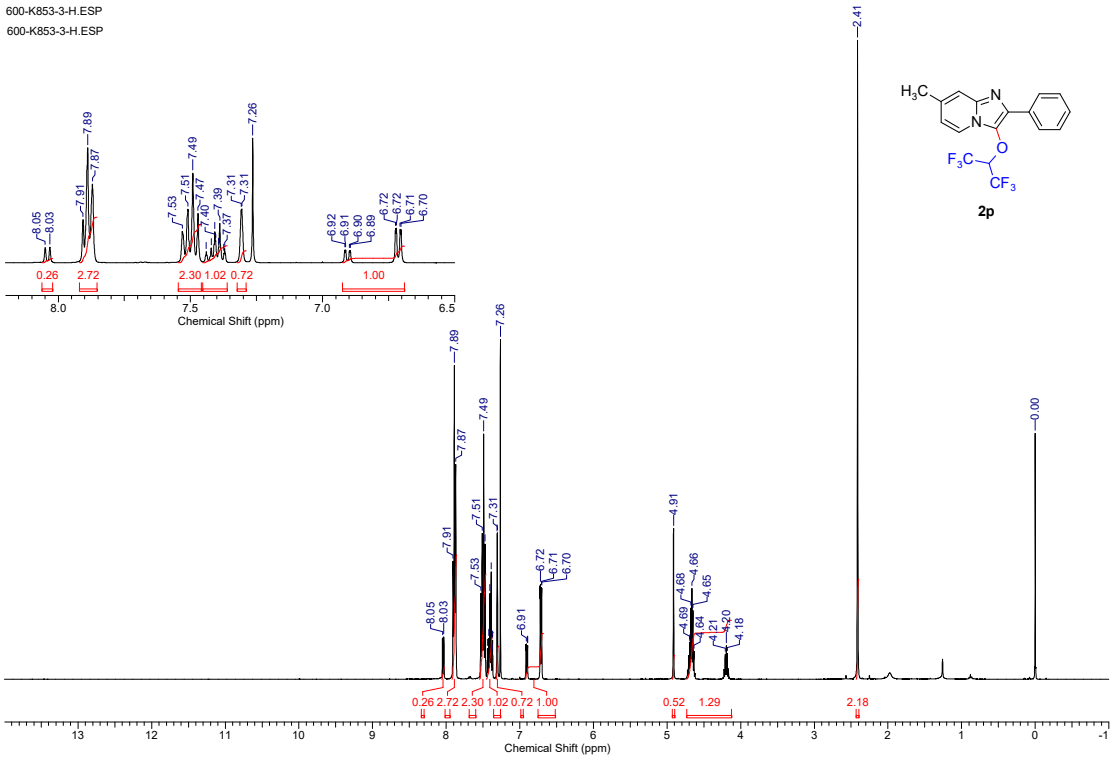


Figure S47. ^{1}H NMR spectrum of compound **2p**

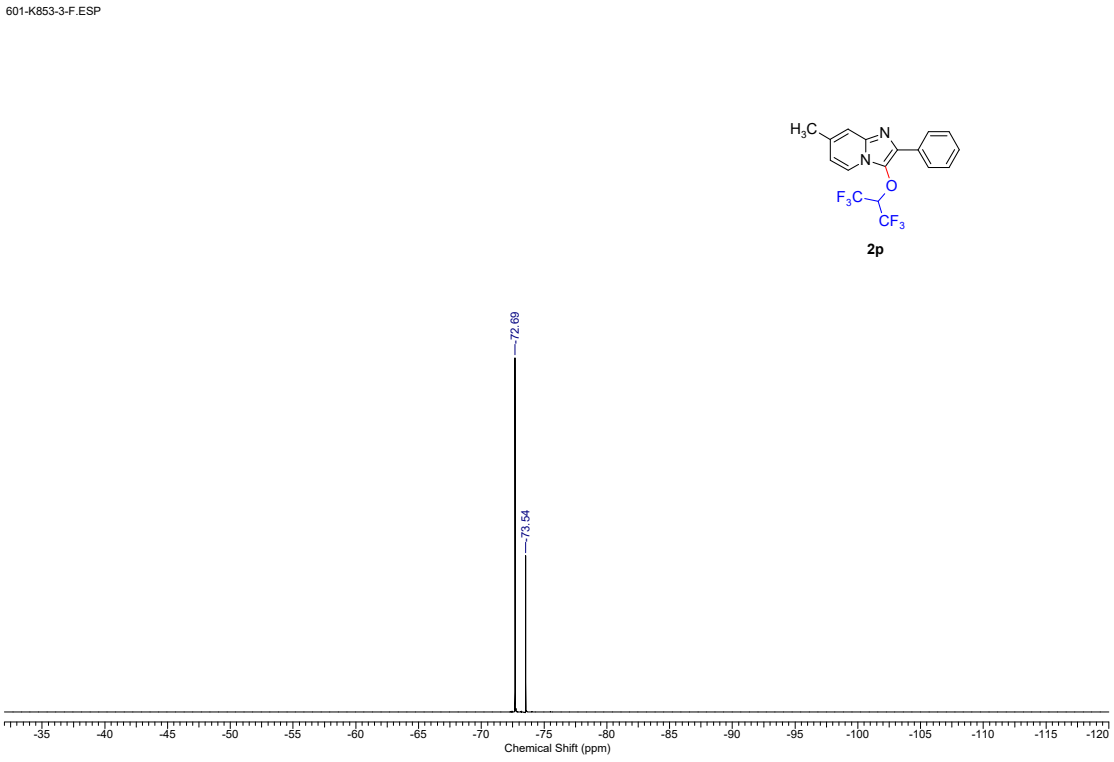


Figure S48. ^{19}F NMR spectrum of compound **2p**

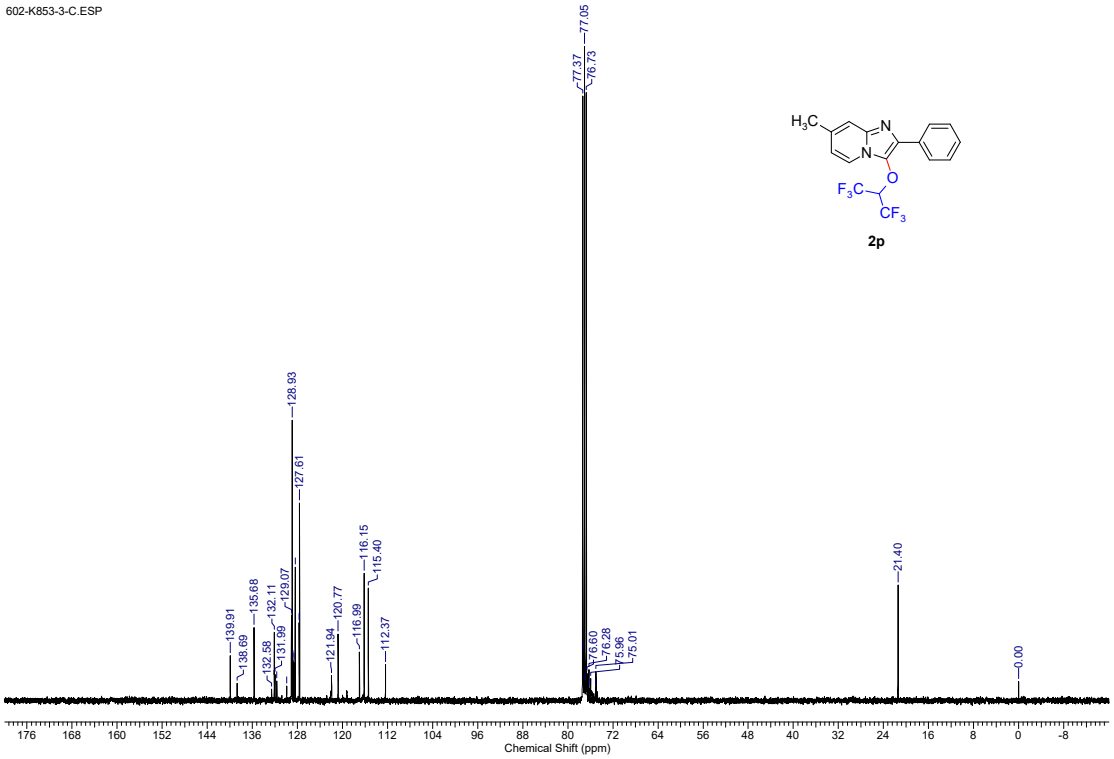


Figure S49. ^{13}C NMR spectrum of compound **2p**

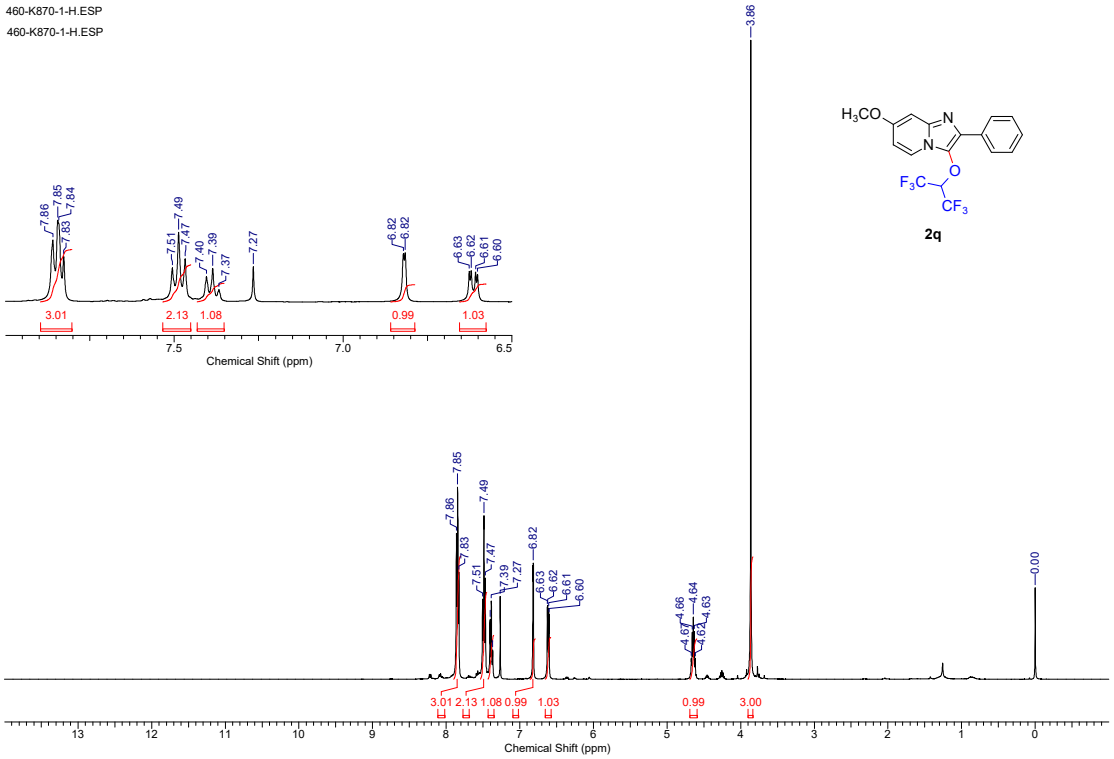


Figure S50. ^{1}H NMR spectrum of compound **2q**

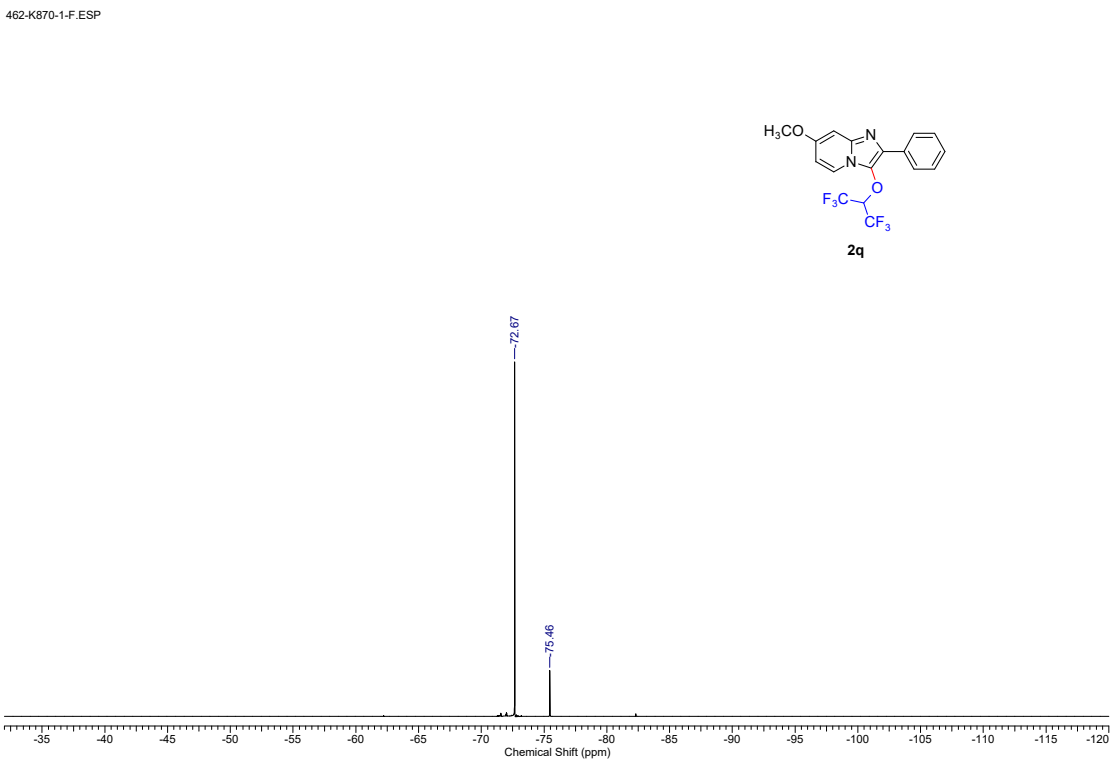


Figure S51. ^{19}F NMR spectrum of compound **2q**

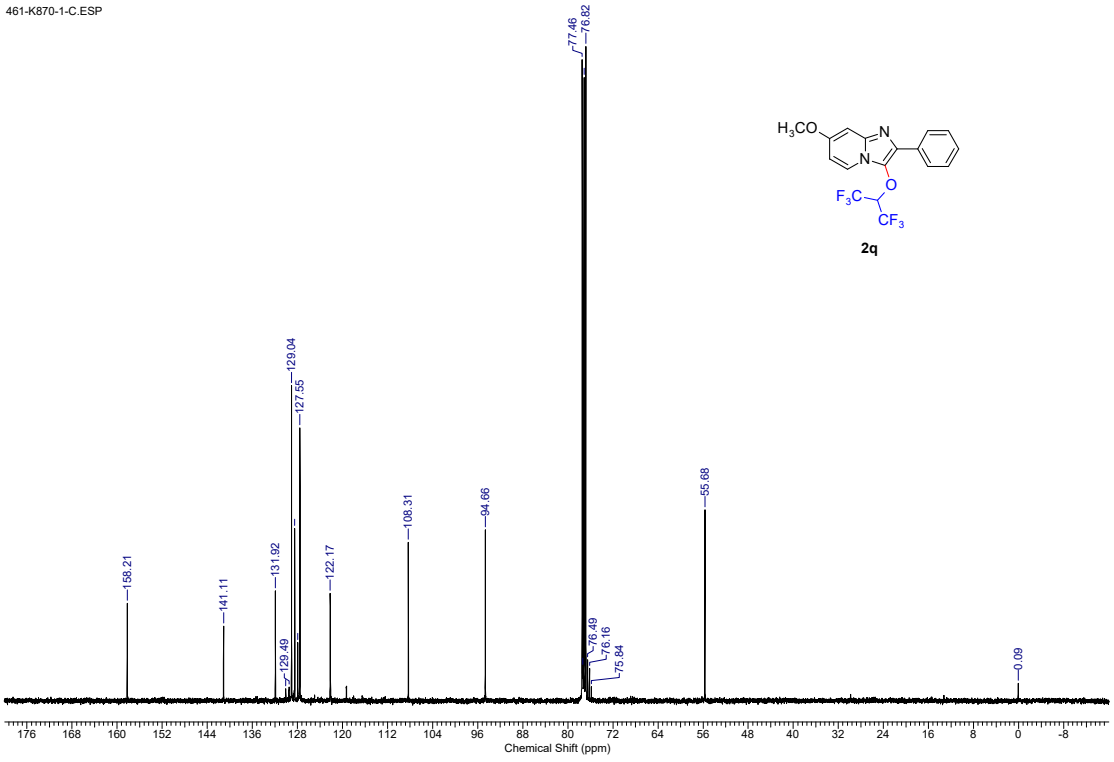


Figure S52. ^{13}C NMR spectrum of compound **2q**

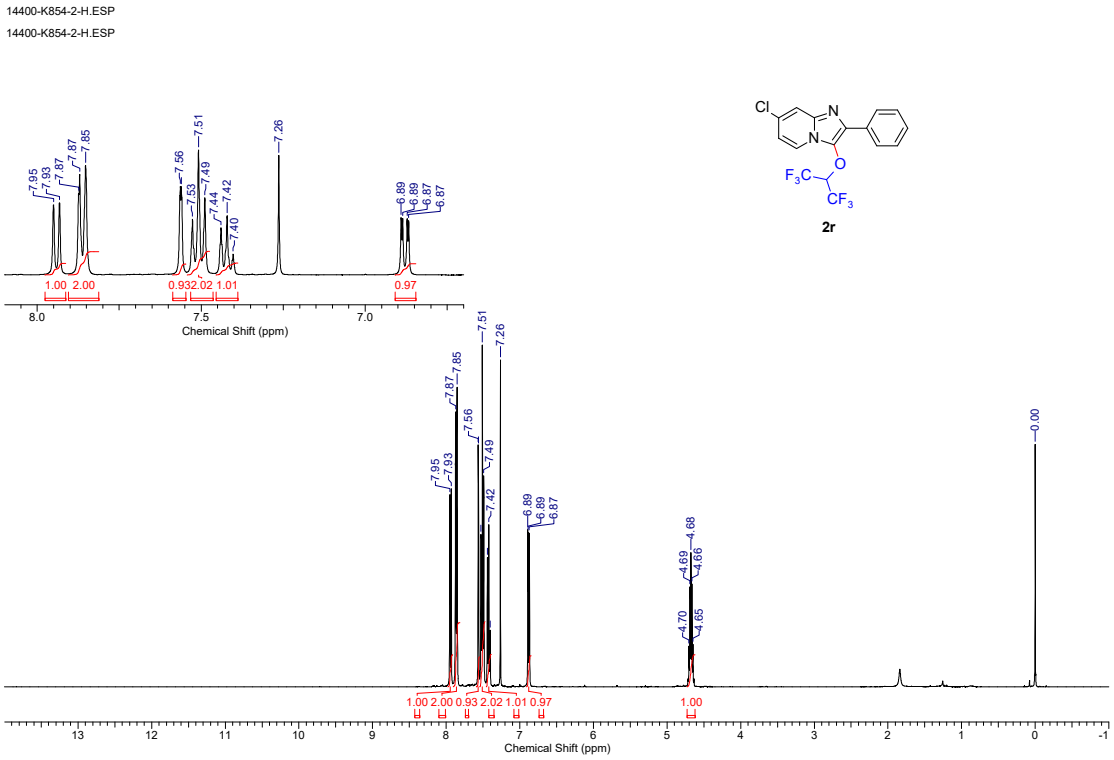


Figure S53. ^{1}H NMR spectrum of compound **2r**

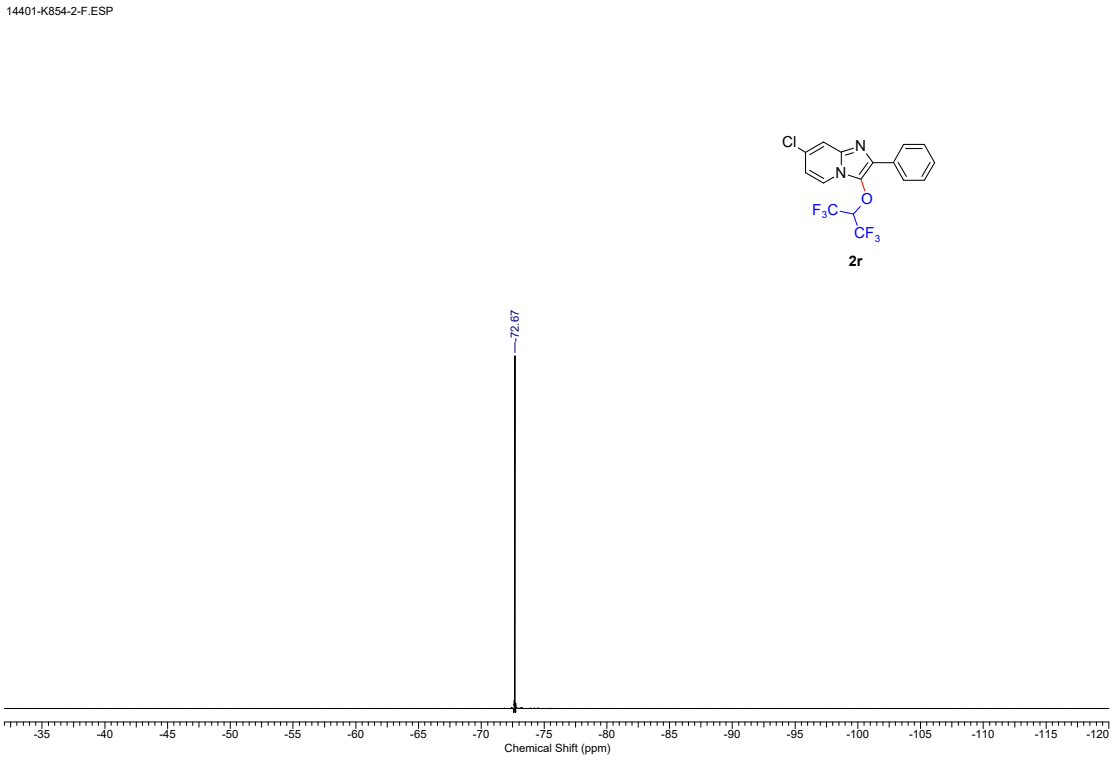


Figure S54. ^{19}F NMR spectrum of compound **2r**

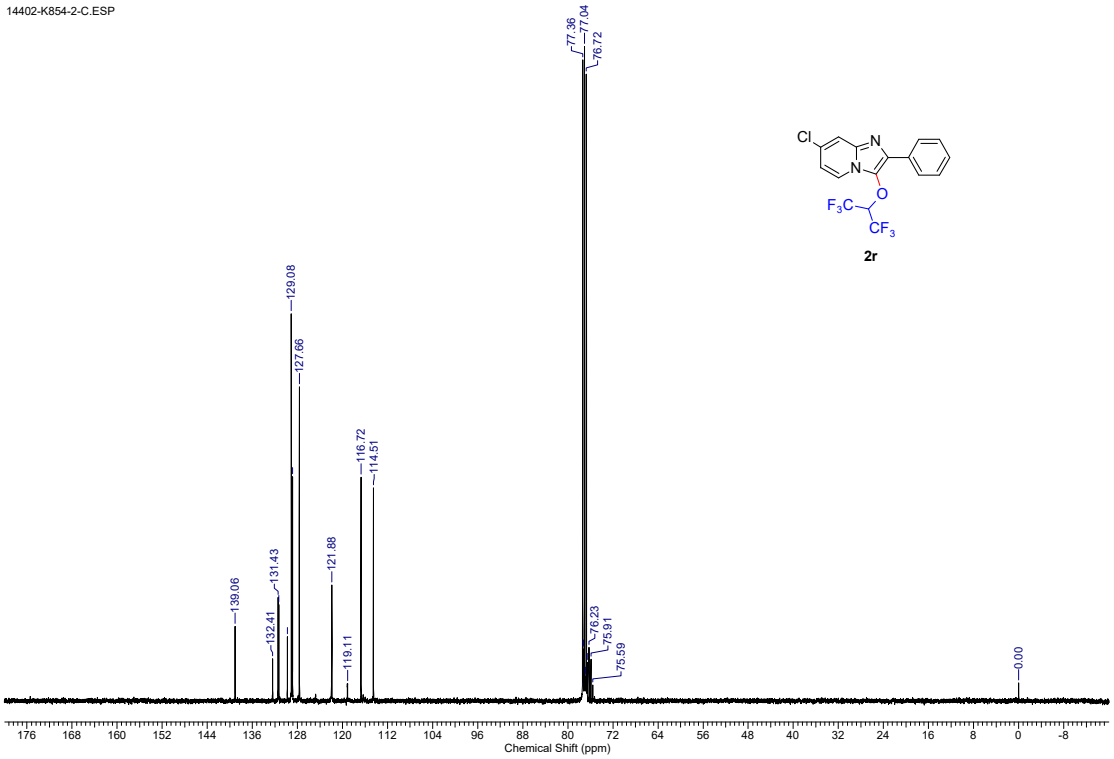


Figure S55. ^{13}C NMR spectrum of compound **2r**

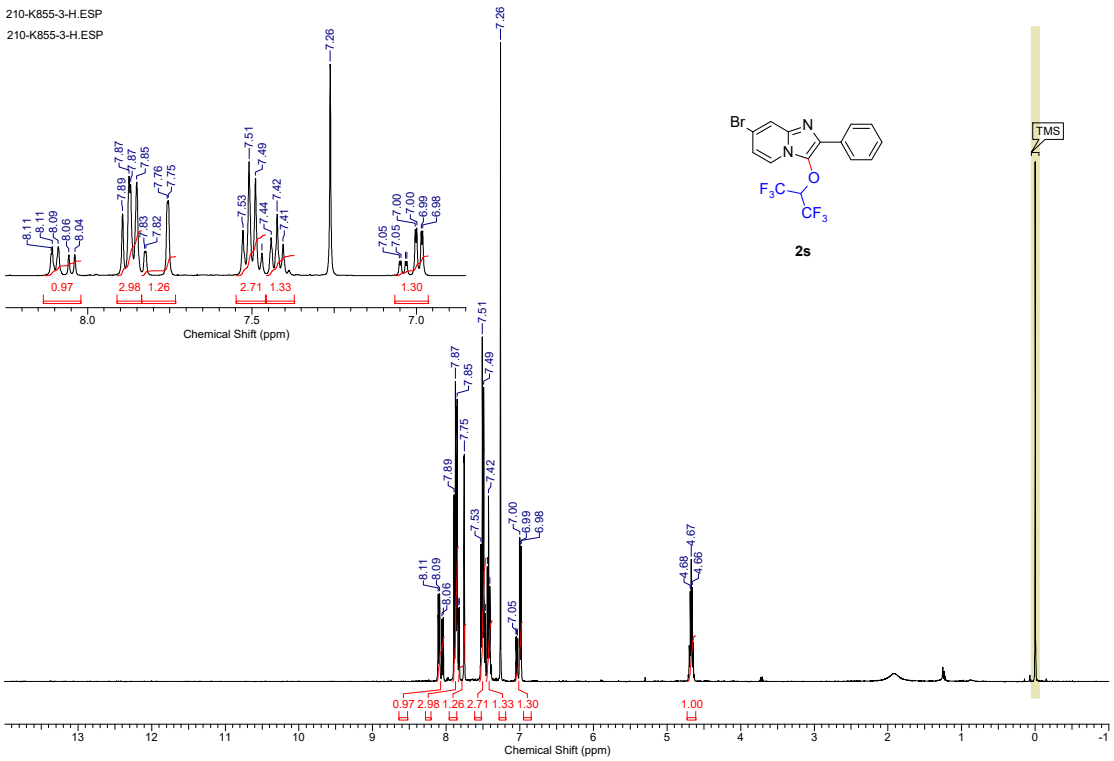


Figure S56. ^{1}H NMR spectrum of compound **2s**

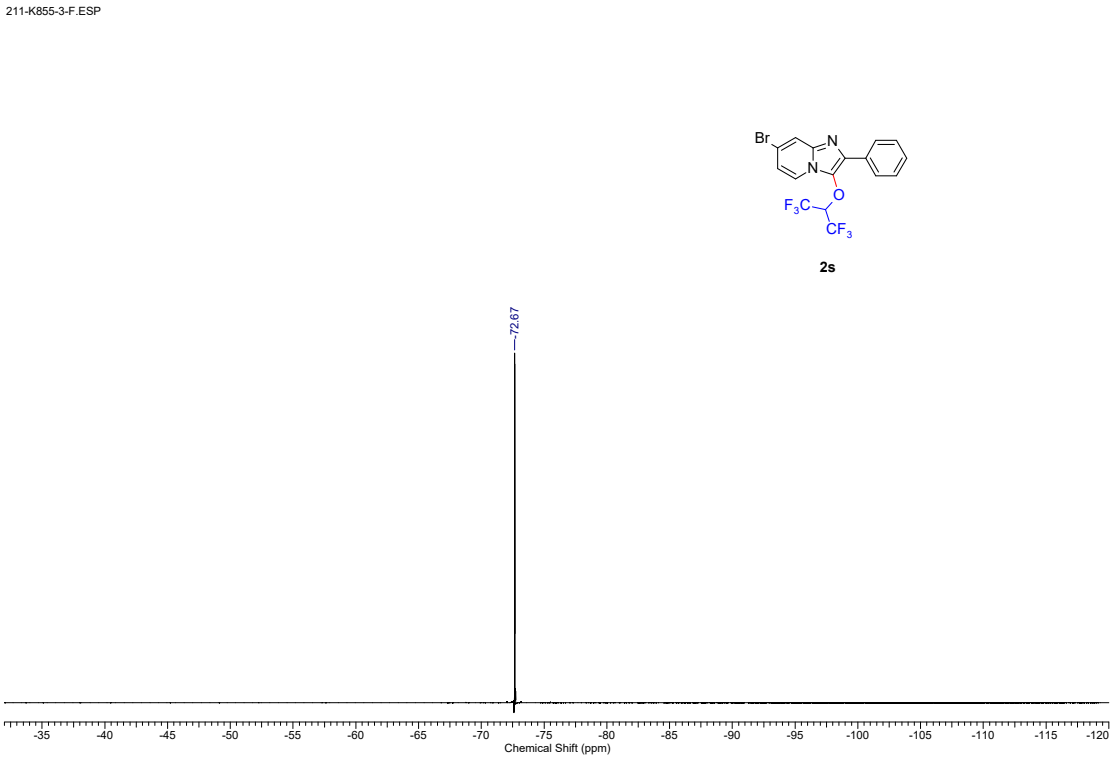


Figure S57. ^{19}F NMR spectrum of compound **2s**

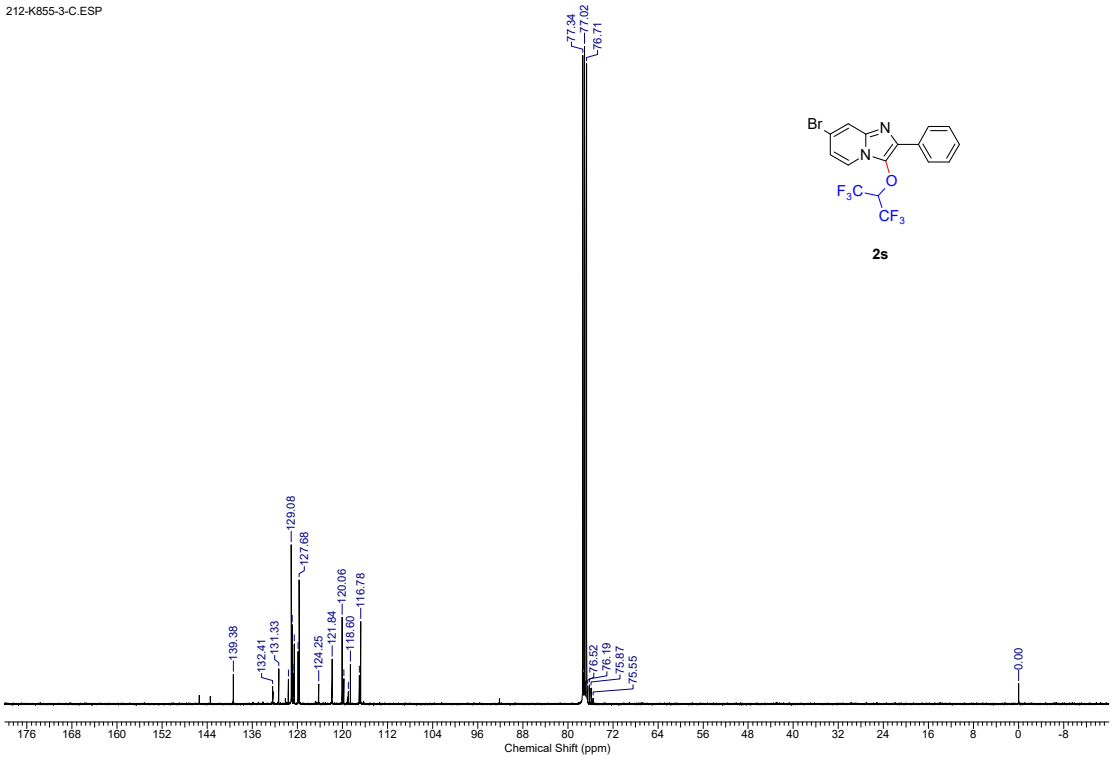


Figure S58. ^{13}C NMR spectrum of compound **2s**

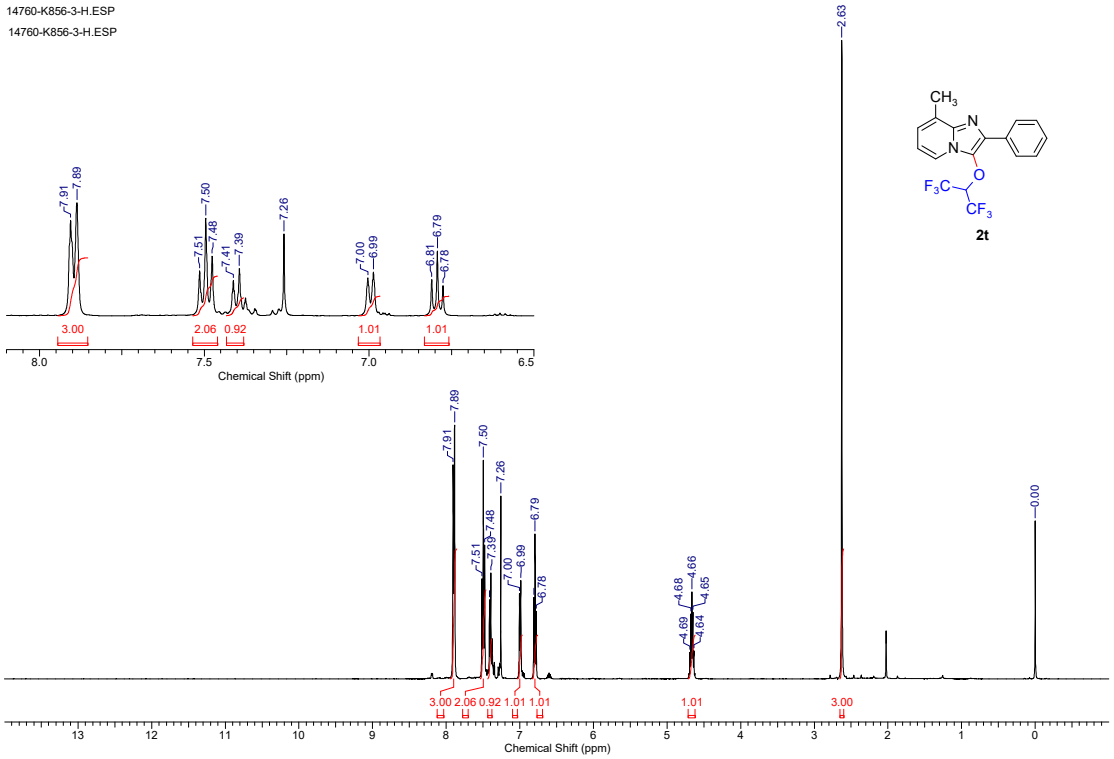


Figure S59. ^{1}H NMR spectrum of compound **2t**

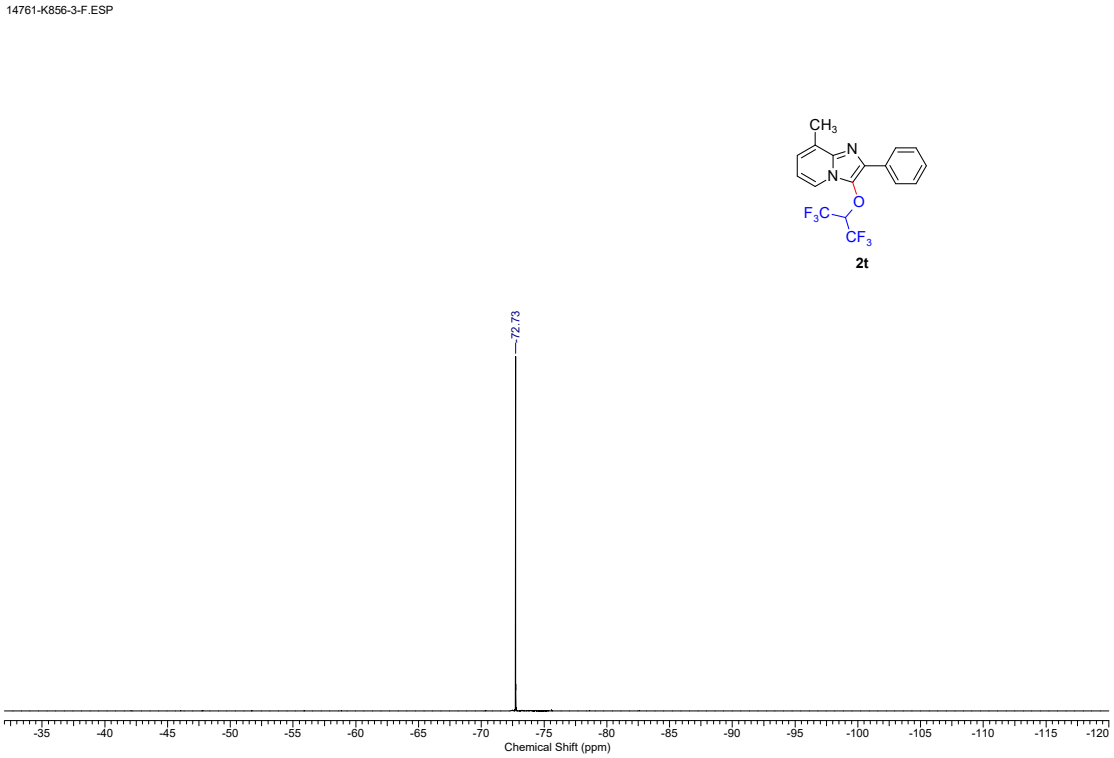


Figure S60. ^{19}F NMR spectrum of compound **2t**

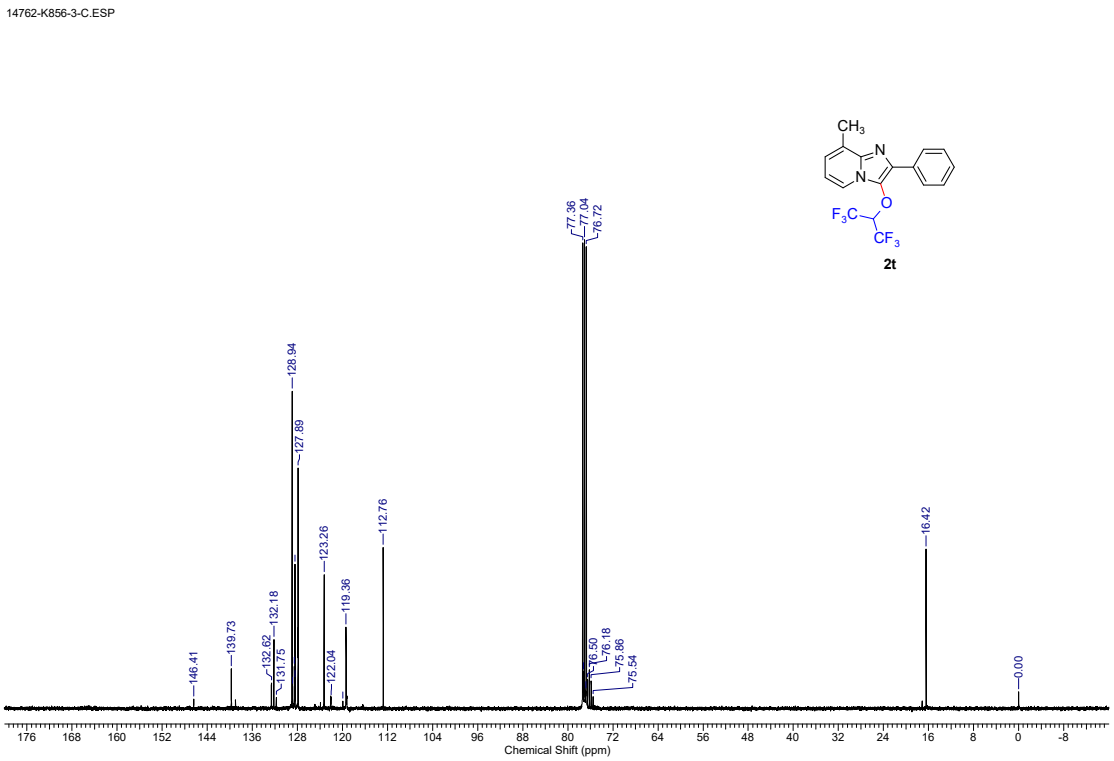


Figure S61. ^{13}C NMR spectrum of compound **2t**

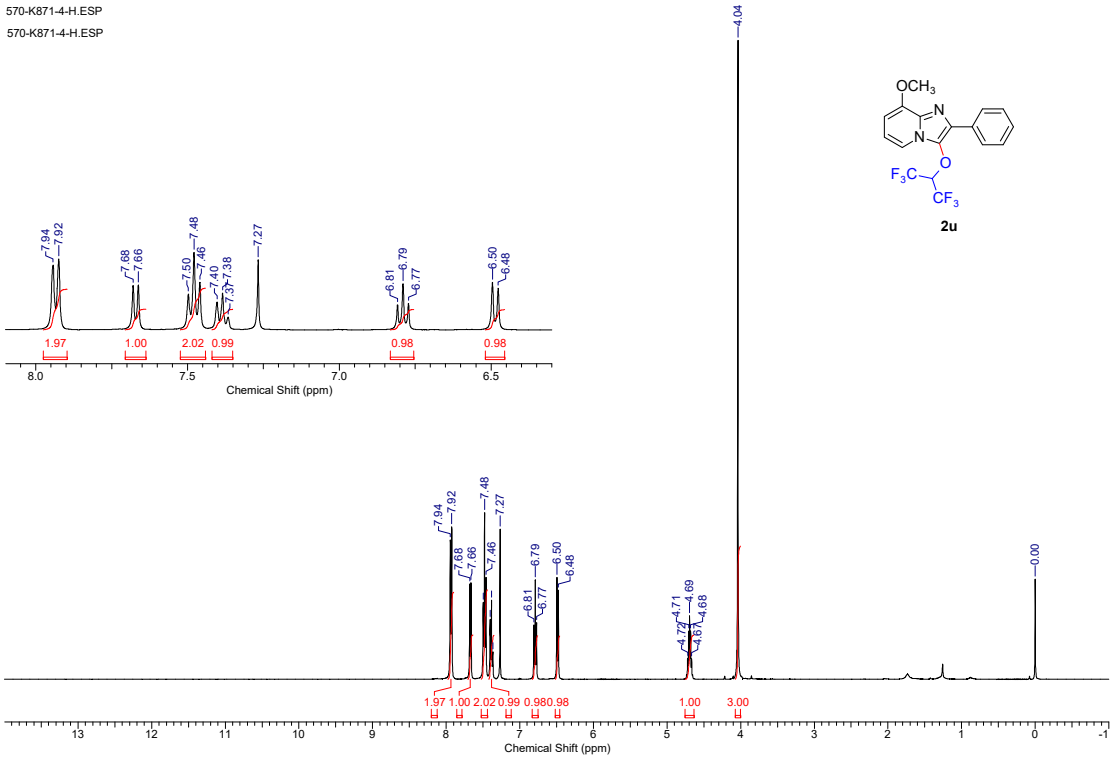


Figure S62. ^{1}H NMR spectrum of compound **2u**

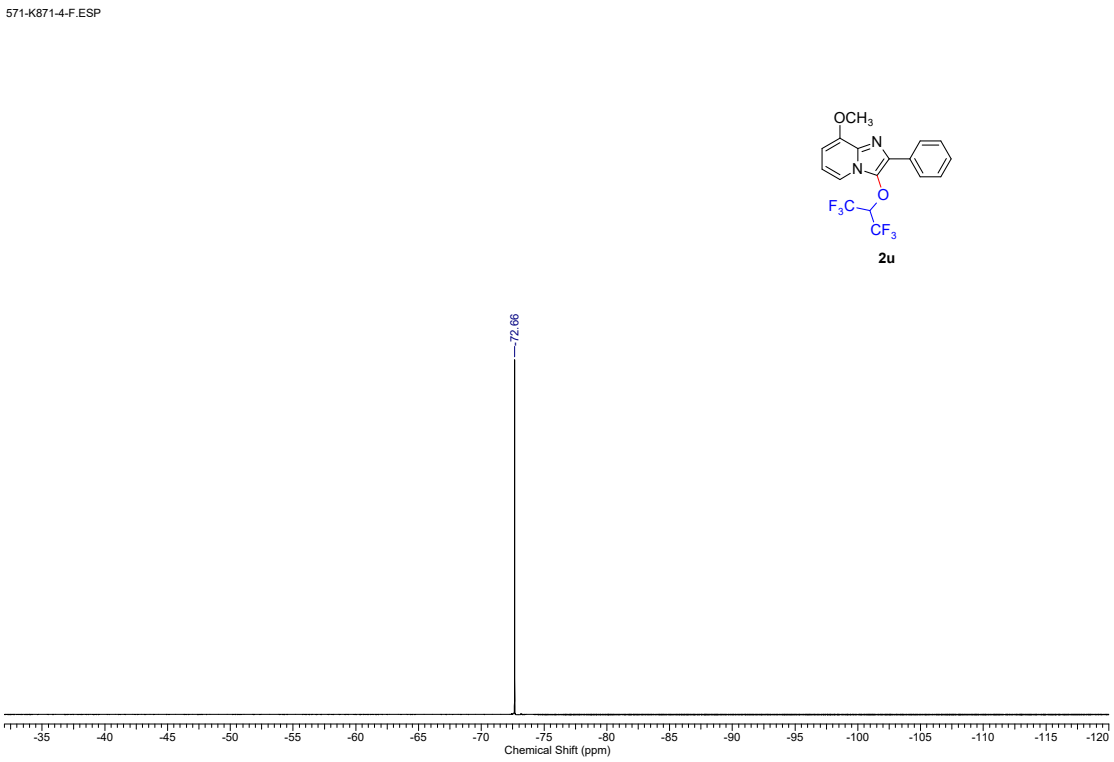


Figure S63. ^{19}F NMR spectrum of compound **2u**

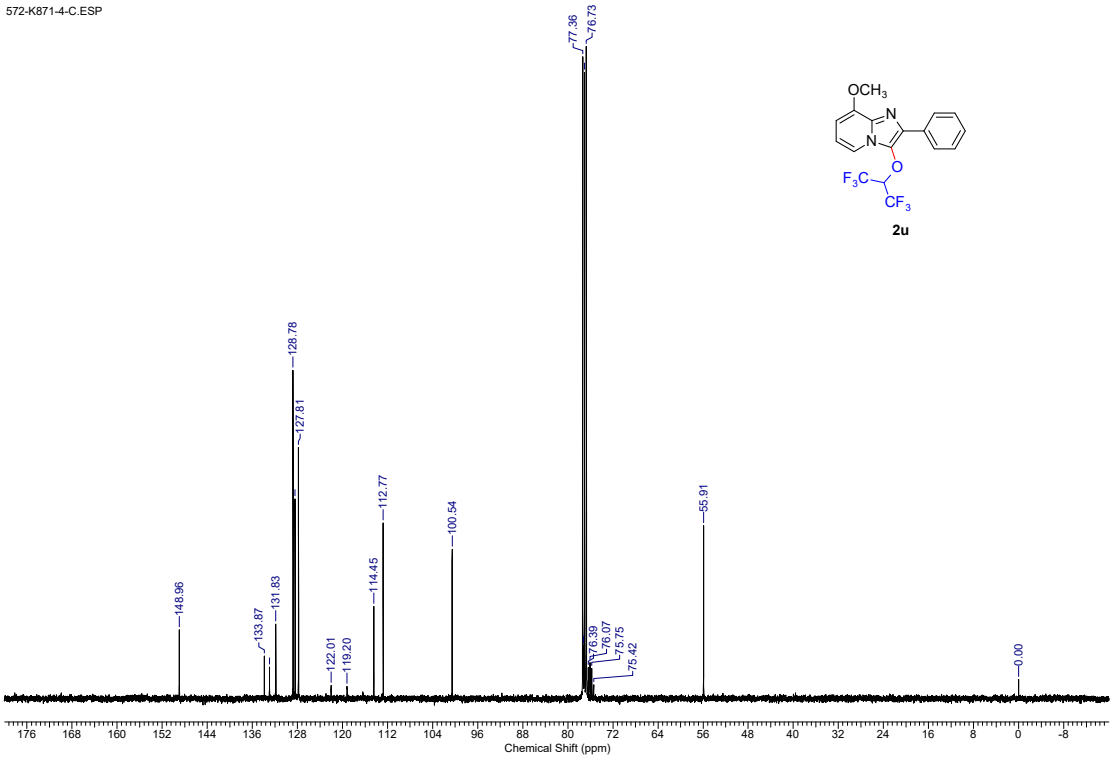


Figure S64. ^{13}C NMR spectrum of compound **2u**

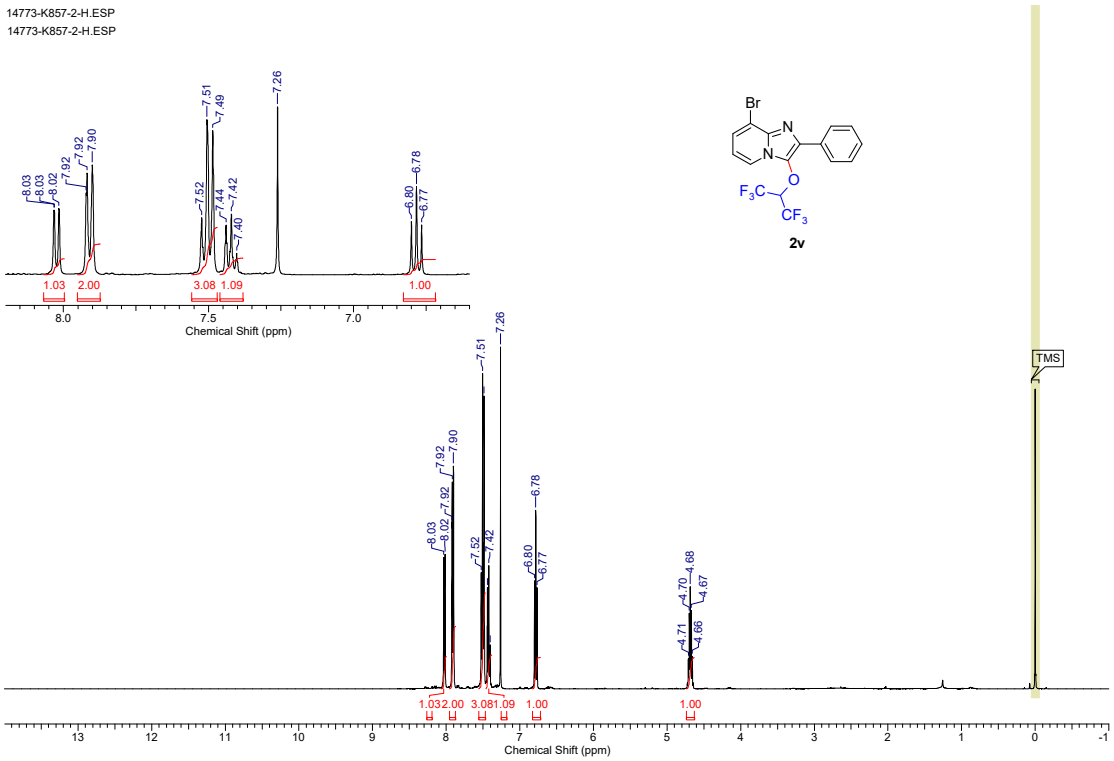


Figure S65. ^{1}H NMR spectrum of compound **2v**

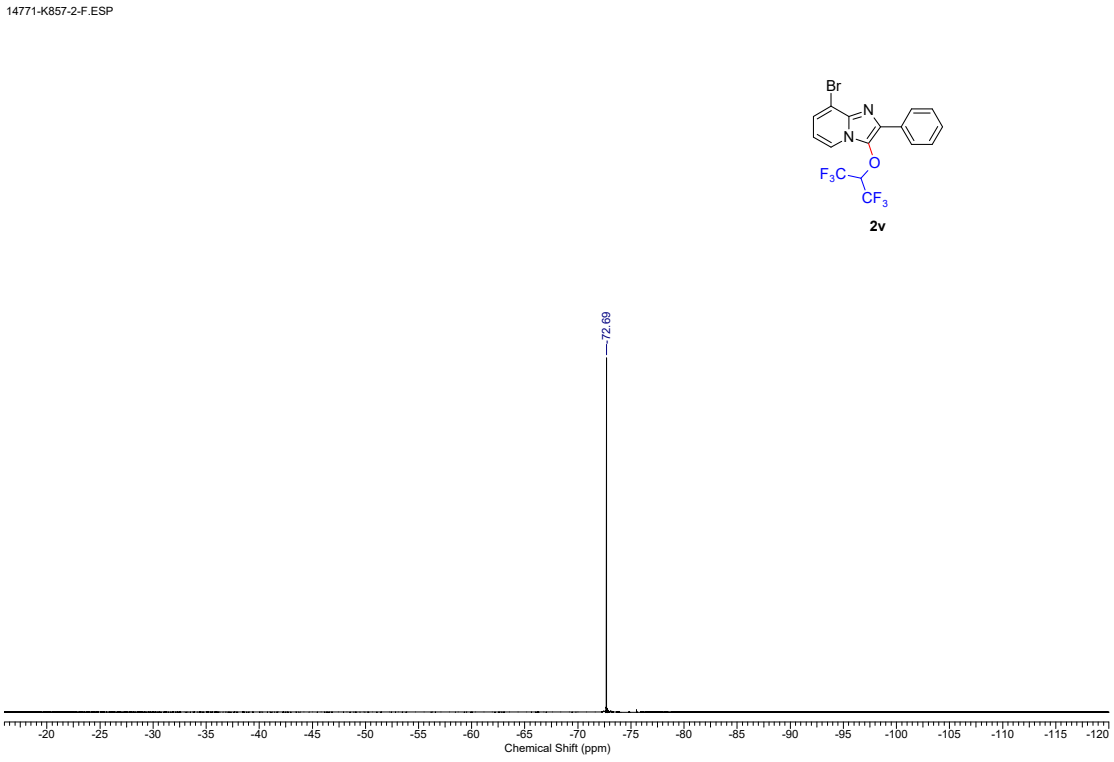


Figure S66. ^{19}F NMR spectrum of compound **2v**

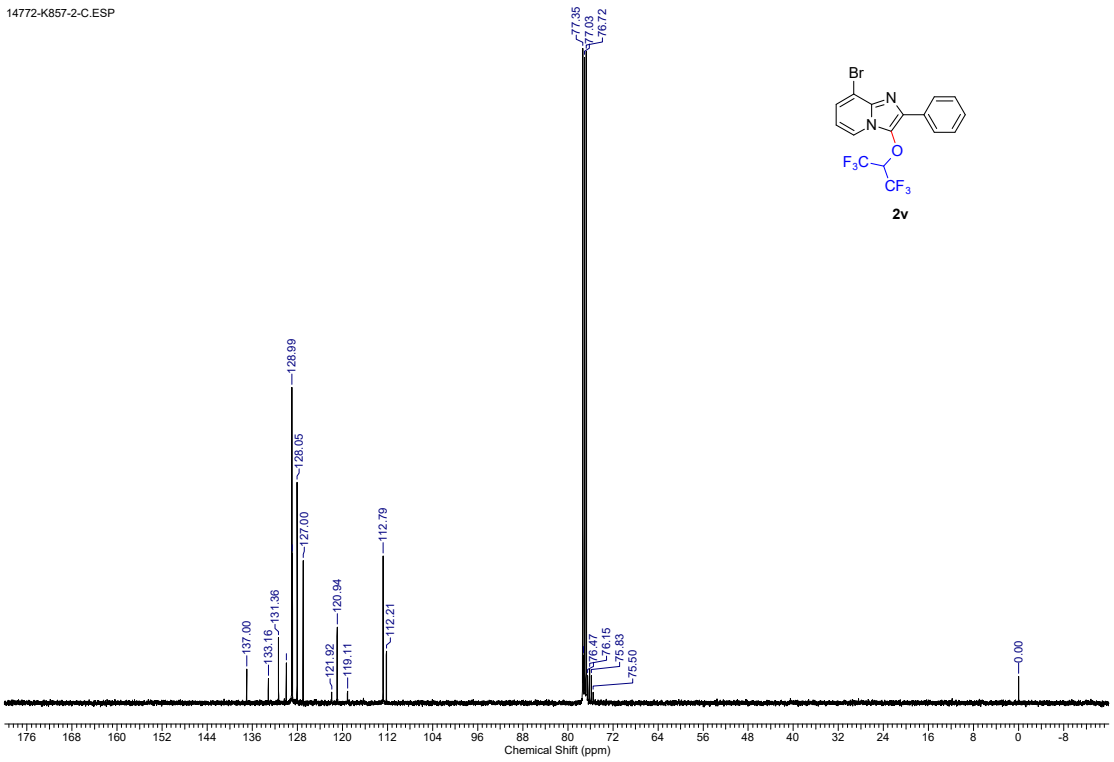


Figure S67. ^{13}C NMR spectrum of compound **2v**

9. Determination of Structure of 2a

The structure of **2a** was determined by the X-ray diffraction. Recrystallized from dichloromethane/n-hexane. Further information can be found in the CIF file. This crystal was deposited in the Cambridge Crystallographic Data Centre and assigned as CCDC 2156712.

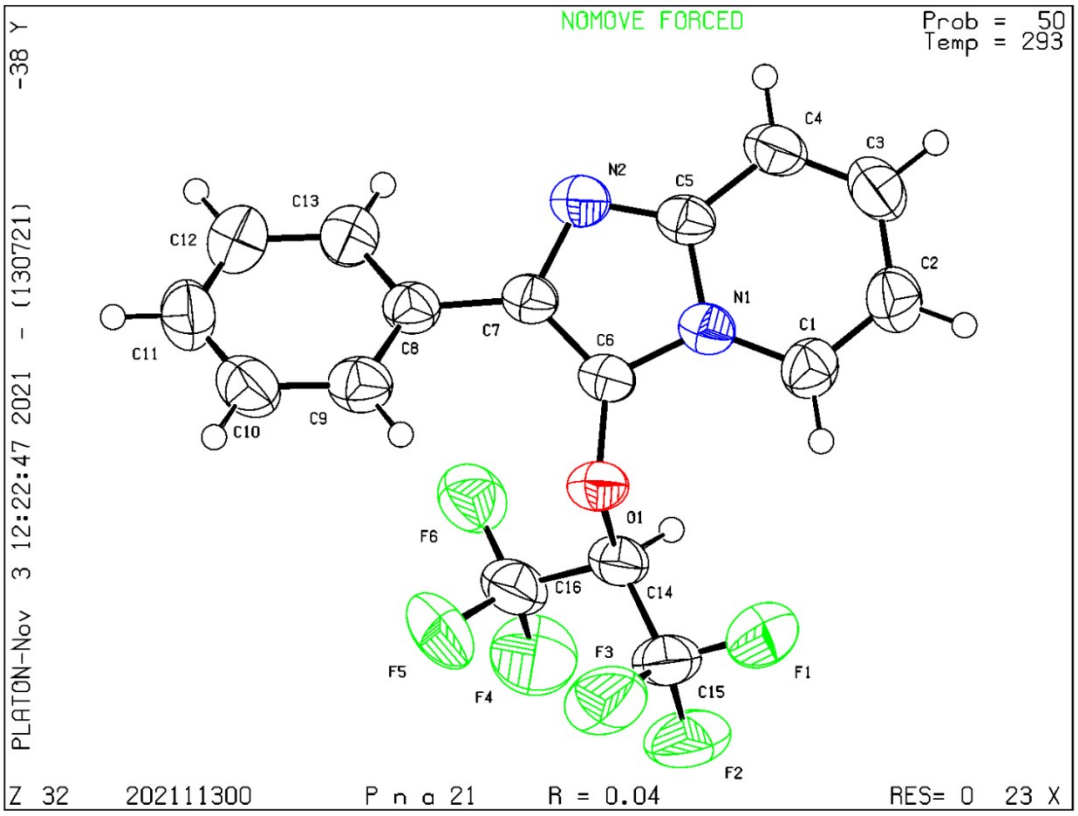


Table 1. Crystal data and structure refinement for 202111300.

Identification code	202111300
Empirical formula	$C_{16}H_{10}F_6N_2O$
Formula weight	360.26
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$Pna2_1$
a/Å	9.4804(2)
b/Å	10.7171(3)
c/Å	14.9246(5)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1516.37(8)
Z	4
ρ_{calc}g/cm^3	1.578
μ/mm^{-1}	1.341
F(000)	728.0
Crystal size/mm^3	0.16 × 0.13 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	10.162 to 141.432

Index ranges	$-11 \leq h \leq 8$, $-13 \leq k \leq 12$, $-18 \leq l \leq 11$
Reflections collected	5527
Independent reflections	2085 [R_{int} = 0.0285, R_{sigma} = 0.0301]
Data/restraints/parameters	2085/1/226
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0399, wR_2 = 0.1016
Final R indexes [all data]	R_1 = 0.0491, wR_2 = 0.1102
Largest diff. peak/hole / e $Å^{-3}$	0.12/-0.18