Supplementary Information

Rh(III)-catalyzed annulation of oxadiazolones with CF_3-imidoyl sulfoxonium ylides: access to trifluoromethyl-substituted fused-dihydroisoquinolines

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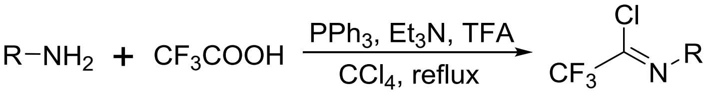
Contents

1. General Information

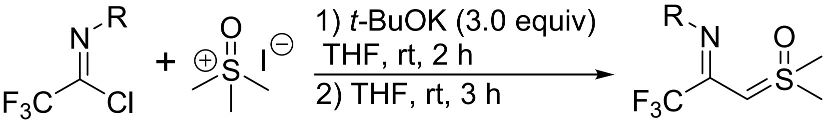
Unless otherwise noted, all reactions were carried out under air atmosphere. All reagents were from commercial sources and used as received without further purification. All solvents were dried by standard techniques and distilled prior to use. Column chromatography was performed on silica gel (200-300 meshes) using petroleum ether (bp. 60~90 °C) and ethyl acetate as eluent. ^{1}NMR spectra were recorded on a Bruker Avance operating at for ^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz and ^{19}F NMR at 376 MHz and spectral data were reported in ppm relative to tetramethylsilane (TMS) as internal standard and $CDCl_3$ (^{1}H NMR δ 7.26, ^{13}C NMR δ 77.16) as solvent. All coupling constants (*J*) are reported in Hz. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, dd = double doublet, ddd = double doublet of doublets, t = triplet, dt = double triplet, q = quatriplet, m = multiplet, br = broad. Gas chromatography (GC) analyses were performed on a Shimadzu GC-2014C chromatograph equipped with a FID detector. Mass spectra (MS) were measured on spectrometer by direct inlet at 70 eV. Mass spectroscopy data of the products were collected on an HRMS-TOF instrument or Waters TOFMS GCT Premier using EI or ESI ionization. Melting points were measured with WRR digital point apparatus and not corrected.

1.1 Preparation of Trifluoroacetimidoyl Chlorides[1]



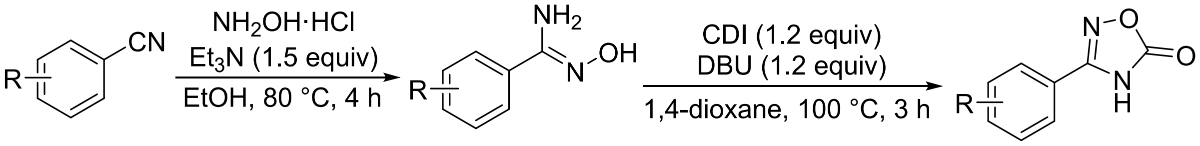
A 100 mL two-necked flask equipped with a septum cap, a condenser, and a Tefloncoated magnetic stir bar was charged with PPh_3 (9.84 g, 37.5 mmol), Et_3N (2.1 mL, 15 mmol), CCl_4 (20.0 mL), and TFA (1.2 mL, 15 mmol). After the solution was stirred for about 10 min (ice bath), amine (15 mmol) dissolved in CCl_4 (20.0 mL) was added. The mixture was then refluxed under stirring (3 h). After the reaction was completed, residual solid Ph_3PO, PPh_3 and Et_3N-HC1 were washed with hexane several times. Then the hexane was filtered and concentrated under vacuum. The crude product was purified by column chromatography on silica gel or neutral alumina to afford the corresponding trifluoroacetimidoyl chloride products.

1.2 Preparation of CF_3-Imidoyl Sulfoxonium Ylides[2]



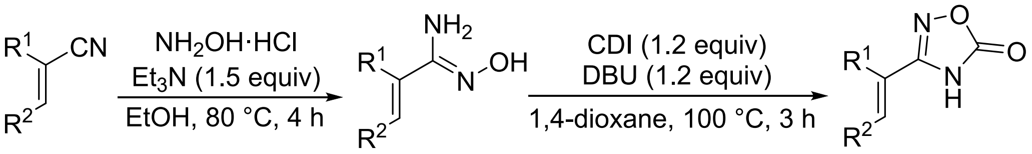
Trimethylsulfoxonium iodide (30 mmol, 3.0 equiv) was suspended in THF (150 mL) in a 250 mL round bottom flask, *t*-BuOK (30 mmol, 3.0 equiv) was added and the mixture was stirred at room temperature for 2 hours. After, trifluoroacetimidoyl chloride (10 mmol, 1.0 equiv) was added. The mixture was stirred at room temperature for 3 hours and then filtered through a plug of celite before all volatiles were removed under vacuum. Purification by flash chromatography (petroleum ether/EtOAc = 2: 1) afforded TFISY products. All the CF_3-imidoyl sulfoxonium ylides (TFISYs) are known compounds and have been reported previously by Cheng and our group.[2]

1.3 Preparation of Oxadiazolones[3,4]



To a round bottom flask (100 mL) containing arylnitrile (50 mmol, 1.0 equiv) were added hydroxylamine hydrochloride (5.21 g, 75 mmol, 1.5 equiv) and Et_3N (10.4 mL, 75 mmol, 1.5 equiv). Then, ethyl alcohol (50 mL) was sequentially added to the system, and the reaction mixture was stirred at 80 °C for 4 h. After cooling to ambient temperature, the mixture was concentrated in vacuo. Then, 50 mL of EtOAc was used to extract the product from the aqueous layer. The combined organic layer was washed with water (3 × 50 mL), dried over Na_2SO_4, filtered, and concentrated to afford the crude *N'*-hydroxybenzimidamide product. This residue was pure enough for further reaction as a white solid.

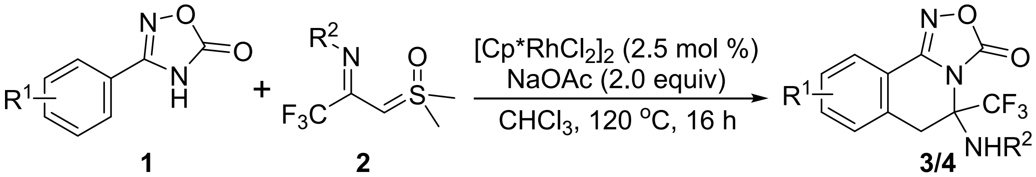
Then, to a round bottom flask (100 mL) containing substituted *N'*-hydroxybenzimidamide (30.0 mmol) were added *N*,*N'*-carbonyldiimidazole (CDI) (5.84 g, 36.0 mmol, 1.2 equiv) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (5.02 g, 33.0mmol, 1.1 equiv). Then, 1,4-dioxane (30 mL) was sequentially added to the system, and the reaction mixture was stirred at 100 °C for 3 h. After cooling to ambient temperature, the mixture was diluted with water, adjusted to pH ≈ 2 with 3 M HCl, and extracted with EtOAc. The combined organic layer was washed with water (3 × 50 mL), dried over Na_2SO_4, filtered, and concentrated to afford the crude product. The crude product was filtered through a Buchner funnel, and the precipitate was washed with cold $CHCl_3$ (3 × 10 mL). The obtained residue was pure enough for further reaction.



The oxadiazolones with substituted alkene moiety are prepared according to the above similar synthetic procedures.

2. Experimental Procedures

2.1. General Procedure for the Synthesis of Fused-Dihydroisoquinoline Products 3/4

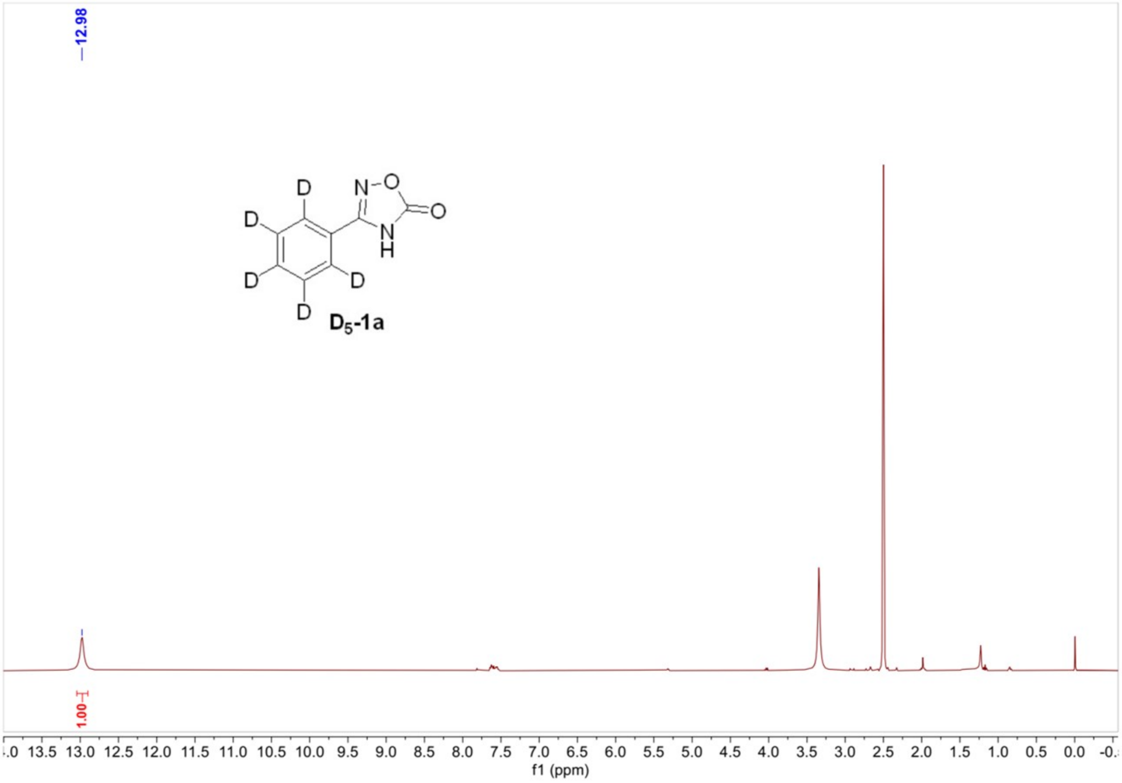


Under air atmosphere, 3-aryl-1,2,4-oxadiazol-5(4*H*)-ones **1** (0.3 mmol, 1.5 equiv) and TFISYs **2** (0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 120 °C (oil bath) for 16 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3 × 10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc) to yield the fused-dihydroisoquinoline products **3/4**.

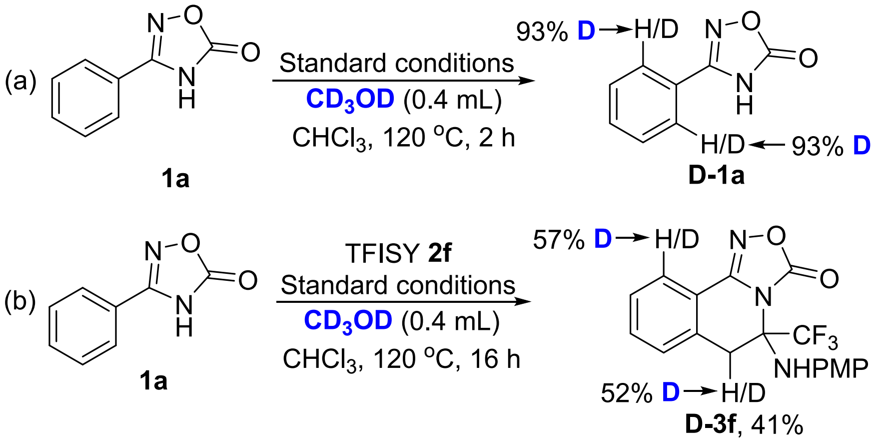
2.2. Mechanistic Studies

The deuterated 3-phenyl-1,2,4-oxadiazol-5(4H)-one **[D]$_5$-1a** was synthesized according to the reported procedure.[4]

^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.98 (1H, s).

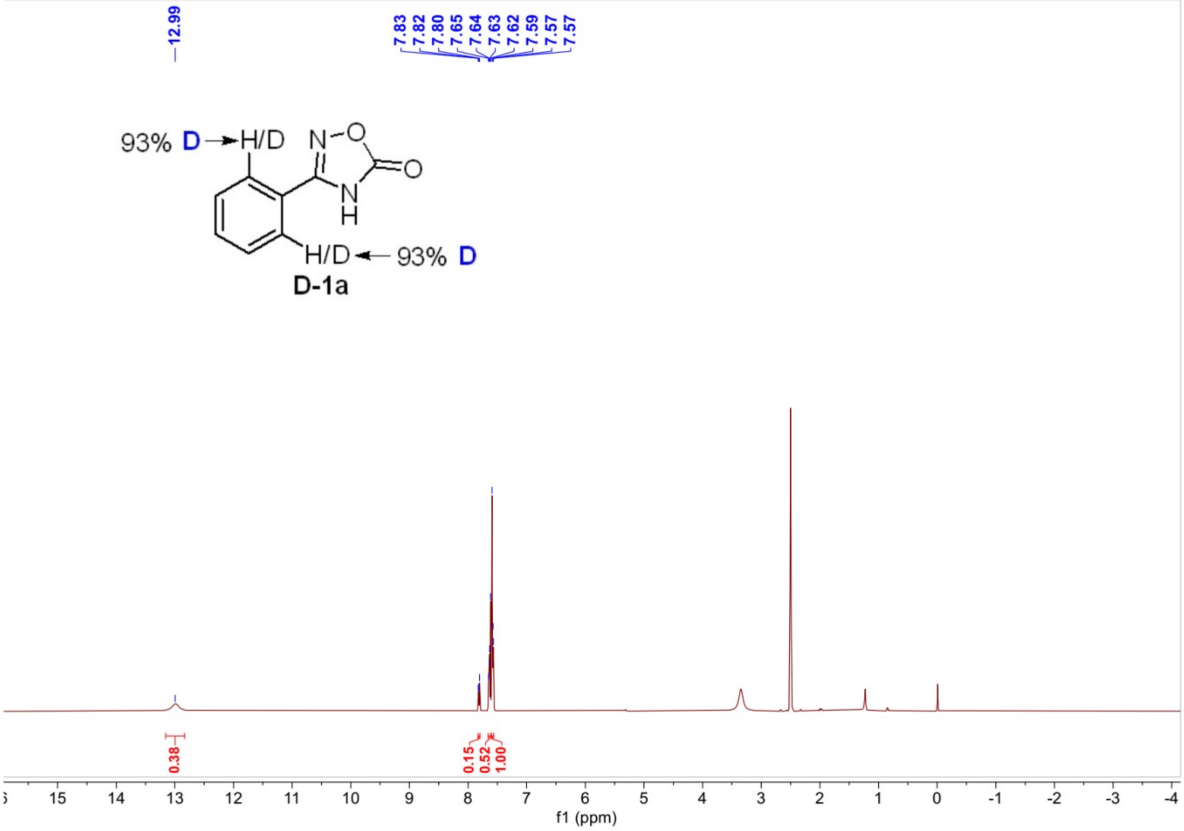


a) H/D Exchange Experiments

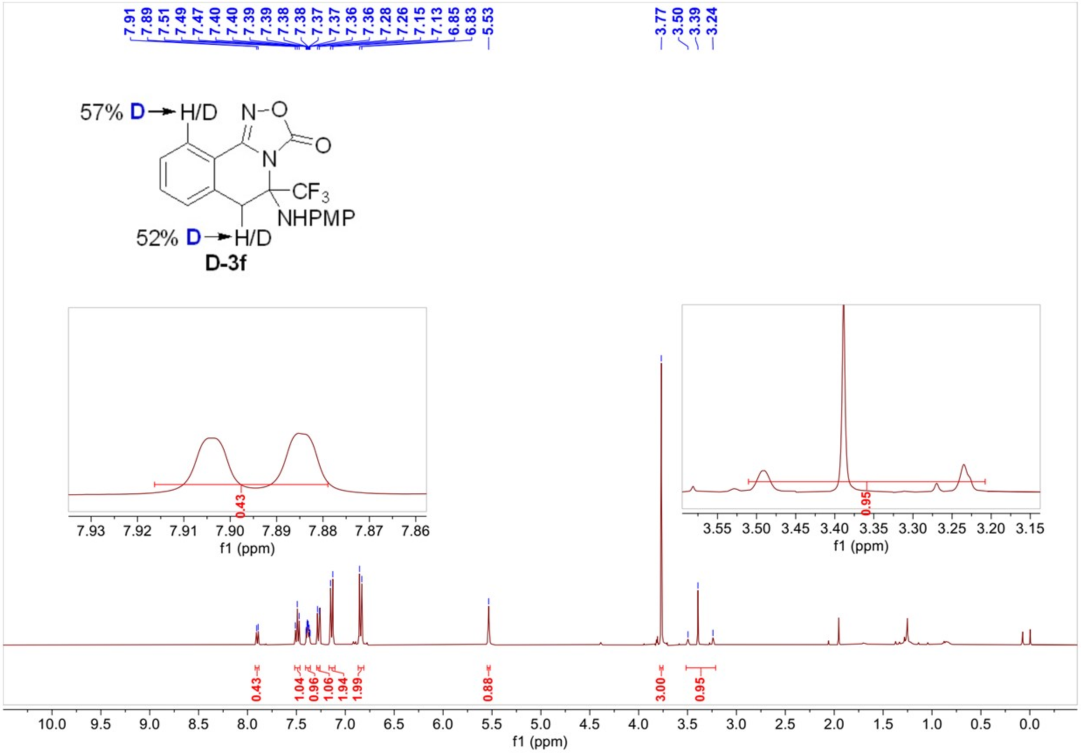


(a) To a 15 mL Schlenk tube with a magneton was added 3-phenyl-1,2,4-oxadiazol-5(4H)-one **1a** (48.64 mg, 0.30 mmol, 1.5 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv), CD_3OD (0.4 mL, 10.0 equiv) and $CHCl_3$ (2.0 mL). The reaction mixture was rapidly degassed several times, then it was sealed up and stirred vigorously at 120 °C (oil bath) for 2 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×10 mL). The extract was combined and concentrated under vacuum.

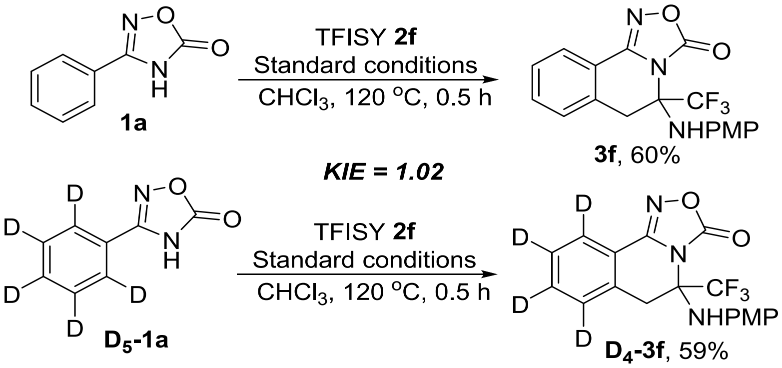
The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 3/1) to yield the product **D-1a**. The D-incorporation in **D-1a** was determined by ^{1}H NMR spectroscopy.



(b) To a 15 mL Schlenk tube with a magneton was added 3-phenyl-1,2,4-oxadiazol-5(4H)-one **1a** (48.6 mg, 0.30 mmol, 1.5 equiv) and TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv), CD_3OD (0.4 mL, 10.0 equiv) and $CHCl_3$ (2.0 mL). The reaction mixture was sealed up and stirred vigorously at 120 °C (oil bath) for 16 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield the product **D-3f** (30.9 mg, 41%). The D-incorporation in compound **D-3f** was determined by ^{1}H NMR spectroscopy.

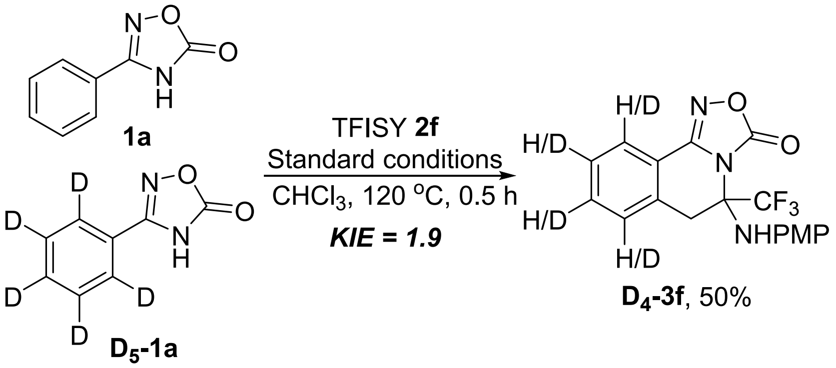


b) KIE by Parallel Experiments

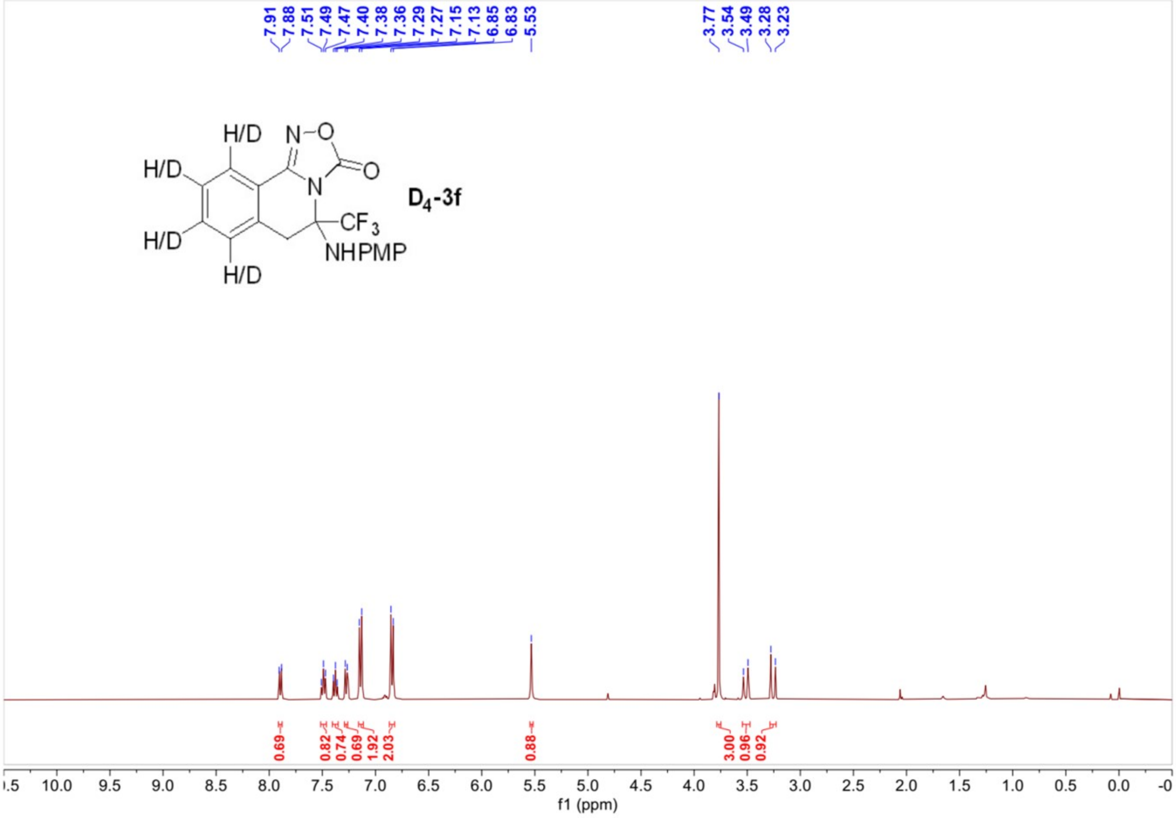


Two pressure tubes each was charged with $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv) and $CHCl_3$ (2.0 mL). To the parallel tubes was then separately added **1a** (48.7 mg, 0.3 mmol) and **$[D]_5$-1a** (50.0 mg, 0.3 mmol), respectively. The reaction was sealed up and stirred vigorously at 120 °C (oil bath) for 0.5 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield the product **3f** (45.2 mg, 60%) and **$[D]_4$-3f** (45.0 mg, 59%), respectively. The KIE value was calculated according to the ratio of isolated yields of **3f** and **$[D]_4$-3f** from the two parallel reactions.

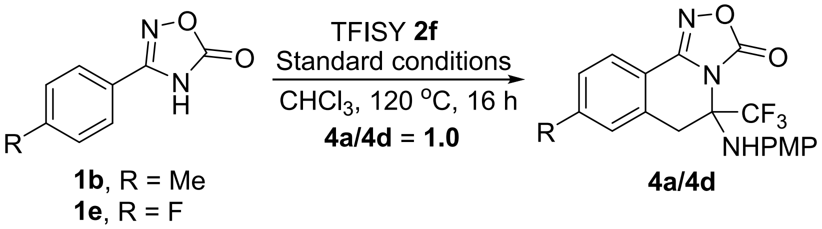
c) KIE by Competitive Experiments



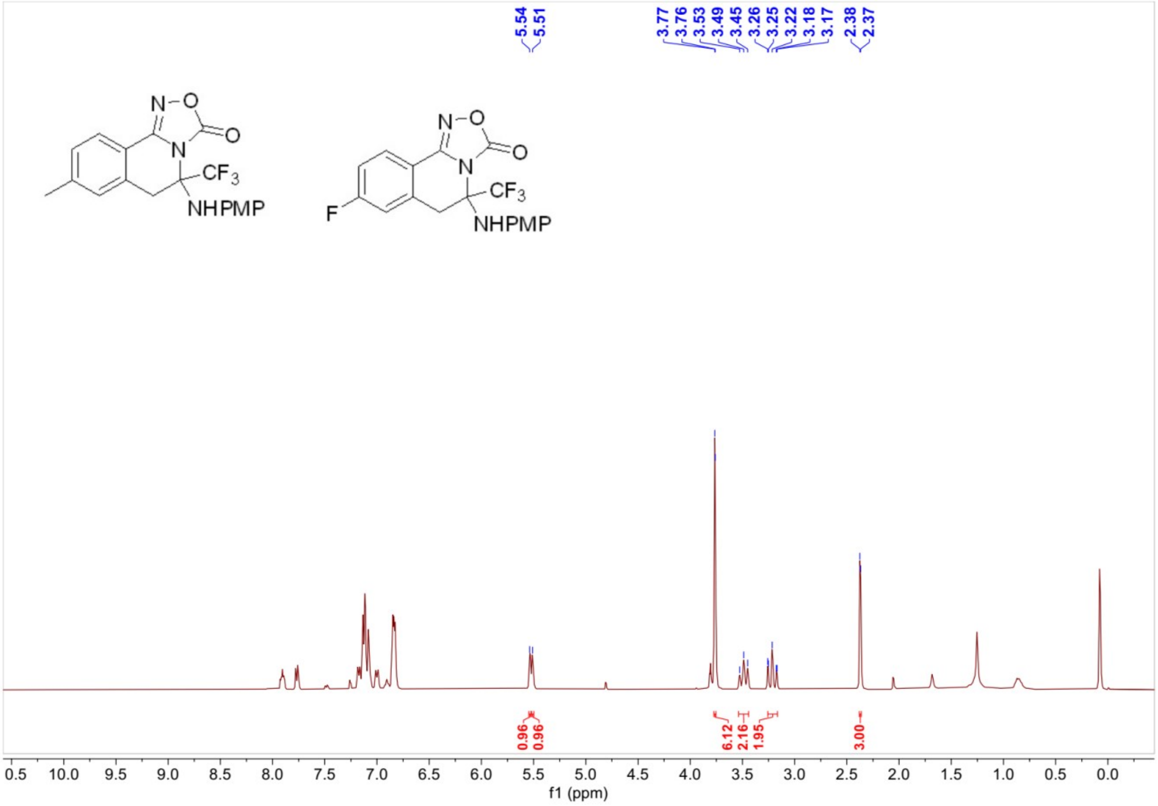
To a 15 mL Schlenk tube with a magneton was added **1a** (24.3 mg, 0.15 mmol, 0.75 equiv), **[D]$_5$-1a** (25.1 mg, 0.15 mmol, 0.75 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). The reaction mixture was sealed up and stirred vigorously at 120 °C (oil bath) for 0.5 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield the product **3f** and **D$_4$-3f**. The KIE value (1.9) was determined by ^{1}H NMR spectroscopy.



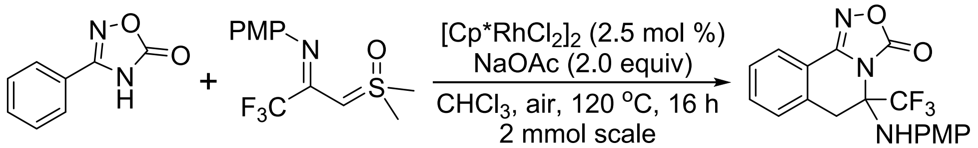
2.3. Competition Experiments



Under air atmosphere, oxadiazolone **1b** (26.4 mg, 0.15 mmol, 0.75 equiv), oxadiazolone **1e** (27.0 mg, 0.15 mmol, 0.75 equiv) TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2 mL) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 120 °C (oil bath) for 16 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3× 10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield the product **4a** and **4d** as a mixture of yellow solid. The ratio of **4a** and **4d** was determined by ^{1}H NMR spectroscopy.



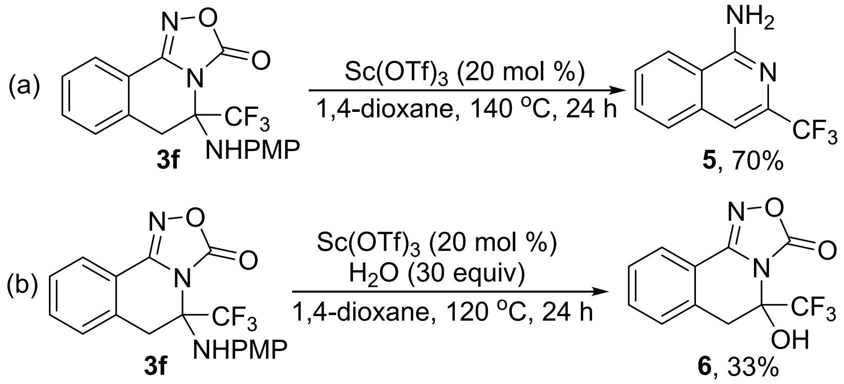
2.4. Scale-up Reaction



1a **2f** **3f**, 0.57 g, 75%

Under air atmosphere, 3-phenyl-1,2,4-oxadiazol-5(4*H*)-one **1a** (486 mg, 3.0 mmol, 1.5 equiv), TFISY **2f** (587 mg, 2.0 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (31 mg, 0.05 mmol, 2.5 mol %), NaOAc (328 mg, 4.0 mmol, 2.0 equiv) and CHCl$_3$ (20 mL) were added to an oven-dried 100 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 120 °C (oil bath) for 16 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×30 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield the product **3f** as a white solid (0.57 g, 75%).

2.5. Synthetic Transformation



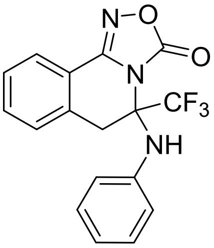
(a) **3f** → **5**, 70%

(b) **3f** → **6**, 33%

(a) Under air atmosphere, compound **3f** (57.8 mg, 0.2 mmol, 1.0 equiv), Sc(OTf)$_3$ (19.7 mg, 0.04 mmol, 20 mol %) and 1,4-dioxane (2.0 mL) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 140 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield the isoquinolin-1-amine product **5** as a white solid (29.7 mg, 70%).

(b) Under air atmosphere, compound **3f** (57.8 mg, 0.2 mmol, 1.0 equiv), $Sc(OTf)_3$ (19.7 mg, 0.04 mmol, 20 mol %), H_2O (108.0 mg, 6.0 mmol, 30.0 equiv) and 1,4-dioxane (2.0 mL) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 120 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 3/1) to yield the tertiary alcohol product **6** as a white solid (18.0 mg, 33%).

3. Characterization Data of the Corresponding Products



5-(phenylamino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3a**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2a** (52.7 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, $R_f = 0.5$) to give the titled product **3a** as a brown solid (43.1 mg, 62%).

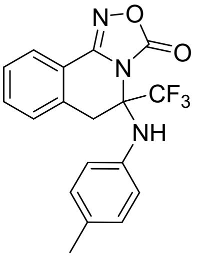
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (d, J = 7.8 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.35 – 7.28 (m, 3H), 7.19 (t, J = 7.4 Hz, 1H), 7.14 (d, J = 7.5 Hz, 2H), 5.68 (s, 1H), 3.69 (d, J = 17.4 Hz, 1H), 3.34 (d, J = 17.3 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.2, 154.1, 139.1, 133.2, 132.4, 129.7, 128.4, 128.4, 126.5, 126.1, 124.7, 123.9 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.3 Hz), 118.8, 75.4 (C-F, q, $^2J_{(C\text{-}F)}$ = 30.1 Hz), 32.4.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.21.

M.p. 127.5-128.6 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{17}H_{13}F_3N_3O_2^+$ 348.0954, found 348.0955.



5-(p-tolylamino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3b**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2b** (55.5 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3b** as a purple solid (50.6 mg, 70%).

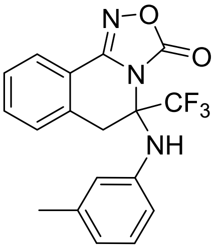
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.8 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 7.12 (d, J = 8.3 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 5.60 (s, 1H), 3.62 (d, J = 17.3 Hz, 1H), 3.30 (d, J = 17.3 Hz, 1H), 2.31 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 154.2, 136.3, 136.2, 133.2, 132.5, 130.3, 130.0, 128.4, 128.3, 127.2, 124.0 (C-F, q, $^1J_{(C-F)}$ = 288.1 Hz), 124.6, 120.6, 119.7, 118.9, 75.7 (C-F, q, $^2J_{(C-F)}$ = 29.6 Hz), 32.5, 20.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -80.14 .

M.p. 128.3-129.5 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{18}H_{15}F_3N_3O_2^+$ 362.1111, found 362.1110.



5-(m-tolylamino)-5-(trifluoromethyl)-5,6-dihydro-3H-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3c**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2c** (55.5 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3c** as a brown solid (43.4 mg, 60%).

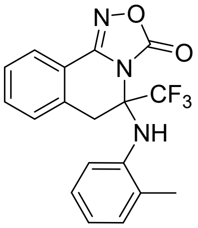
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.40 (t, J = 7.4 Hz, 1H), 7.30 (d, J = 7.7 Hz, 1H), 7.19 (t, J = 7.7 Hz, 1H), 7.00 (d, J = 7.7 Hz, 1H), 6.97 (s, 1H), 6.93 (d, J = 8.3 Hz, 1H), 5.63 (s, 1H), 3.69 (d, J = 17.4 Hz, 1H), 3.33 (d, J = 17.4 Hz, 1H), 2.32 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.3, 154.1, 139.8, 139.0, 133.2, 132.5, 129.4, 128.4, 128.3, 127.4, 127.0, 124.7, 123.4, 124.0 (C-F, q, $^1J_{(C-F)}$ = 273.3 Hz), 118.8, 75.4 (C-F, q, $^2J_{(C-F)}$ = 29.9 Hz), 32.5, 21.5.

^{19}F NMR (376 MHz, CDCl$_3$) -80.23.

M.p. 143.3-144.5 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{18}H_{15}F_3N_3O_2^+$ 362.1111, found 362.1110.



5-(o-tolylamino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3d**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2d** (55.5 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3d** as a brown solid (54.3 mg, 75%).

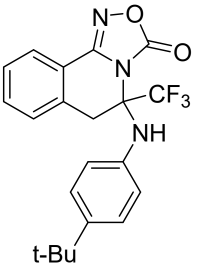
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.96 (d, J = 7.5 Hz, 1H), 7.51 (td, J = 7.6, 1.5 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.28 – 7.20 (m, 2H), 7.15 – 7.06 (m, 2H), 6.99 – 6.89 (m, 1H), 5.23 (s, 1H), 3.61 (d, J = 19.2 Hz, 1H), 3.29 (d, J = 17.7 Hz, 1H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.1, 154.0, 137.7, 135.9, 133.2, 132.4, 131.5, 128.5, 128.3, 127.2, 126.1, 124.9, 124.7, 124.2 (C-F, q, $^1J_{(C-F)}$ = 288.1 Hz), 119.9, 75.5 (C-F, q, $^2J_{(C-F)}$ = 30.3 Hz), 30.9, 18.3.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.68.

M.p. 139.4-141.1 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{18}H_{15}F_3N_3O_2^+$ 362.1111, found 362.1115.



5-((4-(tert-butyl)phenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3e**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2e** (63.8 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3e** as a brown solid (59.7 mg, 74%).

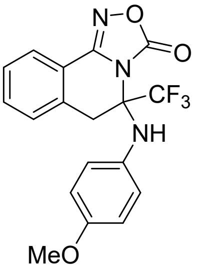
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (d, J = 7.9 Hz, 1H), 7.50 (td, J = 7.6, 1.5 Hz, 2H), 7.39 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 7.7 Hz, 2H), 7.09 (d, J = 8.5 Hz, 2H), 5.60 (s, 1H), 3.68 (d, J = 17.1 Hz, 1H), 3.32 (d, J = 17.3 Hz, 1H), 1.29 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.2, 154.1, 149.2, 136.1, 133.1, 132.5, 128.4, 128.2, 126.5, 126.5, 124.6, 123.9 (C-F, q, $^1J_{(C-F)}$ = 287.9 Hz), 118.8, 75.6 (C-F, q, $^2J_{(C-F)}$ = 29.9 Hz), 34.5, 32.4, 31.3.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.65.

M.p. 115.3-116.7 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{21}H_{21}F_3N_3O_2^+$ 404.1580, found 404.1585.



5-((4-methoxyphenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3f**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3f** as a purple solid (64.9 mg, 86%).

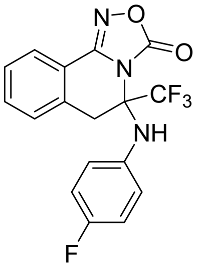
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 7.7 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.14 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 5.53 (s, 1H), 3.77 (s, 3H), 3.52 (d, J = 17.2 Hz, 1H), 3.26 (d, J = 17.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 157.5, 154.3, 133.2, 132.5, 131.3, 129.6, 128.4, 128.3, 124.6, 124.0 (C-F, q, $^1J_{(C-F)}$ = 288.0 Hz), 119.0, 114.8, 76.0 (C-F, q, $^2J_{(C-F)}$ = 29.8 Hz), 55.6, 32.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -80.48.

M.p. 110.8-112.0 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{18}H_{15}F_3N_3O_3^+$ 378.1060, found 378.1064.



5-((4-fluorophenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3g**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2g** (56.3 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3g** as a white solid (48.9 mg, 67%).

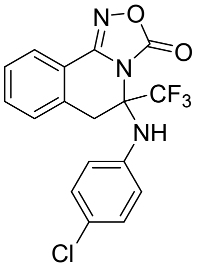
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.21 – 7.14 (m, 2H), 7.02 (t, *J* = 8.5 Hz, 2H), 5.62 (s, 1H), 3.53 (d, *J* = 17.1 Hz, 1H), 3.29 (d, *J* = 16.9 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 162.4, 160.0, 157.4, 154.1, 134.7 (C-F, d, $^3J_{(C-F)}$ = 2.9 Hz), 133.3, 132.2, 129.5 (C-F, d, $^3J_{(C-F)}$ = 8.3 Hz), 128.5, 128.4, 124.7, 123.9 (C-F, q, $^1J_{(C-F)}$ = 288.2 Hz), 118.8, 116.5 (C-F, d, $^2J_{(C-F)}$ = 22.4 Hz), 75.6 (C-F, q, $^2J_{(C-F)}$ = 29.9 Hz), 32.5.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.03, 115.36.

M.p. 143.0-144.5 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{17}H_{12}F_4N_3O_2^+$ 366.0860, found 366.0864.



5-((4-chlorophenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3h**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2h** (59.5 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3h** as a yellow solid (56.5 mg, 74%).

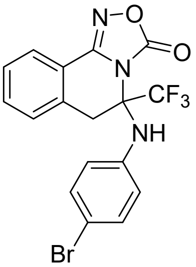
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (d, J = 7.8 Hz, 1H), 7.52 (t, J = 6.9 Hz, 1H), 7.42 (t, J = 7.7 Hz, 1H), 7.33 – 7.26 (m, 3H), 7.09 (d, J = 8.7 Hz, 2H), 5.66 (s, 1H), 3.61 (d, J = 17.5 Hz, 1H), 3.32 (d, J = 17.2 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.2, 154.0, 137.7, 133.3, 132.1, 131.9, 129.8, 128.5, 128.4, 127.9, 125.3, 124.8, 123.8 (C-F, q, $^1J_{(C-F)}$ = 288.4 Hz), 118.8, 75.3 (C-F, q, $^2J_{(C-F)}$ = 29.5 Hz), 32.4.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.68.

M.p. 130.2-131.4 °C.

HRMS (ESI): [M+H]$^+$ calcd. for $C_{17}H_{12}ClF_3N_3O_2^+$ 382.0565, found 382.0569.



5-((4-bromophenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3i**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2i** (68.4 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R$_f$ = 0.5) to give the titled product **3i** as a white solid (58.0 mg, 68%).

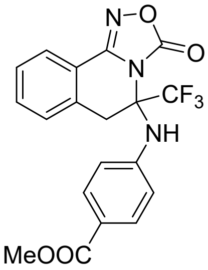
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (d, J = 8.0 Hz, 1H), 7.52 (td, J = 7.6, 1.4 Hz, 1H), 7.47 – 7.38 (m, 3H), 7.30 (d, J = 7.7 Hz, 1H), 7.02 (d, J = 8.7 Hz, 2H), 5.65 (s, 1H), 3.63 (d, J = 17.2 Hz, 1H), 3.33 (d, J = 17.2 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.2, 154.0, 138.2, 133.4, 132.8, 132.0, 128.6, 128.4, 128.1, 128.0, 124.78, 123.8 (C-F, q, $^1J_{(C-F)}$ = 288.4 Hz), 119.6, 118.7, 75.1 (C-F, q, $^2J_{(C-F)}$ = 30.5 Hz), 32.4.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.18.

M.p. 150.4-151.6 °C.

HRMS (ESI): [M+H]$^+$ calcd. for $C_{17}H_{12}BrF_3N_3O_2^+$ 426.0060, found 426.0062.



Methyl 4-((3-oxo-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-5-yl)amino)benzoate (**3j**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2j** (64.3 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, $R_f = 0.5$) to give the titled product **3j** as a yellow solid (36.5 mg, 45%).

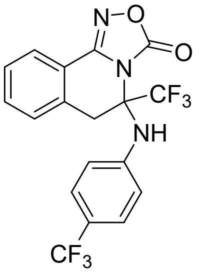
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.92 (m, 3H), 7.55 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.00 (d, J = 8.2 Hz, 2H), 5.79 (s, 1H), 3.91 (d, J = 18.1 Hz, 1H), 3.88 (s, 3H), 3.44 (d, J = 18.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 156.4, 153.8, 144.2, 133.4, 131.9, 131.4, 128.6, 128.5, 126.0, 124.9, 123.8 (C-F, d, $^1J_{(C-F)}$ = 288.9 Hz), 121.8, 118.6, 74.2 (C-F, d, $^2J_{(C-F)}$ = 23.1 Hz), 52.2, 32.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -81.21.

M.p. 173.1-174.9 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{19}H_{15}F_3N_3O_4^+$ 406.1009, found 406.1007.



5-(trifluoromethyl)-5-((4-(trifluoromethyl)phenyl)amino)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3k**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2k** (66.3 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, $R_f = 0.5$) to give the titled product **3k** as a white solid (41.5 mg, 50%).

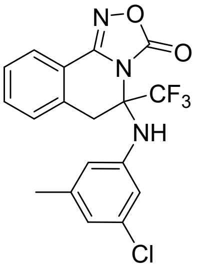
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.8 Hz, 1H), 7.59 – 7.51 (m, 3H), 7.45 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 7.7 Hz, 1H), 7.12 (d, J = 8.3 Hz, 2H), 5.79 (s, 1H), 3.83 (d, J = 17.6 Hz, 1H), 3.43 (d, J = 17.7 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 156.7, 153.8, 143.0, 133.5, 131.8, 128.7, 128.5, 127.0 (C-F, q, $^3J_{(C\text{-}F)}$ = 3.8 Hz), 126.8, 124.9, 124.0 (C-F, q, $^1J_{(C\text{-}F)}$ = 272.0 Hz), 123.4, 123.8 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.6 Hz), 118.6, 74.4 (C-F, q, $^2J_{(C\text{-}F)}$ = 30.3 Hz), 32.0.

^{19}F NMR (376 MHz, CDCl$_3$) δ -62.32, -80.52.

M.p. 156.3-157.9 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{18}H_{12}F_6N_3O_2^+$ 416.0828, found 416.0829.



5-((3-chloro-5-methylphenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3m**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2m** (62.3 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3m** as a yellow solid (45.8 mg, 58%).

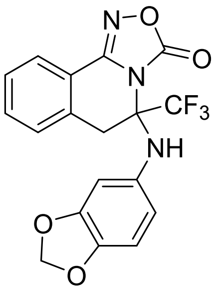
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (d, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 6.93 (s, 1H), 6.84 (s, 1H), 5.67 (s, 1H), 3.67 (d, *J* = 17.3 Hz, 1H), 3.34 (d, *J* = 17.3 Hz, 1H), 2.29 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.2, 154.0, 141.3, 140.2, 134.8, 133.3, 132.1, 128.5, 127.0, 125.1, 124.7, 123.5, 123.8 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.4 Hz), 118.8, 75.1 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.9 Hz), 32.4, 21.4.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.77.

M.p. 113.9-114.9 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{18}H_{14}ClF_3N_3O_2^+$ 396.0721, found 396.0720.



5-(benzo[*d*][1,3]dioxol-5-ylamino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-a]isoquinolin-3-one (**3n**)

General procedure was followed with 3-phenyl-1,2,4-oxadiazol-5(2*H*)-one **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2n** (61.4 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv), CHCl$_3$ (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R$_f$ = 0.5) to give the titled product **3n** **as** a brown solid (60.2 mg, 77%).

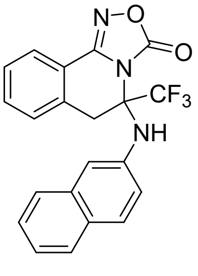
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.7 Hz, 1H), 6.76 – 6.65 (m, 3H), 5.98 – 5.91 (m, 2H), 5.53 (s, 1H), 3.55 (d, *J* = 17.2 Hz, 1H), 3.25 (d, *J* = 17.8 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.5, 154.2, 148.4, 146.5, 133.2, 132.4, 132.4, 128.4, 128.3, 124.6, 123.9 (C-F, q, $^1J_{(C-F)}$ = 288.2 Hz), 121.6, 118.8, 109.6, 108.5, 101.8, 75.9 (C-F, q, $^2J_{(C-F)}$= 29.7 Hz), 32.6.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.56.

M.p. 147.6-149.3 °C.

HRMS (ESI): [M+H]$^+$ calcd. for $C_{18}H_{13}F_3N_3O_4^+$ 392.0853, found 392.0856.



5-(naphthalen-2-ylamino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3o**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2o** (62.7 mg, 0.2 mmol, 1.0 equiv), [Cp*$RhCl_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3o** as a black solid (52.5 mg, 66%).

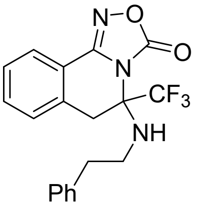
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (d, J = 7.8 Hz, 1H), 7.80 (t, J = 7.0 Hz, 2H), 7.75 (d, J = 7.9 Hz, 1H), 7.56 – 7.36 (m, 5H), 7.33 – 7.26 (m, 2H), 5.87 (s, 1H), 3.78 (d, J = 17.4 Hz, 1H), 3.42 (d, J = 17.3 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.3, 154.1, 136.7, 133.9, 133.2, 132.3, 131.5, 129.6, 128.4, 127.8, 127.7, 126.9, 126.0, 125.8, 124.7, 124.0 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.4 Hz), 123.2, 118.8, 75.5 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.4 Hz), 32.4.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.17.

M.p. 125.2-126.9 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{21}H_{15}F_3N_3O_2^+$ 398.1111, found 398.1115.



5-(phenethylamino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3p**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2p** (58.3 mg, 0.2 mmol, 1.0 equiv), [Cp*$RhCl_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3p** as a white solid (61.6 mg, 82%).

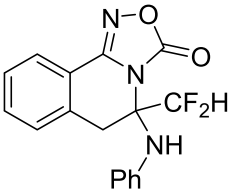
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.29 (q, *J* = 7.1, 6.3 Hz, 3H), 7.26 – 7.19 (m, 3H), 3.61 (d, *J* = 17.4 Hz, 1H), 3.45 (d, *J* = 4.3 Hz, 1H), 3.19 (d, *J* = 17.4 Hz, 1H), 3.04 – 2.95 (m, 2H), 2.94 – 2.86 (m, 2H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 156.8, 154.5, 138.8, 133.2, 132.5, 128.9, 128.7, 128.4, 126.7, 124.7, 123.9 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.3 Hz), 119.1, 76.5 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.2 Hz), 44.2, 36.4, 31.8.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.39.

M.p. 102.3-103.9 °C.

HRMS (ESI): [M+H]$^+$ calcd. for $C_{19}H_{17}F_3N_3O_2^+$ 376.1267, found 376.1266.



5-(difluoromethyl)-5-(phenylamino)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3q**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2q** (49.1 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R$_f$ = 0.5) to give the titled product **3q** as a white solid (42.8 mg, 65%).

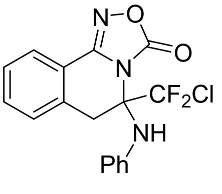
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (d, *J* = 7.6 Hz, 1H), 7.56 – 7.48 (m, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 1H), 7.22 (t, *J* = 7.9 Hz, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.91 (d, *J* = 7.4 Hz, 2H), 6.72 – 6.23 (m, 1H), 4.79 (s, 1H), 3.59 (d, *J* = 17.4 Hz, 1H), 3.47 (d, *J* = 17.4 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.4, 153.9, 139.8, 133.2, 132.5, 129.7, 129.0, 128.3, 125.2, 124.7, 124.3, 118.9, 112.9 (C-F, t, $^1J_{(C\text{-}F)}$ = 251.7 Hz), 74.3 (C-F, t, $^2J_{(C\text{-}F)}$ = 24.1 Hz), 31.9.

^{19}F NMR (376 MHz, CDCl$_3$) δ -129.76 (d, *J* = 54.3 Hz), -130.50 (d, *J* = 54.3 Hz), -134.06 (d, *J* = 55.8 Hz), -134.80 (d, *J* = 56.1 Hz).

M.p. 127.5-128.9 °C.

HRMS (ESI): [M+H]$^+$ calcd. for $C_{17}H_{14}F_2N_3O_2^+$ 330.1049, found 330.1052.



5-(chlorodifluoromethyl)-5-(phenylamino)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3r**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2r** (55.9 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3r** as a yellow solid (33.5 mg, 46%).

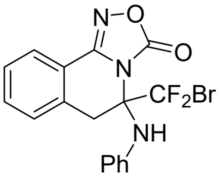
1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.6 Hz, 1H), 7.55 – 7.46 (m, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.36 – 7.26 (m, 3H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.17 – 7.13 (m, 2H), 5.76 (s, 1H), 3.66 (d, *J* = 17.5 Hz, 1H), 3.46 (d, *J* = 17.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 154.3, 139.4, 133.2, 132.7, 129.7, 129.5 (C-F, t, $^1J_{(C\text{-}F)}$ = 303.3 Hz), 128.3, 126.4, 126.0, 124.6, 119.1, 78.9 (C-F, t, $^2J_{(C\text{-}F)}$ = 25.5 Hz), 33.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.47 (d, *J* = 166.9 Hz), -65.81 (d, *J* = 166.9 Hz).

M.p. 130.2-131.9 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{17}H_{13}ClF_2N_3O_2^+$ 364.0659, found 364.0663.



5-(bromodifluoromethyl)-5-(phenylamino)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**3s**)

General procedure was followed with oxadiazolone **1a** (48.6 mg, 0.3 mmol, 1.5 equiv), TFISY **2s** (64.8 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **3s** as a yellow solid (32.7 mg, 40%).

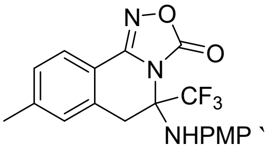
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.31 (q, *J* = 8.2, 7.6 Hz, 3H), 7.23 – 7.13 (m, 3H), 5.76 (s, 1H), 3.62 (d, *J* = 17.3 Hz, 1H), 3.51 (d, *J* = 17.4 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.3, 154.3, 139.4, 133.2, 132.6, 129.7, 128.3, 126.5, 126.0, 124.6, 124.5 (C-F, t, $^1J_{(C\text{-}F)}$ = 316.9 Hz), 119.2, 79.5 (C-F, t, $^2J_{(C\text{-}F)}$ = 23.0 Hz), 34.0.

^{19}F NMR (376 MHz, CDCl$_3$) δ -56.88 (d, *J* = 167.6 Hz), -60.06 (d, *J* = 167.6 Hz).

M.p. 101.9-102.7 °C.

HRMS (ESI): [M+H]$^+$ calcd. for $C_{17}H_{13}BrF_2N_3O_2^+$ 408.0154, found 408.0159.



5-((4-methoxyphenyl)amino)-8-methyl-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**4a**)

General procedure was followed with oxadiazolone **1b** (52.9 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **4a** as a brown solid (54.8 mg, 70%).

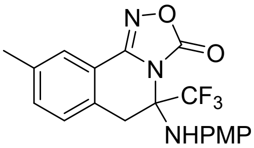
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.8 Hz, 2H), 7.08 (s, 1H), 6.84 (d, *J* = 8.9 Hz, 2H), 5.54 (s, 1H), 3.77 (s, 3H), 3.48 (d, *J* = 17.4 Hz, 1H), 3.20 (d, *J* = 17.2 Hz, 1H), 2.38 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.4, 157.6, 154.3, 144.1, 132.5, 131.4, 129.6, 129.2, 128.9, 124.6, 124.0 (C-F, q, $^1J_{(C\text{-}F)}$ = 287.9 Hz), 116.1, 114.8, 76.0 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.6 Hz), 55.6, 32.6, 21.8 .

^{19}F NMR (376 MHz, CDCl$_3$) δ -79.96.

M.p. 154.2-155.1 °C.

HRMS (ESI): [M+H]$^+$ calcd. for $C_{19}H_{17}F_3N_3O_3^+$ 392.1217, found 392.1218.



5-((4-methoxyphenyl)amino)-9-methyl-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**4b**)

General procedure was followed with oxadiazolone **1c** (52.9 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, $R_f = 0.5$) to give the titled product **4b** as a yellow solid (68.9 mg, 88%).

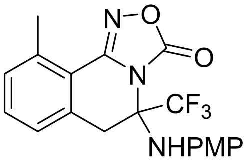
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.14 (t, J = 8.2 Hz, 3H), 6.84 (d, J = 8.9 Hz, 2H), 5.53 (s, 1H), 3.77 (s, 3H), 3.46 (d, J = 17.2 Hz, 1H), 3.21 (d, J = 17.1 Hz, 1H), 2.36 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 157.6, 154.4, 138.4, 134.1, 131.4, 129.5, 129.5, 128.2, 124.8, 124.0 (C-F, q, $^1J_{(C\text{-}F)} = 288.2$ Hz), 118.6, 114.8, 76.1 (C-F, q, $^2J_{(C\text{-}F)} = 29.6$ Hz), 55.6, 32.2, 21.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -79.94.

M.p. 128.3-129.0 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{19}H_{17}F_3N_3O_3^+$ 392.1217, found 392.1220.



5-((4-methoxyphenyl)amino)-10-methyl-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**4c**)

General procedure was followed with oxadiazolone **1d** (52.9 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, $R_f = 0.5$) to give the titled product **4c** as a white solid (47.0 mg, 60%).

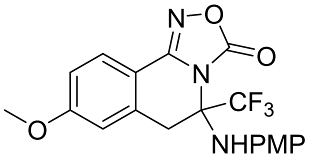
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.35 (t, *J* = 7.7 Hz, 1H), 7.21 (d, *J* = 7.7 Hz, 1H), 7.12 (dd, *J* = 13.9, 8.2 Hz, 3H), 6.84 (d, *J* = 8.9 Hz, 2H), 5.66 (s, 1H), 3.77 (s, 3H), 3.48 (d, *J* = 16.9 Hz, 1H), 3.23 (d, *J* = 16.8 Hz, 1H), 2.60 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.4, 157.3, 155.1, 139.2, 133.3, 132.2, 131.4, 131.1, 129.7, 126.0, 124.0 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.1 Hz), 117.8, 114.7, 75.5 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.4 Hz), 55.5, 33.4, 22.9.

^{19}F NMR (376 MHz, CDCl$_3$) δ -79.79.

M.p. 126.0-127.3 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{19}H_{17}F_3N_3O_3^+$ 392.1217, found 392.1219.



8-methoxy-5-((4-methoxyphenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-a]isoquinolin-3-one (**4d**)

General procedure was followed with 3-(4-methoxyphenyl)-1,2,4-oxadiazol-5(4H)-one **1e** (57.7 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv), CHCl$_3$ (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **4d** as a brown solid (65.5 mg, 80%).

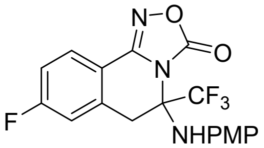
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.81 (d, *J* = 8.7 Hz, 1H), 7.13 (d, *J* = 8.9 Hz, 2H), 6.88 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.86 – 6.81 (m, 2H), 6.75 (d, *J* = 2.2 Hz, 1H), 5.54 (s, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 3.48 (d, *J* = 17.1 Hz, 1H), 3.19 (d, *J* = 17.2 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 163.3, 158.4, 157.6, 154.1, 134.6, 131.3, 129.6, 126.5, 124.0 (C-F, q, $^1J_{(C\text{-}F)}$ = 287.9 Hz), 114.7, 114.3, 113.4, 111.0, 75.8 (C-F, q, $^2J_{(C\text{-}F)}$= 29.7 Hz), 55.7, 55.6, 32.8.

^{19}F NMR (376 MHz, CDCl$_3$) δ -84.74.

M.p. 163.4-164.5 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{19}H_{17}F_3N_3O_4^+$ 408.1166, found 408.1172.



8-fluoro-5-((4-methoxyphenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**4e**)

General procedure was followed with oxadiazolone **1f** (54.0 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **4e** as a brown solid (47.4 mg, 60%).

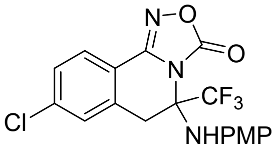
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (dd, J = 8.8, 5.3 Hz, 1H), 7.15 – 7.04 (m, 3H), 7.00 (d, J = 7.8 Hz, 1H), 6.85 (d, J = 8.5 Hz, 2H), 5.52 (s, 1H), 3.77 (s, 3H), 3.51 (d, J = 17.4 Hz, 1H), 3.23 (d, J = 17.3 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 165.3 (C-F, d, $^1J_{(C\text{-}F)}$ = 255.8 Hz), 158.5, 157.4, 153.6, 135.5 (C-F, d, $^3J_{(C\text{-}F)}$ = 8.7 Hz), 131.1, 129.7, 127.2 (C-F, d, $^3J_{(C\text{-}F)}$ = 9.5 Hz), 123.9 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.2 Hz), 116.1 (C-F, d, $^2J_{(C\text{-}F)}$ =22.8 Hz), 115.7 (C-F, d, $^2J_{(C\text{-}F)}$ =23.2 Hz), 115.2 (C-F, d, $^4J_{(C\text{-}F)}$ =3.7 Hz), 114.9, 75.9 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.6 Hz), 55.6, 32.6.

^{19}F NMR (376 MHz, CDCl$_3$) δ -79.98, -103.82.

M.p. 137.5-138.9 °C.

HRMS (ESI): [M+H]$^+$ calcd. for $C_{18}H_{14}F_4N_3O_3^+$ 396.0966, found 396.0968.



8-chloro-5-((4-methoxyphenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**4f**)

General procedure was followed with oxadiazolone **1g** (59.0 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **4f** as a black solid (56.0 mg, 68%).

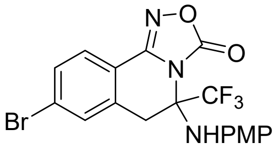
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.83 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.3 Hz, 1H), 7.30 (s, 1H), 7.12 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 5.50 (s, 1H), 3.77 (s, 3H), 3.49 (d, J = 17.2 Hz, 1H), 3.22 (d, J = 17.3 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.5, 157.3, 153.6, 139.4, 134.3, 131.0, 129.7, 128.8, 128.6, 125.9, 123.9 (C-F, q, $^1J_{(C-F)}$ = 287.8 Hz), 121.3, 117.4, 114.9, 75.9 (C-F, q, $^2J_{(C-F)}$ = 29.6 Hz), 55.6, 32.4.

^{19}F NMR (376 MHz, CDCl$_3$) δ -79.94.

M.p. 154.8-155.7 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{18}H_{14}ClF_3N_3O_3^+$ 412.0670, found 412.0669.



8-bromo-5-((4-methoxyphenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**4g**)

General procedure was followed with oxadiazolone **1h** (72.3 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and $CHCl_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **4g** as a purple solid (52.0 mg, 57%).

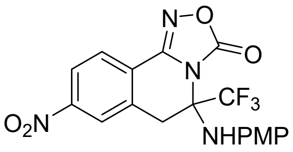
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.46 (s, 1H), 7.12 (d, *J* = 8.9 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 5.50 (s, 1H), 3.77 (s, 3H), 3.49 (d, *J* = 17.3 Hz, 1H), 3.21 (d, *J* = 17.3 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.5, 157.3, 153.7, 134.3, 131.7, 131.5, 131.0, 129.7, 127.8, 126.0, 123.8 (C-F, q, $^1J_{(C-F)}$ = 272.5 Hz), 117.8, 114.9, 75.9 (C-F, q, $^2J_{(C-F)}$ = 29.6 Hz), 55.6, 32.3.

^{19}F NMR (376 MHz, CDCl$_3$) δ -79.92.

M.p. 163.8-164.5 °C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{18}H_{14}BrF_3N_3O_3^+$ 456.0165, found 456.0166.



5-((4-methoxyphenyl)amino)-8-nitro-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**4h**)

General procedure was followed with oxadiazolone **1i** (62.1 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R$_f$ = 0.5) to give the titled product **4h** as a brown solid (36.3 mg, 43%).

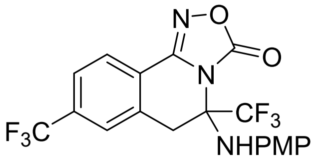
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.24 (d, *J* = 8.7 Hz, 1H), 8.19 (s, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.15 (d, *J* = 7.7 Hz, 2H), 6.86 (d, *J* = 7.9 Hz, 2H), 5.48 (s, 1H), 3.77 (s, 3H), 3.60 (d, *J* = 17.3 Hz, 1H), 3.42 (d, *J* = 17.4 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.8, 157.0, 153.0, 150.3, 134.4, 130.6, 129.8, 126.0, 124.4, 123.7 (C-F, q, $^1J_{(C-F)}$ = 287.8 Hz),123.6, 123.4, 115.0, 76.1 (C-F, q, $^2J_{(C-F)}$ = 29.6 Hz), 55.6, 32.8.

^{19}F NMR (376 MHz, CDCl$_3$) δ -79.84.

M.p. 192.3-193.2 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{18}H_{14}F_3N_4O_5^+$ 423.0911, found 423.0917.



5-((4-methoxyphenyl)amino)-5,8-bis(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-a]isoquinolin-3-one (**4i**)

General procedure was followed with 3-(4-(trifluoromethyl)phenyl)-1,2,4-oxadiazol-5(4H)-one **1j** (69.0 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv), CHCl$_3$ (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R_f = 0.5) to give the titled product **4i** as a brown solid (51.5 mg, 58%).

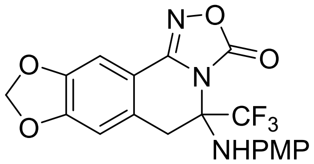
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, J = 8.1 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.57 (s, 1H), 7.16 – 7.11 (m, 2H), 6.87 – 6.83 (m, 2H), 5.50 (s, 1H), 3.77 (s, 3H), 3.56 (d, J = 17.3 Hz, 1H), 3.34 (d, J = 17.4 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.6, 157.2, 153.4, 134.78 (C-F, q, $^2J_{(C\text{-}F)}$ = 33.0 Hz), 133.4, 130.8, 129.8, 125.4 (C-F, q, $^3J_{(C\text{-}F)}$ =3.9 Hz), 125.3, 125.2, 123.2 (C-F, q, $^1J_{(C\text{-}F)}$ = 273.0 Hz), 122.4, 122.2, 114.9, 76.1 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.6 Hz), 55.6, 32.67.

^{19}F NMR (376 MHz, CDCl$_3$) δ -63.35, -79.91.

M.p. 180.6-182.1 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{19}H_{14}F_6N_3O_3^+$ 446.0934, found 446.0939.



5-((4-methoxyphenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,3]dioxolo[4,5-g][1,2,4]oxadiazolo[3,4-a]isoquinolin-3-one (**4j**)

General procedure was followed with 3-(benzo[d][1,3]dioxol-5-yl)-1,2,4-oxadiazol-5(4H)-one **1k** (61.8 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv), $CHCl_3$ (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **4j** as a brown solid (52.4 mg, 62%).

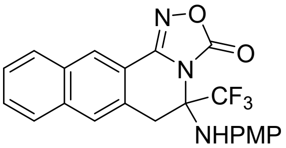
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.48 (d, J = 8.2 Hz, 1H), 7.15 – 7.11 (m, 2H), 6.86 – 6.83 (m, 2H), 6.81 (d, J = 8.1 Hz, 1H), 6.09 – 6.05 (m, 2H), 5.58 (s, 1H), 3.77 (s, 3H), 3.37 (d, J = 17.5 Hz, 1H), 3.24 (d, J = 17.5 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.4, 157.6, 153.9, 151.0, 145.2, 131.2, 129.6, 123.9 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.2 Hz), 114.8, 113.5, 112.4, 108.4, 102.5, 75.7 (C-F, q, $^2J_{(C\text{-}F)}$ =29.8 Hz), 55.6, 26.0.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.15.

M.p. 149.2-151.9 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{19}H_{15}F_3N_3O_5^+$ 422.0958, found 422.0963.



5-((4-methoxyphenyl)amino)-5-(trifluoromethyl)-5,6-dihydro-3*H*-benzo[g][1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**4k**)

General procedure was followed with oxadiazolone **1l** (63.7 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R_f = 0.5) to give the titled product **4k** as a yellow solid (68.4 mg, 80%).

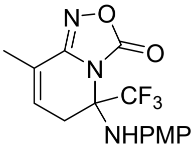
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.45 (s, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.71 (s, 1H), 7.67 – 7.47 (m, 2H), 7.20 (d, J = 8.9 Hz, 2H), 6.87 (d, J = 8.9 Hz, 2H), 5.62 (s, 1H), 3.77 (s, 3H), 3.60 (d, J = 16.8 Hz, 1H), 3.43 (d, J = 16.8 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.5, 157.7, 154.6, 135.2, 132.0, 131.3, 129.7, 129.1, 129.0, 127.8, 127.6, 127.4, 127.3, 125.6, 124.0 (C-F, q, $^1J_{(C\text{-}F)}$ = 287.8 Hz), 116.5, 114.8, 76.3 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.5 Hz), 55.5, 33.2.

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.11.

M.p. 138.2-139.1 °C.

HRMS (ESI): [M+H]+ calcd. for $C_{22}H_{17}F_3N_3O_3^+$ 428.1217, found 428.1221.



5-((4-methoxyphenyl)amino)-8-methyl-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[4,3-*a*]pyridin-3-one (**4n**)

General procedure was followed with oxadiazolone **1o** (37.8 mg, 0.3 mmol, 1.5 equiv), TFISY **2f** (58.7 mg, 0.2 mmol, 1.0 equiv), [Cp*RhCl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (32.8 mg, 0.4 mmol, 2.0 equiv) and CHCl$_3$ (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, $R_f = 0.5$) to give the titled product **4n** as a yellow solid (27.3 mg, 40%).

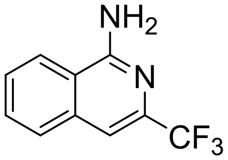
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.00 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.02 (d, J = 5.9 Hz, 1H), 5.35 (s, 1H), 3.78 (s, 3H), 2.99 (d, J = 19.4 Hz, 1H), 2.78 (dd, J = 19.4, 6.1 Hz, 1H), 1.98 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 158.1, 157.2, 154.7, 131.6, 130.1, 128.6, 124.2 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.4 Hz), 120.9, 114.8, 75.1 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.5 Hz), 55.6, 28.5, 14.8.

^{19}F NMR (376 MHz, CDCl$_3$) δ -81.68.

M.p. 110.8-111.6°C.

HRMS (ESI): [M+H]+ calcd. for $C_{15}H_{15}F_3N_3O_3^+$ 342.1060, found 342.1059.



3-(trifluoromethyl)isoquinolin-1-amine (**5**) [5]

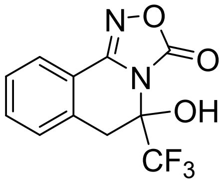
Under air atmosphere, compound **3f** (57.8 mg, 0.2 mmol, 1.0 equiv), Sc(OTf)$_3$ (19.7 mg, 0.04 mmol, 20 mol %) and 1,4-dioxane (2.0 mL) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 140 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield the products **5** as a white solid (29.7 mg, 70%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.85 (d, J = 8.3 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.43 (s, 1H), 5.77 (s, 2H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 157.0, 140.0 (C-F, q, $^2J_{(C\text{-}F)}$ = 32.8 Hz), 136.7, 131.2, 128.4, 128.3, 122.8, 122.4 (C-F, q, $^1J_{(C\text{-}F)}$ = 272.8 Hz), 118.9, 109.9 (C-F, q, $^3J_{(C\text{-}F)}$ = 3.8 Hz).

^{19}F NMR (376 MHz, CDCl$_3$) δ -68.16.

M.p. 231.4-233.2 °C.



5-hydroxy-5-(trifluoromethyl)-5,6-dihydro-3*H*-[1,2,4]oxadiazolo[3,4-*a*]isoquinolin-3-one (**6**)

Under air atmosphere, compound **3f** (57.8 mg, 0.2 mmol, 1.0 equiv), $Sc(OTf)_3$ (19.7 mg, 0.04 mmol, 20 mol %), H_2O (108.0 mg, 6.0 mmol, 30.0 equiv) and 1,4-dioxane (2 mL) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 120 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 3/1) to yield the product **6** as a white solid (18.0 mg, 33%).

^{1}H NMR (400 MHz, DMSO) δ 8.87 (s, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.68 – 7.59 (m, 1H), 7.55 (d, J = 7.1 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 3.62 (d, J = 9.8 Hz, 2H).

^{13}C NMR (101 MHz, DMSO) δ 154.9, 154.2, 133.7, 133.3, 129.2, 128.7, 124.2, 123.5 (C-F, q, $^1J_{(C\text{-}F)}$ = 288.5 Hz), 119.0, 84.1, 83.9 (C-F, q, $^2J_{(C\text{-}F)}$ = 29.5 Hz).

^{19}F NMR (376 MHz, DMSO) δ -79.46.

M.p. 295.3-297.2 ^{o}C.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{11}H_8F_3N_2O_3^+$ 273.0482, found 273.0475.

4. References

(1) Tamura, K.; Mizukami,H.; Maeda, K.; Watanabe, H.; Uneyama, K. One-pot synthesis of trifluoroacetimidoyl Halides. *J. Org. Chem.* **1993**, *58*, 32-35.

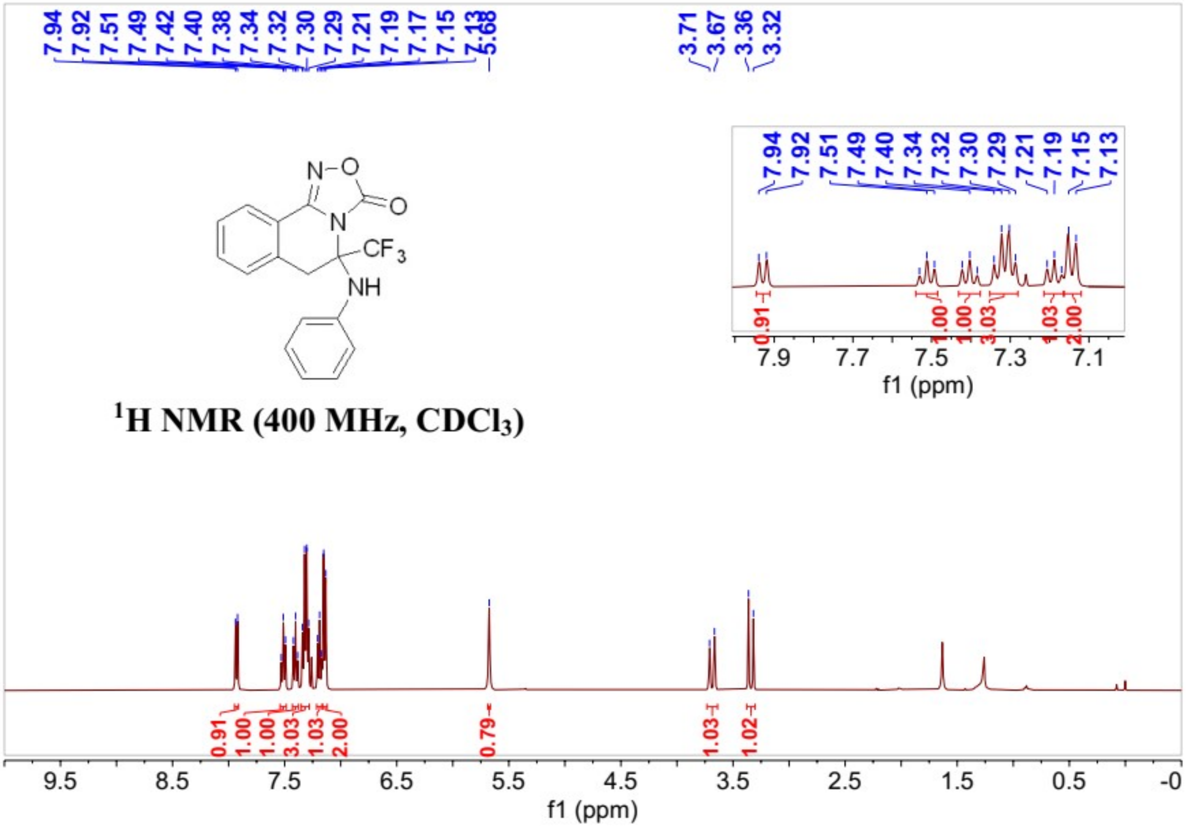
(2) (a) Wen, S.; Tian, Q.; Chen, Y.; Zhang, Y.; Cheng, G. Annulation of CF3-imidoyl sulfoxonium ylides with 1,3-dicarbonyl compounds: Access to 1,2,3-trisubstituted 5-trifluoromethylpyrroles. *Org. Lett.* **2021**, *23*, 7407-7411. (b) Yang, Z.; Tang, J.; Chen, Z.; Wu, X.-F., Ruthenium-Catalyzed Hydroxyl-Directed *peri*-Selective C-H Activation and Annulation of 1-Naphthols with CF_3-Imidoyl Sulfoxonium Ylides for the Synthesis of 2-(Trifluoromethyl)-2,3-dihydrobenzo[de]chromen-2-amines. *Org. Lett.* **2022**, *24*, 7288-7293.

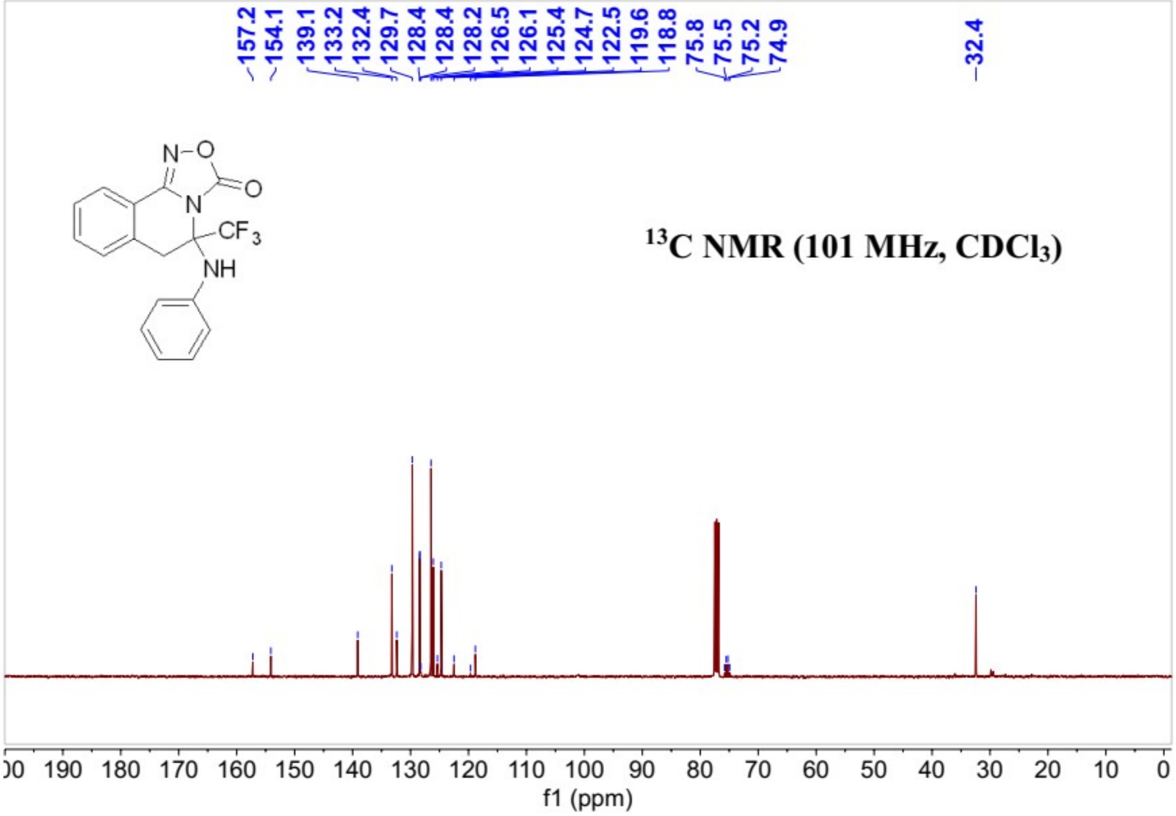
(3) Yu, X.; Chen, K.; Wang, Q.; Guo, S.; Zha, S.; Zhu, J., Associative Covalent Relay: An Oxadiazolone Strategy for Rhodium(III)-Catalyzed Synthesis of Primary Pyridinylamines. *Angew. Chem. Int. Ed.* **2017,** *56*, 5222-5226.

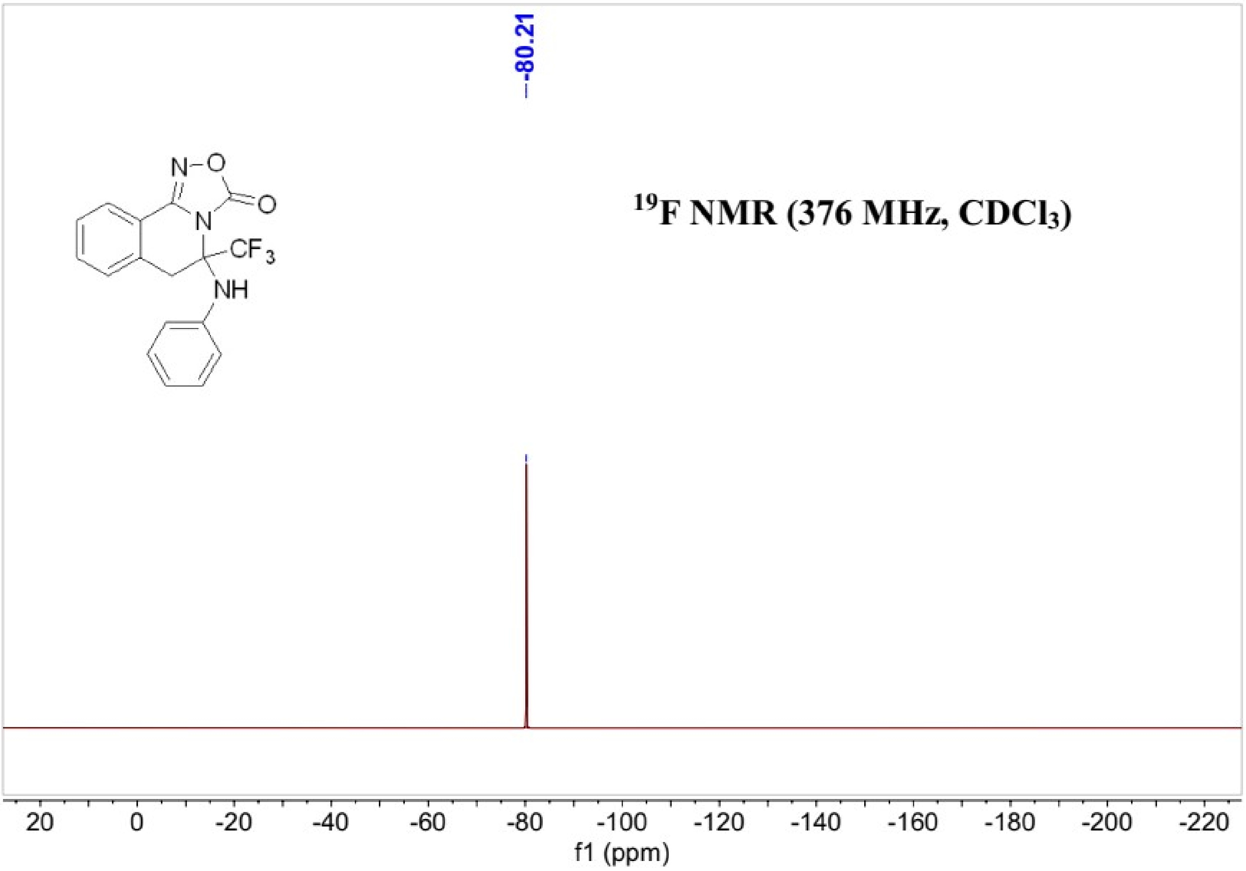
(4) Wang, Y.; Zhang, Q.; Hao, Y.; Luo, C.; Huang, X.; Guo, L.; Wu, Y., C–H Activation-Engaged Synthesis of Diverse Fused-Heterocycles from the Reactions of 3-Phenyl-1,2,4-oxadiazol-5(2H)-ones with Vinylene Carbonate. *Organometallics* **2022,** *41*, 2494-2503.

(5) Wang, X.; Yuan, F.; Szostak, M., Quinazolinone-to-Isoquinoline Metamorphosis by Ruthenium-Catalyzed [4+2] Annulation with Sulfoxonium Ylides. *Org. Lett.* **2024,** *26*, 10951-10957.

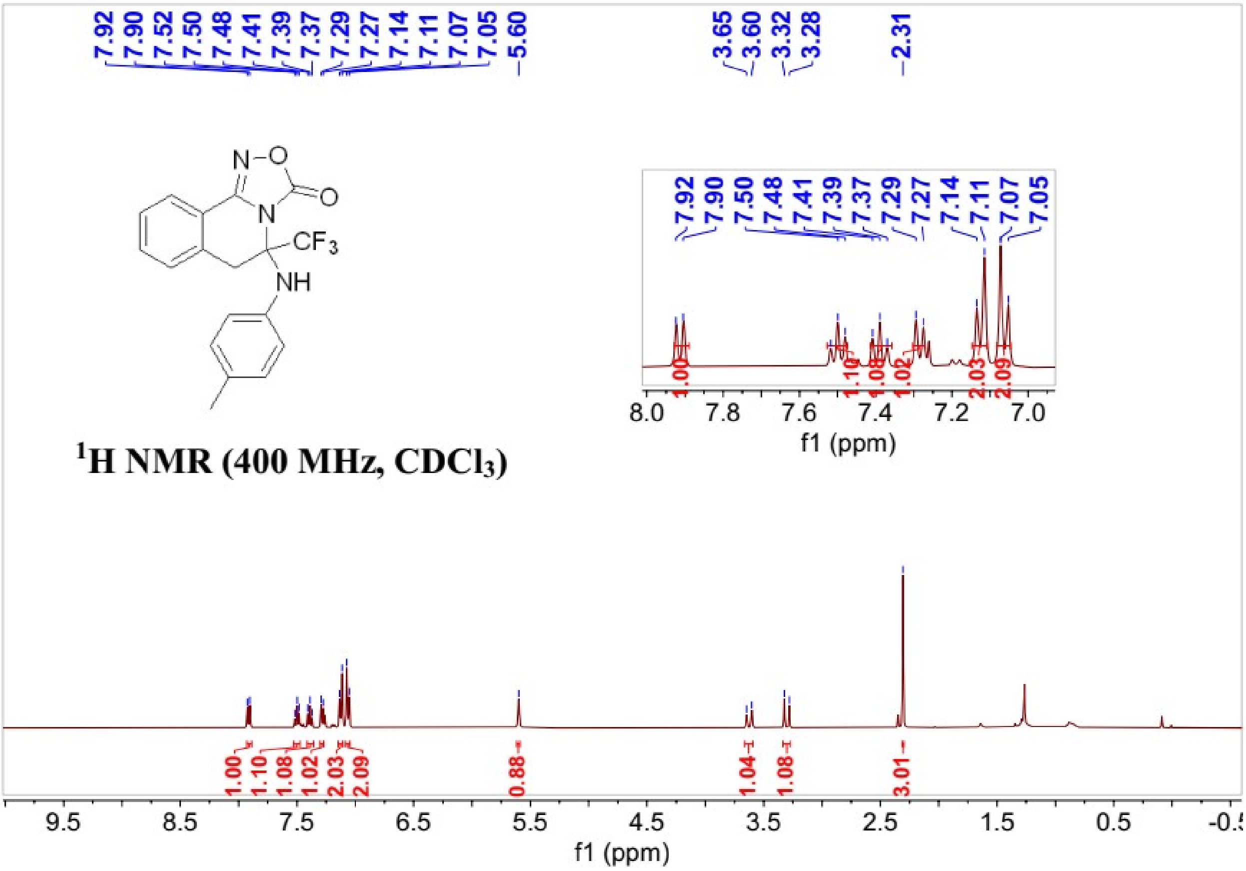
5. Copy of ^{1}H, ^{13}C and ^{19}F NMR Spectra of Products







^{19}F NMR (376 MHz, CDCl$_3$)



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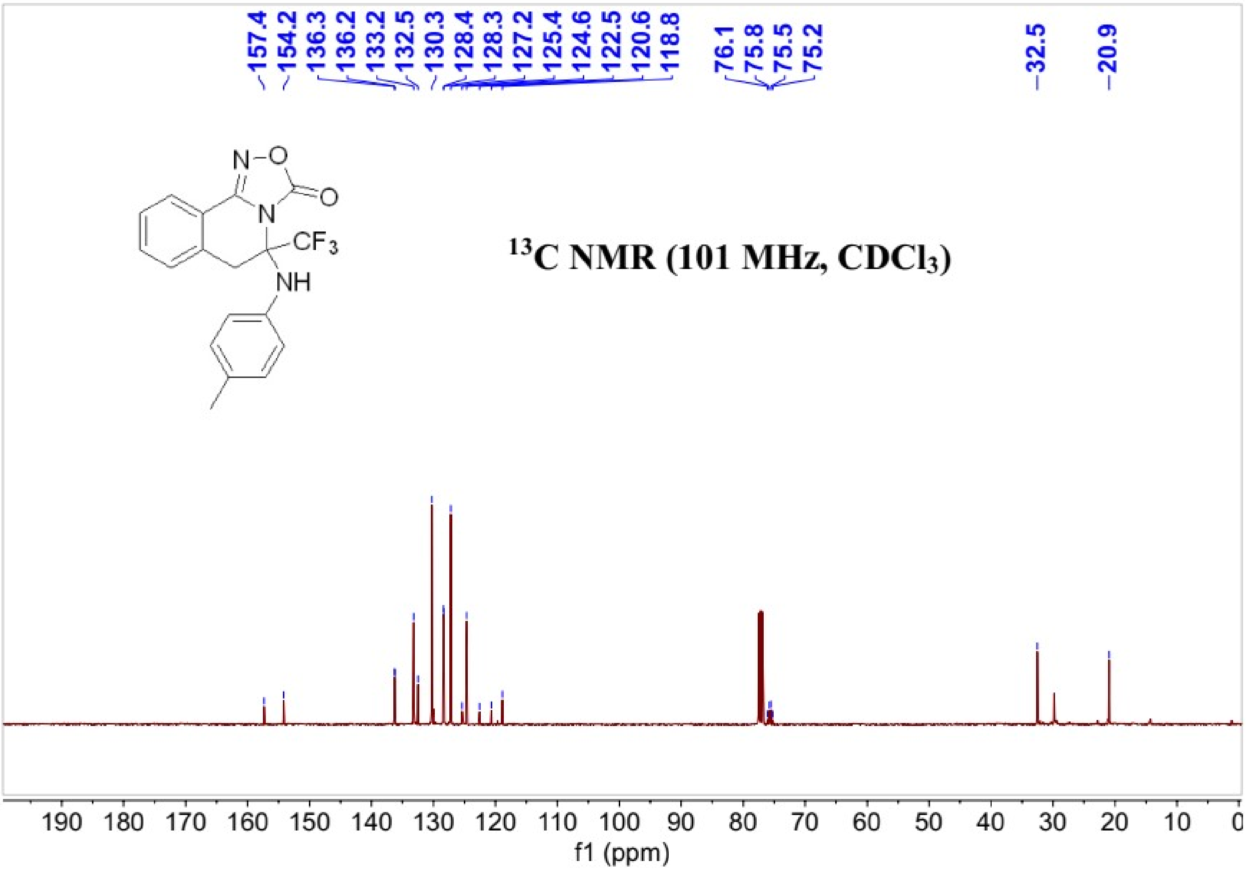
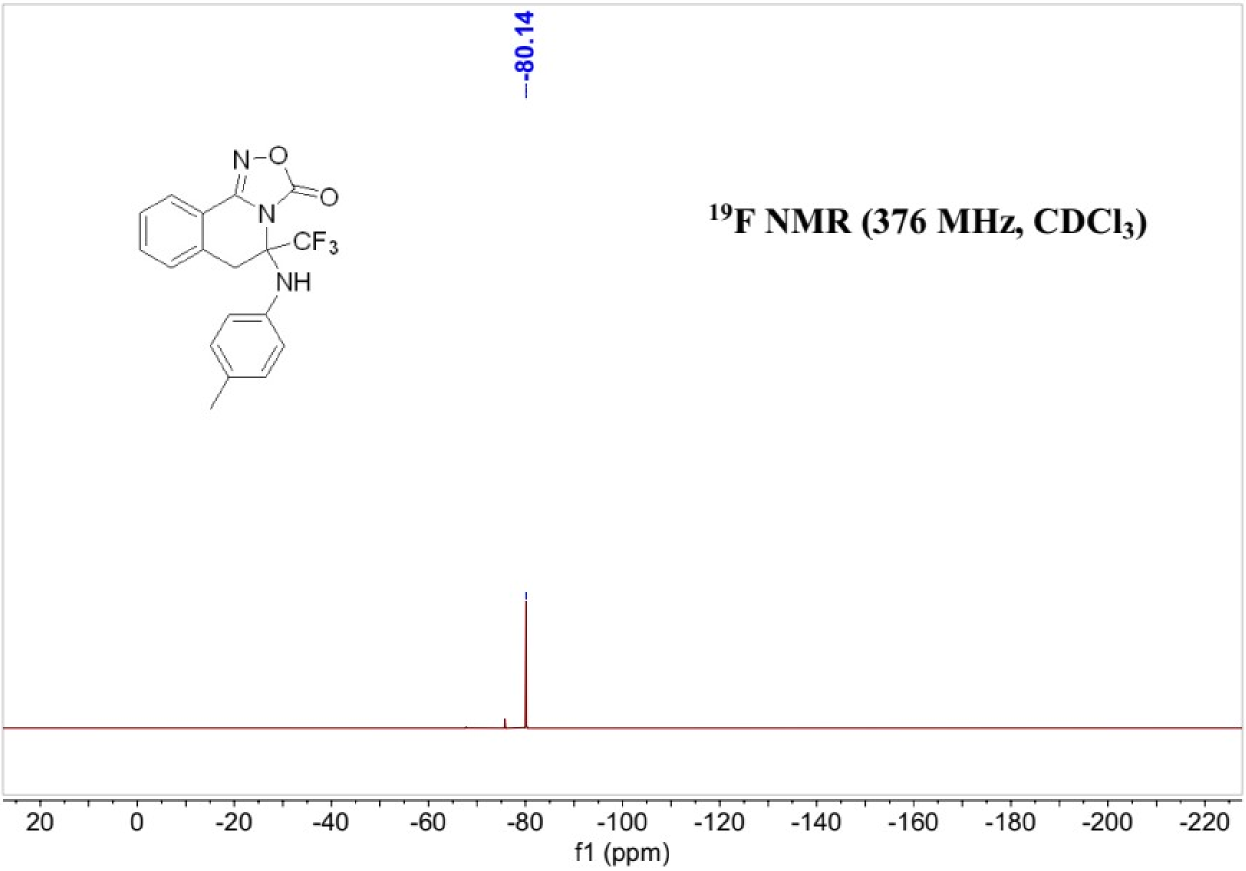
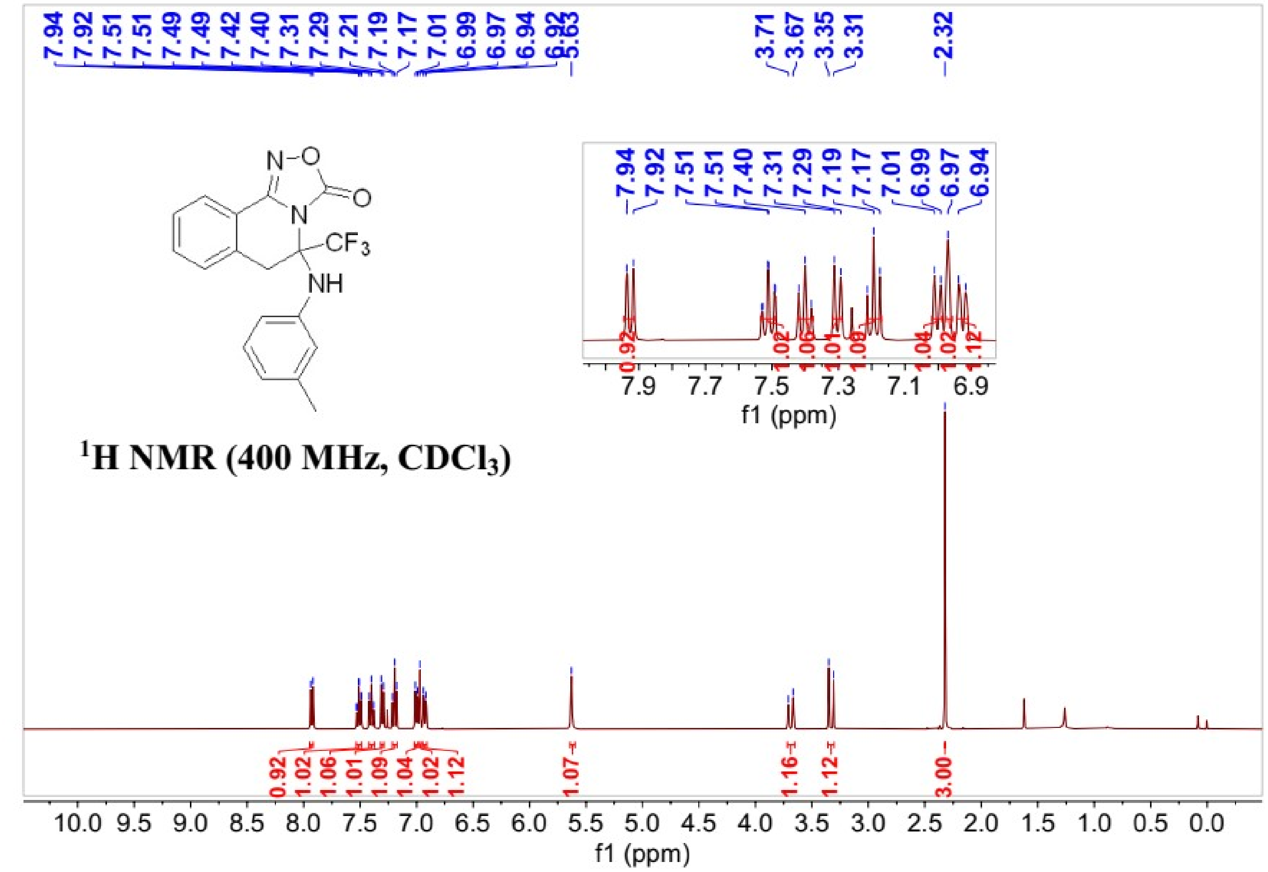


^{13}C NMR (101 MHz, CDCl$_3$)



^{19}F NMR (376 MHz, CDCl$_3$)



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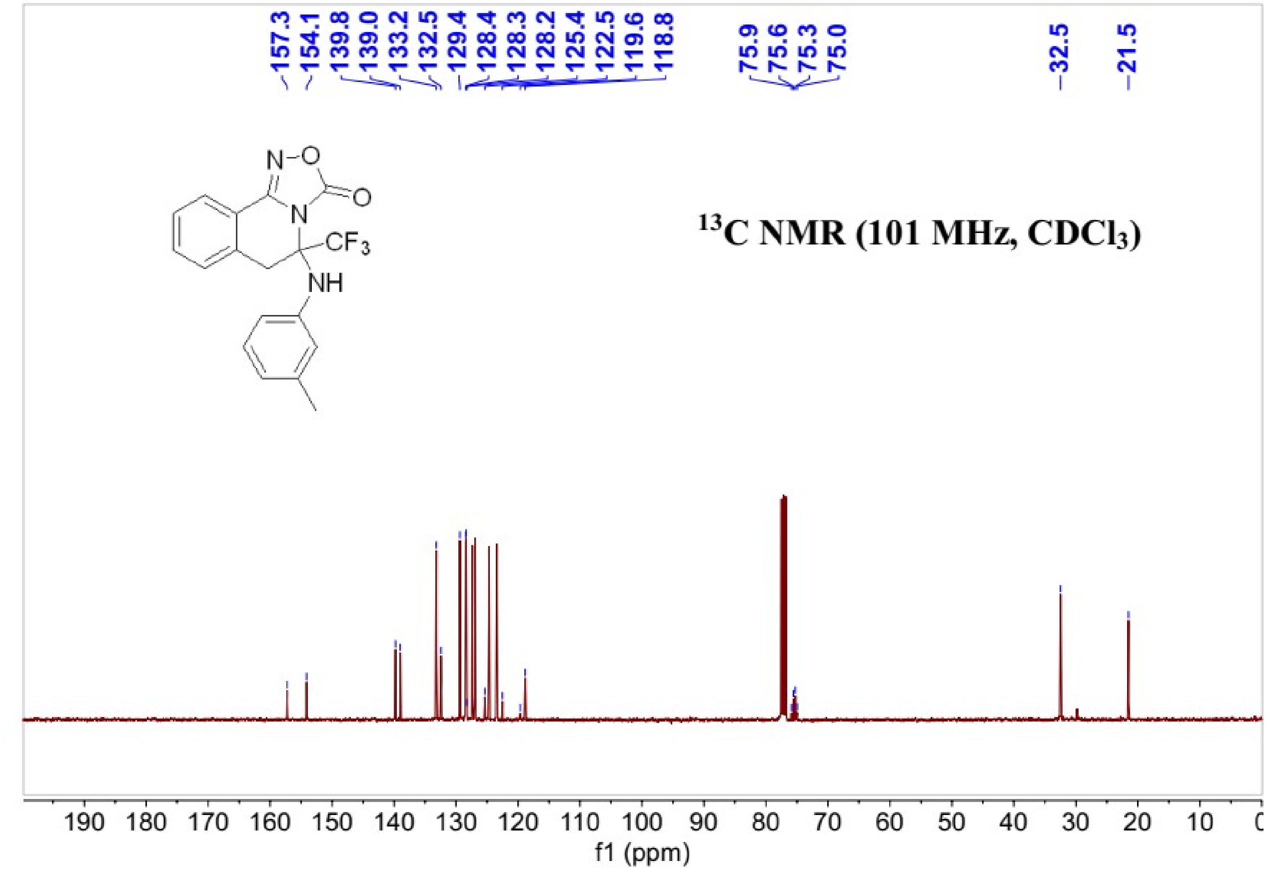
3.71 3.67 3.35 3.31
2.32
N–O
O
N
CF3
NH
1H NMR (400 MHz, CDCl3)
7.94 7.92 7.51 7.51 7.40 7.31 7.29 7.19 7.17 7.01 6.99 6.97 6.94
0.92 1.02 1.06 1.01 1.09 1.04 1.02 1.12
7.9 7.7 7.5 7.3 7.1 6.9
f1 (ppm)
0.92 1.02 1.06 1.01 1.09 1.04 1.02 1.12
1.07
1.16 1.12
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



157.3 154.1 139.8 139.0 133.2 132.5 129.4 128.4 128.3 128.2 125.4 122.5 119.6 118.8
75.9 75.6 75.3 75.0
32.5
21.5
N–O
O
N
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NH
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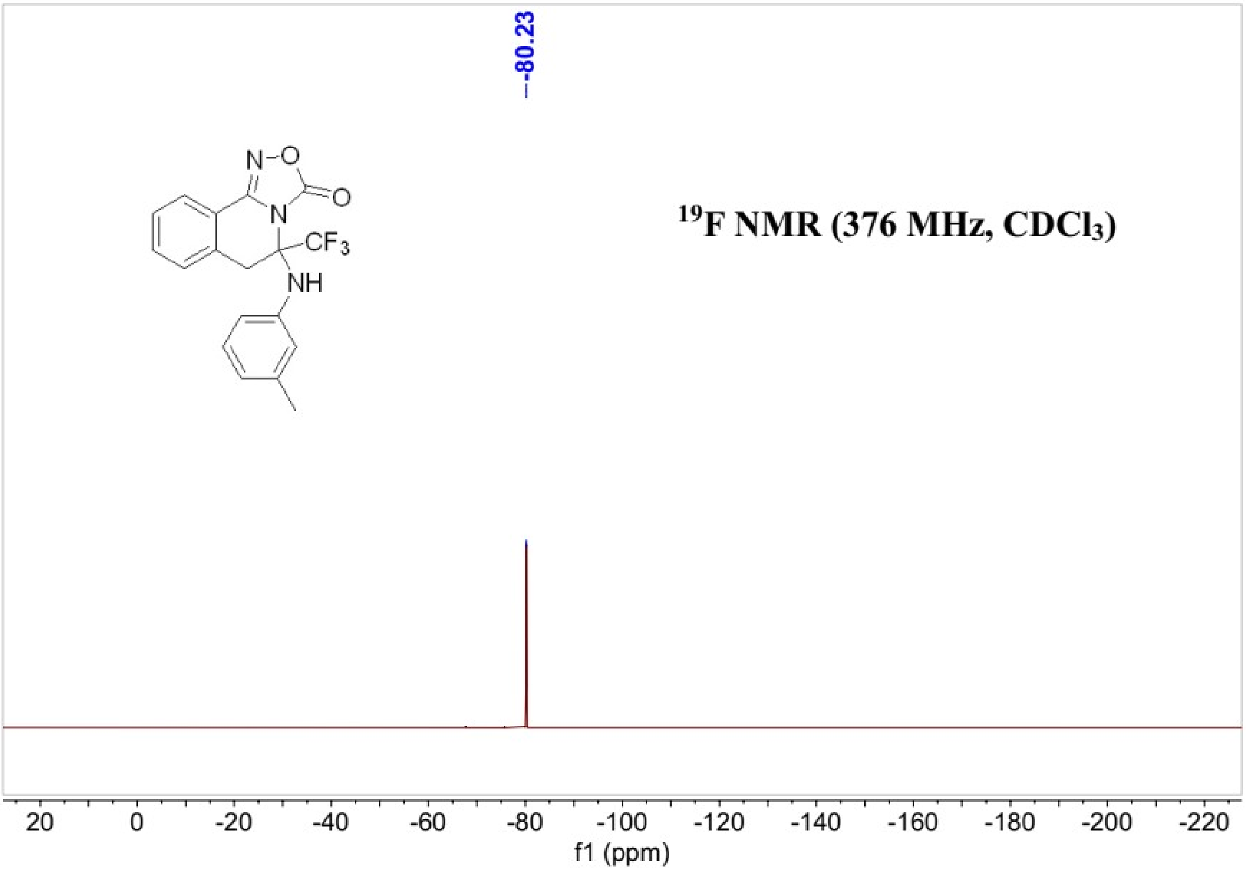
f1 (ppm)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-180
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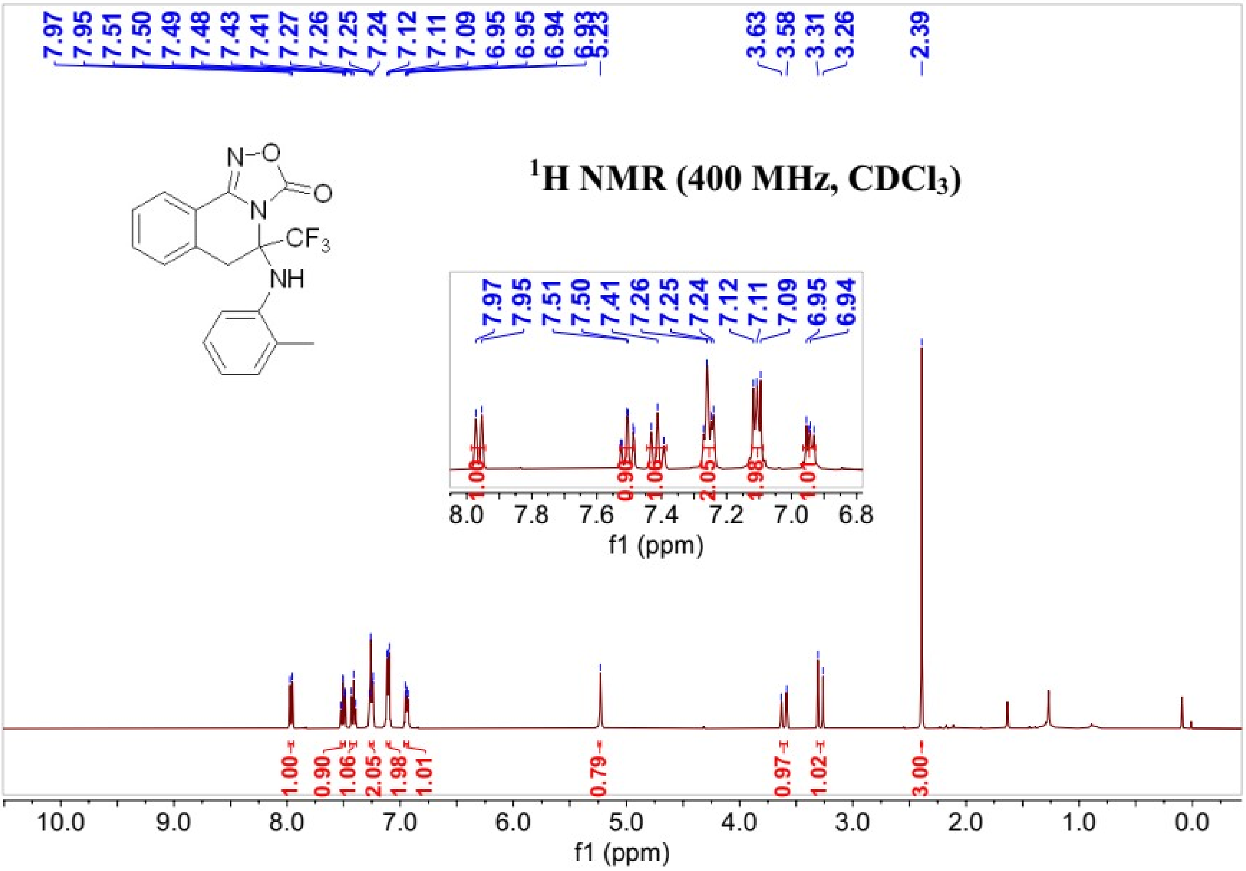
-220
f1 (ppm)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5.23
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3.58
3.31
3.26
2.39
^{1}H NMR (400 MHz, CDCl$_3$)
N–O
O
N
CF$_3$
NH
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7.95
7.51
7.50
7.41
7.26
7.25
7.24
7.12
7.11
7.09
6.95
6.94
1.00
0.90
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2.05
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7.6
7.4
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6.8
f1 (ppm)
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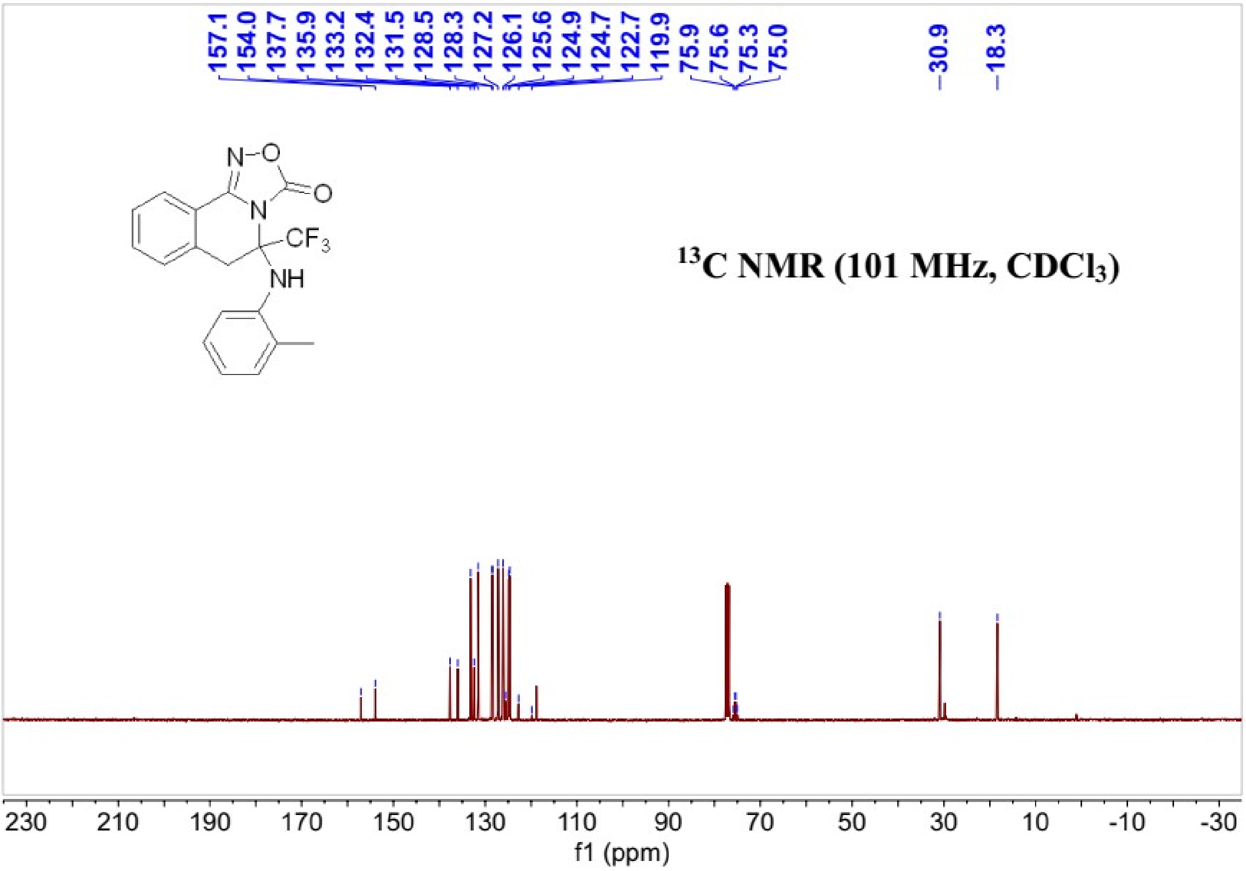
f1 (ppm)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119.9
75.9
75.6
75.3
75.0
30.9
18.3
N
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O
N
CF3
NH
13C NMR (101 MHz, CDCl3)
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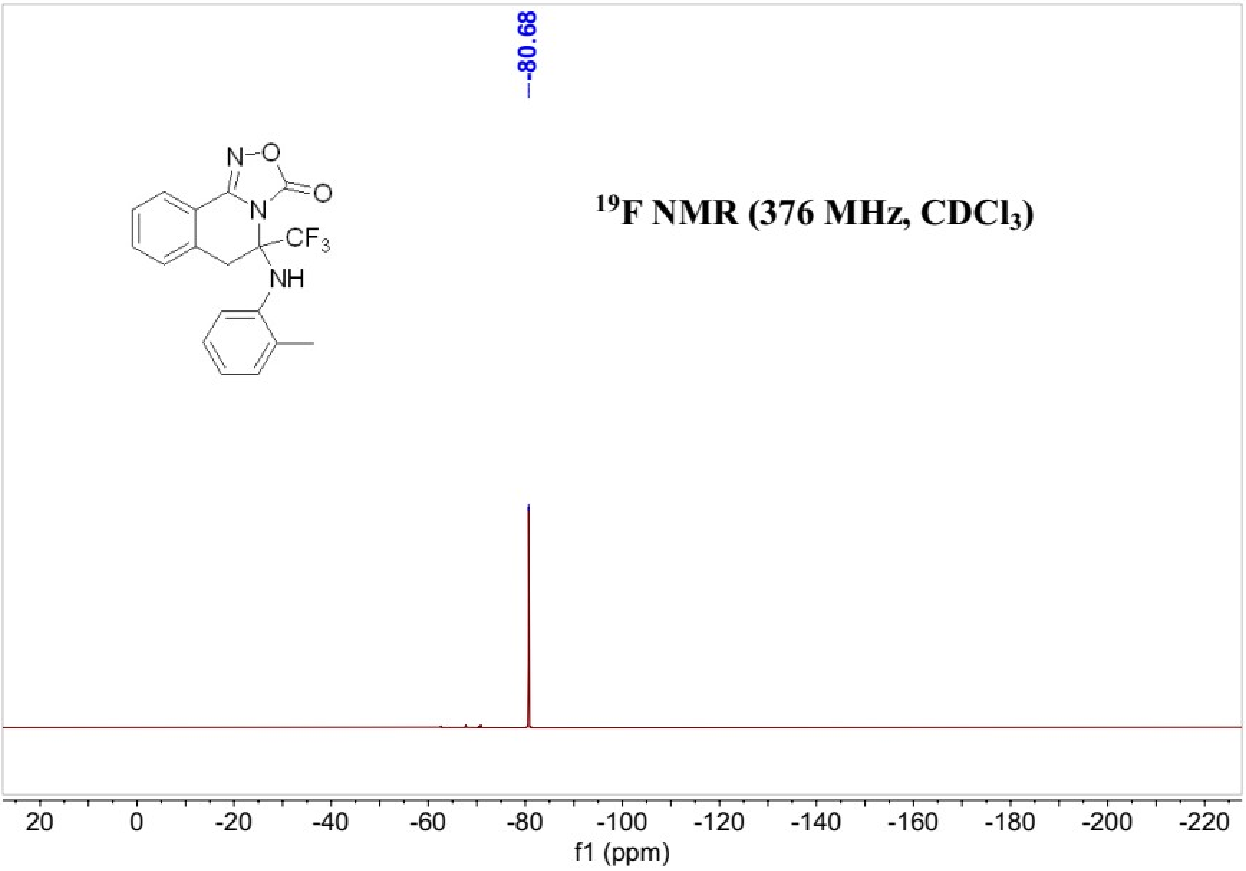
-10
-30
f1 (ppm)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N
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NH
19F NMR (376 MHz, CDCl3)
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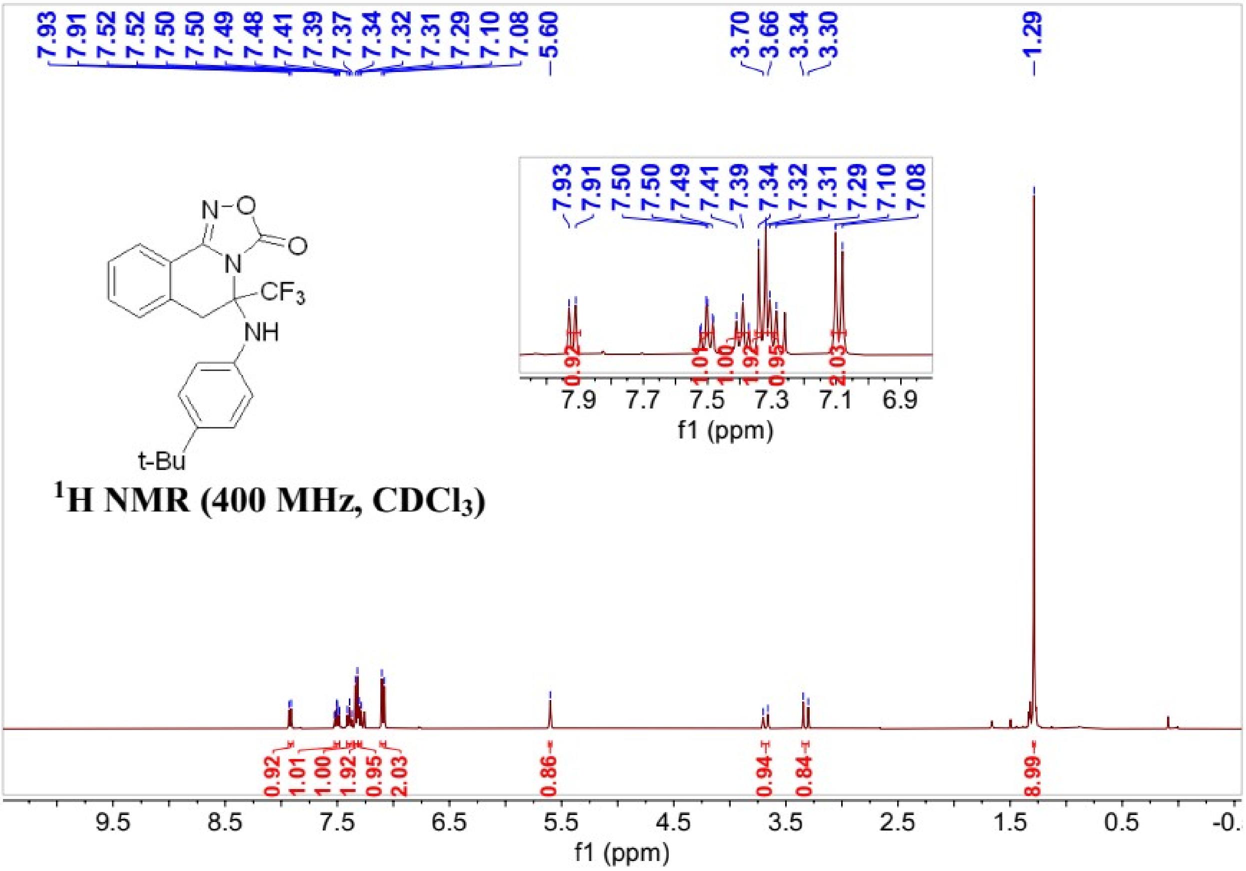
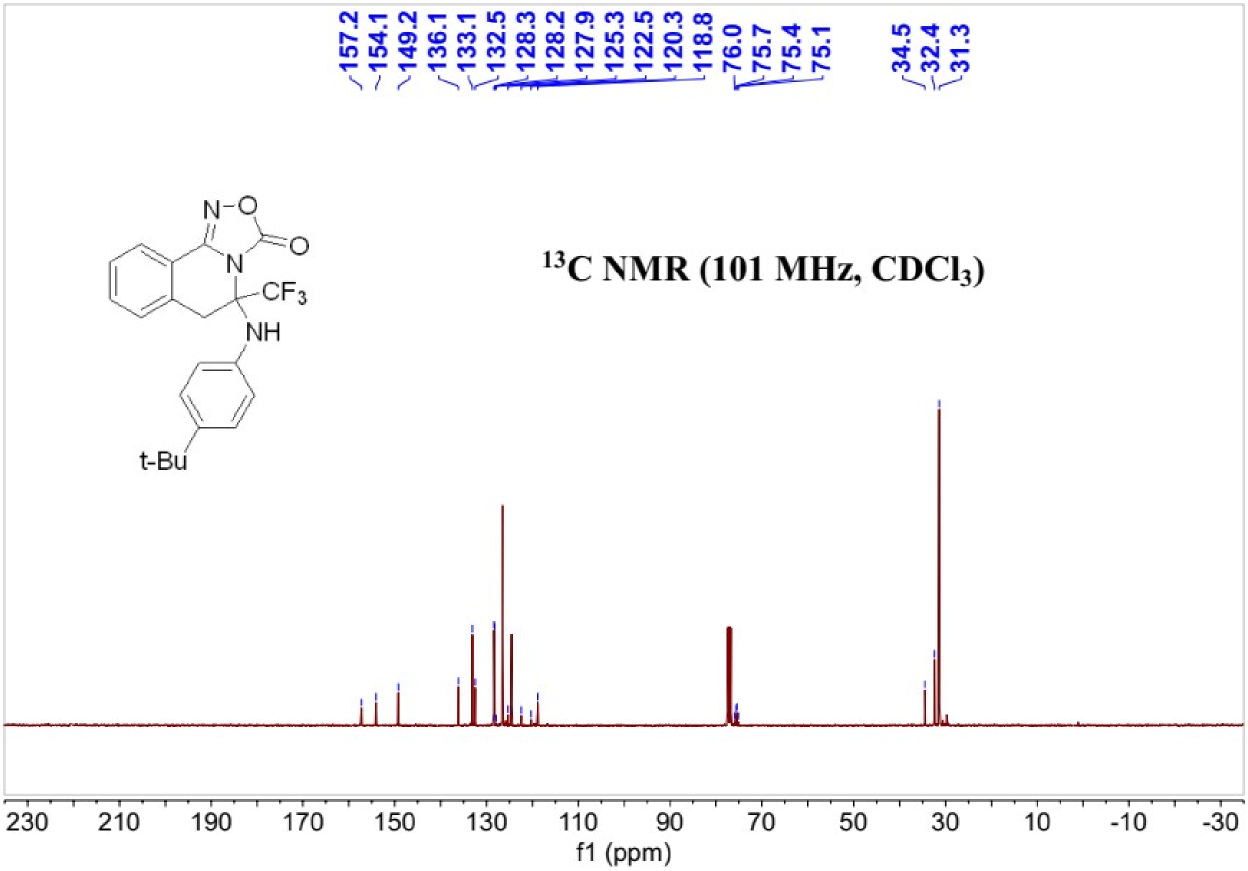
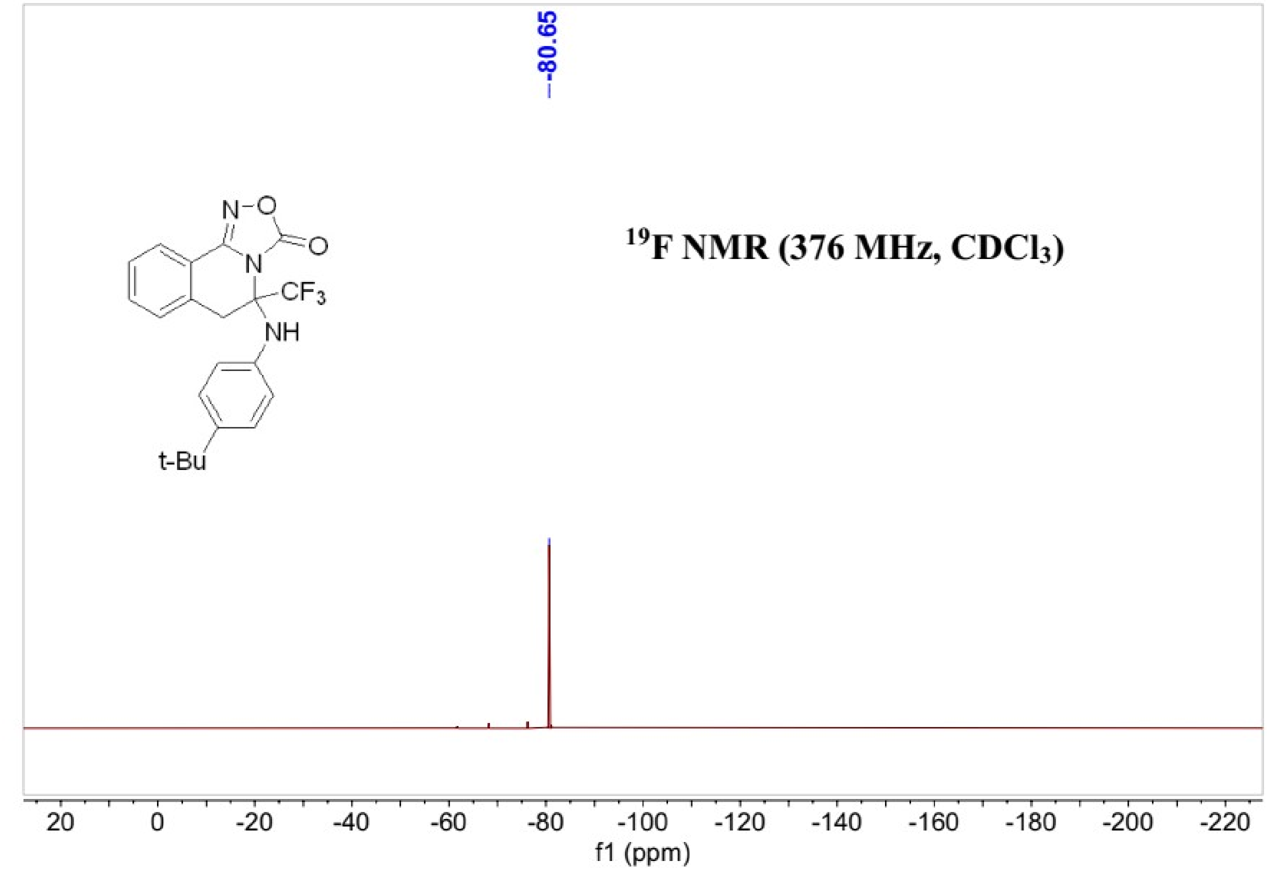
f1 (ppm)



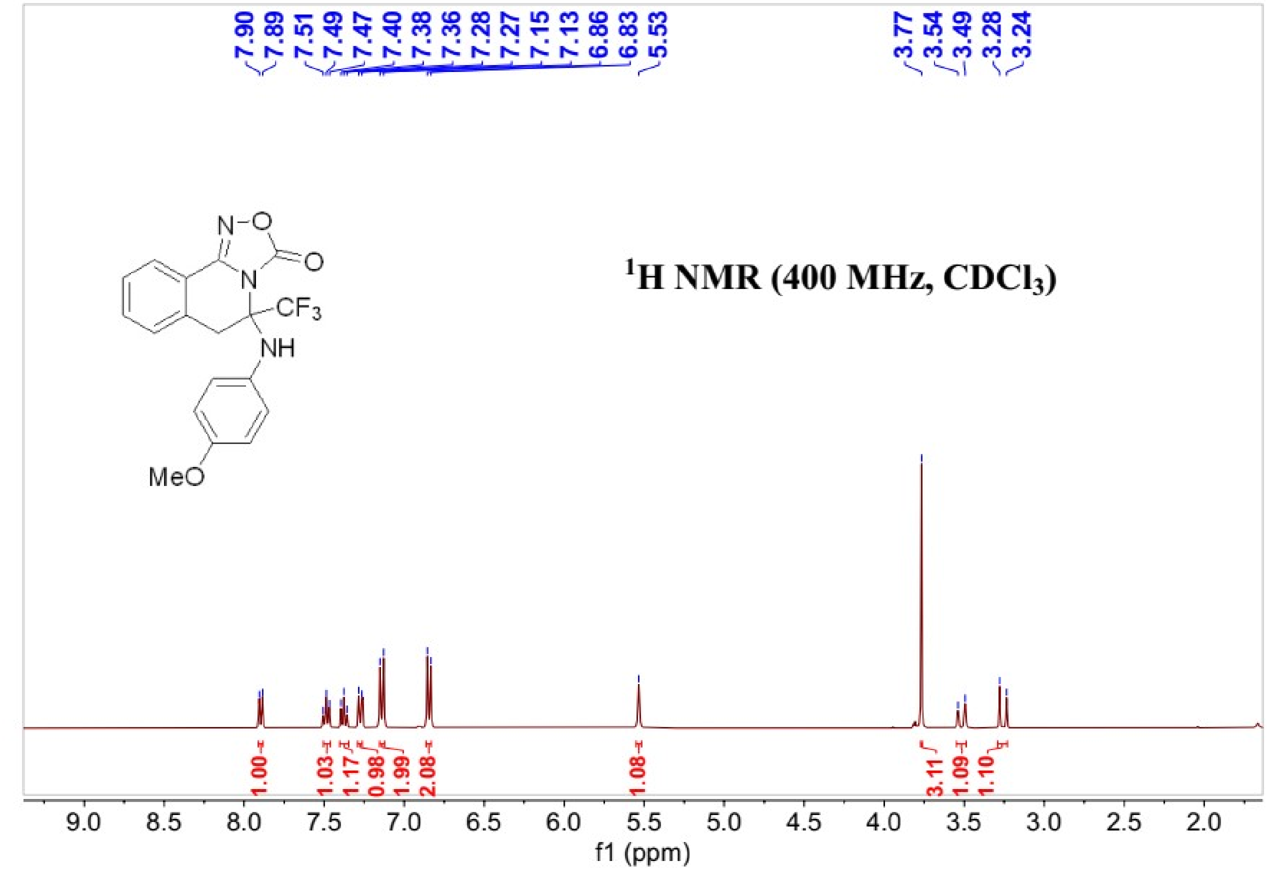
^{1}H NMR (400 MHz, CDCl$_3$)



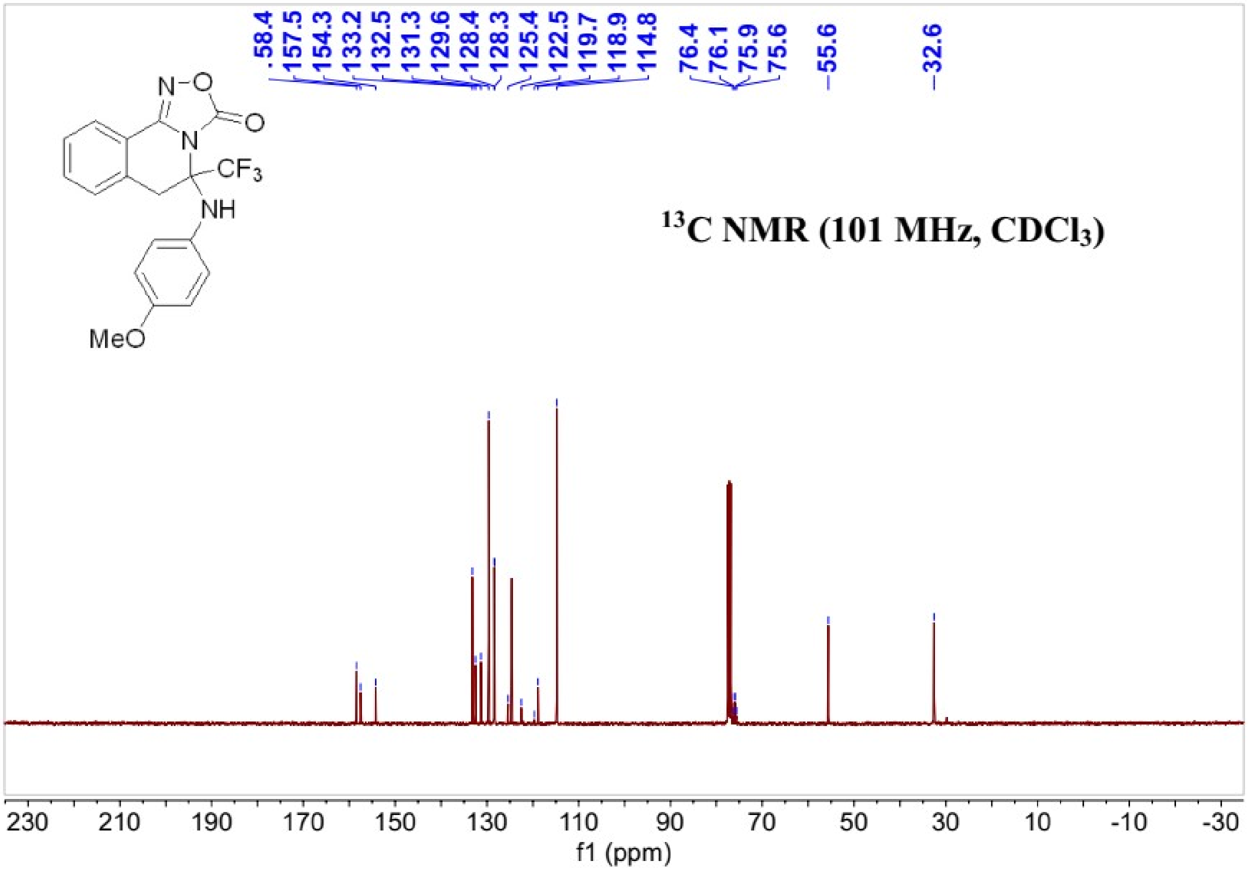
^{13}C NMR (101 MHz, CDCl$_3$)

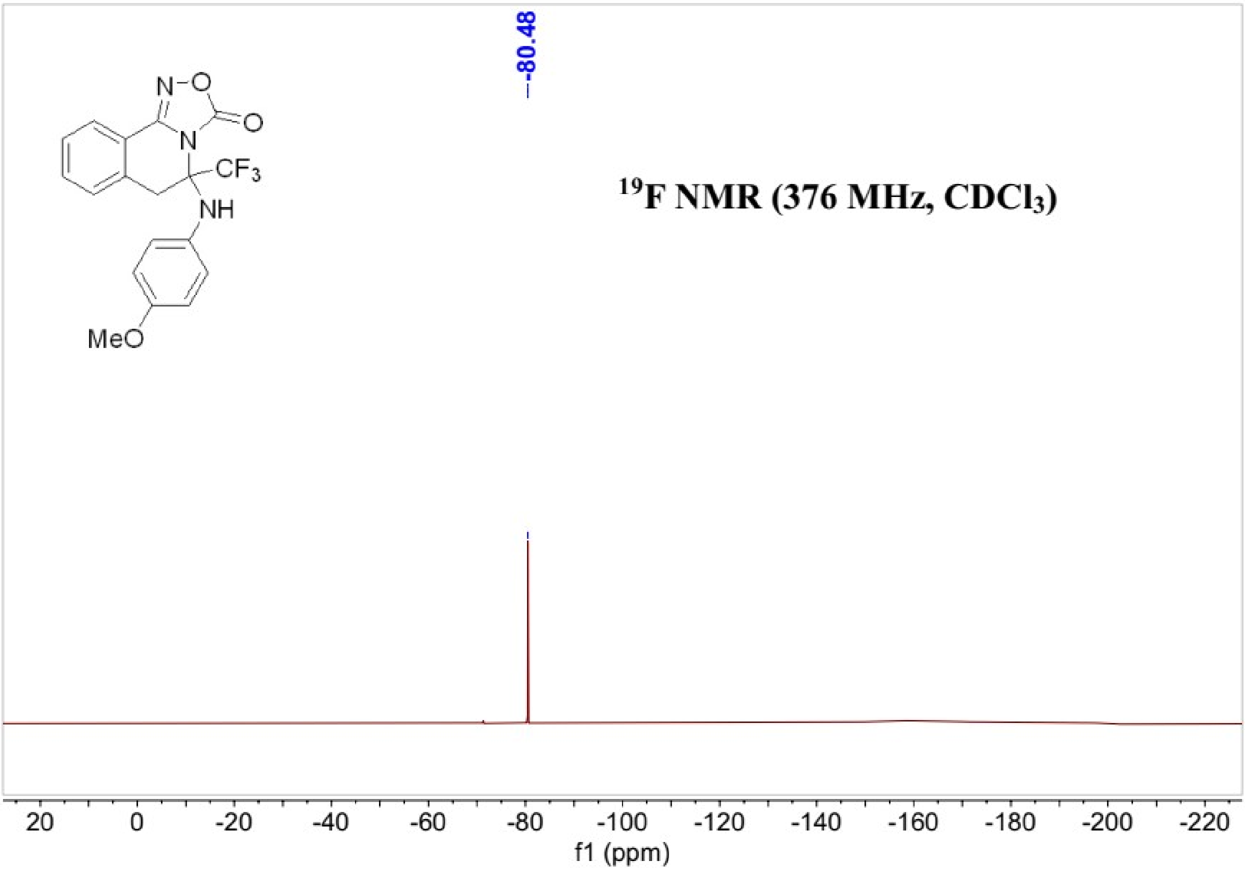


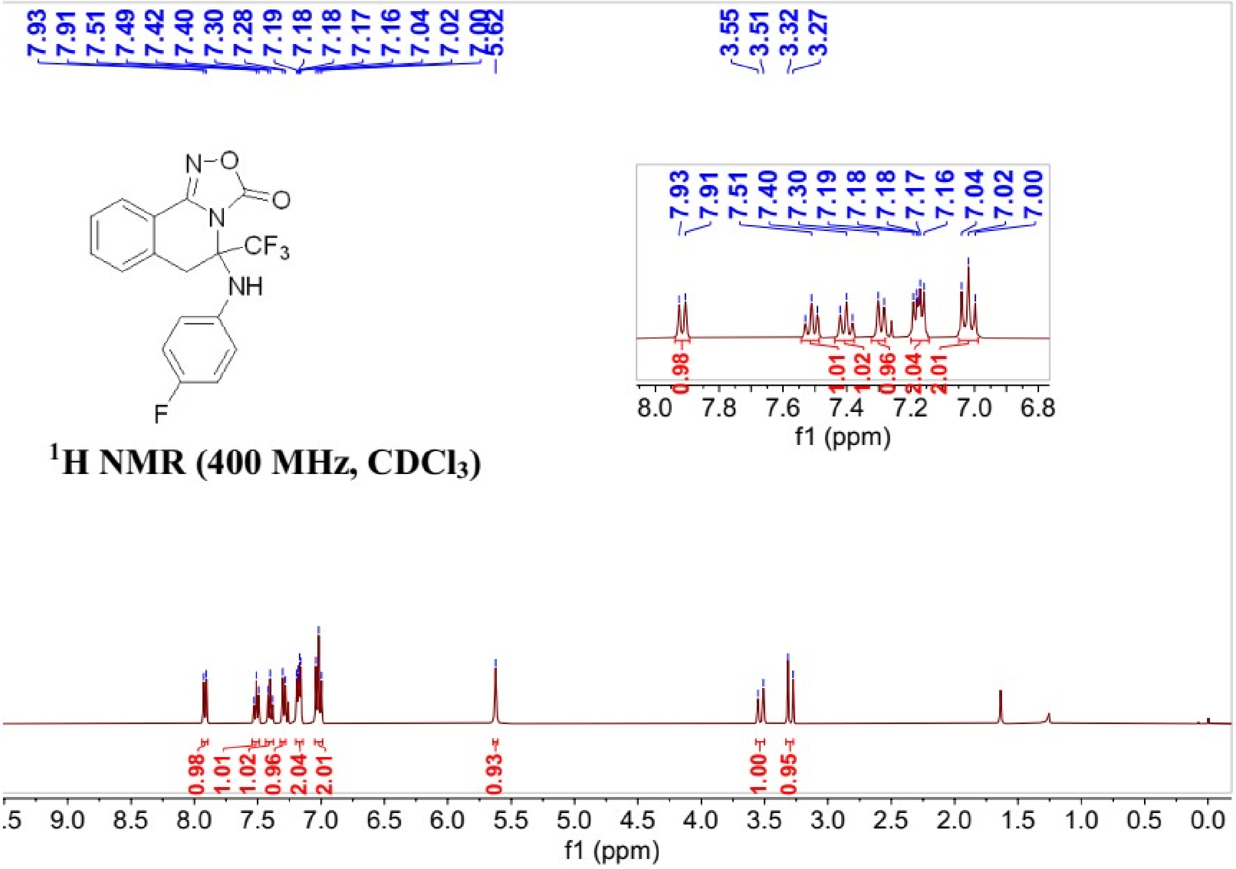
^{19}F NMR (376 MHz, $CDCl_3$)

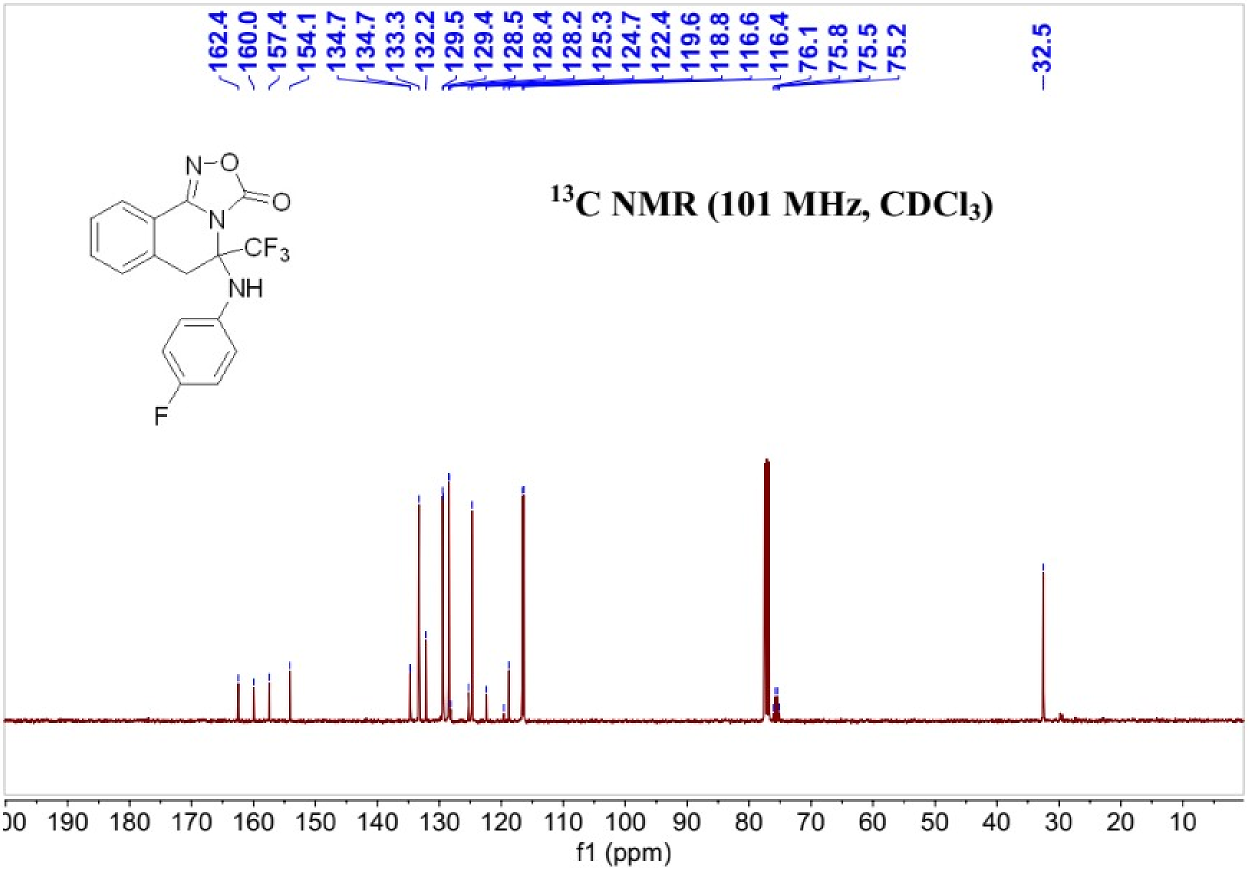


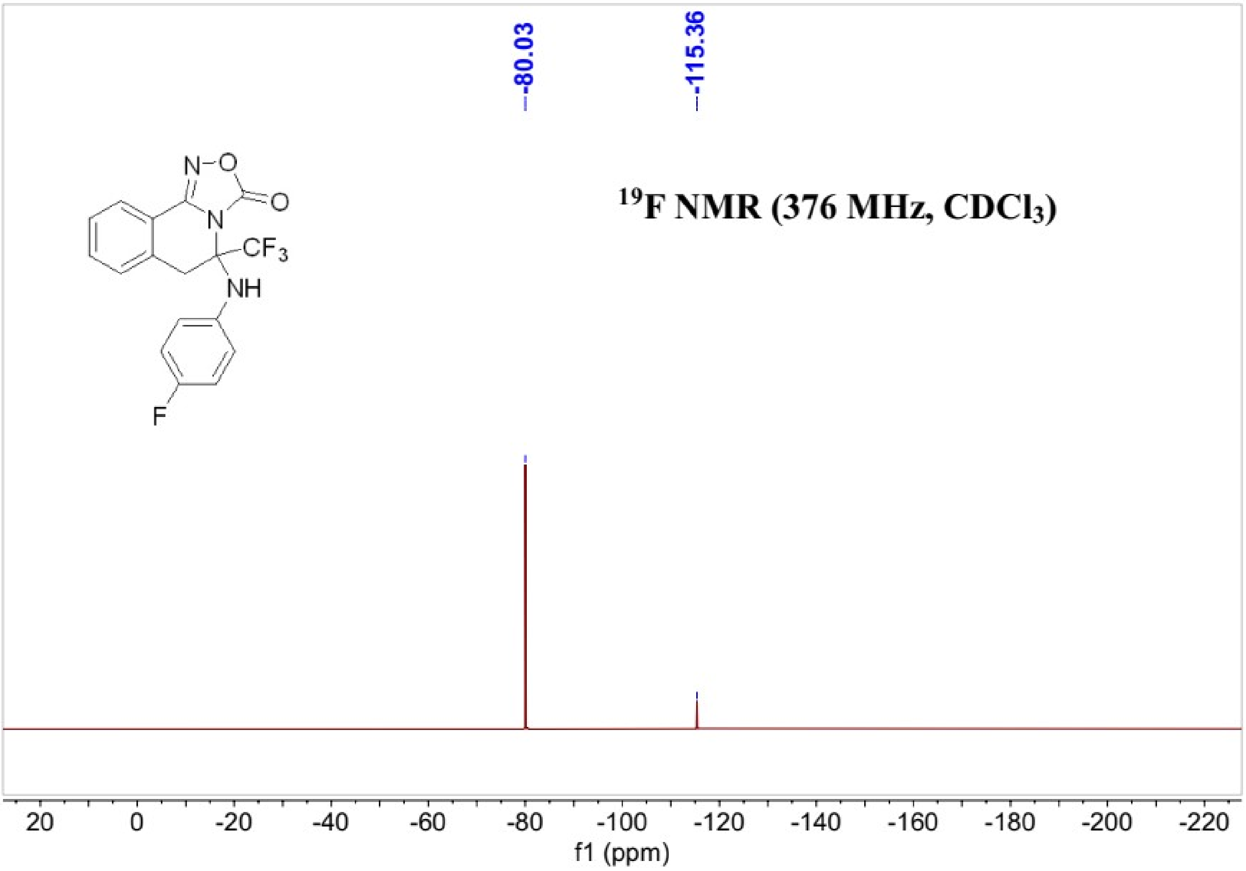
^{1}H NMR (400 MHz, $CDCl_3$)

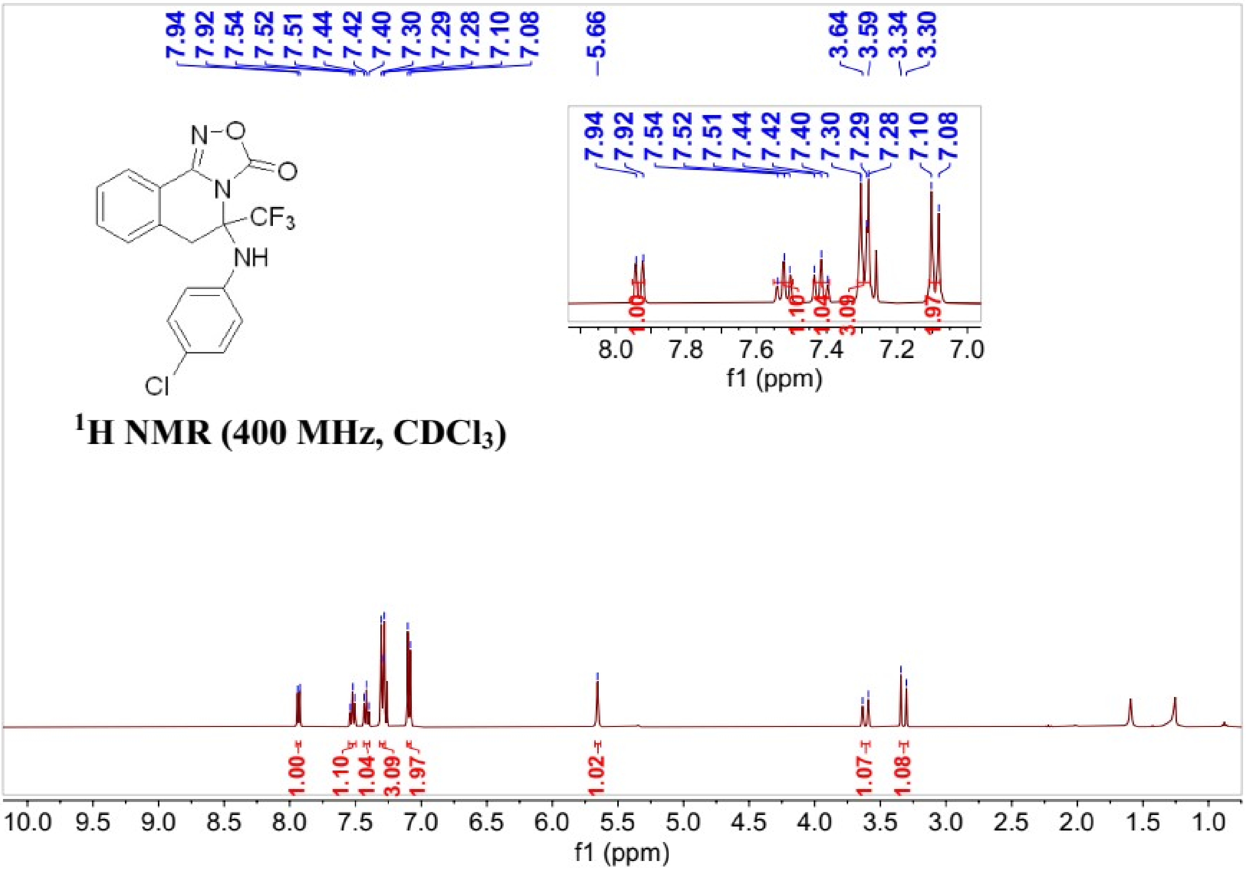

58.4
157.5
154.3
133.2
132.5
131.3
129.6
128.4
128.3
125.4
122.5
119.7
118.9
114.8
76.4
76.1
75.9
75.6
55.6
32.6
N
O
O
N
CF3
NH
MeO
13C NMR (101 MHz, CDCl3)
230
210
190
170
150
130
110
90
70
50
30
10
-10
-30
f1 (ppm)

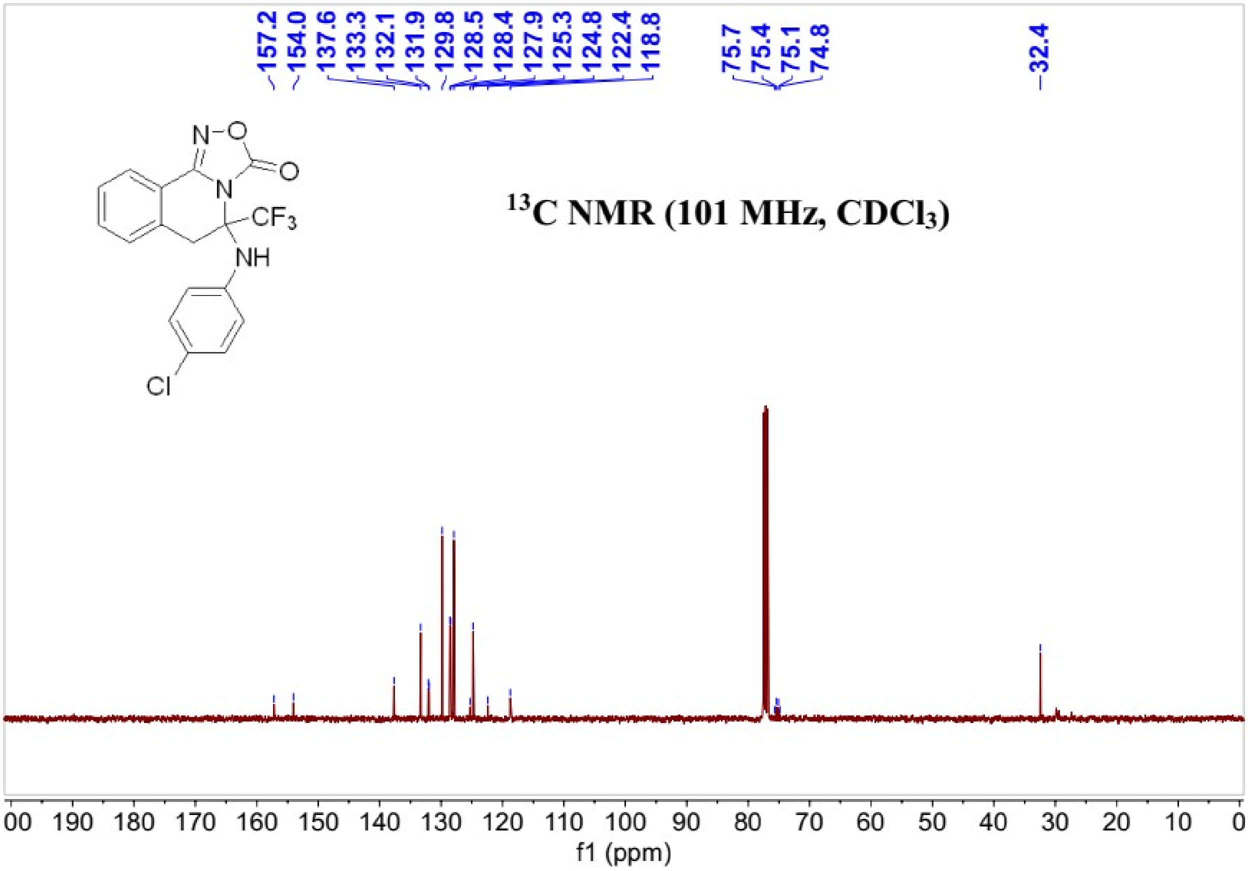

-80.48
N
O
O
N
CF3
NH
MeO
19F NMR (376 MHz, CDCl3)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

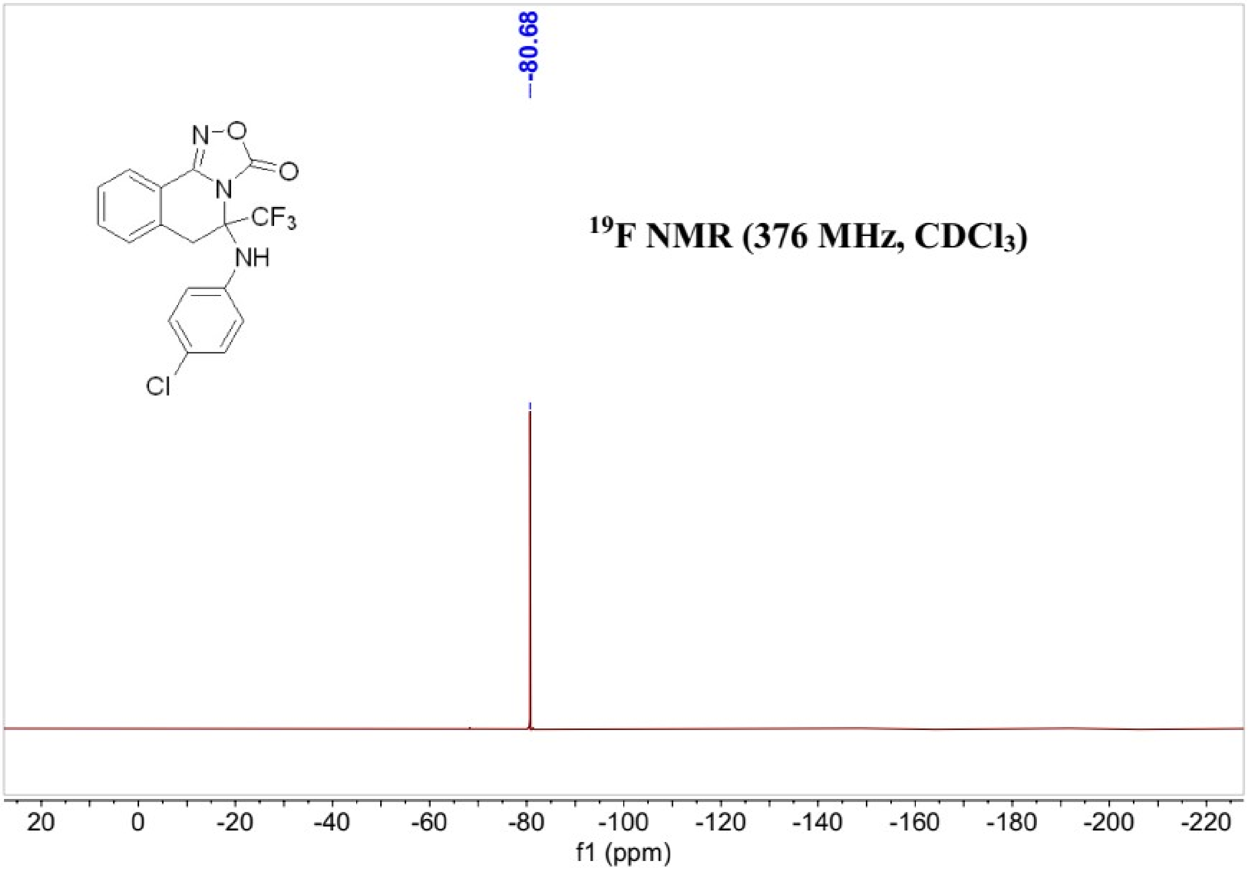

^{1}H NMR (400 MHz, CDCl$_3$)

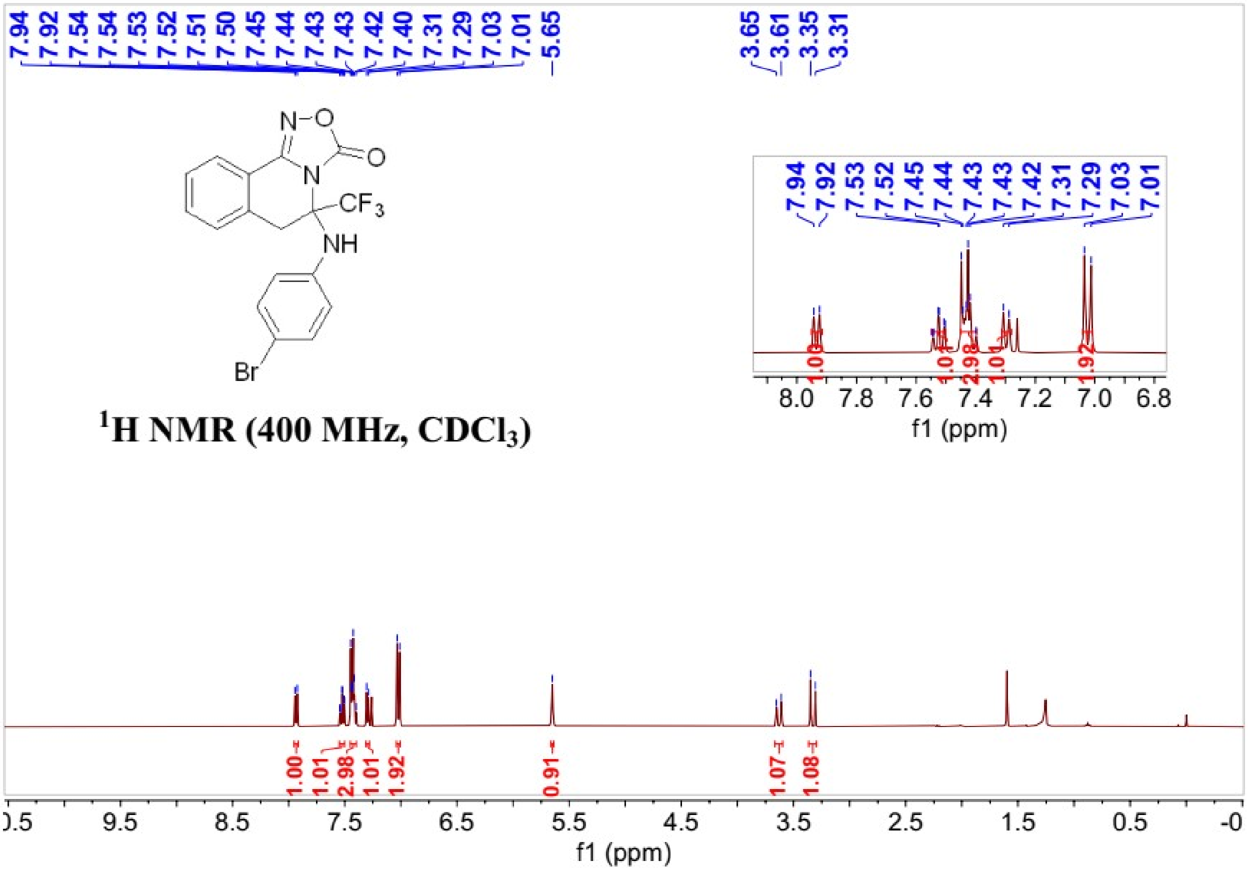

^{13}C NMR (101 MHz, CDCl$_3$)


-80.03
-115.36
^{19}F NMR (376 MHz, CDCl$_3$)
N–O
O
N
CF$_3$
NH
F
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

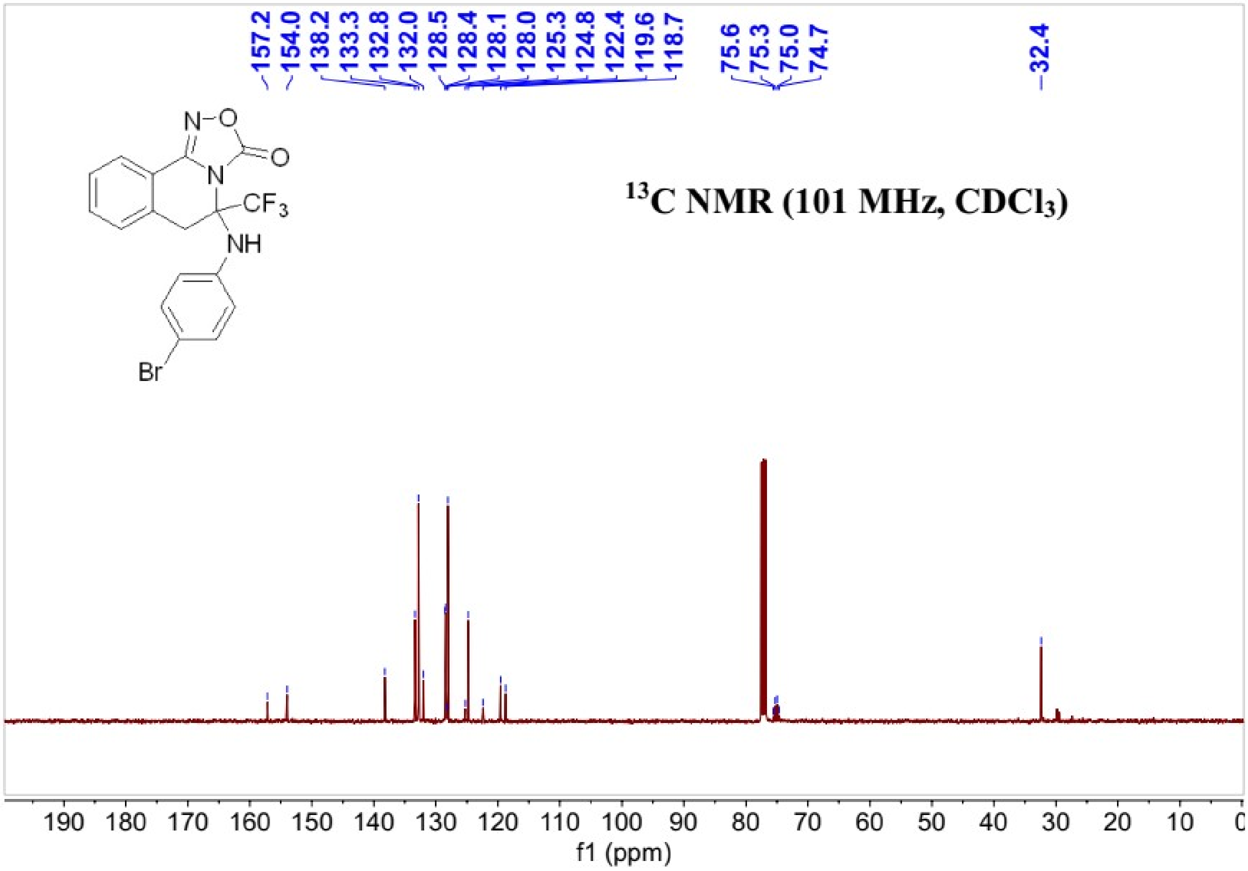

7.94 7.92 7.54 7.52 7.51 7.44 7.42 7.40 7.30 7.29 7.28 7.10 7.08
5.66
3.64 3.59 3.34 3.30
N–O
O
N
CF$_3$
NH
Cl
^{1}H NMR (400 MHz, CDCl$_3$)
1.00 1.10 1.04 3.09 1.97 1.02 1.07 1.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)
8.0 7.8 7.6 7.4 7.2 7.0


157.2
154.0
137.6
133.3
132.1
131.9
129.8
128.5
128.4
127.9
125.3
124.8
122.4
118.8
75.7
75.4
75.1
74.8
32.4
N
O
O
N
CF3
NH
Cl
13C NMR (101 MHz, CDCl3)
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

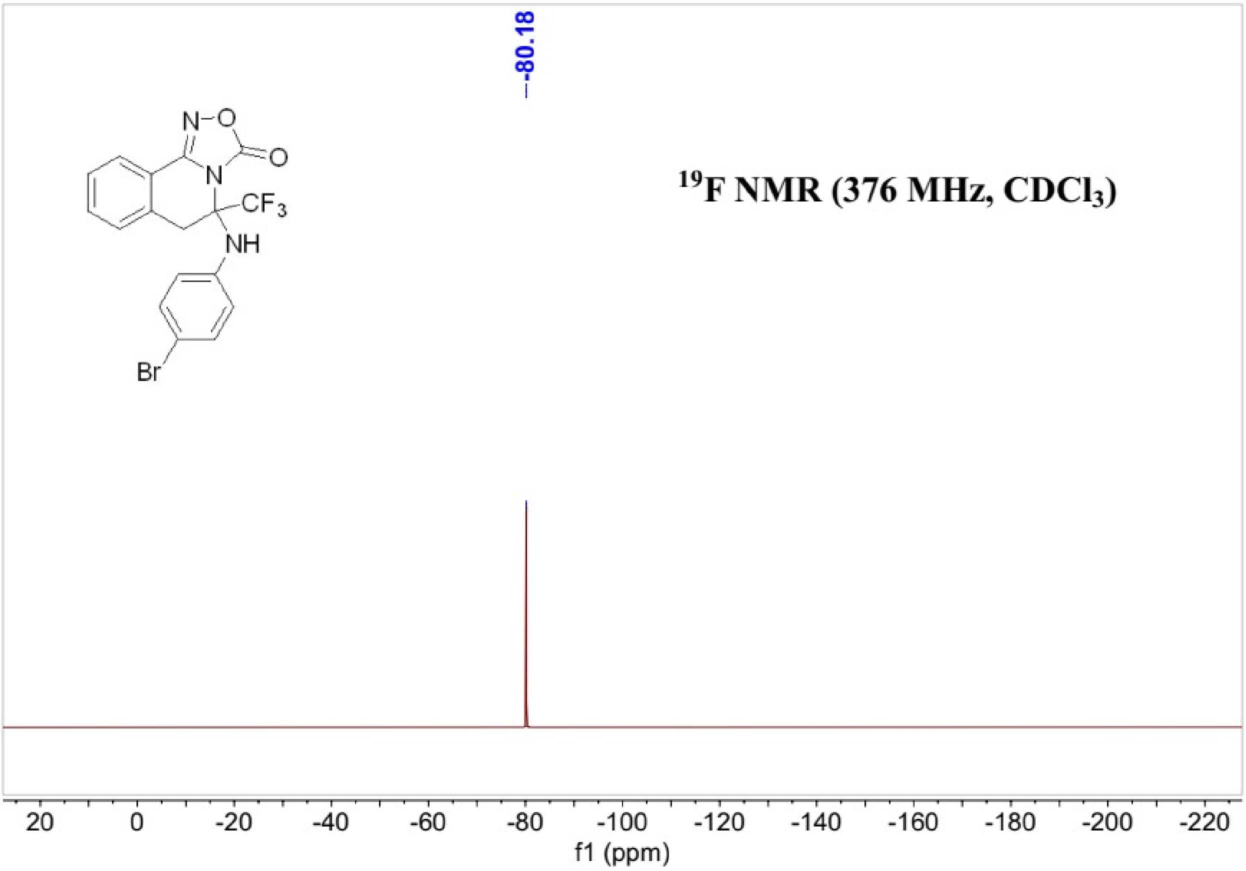

-80.68
N
O
O
N
CF3
NH
Cl
19F NMR (376 MHz, CDCl3)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

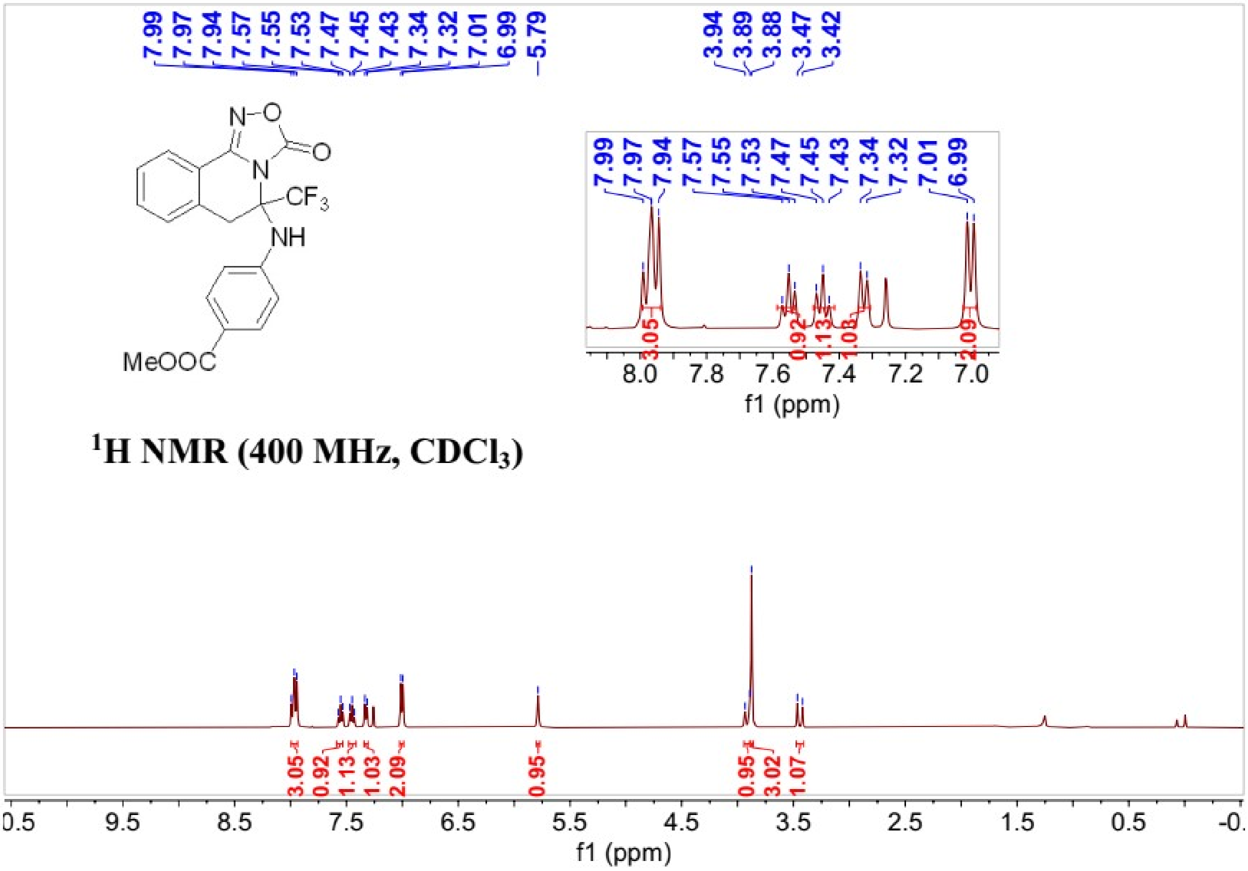


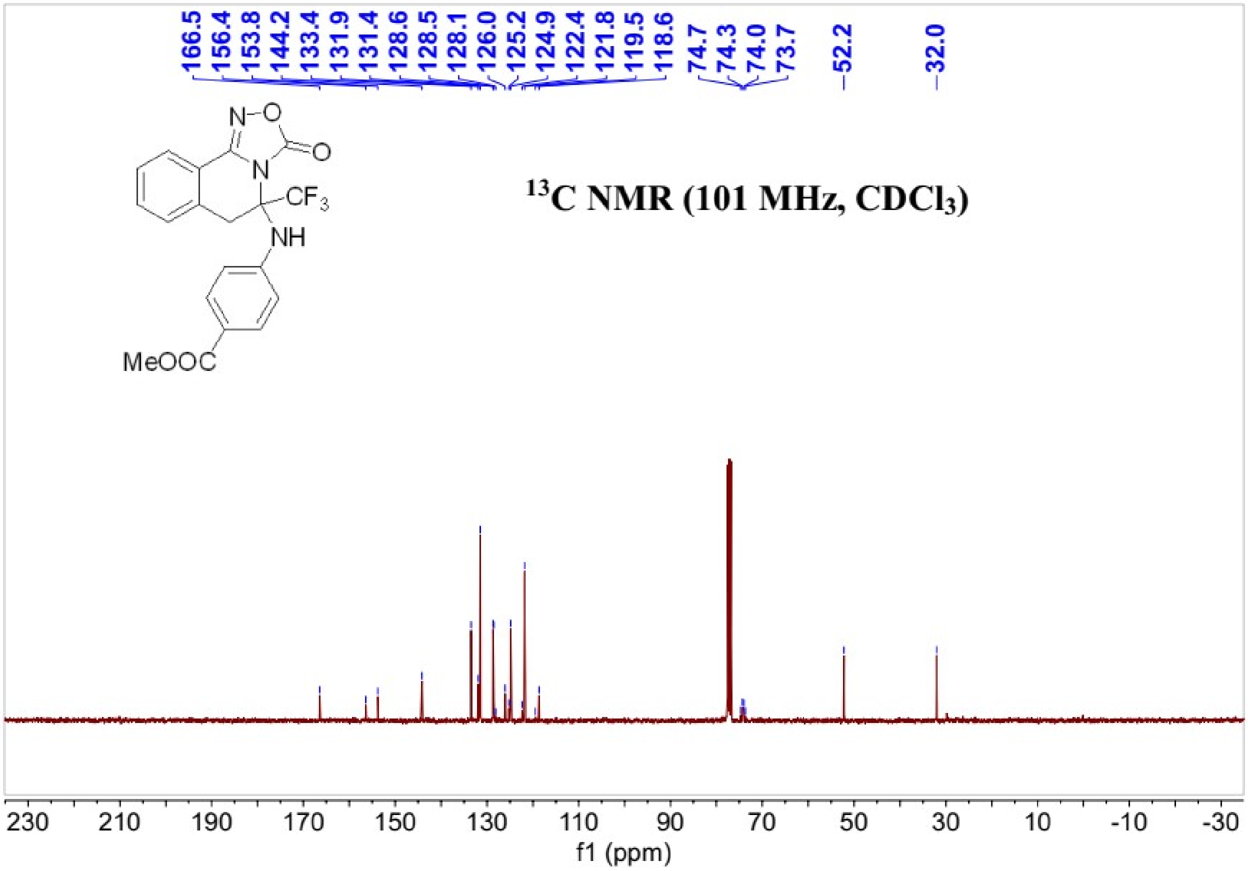
^{1}H NMR (400 MHz, CDCl$_3$)

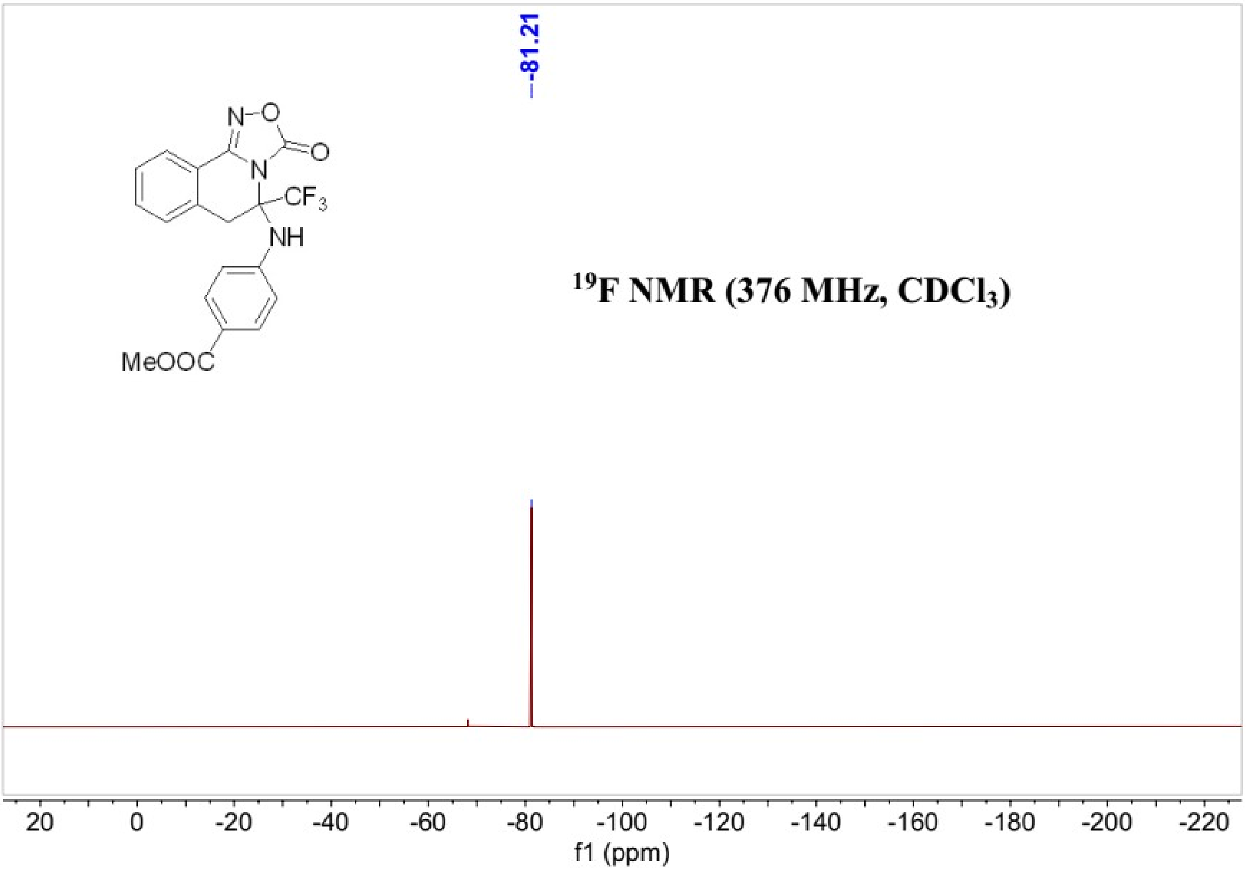


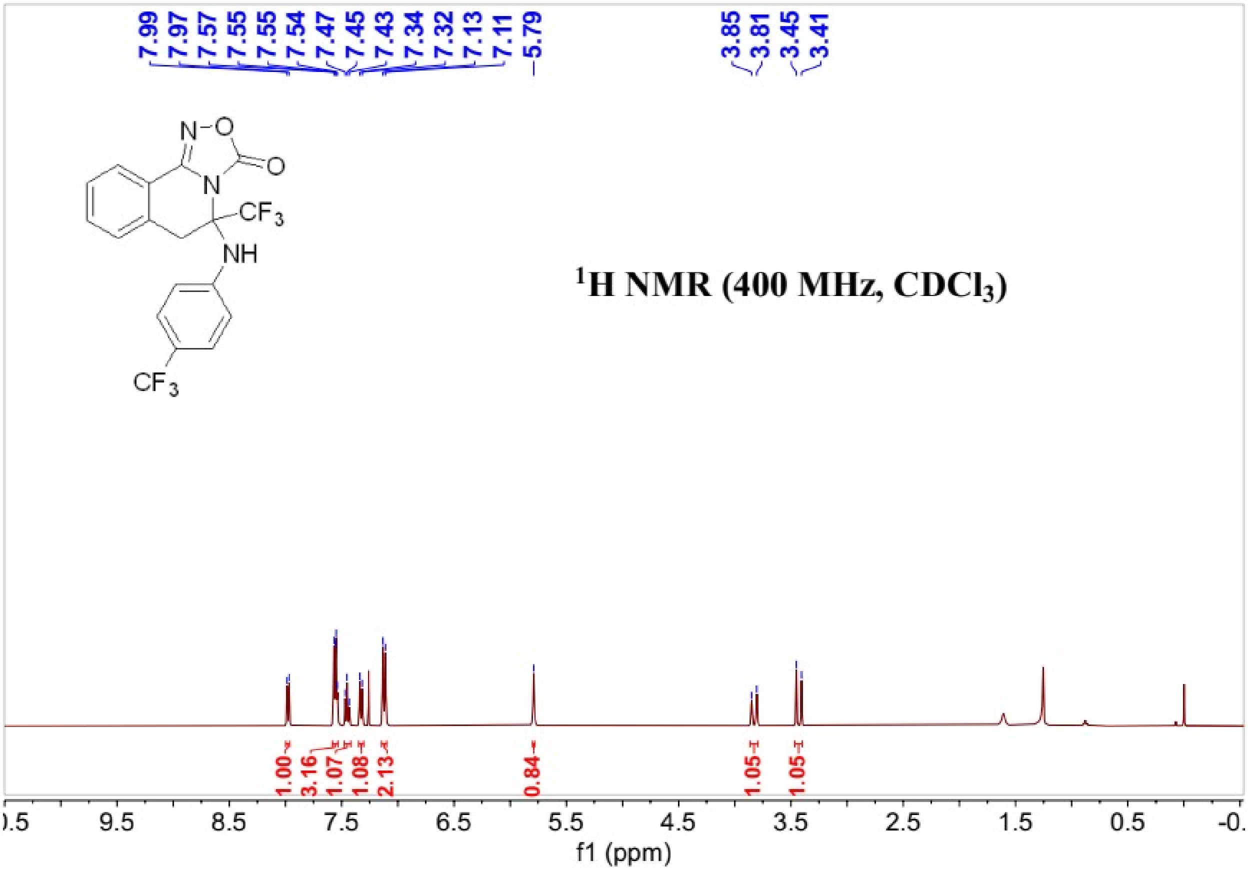
^{13}C NMR (101 MHz, CDCl$_3$)

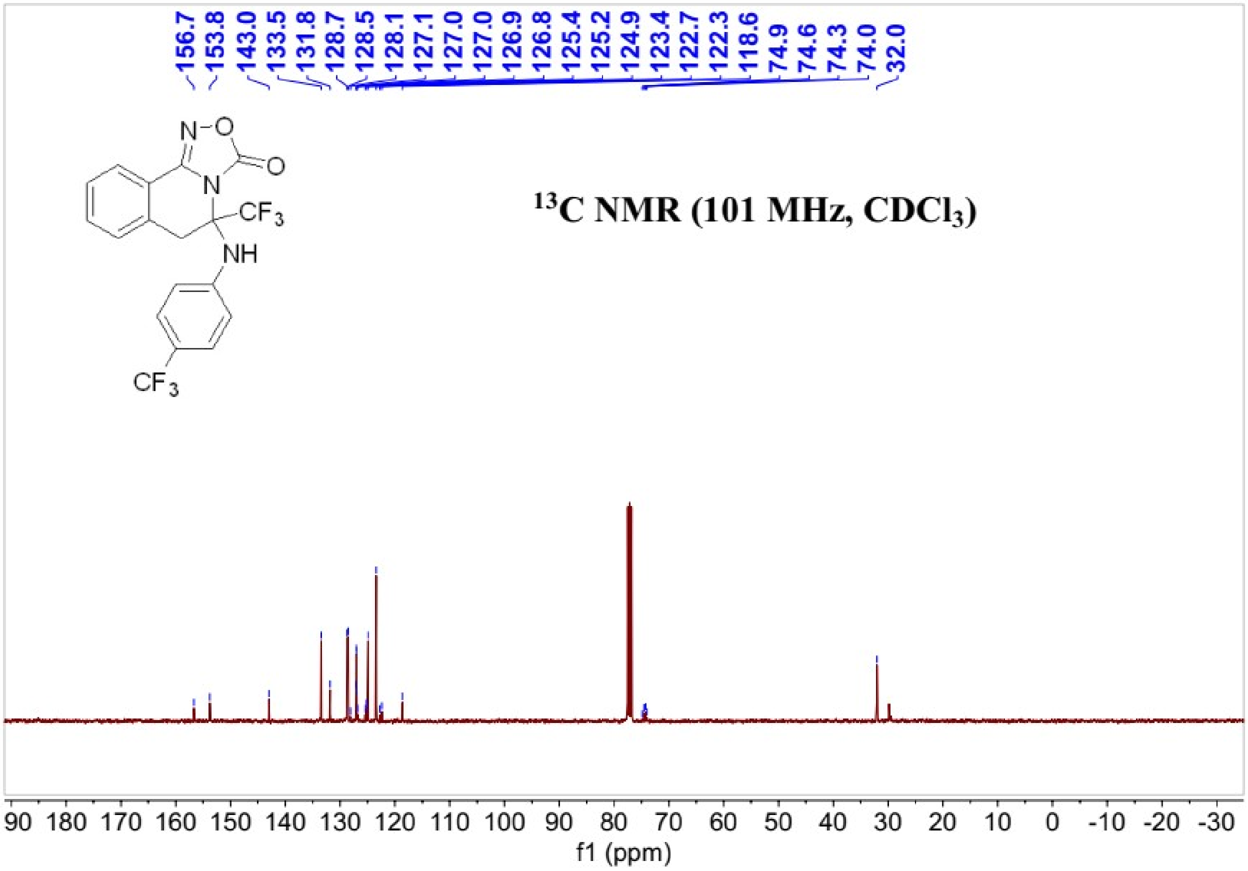

-80.18
N
O
O
N
CF3
NH
Br
19F NMR (376 MHz, CDCl3)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

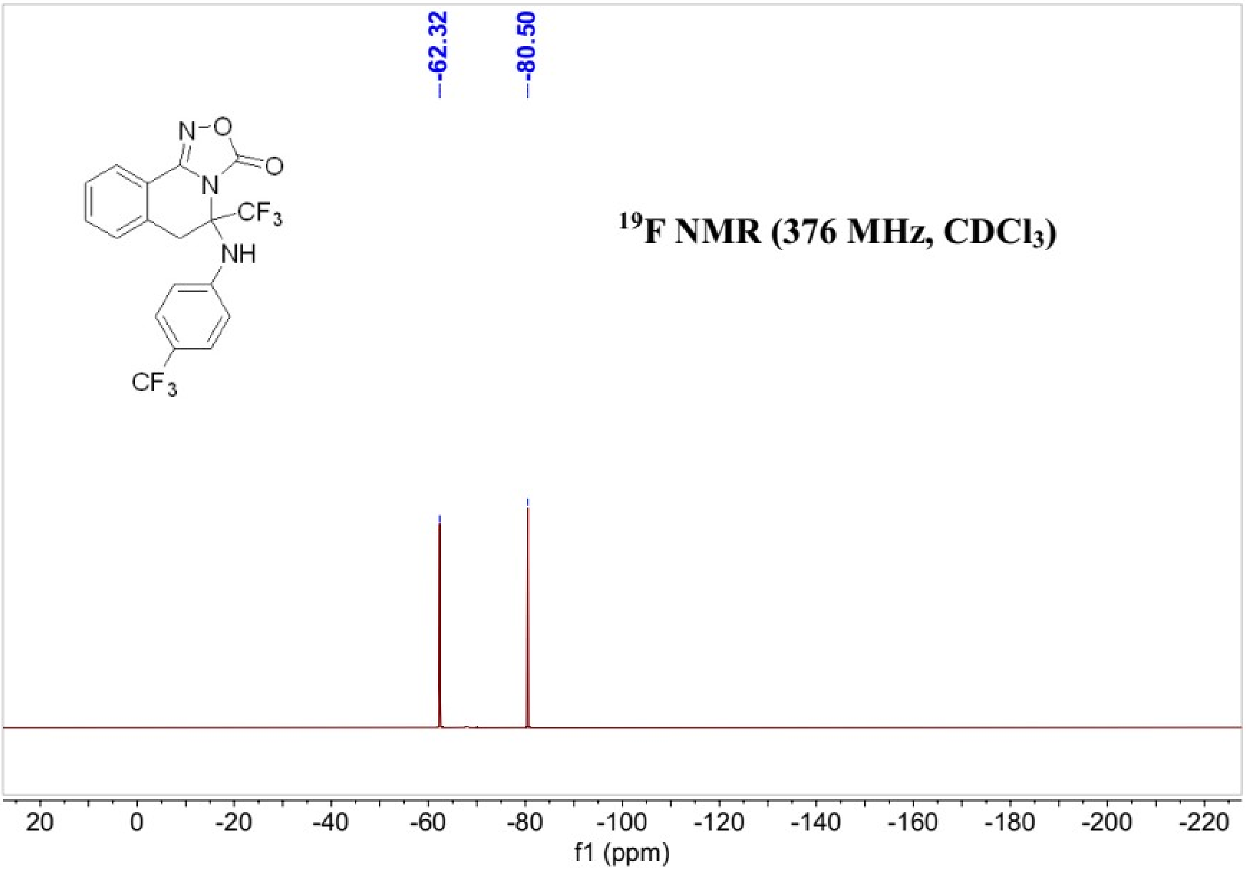

7.99
7.97
7.94
7.57
7.55
7.53
7.47
7.45
7.43
7.34
7.32
7.01
6.99
5.79
3.94
3.89
3.88
3.47
3.42
N
O
O
N
CF3
NH
MeOOC
1H NMR (400 MHz, CDCl3)
3.05
0.92
1.13
1.03
2.09
0.95
0.95
3.02
1.07
8.0
7.8
7.6
7.4
7.2
7.0
f1 (ppm)
0.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.
f1 (ppm)


166.5
156.4
153.8
144.2
133.4
131.9
131.4
128.6
128.5
128.1
126.0
125.2
124.9
122.4
121.8
119.5
118.6
74.7
74.3
74.0
73.7
52.2
32.0
N
O
O
N
CF3
NH
MeOOC
13C NMR (101 MHz, CDCl3)
230
210
190
170
150
130
110
90
70
50
30
10
-10
-30
f1 (ppm)

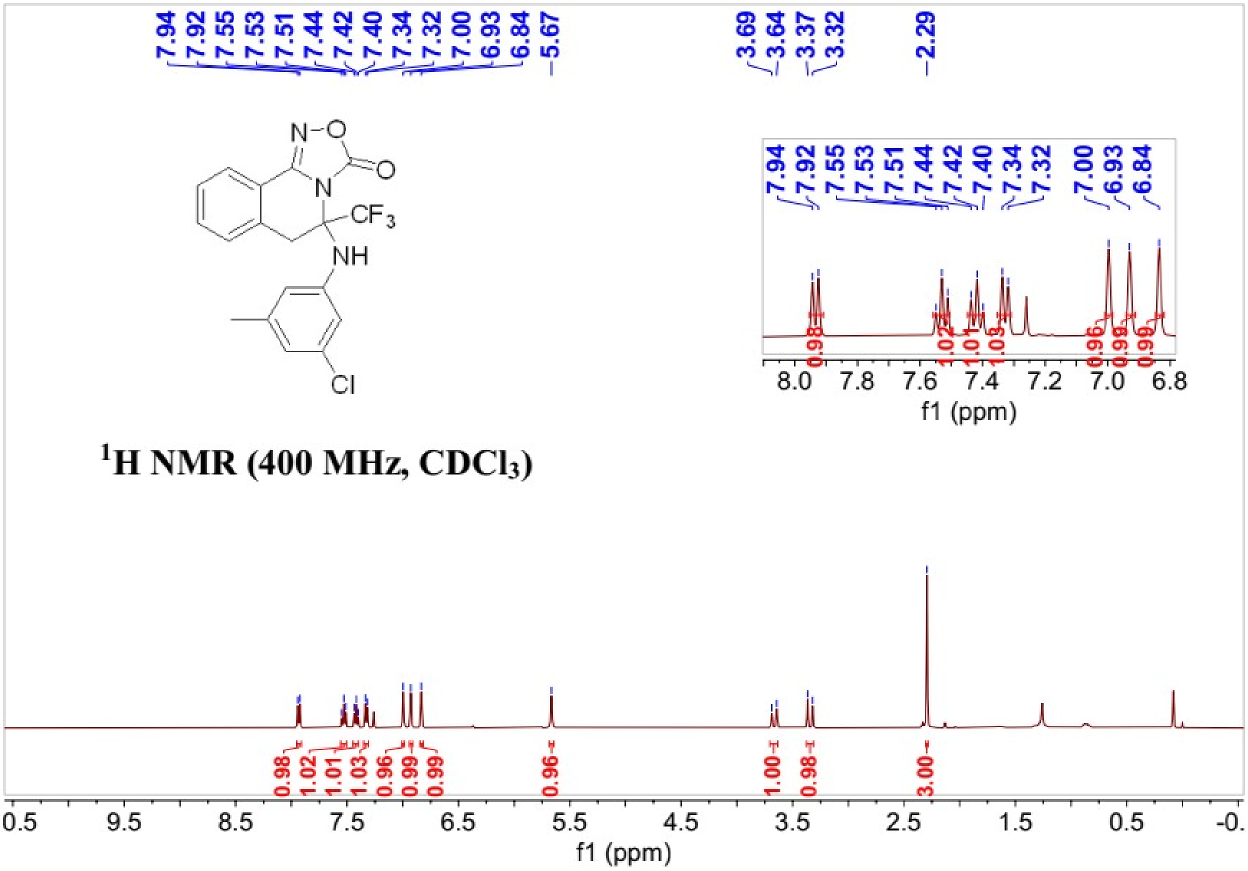

-81.21
N
O
O
N
CF3
NH
MeOOC
19F NMR (376 MHz, CDCl3)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)


7.99
7.97
7.57
7.55
7.55
7.54
7.47
7.45
7.43
7.34
7.32
7.13
7.11
5.79
3.85
3.81
3.45
3.41
N
O
O
N
CF3
NH
CF3
1H NMR (400 MHz, CDCl3)
1.00
3.16
1.07
1.08
2.13
0.84
1.05
1.05
).5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.
f1 (ppm)

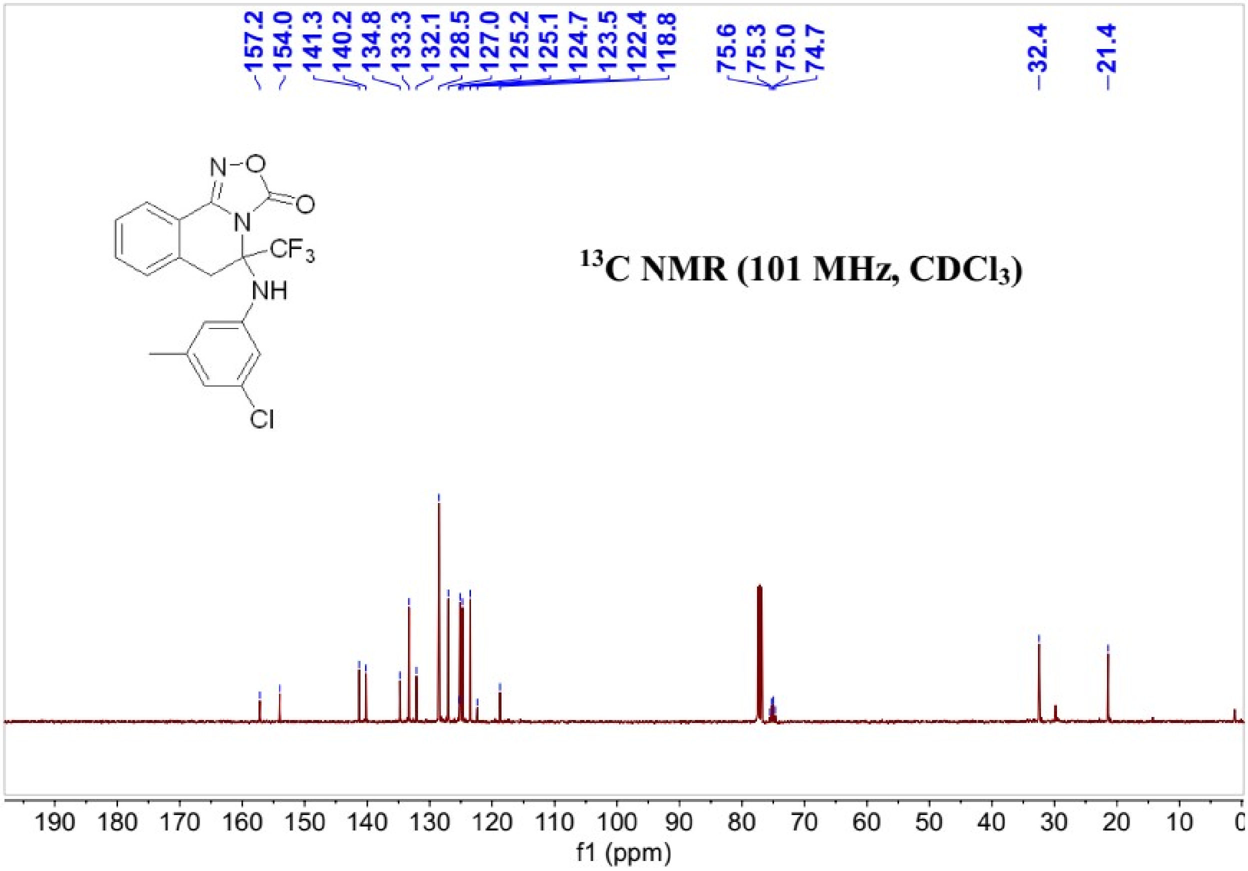

156.7
153.8
143.0
133.5
131.8
128.7
128.5
128.1
127.1
127.0
127.0
126.9
126.8
125.4
125.2
124.9
123.4
122.7
122.3
118.6
74.9
74.6
74.3
74.0
32.0
N
O
O
N
CF3
NH
CF3
13C NMR (101 MHz, CDCl3)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
f1 (ppm)

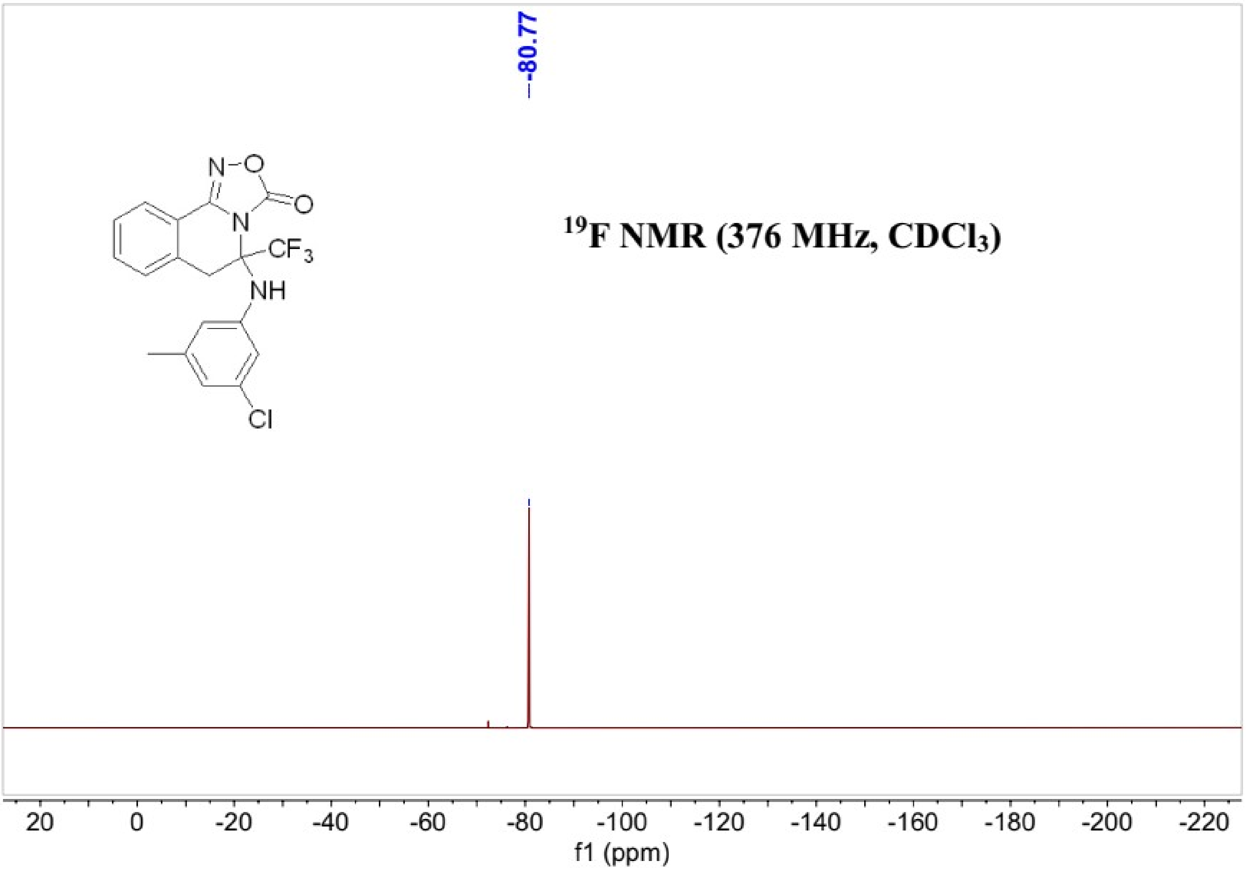


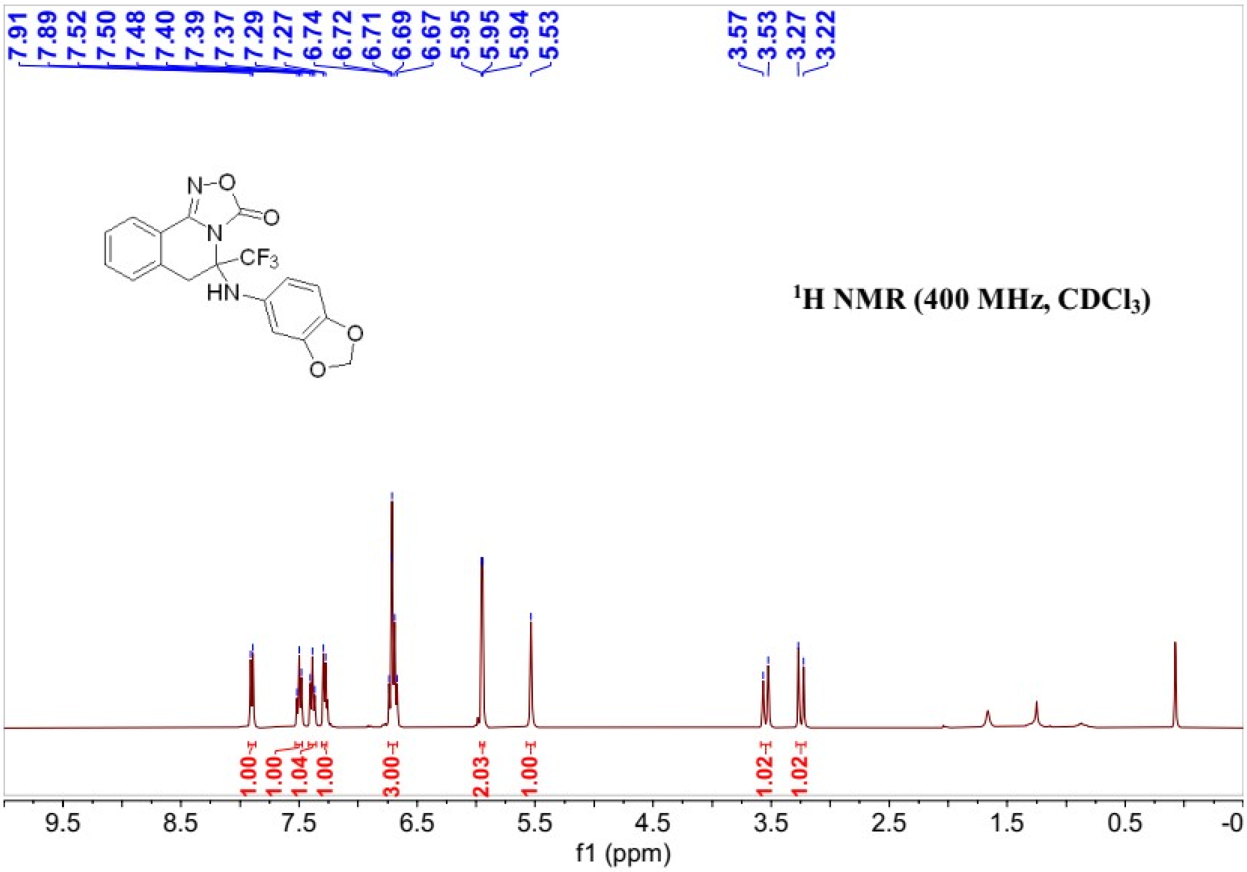
^{19}F NMR (376 MHz, $CDCl_3$)

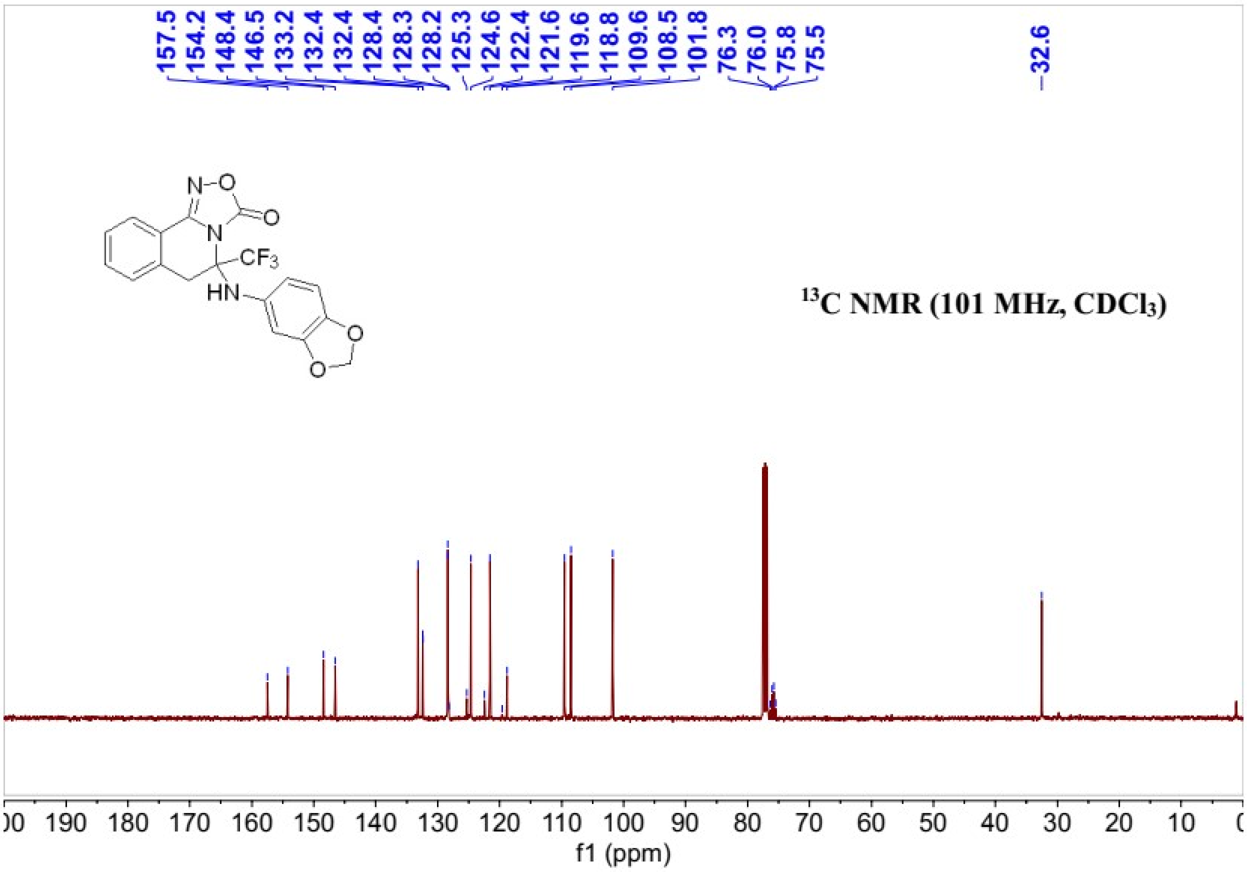


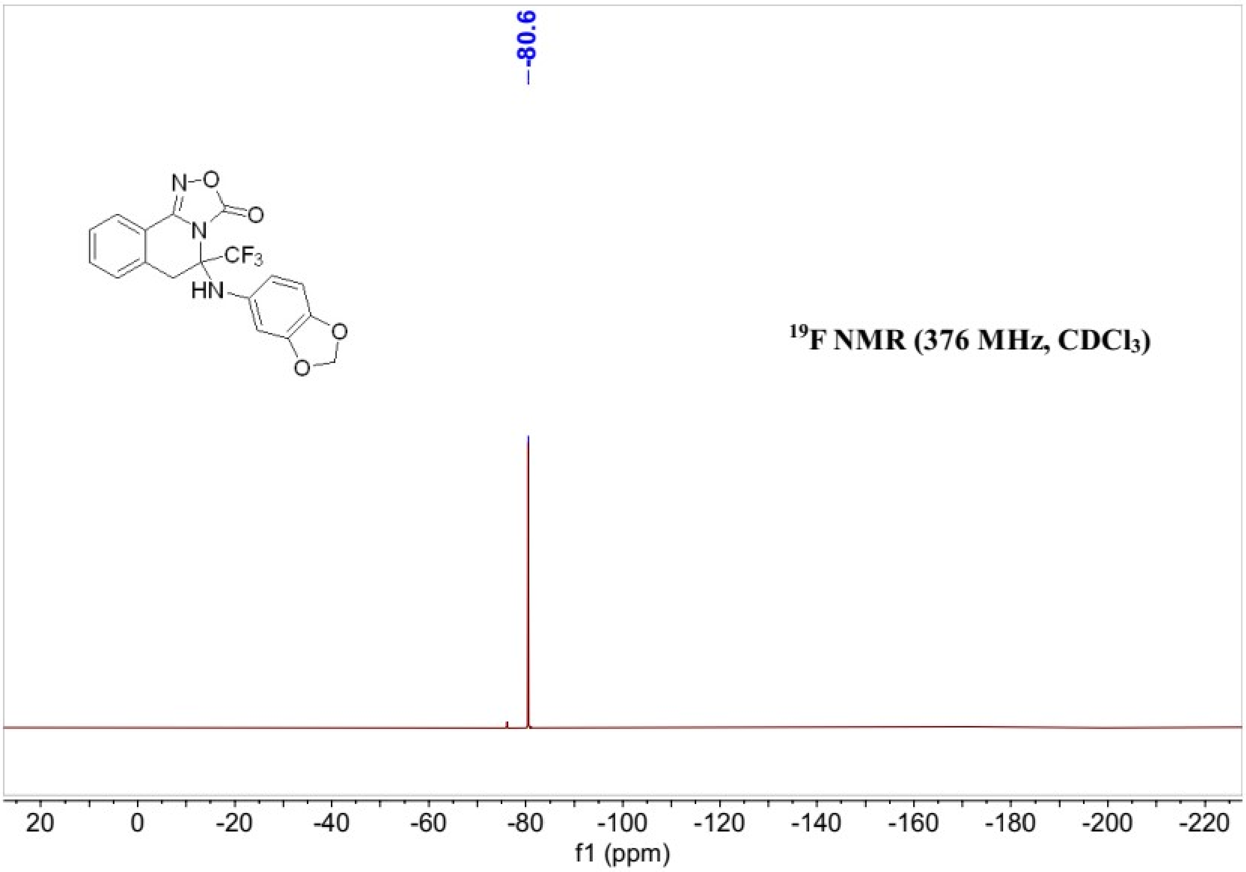
^1H NMR (400 MHz, $CDCl_3$)

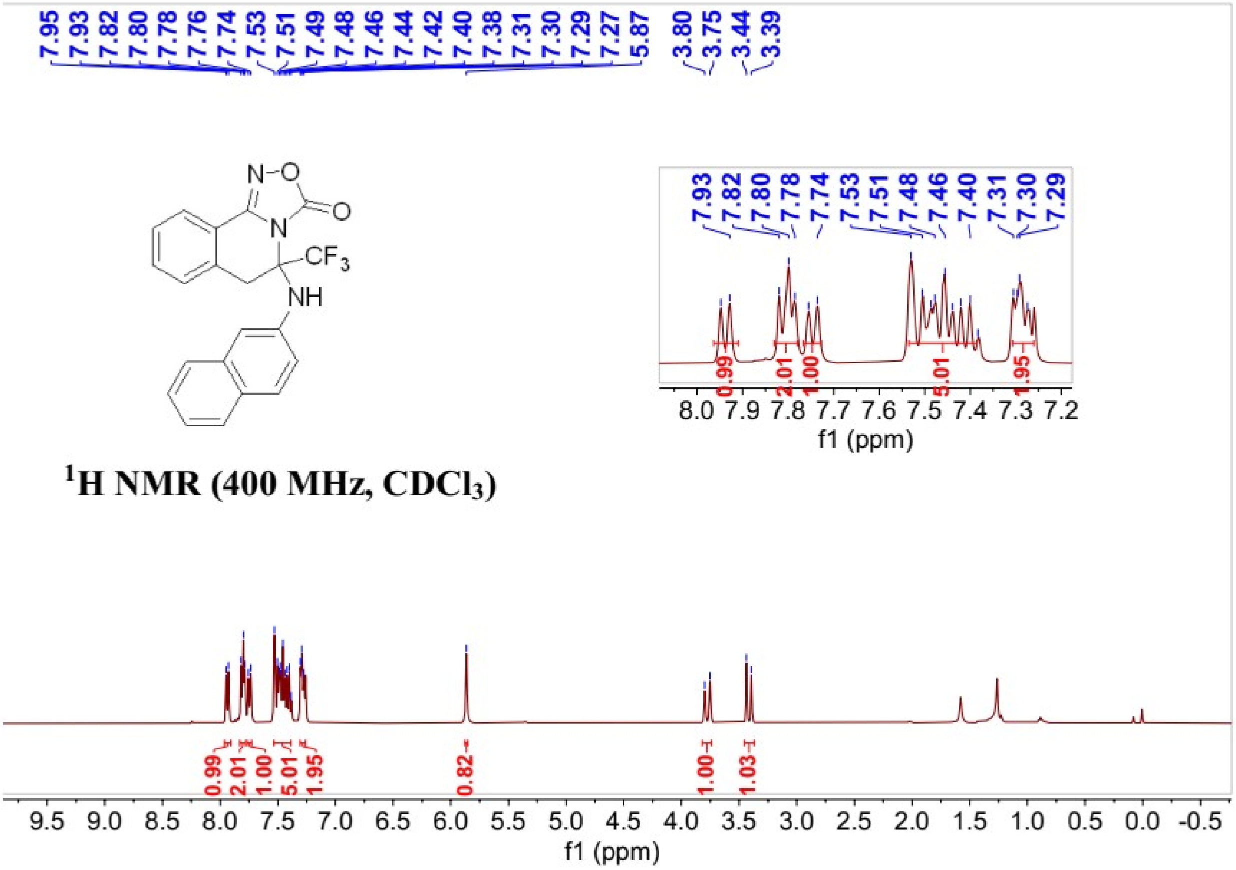

157.2
154.0
141.3
140.2
134.8
133.3
132.1
128.5
127.0
125.2
125.1
124.7
123.5
122.4
118.8
75.6
75.3
75.0
74.7
32.4
21.4
N
O
O
N
CF3
NH
Cl
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

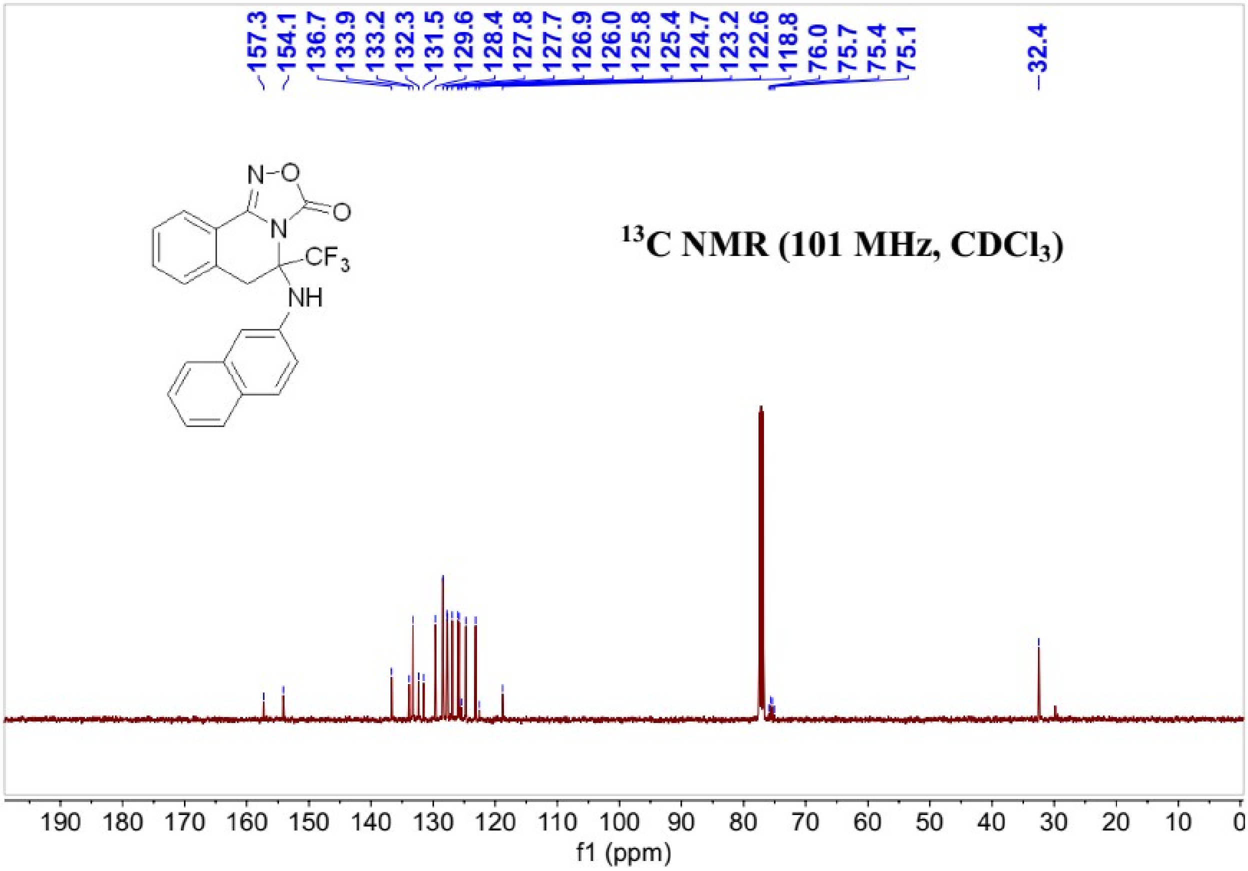

-80.77
N
O
O
N
CF3
NH
Cl
19F NMR (376 MHz, CDCl3)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

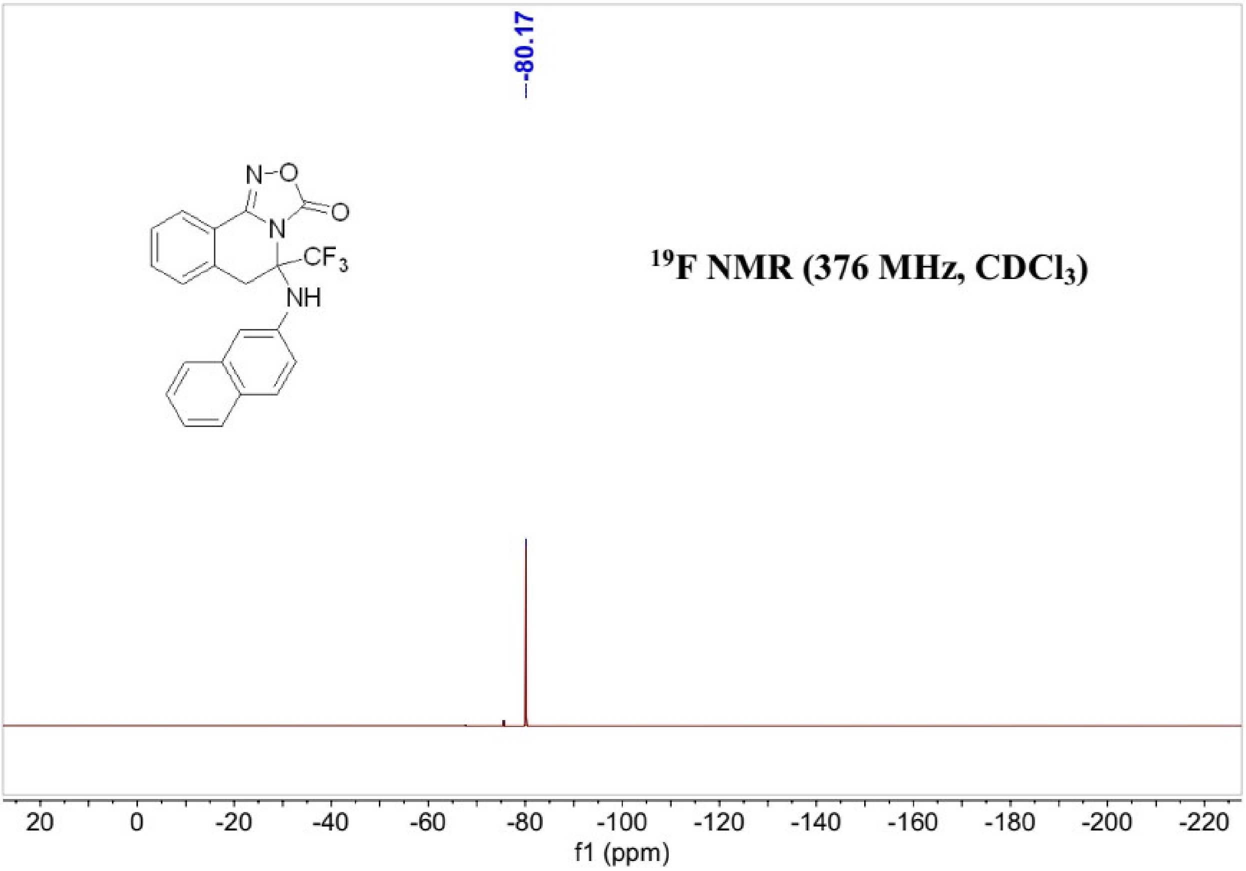

^{1}H NMR (400 MHz, CDCl$_3$)

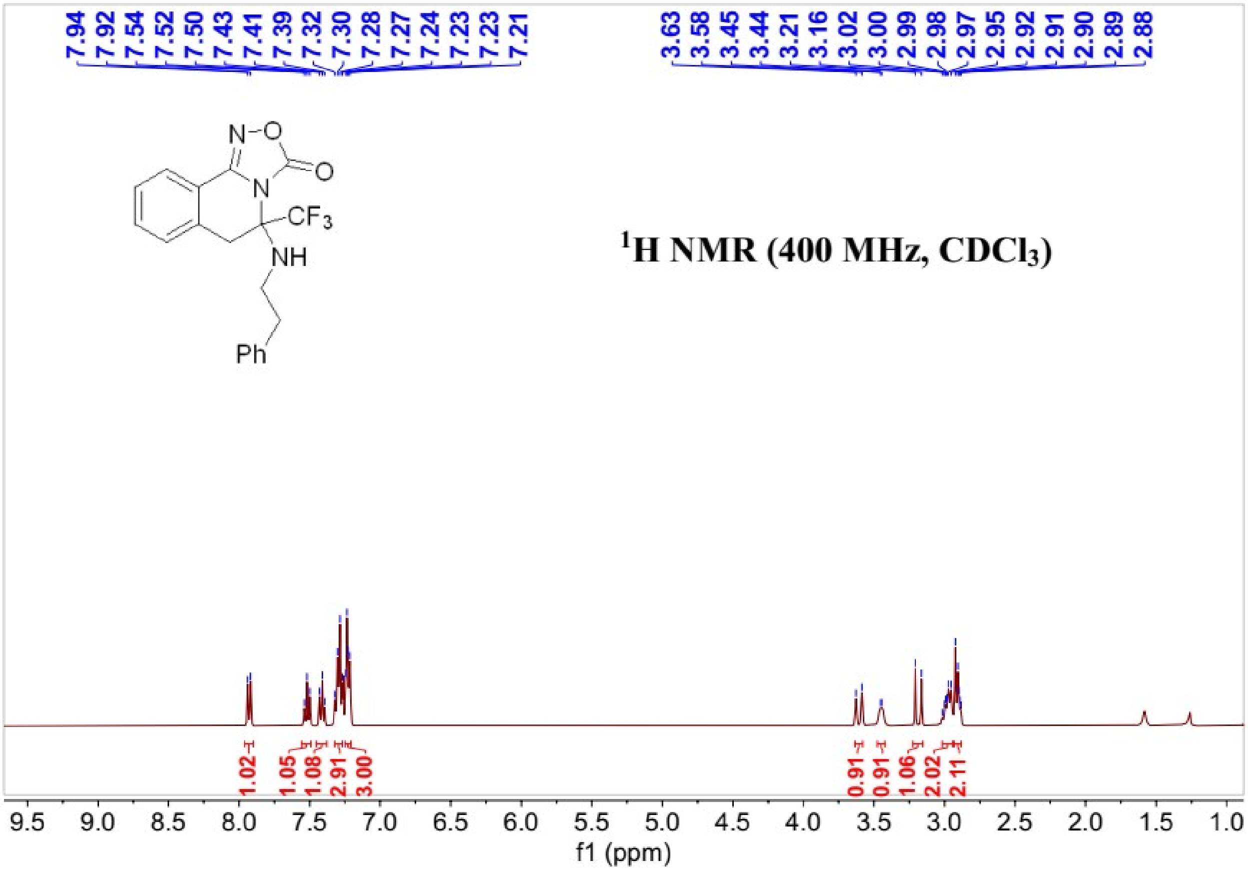

^{13}C NMR (101 MHz, CDCl$_3$)

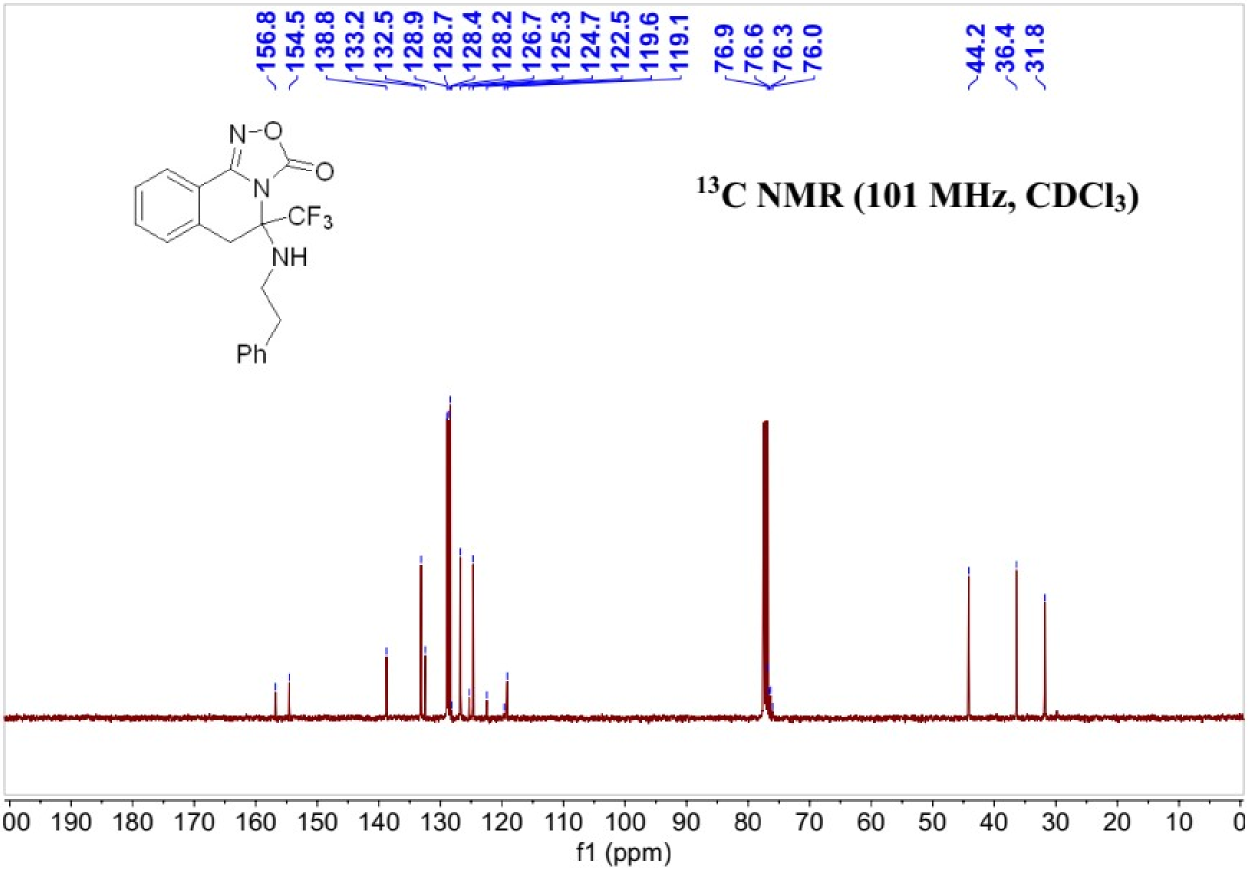

-80.6
N–O
O
N
CF3
HN
O
O
19F NMR (376 MHz, CDCl3)
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

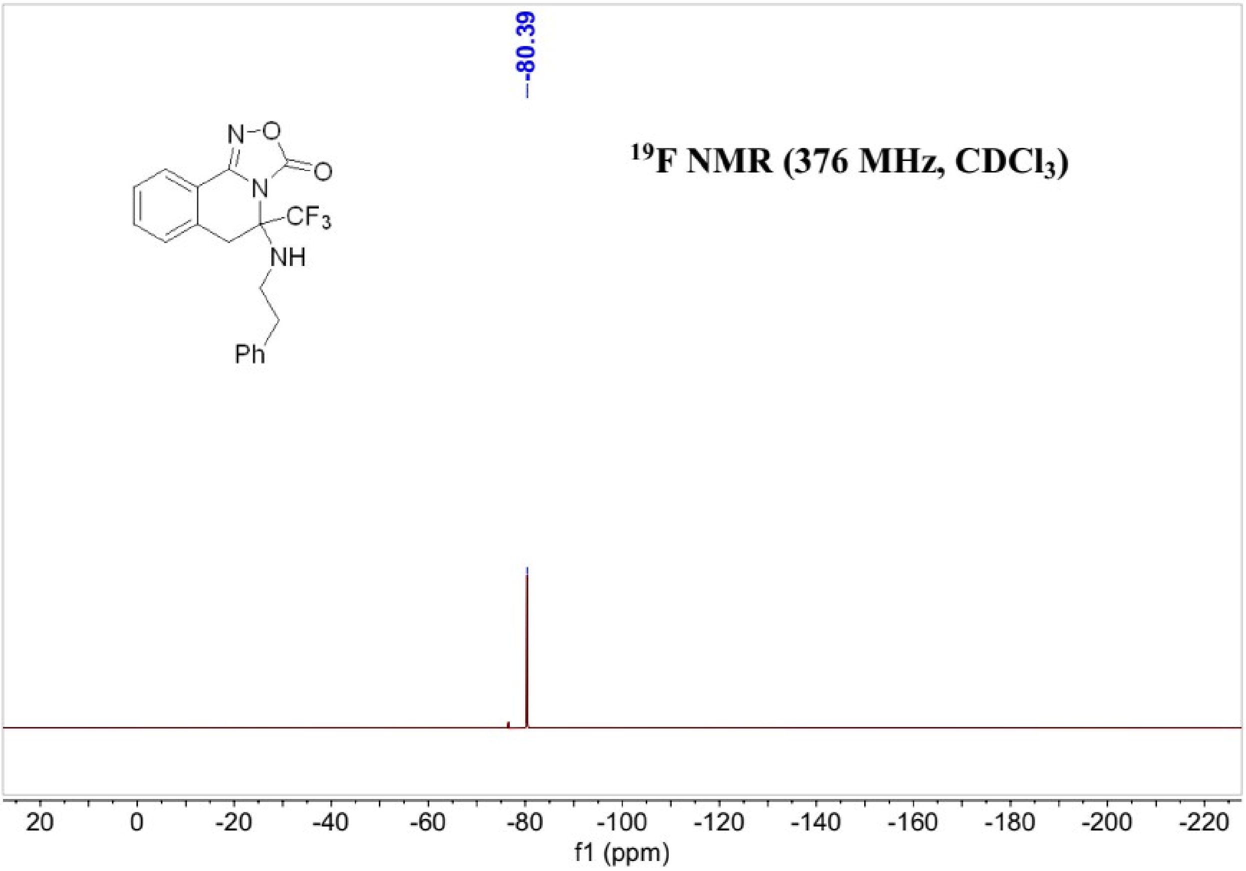

7.95 7.93 7.82 7.80 7.78 7.76 7.74 7.53 7.51 7.49 7.48 7.46 7.44 7.42 7.40 7.38 7.31 7.30 7.29 7.27 5.87 3.80 3.75 3.44 3.39
N–O
O
N
CF3
NH
7.93 7.82 7.80 7.78 7.74 7.53 7.51 7.48 7.46 7.40 7.31 7.30 7.29
0.99 2.01 1.00 5.01 1.95
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)
1H NMR (400 MHz, CDCl3)
0.99 2.01 1.00 5.01 1.95 0.82 1.00 1.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


157.3
154.1
136.7
133.9
133.2
132.3
131.5
129.6
128.4
127.8
127.7
126.9
126.0
125.8
125.4
124.7
123.2
122.6
118.8
76.0
75.7
75.4
75.1
32.4
N
O
O
N
CF3
NH
13C NMR (101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

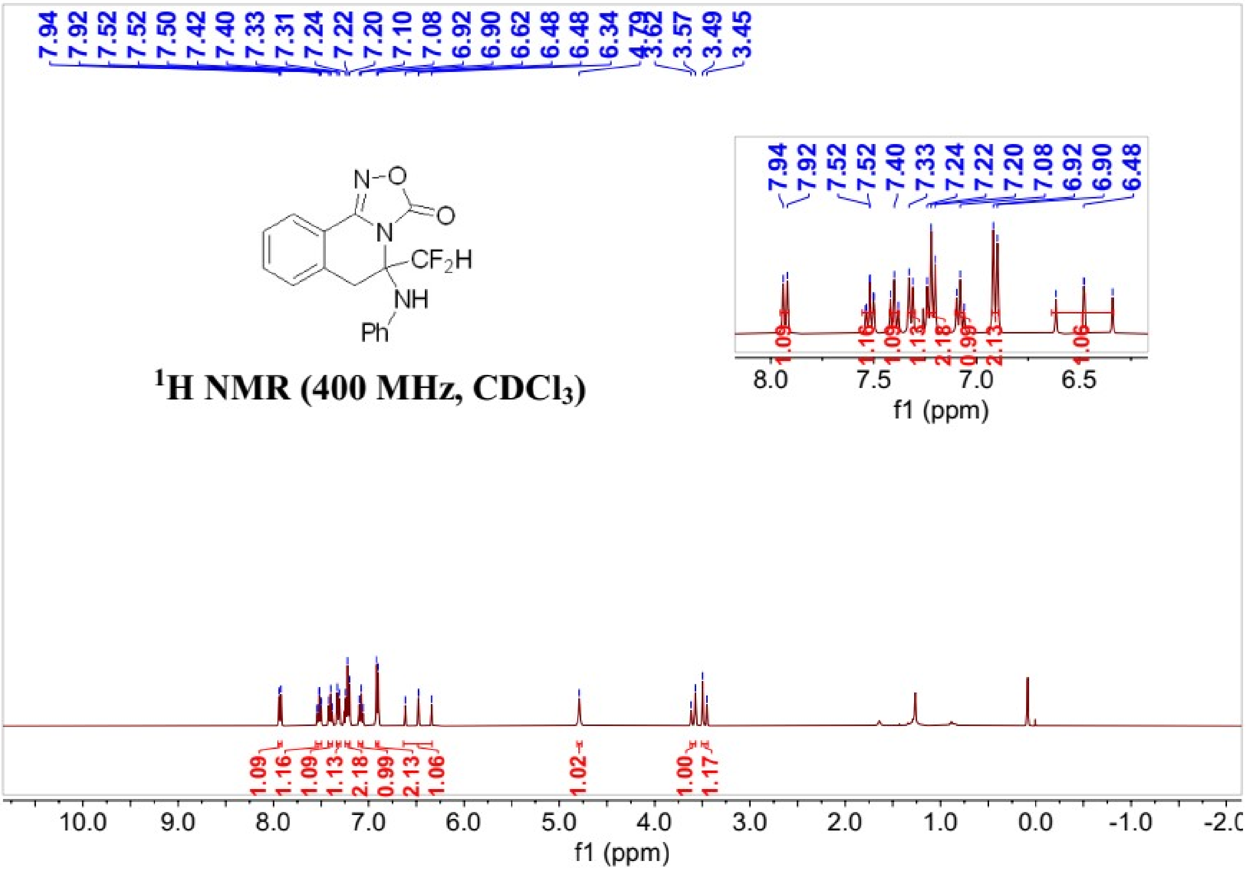

-80.17
N
O
O
N
CF3
NH
19F NMR (376 MHz, CDCl3)
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)


7.94 7.92 7.54 7.52 7.50 7.43 7.41 7.39 7.32 7.30 7.28 7.27 7.24 7.23 7.23 7.21
3.63 3.58 3.45 3.44 3.21 3.16 3.02 3.00 2.99 2.98 2.97 2.95 2.92 2.91 2.90 2.89 2.88
N–O
O
N
CF3
NH
Ph
1H NMR (400 MHz, CDCl3)
1.02 1.05 1.08 2.91 3.00
0.91 0.91 1.06 2.02 2.11
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)

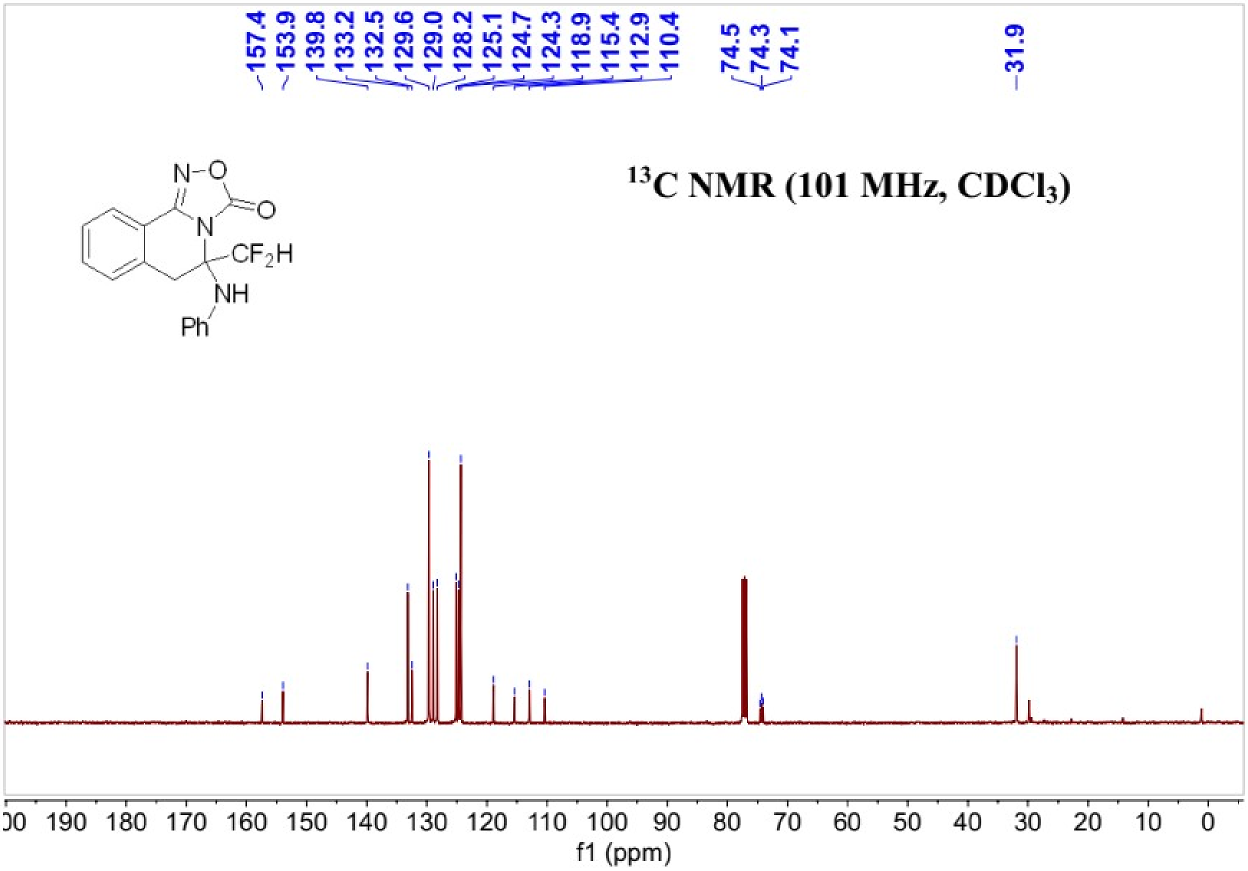

156.8 154.5 138.8 133.2 132.5 128.9 128.7 128.4 128.2 126.7 125.3 124.7 122.5 119.6 119.1
76.9 76.6 76.3 76.0
44.2 36.4 31.8
N–O
O
N
CF3
NH
Ph
13C NMR (101 MHz, CDCl3)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

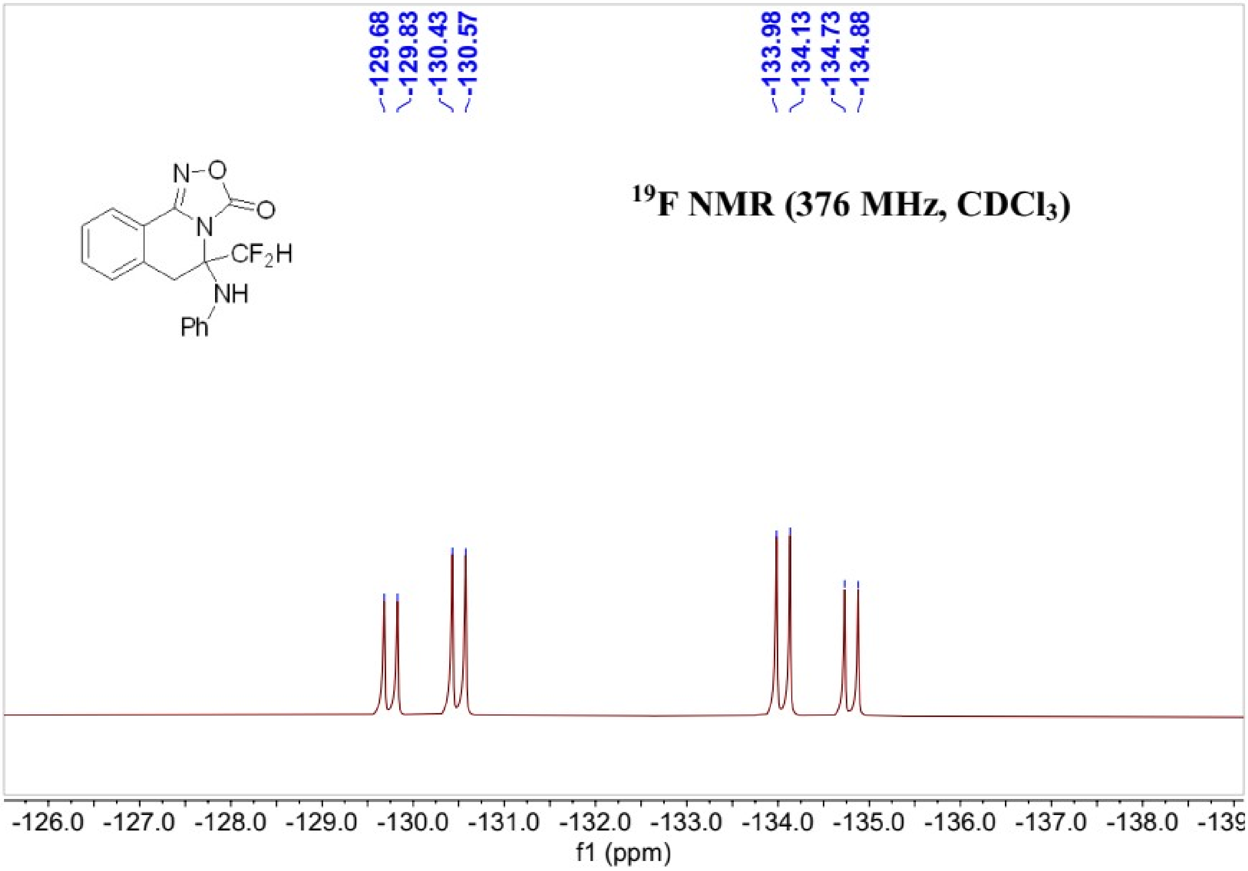


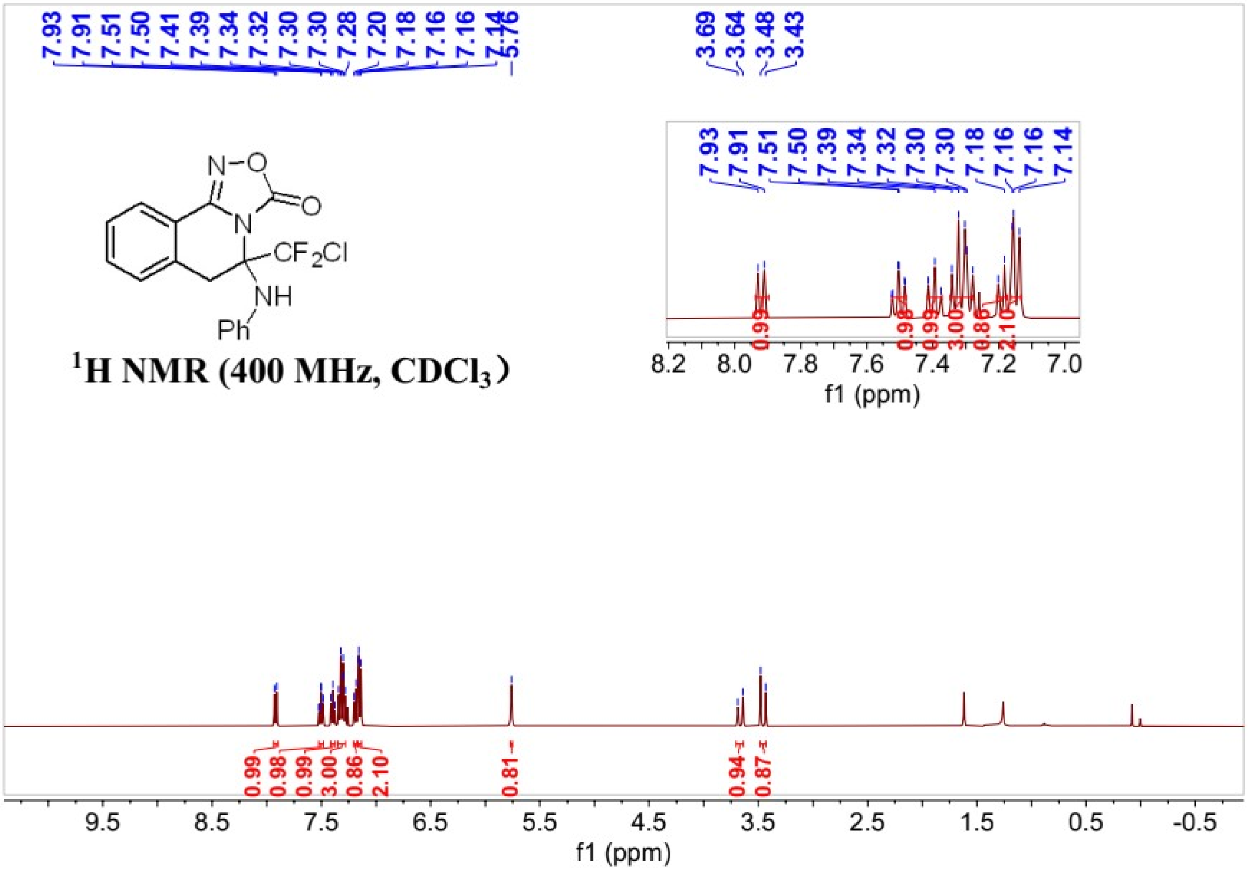
^{19}F NMR (376 MHz, CDCl$_3$)



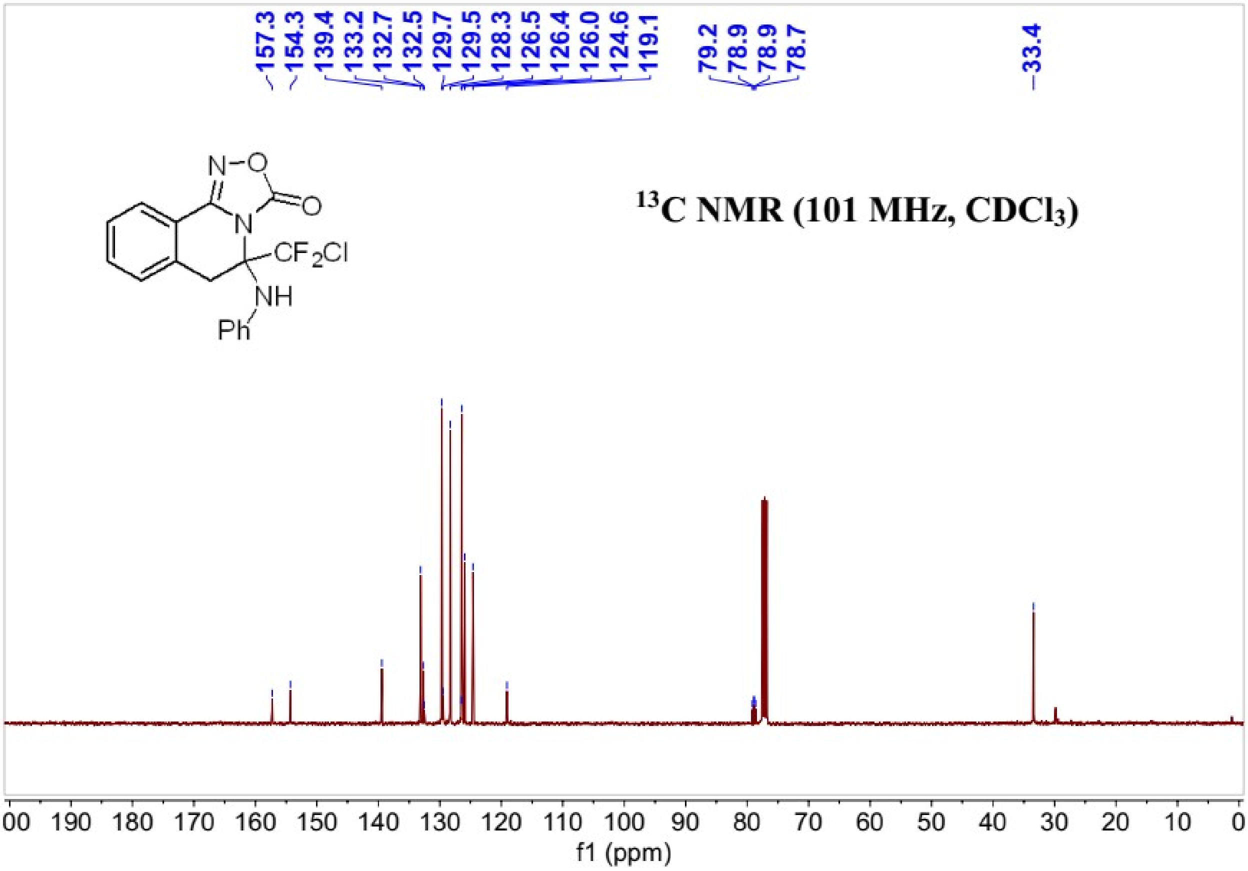
^{1}H NMR (400 MHz, CDCl$_3$)


157.4
153.9
139.8
133.2
132.5
129.6
129.0
128.2
125.1
124.7
124.3
118.9
115.4
112.9
110.4
74.5
74.3
74.1
31.9
N
O
O
N
CF2H
NH
Ph
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

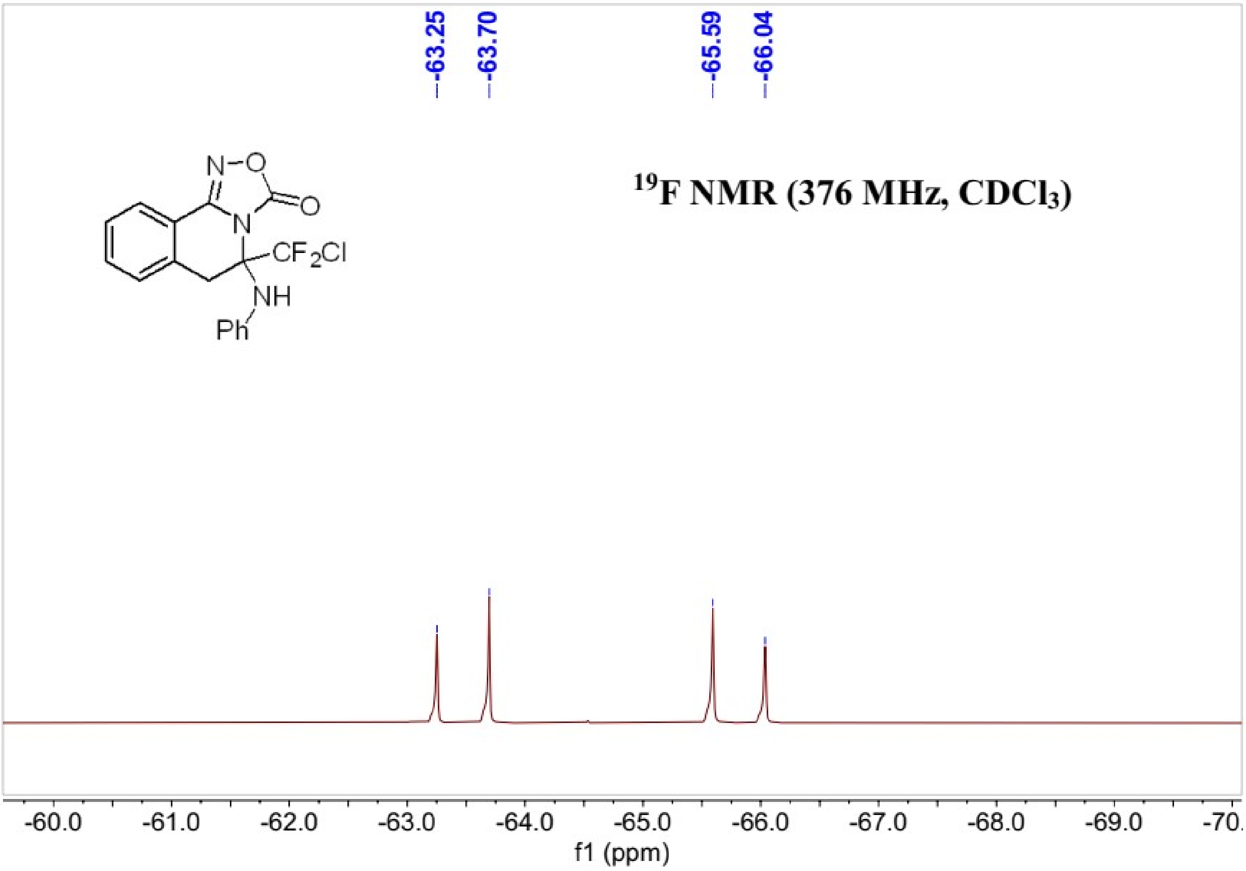

-129.68
-129.83
-130.43
-130.57
-133.98
-134.13
-134.73
-134.88
N
O
O
N
CF2H
NH
Ph
19F NMR (376 MHz, CDCl3)
-126.0
-127.0
-128.0
-129.0
-130.0
-131.0
-132.0
-133.0
-134.0
-135.0
-136.0
-137.0
-138.0
f1 (ppm)

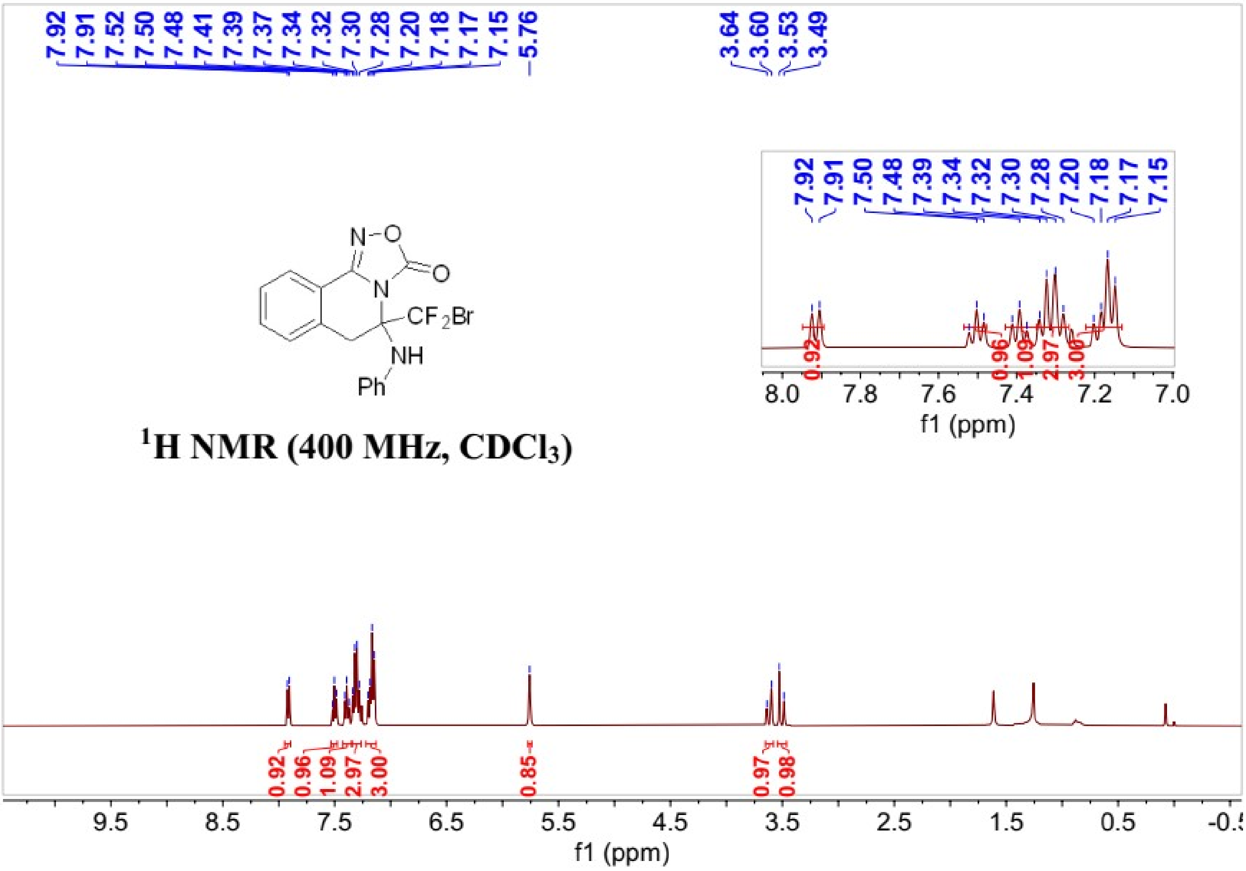


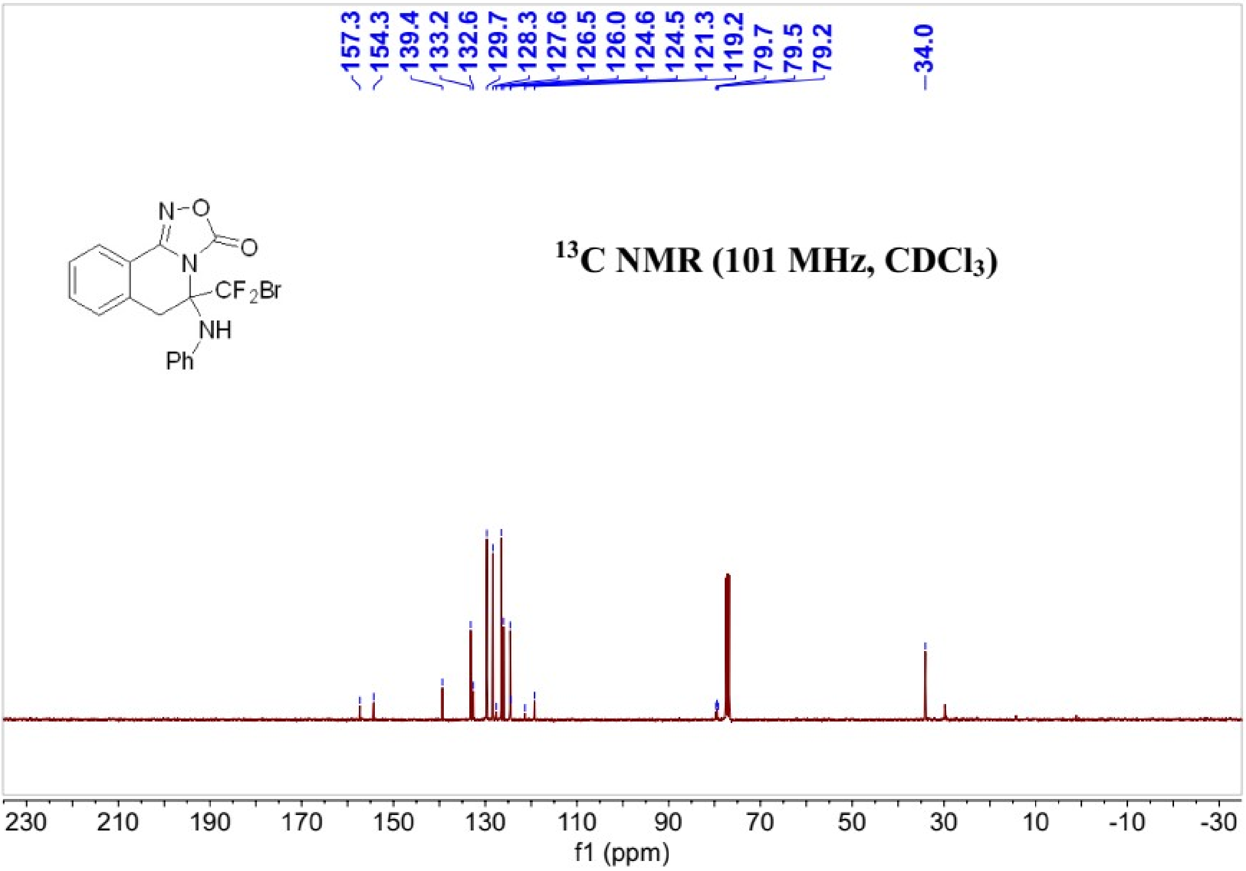
^{1}H NMR (400 MHz, CDCl$_3$)

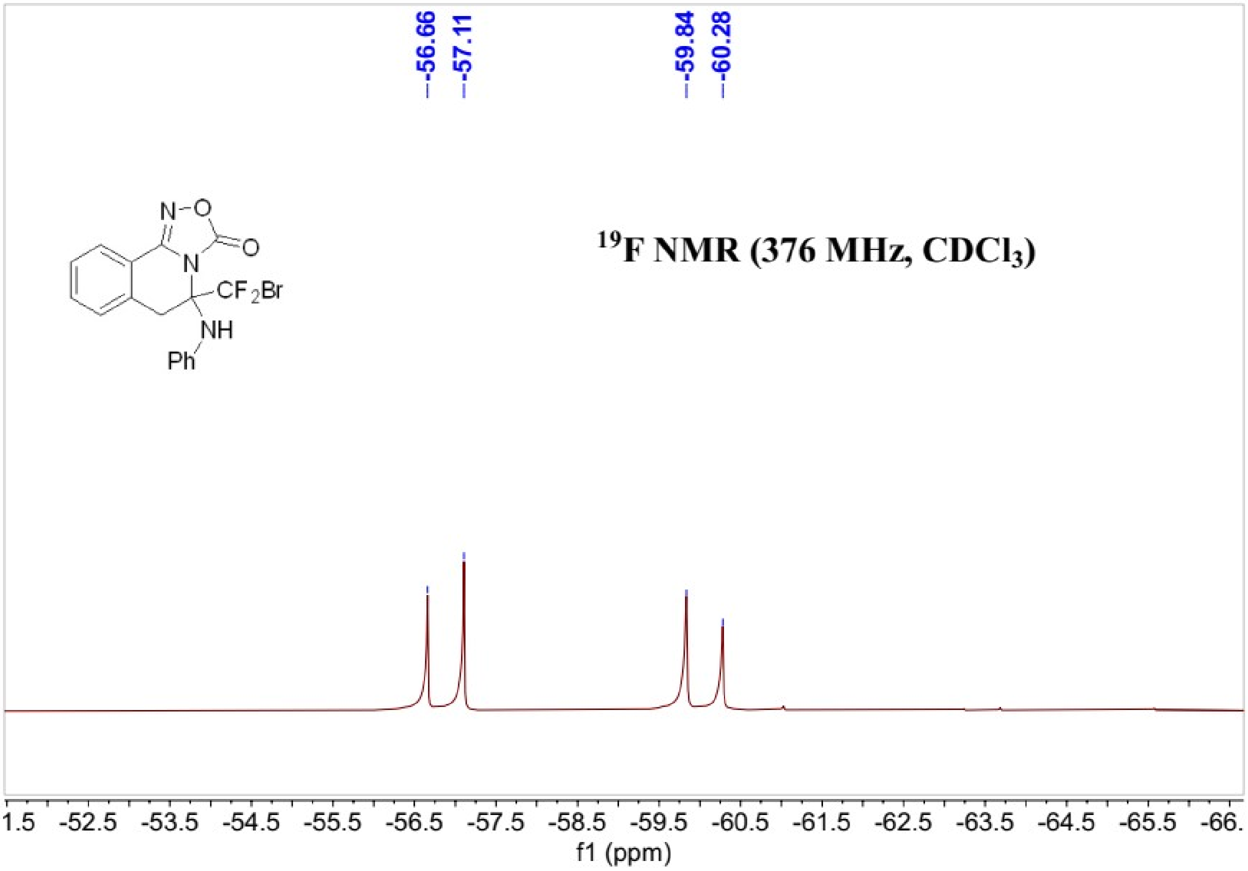


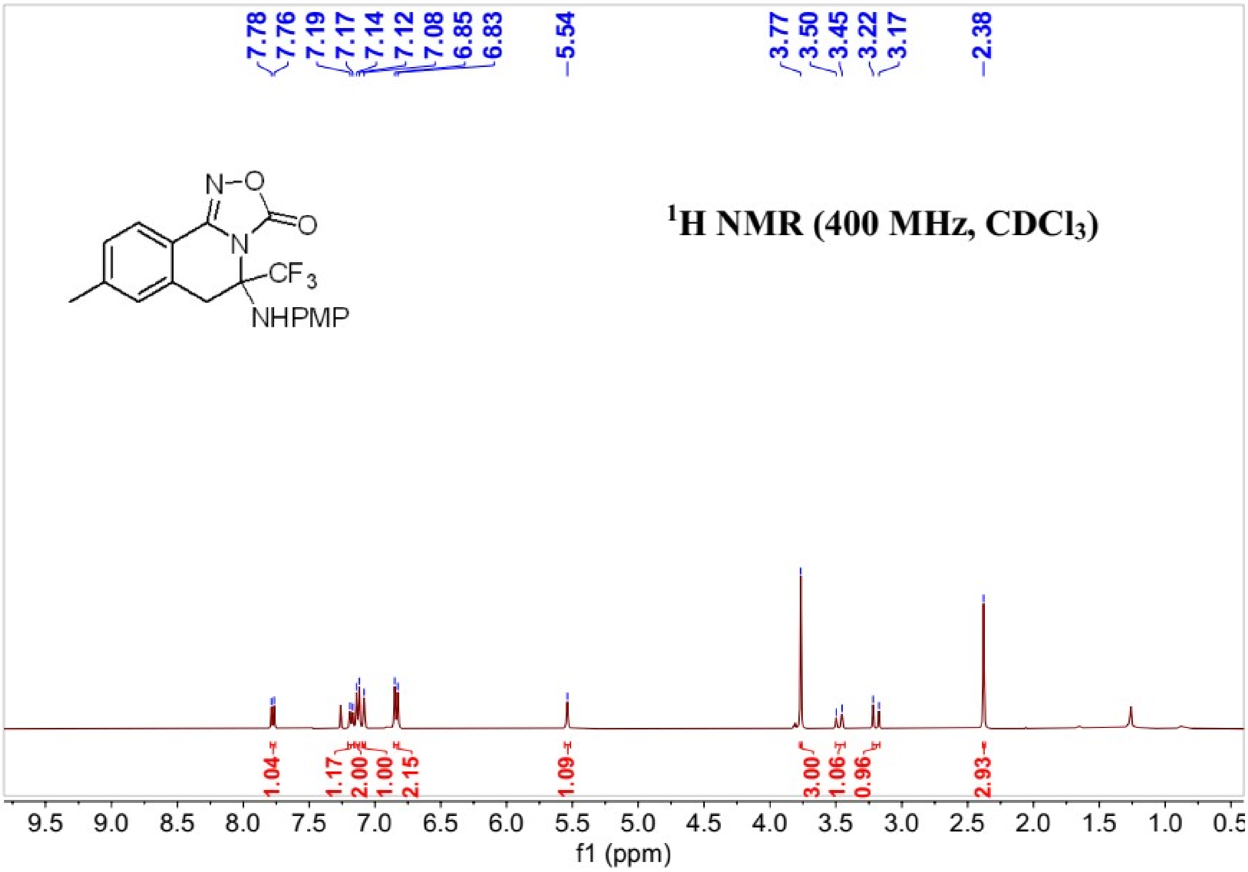
^{13}C NMR (101 MHz, CDCl$_3$)

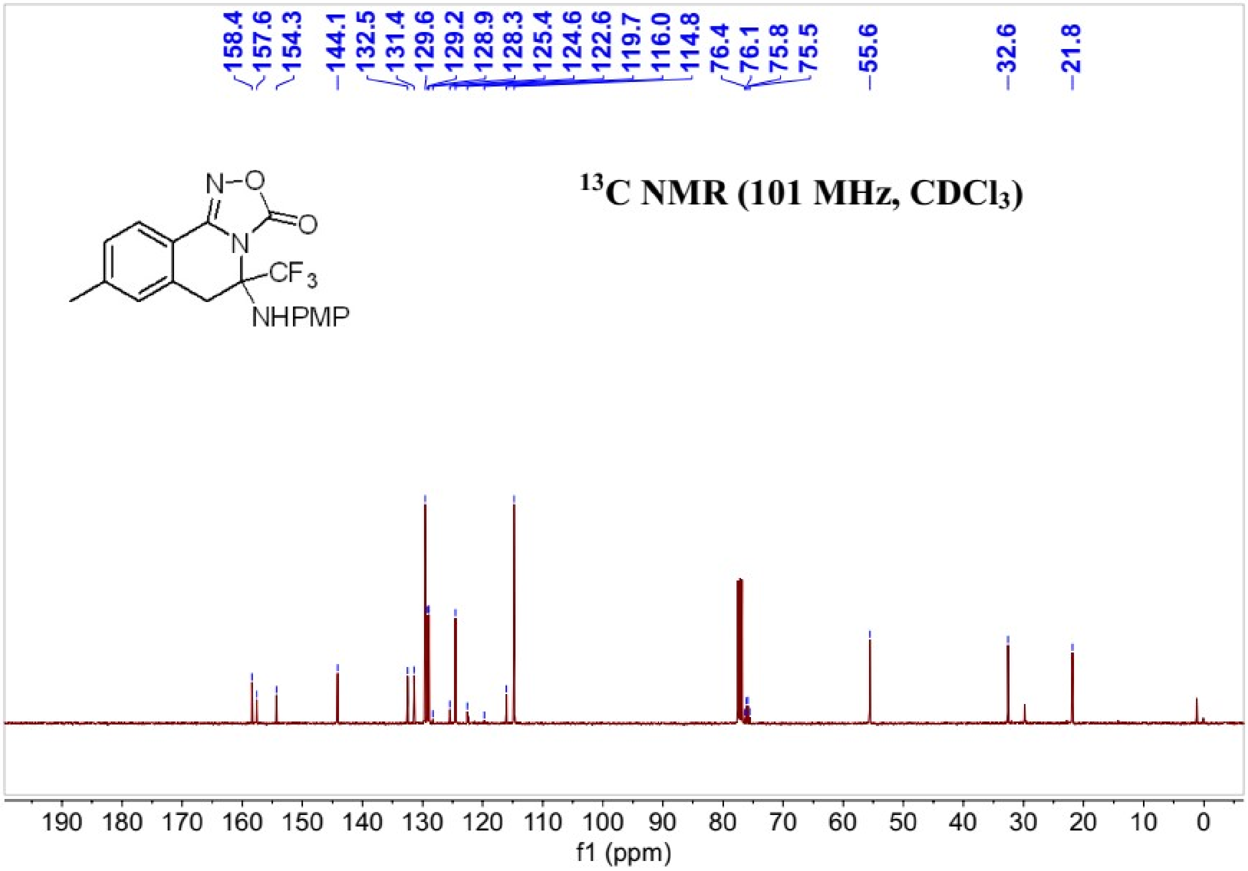

-63.25
-63.70
-65.59
-66.04
N–O
O
N
CF2Cl
NH
Ph
19F NMR (376 MHz, CDCl3)
-60.0 -61.0 -62.0 -63.0 -64.0 -65.0 -66.0 -67.0 -68.0 -69.0 -70.
f1 (ppm)

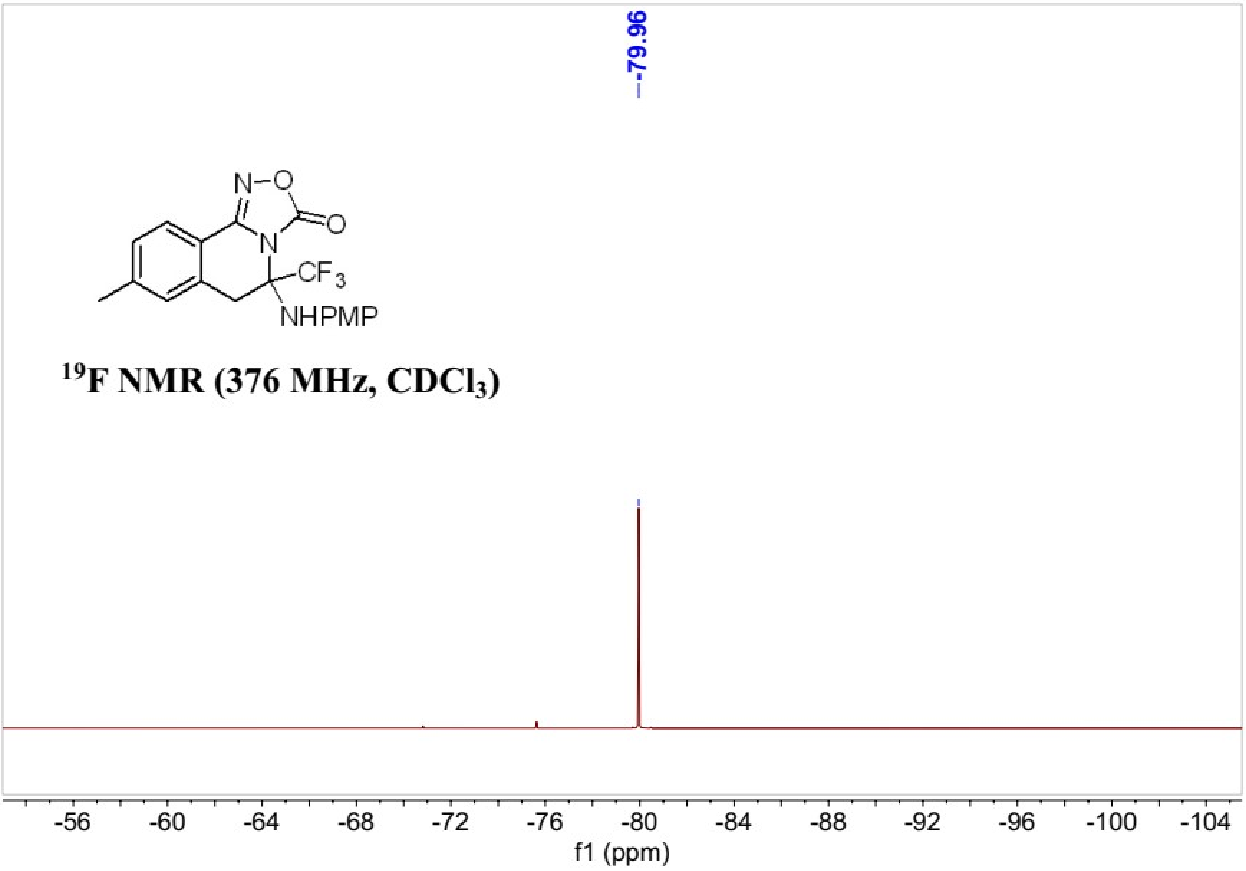

7.92 7.91 7.52 7.50 7.48 7.41 7.39 7.37 7.34 7.32 7.30 7.28 7.20 7.18 7.17 7.15 5.76
3.64 3.60 3.53 3.49
7.92 7.91 7.50 7.48 7.39 7.34 7.32 7.30 7.28 7.20 7.18 7.17 7.15
0.92 0.96 1.09 2.97 3.06
8.0 7.8 7.6 7.4 7.2 7.0
f1 (ppm)
N–O
O
N
CF2Br
NH
Ph
1H NMR (400 MHz, CDCl3)
0.92 0.96 1.09 2.97 3.00 0.85 0.97 0.98
9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)


157.3
154.3
139.4
133.2
132.6
129.7
128.3
127.6
126.5
126.0
124.6
124.5
121.3
119.2
79.7
79.5
79.2
34.0
N
O
O
N
CF2Br
NH
Ph
13C NMR (101 MHz, CDCl3)
230
210
190
170
150
130
110
90
70
50
30
10
-10
-30
f1 (ppm)

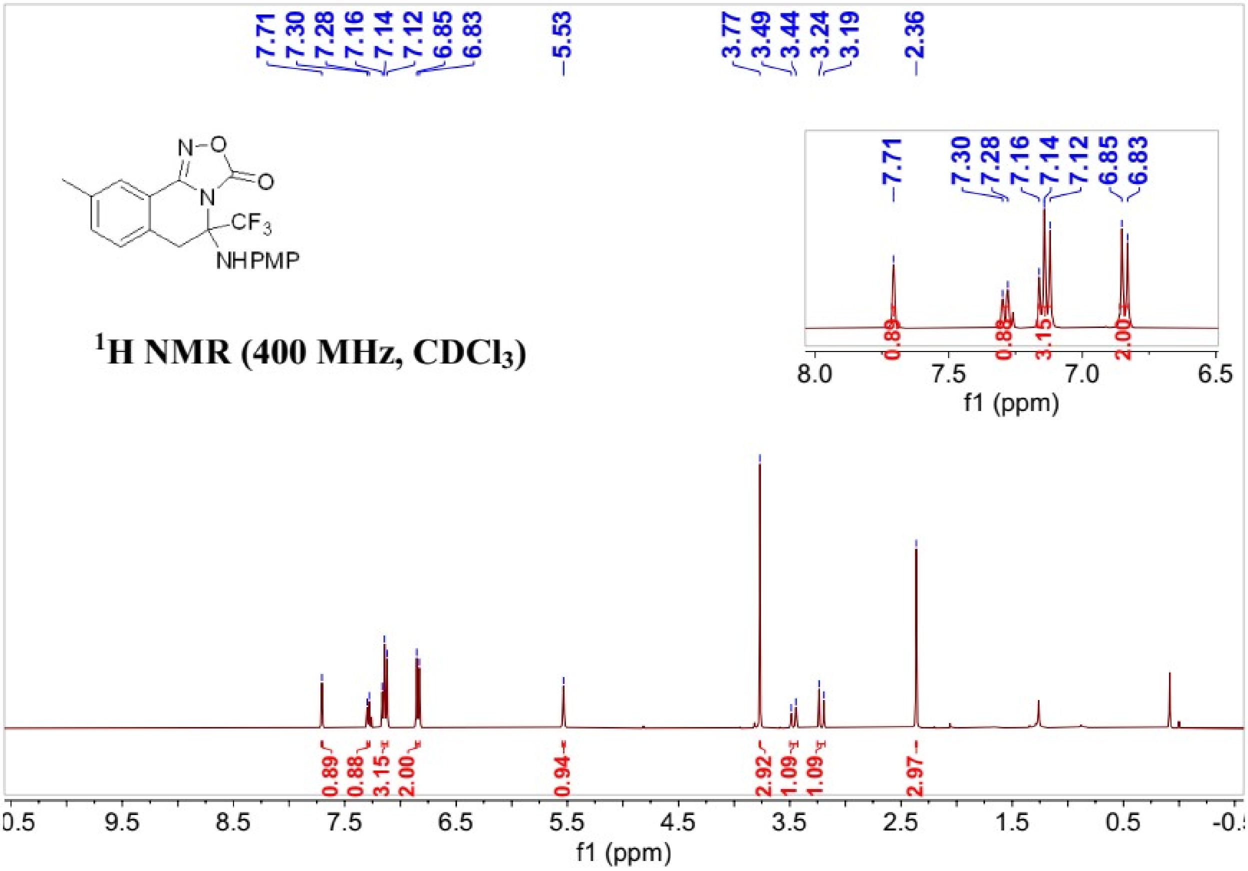

-56.66
-57.11
-59.84
-60.28
N
O
O
N
CF2Br
NH
Ph
19F NMR (376 MHz, CDCl3)
1.5
-52.5
-53.5
-54.5
-55.5
-56.5
-57.5
-58.5
-59.5
-60.5
-61.5
-62.5
-63.5
-64.5
-65.5
-66.
f1 (ppm)


7.78
7.76
7.19
7.17
7.14
7.12
7.08
6.85
6.83
5.54
3.77
3.50
3.45
3.22
3.17
2.38
N–O
O
N
CF3
NHPMP
^{1}H NMR (400 MHz, CDCl$_3$)
1.04
1.17
2.00
1.00
2.15
1.09
3.00
1.06
0.96
2.93
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

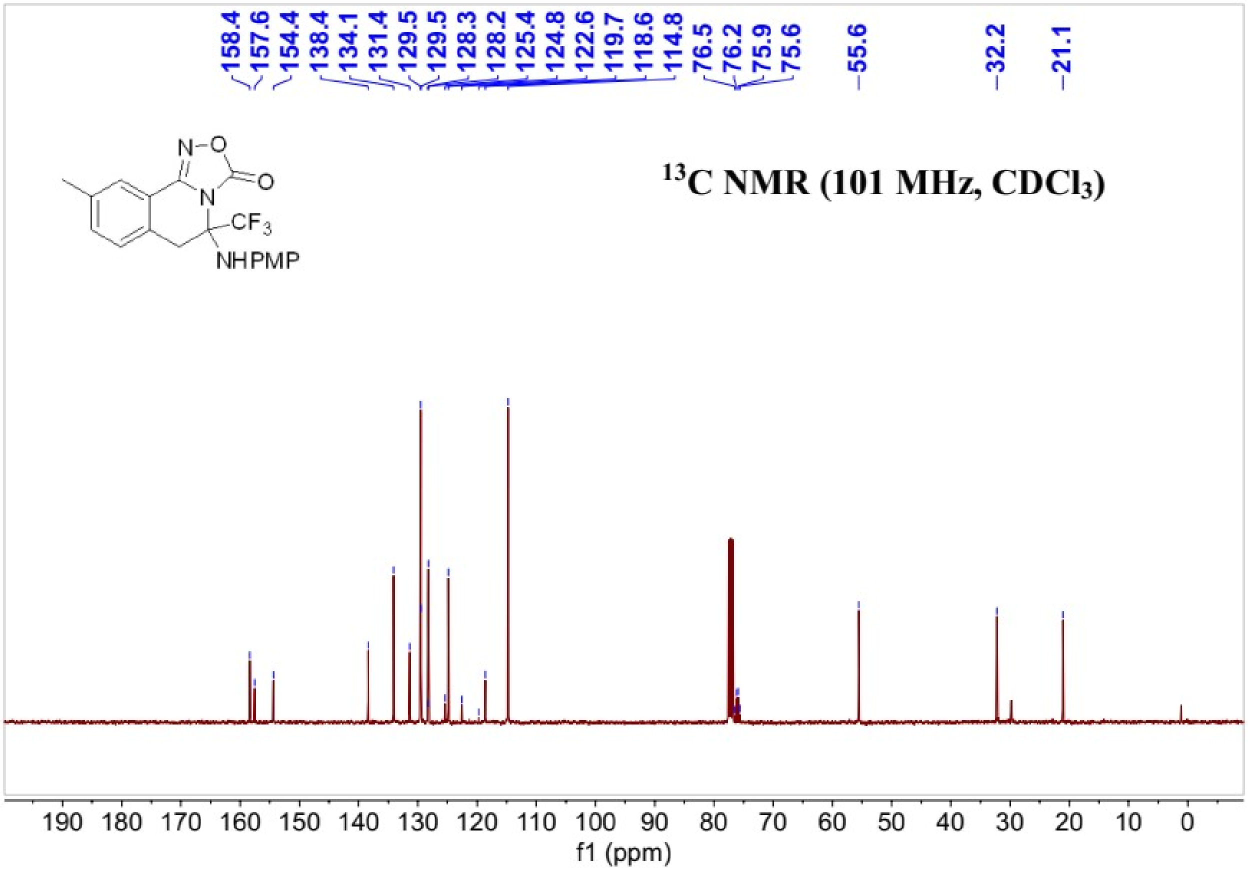

158.4
157.6
154.3
144.1
132.5
131.4
129.6
129.2
128.9
128.3
125.4
124.6
122.6
119.7
116.0
114.8
76.4
76.1
75.8
75.5
55.6
32.6
21.8
N–O
O
N
CF3
NHPMP
^{13}C NMR (101 MHz, CDCl$_3$)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



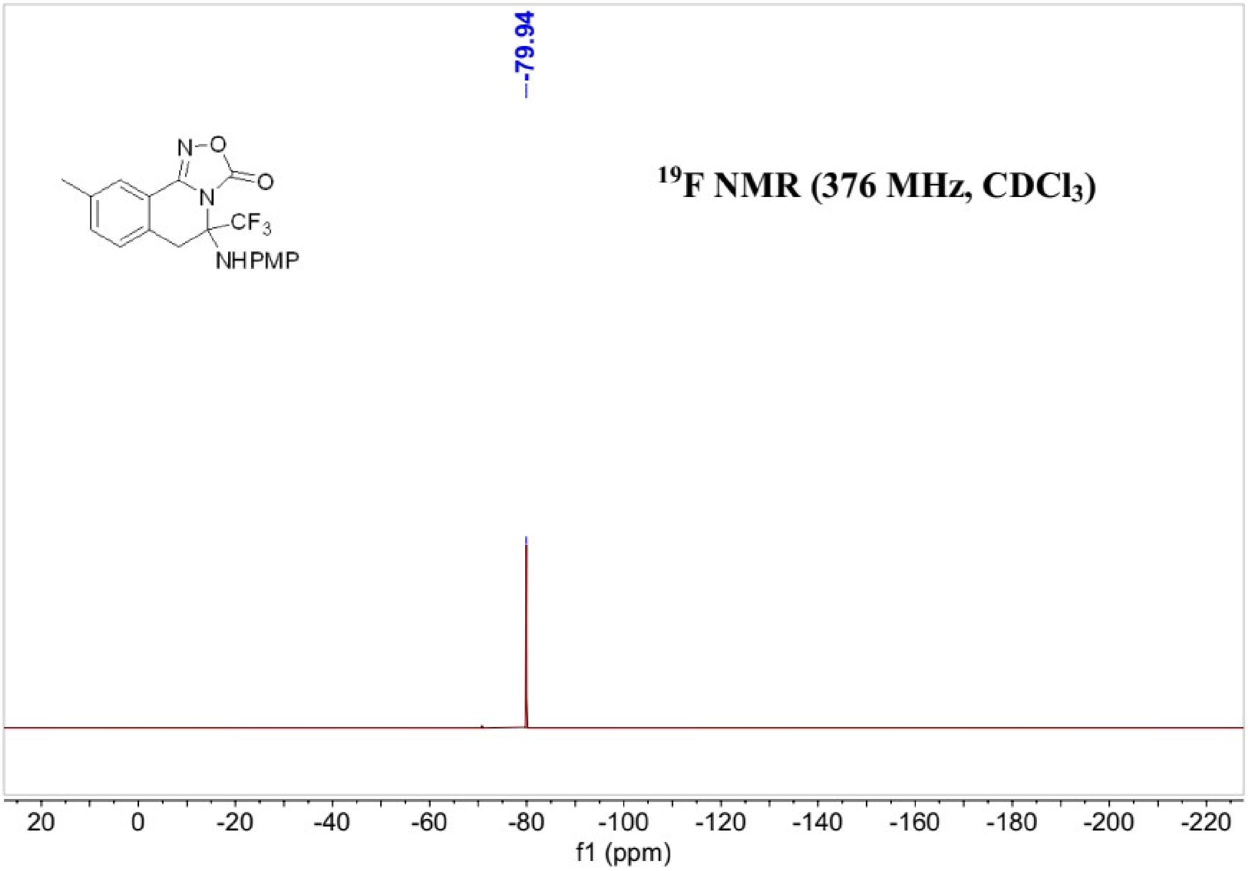
^{19}F NMR (376 MHz, CDCl$_3$)



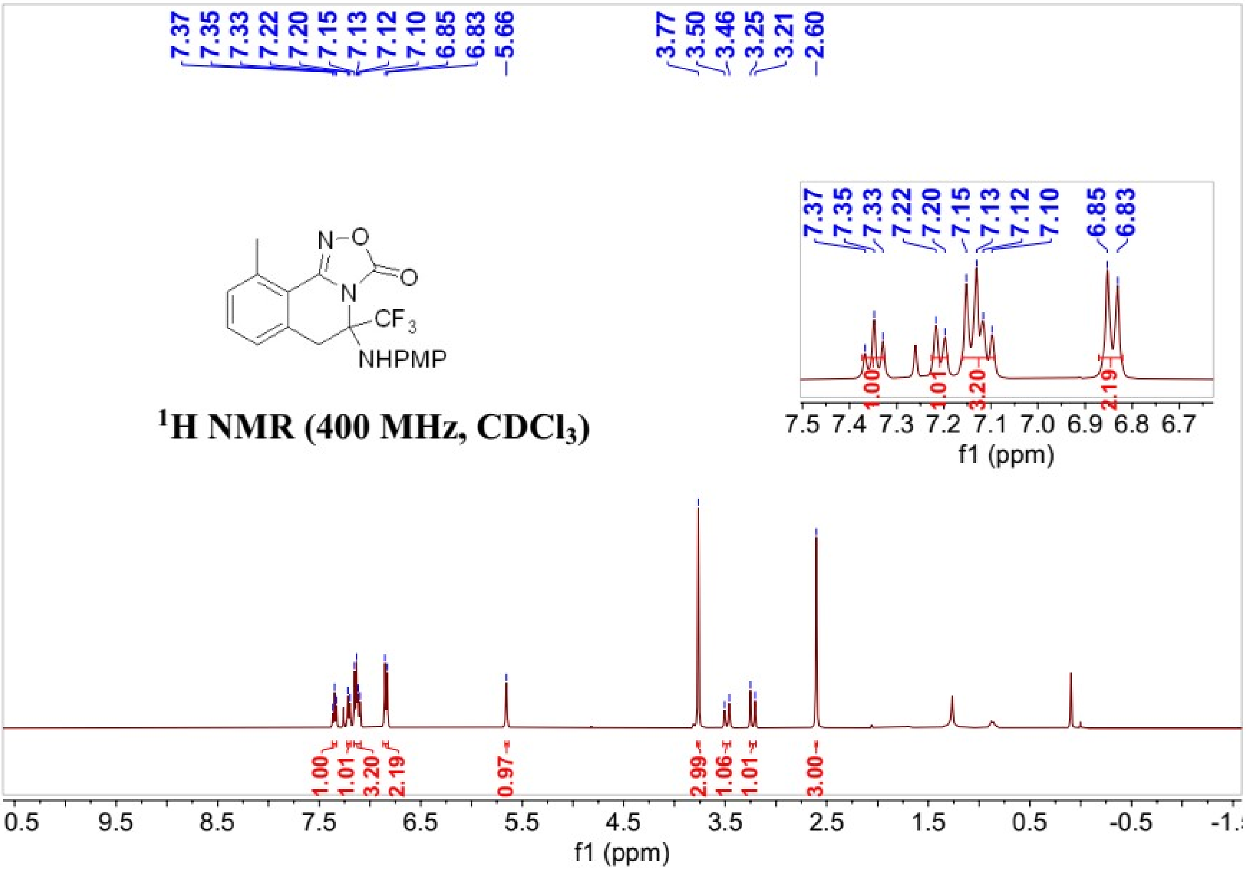
^{1}H NMR (400 MHz, CDCl$_3$)

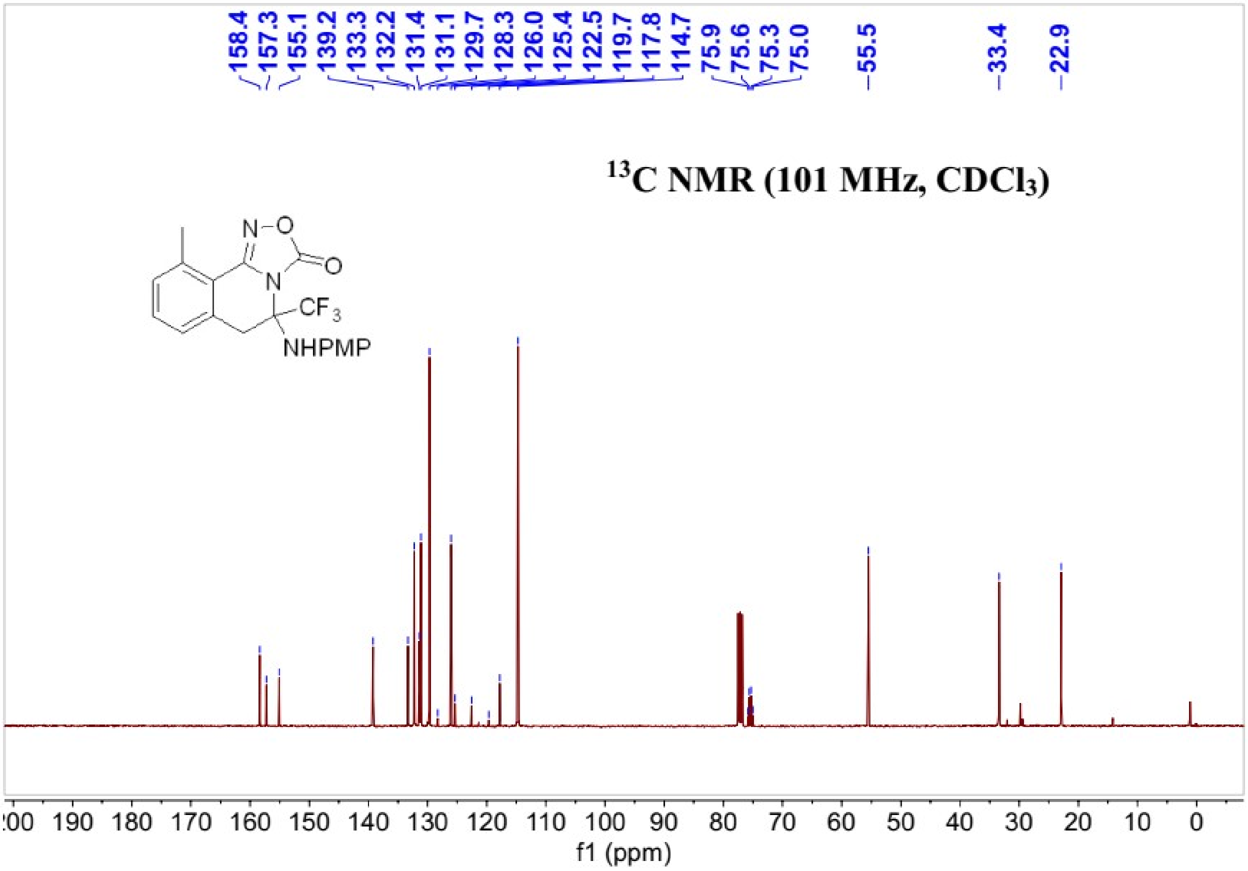


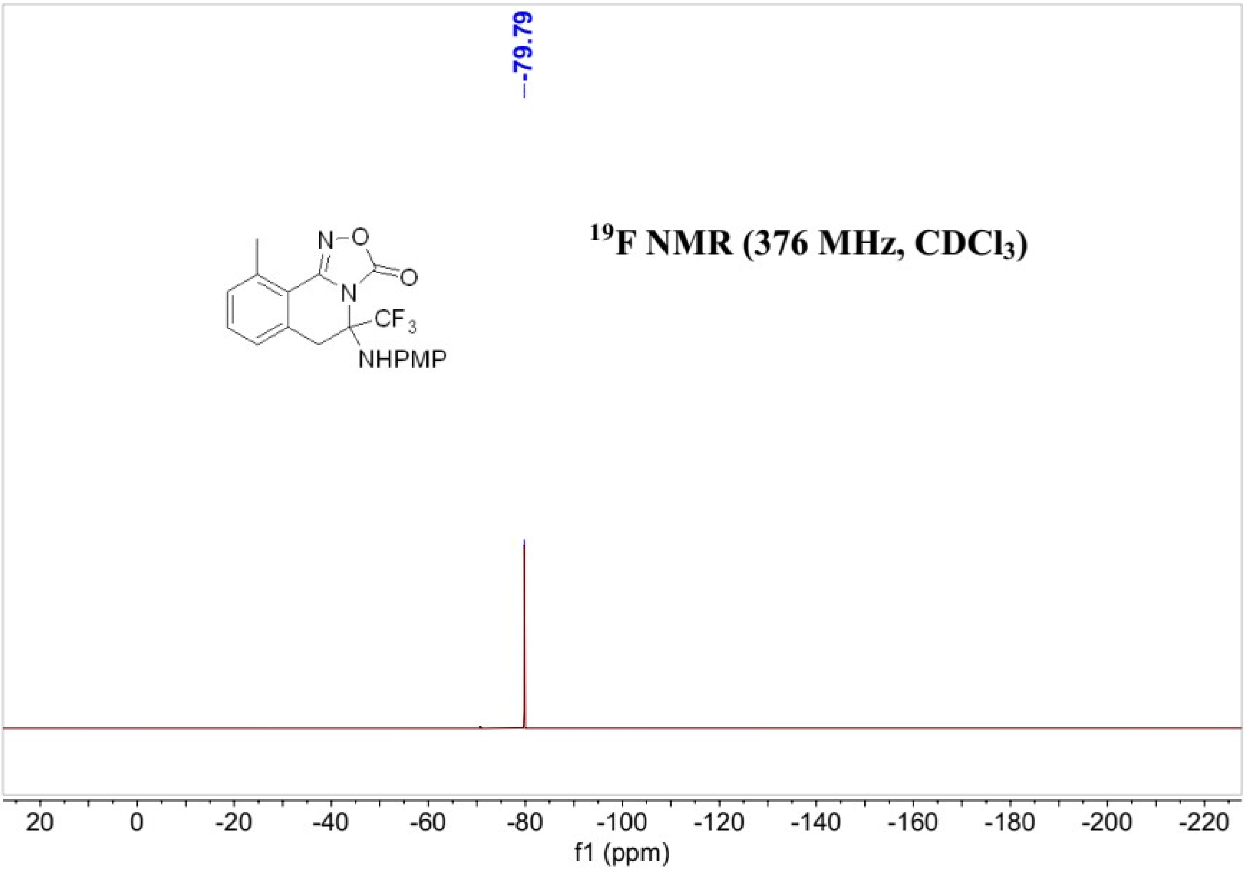
^{13}C NMR (101 MHz, CDCl$_3$)

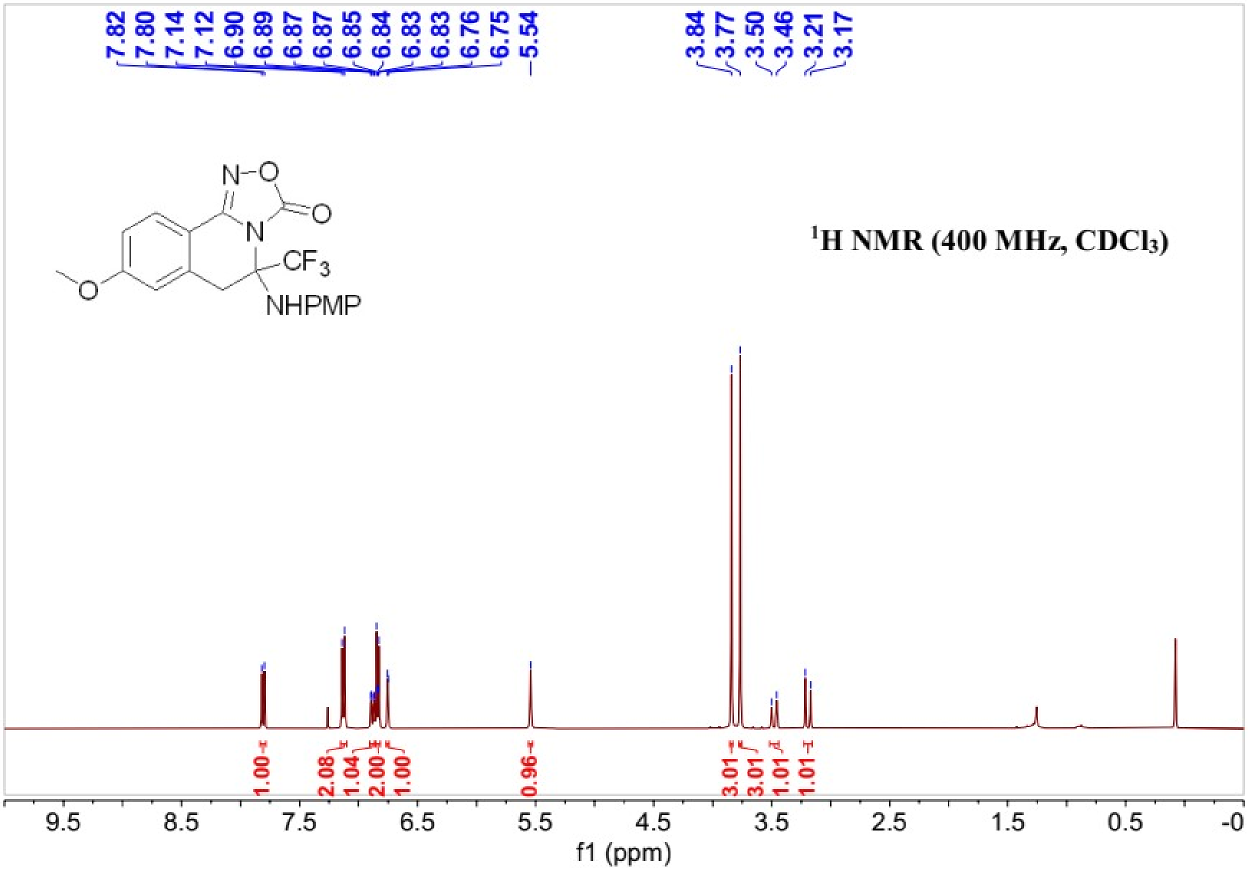


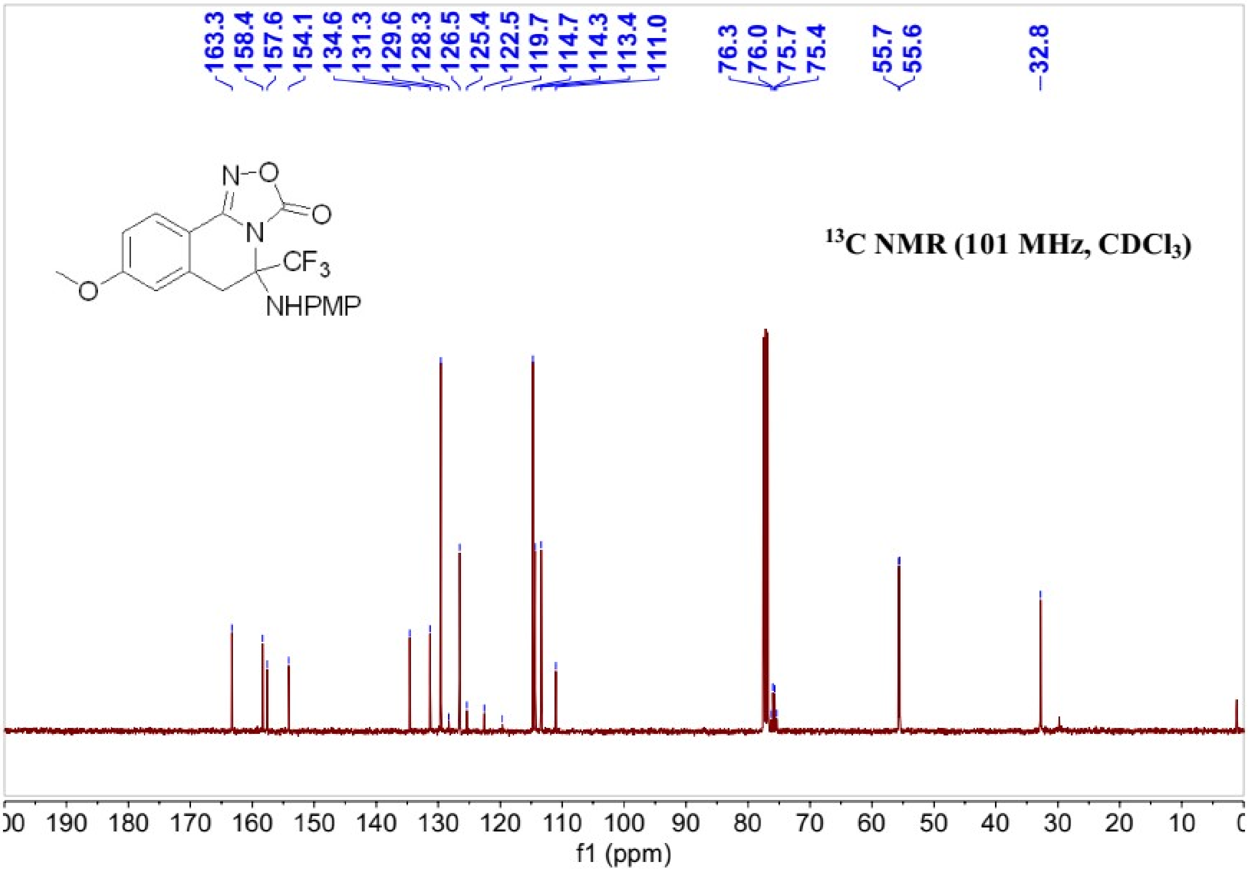
^{19}F NMR (376 MHz, CDCl$_3$)

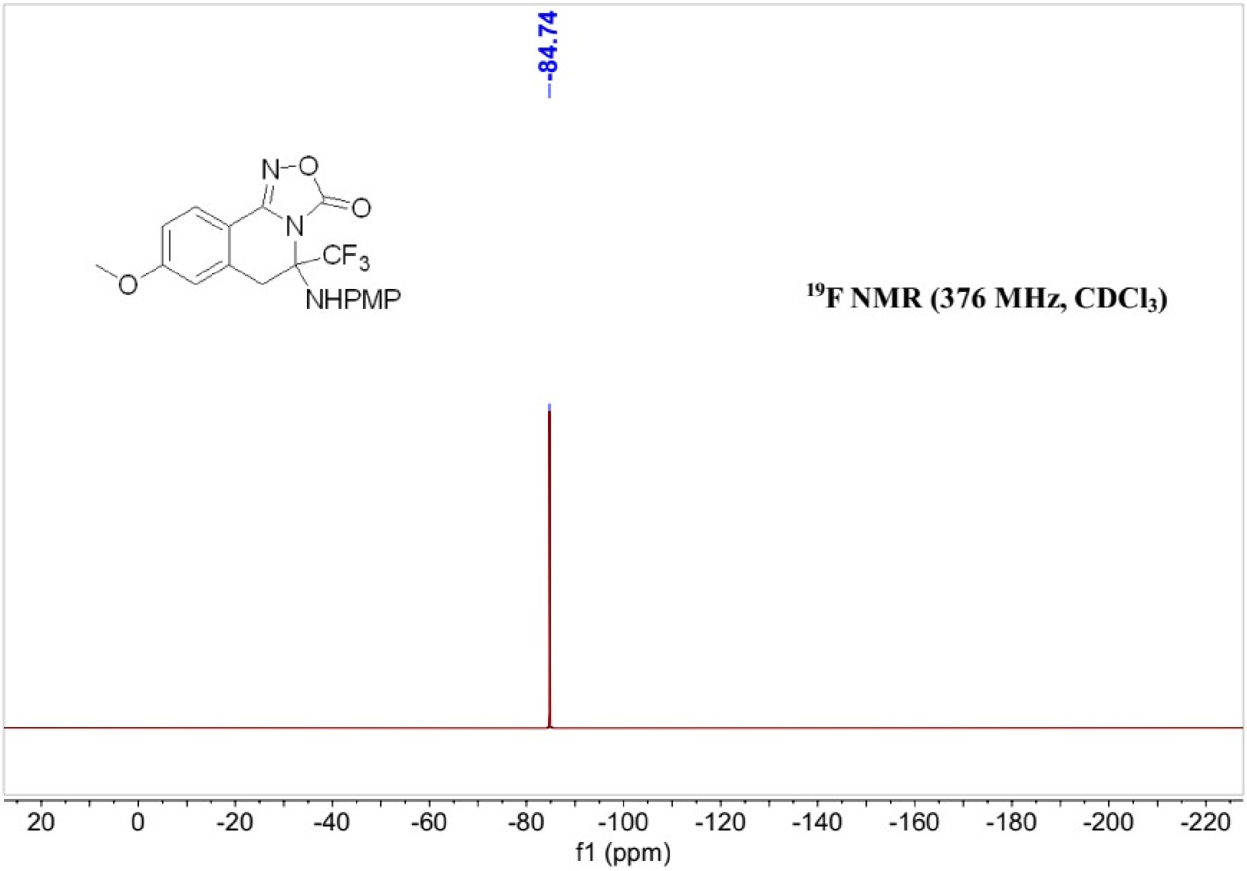

7.37 7.35 7.33 7.22 7.20 7.15 7.13 7.12 7.10 6.85 6.83 5.66
3.77 3.50 3.46 3.25 3.21 2.60
N–O
O
N
CF3
NHPMP
1H NMR (400 MHz, CDCl3)
1.00 1.01 3.20 2.19
7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
1.00 1.01 3.20 2.19 0.97 2.99 1.06 1.01 3.00
0.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5 -1.
f1 (ppm)

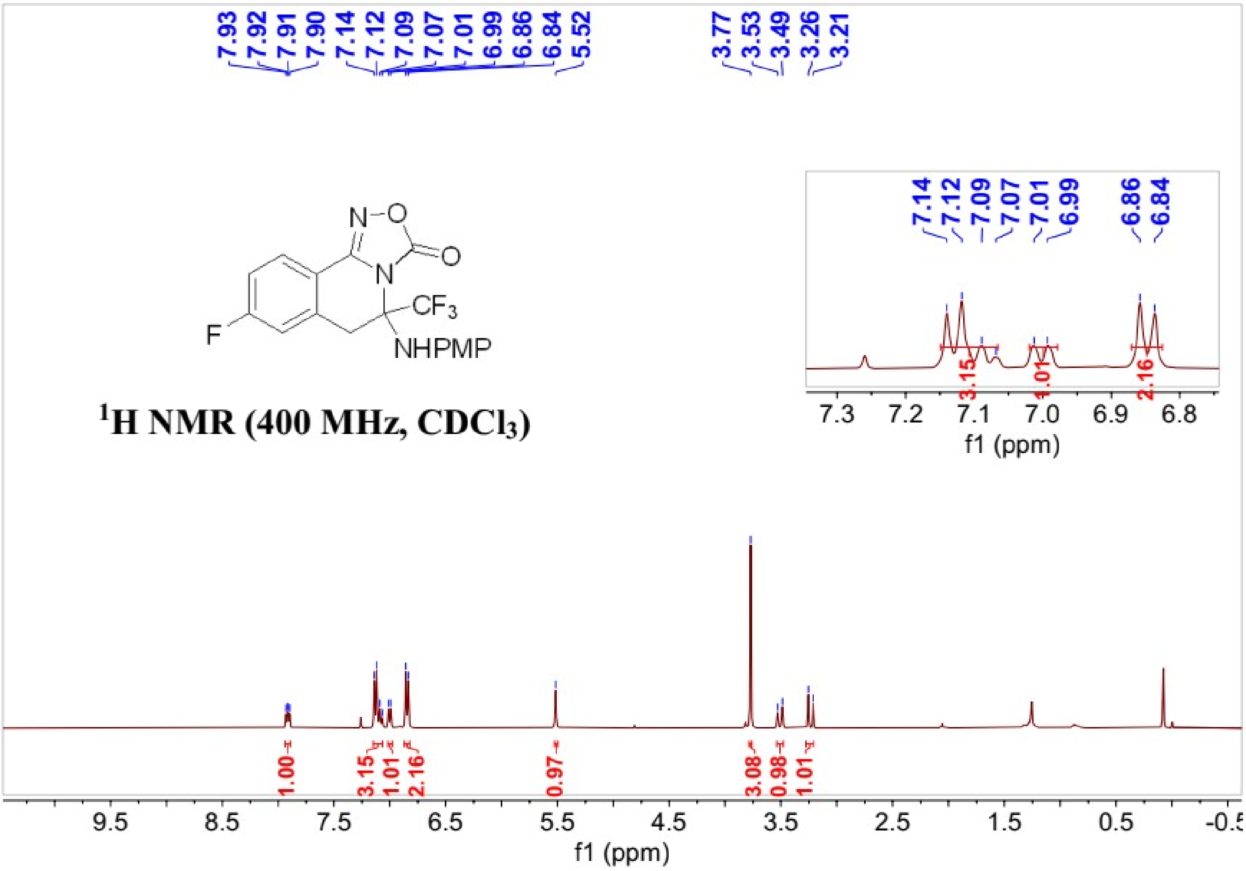

158.4 157.3 155.1 139.2 133.3 132.2 131.4 131.1 129.7 128.3 126.0 125.4 122.5 119.7 117.8 114.7 75.9 75.6 75.3 75.0 55.5 33.4 22.9
13C NMR (101 MHz, CDCl3)
N–O
O
N
CF3
NHPMP
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

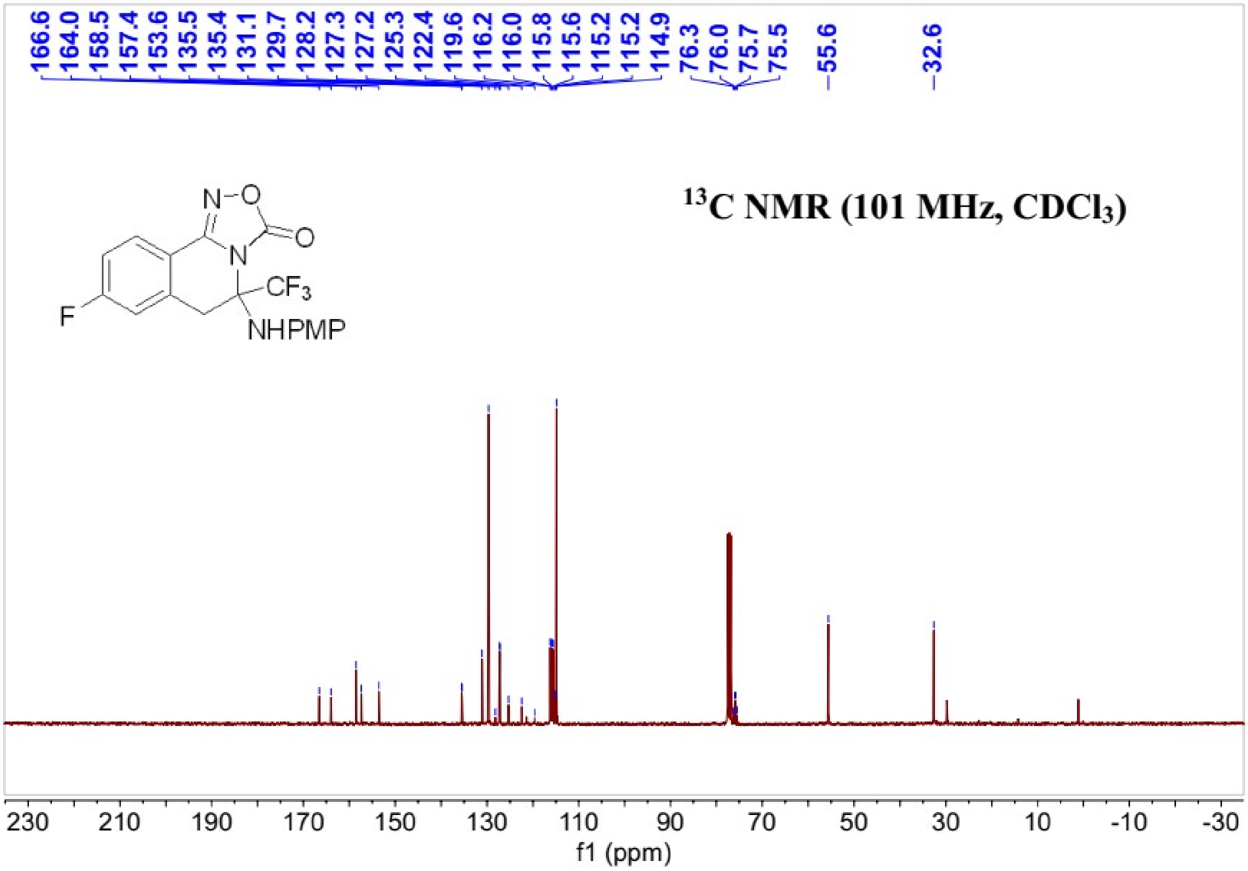

--79.79
^{19}F NMR (376 MHz, CDCl$_3$)
N–O
O
N
CF$_3$
NHPMP
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

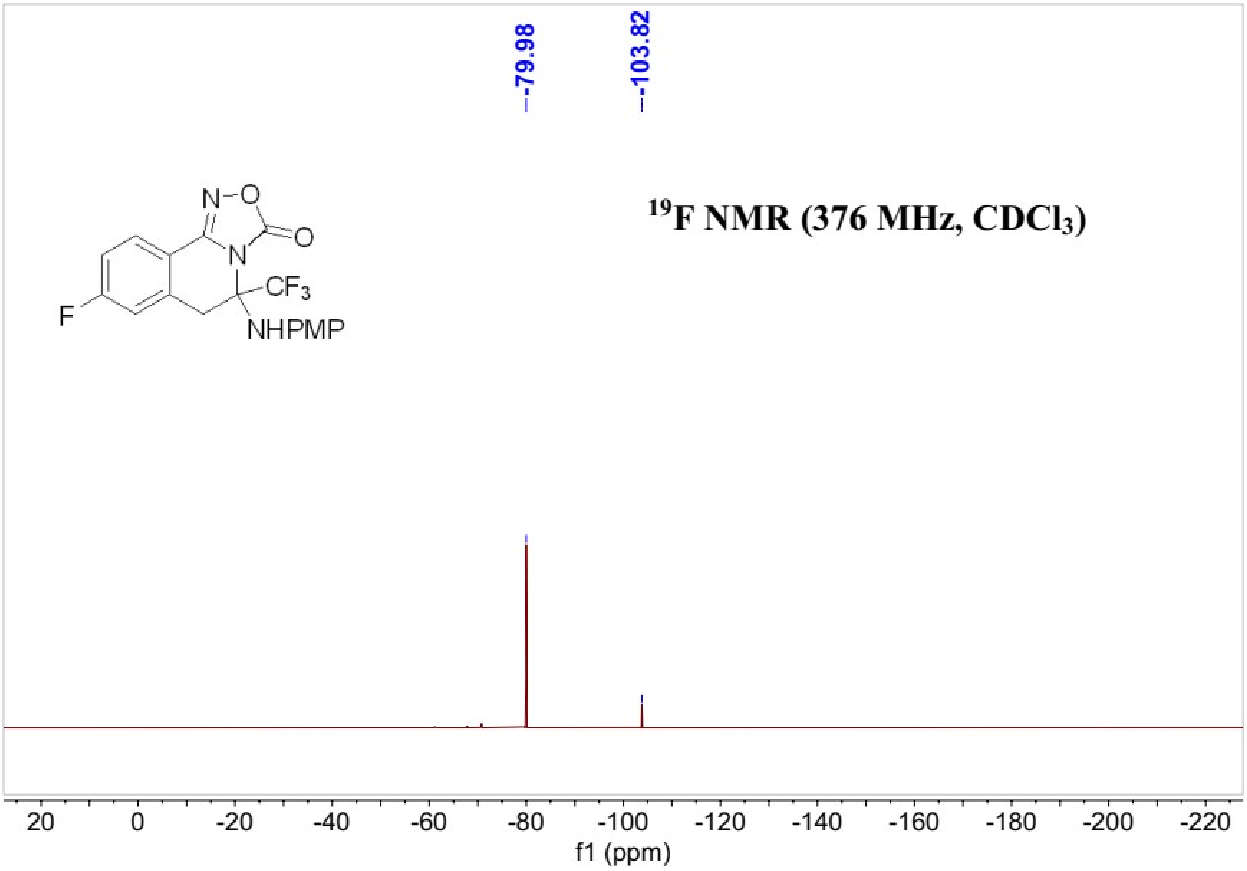

7.82
7.80
7.14
7.12
6.90
6.89
6.87
6.87
6.85
6.84
6.84
6.83
6.83
6.76
6.75
5.54
3.84
3.77
3.50
3.46
3.21
3.17
N–O
O
N
CF$_3$
NHPMP
O
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
2.08
1.04
2.00
1.00
0.96
3.01
3.01
1.01
1.01
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0
f1 (ppm)


163.3
158.4
157.6
154.1
134.6
131.3
129.6
128.3
126.5
125.4
122.5
119.7
114.7
114.3
113.4
111.0
76.3
76.0
75.7
75.4
55.7
55.6
32.8
N
O
O
N
CF3
O
NHPMP
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

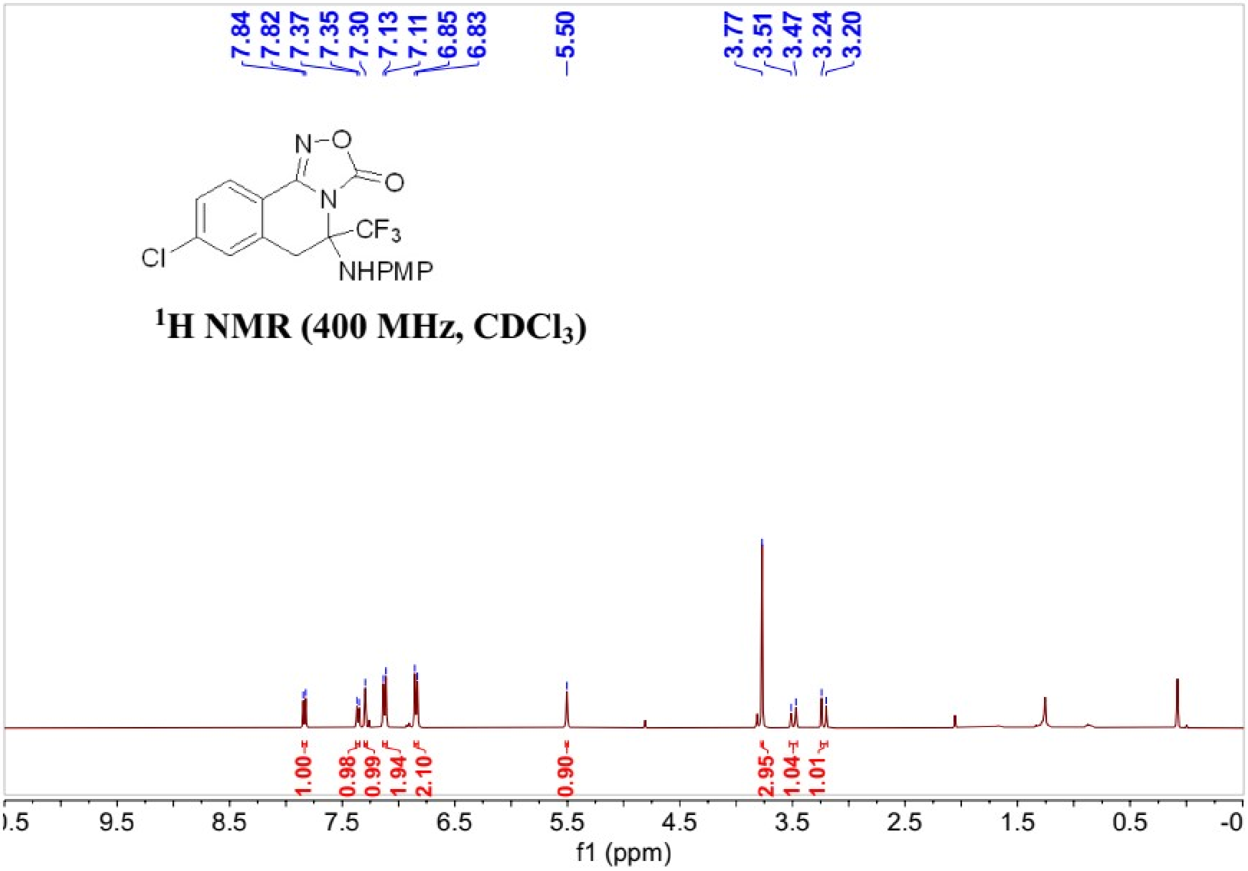

-84.74
N
O
O
N
CF3
O
NHPMP
19F NMR (376 MHz, CDCl3)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)


7.93
7.92
7.91
7.90
7.14
7.12
7.09
7.07
7.01
6.99
6.86
6.84
5.52
3.77
3.53
3.49
3.26
3.21
N
O
O
N
CF$_3$
F
NHPMP
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
3.15
1.01
2.16
0.97
3.08
0.98
1.01
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)

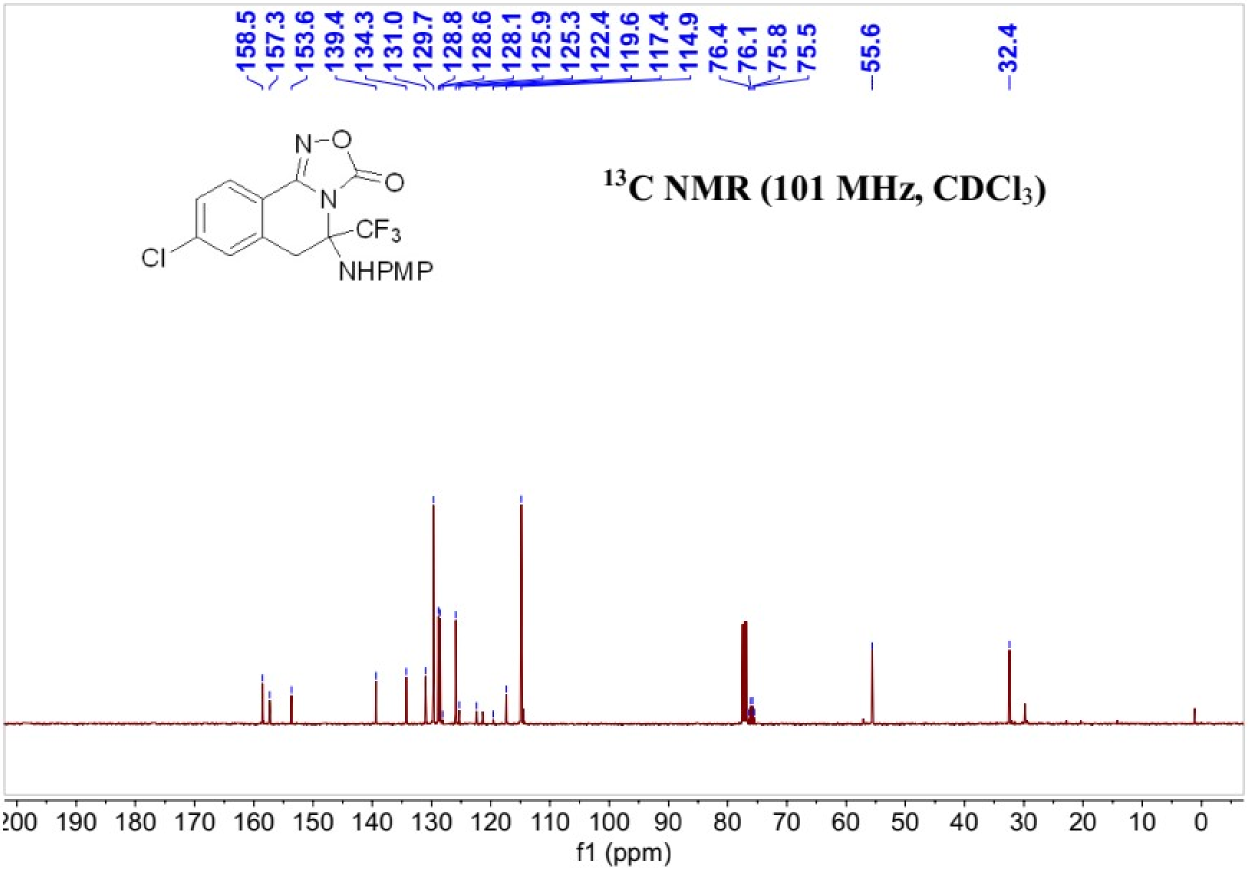

166.6
164.0
158.5
157.4
153.6
135.5
135.4
131.1
129.7
128.2
127.3
127.2
125.3
122.4
119.6
116.2
116.0
115.8
115.6
115.2
115.2
114.9
76.3
76.0
75.7
75.5
55.6
32.6
^{13}C NMR (101 MHz, CDCl$_3$)
N
O
O
N
CF$_3$
F
NHPMP
230
210
190
170
150
130
110
90
70
50
30
10
-10
-30
f1 (ppm)

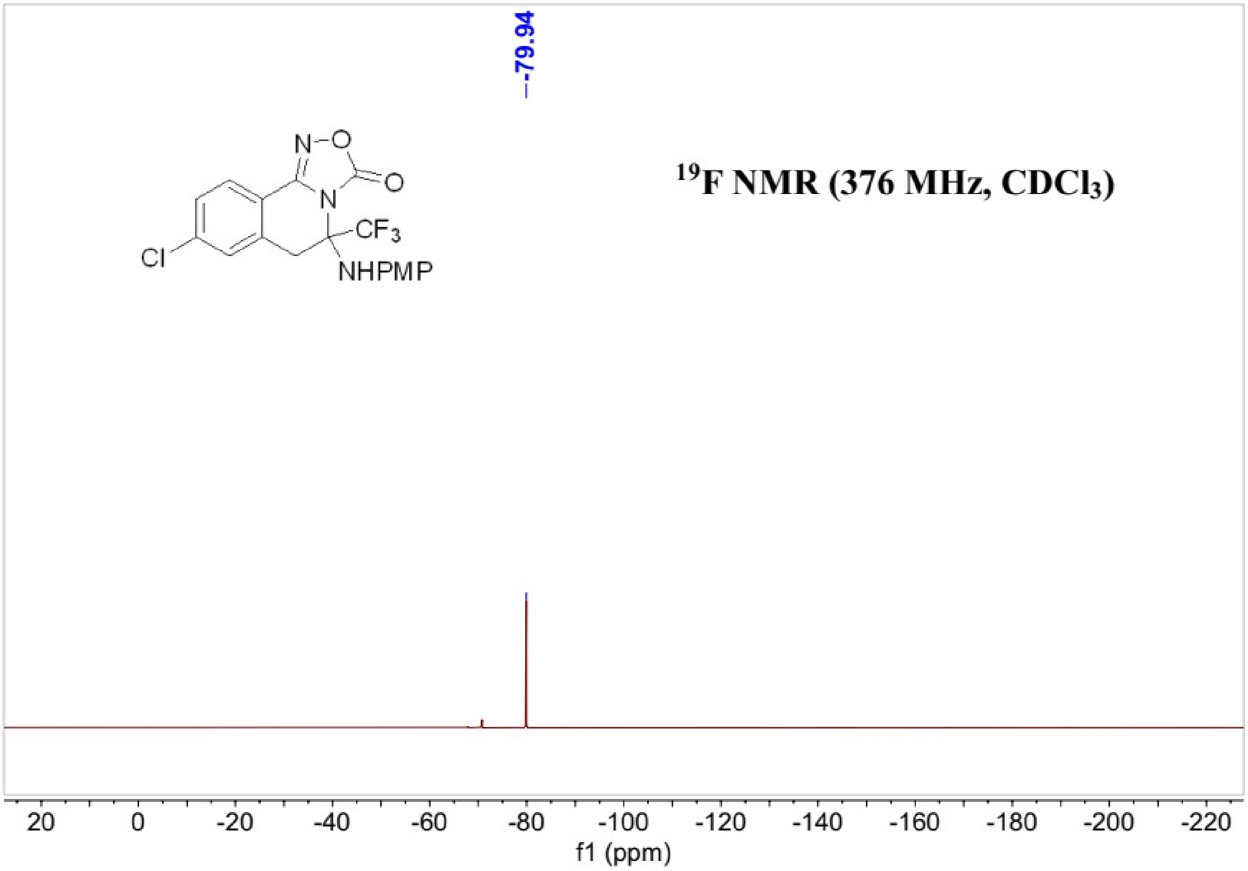


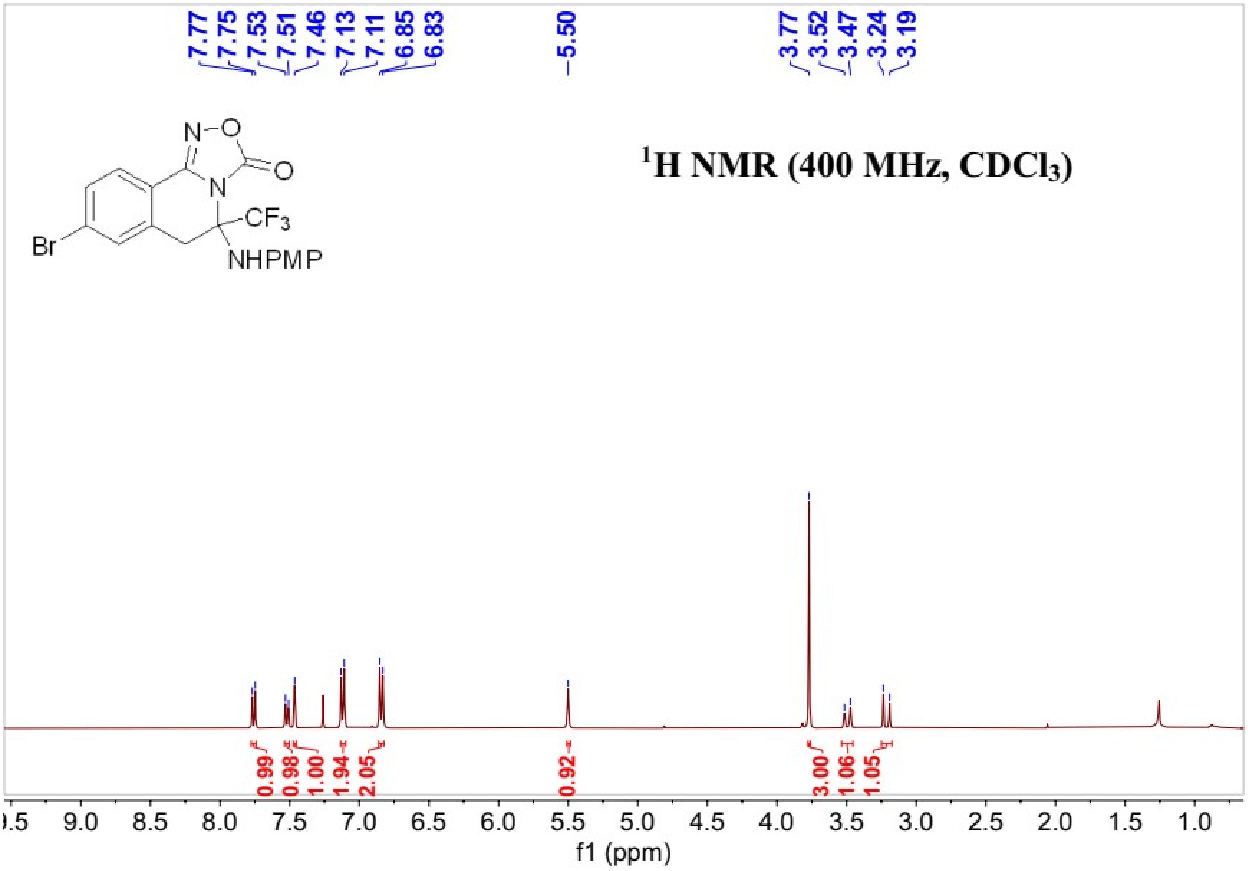
-79.98
-103.82
19F NMR (376 MHz, CDCl3)
N-O
O
N
CF3
F
NHPMP
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

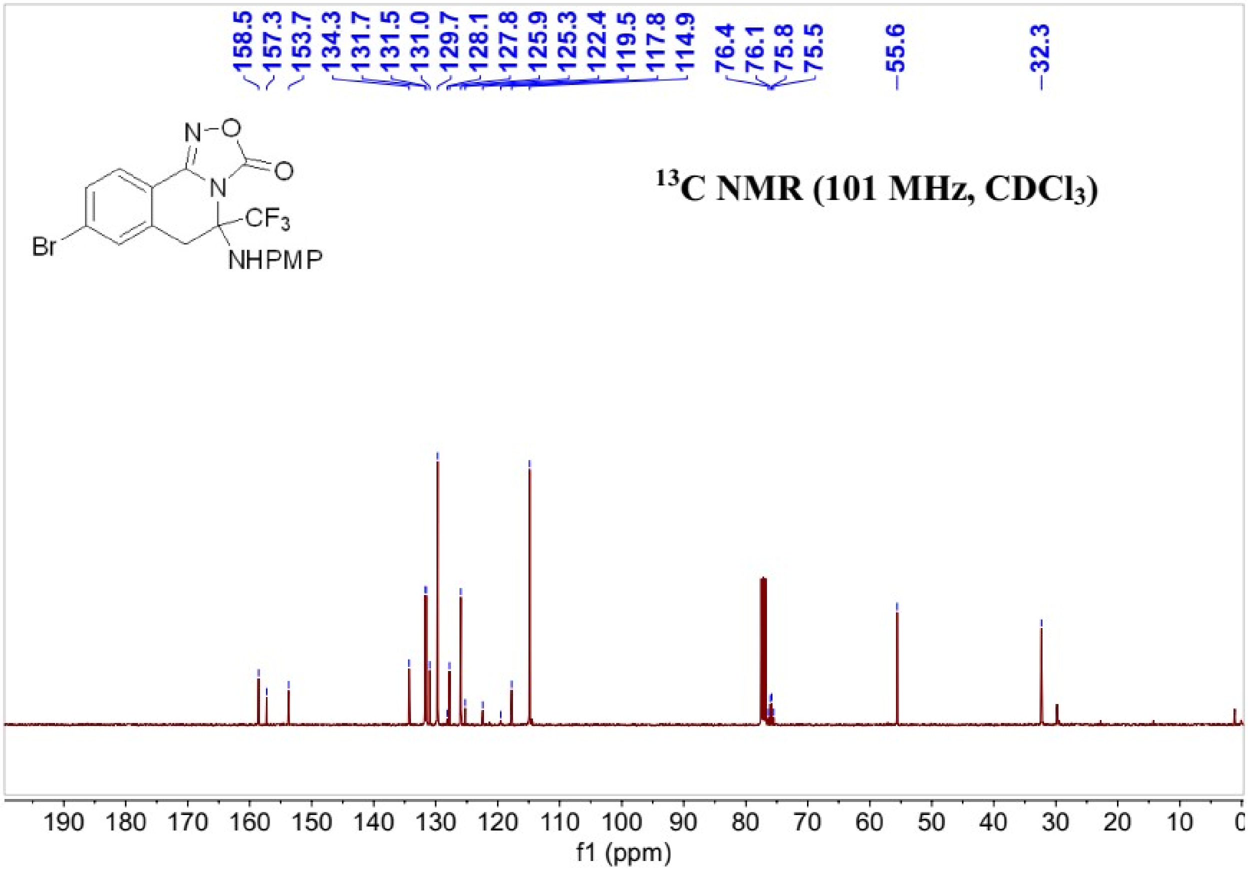


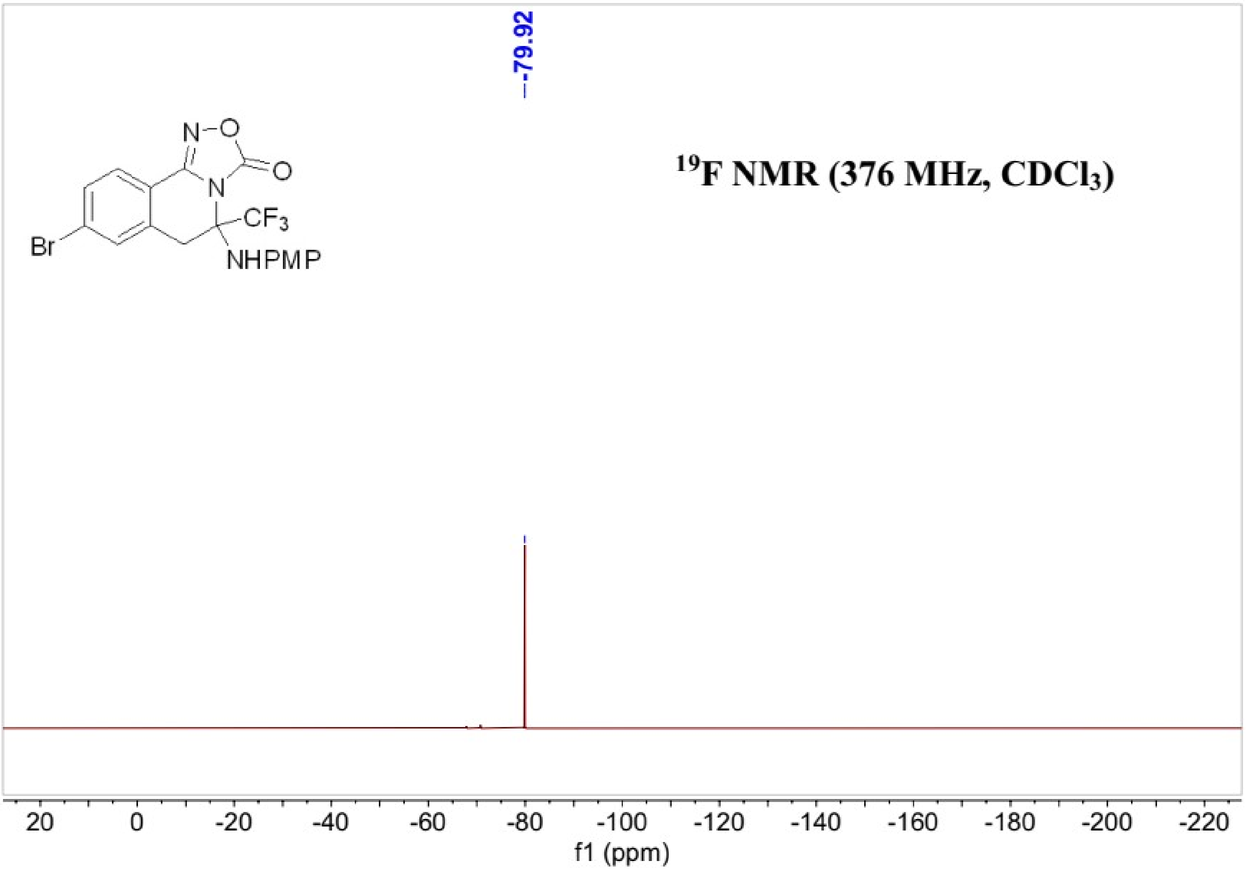
7.84
7.82
7.37
7.35
7.30
7.13
7.11
6.85
6.83
5.50
3.77
3.51
3.47
3.24
3.20
N-O
O
N
CF3
Cl
NHPMP
1H NMR (400 MHz, CDCl3)
1.00
0.98
0.99
1.94
2.10
0.90
2.95
1.04
1.01
).5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0
f1 (ppm)

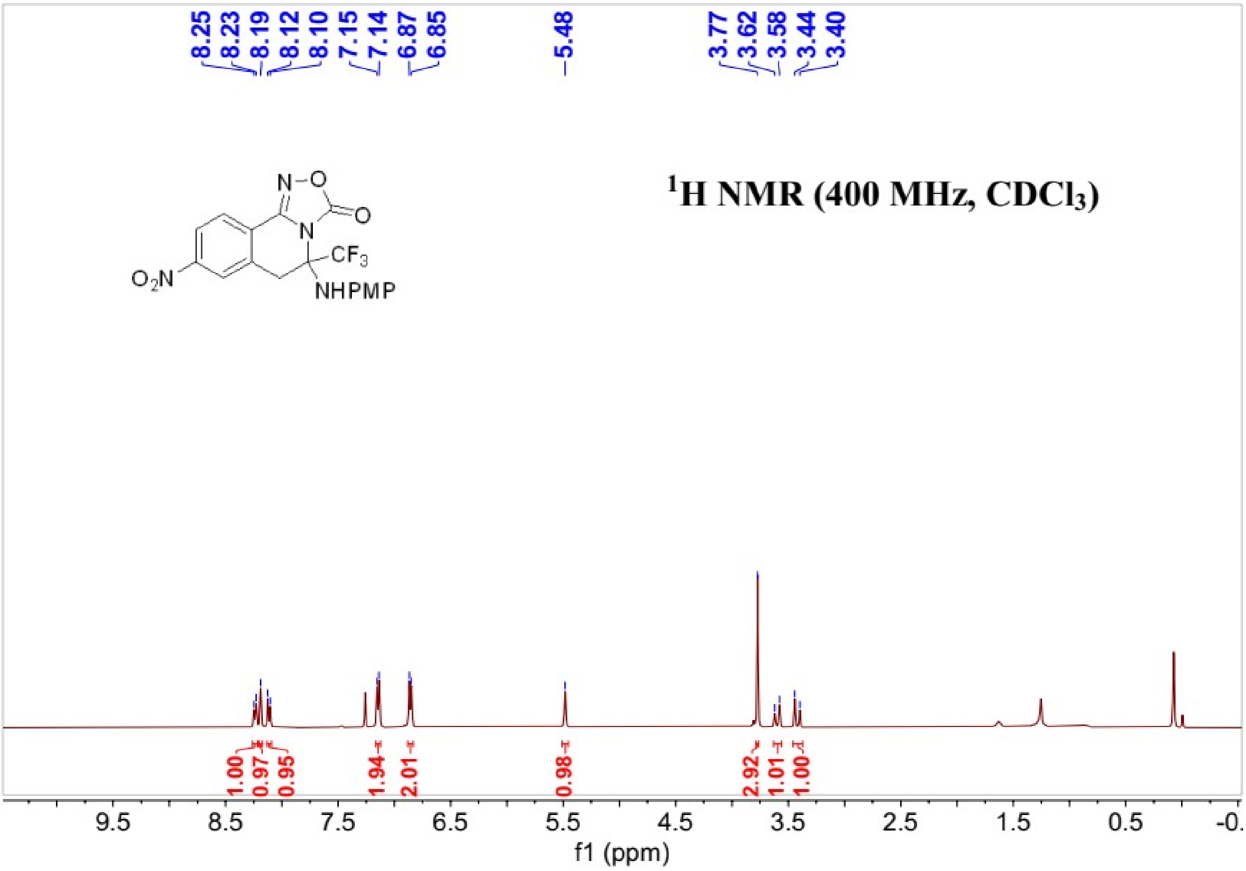

158.5
157.3
153.6
139.4
134.3
131.0
129.7
128.8
128.6
128.1
125.9
125.3
122.4
119.6
117.4
114.9
76.4
76.1
75.8
75.5
55.6
32.4
N
O
N
O
CF$_3$
Cl
NHPMP
^{13}C NMR (101 MHz, CDCl$_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

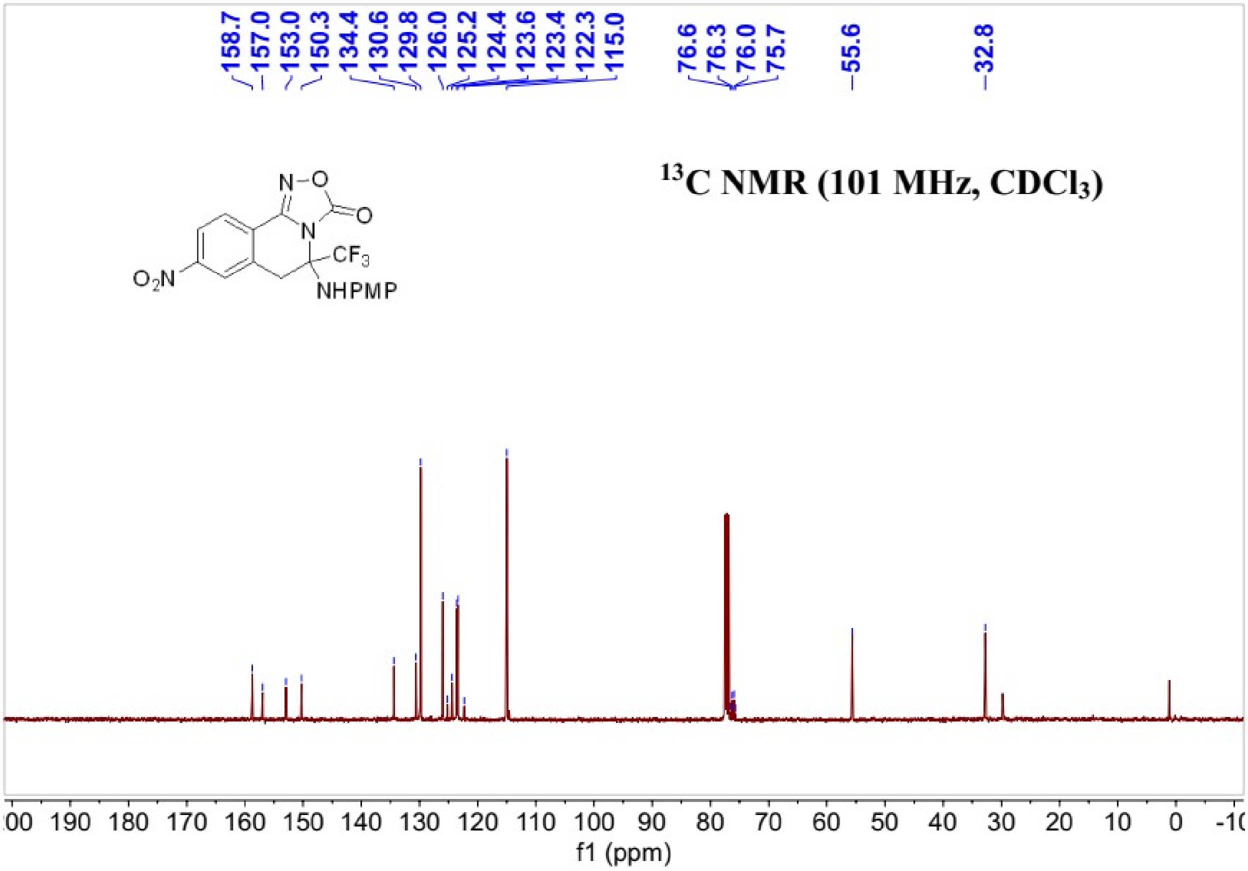

-79.94
N
O
N
O
CF$_3$
Cl
NHPMP
^{19}F NMR (376 MHz, CDCl$_3$)
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

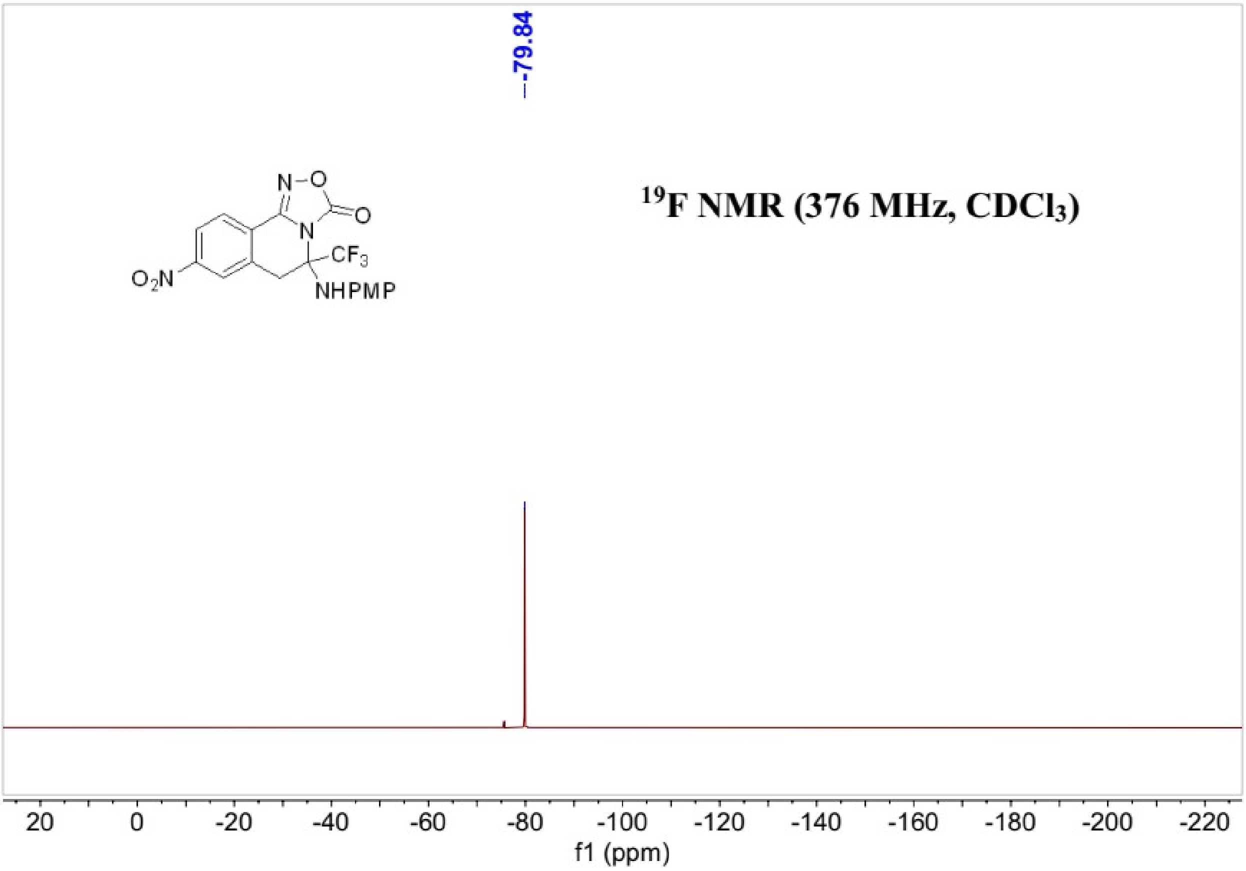

7.77
7.75
7.53
7.51
7.46
7.13
7.11
6.85
6.83
5.50
3.77
3.52
3.47
3.24
3.19
N
O
O
N
CF3
Br
NHPMP
^{1}H NMR (400 MHz, CDCl$_3$)
0.99
0.98
1.00
1.94
2.05
0.92
3.00
1.06
1.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

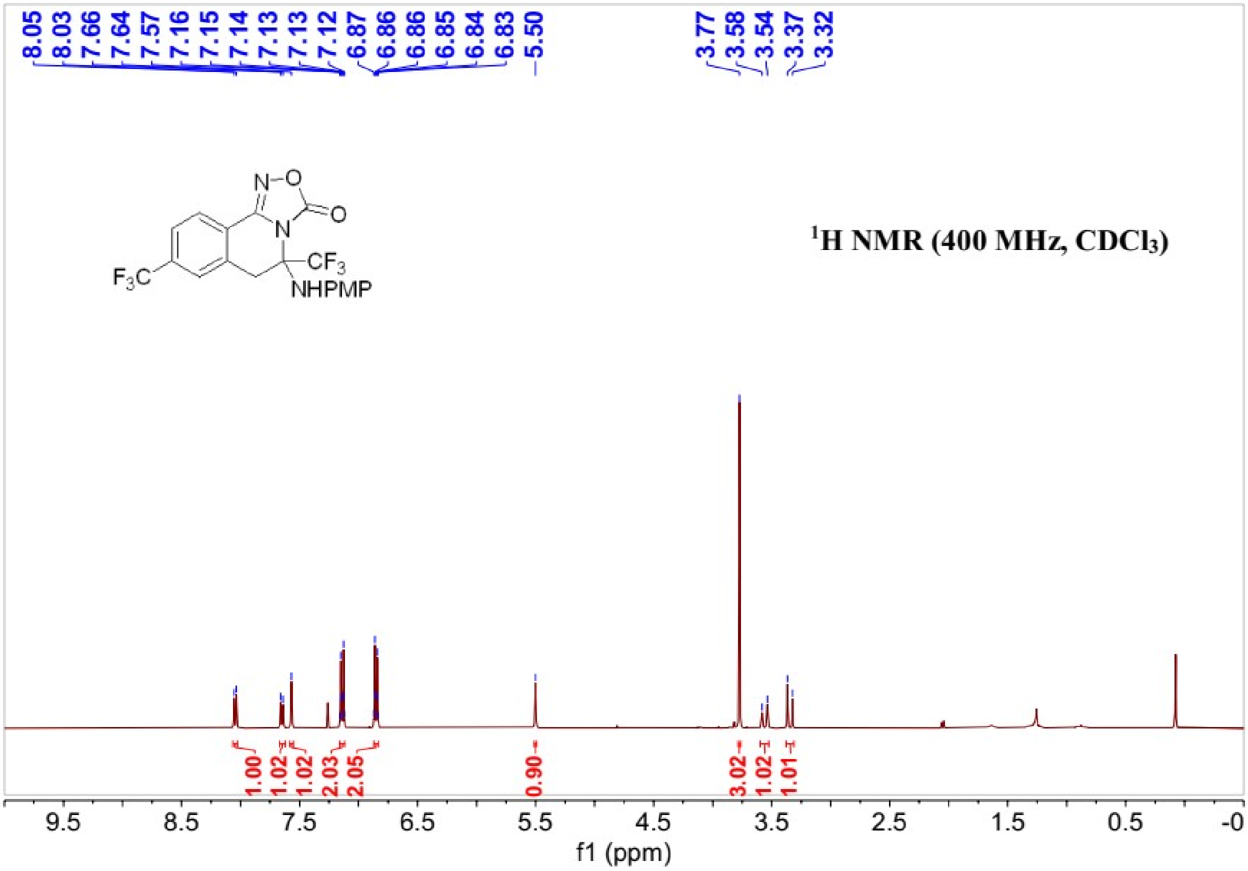

158.5
157.3
153.7
134.3
131.7
131.5
131.0
129.7
128.1
127.8
125.9
125.3
122.4
119.5
117.8
114.9
76.4
76.1
75.8
75.5
55.6
32.3
N
O
O
N
CF3
Br
NHPMP
^{13}C NMR (101 MHz, CDCl$_3$)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

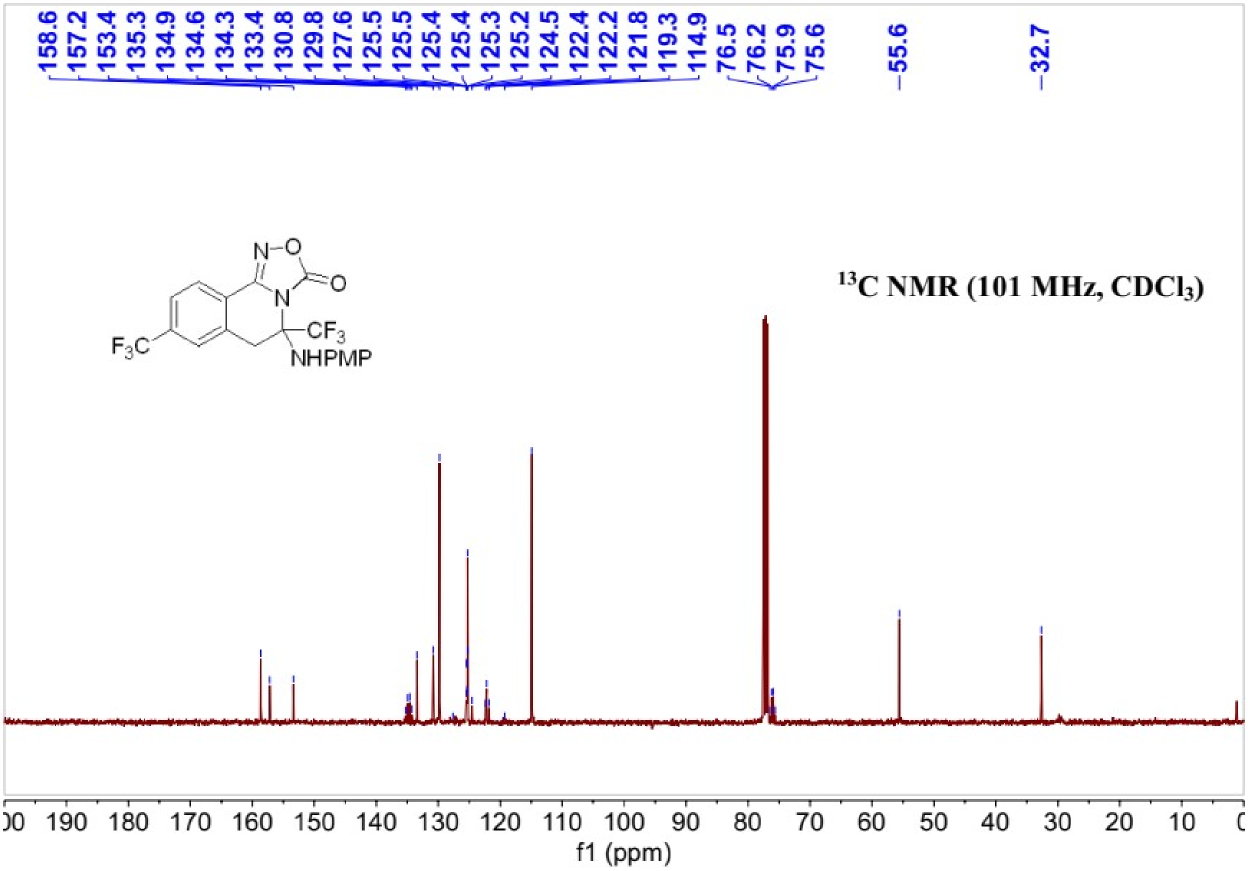

-79.92
N–O
O
N
CF3
Br
NHPMP
^{19}F NMR (376 MHz, CDCl$_3$)
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

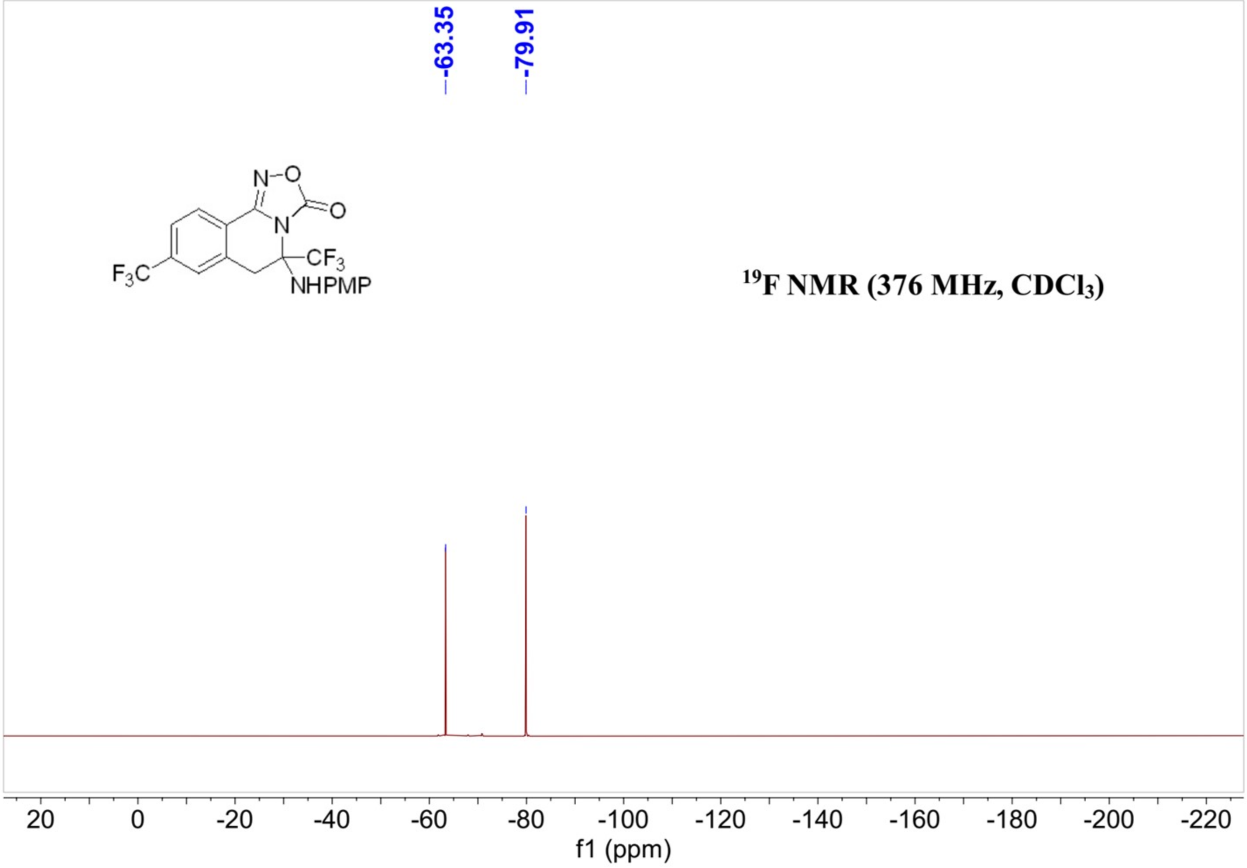

8.25
8.23
8.19
8.12
8.10
7.15
7.14
6.87
6.85
5.48
3.77
3.62
3.58
3.44
3.40
N–O
O
N
CF3
O2N
NHPMP
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
0.97
0.95
1.94
2.01
0.98
2.92
1.01
1.00
9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.
f1 (ppm)

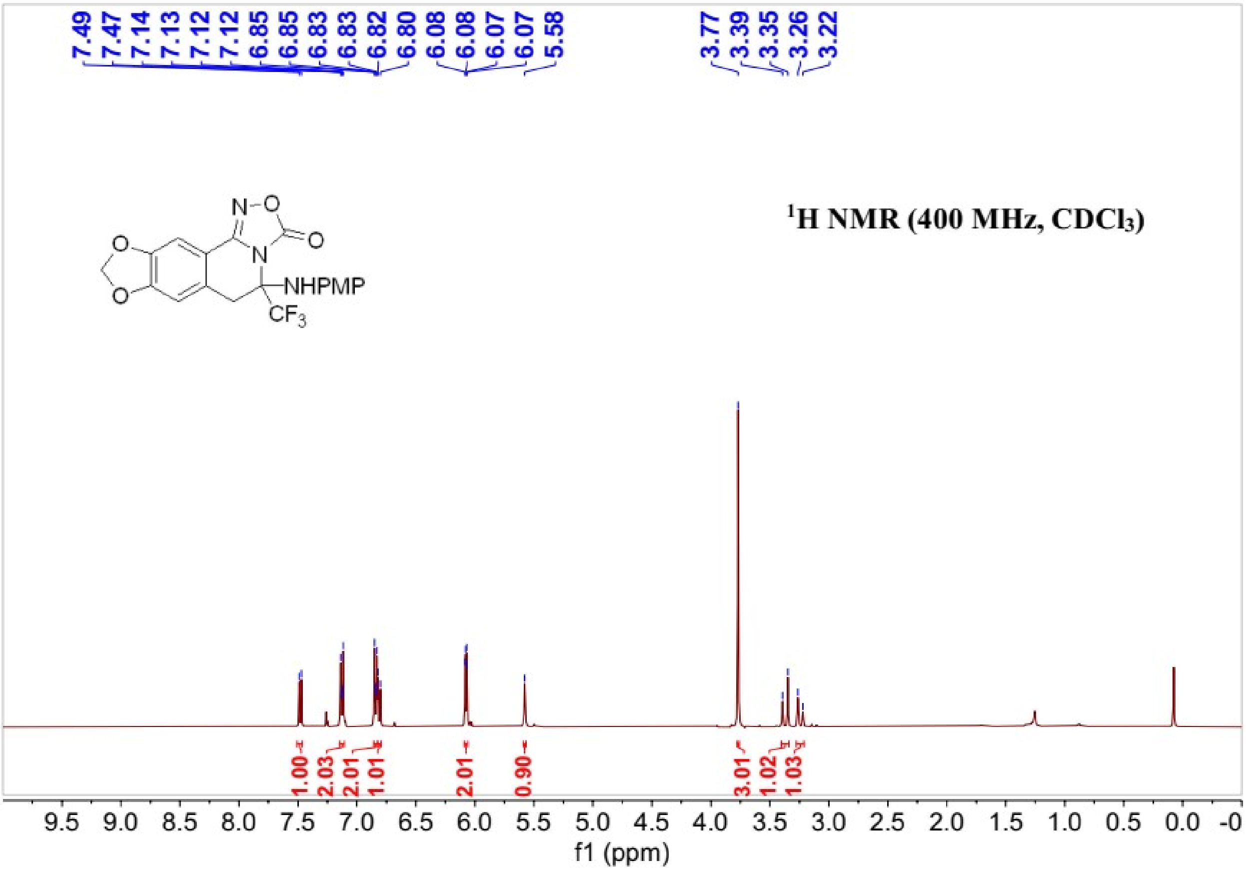

158.7
157.0
153.0
150.3
134.4
130.6
129.8
126.0
125.2
124.4
123.6
123.4
122.3
115.0
76.6
76.3
76.0
75.7
55.6
32.8
13C NMR (101 MHz, CDCl3)
N
O
O
N
CF3
O2N
NHPMP
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

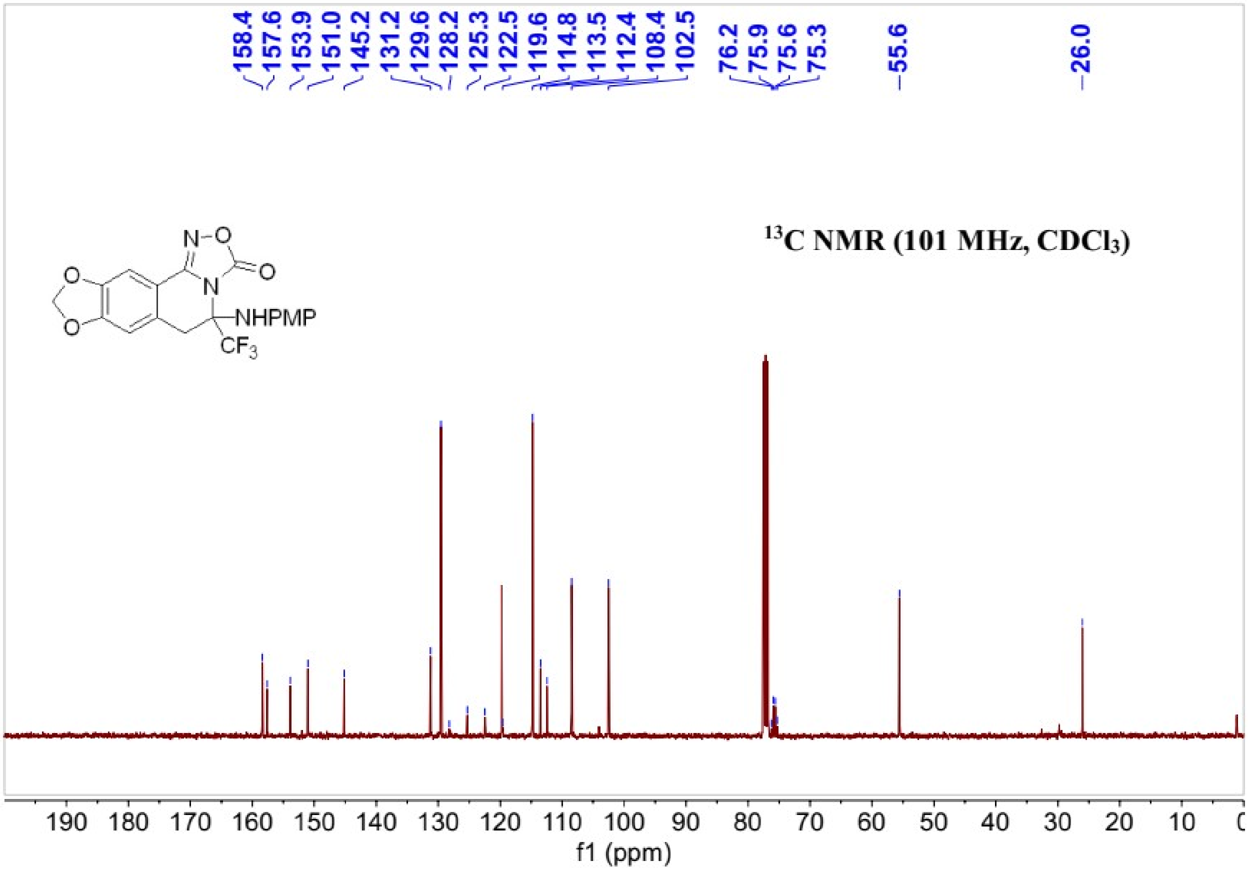

-79.84
19F NMR (376 MHz, CDCl3)
N
O
O
N
CF3
O2N
NHPMP
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

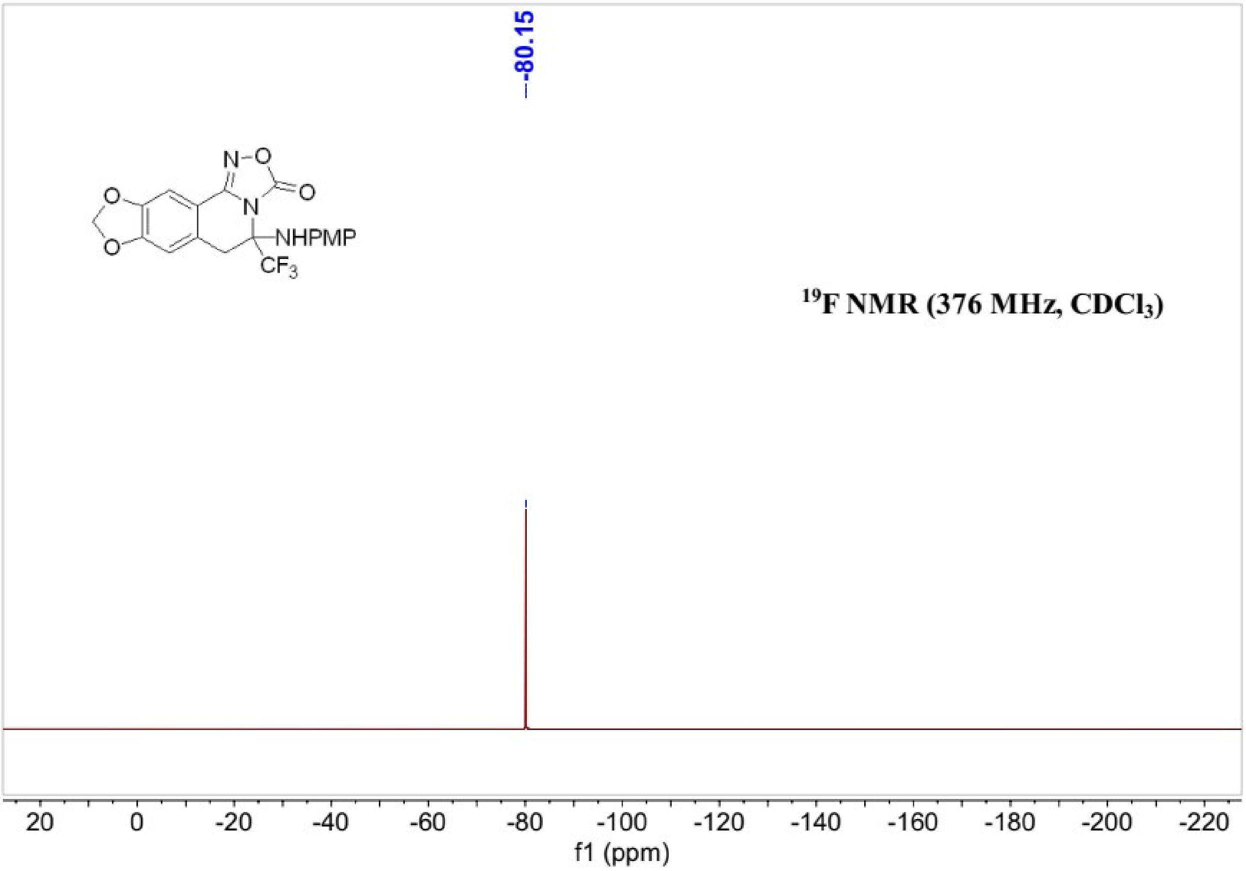

8.05
8.03
7.66
7.64
7.57
7.16
7.15
7.14
7.13
7.13
7.12
6.87
6.86
6.86
6.85
6.84
6.83
5.50
3.77
3.58
3.54
3.37
3.32
N
O
O
N
CF3
F3C
NHPMP
1H NMR (400 MHz, CDCl3)
1.00
1.02
1.02
2.03
2.05
0.90
3.02
1.02
1.01
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0
f1 (ppm)

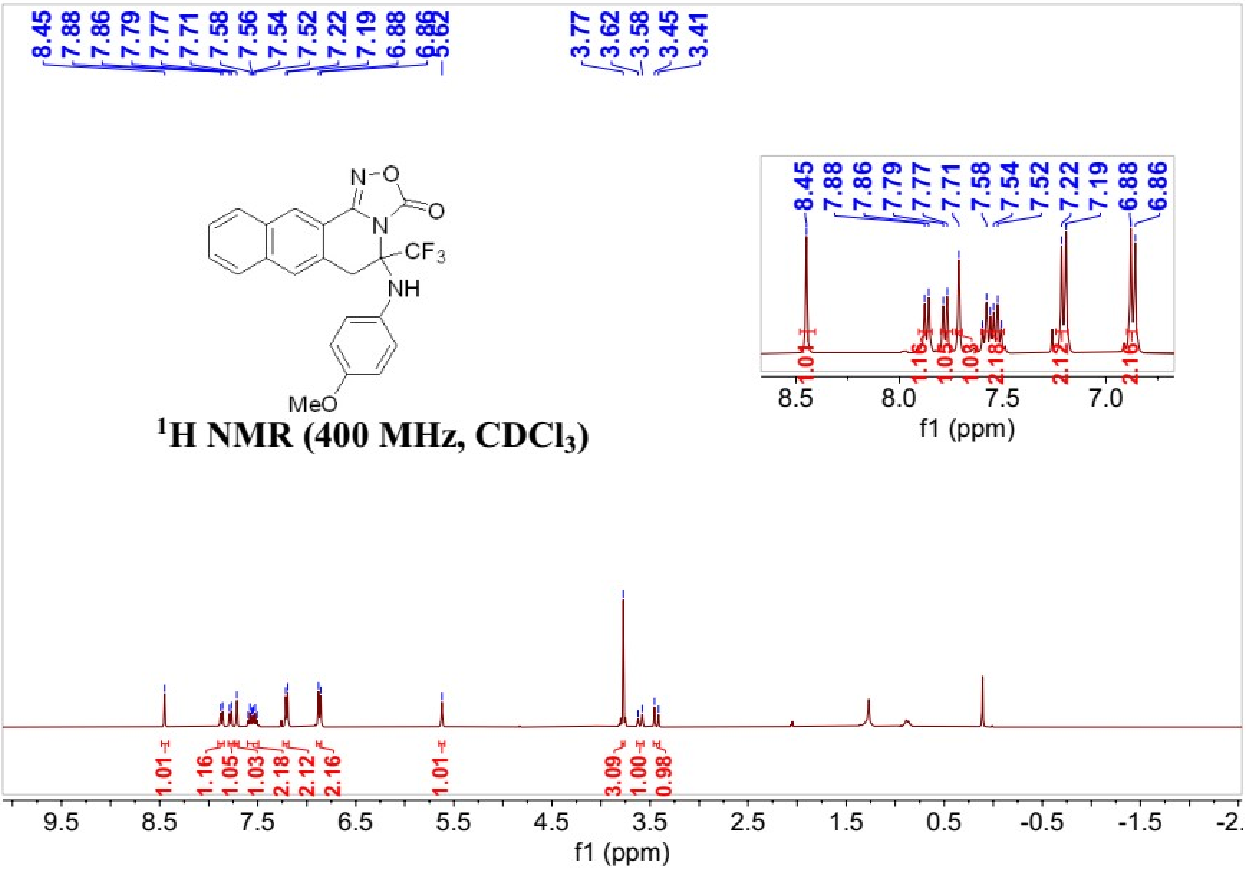

158.6
157.2
153.4
135.3
134.9
134.6
134.3
133.4
130.8
129.8
127.6
125.5
125.5
125.4
125.4
125.3
125.2
124.5
122.4
122.2
121.8
119.3
114.9
76.5
76.2
75.9
75.6
55.6
32.7
N
O
O
N
CF3
F3C
NHPMP
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

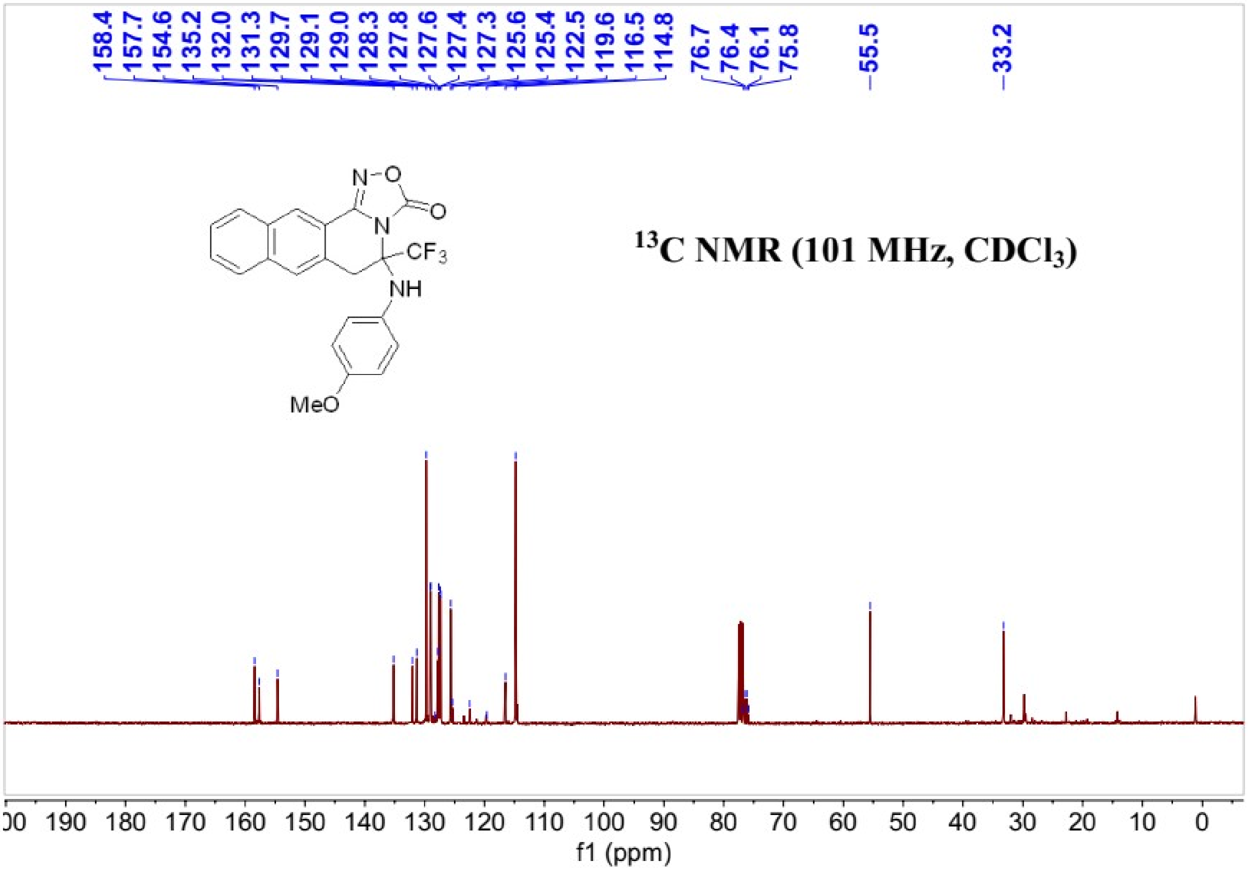

-63.35
-79.91
N–O
O
N
CF$_3$
F$_3$C
NHPMP
^{19}F NMR (376 MHz, CDCl$_3$)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

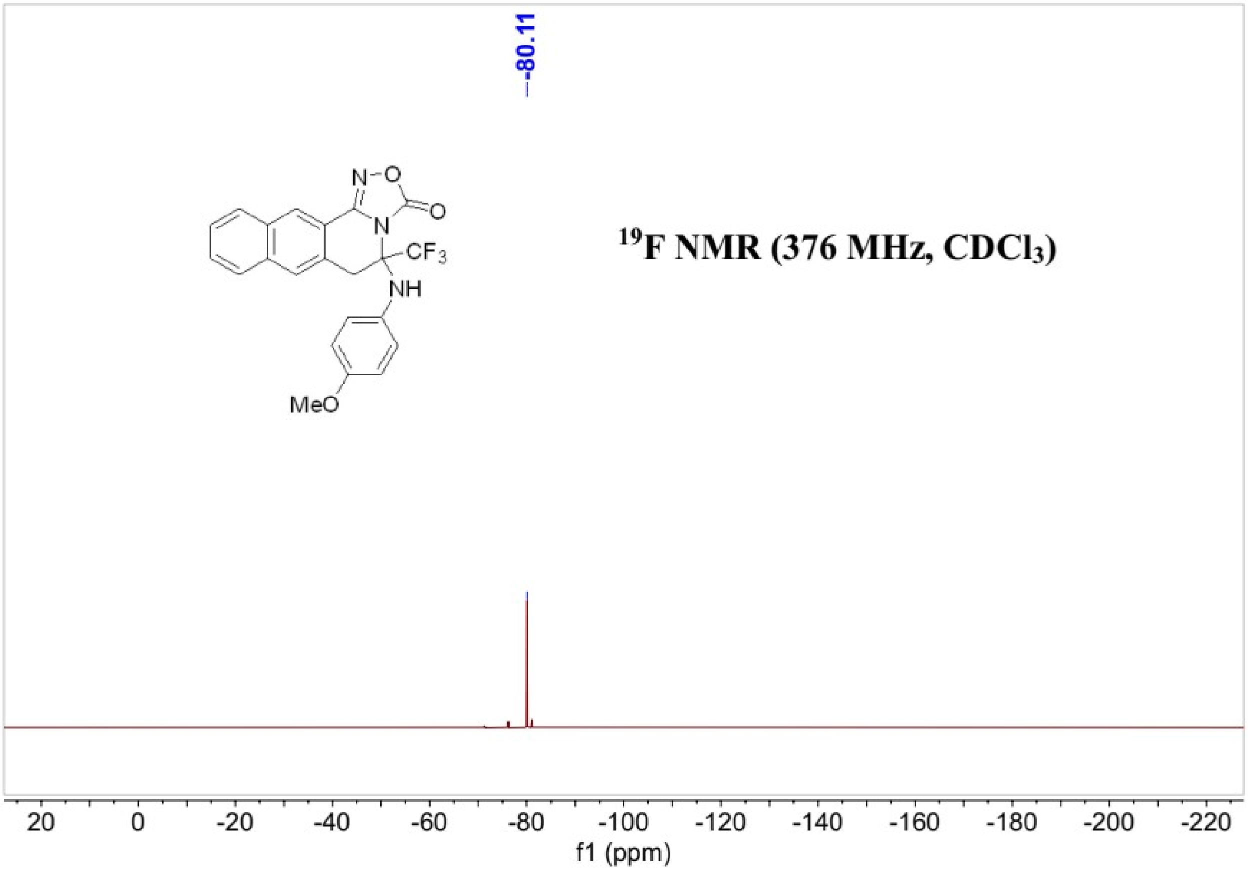

7.49
7.47
7.14
7.13
7.12
7.12
6.85
6.85
6.83
6.83
6.82
6.80
6.08
6.08
6.07
6.07
5.58
3.77
3.39
3.35
3.26
3.22
N–O
O
O
O
N
NHPMP
CF$_3$
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
2.03
2.01
1.01
2.01
0.90
3.01
1.02
1.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

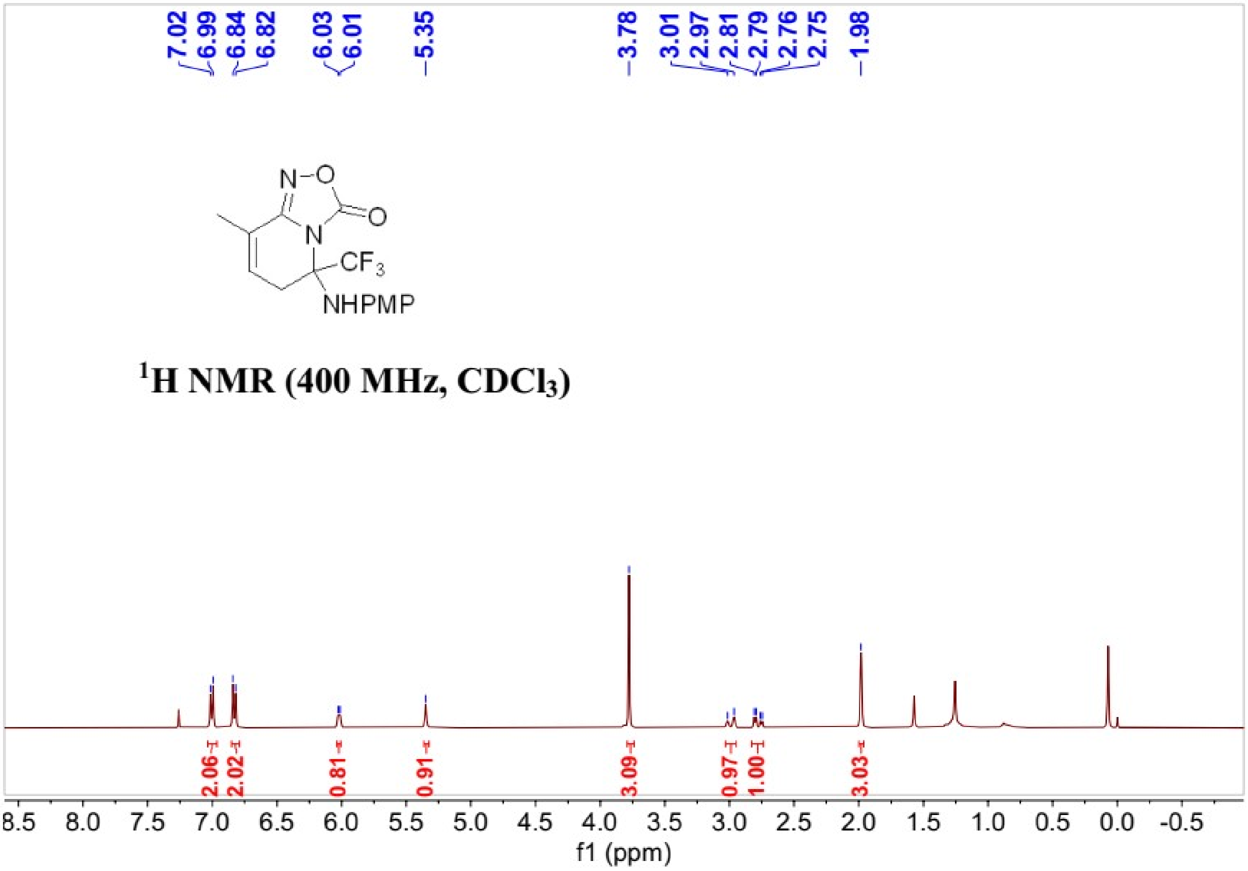

158.4
157.6
153.9
151.0
145.2
131.2
129.6
128.2
125.3
122.5
119.6
114.8
113.5
112.4
108.4
102.5
76.2
75.9
75.6
75.3
55.6
26.0
N
O
O
O
N
O
O
NHPMP
CF3
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

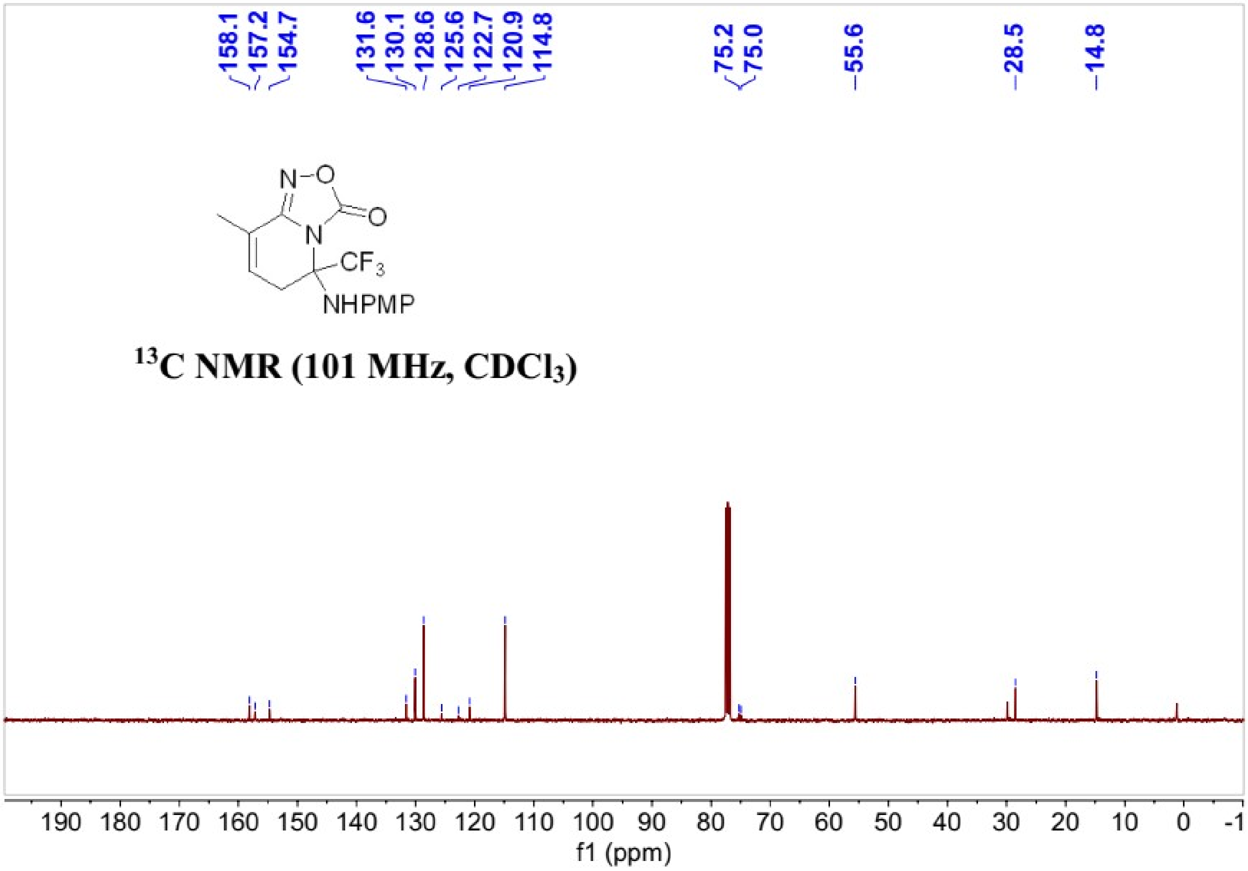

-80.15
N
O
O
O
N
O
O
NHPMP
CF3
19F NMR (376 MHz, CDCl3)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)


8.45
7.88
7.86
7.79
7.77
7.71
7.58
7.56
7.54
7.52
7.22
7.19
6.88
6.86
5.62
3.77
3.62
3.58
3.45
3.41
N
O
O
N
CF3
NH
MeO
1H NMR (400 MHz, CDCl3)
1.01
1.16
1.05
1.03
2.18
2.12
2.16
1.01
3.09
1.00
0.98
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
-2.
f1 (ppm)
8.0
7.0

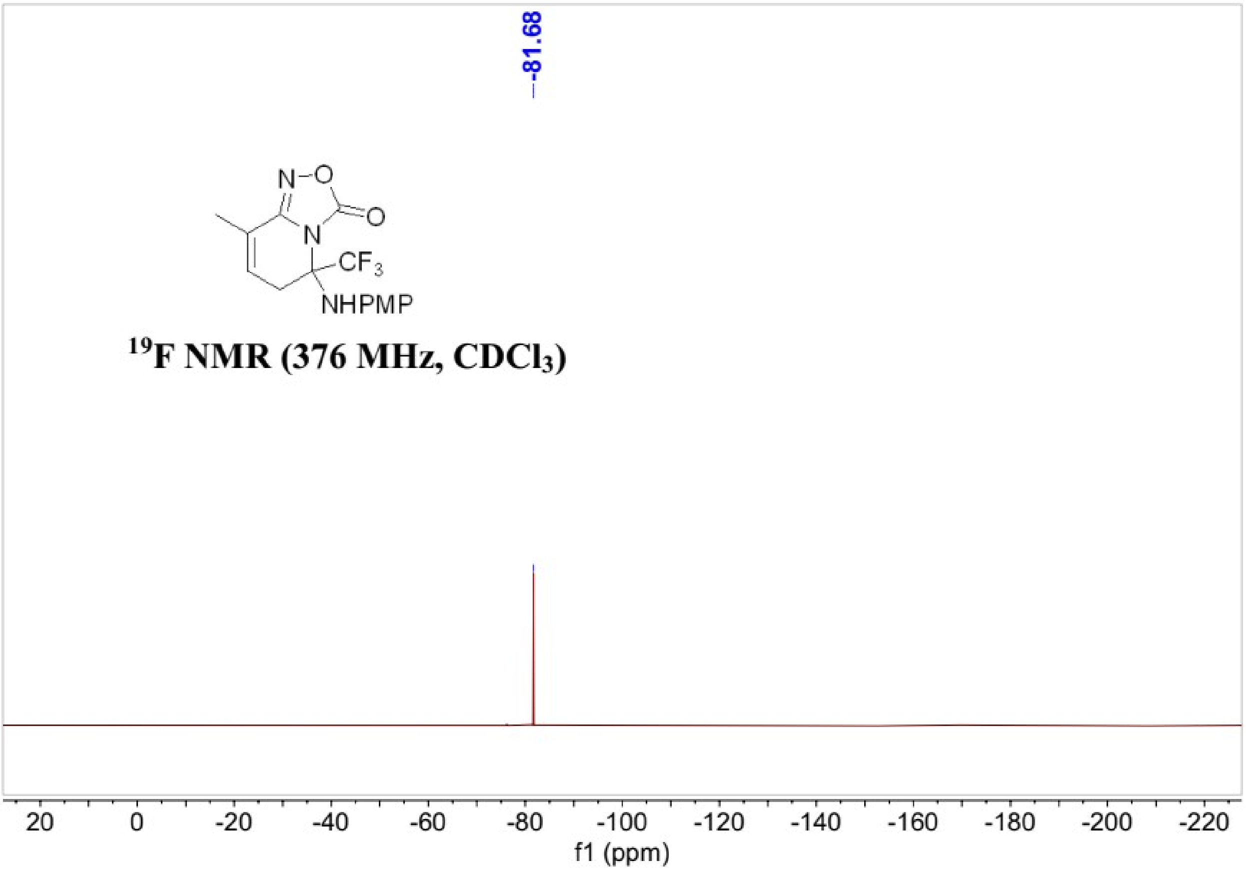

158.4
157.7
154.6
135.2
132.0
131.3
129.7
129.1
129.0
128.3
127.8
127.6
127.4
127.3
125.6
125.4
122.5
119.6
116.5
114.8
76.7
76.4
76.1
75.8
55.5
33.2
N
O
O
N
CF3
NH
MeO
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-80.11
N
O
O
N
CF3
NH
MeO
19F NMR (376 MHz, CDCl3)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

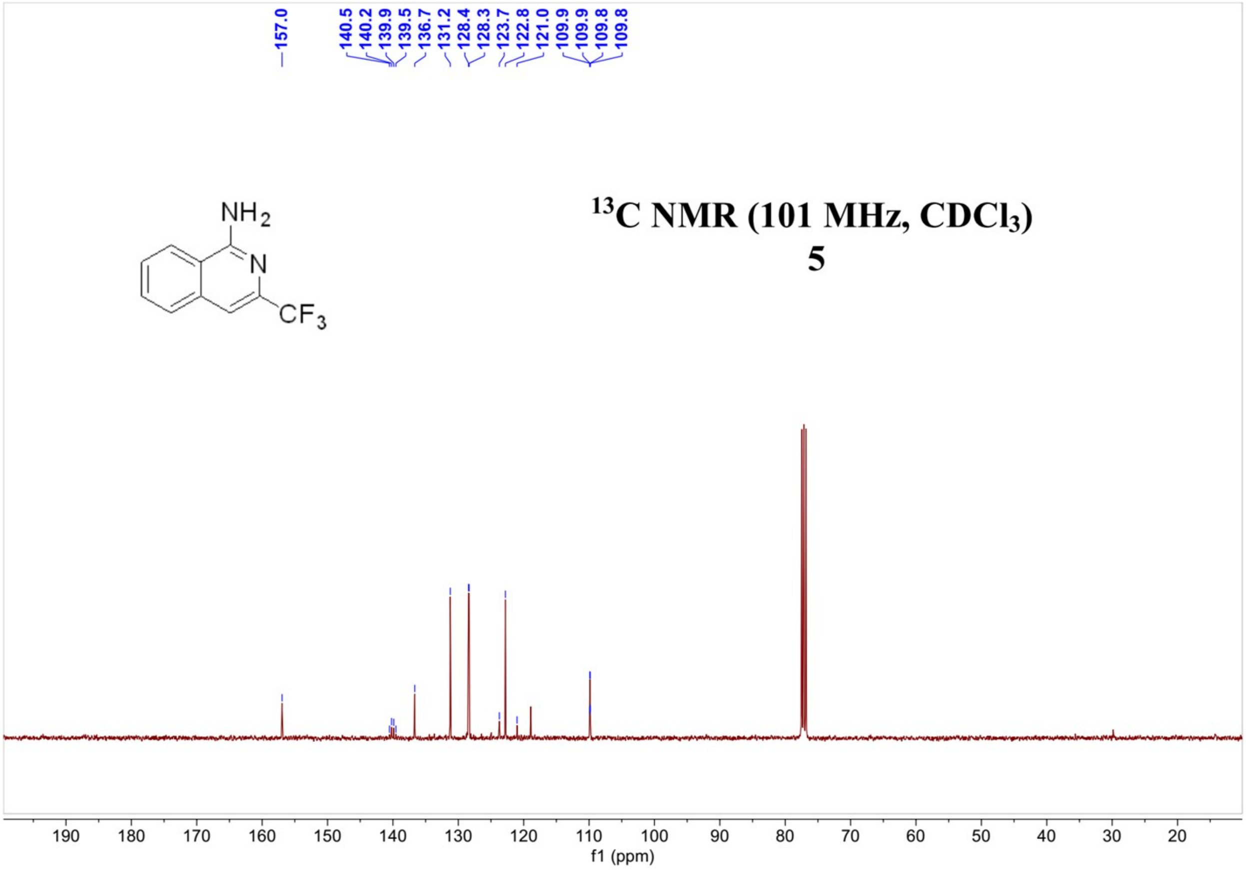

7.02
6.99
6.84
6.82
6.03
6.01
5.35
3.78
3.01
2.97
2.81
2.79
2.76
2.75
1.98
N
O
O
N
CF3
NHPMP
1H NMR (400 MHz, CDCl3)
2.06
2.02
0.81
0.91
3.09
0.97
1.00
3.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



^{13}C NMR (101 MHz, CDCl$_3$)

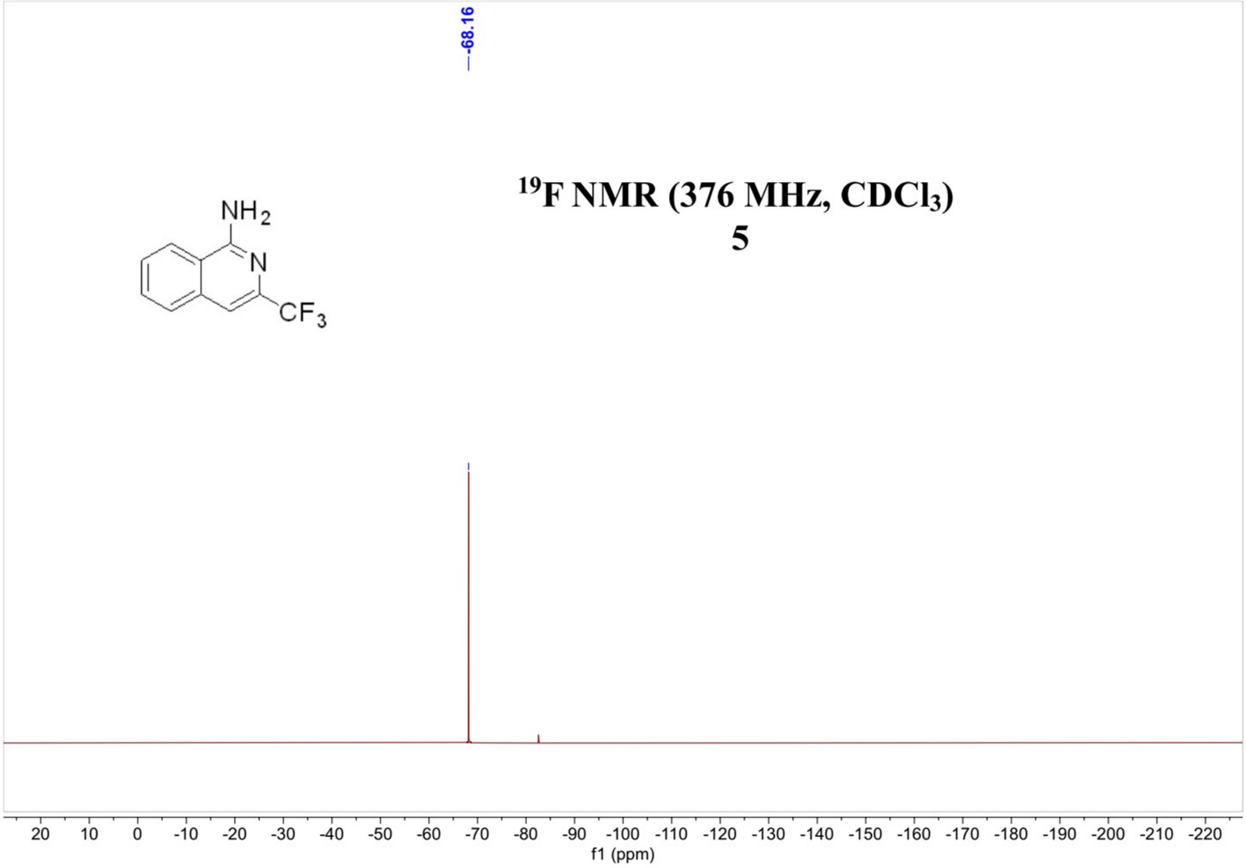


^{19}F NMR (376 MHz, CDCl$_3$)



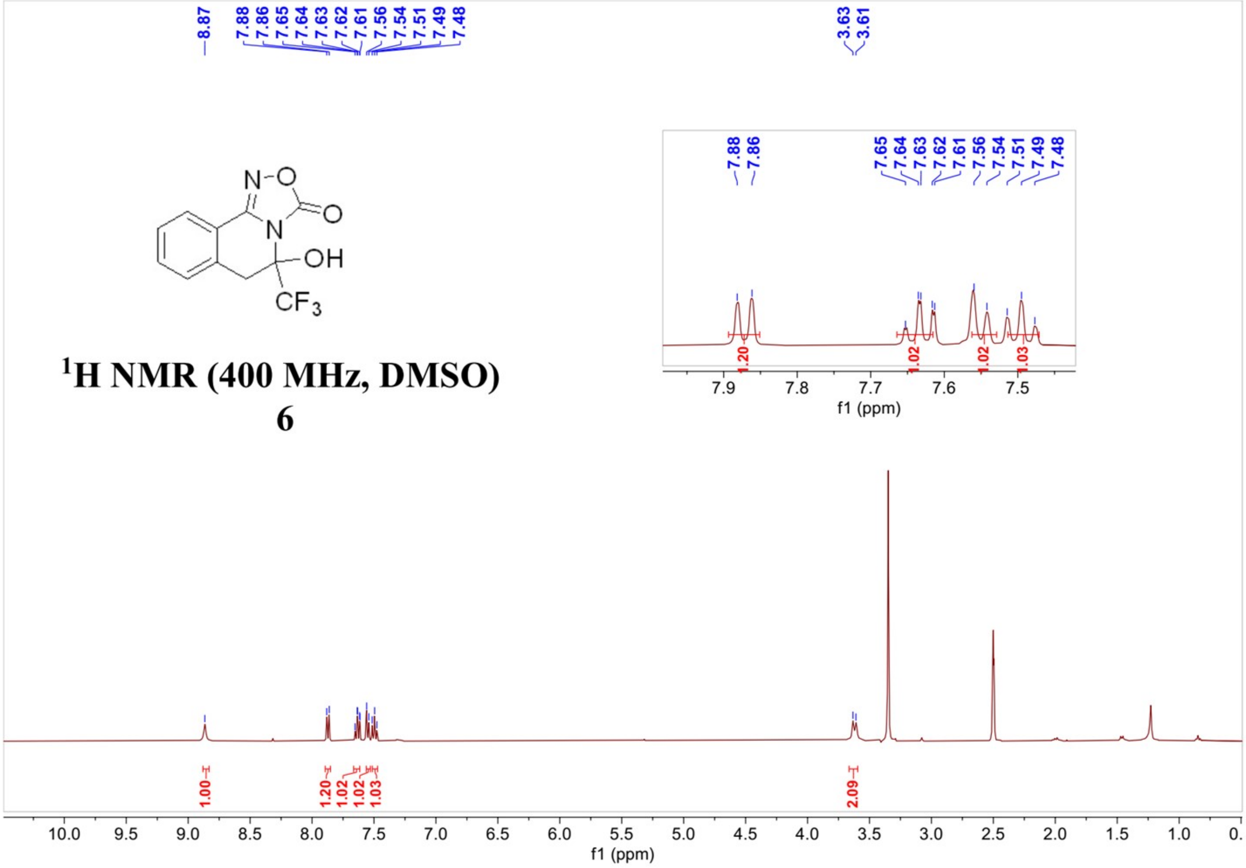
^{13}C NMR (101 MHz, $CDCl_3$)

5



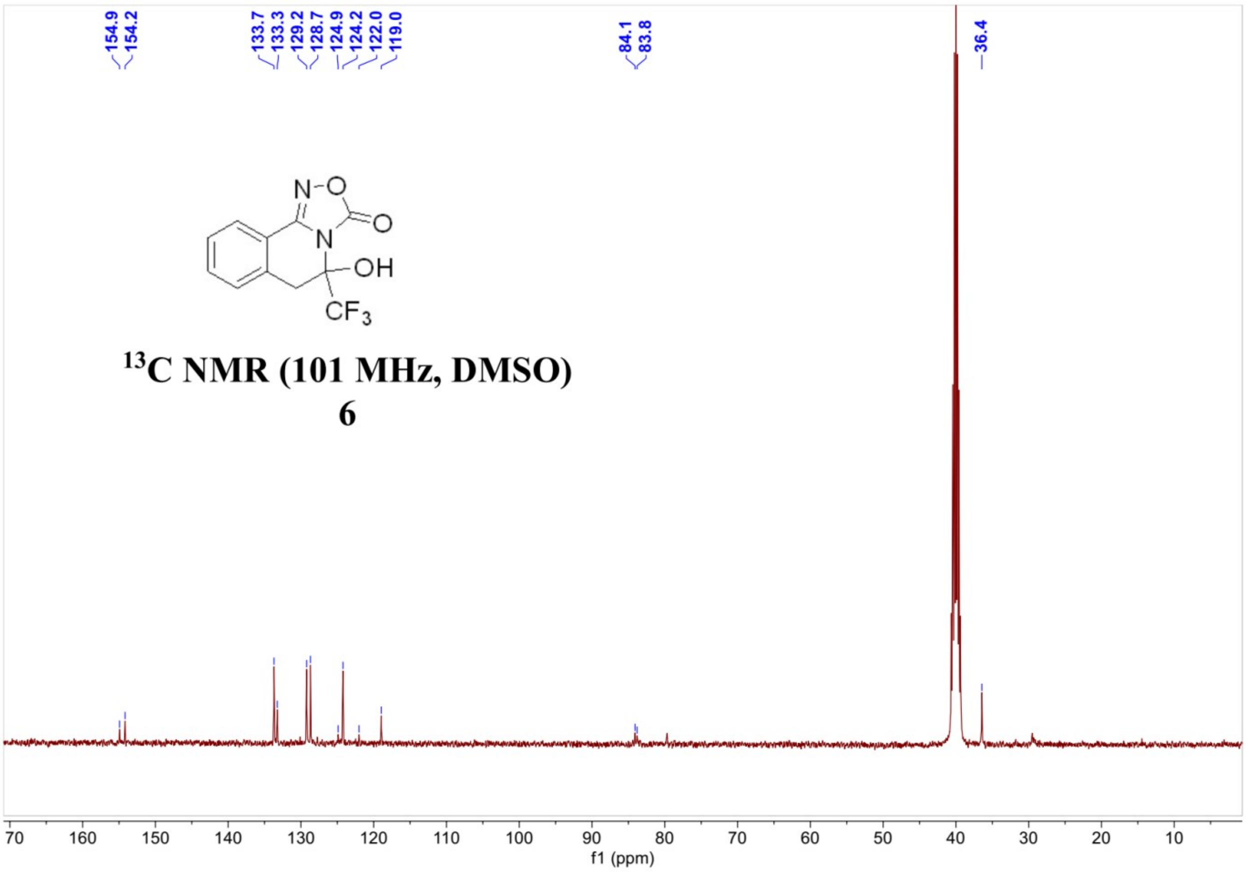
^{19}F NMR (376 MHz, $CDCl_3$)

5



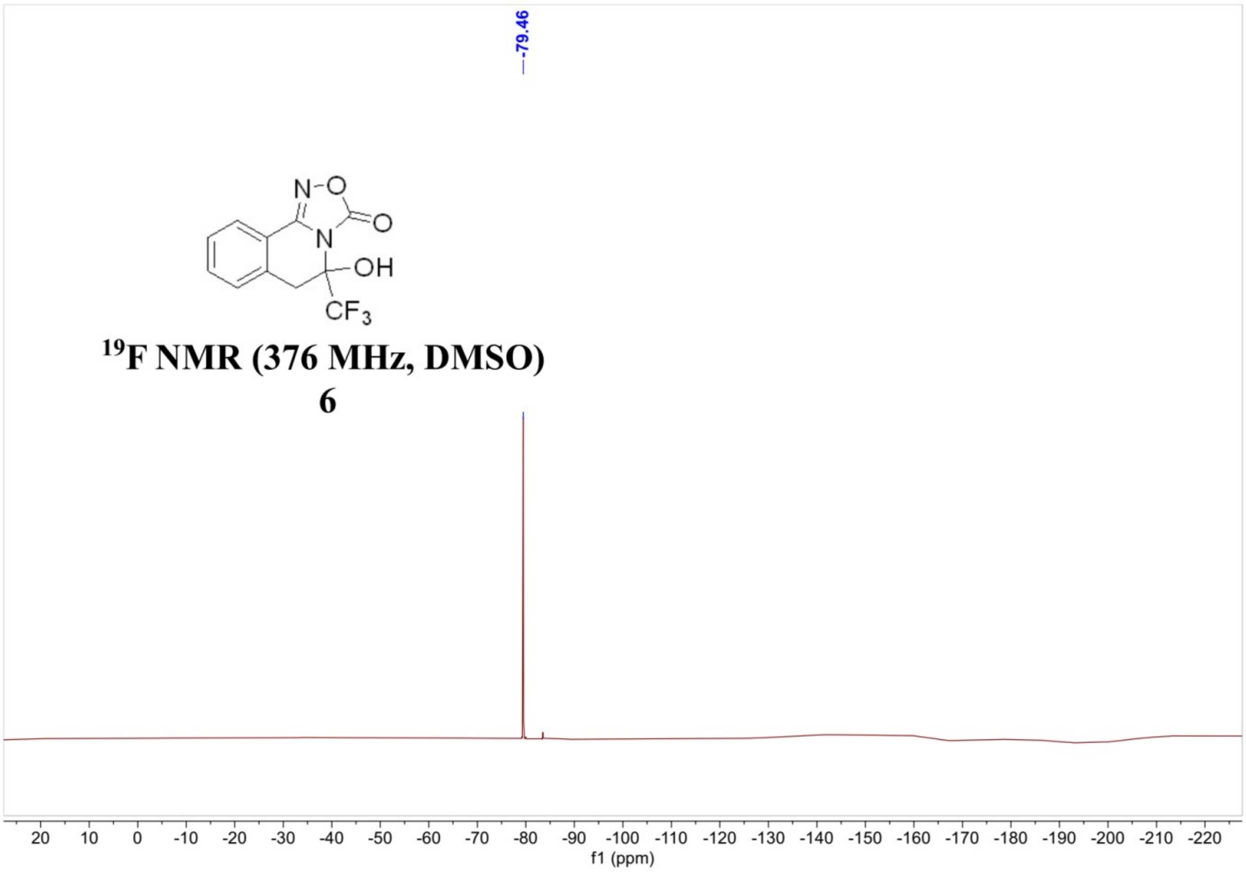
^{1}H NMR (400 MHz, DMSO)

6



^{13}C NMR (101 MHz, DMSO)

6


-79.46
N
O
O
N
OH
CF3
19F NMR (376 MHz, DMSO)
6
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
f1 (ppm)