Supporting Information

Photoinduced amine-mediated hydrodifluoroalkylation of 3-methyleneisoindolin-1-ones

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1. General consideration

Chemicals

All the chemicals were purchased from commercial sources (Sigma-Aldrich, Merck, TCI, ACROS Organics, Spectrochem, BLDpharm) and directly used as received without additional purification. Anhydrous solvents (DMA, DMF, DMSO, CH_3CN, Acetone, $CHCl_3$) were purchased from Acros Organics and used as received.

Chromatography

Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminum 60 F-254 plates. Visualization of TLC was achieved by using a UV lamp (254 nm). Column chromatography was carried out with silica gel (60-120 mesh, 100-200 mesh, and 230-400 mesh) to purify products using appropriate solvents as the eluent system. All the yields of the products are referred to as chromatography-pure compounds.

Nuclear Magnetic Resonance (NMR) Spectroscopy

NMR spectra were recorded at 500 MHz for ^{1}H NMR spectra and 125 MHz for ^{13}C NMR spectra. ^{19}F NMR spectra were recorded in chloroform-*d* at 471 M Hz. The sample to be analyzed was dissolved in chloroform-*d* and DMSO-d_6 solvent. Chemical shifts are quoted in parts per million referenced to the appropriate solvent peak. For ^{13}C NMR and ^{1}H NMR, chemical shifts are reported in parts per million referenced to the center of a triplet at 77.16 ppm and 7.26 ppm of chloroform-*d* respectively. For ^{13}C NMR and ^{1}H NMR, chemical shifts are reported in parts per million referenced to the center of a septet at 39.52 ppm and 2.50 ppm of DMSO-d_6 respectively. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet; d = doublet; t = triplet; q = quartet; quin = quintet; sext = sextet; sept = septet; m = multiplet; brs = broad singlet. Coupling constants, *J* are reported in hertz.

Fourier Transform Infrared Spectroscopy

FT-IR spectra were recorded on the IR Prestige-21 SHIMADZU instrument using a KBr disc or pellet and are reported in terms of frequency of absorption (cm^{-1}).

High-Resolution Mass Spectrometry (HRMS)

Waters Q-TOF mass spectrometer equipped with a Z-spray source was used for the electrospray ionization (ESI) mass spectrometry measurement in positive mode.

UV instrument

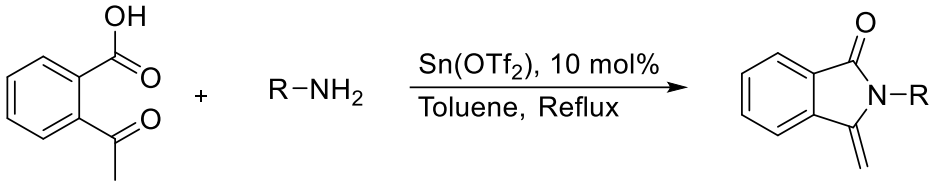
The optical absorption spectra were recorded on a Shimadzu (Model UV3600) spectrophotometer.

Description of Light Source

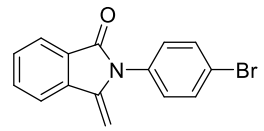
The purple lights were purchased from Kessil (Kessil® PR160-390 nm). The reaction vessels were placed 5 cm away from light sources (Figure S1).

2. Synthesis of Starting Materials

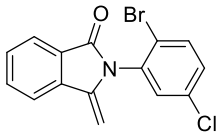
2.1 General procedure (GP1) for synthesis of starting material 1b



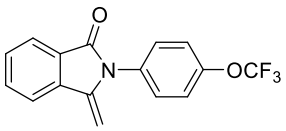
2-Acetylbenzoic acid (1.0 g, 6.09 mmol, 1 equiv) was dissolved in toluene (50 mL), followed by the addition of aniline (1.2 equiv) and $Sn(OTf)_2$ (10 mol%). The reaction mixture was then refluxed for 15 h. After completion of the reaction (monitored by TLC), the mixture was quenched with water and extracted with EtOAc. The organic layer was washed with saturated NaCl solution, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to afford the desired compound.



1a



1b



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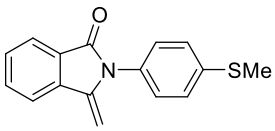

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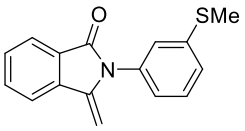

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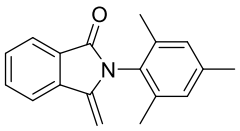

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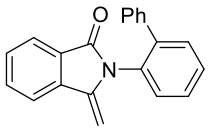

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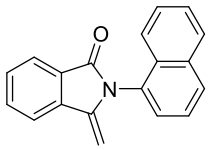

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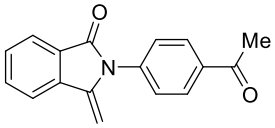
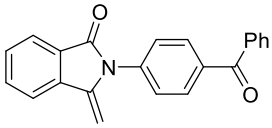


1i



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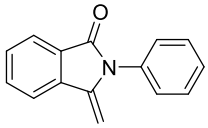
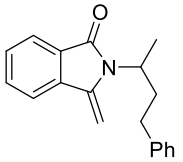
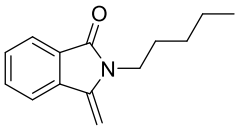


1k



1l



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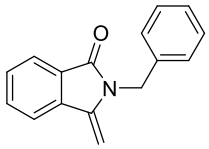
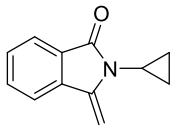
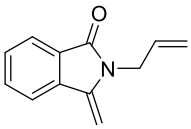


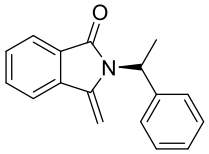
1n



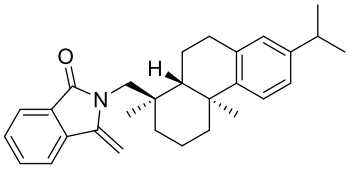
1o



1p



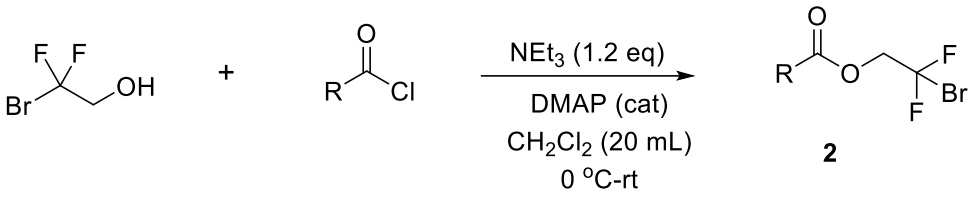
1q



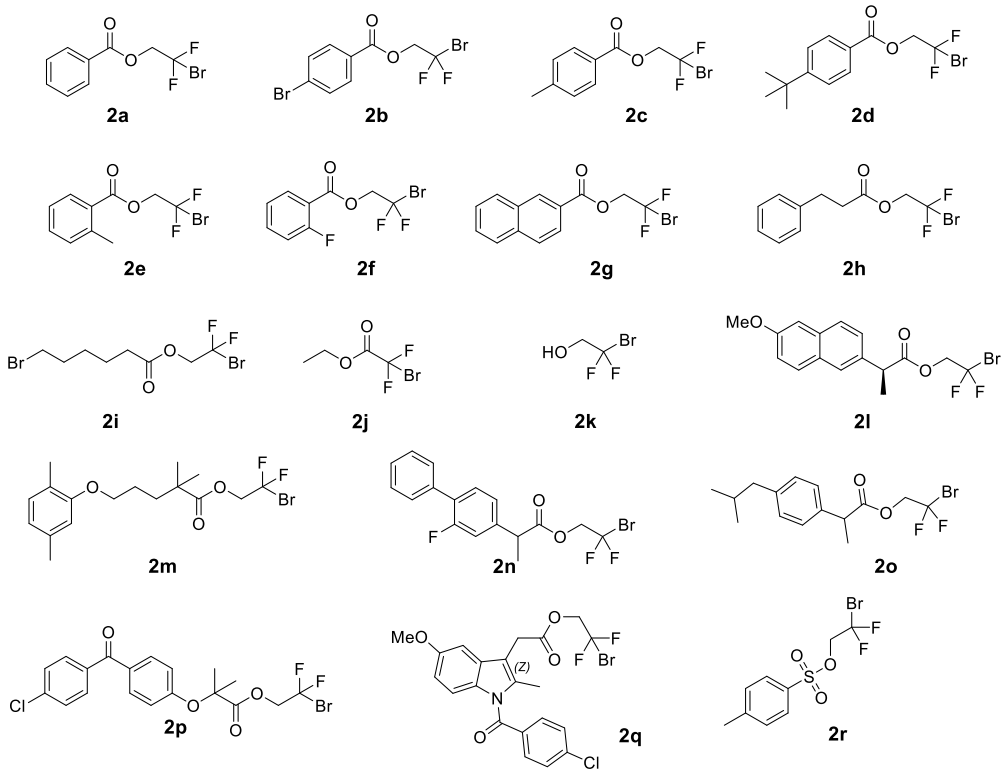
1r

Starting Material **1a, 1c, 1d, 1e, 1f, 1g, 1h, 1i, 1j, 1k, 1l, 1m, 1n, 1o, 1p, 1q, and 1r** were prepared according to known literature procedure[1].

2.2 General procedure (GP2) for synthesis of starting material



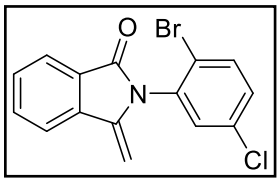
A solution of 2-bromo-2,2-difluoroethan-1-ol (3.12 mmol, 1 equiv) in CH_2Cl_2 (20 mL) was prepared in a 50 mL round-bottom flask and cooled to 0°C. Triethylamine (3.74 mmol, 1.2 equiv), 4-(dimethylamino)pyridine (0.2 mmol), and benzoyl chloride (3.74 mmol, 1.2 equiv) were added sequentially, and the mixture was stirred at room temperature overnight. The reaction was quenched with water, and the organic layer was extracted with hexane (3 × 15 mL). The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using hexane/EtOAc as the eluent to afford the difluorobromoalkanes (**2i, 2o, 2p and 2r**).



Substrate **2j** was purchased from commercial sources.

Starting Material **2a, 2b, 2c, 2d, 2e, 2f, 2g, 2h, 2j, 2k, 2l, 2m 2n and 2r** [3b] were prepared according to known literature procedure[2,3].

3. Synthesis and Characterization of starting materials



2-(2-bromo-6-chlorophenyl)-3-methyleneisoindolin-1-one (1b):

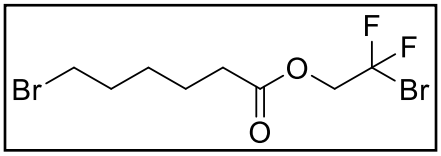
Following GP1, a residue was purified by column chromatography on silica gel (0 to 25% ethyl acetate in hexane) 1b afforded as yellow solid (731 mg, 65%). **M.P.** 150.1-152.9 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 9.0 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.39 (s, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 5.24 (s, 1H), 4.48 (s, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.1, 141.9, 136.4, 135.4, 134.6, 134.1, 132.8, 131.5, 130.8, 130.0, 128.7, 124.0, 122.3, 120.4, 90.7.

IR (neat, cm^{-1}) 1724, 1649, 1475, 776, 701.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{15}H_9BrClNO]^+$ 333.9634; found 333.9630.



2-bromo-2,2-difluoroethyl 6-bromohexanoate (2i):

Following GP2, a residue was purified by column chromatography on silica gel (0 to 10% ethyl acetate in hexane) **2i** afforded as colorless liquid (681 mg, 65%).

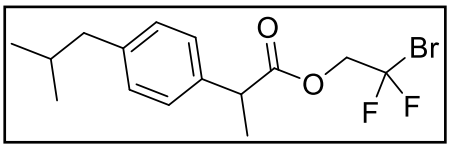
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.59 (t, *J* = 11.5 Hz, 2H), 3.40 – 3.38 (m, 2H), 2.43 (t, *J* = 7.5 Hz, 2H), 1.90 – 1.84 (m, 2H), 1.70 – 1.66 (m, 2H), 1.52 – 1.46 (m, 2H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 171.7, 118.2 (t, $^1J_{CF}$= 306.5 Hz), 66.9 (t, $^2J_{CF}$= 27.1 Hz), 33.6, 33.4, 32.4, 27.6, 23.9.

^{19}F NMR (471 MHz, $CDCl_3$) δ -56.3.

IR (neat, cm^{-1}) 2336, 1760, 1539, 1219, 1139, 943, 786.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_8H_{12}Br_2F_2O_2]^+$ 336.9250; found 336.9246.



2-bromo-2,2-difluoroethyl 2-(4-isobutylphenyl)propanoate (2o):

Following GP2, a residue was purified by column chromatography on silica gel (0 to 10% ethyl acetate in hexane) **2o** afforded as yellow liquid (662 mg, 61%).

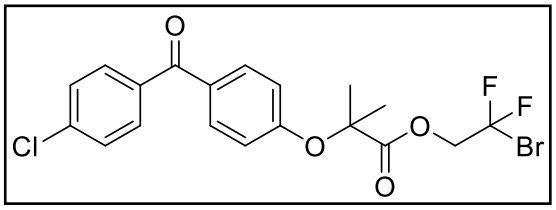
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 4.65 – 4.51 (m, 2H), 3.80 (q, *J* = 7.0 Hz, 1H), 2.45 (d, *J* = 7.0 Hz, 2H), 1.87 – 1.80 (m, 1H), 1.55 (d, *J* = 7.5 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 6H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 173.1, 141.1, 136.6, 129.5 (2C), 127.3 (2C), 118.24 (t, $^{1}J_{CF}$ = 306.5 Hz), 67.1, (t, $^{2}J_{CF}$ = 27.1 Hz), 45.1, 44.9, 30.3, 22.4 (2C), 18.3.

^{19}F NMR (471 MHz, $CDCl_3$) δ -56.1.

IR (neat, cm^{-1}) 2959, 1711, 1646, 1230, 855.

HRMS (ESI-TOF) m/z $[M]^+$ calcd for $[C_{15}H_{19}BrF_2O_2]^+$ 348.0536; found 348.0525.



2-bromo-2,2-difluoroethyl 2-(4-benzoylphenoxy)-2-methylpropanoate (2p):

Following GP2, a residue was purified by column chromatography on silica gel (0 to 10% ethyl acetate in hexane) **2p** afforded as yellow liquid (903 mg, 68%).

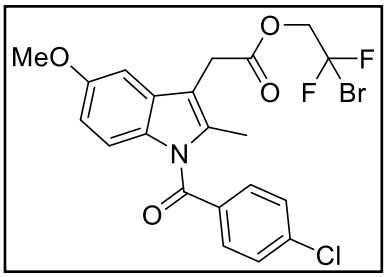
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 16.5, 6.5 Hz, 4H), 7.45 (d, *J* = 7.0 Hz, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 4.70 (t, *J* = 11.0 Hz, 2H), 1.73 (s, 6H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 194.4, 172.3, 159.3, 138.6, 136.4, 132.2 (2C), 131.3 (2C), 131.0, 128.7 (2C), 117.7 (2C), 117.4 (t, $^{1}J_{CF}$ = 307.0 Hz), 79.3, 67.5 (t, $^{2}J_{CF}$ = 27.6 Hz), 25.6 (2C).

^{19}F NMR (471 MHz, $CDCl_3$) δ -56.4.

IR (neat, cm^{-1}) 1736, 1598, 1263, 1132, 937.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{19}H_{16}BrClF_2O_4]^+$ 462.9946; found 462.9947.



2-bromo-2,2-difluoroethyl 2-(1-(4-chlorobenzoyl)-2-methyl-1H-indol-3-yl)acetate (2q):

Following GP2, a residue was purified by column chromatography on silica gel (0 to 10% ethyl acetate in hexane) **2q** afforded as colorless liquid (731 mg, 56%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 6.5 Hz, 2H), 7.47 (d, *J* = 7.0 Hz, 2H), 6.95 – 6.88 (m, 2H), 6.68 (d, *J* = 9.0 Hz, 1H), 4.63 (t, *J* = 12.5 Hz, 2H), 3.84 (s, 3H), 3.78 (s, 2H), 2.39 (s, 3H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.2, 168.4, 156.3, 139.5, 136.4, 133.9, 131.3 (2C), 130.9, 130.4, 129.3 (2C), 118.1 (t, $^{3}J_{CF}$ = 306.3 Hz), 115.1, 112.1, 111.5, 101.1, 67.4 (t, $^{2}J_{CF}$ = 27.6 Hz), 55.8, 22.9, 13.5.

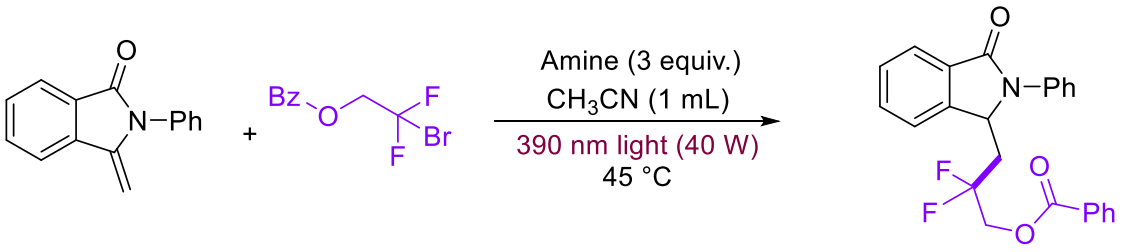
^{19}F NMR (471 MHz, $CDCl_3$) δ -56.3.

IR (neat, cm^{-1}) 2929, 1760, 1688, 1477, 1321, 1230, 1143, 937, 758.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{21}H_{17}BrClF_2NO_4]^+$ 502.0055; found 502.0064.

4. Optimization Details

4.1 General procedure for the optimization of functionalization of 3-methyleneisoindolin-1-ones



1k **2a** **3k**

A 10 mL glass vial was charged with **1k** (0.1 mmol, 32 mg), **2a** (0.2 mmol, 52 mg), the amine (3 equiv), and a PTFE-coated magnetic stir bar under an inert atmosphere (Reaction also proceeds well in aerial atmosphere). The mixture was dissolved in CH_3CN (1 mL), sealed with a PTFE septum, stirred, and irradiated with Kessil® PR160-390 nm light (40 W) at 45 °C (as shown in Figure S1). After 24 h, trimethoxybenzene (0.1 mmol) was added, and the reaction mixture was extracted with EtOAc, followed by washing with brine solution. The organic layer was concentrated under reduced pressure and analyzed by ^1H NMR to determine the reaction yield.

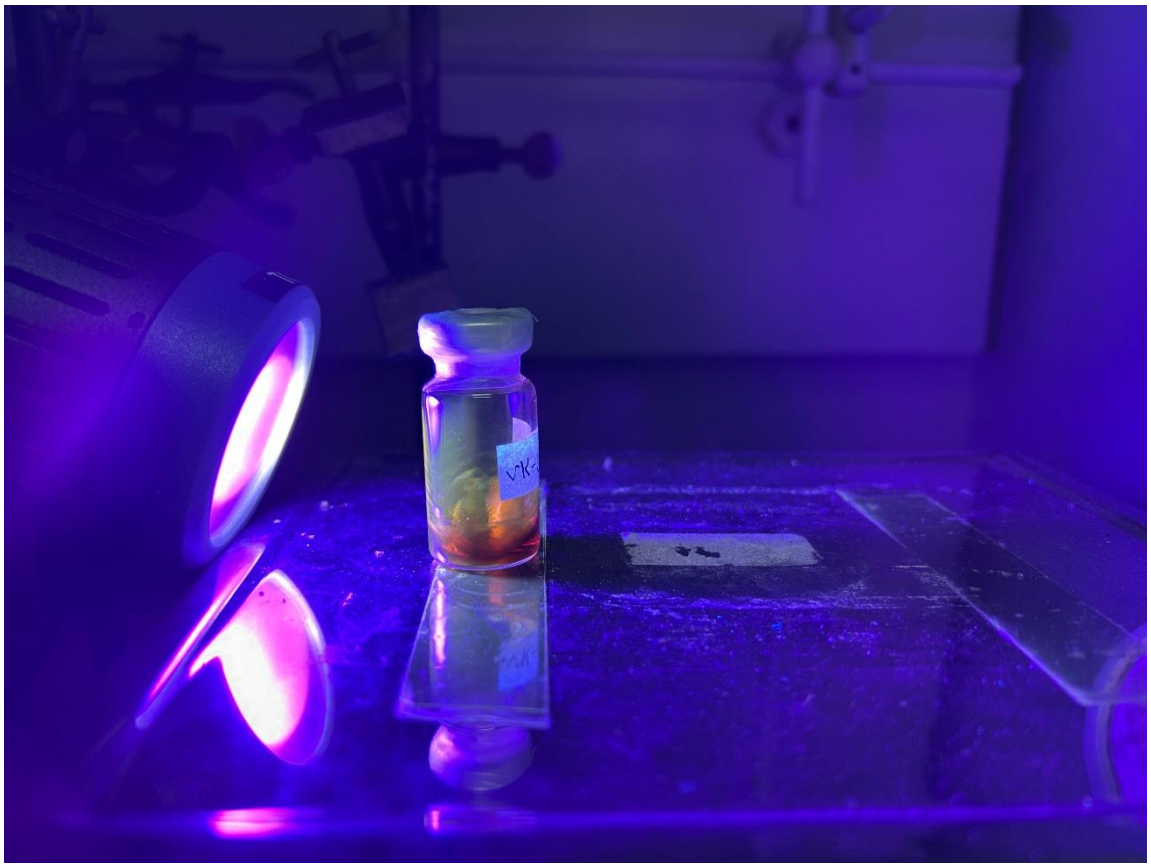
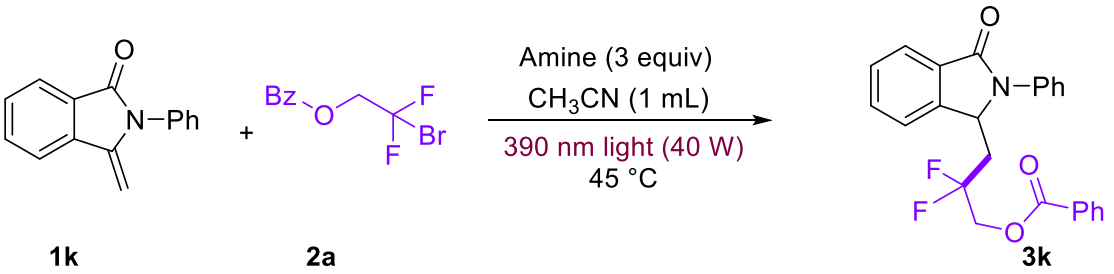


Figure S1: Reaction setup with Kessil® PR160-390 nm light (40 W). Light source placed 3 cm away from reaction vial

Table S1: Screening of amines

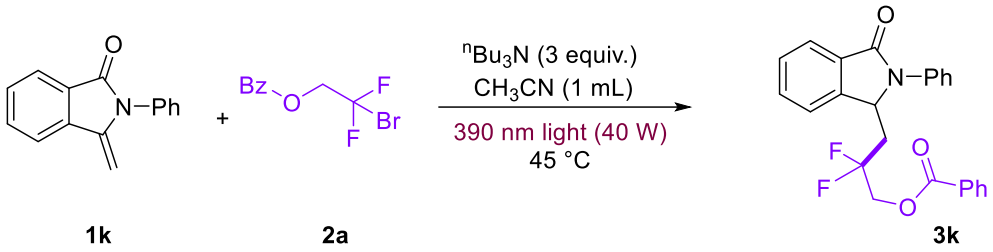


1k **2a** **3k**

Entry	Variation in Amine	Yield %
1	DIPEA	56
2	$^{n}Bu_3N$	71
3	Et_3N	36
4	DABCO	trace
5	1,3,5 Triazine	20
6	MTBD	0
7	TMP	0
8	DIPA	trace
9	DBU	0
10	DMAP	22
11	Pyridine	0

Optimization of reaction condition using **1k** (0.1 mmol), **2a** (0.2 mmol). NMR yield using 1,3,5 Trimethoxy benzene as internal standard.

Table S2: Screening of solvents

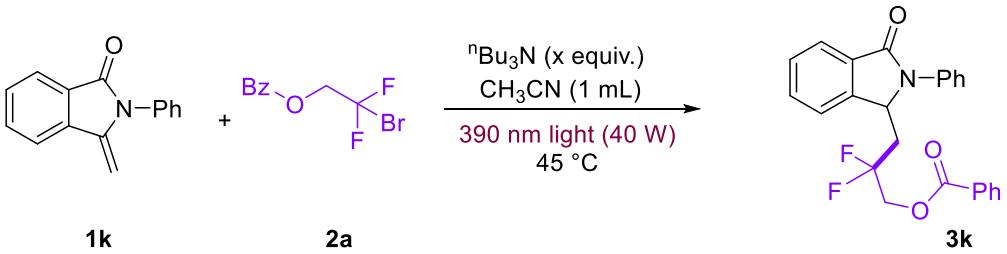


1k **2a** **3k**

Entry	Variation in Solvent	Yield (%)
1	DMF	47
2	DMSO	49
3	Toluene	26
4	Acetone	22
5	MeOH	21
6	THF	61
7	H_2O	40

Optimization of reaction condition using **1k** (0.1 mmol), **2a** (0.2 mmol). NMR yield using 1,3,5 Trimethoxy benzene as internal standard.

Table S3: Screening of different amount of 2-bromo-2,2-difluoroethyl benzoate

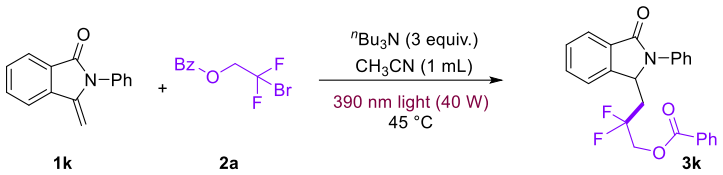


1k **2a** **3k**

Entry	$^{n}Bu_3N$ (x equiv)	Yield (%)
1	1	24
2	2	28

Optimization of reaction condition using **1k** (0.1 mmol), **2a** (0.2 mmol). NMR yield using 1,3,5 Trimethoxy benzene as internal standard.

Table S4: Control Reactions



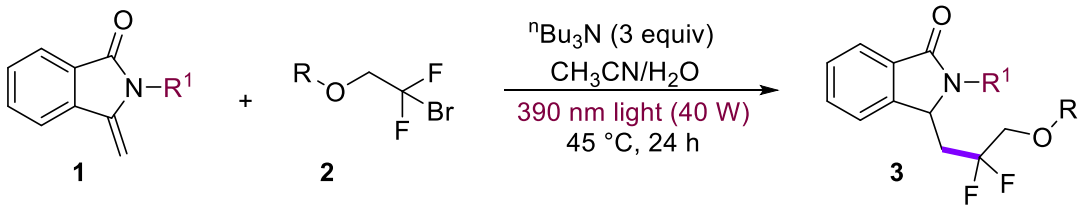
1k 2a 3k

Entry	Deviation from standard condition	Yield %
1	without light	0
2	3W purple light	28
3	40 W Blue light	33
4	3W blue light	13
5	addition of 10 μL of H_2O	85 (79)[a]
6	addition of 20 μL of H_2O	55
7	addition of 12 μL of H_2O	70
8	addition of 15 μL of H_2O	59
9	addition of 17 μL of H_2O	55
10	PPh_3 instead of $^nBu_3N$	0
11	PPh_3 instead of $^nBu_3N$	0

Optimization of reaction condition using **1k** (0.1 mmol), **2a** (0.2 mmol). NMR yield using 1,3,5 Trimethoxy benzene as internal standard.[a]Isolated yield.

5. General Experimental Procedure

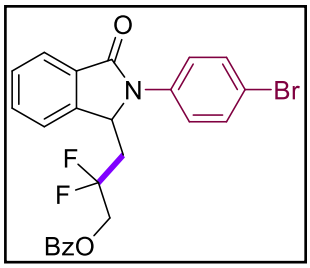
5.1 General Experimental Procedure (GP3) for functionalization of 3-methyleneisoindolin-1-ones:



1 2 3

A 10 mL glass vial was charged with **1** (0.1 mmol, 1 equiv), **2** (0.2 mmol, 2 equiv), $^nBu_3N$ (3 equiv), and a PTFE-coated magnetic stir bar under an inert atmosphere. The mixture was dissolved in CH_3CN (1 mL) and water (10 μL), sealed with a PTFE septum, stirred, and irradiated with Kessil® PR160-390 nm light (40 W) at 40–50 °C (as shown in Figure S1) for 24 h. After completion of the reaction (confirmed by TLC), the mixture was quenched with brine solution and extracted with EtOAc (2 × 5 mL). The combined organic layers were concentrated under reduced pressure, and the crude product **3** was purified by silica gel column chromatography using hexane/EtOAc as the eluent.

6. Characterization of products



3-(2-(4-bromophenyl)-3-oxoisoindolin-1-yl)-2,2-difluoropropyl benzoate (3a):

Following the experimental procedure GP3, two independent reactions of **1a** (0.1 mmol, 59 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3a** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (67 mg, 70% yield). **M.P.** 137.6-139.6 °C

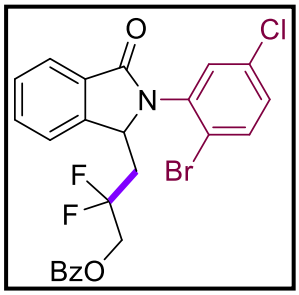
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.84 (d, *J* = 7.5 Hz, 2H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.65 – 7.50 (m, 7H) 7.44 (t, *J* = 8.0 Hz, 2H), 5.53 (d, *J* = 10.0 Hz, 1H), 4.50 – 4.34 (m, 2H), 2.70 -2.61 (m, 1H) 2.38 – 2.26 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 165.2, 144.1, 135.5, 133.9, 132.8, 132.4 (2C), 131.5, 129.8 (2C), 129.1, 128.7, 128.6, 124.9 (2C), 124.3, 123.68, 123.61, 120.8 (t, *J* = 244.3 Hz), 119.04, 64.4 (t, *J* = 34.1 Hz) 55.0 (d, *J* = 2.5 Hz), 36.3 (t, *J* = 22.7 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.5 (d, *J* = 257.4 Hz, 1F), -104.1 (d, *J* = 257.0 Hz, 1F).

IR (neat, cm^{-1}) 3060, 2963, 1706, 1491, 1376, 1260, 1106, 708.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{24}H_{18}BrF_2NO_3]^+$ 486.0516; found 486.0524.



3-(2-(2-bromo-6-chlorophenyl)-3-oxoisoindolin-1-yl)-2,2-difluoropropyl benzoate (3b):

Following experimental procedure GP3, two independent reactions of **1b** (0.1 mmol, 66 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3b** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (70 mg, 68% yield). **M.P.** 138.2-142.6 °C.

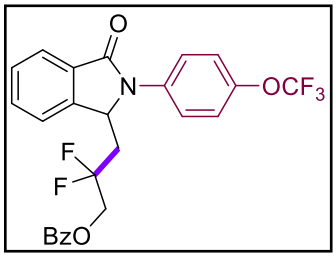
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 23.0, 7.5 Hz, 3H), 7.67 – 7.56 (m, 5H), 7.45 (t, *J* = 7.5 Hz, 3H), 7.19 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.49 -5.35 (m, 1H), 4.45 (t, *J* = 12.5 Hz, 2H), 2.65 – 2.33 (m, 2H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.25, 145.2, 134.7, 134.2, 133.8 (2C), 132.9 (2C), 130.8, 130.3, 129.8 (2C), 129.0, 128.7 (2C), 128.6 (2C), 124.6 (2C), 123.6, 120.5 (t, *J* = 244.3 Hz), 64.2 (t, *J* = 34.0 Hz), 55.7, 36.8.

^{19}F NMR (471 MHz, $CDCl_3$) δ -100.9 (d, *J* = 259.2 Hz, 1F), -103.9 (d, *J* = 258.8 Hz,1F).

IR (neat, cm^{-1}) 1716, 1471, 1272, 1110, 713.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{24}H_{17}BrClF_2NO_3]^+$ 520.0127; found 520.0116.



2,2-difluoro-3-(3-oxo-2-(4-(trifluoromethoxy)phenyl)isoindolin-1-yl)propyl benzoate (3c):

Following experimental procedure GP3, two independent reactions of **1c** (0.1 mmol, 61 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3c** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording as a white solid (71 mg, 73% yield). **M.P.** 142.8-144.6 °C

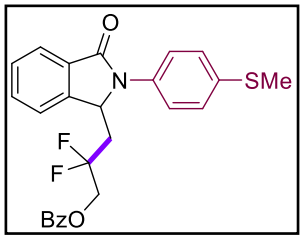
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.5 Hz, 1H), 7.79 – 7.77 (m, 2H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.58 – 7.46 (m, 5H), 7.34 (t, *J* = 8.0 Hz, 2H), 7.20 – 7.18 (m, 2H), 5.48 (d, *J* = 8.5 Hz, 1H), 4.42 – 4.29 (m, 2H), 2.64 – 2.51 (m, 1H), 2.33 – 2.19 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.9, 165.2, 146.57, 146.55, 144.2, 134.9, 133.9, 132.9, 131.5, 129.8 (2C), 129.1, 128.7 (2C), 128.6, 124.6, 124.4, 123.7, 123.6, 121.9, 121.2 (q, *J* = 244.3 Hz), 119.7 (t, *J* = 244.3 Hz), 64.4 (t, *J* = 34.1 Hz), 55.4 (d, *J* = 4.0 Hz), 36.5 (t, *J* = 23.2 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -57.8, -101.5 (d, *J* = 257.1 Hz, 1F), -104.2 (d, *J* = 257.3 Hz, 1F).

IR (neat, cm^{-1}) 1711, 1511, 1382, 1261, 1108, 709.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{25}H_{18}F_5NO_4Na]^+$ 514.1053; found 514.1061.



2,2-difluoro-3-(2-(4-(methylthio)phenyl)-3-oxoisoindolin-1-yl)propyl benzoate (3d):

Following experimental procedure GP3, two independent reactions of **1d** (0.1 mmol, 53 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3d** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (56 mg, 62% yield). **M.P.** 156.8-157.6 °C.

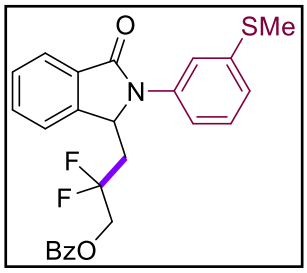
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.84 (dd, *J* = 8.5, 1.5 Hz, 2H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.64 – 7.51 (m, 5H), 7.44 (t, *J* = 8.5 Hz, 2H), 7.31 – 7.30 (m, 2H), 5.53 (d, *J* = 10.5 Hz, 1H), 4.51 – 4.35 (m, 2H), 2.76 – 2.62 (m, 1H), 2.47, (s, 3H), 2.38 – 2.25 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 165.2, 144.2, 136.1, 133.8, 133.5, 132.6, 131.8, 129.8 (2C), 129.0, 128.7 (2C), 127.6 (2C), 124.2, 124.1 (2C), 123.65, 123.62, 120.8 (t, *J* = 244.2 Hz), 64.4 (t, *J* = 34.1 Hz), 55.5, 36.4 (t, *J* = 22.7 Hz), 16.1**.**

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.4 (d, *J* = 256.7 Hz, 1F), -104.2 (d, *J* = 256.9 Hz, 1F).

IR (neat, cm^{-1}) 2922, 1702, 1496, 1381, 1269, 1105, 712.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{25}H_{21}F_2NO_3S]^+$ 454.1288; found 454.1281.



2,2-difluoro-3-(2-(3-(methylthio)phenyl)-3-oxoisoindolin-1-yl)propyl benzoate (3e):

Following experimental procedure GP3, two independent reactions of **1e** (0.1 mmol, 53 mg1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3e** was purified by flash column chromatography of reaction mixture on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (55 mg, 61% yield).

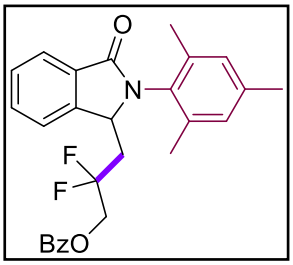
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 1H), 7.85 (dd, *J* = 8.5, 1.5 Hz, 2H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.59 – 7.53 (m, 3H), 7.41 (t, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 5.5 Hz, 2H), 7.12 – 7.09 (m, 1H), 5.57 (d, *J* = 9.0 Hz, 1H), 4.49 – 4.35 (m, 2H), 2.75 – 2.62 (m, 1H), 2.49 (s, 3H), 2.40 – 2.26 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 165.2, 144.3, 140.3, 136.9, 133.8, 132.7, 131.7, 129.8 (2C), 129.0, 128.6 (2C), 124.3, 123.8, 123.69, 123.62, 121.1, 120.8 (t, *J* = 244.7 Hz), 119.7, 64.5 (t, *J* = 33.6 Hz), 55.5, 36.5 (t, *J* = 22.7 Hz), 15.6.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.5 (d, *J* = 256.6 Hz, 1F), -104.2 (d, *J* = 256.6 Hz, 1F).

IR (neat, cm^{-1}) 2964, 1706, 1478, 1379, 1271, 1111, 711.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{25}H_{21}F_2NO_3SNa]^+$ 476.1108; found 476.1116.



2,2-difluoro-3-(2-mesityl-3-oxoisoindolin-1-yl)propyl benzoate (3f):

Following experimental procedure GP3, two independent reactions of **1f** (0.1 mmol, 52 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **1f** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (53 mg, 60% yield).

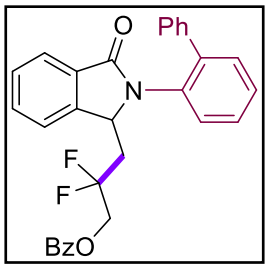
^{1}H NMR (500 MHz, CDCl3) δ 7.96 (d, J = 7.5 Hz, 1H), 7.88 – 7.81 (m, 2H), 7.73 (d, J = 7.5 Hz, 1H), 7.68 – 7.58 (m, 2H), 7.56 (d, J = 7.5 Hz, 1H), 7.43 (t, J = 8.5 Hz, 2H), 6.91 (d, J = 4.0 Hz, 2H), 5.24 (d, J = 6.5 Hz, 1H), 4.45 (t, J = 12.0 Hz, 2H), 2.55 – 2.43 (m, 1H), 2.32 – 2.70 (m, 1H), 2.25 (s, 3H), 2.14 (d, J = 11.0 Hz, 6H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.15, 165.2, 145.6, 138.4, 137.3, 136.3, 133.8, 132.3, 131.6, 130.4, 130.1, 129.8 (2C), 129.6, 128.7, 128.6 (2C), 124.2, 123.8, 123.7, 120.7 (t, *J* = 244.2 Hz), 64.2 (t, *J* = 34.1 Hz), 56.2 (t, *J* = 3.4 Hz), 35.8 (t, *J* = 22.7 Hz), 21.1, 18.7, 18.3.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.0 (d, *J* = 256.0 Hz, 1F), -105.3 (d, *J* = 256.5 Hz, 1F).

IR (neat, cm^{-1}) 2969, 1704, 1385, 1269, 1108, 712.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{27}H_{25}F_2NO_3Na]^+$ 472.1700; found 472.1710.



3-(2-([1,1'-biphenyl]-2-yl)-3-oxoisoindolin-1-yl)-2,2-difluoropropyl benzoate (3g):

Following experimental procedure GP3, two independent reactions of **1g** (0.1 mmol, 59 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3g** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording as a colorless liquid (61 mg, 64% yield).

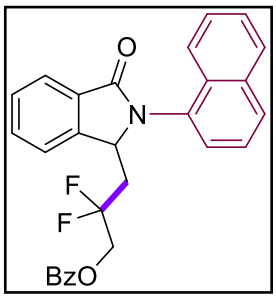
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.5 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.45 – 7.39 (m, 7H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.22 (s, 2H), 4.34 – 4.18 (m, 3H), 2.46 – 2.35 (m, 1H), 2.20 – 2.08 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.6, 165.2, 145.2, 140.4, 138.6, 133.8, 133.2, 132.6, 132.28, 131.3, 131.1, 130.3, 130.0, 129.8 (2C), 128.8, 128.7, 128.6 (2C), 128.5, 128.33, 128.31, 127.8, 124.2, 123.4, 120.4 (t, *J* = 244.2 Hz), 64.1 (t, *J* = 33.2 Hz), 55.5, 36.4 (t, *J* = 23.1 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.4 (d, *J* = 258.0 Hz, 1F), -104.4 (d, *J* = 257.8 Hz, 1F).

IR (neat, cm^{-1}) 3061, 2962, 1701, 1267, 1108, 708.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{30}H_{23}F_2NO_3]^+$ 484.1724; found 484.1719



2,2-difluoro-3-(2-(naphthalen-1-yl)-3-oxoisoindolin-1-yl)propyl benzoate (3h):

Following experimental procedure GP3, two independent reactions of **1h** (0.1 mmol, 54 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3h** (*rotamers*) was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording as a brown liquid (66 mg, 66% yield).

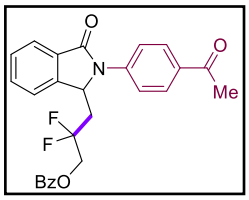
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 – 8.00 (m, 1H), 7.91 – 7.84 (m, 2H), 7.79 – 7.75 (m, 2H), 7.69 (t, *J* = 6.5 Hz, 1H), 7.62 – 7.40 (m, 8H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 5.54 – 5.43 (m, 1H), 4.35 – 4.10 (m, 2H), 2.75 – 2.33 (m, 2H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 171.3, 168.6, 167.4, 165.1, 145.7, 145.1, 134.9, 134.5, 133.7, 133.6, 133.1, 132.59, 132.52, 132.2, 131.7, 131.6, 131.1, 130.9, 129.8, 129.6 (2C), 129.4, 129.08, 129.05, 128.9, 128.6 (2C), 128.5 (2C), 127.4, 127.1, 126.6 (2C), 125.69, 125.60, 125.0, 124.5, 124.4, 123.7, 123.6, 120.55 (t, *J* = 244.2 Hz), 120.45 (t, *J* = 243.2 Hz), 64.1 (t, *J* = 33.2 Hz), 64.0 (t, *J* = 33 Hz), 60.5, 58.9, 57.5, 36.7 (t, *J* = 23 Hz), 36.6 (t, *J* = 22.9 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -100.5 (d, *J* = 257.4 Hz), -101.2 (d, *J* = 256.7 Hz), -104.3 (d, *J* = 257.5 Hz), -105.0 (d, *J* = 256.6 Hz).

IR (neat, cm^{-1}) 3056, 1709, 1403, 1271, 1110, 712.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{28}H_{21}F_2NO_3Na]^+$ 480.1387; found 480.1394.



3-(2-(4-acetylphenyl)-3-oxoisoindolin-1-yl)-2,2-difluoropropyl benzoate (3i):

Following experimental procedure GP3, two independent reactions of **1i** (0.1 mmol, 49 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3i** was purified by flash column chromatography of reaction mixture on silica gel (Gradient 0-10% EtOAc/Hexane), affording as a white solid (65 mg, 73% yield). **M.P.** 89.4-93.6 °C.

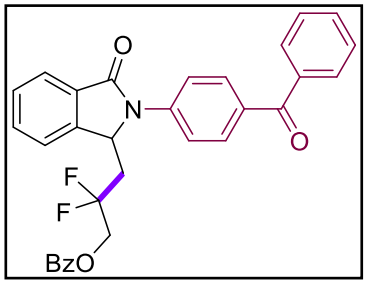
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.5 Hz, 2H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.0 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 5.63 (d, *J* = 8.5 Hz, 1H), 4.50 – 4.33 (m, 2H), 2.77 – 2.63 (m, 1H), 2.55 (s, 3H), 2.44 – 2.32 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 196.9, 167.0, 165.1, 144.1, 133.8, 133.7, 133.1, 131.3, 129.78 (2C), 129.73 (2C), 129.2, 128.6 (2C), 128.5, 124.4, 123.69, 123.62, 122.1 (2C), 120.7 (t, *J* = 244.7 Hz), 64.3 (t, *J* = 34.5 Hz), 55.1, 36.4 (t, *J* = 22.7 Hz), 26.5.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.4 (d, *J* = 257.7 Hz, 1F), -103.7 (d, *J* = 257.5 Hz, 1F).

IR (neat, cm^{-1}) 2958, 1705, 1600, 1369, 1207, 1106, 711.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{26}H_{21}F_2NO_3Na]^+$ 472.1336; found 472.1338.



3-(2-(4-benzoylphenyl)-3-oxoisoindolin-1-yl)-2,2-difluoropropyl benzoate (3j):

Following the experimental procedure GP3, two independent reactions of **1j** (0.1 mmol, 49 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3j** was purified by flash column chromatography of the reaction mixture on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (75 mg, 74% yield).

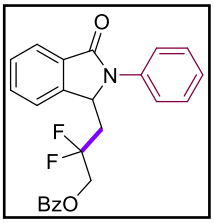
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.0 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 2H), 7.86 (d, *J* = 8.5 Hz, 2H), 7.81 (dd, *J* = 14.0, 8.5 Hz, 3H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.63 – 7.47 (m, 6H), 7.39 (t, *J* = 8.0 Hz, 2H), 5.68 (d, *J* = 7.0 Hz, 1H), 4.53 – 4.37 (m, 2H), 2.80 – 2.69 (m, 1H), 2.45 – 2.33 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 195.6, 167.1, 165.3, 144.2, 140.4, 137.7, 134.1, 133.9, 133.1, 132.5, 131.6 (2C), 131.5, 130.0 (2C), 129.8 (2C), 129.2, 128.7 (2C), 128.6, 128.5 (2C), 124.5, 123.7 (t, *J* = 244.7 Hz), 122.0 (2C), 64.5 (t, *J* = 34.5 Hz), 55.1, 36.6 (t, *J* = 22.7 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.3 (d, *J* = 257.4 Hz, 1F), -104.0 (d, *J* = 257.4 Hz, 1F).

IR (neat, cm^{-1}) 2962, 1716, 1376, 1274, 1106, 718.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{31}H_{23}F_2NO_4Na]^+$ 534.1493; found 534.1448.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl benzoate (3k):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3k** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (64 mg, 79% yield).

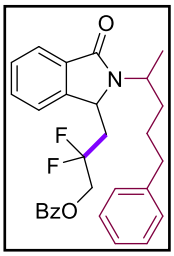
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.85 – 7.82 (m, 2H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.66 – 7.53 (m, 5H), 7.45 – 7.39 (m, 4H), 7.23 (d, *J* = 6.5 Hz, 1H), 5.58 (d, *J* = 6.5 Hz, 1H), 4.49 – 4.34 (m, 2H), 2.76 – 2.63 (m, 1H), 2.38 – 2.26(m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.9, 165.3, 144.4, 136.4, 133.8, 132.6, 131.9, 129.9 (2C), 129.4 (2C), 129.0, 128.8, 128.6 (2C), 125.9, 124.3, 123.8 (2C), 123.7, 120.8 (t, *J* = 244.7 Hz), 64.5 (t, *J* = 34.5 Hz), 55.6, 36.5 (t, *J* = 22.7 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.3 (d, *J* = 257.0 Hz, 1F), -104.3 (d, *J* = 256.6 Hz, 1F).

IR (neat, cm^{-1}) 2916, 1713, 1387, 1108, 714.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{24}H_{19}F_2NO_3Na]^+$ 430.1231; found 430.1236.



2,2-difluoro-3-(3-oxo-2-(5-phenylpentan-2-yl)isoindolin-1-yl)propyl benzoate (3l):

Following the experimental procedure GP3, two independent reactions of **1l** (0.1 mmol, 55 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3l** (*dr* = 1:1) was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (67 mg, 73% yield).

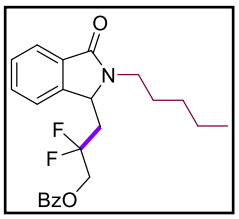
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (t, *J* = 7.0 Hz, 2H), 7.81 (d, *J* = 6.5 Hz, 1H), 7.62 – 7.58 (m, 1H), 7.56 – 7.53 (m, 2H), 7.47 – 7.42 (m, 3H), 7.24 – 7.19 (m, 2H), 7.18 – 7.11 (m, 3H), 4.83 – 4.80 (m, 1H), 4.55 – 4.42 (m, 2H), 3.93 – 3.82 (m, 1H), 2.71 – 2.15 (m, 6H), 2.09 – 1.98 (m, 1H), 1.55 (d, *J* = 7.0 Hz, 2H), 1.44 (d, *J* = 7.0 Hz, 2H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.9, 168.6, 165.40, 165.38, 145.8, 145.5, 141.4, 141.3, 133.9, 132.6, 132.6, 131.9, 131.8, 129.9, 128.8, 128.7, 128.61, 128.60, 128.55, 128.52, 128.47, 128.41, 128.34, 128.26, 126.1, 126.0, 123.49, 123.46, 123.20, 123.16, 123.1, 120.8 (t, *J* = 244 Hz), 120.7 (t, *J* = 243 Hz), 64.8 (t, *J* = 34 Hz), 64.6 (t, J = 35 Hz), 56.0 (t, *J* = 3.8 Hz), 54.6 (t, *J* = 3.8 Hz), 50.6, 49.9, 37.8 (t. *J* = 22.7 Hz), 37.5 (t. *J* = 22.7 Hz), 36.10, 35.87, 33.37, 33.28, 19.19, 18.76.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.9 (d, *J* = 257 Hz), -102.0 (d, *J* = 254 Hz), -104.1 (d, *J* = 257 Hz), -104.6 (d, *J* = 254 Hz),

IR (neat, cm^{-1}) 2969, 1730, 1687, 1270, 1108, 709.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{28}H_{27}F_2NO_3Na]^+$ 486.1857; found 486.1870.



2,2-difluoro-3-(3-oxo-2-pentylisoindolin-1-yl)propyl benzoate (3m):

Following experimental procedure GP3, two independent reactions of **1m** (0.1 mmol, 40 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3m** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane) afforded as a brown liquid (51 mg, 64% yield).

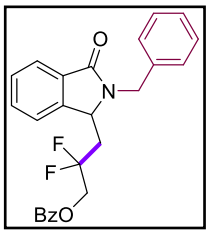
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 9.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 2H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.49 – 7.42 (m, 4H), 4.89 (d, *J* = 7.0 Hz, 1H), 4.53 (t, *J* = 12.0 Hz, 2H), 4.09 – 4.01 (m, 1H), 3.26 – 3.00 (m, 2H), 2.70 – 2.59 (m, 1H), 2.47 – 2.36 (m, 1H), 1.73 – 1.55 (m, 3H), 1.43 – 1.21 (m, 2H), 0.94 (t, *J* = 7.5 Hz, 1H), 0.86 (t, *J* = 7.0 Hz, 2H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.3, 165.4, 145.3, 133.9, 133.0, 131.9, 130.1, 129.9, 128.7, 128.6, 128.4, 123.8, 123.07, 123.03, 120.8 (t, *J* = 244.0 Hz), 64.5 (t, *J* = 33.7 Hz), 53.8, 40.1, 36.6 (t, *J* = 22.9 Hz), 29.1, 27.9, 22.5, 14.0.

^{19}F NMR (471 MHz, $CDCl_3$) δ -102.0 (d, *J* = 257.5 Hz, 1F), -104.0 (d, *J* = 257.6 Hz, 1F).

IR (neat, cm^{-1}) 2965, 1700, 1271, 1106, 721.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{23}H_{25}F_2NO_3Na]^+$ 424.1700; found 424.1705.



3-(2-benzyl-3-oxoisoindolin-1-yl)-2,2-difluoropropyl benzoate (3n):

Following the experimental procedure GP3, two independent reactions of **1n** (0.1 mmol, 47 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3n** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (56 mg, 67% yield).

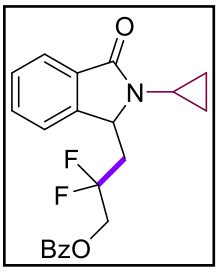
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.92 (m, 2H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.0 Hz, 1H), 7.47 – 7.37 (m, 5H), 7.19 – 7.13 (m, 5H), 5.24 (d, *J* = 15.5 Hz, 1H), 4.65 (dd, *J* = 7.0, 3.0 Hz, 1H), 4.40 – 4.24 (m, 3H), 2.64 – 2.52 (m, 1H), 2.39 – 2.27 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.5, 165.3, 145.3, 136.8, 133.9, 132.1, 131.6, 129.9 (2C), 128.9 (2C), 128.8, 128.77 (2C), 128.74, 128.1, 127.8, 124.0, 123.17, 123.13, 120.7 (t, *J* = 244.2 Hz), 64.5 (t, *J* = 33.6 Hz), 54.0, 44.3, 36.4 (t, *J* = 23.1 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.4 (d, *J* = 258.2 Hz, 1F), -103.4 (d, *J* = 258.2 Hz, 1F).

IR (neat, cm^{-1}) 2971, 1695, 1411, 1271, 1107, 713.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{25}H_{21}F_2NO_3Na]^+$ 444.1387; found 444.1398.



3-(2-cyclopropyl-3-oxoisoindolin-1-yl)-2,2-difluoropropyl benzoate (3o):

Following the experimental procedure GP3, two independent reactions of **1o** (0.1 mmol, 37 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) for 24 h. The product **3o** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (48 mg, 66% yield). **M.P.** 89.9-92.6 °C

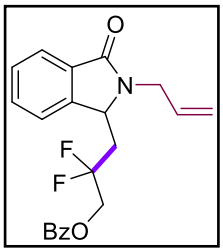
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 2H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.60 (t, *J* = 7.0 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.47 – 7.43 (m, 3H), 4.74 (d, *J* = 8.0 Hz, 1H), 4.54 – 4.44 (m, 2H), 2.95 – 2.83 (m, 1H), 2.72 – 2.67 (m, 1H), 2.45 – 2.35 (m, 1H), 1.16 – 1.08 (m, 1H), 1.00 – 0.93 (m, 1H), 0.85 – 0.73 (m, 2H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.1, 165.4, 144.7, 133.8, 132.2, 131.9, 129.8, 128.75 (2C), 128.70, 123.6, 123.37, 123.32, 120.8 (t, *J* = 244.2 Hz), 64.6 (t, *J* = 33.6 Hz), 55.8, 36.4 (t, *J* = 23.1 Hz), 23.1, 8.0, 4.9.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.2 (d, *J* = 257.4 Hz, 1F), -104.1 (d, *J* = 257.3 Hz, 1F).

IR (neat, cm^{-1}) 3016, 1692, 1404, 1266, 1105, 706.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{21}H_{19}F_2NO_3Na]^+$ 394.1231; found 394.1242.



3-(2-allyl-3-oxoisoindolin-1-yl)-2,2-difluoropropyl benzoate (3p):

Following the experimental procedure GP3, two independent reactions of **1p** (0.1 mmol, 37 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) for 24 h. The product **3p** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (51 mg, 69% yield).

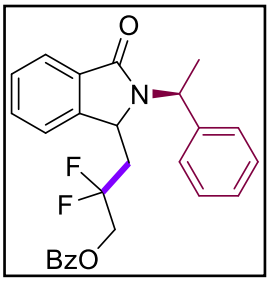
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 9.0 Hz, 1H), 7.56 – 7.54 (m, 2H), 7.49 – 7.45 (m, 3H), 5.86 – 5.79 (m, 1H), 5.22 – 5.18 (m, 2H), 4.89 (dd, *J* = 7.5, 3.5 Hz, 1H), 4.68 – 4.63 (m, 1H), 4.52 – 4.44 (m, 2H), 3.85 (dd, *J* = 15.5, 7.0 Hz, 1H), 2.76 – 2.64 (m, 1H), 2.48 -2.35 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.2, 165.4, 145.4, 133.9, 132.9, 132.1, 131.7, 129.9 (2C), 128.77 (2C), 128.74, 123.9, 123.18, 123.14, 120.7 (t, *J* = 244.7 Hz) 118.2, 64.5 (t, *J* = 34.1 Hz), 54.2, 43.1, 36.6 (t, *J* = 23.6 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.6 (d, *J* = 258.1 Hz, 1F), -103.7 (d, *J* = 258.0 Hz, 1F).

IR (neat, cm^{-1}) 2697, 1701, 1269, 1106, 719.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{21}H_{15}F_2NO_3]^+$ 372.1411; found 372.1420.



2,2-difluoro-3-(3-oxo-2-((*R*)-1-phenylethyl)isoindolin-1-yl)propyl benzoate (3q):

Following the experimental procedure GP3, two independent reactions of **1q** (0.1 mmol, 49 mg, 1 equiv) with **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3q** (*dr* = 1:1) was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a brown liquid (52 mg, 60% yield).

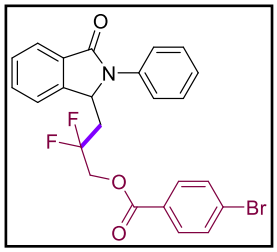
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.73 – 7.71 (m, 1H), 7.69 – 7.65 (m, 1H), 7.43 – 7.40 (m, 1H), 7.38 – 7.36 (m, 1H), 7.35 – 7.30 (m, 2H), 7.30 – 7.27 (m, 2H), 7.18 – 7.16 (m, 1H), 7.10 – 7.08 (m, 1H), 7.04 – 7.02 (m, 2H), 6.96 – 6.92 (m, 1H), 5.47 (q, *J* = 7.5 Hz, 1H), 4.85 (d, *J* = 8.5 Hz, 1H), 4.23 – 4.05 (m, 3H), 2.18 – 2.04 (m, 1H), 1.77 – 1.71 (m, 1H), 1.65 (d, *J* = 7.5 Hz, 2H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.92, 168.90, 165.3, 165.2, 145.9, 145.5, 141.6, 140.4, 133.89 (2C), 133.82 (2C), 132.1 (2C), 131.9, 131.8, 129.96 (2C), 129.91 (2C), 128.86, 128.82, 128.7 (2C), 128.6 (2C), 128.5 (2C), 128.1, 128.0, 127.7, 127.6 127.5, 127.4, 127.3 (2C), 127.1 (2C), 123.7 (2C), 123.6 (2C), 123.3, 123.2, 120.8 (t, *J* = 241 Hz), 120.6 (t, *J* = 240 Hz), 64.65 (t, *J* = 32 Hz), 64.61 (t = *J* = 33 Hz), 55.2, 53.5, 52.7, 49.9 (2C), 37.64 (t, *J* = 22 Hz), 36.9 (t, *J* = 23 Hz), 18.7, 17.1.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.2 (d, *J* = 257.9 Hz), -102.2 (d, *J* = 255.7 Hz), -104.1 (d, *J* = 255.8 Hz), -104.4 (d, *J* = 257.9 Hz).

IR (neat, cm^{-1}) 2969, 1730, 1689, 1270, 1106, 706.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{26}H_{23}F_2NO_3Na]^+$ 458.1544; found 458.1548.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 4-bromobenzoate (3r):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2b** (0.2 mmol, 136 mg, 2 equiv) were carried out for 24 h. The product **3r** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (75 mg, 78% yield). **M.P.** 142.8-144.6 ^{0}C

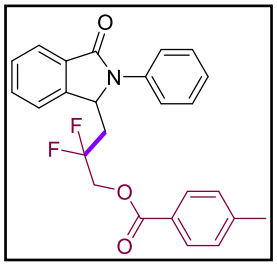
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.85 – 7.82 (m, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.69 – 7.67 (m, 1H), 7.66 – 7.62 (m, 2H), 7.61 – 7.59 (m, 2H), 7.56 – 7.53 (m, 3H), 7.46 – 7.42 (m, 2H), 5.57 (dd, *J* = 8.5, 2.0 Hz, 1H), 4.47 – 4.33 (m, 2H), 2.73 – 2.61 (m, 1H), 2.37 – 2.25 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 164.6, 144.3, 136.3, 132.6, 132.0, 131.9, 131.3, 130.1, 129.9, 129.5, 129.0, 127.6, 125.9, 124.3, 123.8, 123.68, 123.61, 123.3, 122.8, 120.7 (t, *J* = 244.7 Hz) 64.6 (t, *J* = 34.1 Hz), 55.5, 36.4 (t, *J* = 23.6 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -56.1, -101.6 (d, *J* = 256.7 Hz, 1F), -104.3 (d, *J* = 256.8 Hz, 1F).

IR (neat, cm^{-1}) 2968, 1712, 1386, 1272, 1109, 712.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{24}H_{18}BrF_2NO_3Na]^+$ 508.0336; found 508.0329.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 4-methylbenzoate (3s):

Following experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2c** (0.2 mmol, 111 mg, 2 equiv) were carried out for 24 h. The product **3s** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (58 mg, 70% yield). **M.P.** 180.4-182.6 °C

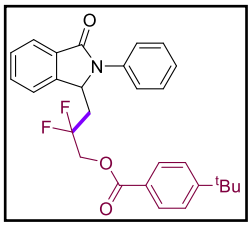
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 3H), 7.64 7.59 (m, 3H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 2H), 7.25 – 7.22 (m, 1H), 7.19 (d, *J* = 8.5 Hz, 2H), 5.57 (d, *J* = 6.5 Hz, 1H), 4.46 – 4.33 (m, 2H), 2.74 – 2.62 (m, 1H), 2.41 (s, 3H), 2.36 – 2.25 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 165.3, 144.6, 144.4, 136.3, 132.5, 131.9, 129.9 (2C), 129.4 (2C), 129.3 (2C), 128.9, 126.0, 125.9, 124.2, 123.8, 123.7, 123.6, 120.8 (t, *J* = 244.2 Hz), 64.3 (t, *J* = 35.9 Hz), 55.6, 36.5 (t, *J* = 23.1 Hz), 21.8.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.3 (d, *J* = 256.6 Hz, 1F), -104.4 (d, *J* = 256.3 Hz, 1F).

IR (neat, cm^{-1}) 2968, 1705, 1383, 1271, 1107, 757.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{25}H_{21}F_2NO_3Na]^+$ 444.1387; found 444.1389.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 4-(tert-butyl)benzoate (3t):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2d** (0.2 mmol, 128 mg, 2 equiv) were carried out for 24 h. The product **3t** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (64 mg, 69% yield). **M.P.** 161.2-161.9 °C

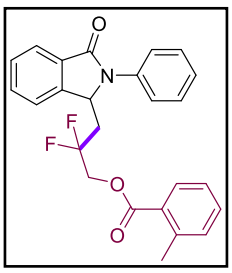
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.65 – 7.59 (m, 3H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.45 – 7.40 (m, 4H), 7.23 (t, *J* = 7.5 Hz, 1H), 5.57 (d, *J* = 6.5 Hz, 1H), 4.47 – 4.35 (m, 2H), 2.73 – 2.62 (m, 1H), 2.37 – 2.25 (m, 1H), 1.34 (s, 9H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 165.2, 157.6, 144.4, 136.4, 132.5, 131.9, 130.8, 129.4 (2C), 129.0, 127.9, 126.0, 125.9, 124.3, 123.8, 123.7, 123.6, 120.8 (t, *J* = 244.7 Hz), 64.3 (t, *J* = 33.6 Hz), 55.6, 36.6 (t, *J* = 22.7 Hz), 35.2, 31.3 (2C).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.2 (d, *J* = 256.5 Hz, 1F), -104.4 (d, *J* = 256.5 Hz, 1F).

IR (neat, cm^{-1}) 2963, 1701, 1378, 1106, 745, 701.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{28}H_{27}F_2NO_3Na]^+$ 486.1857; found 486.1859.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 2-methylcyclohexa-1,3-diene-1-carboxylate (3u):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2e** (0.2 mmol, 111 mg, 2 equiv) were carried out for 24 h. The product **9u** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane) affording a white solid (64 mg, 76% yield). **M.P.** 135.8-136.6 °C.

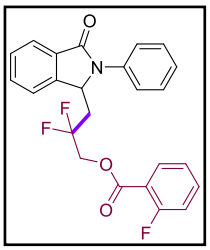
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.67 – 7.58 (m, 4H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.42 (q, *J* = 7.5 Hz, 3H), 7.25 – 7.21 (m, 2H), 7.18 (t, *J* = 8.0 Hz, 1H), 5.57 (d, *J* = 6.5 Hz, 1H), 4.44 – 4.34 (m, 2H), 2.73 – 2.62 (m, 1H), 2.50 (s, 3H), 2.37 – 2.25 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 165.9, 144.4, 141.0, 136.3, 132.8, 132.5, 132.0, 131.9, 130.8, 129.4 (2C), 129.0, 127.9, 126.0 125.9, 124.3, 123.8, 123.7, 123.6, 120.8 (t, *J* = 244.2 Hz), 64.3 (t, *J* = 33.6 Hz), 55.6, 36.6 (t, *J* = 18.0 Hz), 21.9.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.3 (d, *J* = 256.4 Hz, 1F), -104.4 (d, *J* = 256.2 Hz, 1F).

IR (neat, cm^{-1}) 2961, 1703, 1496, 1381, 1250, 1091, 750.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{25}H_{27}F_2NO_3Na]^+$ 444.1387; found 444.1393.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 2-fluorobenzoate (3v):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) and **2f** (0.2 mmol, 112 mg, 2 equiv) were carried out for 24 h. The product **3v** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (63 mg, 74% yield). **M.P.** 175.4-175.8 °C

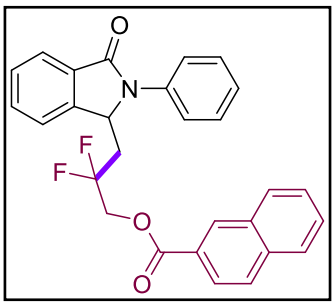
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.89 – 7.72 (m, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.64 – 7.53 (m, 5H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.22 – 7.16 (m, 2H), 7.12 – 7.08 (m, 1H), 5.57 (d, *J* = 6.5 Hz, 1H), 4.40 (t, *J* = 12.0 Hz, 2H), 2.75 – 2.64 (m, 1H), 2.42 – 2.30 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.9, 163.0 (d, *J* = 3.8 Hz), 162.3 (d, *J* = 262 Hz), 161.1, 144.4, 136.3, 135.4 (d, *J* = 8.9 Hz), 132.5, 132.3, 131.9, 129.4 (2C), 128.9, 125.9, 124.29, 124.25, 123.87 (2C), 123.7 (d, *J* = 8.8 Hz), 120.7 (t, *J* = 244.2 Hz), 117.2 (d, *J* = 21 Hz), 64.7 (t, *J* = 34.5 Hz), 55.6, 36.4 (t, *J* = 22.7 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.1 (d, *J* = 257.8 Hz, 1F), -104.4 (d, *J* = 257.5 Hz, 1F), -108.2.

IR (neat, cm^{-1}) 2907, 1710, 1381, 1265, 1098, 751.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{24}H_{18}F_3NO_3]^+$ 426.1317; found 426.1321.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 2-naphthoate (3w):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2g** (0.2 mmol, 125 mg, 2 equiv) were carried out for 24 h. The product **3w** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (59 mg, 65% yield). **M.P.** 123.4-125.8 °C

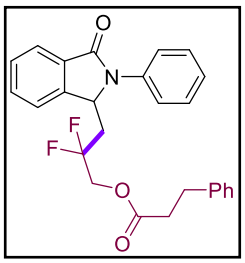
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.95 (d, *J* = 7.5 Hz, 1H), 7.88 (dd, *J* = 8.5, 4.5 Hz, 2H), 7.84 (s, 2H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.64 – 7.59 (m, 4H), 7.55 (q, *J* = 6.5 Hz, 2H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 1H), 5.58 (d, *J* = 8.5 Hz, 1H), 4.55 – 4.41 (m, 2H), 2.79 – 2.68 (m, 1H), 2.42 – 2.30 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 165.4, 144.3, 136.3, 135.8, 132.5, 132.4, 131.9, 131.6, 129.5, 129.4 (2C), 128.9, 128.8, 128.4, 127.8, 126.9, 125.94, 125.91, 125.0, 124.2, 123.7, 123.68, 123.61, 120.8 (t, *J* = 244.7 Hz), 64.5 (t, *J* = 33.6 Hz), 55.5, 36.5 (t, *J* = 23.2 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.2 (d, *J* = 256.6 Hz, 1F), -104.2 (d, *J* = 256.6 Hz, 1F).

IR (neat, cm^{-1}) 2961, 1703, 1496, 1279, 1098, 759.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{28}H_{21}F_2NO_3Na]^+$ 480.1387; found 480.1393.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 4-phenylbutanoate (3x):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2h** (0.2 mmol, 116 mg, 2 equiv) were carried out for 24 h. The product **3x** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (56 mg, 64% yield). **M.P.** 82.4-84.8 °C

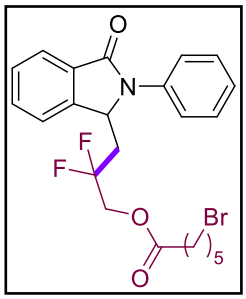
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.68 – 7.54 (m, 5H), 7.47 – 7.44 (m, 2H), 7.24 – 7.14 (m, 4H), 7.10 (d, *J* = 7.0 Hz, 2H), 5.49 (d, *J* = 8.5 Hz, 1H), 4.16 (t, *J* = 11.5 Hz, 2H), 2.84 (t, *J* = 8.0 Hz, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 2.49 – 2.37 (m, 1H), 2.15 – 2.03 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 171.5, 166.8, 144.3, 136.4, 132.5, 131.9, 129.4 (2C), 128.9, 128.6 (2C), 128.2 (2C), 126.5, 125.9, 124.2, 123.7, 123.67, 123.60, 120.6 (t, *J* = 244.2 Hz), 64.0 (t, *J* = 33.6 Hz), 55.4, 36.3 (t, *J* = 22.7 Hz), 35.4, 30.7.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.5 (d, *J* = 256.5 Hz, 1F), -104.5 (d, *J* = 256.3 Hz, 1F).

IR (neat, cm^{-1}) 2961, 1700, 1382, 1149, 758, 700.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{26}H_{23}F_2NO_3Na]^+$ 458.1544; found 458.1534



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 6-bromohexanoate (3y):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2i** (0.2 mmol, 134 mg, 2 equiv) were carried out for 24 h. The product **3y** (*rotamers*) was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (29 mg, 30% yield).

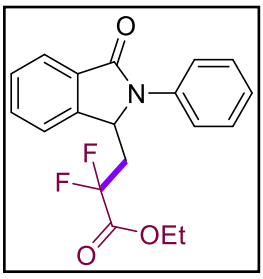
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 8.5 Hz, 2H), 7.54 (t, *J* = 7.0 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.27 (d, *J* = 7.5 Hz, 1H), 5.52 (d, *J* = 5.5 Hz, 1H), 4.24 – 4.13 (m, 2H), 3.50 (t, *J* = 6.5 Hz, 1H), 3.36 (t, *J* = 7.0 Hz, 1H), 2.58 – 2.47 (m, 1H), 2.26 (t, *J* = 7.5 Hz, 2H), 1.84 – 1.79 (m, 1H), 1.76 – 1.70 (m, 1H), 1.58 – 1.52 (m, 2H), 1.44 – 1.38 (m, 2H), 0.97 (t, *J* = 7.0 Hz, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ172.0, 166.8, 144.3, 136.4, 132.5, 131.9, 129.4 (2C), 129.0, 125.9, 124.3, 123.7, 123.68, 123.61, 120.6 (t, *J* = 244.2 Hz), 64.56, 63.9 (t, *J* = 33.2 Hz), 55.5, 55.49, 44.7, 36.5 (t, *J* = 22.7 Hz), 33.63, 33.60, 33.4, 32.3, 32.1, 27.5, 26.3, 24.0, 23.8.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.72 (d, *J* = 255.9 Hz, 1F), -104.47 (d, *J* = 255.8 Hz, 1F).

IR (neat, cm^{-1}) 2957, 1701, 1384, 1157, 760.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{23}H_{24}BrF_2NO_3Na]^+$ 502.0805; found 502.0804.



ethyl 2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propanoate (3z):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) and **2j** (0.2 mmol, 40 mg, 2 equiv) were carried out for 24 h. The product **3z** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording it as a white solid (48 mg, 69% yield). The analytical data are consistent with published ones[1].

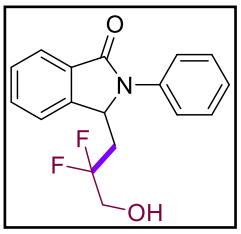
^{1}H NMR (500 MHz, DMSO) δ 7.79 - 7.74 (m, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 1H), 5.79 (d, *J* = 3.5 Hz, 1H), 4.02 – 3.88 (m, 2H), 2.89 – 2.78 (m, 1H), 2.66 – 2.55 (m, 1H), 1.23 (s, 3H).

^{13}C {^{1}H} NMR (126 MHz, DMSO) δ 166.0, 164.3 (t, *J* = 115.3 Hz), 143.7, 136.5, 132.1, 131.4, 128.8 (2C), 128.6, 125.3, 123.6 (2C), 123.27, 123.22, 115.2 (t, *J* = 251.3 Hz), 55.4, 34.5 (t, *J* = 22.5 Hz), 29.0, 13.3.

^{19}F NMR (471 MHz, DMSO) δ -101.1 (d, *J* = 256.5 Hz, 1F), -102.4 (d, *J* = 256.7 Hz, 1F).

Large scale reaction:

A 50 mL round-bottom flask was charged with **1k** (1 gm, 4.5 mmol, 1 equiv), **2j** (1.5 mL, 9.04 mmol, 2 equiv), $^{n}Bu_3N$ (3.2 mL, 13.5 mmol, 3 equiv), and a PTFE-coated magnetic stir bar. CH_3CN (30 mL) and water (4.0 mL) were then added, and the flask was sealed with a PTFE septum. The reaction mixture was stirred and irradiated with Kessil® PR160-390 nm light (40 W) at 45 °C (as shown in Figure S1) for 24 h. After completion, the mixture was quenched with saturated aqueous NaCl solution and extracted with EtOAc. The combined organic layers were concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography using hexane/EtOAc as the eluent to afford **3z** as a yellow liquid (698 mg, 45%).



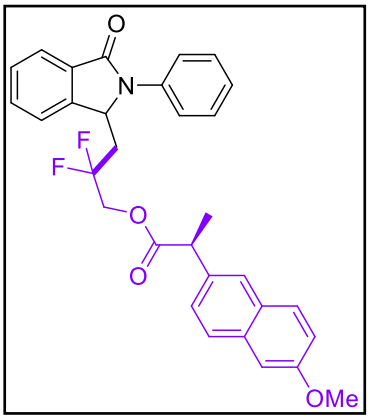
3-(2,2-difluoro-3-hydroxypropyl)-2-phenylisoindolin-1-one (3aa):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) and 2k (0.2 mmol, 31 mg, 2 equiv) were performed for 24 h. The product **3aa** was purified by flash column chromatography of the reaction mixture on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (16 mg, 25% yield). The analytical data are consistent with published ones[1].

^{1}H NMR (500 MHz, CDCl3) δ 7.94 (d, J = 7.5 Hz, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.65 – 7.60 (m, 3H), 7.54 (t, J = 7.5 Hz, 1H), 7.47 (t, J = 8.5 Hz, 1H), 7.25 (s, 1H), 5.54 (d, J = 6.0, Hz, 1H), 3.73 – 3.62 (m, 2H), 2.64 – 2.53 (m, 1H), 2.34 – 2.20 (m, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.0, 144.6, 136.4, 132.5, 129.4, 128.9, 125.9, 124.2, 123.8, 123.7, 123.6, 64.7 (t, *J* = 31.5 Hz), 55.7, 36.0, 35.8, 35.7.

^{19}F NMR (471 MHz, $CDCl_3$) δ -104.0 (d, *J* = 252.9 Hz, 1F), -107.1 (d, *J* = 252.8 Hz, 1F).



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 2-(6-methoxynaphthalen-2-yl)propanoate (3ac):

Following the experimental procedure GP3, two independent reactions of 1k (0.1 mmol, 22 mg, 1 equiv) and 2l (0.2 mmol, 148 mg, 2 equiv) were performed for 24 h. The product **3ac** (*dr* = 1:1) was purified by flash column chromatography of the reaction mixture on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (72 mg, 70% yield).

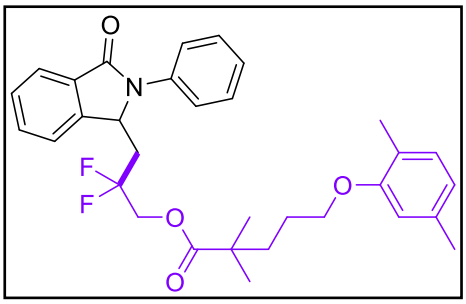
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.88 (m, 1H), 7.60 – 7.42 (m, 10H), 7.25 – 7.22 (m, 2H), 7.12 (d, *J* = 9.0 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 5.37 (d, *J* = 8.0 Hz, 1H), 4.26 – 4.11 (m, 2H), 3.93 (d, *J* = 6.5 Hz, 3H), 3.78 (q, *J* = 7.5 Hz, 1H), 2.41 – 2.23 (m, 1H), 1.98 (s, 1H), 1.52 – 1.49 (m, 3H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 173.33, 173.31, 166.8, 166.7, 157.9, 157.8, 144.3, 144.2, 136.31, 136.30, 134.5, 138.86, 133.84, 132.45, 132.41, 131.77, 131.74, 129.3 (2C), 129.24, 129.1, 128.9, 128.8, 128.83, 128.81, 127.36, 127.34, 126.0 (2C), 125.97, 125.95, 125.93, 125.91, 124.14, 124.12, 123.76, 123.72, 123.51, 123.46, 123.44, 123.40, 120.6 (t, *J* = 244.2 Hz), 119.36, 119.33, 105.7, 64.3 (t, *J* = 33.6 Hz), 64.2 (t, *J* = 32.6 Hz), 55.37 (d, *J* = 2.5 Hz), 55.36 (d, *J* = 2.4 Hz), 45.2, 45.1, 36.46 (t, *J* = 22.5 Hz), 36.16 (t, *J* = 21.5 Hz), 18.15, 18.08.

^{19}F NMR (471 MHz, $CDCl_3$) δ -100.83 (d, *J* = 257.4 Hz), -101.45 (d, *J* = 257.2 Hz), -104.24 (d, *J* = 201.4 Hz), -104.78 (d, *J* = 201.9 Hz).

IR (neat, cm^{-1}) 2968, 1696, 1383, 1157, 756.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{31}H_{27}F_2NO_4Na]^+$ 538.1806; found 538.1791.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (3ad):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) and **2m** (0.2 mmol, 156 mg, 2 equiv) were carried out for 24 h. The product **3ad** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (64 mg, 60% yield).

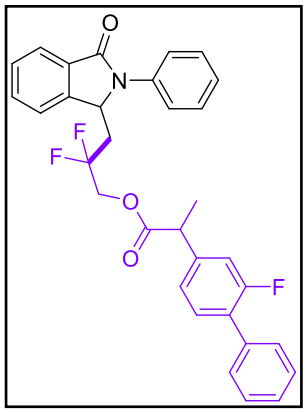
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.63 – 7.51 (m, 3H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.00 – 6.98 (m, 1H), 6.66 – 6.57 (m, 3H), 5.53 (d, *J* = 7.5 Hz, 1H), 4.21 – 4.15 (m, 2H), 3.92 (t, *J* = 5.5 Hz, 1H), 3.84 (t, *J* = 5.5 Hz, 2H), 2.98 – 2.89 (m, 1H), 2.58 – 2.47 (m, 1H), 2.30 (s, 3H), 2.14 (s, 3H), 1.75 – 1.71 (m, 1H), 1.63 (s, 1H), 1.43 – 1.37 (m, 1H), 1.10 (s, 6H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 176.5, 166.9, 157.1, 156.9, 144.5, 136.6, 136.6, 136.3, 132.6, 131.9, 130.5, 130.4, 129.5, 129.0, 126.0, 124.3, 123.7, 123.6, 123.6, 122.7, 120.9, 120.8, 120.7 (t, *J* = 244 Hz), 112.1, 112.1, 68.2, 67.8, 63.9 (t, *J* = 33.6 Hz), 55.5, 52.1, 42.2, 37.1, 36.9, 36.5 (t, *J* = 22.5 Hz), 25.3, 25.3, 25.1, 25.0, 25.0, 21.5, 20.3, 20.0, 15.9, 15.8, 13.9, 13.7.

^{19}F NMR (471 MHz, $CDCl_3$) δ -102.3 (d, *J* = 255.4 Hz, 1F), -105.0 (d, *J* = 255.1 Hz, 1F).

IR (neat, cm^{-1}) 2958, 1708, 1384, 1137, 760.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{32}H_{35}F_2NO_4Na]^+$ 558.2432; found 558.2425.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (3ae):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2n** (0.2 mmol, 142 mg, 2 equiv) were carried out for 24 h. The product **3ae** (*dr* 1:1) was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a brown liquid (75 mg, 71% yield).

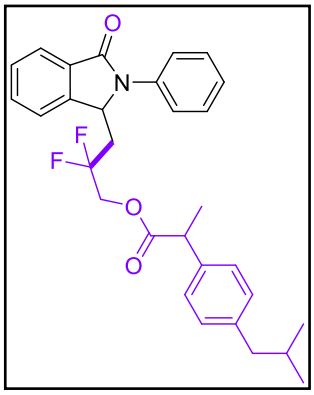
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.90 (m, 1H), 7.63 – 7.56 (m, 4H), 7.52 – 7.43 (m, 7H), 7.39 – 7.36 (m, 1H), 7.32 – 7.28 (m, 2H), 7.02 – 6.98 (m, 2H), 5.49 (d, *J* = 8.5 Hz, 1H), 4.26 – 4.11 (m, 2H), 3.71 – 3.66 (m, 1H), 2.53 – 2.40 (m, 1H), 2.21 – 2.08 (m, 1H), 1.47 – 1.42 (m, 3H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 172.6, 166.8, 159.9 (d, J = 250 Hz), 144.3, 144.2, 140.7 (d, J = 2.5 Hz), 140.6 (d, J = 2.5 Hz), 136.3, 135.3, 132.6, 132.5, 131.8, 130.9, 129.4, 129.05, 129.03, 128.9, 128.62, 127.9, 126.0, 124.29, 124.28, 123.78, 123.75, 123.58, 123.55, 120.5 (t, *J* = 244.2 Hz), 115.4 (d, *J* = 22.5 Hz), 115.2 (d, *J* = 21.5 Hz), 115.2, 115.1, 64.3 (t, *J* = 33.2 Hz), 55.4, 44.7, 36.5 (t, *J* = 64.6 Hz), 18.16, 18.11.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.1.5 (d, *J* =259 Hz), -101.9 (d, *J* =254 Hz), -101.6 (d, *J* =259 Hz), -101.7 (d, *J* =254 Hz),

IR (neat, cm^{-1}) 2970, 1700, 1493, 1381, 1152, 1091, 754, 700.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{32}H_{26}F_3NO_3Na]^+$ 552.1763; found 552.1767



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 2-(4-isobutylphenyl)propanoate (3af):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2o** (0.2 mmol, 139 mg, 2 equiv) were carried out for 24 h. The product **3af** (*dr* = 1:1) was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (59 mg, 60% yield).

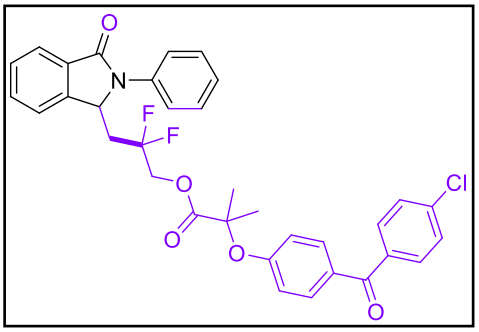
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.62 – 7.52 (m, 5H), 7.49 – 7.45 (m, 2H), 7.26 (s, 1H), 7.07 – 7.03 (m, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 5.45 (d, *J* = 8.5 Hz, 1H), 4.23 – 4.06 (m, 2H), 3.65 – 3.60 (m, 1H), 2.37 – 2.33 (m, 3H), 2.13 – 2.01 (m, 1H), 1.83 – 1.75 (m, 1H), 1.44 – 1.40 (m, 3H), 0.86 (d, *J* = 6.5 Hz, 6H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 173.39, 166.82, 144.46, 144.35, 141.07, 141.04, 136.75, 136.71, 136.37, 132.52, 131.91, 129.50, 129.48, 129.42, 128.93, 127.20, 127.18, 125.95, 124.24, 123.74, 123.72, 123.63, 123.55, 120.67 (t, *J* = 243.6 Hz), 120.68 (t, *J* = 243.6 Hz), 64.24 (t, *J* = 34 Hz), 64.18 (t, *J* = 34 Hz), 55.41, 45.08, 44.91, 44.85, 36.4 (t, *J* = 22.5 Hz), 36.2 (t, *J* = 22.5 Hz), 30.28, 22.46, 18.13, 18.03.

^{19}F NMR (471 MHz, $CDCl_3$) δ -100.8 (d, *J* =259 Hz), -101.3 (d, *J* =267 Hz), -104.3 (d, *J* =259 Hz), -104.6 (d, *J* =267 Hz).

IR (neat, cm^{-1}) 2954, 1703, 1382, 1155, 760.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{30}H_{31}F_2NO_3Na]^+$ 514.2170; found 514.2169.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (3ag):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) and **2p** (0.2 mmol, 183 mg, 2 equiv) were carried out for 24 h. The product **3ag** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (74 mg, 61% yield).

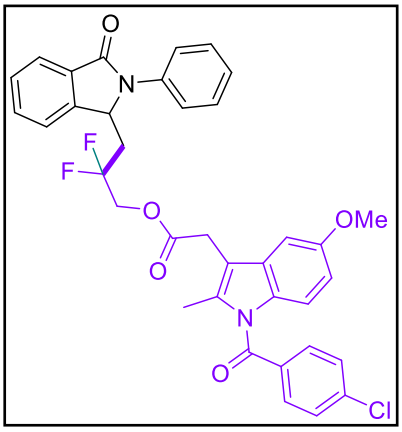
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.68 – 7.64 (m, 4H), 7.59 – 7.49 (m, 5H), 7.45 – 7.42 (m, 4H), 7.24 (d, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 9.0 Hz, 2H), 5.46 (d, *J* = 8.5 Hz, 1H), 4.31 – 4.20 (m, 2H), 2.46 – 2.35 (m, 1H), 2.14 – 2.01 (m, 1H), 1.57 (s, 6H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 194.1, 172.5, 166.7, 159.2, 144.2, 138.6, 136.3, 136.2, 132.5, 132.1 (2C), 131.8, 131.2 (2C), 130.8, 129.9 (2C), 129.0, 128.7 (2C), 126.0, 124.3, 123.7 (2C), 123.5, 123.4, 120.3 (t, *J* = 245.1 Hz), 117.4, 79.2, 64.4 (t, *J* = 33.6 Hz), 55.3, 36.4 (t, *J* = 23.1 Hz), 25.4, 25.3.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.99 (d, *J* = 256.7 Hz, 1F), -104.76 (d, *J* = 256.7 Hz, 1F).

IR (neat, cm^{-1}) 3003, 1703, 1598, 1386, 1275, 1133, 759.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{34}H_{28}ClF_2NO_5Na]^+$ 626.1522; found 626.1514.



2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methylindolin-3-yl)acetate (3ah):

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) with **2q** (0.2 mmol, 200 mg, 2 equiv) were carried out for 24 h. The product **3ah** was purified by flash column chromatography of reaction mixture on silica gel (Gradient 0-10% EtOAc/Hexane), affording a brown liquid (84 mg, 65% yield).

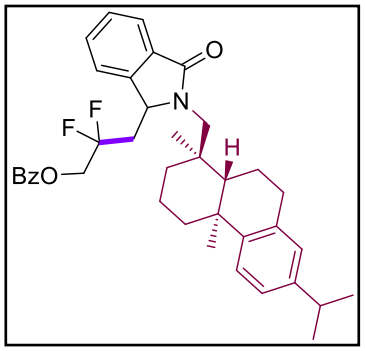
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.5 Hz, 1H), 7.63 – 7.51 (m, 7H), 7.47 – 7.43 (m, 4H), 7.25 – 7.23 (m, 1H), 6.84 (d, *J* = 2.5 Hz, 1H), 6.78 (d, *J* = 9.0 Hz, 1H), 6.63 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.45 (d, *J* = 8.5 Hz, 1H), 4.25 – 4.12 (m, 2H), 3.76 (s, 3H), 3.63 (s, 1H), 2.49 – 2.37 (m, 1H), 2.29 (s, 2H), 2.22 – 2.09 (m, 1H), 1.99 (s, 1H), 1.49 (s, 1H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.5, 168.2, 166.8, 156.1, 144.2, 139.5, 136.2, 133.7, 132.5, 131.8, 131.2 (2C), 130.7, 130.2, 129.4 (2C), 129.2 (2C), 128.9, 126.0, 124.2, 123.7 (2C), 123.47, 123.40, 120.4 (t, *J* = 244.7 Hz), 115.9, 115.0, 111.7, 111.5, 64.5 (t, *J* = 32.2 Hz), 55.7, 36.5 (t, *J* = 18.1 Hz), 31.7, 29.9, 13.3.

^{19}F NMR (471 MHz, $CDCl_3$) δ -101.3 (d, *J* = 256.4 Hz, 1F), -104.6 (d, *J* = 256.3 Hz, 1F).

IR (neat, cm^{-1}) 2962, 1694, 1478, 1375, 1318, 1229, 756.

HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $[C_{36}H_{29}ClF_2N_2O_5Na]^+$ 665.1631; found 665.1629.



2,2-difluoro-3-(2-(((1S,4aR,10aS)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)-3-oxoisoindolin-1-yl)propyl benzoate (3ai):

Following the experimental procedure GP3, two independent reactions of **1r** (0.1 mmol, 82 mg, 1 equiv) and **2a** (0.2 mmol, 105 mg, 2 equiv) were carried out for 24 h. The product **3ai** was purified by flash column chromatography on silica gel (Gradient 0-10% EtOAc/Hexane), affording a white solid (71 mg, 59% yield). **M.P.** 89.4-93.8 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 – 8.04 (m, 2H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.64 – 7.61 (m, 1H), 7.57 – 7.46 (m, 5H), 7.12 (d, *J* = 8.5 Hz, 1H), 6.96 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.86, (s, 1H), 5.14 (d, *J* = 4.5, 1H), 4.49 – 4.37 (m, 2H), 4.19 (d, *J* = 14.5 Hz, 1H), 2.68 – 2.77 (m, 5H), 2.38 – 2.23 (m, 2H), 2.20 – 2.16 (m, 1H), 1.78 – 1.66 (m, 2H), 1.65 – 1.55 (m, 3H), 1.52 – 1.43 (m, 3H), 1.40 – 1.33 (m, 2H), 1.27 (s, 2H), 1.22 – 1.20 (m, 4H), 1.07 (s, 3H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.9, 165.3, 147.2, 145.56, 145.5, 135.1, 133.9, 131.8, 131.5, 129.9 (2C), 128.8, 128.7, 128.6, 127.1, 124.0, 123.9, 123.8, 123.2, 123.1, 120.8 (t, *J* =247 Hz), 64.6 (t, *J* = 33.6 Hz), 56.7, 50.6, 46.2, 39.7, 38.2, 37.7, 37.3, 35.53 (t, *J* = 22.5 Hz), 33.5, 30.4, 25.8, 24.08, 24.05, 20.1, 19.5, 18.8.

^{19}F NMR (471 MHz, $CDCl_3$) δ -100.6 (d, *J* = 258.3 Hz, 1F), -103.4 (d, *J* = 258.2 Hz, 1F).

IR (neat, cm^{-1}) 2957, 1698, 1271, 1107, 714.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{38}H_{43}F_2NO_3]^+$ 622.3109; found 622.3107.

7. Mechanistic studies

ON/OFF experiment:

A 10 mL glass vial was charged with compound **1k** (0.1 mmol, 22.0 mg), **2a** (0.2 mmol, 52.79 mg), $^{n}Bu_3N$ (3 equivalents), trimethoxybenzene (0.1 mmol, used as an internal standard to determine the reaction yield), and a PTFE-coated stirring bar under an inert atmosphere. The vial was sealed with a PTFE septum, followed by the addition of dry CH_3CN (1 mL) and 10 µL of water. The reaction vial was then placed on a magnetic stirrer and irradiated with a Kessil® PR160-390 nm light (40 W) at 45 °C. After the designated reaction time, a small aliquot of the mixture was withdrawn, extracted with EtOAc, and washed with brine. The organic layer was concentrated under reduced pressure and analyzed by ^{1}H NMR to determine the reaction yield.

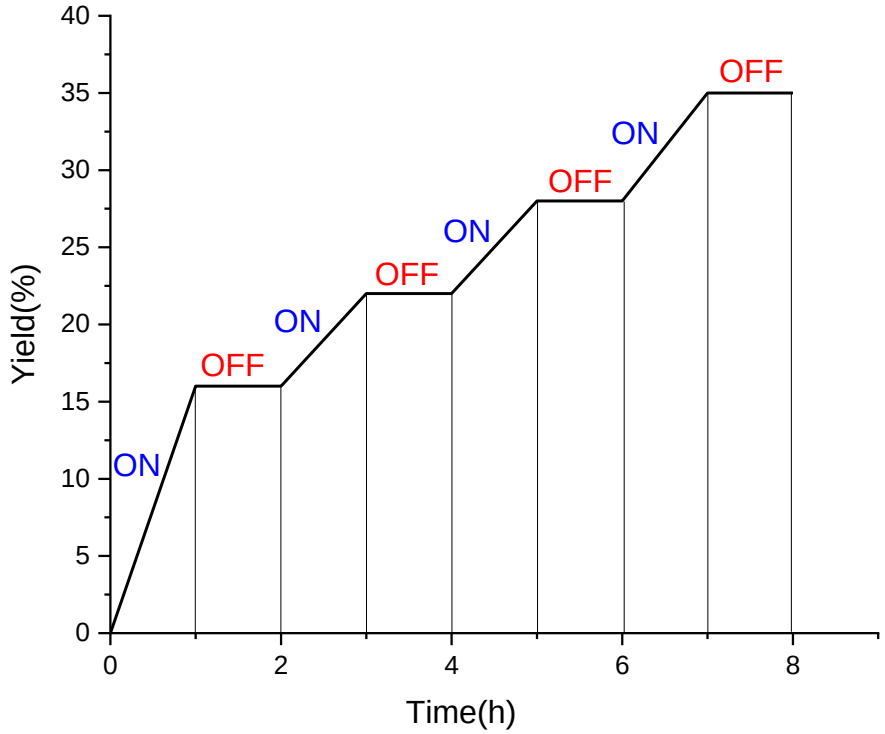
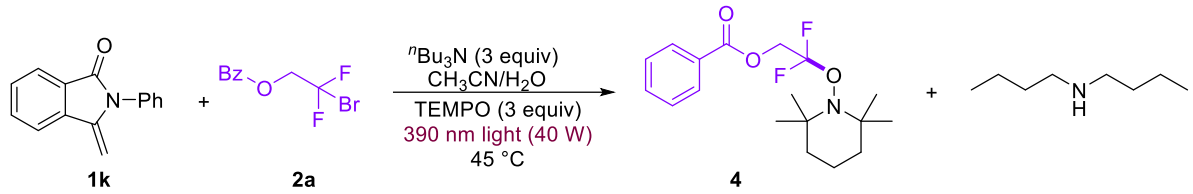


Figure S2: ON/OFF Experiment: The reaction profile during alternating irradiation shows that the reaction proceeds only in the presence of light.

Conclusions: We can conclude that the presence of light is essential for reaction progression, indicating that irradiation plays a key role in radical generation.

Radical Trap Experiment

Reaction in the presence of TEMPO



Detected by HRMS
$[M+H]^+$ Calc 342.1875
Found 342.1876

Detected by HRMS
$[M+H]^+$ Calc 130.1590
Found 130.1592

A 10 ml glass vial was charged with compound **1k** (0.1 mmol, 22.0 mg), **2a** (0.1 mmol,26.3 mg), ^{n}Bu$_3$N (3 equiv), TEMPO (3 equiv), and a PTFE-coated stirring bar in an inert atmosphere, and the glass vial was sealed with a PTFE septum Then dry CH_3CN (1 ml) was added to the reaction vial. The reaction vials were placed on the magnetic stirrer under irradiation with a Kessil® PR160-390 nm light (40 W) at 45 °C. The reaction mixture was filtered with cotton and an aliquot of the mixture was analyzed by HRMS and identified the formation of adduct **4**.

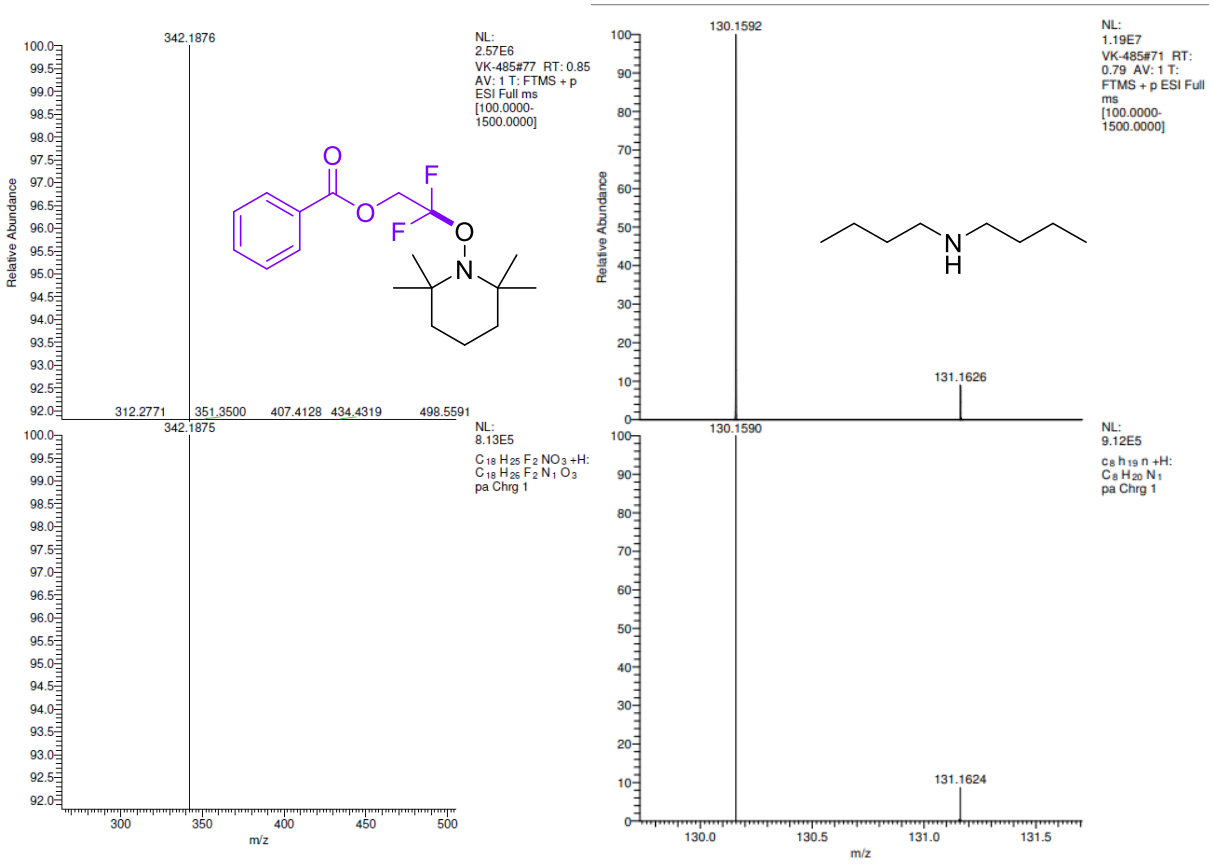
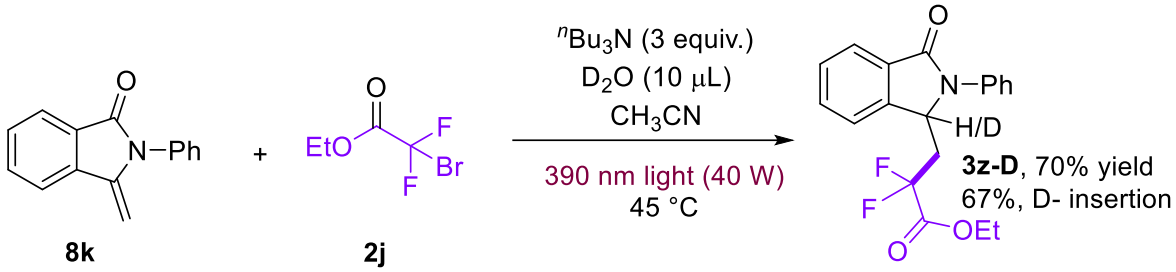


Figure S3. HRMS spectrum of the crude reaction mixture confirming the formation of adduct **4** and secondary amine

Conclusions: We can conclude that the reaction mechanism proceeds via radical intermediates. Additionally, the detection of the secondary amine suggests that an α-amino alkyl radical forms under our reaction conditions, which can get oxidised into the iminium ion, and then undergo hydrolysis to form the secondary amine. This observation is thus in line with our mechanistic claim that the α-amino alkyl radical acts as a reductant species.

Isotope labelling experiment:

Evidence of deuterium incorporation from water



A 10 ml glass vial was charged with **1k** (0.1 mmol, 1.0 equiv.), **2j** (0.2 mmol, 2.0 equiv.), ^{n}Bu$_3$N (3.0 equiv.), and a PTFE-coated stirring bar in an inert atmosphere, and the glass vial was sealed with a PTFE septum. Then CH_3CN (1 mL) D_2O (10 μL) was added to a glass vial sealed with a PTFE septum the reaction mixture was stirred and irradiated with a Kessil® PR160-440 nm light (40 W) and after 24 h, the reaction mixture and extracted with EtOAc, followed by washing with brine solution. The organic layer was concentrated under reduced pressure and was analyzed by ^{1}H NMR to determine the deuterium incorporation. By the analysis of ^{1}H NMR, we concluded that 67 % deuterium incorporates. (24 mg, 70% yield).

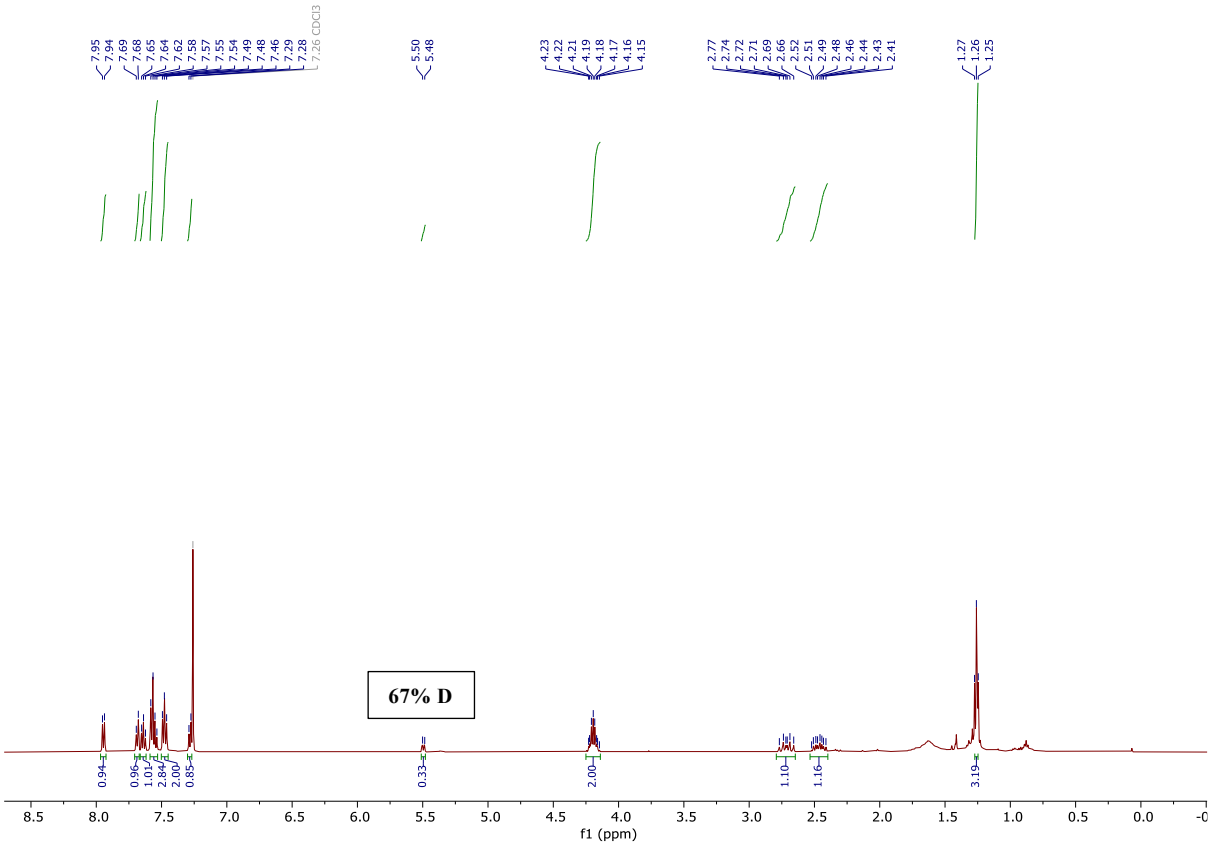


Figure S4. ^{1}H NMR (500 MHz, top) Spectra of **3z-D** in $CDCl_3$ at 298 K.

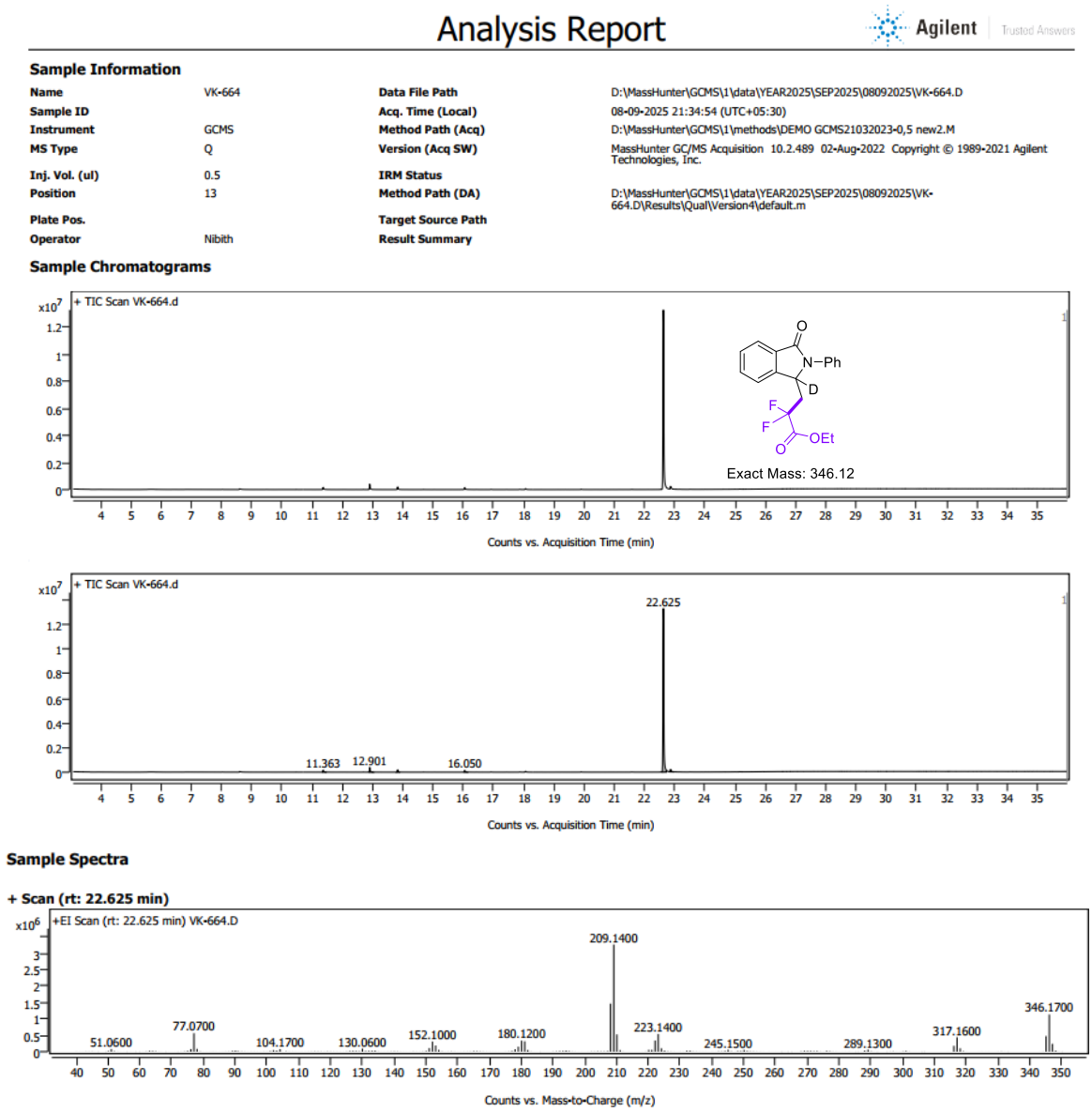
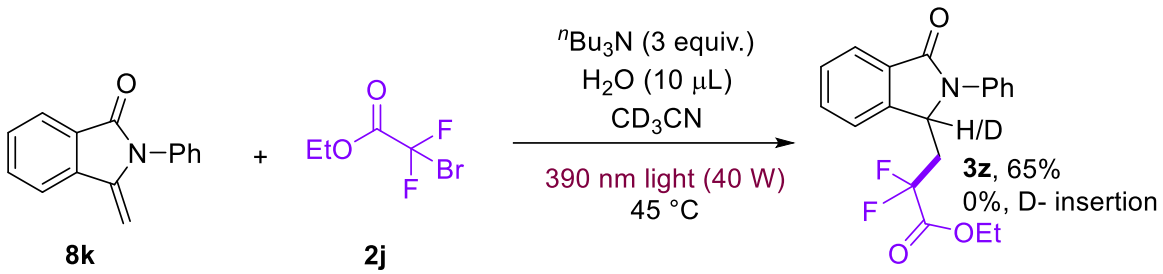


Figure S5 GC-MS analysis of the deuterium incorporated product **3z-D**.

Conclusions: Since the use of D_2O results in a 67% deuterated product **3z-D**, we can conclude that H_2O acts as a proton source in the reaction mechanism, indicating that the role of water might be like that of a terminal protonating agent.



A 10 ml glass vial was charged with **8k** (0.1 mmol, 1.0 equiv.), **2j** (0.2 mmol, 2.0 equiv.), $^{n}Bu_3N$ (3.0 equiv.), and a PTFE-coated stirring bar in an inert atmosphere, and the glass vial was sealed with a PTFE septum. Then CD_3CN (1 mL) H_2O (10 μL) was added to a glass vial sealed with a PTFE septum the reaction mixture was stirred and irradiated with a Kessil® PR160-440 nm light (40 W) and after 24 h, the reaction mixture and extracted with EtOAc, followed by washing with brine solution. The organic layer was concentrated under reduced pressure and was analyzed by ^{1}H NMR to determine the deuterium incorporation. By the analysis of ^{1}H NMR, we concluded that 0 % deuterium incorporates. (22 mg, 65% yield).

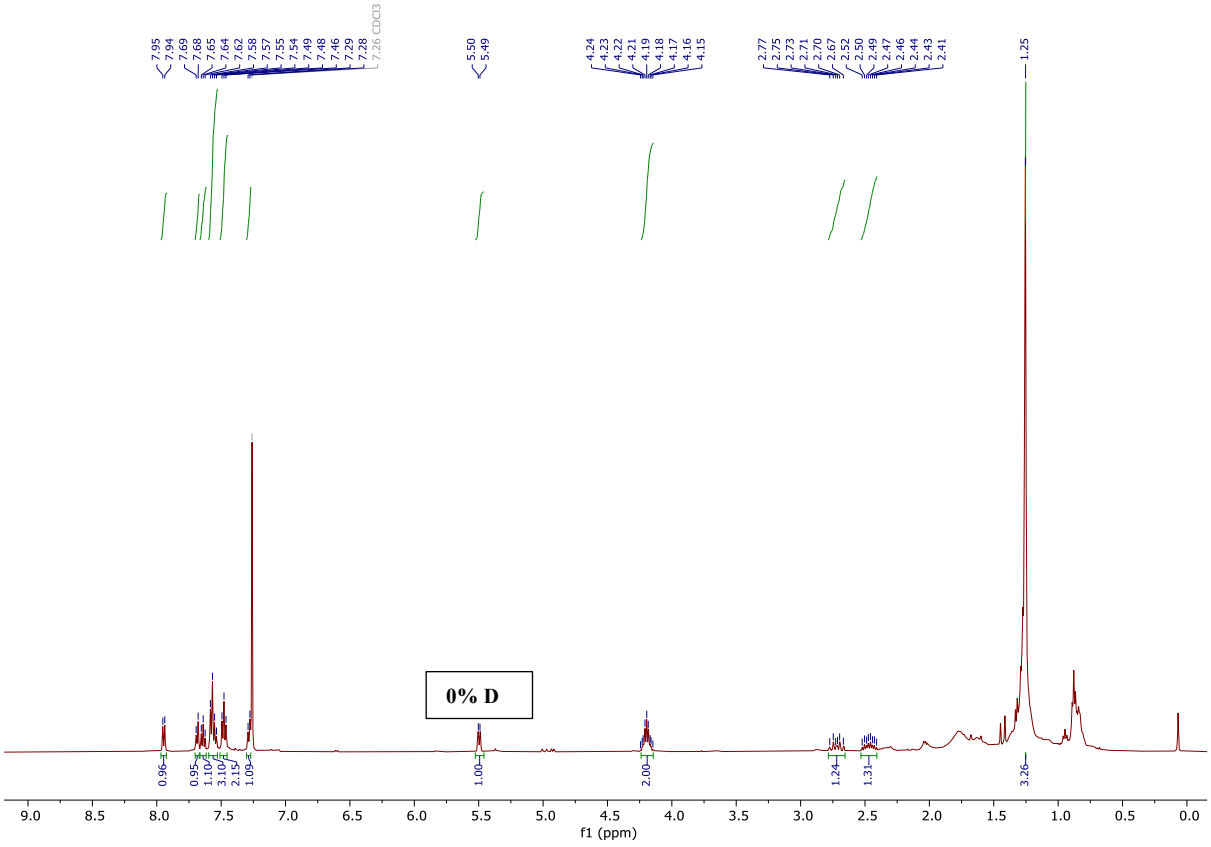


Figure S6. ^{1}H NMR (500 MHz, top) Spectra of **3z** in $CDCl_3$ at 298 K.

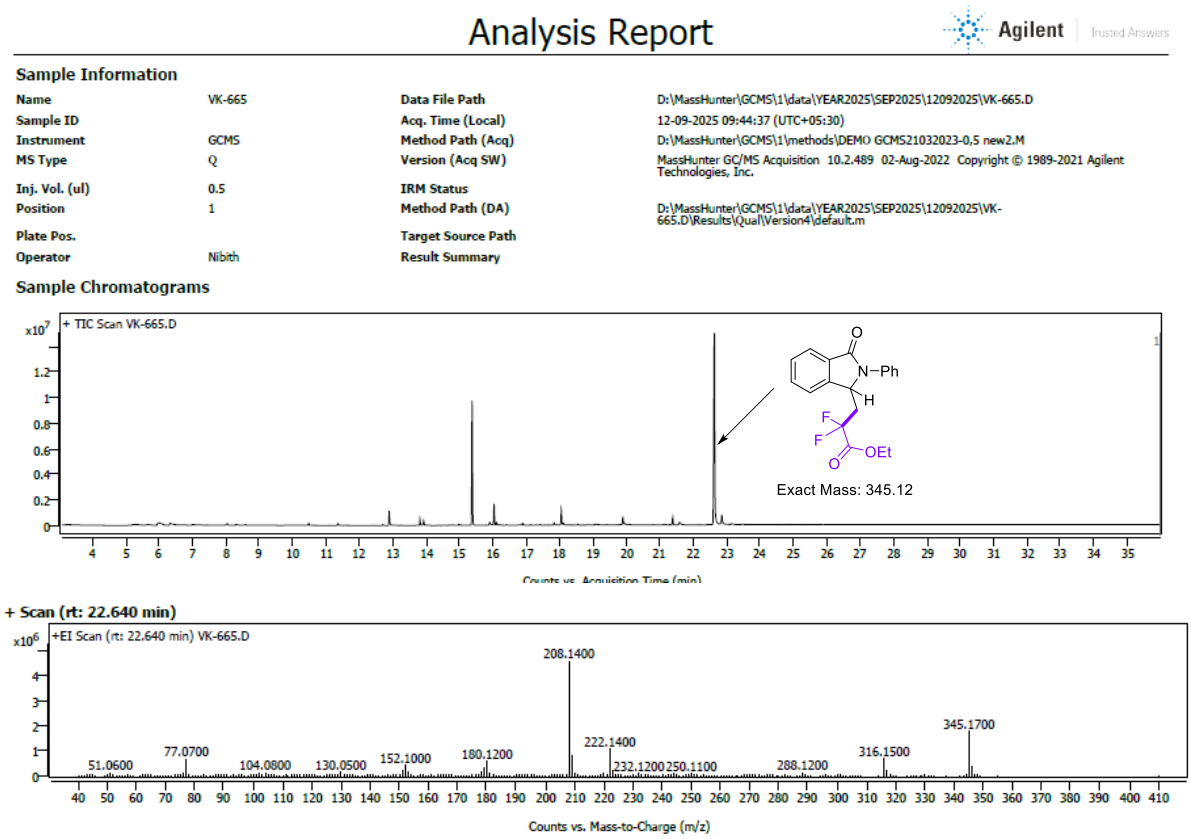


Figure S7 GC-MS analysis

Conclusions: Since the use of CD_3CN results in 0% deuterium incorporation, we can conclude that the solvent does not play a role as a H-atom donor.

UV-Vis Spectroscopic Measurement

A UV-vis absorbance experiment has been carried out to confirm the formation of the EDA complex or halogen-bond interaction. The UV/Vis absorption spectra of different combinations of **1k** (0.05 M), **2a** (0.1 M), and DIPEA (0.15 M), in CH_3CN solvent.

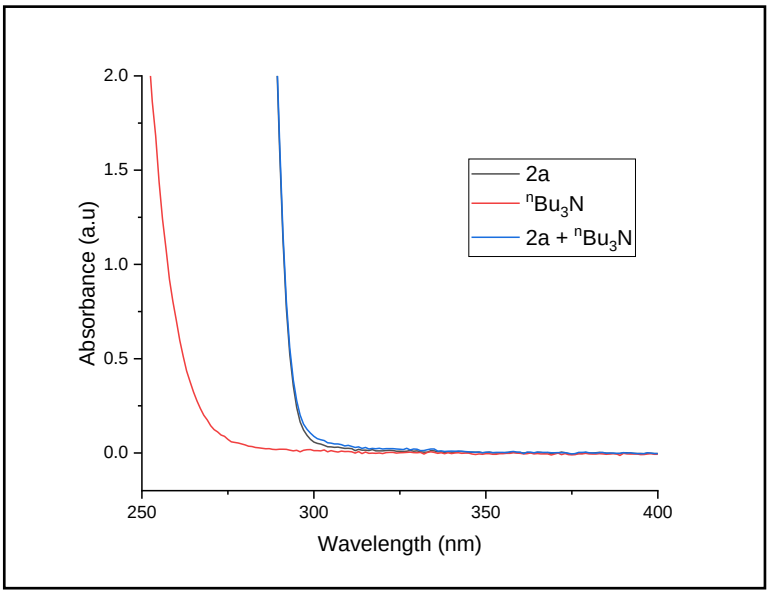


Figure S8. UV-Vis absorption spectra of a mixture of **2a** and **^{n}Bu$_3$N** in CH_3CN.

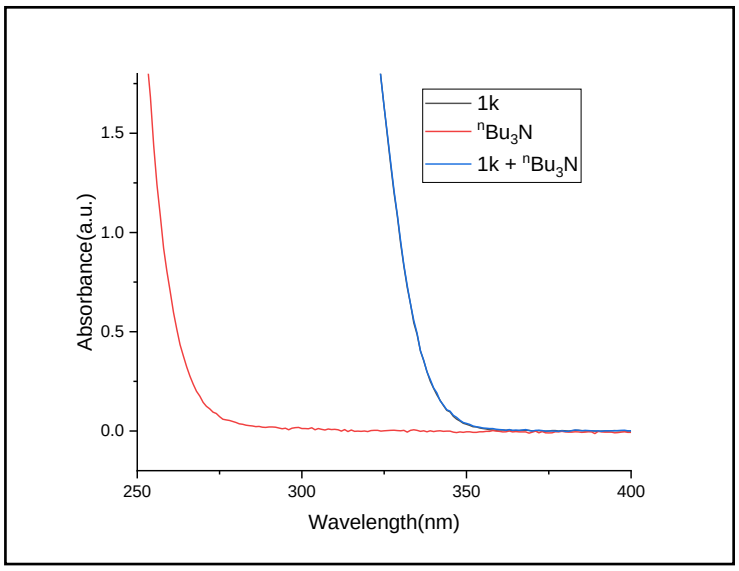


Figure S9. UV-Vis absorption spectra of a mixture of **1** and **^{n}Bu$_3$N** in CH_3CN

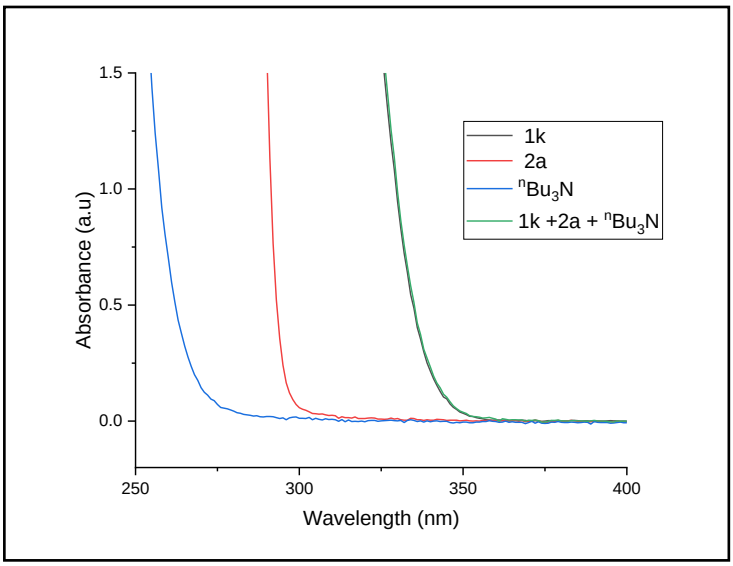


Figure S10. UV-Vis absorption spectra of a mixture of **1k 2a** and **^{n}Bu$_3$N** in CH_3CN.

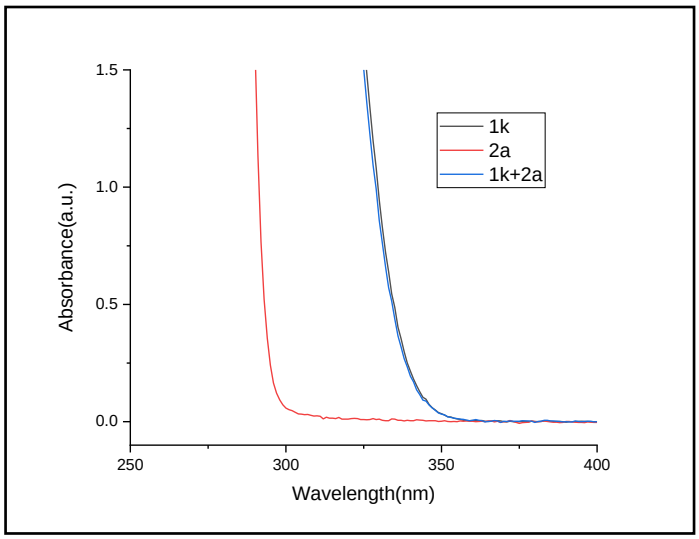


Figure S11. UV-Vis absorption spectra of a mixture of **1k** and **2a** in CH_3CN

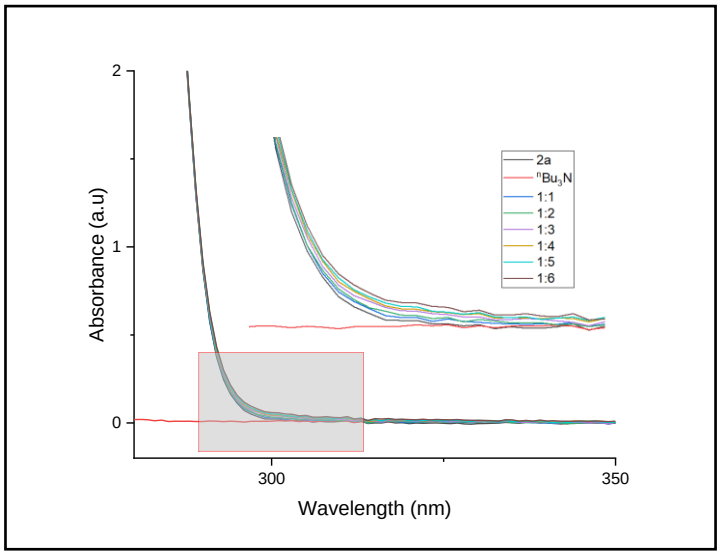


Figure S12. UV-Vis absorption spectra of a mixture of **2a** (0.05 M) and **ⁿBu₃N** (0.05M) in CH_3CN. Change in absorption upon increasing **ⁿBu₃N** concentration.

Conclusions: On the basis of the conducted UV-Vis studies we can conclude that there exists a strong interaction between **ⁿBu₃N** and **2a**. This is most likely to be of a halogen-bonding type. The interactions between **1k** and **ⁿBu₃N** are found to be negligible.

Job's Method Experiment:

The stoichiometry of the Halogen bond interaction complex was determined using Job's method with varying 2-bromo-2,2-difluoroethylbenzoate **2a** and **ⁿBu₃N** ratios in CH_3CN. The total concentration of **2a** and **ⁿBu₃N** was kept constant at 0.1 M (0.05 M), while the amount of $^{n}Bu_3N$ was varied from 0 to 0.05 M. The molar ratios of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0. UV for each sample was recorded, and an absorbance of $^{n}Bu_3N$ was used to draw the plot. The stoichiometry was determined by plotting ratios of absorbance against the ratio of [**ⁿBu₃N**]/[**ⁿBu₃N**]+[**2a**] to afford a maximum at ratio [**ⁿBu₃N**]/[**ⁿBu₃N**]+[**2a**] = 0.5, which meant a 1:1 complex ratio between 2a and $^{n}Bu_3N$.

S. No	[$^{n}Bu_3N$]/[$^{n}Bu_3N$]+[**2a**]	**Absorbance**
1	0	0
2	0.1	0.0882
3	0.2	0.1360
4	0.3	0.1645
5	0.4	0.1488
6	0.5	0.1845
7	0.6	0.1648
8	0.7	0.1314
9	0.8	0.1016
10	0.9	0.0587
11	1	0

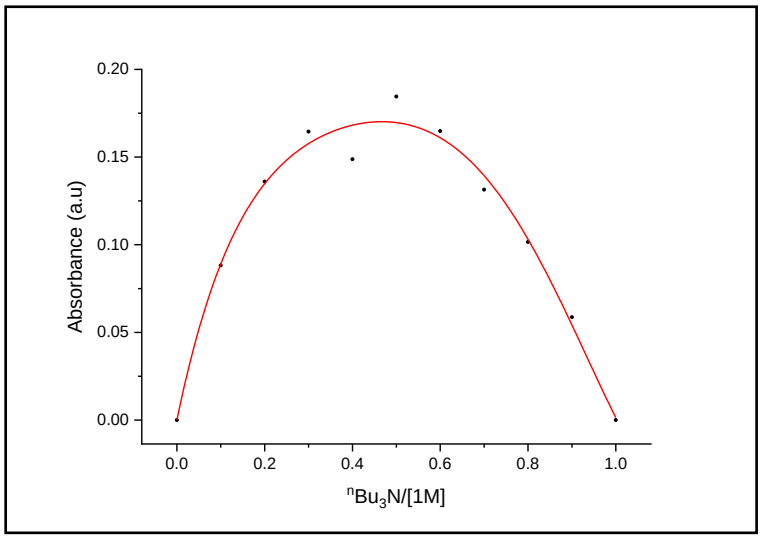


Figure S13: Job's plot of the XB complex (0.01 M total concentration in CH_3CN between **2a** and $^{n}Bu_3N$.

Conclusions: On the basis of the conducted Job's method experiment we can conclude that there is a 1:1 complex formed between **$^{n}Bu_3N$** and **2a**. This is most likely to be of a halogen-bonding type.

Determination of the association constant (K_{XB}) by UV titration

The association constant of the Halogen bonding (XB) complex formed between 2-bromo-2,2-difluoroethylbenzoate (2a) and DIPEA was determined spectrophotometrically in CH_3CN, employing the Hildebrand-Benesi methodology. The absorption at 274.0 nm of the solutions with a constant concentration of 2-bromo-2,2-difluoroethylbenzoate (0.05M) and an increased donor/acceptor ratio by adding an excess of DIPEA was measured. All the absorption spectra were recorded in 3 cm path quartz cuvettes. Data obtained for XB in 1:1 CH_3CN are shown below. Average of 2 readings for absorbance values are taken.

1/[DIPEA] M^{-1}	$1/Abs_{XB}-A_0$
13.4125	250
6.79348	66.6666
4.58716	35.7140
3.48384	25.6410
2.38095	17.2413
2.06543	16.1290
1.82901	13.626

$$\frac{1}{A-A_0}=\frac{1}{A_{max}-A_0}\left(\frac{1}{K_{XB}[NMM]n}+1\right)$$

The above equation obtained a linear plot (shown below) for this XB system. (A_0 = 0.558, A: the absorption in the absence and presence of DIPEA, Amax: the maximum absorption in the presence of DIPEA, K_{XB}: equilibrium constant, n = 1, the stoichiometry of the XB complex). The equilibrium constant K_{XB} (K_{XB}=21.265/44.290 = 0.480 M^{-1}) was readily obtained from the slope of these plots.

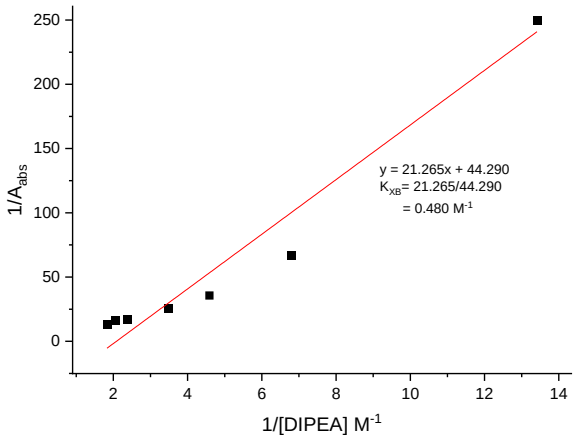
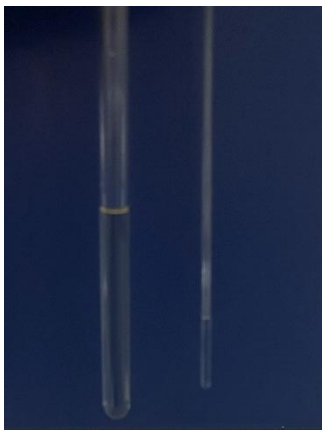


Figure S14: Plot of the determination of the association constant.

NMR titration:

Experiment step-up:



To conduct the NMR titration studies, an external standard (CH_3SO_2Cl in the case of ^{13}C NMR and Ph-CF_3 in the case of ^{19}F NMR) was taken in a previously heat-dried capillary tube and then sealed. This capillary tube was then inserted into the NMR tube containing the solvent. After the NMR signal corresponding to the standard was identified, this was then used to calibrate all subsequent readings.

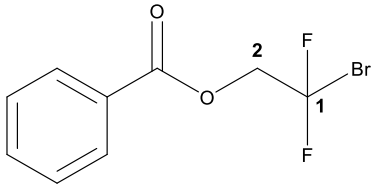
Inside the NMR tube, after adding the external standard, a solution of the difluorobromoalkane (0.5 ml) was prepared in a suitable NMR solvent. Incrementally, DIPEA was added to the tube and the shifts in NMR signals were monitored, to detect proof for interactions between the alkyl bromide species and DIPEA.

Conclusions: Based on the NMR studies conducted (details below), we can infer that there is a strong interaction between the alkyl halide (**2a**) and DIPEA, which exerts a stronger influence on the carbon of the C–Br bond. This is thus strong evidence for the existence of halogen-bonding interactions between **2a** and DIPEA.

We also conducted a titration using the same protocol with triphenylphosphine (Figures S23 and S24), and we were unable to observe any shifts in the NMR signals being monitored, which indicates that this interaction works best with amines as halogen-bond acceptors.

Halogen bonding interaction between 2a and DIPEA by ^{13}C NMR (DMSO):

In the NMR tube, the concentration of (**2a**) was maintained at 0.2 M, while DIPEA was added in varying equivalents. The molar ratios of **2a** to DIPEA were set at 1:0, 1:2 and 1:4 respectively. As the concentration of DIPEA increased, the signals of the ^{13}C NMR showed an upfield shift. Further, it was found that the signal corresponding to the -CF_2Br moiety shifted with a larger magnitude than the other signals, indicating that the interaction is indeed a halogen bonding interaction.



Atom	Signal at 1:0 (ppm)	Signal at 1:4 (ppm)	Difference (ppm)
1	118.7857	118.7785	**0.0072**
2	66.7925	66.7889	**0.0036**

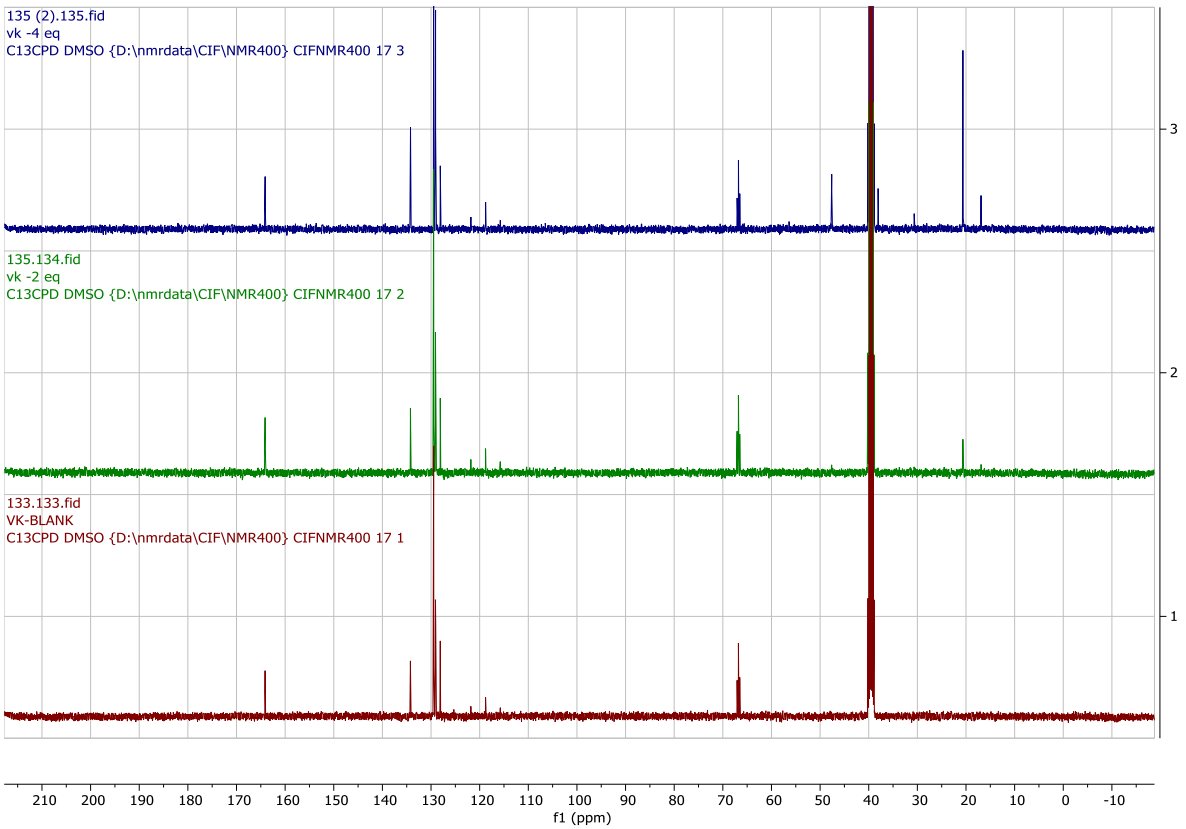


Figure S15. ^{13}C NMR (400 MHz, top) Full NMR titration Spectra.

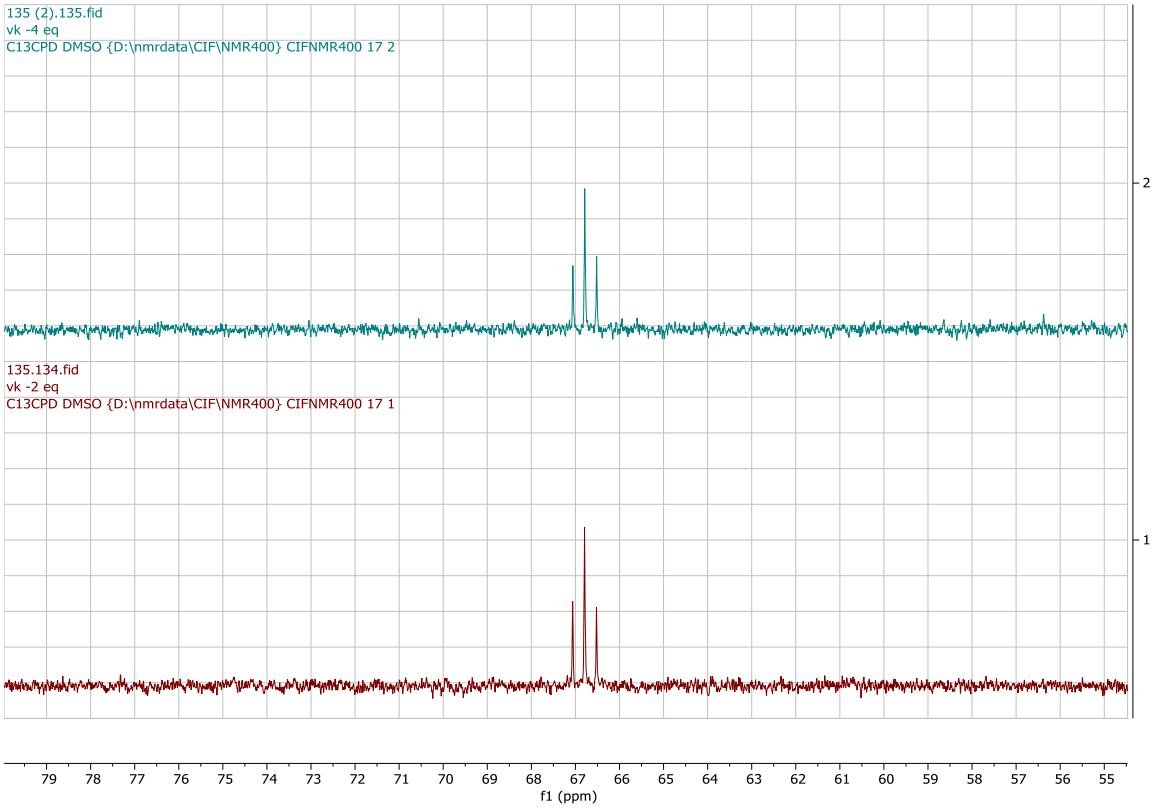


Figure S16. ^{13}C NMR (400 MHz, top) titration Spectra (Shift in carbon 2)

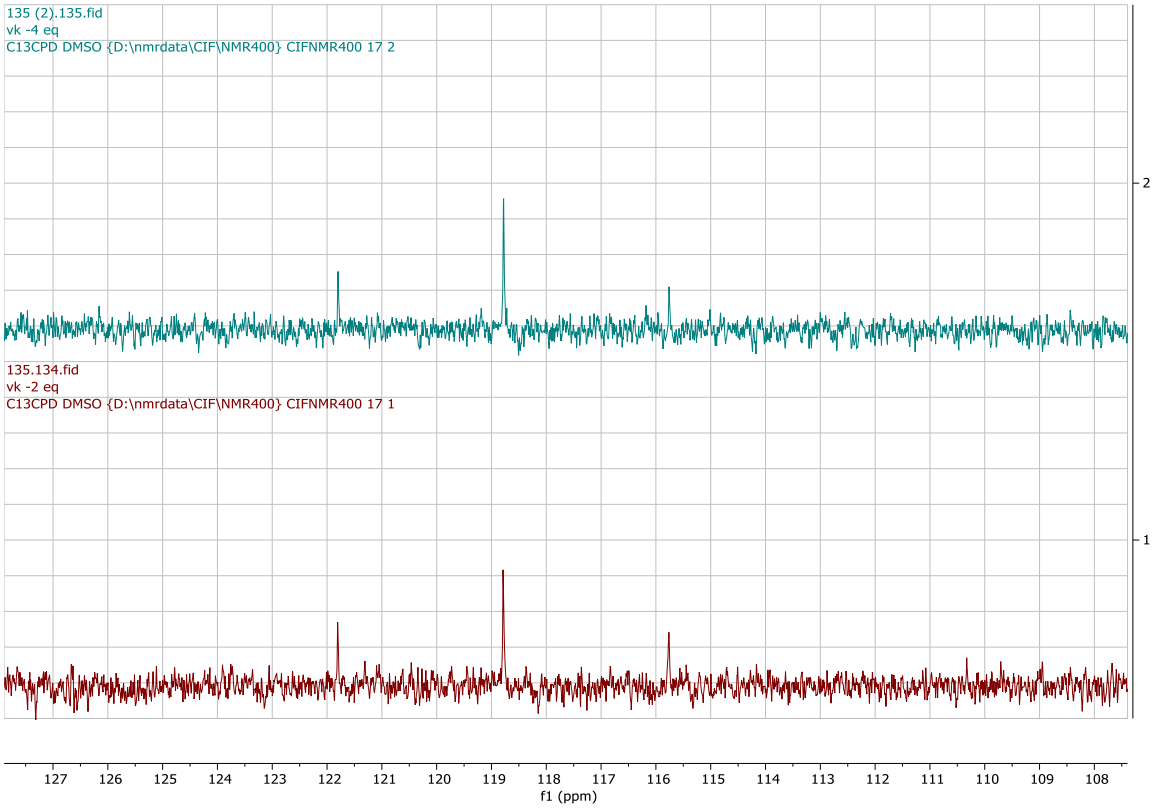
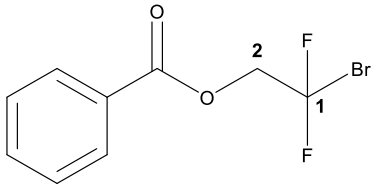


Figure S17. ^{13}C NMR (400 MHz, top) titration Spectra (Shift in carbon 1)

Halogen bonding interaction between 2a and DIPEA by ^{13}C NMR (CD_3CN):

In the NMR tube, the concentration of (**2a**) was maintained at 0.05 M, while DIPEA was added in varying equivalents. The molar ratios of **2a** to DIPEA were set at 1:0, 1:2, and 1:4, respectively. As the concentration of DIPEA increased, the signals of the ^{13}C NMR showed an upfield shift.



Atom	Signal at 1:0 (ppm)	Signal at 1:2 (ppm)	Signal at 1:4 (ppm)	Diff. after 2eq (ppm)	Diff. after 4eq (ppm)
1	119.3082	119.3190	119.3262	**0.0108**	**0.0072**
2	67.5352	67.5460	67.5531	**0.0108**	**0.0071**

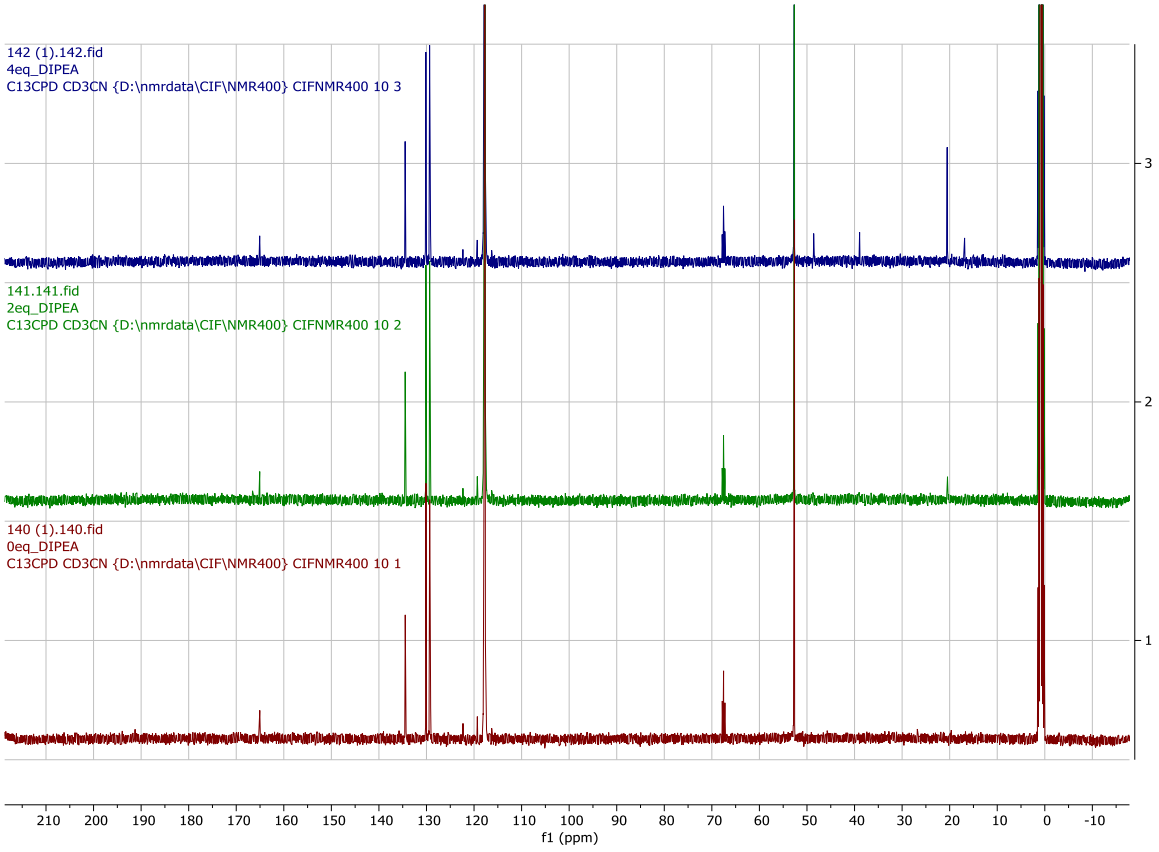


Figure S18. ^{13}C NMR (400 MHz, top) Full NMR titration Spectra.

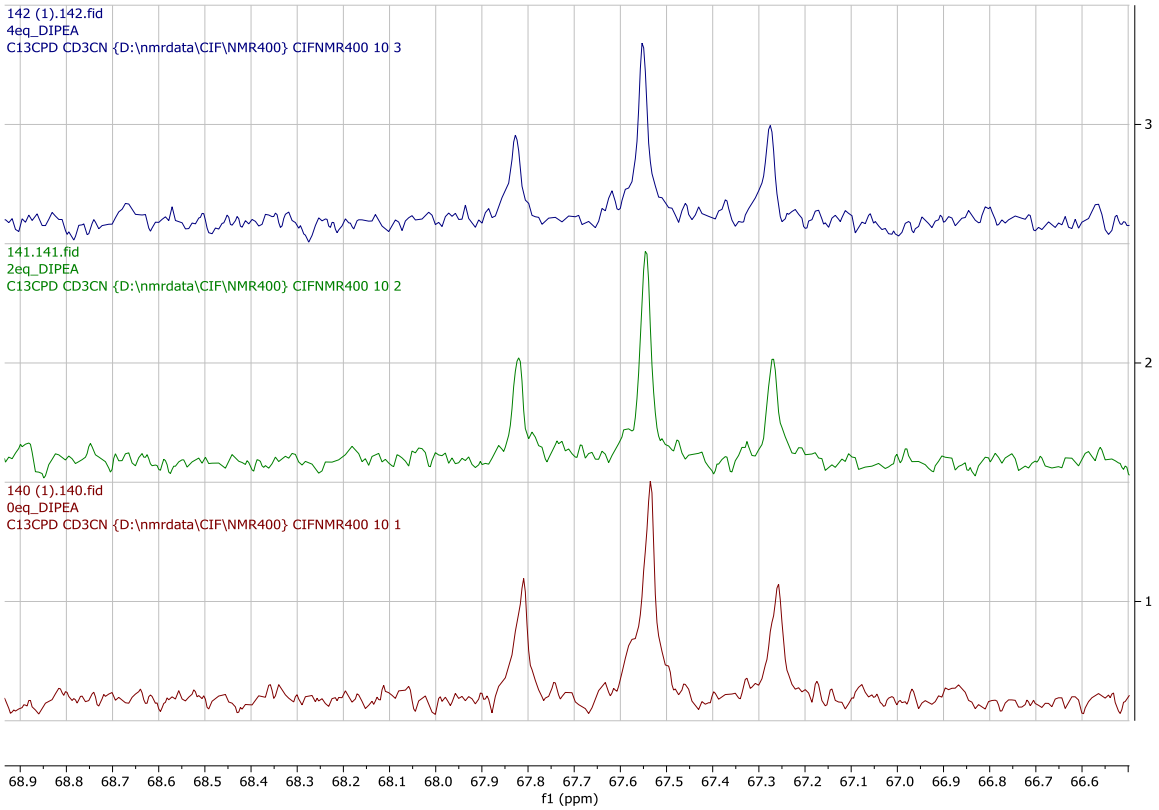


Figure S19. ^{13}C NMR (400 MHz, top) titration Spectra (Shift in carbon 2).

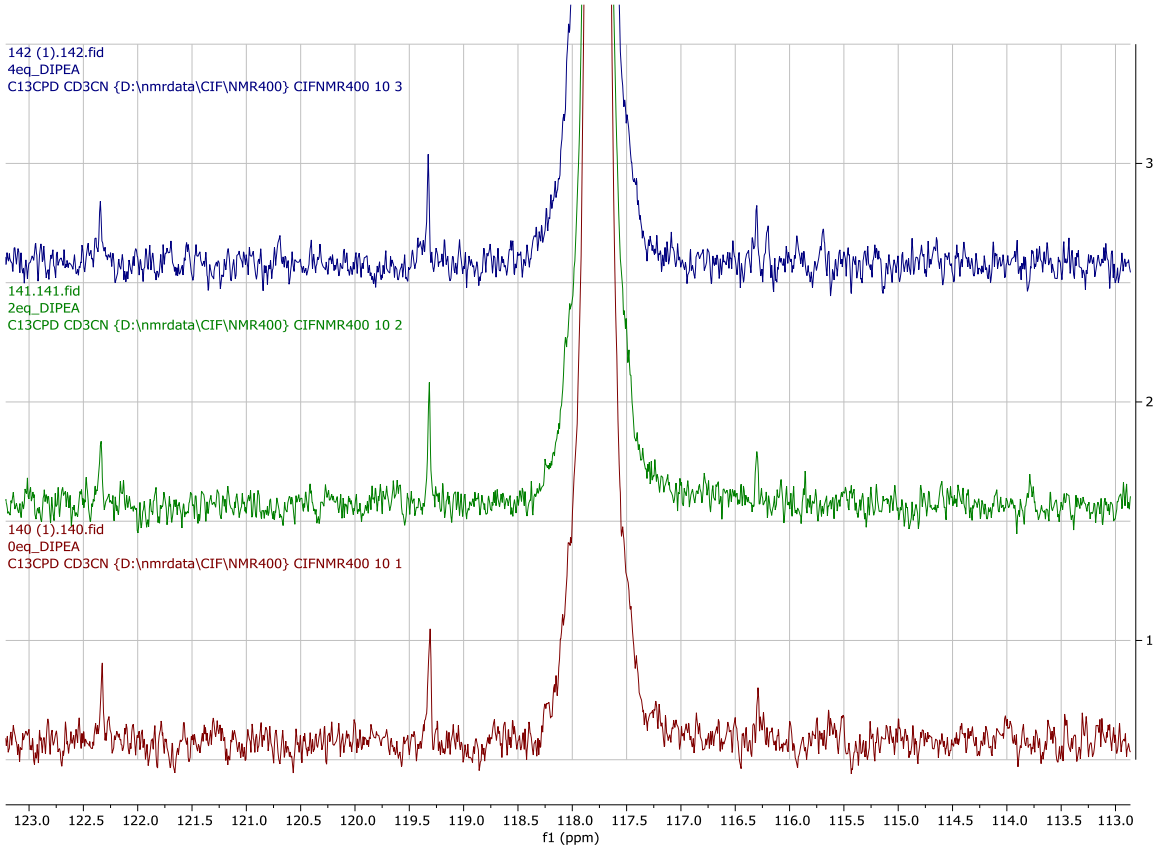
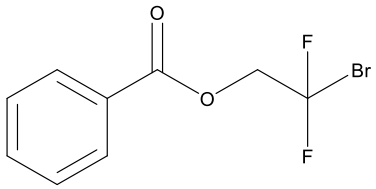


Figure S20. ^{13}C NMR (400 MHz, top) titration Spectra (Shift in carbon 1; Large peak corresponds to acetonitrile).

Halogen bonding interaction between 2a and DIPEA by ^{19}F NMR (CD_3CN):

In the NMR tube, the concentration of (**2a**) was maintained at 0.05 M, while DIPEA was added in varying equivalents. The molar ratio of 2a to DIPEA was increased gradually. As the concentration of DIPEA increased, the signals of the ^{19}F NMR showed an upfield shift.



Molar ratio	**Signal** (ppm)
1:0	-57.0011
1:1	-56.9999
1:2	-56.9990
1:5	-56.9984
1:6	-56.9976
1:8	-56.9976
1:10	-56.9967
1:12	-56.9955

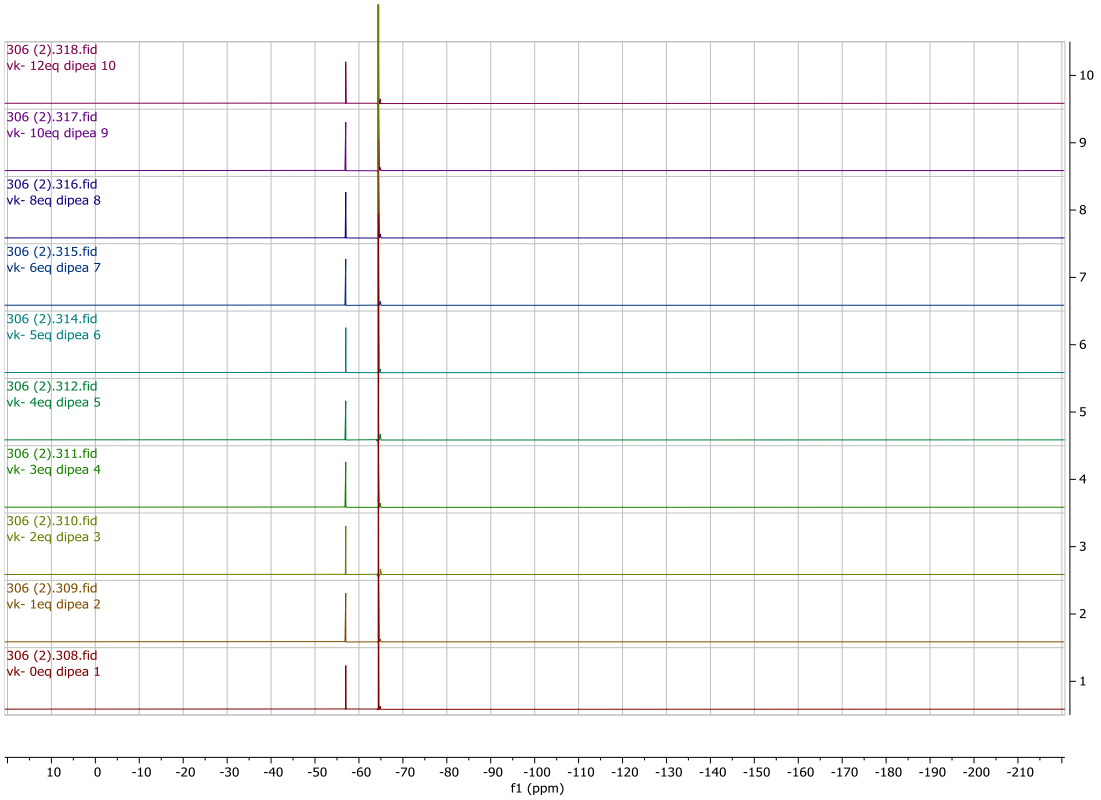


Figure S21. ^{19}F NMR (500 MHz, top) titration full spectra (Large peak corresponds to trifluorotoluene, the chosen external standard).

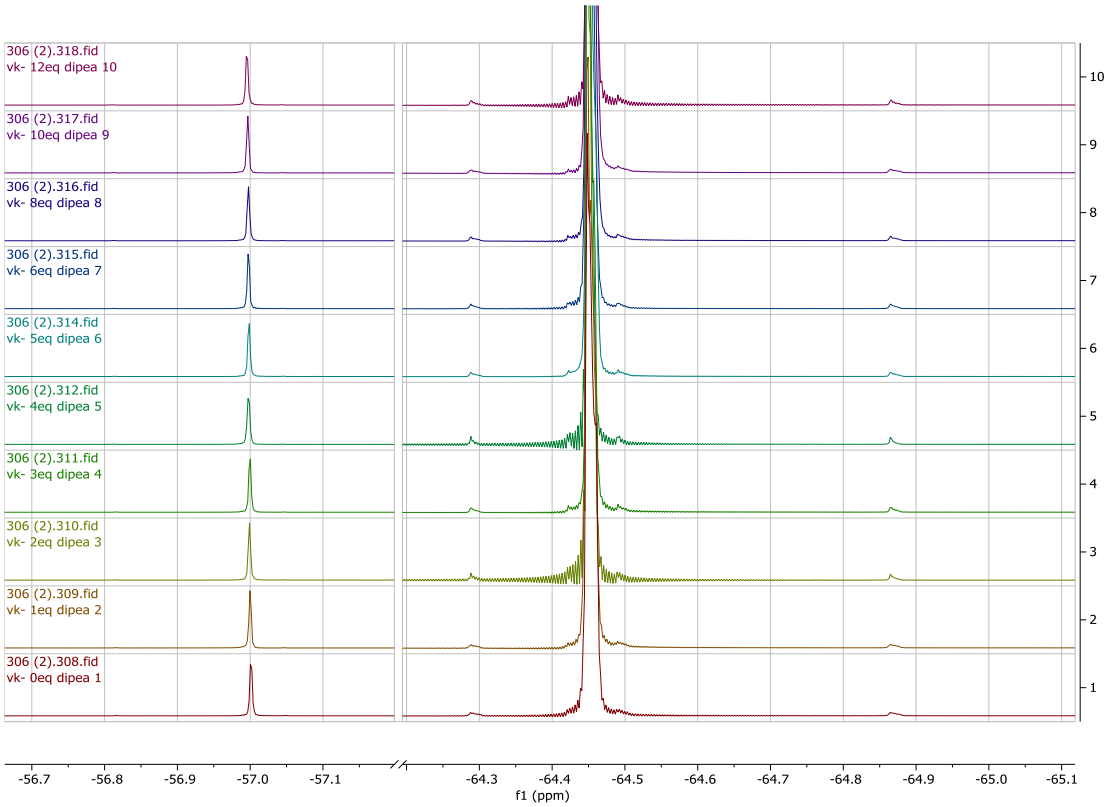


Figure S22. ^{19}F NMR (500 MHz, top) titration zoomed-in spectra (Large peak corresponds to trifluorotoluene, the chosen external standard).

Halogen bonding interaction between 2a and PPh_3 by ^{19}F NMR (CD_3CN):

In the NMR tube, the concentration of (**2a**) was maintained at 0.05 M, while PPh_3 was added in varying equivalents. The molar ratio of 2a to PPh_3 was increased gradually. As the concentration of PPh_3 increased, the signals of the ^{19}F NMR showed no shift.

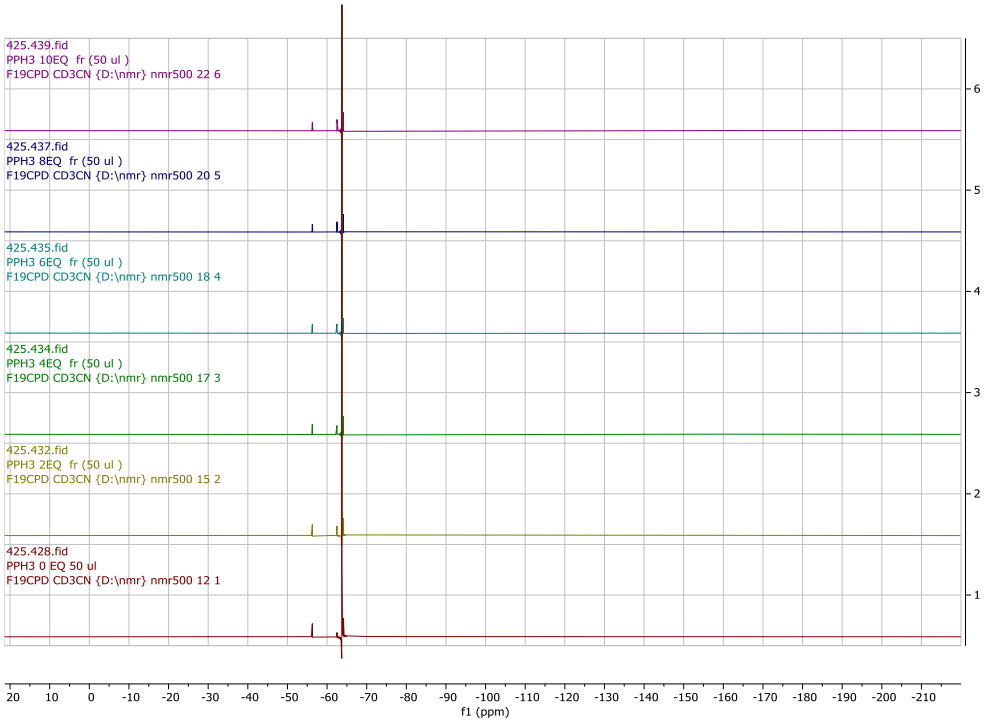


Figure S23. ^{19}F NMR (500 MHz, top) titration full spectra (Large peak corresponds to trifluorotoluene, the chosen external standard).

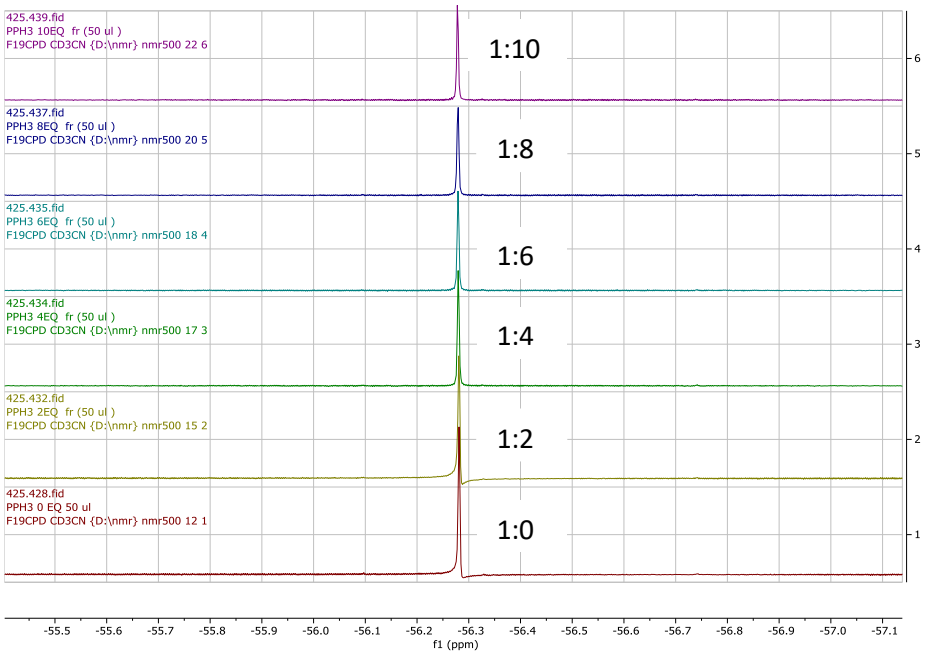
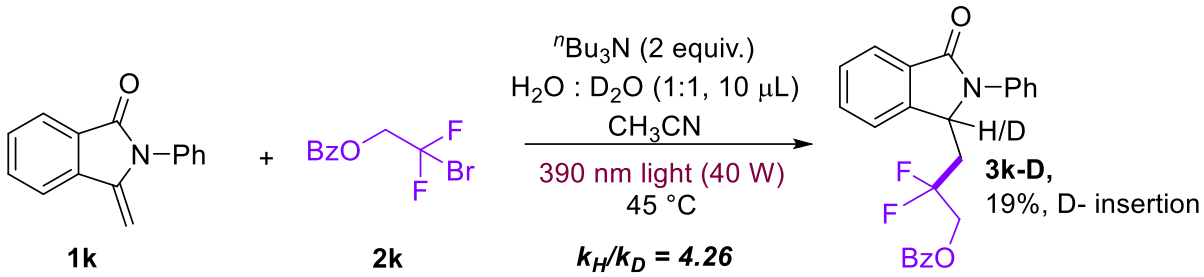


Figure S24. ^{19}F NMR (500 MHz, top) titration zoomed-in spectra (Large peak corresponds to trifluorotoluene, the chosen external standard).

Kinetic Isotope Effect (KIE) Experiment:



A 10 ml glass vial was charged with **1k** (0.1 mmol, 1.0 equiv.), **2k** (0.2 mmol, 2.0 equiv.), ^{n}Bu$_3$N (2.0 equiv.), and a PTFE-coated stirring bar in an inert atmosphere, and the glass vial was sealed with a PTFE septum. Then CH_3CN (1 mL) H_2O: D_2O (1:1, 10 μL) was added to a glass vial sealed with a PTFE septum the reaction mixture was stirred and irradiated with a Kessil® PR160-440 nm light (40 W) and after 24 h, the reaction mixture and extracted with EtOAc, followed by washing with brine solution. The organic layer was concentrated under reduced pressure and was analyzed by ^{1}H NMR to determine the deuterium incorporation. By the analysis of ^{1}H NMR, we concluded that 19 % deuterium incorporates.

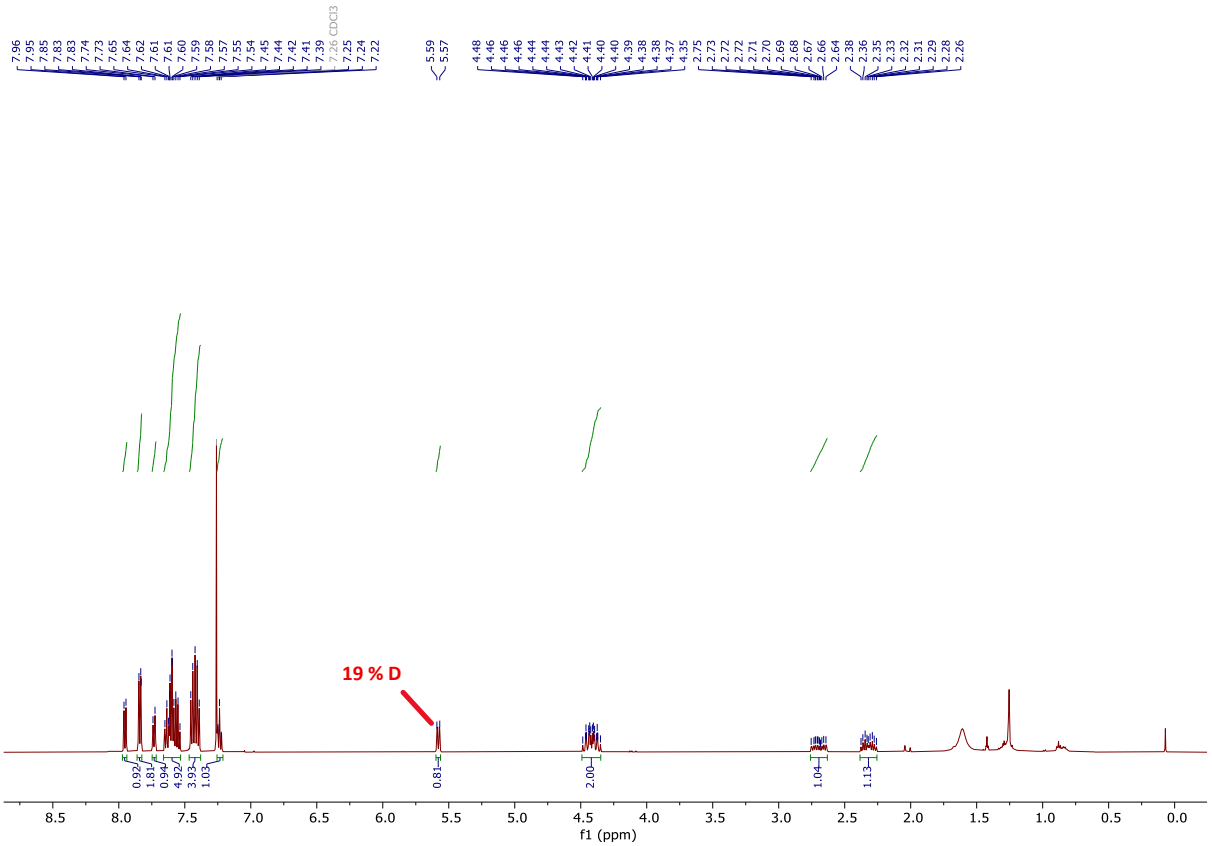
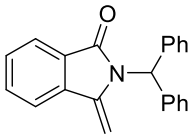
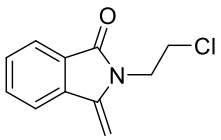


Figure S25. ^{1}H NMR (500 MHz, top) spectra of **3k** in $CDCl_3$ at 298 K.

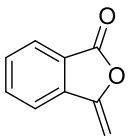
Conclusions: Despite not being the rate-determining step (Figure S108), we see a K.I.E value of 4.26, which indicates that in the presence of water, the protonation event does not proceed classically. It is thus possible that the water-assisted proton shuttling proceeds via quantum tunnelling.

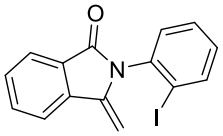
Unsuccessful substrates:



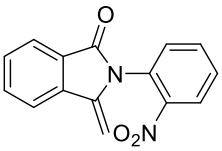


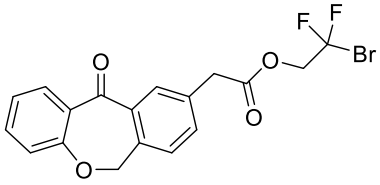
obtained as inseparable mixture



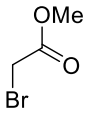


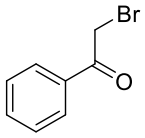
obtained as inseparable mixture





obtained as inseparable mixture





8. NMR Spectra

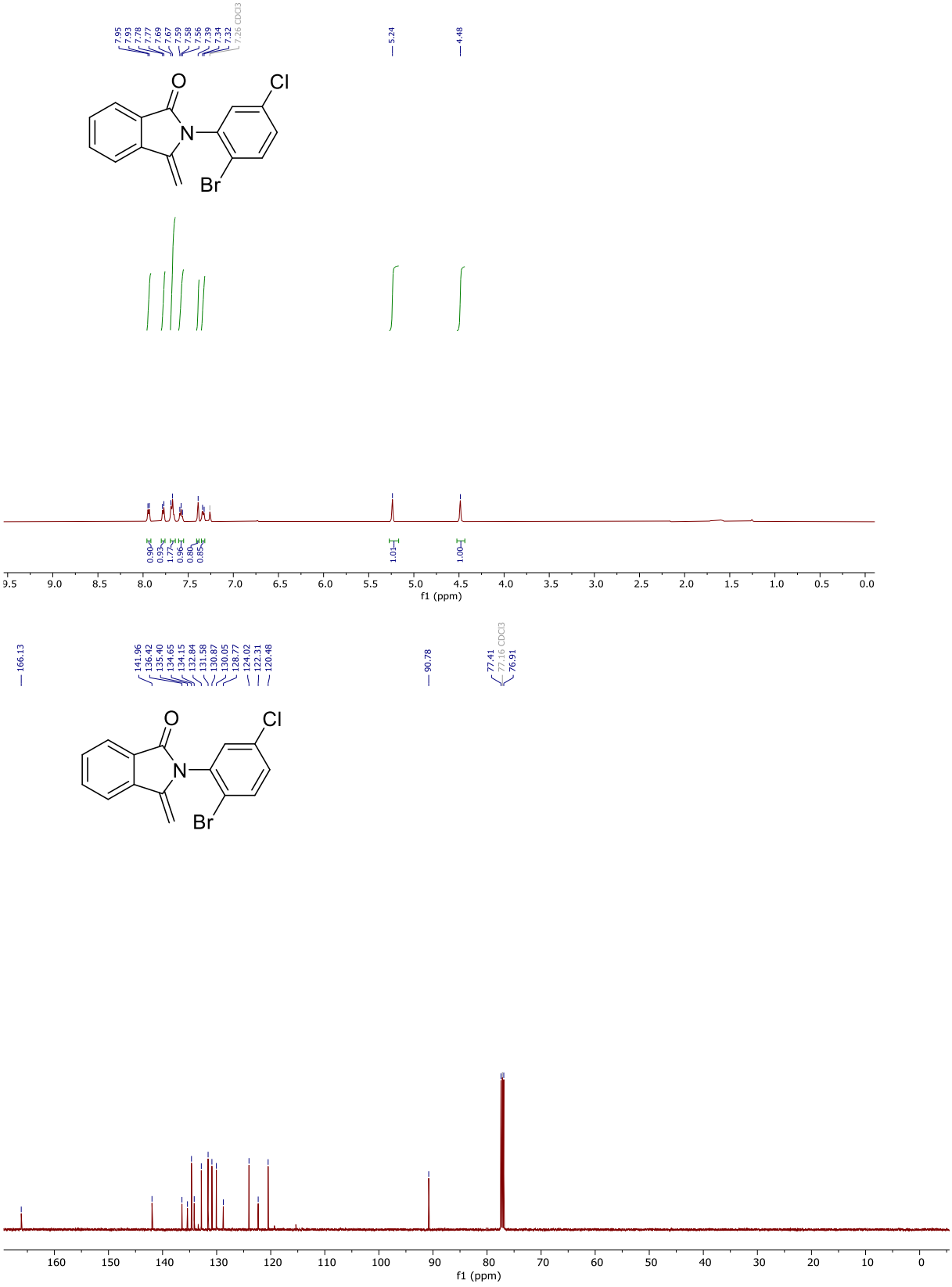


Figure S26. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **1b** in CDCl3 at 298 K.

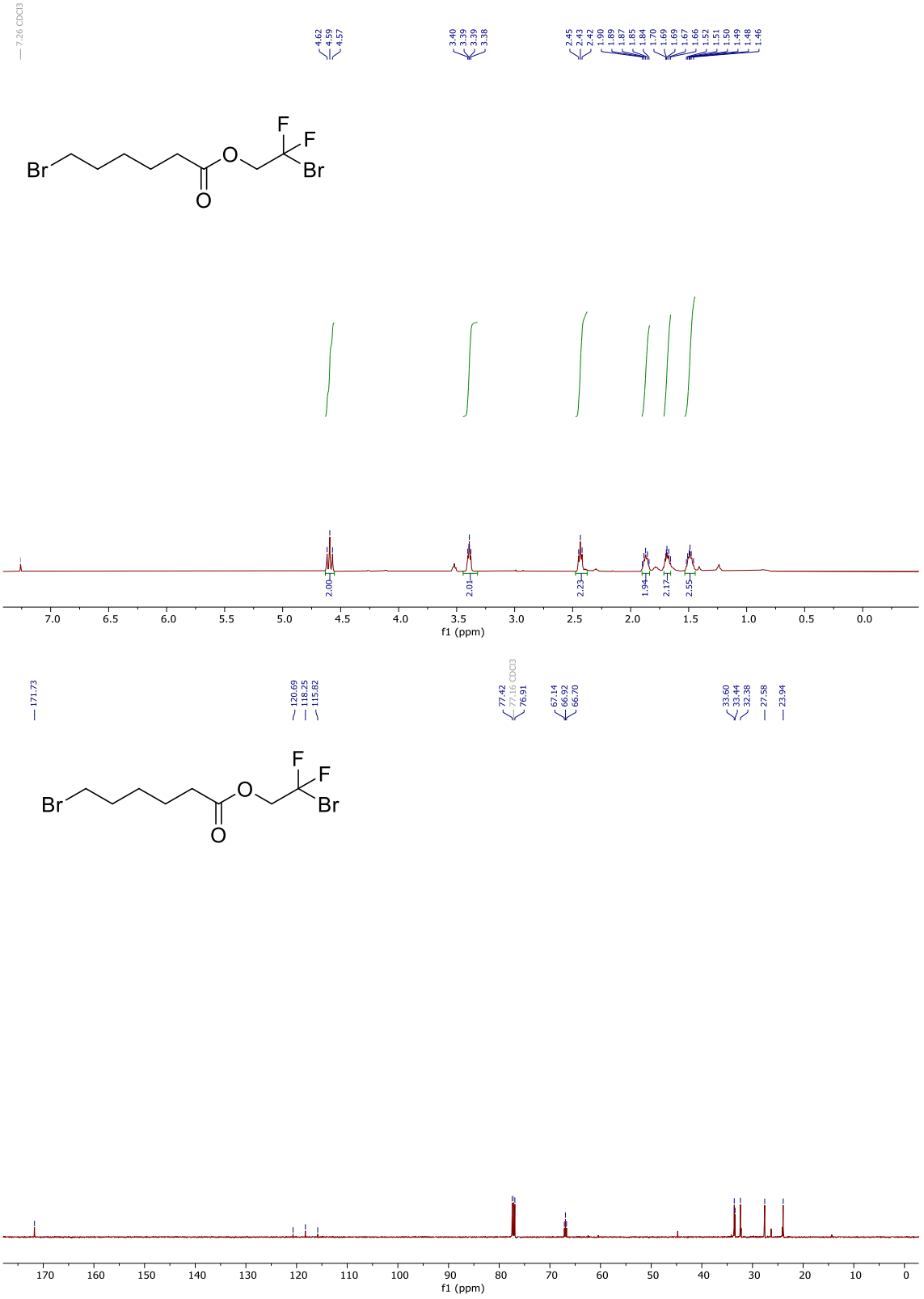


Figure S27. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **2i** in CDCl3 at 298 K.

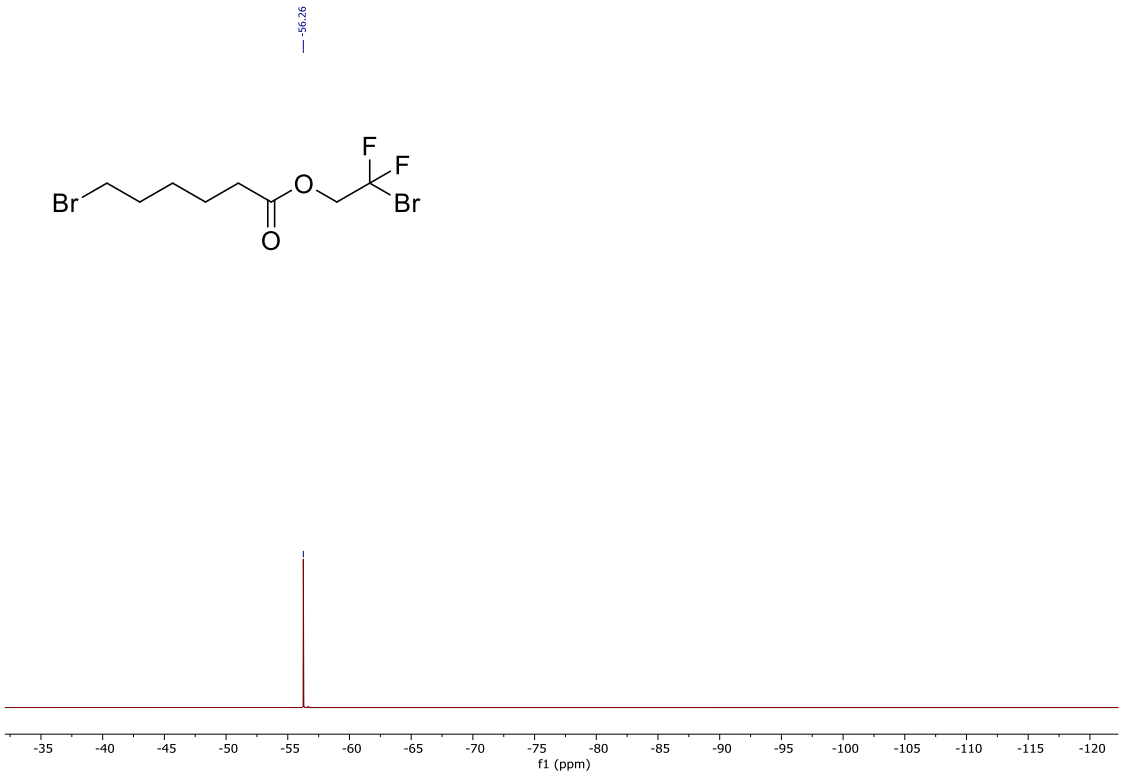


Figure S28. ^{19}F NMR (471 MHz) Spectra of **2i** in $CDCl_3$ at 298 K.

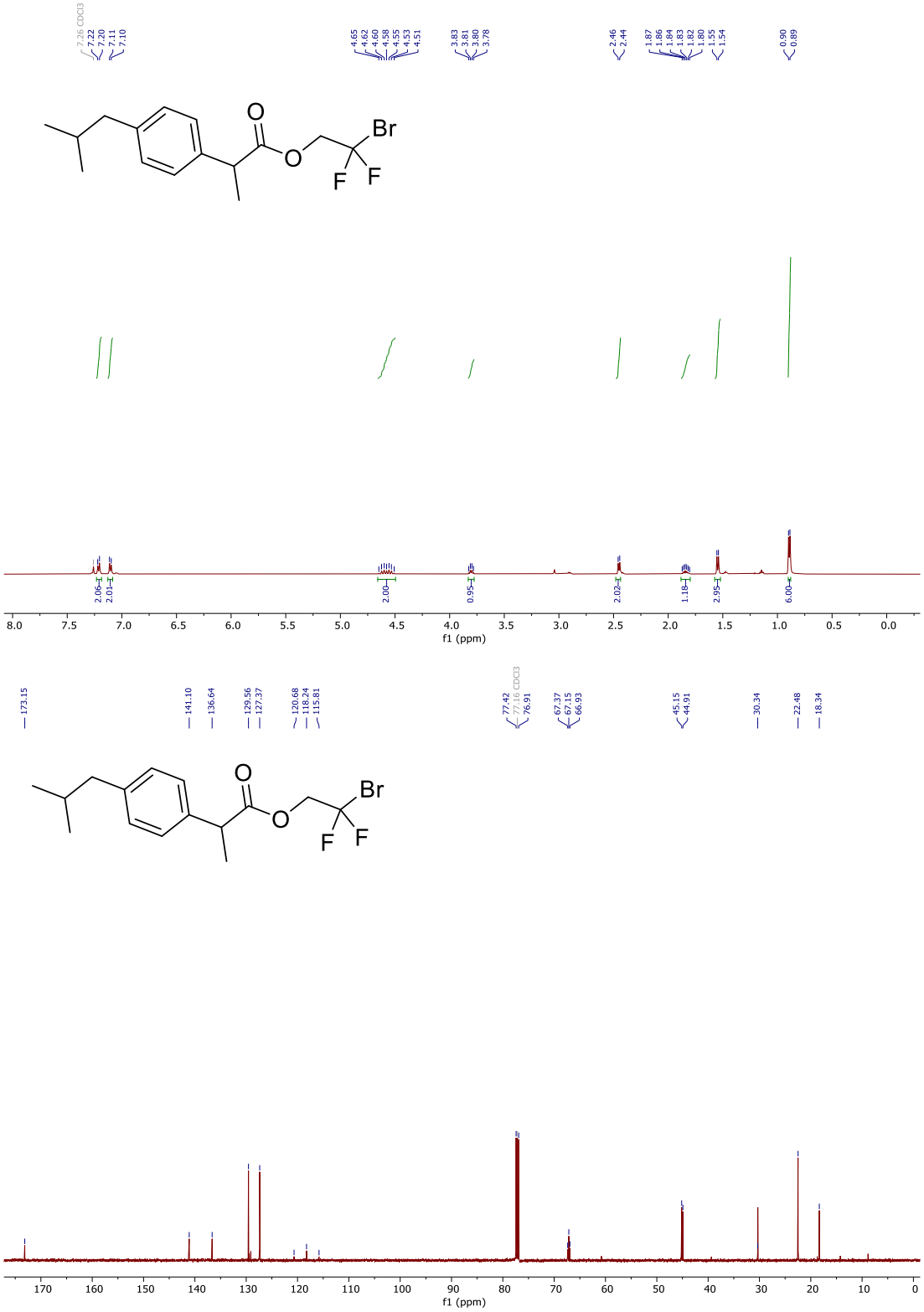


Figure S29. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **2o** in CDCl3 at 298 K.

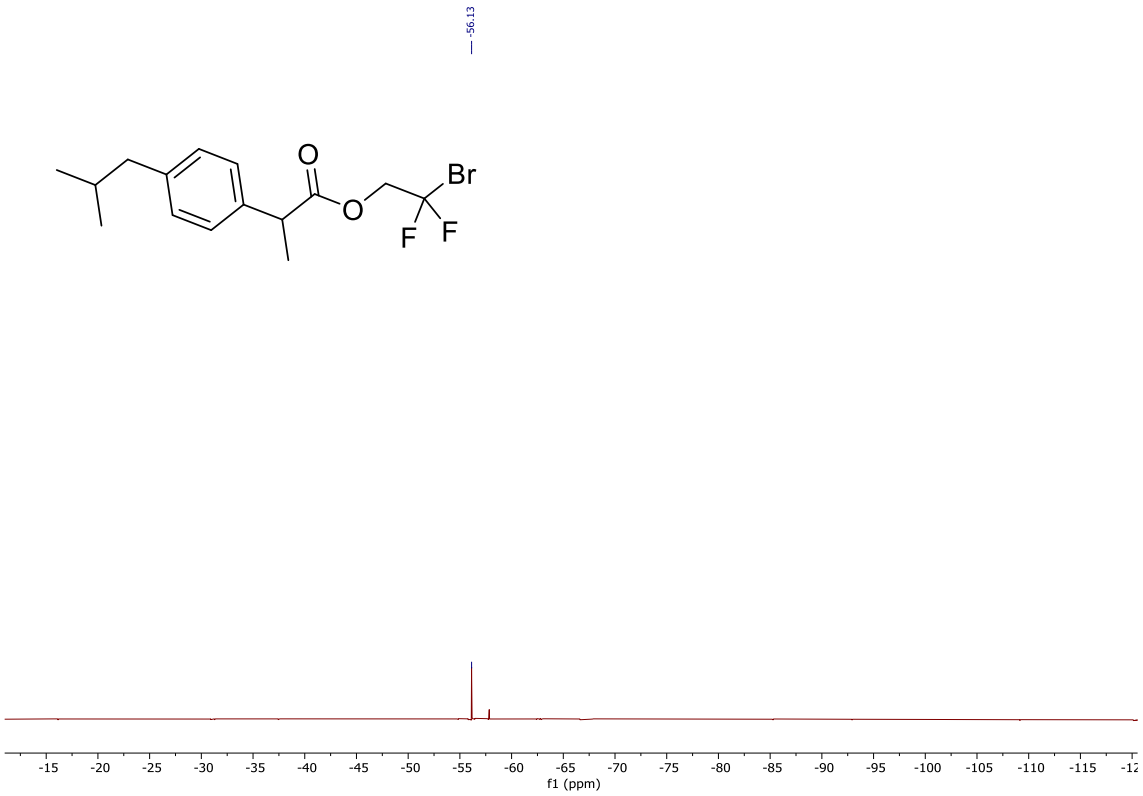


Figure S30. ^{19}F NMR (471 MHz) Spectra of **2o** in $CDCl_3$ at 298 K.

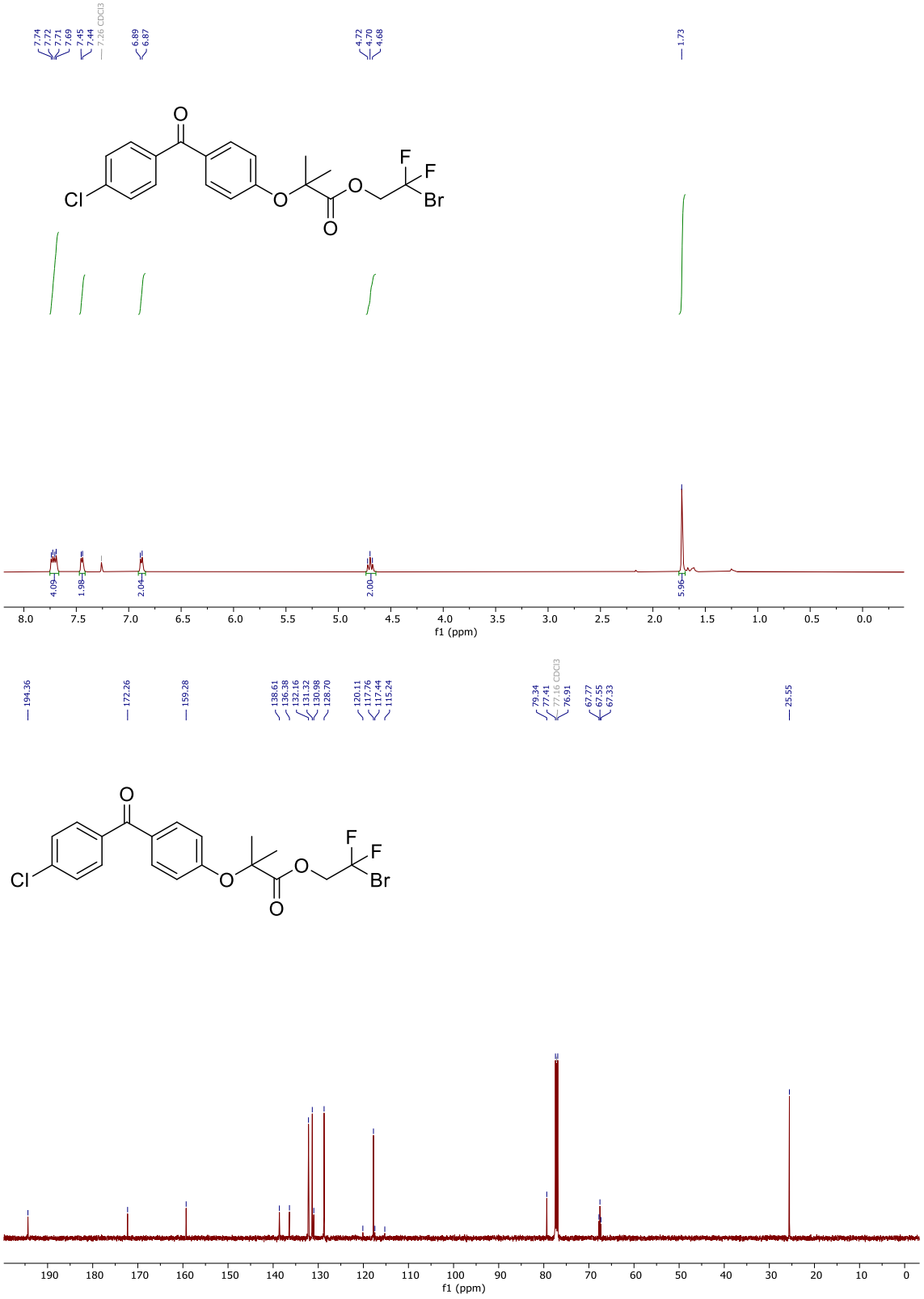


Figure S31. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **2p** in CDCl3 at 298 K.

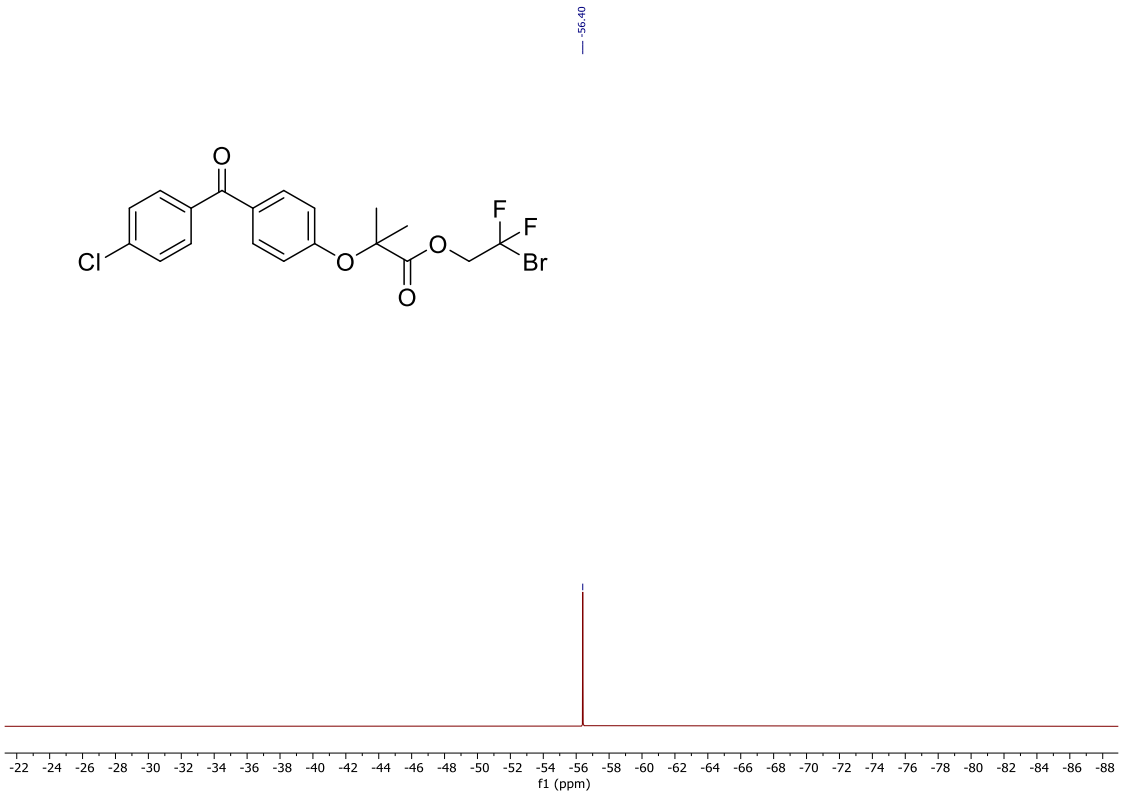


Figure S32. ^{19}F NMR (471 MHz) Spectra of **2p** in $CDCl_3$ at 298 K.

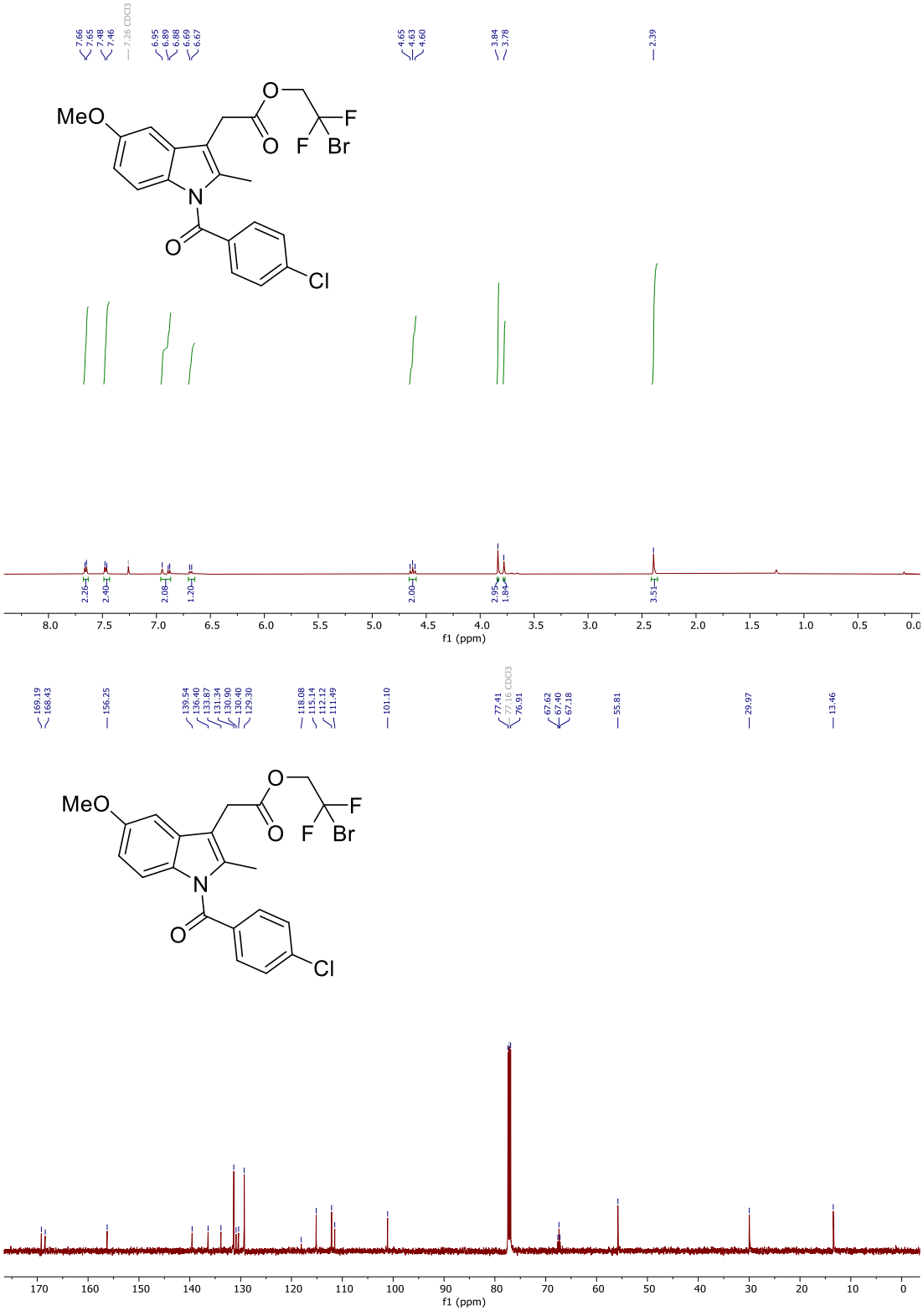


Figure S33. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **2q** in CDCl3 at 298 K.

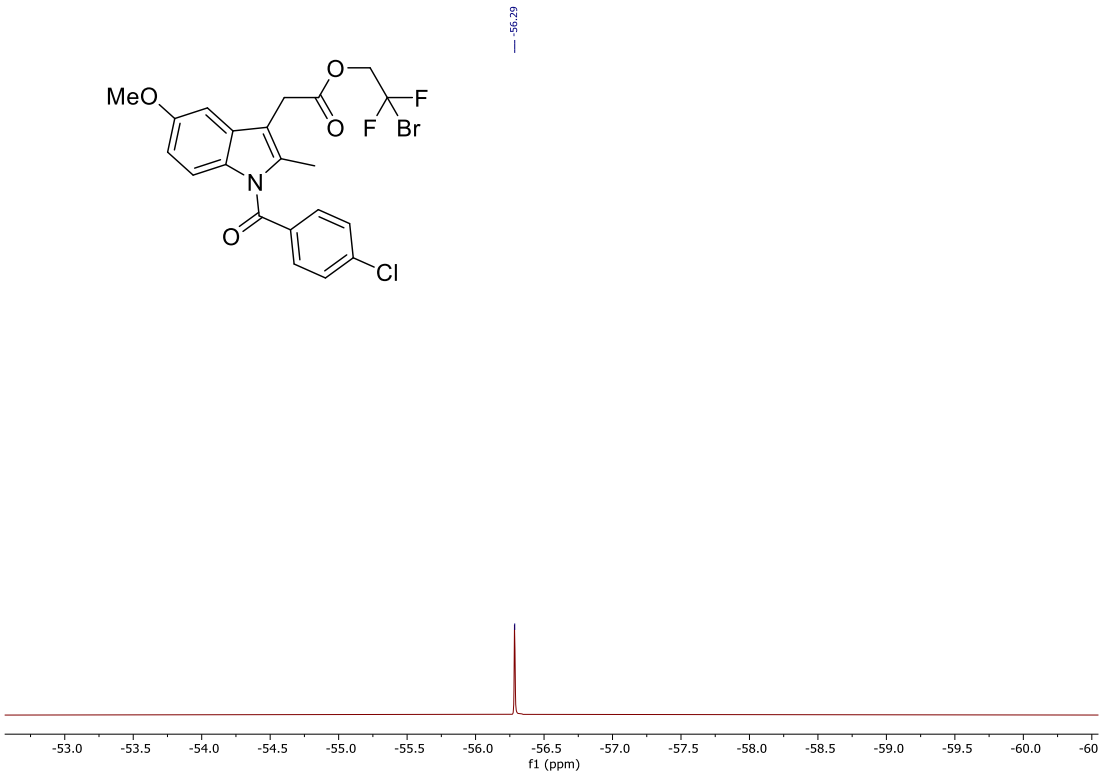


Figure S34. ^{19}F NMR (471 MHz) Spectra of **2q** in $CDCl_3$ at 298 K.

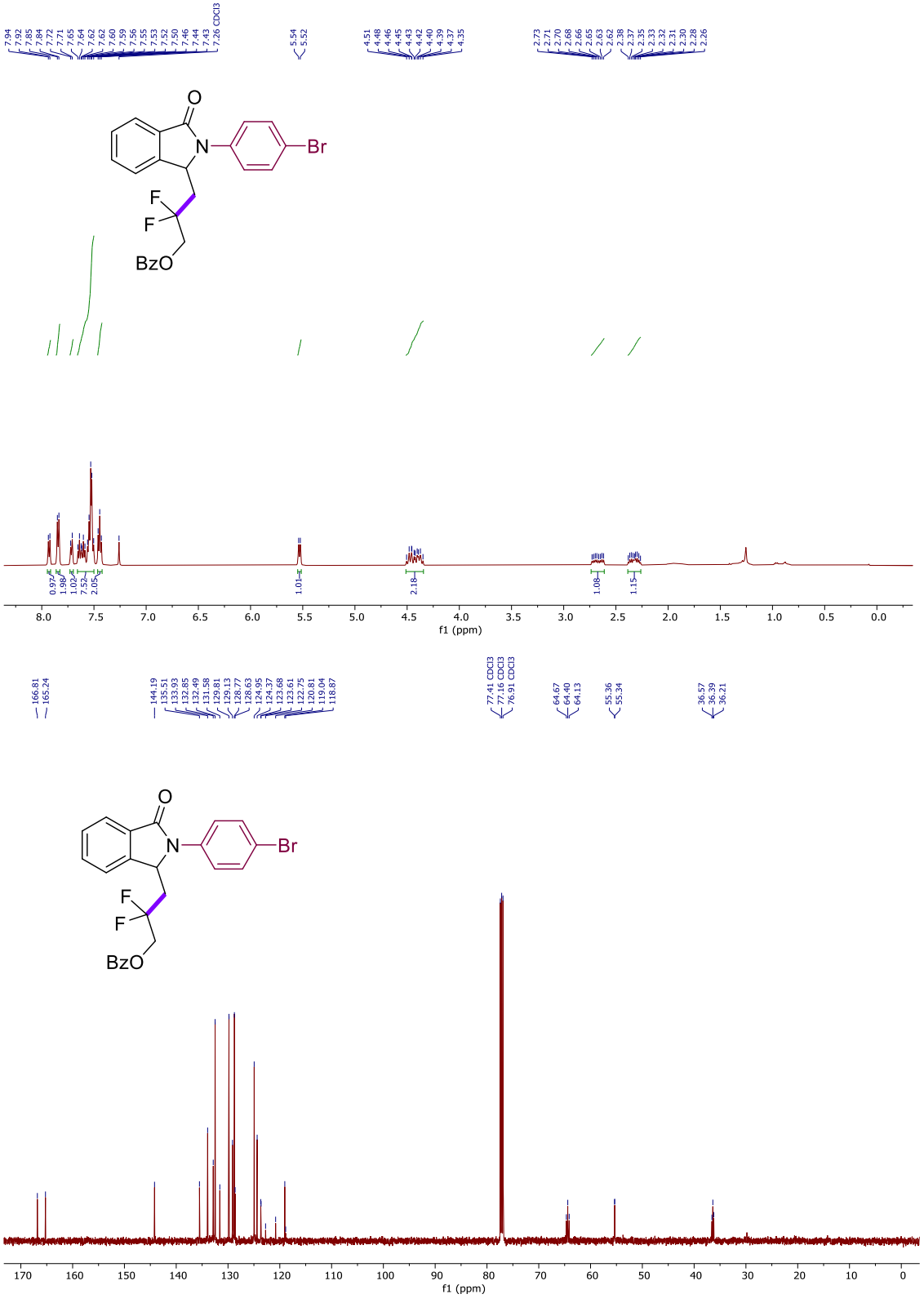


Figure S35. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3a** in $CDCl_3$ at 298 K.

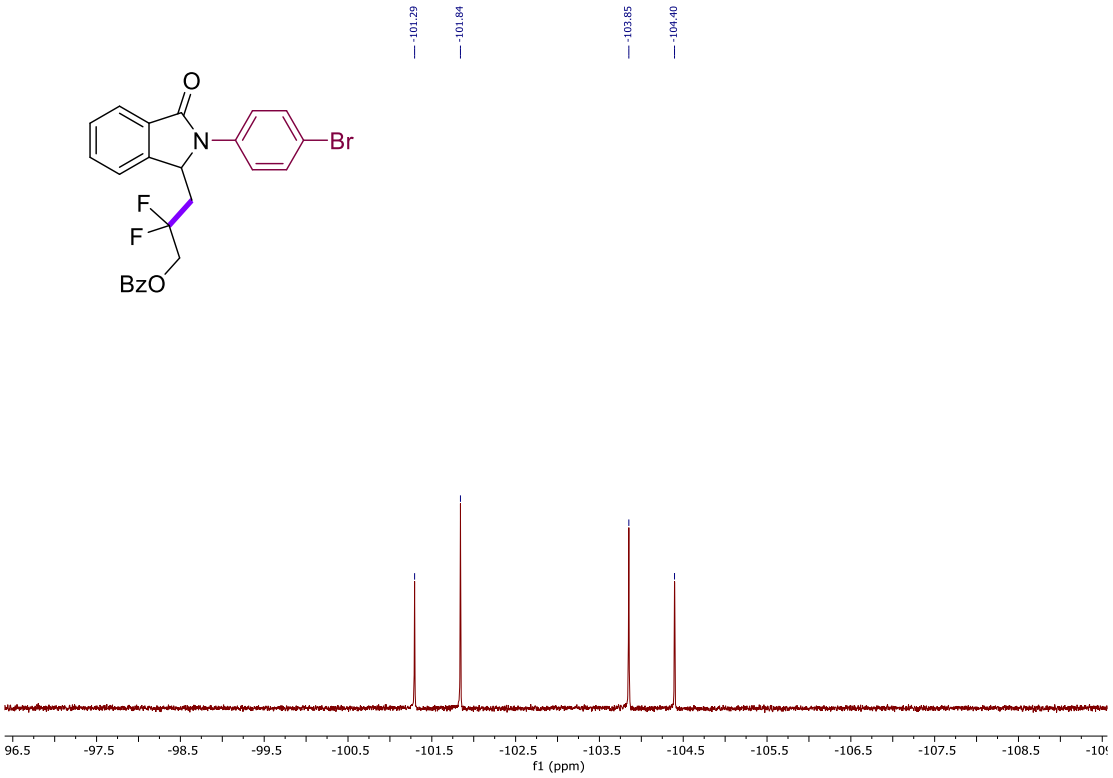


Figure S36. ^{19}F NMR (471 MHz) Spectra of **3a** in $CDCl_3$ at 298 K.

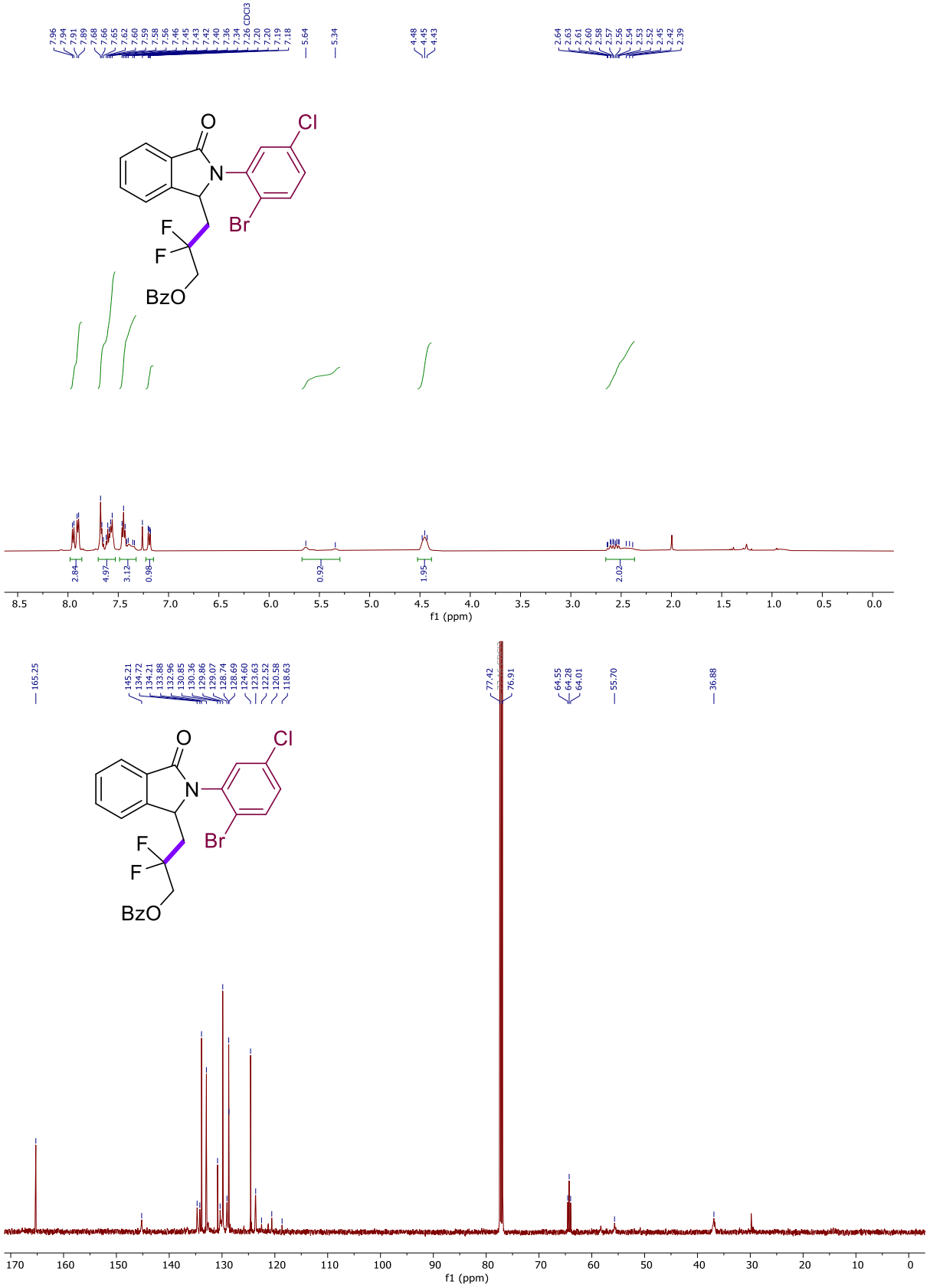


Figure S37. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3b** in $CDCl_3$ at 298 K.

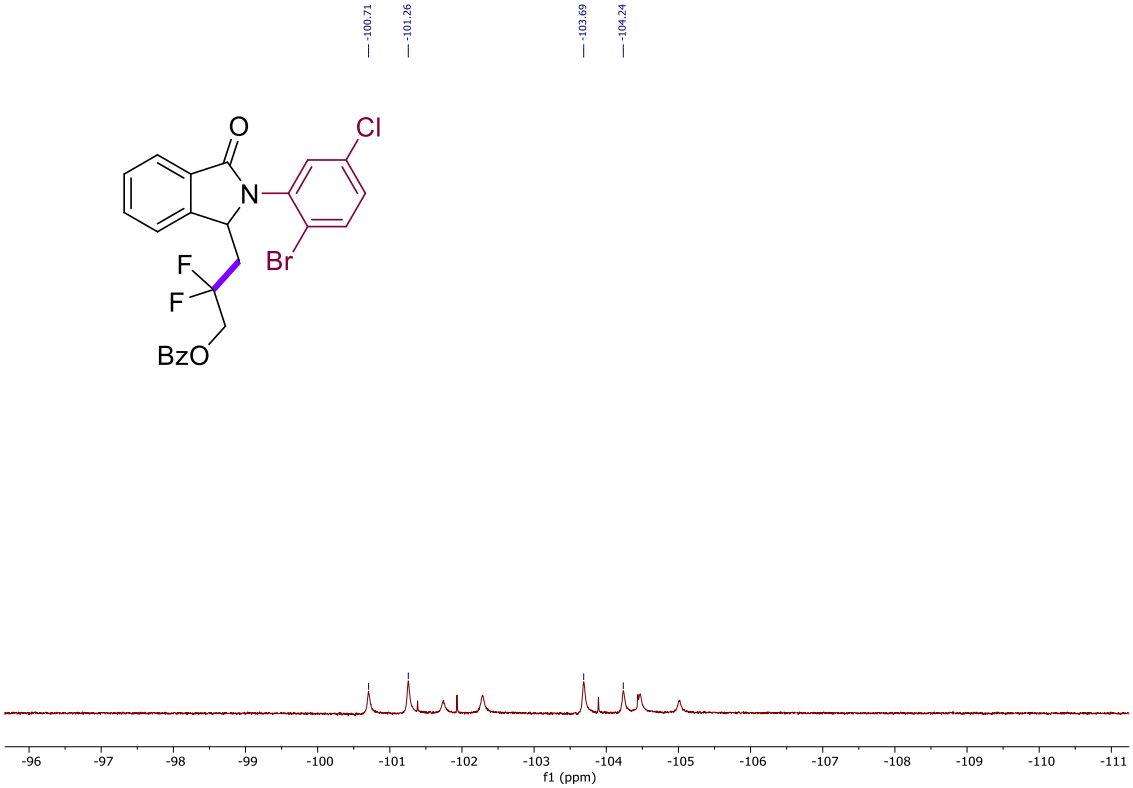


Figure S38. ^{19}F NMR (471 MHz) Spectra of **3b** in $CDCl_3$ at 298 K.

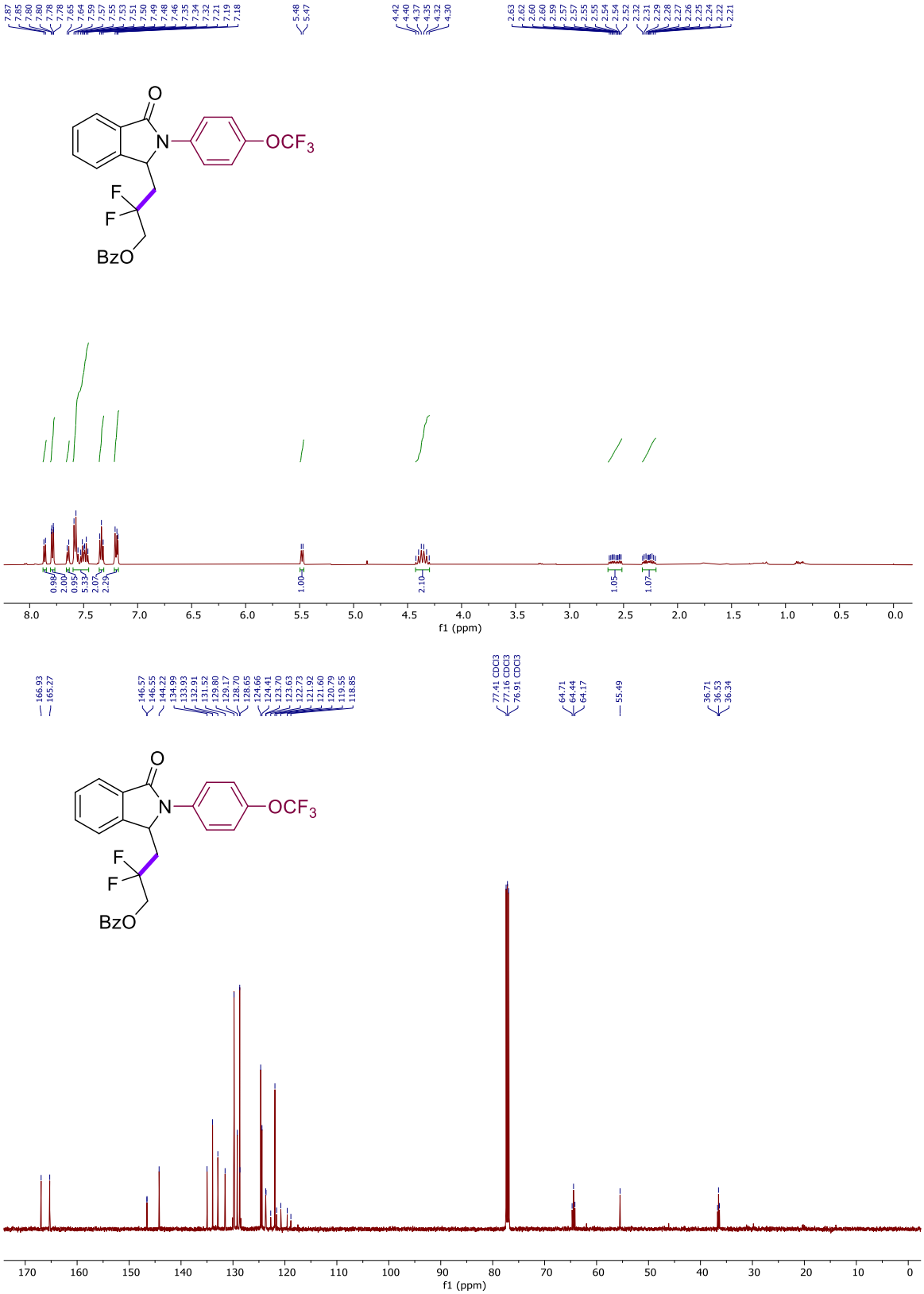


Figure S39. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3c** in $CDCl_3$ at 298 K.

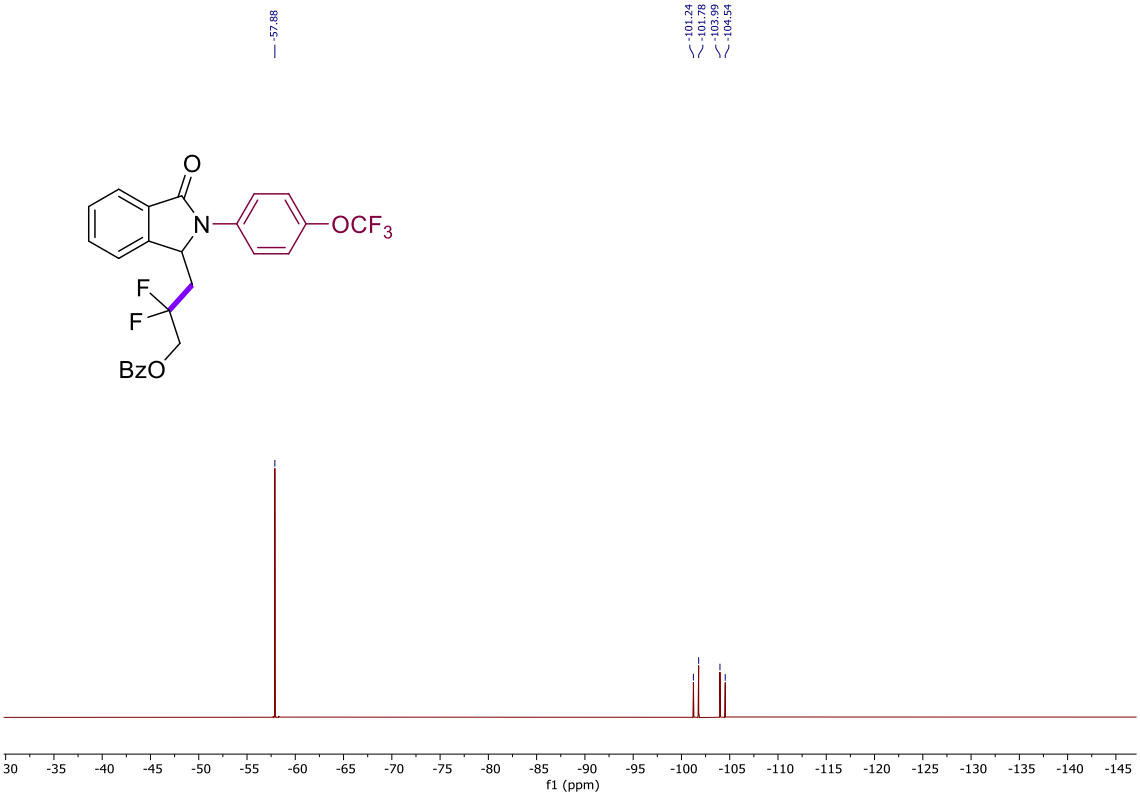


Figure S40. ^{19}F NMR (471 MHz) Spectra of **3c** in $CDCl_3$ at 298 K.

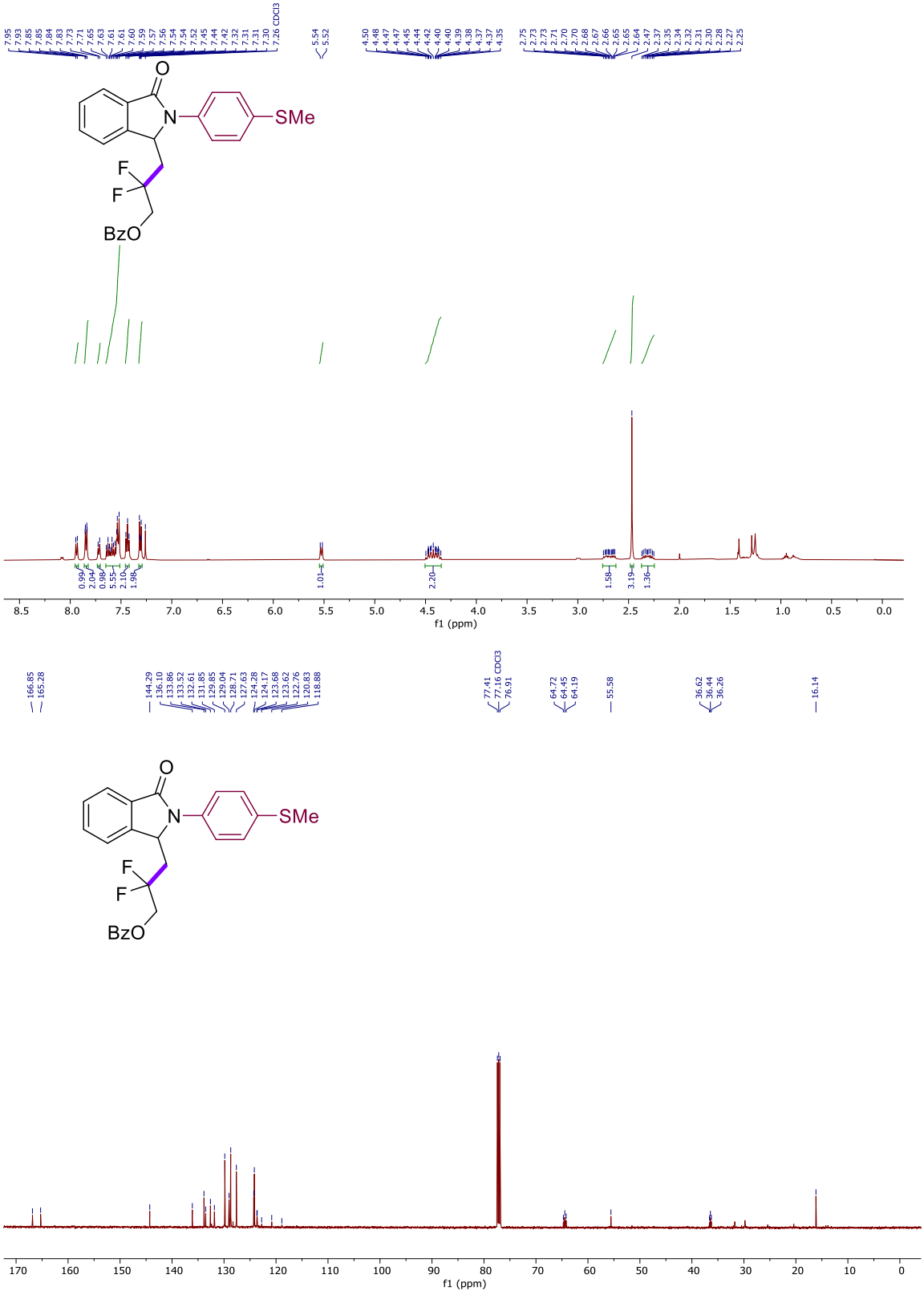


Figure S41. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3d** in $CDCl_3$ at 298 K.

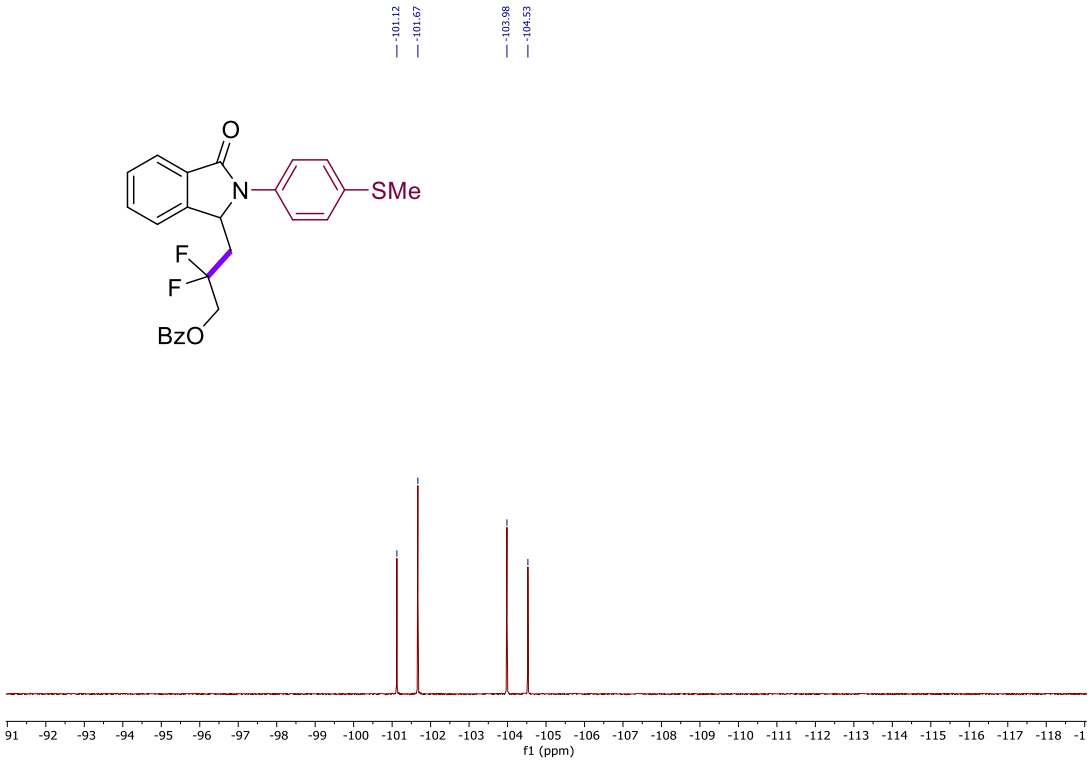


Figure S42. ^{19}F NMR (471 MHz) Spectra of **3d** in $CDCl_3$ at 298 K.

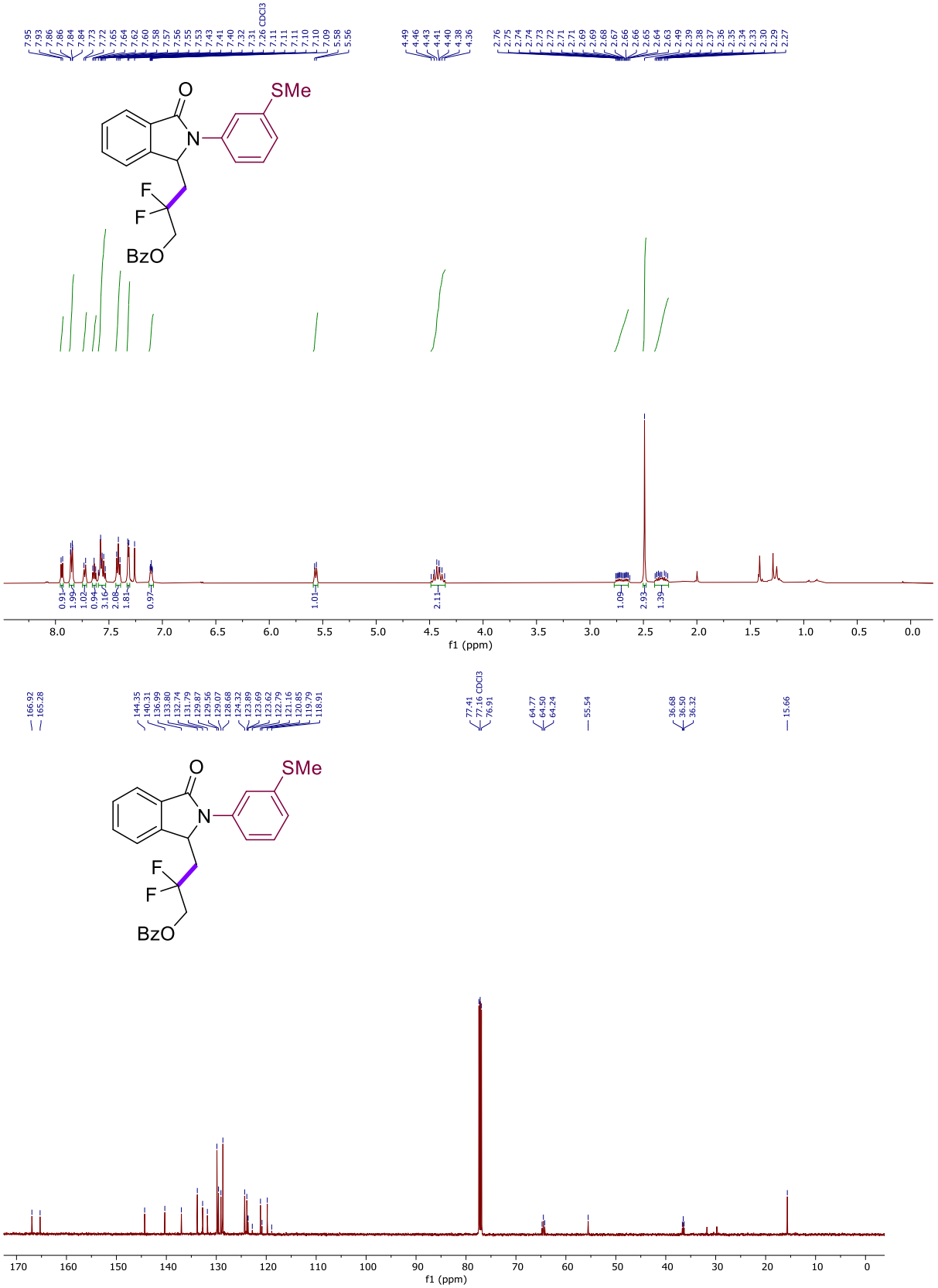


Figure S43. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3e** in $CDCl_3$ at 298 K.

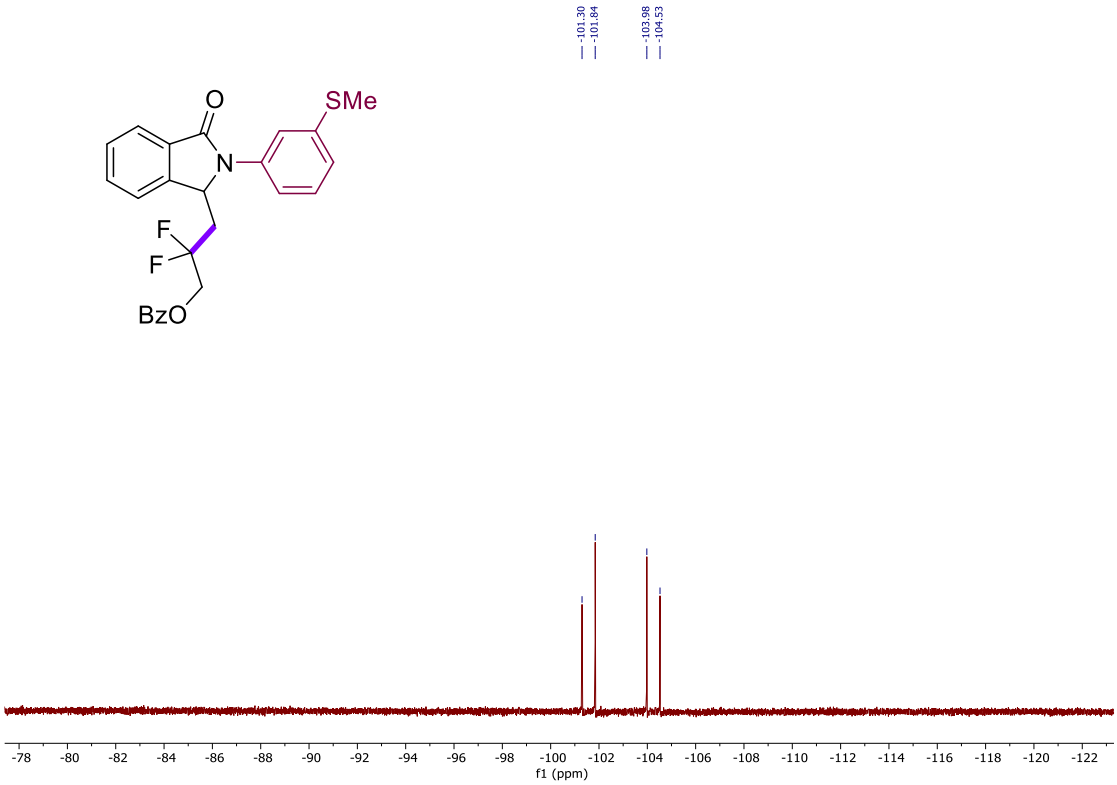


Figure S44. ^{19}F NMR (471 MHz) Spectra of **3e** in $CDCl_3$ at 298 K.

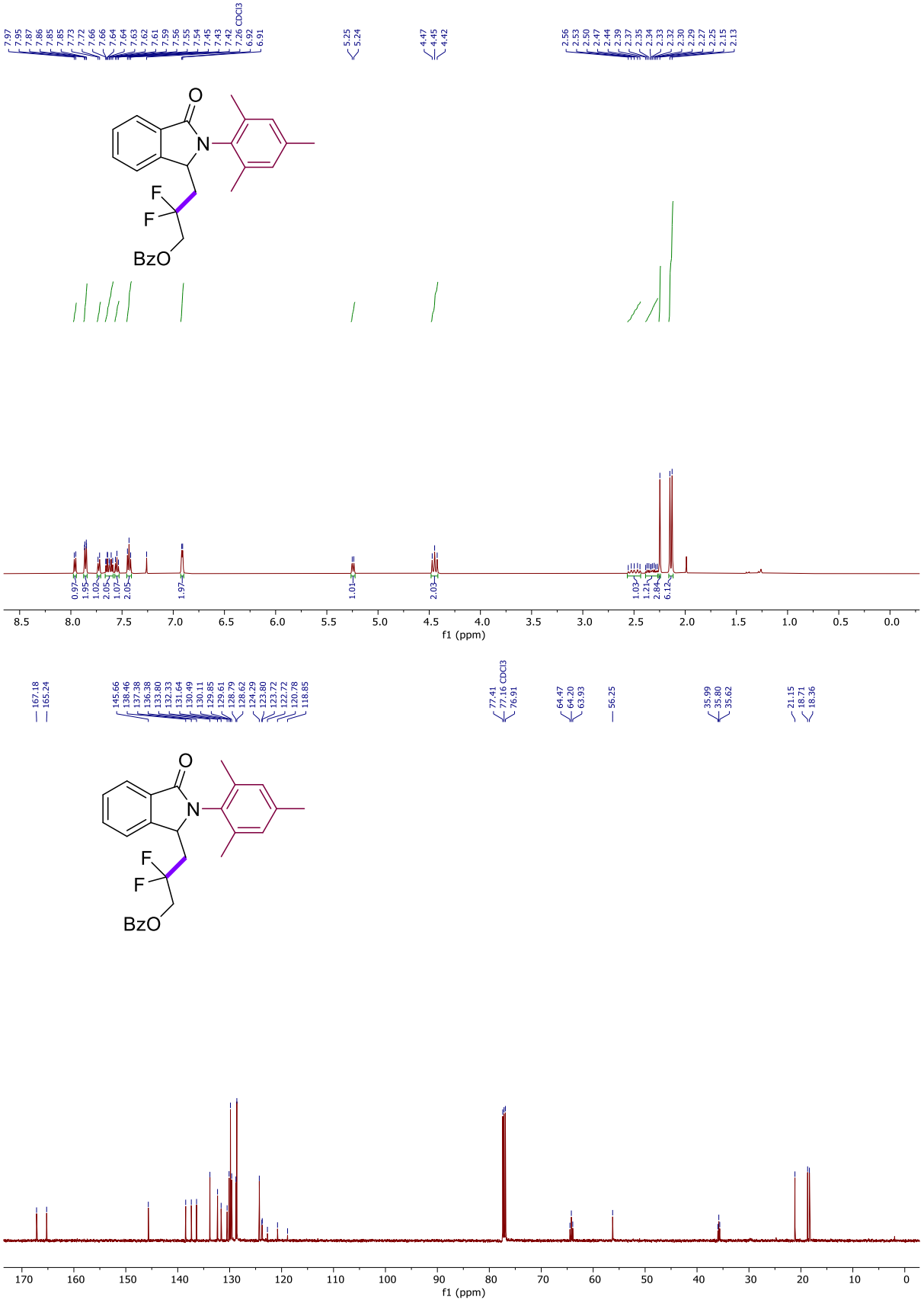


Figure S45. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3f** in $CDCl_3$ at 298 K.

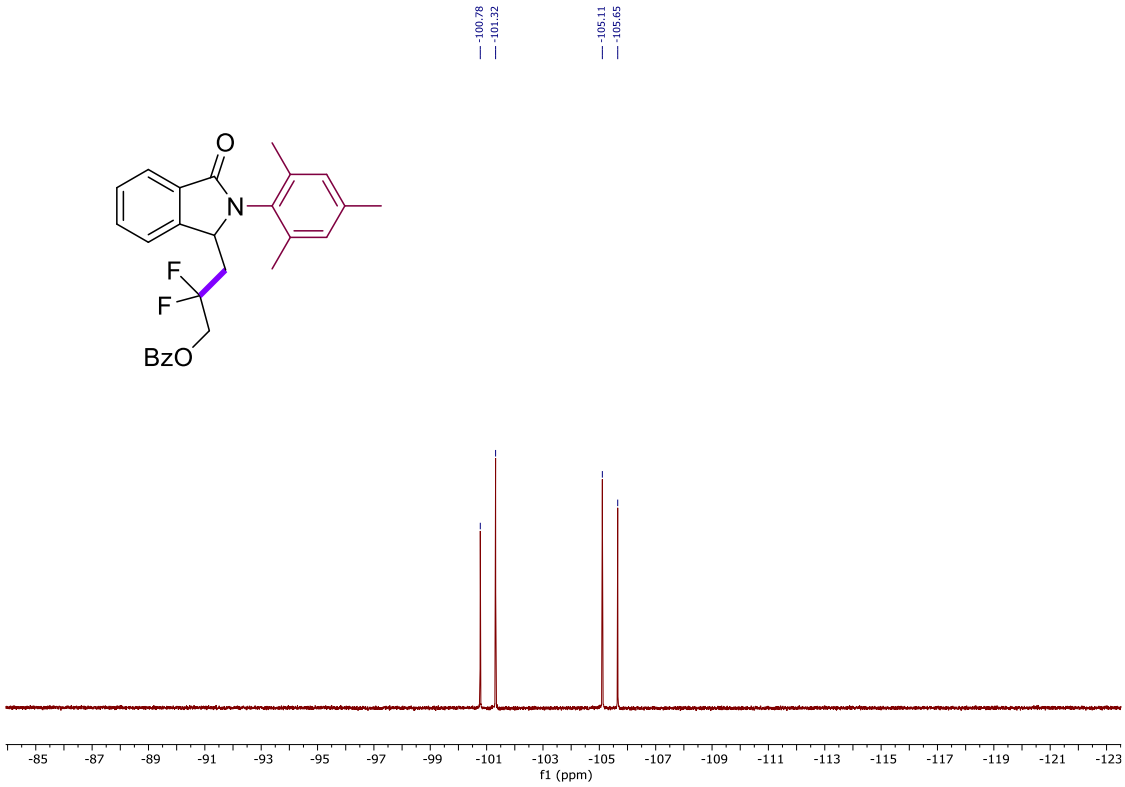


Figure S46. ^{19}F NMR (471 MHz) Spectra of **3f** in $CDCl_3$ at 298 K.

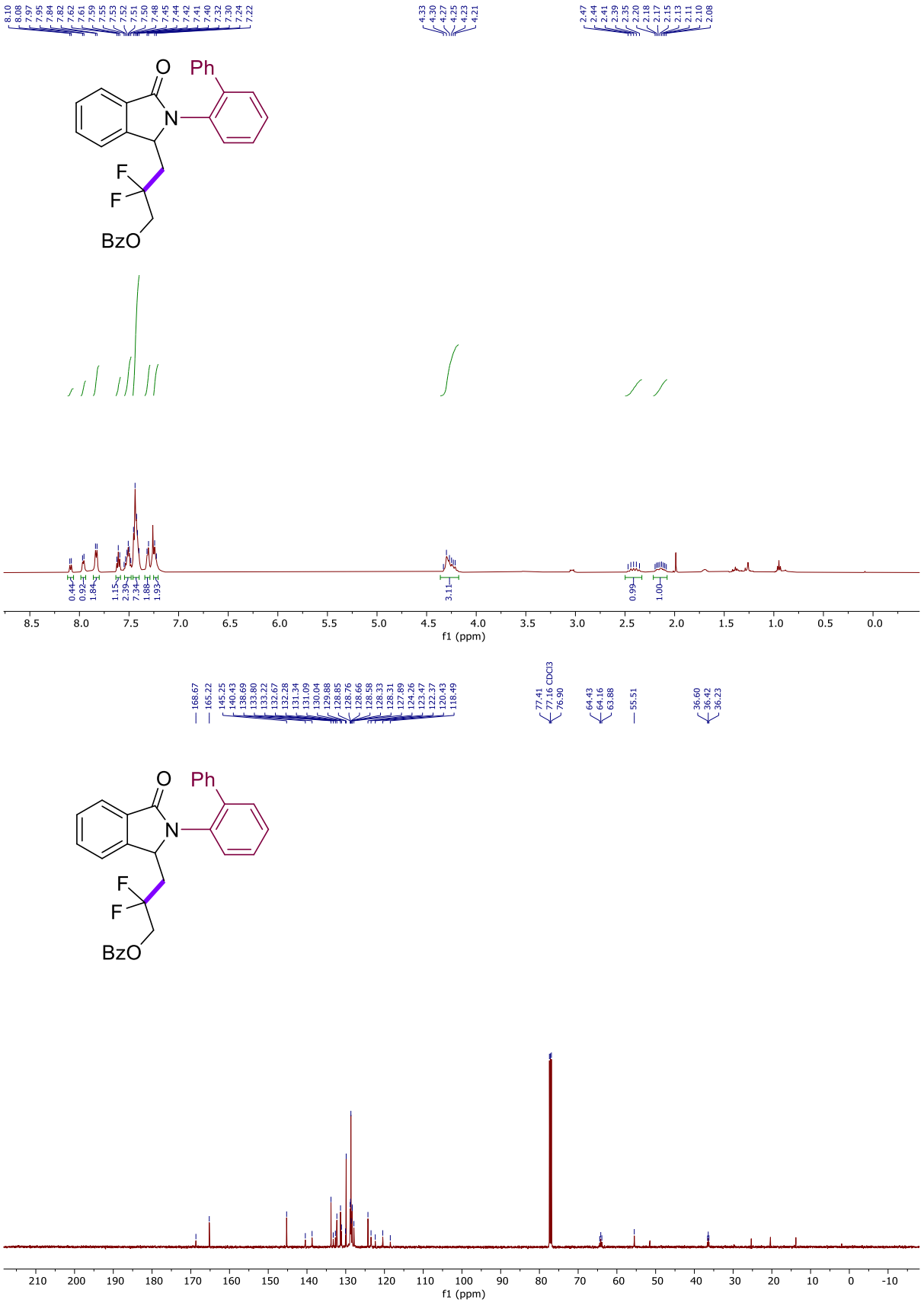


Figure S47. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3g** in $CDCl_3$ at 298 K.

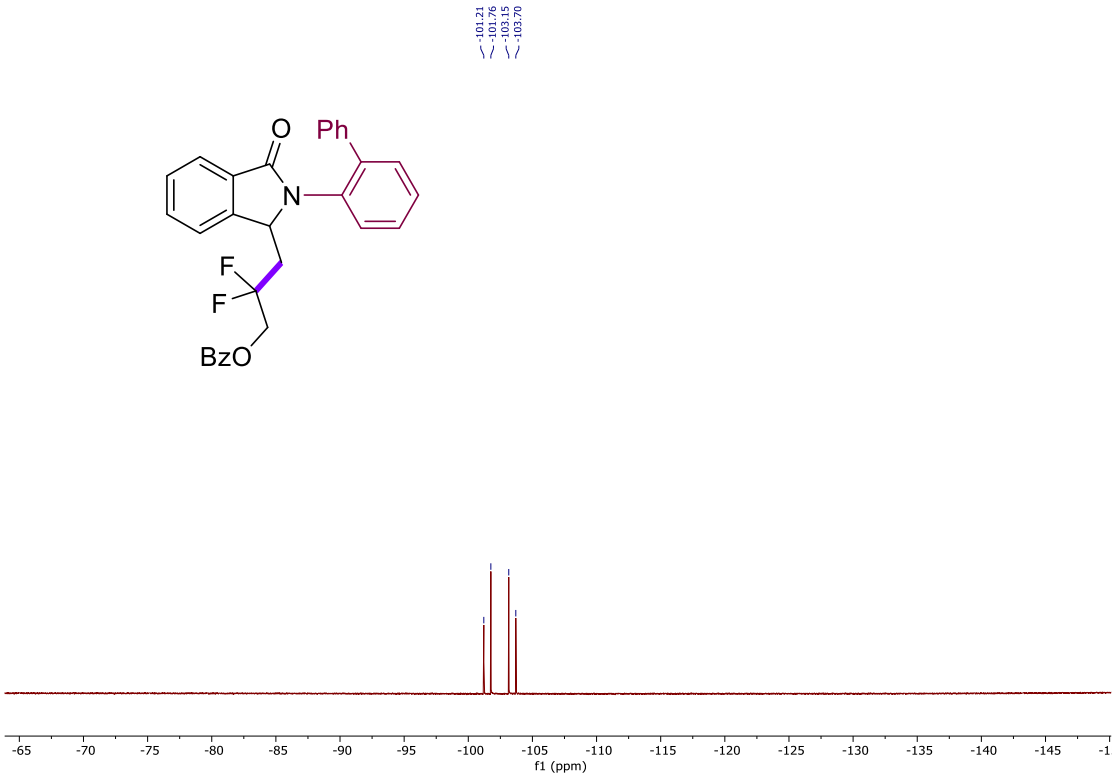


Figure S48. ^{19}F NMR (471 MHz) Spectra of **3g** in $CDCl_3$ at 298 K.

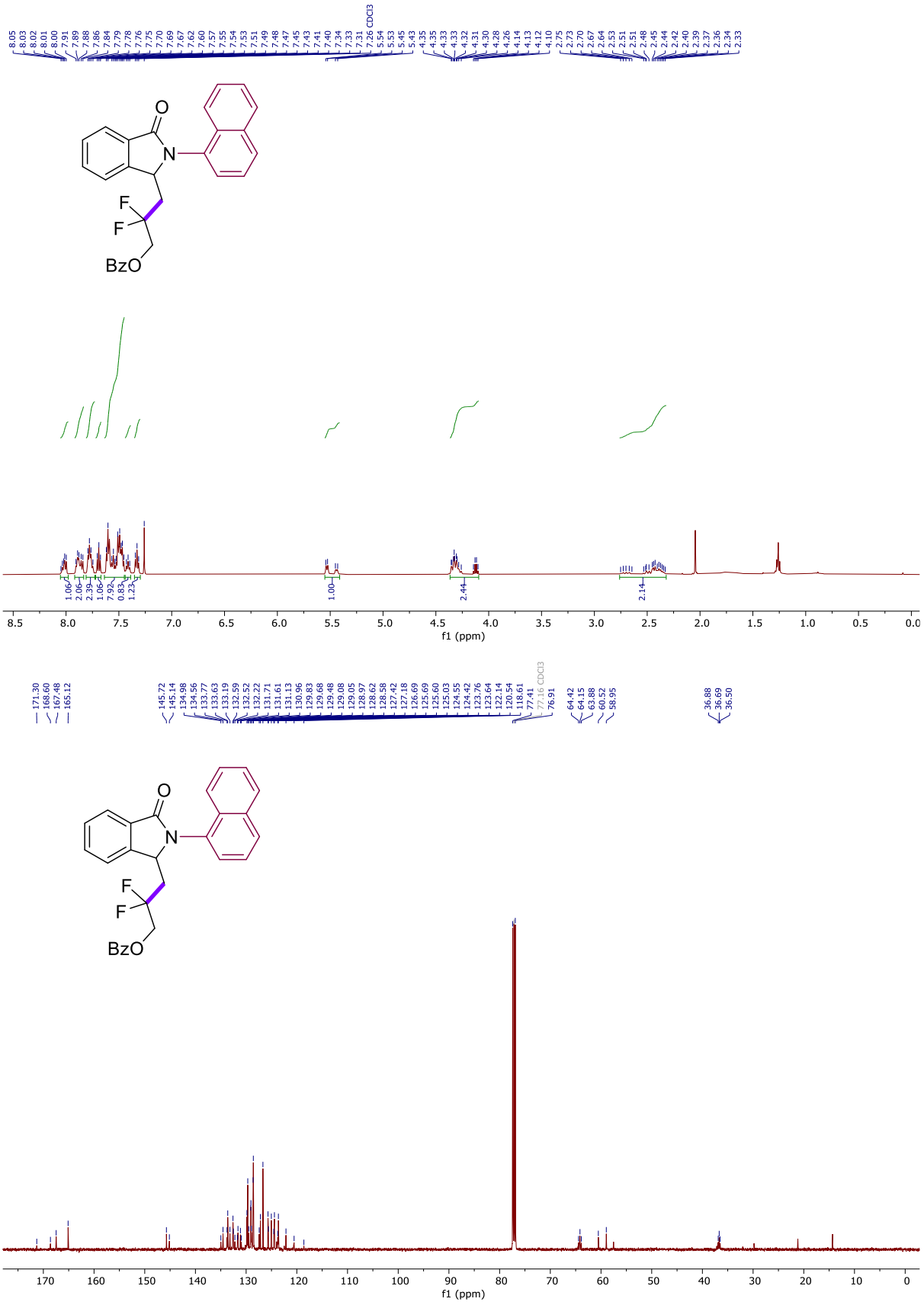


Figure S49. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3h** in $CDCl_3$ at 298 K.

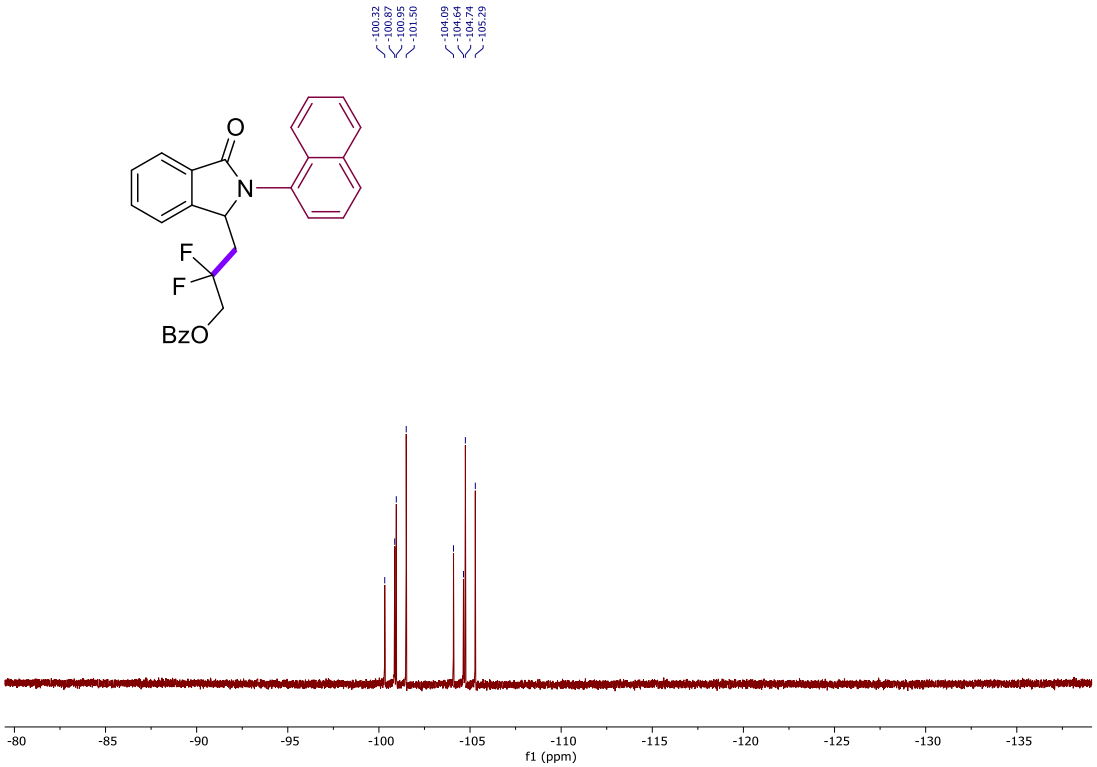


Figure S50. ^{19}F NMR (471 MHz) Spectra of **3h** in $CDCl_3$ at 298 K.

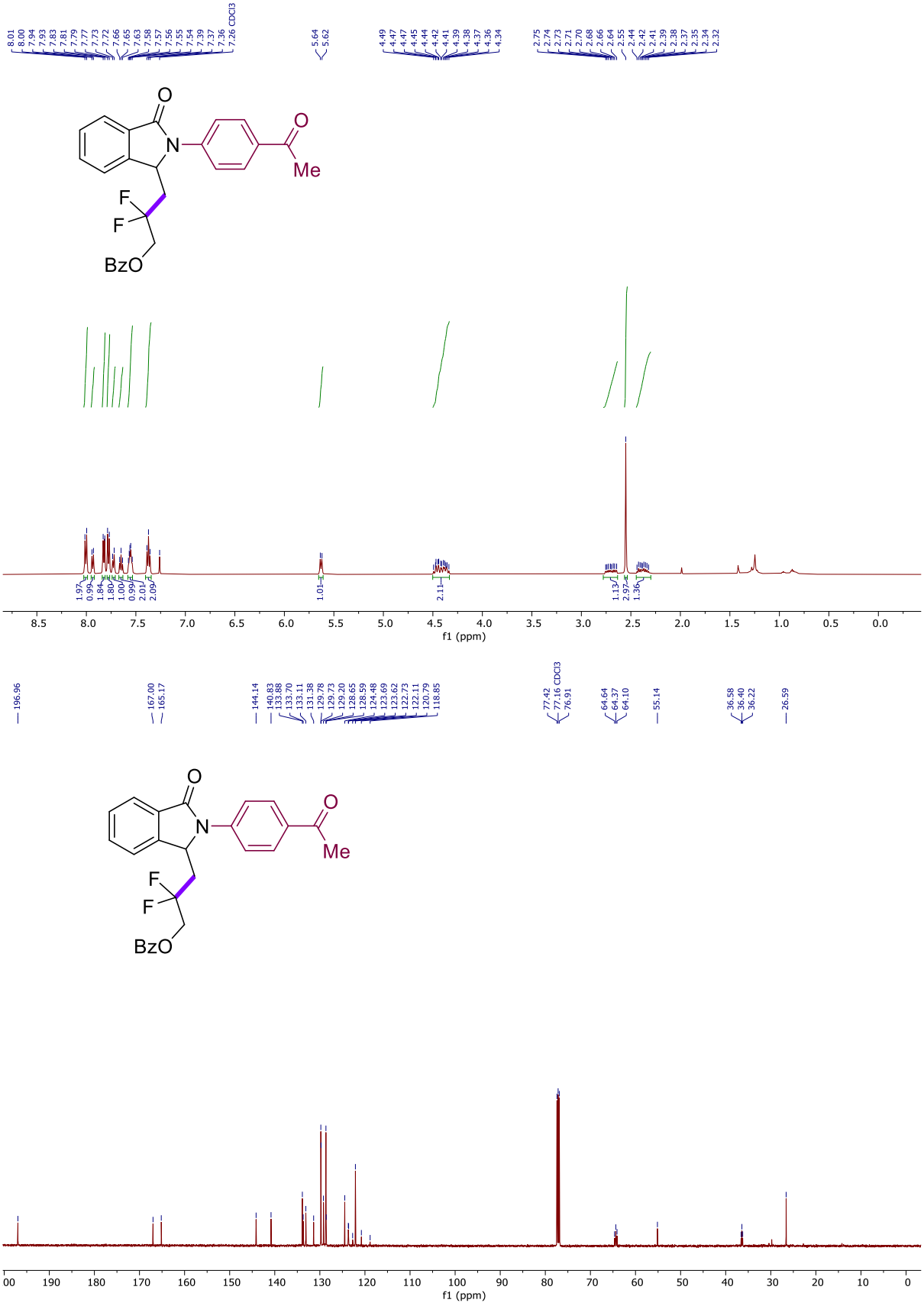


Figure S51. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3i** in $CDCl_3$ at 298 K.

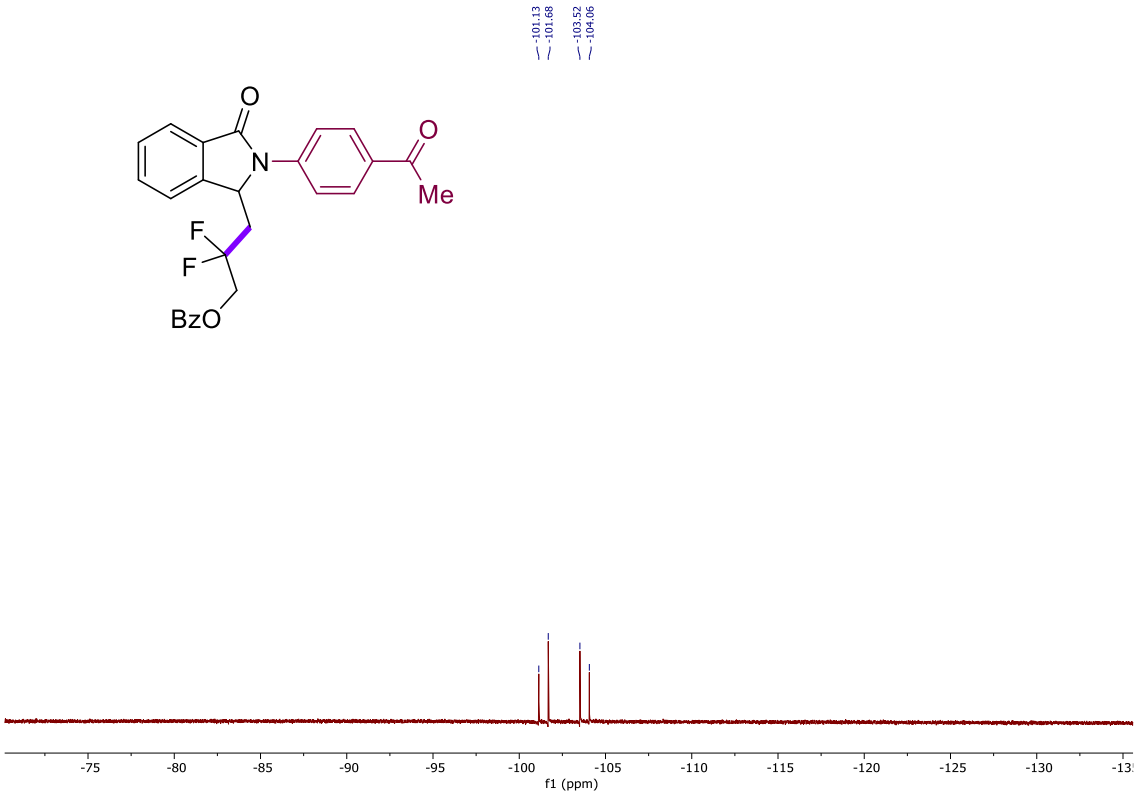


Figure S52. ^{19}F NMR (471 MHz) Spectra of **3i** in $CDCl_3$ at 298 K.

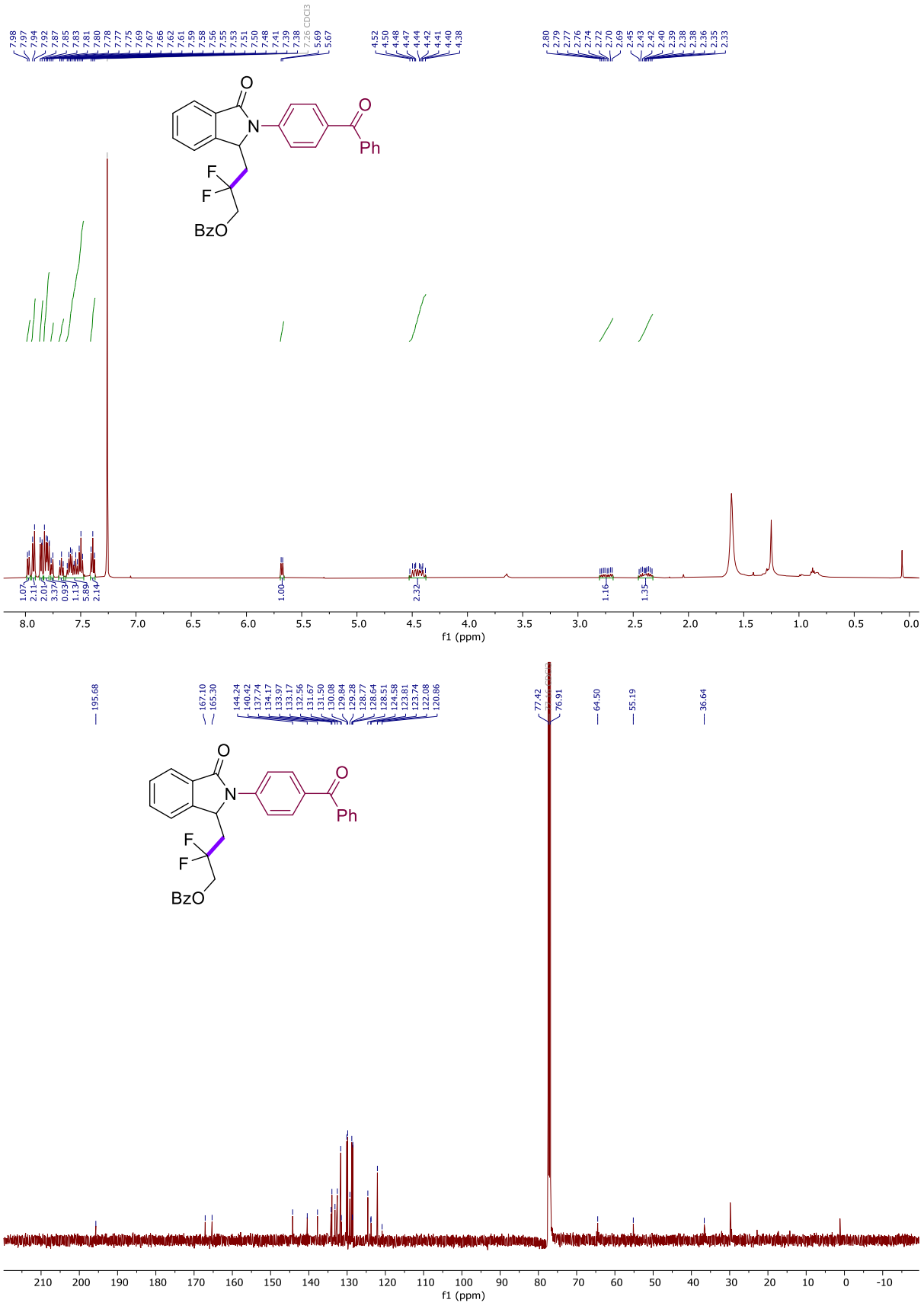


Figure S53. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3j** in $CDCl_3$ at 298 K.

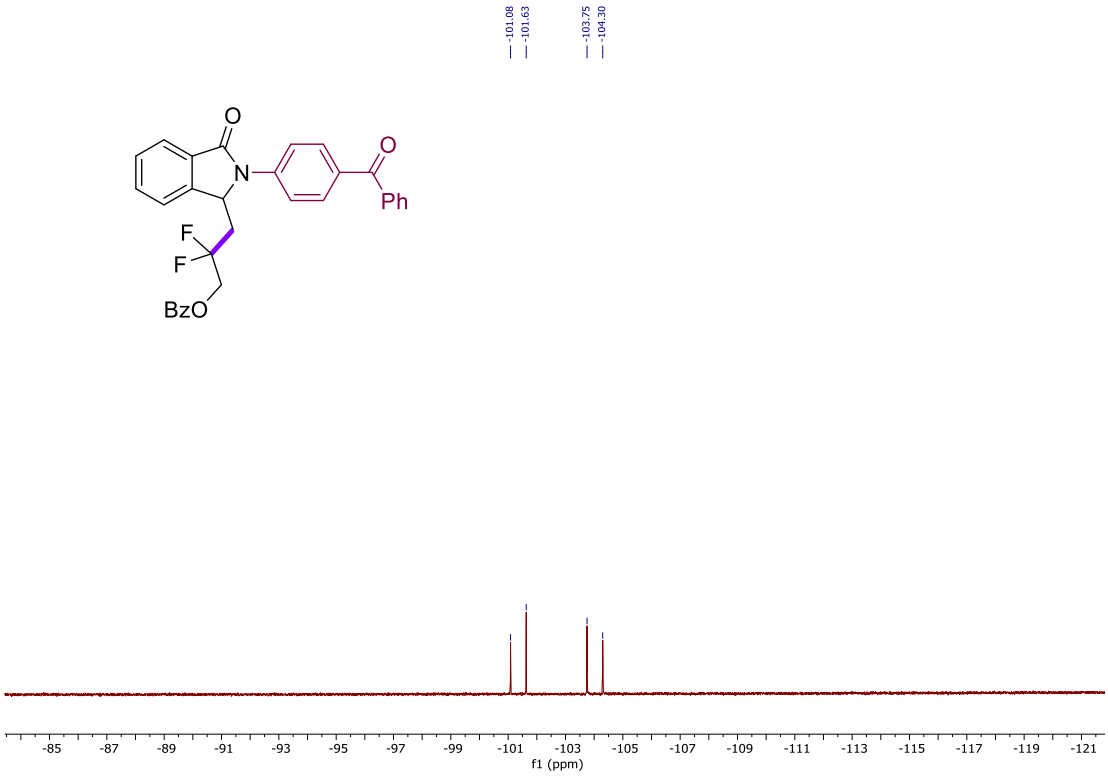


Figure S54. ^{19}F NMR (471 MHz) Spectra of **3j** in $CDCl_3$ at 298 K.

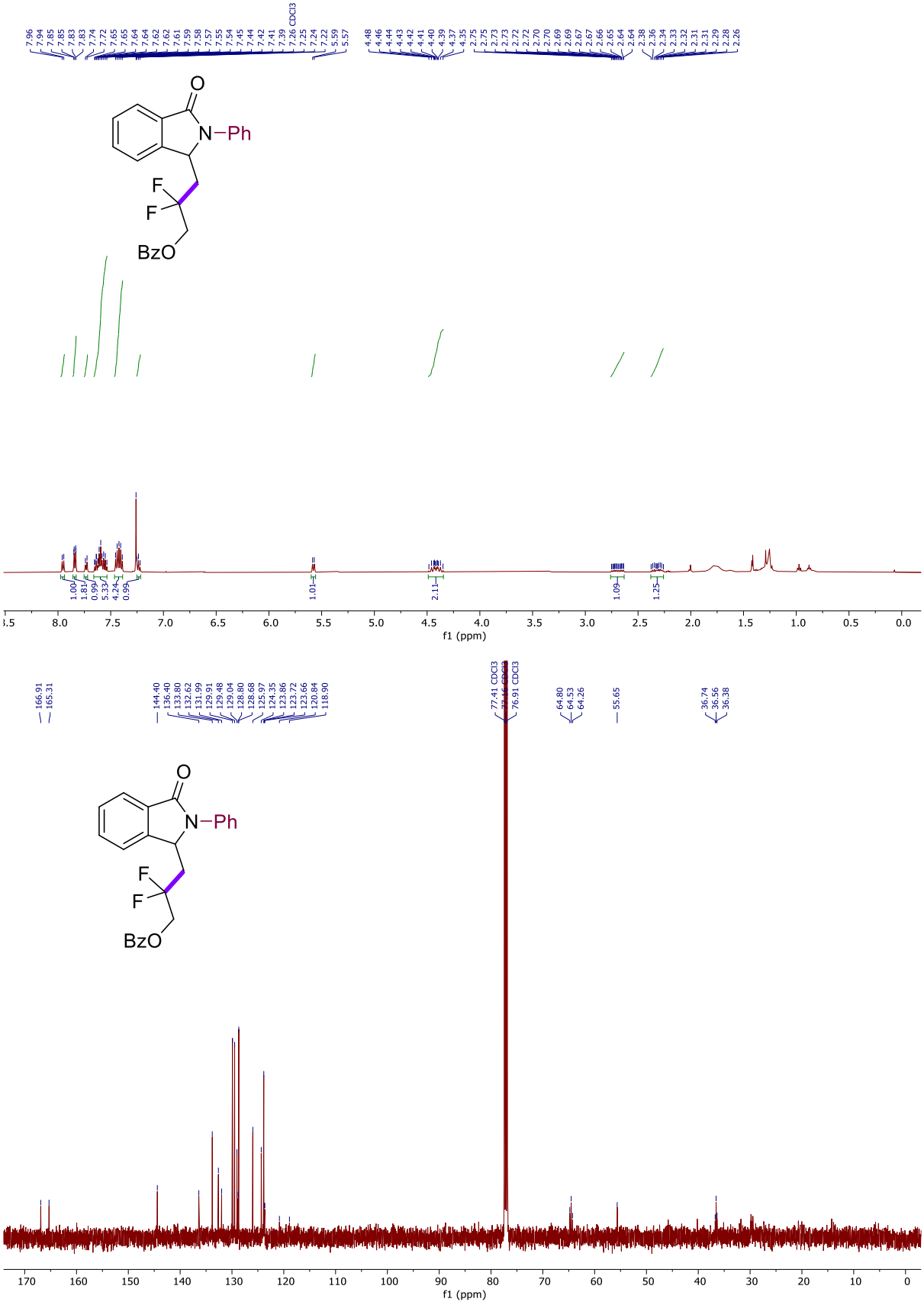


Figure S55. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3k** in $CDCl_3$ at 298 K.

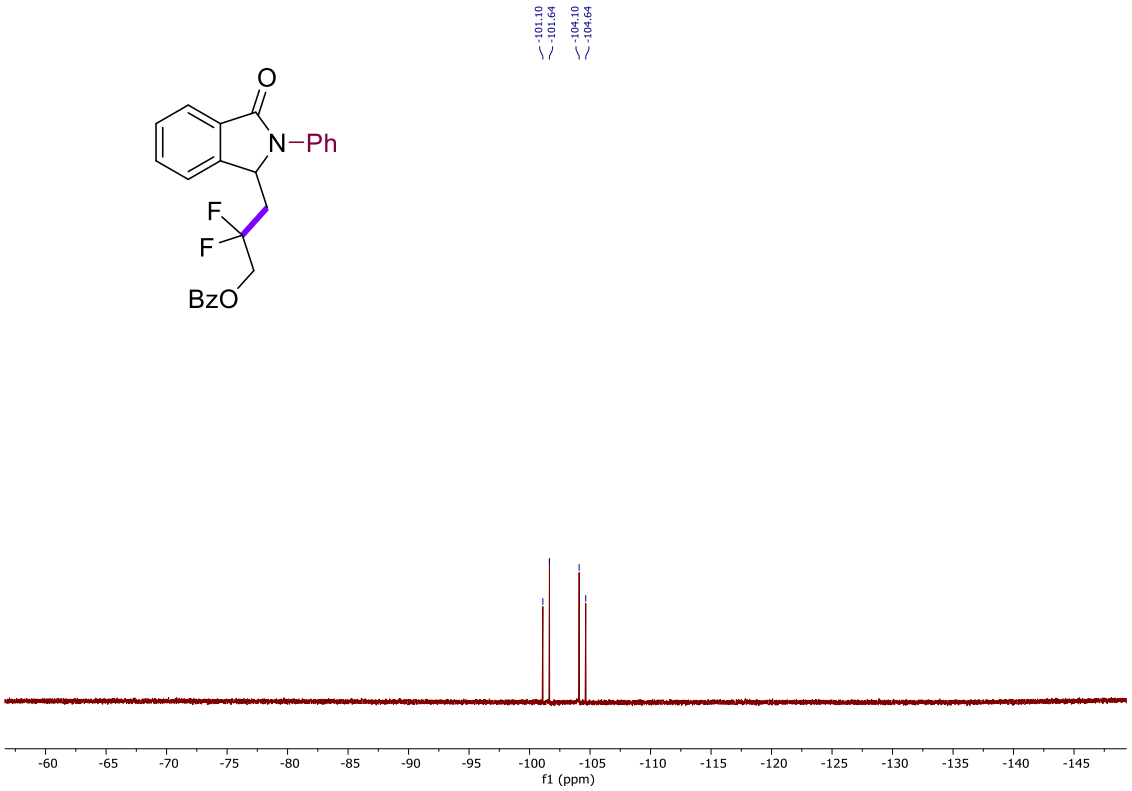


Figure S56. ^{19}F NMR (471 MHz) Spectra of **3k** in $CDCl_3$ at 298 K.

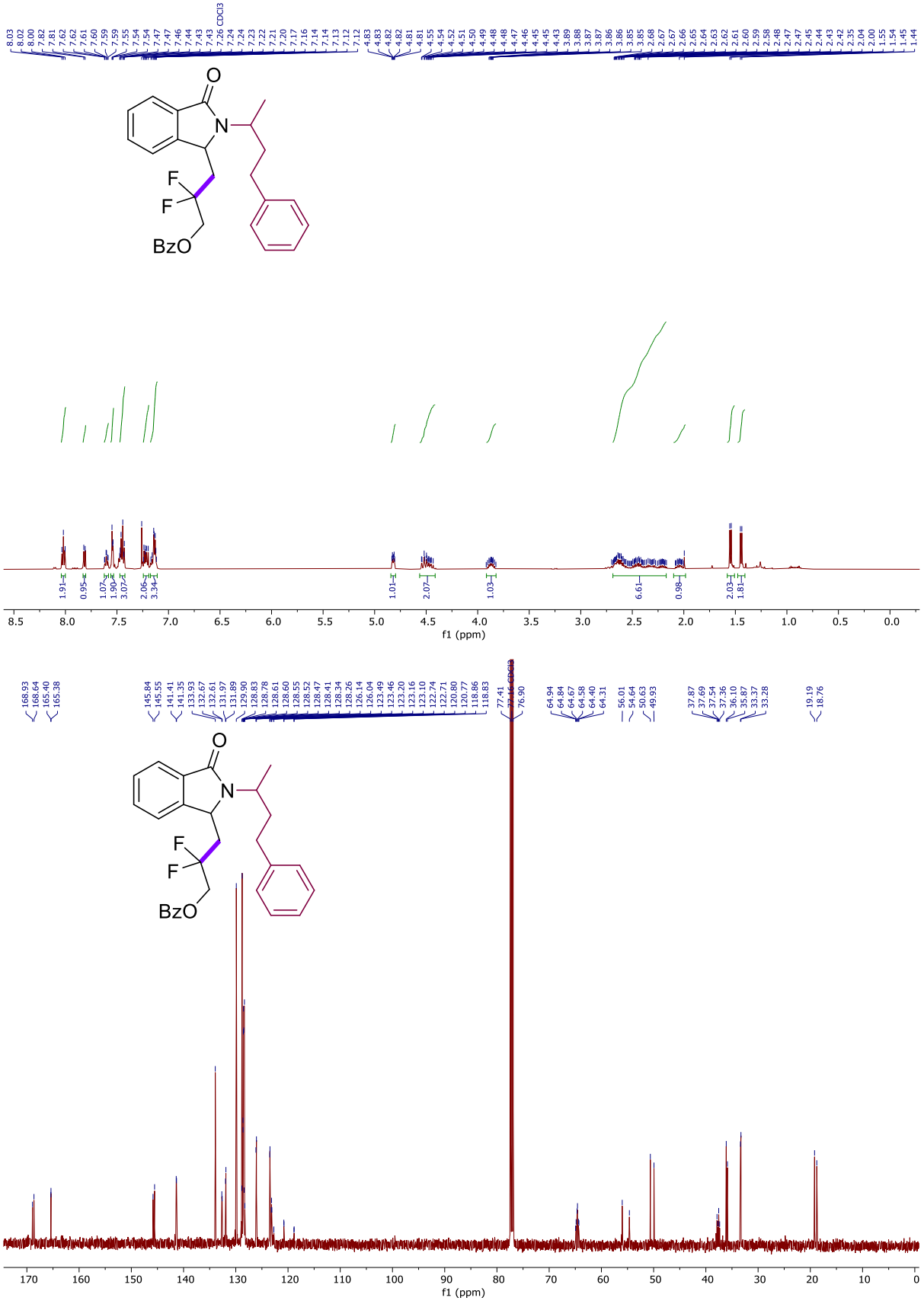


Figure S57. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3l** in $CDCl_3$ at 298 K.

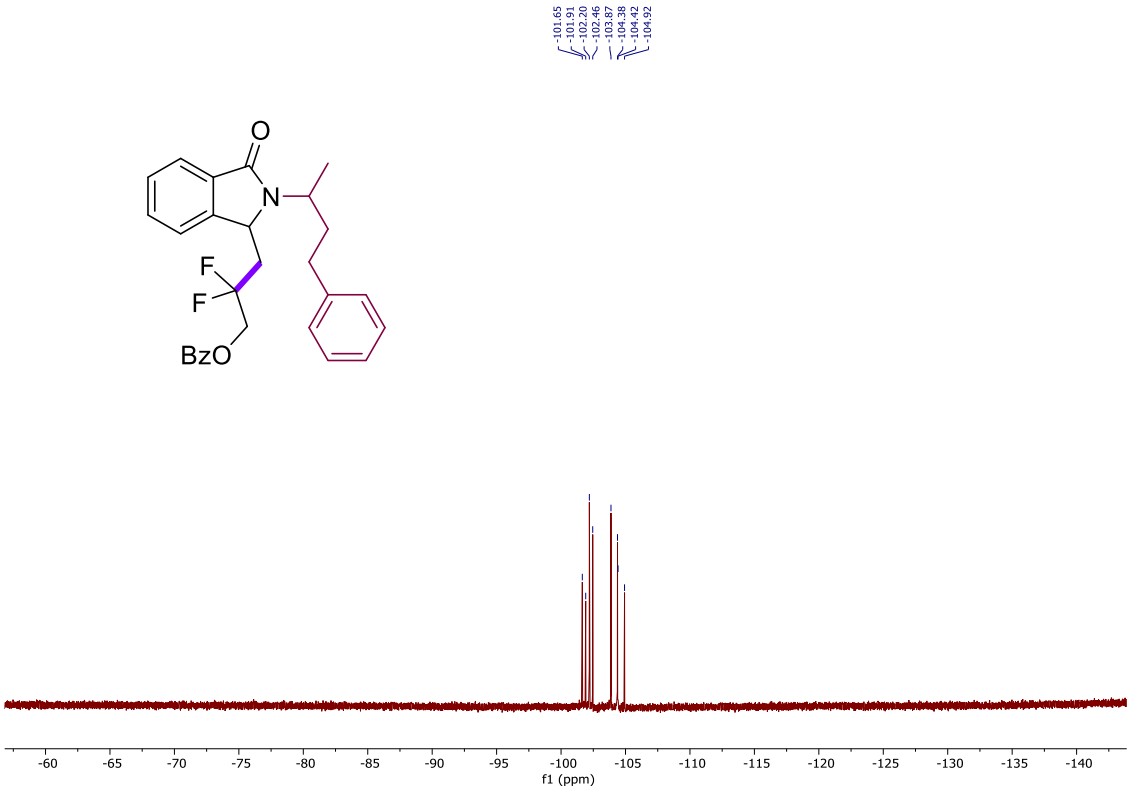


Figure S58. ^{19}F NMR (471 MHz) Spectra of **3l** in $CDCl_3$ at 298 K.

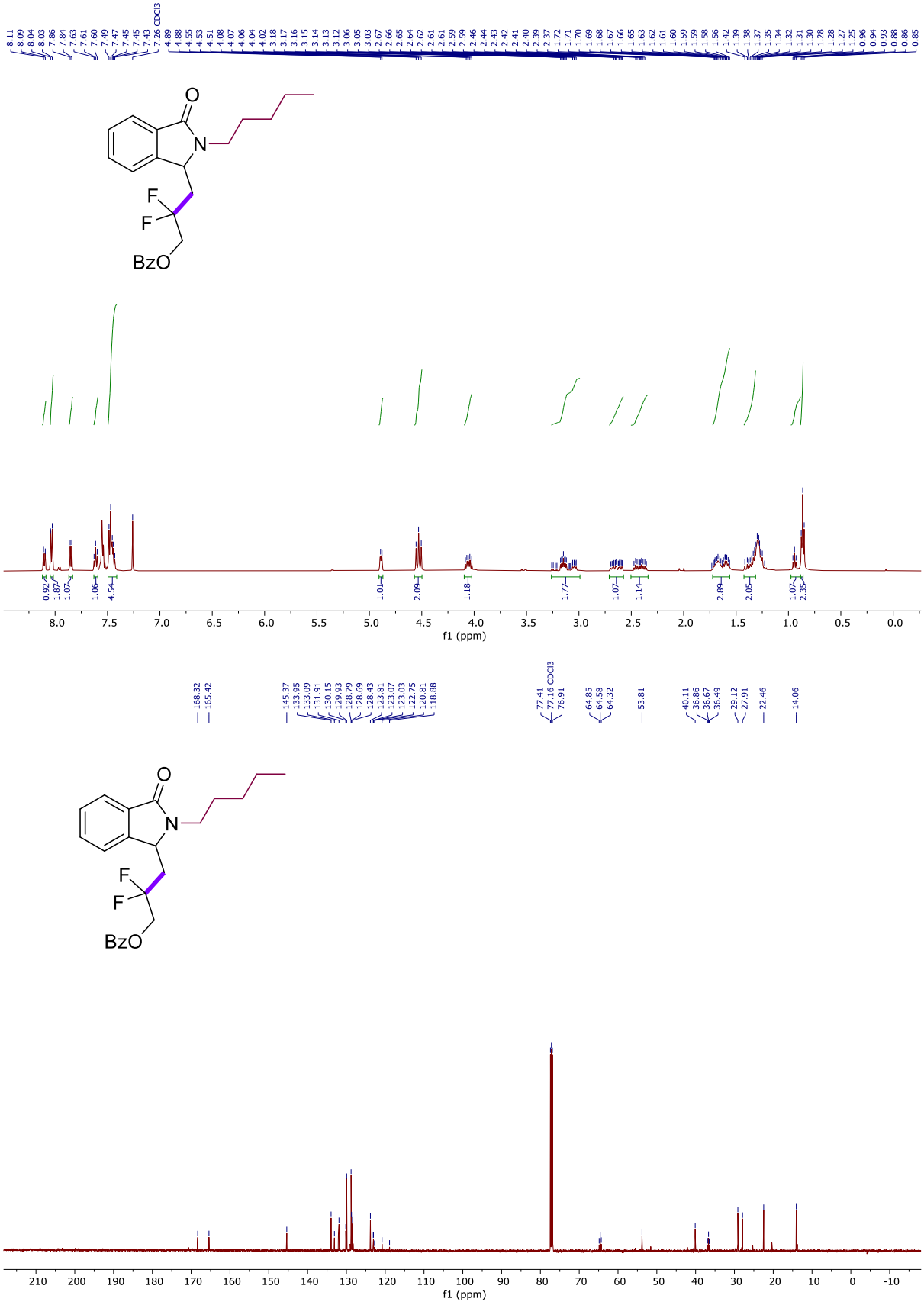


Figure S59. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3m** in $CDCl_3$ at 298 K.

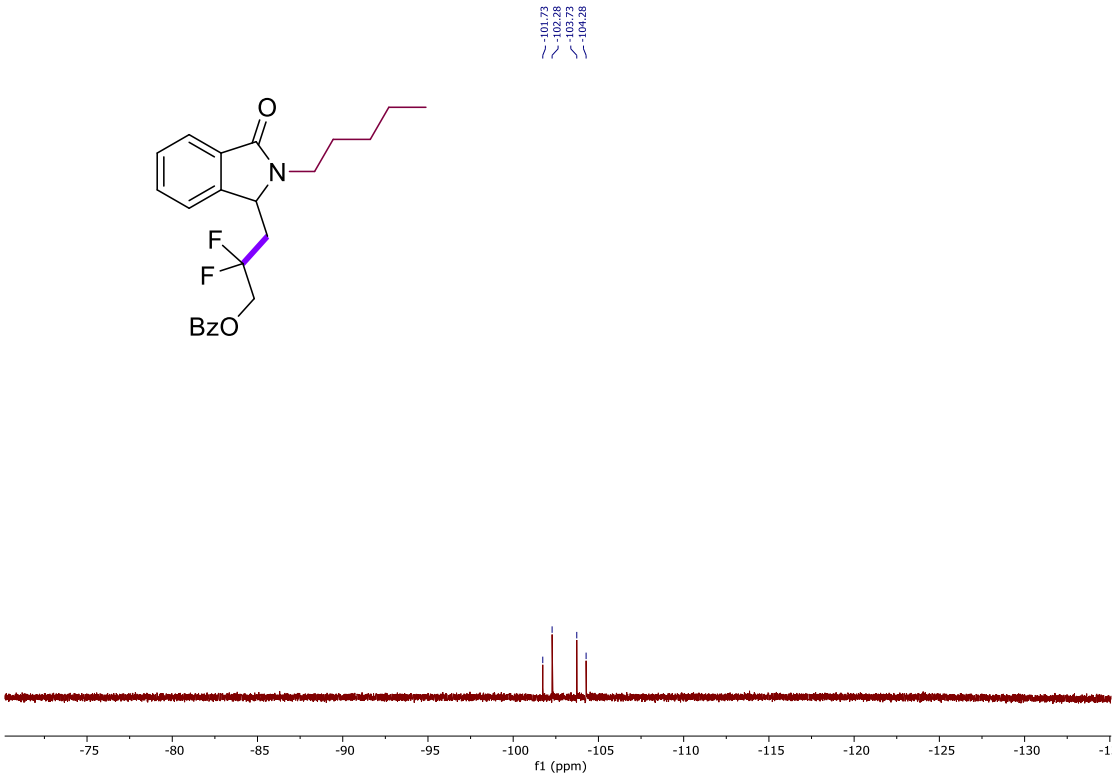


Figure S60. ^{19}F NMR (471 MHz) Spectra of **3m** in $CDCl_3$ at 298 K.

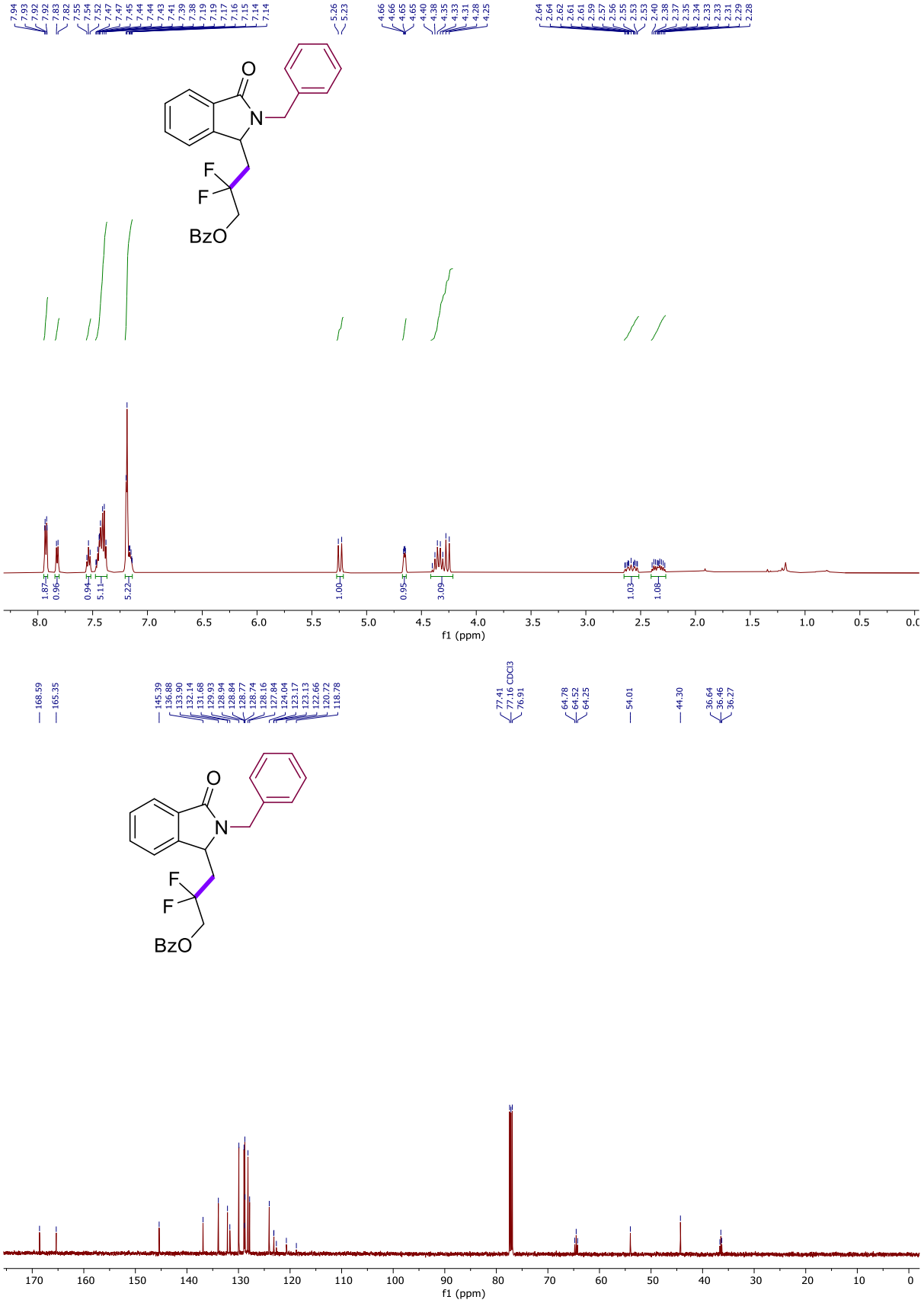


Figure S61. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3n** in $CDCl_3$ at 298 K.

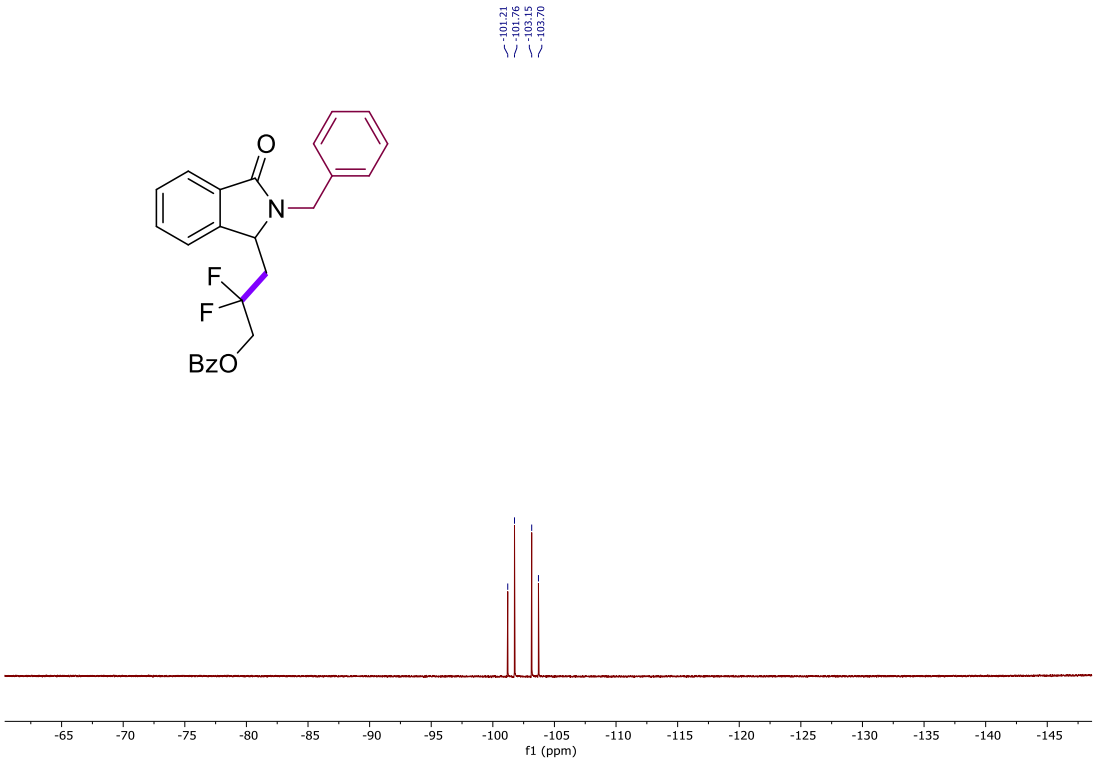


Figure S62. ^{19}F NMR (471 MHz) Spectra of **3n** in $CDCl_3$ at 298 K.

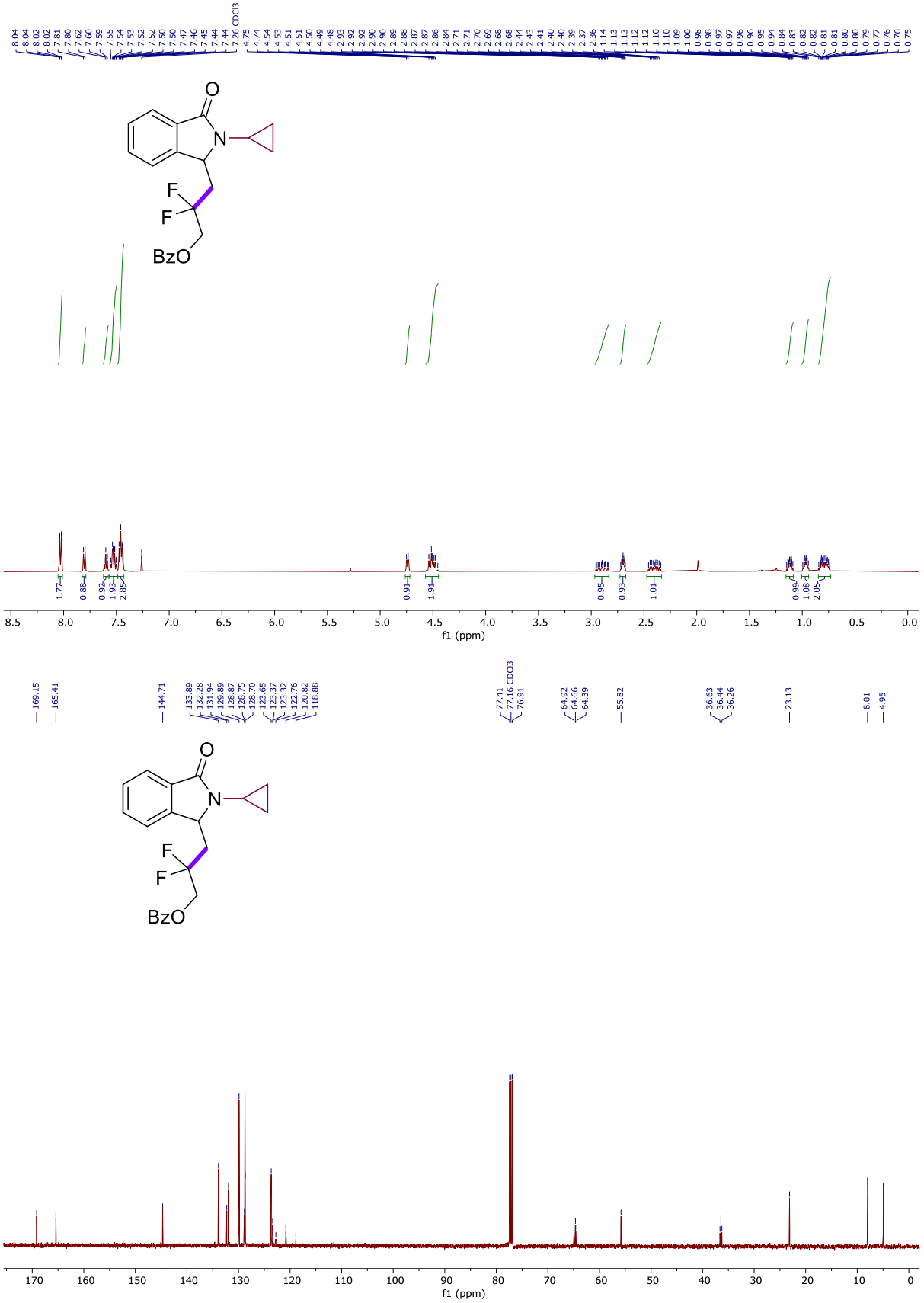


Figure S63. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3o** in $CDCl_3$ at 298 K.

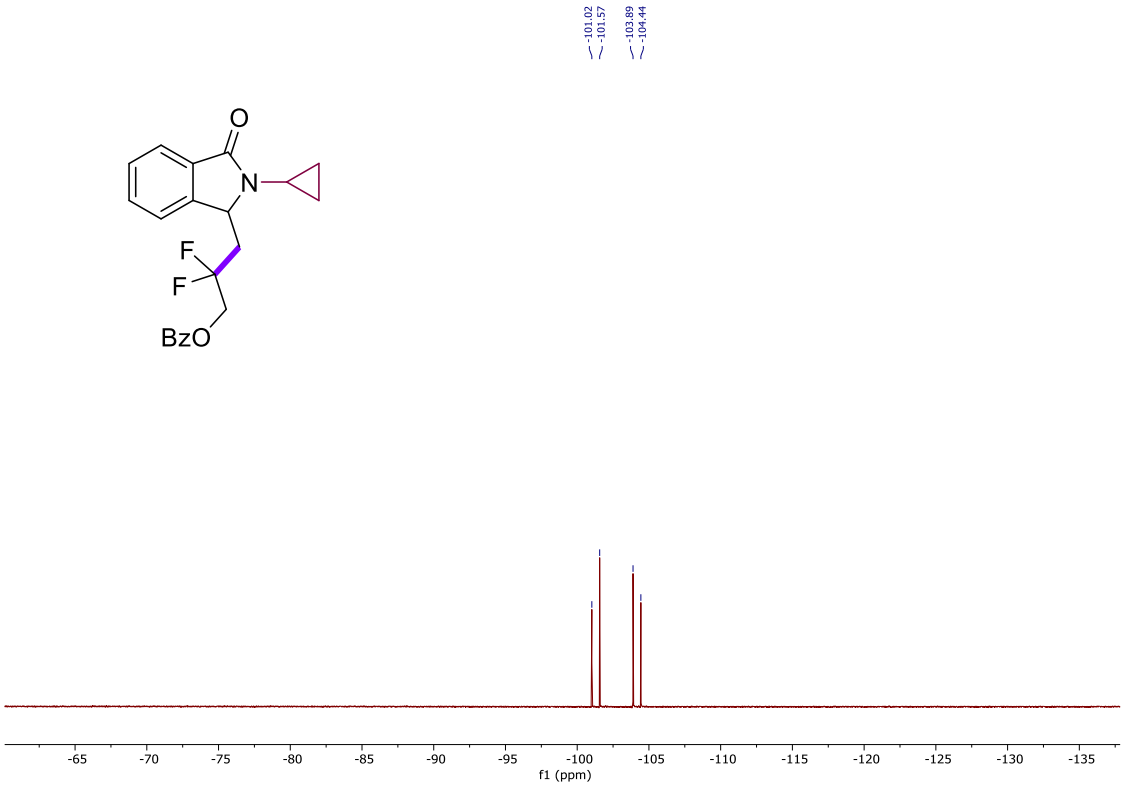


Figure S64. ^{19}F NMR (471 MHz) Spectra of **3o** in $CDCl_3$ at 298 K.

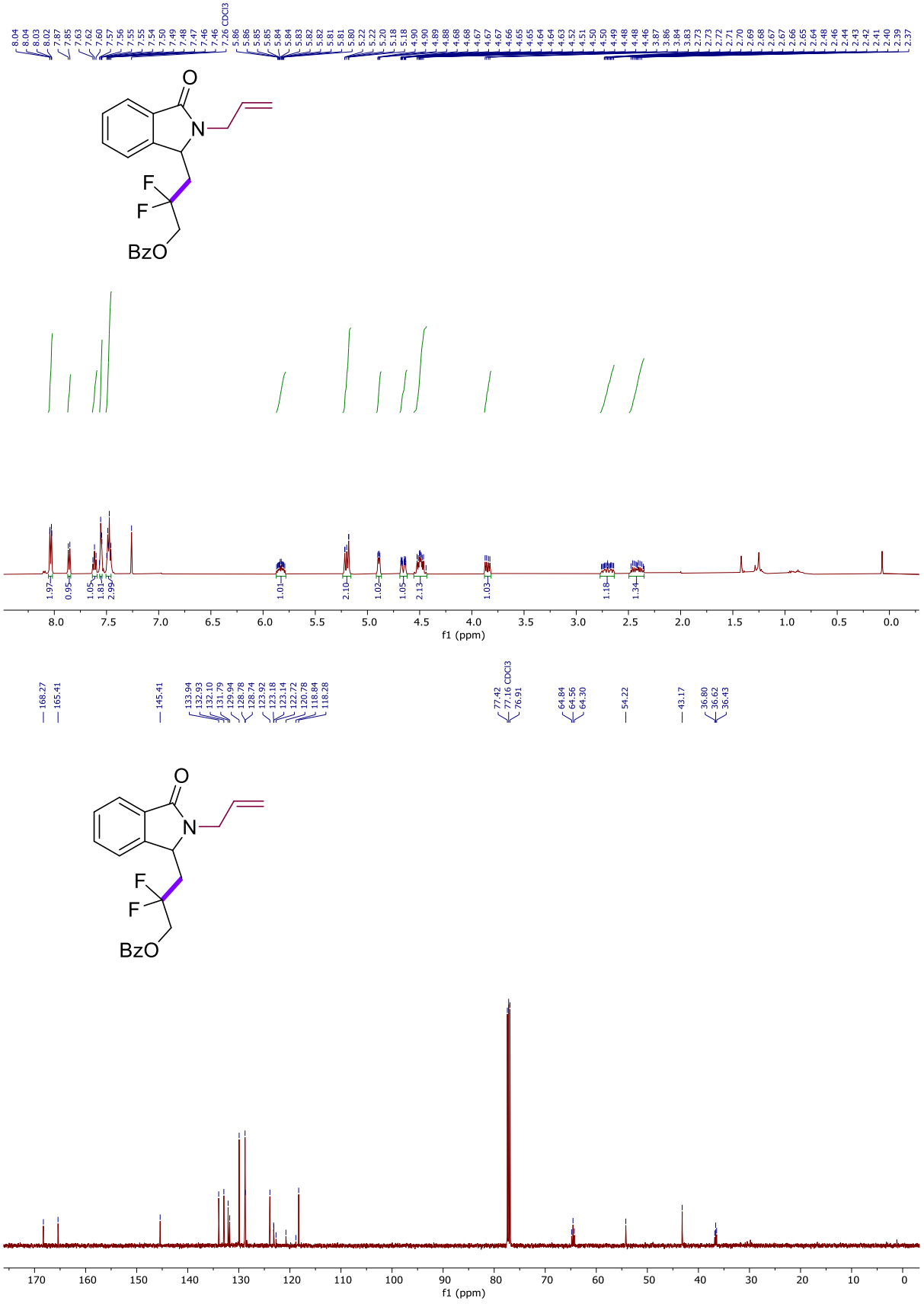


Figure S65. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3p** in $CDCl_3$ at 298 K.

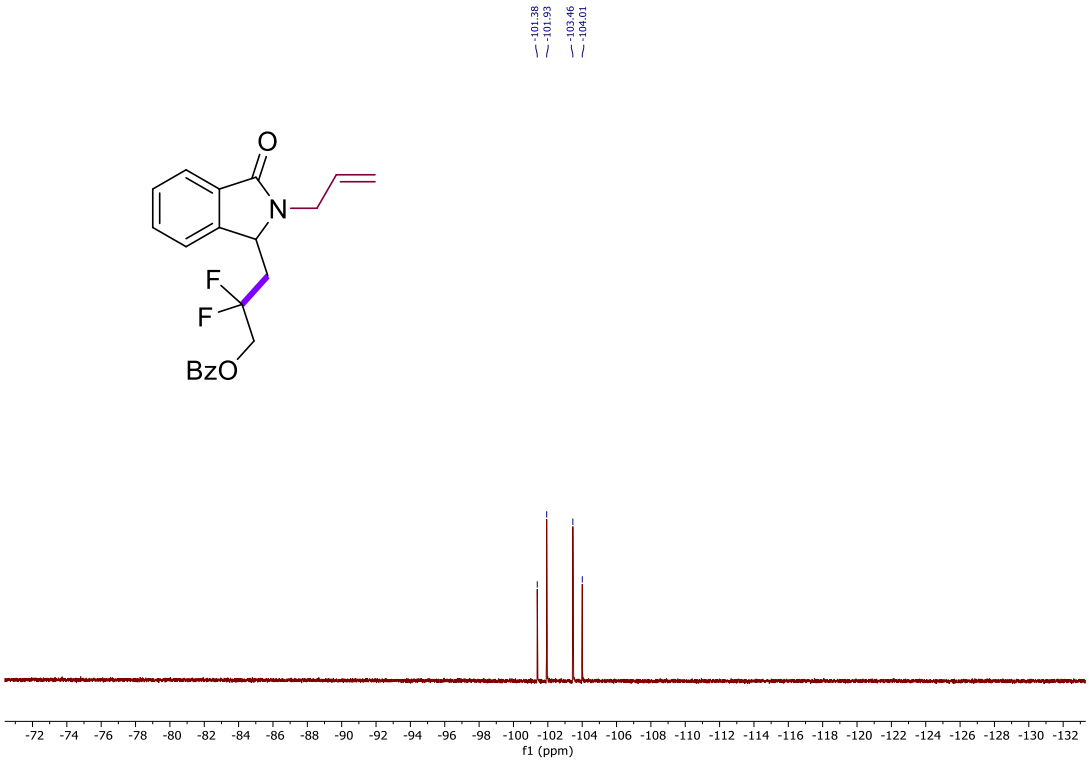


Figure S66. ^{19}F NMR (471 MHz) Spectra of **3p** in $CDCl_3$ at 298 K.

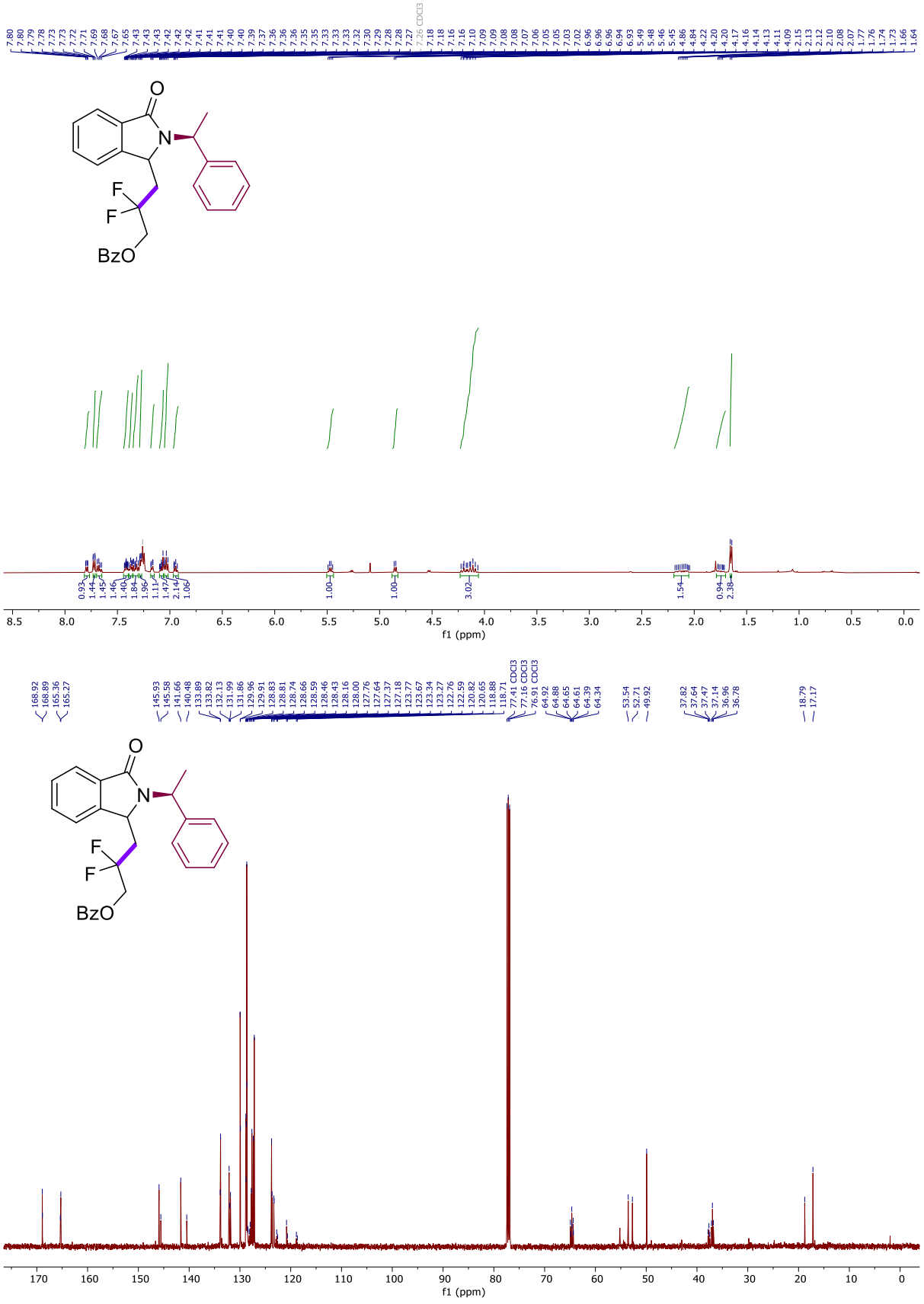


Figure S67. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3q** in $CDCl_3$ at 298 K.

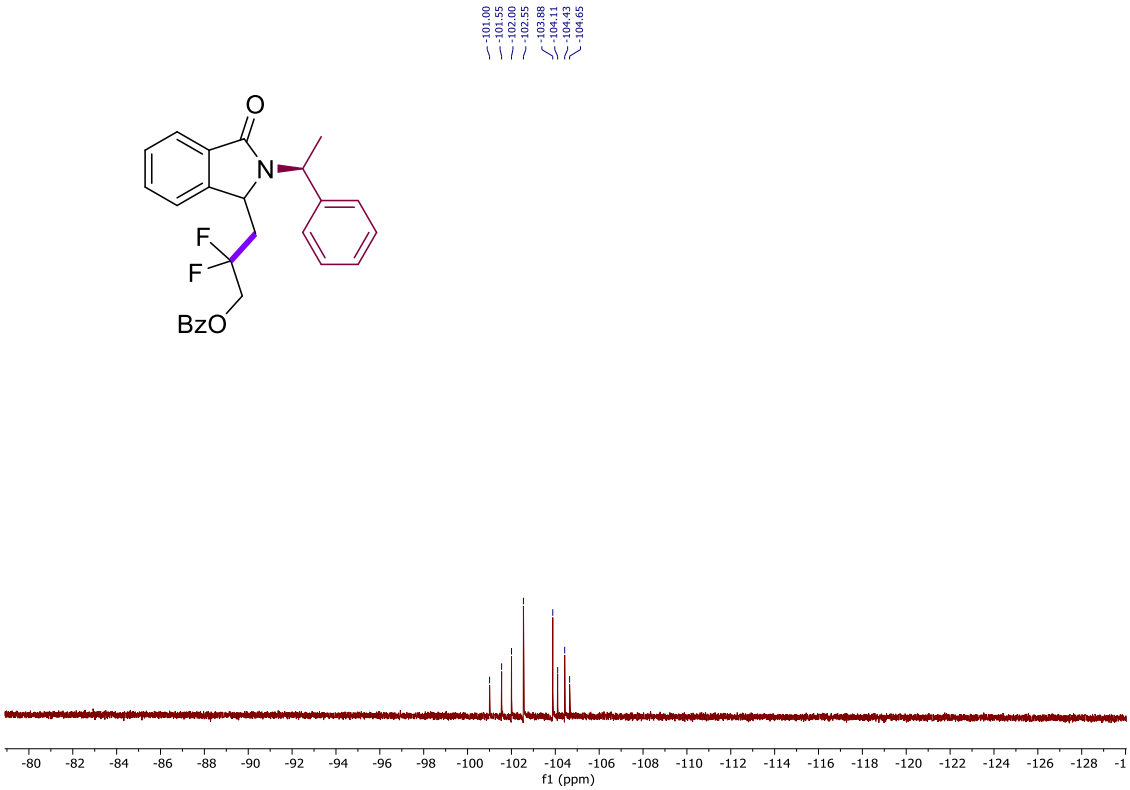


Figure S68. ^{19}F NMR (471 MHz) Spectra of **3q** in $CDCl_3$ at 298 K.

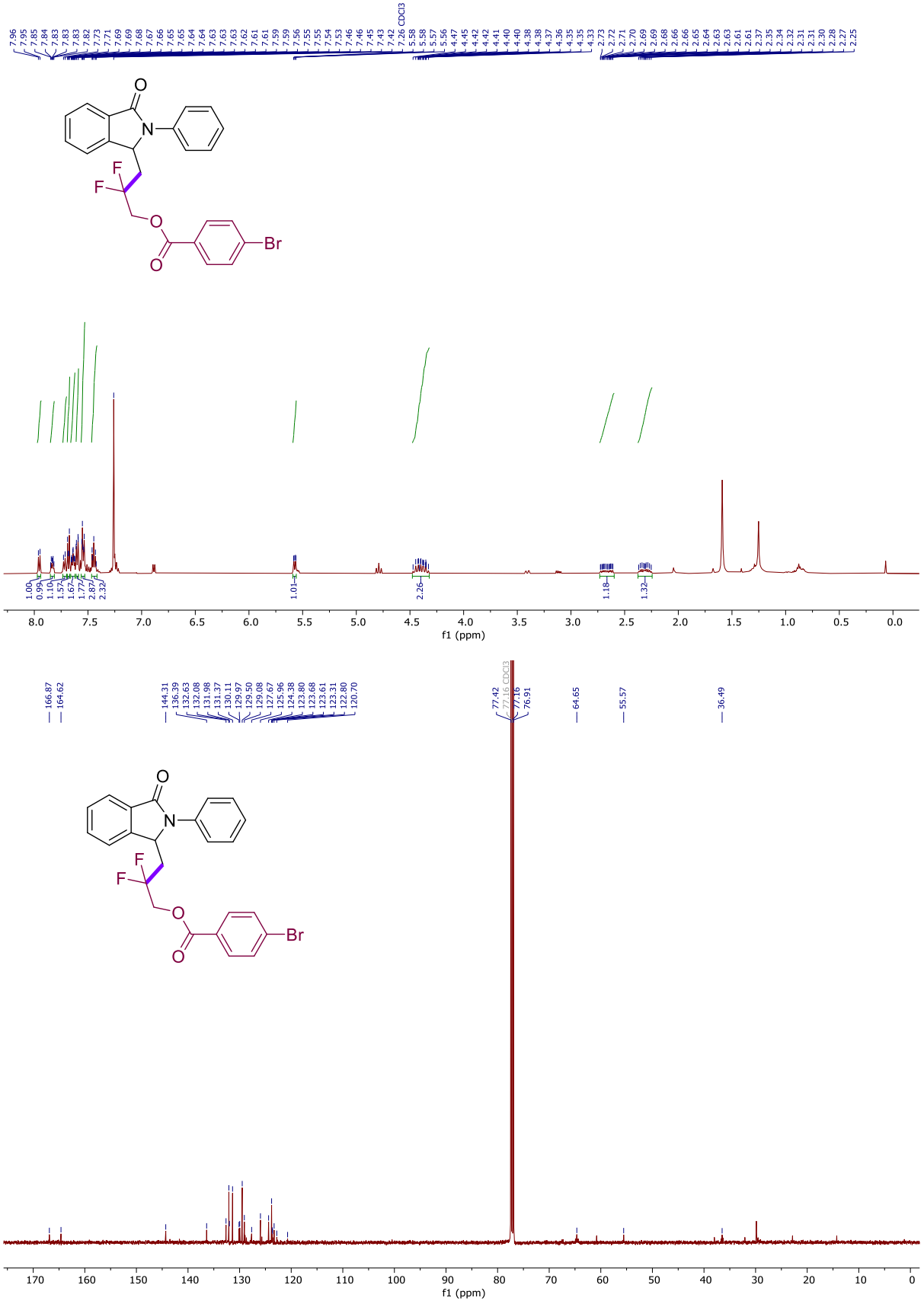


Figure S69. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3r** in $CDCl_3$ at 298 K.

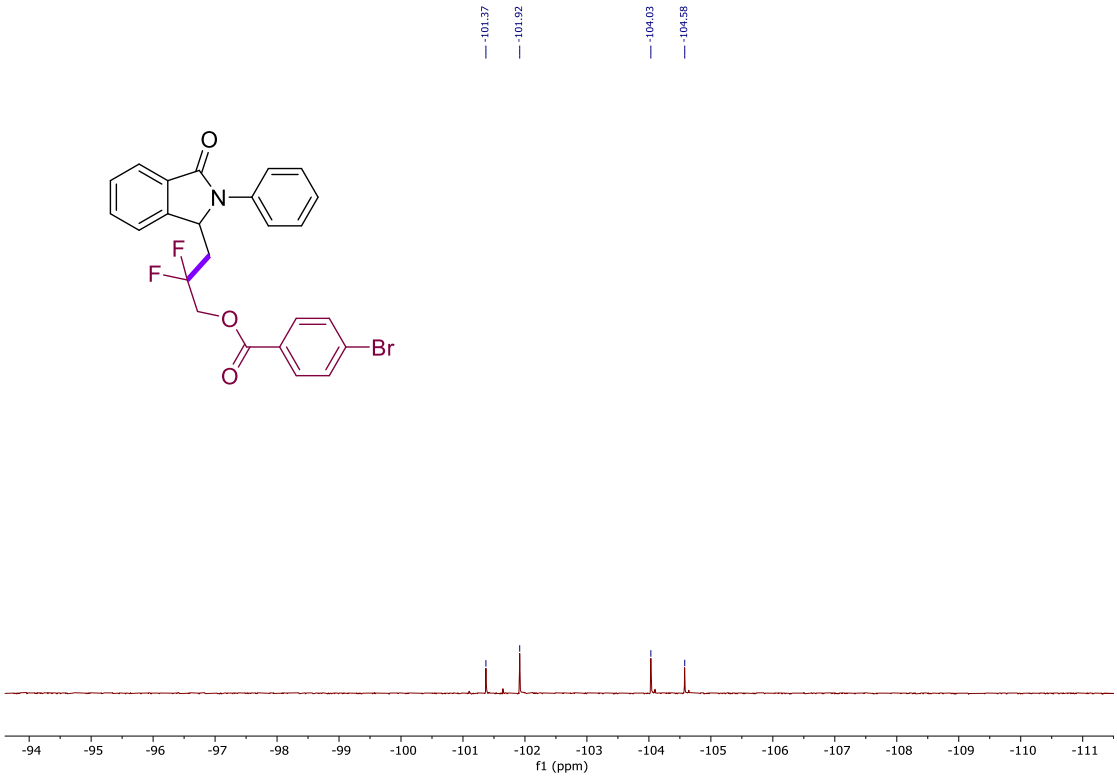


Figure S70. ^{19}F NMR (471 MHz) Spectra of **3r** in $CDCl_3$ at 298 K.

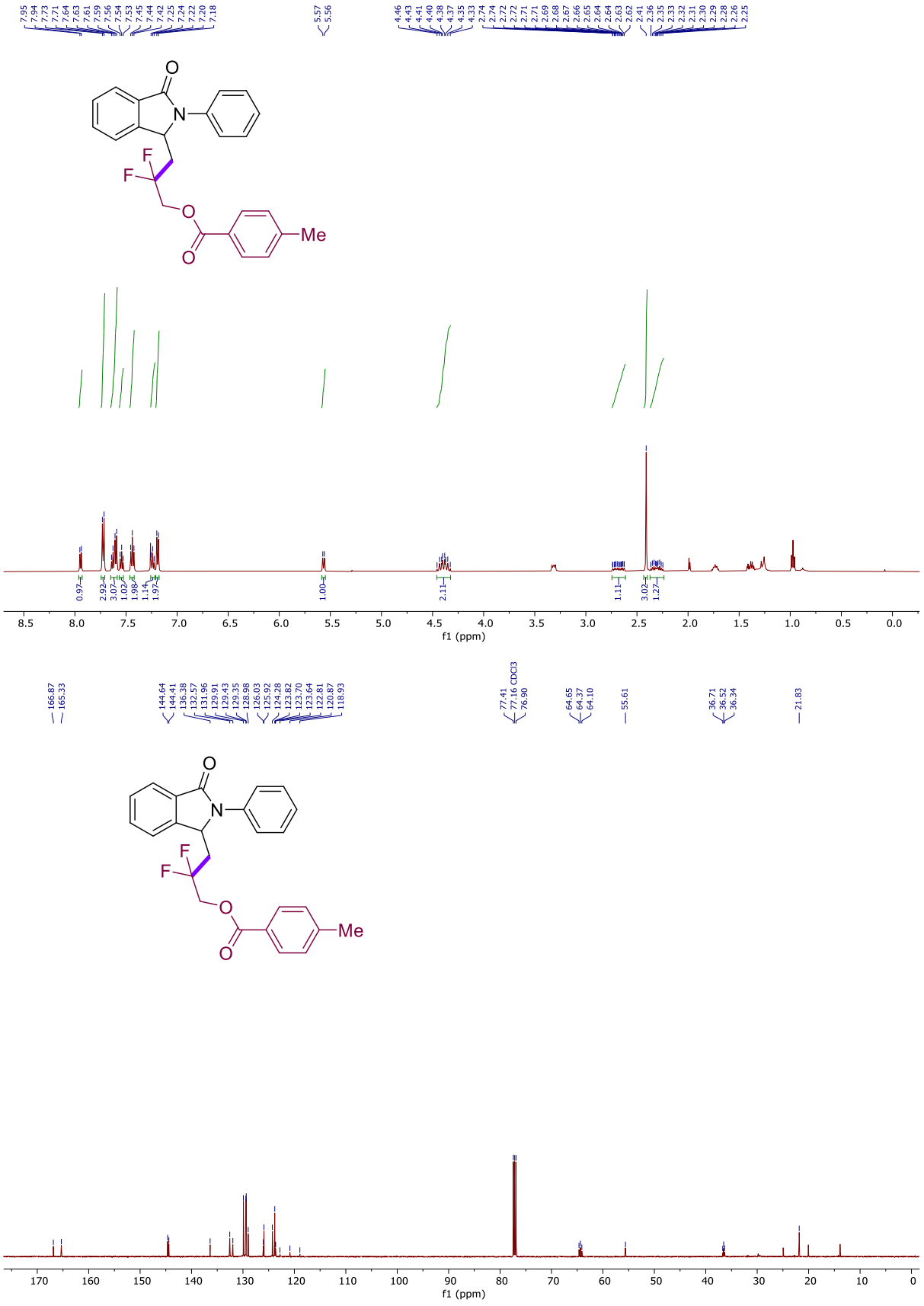


Figure S71. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3s** in $CDCl_3$ at 298 K.

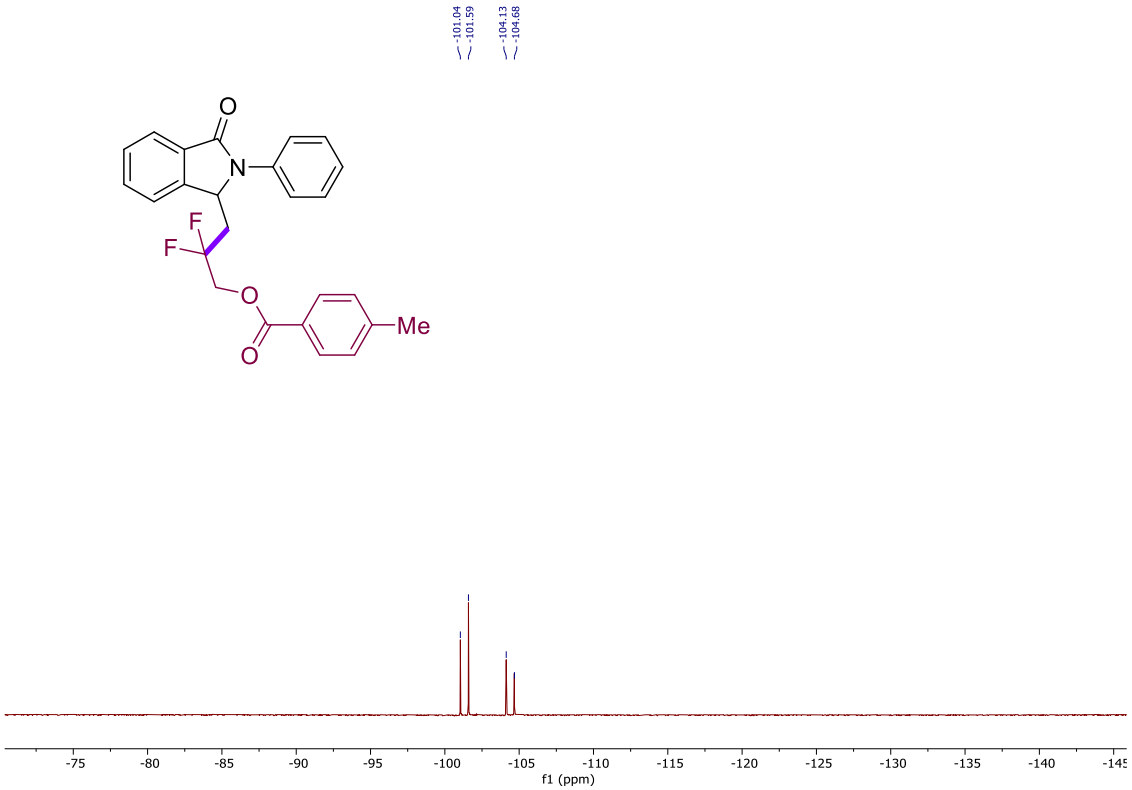


Figure S72. ^{19}F NMR (471 MHz) Spectra of **3s** in $CDCl_3$ at 298 K.

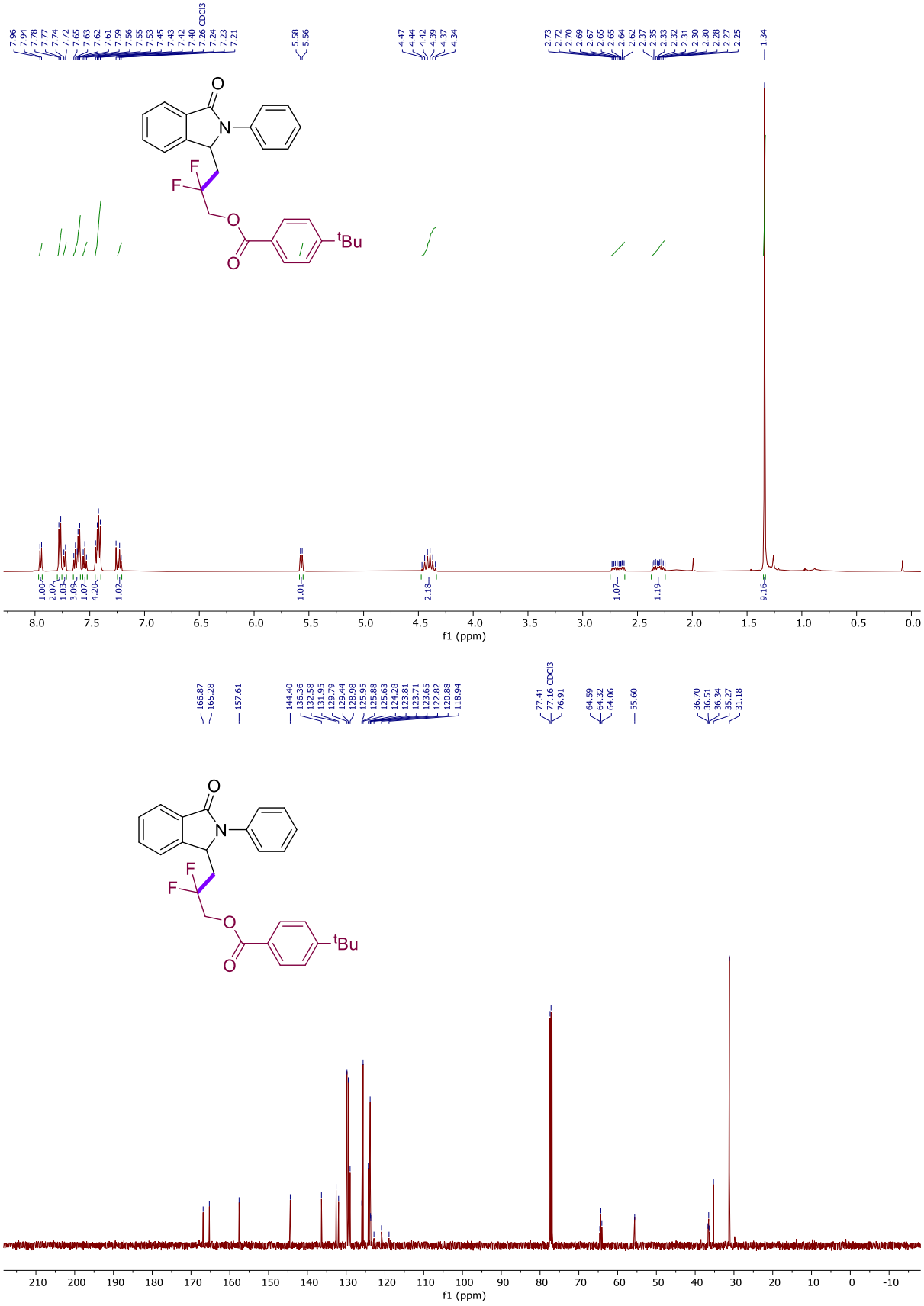


Figure S73. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3t** in $CDCl_3$ at 298 K.

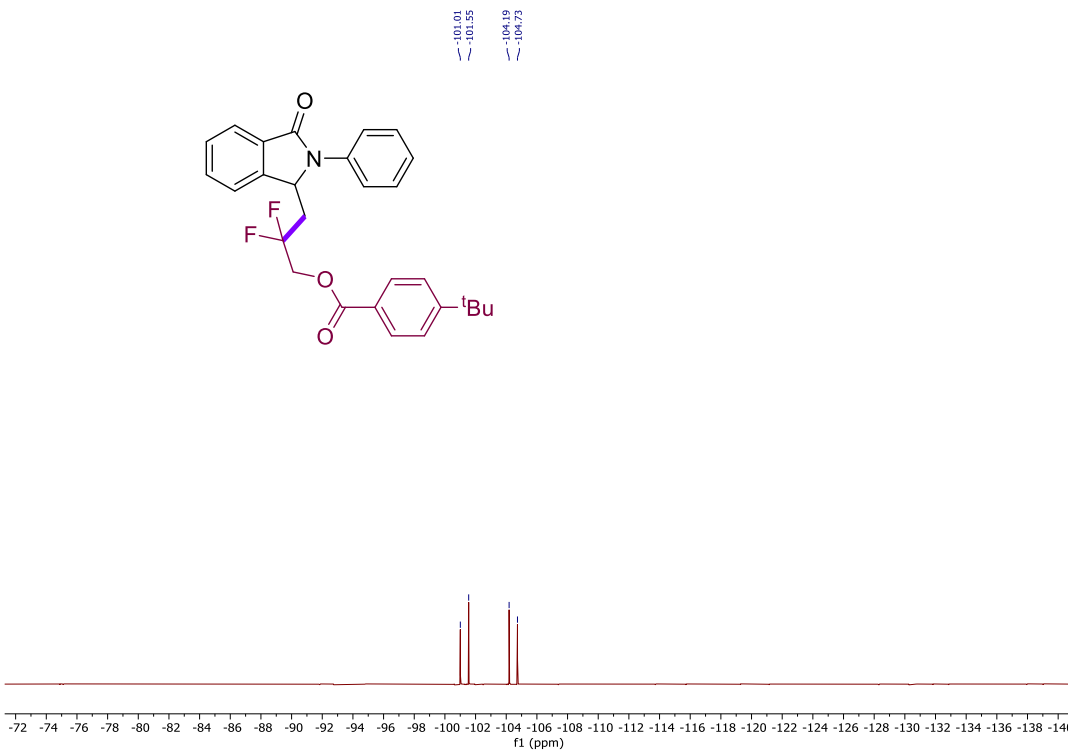


Figure S74. ^{19}F NMR (471 MHz) Spectra of **3t** in $CDCl_3$ at 298 K.

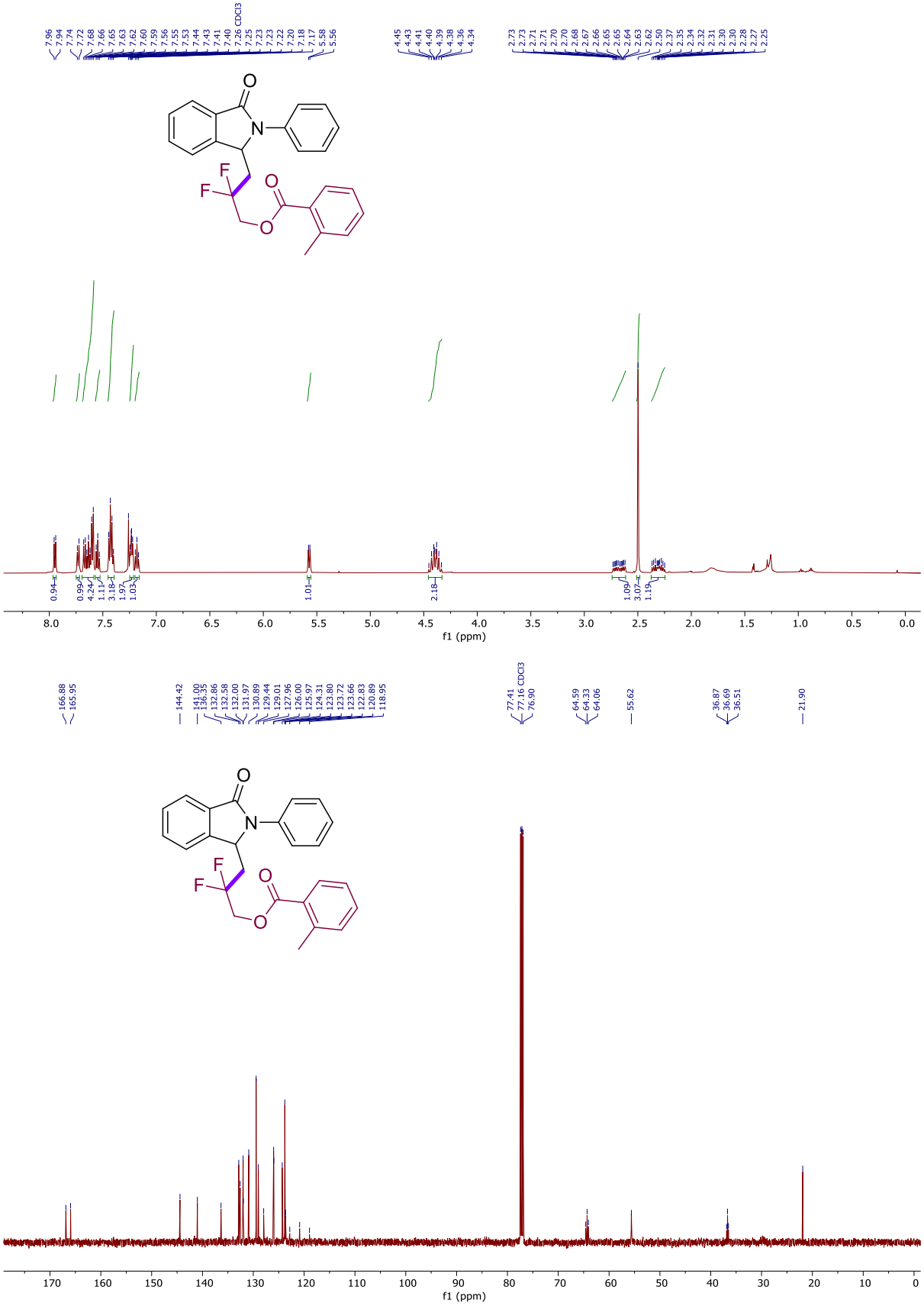


Figure S75. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3u** in $CDCl_3$ at 298 K.

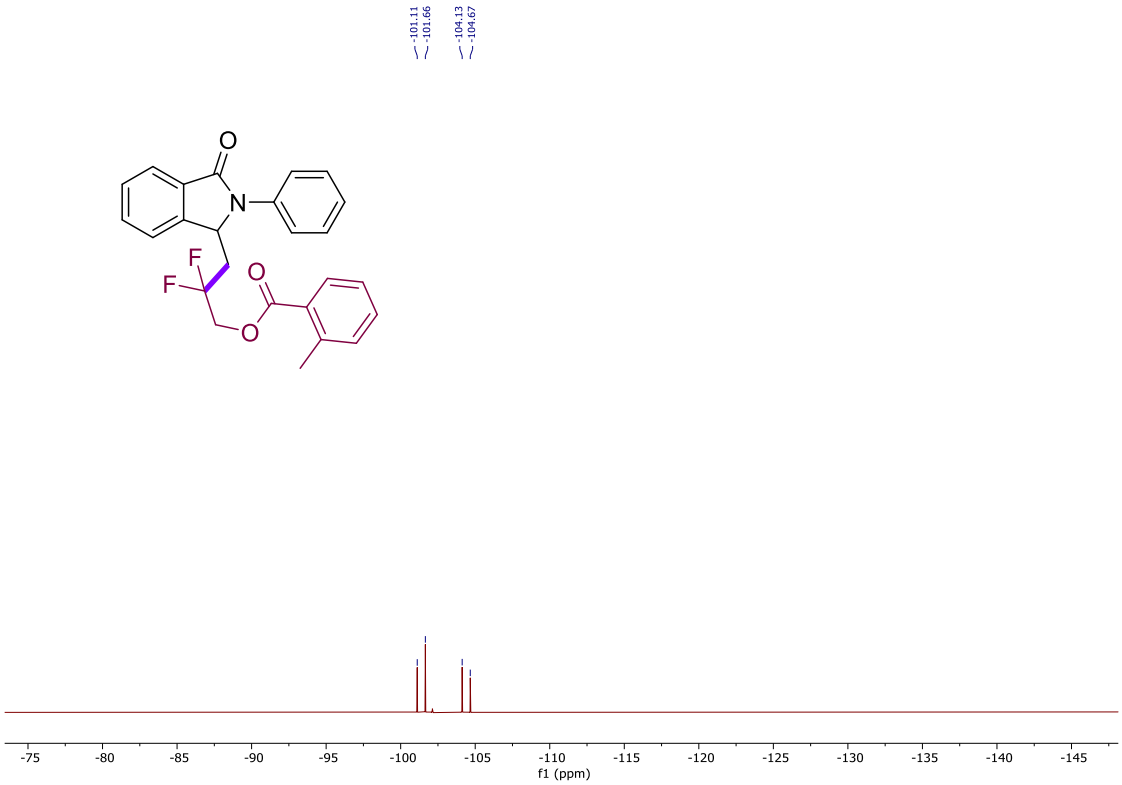


Figure S76. ^{19}F NMR (471 MHz) Spectra of **3u** in $CDCl_3$ at 298 K.

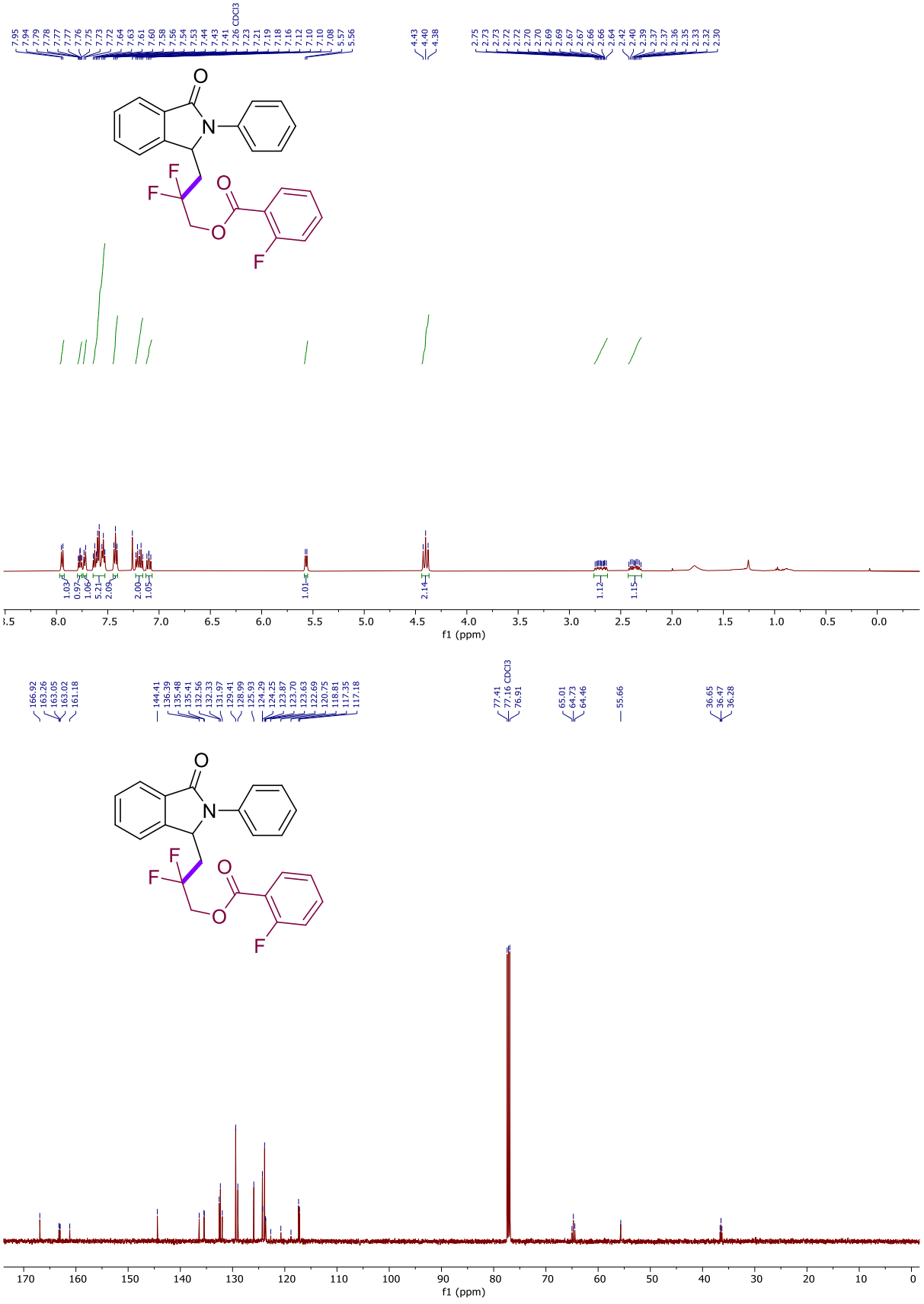


Figure S77. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3v** in $CDCl_3$ at 298 K.

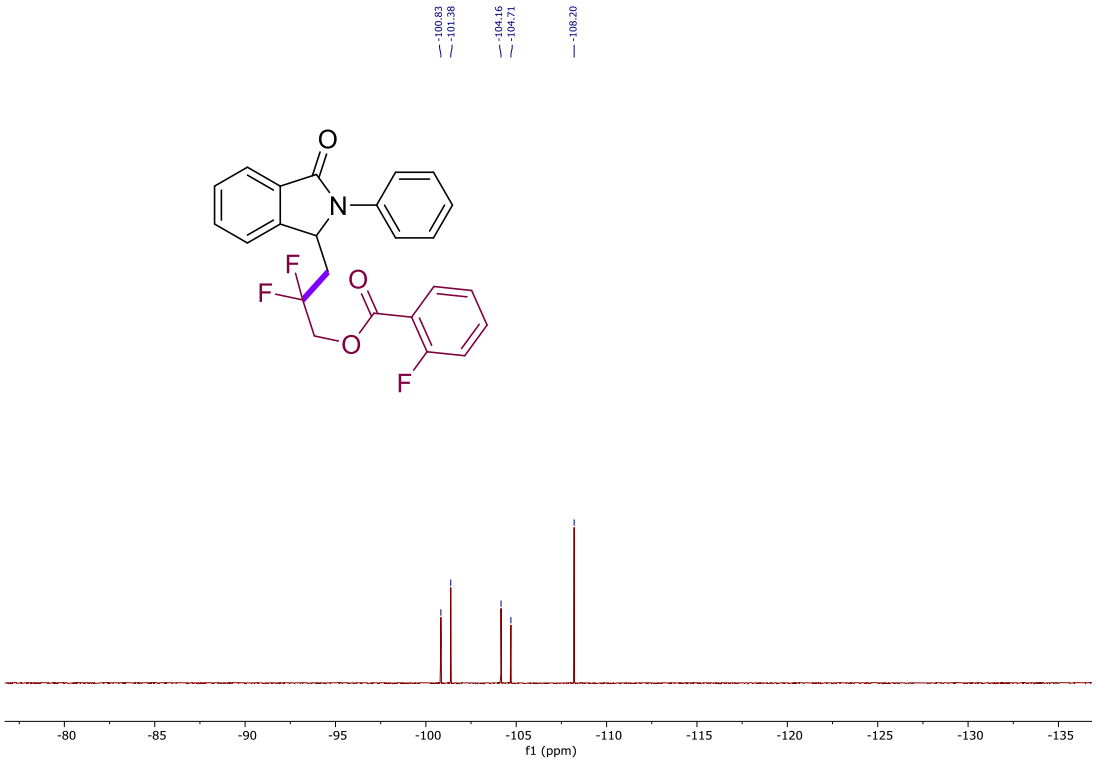


Figure S78. ^{19}F NMR (471 MHz) Spectra of **3v** in $CDCl_3$ at 298 K.

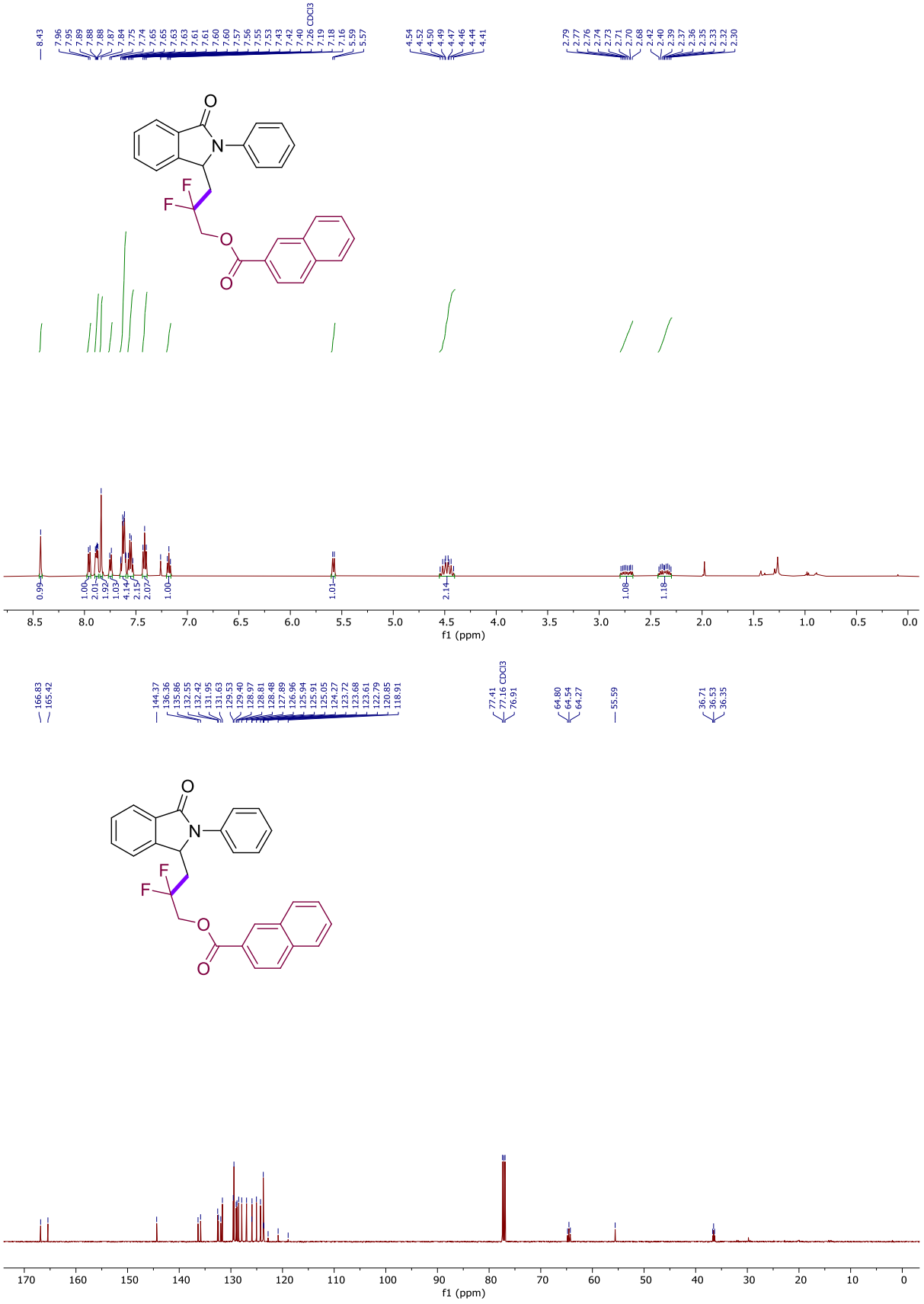


Figure S79. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3w** in $CDCl_3$ at 298 K.

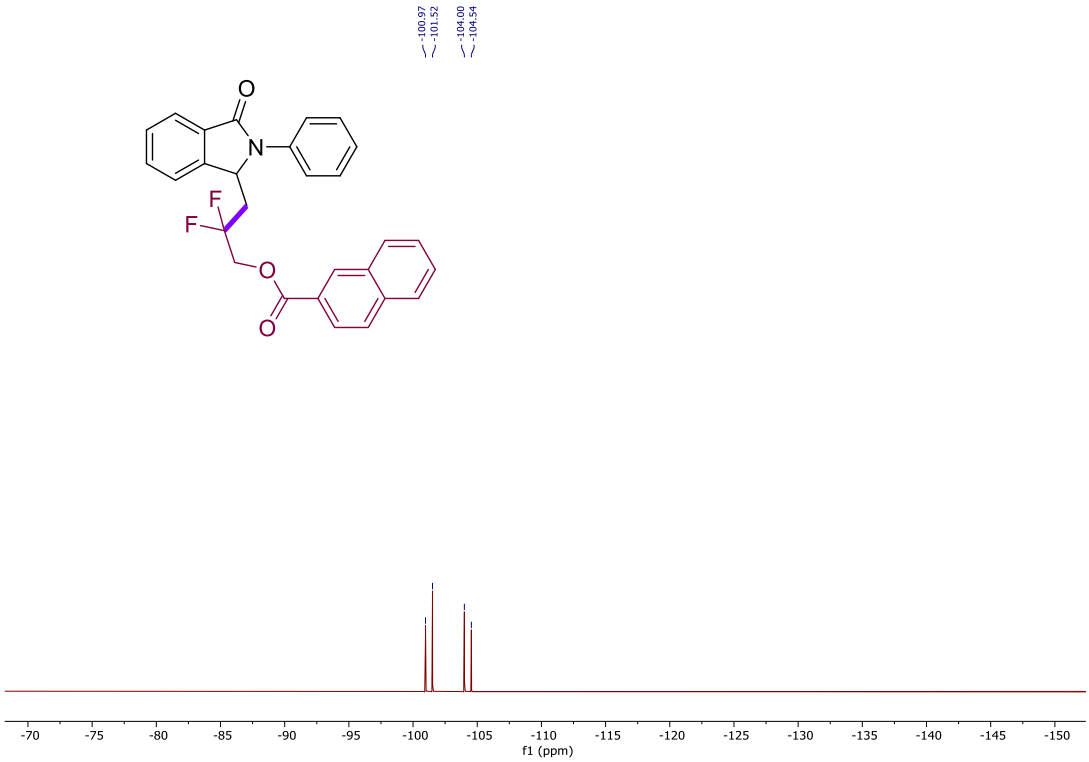


Figure S80. ^{19}F NMR (471 MHz) Spectra of **3w** in $CDCl_3$ at 298 K.

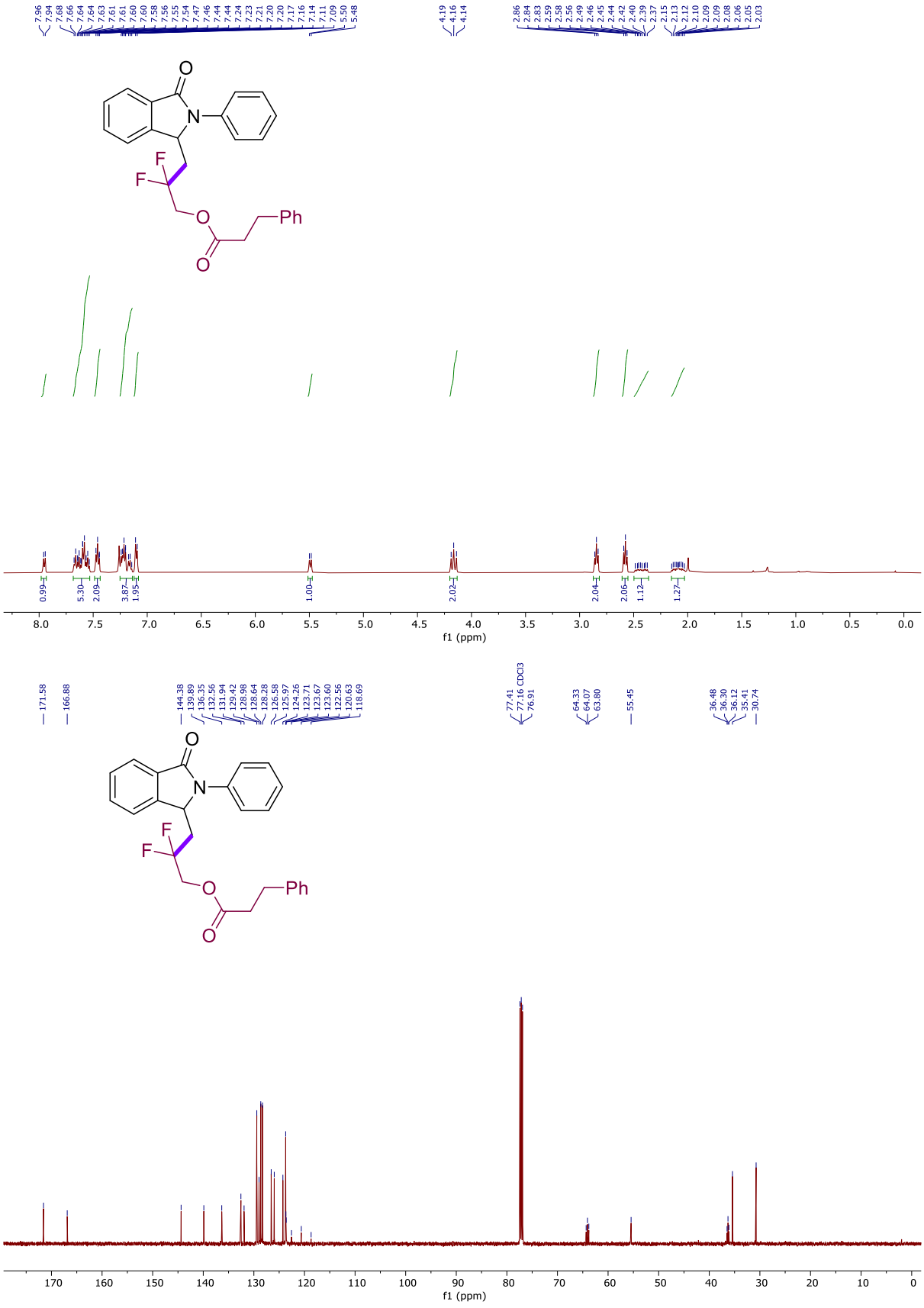


Figure S81. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3x** in $CDCl_3$ at 298 K.

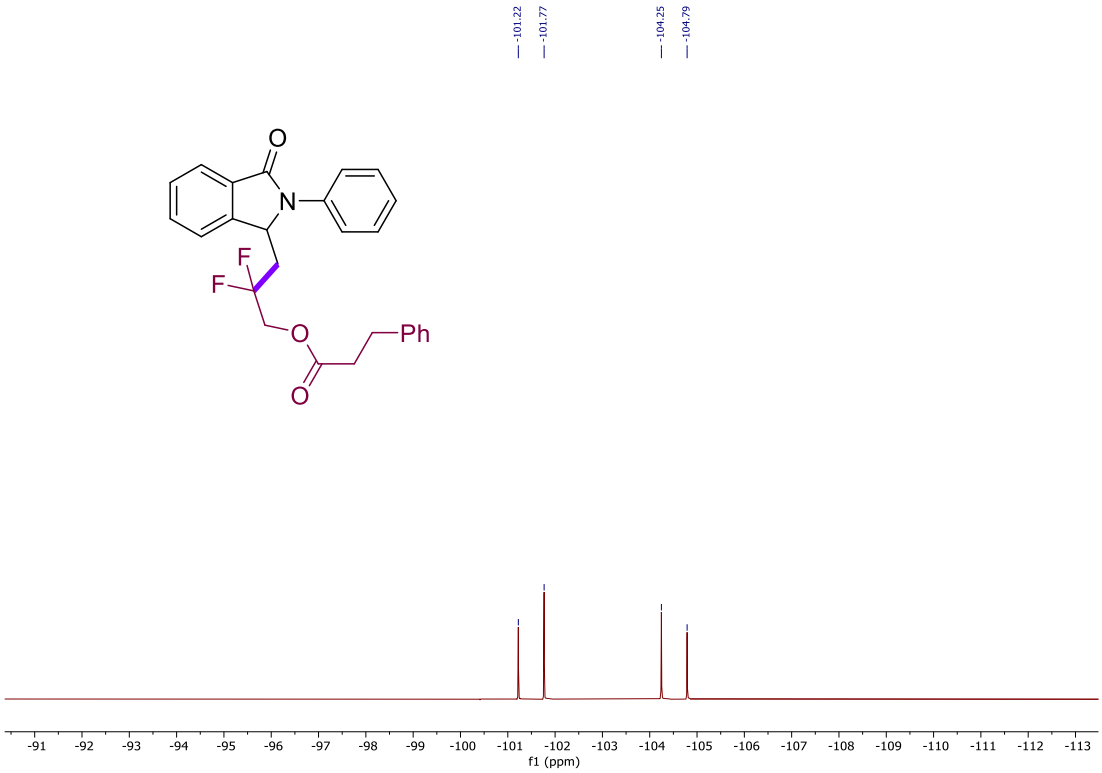


Figure S82. ^{19}F NMR (471 MHz) Spectra of **3x** in $CDCl_3$ at 298 K.

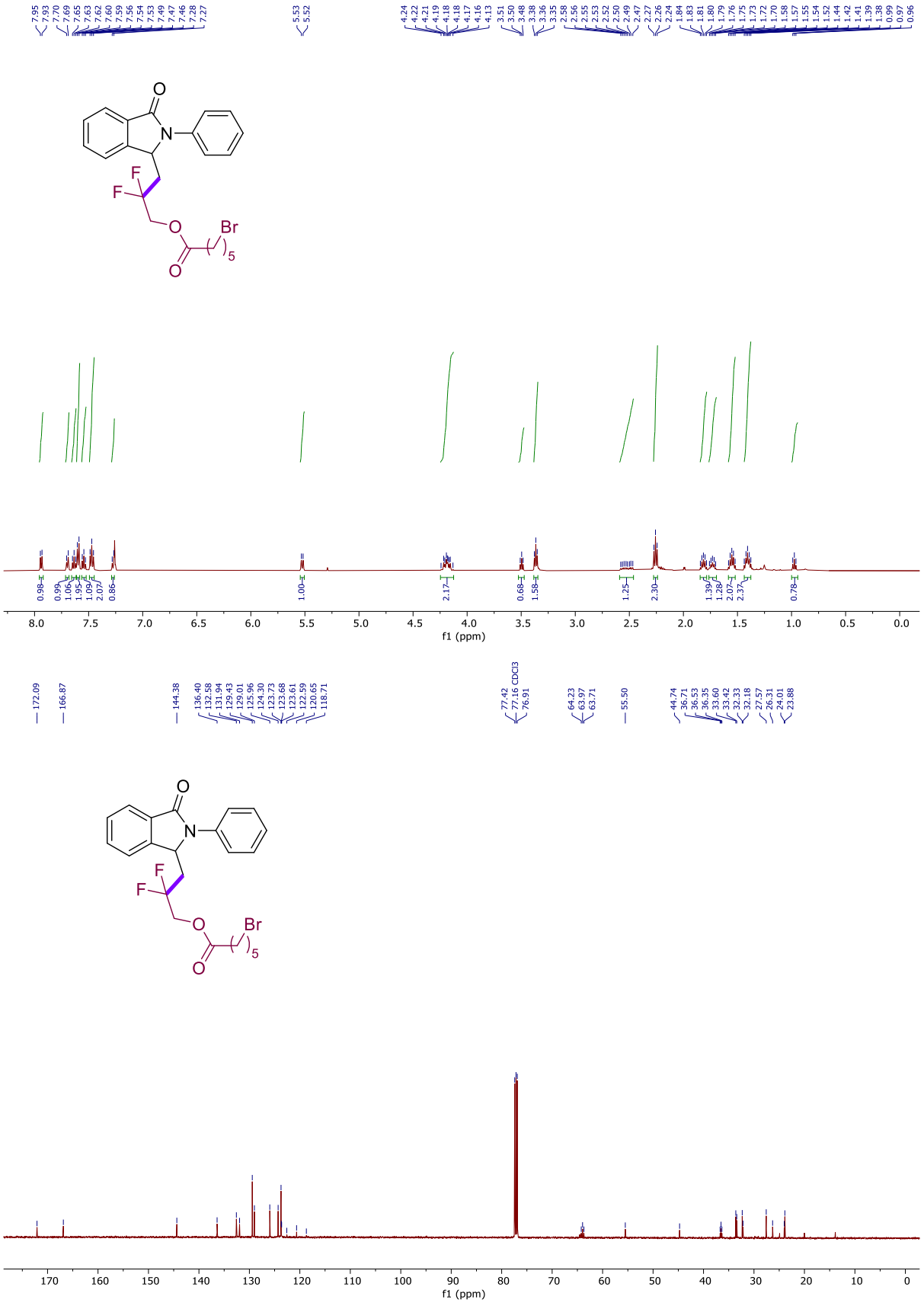


Figure S83. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3y** in $CDCl_3$ at 298 K.

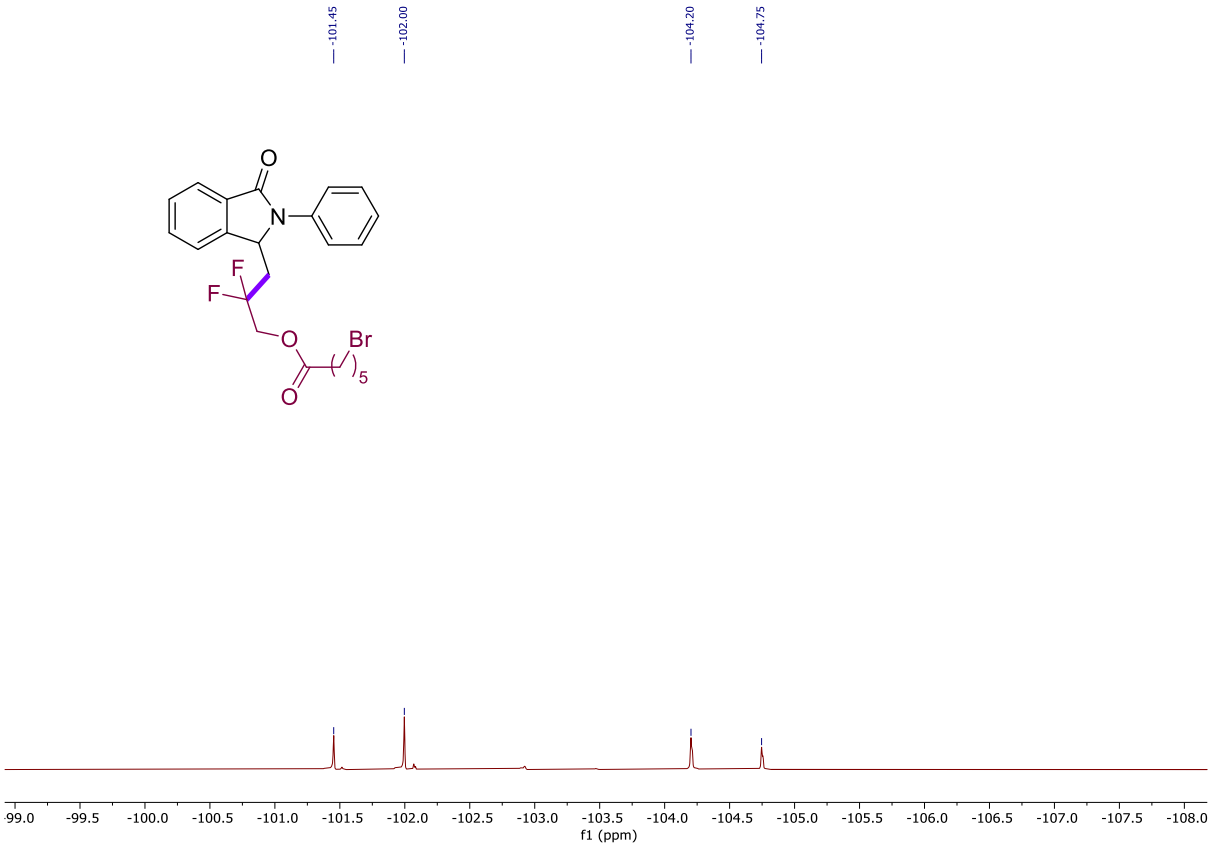


Figure S84. ^{19}F NMR (471 MHz) Spectra of **3y** in $CDCl_3$ at 298 K.

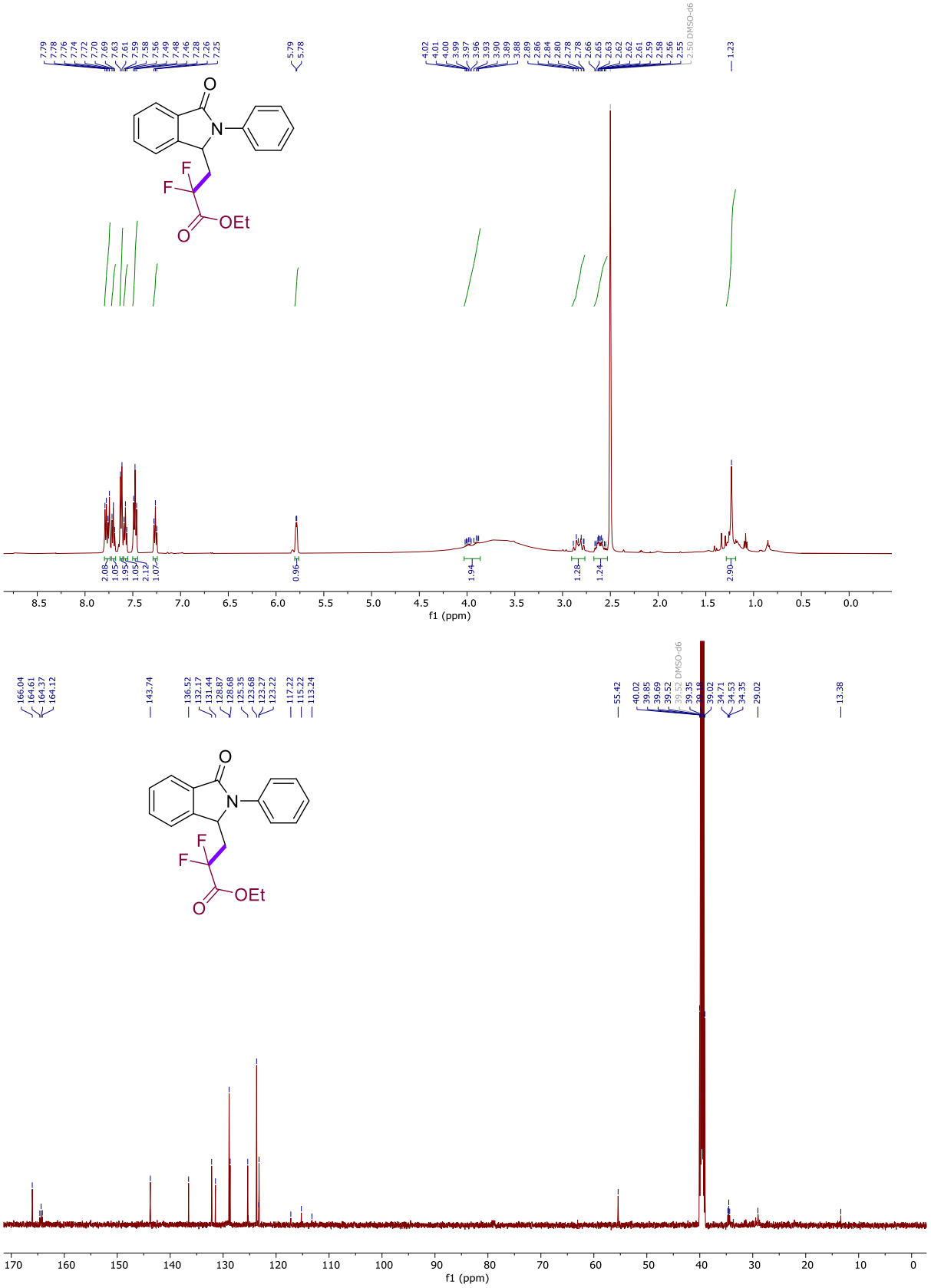


Figure S85. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3z** in DMSO-d6 at 298 K.

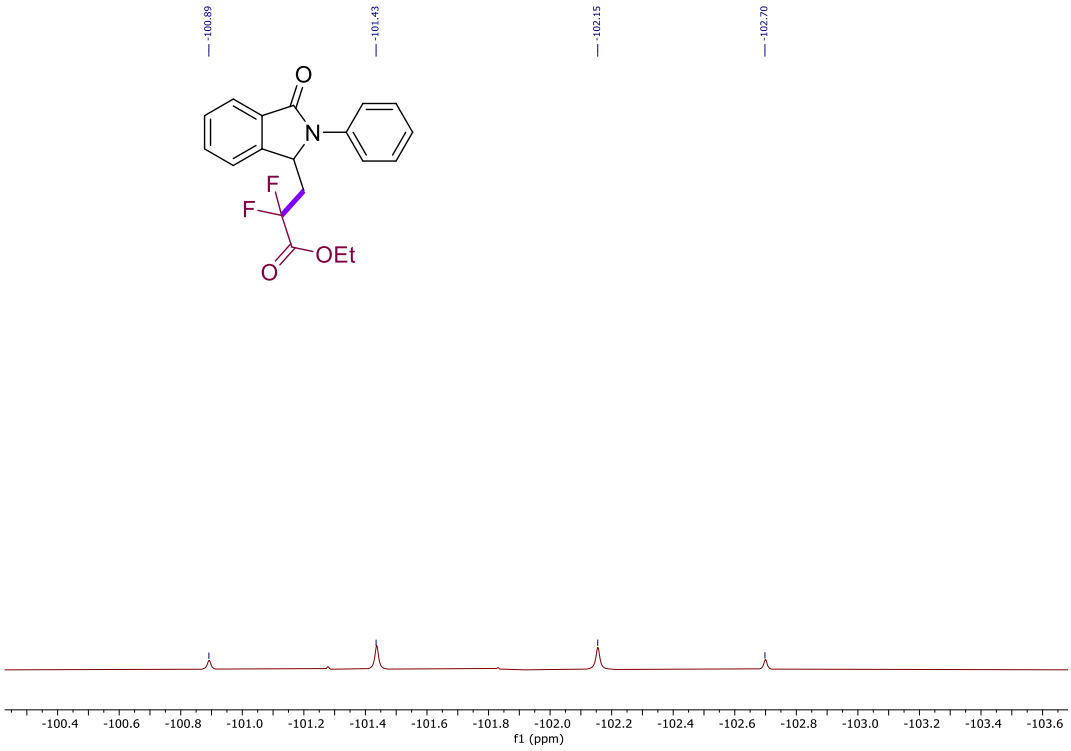


Figure S86. ^{19}F NMR (471 MHz) Spectra of **3z** in DMSO-D6 at 298 K.

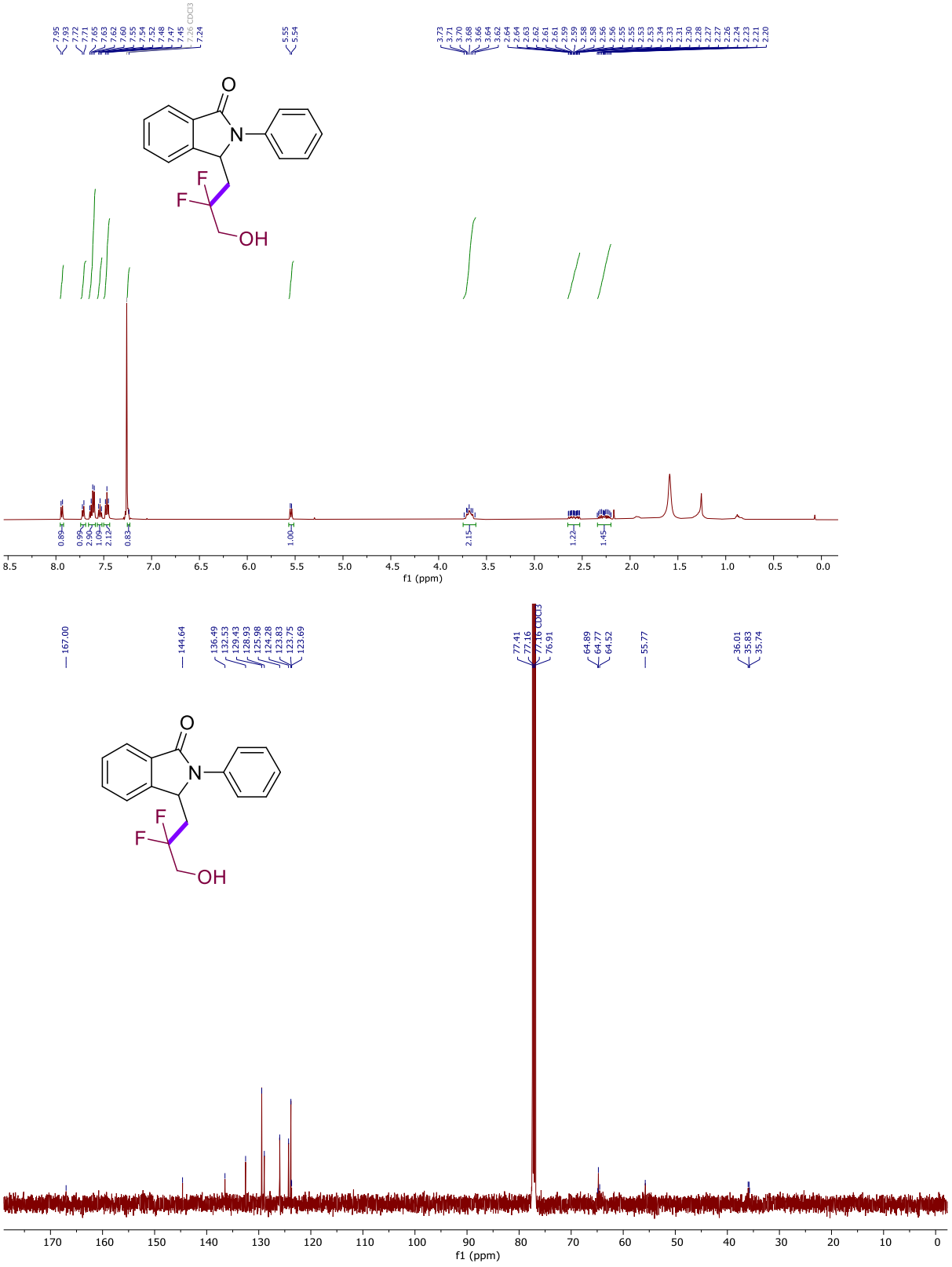


Figure S87. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3aa** in $CDCl_3$ at 298 K.

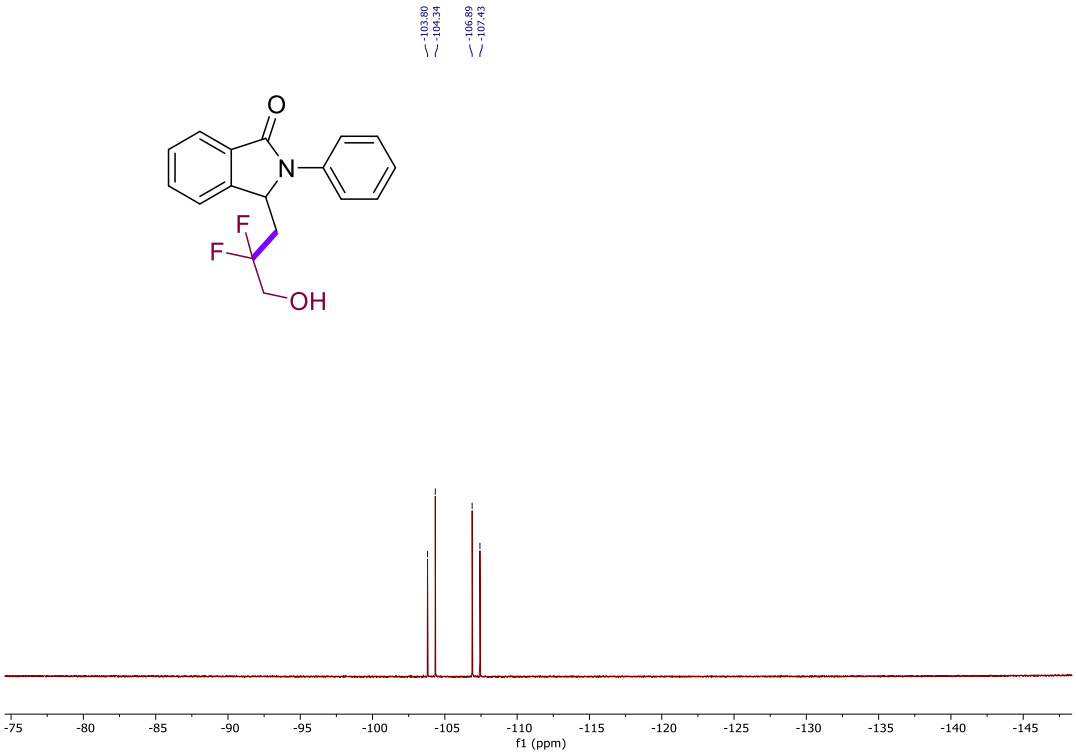


Figure S88. ^{19}F NMR (471 MHz) Spectra of **3aa** in $CDCl_3$ at 298 K.

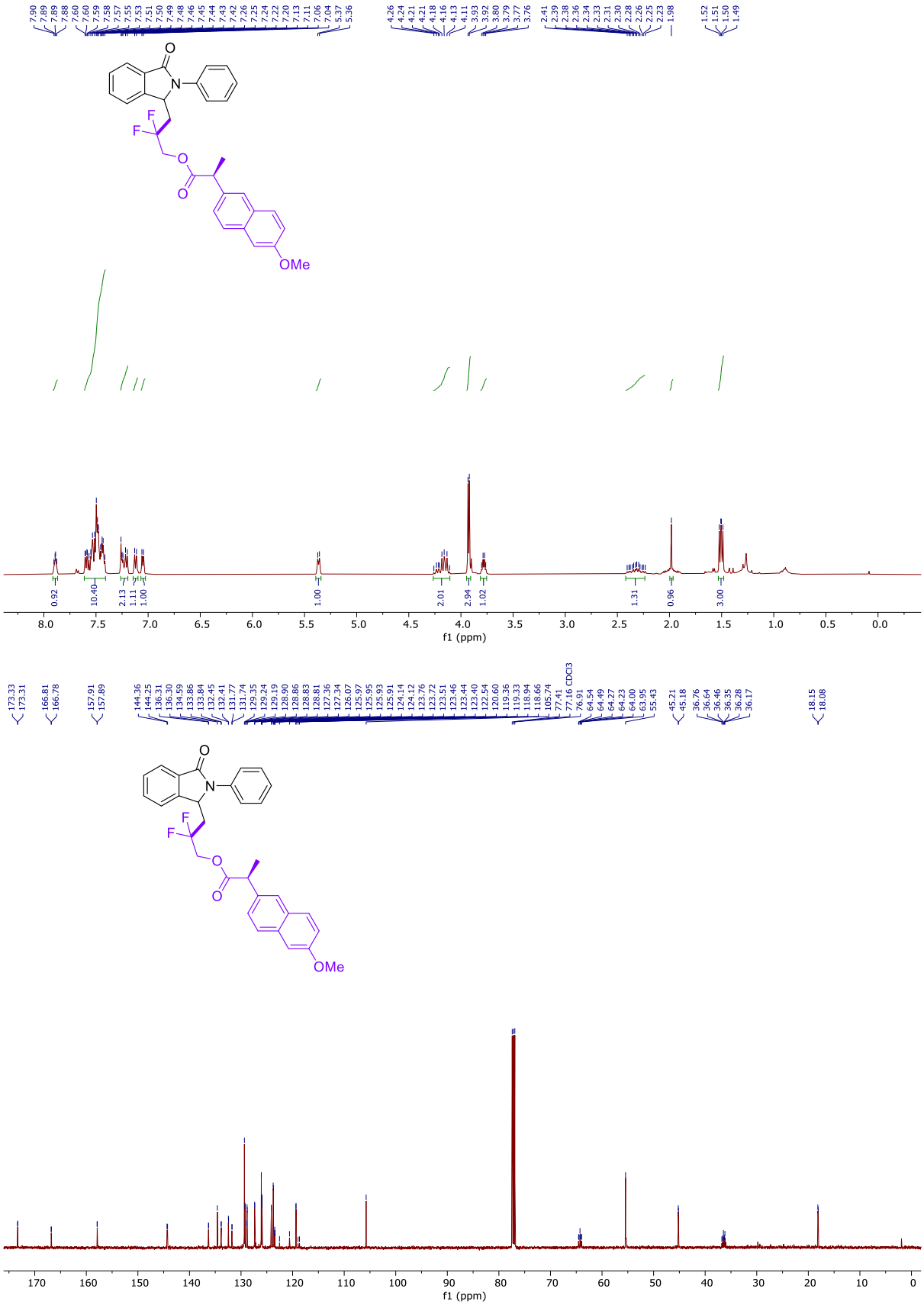


Figure S89. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3ac** in $CDCl_3$ at 298 K.

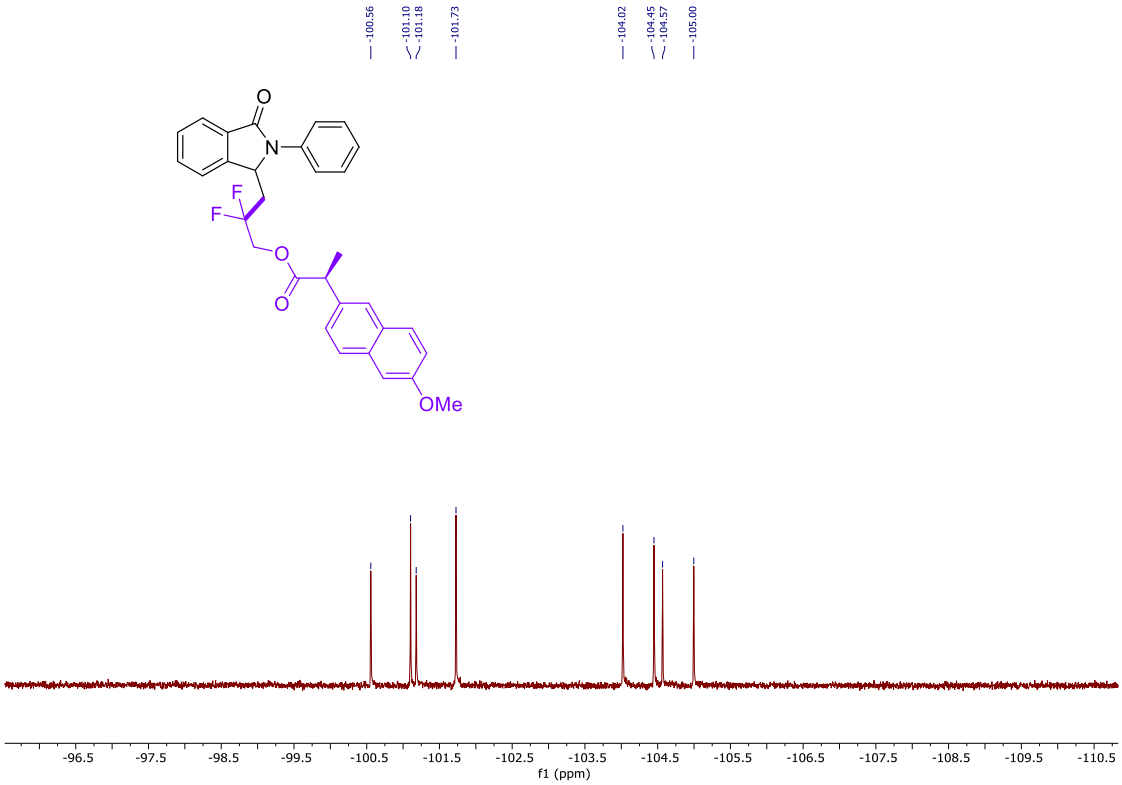


Figure S90. ^{19}F NMR (471 MHz) Spectra of **3ac** in $CDCl_3$ at 298 K.

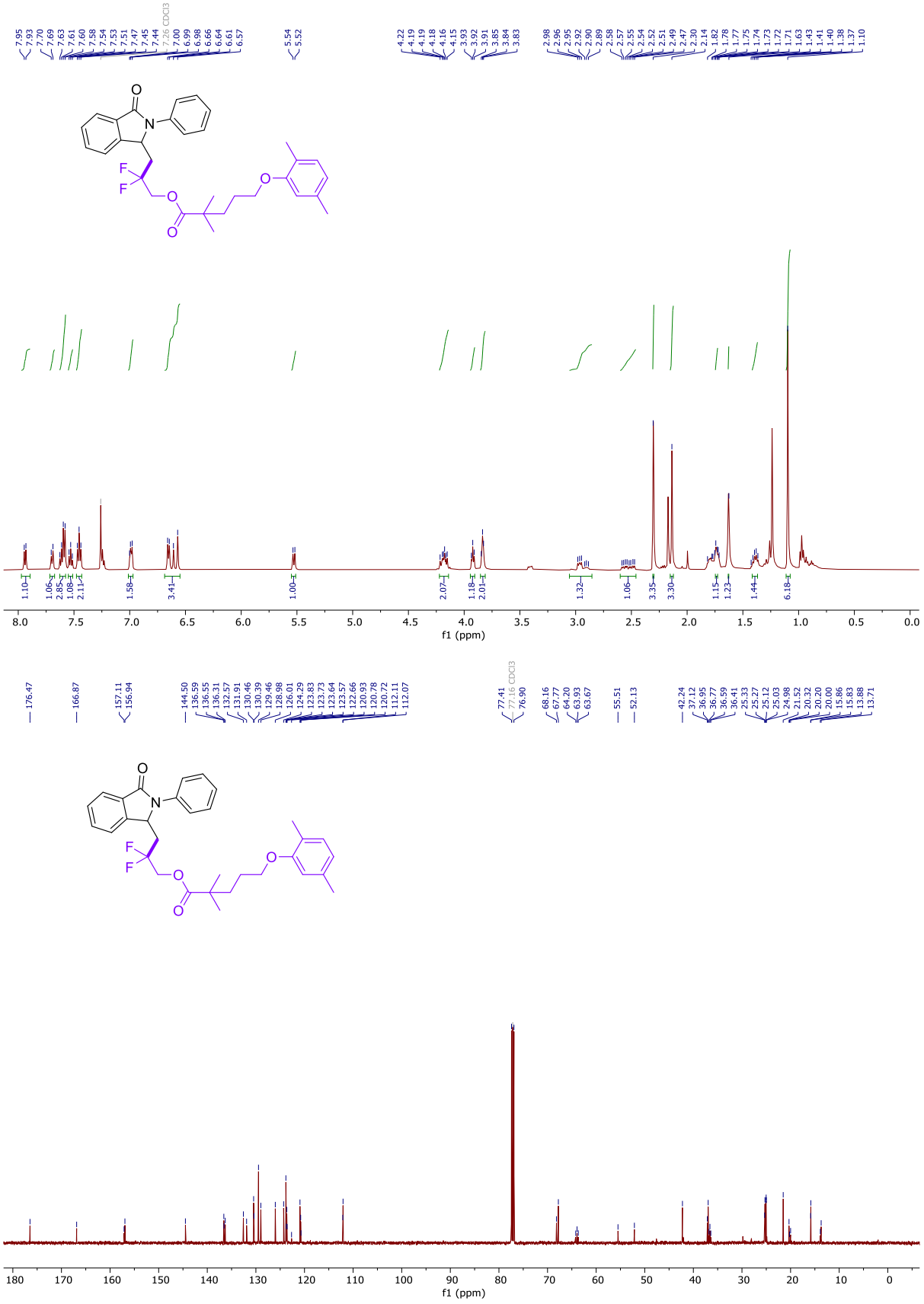


Figure S91. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3ad** in $CDCl_3$ at 298 K.

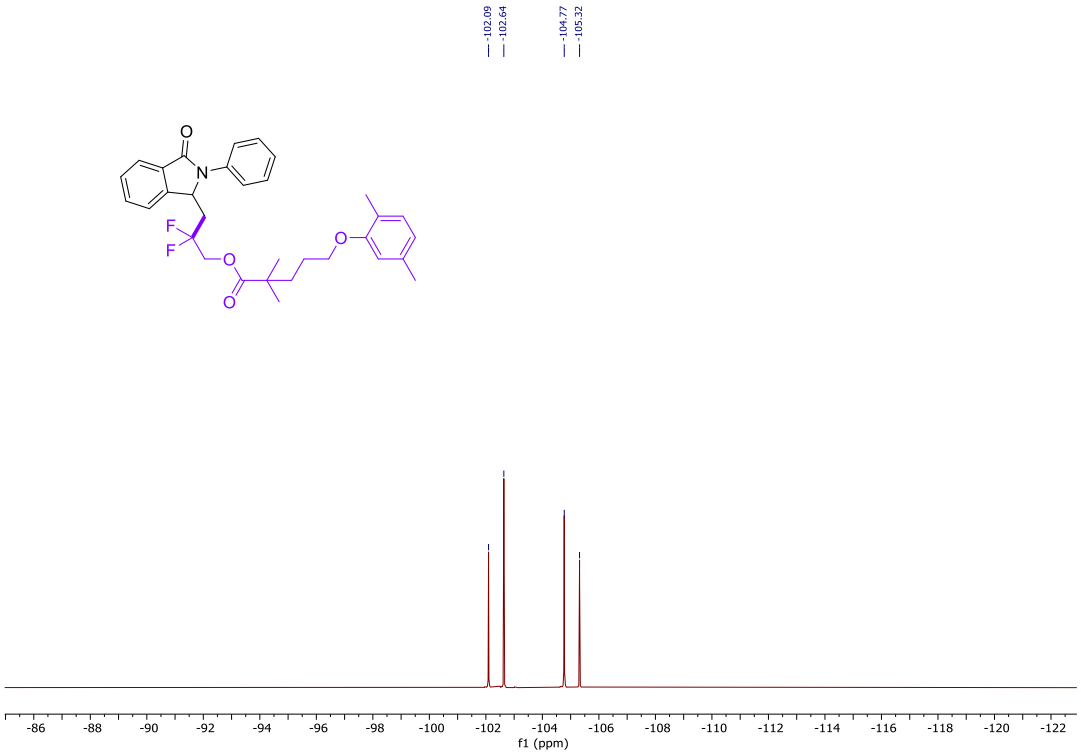


Figure S92. ^{19}F NMR (471 MHz) Spectra of **3ad** in $CDCl_3$ at 298 K.

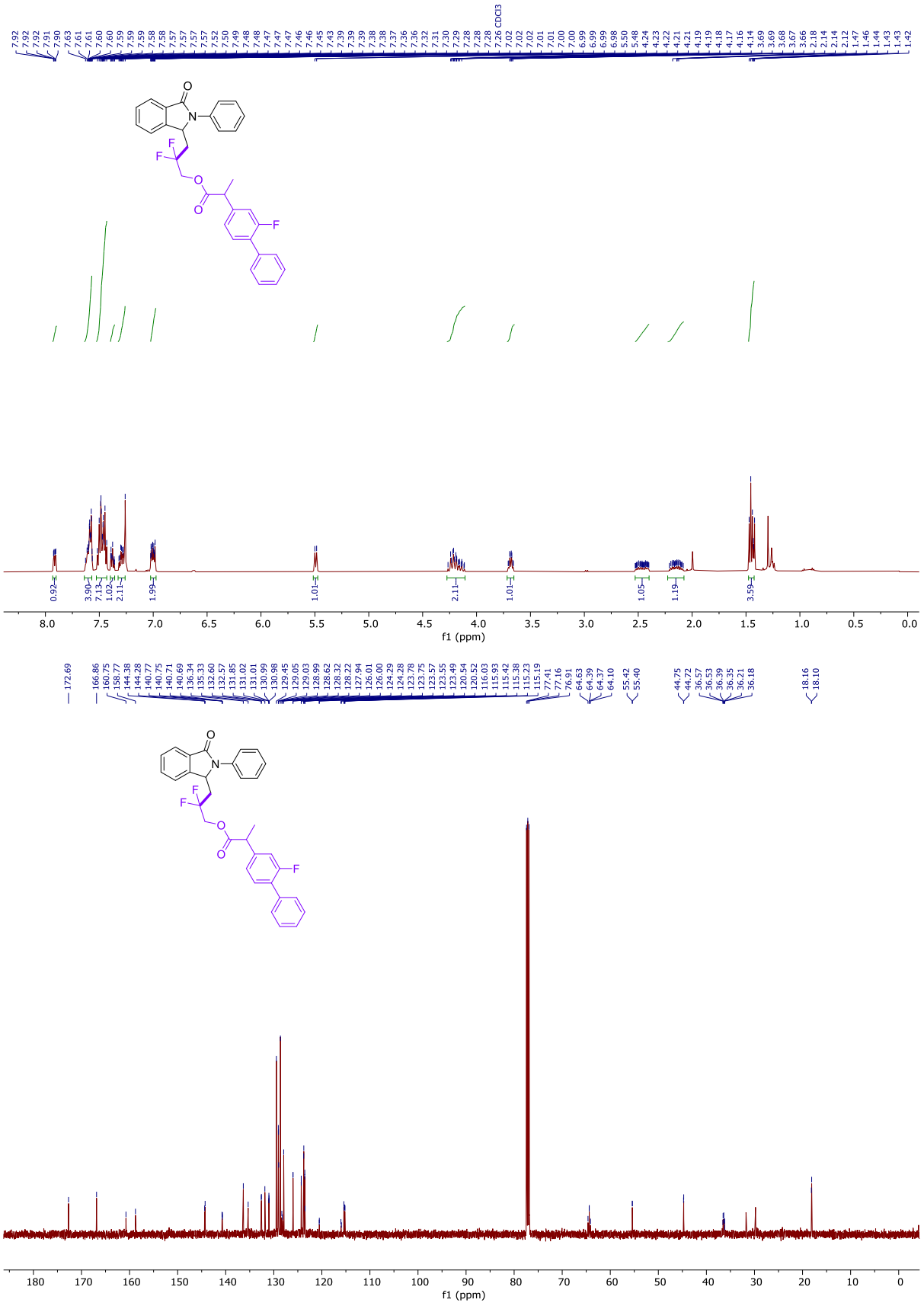


Figure S93. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3ae** in $CDCl_3$ at 298 K.

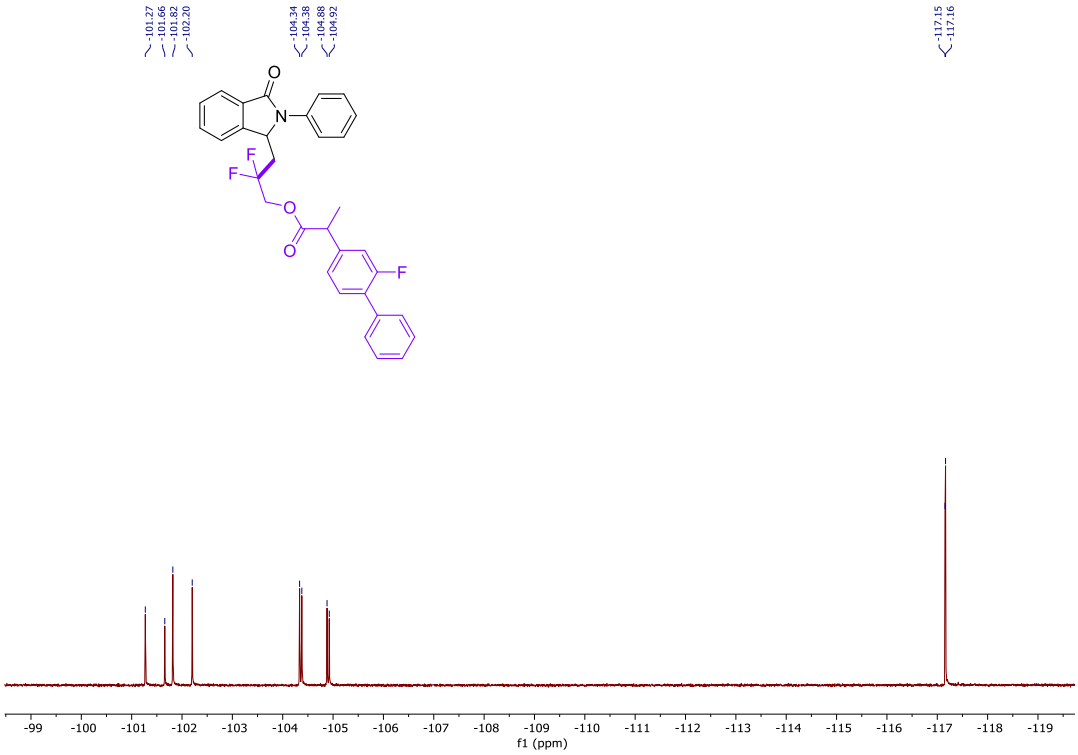


Figure S94. ^{19}F NMR (471 MHz) Spectra of **3ae** in $CDCl_3$ at 298 K.

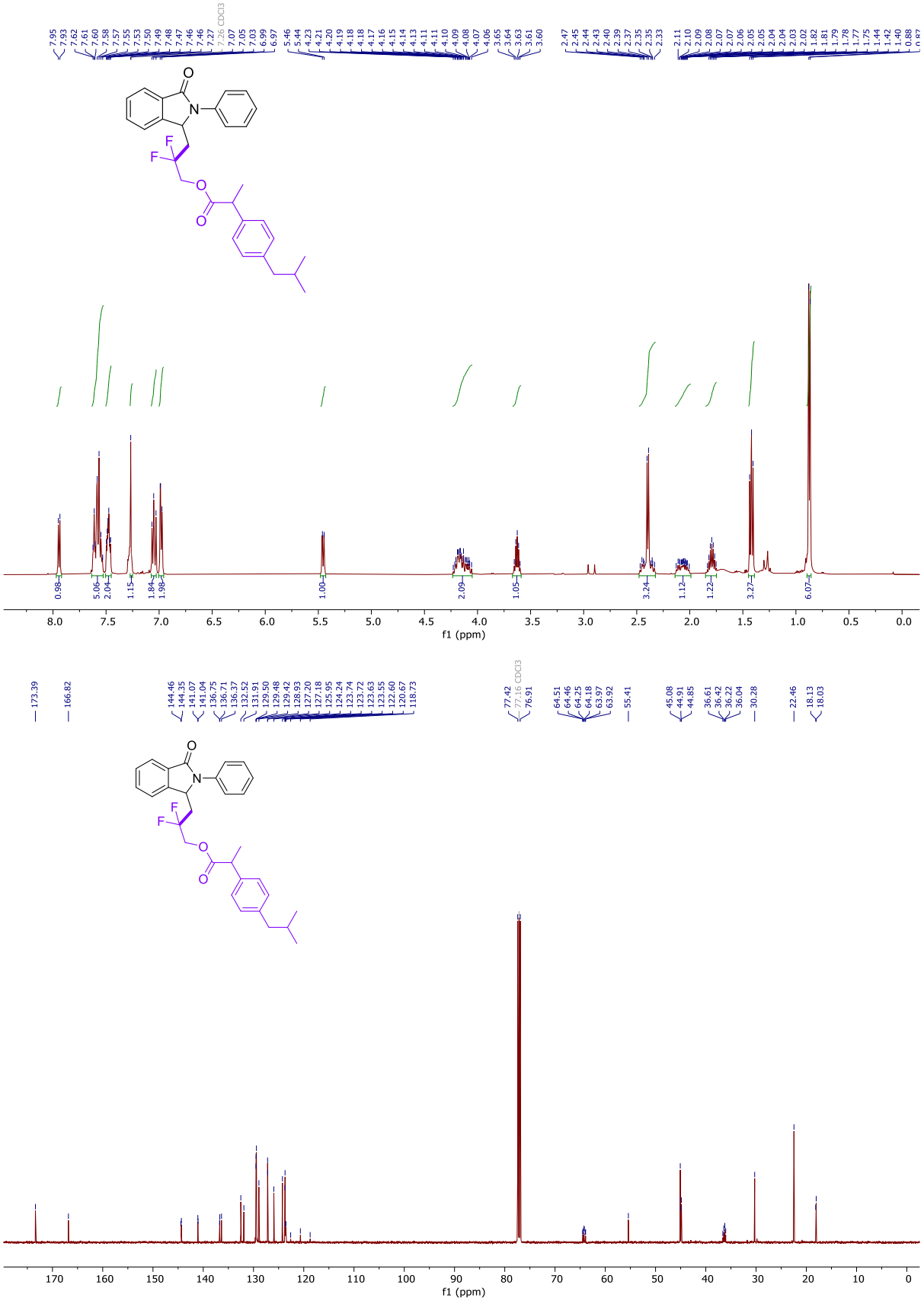


Figure S95. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3af** in $CDCl_3$ at 298 K.

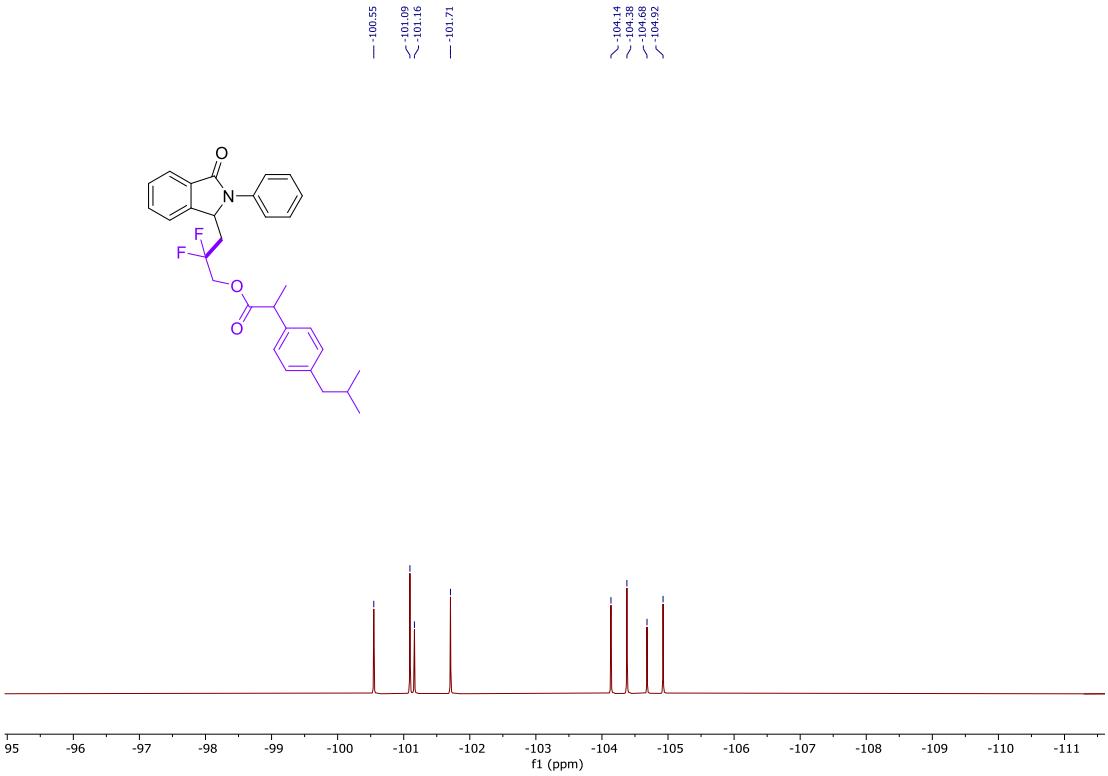


Figure S96. ^{19}F NMR (471 MHz) Spectra of **3af** in $CDCl_3$ at 298 K.

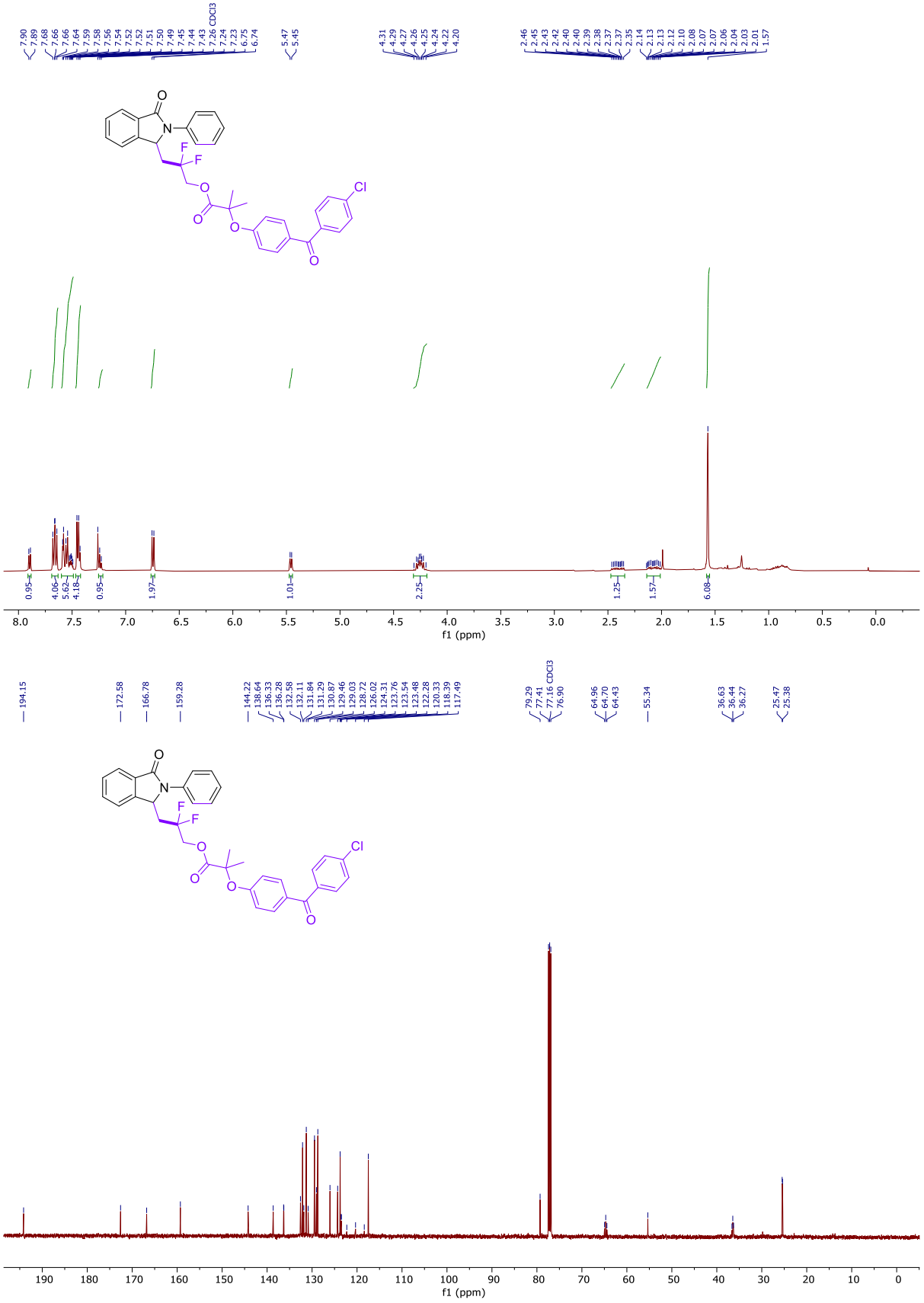


Figure S97. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3ag** in $CDCl_3$ at 298 K.

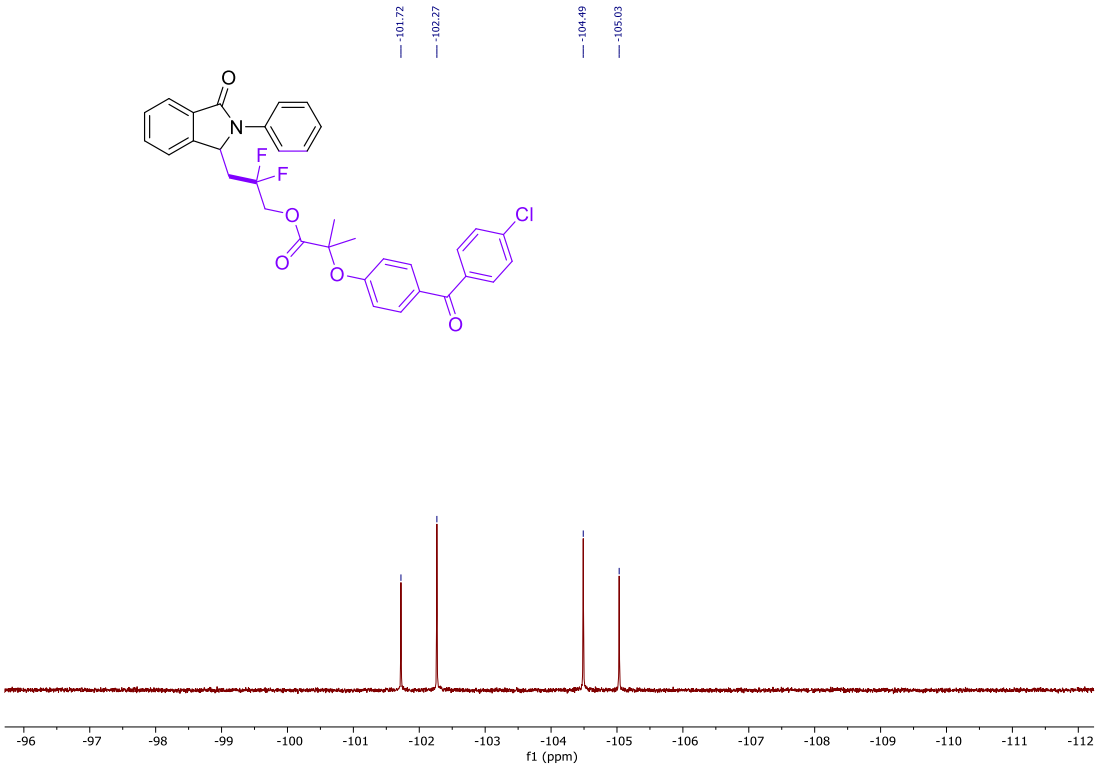


Figure S98. ^{19}F NMR (471 MHz) Spectra of **3ag** in $CDCl_3$ at 298 K.

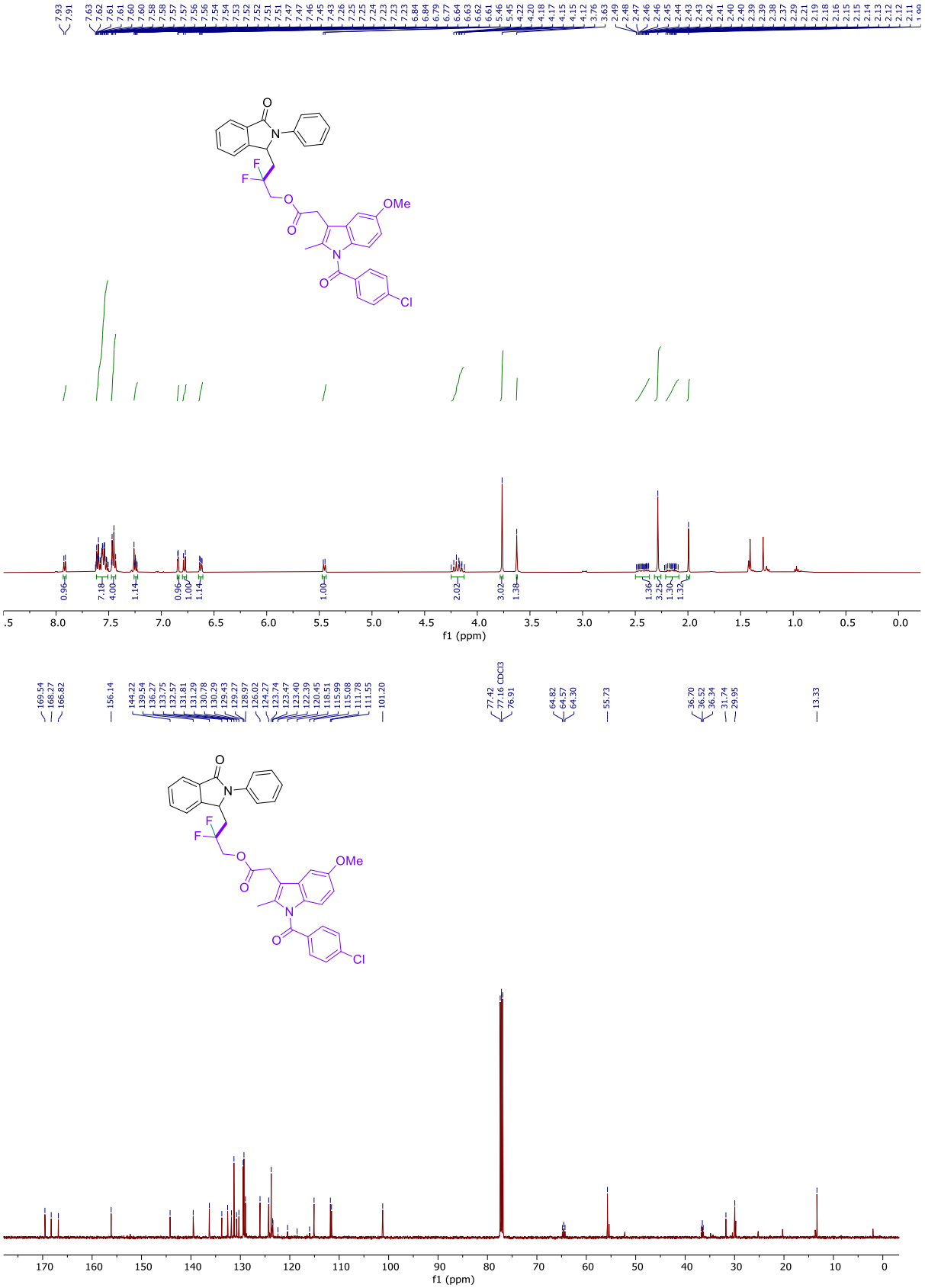


Figure S99. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3ah** in $CDCl_3$ at 298 K.

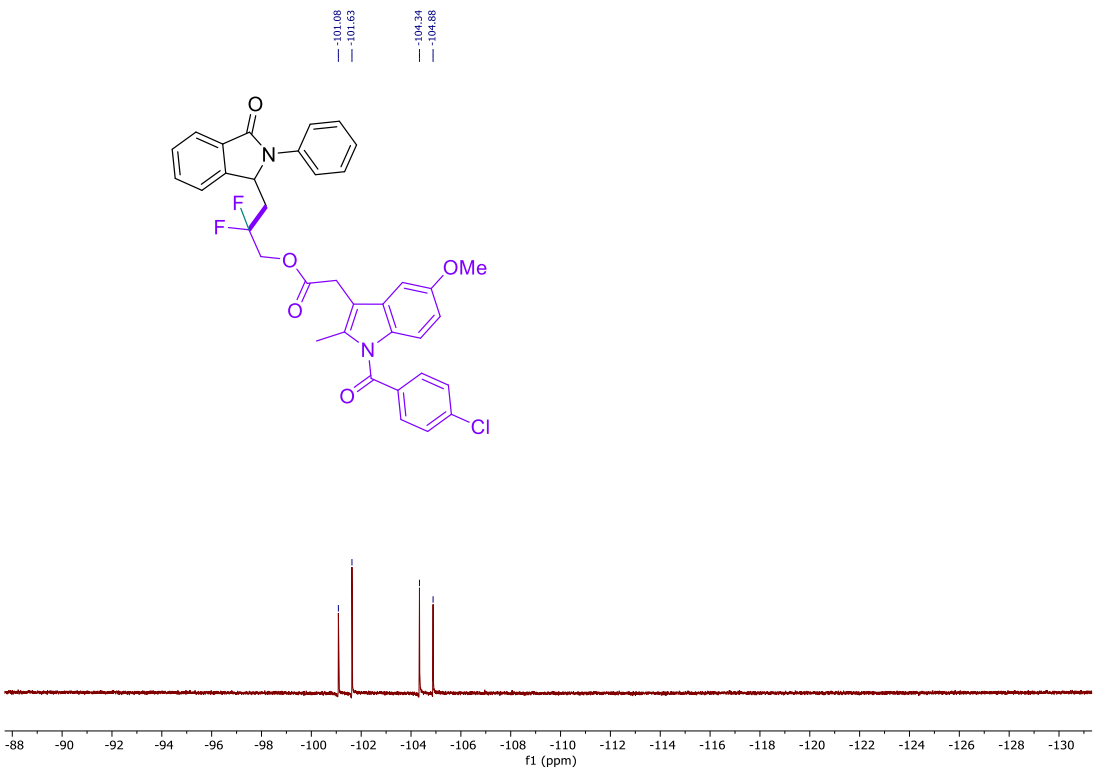


Figure S100. ^{19}F NMR (471 MHz) Spectra of **3ah** in $CDCl_3$ at 298 K.

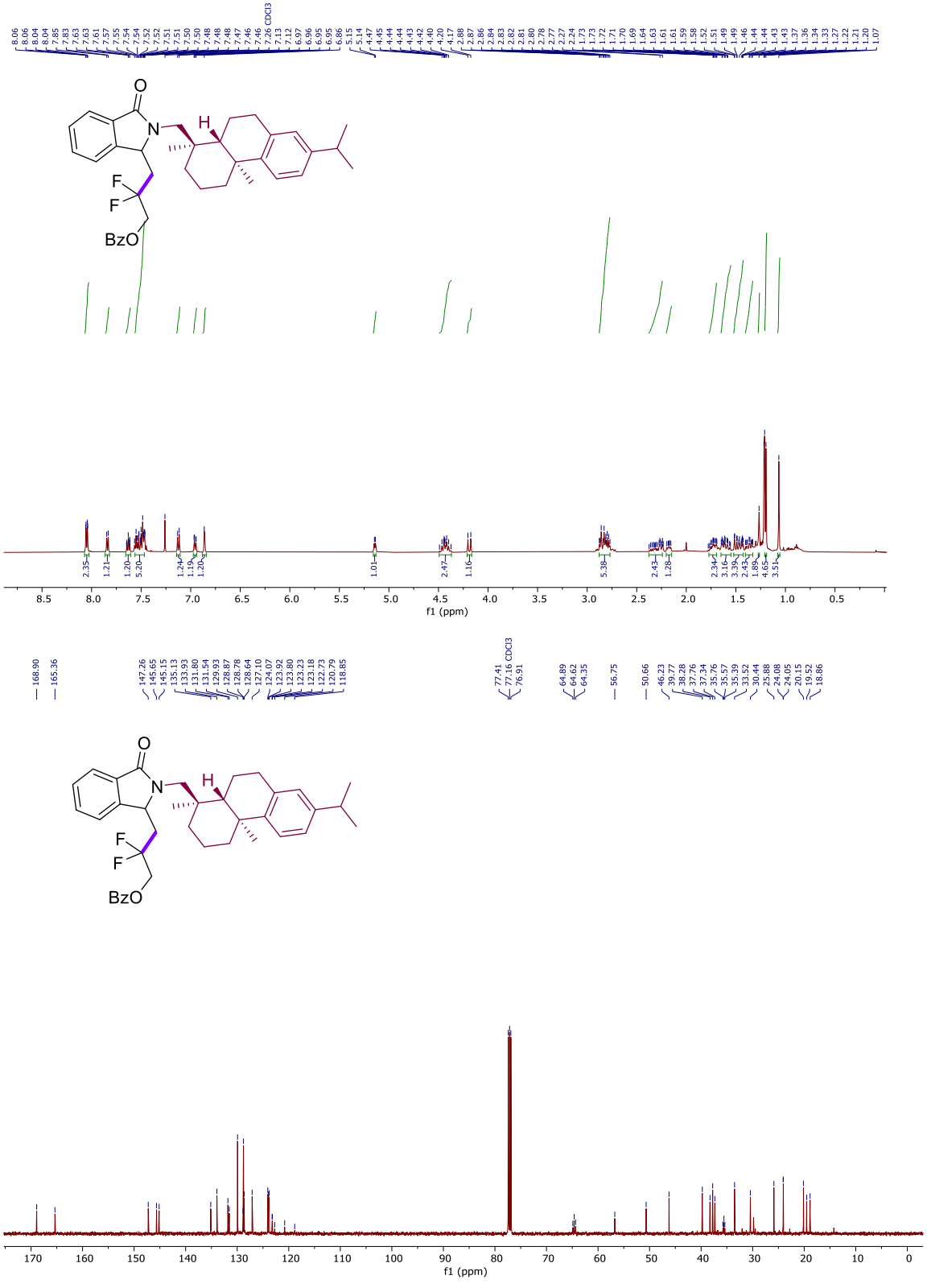


Figure S101. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3ai** in $CDCl_3$ at 298 K.

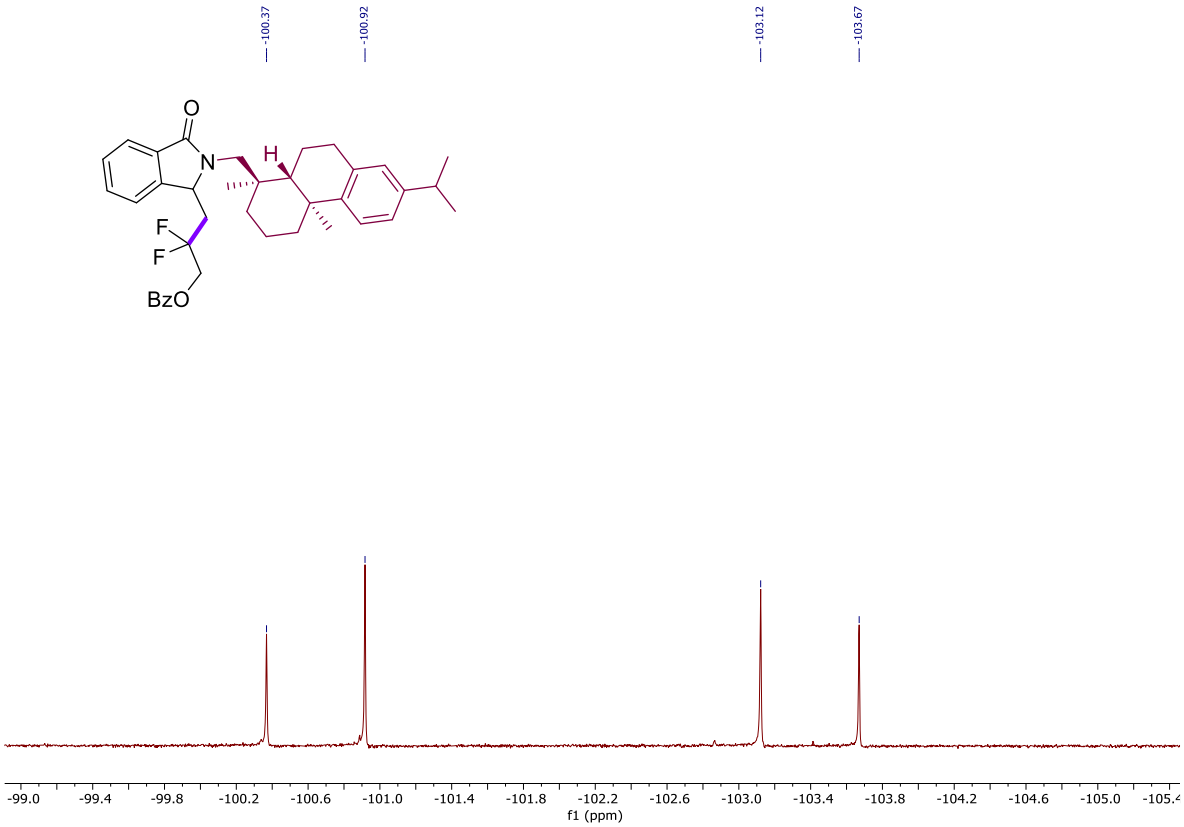


Figure S102. ^{19}F NMR (471 MHz) Spectra of **3ai** in $CDCl_3$ at 298 K.

9. Computational studies

All DFT calculations were performed using the Gaussian 16 package[4]. Geometry optimisations were performed in the solvent phase using the ωB97X functional[5] with a version of Grimme's D2 dispersion correction model[6] (ωB97XD), using the def2-SVP basis set of Alrichs and co-workers[7]. The structure was confirmed to be optimised by the means of frequency analysis at the same level of theory. Single point energies were calculated upon the optimised structures using the same functional, and using the def2-TZVP basis set of Alrichs and co-workers[4]. Solvent effects were incorporated by using the SMD solvent model developed by Truhlar and co-workers[8]. The total Gibbs Free Energy is taken as the sum of the single point electronic energy obtained at the ωB97XD/def2-TZVP+SMD(Acetonitrile) level of theory and the thermal corrections obtained at the ωB97XD/def2-SVP+SMD(Acetonitrile) level of theory. Transition states were identified by means of frequency analyses, and were confirmed to connect relevant intermediates by means of IRC calculations[9].

Computational calculations have been carried out to understand the mechanism of product formation and to determine whether the product forms via a HAT event or a radical polar crossover. Hence, the initial step of radical generation mediated by halogen bonding has not been computationally investigated herein. For computational simplicity, DIPEA has been chosen instead of $^{n}Bu_3N$ to carry out computational calculations.

Electron-transfer barriers

Electron transfer barriers were computed for select reactions by employing the Marcus-Hush theory[10] and Nelsen's four-point formula[11]. Standard notation has been employed in the description below (Table S5).

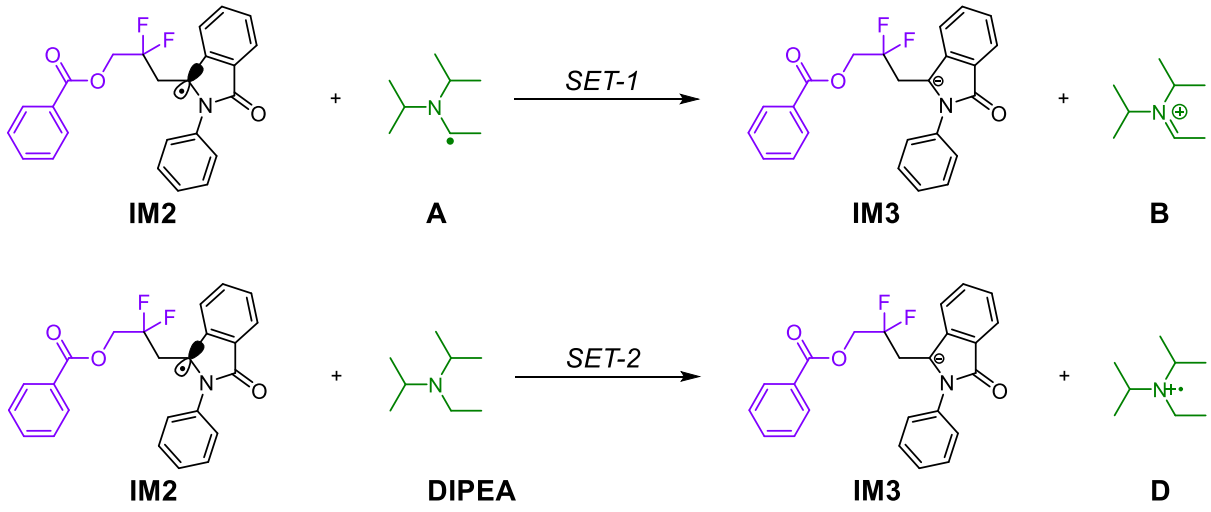


Figure S103. Reaction schemes for the calculation of single-electron transfer barriers

Table S5. Parameters for the calculation of SET barriers.

Reaction	λ_i (kcal/mol)	λ_s (kcal/mol)	ΔG_s (kcal/mol)	r_a (Å)	r_d (Å)	$\Delta G_r^{\ddagger}$ (kcal/mol)
SET-1	19.3	17.2	-12.6	5.76	4.62	3.9
SET-2	28.8	17.6	37.1	5.76	4.48	37.5

Proof for water-assisted quantum tunnelling phenomena during protonation

Based on previous reports, we sought to analyse the vibrational frequency and extent of geometric reorganization in the protonation steps (associated with **TS3a** and **TS3b**, see figure S108). The results are tabulated below.

a) Shuttling in direct protonation event

It is found that the protonation takes place via **TS3a** with a barrier of 5.5 kcal/mol. The imaginary frequency associated with this transition state was analyzed, and it is found to have a value of -1161.99 cm^{-1}. Furthermore, we find (Figure S104, Table S6) that the geometric reorganization during protonation is limited, with a difference of only around 0.2 Å in the distance between the N of aminium ion **C**, and the anionic centre of **IM3** (Table S6) before and after protonation.

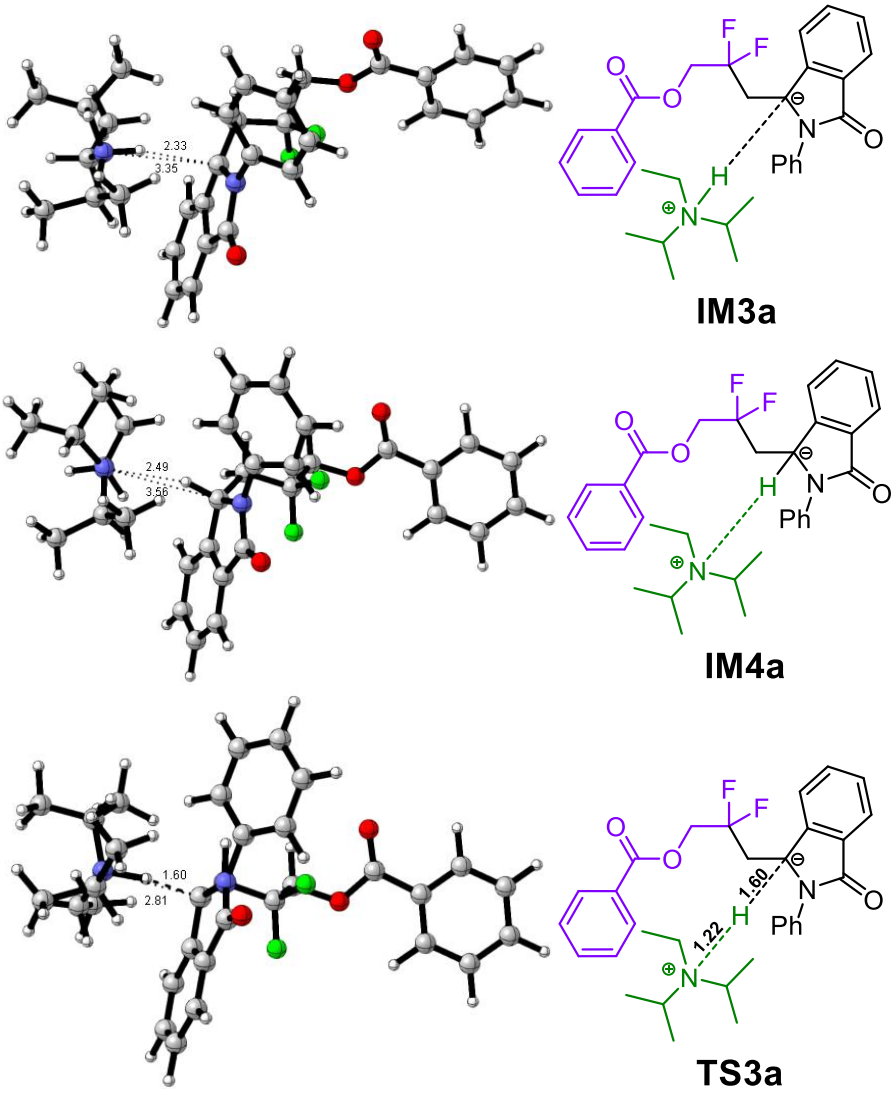


Figure S104. 3D structure of intermediates **IM3a**, **IM4a** and **TS3a** respectively. Distances given in Å. Structures were drawn using CYLView[12].

Table S6. Geometric parameters for the protonation of **IM3** by ion **C**.

Structure	N – C distance (Å)	Difference (Å)
IM3a	3.353	
TS3a	2.813	-0.540
IM4a	3.556	0.203

b) Tunnelling in protonation event via shuttling.

It is found that protonation can also take place via a shuttling event, with water acting as a proton shuttle. This is found to take place via **TS3b**, with a barrier of 5.8 kcal/mol. The imaginary frequency associated with this transition state was analysed, and it is found to have a value of -1164.58 cm^{-1}. Furthermore, we find (Figure S105, Table S7) that the geometric reorganization during protonation is limited, with the N–O, C–O and N–C distances only varying by 0.05 Å, 0.4 Å, and 0.13 Å respectively, during protonation.

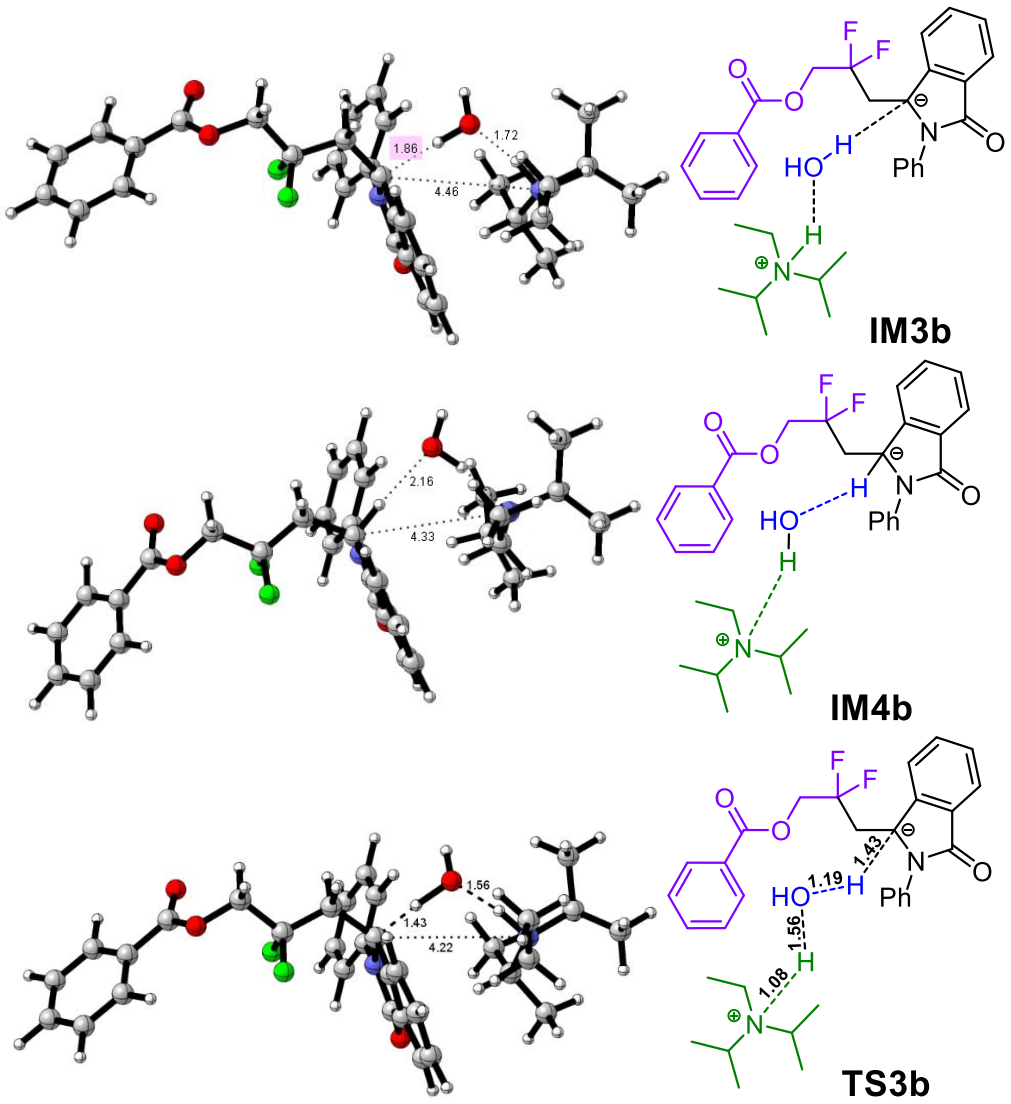


Figure S105. 3D structure of intermediates **IM3b**, **IM4b** and **TS3b** respectively. Distances given in Å. Structures were drawn using CYLView[12].

Table S7. Geometric parameters for the protonation of **IM3** by **C** via a proton shuttle.

Structure	N – O distance (Å)	Difference (Å)	O – C distance (Å)	Difference (Å)	N – C distance (Å)	Difference (Å)
IM3b	2.754		2.863		4.461	
TS3b	2.631	-0.123	2.618	-0.245	4.225	-0.236
IM4b	2.807	0.053	3.265	0.402	4.331	-0.130

The transition states **TS3a** and **TS3b** were analysed. Based upon the high value of imaginary frequencies, we assume that the proton movement is much larger than the movement of other atoms hence we approximate the tunnelling width to be the N–C, N–O and O–C distances respectively. Here, since we are dealing with bond-breaking and bond-forming phenomena, we treat the barrier to be parabolic in nature. Hence, we can estimate the tunnelling probability by the following equation[14].

$$P(E) = e^{-\pi^2 w\sqrt{2mE_a}/h}$$

Using this equation, we have the following tunnelling probabilities:

Table S8. Evaluation of tunnelling probabilities of the proton in **TS3a** and **TS3b**.

Transition state		w (Å)	E_a (kcal/mol)	m (kg)	Probability
TS3a	N-C	2.8125	3.7	1.67262E-27	1.23603E-17
TS3b	N-O	2.63111	0.9	1.67262E-27	1.19922E-08
TS3b	C-O	2.61755	0.9	1.67262E-27	1.31741E-08

On the basis of the low tunnelling probability associated with **TS3a**, we conclude that **TS3a** corresponds to a classical proton transfer event. However, we find that the tunnelling probability associated with **TS3b** is higher than that of **TS3a** by several orders of magnitude. This is perhaps due to the extremely low tunnelling barrier (0.9 kcal/mol) associated with **TS3b** (w.r.t **IM3b**). Hence, it is likely that the water-assisted protonation event proceeds via quantum tunnelling of the proton. This also explains why we see significant deuterium incorporation in the product despite **TS3a** being more stable than **TS3b**.

Alternate complexation events

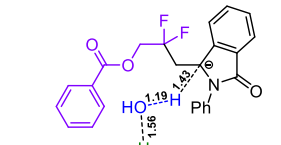
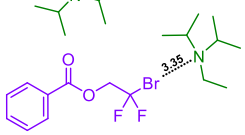
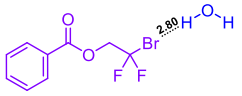
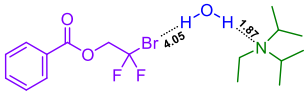
Structure	Complex	ΔG for formation (w.r.t. separated reactants)
	**IM3b**	6.7 kcal/mol
	**XB-1**	9.0 kcal/mol
	**HB-1**	8.6 kcal/mol
	**HB-2**	12.6 kcal/mol

Figure S106. Gibbs free energy for different complexation events, calculated at the ωB97XD/def2-TZVP+SMD(Acetonitrile)//ωB97XD/def2-SVP+SMD(Acetonitrile) level of theory. Interaction lengths are given in Å.

*On the basis of the calculated ΔG values, we can infer that at lower concentrations of water, it will preferentially form the pre-shuttling complex **IM3b**, and only at higher concentrations is it likely to disrupt halogen bonding.*

Computational evaluation of halogen bonding between 2a and DIPEA

To computationally characterise the complex **XB-1**, we carried out NBO, NCI and AIM analyses on the optimised structure using MultiWfn[13] (Figure S107). The existence of a bond critical point (Table S8) between N of DIPEA and Br of **2a** indicates that this interaction is of a halogen-bonding type, and also that there exist stabilizing dispersion interactions between **2a** and DIPEA.

Table S9. AIM analysis of complex **XB-1**.

Interaction	Density of all electrons	Laplacian of electron density	Lagrangian kinetic energy G(r)	Potential energy density V(r)	Energy (kcal/mol)
C-H … Br	0.0058	0.019212689	0.004178441	-0.00355371	-1.1
N … Br	0.0081	0.0274192	0.006161834	-0.005468868	-1.7
C-H … Br	0.0073	0.023449125	0.005395337	-0.004928393	-1.5
C-H … Br	0.0068	0.021625465	0.004908482	-0.004410598	-1.4
C-H … O	0.0052	0.018525249	0.00402465	-0.003417988	-1.1
C-H … π	0.0066	0.015846071	0.003538113	-0.003114708	-1.0
C-H … π	0.0057	0.017205266	0.003505443	-0.002709569	-0.9
C-H … π	0.0051	0.017066473	0.003421088	-0.002575557	-0.8
C-H … π	0.0034	0.009900822	0.001963012	-0.001450818	-0.5

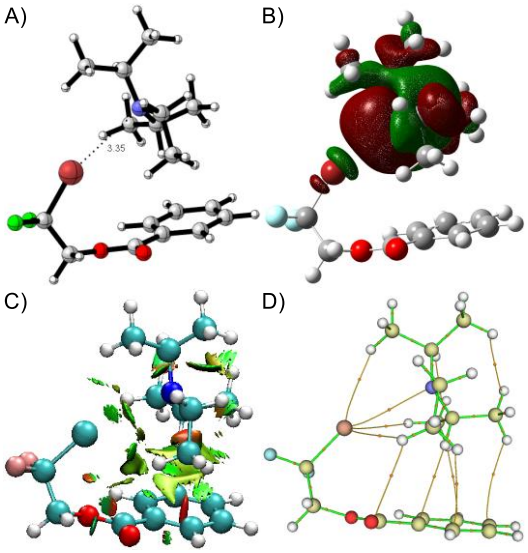


Figure S107. A) Optimised structure of complex **XB-1**. B) HOMO of **XB-1** (*Iso=0.004*). C) NCI plot of **XB-1**. D) AIM analysis, (3,-1) critical points in **XB-1**. Interaction lengths are given in Å.

Table S10. NBO analysis of complex **XB-1**.

Donor orbitals	Acceptor orbitals	Stabilization energy (kcal/mol)	E(a)-E(d) (a.u.)	F(d,a) (a.u.)
LP (1) N	RY*(1)Br	0.39	1.05	0.012
LP (1) N	RY*(1)Br	0.08	1.12	0.009
LP (1) N	BD*(1) C-Br	1.77	0.41	0.024

Reaction profile diagram

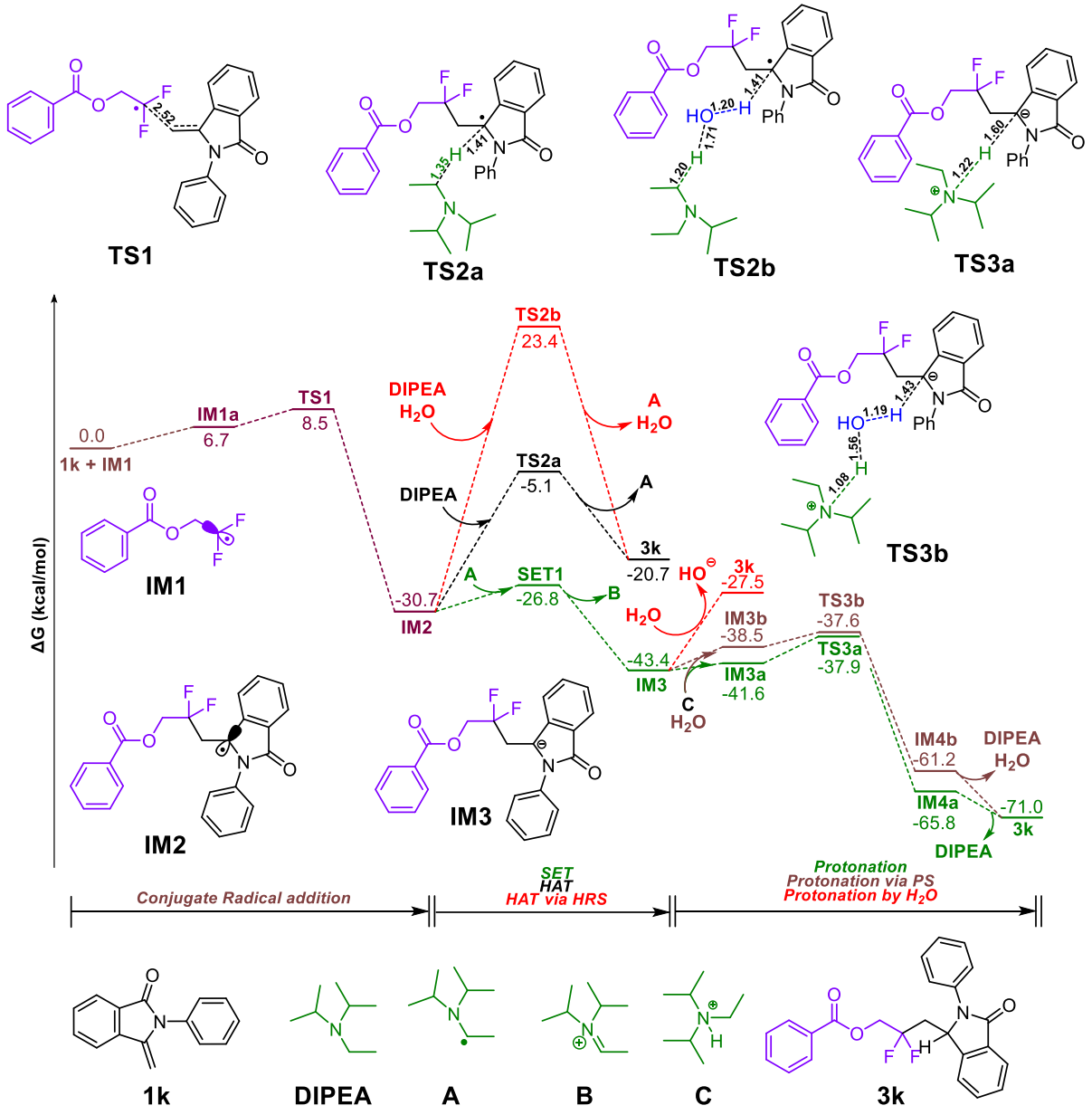


Figure S108. Gibbs free energy profile diagram for the difluoroalkylation of 3-methylene isoindolinones, calculated at the ωB97XD/def2-TZVP+SMD(Acetonitrile)//ωB97XD/def2-SVP+SMD(Acetonitrile) level of theory. Bond lengths are given in Å.

On the basis of the calculated barriers and exergonicity values, HAT events and direct protonation by H_2O are ruled out!

Cartesian coordinates

All energy values are in Hartree units.

Substrate 1k

Thermal correction to Gibbs free energy = 0.18177

Single-point energy = -708.2360823

0 1

C 1.86924800 -0.69404100 0.10091500

C 3.04261100 -1.43135300 0.21403600

C 4.25182300 -0.74184700 0.11921900

C 4.26935300 0.64531400 -0.08314300

C 3.08633900 1.37827600 -0.19539600

C 1.88093300 0.68710900 -0.09934500

H 3.01320800 -2.51173800 0.37116900

H 5.19559900 -1.28514100 0.20270300

H 5.22863700 1.16312200 -0.15442000

H 3.11084200 2.45858100 -0.35347600

C 0.48147100 1.15382000 -0.17638700

N -0.31057000 -0.00170400 -0.00336200

C -1.73170700 -0.00953500 0.00147100

C -2.42803500 0.61572700 1.03905800

C -2.42542500 -0.64829800 -1.02863900

C -3.82188000 0.60737800 1.03894000

H -1.87309900 1.10683200 1.84134500

C -3.81928800 -0.66653200 -1.01464200

H -1.86904000 -1.12902000 -1.83561000

C -4.51893700 -0.03613400 0.01519700

H -4.36550300 1.09970400 1.84844200

H -4.36133500 -1.17066900 -1.81792800

H -5.61132300 -0.04660500 0.02037300

C 0.45583800 -1.15115100 0.16144300

O 0.02326100 -2.27048300 0.32515400

C 0.03888500 2.39876500 -0.38501600

H -1.02546700 2.63644800 -0.43354900

H 0.75800500 3.20929400 -0.51301900

Intermediate IM1

Thermal correction to Gibbs free energy = 0.105164

Single-point energy = -697.3202577

0 2

C 3.53130700 -0.70343400 -0.44501200

C 3.84419200 0.65191000 -0.32338100

C 2.85731100 1.56959500 0.04052900

C 1.55614600 1.13625700 0.28522200

C 1.24029300 -0.22286300 0.16409400

C 2.23212400 -1.14056400 -0.20296100

H 4.30349200 -1.42127300 -0.73004200

H 4.86390600 0.99508800 -0.51377400

H 3.10270000 2.62976100 0.13400300

H 0.78242500 1.85105900 0.56825800

H 1.97235900 -2.19689200 -0.29523400

C -0.13546100 -0.74122600 0.41149500

O -0.46118600 -1.89523400 0.28521100

O -0.97846000 0.22592800 0.80540900

C -2.34833800 -0.12402800 1.02561800

H -2.70055200 0.48410400 1.86720700

H -2.43801100 -1.18994500 1.27033600

C -3.17408600 0.18101100 -0.17352000

F -3.32437800 1.46318800 -0.47677500

F -2.89674300 -0.51178900 -1.26969400

Intermediate IM2

Thermal correction to Gibbs free energy = 0.312484

Single-point energy = -1405.630887

0 2

C 3.82765800 1.22453600 0.71821300

C 4.68569100 2.17700900 1.26651700

C 4.62999600 3.47386100 0.76413800

C 3.72780700 3.81040400 -0.26846000

C 2.87034500 2.86959400 -0.81887900

C 2.92460500 1.55275200 -0.32024700

H 5.37759800 1.90926600 2.06840500

H 5.28845900 4.24383100 1.17219700

H 3.70546400 4.83790700 -0.63937800

H 2.17158300 3.14152300 -1.61238900

C 2.20130800 0.37584100 -0.65800100

N 2.64658300 -0.64236200 0.15987800

C 2.19676600 -1.99356000 0.13172300

C 1.44754800 -2.49248100 1.19814500

C 2.51575100 -2.80934400 -0.95527400

C 1.01342600 -3.81618800 1.17243900

H 1.20221700 -1.83814800 2.03634200

C 2.06659100 -4.12906000 -0.98074800

H 3.11282900 -2.40514200 -1.77572600

C 1.31780600 -4.63385900 0.08274700

H 0.42659600 -4.20875400 2.00583500

H 2.30999700 -4.76657900 -1.83356000

H 0.97005000 -5.66918600 0.06296100

C 3.65674000 -0.19698900 1.03943100

O 4.22406000 -0.90384500 1.85295100

C -6.58798600 -0.25660500 1.21664800

C -6.73715800 1.10182500 1.50335100

C -5.79623100 2.02375100 1.04155100

C -4.70580000 1.59188400 0.28984400

C -4.55500000 0.22988100 0.00044700

C -5.49820900 -0.69290600 0.46843200

H -7.32376700 -0.97771200 1.57920600

H -7.59175400 1.44388800 2.09199700

H -5.91195900 3.08566700 1.26930600

H -3.96537100 2.30782200 -0.06909000

H -5.36715000 -1.75208600 0.23840300

C -3.40076300 -0.28444000 -0.78982800

O -3.17352100 -1.45197300 -0.98434400

O -2.64439300 0.71106100 -1.27904800

C -1.44163700 0.38151600 -1.94364100

H -1.33888900 1.05240800 -2.80584500

H -1.45245800 -0.66183600 -2.28364400

F -0.25614500 1.89533700 -0.58898500

F -0.47719800 -0.13851500 0.13186700

C -0.27081200 0.59505900 -1.00135100

C 1.07386700 0.23129300 -1.61608000

H 1.23411400 0.89483700 -2.47811100

H 1.00341500 -0.79715000 -1.99516000

α-amino alkyl radical A

Thermal correction to Gibbs free energy = 0.210619

Single-point energy = -370.4226629

0 2

N -0.02515700 0.25144100 0.12920100

C -1.25759800 -0.53372300 0.06809900

C -1.36380200 -1.51994900 1.23140100

C -1.45526900 -1.22086500 -1.28617500

H -2.08036700 0.18309800 0.19249000

H -1.24536500 -0.99926200 2.19374600

H -2.35110700 -2.00681200 1.22318100

H -0.60516400 -2.31636300 1.17465400

H -2.43681500 -1.71835500 -1.32799400

H -1.40890800 -0.48598000 -2.10481200

H -0.68432500 -1.98757000 -1.46551500

C 1.25027500 -0.46248000 0.02511300

C 2.17063900 -0.12265800 1.19849400

C 1.95419100 -0.26116300 -1.32038700

H 1.01068300 -1.53280800 0.10207400

H 1.67128200 -0.33239900 2.15662200

H 3.09472300 -0.71955000 1.15271000

H 2.45745200 0.94101700 1.18732100

H 1.28174300 -0.49988200 -2.15779100

H 2.30145800 0.77594100 -1.44595100

H 2.83384300 -0.91978400 -1.38951000

C -0.04243000 1.60800200 -0.17492800

C -1.24049700 2.45603900 0.11363000

H 0.93816900 2.08825700 -0.10306300

H -0.99707000 3.51090800 -0.08214400

H -2.11801600 2.21048000 -0.51117200

H -1.57917400 2.38975400 1.16926500

Iminium ion B

Thermal correction to Gibbs free energy = 0.216048

Single-point energy = -370.3327135

1 1

N 0.03762600 0.27601700 -0.00516700

C 1.28143400 -0.53696700 -0.00429400

C 1.35310600 -1.39469900 -1.26142200

C 1.38990000 -1.32945500 1.29237300

H 2.10976800 0.17870400 -0.03496500

H 1.27363400 -0.77452300 -2.16596600

H 2.32648100 -1.90510400 -1.27929900

H 0.56939100 -2.16599000 -1.28695400

H 2.36178900 -1.84273900 1.30771000

H 1.33882200 -0.66330600 2.16577500

H 0.60465500 -2.09470200 1.38071800

C -1.26657000 -0.45859500 0.01287800

C -2.04572000 -0.19454700 -1.26790600

C -2.04419100 -0.14069100 1.28213300

H -0.99195500 -1.51943600 0.03606900

H -1.43885400 -0.42968800 -2.15400600

H -2.93906700 -0.83486500 -1.28085300

H -2.37818400 0.85280400 -1.33253000

H -1.43602500 -0.33766400 2.17661800

H -2.37916500 0.90744800 1.30352400

H -2.93641400 -0.78144200 1.32273400

C 0.05144000 1.55989100 -0.01861500

C 1.25828100 2.41676400 -0.03371000

H -0.92921900 2.04753100 -0.01752800

H 0.96345300 3.47143800 -0.03566800

H 1.88433500 2.21830400 0.85031800

H 1.86709700 2.21090700 -0.92814900

DIPEA

Thermal correction to Gibbs free energy = 0.225067

Single-point energy = -371.0745393

0 1

N 0.00374700 0.26161700 0.15449700

C -1.39453400 -0.15747400 0.05737400

C -1.87958300 -0.79091000 1.36166900

C -1.72584900 -1.04888200 -1.14699300

H -1.97127100 0.77276500 -0.06946400

H -1.67858400 -0.12156600 2.21203200

H -2.96276400 -0.98554200 1.32048700

H -1.38187800 -1.75389600 1.56044300

H -2.81387200 -1.20267600 -1.22338300

H -1.38625800 -0.59185800 -2.08967100

H -1.25617300 -2.04149600 -1.05571800

C 1.01615400 -0.79527300 0.20794200

C 2.10336800 -0.44020200 1.22413900

C 1.64288300 -1.17890800 -1.14120400

H 0.50314800 -1.69268300 0.58762500

H 1.66021700 -0.25636500 2.21464200

H 2.84205200 -1.25222200 1.31800000

H 2.64771000 0.46986000 0.92151300

H 0.87905400 -1.41048500 -1.89659700

H 2.27913100 -0.37221600 -1.53856200

H 2.28078200 -2.06906600 -1.02309800

C -0.14830100 2.73841400 -0.00309900

H 0.15585000 3.60221300 -0.61530100

H -1.24560600 2.76822500 0.08510500

H 0.27499900 2.86125800 1.00636300

C 0.34257400 1.43708600 -0.62855900

H -0.03111500 1.36563100 -1.67302200

H 1.43807200 1.49568800 -0.71049200

Intermediate IM3

Thermal correction to Gibbs free energy = 0.312271

Single-point energy = -1405.746192

-1 1

C 3.77879500 -1.12851800 -0.76229700

C 4.65197400 -2.06793900 -1.33823400

C 4.75269600 -3.33420600 -0.79030500

C 3.95520500 -3.67550000 0.34732600

C 3.09552200 -2.77916200 0.93777900

C 3.00250000 -1.44640100 0.41347700

H 5.23831700 -1.79044800 -2.22055000

H 5.42456000 -4.07915400 -1.22382500

H 4.02978200 -4.68840300 0.75602000

H 2.49043400 -3.07980500 1.79825400

C 2.26667600 -0.33000400 0.77413800

N 2.54302400 0.66526400 -0.20753400

C 2.10045800 2.00033700 -0.14863700

C 1.56939300 2.61797300 -1.28894700

C 2.19623200 2.73182300 1.04257800

C 1.13512000 3.94002800 -1.23130100

H 1.49966900 2.04986100 -2.21664100

C 1.74301000 4.04973400 1.09871200

H 2.63925600 2.26447700 1.92467600

C 1.21199900 4.66079000 -0.03720000

H 0.72089100 4.40950500 -2.12718400

H 1.81825500 4.60528200 2.03683400

H 0.86143100 5.69464500 0.00598000

C 3.47647900 0.22373200 -1.16173400

O 3.92334000 0.92283300 -2.08478000

C -6.57673400 0.19155900 -1.15693500

C -6.61266700 -1.11218000 -1.65582000

C -5.60147600 -2.01685500 -1.32764500

C -4.55491500 -1.62327000 -0.49660500

C -4.51803900 -0.31665500 0.00598500

C -5.52999000 0.59034600 -0.33018900

H -7.36745700 0.89944500 -1.41490900

H -7.43316900 -1.42438900 -2.30633900

H -5.62764800 -3.03488500 -1.72241900

H -3.75853900 -2.32364700 -0.24165900

H -5.48639700 1.60742900 0.06433100

C -3.41165700 0.15497000 0.88786900

O -3.25818300 1.30038100 1.23228400

O -2.61480200 -0.85150600 1.27096400

C -1.42644500 -0.54737600 1.97795300

H -1.30893700 -1.29751000 2.77022300

H -1.48266700 0.45468600 2.42187900

F -0.18246100 -1.87703500 0.49746400

F -0.48247900 0.20940800 -0.02693400

C -0.23907900 -0.62144000 1.03466300

C 1.08985900 -0.26693300 1.68836300

H 1.23552100 -0.98045100 2.51415200

H 0.95764500 0.72236600 2.15344200

Aminium ion C

Thermal correction to Gibbs free energy = 0.243956

Single-point energy = -371.5553134

1 1

N 0.03338400 -0.28044000 -0.37014400

C 1.53263600 -0.51364700 -0.23767400

C 1.99756100 -0.50539600 1.20759800

C 2.29459100 0.46434400 -1.11806600

H 1.67112200 -1.52201900 -0.65152800

H 1.44259700 -1.22206800 1.82884900

H 3.05636400 -0.79955200 1.22510800

H 1.92270900 0.49515900 1.65802800

H 3.35026100 0.15975200 -1.14042400

H 1.91755600 0.45054800 -2.15216500

H 2.25456000 1.49559600 -0.73809900

C -0.43122500 1.06046700 0.20308600

C -1.33294600 1.76712700 -0.79803000

C -1.04859200 0.94530500 1.58682600

H 0.48832000 1.65079100 0.29218000

H -2.29160000 1.24778200 -0.93468800

H -1.54540800 2.77980200 -0.42741700

H -0.83821800 1.86490500 -1.77651000

H -2.02722400 0.44599600 1.57104500

H -0.39336600 0.42389700 2.29680100

H -1.20241800 1.96579900 1.96546600

C -0.75506700 -1.48966800 0.04037100

C -2.16087800 -1.51695700 -0.52328900

H -0.74983000 -1.54582000 1.13455500

H -0.18834100 -2.34918400 -0.33932000

H -2.59873700 -2.50043300 -0.30148300

H -2.81533400 -0.75331300 -0.08307500

H -2.15289200 -1.38985400 -1.61675700

H -0.11028300 -0.20415600 -1.38448400

Radical cation D

Thermal correction to Gibbs Free Energy= 0.225572

Single-point energy= -370.9004412

1 2

N -0.00188300 0.10750500 -0.25906400

C -1.45277000 0.03268000 -0.11217300

C -1.84650600 0.18470600 1.35895000

C -1.98279300 -1.25510500 -0.74687700

H -1.85281400 0.88645400 -0.67513200

H -1.43932400 1.11313800 1.78298200

H -2.94336300 0.23034700 1.41204000

H -1.50915900 -0.66794400 1.96541600

H -3.08064500 -1.22178600 -0.70797800

H -1.67505700 -1.33147400 -1.79914800

H -1.64722800 -2.15055200 -0.20449800

C 0.85966400 -0.89741100 0.35507500

C 1.82274300 -0.23954100 1.34461800

C 1.58042800 -1.70708100 -0.72722600

H 0.19671600 -1.57397000 0.90805000

H 1.27668100 0.32624600 2.11206300

H 2.39268400 -1.03720700 1.84140600

H 2.53585300 0.42806200 0.83992700

H 0.86392500 -2.14561700 -1.43528400

H 2.30804900 -1.09614900 -1.28035500

H 2.12311700 -2.52351700 -0.23054900

C 0.40757300 2.54189400 -0.30171700

H 0.84483600 3.31794900 -0.94459800

H -0.64732200 2.79307000 -0.12555600

H 0.94277700 2.53660700 0.65737000

C 0.56016000 1.19850500 -1.02096800

H 0.01587900 1.22499300 -1.97963100

H 1.61658700 0.98692800 -1.22116700

Product 3k

Thermal correction to Gibbs free energy = 0.32732

Single-point energy = -1406.267068

0 1

C -2.89127300 -1.63665000 0.93467300

C -3.12935100 -2.79690000 1.66724600

C -3.27092300 -3.99080900 0.96277700

C -3.17768600 -4.00669000 -0.43657100

C -2.93963200 -2.83711200 -1.16031900

C -2.79624300 -1.64891500 -0.45091200

H -3.20158600 -2.76382200 2.75662500

H -3.45743200 -4.92291700 1.50080200

H -3.29357000 -4.95341700 -0.96954900

H -2.86388900 -2.85979900 -2.24969300

C -2.54180200 -0.24978700 -0.94949500

N -2.52851300 0.52894500 0.29282200

C -2.36646100 1.93079100 0.30135300

C -1.62676900 2.56048000 1.31186600

C -2.93121600 2.70565600 -0.72057900

C -1.47200500 3.94471600 1.30090000

H -1.17498400 1.96320400 2.10200100

C -2.75740200 4.08863900 -0.72999900

H -3.51323600 2.23054900 -1.51236000

C -2.03212500 4.71646100 0.28195900

H -0.89435600 4.42337200 2.09537600

H -3.20187700 4.67835400 -1.53521800

H -1.90051300 5.80075700 0.27517400

C -2.71390000 -0.24570400 1.42223600

O -2.74753600 0.14646300 2.57199200

C 6.31396800 0.49496600 1.11812400

C 6.45195800 -0.85656700 1.44080300

C 5.51423100 -1.78552600 0.98663100

C 4.43851300 -1.36772000 0.20626800

C 4.29916600 -0.01275600 -0.11946000

C 5.23853100 0.91731300 0.34163700

H 7.04705800 1.22165900 1.47497200

H 7.29505500 -1.18759900 2.05191700

H 5.62075900 -2.84184700 1.24306700

H 3.69990400 -2.08872800 -0.14627400

H 5.11588300 1.97111000 0.08389400

C 3.15901300 0.48633500 -0.93982700

O 2.93041700 1.65072800 -1.15168000

O 2.41988900 -0.51837600 -1.43443200

C 1.21902000 -0.20547700 -2.11106800

H 1.13433200 -0.87895600 -2.97320100

H 1.22051100 0.83756900 -2.45191800

F 0.05139700 -1.74293200 -0.77787900

F 0.25788500 0.28508300 -0.03342500

C 0.04240100 -0.43601800 -1.17542500

C -1.28454900 -0.06961300 -1.80804200

H -1.40060600 -0.67663200 -2.71792100

H -1.21664900 0.97818600 -2.13505300

H -3.39369000 0.06177800 -1.57635400

Transition state TS1

Thermal correction to Gibbs free energy = 0.3058

Single-point energy = -1405.561693

Imaginary frequency = -168.79 cm^{-1}

0 2

C 4.03280500 -1.02671600 0.76977700

C 4.85258000 -1.90036300 1.47596100

C 5.00207700 -3.19473000 0.97767000

C 4.34228600 -3.59010000 -0.19559600

C 3.52272900 -2.70833400 -0.90084200

C 3.37579800 -1.41440400 -0.40172600

H 5.35766200 -1.58026000 2.38991400

H 5.63687200 -3.91045500 1.50461700

H 4.47348100 -4.61009600 -0.56431100

H 3.01373400 -3.02597300 -1.81322200

C 2.60030800 -0.26883400 -0.89110700

N 2.83281900 0.77326300 0.02650400

C 2.18110700 2.03470400 -0.02073900

C 2.45582500 2.92564500 -1.06038400

C 1.24971700 2.36708500 0.96623800

C 1.78541800 4.14677900 -1.11857100

H 3.18990700 2.65476200 -1.82221300

C 0.59495000 3.59615400 0.91116700

H 1.03565600 1.65600200 1.76587700

C 0.85703000 4.48459900 -0.13311800

H 1.99560800 4.84040200 -1.93577200

H -0.13190100 3.85623800 1.68393200

H 0.33609700 5.44367400 -0.17854800

C 3.67534400 0.38389400 1.06507600

O 4.01821400 1.08271600 1.99421700

C 1.74626000 -0.22704300 -1.93617900

H 1.27195900 0.70191600 -2.25488400

H 1.65469200 -1.09953500 -2.58434800

C -7.08875600 -1.01511800 0.21382300

C -7.03136800 -0.70760500 1.57463100

C -5.84193400 -0.24380600 2.13917100

C -4.70763300 -0.08476000 1.34625100

C -4.76306000 -0.39248300 -0.01897900

C -5.95719700 -0.85898000 -0.58180600

H -8.01924100 -1.37856500 -0.22769400

H -7.91924600 -0.83093300 2.19935400

H -5.79740500 -0.00512100 3.20404100

H -3.77578400 0.27503500 1.78429100

H -5.98674200 -1.09650300 -1.64695500

C -3.57689300 -0.24633100 -0.91090100

O -3.56425200 -0.54066300 -2.08040400

O -2.51876600 0.26378100 -0.26439500

C -1.28628400 0.39116100 -0.97901600

H -0.80099000 1.30438500 -0.61324600

H -1.47232900 0.47262300 -2.05743200

C -0.39035800 -0.76763000 -0.71903300

F 0.02476400 -0.90183700 0.53874600

F -0.82008100 -1.94525300 -1.16595500

Transition state TS2a

Thermal correction to Gibbs free energy = 0.557136

Single-point energy = -1776.684089

Imaginary frequency = -1296.84 cm^{-1}

0 2

C -1.55224200 -1.27561200 1.81427400

C -1.97262100 -2.30636700 2.65600400

C -2.19364700 -3.55981900 2.09522100

C -1.99838300 -3.76575200 0.71571800

C -1.58666300 -2.73521100 -0.12206400

C -1.36045500 -1.47173900 0.44130100

H -2.11621300 -2.12679100 3.72414500

H -2.52040200 -4.39151800 2.72330900

H -2.17495100 -4.75911000 0.29560500

H -1.43436700 -2.91165600 -1.18924600

C -0.97409700 -0.20529800 -0.17736200

N -0.82643600 0.69786000 0.93664800

C -0.43462100 2.04873100 0.81697500

C 0.38704700 2.63169000 1.79168000

C -0.84709800 2.81795700 -0.27783200

C 0.77525500 3.96325600 1.67198700

H 0.72060900 2.03582300 2.64014000

C -0.44094900 4.14664700 -0.39740000

H -1.48969900 2.37992000 -1.04078200

C 0.36695000 4.72852800 0.57786500

H 1.41604000 4.40412900 2.43951100

H -0.76890000 4.73015200 -1.26090400

H 0.68032900 5.77082300 0.48561100

C -1.21891800 0.12100100 2.14167200

O -1.28674200 0.68609300 3.22122200

C 8.09307100 0.22632100 0.25103000

C 8.22061000 -1.07209600 0.74871900

C 7.17746800 -1.98721300 0.59676000

C 6.00602900 -1.60893800 -0.05531600

C 5.87683900 -0.30753500 -0.55632600

C 6.92283900 0.60940800 -0.39837800

H 8.90881600 0.94253400 0.37132500

H 9.13828600 -1.37191200 1.26041400

H 7.27659000 -3.00133700 0.99000600

H 5.18493900 -2.31750900 -0.17186200

H 6.80741300 1.62204300 -0.78974100

C 4.63796300 0.14853500 -1.24871600

O 4.43238600 1.28289200 -1.60117100

O 3.77788000 -0.86071200 -1.45147100

C 2.49103200 -0.56302500 -1.95575600

H 2.22262500 -1.34913100 -2.67252800

H 2.48194100 0.41428600 -2.45471000

F 1.49607100 -1.79476700 -0.22310100

F 1.93896400 0.29557400 0.15212600

C 1.48921800 -0.56251600 -0.81259000

C 0.08557000 -0.18843000 -1.25600300

H -0.20949800 -0.90121400 -2.03933600

H 0.14480200 0.79838700 -1.73756300

N -4.40754500 0.02654100 -0.94033500

C -4.92694600 -1.33992900 -0.94819700

C -6.21714200 -1.43944200 -1.76566300

C -5.10810100 -1.91839700 0.45572400

H -4.16449000 -1.95543900 -1.44474700

H -6.05829900 -1.08467600 -2.79509700

H -6.56983800 -2.48176300 -1.81029500

H -7.01912200 -0.83360400 -1.31327600

H -5.34311700 -2.99164000 0.38966900

H -4.19079600 -1.80460000 1.04901000

H -5.93395300 -1.43429800 0.99985200

C -5.07428900 1.02837700 -0.10941200

C -5.52586000 2.24839700 -0.91480000

C -4.23039700 1.43084600 1.10079900

H -5.98755800 0.54718900 0.26843600

H -6.10398300 1.93963100 -1.79899600

H -6.16445300 2.89401800 -0.29291400

H -4.67458800 2.85962300 -1.25341900

H -3.96221500 0.55114400 1.70360500

H -3.30054300 1.92770200 0.78446400

H -4.78404300 2.13221500 1.74394600

C -2.92693600 -0.34044900 -2.92541400

H -2.06030500 0.13963600 -3.40163900

H -2.67485400 -1.40113600 -2.77647300

H -3.77329500 -0.28949500 -3.63126400

C -3.24799200 0.37515400 -1.63020900

H -2.14433700 0.14599400 -0.88067800

H -3.17941000 1.46483000 -1.74338000

Transition state TS2b

Thermal correction to Gibbs free energy = 0.576657

Single-point energy = -1853.100098

Imaginary frequency = -1325.15 cm^{-1}

0 2

C 0.46859100 3.75599400 -0.94985700

C 0.43119800 4.83810500 -1.83388300

C 0.84491000 4.63443000 -3.14480800

C 1.28401600 3.35816200 -3.55396900

C 1.32959800 2.28512500 -2.67280900

C 0.92809900 2.48747000 -1.33939500

H 0.07666600 5.81514600 -1.49468200

H 0.82698600 5.45709500 -3.86348200

H 1.59641600 3.21146900 -4.59164300

H 1.67284700 1.30402000 -3.01139200

C 0.93496400 1.58958100 -0.19367200

N 0.31300000 2.39578500 0.85887800

C 0.18982800 1.94811600 2.18687000

C -0.89531200 2.34720600 2.98172700

C 1.14764300 1.07619500 2.72523600

C -1.01089100 1.88260400 4.28976400

H -1.64392400 3.02068600 2.56682600

C 1.01486100 0.60787900 4.03160200

H 2.00305900 0.78602100 2.11203700

C -0.06168800 1.00831300 4.82305900

H -1.86242200 2.20099000 4.89660000

H 1.77033700 -0.07106800 4.43574900

H -0.16166300 0.64221400 5.84747800

C 0.06196600 3.69778400 0.46330400

O -0.36629600 4.60490700 1.16927300

C -7.30404100 -2.41777500 0.42188700

C -7.83879100 -1.70906500 -0.65584800

C -6.99253400 -1.08329800 -1.57283500

C -5.61057900 -1.16667300 -1.41791600

C -5.07226800 -1.87822100 -0.33844900

C -5.92368000 -2.50056100 0.58228700

H -7.96631100 -2.90607300 1.14012100

H -8.92219300 -1.64257100 -0.78097600

H -7.41182700 -0.52578200 -2.41324200

H -4.94518300 -0.67507700 -2.12878600

H -5.49117600 -3.04848000 1.42171400

C -3.60088400 -1.98781800 -0.12289400

O -3.09135500 -2.49698700 0.84420700

O -2.90452700 -1.46955200 -1.14413300

C -1.49849000 -1.37082100 -1.02268900

H -1.06316500 -1.61415500 -2.00025500

H -1.12108000 -2.07065200 -0.26599800

F -1.51330800 0.89466500 -1.63773600

F -1.83837100 0.41614200 0.45517500

C -1.10816800 0.04846000 -0.64350100

C 0.37762500 0.19219600 -0.37619800

H 0.90325600 -0.26865600 -1.22496700

H 0.59951500 -0.43734500 0.49983900

N 4.03105800 -2.37618000 -0.12509200

C 2.95465100 -2.48419600 -1.10875500

C 2.84025900 -3.91222000 -1.63730100

C 3.14407700 -1.43674200 -2.21039000

H 2.03102900 -2.24017900 -0.57168400

H 2.68673600 -4.62573200 -0.81510600

H 1.97066600 -3.96574900 -2.30789700

H 3.72946100 -4.21341600 -2.21040900

H 2.24913900 -1.44442800 -2.84995100

H 3.25988100 -0.43801400 -1.76436800

H 4.01461700 -1.65696100 -2.84558500

C 5.41385600 -2.60725800 -0.54743800

C 5.99238200 -3.80879500 0.19983700

C 6.25375900 -1.33884700 -0.38385400

H 5.37049600 -2.85534000 -1.61530300

H 5.37865800 -4.70654200 0.03894900

H 7.00423900 -4.00663200 -0.18202700

H 6.06442800 -3.61502300 1.28027900

H 5.74395700 -0.47026200 -0.82344300

H 6.46474700 -1.12185500 0.67323400

H 7.21307000 -1.48788000 -0.89937400

C 2.56659600 -2.38055600 1.90509900

H 2.52534500 -1.89418900 2.88930800

H 1.61113900 -2.18236500 1.40163800

H 2.66516800 -3.46536100 2.06126100

C 3.77165800 -1.82609600 1.15763800

H 2.28672200 1.28394400 0.07378500

H 4.67860800 -1.90520500 1.77029300

O 3.39611200 0.85751000 0.26991700

H 3.86092500 1.54426300 0.76323700

H 3.61680000 -0.70443000 0.92957200

Transition state TS3a

Thermal correction to Gibbs free energy = 0.575599

Single-point energy = -1777.312162

Imaginary frequency = -1161.99 cm^{-1}

0 1

C -1.46317400 -1.74778100 1.80921100

C -1.78440200 -2.90847000 2.52040200

C -1.97251700 -4.08712600 1.81179500

C -1.82300700 -4.09246800 0.40765000

C -1.51892700 -2.93820400 -0.29898900

C -1.36321900 -1.72750900 0.40704600

H -1.87408700 -2.87810400 3.60959100

H -2.22148400 -5.01371500 2.33414700

H -1.94955600 -5.03283000 -0.13601100

H -1.40651500 -2.97103100 -1.38502300

C -1.14912800 -0.36564500 -0.05652700

N -0.93998000 0.37087900 1.19627200

C -0.62994300 1.74029000 1.25604000

C 0.13567400 2.26143500 2.31225500

C -1.06294200 2.61196600 0.24734900

C 0.44339400 3.61875300 2.35237000

H 0.48468400 1.59689300 3.10004800

C -0.74205600 3.96767000 0.29026800

H -1.65861600 2.22522100 -0.57580700

C 0.00949500 4.48293700 1.34488000

H 1.04151900 4.00406700 3.18210500

H -1.09185000 4.62402900 -0.51049400

H 0.25861700 5.54586300 1.38117900

C -1.18828400 -0.40216600 2.32015900

O -1.21011900 -0.01294900 3.48491300

C 7.93267700 0.51140000 0.13030000

C 8.12142000 -0.82144200 0.50157000

C 7.10323700 -1.75569900 0.30365000

C 5.89613900 -1.36205800 -0.26960500

C 5.70556700 -0.02605000 -0.64383500

C 6.72605000 0.90992300 -0.43836500

H 8.72905200 1.24236100 0.28641800

H 9.06757900 -1.13352800 0.95017600

H 7.24990000 -2.79692800 0.59907900

H 5.09383900 -2.08541900 -0.42119700

H 6.56257600 1.94927100 -0.72988900

C 4.42525200 0.44481400 -1.24589300

O 4.15585100 1.60140100 -1.45477800

O 3.61054500 -0.57591900 -1.54714100

C 2.28843200 -0.29048700 -1.96247100

H 2.03335300 -0.99145600 -2.76711300

H 2.20810100 0.74068000 -2.32920700

F 1.43772500 -1.79084700 -0.37409600

F 1.78836600 0.25605900 0.25650700

C 1.33520500 -0.49431700 -0.79570000

C -0.10548000 -0.14302500 -1.13439700

H -0.37622600 -0.74833000 -2.01249100

H -0.09263000 0.90210400 -1.47936900

N -3.80308700 0.02269300 -0.90261700

C -4.42056800 -0.12249900 0.47629600

C -5.87102700 -0.59985500 0.51508200

C -4.24781600 1.12598700 1.32949800

H -3.80981100 -0.91957800 0.92515400

H -6.01807400 -1.57434900 0.03217300

H -6.15111600 -0.71884500 1.57210500

H -6.56784700 0.12280200 0.07011500

H -4.41442700 0.85202500 2.38110600

H -3.23784400 1.54604400 1.25499500

H -4.97690700 1.90872300 1.06971500

C -4.03842100 1.33998800 -1.58246800

C -3.00163400 1.63800900 -2.66924100

C -5.45042300 1.53047200 -2.12229500

H -3.87724600 2.08008100 -0.79072000

H -3.28761700 1.22821700 -3.64603800

H -2.91998000 2.72893700 -2.78258900

H -2.00698600 1.25105700 -2.41518300

H -5.70195500 0.78130600 -2.88831800

H -6.21324700 1.49990000 -1.33429500

H -5.50829500 2.51999000 -2.59956000

C -4.11162800 -1.19018500 -1.70647000

C -3.28777600 -1.40593100 -2.96365500

H -5.17977800 -1.18791500 -1.96415900

H -3.94990300 -2.03593500 -1.02491600

H -3.41215500 -2.45394200 -3.27353300

H -3.61808300 -0.77679700 -3.79899900

H -2.21717600 -1.23132300 -2.79729200

H -2.61438300 -0.05808200 -0.62260700

Transition state TS3b

Thermal correction to Gibbs free energy = 0.595975

Single-point energy = -1853.773906

Imaginary frequency = -1164.58 cm^{-1}

0 1

C -1.21695300 -1.33740900 1.43097300

C -1.73876900 -2.35935600 2.23021000

C -1.97742300 -3.59648400 1.64622900

C -1.68802700 -3.79726100 0.27930000

C -1.18416100 -2.77833500 -0.51750300

C -0.95666100 -1.51498600 0.06195400

H -1.95130600 -2.17760800 3.28703600

H -2.38397600 -4.41853600 2.23971000

H -1.87305900 -4.77982500 -0.16347100

H -0.97722400 -2.95491300 -1.57597900

C -0.55933000 -0.25055900 -0.53288600

N -0.46194600 0.64183300 0.62385300

C -0.17029900 2.01237100 0.51154400

C 0.50256200 2.69006400 1.53948700

C -0.53730700 2.72029100 -0.64189700

C 0.79099700 4.04675200 1.41057800

H 0.79558700 2.14708500 2.43663700

C -0.23360900 4.07445700 -0.76698600

H -1.07917400 2.20343500 -1.43317200

C 0.42937100 4.74790500 0.25876500

H 1.31617100 4.55980700 2.22021500

H -0.52817000 4.60736900 -1.67444000

H 0.66430400 5.81028000 0.16146900

C -0.90060900 0.05060800 1.79466400

O -1.05827200 0.60501100 2.87984600

C 8.48918900 0.33728500 0.52006500

C 8.56481400 -0.89950600 1.16387700

C 7.52423900 -1.82130100 1.03659200

C 6.40771300 -1.51177500 0.26304400

C 6.33083800 -0.27252500 -0.38469600

C 7.37339600 0.65202100 -0.25066400

H 9.30281900 1.05889100 0.62109400

H 9.43969500 -1.14579400 1.77033300

H 7.58217400 -2.78648800 1.54449300

H 5.58815800 -2.22488100 0.16465300

H 7.29835600 1.61635000 -0.75696000

C 5.15020100 0.11055800 -1.21108800

O 4.97823000 1.20610100 -1.68462400

O 4.30577000 -0.91578600 -1.38293700

C 3.05661800 -0.67098300 -2.00153500

H 2.84135800 -1.51852000 -2.66429100

H 3.08476000 0.25822400 -2.58466600

F 1.93473200 -1.75818900 -0.25235400

F 2.36294700 0.35755100 -0.01660200

C 1.97335200 -0.57690600 -0.93966800

C 0.60494500 -0.23446100 -1.50252400

H 0.39057000 -0.95730000 -2.30491300

H 0.70375800 0.74557600 -1.99539400

N -4.77343300 -0.10453800 -0.27508100

C -4.24155800 0.48534300 1.01120300

C -5.17731400 0.31291900 2.19527700

C -3.80507100 1.92868800 0.80723200

H -3.33857600 -0.10650100 1.19958500

H -5.46384700 -0.73696600 2.35114000

H -4.64944600 0.65030300 3.09902600

H -6.08863600 0.92140400 2.09324900

H -3.18646400 2.22595600 1.66633100

H -3.19117100 2.02143800 -0.09869900

H -4.65366300 2.62648200 0.74337300

C -6.06266300 0.53577700 -0.74956300

C -5.98357300 0.85907800 -2.23665300

C -7.31189200 -0.25588700 -0.38852300

H -6.11237100 1.49133000 -0.21241500

H -5.91362200 -0.04614100 -2.85570900

H -6.89336900 1.40211600 -2.53102200

H -5.11932500 1.50077100 -2.45830700

H -7.39829200 -1.18863100 -0.96395800

H -7.35845400 -0.49688500 0.68174300

H -8.18806200 0.36383100 -0.62816000

C -4.74995100 -1.59895000 -0.23070700

C -4.79070100 -2.25719600 -1.59715300

H -5.56439000 -1.95178600 0.41385000

H -3.80499400 -1.86068800 0.26381200

H -4.59404800 -3.33158600 -1.46905000

H -5.76645500 -2.15437000 -2.09162600

H -4.01276500 -1.83287000 -2.24783800

H -4.00341800 0.14000800 -0.99216700

O -2.73480600 0.24694200 -1.90087300

H -1.72555400 0.06599600 -1.30436000

H -2.62088600 0.97874900 -2.51692300

Complex XB-1

Thermal correction to Gibbs Free Energy= 0.353369

Single-point energy= -3642.687976

0 1

C -0.59769700 4.14314700 0.51525300

C -0.73849600 4.21840200 -0.87235200

C 0.04124400 3.41155500 -1.70214800

C 0.95707800 2.51963500 -1.14893300

C 1.09897000 2.44320900 0.24162700

C 0.32177500 3.25973700 1.07197900

H -1.20858100 4.77466900 1.16371700

H -1.46228500 4.91027200 -1.30948800

H -0.07195600 3.47021100 -2.78670300

H 1.55259300 1.87084200 -1.79207400

H 0.43969100 3.18481400 2.15448200

C 2.01548000 1.46388800 0.88307600

O 2.09764700 1.27356400 2.06984400

O 2.75138100 0.79116900 -0.02342500

C 3.44383200 -0.35926600 0.39072100

H 3.36846800 -0.51079100 1.47532600

H 4.50231900 -0.26836900 0.10538200

C 2.87718600 -1.56792500 -0.33706500

F 3.10438900 -1.48003000 -1.65554000

F 3.49213600 -2.67239300 0.10250100

Br 0.95298000 -1.74114100 -0.07171600

N -2.26506800 -0.84481000 0.20598600

C -3.13957100 -1.89663100 -0.33296600

C -4.57765900 -1.90749000 0.20893700

C -2.49832700 -3.27546900 -0.16323000

H -3.21423000 -1.71613300 -1.41387600

H -5.04706000 -0.91482500 0.15101900

H -5.19284800 -2.60400300 -0.38193000

H -4.61943900 -2.24297500 1.25724600

H -3.14865700 -4.06317500 -0.57604800

H -1.53121000 -3.32300500 -0.68508800

H -2.32482900 -3.51299300 0.89896200

C -2.17557600 0.40396600 -0.56058200

C -3.41587500 1.30578700 -0.49754800

C -1.76247400 0.16953400 -2.01265900

H -1.34607800 0.96651300 -0.10297300

H -3.72336200 1.50846900 0.54027200

H -3.20447800 2.27571300 -0.97539000

H -4.27057400 0.85368900 -1.02627200

H -0.89815900 -0.50790400 -2.07272700

H -2.57693700 -0.25086700 -2.62321500

H -1.47869500 1.12739700 -2.47345800

C -2.39097100 -0.67348600 1.64682100

C -1.33954000 0.22169100 2.28632400

H -2.31820100 -1.67360300 2.10395000

H -3.38971700 -0.28412300 1.93959400

H -1.41722300 0.15084400 3.38218800

H -0.32134600 -0.07536800 1.99752100

H -1.47324900 1.28055300 2.02020300

Complex HB-1

Thermal correction to Gibbs Free Energy= 0.126035

Single-point energy= -3348.053686

0 1

C -4.55848800 -0.28212600 0.33620200

C -4.60044100 1.03470800 -0.12535900

C -3.45606500 1.62553400 -0.66428200

C -2.26796400 0.90301900 -0.74392100

C -2.22389300 -0.41726500 -0.27762500

C -3.37221800 -1.00699900 0.26223000

H -5.45346700 -0.74438300 0.75812200

H -5.53048900 1.60471800 -0.06446500

H -3.48950700 2.65580100 -1.02500300

H -1.37188600 1.36436800 -1.16097000

H -3.32325200 -2.03535100 0.62520900

C -0.97403600 -1.22531400 -0.31387400

O -0.87110100 -2.35469800 0.08665700

O 0.04205100 -0.55123000 -0.89266100

C 1.28087200 -1.19366500 -1.04476700

H 1.65851900 -0.99116000 -2.05551200

H 1.19236000 -2.27954400 -0.89148100

C 2.28970700 -0.68618800 -0.02857100

F 1.95198600 -1.03454200 1.21375700

F 3.48424200 -1.21705900 -0.29372400

Br 2.46998400 1.26840100 -0.06536600

O -0.48685100 0.63002800 2.07829600

H 0.11300000 1.02195200 1.43316700

H -1.34841800 0.97093900 1.80991900

Complex XB-2

Thermal correction to Gibbs Free Energy= 0.376273

Single-point energy= -3719.147048

0 1

C 1.57466900 3.56097000 -0.93324400

C 1.97770900 3.73734700 0.39170600

C 1.13178800 3.36569000 1.43857200

C -0.11311400 2.80540000 1.16475900

C -0.51588000 2.62183100 -0.16374200

C 0.32731900 3.00942200 -1.21161800

H 2.23701800 3.85023900 -1.75180100

H 2.95780300 4.16764700 0.61025700

H 1.44729000 3.50719500 2.47440500

H -0.77058600 2.50366500 1.98073500

H 0.00159700 2.86017300 -2.24282300

C -1.81838600 1.99586200 -0.51457500

O -2.30211600 1.98129000 -1.61637800

O -2.40804600 1.42792300 0.55898200

C -3.65341800 0.79921900 0.39589900

H -4.08358900 0.99159600 -0.59545000

H -4.33476100 1.17253000 1.17510600

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F -3.01689100 -0.96582900 1.82394000

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Br -2.39960600 -1.57872900 -0.71548400

N 2.52947500 -1.11912000 0.07166700

C 3.01335600 -1.12699800 -1.32544300

C 2.94383900 0.22252700 -2.05233600

C 2.29387700 -2.20691700 -2.13508800

H 4.07397300 -1.41366900 -1.28107300

H 3.40246400 1.03341400 -1.47004900

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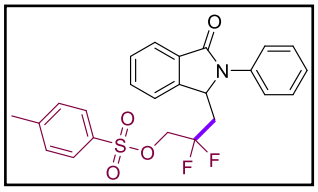

2,2-difluoro-3-(3-oxo-2-phenylisoindolin-1-yl)propyl 4-methylbenzenesulfonate (3ab)

Following the experimental procedure GP3, two independent reactions of **1k** (0.1 mmol, 22 mg, 1 equiv) and **2r** (0.2 mmol, 59 mg, 2 equiv) were performed for 24 h. The product **3ab** was purified by flash column chromatography of the reaction mixture on silica gel (Gradient 0-10% EtOAc/Hexane), affording a yellow liquid (61 mg, 66% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 4.5 Hz, 2H), 7.57 – 7.53 (m, 3H), 7.48 – 7.45 (m, 2H), 7.33 – 7.27 (m, 3H), 5.48 (d, *J* = 8.0 Hz, 1H), 4.10 – 3.98 (m, 2H), 2.55 – 2.49 (m, 1H), 2.46 (s, 3H), 2.29 – 2.17 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.80, 145.8, 144.0, 136.2, 132.6, 131.9, 131.9, 130.2 (2C), 129.4 (2C), 129.0, 128.0 (2C), 126.0, 124.2, 123.7, 123.6, 123.5, 119.7, (t, *J* = 245.7 Hz), 68.3(t, *J* = 35.8 Hz), 55.3, 36.1 (t, *J* = 22.1 Hz), 21.8.

^{19}F NMR (471 MHz, $CDCl_3$) δ -100.9 (d, *J* = 253.4 Hz, 1F), -104.4 (d, *J* = 259.3 Hz, 1F).

IR (neat, cm^{-1}) 3005, 1706, 1362, 1220, 1180, 1021, 913, 822, 736.

HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $[C_{24}H_{22}F_2NO_4S]^+$ 458.1232; found 458.1221.

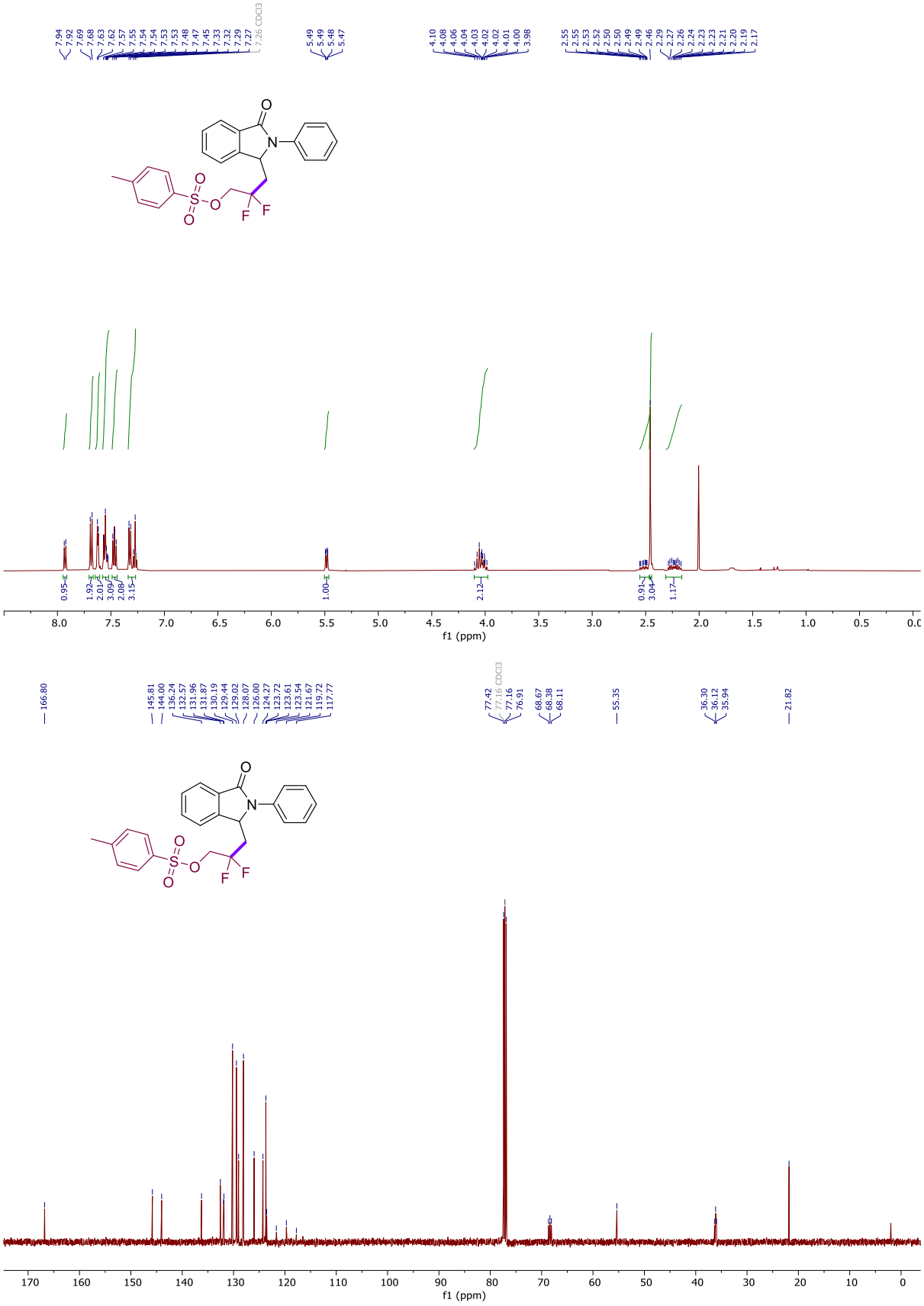

Figure S109. ^{1}H NMR (500 MHz, top) and ^{13}C {1H} NMR (126 MHz, bottom) Spectra of **3ab** in $CDCl_3$ at 298 K.

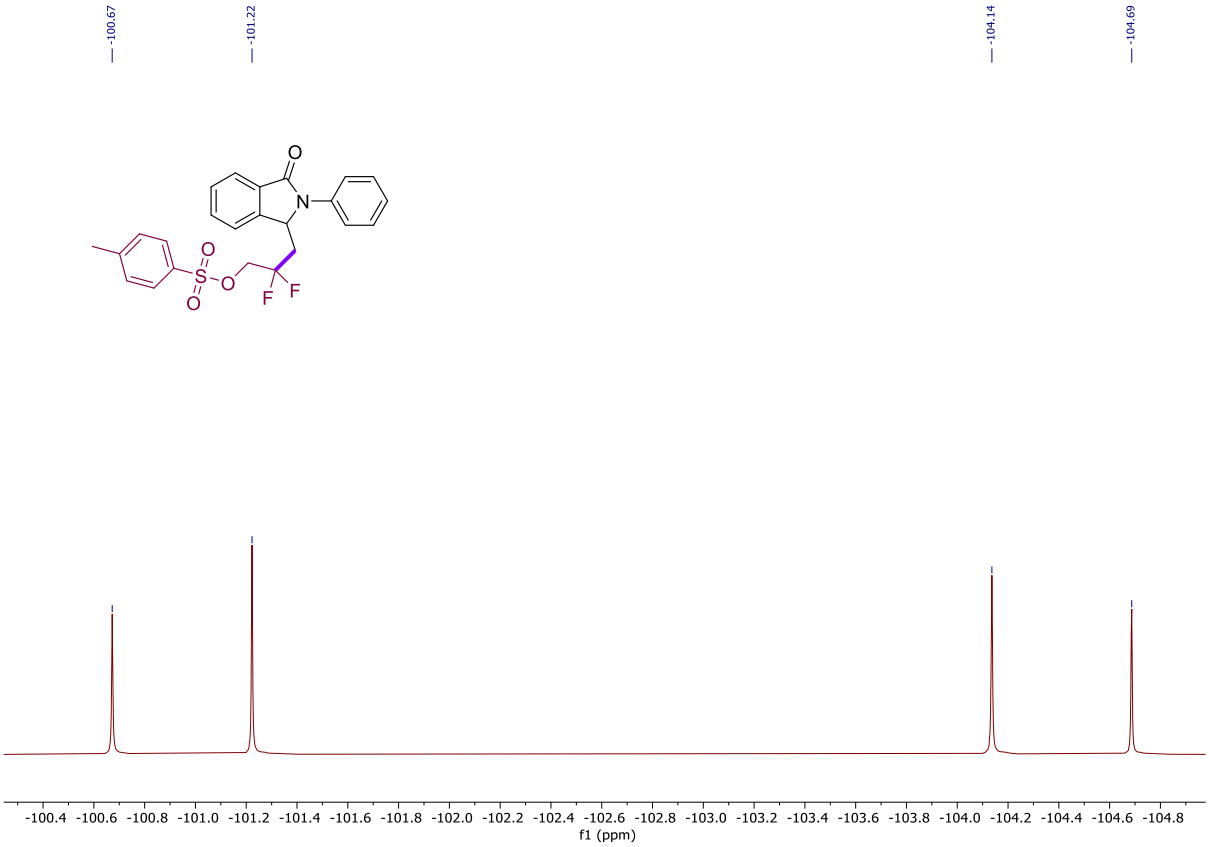

Figure S110. ^{19}F NMR (471 MHz) Spectra of **3ab** in $CDCl_3$ at 298 K.

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