Supporting Information

A quick access to CF_3-containing functionalized benzofuranyl, benzothiophene and indolyl heterocycles under catalyst-free conditions

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1. General Information

All the chemicals were purchased from Sigma-Aldrich (Sigma-Aldrich, Germany). The solvents used were of analytical and HPLC reagent grade. Magnetic resonance spectra (^{1}H and ^{13}C) were recorded with Bruker, and chemical shift values are reported in δ units (ppm) using TMS as internal standard. Follow-up of the reactions and checks of the purity of the compound were done by TLC on silica-gel-protected aluminum sheets 60 F254 (Merck), and the spots were detected by exposure to UV light at λ = 254 nm. Analytical HPLC was performed on Shimadzu system using a Phenomenax C18 column (3µm, 4.6×50 mm) by dissolving the sample in CH_3CN only. Labsolution software was used for data processing. Buffer A: 0.1% TFA in H_2O, buffer B: 0.1% TFA in CH_3CN were used in HPLC. High resolution mass spectrometry (HRMS) was performed using a Bruker ESI-QTOF mass spectrometer in positive-ion mode.

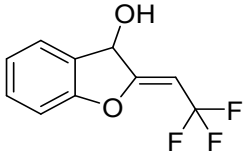
2. Preparation of benzofuran derivative

2.1. General procedure for preparation of benzofuran derivative

In an oven-dried flask was added THF (10.0 vol) and DIPA (4.0 eq.) under nitrogen atmosphere. The flask was then cooled to -78°C and then *n*-butyllithium (4.0 eq. of 2.5 M in THF) was added dropwise in inert atmosphere. The reaction mixture was allowed to stir at -78°C for 40 min to generate LDA. After generation of LDA, **2-BTP** (1.7 eq.) was added dropwise to the flask. The reaction mixture was stirred at -78°C for 15 min. In parallel, **1** (1 eq.) was dissolved in dry THF and was added dropwise to the stirring reaction for next 30-90 min while maintaining temperature -78°C. The reaction was monitored by TLC for completion of reaction. After completion, reaction was quenched with aq. NH_4Cl and extracted three times with EtOAc. The combined organic phase was washed twice with brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by 100-200 silica gel column chromatography using ethyl acetate: hexane as mobile phase to afford **2a-2p** in 40-90 % yield.

2.2. Physical and spectral data

(Z)-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2a)**



Yield: 90 %
Colour: Pale yellow solid
Melting point: 135-137°C

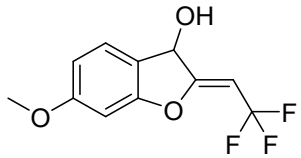
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 7.5 Hz, 1H), 7.37 (t, J = 7.8 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 8.2 Hz, 1H), 5.67 (s, 1H), 5.37 (qd, $^3J_{H-F}$ = 7.9, 1.6 Hz, 1H), 2.44 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 164.9 (d, $^3J_{C-F}$ = 5.0 Hz), 157.2, 131.4, 126.0, 125.6, 124.0, 123.1 (q, $^1J_{C-F}$ = 267.5 Hz), 111.1, 94.6 (q, $^2J_{C-F}$ = 37.5 Hz), 72.4

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.6

HRMS (APCI) m/z: Calcd for $C_{10}H_7O_2F_3$: 215.0314 $[M–H]^+$; found 215.0325

(Z)-6-methoxy-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2b)**



Yield: 80 %
Colour: Pale orange solid
Melting point: 110-112°C

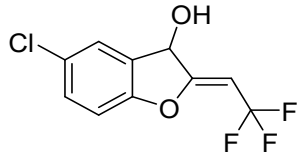
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, J = 8.3 Hz, 1H), 6.66-6.61 (m, 1H), 6.61 (s, 1H), 5.60 (s, 1H), 5.35 (qd, $^3J_{H-F}$ = 7.9, 0.8 Hz, 1H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6 (q, $^3J_{C-F}$ = 5.0 Hz), 162.6, 158.6, 125.9, 117.8, 123.1 (q, $^1J_{C-F}$ = 267.0 Hz), 110.3, 97.0, 94.6 (q, $^2J_{C-F}$ = 36.0 Hz). 72.0, 55.8

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.6

HRMS (APCI) m/z: Calcd for $C_{11}H_9O_3F_3$: 229.0471 $[M\text{-}OH]^+$; found 229.0475

(Z)-5-chloro-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2c)**



Yield: 80 %
Colour: White solid
Melting point: 125-127°C

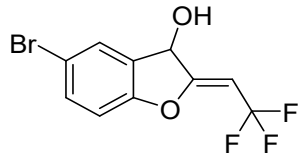
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (d, J = 1.8 Hz, 1H), 7.34-7.32 (m, 1H), 7.01 (d, J = 8.6 Hz, 1H), 5.69 (s, 1H), 5.39 (qd, $^3J_{H-F}$ = 7.8, 1.8 Hz, 1H), 2.45 (bs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4 (d, $^3J_{C-F}$ = 5.0 Hz), 155.6, 131.3, 129.1, 127.7, 125.8, 122.7 (q, $^1J_{C-F}$ = 267.0 Hz), 112.2, 95.1 (q, $^2J_{C-F}$ = 36.0 Hz), 72.1

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.7

HRMS (APCI) m/z: Calcd for $C_{10}H_6O_2ClF_3$: 248.9925 $[M–H]^-$; found 248.9938

(Z)-5-bromo-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2d)**



Yield: 80 %
Colour: Light orange solid
Melting point: 119-121°C

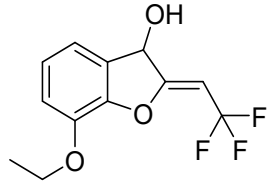
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 1.6 Hz, 1H), 7.49-7.46 (m, 1H), 6.96 (d, J = 8.6 Hz, 1H), 5.68 (s, 1H), 5.39 (qd, $^3J_{H-F}$ = 7.8, 1.7 Hz, 1H), 2.51 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3 (q, $^3J_{C-F}$ = 5.0 Hz), 156.0, 134.2, 128.7, 128.1, 122.8 (q, $^1J_{C-F}$ = 267.0 Hz), 116.3, 112.8, 95.2 (q, $^2J_{C-F}$ = 36.0 Hz), 72.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.7

HRMS (APCI) m/z: Calcd for $C_{10}H_6O_2BrF_3$: 292.9420 $[M–H]^+$; found 292.9439

(Z)-7-ethoxy-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2e)**



Yield: 70 %
Colour: White solid
Melting point: 102-104°C

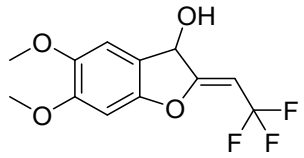
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.06 – 7.01 (m, 2H), 6.95 – 6.91 (m, 1H), 5.67 (d, J = 9.7 Hz, 1H), 5.37 (qd, $^3J_{H-F}$ = 7.9, 1.2 Hz, 1H), 4.19 (q, J = 7.0 Hz, 2H), 2.42 (bs, 1H), 1.43 (t, J = 7.0 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7 (q, $^3J_{C-F}$ = 5.3 Hz), 145.8, 143.6, 127.5, 124.7, 123.1 (q, $^1J_{C-F}$ = 267.8 Hz), 117.1, 117.1, 94.6 (q, $^2J_{C-F}$ = 36.0 Hz), 72.7, 65.6, 15.0

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.6

HRMS (APCI) m/z: Calcd for $C_{12}H_{11}O_3F_3$: 243.0627 $[M\text{-}OH]^+$; found 243.0629

(Z)-5,6-dimethoxy-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2f)**



Yield: 70 %
Colour: Pale orange
Melting point: 128-130°C

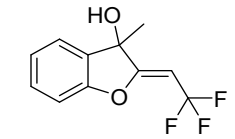
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.89 (s, 1H), 6.62 (s, 1H), 5.59 (s, 1H), 5.34 (qd, $^3J_{H-F}$ = 7.9, 1.7 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9 (q, $^3J_{C-F}$ = 5.0 Hz), 151.7, 151.5, 145.9, 123.2 (q, $^1J_{C-F}$ = 267.0 Hz), 115.9, 107.9, 95.6, 94.7 (q, $^2J_{C-F}$ = 36.0 Hz), 72.9, 56.7, 56.3

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.5

HRMS (APCI) m/z: Calcd for $C_{12}H_{11}O_4F_3$: 259.0577 $[M\text{-}H_2O]^+$; found 259.0580

(Z)-3-methyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2g)**



Yield:70% yield
Colour: Light brown solid
Melting point: 110-112°C

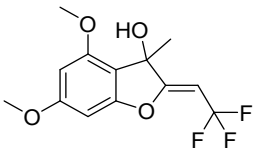
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.40 (m, 1H), 7.38 – 7.32 (m, 1H), 7.13 (t, J = 7.5 Hz, 1H), 7.08 (d, J = 8.2 Hz, 1H), 5.28 (q, $^3J_{H\text{-}F}$ = 7.9 Hz, 1H), 2.42 (s, 1H), 1.67 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): 169.1 (q, $^3J_{C\text{-}F}$ = 5.3 Hz), 155.8, 131.0, 130.1, 124.0, 123.7, 123.4 (q, $^1J_{C\text{-}F}$ = 267.0 Hz), 111.1, 92.0 (q, $^2J_{C\text{-}F}$ = 36.0 Hz), 77.6, 28.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.2.

HRMS (APCI) m/z: Calcd for $C_{11}H_9O_2F_3$: 213.0522 $[M\text{-}OH]^+$; found: 213.0526.

(Z)-4,6-dimethoxy-3-methyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2h)**



Yield: 60 % yield
Colour: Brown solid
Melting point: 102-104°C

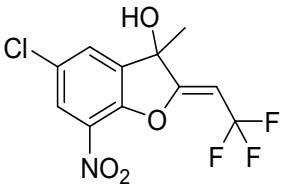
^{1}H NMR (500 MHz, $CDCl_3$): δ 6.26 (d, J = 1.9 Hz, 1H), 6.16 (d, J = 1.9 Hz, 1H), 5.24 (q, $^3J_{H\text{-}F}$ = 7.9 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 2.49 (bs, 1H), 1.75 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5 (q, $^3J_{C\text{-}F}$= 5.0 Hz), 163.5, 157.8, 157.4, 123.5 (q, $^1J_{C\text{-}F}$ = 267.0 Hz), 108.9, 94.3, 91.6 (q, $^2J_{C\text{-}F}$ = 36.0 Hz), 89.0, 77.8, 55.9, 55.7, 27.0

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.2

HRMS (APCI) m/z: Calcd for $C_{13}H_{13}O_4F_3$: 273.0733 $[M\text{-}OH]^+$; found 273.0737

(Z)-4-chloro-3-methyl-7-nitro-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2i)**



Yield: 70 %
Colour: Yellow solid
Melting point: 107-109°C

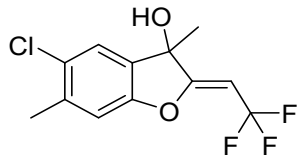
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.67 (d, J = 2.2 Hz, 1H), 5.47 (q, $^3J_{H\text{-}F}$ = 8.0 Hz, 1H), 2.81 (bs, 1H), 1.74 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1 (q, $^3J_{C\text{-}F}$= 5.0 Hz), 147.9, 136.3, 133.1, 130.0, 129.5, 126.1, 122.4 (q, $^1J_{C\text{-}F}$ = 269.0 Hz), 95.4 (q, $^2J_{C\text{-}F}$ = 37.0 Hz), 76.5, 28.7

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.8

HRMS (APCI) m/z: Calcd for $C_{11}H_7O_4NClF_3$: 291.9983 $[M\text{-}OH]^+$; found 291.9984

(Z)-5-chloro-3,6-dimethyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2j)**



Yield: 60 %
Colour: Yellow solid
Melting point: 90-92°C

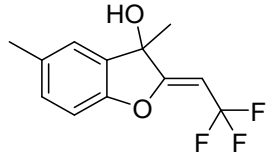
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (s, 1H), 6.98 (s, 1H), 5.28 (q, $^3J_{H\text{-}F}$ = 7.8 Hz, 1H), 2.39 (s, 3H), 2.32 (s, 1H), 1.67 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1 (q, $^3J_{C\text{-}F}$ = 5.0 Hz), 154.3, 139.3, 129.2, 124.7, 123.3 (q, $^1J_{C\text{-}F}$= 268.0 Hz), 124.15, 113.2, 92.3 (q, $^2J_{C\text{-}F}$ = 36.0 Hz), 77.3, 28.6, 20.9

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.3

HRMS (APCI) m/z: Calcd for $C_{12}H_{10}O_2ClF_3$: 261.0289 $[M\text{-}OH]^+$; found 261.0291

(Z)-3,5-dimethyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2k)**



Yield: 50 %
Colour: Yellow solid
Melting point: 95-97°C

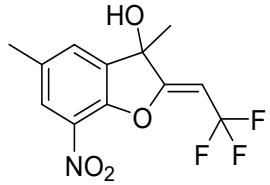
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (s, 1H), 7.15 – 7.12 (m, 1H), 6.96 (d, J = 8.3 Hz, 1H), 5.24 (q, $^3J_{H\text{-}F}$ = 7.9 Hz, 1H), 2.35 (s, 3H), 1.66 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4 (q, $^3J_{C\text{-}F}$ = 5.0 Hz), 153.7, 133.6, 131.3, 129.9, 123.9 123.3 (q, $^1J_{C\text{-}F}$ = 268.0 Hz), 110.5, 91.5 (q, $^2J_{C\text{-}F}$ = 36.0 Hz), 77.6, 28.4, 21.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.2

HRMS (APCI) m/z: Calcd for $C_{12}H_{11}O_2F_3$: 227.0678 $[M\text{-}OH]^+$; found 227.0683

(Z)-3,5-dimethyl-7-nitro-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2l)**



Yield: 55 %
Colour: Brown solid
Melting point: 123-125°C

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, J = 2.4 Hz, 1H), 7.51 (d, J = 1.5 Hz, 1H), 5.43 (q, $^3J_{H\text{-}F}$ = 7.9 Hz, 1H), 2.54 (s, 1H), 2.45 (s, 3H), 1.72 (s, 3H)

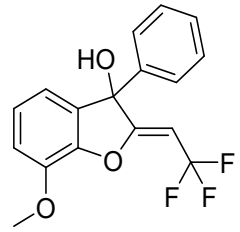
^{13}C NMR δ 167.7 (q, $^3J_{C\text{-}F}$ = 5.0 Hz), 147.4, 134.7, 134.3, 132.7, 130.2, 126.3,

(125 MHz, $CDCl_3$): 122.6 (q, $^1J_{C-F}$ = 268.8 Hz), 94.5 (q, $^2J_{C-F}$ = 36.3 Hz), 76.6, 28.6, 20.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.7

HRMS (APCI) m/z: $C_{12}H_{10}O_4NF_3$: 272.0529 $[M\text{-}OH]^+$; found 272.0533

(Z)-7-methoxy-3-phenyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2m)**



Yield: 50 %
Colour: Pale yellow solid
Melting point: 108-110°C

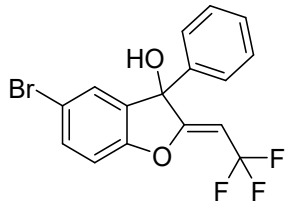
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.35 (m, 4H), 7.34 – 7.30 (m, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.72 (d, *J* = 2.2 Hz, 1H), 6.65 – 6.62 (m, 1H), 5.08 (q, $^3J_{H-F}$ = 7.9 Hz, 1H), 3.83 (s, 3H), 2.69 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0 (q, $^3J_{C-F}$ = 5.1 Hz), 162.5, 157.8, 142.3, 128.6, 128.2, 125.4, 123.3 (q, $^1J_{C-F}$ = 269.0 Hz), 122.6, 110.8, 96.9, 94.4 (q, $^2J_{C-F}$ = 36.5 Hz), 81.4, 55.9

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.3

HRMS (APCI) m/z: Calcd for $C_{17}H_{13}O_3F_3$: 305.0784 $[M\text{-}H_2O]^+$; found 305.0786

(Z)-5-bromo-3-phenyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2n)**



Yield: 70 %
Colour: Brown liquid
Melting point: NA

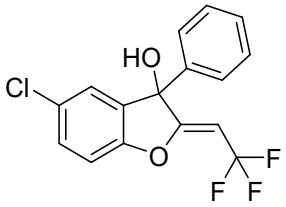
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.40 (m, 1H), 7.34 – 7.27 (m, 5H), 7.25 (d, *J* = 2.1 Hz, 1H), 7.00 (d, *J* = 8.6 Hz, 1H), 5.05 (q, $^3J_{H-F}$ = 8.0 Hz, 1H), 2.76 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7 (d, $^3J_{C-F}$ = 5.0 Hz), 154.1, 140.2, 133.0, 131.8, 127.7, 127.5, 126.9, 124.1, 115.4, 111.7, 94.0 (q, $^2J_{C-F}$ = 37.0 Hz), 80.4

^{19}F NMR (376 MHz, $CDCl_3$): δ -57.4

HRMS (APCI) m/z: Calcd for $C_{16}H_{10}O_2BrF_3$: 352.9783 $[M\text{-}OH]^+$; found 352.9786

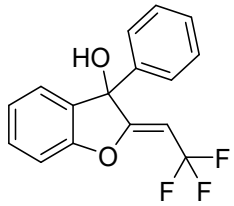
(Z)-5-chloro-3-phenyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2o)**



Yield: 70 %
Colour: Yellow solid
Melting point: 138-140°C

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.50 – 7.48 (m, 1H), 7.39 – 7.38 (m, 1H), 7.38 – 7.36 (m, 3H), 7.36 – 7.34 (m, 1H), 7.33 – 7.32 (m, 1H), 7.07 (d, J = 8.6 Hz, 1H), 5.12 (q, $^3J_{H\text{-}F}$ = 7.8 Hz, 1H), 1.25 (s, 1H)
^{13}C NMR (100 MHz, $CDCl_3$):	δ 168.8, 155.2, 141.3, 134.0, 132.9, 128.8, 128.5, 128.0, 125.1, 116.5, 112.8, 95.0 (q, $^1J_{C\text{-}F}$ = 36.0 Hz), 81.4.
^{19}F NMR (376 MHz, $CDCl_3$):	δ -57.5
HRMS (APCI) m/z:	Calcd for $C_{16}H_{10}ClO_2F_3$: 309.0289 $[M\text{-}OH]^+$; found 309.0289

(Z)-3-phenyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran-3-ol **(2p)**



Yield: 55 %
Colour: Brown liquid
Melting point: NA

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.41 – 7.31 (m, 6H), 7.24 – 7.16 (m, 2H), 7.13 – 7.08 (m, 1H), 5.11 (q, $^3J_{H\text{-}F}$ = 8.0 Hz, 1H), 2.75 (s, 1H)
^{13}C NMR (100 MHz, $CDCl_3$):	δ 169.1 (q, $^3J_{C\text{-}F}$ = 5.0 Hz), 156.3, 141.9, 131.1, 130.6, 128.6, 128.2, 125.2, 124.8, 124.2, 123.2 (q, $^1J_{C\text{-}F}$ = 267.0 Hz), 111.1, 94.4 (q, $^2J_{C\text{-}F}$ = 37.0 Hz), 81.6
^{19}F NMR (376 MHz, $CDCl_3$):	δ -57.3
HRMS (APCI) m/z:	Calcd for $C_{16}H_{11}O_2F_3$ = 275.0678 $[M\text{-}OH]^+$; found 275.0681

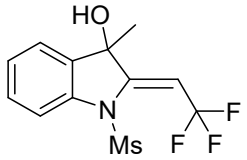
3. Preparation of indolin derivatives

3.1. General Procedure for preparation of indolin derivative

Similar procedure as described above was followed for the synthesis of **4a-o** and the product was obtained in 40-90% yield.

3.2. Physical and spectral data

(Z)-3-methyl-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4a)**



Yield: 80 %
Colour: Brown liquid
Melting point: NA

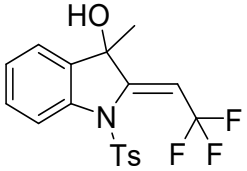
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 – 7.40 (m, 3H), 7.28 (s, 1H), 5.74 (q, $^3J_{H-F}$ = 8.5 Hz, 1H), 3.13 (s, 3H), 2.28 (s, 1H) 1.69 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4 (d, $^3J_{C-F}$ = 4.0 Hz), 140.7, 135.5, 130.5, 126.7, 123.4, 122.5 (q, $^1J_{C-F}$ = 267.0 Hz), 117.0, 104.8 (q, $^2J_{C-F}$ = 37.0 Hz), 78.8, 40.4, 27.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ -59.5

HRMS (APCI) m/z: Calcd for $C_{12}H_{12}O_3NF_3S$: 290.0457 $[M\text{-}OH]^+$; found 290.0458

(Z)-3-methyl-1-tosyl-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4b)**



Yield: 70 %
Colour: White solid
Melting point: 167-169°C

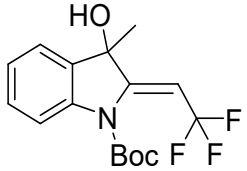
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 – 7.66 (m, 1H), 7.54 – 7.48 (m, 2H), 7.40 – 7.34 (m, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 7.4 Hz, 1H), 7.16 (d, *J* = 8.5 Hz, 2H), 5.79 (qd, $^3J_{H-F}$ = 8.6, 1.4 Hz, 1H), 2.34 (s, 3H), 1.77 (s, 1H), 1.05 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.0 (d, $^3J_{C-F}$ = 6.0 Hz), 145.3, 140.3, 136.0, 134.0, 130.1, 130.0, 128.2, 126.8, 123.1, 122.3 (q, $^1J_{C-F}$= 268.0 Hz), 118.7, 107.2 (q, $^2J_{C-F}$ = 38.0 Hz), 27.1, 21.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ -58.8

HRMS (APCI) m/z: Calcd for $C_{18}H_{16}O_3NF_3S$: 366.0770 $[M\text{-}H_2O]^+$; found 366.0771

tert-butyl (Z)-3-hydroxy-3-methyl-2-(2,2,2-trifluoroethylidene)indoline-1-carboxylate **(4c)**



Yield: 60 %
Colour: White solid
Melting point: 153-155°C

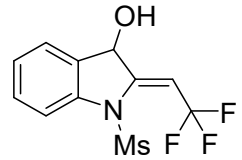
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.2 Hz, 1H), 7.50 – 7.42 (m, 1H), 7.39 – 7.29 (m, 1H), 7.21 – 7.09 (m, 1H), 5.65 (s, 1H), 1.68 (s, 3H), 1.64 (s, 9H), 1.63 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 173.3, 149.7, 143.2, 130.7, 130.3, 124.9, 123.4, 115.9, 96.3, 87.8, 85.2, 31.1, 28.1

^{19}F NMR (470 MHz, $CDCl_3$): δ -57.2

HRMS (APCI) m/z: Calcd for $C_{16}H_{18}O_3NF_3$: 330.1312 $[M+H]^+$; found 330.1349

(Z)-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4d)**



Yield: 80 %
Colour: Brown solid
Melting point: 130-132°C

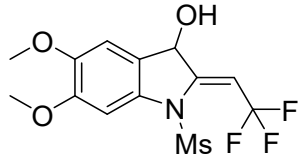
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 – 7.49 (m, 2H), 7.45 – 7.41 (m, 1H), 7.31 – 7.27 (m, 1H), 5.81 (qd, $^3J_{H\text{-}F}$ = 8.4, 1.6 Hz, 1H), 5.55 (s, 1H), 2.97 (s, 3H), 2.53 (bs, 1H)

^{13}C NMR (125 MHz, $CDCl_3$): δ 149.3 (q, $^3J_{C\text{-}F}$ = 5.0 Hz), 142.2, 131.4, 130.9, 126.9, 125.4, 122.2 (q, $^1J_{C\text{-}F}$ = 267.5 Hz), 117.8, 109.2 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 73.9, 39.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -59.7

HRMS (APCI) m/z: Calcd for $C_{11}H_{10}O_3NF_3S$: 276.0301 $[M-OH]^+$; found 276.0300

(Z)-5,6-dimethoxy-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4e)**



Yield: 50 %
Colour: White solid
Melting point: 153-155°C

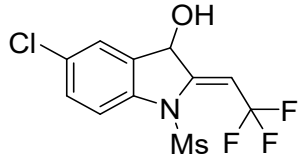
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (s, 1H), 7.00 (s, 1H), 5.81 (q, $^3J_{H\text{-}F}$ = 8.4 Hz, 1H), 5.47 (d, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 2.87 (s, 3H), 2.34 (bs, 1H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 151.4, 149.9 (q, $^3J_{C\text{-}F}$ = 5.0 Hz), 148.6, 135.6, 122.5, 121.8 (q, $^1J_{C\text{-}F}$ = 267.5 Hz), 110.3 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 107.4, 102.1, 74.0, 56.4, 56.4, 37.6

^{19}F NMR (376 MHz, $CDCl_3$): δ -50.6

HRMS (APCI) m/z: Calcd for $C_{13}H_{14}O_5NF_3S$: 336.0512 $[M-OH]^+$; found 336.0513

(Z)-5-chloro-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4f)**

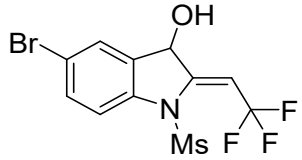


Yield: 70 %
Colour: Off white solid
Melting point: 147-149°C

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.47 (m, 1H), 7.43 (d, J = 8.3 Hz, 1H), 7.42 – 7.38 (m, 1H), 5.81 (qd, $^3J_{H\text{-}F}$ = 8.3, 1.7 Hz, 1H), 5.54 (d, J = 7.6 Hz, 1H), 3.00 (s, 3H), 2.49 (d, J = 7.8 Hz, 1H)

^{13}C NMR (125 MHz, DMSO-d_6+$CDCl_3$):	δ 155.2 (q $^3J_{C\text{-}F}$ = 5.0 Hz), 145.2, 140.0, 136.4, 134.7, 130.5, 127.0 (q, $^1J_{C\text{-}F}$ = 267.5 Hz), 123.5, 112.9 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 77.4, 43.1.
^{19}F NMR (376 MHz, $CDCl_3$):	δ -59.8
HRMS (APCI) m/z:	Calcd for $C_{11}H_9O_3ClNF_3S$: 309.9911 $[M\text{-}OH]^+$; found 309.9910

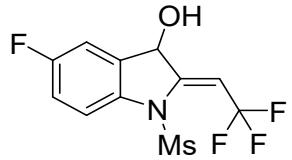
(Z)-5-bromo-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4g)**



Yield: 70 %
Colour: Pale yellow solid
Melting point: 140-142°C

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.63 (d, J = 1.6 Hz, 1H), 7.59 – 7.50 (m, 1H), 7.37 (d, J = 8.5 Hz, 1H), 5.81 (qd, $^3J_{H\text{-}F}$ = 8.3, 1.6 Hz, 1H), 5.54 (s, 1H), 2.99 (s, 3H), 2.62 (bs, 1H)
^{13}C NMR (100 MHz, DMSO-d_6+$CDCl_3$):	δ 149.0 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 139.8, 134.3, 131.6, 127.4, 121.0 (q, $^1J_{C\text{-}F}$ = 266.0 Hz) 118.3, 117.9, 107.1 (q, $^2J_{C\text{-}F}$ = 36.0 Hz), 71.4, 37.2.
^{19}F NMR (376 MHz, $CDCl_3$):	δ -59.7
HRMS (APCI) m/z:	Calcd for $C_{11}H_9O_3BrNF_3S$: 353.9406 $[M\text{-}OH]^+$; found 353.9404

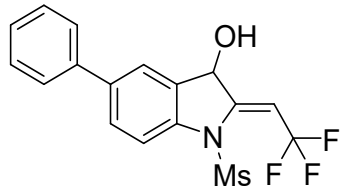
(Z)-5-fluoro-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol (**4h**)



Yield: 65 %
Colour: Brown
Melting point: 138-140°C

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.63 – 7.62 (m, 1H), 7.56 – 7.54 (m, 1H), 7.38 – 7.36 (m, 1H), 5.81 (qd, $^3J_{H\text{-}F}$ = 8.3, 1.6 Hz, 1H), 5.54 (m, 1H), 2.99 (s, 3H), 2.62 (bs, 1H).
^{13}C NMR (100 MHz, DMSO-d_6+$CDCl_3$):	δ 159.7 (d, $^{Ar}J_{C\text{-}F}$= 245.4 Hz), 149.5 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 136.4, 134.2 (d, $^{Ar}J_{C\text{-}F}$ = 8.2 Hz), 121.0 (q, $^1J_{C\text{-}F}$ = 268.0 Hz), 117.7 (d, $^{Ar}J_{C\text{-}F}$ = 8.4 Hz), 115.4 (d, $^{Ar}J_{C\text{-}F}$ = 24.0 Hz), 111.5 (d, $^{Ar}J_{C\text{-}F}$ = 24.6 Hz), 107.0 (q, $^2J_{C\text{-}F}$ = 36.0 Hz), 71.4, 36.7
^{19}F NMR (376 MHz, $CDCl_3$):	δ -59.8, -114.0
HRMS (APCI) m/z:	Calcd for $C_{11}H_9O_3NF_4S$: 294.0206 $[M\text{-}OH]^+$; found 294.0205

(Z)-1-(methylsulfonyl)-5-phenyl-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4i)**



Yield: 80 %
Colour: Pale yellow
Melting point: 140-142°C

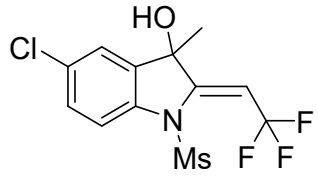
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, J = 1.7 Hz, 1H), 7.66 – 7.63 (m, 1H), 7.58 – 7.54 (m, 3H), 7.49 – 7.44 (m, 2H), 7.41 – 7.37 (m, 1H), 5.84 (qd, $^3J_{H\text{-}F}$ = 8.3, 1.6 Hz, 1H), 5.62 (s, 1H), 3.03 (s, 3H), 2.43 (bs, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 149.5, 141.4, 140.4, 139.8, 132.0, 129.8, 129.1, 128.0, 127.1, 127.0 (q, $^1J_{C\text{-}F}$ = 268.8 Hz), 123.9, 118.1, 109.0 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 74.2, 39.2

^{19}F NMR (376 MHz, $CDCl_3$): δ -59.7

HRMS (APCI) m/z: Calcd for $C_{17}H_{14}O_3NF_3S$: 352.0614 $[M\text{-}OH]^+$; found 352.0612

(Z)-5-chloro-3-methyl-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4j)**



Yield: 50 %
Colour: Light yellow liquid
Melting point: NA

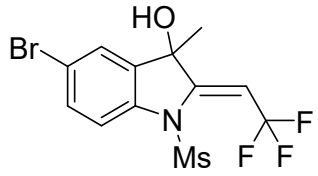
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.36 (m, 2H), 7.32 (d, J = 8.5 Hz, 1H), 5.74 (q, $^3J_{C\text{-}F}$ = 8.5 Hz, 1H), 3.15 (s, 3H), 2.33 (bs, 1H), 1.68 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 153.0 (d, $^3J_{C\text{-}F}$ = 5.0 Hz), 139.2, 137.3, 132.1, 130.4, 123.7, 122.2 (q, $^1J_{C\text{-}F}$ = 267.5 Hz), 118.2, 105.0 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 78.7, 40.7, 27.4

^{19}F NMR (376 MHz, $CDCl_3$): δ -59.5

HRMS (APCI) m/z: Calcd for $C_{12}H_{11}O_3NClF_3S$: 324.0067 $[M\text{-}OH]^+$; found 324.0069

(Z)-5-bromo-3-methyl-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4k)**



Yield: 70 %
Colour: Light yellow liquid
Melting point: NA

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 – 7.51 (m, 2H), 7.28 (s, 1H), 5.74 (q, $^3J_{H\text{-}F}$ = 8.5 Hz, 1H), 3.15 (s, 3H), 2.38 (s, 1H), 1.68 (s, 3H).

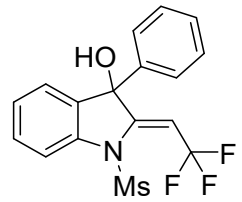
^{13}C NMR δ 152.9 (q, $^3J_{C\text{-}F}$ = 5.0 Hz), 139.7, 137.6, 133.3, 126.7, 122.2 (q,

(100 MHz, $CDCl_3$): $^1J_{C-F}$ = 267.0 Hz), 119.6, 118.5, 104.9 (q, $^2J_{C-F}$ = 37.0 Hz), 78.8, 40.8, 27.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -59.5

HRMS (APCI) m/z: Calcd for $C_{12}H_{11}O_3NBrF_3S$: 367.9562 $[M\text{-}OH]^+$; found 367.9561

(Z)-1-(methylsulfonyl)-3-phenyl-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4l)**



Yield: 60 %
Colour: Pale brown
Melting point: 157-159°C

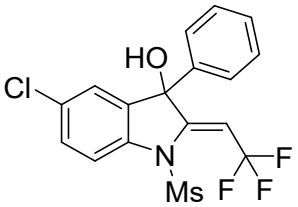
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.1 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.42 – 7.33 (m, 5H), 7.30 – 7.25 (m, 2H), 5.57 (q, $^3J_{H-F}$ = 8.0 Hz, 1H), 2.94 (s, 3H), 2.77 (s, 1H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4 (q, $^3J_{C-F}$ = 5.0 Hz), 141.8, 140.3, 131.0, 128.9, 128.8, 126.9, 126.4, 125.1, 122.4 (q, $^1J_{C-F}$ = 268.0 Hz), 117.2, 108.4 (q, $^2J_{C-F}$ = 37.0 Hz), 83.0, 39.7

^{19}F NMR (471 MHz, $CDCl_3$): δ -59.6

HRMS (APCI) m/z: Calcd for $C_{17}H_{14}O_3NF_3S$: 352.0614 $[M\text{-}OH]^+$; found 352.0613

(Z)-5-chloro-1-(methylsulfonyl)-3-phenyl-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4m)**



Yield: 70 %
Colour: Light yellow liquid
Melting point: NA

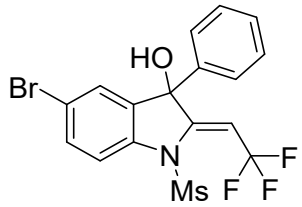
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 – 7.56 (m, 1H), 7.43 – 7.38 (m, 7H), 5.55 (q, $^3J_{H-F}$ = 8.5 Hz, 1H), 2.98 (s, 3H), 2.88 (s, 1H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 153.0 (q, $^3J_{C-F}$ = 5.3 Hz), 140.8, 139.7, 137.9, 133.8, 129.2, 129.1, 128.3, 126.3, 122.2 (q, $^1J_{C-F}$ = 268.8 Hz), 119.9, 118.8, 108.7 (q, $^2J_{C-F}$ = 36.8 Hz). 82.9, 39.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -59.6

HRMS (APCI) m/z: Calcd for $C_{17}H_{13}O_3NClF_3S$: 386.0224 $[M\text{-}OH]^+$; found 386.0221

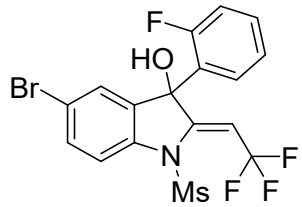
(Z)-5-bromo-1-(methylsulfonyl)-3-phenyl-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4n)**



Yield: 70 %
Colour: Pale yellow liquid
Melting point: NA

^{1}H NMR (500 MHz, $CDCl_3$):	δ 7.58-7.56 (m, 1H), 7.42 – 7.38 (m, 7H), 5.54 (q, $^{3}J_{H-F}$ = 8.0 Hz, 1H), 2.98 (s, 3H), 2.90 (bs, 1H)
^{13}C NMR (100 MHz, $CDCl_3$):	δ 152.9 (q, $^{3}J_{C-F}$ = 5.0 Hz), 140.7, 139.5, 137.8, 133.7, 129.1, 128.9, 128.2, 126.2, 122.0 (q, $^{1}J_{C-F}$ = 267.0 Hz), 119.8, 118.7, 108.6 (q, $^{2}J_{C-F}$ = 37.0 Hz), 82.8, 39.8.
^{19}F NMR (471 MHz, $CDCl_3$):	δ -59.6
HRMS (APCI) m/z:	Calcd for $C_{17}H_{13}O_3NBrF_3S$: 429.9719 $[M\text{-}OH]^+$; found 429.9718

(Z)-5-bromo-3-(2-fluorophenyl)-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol **(4o)**



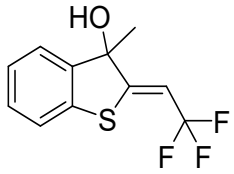
Yield: 65 %
Colour: Pale orange liquid
Melting point: NA

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.80 – 7.74 (m, 1H), 7.59 – 7.54 (m, 1H), 7.47 – 7.39 (m, 2H), 7.34 – 7.26 (m, 2H), 7.11 – 7.02 (m, 1H), 5.36 (q, $^{3}J_{H-F}$= 8.0 Hz, 1H), 3.13 (s, 3H), 3.06 (bs, 1H).
^{13}C NMR (100 MHz, $CDCl_3$):	δ 159.3 (d, $^{Ar}J_{C-F}$ = 249.2 Hz), 151.3 (q, $^{3}J_{C-F}$ = 4.0 Hz), 140.8, 137.0, 133.8, 131.4 (d, $^{Ar}J_{C-F}$ = 8.4 Hz), 127.9, 127.4, 127.1 (d, $^{Ar}J_{C-F}$ = 10.9 Hz), 124.4 (d, $^{Ar}J_{C-F}$ = 3.1 Hz), 122.1 (q $^{1}J_{C-F}$ = 268.0 Hz), 119.7, 118.9, 116.7 (d, $^{Ar}J_{C-F}$ = 21.4 Hz), 107.7 (q $^{2}J_{C-F}$ = 38.0 Hz), 80.2, 39.9.
^{19}F NMR (376 MHz, $CDCl_3$):	δ -59.6, -108.3
HRMS (APCI) m/z:	Calcd for $C_{17}H_{12}O_3NBrF_4S$: 447.9625 $[M\text{-}OH]^+$; found 447.9624

4. Preparation of benzothiophene derivative

Similar procedure as described above was followed for the synthesis of **6a** and the product was obtained in 80% yield.

(Z)-3-methyl-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzo[b]thiophen-3-ol **(6a)**



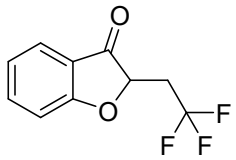
Yield: 80 %
Colour: White solid
Melting point: 86-88°C

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.42 – 7.40 (m, 1H), 7.33 – 7.29 (m, 1H), 7.24 – 7.20 (m, 2H), 6.13 (q, $^{3}J_{H\text{-}F}$ = 8.0 Hz, 1H), 2.48 (s, 1H), 1.63 (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$):	δ 158.9 (q, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 141.8, 134.7, 130.2, 126.2, 124.3, 123.9 (q, $^{1}J_{C\text{-}F}$ = 268.0 Hz), 122.1, 109.1 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 85.3, 31.4
^{19}F NMR (376 MHz, $CDCl_3$):	δ -59.7
HRMS (APCI) m/z:	Calcd for $C_{11}H_9OF_3S$: 229.0293 $[M\text{-}OH]^+$; found 229.0291

5. Further derivatization

5.1. Synthesis of *2-(2,2,2-trifluoroethyl)benzofuran-3(2H)-one* (2aa)

In an oven dried nitrogen purged flask, **2a** (50 mg, 1.0 eq.) and triethylamine (1.5 eq.) was suspended in toluene (1.0 mL). The reaction mixture was refluxed for 2 h. After completion (as monitored by TLC), the solvent was removed under reduced pressure. The crude was then purified using silica gel column chromatography to obtain pure product (**2aa**).

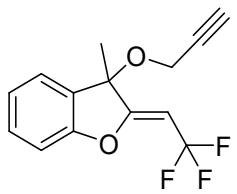


Yield: 95 %
Colour: Colourless liquid
Melting point: NA

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.71 – 7.65 (m, 2H), 7.21 – 7.13 (m, 2H), 4.77 (d, J = 10.0 Hz, 1H), 2.91 – 2.81 (m, 1H), 2.47 – 2.39 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$):	δ 199.0, 172.8, 138.8, 124.7, 122.8, 118.6 (q $^{1}J_{C\text{-}F}$ = 263.0 Hz), 114.0, 78.8, 36.1 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz)
^{19}F NMR (376 MHz, $CDCl_3$):	δ -64.2
HRMS (APCI) m/z:	Calcd for $C_{10}H_7O_2F_3$: 215.0314 $[M\text{-}H]^+$; found 215.0327

5.2. Synthesis of *(Z)-3-methyl-3-(prop-2-yn-1-yloxy)-2-(2,2,2-trifluoroethylidene)-2,3-dihydrobenzofuran* (2ga)

In a round bottom flask, **2g** (100 mg, 1.0 eq) and sodium hydride (1.5 eq.) were suspended in DMF (2.0 mL) at 0°C. The reaction was stirred for 30 min maintaining the temperature. To the stirring mixture, propargyl bromide (1.1 eq.) was added dropwise. The reaction mixture was then stirred for 2 h. After completion (as monitored by TLC), the reaction was quenched with ice cold water and extracted 3 times with ethyl acetate. Combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was then purified using silica gel column chromatography to obtain pure product (**2ga**).

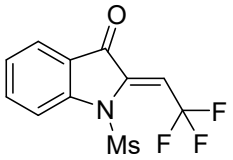


Yield: 80 %
Colour: Colourless liquid
Melting point: NA

^{1}H NMR (500 MHz, $CDCl_3$):	δ 7.40 – 7.37 (m, 2H), 7.18 – 7.14 (m, 1H), 7.10 – 7.08 (m, 1H), 5.30 (q, $^3J_{H\text{-}F}$ = 8.0 Hz, 1H), 3.80 (dd, J = 14.6, 2.4 Hz, 1H), 3.59 (dd, J = 14.6, 2.5 Hz, 1H), 2.38 (t, J = 2.5 Hz, 1H), 1.71 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$):	δ 165.1 (q, $^3J_{C\text{-}F}$= 5.0 Hz), 156.6, 131.4, 125.6, 124.5, 124.1, 123.2 (q, $^1J_{C\text{-}F}$ = 267.5 Hz), 111.2, 93.1 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 83.3, 79.2, 74.6, 53.2, 28.8
^{19}F NMR (376 MHz, $CDCl_3$):	δ -57.2
HRMS (APCI) m/z:	Calcd for $C_{14}H_{11}O_2F_3$: 269.0784 $[M+H]^+$; found 269.0784

5.3. Synthesis of *(Z)-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)indolin-3-one* (4da)

In an oven dried nitrogen purged flask, **4d** (20 mg, 1 eq.) and pyridinium chlorochromate (1.5 eq.) was suspended in DCM (1 mL). The reaction mixture was stirred at rt for 2 h. After completion (as monitored by TLC), the reaction was filtered through celite. The celite was washed several times with DCM. The combined organic filtrate was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was then purified using silica gel column chromatography to obtain pure product (**4da**).

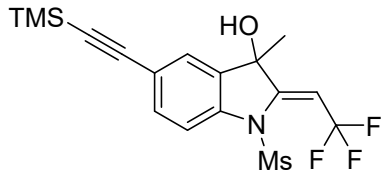


Yield: 95 %
Colour: Brown liquid
Melting point: NA

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.94 (d, J = 8.4 Hz, 1H), 7.87 – 7.85 (m, 1H), 7.73 – 7.69 (m, 1H), 7.34 (t, J = 7.5 Hz, 1H), 6.81 (q, $^3J_{H\text{-}F}$ = 9.0 Hz, 1H), 3.10 (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$):	δ 184.4, 151.1, 137.8, 126.7, 125.7, 123.8, 118.4, 116.2, 109.0 (q, $^2J_{C\text{-}F}$ = 39.0 Hz), 40.5.
^{19}F NMR (470 MHz, $CDCl_3$):	δ -57.2
HRMS (APCI) m/z:	Calcd for $C_{11}H_8O_3NF_3S$: 292.0250 $[M+H]^+$; found 292.0248

5.4. Synthesis of *(Z)-3-methyl-1-(methylsulfonyl)-2-(2,2,2-trifluoroethylidene)-5-((trimethylsilyl)ethynyl)indolin-3-ol* (4ga)

In an oven dried nitrogen purged flask, **4g** (100 mg, 1.0 eq.), triethylamine (5.0 eq.), CuI (0.01 eq.) and $Pd(PPh_3)_2Cl_2$ (0.03 eq.) was suspended in dry THF (1.0 mL). The mixture was purged with nitrogen and TMS-acetylene (1.1 eq.) was added. The reaction mixture was stirred at 80°C for 8 h. After completion (as monitored by TLC), the reaction was cooled to rt and filtered through celite. The celite was washed several times with diethyl ether. The combined organic filtrate was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was then purified using silica gel column chromatography to obtain pure product (**4ga**).

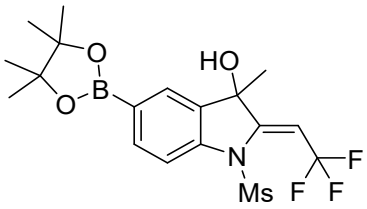


Yield: 90 %
Colour: Colourless liquid
Melting point: NA

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.54 (d, J = 1.2 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.33 (d, J = 8.3 Hz, 1H), 5.74 (q, $^3J_{H\text{-}F}$ = 8.0 Hz, 1H), 3.12 (s, 3H), 1.67 (s, 3H), 0.26 (s, 9H)
^{13}C NMR (125 MHz, $CDCl_3$):	δ 153.1 (d, $^3J_{C\text{-}F}$ = 5.0 Hz), 140.5, 135.7, 134.3, 127.0, 122.4 (q, $^1J_{C\text{-}F}$ = 267.5 Hz), 121.7, 116.8, 104.9 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 103.7, 95.6, 78.8, 40.7, 27.5
^{19}F NMR (376 MHz, $CDCl_3$):	δ -59.5
HRMS (APCI) m/z:	Calcd for $C_{17}H_{20}O_3NF_3SSi$: 404.0958 $[M+H]^+$; found 404.0955

5.5. Synthesis of (*Z*)-3-methyl-1-(methylsulfonyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(2,2,2-trifluoroethylidene)indolin-3-ol (4gb)

In an oven dried nitrogen purged flask, **4g** (20 mg, 1.0 eq.), bis(pinacolato)diboron (1.2 eq.) and KOAc (3.0 eq.) was suspended in dry 1,4-dioxane (1.0 mL). To this mixture, catalytic amount of $Pd(dppf)Cl_2$ (< 1 mg) was added. The reaction mixture was stirred at 90°C for 2 h. After completion (as monitored by TLC), the reaction was cooled to rt and filtered through celite. The celite was washed several times with diethyl ether. The combined organic filtrate was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was then purified using silica gel column chromatography to obtain pure product (**4gb**).

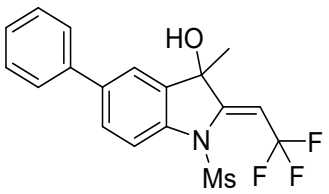


Yield: 80 %
Colour: Viscous colourless liquid
Melting point: NA

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.88 (s, 1H), 7.87-7.84 (m, 1H), 7.41 (d, J = 8.0 Hz, 1H), 5.74 (q, $^3J_{H\text{-}F}$ = 8.0 Hz, 1H), 3.12 (s, 3H), 2.11 (s, 1H), 1.70 (s, 3H), 1.35 (d, J = 1.9 Hz, 12H)
^{13}C NMR (175 MHz, DMSO-d_6+$CDCl_3$):	δ 153.4, 143.1, 142.3, 136.7, 135.6, 129.9, 115.9, 104.7 (q, $^2J_{C\text{-}F}$ = 36.8 Hz), 84.0, 39.4, 29.6, 24.9, 24.7
^{19}F NMR (376 MHz, $CDCl_3$):	δ -59.5
HRMS (APCI) m/z:	Calcd for $C_{18}H_{23}NBF_3O_3S$: 416.1309 $[M\text{-}OH]^+$; found 416.1307

5.6. Synthesis of *(Z)-3-methyl-1-(methylsulfonyl)-5-phenyl-2-(2,2,2-trifluoroethylidene)indolin-3-ol* (4gc)

In an oven dried nitrogen purged flask, **4g** (100 mg, 1 eq.), phenyl boronic acid (1.2 eq.), K_2CO_3 (3.0 eq.) were suspended in 1,4-dioxane:H_2O (1:1; 2.0 mL). The mixture was purged with nitrogen and $Pd(PPh_3)_4$ (0.05 eq.) was added. The reaction mixture was stirred at 100°C for 8 h. After completion (as monitored by TLC), the reaction was cooled to rt and filtered through celite. The celite was washed several times with diethyl ether. The combined organic filtrate was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was then purified using silica gel column chromatography to obtain pure product (**4gc**).



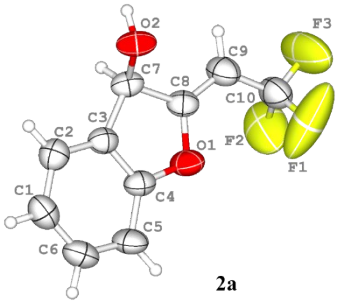
Yield: 90 %
Colour: Brown liquid
Melting point: NA

^{1}H NMR (400 MHz, $CDCl_3$):	δ 7.65 – 7.56 (m, 4H), 7.48 – 7.44 (m, 3H), 7.40 – 7.36 (m, 1H), 5.77 (q, $^3J_{H\text{-}F}$ = 8.0 Hz, 1H), 3.18 (s, 3H), 2.26 (s, 1H), 1.73 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$):	δ 149.5 (q, $^3J_{C\text{-}F}$ = 5.0 Hz), 141.4, 140.4, 139.8, 132.0, 129.8, 129.1, 128.0, 127.1, 123.9, 121.9 (q, $^1J_{C\text{-}F}$ = 267.5 Hz), 118.0, 109.0 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 74.1, 39.1
^{19}F NMR (376 MHz, $CDCl_3$):	δ -59.5
HRMS (APCI) m/z:	Calcd for $C_{18}H_{16}O_3NF_3S$: 366.0770 $[M\text{-}OH]^+$; found 366.0769

6. X-Ray Crystal Data

X-ray data for the compound was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 A) and a PHOTON-III detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [1]. The structure was solved using intrinsic phasing method and further refined with the SHELXL program and expanded using Fourier techniques [2]. Anisotropic displacement parameters were included for all non-hydrogen atoms. All C bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms].

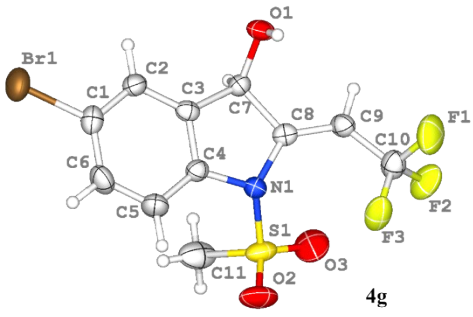
Crystal structure determination of 2a



2a

Crystal Data for $C_{10}H_7O_2F_3$ (M =216.16 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 8.510(8) Å, b = 4.956(4) Å, c = 11.481(9) Å, β = 106.91(3)°, V = 463.3(7) Å^3, Z = 2, T = 294.15 K, μ(MoKα) = 0.146 mm^{-1}, *Dcalc* = 1.549 g/cm^3, 9200 reflections measured (5.002° ≤ 2Θ ≤ 60.688°), 2488 unique (R_{int} = 0.0696, R_{sigma} = 0.0724) which were used in all calculations. The final R_1 was 0.0629 (I > 2σ(I)) and wR_2 was 0.1962 (all data). CCDC 2352135 deposition number contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Crystal structure determination of 4g



4g

Crystal Data for $C_{11}H_9BrF_3NO_3S$ (M =372.16 g/mol): orthorhombic, space group $Pna2_1$ (no. 33), a = 5.4629(7) Å, b = 21.481(3) Å, c = 11.2799(13) Å, V = 1323.7(3) Å^3, Z = 4, T = 294.15 K, μ(MoKα) = 3.305 mm^{-1}, *Dcalc* = 1.868 g/cm^3, 9707 reflections measured (6.74° ≤ 2Θ ≤ 56.542°), 2982 unique (R_{int} = 0.0297, R_{sigma} = 0.0459) which were used in all calculations. The final R_1 was 0.0293 (I > 2σ(I)) and wR_2 was 0.0628 (all data). **CCDC 2366081** deposition numbers contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

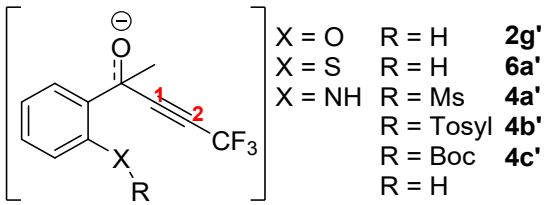
7. Computational Data

For better understanding of the electronic effect of the intermediate formed in the plausible reaction mechanism, density functional theory (DFT) was performed in the gas phase using Gaussian09 software. To perform the DFT calculations, B3LYP (Becke three-parameter Lee−Yang−Parr exchange correlation functional) and the 6-311G++(d,p) as basis set was used [3]. Geometries were optimized, and the frequency calculations showed no negative eigenvalue. The optimized geometries were used to perform natural bond orbital (NBO) calculations to calculate the atomic charges present in the molecule [4]. Later this was used to evaluate Fukui indices for calculating nucleophilic centre whether at position 1 or 2 (**Table S1**) using below equation.

$f += Qk(N+1) - Qk(N)$

Where, Qk is charge on atom k; N is neutral system (or system which participates in the reaction mechanism); N+1 is one electron added to the N system. The data are tabulated in **Table 2**. Fukui indices provide an insight into the most probable nucleophilic (and electrophilic) attack site. Based on the reaction mechanism there arise two possibilities, the attack can probably take place *via* site 1 or site 2. Upon comparison, site 1 is favoured for nucleophilic attack compared to position 2. The Fukui indices are positive at site 1 compared to the negative values at site 2. The formation of 5-exo-dig cyclization is justified as negative Fukui indices are insignificant [5, 6].

Table S1. Fukui indices for understanding the nucleophilic probability at the respective atom.



Intermediate	Charge on atom			f+	
	X	1	2	For 1	For 2
2g'	-0.673	0.089	-0.214	0.108	-0.105
4a'	-0.855	0.139	-0.275	0.014	-0.006
4b'	-0.845	0.086	-0.196	0.065	-0.100
4c'	-0.745	0.146	-0.216	0.136	-0.057

6a'	0.121	0.145	-0.277	0.054	-0.012
-NH_2	-0.832	0.157	-0.277	0.056	-0.014

References

[1] B. APEX, *Madison, WI, USA*, (2016).

[2] G.M. Sheldrick, *Acta Crystallographica Section A: Foundations and Advances*, **71** (2015) 3-8.

[3] A. Frisch, *Wallingford, USA, 25p*, **470** (2009).

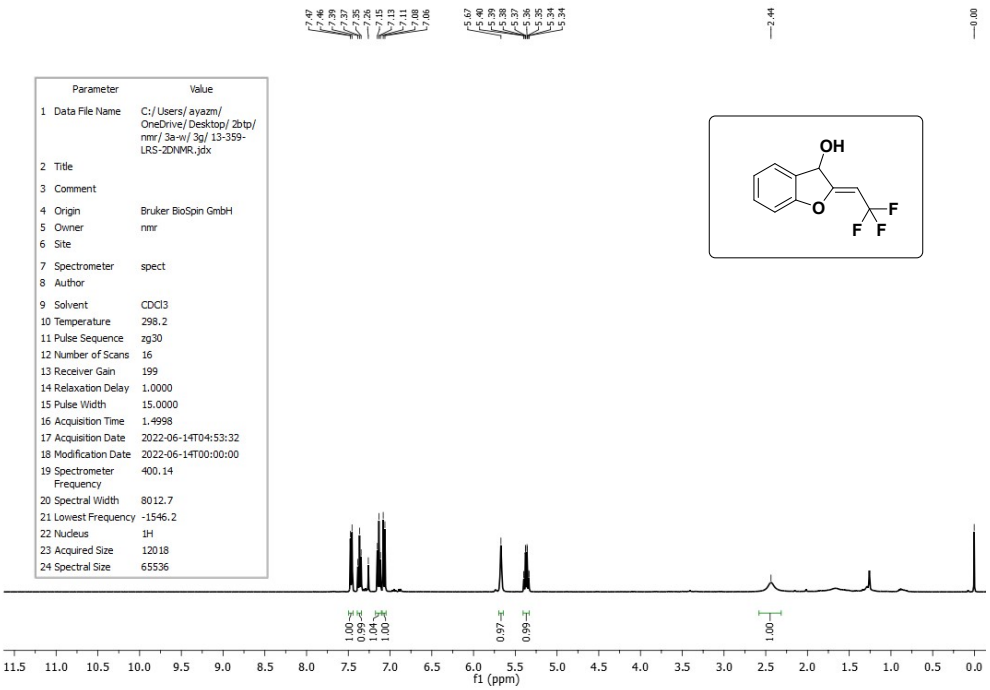
[4] A.E. Reed, L.A. Curtiss, F. Weinhold, *Chem. Rev.*, **88** (1988) 899-926.

[5] T. Otsuka, N. Okimoto, H. Saito, M. Taiji, *J. Phys. Conf. Ser.*, **1290** (2019) 012021.

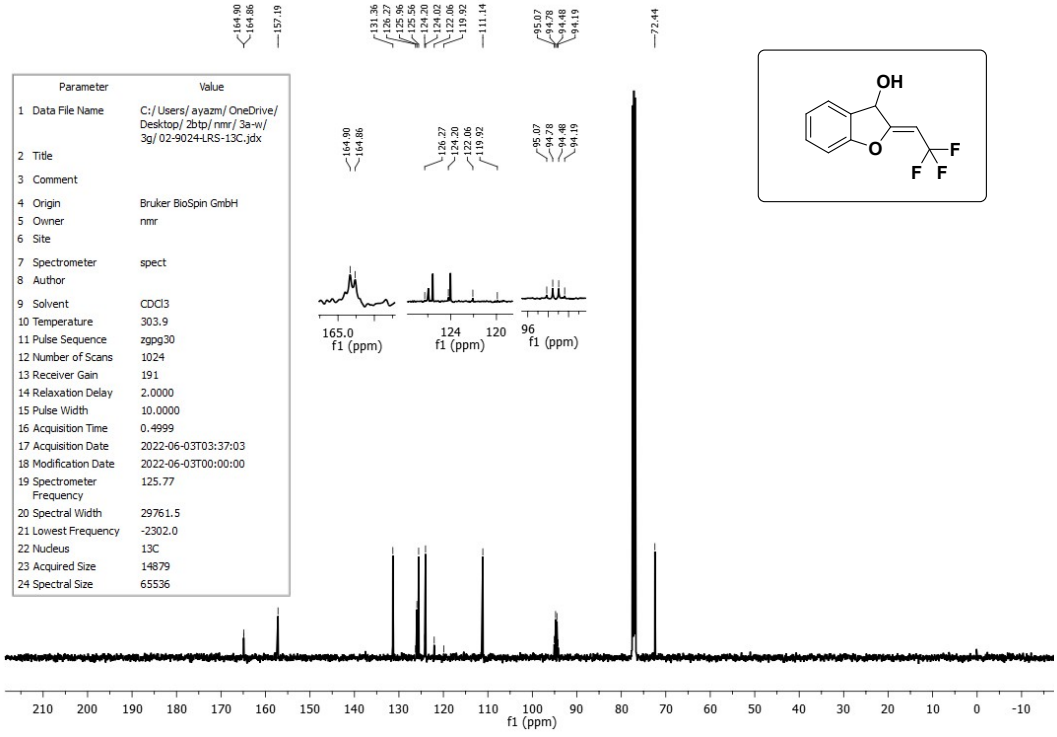
[6] P. Bultinck, D. Clarisse, P.W. Ayers, R. Carbo-Dorca, *Phys. Chem. Chem. Phys.*, **13** (2011) 6110-6115.

8. Spectra of the synthesized compounds

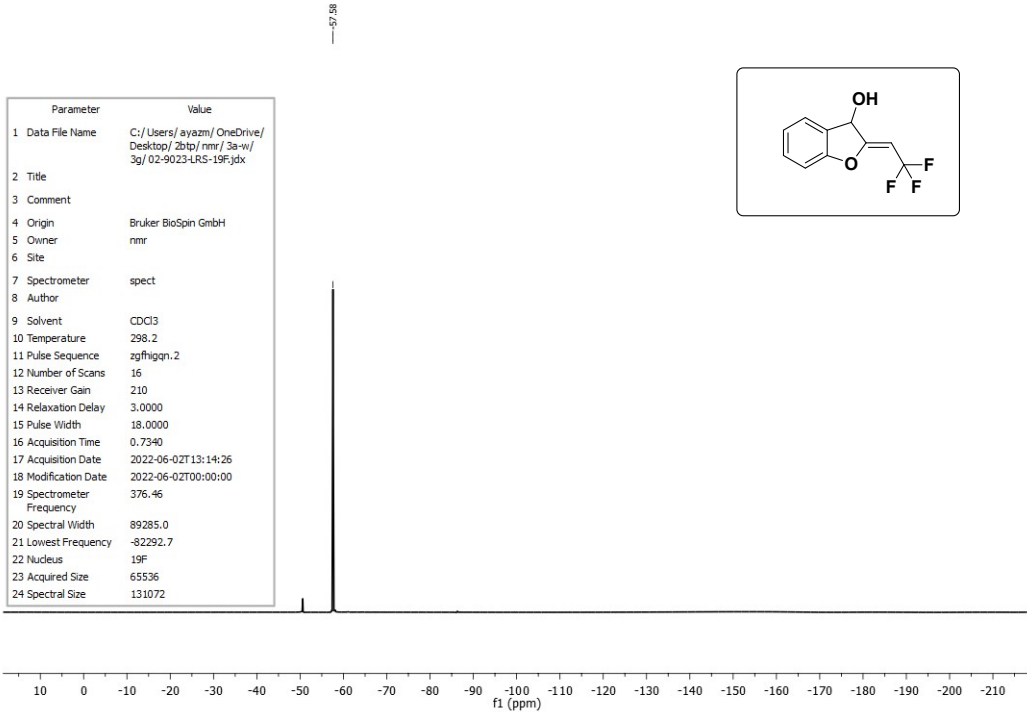
^{1}H NMR for 2a at 400 MHz



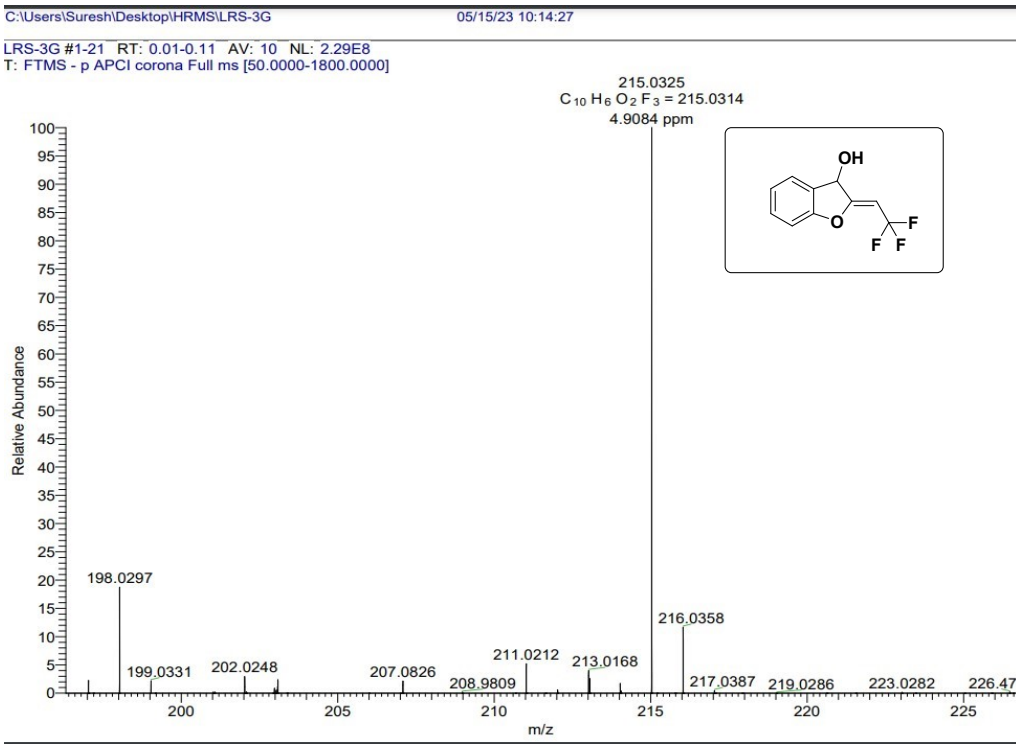
^{13}C NMR for 2a at 125 MHz



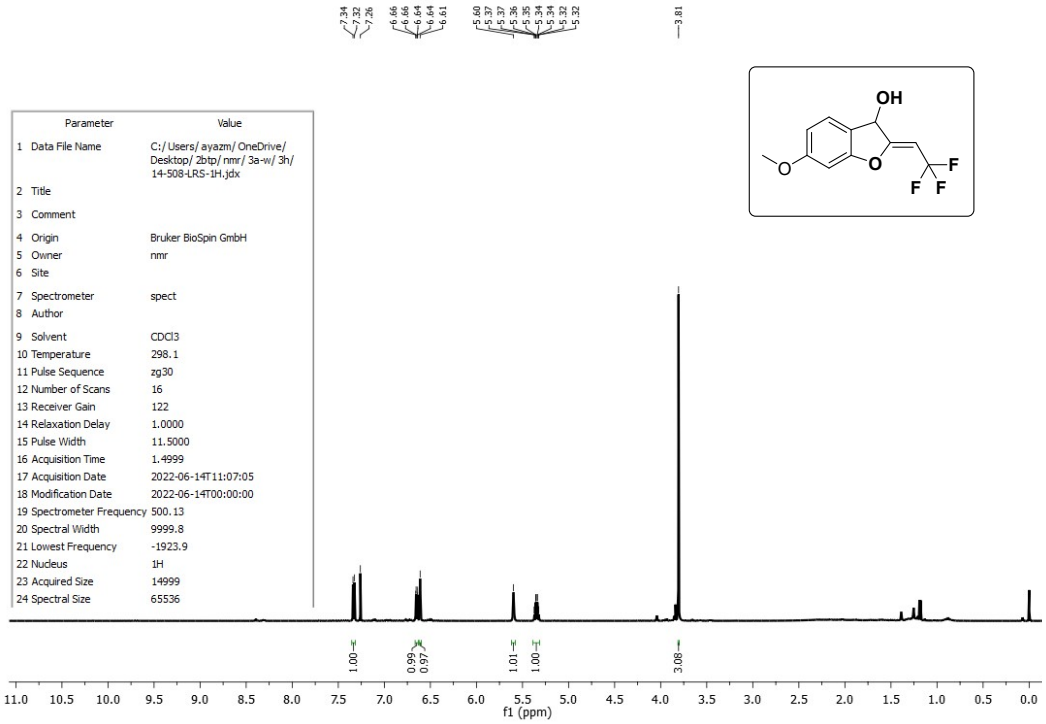
^{19}F NMR for 2a at 376 MHz



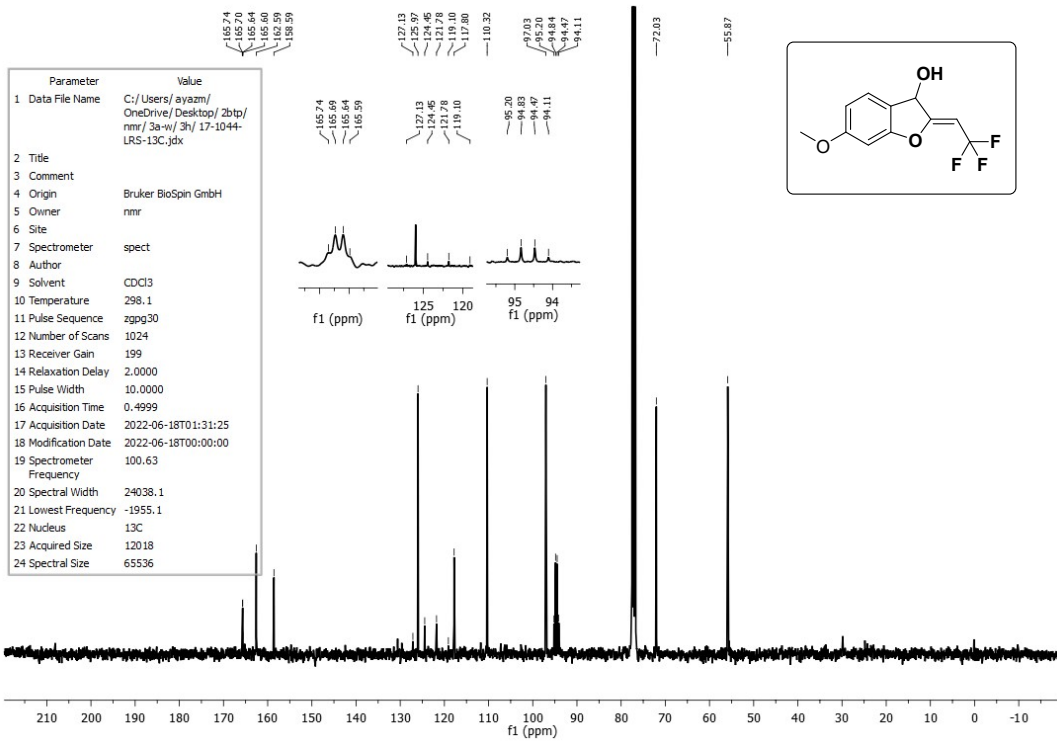
HRMS for 2a in APCI (-) MODE.



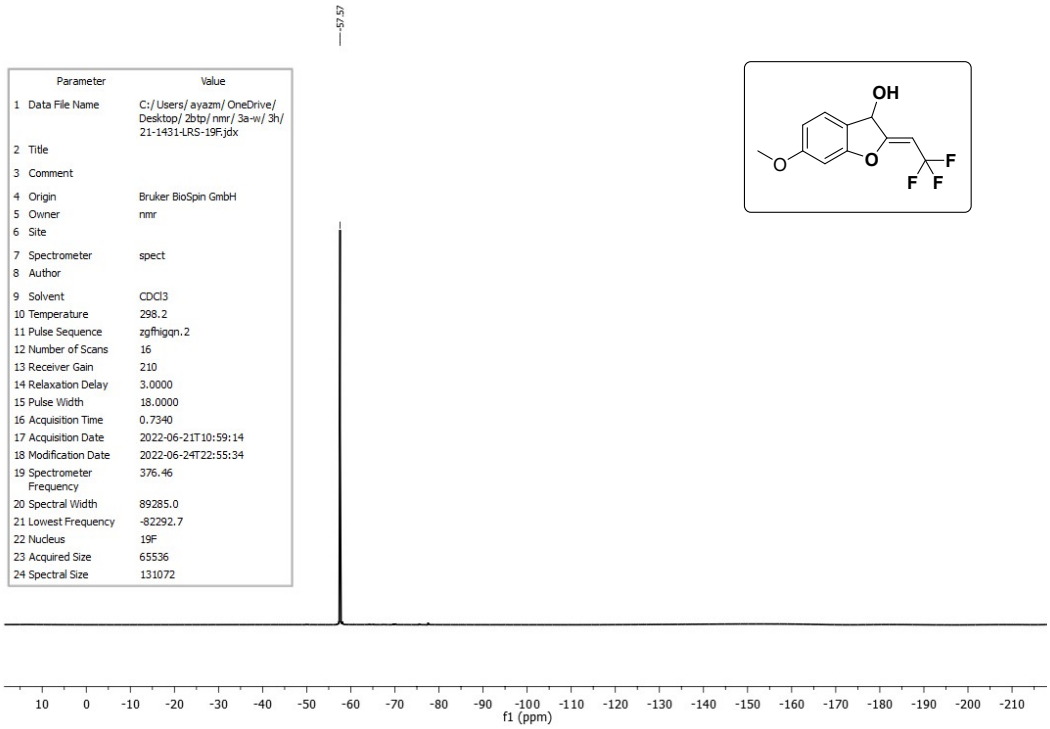
^{1}H NMR for 2b at 500 MHz



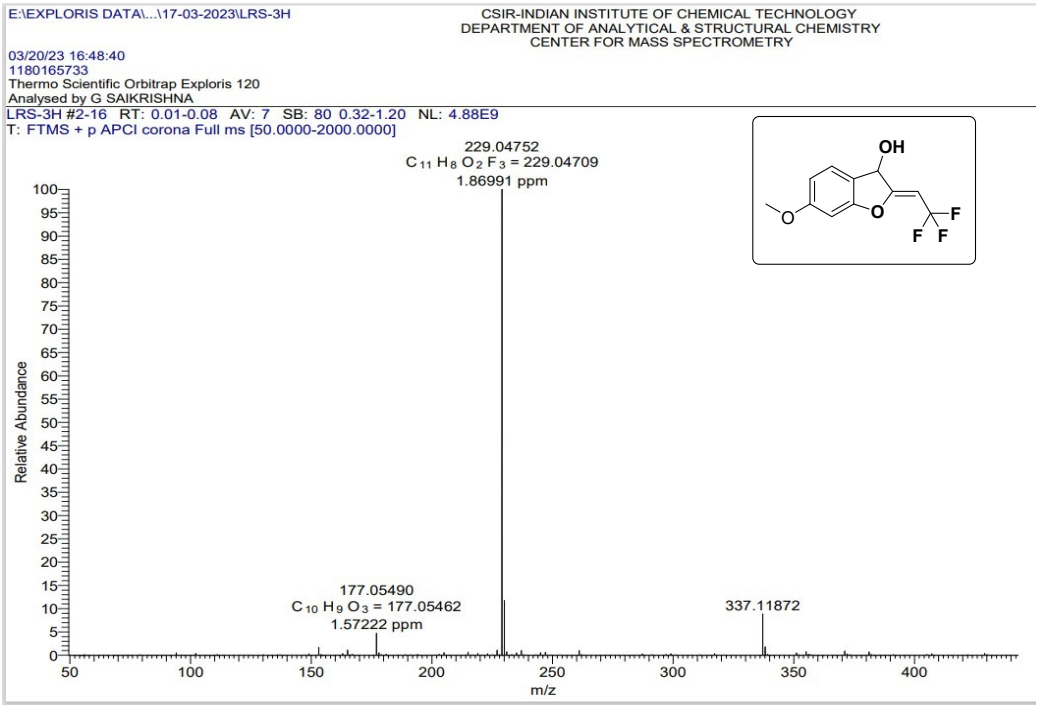
^{13}C NMR for 2b at 100 MHz



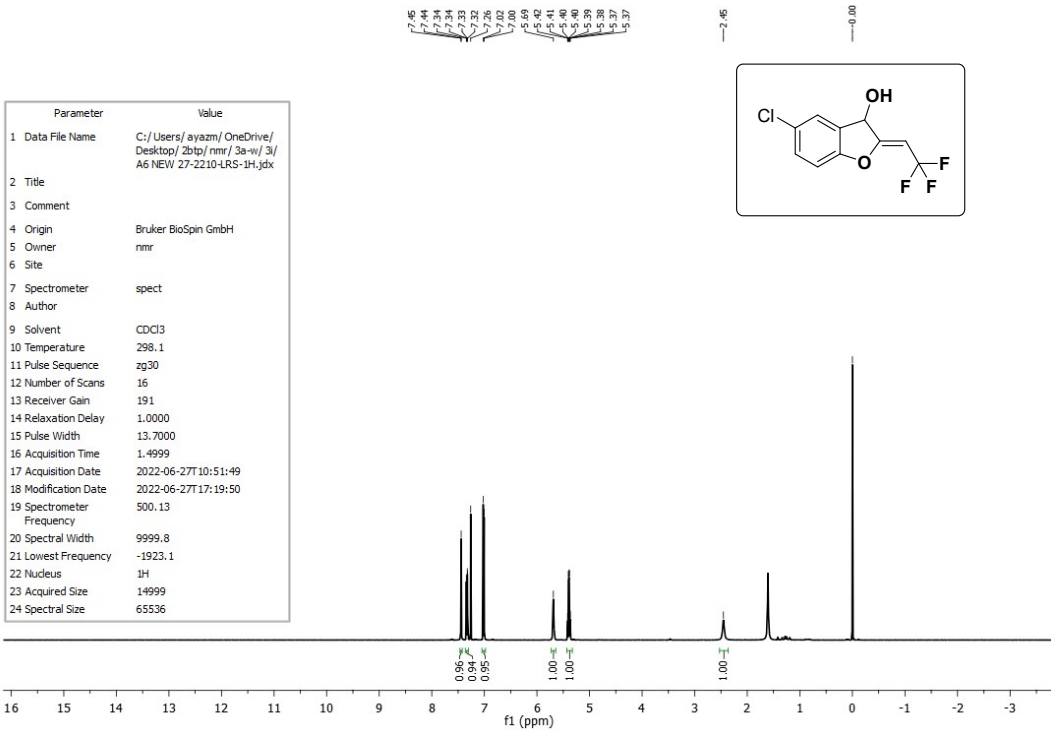
^{19}F NMR for 2b at 376 MHz



HRMS for 2b in APCI (+) MODE.



^{1}H NMR for 2c at 500 MHz



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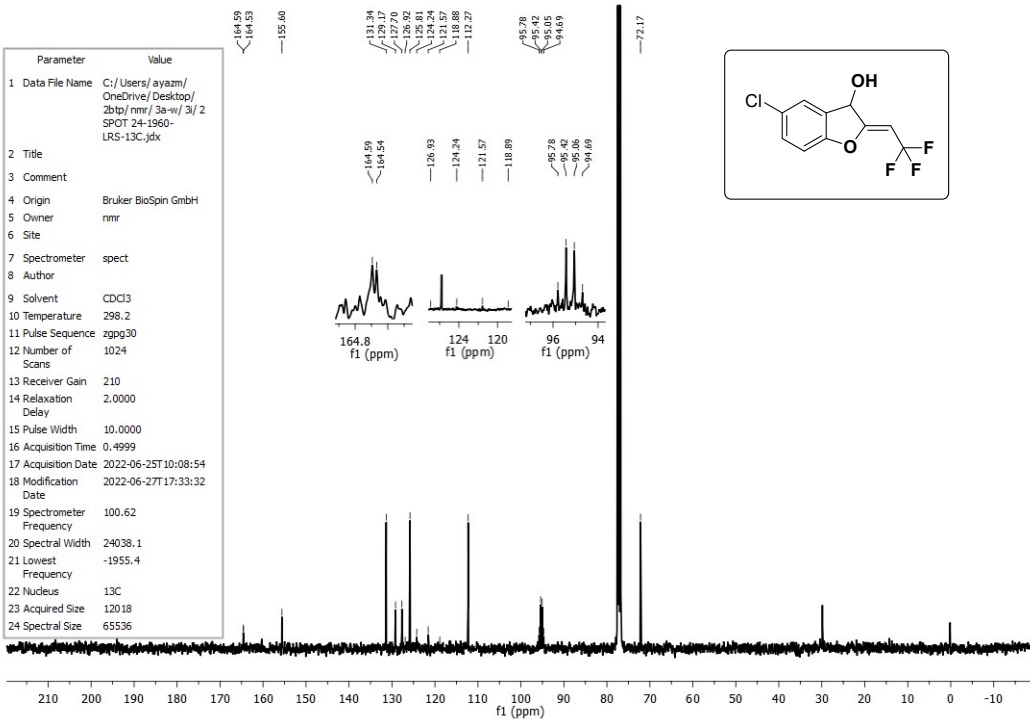
2	Title	
3	Comment	
4	Origin	Bruker BioSpin GmbH
5	Owner	nmr
6	Site	
7	Spectrometer	spect
8	Author	
9	Solvent	CDCl3
10	Temperature	298.1
11	Pulse Sequence	zg30
12	Number of Scans	16
13	Receiver Gain	191
14	Relaxation Delay	1.0000
15	Pulse Width	13.7000
16	Acquisition Time	1.4999
17	Acquisition Date	2022-06-27T10:51:49
18	Modification Date	2022-06-27T17:19:50
19	Spectrometer Frequency	500.13
20	Spectral Width	9999.8
21	Lowest Frequency	-1923.1
22	Nucleus	1H
23	Acquired Size	14999
24	Spectral Size	65536

^{13}C NMR for 2c at 100 MHz



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2	Title	
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6	Site	
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8	Author	
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11	Pulse Sequence	zgpg30
12	Number of Scans	1024
13	Receiver Gain	210
14	Relaxation Delay	2.0000
15	Pulse Width	10.0000
16	Acquisition Time	0.4999
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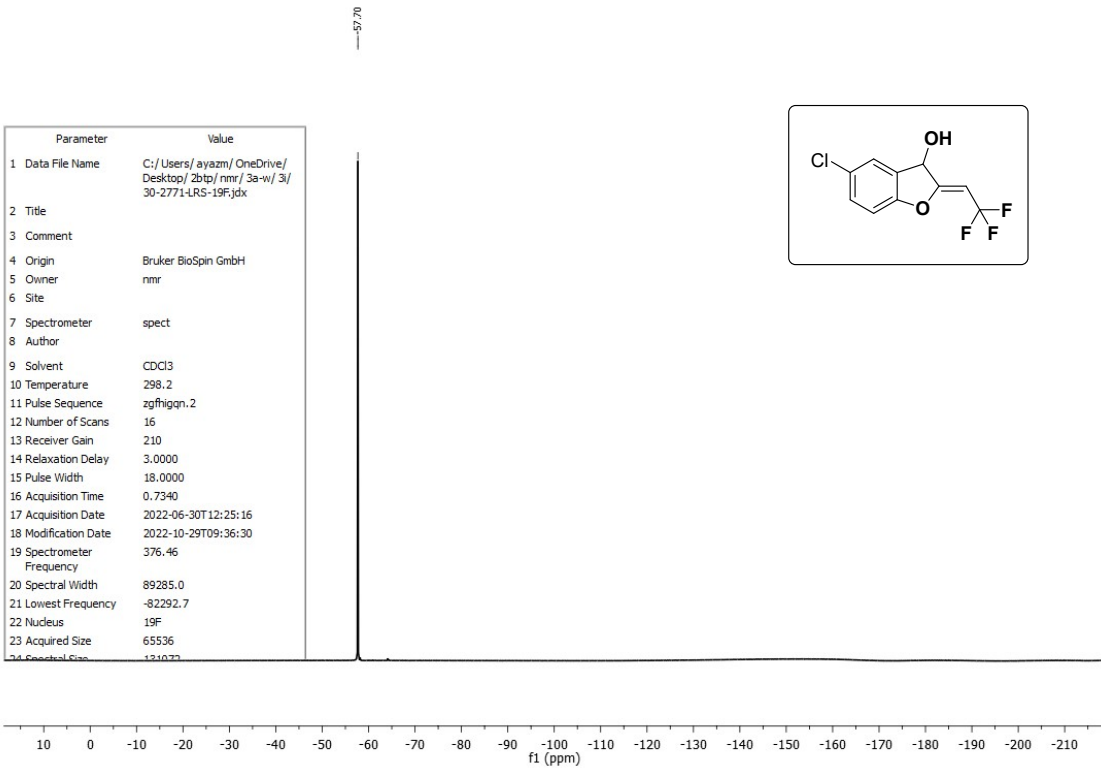
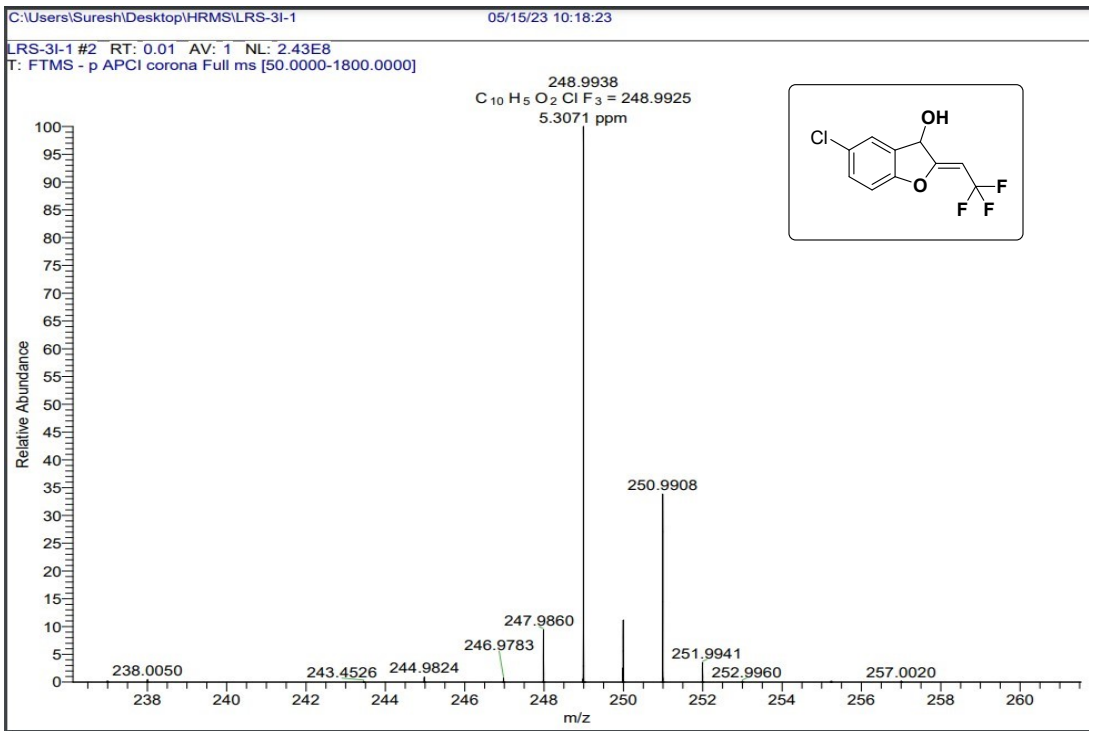
18	Modification Date	2022-06-27T17:33:32
19	Spectrometer Frequency	100.62
20	Spectral Width	24038.1
21	Lowest Frequency	-1955.4
22	Nucleus	13C
23	Acquired Size	12018
24	Spectral Size	65536

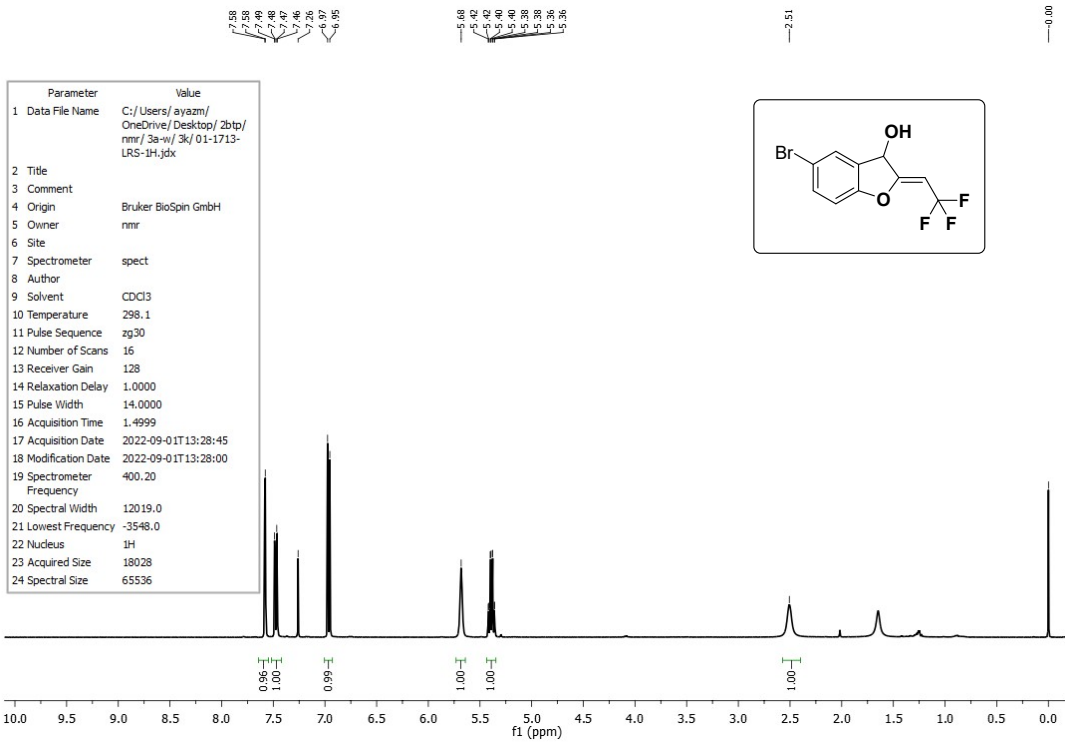
^{19}F NMR for 2c at 376 MHz



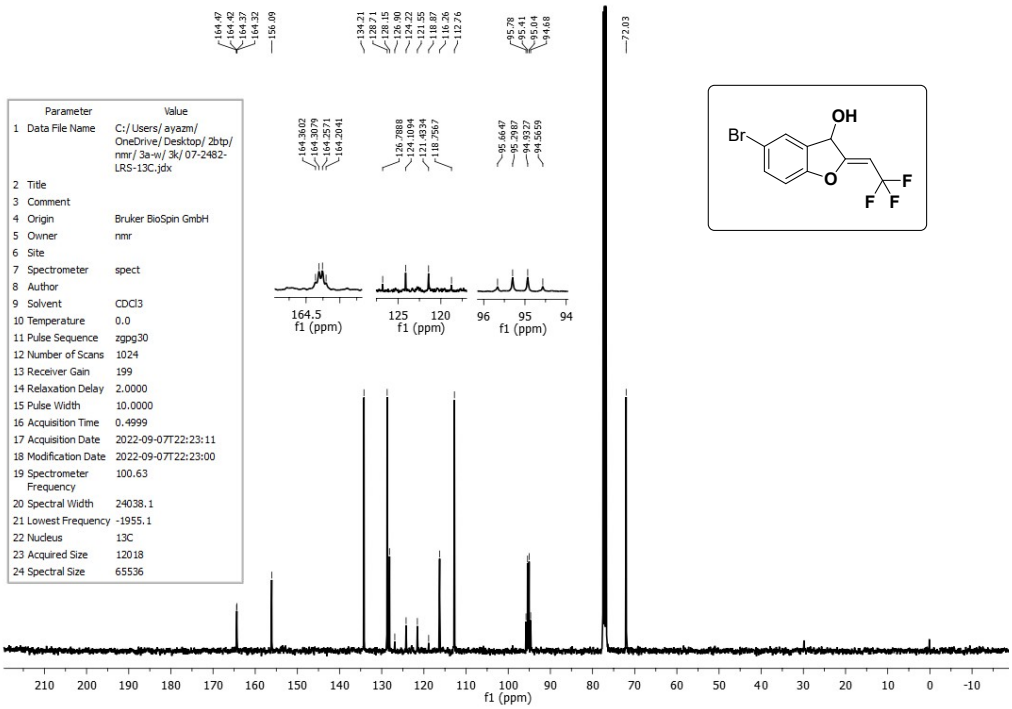
HRMS for 2c in APCI (-) MODE.



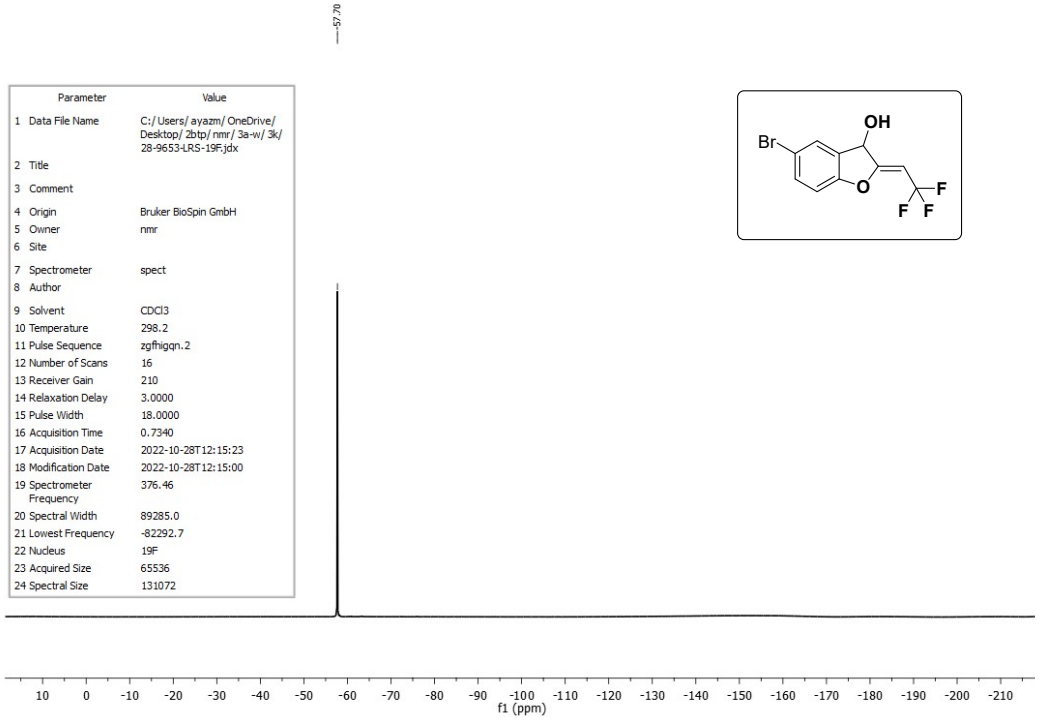
^{1}H NMR for 2d at 400 MHz



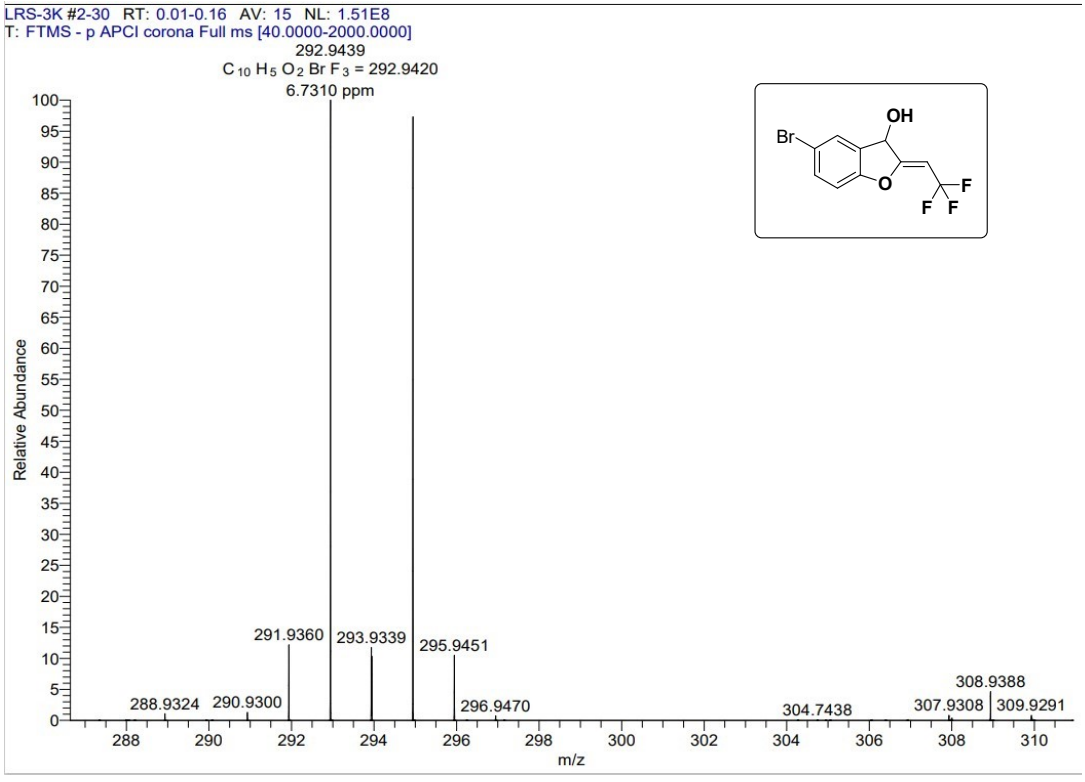
^{13}C NMR for 2d at 100 MHz



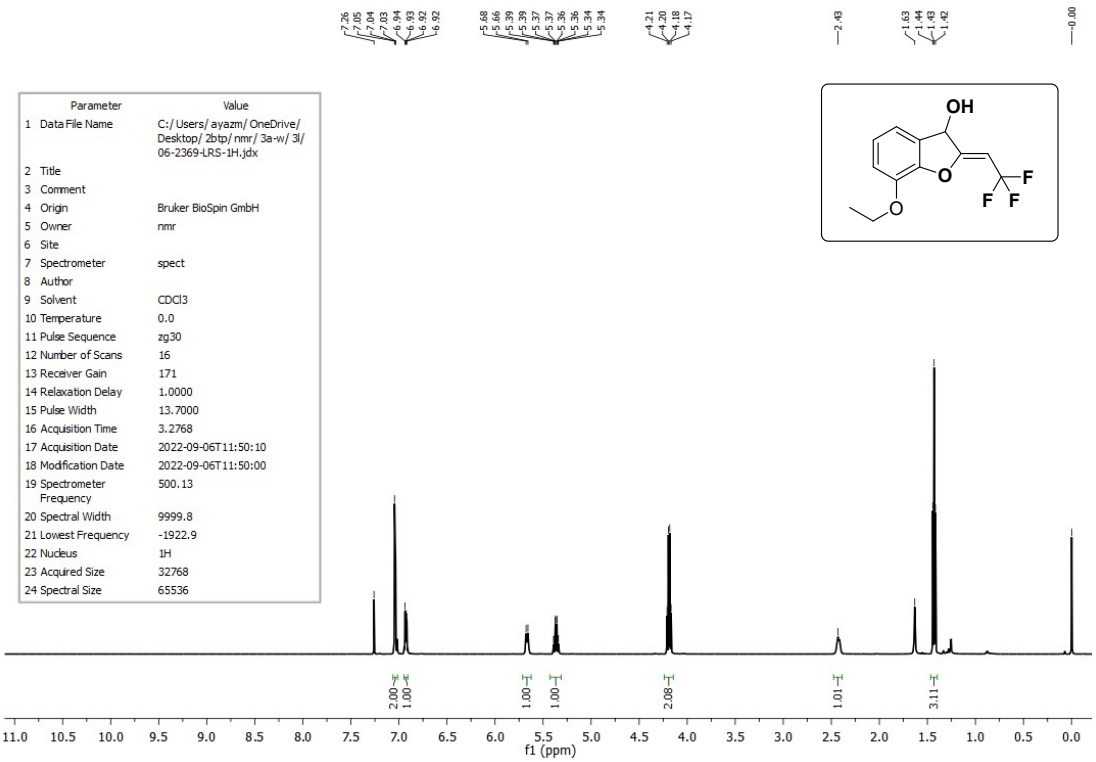
^{19}F NMR for 2d at 376 MHz



HRMS for 2d in APCI (-) MODE.



^{1}H NMR for 2e at 500 MHz



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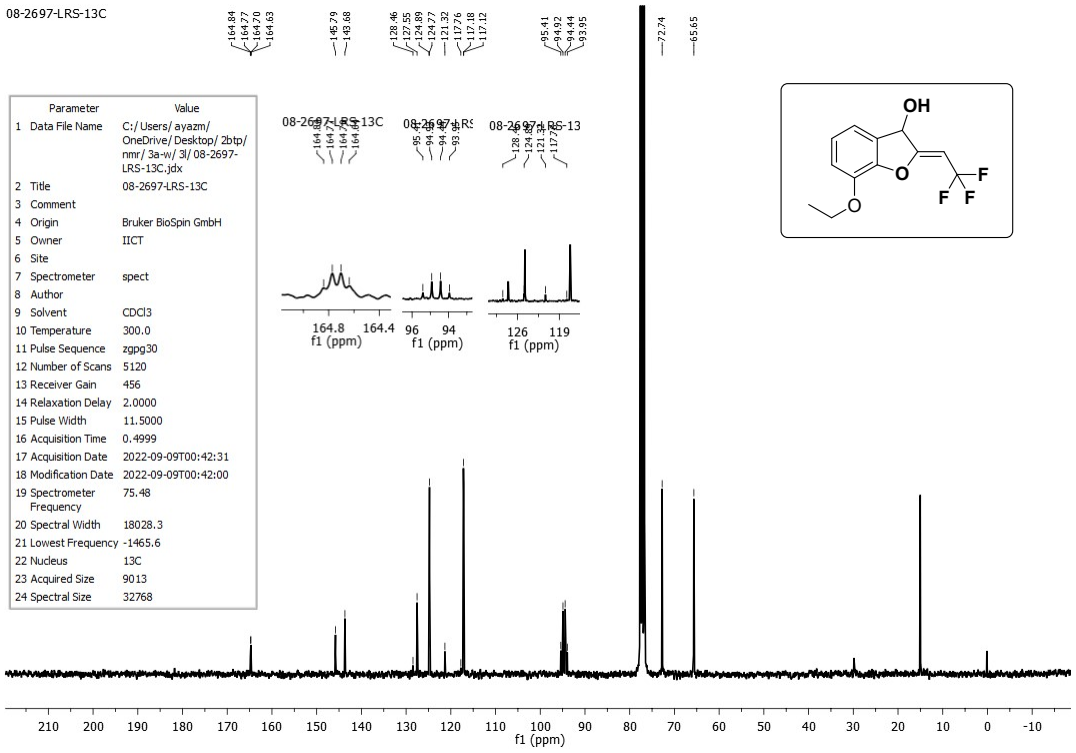
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Spectrometer	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	0.0
11 Pulse Sequence	zg30
12 Number of Scans	16
13 Receiver Gain	171
14 Relaxation Delay	1.0000
15 Pulse Width	13.7000
16 Acquisition Time	3.2768
17 Acquisition Date	2022-09-06T11:50:10
18 Modification Date	2022-09-06T11:50:00
19 Spectrometer Frequency	500.13
20 Spectral Width	9999.8
21 Lowest Frequency	-1922.9
22 Nucleus	1H
23 Acquired Size	32768
24 Spectral Size	65536

^{13}C NMR for 2e at 75 MHz



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5 Owner	IICT
6 Site	
7 Spectrometer	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zgpg30
12 Number of Scans	5120
13 Receiver Gain	456
14 Relaxation Delay	2.0000
15 Pulse Width	11.5000
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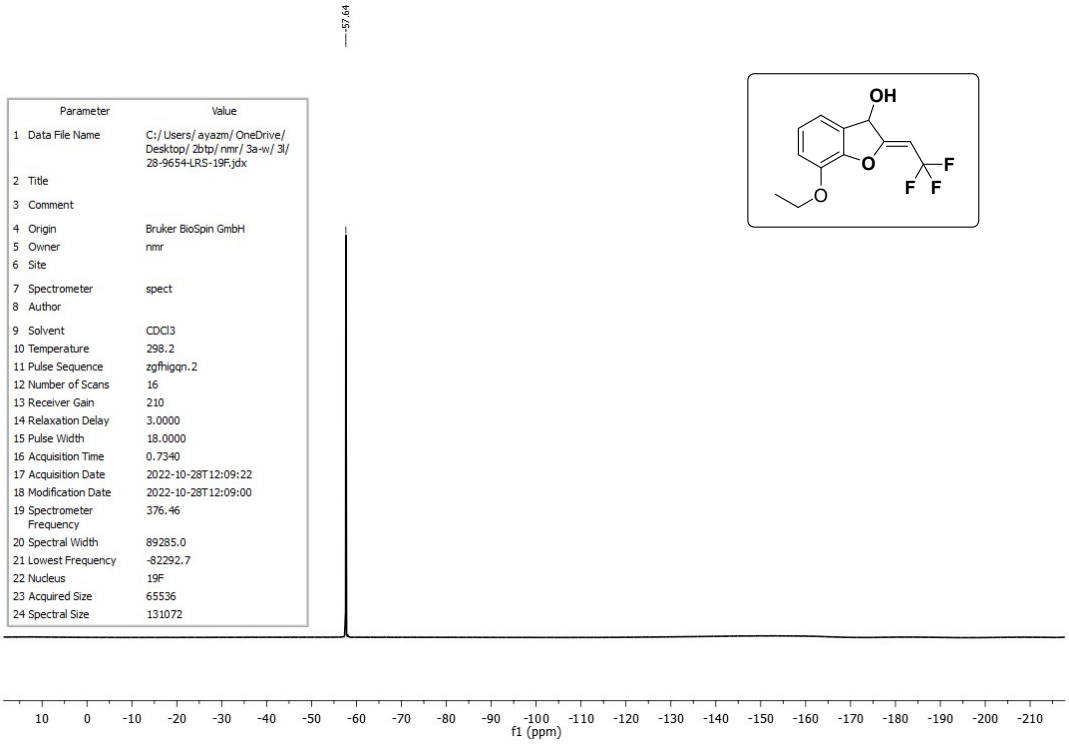
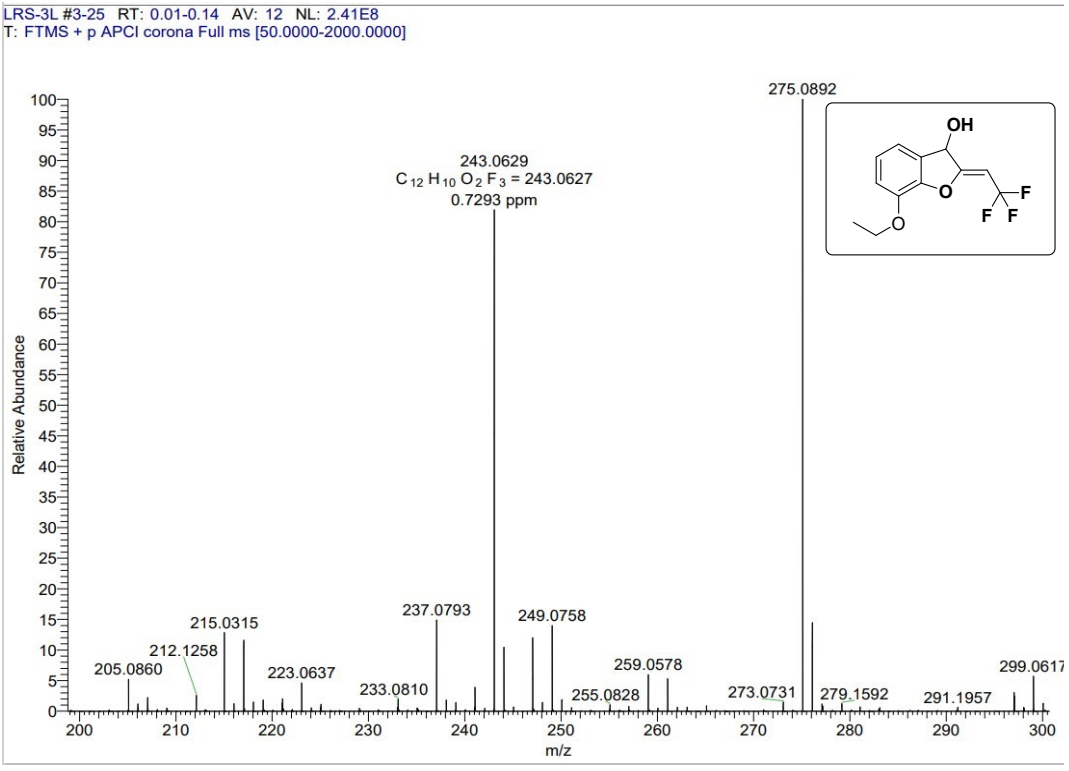
17 Acquisition Date	2022-09-09T00:42:31
18 Modification Date	2022-09-09T00:42:00
19 Spectrometer Frequency	75.48
20 Spectral Width	18028.3
21 Lowest Frequency	-1465.6
22 Nucleus	13C
23 Acquired Size	9013
24 Spectral Size	32768

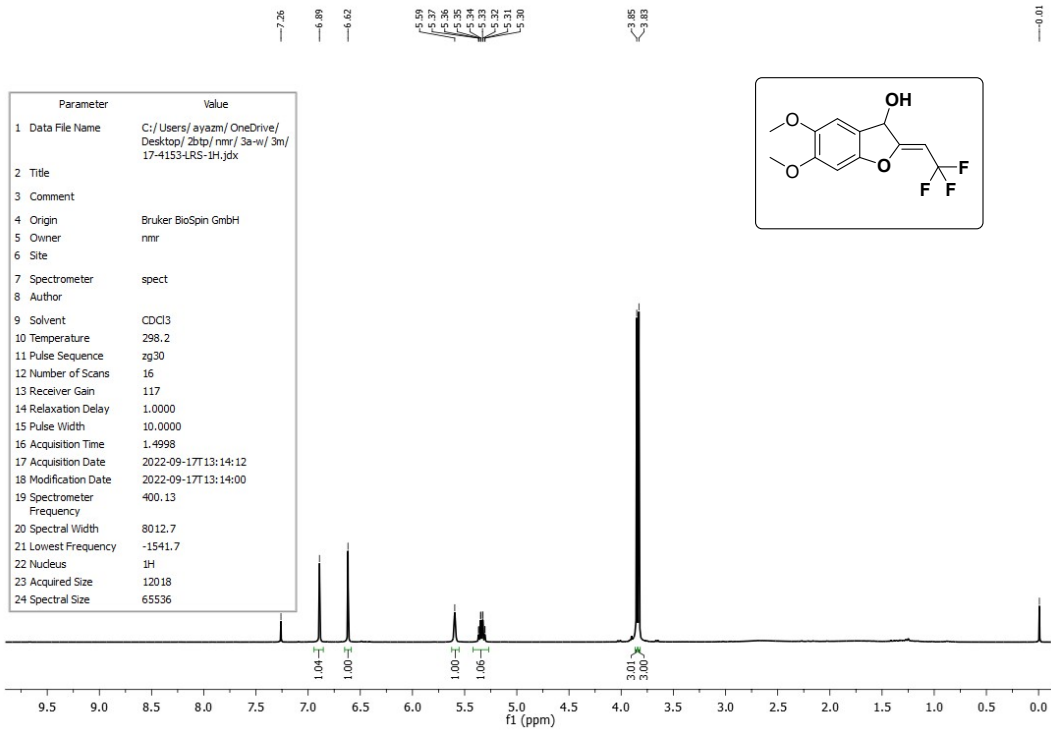
^{19}F NMR for 2e at 376 MHz



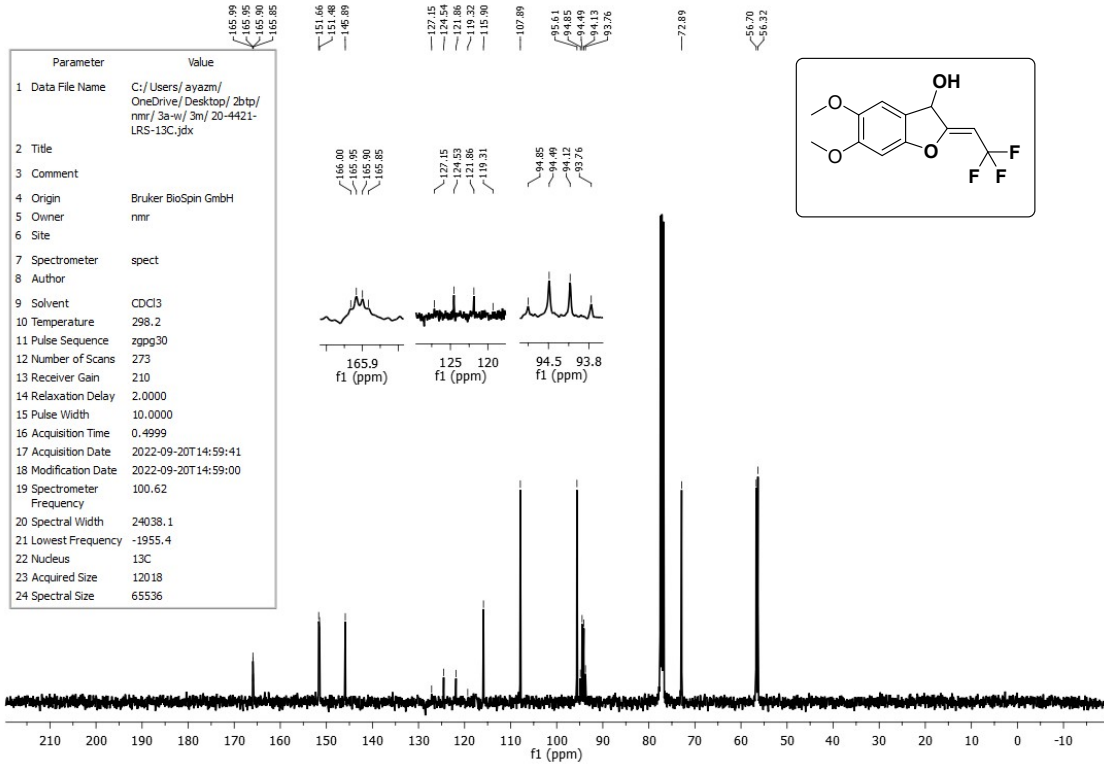
HRMS for 2e in APCI (+) MODE.



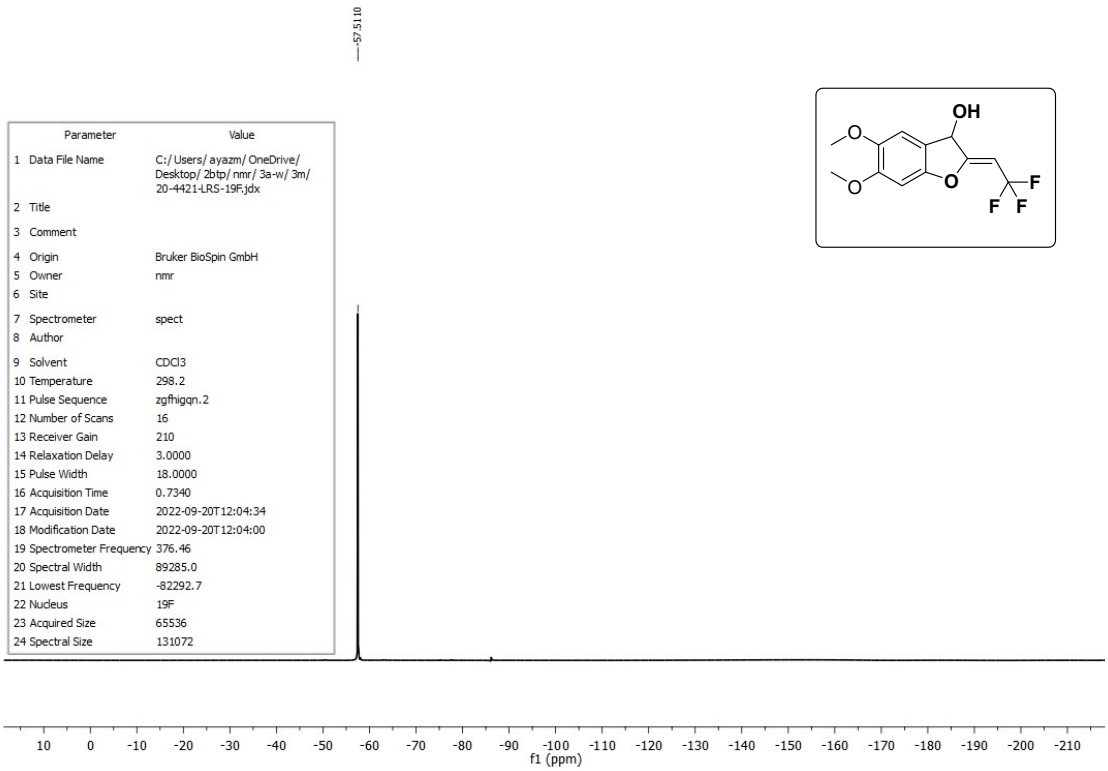
^{1}H NMR for 2f at 400 MHz



^{13}C NMR for 2f at 100 MHz



^{19}F NMR for 2f at 376 MHz



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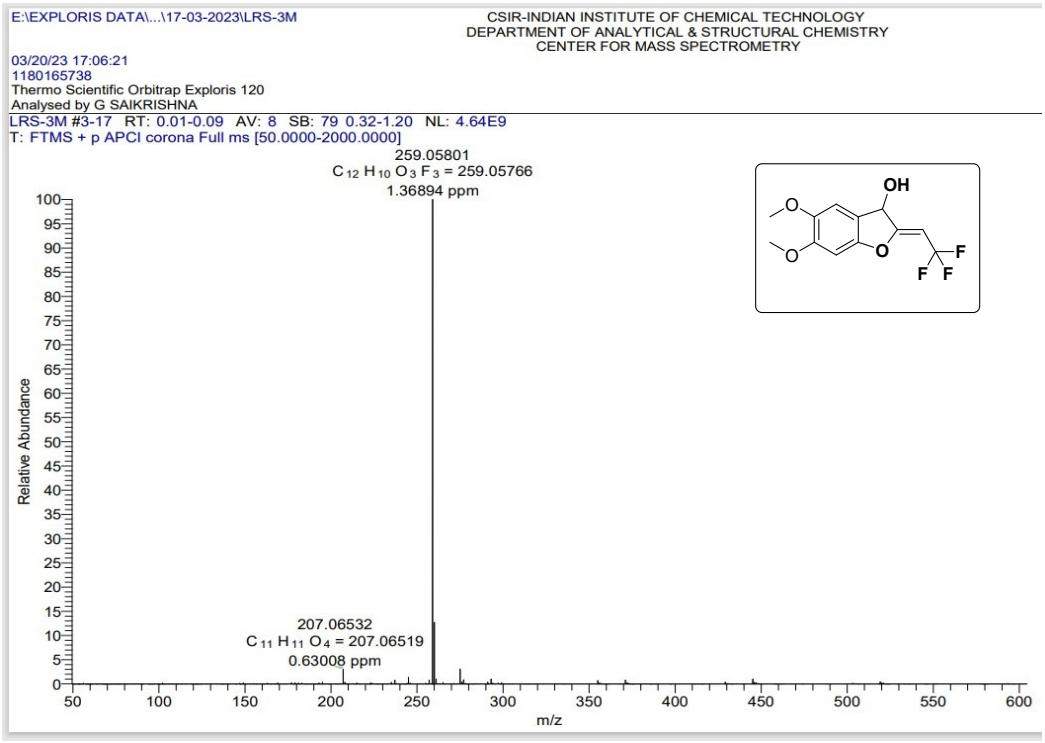
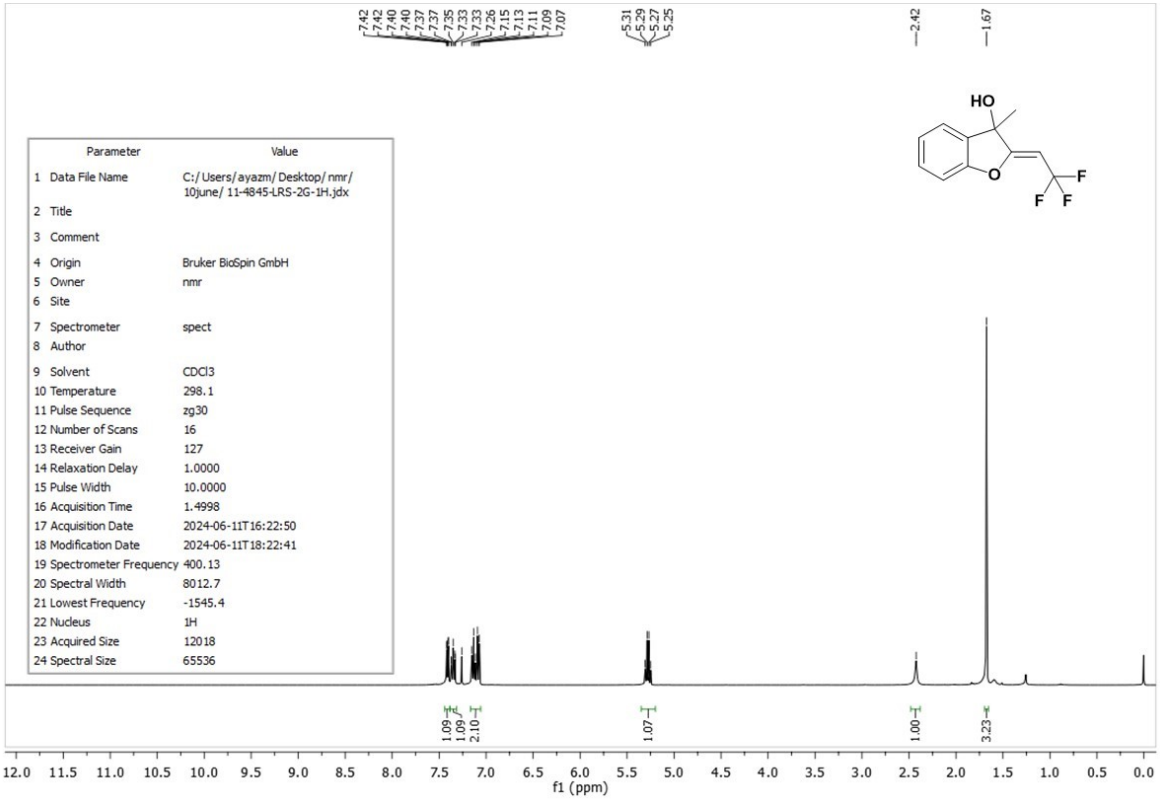
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Spectrometer	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.2
11 Pulse Sequence	zgfhigqn.2
12 Number of Scans	16
13 Receiver Gain	210
14 Relaxation Delay	3.0000
15 Pulse Width	18.0000
16 Acquisition Time	0.7340
17 Acquisition Date	2022-09-20T12:04:34
18 Modification Date	2022-09-20T12:04:00
19 Spectrometer Frequency	376.46
20 Spectral Width	89285.0
21 Lowest Frequency	-82292.7
22 Nucleus	19F
23 Acquired Size	65536
24 Spectral Size	131072

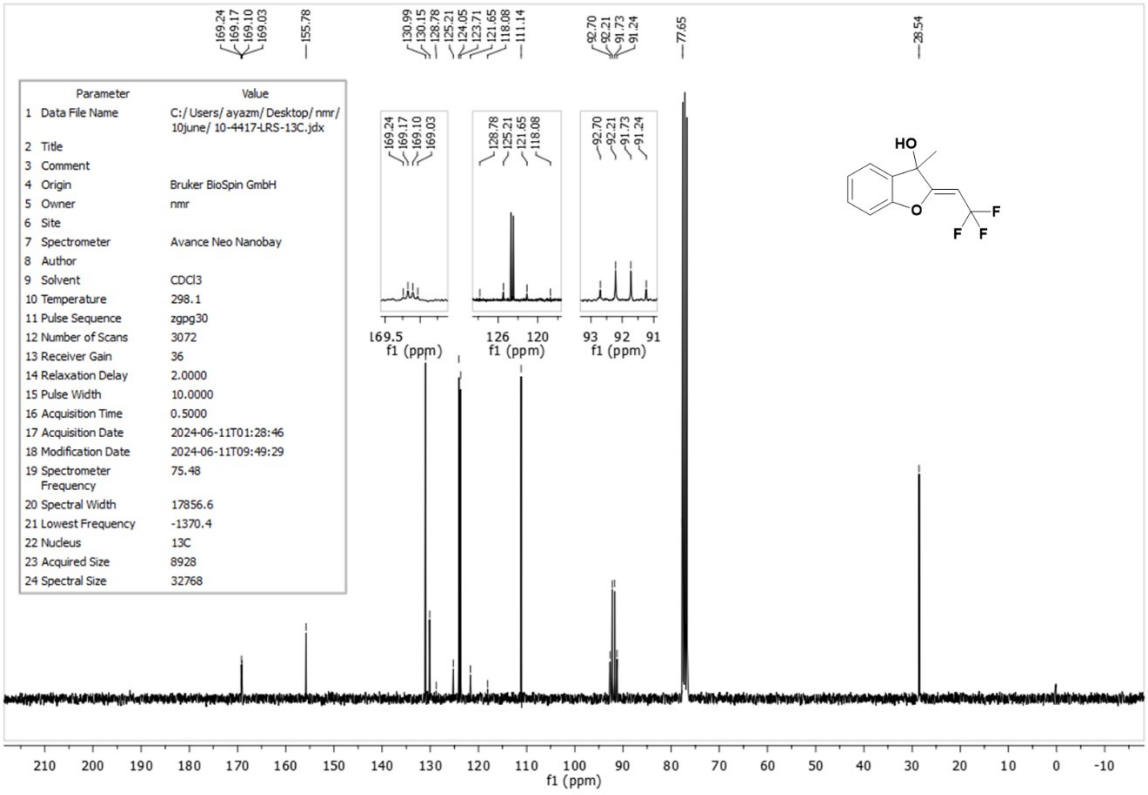
HR MS for 2f in APCI (+) MODE.



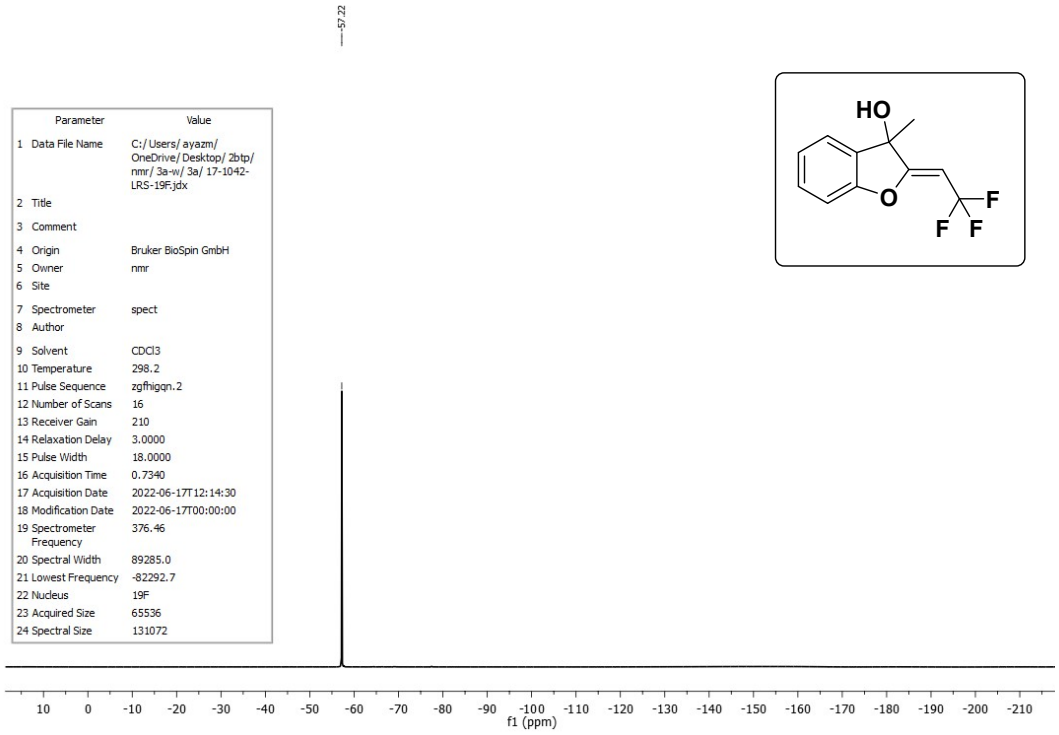
^{1}H NMR for 2g at 400 MHz



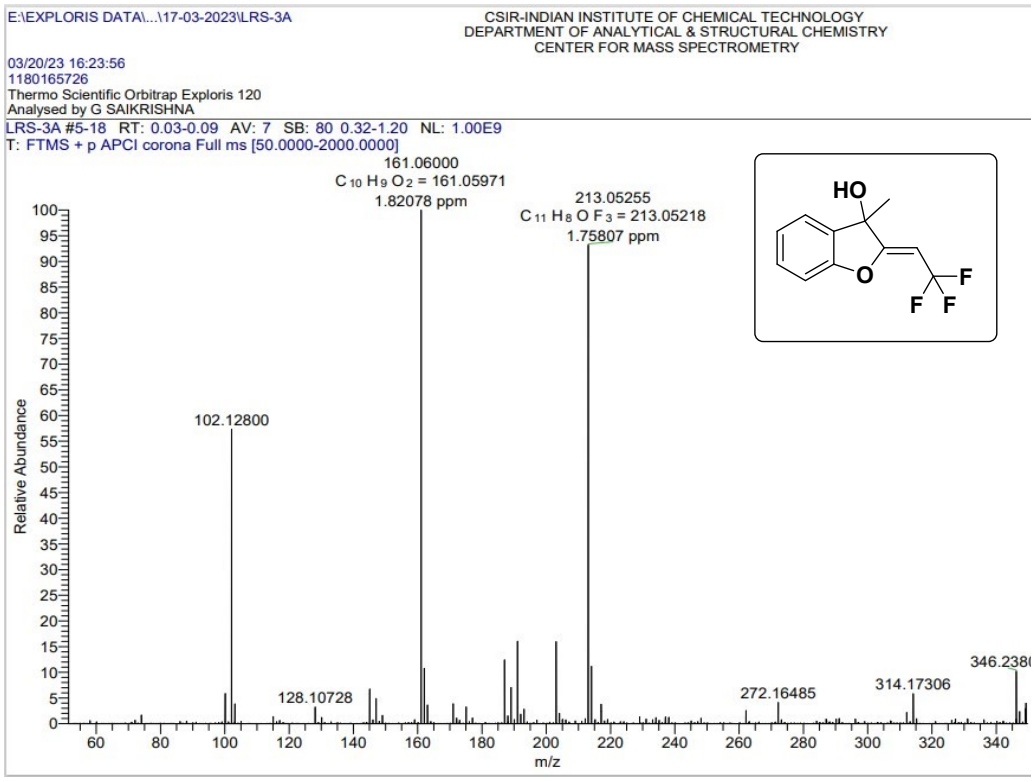
^{13}C NMR for 2g at 75 MHz



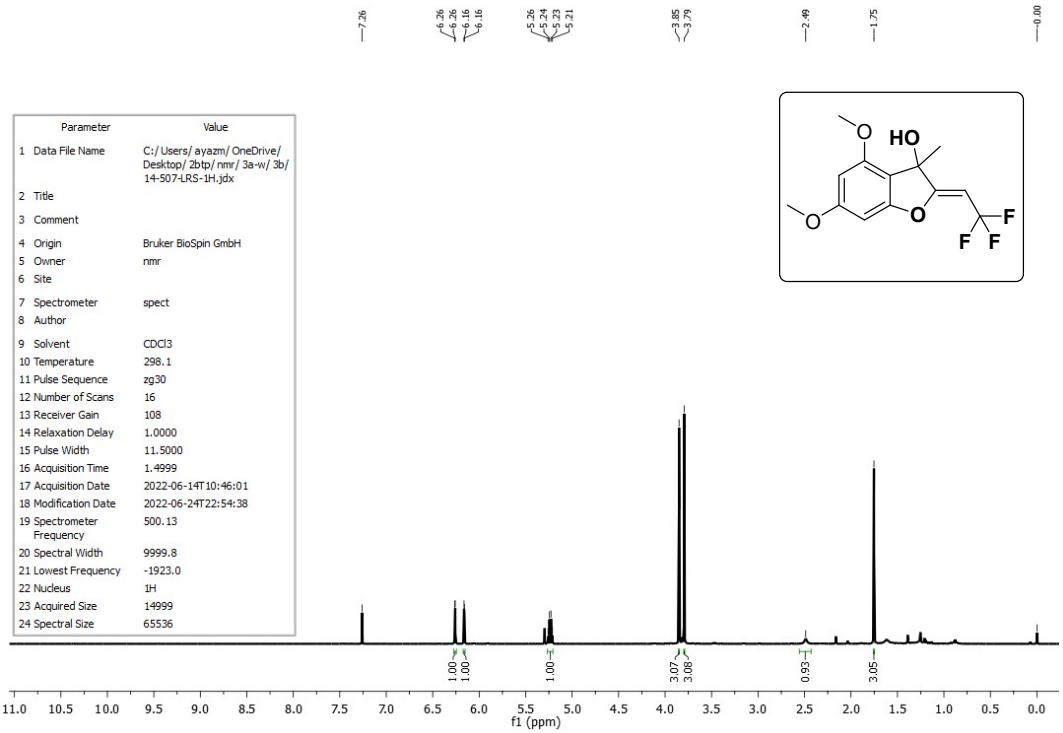
^{19}F NMR for 2g at 376 MHz



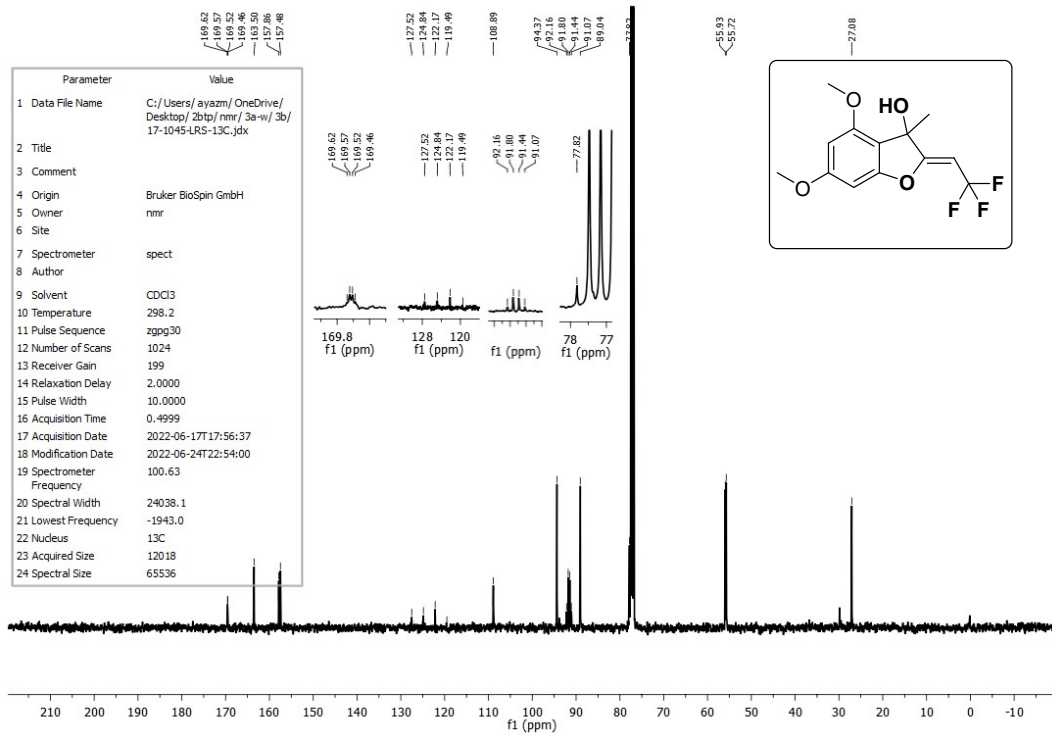
HRMS for 2g in APCI (+) MODE.



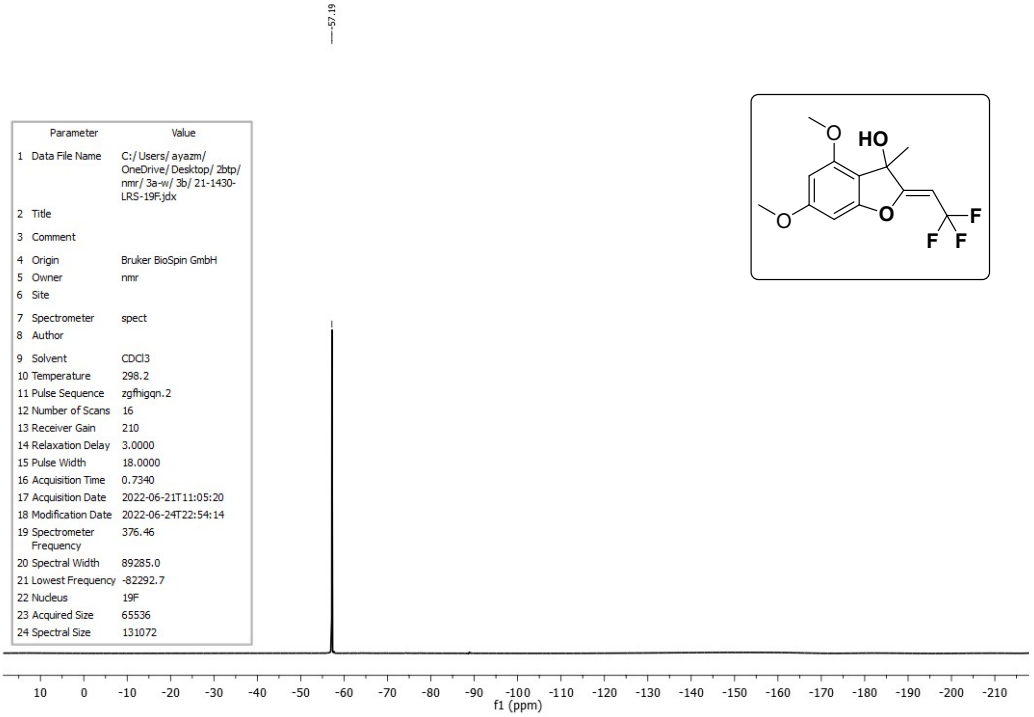
^{1}H NMR for 2h at 500 MHz



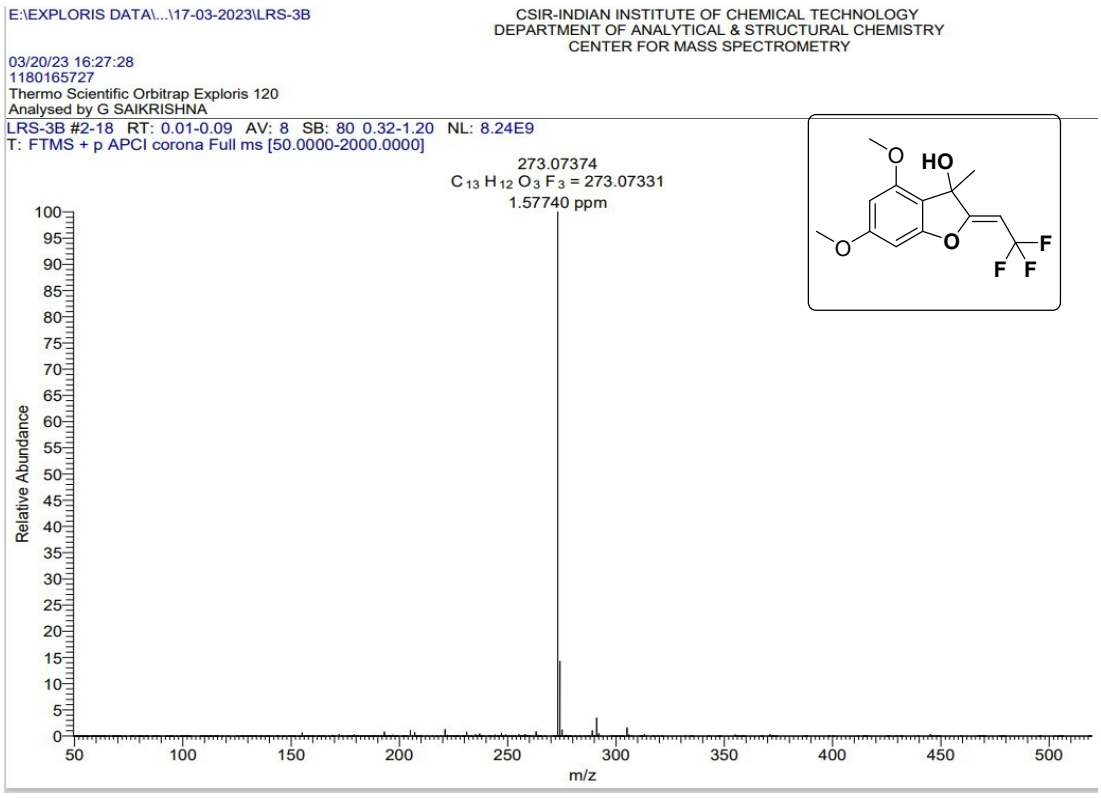
^{13}C NMR for 2h at 100 MHz



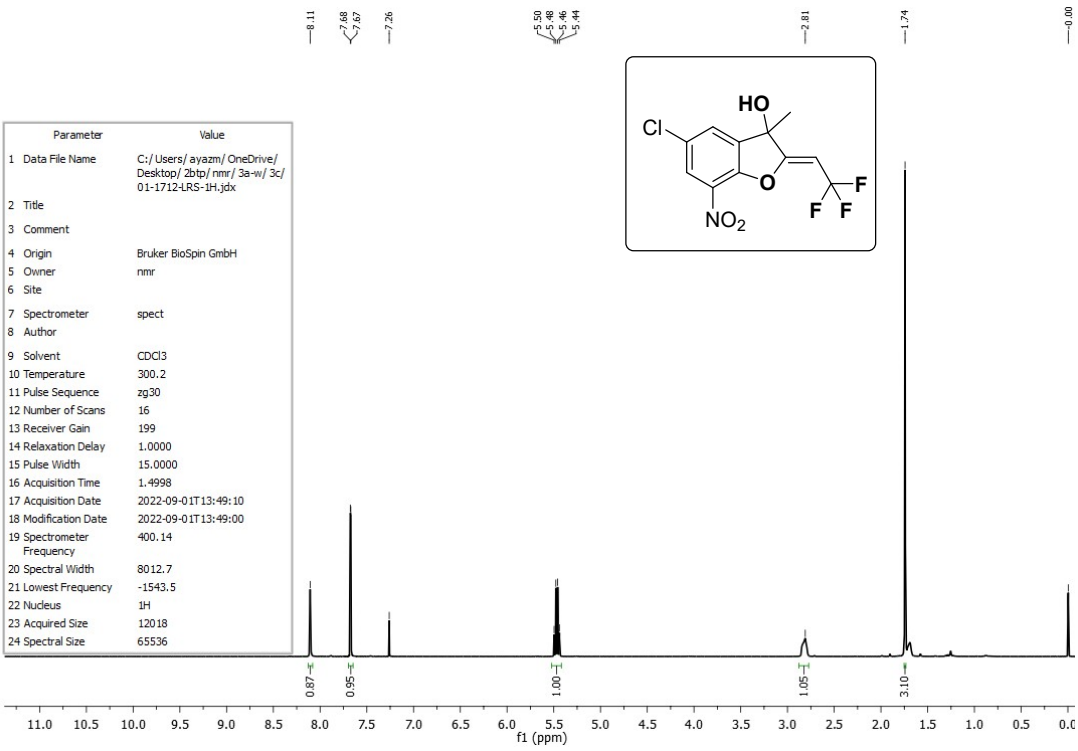
^{19}F NMR for 2h at 376 MHz



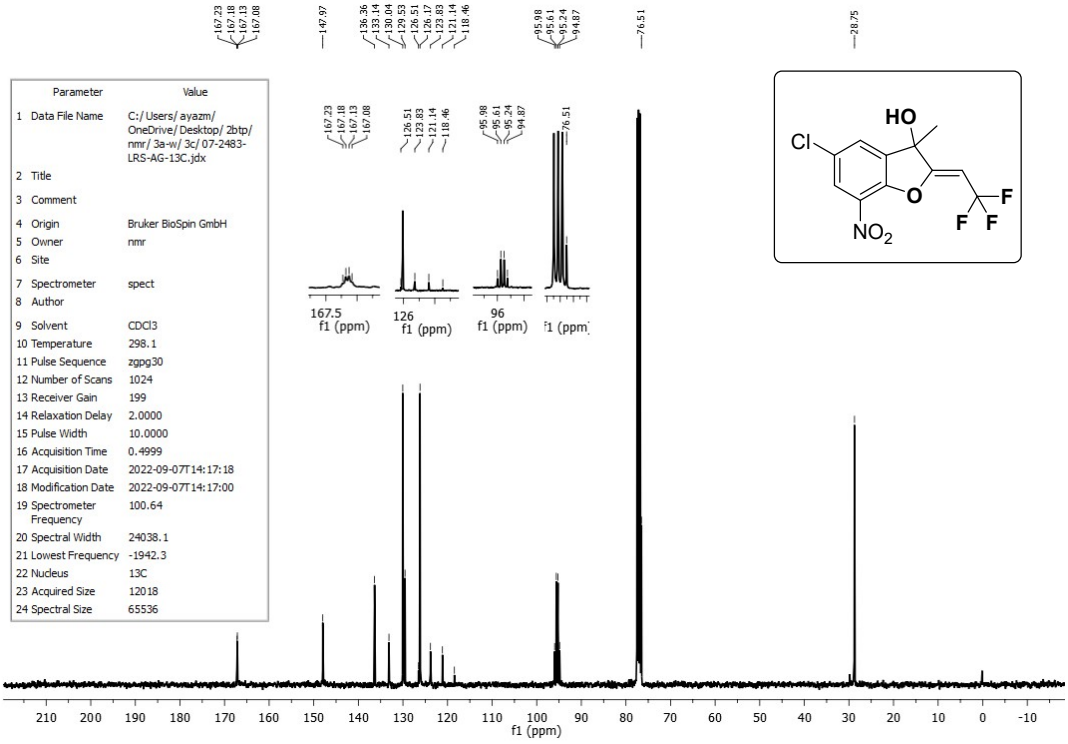
HRMS for 2h in APCI (+) MODE.



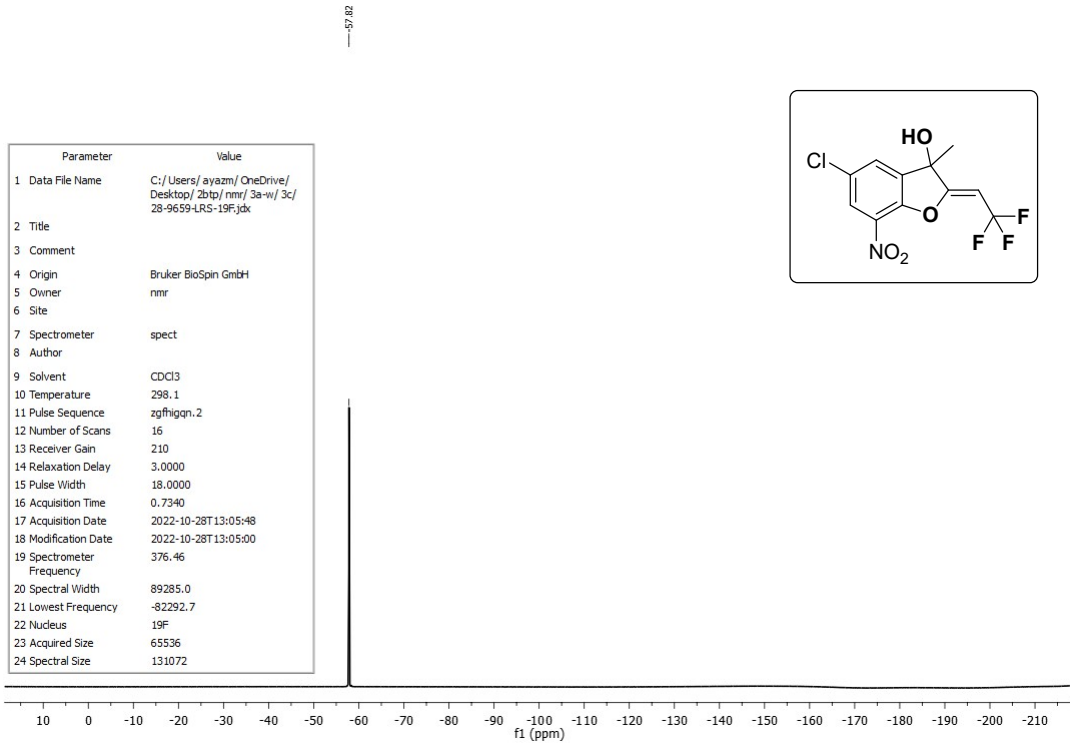
^{1}H NMR for 2i at 400 MHz



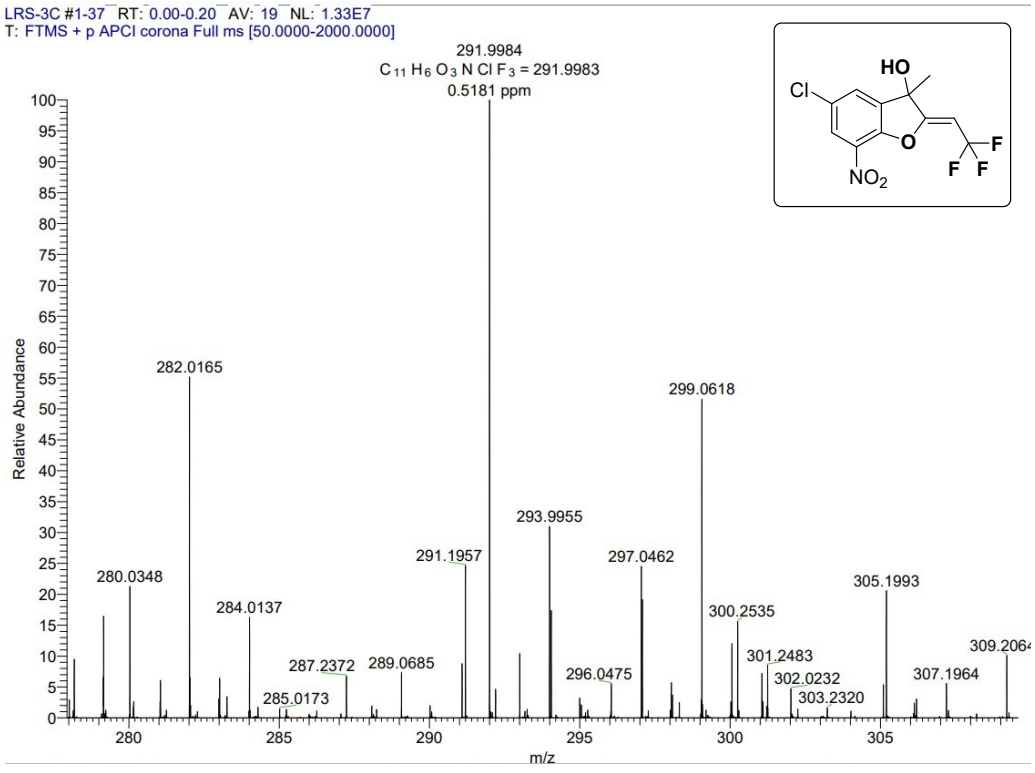
^{13}C NMR for 2i at 100 MHz



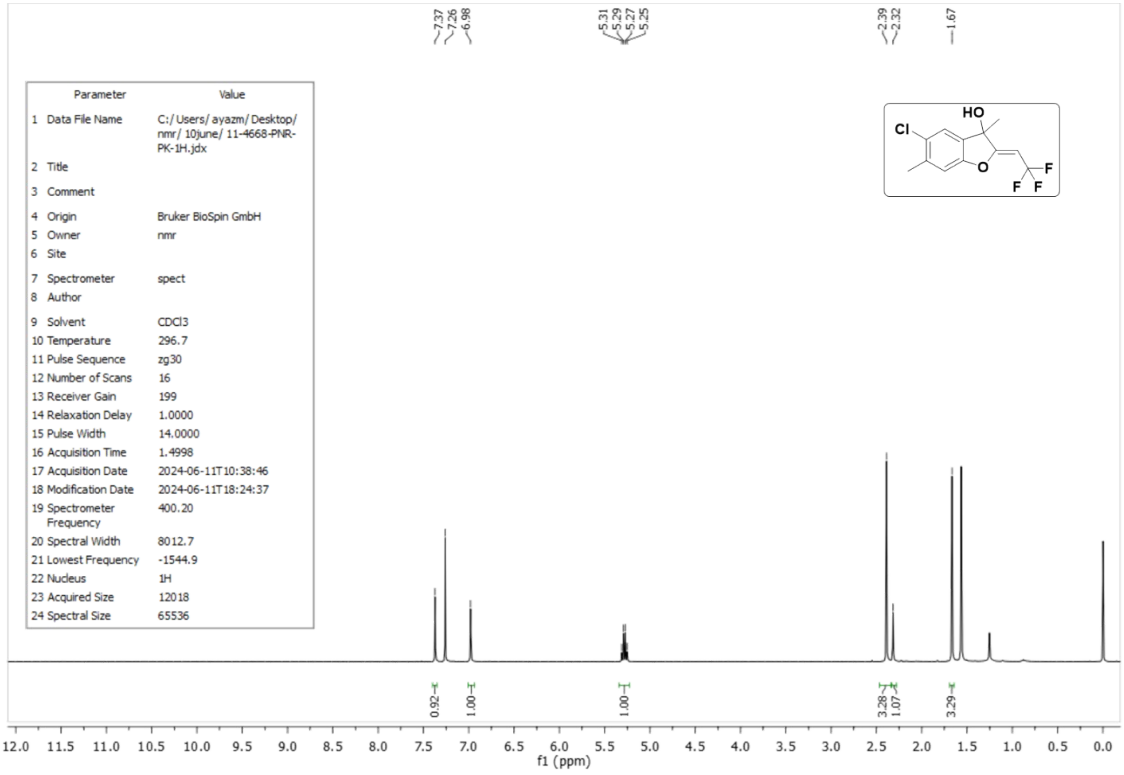
^{19}F NMR for 2i at 376 MHz



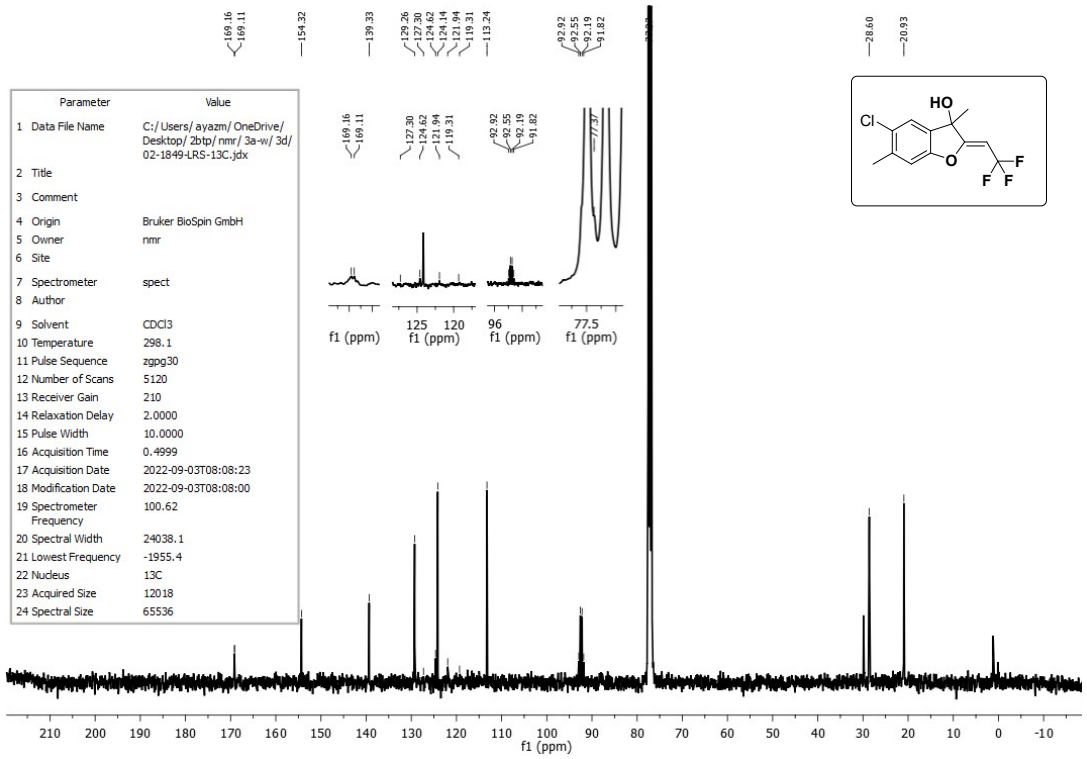
HRMS for 2i in APCI (+) MODE.



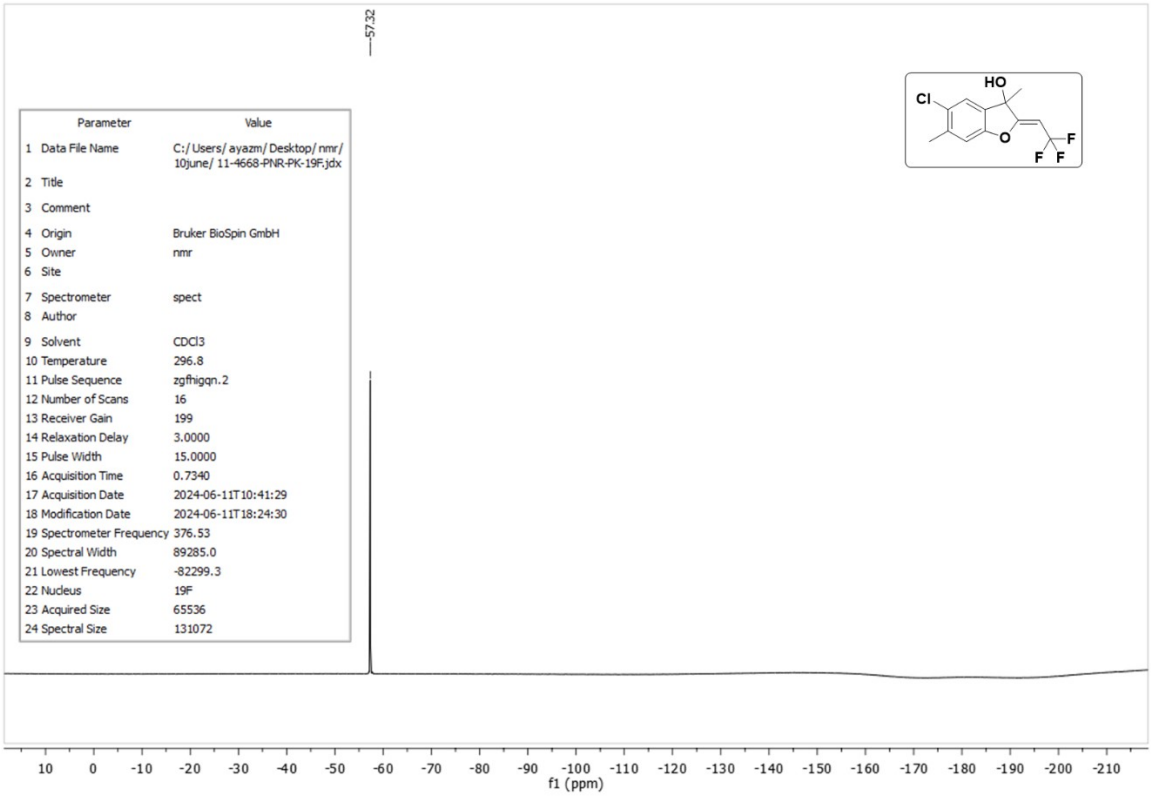
^{1}H NMR for 2j at 400 MHz



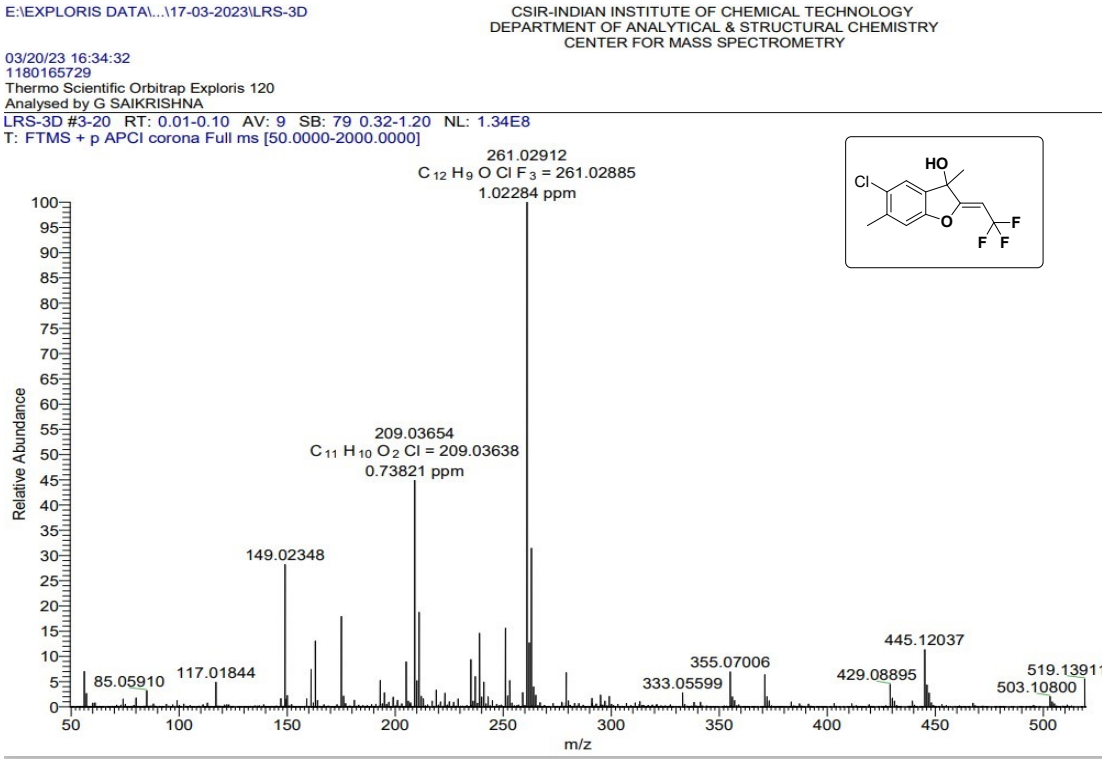
^{13}C NMR for 2j at 100 MHz



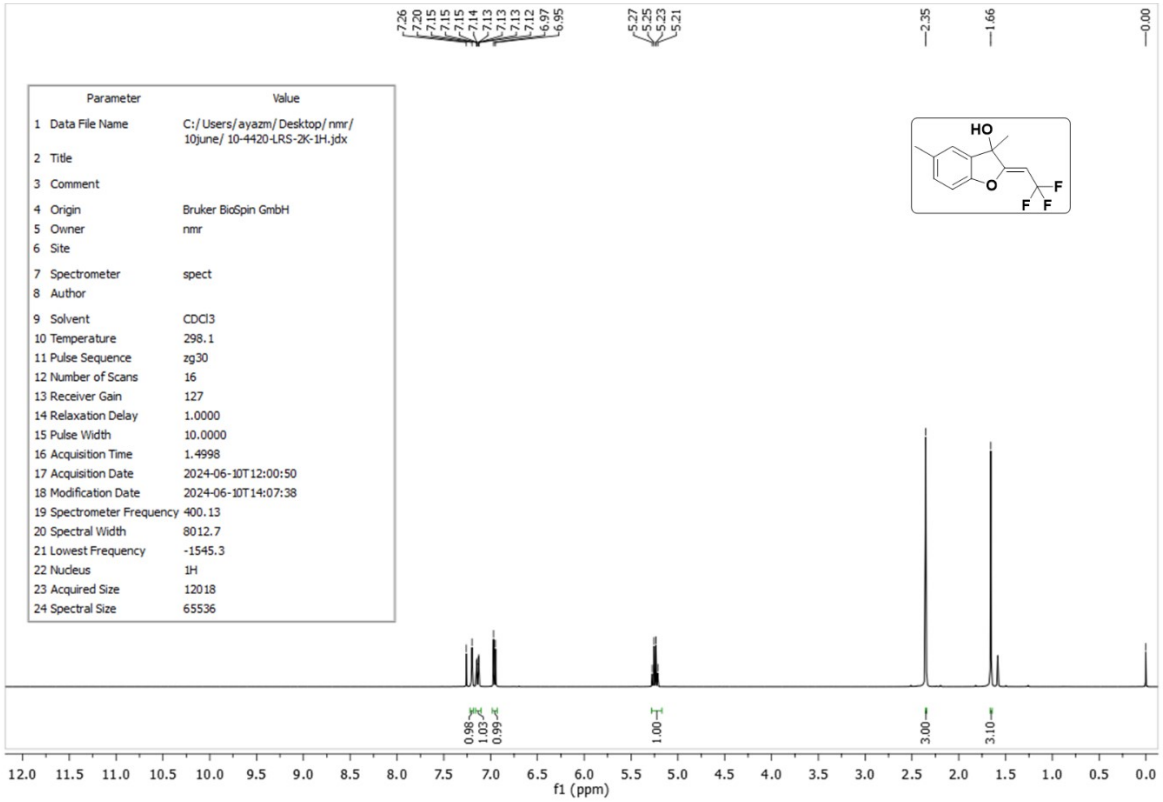
^{19}F NMR for 2j at 376 MHz



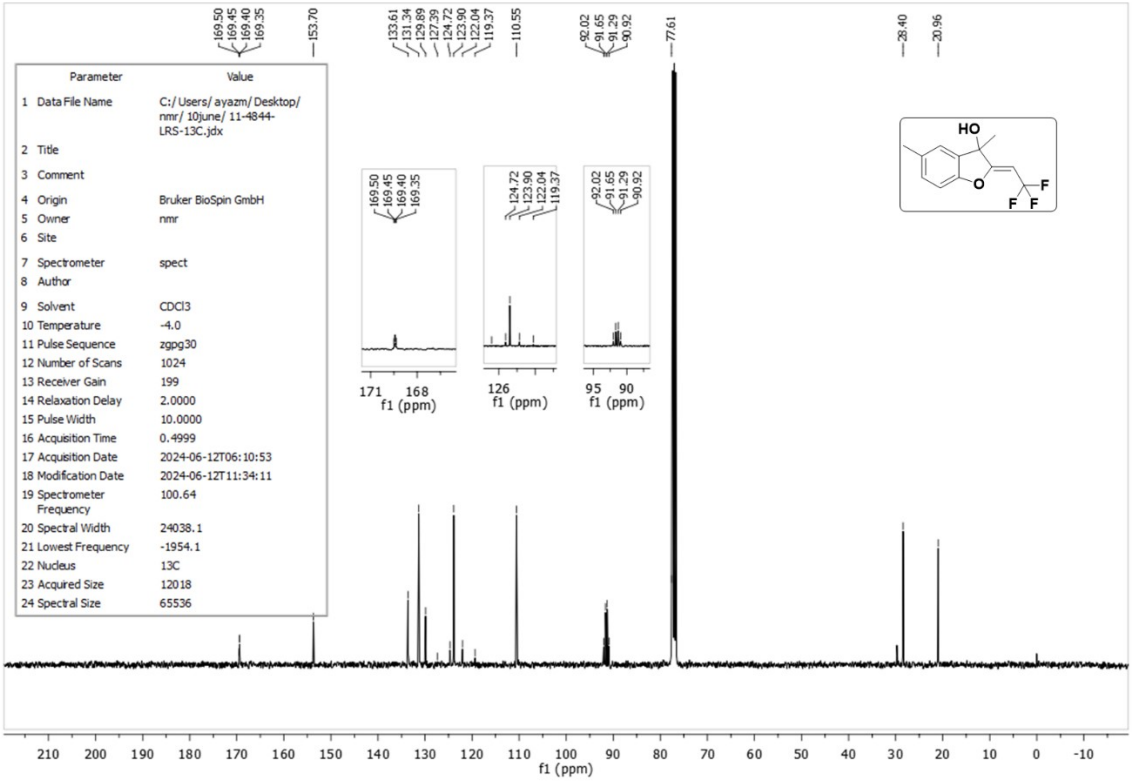
HRMS for 2j in APCI (+) MODE.



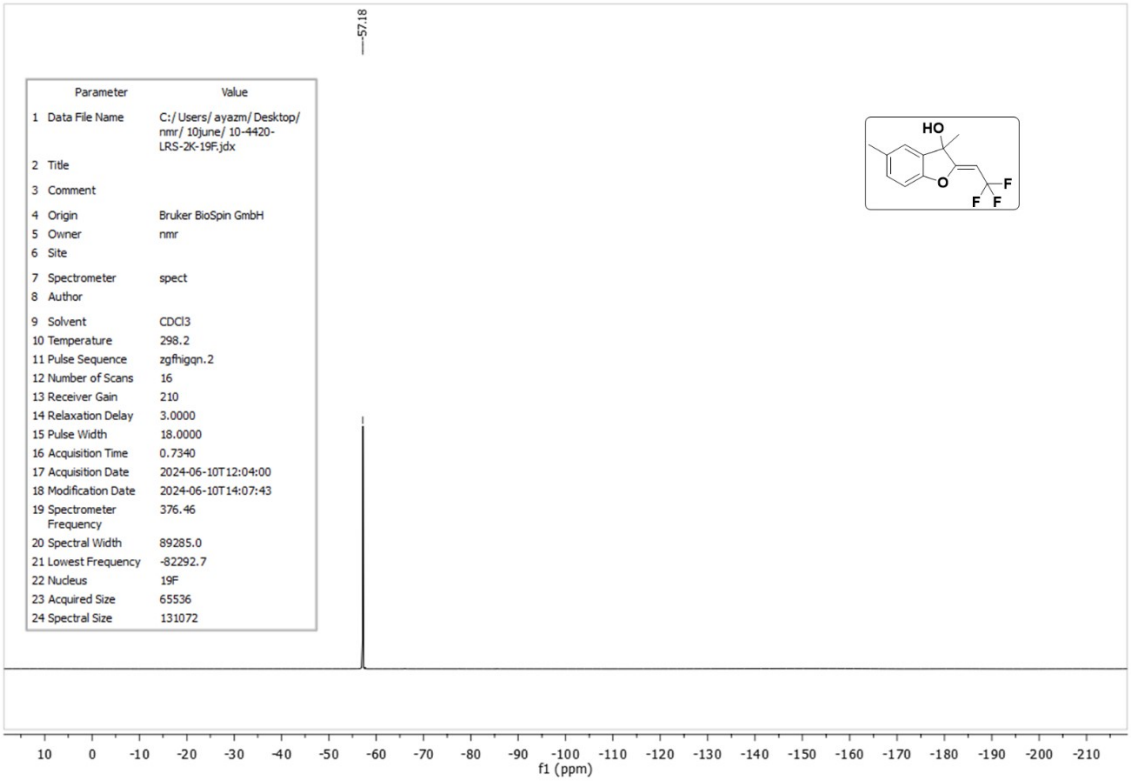
^{1}H NMR for 2k at 400 MHz



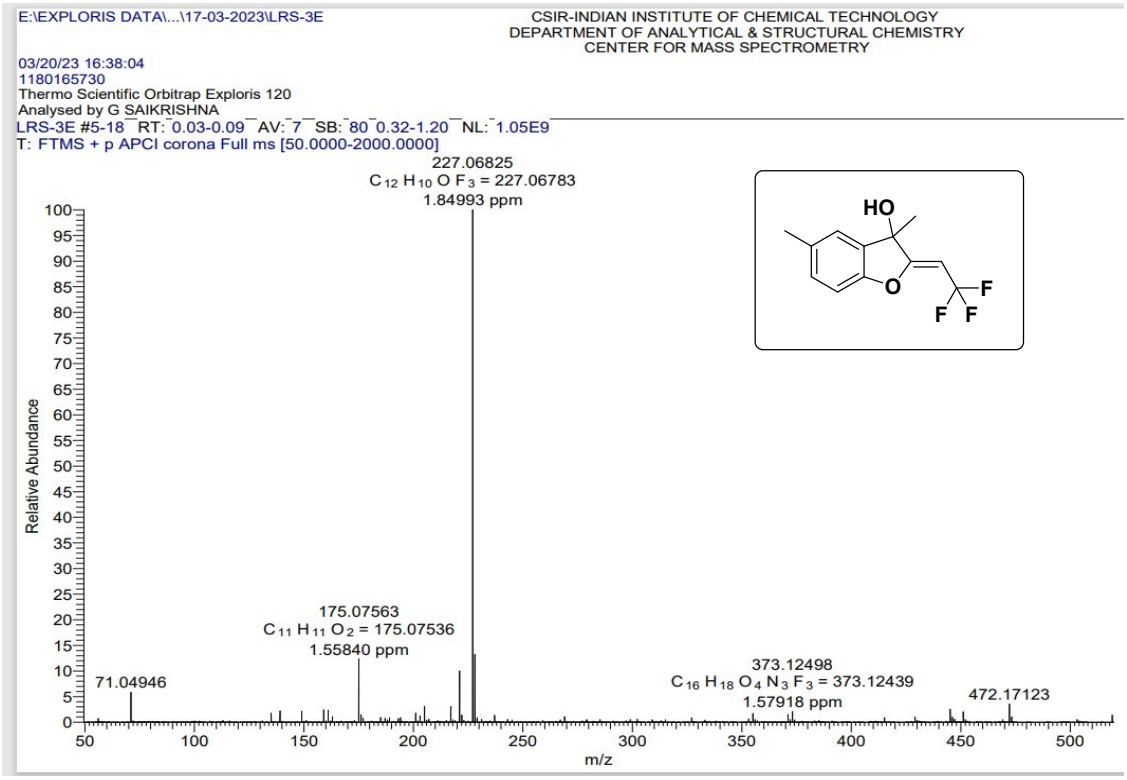
^{13}C NMR for 2k at 100 MHz



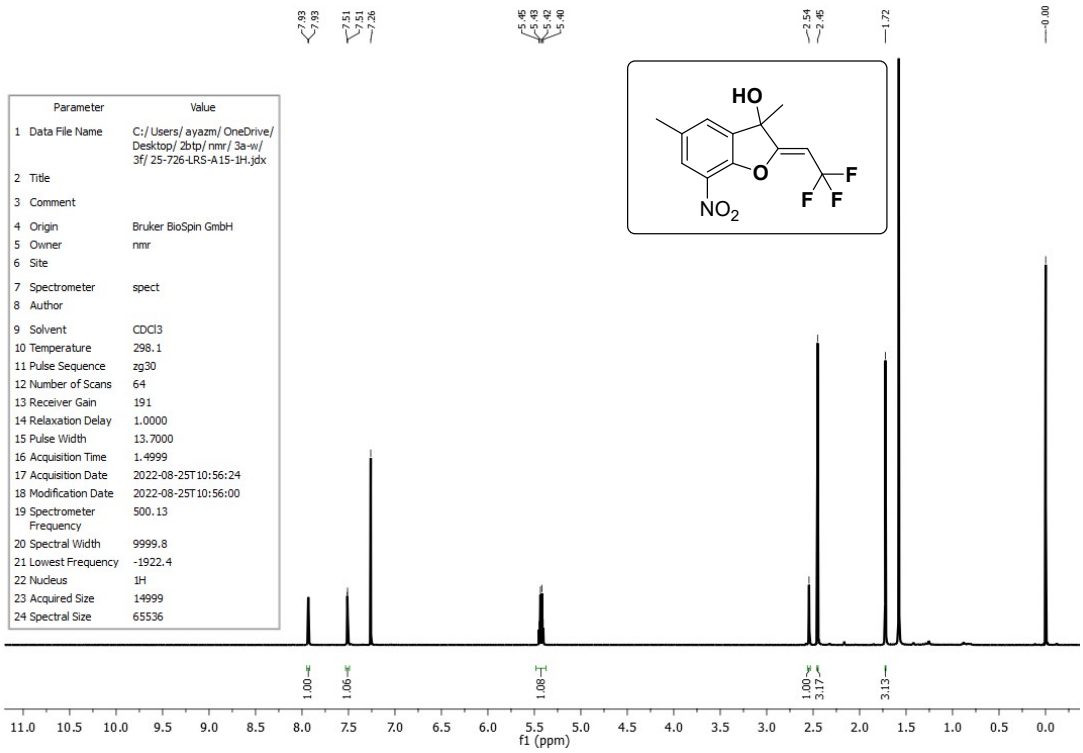
^{19}F NMR for 2k at 376 MHz



HRMS for 2k in APCI (+) MODE.



^{1}H NMR for 2l at 500 MHz



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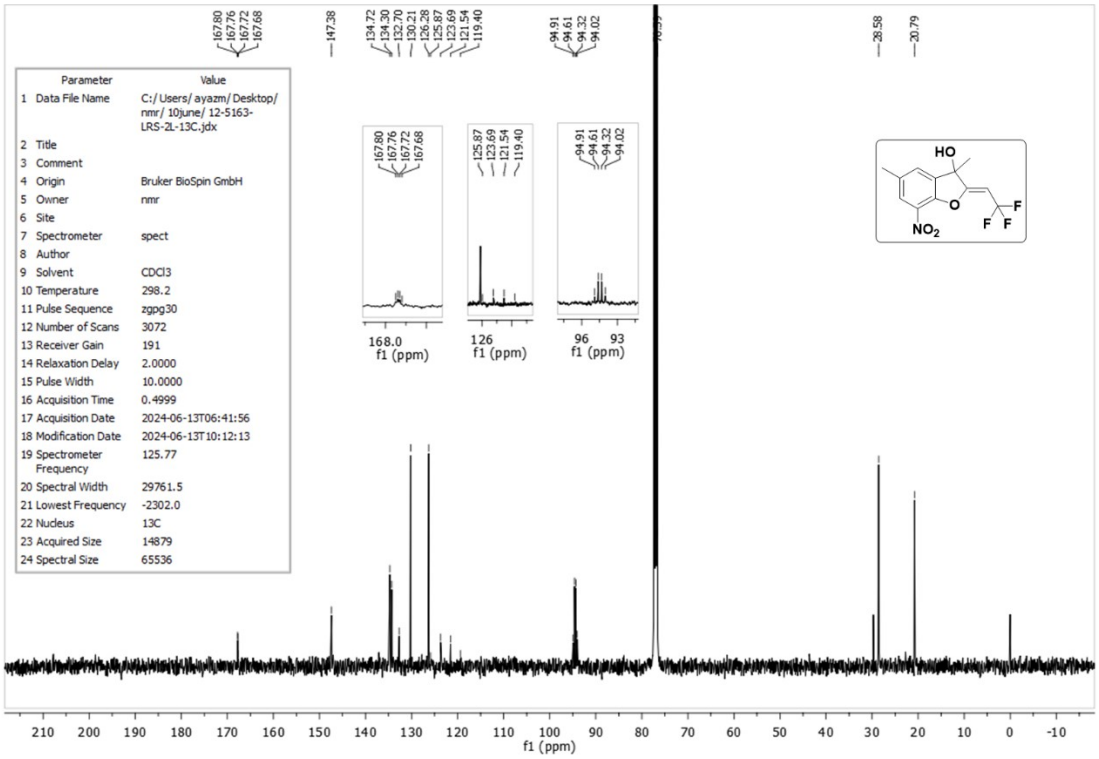
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Spectrometer	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.1
11 Pulse Sequence	zg30
12 Number of Scans	64
13 Receiver Gain	191
14 Relaxation Delay	1.0000
15 Pulse Width	13.7000
16 Acquisition Time	1.4999
17 Acquisition Date	2022-08-25T10:56:24
18 Modification Date	2022-08-25T10:56:00
19 Spectrometer Frequency	500.13
20 Spectral Width	9999.8
21 Lowest Frequency	-1922.4
22 Nucleus	1H
23 Acquired Size	14999
24 Spectral Size	65536

^{13}C NMR for 2l at 125 MHz



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2 Title	
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4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Spectrometer	spect
8 Author	
9 Solvent	CDCl3
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11 Pulse Sequence	zgpg30
12 Number of Scans	3072
13 Receiver Gain	191
14 Relaxation Delay	2.0000
15 Pulse Width	10.0000
16 Acquisition Time	0.4999
17 Acquisition Date	2024-06-13T06:41:56
18 Modification Date	2024-06-13T10:12:13
19 Spectrometer Frequency	125.77
20 Spectral Width	29761.5
21 Lowest Frequency	-2302.0
22 Nucleus	13C
23 Acquired Size	14879
24 Spectral Size	65536

^{19}F NMR for 2l at 376 MHz

	Parameter	Value
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5	Owner	nmr
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7	Spectrometer	spect
8	Author	
9	Solvent	CDCl3
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11	Pulse Sequence	zgfhigqn.2
12	Number of Scans	16
13	Receiver Gain	210
14	Relaxation Delay	3.0000
15	Pulse Width	18.0000
16	Acquisition Time	0.7340
17	Acquisition Date	2022-10-20T12:22:52
18	Modification Date	2022-10-28T17:43:52
19	Spectrometer Frequency	376.46
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21	Lowest Frequency	-82292.7
22	Nucleus	19F
23	Acquired Size	65536
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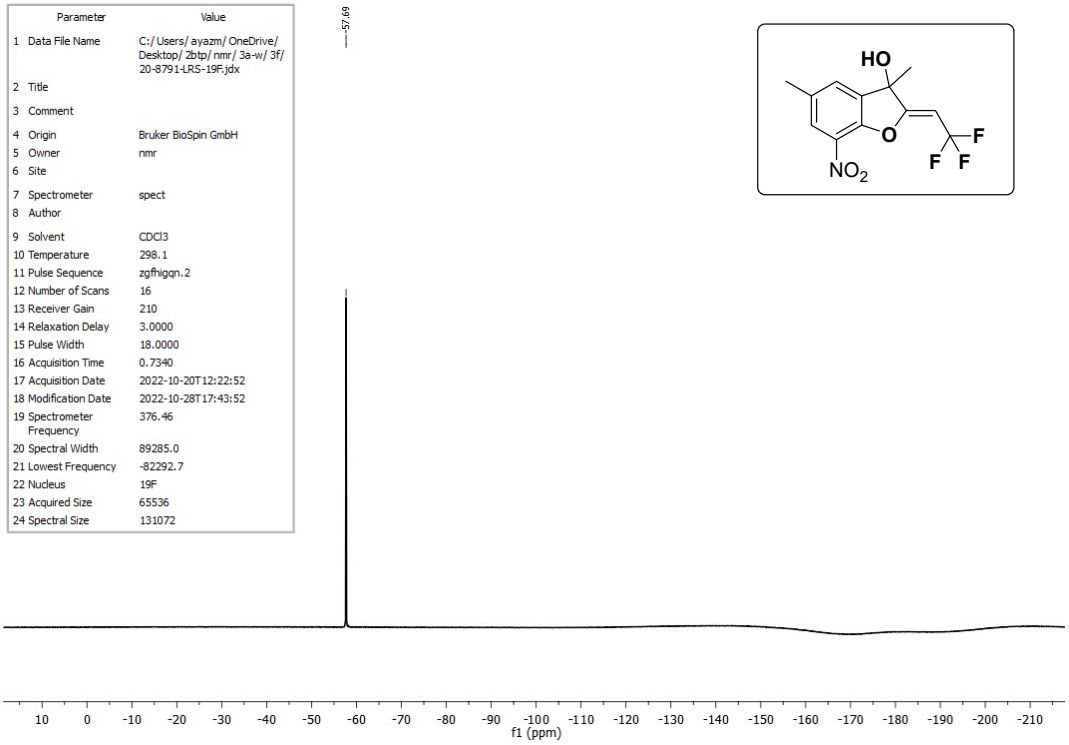
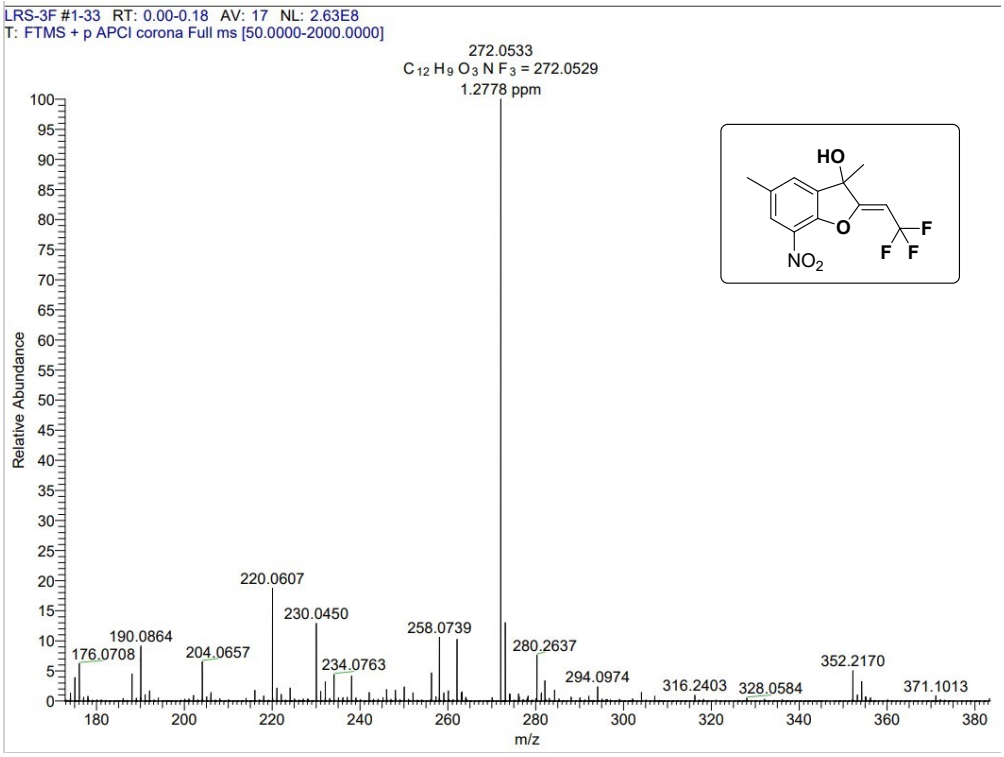
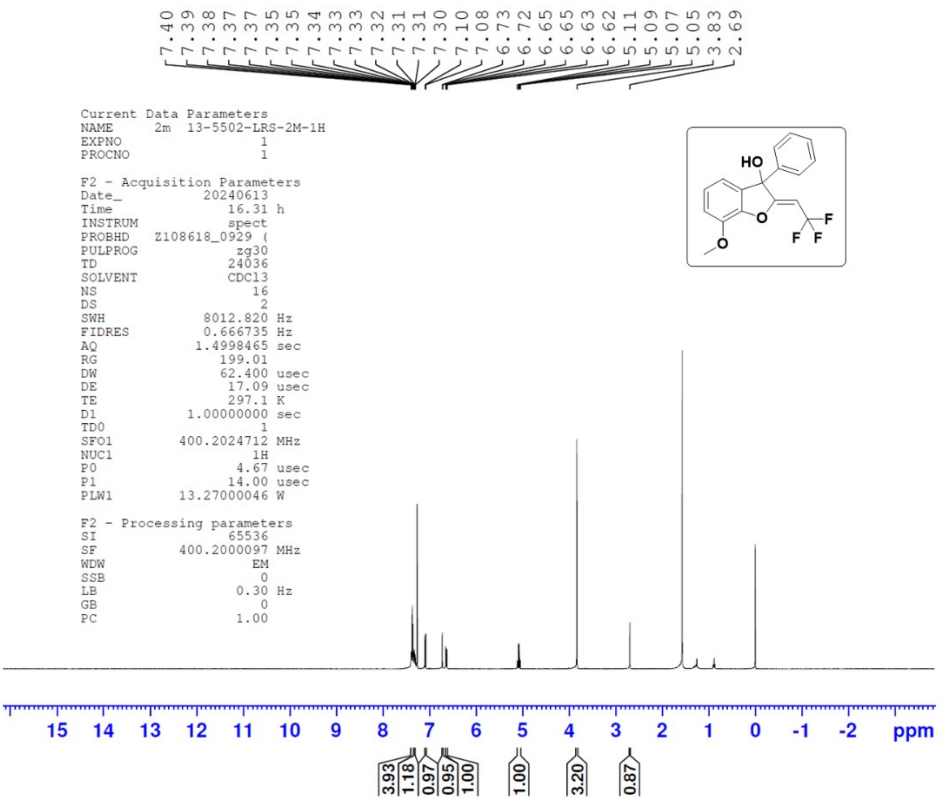


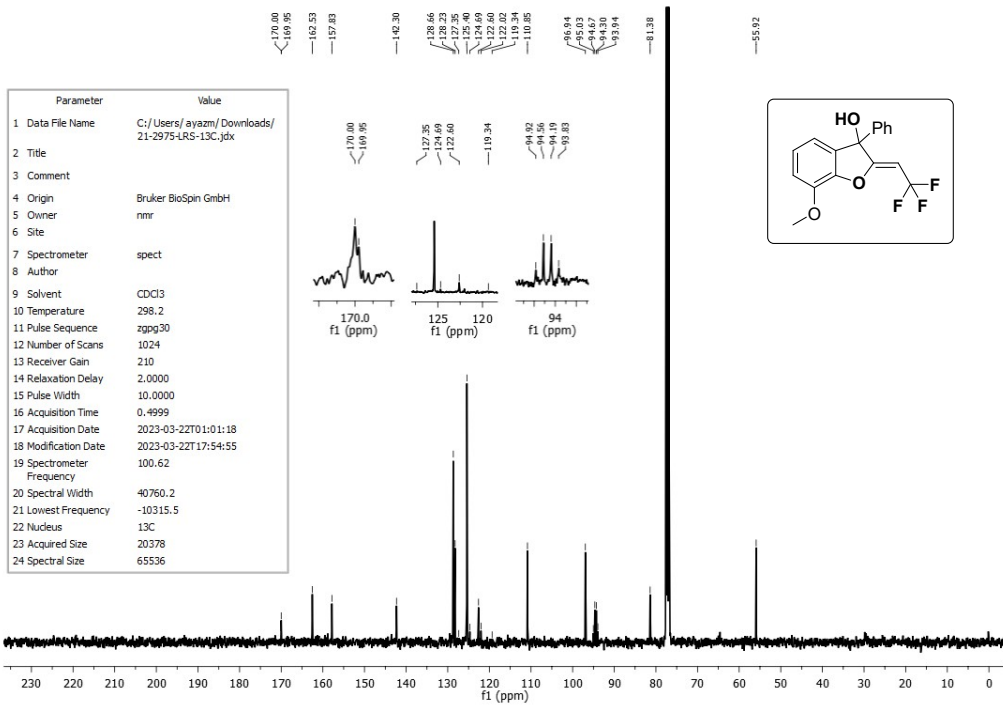
HRMS for 2l in APCI (+) MODE.



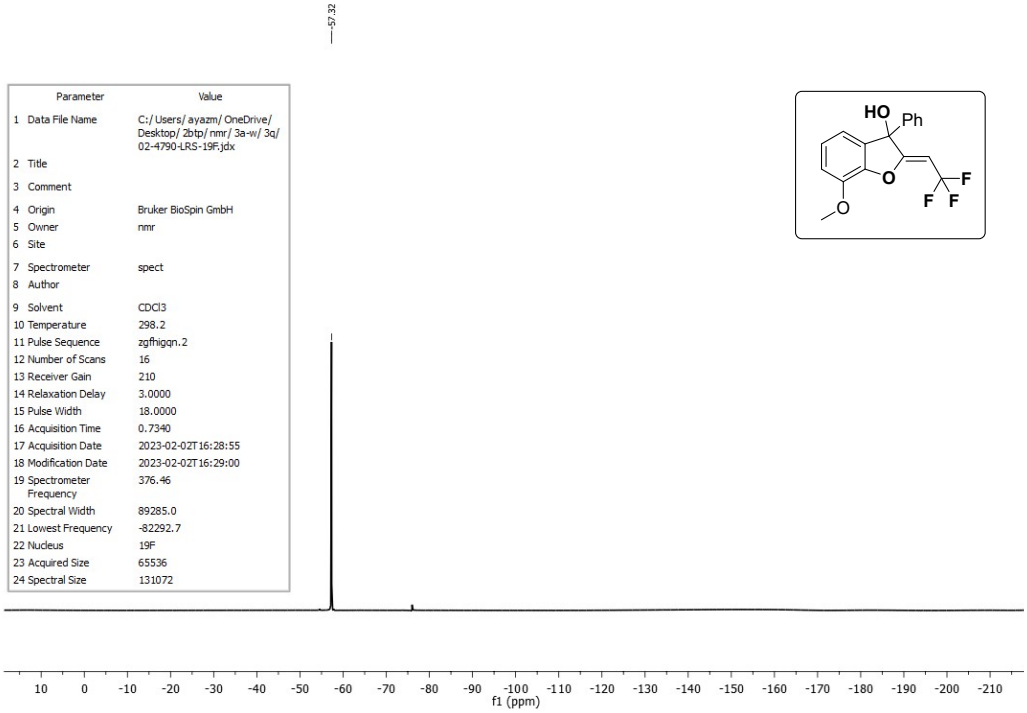
^{1}H NMR for 2m at 400 MHz



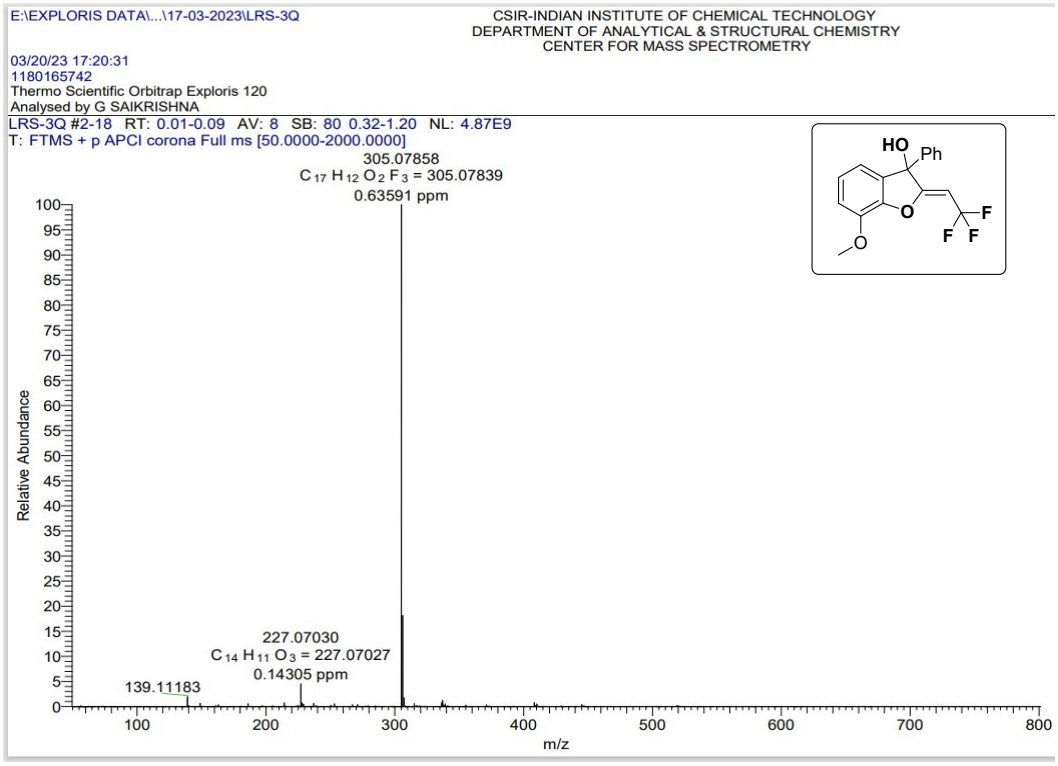
^{13}C NMR for 2m at 100 MHz



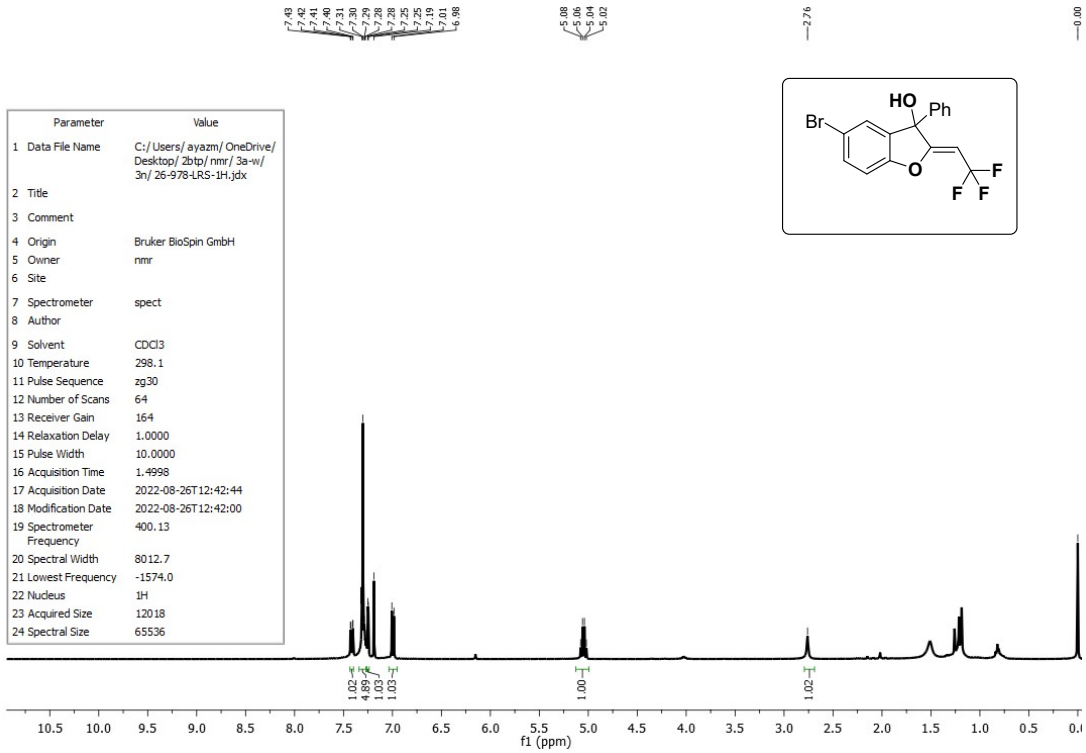
^{19}F NMR for 2m at 376 MHz



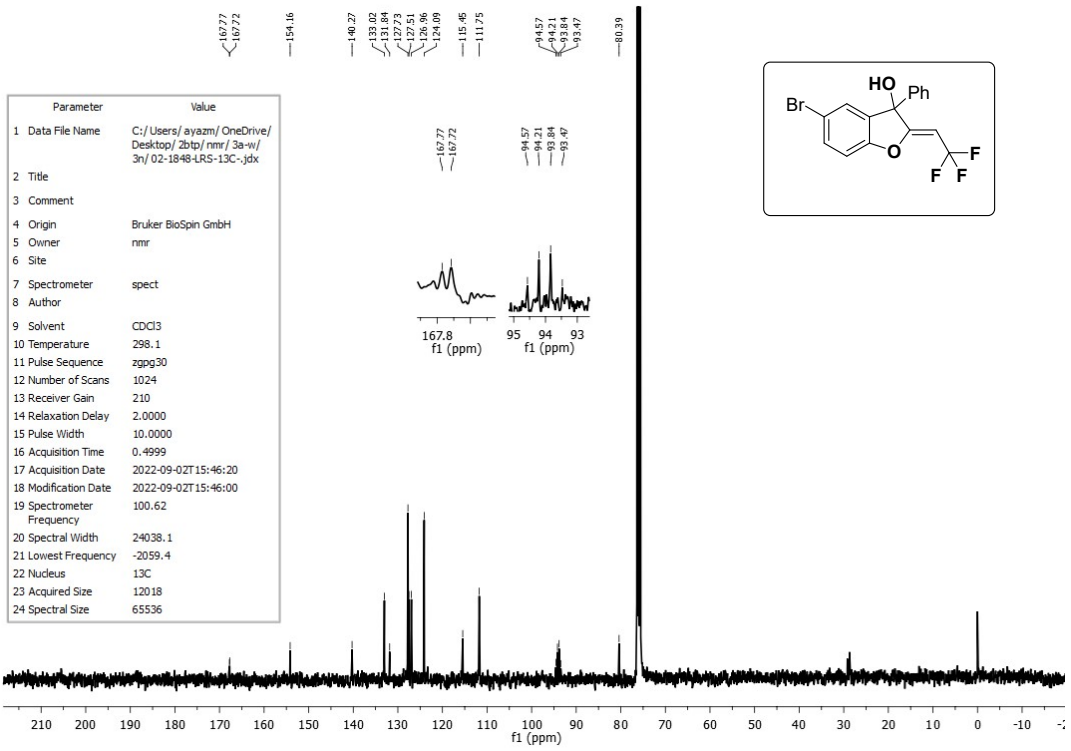
HRMS for 2m in APCI (+) MODE.



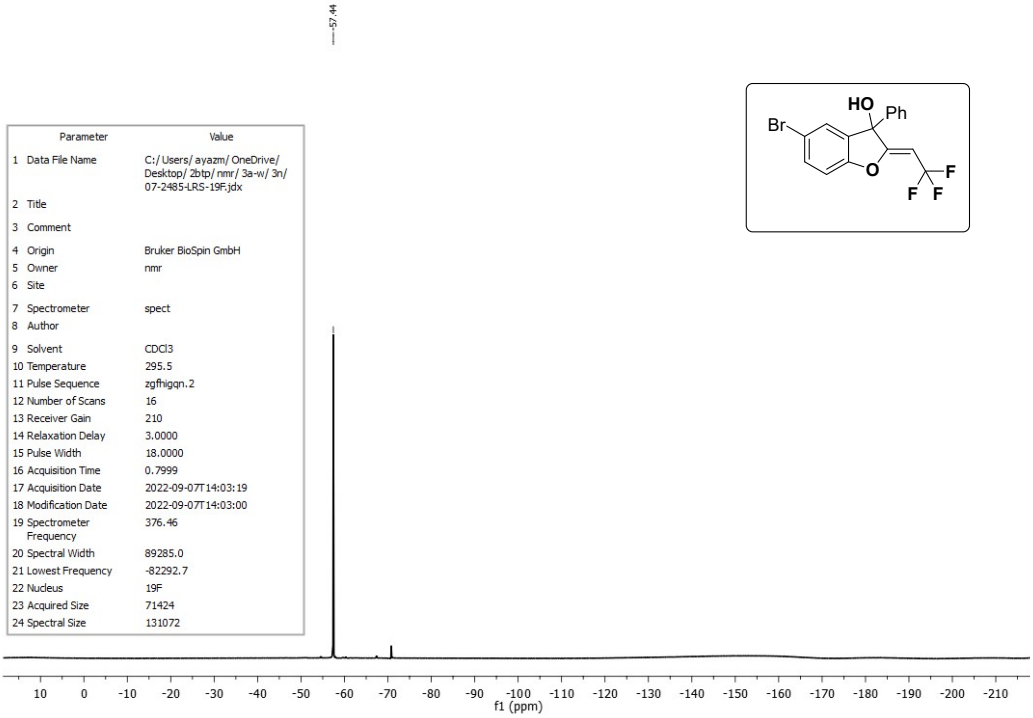
^{1}H NMR for 2n at 400 MHz



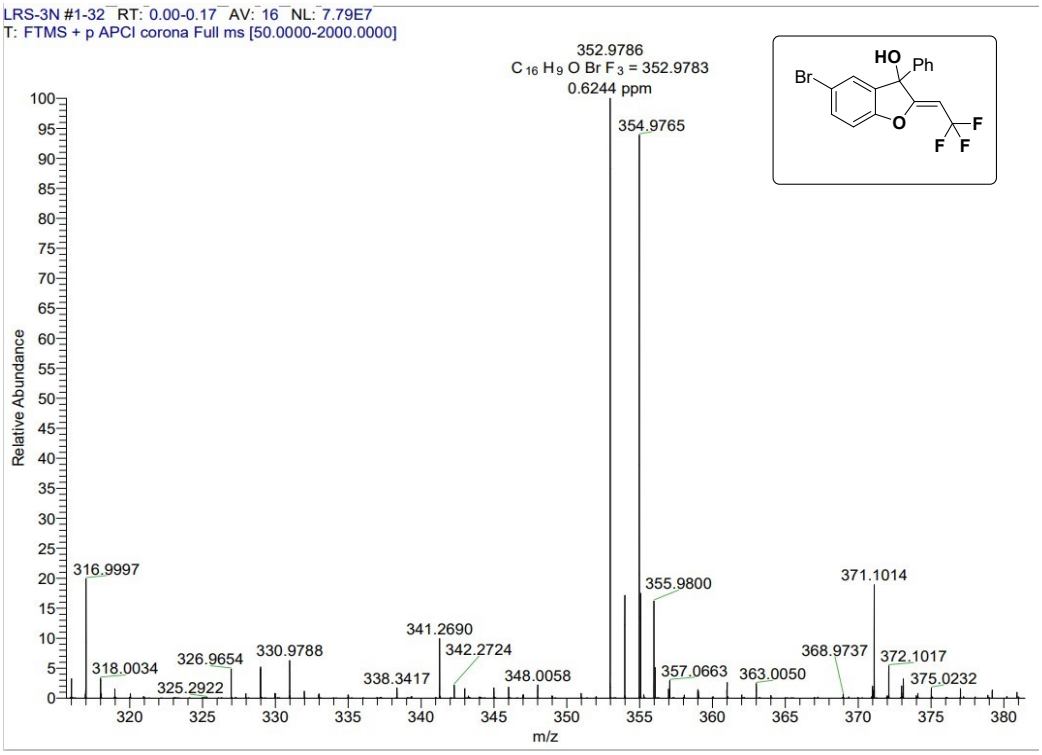
^{13}C NMR for 2n at 100 MHz



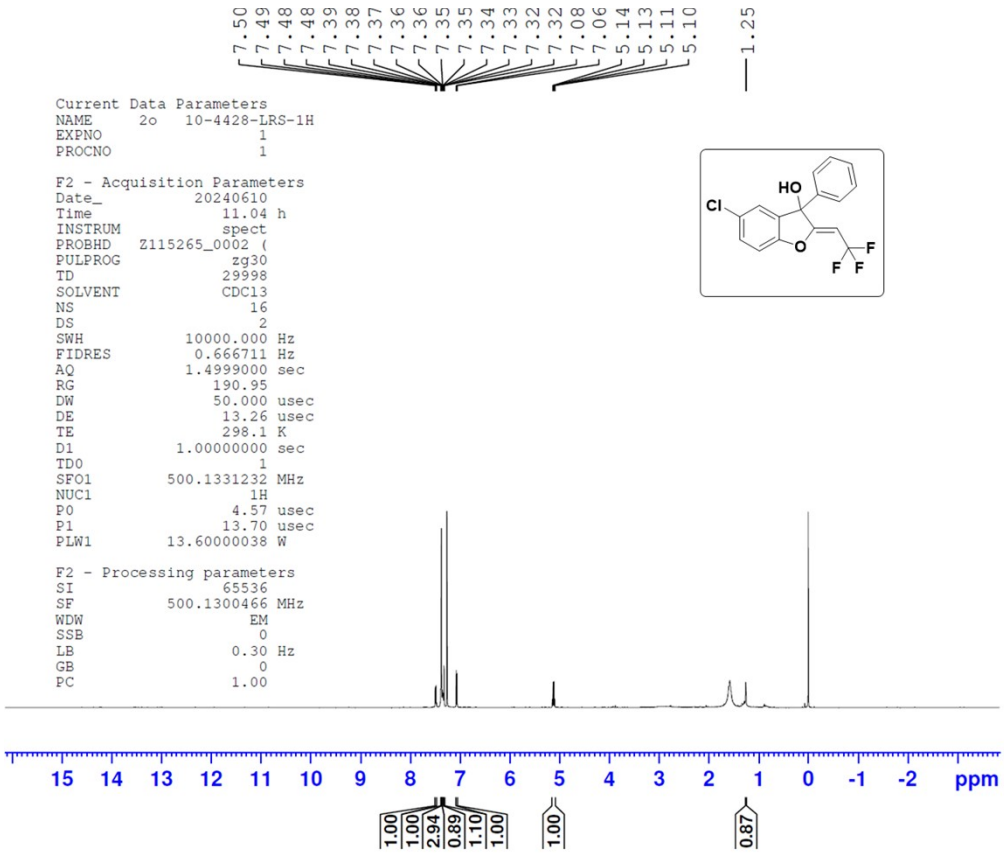
^{19}F NMR for 2n at 376 MHz



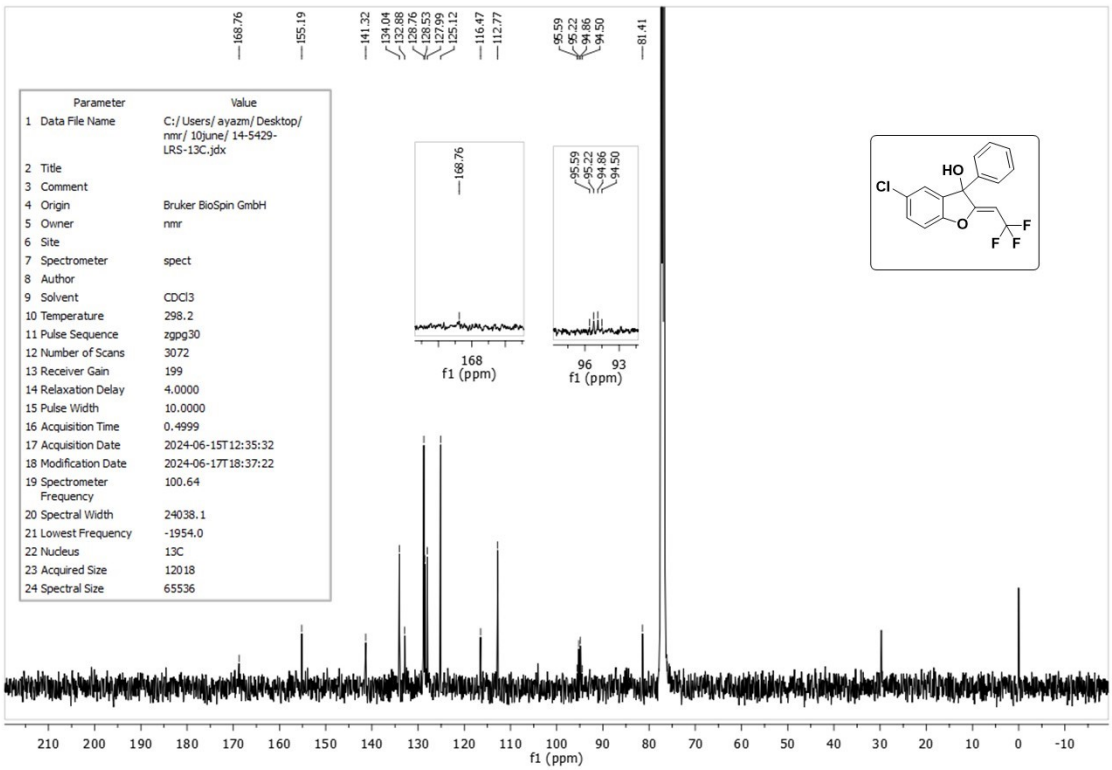
HRMS for 2n in APCI (+) MODE.



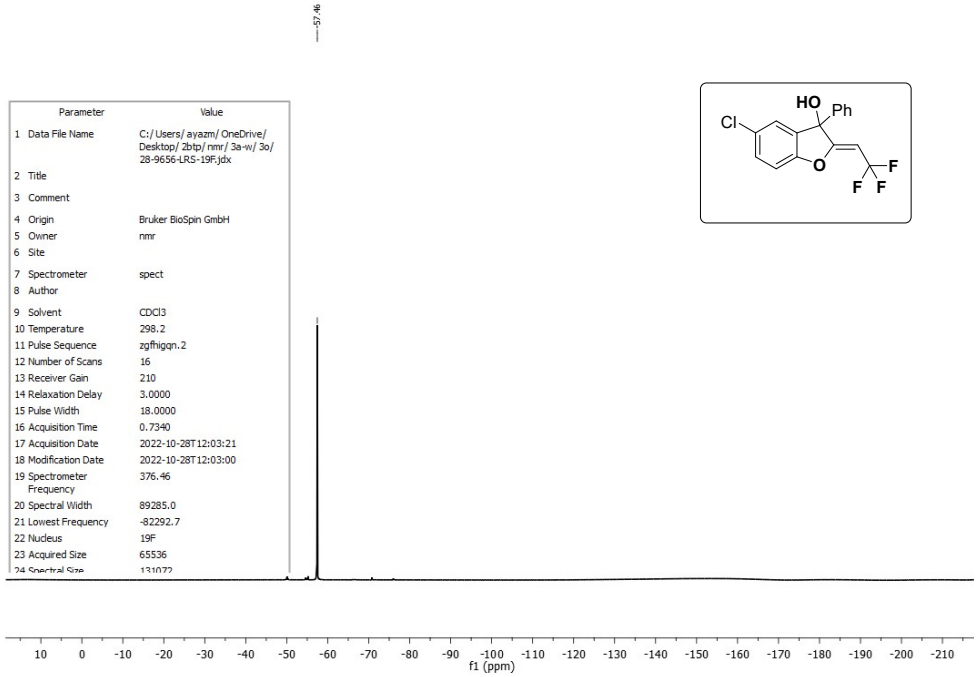
^{1}H NMR for 2o at 500 MHz



^{13}C NMR for 2o at 100 MHz



^{19}F NMR for 2o at 376 MHz



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9 Solvent	CDCl3
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12 Number of Scans	16
13 Receiver Gain	210
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15 Pulse Width	18.0000
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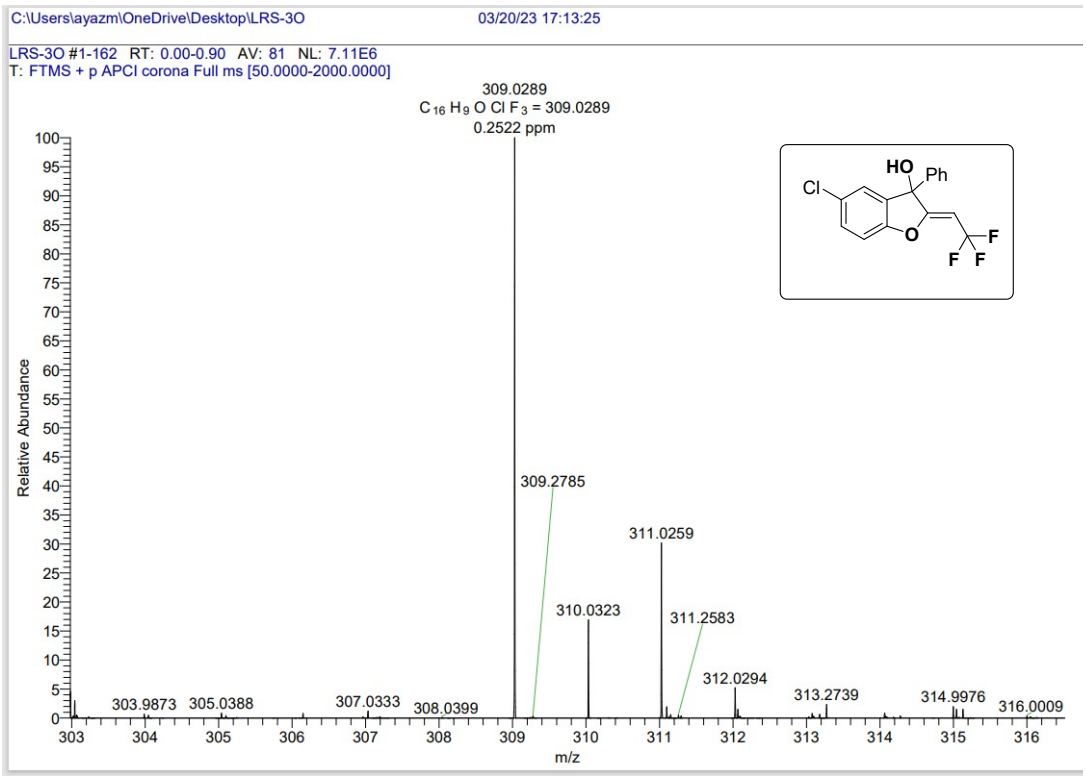
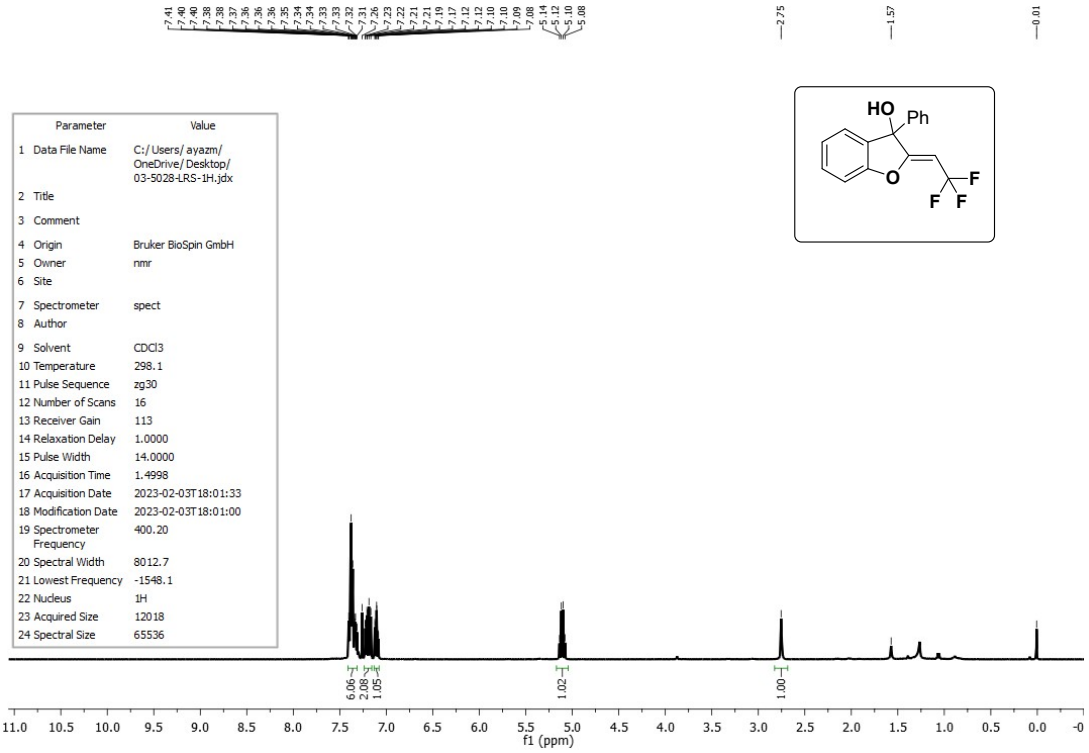
17 Acquisition Date	2022-10-28T12:03:21
18 Modification Date	2022-10-28T12:03:00
19 Spectrometer Frequency	376.46
20 Spectral Width	89285.0
21 Lowest Frequency	-82292.7
22 Nucleus	19F
23 Acquired Size	65536
24 Spectral Size	131072

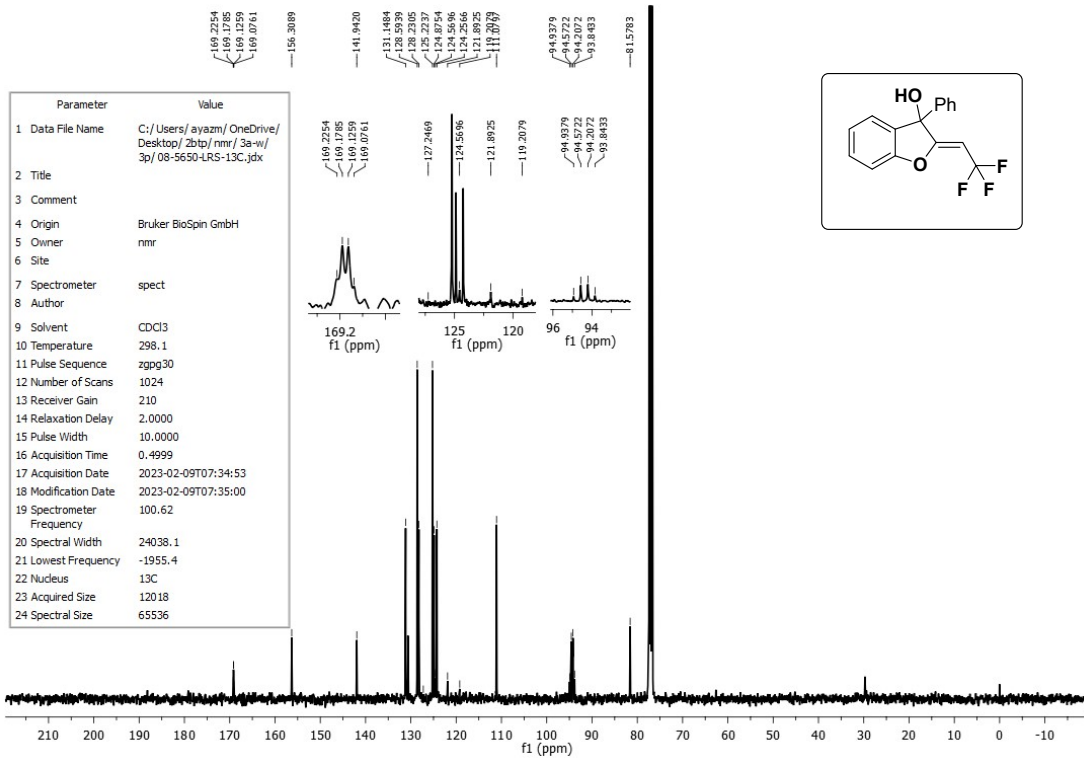
HRMS for 2o in APCI (+) MODE.



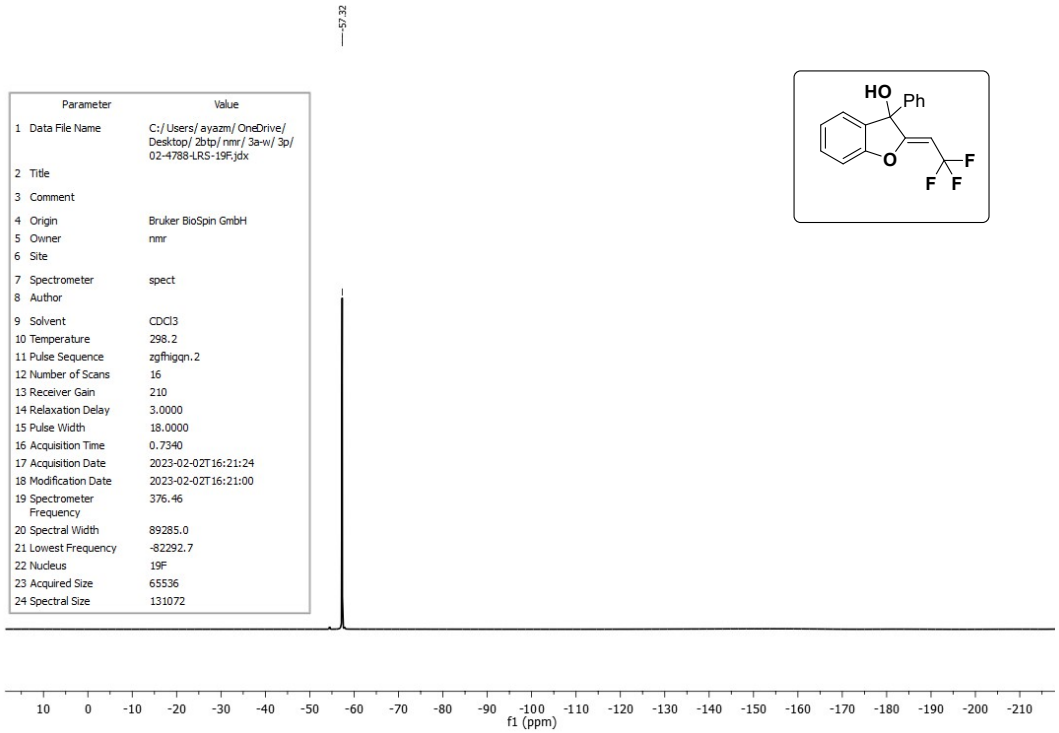
^{1}H NMR for 2p at 400 MHz



^{13}C NMR for 2p at 100 MHz



^{19}F NMR for 2p at 376 MHz



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12	Number of Scans	16
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14	Relaxation Delay	3.0000
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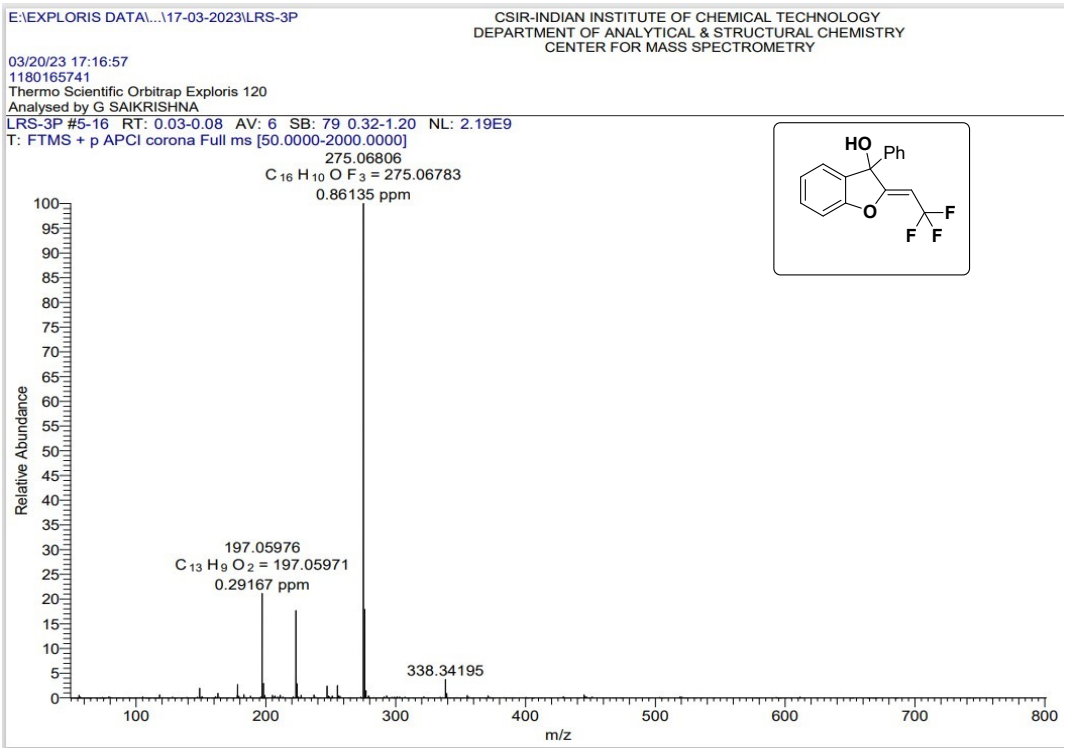
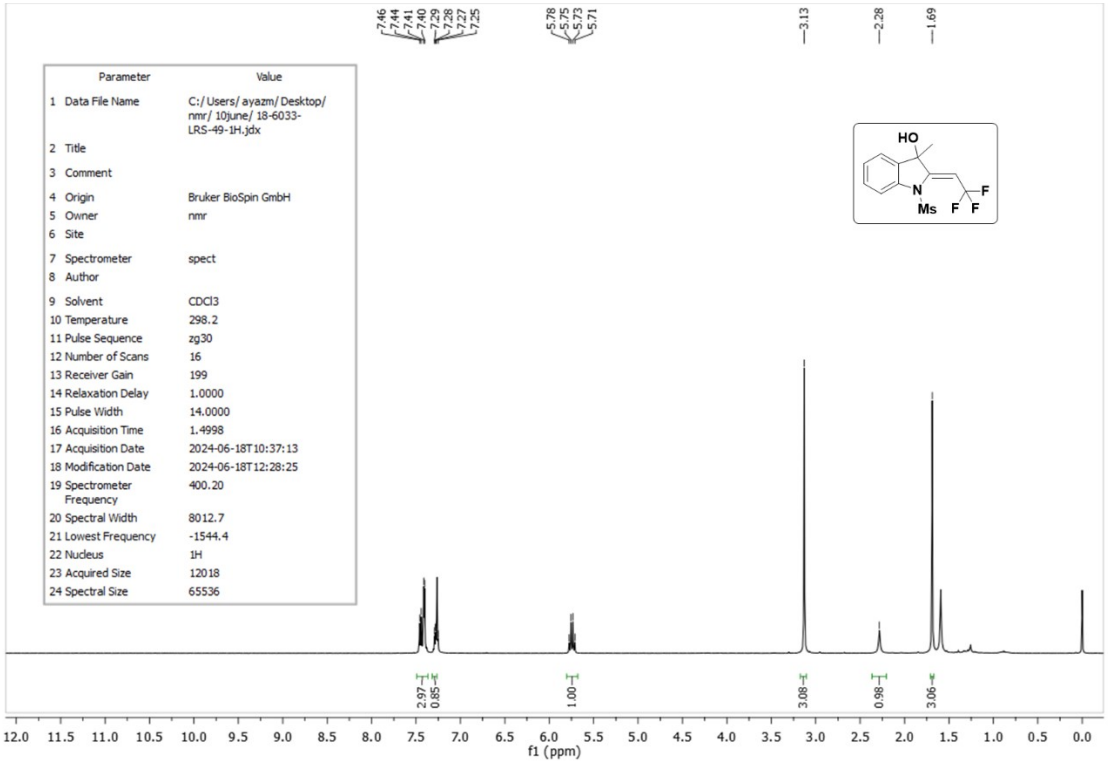
19	Spectrometer Frequency	376.46
20	Spectral Width	89285.0
21	Lowest Frequency	-82292.7
22	Nucleus	19F
23	Acquired Size	65536
24	Spectral Size	131072

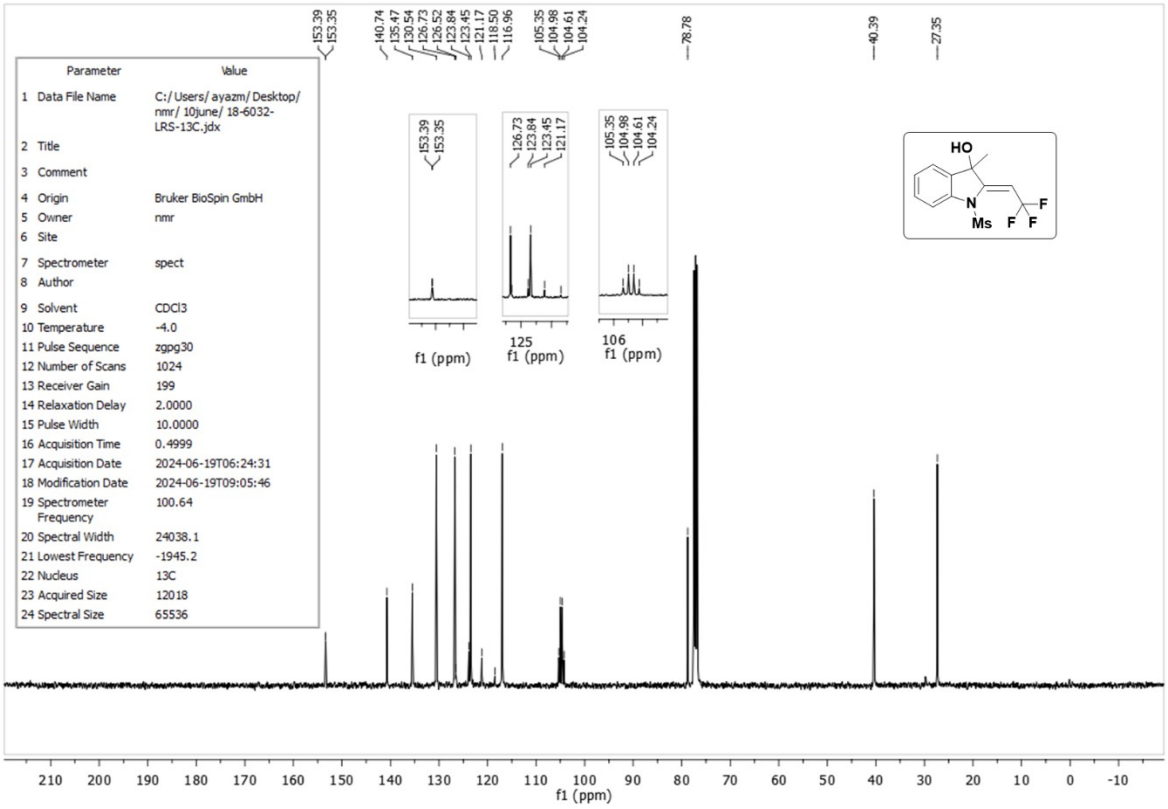
HRMS for 2p in APCI (+) MODE.



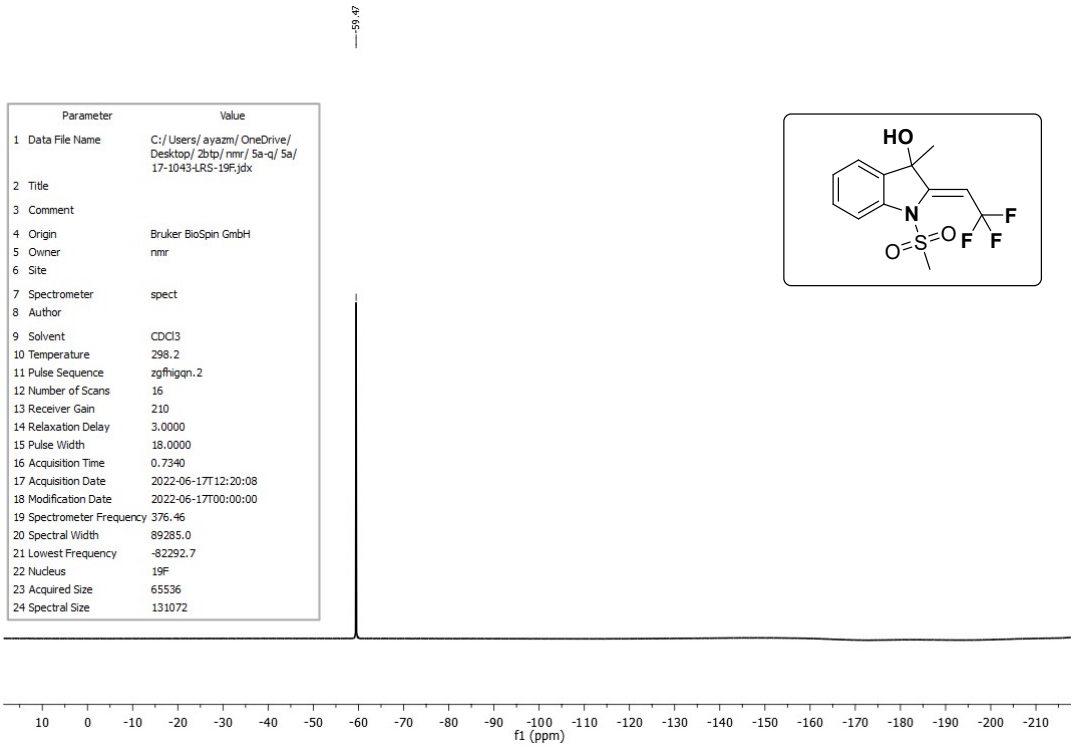
^{1}H NMR for 4a at 400 MHz



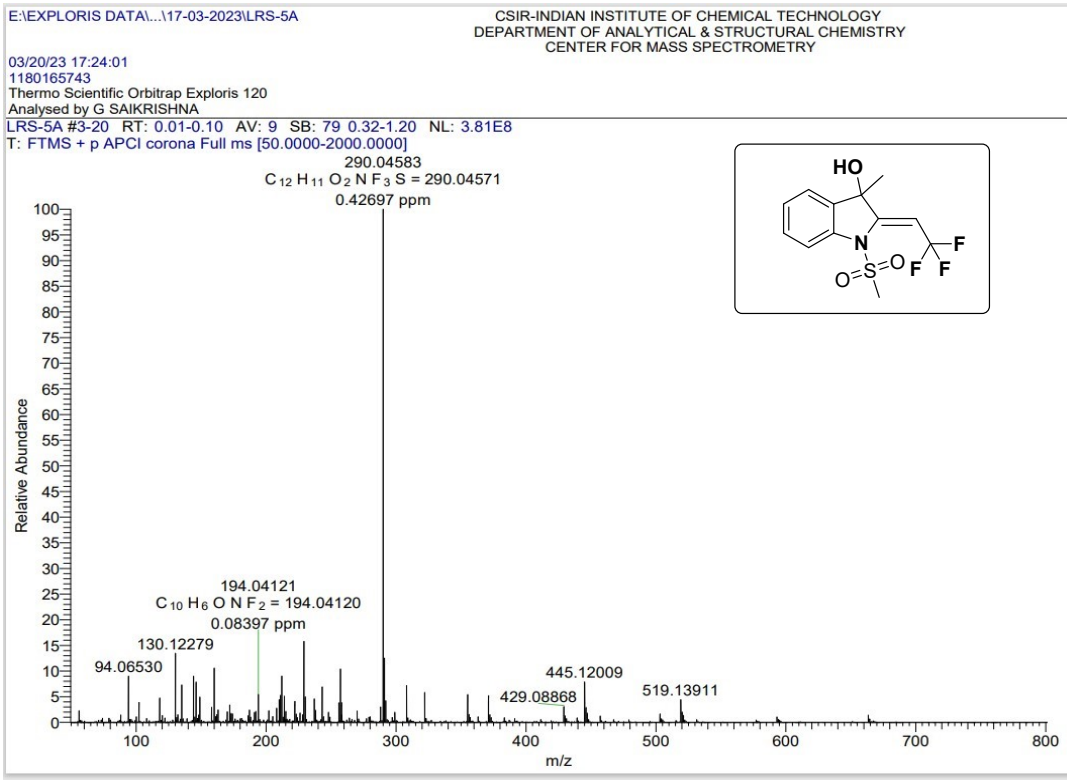
^{13}C NMR for 4a at 100 MHz



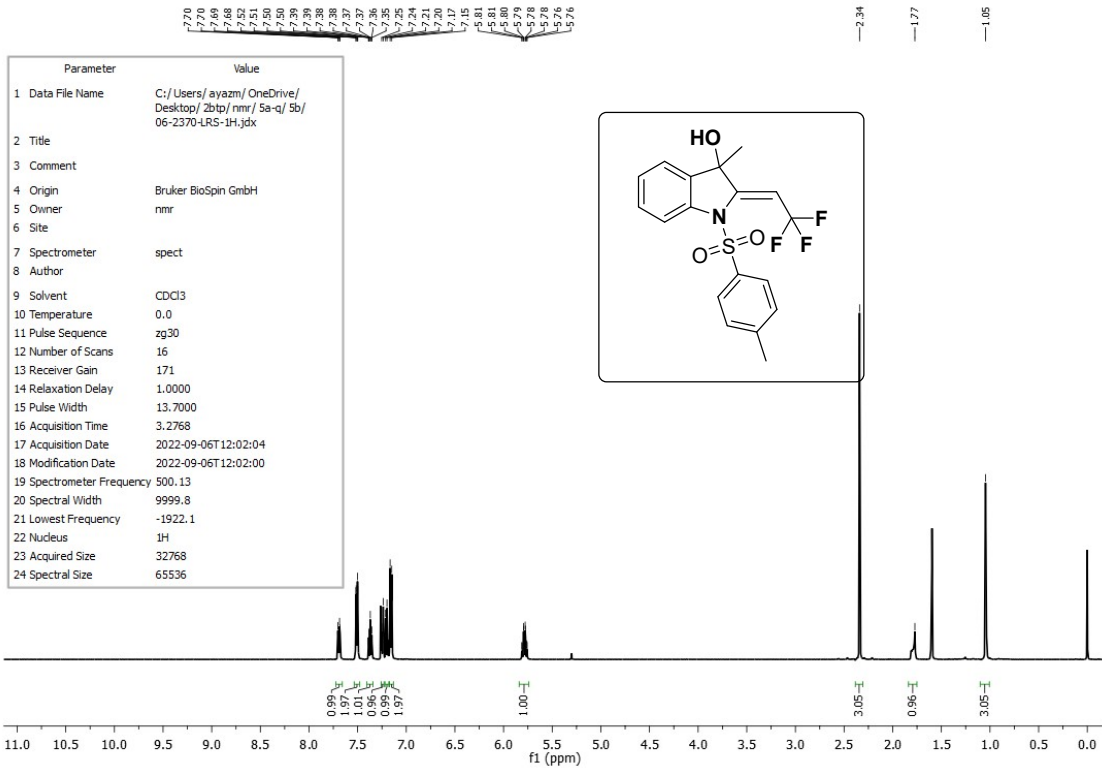
^{19}F NMR for 4a at 376 MHz



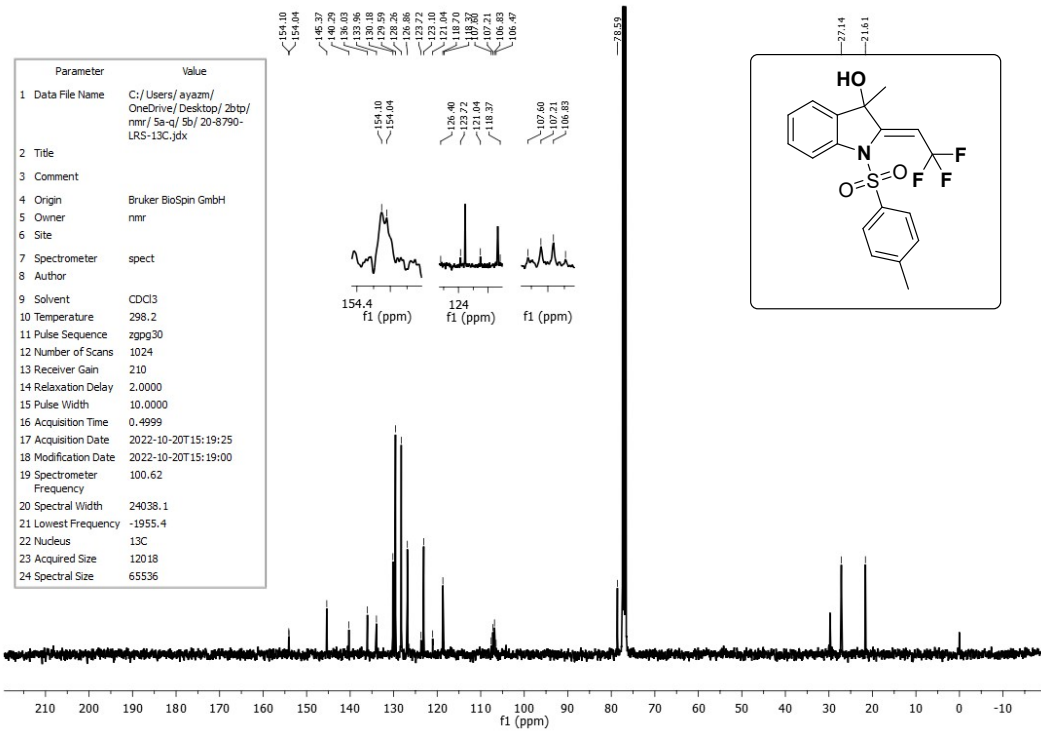
HRMS for 4a in APCI (+) MODE.



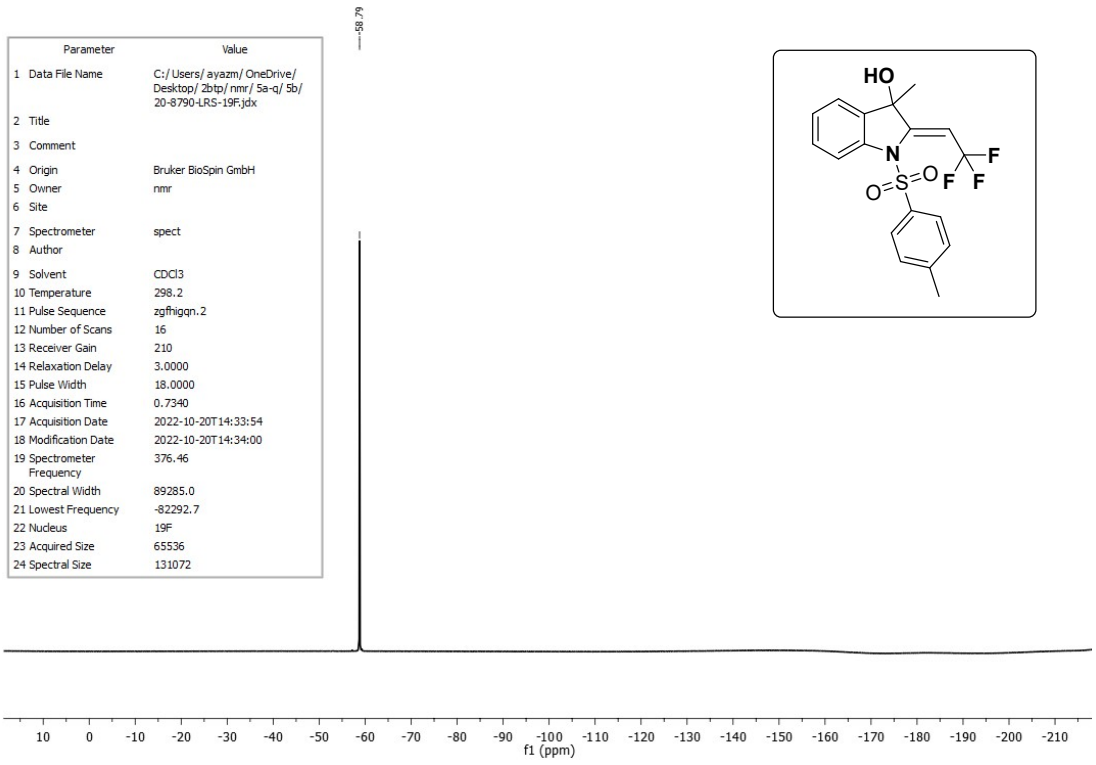
^{1}H NMR for 4b at 500 MHz



^{13}C NMR for 4b at 100 MHz



^{19}F NMR for 4b at 376 MHz



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8	Author	
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11	Pulse Sequence	zgfhigqn.2
12	Number of Scans	16
13	Receiver Gain	210
14	Relaxation Delay	3.0000
15	Pulse Width	18.0000
16	Acquisition Time	0.7340
17	Acquisition Date	2022-10-20T14:33:54
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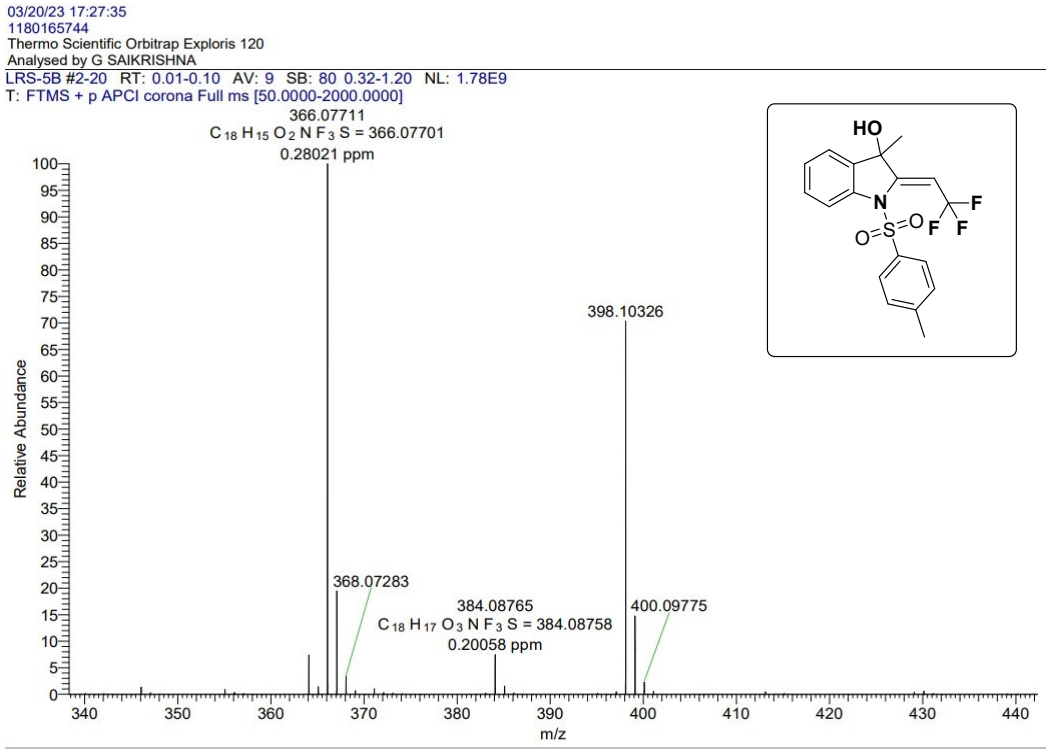
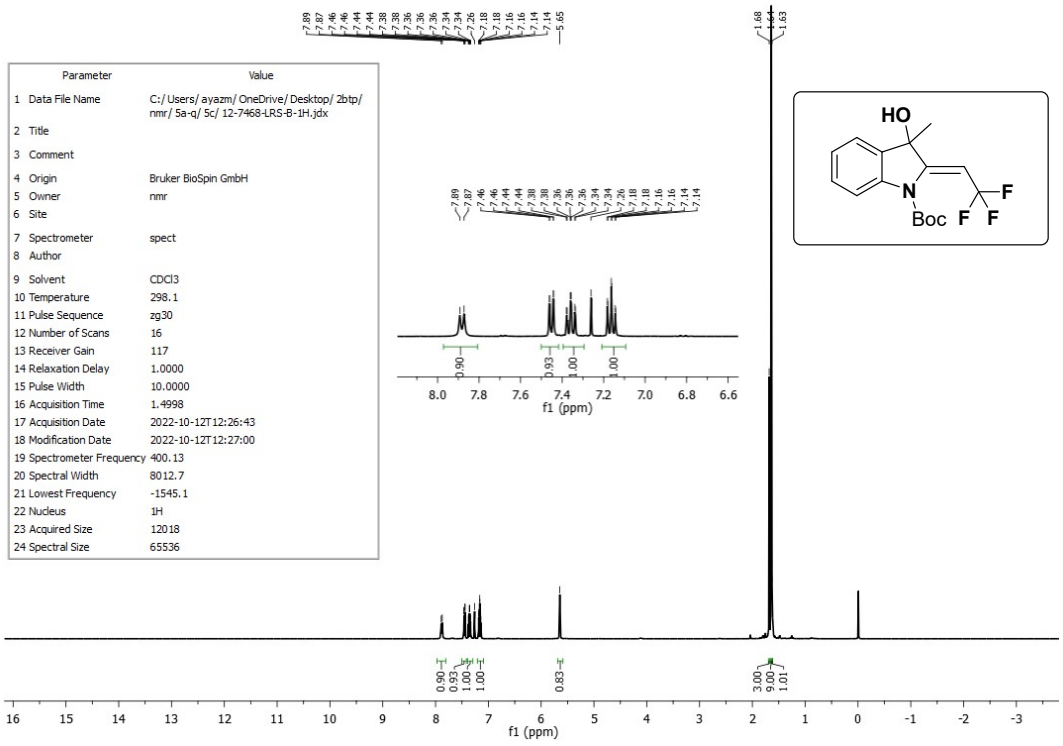
19	Spectrometer Frequency	376.46
20	Spectral Width	89285.0
21	Lowest Frequency	-82292.7
22	Nucleus	19F
23	Acquired Size	65536
24	Spectral Size	131072

HRMS for 4b in APCI (+) MODE.



^{1}H NMR for 4c at 400 MHz



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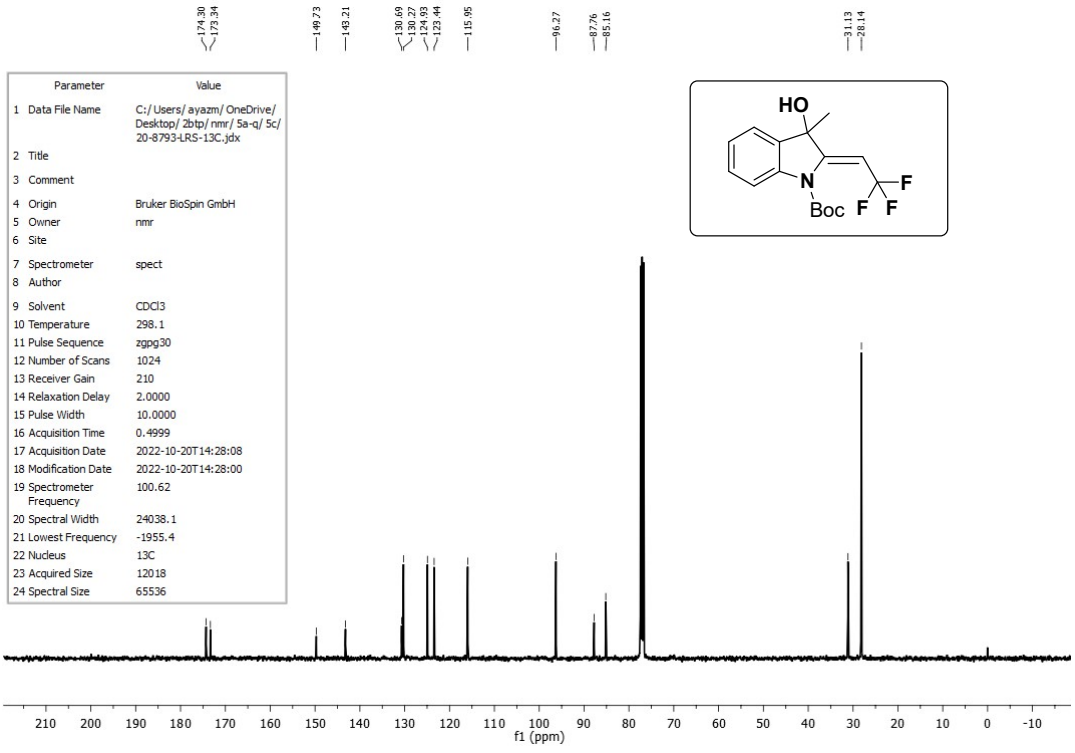
22	Nucleus	1H
23	Acquired Size	12018
24	Spectral Size	65536

^{13}C NMR for 4c at 100 MHz



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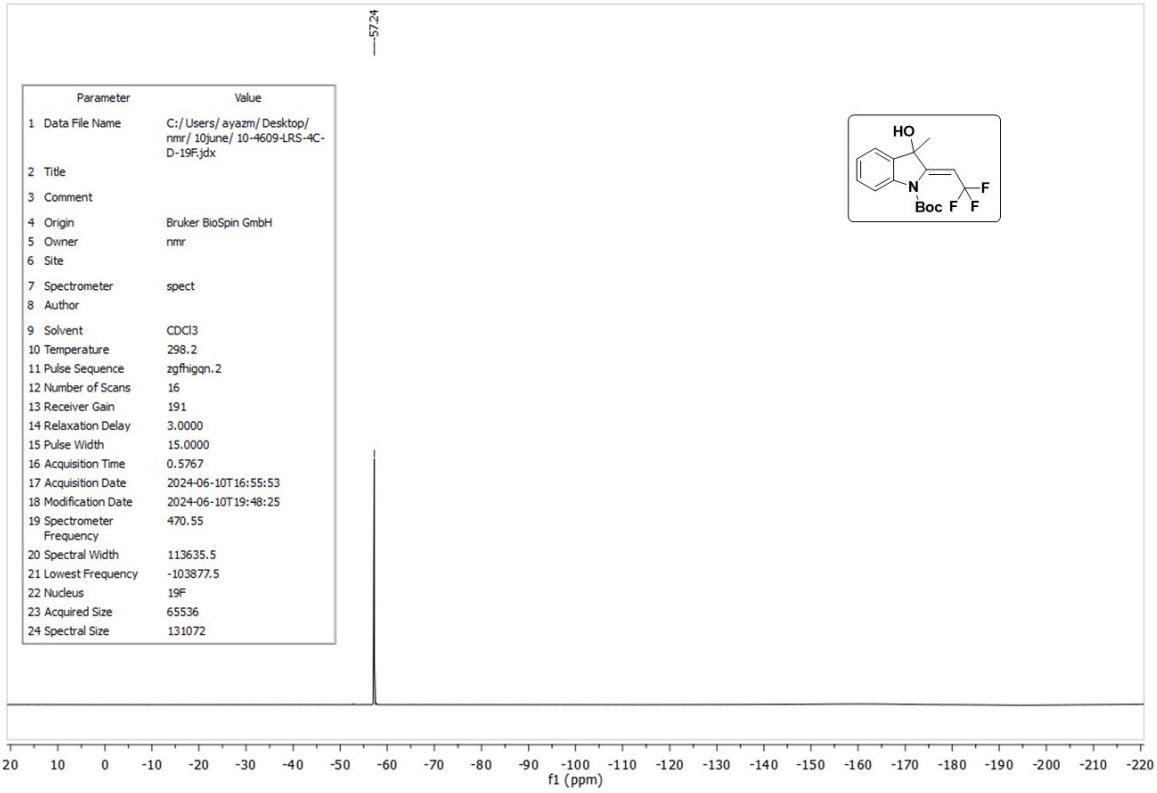
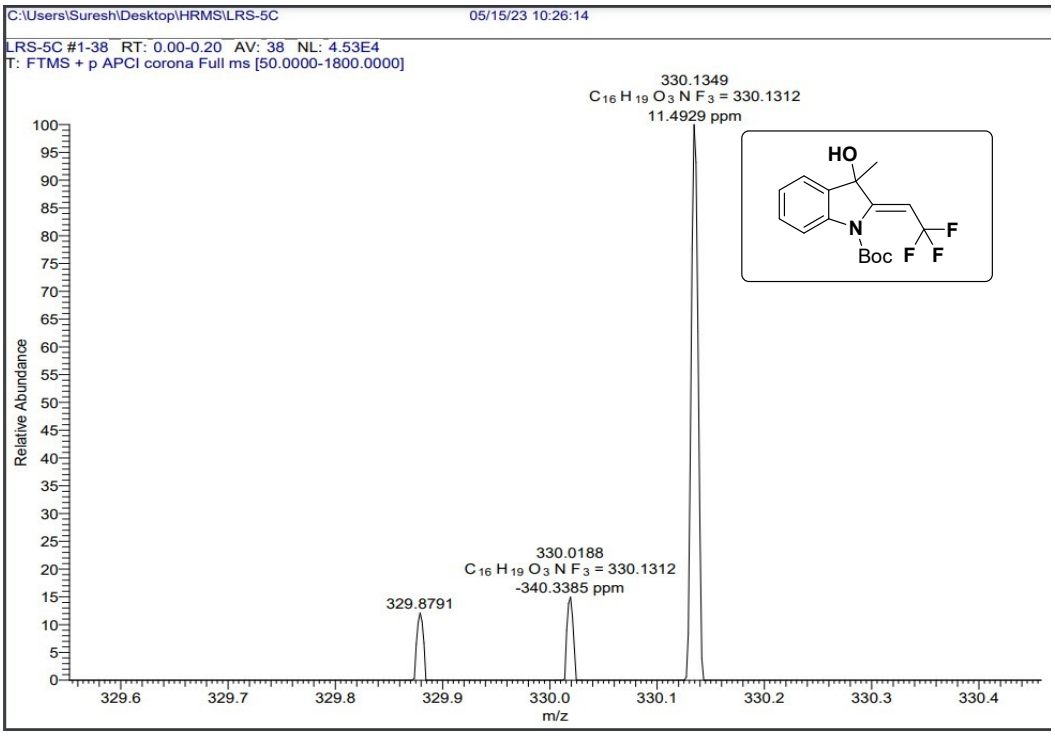
22	Nucleus	13C
23	Acquired Size	12018
24	Spectral Size	65536

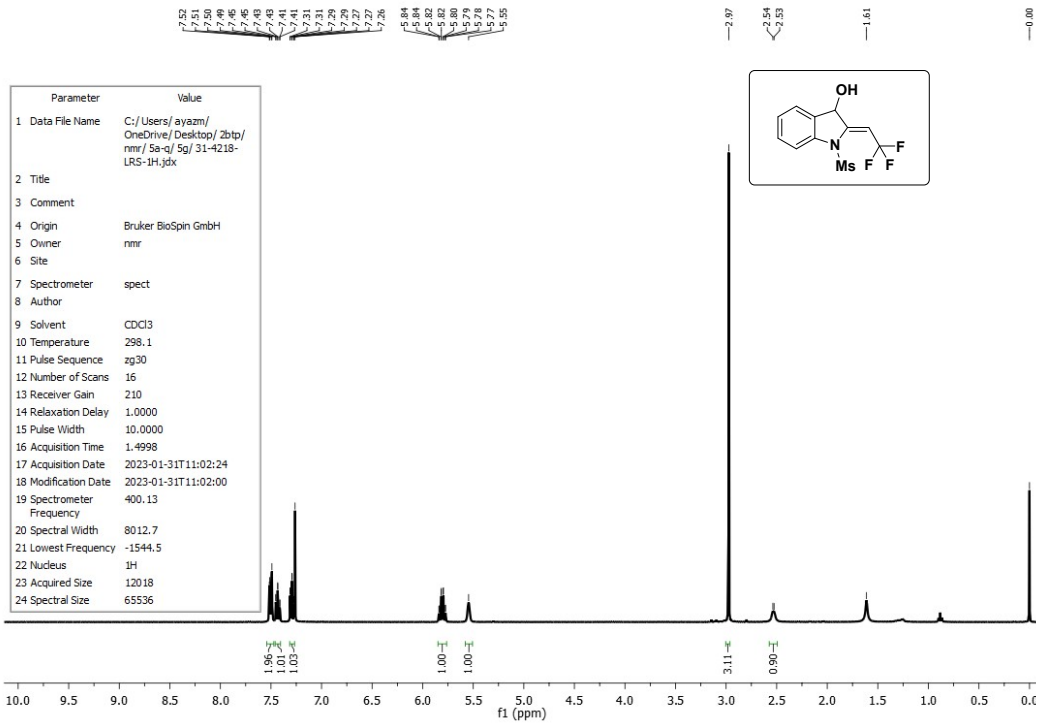
^{19}F NMR for 4c at 470 MHz



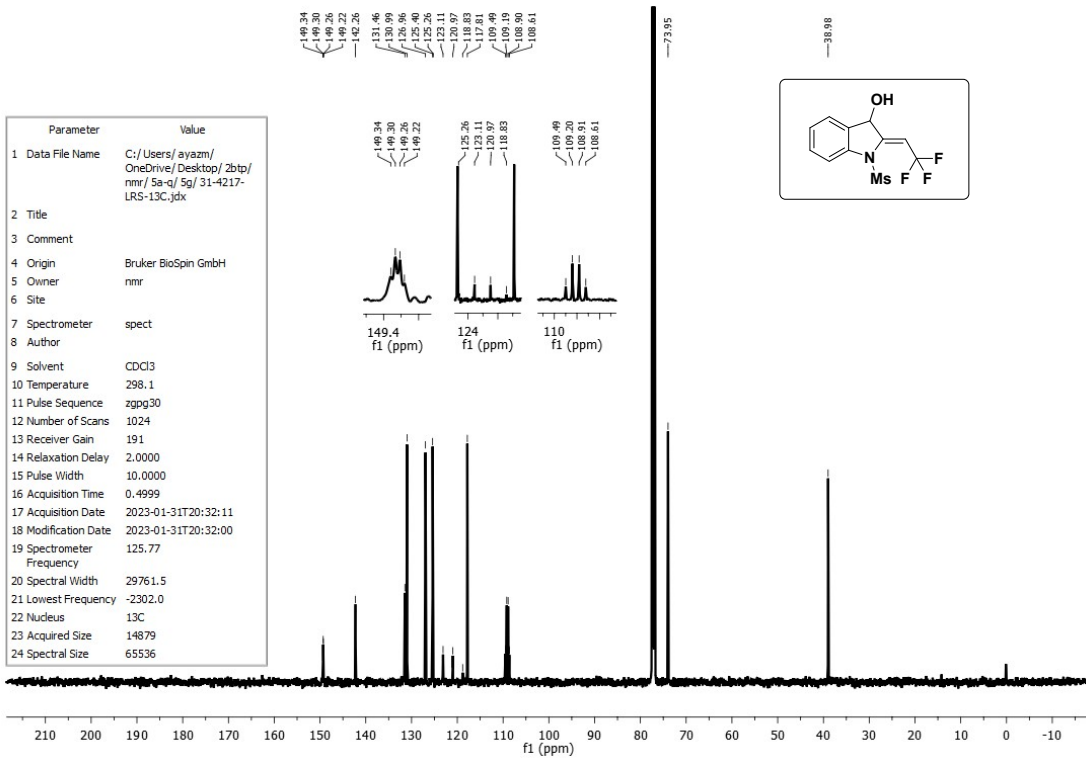
HRMS for 4c in APCI (+) MODE.



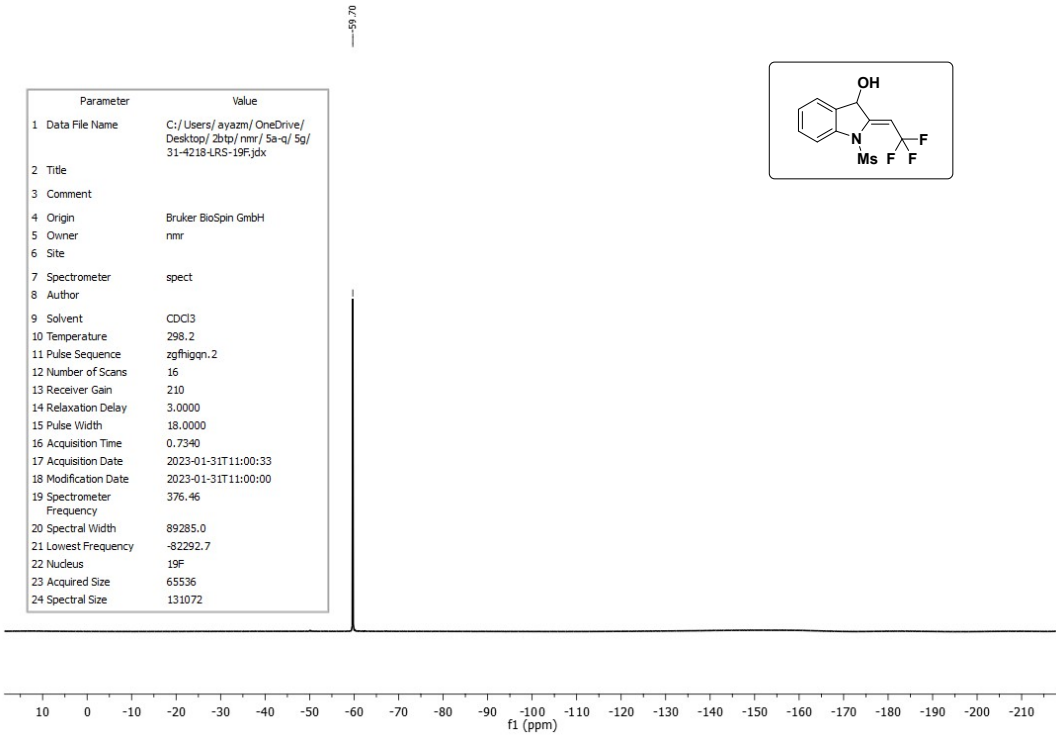
^{1}H NMR for 4d at 400 MHz



^{13}C NMR for 4d at 125 MHz



^{19}F NMR for 4d at 376 MHz



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15 Pulse Width	18.0000
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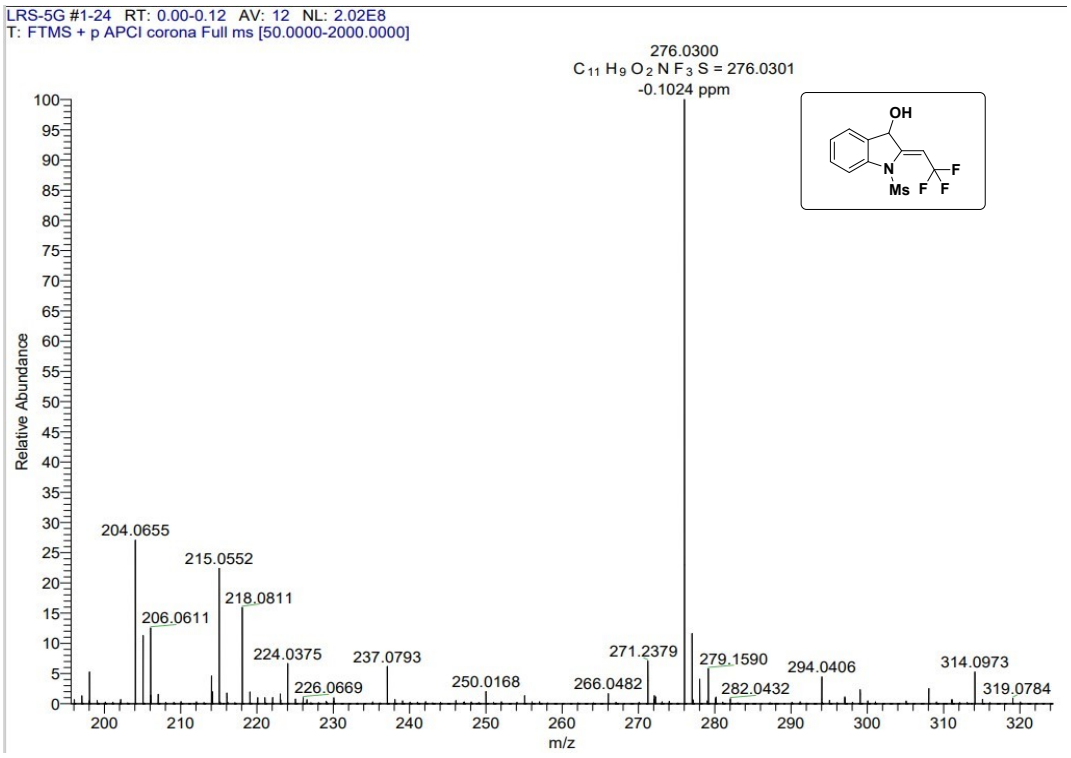
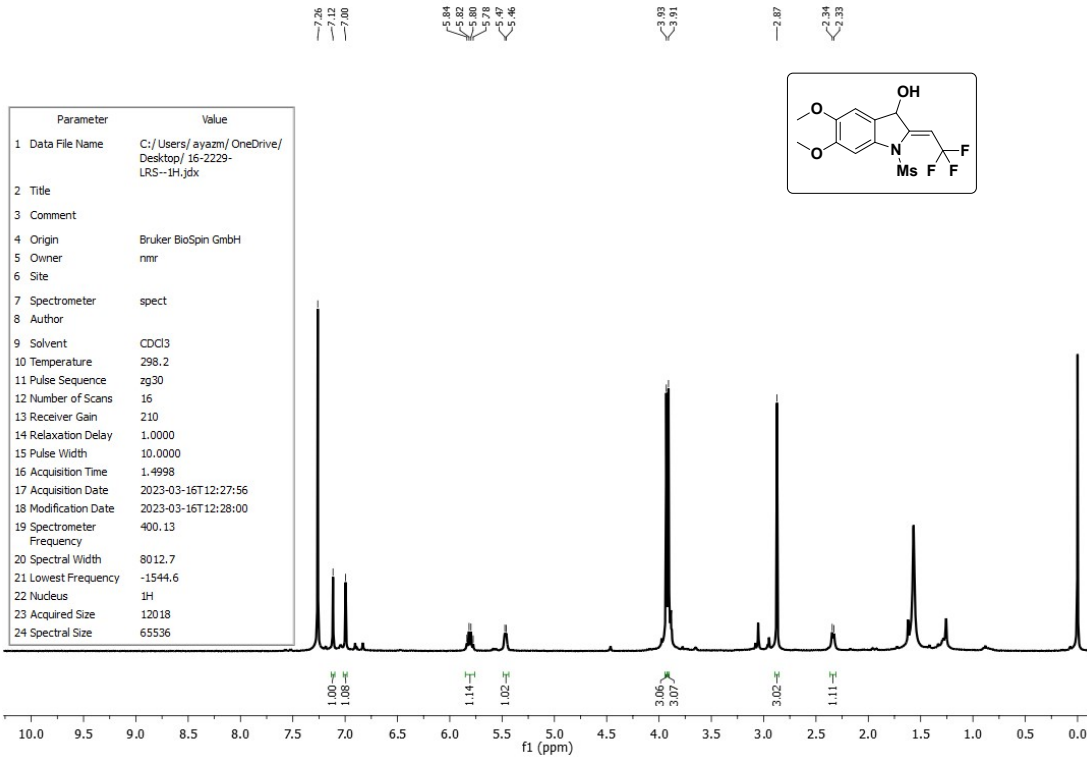
17 Acquisition Date	2023-01-31T11:00:33
18 Modification Date	2023-01-31T11:00:00
19 Spectrometer Frequency	376.46
20 Spectral Width	89285.0
21 Lowest Frequency	-82292.7
22 Nucleus	19F
23 Acquired Size	65536
24 Spectral Size	131072

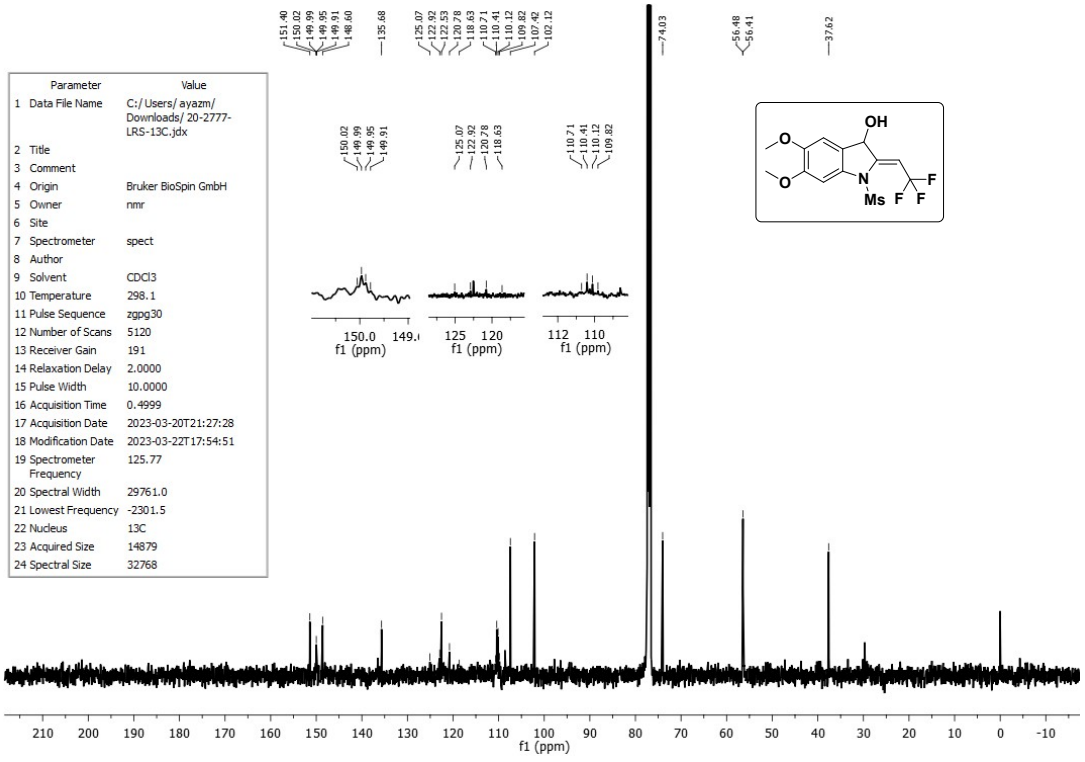
HRMS for 4d in APCI (+) MODE.



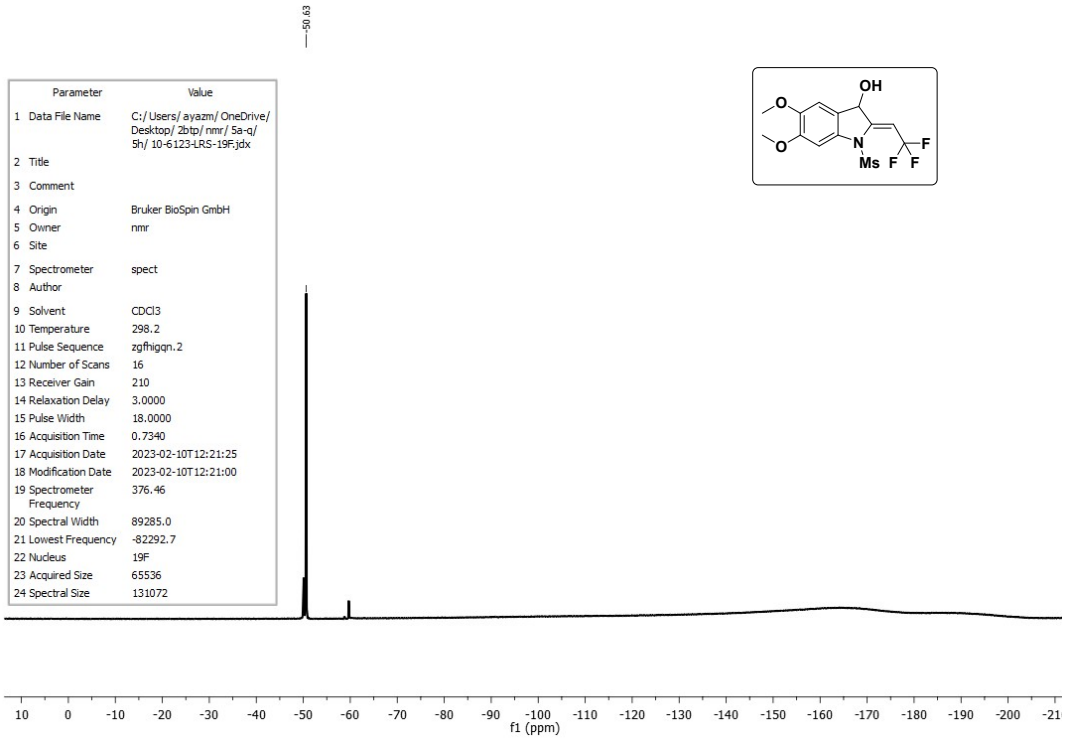
^{1}H NMR for 4e at 400 MHz



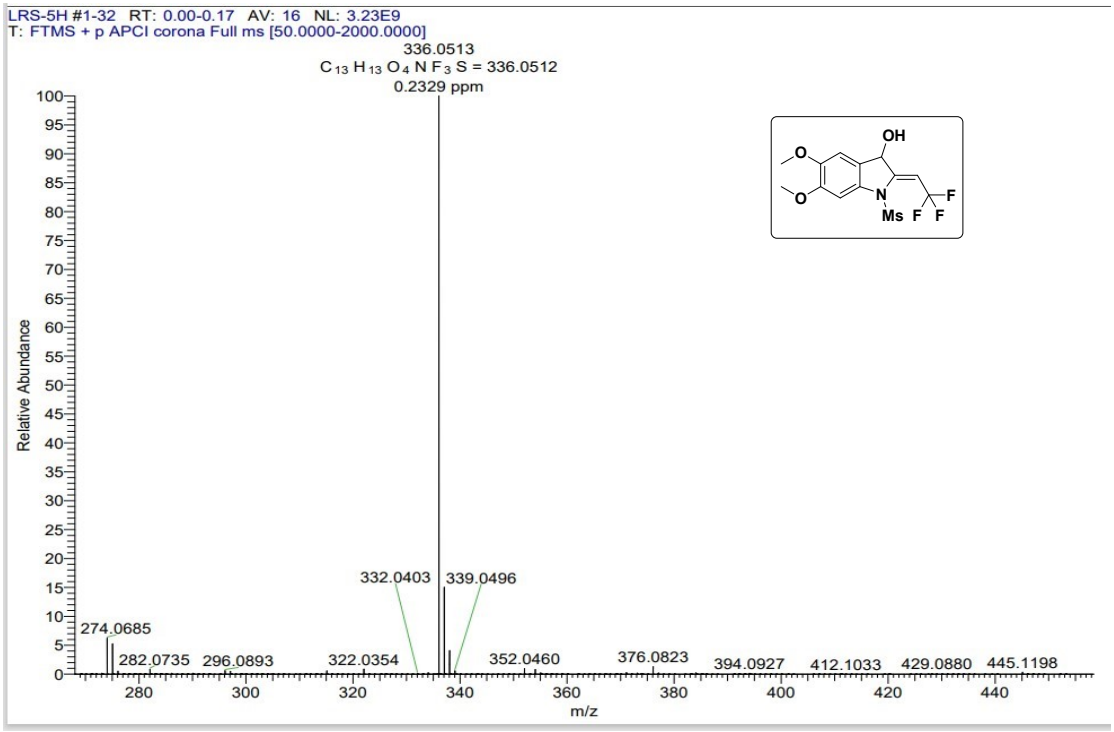
^{13}C NMR for 4e at 100 MHz



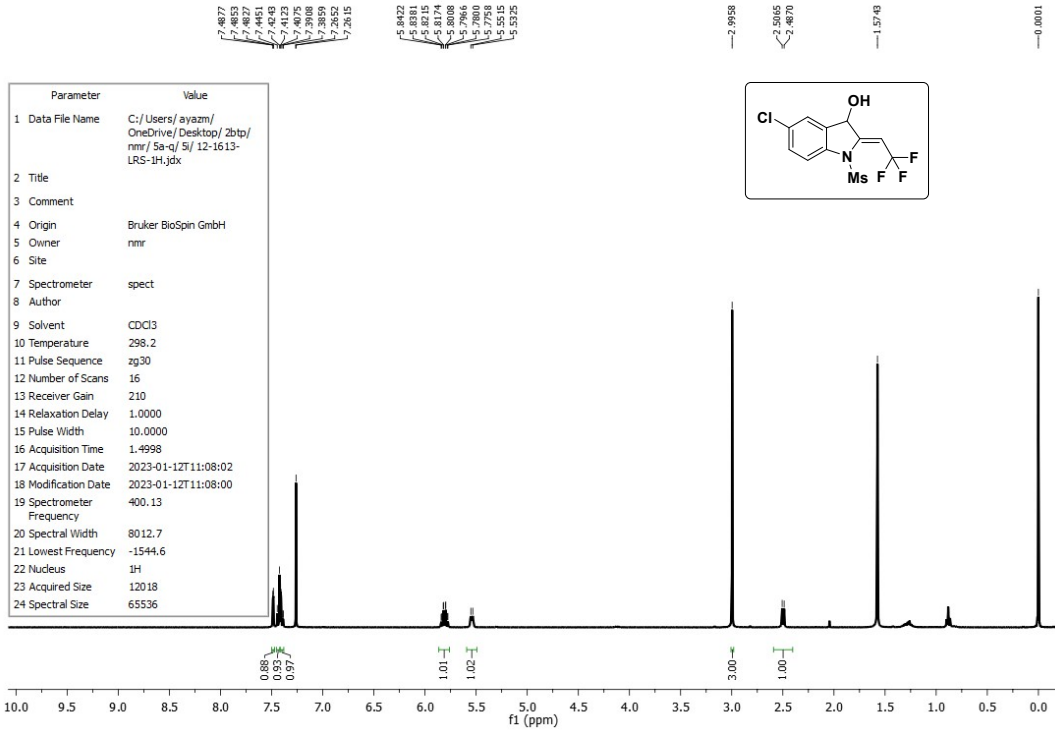
^{19}F NMR for 4e at 376 MHz



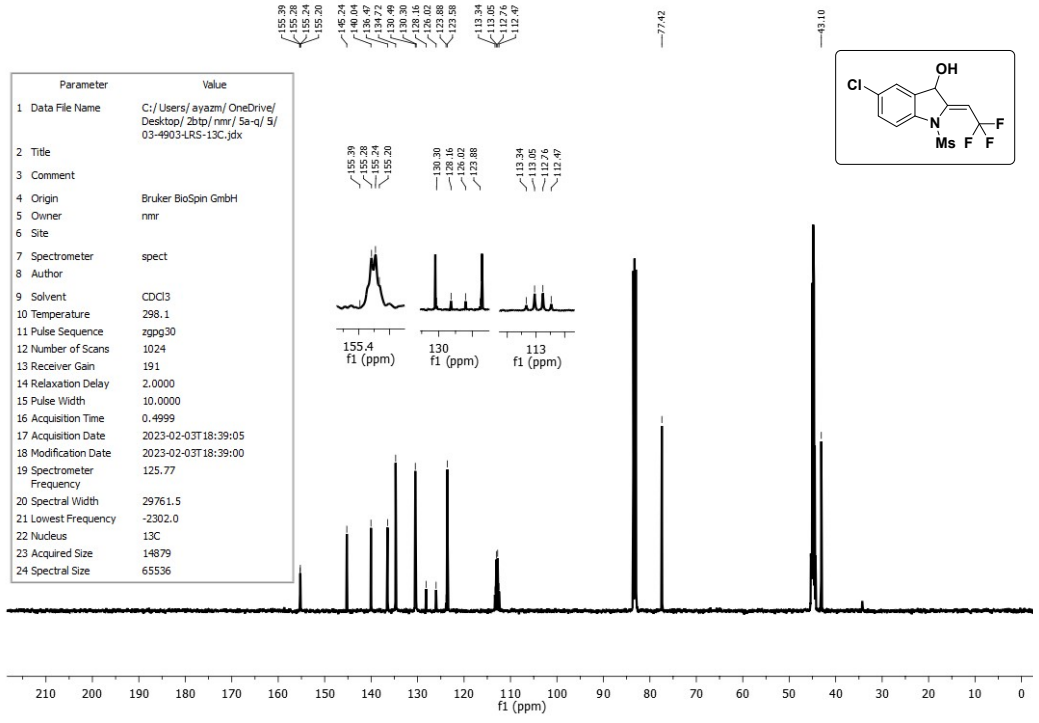
HRMS for 4e in APCI (+) MODE.



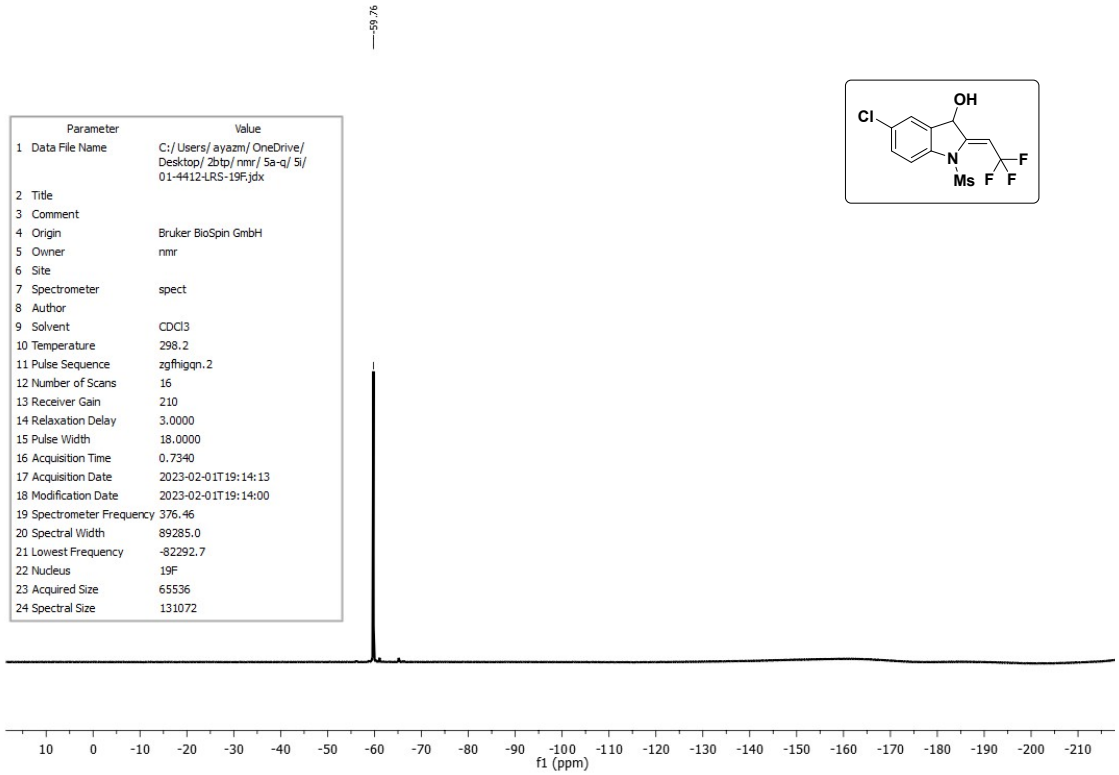
^{1}H NMR for 4f at 400 MHz



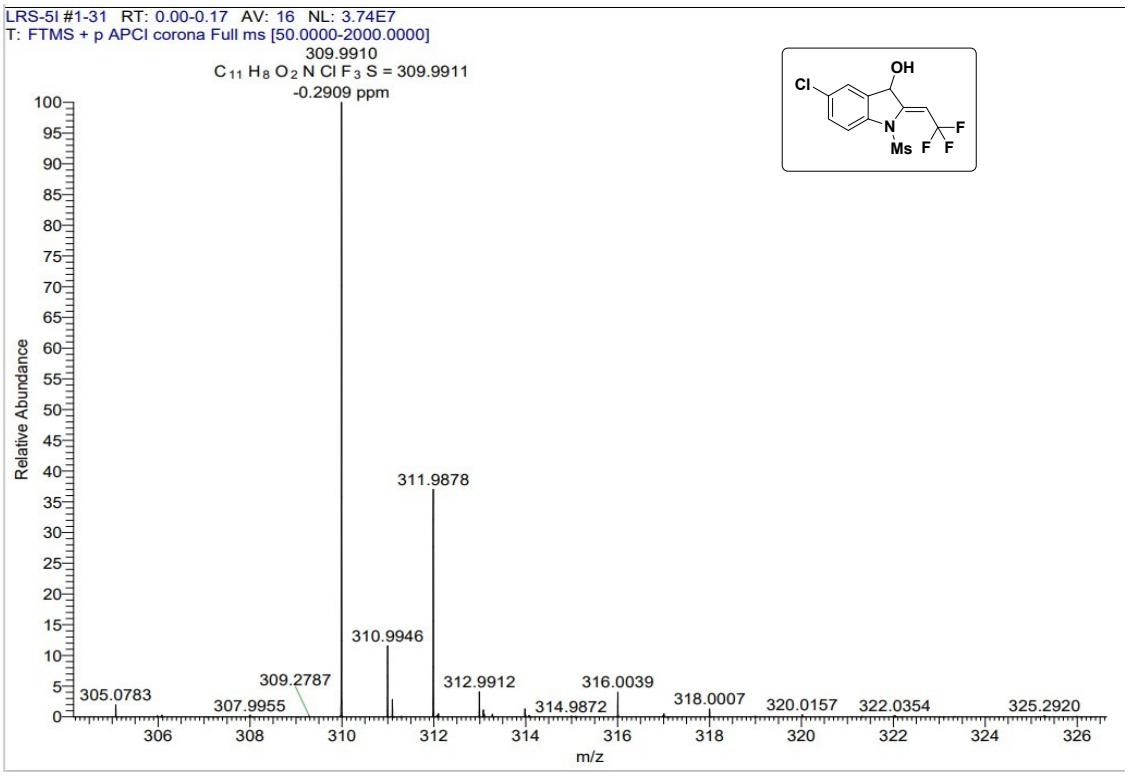
^{13}C NMR for 4f at 125 MHz in $CDCl_3$ and DMSO-d_6 mixture.



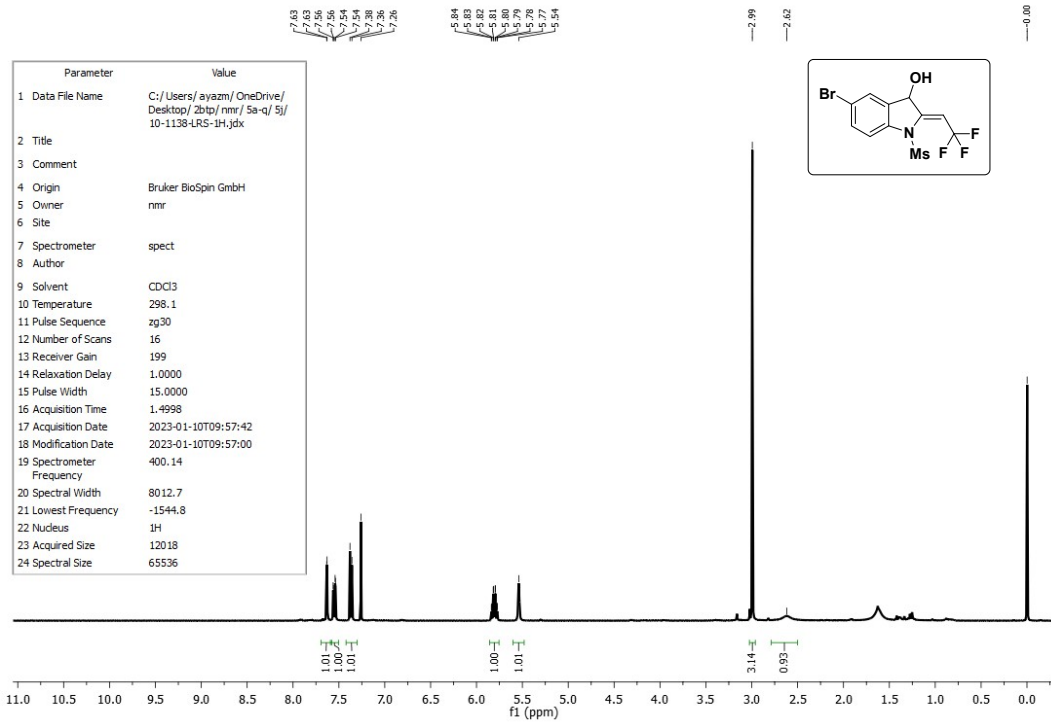
^{19}F NMR for 4f at 376 MHz



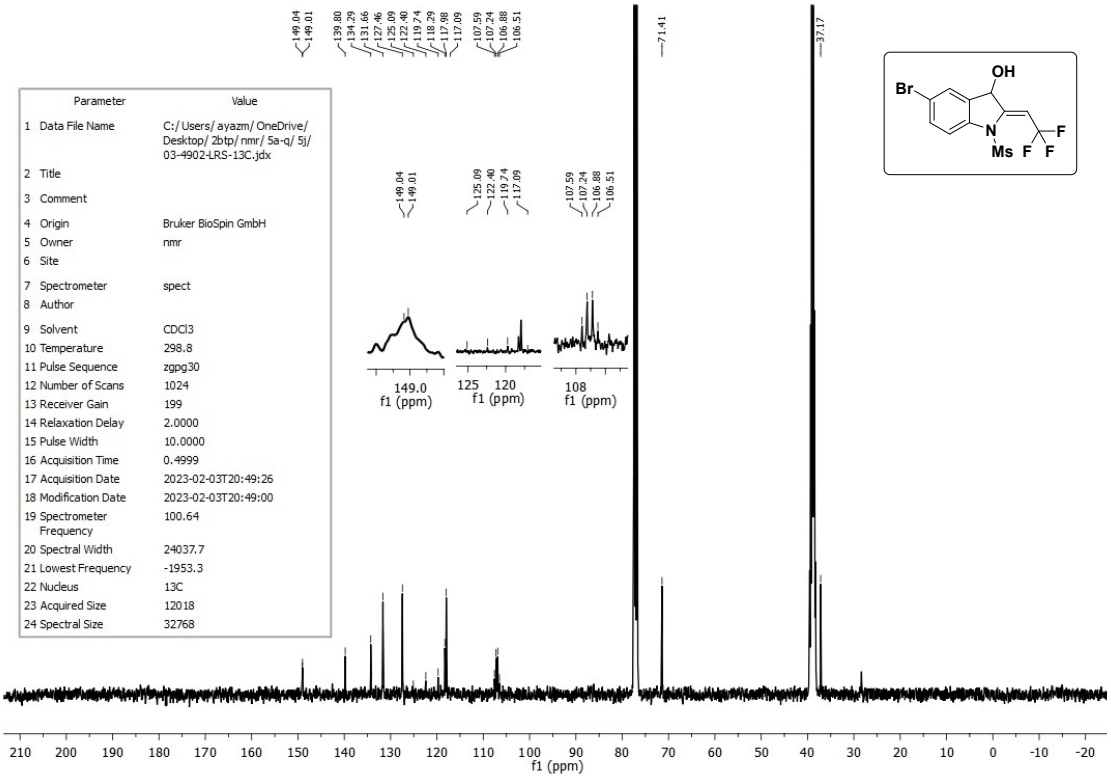
HRMS for 4f in APCI (+) MODE.



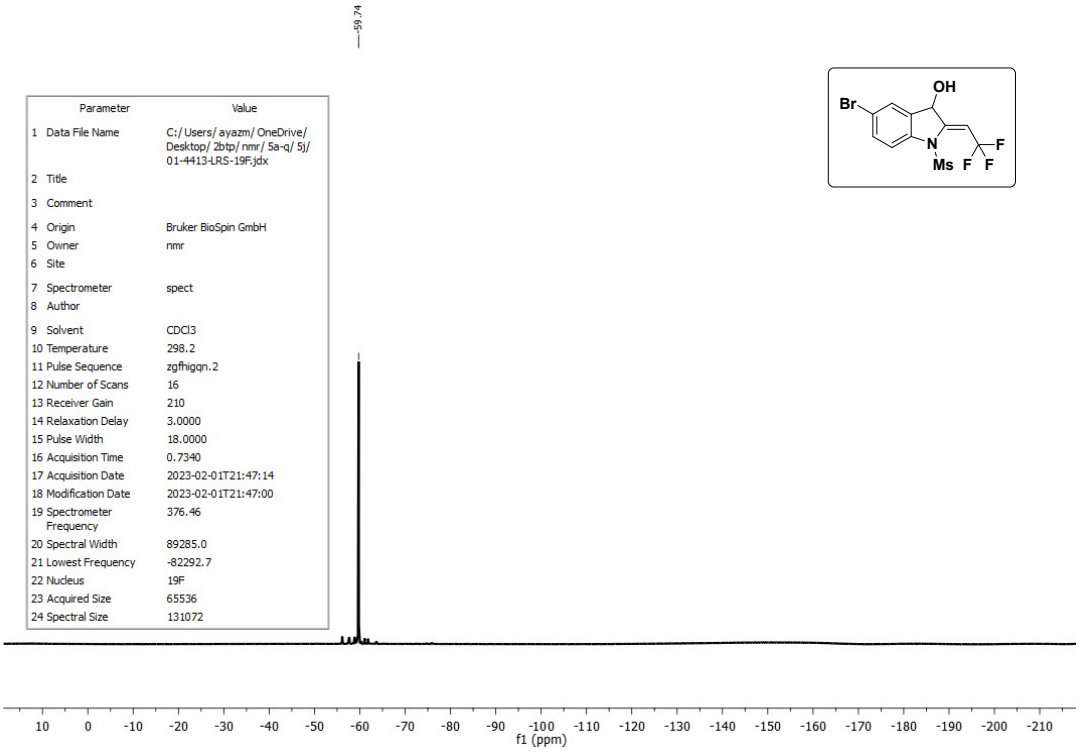
^{1}H NMR for 4g at 400 MHz



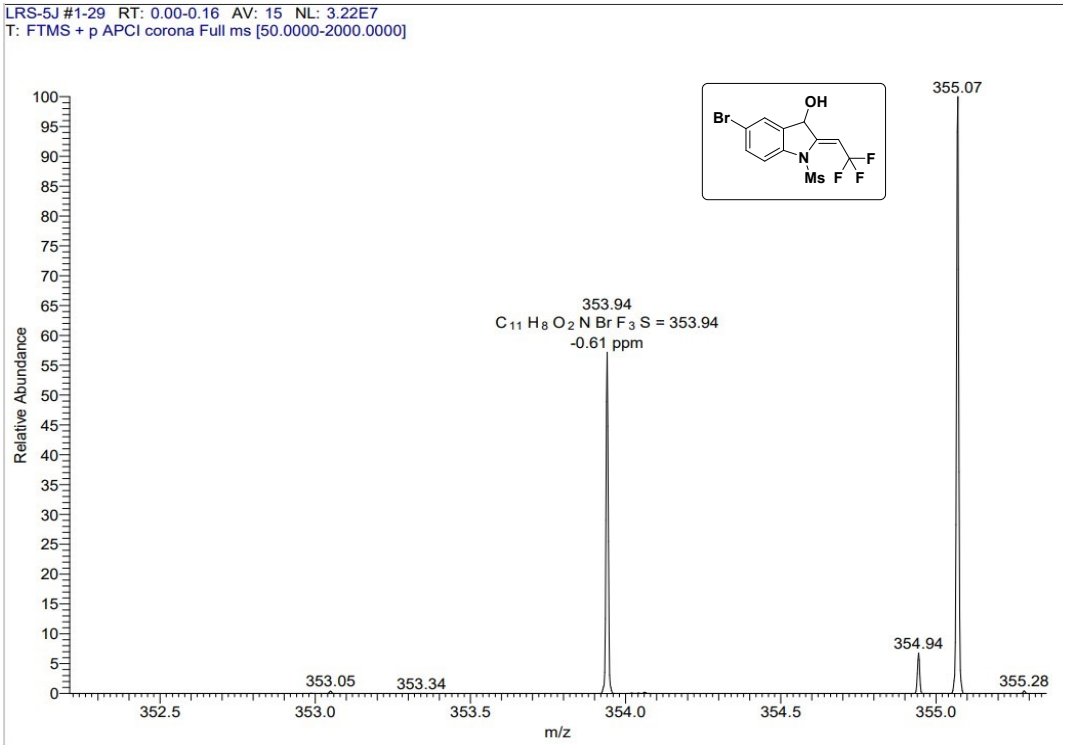
^{13}C NMR for 4g at 125 MHz in $CDCl_3$ and DMSO-d_6 mixture.



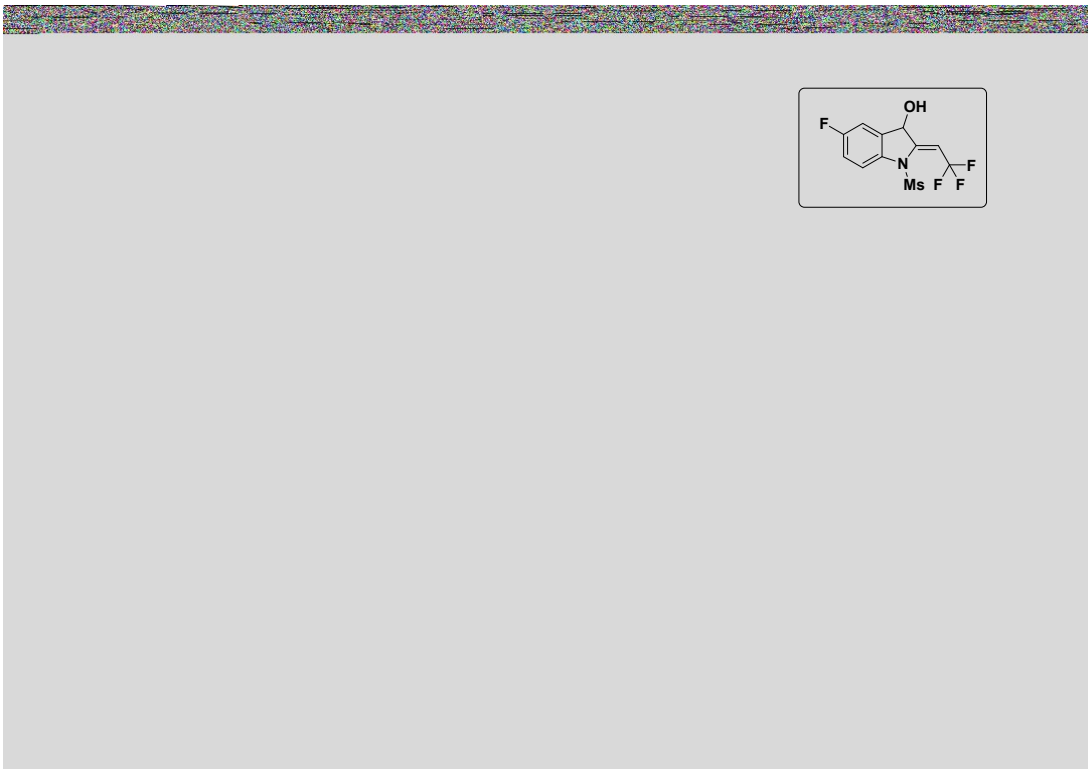
^{19}F NMR for 4g at 376 MHz



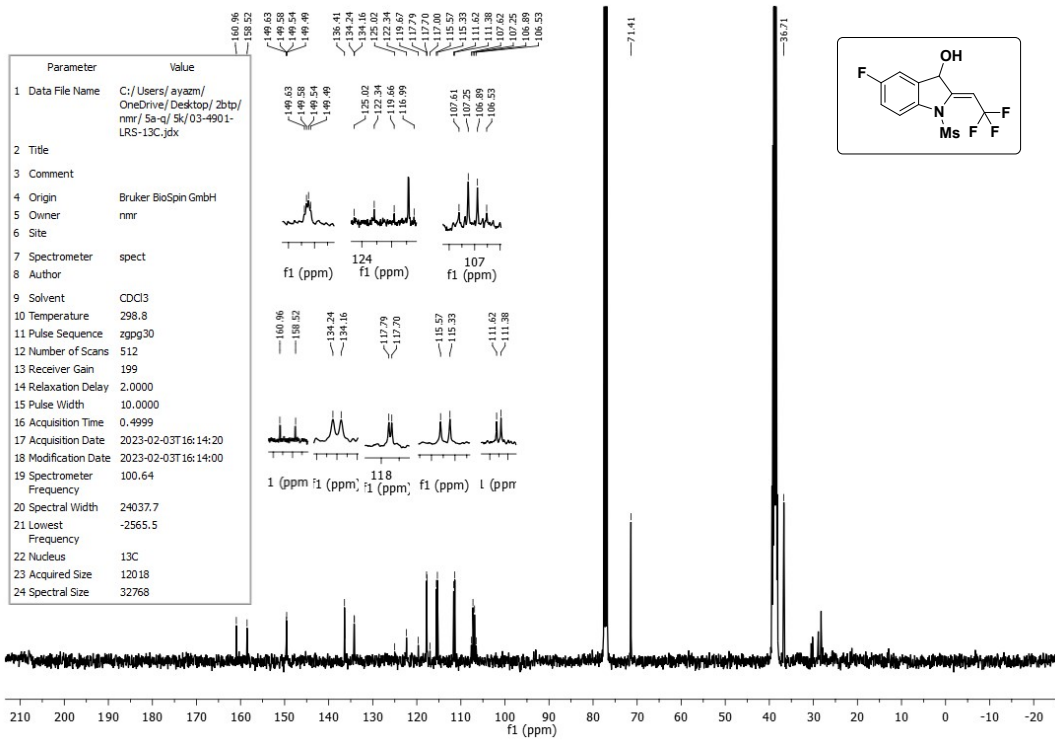
HRMS for 4g in APCI (+) MODE.



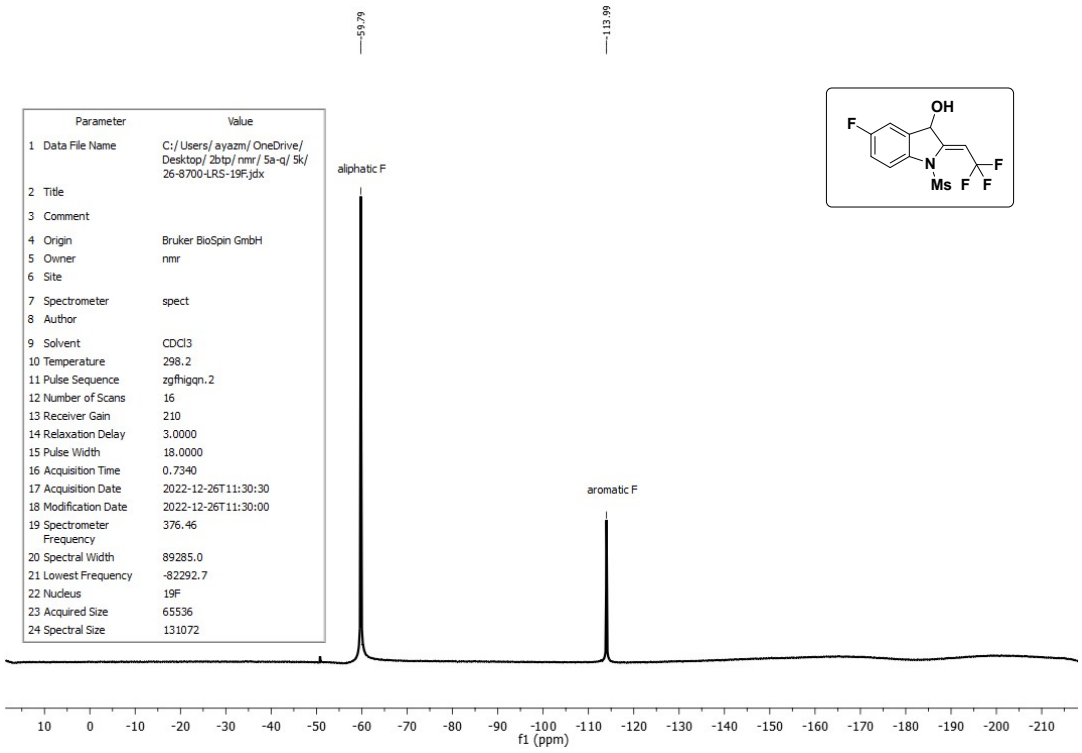
^{1}H NMR for 4h at 400 MHz



^{13}C NMR for 4h at 125 MHz in $CDCl_3$ and DMSO-d_6 mixture.



^{19}F NMR for 4h at 376 MHz



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8	Author	
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16	Acquisition Time	0.7340
17	Acquisition Date	2022-12-26T11:30:30
18	Modification Date	2022-12-26T11:30:00
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22	Nucleus	19F
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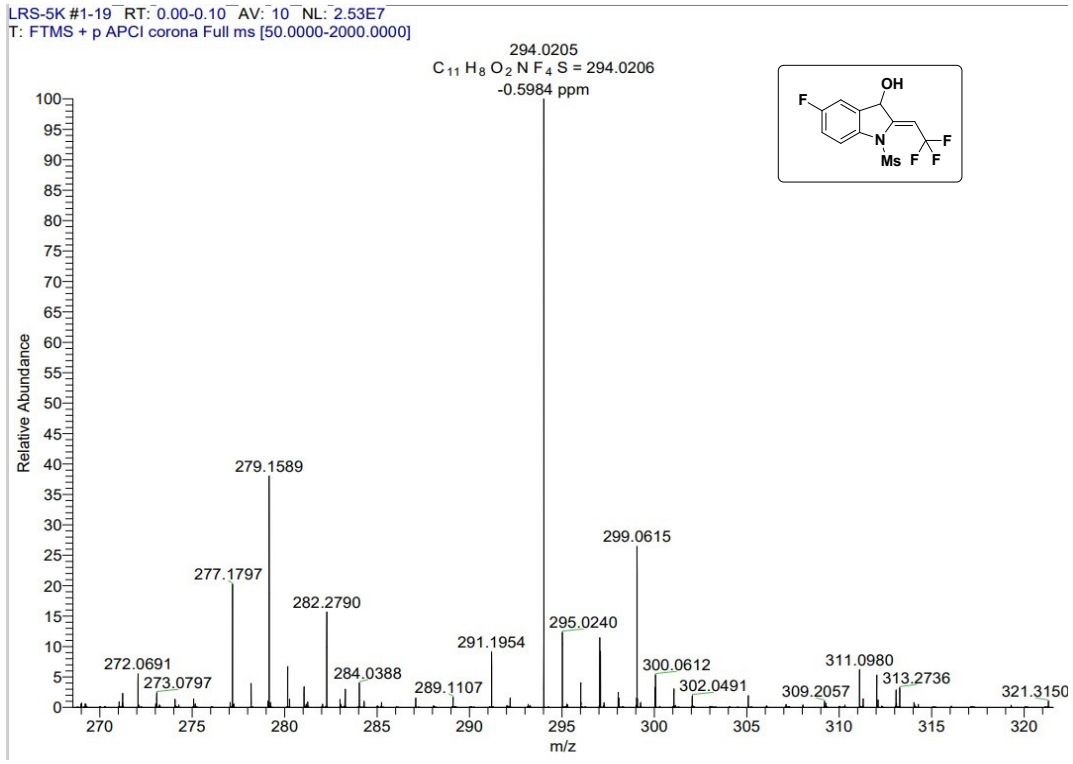
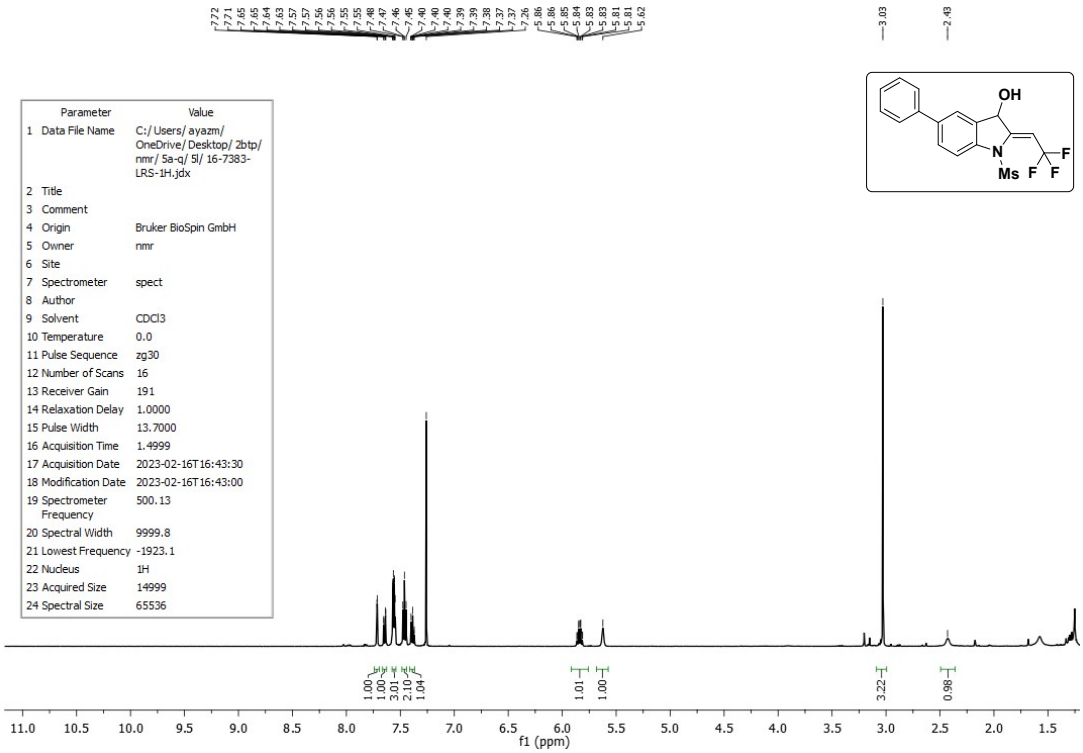
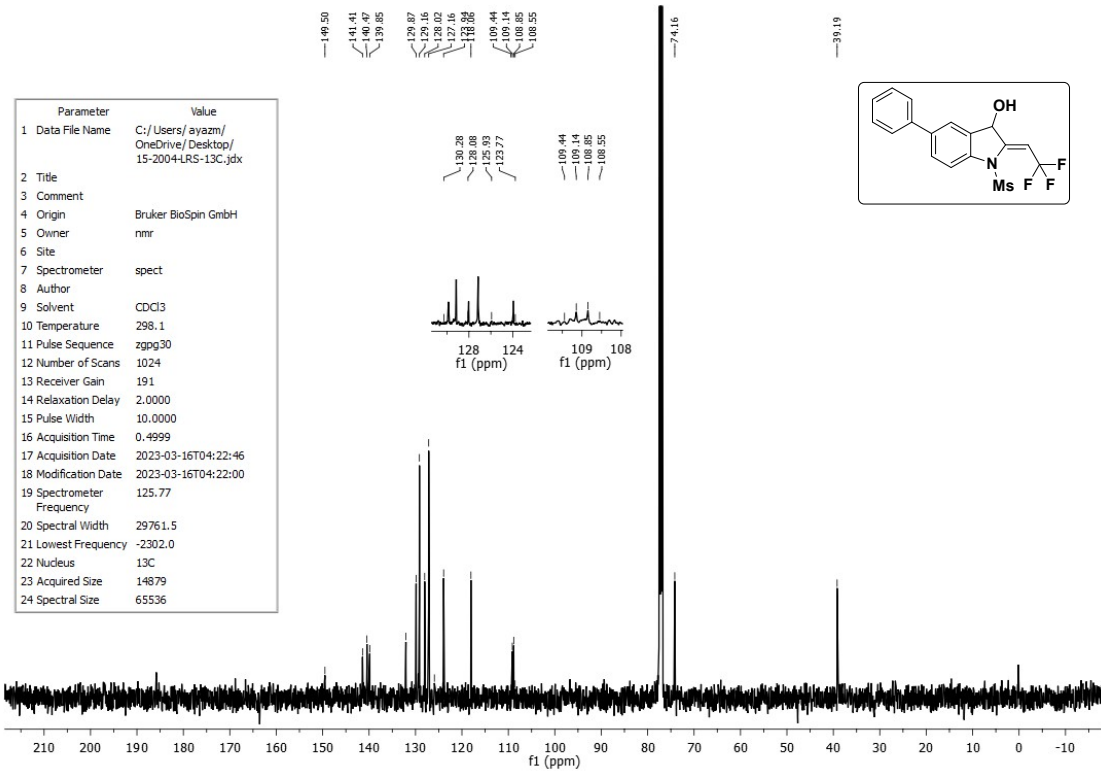
HRMS for 4h in APCI (+) MODE.



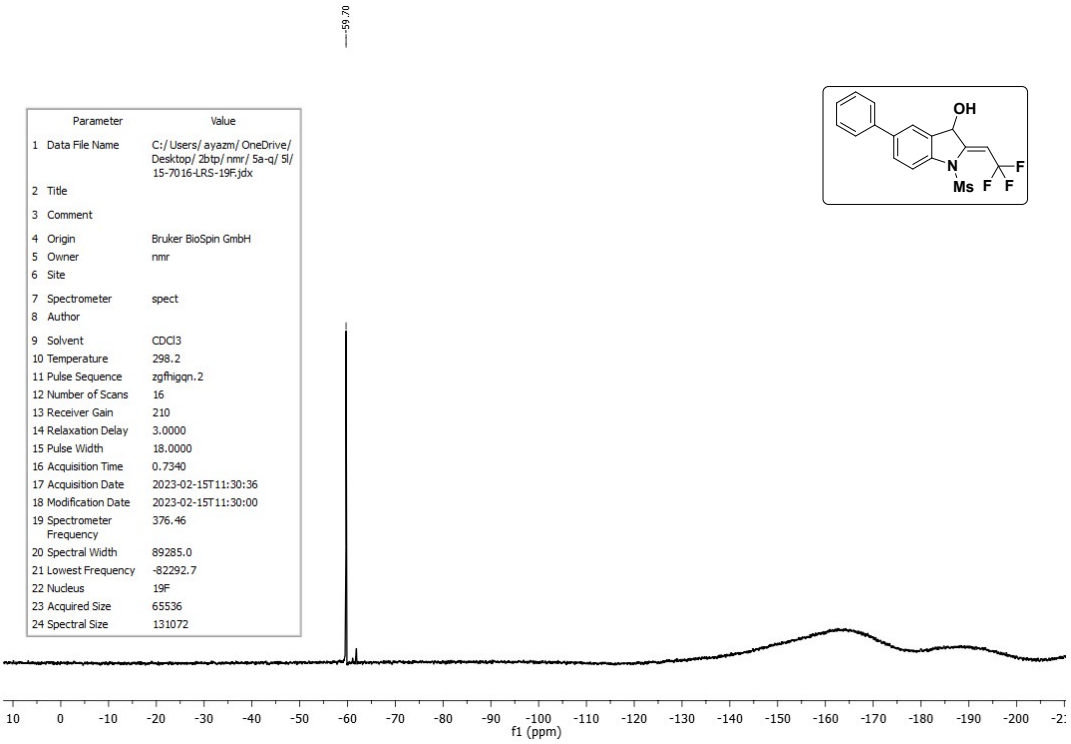
^{1}H NMR for 4i at 500 MHz



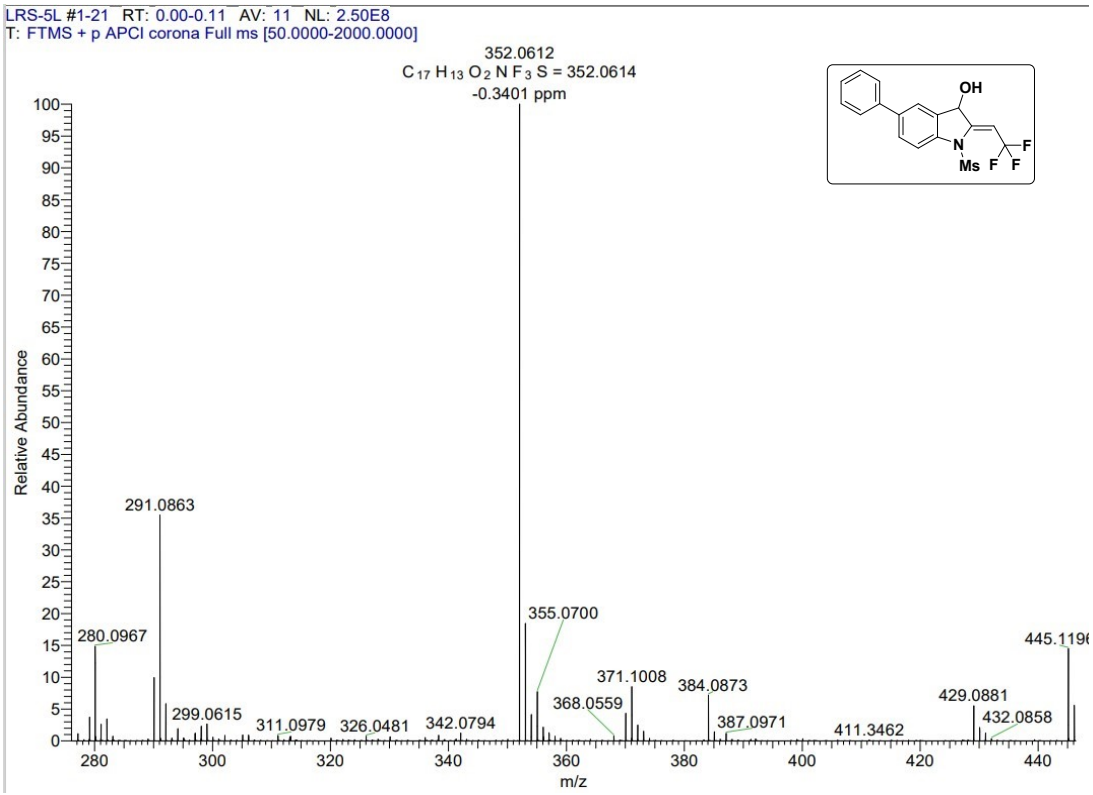
^{13}C NMR for 4i at 100 MHz



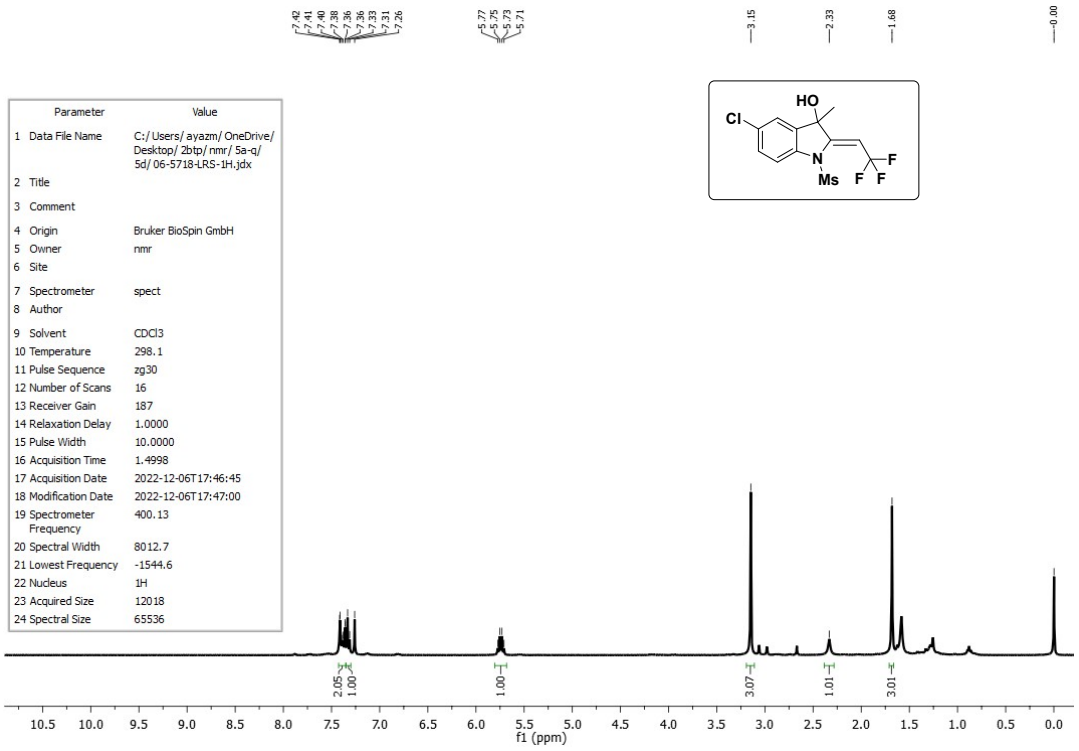
^{19}F NMR for 4i at 376 MHz



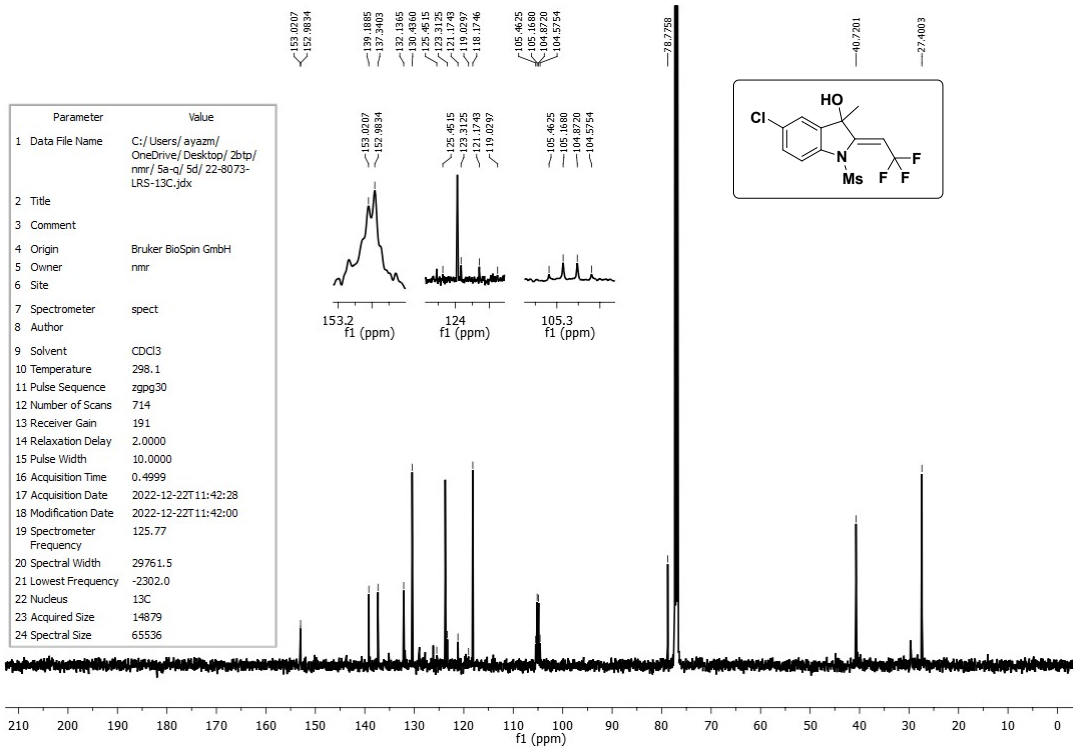
HRMS for 4i in APCI (+) MODE.



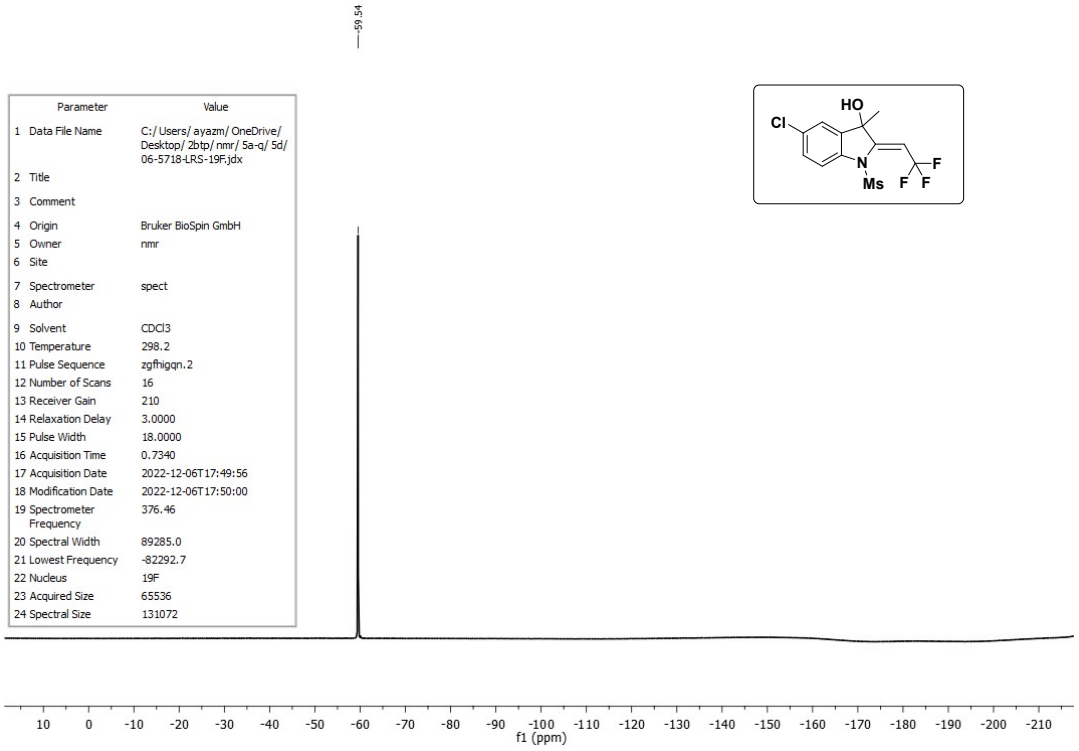
^{1}H NMR for 4j at 400 MHz



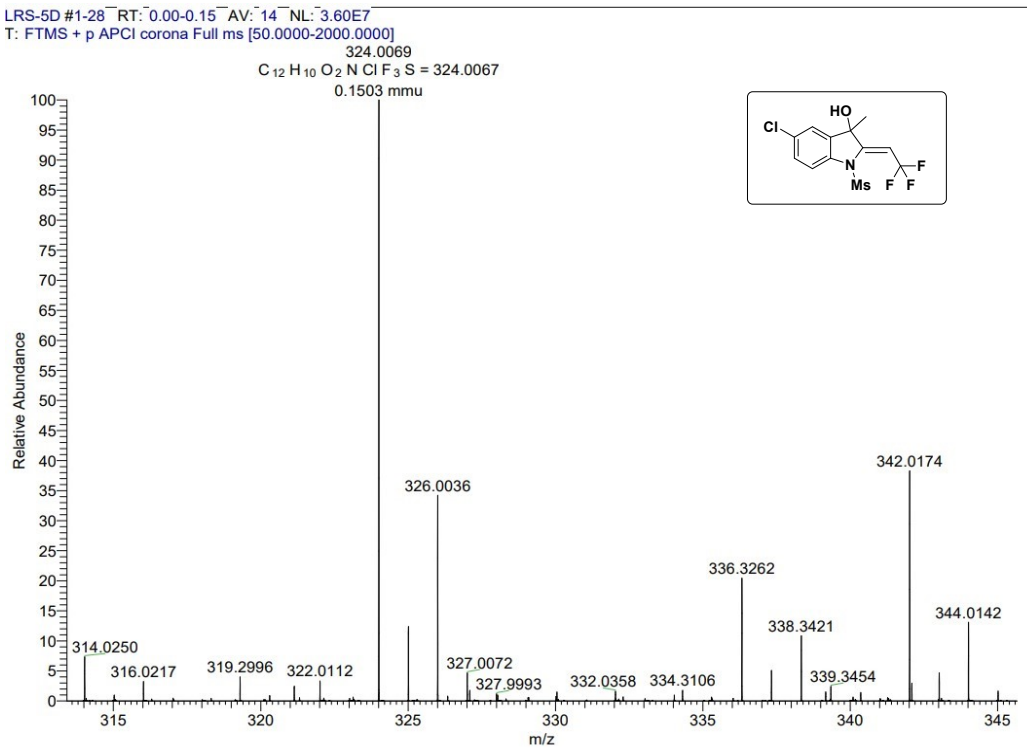
^{13}C NMR for 4j at 100 MHz



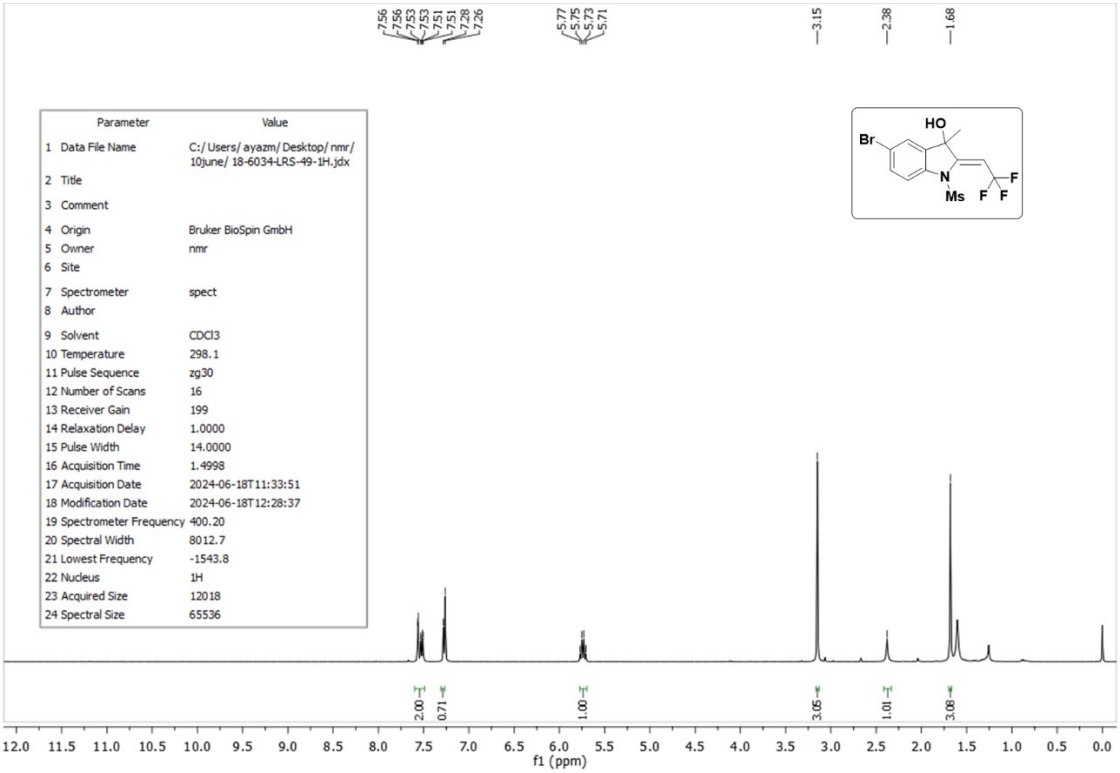
^{19}F NMR for 4j at 376 MHz



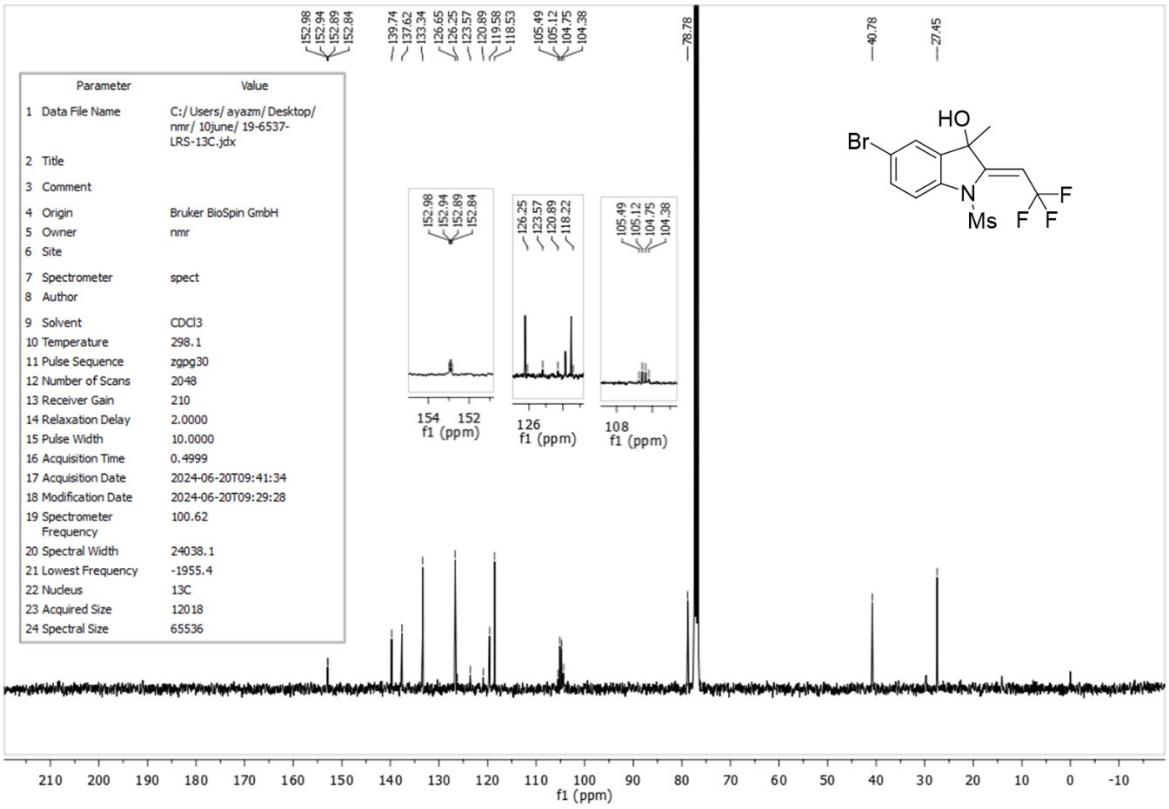
HRMS for 4j in APCI (+) MODE.



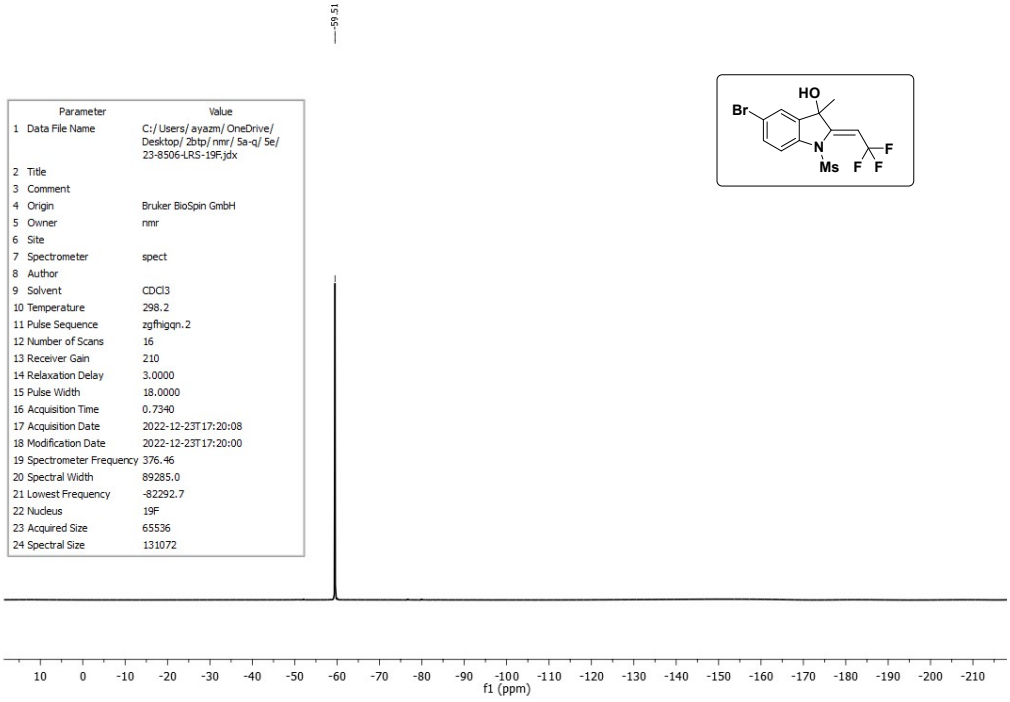
^{1}H NMR for 4k at 400 MHz



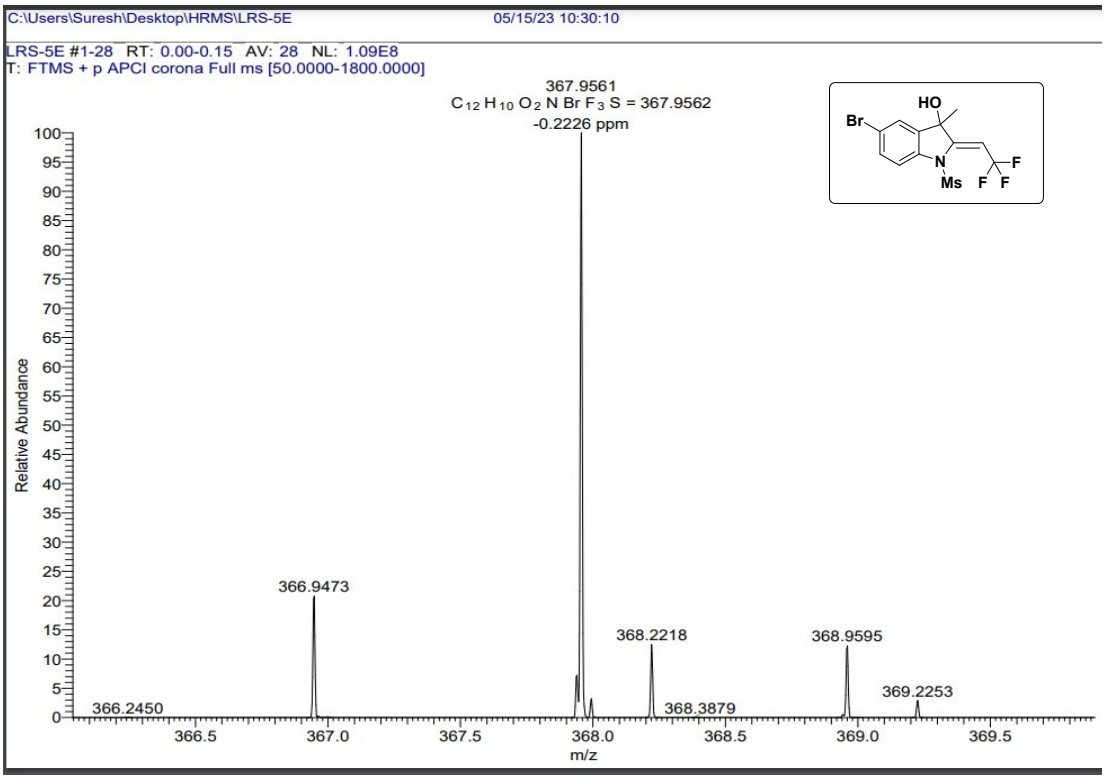
^{13}C NMR for 4k at 100 MHz



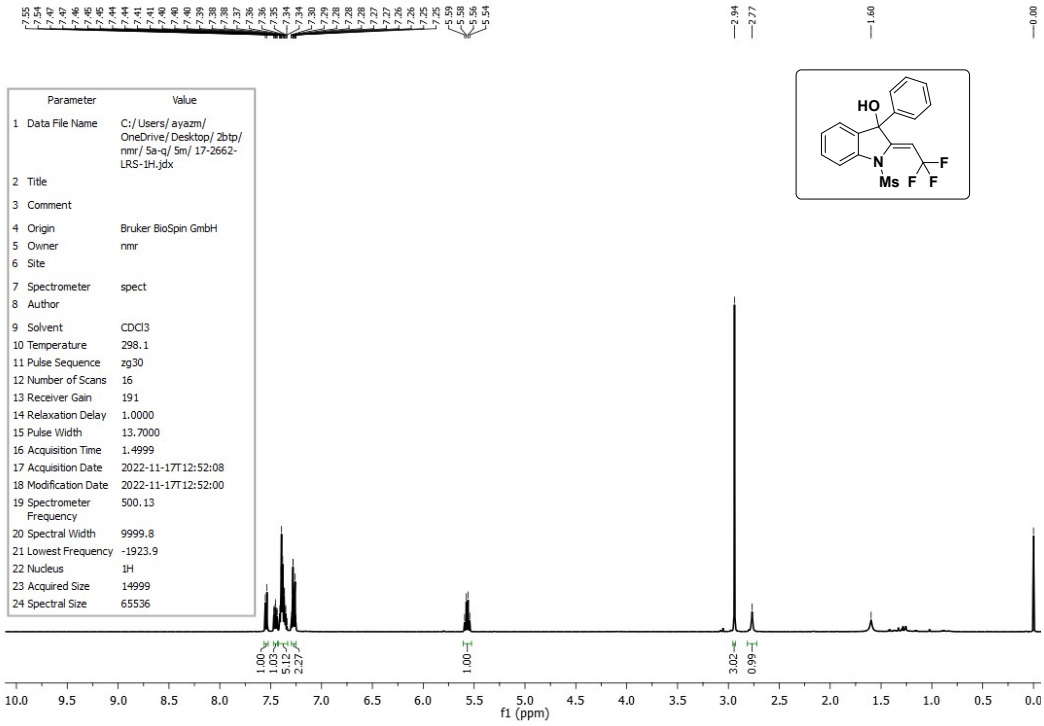
^{19}F NMR for 4k at 376 MHz



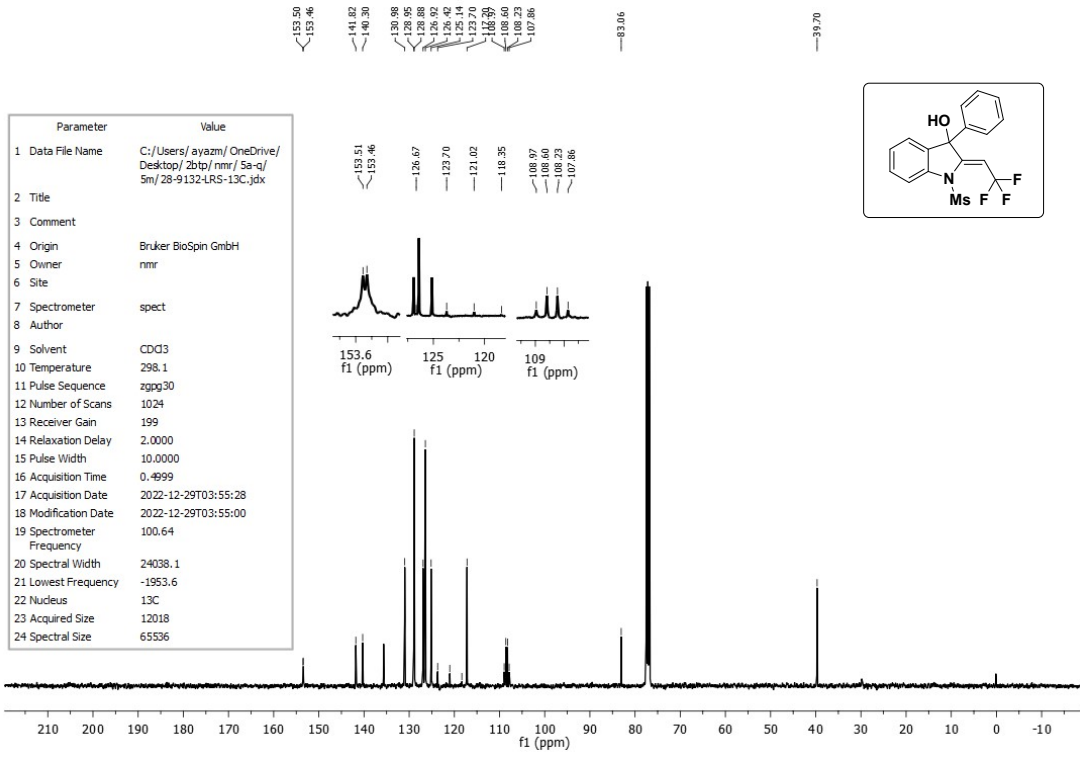
HRMS for 4k in APCI (+) MODE.



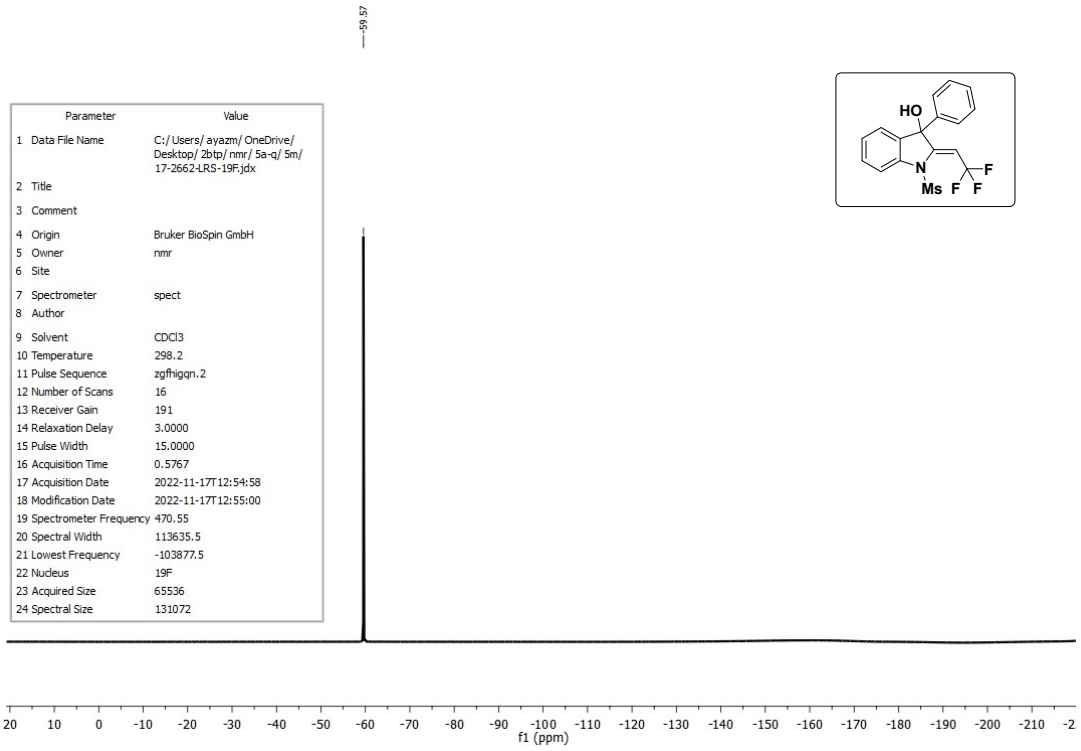
^{1}H NMR for 4l at 400 MHz



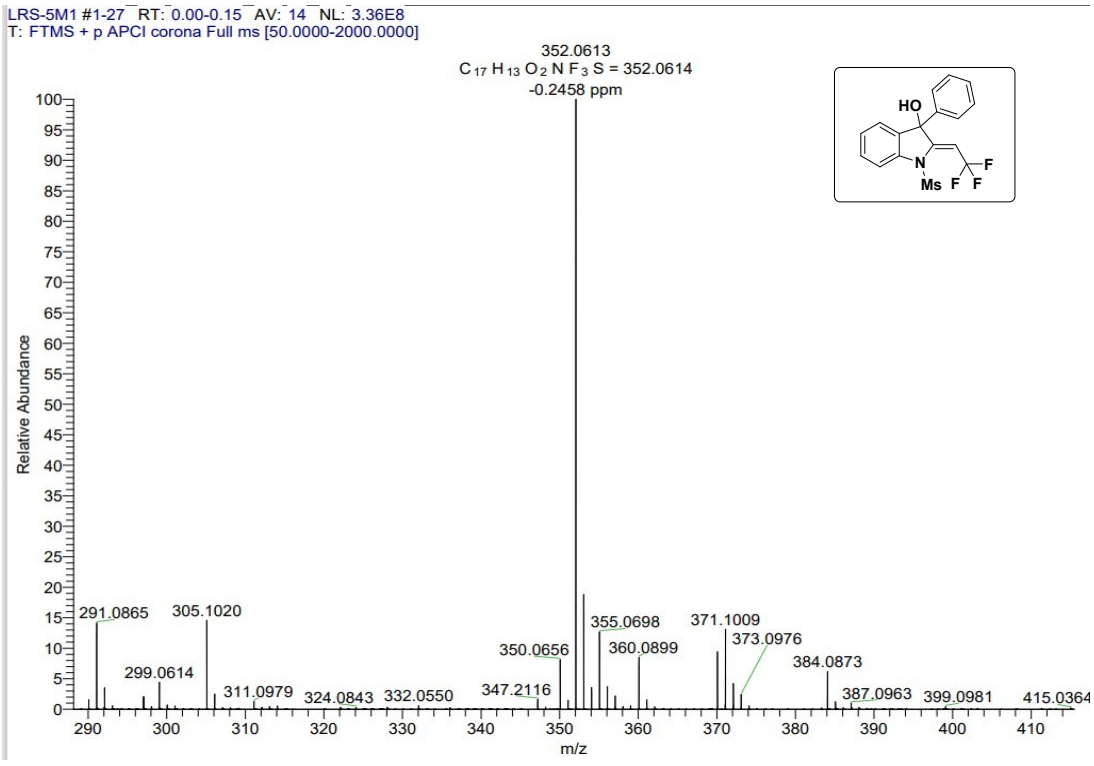
^{13}C NMR for 4l at 100 MHz



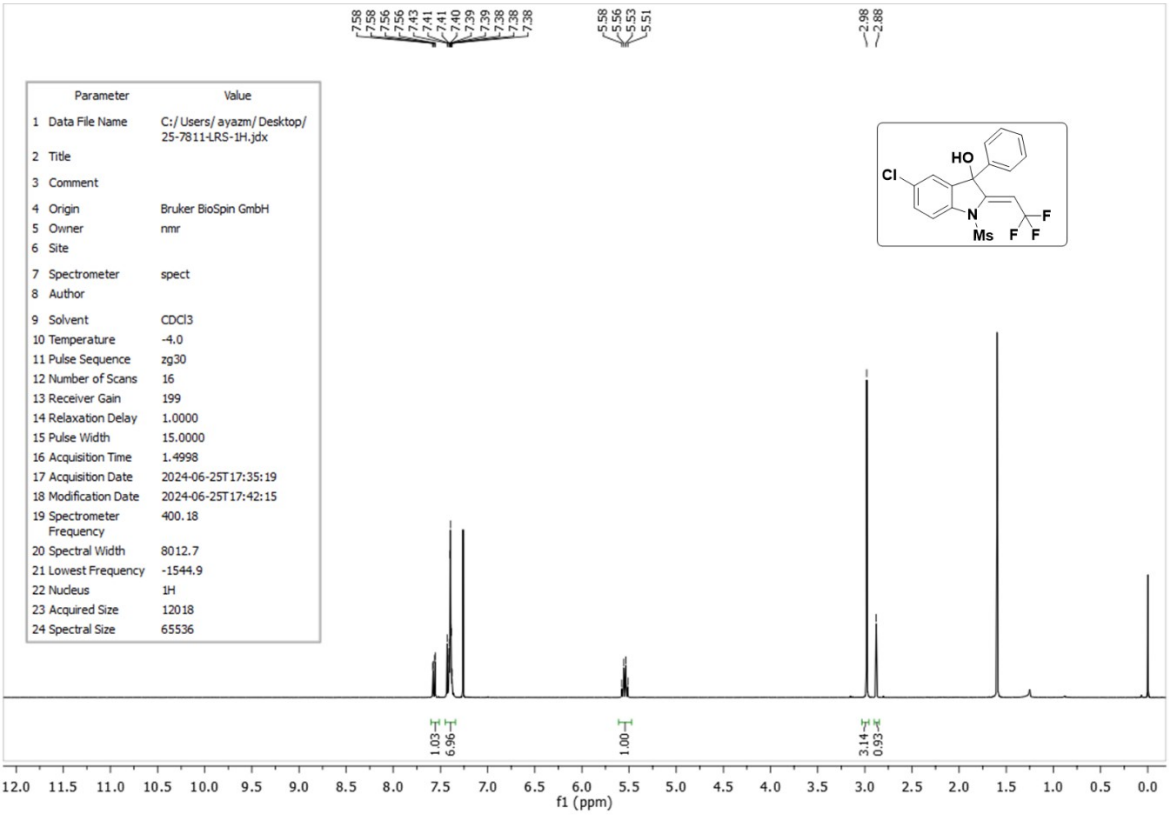
^{19}F NMR for 4l at 376 MHz



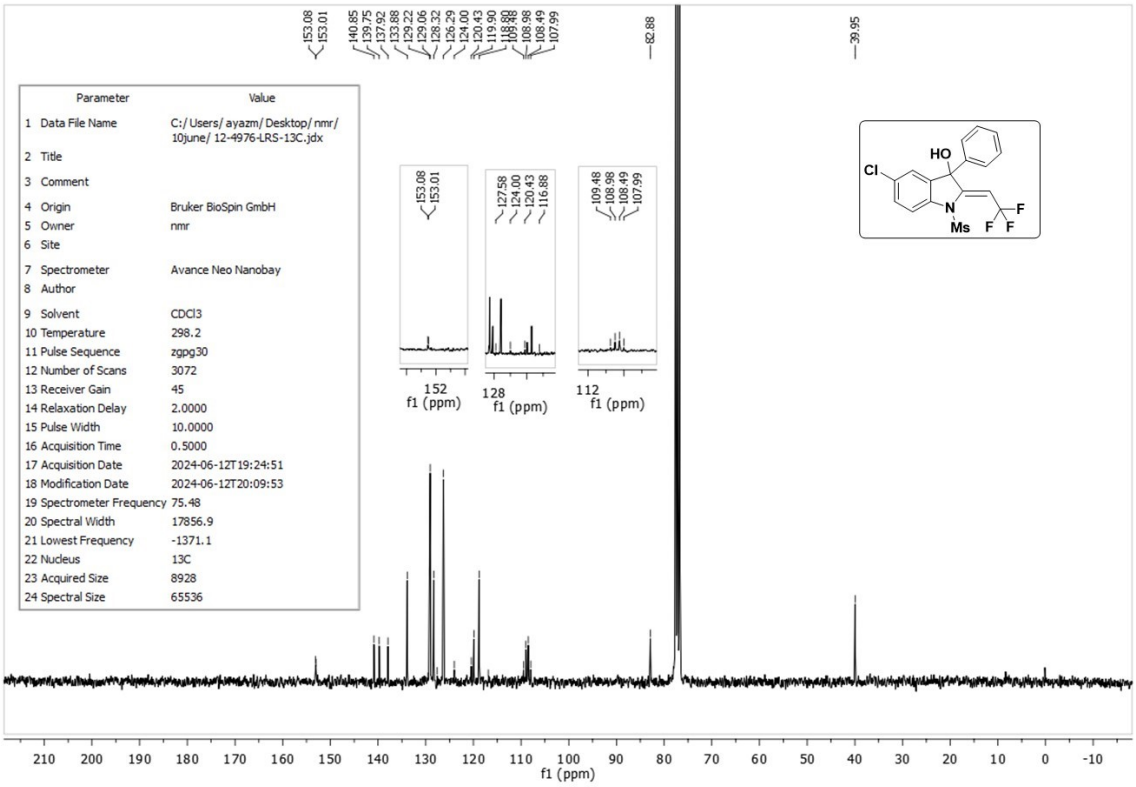
HRMS for 4l in APCI (+) MODE.



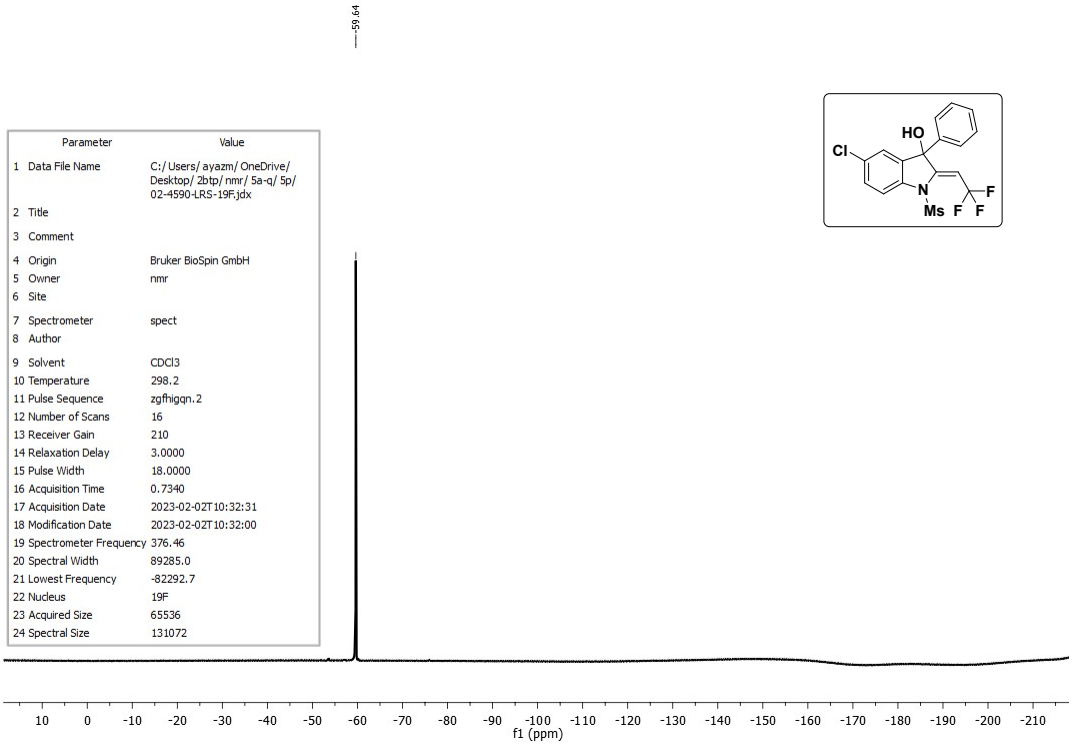
^{1}H NMR for 4m at 300 MHz



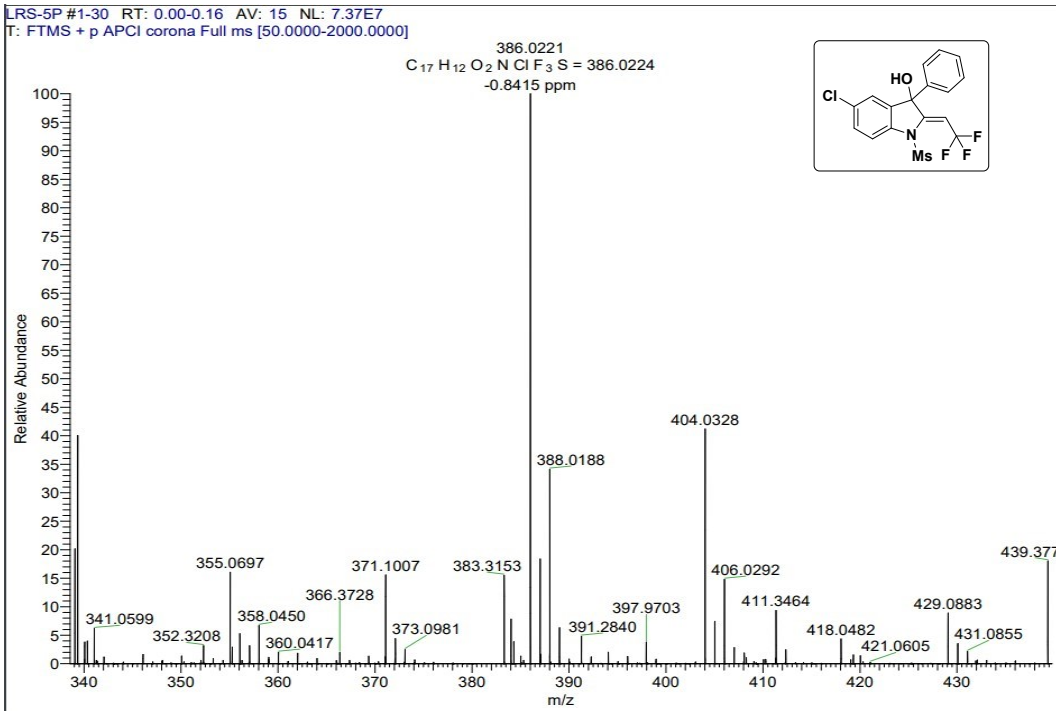
^{13}C NMR for 4m at 75 MHz



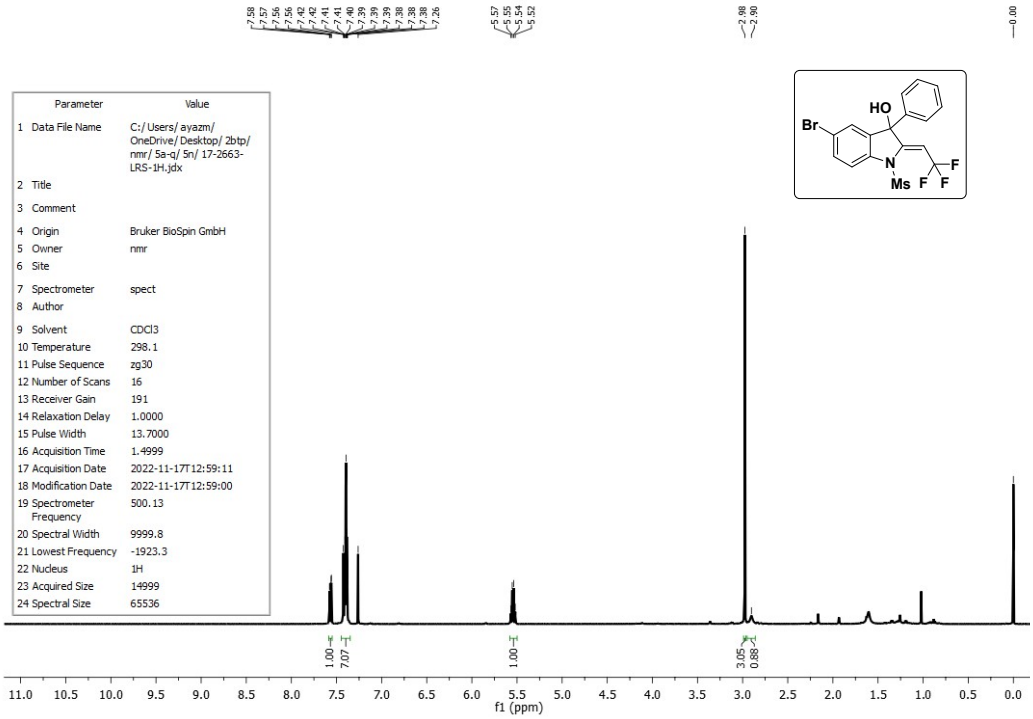
^{19}F NMR for 4m at 376 MHz



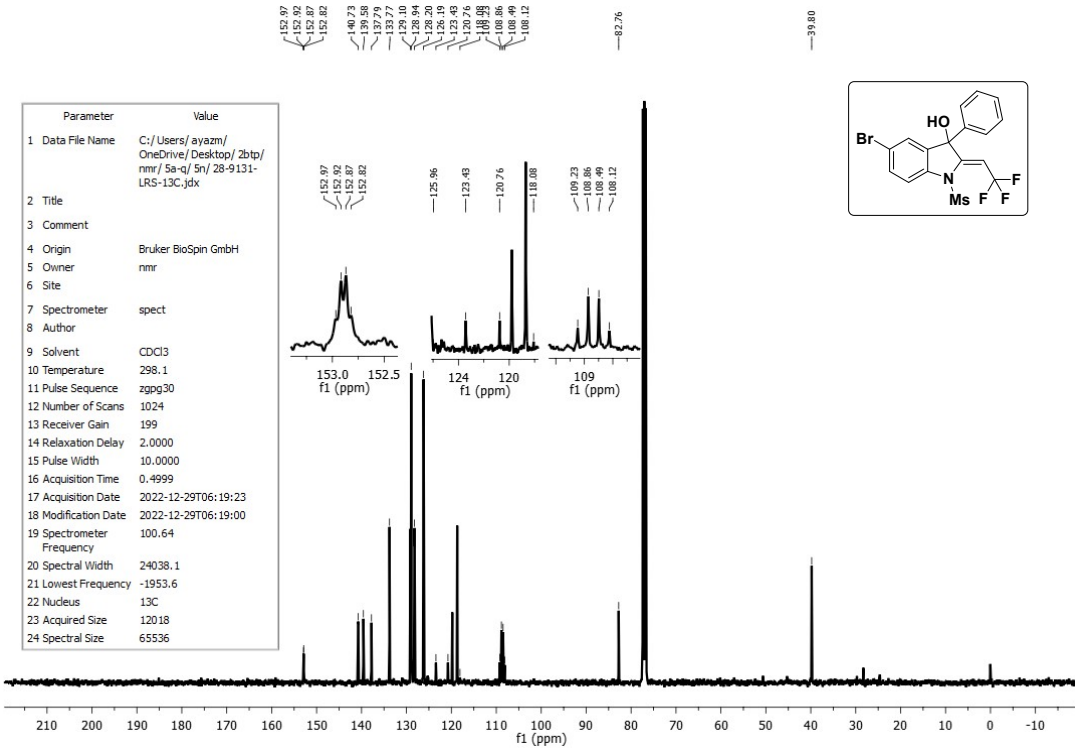
HRMS for 4m in APCI (-) MODE.



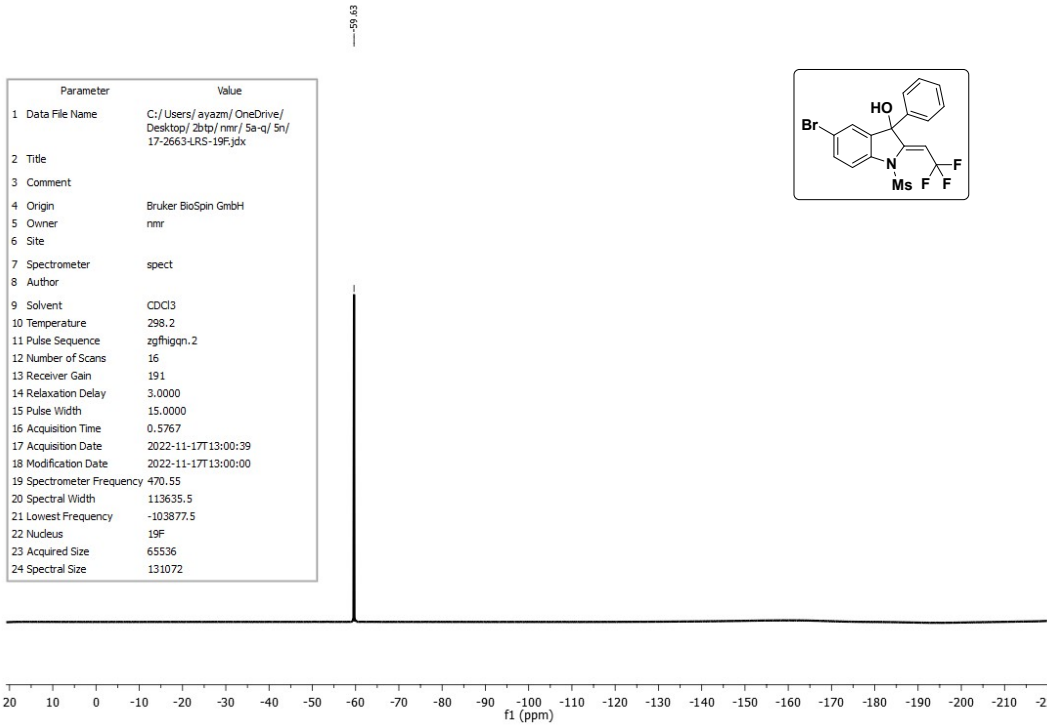
^{1}H NMR for 4n at 400 MHz



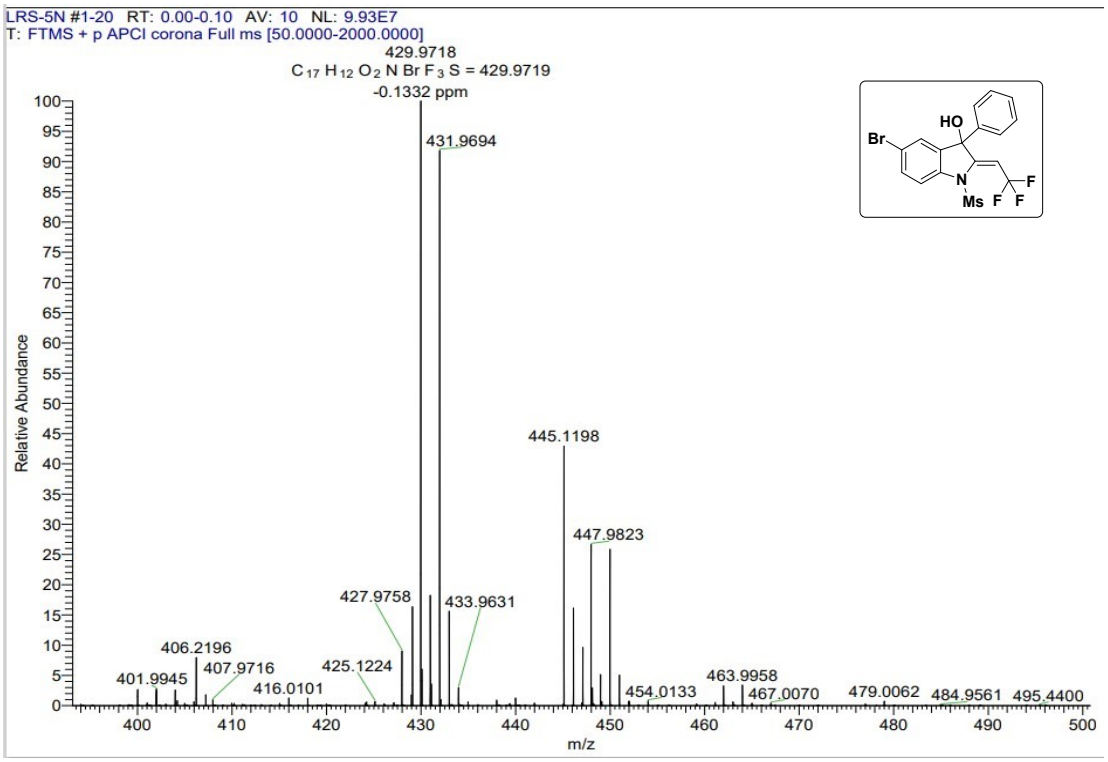
^{13}C NMR for 4n at 100 MHz



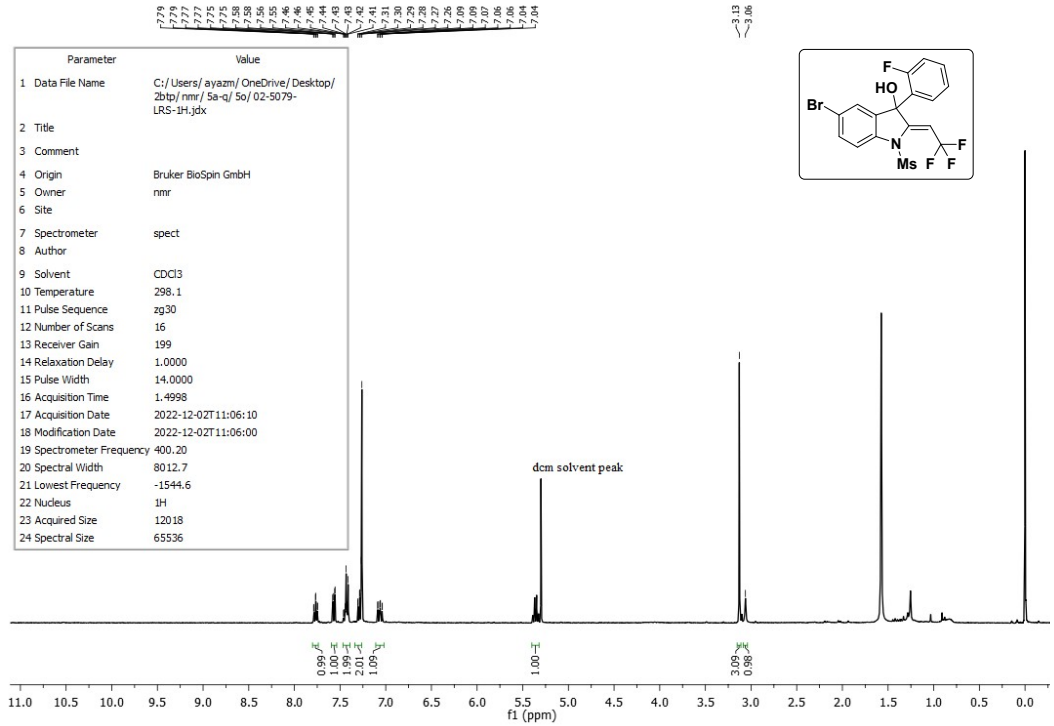
^{19}F NMR for 4n at 470 MHz



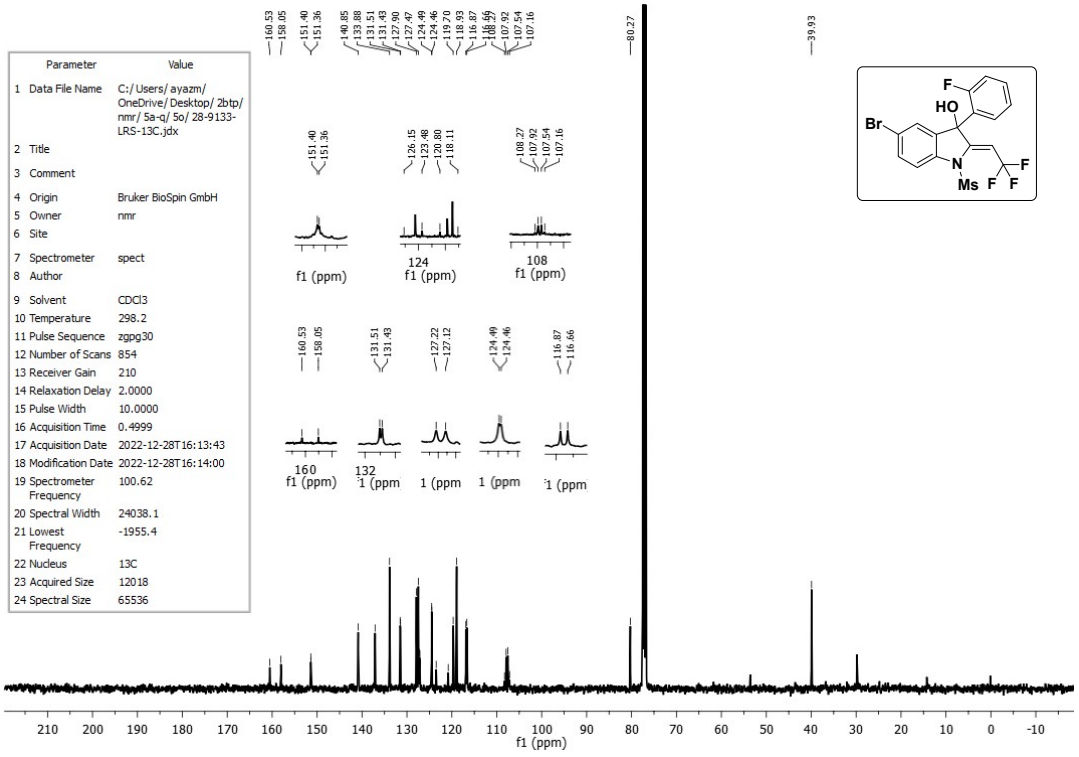
HRMS for 4n in APCI (+) MODE.



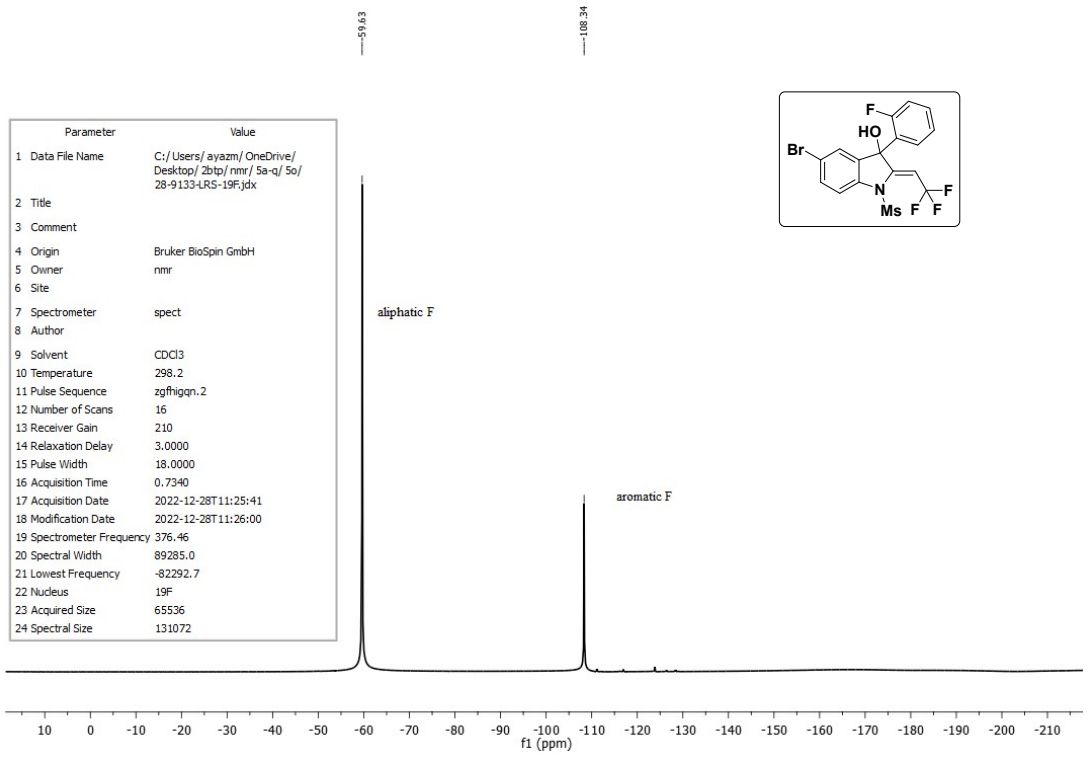
^{1}H NMR for 4o at 400 MHz



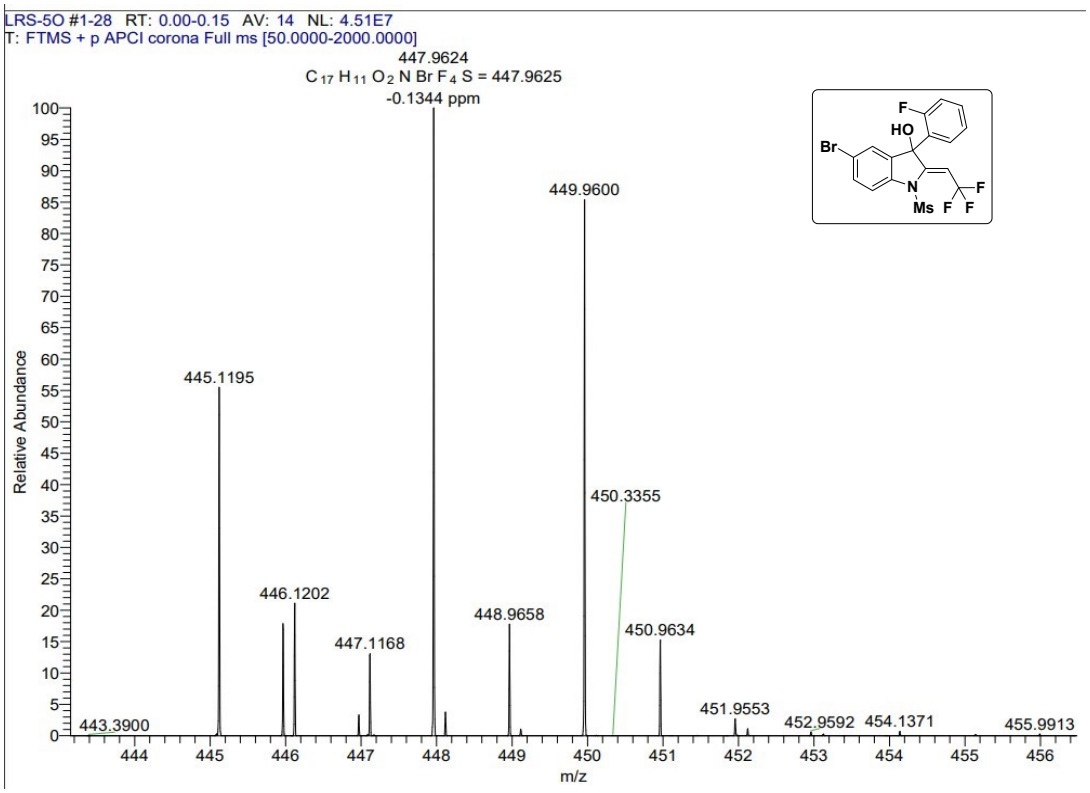
^{13}C NMR for 4o at 100 MHz



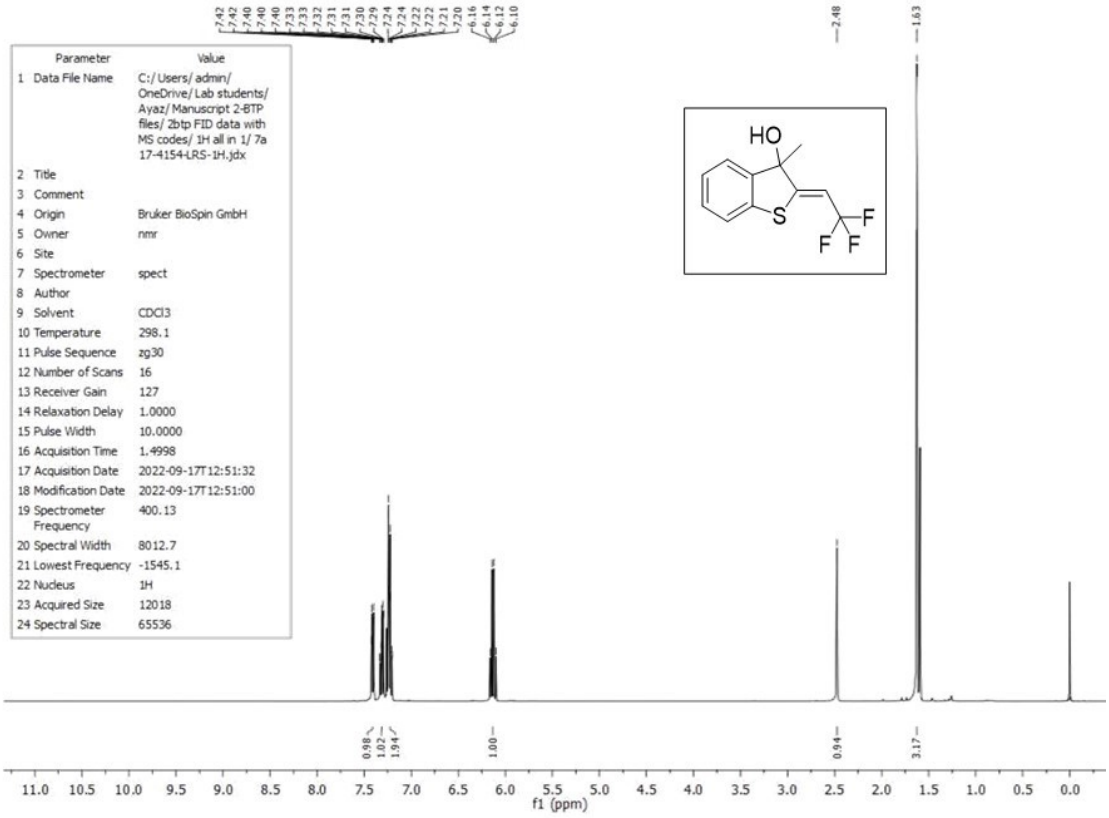
^{19}F NMR for 4o at 376 MHz



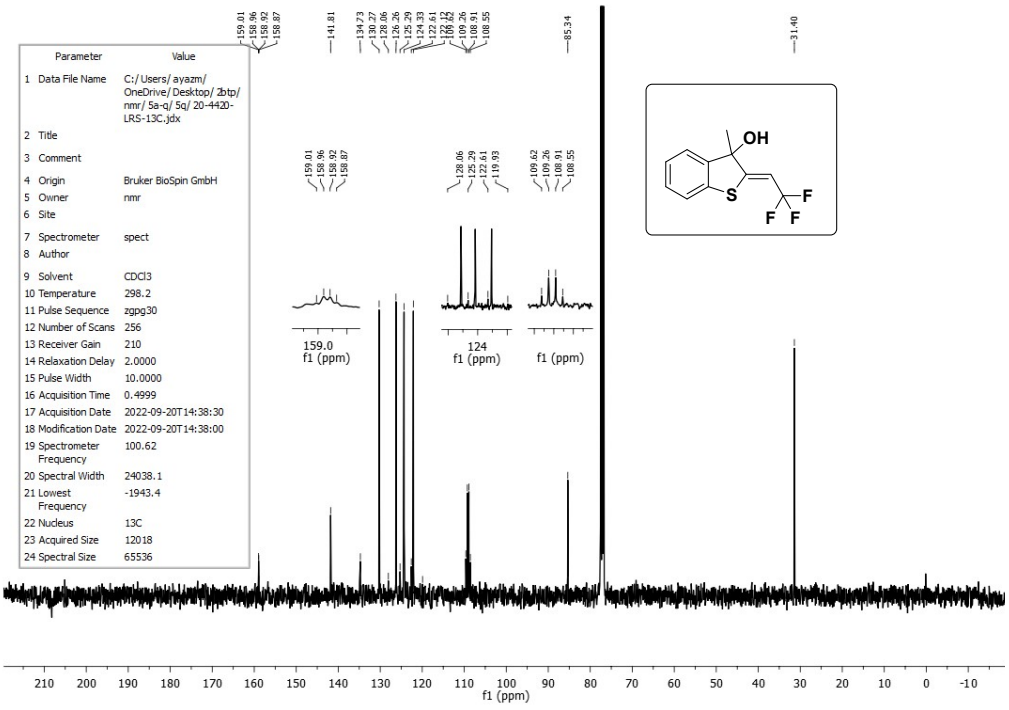
HRMS for 4o in APCI (+) MODE.



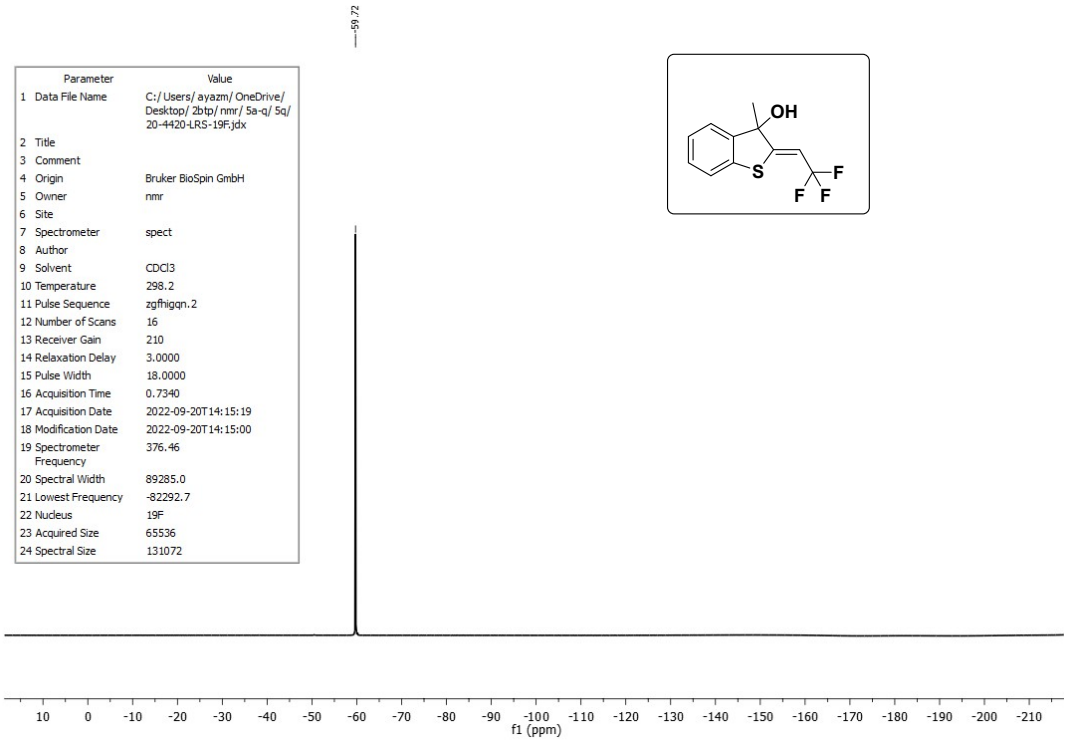
^{1}H NMR for 6a at 400 MHz



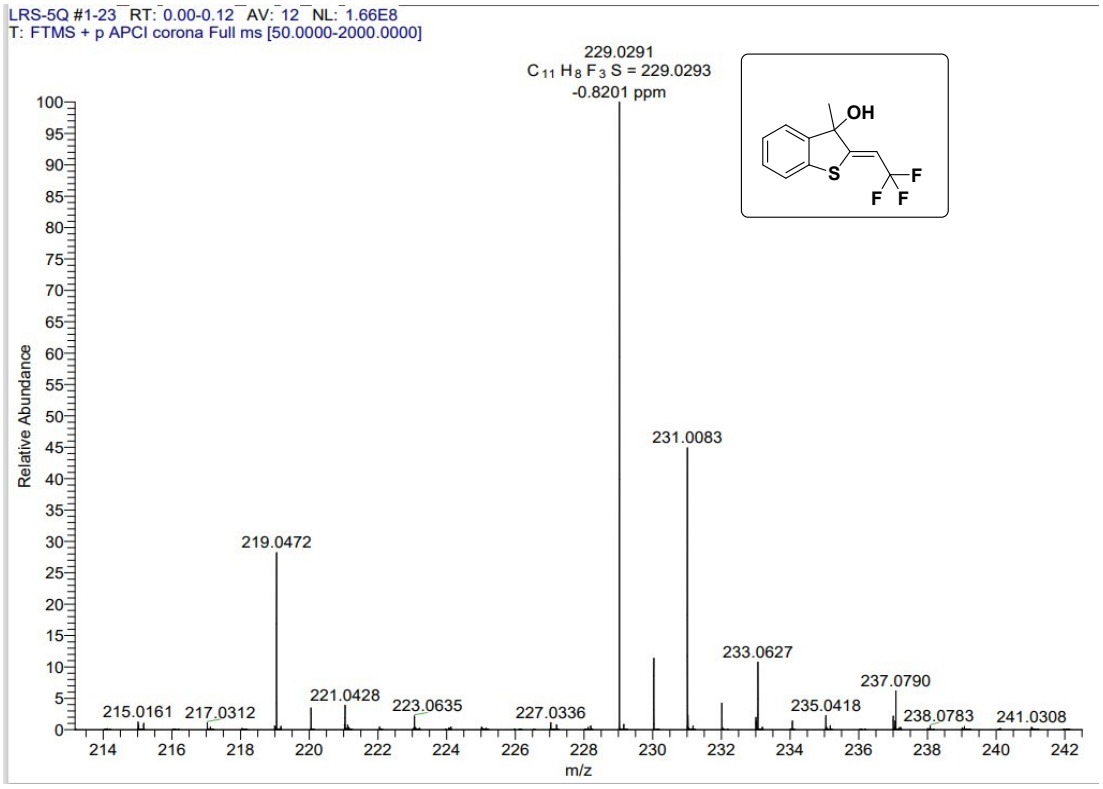
^{13}C NMR for 6a at 100 MHz



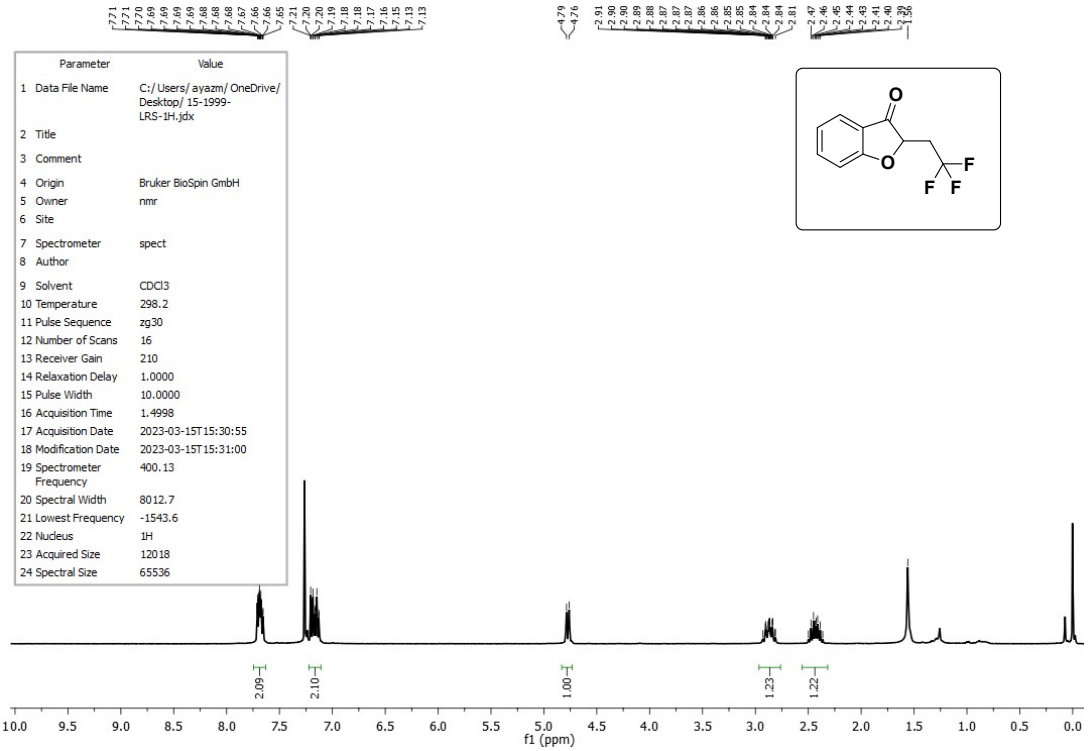
^{19}F NMR for 6a at 376 MHz



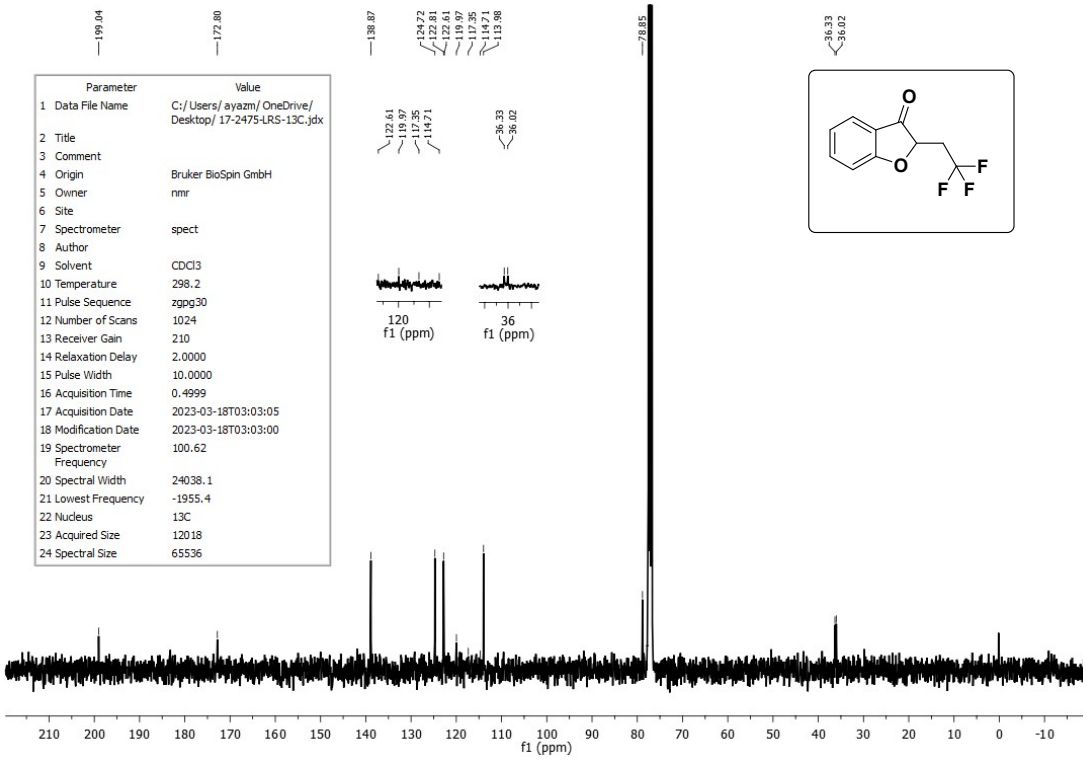
HRMS for 6a in APCI (+) MODE.



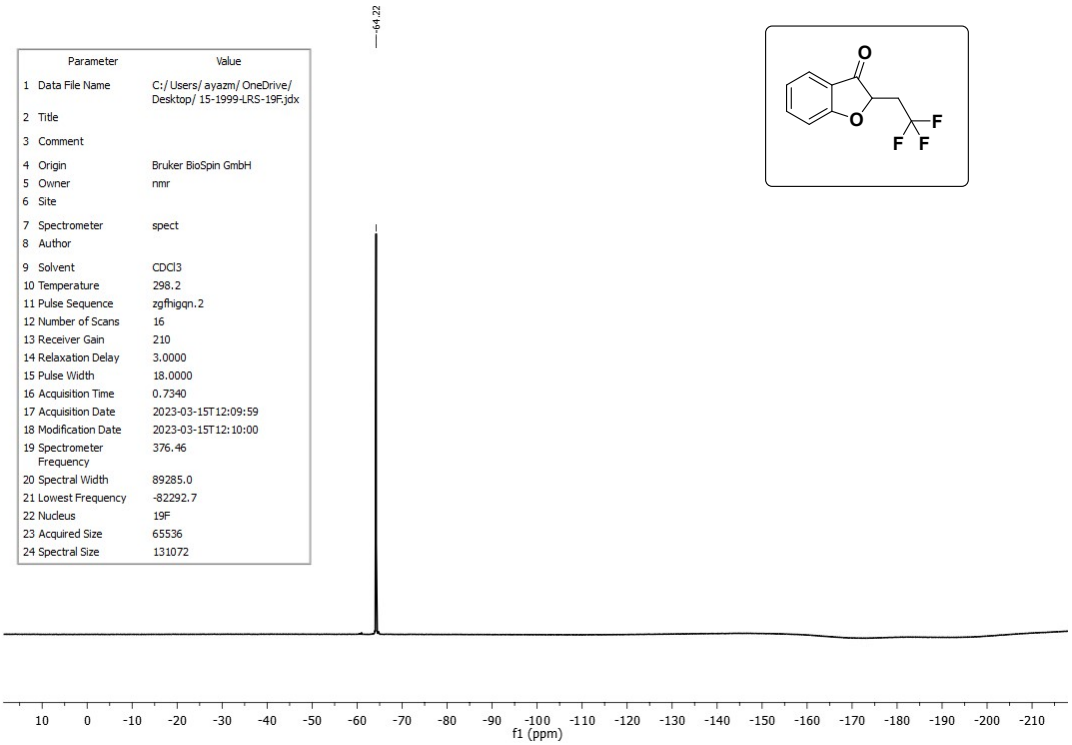
^{1}H NMR for 2aa at 400 MHz



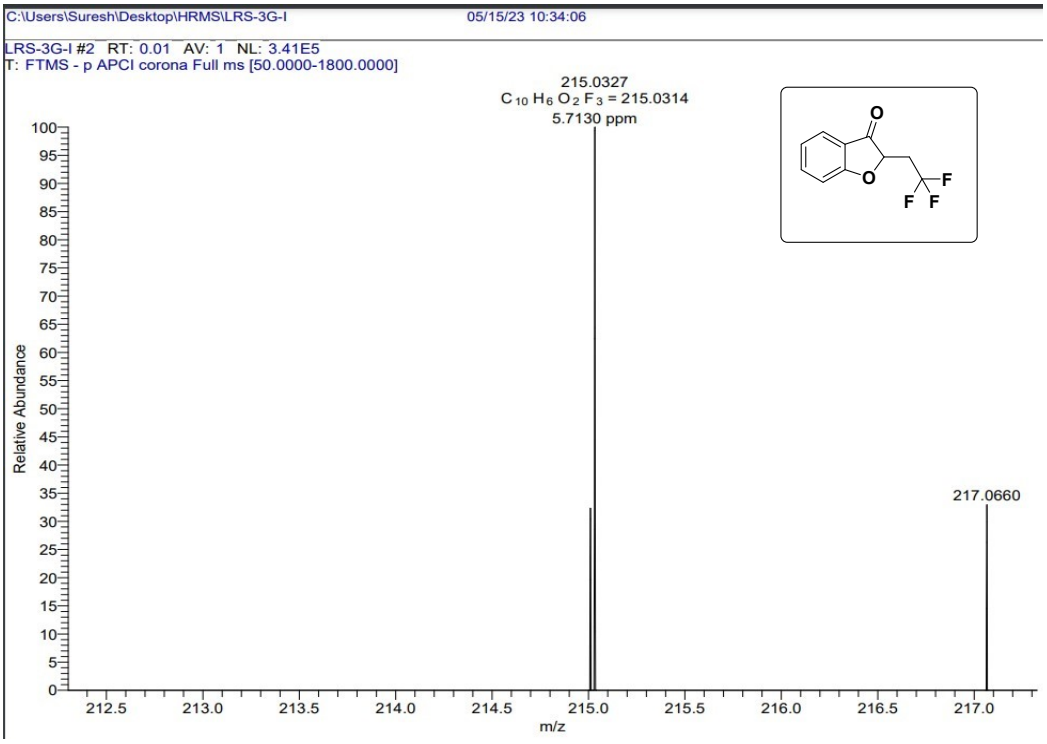
^{13}C NMR for 2aa at 100 MHz



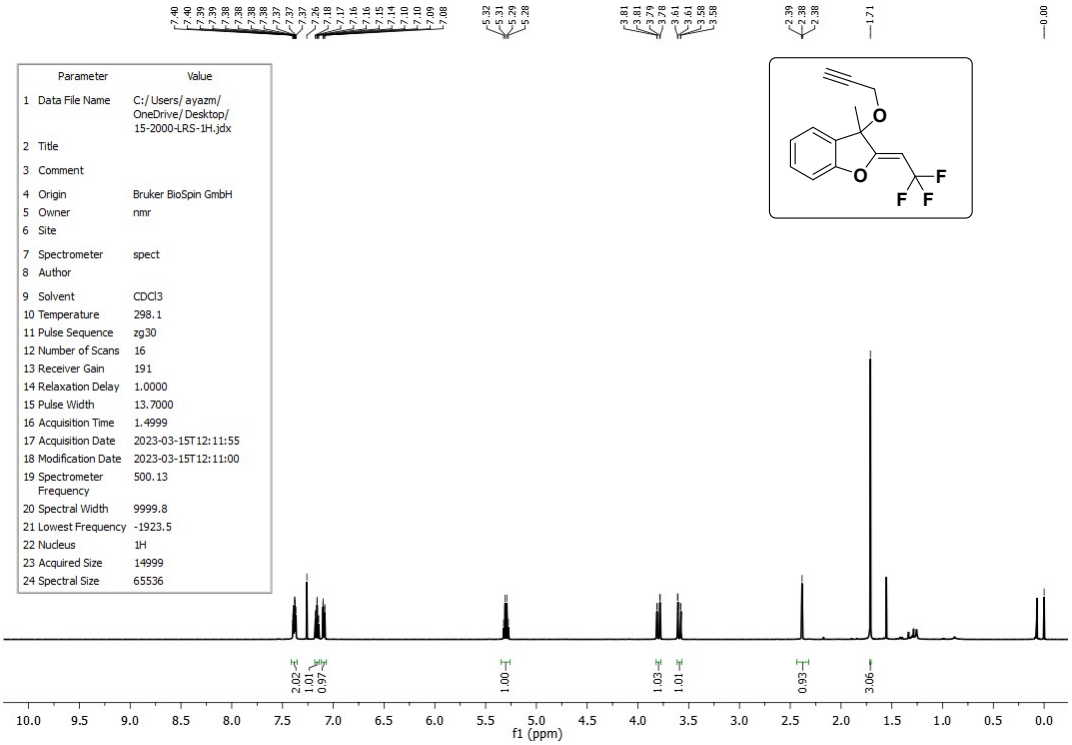
^{19}F NMR for 2aa at 376 MHz



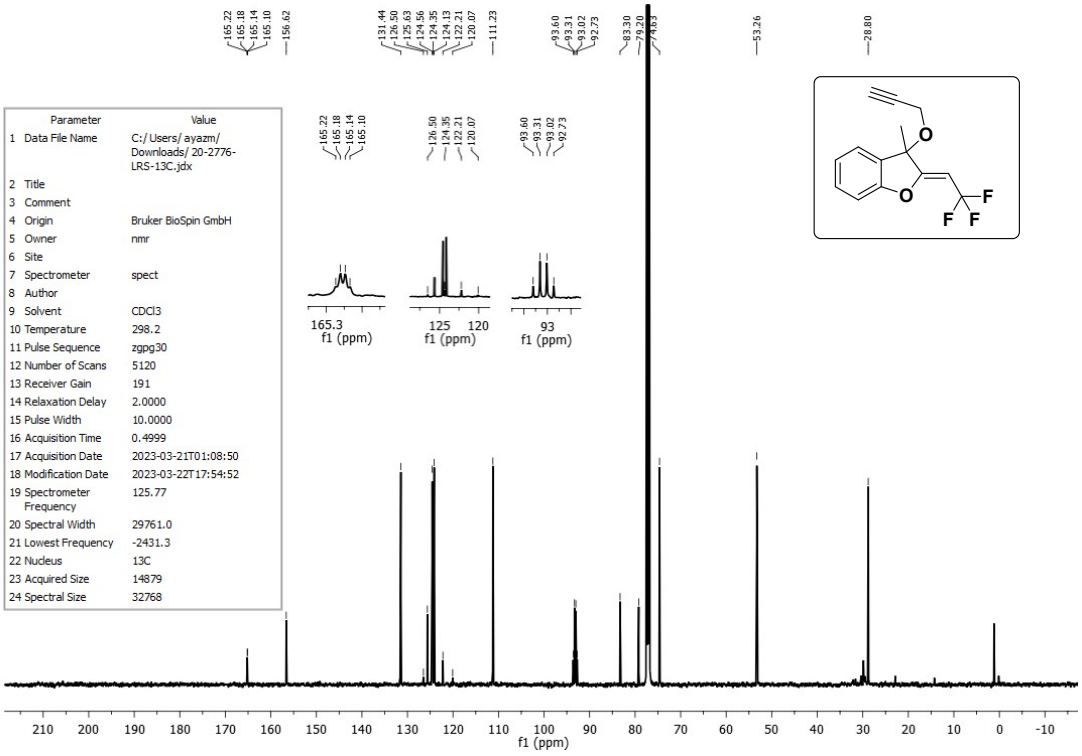
HRMS for 2aa in APCI (-) MODE.



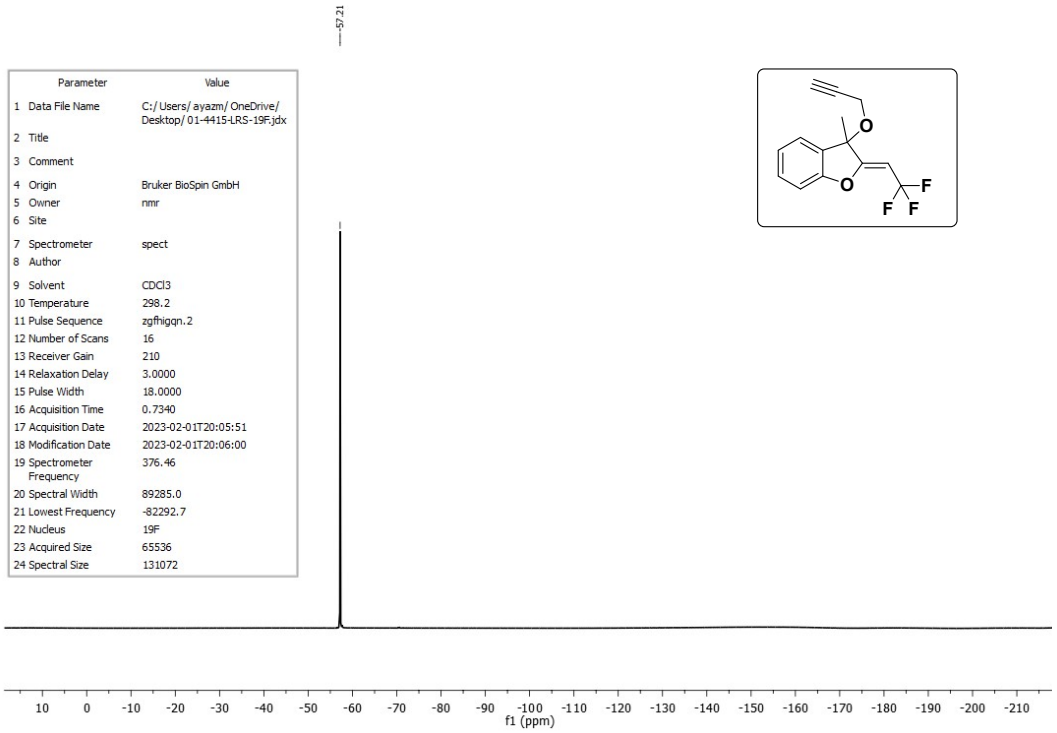
^{1}H NMR for 2ga at 400 MHz



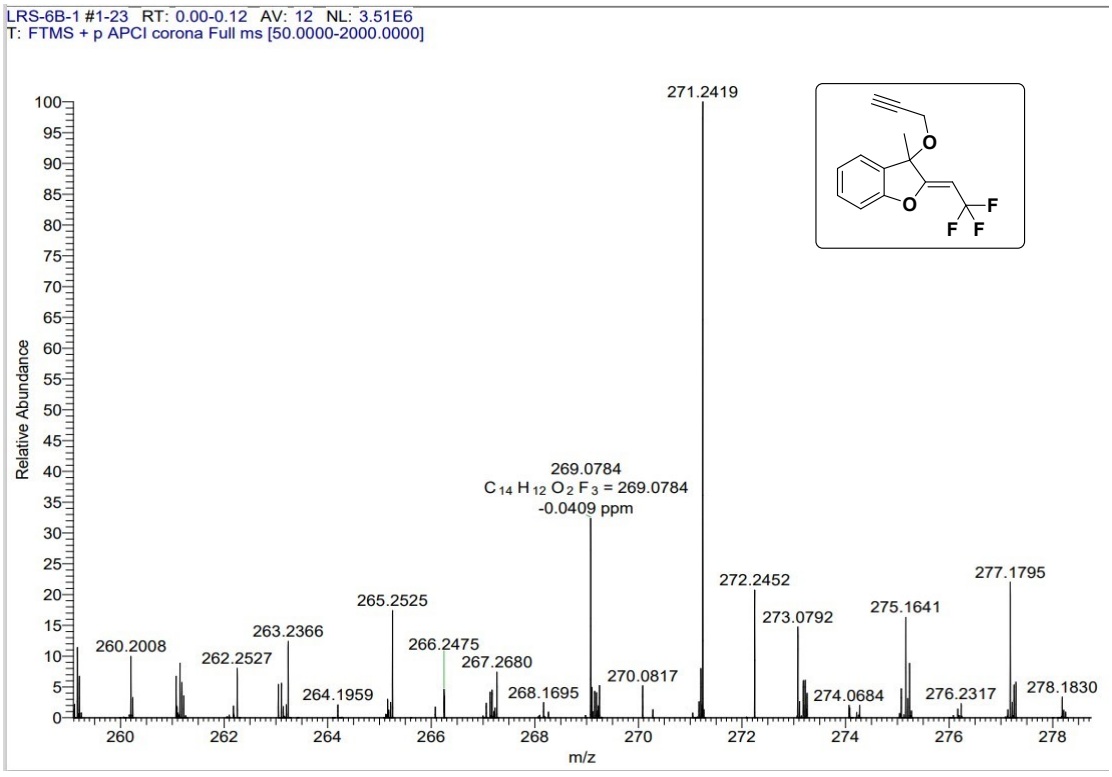
^{13}C NMR for 2ga at 100 MHz



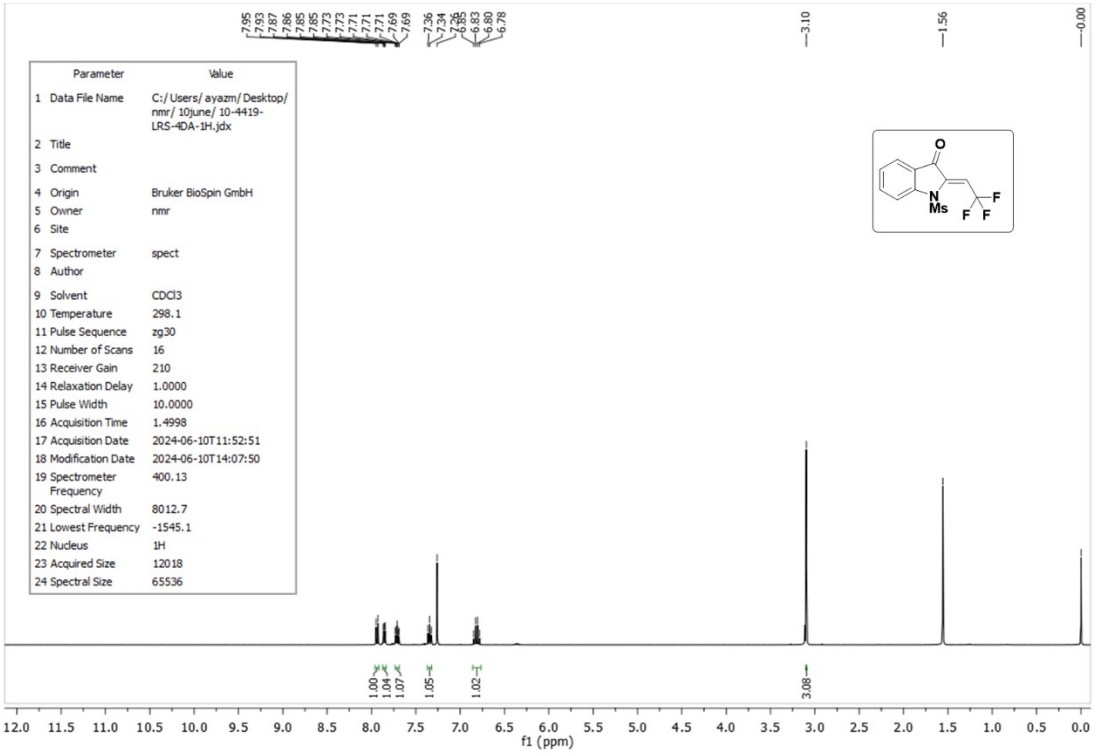
^{19}F NMR for 2ga at 376 MHz



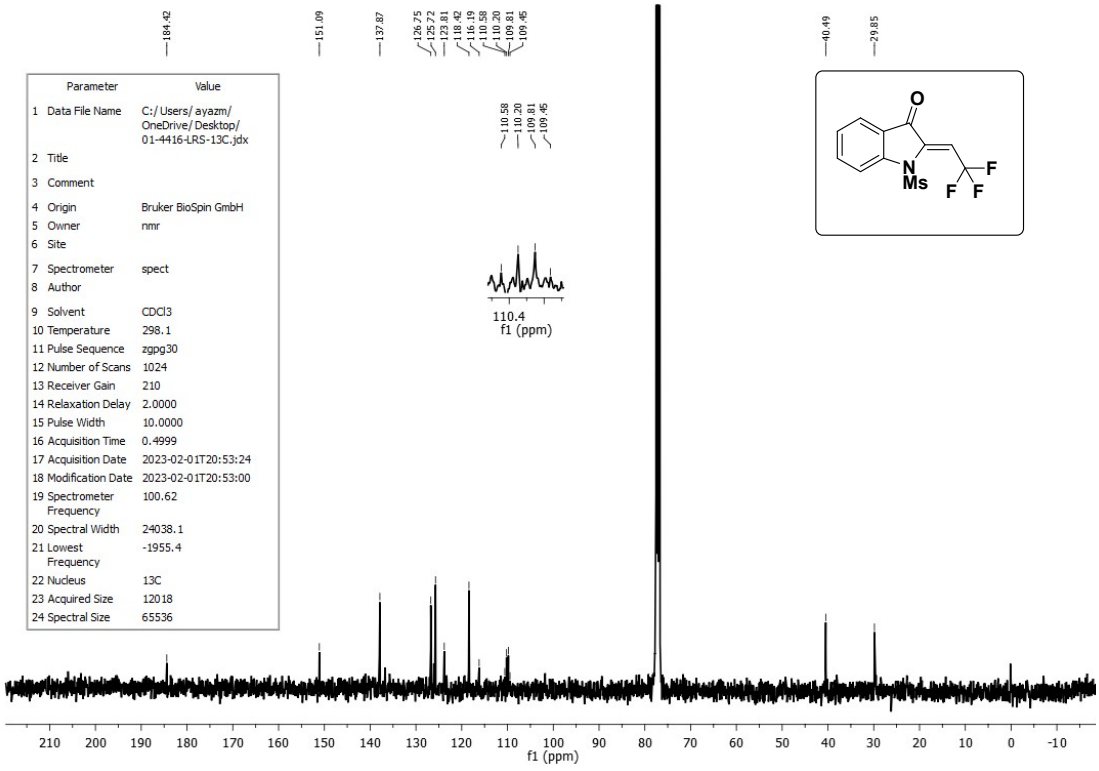
HRMS for 2ga in APCI (+) MODE.



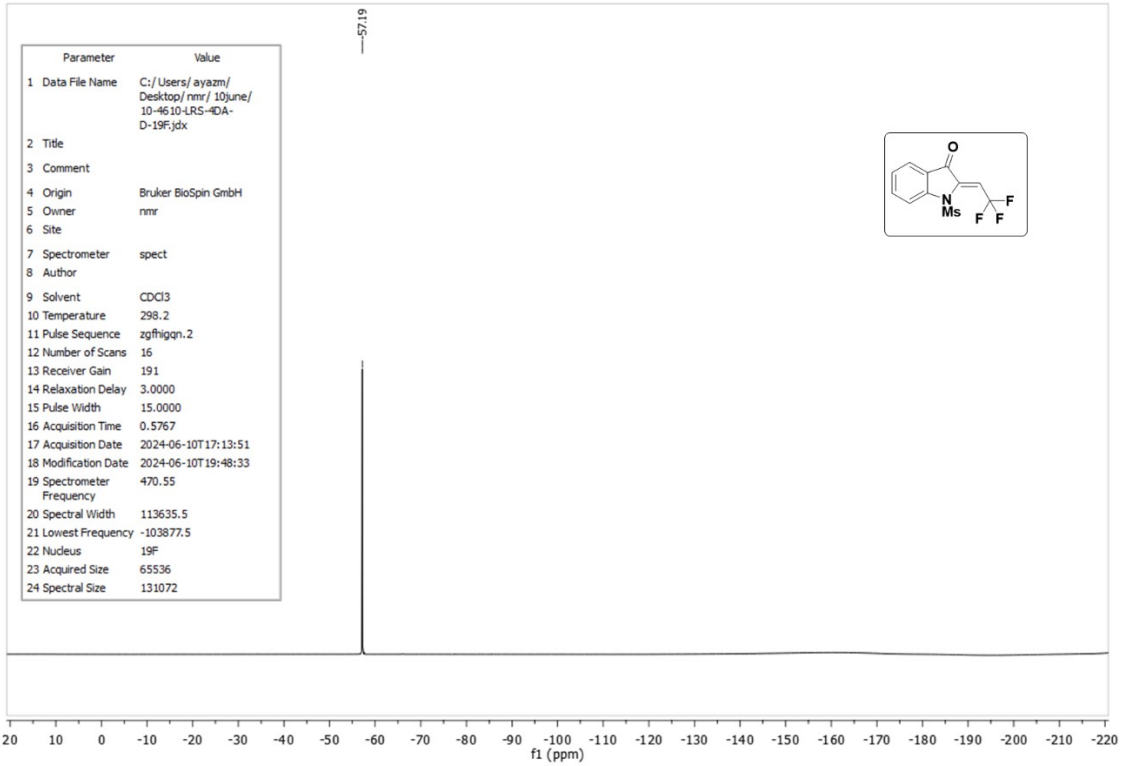
^{1}H NMR for 4da at 400 MHz



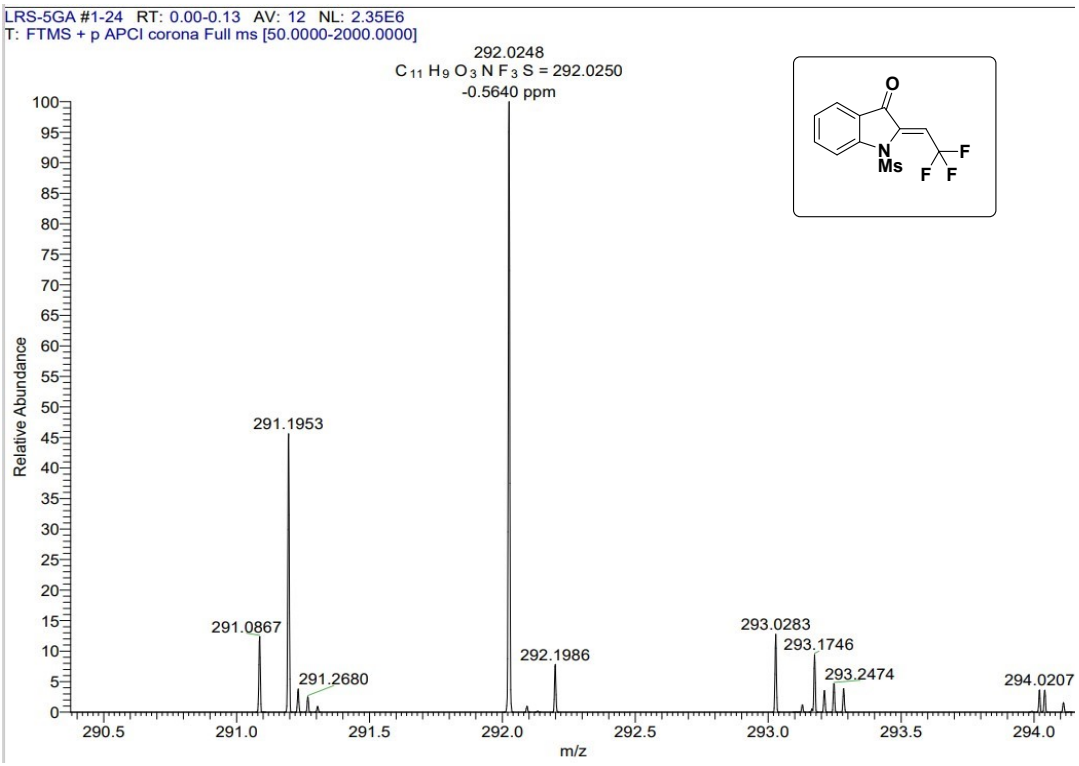
^{13}C NMR for 4da at 100 MHz



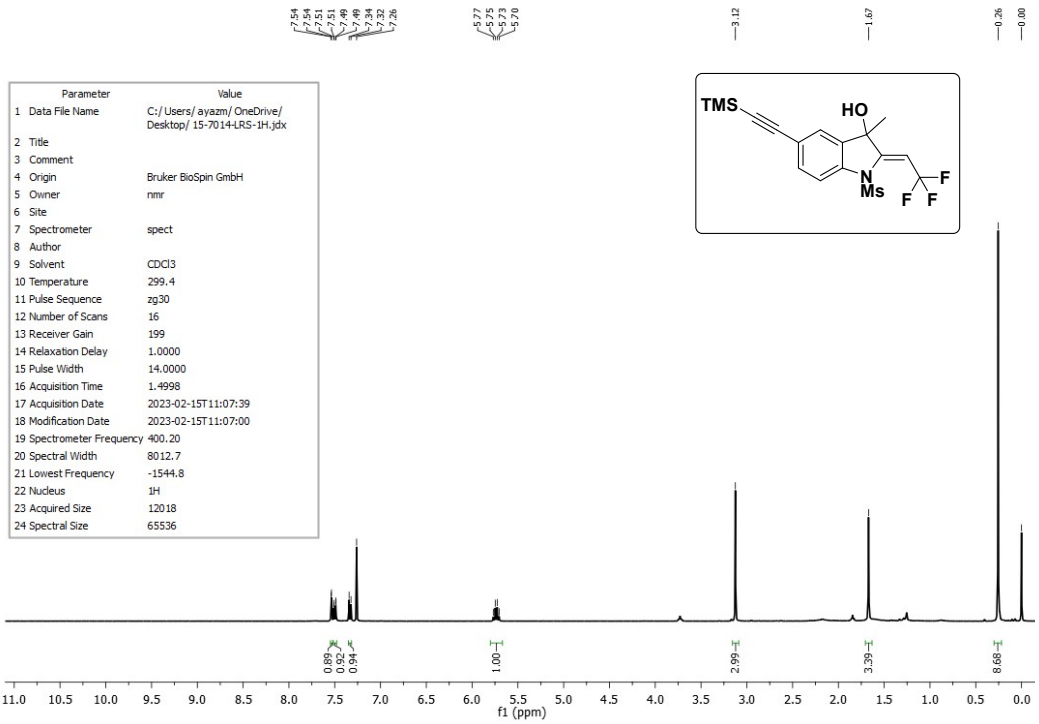
^{19}F NMR for 4da at 470 MHz



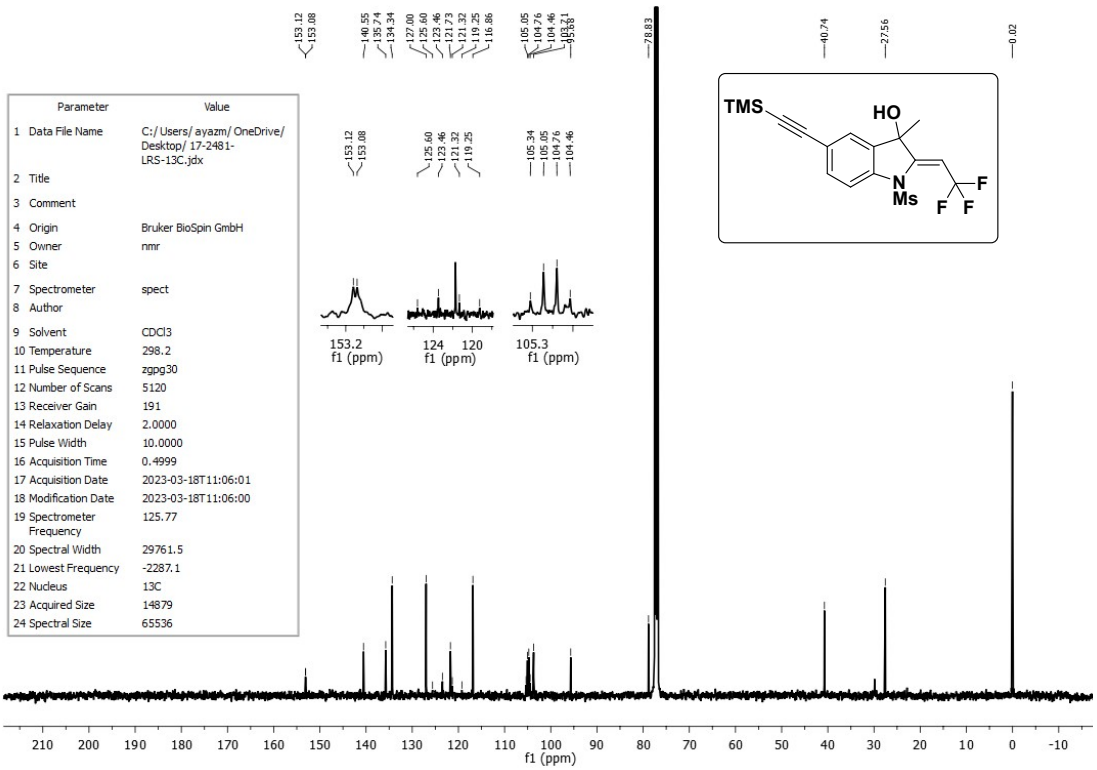
HRMS for 4da in APCI (+) MODE.



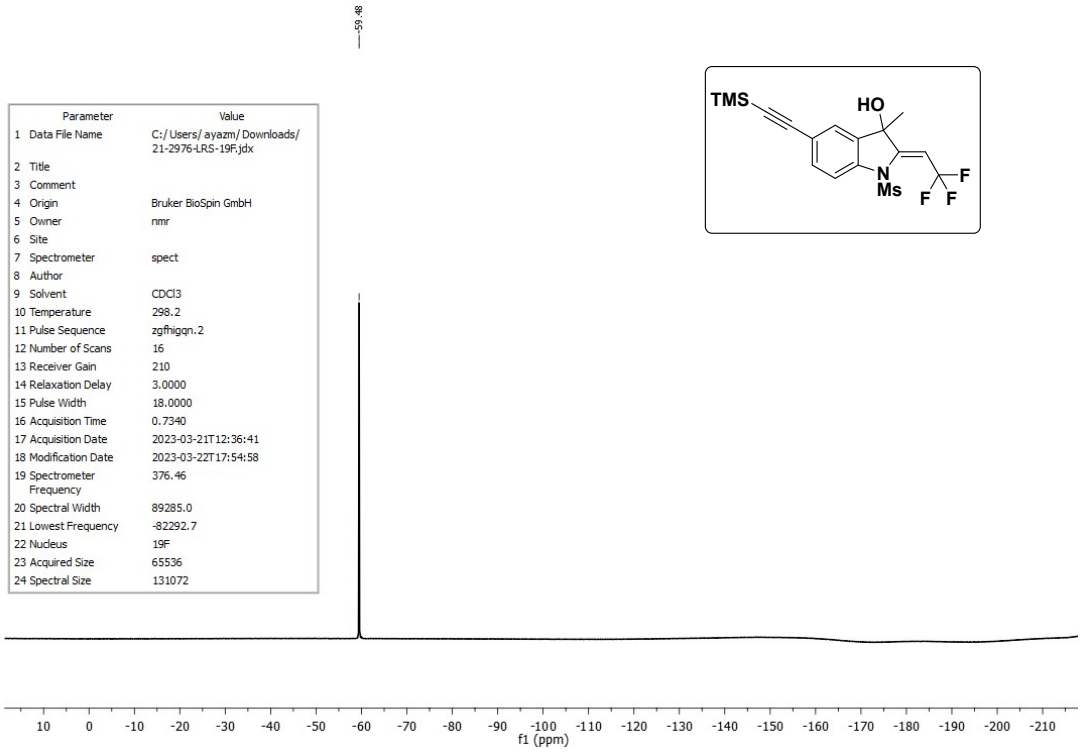
^{1}H NMR for 4ga at 400 MHz



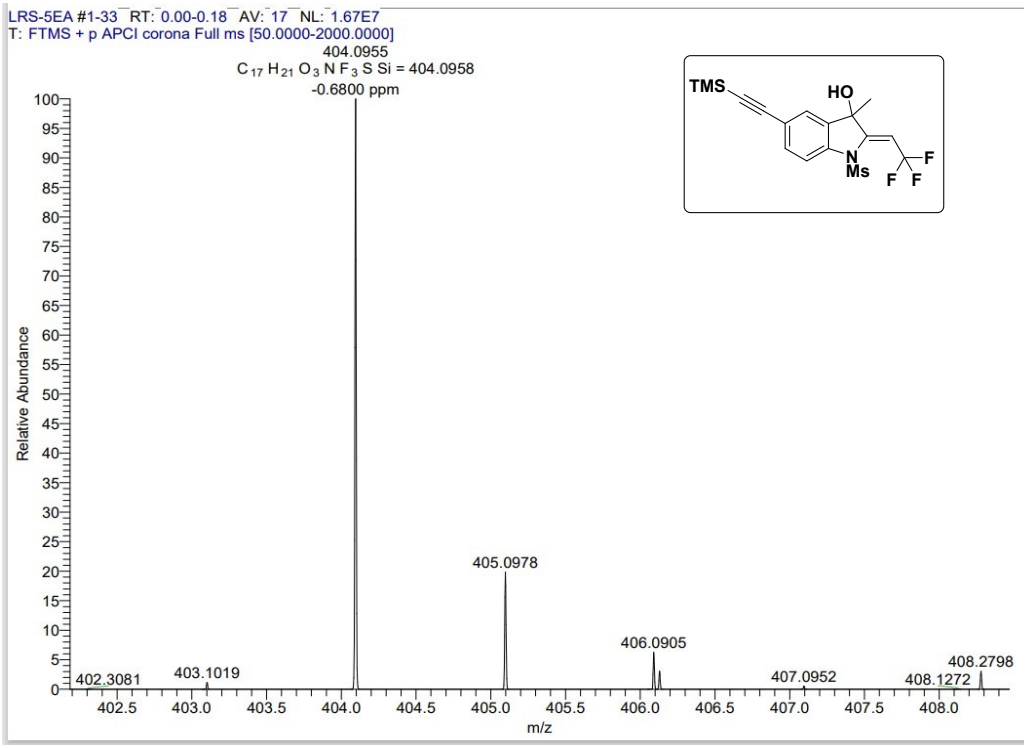
^{13}C NMR for 4ga at 125 MHz



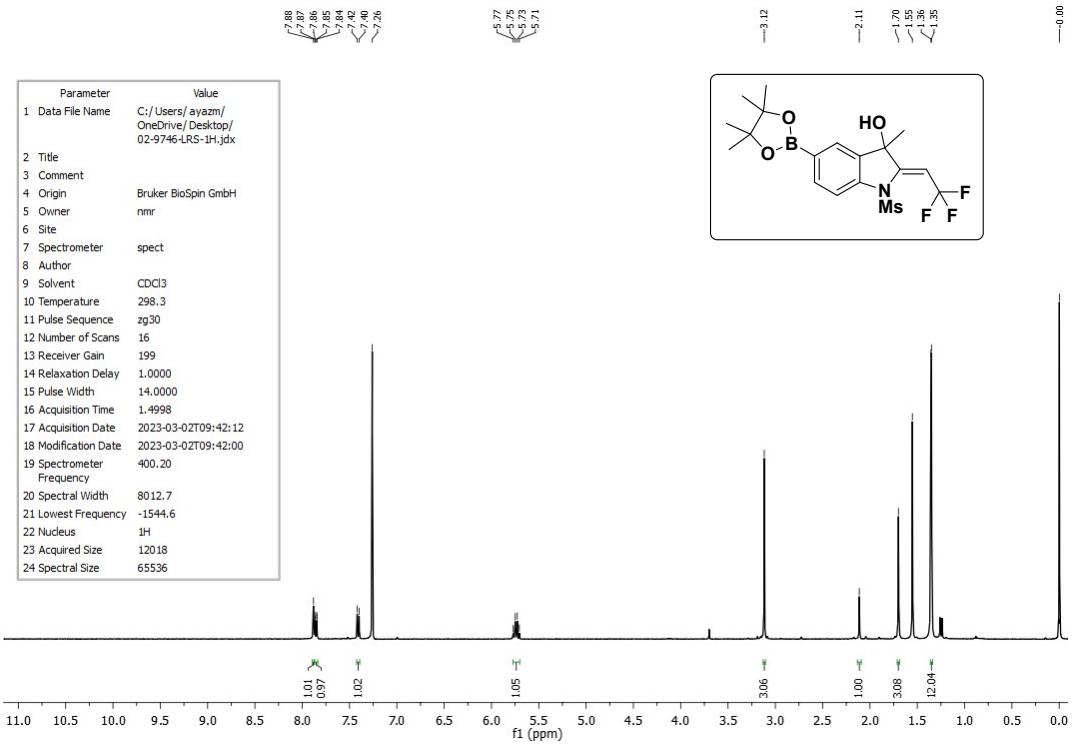
^{19}F NMR for 4ga at 376 MHz



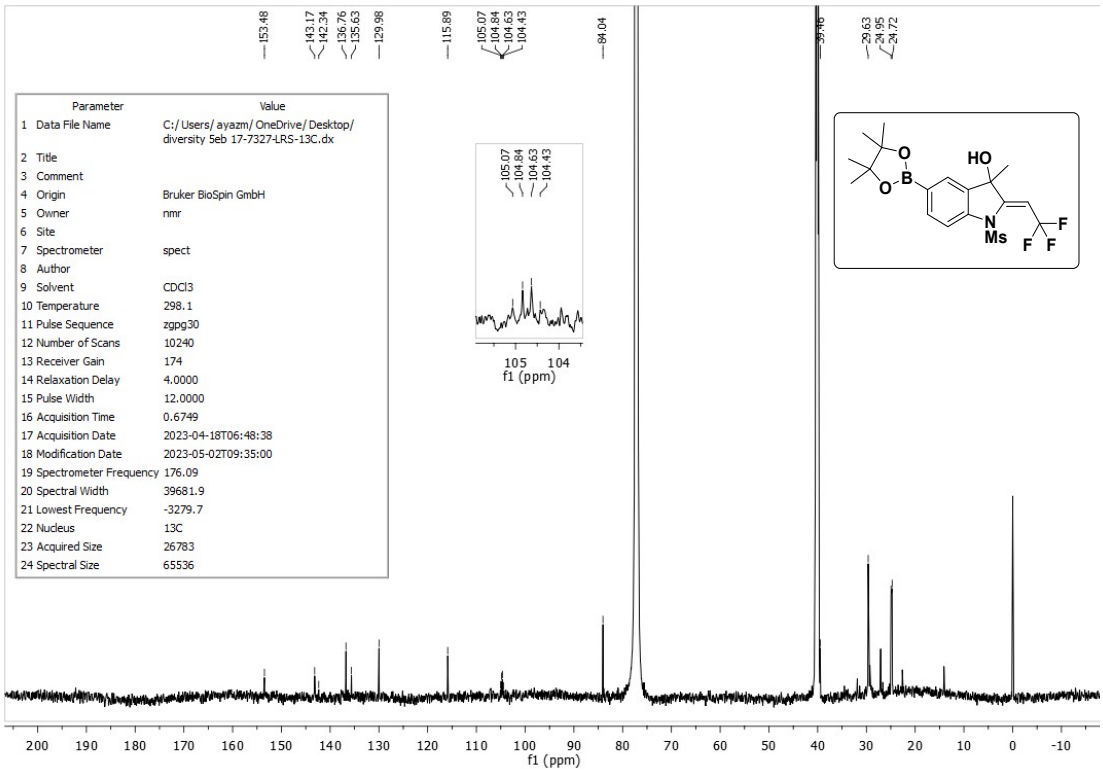
HRMS for 4ga in APCI (+) MODE.



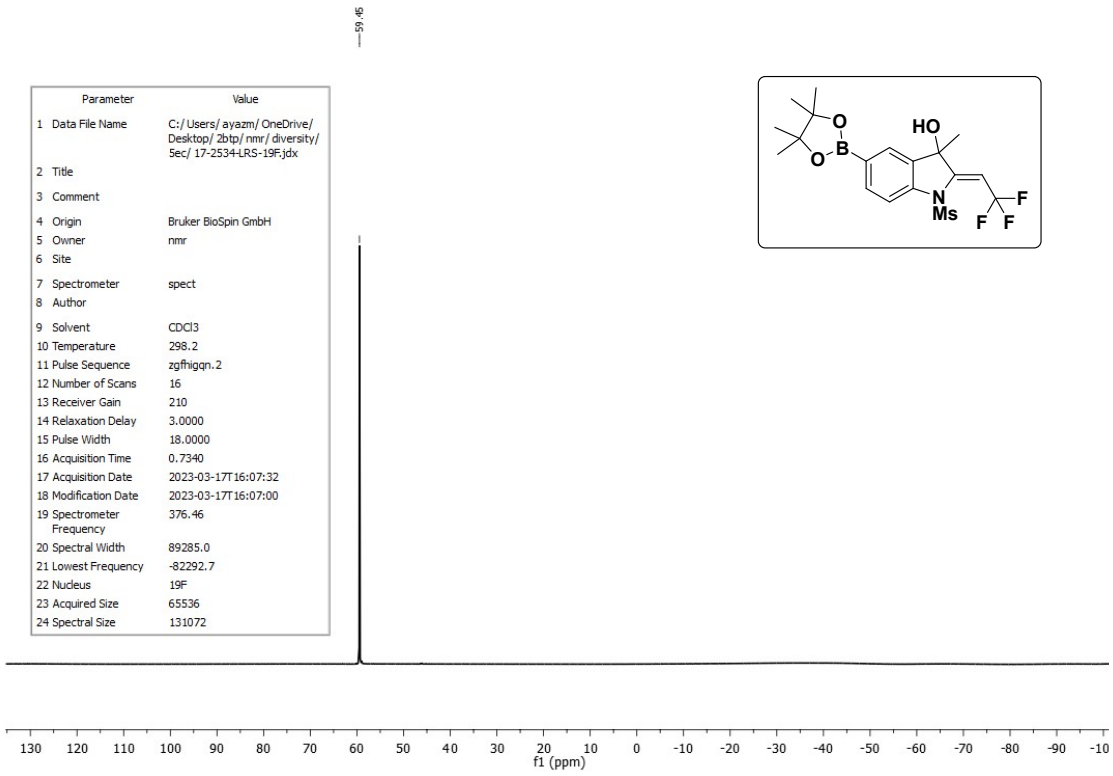
^{1}H NMR for 4gb at 400 MHz



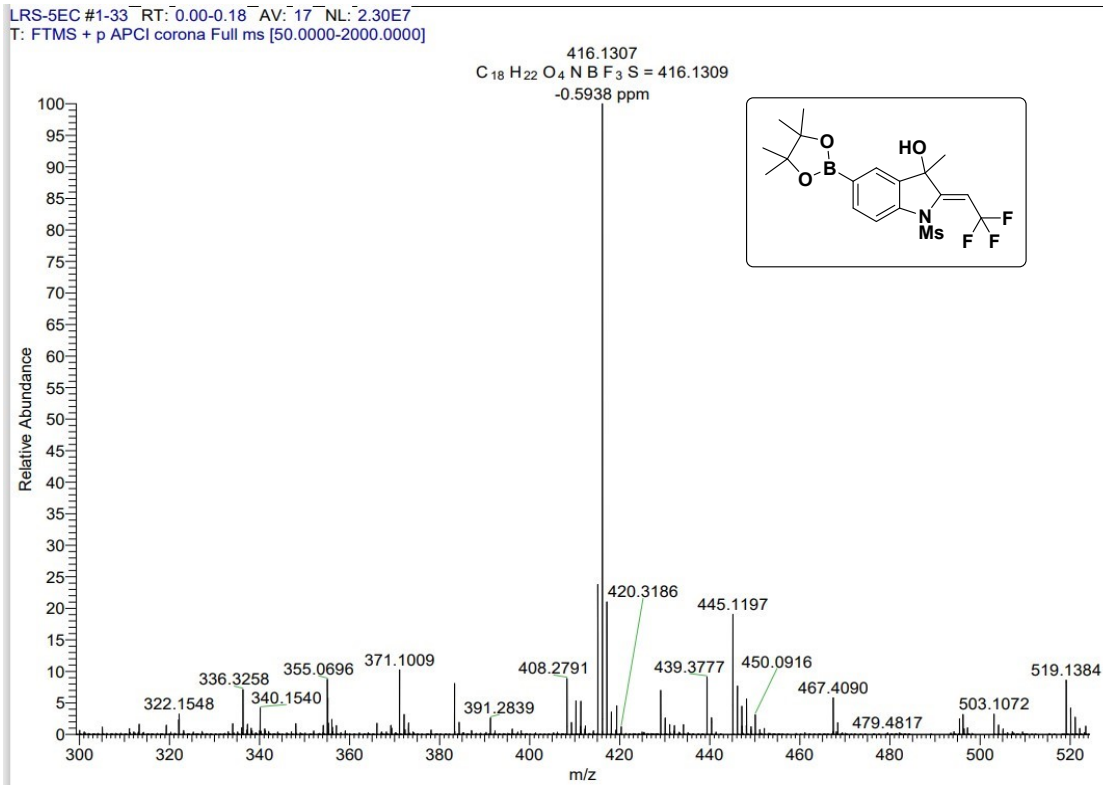
^{13}C NMR for 4gb at 100 MHz



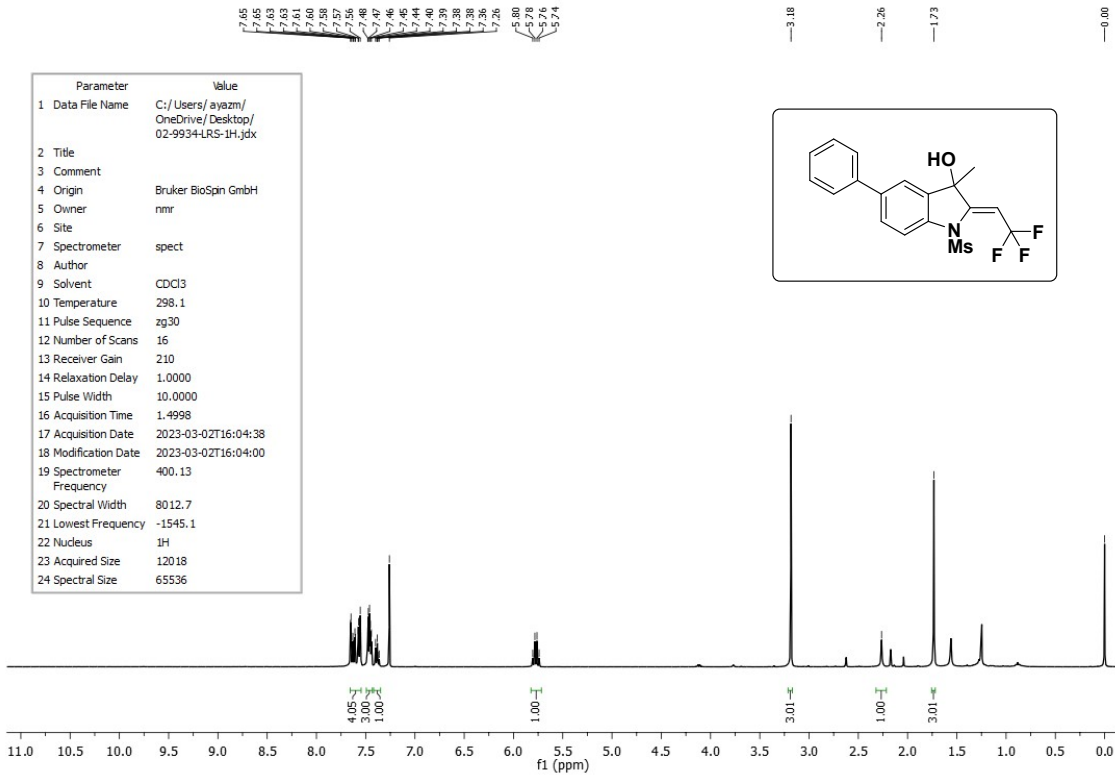
^{19}F NMR for 4gb at 376 MHz



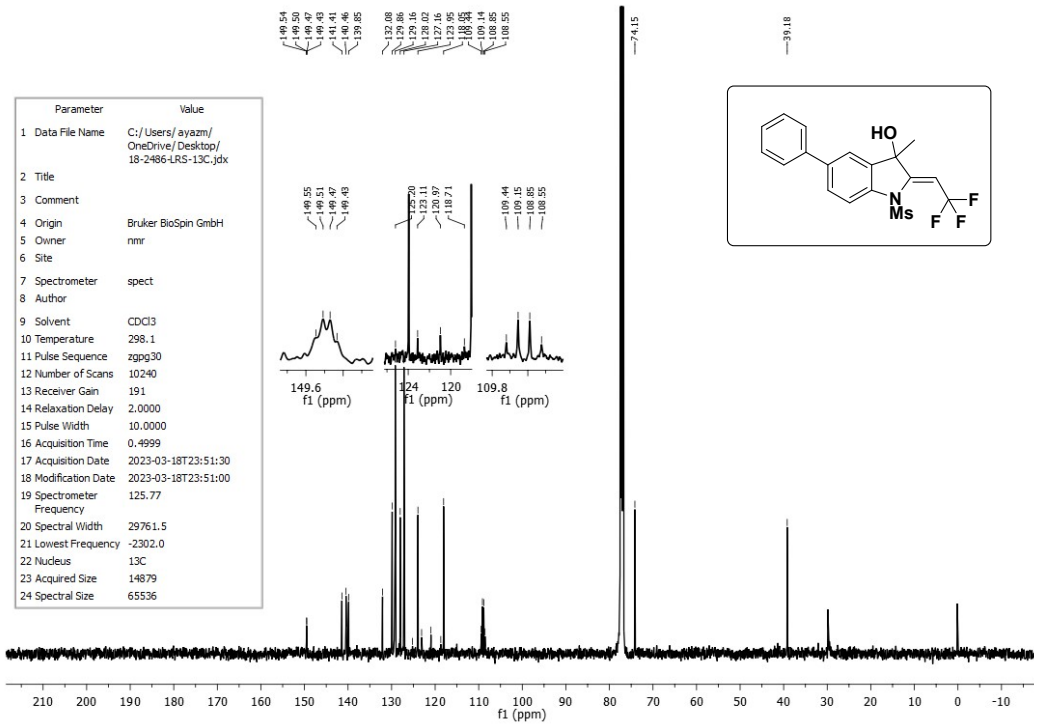
HRMS for 4gb in APCI (+) MODE.



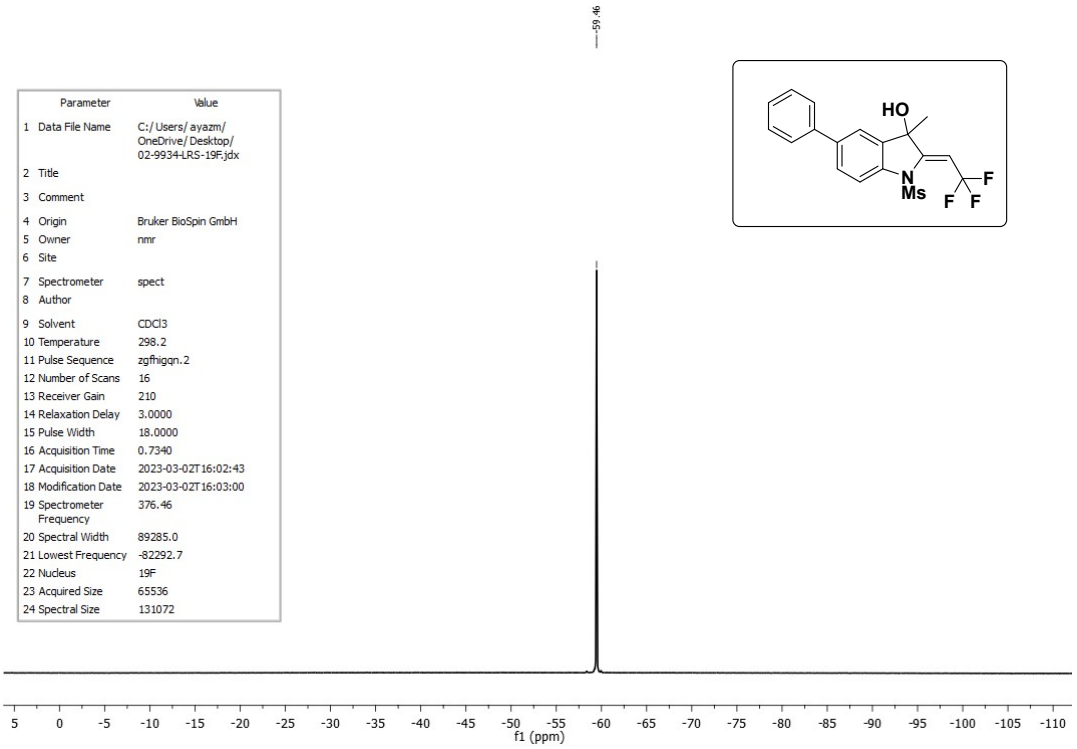
^{1}H NMR for 4gc at 400 MHz



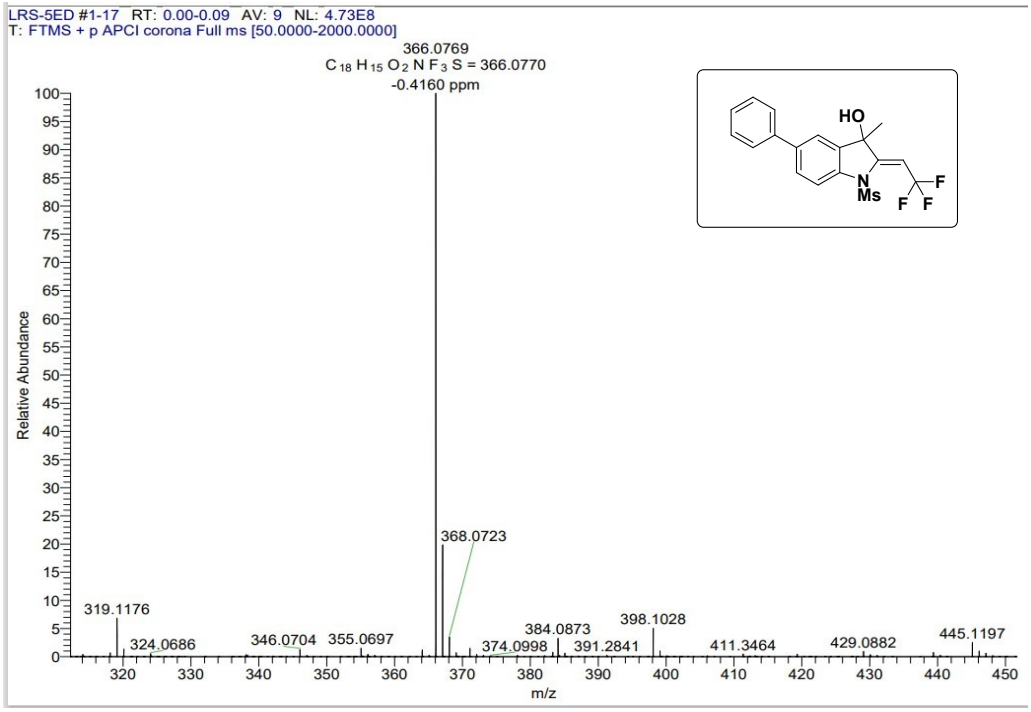
^{13}C NMR for 4gc at 100 MHz



^{19}F NMR for 4gc at 376 MHz

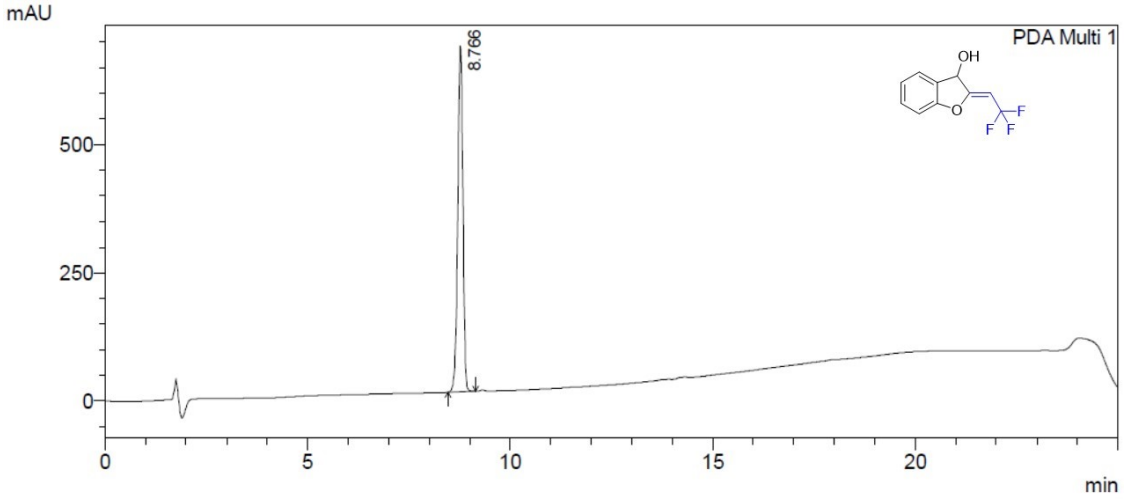


HRMS for 4gc in APCI (+) MODE.

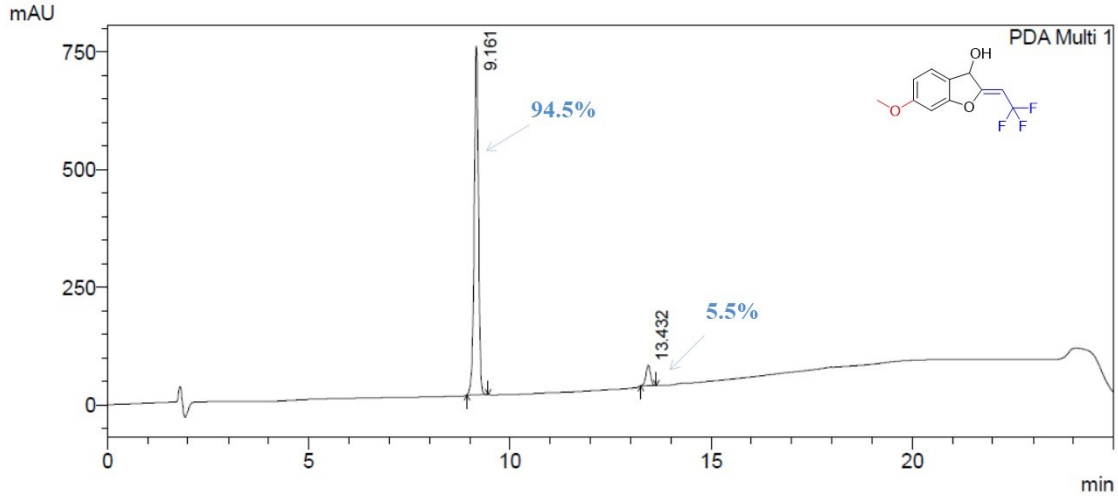


HPLC chromatogram for peak purity

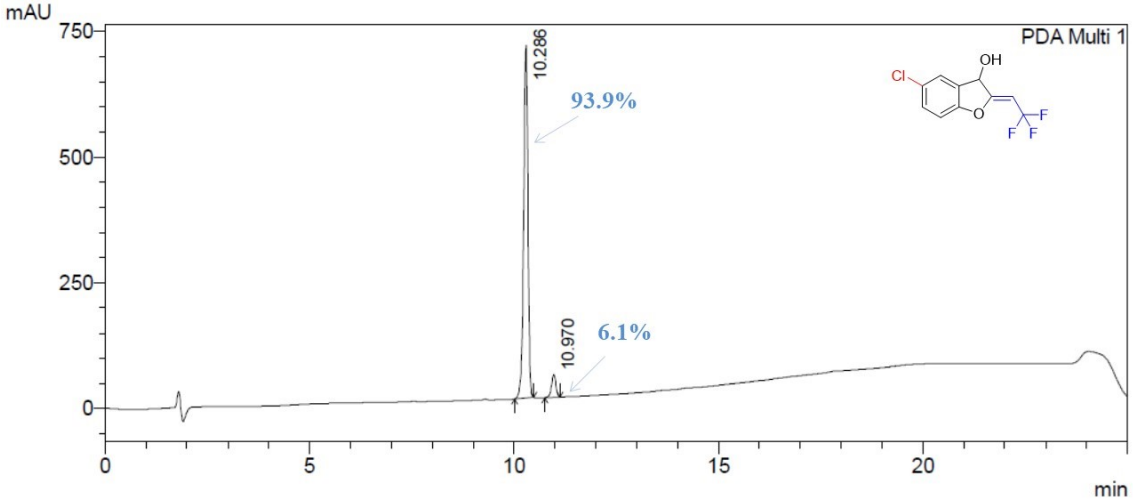
HPLC for 2a



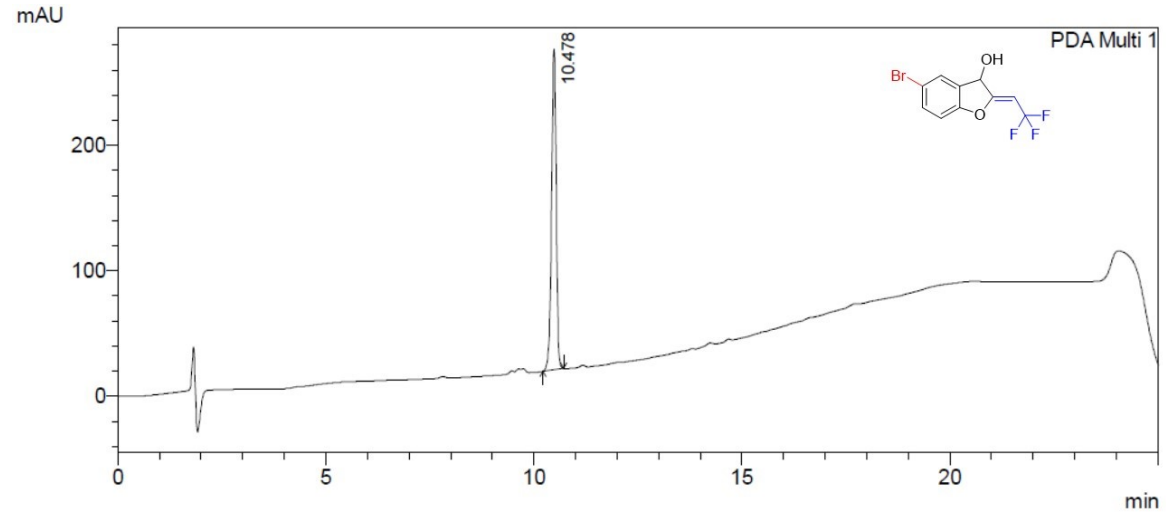
HPLC for 2b



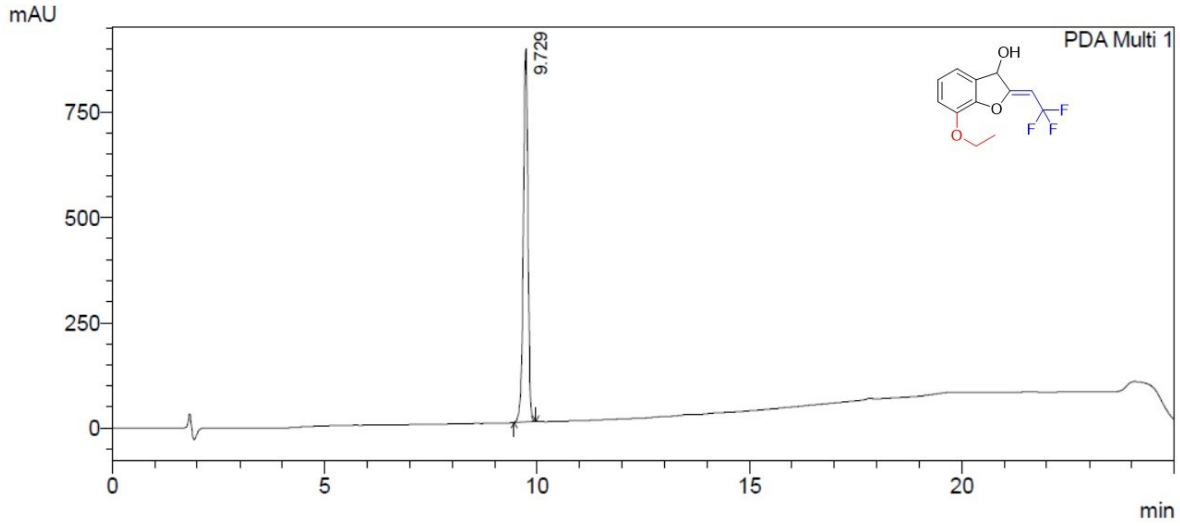
HPLC for 2c



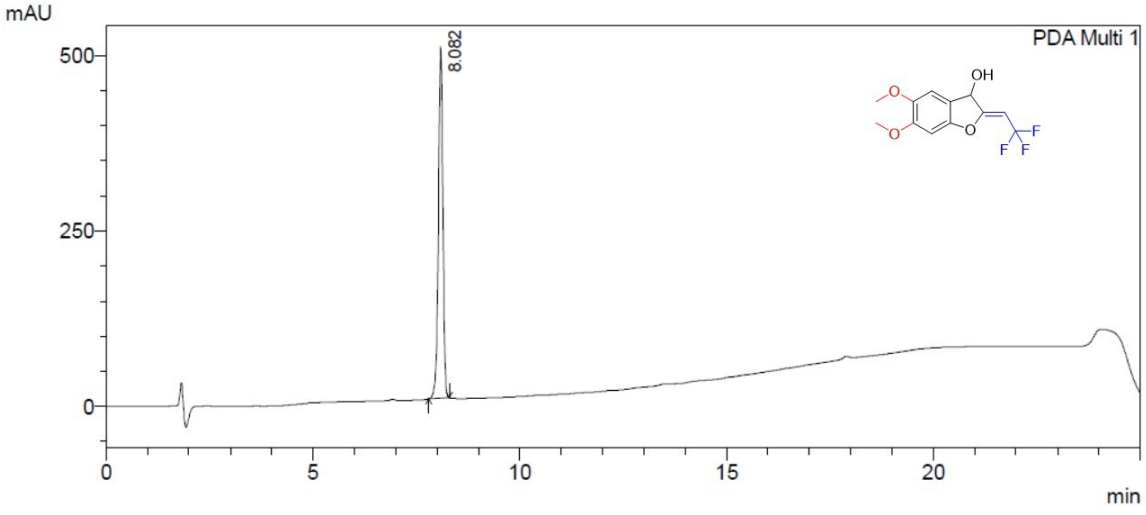
HPLC for 2d



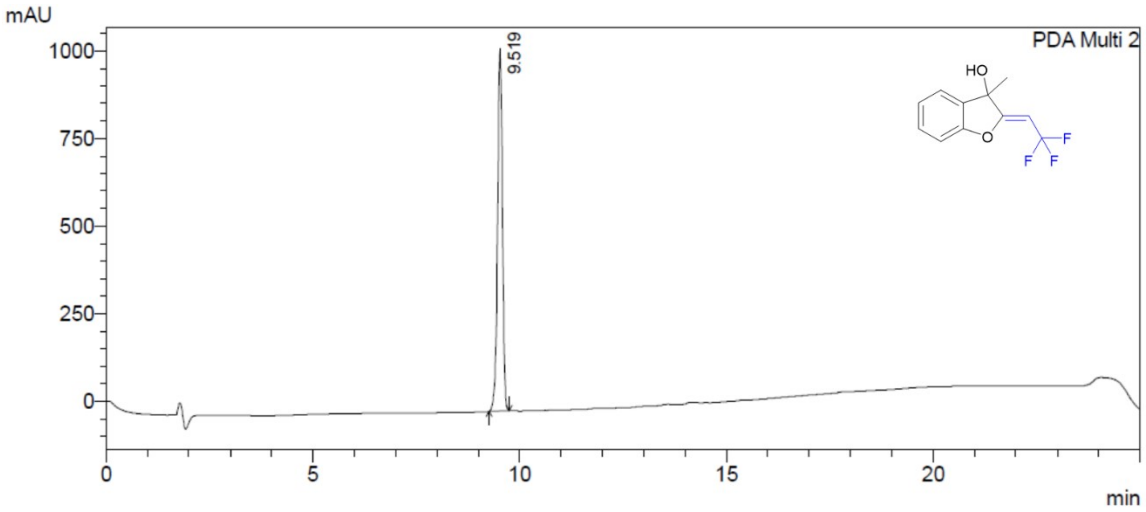
HPLC for 2e



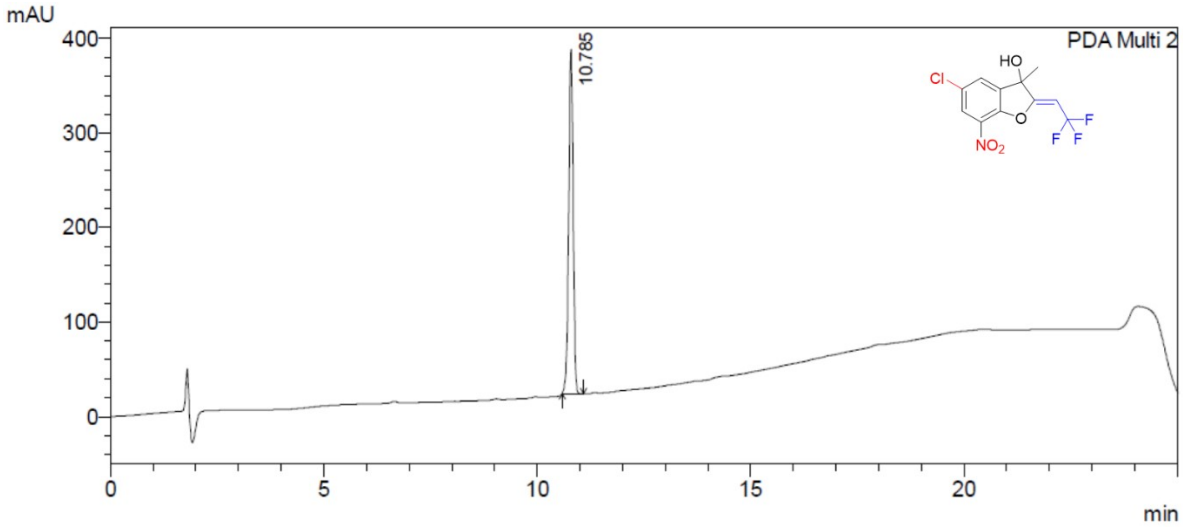
HPLC for 2f



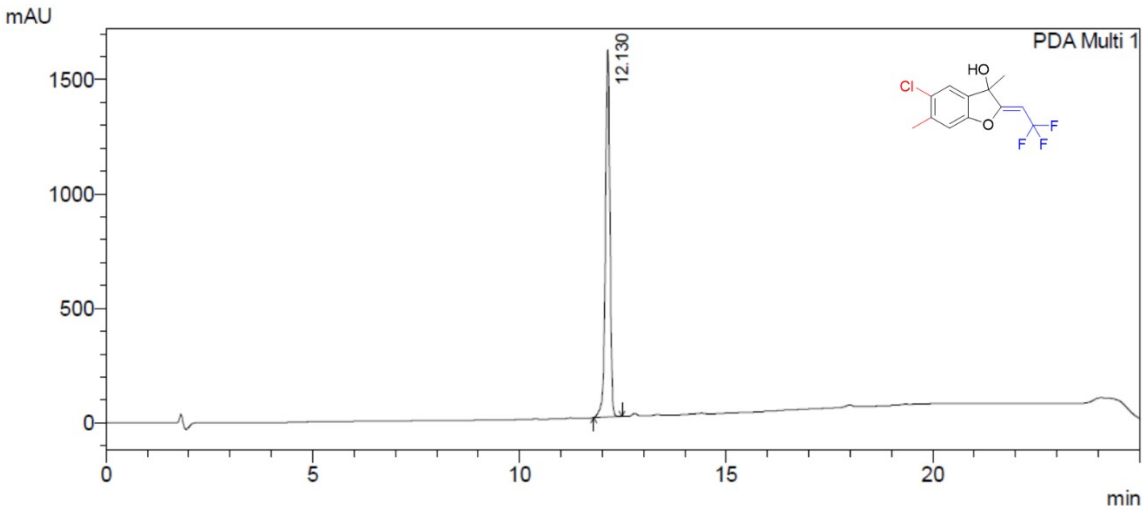
HPLC for 2g



HPLC for 2i



HPLC for 2j



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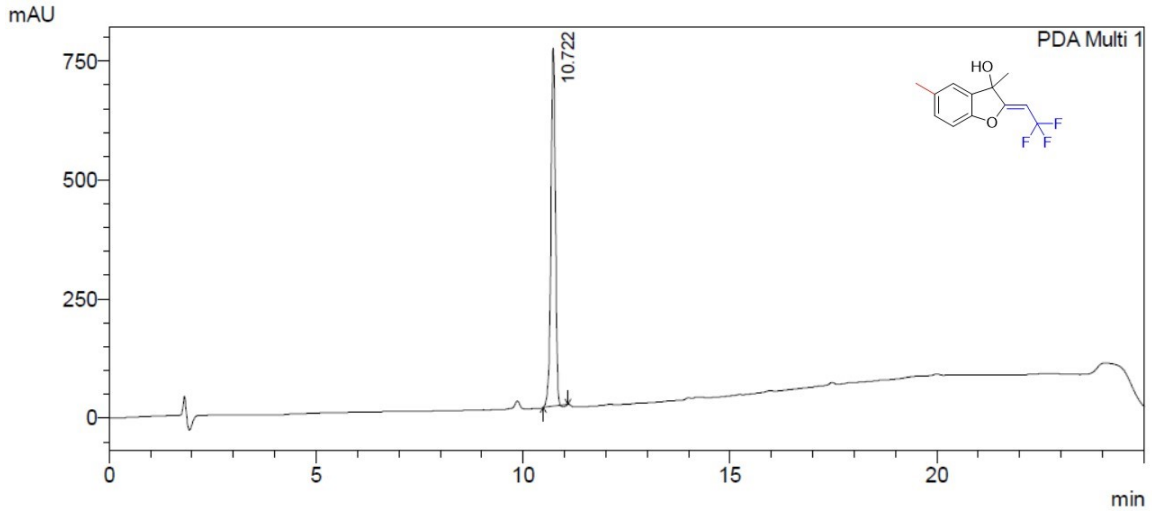

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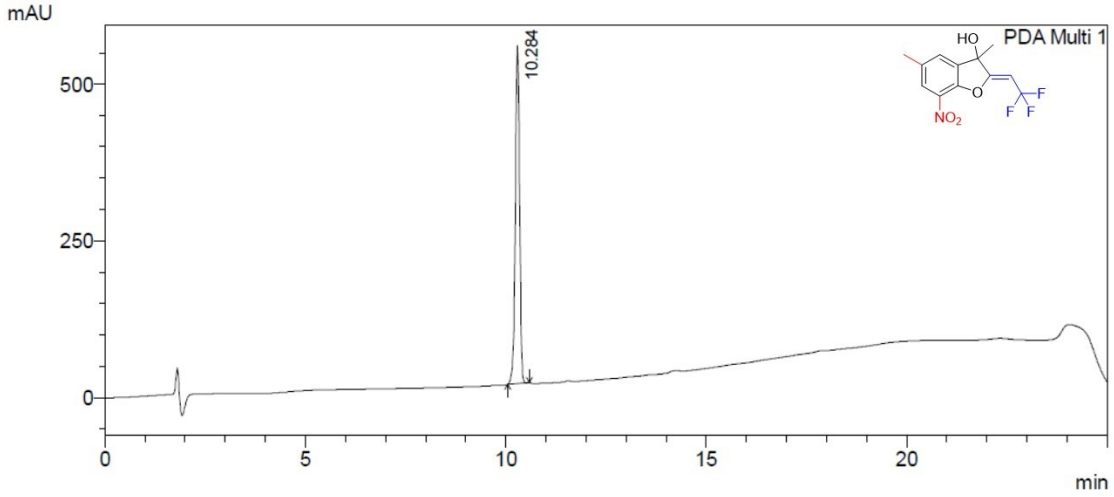

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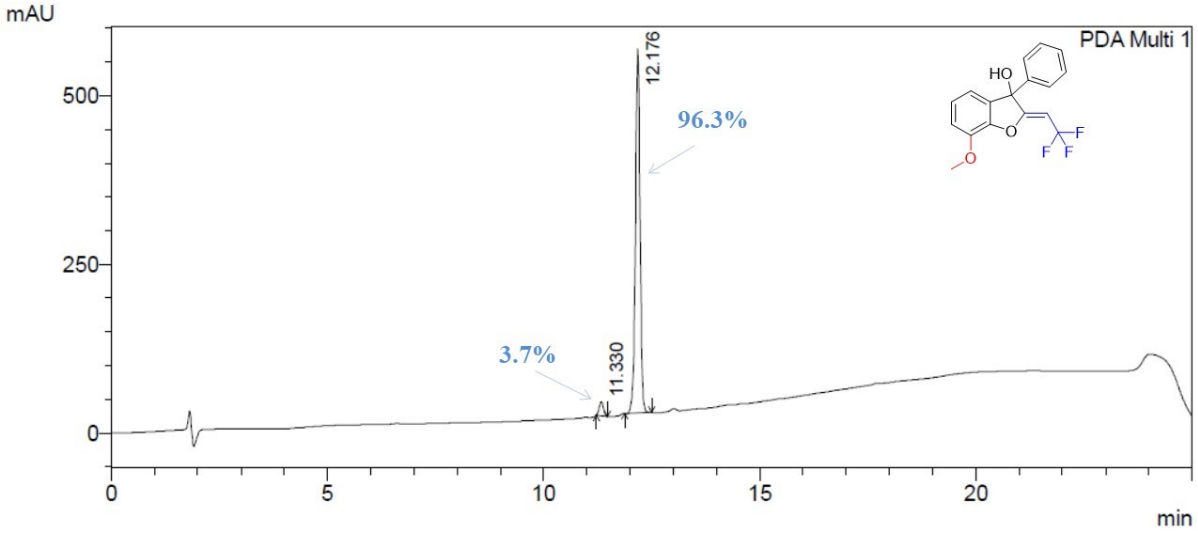
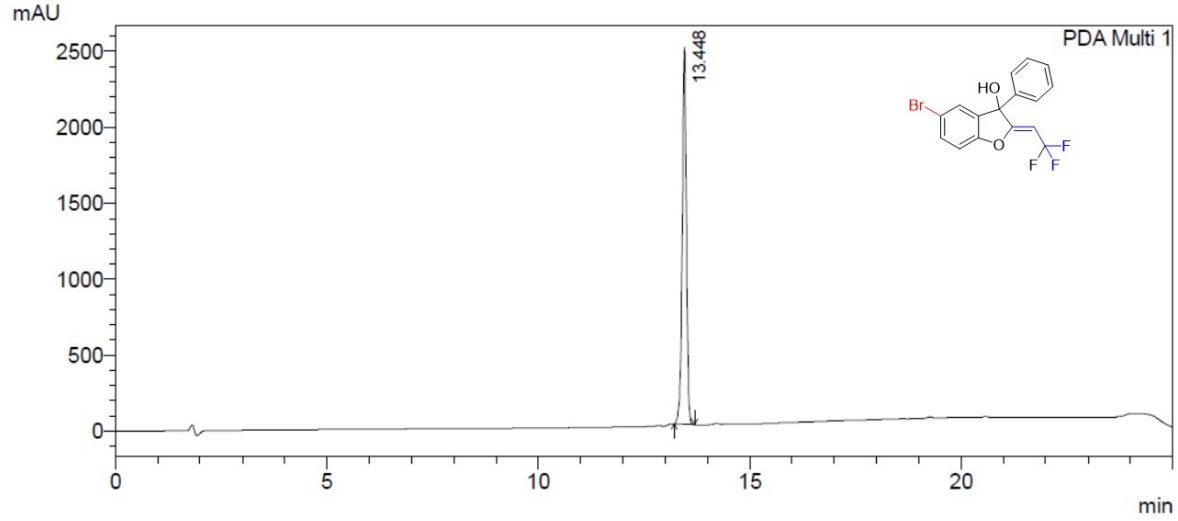


HPLC for 2n



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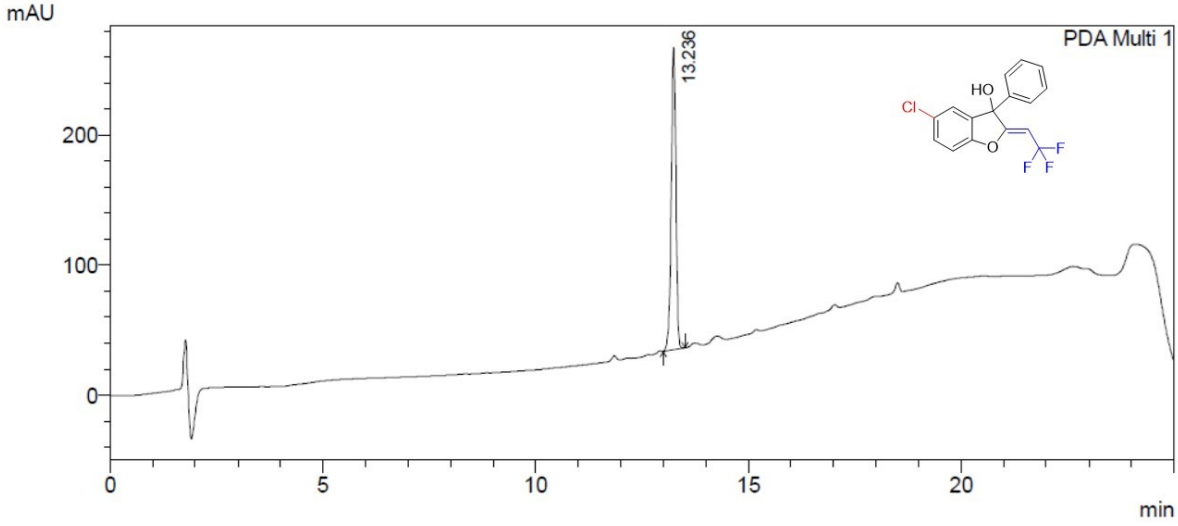

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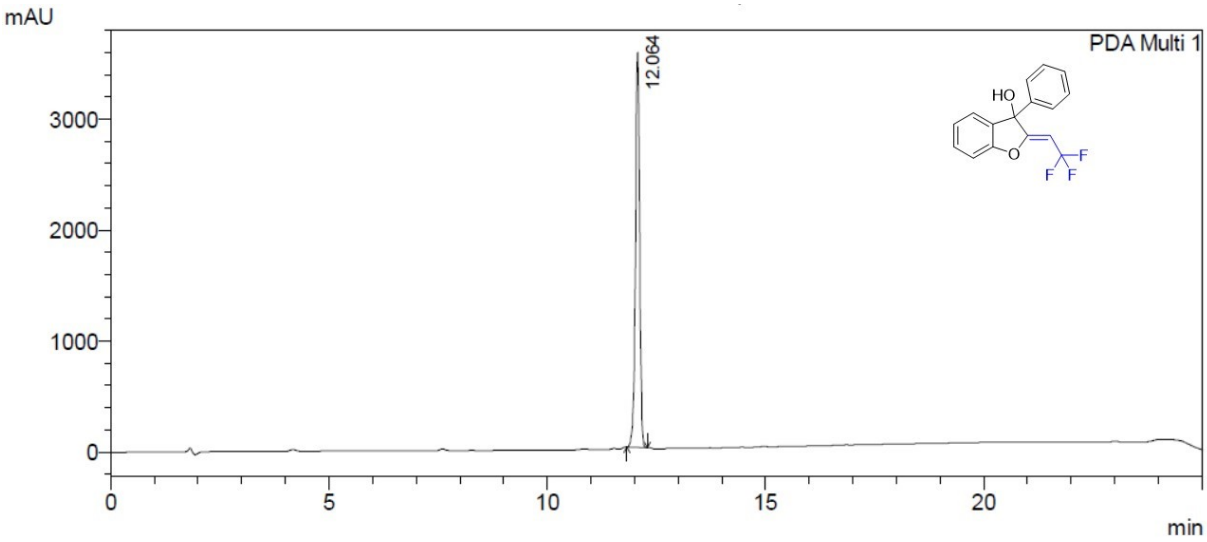
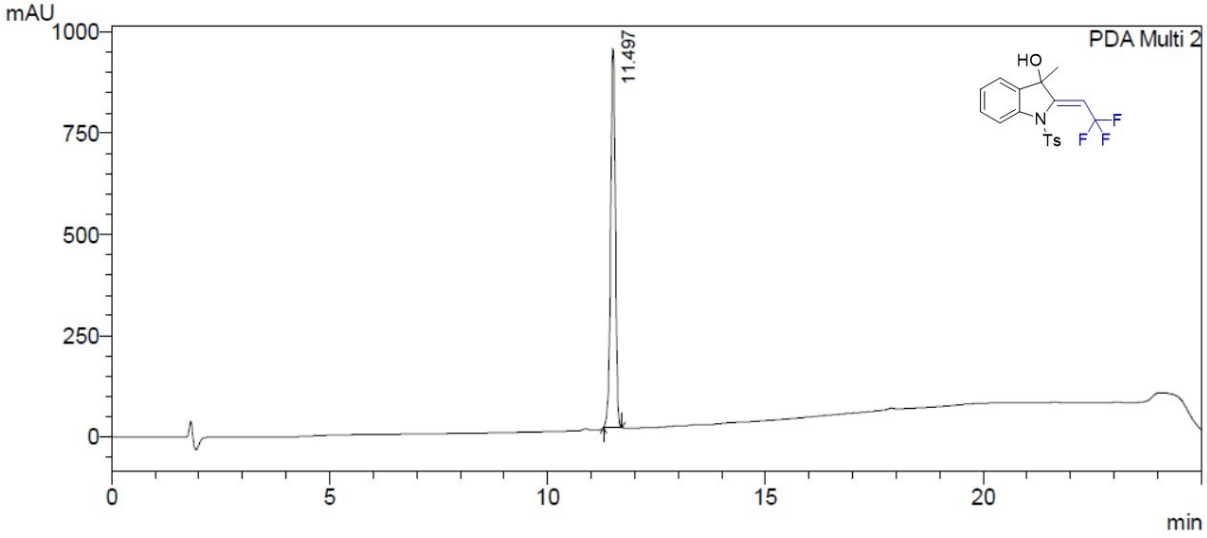
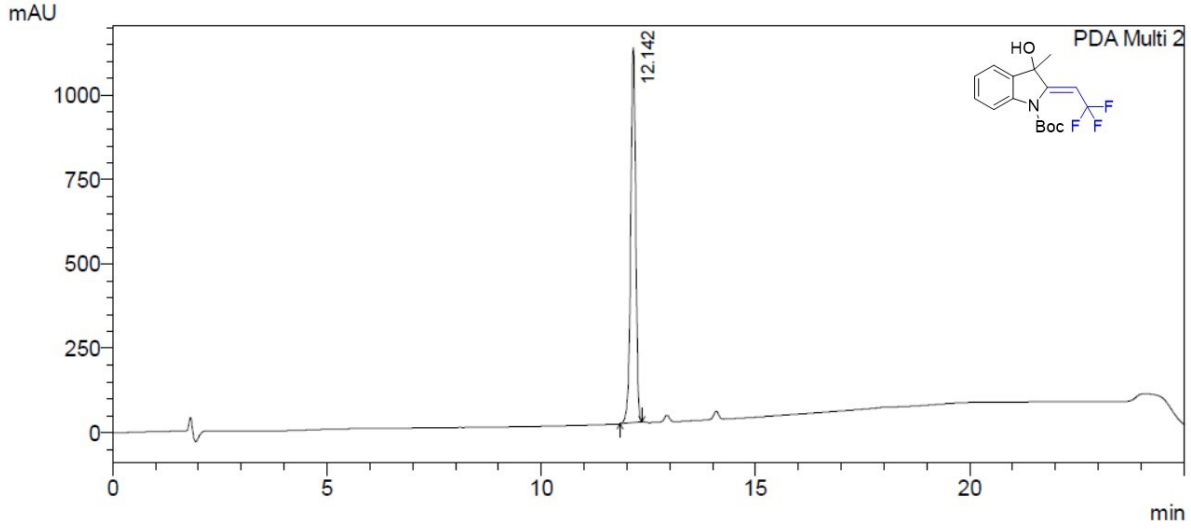


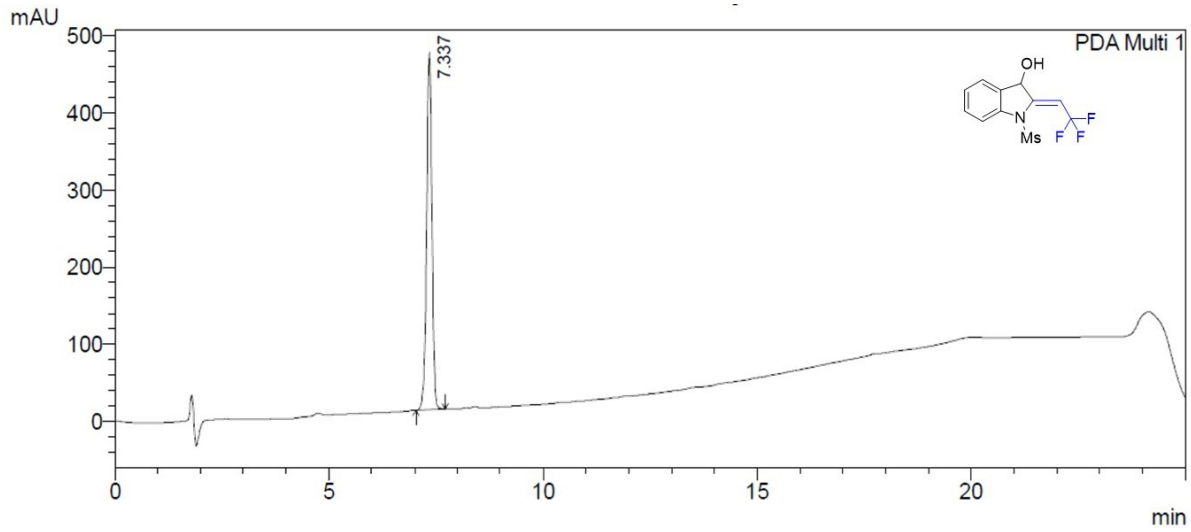
HPLC for 4b



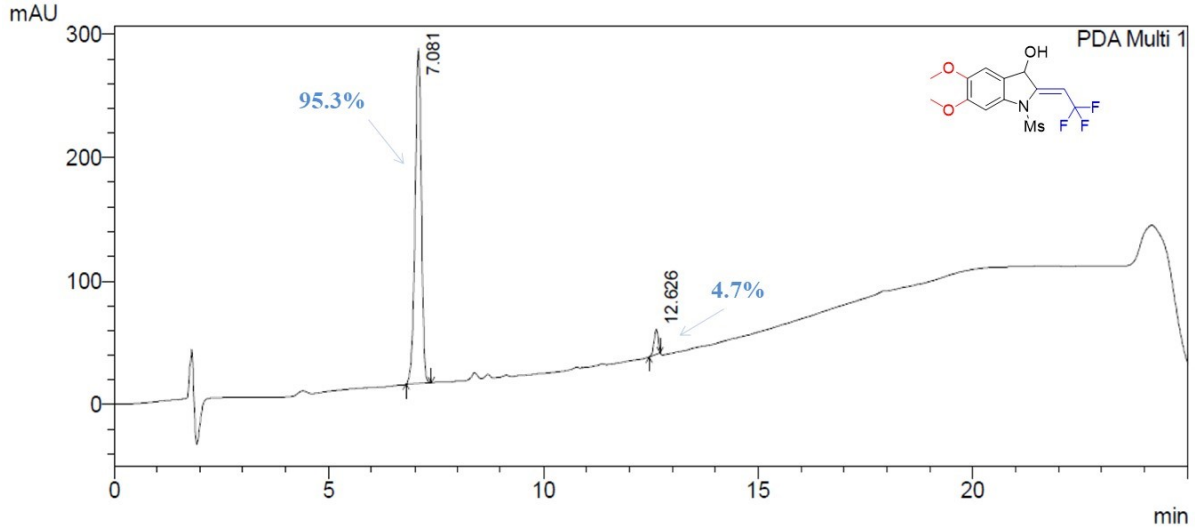
HPLC for 4c



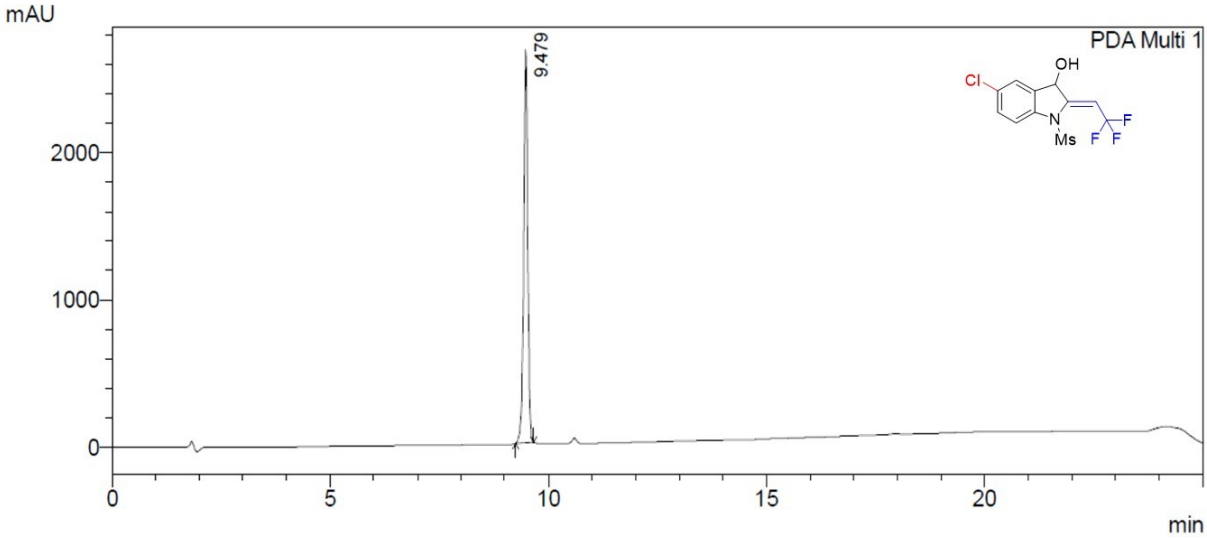
HPLC for 4d



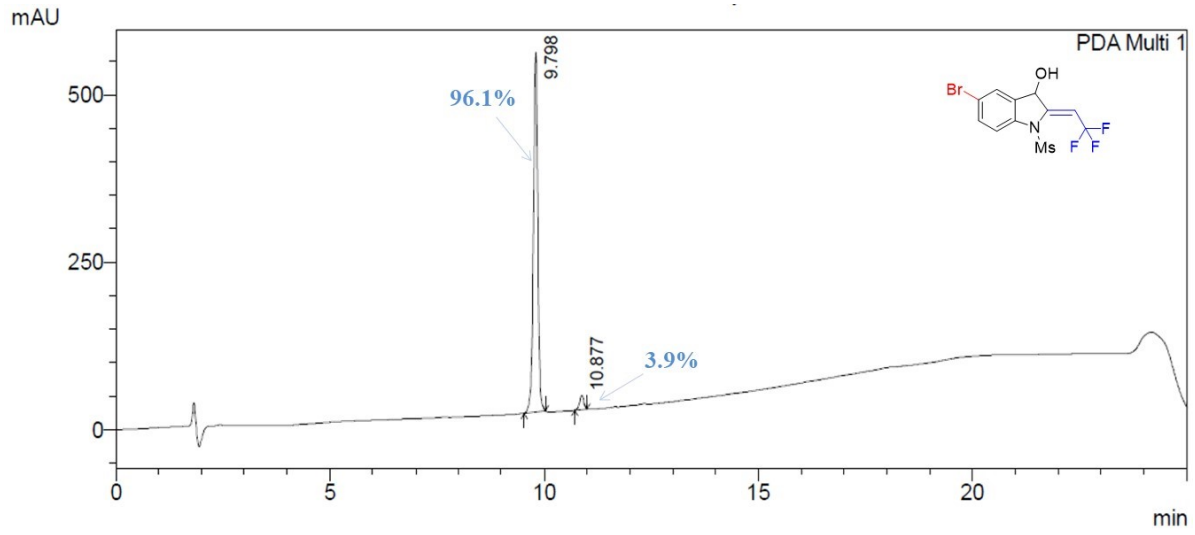
HPLC for 4e



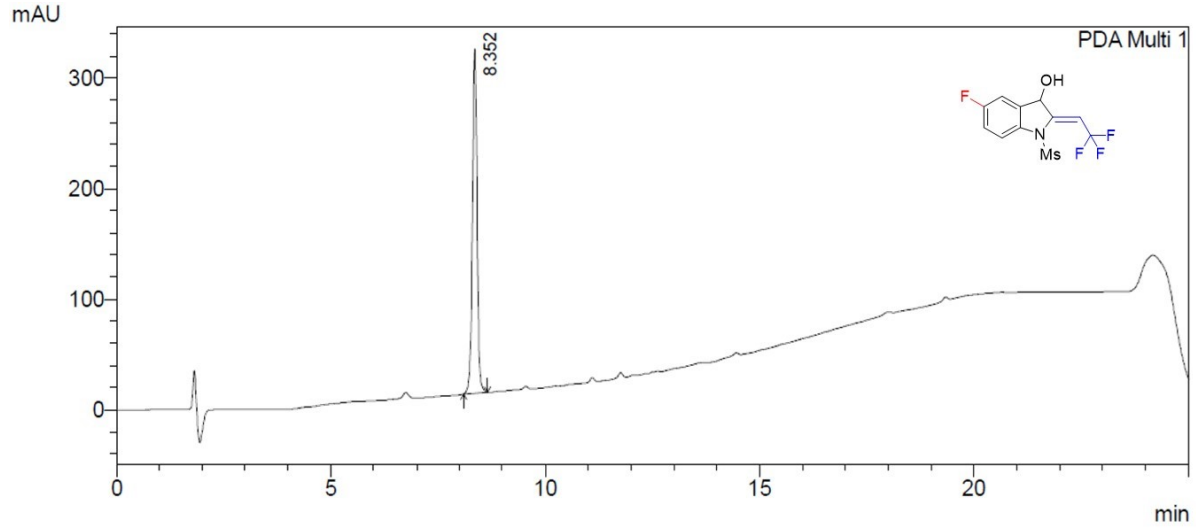
HPLC for 4f



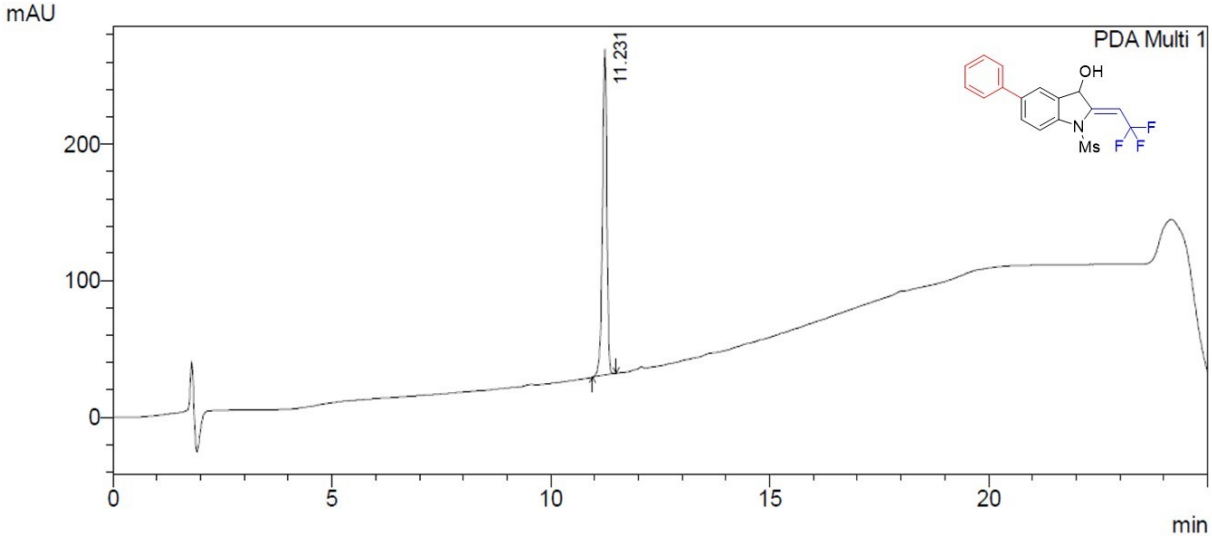
HPLC for 4g



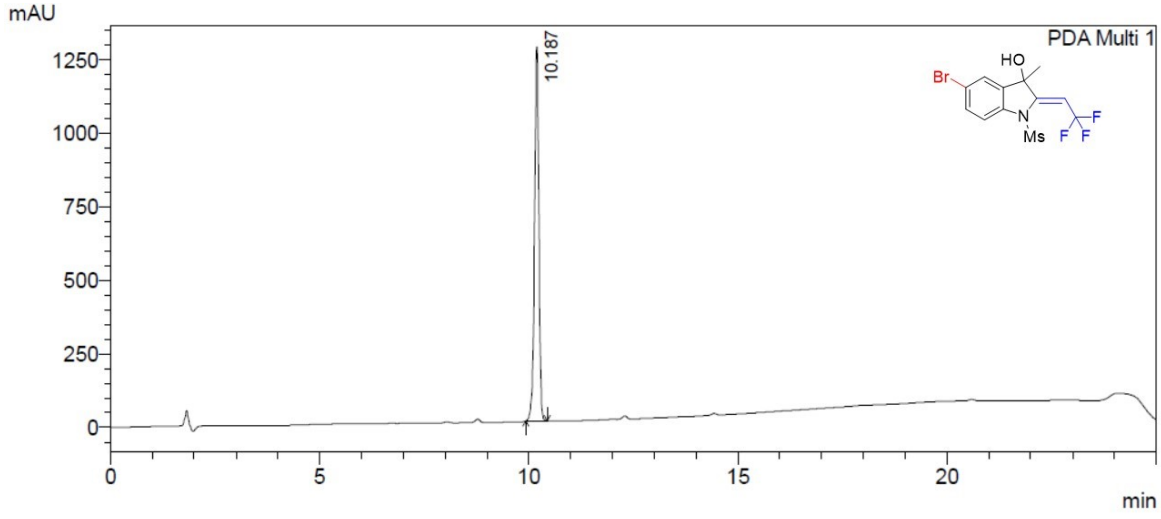
HPLC for 4h



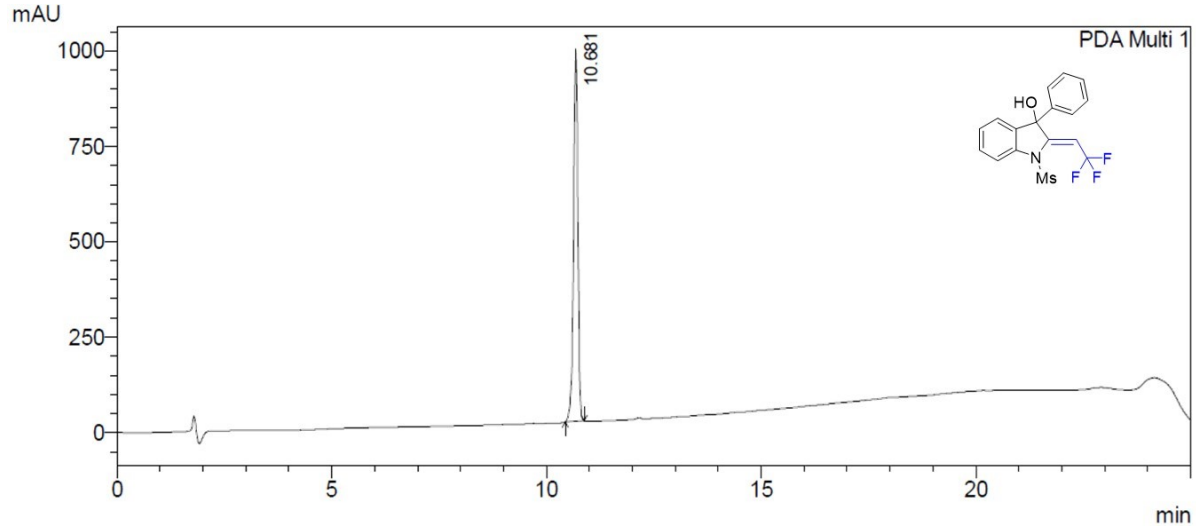
HPLC for 4i



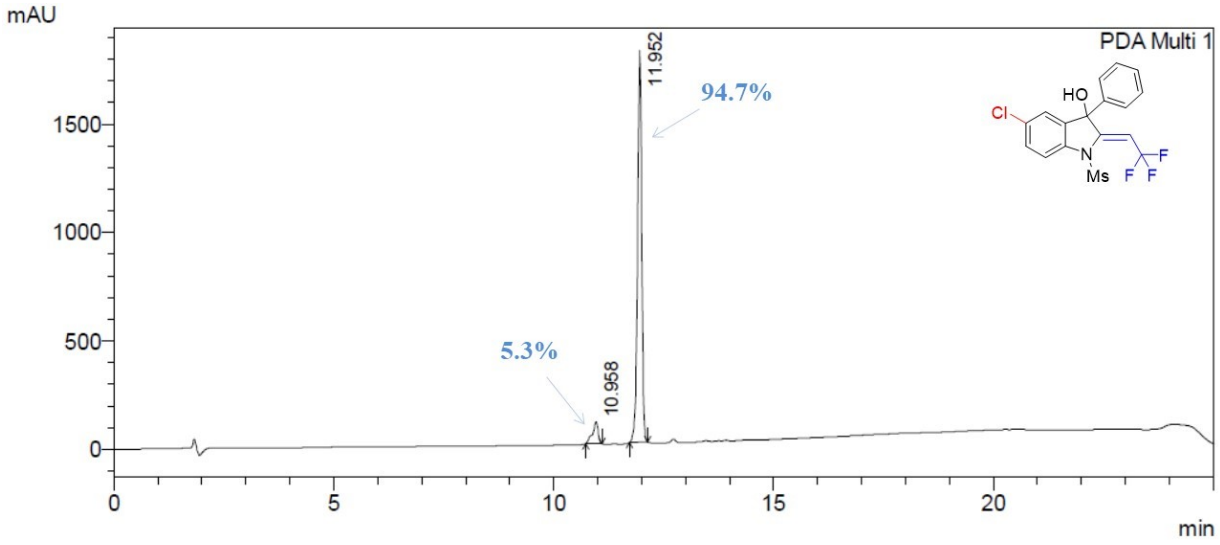
HPLC for 4k



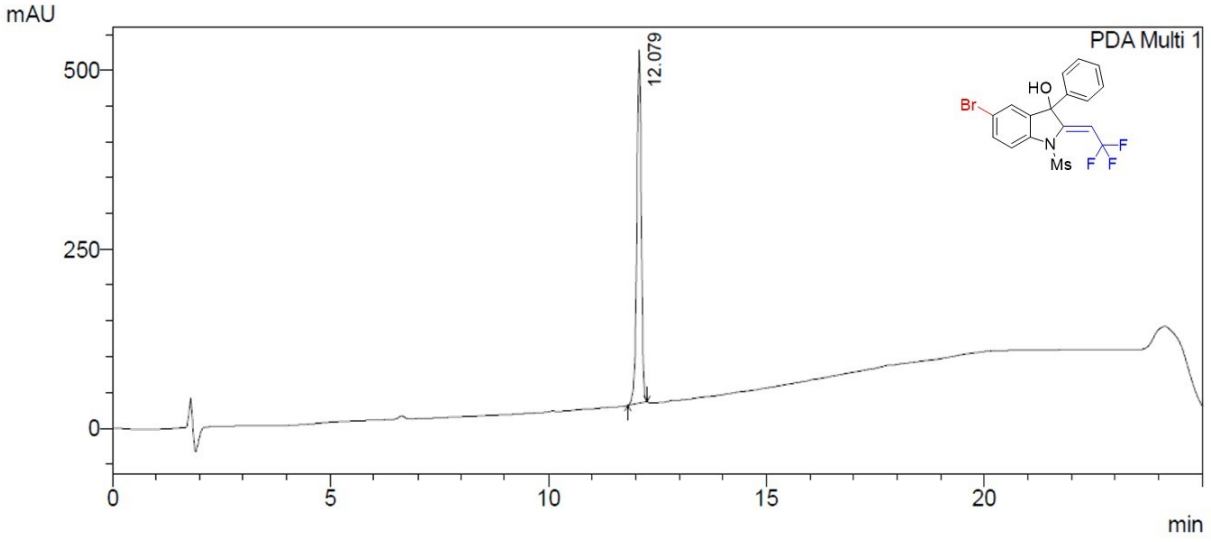
HPLC for 4l



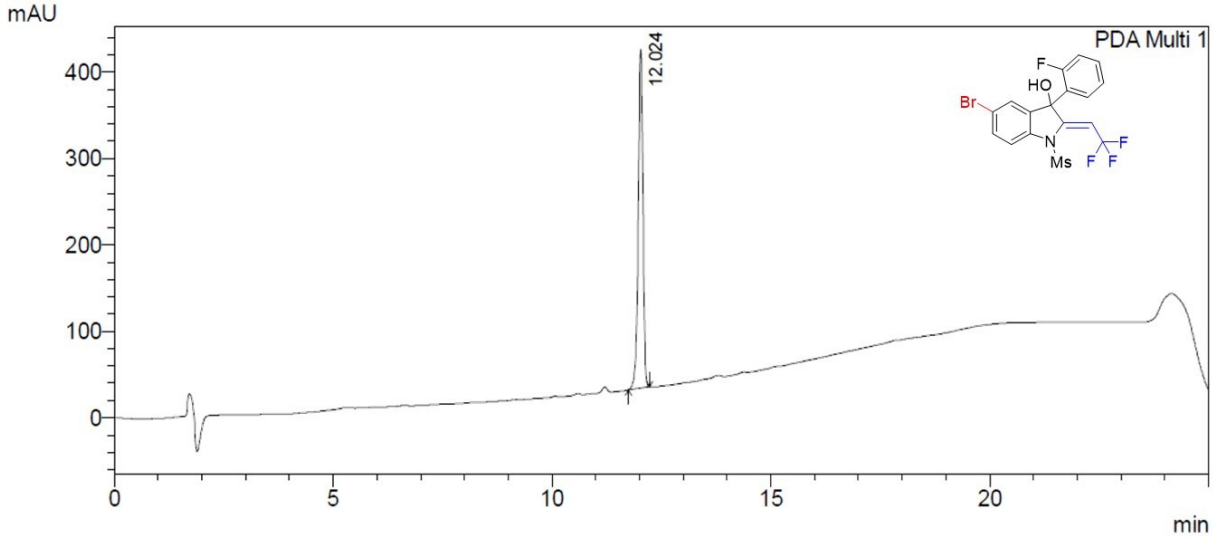
HPLC for 4m



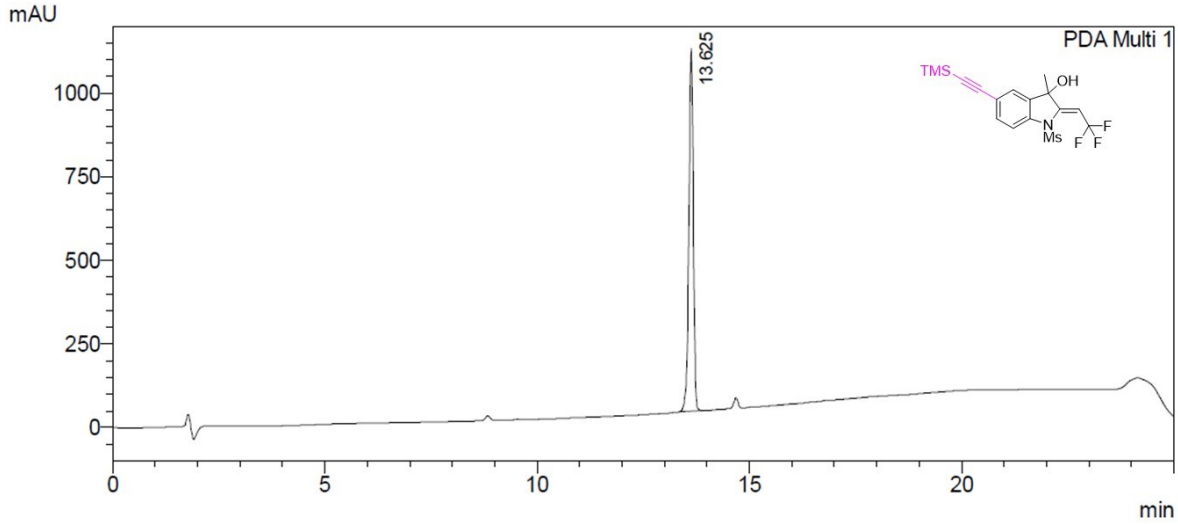
HPLC for 4n



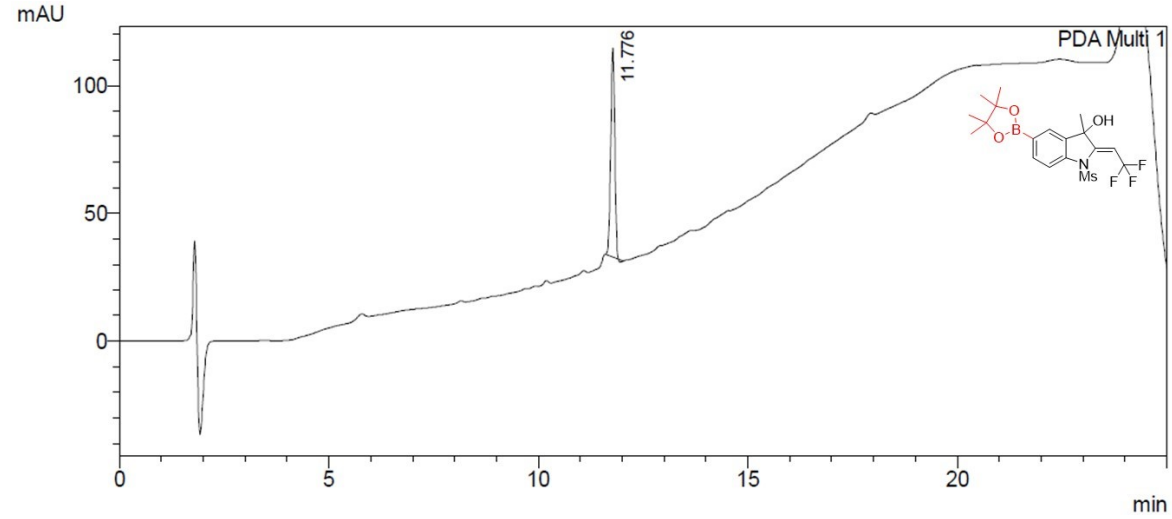
HPLC for 4o



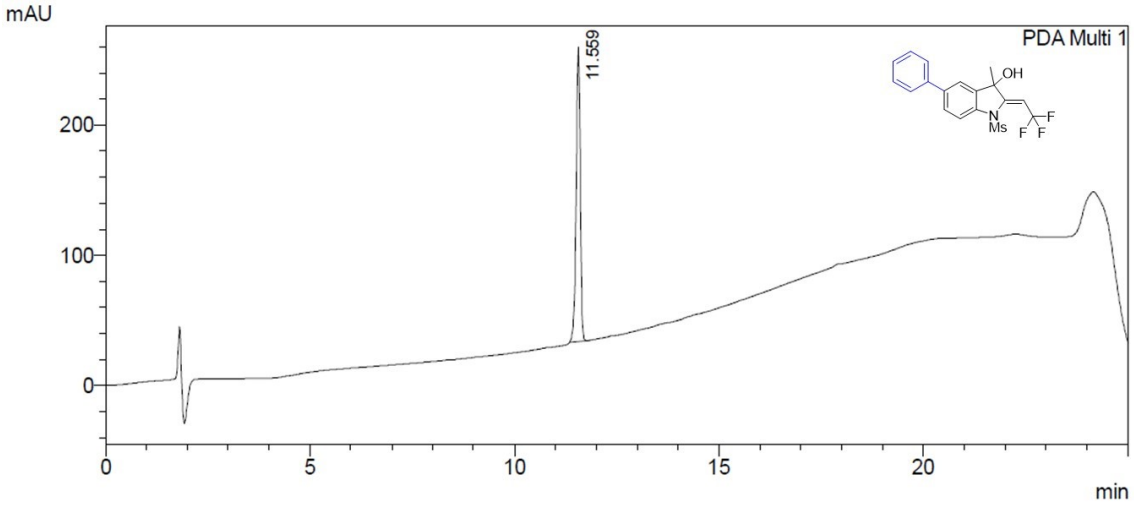
HPLC for 4ga



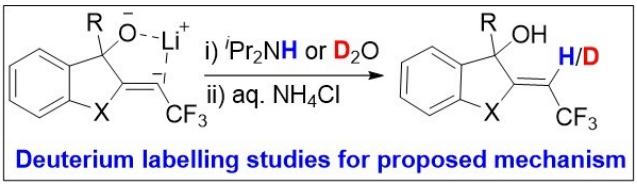
HPLC for 4gb

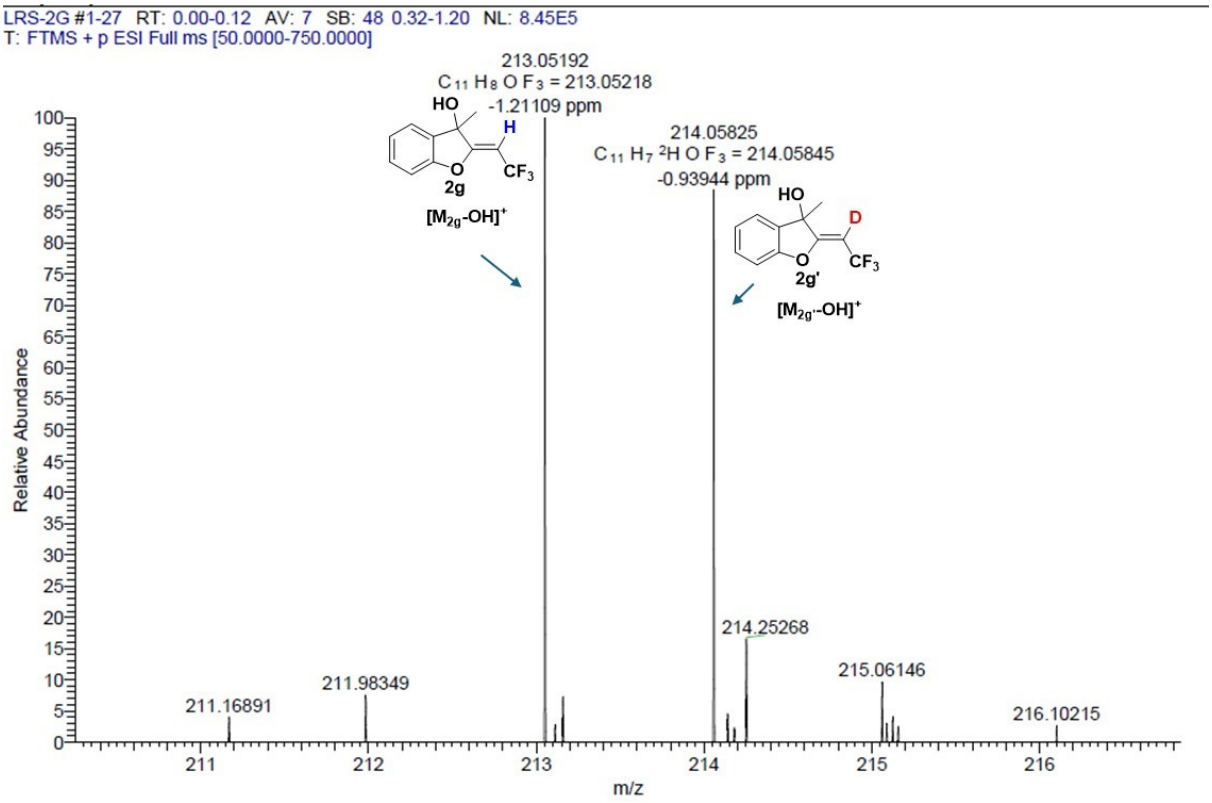


HPLC for 4gc



9. Deuterium labelling of compound 2g (HRMS of 2g')





10. Cartesian Coordinates of the optimized geometries of molecules

Table 1. Cartesian Coordinates of the optimized geometry of intermediate of **2g′**.
Free Energy = -874.17189674 Hartree

```
-1 1
 C                  3.52133500    2.03971100   -0.03925600
 C                  2.17140000    2.36920700   -0.04691000
 C                  1.21485100    1.35088800   -0.04002300
 C                  1.54308400   -0.00859500   -0.02336000
 C                  2.92022600   -0.31461200   -0.02242200
 C                  3.88620100    0.69391300   -0.03250700
 H                  4.28622400    2.80963800   -0.04198800
 H                  1.85664700    3.40786400   -0.05186700
 H                  0.16535500    1.62160300   -0.03103800
 H                  4.93859200    0.41522000   -0.04113500
 C                  0.45559200   -1.12651600    0.16474100
 C                  0.54998300   -2.17339100   -1.00427400
 H                  1.49176100   -2.71095100   -0.90860000
 H                 -0.27397500   -2.88193400   -0.88678400
 H                  0.48673400   -1.70788200   -1.99709800
 O                  3.32456300   -1.63021900   -0.02595200
 H                  4.25979000   -1.65963300    0.19617200
 O                  0.52023500   -1.65986700    1.38234900
 C                 -0.91988900   -0.49865300   -0.01611100
 C                 -2.07794200   -0.13922600   -0.03852200
 C                 -3.44122500    0.28521100   -0.01780100
 F                 -4.21912500   -0.34928100   -0.94956700
 F                 -3.59076500    1.62450000   -0.27237500
 F                 -4.06913300    0.07579500    1.17859000

 1 2 1.5 6 1.5 7 1.0
 2 3 1.5 8 1.0
 3 4 1.5 9 1.0
 4 5 1.5 11 1.0
 5 6 1.5 16 1.0
 6 10 1.0
 7
 8
 9
 10
 11 12 1.0 18 1.5 19 1.0
 12 13 1.0 14 1.0 15 1.0
 13
 14
 15
 16 17 1.0
 17
 18
 19 20 3.0
 20 21 1.5
 21 22 1.0 23 1.0 24 1.0
 22
 23
 24
```

Table 2. Cartesian Coordinates of the optimized geometry of intermediate of **4a'**.
Free Energy = -1442.28876931 Hartree

```
-1 1
 C                  -3.83578100    0.62845500    1.10602800
 C                  -3.39404500    1.94113900    1.25609100
 C                  -2.19171400    2.32945800    0.67077500
 C                  -1.40026800    1.44003200   -0.05561200
 C                  -1.84756200    0.10918800   -0.17628600
 C                  -3.07101200   -0.28368900    0.38434700
 H                  -4.77765200    0.30740100    1.53970700
 H                  -3.98303500    2.65740800    1.82064300
 H                  -1.79010100    3.33517600    0.75038800
 H                  -3.41247400   -1.30132200    0.24941100
 C                  -0.11101900    2.09241700   -0.71194400
 C                  -0.27931000    2.02572600   -2.27268600
 H                  -1.12602300    2.66932000   -2.52262800
 H                   0.62203000    2.44574700   -2.72386700
 H                  -0.46089100    1.02804800   -2.69171100
 O                   0.11803300    3.33172200   -0.29472200
 C                   1.09039900    1.25085000   -0.33428700
 C                   2.13597000    0.73379200   -0.00275200
 C                   3.40038900    0.22024800    0.43335100
 F                   4.15209500   -0.28828300   -0.58284200
 F                   3.26906100   -0.80097000    1.34231600
 F                   4.18486900    1.15032600    1.04649700
 N                  -1.07603900   -0.85336900   -0.91209700
 H                  -0.21840400   -0.48230000   -1.30685800
 O                   0.26849500   -2.93554800   -1.25453800
 O                  -2.01268200   -3.12501600   -0.16932400
 C                  -0.01618800   -2.20969200    1.29162100
 H                   0.93015400   -1.68377800    1.18595100
 H                  -0.71483900   -1.65052300    1.91252800
 H                   0.13157600   -3.21535900    1.68459100
 S                  -0.74951300   -2.40766800   -0.34690100

 1 2 1.5 6 1.5 7 1.0
 2 3 1.5 8 1.0
 3 4 1.5 9 1.0
 4 5 1.5 11 1.0
 5 6 1.5 23 1.0
 6 10 1.0
 7
 8
 9
 10
 11 12 1.0 16 1.5 17 1.0
 12 13 1.0 14 1.0 15 1.0
 13
 14
 15
 16
 17 18 3.0
 18 19 1.5
 19 20 1.0 21 1.0 22 1.0
```

```
 20
 21
 22
 23 24 1.0 31 1.0
 24
 25 31 2.0
 26 31 2.0
 27 28 1.0 29 1.0 30 1.0 31 1.0
 28
 29
 30
 31
```

Table 3. Cartesian Coordinates of the optimized geometry of intermediate of **4b'**.
Free Energy = -1673.37611586 Hartree

```
-1 1
 C                  0.61878700    0.49500900   -3.36441600
 C                 -0.59671500    1.05364700   -2.97887200
 C                 -1.21974900    0.61290700   -1.81709600
 C                 -0.69437000   -0.39636300   -0.99192400
 C                  0.54788900   -0.94028800   -1.38943200
 C                  1.18039600   -0.48490800   -2.55731000
 H                  1.12691900    0.81982500   -4.26602200
 H                 -1.06326800    1.82816300   -3.57938100
 H                 -2.16331300    1.06106900   -1.53180100
 H                  2.13666900   -0.92258900   -2.82883700
 C                 -1.41084000   -0.70107400    0.36791200
 C                 -1.53933000   -2.23239700    0.65716700
 H                 -0.55866200   -2.64994900    0.86314000
 H                 -2.15743700   -2.34900000    1.55043300
 H                 -2.00694500   -2.77357400   -0.17508000
 O                 -0.80035800   -0.00527300    1.34265100
 C                 -2.85357200   -0.24167900    0.26873200
 C                 -4.00316900    0.12554300    0.36063700
 C                 -5.35192100    0.59101700    0.47785200
 F                 -6.27516500   -0.41497000    0.40587300
 F                 -5.69647600    1.47527700   -0.50798000
 F                 -5.60539600    1.23517600    1.65314200
 N                  1.20420400   -2.03795400   -0.71807900
 H                  1.70798100   -2.59890100   -1.39733300
 O                  3.50351700   -2.68154000    0.07004300
 O                  1.75543600   -2.20686300    1.82655200
 S                  2.36983200   -1.86828700    0.55207900
 C                  2.88932100   -0.14457000    0.59213200
 C                  4.17548400    0.16913500    0.16005900
 C                  2.01625600    0.82443900    1.08476800
 C                  4.60312100    1.49291400    0.23098000
 H                  4.82503200   -0.61274600   -0.21334100
 C                  2.46798100    2.14133800    1.13293900
 H                  0.98688700    0.55592200    1.36580300
 C                  3.75732000    2.49558600    0.71858600
 H                  5.60580200    1.74747900   -0.09912100
 H                  1.79120700    2.90857800    1.49664700
```

```
 C                  4.22872600    3.92732600    0.81385800
 H                  4.53171000    4.17356200    1.83795000
 H                  5.08719100    4.11025100    0.16272800
 H                  3.43438300    4.62474000    0.53479400

 1 2 1.5 6 1.5 7 1.0
 2 3 1.5 8 1.0
 3 4 1.5 9 1.0
 4 5 1.5 11 1.0
 5 6 1.5 23 1.0
 6 10 1.0
 7
 8
 9
 10
 11 12 1.0 16 1.0 17 1.0
 12 13 1.0 14 1.0 15 1.0
 13
 14
 15
 16
 17 18 3.0
 18 19 1.5
 19 20 1.0 21 1.0 22 1.0
 20
 21
 22
 23 24 1.0 27 1.0
 24
 25 27 2.0
 26 27 2.0
 27 28 1.0
 28 29 1.5 30 1.5
 29 31 1.5 32 1.0
 30 33 1.5 34 1.0
 31 35 1.5 36 1.0
 32
 33 35 1.5 37 1.0
 34
 35 38 1.0
 36
 37
 38 39 1.0 40 1.0 41 1.0
 39
 40
 41
```

Table 4. Cartesian Coordinates of the optimized geometry of intermediate of **4c'**.
Free Energy = -1200.27486663 Hartree

```
-1 1
 C                 -0.12936600    3.71250400   -0.21005800
 C                  1.22794300    3.45187000   -0.03487300
 C                  1.63442900    2.13086500    0.16135700
```

```
C                  0.72306200    1.07871100    0.18586800
C                 -0.67308100    1.33498800    0.00505900
C                 -1.06350800    2.68283900   -0.19228800
H                 -0.47078400    4.73249200   -0.36569200
H                  1.95956600    4.25270000   -0.05267900
H                  2.69003800    1.91997500    0.29563600
H                 -2.11524000    2.88855300   -0.32425400
C                  1.18792000   -0.36627700    0.48584500
C                  0.97668200   -0.67330600    1.99489900
H                 -0.08604900   -0.56143600    2.21370300
H                  1.27997000   -1.70249500    2.20258400
H                  1.55072900    0.01288900    2.62338800
O                  0.51258100   -1.33238500   -0.30520800
C                  2.62263600   -0.54743800    0.18529200
C                  3.79166400   -0.74642400   -0.02109100
C                  5.18729600   -0.98550500   -0.28284400
F                  5.46835100   -2.30396300   -0.45674000
F                  5.98727600   -0.55910600    0.73470200
F                  5.63148500   -0.35177100   -1.40052100
N                 -1.51058300    0.23569300    0.02455900
H                 -0.44171900   -1.00715400   -0.27376800
C                 -2.83941800    0.32669600   -0.05437200
C                 -4.79344700   -1.20158400   -0.15368000
C                 -4.89025700   -2.73294200   -0.14195600
H                 -4.45514400   -3.13269700    0.77738400
H                 -5.93520800   -3.05265200   -0.20599800
H                 -4.34027900   -3.15316600   -0.98754300
C                 -5.36553400   -0.65499100   -1.47119600
H                 -5.30080200    0.43154800   -1.49672600
H                 -4.80257400   -1.06043700   -2.31699000
H                 -6.41294400   -0.95760600   -1.57925900
C                 -5.53178700   -0.62425600    1.06428500
H                 -6.58583600   -0.92242000    1.03984800
H                 -5.08762900   -1.01121200    1.98618300
H                 -5.46553900    0.46248900    1.07346700
O                 -3.36967100   -0.96983200   -0.06333800
O                 -3.59064600    1.30594700   -0.10640900

1 2 1.5 6 1.5 7 1.0
2 3 1.5 8 1.0
3 4 1.5 9 1.0
4 5 1.5 11 1.0
5 6 1.5 23 1.0
6 10 1.0
7
8
9
10
11 12 1.0 16 1.0 17 1.0
12 13 1.0 14 1.0 15 1.0
13
14
15
16 24 1.0
17 18 3.0
18 19 1.5
```

```
 19 20 1.0 21 1.0 22 1.0
 20
 21
 22
 23 25 1.5
 24
 25 39 1.0 40 2.0
 26 27 1.0 31 1.0 35 1.0 39 1.0
 27 28 1.0 29 1.0 30 1.0
 28
 29
 30
 31 32 1.0 33 1.0 34 1.0
 32
 33
 34
 35 36 1.0 37 1.0 38 1.0
 36
 37
 38
 39
 40
```

Table 5. Cartesian Coordinates of the optimized geometry of intermediate of **6a'**.
Free Energy = -1197.15275796 Hartree

```
-1 1
 C                  -3.13075800    2.34931500   -0.20075500
 C                  -1.87854300    2.63859800    0.33817600
 C                  -0.98344000    1.59463700    0.56258800
 C                  -1.29978900    0.26695800    0.26291300
 C                  -2.56231900   -0.01976200   -0.28347600
 C                  -3.46318600    1.03339000   -0.50638100
 H                  -3.84691900    3.14261900   -0.39233200
 H                  -1.59946200    3.66070000    0.57383900
 H                  -0.00279700    1.81235200    0.97408400
 H                  -4.43700800    0.81541500   -0.93359000
 C                  -0.31453100   -0.91114600    0.54377800
 C                  -0.40453700   -1.24307100    2.07752000
 H                  -1.42116700   -1.59048200    2.27721200
 H                   0.29124900   -2.05799400    2.29218100
 H                  -0.17812100   -0.38605400    2.72325500
 O                  -0.56309300   -1.97268400   -0.23262900
 C                   1.08949500   -0.42567100    0.28844700
 C                   2.24294200   -0.15719900    0.03874200
 C                   3.60254500    0.15214800   -0.28180400
 F                   4.47964000   -0.21067300    0.70352600
 F                   3.81387700    1.48979200   -0.48248100
 F                   4.05196800   -0.46076500   -1.41501800
 S                  -3.02892800   -1.70739200   -0.69049500
 H                  -4.33482300   -1.33117500   -0.89843900

 1 2 1.5 6 1.5 7 1.0
 2 3 1.5 8 1.0
```

```
 3 4 1.5 9 1.0
 4 5 1.5 11 1.0
 5 6 1.5 23 1.0
 6 10 1.0
 7
 8
 9
 10
 11 12 1.0 16 1.5 17 1.0
 12 13 1.0 14 1.0 15 1.0
 13
 14
 15
 16
 17 18 3.0
 18 19 1.5
 19 20 1.0 21 1.0 22 1.0
 20
 21
 22
 23 24 1.0
 24
```

Table 6. Cartesian Coordinates of the optimized geometry of intermediate of **amine** analogue with no protecting group.
Free Energy = -854.32325388 Hartree

```
-1 1
 C                 -3.51119600    2.00566200   -0.08603200
 C                 -2.24085200    2.33346700    0.38264100
 C                 -1.27536100    1.32578600    0.47700100
 C                 -1.53696800    0.00308500    0.12733000
 C                 -2.83748200   -0.32686800   -0.34048000
 C                 -3.80192300    0.69281800   -0.44369300
 H                 -4.27771600    2.76991600   -0.17800900
 H                 -1.99747400    3.35332900    0.66196700
 H                 -0.27902500    1.58377900    0.82233600
 H                 -4.79390000    0.43506700   -0.80755100
 C                 -0.46393200   -1.13312200    0.24513700
 C                 -0.57450800   -1.72493100    1.69566800
 H                 -1.57028700   -2.16273500    1.80060500
 H                  0.17009200   -2.51820000    1.80219800
 H                 -0.42660100   -0.97136400    2.47819200
 O                 -0.56673500   -2.09273200   -0.70805400
 C                  0.90372200   -0.52467400    0.13902000
 C                  2.04422100   -0.14255100    0.00825300
 C                  3.39106500    0.30334100   -0.17341500
 F                  4.27561900   -0.30503700    0.67406100
 F                  3.54504200    1.64681000    0.04379500
 F                  3.87681300    0.08190500   -1.42986800
 N                 -3.14421400   -1.64591600   -0.64624900
 H                 -3.88617100   -1.75377400   -1.32433400
 H                 -2.25352600   -2.15792700   -0.84771000
```

```
1 2 1.5 6 1.5 7 1.0
2 3 1.5 8 1.0
3 4 1.5 9 1.0
4 5 1.5 11 1.0
5 6 1.5 23 1.0
6 10 1.0
7
8
9
10
11 12 1.0 16 1.0 17 1.0
12 13 1.0 14 1.0 15 1.0
13
14
15
16
17 18 3.0
18 19 1.5
19 20 1.0 21 1.0 22 1.0
20
21
22
23 24 1.0 25 1.0
24
25
```