Supplementary Information

A boron effect in radical difluoromethylation of the *N*-sulfonyl cyclic ketimines

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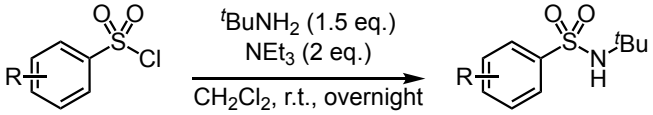
Contents

Experimental Section

General

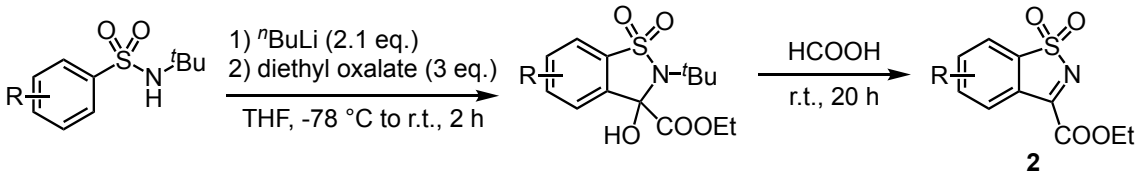
All experiments were carried out under inert atmosphere (nitrogen or argon) unless otherwise noted. ^{1}H NMR, ^{13}C{^{1}H} NMR, and ^{19}F NMR spectra were measured on a Bruker Avance Neo (400 MHz) spectrometer. Chemical shifts of ^{1}H NMR were expressed in parts per million downfield from $CHCl_3$ as an internal standard (δ = 7.26) in $CDCl_3$. Chemical shifts of ^{13}C{^{1}H} NMR were expressed in parts per million relative to the central line of the triplet (δ = 77.10) for $CDCl_3$. Chemical shifts of ^{19}F NMR were expressed in parts per million downfield from benzotrifluoride as an internal standard (δ = –63.24) in $CDCl_3$. Important NMR data were tabulated in the following order: multiplicity (s: singlet, d: doublet, t: triplet, pt: pseudo triplet, q: quartet, m: multiplet, br: broad) and coupling constant *J* (Hz). Mass spectra were measured on a JEOL JMS-T100LC spectrometer. Analytical thin layer chromatography (TLC) was performed on a glass plate pre-coated with silica gel (Merck Kieselgel 60 F_{254}, layer thickness 0.25 mm). Visualization was accomplished by UV light (254 nm) and anisaldehyde. Column chromatography was performed on KANTO Silica Gel 60N (spherical, neutral). All experiments were conducted under inert atmospheres (N_2 or argon) unless otherwise noted. Difluoromethylborates **1** were prepared according to our previous paper.[14] The oxazoline ligand (Table S1) was synthesized according to the published procedure.[12]

Preparation of sulfonamides[24]



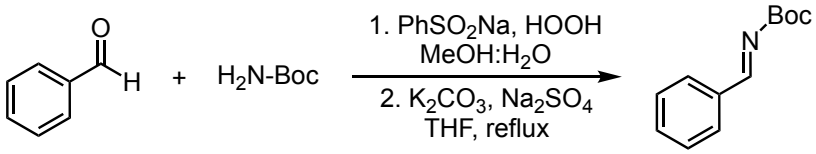
^{t}BuNH$_2$ (0.80 mL, 7.5 mmol) and NEt$_3$ (1.4 mL, 10 mmol) were dissolved in CH_2Cl_2 (5 mL). To the solution, aryl sulfonyl chloride (5 mmol) dissolved in CH_2Cl_2 (5 mL) was added dropwise at 0 °C, and the mixture was stirred overnight at room temperature. The reaction was quenched by saturated Na_2CO_3 aq. and extracted with CH_2Cl_2 three times. The organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in vacuo to give the title compound as a solid.

Preparation of cyclic sulfonyl imines (cyclic ketimines) 2[24]



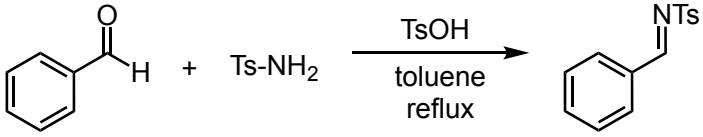
A sulfonamide (4 mmol) was dissolved in THF (24 mL). To the solution, ^{n}BuLi (2.6 M in hexane, 3.2 mL, 8.4 mmol) was added dropwise for 20 min at 0 °C, and the mixture was stirred 25 min at 0 °C. Then the resulting suspension was cooled to –78 °C, and diethyl oxalate (1.6 mL, 12 mmol) was added dropwise at –78 °C. The mixture was stirred for 2 h at room temperature. The reaction was quenched by 1 M aqueous HCl and extracted with Et_2O three times. The organic layer was dried over anhydrous Na_2SO_4 and filtered. After the solvent was removed in vacuo, formic acid (6.6 mL) was added, and the mixture was stirred 20 h at room temperature. The resulting suspension was dissolved in CH_2Cl_2 and concentrated in vacuo to remove formic acid. Purification by recrystallization or silica-gel column chromatography gave the title compound as a solid. The NMR spectroscopic data were identical to the published results.[25]

Preparation of the *N*-Boc aldimine[26]



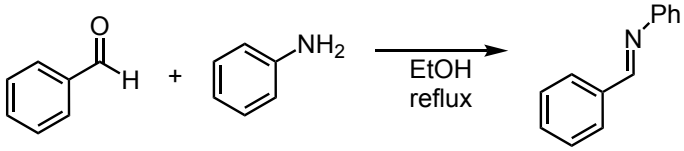
A methanol (2.5 mL) solution of benzaldehyde (0.50 g, 4.7 mmol) was added to a water (10 mL) solution of *t*-butyl carbamate (0.52 g, 4.5 mmol) and benzene sulfinic acid sodium salt (0.73 g, 4.5 mmol). This mixture was stirred for five minutes before treatment with formic acid (1.5 mL). The reaction mixture was stirred at 70 °C for 2 h and then stirred at room temperature for 12 h. After 12 h, the resulting solution was filtered through sintered funnel, and insoluble product was washed with Et_2O and dried in air to give tert-butyl (phenyl(phenylsulfonyl)methyl) carbamate as a white solid. A mixture of this crude product (0.50 g, 1.4 mmol), potassium carbonate (1.20 g, 8.50 mmol) and sodium sulfate (1.40 g, 10.0 mmol) were refluxed in THF for 12 h. After 12 h, the reaction mixture was cooled to room temperature, filtered through a Celite bed, and washed with Et_2O. The filtrate was concentrated to give the desired aldimine as a colorless oil and was used without further purification for the catalytic reaction.

Preparation of *N*-Benzylidene-4-methylbenzenesulfonamide[27]



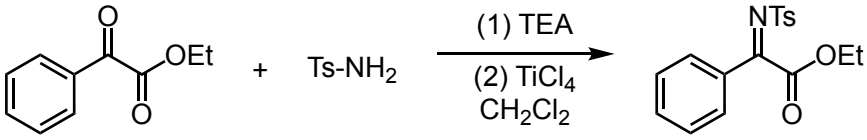
To a mixture of *p*-toluenesulfamide (1.71 g, 10.0 mmol) and 4-methylbenzenesulfonic acid (0.095 g, 0.50 mmol) in 12 mL of toluene, was added benzaldehyde (1.10 mL, 10.0 mmol) at room temperature. After refluxing overnight, the reaction mixture was cooled to room temperature and quenched with sat. $NaHCO_3$, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4 and concentrated. Purification by silica-gel column chromatography (hexane/AcOEt) gave the desired imine as a white solid.

Preparation of the *N*,1-diphenylmethanimine[28]



A solution of the aniline (0.91 ml, 10 mmol), benzaldehyde (1.01 ml, 10.0 mmol) in EtOH was refluxed for 6 h. After refluxing, the reaction mixture was concentrated. Purification by recrystallization gave the desired imine as a solid.

Preparation of ethyl-2-phenyl-2-(tosylimino)acetate[29]



A solution of the ethyl benzoylformate (0.80 ml, 5.0 mmol), *p*-toluenesulfonamide (0.86 ml, 5.0 mmol), and triethylamine (0.70 ml, 5.0 mmol) in CH_2Cl_2 was cooled to 0 °C. To this mixture was added a solution of $TiCl_4$ (5.0 ml, 5.0 mmol) in CH_2Cl_2 under N_2. The mixture was stirred at 0 ºC for 30 min and then warmed to room temperature and stirred for 1.5 h. The mixture was then quenched with sat. $NaHCO_3$ and extracted three times with CH_2Cl_2. The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated. Washing by hexane gave the desired imine and ethyl benzoylformate as a 1 : 2.4 mixture (determined by ^1H NMR, Figure S1). Spectral data of ethyl-2-phenyl-2-(tosylimino)acetate were identical to the literature.

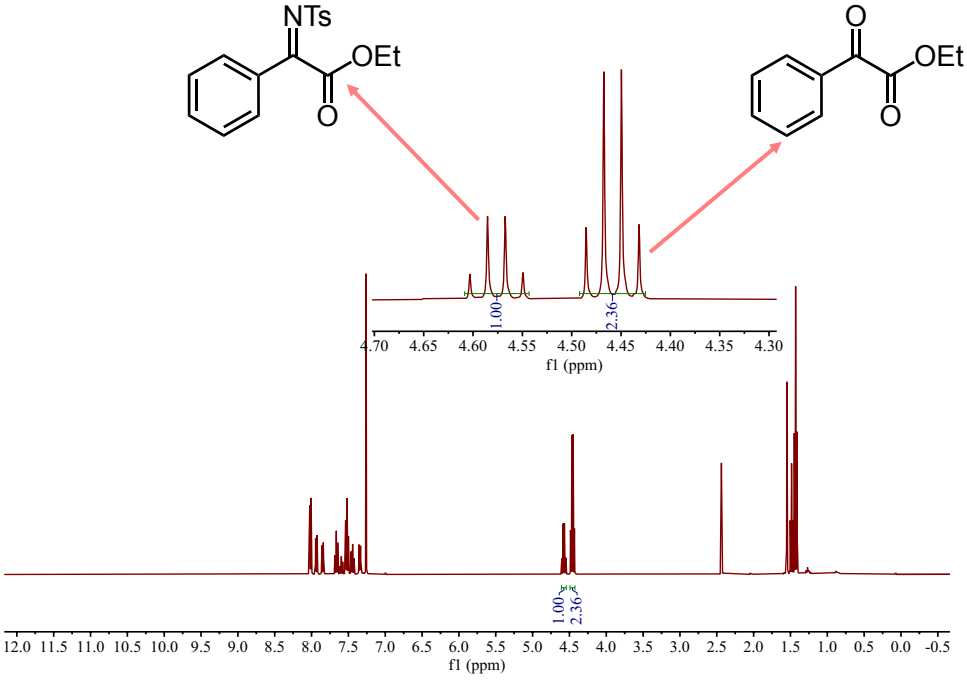
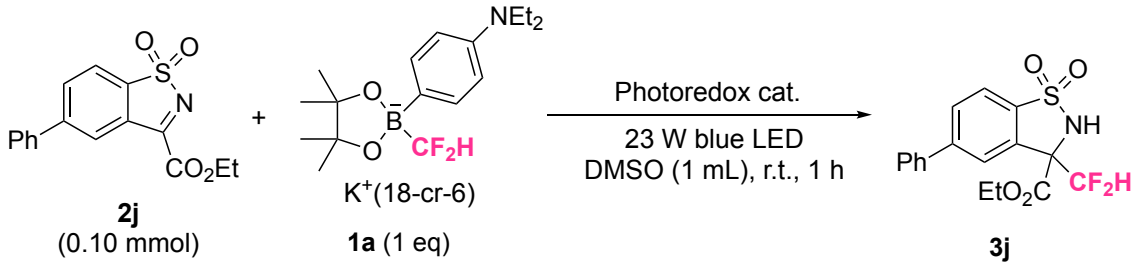


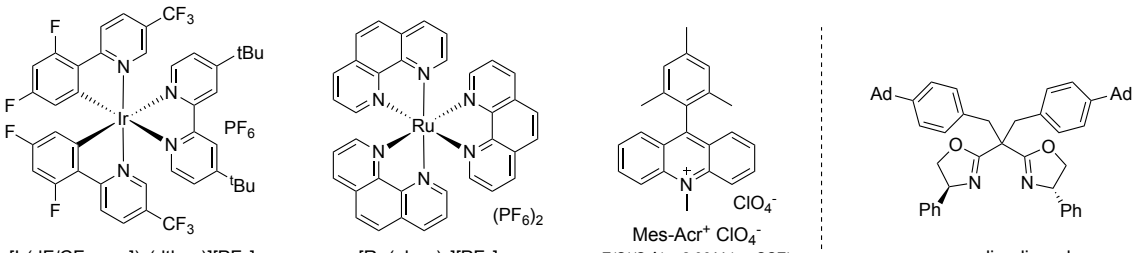
Figure S1. ^1H NMR ($CDCl_3$) of ethyl-2-phenyl-2-(tosylimino)acetate and ethyl benzoylformate.

Table S1. Difluoromethylation of ketimine **2j** with difluoromethylborate **1a**



Entry	Photoredox cat.	Yield[a)]
1	$[Ru(phen)_3][PF_6]_2$	75
2	$[Ir(dF/CF_3\text{-}ppy)_2(dtbpy)]\ PF_6$	76
3	Mes-acr$^+$ ClO_4^-	56
4	$Cu(BF_4)_2{\cdot}H_2O$ + oxazoline ligand	20

a) Determined by ^{19}F NMR using benzotrifluoride (BTF) as an internal standard.



*The oxazoline ligand was synthesized according to the published procedure.[12]

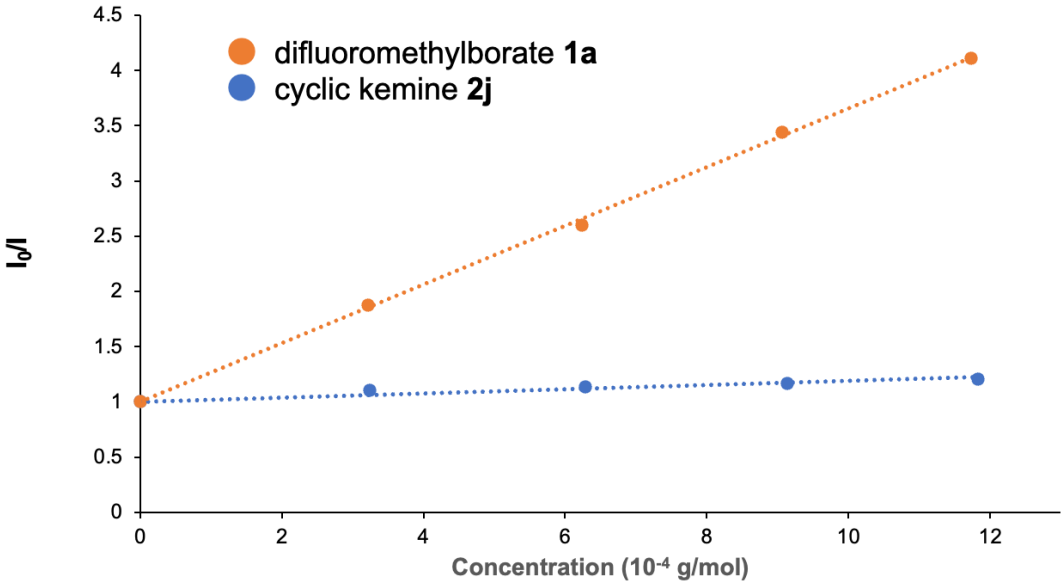
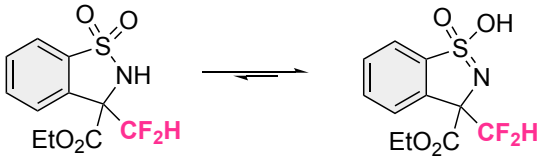


Figure S2. Stern-Volmer quenching with **1a** and **2j** in DMSO.

Fluorescence quenching studies were performed using a JACSO FP-6500 spectrofluorometer. In each experiment, $[Ru(phen)_3][PF_6]_2$ and various concentrations of borate **1a** or cyclic ketimine **3j** were dissolved in DMSO. The emission quenching of the $[Ru(phen)_3][PF_6]_2$ was achieved using a concentration of 9.5 x 10^{-5} mol/L under excitation at 450 nm. The emission intensity was observed at 622 nm. Plots were constructed according to the Stern–Volmer equation $I_0/I = 1 + k_Q\tau_0[Q]$ (I is the emission intensity. I_0 is the emission intensity without quencher. k_Q is the rate constant of quenching process. τ_0 is the fluorescence lifetime without quencher. [Q] is the concentration of quencher.

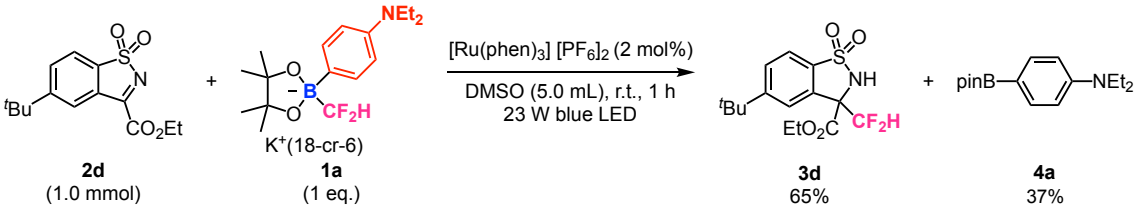
Table S2. Tautomeric properties of γ-sultams **3**



3 **3-iso**

3	**3** : **3-iso**	Diastereomers ratio of **3-iso**
3a	>99 : 1	-
3b	13 : 1	not determined
3c	9 : 1	not determined
3d	>99 : 1	-
3e	>99 : 1	-
3f	14 : 1	3 : 5
3g	9 : 1	1 : 1
3h	17 : 1	1 : 1
3i	> 99 : 1	-
3j	12 : 1	4 : 5
3k	> 99 : 1	-

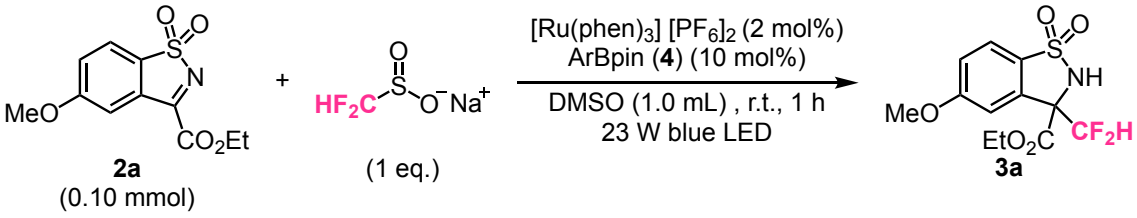
Large scale Synthesis of γ-sultam 3d



2d (1.0 mmol) **1a** (1 eq.) **3d** 65% **4a** 37%

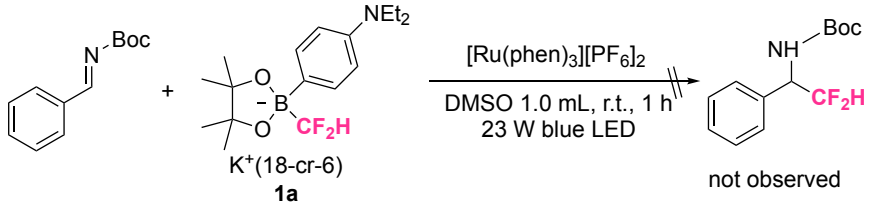
To a suspension of the difluoroborate **1a** (630 mg, 1.0 mmol), cyclic N-sulfonyl α-iminoester **2d** (295 mg, 1.0 mmol) and tris(1,10-phenanthroline)ruthenium(II) Bis(hexafluorophosphate) (19 mg, 0.020 mmol) in DMSO (5.0 mL) were mixed at room temperature. The resulting suspension was stirred upon blue LED irradiation under a nitrogen balloon at room temperature for 1 h, and was quenched by 1 M aqueous HCl and extracted with CH_2Cl_2 three times. The organic layer was dried over anhydrous Na_2SO_4 and filtered. After the solvent was removed in vacuo, the resulting mixture was purified by silica-gel column chromatography (hexane/AcOEt = 2:1) to give desired products **3d** (226.1 mg, 65%) and 4-$Et_2NC_6H_4$Bpin (**4a**, 102.2 mg, 37%) as solids.

Synthesis of γ-sultam 3a by HCF_2SO_2Na under catalytic amounts of ArylBpin (4) and photo-redox Catalytic reaction conditions



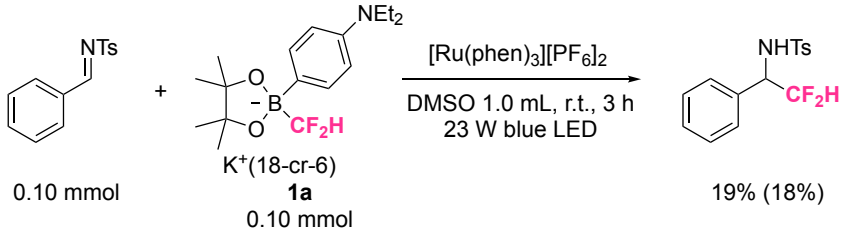
To a suspension of HCF_2SO_2Na (14.0 mg, 0.10 mmol) in DMSO (1.0 mL), cyclic N-sulfonyl α-iminoester **2a** (27mg, 0.10 mmol), ArylBpin (**4**, 0.010 mmol) and tris(1,10-phenanthroline)ruthenium(II) bis(hexafluorophosphate) (1.9 mg, 0.0020 mmol) were added. The resulting suspension was stirred upon blue LED irradiation under a nitrogen balloon for 1 h at room temperature. After 1 h, BTF was added, and the mixture was analyzed by ^{19}F NMR spectroscopy.

Attempted synthesis of tert-butyl (2,2-difluoro-1-phenylethyl)carbamate



Difluoromethylborate **1a** (62.9 mg, 0.10 mmol), *N*-Boc aldimine (20.5 mg, 0.10 mmol) and tris(1,10-phenanthroline)ruthenium(II) bis(hexafluorophosphate) (1.9 mg, 0.0020 mmol) were mixed in DMSO (1.0 mL) at room temperature. The resulting suspension was stirred upon the blue LED irradiation under a nitrogen balloon for 1 h, BTF was added and the mixture was analyzed by ^{19}F NMR spectroscopy showing no desired product.

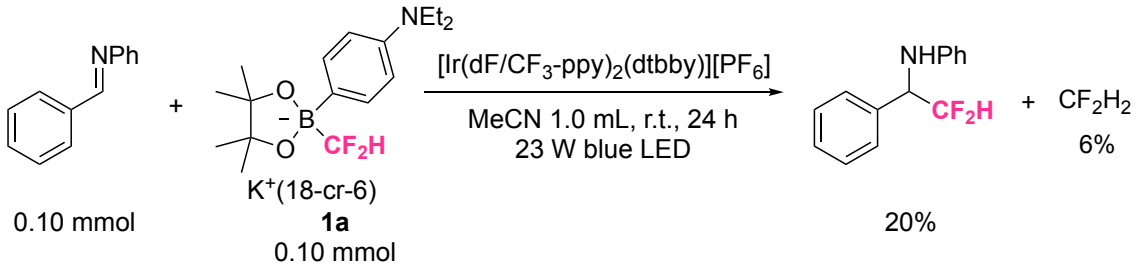
Synthesis of *N*-(2,2-difluoro-1-phenylethyl)-4-methylbenzenesulfonamide



1a (62.9 mg, 0.10 mmol), *N*-benzylidene-4-methylbenzenesulfonamide (25.9 mg, 0.10 mmol) and tris(1,10-phenanthroline)ruthenium(II) bis(hexafluorophosphate) (1.9 mg, 0.0020 mmol) were mixed in DMSO (1.0 mL). The resulting suspension was stirred upon blue LED irradiation under a nitrogen balloon for 3 h at room temperature, and was quenched by 1 M aqueous HCl, and extracted with CH_2Cl_2 three times. The organic layer was dried over anhydrous Na_2SO_4 and filtered. After the solvent was removed in vacuo, BTF was added and the mixture was analyzed by ^{19}F NMR spectroscopy. The resulting mixture was purified by PTLC (hexane/AcOEt = 3:1) to give the desired product[30] as a solid (5.5 mg, 18%).

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.60 (d, J = 8.3 Hz, 2H), 7.31–7.11 (m, 7H), 5.93 (td, J = 55.4, 2.4 Hz, 1H), 5.19 (s, 1H), 4.66 (dddd, J = 15.2, 12.9, 8.4, 2.4 Hz, 1H), 2.37 (s, 3H).

Synthesis of *N*-(2,2-difluoro-1-phenylethyl)-4-methylbenzenesulfonamide (Scheme S1)



Scheme S1. Difluoromethylation of *N*-benzylideneaniline.

To a suspension of the difluoroborate **1a** (62.9 mg, 0.10 mmol), *N*-Benzylideneaniline (18.0 mg, 0.10 mmol) and Ir[dF(CF_3)ppy]$_2$(dtbpy) PF_6 (2.3 mg, 0.0020 mmol) in MeCN (1.0 mL) at room temperature. The resulting suspension was stirred upon blue LED irradiation under nitrogen balloon for 24 h, BTF was added and the mixture was analyzed by ^{19}F NMR spectroscopy[31] (Figure S3).

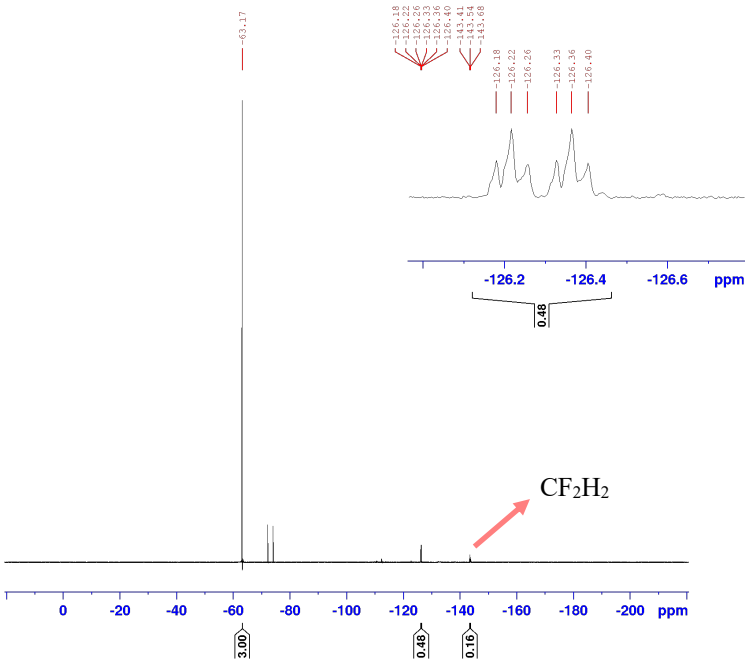
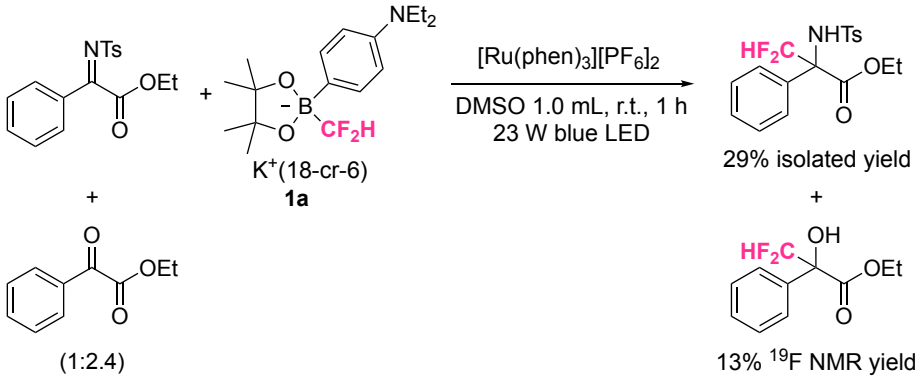


Figure S3. ^{19}F NMR of a reaction mixture of Scheme S1.

Synthesis of ethyl 3,3-difluoro-2-((4-methylphenyl)sulfonamido)-2-phenylpropanoate (Scheme S2)



Scheme S2. Difluoromethylation of a mixture of 2-phenyl-2-(tosylimino)acetate and benzoylformate.

1a (188.7 mg, 0.30 mmol), a mixture of ethyl 2-phenyl-2-(tosylimino)acetate (0.10 mmol) and ethyl benzoylformate (0.24 mmol) and tris(1,10-phenanthroline)ruthenium(II) bis(hexafluorophosphate) (5.7 mg, 0.0060 mmol) in DMSO (1.0 mL) were mixed at room temperature. The resulting suspension was stirred upon blue LED irradiation under a nitrogen balloon for 1 h, BTF was added, and the mixture was analyzed by ^{19}F NMR spectroscopy. The mixture was quenched by 1 M aqueous HCl and extracted with CH_2Cl_2 three times. The organic layer was dried over anhydrous Na_2SO_4 and filtered. After the solvent was removed in vacuo, the resulting mixture was purified by PTLC (hexane/AcOEt = 3:1) to give 3,3-difluoro-2-((4-methylphenyl)sulfonamido)-2-phenylpropanoate together with inseparable materials in 29% yield. The reaction mixture included the difluoromethylated ethyl benzoylformate (ethyl 3,3-difluoro-2-hydroxy-2-phenylpropanoate, 13% ^{19}F NMR yield).[32]

^{1}H NMR ($CDCl_3$, 400 MHz): δ7.30–7.27 (m, 2H), 7.25–7.22 (m, 1H), 7.17–7.03 (m, 6H), 6.82 (t, J = 54.7 Hz, 1H), 6.04 (s, 1H), 4.30 (dp, J = 10.8, 7.2 Hz, 2H), 2.35 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −123.1 (dd, J_{FF} = 281.8 Hz, J_{HF} = 54.7 Hz, 1F); −129.8 (dd, J_{FF} = 282.0 Hz, J_{HF} = 54.7 Hz, 1F). HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{18}H_{19}F_2NO_4S$: 406.0901, found 405.9884.

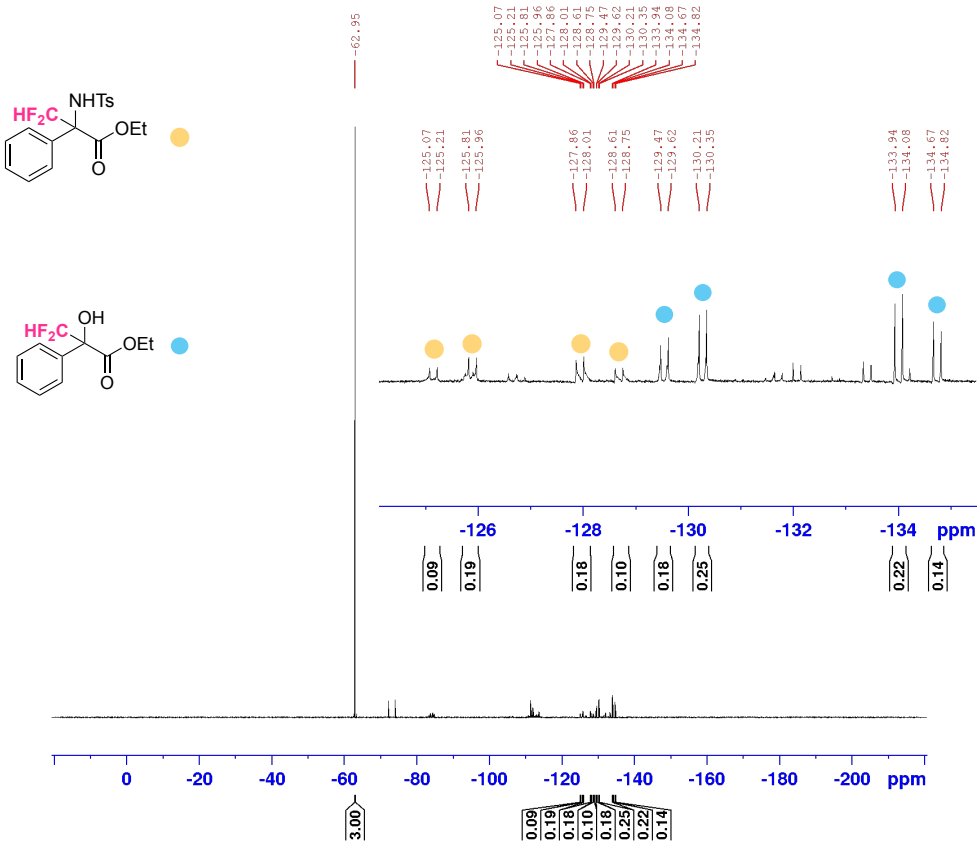
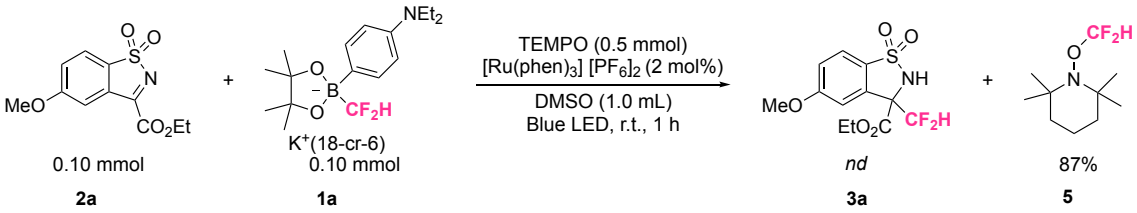


Figure S4. ^{19}F NMR of a reaction mixture of Scheme S2.

Mechanistic study: TEMPO trapping



A suspension of **1a** (62.9 mg, 0.10 mmol), ethyl 5-methoxybenzo[d]isothiazole-3-carboxylate 1,1-dioxide (**2a**, 26.9 mg, 0.10 mmol), TEMPO (2,2,6,6-tetramethylpiperidine 1-oxyl, 78.1 mg, 0.50 mmol) and tris(1,10-phenanthroline)ruthenium(II) bis(hexafluorophosphate) (1.9 mg, 0.0020 mmol) in DMSO (1.0 mL) was stirred upon blue LED irradiation under a nitrogen balloon for 1 h at room temperature. α,α,α-Trifluorotoluene (10.0 μL, 0.08145 mmol) was added and the mixture was analyzed by ^{19}F NMR spectroscopy characterizing **5** (Tempo-CF_2H) and absence of **3a**.

^{19}F NMR ($CDCl_3$, 376 MHz): δ –79.6 (d, J = 71.7 Hz, 2F).[33]

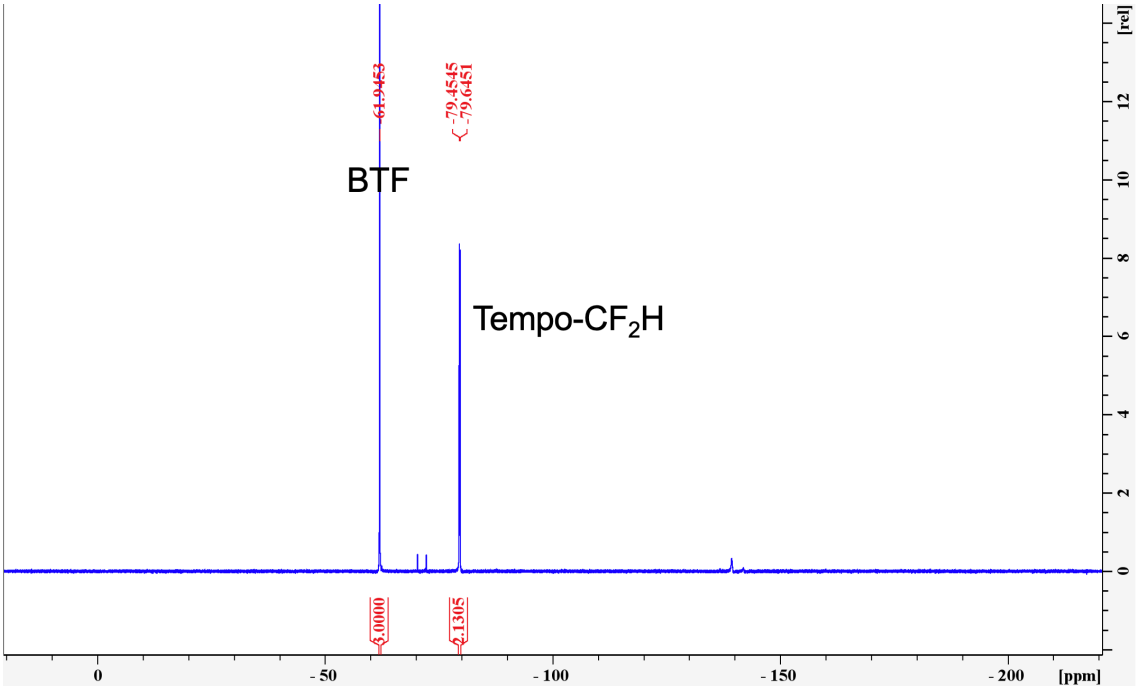
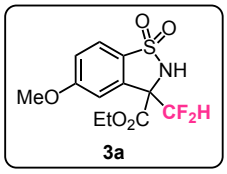


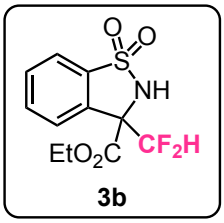
Figure S5. ^{19}F NMR ($CDCl_3$) of a resultant mixture of **1a**, **2a**, TEMPO, and the photoredox catalyst after irradiation.

Characterization of diluoromethylated γ-sultams 3



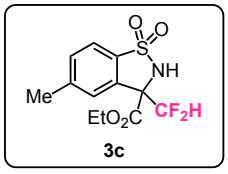
3a

Ethyl 3-(difluoromethyl)-5-methoxy-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3a**): yellow solid (23.5 mg, 73%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72 (d, J = 8.7 Hz, 1H), 7.25 (s, 1H), 7.17 (dd, J = 8.7, 2.3 Hz, 1H), 6.08 (pt, J = 54.6 Hz, 1H), 5.82 (s, 1H), 4.43 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –123.7 (dd, J_{FF} = 278.7 Hz, J_{HF} = 54.4 Hz, 1F), –127.4 (dd, J_{FF} = 278.7 Hz, J_{HF} = 54.4 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.3 (d, J = 4.4 Hz), 164.1, 132.9 (t, J = 2.7 Hz), 127.9, 123.5, 118.2, 113.8 (t, J = 251.5 Hz), 110.6 (d, J = 2.2 Hz), 68.6 (t, J = 23.4 Hz), 64.8, 56.2, 14.1. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{12}H_{13}F_2NO_5S$: 344.0380, found 344.0525.



3b

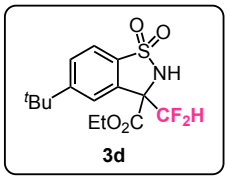
Ethyl 3-(difluoromethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3b**): yellow oil (19.0 mg, 65%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85 (t, J = 7.1 Hz, 2H), 7.72 (pd, J = 7.4, 1.5 Hz, 2H), 6.10 (pt, J = 54.6 Hz, 1H), 5.84 (s, 1H), 4.43 (qq, J = 7.3, 3.6 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –123.6 (dd, J_{FF} = 279.2 Hz, J_{HF} = 54.7 Hz, 1F), –127.4 (dd, J_{FF} = 279.2 Hz, J_{HF} = 54.7 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.4 (d, J = 4.3 Hz), 136.1, 133.9, 132.0, 130.5 (t, J = 2.8 Hz), 126.1 (d, J = 2.2 Hz), 122.1, 113.8 (t, J = 251.5 Hz), 69.0 (t, J = 23.5 Hz), 64.9, 14.1. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{11}H_{11}F_2NO_4S$: 314.0275, found 314.0361.



3c

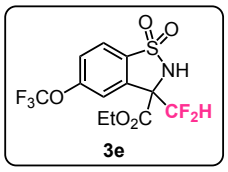
Ethyl 3-(difluoromethyl)-5-methyl-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3c**): yellow solid (26.7 mg, 88%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.71 (d, J =

7.9 Hz, 1H), 7.61 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 6.09 (pt, J = 54.6 Hz, 1H), 5.78 (s, 1H), 4.43 (qp, J = 7.0, 3.5 Hz, 2H), 2.52 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –123.8 (dd, J_{FF} = 278.7 Hz, J_{HF} = 54.4 Hz, 1F), –127.6 (dd, J_{FF} = 278.7 Hz, J_{HF} = 54.4 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.5 (d, J = 4.7 Hz), 145.3, 133.4, 132.9, 130.8 (t, J = 2.7 Hz),126.2 (d, J = 2.1 Hz), 121.8, 113.8 (t, J = 251.3 Hz), 68.8 (t, J = 23.4 Hz), 64.7, 22.0, 14.1. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{12}H_{13}F_2NO_4S$: 328.0431, found 328.0428.



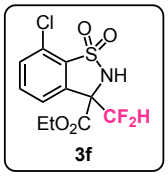
3d

Ethyl 5-(tert-butyl)-3-(difluoromethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3d**): white solid (28.2 mg, 81%). ^{19}F NMR yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (s, 1H), 7.77–7.70 (m, 2H), 6.10 (pt, J = 54.6 Hz, 1H), 5.83 (s, 1H), 4.52–4.35 (m, 2H), 1.39 (t, J = 7.1 Hz, 3H), 1.37 (s, 1H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –123.8 (dd, J_{FF} = 278.7 Hz, J_{HF} = 54.4 Hz, 1F), –127.6 (dd, J_{FF} = 278.7 Hz, J_{HF} = 54.4 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.5 (d, J = 4.4 Hz), 158.5, 133.2, 130.6 (d, J = 2.6 Hz), 129.5, 122.7 (d, J = 2.2 Hz), 121.6, 113.8 (t, J = 251.3 Hz), 68.9 (t, J = 23.4 Hz), 64.6, 35.7, 31.2, 14.1. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{15}H_{19}F_2NO_4S$: 370.0901, found 370.0872.



3e

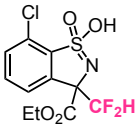
Ethyl 3-(difluoromethyl)-5-(trifluoromethoxy)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3e**): white solid (27.5 mg, 73%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (d, J = 8.5 Hz, 1H), 7.69 (s, 1H), 7.54 (ddd, J = 8.5, 2.1, 1.0 Hz, 1H), 6.06 (pt, J = 54.5 Hz, 1H), 5.98 (s, 1H), 4.46 (qd, J = 7.1, 1.8 Hz, 2H), 1.40 (t, J = 7.2 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –57.9 (s, 3F), −123.3 (dd, J_{FF} = 280.0 Hz, J_{HF} = 54.2 Hz, 1F), −126.6 (dd, J_{FF} = 280.0 Hz, J_{HF} = 54.2 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.7 (d, J = 3.8 Hz), 152.9 (d, J = 2.0 Hz), 134.4, 133.1 (t, J = 2.8 Hz), 124.5, 123.9, 120.2 (q, J = 258.9 Hz), 118.6, 113.5 (d, J = 252.4 Hz), 68.4 (t, J = 24.2 Hz), 65.2, 13.9. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{12}H_{10}F_5NO_5S$: 398.0098, found 397.9112.



3f

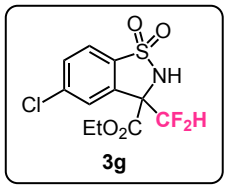
Ethyl 7-chloro-3-(difluoromethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3f**): white solid (20.9 mg, 64%). The reaction in acetonitrile gave 87% ^{19}F NMR yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, J = 7.3 Hz, 1H), 7.66 (t, J = 7.9 Hz, 1H), 7.63 (dd, J = 7.9, 1.4 Hz, 1H), 6.08 (pt, J = 54.5 Hz, 1H), 4.44 (qq, J = 7.0, 3.6 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –123.4 (dd, J_{FF} = 279.5 Hz, J_{HF} = 54.5 Hz, 1F), −127.2 (dd, J_{FF} = 279.5 Hz, J_{HF} = 54.5 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.0 (d, J = 4.3 Hz), 135.0, 134.2, 133.1 (t, J = 2.8 Hz), 132.8, 129.9, 124.4 (d, J = 2.5 Hz), 113.5 (t, J = 251.8 Hz), 67.9 (t, J = 23.8 Hz), 65.1, 14.1. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{11}H_{10}ClF_2NO_4S$: 347.9885, found 347.9918.

Tautomer **3f-iso**



3f-iso

^{19}F NMR ($CDCl_3$, 376 MHz): Diastereomer A: δ –116.2 (dd, J_{FF} = 305.0 Hz, J_{HF} = 56.5 Hz, 1F), −117.8 (dd, J_{FF} = 305.0 Hz, J_{HF} = 56.5 Hz, 1F). Diastereomer B: δ –123.3 (dd, J_{FF} = 282.4 Hz, J_{HF} = 56.5 Hz, 1F), −126.6 (dd, J_{FF} = 282.4 Hz, J_{HF} = 56.5 Hz, 1F). ^{1}H NMR ($CDCl_3$, 400 MHz): Diastereomer A: δ 6.97 (pt, J = 54.5 Hz, 1H). Diastereomer B: δ 6.9 (pt, J = 54.5 Hz, 1H).

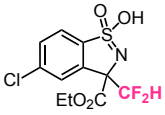


3g

Ethyl 5-chloro-3-(difluoromethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3g**): white solid (25.2 mg, 77%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (s, 1H), 7.76 (dd, J = 8.3, 0.5 Hz, 1H), 7.67 (dd, J = 8.3, 1.8 Hz, 1H), 6.07 (pt, J = 54.5 Hz, 1H), 5.92 (s, 1H), 4.50–4.40 (m, 2H), 1.40 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –123.5 (dd, J_{FF} = 282.4 Hz, J_{HF} = 54.5 Hz, 1F), −127.2 (dd, J_{FF} = 282.4 Hz, J_{HF} = 54.5 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.8 (d, J = 4.2 Hz), 140.5, 134.6, 132.5,

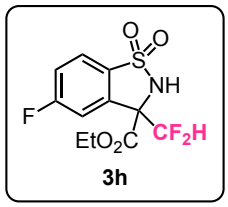
132.4 (t, J = 2.6 Hz), 126.5 (d, J = 2.3 Hz), 123.2, 113.5 (t, J = 252.0 Hz), 68.5 (t, J = 23.9 Hz), 65.2, 14.1. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{11}H_{10}ClF_2NO_4S$: 347.9885, found 347.9014.

Tautomer **3g-iso**



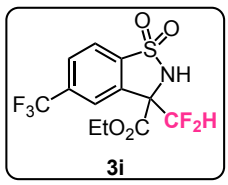
3g-iso

^{19}F NMR ($CDCl_3$, 376 MHz): Diastereomer A: δ –116.2 (dd, J_{FF} = 305.0 Hz, J_{HF} = 56.5 Hz, 1F), −117.8 (dd, J_{FF} = 305.0 Hz, J_{HF} = 56.5 Hz, 1F). Diastereomer B: δ –123.3 (dd, J_{FF} = 282.4 Hz, J_{HF} = 56.5 Hz, 1F), −126.6 (dd, J_{FF} = 282.4 Hz, J_{HF} = 56.5 Hz, 1F). ^{1}H NMR ($CDCl_3$, 400 MHz): Diastereomer A or B: δ 6.97 (pt, J = 54.5 Hz, 1H).



3h

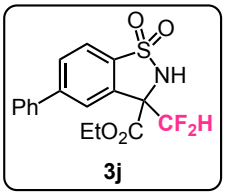
Ethyl 3-(difluoromethyl)-5-fluoro-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3h**): yellow solid (32.2 mg, quant). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (dd, J = 8.6, 4.7 Hz, 1H), 7.53 (d, J = 8.3 Hz, 1H), 7.40 (td, J = 8.3, 2.3 Hz, 1H), 6.06 (pt, J = 54.5 Hz, 1H), 5.95 (s, 1H), 4.50–4.39 (m, 2H), 1.40 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –102.05 ~ –102.11 (m, 1F), –123.4 (ddd, J_{FF} = 282.4 Hz, J_{HF} = 54.5 Hz, J = 7.5 Hz, 1F), −127.0 (ddd, J_{FF} = 282.4 Hz, J_{HF} = 54.5 Hz, J = 7.5 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.7 (d, J = 255.3 Hz), 164.8 (d, J = 4.0 Hz), 133.5 (dt, J = 9.7, 2.8 Hz), 132.2 (d, J = 3.0 Hz), 124.3 (d, J = 9.9 Hz), 120.0 (d, J = 23.9 Hz), 113.8 (dd, J = 25.6, 2.4 Hz), 113.5 (t, J = 252.1 Hz), 68.4 (td, J = 24.0, 2.2 Hz), 65.2, 14.1. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{11}H_{10}F_3NO_4S$: 332.0180, found 331.9397.



3i

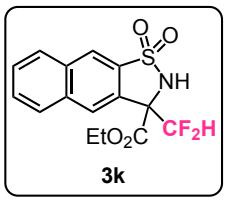
Ethyl 3-(difluoromethyl)-5-(trifluoromethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3i**): yellow solid (22.8 mg, 64%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.12 (s, 1H), 7.98 (d, J = 1.1 Hz, 2H), 6.10 (pt, J = 54.5 Hz, 1H), 5.97 (s, 1H), 4.47 (q,

J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –62.9 (s, 3F), –123.4 (dd, J_{FF} = 282.4 Hz, J_{HF} = 54.6 Hz, 1F), −126.7 (dd, J_{FF} = 282.4 Hz, J_{HF} = 54.6 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.6 (d, J = 4.0 Hz), 139.5, 136.1 (q, J = 33.4 Hz), 131.6 (t, J = 2.9 Hz), 129.3 (q, J = 3.6 Hz), 123.8 (quintet, J = 3.6 Hz), 123, 122.8 (q, J = 272.0 Hz), 113.5 (t, J = 252.43 Hz), 68.7 (t, J = 24.1 Hz), 65.3, 14.0. HRMS (ESI$^-$-TOF) m/z [M-H]$^-$ calcd for $C_{12}H_{10}F_5NO_4S$: 358.0172, found 358.0096.



3j

Ethyl 3-(difluoromethyl)-5-phenyl-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (**3j**): yellow solid (22.0 mg, 60%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (s, 1H), 7.89 (d, J = 1.1 Hz, 2H), 7.61–7.47 (m, 5H), 6.16 (pt, J = 54.6 Hz, 1H), 5.91 (s, 1H), 4.46 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –123.6 (dd, J_{FF} = 278.6 Hz, J_{HF} = 54.6 Hz, 1F), −127.3 (dd, J_{FF} = 278.6 Hz, J_{HF} = 54.6 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.4 (d, J = 4.3 Hz), 147.6, 138.7, 134.5, 131.3 (t, J = 2.6 Hz), 131.1, 129.4, 129.2, 127.5, 124.5 (d, J = 2.2 Hz), 122.4, 113.8 (t, J = 251.6 Hz), 68.9 (t, J = 23.7 Hz), 64.9, 14.2. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{17}H_{15}F_2NO_4S$: 390.0588, found 390.0606.



3k

Ethyl 3-(difluoromethyl)-2,3-dihydronaphtho[2,3-*d*]isothiazole-3-carboxylate 1,1-dioxide (**3k**): yellow solid (16.9 mg, 50%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.36 (s, 1H), 8.31 (s, 1H), 8.02 (t, J = 9.2 Hz, 2H), 7.75–7.67 (m, 2H), 6.21 (pt, J = 54.6 Hz, 1H), 5.94 (s, 1H), 4.46 (qq, J = 7.0, 3.6 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz): δ –123.5 (dd, J_{FF} = 278.6 Hz, J_{HF} = 54.6 Hz, 1F), −127.3 (dd, J_{FF} = 278.6 Hz, J_{HF} = 54.6 Hz, 1F); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.7 (d, J = 4.5 Hz), 135.3, 133.8, 132.9, 129.6, 129.4, 129.0 (d, J = 2.5 Hz), 126.3 (d, J = 2.0 Hz), 126.1 (t, J = 2.7 Hz), 122.8, 114.0 (t, J = 251.4 Hz), 68.7 (t, J = 23.3 Hz), 64.8, 14.2. HRMS (ESI+-TOF) m/z [M+Na]+ calcd for $C_{15}H_{13}F_2NO_4S$: 328.0431, found 328.0428.

References (additional)

24 H. Wang, T. Jiang and M.-H. Xu, *J. Am. Chem. Soc.*, 2013, **135**, 971-974.

25 a) J. Pan, J. H. Wu, H. Zhang, X. Ren, J. P. Tan, L. Zhu, H. S. Zhang, C. Jiang and T. Wang, *Angew. Chem. Int. Ed.*, 2019, **58,** 7425-7430; b) L. Wu, R.-R. Liu, G. Zhang, D.-J.Wang, H. Wu, J. Gao and Y.-X. Jia, *Adv. Synth. Catal.*, 2015, **357**, 709-713; c) S. Nakamura, M. Sano, A. Toda, D. Nakane and H. Masuda, *Chem. Eur. J.*, 2015, **21**, 3929-3932.

26 R. D. Kardile and R.-S. Liu, *Org. Lett.*, 2019, **21**, 6452-6456.

27 D. Chen, X. Chen, T. Du, L. Kong, R. Zhen, S. Zhen, Y. Wen and G. Zhu, *Tetrahedron Lett.*, 2010, **51**, 5131-5133.

28 A. F. Garrido-Castro, A. Gini, M. C. Maestro and J. Alemán, *Chem. Commun.*, 2020, **56**, 3769-3772.

29 a) S. Takizawa,F. A. Arteaga, Y. Yoshida, M. Suzuki and H. Sasai, *Org. Lett.*, 2013, **15**, 4142-4145; b) J. Y. Ying, N. Erathodiyil, H. Gu, H. Shao and J. Jiang, *PCT Int. Appl.*, WO 2010114490 A1 20101007, 2010.

30 V. V. Levin, A. L. Trifonov, A. A. Zemtsov, M. I. Struchkova, D. E. Arkhipov and A. D. Dilman, *Org. Lett.*, 2014, **16**, 6256-6259.

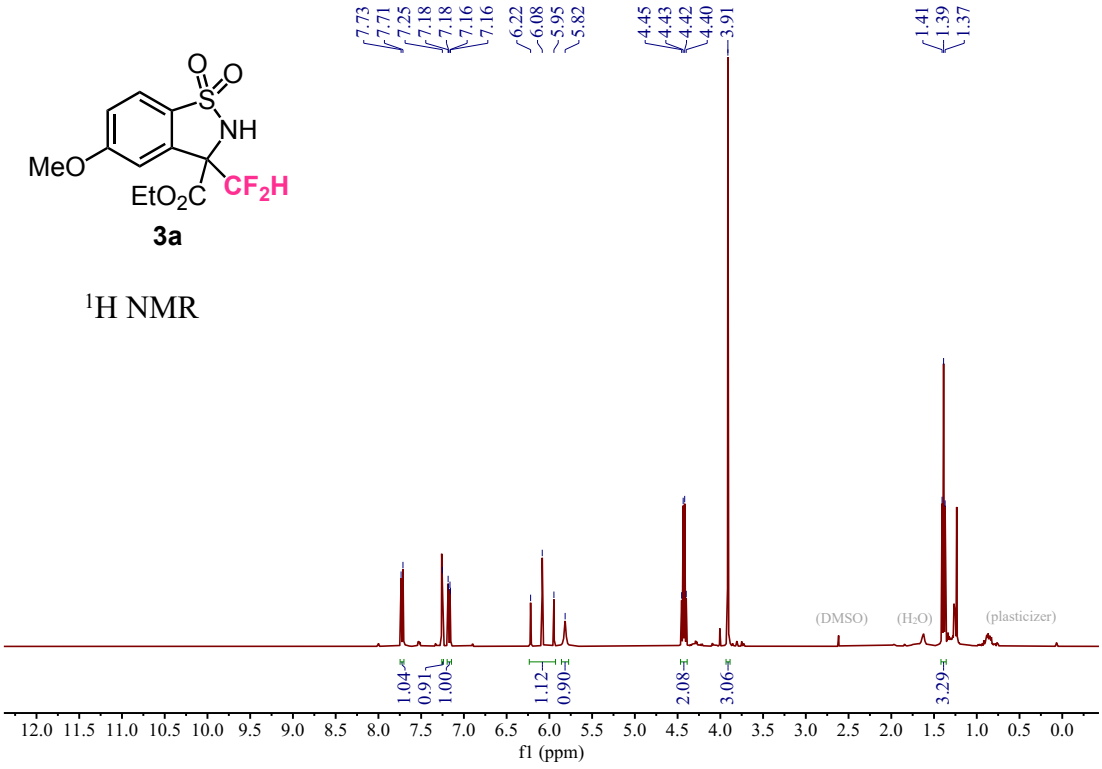
31 G. K. S. Prakash, R. Mogi and G. A. Olah, *Org. Lett.*, 2006, **8**, 3589-3592.

32 M. Pohmakotr, D. Panichakul, P. Tuchinda and V. Reutrakul, *Tetrahedron*, 2007, **63**, 9429-9436.

33 R. Sakamoto, H. Kashiwagi and K. Maruoka, *Org. Lett.*, 2017, **19**, 5126-5129.

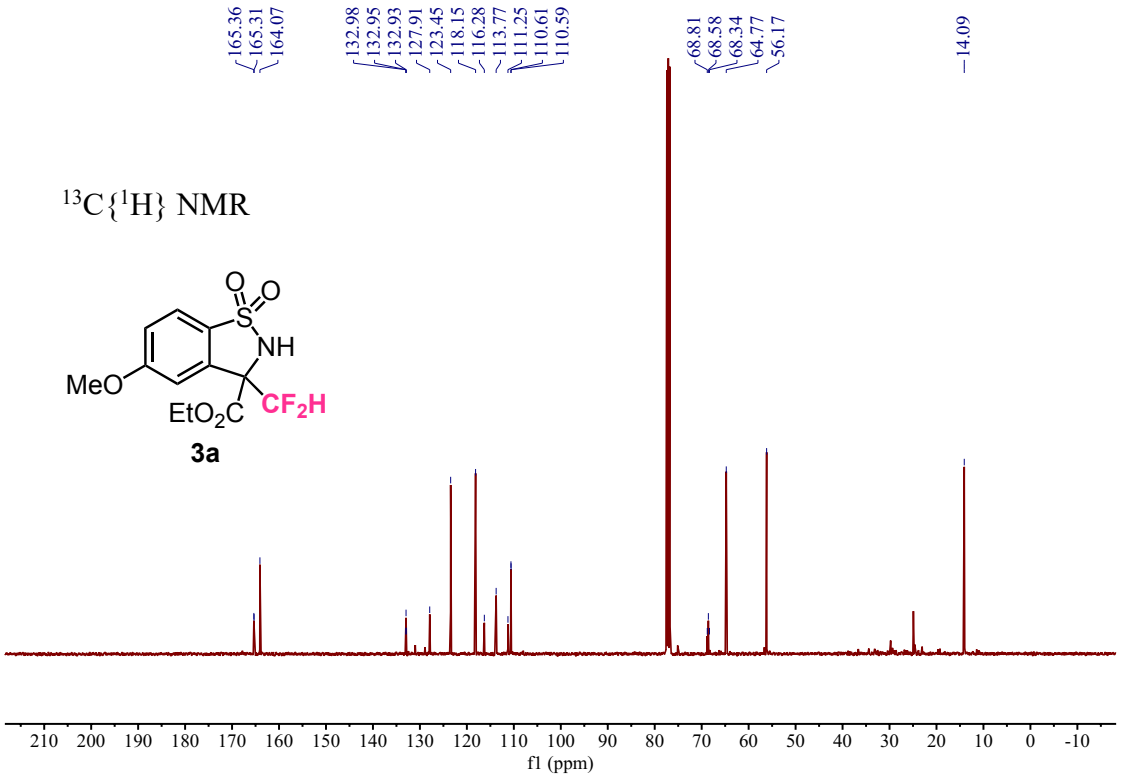
NMR charts of difluoromethylated γ-sultams 3

Note: The corresponding tautomer is included in each γ-sultam **3** (Table S2)



3a

^{1}H NMR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113.77
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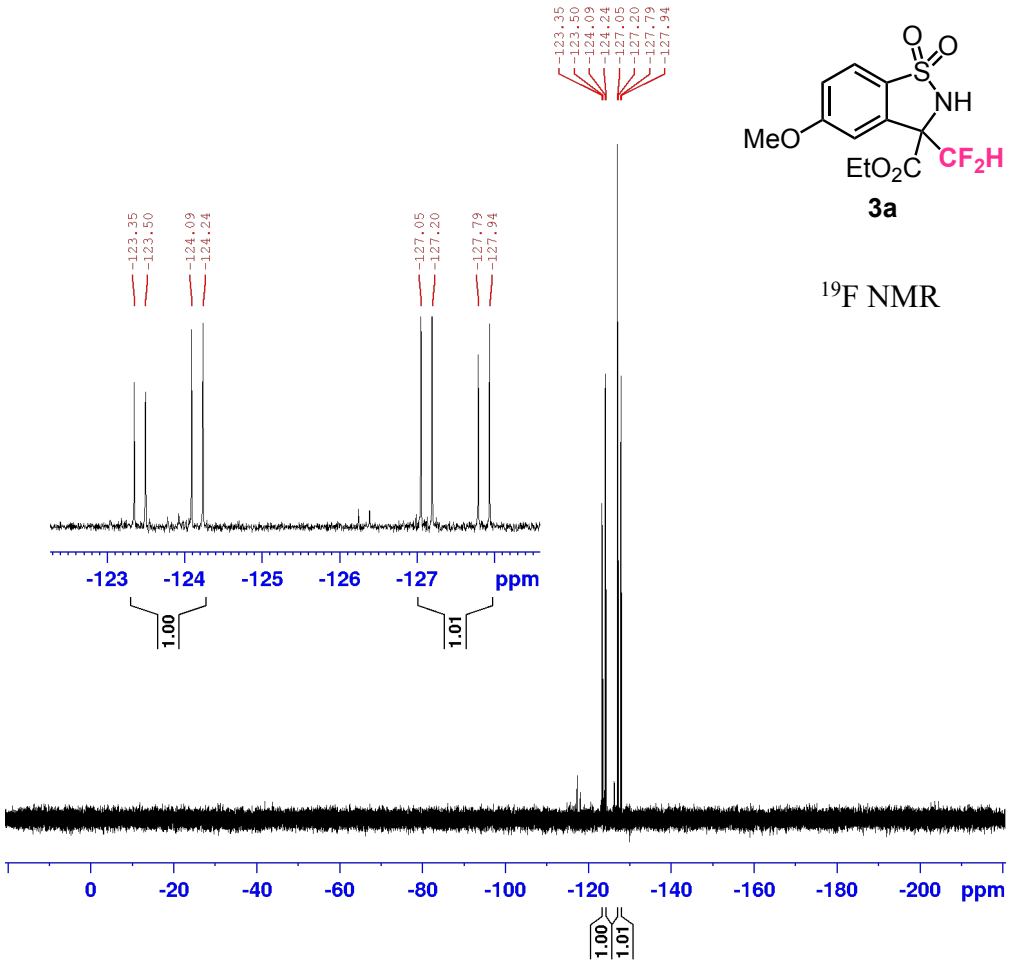
110.61
110.59
68.81
68.58
68.34
64.77
56.17
14.09
$^{13}C\{^{1}H\}$ NMR
O
O
S
NH
MeO
EtO_2C
CF_2H
3a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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ppm
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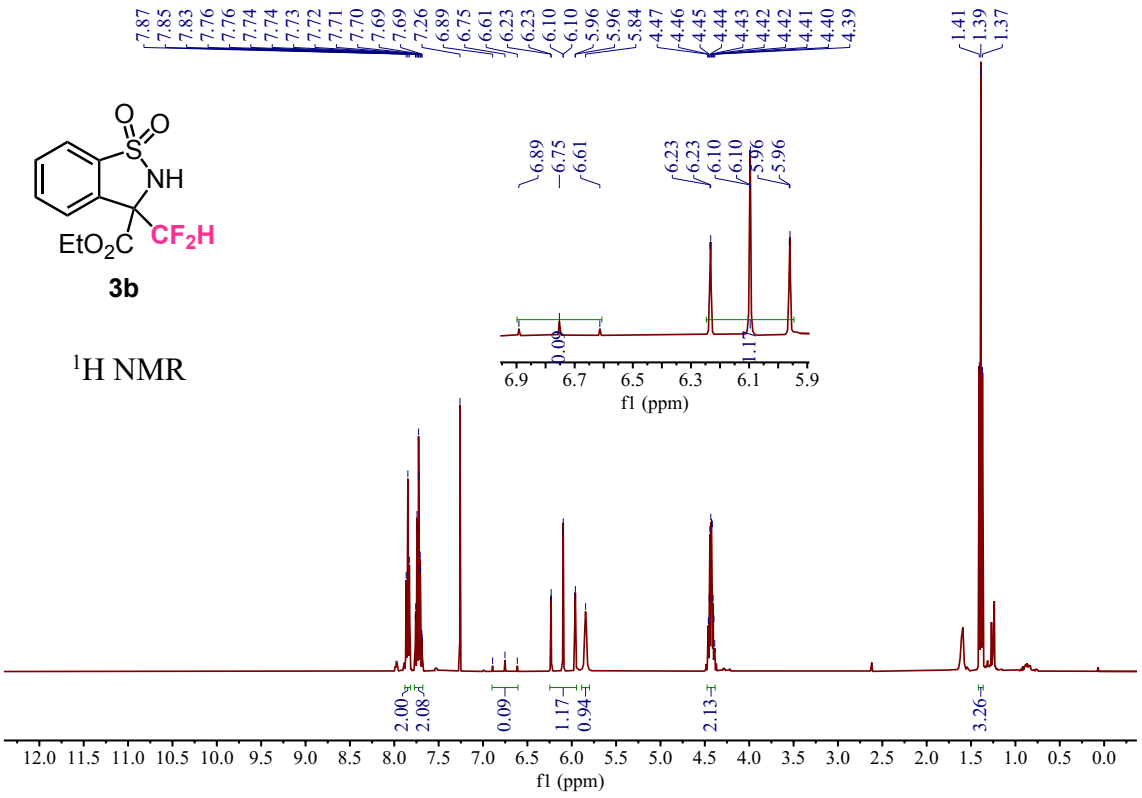
O
O
S
NH
MeO
EtO2C
CF2H

3a

^{19}F NMR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CF2H
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1H NMR
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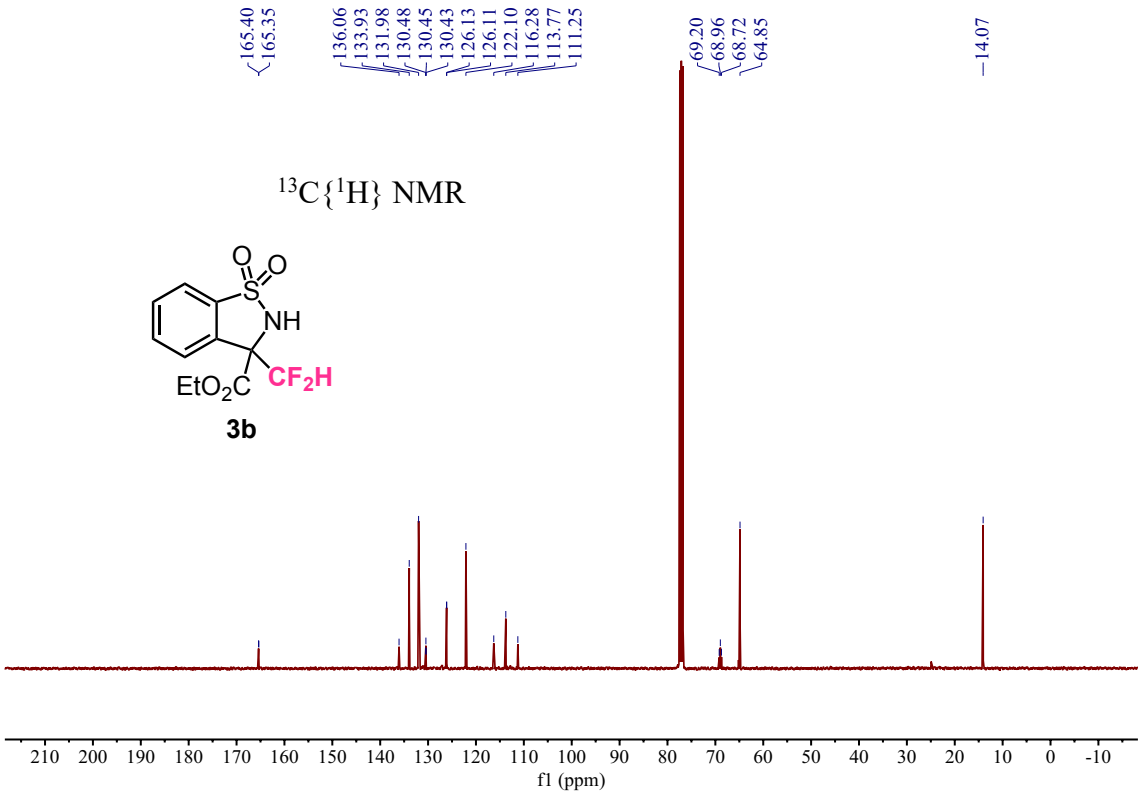
6.75
6.61
6.23
6.23
6.10
6.10
5.96
5.96
0.09
1.17
6.9 6.7 6.5 6.3 6.1 5.9
f1 (ppm)
2.00
2.08
0.09
1.17
0.94
2.13
3.26
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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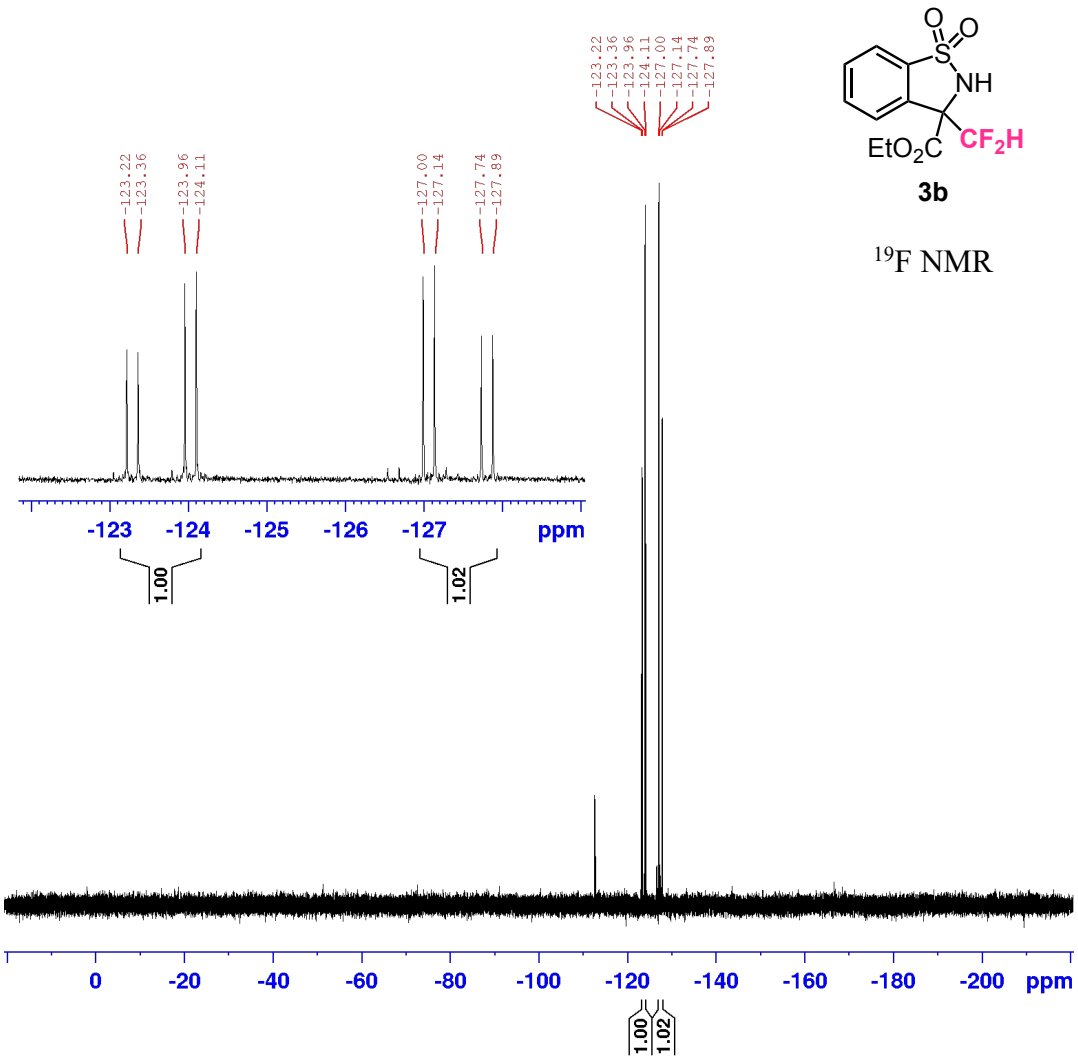
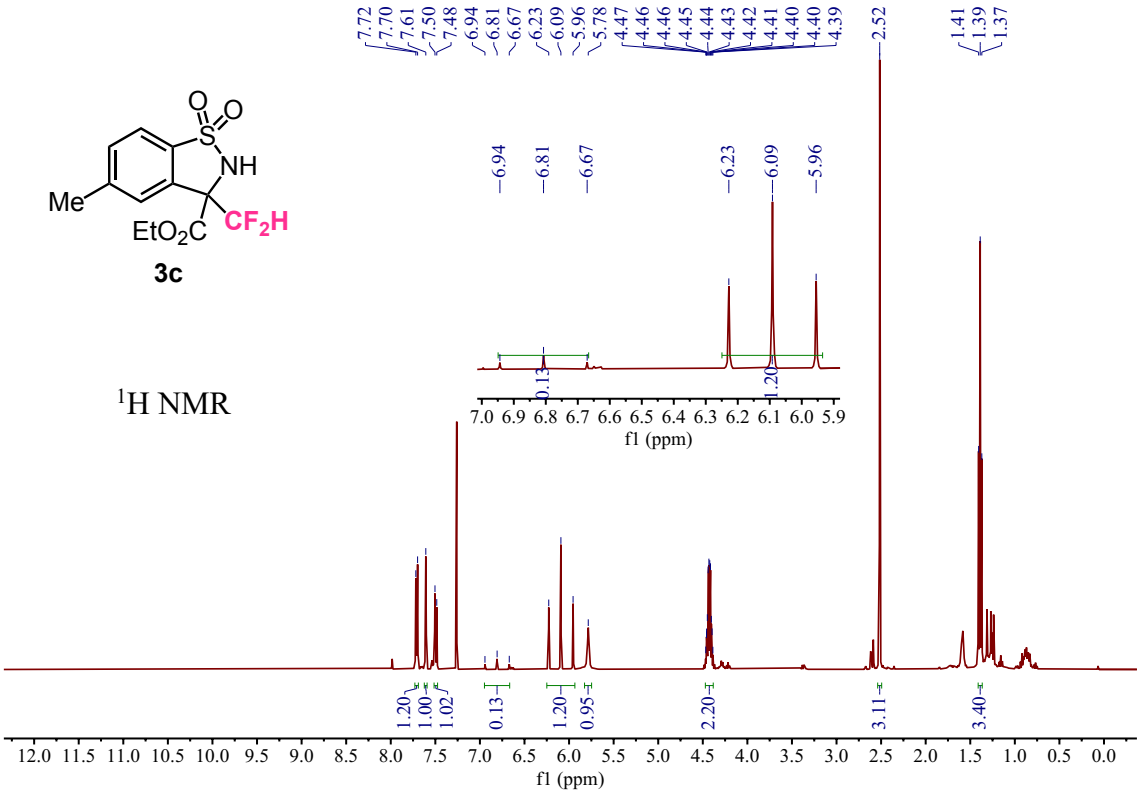
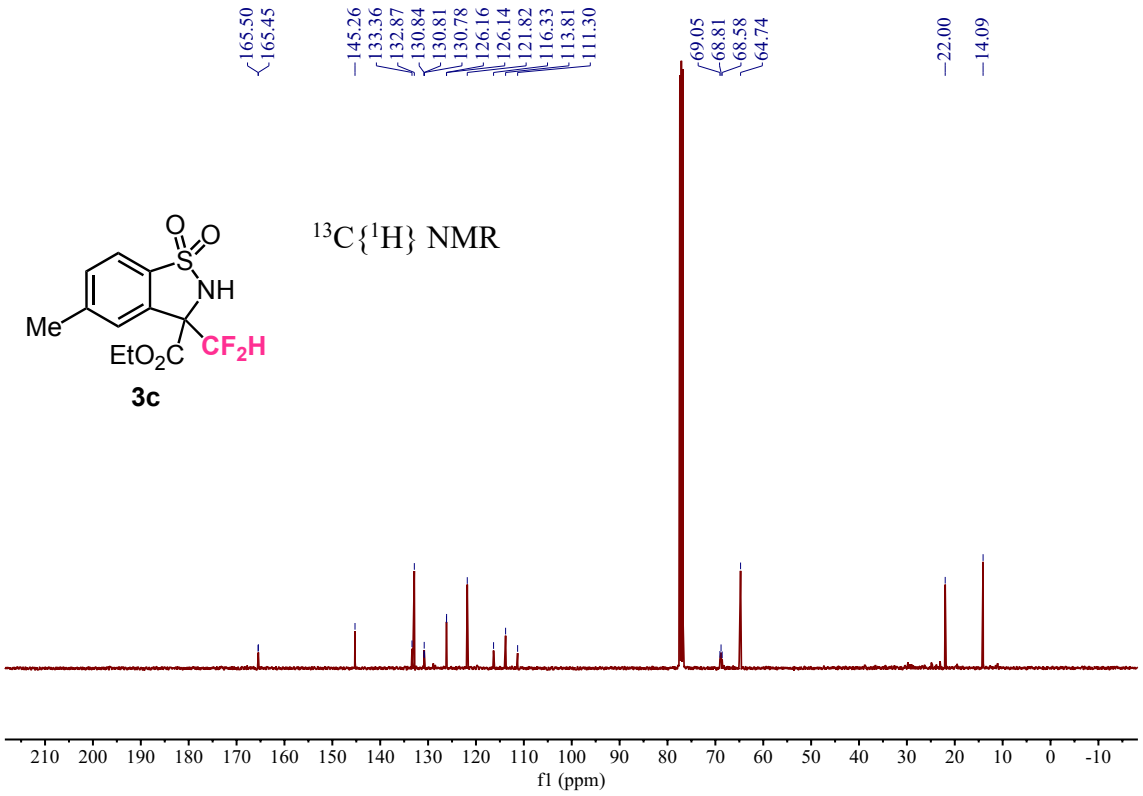
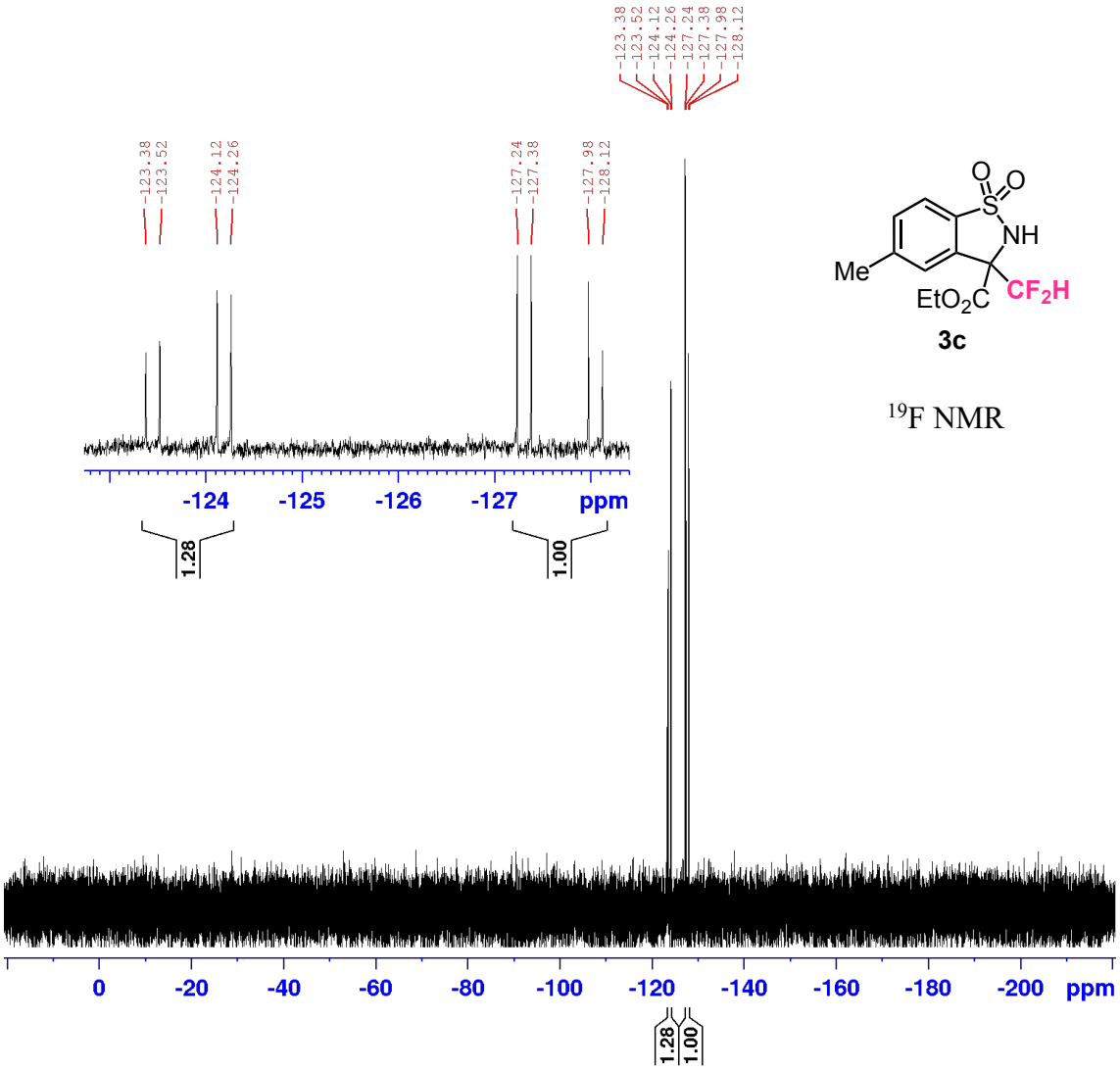
165.35
136.06
133.93
131.98
130.48
130.45
130.43
126.13
126.11
122.10
116.28
113.77
111.25
69.20
68.96
68.72
64.85
14.07
$^{13}C\{^{1}H\}$ NMR
O
O
S
NH
EtO_2C
CF_2H
3b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-123.22
-123.36
-123.96
-124.11
-127.00
-127.14
-127.74
-127.89
O
O
S
NH
EtO2C
CF2H
3b
19F NMR
-123
-124
-125
-126
-127
ppm
1.00
1.02
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
1.00
1.02


Me
EtO2C
CF2H
3c
1H NMR
f1 (ppm)

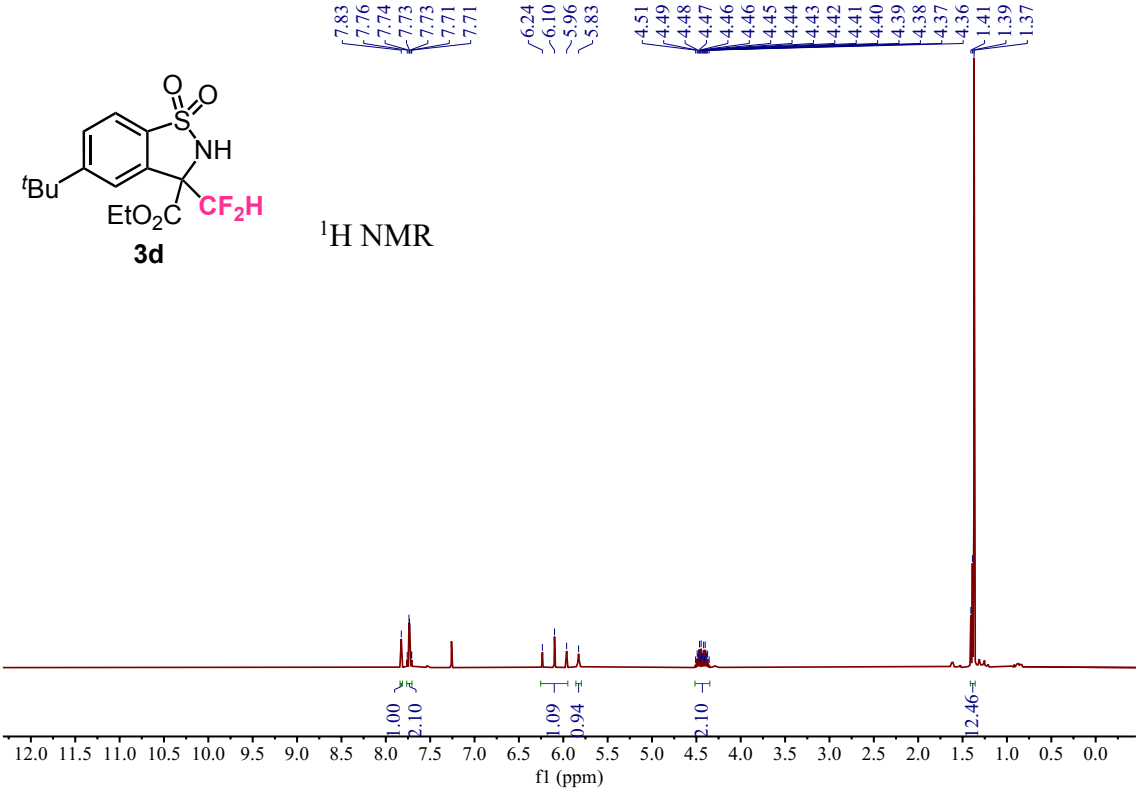

165.50
165.45
145.26
133.36
132.87
130.84
130.81
130.78
126.16
126.14
121.82
116.33
113.81
111.30
69.05
68.81
68.58
64.74
22.00
14.09
$^{13}C\{^{1}H\}$ NMR
Me
EtO_2C
CF_2H
3c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

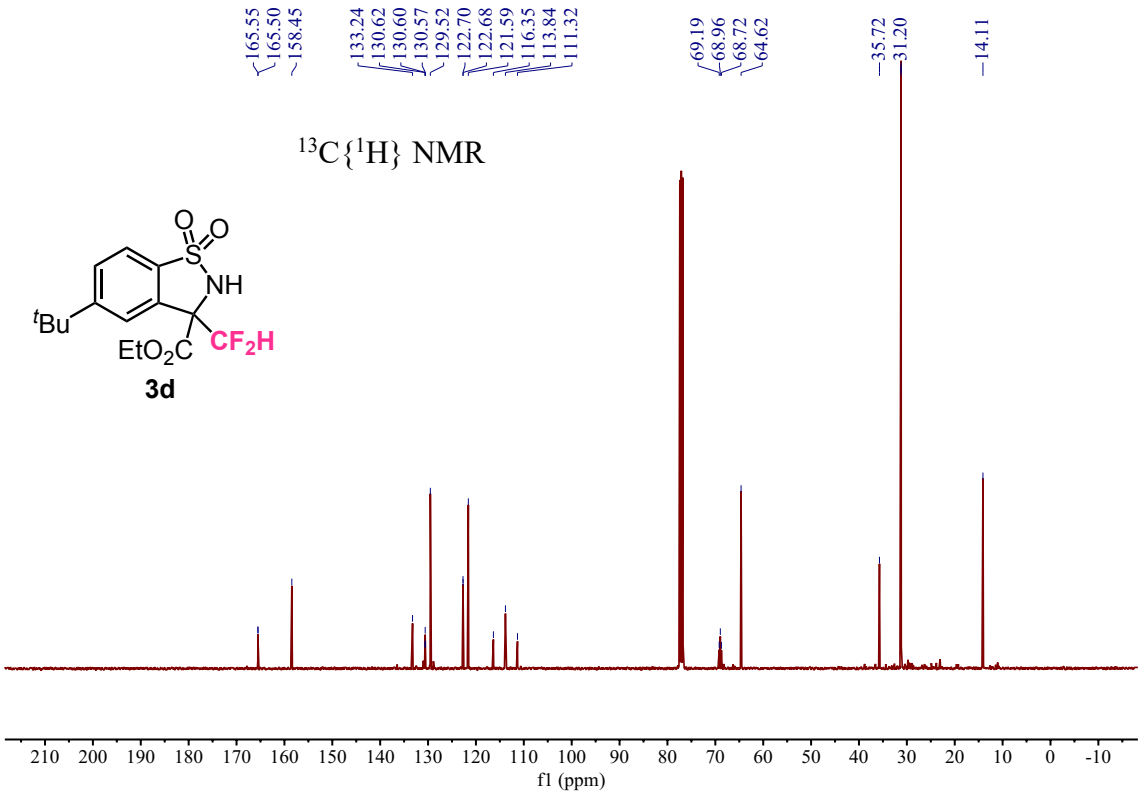

-123.38
-123.52
-124.12
-124.26
-127.24
-127.38
-127.98
-128.12
-124
-125
-126
-127
ppm
1.28
1.00
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
1.28
1.00

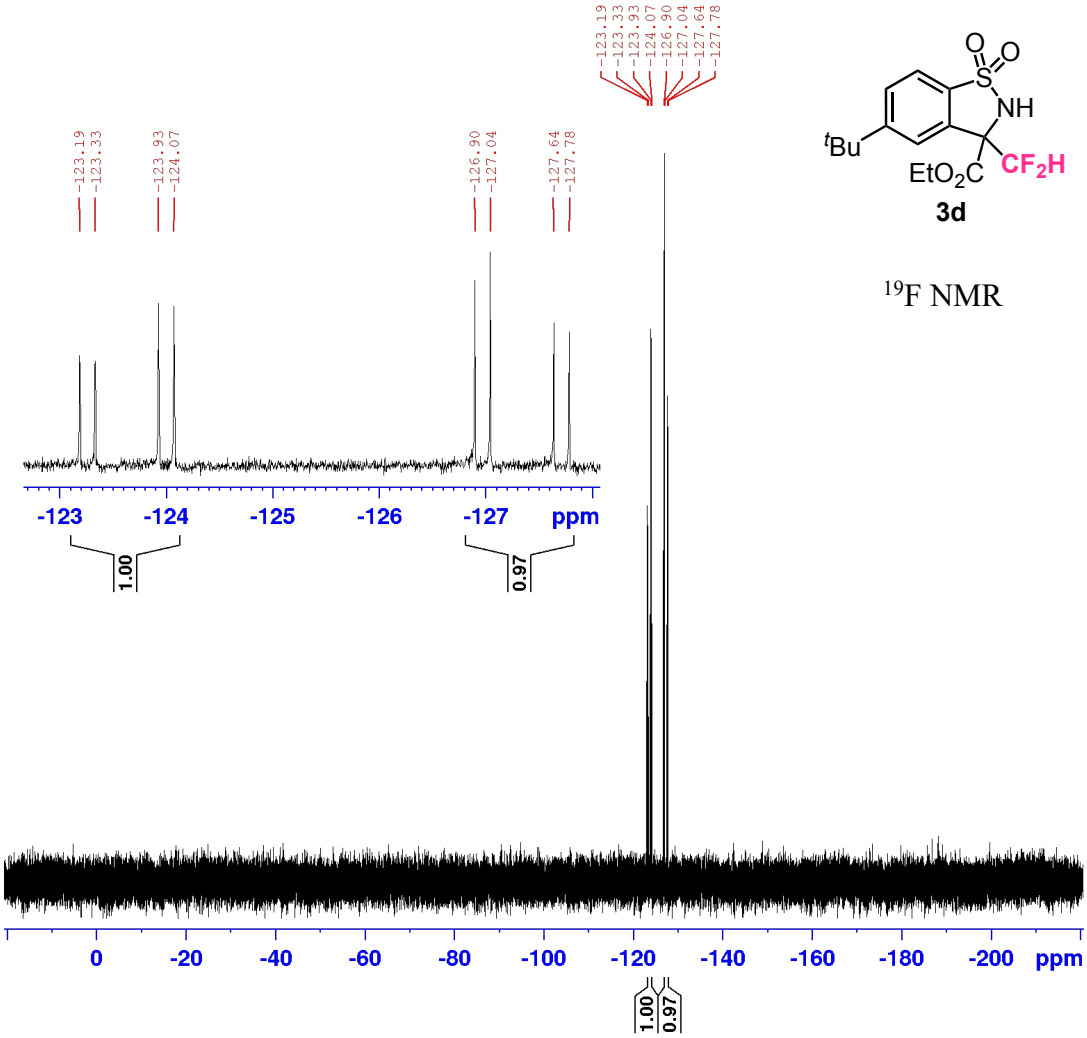
O
O
S
NH
Me
EtO2C
CF2H

3c

^{19}F NMR


7.83
7.76
7.74
7.73
7.73
7.71
7.71
6.24
6.10
5.96
5.83
4.51
4.49
4.48
4.47
4.46
4.46
4.45
4.44
4.43
4.42
4.41
4.40
4.39
4.38
4.37
4.36
1.41
1.39
1.37
O
O
S
NH
tBu
EtO2C
CF2H
3d
1H NMR
1.00
2.10
1.09
0.94
2.10
12.46
12.0 11.5 11.0 10.5 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)

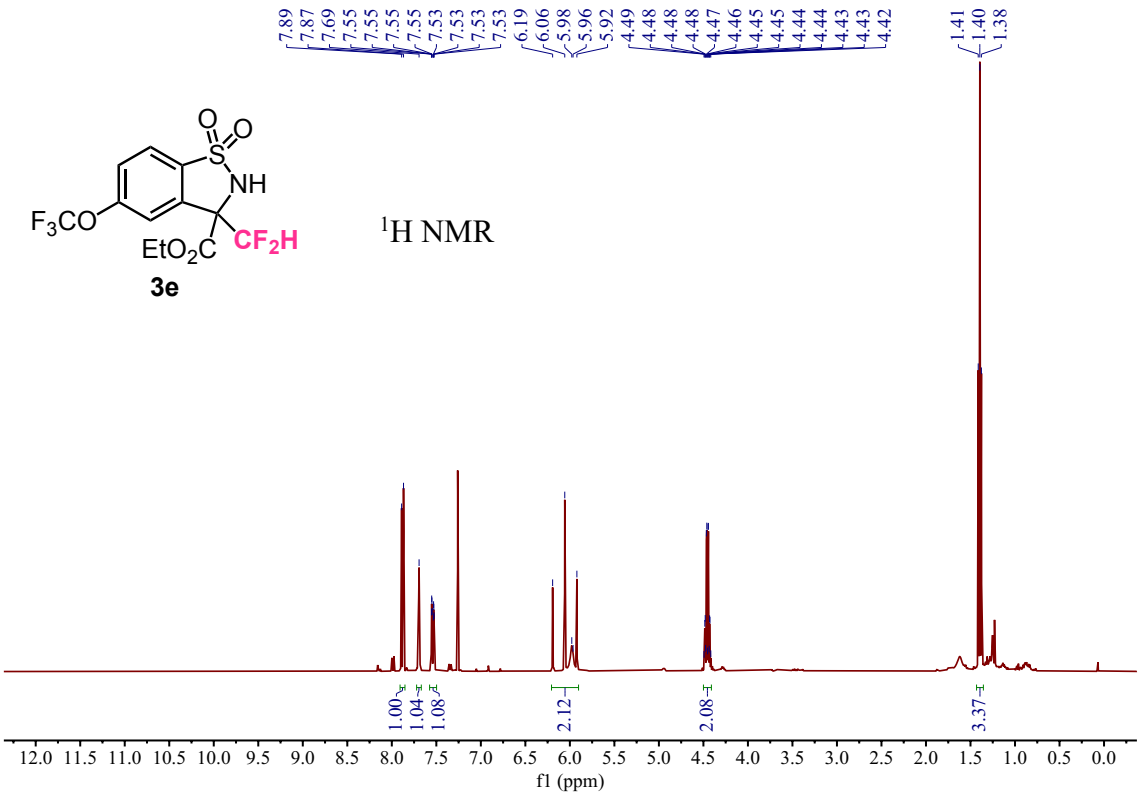

165.55
165.50
158.45
133.24
130.62
130.60
130.57
129.52
122.70
122.68
121.59
116.35
113.84
111.32
69.19
68.96
68.72
64.62
35.72
31.20
14.11
$^{13}C\{^{1}H\}$ NMR
O
O
S
NH
^{t}Bu
EtO_2C
CF_2H
3d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

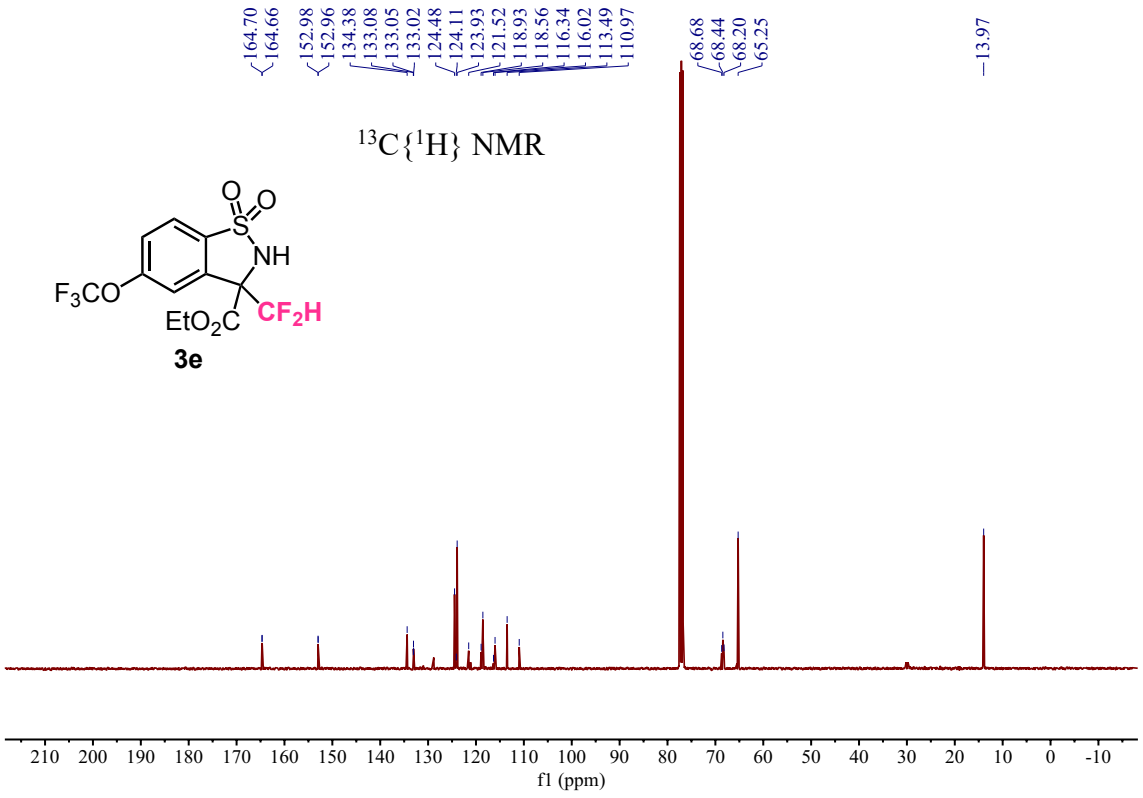

-123.19
-123.33
-123.93
-124.07
-126.90
-127.04
-127.64
-127.78
-123
-124
-125
-126
-127
ppm
1.00
0.97
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
1.00
0.97

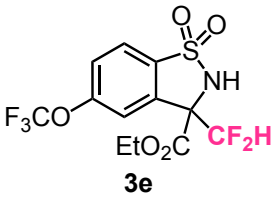
O
O
S
NH
tBu
EtO2C
CF2H

3d

^{19}F NMR


7.89
7.87
7.69
7.55
7.55
7.55
7.55
7.53
7.53
7.53
7.53
6.19
6.06
5.98
5.96
5.92
4.49
4.48
4.48
4.48
4.47
4.46
4.45
4.45
4.44
4.44
4.43
4.43
4.42
1.41
1.40
1.38
O
O
S
NH
F3CO
EtO2C
CF2H
3e
1H NMR
1.00
1.04
1.08
2.12
2.08
3.37
12.0 11.5 11.0 10.5 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)

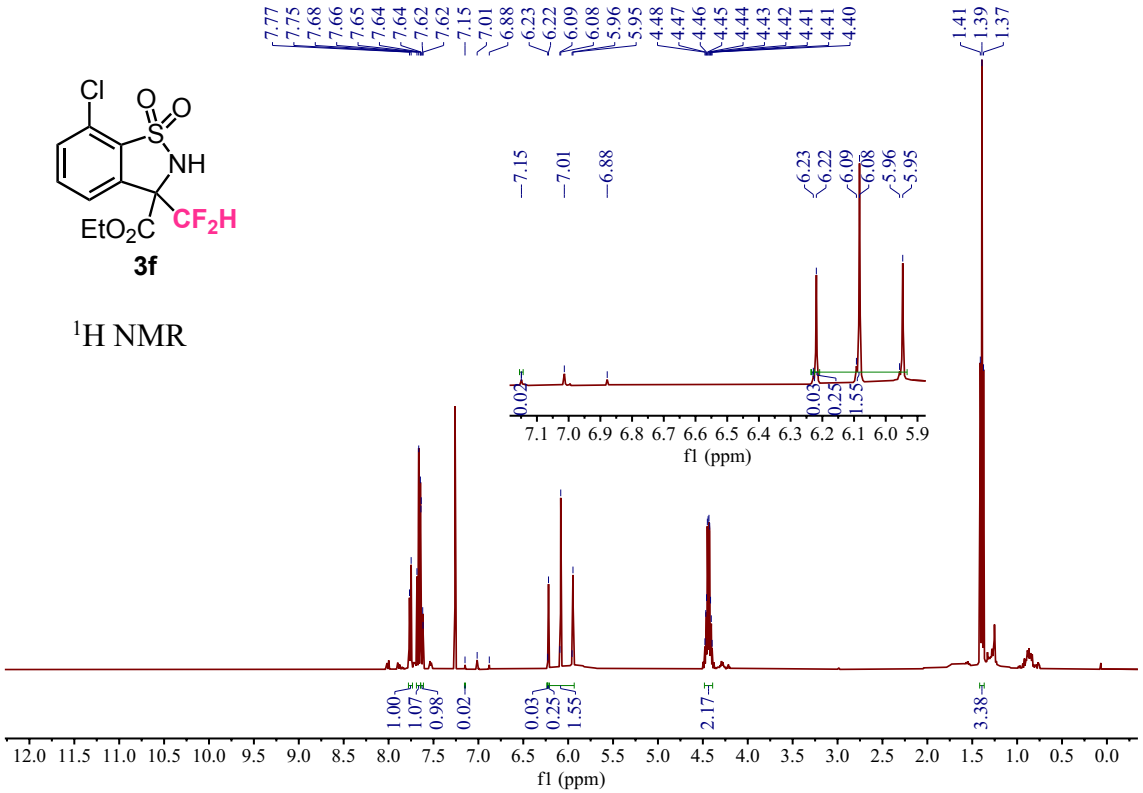

164.70
164.66
152.98
152.96
134.38
133.08
133.05
133.02
124.48
124.11
123.93
121.52
118.93
118.56
116.34
116.02
113.49
110.97
68.68
68.44
68.20
65.25
13.97
$^{13}C\{^{1}H\}$ NMR
O
O
S
NH
F_3CO
EtO_2C
CF_2H
3e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

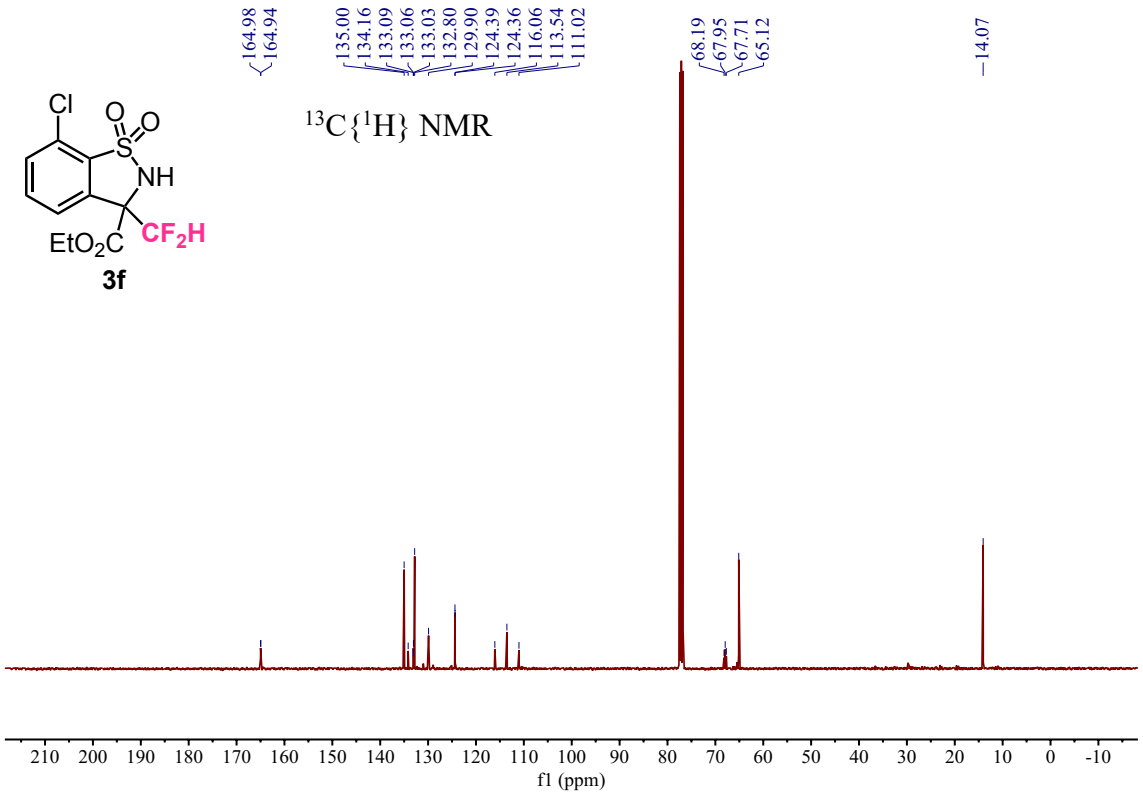

O
O
S
NH
F3CO
EtO2C
CF2H

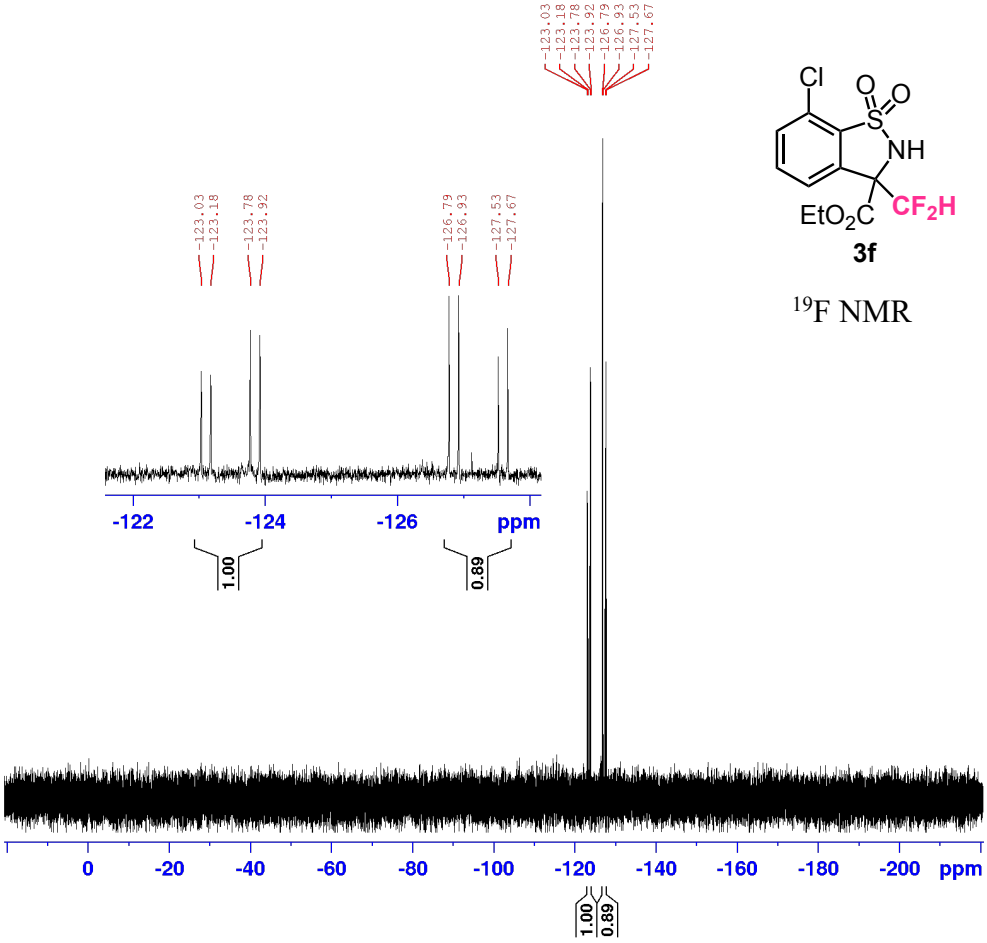
3e

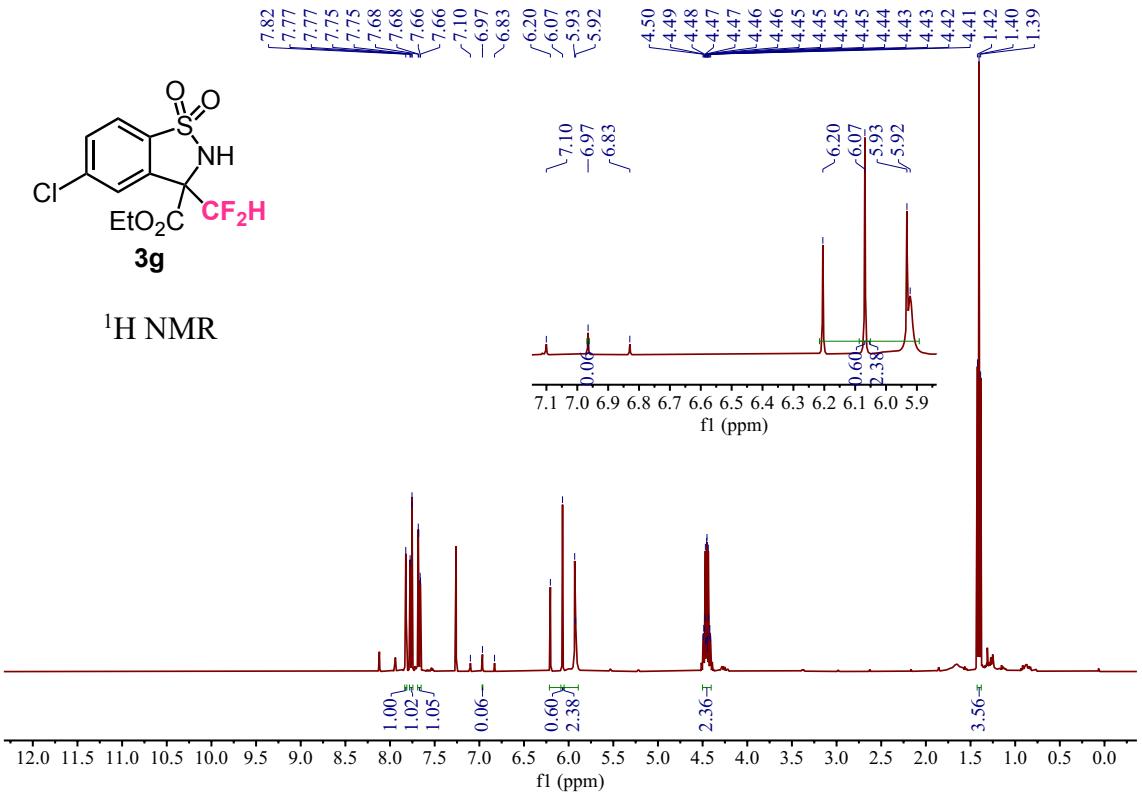
^{19}F NMR

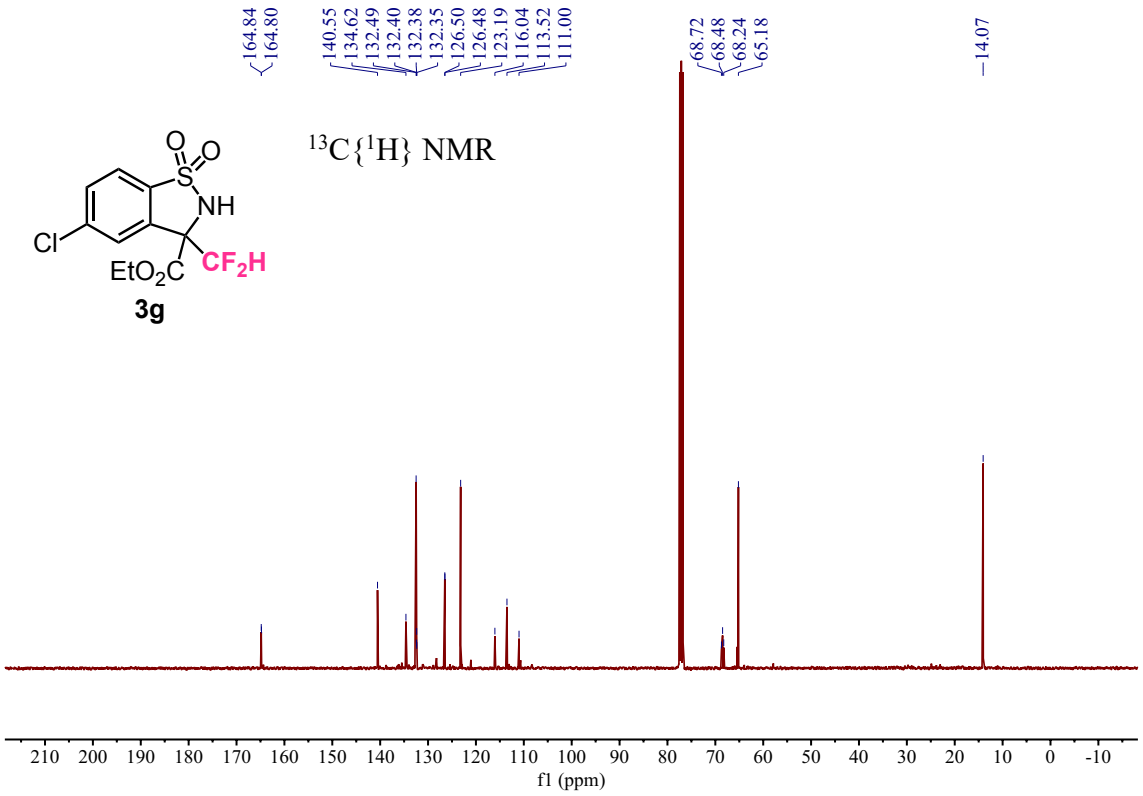
-57.89
-122.97
-123.12
-123.72
-123.86
-126.26
-126.40
-127.00
-127.15
-123
-124
-125
-126
ppm
0.50
0.67
0.77
0.45
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
3.00
0.50
0.67
0.77
0.45

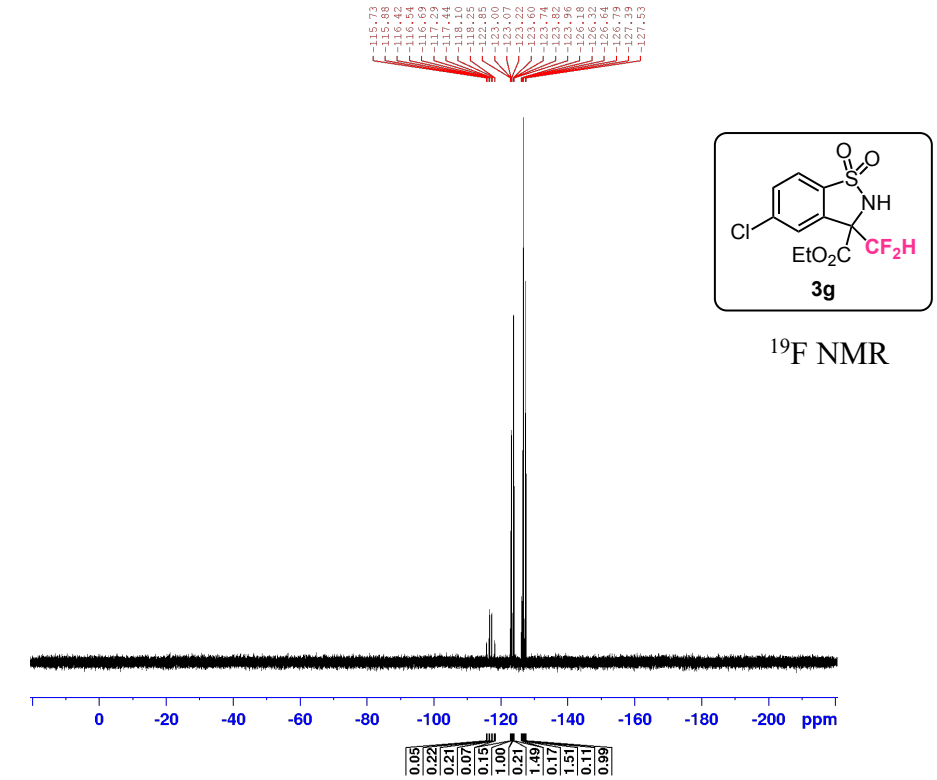

Cl
O
O
S
NH
EtO2C
CF2H
3f
1H NMR
7.77
7.75
7.68
7.66
7.65
7.64
7.64
7.62
7.62
7.15
7.01
6.88
6.23
6.22
6.09
6.08
5.96
5.95
4.48
4.47
4.46
4.45
4.44
4.43
4.42
4.41
4.41
4.40
1.41
1.39
1.37
1.00
1.07
0.98
0.02
0.03
0.25
1.55
2.17
3.38
f1 (ppm)

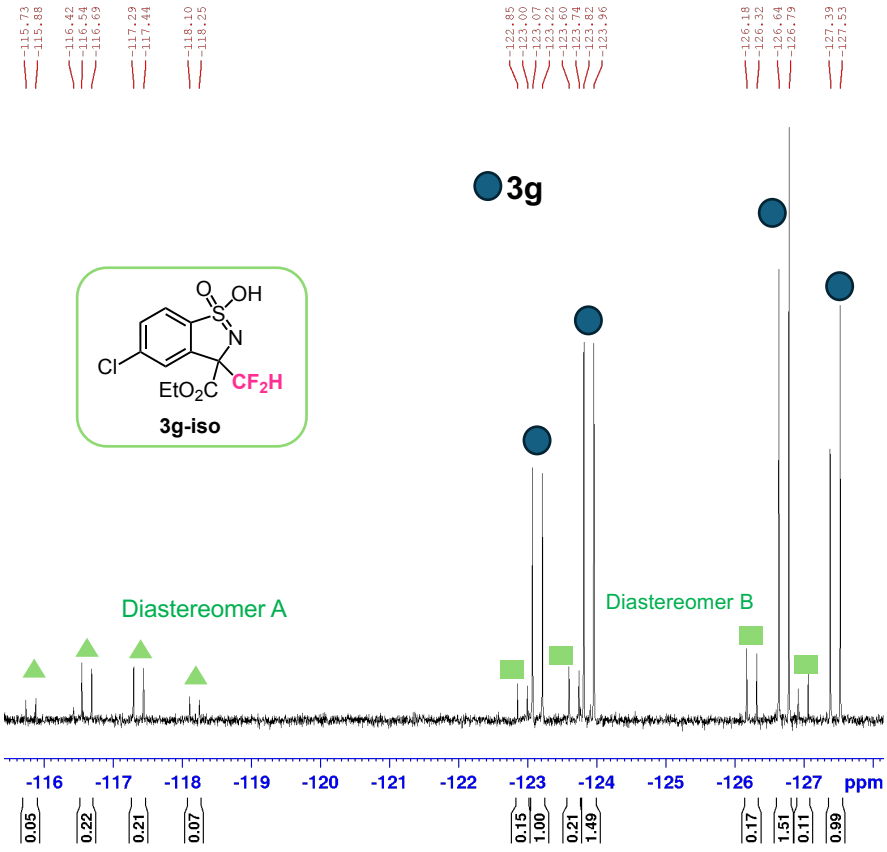

164.98
164.94
135.00
134.16
133.09
133.06
133.03
132.80
129.90
124.39
124.36
116.06
113.54
111.02
68.19
67.95
67.71
65.12
14.07
Cl
O
O
S
NH
EtO2C
CF2H
3f
13C{1H} NMR
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

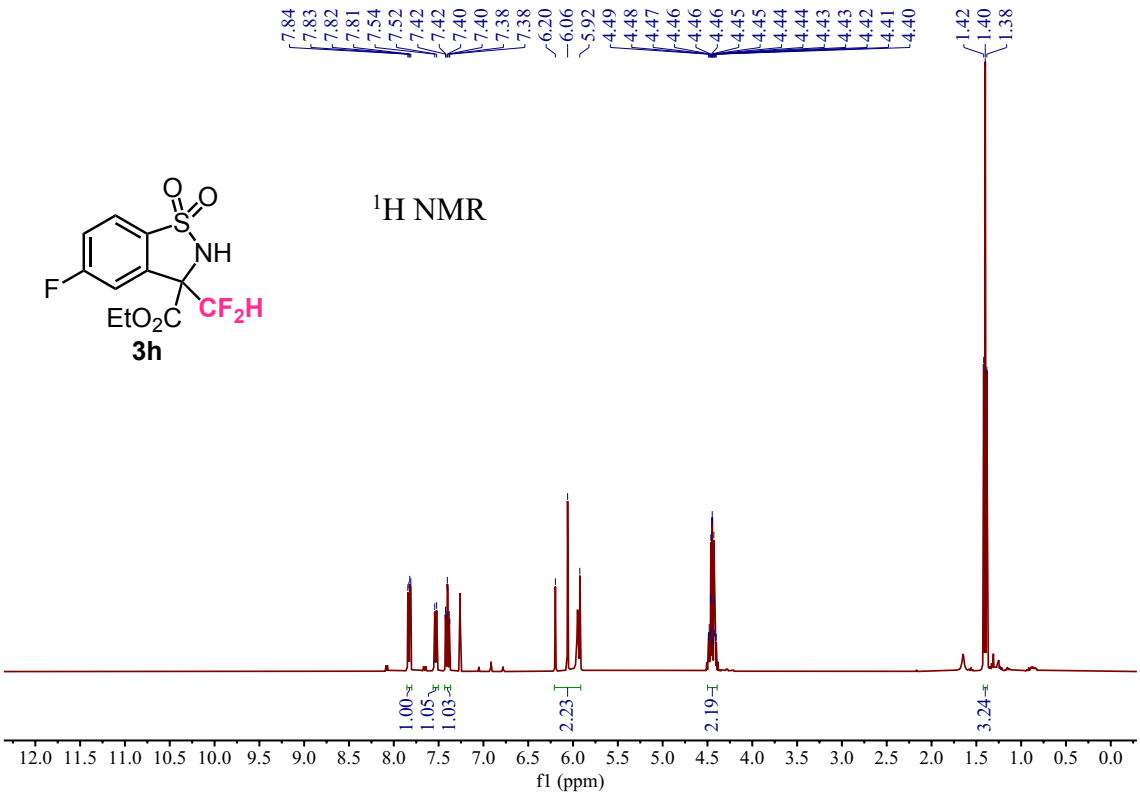

-123.03
-123.18
-123.78
-123.92
-126.79
-126.93
-127.53
-127.67
Cl
O
O
S
NH
EtO2C
CF2H
3f
19F NMR
-122
-124
-126
ppm
1.00
0.89
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
1.00
0.89

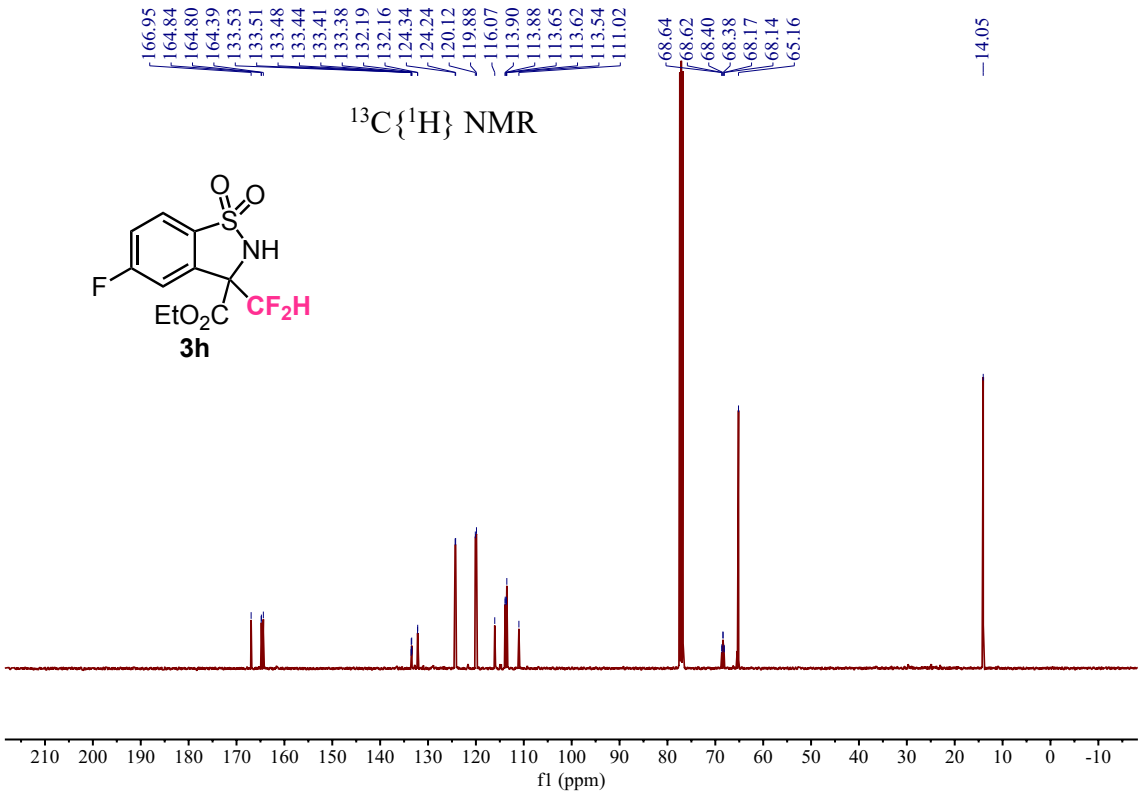

Cl
EtO2C
CF2H
3g
1H NMR
f1 (ppm)

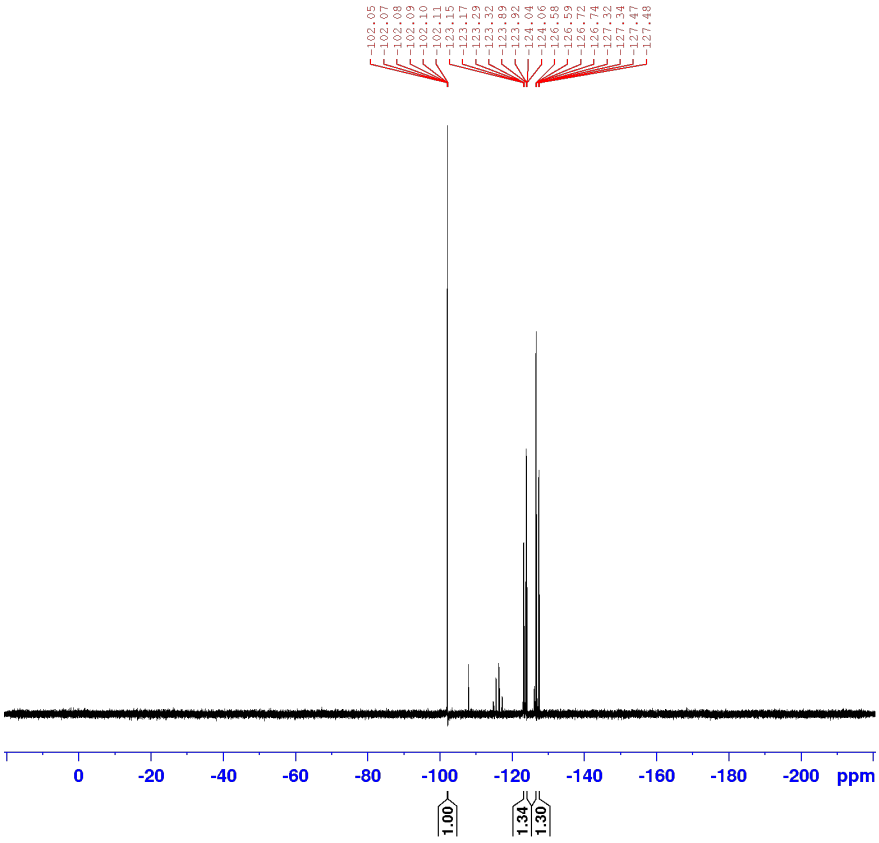

164.84
164.80
140.55
134.62
132.49
132.40
132.38
132.35
126.50
126.48
123.19
116.04
113.52
111.00
68.72
68.48
68.24
65.18
14.07
$^{13}C\{^{1}H\}$ NMR
Cl
NH
EtO_2C
CF_2H
3g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

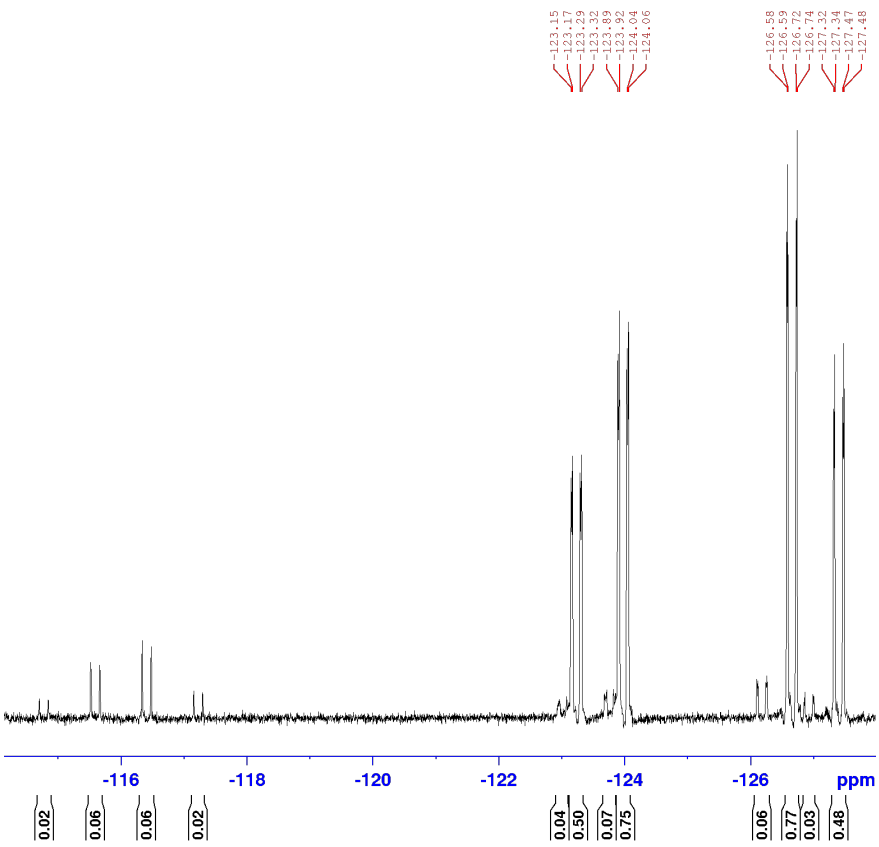

3g
^{19}F NMR
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

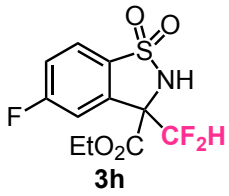

3g
3g-iso
Diastereomer A
Diastereomer B
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
-127
ppm


7.84
7.83
7.82
7.81
7.54
7.52
7.42
7.42
7.40
7.40
7.38
7.38
6.20
6.06
5.92
4.49
4.48
4.47
4.46
4.46
4.46
4.45
4.45
4.44
4.44
4.43
4.43
4.42
4.41
4.40
1.42
1.40
1.38
O
O
S
NH
F
EtO2C
CF2H
3h
1H NMR
1.00
1.05
1.03
2.23
2.19
3.24
12.0 11.5 11.0 10.5 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)


166.95
164.84
164.80
164.39
133.53
133.51
133.48
133.44
133.41
133.38
132.19
132.16
124.34
124.24
120.12
119.88
116.07
113.90
113.88
113.65
113.62
113.54
111.02
68.64
68.62
68.40
68.38
68.17
68.14
65.16
14.05
13C{1H} NMR
O
O
S
NH
F
EtO2C
CF2H
3h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

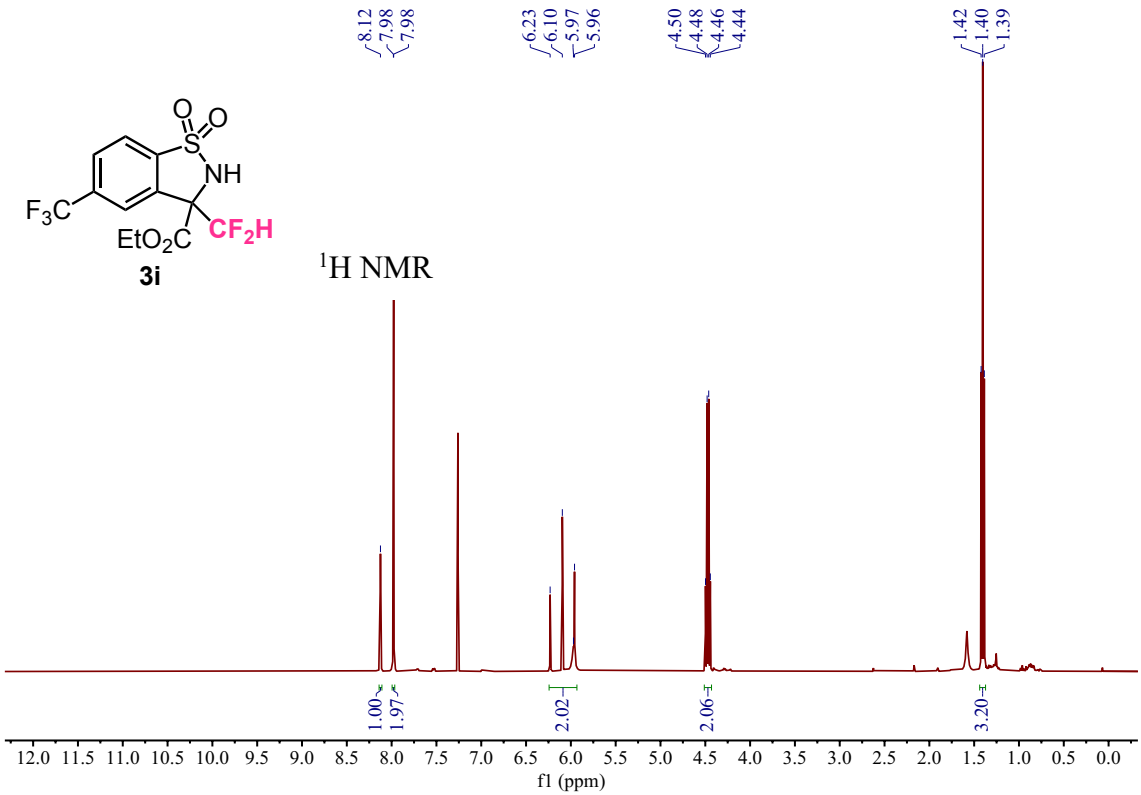

-102.05
-102.07
-102.08
-102.09
-102.10
-102.11
-123.15
-123.17
-123.29
-123.32
-123.89
-123.92
-124.04
-124.06
-126.58
-126.59
-126.72
-126.74
-127.32
-127.34
-127.47
-127.48
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
1.00
1.34
1.30

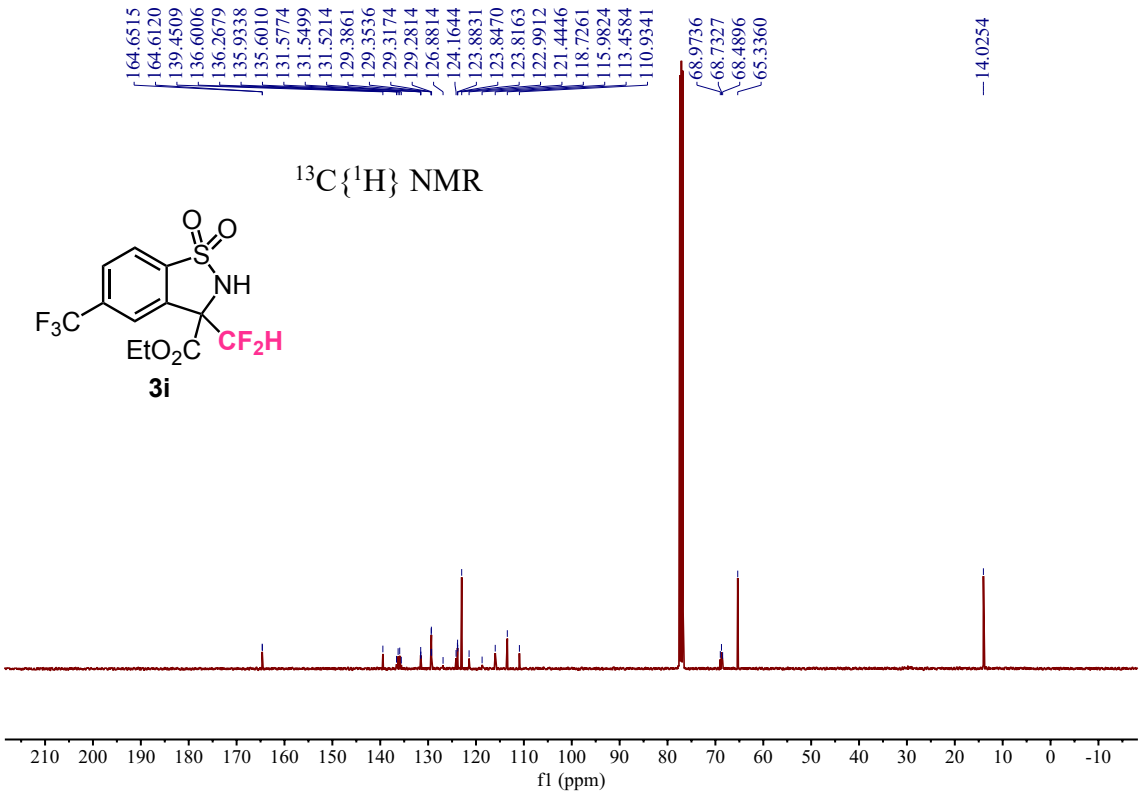

-123.15
-123.17
-123.29
-123.32
-123.89
-123.92
-124.04
-124.06
-126.58
-126.59
-126.72
-126.74
-127.32
-127.34
-127.47
-127.48
-116
-118
-120
-122
-124
-126
ppm
0.02
0.06
0.06
0.02
0.04
0.50
0.07
0.75
0.06
0.77
0.03
0.48


O
O
S
NH
F
CF2H
EtO2C

3h

^{19}F NMR


8.12
7.98
7.98
6.23
6.10
5.97
5.96
4.50
4.48
4.46
4.44
1.42
1.40
1.39
O
O
S
NH
F3C
EtO2C
CF2H
3i
1H NMR
1.00
1.97
2.02
2.06
3.20
12.0 11.5 11.0 10.5 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)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164.6120
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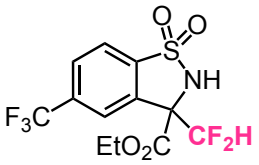
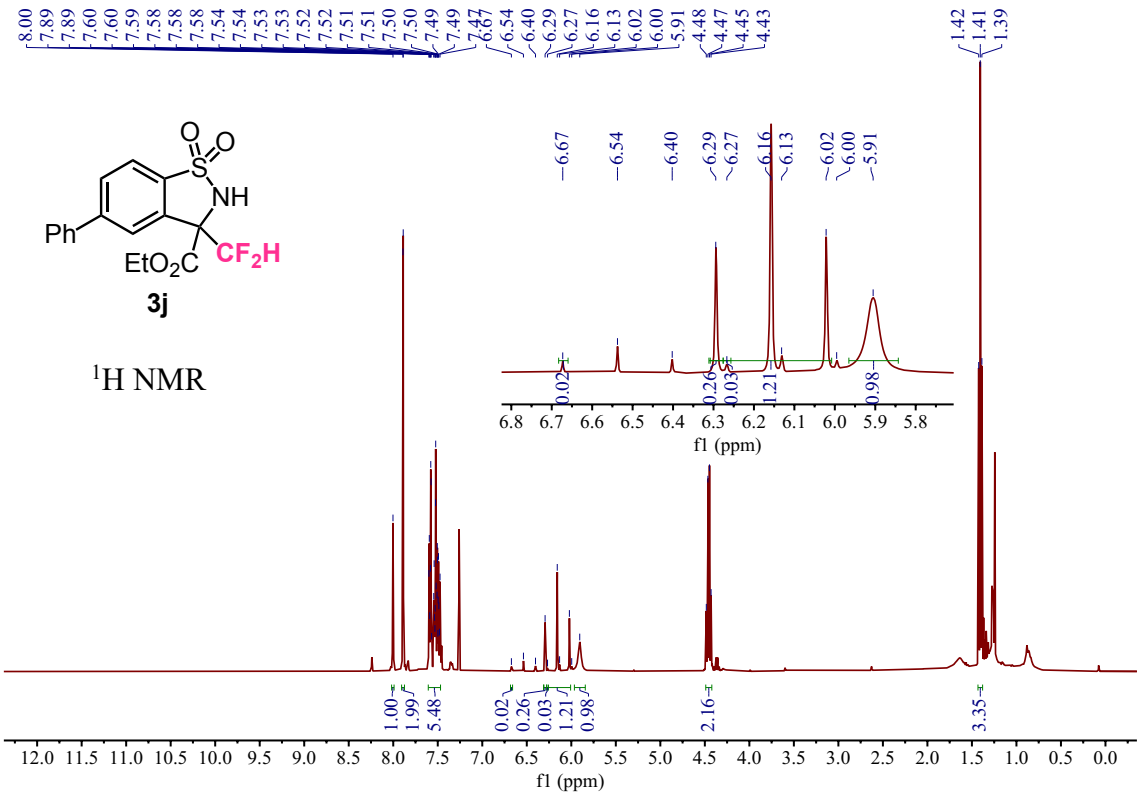
136.6006
136.2679
135.9338
135.6010
131.5774
131.5499
131.5214
129.3861
129.3536
129.3174
129.2814
126.8814
124.1644
123.8831
123.8470
123.8163
122.9912
121.4446
118.7261
115.9824
113.4584
110.9341
68.9736
68.7327
68.4896
65.3360
14.0254
$^{13}C\{^{1}H\}$ NMR
O
O
S
NH
F_3C
EtO_2C
CF_2H
3i
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

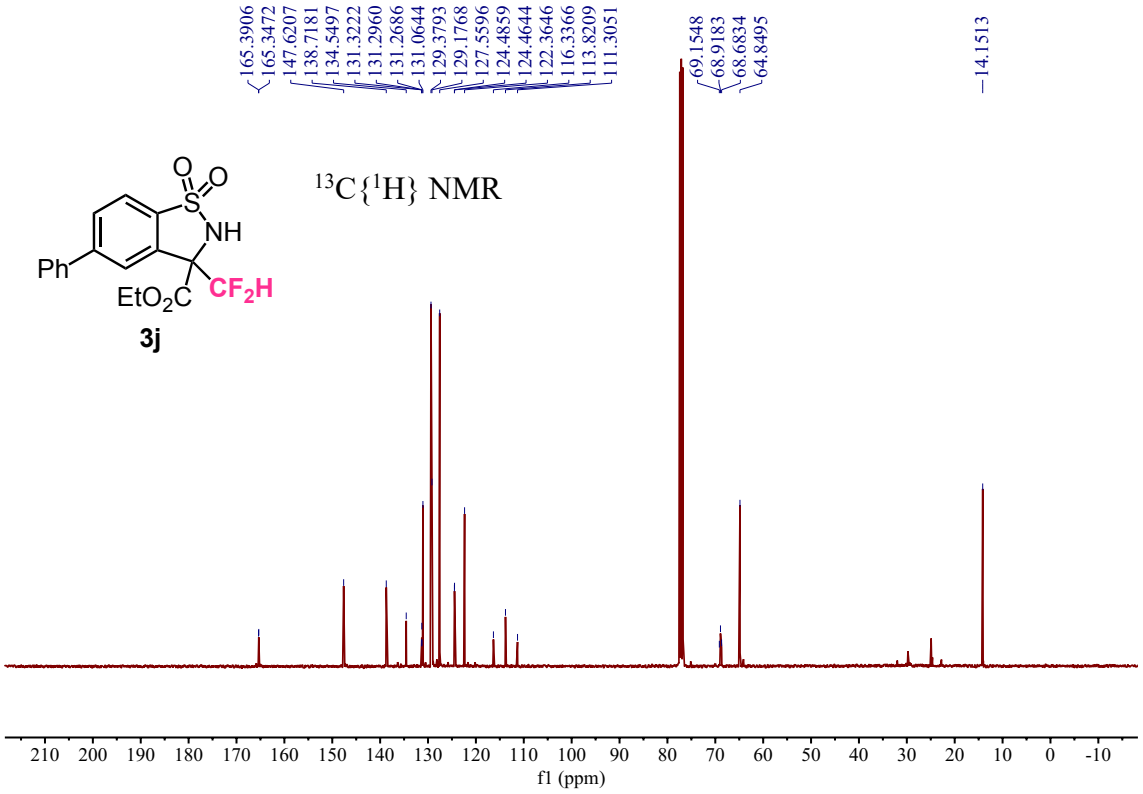

O
O
S
NH
F3C
EtO2C
CF2H

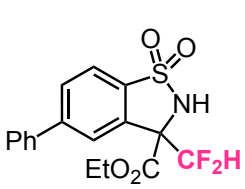
3i

^{19}F NMR

-62.89
-122.91
-123.05
-123.65
-123.80
-126.30
-126.44
-127.05
-127.19
-123
-124
-125
-126
ppm
1.22
1.25
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
3.00
1.22
1.25

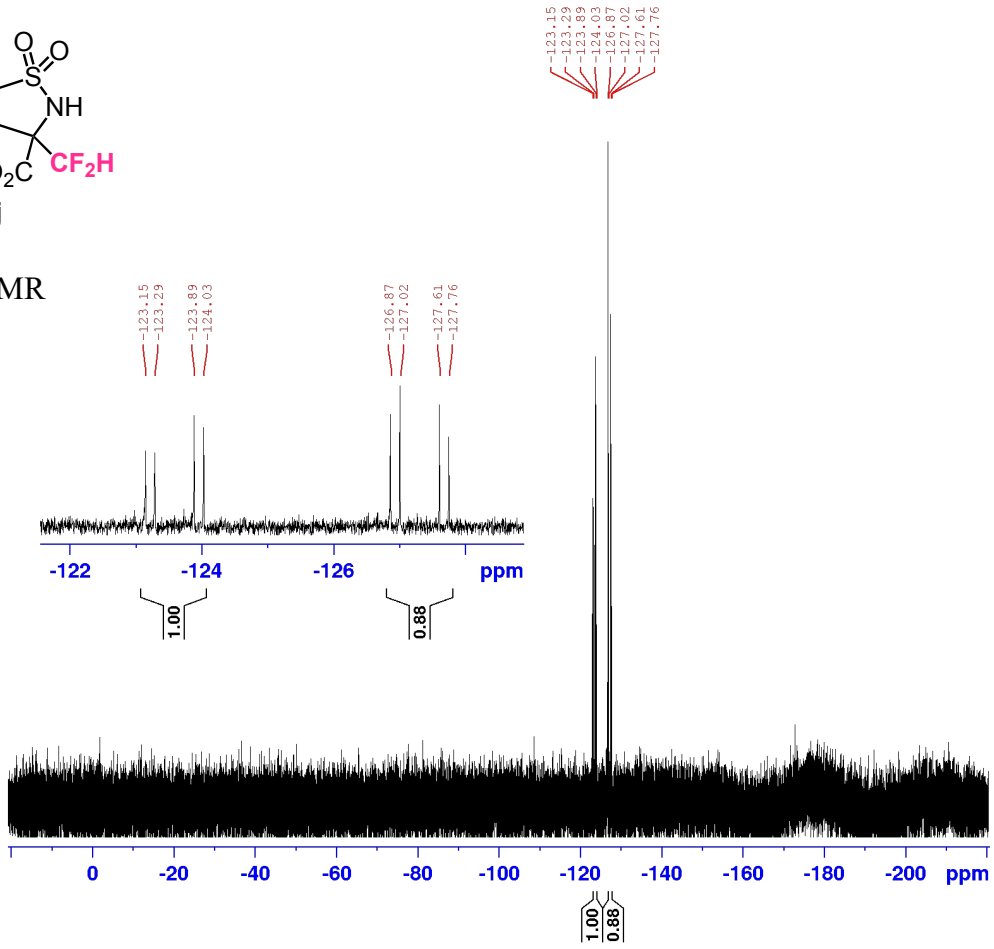

8.00 7.89 7.89 7.60 7.60 7.59 7.58 7.58 7.58 7.54 7.54 7.53 7.53 7.52 7.52 7.51 7.51 7.50 7.50 7.49 7.49 7.47 6.67 6.54 6.40 6.29 6.27 6.16 6.13 6.02 6.00 5.91 4.48 4.47 4.45 4.43 1.42 1.41 1.39
O
O
S
NH
Ph
CF2H
EtO2C
3j
1H NMR
6.67 6.54 6.40 6.29 6.27 6.16 6.13 6.02 6.00 5.91
0.02 0.26 0.03 1.21 0.98
6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8
f1 (ppm)
1.00 1.99 5.48 0.02 0.26 0.03 1.21 0.98 2.16 3.35
12.0 11.5 11.0 10.5 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)

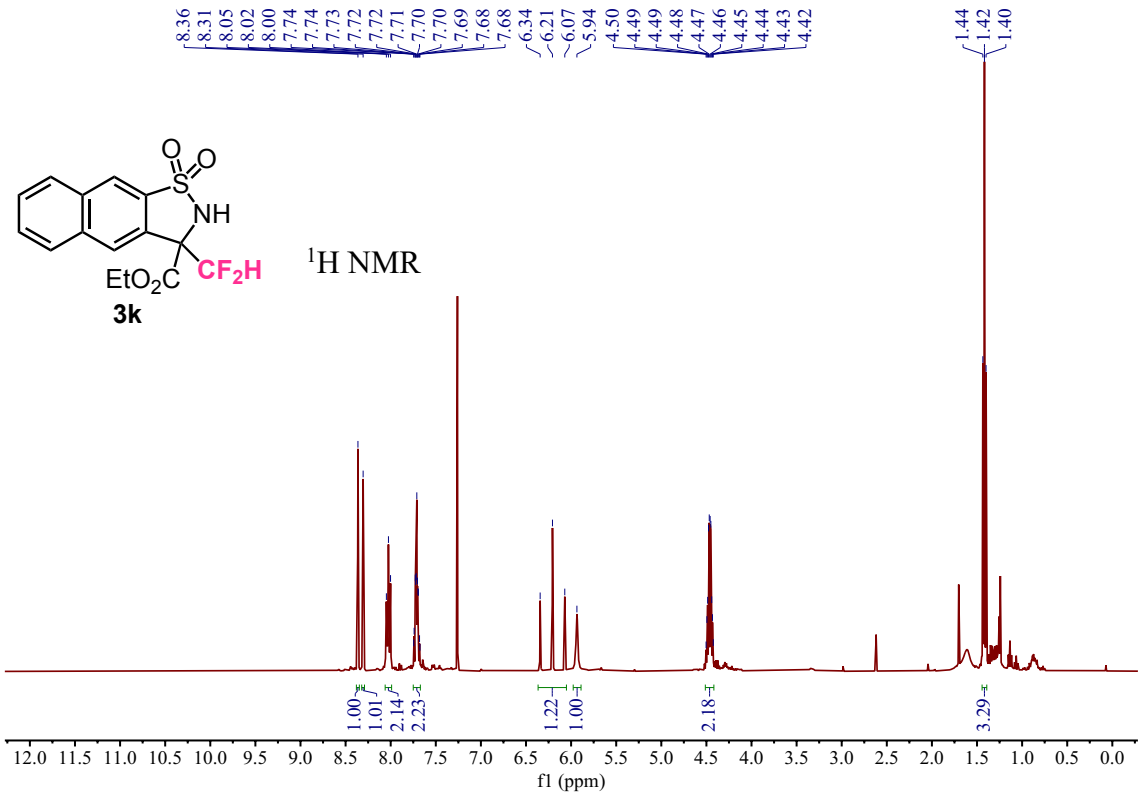

165.3906
165.3472
147.6207
138.7181
134.5497
131.3222
131.2960
131.2686
131.0644
129.3793
129.1768
127.5596
124.4859
124.4644
122.3646
116.3366
113.8209
111.3051
69.1548
68.9183
68.6834
64.8495
14.1513
$^{13}C\{^{1}H\}$ NMR
Ph
NH
EtO_2C
CF_2H
3j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

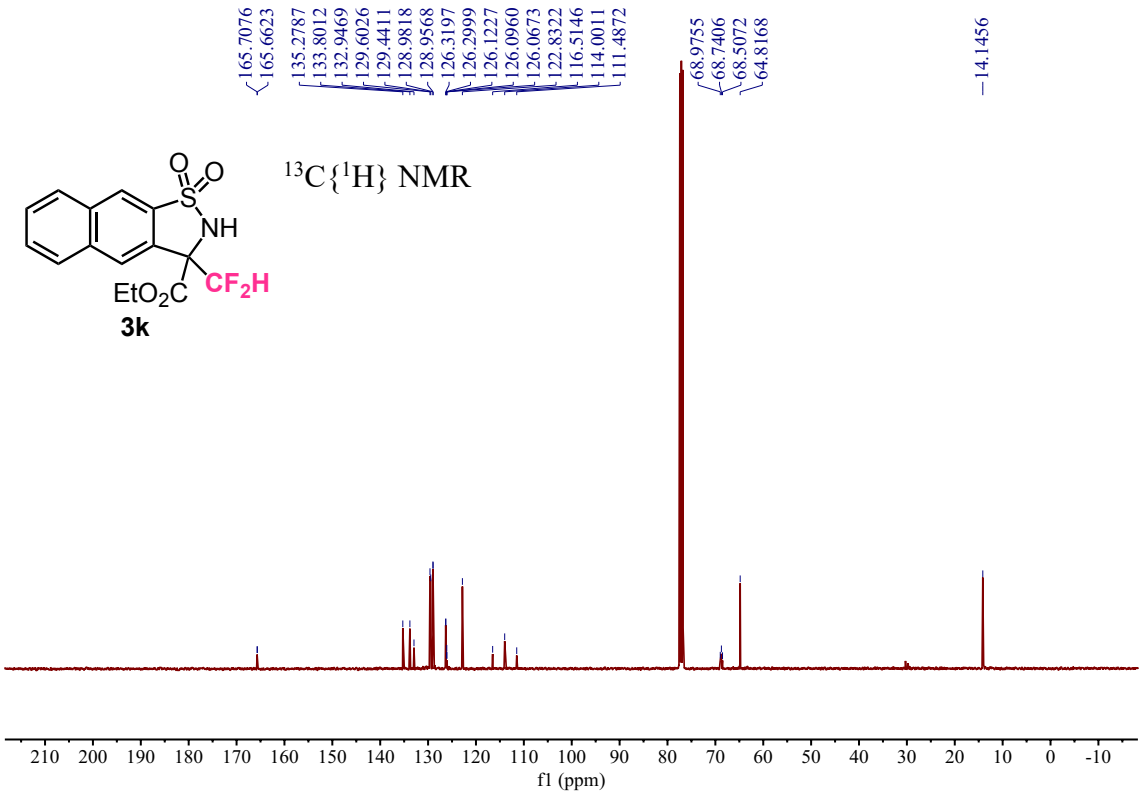

O
O
S
NH
Ph
EtO2C
CF2H

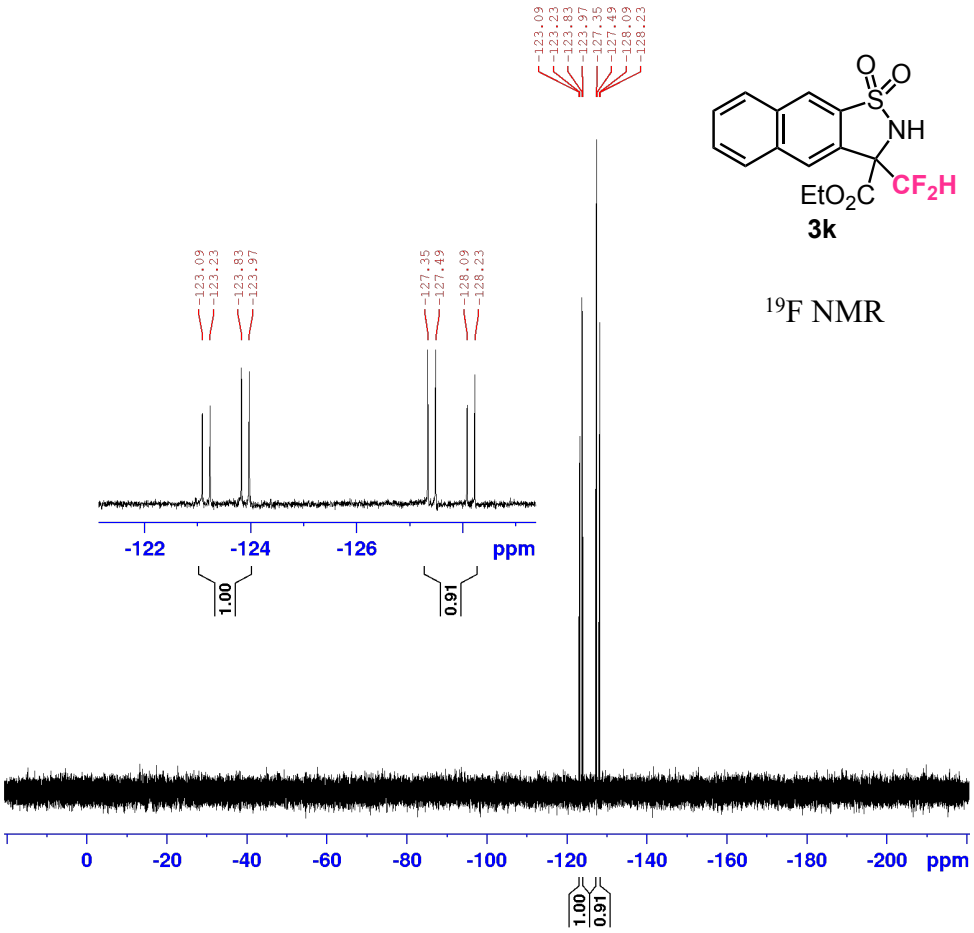
3j

^{19}F NMR


-123.15
-123.29
-123.89
-124.03
-126.87
-127.02
-127.61
-127.76
-122
-124
-126
ppm
1.00
0.88
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
1.00
0.88


8.36
8.31
8.05
8.02
8.00
7.74
7.74
7.73
7.72
7.72
7.71
7.70
7.70
7.69
7.68
7.68
6.34
6.21
6.07
5.94
4.50
4.49
4.49
4.48
4.47
4.46
4.45
4.44
4.43
4.42
1.44
1.42
1.40
O
O
S
NH
EtO2C
CF2H
3k
1H NMR
1.00
1.01
2.14
2.23
1.22
1.00
2.18
3.29
12.0 11.5 11.0 10.5 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)


165.7076
165.6623
135.2787
133.8012
132.9469
129.6026
129.4411
128.9818
128.9568
126.3197
126.2999
126.1227
126.0960
126.0673
122.8322
116.5146
114.0011
111.4872
68.9755
68.7406
68.5072
64.8168
14.1456
O
O
S
NH
EtO2C
CF2H
3k
13C{1H} NMR
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-123.09
-123.23
-123.83
-123.97
-127.35
-127.49
-128.09
-128.23
O
O
S
NH
EtO2C
CF2H
3k
19F NMR
-122
-124
-126
ppm
1.00
0.91
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm
1.00
0.91