Pd-Catalyzed Enantioselective Reductive Heck Reaction of *mono*-Fluoro, *gem*-Difluoro, and Trifluoromethyl tethered-Alkenes

Naveen Sihag,[a] Hemaang Bhartiya,[a] Swati Jain,[a] Jitendra Singh,[b] S. Rajagopala Reddy[b],* and M Ramu Yadav[a]*

[a]Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi, 110016, India. Phone number: (+91) 11-2659-1506; e-mail address: ramuyadav@chemistry.iitd.ac.in.

[b]Department of Chemistry, School of Chemical Sciences and Pharmacy, Central University of Rajasthan, NH-8, Bandarsindri, Ajmer, Rajasthan 305817, India; e-mail address: rajagopala.seelam@curaj.ac.in.

Table of Contents

1. General Information

Experimental: All the inert condition reactions were performed in a nitrogen atmosphere using Glove box and Schlenk line techniques. All glassware was oven-dried overnight at 100 ºC before use. Catalytic reactions were performed in commercially available 7.0 mL screw cap vials fitted with PTFE/silicone septa purchased from Sigma-Aldrich.

Chromatography: Analytical Thin Layer Chromatography (TLC) was performed on Merck and GLR precoated silica gel 60 F_{254} plates, using UV light as the visualization agent. Chromatographic purification of products was accomplished by column chromatography on Finar silica gel (100-200 mesh). The solvents were removed under reduced pressure using a rotary evaporator to obtain the desired compounds.

Characterization: All proton nuclear magnetic resonance spectra (^{1}H NMR), proton decoupled carbon nuclear magnetic resonance spectra [^{13}C{^{1}H} NMR], and fluorine nuclear magnetic resonance spectra (^{19}F NMR) were collected on Bruker Ascend 500 MHz and JEOL 400 MHz (the respective frequencies are for ^{1}H (500 MHz and 400 MHz), ^{13}C (126 MHz and 101 MHz), and ^{19}F (471 MHz and 377 MHz). Chemical shifts are reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS, 0.0 ppm), all ^{1}H NMR and ^{13}C NMR spectra referenced to residual solvent signal (^{1}H, $CDCl_3$ = 7.26 ppm) and (^{13}C, CDC_{l3} = 77.00 ppm). Coupling constants (*J*) are reported in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; m, multiplet; dd, doublet of doublets; ddd, doublet of doublet of doublets; dq, doublet of quartet; dp, doublet of pentet; bs, broad singlet; bd, broad doublet; bt, broad triplet; bq, broad quartet; tq, triplet of quartet. High-resolution mass spectra (HRMS) were obtained using Waters Xevo-G2XQTOF instruments with the electrospray ionization (ESI) method. The gas chromatography-mass spectrometry (GC-MS) analysis was performed using an Agilent 5977B GC/MSD spectrometer. Single crystal X-ray diffractions were recorded using Bruker AXS Smart Apex CCD diffractometer and Rigaku XtaLab Synergy Custom X-Ray Diffractometer. Optical rotations were recorded on Rudolph, AUTOPOL V digital polarimeter using a 10 cm sample cell, and $[\alpha]_D$ values are given in $deg.dm^{-1}.g^{-1}.mL$; concentration c is listed in $g.mL^{-1}$ and all data are reported as follows: $[\alpha]_D^{temp}$ (c = $g.mL^{-1}$, solvent). Enantiomeric excesses (*ee*) were determined by chiral HPLC analysis (Shimadzu) LC-20AD using Chiralcel OJ-H, AD-H, and OD-H columns with *n*-Hexane and ^{i}PrOH as solvents. Retention times are reported

using the following abbreviation: t_r. Preparative HPLC (Shimadzu) LC-20AP having a C18 column with acetonitrile (CH_3CN) and H_2O as solvents have been used in purification. The melting points of compounds were recorded using DIGITAL MELTING POINT APP. by UNITECH SALES.

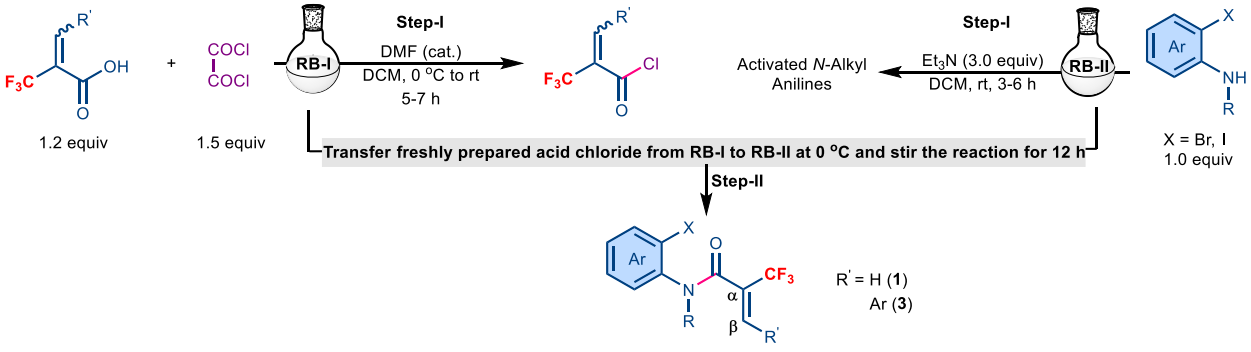
Materials: Unless specified otherwise, all reagents, chiral ligands, and metal salts were obtained from commercial suppliers (BLD Pharma, Spectrochem, GLR, TCI, Sigma-Aldrich, SRL chemical) and used without further purification. Acrylamide derivatives were synthesized according to the literature. Anhydrous solvents were dried using CaH_2 pre-drying followed by vacuum distillation, and solvents like tetrahydrofuran (THF), and toluene (PhMe) were dried via sodium wire/benzophenone conventional drying agents. Oxalyl chloride was purchased from Spectrochem and distilled under N_2. Triethylamine was distilled and stored over KOH pellets for usage.

2. Synthesis of Substrates

All disubstituted acrylamides were prepared according to the previous reports.[1,2] The known substrates (**1a**, **1a′**, **1b–1j**, **1l–1p**) characterization data were consistent with the reported literature. Further, the general procedure and characterization data for unreported substrates are given.

2.1 General Procedure for the Synthesis of *o*-Halo Trifluoromethyl Acrylamides and *o*–Iodo *β*–Phenyl Trifluoromethyl Acrylamides.

General procedure-I (GP–I):



Scheme S1. Synthesis of trifluoromethyl acrylamides from di- and trisubstituted olefins.

Step 1. Round Bottom Flask I (RB–I): A two–necked round bottom flask equipped with a magnetic stir bar was charged with acrylic acid (1.2 equiv) and dry DCM (0.2 M) was added under

nitrogen atmosphere. The flask was then cooled to 0 ^{o}C using an ice bath and 4−6 drops of dry DMF were added. Afterward, freshly distilled oxalyl chloride (1.5 equiv) was added dropwise to the solution. Then, the solution was slowly allowed to attain room temperature and stirred for 5 to 7 hours with nitrogen (N_2) ballon until the solution turned yellow-orange. The acyl chloride was directly used for the next step without further purification.

Round Bottom Flask II (RB–II): In a separate two−necked round−bottom flask equipped with a magnetic stir bar, *o*-halo aniline derivatives (1.0 equiv), triethylamine (3.0 equiv), and dry DCM (0.2 M) were added and stirred for 3-6 h at room temperature to activate anilines.

Step 2. Then, freshly prepared acryloyl chloride **RB–I** was added dropwise to **RB–II** for 10 to 15 min at 0 ^{o}C under a nitrogen atmosphere. The resultant mixture was allowed to warm up to room temperature and stirred overnight with nitrogen (N_2) ballon until the aniline derivative was consumed completely (monitored by TLC). The reaction mixture was washed with water and extracted with DCM (3.0 times). The organic layer was sequentially washed with 1.0 N HCl solution, 1.0 N NaOH solution, and brine. The final organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated using a rotary evaporator. The residue was purified by SiO_2 column chromatography (100−200 mesh) using a mixture of hexane, DCM, and ethyl acetate to afford the desired acrylamides.

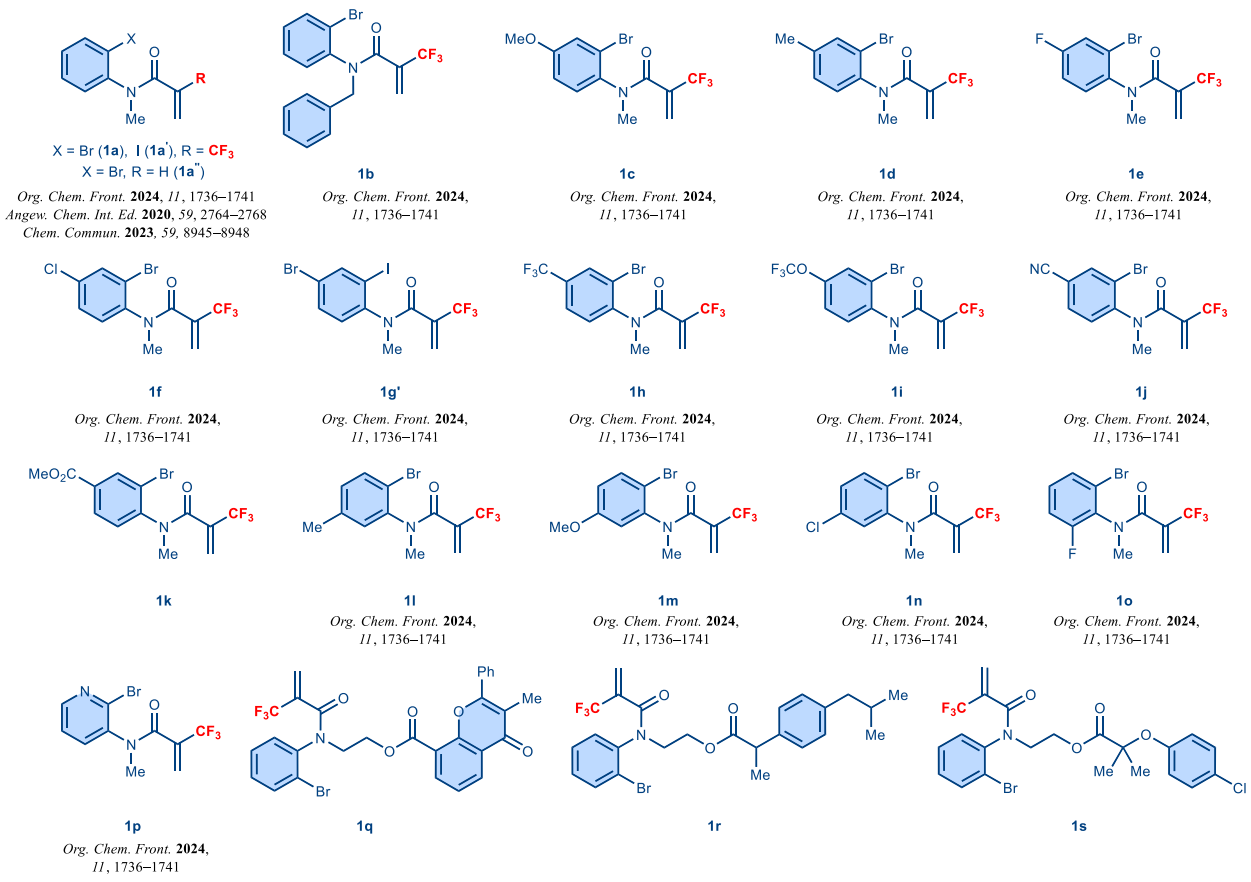


Figure S1. *N*–(2–Haloaryl)–trifluoromethyl acrylamides.

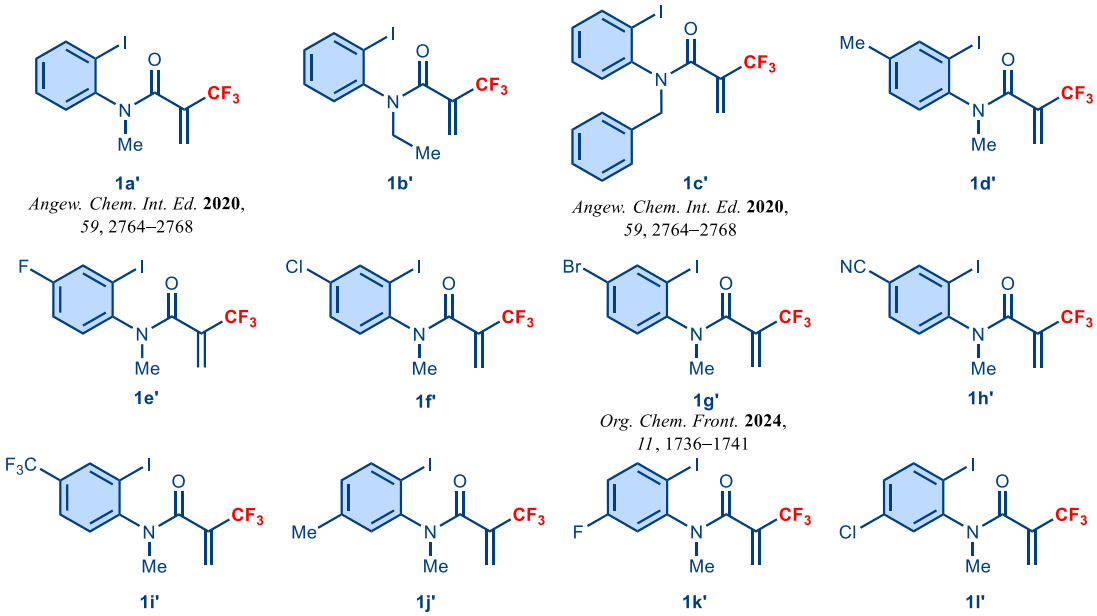


Figure S2. *N*–(2–Iodoaryl)–trifluoromethyl acrylamides.

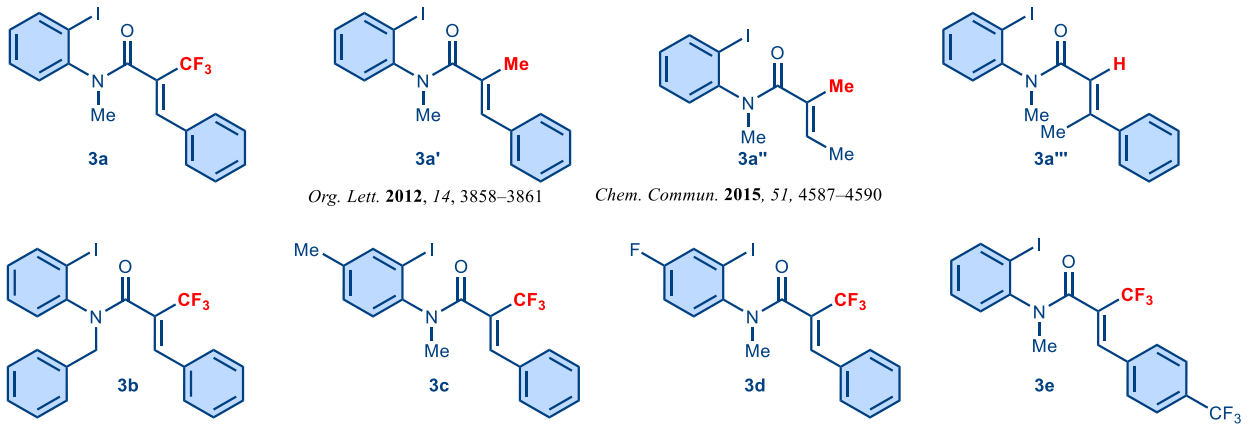
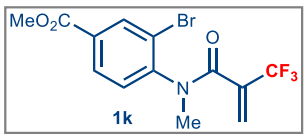


Figure S3. *N*–(2–Haloaryl)–*N*–substituted *β*-phenyl trifluoromethyl acrylamides.

Characterization data of starting materials:

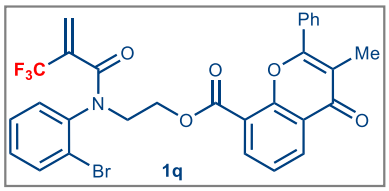
Methyl 3-bromo-4- (*N*-methyl-2-(trifluoromethyl)acrylamido)benzoate (1k):



According to **GP–I**, amide coupling of 2-(trifluoromethyl)acrylic acid (420 mg, 3.0 mmol) with methyl 3–bromo–4–(methylamino)benzoate (610 mg, 2.5 mmol) afforded the desired amide **1k** (130 mg) in 14% yield as a white solid; R_f = 0.35 (3% EtOAc, 30% DCM in hexane); Melting point: 94–96 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.01 (d, J = 7.9 Hz, 1H), 7.30–7.24 (m, 1H), 5.80 (s, 1H), 5.63 (s, 1H), 3.95 (s, 3H), 3.32 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 164.7, 163.4, 146.2, 135.2, 133.9 (q, J = 31.9 Hz), 131.7, 130.04, 129.98, 124.9 (q, J = 5.0 Hz), 122.5, 121.2 (q, J = 274.0 Hz), 52.7, 36.3; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -64.4 ppm; **HRMS (ESI–TOF) *m/z***: $[M+H]^+$ calcd. for $C_{13}H_{12}BrF_3NO_3$: 365.9947, found 365.9953.

2-(*N*-(2-Bromophenyl)-2-(trifluoromethyl)acrylamido)ethyl-3-methyl-4-oxo-2-phenyl-4H-chromene-8-carboxylate (1q):

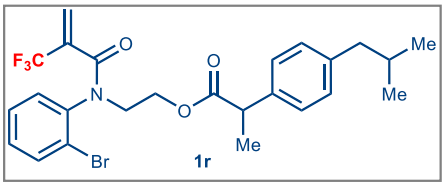


According to **GP–I**, amide coupling of 2-(trifluoromethyl)acrylic acid (336 mg, 2.4 mmol) with 2-((2-bromophenyl)amino)ethyl 3-methyl-4-oxo-2-phenyl-4*H*-chromene-8-carboxylate (957 mg, 2.0 mmol) afforded the desired amide **1q** (302 mg) in 25% yield as a yellow solid; R_f = 0.08 (3% EtOAc, 30% DCM in hexane); Melting point: 78–80 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (dd, J = 7.9, 1.5 Hz, 1H), 8.11 (dd, J = 7.4, 1.2 Hz, 1H), 7.79–7.74 (m, 2H), 7.62–7.49 (m, 4H), 7.41 (t, J = 7.7 Hz, 1H), 7.15 (d, J = 3.3 Hz, 3H), 5.75 (s, 1H),

5.58 (s, 1H), 4.76–4.67 (m, 1H), 4.65–4.57 (m, 1H), 4.50–4.43 (m, 1H), 3.69–3.61 (m, 1H), 2.25 (s, 3H); **$^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)** δ 178.2, 163.8, 163.6, 160.9, 154.5, 140.3, 136.2, 134.1, 133.9 (q, J = 32.3 Hz), 132.9, 131.4, 131.0, 130.6, 130.1, 129.3, 128.6, 128.5, 124.4 (q, J = 5.8 Hz), 124.0, 123.2, 122.8, 121.2 (q, J = 274.0 Hz, one of the quartet peak merged with other peaks), 119.8, 117.6, 61.9, 46.9, 11.8; **$^{19}F\{^{1}H\}$ NMR (471 MHz, $CDCl_3$)** δ -64.4 ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{29}H_{21}BrF_3NO_5Na$: 622.0447, found 622.0466.

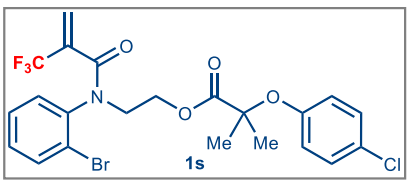
2-(*N*-(2-Bromophenyl)-2-(trifluoromethyl)acrylamido)ethyl 2-(4-isobutylphenyl)propanoate (1r):



According to **GP–I**, amide coupling of 2-(trifluoromethyl)acrylic acid (504 mg, 3.6 mmol) with 2-((2-Bromophenyl)amino)ethyl 2-(4-isobutylphenyl)propanoate (1.2 g, 3.0 mmol) afforded the desired amide **1r** (364 mg) in 23% yield as a yellow liquid; R_f = 0.46 (3% EtOAc, 30% DCM in hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65–7.56 (m, 1H), 7.24–7.16 (m, 2H), 7.16–7.11 (m, 2H), 7.11–7.06 (m, 2H), 7.05–6.96 (m, 1H), 5.72 (s, 1H), 5.53 (d, J = 10.7 Hz, 1H), 4.73–4.63 (m, 0.5H), 4.56–4.48 (m, 0.5H), 4.37–4.30 (m, 0.5H), 4.29–4.22 (m, 1H), 4.02–3.95 (m, 0.5H), 3.65–3.54 (m, 1H), 3.52–3.38 (m, 1H), 2.44 (d, J = 7.2 Hz, 2H), 1.84 (sept, J = 6.8 Hz, 1H), 1.41 (dd, J = 20.5, 7.1 Hz, 3H), 0.89 (bd, J = 6.6 Hz, 6H); **$^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)** δ 174.40, 174.38, 163.7, 163.6, 140.59, 140.55, 139.8, 137.52, 137.49, 134.2, 134.1, 133.9, 133.8, 131.6, 130.12, 130.07, 129.34, 129.31, 128.63, 128.61, 127.14, 127.10, 124.3 (dq, J = 10.8, 5.5 Hz, this due to two quartet merging), 122.9, 122.8, 121.23 (q, J = 274.1 Hz), 121.21 (q, J = 274.2 Hz), 61.6, 60.9, 47.5, 46.2, 45.0, 44.9, 30.14, 30.13, 22.4, 22.3, 18.5, 18.3; **$^{19}F\{^{1}H\}$ NMR (471 MHz, $CDCl_3$)** δ -64.2 ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{25}H_{27}BrF_3NO_3Na$: 548.1019, found 548.1031.

2-(*N*-(2-Bromophenyl)-2-(trifluoromethyl)acrylamido)ethyl-2-(4-chlorophenoxy)-2-methylpropanoate (1s):

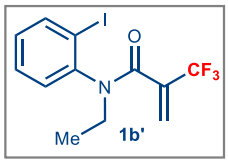


According to **GP–I**, amide coupling of 2-(trifluoromethyl)acrylic acid (840 mg, 6.0 mmol) with 2-((2-Bromophenyl)amino)ethyl 2-(4-chlorophenoxy)-2-

methylpropanoate (2.1 g, 5.0 mmol) afforded the desired amide **1s** (1.06 g) in 40% yield as a yellow liquid; R_f = 0.42 (3% EtOAc, 30% DCM in hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (dd, J = 7.9, 1.3 Hz, 1H), 7.28 (td, J = 7.5, 1.2 Hz, 1H), 7.22 (td, J = 7.7, 1.7 Hz, 1H), 7.20–7.14 (m, 3H), 6.78–6.72 (m, 2H), 5.76 (s, 1H), 5.56 (s, 1H), 4.64 (ddd, J = 14.6, 7.4, 4.1 Hz, 1H), 4.43 (ddd, J = 11.4, 5.6, 4.3 Hz, 1H), 4.26 (ddd, J = 11.6, 7.4, 3.9 Hz, 1H), 3.48 (ddd, J = 14.6, 5.6, 4.1 Hz, 1H), 1.52 (s, 6H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 173.5, 163.6, 153.8, 140.0, 134.0, 133.7 (q, J = 32.0 Hz), 131.4, 130.2, 129.0, 128.7, 127.2, 124.5 (q, J = 5.2 Hz), 122.6, 121.1 (q, J = 274.0 Hz), 120.6, 79.3, 61.9, 46.8, 25.2, 24.8; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -64.2 ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{22}H_{20}BrClF_3NO_4Na$: 556.0109, found 556.0103.

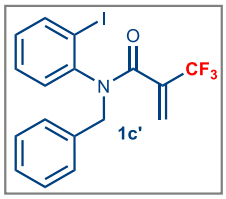
***N*-Ethyl-*N*-(2-iodophenyl)-2-(trifluoromethyl)acrylamide (1b′):**



According to **GP–I**, amide coupling of *N*-ethyl-2-iodoaniline (1.6 mL, 10 mmol) with 2-(trifluoromethyl)acrylic acid (1.68 g, 12 mmol) afforded **1b′** (1.18 g) in 32% yield as a white solid; R_f = 0.21 (5% EtOAc in hexane); Melting point: 70–72 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 5.5 Hz, 1H), 7.37 (t, J = 6.8 Hz, 1H), 7.11 (bd, J = 7.0 Hz, 1H), 7.05 (t, J = 7.1 Hz, 1H), 5.74 (s, 1H), 5.65 (s, 1H), 4.40–4.39 (m, 1H), 3.30–3.17 (m, 1H), 1.20–1.11 (m, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 163.1, 143.6, 140.5, 134.3 (q, J = 31.3 Hz), 131.0, 129.9, 129.4, 124.1 (q, J = 5.0 Hz), 121.4 (q, J = 273.9 Hz), 99.6, 43.9, 11.9; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -64.2 ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{12}H_{11}F_3INNaO$: 391.9730, found 391.9727.

***N*-Benzyl-*N*-(2-iodophenyl)-2-(trifluoromethyl)acrylamide (1c′):[1]**

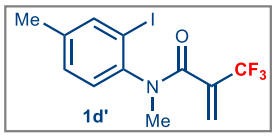


According to **GP–I**, amide coupling of *N*-benzyl-2-iodoaniline (1.3 mL, 7 mmol) with 2-(trifluoromethyl)acrylic acid (1.18 g, 8.4 mmol) afforded **1c′** (875 mg) in 29% yield as a white solid; R_f = 0.26 (5% EtOAc in hexane); Melting point: 53–55 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.9 Hz, 1H), 7.27–7.23 (m, 3H), 7.21–7.12 (m, 3H), 6.99 (td, J = 7.9, 1.0 Hz, 1H), 6.60 (d, J = 7.5 Hz, 1H), 5.83–5.69 (m, 3H), 4.14 (d, J = 14.3 Hz, 1H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 163.4, 142.9, 140.3, 135.7, 134.2 (q, J = 31.5 Hz), 131.7,

130.0, 129.4, 129.1, 128.5, 127.9, 124.2 (bq, J = 5.0 Hz), 121.4 (q, J = 274.7 Hz), 99.3, 51.8; **^{19}F NMR (377 MHz, CDCl$_3$)** δ -64.0 ppm.

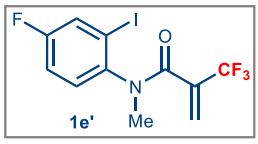
***N*-(2-Iodo-4-methylphenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (1d′):**



According to **GP–I**, amide coupling of 2-iodo-*N*,4-dimethylaniline (2.4 mL, 15 mmol) with 2-(trifluoromethyl)acrylic acid (2.52 g, 18 mmol) afforded **1d′** (2.0 g) in 36% yield as a yellow liquid; R_f = 0.26 (5% EtOAc in hexane).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.71 (s, 1H), 7.16 (bd, J = 7.8 Hz, 1H), 7.03 (bd, J = 8.0 Hz, 1H), 5.78 (s, 1H), 5.68 (s, 1H), 3.26 (s, 3H), 2.32 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 163.7 143.0, 140.7, 140.4, 134.0 (q, J = 31.5 Hz), 130.6, 128.9, 124.6 (q, J = 5.2 Hz), 121.4 (q, J = 274.0 Hz, one of quartet peak merged with other peaks), 98.3, 36.9, 20.4; **^{19}F NMR (377 MHz, CDCl$_3$)** δ -64.2 ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{12}H_{12}F_3INO$: 369.9910, found 369.9906.

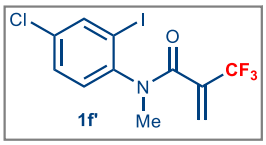
***N*-(4-Fluoro-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (1e′):**



According to **GP–I**, amide coupling of 4-fluoro-2-iodo-*N*-methylaniline (2.1 mL, 15 mmol) with 2-(trifluoromethyl)acrylic acid (2.52 g, 18 mmol) afforded **1e′** (3.14 g) in 56% yield as a white solid; R_f = 0.18 (5% EtOAc in hexane); Melting point: 59–61 ºC. (Due to rotamers of **1e′**, we obtained the product as a mixture with minor isomer).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.60–7.54 (m, 1H), 7.17–7.04 (m, 2H), 5.78 (s, 1H), 5.67 (s, 1H), 3.241 (s, 1.67H), 3.235 (s, 1.32H); **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 163.5, 161.1 (d, J = 254.5 Hz), 141.9 (d, J = 3.2 Hz), 133.9 (q, J = 32.2 Hz), 130.1 (d, J = 8.7 Hz), 127.1 (d, J = 24.7 Hz), 124.6 (bq, J = 5.0 Hz), 121.2 (q, J = 273.9 Hz), 116.8 (d, J = 22.2 Hz), 98.5 (d, J = 8.6 Hz), 36.9; **^{19}F NMR (377 MHz, CDCl$_3$)** δ -64.1, -64.8 (minor isomer), -(110.6–110.7) ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{11}H_9F_4INO$: 373.9659, found 373.9661.

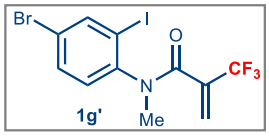
***N*-(4-Chloro-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (1f′):**



According to **GP–I**, amide coupling of 4-chloro-2-iodo-*N*-methylaniline (2.82 mL, 20 mmol) with 2-(trifluoromethyl)acrylic acid (3.36 g, 24 mmol) afforded **1f′** (2.89 g) in 37% yield as a yellow liquid; R_f = 0.21 (5% EtOAc in hexane). (Due to rotamers of **1f′**, we obtained the product as a mixture with minor isomer).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (bs, 1H), 7.36 (d, J = 8.2 Hz, 1H), 7.09 (bd, J = 8.3 Hz, 1H), 5.82 (s, 1H), 5.69 (s, 1H), 3.26 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 163.5, 144.4, 139.7, 134.8, 134.0 (q, J = 31.8 Hz), 130.04, 129.96, 124.88 (q, J = 5.0 Hz), 121.3 (q, J = 274.0 Hz), 98.9, 36.9; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -64.1, -64.7 (minor isomer) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_9ClF_3INO$: 389.9364, found 389.9360.

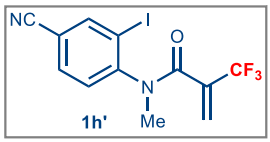
_N_-(4-Bromo-2-iodophenyl)-_N_-methyl-2-(trifluoromethyl)acrylamide (1g′):



According to **GP–I**, amide coupling of 4-bromo-2-iodo-*N*-methylaniline (4.0 g 15.1 mmol) with 2-(trifluoromethyl)acrylic acid (2.54 g, 18.12 mmol) afforded **1g′** (3.22 g) in 49% yield as a white solid; R_f = 0.39 (10% EtOAc in hexane); Melting point: 45–47 °C. (Due to rotamers of **1g′**, we obtained the product as a mixture with minor isomer).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 2.0 Hz, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.03 (d, J = 8.3, 1H), 5.83 (s, 1H), 5.69 (s, 1H), 3.26 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 163.5, 144.9, 142.5, 133.9 (q, J = 32.8 Hz), 133.1, 130.4, 124.9 (q, J = 5.0 Hz), 122.8, 121.3 (q, J = 274.0 Hz), 99.4, 36.8; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -64.2, -64.7 (minor isomer) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_9BrF_3INO$: 433.8859, found 433.8858.

_N_-(4-Cyano-2-iodophenyl)-_N_-methyl-2-(trifluoromethyl)acrylamide (1h′):

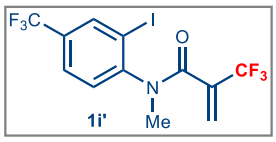


According to **GP–I**, amide coupling of 3-iodo-4-(methylamino)benzonitrile (2.64 g, 10.23 mmol) with 2-(trifluoromethyl)acrylic acid (1.72 g, 12.27 mmol) afforded **1h′** (1.5 g) in 39% yield as a white solid; R_f = 0.17 (10% EtOAc in hexane); Melting point: 84–86 °C. (Due to rotamers of **1h′**, we obtained the product as a mixture with minor isomer).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (bs, 1H), 7.69 (d, J = 7.7 Hz, 1H), 7.33–7.23 (m, 1H), 5.85 (s, 1H), 5.67 (s, 1H), 3.29 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 163.2, 149.8, 143.7, 133.9 (q, J = 31.5 Hz, one quartet peak is merged with other peak), 133.4, 130.0, 125.4 (bq, J = 2.1 Hz,

quartet splitting is not clear), 121.1 (q, J = 273.9 Hz), 116.0, 113.9, 98.8, 36.8; **^{19}F NMR (377 MHz, CDCl$_3$)** δ -64.2, -64.7 (minor isomer) ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{12}H_9F_3IN_2O$: 380.9706, found 380.9698.

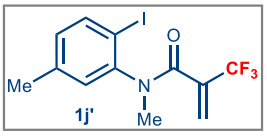
***N*-(2-Iodo-4-(trifluoromethyl)phenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (1i′):**



According to **GP–I**, amide coupling of 2-iodo-*N*-methyl-4-(trifluoromethyl)aniline (2.48 mL, 15 mmol) with 2-(trifluoromethyl)acrylic acid (2.52 g, 18 mmol) afforded **1i′** (3.0 g) in 47% yield as a yellow liquid; R_f = 0.50 (10% EtOAc in hexane). (Due to rotamers of **1i′**, we obtained the product as a mixture with minor isomer).

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.13 (s, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.28 (bd, J = 7.8 Hz, 1H), 5.83 (s, 1H), 5.68 (s, 1H), 3.28 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 163.3, 149.0, 137.4, 133.8 (q, J = 32.4 Hz), 131.8 (q, J = 33.5 Hz), 129.8, 127.0 (q, J = 3.5 Hz), 125.3 (bq, J = 4.6 Hz, quartet splitting is not clear), 122.3 (q, J = 273.4 Hz), 121.2 (q, J = 273.9 Hz), 98.6, 36.7; **^{19}F NMR (377 MHz, CDCl$_3$)** δ -62.6, -64.2, -64.7 (minor isomer) ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{12}H_9F_6INO$: 423.9628, found 423.9622.

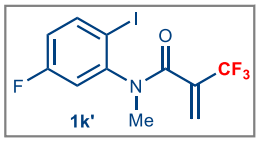
***N*-(2-Iodo-5-methylphenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (1j′):**



According to **GP–I**, amide coupling of 2-iodo-*N*,5-dimethylaniline (2.94 g, 14.67 mmol) with 2-(trifluoromethyl)acrylic acid (2.46 g, 17.6 mmol) afforded **1j′** (3.07 g) in 57% yield as a white solid; R_f = 0.17 (5% EtOAc in hexane); Melting point: 81–83 °C. (Due to rotamers of **1j′**, we obtained the product as a mixture with minor isomer).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.73 (d, J = 8.1 Hz, 1H), 6.99 (s, 1H), 6.87 (d, J =8.0 Hz, 1H), 5.78 (s, 1H), 5.68 (s, 1H), 3.27 (s, 3H), 2.29 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 163.7, 145.5, 140.4, 139.9, 134.0 (q, J = 31.7 Hz), 130.9, 130.2, 124.6 (q, J = 5.0 Hz), 121.4 (q, J = 277.2 Hz), 94.2, 36.8, 20.7; **^{19}F NMR (377 MHz, CDCl$_3$)** δ -64.2, -64.8 (minor isomer) ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{12}H_{12}F_3INO$: 369.9910, found 369.9906.

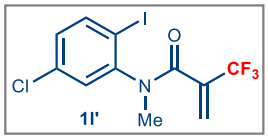
***N*-(5-Fluoro-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (1k′):**



According to **GP–I**, amide coupling of 5-fluoro-2-iodo-*N*-methylaniline (2.41 g, 11.8 mmol) with 2-(trifluoromethyl)acrylic acid (1.98 g, 14.2 mmol) afforded **1k′** (1.18 g) in 27% yield as a white solid; R_f = 0.14 (5% EtOAc in hexane); Melting point: 50–52 °C. (Due to rotamers of **1k′**, we obtained the product as a mixture with minor isomer).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, J = 8.7, 5.9, Hz, 1H), 6.94 (d, J = 7.5 Hz, 1H), 6.85 (td, J = 8.3, 2.7 Hz, 1H), 5.83 (s, 1H), 5.71 (s, 1H), 3.28 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 163.5, 163.2 (d, J = 252.3 Hz), 146.9 (d, J = 8.8 Hz), 141.2 (d, J = 8.3 Hz), 133.9 (q, J = 31.9 Hz), 125.0 (bq, J = 4.6 Hz), 121.2 (q, J = 273.8 Hz), 117.7 (d, J = 21.5 Hz), 117.2 (d, J = 22.8 Hz), 91.9 (d, J = 2.9 Hz), 36.8; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -64.2, -64.8 (minor isomer) -110.3 (dd, J = 13.4, 6.8 Hz) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_9F_4INO$: 373.9659, found 373.9655.

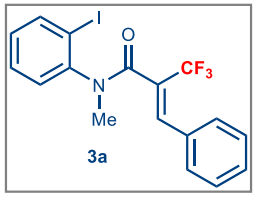
_N_-(5-Chloro-2-iodophenyl)-_N_-methyl-2-(trifluoromethyl)acrylamide (1l′):



According to **GP–I**, amide coupling of 5-chloro-2-iodo-*N*-methylaniline (4.01 g, 15 mmol) with 2-(trifluoromethyl)acrylic acid (2.52 g, 18 mmol) afforded **1l′** (3.0 g) in 51% yield as a white solid; R_f = 0.19 (5% EtOAc in hexane); Melting point: 85–87 °C. (Due to rotamers of **1l′**, we obtained the product as a mixture with minor isomer).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 8.5 Hz, 1H), 7.18 (bs, 1H), 7.06 (dd, J = 8.5, 2.1 Hz, 1H), 5.84 (s, 1H), 5.69 (s, 1H), 3.28 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 163.4, 146.7, 141.0, 135.6, 134.0 (q, J = 31.9 Hz), 130.2, 129.8, 125.0 (bq, J = 4.5 Hz), 121.3 (q, J = 276.4 Hz), 96.0, 36.8; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -64.2, -64.7 (minor isomer) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_9ClF_3INO$: 389.9364, found 389.9366.

(*Z*)-*N*-(2-Iodophenyl)-*N*-methyl-3-phenyl-2-(trifluoromethyl)acrylamide (3a):



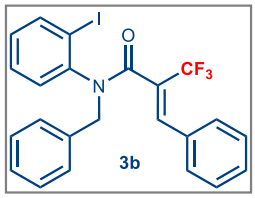
According to **GP–I**, amide coupling of 3-phenyl-2-(trifluoromethyl)acrylic acid[3] (864 mg, 4.0 mmol, used ~30:70 to ~40:60 ratio of *Z*/*E* isomer compound) with 2-iodo-*N*-methylaniline (769 mg, 3.3 mmol) afforded the desired amide **3a** (714 mg) in 50% yield as a white solid; R_f = 0.22 (3% EtOAc, 30% DCM in hexane); Melting point: 83–85 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.9 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.31–7.21 (m, 4H), 7.15 (s, 1H), 7.10–7.04 (m, 3H), 3.35 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.4 (q, J = 2.7 Hz), 145.8, 140.4, 140.0 (q, J = 3.7 Hz), 132.3, 129.95, 129.94, 129.8, 129.4, 128.7 (q, J = 2.6 Hz), 128.2, 126.1 (q, J = 32.4 Hz), 121.6 (q, J = 274.9 Hz), 98.4, 36.7; **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -56.7 ppm; **HRMS (ESI−TOF) *m/z***: $[M+Na]^+$ calcd. for $C_{17}H_{13}IF_3NONa$: 453.9886, found 453.9892.

Note: The independent amide coupling with *E*-isomer resulted in the *E/Z* isomerization. Therefore, the overall yield of *Z*-amide is higher.

Note: Compounds **3a'** and **3a''** are prepared according to the reported procedure.[2]

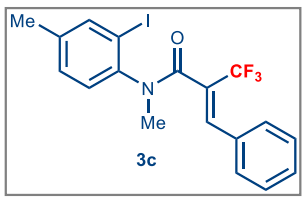
(*Z*)-*N*-Benzyl-*N*-(2-iodophenyl)-3-phenyl-2-(trifluoromethyl)acrylamide (3b):



According to **GP–I**, amide coupling of 3-phenyl-2-(trifluoromethyl)acrylic acid[3] (864 mg, 4.0 mmol, used ~30:70 to ~40:60 ratio of *Z*/*E* isomer compound) with *N*-benzyl-2-iodoaniline (1.0 g, 3.3 mmol) afforded the desired amide **3b** (949 mg) in 47% yield as a white solid; R_f = 0.38 (3% EtOAc, 30% DCM in hexane); Melting point: 74–76 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.9 Hz, 1H), 7.30–7.20 (m, 8H), 7.18 (s, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.10–7.03 (m, 2H), 6.99 (t, J = 7.7 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 5.82 (d, J = 14.3 Hz, 1H), 4.21 (d, J = 14.3 Hz, 1H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.0 (q, J = 2.4 Hz), 142.9, 140.2, 139.4 (q, J = 4.0 Hz), 135.8, 132.2, 131.8, 129.9, 129.34, 129.32, 129.2, 128.7 (bq, J = 2.4 Hz), 128.4, 128.2, 127.8, 126.1 (q, J = 32.5 Hz), 121.6 (q, J = 274.9 Hz), 99.1, 51.6; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -56.5 ppm; **HRMS (ESI−TOF) *m/z***: $[M+Na]^+$ calcd. for $C_{23}H_{17}IF_3NONa$: 530.0199, found 530.0215.

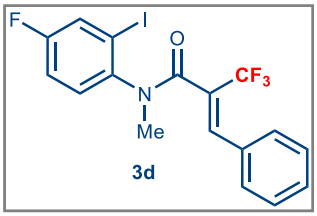
(*Z*)-*N*-(2-Iodo-4-methylphenyl)-*N*-methyl-3-phenyl-2-(trifluoromethyl)acrylamide (3c):



According to **GP–I**, amide coupling of 3-phenyl-2-(trifluoromethyl)acrylic acid[3] (1.3 g, 6.0 mmol, used ~30:70 to ~40:60 ratio of *Z*/*E* isomer compound) with 2-iodo-*N*,4-dimethylaniline (1.2 g, 5.0 mmol) afforded the desired amide **3c** (796 mg) in 36% yield as a yellow solid; R_f = 0.22 (3% EtOAc, 30% DCM in hexane); Melting point: 61–63 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.32–7.27 (m, 3H), 7.20–7.14 (m, 2H), 7.14–7.08 (m, 3H), 3.32 (s, 3H), 2.33 (s, 3H); **$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$)** δ 165.6 (bq, J = 2.7 Hz), 143.1, 140.7, 140.3, 139.8 (q, J = 3.7 Hz), 132.4, 130.6, 129.4, 129.2, 128.9 (bq, J = 2.6 Hz), 128.3, 126.2 (q, J = 32.5 Hz), 121.6 (q, J = 275.0 Hz), 98.2, 36.8, 20.5; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -56.6 ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{18}H_{15}IF_3NONa$: 468.0043, found 468.0045.

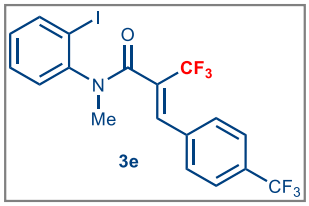
(*Z*)-*N*-(4-Fluoro-2-iodophenyl)-*N*-methyl-3-phenyl-2-(trifluoromethyl)acrylamide (3d):



The above method **GP–I**, amide coupling of 3-phenyl-2-(trifluoromethyl)acrylic acid[3] (259 mg, 1.2 mmol, used ~30:70 to ~40:60 ratio of *Z*/*E* isomer compound) with 4-fluoro-2-iodo-*N*-methylaniline (251 mg, 1.0 mmol) afforded the desired amide **3d** (145 mg) in 32% yield as a yellow solid; R_f = 0.22 (3% EtOAc, 30% DCM in hexane); Melting point: 65–67 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dd, J = 7.5, 2.7 Hz, 1H), 7.34–7.27 (m, 3H), 7.22 (dd, J = 8.6, 5.3 Hz, 1H), 7.17 (s, 1H), 7.15–7.08 (m, 3H), 3.32 (s, 3H); **$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$)** δ 165.4 (bq, J = 2.0 Hz), 161.2 (d, J = 254.7 Hz), 142.1 (d, J = 3.3 Hz), 140.1 (q, J = 3.7 Hz), 132.1, 130.5 (d, J = 8.6 Hz), 129.6, 128.9 (q, J = 2.3 Hz), 128.4, 127.2 (d, J = 24.6 Hz), 126.2 (q, J = 32.5 Hz), 121.5 (q, J = 274.8 Hz), 116.9 (d, J = 22.1 Hz), 98.5 (d, J = 8.8 Hz), 36.9; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -56.5, -110.5 (q, J = 7.0 Hz); **HRMS (ESI−TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{17}H_{12}IF_4NONa$: 471.9792, found 471.9792.

(*Z*)-*N*-(2-Iodophenyl)-*N*-methyl-2-(trifluoromethyl)-3-(4-trifluoromethyl)phenyl acrylamide (3e):

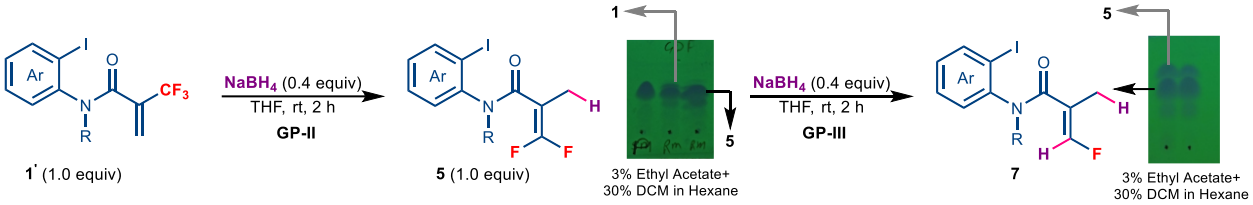


The above method **GP–I**, amide coupling of 2-(trifluoromethyl)-3-(4-(trifluoromethyl)phenyl)acrylic acid[3] (444 mg, 1.2 mmol, used ~30:70 to ~40:60 ratio of *Z*/*E* isomer compound) with 2-iodo-*N*-methylaniline (303 mg, 1.3 mmol) afforded the desired amide **3e** (306 mg) in 47% yield as a white solid; R_f = 0.28 (3% EtOAc, 30% DCM in hexane); Melting point: 45–47 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 7.9 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 7.4 Hz, 1H), 7.19 (s, 1H), 7.16–7.08 (m, 3H), 3.36 (s, 3H); **$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$)** δ 164.7 (bq, J = 2.5 Hz), 145.5, 140.5, 138.2 (q, J = 3.8 Hz), 135.9, 131.1 (q,

J = 32.8 Hz), 130.2, 130.1, 129.8, 128.7 (bq, J = 2.4 Hz), 128.4 (q, J = 32.6 Hz), 125.3 (q, J = 3.7 Hz), 123.7 (q, J = 272.3 Hz), 121.2 (q, J = 275.1 Hz), 98.5, 36.7; **^{19}F NMR (377 MHz, CDCl$_3$)** δ -56.5, -62.9 ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{18}H_{13}IF_6NO$: 499.9941, found 499.9954.

2.2 General Procedure for the Synthesis of *o*-Iodoaryl *gem*-Difluoro and Monofluoro Acrylamides (GP-II & III):



Scheme S2. Synthesis of *o*-iodoaryl *gem*-difluoro and monofluoromethyl acrylamides.

General Procedure-II (GP-II): A round bottom flask equipped with a magnetic stir bar was charged with *o*-iodo trifluoromethyl acrylamide **1'** (1.0 equiv) and sodium borohydride (0.4 equiv). Later, the RB was introduced into the glove box to add THF (0.5 M). Then, the reaction was stirred inside the glove box at room temperature for 2 hours. After completion of the reaction (monitored by TLC), the reaction mixture was washed with water and extracted with DCM (3 times). The combined organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated in a rotary evaporator. The residue was purified by SiO_2 column chromatography (100−200 mesh) using a mixture of hexane, DCM, and ethyl acetate to afford the desired acrylamides (**5a-5l**).

A similar procedure has been followed to prepare monofluoromethyl acrylamides (**7a-7e**) from *gem*-difluoro methyl acrylamides (**GP-III**).

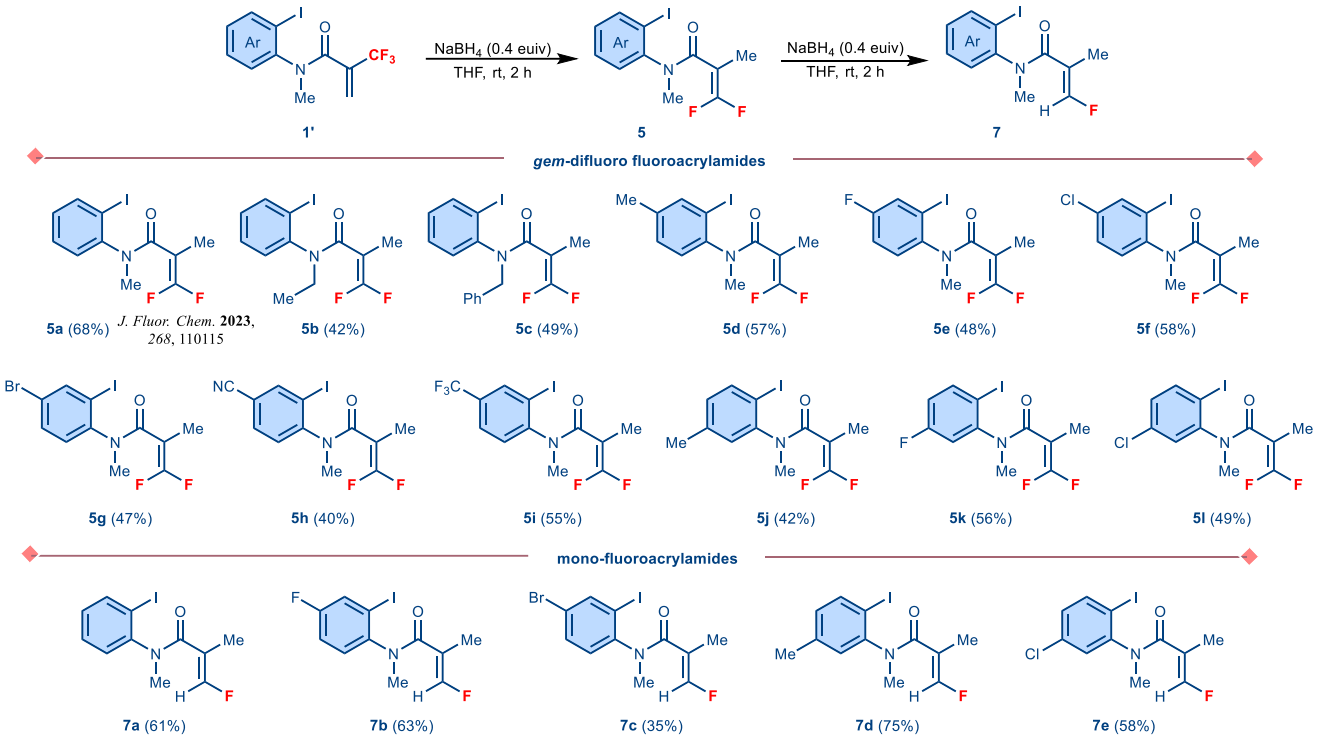
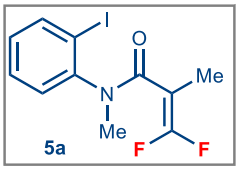


Figure S4. *N*–(2–Haloaryl) *gem*-difluoro and monofluoro methyl acrylamides.

Characterization Data of *o*-Iodoaryl *gem*-Difluoro and Monofluoro Acrylamides:

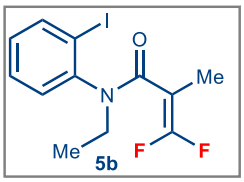
3,3-Difluoro-*N*-(2-iodophenyl)-*N*, 2-dimethyl acrylamide (5a)[4]:



According to **GP–II**, the reaction of *N*-(2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1a'**, 178 mg, 0.5 mmol) with $NaBH_4$ (7.5 mg, 0.2 mmol) afforded the desired amide **5a** (115 mg) in 68% yield as a white solid; R_f = 0.28 (3% EtOAc, 30% DCM in hexane); Melting point: 71–73 ºC *(89:11 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.9 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.28–7.23 (m, 1H), 7.06 (t, J = 7.5 Hz, 1H), 3.30 (s, 0.3H), 3.27-3.22 (m, 2.7H), 1.65 (bq, J = 3.2 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 166.0 (dd, J = 9.2, 3.5 Hz), 153.2 (t, J = 290.6 Hz), 145.4, 144.9*, 140.2, 140.0*, 129.8, 129.6*, 129.4, 129.1 (d, J = 2.7 Hz), 128.5*, 98.3, 97.6*, 86.0 (dd, J = 22.0, 17.8 Hz), 38.5*, 36.9, 11.2, 10.7*; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(78.95–79.35) (m, 1F), -81.7* (d, J = 37.0 Hz, 0.13F), -(89.36–89.60) (m, 1F), -90.3* (d, J = 36.6 Hz, 0.13F) ppm; **HRMS (ESI–TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}IF_2NO$: 337.9848, found 337.9843.

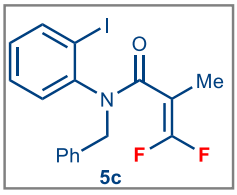
***N*-Ethyl-3,3-difluoro-*N*-(2-iodophenyl)-2-methylacrylamide (5b):**



According to **GP–II**, the reaction of *N*-(2-iodophenyl)-*N*-ethyl-2-(trifluoromethyl)acrylamide (**1b'**, 369 mg, 1.0 mmol) with $NaBH_4$ (15 mg, 0.4 mmol) afforded the desired amide **5b** (147 mg) in 42% yield as a yellow liquid along with (*E*)-*N*-ethyl-3-fluoro-*N*-(2-iodophenyl)-2-methylacrylamide (85 mg, 25% yield); R_f = 0.32 (3% EtOAc, 30% DCM in hexane). *(89:11 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 8.0 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.20 (bd, J = 7.8 Hz, 1H), 7.07 (t, J = 7.6 Hz, 1H), 4.22 (dq, J = 14.2, 7.2 Hz, 1H), 3.80 (td, J = 13.9, 6.8 Hz, 0.16H), 3.56 (dt, J = 21.3, 7.0 Hz, 0.16H), 3.28 (dq, J = 14.2, 7.1 Hz, 1H), 1.95 (s, 0.31H), 1.71 (s, 0.29H), 1.62 (bt, J = 3.0 Hz, 3H), 1.16 (t, J = 7.2 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.5 (dd, J = 9.2, 3.1 Hz), 153.1 (dd, J = 291.2, 289.6 Hz), 143.5, 140.2, 130.3 (d, J = 2.8 Hz), 129.8, 128.9, 99.4, 86.3 (dd, J = 21.6, 18.2 Hz), 43.9, 12.5, 11.1; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -79.9 (dp, J = 33.8, 3.8 Hz, 1F), -82.7* (d, J = 39.4 Hz, 0.11F), -90.2 (dq, J = 33.2, 3.0 Hz, 1F), -91.2* (d, J = 37.4 Hz, 0.11F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{13}IF_2NO$: 352.0004, found 351.9995.

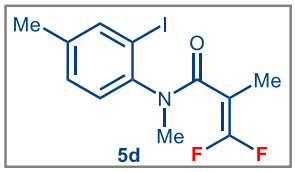
***N*-Benzyl-3,3-difluoro-*N*-(2-iodophenyl)-2-methylacrylamide (5c):**



According to **GP–II**, the reaction of *N*-(2-iodophenyl)-*N*-benzyl-2-(trifluoromethyl)acrylamide (**1c'**, 790 mg, 1.5 mmol) with $NaBH_4$ (23 mg, 0.6 mmol) afforded the desired amide **5c** (304 mg) in 49% yield as a white solid; R_f = 0.46 (3% EtOAc, 30% DCM in hexane); Melting point: 47–49 °C. *(91:09 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.9 Hz, 1H), 7.30–7.23 (m, 3H), 7.22–7.13 (m, 3H), 7.01 (t, J = 7.6 Hz, 1H), 6.77 (d, J = 7.8 Hz, 1H), 5.68 (d, J = 14.4 Hz, 1H), 4.11 (d, J = 14.4 Hz, 1H), 1.67 (bt, J = 2.9 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.9 (dd, J = 9.1, 3.2 Hz), 153.0 (dd, J = 291.6, 289.5 Hz), 143.0, 140.0, 136.2, 130.7 (d, J = 3.0 Hz), 129.9, 129.1, 128.6, 128.4, 127.6, 99.2, 86.1 (dd, J = 21.9, 18.2 Hz), 52.0, 11.2; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(79.30–79.65) (m, 1F), -80.8* (d, J = 36.0 Hz, 0.07F), -(89.85–90.10) (m, 1F), -90.3* (d, J = 35.1 Hz, 0.09F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{17}H_{15}IF_2NO$: 414.0161, found 414.0160.

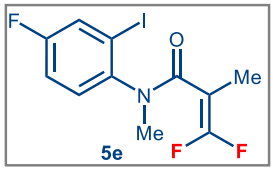
3,3-Difluoro-*N*-(2-iodo-4-methylphenyl)-*N*, 2-dimethylacrylamide (5d):



According to **GP–II**, the reaction of *N*-(2-iodo-4-methylphenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1d'**, 369 mg, 1.0 mmol) with $NaBH_4$ (15 mg, 0.4 mmol) afforded the desired amide **5d** (202 mg) in 57% yield as a yellow liquid; R_f = 0.31 (3% EtOAc, 30% DCM in hexane). *(88:12 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (bd, J = 1.0 Hz, 1H), 7.19–7.09 (m, 2H), 3.21 (s, 3H), 2.32 (s, 3H), 1.64 (t, J = 3.1 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 166.2 (dd, J = 9.1, 3.0 Hz), 153.1 (t, J = 290.6 Hz), 142.7, 140.4, 140.2, 130.1, 128.5 (d, J = 2.6 Hz), 98.0, 86.0 (dd, J = 22.0, 18.0 Hz), 36.9, 20.5, 11.2; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(79.32–79.53) (m, 1F), -81.8* (d, J = 37.2 Hz, 0.12F), -(89.75–89.86) (m, 1F), -90.4* (dd, J = 37.3, 2.1 Hz, 0.12F, broad peaks) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{13}IF_2NO$: 352.0004, found 351.9994.

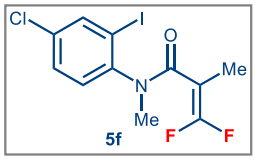
3,3-Difluoro-*N*-(4-fluoro-2-iodophenyl)-*N*, 2-dimethylacrylamide (5e):



According to **GP–II**, the reaction of *N*-(4-fluoro-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1e'**, 186.5 mg, 0.5 mmol) with $NaBH_4$ (7.5 mg, 0.2 mmol) afforded the desired amide **5e** (85 mg) in 48% yield as a white solid; R_f = 0.31 (3% EtOAc, 30% DCM in hexane); Melting point: 50–52 ºC. *(87:13 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, J = 7.6, 2.8 Hz, 1H), 7.26–7.21 (m, 1H), 7.14–7.08 (m, 1H), 3.28* (s, 0.4H), 3.22 (s, 3H), 1.90* (t, J = 2.4 Hz, 0.4H), 1.67 (bt, J = 3.1 Hz, 3H); **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 165.9 (dd, J = 10.2, 3.8 Hz), 161.0 (d, J = 254.2 Hz), 152.9 (dd, J = 291.9, 290.2 Hz), 141.6 (d, J = 4.1 Hz), 129.6 (dd, J = 9.2, 3.3 Hz), 126.7 (d, J = 24.8 Hz), 116.3 (d, J = 22.4 Hz), 98.1 (d, J = 8.9 Hz), 85.8 (dd, J = 22.2, 17.9 Hz), 36.8, 11.2; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(78.78–79.06) (m, 1F), -81.6* (d, J = 36.2 Hz, 0.16F), -(89.20–89.50) (m, 1F), -90.0* (d, J = 36.4 Hz, 0.15F), 110.9 (dd, J =13.3, 7.4 Hz, 1F), -111.9 (dd, J =13.1, 7.1 Hz, 0.14F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}IF_3NO$: 355.9754, found 355.9751.

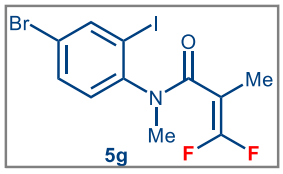
***N*-(4-Chloro-2-iodophenyl)-3,3-difluoro-*N*, 2-dimethylacrylamide (5f):**



According to **GP–II**, the reaction of *N*-(4-chloro-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1f'**, 389 mg, 1.0 mmol) with $NaBH_4$ (15 mg, 0.4 mmol) afforded the desired amide **5f** (216 mg) in 58% yield as a white solid; R_f = 0.31 (3% EtOAc, 30% DCM in hexane); Melting point: 44–46 ºC. *(85:15 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 2.3 Hz, 1H), 7.35 (dd, J = 8.4, 2.3 Hz, 1H), 7.16 (dd, J = 8.4, 2.8 Hz, 1H), 3.26* (s, 0.45H), 3.20 (s, 3H), 1.91* (bt, J = 4.0 Hz, 0.6H), 1.65 (t, J = 3.2 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.8 (dd, J = 9.2, 3.3 Hz), 153.1 (dd, J = 292.2, 290.4 Hz), 144.0, 139.4, 134.6, 129.53, 129.46 (d, J = 2.9 Hz), 98.5, 85.8 (dd, J = 21.9, 17.7 Hz), 36.8, 11.2; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(78.48–78.64) (m, 1F), -81.3* (d, J = 35.8 Hz, 0.18F), -(88.71–88.88) (m, 1F), -89.7* (dd, J = 36.0, 1.5 Hz, 0.18F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}ClIF_2NO$: 371.9458, found 371.9455.

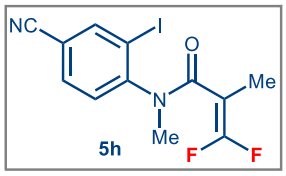
***N*-(4-Bromo-2-iodophenyl)-3,3-difluoro-*N*, 2-dimethylacrylamide (5g):**



According to **GP–II**, the reaction of *N*-(4-bromo-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1g'**, 217 mg, 0.5 mmol) with $NaBH_4$ (7.5 mg, 0.2 mmol) afforded the desired amide **5g** (85 mg) in 47% yield as a white solid; R_f = 0.33 (3% EtOAc, 30% DCM in hexane); Melting point: 46–48 ºC. *(86:14 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 2.1 Hz, 1H), 7.51 (dd, J = 8.4, 1.9 Hz, 1H), 7.12 (dd, J = 8.4, 2.6 Hz, 1H), 3.27* (s, 0.43H), 3.22 (s, 3H), 1.93* (bs, 0.45H), 1.67 (bt, J = 3.0 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.9 (dd, J = 9.2, 3.2 Hz), 153.2 (dd, J = 292.3, 290.5 Hz), 144.6, 142.2, 132.6, 129.9 (d, J = 2.9 Hz), 122.6, 99.1, 85.9 (dd, J = 22.0, 17.7 Hz), 36.8, 11.3; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(78.36–78.60) (m, 1F), -81.2* (d, J = 35.5 Hz, 0.17F), -(88.56–88.74) (m, 1F), -89.6* (d, J = 35.5 Hz, 0.17F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}BrIF_2NO$: 415.8953, found 415.8946.

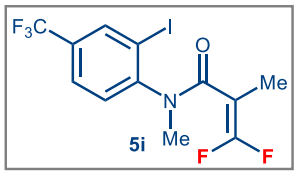
***N*-(4-Cyano-2-iodophenyl)-3,3-difluoro-*N*, 2-dimethylacrylamide (5h):**



According to **GP–II**, the reaction of *N*-(4-cyano-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1h'**, 362 mg, 1.0 mmol) with $NaBH_4$ (15 mg, 0.4 mmol) afforded the desired amide **5h** (144 mg) in 40% yield as a white solid; R_f = 0.11 (3% EtOAc, 30% DCM in hexane); Melting point: 84–86 ºC. *(78:22 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.34 (d, J = 8.1 Hz, 1H), 3.25 (bs, 3H), 1.70 (bs, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.6 (bd, J = 10.1 Hz), 153.4 (dd, J = 293.5, 291.2 Hz), 149.7, 143.5, 132.9, 129.6, 116.2, 113.8, 98.6, 85.9 (dd, J = 22.0, 16.6 Hz), 36.9, 11.4; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -77.3 (d, J = 28.3, 1F), -80.4* (d, J = 34.1 Hz, 0.28F), -87.2 (d, J = 28.4 Hz, 1F), -88.7* (d, J = 32.5 Hz, 0.31F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{10}F_2IN_2O$: 362.9800, found 362.9796.

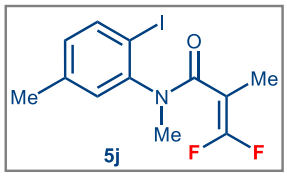
3,3-Difluoro-*N*-(2-iodo-4-(trifluoromethyl)phenyl)-*N*, 2-dimethylacrylamide (5i):



According to **GP–II**, the reaction of *N*–(2-iodo-4-(trifluoromethyl)phenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1i'**, 405 mg, 1.0 mmol) with $NaBH_4$ (15 mg, 0.4 mmol) afforded the desired amide **5i** (223 mg) in 55% yield as a white solid along with (*E*)-3-Fluoro-*N*-(2-iodo-4-(trifluoromethyl)phenyl)-*N*,2-dimethylacrylamide (66 mg, 17% yield); R_f = 0.30 (3% EtOAc, 30% DCM in hexane); Melting point: 66–68 ºC. *(82:18 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 1.0 Hz, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 3.30* (s, 0.51H), 3.25 (s, 3H), 1.94* (bs, 0.54H), 1.68 (bt, J = 2.9 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.7 (dd, J = 9.3, 3.3 Hz), 153.3 (dd, J = 292.7, 291.1 Hz), 148.7, 137.2 (bq, J = 3.6 Hz), 131.7 (q, J = 33.4 Hz), 129.3 (d, J = 2.7 Hz), 126.4 (bq, J = 3.3 Hz), 122.4 (q, J = 273.1 Hz), 98.3, 85.8 (dd, J = 21.9, 17.4 Hz), 36.8, 11.3; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -62.61 (3F), -62.64 (0.5F), -(77.84−78.02) (m, 1F), -80.9* (d, J = 35.9 Hz, 0.22F), -(87.82−88.00) (m, 1F), -89.2* (d, J = 35.9 Hz, 0.22F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{10}F_5INO$: 405.9722, found 405.9716.

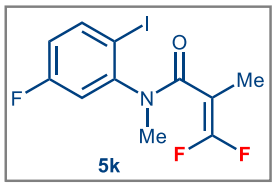
3,3-Difluoro-*N*-(2-iodo-5-methylphenyl)-*N*, 2-dimethylacrylamide (5j):



According to **GP–II**, the reaction of *N*-(2-iodo-5-methylphenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1j'**, 2.0 g, 5.4 mmol) with $NaBH_4$ (82 mg, 2.17 mmol) afforded the desired amide **5j** (793 mg) in 42% yield as a yellow liquid; R_f = 0.30 (3% EtOAc, 30% DCM in hexane). *(86:14 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.1 Hz, 1H), 7.06 (s, 1H), 6.87 (d, J = 7.3 Hz, 1H), 3.27* (s, 0.42H), 3.22 (s, 3H), 2.31 (s, 3H), 1.93* (bs, 0.43H), 1.64 (bt, J = 3.0 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 166.0 (dd, J = 9.1, 3.3 Hz), 153.1 (t, J = 290.6 Hz), 145.1, 139.8, 139.7, 130.8, 129.7 (d, J = 2.6 Hz), 93.9, 86.1 (dd, J = 21.9, 17.9 Hz), 36.8, 20.7, 11.2; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(79.42–79.56) (m, 1F), -81.8* (d, J = 37.0 Hz, 0.17F), -(89.63–89.79) (m, 1F), -(90.31−90.46)* (m, 0.16F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{13}F_2INO$: 352.0004, found 351.9995.

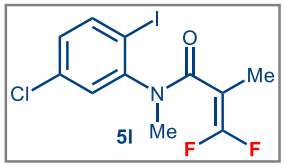
3,3-Difluoro-*N*-(5-fluoro-2-iodophenyl)-*N*, 2-dimethylacrylamide (5k):



According to **GP–II**, the reaction of *N*-(5-fluoro-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1k'**, 1.18 g, 3.17 mmol) with $NaBH_4$ (48 mg, 1.27 mmol) afforded the desired amide **5k** (634 mg) in 56% yield as a yellow liquid; R_f = 0.33 (3% EtOAc, 30% DCM in hexane). *(83:17 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).*

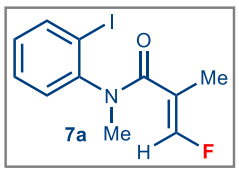
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, J = 8.8, 6.0 Hz 1H), 7.01 (dt, J = 8.8, 2.6 Hz, 1H), 6.86 (td, J = 8.6, 2.8 Hz, 1H), 3.28* (s, 0.49H), 3.22 (s, 3H), 1.92* (bs, 0.48H), 1.67 (bt, J = 3.1 Hz, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.8 (dd, J = 9.1, 3.5 Hz), 162.9 (d, J = 251.0 Hz), 153.2 (t, J = 291.5 Hz), 146.6 (d, J = 9.6 Hz), 140.8 (d, J = 8.5 Hz), 117.5 (d, J = 21.5 Hz), 116.7 (dd, J = 22.6, 2.8 Hz), 91.5 (d, J = 3.8 Hz), 85.9 (dd, J = 22.0, 17.6 Hz), 36.8, 11.2; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(78.39–78.55) (m, 1F), -81.1* (d, J = 35.5 Hz, 0.20F), -(88.47–88.67) (m, 1F), -89.6* (d, J = 35.4 Hz, 0.20F), -111.1 (bq, J = 6.4 Hz, 1F), -111.3 (bq, J = 6.4 Hz, 0.20F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}F_3INO$: 355.9754, found 355.9750.

***N*-(5-Chloro-2-iodophenyl)-3,3-difluoro-*N*, 2-dimethylacrylamide (5l):**



According to **GP–II**, the reaction of *N*-(5-chloro-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1l'**, 389 mg, 1.0 mmol) with $NaBH_4$ (15 mg, 0.4 mmol) afforded the desired amide **5l** (181 mg) in 49% yield as a white solid; R_f = 0.41 (3% EtOAc, 30% DCM in hexane); Melting point: 68–70 °C. *(82:18 mixture of isomers based on ^{19}F NMR ratio, the minor isomer highlighted with star mark).* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (d, J = 8.4 Hz, 1H), 7.26 (bs, 1H), 7.08 (bd, J = 8.3 Hz, 1H), 3.29* (s, 0.60H), 3.23 (s, 2.4H), 1.94* (bs, 0.54H), 1.69 (bs, 2.4H); **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 165.7 (dd, J = 9.0, 3.3 Hz), 153.2 (t, J = 291.7 Hz), 146.4, 140.7, 135.0, 130.1, 129.3 (d, J = 2.8 Hz), 95.6, 85.8 (dd, J = 22.0, 17.5 Hz), 36.8, 11.3; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(78.25−78.42) (m, 1F), -81.0* (d, J = 35.3 Hz, 0.22F), -(88.31−88.48) (dd, J = 30.7, 2.4 Hz, 1F), -89.5* (d, J = 35.5 Hz, 0.22F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}ClIF_2NO$: 371.9458, found 371.9455.

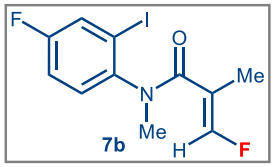
(*E*)-3-Fluoro-*N*-(2-iodophenyl)-*N*,2-dimethyl acrylamide (7a):



According to **GP–III**, the reaction of 3,3-difluoro-*N*-(2-iodophenyl)-*N*,2-dimethyl acrylamide (**5a**, 101 mg, 0.3 mmol) with $NaBH_4$ (4.5 mg, 0.12 mmol) afforded the desired amide **7a** (42 mg) in 44% yield as a white solid; R_f = 0.18 (3% EtOAc 30% DCM in hexane); Melting point: 60–62 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.1 Hz, 1H), 7.38 (bt, J = 6.8 Hz, 1H), 7.16 (bd, J = 6.7 Hz, 1H), 7.04 (bt, J = 7.8 Hz, 1H), 6.75 (d, J = 82.7 Hz, 1H), 3.23 (s, 3H), 1.64 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 168.7 (d, J = 15.1 Hz), 152.7 (d, J = 267.6 Hz), 146.5, 140.4, 129.7, 129.5, 129.1, 116.7 (d, J = 9.2 Hz), 99.0, 37.4, 10.7 (d, J = 5.3 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -123.6 (d, J = 82.0 Hz) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{12}FINO$: 319.9942, found 319.9958.

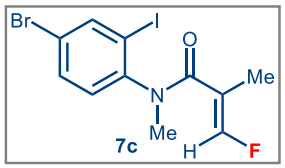
***(E)*-3-Fluoro-*N*-(4-fluoro-2-iodophenyl)-*N*, 2-dimethylacrylamide (7b):**



According to **GP–III**, the reaction of 3,3-difluoro-*N*-(4-fluoro-2-iodophenyl)-*N*,2-dimethylacrylamide (**5e**, 476 mg, 1.3 mmol) with $NaBH_4$ (18 mg, 0.48 mmol) afforded the desired amide **7b** (274 mg) in 63% yield as a white solid; R_f = 0.20 (3% EtOAc, 30% DCM in hexane); Melting point: 56–58 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J = 6.8 Hz, 1H), 7.17–7.03 (m, 2H), 6.74 (d, J = 82.7 Hz, 1H), 3.18 (s, 3H), 1.62 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 168.6 (d, J = 15.1 Hz), 160.8 (d, J = 254.0 Hz), 152.4 (d, J = 276.2 Hz), 142.7, 129.6 (d, J = 8.6 Hz), 127.0 (d, J = 24.6 Hz), 116.7 (d, J = 22.3 Hz), 116.5 (d, J = 9.2 Hz), 98.8 (d, J = 8.5 Hz), 37.4, 10.6 (d, J = 5.3 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -111.4, -123.2 (bd, J = 79.4 Hz) ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}F_2INO$: 337.9848, found 337.9844.

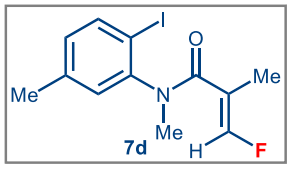
(*E*)-*N*-(4-Bromo-2-iodophenyl)-3-fluoro-*N*, 2-dimethylacrylamide (7c):



According to **GP–III**, the reaction of *N*-(4-bromo-2-iodophenyl)-3,3-difluoro-*N*,2-dimethylacrylamide (**5g**, 250 mg, 0.6 mmol) with $NaBH_4$ (9.0 mg, 0.24 mmol) afforded the desired amide **7c** (150 mg) in 63% yield as a white solid; R_f = 0.21 (3% EtOAc, 30% DCM in hexane); Melting point: 65–67 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.51 (d, J = 8.3 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H), 6.76 (d, J = 82.4 Hz, 1H), 3.20 (s, 3H), 1.66 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 168.6 (d, J = 15.1 Hz), 152.7 (d, J = 270.4 Hz), 145.7, 142.4, 132.9, 130.0, 122.1, 116.6 (d, J = 9.4 Hz), 99.7, 37.4, 10.7 (d, J = 5.2 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -123.8 (d, J = 79.4 Hz) ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}BrFINO$: 397.9047, found 397.9066.

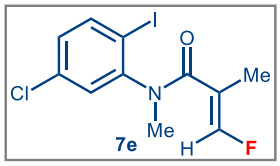
***(E)*-3-Fluoro-*N*-(2-iodo-5-methylphenyl)-*N*, 2-dimethylacrylamide (7d):**



According to **GP–III**, the reaction of 3,3-difluoro-*N*-(2-iodo-5-methylphenyl)-*N*,2-dimethylacrylamide (**5j**, 420 mg, 1.2 mmol) with $NaBH_4$ (18 mg, 0.48 mmol) afforded the desired amide **7d** (300 mg) in 75% yield as a white solid; R_f = 0.21 (3% EtOAc, 30% DCM in hexane); Melting point: 58–60 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 8.1 Hz, 1H), 6.97 (s, 1H), 6.84 (d, J = 8.2 Hz, 1H), 6.76 (d, J = 80.5 Hz, 1H, one of the doublet peak merged with previous peak), 3.20 (s, 3H), 2.30 (s, 3H), 1.64 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 168.6 (d, J = 15.1 Hz), 152.5 (d, J = 270.0 Hz), 146.2, 140.1, 139.9, 130.4, 129.7, 116.6 (d, J = 9.0 Hz), 94.6, 37.3, 20.8, 10.7 (d, J = 5.3 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -123.8 (d, J = 89.2 Hz, 1F) ppm; **HRMS (ESI−TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{12}H_{13}FINNaO$: 355.9918, found 355.9922.

***(E)*-*N*-(5-Chloro-2-iodophenyl)-3-fluoro-*N*, 2-dimethylacrylamide (7e):**

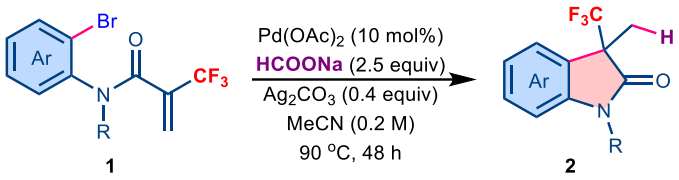


According to **GP–III**, the reaction of *N*-(5-chloro-2-iodophenyl)-3,3-difluoro-*N*,2-dimethylacrylamide (**5l**, 175 mg, 0.47 mmol) with $NaBH_4$ (7.1 mg, 0.19 mmol) afforded the desired amide **7e** (96 mg) in 58% yield as a white solid; R_f = 0.28 (3% EtOAc, 30% DCM in hexane); Melting point: 68–70 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 8.5 Hz, 1H), 7.17 (s, 1H), 7.05 (d, J = 8.5 Hz, 1H), 6.78 (d, J = 82.4 Hz, 1H), 3.22 (s, 3H), 1.69 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 168.5 (d, J = 15.2 Hz), 152.7 (d, J = 267.1 Hz), 147.6, 141.0, 135.4, 129.8, 129.3, 116.5 (d, J = 9.3 Hz), 96.3, 37.5, 10.7 (d, J = 5.2 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -123.8 (d, J = 82.8 Hz, 1F) ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}ClFINO$: 353.9552, found 353.9550.

3. Experimental Procedures:

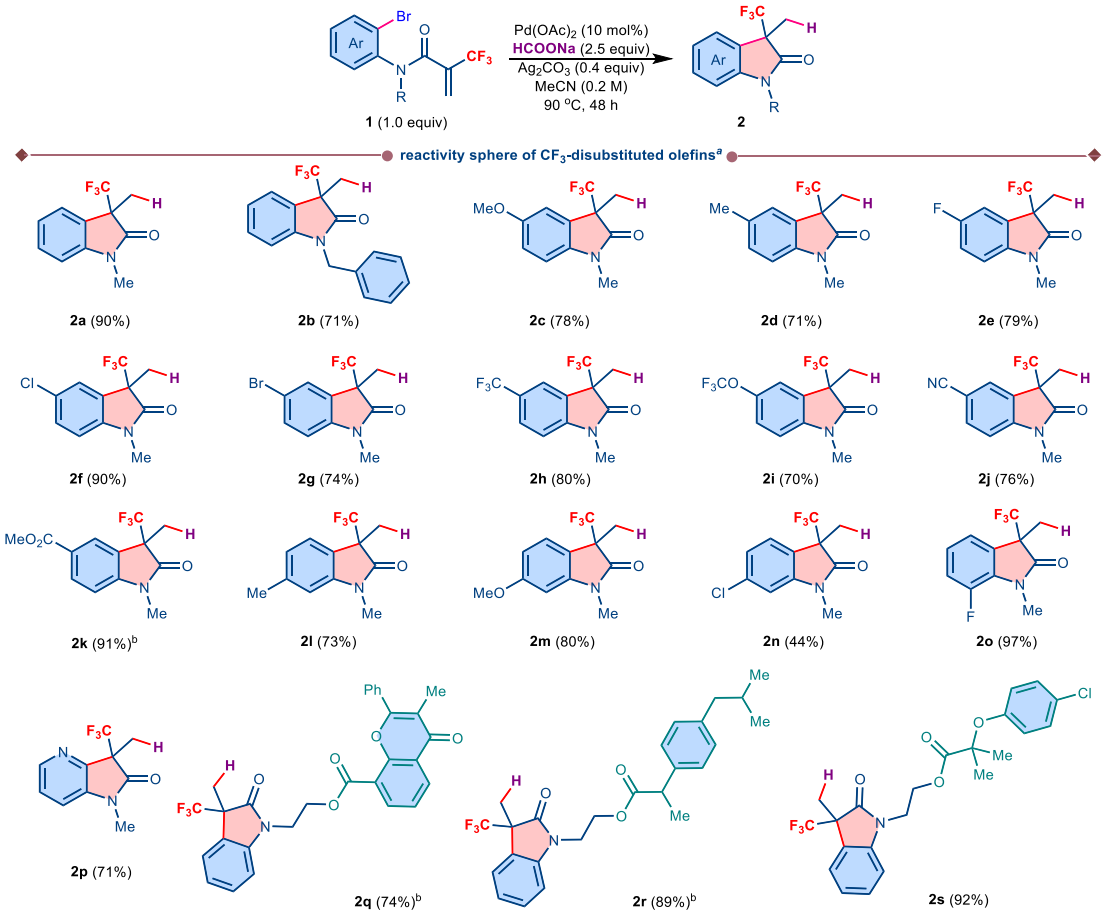
3.1 General Procedure for Palladium-Catalyzed Reductive Heck Cyclization of Di-substituted CF_3-Acrylamides (GP-IV, racemic):



Scheme S3. Reductive Heck cyclization of *o*-halo trifluoromethyl acrylamide.

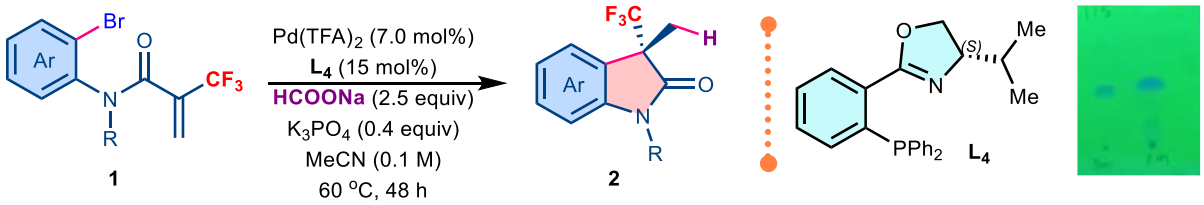
General Procedure-IV (GP-IV): An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-halo trifluoromethyl acrylamide (**1**, 1.0 equiv), $Pd(OAc)_2$ (10 mol%), HCOONa (2.5 equiv) and Ag_2CO_3 (0.4 equiv). Then the reaction vial was introduced inside the glove box and acetonitrile solvent (MeCN, 0.2 M) was added. The reaction vial was capped, taken outside, and stirred at 90 °C (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Hexane/Ethyl acetate/DCM) to afford the desired products (**2**).

Table S1. Scope study.



[a]**Reaction Conditions: 1** (0.2 mmol), $Pd(OAc)_2$ (10 mol %), HCOONa (2.5 equiv), Ag_2CO_3 (0.4 equiv), MeCN (0.2 M), 90 °C, 48 h. [b]0.1 mmol reaction scale.

3.2 General Procedure for Palladium-Catalyzed Asymmetric Reductive Heck Cyclization of Di-substituted CF_3-Acrylamides (GP-V):

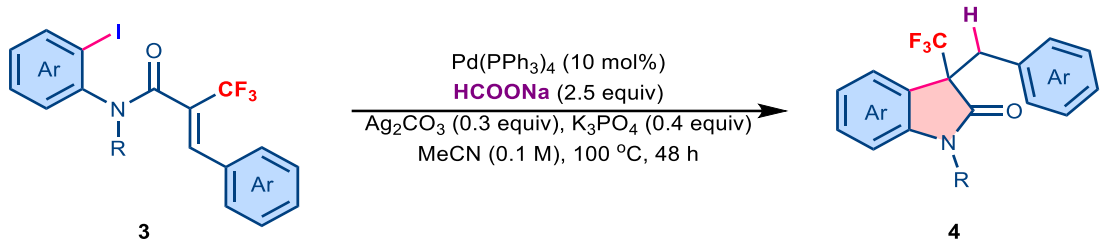


Scheme S4. Asymmetric reductive Heck cyclization of *o*-halo trifluoromethyl acrylamide **1**.

General Procedure-V (GP-V): An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-halo trifluoromethyl acryl amide (**1**, 0.1 mmol), $Pd(TFA)_2$ (7 mol%), **L4** (15 mol%), HCOONa (0.25 mmol) and K_3PO_4 (0.04 mmol). Then, the reaction vial was introduced inside the glove box, and acetonitrile solvent (MeCN, 0.1 M) was added. The reaction vial was

capped, taken outside and stirred at 60 °C (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Hexane/Ethyl acetate/DCM) to afford the desired products.

3.6 General Procedure for Palladium-Catalyzed Reductive Heck of Tri-substituted *β*-Phenyl-CF_3-Acrylamides (GP-VI, racemic):

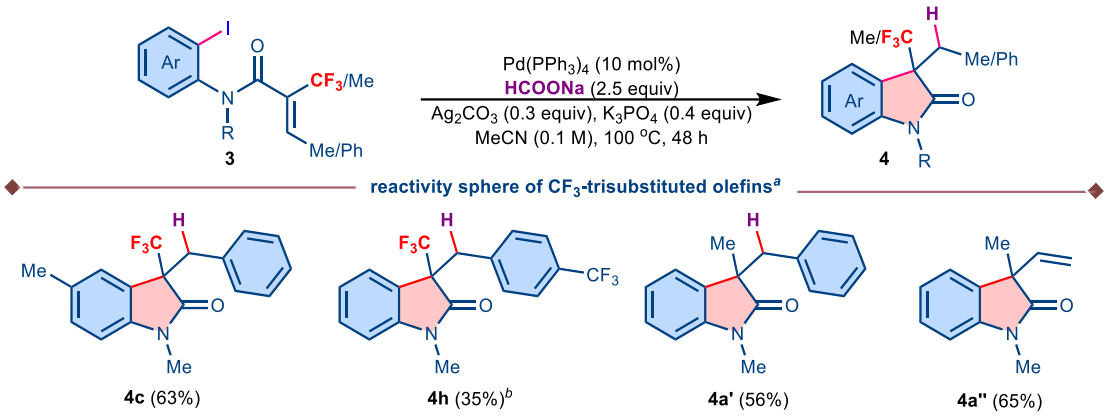


Scheme S5. Reductive Heck cyclization of *o*-halo *β*-phenyl trifluoromethyl acrylamides.

General procedure-VI (GP-VI): An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-iodo *β*-phenyl trifluoromethyl acryl amides (**3**, 0.1 mmol), $Pd(PPh_3)_4$ (10 mol%), HCOONa (0.25 mol), Ag_2CO_3 (0.03 mmol) and K_3PO_4 (0.04 mmol). Then the reaction vial was introduced inside the glove box and acetonitrile solvent (MeCN, 0.1 M) was added. The reaction vial was capped, taken outside and stirred at 100 °C (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Hexane/Ethyl acetate/DCM) to afford the desired products (**4**).

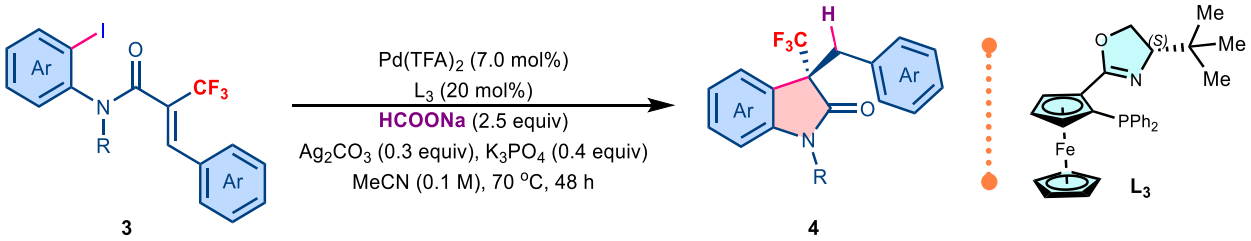
Note: Compounds **4a–b** and **4d** reported in the literature.[2,6]

Table S2. Scope study.[a]



[a]**Reaction Conditions: 3** (0.1 mmol), $Pd(PPh_3)_4$ (10 mol%), HCOONa (2.5 equiv), K_3PO_4 (0.4 equiv), Ag_2CO_3 (0.3 equiv), MeCN (0.1 M), 100 °C, 48 h. [b]$Pd(TFA)_2$ (7.0 mol%) at 70 °C.

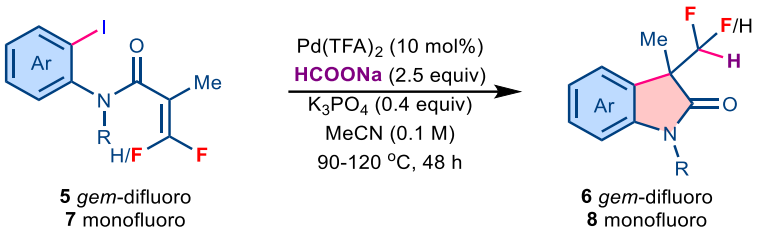
3.7 General Procedure for Palladium-Catalyzed Asymmetric Reductive Heck of Tri-substituted *β*-Phenyl-CF_3-Acrylamides (GP-VII):



Scheme S6. Asymmetric Reductive Heck cyclization of *o*-halo *β*-phenyl trifluoromethyl acrylamides.

General Procedure- VII (GP- VII): An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-iodo *β*-phenyl trifluoromethyl acryl amides (**3**, 1.0 equiv), $Pd(TFA)_2$ (7 mol%), **L_3** (20 mol%), HCOONa (2.5 equiv) and Ag_2CO_3 (0.3 equiv) and K_3PO_4 (0.4 equiv). Then the reaction vial was introduced inside the glove box and acetonitrile solvent (MeCN, 0.1 M) was added. The reaction vial was capped, taken outside and stirred at 70 °C (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Hexane/Ethyl acetate/DCM) to afford the desired products (**4**).

3.8 General Procedure for Palladium-Catalyzed Reductive Heck of Tri/Tetra-substituted *gem*-Difluoro and Monolfuoro-Acrylamides (GP-VIII, racemic):



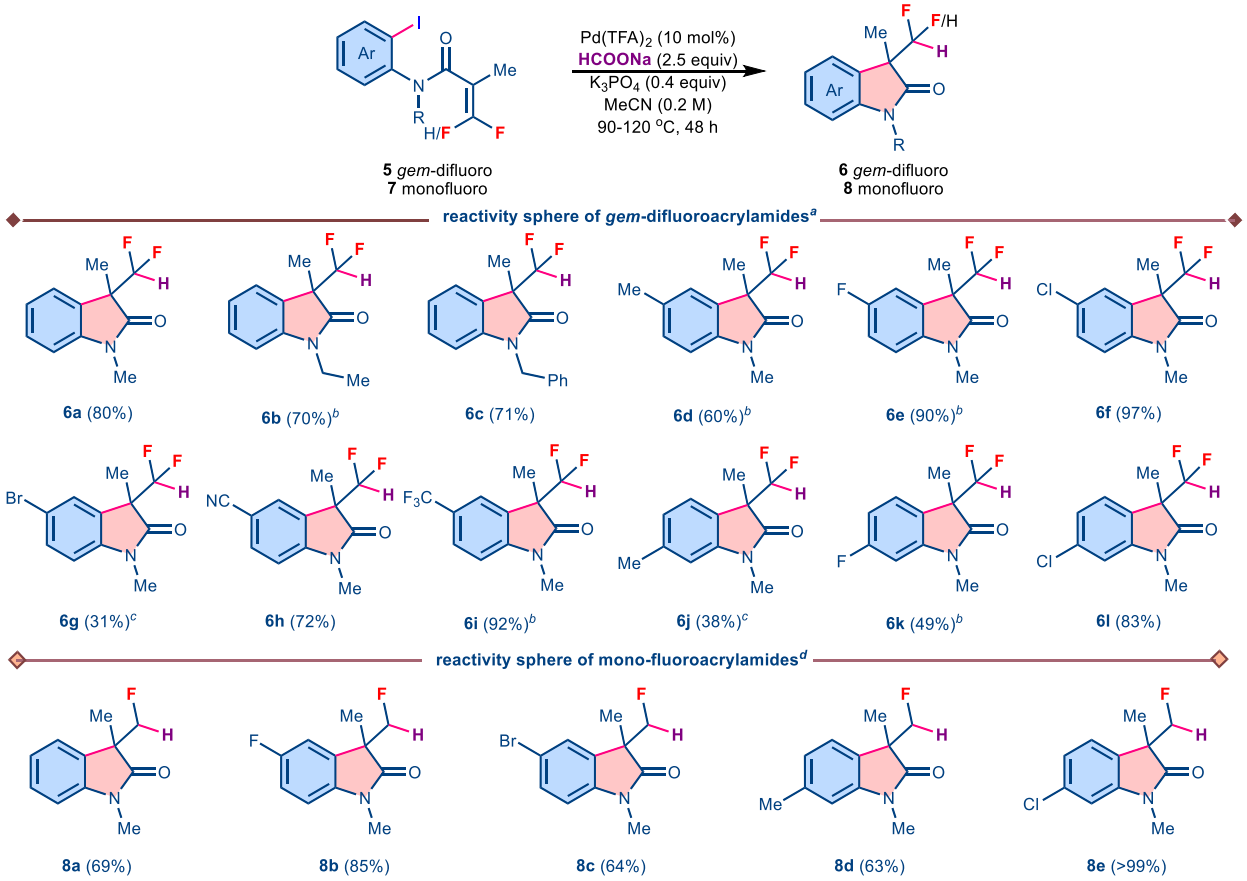
5 *gem*-difluoro
7 monofluoro

6 *gem*-difluoro
8 monofluoro

Scheme S7. Reductive Heck cyclization of *o*-iodo *gem*-difluoromethyl and monofluoromethyl acrylamide.

General Procedure-VIII (GP-VIII): An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-iodo *gem*-difluoro (**5**) or monofluoro methyl acrylamide (**7**) (1.0 equiv), $Pd(TFA)_2$ (10 mol%), HCOONa (2.5 equiv), K_3PO_4 (0.4 equiv). Then the reaction vial was introduced inside the glove box and acetonitrile solvent (MeCN, 0.1 M) was added. The reaction vial was capped, taken outside and stirred at 90-120 °C (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Hexane/Ethyl acetate/DCM) to afford the desired products (**6/8**).

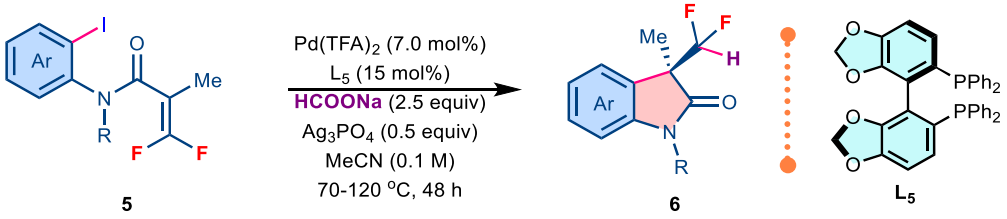
Table S3. Scope study.



[a]**Reaction Conditions: 5** (0.2 mmol), $Pd(TFA)_2$ (15 mol%), HCOONa (2.5 equiv), K_3PO_4 (1.5 equiv), MeCN (0.2 M), 120 °C, 36 h. [b](0.15 mmol), MeCN (0.15 M). [c](0.1 mmol), MeCN (0.1 M).

[d]**Reaction Conditions: 7** (0.1 mmol), $Pd(TFA)_2$ (10 mol%), HCOONa (2.5 equiv), K_3PO_4 (1.5 equiv), MeCN (0.1 M), 90 °C, 36 h.

3.9 General Procedure for Palladium-Catalyzed Asymmetric Reductive Heck of Tetra-substituted *gem*-Difluoro Acrylamides (GP-IX):

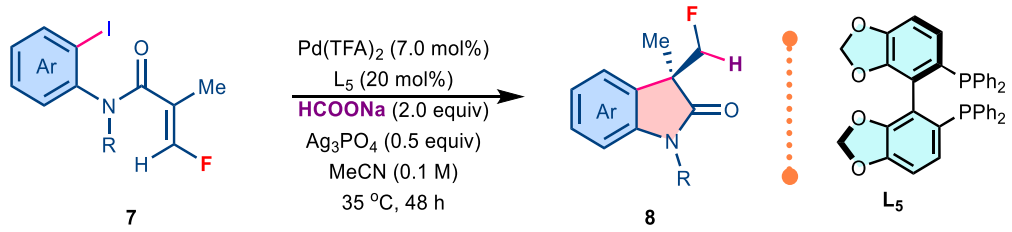


Scheme S8. Asymmetric reductive Heck cyclization of *o*-iodo *gem*-difluoro acrylamide.

General Procedure- IX (GP- IX): An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-iodo *gem*-difluoro acrylamides (**5**, 1.0 equiv), $Pd(TFA)_2$ (7 mol%), **L5** (15 mol%), HCOONa (2.5 equiv) and Ag_3PO_4 (0.5 equiv). Then the reaction vial was introduced

inside the glove box and acetonitrile solvent (MeCN, 0.1 M) was added. The reaction vial was capped, taken outside and stirred at desired temperature (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Hexane/Ethyl acetate/DCM) to afford the desired products (**6**).

3.10 General Procedure for Palladium-Catalyzed Asymmetric Reductive Heck of Tri-substituted Monofluoro Acrylamides (GP-X):

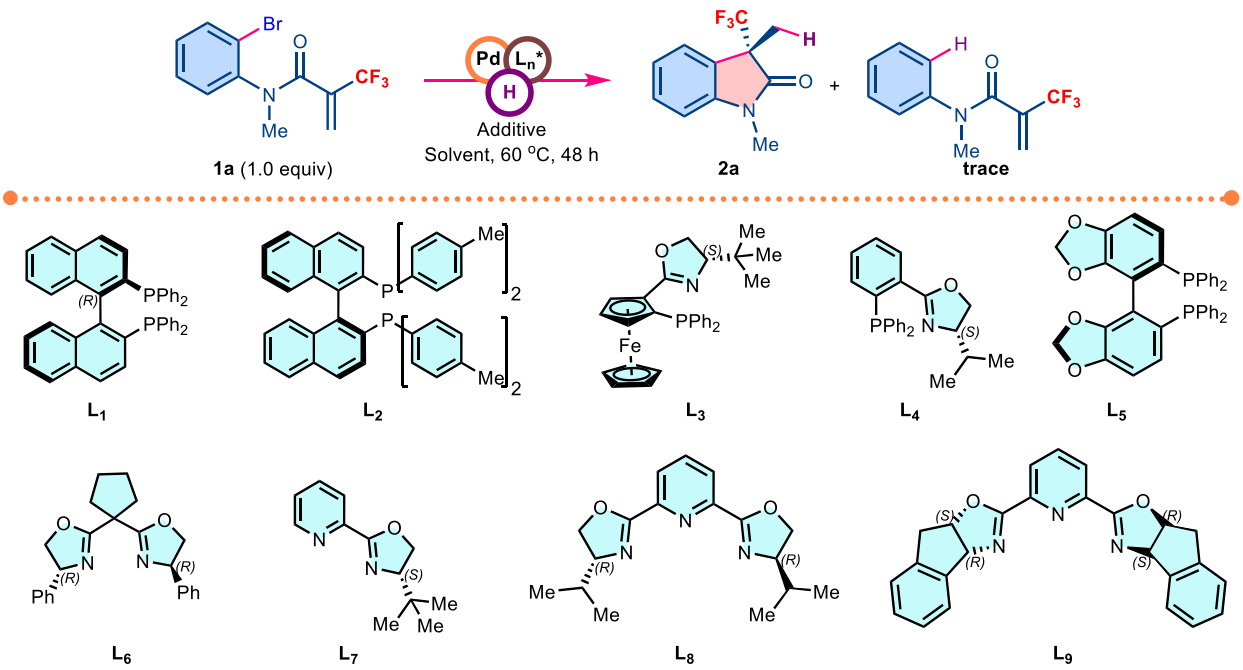


Scheme S9. Asymmetric reductive Heck cyclization of *o*-iodo monofluoro acrylamide.

General Procedure-X (GP-X): An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-iodo monofluoromethyl acrylamide (**7**, 1.0 equiv), $Pd(TFA)_2$ (7 mol%), **L_5** (20 mol%), HCOONa (2.5 equiv) and Ag_3PO_4 (0.4 equiv). Then, the reaction vial was introduced inside the glove box, and acetonitrile solvent (MeCN, 0.1 M) was added. The reaction vial was capped, taken outside and stirred at 35 °C (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Hexane/Ethyl acetate/DCM). Afterward, all the compounds were further purified by preparative HPLC (Shim-pack, SHIMADZU, C18 column, 70% acetonitrile in water, flow rate 20 mL/min, T = 25 °C, λ = 254 nm) to afford the desired products (**8**).

4. Optimization of Reaction Conditions:

Table S4: Optimization of Asymmetric Reaction Conditions for Di-substituted Trifluoromethyl Acrylamides[a]

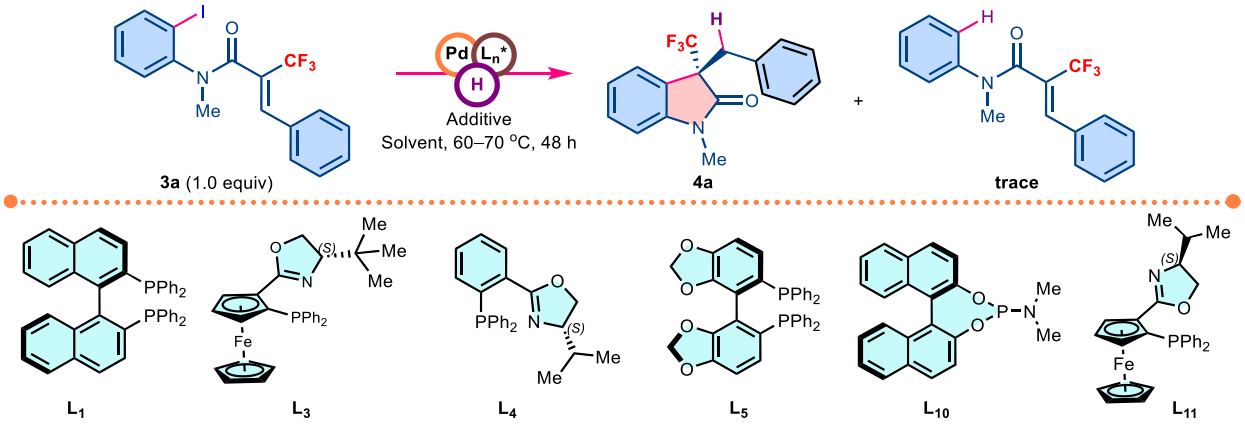


Entry	Metal	Ligand	[H]	Additive	Solvent	Conversion(%)[b]	*ee*[c] %
1	$Pd(OAc)_2$	**L_1**	HCOONa	K_3PO_4	MeCN	<5	14
2	$Pd(OAc)_2$	**L_2**	HCOONa	K_3PO_4	MeCN	<5	<5
3	$Pd(OAc)_2$	**L_3**	HCOONa	K_3PO_4	MeCN	60	90
4	$Pd(OAc)_2$	**L_4**	HCOONa	K_3PO_4	MeCN	50	96
5	$Pd(OAc)_2$	**L_5**	HCOONa	K_3PO_4	MeCN	<5	-8
6	$Pd(OAc)_2$	**L_6**	HCOONa	K_3PO_4	MeCN	30	<5
7	$Pd(OAc)_2$	**L_7**	HCOONa	K_3PO_4	MeCN	10	15
8	$Pd(OAc)_2$	**L_8**	HCOONa	K_3PO_4	MeCN	45	<5
9	$Pd(OAc)_2$	**L_9**	HCOONa	K_3PO_4	MeCN	89	-12
10[d]	$Pd(OAc)_2$	L_4	HCOONa	K_3PO_4	MeCN	76[e]	95[e]
11[d]	$Pd(OAc)_2$	L_4	**$HCOONH_4$**	K_3PO_4	MeCN	10	90
12[d]	$Pd(OAc)_2$	L_4	**$HSiEt_3$**	K_3PO_4	MeCN	27	40
13[d]	$Pd(OAc)_2$	L_4	HCOONa	**Cs_2CO_3**	MeCN	56	97
14[d]	$Pd(OAc)_2$	L_4	HCOONa	**Ag_2CO_3**	MeCN	62[e]	96[e]
15[d]	$Pd(OAc)_2$	L_4	HCOONa	K_3PO_4	**1,4-Dioxane**	10	-20

16[d]	$Pd(OAc)_2$	L_4	HCOONa	K_3PO_4	**DMA**	25	64
17[d]	$Pd(OAc)_2$	L_4	HCOONa	K_3PO_4	**Toluene**	18	-38
18[d]	$Pd(OAc)_2$	-	HCOONa	K_3PO_4	MeCN	65	-
19[d]	$Pd(OAc)_2$	L_4	-	K_3PO_4	MeCN	NR	-
20[d]	$Pd(OAc)_2$	L_4	HCOONa	-	MeCN	17	94
21[d]	**$Pd(acac)_2$**	L_4	HCOONa	K_3PO_4	MeCN	88	96
22[d]	**$Pd(TFA)_2$**	L_4	HCOONa	K_3PO_4	MeCN	>98	97
23[d]	**Pd_2dba_3**	L_4	HCOONa	K_3PO_4	MeCN	95	96
24[f, g]	$Pd(TFA)_2$	L_4	HCOONa	K_3PO_4	MeCN	88	95
25[g, h]	$Pd(TFA)_2$	L_4	HCOONa	K_3PO_4	MeCN	96	95
26[g, i]	**$Pd(TFA)_2$**	**L_4**	**HCOONa**	**K_3PO_4**	**MeCN**	**>98 (89)[e]**	**96 (94)[e]**
27[g, j]	$Pd(TFA)_2$	L_4	HCOONa	K_3PO_4	MeCN	>98	91
28[g, i]	$Pd(TFA)_2$	L_4	DMP	K_3PO_4	MeCN	10	91
29[g, i]	$Pd(TFA)_2$	L_4	*L*-Menthol	K_3PO_4	MeCN	-	-
30[g, i]	$Pd(TFA)_2$	L_4	IPA	K_3PO_4	MeCN	-	-
31[g, i]	$Pd(TFA)_2$	L_4	HCOONa	Na_3PO_4	MeCN	33	94
32[g, i]	$Pd(TFA)_2$	L_4	HCOONa	Ag_3PO_4	MeCN	>90	94

[a]**Reactions Conditions:** Reaction conditions: **1a** (0.025 mmol), [**Pd**] (5 mol%), $\mathbf{L_n}$***** (10 mol%), [**H**] (2.5 equiv), additive (0.4 equiv), solvent (0.05 M) at 60 °C for 48 h. [b]Crude ^{19}F NMR conversion. [c]Enantiomeric excess (*ee*) determined by chiral HPLC. [d][**Pd**] (10 mol%), $\mathbf{L_4}$ (20 mol%). [e]0.1 mmol scale, isolated yield. [f][**Pd**] (5 mol%), $\mathbf{L_4}$ (10 mol%). [g]0.05 mmol reaction scale. [h][**Pd**] (5 mol%), $\mathbf{L_4}$ (15 mol%). [i][**Pd**] (7 mol%), $\mathbf{L_4}$ (15 mol%), [j][**P**d] (7 mol%), $\mathbf{L_4}$ (10 mol%). NR = No Reaction. DMP = 2,4-Dimethyl-3-pentanol, IPA = Isopropanol.

Table S5: Optimization of Asymmetric Reaction Conditions for Tri-substituted *β*-Phenyl Trifluoromethyl Acrylamides[a]

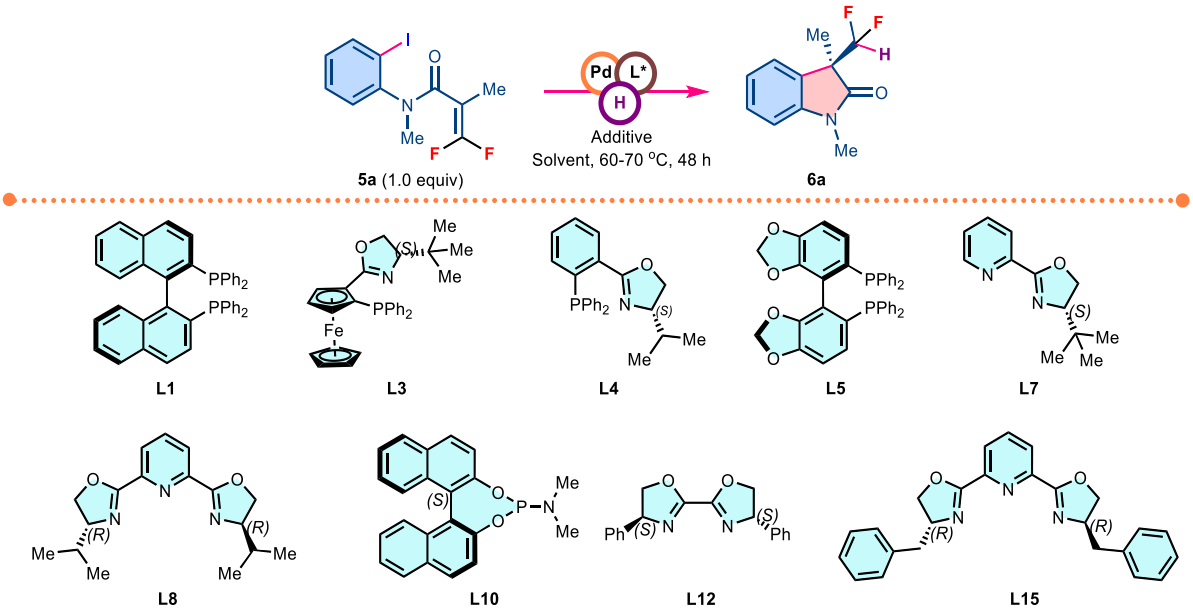


Entry	Metal	Ligand	[H]	Additive	Solvent	Conversion(%)[b]	ee[c] %
1	$Pd(TFA)_2$	**L_1**	HCOONa	K_3PO_4	MeCN	63	-32
2	$Pd(TFA)_2$	**L_3**	HCOONa	K_3PO_4	MeCN	36	85
3	$Pd(TFA)_2$	**L_4**	HCOONa	K_3PO_4	MeCN	30	31
4	$Pd(TFA)_2$	**L_5**	HCOONa	K_3PO_4	MeCN	29	-10
5	$Pd(TFA)_2$	**L_{10}**	HCOONa	K_3PO_4	MeCN	48	06
6	$Pd(TFA)_2$	**L_{11}**	HCOONa	K_3PO_4	MeCN	27	72
7[d]	$Pd(TFA)_2$	L_3	HCOONa	K_3PO_4	MeCN	28	82
8[e]	$Pd(TFA)_2$	L_3	HCOONa	K_3PO_4	MeCN	20	52
9[e]	**$Pd(OAc)_2$**	L_3	HCOONa	K_3PO_4	MeCN	58	18
10[e]	**Pd(allyl)Cl$_2$**	L_3	HCOONa	K_3PO_4	MeCN	23	78
11[f, g]	**$Pd(TFA)_2$**	**L_3**	**HCOONa**	**K_3PO_4 (0.4 equiv)+Ag_2CO_3 (0.3 equiv)**	**MeCN**	**42**	**83**
12[f, h]	$Pd(TFA)_2$	L_3	HCOONa	K_3PO_4 (0.4 equiv)+Ag_2CO_3 (0.3 equiv)	MeCN	49	26
13[f, i]	$Pd(TFA)_2$	L_3	HCOONa	K_3PO_4 (0.4 equiv)+Ag_2	MeCN	56	20

				CO_3 (0.3 equiv)			
14[f, g]	$Pd(TFA)_2$	L_3	HCOONa	Ag_2CO_3 (1.0 equiv)	MeCN	<5	16

[a]**Reaction Conditions: 3a** (0.025 mmol), [**Pd**] (7 mol%), **L_n*** (15 mol%), HCOONa (2.5 equiv), additive (0.4 equiv), solvent (0.05 M) at 60 °C for 48 h. [b]Crude ^{19}F NMR conversion. [c]Enantiomeric excess (*ee*) determined by chiral HPLC. [d][**Pd**] (10 mol%), **L_3** (15 mol%), [e][**Pd**] (10 mol%), **L_3** (20 mol). [f][**Pd**] (7.0 mol%), **L_3** (20 mol%), [g]70 °C. [h]75 °C. [i]80 °C.

Table S6: Optimization of Asymmetric Reaction Conditions for Tetra-substituted *gem*-Difluoromethyl Acrylamides[a]



Entry	Metal	Ligand	[H]	Additive	Solvent	Yield[b] %	*ee*[c] %
1	$Pd(TFA)_2$	**L_1**	HCOONa	K_3PO_4	MeCN	05	40
2	$Pd(TFA)_2$	**L_3**	HCOONa	K_3PO_4	MeCN	04	-36
3	$Pd(TFA)_2$	**L_4**	HCOONa	K_3PO_4	MeCN	04	15
4	$Pd(TFA)_2$	**L_5**	HCOONa	K_3PO_4	MeCN	13	59
5	$Pd(TFA)_2$	**L_7**	HCOONa	K_3PO_4	MeCN	16	20
6	$Pd(TFA)_2$	**L_8**	HCOONa	K_3PO_4	MeCN	20	<5
7	$Pd(TFA)_2$	**L_{10}**	HCOONa	K_3PO_4	MeCN	69	17

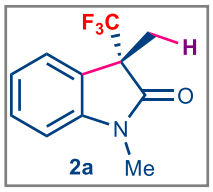
8	$Pd(TFA)_2$	**L_{12}**	HCOONa	K_3PO_4	MeCN	33	<5
9	$Pd(TFA)_2$	**L_{15}**	HCOONa	K_3PO_4	MeCN	20	<5
10[d]	$Pd(TFA)_2$	L_5	HCOONa	Ag_2CO_3	MeCN	19	94
11[d]	$Pd(TFA)_2$	L_5	HCOONa	$AgNO_3$	MeCN	15	90
12[d]	$Pd(TFA)_2$	L_5	HCOONa	Ag_3PO_4	MeCN	17	96
13[e]	$Pd(TFA)_2$	L_5	HCOONa	Ag_3PO_4	MeCN	49	94
14[f]	**$Pd(TFA)_2$**	**L_5**	**HCOONa**	**Ag_3PO_4**	**MeCN**	**70**	**93**

[a]**Reactions Conditions:** Reaction conditions: **5a** (0.025 mmol), $Pd(TFA)_2$ (7 mol%), **L_n*** (15 mol%), HCOONa (2.5 equiv), K_3PO_4 (0.4 equiv), MeCN (0.05 M) at 60 °C for 48 h. [b]Crude ^1H NMR yield (yields measured with tri-methoxybenzene as internal standard). [c]Enantiomeric excess (*ee*) determined by chiral HPLC. [d]At 50 °C. [e]At 60 °C. [f]**5a** (0.1 mmol) at 70 °C, 48 h, isolated yield.

5. Characterization data and HPLC Spectra of Products:

Di-substituted Trifluoromethyl Acrylamides (2):

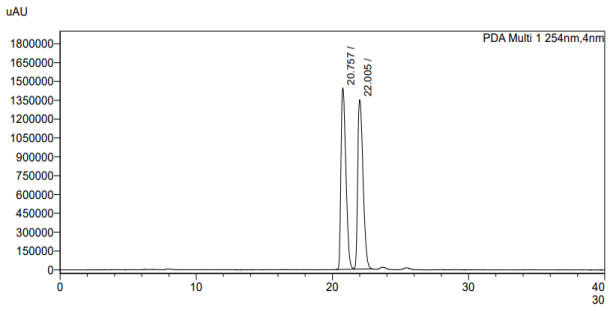
(*S*)-1,3-Dimethyl-3-(trifluoromethyl)indolin-2-one (2a):[5]



According to **GP–V**, the reaction of *N*-(2-bromophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide **1a** (31 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L_4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2a** (20.3 mg) in 89% yield and 94% *ee* as a white solid; R_f = 0.50 (3% EtOAc, 30% DCM in hexane). Melting point: 59–61 °C. For 1.0 mmol reaction, **2a** (218.3 mg) in 95% yield and 96% *ee*.

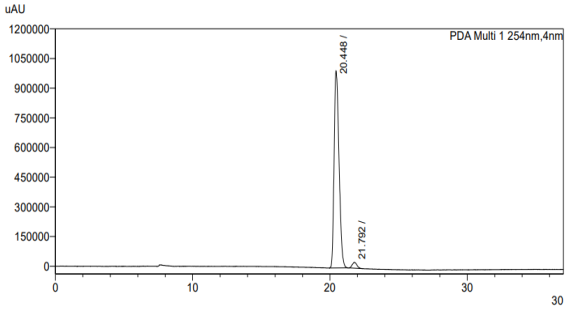
^1H NMR (500 MHz, $CDCl_3$) δ 7.42–7.35 (m, 2H), 7.12 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 3.25 (s, 3H), 1.64 (s, 3H); **$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$)** δ 172.3 (q, J = 2.1 Hz) 143.7, 129.9, 126.2, 124.9 (q, J = 281.8 Hz), 124.5, 123.2, 108.6, 52.1 (q, J = 27.6 Hz), 26.6, 17.7 (q, J = 2.2 Hz); **$^{19}F\{^1H\}$ NMR (471 MHz, $CDCl_3$)** δ -73.6 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}F_3NO$: 230.0787, found 230.0783.

Enantiomeric excess = 94%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 20.45 min (major), t_R = 21.79 min (minor). $[\alpha]_D^{26.3}$ = +17° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	20.757	36229239	1443704	49.722	49.722
2	22.005	36634805	1348430	50.278	50.278
Total		72864043	2792134		100.000

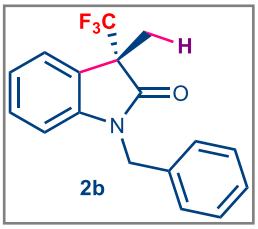


PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	20.448	24826309	996401	97.238	97.238
2	21.792	705187	29537	2.762	2.762
Total		25531496	1025938		100.000

Figure S5. HPLC chromatograms for racemic **2a** and enantioenriched **2a**.

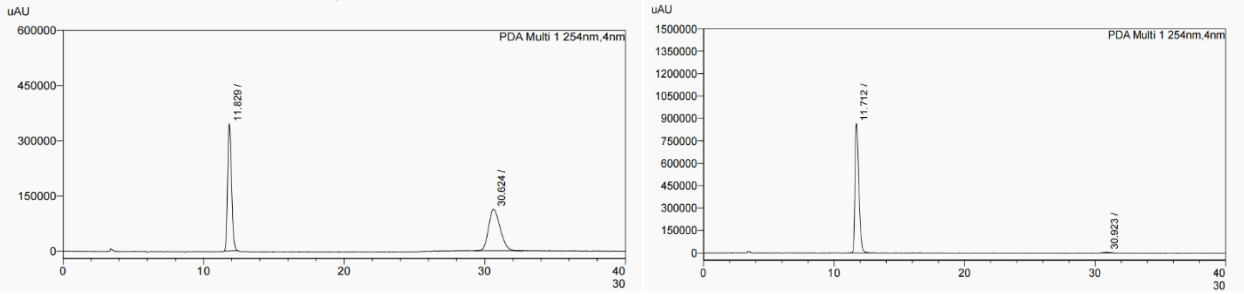
(*S*)-1-Benzyl-3-methyl-3-(trifluoromethyl)indolin-2-one (2b):



According to **GP–V**, the reaction of *N*-benzyl-*N*-(2-bromophenyl)-2-(trifluoromethyl)acrylamide **1b** (38 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2b** (30.4 mg) in >99% yield and 98% *ee* as a white solid; R_f = 0.64 (3% EtOAc, 30% DCM in hexane); Melting point: 46–48 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 7.3 Hz, 1H), 7.26–7.21 (m, 2H), 7.20–7.14 (m, 4H), 7.00 (t, J = 7.5 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 4.99 (d, J = 15.7 Hz, 1H), 4.73 (d, J = 15.7 Hz, 1H), 1.63 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 172.5 (bq, J = 2.3 Hz), 142.7, 135.1, 129.8, 128.9, 127.8, 127.0, 126.2, 125.0 (q, J = 281.8 Hz), 124.6, 123.2, 109.6, 52.2 (q, J = 27.6 Hz), 43.9, 17.9 (bq, J = 2.3 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.5 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{17}H_{15}F_3NO$: 306.1100, found 306.1104.

Enantiomeric excess = 98%, determined by HPLC (Daicel Chiralpak OJ-H Column, 2.5% ^{i}PrOH in *n*-Hexane, flow rate 1.0 mL/min, T = 25 °C, λ = 254 nm): t_R = 11.71 min (major), t_R = 30.92 min (minor). $[\alpha]_D^{28.4}$ = +2° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

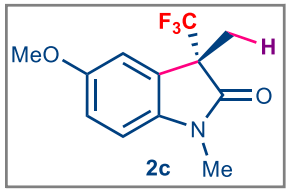
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.829	6715897	345034	50.991	50.991
2	30.624	6454817	112794	49.009	49.009
Total		13170714	457828		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.712	17604895	865478	98.847	98.847
2	30.923	205279	4131	1.153	1.153
Total		17810174	869609		100.000

Figure S6. HPLC chromatograms for racemic **2b** and enantioenriched **2b**.

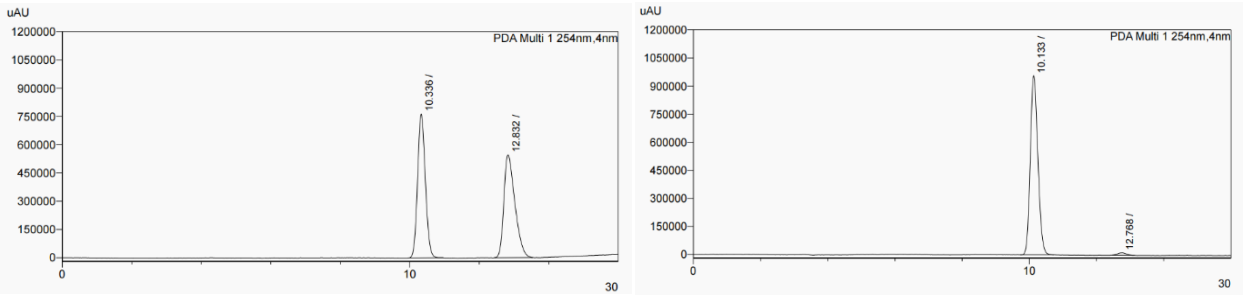
(*S*)-5-Methoxy-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2c):



According to **GP–V**, the reaction of *N*-(2-bromo-4-methoxyphenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide **1c** (34 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2c** (23.4 mg) in 90% yield and 97% *ee* as a white solid; R_f = 0.42 (3% EtOAc, 30% DCM in hexane); Melting point: 59–61 °C.

^{1}H NMR (500 MHz, $CDCl_3$) 6.98 (bs, 1H), 6.90 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 3.81 (s, 3H), 3.22 (s, 3H), 1.63 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** *δ* 171.9 (bq, *J* = 2.1 Hz), 156.3, 137.0, 127.4, 124.9 (q, *J* = 281.8 Hz), 114.0, 112.0, 108.9, 55.8, 52.4 (q, *J* = 27.6 Hz), 26.6, 17.8 (bq, *J* = 2.2 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** *δ* -73.6 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{13}F_3NO_2$: 260.0893, found 260.0911.

Enantiomeric excess = 97%, determined by HPLC (Daicel Chiralpak OD-H Column, 2.5% ^{i}PrOH in *n*-Hexane, flow rate 1.0 mL/min, T = 15 °C, λ = 254 nm): t_R = 10.13 min (major), t_R = 12.77 min (minor). **$[\alpha]_D^{28}$** = +31° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

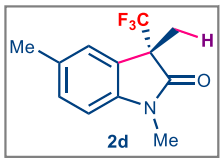
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.336	11856155	763076	49.709	49.709
2	12.832	11994856	546257	50.291	50.291
Total		23851011	1309333		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10.133	15048315	955462	98.417	98.417
2	12.768	242081	13063	1.583	1.583
Total		15290396	968525		100.000

Figure S7. HPLC chromatograms for racemic **2c** and enantioenriched **2c**.

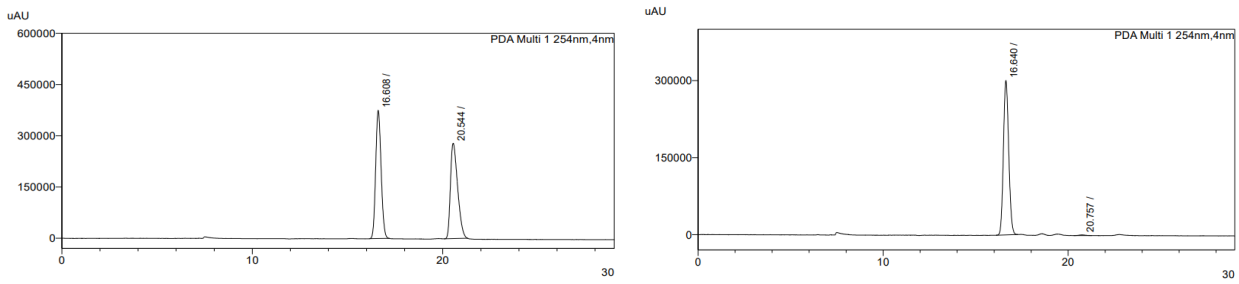
(*S*)-1,3,5-Trimethyl-3-(trifluoromethyl)indolin-2-one (2d):



According to **GP–V**, the reaction of *N*-(2-bromo-4-methylphenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide **1d** (32.2 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L_4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2d** (20.2 mg) in 83% yield and 99% *ee* as a white solid; R_f = 0.50 (3% EtOAc, 30% DCM in hexane); Melting point: 81–83 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20–7.15 (m, 2H), 6.77 (d, J = 7.8 Hz, 1H), 3.22 (s, 3H), 2.36 (s, 3H), 1.63 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 172.2 (q, J = 3.3 Hz), 141.2, 132.8, 130.1, 126.2, 125.3, 125.0 (q, J = 282.0 Hz), 108.3, 52.2 (q, J = 27.5 Hz), 26.6, 21.1, 17.8 (q, J = 2.1 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.6 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{13}F_3NO$: 244.0944, found 244.0942.

Enantiomeric excess = 99%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 16.64 min (major), t_R = 20.76 min (minor). **$[\alpha]_D^{26.7}$** = +29° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

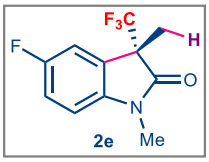
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	16.608	7431500	374828	50.411	50.411
2	20.544	7310360	279249	49.589	49.589
Total		14741860	654077		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	16.640	5981700	300627	99.528	99.528
2	20.757	28361	1336	0.472	0.472
Total		6010061	301963		100.000

Figure S8. HPLC chromatograms for racemic **2d** and enantioenriched **2d**.

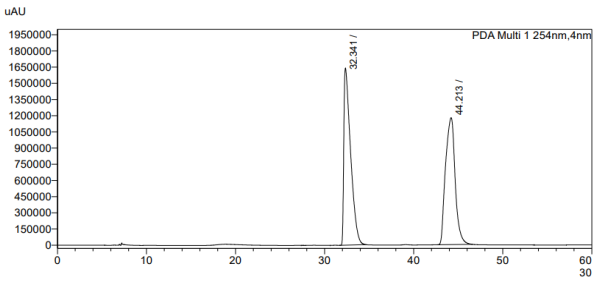
(*S*)-5-Fluoro-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2e):



Using the above method **GP–V**, the reaction of *N*-(2-Bromo-4-fluorophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1e**; 32.6 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded the **2e** (13.1 mg) in 53% yield and 91% *ee* as a white solid; R_f = 0.46 (3% EtOAc, 30% DCM in hexane); Melting point: 76–78 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16–7.06 (m, 2H), 6.82 (dd, J = 8.3, 3.8 Hz, 1H), 3.24 (s, 3H), 1.64 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 171.8 (bd, J = 1.3 Hz), 159.3 (d, J = 242.1 Hz), 139.6 (d, J = 2.0 Hz), 127.5 (d, J = 8.3 Hz), 124.6 (q, J = 281.8 Hz), 116.2 (d, J = 23.5 Hz), 112.9 (d, J = 25.6 Hz), 109.2 (d, J = 8.1 Hz), 52.5 (qd, J = 29.1, 1.5 Hz), 26.7, 17.7 (bq, J = 2.4 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.6, -119.3 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}F_4NO$: 248.0693, found 248.0688.

Enantiomeric excess = 91%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 32.38 min (major), t_R = 44.10 min (minor). **$[\alpha]_D^{28.5}$** = +6° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

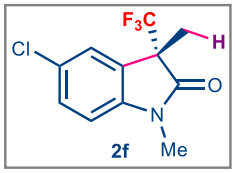
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	32.341	86782897	1639784	49.608	49.608
2	44.213	88154410	1176083	50.392	50.392
Total		174937307	2815867		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	32.384	50439462	1030193	95.398	95.398
2	44.096	2433310	38400	4.602	4.602
Total		52872772	1068594		100.000

Figure S9. HPLC chromatograms for racemic **2e** and enantioenriched **2e**.

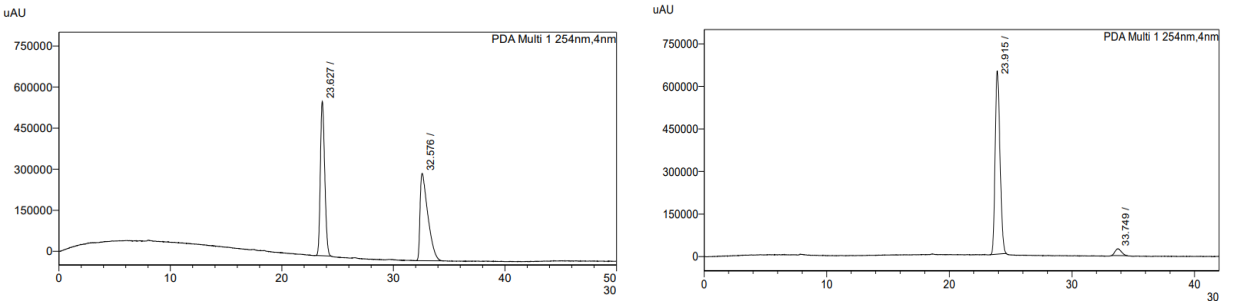
(*S*)-5-Chloro-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2f):



According to **GP–V**, the reaction of *N*-(2-Bromo-4-chlorophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1f**; 34 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2f** (23.5 mg) in 89% yield and 91% *ee* as a white solid; R_f = 0.54 (3% EtOAc, 30% DCM in hexane); Melting point: 68–70 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.33 (m, 2H), 6.82 (d, J = 8.2 Hz, 1H), 3.23 (s, 3H), 1.64 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 171.7 (d, J = 1.7 Hz), 142.2, 130.0, 128.6, 127.7, 125.1, 124.6 (q, J = 281.9 Hz), 109.5, 52.3 (q, J = 28.0 Hz), 26.7, 17.7 (bq, J = 2.1 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.6 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}ClF_3NO$: 264.0398, found 264.0406.

Enantiomeric excess = 91%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 23.92 min (major), t_R = 33.75 min (minor). **$[\alpha]_D^{27.4}$** = +40° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

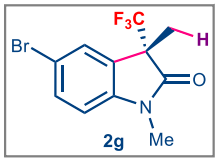
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.627	15325638	564100	49.734	49.734
2	32.576	15489365	319165	50.266	50.266
Total		30815003	883265		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.915	17781746	645520	95.435	95.435
2	33.749	850483	23511	4.565	4.565
Total		18632230	669030		100.000

Figure S10. HPLC chromatograms for racemic **2f** and enantioenriched **2f**.

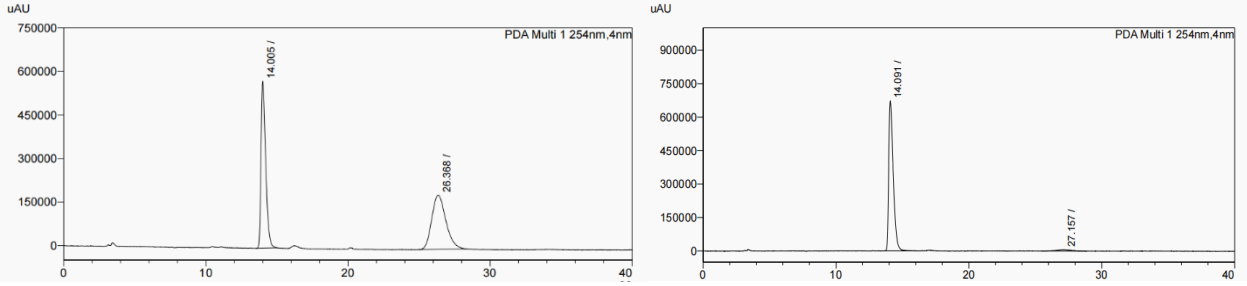
(*S*)-5-Bromo-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2g):



According to **GP–V**, the reaction of *N*-(4-bromo-2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1g′**; 86.8 mg, 0.2 mmol) using $Pd(TFA)_2$ (4.65 mg, 7 mol%), *S*-PHOX (**L4**, 11.2 mg, 15 mol%), HCOONa (34 mg, 0.5 mmol) and K_3PO_4 (17 mg, 0.08 mmol) afforded **2g** (39.6 mg) in 59% yield and 94% *ee* as a white solid; R_f = 0.54 (3% EtOAc, 30% DCM in hexane); Melting point: 97–99 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (bd, J = 8.3 Hz, 1H), 7.48 (bs, 1H), 6.77 (d, J = 8.2 Hz, 1H), 3.23 (s, 3H), 1.64 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 171.6 (bq, J = 2.0 Hz), 142.7, 132.8, 128.0, 127.8, 124.6 (q, J = 281.9 Hz), 115.7, 110.0, 52.2 (q, J = 27.9 Hz), 26.7, 17.7 (q, J = 1.8 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -73.4 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}BrF_3NO$: 307.9892, found 307.9889.

Enantiomeric excess = 94%, determined by HPLC (Daicel Chiralpak OJ-H Column, 2.5% ^{i}PrOH in *n*-Hexane, flow rate 1.0 mL/min, T = 25 °C, λ = 254 nm): t_R = 14.09 min (major), t_R = 27.16 min (minor). **$[\alpha]_D^{28.7}$** = +30° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

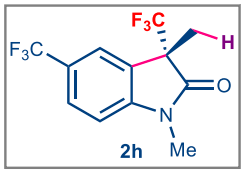
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.005	13121948	574360	50.325	50.325
2	26.368	12952598	187265	49.675	49.675
Total		26074546	761625		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.091	15886931	671104	96.983	96.983
2	27.157	494209	6773	3.017	3.017
Total		16381140	677877		100.000

Figure S11. HPLC chromatograms for racemic **2g** and enantioenriched **2g**.

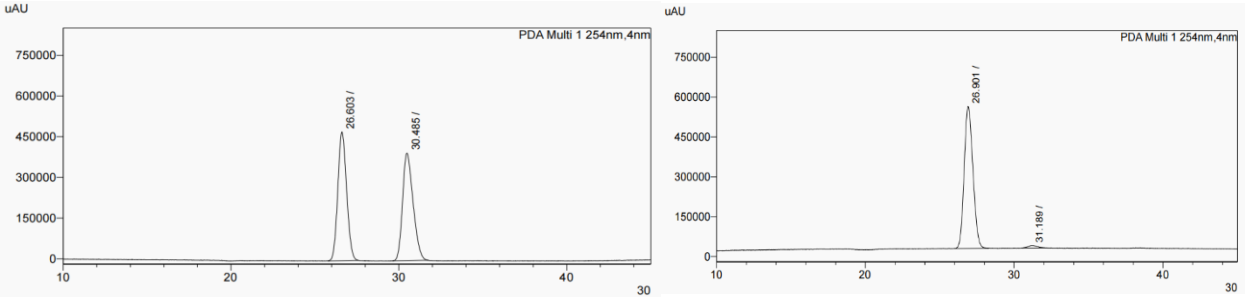
(*S*)-1,3-Dimethyl-3,5-bis(trifluoromethyl)indolin-2-one (2h):



According to **GP–V**, the reaction of *N*-(2-bromo-4-(trifluoromethyl)phenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1h**; 37.6 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2h** (14.2 mg) in 48% yield and 97% *ee* as a white solid; R_f = 0.54 (3% EtOAc, 30% DCM in hexane); Melting point: 82–84 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 1H), 7.60 (s, 1H) 6.98 (d, J = 8.1 Hz, 1H), 3.28 (s, 3H), 1.68 (s, 3H);**^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 172.1 (bq, J = 2.1 Hz), 146.6, 127.7 (q, J = 3.8 Hz), 126.7, 125.6 (q, J = 33.1 Hz), 124.6 (q, J = 276.5 Hz), 124.0 (q, J = 271.6 Hz), 121.7 (q, J = 3.7 Hz), 108.5, 52.1 (q, J = 28.1 Hz), 26.8, 17.6 (bq, J =1.9 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -61.7, -73.5 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{10}F_6NO$: 298.0661, found 298.0668.

Enantiomeric excess = 97%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 26.90 min (major), t_R = 31.19 min (minor). **$[\alpha]_D^{28}$** = +2° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

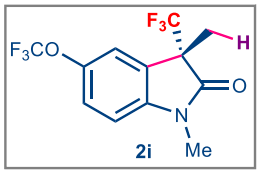
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	26.603	17311033	474056	50.118	50.118
2	30.485	17229795	395864	49.882	49.882
Total		34540827	869920		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	26.901	21828074	534436	98.214	98.214
2	31.189	396991	9028	1.786	1.786
Total		22225065	543464		100.000

Figure S12. HPLC chromatograms for racemic **2h** and enantioenriched **2h**.

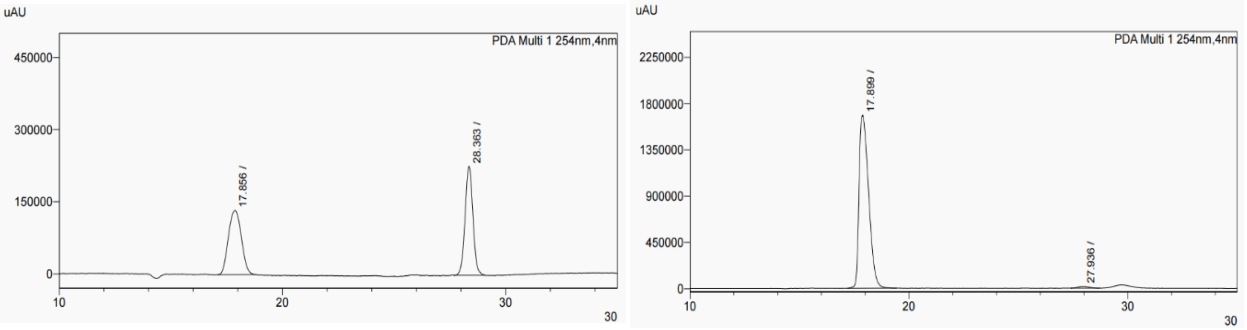
(*S*)-1,3-Dimethyl-5-(trifluoromethoxy)-3-(trifluoromethyl)indolin-2-one (2i):



According to **GP–V**, the reaction of *N*-(2-bromo-4-(trifluoromethoxy)phenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1i**; 39.2 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2i** (19.7 mg) in 63% yield and 98% *ee* as a yellow liquid; R_f = 0.54 (3% EtOAc, 30% DCM in hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.24 (m, 2H), 6.89 (d, J = 8.2 Hz, 1H), 3.26 (s, 3H), 1.66 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 171.9 (bq, J = 1.8 Hz), 145.0, 142.4, 127.5, 124.5 (q, J = 281.8 Hz), 123.1, 120.5 (q, J = 257.1 Hz), 118.7, 109.1, 52.4 (q, J = 28.0 Hz), 26.8, 17.7 (bq, J = 2.1 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -58.5, -73.6 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{10}F_6NO_2$: 314.0610, found 314.0610.

Enantiomeric excess = 98%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 17.90 min (major), t_R = 27.94 min (minor). **$[\alpha]_D^{28.6}$** = +13° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

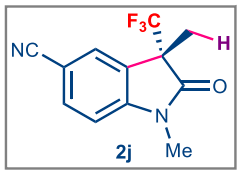
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	17.856	5378953	133735	49.290	49.290
2	28.363	5533850	226524	50.710	50.710
Total		10912803	360259		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	17.899	51120721	1682495	98.851	98.851
2	27.936	594346	17494	1.149	1.149
Total		51715067	1699989		100.000

Figure S13. HPLC chromatograms for racemic **2i** and enantioenriched **2i**.

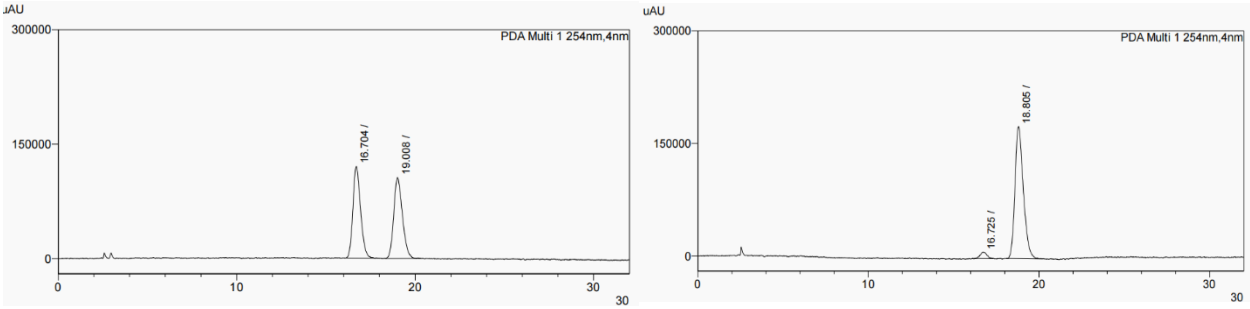
(*S*)-1,3-Dimethyl-2-oxo-3-(trifluoromethyl)indoline-5-carbonitrile (2j):



According to **GP–V**, the reaction of *N*-(2-bromo-4-cyanophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1j**; 33.3 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol), K_3PO_4 (42.5 mg, 0.2 mmol) and Ag_2CO_3 (55.2 mg, 0.2 mmol) afforded **2j** (17 mg) in 67% yield and 93% *ee* as a white solid; R_f = 0.17 (3% EtOAc, 30% DCM in hexane); Melting point: 123–125 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, J = 8.2, 1.5 Hz, 1H), 7.63 (s, 1H), 6.98 (d, J = 8.2 Hz 1H), 3.28 (s, 3H), 1.67 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 171.7 (bq, J = 2.0 Hz), 147.4 135.1, 128.0, 127.1, 124.3 (q, J = 281.9 Hz), 118.4, 109.2, 106.6, 51.9 (q, J = 28.3 Hz), 26.8, 17.5 (bq, J = 1.9 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.5 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{10}F_3N_2O$: 255.0740, found 255.0755.

Enantiomeric excess = 93%, determined by HPLC (Daicel Chiralpak OD-H Column, 3% ^{i}PrOH in *n*-Hexane, flow rate 1.3 mL/min, T = 15 °C, λ = 254 nm): t_R = 16.72 min (minor), t_R = 18.80 min (major). **$[\alpha]_D^{28}$** = +36° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

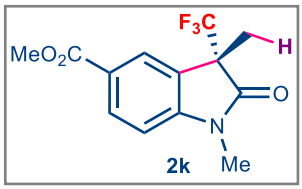
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	16.704	3578850	120089	49.958	49.958
2	19.008	3584826	106120	50.042	50.042
Total		7163677	226210		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	16.725	226043	8664	3.628	3.628
2	18.805	6005144	176027	96.372	96.372
Total		6231187	184691		100.000

Figure S14. HPLC chromatograms for racemic **2j** and enantioenriched **2j**.

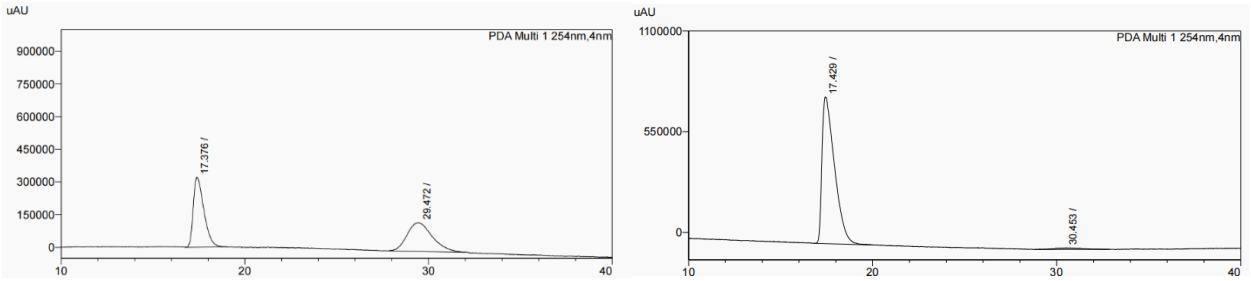
Methyl (*S*)-1,3-dimethyl-2-oxo-3-(trifluoromethyl)indoline-5-carboxylate (2k):



According to **GP–V**, the reaction of methyl 3-bromo-4-(*N*-methyl-2-(trifluoromethyl)acrylamido)benzoate (**1k**; 36.6 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded the desired amide **2k** (27.4 mg) in 95% yield and 96% *ee* as a white solid; R_f = 0.32 (3% EtOAc, 30% DCM in hexane); Melting point: 96–98 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, J = 8.2, 1.6 Hz, 1H), 8.04 (s, 1H), 6.94 (d, J = 8.2 Hz, 1H), 3.92 (s, 3H), 3.28 (s, 3H), 1.67 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 172.5 (q, J = 1.8 Hz), 166.3, 147.6, 132.5, 126.1, 125.9, 125.3, 124.6 (q, J = 281.3 Hz), 108.2, 52.2, 52.0 (q, J = 28.0 Hz), 26.8, 17.6 (bq, J = 2.0 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.5 ppm; **HRMS (ESI-TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{13}H_{13}F_3NO_3$: 288.0842, found 288.0854.

Enantiomeric excess = 96%, determined by HPLC (Daicel Chiralpak OD-H Column, 12% ^{i}PrOH in *n*-Hexane, flow rate 1.0 mL/min, T = 15 °C, λ = 254 nm): t_R = 17.43 min (major), t_R = 30.45 min (minor). **$[\alpha]_D^{28.2}$** = +35° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

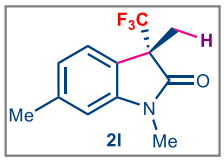
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	17.376	12923581	321741	50.389	50.389
2	29.472	12723834	133063	49.611	49.611
Total		25647415	454804		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	17.429	38027417	802053	97.859	97.859
2	30.453	831783	8196	2.141	2.141
Total		38859200	810249		100.000

Figure S15. HPLC chromatograms for racemic **2k** and enantioenriched **2k**.

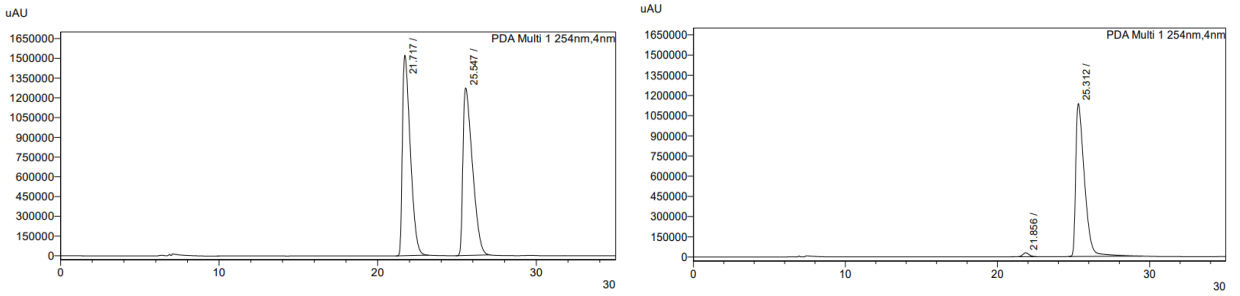
(*S*)-1,3,6-Trimethyl-3-(trifluoromethyl)indolin-2-one (2l):



According to **GP–V**, the reaction of *N*-(2-bromo-5-methylphenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1l**; 32.2 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2l** (21.3 mg) in 88% yield and 96% *ee* as a white solid; R_f = 0.56 (3% EtOAc, 30% DCM in hexane); Melting point: 69–71 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.23 (m, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.72 (s, 1H), 3.23 (s, 3H), 2.41 (s, 3H), 1.62 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 172.6 (bd, J = 1.6 Hz), 143.7, 140.3, 125.0 (q, J = 281.6 Hz), 124.2, 123.7, 123.3, 109.5, 51.9 (q, J = 27.6 Hz), 26.6, 21.8, 17.8 (bd, J = 2.0 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.8 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{13}F_3NO$: 244.0944, found 244.0947.

Enantiomeric excess = 96%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 21.86 min (minor), t_R = 25.31 min (major). **$[\alpha]_D^{28.3}$** = +8° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

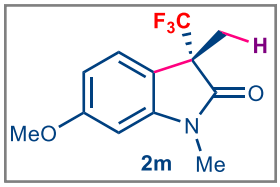
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	21.717	52739422	1521029	49.865	49.865
2	25.547	53025068	1272612	50.135	50.135
Total		105764490	2793641		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	21.856	811465	28231	1.754	1.754
2	25.312	45454848	1136145	98.246	98.246
Total		46266313	1164375		100.000

Figure S16. HPLC chromatograms for racemic **2l** and enantioenriched **2l**.

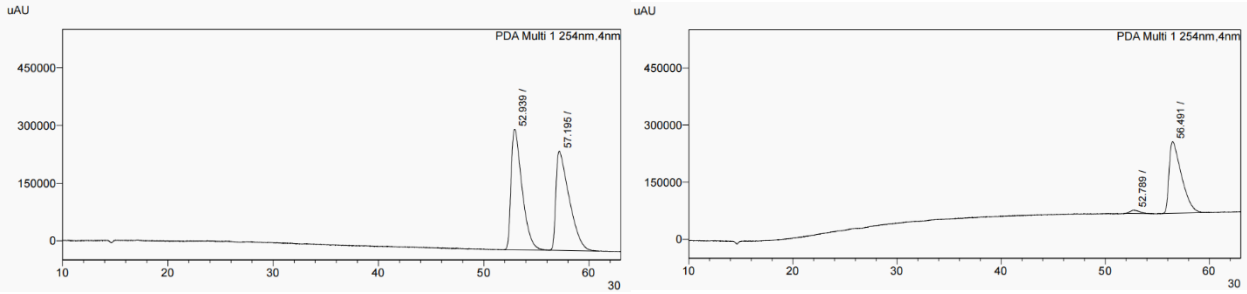
(*S*)-6-Methoxy-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2m):



According to **GP–V**, the reaction of *N*-(2-bromo-5-methoxyphenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1m**; 33.8 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2m** (14.8 mg) in 57% yield and 93% *ee* as a white solid; R_f = 0.44 (3% EtOAc, 30% DCM in hexane); Melting point: 55–57 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.23 (m, 1H), 6.61 (dd, J = 8.2, 1.8 Hz, 1H), 6.46 (d, J = 1.6 Hz, 1H), 3.84 (s, 3H), 3.22 (s, 3H), 1.61 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 172.9 (bs), 161.4, 145.0, 125.3, 125.0 (q, J = 283.4 Hz), 118.1, 106.9, 96.6, 55.6, 51.7 (q, J = 28.6 Hz), 26.6, 17.8 (bd, J = 1.6 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.9 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{13}F_3NO_2$: 260.0893, found 260.0903.

Enantiomeric excess = 93%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 52.79 min (minor), t_R = 56.49 min (major). **$[\alpha]_D^{28.4}$** = +2° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

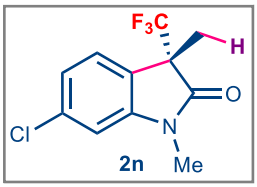
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	52.939	22790095	313914	50.207	50.207
2	57.195	22602347	258044	49.793	49.793
Total		45392442	571959		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	52.789	536200	8519	3.326	3.326
2	56.491	15583995	188706	96.674	96.674
Total		16120195	197225		100.000

Figure S17. HPLC chromatograms for racemic **2m** and enantioenriched **2m**.

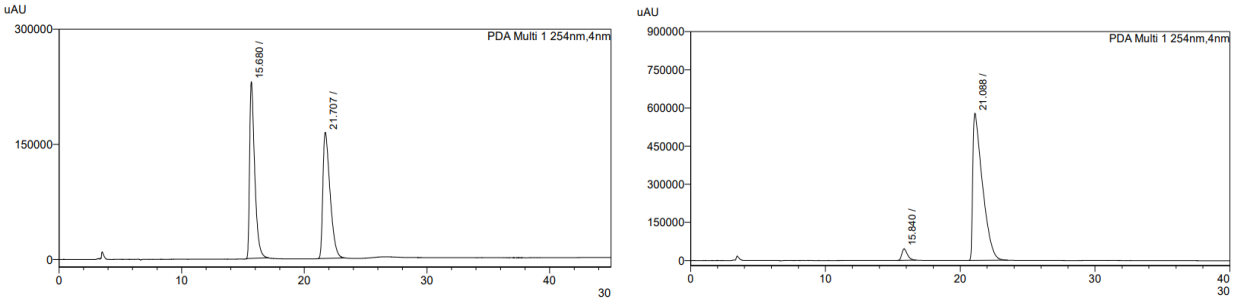
(*S*)-6-Chloro-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2n):



Using the above method **GP–V**, the reaction of *N*-(2-bromo-5-chlorophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1n**; 34 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2n** (22.7 mg) in 86% yield and 91% *ee* as a white solid; R_f = 0.56 (3% EtOAc, 30% DCM in hexane); Melting point: 80–82 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, J = 7.9 Hz, 1H), 7.10 (d, J = 8.0 Hz 1H), 6.89 (s, 1H), 3.23 (s, 3H), 1.63 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 172.2 (bq, J = 1.6 Hz), 144.8, 135.9, 125.5, 124.6 (q, J = 281.8 Hz), 124.5, 123.0, 109.4, 51.9 (q, J = 28.0 Hz), 26.7, 17.7 (bq, J = 1.8 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.6 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}ClF_3NO$: 264.0398, found 264.0392.

Enantiomeric excess = 91%, determined by HPLC (Daicel Chiralpak OJ-H Column, 2% ^{i}PrOH in *n*-Hexane, flow rate 1.0 mL/min, T = 15 °C, λ = 254 nm): t_R = 15.84 min (minor), t_R = 21.09 min (major). **$[\alpha]_D^{27.1}$** = +7° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

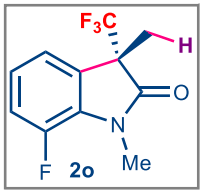
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	15.680	6614248	230122	49.660	49.660
2	21.707	6704935	164452	50.340	50.340
Total		13319184	394574		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	15.840	1289534	45434	4.283	4.283
2	21.088	28819164	578625	95.717	95.717
Total		30108698	624058		100.000

Figure S18. HPLC chromatograms for racemic **2n** and enantioenriched **2n**.

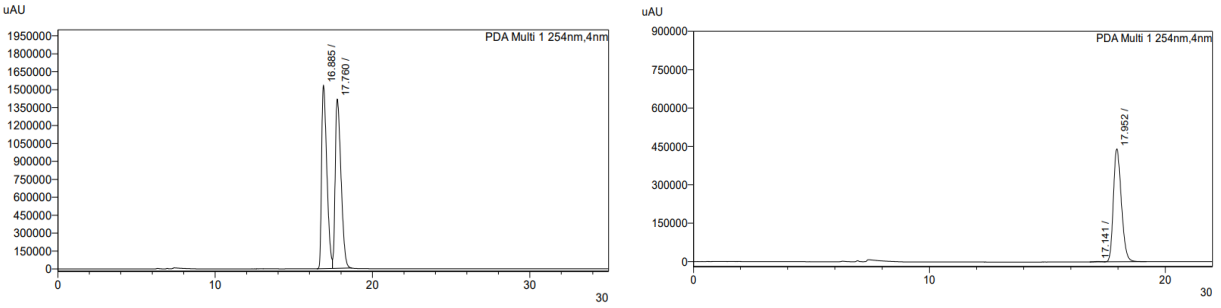
(*S*)-7-Fluoro-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2o):



According to **GP–V**, the reaction of *N*-(2-bromo-6-fluorophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1o**; 32.6 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2o** (7 mg) in 28% yield and 99% *ee* as a yellow solid; R_f = 0.64 (3%, EtOAc 30% DCM in hexane); Melting point: 106–108 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (bd, J = 7.1 Hz, 1H), 7.12 (bt, J = 9.8 Hz, 1H), 7.09–7.03 (m, 1H), 3.47 (s, 3H), 1.66 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 171.8 (q, J = 2.1 Hz), 147.6 (d, J = 244.4 Hz), 130.5 (d, J = 8.8 Hz), 128.8 (d, J = 2.4 Hz), 124.6 (q, J = 281.9 Hz), 123.8 (d, J = 6.4 Hz), 120.4 (d, J = 3.0 Hz), 117.9 (d, J = 19.1 Hz), 52.3 (qd, J = 27.9, 2.0 Hz), 29.1 (d, J = 6.0 Hz), 17.9 (q, J = 2.2 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -73.7, -(135.6–135.8) (m, 1F) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}F_4NO$: 248.0693, found 248.0712.

Enantiomeric excess = 99%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 17.14 min (minor), t_R = 18.00 min (major). **$[\alpha]_D^{27.6}$** = +10° (c = 2*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

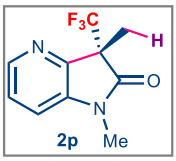
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	16.885	35450208	1532254	49.413	49.413
2	17.760	36292586	1415095	50.587	50.587
Total		71742794	2947350		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	17.141	27674	1394	0.266	0.266
2	17.952	10384170	440967	99.734	99.734
Total		10411844	442361		100.000

Figure S19. HPLC chromatograms for racemic **2o** and enantioenriched **2o**.

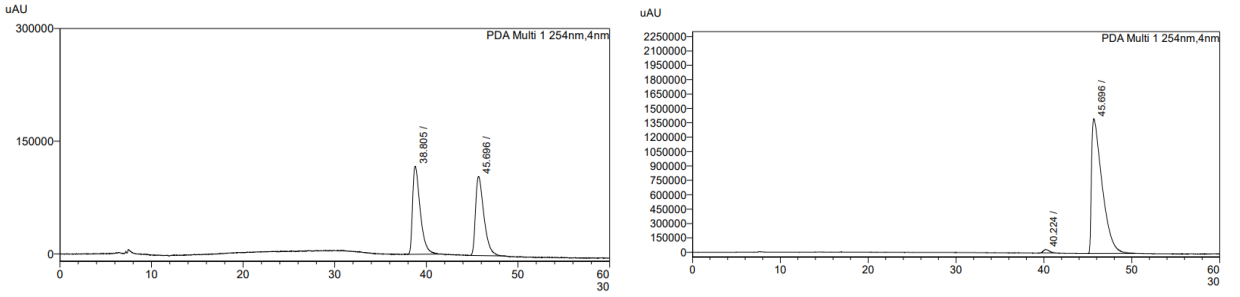
(*S*)-1,3-Dimethyl-3-(trifluoromethyl)-1,3-dihydro-2H-pyrrolo[3,2-b]pyridin-2-one (2p):



According to **GP–V**, the reaction of *N*-(2-bromopyridin-3-yl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1p**; 30.9 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2p** (19.3 mg) in 84% yield and 97% *ee* as a brown solid; R_f = 0.12 (3.0%, EtOAc, 30% DCM in hexane); Melting point: 75–77 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 4.8 Hz, 1H), 7.29 (bt, J = 6.2 Hz, 1H), 7.15 (d, J = 7.9 Hz, 1H), 3.26 (s, 3H), 1.71 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 170.9 (bq, J = 1.9 Hz), 147.1, 143.8, 139.1, 124.4, 124.2 (q, J = 282.9 Hz), 115.0, 52.2 (q, J = 27.7 Hz), 26.4, 15.9 (bq, J = 1.8 Hz); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -72.6 ppm; **HRMS (ESI-TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{10}H_{10}F_3N_2O$: 231.0740, found 231.0743.

Enantiomeric excess = 97%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 40.22 min (minor), t_R = 45.70 min (major). **$[\alpha]_D^{28.6}$** = +2° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

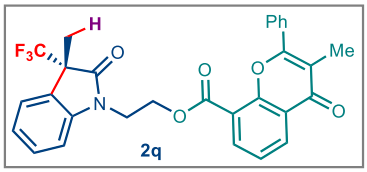
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	38.805	6786049	117193	0.000	50.354
2	45.696	6690556	105561	0.000	49.646
Total		13476605	222755		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	40.224	1805755	35990	1.504	1.504
2	45.696	118230677	1404676	98.496	98.496
Total		120036432	1440666		100.000

Figure S20. HPLC chromatograms for racemic **2p** and enantioenriched **2p**.

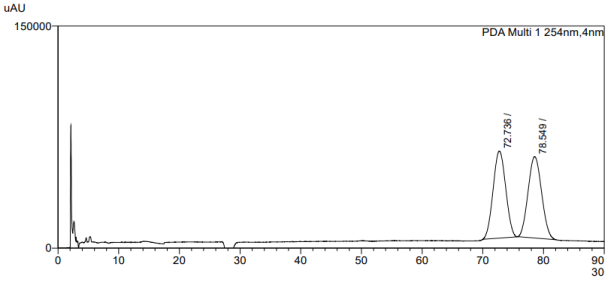
(*S*)-2-(3-Methyl-2-oxo-3-(trifluoromethyl)indolin-1-yl)ethyl-3-methyl-4-oxo-2-phenyl-4*H*-chromene-8-carboxylate (2q):

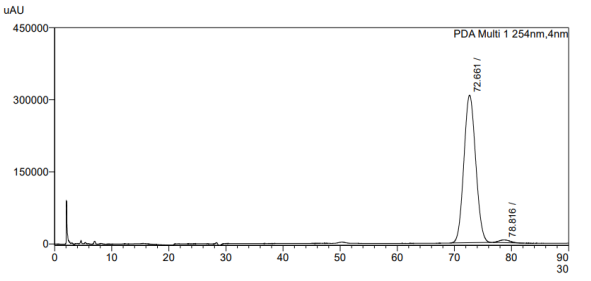


According to **GP–V**, the reaction of 2-(*N*-(2-bromophenyl)-2-(trifluoromethyl)acrylamido)ethyl-3-methyl-4-oxo-2-phenyl-4*H*-chromene-8-carboxylate (**1q**; 60 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2q** (32.2 mg) in 62% yield and 96% *ee* as a white solid; R_f = 0.04 (3% EtOAc, 30% DCM in hexane); Melting point: 153–155 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (dd, J = 7.9, 1.6 Hz, 1H), 8.09 (dd, J = 7.5, 1.6 Hz, 1H), 7.79 (dd, J = 7.4, 1.9 Hz, 2H), 7.57–7.48 (m, 3H), 7.38 (t, J = 7.7 Hz, 1H), 7.34 (d, J = 7.4 Hz, 1H), 7.29–7.24 (m, 1H), 7.09 (t, J = 7.6 Hz, 1H), 6.90 (d, J = 7.9 Hz, 1H), 4.66–4.55 (m, 2H), 4.20–4.06 (m, 2H), 2.24 (s, 3H), 1.60 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 178.2, 172.5 (bq, J = 1.8 Hz), 163.5, 160.9, 154.6, 142.5, 136.2, 133.0, 131.2, 130.5, 129.8, 129.3, 128.5, 126.1, 124.85, 124.78 (q, J = 281.5 Hz), 123.9, 123.3, 123.2, 119.5, 117.6, 108.6, 61.3, 52.0 (q, J = 27.7 Hz), 39.2, 17.6 (bq, J = 2.0 Hz), 11.8; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -73.6 ppm; **HRMS (ESI-TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{29}H_{22}F_3N\,Na\,O_5$: 544.1342, found 544.1348.

Enantiomeric excess = 96%, determined by HPLC (Daicel Chiralpak AD-H Column, 2.5% ^{i}PrOH in *n*-Hexane, flow rate 1.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 72.66 min (major), t_R = 78.82 min (minor). **$[\alpha]_D^{27.8}$** = +6° (c = 5*10^{-4}, $CHCl_3$).





PDA Ch1 254nm

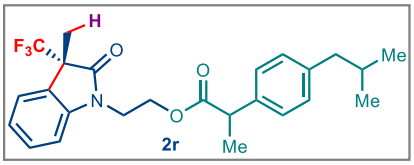
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	72.736	8483179	58827	49.927	49.927
2	78.549	8508146	54958	50.073	50.073
Total		16991325	113785		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	72.661	44104912	307121	98.250	98.250
2	78.816	785740	5746	1.750	1.750
Total		44890652	312867		100.000

Figure S21. HPLC chromatograms for racemic **2q** and enantioenriched **2q**.

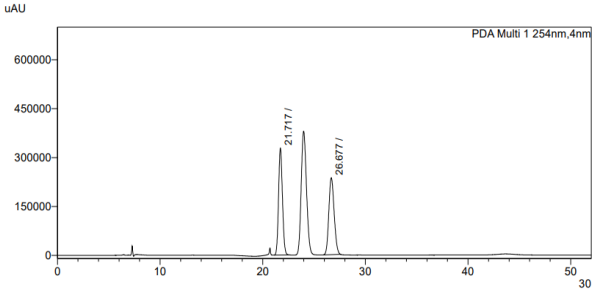
2-((*S*)-3-Methyl-2-oxo-3-(trifluoromethyl)indolin-1-yl)ethyl 2-(4-isobutylphenyl)propanoate (2r):



According to **GP–V**, the reaction of 2-(*N*-(2-bromophenyl)-2-(trifluoromethyl)acrylamido)ethyl 2-(4-isobutylphenyl)propanoate (**1r**; 52.6 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2r** (41.5 mg) in 93% yield and 96% *ee* as a yellow liquid; R_f = 0.42 (3% EtOAc, 30% DCM in hexane). Based on ^{1}H NMR 1:1 diastereomeric ratio observed.

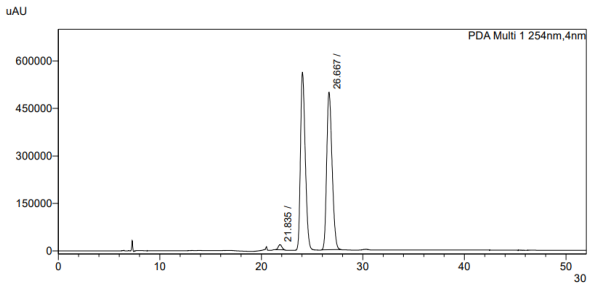
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 7.4 Hz, 1H), 7.32 (tt, J = 7.8, 1.6 Hz, 1H), 7.12 (bt, J = 7.6 Hz, 1H), 7.09–6.98 (m, 4H), 6.87 (t, J = 7.2 Hz, 1H), 4.43–4.31 (m, 1H), 4.30–4.20 (m, 1H), 4.10–3.97 (m, 1H), 3.96–3.86 (m, 1H), 3.57 (q, J = 7.2 Hz, 1H), 2.41 (d, J = 7.2 Hz, 2H), 1.82 (sept, J = 6.8 Hz, 1H), 1.61 (s, 1.5H), 1.59(s, 1.5H), 1.40 (d, J = 7.2 Hz, 1.5H), 1.35 (d, J = 7.2 Hz, 3H), 0.88 (d, J = 6.6 Hz, 6H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 174.51, 174.50, 172.4 (bq, J = 2.3 Hz, 1H), 142.9, 142.8, 140.59, 140.56, 137.21, 137.16, 129.79, 129.78, 129.3 (bs), 127.09, 127.07, 126.12, 126.08, 124.8 (q, J = 281.7 Hz), 124.6, 123.1, 108.94, 108.90, 61.25, 61.18, 52.0 (q, J = 27.8 Hz), 45.00, 44.96, 44.93, 39.2, 30.1, 22.4, 18.23, 18.18, 17.7 (bq, J = 2.1 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -73.5 ppm; **HRMS (ESI-TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{25}H_{28}F_3NNaO_3$: 470.1913, found 470.1922.

Enantiomeric excess = 96%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 21.84 min (minor), t_R = 26.67 min (major). $[\alpha]_D^{29.3}$ = +6.5° (c = 2*10^{-3}, $CHCl_3$).



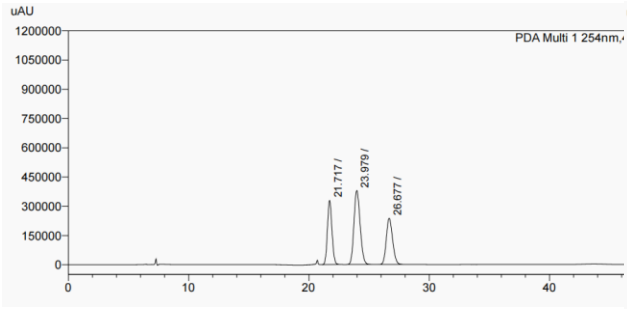
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	21.717	8614619	328053	50.363	50.363
2	26.677	8490345	236140	49.637	49.637
Total		17104964	564193		100.000



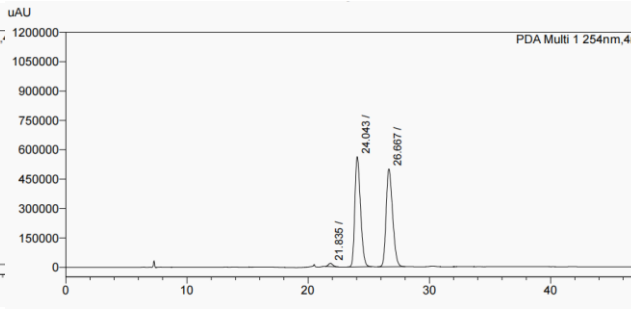
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	21.835	400373	16323	2.130	2.130
2	26.667	18392822	497997	97.870	97.870
Total		18793195	514320		100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	21.717	8614619	328053	27.974	27.974
2	23.979	13584040	379630	44.111	44.111
3	26.677	8596548	237049	27.915	27.915
Total		30795207	944732		100.000

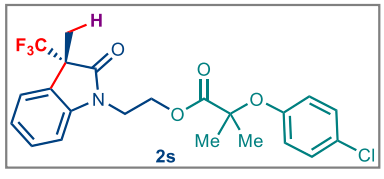


PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	21.835	421775	16664	1.131	1.131
2	24.043	18381771	562073	49.288	49.288
3	26.667	18491367	498821	49.581	49.581
Total		37294913	1077559		100.000

Figure S22. HPLC chromatograms for racemic **2r** and enantioenriched **2r**.

(*S*)-2-(3-Methyl-2-oxo-3-(trifluoromethyl)indolin-1-yl)ethyl-2-(4-chlorophenoxy)-2-methylpropanoate (2s):

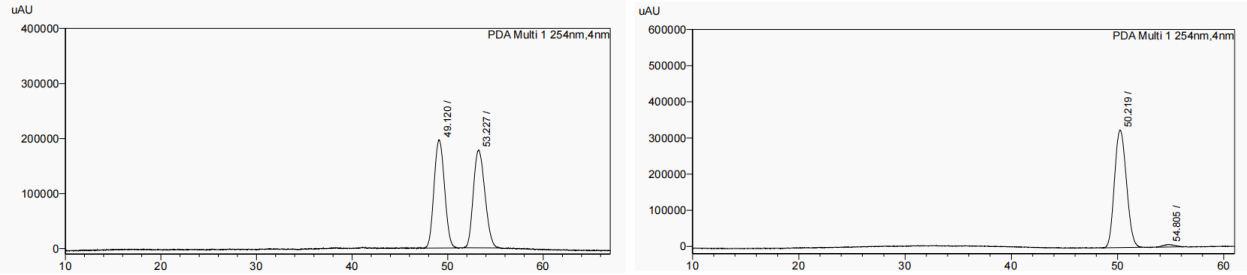


According to **GP–V**, the reaction of 2-(*N*-(2-bromophenyl)-2-(trifluoromethyl)acrylamido)ethyl 2-(4-chlorophenoxy)-2-methylpropanoate (**1s**; 53.47 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), *S*-PHOX (**L4**, 5.6 mg, 15 mol%), HCOONa (17 mg,

0.25 mmol) and K_3PO_4 (8.5 mg, 0.04 mmol) afforded **2s** (43.5 mg) in 95% yield and 96% *ee* as a yellow liquid; R_f = 0.35 (3% EtOAc, 30% DCM in hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (bd, J = 7.5 Hz, 1H), 7.33 (td, J = 7.8, 1.0 Hz, 1H), 7.14–7.09 (m, 3H), 6.90 (d, J = 7.9 Hz, 1H), 6.72–6.67 (m, 2H), 4.46–4.36 (m, 2H), 4.09–4.02 (m, 1H), 4.00–3.93 (m, 1H), 1.61 (s, 3H), 1.47 (s, 3H), 1.45 (s, 3H); **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 173.7, 172.4 (bq, J = 2.1 Hz), 153.7, 142.5, 129.8, 129.0, 127.4, 126.0, 124.8 (q, J = 281.9 Hz), 124.7, 123.3, 120.7, 108.9, 79.4, 62.0, 52.0 (q, J = 27.8 Hz), 39.1, 25.2, 25.0, 17.6 (bq, J = 1.7 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -73.6 ppm; **HRMS (ESI-TOF)** ***m/z***: $[M+Na]^+$ calcd. for $C_{22}H_{21}ClF_3N\ NaO_4$: 478.1003, found 478.1003.

Enantiomeric excess = 96%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 50.22 min (major), t_R = 54.80 min (minor). **$[\alpha]_D^{28.3}$** = +14° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	49.120	15004992	196560	0.000	50.066
2	53.227	14965630	177877	0.000	49.934
Total		29970622	374437		100.000

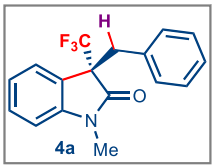
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	50.219	25352460	324535	97.959	97.959
2	54.805	528136	7050	2.041	2.041
Total		25880596	331585		100.000

Figure S23. HPLC chromatograms for racemic **2s** and enantioenriched **2s**.

Tri-substituted *β*-Phenyl Trifluoromethyl Acrylamides (4):

(*S*)-3-Benzyl-1-methyl-3-(trifluoromethyl)indolin-2-one (4a):[6]

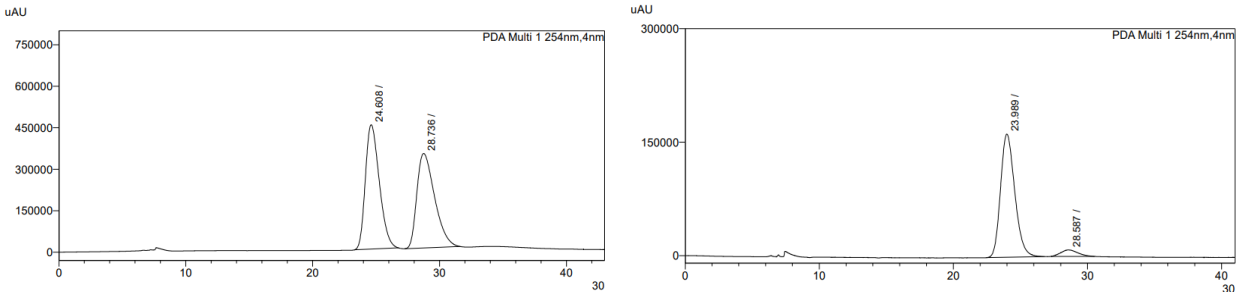


According to **GP–VII**, the reaction of (*Z*)-*N*-(2-iodophenyl)-*N*-methyl-3-phenyl-2-(trifluoromethyl)acrylamide (**3a**; 21.56 mg, 0.05 mmol) using $Pd(TFA)_2$ (1.2 mg, 7 mol%), (*S*, *Sp*)-^{t}Bu-Phosferrox (**L3**, 4.95 mg, 20 mol%), HCOONa (8.5 mg, 0.125 mmol), K_3PO_4 (4.25 mg, 0.02 mmol) and Ag_2CO_3 (4.13 mg, 0.015

mmol) afforded **4a** (6.7 mg) in 44% yield and 88% *ee* as a white solid; R_f = 0.35 (3% EtOAc, 30% DCM in hexane); Melting point: 83–85 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 7.4 Hz, 1H), 7.30–7.25 (m, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.08–7.04 (m, 1H), 7.01 (t, J = 7.2 Hz, 2H), 6.85–6.80 (m, 2H), 6.58 (d, J = 7.8 Hz, 1H), 3.61 (d, J = 12.9 Hz, 1H), 3.31 (d, J = 12.9 Hz, 1H), 2.94 (s, 3H); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -71.5 ppm.

Enantiomeric excess = 88%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 23.99 min (major), t_R = 28.59 min (minor). **$[\alpha]_D^{28.3}$** = +39° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

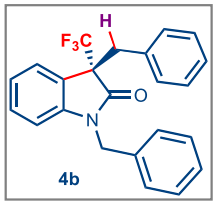
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	24.608	34323025	449509	50.828	50.828
2	28.736	33205263	341655	49.172	49.172
Total		67528288	791164		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.989	12055000	162941	94.169	94.169
2	28.587	746481	8495	5.831	5.831
Total		12801481	171436		100.000

Figure S24. HPLC chromatograms for racemic **4a** and enantioenriched **4a**.

(*S*)-1,3-Dibenzyl-3-(trifluoromethyl)indolin-2-one (4b)[6]:

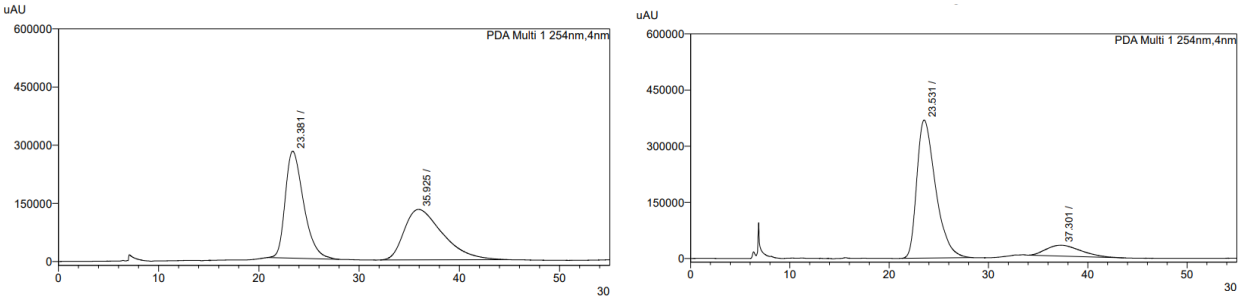


According to **GP–VII**, the reaction of (Z)-*N*-benzyl-*N*-(2-iodophenyl)-3-phenyl-2-(trifluoromethyl)acrylamide (**3b**; 25.36 mg, 0.05 mmol) using $Pd(TFA)_2$ (1.2 mg, 7 mol%), (*S*, *Sp*)-^{t}Bu-Phosferrox (**L_3**, 4.95 mg, 20 mol%), HCOONa (8.5 mg, 0.125 mmol), K_3PO_4 (4.25 mg, 0.02 mmol) and Ag_2CO_3 (4.13 mg, 0.015 mmol) afforded **4b** (7.3 mg) in 38% yield and 75% *ee* as a white solid; R_f = 0.46 (3% EtOAc, 30% DCM in hexane); Melting point: 76–78 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.2 Hz, 1H), 7.20–7.10 (m, 6H), 7.06 (t, J = 7.6 Hz, 2H), 6.91 (d, J = 7.7 Hz, 2H), 6.63 (d, J = 7.2 Hz, 2H), 6.41 (d, J = 7.7 Hz, 1H), 4.90 (d, J = 16.0

Hz, 1H), 4.56 (d, J = 16.0 Hz, 1H), 3.71 (d, J = 13.0 Hz, 1H), 3.42 (d, J = 13.0 Hz, 1H); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -71.8 ppm.

Enantiomeric excess = 75%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 23.53 min (major), t_R = 37.30 min (minor). **$[\alpha]_D^{28.8}$** = +20° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

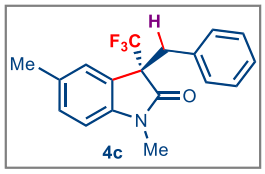
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.381	35295591	276255	50.418	50.418
2	35.925	34709759	130122	49.582	49.582
Total		70005350	406377		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.531	48498079	369186	87.341	87.341
2	37.301	7029007	29111	12.659	12.659
Total		55527086	398297		100.000

Figure S25. HPLC chromatograms for racemic **4b** and enantioenriched **4b**.

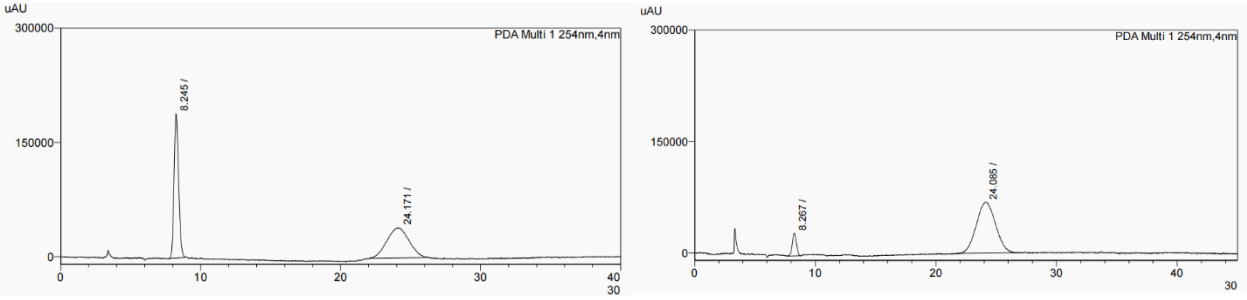
(*S*)-3-Benzyl-1,5-dimethyl-3-(trifluoromethyl)indolin-2-one (4c):



According to **GP–VII**, the reaction of (*Z*)-*N*-(2-iodo-4-methylphenyl)-*N*-methyl-3-phenyl-2-(trifluoromethyl)acrylamide (**3c**; 44.52 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*S*, *Sp*)-^{t}Bu-Phosferrox (**L_3**, 10 mg, 20 mol%), HCOONa (17 mg, 0.25 mmol), K_3PO_4 (8.5 mg, 0.04 mmol) and Ag_2CO_3 (8.3 mg, 0.03 mmol) afforded **4c** (12 mg) in 38% yield and 82% *ee* as a semi-solid; R_f = 0.22 (3% EtOAc, 30% DCM in hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (s, 1H), 7.09–7.05 (m, 2H), 7.04–7.00 (m, 2H), 6.83 (d, J = 7.1 Hz, 2H), 6.47 (d, J = 7.9 Hz, 1H), 3.59 (d, J = 12.9 Hz, 1H), 3.29 (d, J = 12.9 Hz, 1H), 2.91 (s, 3H), 2.39 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 170.8 (q, J = 2.2 Hz), 141.8, 133.0, 132.3, 130.1, 130.0, 127.7, 127.0, 125.9, 124.7 (q, J = 281.9 Hz), 123.6, 108.0, 58.2 (q, J = 26.1 Hz), 37.3 (bq, J = 2.5 Hz), 26.1, 21.2; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -71.4 ppm; **HRMS (ESI-TOF) *m/z***: $[M+Na]^+$ calcd. for $C_{18}H_{16}F_3NNaO$: 342.1076, found 342.1067.

Enantiomeric excess = 82%, determined by HPLC (Daicel Chiralpak OJ-H Column, 2.5% ^{i}PrOH in *n*-Hexane, flow rate 1.0 mL/min, T = 25 °C, λ = 254 nm): t_R = 8.27 min (minor), t_R = 24.08 min (major). **$[\alpha]_D^{28.6}$** = +84° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

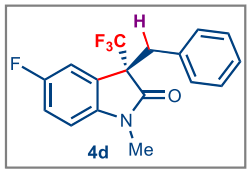
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.245	4310722	189386	49.833	49.833
2	24.171	4339612	39575	50.167	50.167
Total		8650334	228961		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8.267	723193	30566	8.703	8.703
2	24.085	7586213	68594	91.297	91.297
Total		8309406	99160		100.000

Figure S26. HPLC chromatograms for racemic **4c** and enantioenriched **4c**.

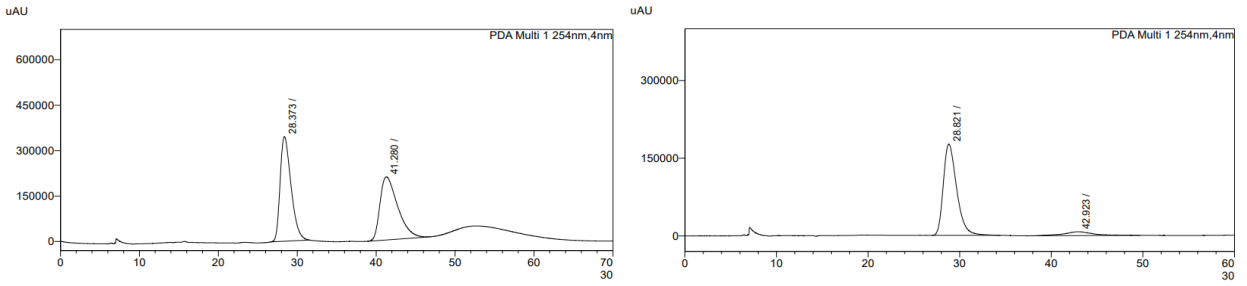
(*S*)-3-Benzyl-5-fluoro-1-methyl-3-(trifluoromethyl)indolin-2-one (4d):[2]



According to **GP–VII**, the reaction of (*Z*)-*N*-(4-fluoro-2-iodophenyl)-*N*-methyl-3-phenyl-2-(trifluoromethyl)acrylamide (**3d**; 44.9 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*S*, *Sp*)-^{t}Bu-Phosferrox (**L_3**, 10 mg, 20 mol%), HCOONa (17 mg, 0.25 mmol), K_3PO_4 (8.5 mg, 0.04 mmol) and Ag_2CO_3 (8.3 mg, 0.03 mmol) afforded **4d** (13.1 mg) in 41% yield and 83% *ee* as a white solid; R_f = 0.35 (3% EtOAc, 30% DCM in hexane); Melting point: 106–108 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, J = 7.6 Hz, 1H), 7.12–7.02 (m, 3H), 6.98 (t, J = 8.7 Hz, 1H), 6.85 (d, J = 7.3 Hz, 2H), 6.51 (dd, J = 8.5, 4.0 Hz, 1H), 3.62 (d, J = 13.0 Hz, 1H), 3.28 (d, J = 13.0 Hz, 1H), 2.94 (s, 3H); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -119.4 (td, J = 8.5, 4.2 Hz), -71.4 ppm.

Enantiomeric excess = 83%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 28.82 min (major), t_R = 42.92 min (minor). **$[\alpha]_D^{28.5}$** = +42° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

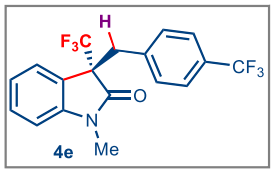
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	28.373	33239963	345544	50.646	50.646
2	41.280	32392540	208432	49.354	49.354
Total		65632503	553976		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	28.821	17841435	176366	91.328	91.328
2	42.923	1694063	7450	8.672	8.672
Total		19535498	183816		100.000

Figure S27. HPLC chromatograms for racemic **4d** and enantioenriched **4d**.

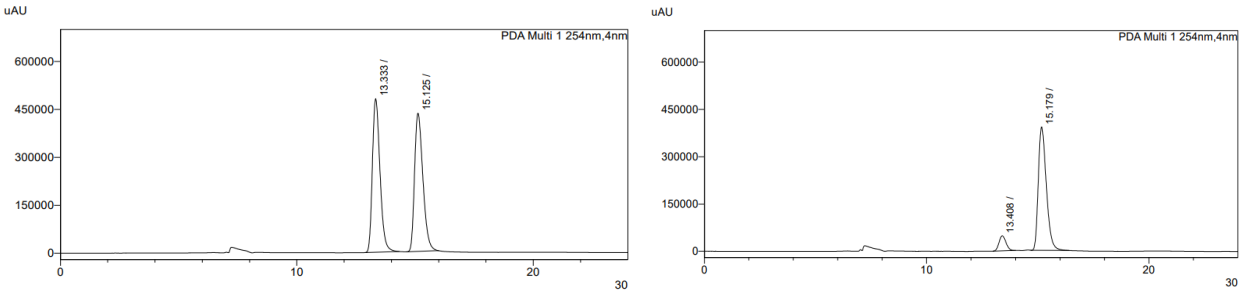
(*S*)-1-Methyl-3-(trifluoromethyl)-3-(4-(trifluoromethyl)benzyl)indolin-2-one (4e):



According to **GP–VII**, the reaction of (*Z*)-*N*-(2-iodophenyl)-*N*-methyl-2-(trifluoromethyl)-3-(4-(trifluoromethyl)phenyl)acrylamide (**3e**; 25 mg, 0.05 mmol) using $Pd(TFA)_2$ (1.2 mg, 7 mol%), (*S*, *Sp*)-^{t}Bu-Phosferrox (**L3**, 4.95 mg, 20 mol%), HCOONa (2.5 mg, 0.125 mmol), K_3PO_4 (4.25 mg, 0.02 mmol) and Ag_2CO_3 (4.13 mg, 0.015 mmol) afforded **4e** (14.6 mg) in 78% yield and 81% *ee* as a white solid; R_f = 0.44 (3% EtOAc, 30% DCM in hexane); Melting point: 71–73 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 1H), 7.34–7.25 (m, 3H), 7.14 (td, J = 7.6, 1.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 2H), 6.62 (d, J = 7.8 Hz, 1H), 3.65 (d, J = 12.9 Hz, 1H), 3.36 (d, J = 12.9 Hz, 1H), 2.94 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 170.4 (bq, J = 1.7 Hz), 144.0, 137.0, 130.4, 130.3, 129.5 (q, J = 32.4 Hz), 125.1, 124.6 (q, J = 3.6 Hz), 124.5 (q, J = 282.2 Hz), 123.9 (q, J = 272.0 Hz), 123.0, 108.6, 57.9 (q, J = 26.4 Hz), 36.9 (bq, J = 1.9 Hz), 26.2 (one of the aromatic ^{13}C merged with other peaks); **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$)** δ -62.7, -71.7 ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{18}H_{14}F_6NO$: 374.0974, found 374.0990.

Enantiomeric excess = 81%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 13.41 min (minor), t_R = 15.18 min (major). **$[\alpha]_D^{28.9}$** = +28° (c = 5*10^{-4}, $CHCl_3$).



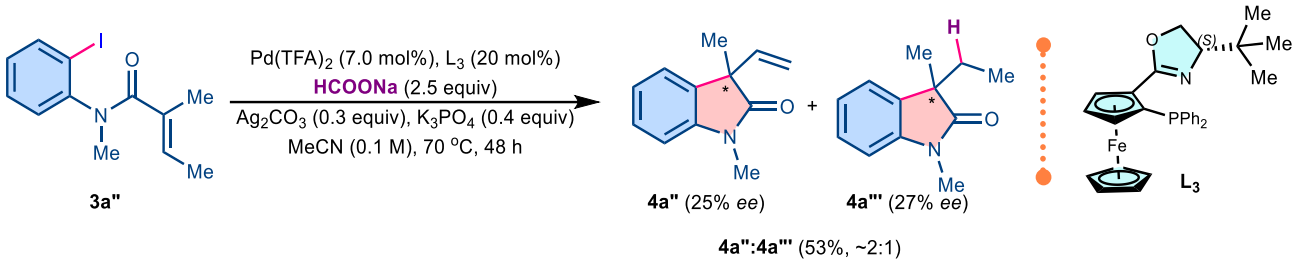
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	13.333	10737809	479728	50.369	50.369
2	15.125	10580413	432078	49.631	49.631
Total		21318222	911806		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	13.408	1038745	47683	9.535	9.535
2	15.179	9855410	391634	90.465	90.465
Total		10894155	439317		100.000

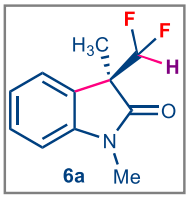
Figure S28. HPLC chromatograms for racemic **4e** and enantioenriched **4e**.



Scheme S10. Asymmetric Reductive Heck cyclization of *o*-halo *β*-methyl meth-acrylamides.

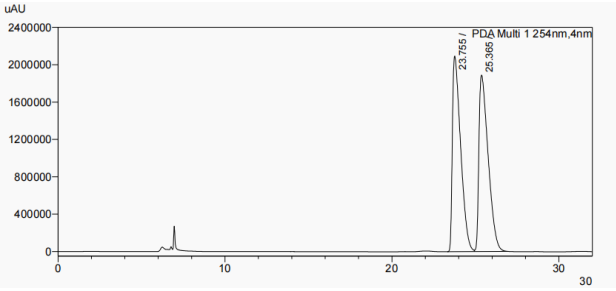
Tetra-substituted *gem*-Difluoromethyl Acrylamides (6):

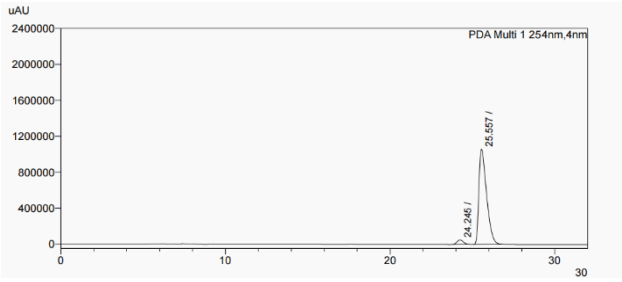
(*R*)-3-(Difluoromethyl)-1,3-dimethylindolin-2-one (6a):



According to **GP–IX**, the reaction of **5a** (33.7 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L_5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **6a** (14.7 mg) in 70% yield and 93% *ee* as a colorless liquid; $R_f = 0.32$ (3% EtOAc, 30% DCM in hexane). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.40–7.33 (m, 2H), 7.12 (t, J = 7.6 Hz, 1H), 6.88 (d, J = 7.8 Hz, 1H), 5.95 (t, J = 56.0 Hz, 1H), 3.23 (s, 3H), 1.52 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 174.9 (dd, J = 9.2, 1.6 Hz), 143.8, 129.2, 127.0, 124.8, 123.0, 116.7 (dd, J = 247.7, 244.8 Hz), 108.4, 51.9 (t, J = 21.1 Hz), 26.4, 17.7 (dd, J = 5.2, 2.7 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -122.1 (dd, J = 280.9, 55.7 Hz), -129.8 (dd, J = 280.9, 56.3 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{12}F_2NO$: 212.0881, found 212.0878.

Enantiomeric excess = 93%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 24.24 min (minor), t_R = 25.56 min (major). **$[\alpha]_D^{28.3}$** = -6° (c = 5*10^{-4}, $CHCl_3$).





PDA Ch1 254nm

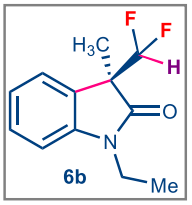
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.755	72076242	2094132	49.776	49.776
2	25.365	72723523	1889529	50.224	50.224
Total		144799765	3983661		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	24.245	1305687	49364	3.665	3.665
2	25.557	34317018	1058326	96.335	96.335
Total		35622705	1107690		100.000

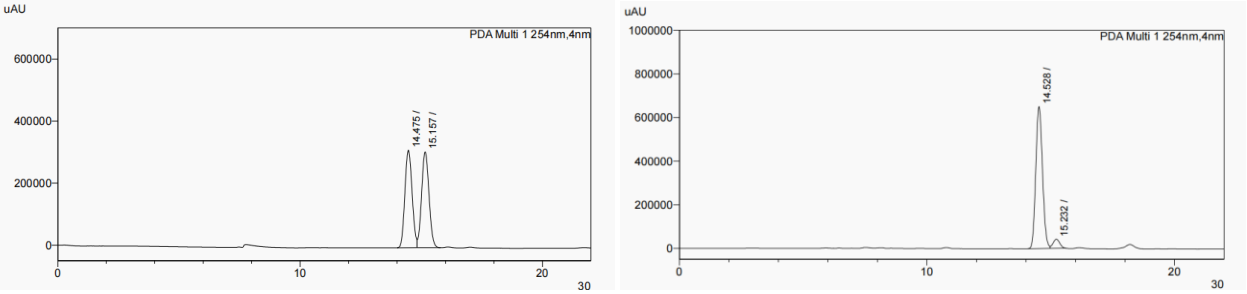
Figure S29. HPLC chromatograms for racemic **6a** and enantioenriched **6a**.

***(R)*-3-(Difluoromethyl)-1-ethyl-3-methylindolin-2-one (6b):**



According to **GP–IX**, the reaction of **5b** (35 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L_5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) at 115 ºC afforded **6b** (19.6 mg) in 87% yield and 88% *ee* as a yellow liquid; R_f = 0.39 (3% EtOAc, 30% DCM in hexane). **^{1}H NMR (500 MHz, $CDCl_3$)** *δ* 7.39 (d, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 5.95 (t, *J* = 56.0 Hz, 1H), 3.85–3.70 (m, 2H), 1.51 (s, 3H), 1.26 (bt, *J* = 7.2 Hz, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** *δ* 174.5 (dd, *J* = 9.2, 1.4 Hz), 142.9, 129.2, 127.3, 125.0, 122.8, 116.8 (dd, *J* = 247.7, 244.7 Hz), 108.5, 51.8 (t, *J* = 21.0 Hz), 34.8, 17.7 (dd, *J* = 5.2, 2.6 Hz), 12.5; **^{19}F NMR (377 MHz, $CDCl_3$)** δ -122.4 (dd, *J* = 280.9, 55.8 Hz), -129.9 (dd, *J* = 280.9, 56.3 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{14}F_2NO$: 226.1038, found 226.1037.

Enantiomeric excess = 88%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 14.53 min (major), t_R = 15.23 min (minor). **$[\alpha]_D^{28.2}$** = -2.7° (c = 1.5*10^{-3}, $CHCl_3$).



PDA Ch1 254nm

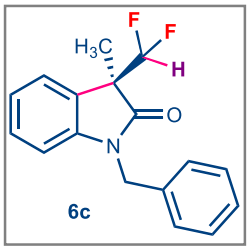
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.475	6493515	313794	49.667	49.667
2	15.157	6580493	308299	50.333	50.333
Total		13074008	622093		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.528	12272503	650464	93.907	93.907
2	15.232	796283	42018	6.093	6.093
Total		13068786	692482		100.000

Figure S30. HPLC chromatograms for racemic **6b** and enantioenriched **6b**.

***(R)*-1-Benzyl-3-(difluoromethyl)-3-methylindolin-2-one (6c):**

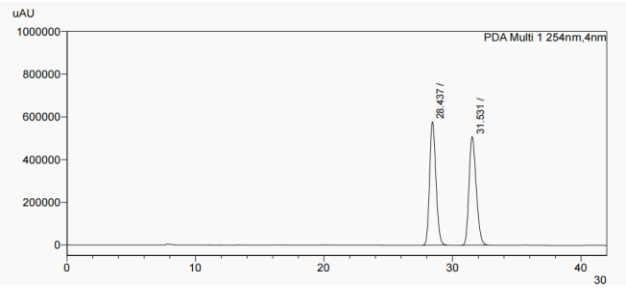


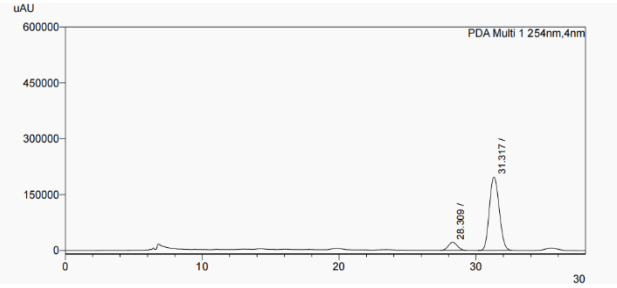
According to **GP–IX**, the reaction of **5c** (62 mg, 0.15 mmol) using $Pd(TFA)_2$ (3.5 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 18.3 mg, 20 mol%), HCOONa (26 mg, 0.375 mmol) and Ag_3PO_4 (32 mg, 0.075mmol) at 110 °C afforded **6c** (10.4 mg) in 24% yield and 82% *ee* as a yellow liquid; R_f = 0.46 (3% EtOAc, 30% DCM in hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 7.4 Hz, 1H), 7.34–7.29 (m, 2H), 7.28–7.20 (m, 4H), 7.08 (t, J = 7.6 Hz, 1H), 6.74 (d, J = 7.9 Hz, 1H), 6.05 (t, J = 56.0 Hz, 1H), 5.04 (d, J = 15.8 Hz, 1H), 4.83 (d, J = 15.8 Hz, 1H), 1.59 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 175.1 (dd, J = 9.3, 1.0 Hz), 142.9, 135.2, 129.1, 128.8, 127.7, 126.99 (d, J = 1.3 Hz), 126.95, 124.8 (d, J = 1.2 Hz), 123.0, 116.9 (dd, J = 247.8, 244.6 Hz), 109.5, 51.9 (t, J = 21.1 Hz), 43.7, 18.0 (dd, J = 5.2, 2.4 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -122.1 (ddd, J = 280.9, 55.8, 1.1 Hz), -129.8 (dd, J = 280.9, 56.2 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{17}H_{16}F_2NO$: 288.1194, found 288.1192.

Note: Each ^{19}F peak appears as a broad quartet and quintet (four peaks for each fluorine atom), but not distinctly enough for clear assignment. As a result, MestReNova software could not assign values to all peaks, so we have provided the ^{19}F values accordingly.

Enantiomeric excess = 82%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 28.31 min (minor), t_R = 31.32 min (major). **$[\alpha]_D^{28.5}$** = -34° (c = 5*10^{-4}, $CHCl_3$).





PDA Ch1 254nm

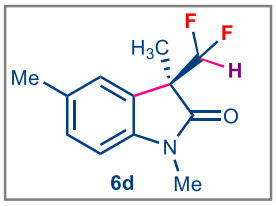
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	28.437	19821094	578211	49.970	49.970
2	31.531	19844917	508352	50.030	50.030
Total		39666011	1086564		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	28.309	948319	20972	8.820	8.820
2	31.317	9803311	196676	91.180	91.180
Total		10751631	217649		100.000

Figure S31. HPLC chromatograms for racemic **6c** and enantioenriched **6c**.

***(R)*-3-(Difluoromethyl)-1,3,5-trimethylindolin-2-one (6d):**

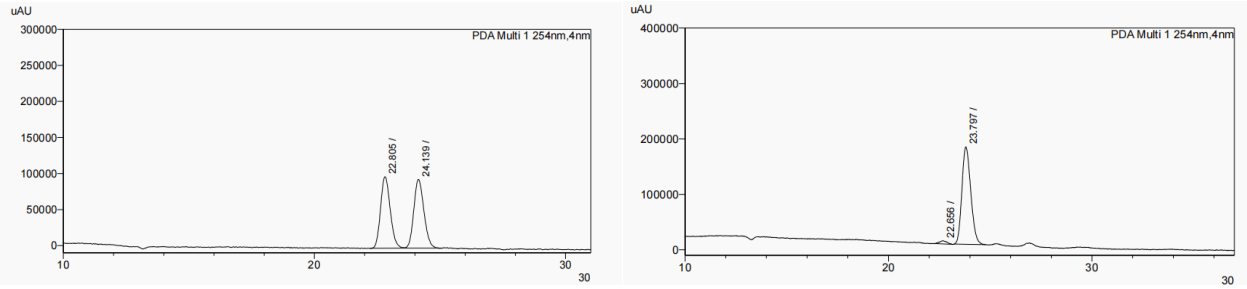


According to **GP–IX**, the reaction of **5d** (35 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **6d** (15.6 mg) in 69% yield and 94% *ee* as a white solid; R_f = 0.31 (3% EtOAc, 30% DCM in hexane); Melting point: 116–118 °C.

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.20 (s, 1H), 7.15 (d, *J* = 7.9 Hz, 1H), 6.77 (d, *J* = 7.9 Hz, 1H), 5.94 (t, *J* = 56.1 Hz, 1H), 3.20 (s, 3H), 2.36 (s, 3H), 1.50 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** *δ* 174.9 (dd, *J* = 9.4, 1.5 Hz), 141.4, 132.6, 129.5, 127.1, 125.6, 116.8 (dd, *J* = 247.6, 244.7 Hz), 108.1, 51.9 (t, *J* = 21.0 Hz), 26.4, 21.1, 17.8 (dd, *J* = 5.3, 2.6 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** *δ* -122.1 (ddd, *J* = 280.5, 55.9, 1.0 Hz), -129.8 (ddd, *J* = 280.6, 56.3, 0.9 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{14}F_2NO$: 226.1038, found 226.1036.

Note: Each ^{19}F peak appears as a broad quartet and quintet (four peaks for each fluorine atom), but not distinctly enough for clear assignment. As a result, MestReNova software could not assign values to all peaks, so we have provided the ^{19}F values accordingly.

Enantiomeric excess = 94%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 22.66 min (minor), t_R = 23.80 min (major). $[\alpha]_D^{28.2}$ = -6° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

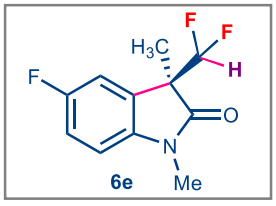
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.805	2660094	99129	49.813	49.813
2	24.139	2680061	95476	50.187	50.187
Total		5340155	194605		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.656	145609	5774	2.662	2.662
2	23.797	5324416	175792	97.338	97.338
Total		5470025	181566		100.000

Figure S32. HPLC chromatograms for racemic **6d** and enantioenriched **6d**.

***(R)*-3-(Difluoromethyl)-5-fluoro-1,3-dimethylindolin-2-one (6e):**

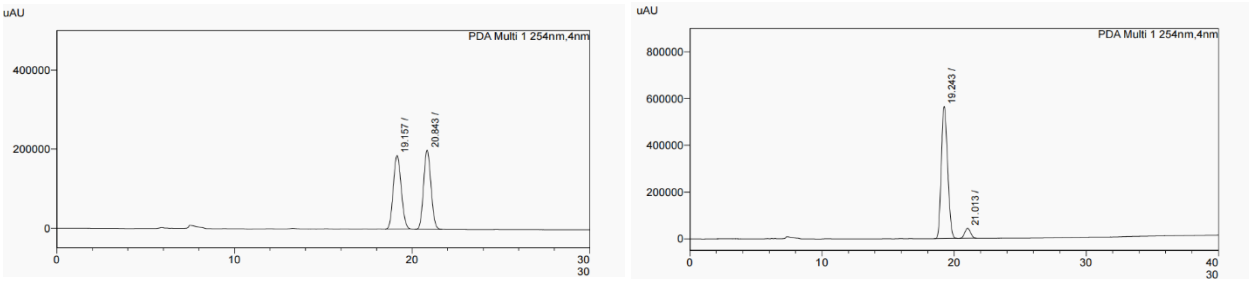


According to **GP–IX**, the reaction of **5e** (35.5 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) at 115 °C afforded **6e** (12.5 mg) in 55% yield and 87% *ee* as a white solid; R_f = 0.35 (3% EtOAc, 30% DCM in hexane); Melting point: 87–89 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, J = 7.6 Hz, 1H), 7.06 (td, J = 8.8, 1.9 Hz, 1H), 6.80 (dd, J = 8.4, 3.9 Hz, 1H), 5.96 (t, J = 55.8 Hz, 1H), 3.22 (s, 3H), 1.52 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 174.5 (d, J = 8.7 Hz), 159.4 (d, J = 241.5 Hz), 139.8 (d, J = 1.9 Hz), 128.5 (d, J = 8.7 Hz), 116.5 (dd, J = 247.9, 245.0 Hz), 115.5 (d, J = 23.5 Hz), 113.1 (dd, J = 25.2, 1.4 Hz), 108.9 (d, J = 8.2 Hz), 52.3 (td, J = 21.1, 1.7 Hz), 26.5, 17.8 (dd, J = 5.2, 2.5 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -119.7 (ddd, J = 9.2, 7.8, 4.1 Hz), -122.0 (ddd, J = 281.8, 55.6, 1.1 Hz), -122.3 (dd, J = 5.6, 1.1 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}F_3NO$: 230.0787, found 230.0782.

Note: Each ^{19}F peak appears as a broad quartet and quintet (four peaks for each fluorine atom), but not distinctly enough for clear assignment. As a result, MestReNova software could not assign values to all peaks, so we have provided the ^{19}F values accordingly.

Enantiomeric excess = 87%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 19.24 min (major), t_R = 21.01 min (minor). **$[\alpha]_D^{28.3}$** = -24° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

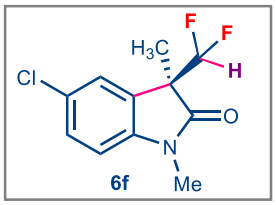
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	19.157	5768100	186184	49.874	49.874
2	20.843	5797149	200440	50.126	50.126
Total		11565249	386623		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	19.243	18811499	564615	93.528	93.528
2	21.013	1301738	42236	6.472	6.472
Total		20113236	606852		100.000

Figure S33. HPLC chromatograms for racemic **6e** and enantioenriched **6e**.

***(R)*-5-Chloro-3-(difluoromethyl)-1,3-dimethylindolin-2-one (6f):**

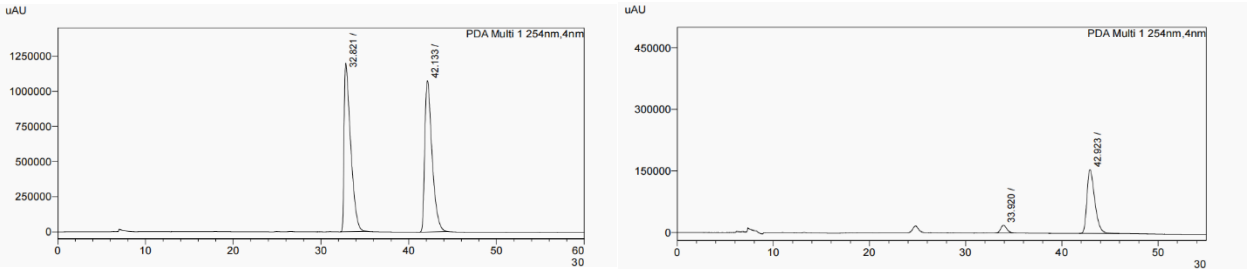


According to **GP–IX**, the reaction of **5f** (37 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L_5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **6f** (11.4 mg) in 46% yield and 82% *ee* as a white solid; R_f = 0.31 (3% EtOAc, 30% DCM in hexane); Melting point: 93–95 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.34 (d, J = 8.6 Hz, 1H), 6.81 (d, J = 8.2 Hz, 1H), 5.95 (t, J = 55.8 Hz, 1H), 3.21 (s, 3H), 1.52 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 174.4 (dd, J = 9.3, 1.1 Hz), 142.4, 129.2, 128.6, 128.5, 125.4 (d, J = 1.4 Hz), 116.4 (dd, J = 248.1, 245.0 Hz), 109.3, 52.1 (t, J = 21.0 Hz), 26.5, 17.8 (dd, J = 5.2, 2.6 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -121.9 (ddd, J = 281.9, 55.6, 1.0 Hz), -129.8 (dd, J = 281.9, 56.0 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}ClF_2NO$: 246.0492, found 246.0490.

Note: Each ^{19}F peak appears as a broad quartet and quintet (four peaks for each fluorine atom), but not distinctly enough for clear assignment. As a result, MestReNova software could not assign values to all peaks, so we have provided the ^{19}F values accordingly.

Enantiomeric excess = 82%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 33.92 min (minor), t_R = 42.92 min (major). **$[\alpha]_D^{28.3}$** = -22° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

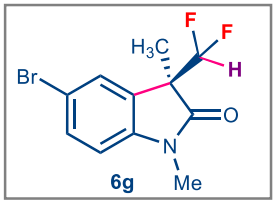
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	32.821	62421036	1199700	50.086	50.086
2	42.133	62207831	1075686	49.914	49.914
Total		124628867	2275387		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	33.920	843674	19001	8.737	8.737
2	42.923	8812160	155646	91.263	91.263
Total		9655834	174646		100.000

Figure S34. HPLC chromatograms for racemic **6f** and enantioenriched **6f**.

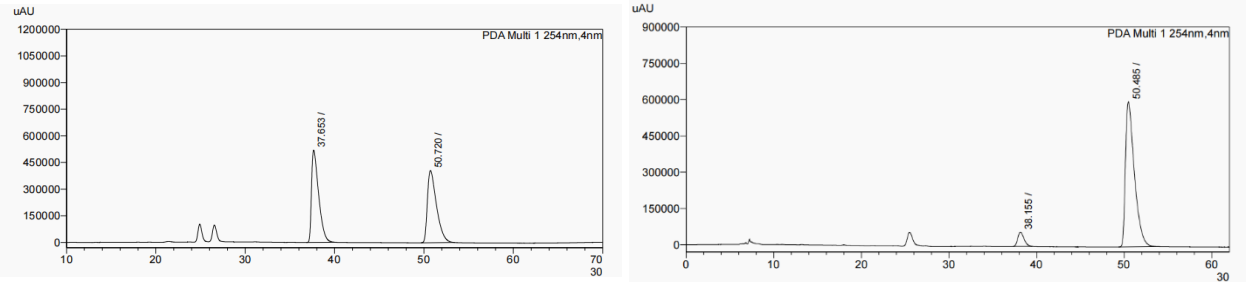
***(R)*-5-Bromo-3-(difluoromethyl)-1,3-dimethylindolin-2-one (6g):**



According to **GP–IX**, the reaction of **5g** (41.6 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 12.2 mg, 20 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) at 100 °C afforded **6g** (9.9 mg) in 34% yield and 87% *ee* as a white solid; R_f = 0.33 (3% EtOAc, 30% DCM in hexane); Melting point: 96–98 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.47 (m, 2H), 6.76 (bd, J = 8.9 Hz, 1H), 5.95 (t, J = 55.8 Hz, 1H), 3.21 (s, 3H), 1.52 (bt, 3H); **^{13}C{^{1}H} (101 MHz, $CDCl_3$)** δ 174.3 (bd, J = 9.5 Hz), 142.9, 132.1, 128.9, 128.1 (d, J = 1.6 Hz), 116.4 (dd, J = 248.1, 245.1 Hz), 115.7, 109.8, 52.1 (t, J = 21.2 Hz), 26.5, 17.8 (dd, J = 5.1, 2.6 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -121.8 (dd, J = 281.9, 55.6 Hz), -129.8 (dd, J = 281.8, 56.0 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}BrF_2NO$: 289.9987, found 289.9986.

Enantiomeric excess = 87%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 38.16 min (minor), t_R = 50.48 min (major). **$[\alpha]_D^{28.3}$** = -4° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

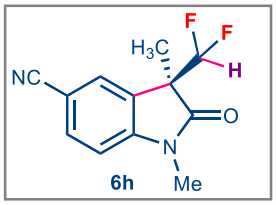
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	37.653	28880534	520547	50.088	50.088
2	50.720	28779079	406473	49.912	49.912
Total		57659613	927021		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	38.155	2908035	58816	6.392	6.392
2	50.485	42585744	599640	93.608	93.608
Total		45493780	658456		100.000

Figure S35. HPLC chromatograms for racemic **6g** and enantioenriched **6g**.

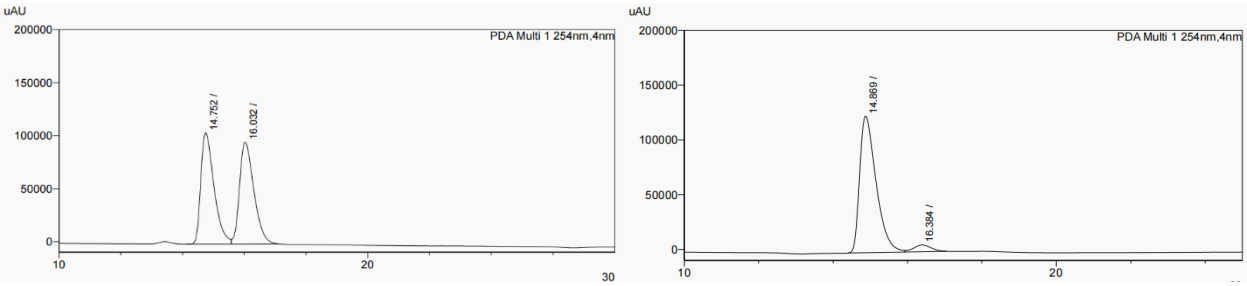
***(R)*-3-(Difluoromethyl)-1,3-dimethyl-2-oxoindoline-5-carbonitrile (6h):**



According to **GP–IX**, the reaction of **5h** (36 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L_5**, 12.2 mg, 20 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) at 100 °C afforded **6h** (18.8 mg) in 80% yield and 90% *ee* as a white solid; R_f = 0.11 (3% EtOAc, 30% DCM in hexane); Melting point: 143–145 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 1H), 7.63 (s, 1H), 6.96 (d, J = 8.1 Hz, 1H), 5.97 (t, J = 55.7 Hz, 1H), 3.26 (s, 3H), 1.54 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 174.6 (dd, J = 9.6, 0.8 Hz), 147.7, 134.6, 128.3 (d, J = 1.5 Hz), 128.0, 118.7, 116.2 (dd, J = 248.7, 245.2 Hz), 108.9, 106.5, 51.8 (t, J = 21.2 Hz), 26.7, 17.8 (dd, J = 5.0, 2.4 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -121.7 (dd, J = 282.9, 55.5 Hz), -129.7 (dd, J = 282.8, 55.8 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{11}F_2N_2O$: 237.0834, found 237.0832.

Enantiomeric excess = 90%, determined by HPLC (Daicel Chiralpak OD-H Column, 2.5% ^{i}PrOH in *n*-Hexane, flow rate 2.0 mL/min, T = 25 °C, λ = 254 nm): t_R = 14.87 min (major), t_R = 16.38 min (minor). **$[\alpha]_D^{26.5}$** = -16° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

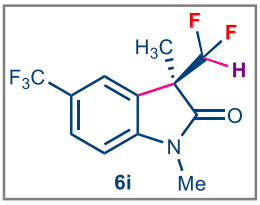
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.752	3122556	104905	50.172	50.172
2	16.032	3101104	96208	49.828	49.828
Total		6223659	201113		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.869	3819752	124658	94.969	94.969
2	16.384	202367	6221	5.031	5.031
Total		4022119	130878		100.000

Figure S36. HPLC chromatograms for racemic **6h** and enantioenriched **6h**.

***(R)*-3-(Difluoromethyl)-1,3-dimethyl-5-(trifluoromethyl)indolin-2-one (6i):**

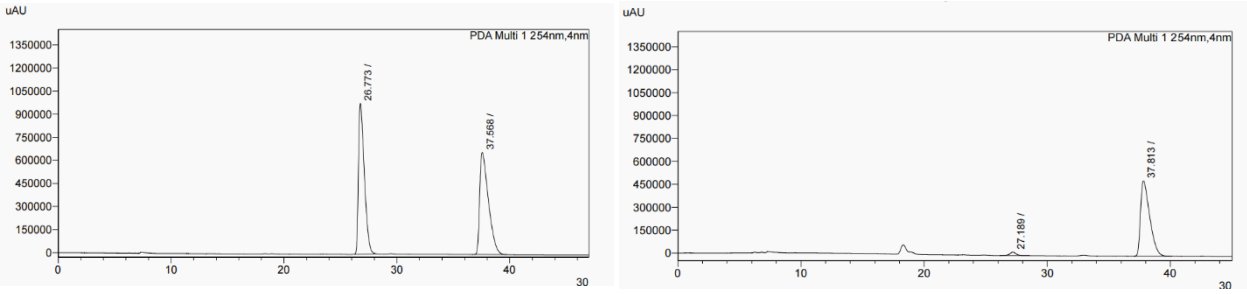


According to **GP–IX**, the reaction of **5i** (61 mg, 0.15 mmol) using $Pd(TFA)_2$ (3.5 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 18.3 mg, 20 mol%), HCOONa (26 mg, 0.375 mmol) and Ag_3PO_4 (32 mg, 0.075 mmol) at 110 ºC afforded **6i** (11.9 mg) in 29% yield and 94% *ee* as a yellow liquid; $R_f = 0.33$ (3% EtOAc, 30% DCM in hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.1 Hz, 1H), 7.61 (s, 1H), 6.96 (d, J = 8.2 Hz, 1H), 5.98 (t, J = 55.8 Hz, 1H), 3.26 (s, 3H), 1.55 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 174.8 (dd, J = 9.4, 1.4 Hz), 146.8 (q, J = 1.3 Hz), 127.6 (bq, J = 1.3 Hz), 127.1 (q, J = 4.1 Hz), 125.4 (q, J = 32.7 Hz), 124.2 (q, J = 271.4 Hz), 121.9 (qd, J = 3.9, 1.7 Hz), 116.4 (dd, J = 248.1, 245.4 Hz), 108.2, 51.9 (t, J = 21.2 Hz), 26.6, 17.8 (dd, J = 5.0, 2.7 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -61.5 (d, J = 0.6 Hz), -CF_3), -121.8 (ddd, J = 282.3, 55.6, 1.1 Hz), -(129.3–130.3, m) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{11}F_5NO$: 280.0755, found 280.0753.

Note: Each ^{19}F peak appears as a broad quartet and quintet (four peaks for each fluorine atom), but not distinctly enough for clear assignment. As a result, MestReNova software could not assign values to all peaks, so we have provided the ^{19}F values accordingly.

Enantiomeric excess = 94%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 27.19 min (minor), t_R = 37.81 min (major). **$[\alpha]_D^{28.2}$** = -12° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

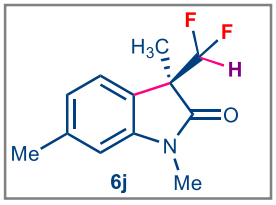
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	26.773	35417391	978528	49.851	49.851
2	37.568	35628631	663666	50.149	50.149
Total		71046021	1642193		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	27.189	790934	21864	3.013	3.013
2	37.813	25456340	493511	96.987	96.987
Total		26247274	515375		100.000

Figure S37. HPLC chromatograms for racemic **6i** and enantioenriched **6i**.

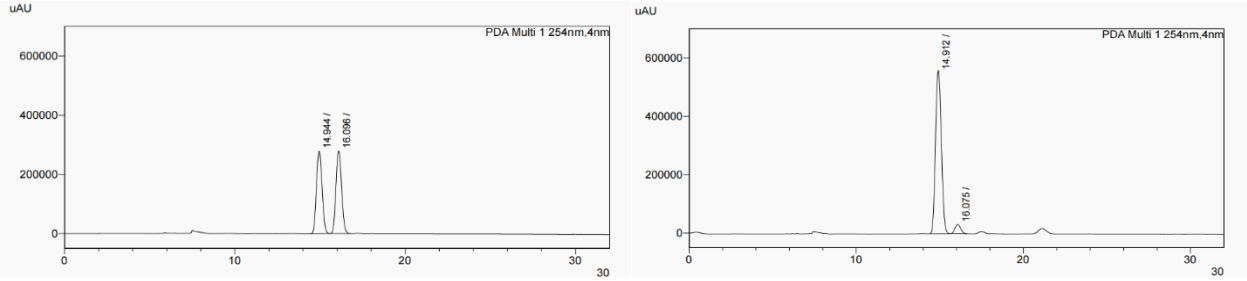
***(R)*-3-(Difluoromethyl)-1,3,6-trimethylindolin-2-one (6j):**



According to **GP–IX**, the reaction of **5j** (35 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) at 90 °C afforded **6j** (13.2 mg) in 59% yield and 90% *ee* as a white solid; R_f = 0.30 (3% EtOAc, 30% DCM in hexane); Melting point: 120–122 °C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.27–7.24 (m, 1H), 6.93 (dq, *J* = 7.6, 0.8 Hz, 1H), 6.71 (s, 1H), 5.93 (t, *J* = 56.1 Hz, 1H), 3.21 (s, 3H), 2.40 (s, 3H), 1.50 (bs, 3H, appears like triplet but not splitted clearly); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** *δ* 175.2 (dd, *J* = 9.6, 1.4 Hz), 143.9, 139.5, 124.5 (d, *J* = 0.8 Hz), 124.0 (bd, *J* = 0.8 Hz), 123.5, 116.7 (dd, *J* = 247.6, 244.6 Hz), 109.3, 51.7 (t, *J* = 21.2 Hz), 26.3, 21.8, 17.8 (dd, *J* = 5.1, 2.6 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** *δ* -122.1 (dd, *J* = 280.6, 56.0 Hz), -129.8 (dd, *J* = 280.6, 56.3 Hz) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{12}H_{14}F_2NO$: 226.1038, found 226.1035.

Enantiomeric excess = 90%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 14.91 min (major), t_R = 16.08 min (minor). $[\alpha]_D^{28.4}$ = -2° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

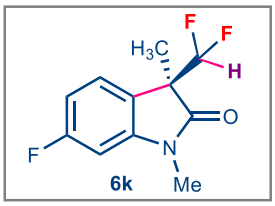
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.944	6437632	278973	49.872	49.872
2	16.096	6470749	278725	50.128	50.128
Total		12908381	557698		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.912	13567126	559062	94.922	94.922
2	16.075	725864	30935	5.078	5.078
Total		14292990	589998		100.000

Figure S38. HPLC chromatograms for racemic **6j** and enantioenriched **6j**.

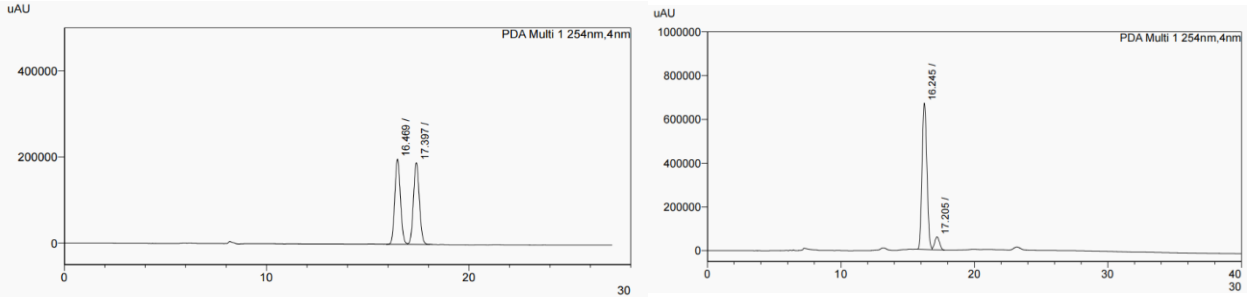
***(R)*-3-(Difluoromethyl)-6-fluoro-1,3-dimethylindolin-2-one (6k):**



According to **GP–IX**, the reaction of **5k** (35.5 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25mmol) and Ag_3PO_4 (21 mg, 0.05mmol) at 115 °C afforded **6k** (11 mg) in 48% yield and 84% *ee* as a yellow liquid; R_f = 0.37 (3% EtOAc, 30% DCM in hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 6.6 Hz, 1H), 6.79 (t, *J* = 8.8 Hz, 1H), 6.62 (d, *J* = 8.7 Hz, 1H), 5.93 (t, *J* = 56.0 Hz, 1H), 3.21 (s, 3H), 1.50 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 175.2 (dd, *J* = 9.5, 1.2 Hz), 163.8 (d, *J* = 246.5 Hz), 145.4 (d, *J* = 11.7 Hz), 125.9 (dd, *J* = 9.8, 1.2 Hz), 122.2 (bd, *J* = 1.7 Hz), 116.5 (dd, *J* = 247.7, 244.9 Hz), 109.1 (d, *J* = 22.4 Hz), 97.4 (d, *J* = 27.7 Hz), 51.6 (t, *J* = 21.2 Hz), 26.5, 17.8 (dd, *J* = 4.9, 2.4 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -110.5 (td, *J* = 9.1, 5.3 Hz, 1F), -122.1 (dd, *J* = 281.4, 55.8 Hz, 1F), -129.9 (dd, *J* = 281.3, 56.2 Hz, 1F) ppm; **HRMS (ESI-TOF)** ***m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}F_3NO$: 230.0787, found 230.0793.

Enantiomeric excess = 84%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 16.24 min (major), t_R = 17.20 min (minor). **$[\alpha]_D^{28}$** = -4° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

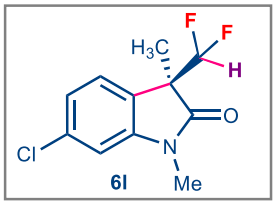
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	16.469	3864840	197665	50.098	50.098
2	17.397	3849656	189599	49.902	49.902
Total		7714496	387264		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	16.245	17009694	668028	91.919	91.919
2	17.205	1495322	58974	8.081	8.081
Total		18505016	727003		100.000

Figure S39. HPLC chromatograms for racemic **6k** and enantioenriched **6k**.

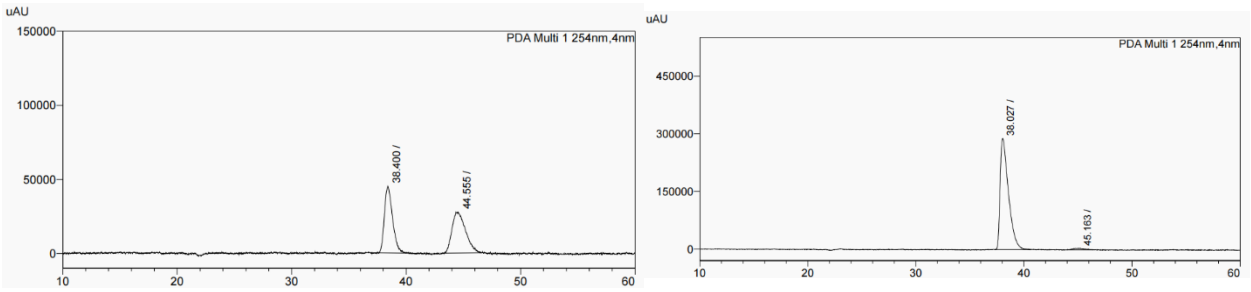
***(R)*-6-Chloro-3-(difluoromethyl)-1,3-dimethylindolin-2-one (6l):**



According to **GP–IX**, the reaction of **5l** (37 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) at 90 °C afforded **6l** (14.6 mg) in 59% yield and 96% *ee* as a white solid; R_f = 0.33 (3% EtOAc, 30% DCM in hexane); Melting point: 97–99 °C.

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.29 (d, *J* = 7.8 Hz, 1H), 7.09 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.88 (bd, *J* = 1.1 Hz, 1H), 5.94 (t, *J* = 55.9 Hz, 1H), 3.21 (s, 3H), 1.50 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** *δ* 174.8 (dd, *J* = 9.2, 1.2 Hz), 145.0, 135.2, 125.7 (bd, *J* = 0.6 Hz), 125.3, 122.9, 116.4 (dd, *J* = 248.0, 244.9 Hz), 109.2, 51.7 (t, *J* = 21.2 Hz), 26.5, 17.7 (dd, *J* = 5.0, 2.4 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -122.1 (dd, *J* = 280.6, 56.0 Hz, 1F), -129.8 (dd, *J* = 280.6, 56.3 Hz, 1F) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{11}ClF_2NO$: 246.0492, found 246.0486.

Enantiomeric excess = 96%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 38.03 min (major), t_R = 45.16 min (minor). **$[\alpha]_D^{28.6}$** = -6° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	38.400	2226976	45019	49.394	49.394
2	44.555	2281666	27596	50.606	50.606
Total		4508642	72615		100.000

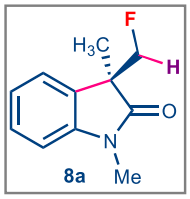
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	38.027	15472916	288798	98.039	98.039
2	45.163	309554	4234	1.961	1.961
Total		15782470	293032		100.000

Figure S40. HPLC chromatograms for racemic **6l** and enantioenriched **6l**.

Tri-substituted Monofluoromethyl Acrylamides:

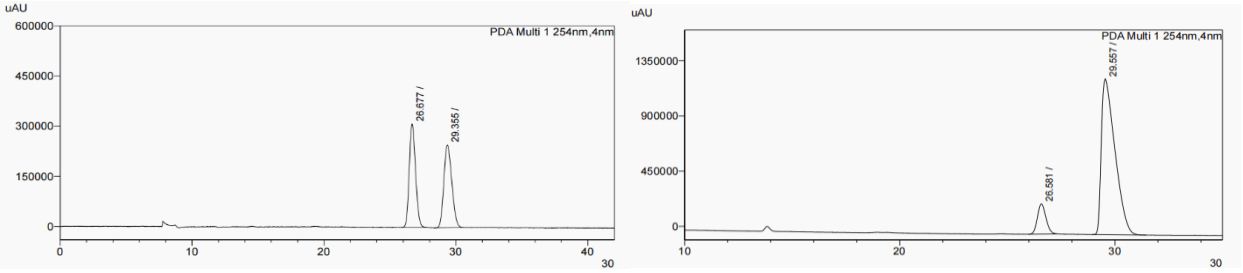
(*R*)-3-(Fluoromethyl)-1,3-dimethylindolin-2-one (8a):



According to **GP–X**, the reaction of **7a** (31.91 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 12.21 mg, 20 mol%), HCOONa (13.6 mg, 0.20 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **8a** (8.6 mg) in 45% yield and 78% *ee* as a white solid; R_f = 0.21 (3% EtOAc, 30% DCM in hexane); Melting point: 50–52 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.28 (m, 2H), 7.10 (t, J = 7.5 Hz, 1H), 6.88 (d, J = 7.7 Hz, 1H), 4.57 (d, J = 47.0 Hz, 2H), 3.23 (s, 3H), 1.40 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 177.4 (d, J = 6.2 Hz), 143.4, 131.0 (d, J = 0.8 Hz), 128.5, 123.2 122.8, 108.3, 86.3 (d, J = 177.4 Hz), 49.3 (d, J = 19.6 Hz), 26.3, 18.5 (d, J = 6.2 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -223.6 (t, J = 47.0 Hz, 1F) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{13}FNO$: 194.0976, found 194.0974.

Enantiomeric excess = 78%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 26.58 min (minor), t_R = 29.56 min (major). **$[\alpha]_D^{27.9}$** = -2° (c = $5*10^{-4}$, $CHCl_3$).



PDA Ch1 254nm

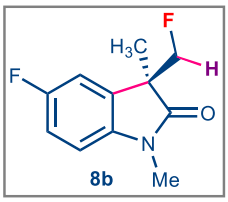
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	26.677	10299349	309570	49.840	49.840
2	29.355	10365480	247250	50.160	50.160
Total		20664829	556821		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	26.581	6739910	245726	10.756	10.756
2	29.557	55919654	1269384	89.244	89.244
Total		62659563	1515111		100.000

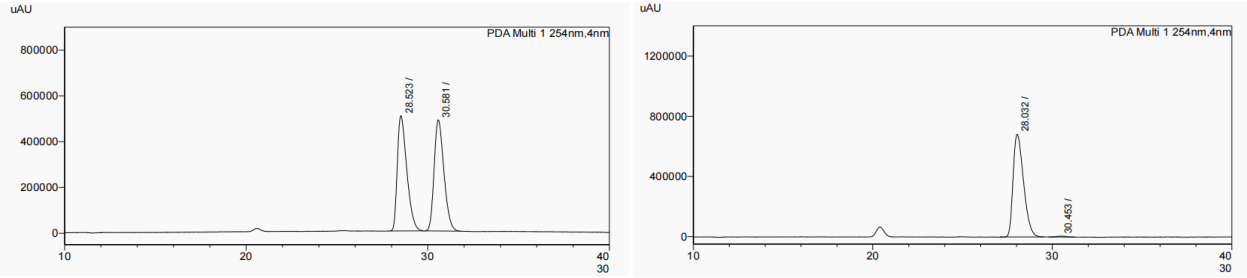
Figure S41. HPLC chromatograms for racemic **8a** and enantioenriched **8a**.

(*R*)-5-Fluoro-3-(fluoromethyl)-1,3-dimethylindolin-2-one (8b):



According to **GP–X**, the reaction of **7b** (33.71 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 12.21 mg, 20 mol%), HCOONa (13.6 mg, 0.20 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **8b** (12.8 mg) in 61% yield and >99% *ee* as a white solid; R_f = 0.20 (3% EtOAc, 30% DCM in hexane); Melting point: 88–90 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07–6.96 (m, 2H), 6.81 (dd, J = 8.4, 4.0 Hz, 1H), 4.55 (d, J = 47.0 Hz, 2H), 3.21 (s, 3H), 1.39 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 176.9 (d, J = 6.3 Hz), 159.4 (d, J = 241.1 Hz), 139.3 (d, J = 1.9 Hz), 132.6 (dd, J = 8.1, 0.6 Hz), 114.7 (d, J = 23.5 Hz), 111.6 (d, J = 24.8 Hz), 108.7 (d, J = 8.1 Hz), 86.0 (d, J = 177.8 Hz), 49.7 (dd, J = 19.5, 1.6 Hz), 26.4, 18.4 (d, J = 6.1 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -(120.17–120.25) (m, 1F), -223.8 (t, J = 47.0 Hz, 1F) ppm; **HRMS (ESI-TOF) *m/z***: $[M+Na]^+$ calcd. for $C_{11}H_{11}F_2NNaO$: 234.0701, found 234.0702. **Enantiomeric excess** = >99%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 28.03 min (major), t_R = 30.45 min (minor). **$[\alpha]_D^{26.4}$** = -4° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

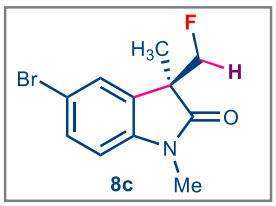
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	28.523	18252062	503012	50.101	50.101
2	30.581	18178263	484891	49.899	49.899
Total		36430324	987903		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	28.032	27586808	681626	99.279	99.279
2	30.453	200309	5839	0.721	0.721
Total		27787116	687465		100.000

Figure S42. HPLC chromatograms for racemic **8b** and enantioenriched **8b**.

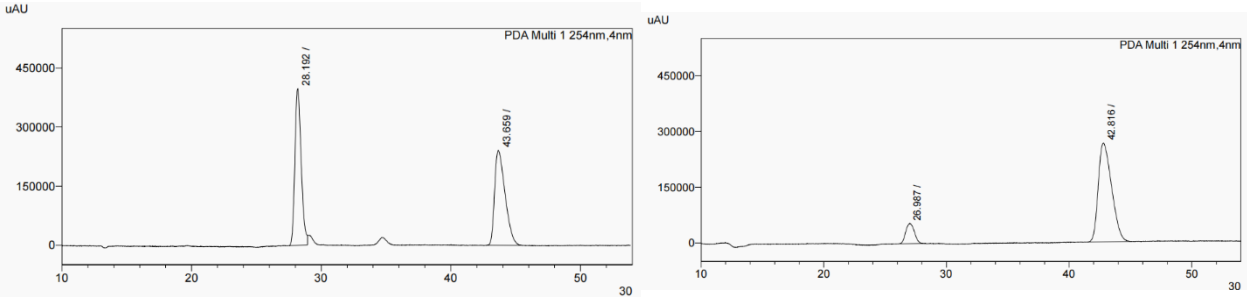
***(R)*-5-Bromo-3-(fluoromethyl)-1,3-dimethylindolin-2-one (8c):**



According to **GP–X**, the reaction of **7c** (39.80 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 12.21 mg, 20 mol%), HCOONa (13.6 mg, 0.20 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **8c** (21.8 mg) in 80% yield and 77% *ee* as a white solid; R_f = 0.20 (3% EtOAc, 30% DCM in hexane); Melting point: 96–98 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 8.2 Hz, 1H), 7.41 (s, 1H), 6.75 (d, J = 8.2 Hz, 1H), 4.55 (d, J = 46.9 Hz, 2H), 3.21 (s, 3H), 1.39 (s, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 176.8 (d, J = 6.1 Hz), 142.5, 133.0, 131.4, 126.6, 115.5, 109.7, 86.0 (d, J = 177.9 Hz), 49.5 (d, J = 19.6 Hz), 26.4, 18.4 (d, J = 6.1 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -223.5 (t, J = 46.9 Hz, 1F) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{12}BrFNO$: 272.0081, found 272.0081.

Enantiomeric excess = 77%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 26.99 min (minor), t_R = 42.82 min (major). **$[\alpha]_D^{28.6}$** = -7° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

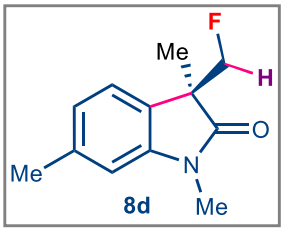
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	28.192	13482384	397876	49.993	49.993
2	43.659	13486418	241205	50.007	50.007
Total		26968803	639080		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	26.987	2644023	53824	11.632	11.632
2	42.816	20086491	266384	88.368	88.368
Total		22730514	320209		100.000

Figure S43. HPLC chromatograms for racemic **8c** and enantioenriched **8c**.

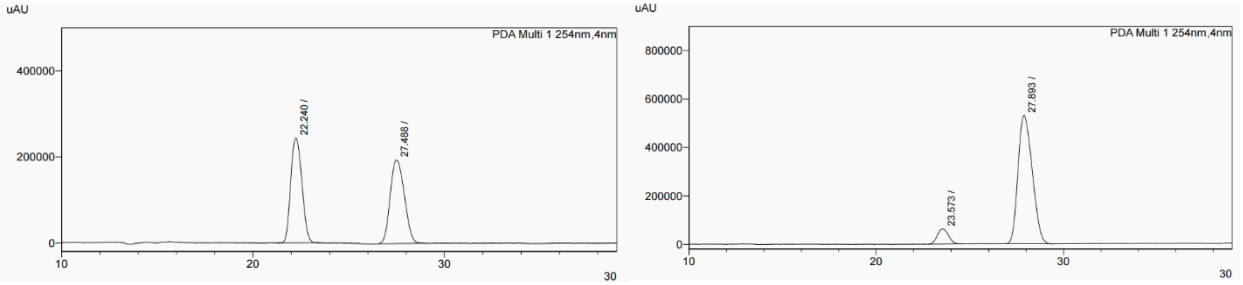
(*R*)-3-(Fluoromethyl)-1,3,6-trimethylindolin-2-one (8d):



According to **GP–X**, the reaction of **7d** (33.31 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 12.21 mg, 20 mol%), HCOONa (13.6 mg, 0.20 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **8d** (9.3 mg) in 45% yield and 83% *ee* as a white solid; R_f = 0.21 (3% EtOAc, 30% DCM in hexane); Melting point: 131–133 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 7.5 Hz, 1H), 6.91 (d, J = 7.5 Hz, 1H), 6.70 (bs, 1H), 4.62–4.56 (m, 1H), 4.53–4.46 (m, 1H), 3.21 (s, 3H), 2.40 (s, 3H), 1.37 (bd, J = 1.2 Hz, 3H); **^{13}C{^{1}H} (126 MHz, $CDCl_3$)** δ 177.7 (d, J = 6.0 Hz), 143.5, 138.7, 128.0 (d, J = 1.2 Hz), 123.2, 122.9, 109.2, 86.4 (d, J = 177.2 Hz), 49.1 (d, J = 19.4 Hz), 26.3, 21.8, 18.5 (d, J = 6.1 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -223.5 (t, J = 47.1 Hz, 1F) ppm; **HRMS (ESI-TOF) *m/z***: $[M+Na]^+$ calcd. for $C_{12}H_{14}FNNaO$: 230.0952, found 230.0948.

Enantiomeric excess = 83%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 23.57 min (minor), t_R = 27.89 min (major). **$[\alpha]_D^{26.3}$** = -16° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

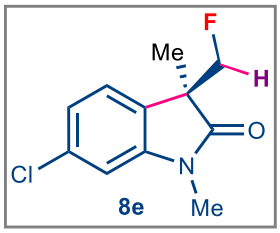
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.240	9867624	243664	49.749	49.749
2	27.488	9967024	194778	50.251	50.251
Total		19834648	438442		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.573	2561258	62385	8.391	8.391
2	27.893	27963233	529844	91.609	91.609
Total		30524490	592229		100.000

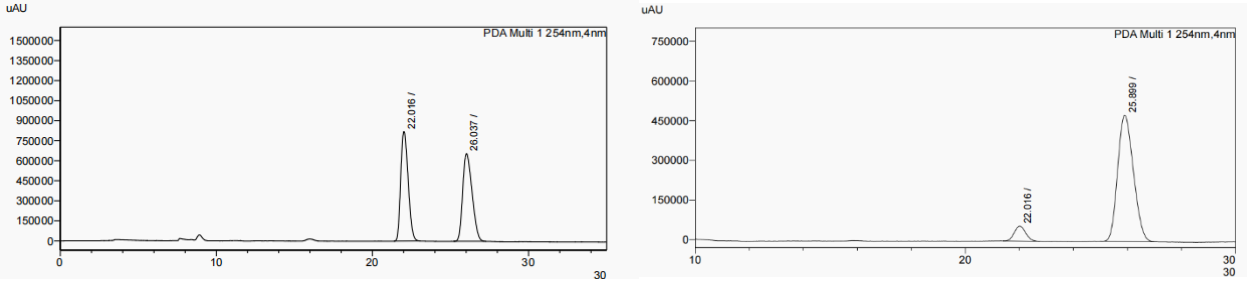
Figure S44. HPLC chromatograms for racemic **8d** and enantioenriched **8d**.

(*R*)-6-Chloro-3-(fluoromethyl)-1,3-dimethylindolin-2-one (8e):



According to **GP–X**, the reaction of **7e** (35.36 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 12.21 mg, 20 mol%), HCOONa (13.6 mg, 0.20 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **8e** (14.3 mg) in 63% yield and 84% *ee* as a white solid; R_f = 0.25 (3% EtOAc, 30% DCM in hexane); Melting point: 87–89 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, J = 7.9 Hz, 1H), 7.07 (d, J = 7.8 Hz, 1H), 6.87 (bs, 1H), 4.54 (d, J = 47.0 Hz, 2H), 3.21 (s, 3H), 1.38 (s, 3H); **^{13}C{1H} (126 MHz, $CDCl_3$)** δ 177.2 (d, J = 6.1 Hz), 144.6, 134.4, 129.3 (d, J = 0.7 Hz), 124.1, 122.6, 109.1, 86.0 (d, J = 177.8 Hz), 49.1 (d, J = 19.5 Hz), 26.4, 18.4 (d, J = 6.0 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -223.5 (t, J = 47.0 Hz, 1F) ppm; **HRMS (ESI-TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{12}ClFNO$: 228.0586, found 228.0581. **Enantiomeric excess** = 84%, determined by HPLC (Daicel Chiralpak AD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 22.02 min (minor), t_R = 25.90 min (major). **$[\alpha]_D^{28.4}$** = -2° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.016	27105597	820234	49.835	49.835
2	26.037	27285345	656018	50.165	50.165
Total		54390942	1476253		100.000

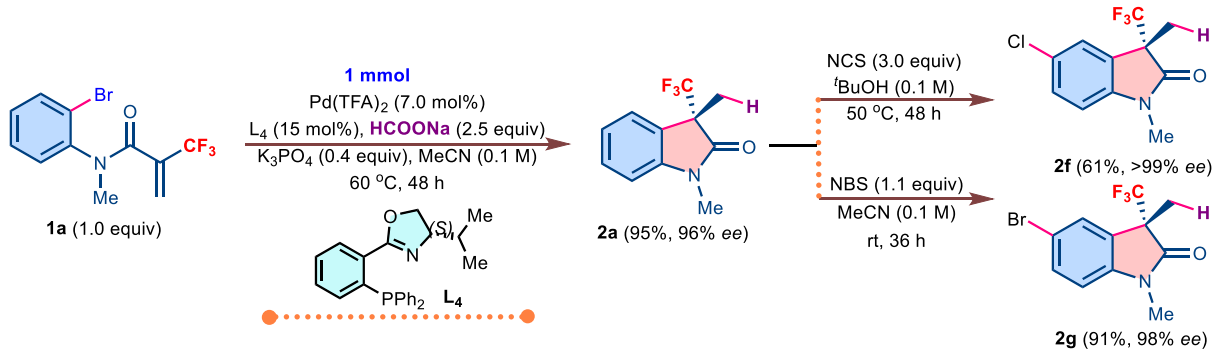
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.016	1656590	56463	7.904	7.904
2	25.899	19301002	477118	92.096	92.096
Total		20957592	533581		100.000

Figure S45. HPLC chromatograms for racemic **8e** and enantioenriched **8e**.

6. Synthetic Applications:

Halogenation Reactions: Chlorination using NCS and Bromination using NBS:

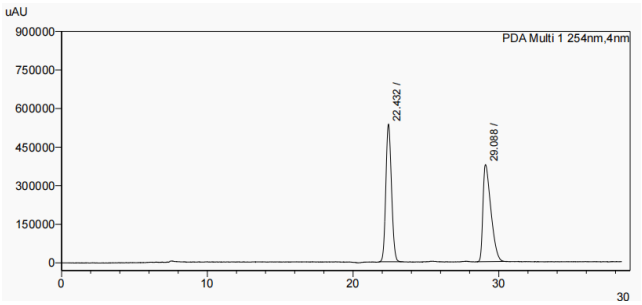


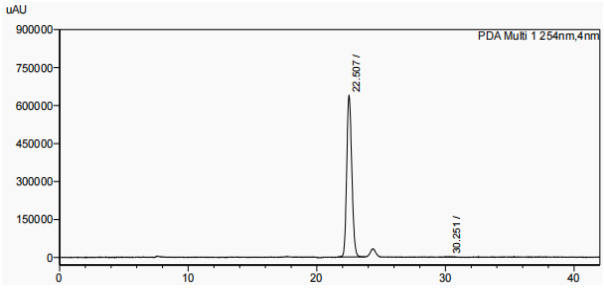
Scheme S11. Chlorination of **2a** using NCS provides **2f** and Bromination of **2a** using NBS provides **2g**.

Chlorination using NCS: Compound **2a** (22.92 mg, 0.1 mmol) and *N*−chlorosuccinimide (40 mg, 0.3 mmol) were taken in a 7.0 ml reaction vial equipped with a magnetic stir bar. Then, ^{t}BuOH (0.1 M) was added to the reaction mixture, vial was sealed and purged with N_2 gas. Afterwards, the reaction was kept for stirring at 50 °C for 48 h. The reaction mixture was concentrated under reduced pressure, and the crude mixture was purified on silica gel column chromatography to afford the desired chlorinated product **2f** (16 mg, 61%, >99% *ee*) as yellow liquid; R_f = 0.54 (3.0%, EtOAc, 30% DCM in hexane).

(*S*)-5-Chloro-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2f)

Enantiomeric excess = >99%, determined by HPLC (Daicel Chiralpak OD-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 15 °C, λ = 254 nm): t_R = 22.51 min (major), t_R = 30.25 min (minor). $[\alpha]_D^{28.6}$ = +38° (c = 5*10^{-4}, $CHCl_3$).





PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.432	14293963	534973	49.795	49.795
2	29.088	14411488	377342	50.205	50.205
Total		28705451	912315		100.000

PDA Ch1 254nm

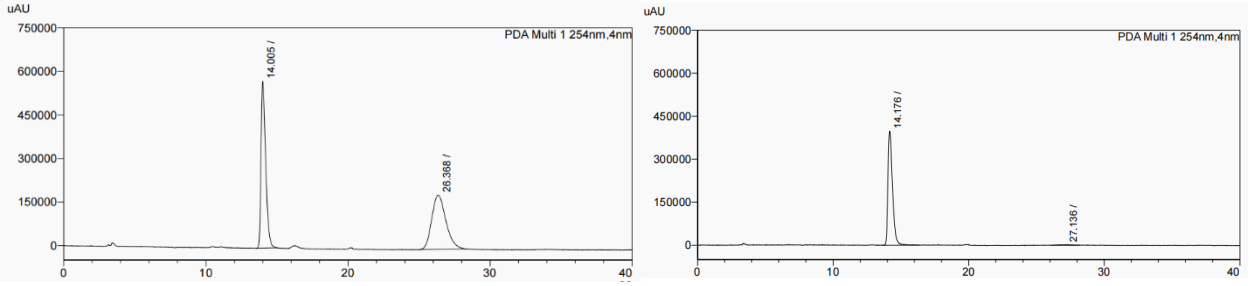
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.507	17554330	638471	99.679	99.679
2	30.251	56470	1734	0.321	0.321
Total		17610801	640204		100.000

Figure S46. HPLC chromatography of the enantioenriched **2f**.

Bromination using NBS: Compound **2a** (22.92 mg, 0.1 mmol) and *N*−bromosuccinimide (19.5 mg, 0.11 mmol) were taken in a 7.0 ml reaction vial equipped with a magnetic stir bar. Then the reaction vial was taken under the glove box to add acetonitrile solvent (MeCN, 0.1 M). The reaction mixture was allowed to stir at room temperature for 36 hours. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure, and the crude mixture was purified on silica gel column chromatography to afford the desired brominated product **2g** (27.7 mg, 91%, 98% *ee*) as white solid; R_f = 0.26 (3.0%, EtOAc, 30% DCM in hexane).

(*S*)-5-Bromo-1,3-dimethyl-3-(trifluoromethyl)indolin-2-one (2g)

Enantiomeric excess = 98%, determined by HPLC (Daicel Chiralpak OJ-H Column, 2.5% ^{i}PrOH in *n*-Hexane, flow rate 1.0 mL/min, T = 25 °C, λ = 254 nm): t_R = 14.18 min (major), t_R = 27.14 min (minor). $[\alpha]_D^{29.1}$ = +38° (c = 10^{-3}, $CHCl_3$).



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.005	13121948	574360	50.325	50.325
2	26.368	12952598	187265	49.675	49.675
Total		26074546	761625		100.000

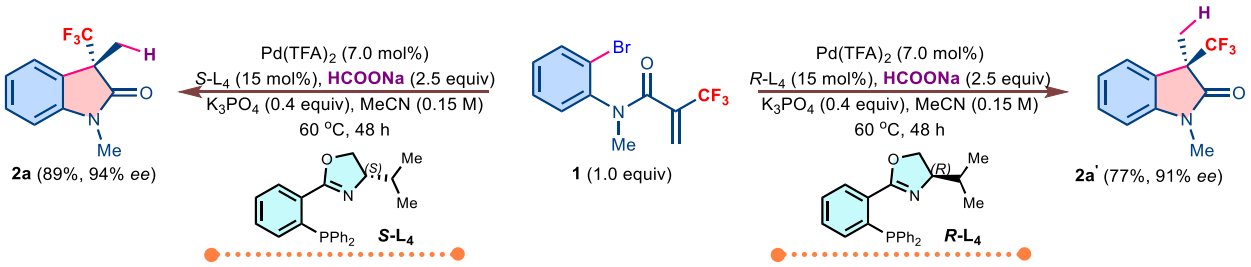
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14.176	9307632	398259	98.955	98.955
2	27.136	98339	1883	1.045	1.045
Total		9405970	400141		100.000

Figure S47. HPLC chromatography of the enantioenriched **2g**.

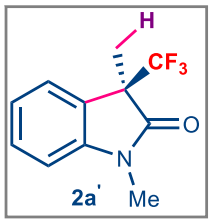
7. Stereo-divergent reactions:

(*S*)-1,3-Dimethyl-3-(trifluoromethyl)indolin-2-one (2a) and (*R*)-1,3-Dimethyl-3-(trifluoromethyl)indolin-2-one (2a'):



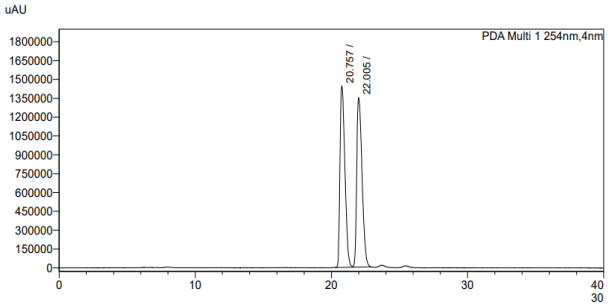
Scheme S12. Stereo-divergent products with ligands *S*-L4 and *R*-L4.

(*R*)-1,3-Dimethyl-3-(trifluoromethyl)indolin-2-one (2a'):



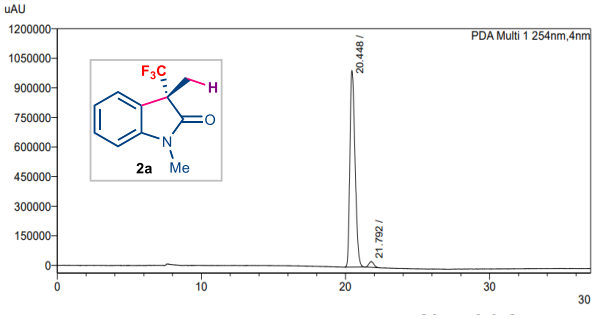
According to **GP–V**, the reaction of *N*-(2-bromophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1a**, 46.2 mg, 0.15 mmol) using $Pd(TFA)_2$ (3.5 mg, 7 mol%), (*R*)-PHOX (**L4**, 8.4 mg, 15 mol%), HCOONa (26 mg, 0.375 mmol) and K_3PO_4 (18 mg, 0.06 mmol) afforded the desired amide **2a'** (26.5 mg) in 77% yield and 91% *ee* as a white solid; R_f = 0.50 (3% EtOAc, 30% DCM in hexane).

Enantiomeric excess = 91%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 21.45 min (minor), t_R = 22.67 min (major). $[\alpha]_D^{28.3}$ = –17° (c = 10^{-3}, $CHCl_3$).



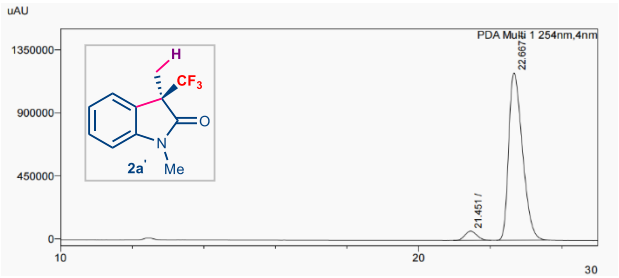
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	20.757	36229239	1443704	49.722	49.722
2	22.005	36634805	1348430	50.278	50.278
Total		72864043	2792134		100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	20.448	24826309	996401	97.238	97.238
2	21.792	705187	29537	2.762	2.762
Total		25531496	1025938		100.000

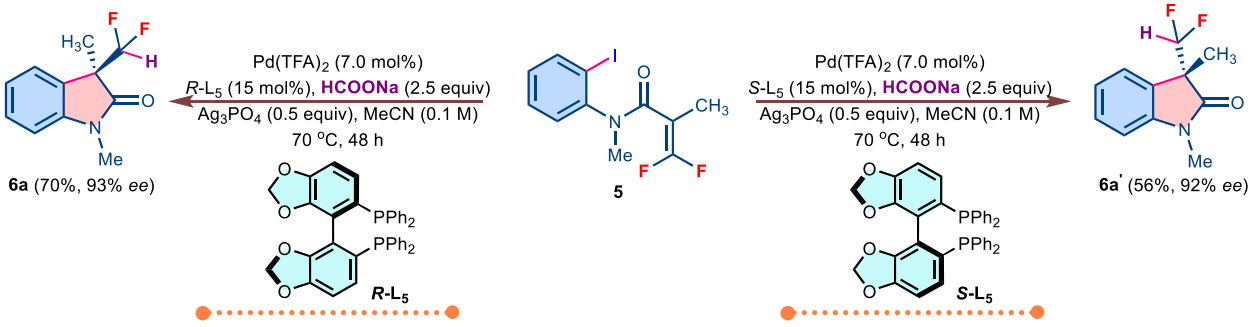


PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	21.451	1540473	66275	4.604	4.604
2	22.667	31918270	1194743	95.396	95.396
Total		33458743	1261018		100.000

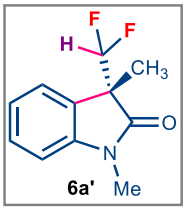
Figure S48. HPLC chromatography of the racemic **2a** and enantioenriched **2a** and **2a'**.

(*R*)-3-(Difluoromethyl)-1,3-dimethylindolin-2-one (6a) and (*S*)-3-(Difluoromethyl)-1,3-dimethylindolin-2-one (6a'):



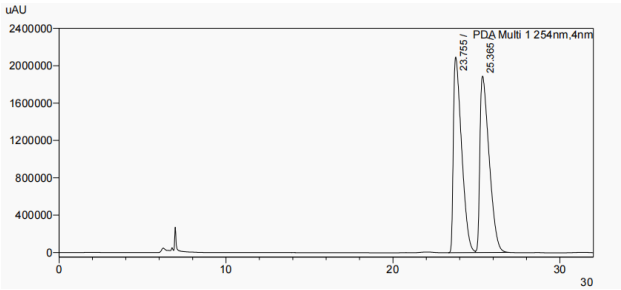
Scheme S13. Stereo-divergent products with ligands *R*-L_5 and *S*-L_5.

(*S*)-3-(Difluoromethyl)-1,3-dimethylindolin-2-one (6a'):



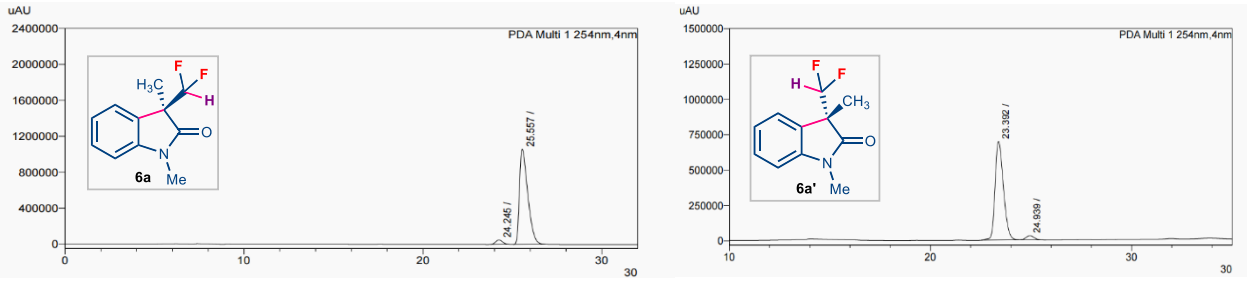
According to **GP–IX**, the reaction of **5a** (33.71 mg, 0.1 mmol) using $Pd(TFA)_2$ (2.33 mg, 7 mol%), (*R*)-SEGPHOS (**L5**, 9.2 mg, 15 mol%), HCOONa (17 mg, 0.25 mmol) and Ag_3PO_4 (21 mg, 0.05 mmol) afforded **6a'** (11.8 mg) in 56% yield and 92% *ee* as a colorless liquid; R_f = 0.32 (3% EtOAc, 30% DCM in hexane).

Enantiomeric excess = 92%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 23.39 min (major), t_R = 24.94 min (minor). $[\alpha]_D^{28.5}$ = +6° (c = 5*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.755	72076242	2094132	49.776	49.776
2	25.365	72723523	1889529	50.224	50.224
Total		144799765	3983661		100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	24.245	1305687	49364	3.665	3.665
2	25.557	34317018	1058326	96.335	96.335
Total		35622705	1107690		100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	23.392	20151942	696337	96.161	96.161
2	24.939	804453	28945	3.839	3.839
Total		20956395	725282		100.000

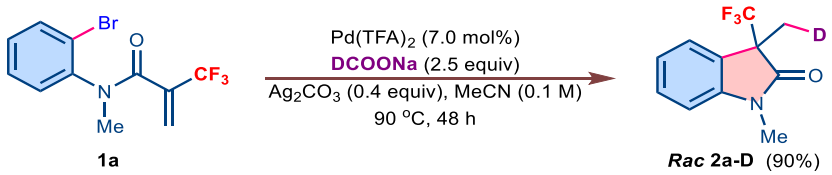
Figure S49. HPLC chromatography of the racemic **6a** and enantioenriched **6a** and **6a'**.

8. Mechanistic Studies:

Control Experiments:

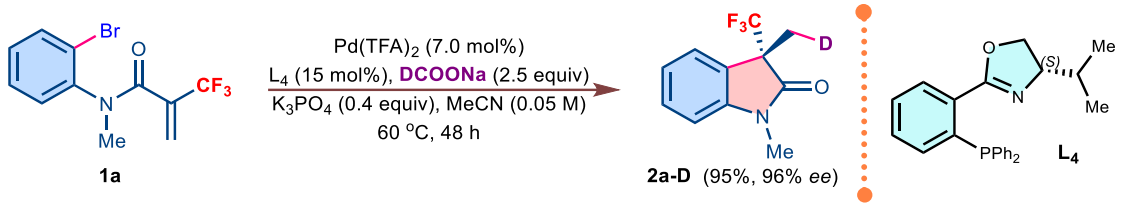
Deuterium Incorporation Experiment:

An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-bromo trifluoromethyl acryl amide (**1a**, 1.0 equiv., 0.1 mmol), $Pd(TFA)_2$ (2.33 mg, 7 mol%), DCOONa (18 mg, 0.25 mmol) and Ag_2CO_3 (11 mg, 0.04 mmol). Then the reaction vial was introduced inside the glove box and acetonitrile solvent (MeCN, 0.1 M) was added. The reaction vial was capped, taken outside, and stirred at 90 °C (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was purified on silica gel column chromatography to afford the desired product ***Rac* 2a-D** (20.7 mg, 90%) as a white solid; R_f = 0.22 (3.0%, EtOAc, 30% DCM in hexane).



Scheme S14. The racemic reductive Heck reaction of **1a** with DCOONa as hydride source.

An oven-dried reaction vial (7.0 mL) equipped with a magnetic bead was charged with *o*-bromo trifluoromethyl acryl amide (**1a**, 1.0 equiv., 0.05 mmol), $Pd(TFA)_2$ (1.2 mg, 7 mol%), L_4 (2.8 mg, 15 mol%), DCOONa (8.63 mg, 0.125 mmol) and K_3PO_4 (4.25 mg, 0.02 mmol). Then the reaction vial was introduced inside the glove box and acetonitrile solvent (MeCN, 0.05 M) was added. The reaction vial was capped, taken outside, and stirred at 60 °C (oil bath/heating block) for 48 hours. After completion of the reaction (monitored by TLC), the vial was cooled to room temperature, the reaction mixture was diluted with DCM (10 mL) and filtered through a celite pad, and the filtrate was concentrated under vacuum. The crude mixture was purified on silica gel column chromatography to afford the desired product **2a-D** (11 mg, 95%) and 96% *ee* a white solid; R_f = 0.22 (3.0%, EtOAc, 30% DCM in hexane).

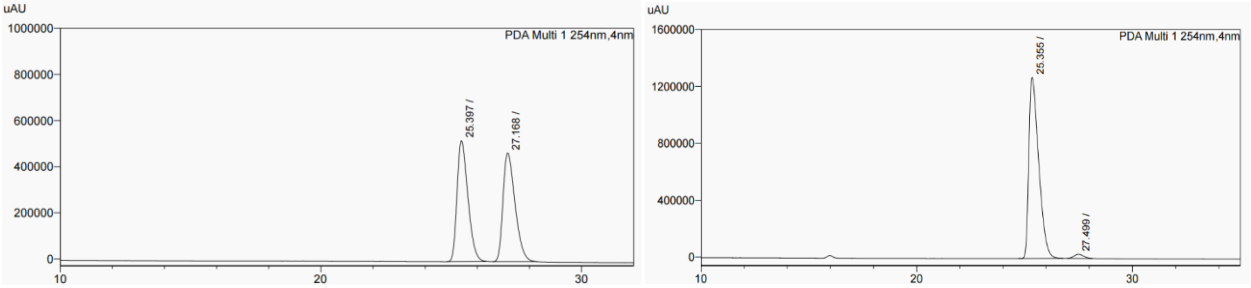


Scheme S15. The asymmetric reductive Heck reaction of **1a** with DCOONa as hydride source.

(*S*)-1-Methyl-3-(methyl-*D*)-3-(trifluoromethyl)indolin-2-one (2a-D)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.35 (m, 2H), 7.12 (t, J = 7.5 Hz, 1H), 6.89 (d, J = 7.8 Hz, 1H), 3.24 (s, 3H), 1.63 (s, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.2 (q, J = 2.8 Hz), 143.6, 129.8, 126.2, 124.9 (q, J = 281.7 Hz), 124.5, 123.1, 108.6, 52.0 (q, J = 27.7 Hz), 26.5, 17.5 (tq, J = 20.2, 2.6 Hz); **^{19}F NMR (377 MHz, $CDCl_3$)** δ -73.5 ppm; **HRMS (ESI−TOF) *m/z***: $[M+H]^+$ calcd. for $C_{11}H_{10}DF_3NO$: 231.0851, found 231.0860.

Enantiomeric excess = 96%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 25.36 min (major), t_R = 27.50 min (minor). $[\alpha]_D^{27.8}$ = +17° (c = 3*10^{-4}, $CHCl_3$).



PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	25.397	15237341	524173	50.129	50.129
2	27.168	15158838	471552	49.871	49.871
Total		30396179	995725		100.000

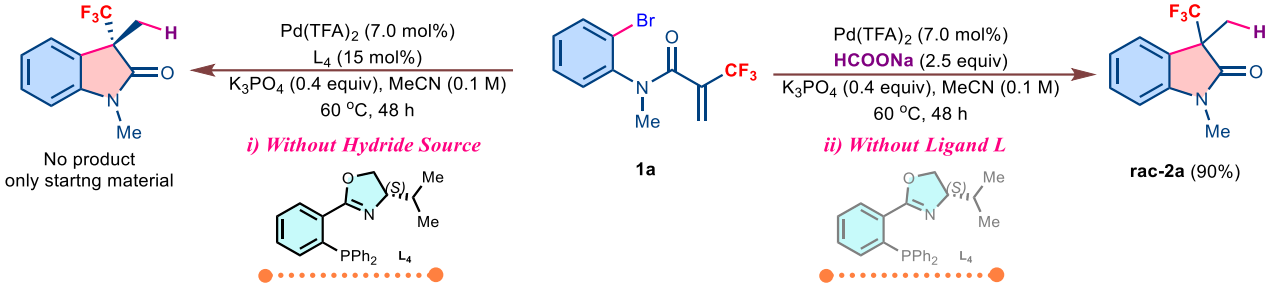
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	25.355	40391053	1271044	97.922	97.922
2	27.499	857150	28307	2.078	2.078
Total		41248204	1299351		100.000

Figure S50. HPLC chromatography of the enantioenriched **2a-D**.

Reactivity Profile without Hydride Source and Ligand:

According to **GP–IX**, the reaction of *N*-(2-bromophenyl)-*N*-methyl-2-(trifluoromethyl)acrylamide (**1a**, 0.025 mmol) was conducted under two conditions: (i) without a hydride source and (ii) without a ligand. *Without a hydride source, the reaction did not yield the desired product, leaving only the starting material. However, when the reaction was carried out without a ligand, 90% of the racemic product was obtained (by crude ^{19}F NMR analysis), suggesting the presence of a rapid background reaction.*

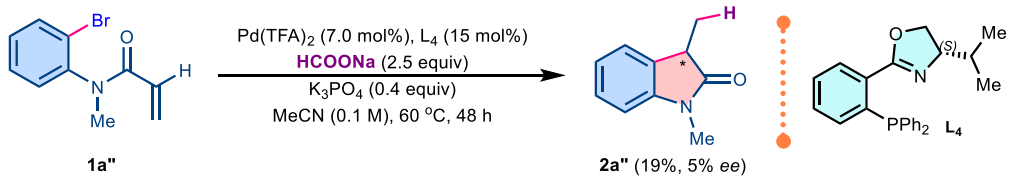


Scheme S16. Role of hydride source and ligand in the reaction medium.

Asymmetric reductive Heck cyclization of monosubstituted terminal alkenes (1a"):

Following the general procedure (**GP-V**), the reaction of **1a"** afforded **2a"** in 19% yield and 5% *ee*. The NMR data matched with the reported data.[7a]

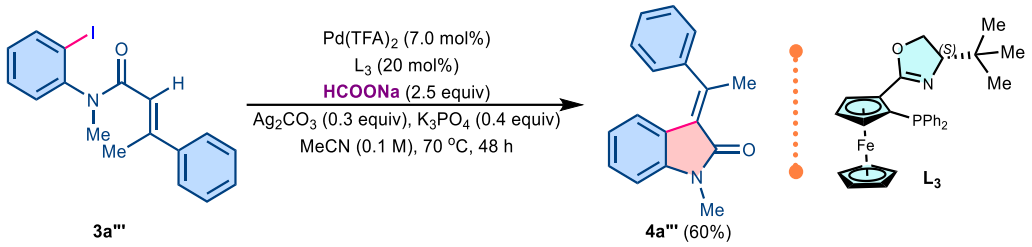
Enantiomeric excess = 5%, determined by HPLC (Daicel Chiralpak OJ-H Column, 1% ^{i}PrOH in *n*-Hexane, flow rate 0.5 mL/min, T = 25 °C, λ = 254 nm): t_R = 25.26 min (minor), t_R = 30.59 min (major).



Scheme S17. Asymmetric Reductive Heck cyclization of *o*-bromo-acrylamides.

Asymmetric reductive Heck cyclization of terminally disubstituted (3a"') acrylamides:

Following the general procedure (**GP-VII**), the reaction of **3a"'** afforded **4a"'** in 60% yield. The NMR data matched with the reported data.[7b]



Scheme S18. Asymmetric Reductive Heck cyclization of *o*-iodo-*β*, *β*-methy, phenyl acrylamides.

9. Computational Studies:

The reaction mechanisms were studied through Density Functional Theory (DFT) using the B3LYP functional.[8] Mixed basis sets were used to account for the relativistic effects from the heavy elements such as Pd. Lanl2DZ basis set[9] was used for Pd, Br and I and for lighter atoms H, C, N, P, F and O the basis set 6-31G(D,P)[10] was used. The Gaussian Program Package was used for all the calculations.[11] All the structures were optimized and stable geometries were found on the account of positive frequencies. We have located the species **A, TS$_S$, TS$_R$, *S*-B** and ***R*-B** pertinent to the enantio-selectivity in the migratory insertion step.

For the reaction involving substrate **1a** with ***S*-L$_4$**, the energies with respect to the energy of **A** is given in Table S7. The location of possible transition state points (TS$_R$, TS$_S$) for both the *re* and *si* face based on interaction of ligand is done. The pictorial representation of optimized geometries can be seen in Figure S51.

Table S7: The energies (in kcal/mol) with respect to the energy of **A** for both the pathways ***R*** and ***S*** respectively for the reaction involving substrate **1a** and ligand ***S*-L$_4$**.

Pathway	E_A	E_{TS}	E_B
R	0.0	25.79	-15.83
S		21.27	-16.96

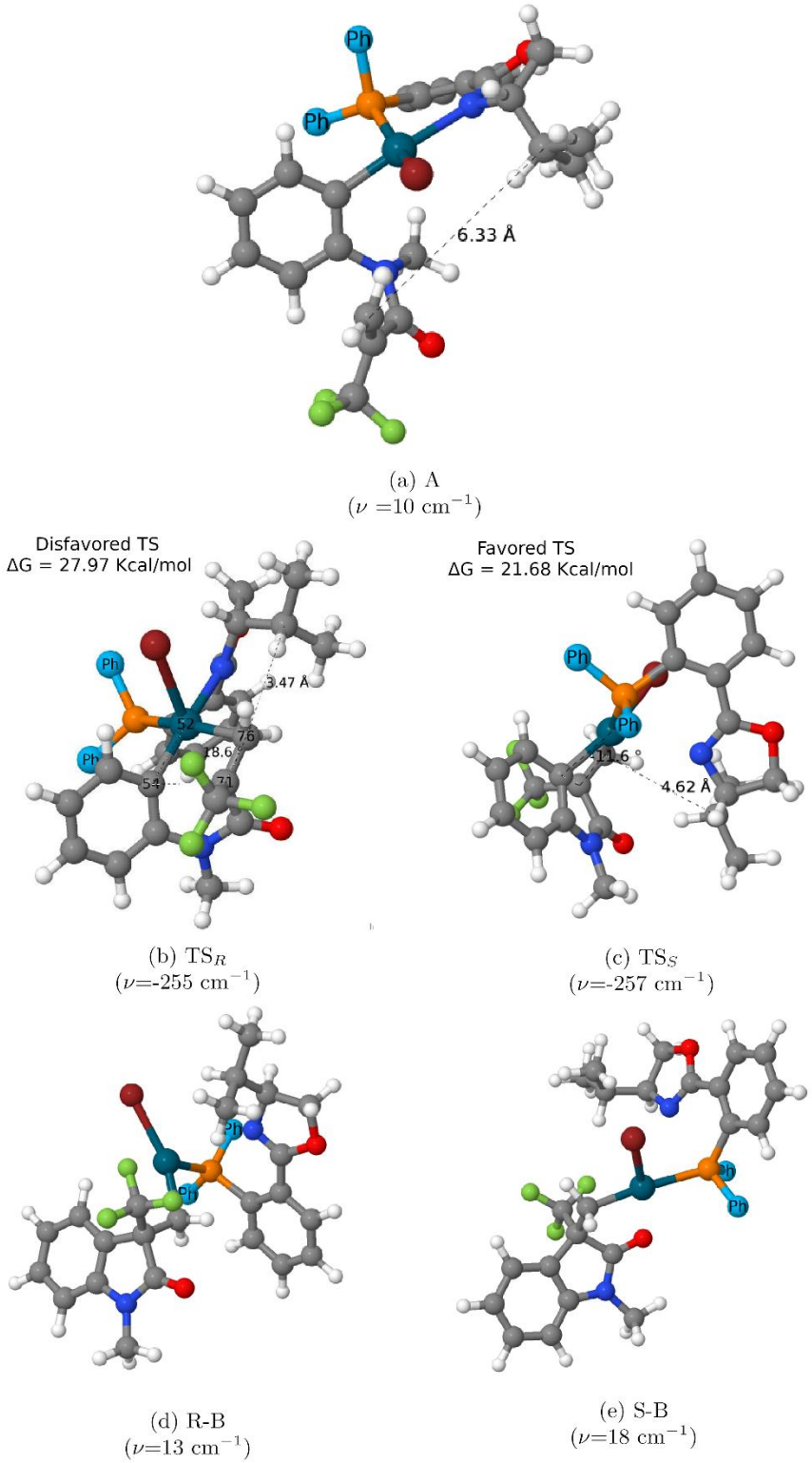


Figure S51. The pictorial representation of A, TS_R , TS_S, ***R***-B, ***S***-B for the reaction involving **1a** with ligand ***S***-$\mathbf{L_4}$. The values in the parenthesis are the first vibrational frequency in cm^{-1} units.

The enantioselectivity is determined by the interaction between the isopropyl group of the ligand (**L4**) and the *Re* or *Si*-face of alkene (**1a**) during the migratory insertion step. Two intermediates (***R*-B** and ***S*-B**) can be formed through the transition states ($\mathbf{TS}_{\boldsymbol{R}}$ and $\mathbf{TS}_{\boldsymbol{S}}$). We have calculated the energies of the oxidative addition intermediate **A**, the two transition states ($\mathbf{TS_R}$, $\mathbf{TS_S}$), and two intermediates (***R*-B** and ***S*-B**). The activation energies computed are ~21 kcal/mol for $\mathbf{TS}_{\boldsymbol{S}}$ and ~26 kcal/mol for $\mathbf{TS}_{\boldsymbol{R}}$, corresponding to the *Si* and *Re* attack of the alkene, respectively (Scheme 17). The steric interactions between the isopropyl group and the alkene destabilize $\mathbf{TS}_{\boldsymbol{R}}$ more than $\mathbf{TS}_{\boldsymbol{S}}$. For instance, the distance between these two carbons is 3.47 Å in $\mathbf{TS}_{\boldsymbol{R}}$ and 4.62 Å in $\mathbf{TS}_{\boldsymbol{S}}$. Additionally, we identified a dihedral angle (52-54-71-76) that governs the positioning of the isopropyl and alkene groups. This dihedral angle is 18° for $\mathbf{TS}_{\boldsymbol{R}}$ and -11° for $\mathbf{TS}_{\boldsymbol{S}}$, which results in the alkene being pushed toward the isopropyl group in $\mathbf{TS}_{\boldsymbol{R}}$, while it is pushed away in $\mathbf{TS}_{\boldsymbol{S}}$. Furthermore, the reaction Gibbs free energy (ΔG) was calculated at the reaction temperature of 60 °C for both processes. The formation of ***S*-B** (21.68 kcal/mol) was found to be more favorable than the formation of ***R*-B** (27.97 kcal/mol), supporting the preferential formation of ***S*-2a** under the given conditions.

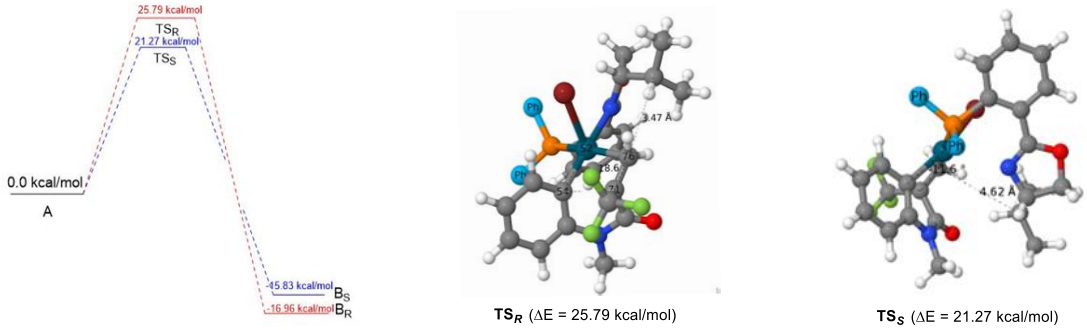


Figure S52. Transition states for enantio-induction step.

Optimized cartesian coordinates (in XYZ format):

Substrate 1a with ligand *S*-L4

A (E = -2394.42243645 au)

P	-1.84375	-1.08355	-0.10486
C	-2.77010	-0.55590	-1.61220
C	-3.14001	0.79931	-1.79333
C	-3.15699	-1.49141	-2.58087
C	-3.90450	1.16262	-2.91387
C	-3.89347	-1.11165	-3.70446
H	-2.88330	-2.53249	-2.45455
C	-4.27259	0.21810	-3.86878
H	-4.19501	2.19926	-3.03383
H	-4.17405	-1.85907	-4.44056
H	-4.85133	0.52400	-4.73469
C	-1.50120	-2.86974	-0.36354
C	-2.20580	-3.87684	0.31169
C	-0.47033	-3.23192	-1.24716
C	-1.89219	-5.22057	0.09632
H	-2.99492	-3.61876	1.00883
C	-0.16709	-4.57402	-1.46543
H	0.10551	-2.46586	-1.75420
C	-0.87704	-5.57181	-0.79298
H	-2.44273	-5.99078	0.62857
H	0.63389	-4.83892	-2.14887
H	-0.63288	-6.61740	-0.95616
C	-3.14021	-1.01372	1.20635
C	-2.78635	-0.60024	2.50011
C	-4.47514	-1.36191	0.94009
C	-3.74792	-0.54972	3.51118
H	-1.76390	-0.29904	2.70897
C	-5.43296	-1.30773	1.95278
H	-4.76957	-1.67008	-0.05853
C	-5.07031	-0.90348	3.23981
H	-3.46125	-0.22608	4.50729
H	-6.46239	-1.57698	1.73481
H	-5.81831	-0.85875	4.02608

C	-2.74526	1.89743	-0.88261
C	-3.06612	3.89819	0.08732
C	-1.63506	3.40245	0.35384
H	-3.12735	4.90431	-0.32880
H	-3.72011	3.82284	0.96214
H	-1.39371	3.38514	1.41830
N	-1.69722	1.99800	-0.13780
O	-3.56761	2.97150	-0.91524
C	-0.52531	4.20401	-0.37474
C	-0.34733	5.57348	0.29843
H	-0.11600	5.46188	1.36234
H	0.47915	6.11978	-0.16626
H	-1.24326	6.20075	0.20489
C	-0.74523	4.34126	-1.88790
H	-0.83411	3.36618	-2.37697
H	-1.63876	4.92927	-2.13098
H	0.10945	4.85329	-2.34082
H	0.39534	3.63611	-0.21030
Pd	-0.19361	0.44217	0.47615
Br	1.16886	2.03325	1.99959
C	1.18913	-0.98941	0.83198
C	1.00603	-1.89166	1.88756
C	2.34188	-1.12909	0.02944
C	1.91108	-2.92518	2.13961
H	0.14288	-1.78659	2.53762
C	3.22341	-2.19915	0.26028
C	3.02108	-3.08686	1.31305
H	1.73959	-3.60135	2.97293
H	4.09012	-2.30951	-0.38347
H	3.72587	-3.89583	1.48144
N	2.65238	-0.22137	-1.04366
C	1.74285	-0.15699	-2.18877
H	1.99465	0.71719	-2.78695
H	1.84254	-1.04834	-2.82388

H	0.71376	-0.07780	-1.83141
C	3.90095	0.33425	-1.24958
O	4.21716	0.83643	-2.32495
C	4.89670	0.36263	-0.11744
C	6.28139	-0.09775	-0.50125
F	6.22842	-1.30177	-1.13512
F	7.07514	-0.26048	0.58163
F	6.91345	0.75170	-1.32939
C	4.65983	0.87592	1.09017
H	3.67359	1.22631	1.37812
H	5.45859	0.95471	1.82021

TS_R (E = -2394.38132934 au)

P	1.08540	1.36762	0.06175
C	1.86193	1.40873	-1.62589
C	2.43341	0.22325	-2.14479
C	1.93974	2.57202	-2.40266
C	3.06087	0.22964	-3.39731
C	2.54093	2.56350	-3.66344
H	1.53529	3.50105	-2.01917
C	3.09956	1.39054	-4.16618
H	3.51632	-0.68495	-3.76100
H	2.58033	3.48103	-4.24333
H	3.57306	1.37889	-5.14287
C	0.46405	3.07721	0.34225
C	0.87629	3.82769	1.45448
C	-0.49268	3.62782	-0.52705
C	0.35773	5.10395	1.67841
H	1.60371	3.41809	2.14605
C	-0.99549	4.90992	-0.30990
H	-0.84051	3.05508	-1.38034
C	-0.57222	5.65164	0.79451
H	0.68744	5.67067	2.54427
H	-1.72643	5.32469	-0.99798

H	-0.96880	6.64798	0.96677
C	2.55580	1.23625	1.16482
C	2.47398	0.45019	2.32317
C	3.74551	1.92850	0.87649
C	3.57235	0.36607	3.18423
H	1.57360	-0.12138	2.54372
C	4.83582	1.83730	1.73957
H	3.82201	2.53515	-0.02101
C	4.74953	1.05633	2.89646
H	3.49887	-0.25068	4.07506
H	5.75248	2.37264	1.50874
H	5.60166	0.98508	3.56683
C	2.47140	-1.03826	-1.37339
C	3.56670	-2.77378	-0.46122
C	2.06956	-2.84023	-0.08597
H	3.95194	-3.67538	-0.93994
H	4.20941	-2.50593	0.38199
H	1.90913	-2.78629	0.99461
N	1.53790	-1.57170	-0.66541
O	3.65112	-1.68898	-1.42857
C	1.33475	-4.09781	-0.60272
C	1.85972	-5.34294	0.13018
H	1.76180	-5.22714	1.21392
H	1.28835	-6.22811	-0.16663
H	2.91277	-5.54608	-0.10157
C	1.38769	-4.26531	-2.12729
H	0.98661	-3.38916	-2.64722
H	2.41025	-4.43062	-2.48849
H	0.79521	-5.13258	-2.43582
H	0.29226	-3.97493	-0.30098
Pd	-0.35911	-0.57049	-0.02593
Br	-0.11077	-2.15456	2.63537
C	-2.16296	0.46687	0.44602
C	-2.26295	0.69787	1.82755

C	-2.94809	1.24460	-0.43128
C	-2.98617	1.79347	2.30012
H	-1.72850	0.04427	2.51148
C	-3.67193	2.34500	0.04483
C	-3.66550	2.62924	1.40783
H	-3.01142	1.99713	3.36652
H	-4.27398	2.93818	-0.63581
H	-4.22599	3.48249	1.77858
N	-3.08765	0.77664	-1.75237
C	-3.52216	1.61586	-2.85775
H	-4.57725	1.89551	-2.75632
H	-2.91710	2.52583	-2.90627
H	-3.39503	1.03899	-3.77358
C	-2.91205	-0.57429	-1.94373
O	-2.93843	-1.13013	-3.03129
C	-2.65413	-1.32339	-0.64165
C	-3.89577	-1.69833	0.17244
F	-4.82136	-0.72165	0.23072
F	-3.59872	-2.07684	1.41806
F	-4.48358	-2.74778	-0.45135
C	-1.60217	-2.24997	-0.62444
H	-1.10574	-2.46499	-1.56542
H	-1.57536	-2.99659	0.16023

TSs(E=-2394.38852991 au)

P	-1.41432	-0.80034	0.21925
C	-2.99350	-0.14443	-0.51929
C	-3.34898	1.22937	-0.48844
C	-3.88503	-1.03815	-1.12653
C	-4.56059	1.64722	-1.05936
C	-5.08487	-0.60809	-1.69593
H	-3.64379	-2.09264	-1.16328
C	-5.42480	0.74051	-1.66530
H	-4.81136	2.70030	-1.02364

H	-5.74609	-1.33374	-2.16052
H	-6.35376	1.08821	-2.10688
C	-1.54011	-2.63451	-0.04193
C	-1.83655	-3.54307	0.98463
C	-1.23236	-3.13685	-1.32144
C	-1.83191	-4.91898	0.73872
H	-2.06852	-3.18327	1.98077
C	-1.23964	-4.51014	-1.56477
H	-0.99512	-2.44661	-2.12704
C	-1.53585	-5.40625	-0.53403
H	-2.06157	-5.60811	1.54675
H	-1.00789	-4.87880	-2.55999
H	-1.53321	-6.47604	-0.72284
C	-1.74617	-0.61383	2.02890
C	-0.69373	-0.36265	2.91725
C	-3.04795	-0.74212	2.54080
C	-0.93314	-0.24741	4.28746
H	0.31213	-0.24733	2.53646
C	-3.28622	-0.62394	3.91096
H	-3.87983	-0.93110	1.86997
C	-2.22903	-0.37685	4.78865
H	-0.10351	-0.05349	4.96169
H	-4.29933	-0.72381	4.29031
H	-2.41539	-0.28412	5.85490
C	-2.50225	2.26241	0.13014
C	-2.09597	4.33247	0.91286
C	-0.86596	3.40299	1.11318
H	-1.89017	5.22086	0.31052
H	-2.55764	4.64190	1.85566
H	-0.64052	3.29719	2.18258
N	-1.33186	2.09916	0.61563
O	-3.04789	3.51453	0.19620
C	0.43565	3.85705	0.41039
C	1.00840	5.11331	1.08328

H	1.15274	4.96722	2.16052
H	1.97717	5.37365	0.64575
H	0.34835	5.97961	0.95113
C	0.28179	4.04968	-1.10414
H	-0.12524	3.15616	-1.58621
H	-0.37135	4.89697	-1.34570
H	1.25912	4.25912	-1.55125
H	1.14723	3.03723	0.56650
Pd	0.67534	-0.14419	-0.92246
C	2.04597	-0.89362	0.59468
C	1.84925	-2.27310	0.75400
C	2.71223	-0.19328	1.61957
C	2.11743	-2.88990	1.97730
H	1.42092	-2.85801	-0.05261
C	2.98556	-0.80601	2.85003
C	2.65779	-2.14807	3.03158
H	1.89030	-3.94342	2.10783
H	3.48991	-0.25483	3.63667
H	2.86586	-2.62569	3.98433
N	3.20063	1.08335	1.29881
C	3.60845	2.05433	2.30346
H	3.80628	2.99365	1.78848
H	2.81020	2.19233	3.03776
H	4.52030	1.73256	2.81962
C	3.41793	1.34065	-0.03357
O	3.81787	2.40744	-0.47325
C	3.07262	0.16248	-0.94504
C	4.17231	-0.88382	-1.13853
F	3.69887	-2.00498	-1.71253
F	4.81051	-1.22685	-0.00511
F	5.10563	-0.36588	-1.96592
C	2.33865	0.47915	-2.10927
Br	-0.66750	0.35296	-3.08807
H	2.09530	1.51902	-2.29648

H	2.40721	-0.16370	-2.97912

***R*-B(E=-2394.44767058 au)**

P	1.11015	-1.26892	0.18849
C	1.18470	-1.03360	2.02915
C	1.83066	0.07054	2.65011
C	0.51901	-1.95357	2.85188
C	1.81208	0.19043	4.04740
C	0.49769	-1.81375	4.24111
H	0.01378	-2.80155	2.40580
C	1.14954	-0.74101	4.84247
H	2.32111	1.03414	4.49810
H	-0.02729	-2.54822	4.84461
H	1.14122	-0.62398	5.92173
C	0.35839	-2.94301	-0.04501
C	1.06817	-4.11940	0.25427
C	-0.93738	-3.04874	-0.56991
C	0.48268	-5.36779	0.04948
H	2.08217	-4.06286	0.63610
C	-1.52108	-4.30058	-0.77469
H	-1.48351	-2.14945	-0.83511
C	-0.81374	-5.46138	-0.46386
H	1.04340	-6.26839	0.28264
H	-2.52429	-4.36075	-1.18602
H	-1.26410	-6.43603	-0.62879
C	2.85930	-1.54474	-0.32504
C	3.22496	-1.42489	-1.67196
C	3.81577	-1.96561	0.61428
C	4.53004	-1.72114	-2.06929
H	2.50307	-1.07586	-2.40373
C	5.11804	-2.25988	0.20834
H	3.55409	-2.05872	1.66320
C	5.47858	-2.13834	-1.13475
H	4.80170	-1.61707	-3.11566

H	5.84901	-2.58126	0.94499
H	6.49345	-2.36504	-1.44908
C	2.53234	1.11304	1.88110
C	3.85765	2.91090	1.63347
C	3.37756	2.37210	0.25565
H	3.44751	3.89485	1.87938
H	4.94365	2.93635	1.74496
H	4.21880	1.91797	-0.28627
N	2.46392	1.27583	0.61816
O	3.33432	1.95621	2.59478
C	2.73014	3.40171	-0.69552
C	3.78076	4.40747	-1.19101
H	4.63178	3.90310	-1.66244
H	3.34459	5.08543	-1.93115
H	4.16820	5.02700	-0.37173
C	1.51358	4.11525	-0.09299
H	0.77357	3.40497	0.28205
H	1.79037	4.78608	0.72983
H	1.02488	4.72881	-0.85637
H	2.38004	2.81753	-1.55540
Pd	-0.14719	0.30399	-0.87866
Br	0.69170	0.58143	-3.32436
C	-3.60758	0.17380	-0.47107
C	-3.45599	-0.28018	-1.77502
C	-4.75969	-0.16470	0.25709
C	-4.45895	-1.08795	-2.33412
H	-2.58253	-0.01513	-2.36402
C	-5.76121	-0.96615	-0.28008
C	-5.59157	-1.42580	-1.59285
H	-4.35041	-1.44415	-3.35356
H	-6.64696	-1.22384	0.29111
H	-6.36050	-2.05061	-2.03800
N	-4.71259	0.41368	1.53434
C	-5.73955	0.29164	2.54901

H	-5.40791	0.86209	3.41731
H	-6.69219	0.69657	2.19019
H	-5.88403	-0.75657	2.83321
C	-3.56744	1.16546	1.71378
O	-3.27581	1.79154	2.71388
C	-2.70504	1.01607	0.41579
C	-2.45479	2.40029	-0.17664
F	-3.59172	3.03457	-0.50649
F	-1.71310	2.27961	-1.32791
F	-1.75897	3.19992	0.64590
C	-1.36571	0.35016	0.80271
H	-1.57486	-0.64009	1.21117
H	-0.86305	0.94971	1.56515

_S_-B(E=-2394.44946953 au)

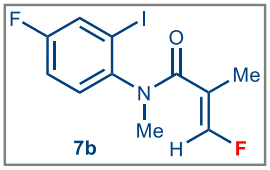
P	1.66434	1.05601	0.14072
C	3.26077	0.68628	-0.74086
C	3.89632	-0.58265	-0.70540
C	3.86252	1.69676	-1.50397
C	5.09553	-0.78098	-1.40723
C	5.04737	1.48199	-2.20947
H	3.40201	2.67523	-1.55238
C	5.66953	0.23840	-2.16045
H	5.56704	-1.75486	-1.35649
H	5.47809	2.29239	-2.79043
H	6.59314	0.05879	-2.70247
C	1.46035	2.88545	-0.10978
C	1.88052	3.85276	0.81550
C	0.79821	3.30962	-1.27691
C	1.64651	5.20956	0.58000
H	2.38792	3.54962	1.72503
C	0.57670	4.66652	-1.51495
H	0.46391	2.57141	-2.00126
C	0.99666	5.62014	-0.58476

H	1.97513	5.94533	1.30902
H	0.07133	4.97649	-2.42539
H	0.81738	6.67628	-0.76636
C	2.11357	0.94628	1.92939
C	1.09670	0.71566	2.86822
C	3.43071	1.11530	2.38280
C	1.39418	0.65576	4.23073
H	0.07383	0.58234	2.53265
C	3.72526	1.05101	3.74602
H	4.23069	1.29158	1.67062
C	2.70783	0.82074	4.67351
H	0.59728	0.47320	4.94653
H	4.75069	1.18027	4.08129
H	2.93791	0.76894	5.73406
C	3.35886	-1.72958	0.04713
C	3.51835	-3.75130	1.01701
C	2.09065	-3.15861	1.18014
H	3.54342	-4.72346	0.51861
H	4.06327	-3.82331	1.96390
H	1.84513	-3.03742	2.24265
N	2.20221	-1.81949	0.57876
O	4.20596	-2.79787	0.17635
C	0.95623	-3.98929	0.53189
C	0.76643	-5.31746	1.28129
H	0.59483	-5.15706	2.35217
H	-0.09519	-5.86315	0.88347
H	1.63932	-5.97425	1.17753
C	1.14966	-4.20648	-0.97471
H	1.20867	-3.25471	-1.50952
H	2.05334	-4.78842	-1.19491
H	0.30153	-4.76511	-1.38502
H	0.04577	-3.39589	0.66434
Pd	-0.48473	0.11815	-0.65616
C	-4.77736	-0.22015	-0.34876

C	-5.73370	-0.85827	-1.12242
C	-5.13449	0.89326	0.42802
C	-7.04551	-0.36042	-1.11971
H	-5.47051	-1.72515	-1.71950
C	-6.42584	1.39976	0.44786
C	-7.38312	0.74970	-0.34478
H	-7.80415	-0.84476	-1.72631
H	-6.69232	2.26139	1.05102
H	-8.40321	1.12151	-0.35249
N	-3.99239	1.38729	1.10941
C	-3.94677	2.61129	1.89003
H	-2.90952	2.78585	2.17642
H	-4.30680	3.45585	1.29393
H	-4.56443	2.51581	2.78831
C	-2.89889	0.65676	0.78042
O	-1.72181	0.92586	1.07745
C	-3.29999	-0.50402	-0.12956
C	-3.14805	-1.82505	0.64211
F	-3.52430	-2.86779	-0.12500
F	-3.91857	-1.83792	1.75430
F	-1.88152	-2.05127	1.04518
C	-2.35223	-0.45926	-1.35151
H	-2.67074	0.32503	-2.04226
H	-2.32027	-1.41289	-1.87792
Br	0.41098	-0.53042	-2.93587

10. X-ray Structural Analysis:

Crystal Growth of Compound 7b:



A saturated solution of **7b** in DCM was kept at room temperature to obtain crystals. Colorless crystals were observed after DCM evaporation. A suitable crystal was selected and visualized on a Bruker APEX−II CCD diffractometer. The crystal was kept at 298.00 K during data collection. Using Olex2, the structure was solved with the olex2.solve structure solution program using Charge Flipping and refined with the olex2.refine refinement package using Gauss−Newton minimization. The crystal structure was drawn on diamond−3 software.

Crystal Structure of Compound 7b:

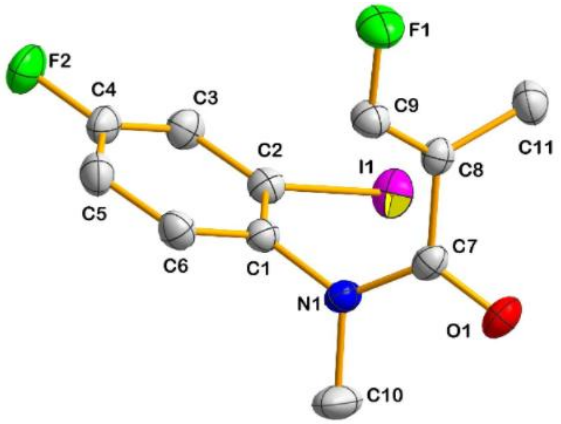


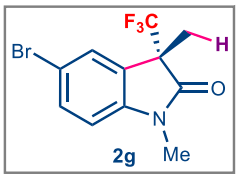
Figure S53. Crystal Structure of compound **7b**. The ellipsoid contour has been drawn at 25% probability levels.

Table S8: Crystal data and structure refinement for 7b:

Empirical formula	**$C_{11}H_{10}F_2INO$**
CCDC	**2384466**
Formula weight	337.11
Temperature/K	298.00
Crystal system	monoclinic
Space group	C2/c
a/Å	20.4768(11)
b/Å	11.5083(6)
c/Å	14.1850(8)

α/°	90
β/°	132.601(1)
γ/°	90
Volume/Å^3	2460.5(2)
Z	8
ρ_{calc}(g/cm^3)	1.820
μ/mm^{-1}	2.607
F(000)	1293.7
Crystal size/mm^3	0.015 × 0.014 × 0.012
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.46 to 55.42
Index ranges	-26 ≤ h ≤ 26, -15 ≤ k ≤ 15, -18 ≤ l ≤ 18
Reflections collected	25756
Independent reflections	2895 [R_{int} = 0.0368, R_{sigma} = 0.0192]
Data/restraints/parameters	2895/0/147
Goodness−of−fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0285, wR_2 = 0.0622
Final R indexes [all data]	R_1 = 0.0398, wR_2 = 0.0682
Largest diff. peak/hole/ e Å^{-3}	0.77/-0.83

Crystal Growth of Compound 2g:



A saturated solution of **2g** in DCM was kept at room temperature to obtain crystals. Colorless crystals were observed after DCM evaporation. A suitable crystal was selected and visualized on a Bruker APEX−II CCD diffractometer. The crystal was kept at 295.00 K during data collection. Using Olex2, the structure was solved with the olex2.solve structure solution program using Charge Flipping and refined with the olex2.refine refinement package using Gauss−Newton minimization. The crystal structure was drawn on diamond−3 software.

Crystal Structure of Compound 2g:

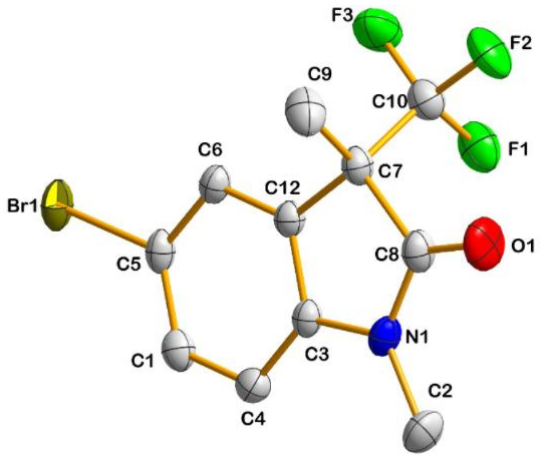


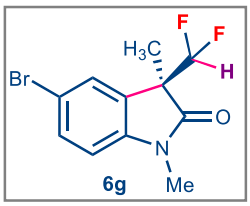
Figure S54. Crystal Structure of compound **2g**. The ellipsoid contour has been drawn at 25% probability levels.

Table S9: Crystal data and structure refinement for 2g:

Empirical formula	**$C_{11}H_9BrF_3NO$**
CCDC	**2384458**
Formula weight	308.10
Temperature/K	295.00
Crystal system	orthorhombic
Space group	$P2_1/ac$
a/Å	7.084(3)
b/Å	10.507(5)
c/Å	16.180(8)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1204.3(10)
Z	4
ρ_{calc}(g/cm^3)	1.699
μ/mm^{-1}	0.063
F(000)	608
Crystal size/mm^3	0.22 × 0.14 × 0.102
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.62 to 52.90
Index ranges	$-8 \le h \le 8, -13 \le k \le 13, -20 \le l \le 20$
Reflections collected	17814
Independent reflections	2419 [R_{int} = 0.0476, R_{sigma} = 0.0364]

Data/restraints/parameters	2419/0/156
Goodness−of−fit on F^2	1.028
Final R indexes [I>=2σ (I)]	R_1 = 0.0265, wR_2 = 0.0589
Final R indexes [all data]	R_1 = 0.0388, wR_2 = 0.0630
Largest diff. peak/hole/ e $Å^{-3}$	0.25/−0.32
Flack parameter	0.048(6)

Crystal Growth of Compound 6g:



A saturated solution of **6g** in DCM was kept at room temperature to obtain crystals. Colorless crystals were observed after DCM evaporation. A suitable crystal was selected and visualized on a Rigaku XtaLab Synergy Custom, X-Ray Diffractometer with RA-MicroMax 007HF Generator and HyPix 6000 Detector. The crystal was kept at 100.00 K during data collection. Using CrysAlisPro, the structure was solved and refined with the olex2.refine refinement package using Gauss−Newton minimization. The crystal structure was drawn on diamond−3 software.

Crystal Structure of compound 6g:

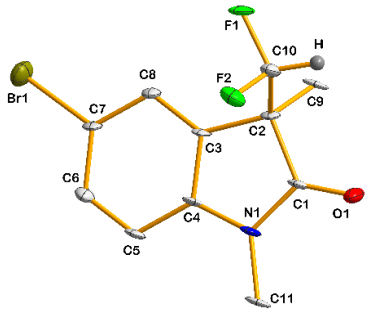


Figure S55. Crystal Structure of compound **6g**. The ellipsoid contour has been drawn at 50% probability levels.

Table S10: Crystal data and structure refinement for 6g:

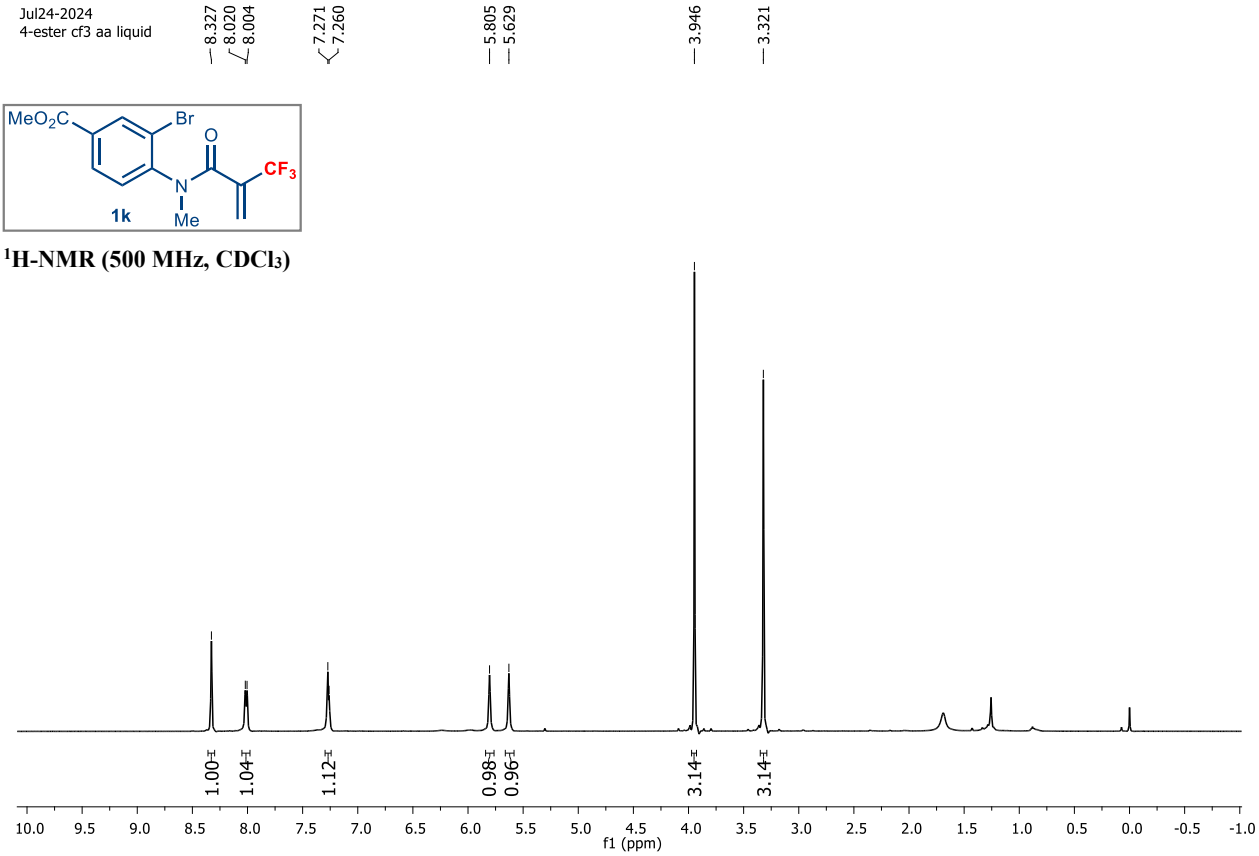
Empirical formula	**$C_{11}H_{10}BrF_2NO$**
CCDC	**2407321**
Formula weight	290.11
Temperature/K	100.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$

a/Å	7.2114(5)
b/Å	8.6463(5)
c/Å	17.6697(11)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1101.74(12)
Z	4
ρ_{calc}(g/cm^3)	1.749
μ/mm^{-1}	5.180
F(000)	576.0
Crystal size/mm^3	0.192 × 0.134 × 0.094
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	5.006 to 81.420
Index ranges	-8 ≤ h ≤ 9, -10 ≤ k ≤ 4, -22 ≤ l ≤ 22
Reflections collected	4283
Independent reflections	2105 [Rint = 0.0800, Rsigma = 0.0658]
Data/restraints/parameters	2105/0/129
Goodness−of−fit on F^2	1.171
Final R indexes [I > 4σ (I)]	R_1 = 0.0649, wR_2 = 0.1874
Final R indexes [all data]	R_1 = 0.0680, wR_2 = 0.1857
Largest diff. peak/hole/ e Å^{-3}	1.366/-1.443
Flack parameter	0.02(5)

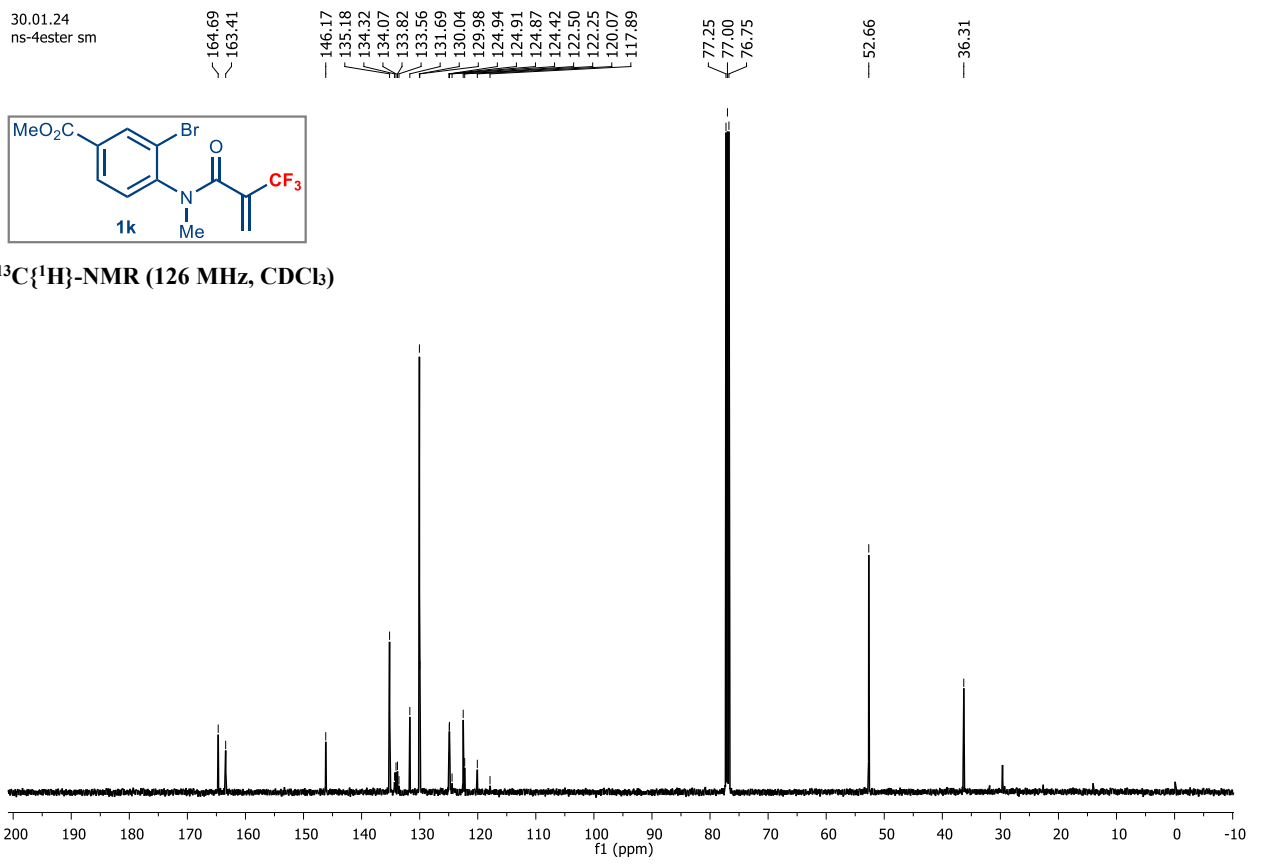
11. References:

1. Bai, X.; Wu, C.; Ge, S.; Lu, Y. *Angew. Chem. Int. Ed.* **2020**, *59*, 2764–2768.
2. (a) Sharma, R.; Sihag, N.; Bhartiya, H.; Saini, S.; Kumar, A.; Yadav, M. R. *Org. Chem. Front*. **2024**, *11*, 1736−1741. (b) Dong, W.; Liu, Y.; Hu, B.; Ren, K.; Li, Y.; Xie, X.; Jiang, Y.; Zhang, Z. *Chem. Commun.* **2015**, *51*, 4587−4590. (c) Seashore-Ludlow, B.; Somfai, P. *Org. Lett.* **2012**, *14*, 3858–3861.
3. Xiao, P.; Pannecoucke, X.; Bouillon, J.P.; Couve-Bonnaire, S. *Adv. Synth. Catal*. **2020**, *362,* 949–954.
4. Li, Y.; Sun, G.; He, X.; Lv, H.; Gao, B. *J. Fluor. Chem.* **2023**, *268*, 110115.

5. (a) Kilaru, P.; Acharya, S.P.; Zhao, P. *Chem. Commun*. **2018**, *54*, 924−927. (b) Liu, Z.; Zhong, S.; Ji, X.; Deng, G.J.; Huang, H. *ACS Catal.* **2021**, *11*, 4422−4429.
6. Shaw, R.; Sihag, N.; Jain, S.; Sharma, R.; Yadav, M. R. *J. Org. Chem.* **2023**, *88*, 5652−5660.
7. (a) Giraldo, J. J. A.; Lindsay, A. C.; Seo, R. C.-Y.; Kilmartina, P. A.; Sperry, J. *Org. Biomol. Chem.* **2023**, *21*, 5609−5615. (b) Tang, S.; Peng, P.; Zhong, P.; Li, J.-H. *J. Org. Chem.* **2008**, *73*, 5476–5480.
8. Becke A. D. *J. Chem. Phys.* **1993**, *98*, 5648.
9. Dunning Jr., T. H; Hay, P. J. in Modern Theoretical Chemistry, Ed. H. F. Schaefer III, Vol. 3 (Plenum, New York, 1977) 1–28.
10. Ditchfield, R.; Hehre, W. J.; Pople J. A. *J. Chem. Phys.* **1971**, *54*, 724.
11. Gaussian 09, Revision E. 01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.;Robb, M. A. ; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, Jr. J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; 57 Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, A. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D.-J.; Gaussian, Inc., Wallingford CT, 2016.

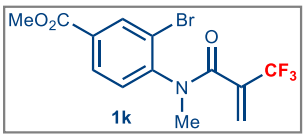


^{1}H-NMR (500 MHz, $CDCl_3$)

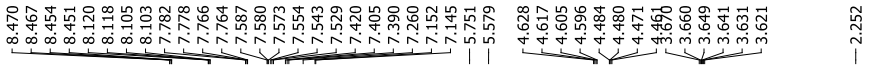


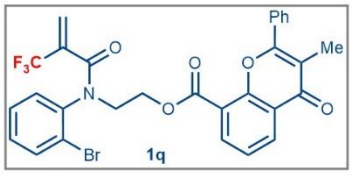
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-4-ester SM
19F

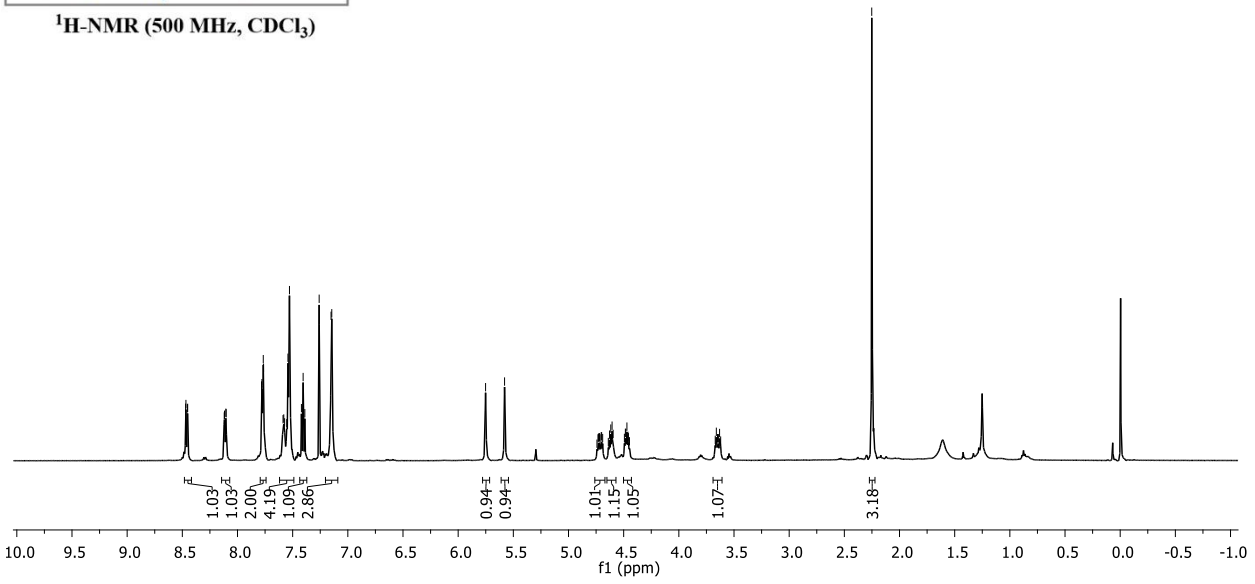


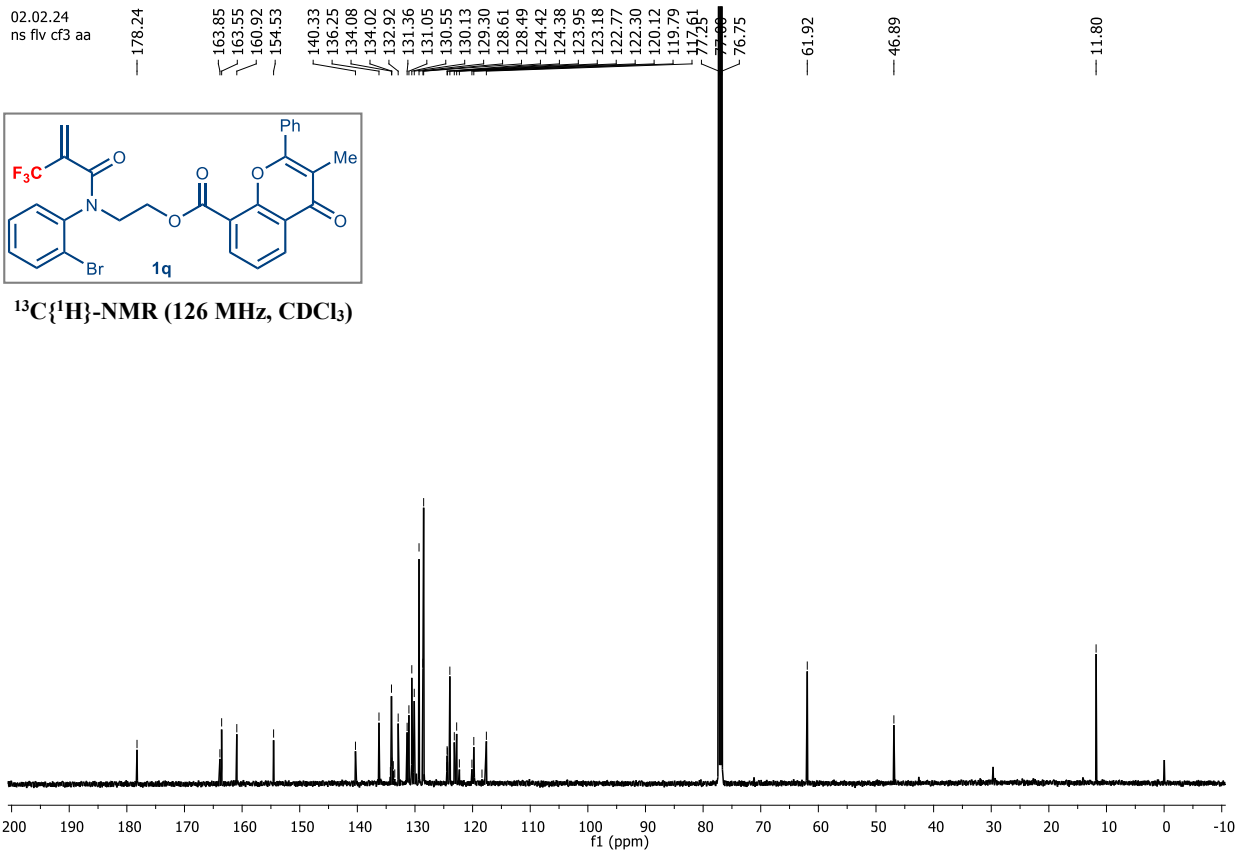
^{19}F-NMR (377 MHz, $CDCl_3$)



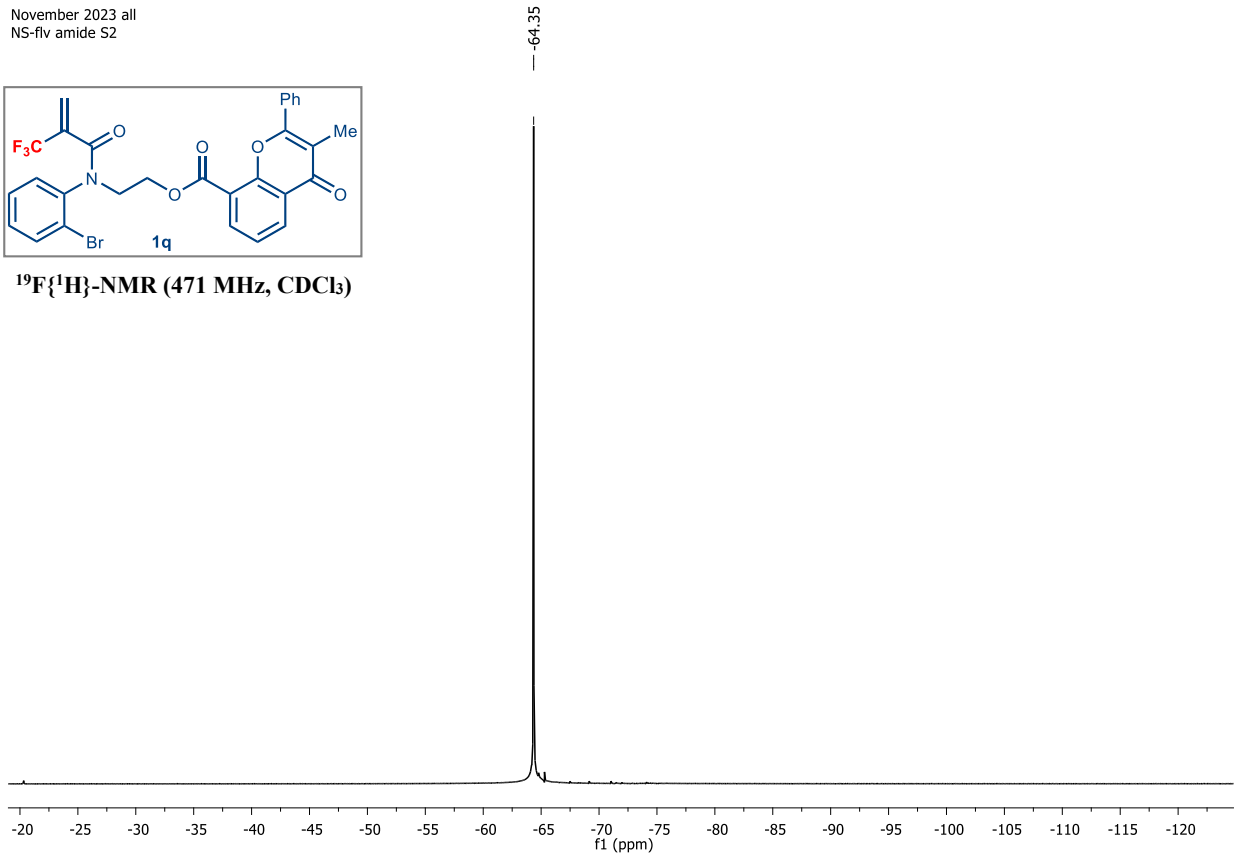


^{1}H-NMR (500 MHz, $CDCl_3$)

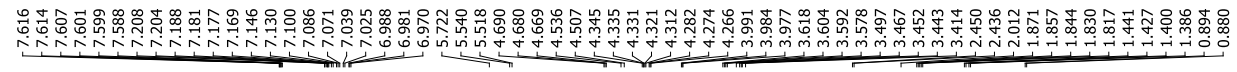


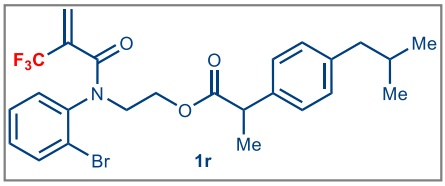


$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)

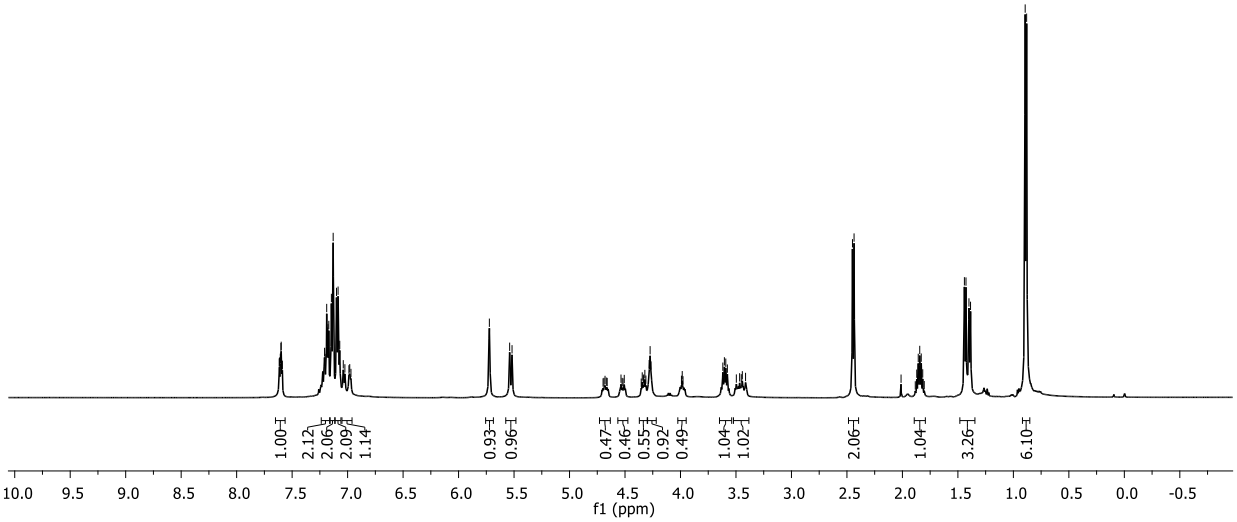


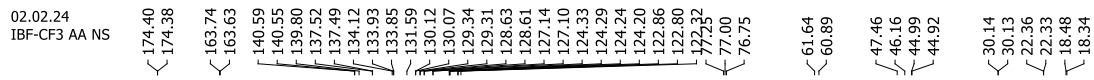
$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

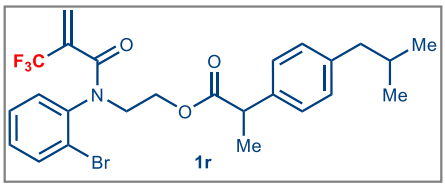




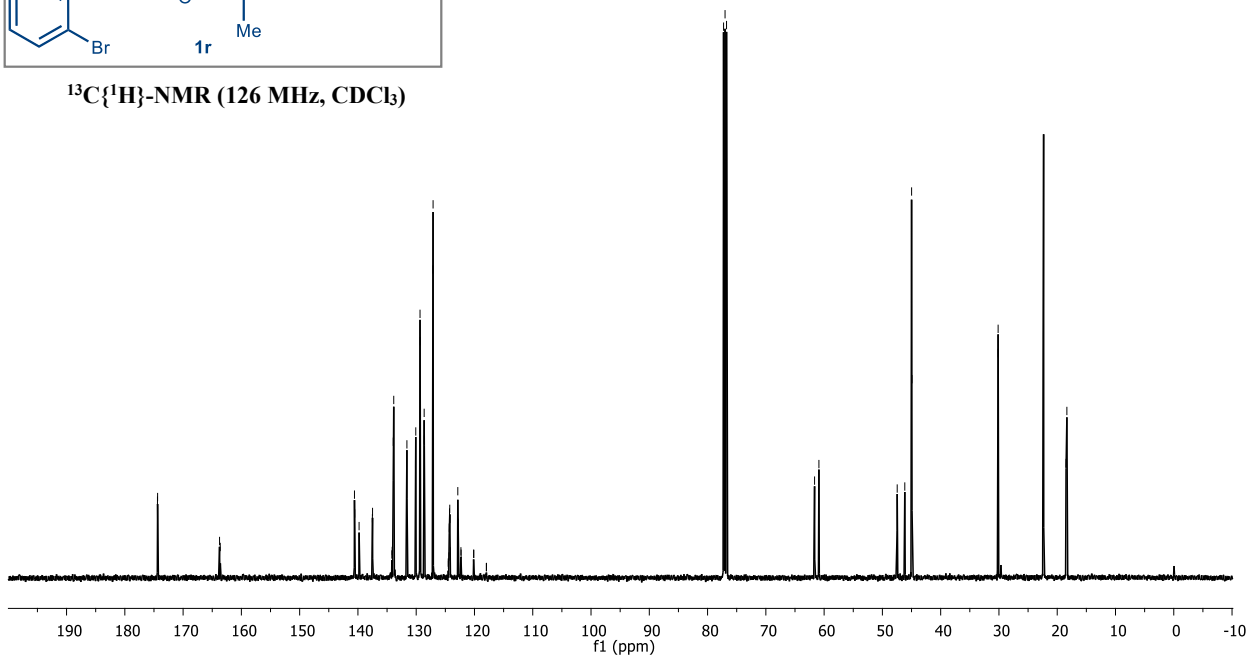
^{1}H-NMR (500 MHz, $CDCl_3$)



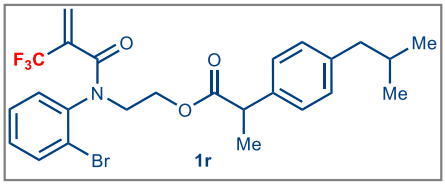




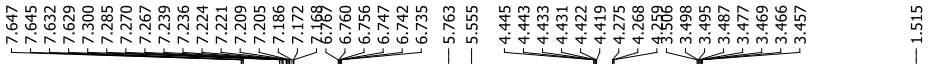
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

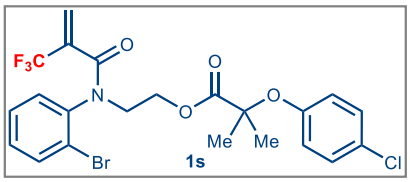


November 2023 all
NS-ibf amide P

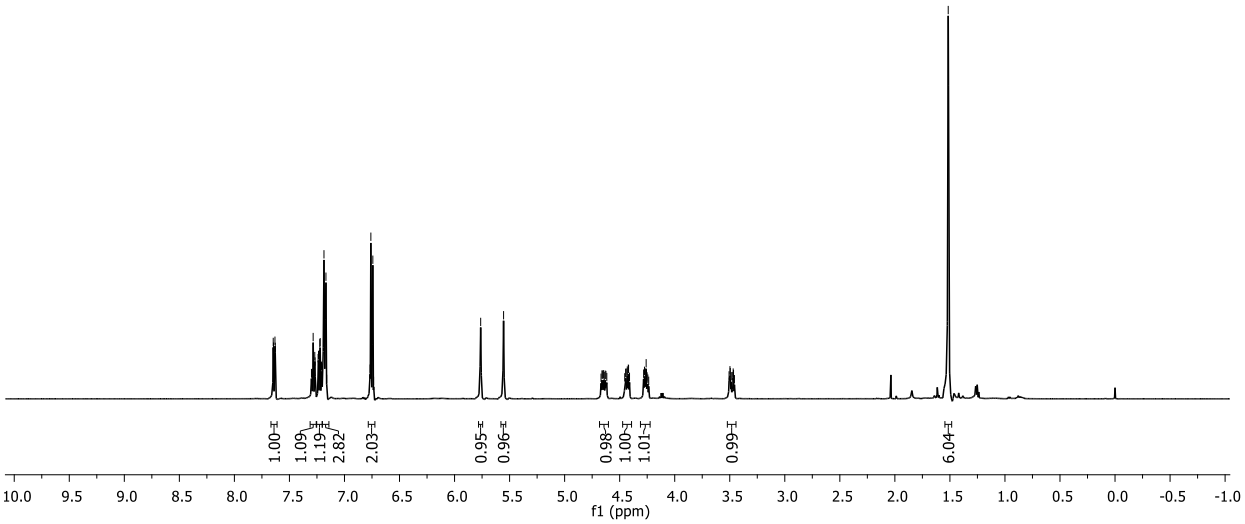


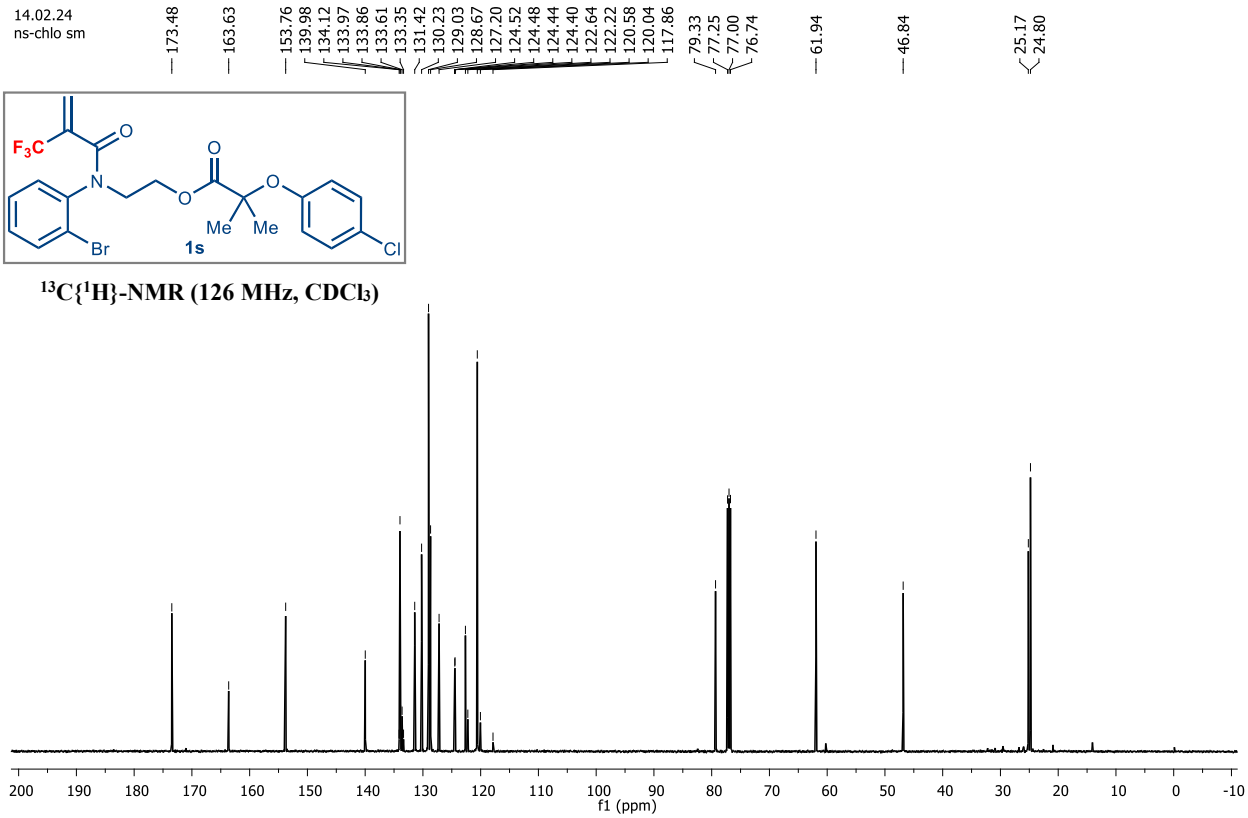
$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)



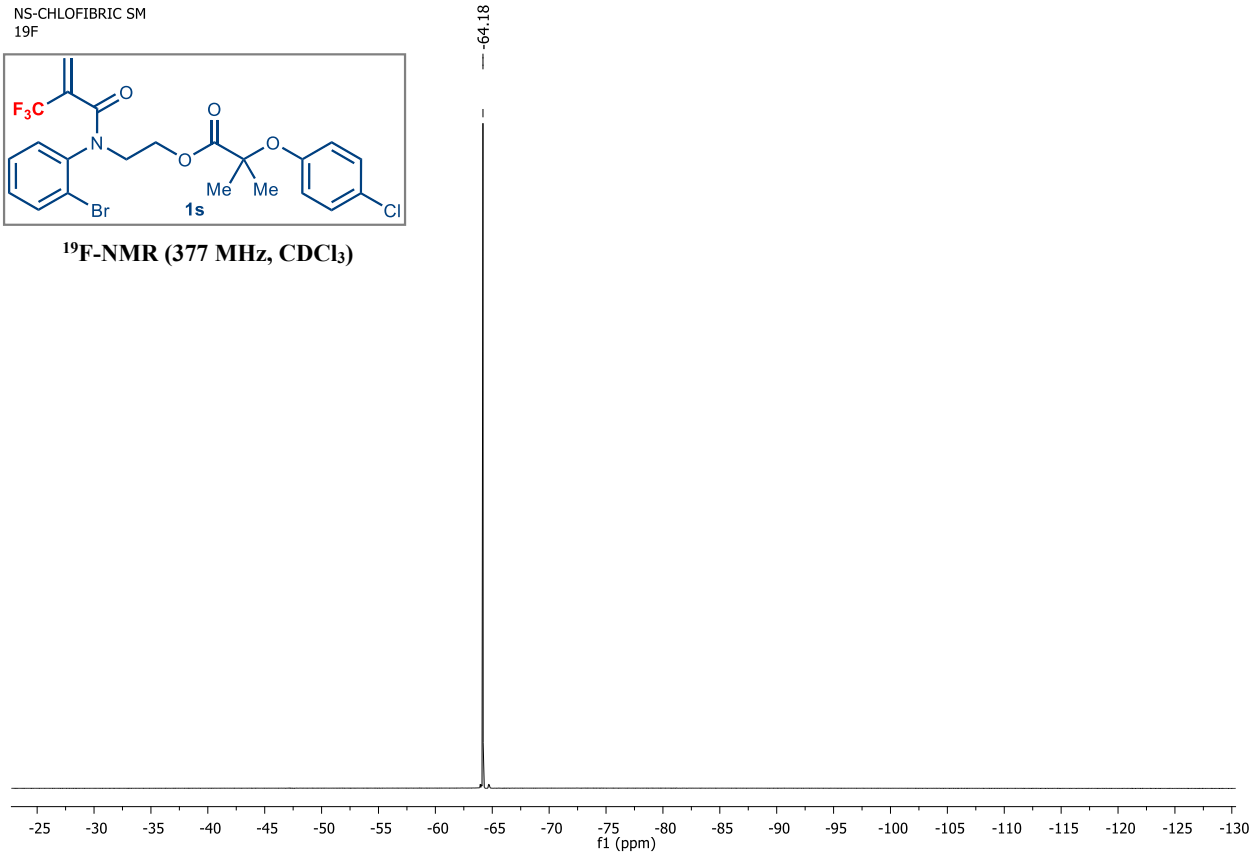


^{1}H-NMR (500 MHz, $CDCl_3$)

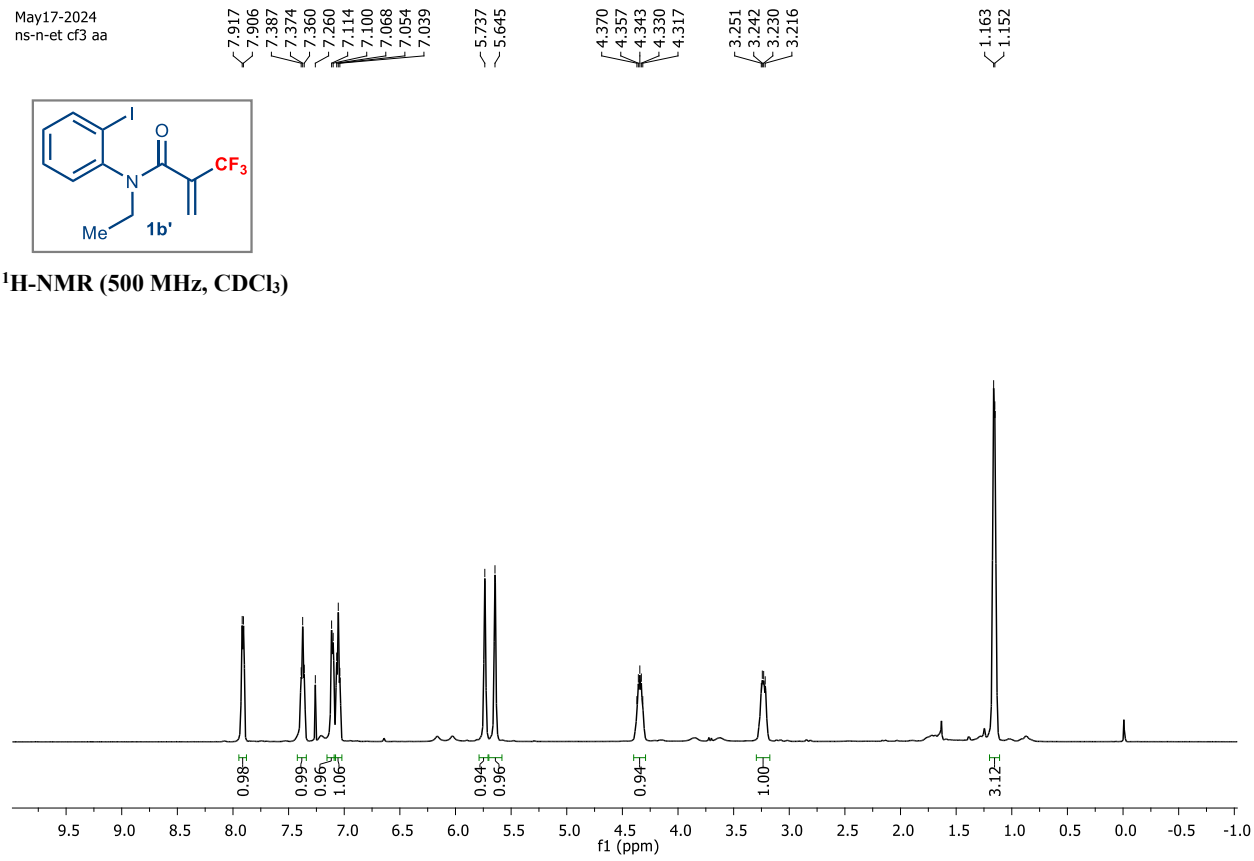




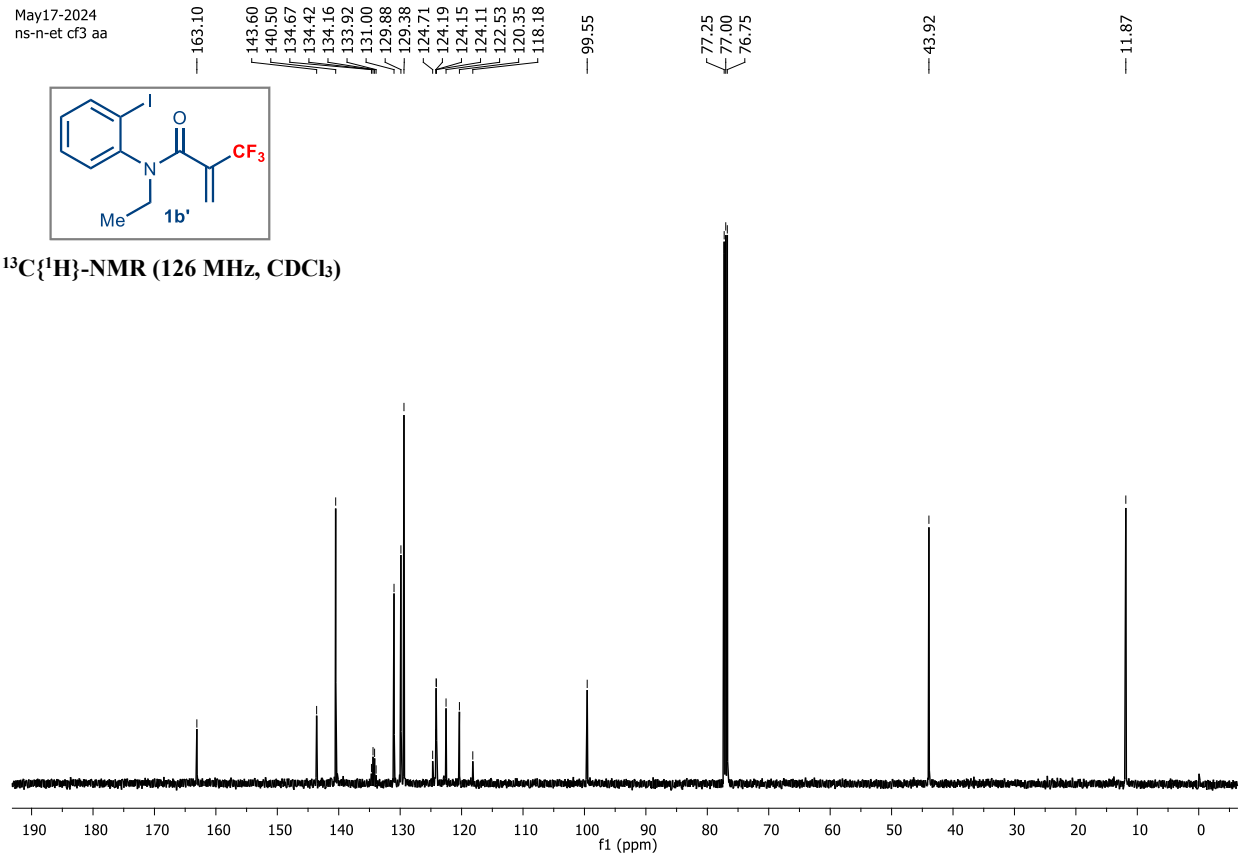
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

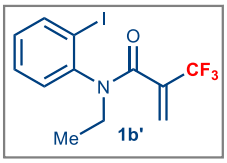


^{1}H-NMR (500 MHz, $CDCl_3$)



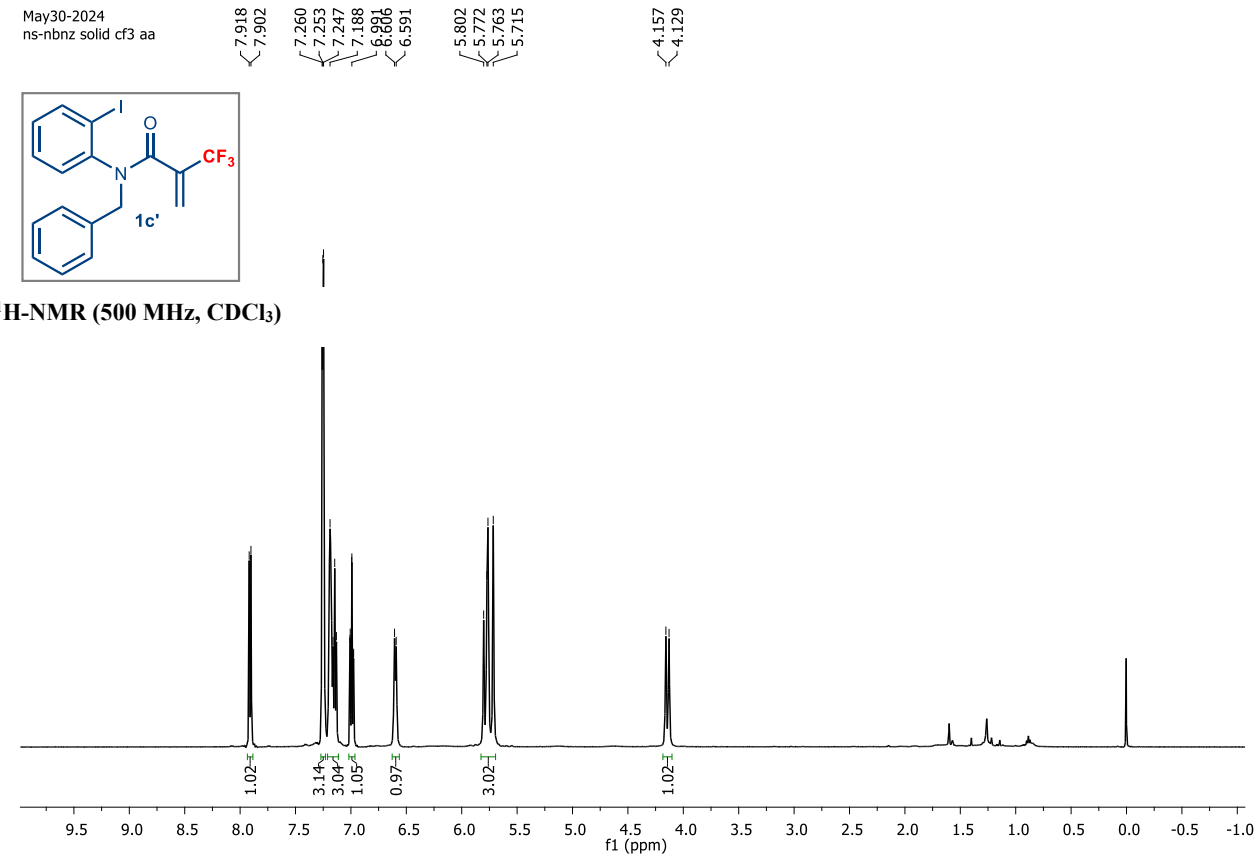
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-N-ET
19F



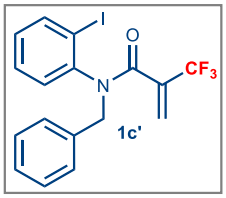
^{19}F-NMR (377 MHz, $CDCl_3$)

May30-2024
ns-nbnz solid cf3 aa



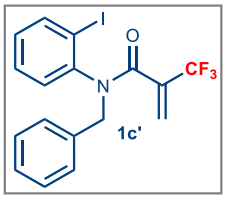
^{1}H-NMR (500 MHz, $CDCl_3$)

May30-2024
ns-nbnz solid cf3 aa

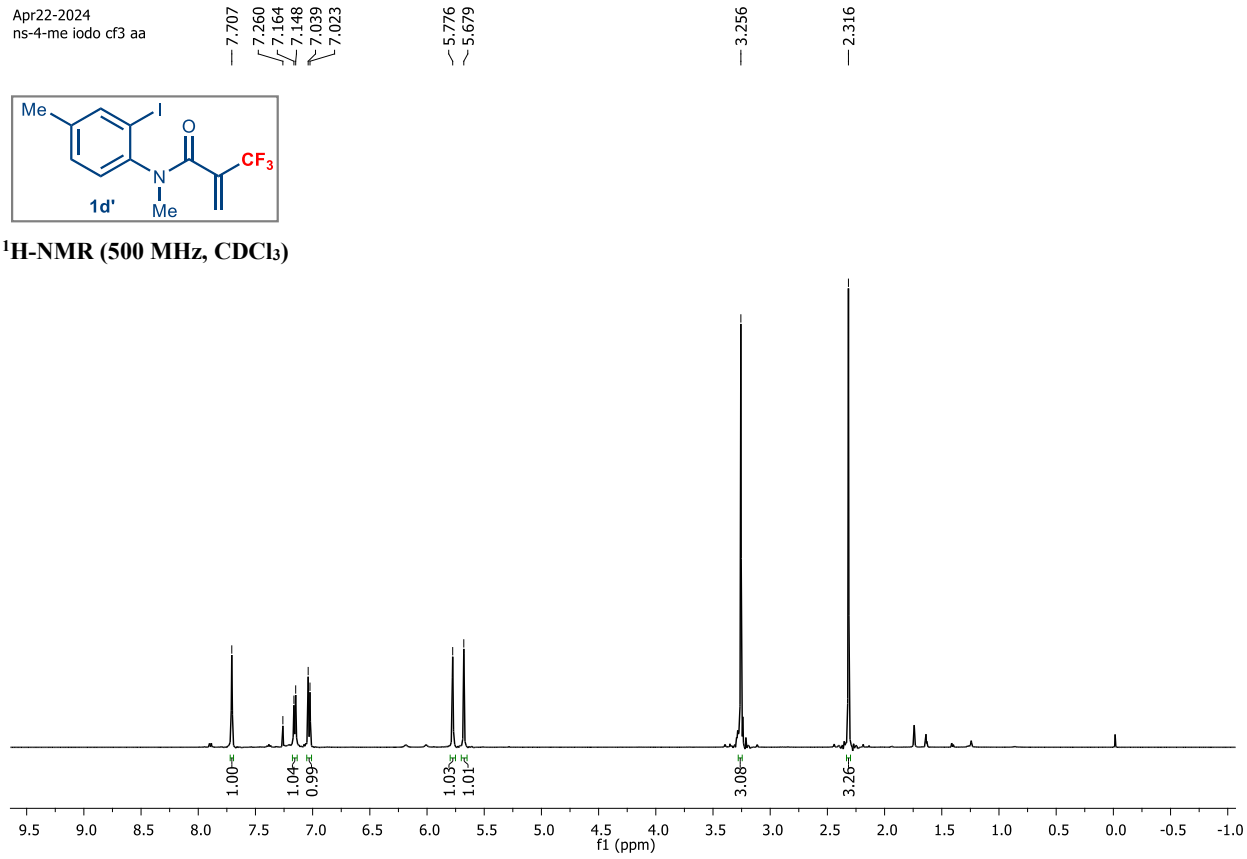


$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)

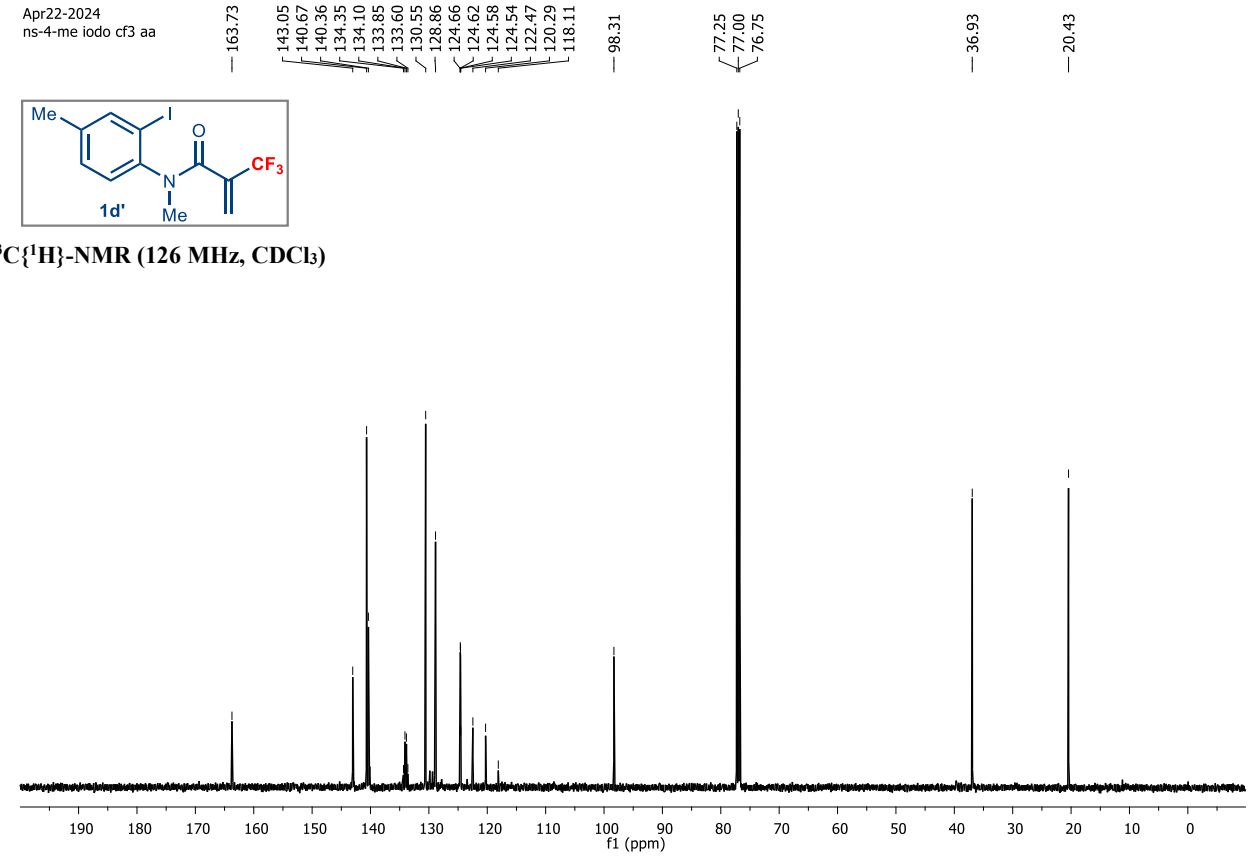
NS-BNZ O-I AMIDE
19F



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

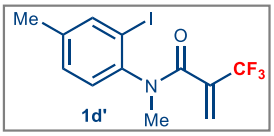


^{1}H-NMR (500 MHz, $CDCl_3$)



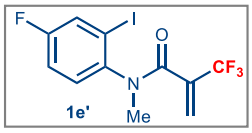
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

4-Me

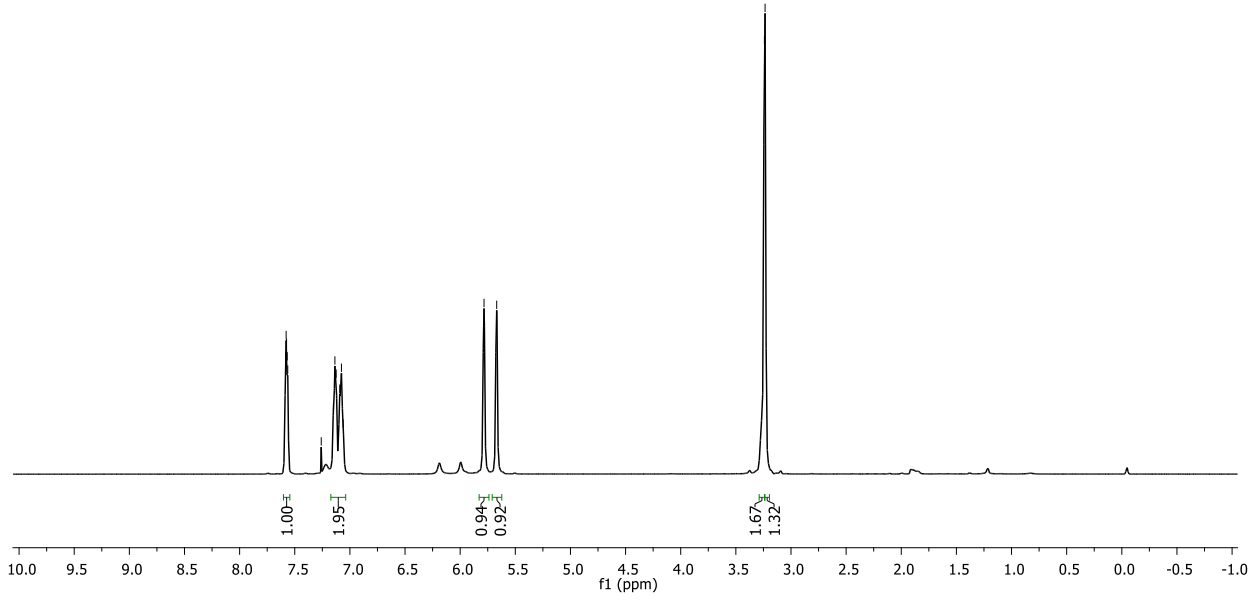


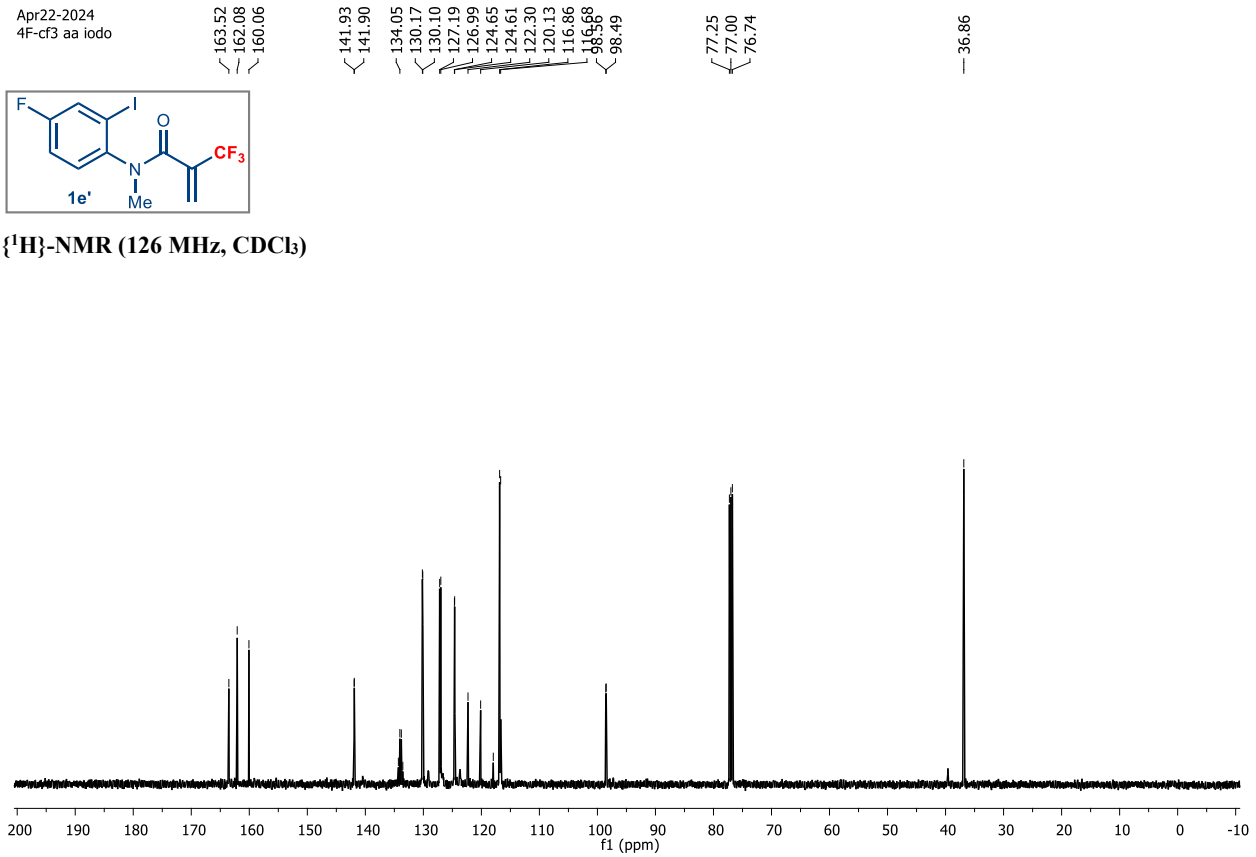
^{19}F-NMR (377 MHz, $CDCl_3$)

Apr22-2024
4F-cf3 aa iodo

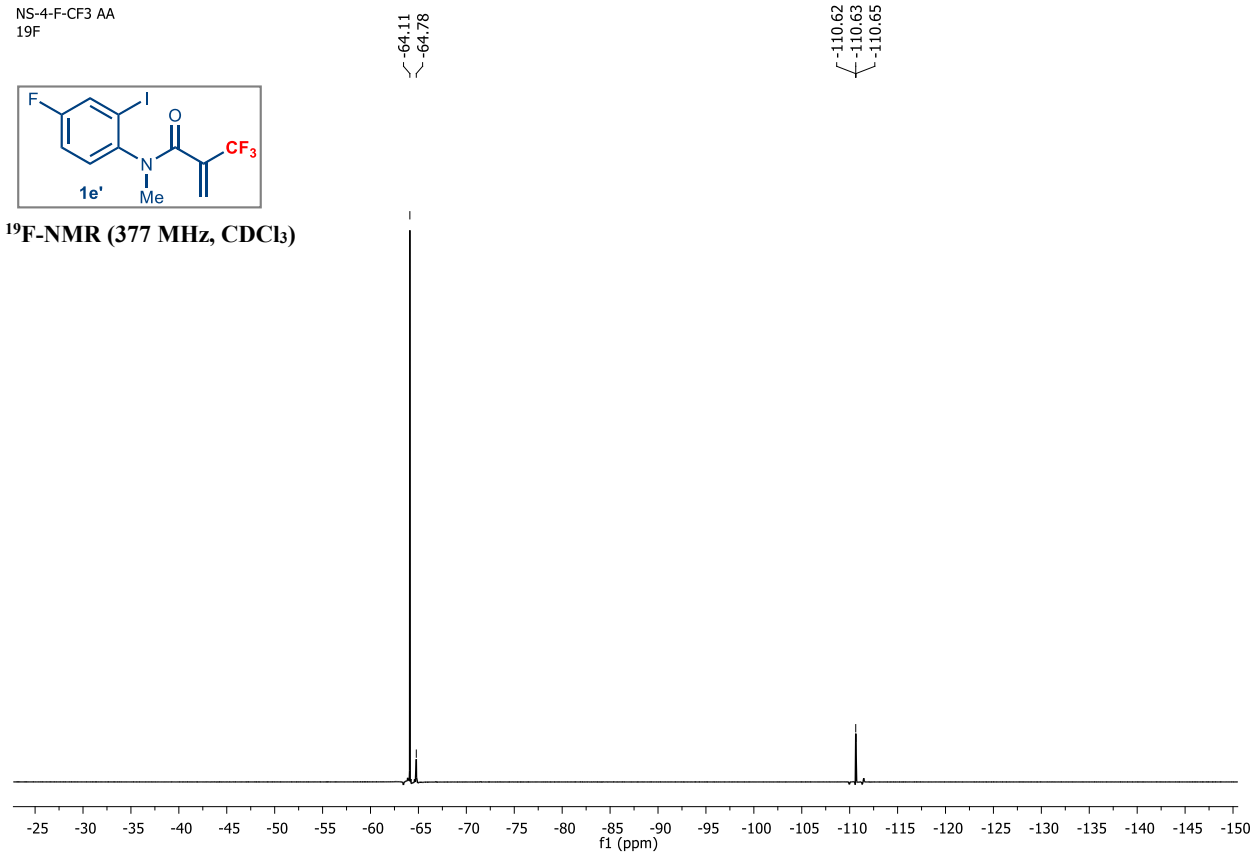


^{1}H-NMR (500 MHz, $CDCl_3$)

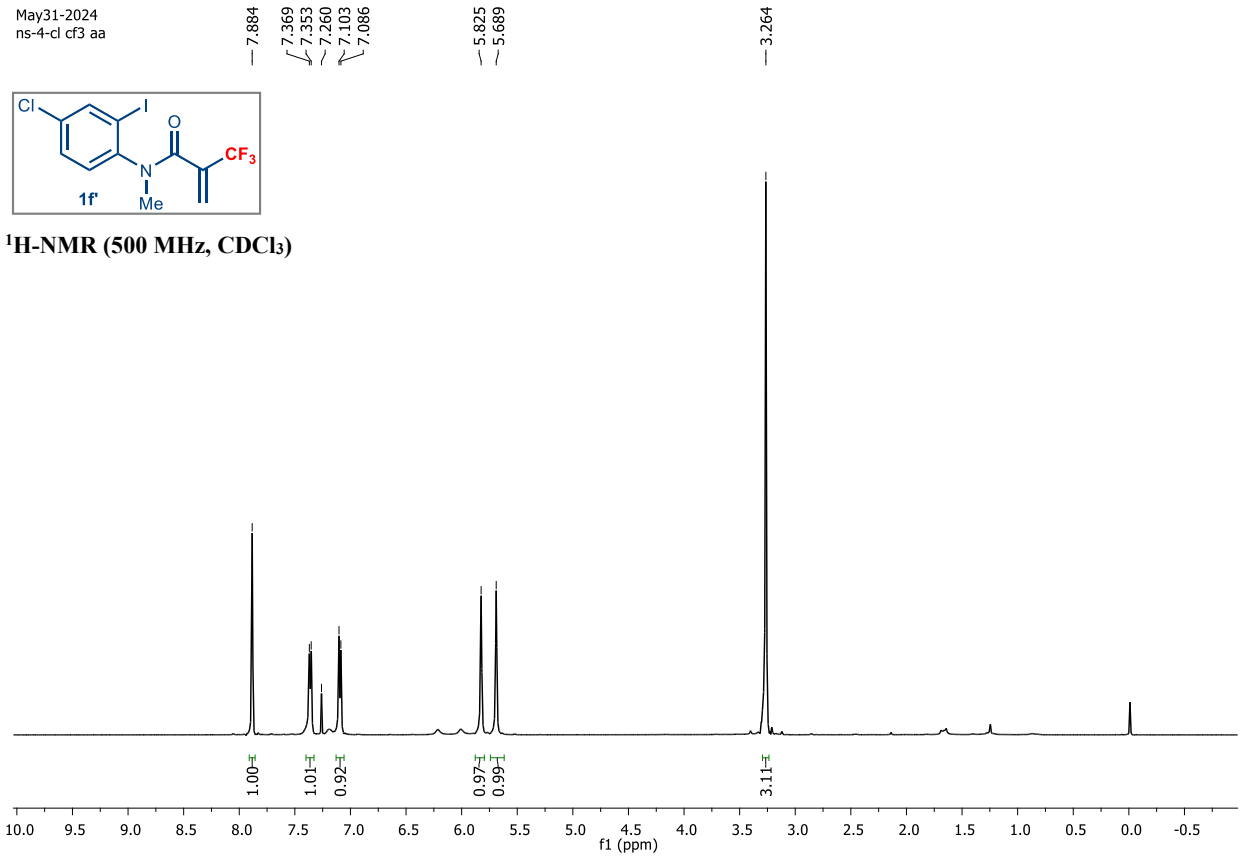




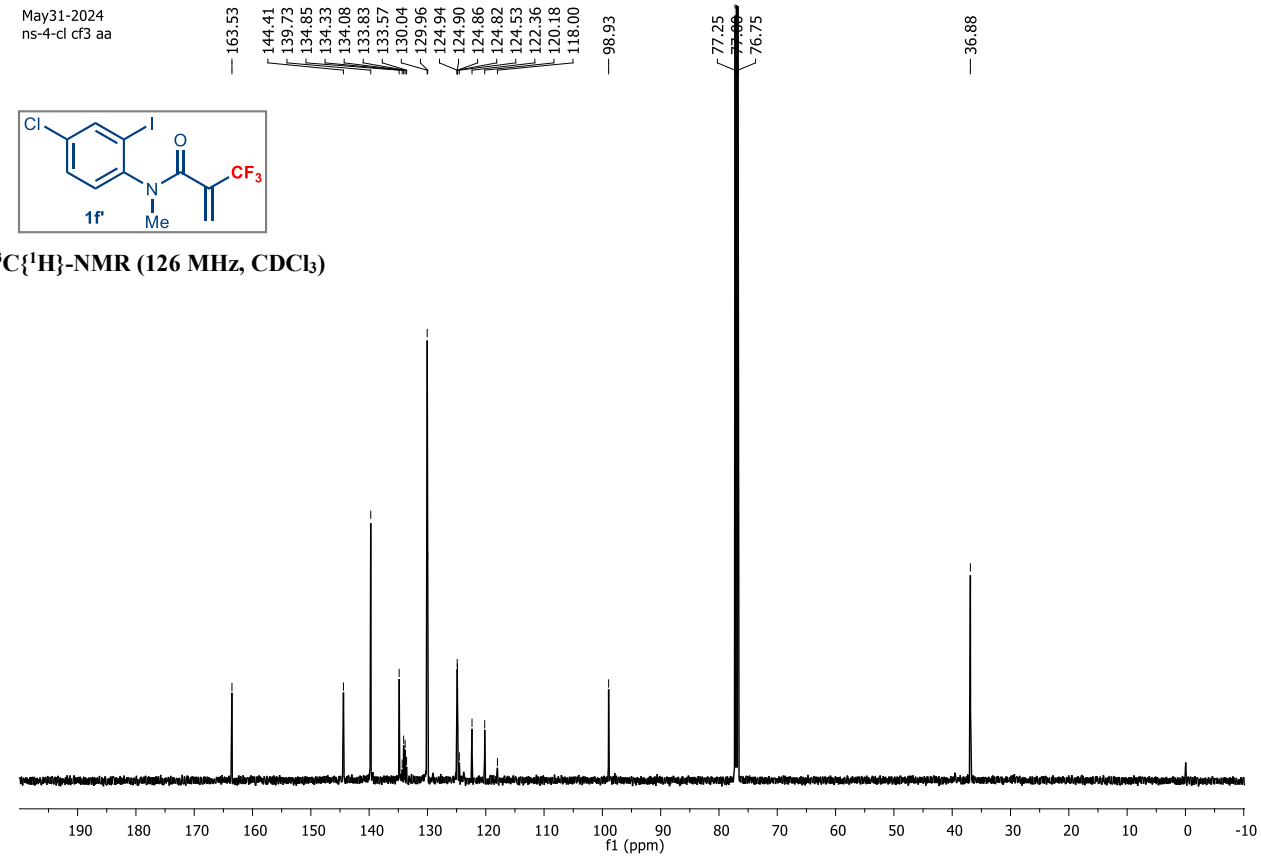
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



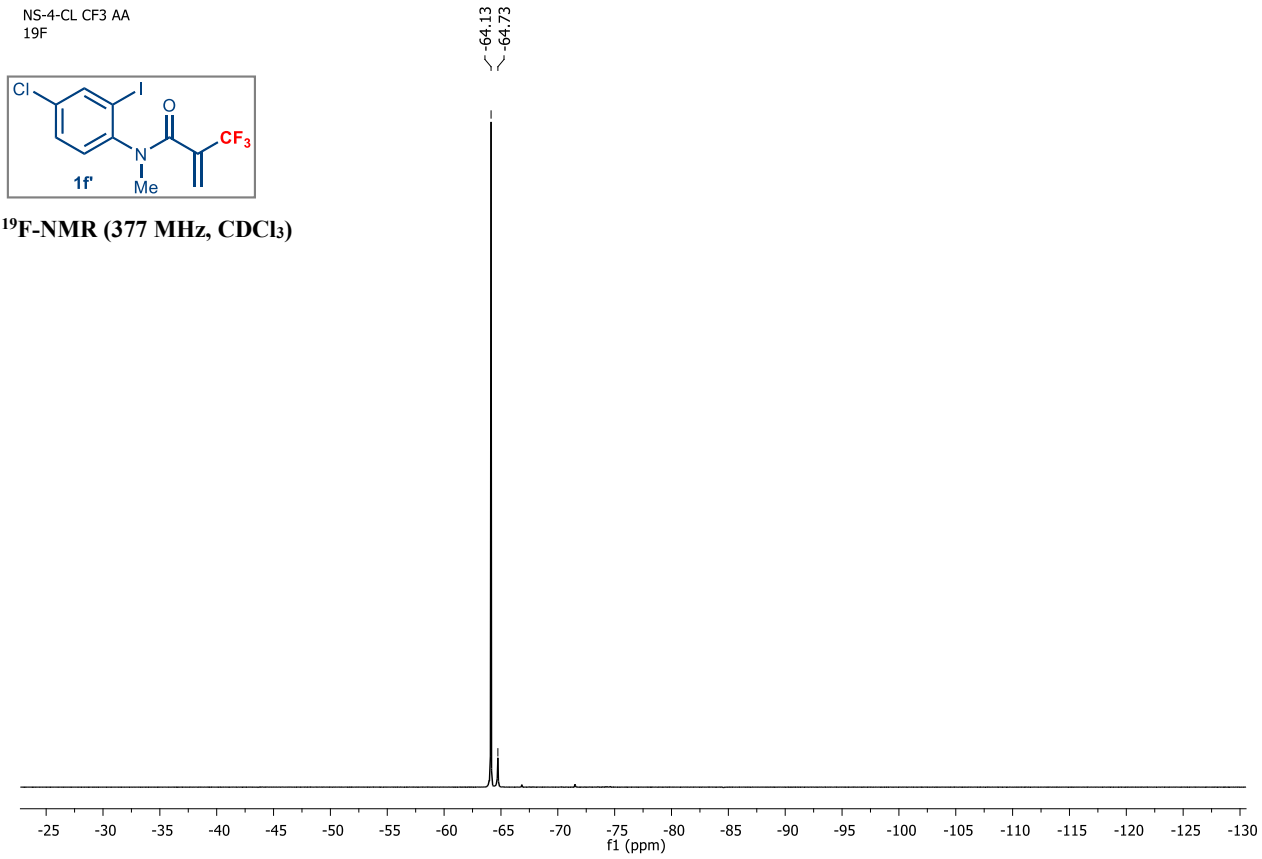
^{19}F-NMR (377 MHz, $CDCl_3$)



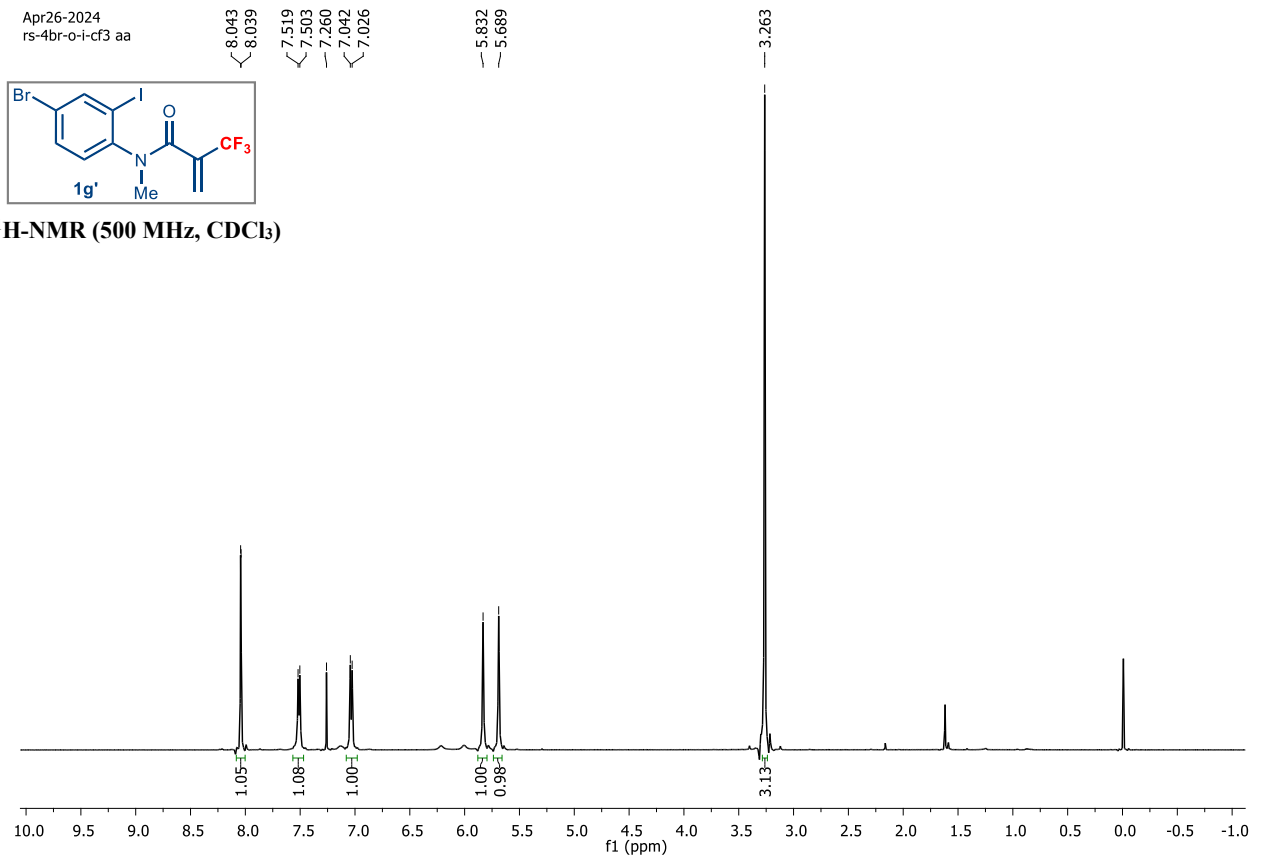
^{1}H-NMR (500 MHz, $CDCl_3$)



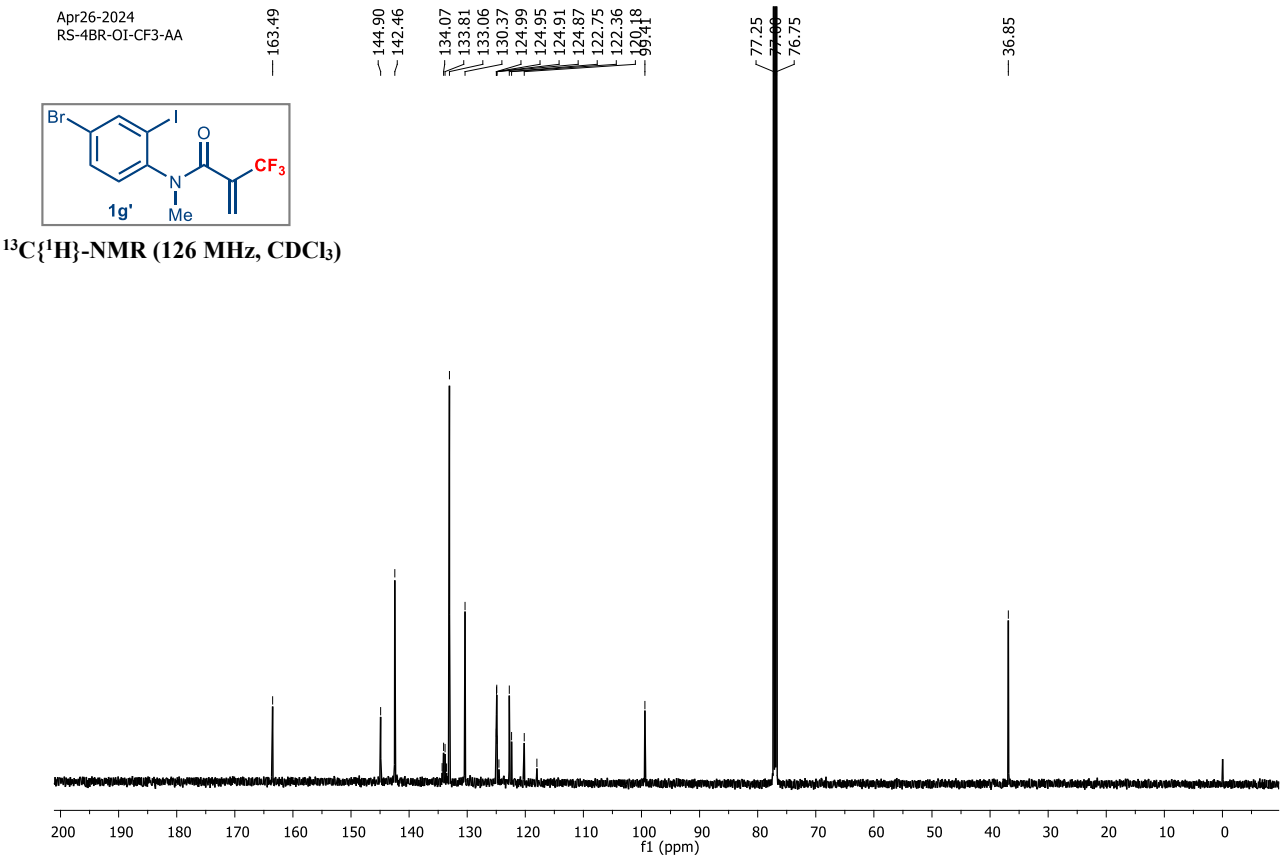
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)



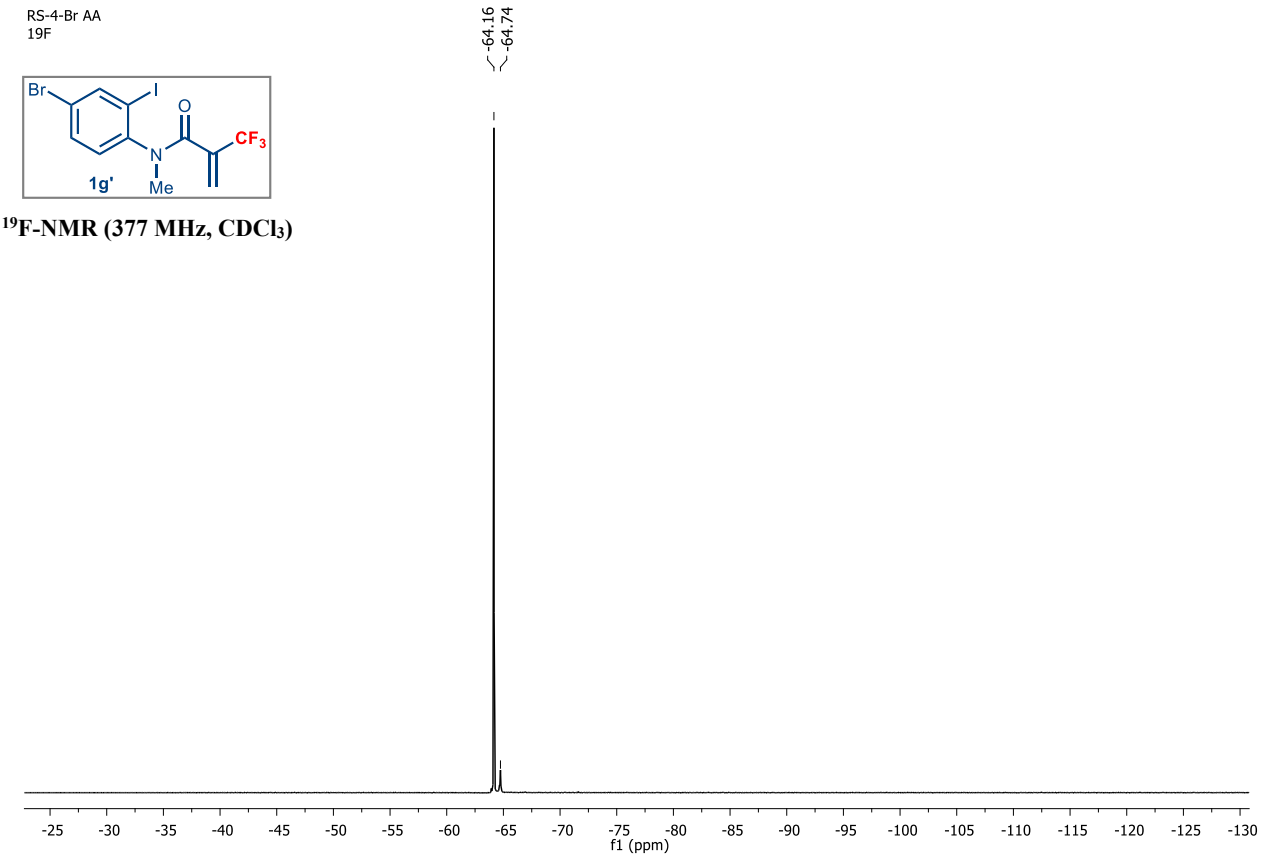
^{19}F-NMR (377 MHz, $CDCl_3$)



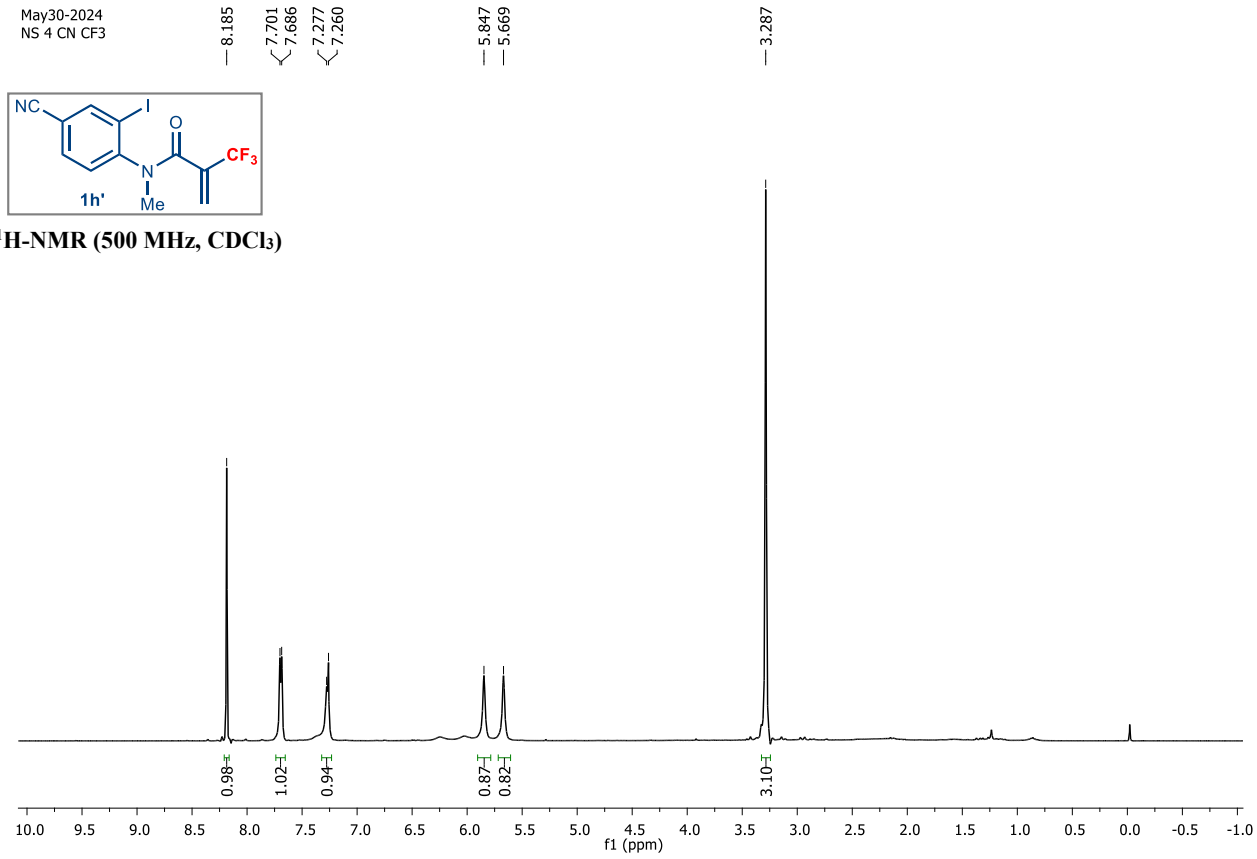
^{1}H-NMR (500 MHz, $CDCl_3$)



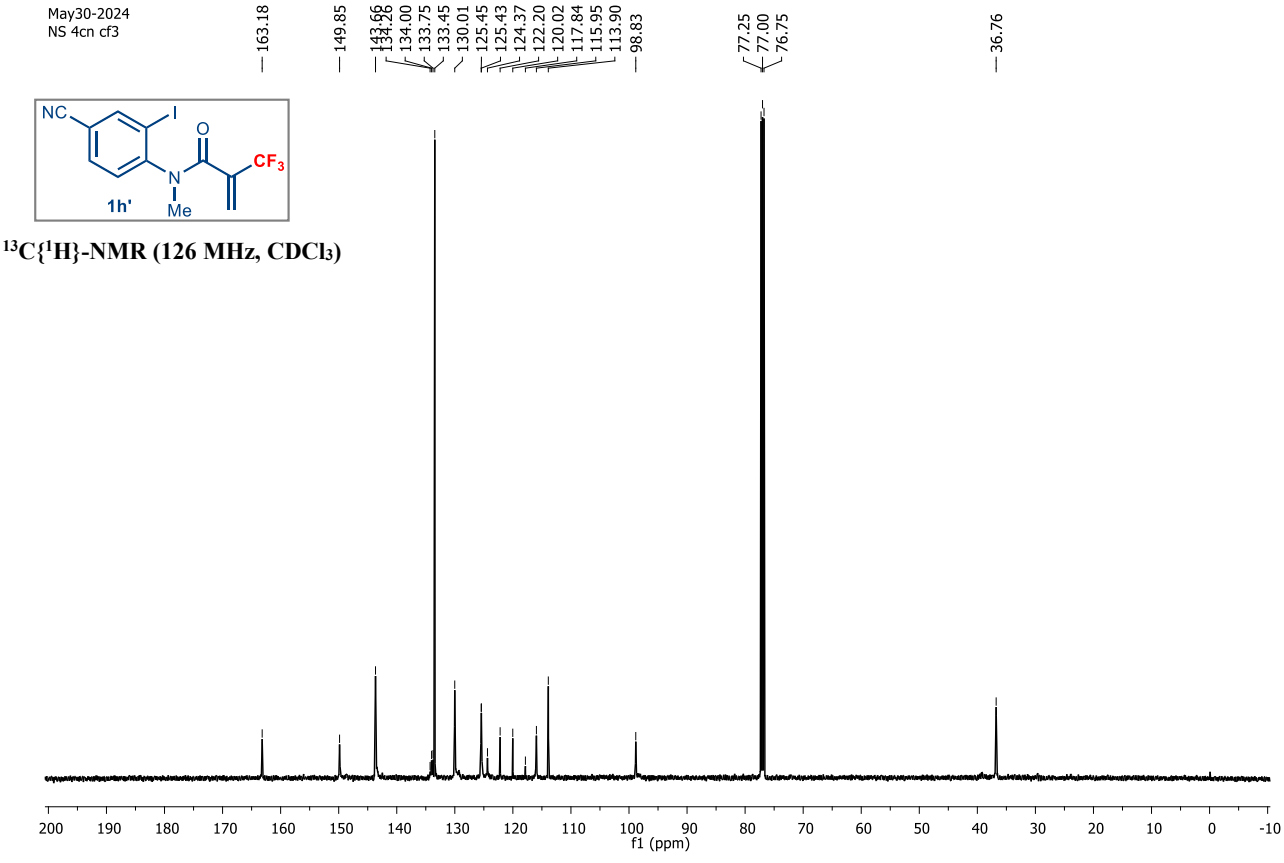
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

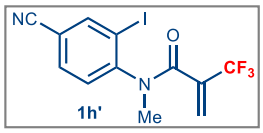


^{1}H-NMR (500 MHz, $CDCl_3$)



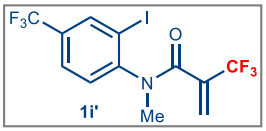
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS 4 CN

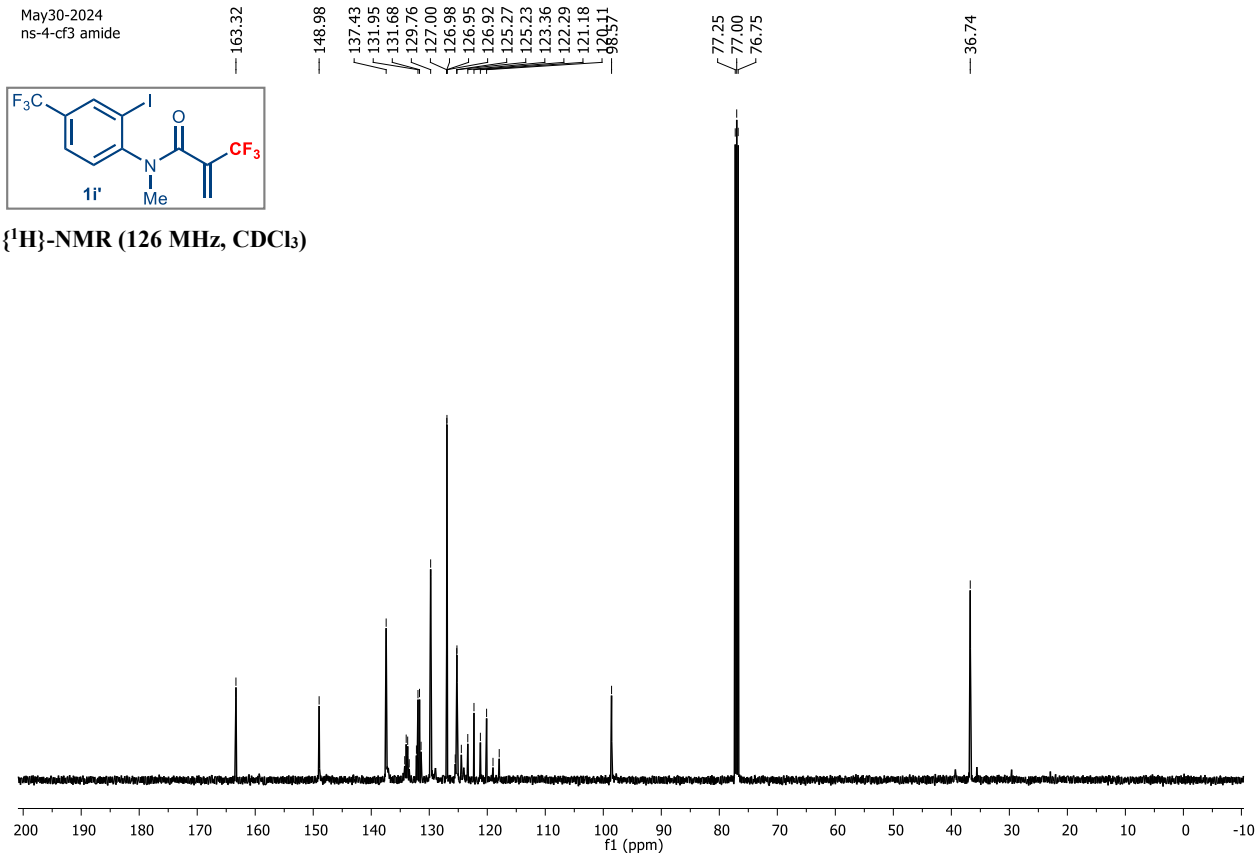


^{19}F-NMR (377 MHz, $CDCl_3$)

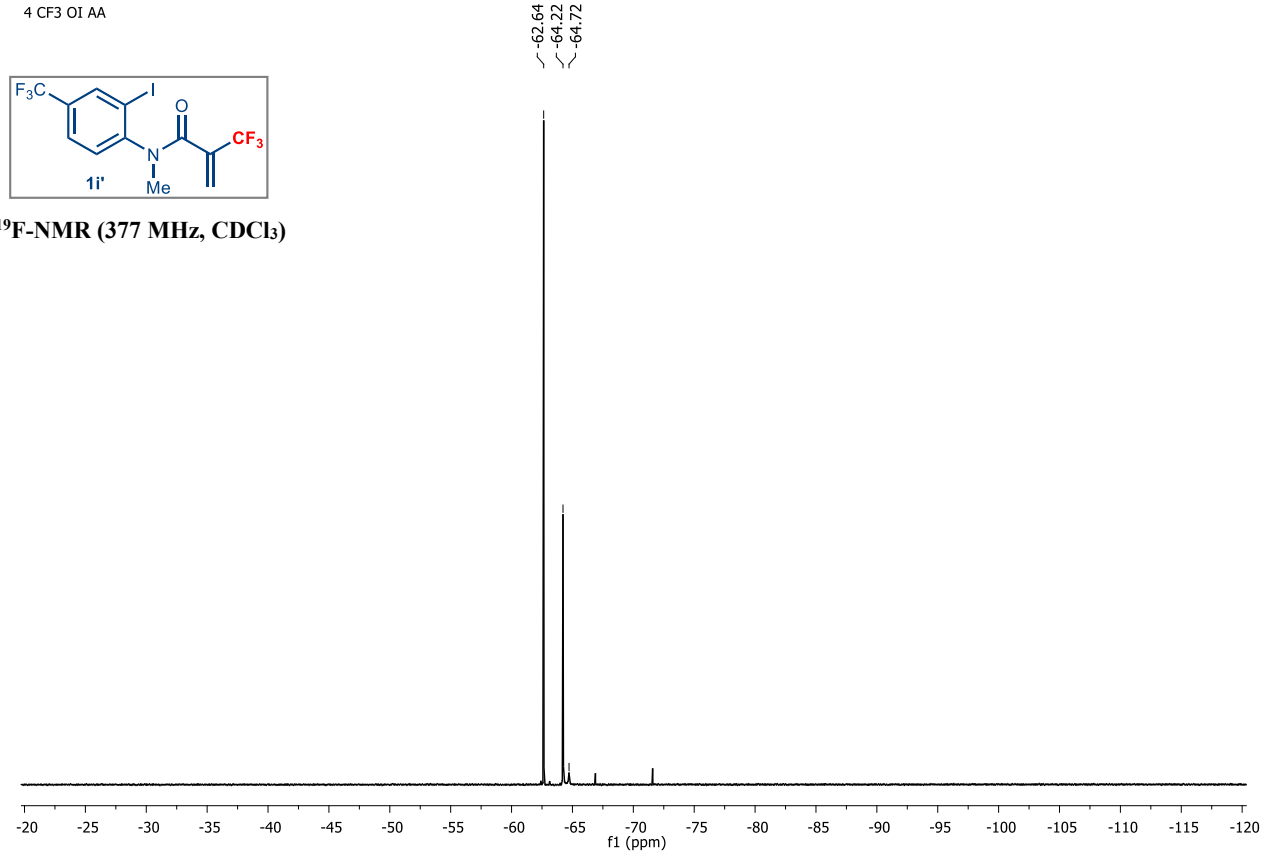
May30-2024
ns-4-cf3 amide



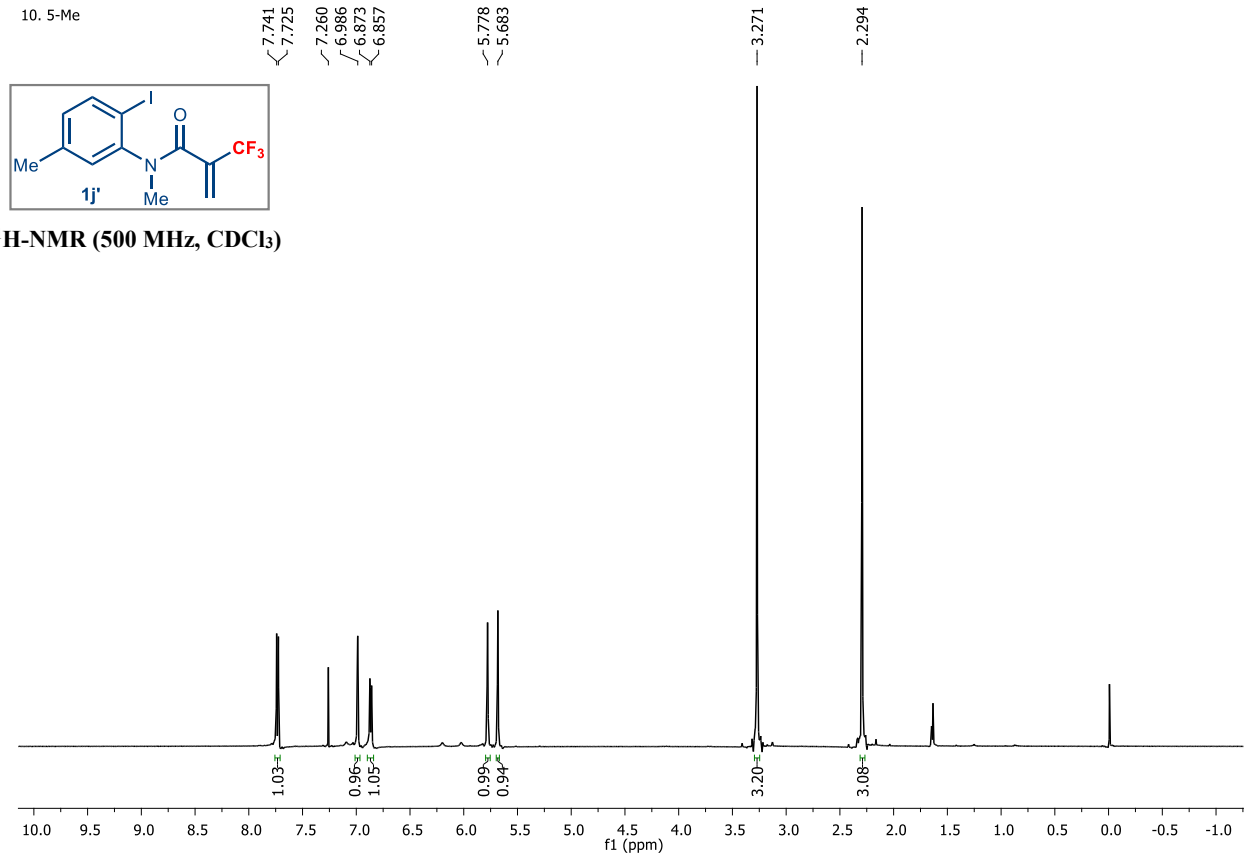
^{1}H-NMR (500 MHz, $CDCl_3$)



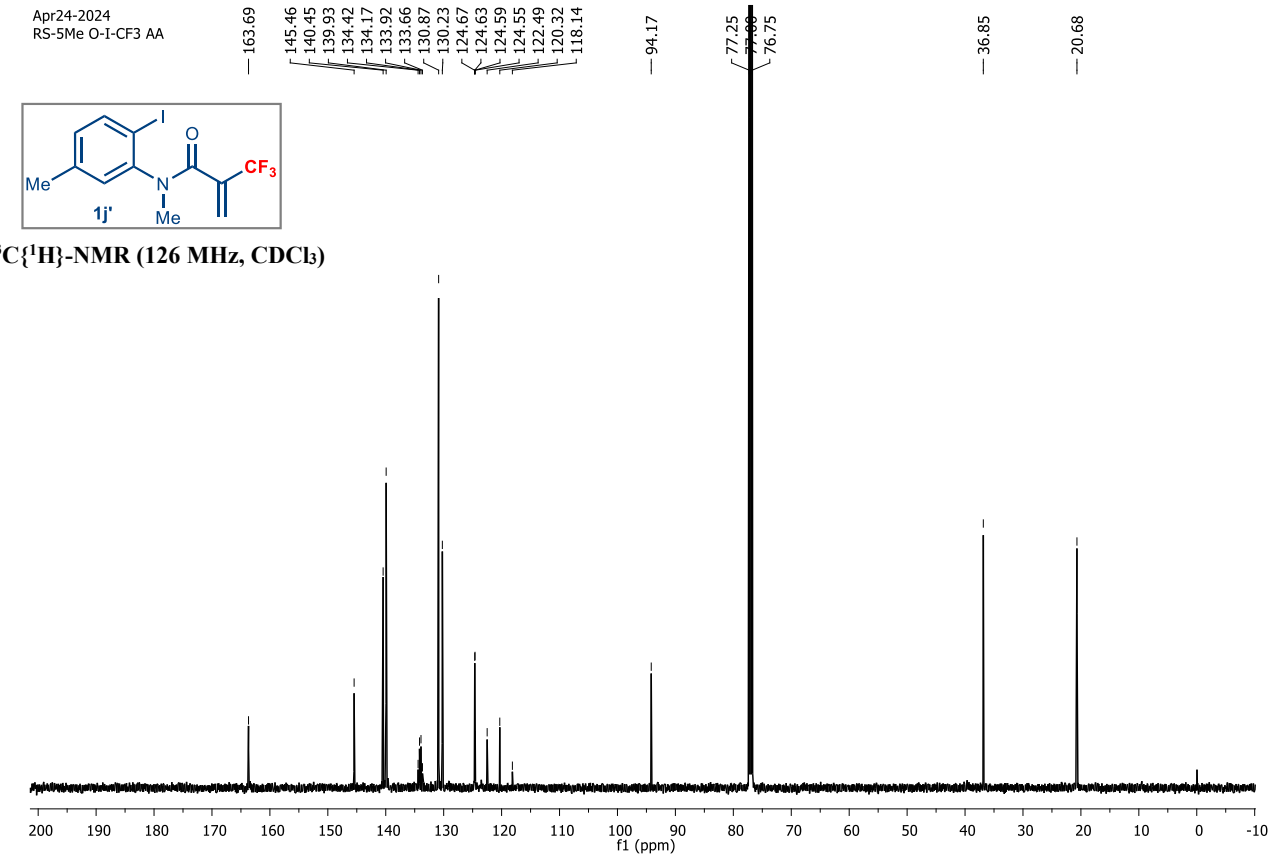
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

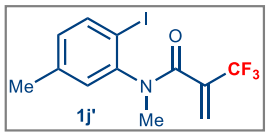


^{1}H-NMR (500 MHz, $CDCl_3$)



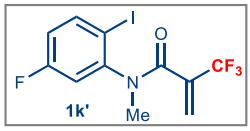
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

RS-5-Me o-I CF3 AA
19F

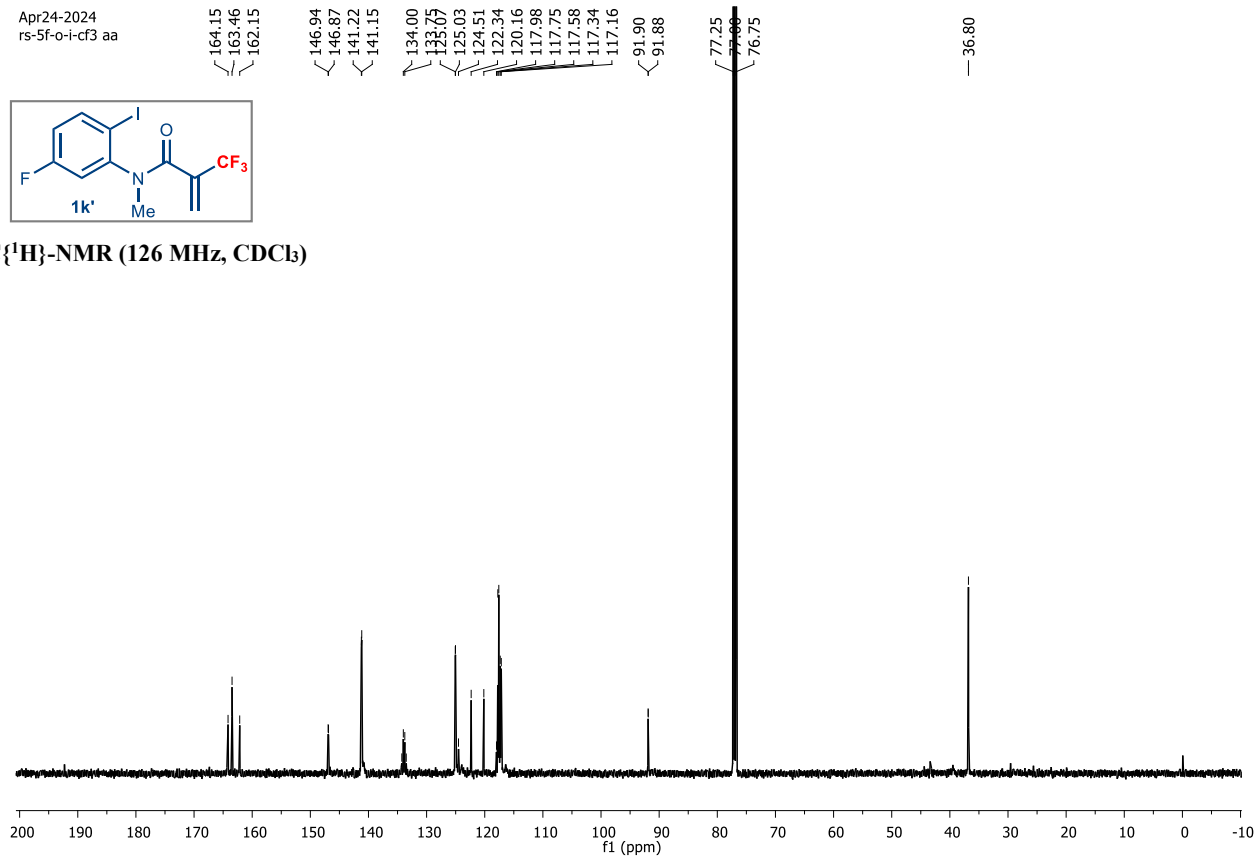


^{19}F-NMR (377 MHz, $CDCl_3$)

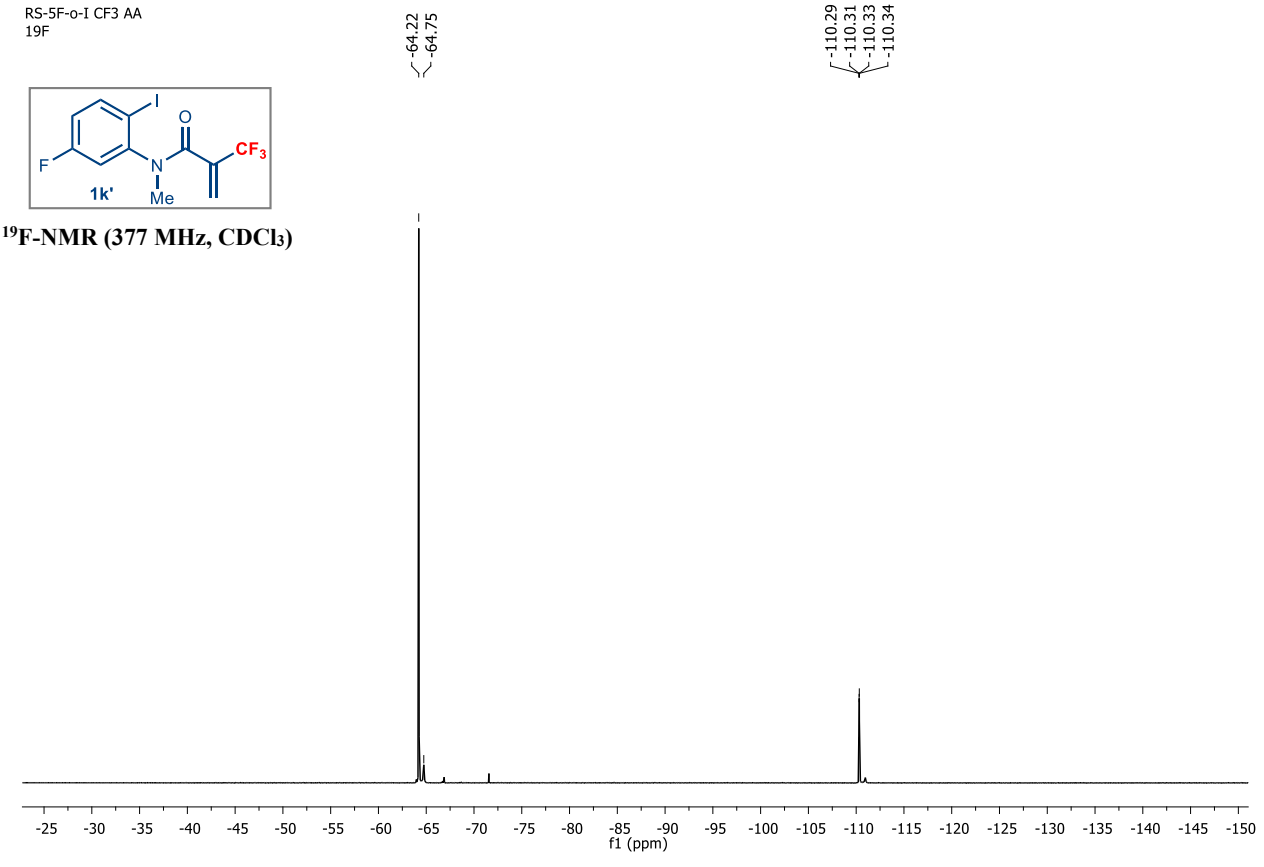
Apr24-2024
rs-5f-o-i-cf3 aa



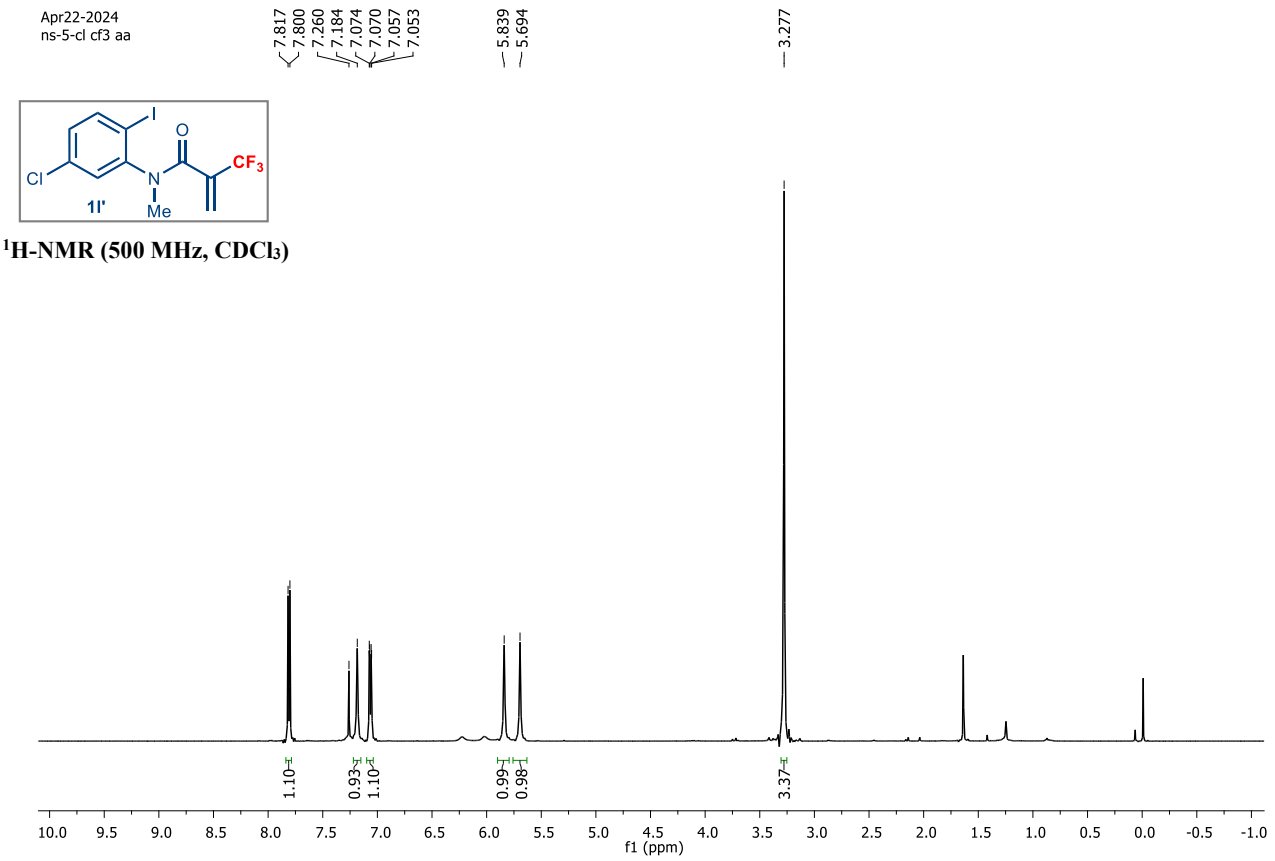
^{1}H-NMR (500 MHz, $CDCl_3$)



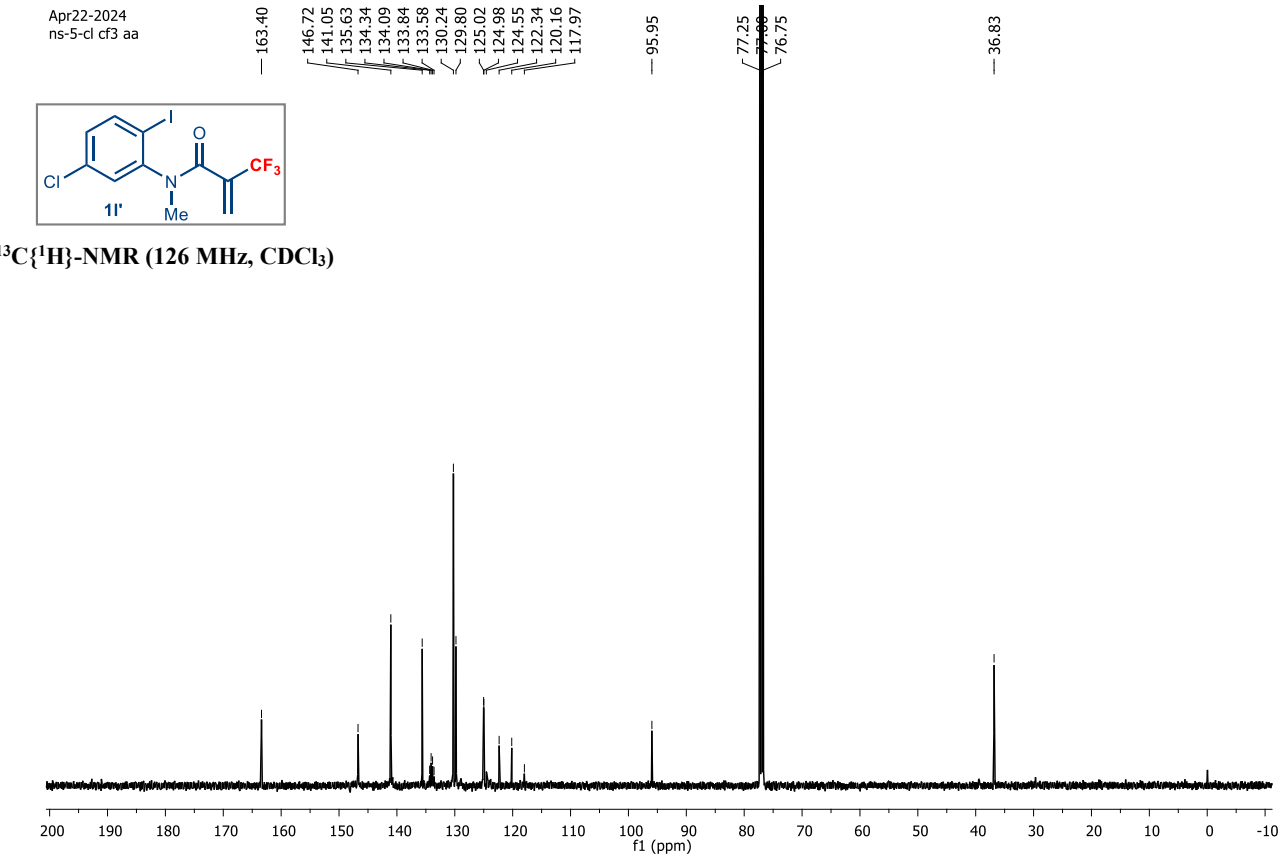
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

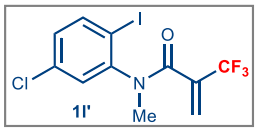


^{1}H-NMR (500 MHz, $CDCl_3$)



^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

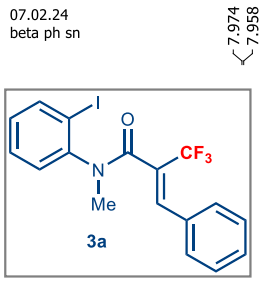
NS 5 CL
19F



1l'

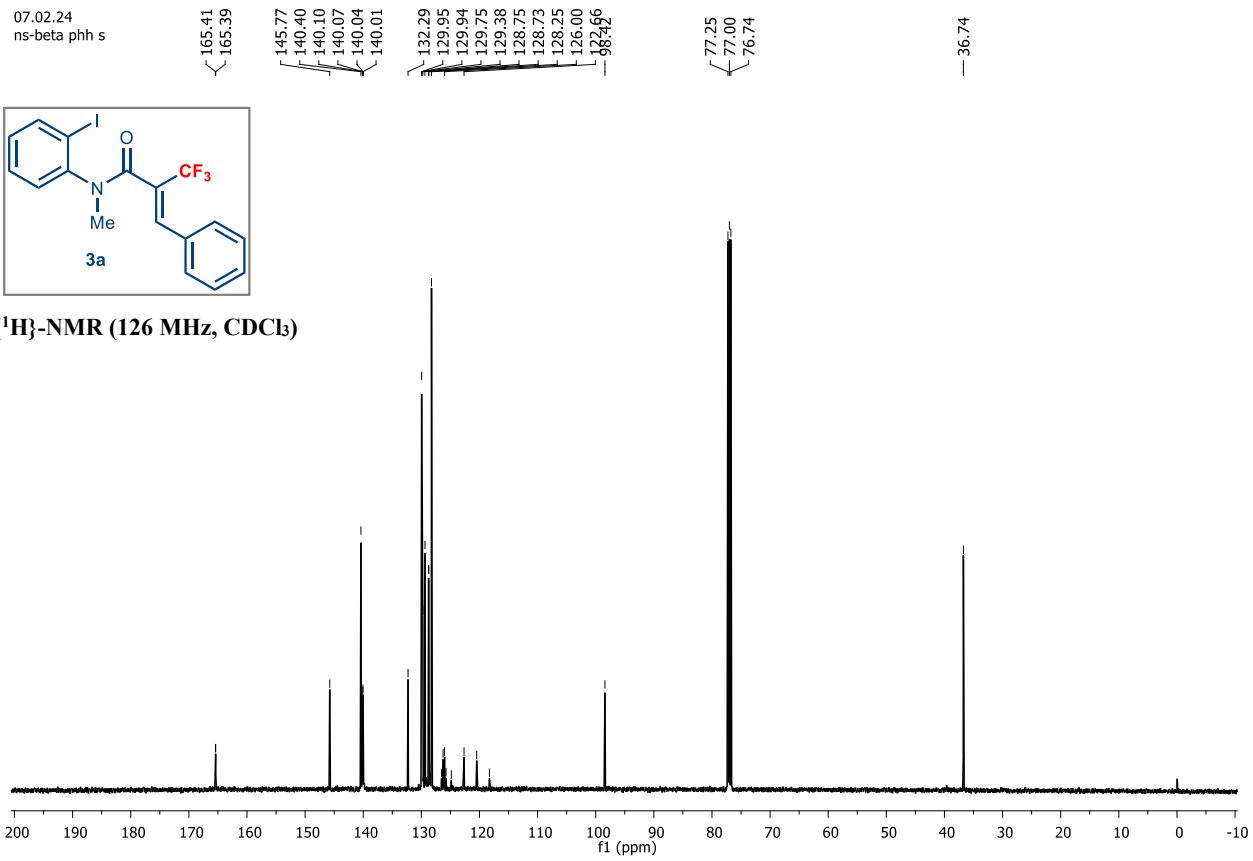
^{19}F-NMR (377 MHz, CDCl$_3$)

07.02.24
beta ph sn

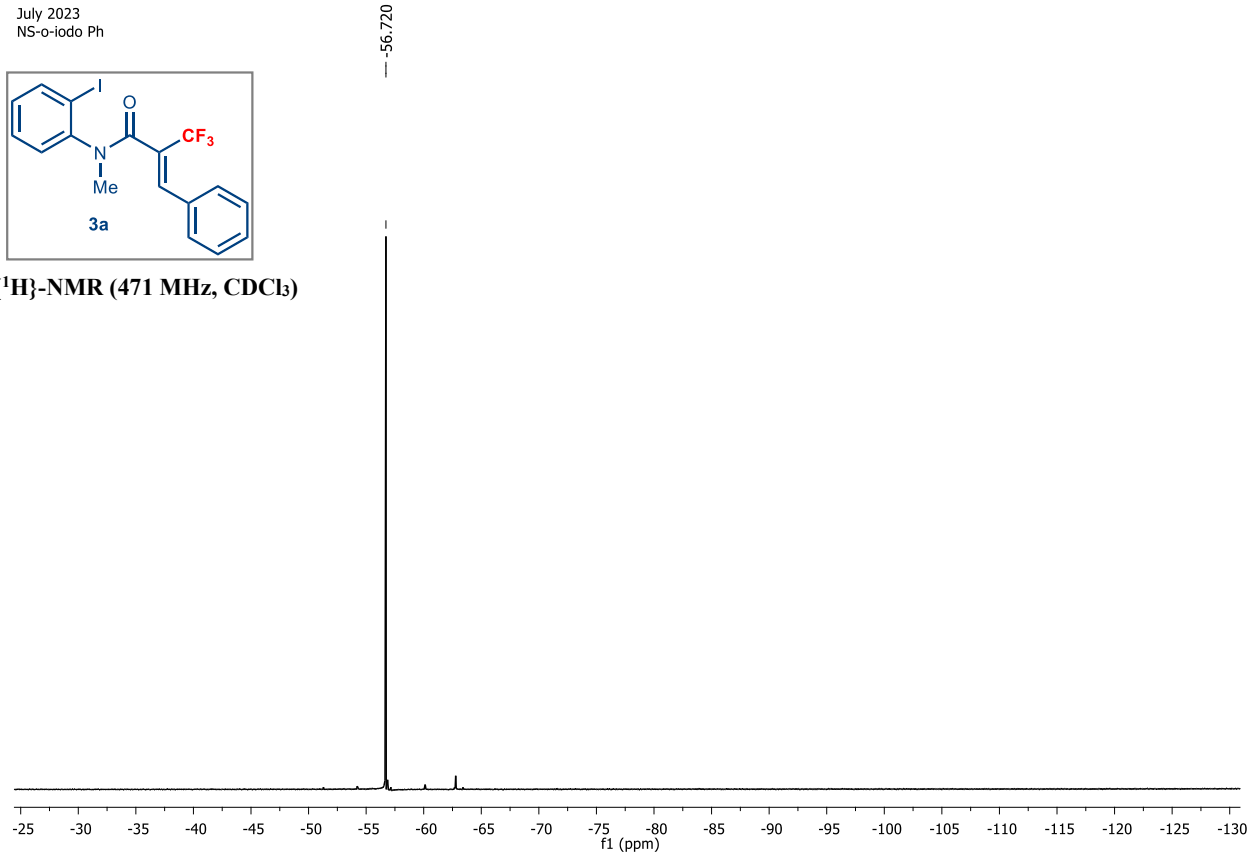


3a

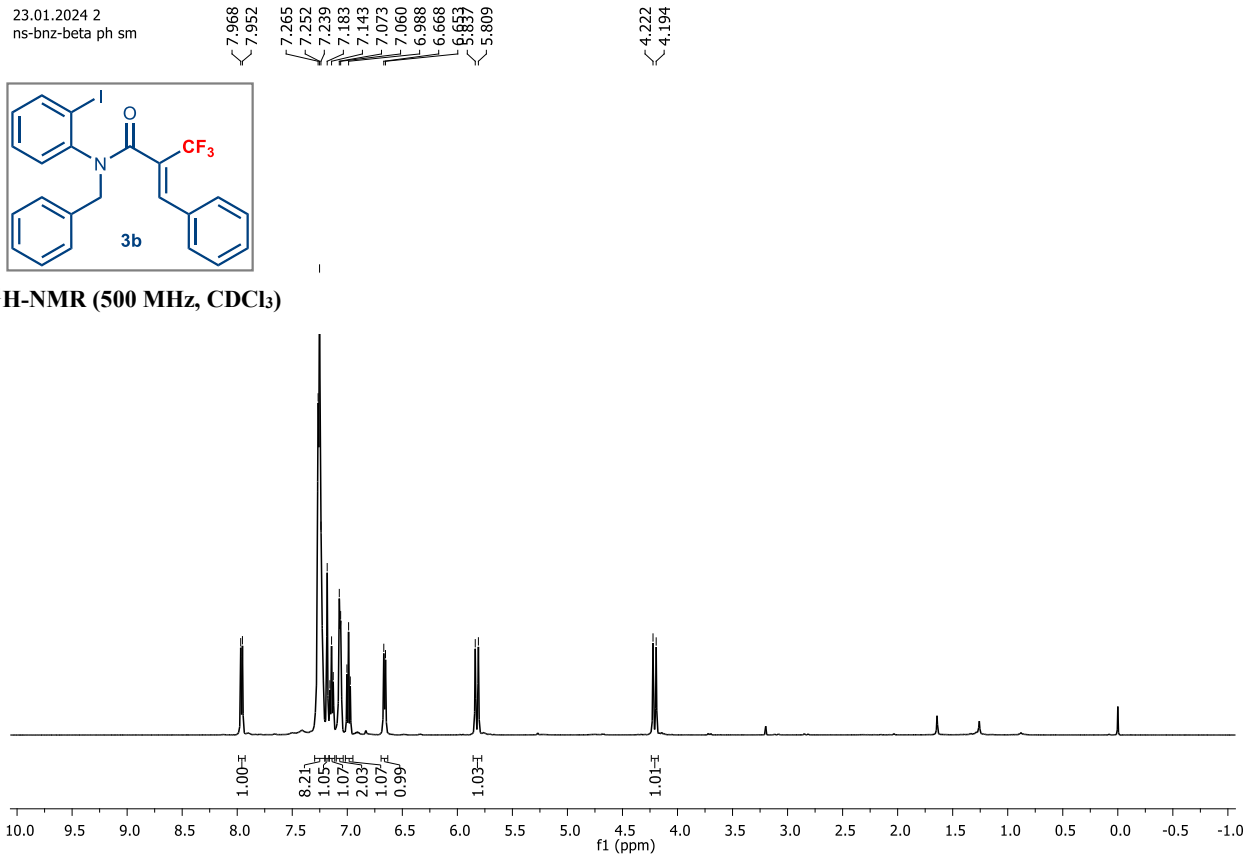
^{1}H-NMR (500 MHz, CDCl$_3$)



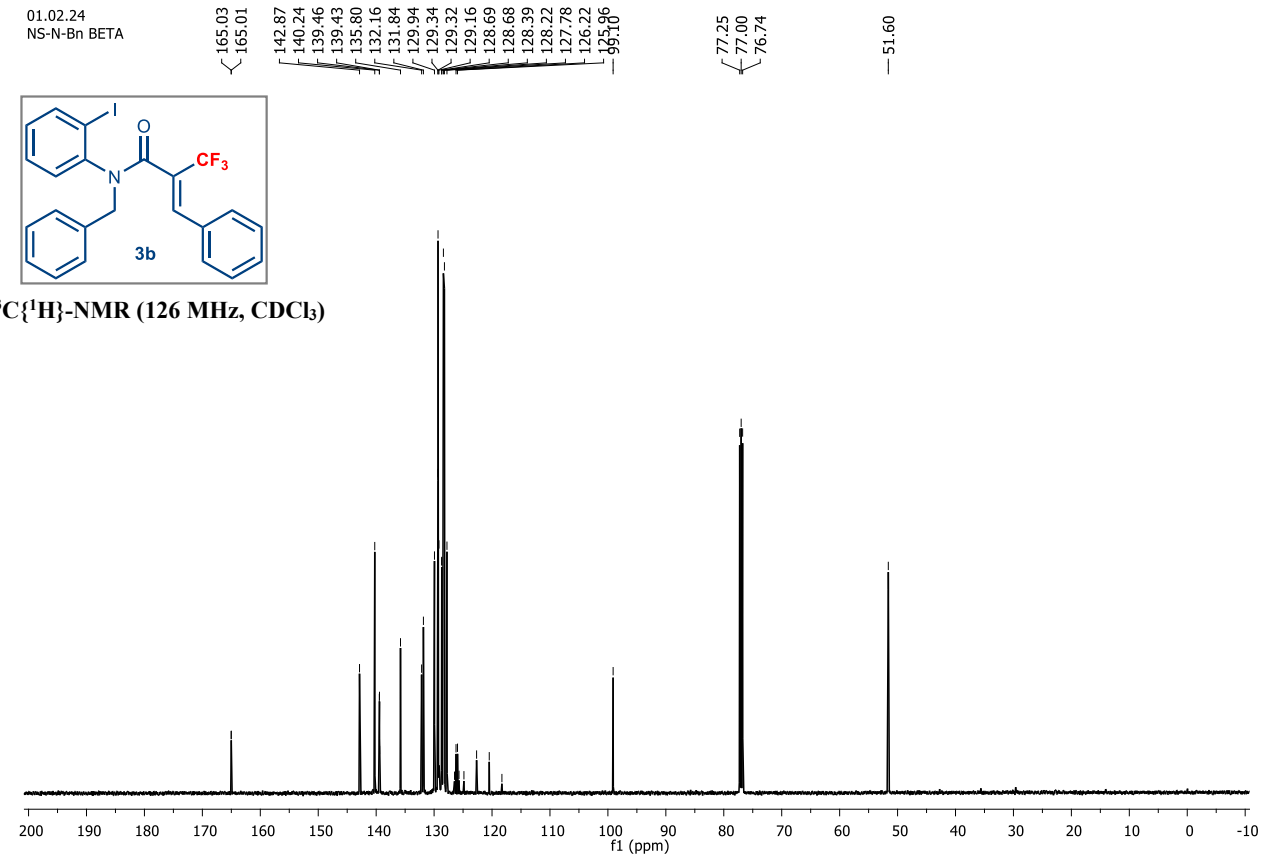
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

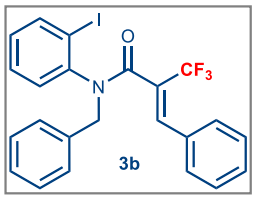


^{1}H-NMR (500 MHz, $CDCl_3$)



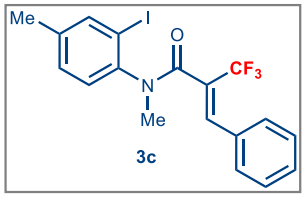
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-NBNZ BETA
19F

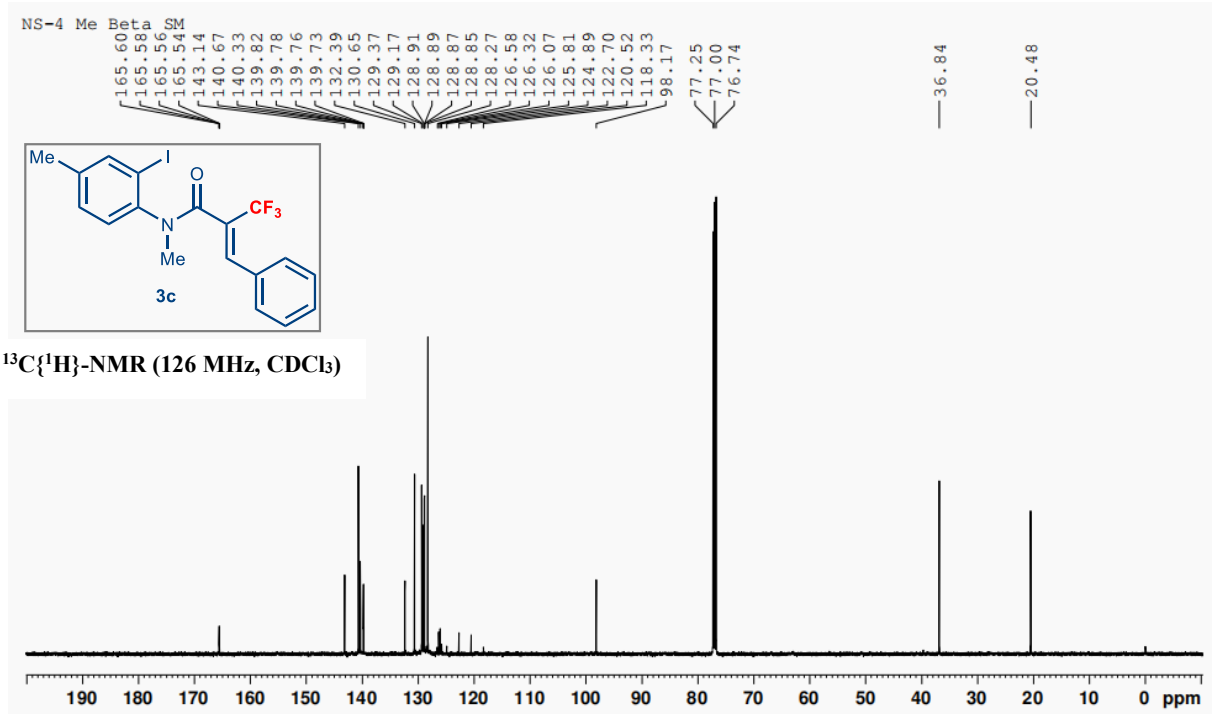


^{19}F-NMR (377 MHz, $CDCl_3$)

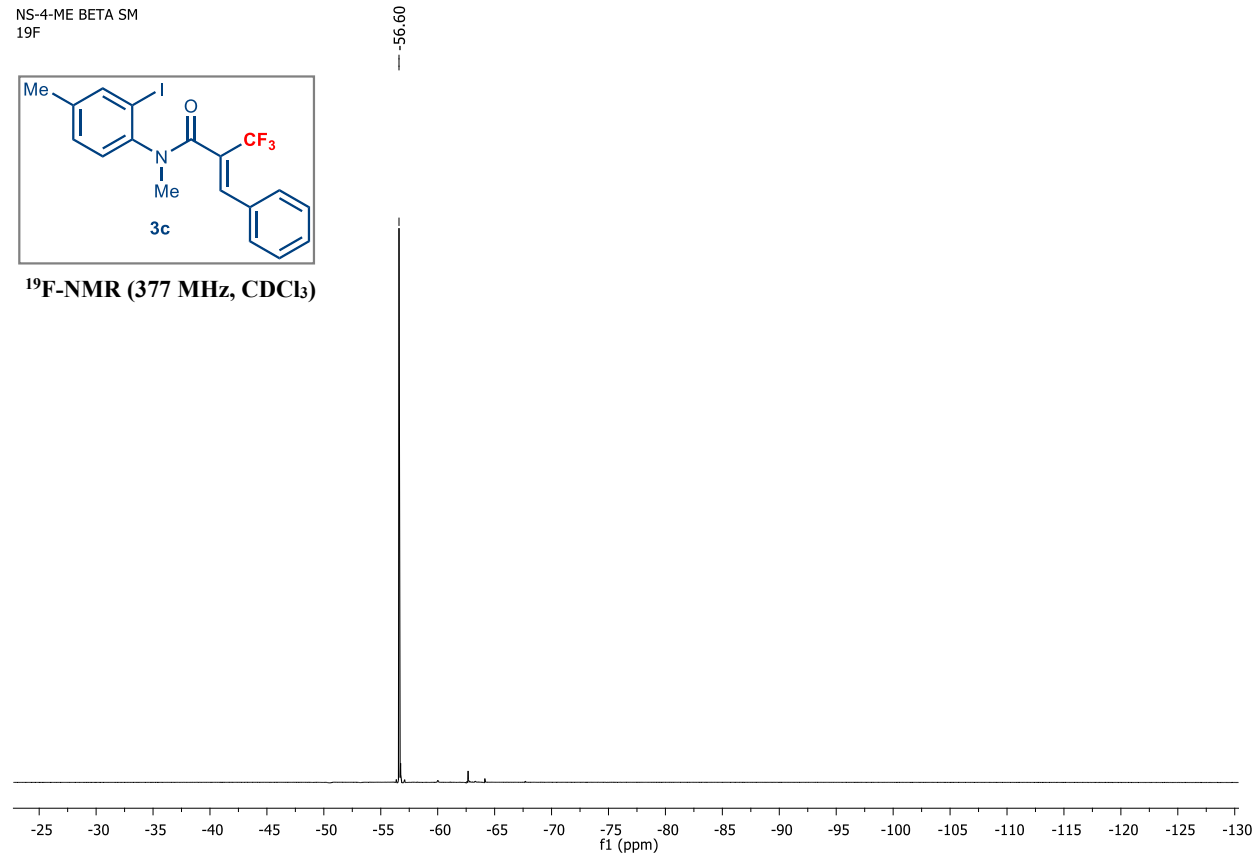
28.02.24
NS-4 Me Beta SM



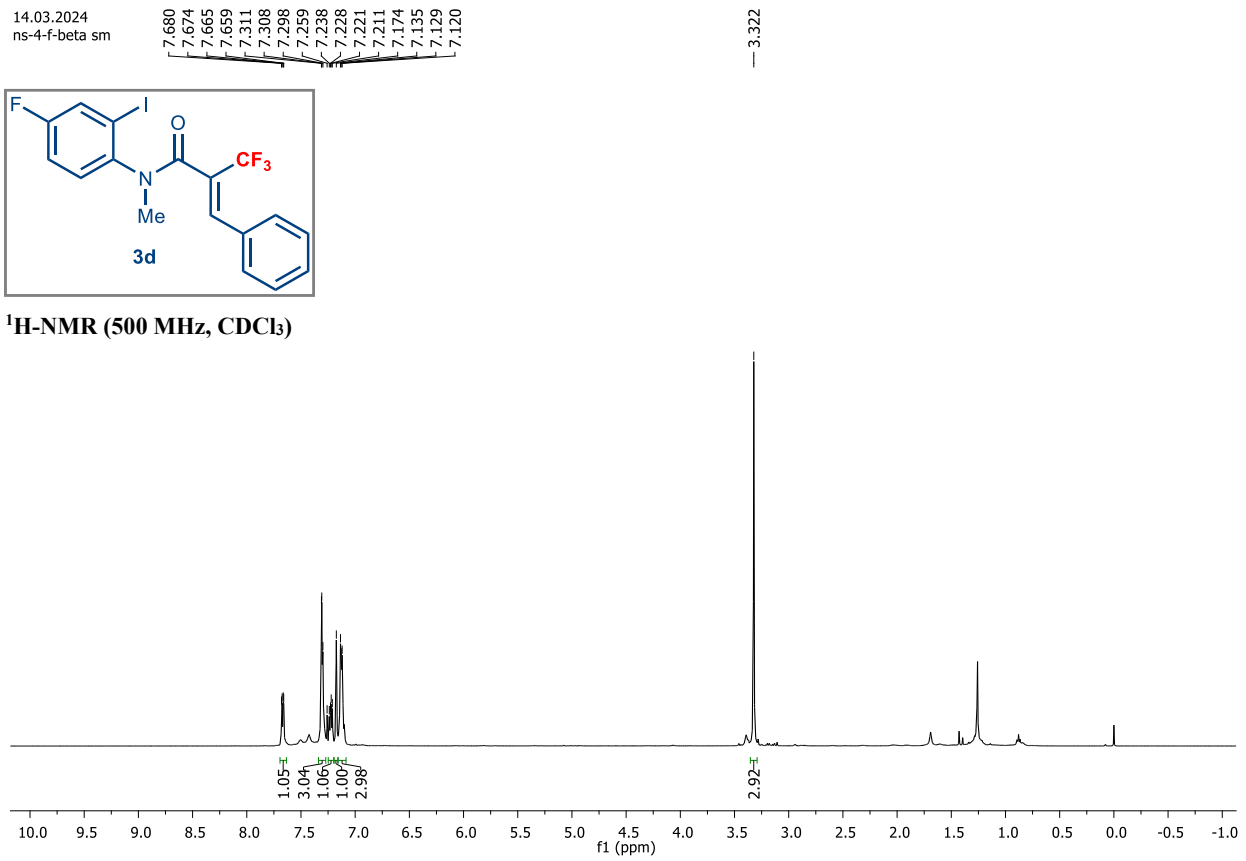
^{1}H-NMR (500 MHz, $CDCl_3$)



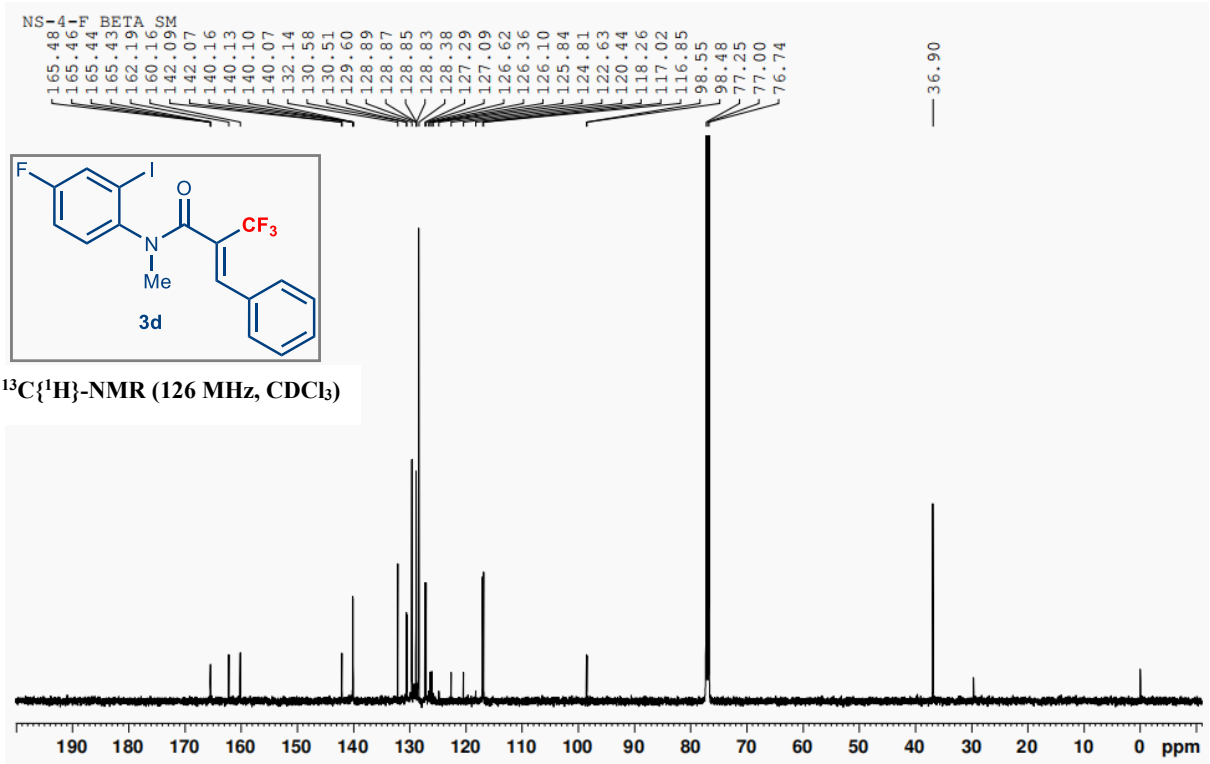
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

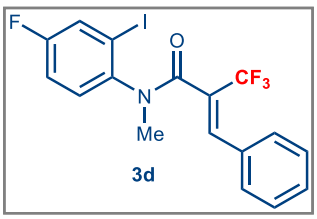


^{1}H-NMR (500 MHz, $CDCl_3$)



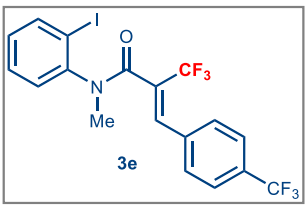
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS 4F BETA PH SM

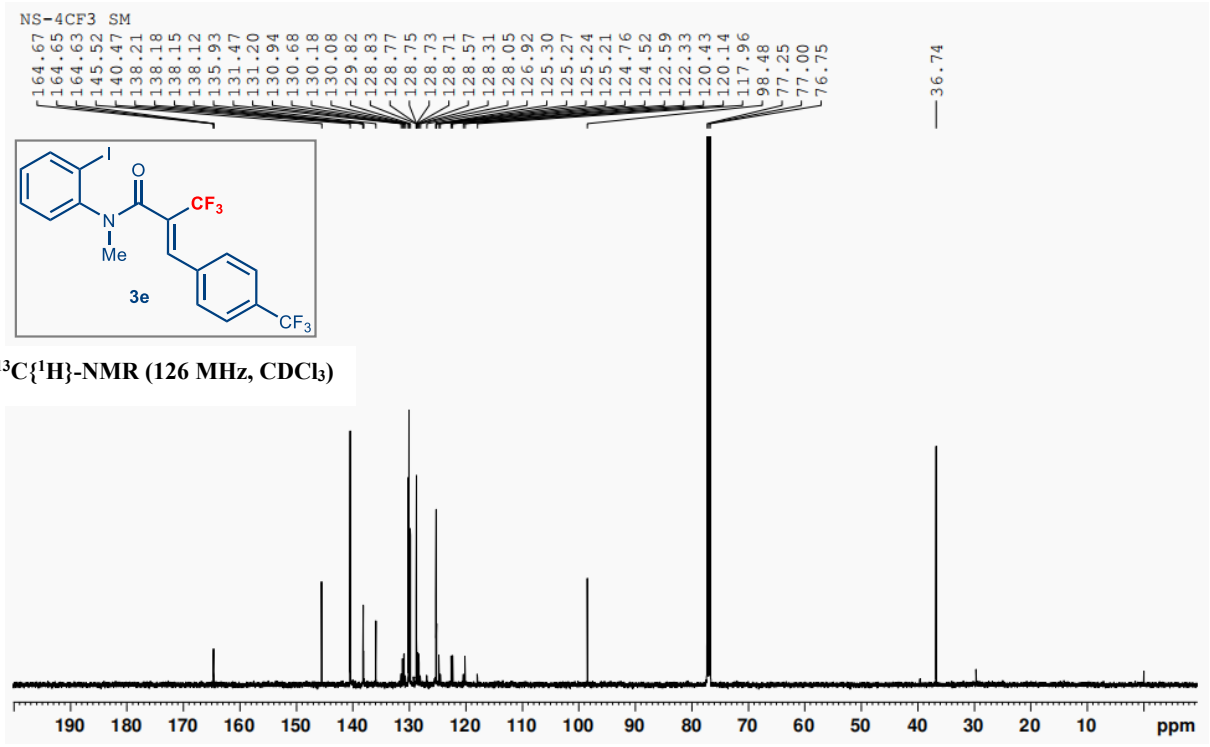


^{19}F-NMR (377 MHz, $CDCl_3$)

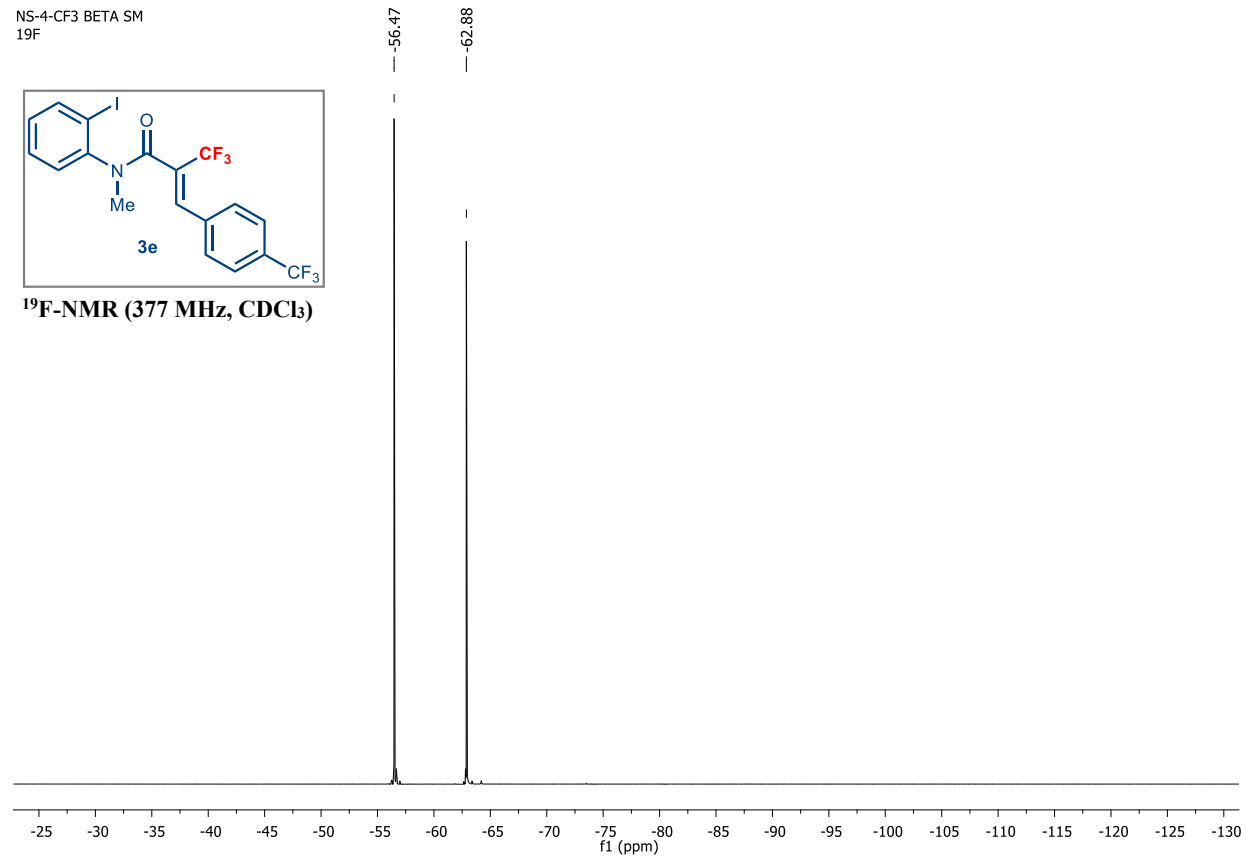
14.02.24
ns-4-cf3 sm beta



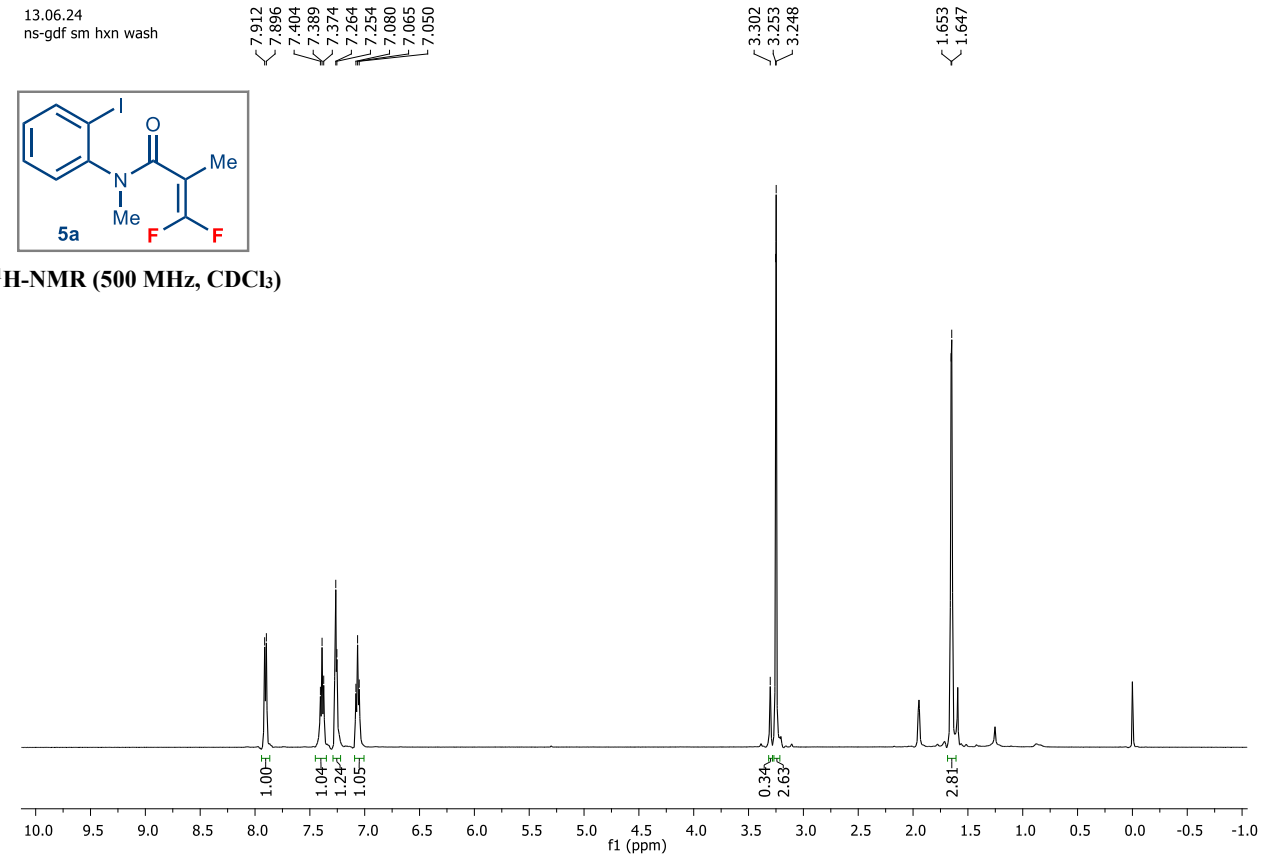
^{1}H-NMR (500 MHz, $CDCl_3$)



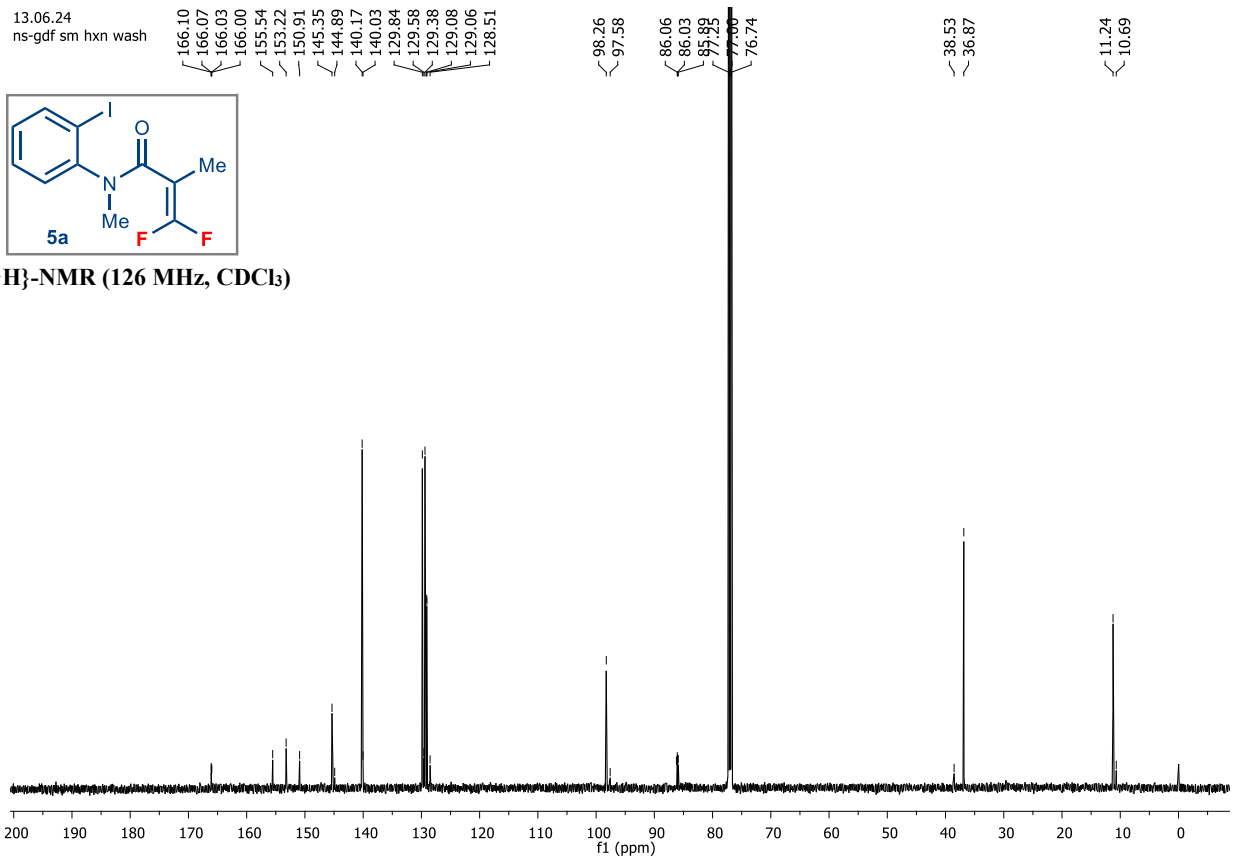
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

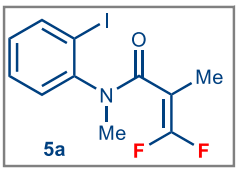


^{1}H-NMR (500 MHz, $CDCl_3$)



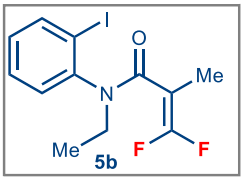
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-STD GDF HXN WASH
19F

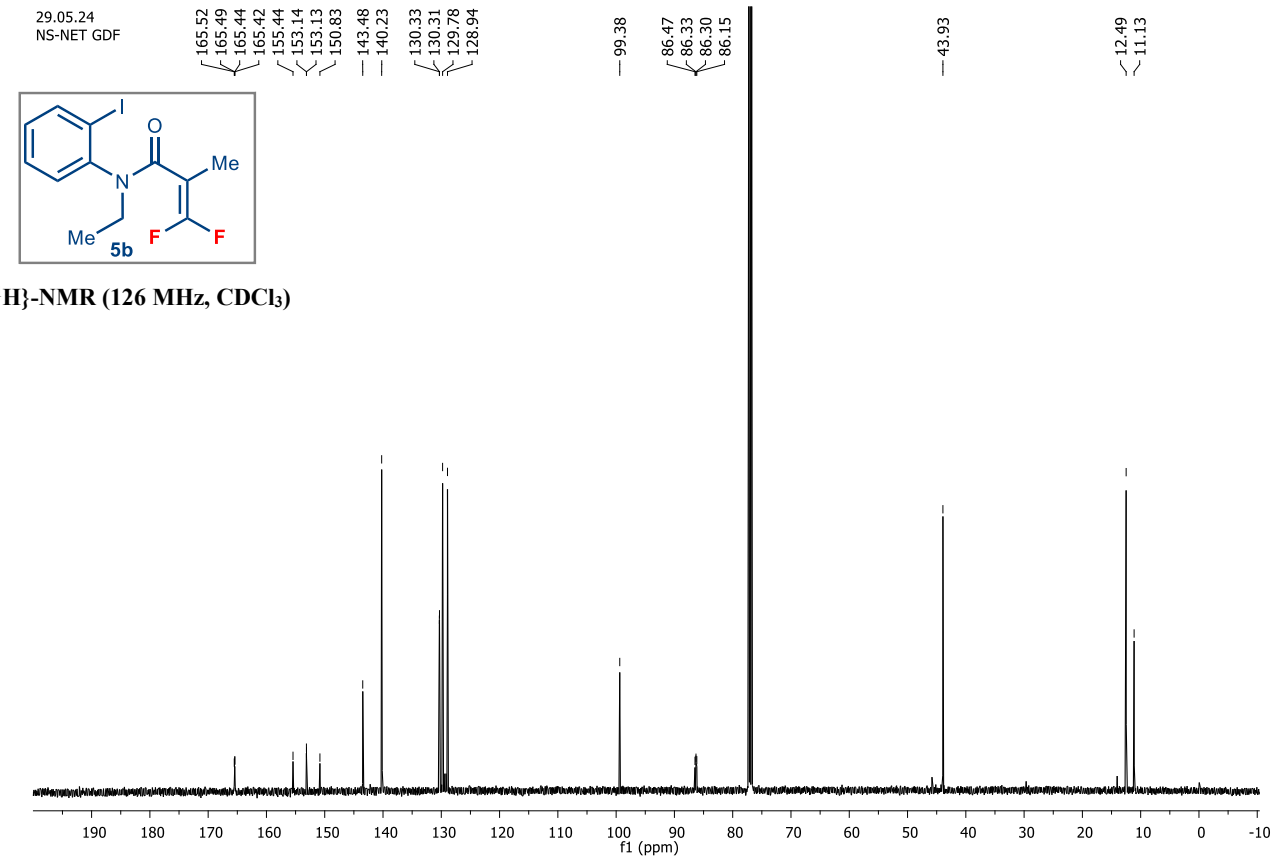


^{19}F-NMR (377 MHz, $CDCl_3$)

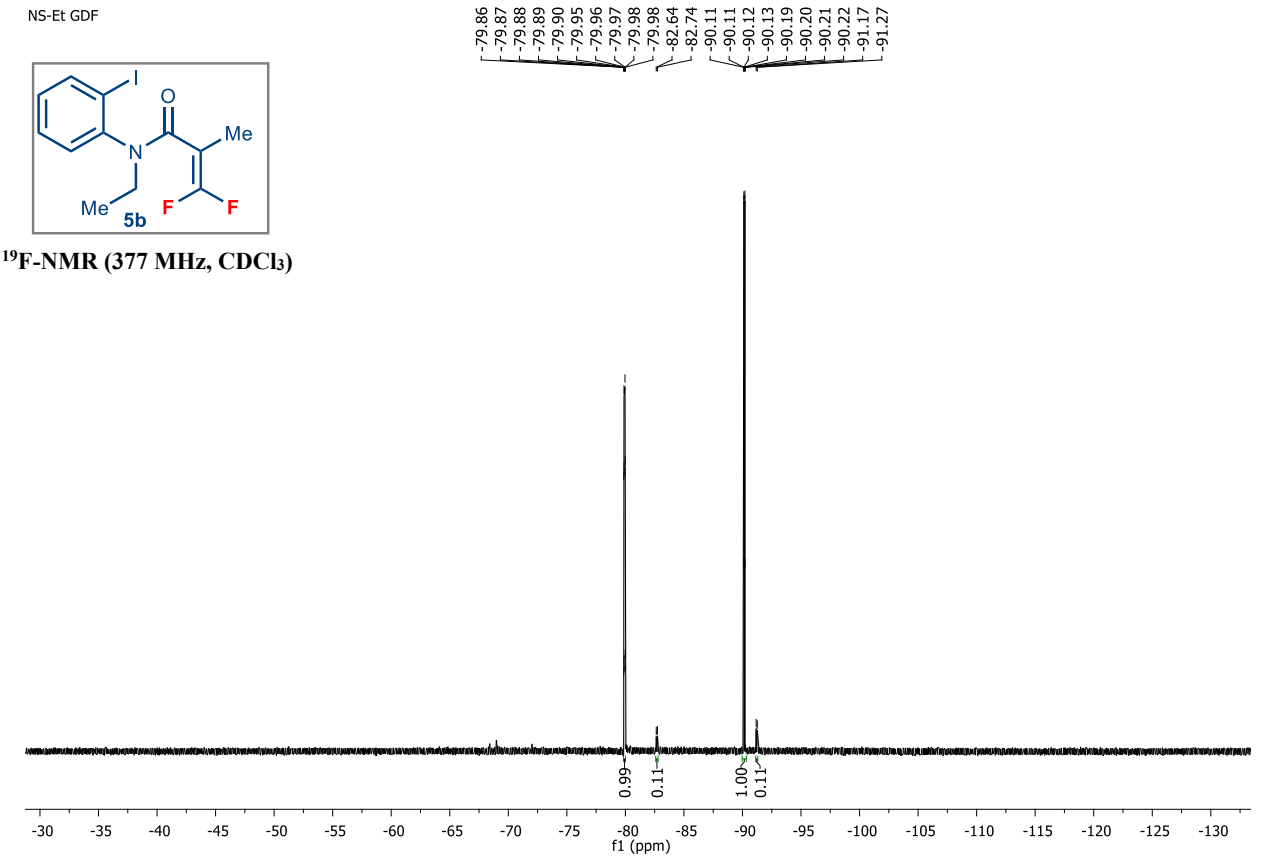
29.05.24
NS-NET GDF



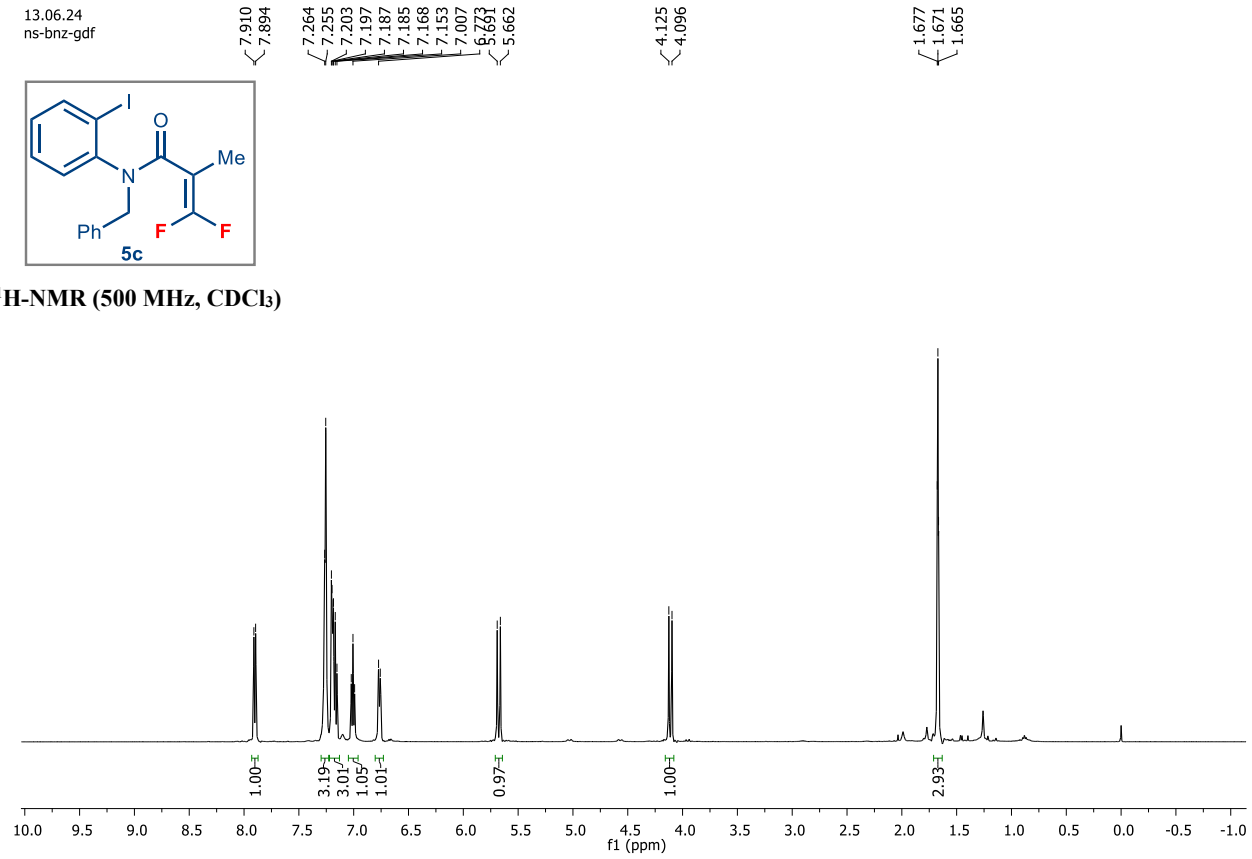
^{1}H-NMR (500 MHz, $CDCl_3$)



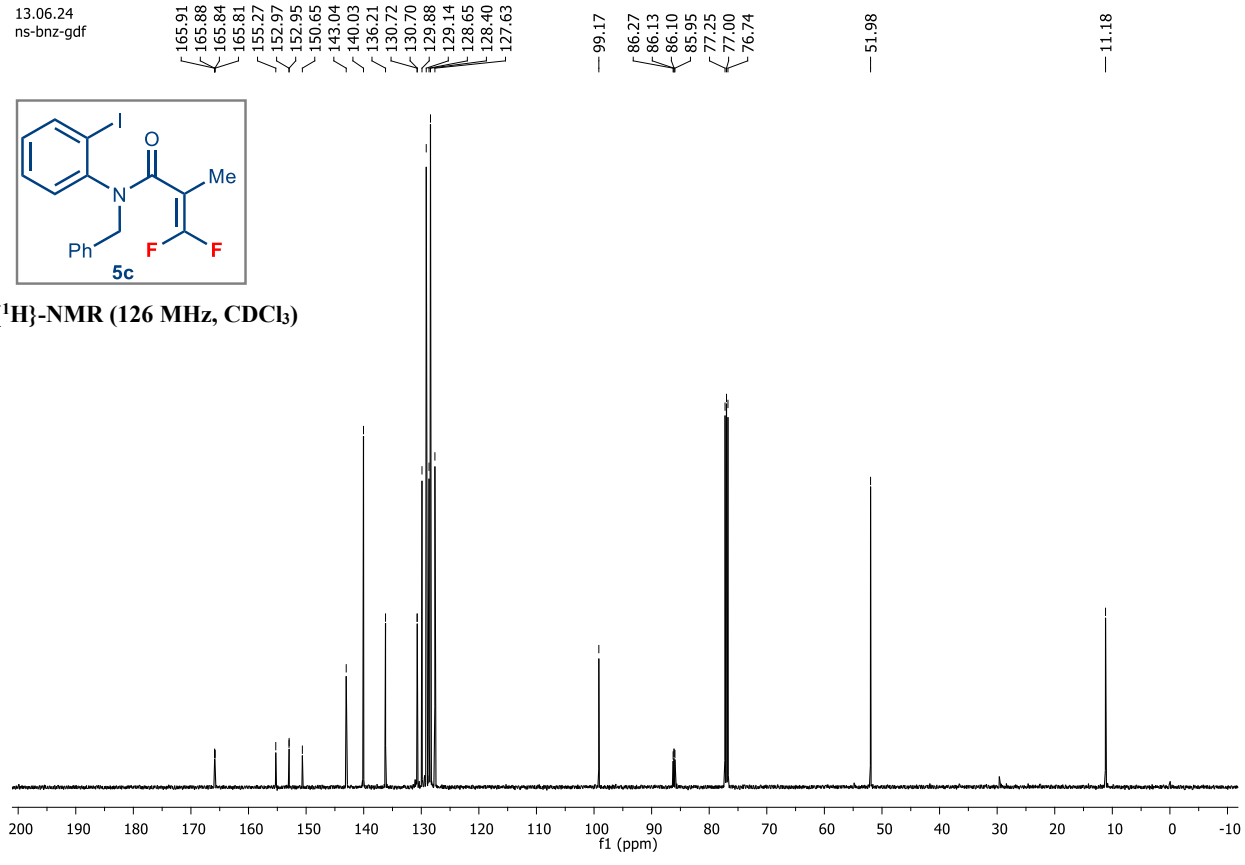
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

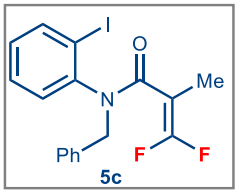


^{1}H-NMR (500 MHz, $CDCl_3$)



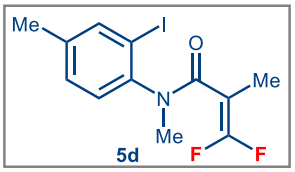
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-BNZ-SM-2 1
19F

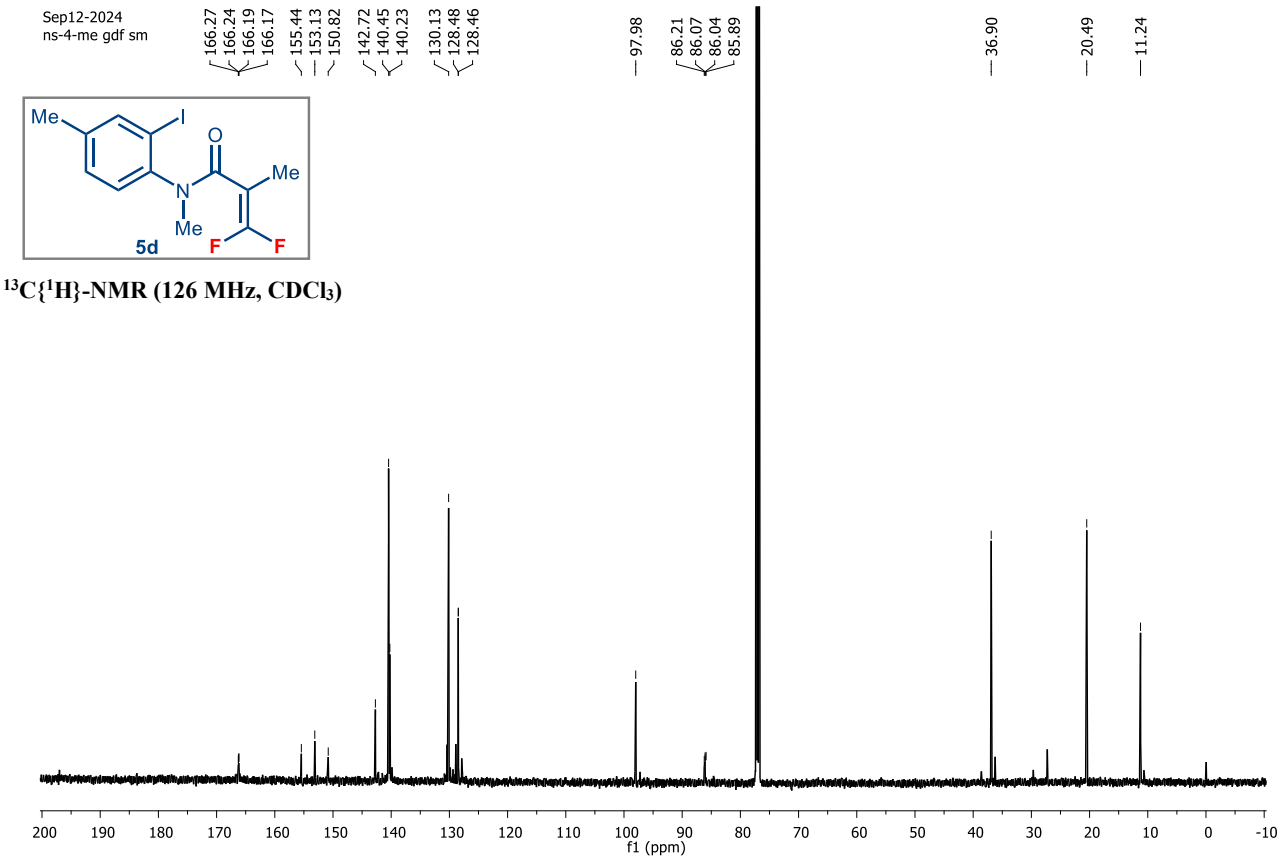


^{19}F-NMR (377 MHz, $CDCl_3$)

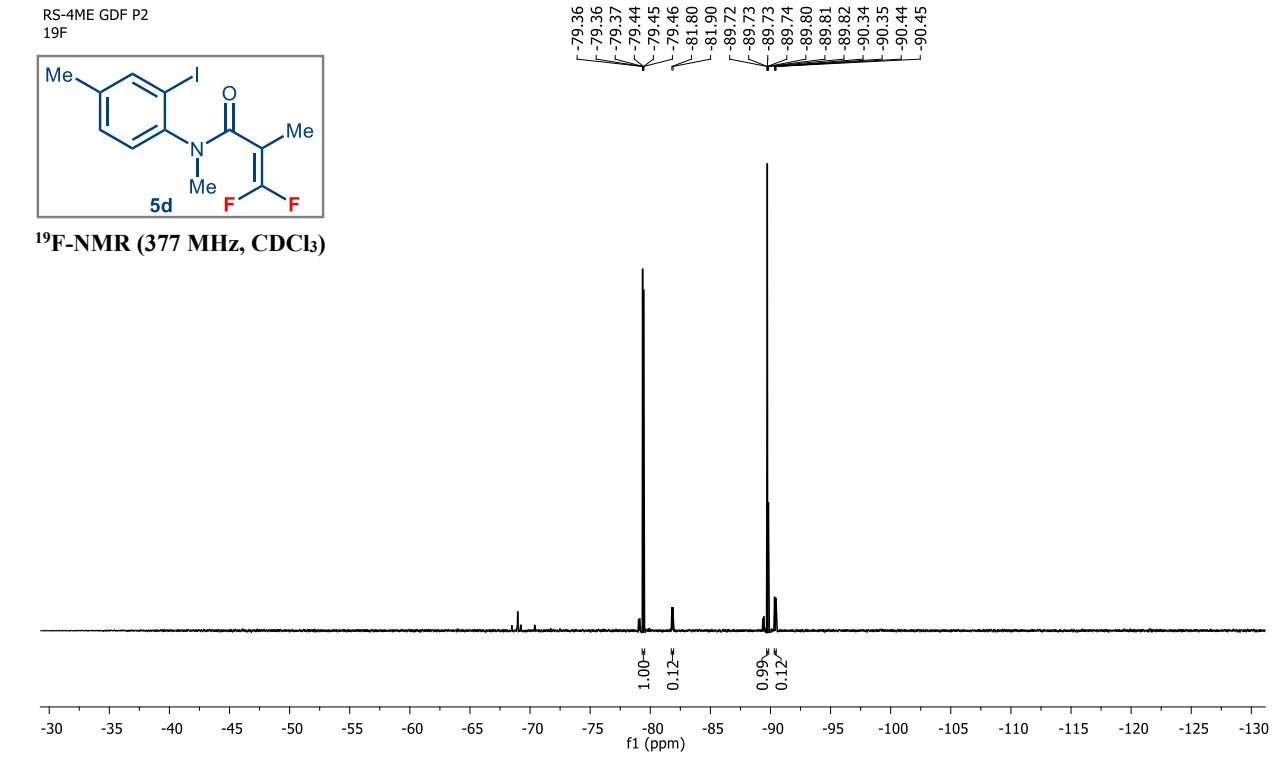
RS-4ME GDF P2



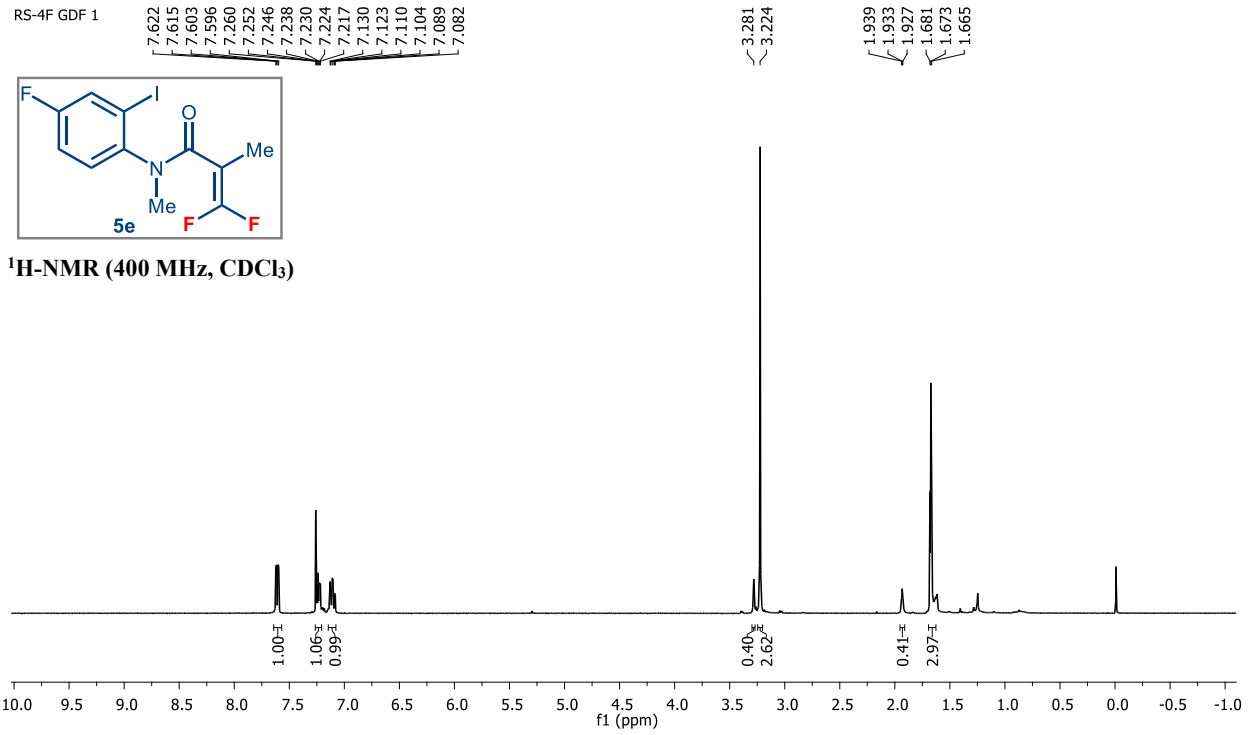
^{1}H-NMR (400 MHz, $CDCl_3$)



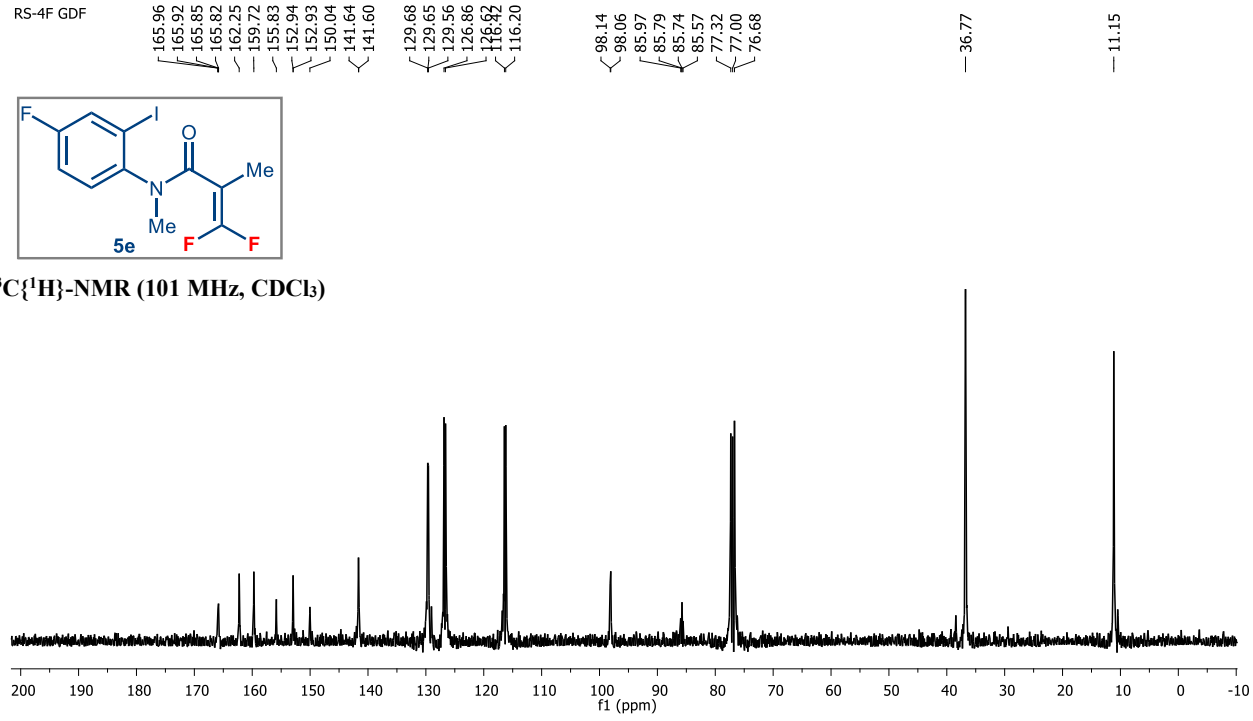
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

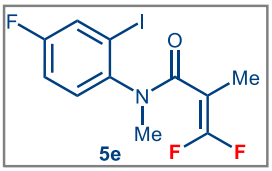


^{1}H-NMR (400 MHz, $CDCl_3$)

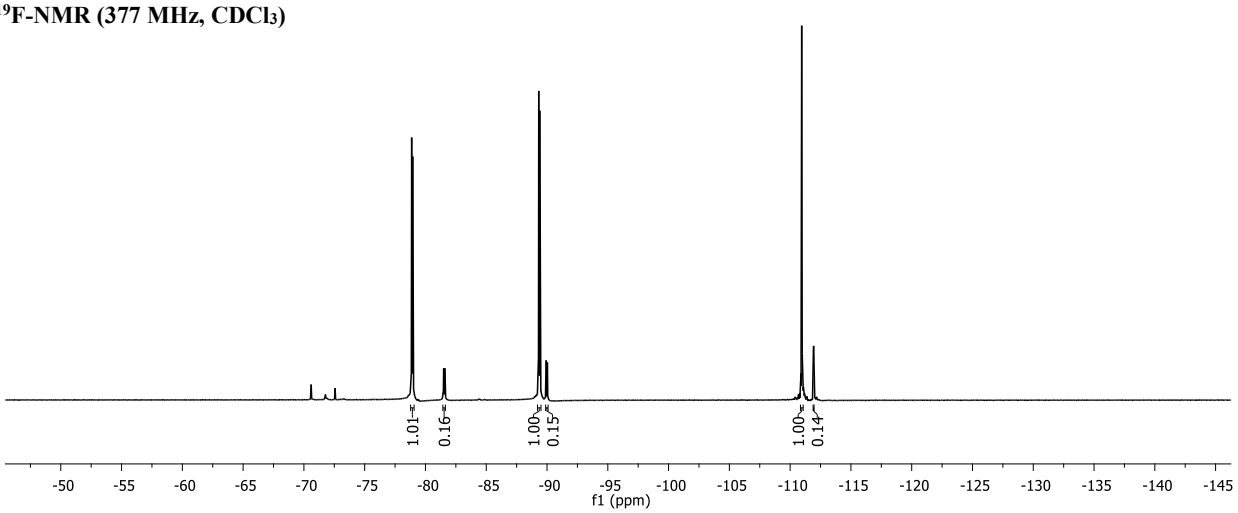


^{13}C{^{1}H}-NMR (101 MHz, $CDCl_3$)

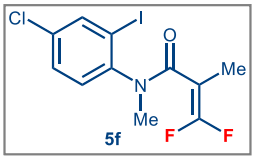
RS-4-F GDF P2
19F



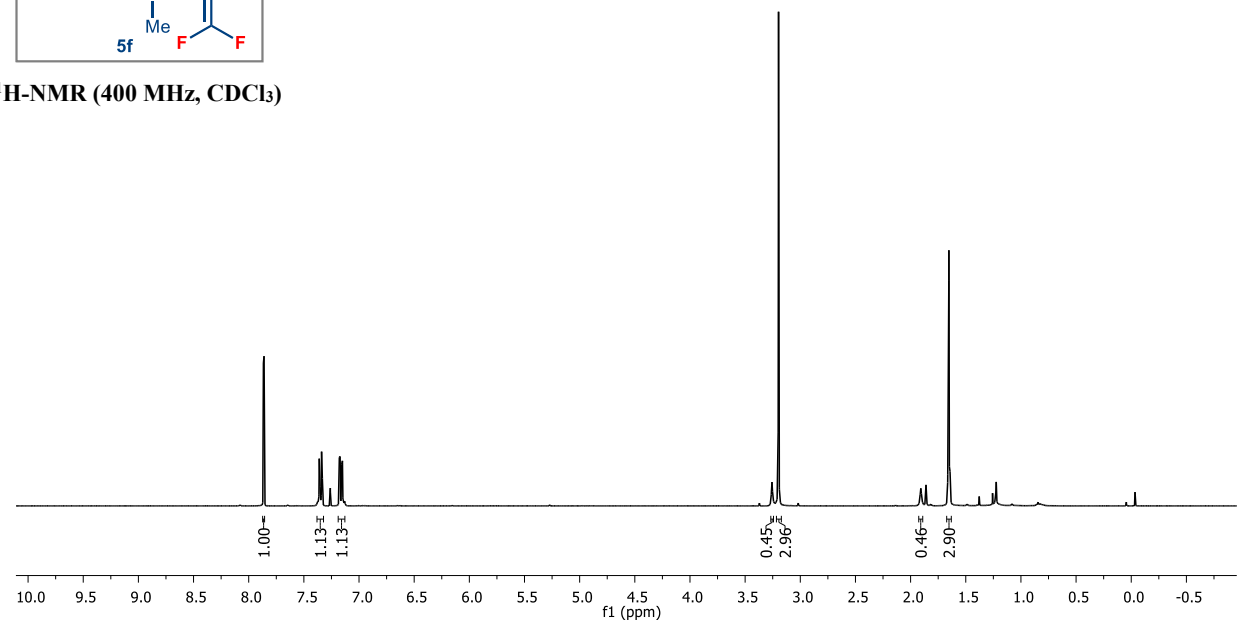
^{19}F-NMR (377 MHz, $CDCl_3$)

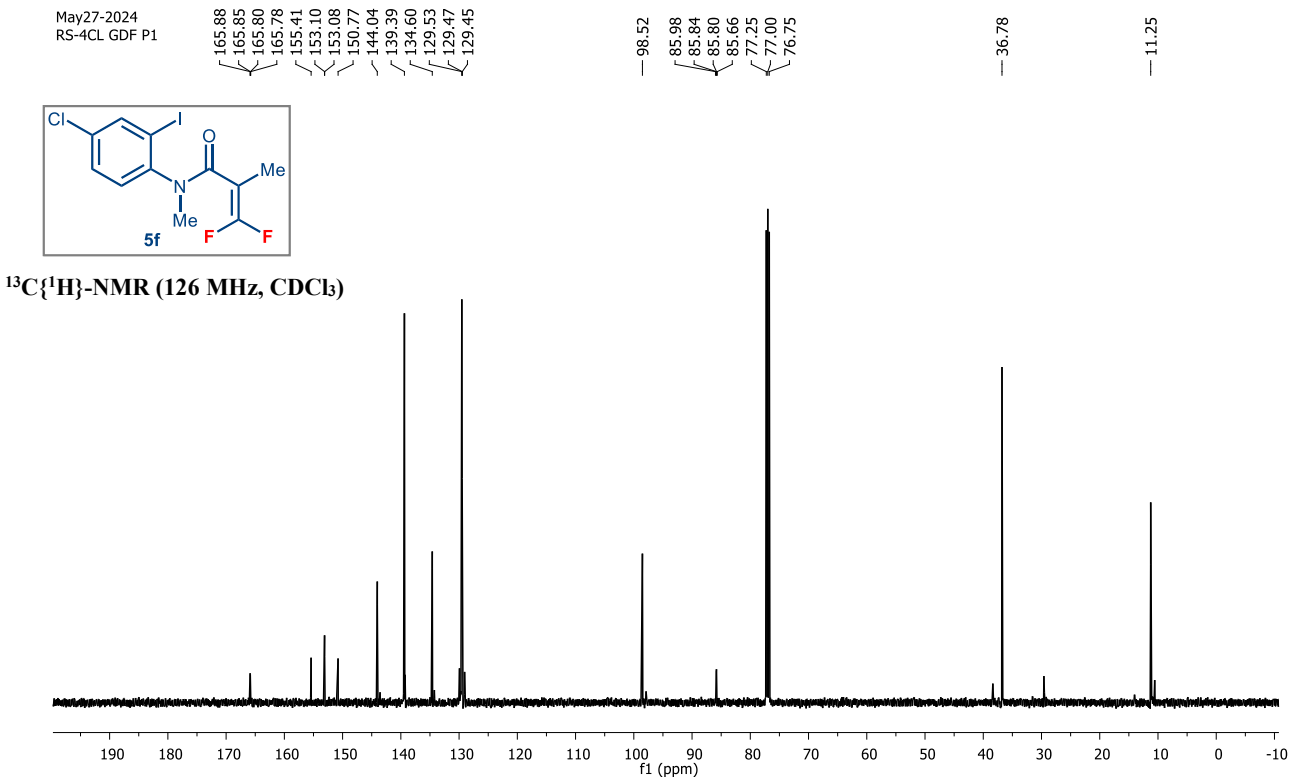


RS-4-CL GDF P1

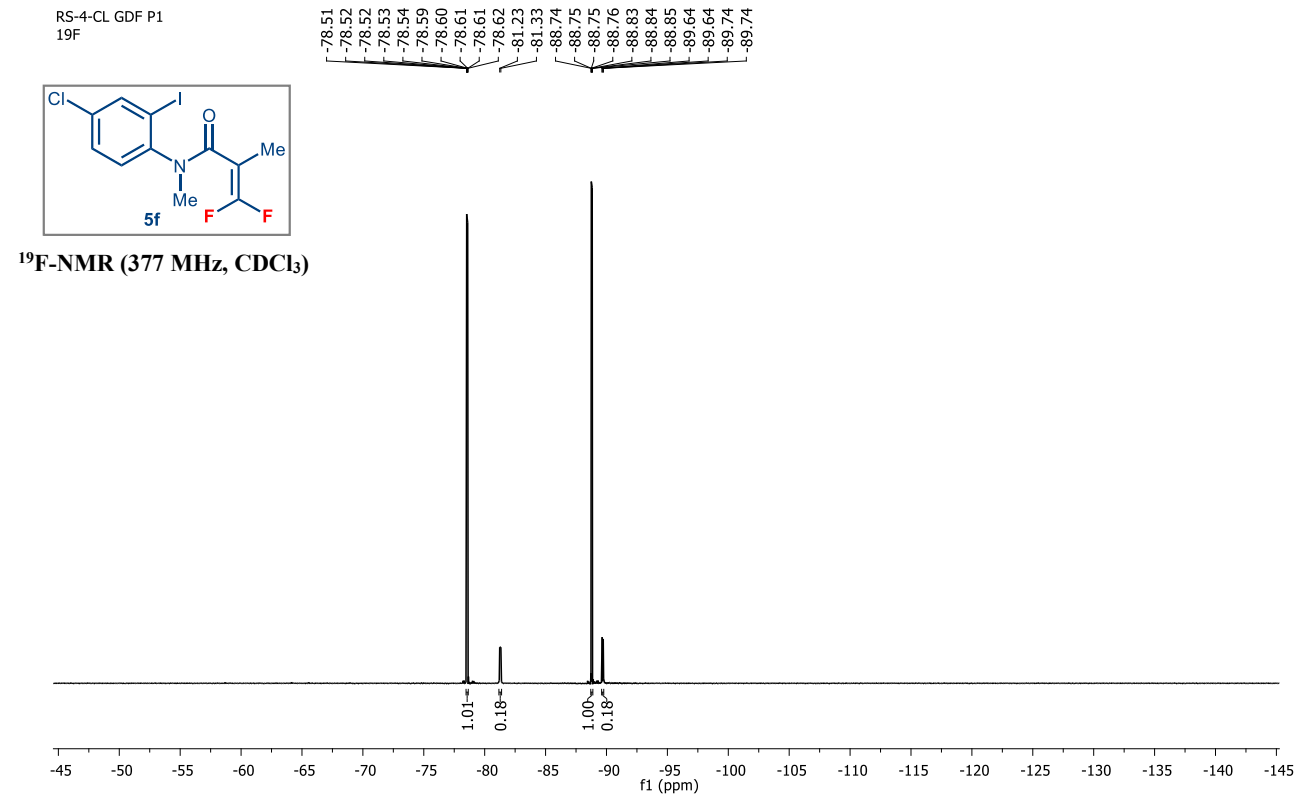


^{1}H-NMR (400 MHz, $CDCl_3$)

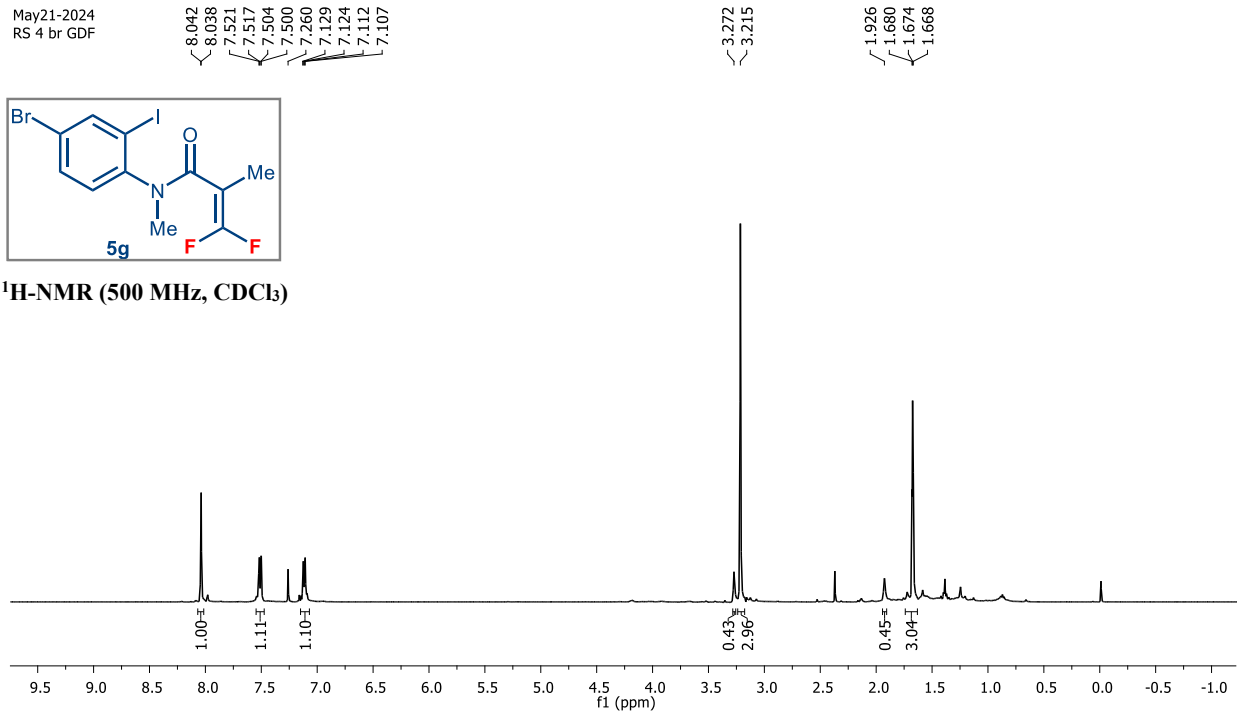




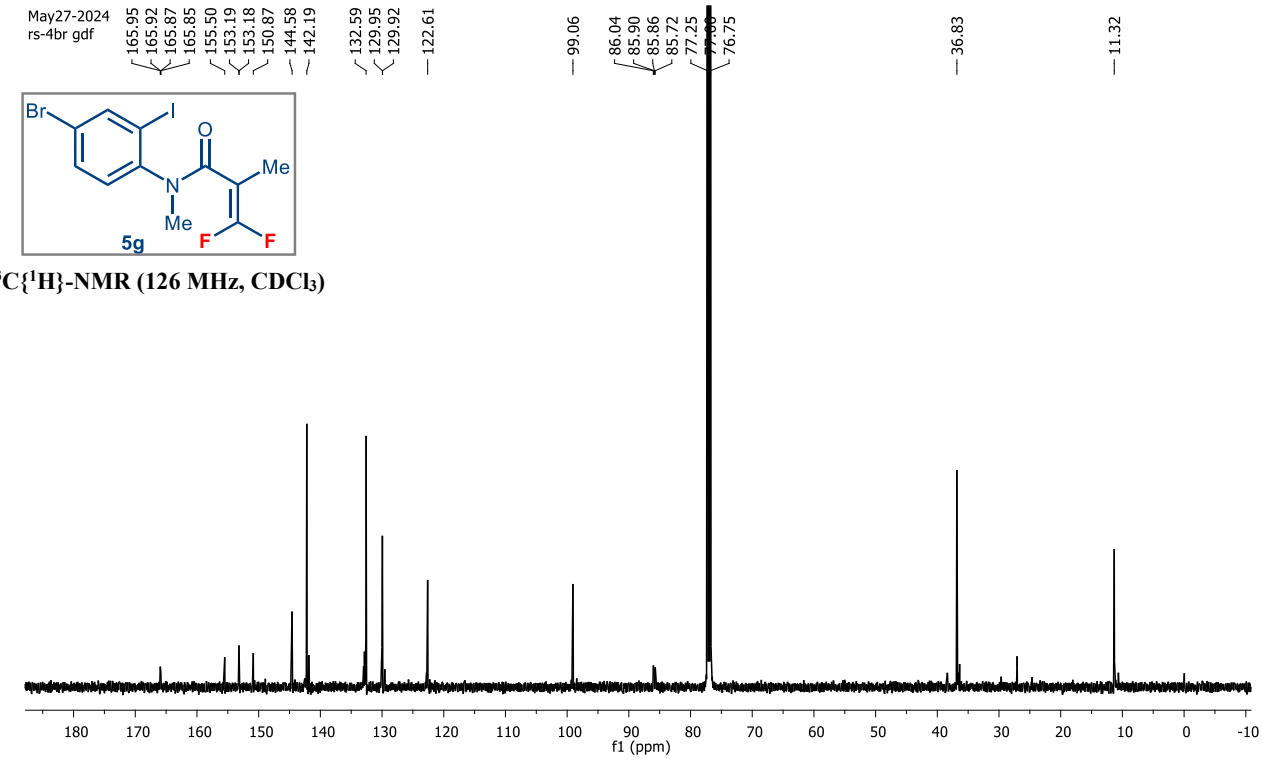
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

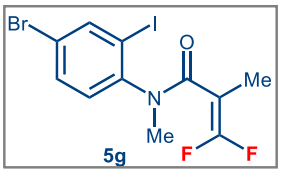


^{1}H-NMR (500 MHz, $CDCl_3$)



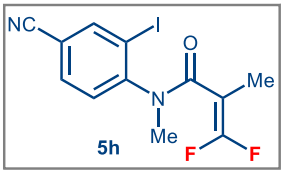
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

RS-4BR GDF P3
19F

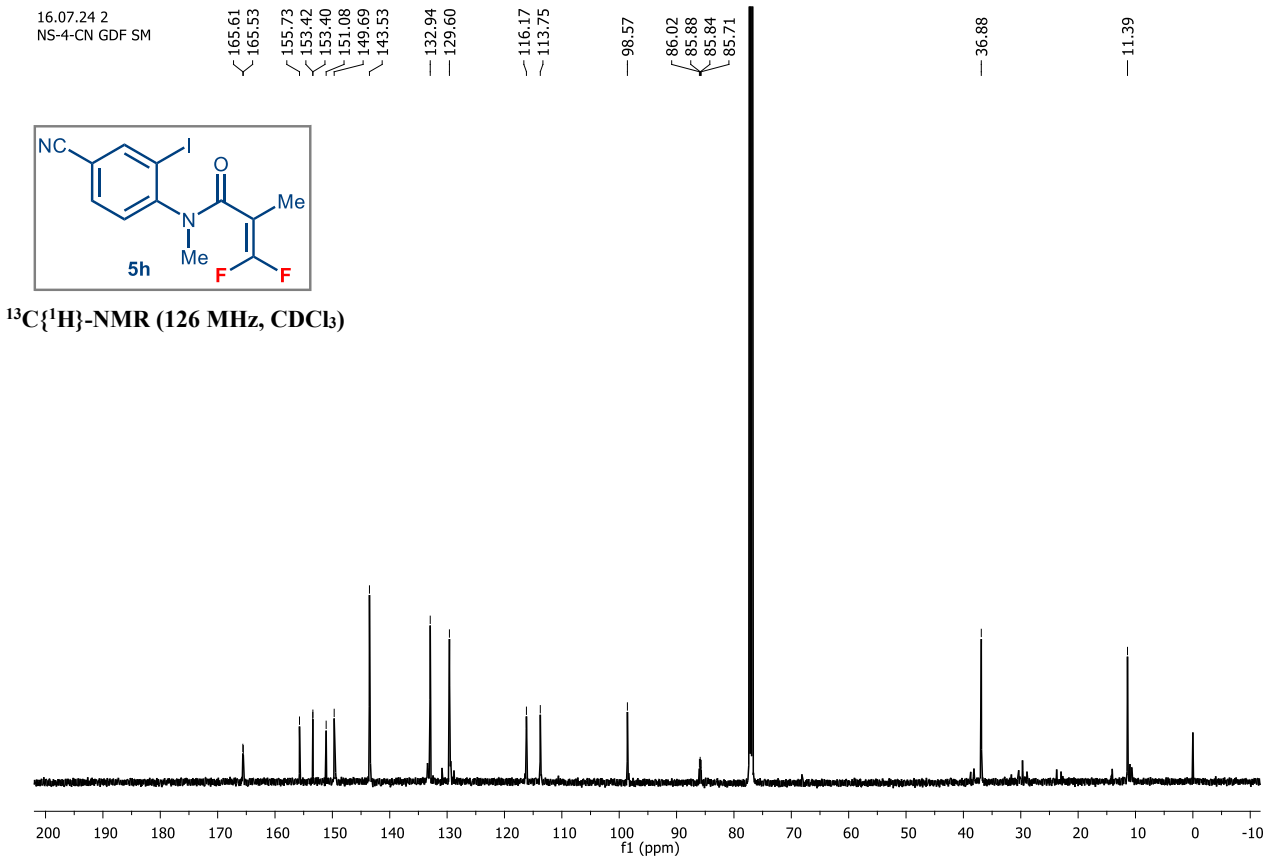


^{19}F-NMR (377 MHz, $CDCl_3$)

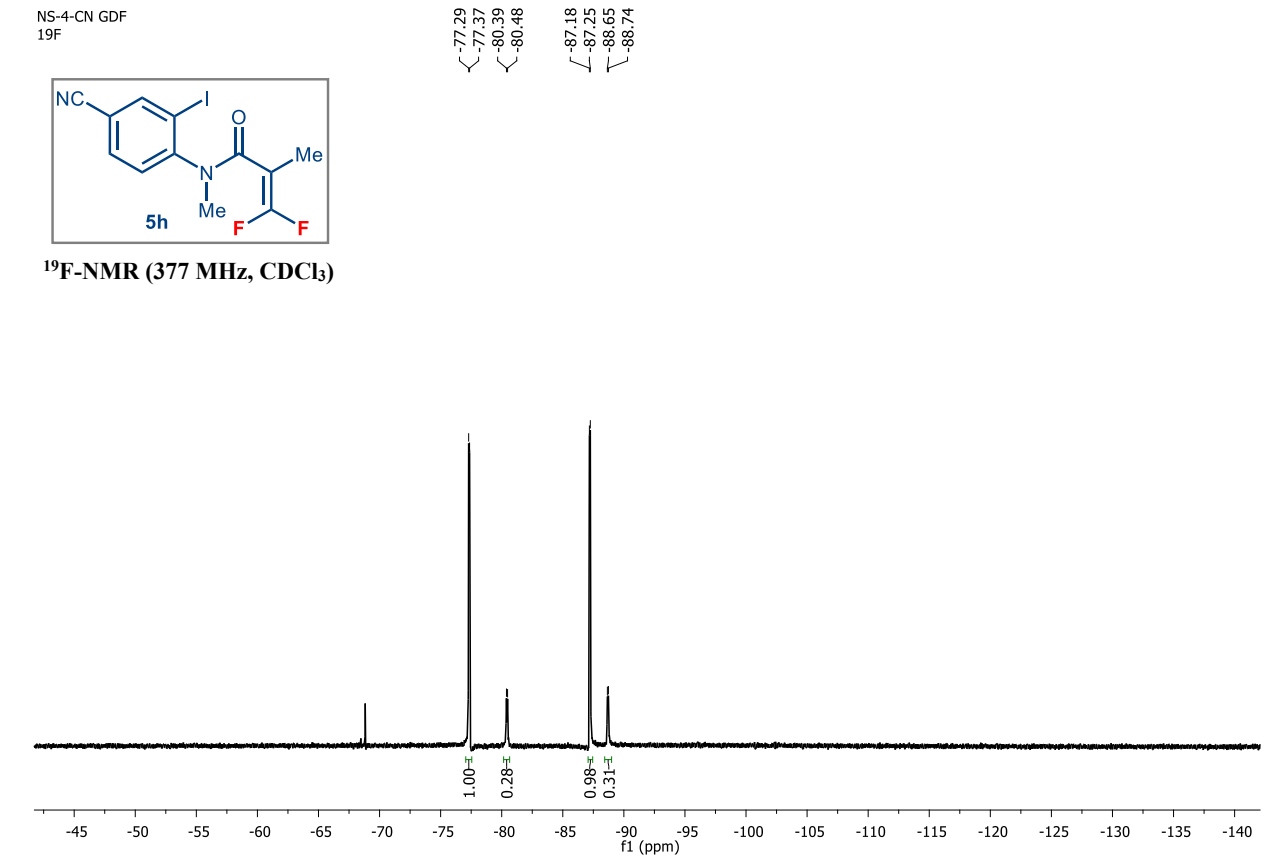
16.07.24 2
NS-4-CN GDF SM



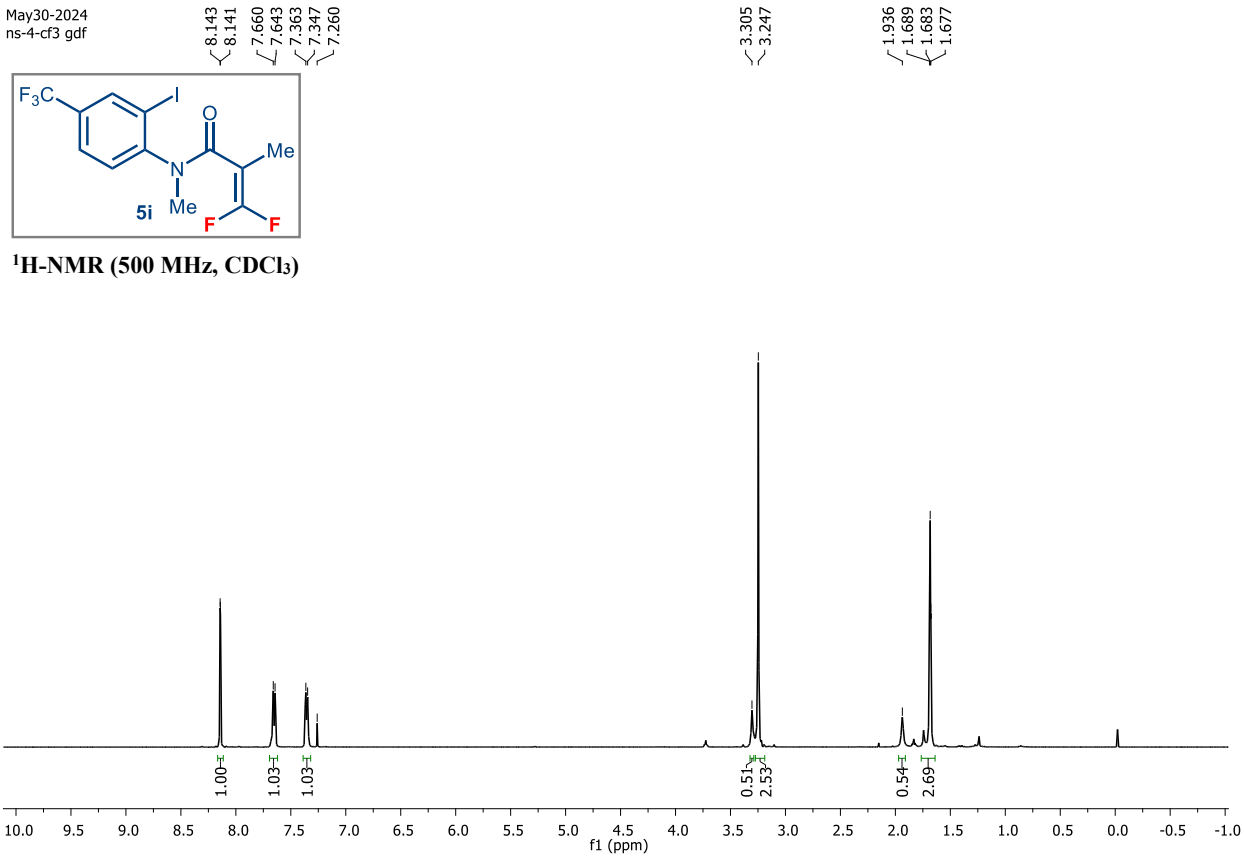
^{1}H-NMR (500 MHz, $CDCl_3$)



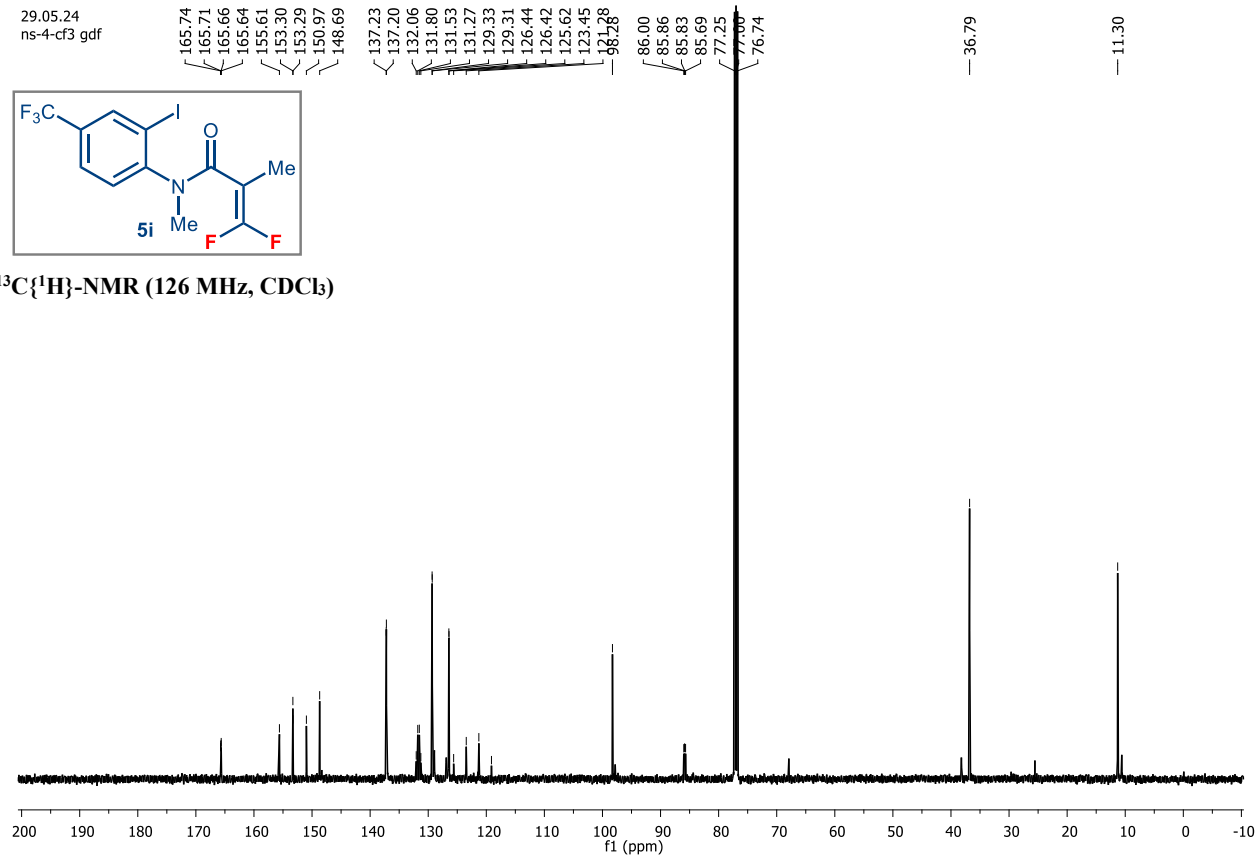
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

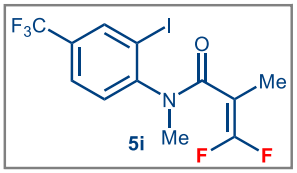


^{1}H-NMR (500 MHz, $CDCl_3$)



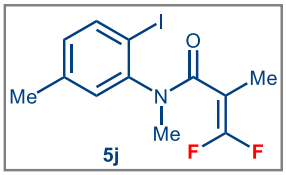
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS 4 CF3

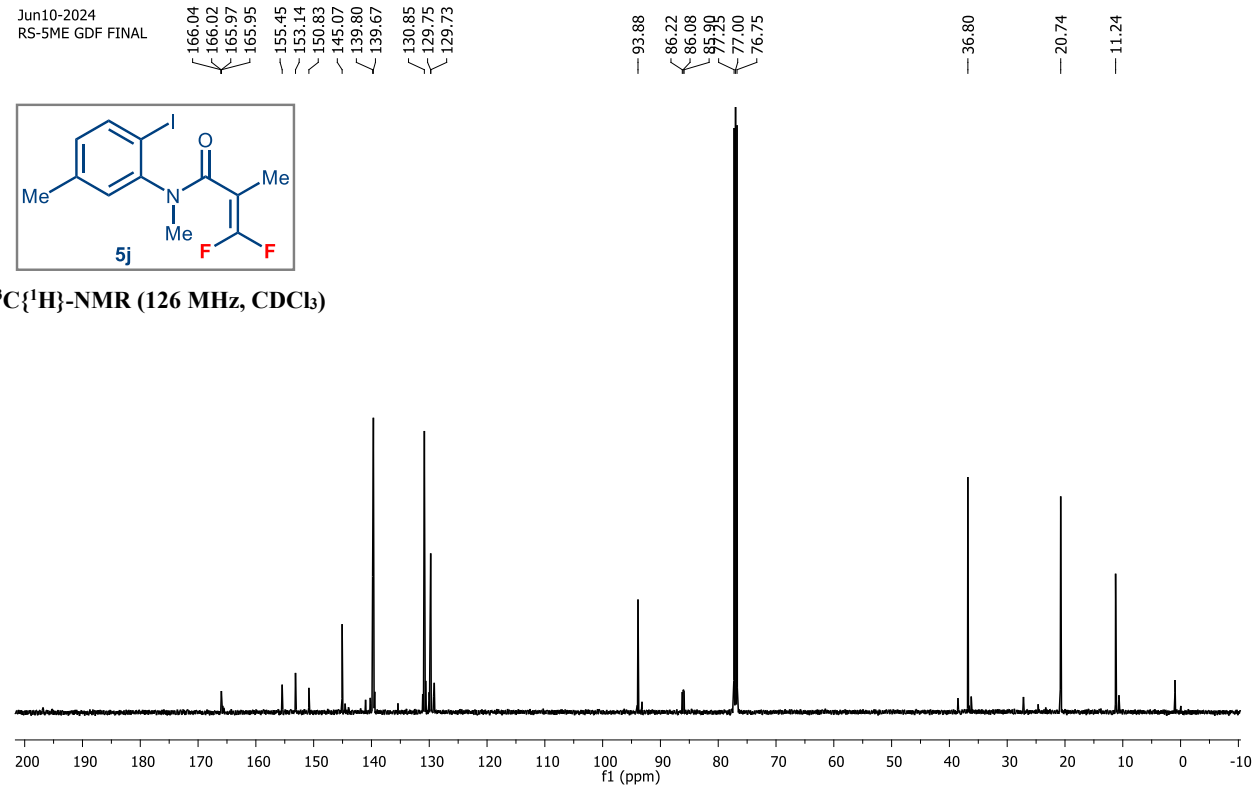


^{19}F-NMR (377 MHz, $CDCl_3$)

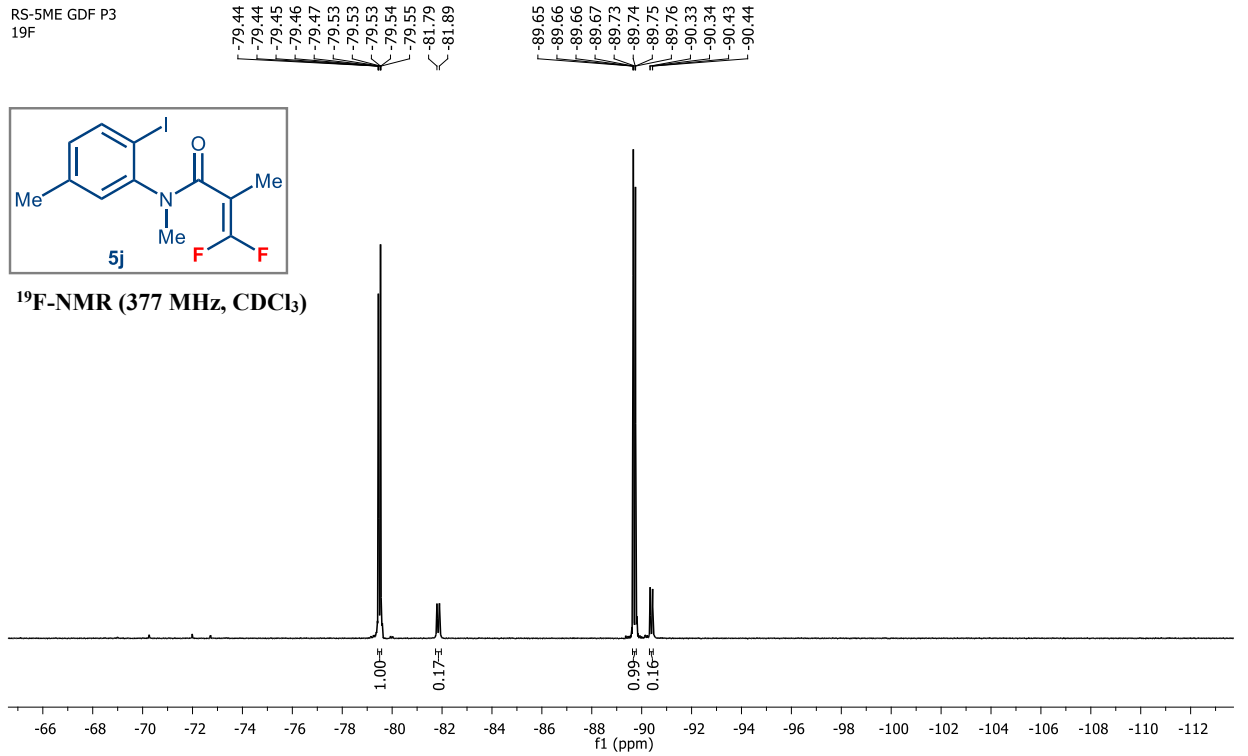
Jun10-2024
RS-5ME GDF FINAL



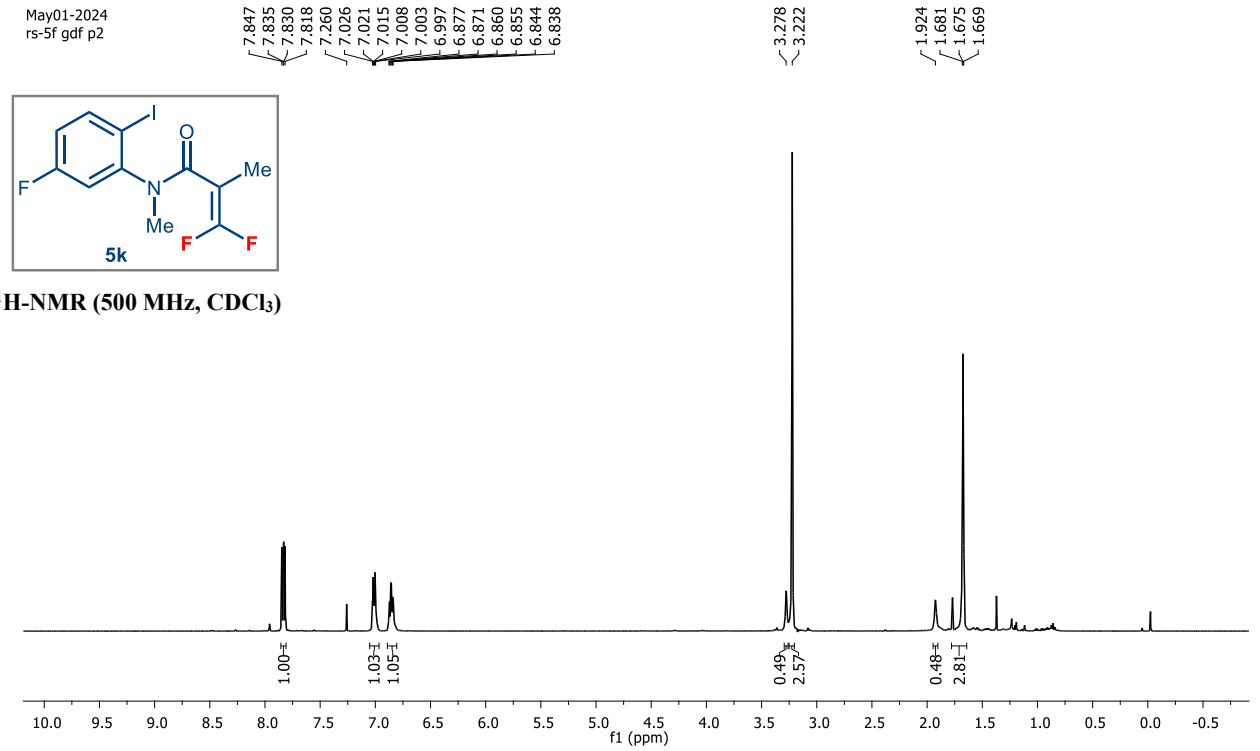
^{1}H-NMR (500 MHz, $CDCl_3$)



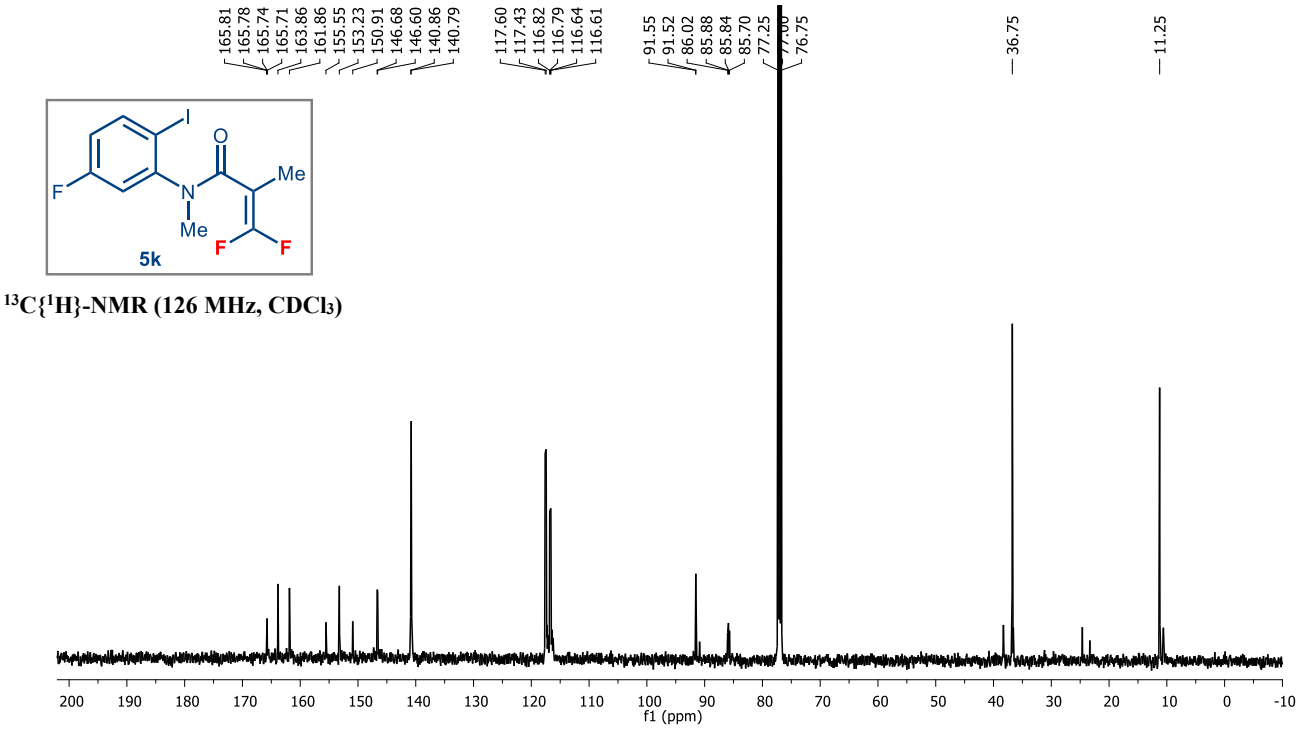
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



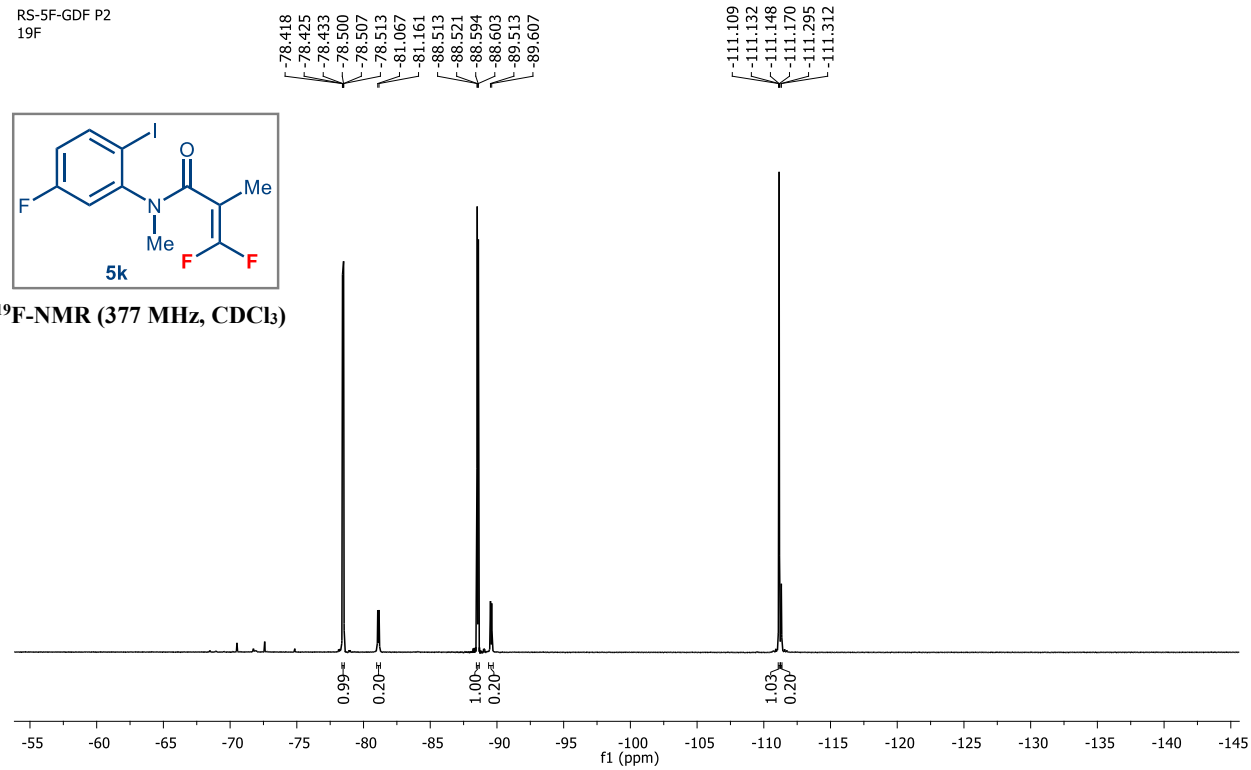
^{19}F-NMR (377 MHz, $CDCl_3$)



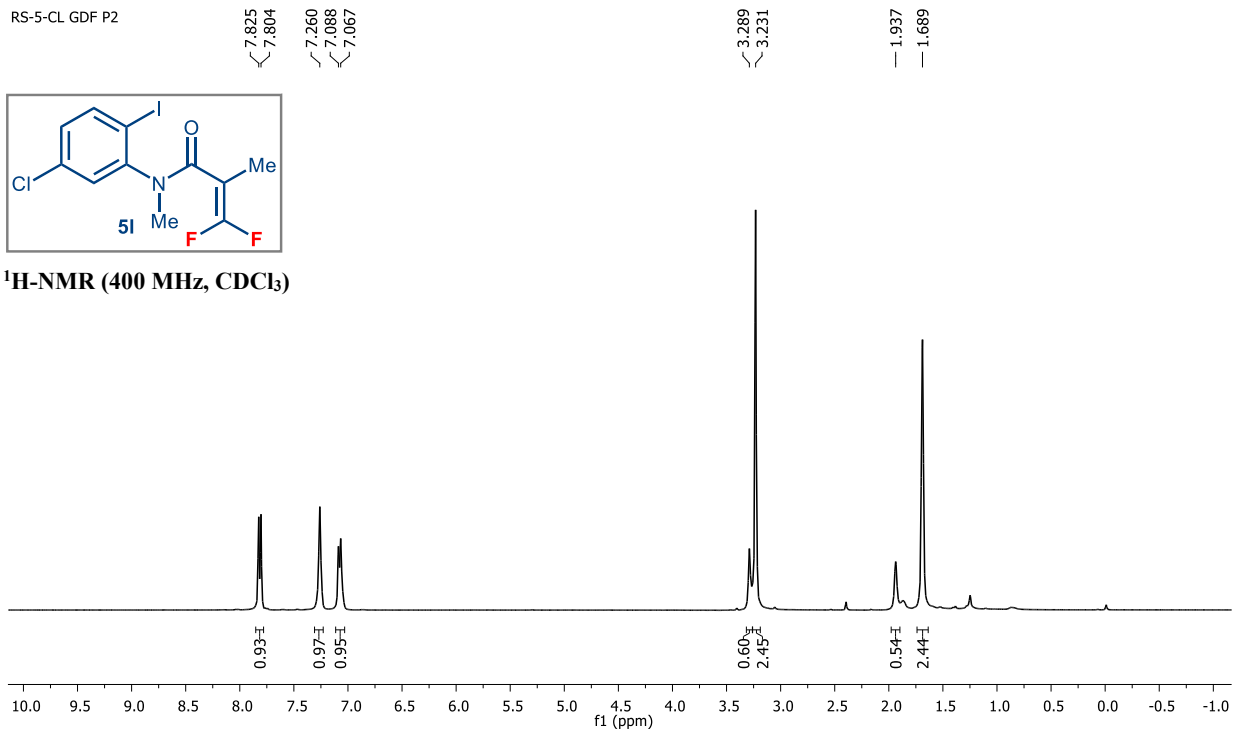
^{1}H-NMR (500 MHz, $CDCl_3$)



^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

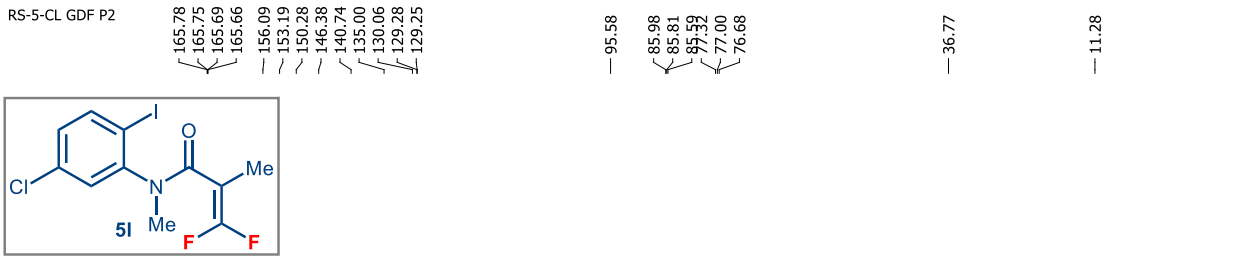


^{19}F-NMR (377 MHz, $CDCl_3$)

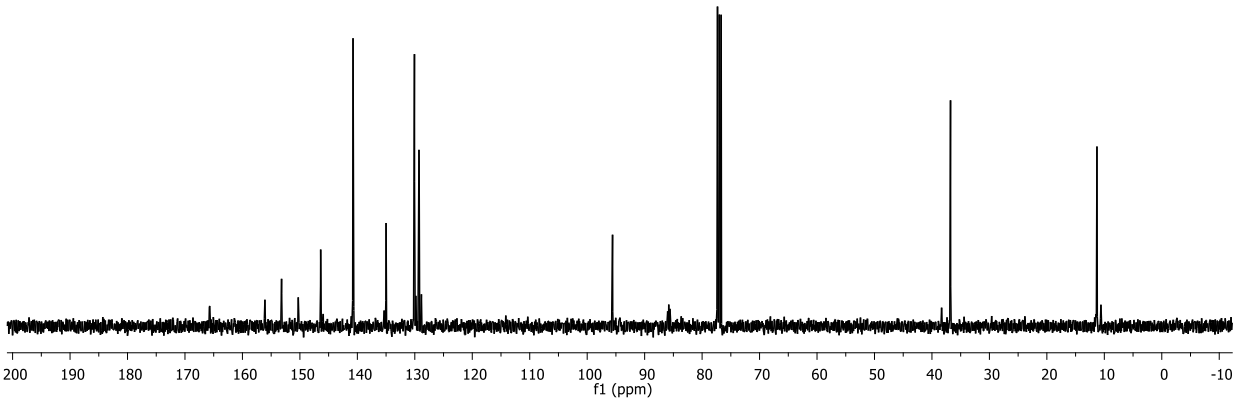


^{1}H-NMR (400 MHz, $CDCl_3$)

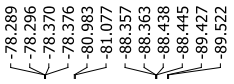
RS-5-CL GDF P2

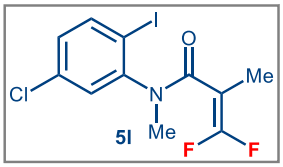


$^{13}C\{^{1}H\}$-NMR (101 MHz, $CDCl_3$)

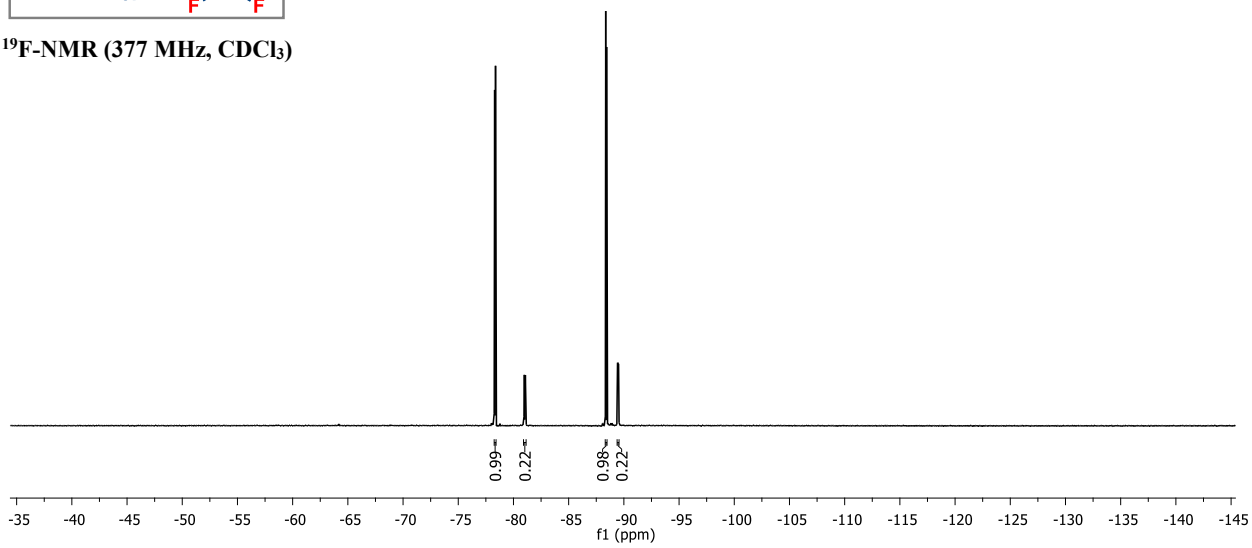


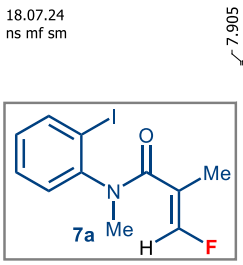
RS-5-CL GDF P2
19F



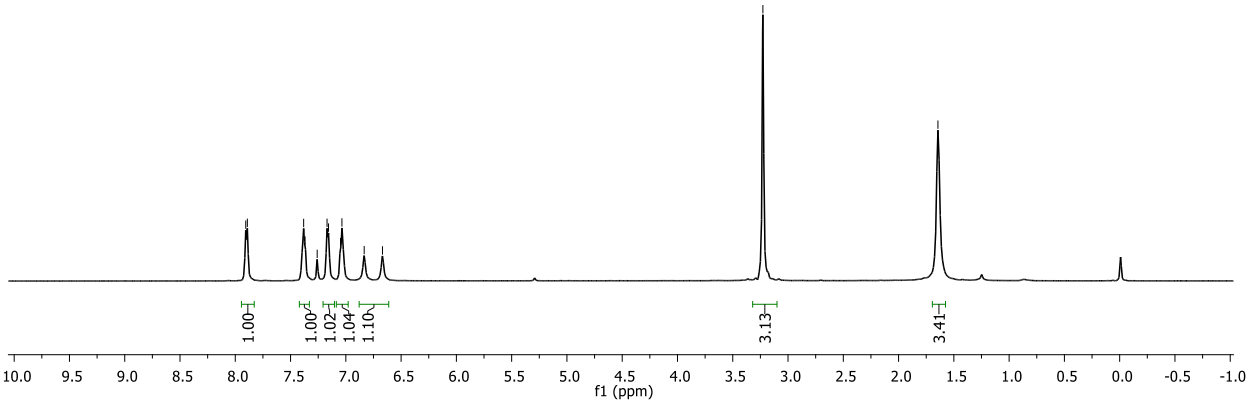


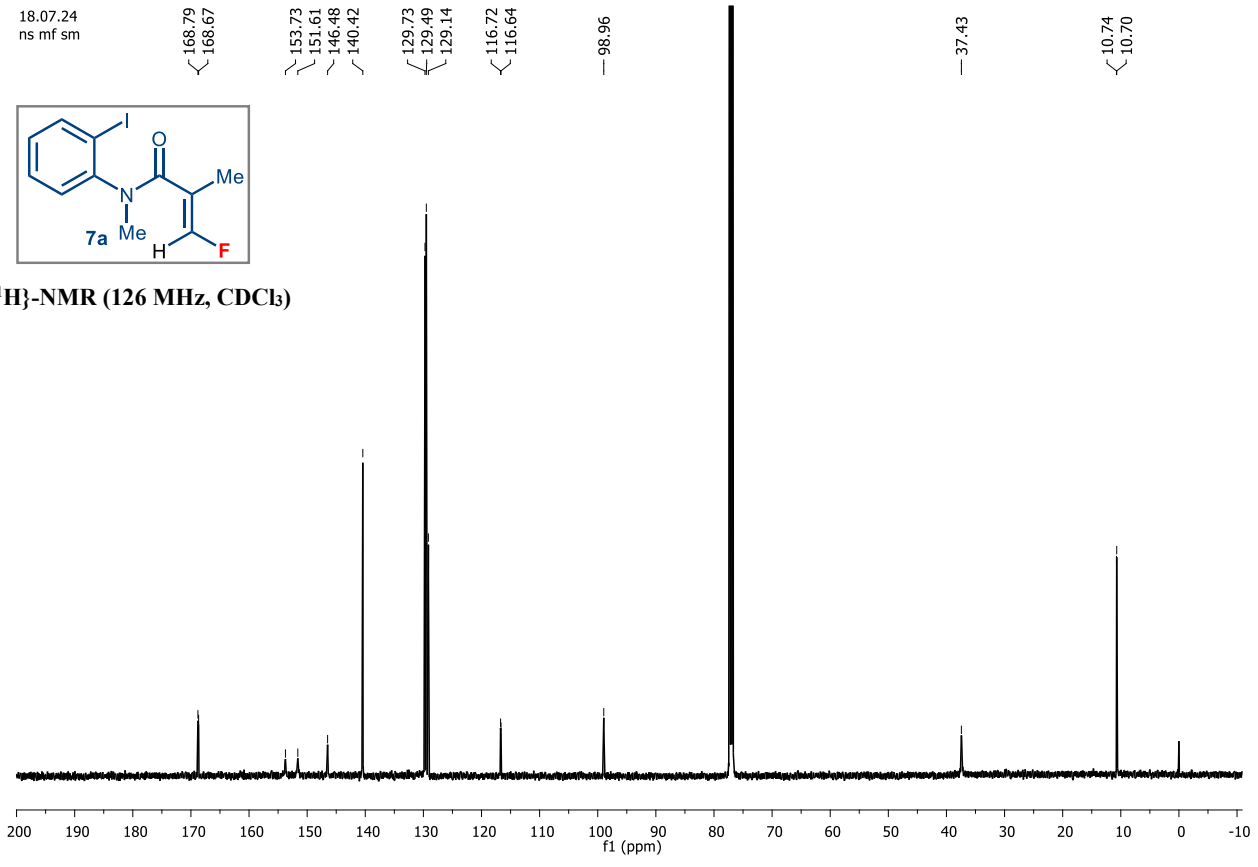
^{19}F-NMR (377 MHz, $CDCl_3$)



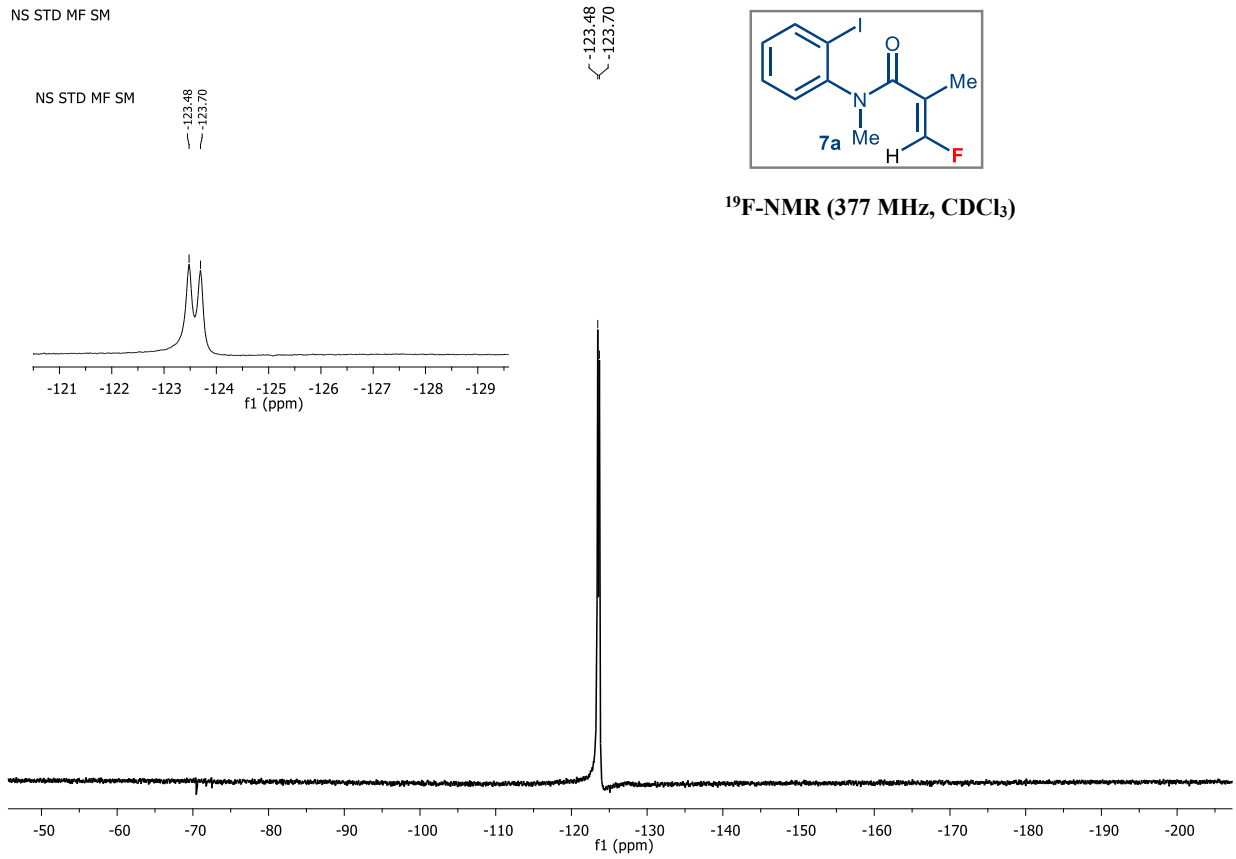


^{1}H-NMR (500 MHz, $CDCl_3$)

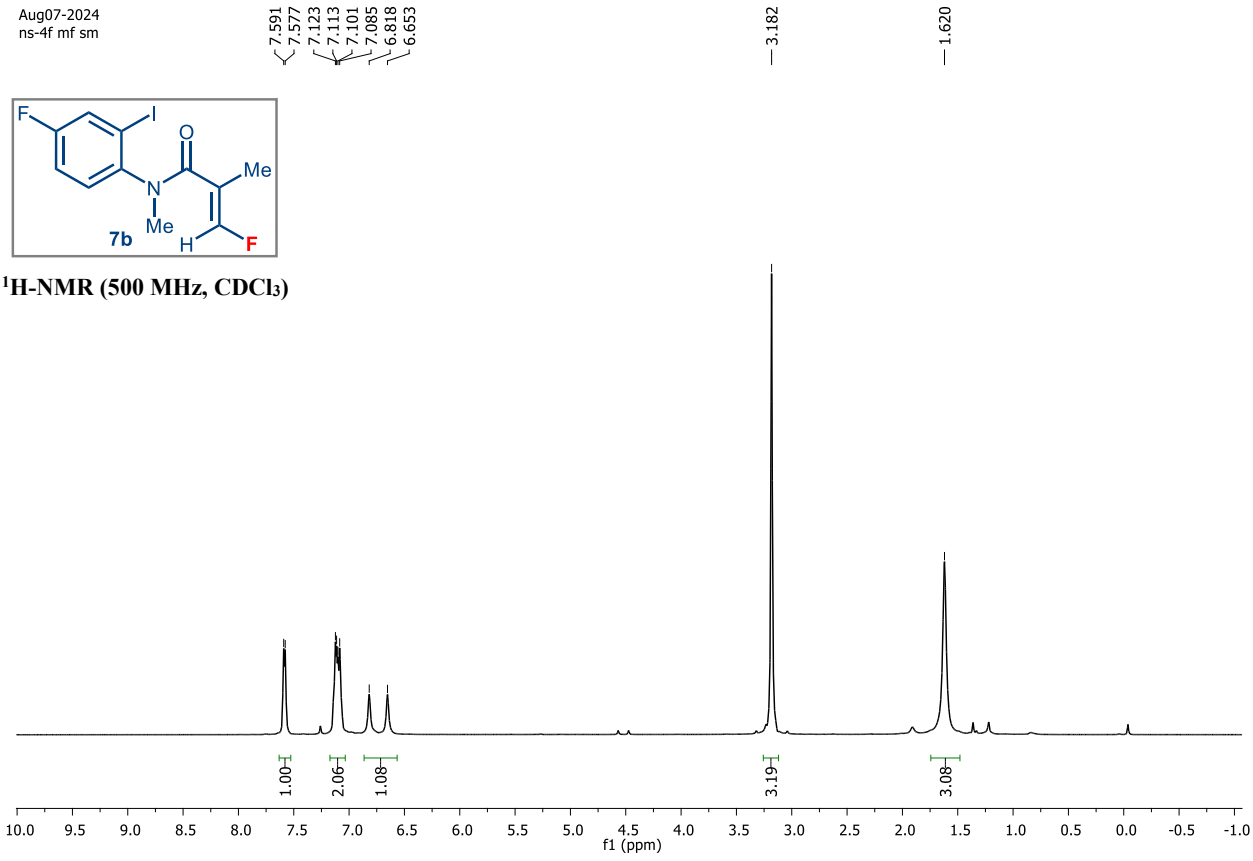




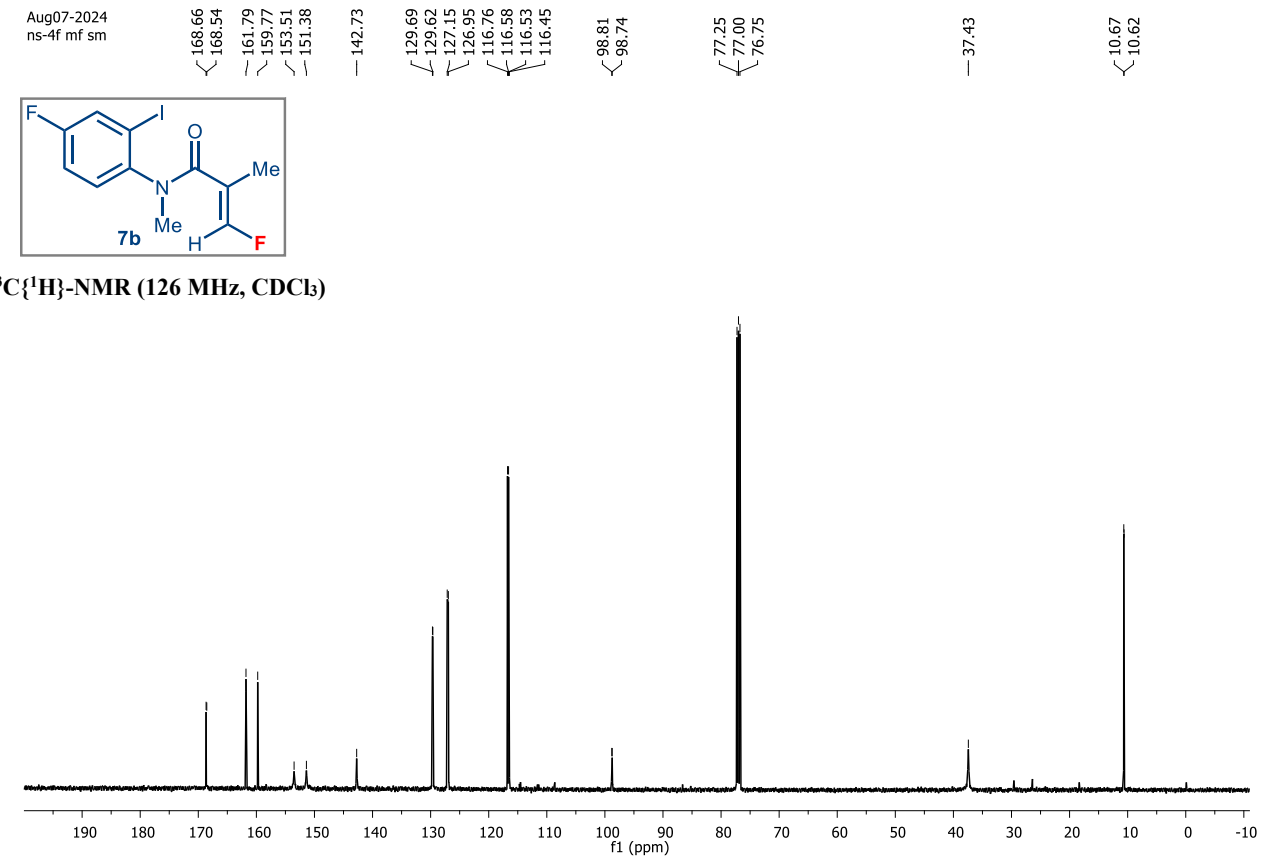
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)



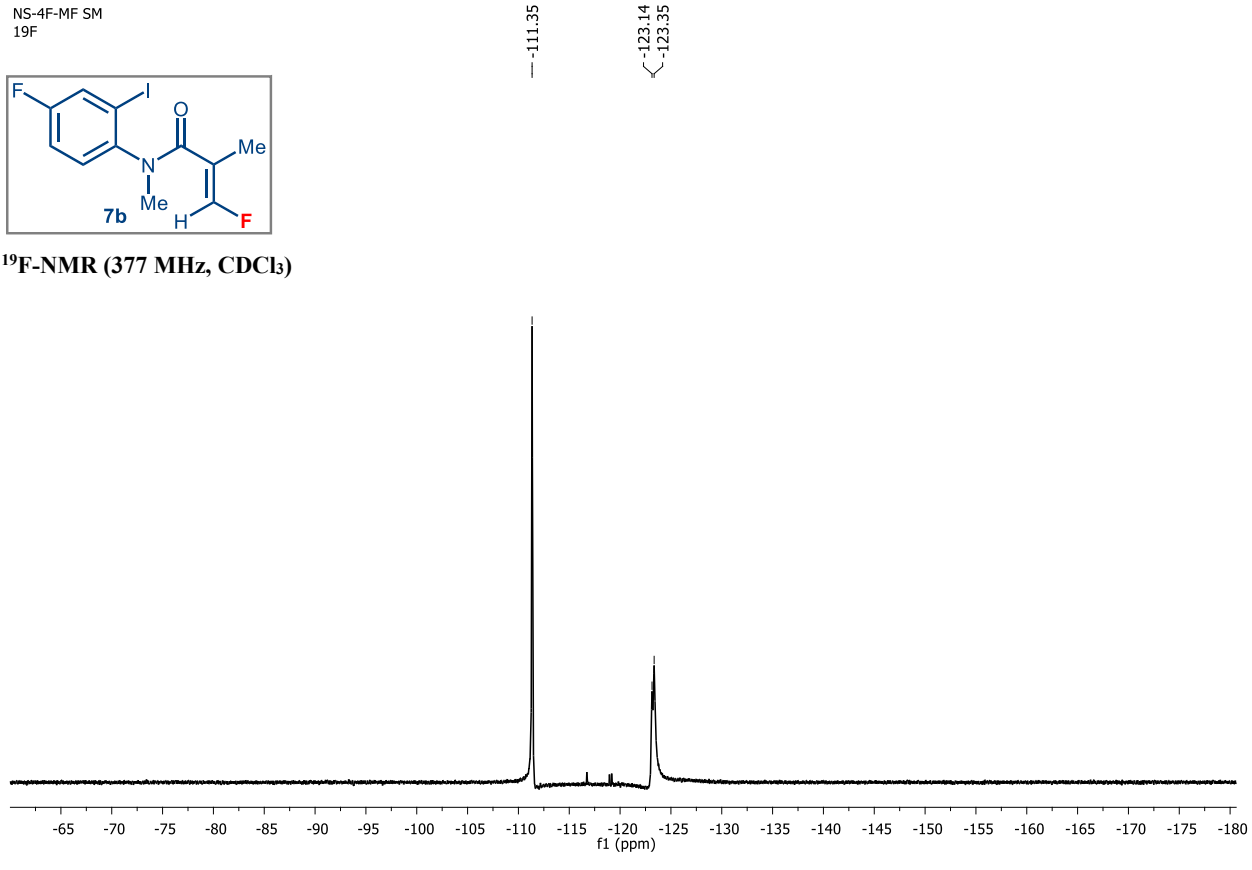
^{19}F-NMR (377 MHz, $CDCl_3$)



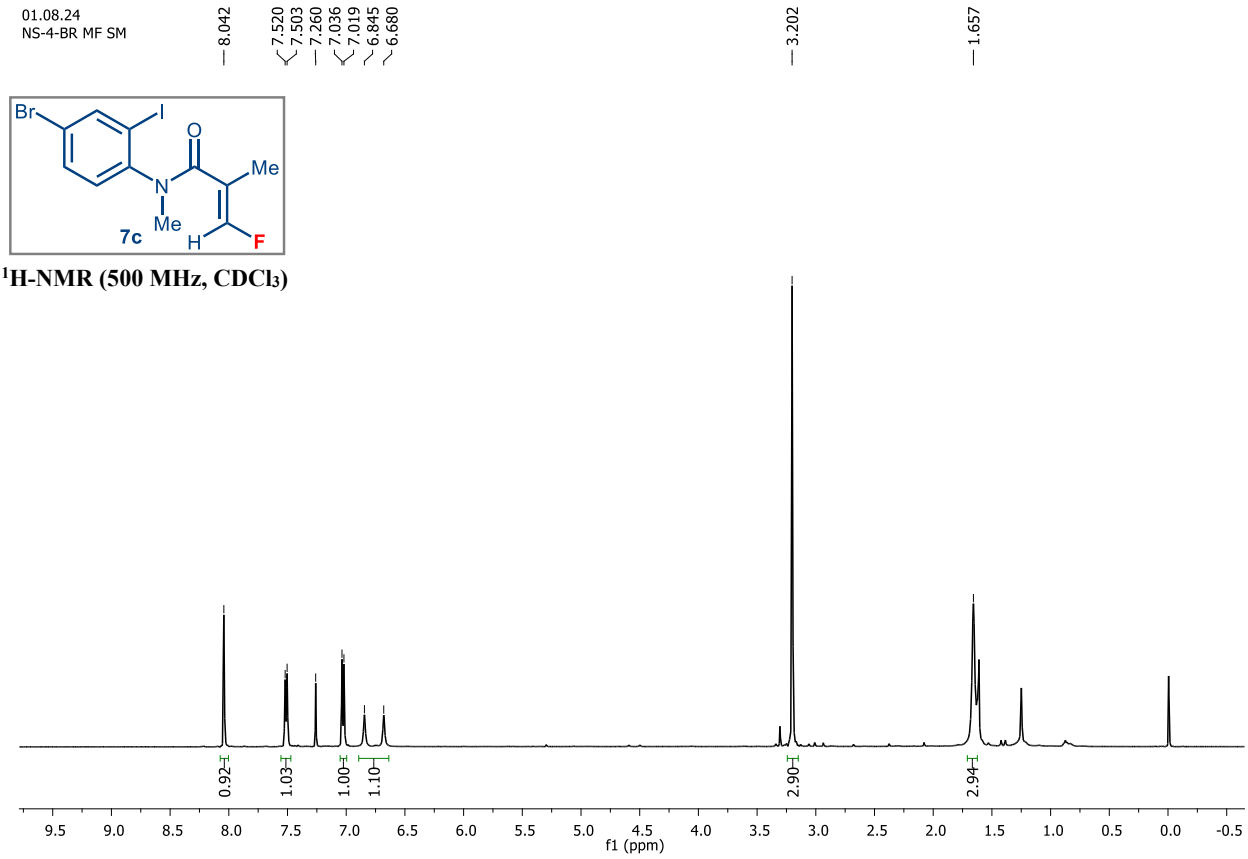
^{1}H-NMR (500 MHz, $CDCl_3$)



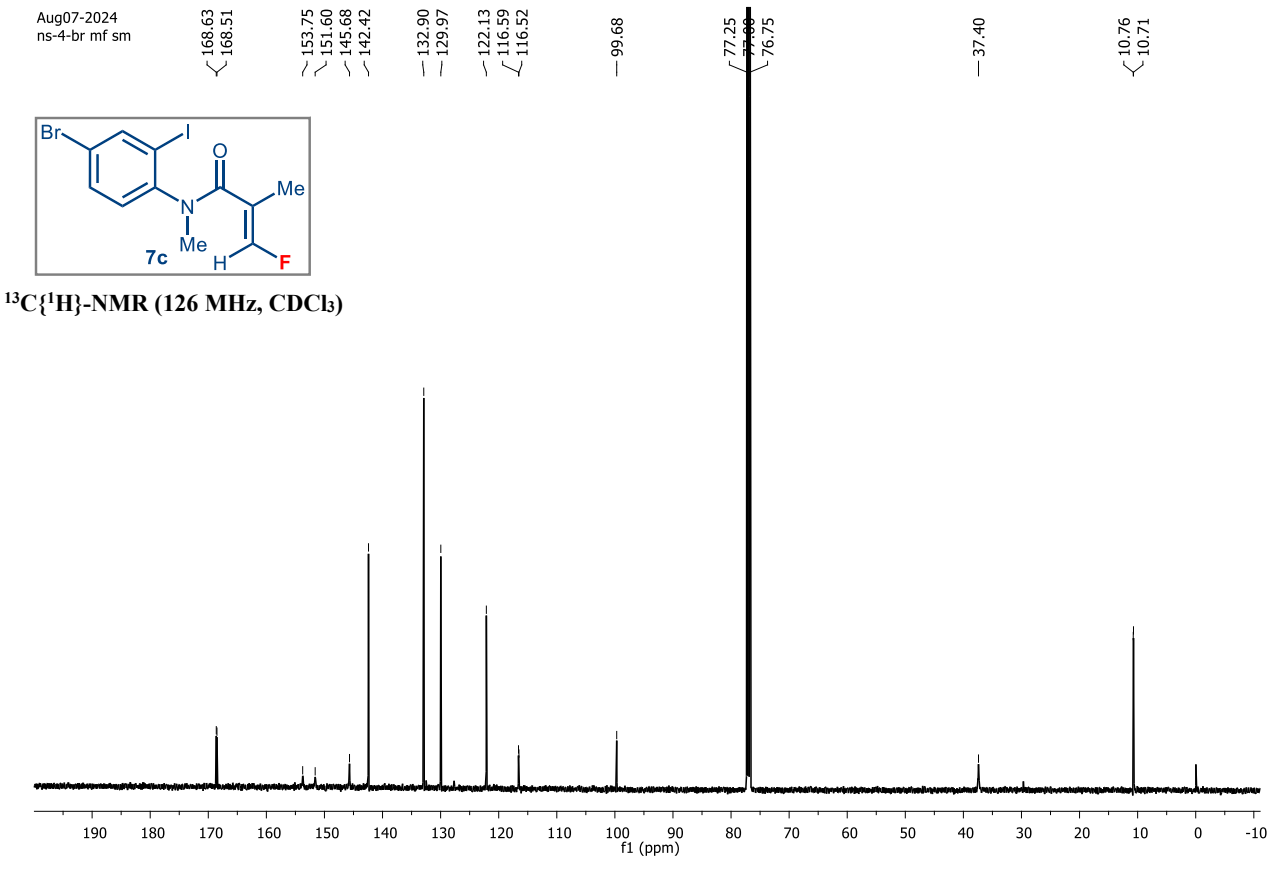
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

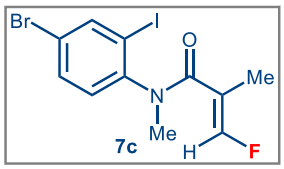


^{1}H-NMR (500 MHz, $CDCl_3$)



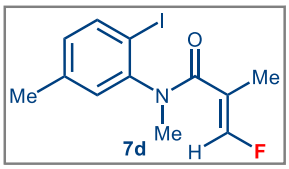
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

4-br

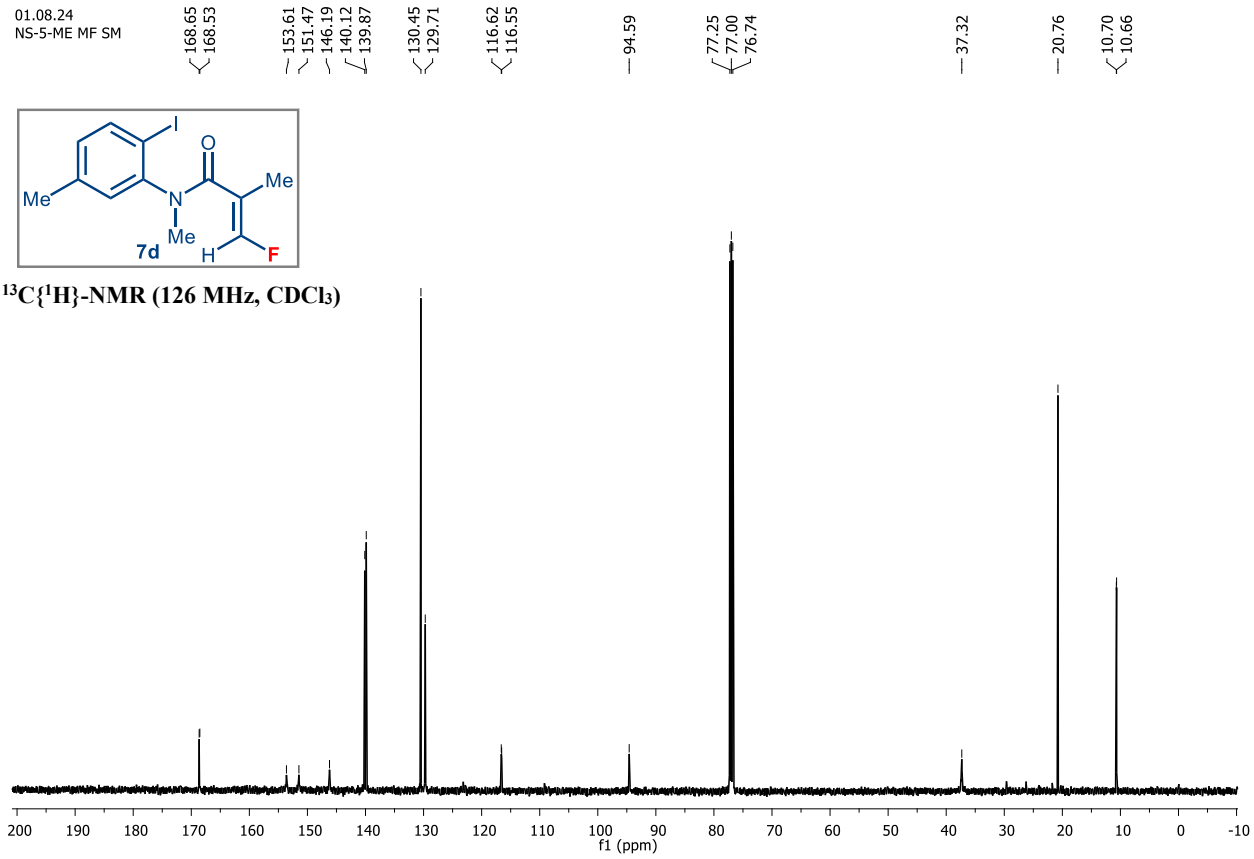


^{19}F-NMR (377 MHz, $CDCl_3$)

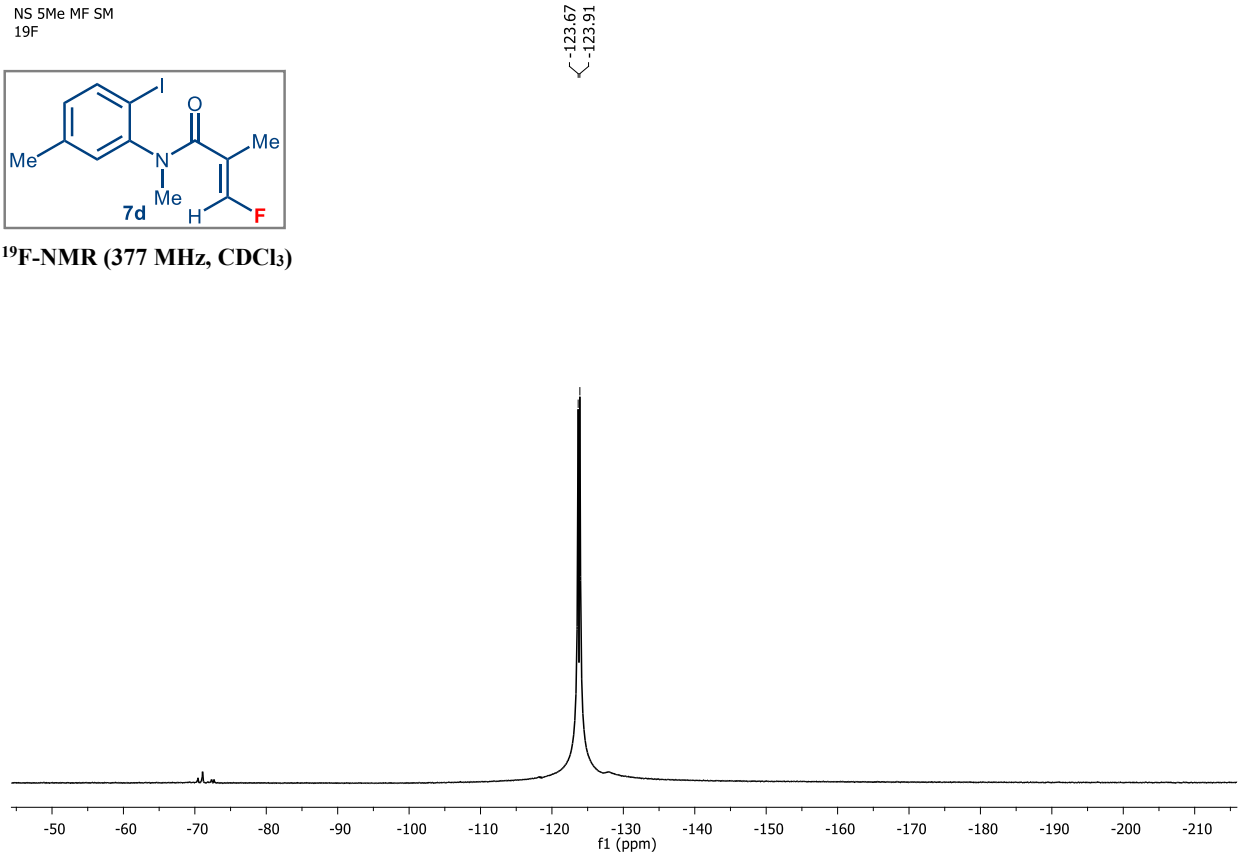
01.08.24
NS-5ME SOLIDE MF SM



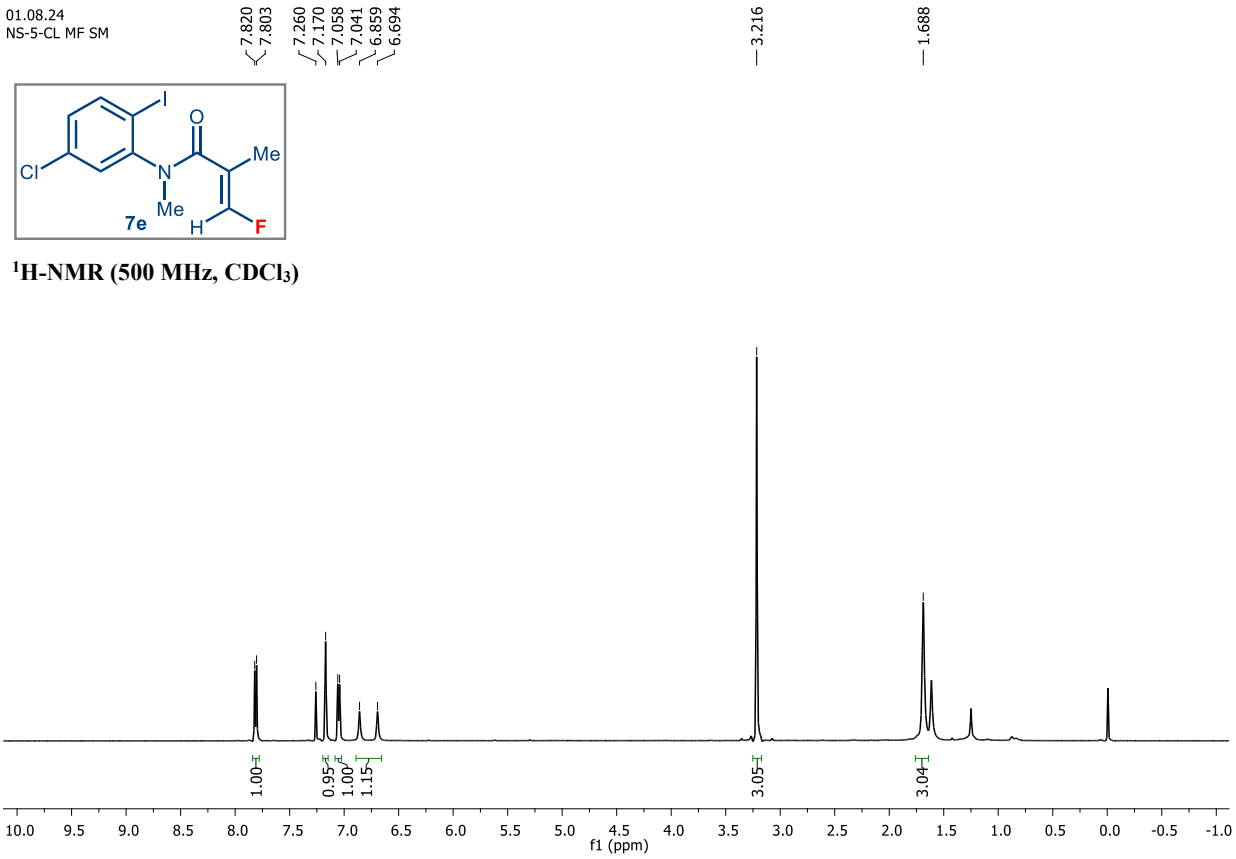
^{1}H-NMR (500 MHz, $CDCl_3$)



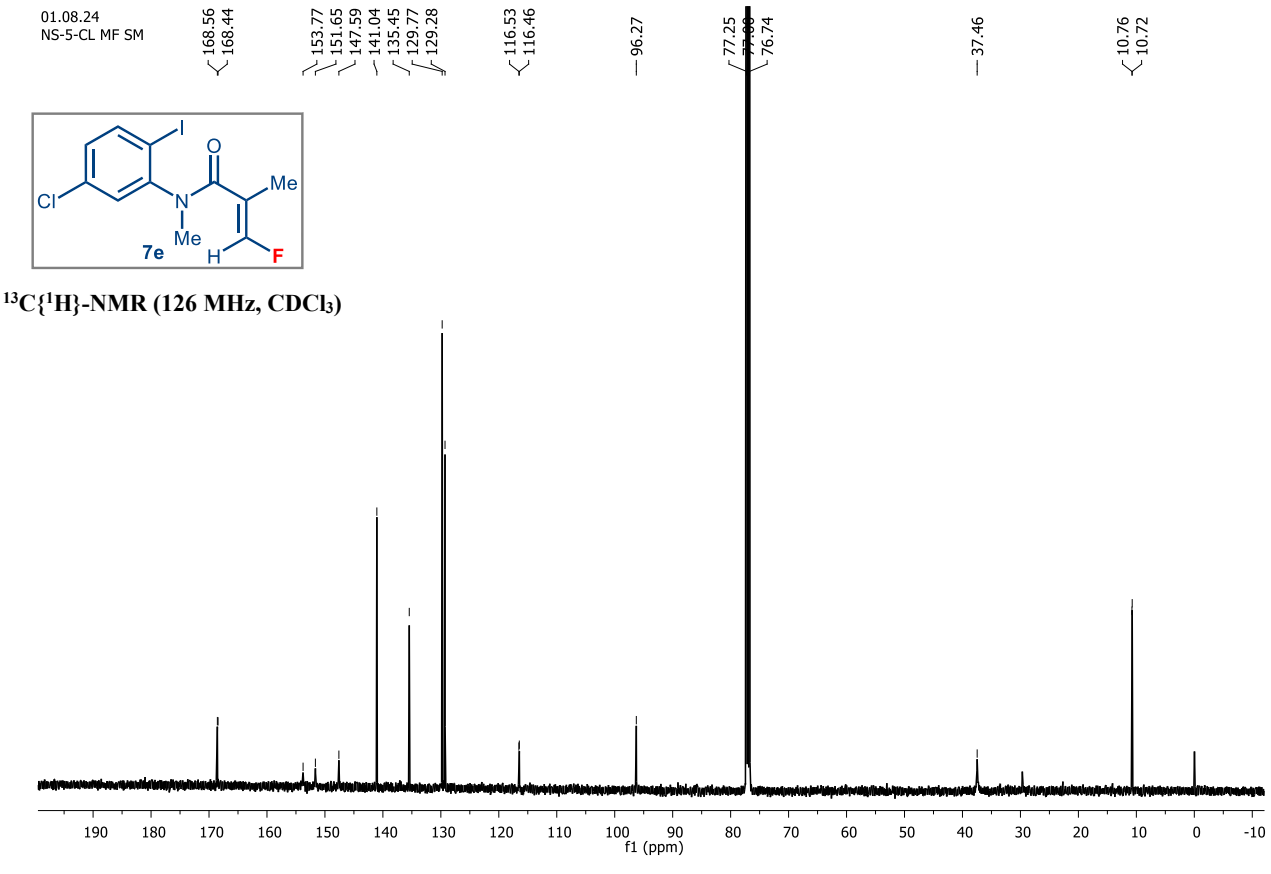
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

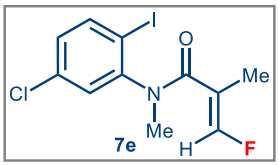


^{1}H-NMR (500 MHz, $CDCl_3$)



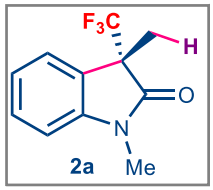
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-5-Cl-MF

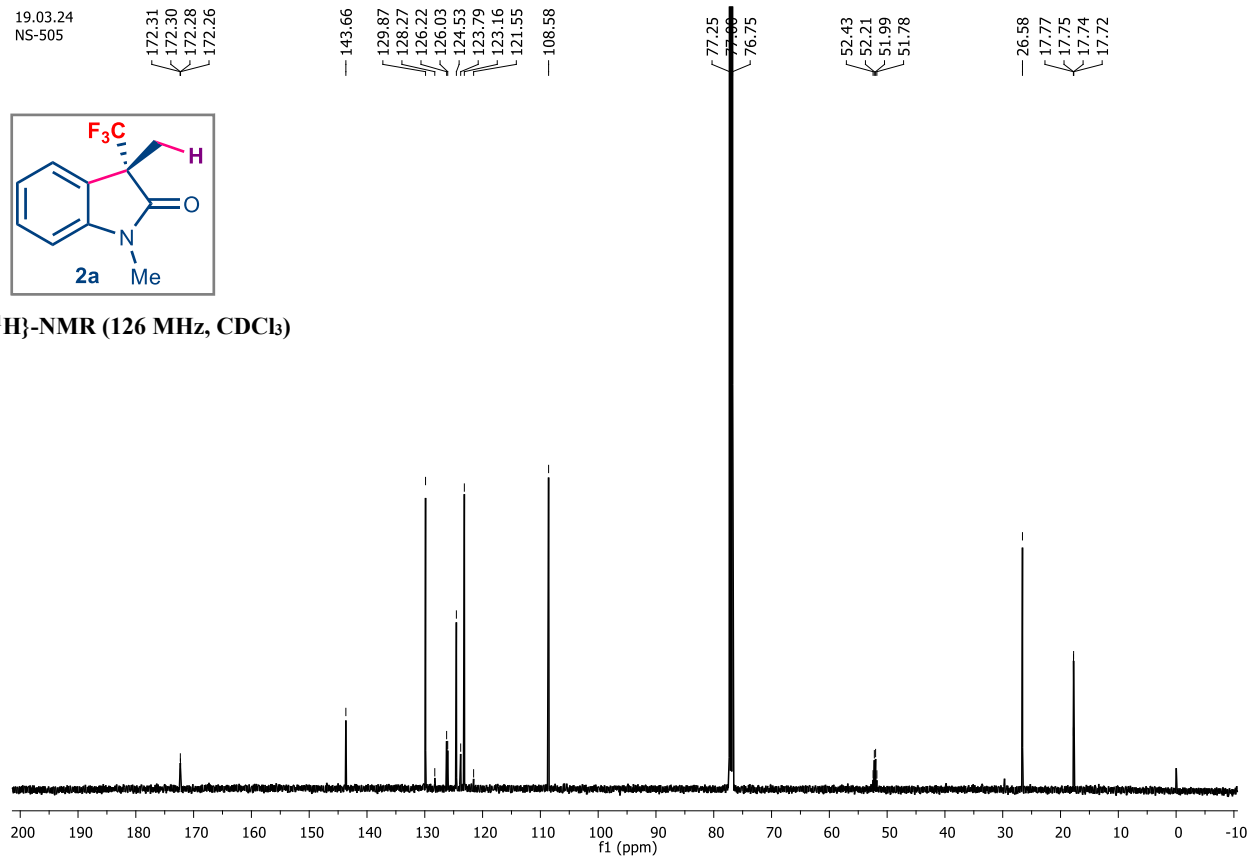


^{19}F-NMR (377 MHz, $CDCl_3$)

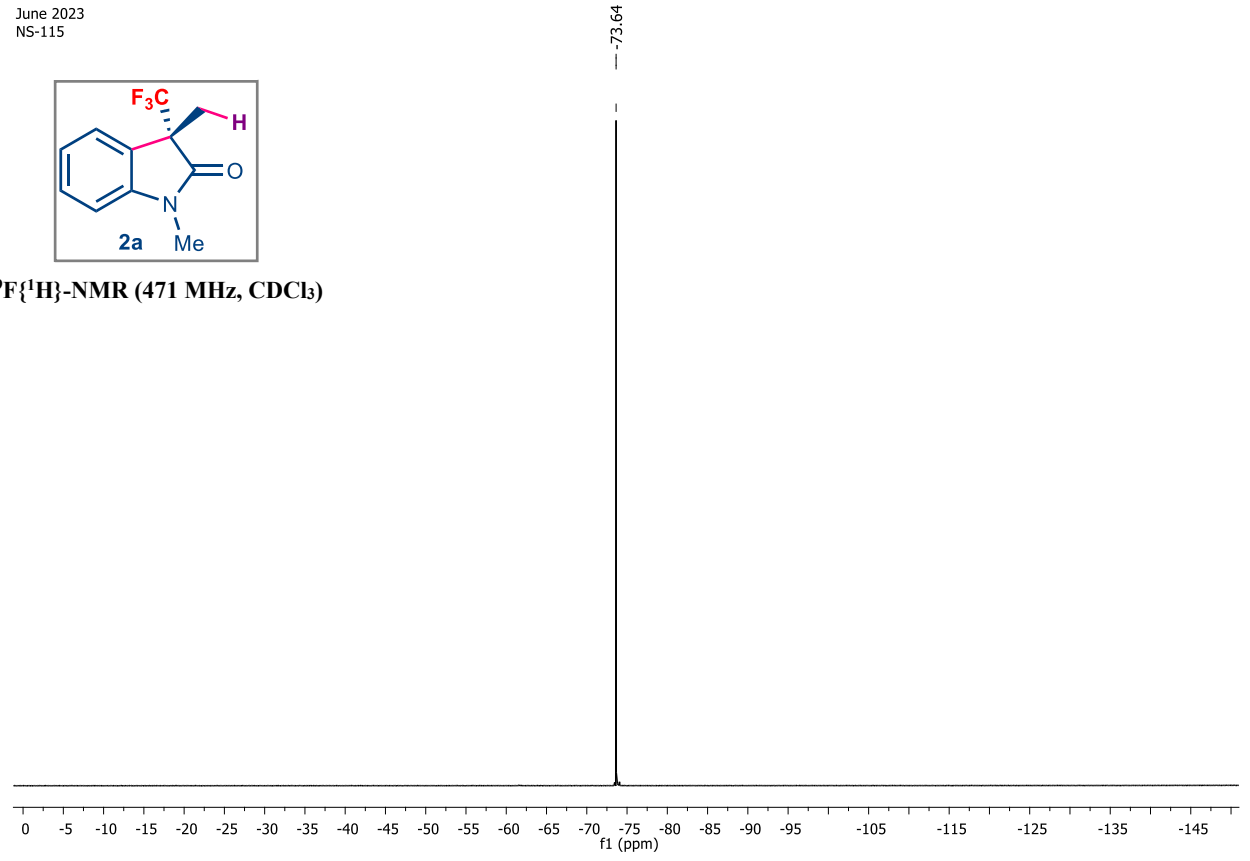
June 2023
NS-115



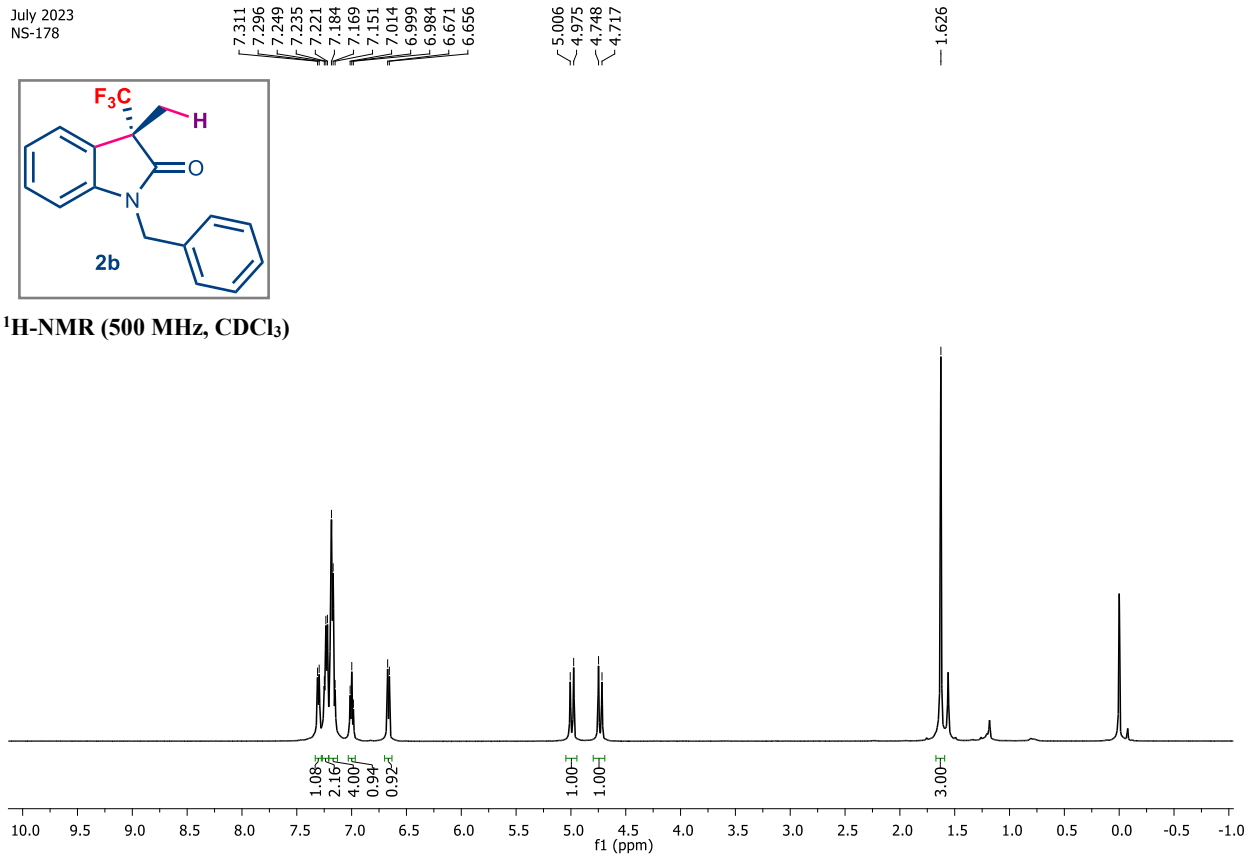
^{1}H-NMR (500 MHz, $CDCl_3$)



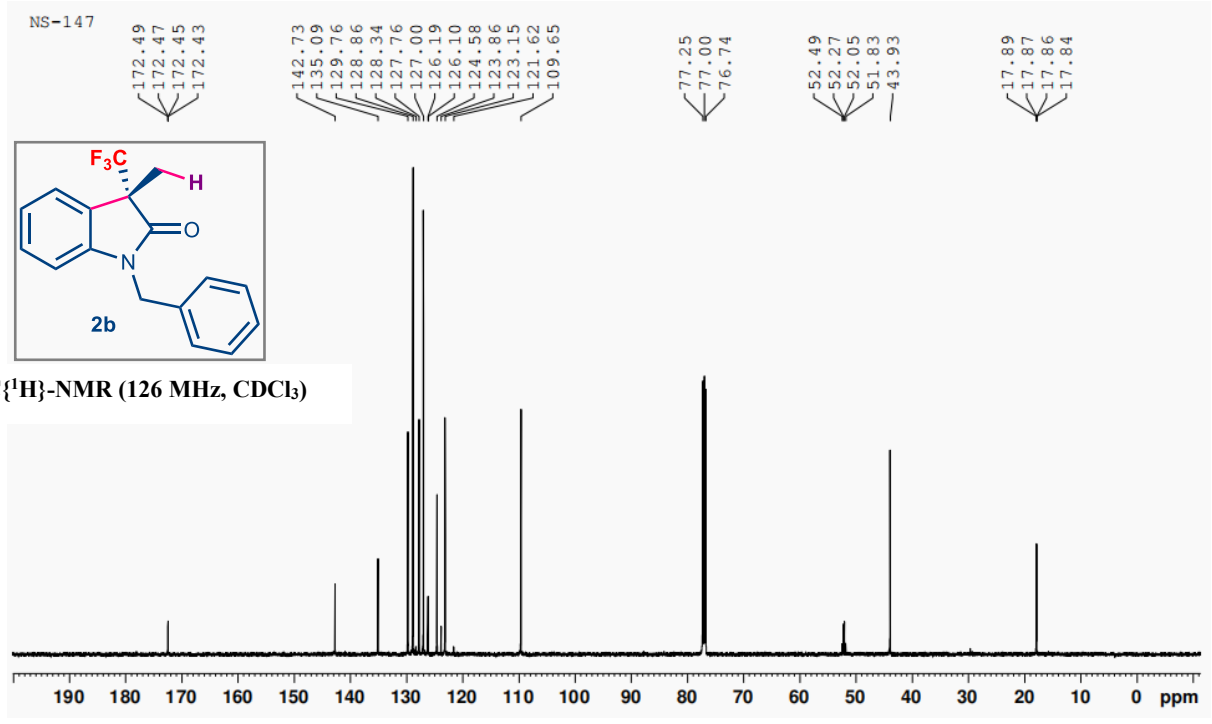
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

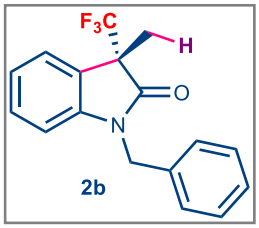


^{1}H-NMR (500 MHz, $CDCl_3$)



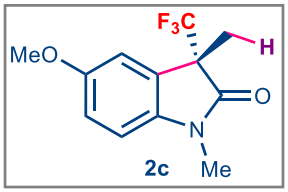
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

July 2023
NS-178

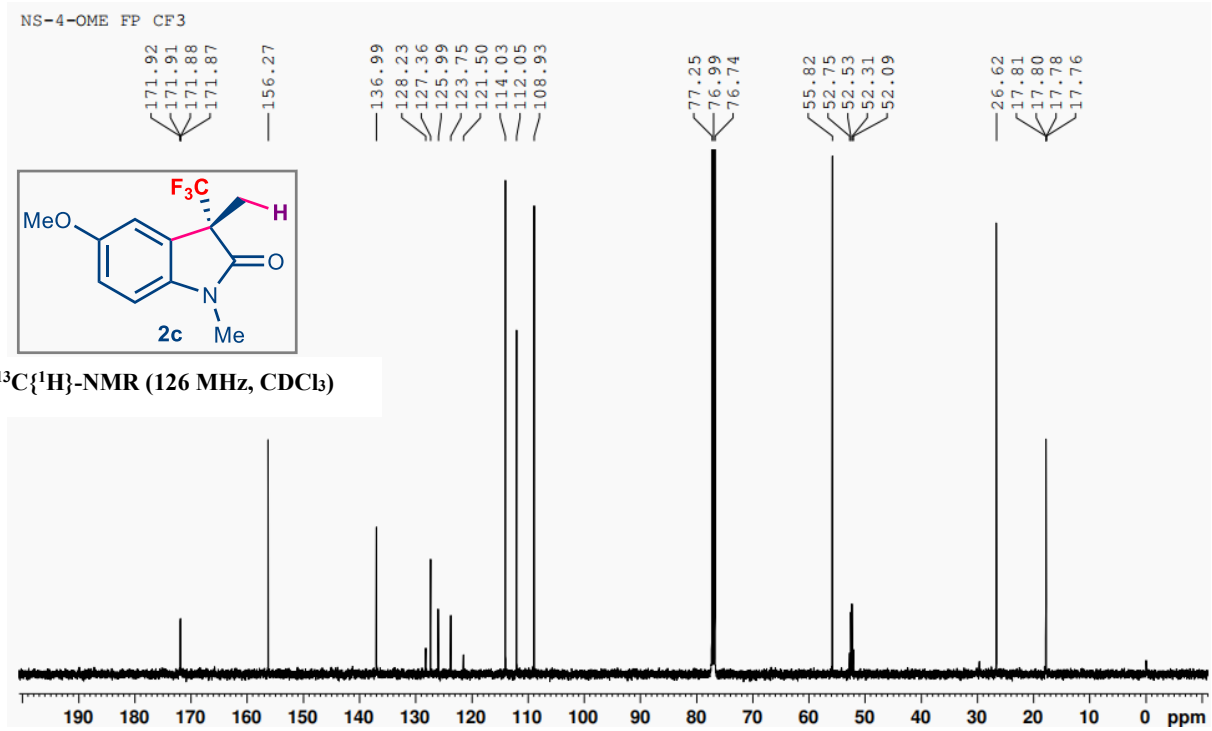


$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

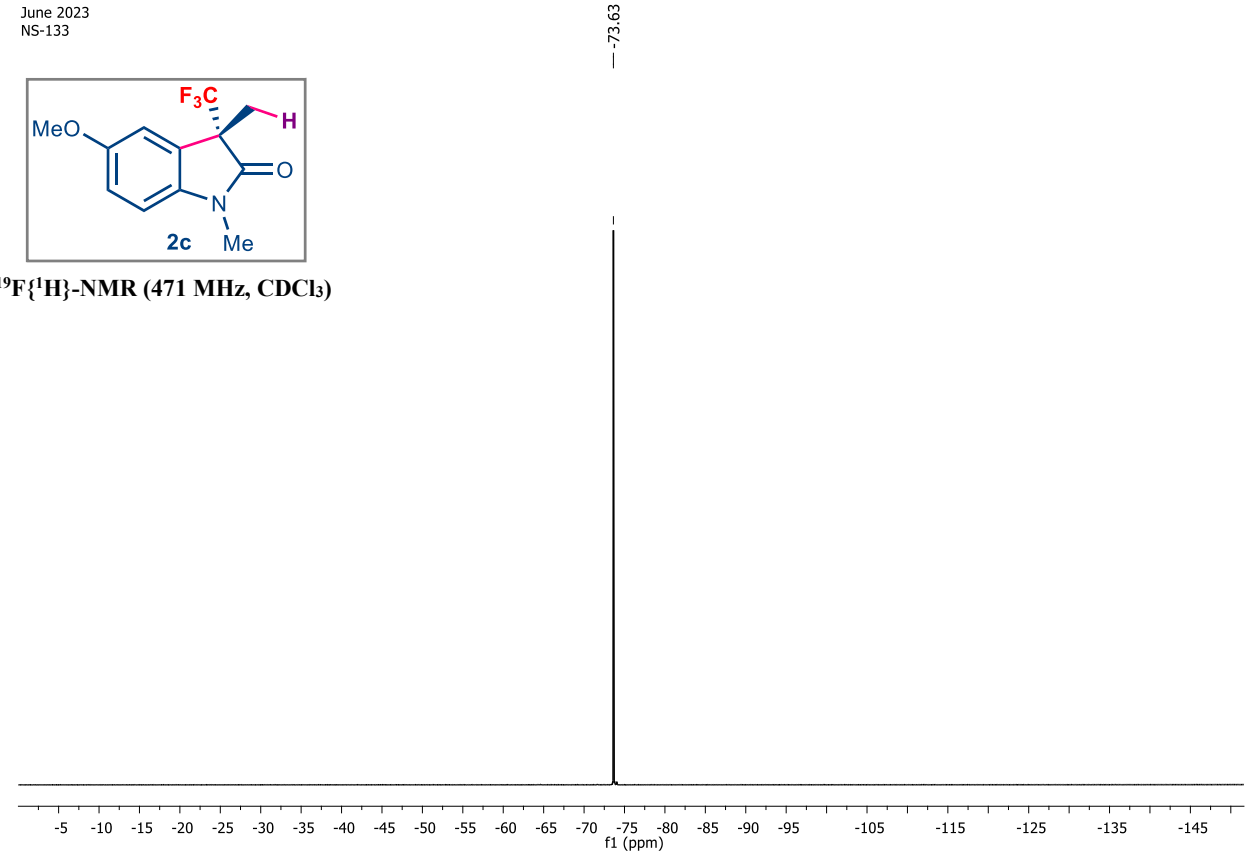
June 2023
NS-133



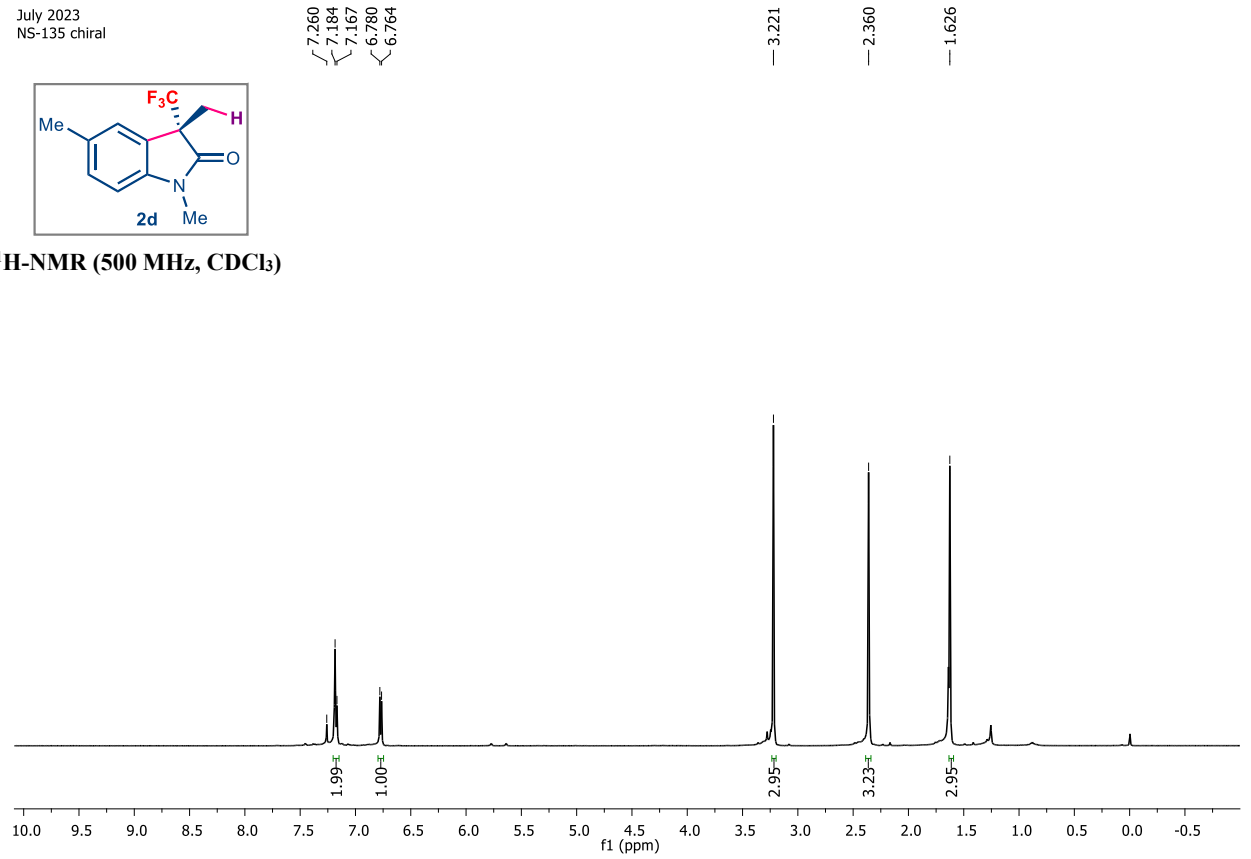
^{1}H-NMR (500 MHz, $CDCl_3$)



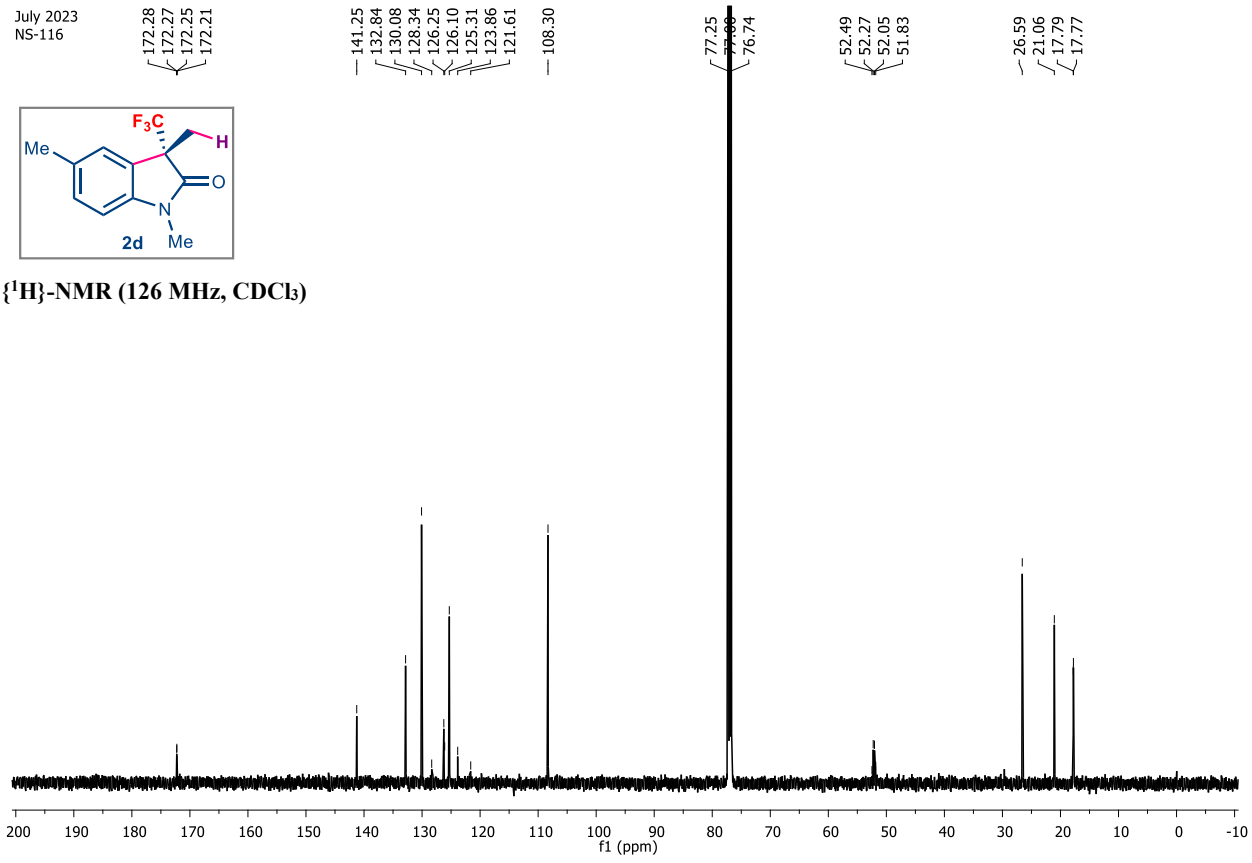
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

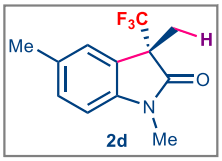


^{1}H-NMR (500 MHz, $CDCl_3$)

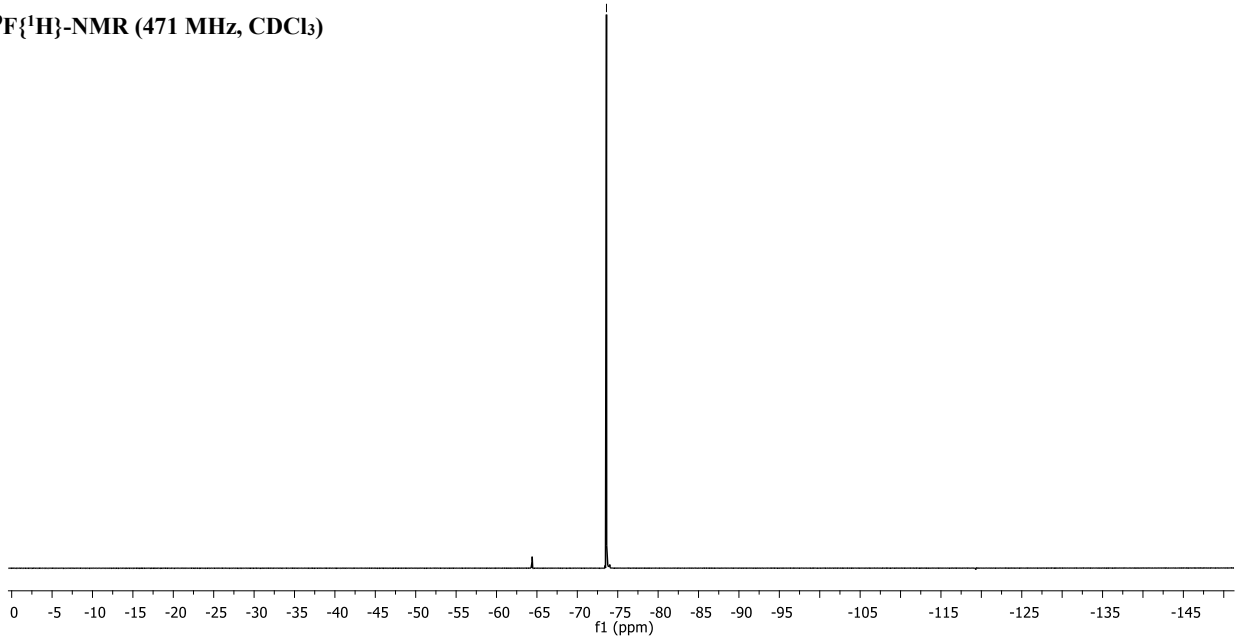


^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

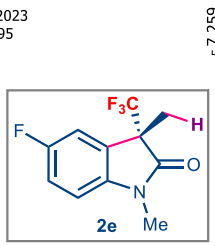
July 2023
NS-135 chiral



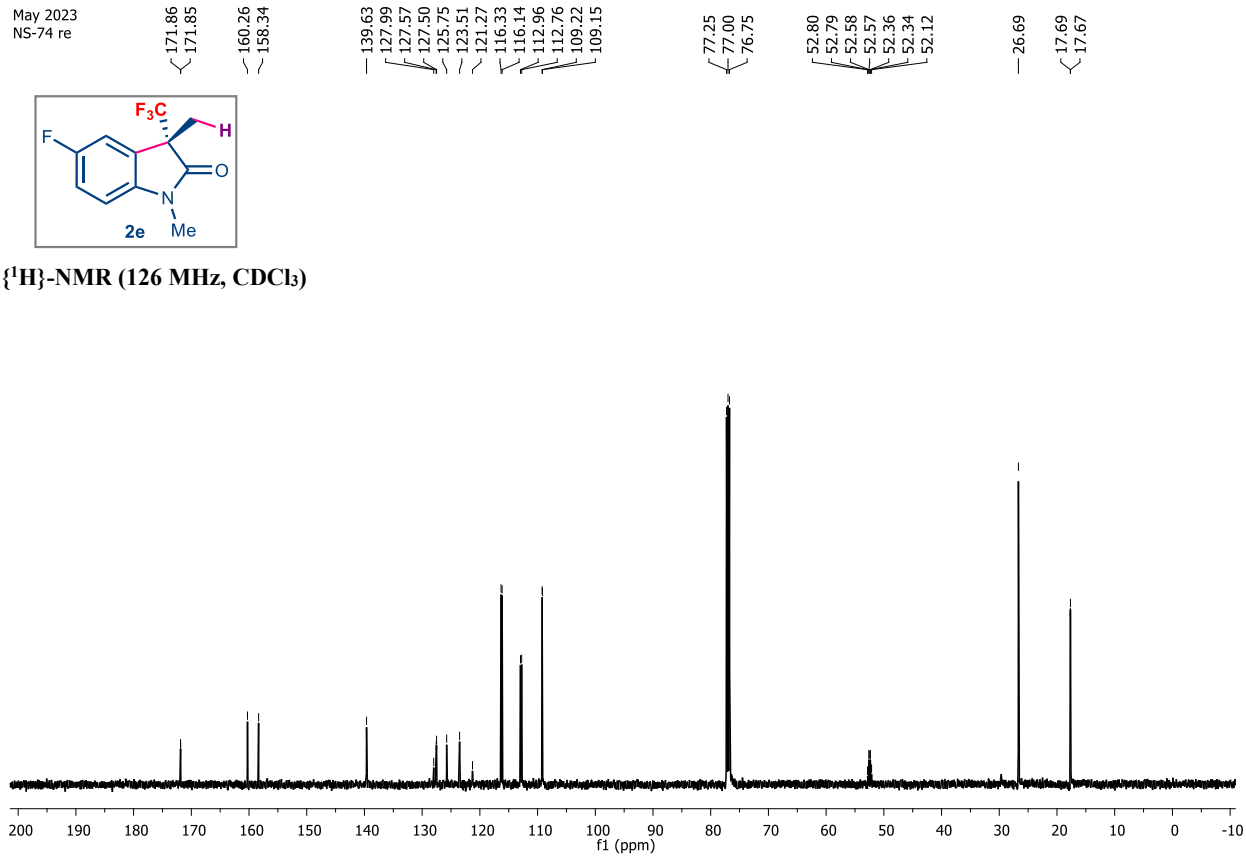
$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)



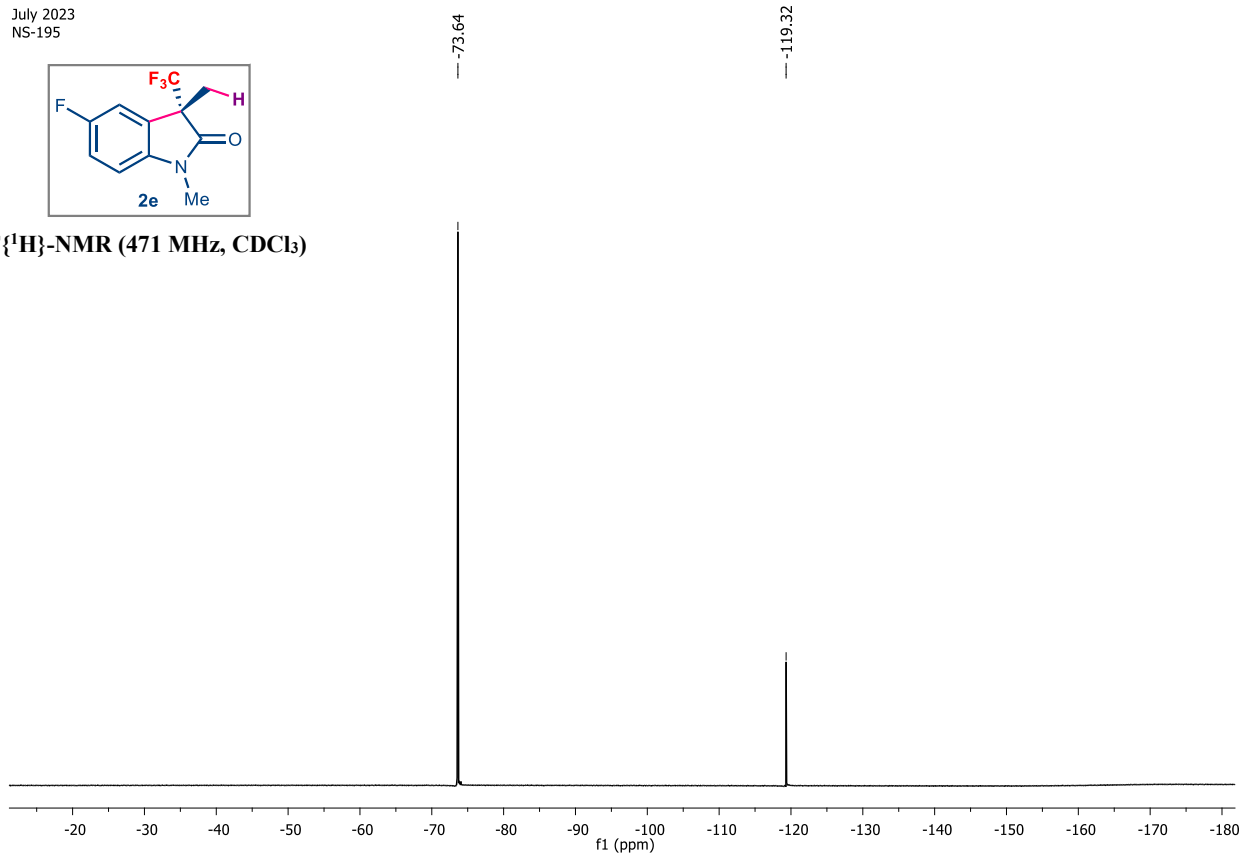
July 2023
NS-195



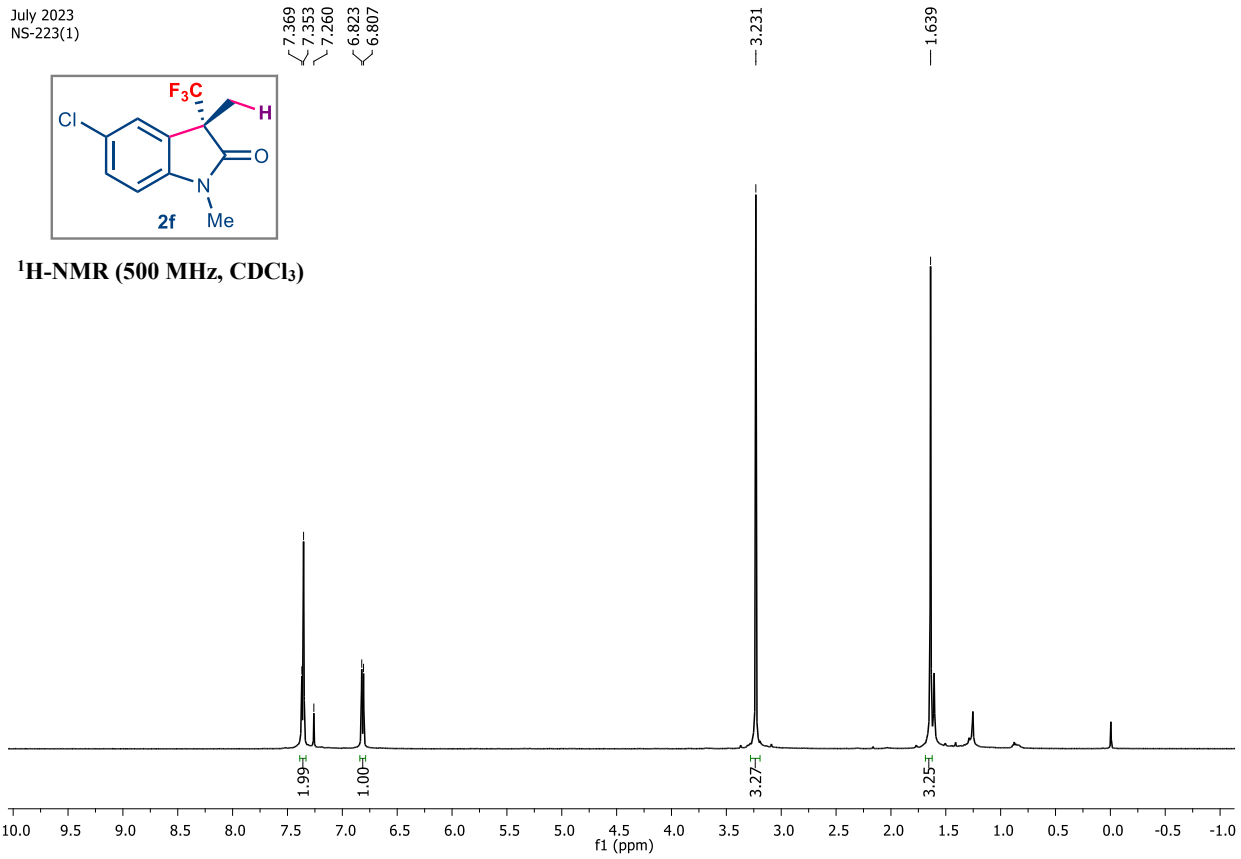
^{1}H-NMR (500 MHz, $CDCl_3$)



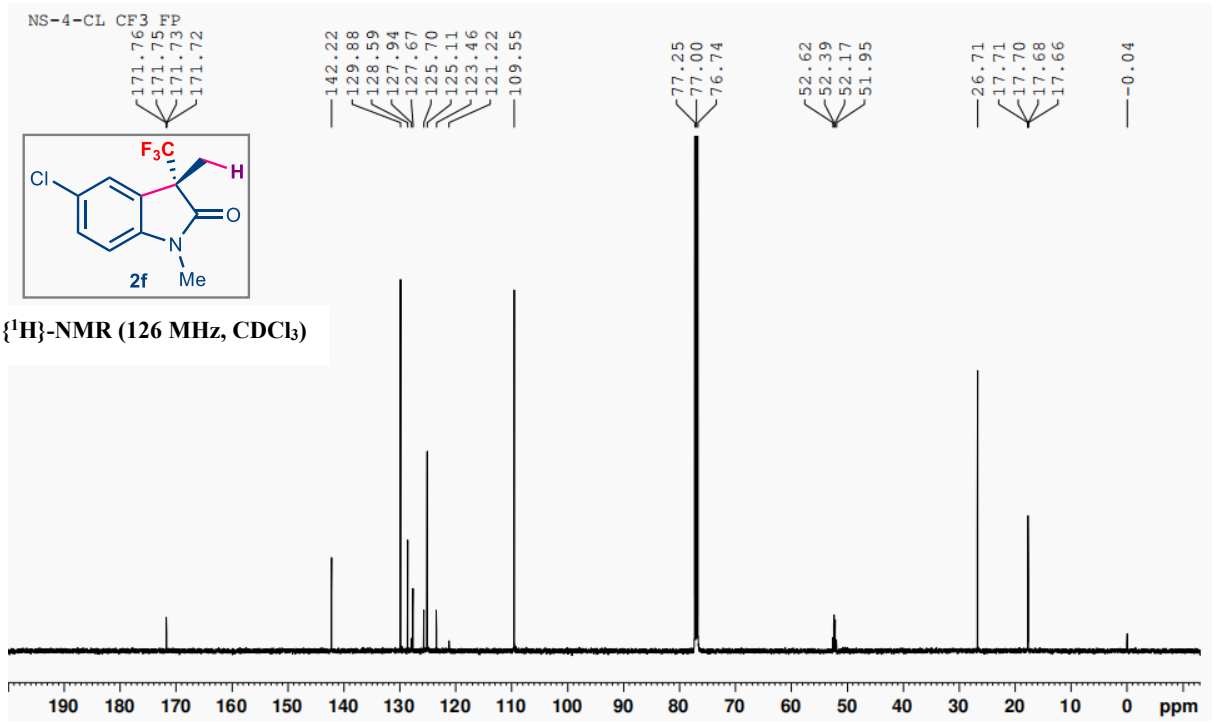
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

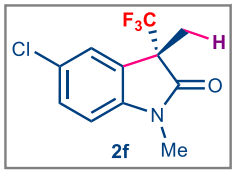


^{1}H-NMR (500 MHz, $CDCl_3$)



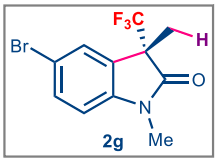
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

July 2023
NS-223(1)

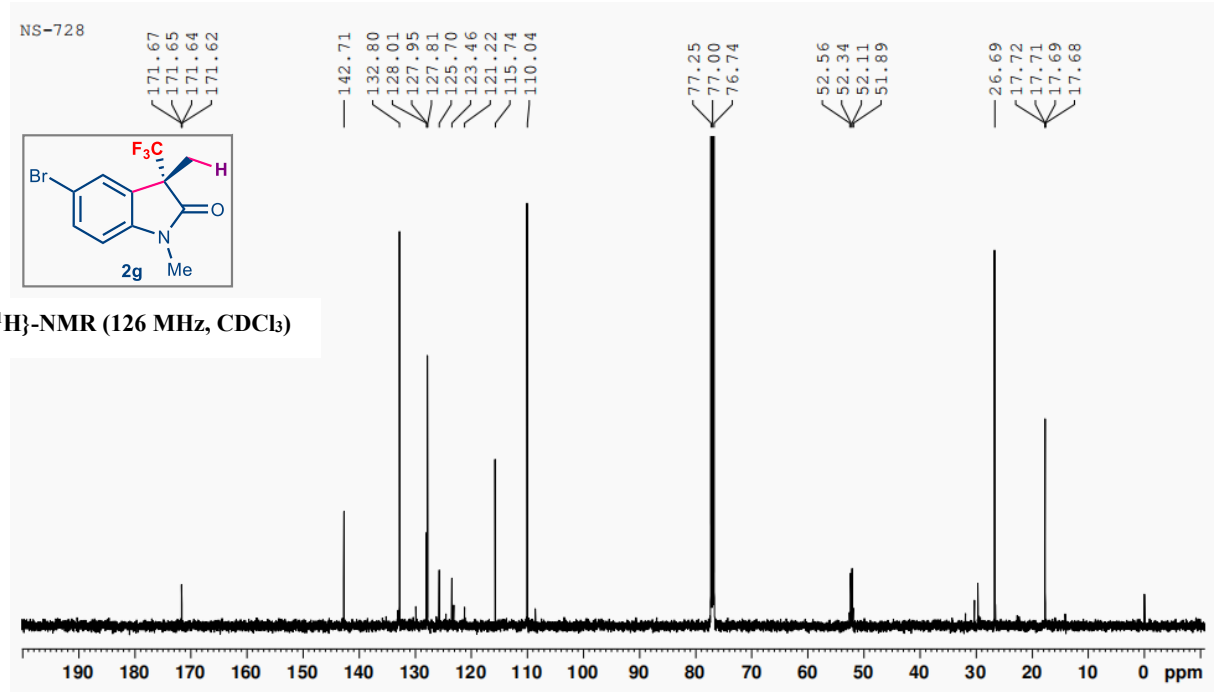


$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

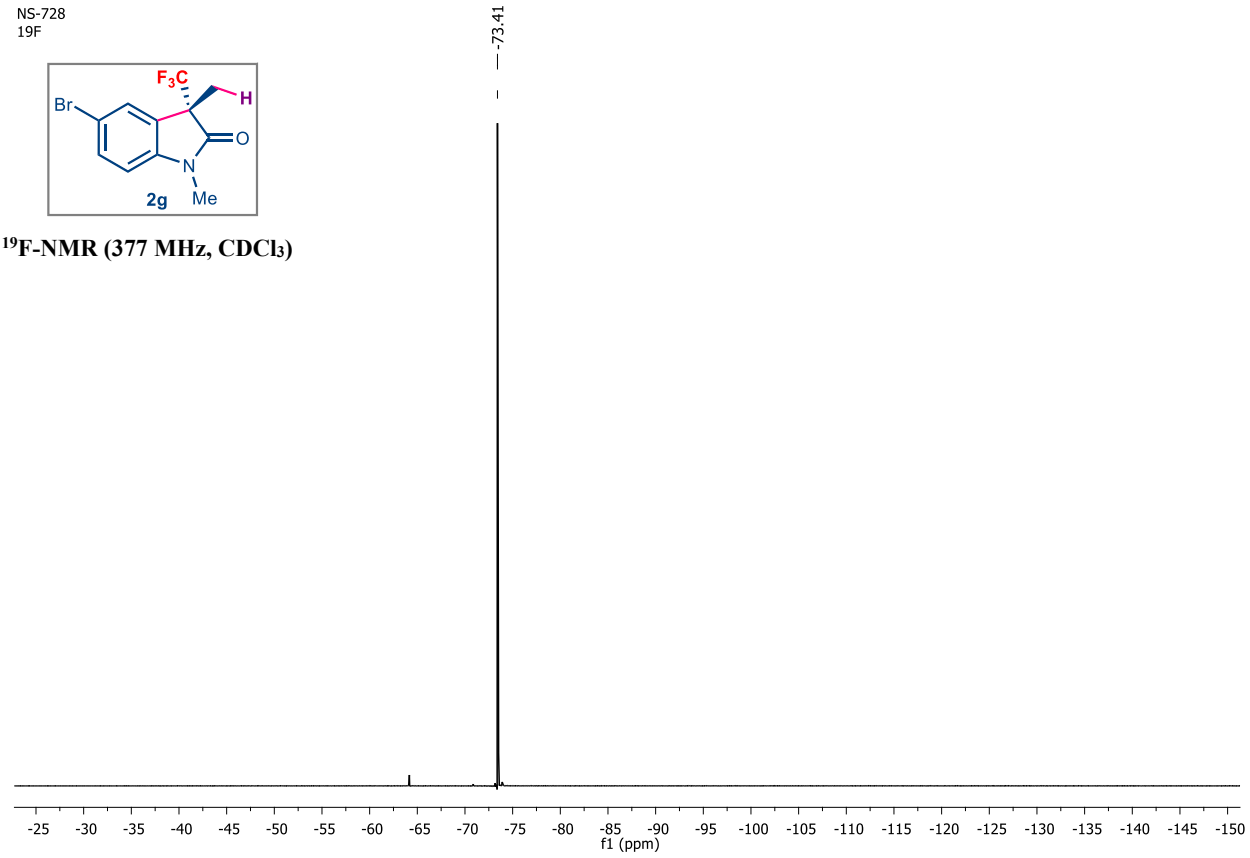
24.08.24
NS-728



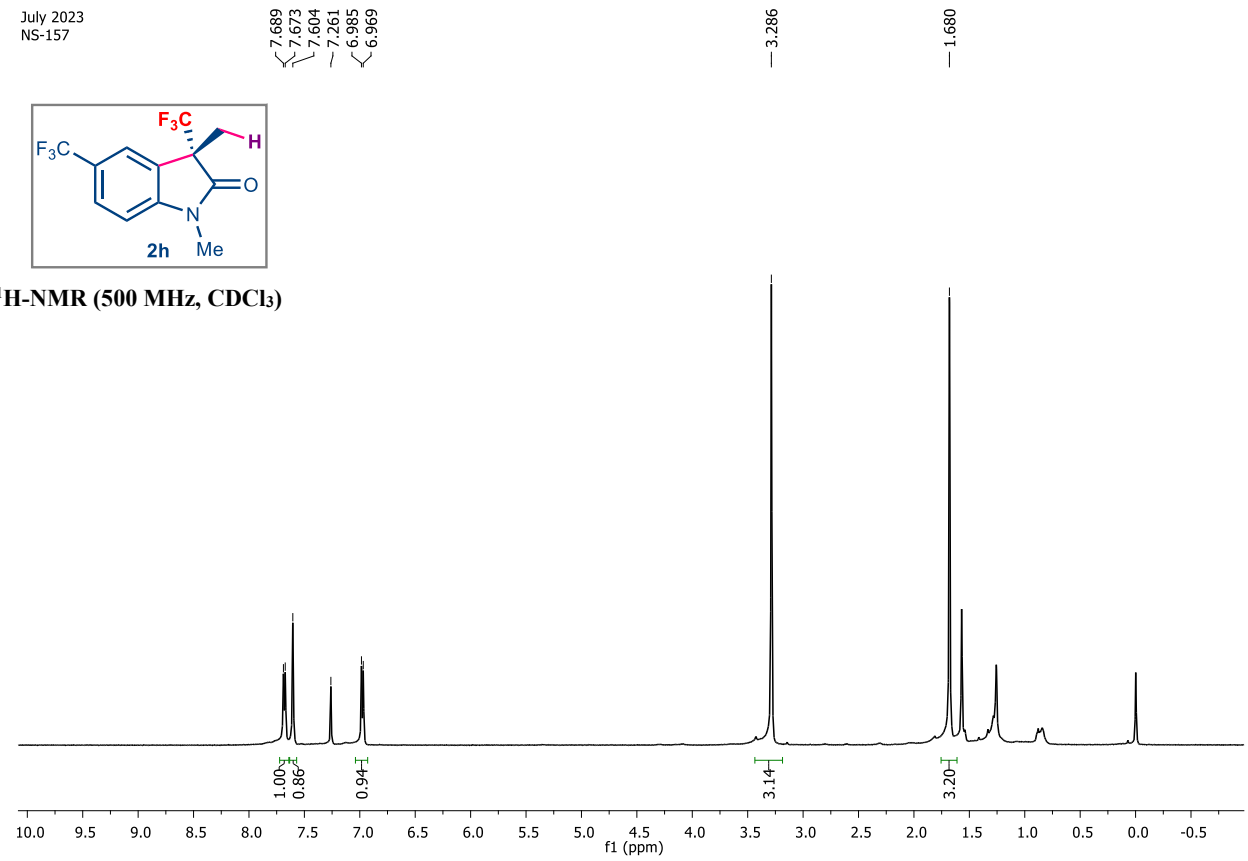
^{1}H-NMR (500 MHz, $CDCl_3$)



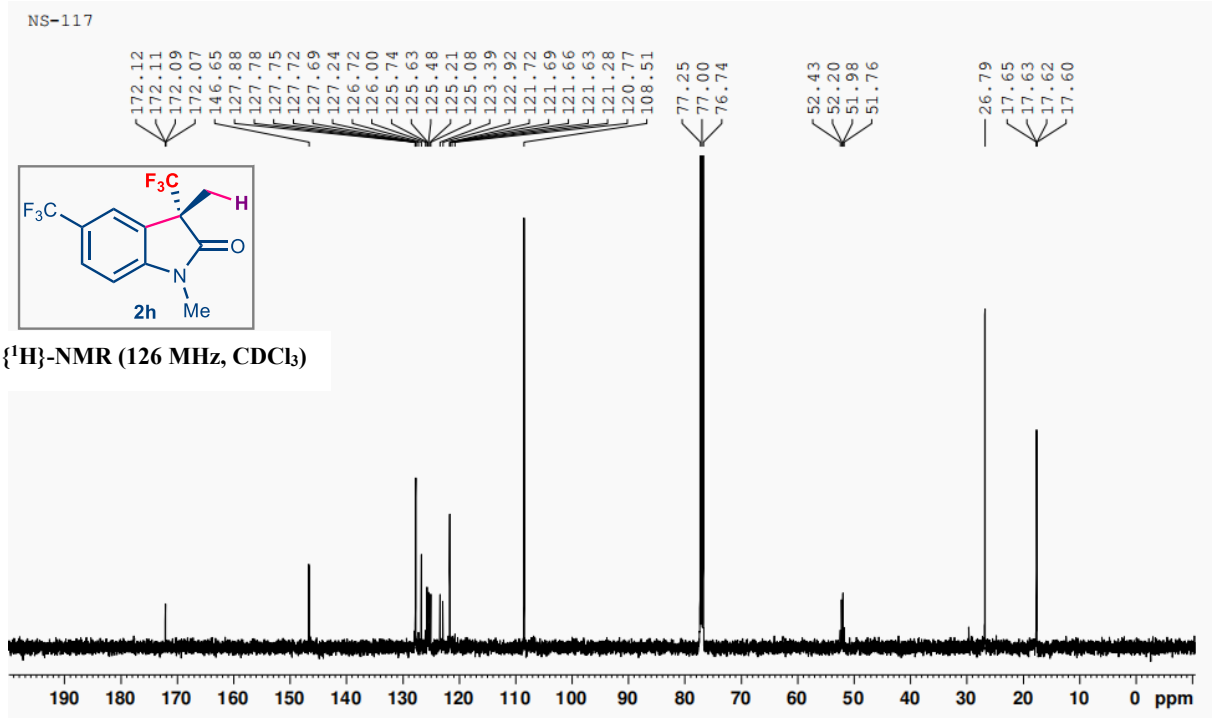
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

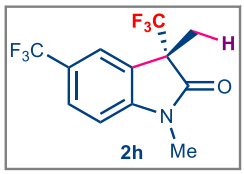


^{1}H-NMR (500 MHz, $CDCl_3$)



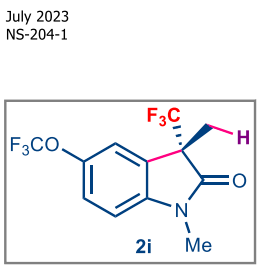
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

July 2023
NS-157

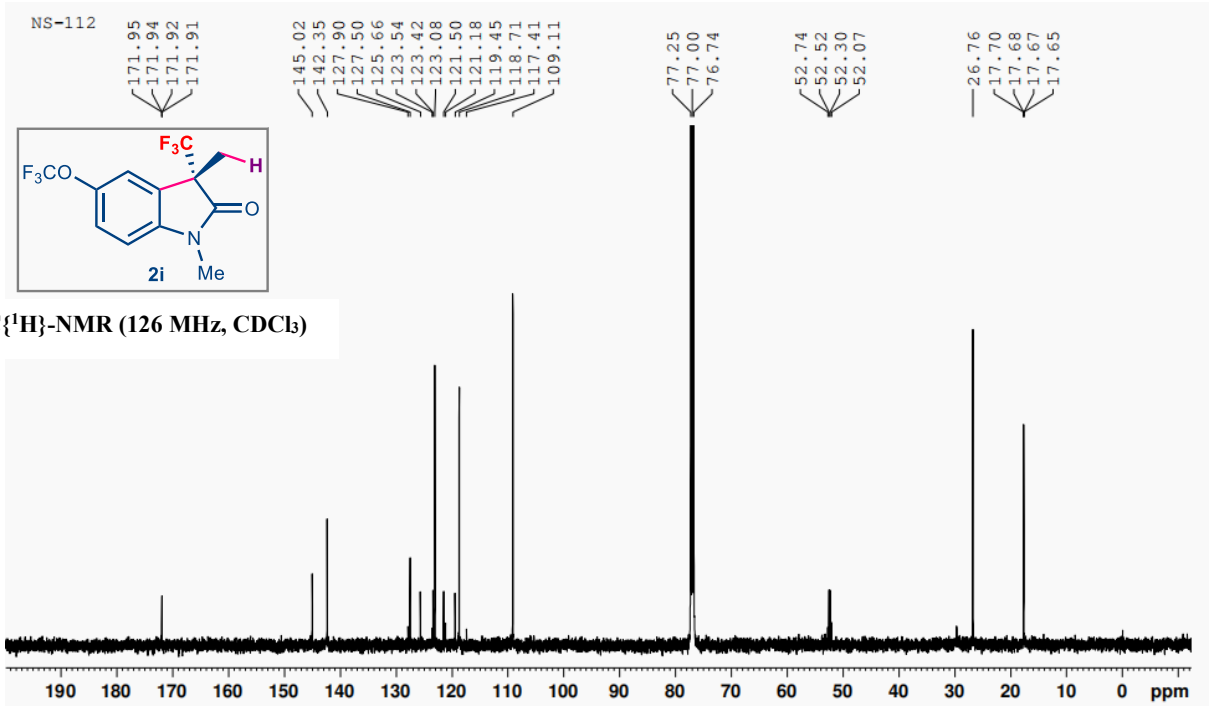


$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

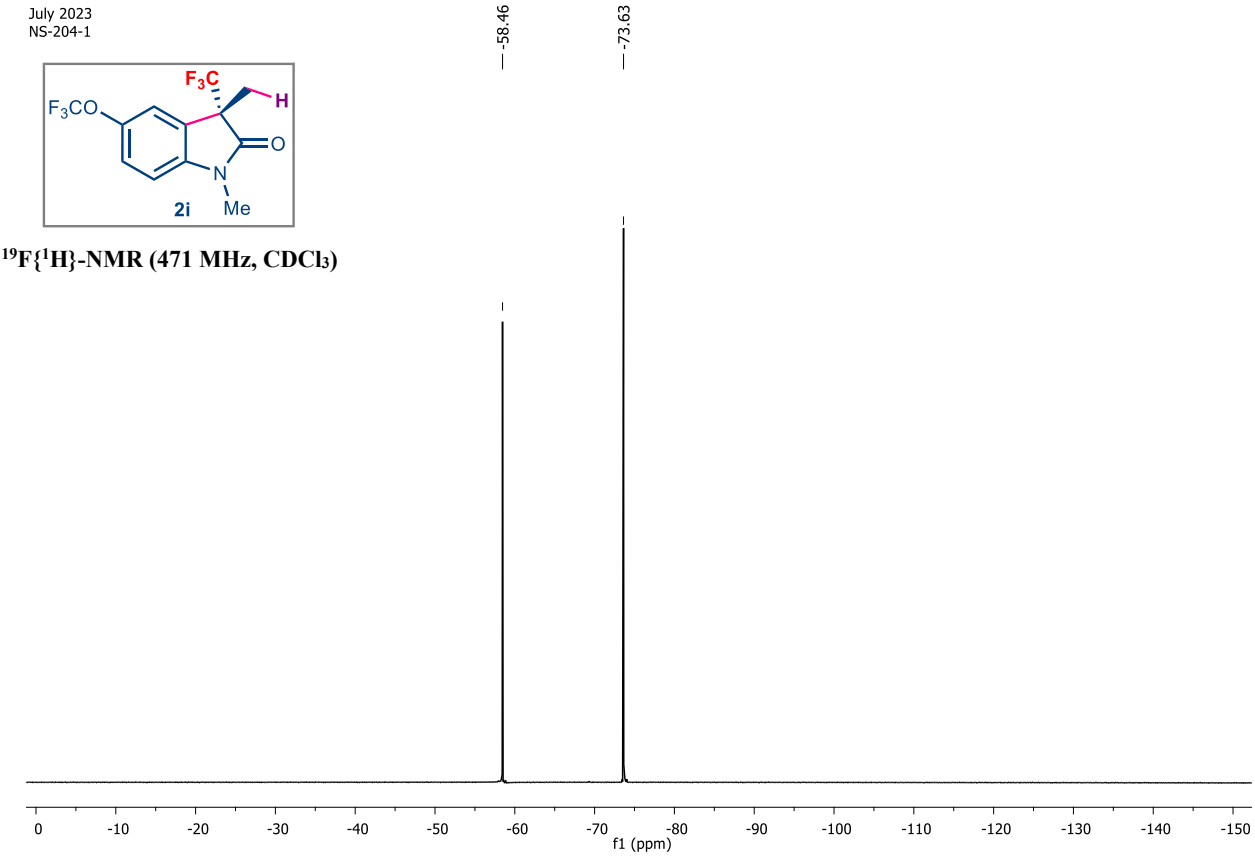
July 2023
NS-204-1



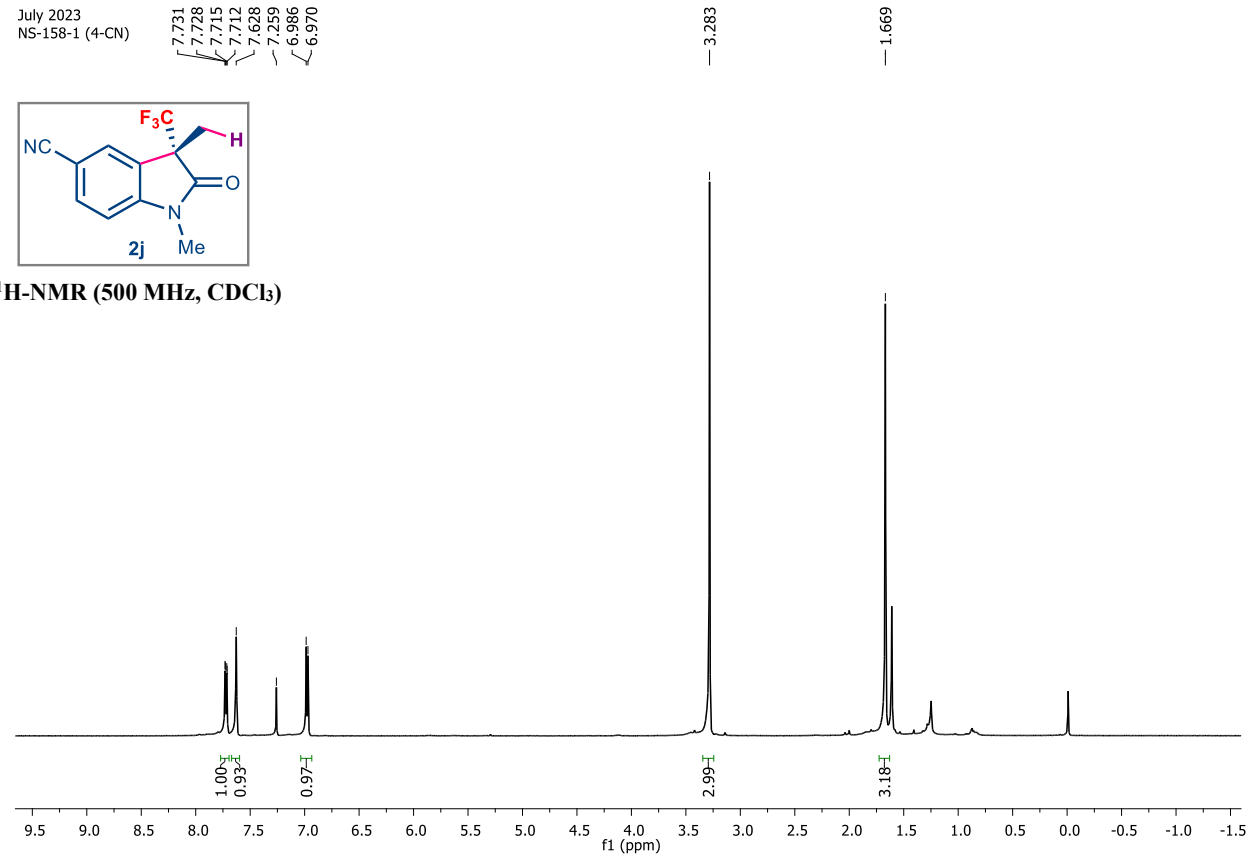
^{1}H-NMR (500 MHz, $CDCl_3$)



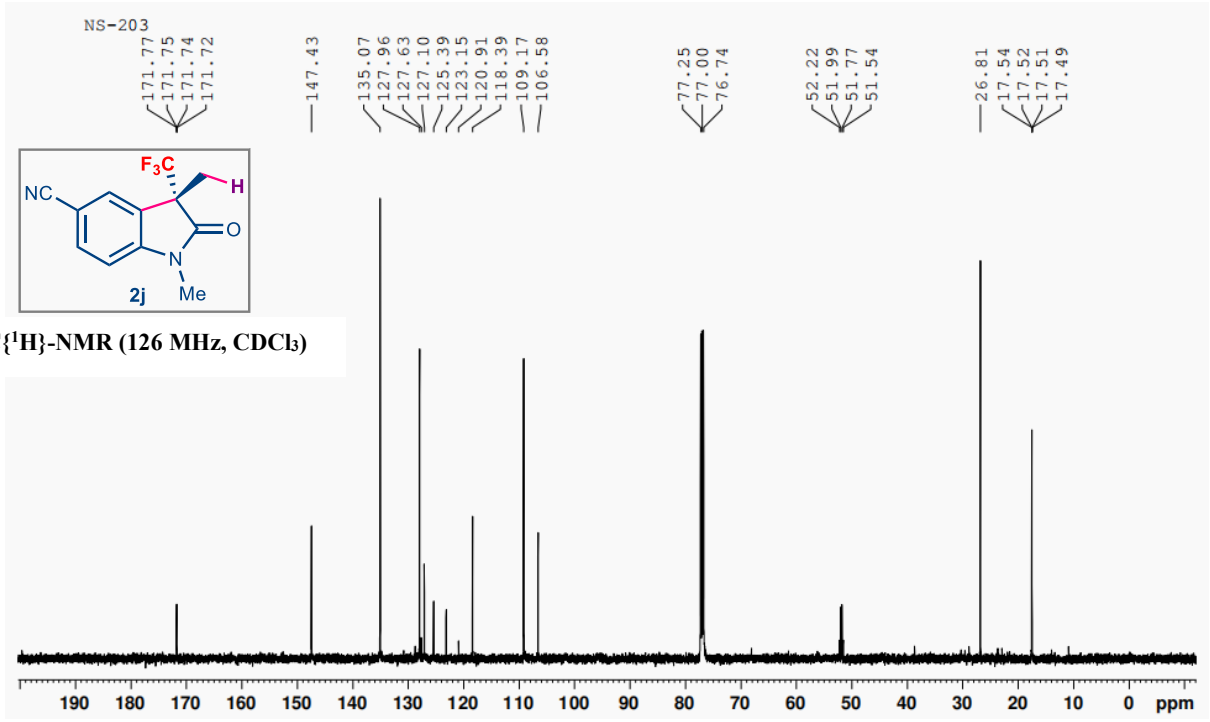
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

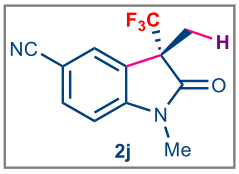


^{1}H-NMR (500 MHz, $CDCl_3$)



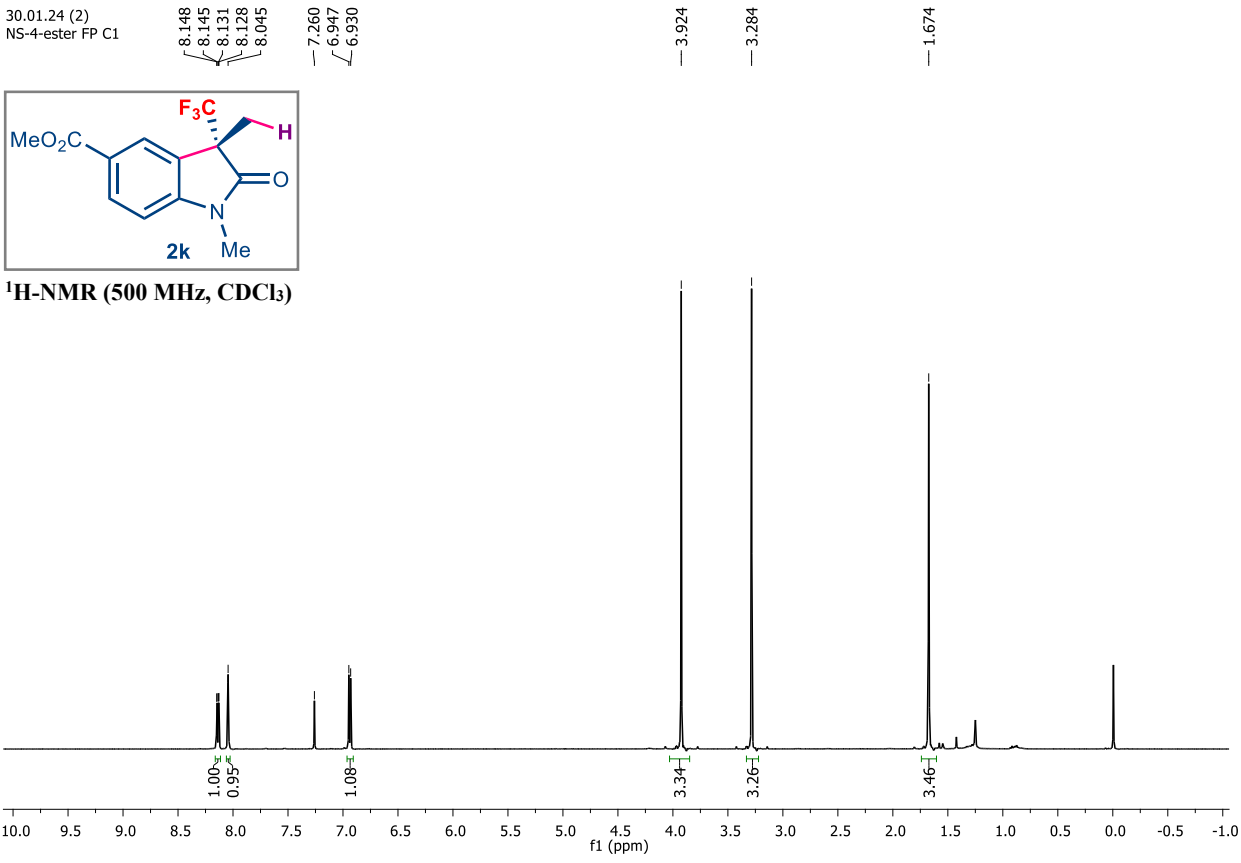
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

July 2023
NS-158-1 (4-CN)

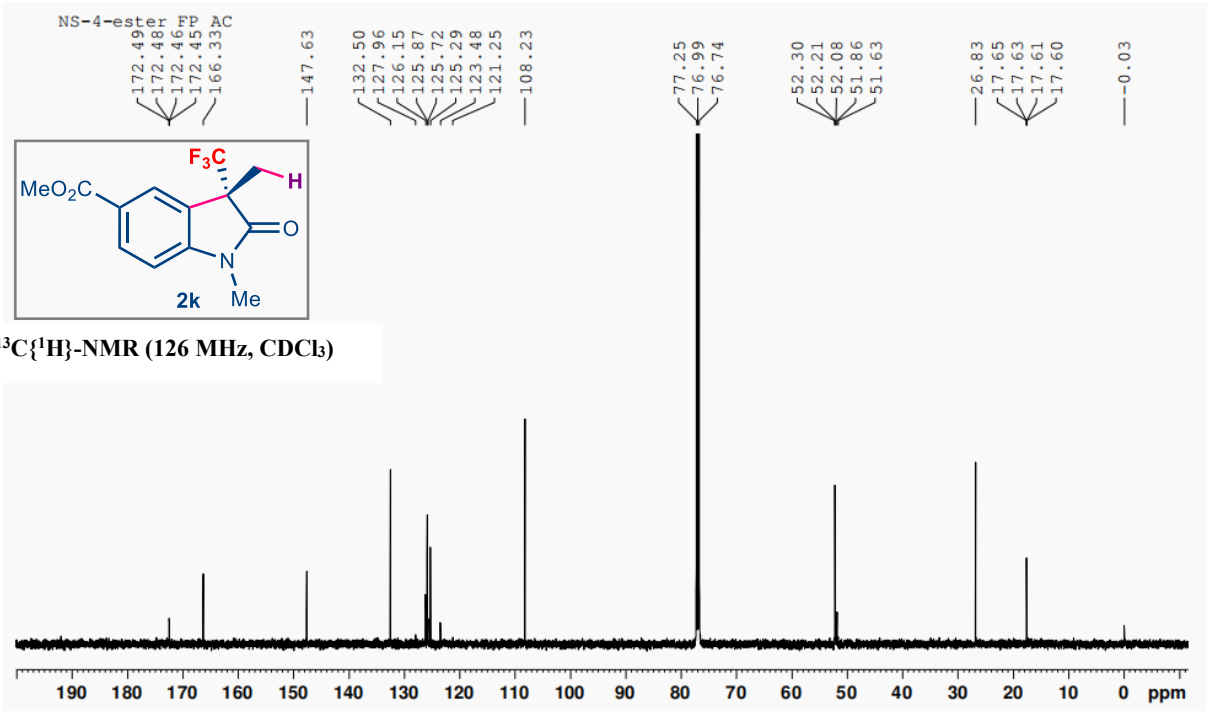


$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

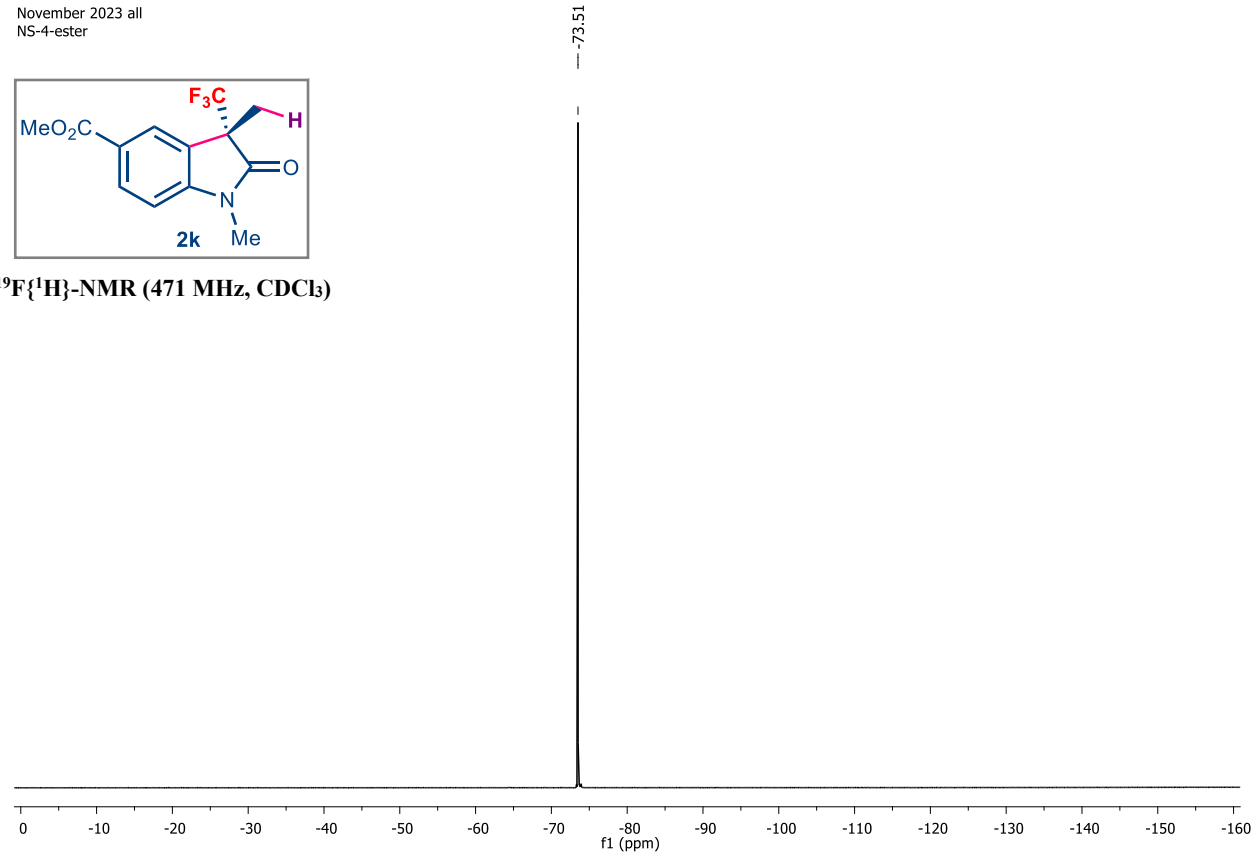
30.01.24 (2)
NS-4-ester FP C1



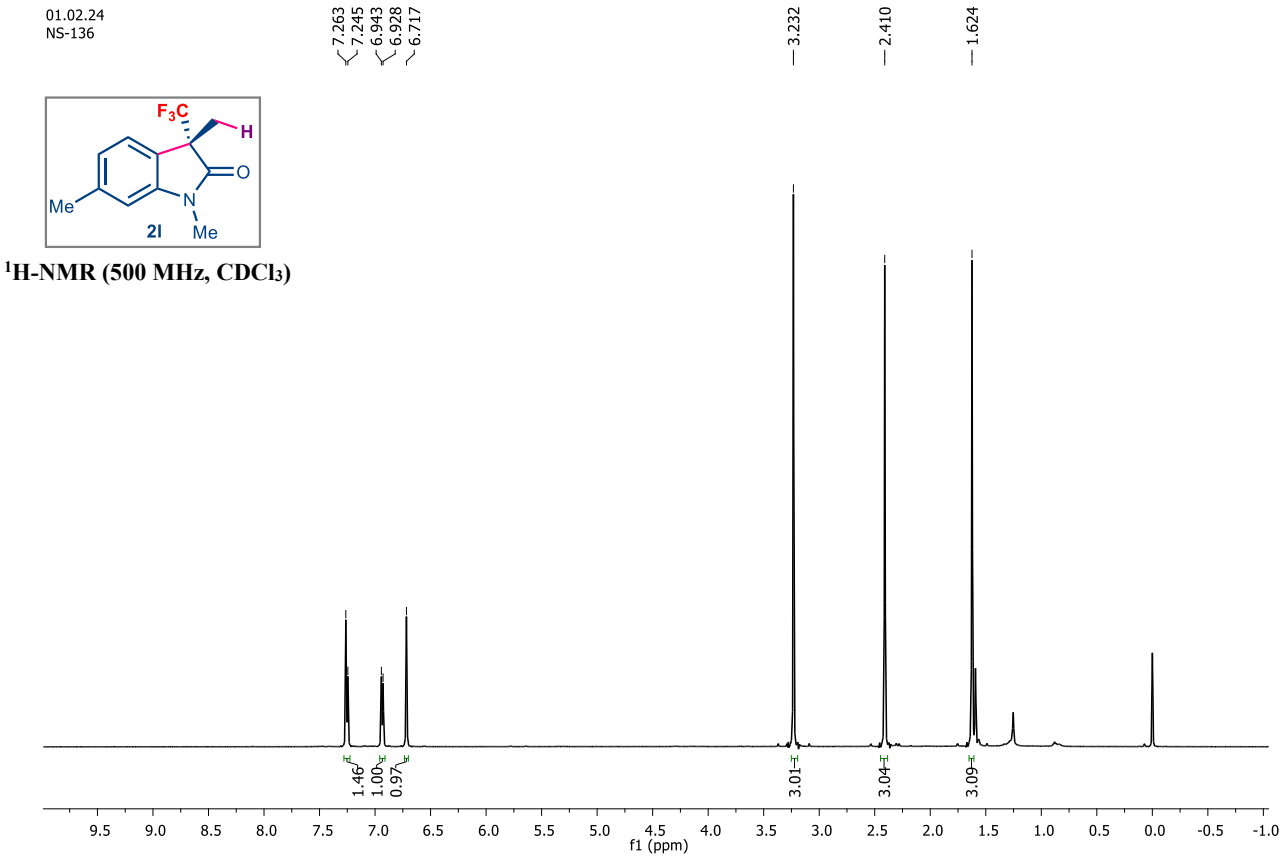
^{1}H-NMR (500 MHz, $CDCl_3$)



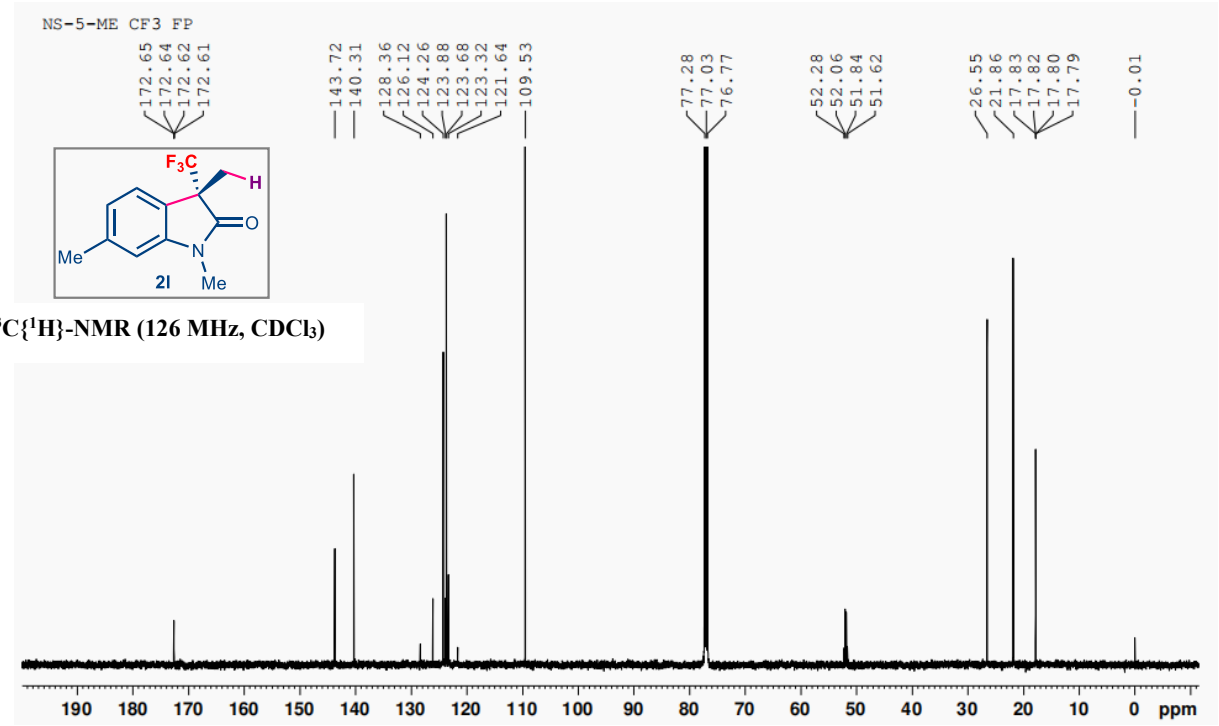
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

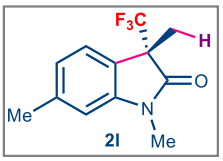


^{1}H-NMR (500 MHz, $CDCl_3$)



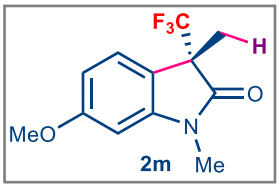
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

June 2023
NS-5Me-1

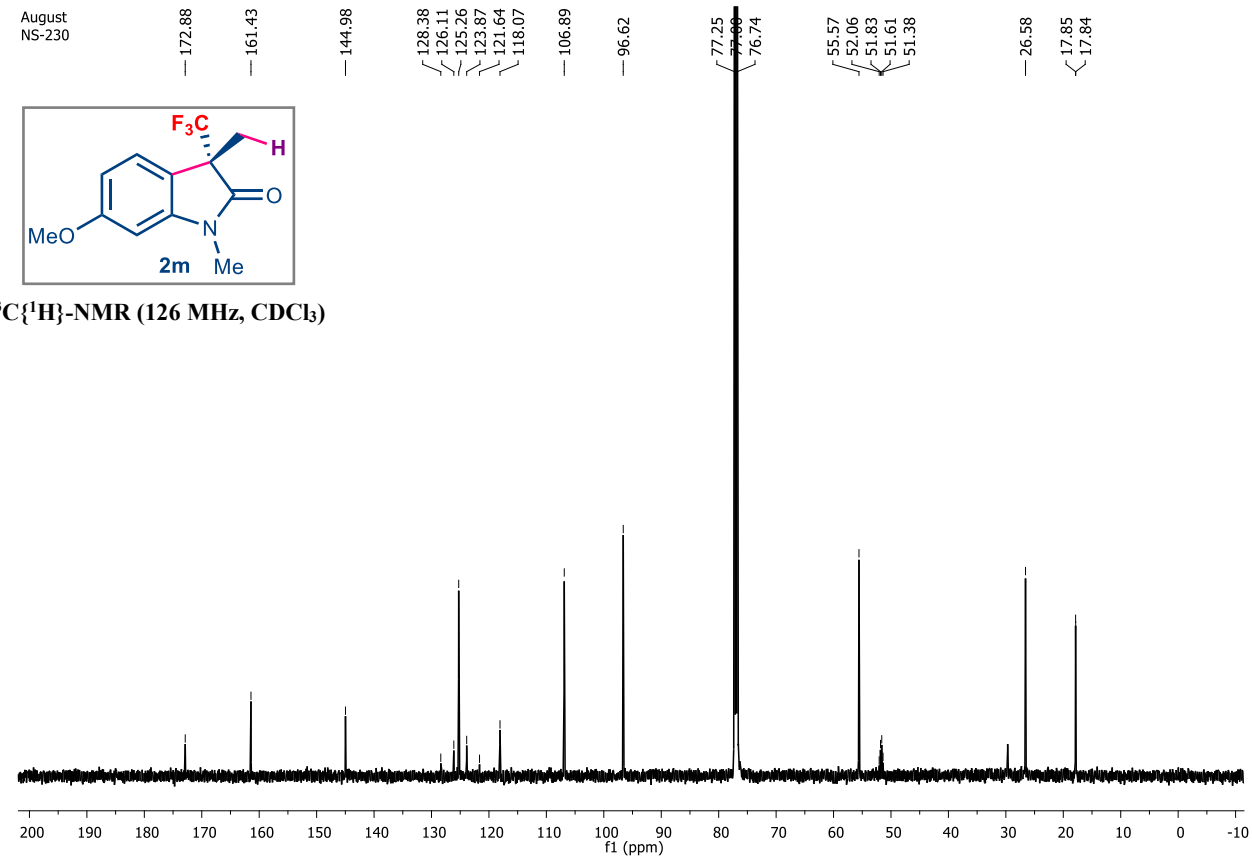


$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

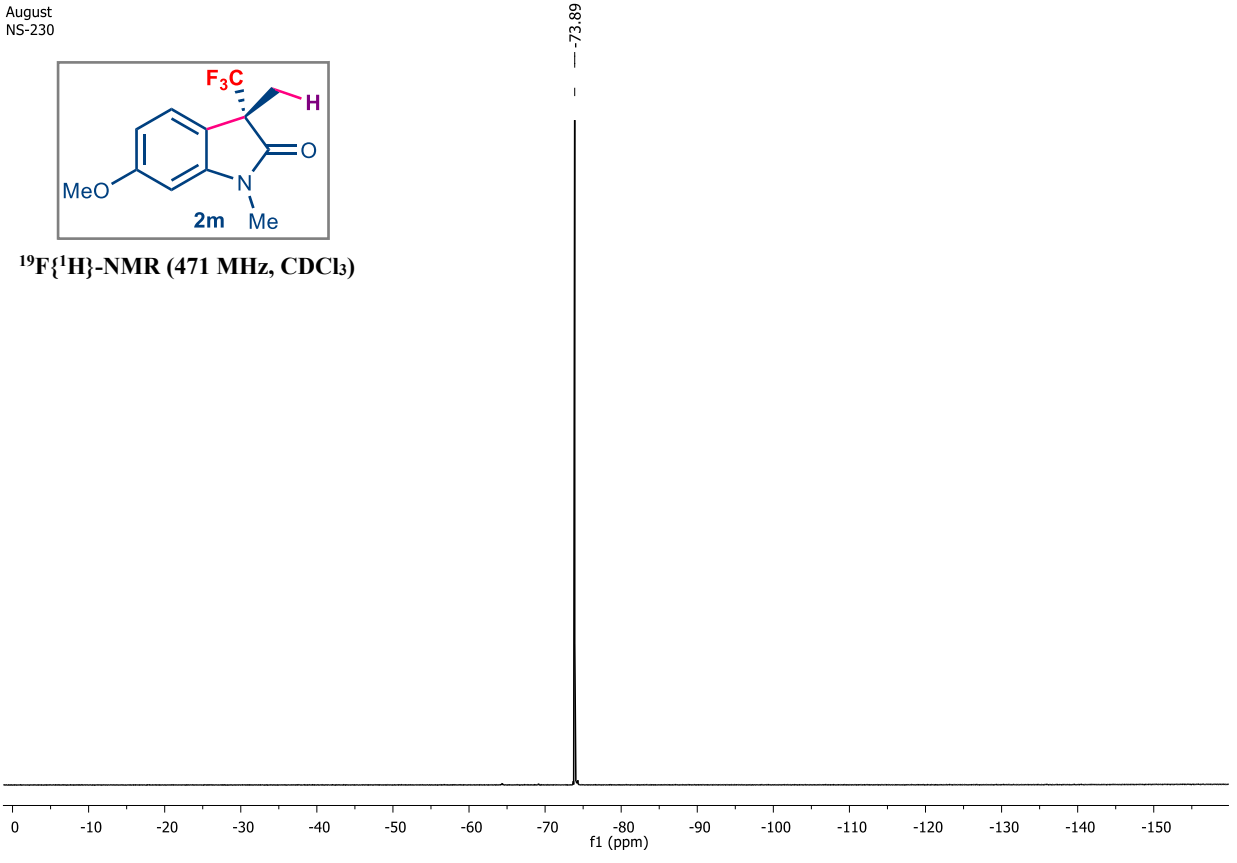
August
NS-230



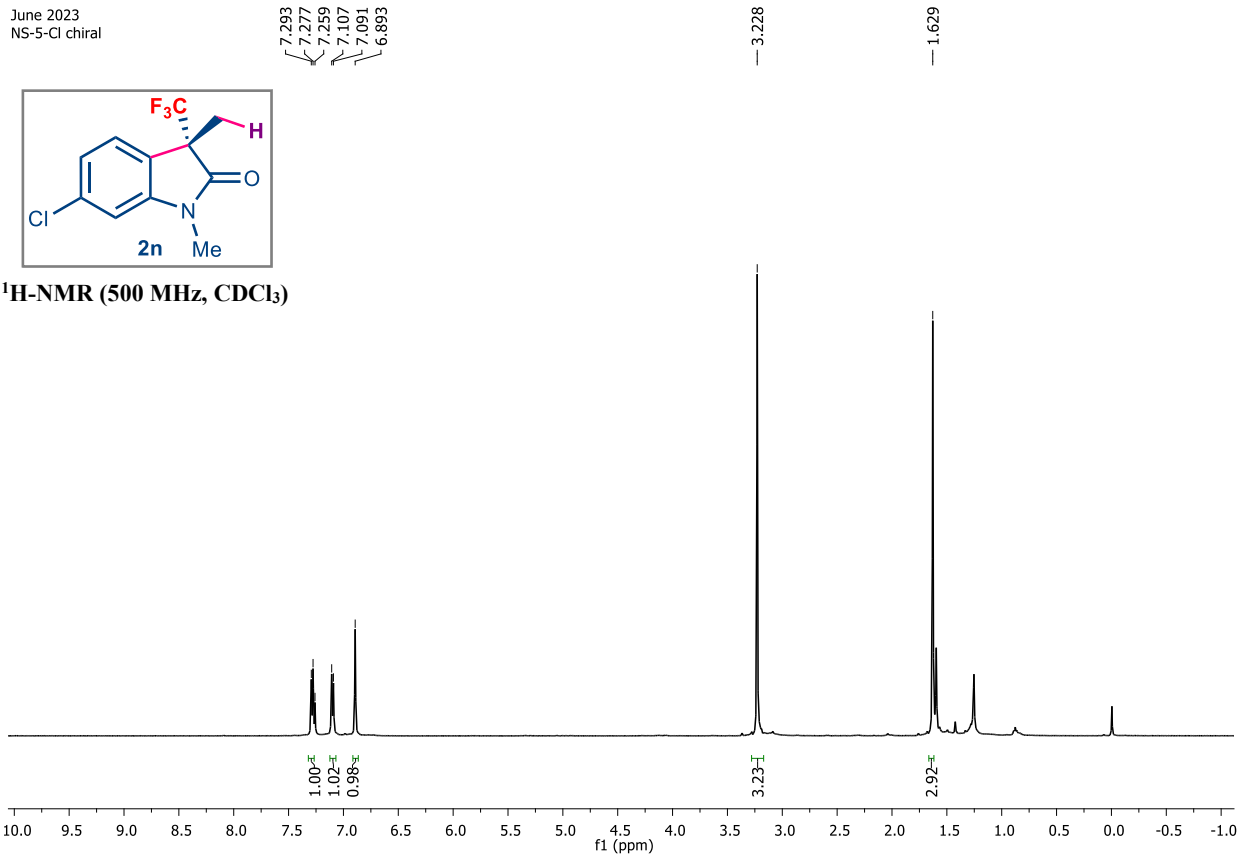
^{1}H-NMR (500 MHz, $CDCl_3$)



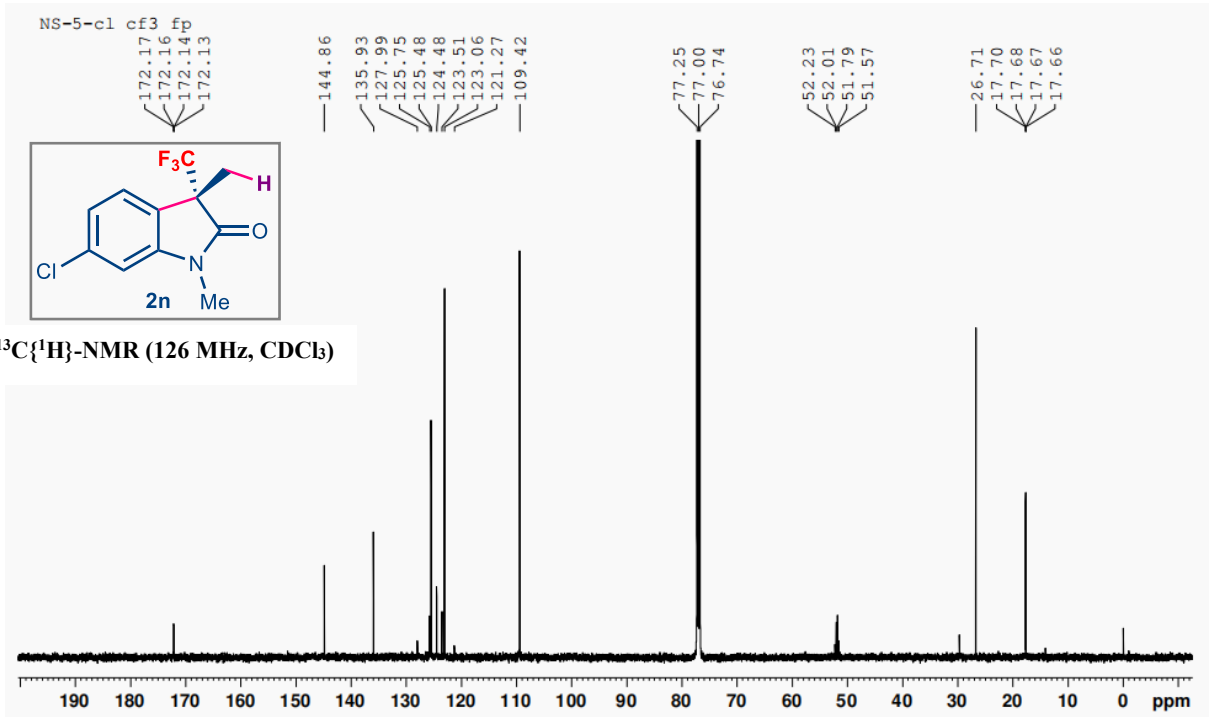
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

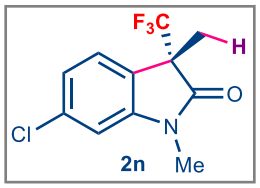


^{1}H-NMR (500 MHz, $CDCl_3$)



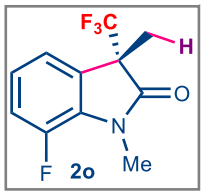
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

June 2023
NS-5-Cl chiral

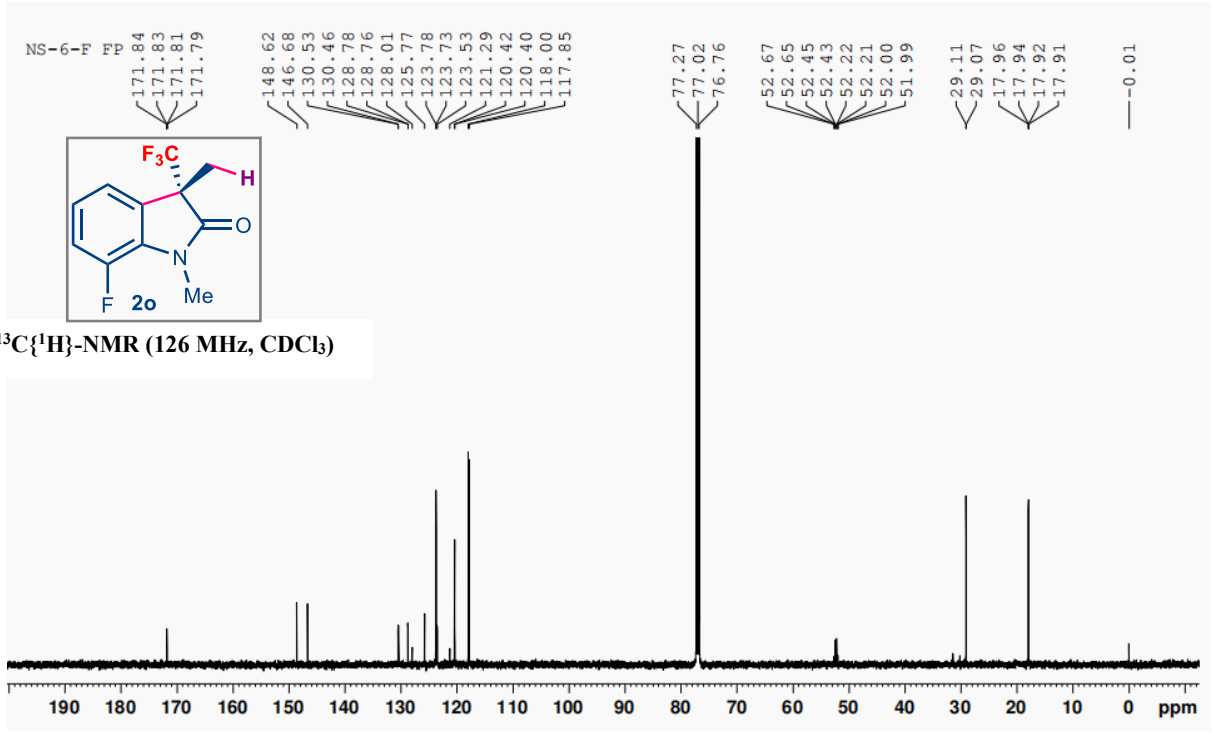


$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

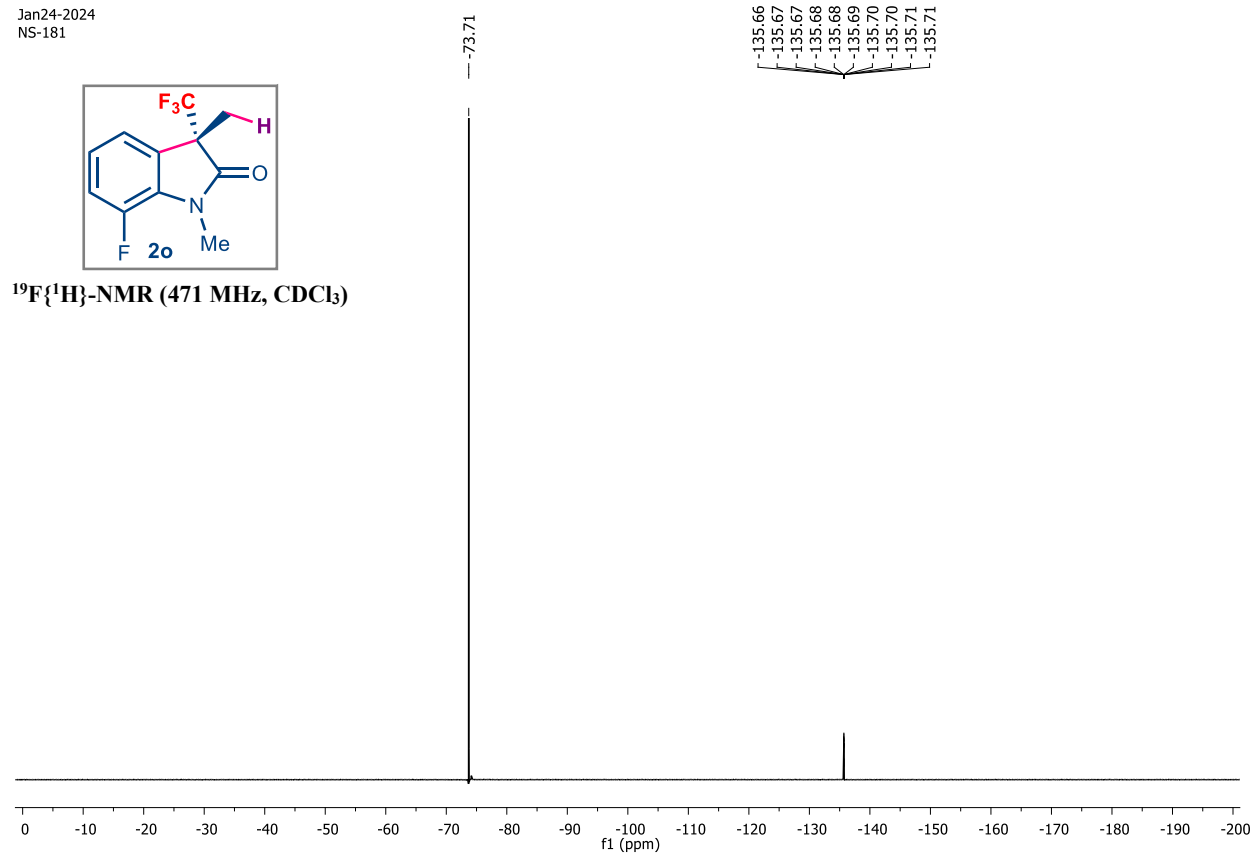
July 2023
NS-180



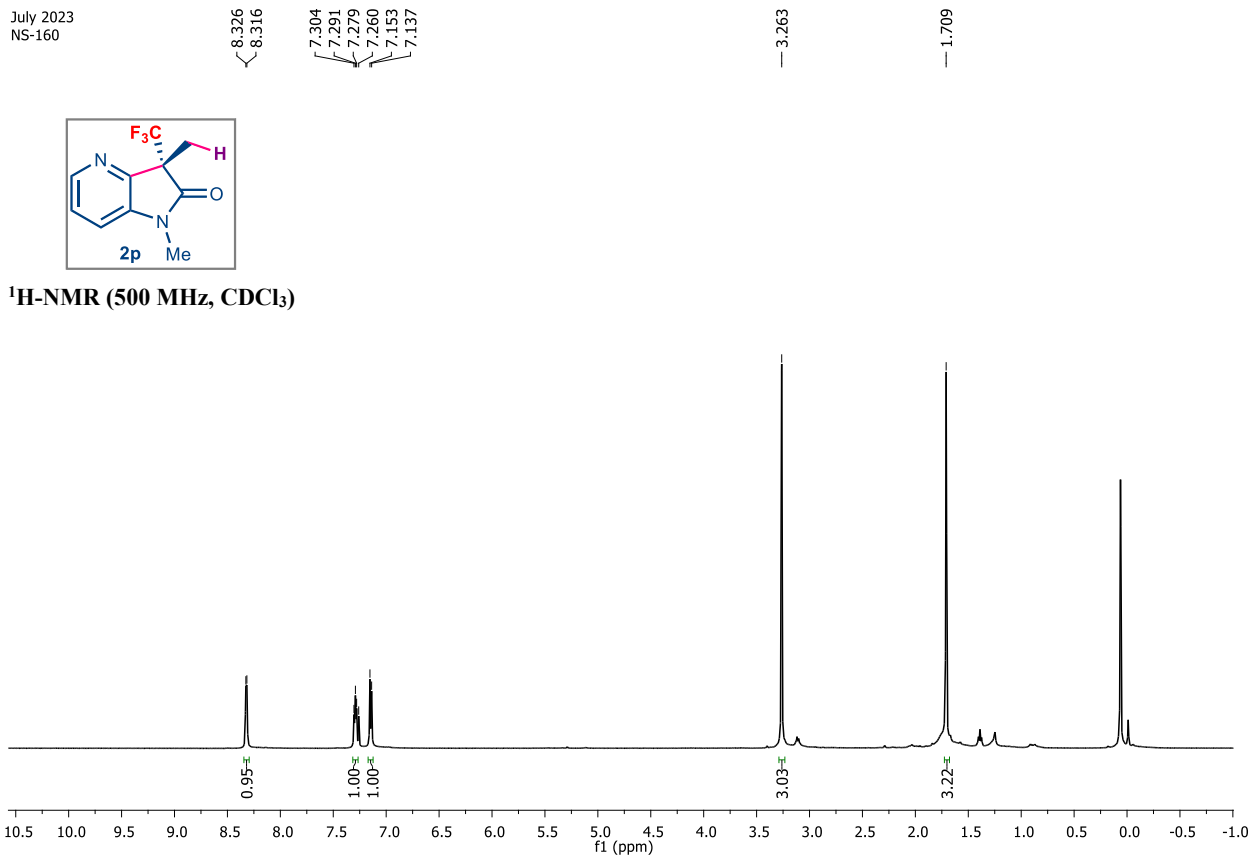
^{1}H-NMR (500 MHz, $CDCl_3$)



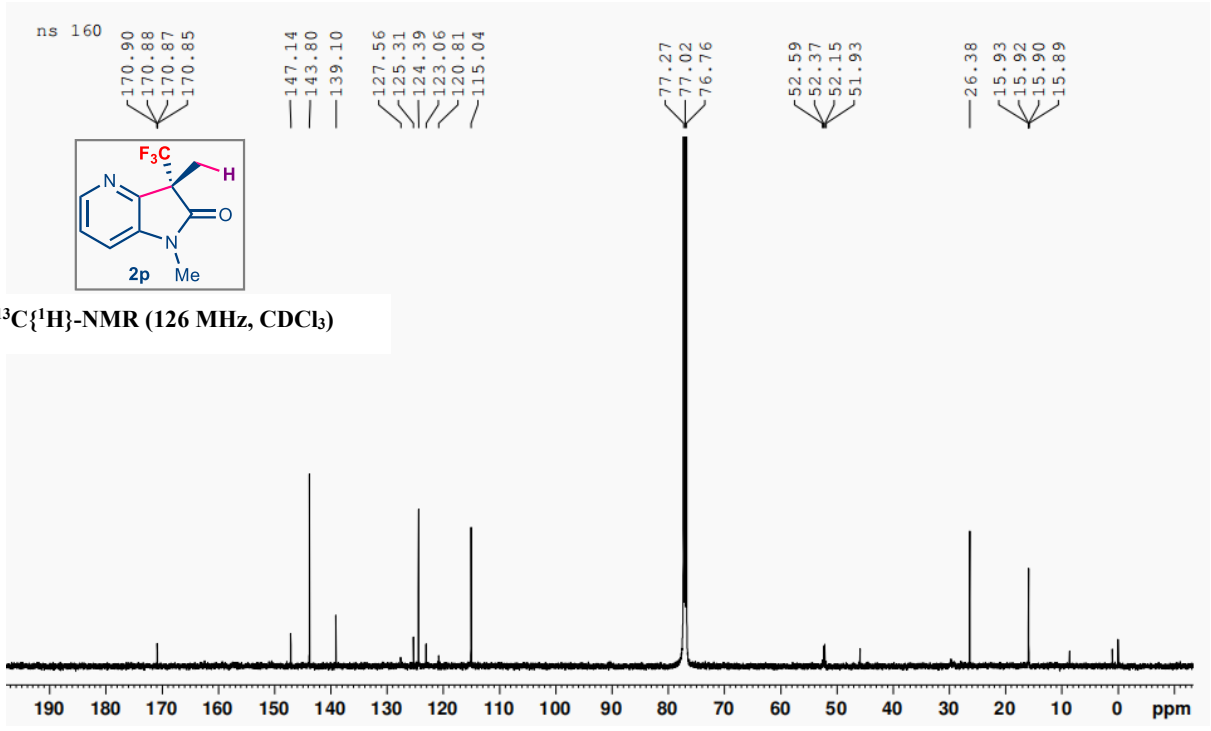
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)

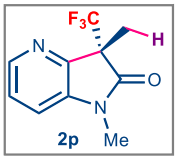


^{1}H-NMR (500 MHz, $CDCl_3$)

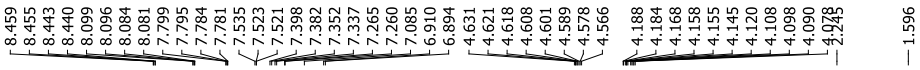


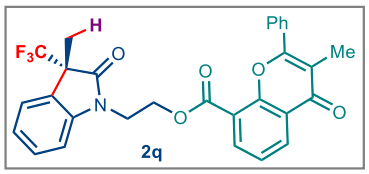
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

July 2023
NS-160

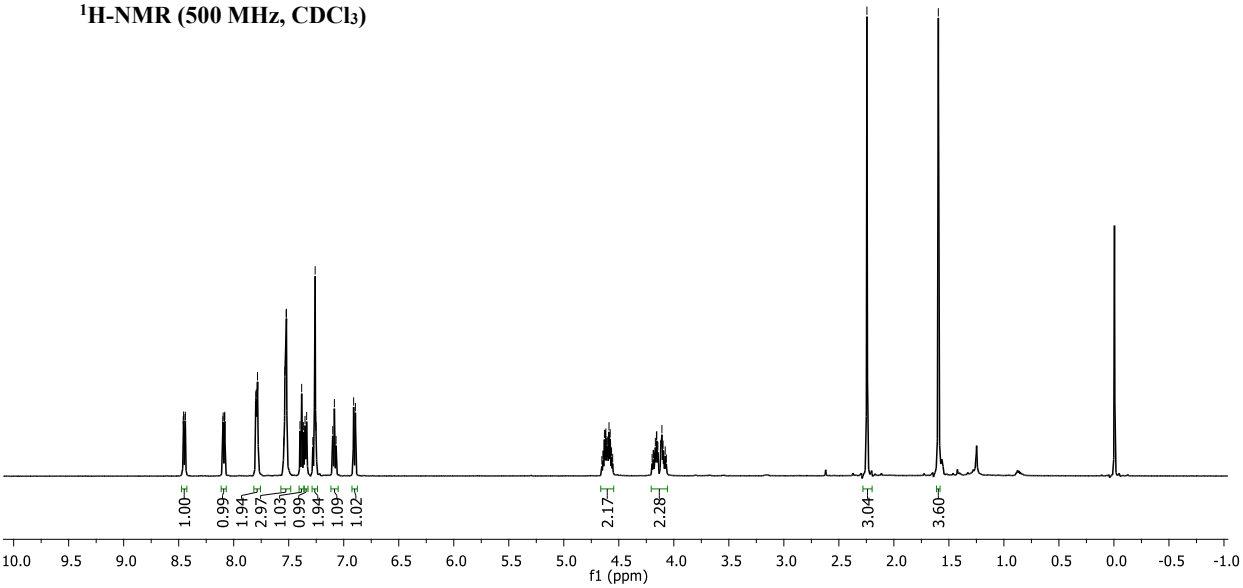


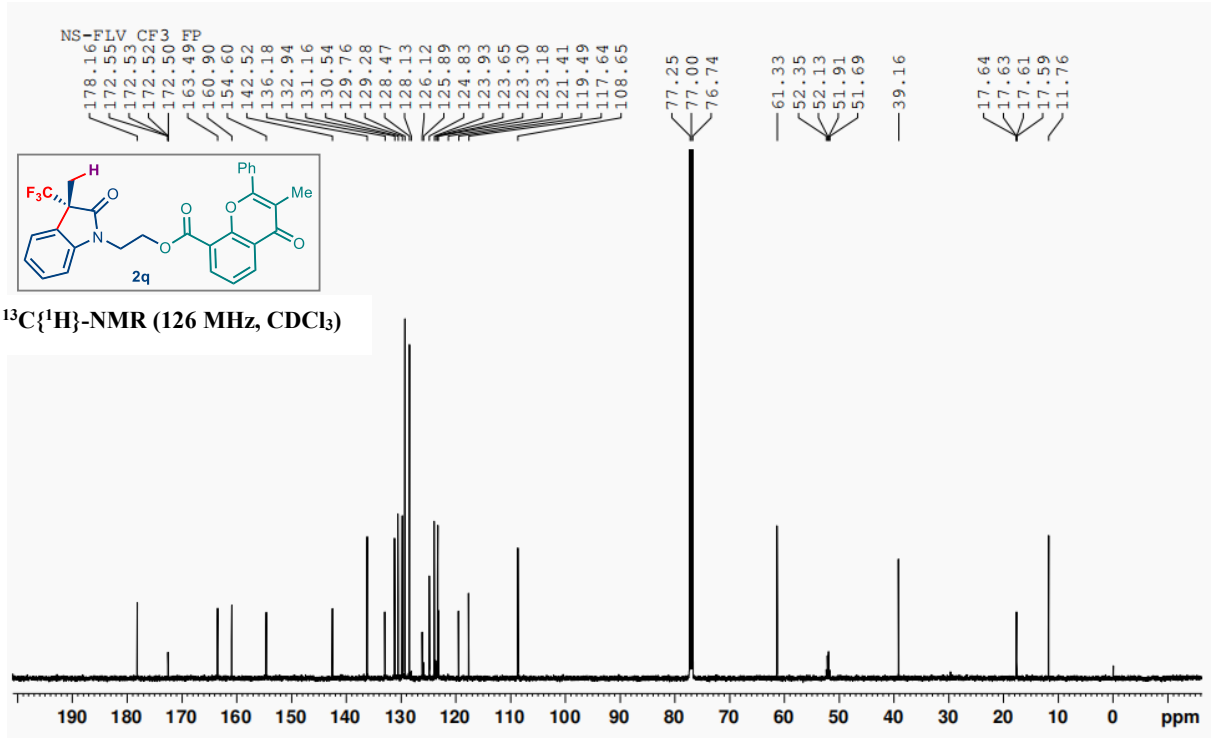
$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)



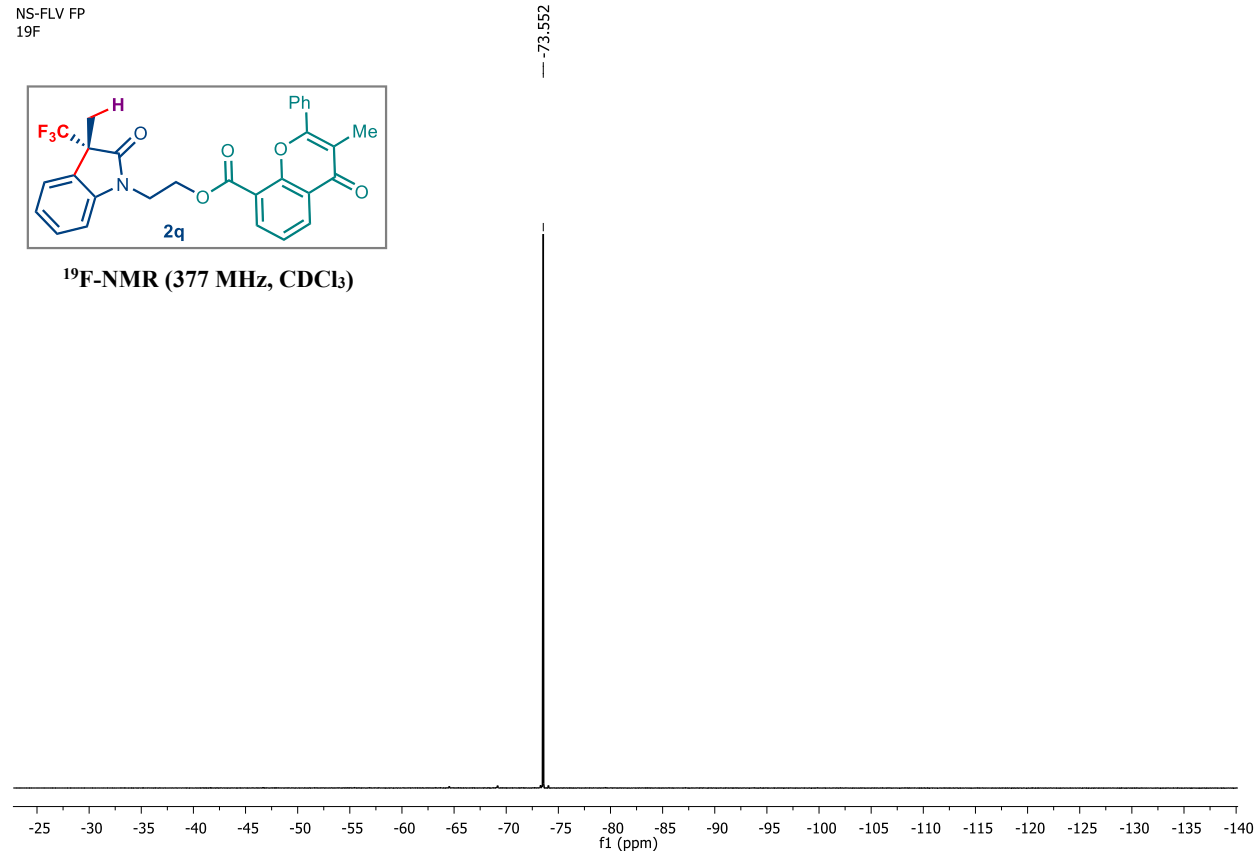


^{1}H-NMR (500 MHz, $CDCl_3$)

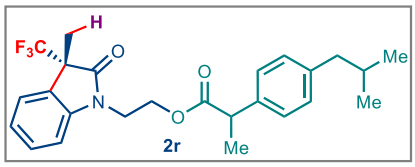




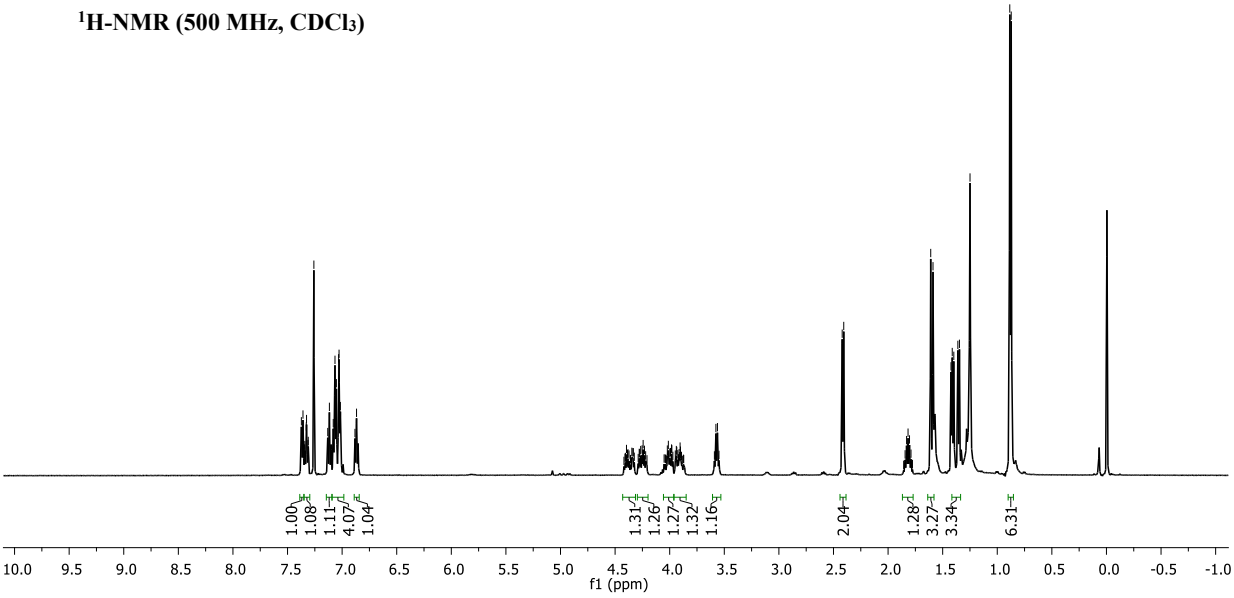
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)

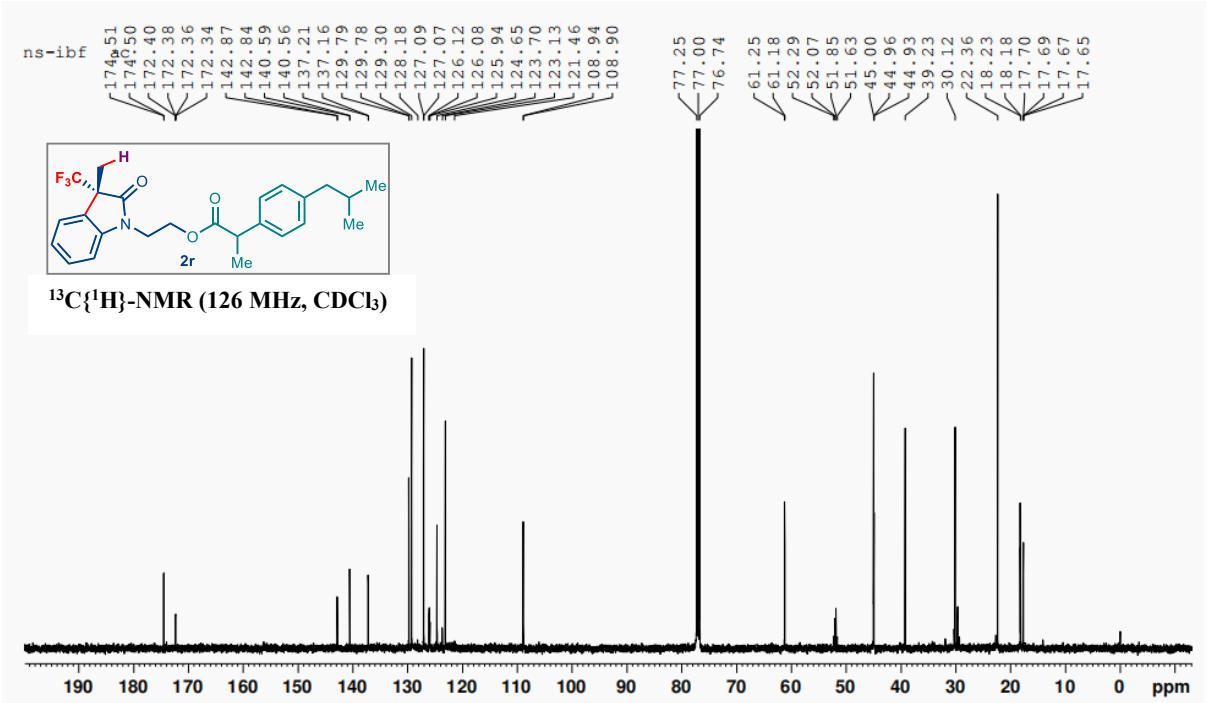


^{19}F-NMR (377 MHz, $CDCl_3$)



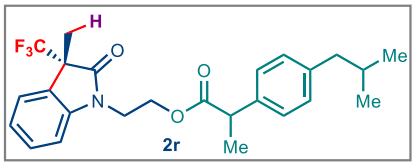
^{1}H-NMR (500 MHz, $CDCl_3$)





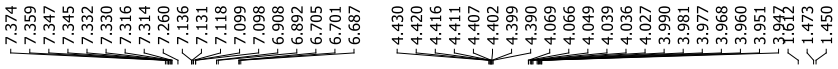
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

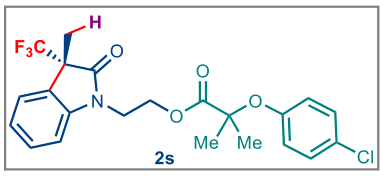
Ns-IBF fP
19F



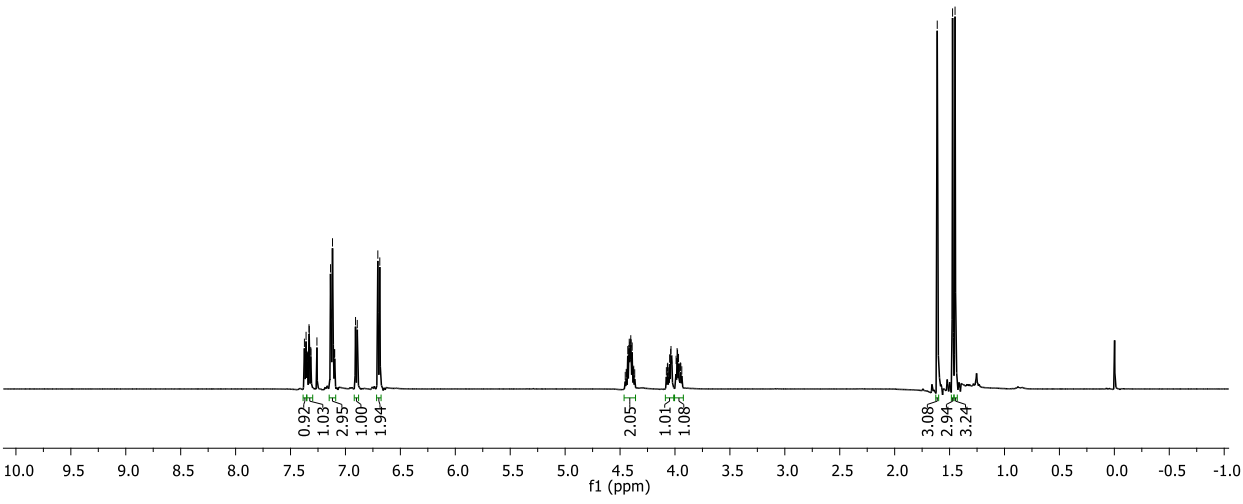
^{19}F-NMR (377 MHz, $CDCl_3$)

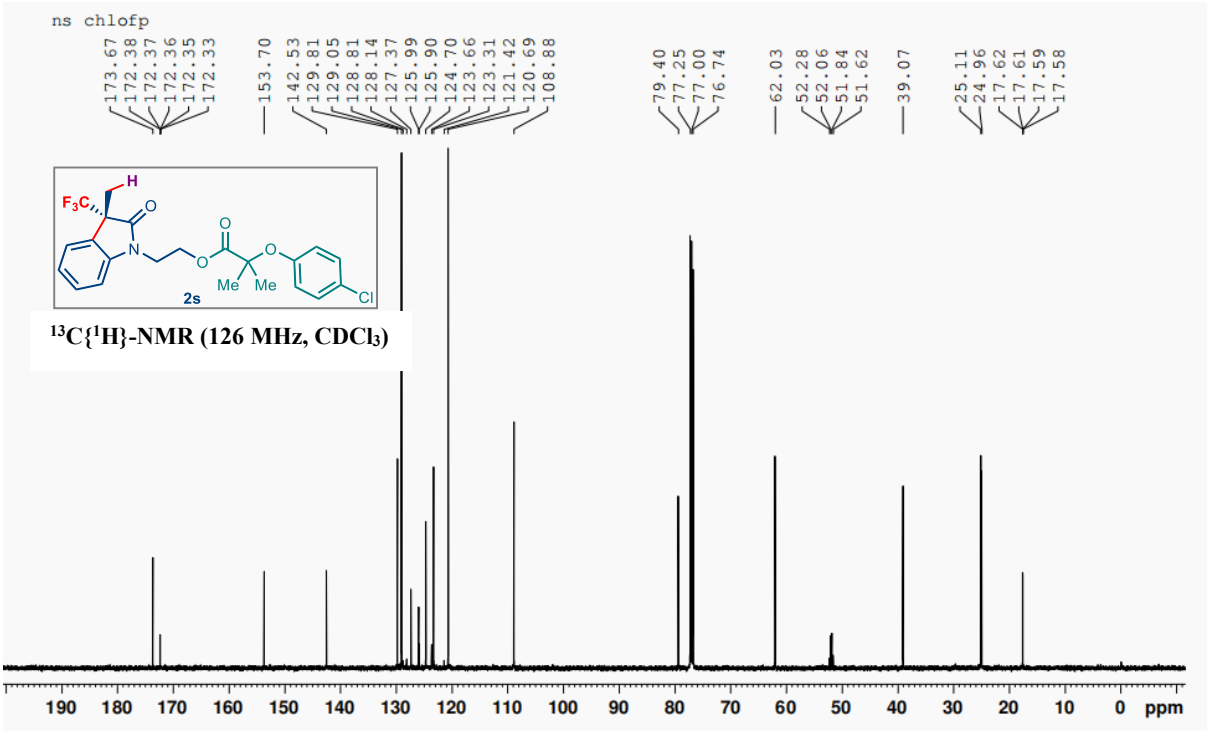
05.03.24
ns-482



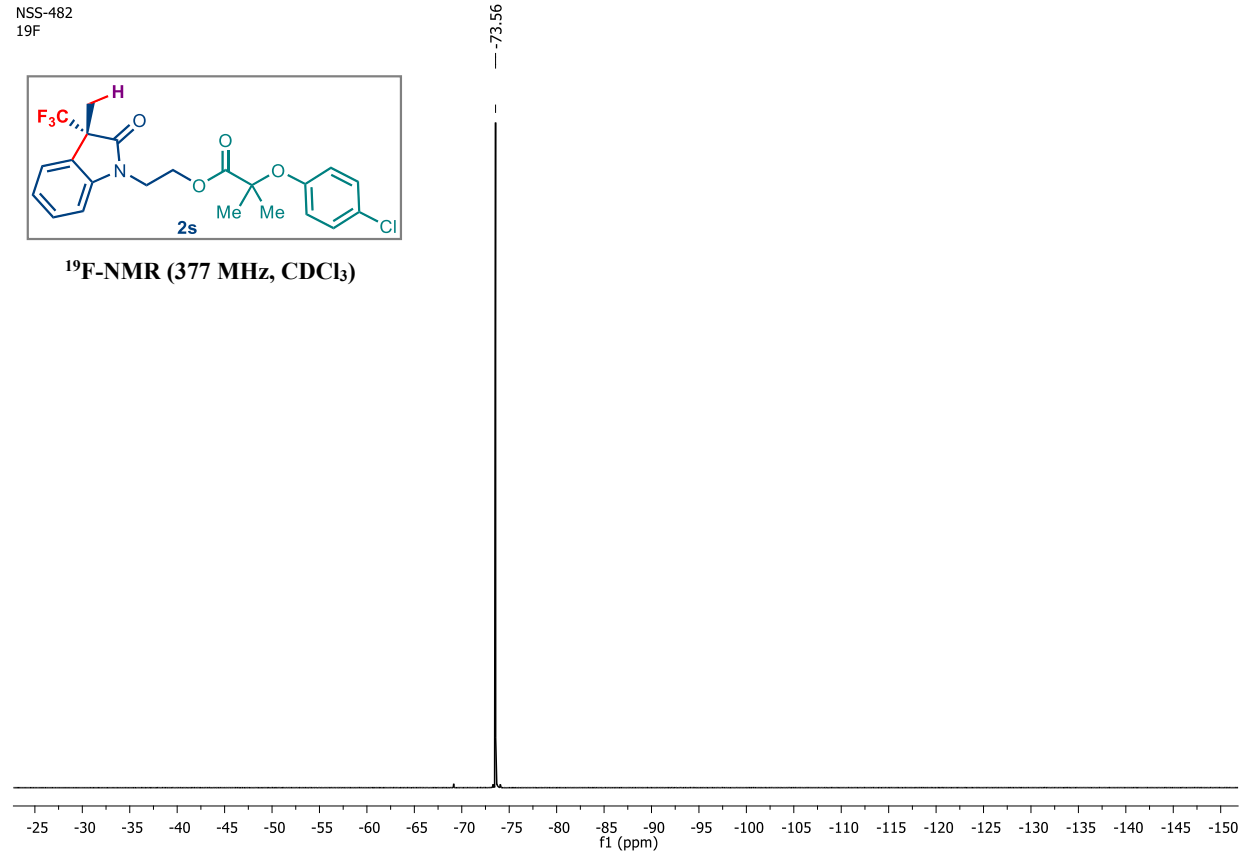


^{1}H-NMR (500 MHz, $CDCl_3$)

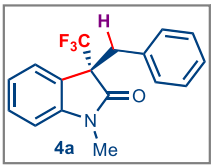




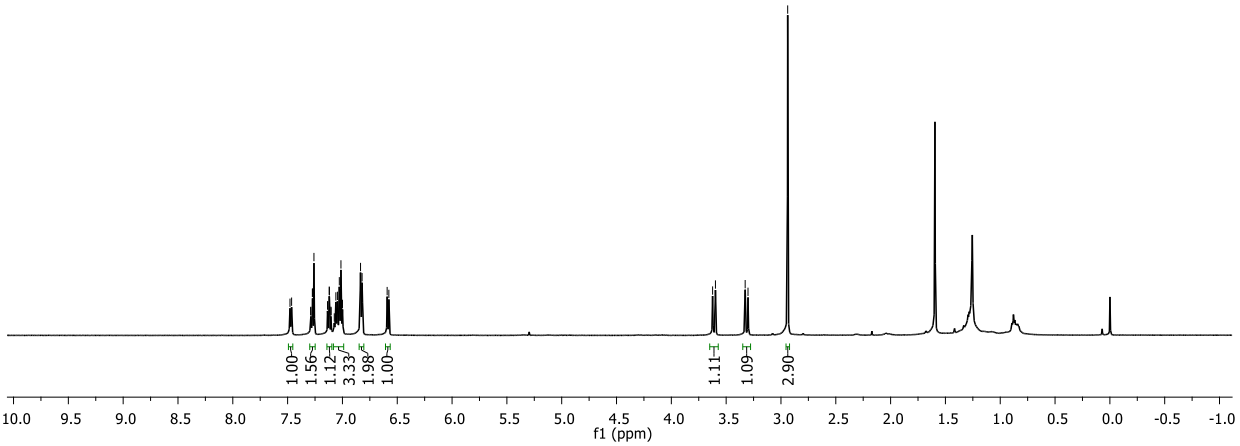
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)

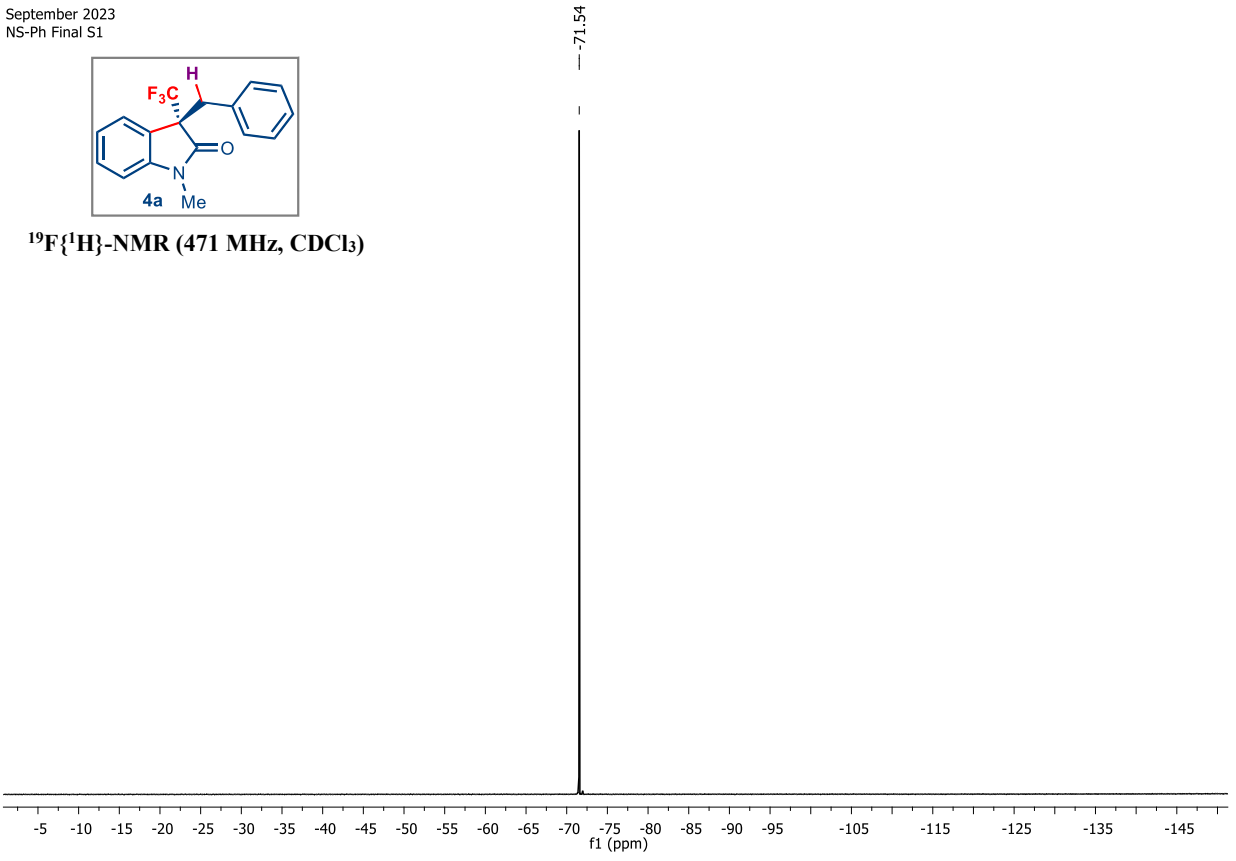


^{19}F-NMR (377 MHz, $CDCl_3$)

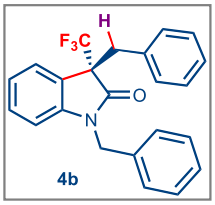


^{1}H-NMR (500 MHz, $CDCl_3$)

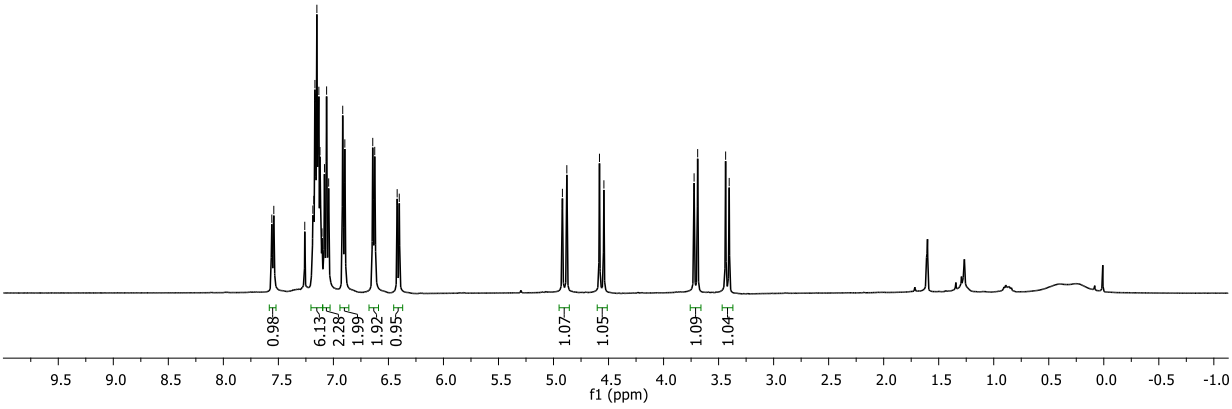


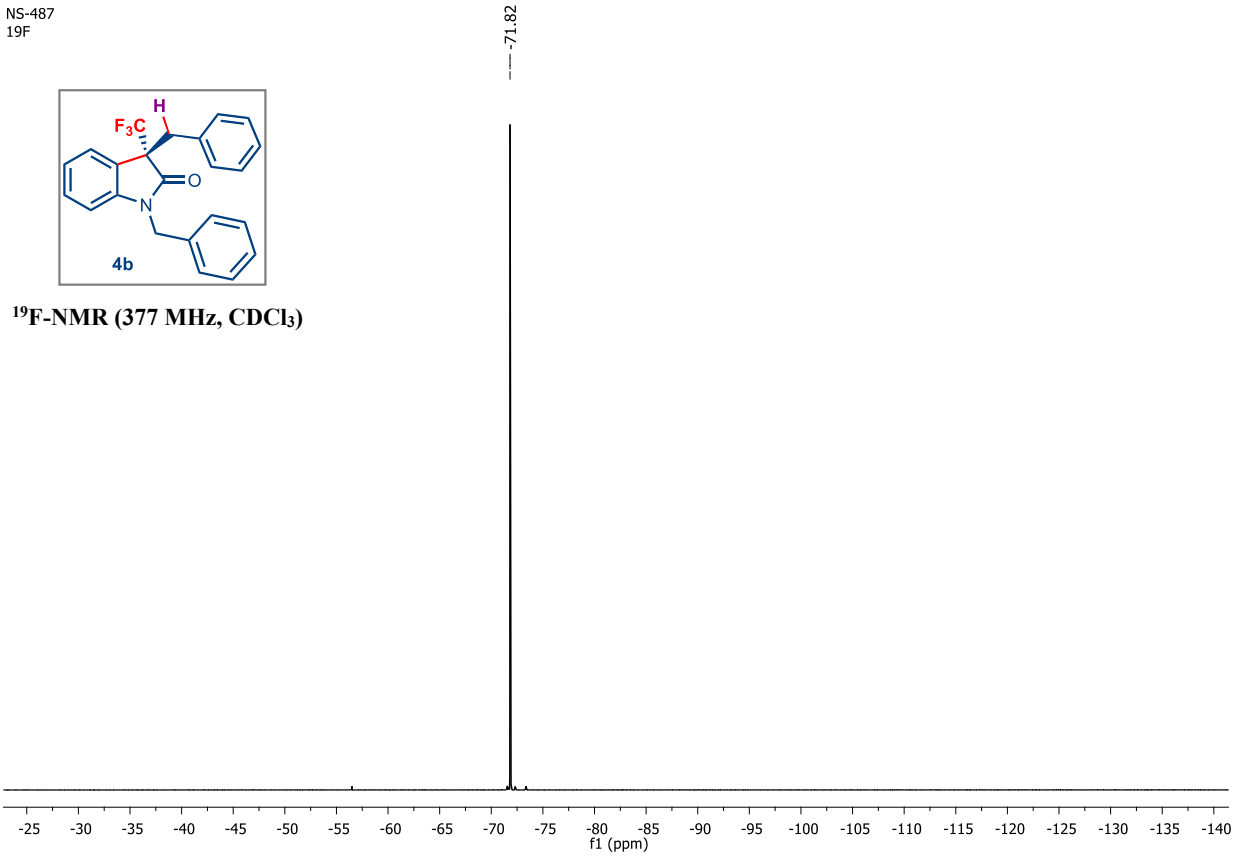


^{19}F{^{1}H}-NMR (471 MHz, $CDCl_3$)

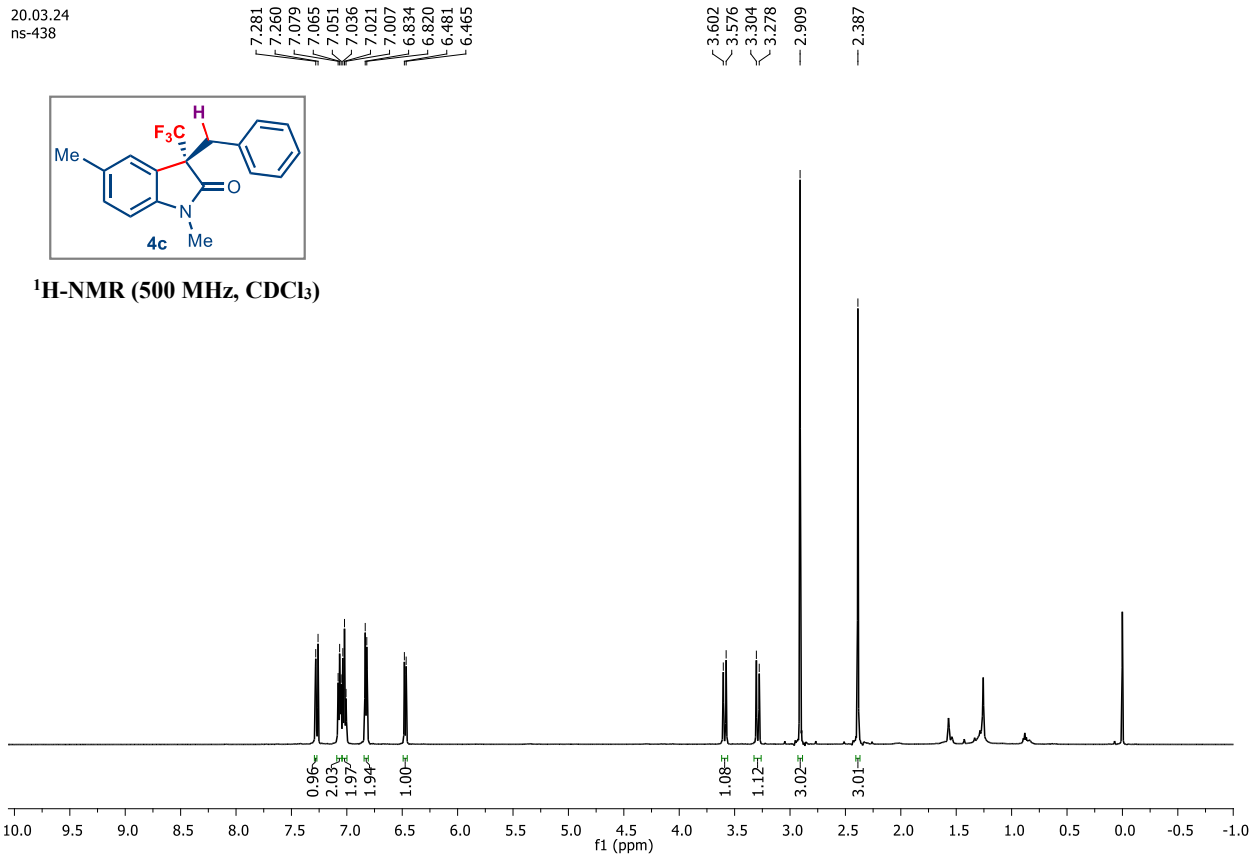


^{1}H-NMR (400 MHz, $CDCl_3$)

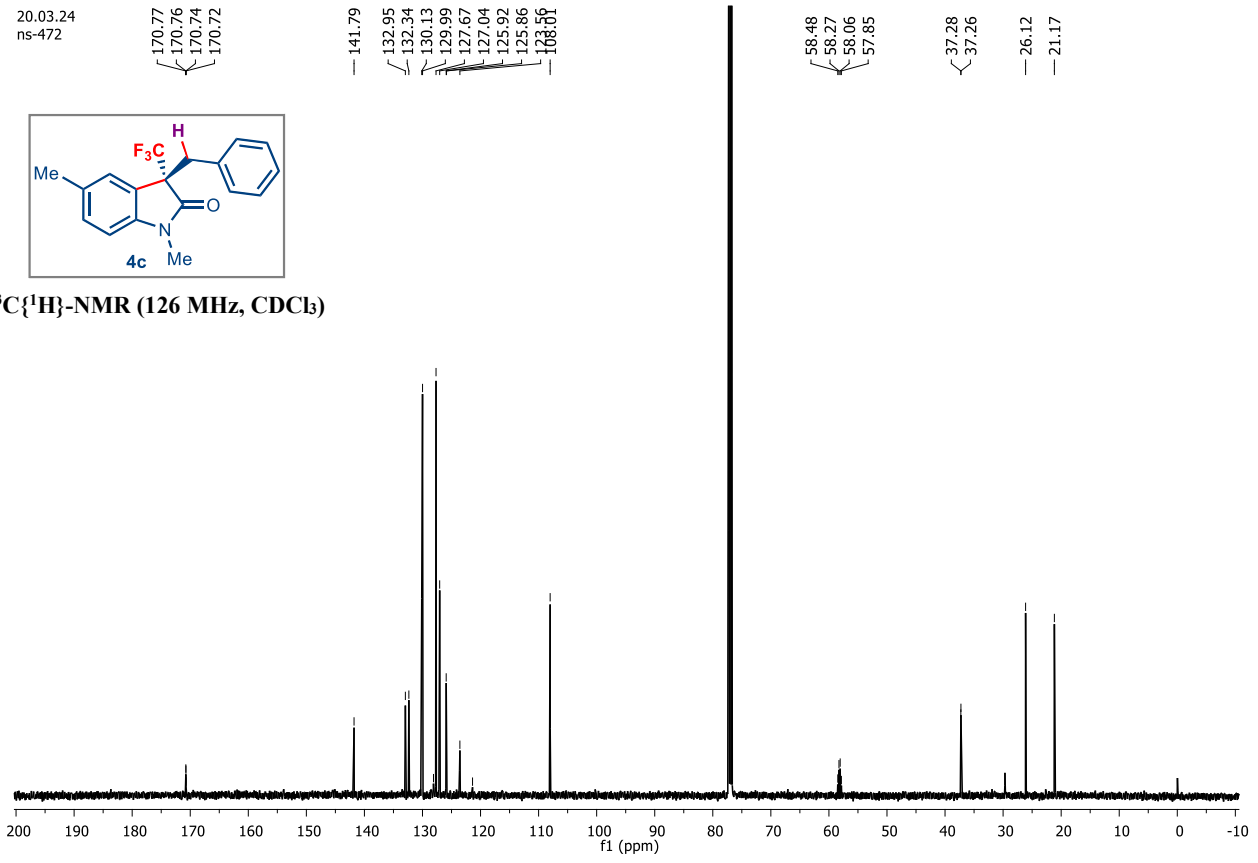




^{19}F-NMR (377 MHz, $CDCl_3$)

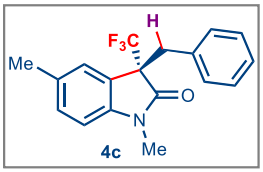


^{1}H-NMR (500 MHz, $CDCl_3$)



^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-438P
19F

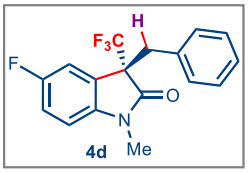


^{19}F-NMR (377 MHz, $CDCl_3$)

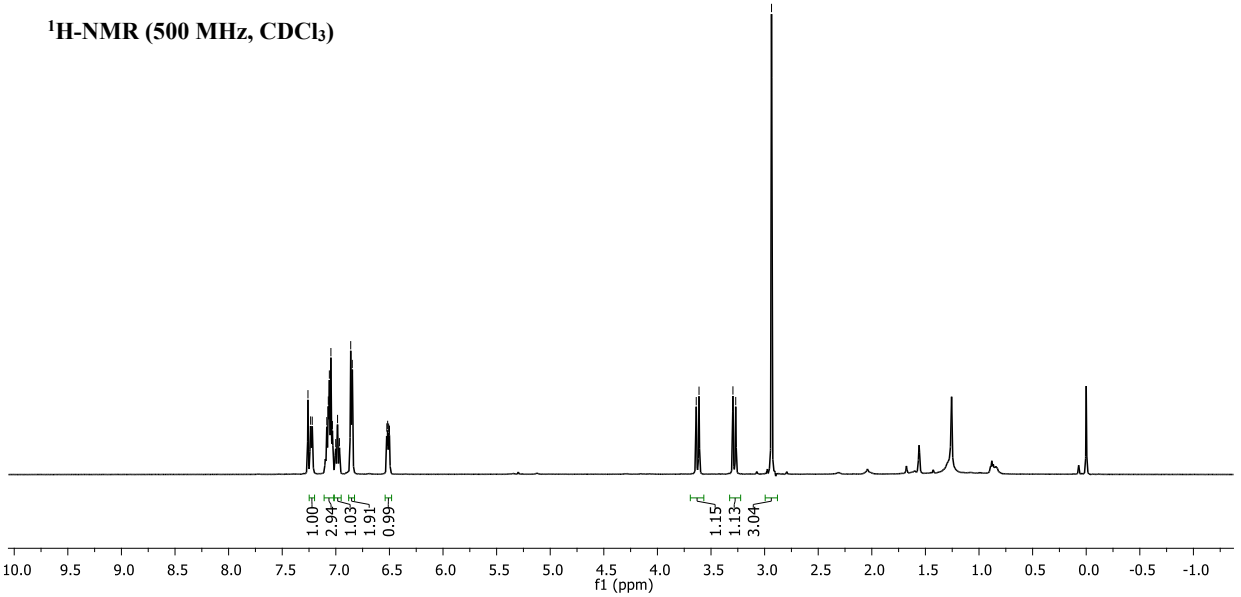
23-01-2024
ns-439

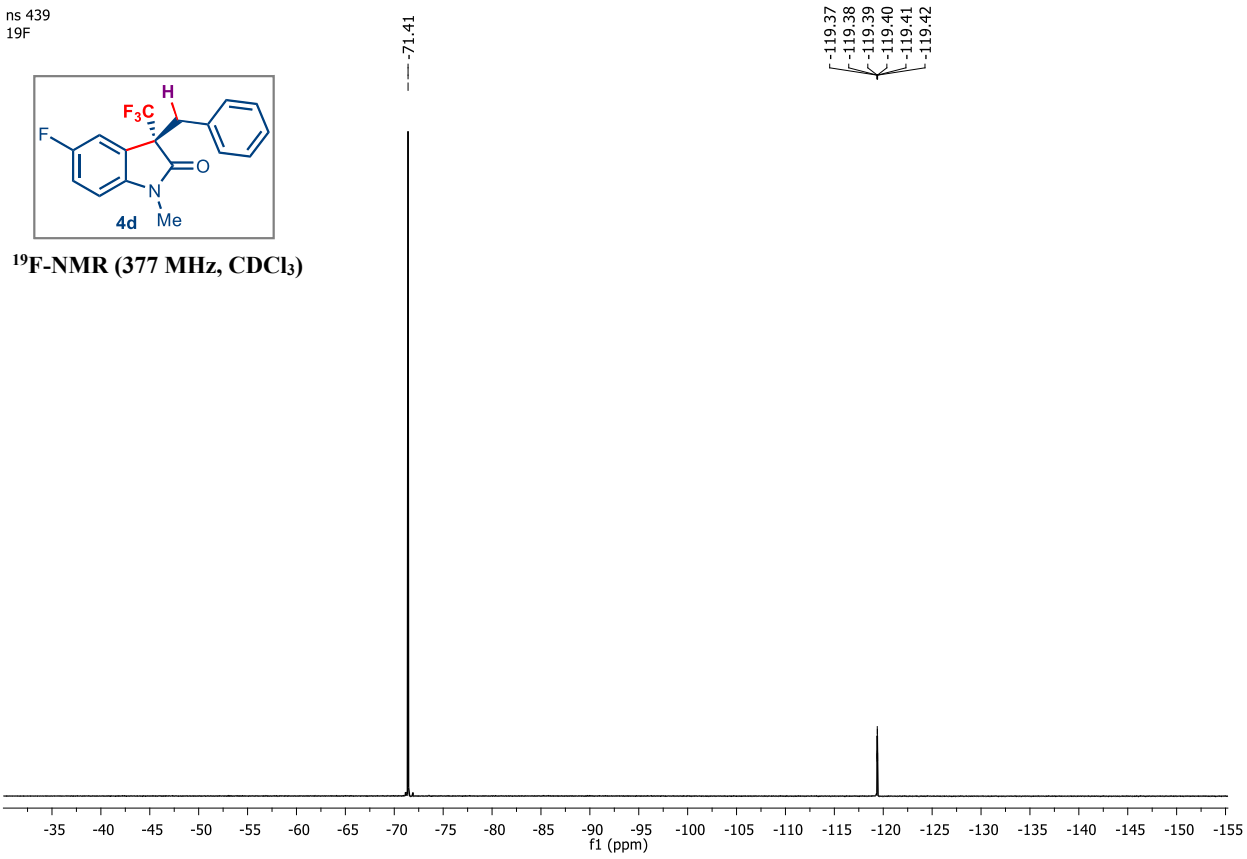
7.260 7.235 7.220 7.084 7.070 7.060 7.046 7.032 7.001 6.984 6.966 6.861 6.846 6.524 6.516 6.507 6.499

3.638 3.612 3.295 3.270 2.935

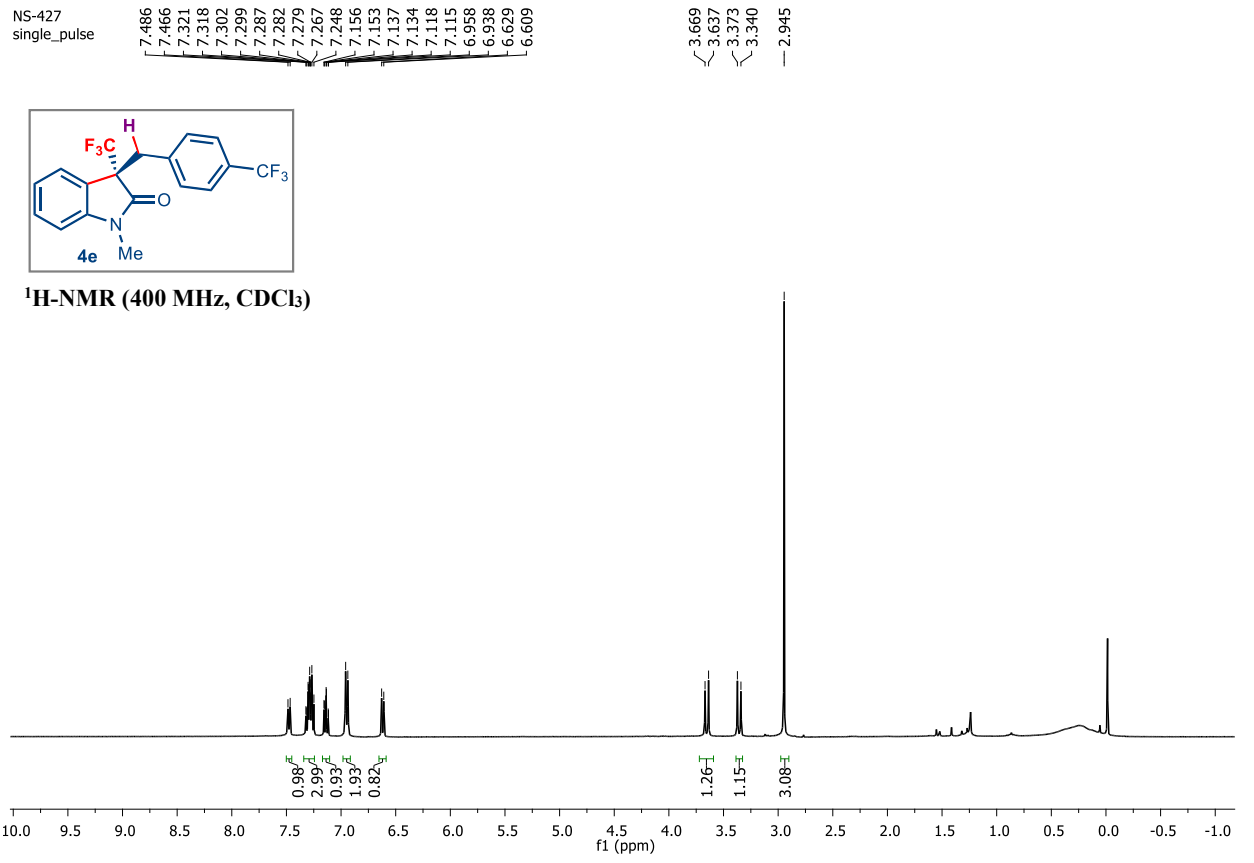


^{1}H-NMR (500 MHz, $CDCl_3$)

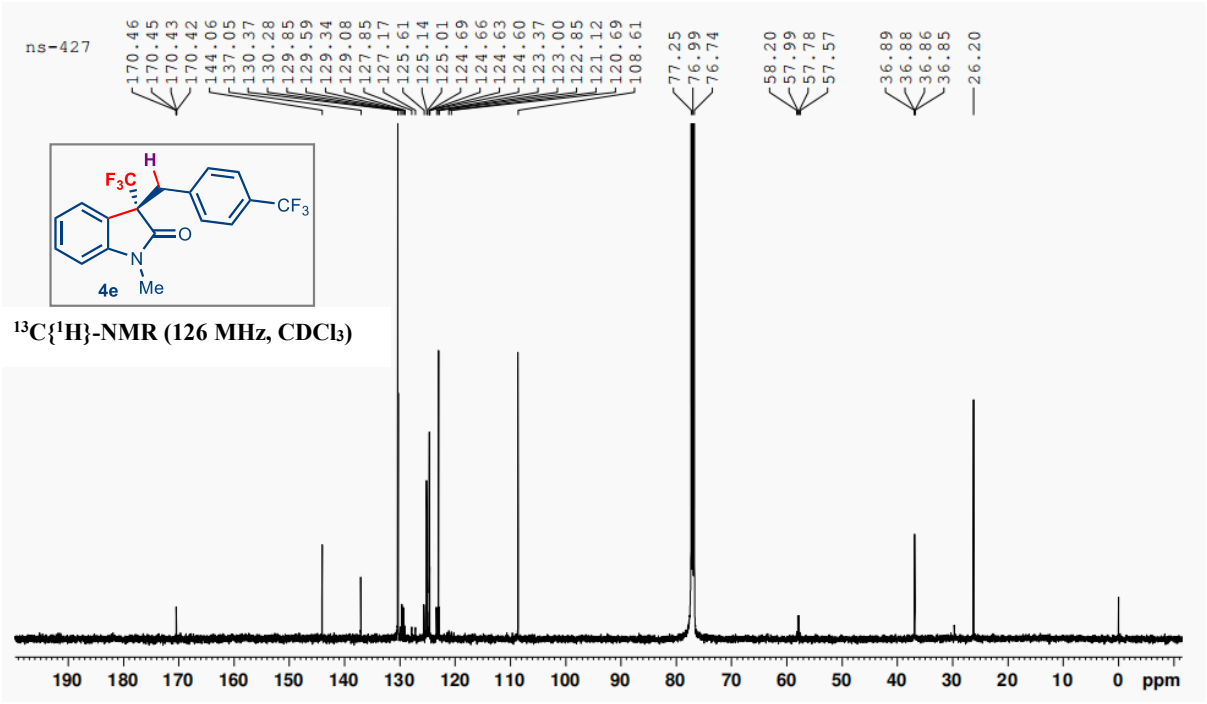




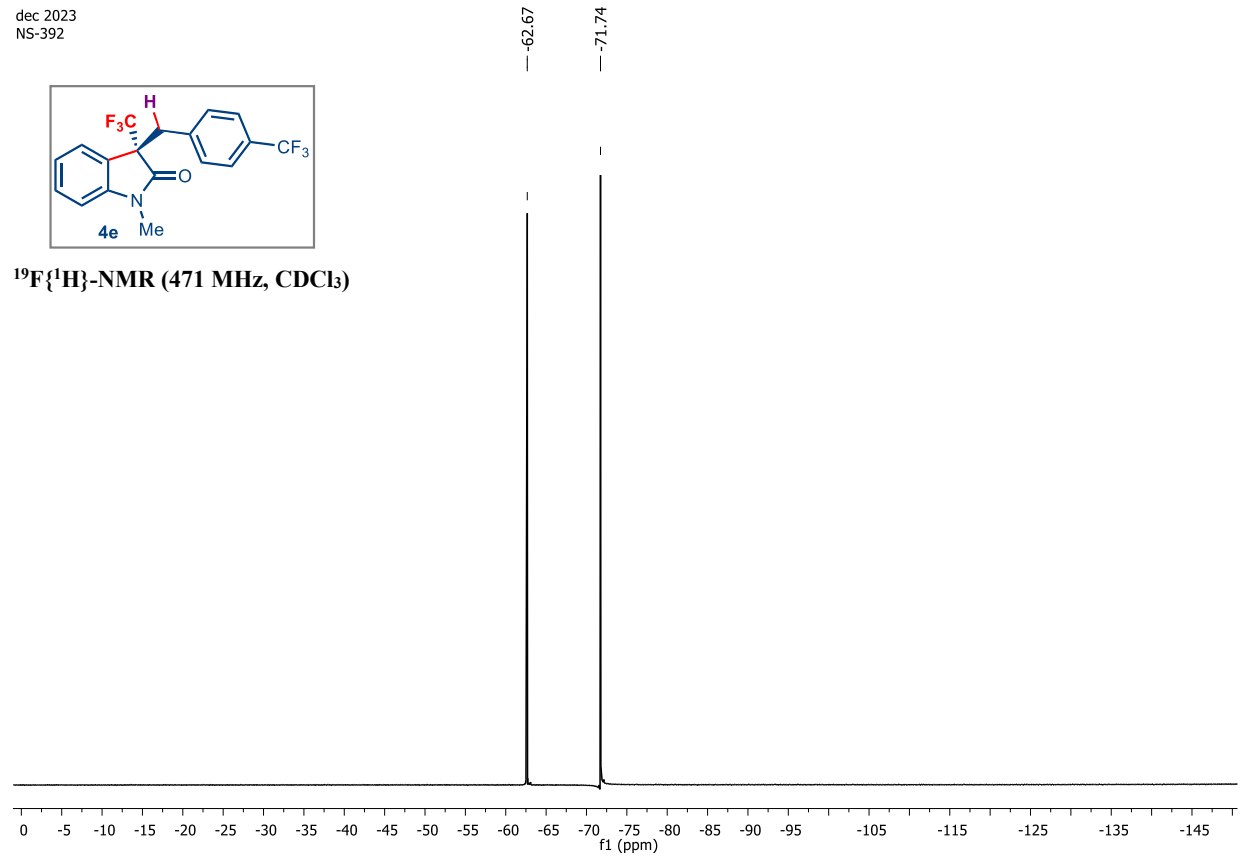
^{19}F-NMR (377 MHz, $CDCl_3$)



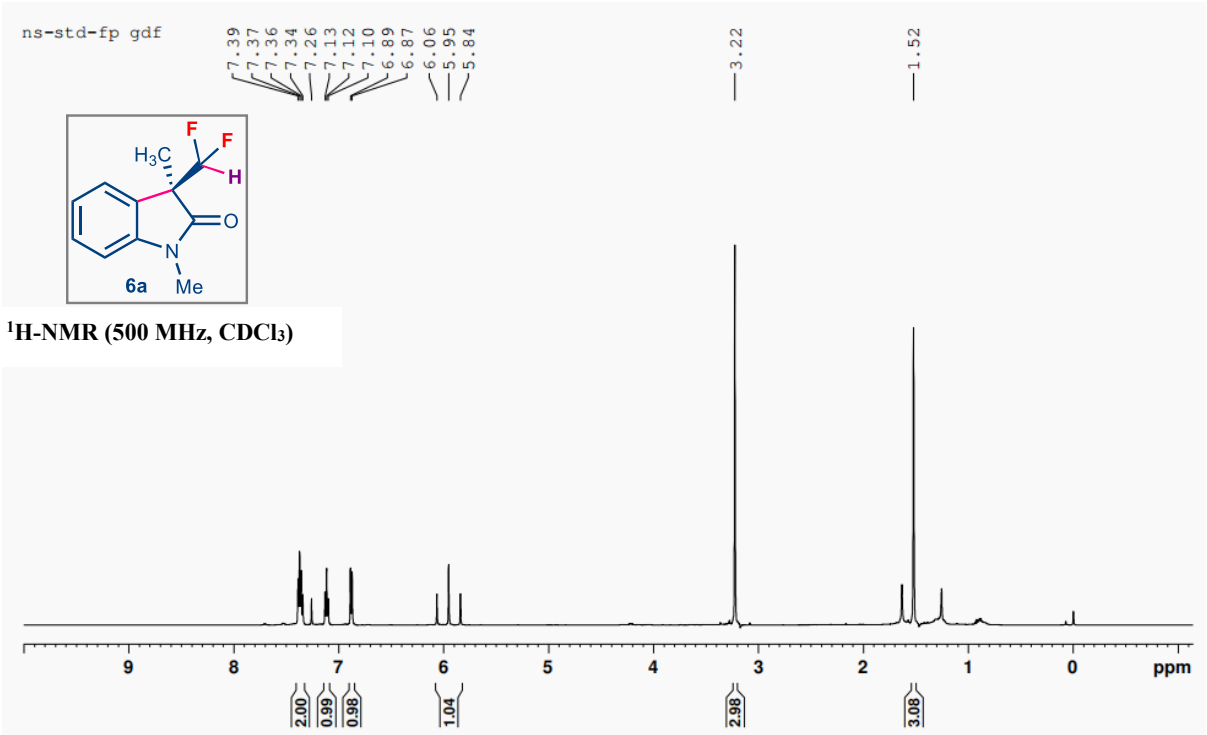
^{1}H-NMR (400 MHz, $CDCl_3$)



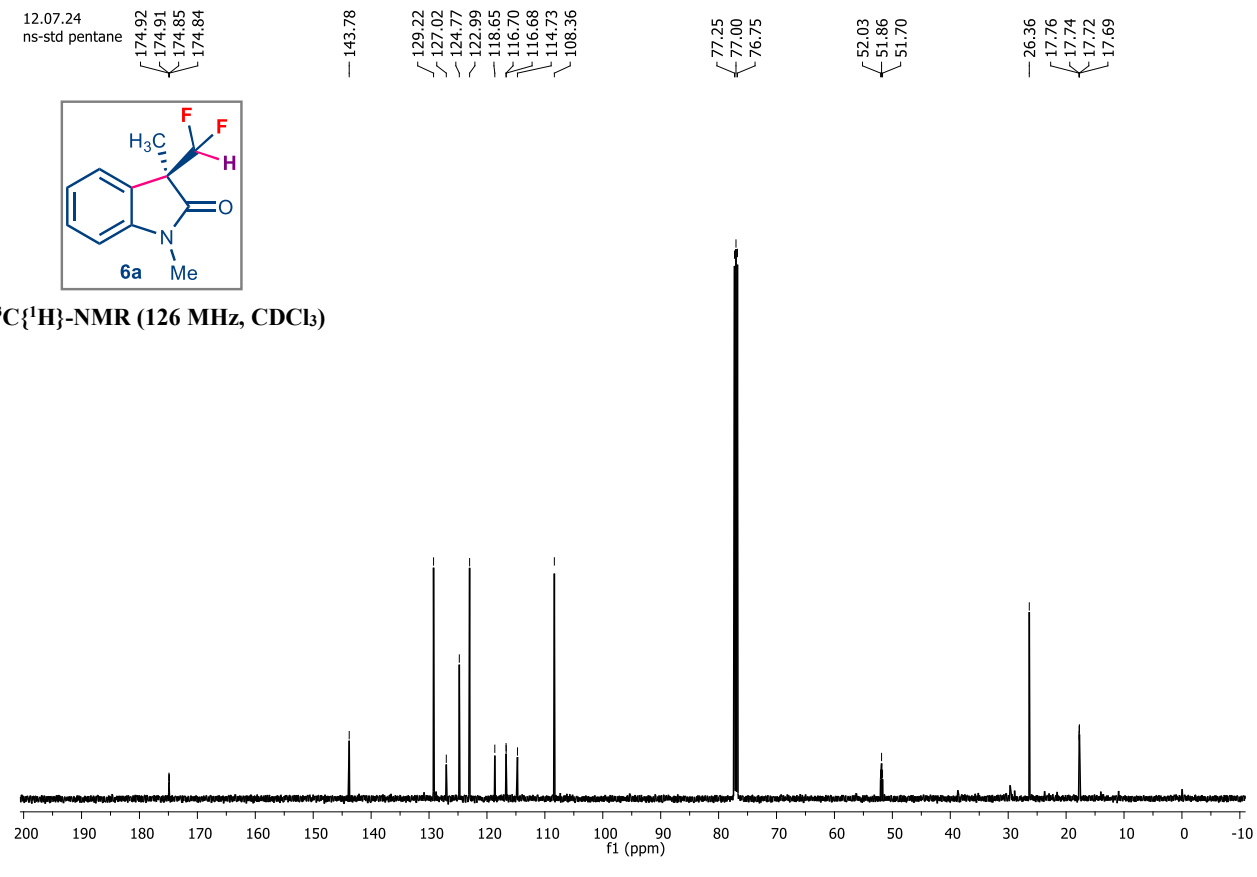
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



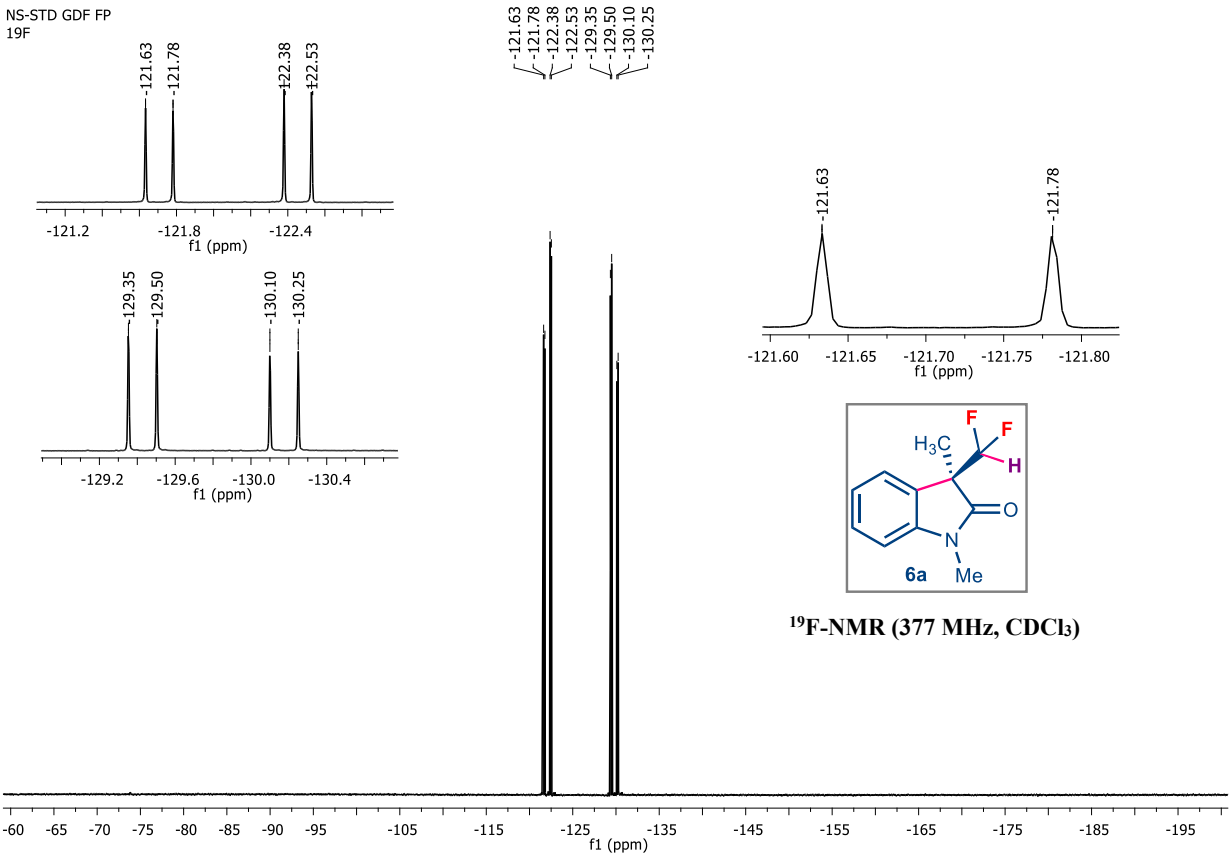
$^{19}F\{^{1}H\}$-NMR (471 MHz, $CDCl_3$)



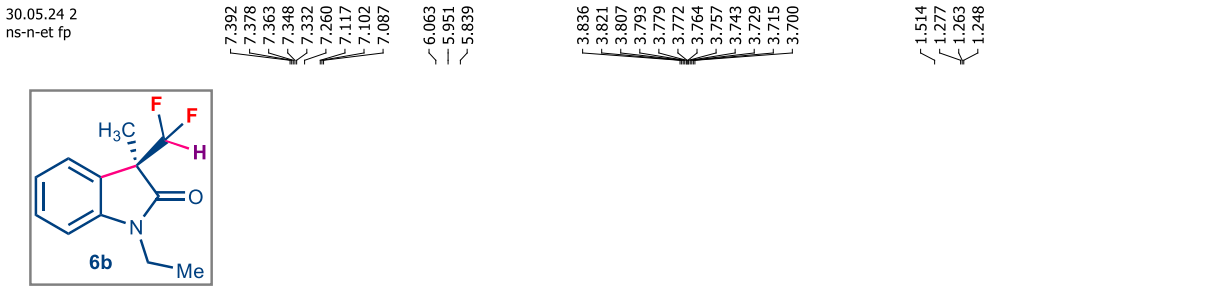
^{1}H-NMR (500 MHz, $CDCl_3$)



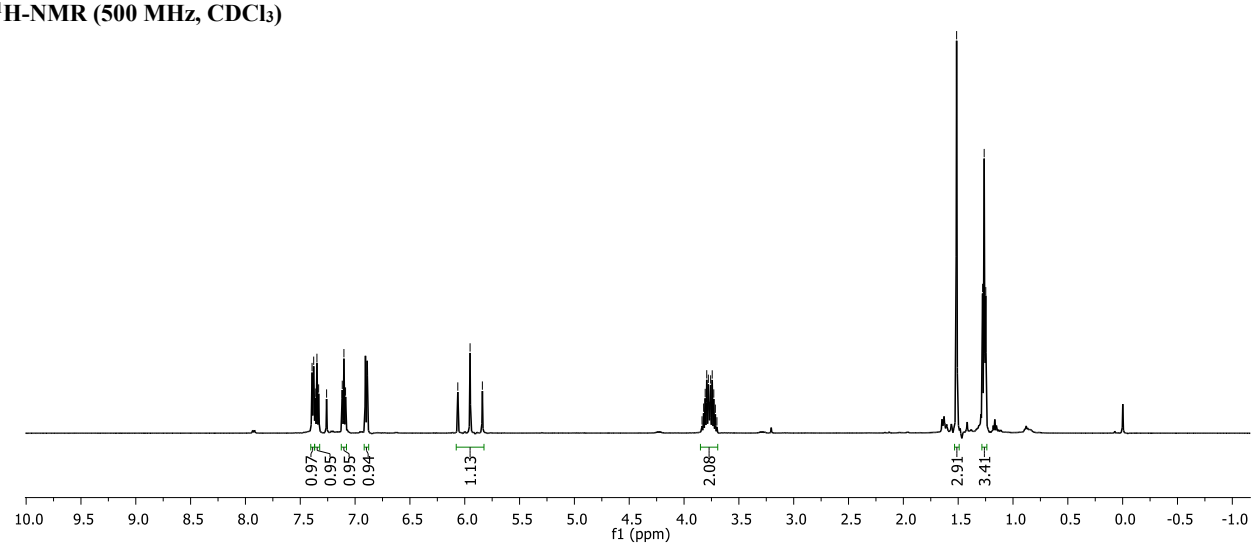
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

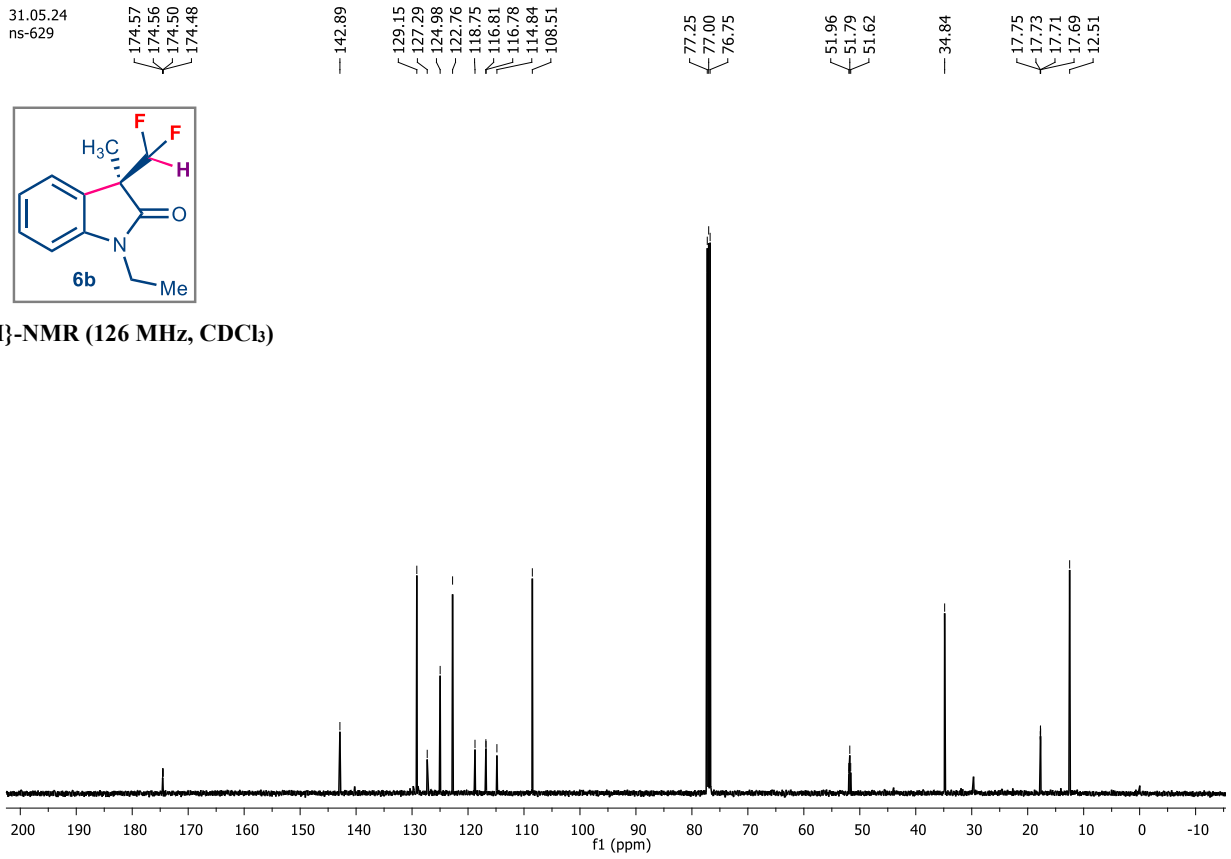


^{19}F-NMR (377 MHz, $CDCl_3$)

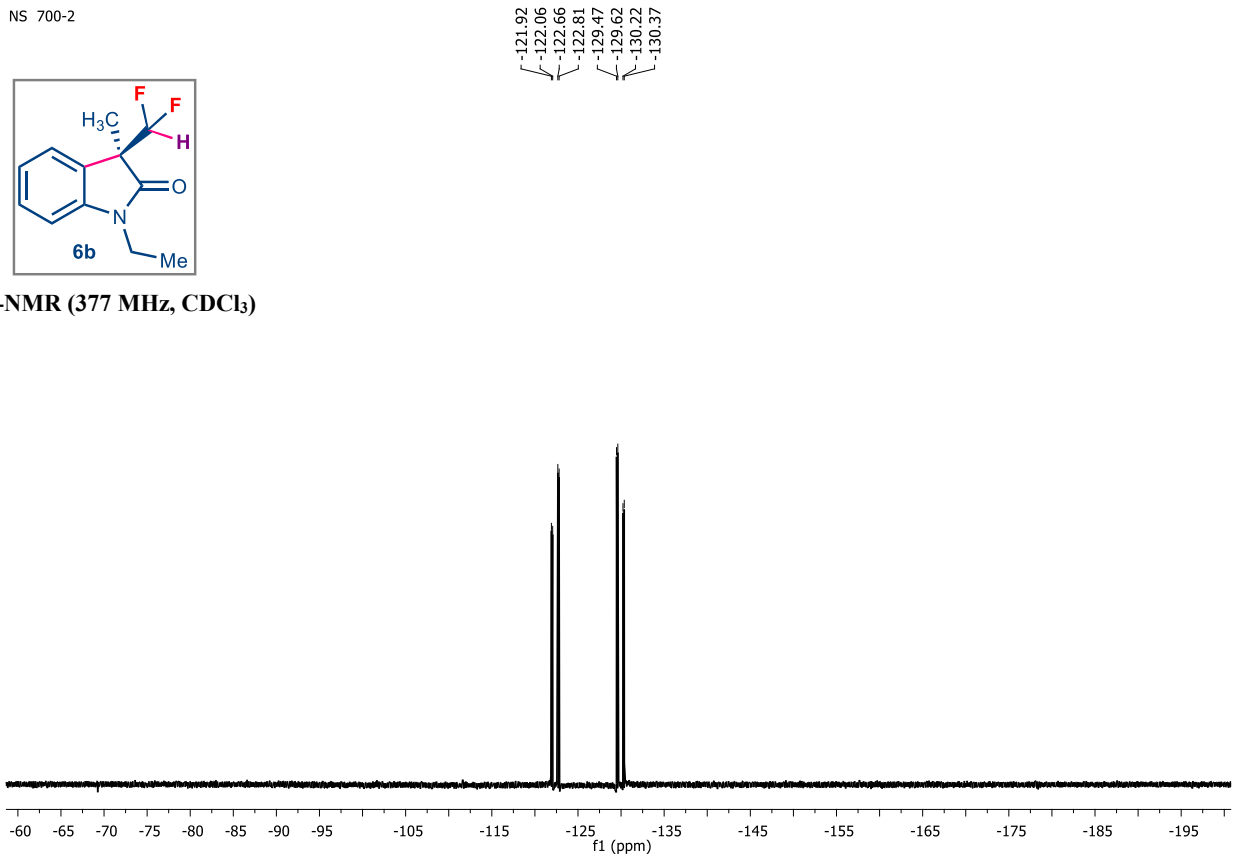


^{1}H-NMR (500 MHz, $CDCl_3$)

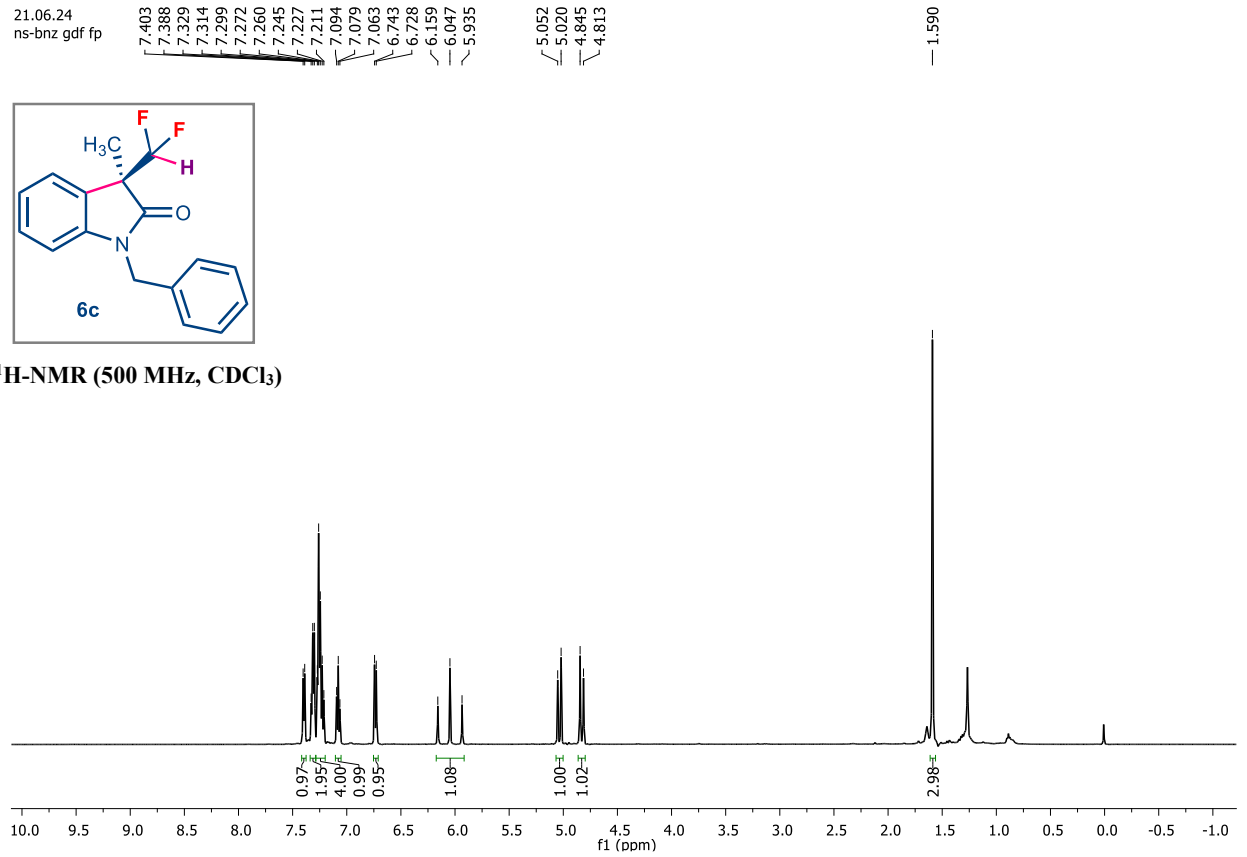




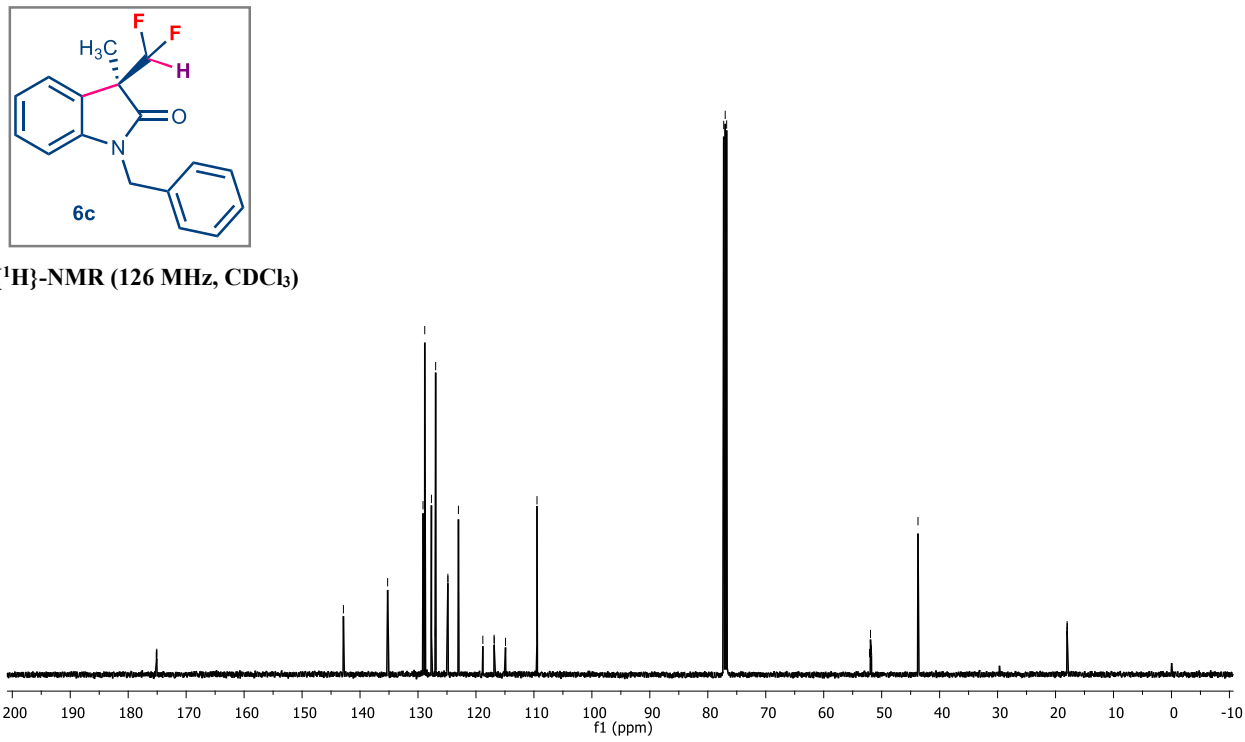
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



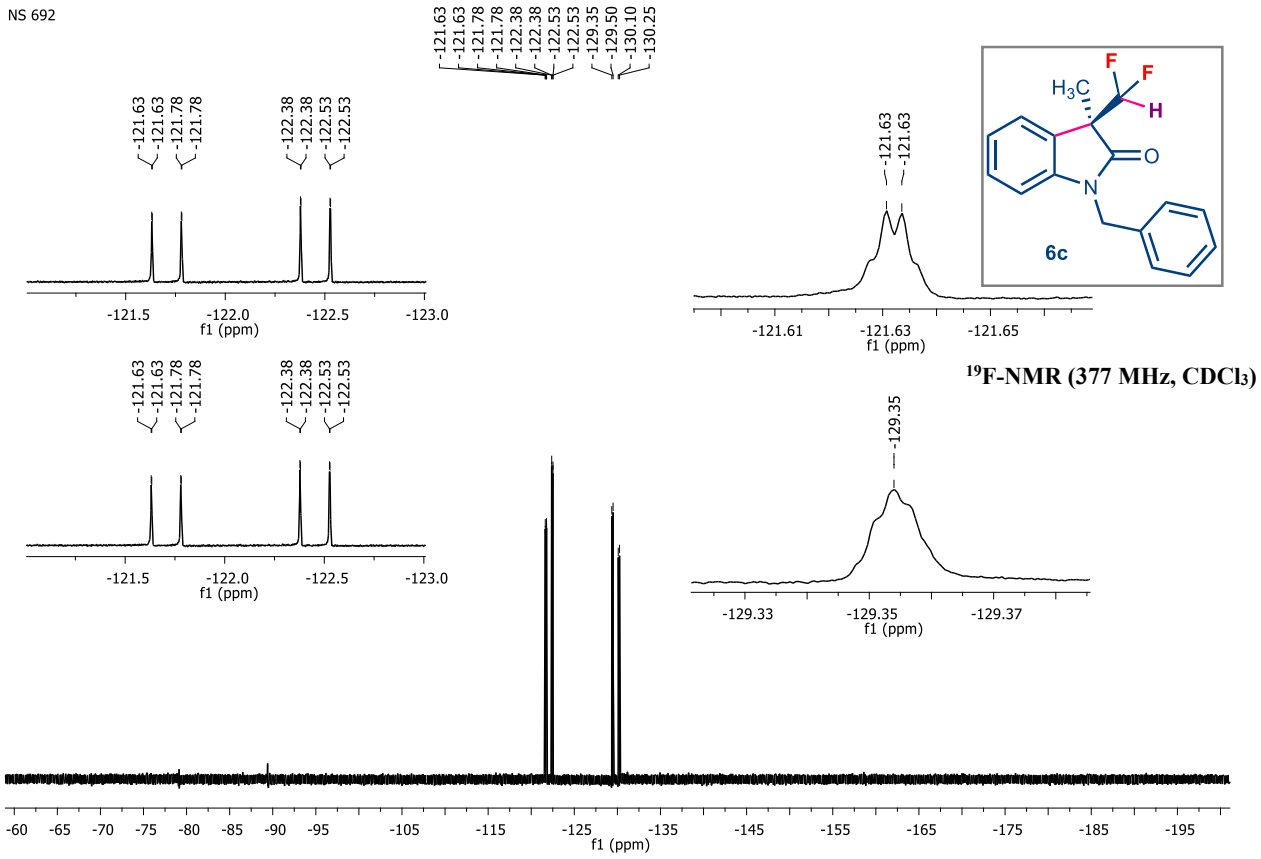
^{19}F-NMR (377 MHz, $CDCl_3$)



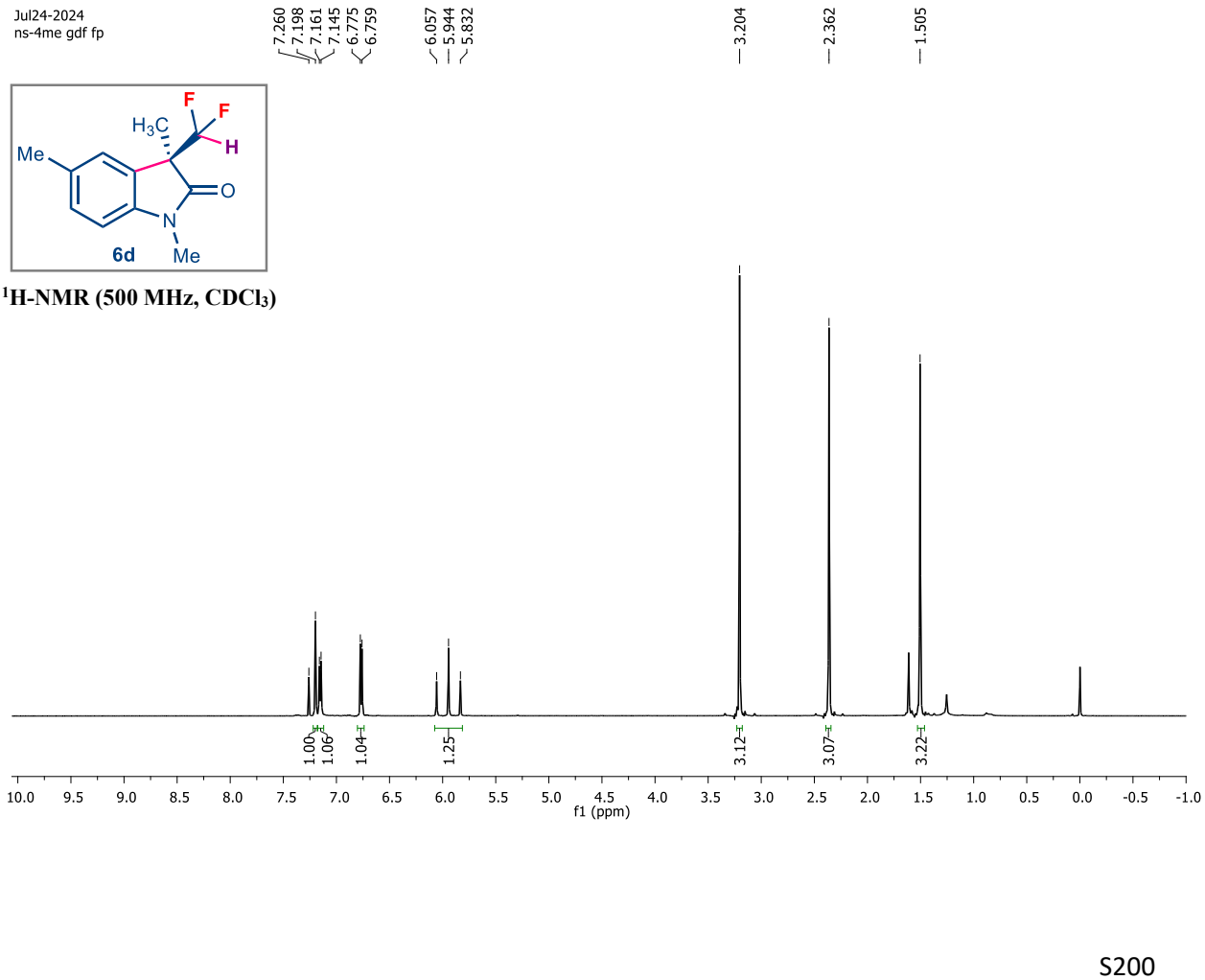
^{1}H-NMR (500 MHz, $CDCl_3$)



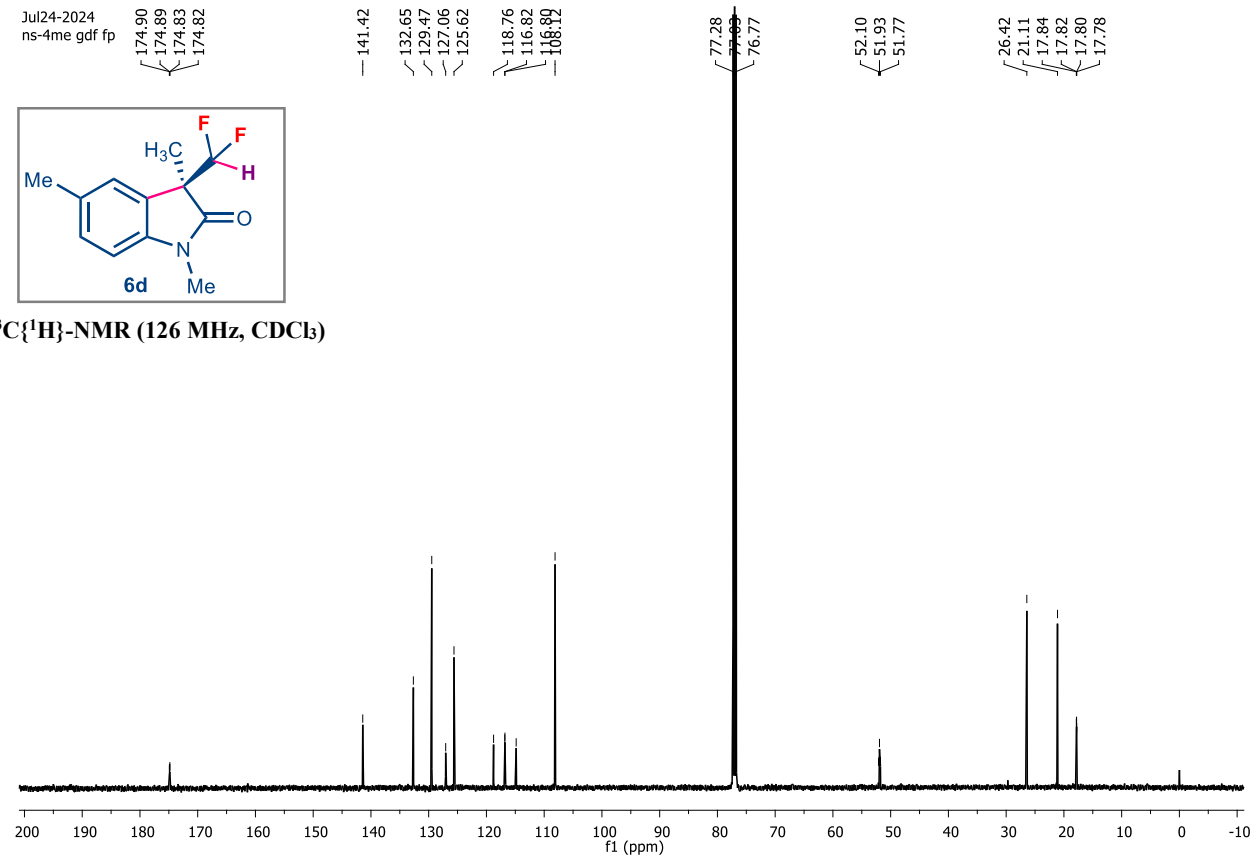
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)



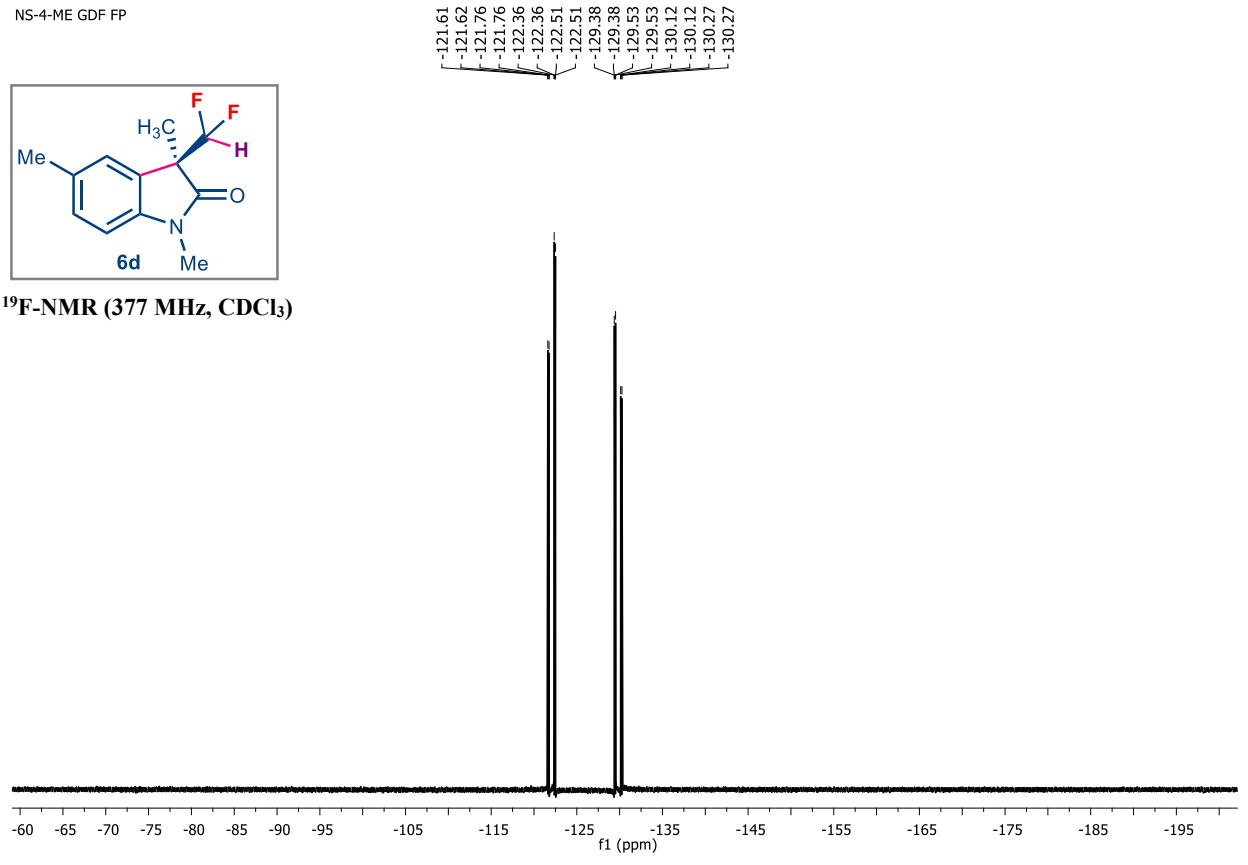
^{19}F-NMR (377 MHz, $CDCl_3$)



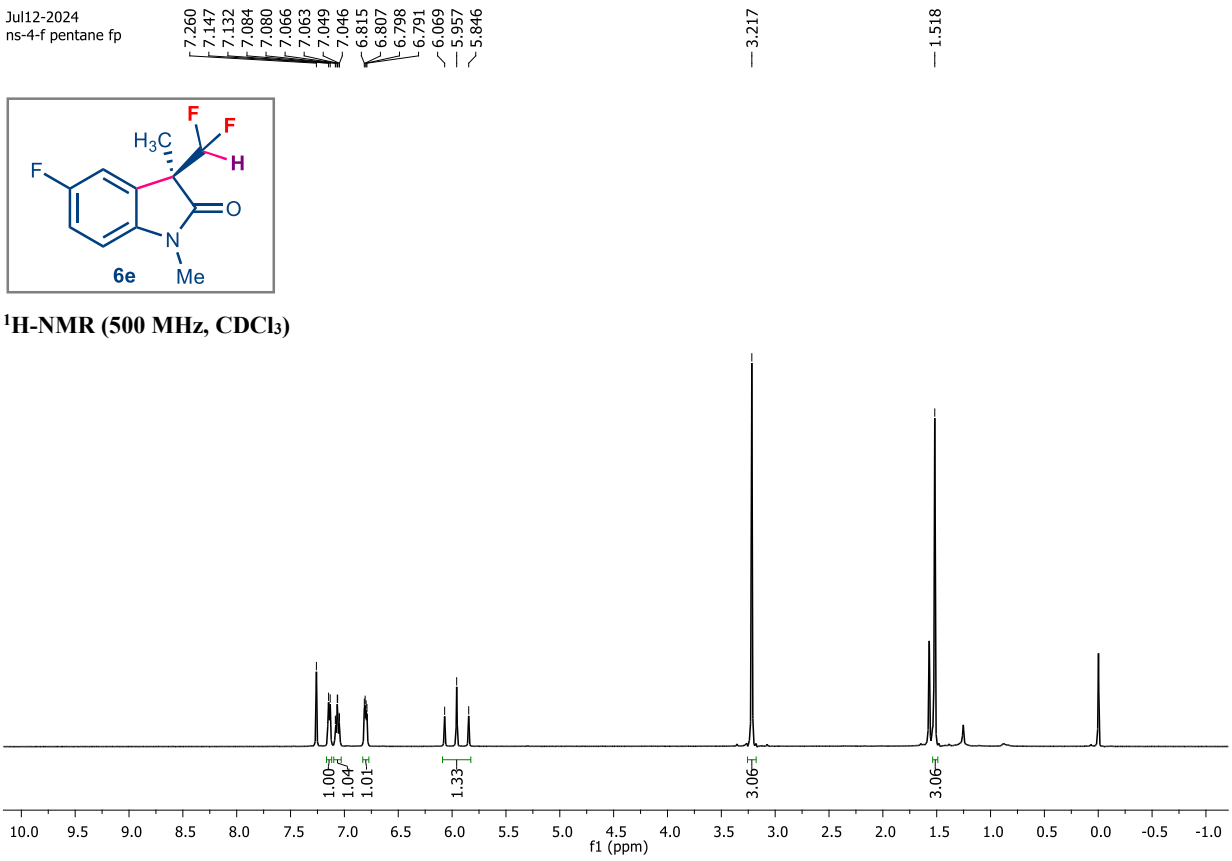
^{1}H-NMR (500 MHz, $CDCl_3$)



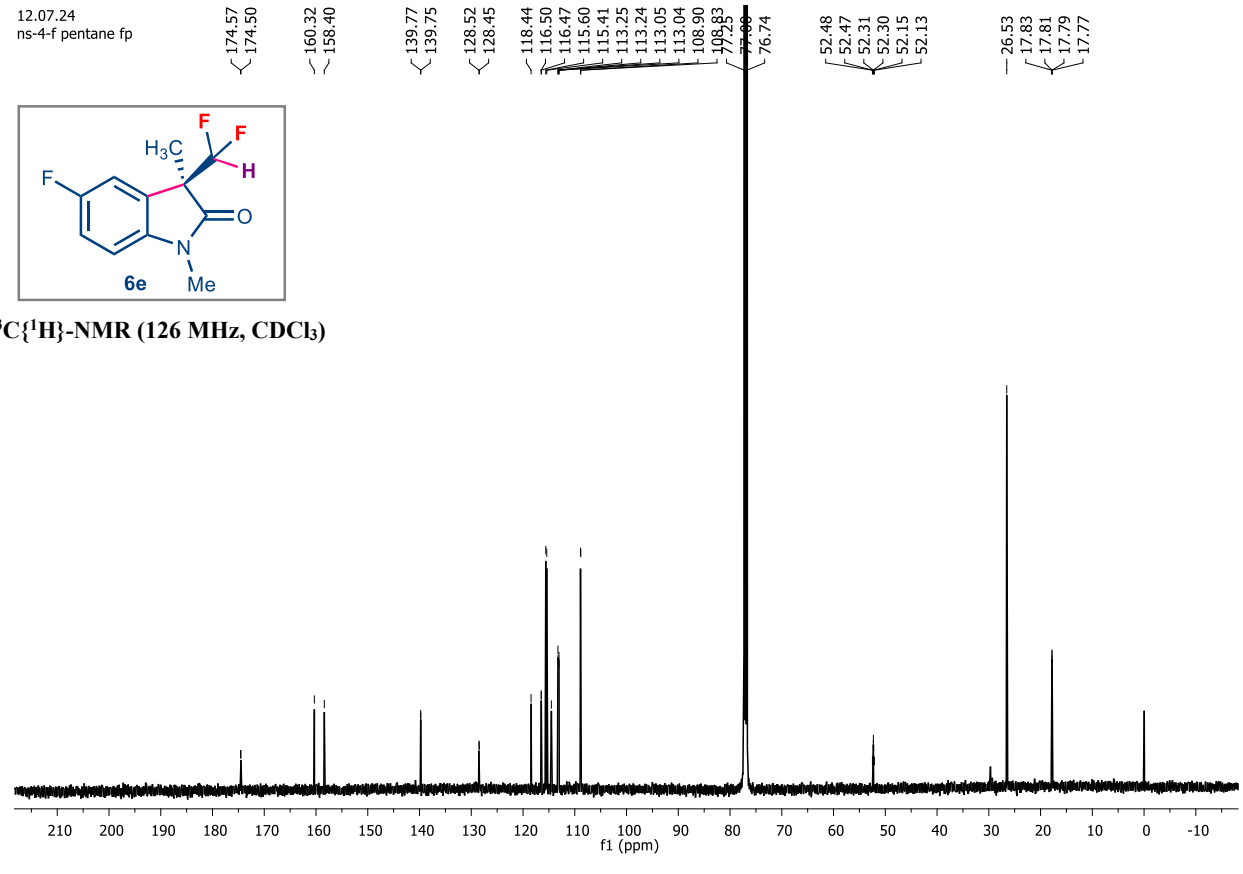
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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



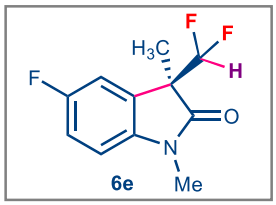
^{1}H-NMR (500 MHz, $CDCl_3$)



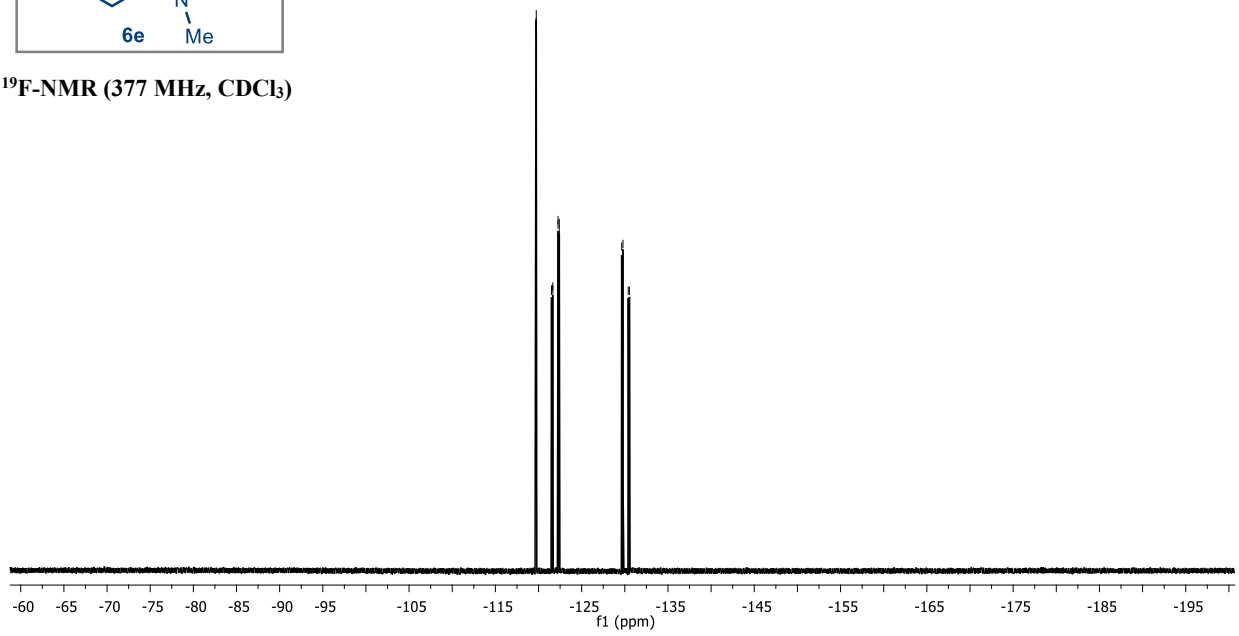
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-4-F GDF FP

-119.71
-119.72
-119.73
-119.73
-119.74
-119.74
-119.75
-119.76
-121.51
-121.51
-121.65
-121.66
-122.26
-122.26
-122.40
-122.41
-129.63
-129.64
-129.64
-129.78
-129.79
-129.79
-130.39
-130.54

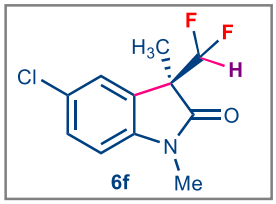


^{19}F-NMR (377 MHz, $CDCl_3$)

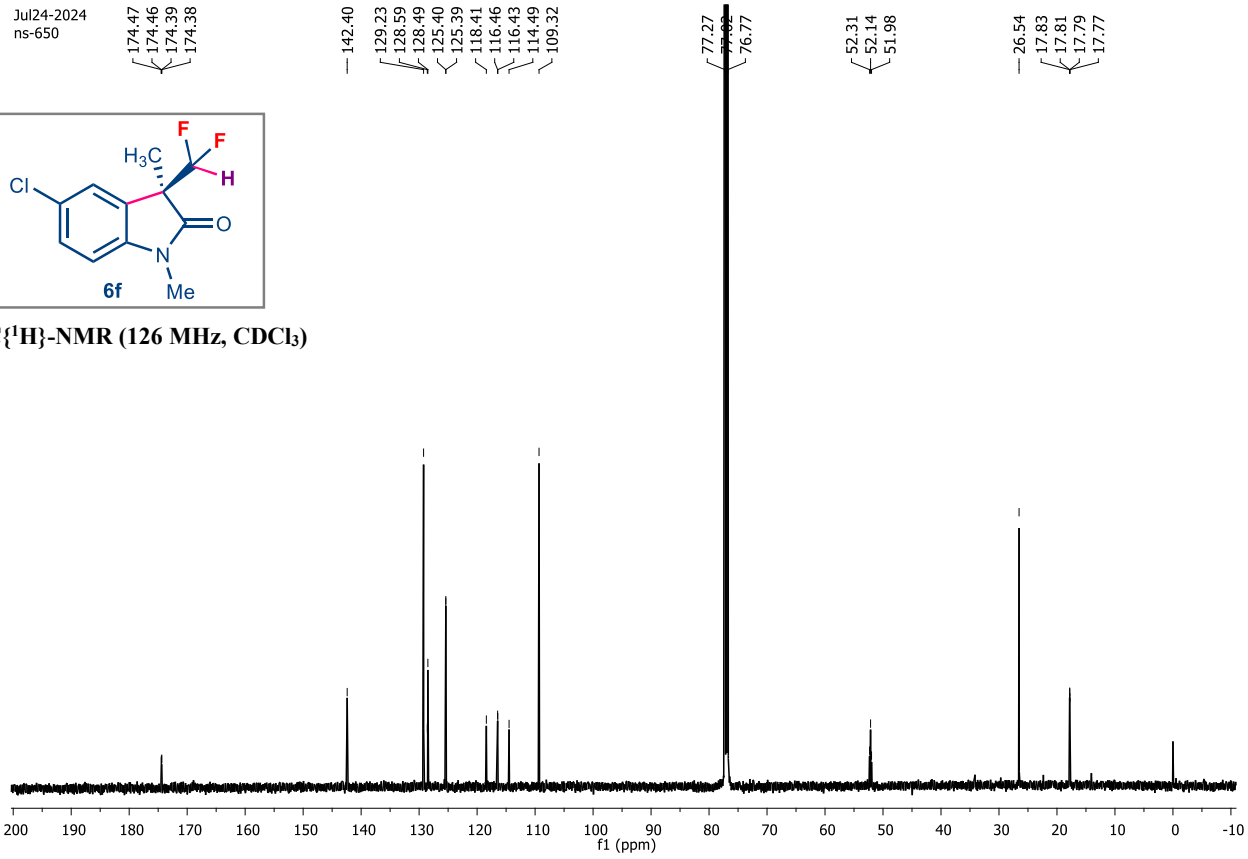


694

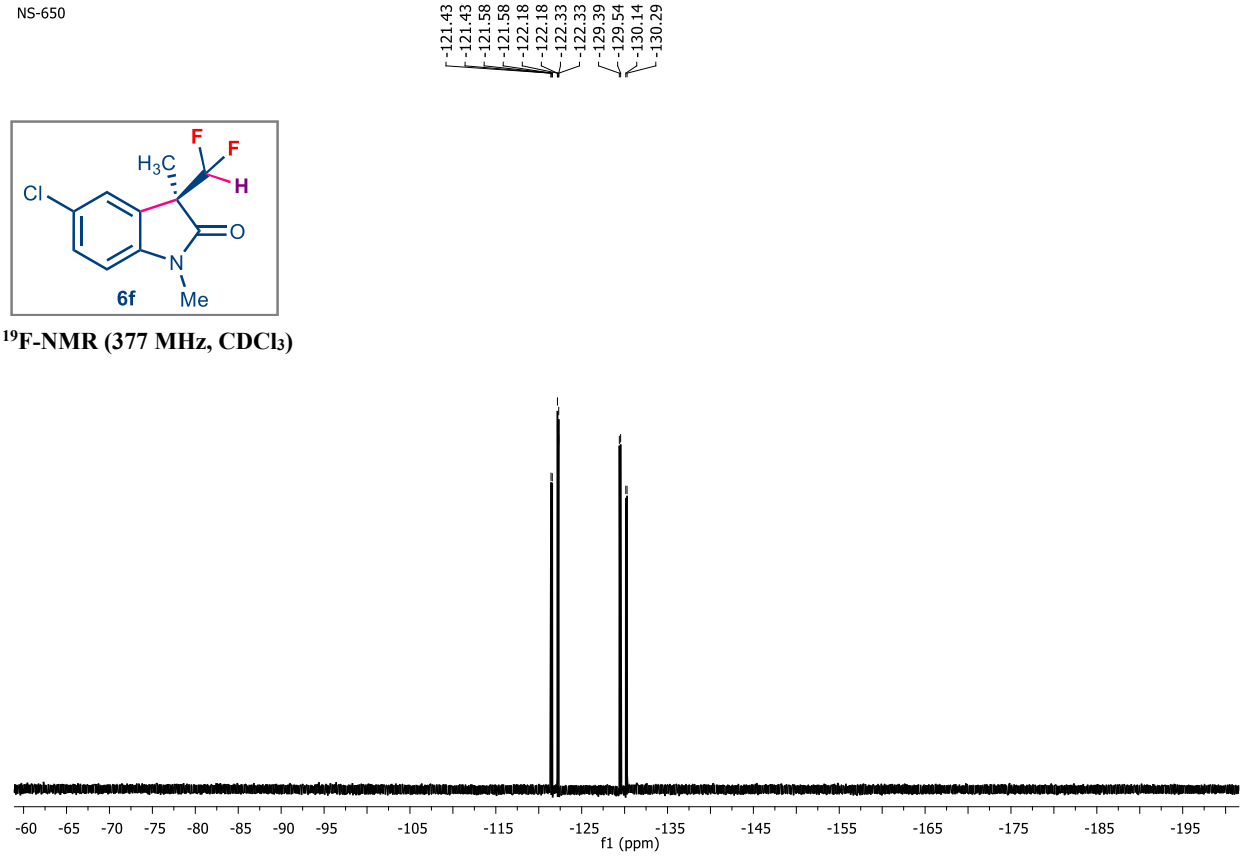
7.361
7.347
7.330
7.260
6.812
6.796
6.062
5.950
5.839
3.213
1.516



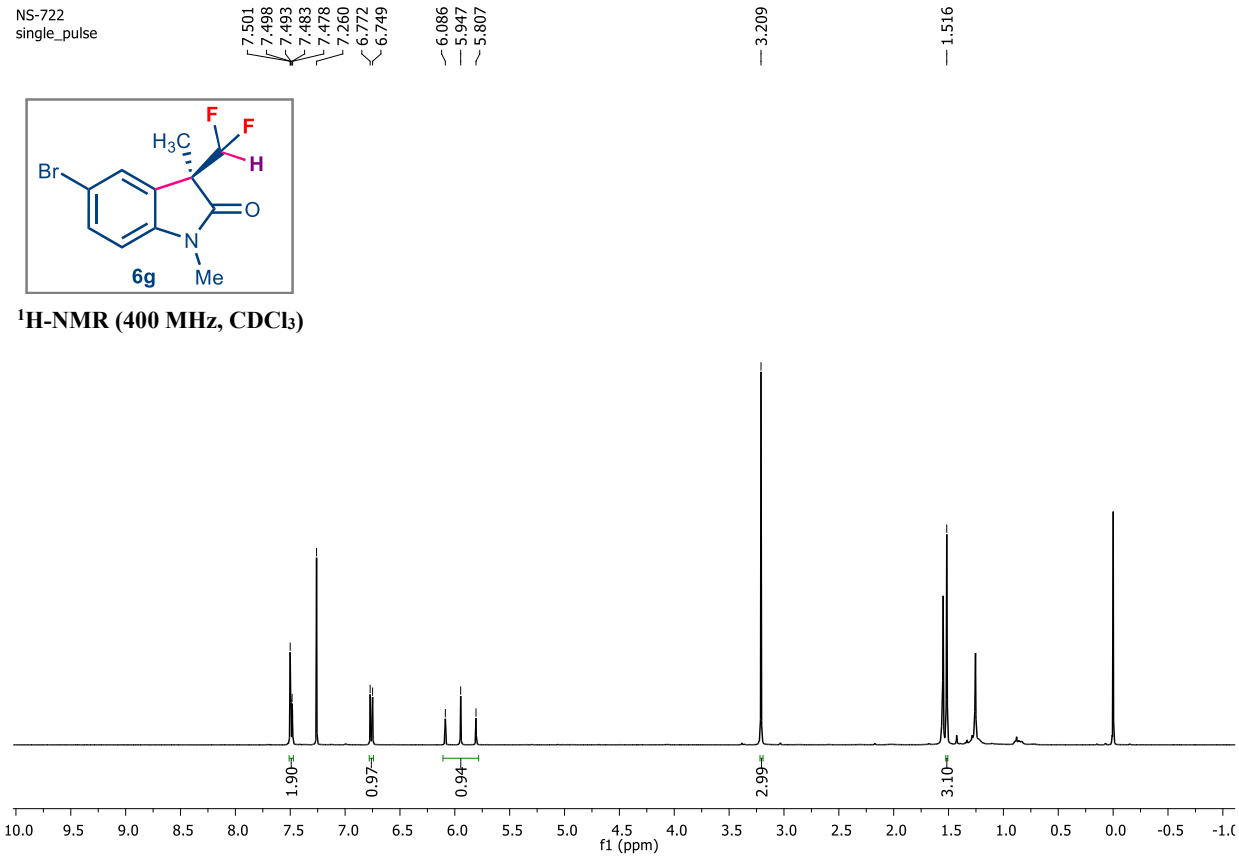
^{1}H-NMR (500 MHz, $CDCl_3$)



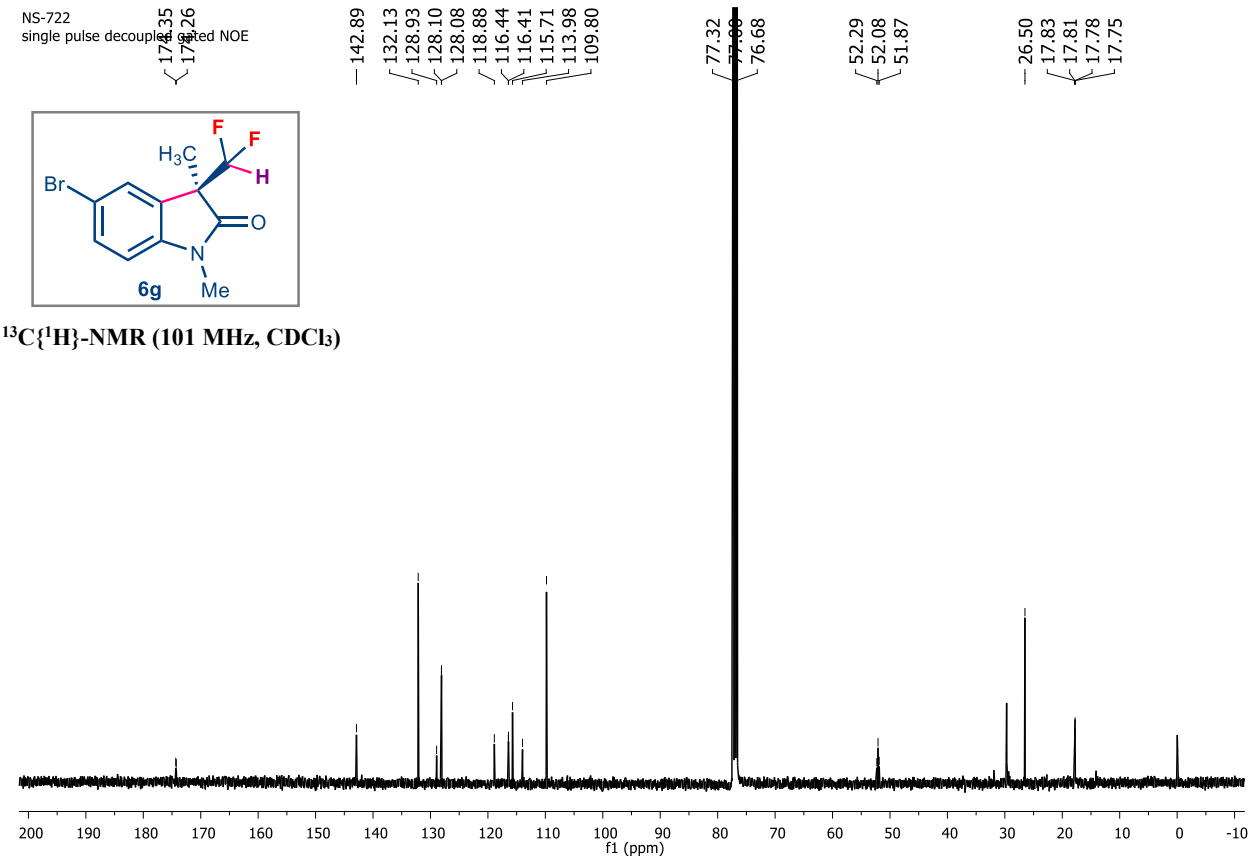
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

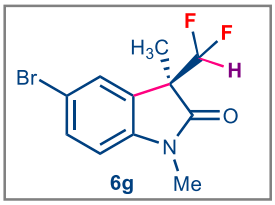


^{1}H-NMR (400 MHz, $CDCl_3$)



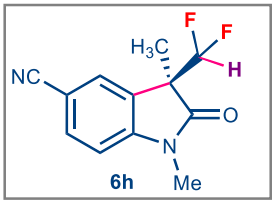
^{13}C{^{1}H}-NMR (101 MHz, $CDCl_3$)

NS-722
19F

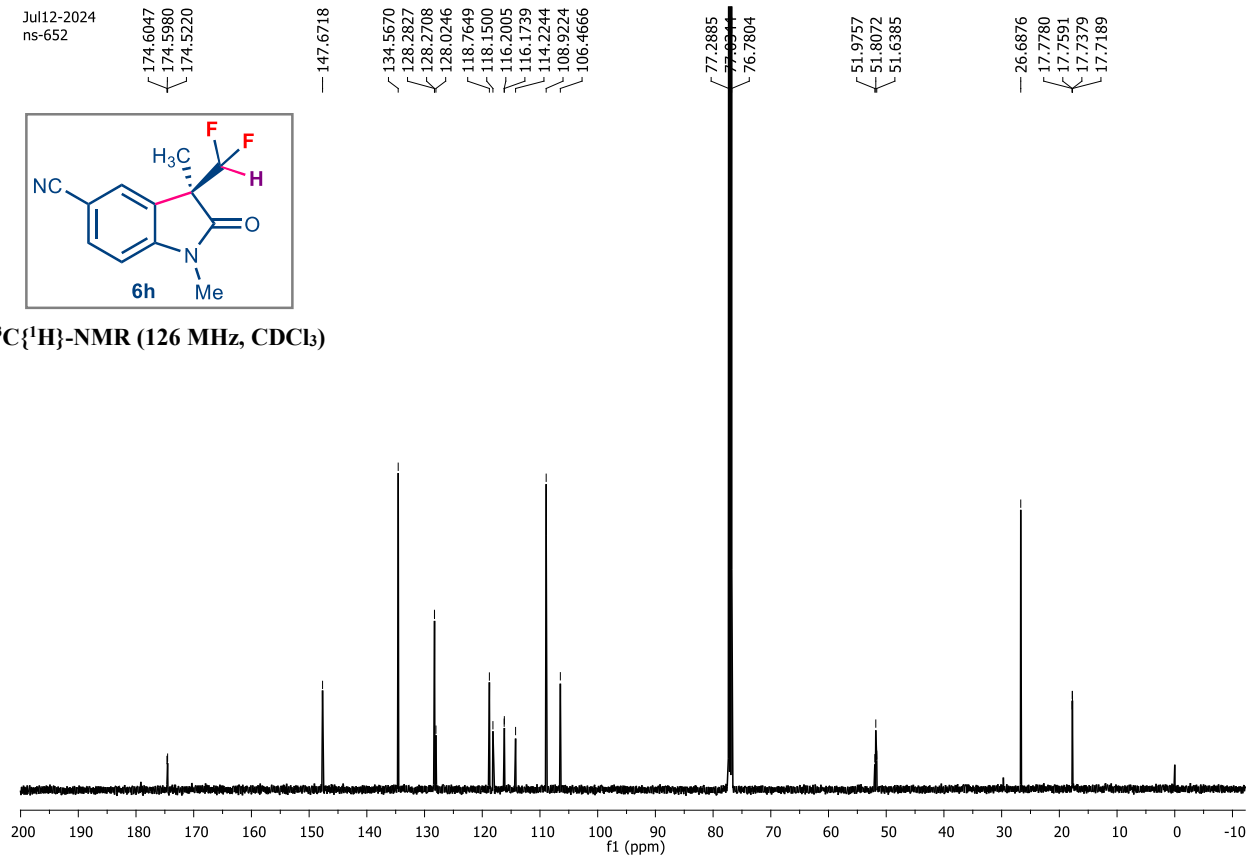


^{19}F-NMR (377 MHz, $CDCl_3$)

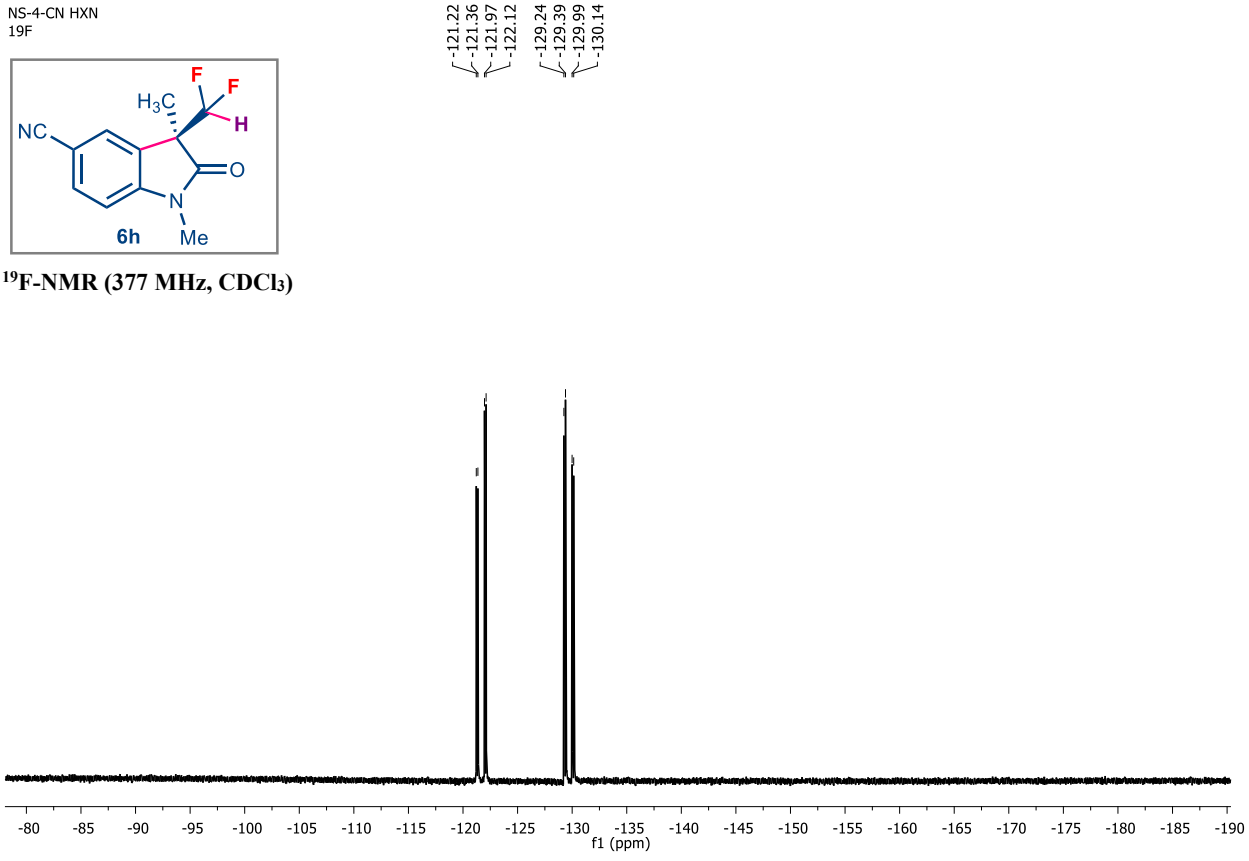
4-cn



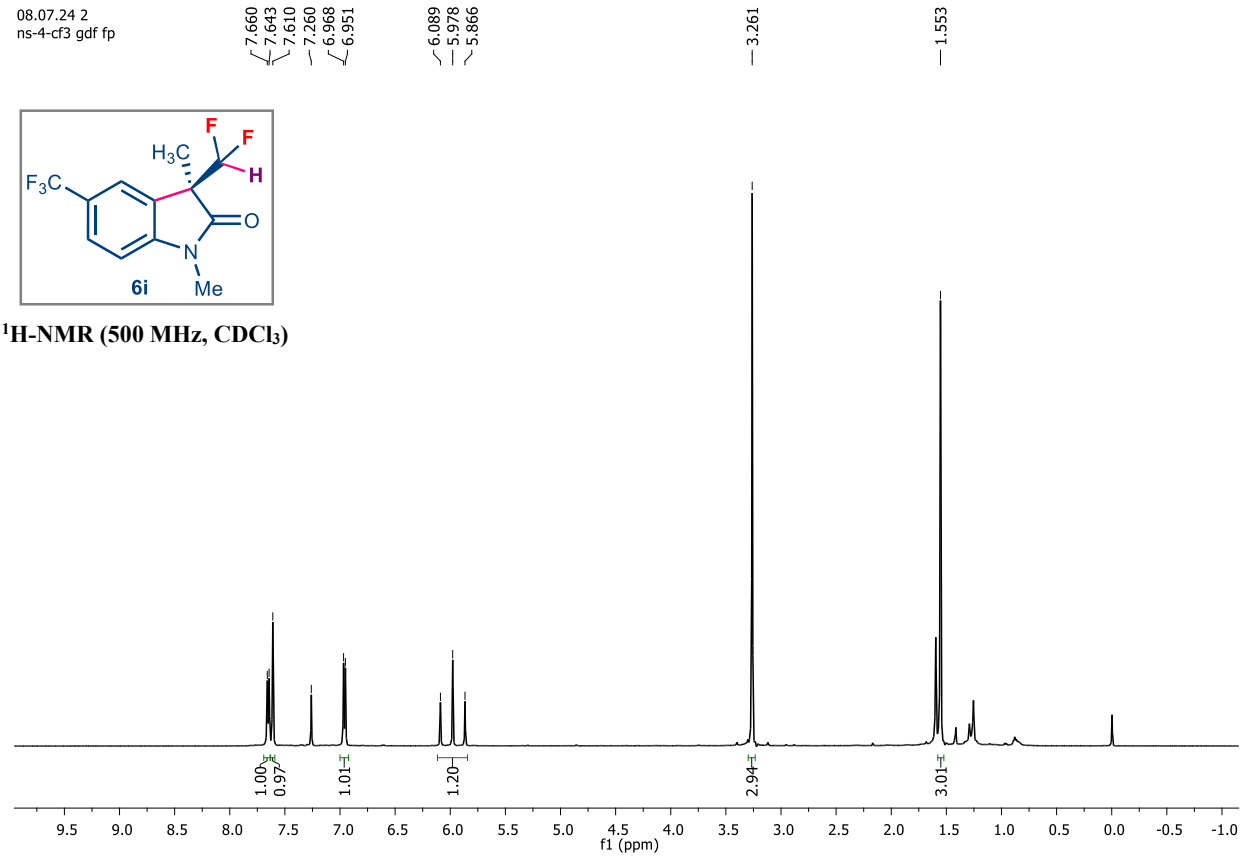
^{1}H-NMR (500 MHz, $CDCl_3$)



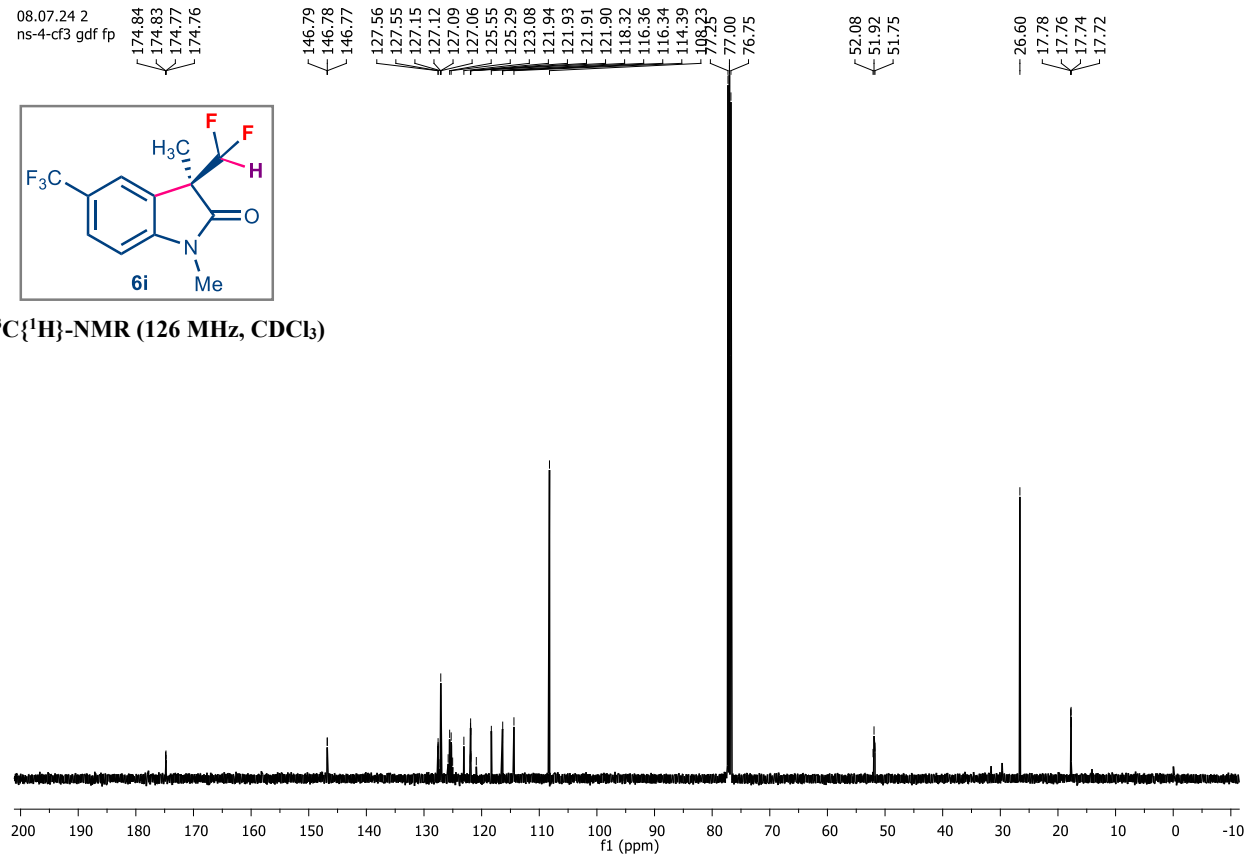
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

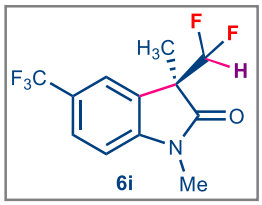


^{1}H-NMR (500 MHz, $CDCl_3$)



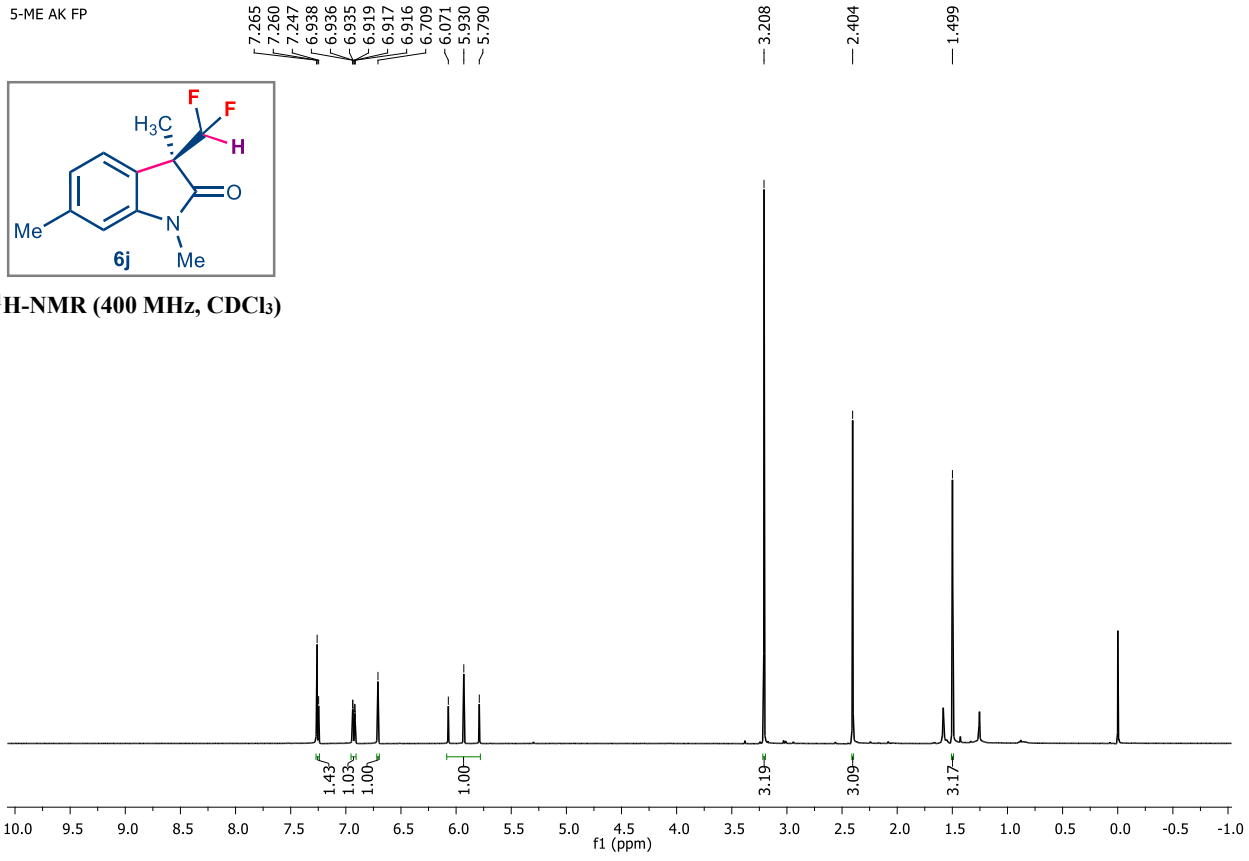
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-627

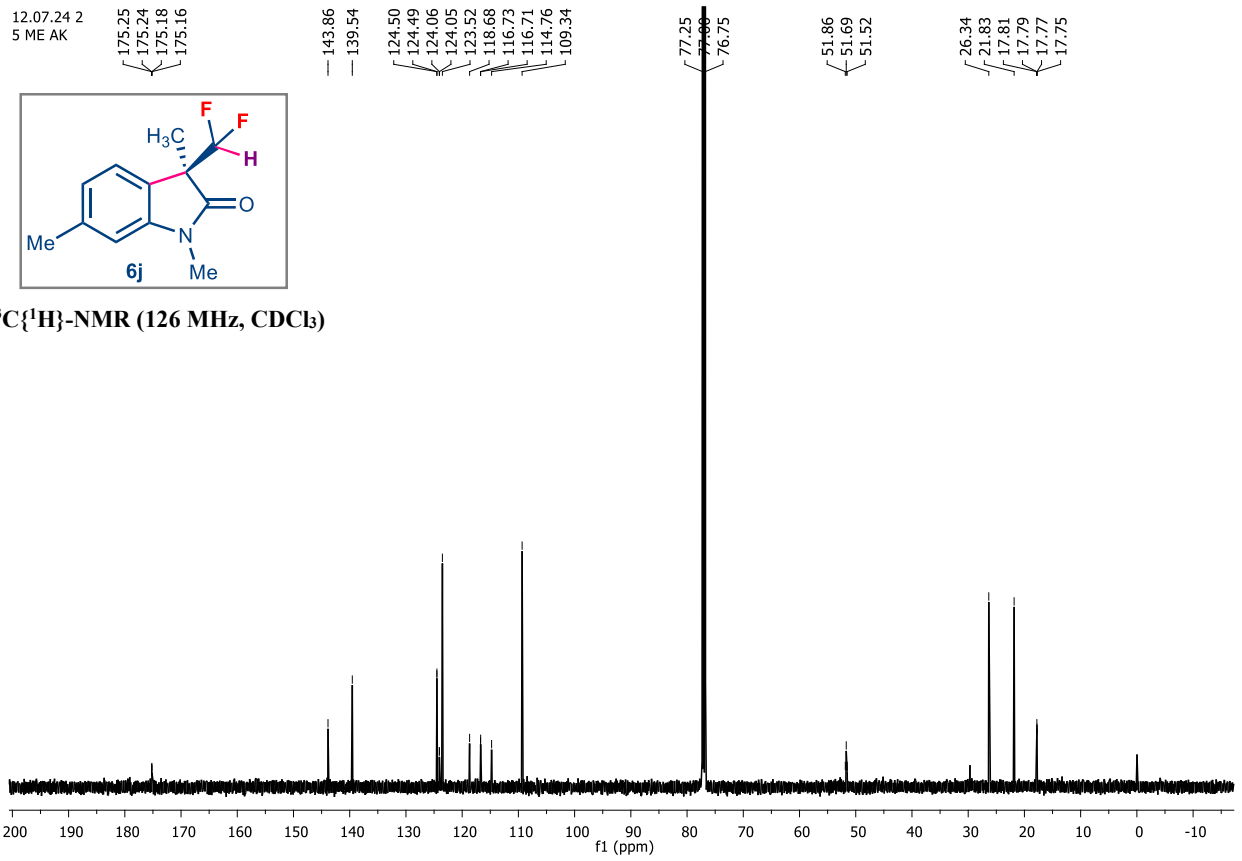


^{19}F-NMR (377 MHz, CDCl$_3$)

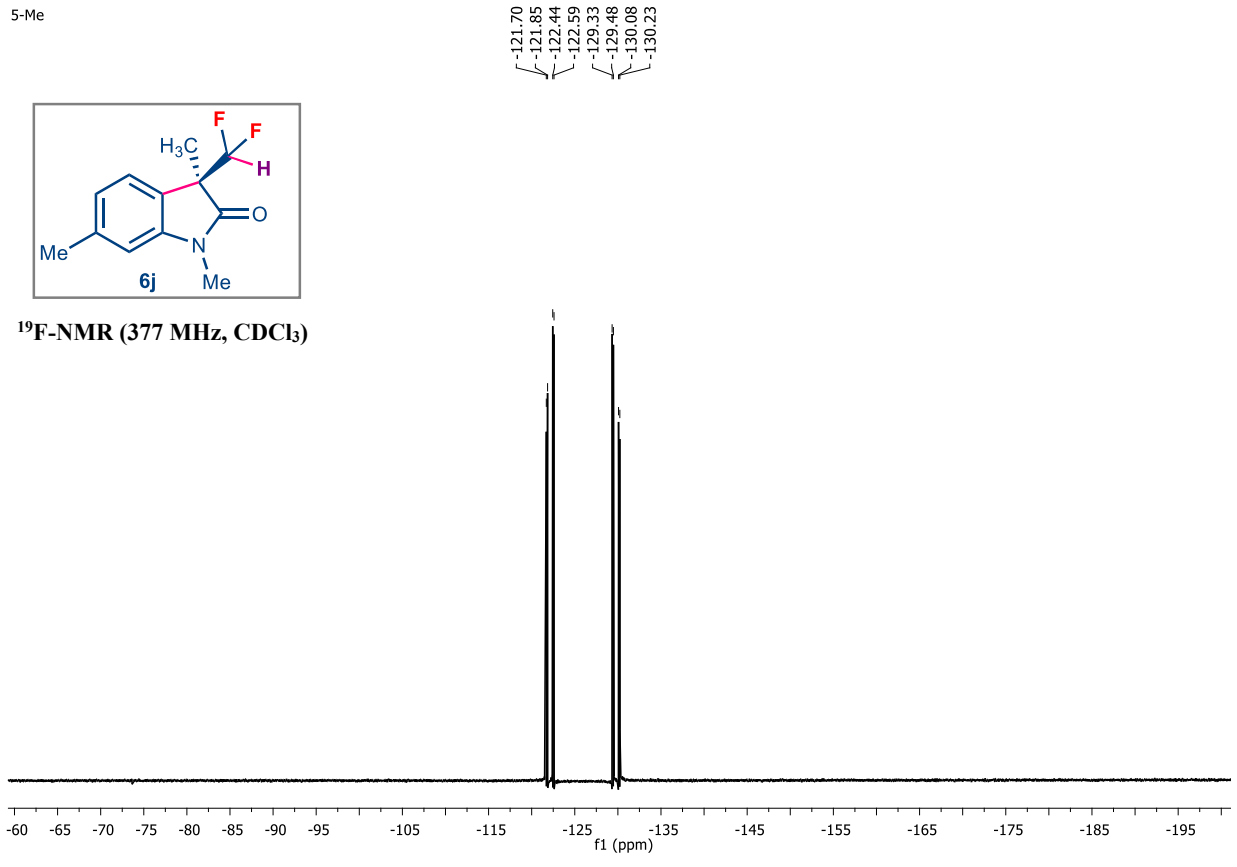
5-ME AK FP



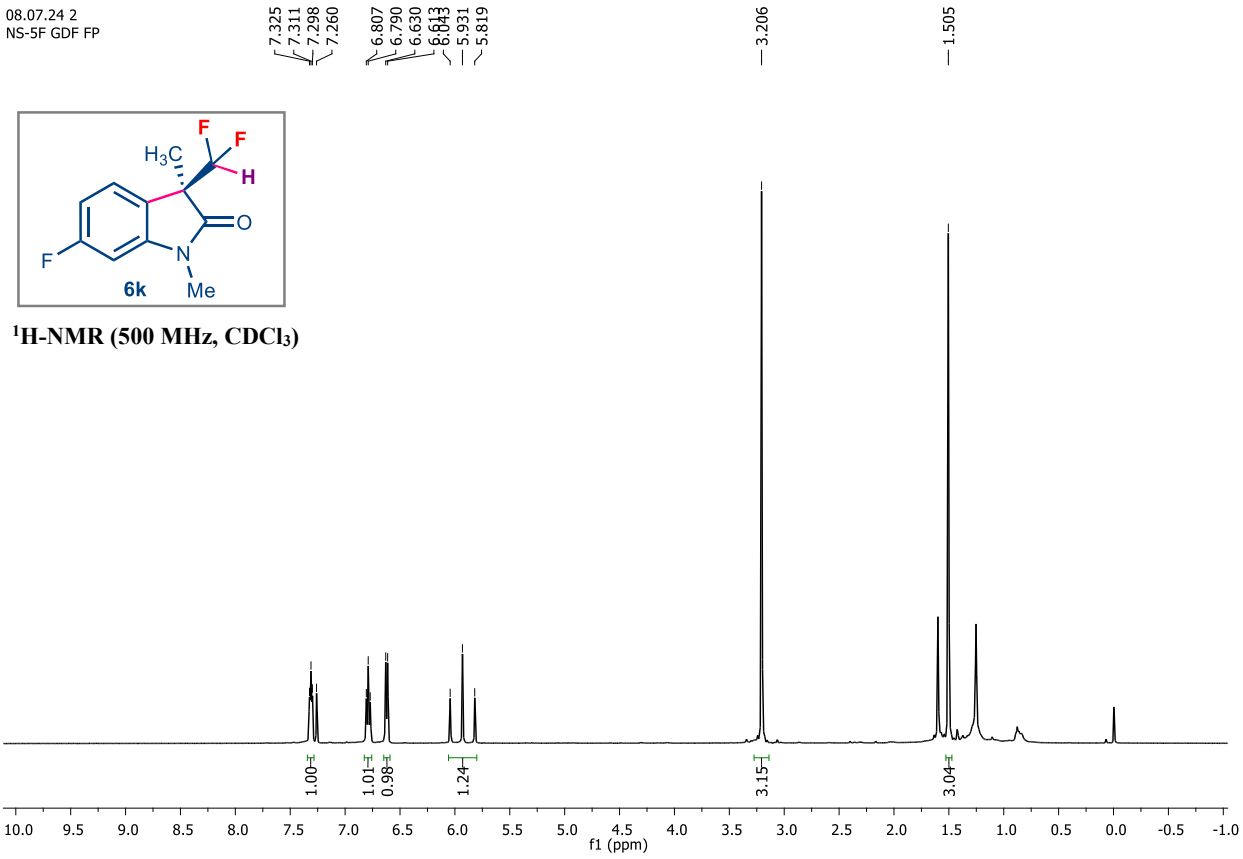
^{1}H-NMR (400 MHz, CDCl$_3$)



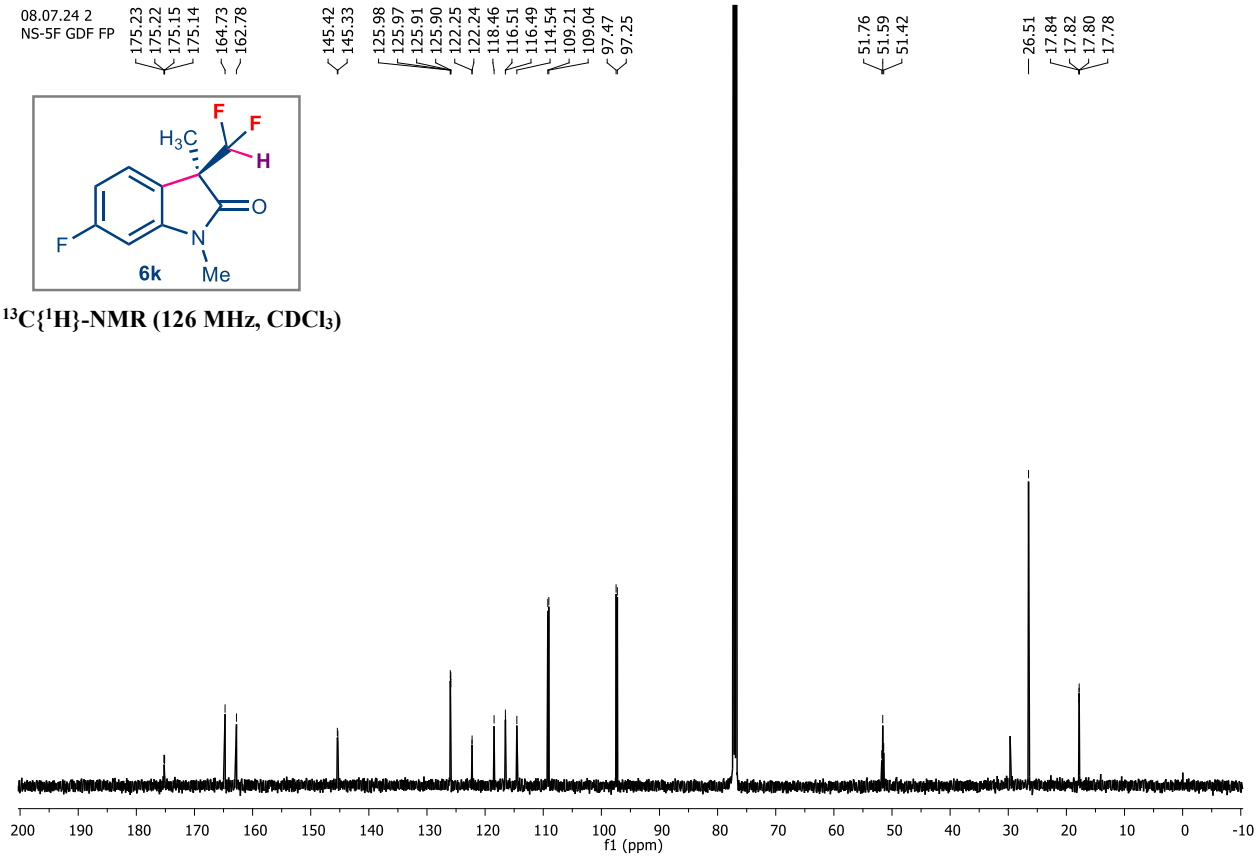
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

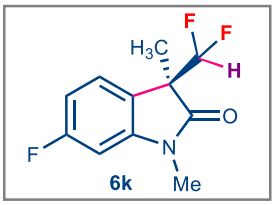


^{1}H-NMR (500 MHz, $CDCl_3$)



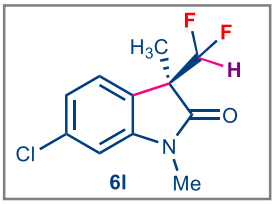
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-5-F GDF FP
19F

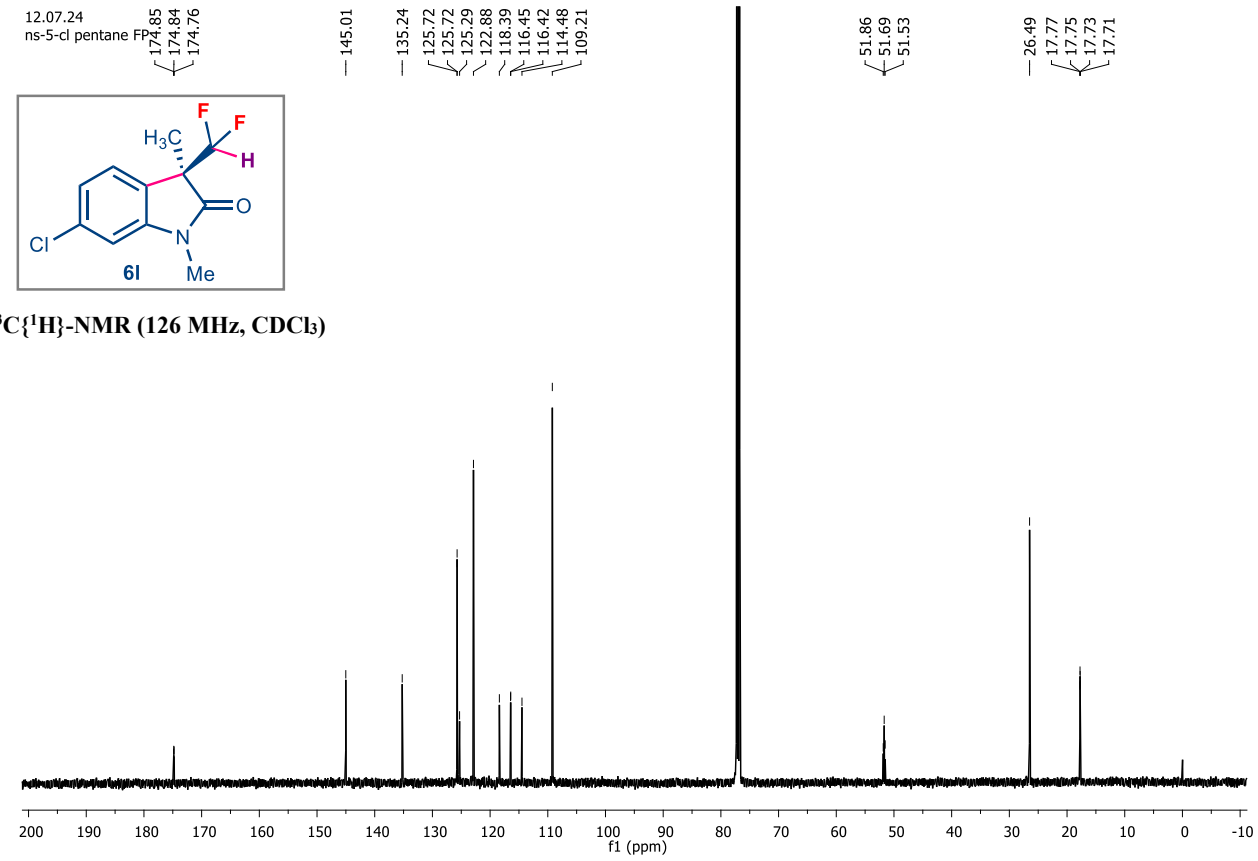


^{19}F-NMR (377 MHz, $CDCl_3$)

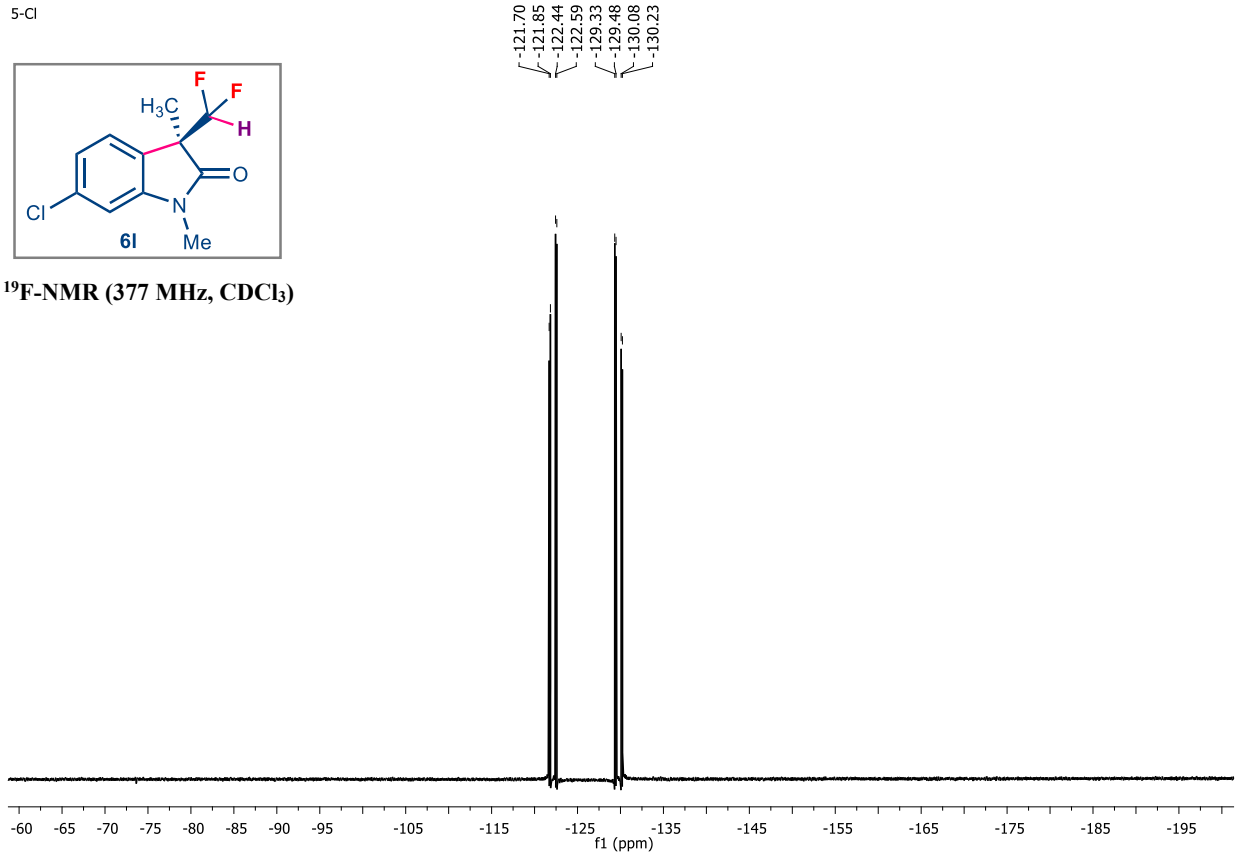
12.07.24
ns-5-cl pentane FP



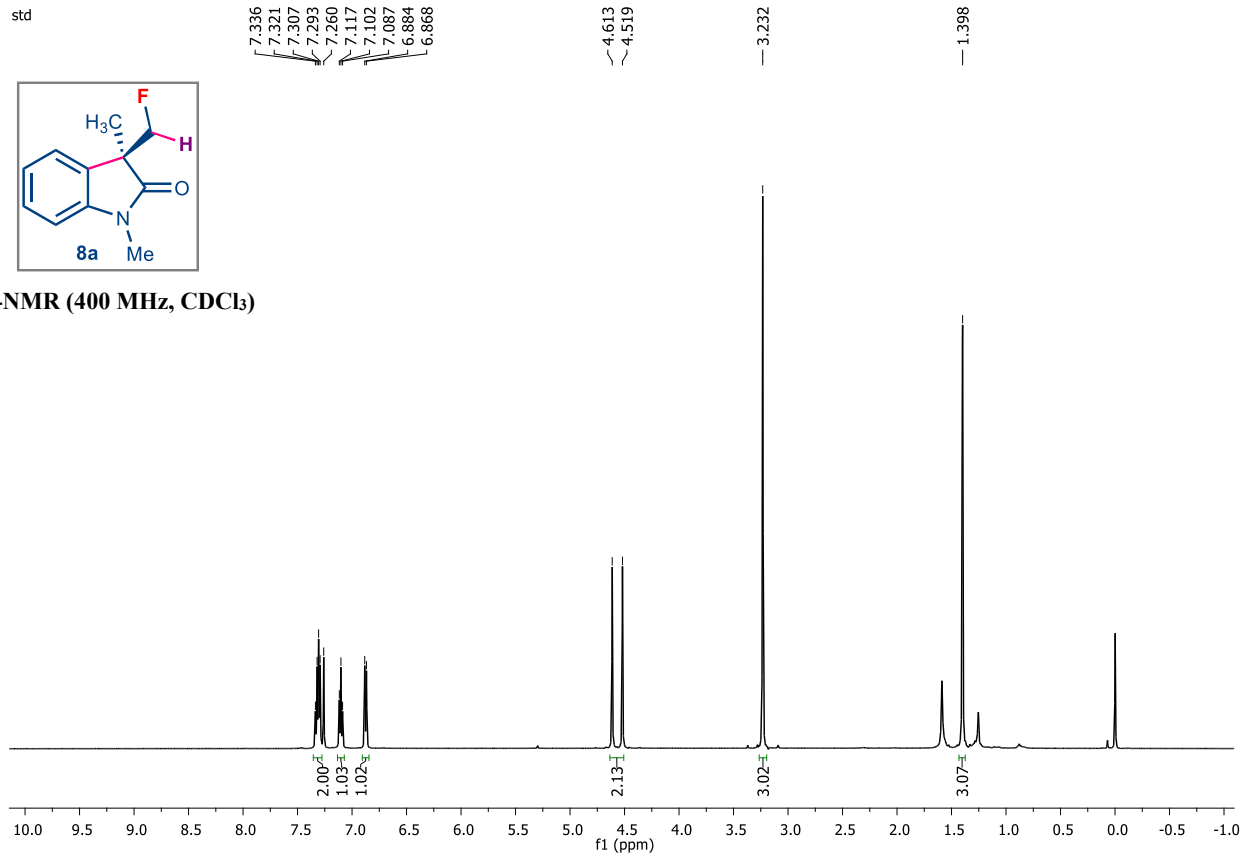
^{1}H-NMR (500 MHz, $CDCl_3$)



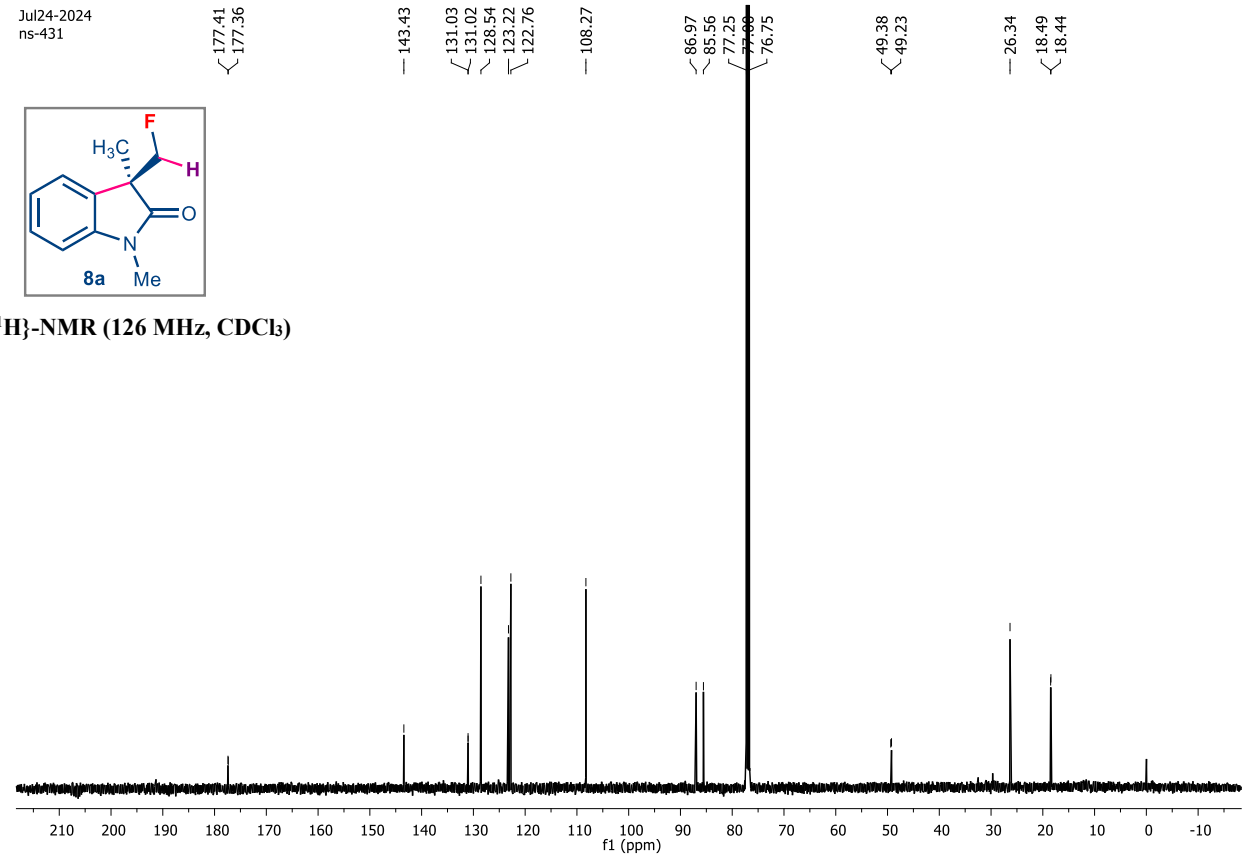
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



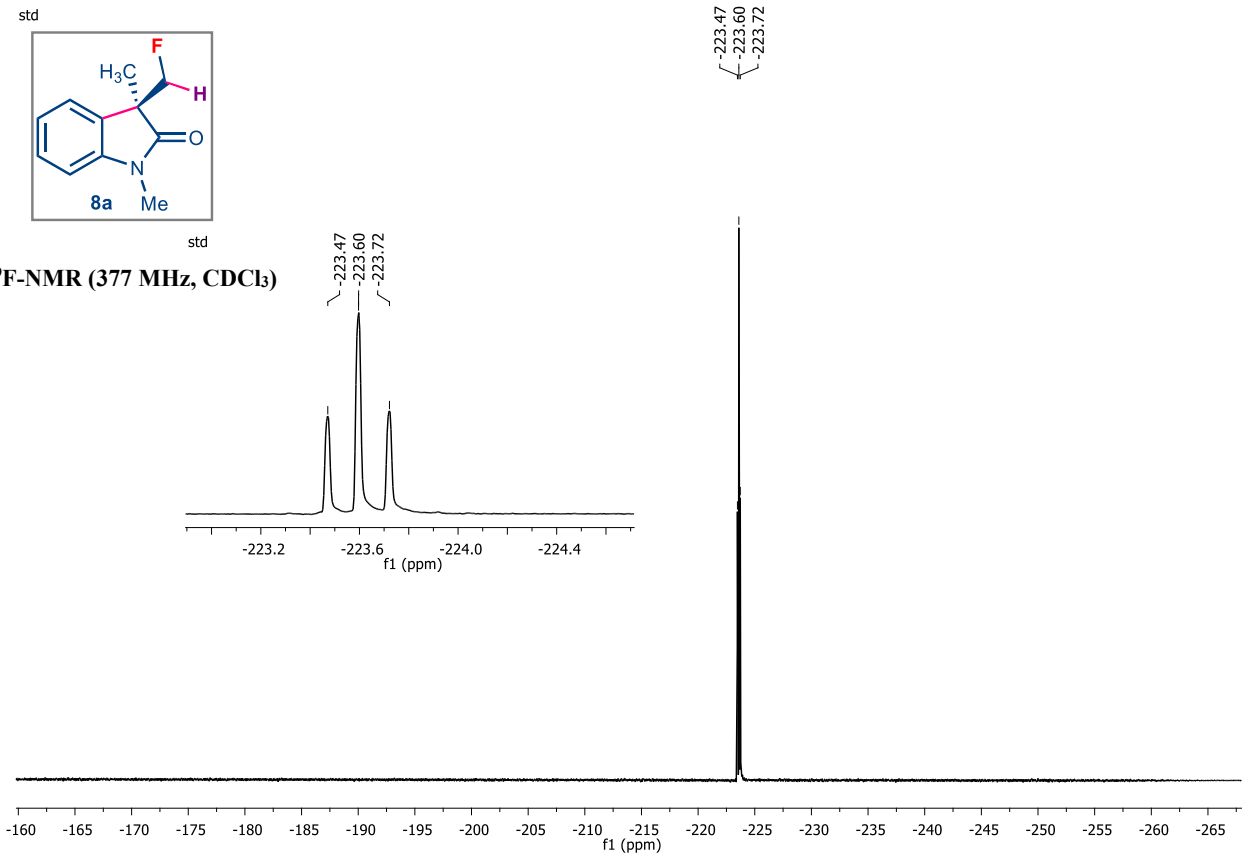
^{19}F-NMR (377 MHz, $CDCl_3$)



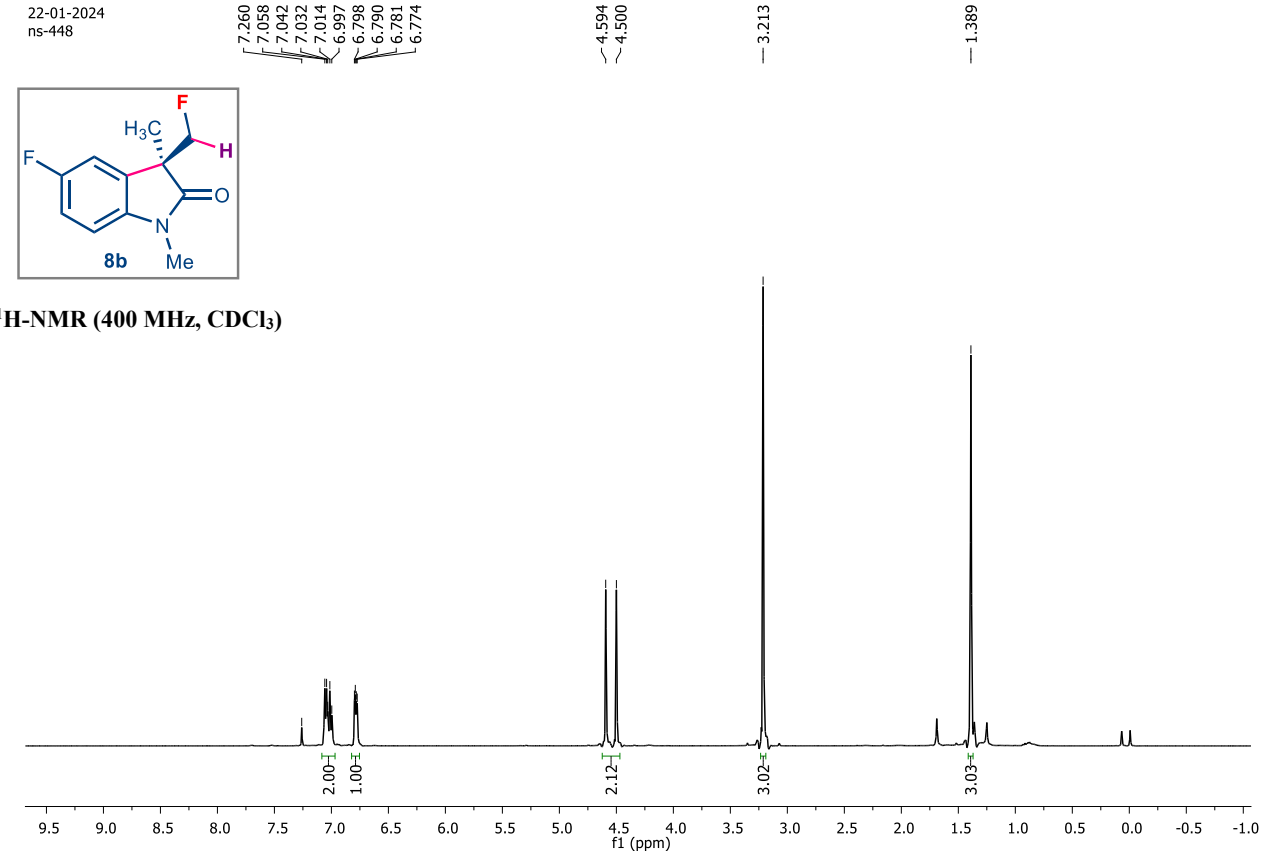
^{1}H-NMR (400 MHz, $CDCl_3$)



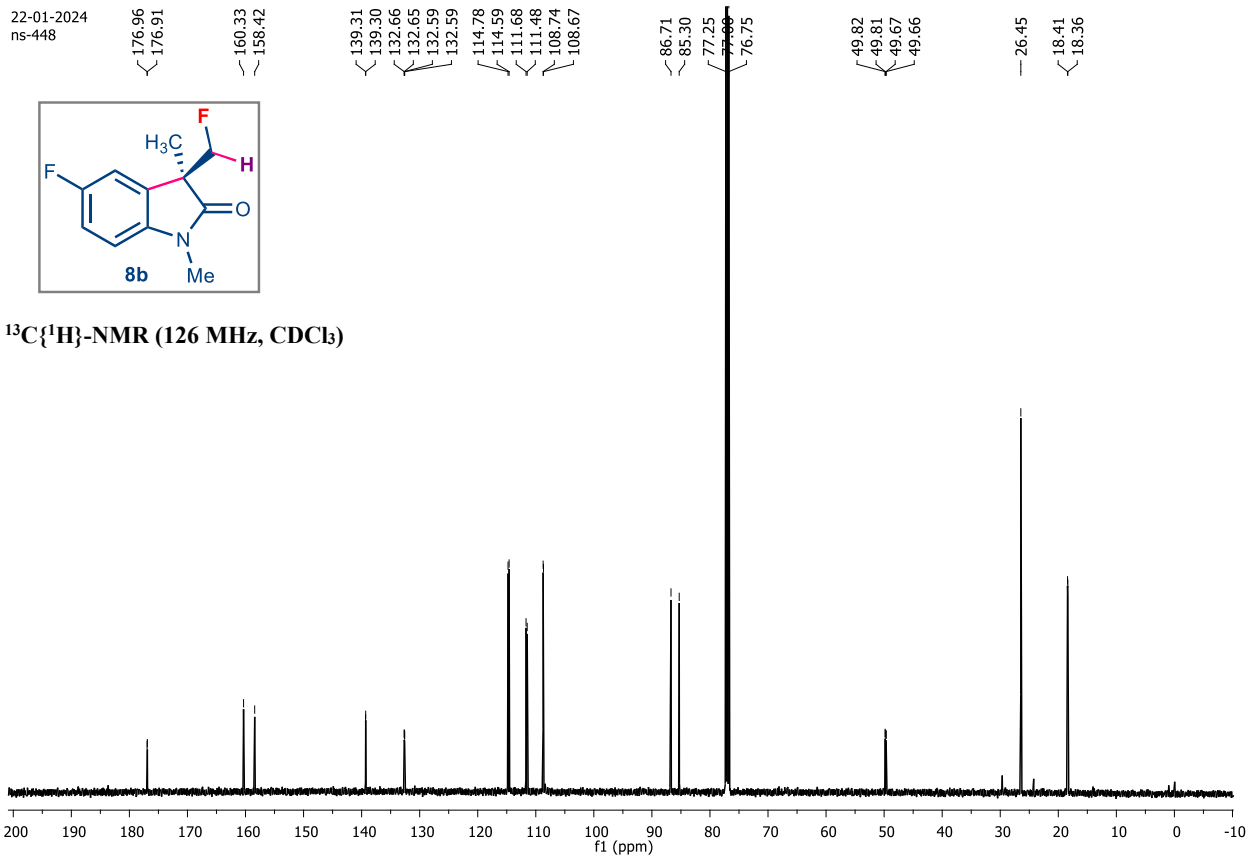
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)



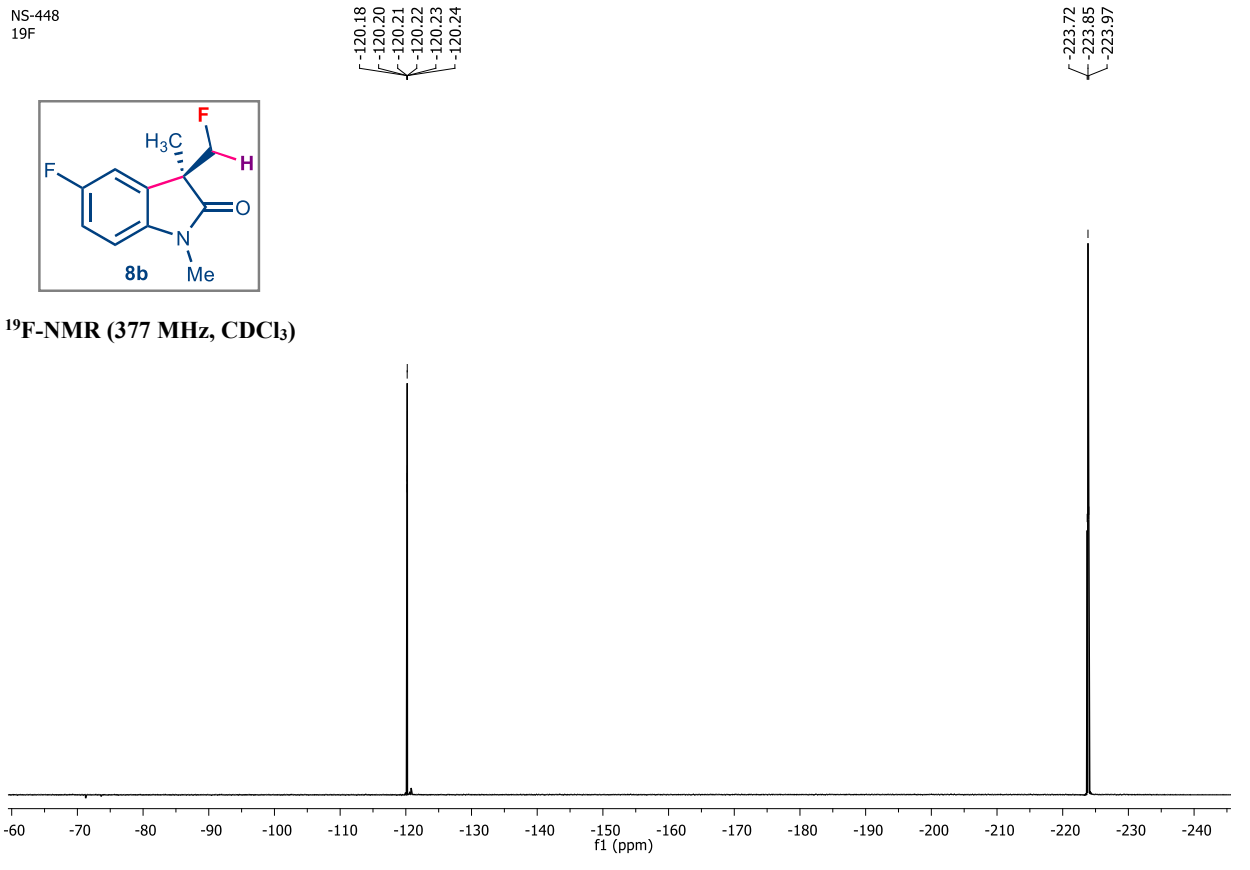
^{19}F-NMR (377 MHz, $CDCl_3$)



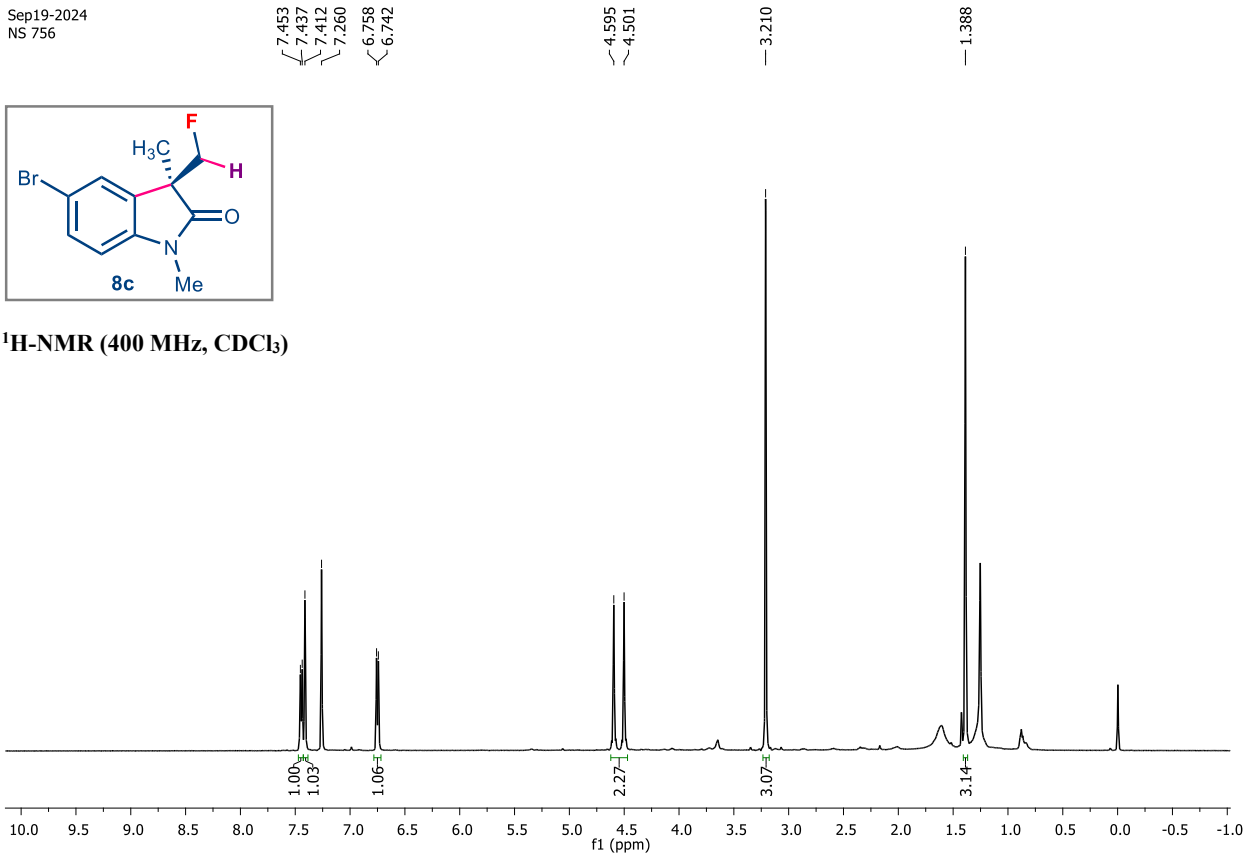
^{1}H-NMR (400 MHz, $CDCl_3$)



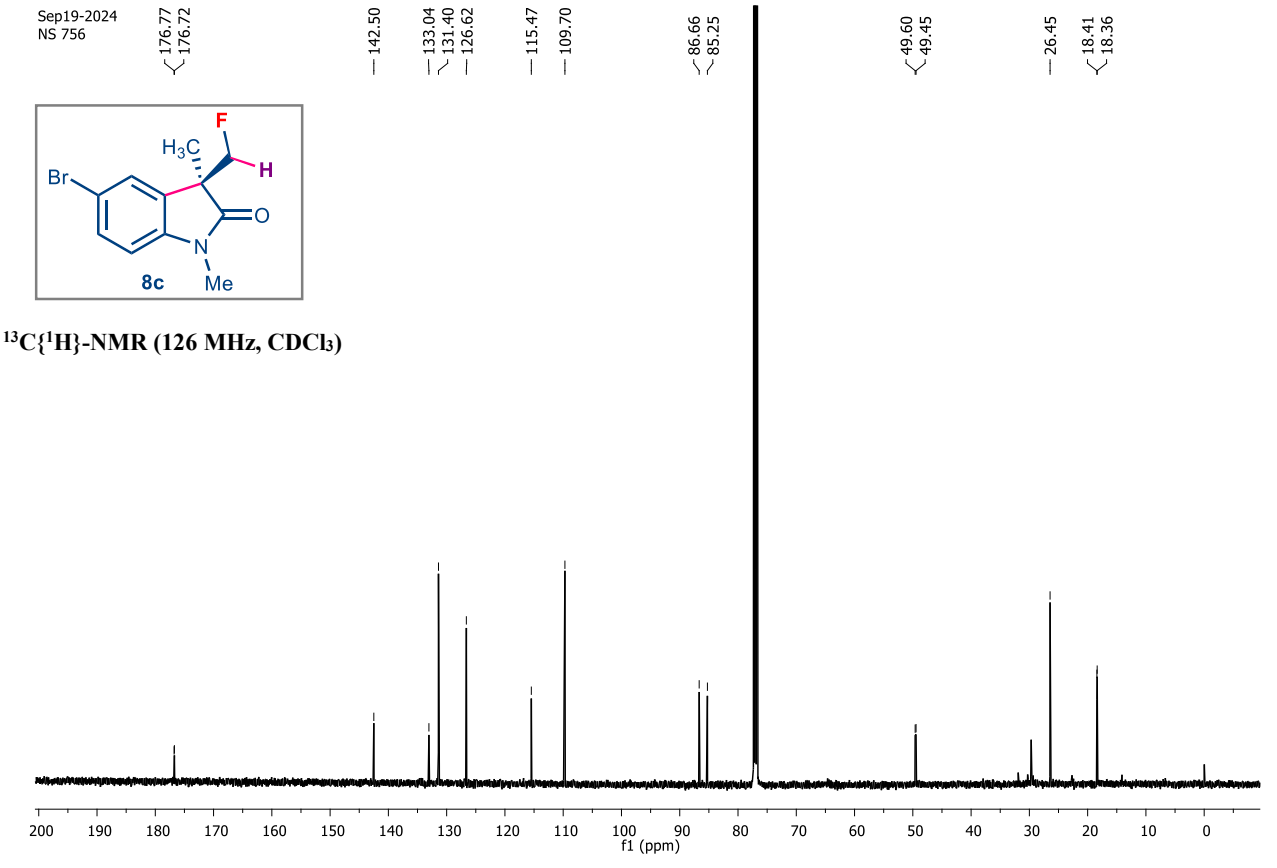
$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)



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

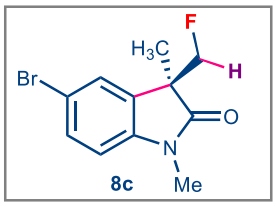


^{1}H-NMR (400 MHz, $CDCl_3$)



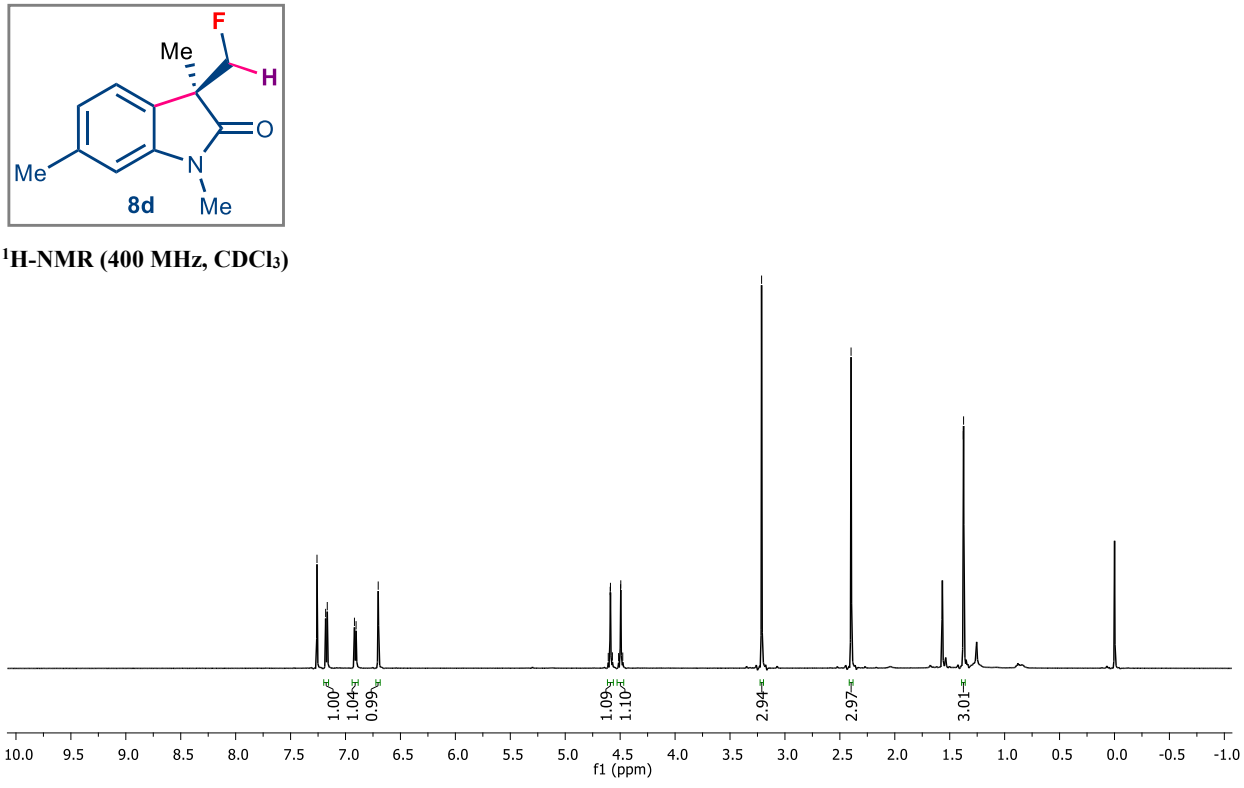
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

NS-756
19F

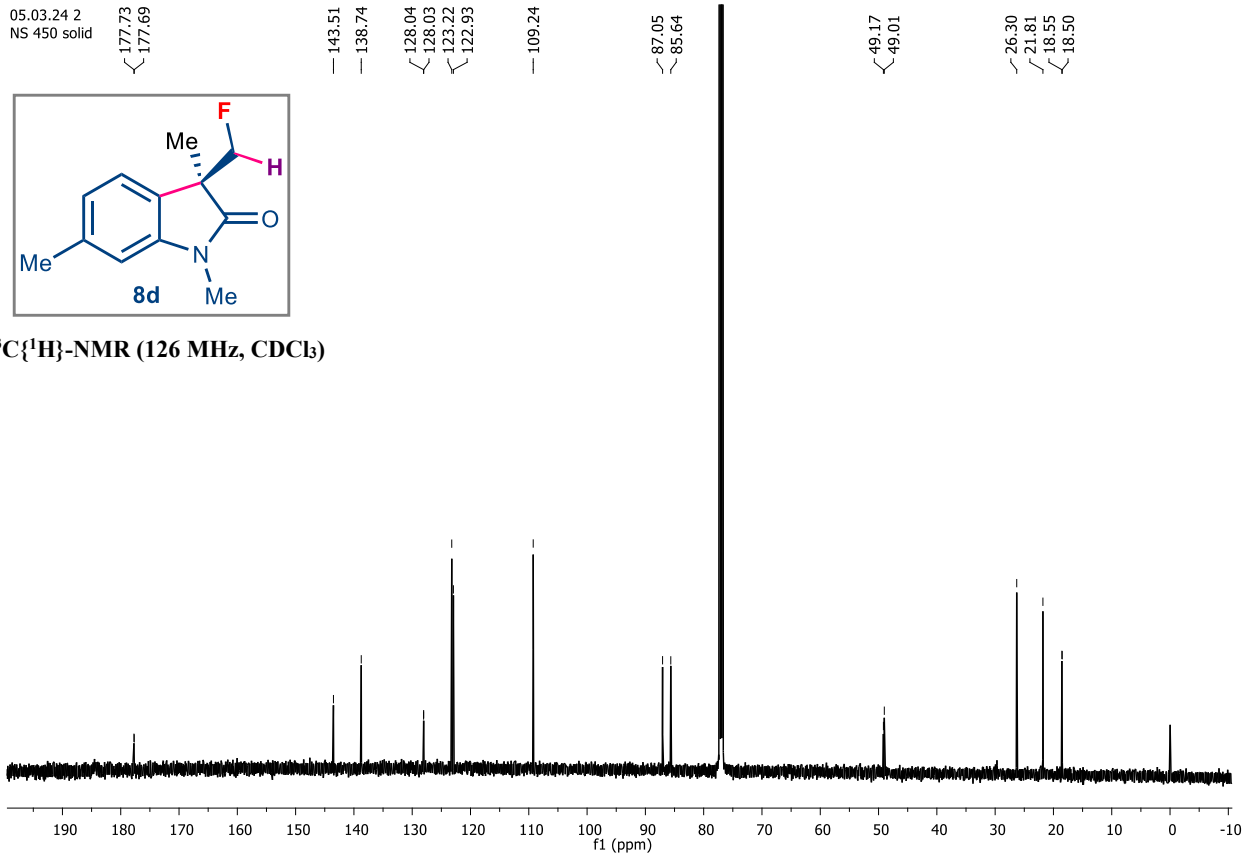


^{19}F-NMR (377 MHz, CDCl$_3$)

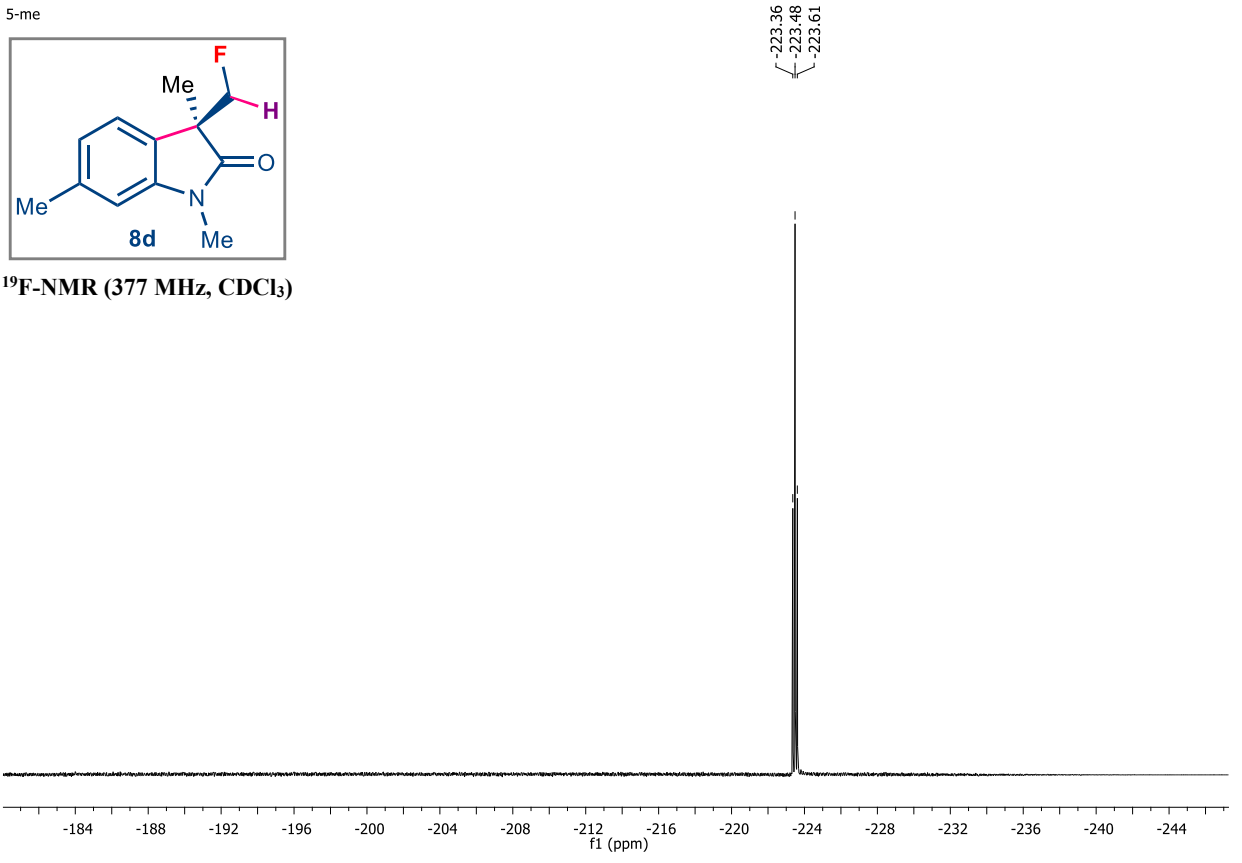
5-me



^{1}H-NMR (400 MHz, CDCl$_3$)

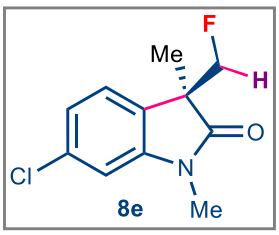


$^{13}C\{^{1}H\}$-NMR (126 MHz, $CDCl_3$)

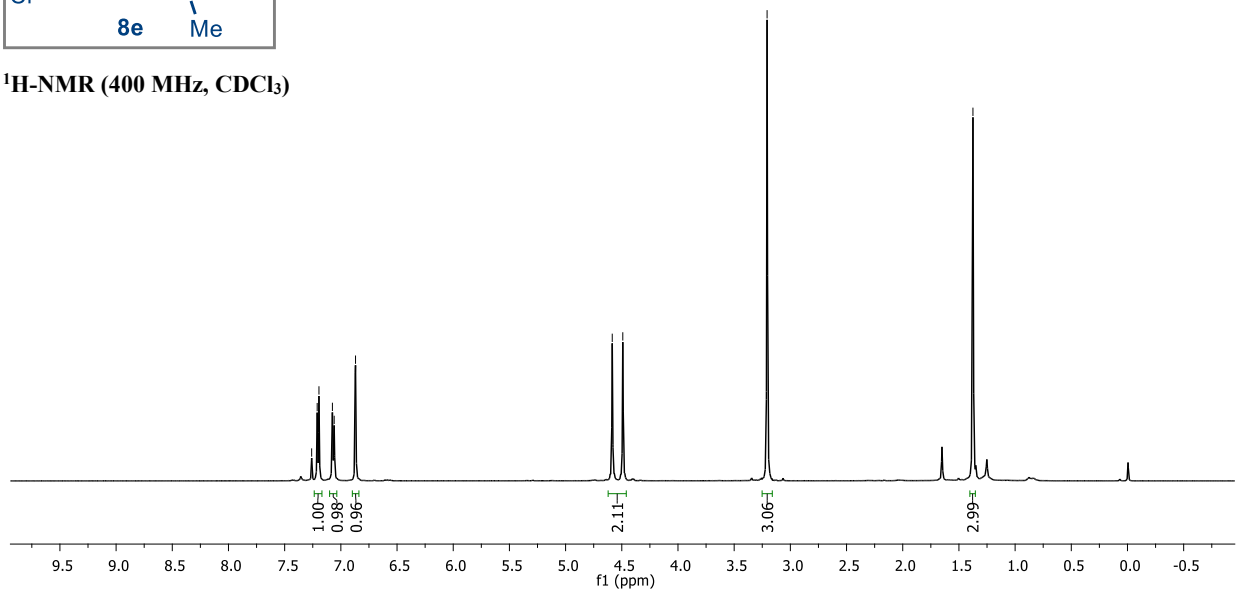


^{19}F-NMR (377 MHz, $CDCl_3$)

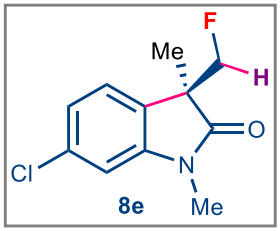
5-Cl



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

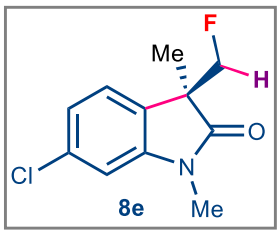


23-01-2024
ns 451



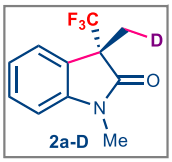
^{13}C{^{1}H}-NMR (126 MHz, $CDCl_3$)

5-Cl

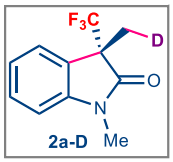


^{19}F-NMR (377 MHz, $CDCl_3$)

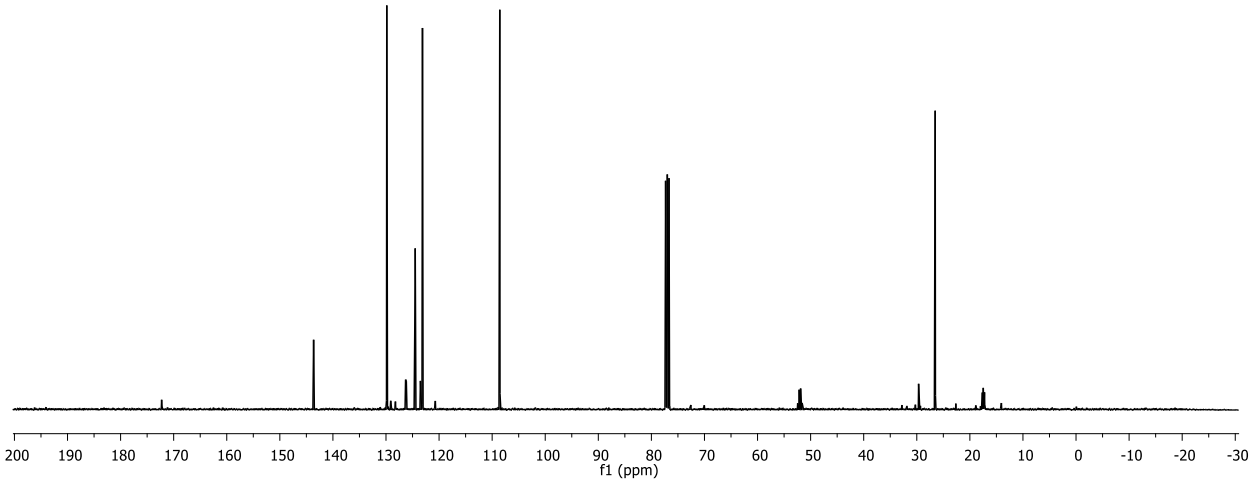
NSD
single_pulse

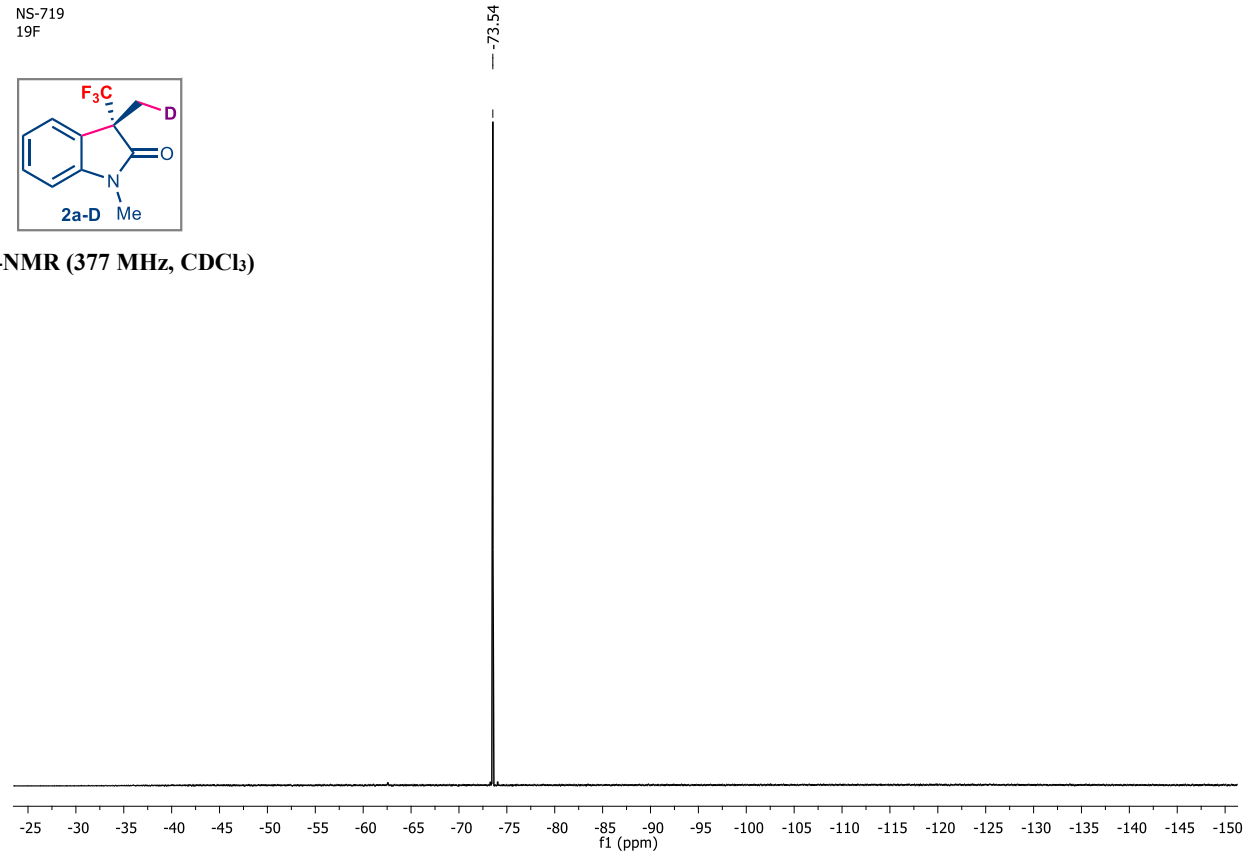


^{1}H-NMR (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-NMR (101 MHz, $CDCl_3$)





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