Supplementary Information

3,3-Dibromo-2-trifluoromethyl-acrylic acid ethyl ester: A Versatile Platform for the Stereoselective Preparation of Functionalized- α-Trifluoromethyl α,β-Unsaturated Lactones and Trifluoromethyl Pyrazolinones

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1. General Information

All NMR spectra were recorded on Varian 500PS spectrometers. ^{1}H ^{13}C and ^{19}F NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) relative to the solvent peak using tetramethylsilane, and trichlorofluoromethane (^{19}F) as an internal standard. Chemical shifts (δ) are quoted in parts per million (ppm) and coupling constants (*J*) are measured in hertz (Hz). The following abbreviations are used to describe multiplicities s=singlet, d=doublet, t=triplet, q=quartet, quint.=quintet, sext.=sextet, sept.=septet br=broad, m=multiplet. NMR spectra were processed in ACD/SpecManager. High resolution mass spectra (HRMS, *m*/*z*) were obtained on JEOL JMS-

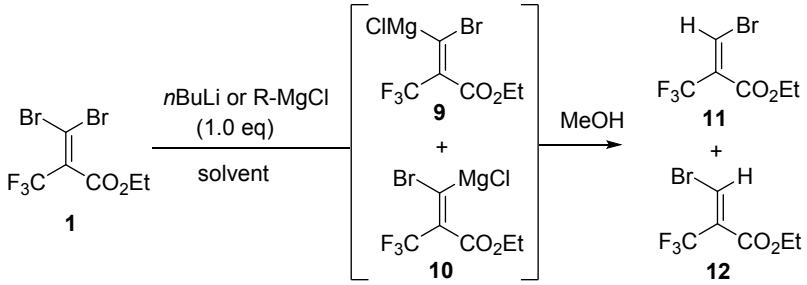
700N for FAB using m-nitrobenzylalcohol as a matrix or on JEOL JMS-T100TD for electrospray ionization (ESI+). All reactions were performed in apparatuses with magnetic stirring under an inert atmosphere. Flash column chromatography was performed over Fuji Silysia Chemical Ltd. silica gel C60 (50-200 μm) using an eluent system as described for each experiment. Thin-layer chromatography was performed using TLC Silica gel 60 F_{254} aluminum sheets (Merck) and silica gel F_{254} glass plates (Merck).

Materials.

Ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) was prepared according to a literature procedure.[1] *i*-PrMgCl (2.0 M, in Et_2O) were purchased from Sigma-Aldrich. Unless noted otherwise, all starting materials and reagents were obtained from commercial suppliers and were used without further purification. All chemicals were purchased from Sigma-Aldrich, Nacalai tesque, Tokyo Chemical Industry and Wako Pure Chemical Industries and used as received. All solvents were purchased from Wako Pure Chemical Industries.

2. Experiments for mono-metalation of 1 and 13

Table 1. Bromine-magnesium exchange reaction of **1**



Entry	*n*BuLi or R-MgCl	solvent	temp. (°C)	conv. (%)[a]	**11**/**12**[b]
1	iPrMgCl	THF	–80	40	60:40 (30)[c]
2	iPrMgCl	THF	–50	93	58:42 (34)[c]
3	iPrMgCl	Et_2O	–80	>95	27:73 (60)[c]
4	iPrMgCl	Et_2O	–50	>95	20:80 (46)[c]
5	iPrMgCl	hexane	–50	>95	40:60 (20)[c]
6	MeMgCl	Et_2O	–80	<5%	ND
7	*n*BuLi	Et_2O	–80	<5%	ND

[a] The conversion was determined by ^{19}F NMR analysis. [b] The ratio was based on the relative integration ratio in ^{19}F NMR spectrum. [c] Numbers in parenthese represent the yield base on internal standard of benzotrifluoride

General procedure for monometalation of 1

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (98 mg, 0.3 mmol) in Et_2O (2.0 mL) was added *i*-PrMgCl (150 μL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min, methanol (500 μL) was added at same temperature and the mixture was allowed to warm to room temperature. The mixture was extracted with Et_2O, washed with H_2O and brine. The organic layers were dried over $MgSO_4$ and concentrated carefully under vacuum. The ratio of isomers was carefully determined by ^1H and ^{19}F NMR of the crude mixtures because it was difficult to isolate products due to their volatility. A mixture of **11** and **12** was obtained in a ratio of 27:73 (Entry 3, Table 1). The stereochemistry for **11** is determined to (*E*)-configuration by analogy based on the H-F coupling constant. [2],[3] According to the data in the reference,[2] the H-F coupling constant values $J_{H\text{-}F}$ of (*E*)-1-bromo-3,3,3-trifluoro-2-{[(methoxymethoxy]methyl}prop-1-ene is 1.7 Hz (quartet). It is also notable that the chemical shift of C3 proton of the *Z* isomer appeared at a higher field (Δδ 0.4 Hz) than the corresponding (*E*) isomer. These tendencies are supportive to the assignment of *E/Z* stereochemistry for 3-bromoacrylate **11** and **12**. Moreover, the crude mixture were detectable by Mass spectrometry ($[M+1]^+ = 248$).

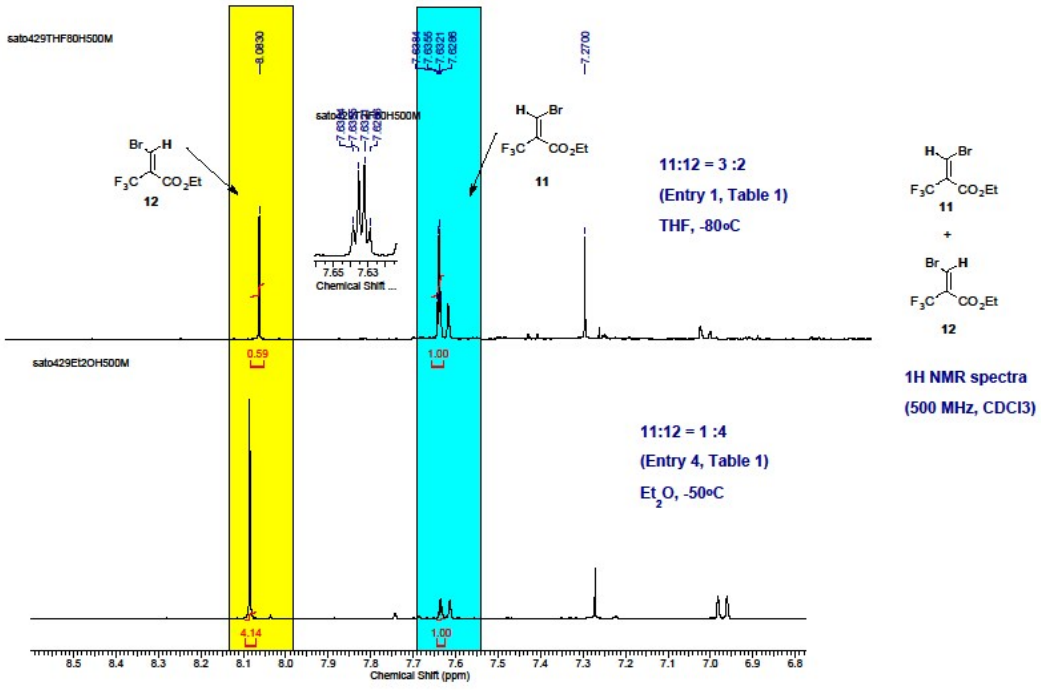
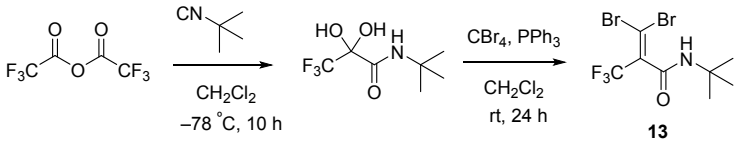


Fig. 1

(Top): ^1H NMR spectrum of crude mixture of reaction for while stirring 15 min at –80 °C in THF before quenching methanol (Entry 1 , Tabel 1) , (bottom) ^1H NMR spectrum of crude mixture of reaction for while stirring for 15 min at -50 °C in Et_2O before quenching methanol (Entry 4, Table 1).

Synthetic procedure for 3,3-dibromo-*N*-(*tert*-butyl)-2-(trifluoromethyl)acrylamide 13

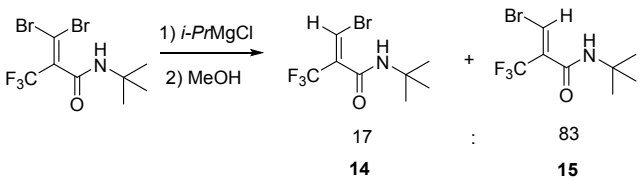


***N*-(tert-butyl)-3,3,3-trifluoro-pyruvylamide acetal**: To a solution of tert-butyl isocyanide (830 mg, 10 mmol) in CH_2Cl_2 (20 mL) was added trifluoroacetic anhydride (1.69 mmol,. 12 mnol) at –50 °C under argon. After stirring for 10 hrs at same temperature, distilled water (10 mL) was added, the mixture was allowed to wart to room temperature. The organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washced with brine , dried over $MaSO_4$, and concentrated in *vacuo*. The residue was purified by column chromatography on SiO_2 gel (Elute: hexane-AcOEt = 8:1 to 4:1) to afford the product (715 mg, 33%) as a white solid. **^{1}H NMR** (500 MHz, acetone-d6) δ 1.34 (s, 9H), 6.60 (br. s, 2O*H*), 6.95 (br. s, N*H*); **^{13}C NMR** (125 MHz, acetone-d6) δ28.5, 52.5, 91.7 (q, *J* = 32.2 Hz), 123.6 (q, *J* = 286.1 Hz), 166.6; **^{19}F NMR** (470 MHz, acetone-d6) δ –84.0 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_7H_{13}F_3NO_3$ $[M+H]^+$ 216.0848, found 216.0848. M.p. = 113 °C.

3,3-dibromo-*N*-(*tert*-butyl)-2-(trifluoromethyl)acrylamide (13): To a solution of PPh_3 (843 mg, 3.2 mmol) in CH_2Cl_2 (5.0 mL) was added CBr_4 (637 mg, 2.0 mmol) at 0 °C. After stirring for 10 min at same temperature, *N*-(tert-butyl)-3,3,3-trifluoro-pyruvylamide acetal (350 mg, 1.6 mmol) was added to the mixture, then it was stirred for 12 hrs at room temperature. The precipitate was filtered off through a pad of Celite, washed with CH_2Cl_2. The filtrate was concentrated in *vacuo.* The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 8:1) to afford the product (44 mg, 8%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 9H), 5.59 (br. s, N*H*); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 28.3, 52.9, 102.3 (q, *J* = 4.7 Hz), 120.6 (q, *J* = 274.7), 135.7 (q, *J* = 34.1 Hz), 159.8; **^{19}F NMR** (470 MHz, $CDCl_3$) δ –59.8 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_8H_{11}Br_2F_3NO$ $[M+H]^+$ 351.9159, found 351.9160. M.p. = 140 °C.

General procedure for monometalation of 13



To a solution of 3,3-dibromo-*N*-(*tert*-butyl)-2-(trifluoromethyl)acrylamide (**13**) (35 mg, 0.1 mmol) in Et_2O (2.0 mL) was added *i*-PrMgCl (50 μL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min, methanol (200 μL) was added at same temperature and the mixture was allowed

to warm to room temperature. The mixture was extracted with Et_2O, washed with H_2O and brine. The organic layers were dried over $MgSO_4$ and concentrated carefully under vacuum. The ratio of isomers was carefully determined by ^1H and ^{19}F NMR of the crude mixtures.

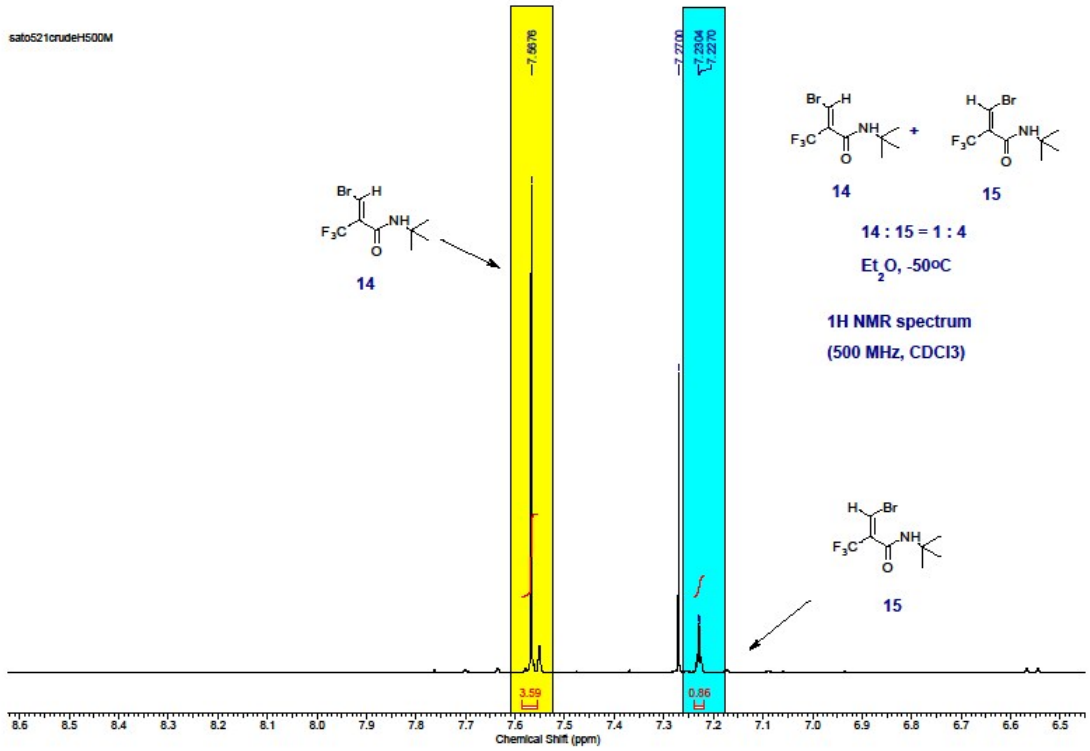


Fig. 2

^1H NMR spectrum of crude mixture of reaction for while stirring for 15 min at -50 °C in Et_2O before quenching methanol.

3. Computational methods

All DFT calculations were performed by using Gaussian 09, Revision D.01. Initial four structures were generated and optimized with UFF force field by using *Avogadro*.[4] The geometries were further optimized at B3LYP/cc-pVDZ level of theory, and it found that the geometry of the 5-membered metallacycle **10b** is most stable than alternative geometries **9a**, **9b** and **10a** (Fig. 2).

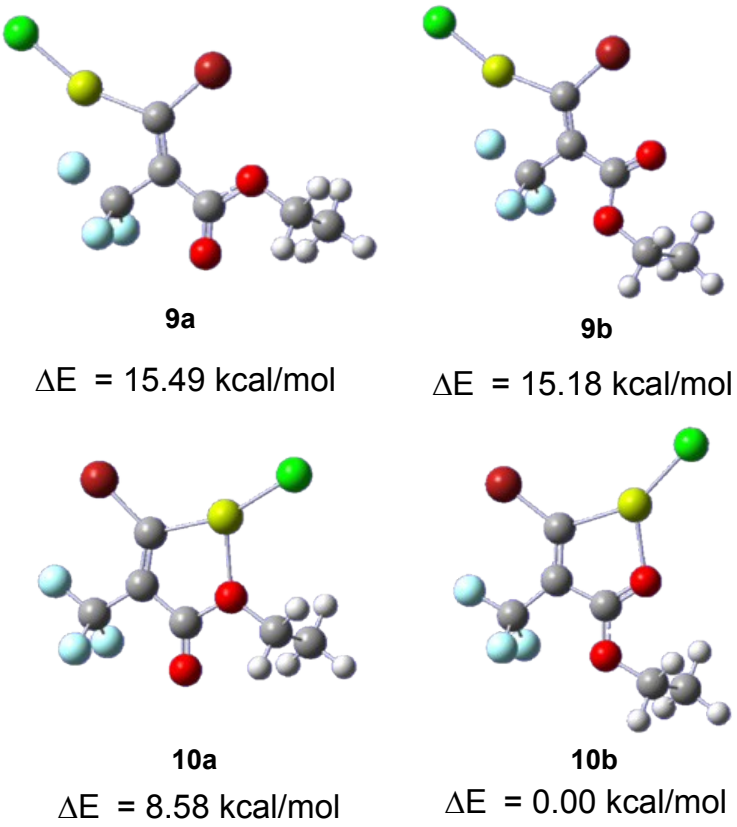
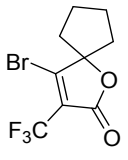


Fig. 2

4. Experimental Procedures and Characterization Data

4-1. General procedure for reaction of 1 with ketones

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (652 mg, 2.0 mmol) in Et_2O (8.0 mL) was added *i*-PrMgCl (1.0 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, cyclopentanone (212 μL, 2.4 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-acetone, 10:1) to afford the product (251 mg, 44%) as a white solid.

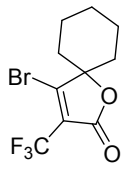


16a

4-Bromo-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-2-one (16a)

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.92–2.05 (m, 6H), 2.20–2.24 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$)

δ 25.3, 37.4, 97.5, 119.4 (q, *J* = 270.0 Hz), 122.0 (q, *J* = 36.0 Hz), 156.7 (q, *J* = 2.8 Hz), 163.6 (m); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.7 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_9H_9BrF_3O_2$ $[M+H]^+$ 284.9738, found 284.9738. M.p. = 73 °C.

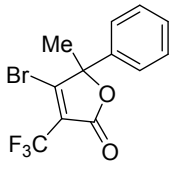


16b

4-Bromo-3-(trifluoromethyl)-1-oxaspiro[4.5]dec-3-en-2-one (16b)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (652 mg, 2.0 mmol) in Et_2O (8.0 mL) was added *i*-PrMgCl (1.0 mL, 2.0 M, in Et_2O) dropwise at –80 °C under argon. After stirring for 15 min at same temperature, cyclohexanone (248 μL, 2.4 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 10:1) to afford the product (228 mg, 38%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23–1.33 (m, 1H), 1.59–1.62 (m, 2H), 1.70–1.83 (m, 5H), 1.95 (dt, *J* = 4.4 Hz, 13.5 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.3, 24.0, 33.3, 89.5, 119.5 (q, *J* = 270.0 Hz), 121.4 (q, *J* = 36.0 Hz), 158.9 (t, *J* = 2.8 Hz), 163.6 (d, *J* = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.7 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{10}H_{11}BrF_3O_2$ $[M+H]^+$ 298.9895, found 298.9889. M.p. = 123 °C.



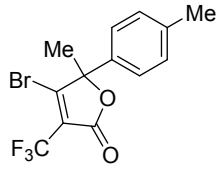
17a

4-Bromo-5-methyl-5-phenyl-3-(trifluoromethyl)furan-2-one (17a)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (652 mg, 2.0 mmol) in Et_2O (8.0 mL) was added *i*-PrMgCl (1.0 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, acetophenone (240 μL, 2.0 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-acetone, 10:1) to afford the product (265 mg, 41%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.03 (s, 3H), 7.39–7.45 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 23.4, 89.6, 119.4 (q, *J* = 270.0 Hz), 121.2 (q, *J* = 36.0 Hz), 125.6, 129.0, 129.7, 134.9, 158.9 (t, *J* = 2.8

Hz), 164.0 (m); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.7 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{12}H_9BrF_3O_2$ $[M+H]^+$ 320.9738, found 320.9740. M.p.= 65 °C.

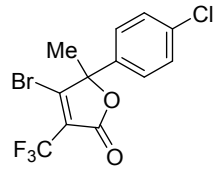


17b

4-Bromo-5-methyl-5-(p-tolyl)-3-(trifluoromethyl)furan-2-one (17b)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in Et_2O (4.0 mL) was added *i*-PrMgCl (0.5 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, 4'-methylacetophenone (161 μL, 1.2 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-acetone, 95:5) to afford the product (124 mg, 37%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.00 (s, 3H), 2.37 (s, 3H), 7.23–7.26 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.0, 23.3, 89.6, 119.5 (q, J = 270.0 Hz), 121.0 (q, J = 36.0 Hz), 125.5, 129.7, 131.9, 139.9, 159.1 (t, J = 2.8 Hz), 164.1 (d, J = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.7 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{13}H_{11}BrF_3O_2$ $[M+H]^+$ 334.9895, found 334.9895. M.p.= 43 °C.



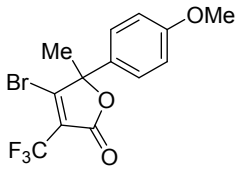
17c

4-Bromo-5-(4-chlorophenyl)-5-methyl-3-(trifluoromethyl)furan-2-one (17c)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in Et_2O (4.0 mL) was added *i*-PrMgCl (0.5 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, 4'-chloroacetophenone (156 μL, 1.2 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-acetone, 95:5) to afford the product (110 mg, 31%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.00 (s, 3H), 7.32 (d, J = 8.8 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 23.6, 89.0, 119.3 (q, J = 270.0 Hz), 121.4 (q, J = 36.0 Hz), 127.1, 129.3, 133.6, 136.0, 158.4 (q, J = 2.8 Hz), 163.7 (d, J = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.7 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{12}H_8BrClF_3O_2$ $[M+H]^+$ 354.9348, found 354.9244. M.p. = 105

°C.

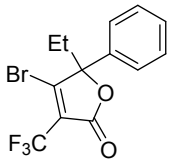


17d

4-Bromo-5-(4-methoxyphenyl)-5-methyl-3-(trifluoromethyl)furan-2-one (17d)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in Et_2O (4.0 mL) was added *i*-PrMgCl (0.5 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, 4'-methoxyacetophenone (180 mg, 1.2 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 8:1) to afford the product (111 mg, 32%) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.00 (s, 3H), 3.83 (s, 3H), 6.93 (d, J = 9.1 Hz, 2H), 7.28 (d, J = 9.1 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 23.4, 55.4, 114.4, 119.5 (q, J = 270.0 Hz), 121.2 (q, J = 37.0 Hz), 126.6, 127.1, 159.1 (t, J = 2.8 Hz), 160.6, 164.1 (d, J = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.7 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{13}H_{11}BrF_3O_3$ $[M+H]^+$ 350.9844, found 350.9849. M.p. = 77 °C.



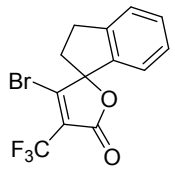
18

4-Bromo-5-ethyl-5-phenyl-3-(trifluoromethyl)furan-2-one (18)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in Et_2O (4.0 mL) was added *i*-PrMgCl (0.5 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, propiophenone (159 μL, 1.2 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (Elute: hexane-acetone = 98:2 to 95:5) to afford the product (100 mg, 30%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.96 (t, J = 7.4 Hz, 3H), 2.34 (dq, J = 7.1, 14.4 Hz, 1H), 2.48 (dq, J = 7.4, 14.4 Hz, 1H), 7.42–7.44 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 6.94, 29.1, 92.0 , 119.4 (q, J = 270.0 Hz), 122.0 (q, J = 36.0 Hz), 125.7, 129.0, 129.5, 134.6, 157.9 (q, J = 2.8 Hz), 164.3 (d, J = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.5 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{13}H_{11}BrF_3O_2$

$[M+H]^+$ 334.9895, found 334.9894. M.p. = 63 °C.

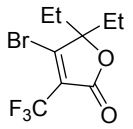


19

3-Bromo-4-(trifluoromethyl)-2',3'-dihydro-5H-spiro[furan-2,1'-inden]-5-one (19)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in Et_2O (4.0 mL) was added *i*-PrMgCl (0.5 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, 1-indanone (120 μL, 1.0 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 10:1) to afford the product (105 mg, 32%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.57 (ddd, *J* = 4.4, 8.6, 14.4 Hz, 1H), 2.77 (ddd, *J* = 6.4, 8.8, 14.4 Hz, 1H), 3.18 (ddd, *J* = 4.4, 8.6, 16.2 Hz, 1H), 3.33 (m, 1H), 7.06 (dd, *J* = 0.5, 7.9 Hz, 1H), 7.32 (tq, *J* = 1.3, 7.6 Hz, 1H), 7.38 (d,quint., *J* = 1.0, 7.6 Hz, 1H), 7.44 (dt, *J* = 1.0, 7.4 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 30.4, 35.7, 98.2, 121.6 (q, *J* = 270.0 Hz), 122.4 (q, *J* = 36.0 Hz), 123.2, 125.5, 127.8, 131.0, 136.3, 145.3, 155.5 (t, *J* = 2.8 Hz), 163.5 (t, *J* = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.5 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{13}H_9BrF_3O_2$ $[M+H]^+$ 332.9738, found 332.9739. M.p.= 142 °C.



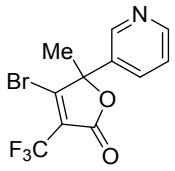
20

4-Bromo-5,5-diethyl-3-(trifluoromethyl)furan-2(5H)-one (20)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in Et_2O (4.0 mL) was added *i*-PrMgCl (0.5 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, 3-pentanone (122 μL, 1.2 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 10:1) to afford the product (112 mg, 39%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.4 Hz, 6H), 1.89 (dq, *J* = 7.6, 14.7 Hz, 2H), 2.02 (dq, *J* = 7.4, 14.7 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 6.53, 29.3, 92.9, 119.4 (q, *J* = 270 Hz), 233.7 (t, *J*

= 36.0 Hz), 156.1 (t, *J* = 2.9 Hz), 164.2 (d, *J* = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.6 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_9H_{11}BrF_3O_2$ $[M+H]^+$ 286.9895, found 286.9894. M.p.= 71 °C.

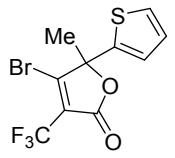


21

4-Bromo-5-(pyridin-3-yl)-5-methyl-3-(trifluoromethyl)furan-2-one (21)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in Et_2O (4.0 mL) was added *i*-PrMgCl (0.5 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, 3-acetylpyridine (132μL, 1.2 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 8:1) to afford the product (106 mg, 33%) as an orange oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.05 (s, 3H), 7.39 (dd, *J* = 4.9, 8.1 Hz, 1H), 7.70–7.72 (m, 1H), 8.67 (d, *J* = 4.7 Hz, 1H), 8.71 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 23.6, 88.1, 119.2 (q, *J* = 270.0 Hz), 121.7 (q, *J* = 36.0 Hz), 123.8, 131.4, 133.5, 146.8, 150.6, 157.8 (q, *J* = 2.8 Hz), 163.3 (t, *J* = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.8 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{11}H_9BrF_3NO_2$ $[M+H]^+$ 321.9691, found 321.9691.



22

4-Bromo-5-(thiophen-2-yl)-5-methyl-3-(trifluoromethyl)furan-2-one (22)

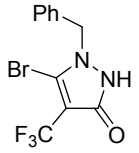
To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in Et_2O (4.0 mL) was added *i*-PrMgCl (0.5 mL, 2.0 M, in Et_2O) dropwise at –50 °C under argon. After stirring for 15 min at same temperature, 2-acetylthiophen (131μL, 1.2 mmol) was added and the mixture was allowed to warm to room temperature. The mixture was stirred for 20 h, quenched with sat. NH_4Cl solution and extracted with AcOEt. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 8:1) to afford the product (115 mg, 35%) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.06 (s, 3H), 7.05 (dd, *J* = 3.7, 5.1 Hz, 1H), 7.14 (dd, *J* = 1.2, 3.7 Hz, 1H), 7.41 (dd, *J* = 1.2, 5.2 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 24.9, 87.7, 119.3 (q, *J* = 270.0

Hz), 121.4 (q, J = 37.0 Hz), 127.0, 127.5, 127.6, 138.4, 157.5 (t, J = 2.8 Hz), 163.1; **^{19}F NMR** (470 MHz, $CDCl_3$) δ –62.8 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{10}H_7BrF_3O_2S$ $[M+H]^+$ 326.9302, found 326.9305. M.p.= 70 °C.

4-2. General procedure for reaction of 1 with hydrazine derivatives

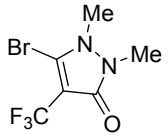
To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in 1,4-dioxane (7.5 mL) was added *N*-benzylhydradine dihydrobromide (341 mg, 1.2 mmol) and *i*-Pr_2NEt (708 μL, 4.0 mmol) under argon. The mixture was stirred for 10 h at 80 °C. After the reaction was completed the mixture was cooled to room temperature, evaporated to remove the solvent. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 4:1) to afford the product (218 mg, 68%) as a white solid.



23

1-Benzyl-5-bromo-4-(trifluoromethyl)-1,2-dihydro-pyrazol-3-one (23)

^{1}H NMR (500 MHz, acetone-d6) δ 5.27 (s, 2H), 7.25–7.27 (m, 2H), 7.30–7.32 (m, 1H), 7.34–7.37 (m, 2H); **^{13}C NMR** (125 MHz, acetone-d6) δ 54.3, 98.1 (q, J = 37.9), 114.2 (q, J = 2.9 Hz), 123.2 (q, J = 264.2 Hz), 128.4, 128.9, 129.2, 136.9, 159.4 (q, J = 1.9 Hz); **^{19}F NMR** (470 MHz, acetone-d6) δ –57.1 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{11}H_9BrF_3N_2O$ $[M+H]^+$ 320.9850, found 320.9851. M.p.= 159 °C.



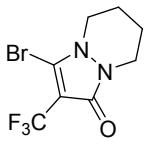
24

5-Bromo-1,2-dimethyl-4-(trifluoromethyl)-1,2-dihydro-pyrazol-3-one (24)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (111 mg, 0.34 mmol) in 1,4-dioxane (5.0 mL) was added *N,N'*-dimethylhydradine dihydrobromide (130 mg, 0.41 mmol) and *i*-Pr_2NEt (210 μL, 3.5 mmol) under argon. The mixture was stirred for 10 h at 80 °C. After the reaction was completed the mixture was cooled to room temperature, evaporated to remove the solvent. The residue was purified by column chromatography on SiO_2 gel (Elute: hexane-AcOEt = 1:1 to AcOEt) to afford the product (56 mg, 63%) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.42 (s, 3H), 3.56 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 29.4, 34.5, 100.3 (q, J = 36.0 Hz), 121.7 (q, J = 265.2 Hz), 126.3 (q, J = 2.8 Hz), 159.5 (q, J = 1.9Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –58.5 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_6H_7BrF_3N_2O$ $[M+H]^+$

258.9694, found 258.9693. M.p.= 127 °C.

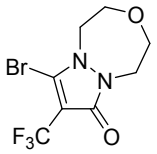


25

5-Bromo-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (25)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (630 mg, 1.9 mmol) in 1,4-dioxane (15.0 mL) was added hexahydropyridazine dihydrobromide (528 mg, 2.1 mmol) and *i*-Pr_2NEt (1.2 mL, 6.7 mmol) under argon. The mixture was stirred for 10 h at 100 °C. After the reaction was completed the mixture was cooled to room temperature, evaporated to remove the solvent. The residue was purified by column chromatography on SiO_2 gel (Elute: hexane-AcOEt = 1:1 to AcOEt) to afford the product (393 mg, 71%) as a brown solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.89–1.95 (m, 2H), 2.00–2.04 (m, 2H), 3.73–3.79 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.6, 22.5, 41.9, 47.9, 121.7 (q, J = 266.2 Hz), 128.2 (q, J = 2.9 Hz), 160.1 (q, J = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –58.6 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_8H_9BrF_3N_2O$ $[M+H]^+$ 284.9850, found 284.9854. M.p.= 105 °C.

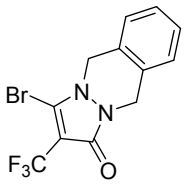


26

5-Bromo-4-(trifluoromethyl)- 1,2-oxydiethylene-1,2-dihydro-pyrazol-3-one (26)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in 1,4-dioxane (10 mL) was added [1,3,5]oxadiazepane dihydrobromide (314 mg, 1.2 mmol) and *i*-Pr_2NEt (708 μL, 4.0 mmol) under argon. The mixture was stirred for 12 h at 100 °C. After the reaction was completed the mixture was cooled to room temperature, evaporated to remove the solvent. The residue was purified by column chromatography on SiO_2 gel (AcOEt) to afford the product (250 mg, 83%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87–3.88 (m, 1H), 3.90–3.92 (m, 1H), 4.25–4.27 (m, 1H), 4.33 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 45.7, 51.6, 69.3, 70.3, 99.3 (t, J = 37.0 Hz), 121.7 (q, J = 265.2 Hz), 122.8 (q, J = 2.8 Hz), 157.7 (q, J = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –58.4 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_8H_9BrF_3N_2O_2$ $[M+H]^+$ 300.9799, found 300.9799. M.p.= 226 °C.



27

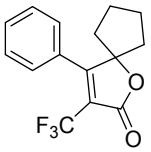
3-Bromo-2-(trifluoromethyl)-5,10-dihydro-pyrazolo[1,2-b]phthalazin-1-one (27)

To a solution of ethyl 3,3-dibromo-2-trifluoromethylacrylate (**1**) (326 mg, 1.0 mmol) in 1,4-dioxane (10 mL) was added 1,2,3,4-tetrahydrophthalazine (155 mg, 1.2 mmol) and *i*-Pr_2NEt (349 μL, 2.0 mmol) under argon. The mixture was stirred for 12 h at 100 °C. After the reaction was completed the mixture was cooled to room temperature, evaporated to remove the solvent. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt, 2:1) to afford the product (193 mg, 58%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.99 (s, 2H), 4.99 (s, 2H), 7.28–7.41 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 44.4, 49.0, 101.7 (q, *J* = 36.0 Hz), 120.6 (q, *J* = 266.2 Hz), 126.2 (q, *J* = 2.9 Hz), 126.3, 126.7, 127.0 128.1, 128.1, 128.6, 159.6 (q, *J* = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –58.5 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{12}H_9BrF_3N_2O$ $[M+H]^+$ 332.9850, found 332.9849. . M.p.= 201 °C.

4-3. General procedure for Pd-catalyzed cross-coupling reactions

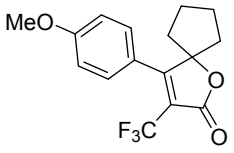
A 10 mL test tube equipped with a magnetic stirring bar and a screw cap was charged with 4-bromo-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-2-one (**16a**) (114mg, 0.4 mmol), $PhB(OH)_2$ (92 mg, 0.6 mmol), $Pd(PPh_3)_4$ (23 mg, 0.02 mmol), Na_2CO_3 (85 mg, 0.8 mmol), toluene (1.6 mL) and H_2O (0.4 mL). The mixture was stirred for 10 h at 90 °C. The mixture was diluted with H_2O (10 mL), extracted with AcOEt (20 mL). The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on SiO_2 gel (hexane-AcOEt , 8:1) to afford the product (104 mg, 92%) as a white solid.



30a

4-Phenyl-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-2-one (30a)

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.71–1.74 (m, 2H), 1.95–2.07 (m, 4H), 7.20–7.22 (m, 2H), 7.48–7.50 (m, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 24.4, 35.8, 97.1, 120.0 (q, *J* = 269.0 Hz), 126.8, 128.7, 129.4, 129.9, 165.7 (m); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –60.8 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{15}H_{14}F_3O_2$ $[M+H]^+$ 283.0946, found 283.0944. . M.p.= 78 °C.

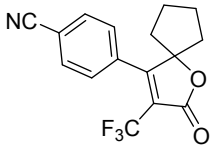


30b

4-(4-Methoxyphenyl)-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-2-one (30b)

Synthesized following general procedure. A mixture of 4-bromo-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-2-one (**16a**) (114 mg, 0.4 mmol), 4-methoxyphenyl boronic acid (92 mg, 0.6 mmol), $Pd(PPh_3)_4$ (23 mg, 0.02 mmol), Na_2CO_3 (85 mg, 0.8 mmol), toluene (1.6 mL) and H_2O (0.4 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt , 10:1) to give the product (103 mg, 83%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.70–1.74 (m, 2H), 1.92–2.07 (m, 6H), 3.84 (s, 3H), 6.99 (d, *J* = 9.1 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 24.6, 36.1, 55.4, 97.1, 114.2, 118.0 (q, *J* = 270,0 Hz), 118.9 (q, *J* = 34.1 Hz), 121.3, 128.6, 161.0, 165.9 (q, *J* = 1.9 Hz), 173.9 (q, *J* = 2.8 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –60.6 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{16}H_{16}F_3O_3$ $[M+H]^+$ 313.1052, found 313.1054. . M.p.= 55 °C.

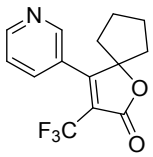


30c

4-(2-Oxo-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-4-yl)benzonitrile (30c)

Synthesized following general procedure. A mixture of 4-bromo-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-2-one (**16a**) (114 mg, 0.4 mmol), 4-cyanophenyl boronic acid (88 mg, 0.6 mmol), $Pd(PPh_3)_4$ (23 mg, 0.02 mmol), Na_2CO_3 (85 mg, 0.8 mmol), toluene (1.6 mL) and H_2O (0.4 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (Elute: hexane-AcOEt = 8:1 to 4:1) to give the product (103mg, 76%) as a white solid. Single crystals suitable for X-ray crystallography were grown from a mixture solution of hexane/AcOEt.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.69–1.79 (m, 2H), 1.92–2.08 (m, 6H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.79–7.82 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 24.2, 35.8, 96.7, 114.1, 117.6, 119.6 (q, *J* = 270.0 Hz), 120.7 (m), 127.8, 132.4, 133.9, 164.7, 170.3 (m); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –60.8 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{16}H_{13}F_3NO_2$ $[M+H]^+$ 308.0898, found 308.0884. . M.p.= 138 °C.

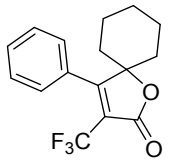


30d

4-(Pyridin-3-yl)-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-2-one (30d)

Synthesized following general procedure. A mixture of 4-bromo-3-(trifluoromethyl)-1-oxaspiro[4.4]non-3-en-2-one (**16a**) (89 mg, 0.3 mmol), 3-pyridineboronic acid (55 mg, 0.45 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), Na_2CO_3 (64 mg, 0.6 mmol), toluene (1.6 mL) and H_2O (0.4 mL) was stirred for 12 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt, 2:1) to give the product (12 mg, 14%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.89–1.92 (m, 2H), 2.04–2.11 (m, 4H), 2.23–2.30 (m, 2H), 7.38–7.41 (dd, *J* = 4.7, 8.6 Hz, 1H), 7.43–7.46 (m, 1H), 8.50 (d, *J* = 2.4 Hz, 1H), 8.57 (d, *J* = 4.7 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 25.8, 36.7, 91.9, 119.3 (q, *J* = 268 Hz), 124.4, 125.3, 140.4, 147.6, 152.3, 164.8 (q, *J* = 1.9 Hz), 178.1 (q, *J* = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –58.3 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{14}H_{13}F_3NO_2$ $[M+H]^+$ 284.0898, found 284.0889. M.p.= 111 °C.

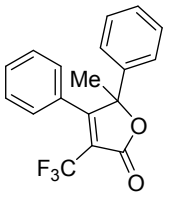


30e

4-Phenyl-3-(trifluoromethyl)-1-oxaspiro[4.5]dec-3-en-2-one (30e)

Synthesized following general procedure. A mixture of 4-bromo-3-(trifluoromethyl)-1-oxaspiro[4.5]dec-3-en-2-one (**16b**) (120 mg, 0.4 mmol), $PhB(OH)_2$ (92 mg, 0.6 mmol), $Pd(PPh_3)_4$ (23 mg, 0.02 mmol), Na_2CO_3 (85 mg, 0.8 mmol), toluene (1.6 mL) and H_2O (0.4 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt, 10:1) to give the product (103 mg, 87%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07–1.13 (m, 1H), 1.64–1.82 (m, 9H), 7.14–7.18 (m, 2H), 7.45–7.51 (m, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.6, 24.1, 32.7, 88.8, 119.0 (q, *J* = 35.0 Hz), 120.1 (q, *J* = 270.0 Hz), 126.4, 128.6, 129.6, 129.8, 165.8 (q, *J* = 1.9 Hz), 175.6 (q, *J* = 2.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –60.8 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{16}H_{16}F_3O_2$ $[M+H]^+$ 297.1102, found 297.1103. M.p.= 117 °C.



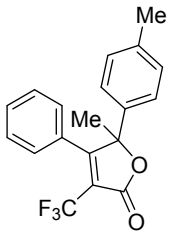
30

5-Methyl-4,5-diphenyl-3-(trifluoromethyl)furan-2-one (30f)

Synthesized following general procedure. A mixture of 4-bromo-5-methyl-5-phenyl-3-(trifluoromethyl)furan-2-one (**17a**) (127 mg, 0.4 mmol), $PhB(OH)_2$ (92 mg, 0.6 mmol), $Pd(PPh_3)_4$

(23 mg, 0.02 mmol), Na_2CO_3 (85 mg, 0.8 mmol), toluene (1.6 mL) and H_2O (0.4 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt, 95:5) to give the product (111 mg, 87%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.90 (s, 3H), 6.74–6.75 (m, 2H), 7.20–7.22 (m, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.38–7.44 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 22.8, 88.8, 117.7 (*J* = 35.0 Hz), 120.2 (q, *J* = 270.0 Hz), 125.9, 127.0, 128.2, 128.7, 128.8, 129.3, 130.3, 135.0, 166.2 (q, *J* = 1.9Hz), 174.8 (q, *J* = 2.8 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –60.6 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{18}H_{14}F_3O_2$ $[M+H]^+$ 319.0946, found 319.0947. M.p.= 65 °C.



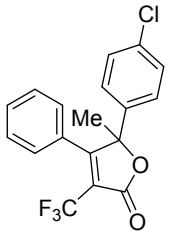
30g

5-Methyl-4-phenyl-5-(*p*-tolyl)-3-(trifluoromethyl)furan-2-one (30g)

Synthesized following general procedure. A mixture of 4-bromo-5-methyl-5-(p-tolyl)-3-(trifluorome-

thyl)furan-2-one (**17b**) (100 mg, 0.3 mmol), $PhB(OH)_2$ (55 mg, 0.45 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), Na_2CO_3 (64 mg, 0.6 mmol), toluene (1.6 mL) and H_2O (0.4 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt, 10:1) to give the product (77 mg, 77%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.87 (s, 3H), 2.39 (s, 3H), 6.76 (dd, *J* = 1.5, 8.1 Hz, 2H), 7.09 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.42 (tt, *J* = 1.2, 7.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.1, 22.8, 88.9, 117.7 (q, *J* = 35.0 Hz), 120.2 (q, *J* = 270.0 Hz), 125.9, 127.2, 128.3, 128.9, 129.6, 130.3, 132.0, 139.5, 166.4 (q, *J* = 1.9Hz), 174.9 (q, *J* = 2.8 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –60.6 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{19}H_{16}F_3O_2$ $[M+H]^+$ 333.1102, found 333.1103. M.p.= 89 °C.



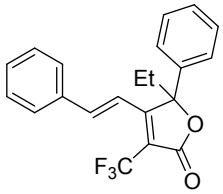
30h

5-(4-Chlorophenyl)-5-methyl-4-phenyl-3-(trifluoromethyl)furan-2-one (30h)

Synthesized following general procedure. A mixture of 4-bromo-5-(4-chlorophenyl)-5-methyl-3-

(trifluoromethyl)furan-2-one (**17c**) (87 mg, 0.24 mmol), $PhB(OH)_2$ (44 mg, 0.36 mmol), $Pd(PPh_3)_4$ (13 mg, 0.012 mmol), Na_2CO_3 (51 mg, 0.48 mmol), toluene (1.5 mL) and H_2O (370 μL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt, 10:1) to give the product (64 mg, 75%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.89 (s, 3H), 6.77 (d, *J* = 8.6 Hz, 2H), 7.13 (d *J* = 8.8 Hz, 2H), 7.33–7.37 (m, 4H), 7.45 (tt, *J* = 1.2, 7.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 23.1, 88.3, 118.1 (q, *J* = 35.0 Hz), 120.0 (q, *J* = 270.0 Hz), 127.0, 127.3, 128.4, 128.6, 129.1, 130.4, 133.9, 135.5, 165.9 (q, *J* = 1.9 Hz), 174.3 (q, *J* = 2.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –60.7 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{18}H_{13}ClF_3O_2$ $[M+H]^+$ 353.0561, found 353.0556. M.p.= 77 °C.

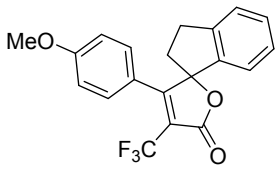


30i

(*E*)-5-Ethyl-5-phenyl-4-styryl-3-(trifluoromethyl)furan-2-one (30i)

Synthesized following general procedure. A mixture of 4-bromo-5-ethyl-5-phenyl-3-(trifluoromethyl)furan-2-one (**18**) (90 mg, 0.27 mmol), (*E*)- strylboronic acid (60 mg, 0.41 mmol) , $Pd(PPh_3)_4$ (15 mg, 0.013 mmol), Na_2CO_3 (58 mg, 0.48 mmol), toluene (1.6 mL) and H_2O (0.4 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt, 10:1) to give the product (59 mg, 60%) as a glassy oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.1 Hz, 3H), 2.45 (dq, *J* = 7.1, 14.4 Hz, 1H), 2.77 (dq, *J* =7.1, 14.4 Hz, 1H), 6.84 (d, *J* = 16.7 Hz, 1H), 7.20 (dd, *J* = 0.8, 16.6 Hz, 1H), 7.36–7.47 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 7.17, 29.0, 89.5, 115.1 (q, *J* = 1.9 Hz), 116.7 (q, *J* = 34.1 Hz), 123.3 (q, *J* = 270.0 Hz), 126.1, 128.0, 129.1, 129.2, 129.5, 131.0, 134.5, 137.4, 144.4, 166.2 (q, *J* = 1.9 Hz), 166.5 (q, *J* = 2.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –59.3 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{21}H_{18}F_3O_2$ $[M+H]^+$ 359.1259, found 359.1255.



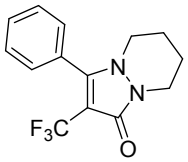
30j

3-(4-Methoxyphenyl)-4-(trifluoromethyl)-2',3'-dihydro-spiro[furan-2,1'-inden]-5-one (30j)

Synthesized following general procedure. A mixture of 3-bromo-4-(trifluoromethyl)-2',3'-dihydro-5H-spiro[furan-2,1'-inden]-5-one (**19**) (100 mg, 0.3 mmol), 4-methoxyphenyl boronic acid (55 mg, 0.36 mmol) , $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), Na_2CO_3 (64 mg, 0.6 mmol), toluene (1.6 mL) and

H_2O (0.4 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt, 10:1) to give the product (60 mg, 55%) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.40 (ddd, *J* = 5.4, 8.8, 13.9 Hz, 1H), 2.55 (ddd, *J* = 5.4, 8.6, 13.9 Hz, 1H), 2.60–2.66 (m, 1H), 3.10–3.16 (m, 1H), 3.79 (s, 3H), 6.79 (d, *J* = 9.3 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 7.28 (d, *J* = 6.6 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.37 (dt, *J* = 1.0, 7.6 Hz, 1H), 7.44 (dt, *J* = 1.3, 7.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 30.2, 35.4, 55.3, 97.0, 114.0, 116.5 (q, *J* = 35.0 Hz), 120.0 (q, *J* = 270 Hz), 120.9, 123.6, 125.5, 127.8, 129.6 (t, *J* = 1.9 Hz), 130.6, 137.2, 145.1, 161.5, 166.2 (q, *J* = 1.9 Hz), 171.1 (q, *J* = 2.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –60.0 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{20}H_{16}F_3O_3$ $[M+H]^+$ 361.1052, found 361.1050. M.p.= 87 °C.

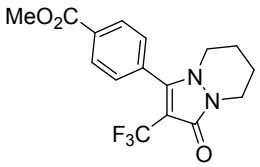


31a

5-Phenyl-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (31a)

Synthesized following general procedure. A mixture of 5-bromo-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (**25**) (143 mg, 0.5 mmol), $PhB(OH)_2$ (92 mg, 0.75 mmol) , $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), Na_2CO_3 (106 mg, 1.0 mmol), toluene (2.0 mL) and H_2O (0.5 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (AcOEt only) to give the product (104 mg, 73%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.91–1.93 (m, 4H), 3.32–3.34 (m, 2H), 3.85–3.88 (m, 2H), 7.38 (d, *J* = 6.6 Hz, 2H), 7.48–7.55 (m, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 22.0, 22.8, 41.3, 47.7, 122.5 (q, *J* = 266.2 Hz), 126.6, 128.7, 129.0, 130.7, 153.5 (m), 160.9 (q, *J* = 1.9 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –56.5 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{14}H_{14}F_3N_2O$ $[M+H]^+$ 283.1058, found 283.1053. M.p.=125 °C.



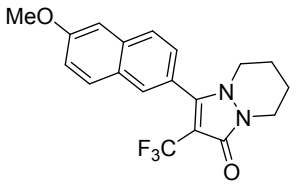
31b

5-(4-methoxycarbonylphenyl)-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (31b)

Synthesized following general procedure. A mixture of 5-bromo-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (**25**) (143 mg, 0.5 mmol), 4-(methoxycarbonyl)phenylboronic acid (135 mg, 0.75 mmol) , $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), Na_2CO_3 (106 mg, 1.0 mmol), toluene (2.0 mL) and H_2O (0.5 mL) was stirred for 10 h at 90 °C.

Purified by SiO_2 gel column chromatography (AcOEt only) to give the product (105 mg, 62%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.92–1.93 (m, 4H), 3.31–3.30 (m, 2H), 3.85–3.87 (m, 2H), 3.96 (s, 3H), 7.46 (d, *J* = 8.3 Hz, 2H), 8.16 (d, *J* = 8.1 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.9, 22.8, 41.4, 47.8, 52.5, 122.3 (q, *J* = 266.2 Hz), 129.3, 129.9, 130.9, 132.3, 152.2 (q, *J* = 2.8 Hz), 160.0 (q, *J* = 1.9 Hz), 165.9; **^{19}F NMR** (470 MHz, $CDCl_3$) δ –56.5 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{16}H_{16}F_3N_2O_3$ $[M+H]^+$ 341.1113, found 341.1114. . M.p.=196 °C.

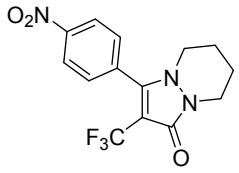


31c

5-(6-Methoxynaphthalen-2-yl)-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (31c)

Synthesized following general procedure. A mixture of 5-bromo-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (**25**) (143 mg, 0.5 mmol), 6-methoxy-2-naphthalenebonoronic acid (152 mg, 0.75 mmol) , $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), Na_2CO_3 (106 mg, 1.0 mmol), toluene (2.0 mL) and H_2O (0.5 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (AcOEt only) to give the product (140 mg, 77%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.90–1.97 (m, 4H), 3.33–3.39 (m, 2H), 3.86–3.92 (m, 2H), 3.96 (s, 3H), 7.19 (br.s, 1H), 7.25 (dd, *J* = 2.2, 8.8 Hz, 1H), 7.38 (d, *J* = 8.6 Hz, 1H), 7.80–7.85 (m, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 22.1, 22.9, 41.3, 48.0, 55.4, 100.1 (q, *J* = 35.0 Hz), 105.7, 120.1, 121.4, 122.6 (q, *J* = 266.2 Hz), 126.1, 127.4, 128.0, 129.1, 129.9, 135.4, 153.9 (q, *J* = 2.8 Hz), 159.1, 161.0 (m); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –56.4 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{19}H_{18}F_3N_2O_2$ $[M+H]^+$ 363.1320, found 363.1318. . M.p.=194 °C.

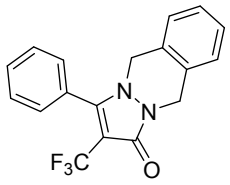


31d

5-(4-nitrophenyl)-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (31d)

Synthesized following general procedure. A mixture of 5-bromo-4-(trifluoromethyl)-1,2-tetramethylene-1,2-dihydro-pyrazol-3-one (**25**) (143 mg, 0.5 mmol), 4-nitrophenylbonoronic acid (125 mg, 0.75 mmol) , $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), Na_2CO_3 (106 mg, 1.0 mmol), toluene (2.0 mL) and H_2O (0.5 mL) was stirred for 22 h at 90 °C. Purified by SiO_2 gel column chromatography (AcOEt only) to give the product (100 mg, 61%) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.92–1.99 (m, 4H), 3.32–3.34 (m, 2H), 3.89–3.91 (m, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 8.37 (d, *J* = 8.8 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.8, 22.7, 41.4, 47.9, 101.4 (q, *J* = 36.0 Hz), 122.1 (q, *J* = 266.2 Hz), 124.0, 130.5, 132.9, 149.2, 150.7 (q, *J* = 2.8 Hz), 160.2 (m); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –56.6 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{14}H_{13}F_3N_3O_3$ $[M+H]^+$ 328.0909, found 328.0912. . . M.p.=233 °C.



31e

3-Phenyl -2-(trifluoromethyl)-5,10-dihydro-pyrazolo[1,2-b]phthalazin-1-one (31e)

Synthesized following general procedure. A mixture of -bromo-2-(trifluoromethyl)-5,10-dihydro-pyrazolo[1,2-b]phthalazin-1-one (**27**) (60 mg, 0.2 mmol), phenylbonoronic acid (33 mg, 0.3 mmol) , $Pd(PPh_3)_4$ (10 mg, 0.01 mmol), Na_2CO_3 (38 mg, 0.4 mmol), toluene (1.6 mL) and H_2O (0.4 mL) was stirred for 10 h at 90 °C. Purified by SiO_2 gel column chromatography (hexane-AcOEt, 1:1) to give the product (33 mg, 56%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.58 (s, 2H), 5.09 (s, 2H), 7.10 (d, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.36–7.41 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.54–7.61 (m, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 44.0, 48.8, 100.1 (q, *J* = 35.1 Hz), 122.5 (d, *J* = 266.2 Hz),126.2, 126.6, 126.9, 127.8, 128.1, 128.4, 128.5, 128.8, 129.0, 129.3, 131.0, 132.1, 152.0 (q, *J* = 2.9 Hz), 160.6 (m); **^{19}F NMR** (470 MHz, $CDCl_3$) δ –56.3 (s, 3F); **HRMS** (FAB) *m/z* Calcd for $C_{18}H_{14}F_3N_2O_3$ $[M+H]^+$ 331.1058, found 331.1061. . M.p.=184 °C.

4-4. Crystal data for 30c

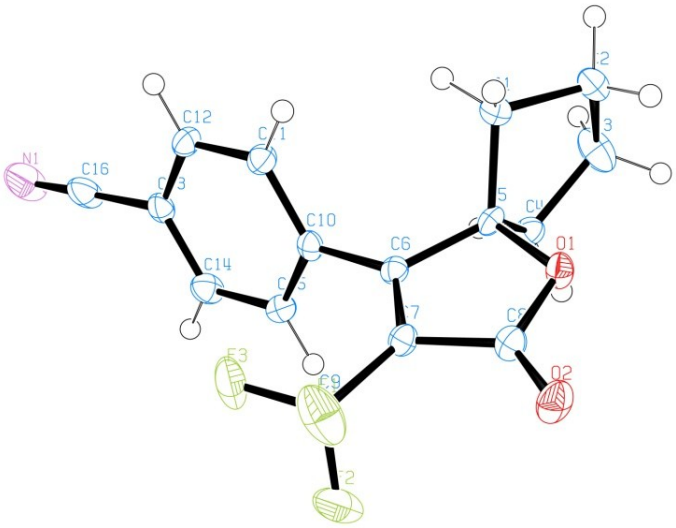


Fig. 2 ORTEP drawing of the X-ray structure of **22c**. Hydrogen atoms are omitted for clarity and ellipsoids displayed at 50% probability.

The crystallographic data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.jk/data_request/cif (CCDC 1491776)

A. Crystal Data

Empirical Formula	$C_{16}H_{12}F_3NO_2$
Formula Weight	307.27
Crystal Color, Habit	colorless, block
Crystal Dimensions	0.220 X 0.070 X 0.040 mm
Crystal System	monoclinic
Lattice Type	Primitive
Lattice Parameters	a = 12.057(4) Å b = 8.771(2) Å c = 14.736(5) Å β = 113.287(5) ° V = 1431.4(8) Å^3
Space Group	$P2_1/c$ (#14)
Z value	4
D_{calc}	1.426 g/cm^3
F_{000}	632.00
μ(MoKα)	1.202 cm^{-1}

B. Intensity Measurements

Diffractometer	Saturn724
Radiation	MoKα (λ = 0.71075 Å)
	multi-layer mirror monochromated
Voltage, Current	50kV, 24mA
Temperature	-180.0°C
Detector Aperture	72.8 x 72.8 mm
Data Images	720 exposures
ω oscillation Range (χ=45.0, ϕ=0.0)	-110.0 - 70.0°
Exposure Rate	16.0 sec./°
Detector Swing Angle	-20.10°
ω oscillation Range (χ=45.0, ϕ=90.0)	-110.0 - 70.0°
Exposure Rate	16.0 sec./°
Detector Swing Angle	-20.10°
Detector Position	44.98 mm
Pixel Size	0.141 mm
$2\theta_{max}$	55.0°
No. of Reflections Measured	Total: 11584
	Unique: 3283 (R_{int} = 0.0548)
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.881 - 0.995)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR2008)
Refinement	Full-matrix least-squares on F^2
Function Minimized	$\Sigma\, w\,(Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/[\,\sigma^2(Fo^2) + (0.0389 \cdot P)^2$
	$+ 0.5104 \cdot P\,]$
	where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	55.0°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3283
No. Variables	199
Reflection/Parameter Ratio	16.50
Residuals: R1 (I>2.00σ(I))	0.0578

Residuals: R (All reflections)	0.0921
Residuals: wR2 (All reflections)	0.1121
Goodness of Fit Indicator	1.068
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.34 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.28 $e^-/Å^3$

5. References

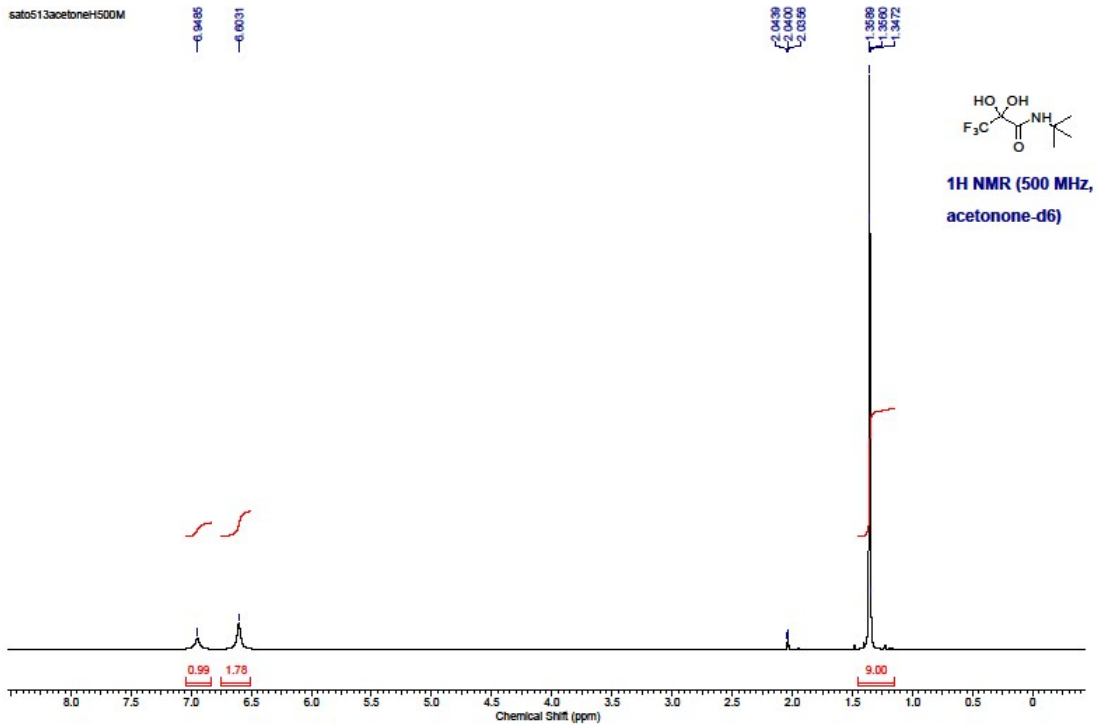
[1] Y.-H. Li, X.-M. Zhao, L. Lu, *J. Fluorine Chem.* 2004, **125**, 1821–1824.

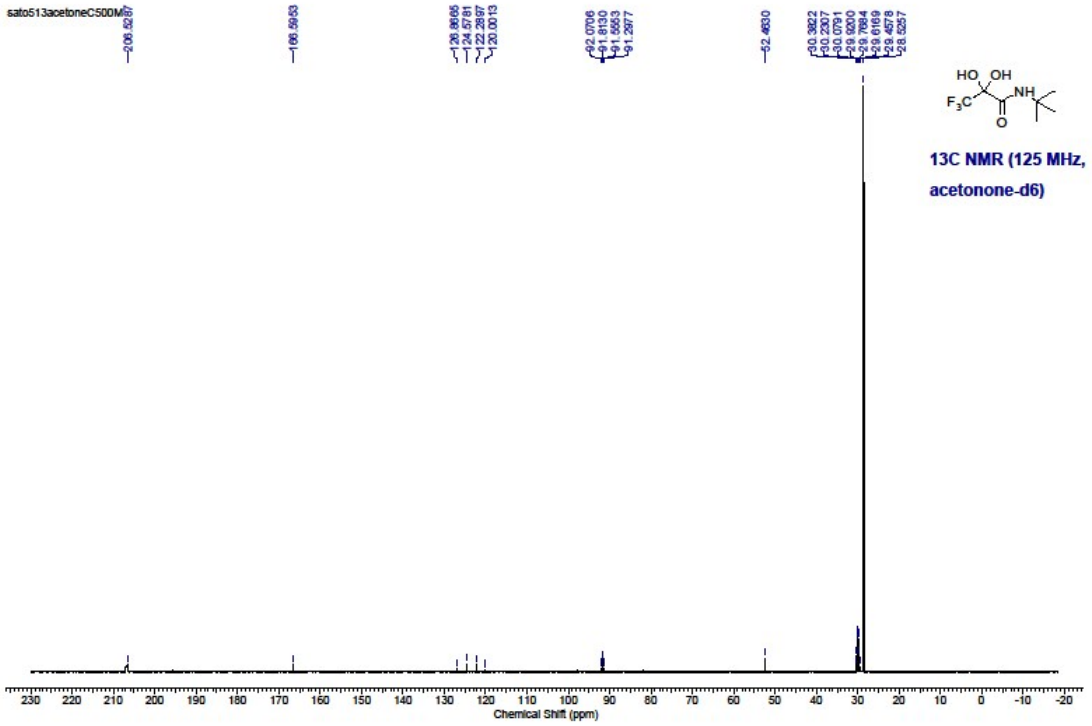
[2] Y. Li, X. Zhao, *Org. Lett.* 2004, **6**, 4467–4470.

[3] U. Matteoli, C. Botteghi, F. Sbrogio, V. Beghetto, S. Paganelli, A. Scrivanti, *Journal of Molecular Catalysis A: Chemical* 1999, 143, 287–295.

[4] M. D Hanwell, D. E. Curtis, D. C. Lonie, T. Vandermeersch, E. Zurek, G. R. Hutchison, *Journal of Cheminformatics* 2012, **4:17,** 2–17.

6. NMR spectra

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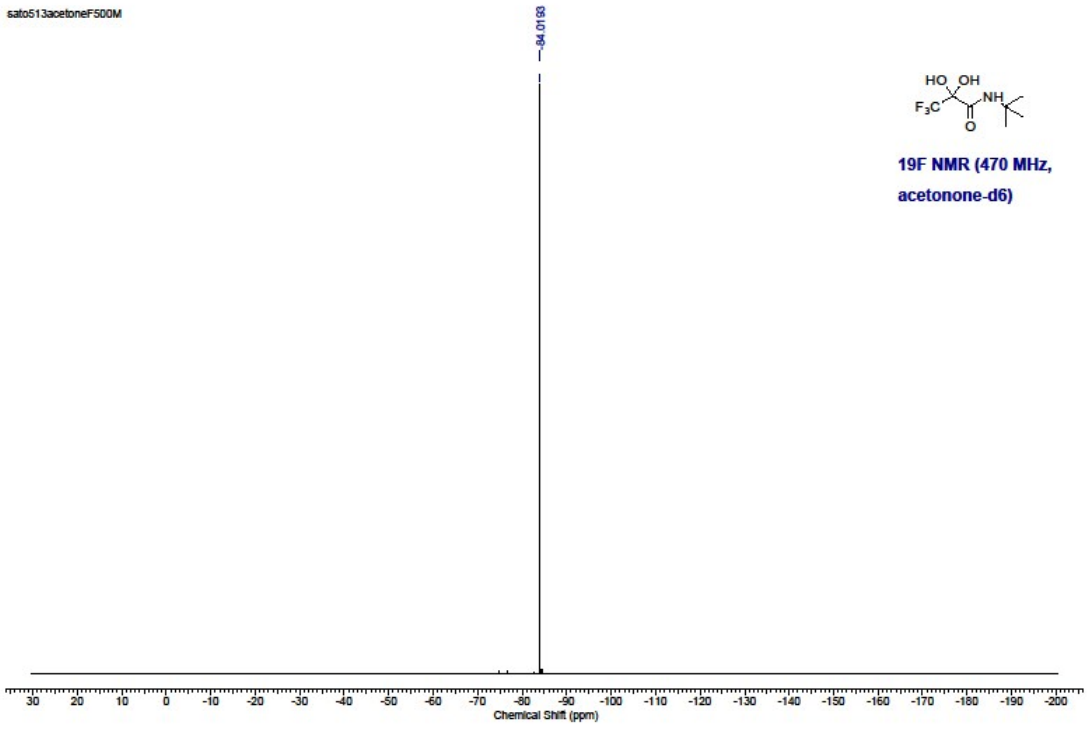
166.5953
126.8665
124.5781
122.2897
120.0013
92.0706
91.8130
91.5553
91.2977
52.4630
30.3822
30.2307
30.0791
29.9200
29.7684
29.6168
29.4578
28.5257
HO OH
F3C
NH
O
13C NMR (125 MHz, acetonone-d6)
Chemical Shift (ppm)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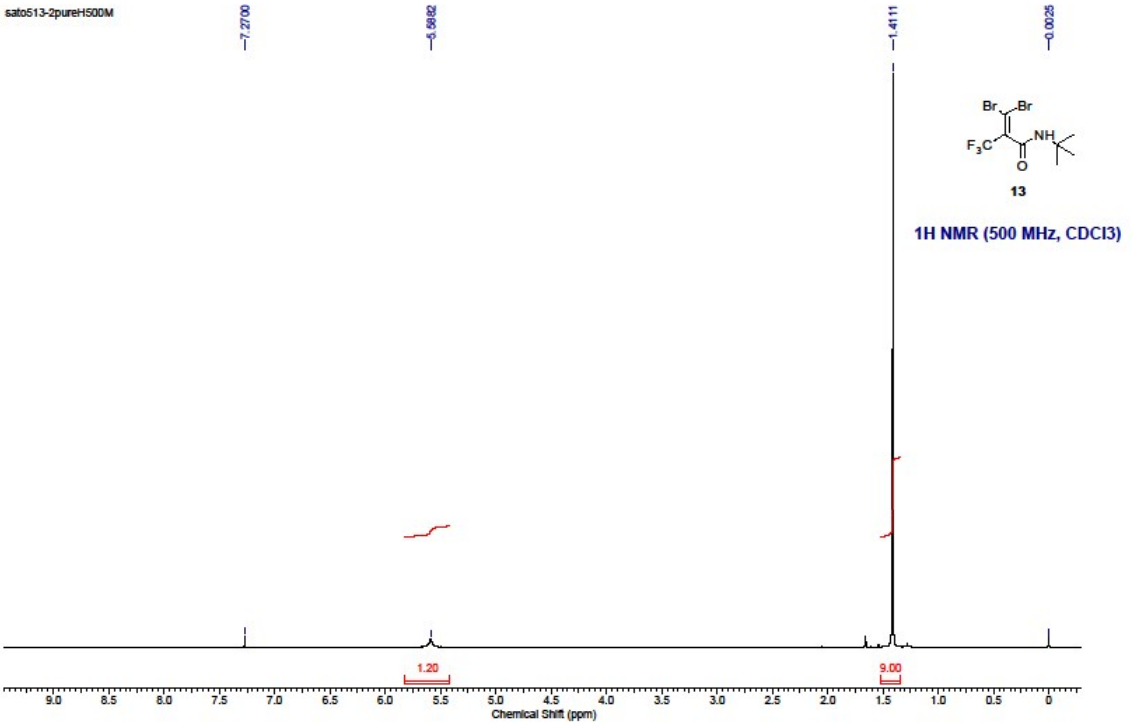
HO OH
F3C
NH
O
19F NMR (470 MHz, acetonone-d6)
Chemical Shift (ppm)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5.6882
1.4111
0.0025
Br
Br
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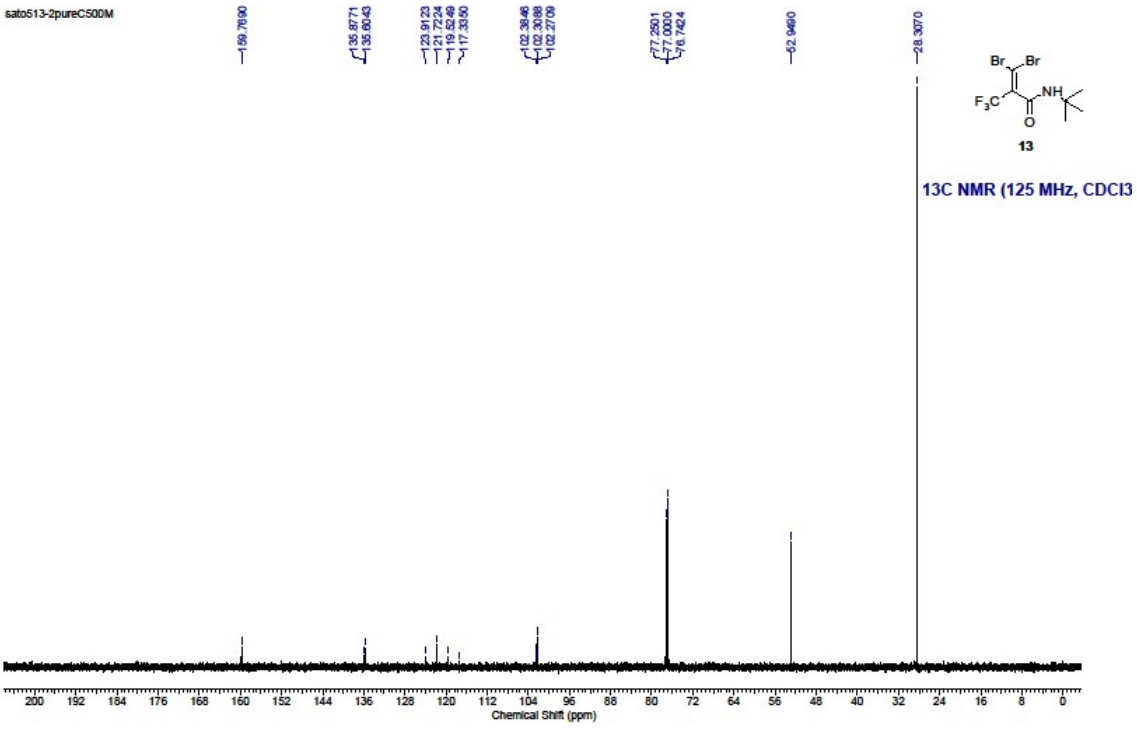
NH
O
13
1H NMR (500 MHz, CDCl3)
1.20
9.00
Chemical Shift (ppm)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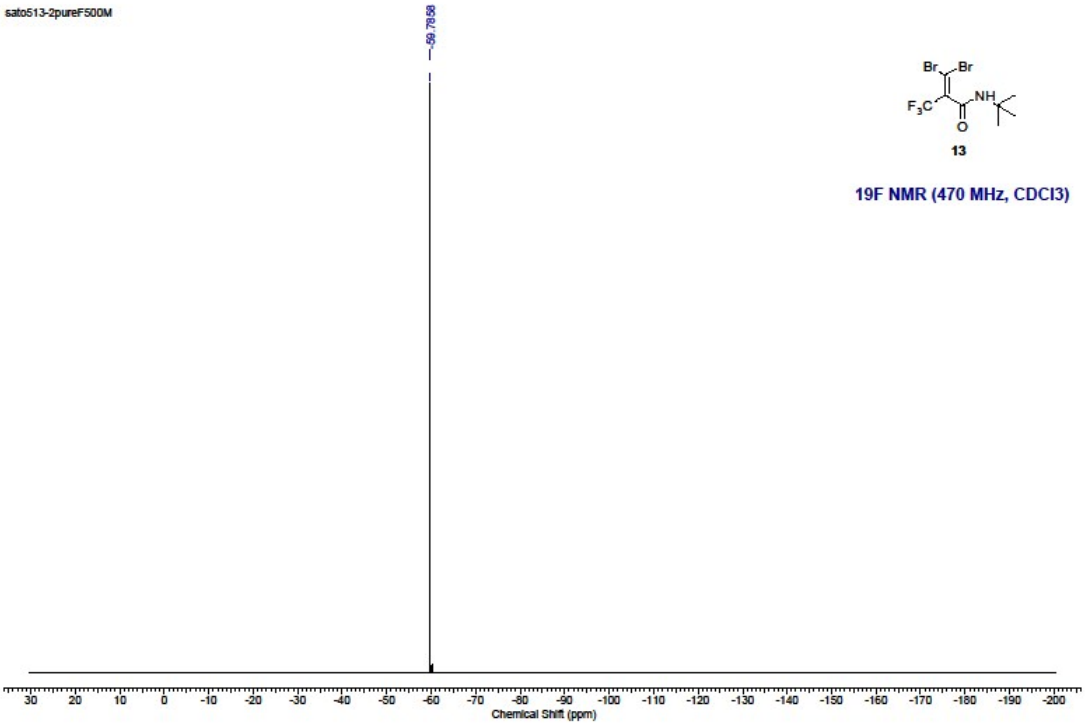
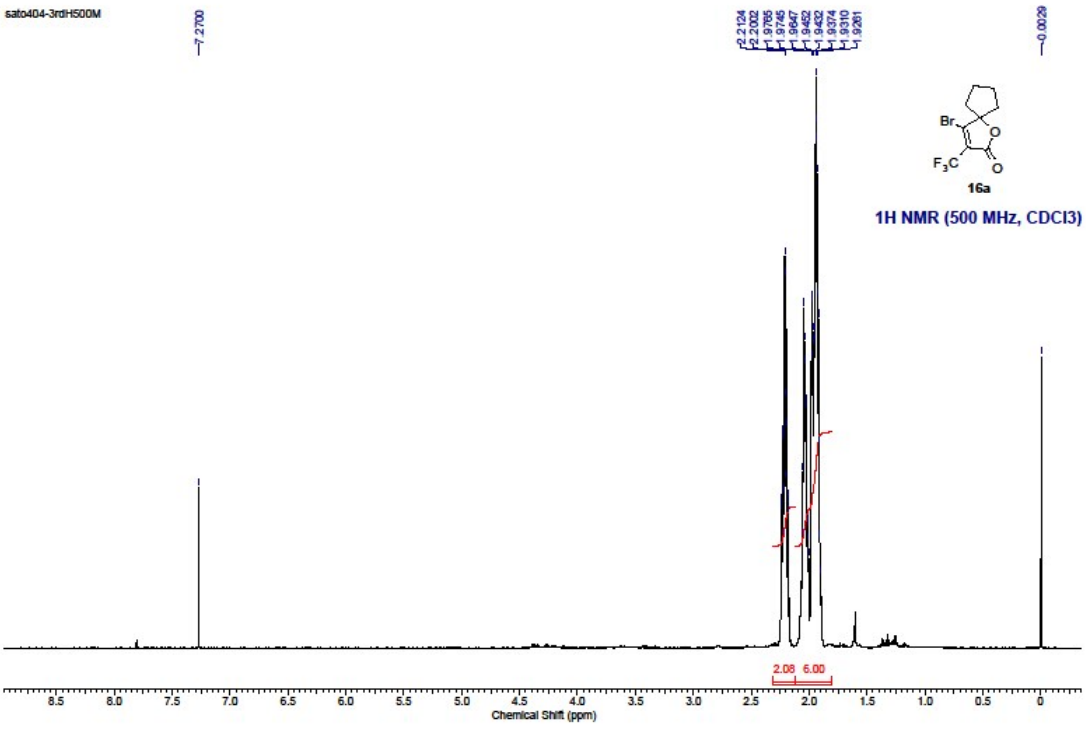
123.9123
121.7224
119.5249
117.3950
103.3846
103.3398
102.2709
77.2501
77.0000
76.7424
52.9460
28.3070
Br
Br
F3C
NH
O
13
13C NMR (125 MHz, CDCl3
Chemical Shift (ppm)


sato513-2pureF500M
-59.7858
Br
Br
F3C
NH
O
13
19F NMR (470 MHz, CDCl3)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)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2.2002
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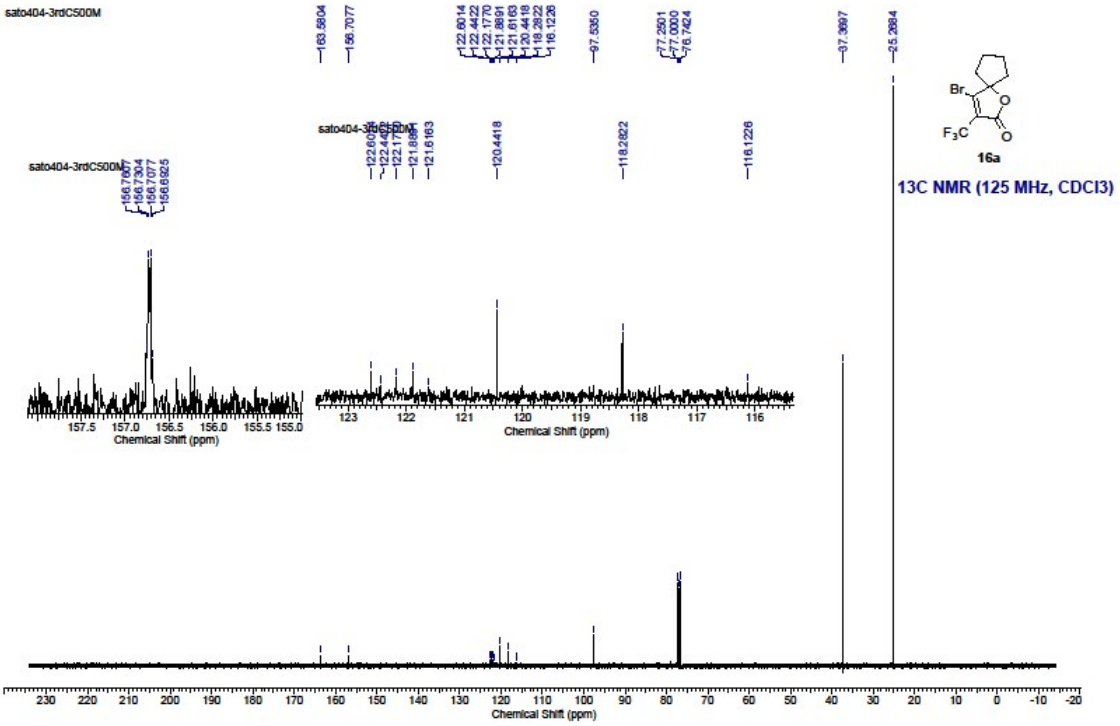
1.9745
1.9647
1.9452
1.9374
1.9310
1.9281
0.0029
Br
O
F3C
O
16a
1H NMR (500 MHz, CDCl3)
2.08 6.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)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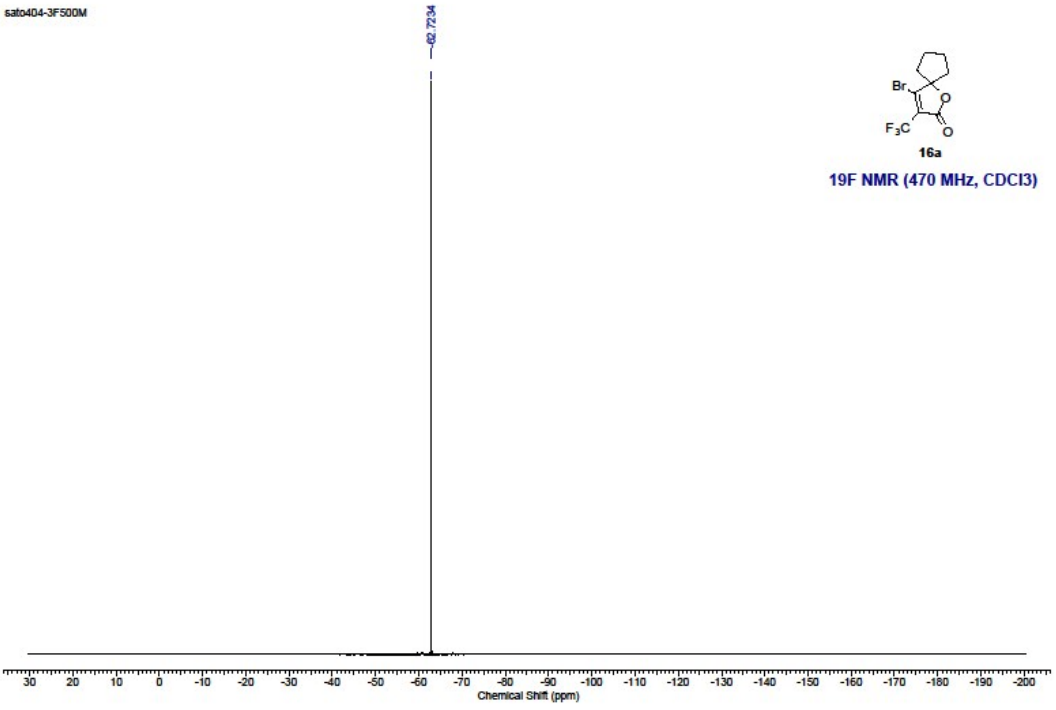
156.7077
122.6014
122.4422
122.1770
121.8891
121.6163
120.4418
118.2822
116.1226
97.5350
77.2501
77.0000
76.7424
37.3997
25.2884
sato404-3rdC500M
156.7077
156.7304
156.7077
156.6825
sato404-3rdC500M
122.6014
122.4422
122.1770
121.8891
121.6163
120.4418
118.2822
116.1226
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
Br
O
F3C
O
16a
13C NMR (125 MHz, CDCl3)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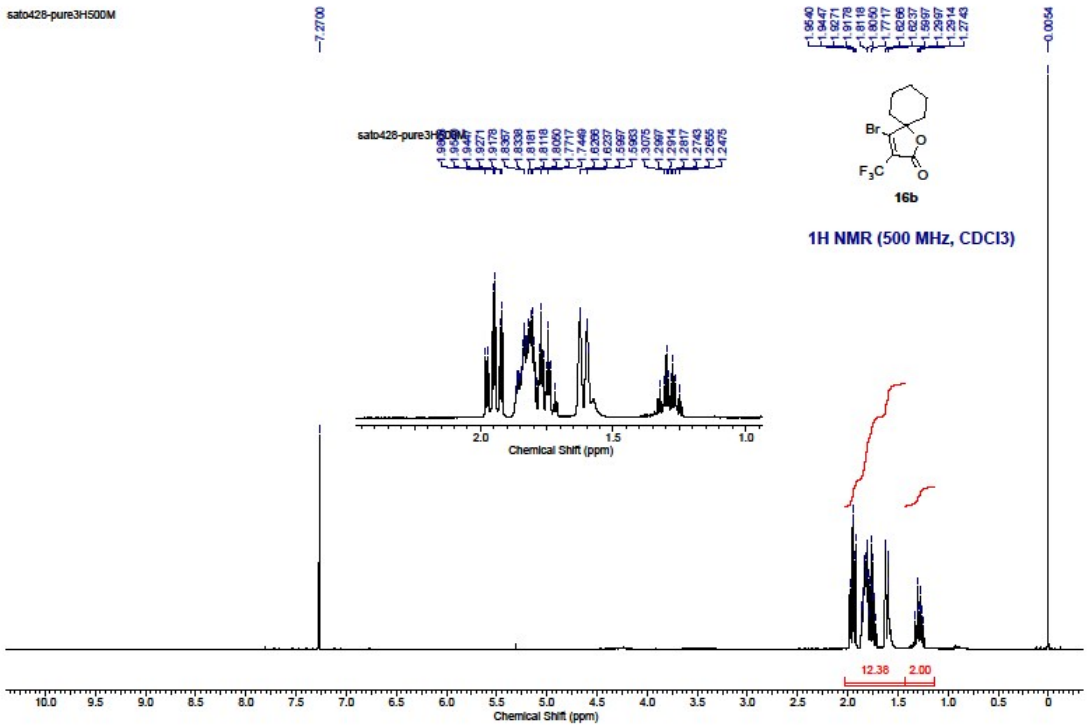
O
F3C
O
16a
19F NMR (470 MHz, CDCl3)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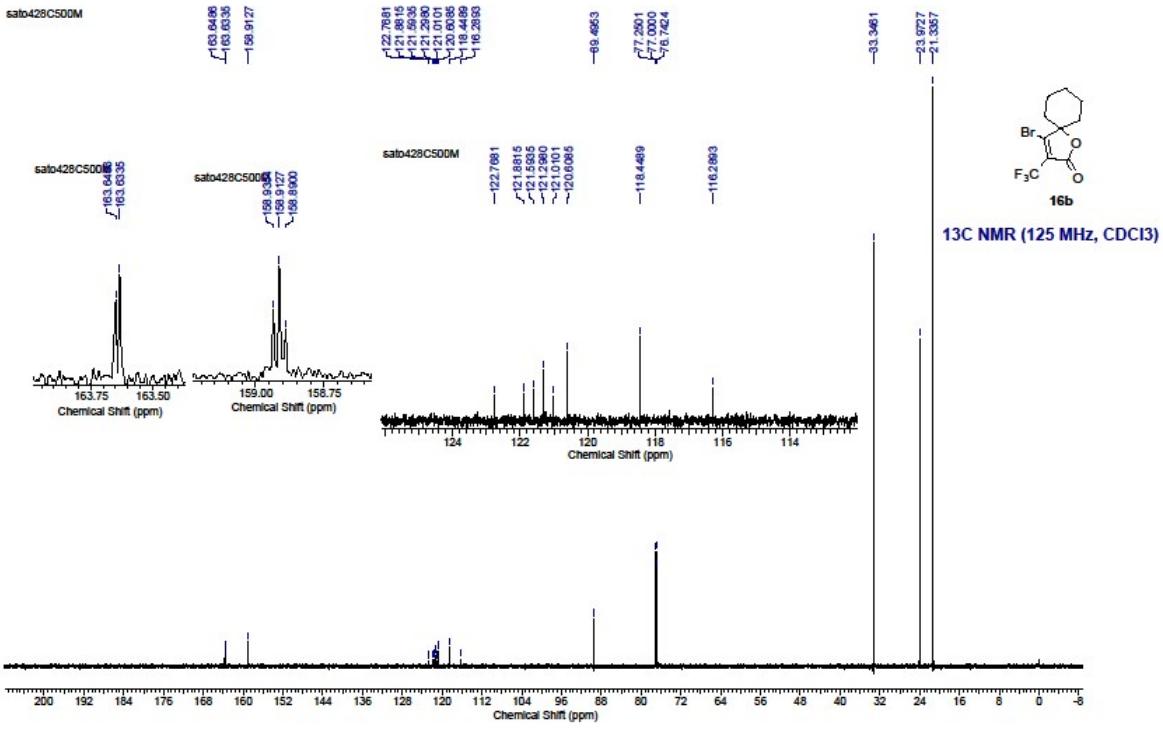
Br
O
F3C
O
16b
1H NMR (500 MHz, CDCl3)
Chemical Shift (ppm)
12.38
2.00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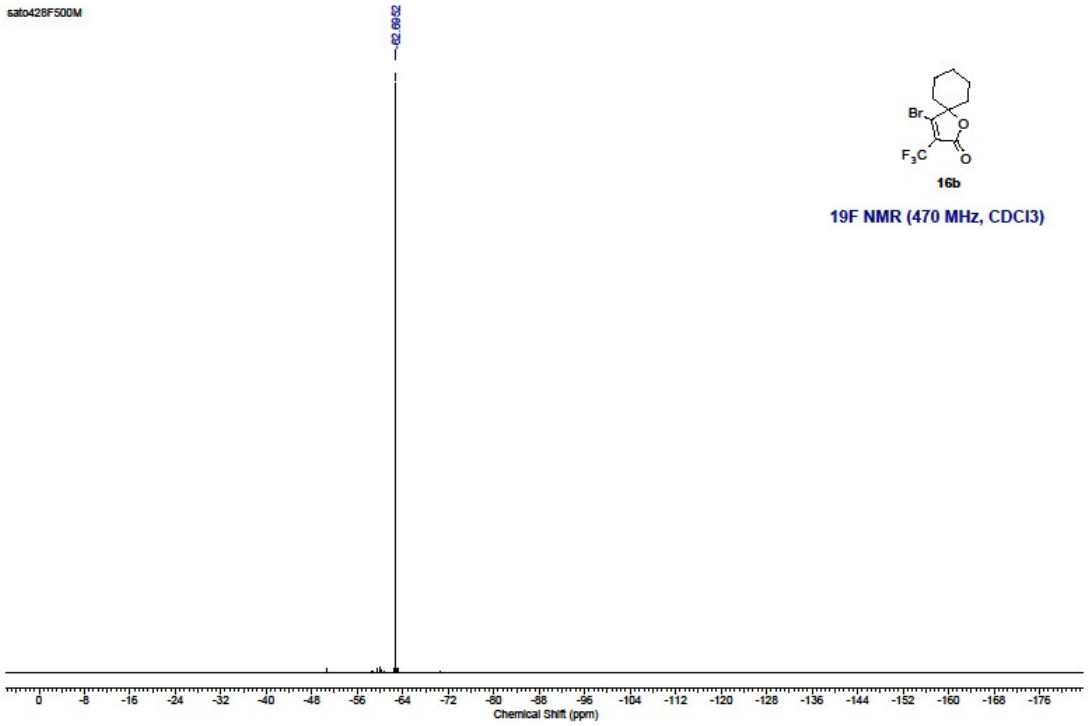
Br
O
F3C
O
16b
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)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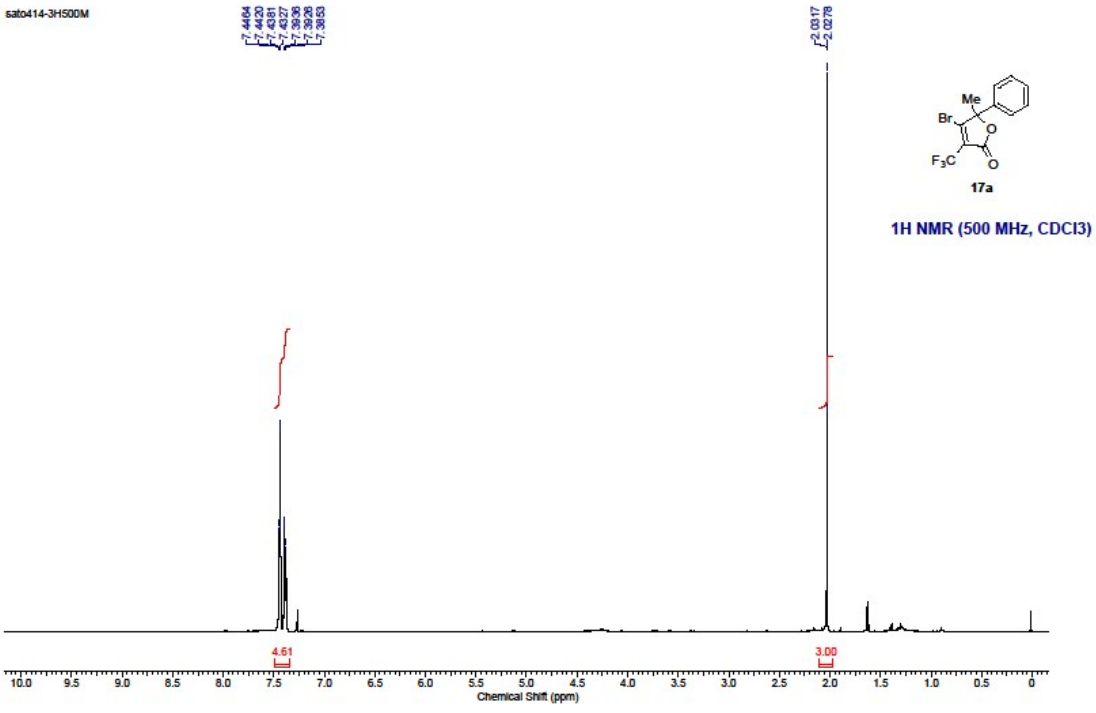
Br
O
F3C
O
16b
19F NMR (470 MHz, CDCl3)
0 -8 -16 -24 -32 -40 -48 -56 -64 -72 -80 -88 -96 -104 -112 -120 -128 -136 -144 -152 -160 -168 -176
Chemical Shift (ppm)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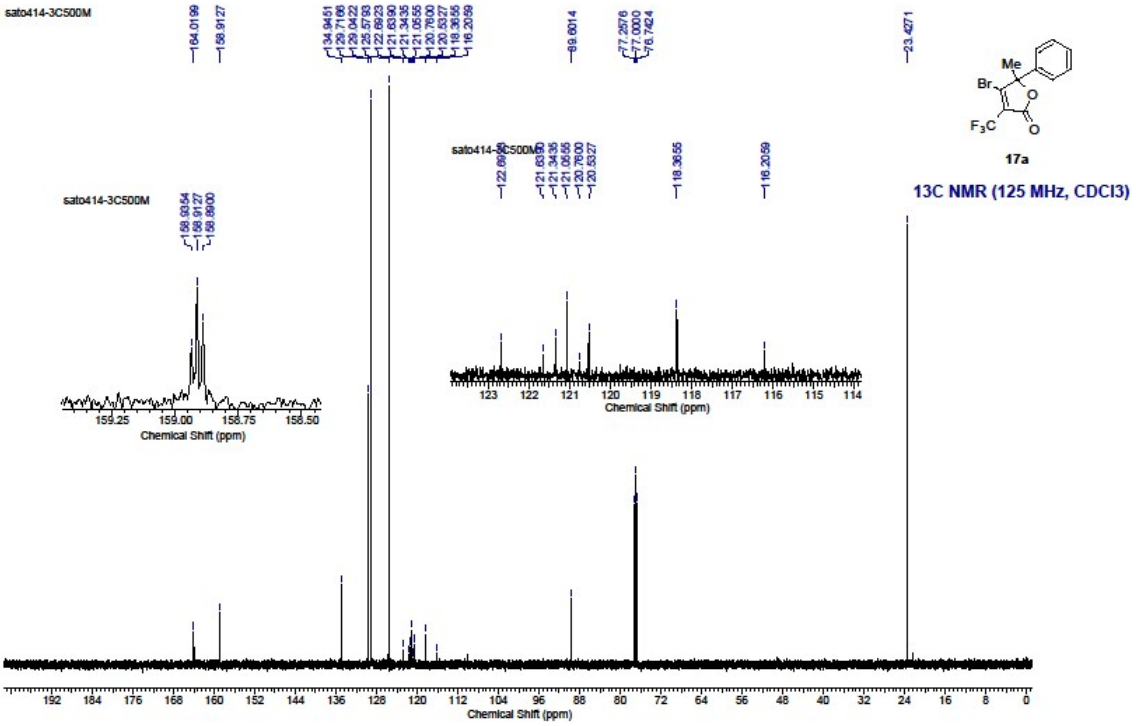
7.4420
7.4381
7.4327
7.3936
7.3929
7.3853
2.0317
2.0278
Me
Br
O
F3C
O
17a
1H NMR (500 MHz, CDCl3)
4.61
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)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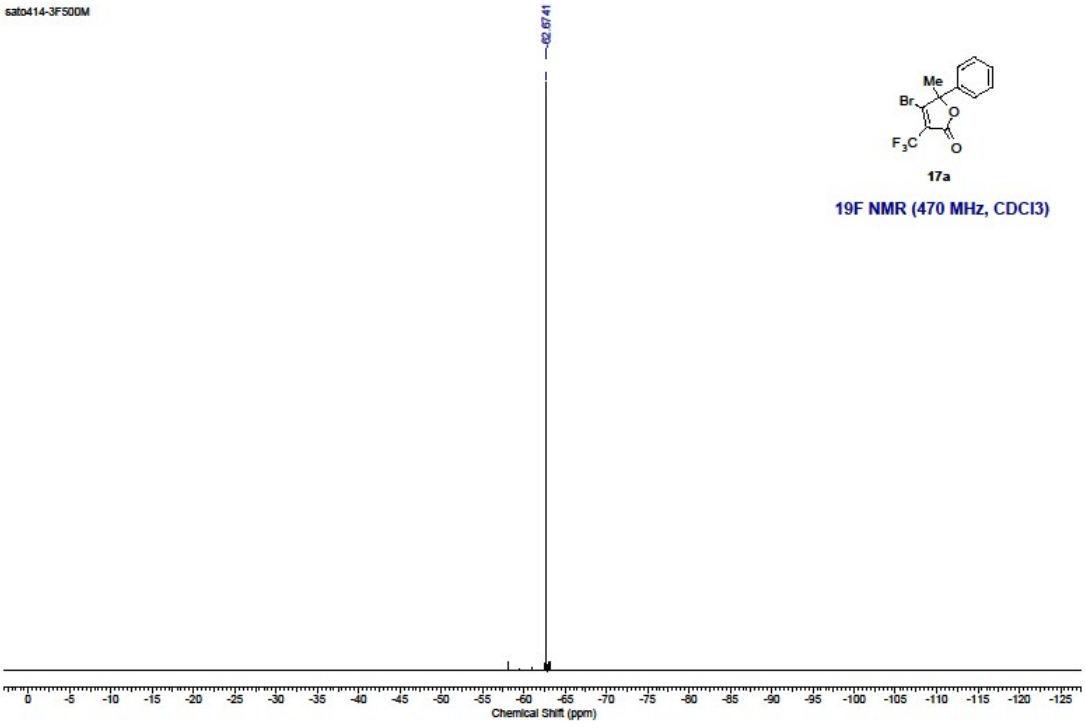
134.9451
129.7166
129.0422
125.5793
122.6923
121.6390
121.3435
121.0555
120.7600
120.5327
118.3655
116.2059
89.6014
77.2576
77.0000
76.7424
23.4271
sato414-3C500M
158.9354
158.9127
158.8900
122.6923
121.6390
121.3435
121.0555
120.7600
120.5327
118.3655
116.2059
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
Me
Br
O
F3C
O
17a
13C NMR (125 MHz, CDCl3)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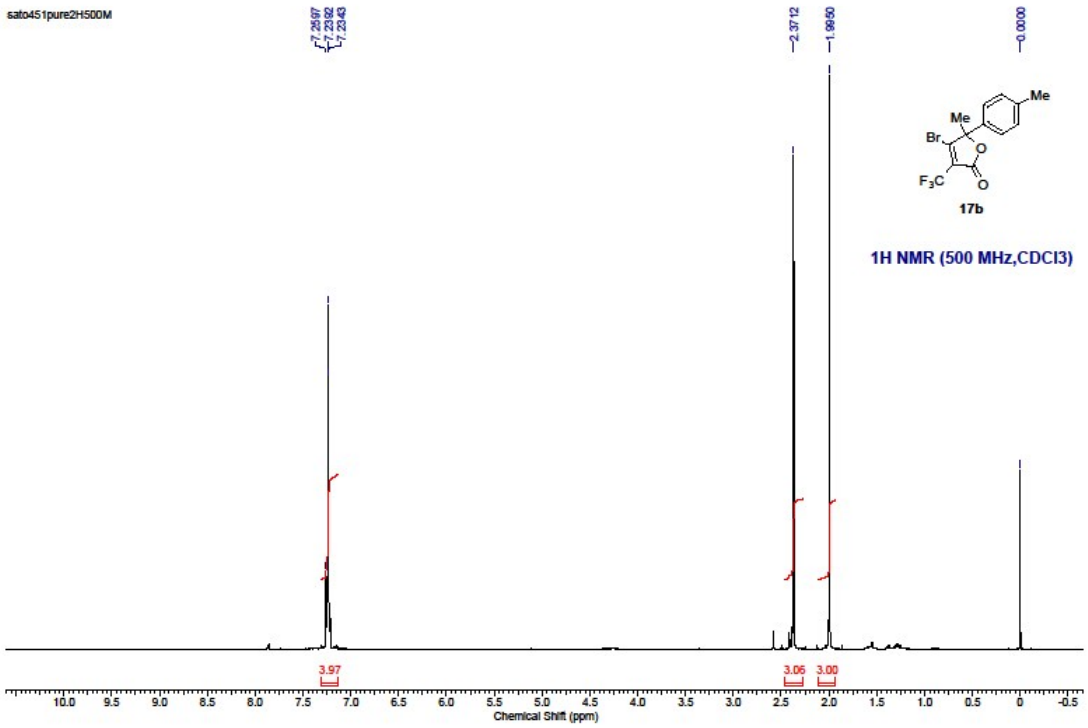
Chemical Shift (ppm)
Me
Br
O
F3C
O
17a
19F NMR (470 MHz, CDCl3)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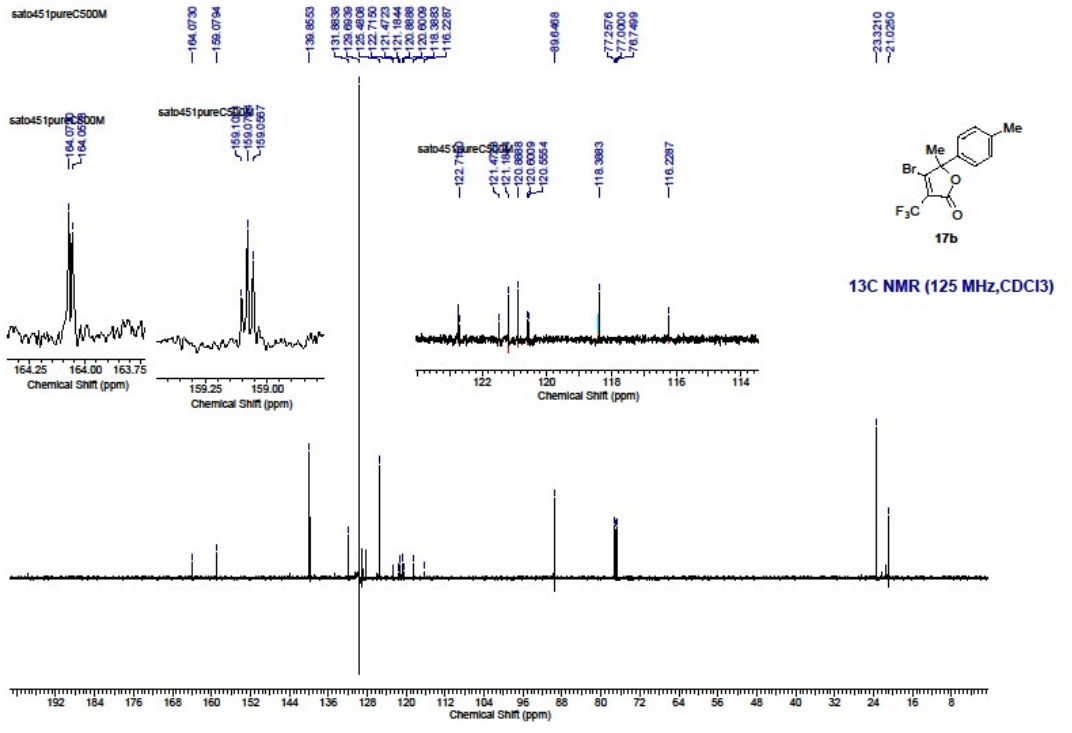
7.2392
7.2343
2.3712
1.9950
0.0000
Me
Me
Br
O
F3C
O
17b
1H NMR (500 MHz,CDCl3)
3.97
3.06
3.00
Chemical Shift (ppm)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159.0794
139.8553
131.8838
129.6939
125.4808
122.7150
121.4723
121.1844
120.8888
120.6009
118.3883
116.2287
99.6408
77.2576
77.0000
76.7499
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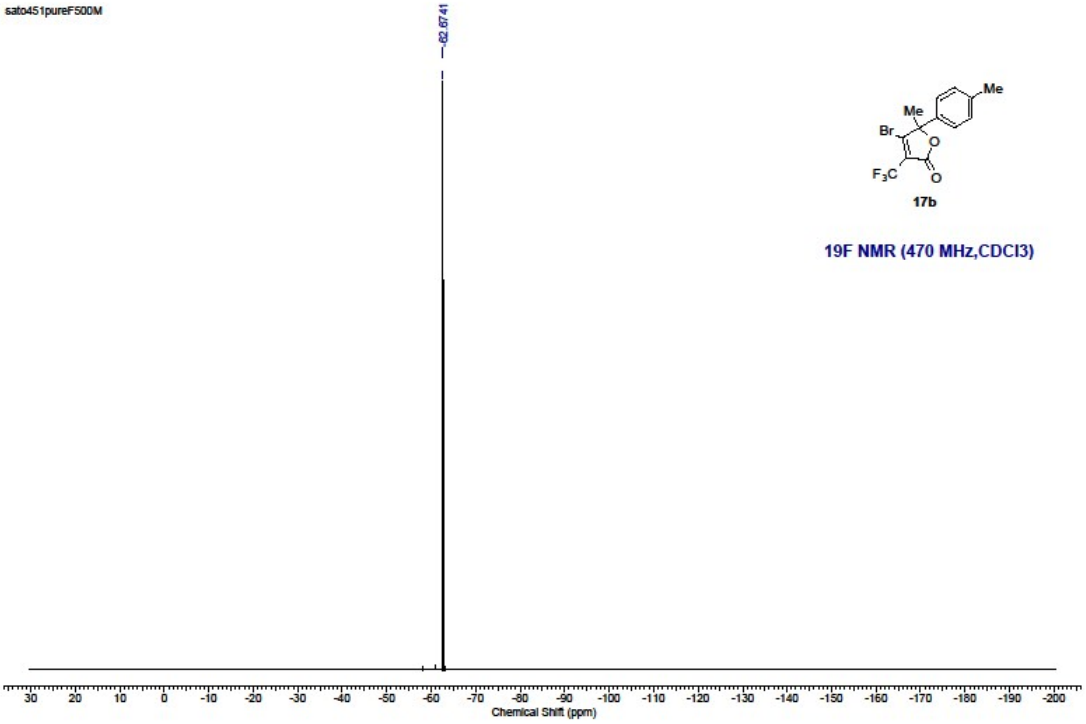
Me
Me
Br
O
F3C
O
17b
13C NMR (125 MHz,CDCl3)
Chemical Shift (ppm)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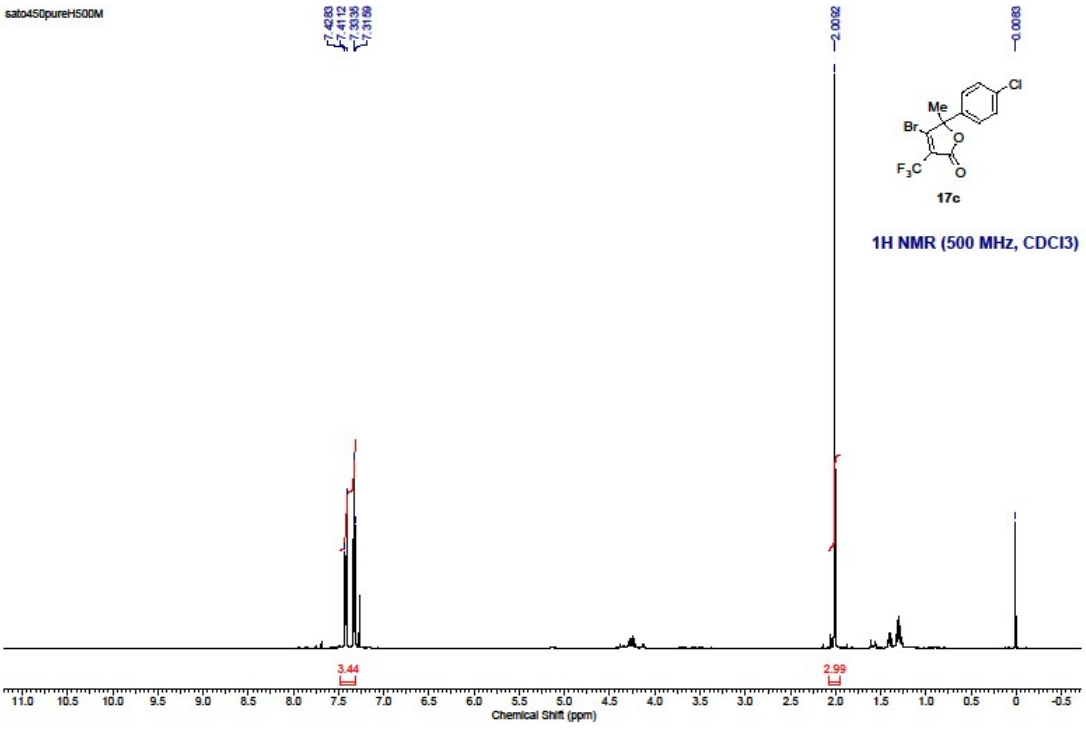
-62.6741
Me
Me
Br
O
F3C
O
17b
19F NMR (470 MHz,CDCl3)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)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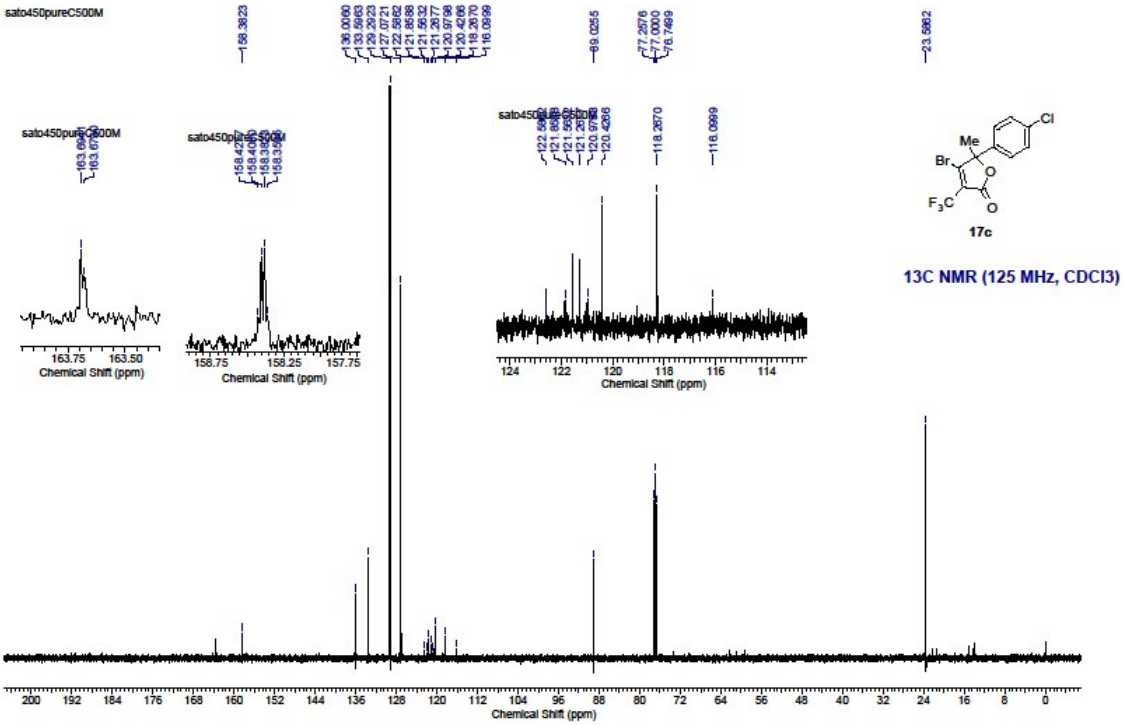
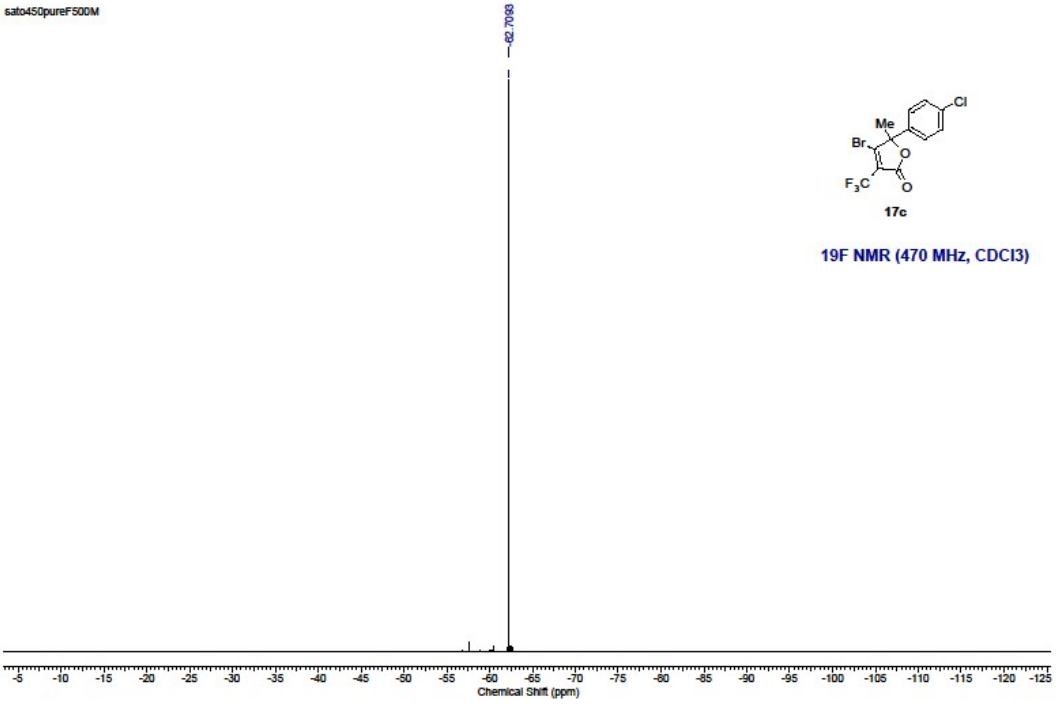
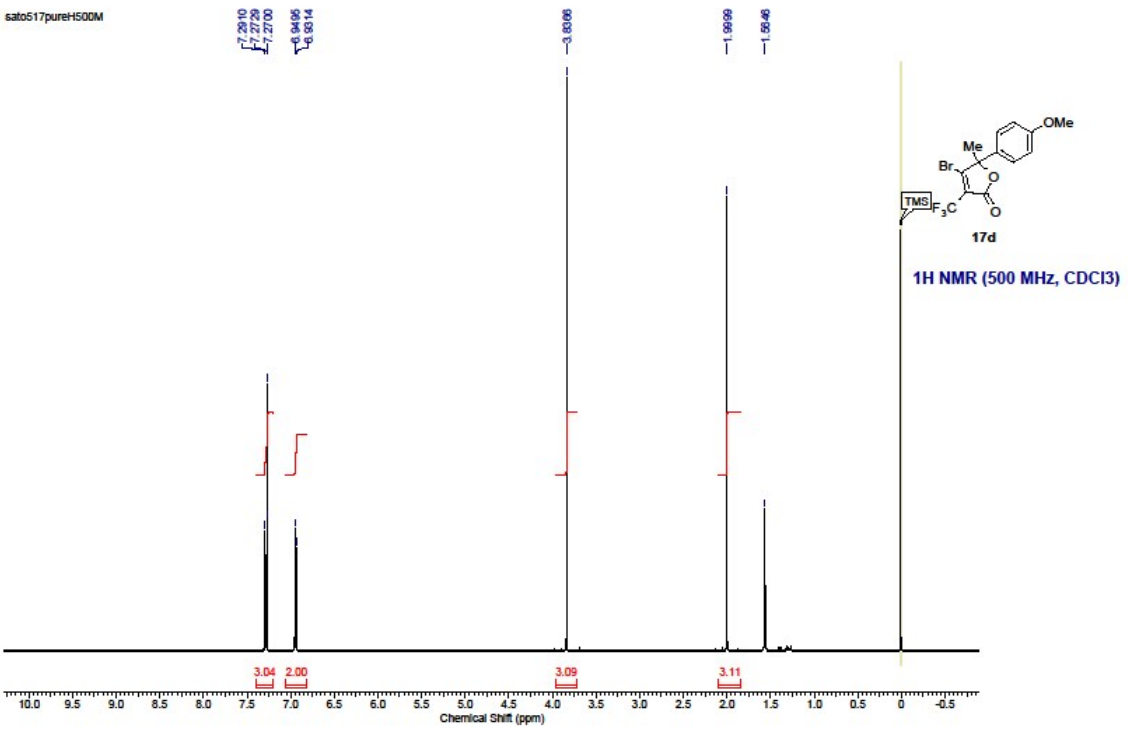
7.4112
7.3335
7.3159
2.0092
0.0083
Cl
Me
Br
O
F3C
O
17c
1H NMR (500 MHz, CDCl3)
3.44
2.99
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)



13C NMR (125 MHz, CDCl3)



19F NMR (470 MHz, CDCl3)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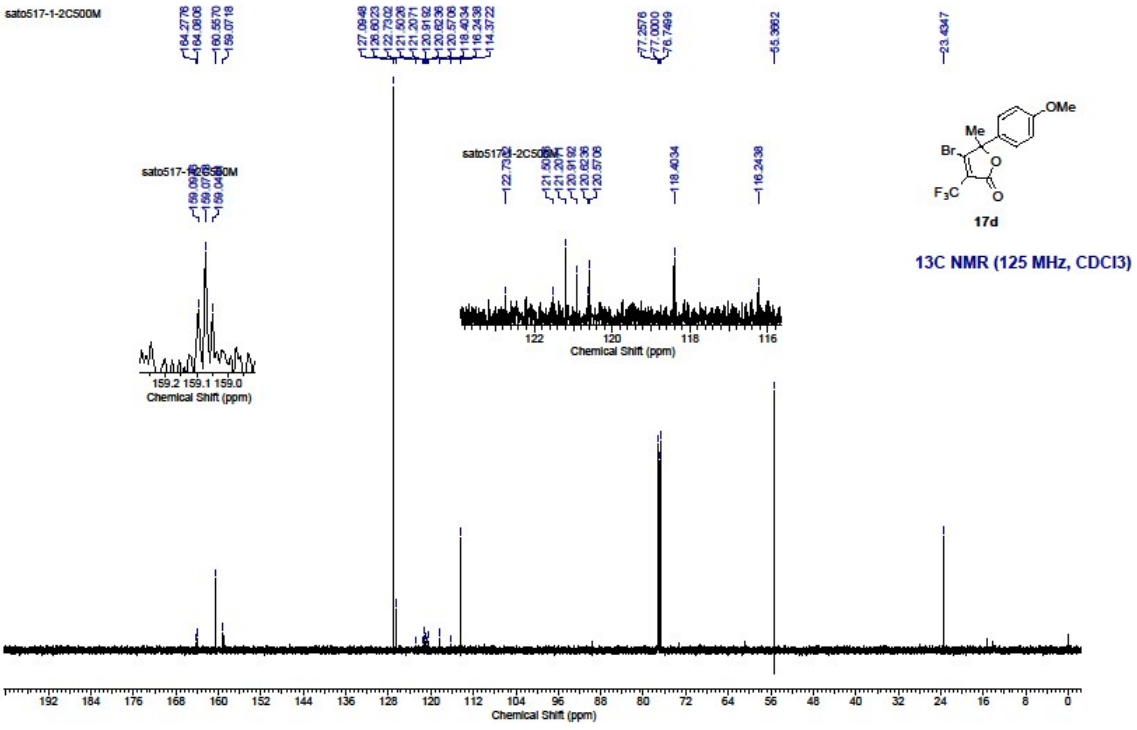
7.2729
7.2700
6.9495
6.9314
3.8366
1.9999
1.5548
OMe
Me
Br
O
TMS
F3C
O
17d
1H NMR (500 MHz, CDCl3)
3.04
2.00
3.09
3.11
Chemical Shift (ppm)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127.0948
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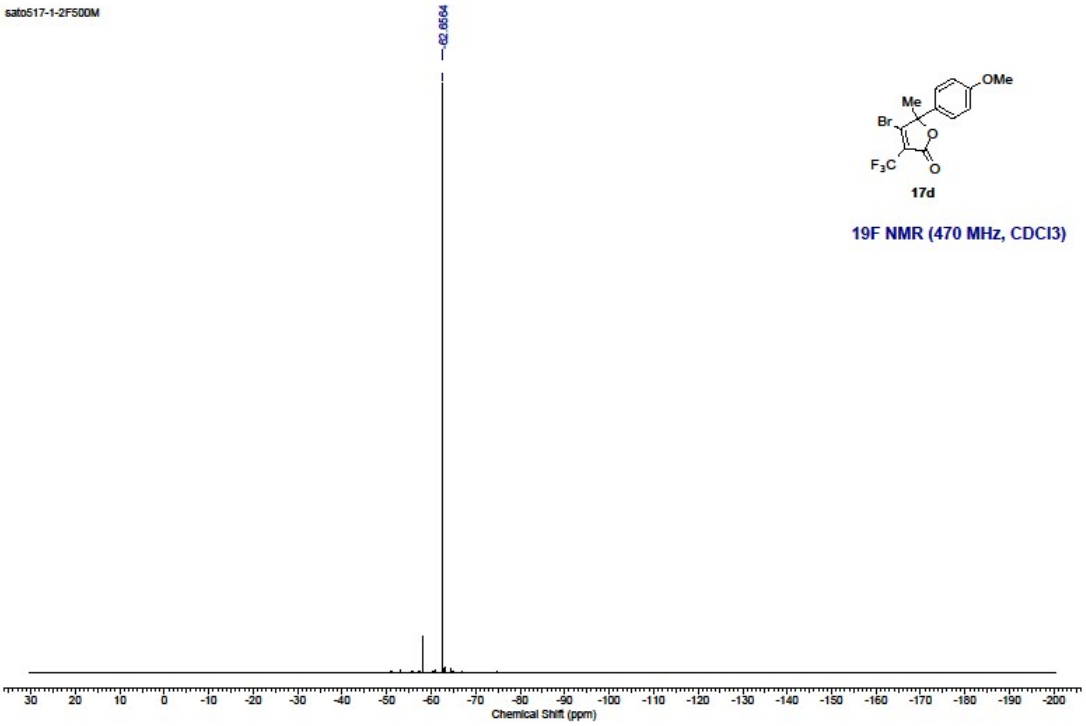
122.7302
121.5026
121.2771
120.9162
120.6236
120.5706
118.4034
116.2438
114.3722
77.2576
77.0000
76.7469
55.3662
23.4347
OMe
Me
Br
O
F3C
O
17d
13C NMR (125 MHz, CDCl3)
159.2 159.1 159.0
Chemical Shift (ppm)
122
120
118
116
Chemical Shift (ppm)
Chemical Shift (ppm)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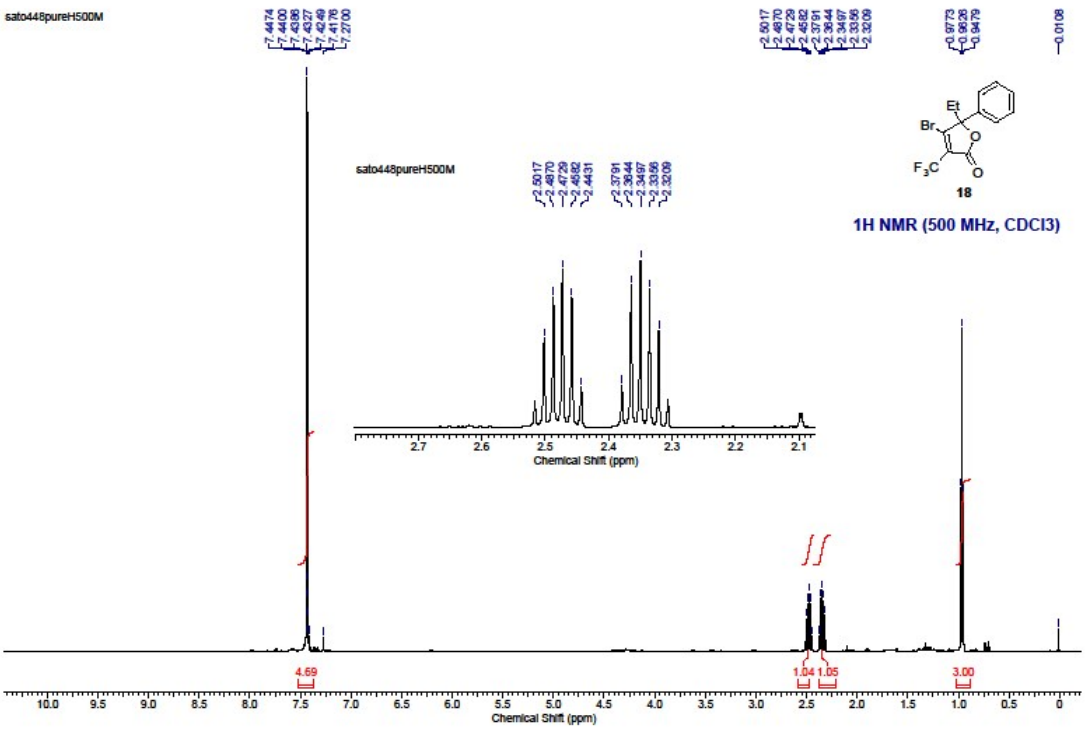
Me
Br
O
F3C
O
17d
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)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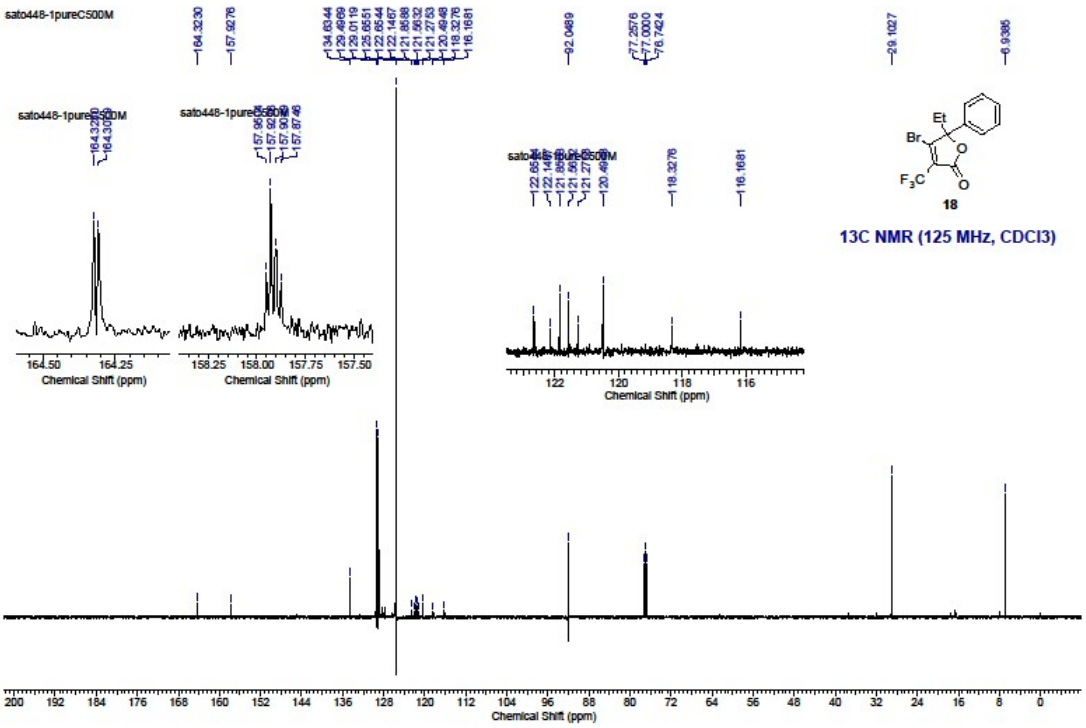
7.4386
7.4327
7.4249
7.4176
7.2700
2.5017
2.4870
2.4729
2.4582
2.4431
2.3791
2.3644
2.3497
2.3356
2.3209
0.9773
0.9626
0.9479
0.0108
Et
Br
O
F3C
O
18
1H NMR (500 MHz, CDCl3)
4.69
1.04
1.05
3.00
Chemical Shift (ppm)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134.6344
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129.0119
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122.6544
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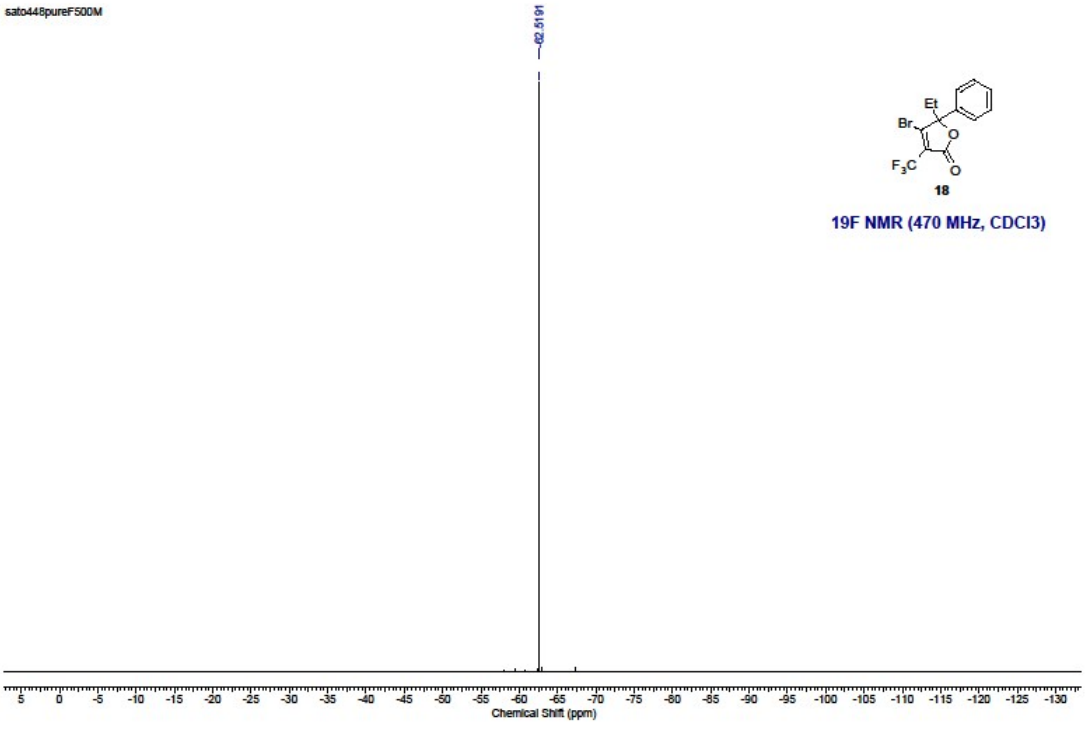
121.8888
121.5932
121.2753
120.4648
118.3276
116.1681
92.0489
77.2576
77.0000
76.7424
29.1027
9.9385
Et
Br
O
F3C
O
18
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)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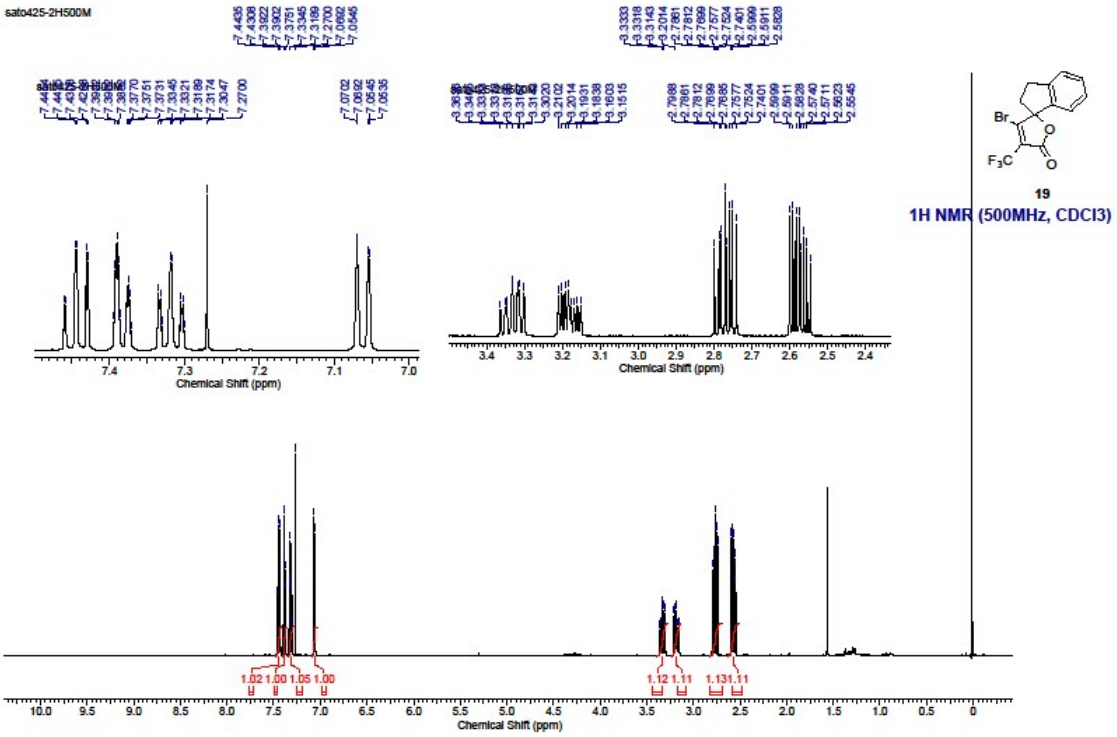
Br
O
F3C
O
18
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)


sato425-2H500M
Chemical Shift (ppm)
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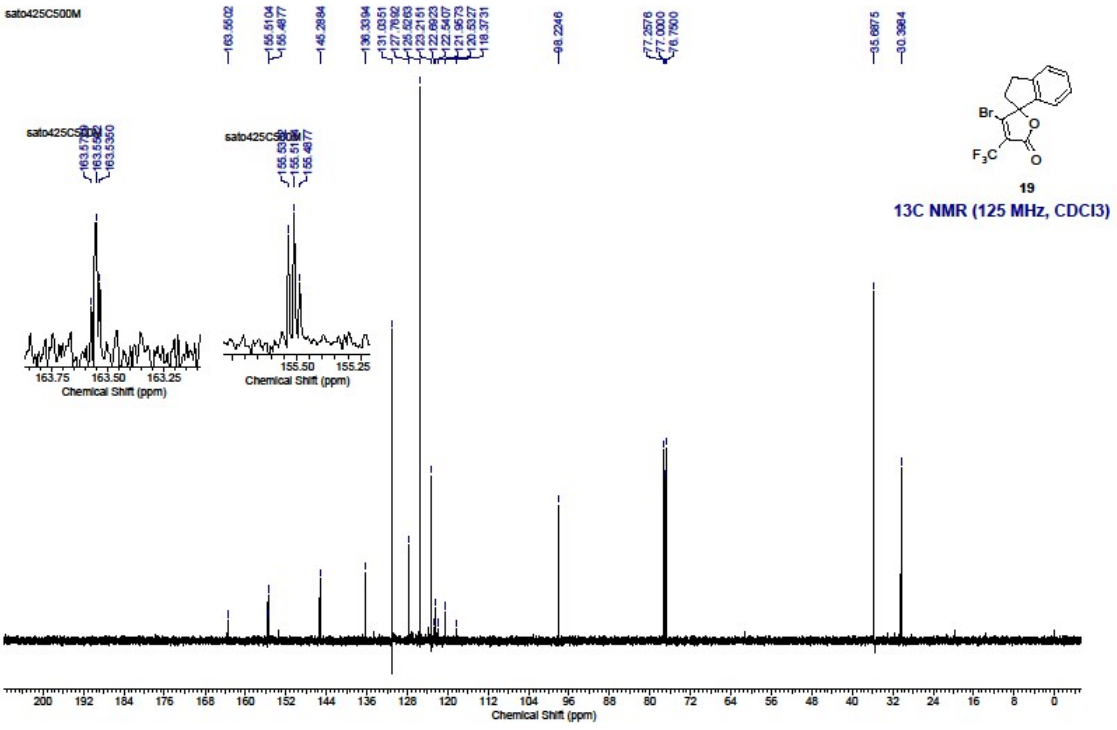
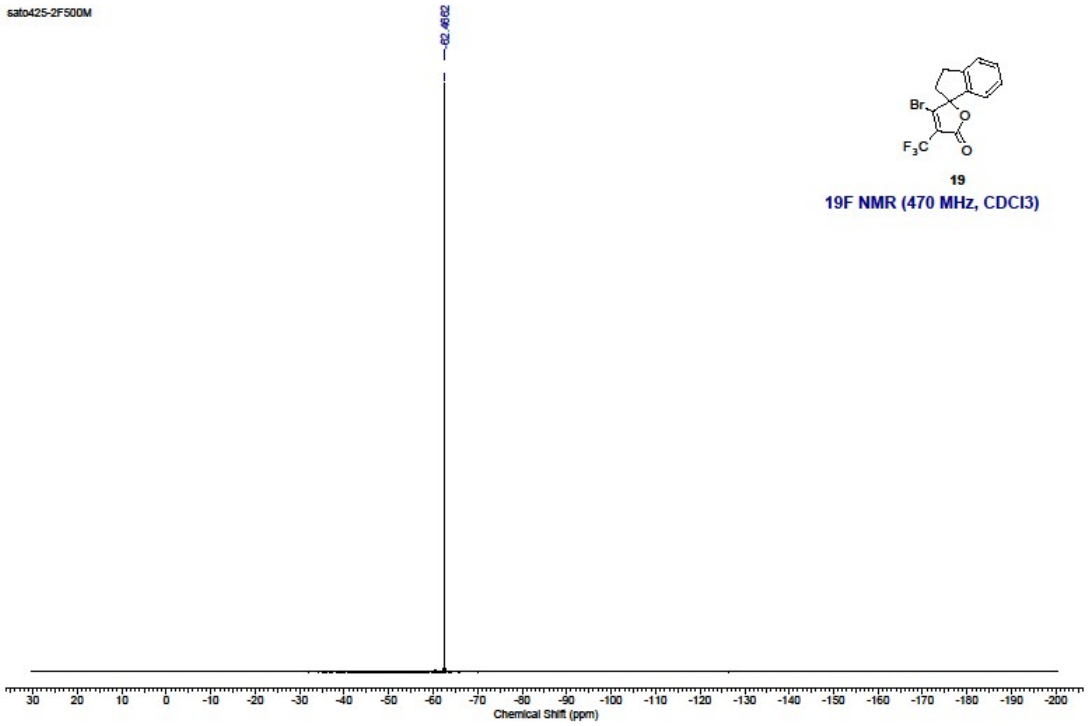
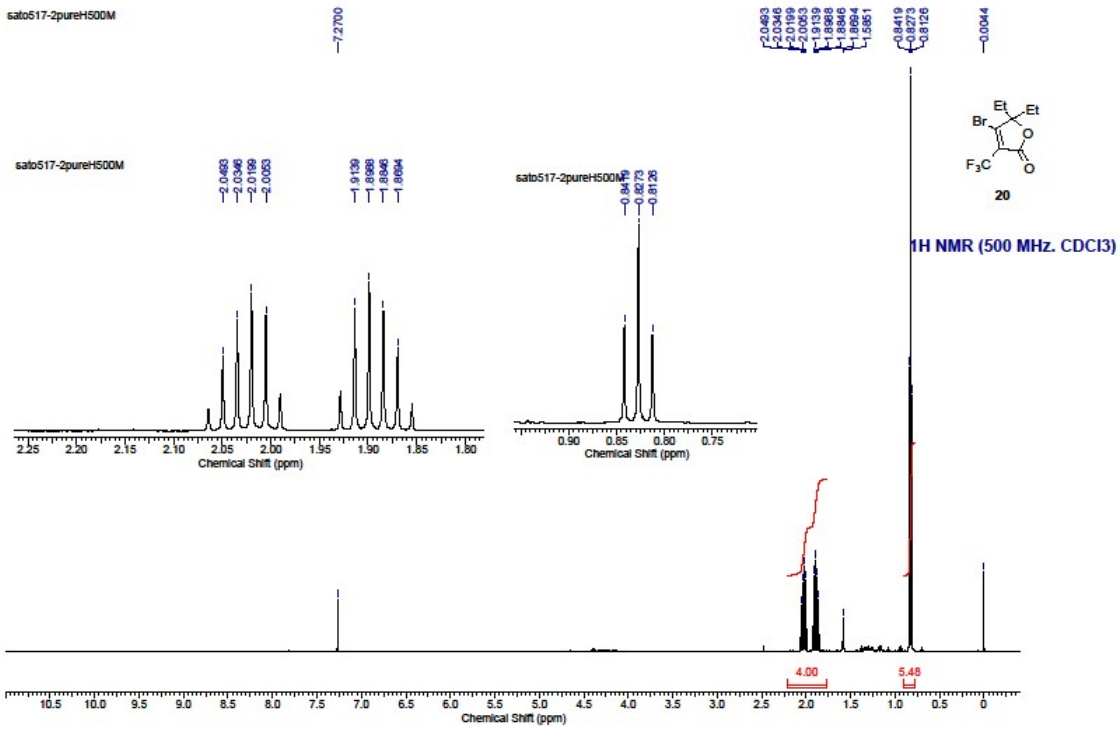
1.12 1.11 1.13 1.11
Br
F3C
O
19
1H NMR (500MHz, CDCl3)


sato425C500M
Chemical Shift (ppm)
Br
F3C
O
19
13C NMR (125 MHz, CDCl3)



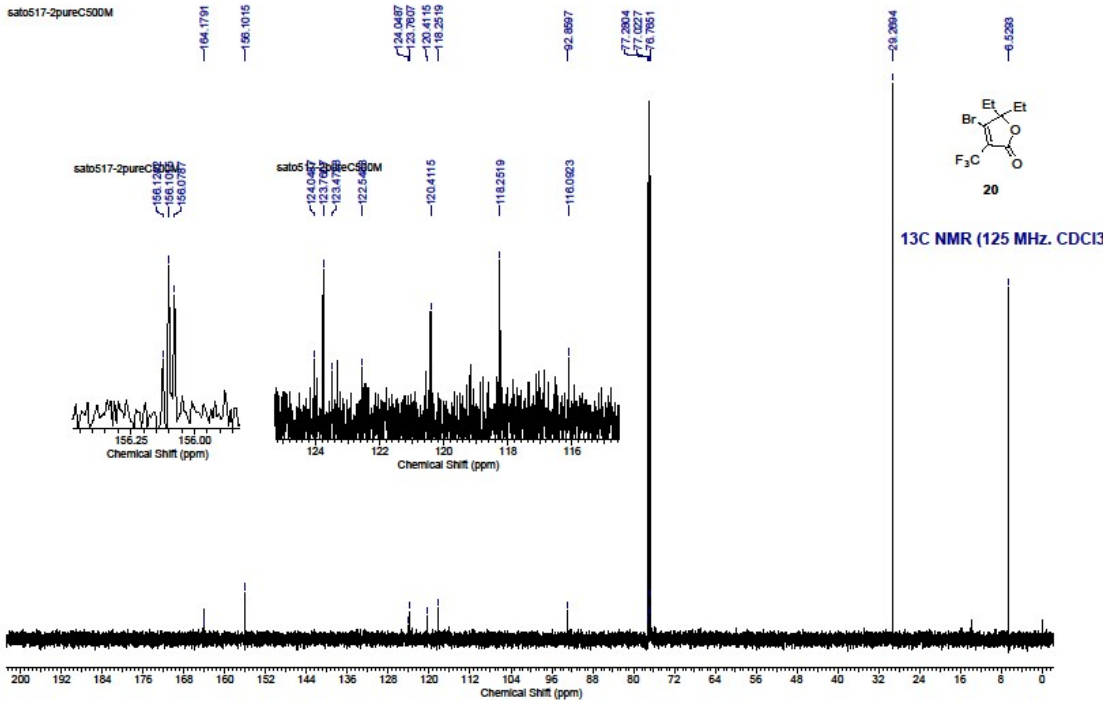
19

19F NMR (470 MHz, CDCl3)



20

1H NMR (500 MHz. CDCl3)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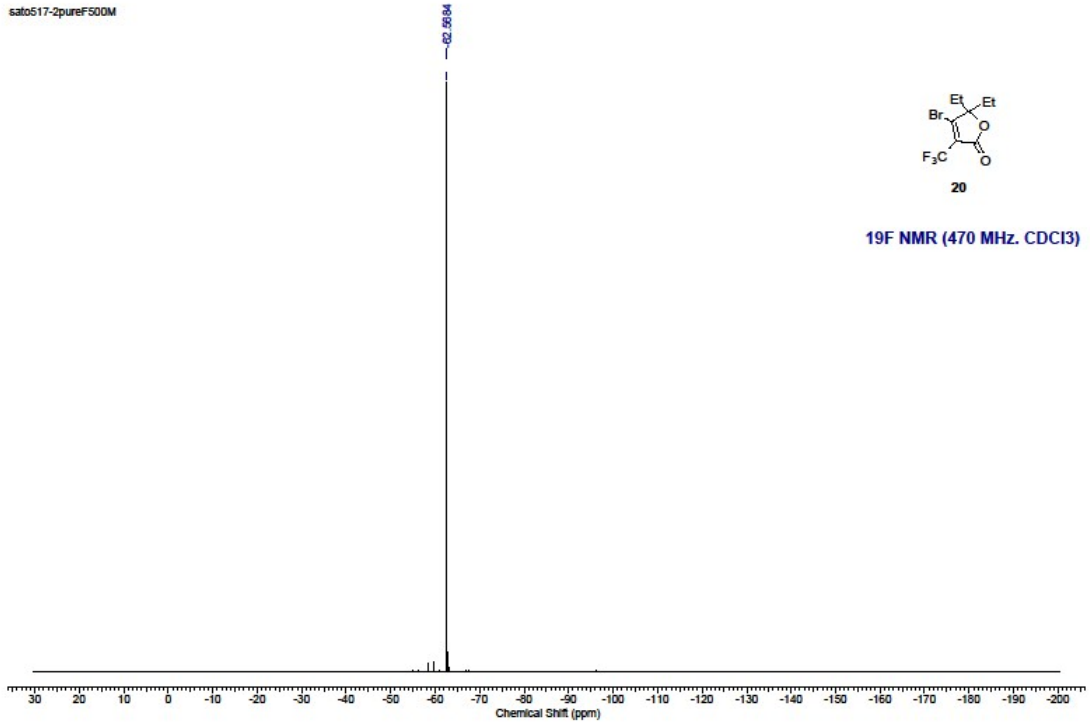
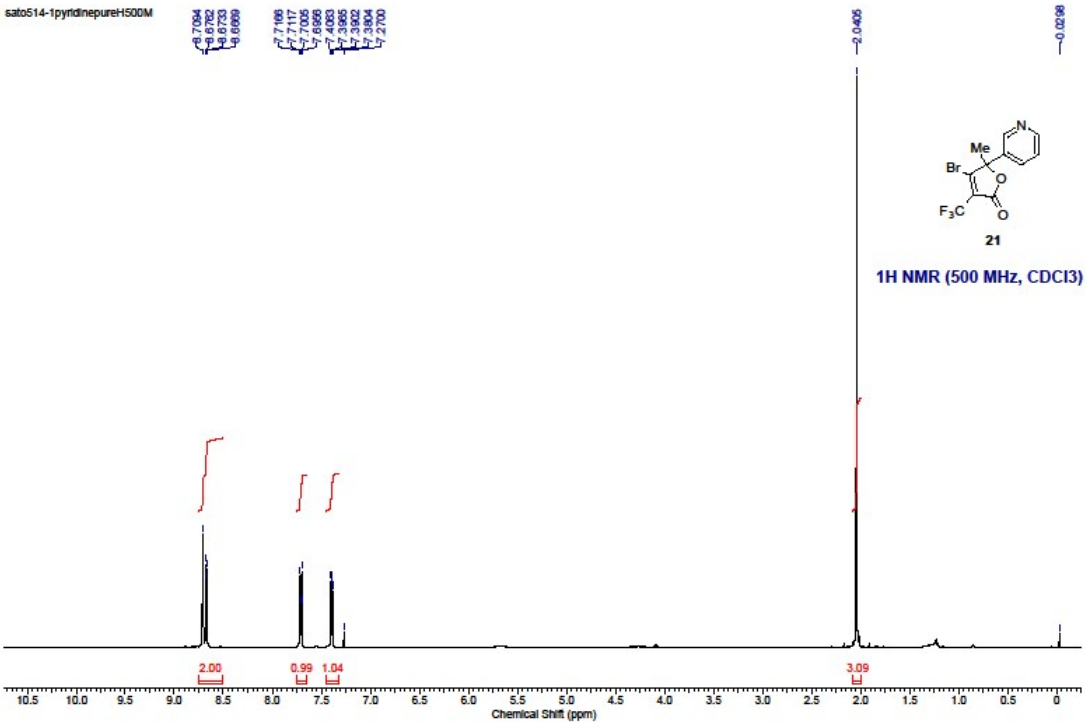
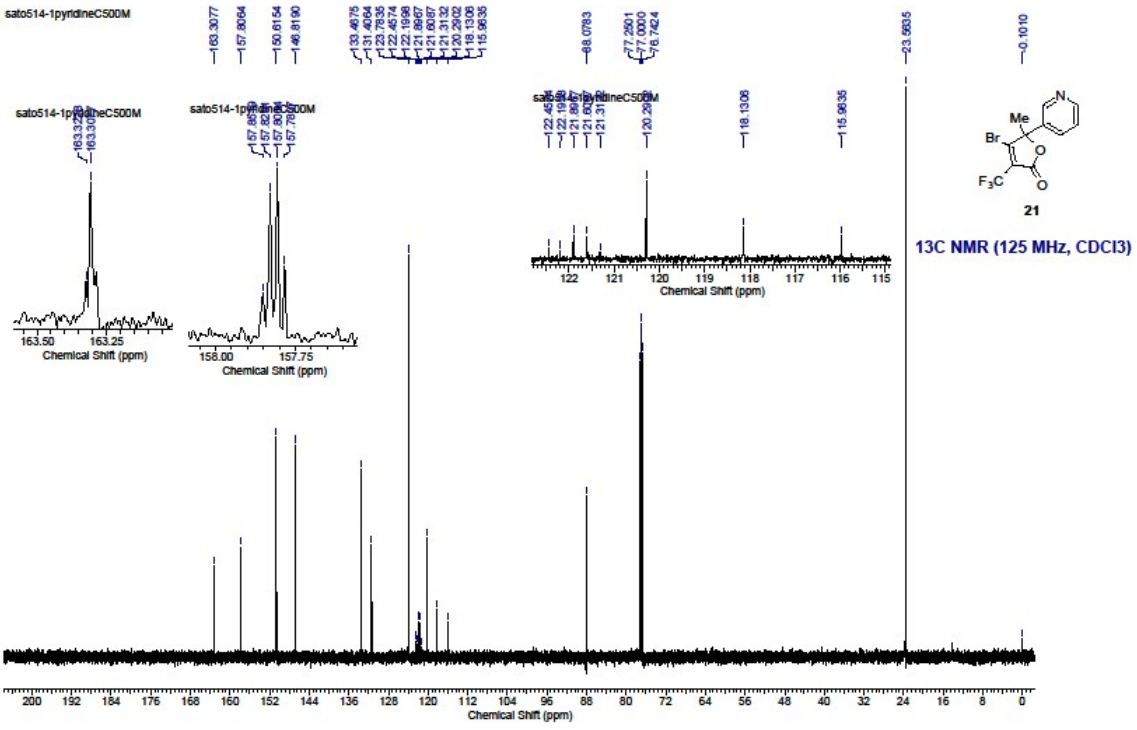
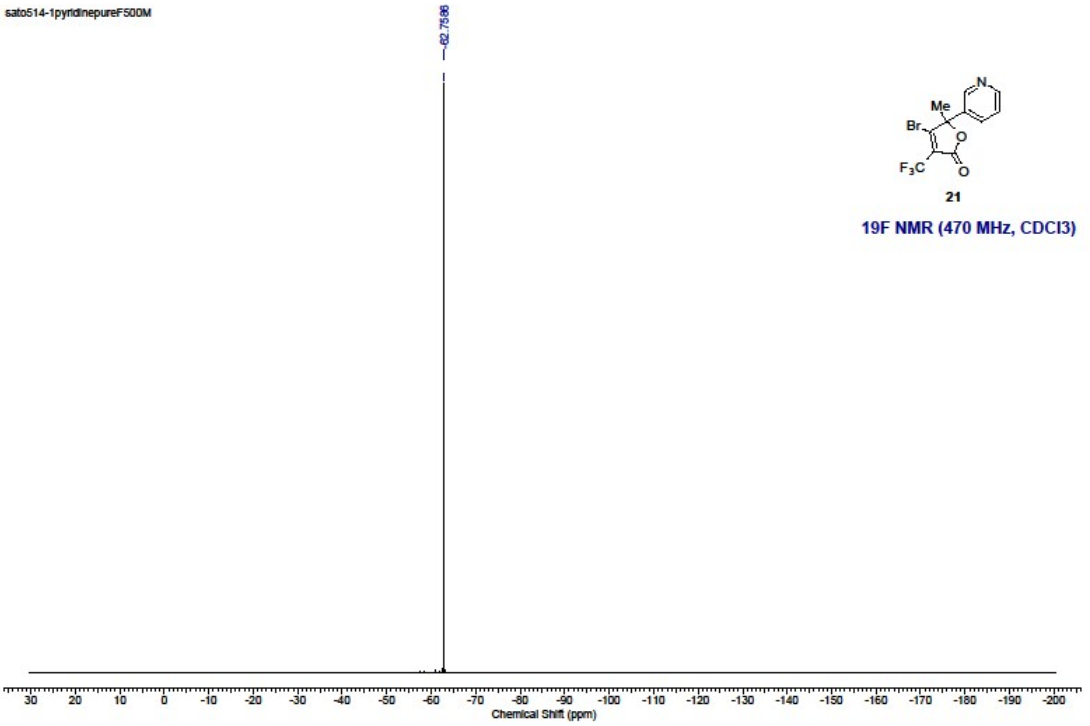
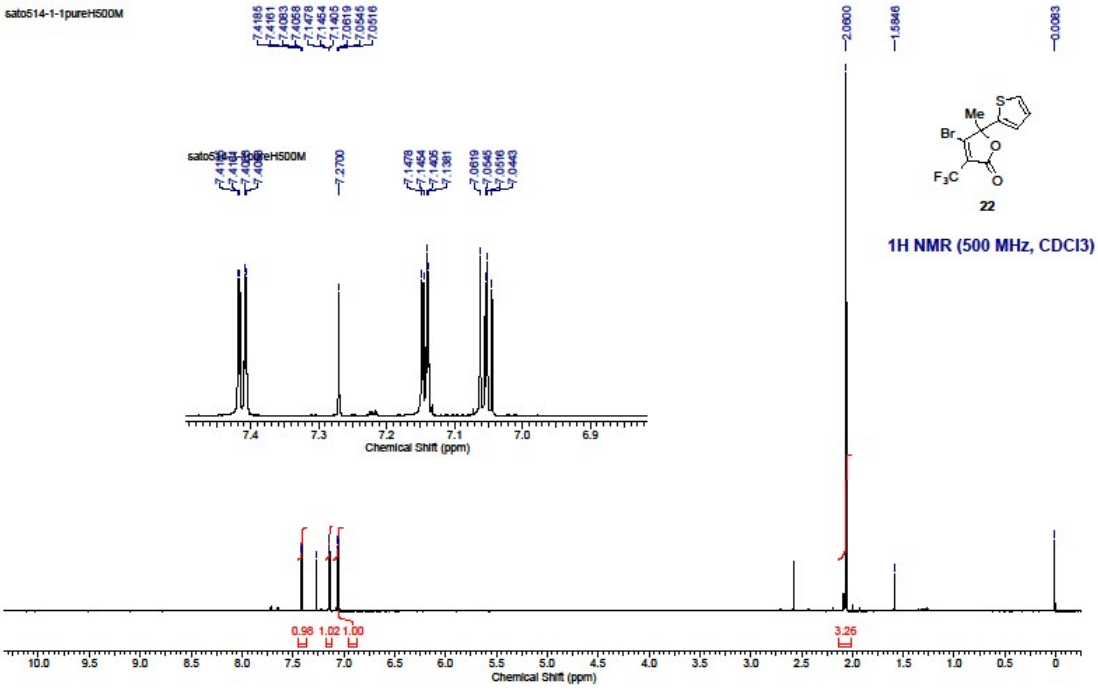
124.0487
123.7607
120.4115
118.2519
92.8597
77.2804
77.0227
76.7651
29.2694
8.5293
Et
Et
Br
O
F3C
O
20
13C NMR (125 MHz. CDCl3
156.25
156.00
Chemical Shift (ppm)
124
122
120
118
116
Chemical Shift (ppm)
Chemical Shift (ppm)

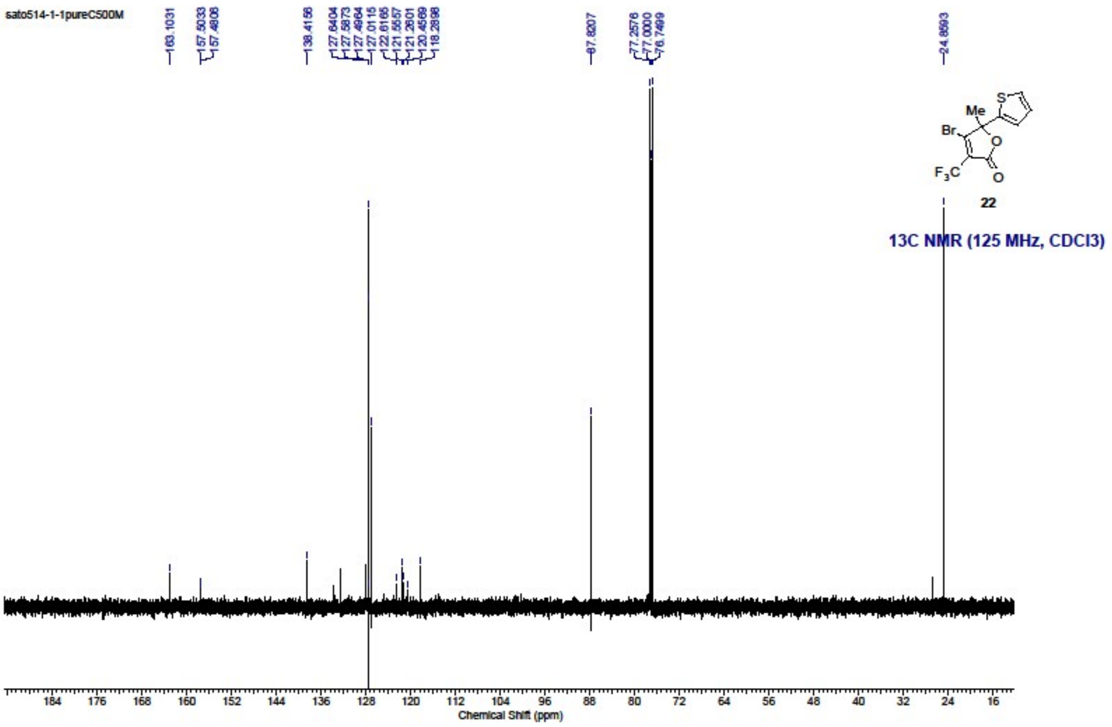

sato517-2pureF500M
62.5884
Et
Et
Br
O
F3C
O
20
19F NMR (470 MHz. CDCl3)
Chemical Shift (ppm)


sato514-1pyridinepureH500M
8.7094
8.6762
8.6733
8.6699
7.7166
7.7117
7.7005
7.6966
7.4063
7.3965
7.3902
7.3804
7.2700
2.0405
0.0298
Me
Br
O
F3C
O
N
21
1H NMR (500 MHz, CDCl3)
2.00
0.99
1.04
3.09
Chemical Shift (ppm)

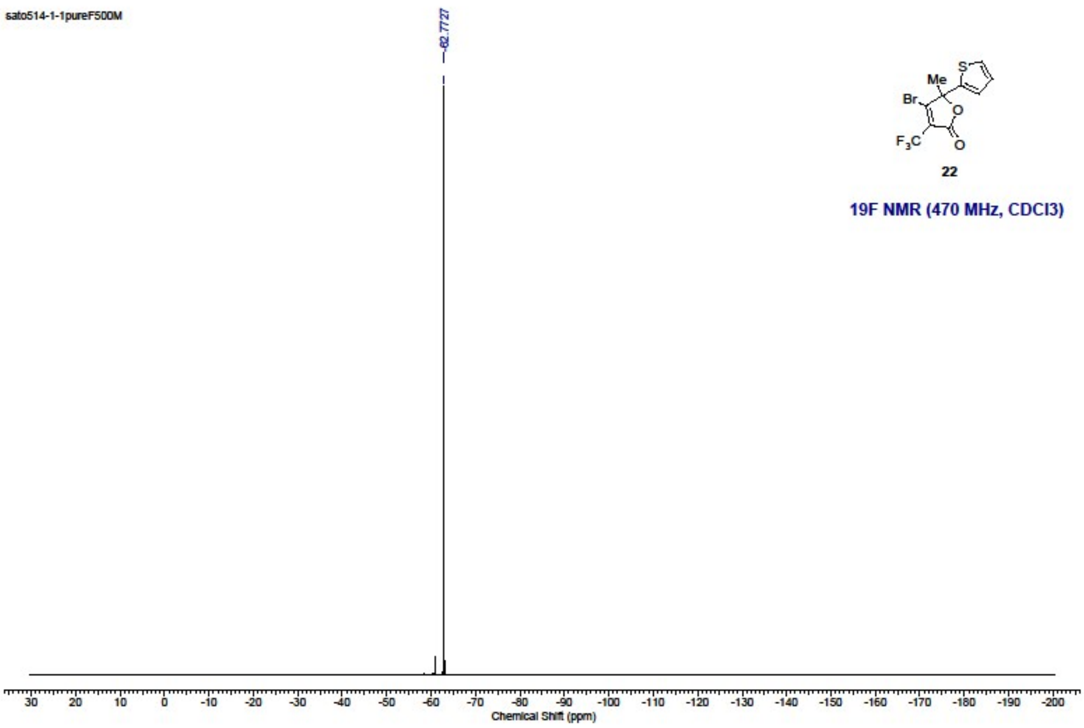

sato514-1pyridineC500M
163.3077
157.8064
150.6154
146.8190
133.4675
131.4064
123.7835
122.4574
122.1998
121.8867
121.6087
121.3132
120.2302
118.1306
115.9835
88.0793
77.2901
77.0000
76.7424
23.5635
0.1010
Me
Br
O
F3C
O
N
21
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)


sato514-1pyridinepureF500M
-62.7686
Me
Br
O
F3C
O
N
21
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

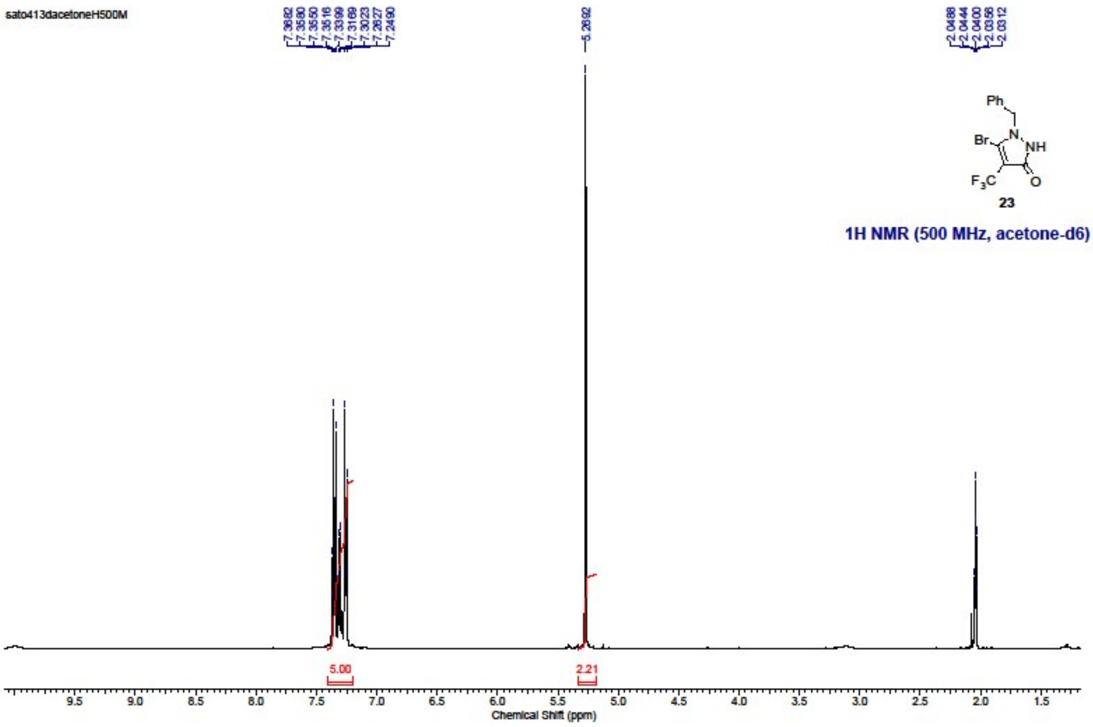

sato514-1-1pureH500M
7.4195
7.4161
7.4083
7.4058
7.1478
7.1454
7.1405
7.0619
7.0545
7.0516
2.0600
1.5846
0.0083
7.2700
Me
S
Br
O
F3C
O
22
1H NMR (500 MHz, CDCl3)
0.98
1.02
1.00
3.26
Chemical Shift (ppm)

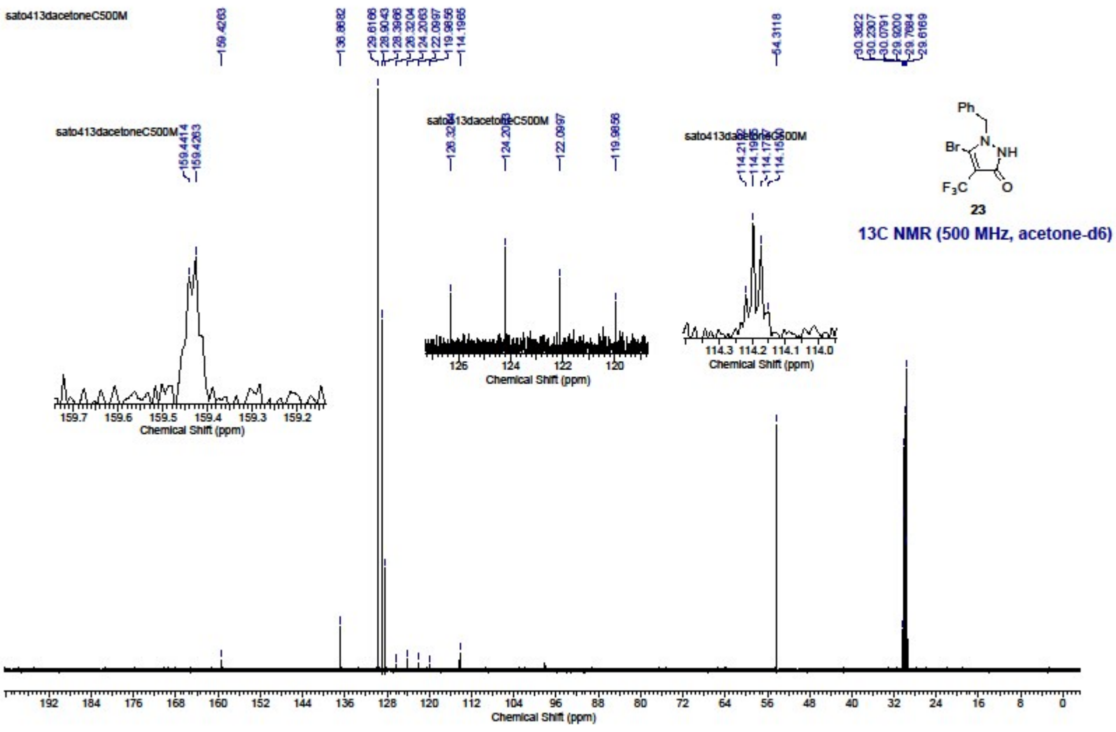


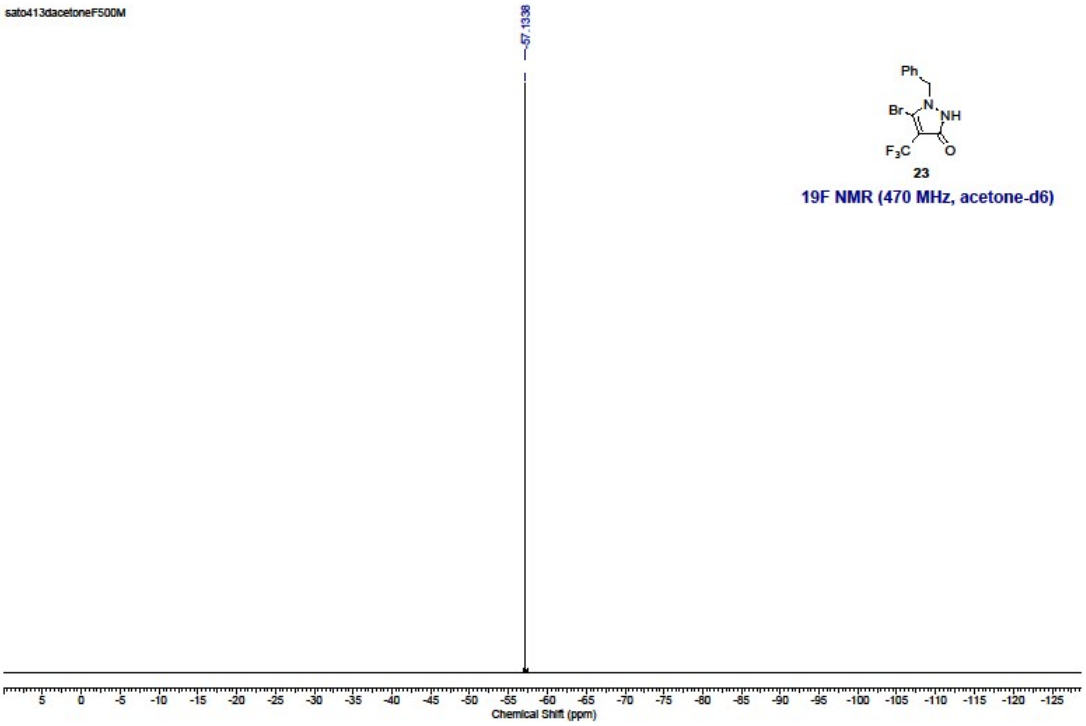
sato514-1-1pureC500M
163.1031
157.5033
157.4808
138.4156
127.6404
127.5873
127.4964
127.0115
122.6165
121.5557
121.2601
120.4569
118.2898
87.8207
77.2576
77.0000
76.7499
24.8593
Me
Br
S
O
F3C
O
22
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)

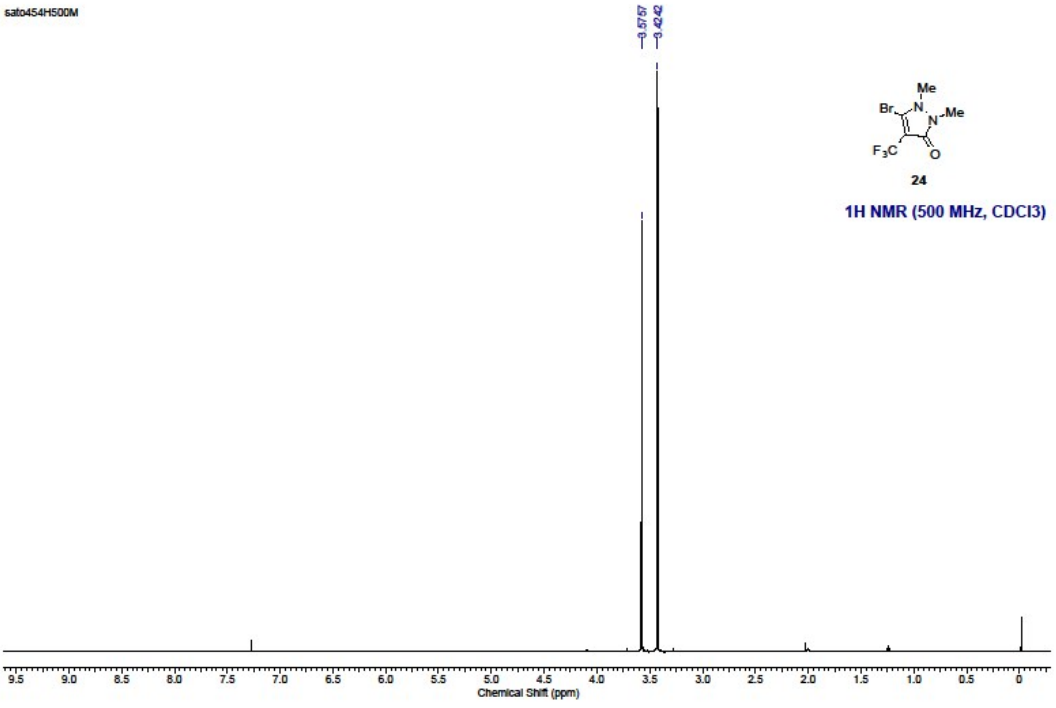


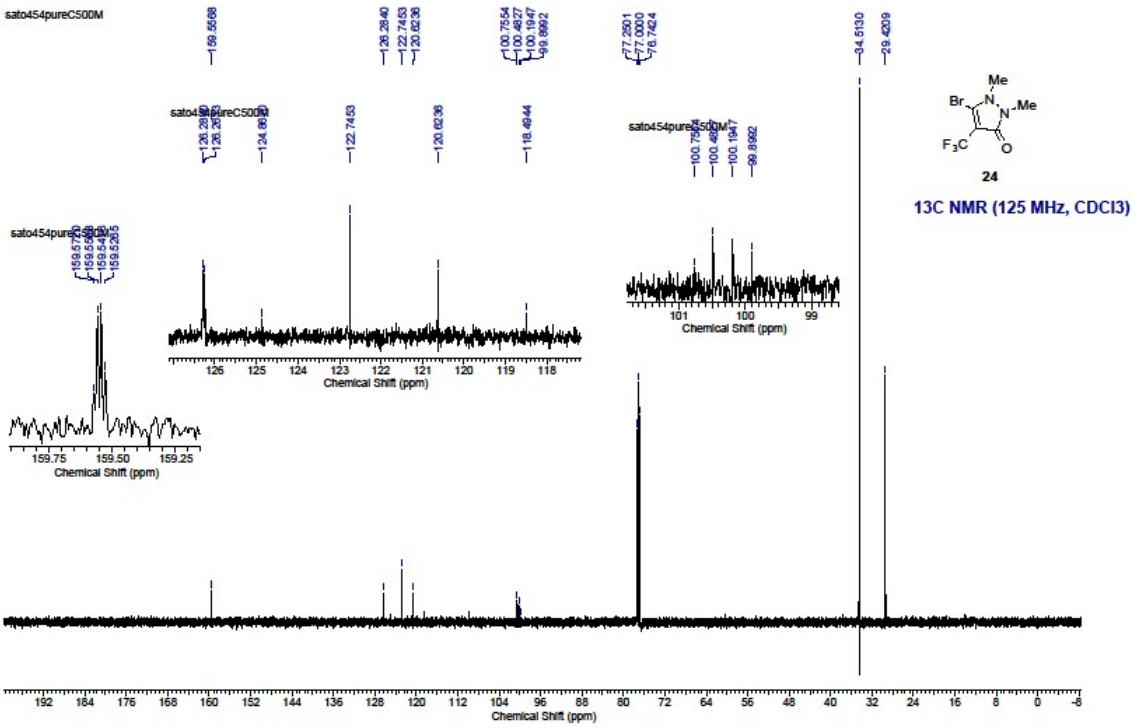
sato514-1-1pureF500M
-62.7727
Me
Br
S
O
F3C
O
22
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)


sato413dacetoneH500M
5.2692
23
1H NMR (500 MHz, acetone-d6)
5.00
2.21
Chemical Shift (ppm)


sato413dacetoneC500M
159.4263
136.8682
54.3118
23
13C NMR (500 MHz, acetone-d6)
Chemical Shift (ppm)

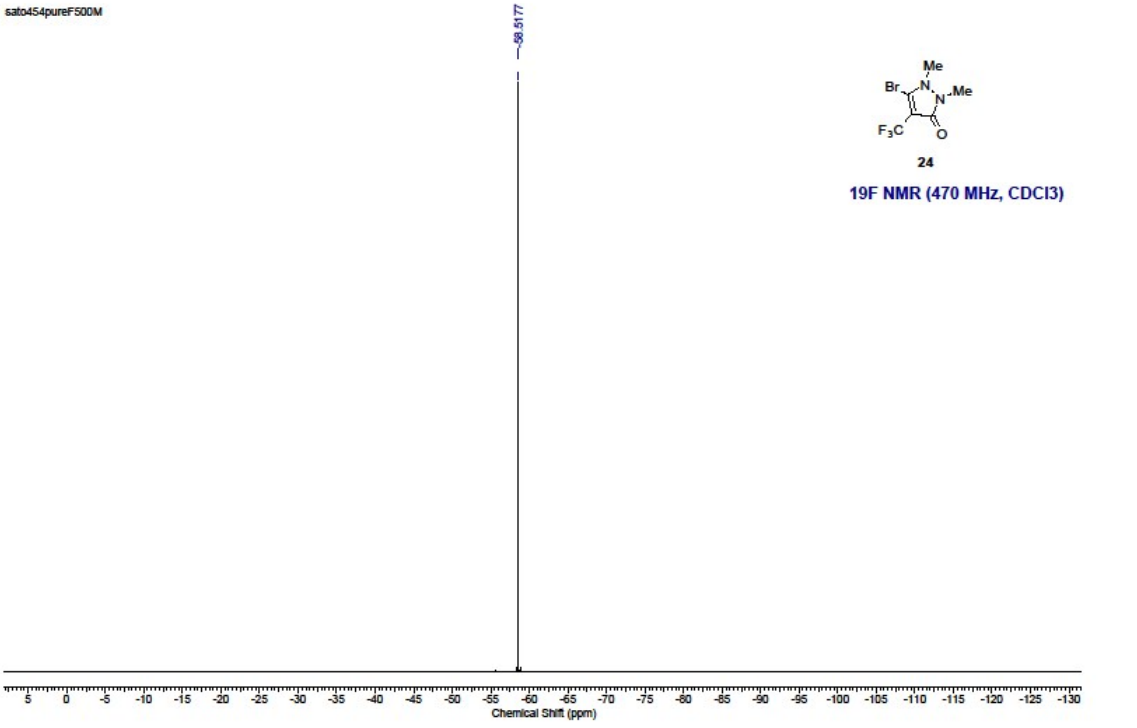

sato413dacetoneF500M
-57.1338
Ph
Br
N
NH
F3C
O
23
19F NMR (470 MHz, acetone-d6)
5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125
Chemical Shift (ppm)


sato454H500M
3.5757
3.4242
Me
Br
N
N
Me
F3C
O
24
1H NMR (500 MHz, CDCl3)
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
Chemical Shift (ppm)



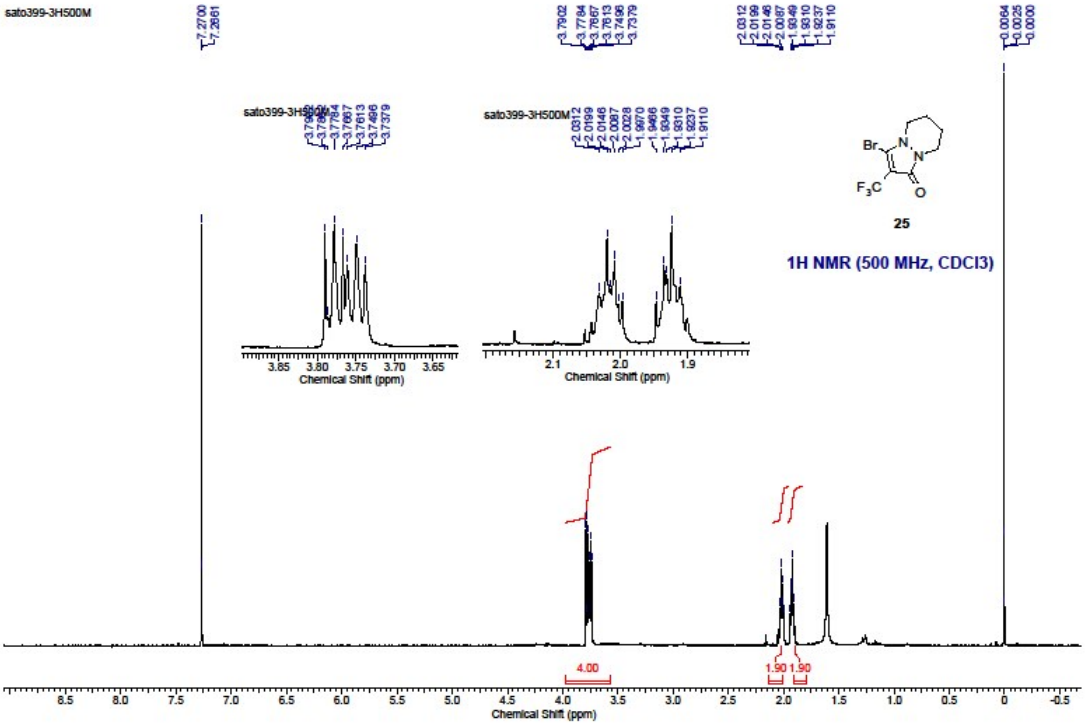
24

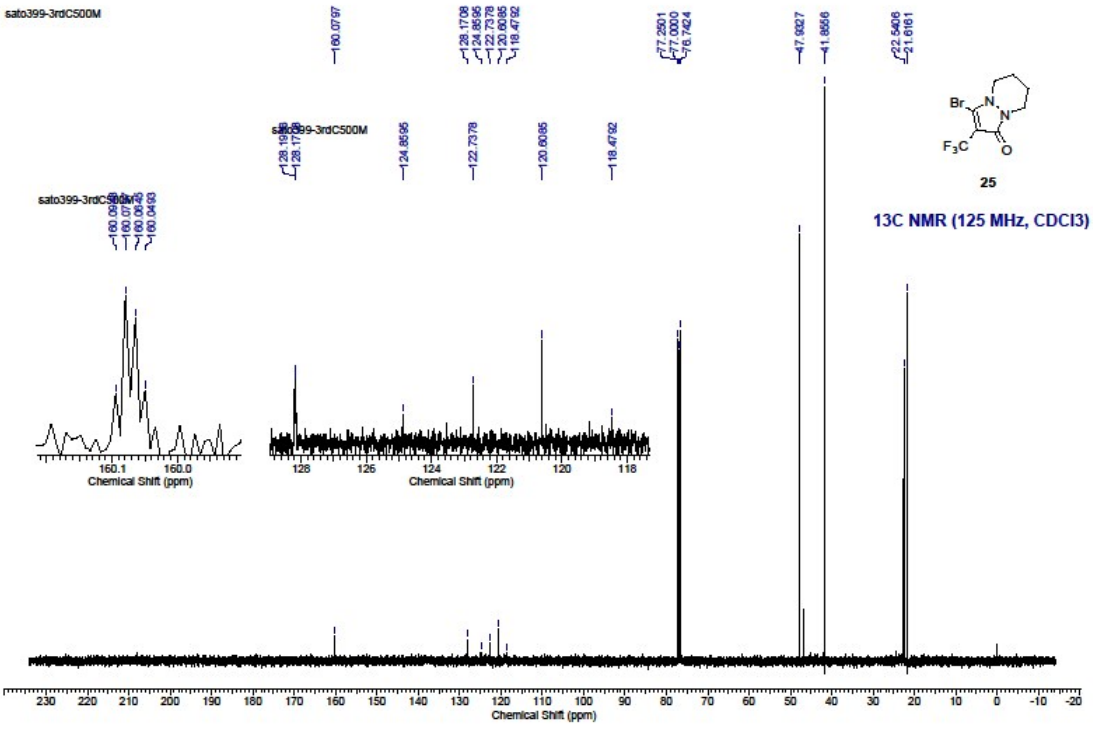
13C NMR (125 MHz, CDCl3)

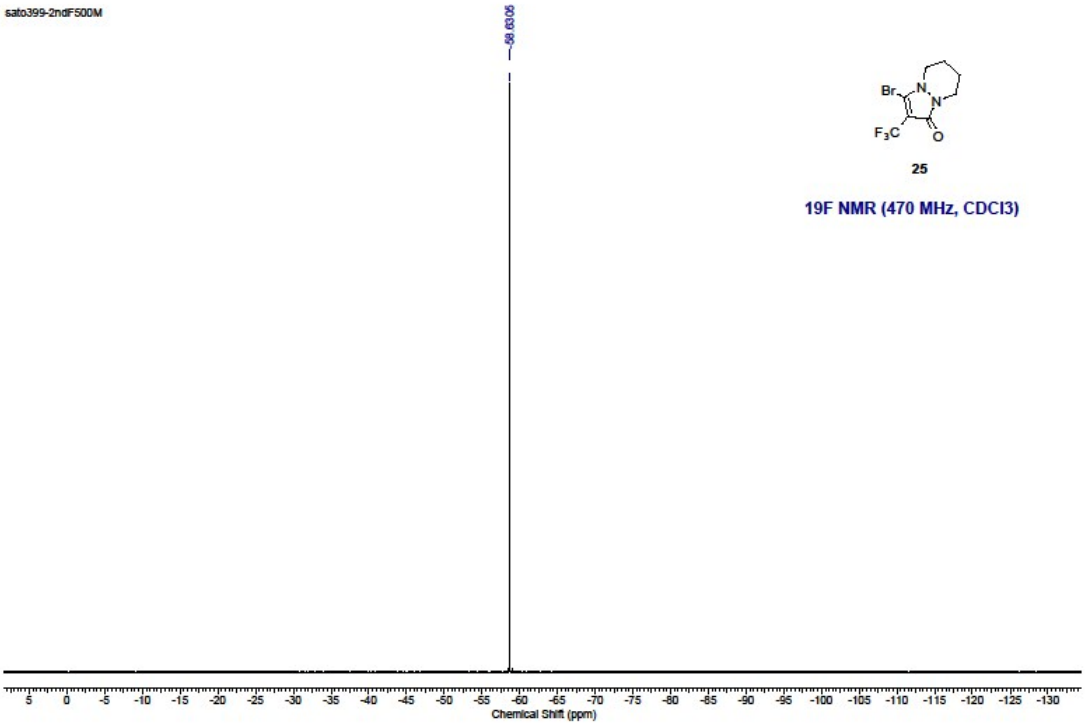


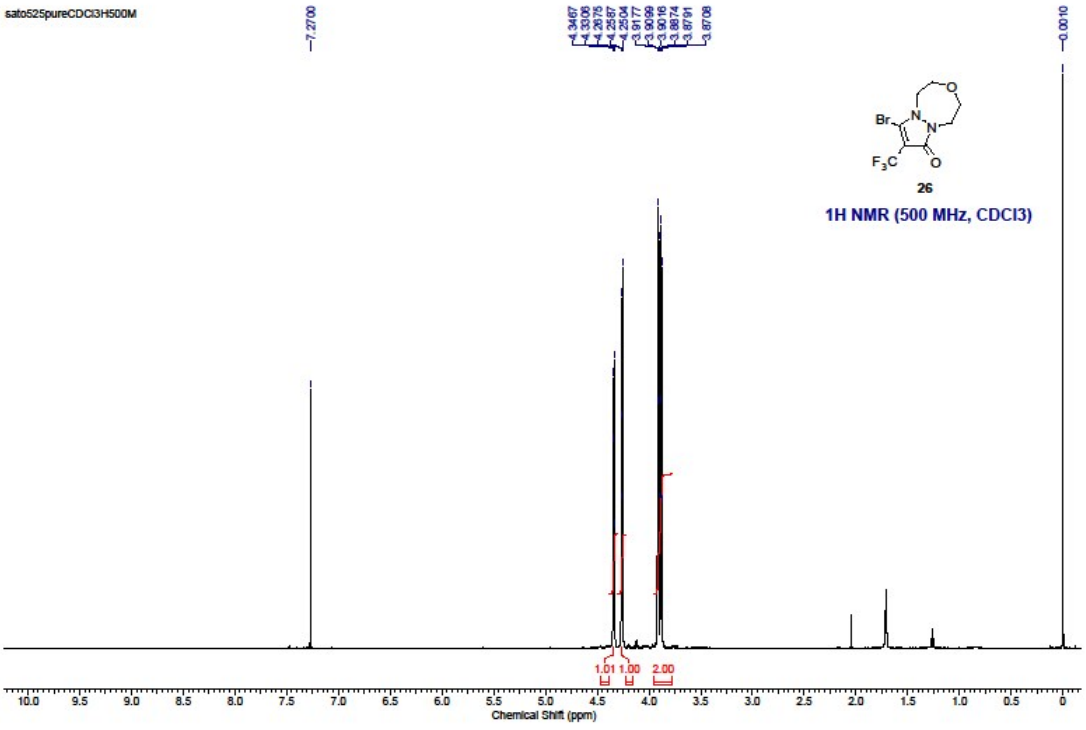
24

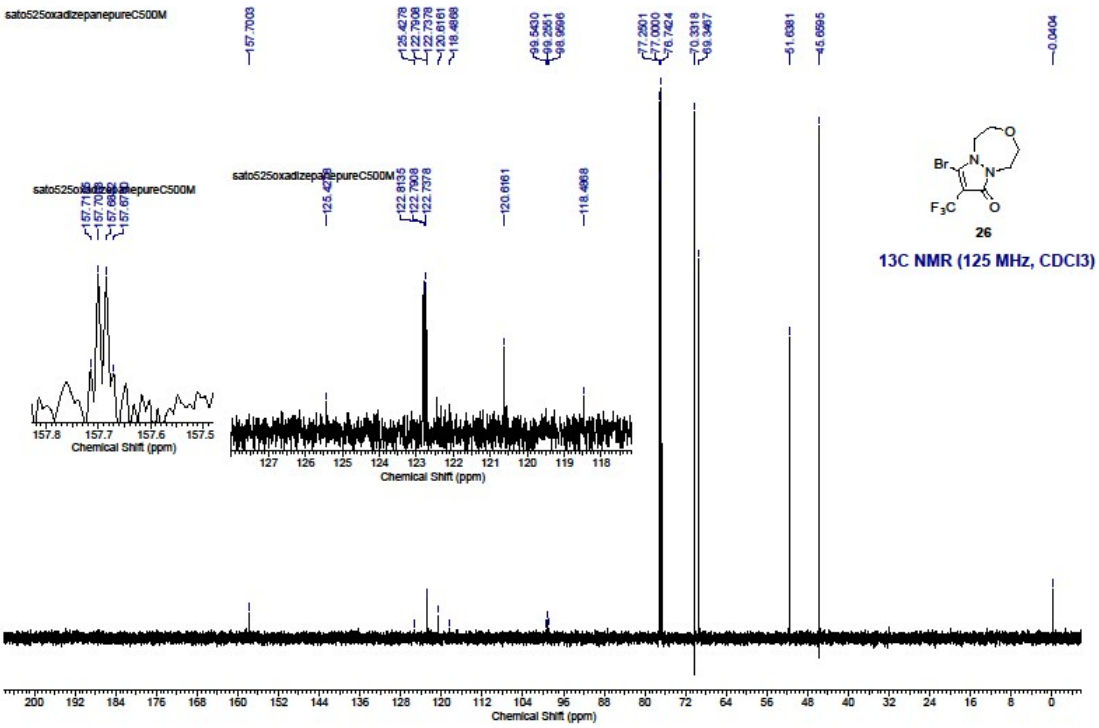
19F NMR (470 MHz, CDCl3)


sato399-3H500M
Br
N
N
F3C
O
25
1H NMR (500 MHz, CDCl3)
Chemical Shift (ppm)
4.00
1.90
1.90


sato399-3rdC500M
Br
N
N
F3C
O
25
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)

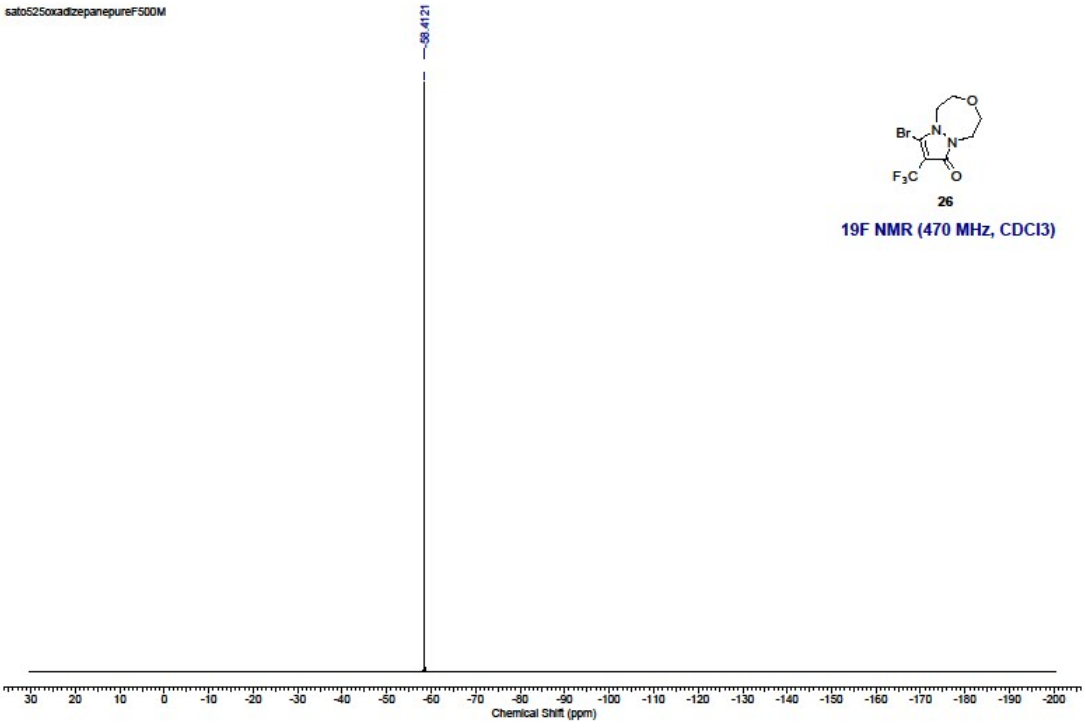

sato399-2ndF500M
-59.6305
Br
N
N
F3C
O
25
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)


sato525pureCDCl3H500M
7.2700
4.3467
4.3306
4.2675
4.2587
4.2504
4.0177
3.9099
3.9016
3.8874
3.8791
3.6708
0.0010
Br
N
N
O
F3C
O
26
1H NMR (500 MHz, CDCl3)
1.01
1.00
2.00
Chemical Shift (ppm)



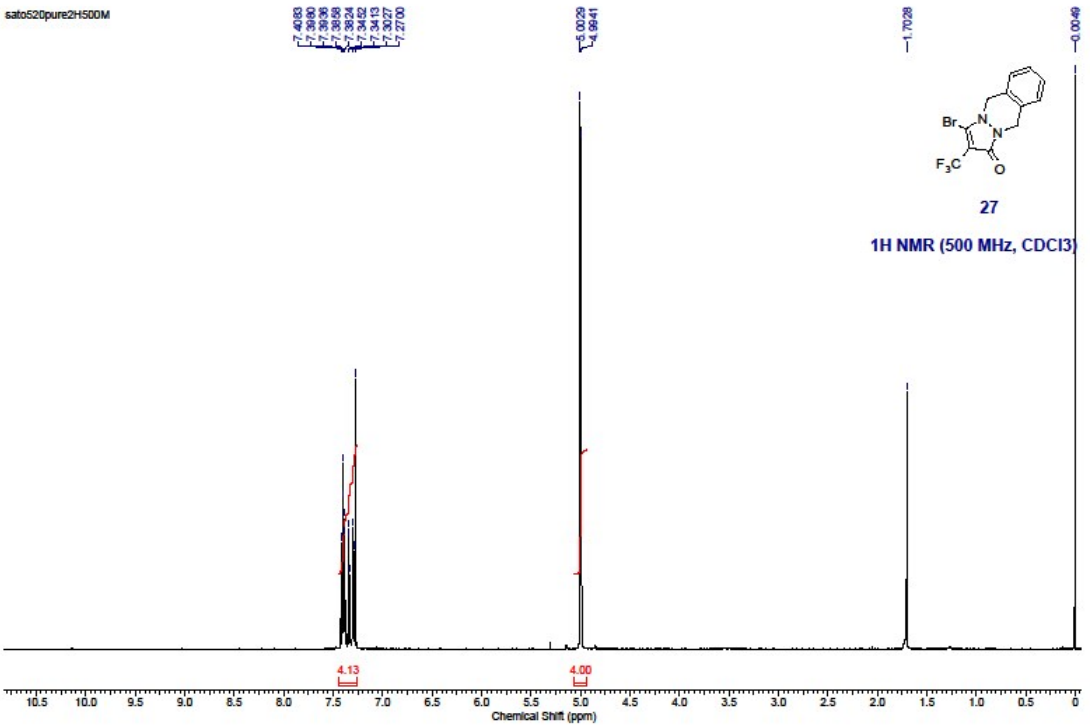
26

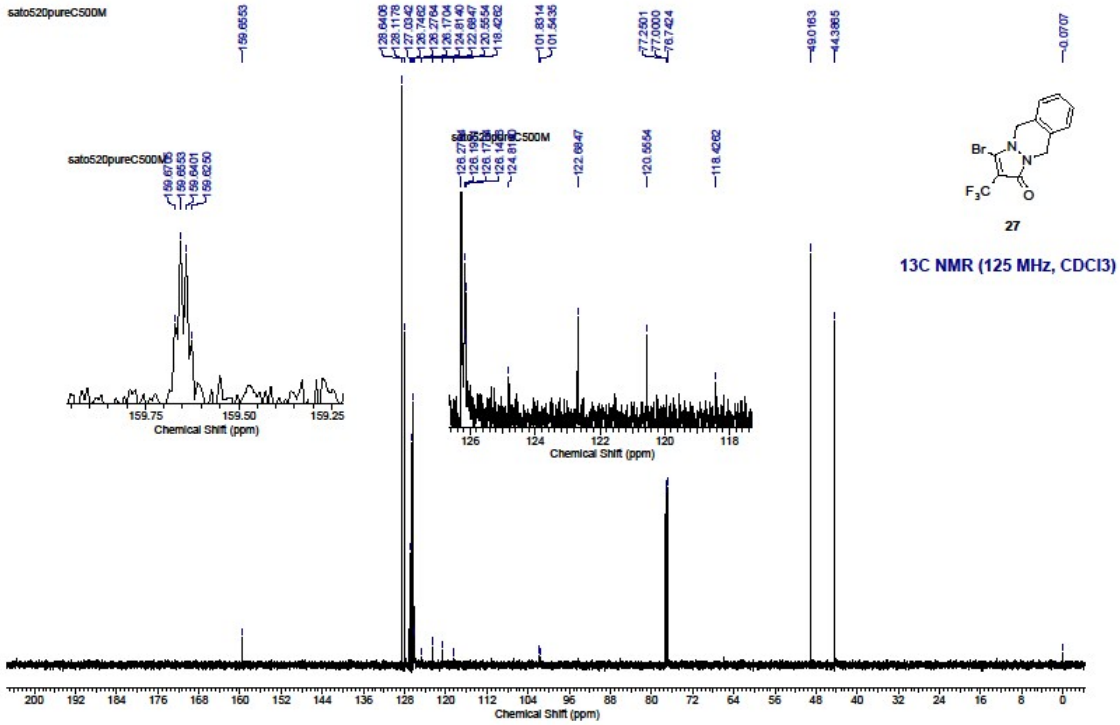
13C NMR (125 MHz, CDCl3)

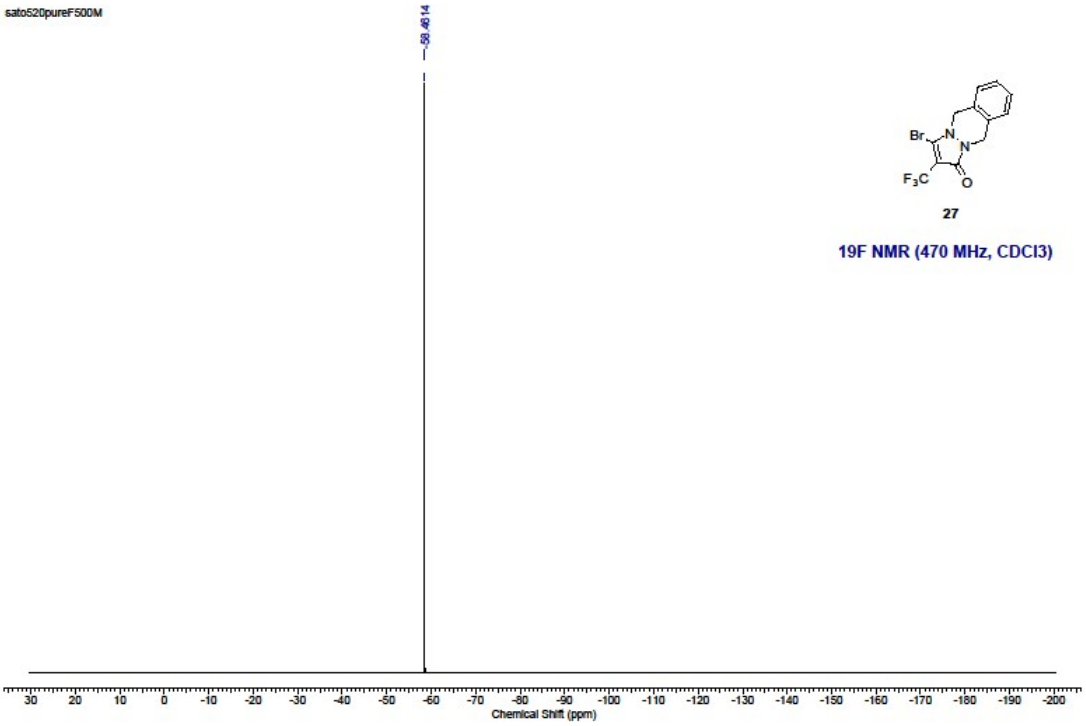


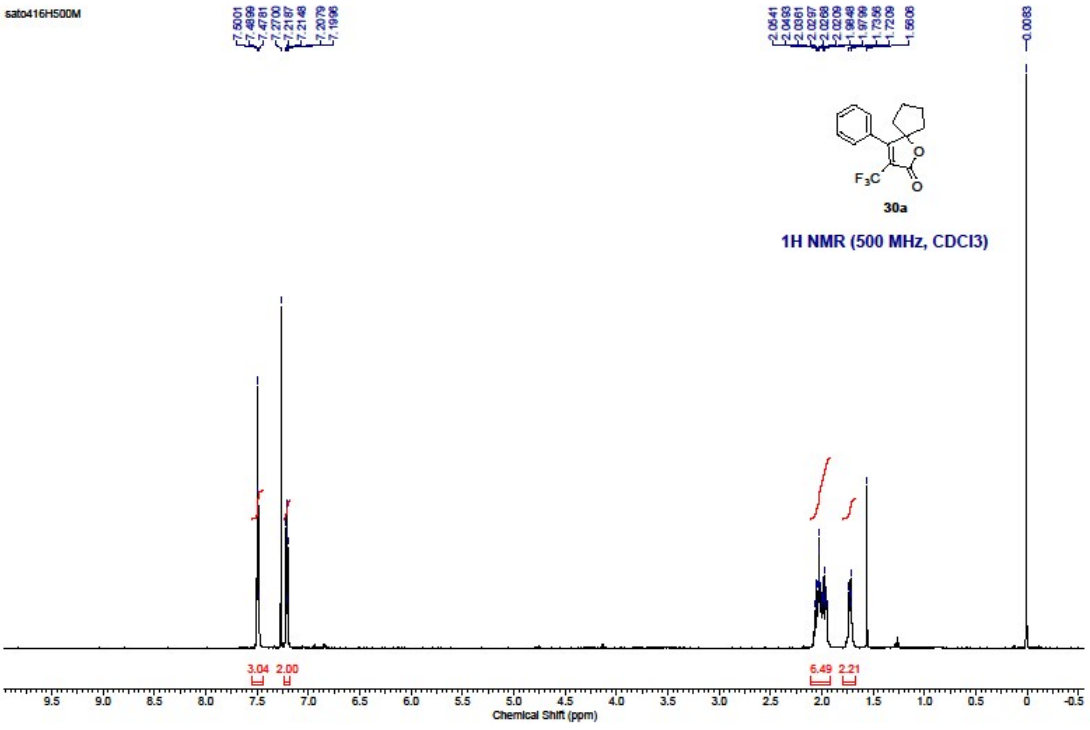
26

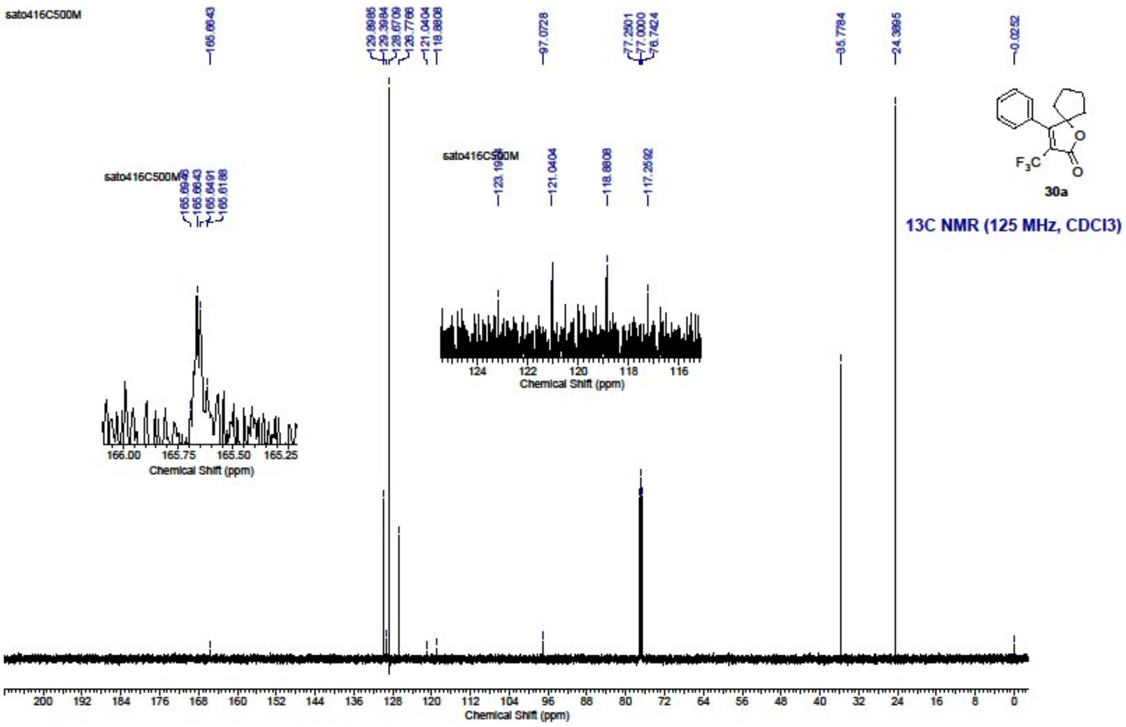
19F NMR (470 MHz, CDCl3)


sato520pure2H500M
7.4083
7.3980
7.3936
7.3856
7.3824
7.3452
7.3413
7.3027
7.2700
5.0029
4.9941
1.7028
0.0049
Br
N
N
F3C
O
27
1H NMR (500 MHz, CDCl3)
4.13
4.00
Chemical Shift (ppm)

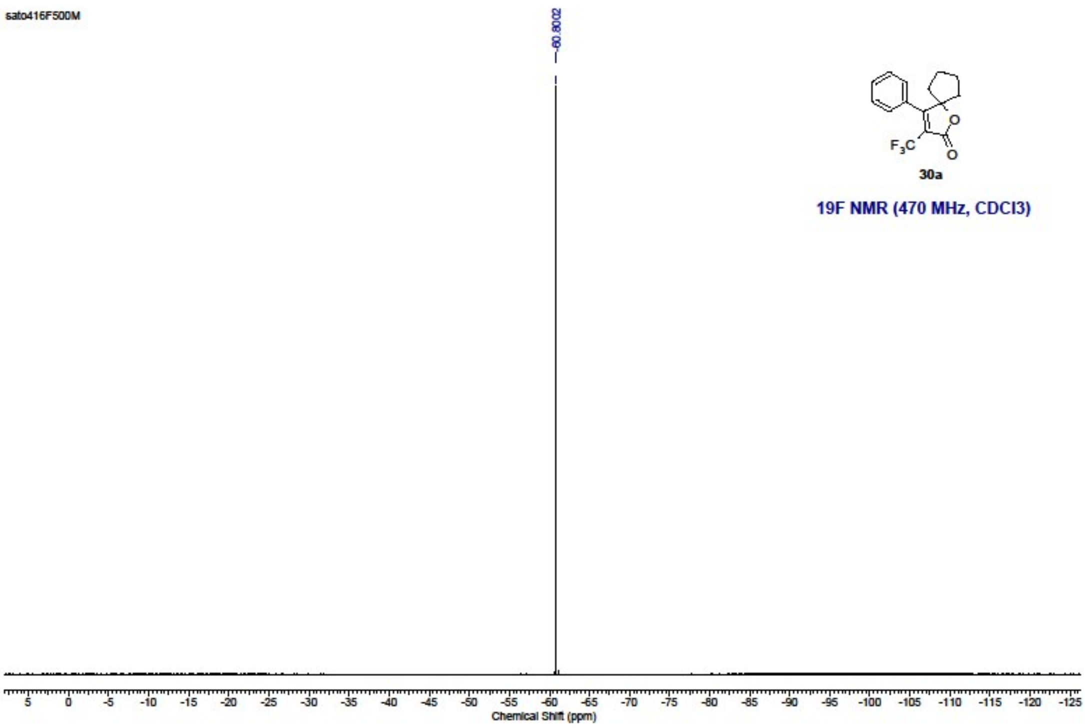

sato520pureC500M
159.6553
128.6406
128.1178
127.0342
126.7462
126.2764
126.1704
124.8140
122.6847
120.5554
118.4262
101.8314
101.5435
77.2501
77.0000
76.7424
49.0163
44.3885
-0.0707
sato520pureC500M
159.6706
159.6553
159.6401
159.6250
159.75
159.50
159.25
Chemical Shift (ppm)
sato520pureC500M
126
124
122
120
118
Chemical Shift (ppm)
Br
N
N
F3C
O
27
13C NMR (125 MHz, CDCl3)
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


sato520pureF500M
-59.4614
Br
N
N
F3C
O
27
19F NMR (470 MHz, CDCl3)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

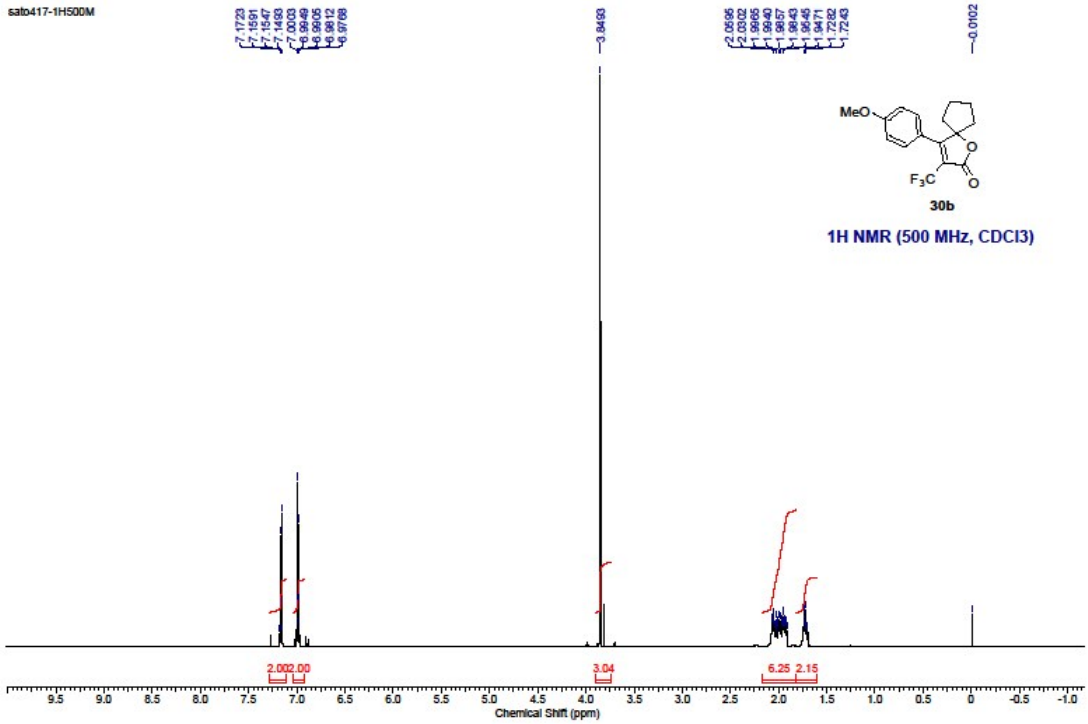

sato416H500M
7.5001
7.4899
7.4781
7.2700
7.2157
7.2148
7.2079
7.1996
2.0541
2.0493
2.0361
2.0297
2.0268
2.0209
1.9848
1.9799
1.7356
1.7209
1.5806
0.0083
O
O
F3C
O
30a
1H NMR (500 MHz, CDCl3)
3.04
2.00
6.49
2.21
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)

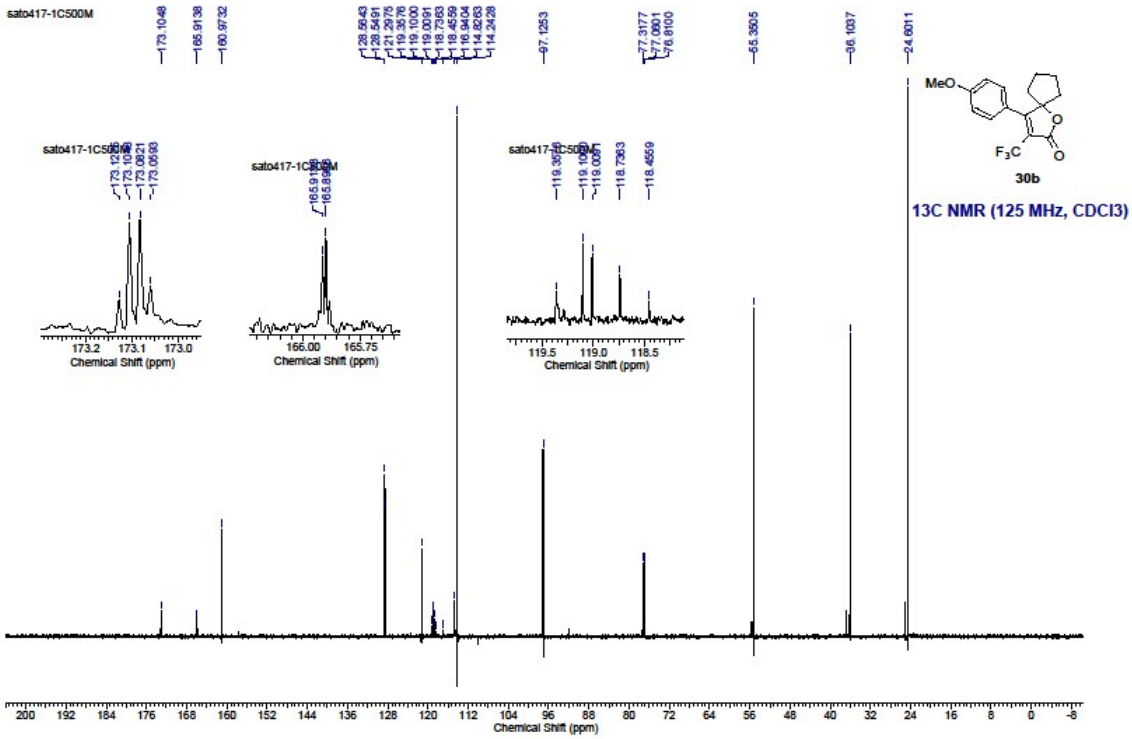


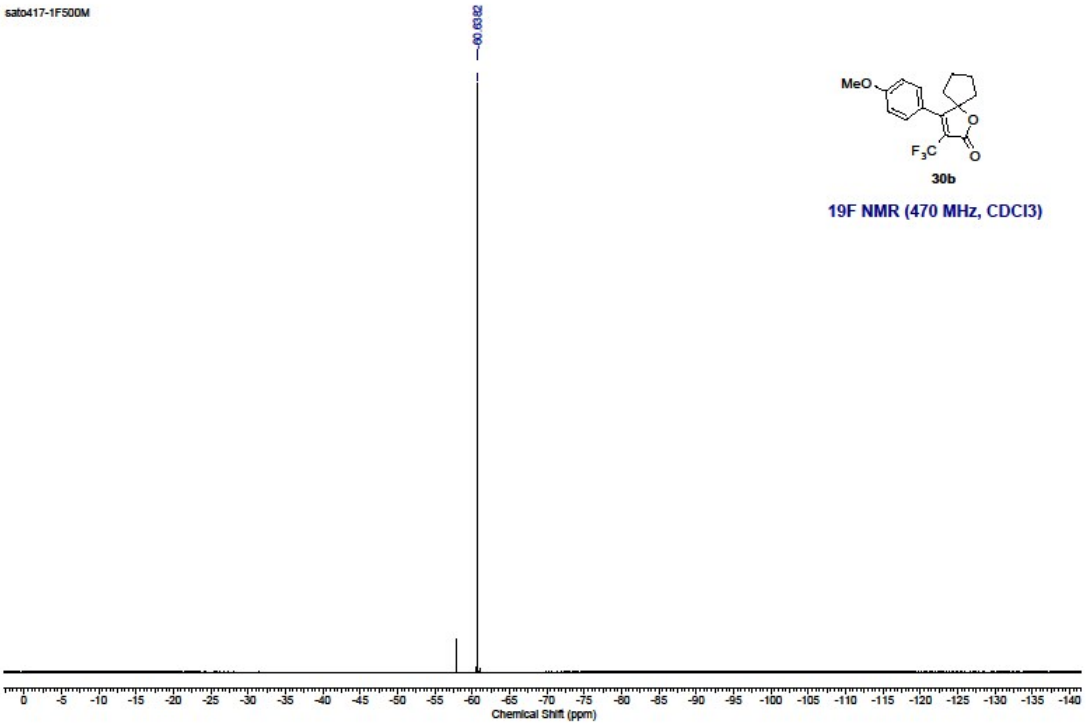
sato416C500M
13C NMR (125 MHz, CDCl3)
30a
Chemical Shift (ppm)

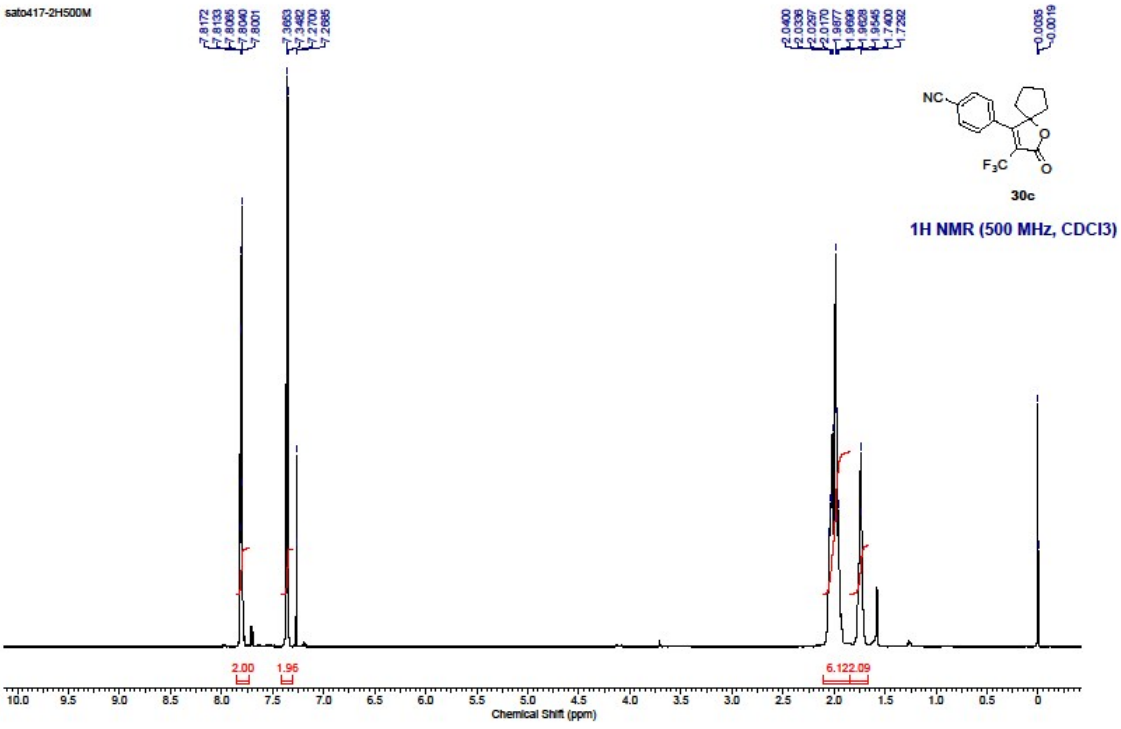


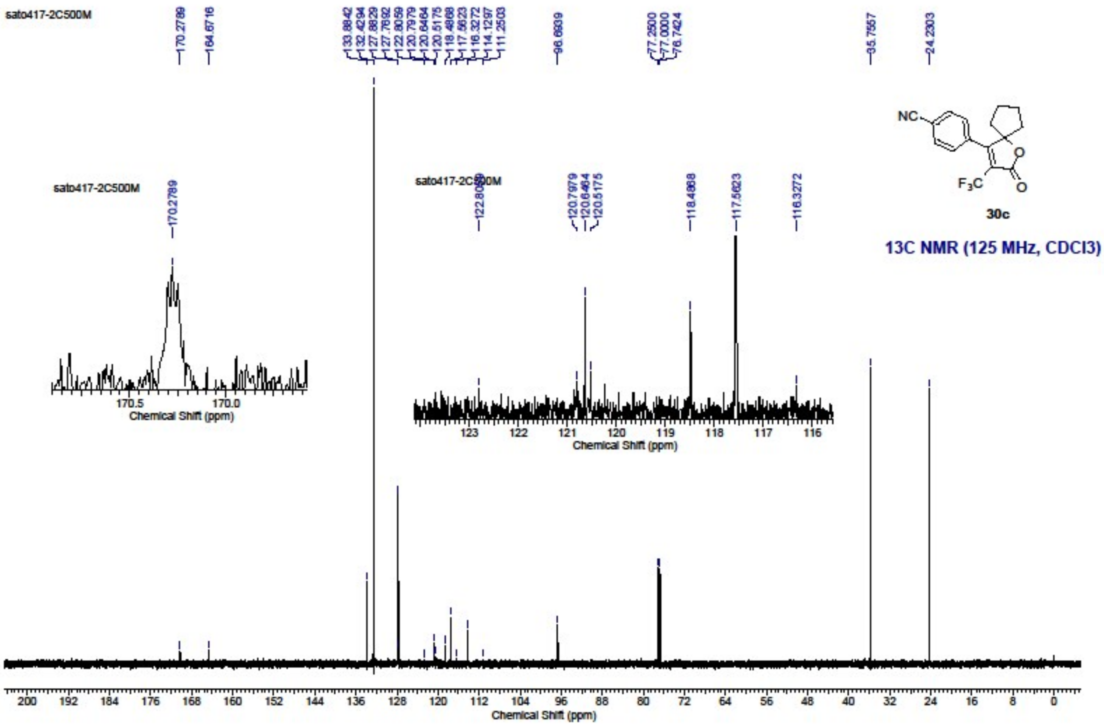
sato416F500M
-60.8002
19F NMR (470 MHz, CDCl3)
30a
Chemical Shift (ppm)

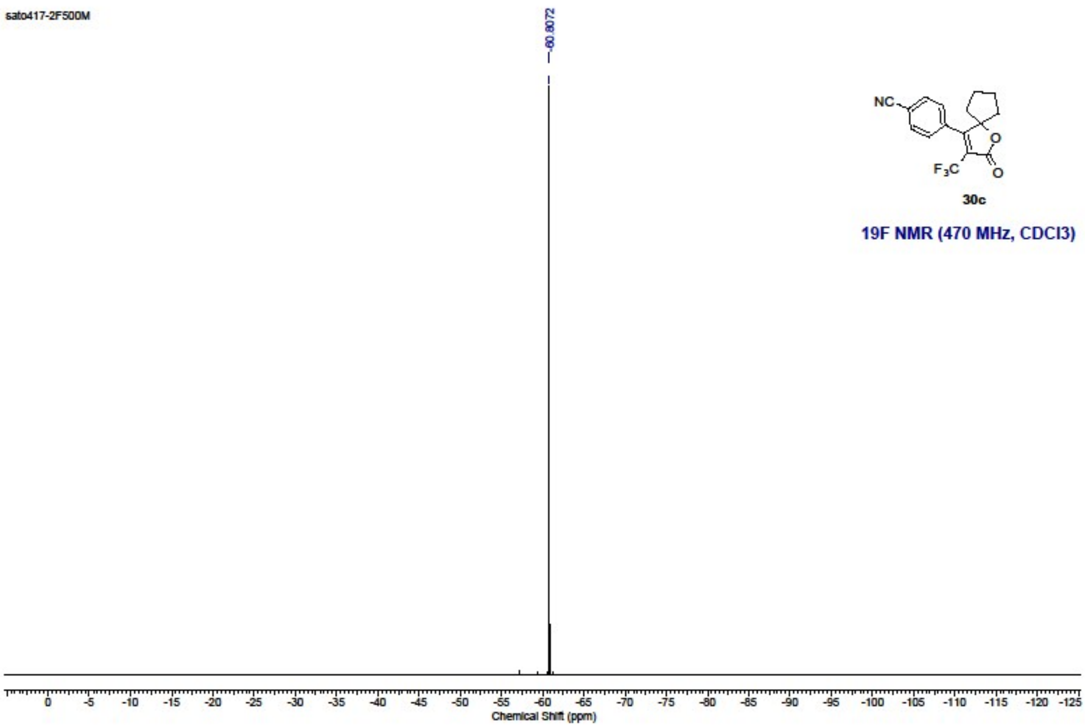

sato417-1H500M
MeO
F3C
O
30b
1H NMR (500 MHz, CDCl3)
2.00 2.00
3.04
6.25 2.15
Chemical Shift (ppm)

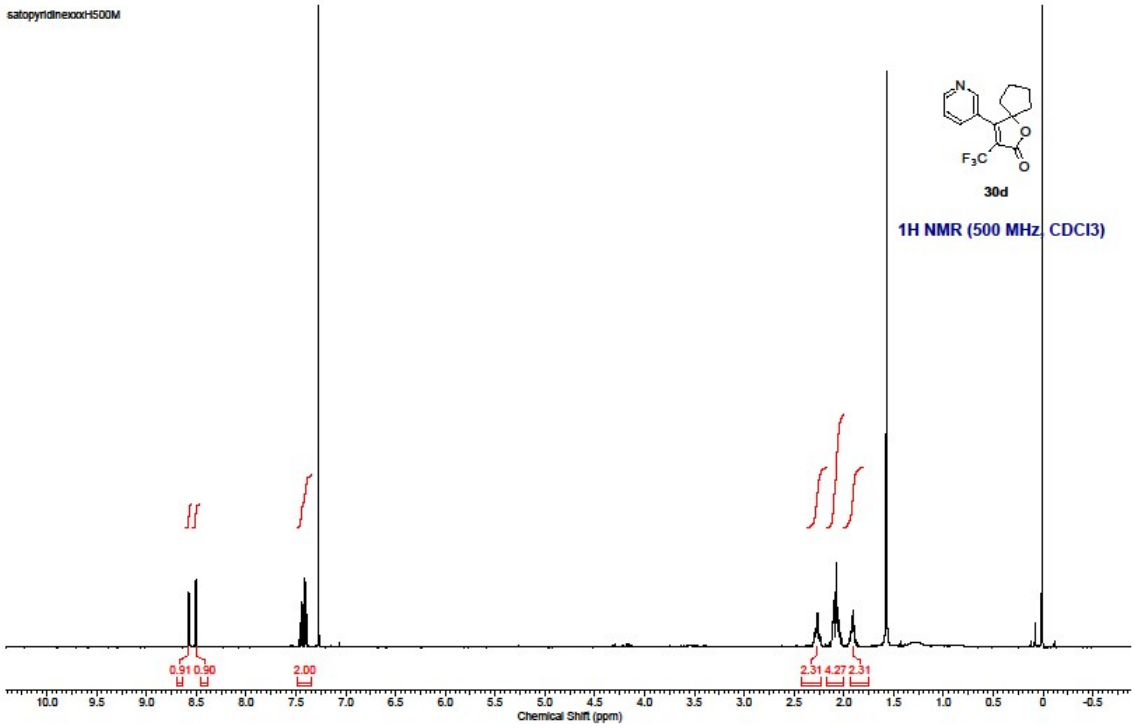

sato417-1C500M
MeO
F3C
O
30b
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)

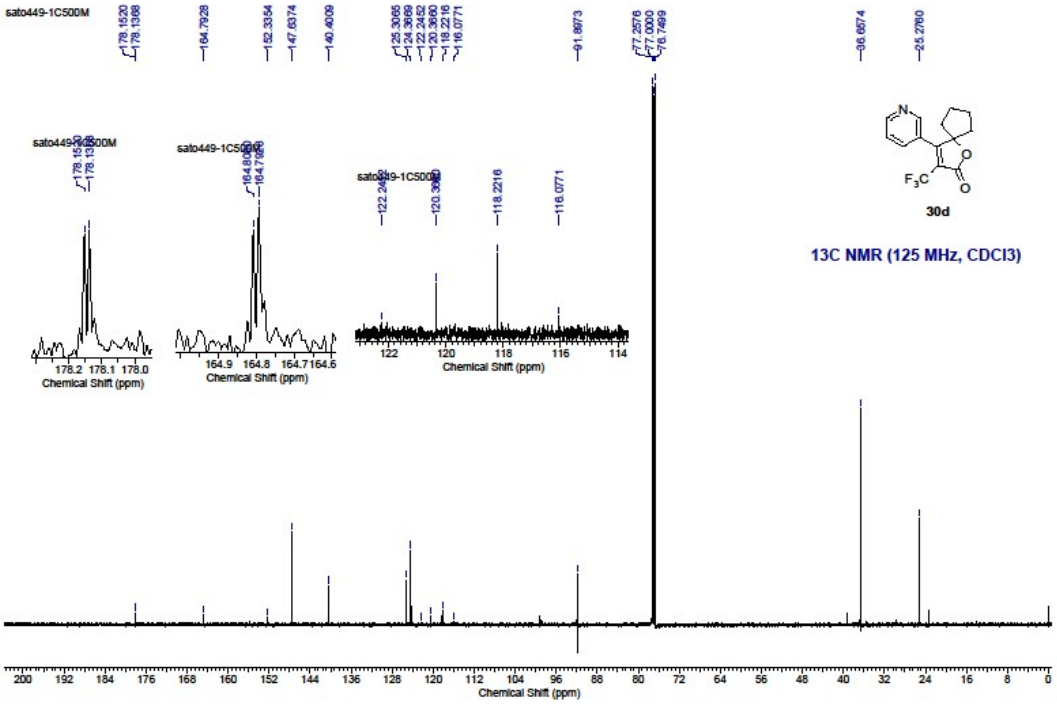

sato417-1F500M
-60.6382
MeO
O
F3C
O
30b
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

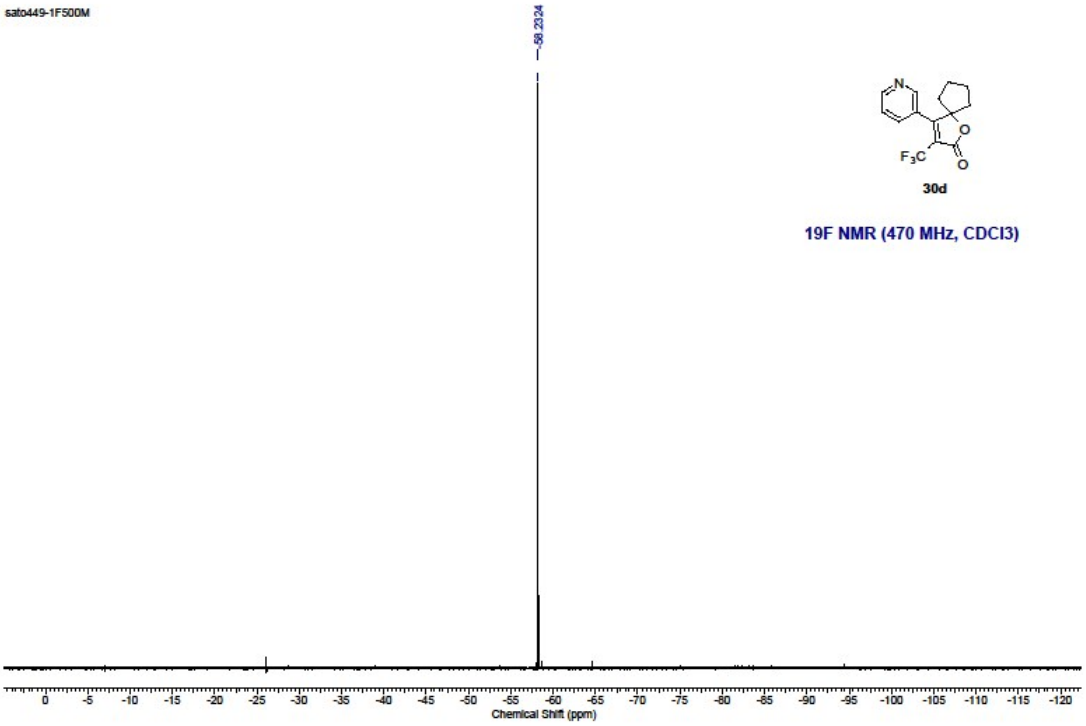

sato417-2H500M
7.8172
7.8133
7.8096
7.8040
7.8001
7.3663
7.3482
7.2700
7.2686
2.0400
2.0336
2.0297
2.0170
1.9977
1.9666
1.9628
1.9445
1.7400
1.7292
0.0035
0.0019
NC
O
F3C
O
30c
1H NMR (500 MHz, CDCl3)
2.00
1.96
6.122.09
Chemical Shift (ppm)

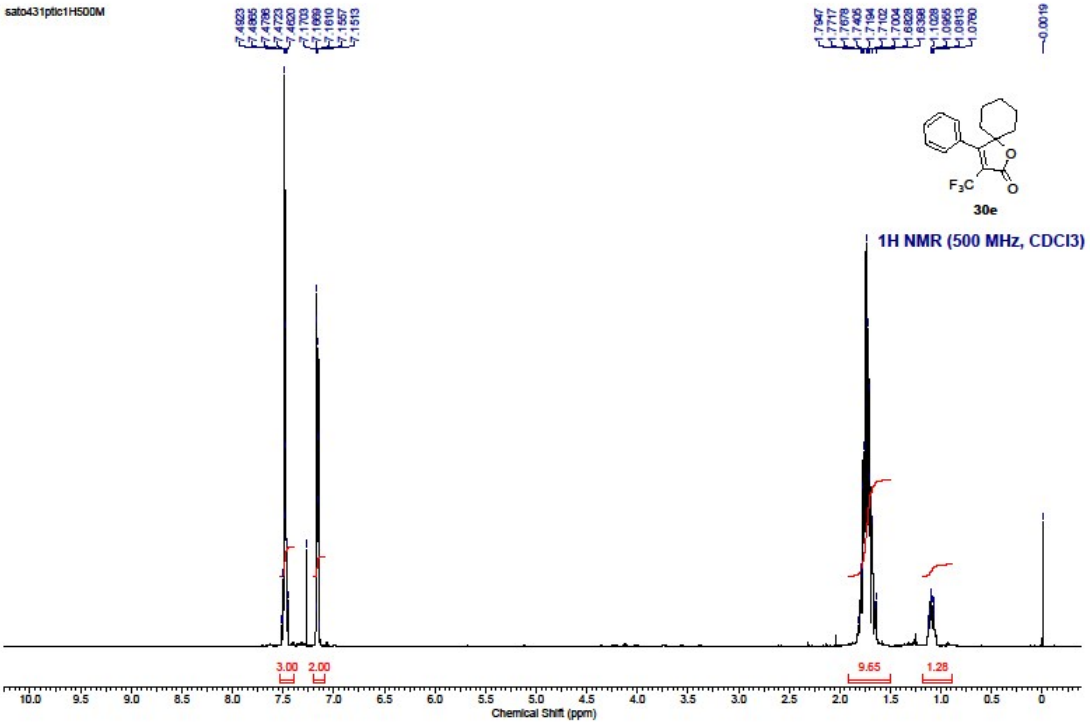

sato417-2C500M
NC
F3C
O
O
30c
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)

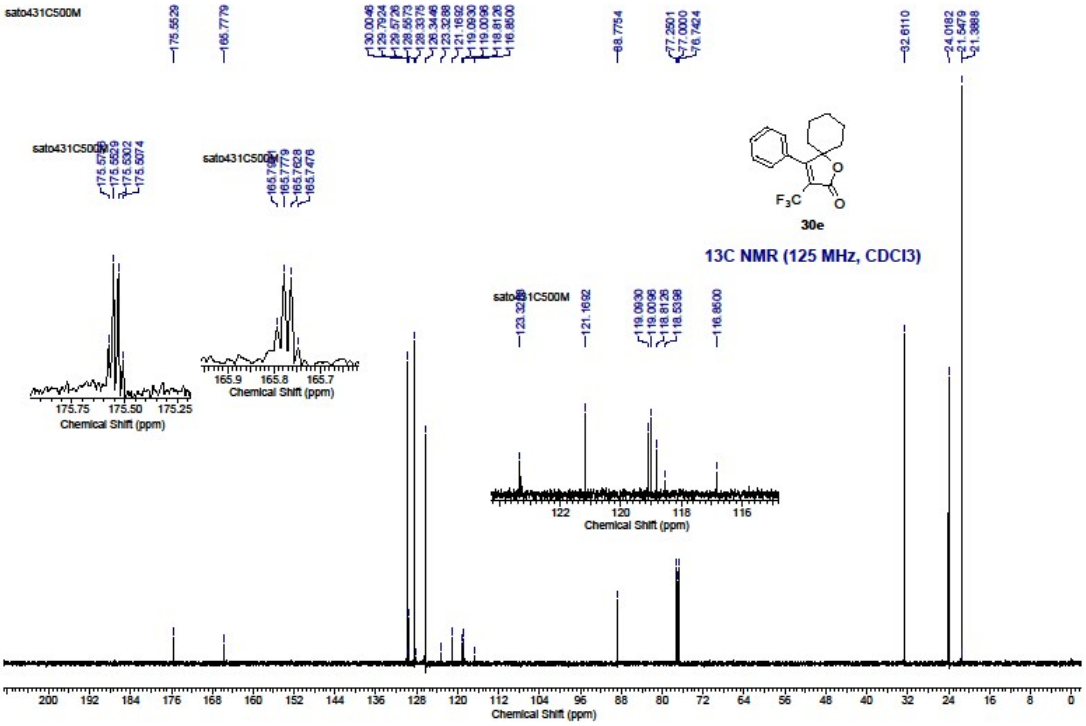

sato417-2F500M
-60.8072
NC
F3C
O
O
30c
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

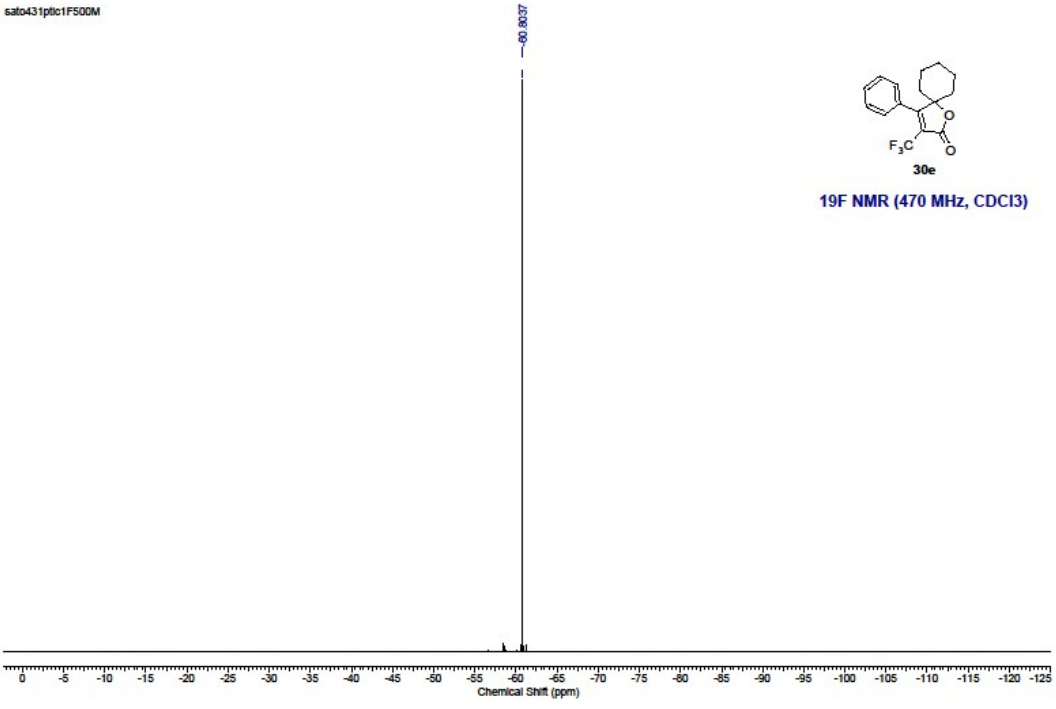

satopyridinexxxH500M
30d
1H NMR (500 MHz, CDCl3)
0.91 0.90
2.00
2.31 4.27 2.31
Chemical Shift (ppm)

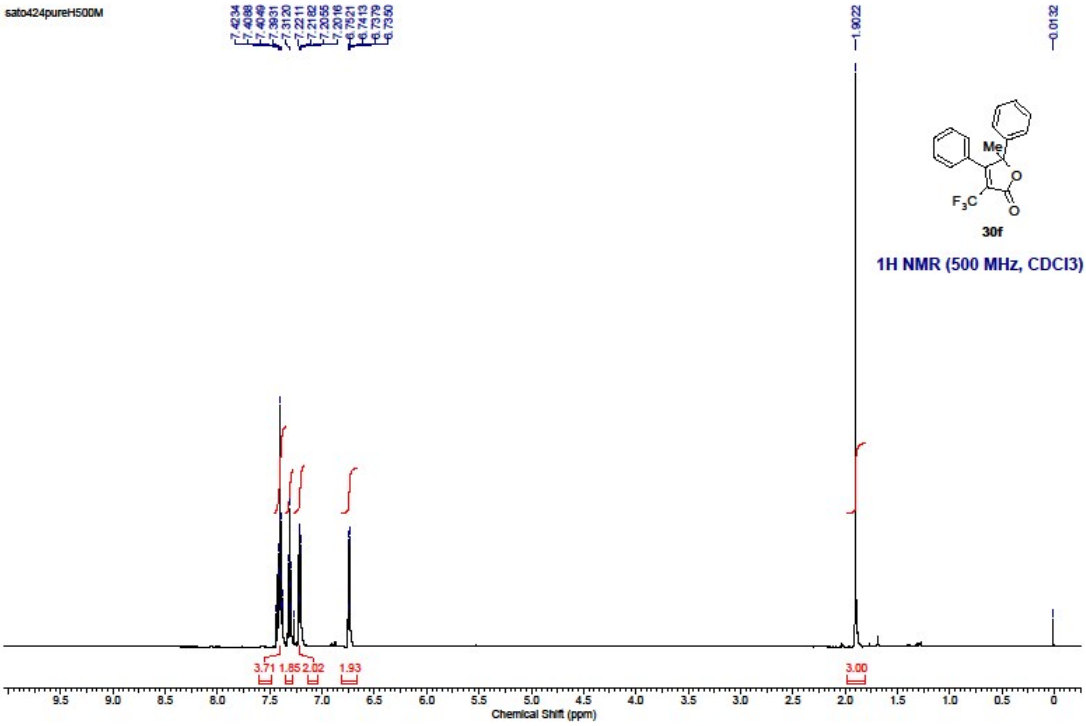

sato449-1CS00M
178.1520
178.1368
164.7928
152.3354
147.6374
140.4009
125.3065
124.3669
122.2452
120.3660
118.2216
116.0771
91.8673
77.2576
77.0000
76.7499
66.6574
25.2760
30d
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)

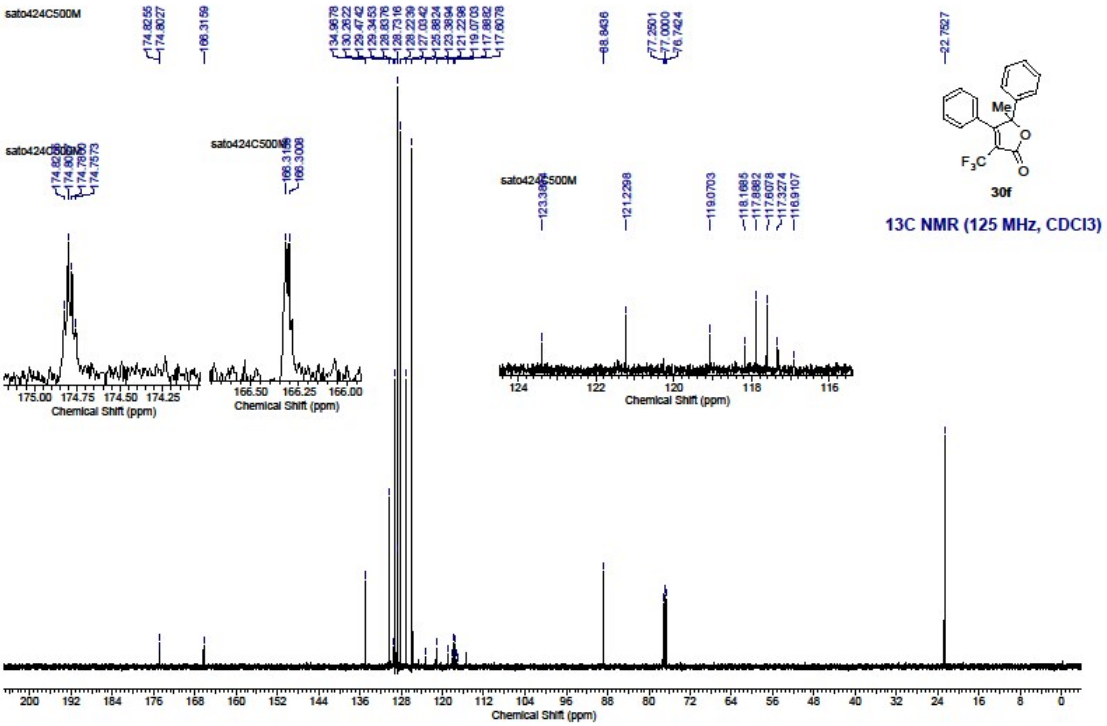

sato449-1F500M
-58.2324
N
O
O
F3C
30d
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

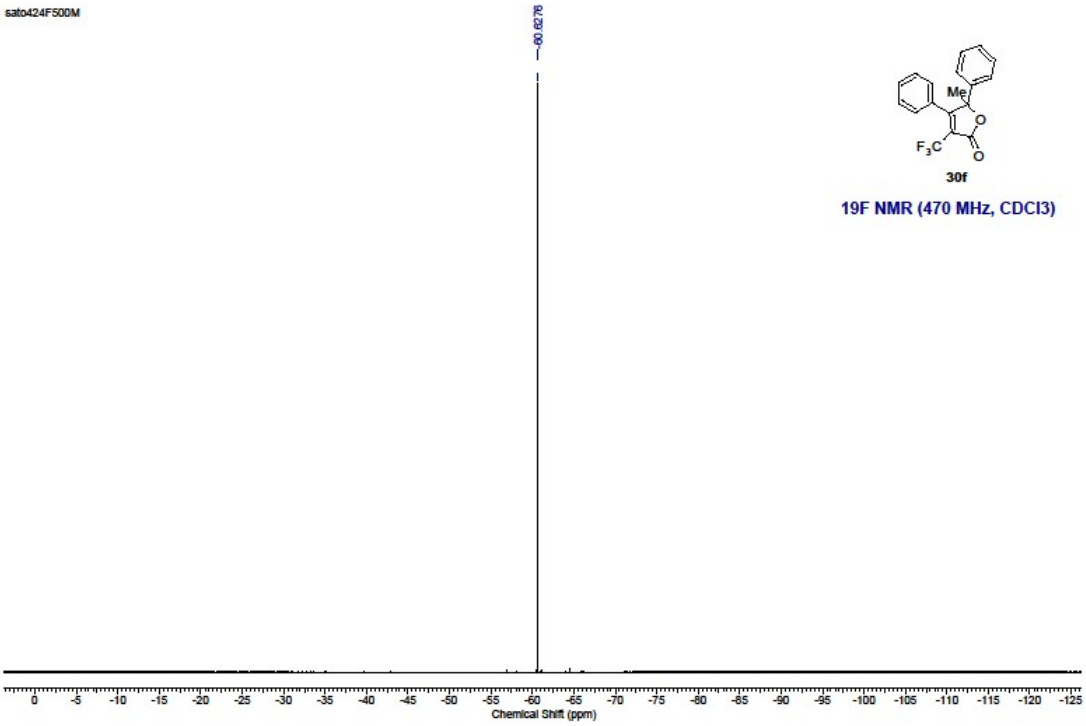

sato431ptic1H500M
7.4923
7.4865
7.4798
7.4723
7.4620
7.1703
7.1669
7.1610
7.1557
7.1513
1.7947
1.7717
1.7676
1.7405
1.7194
1.7102
1.7004
1.6828
1.6368
1.1028
1.0955
1.0913
1.0760
-0.0019
O
O
F3C
30e
1H NMR (500 MHz, CDCl3)
3.00
2.00
9.65
1.28
Chemical Shift (ppm)

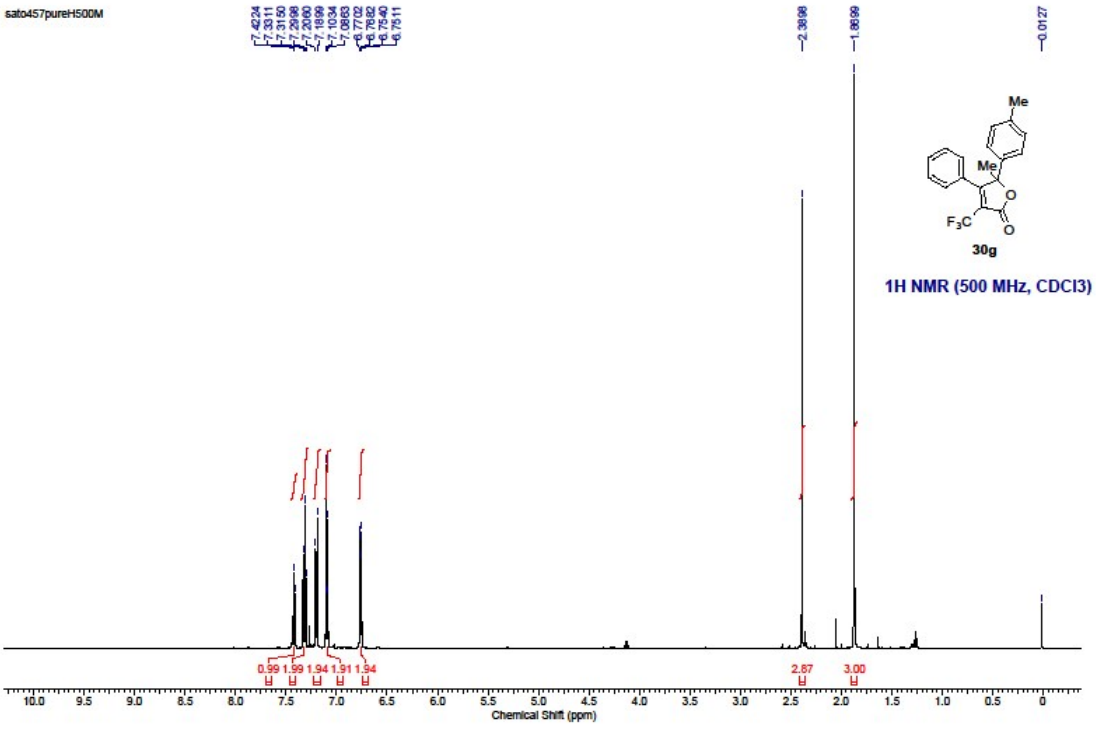

sato431C500M
175.5529
165.7779
88.7754
77.2501
77.0000
76.7424
32.6110
24.0182
21.5479
21.3888
30e
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)

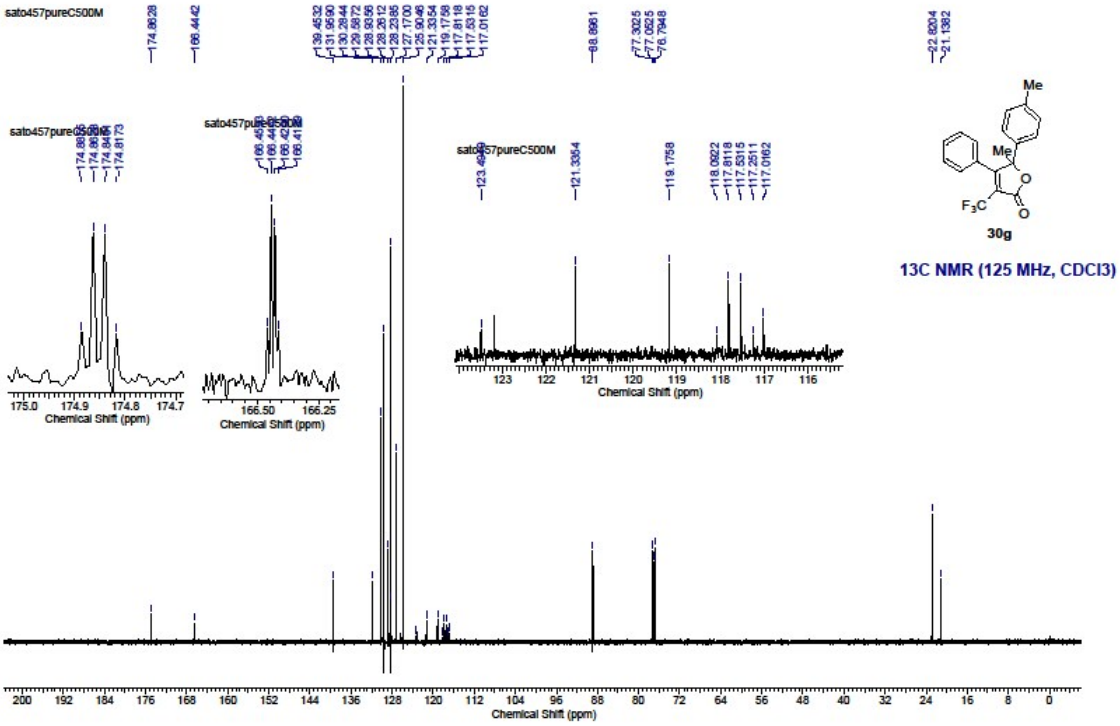

sato431ptic1F500M
-60.8037
30e
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

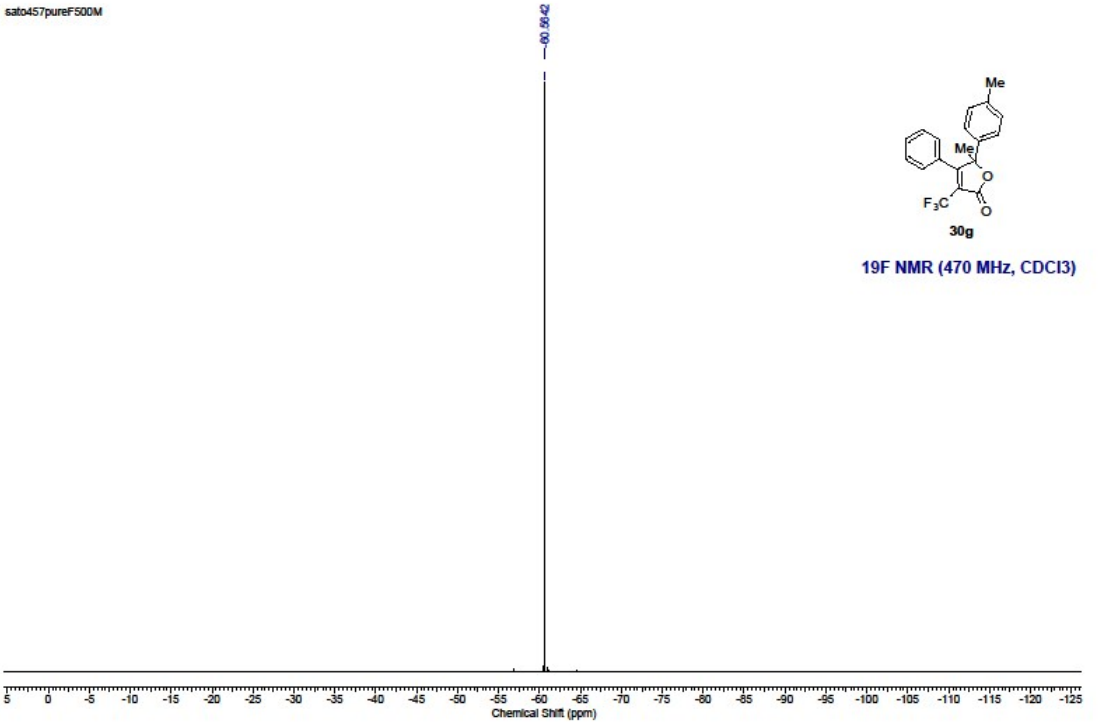

sato424pureH500M
1.9022
0.0132
Me
O
F3C
O
30f
1H NMR (500 MHz, CDCl3)
3.71
1.85
2.02
1.93
3.00
Chemical Shift (ppm)

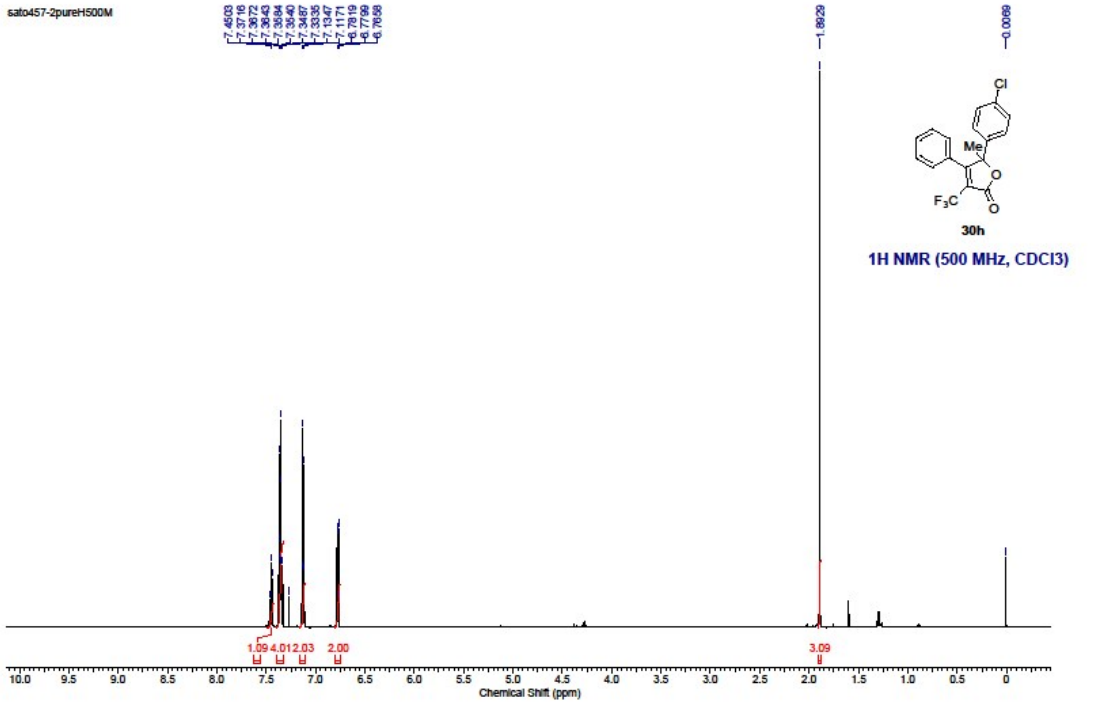

sato424C500M
22.7627
Me
O
F3C
O
30f
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)

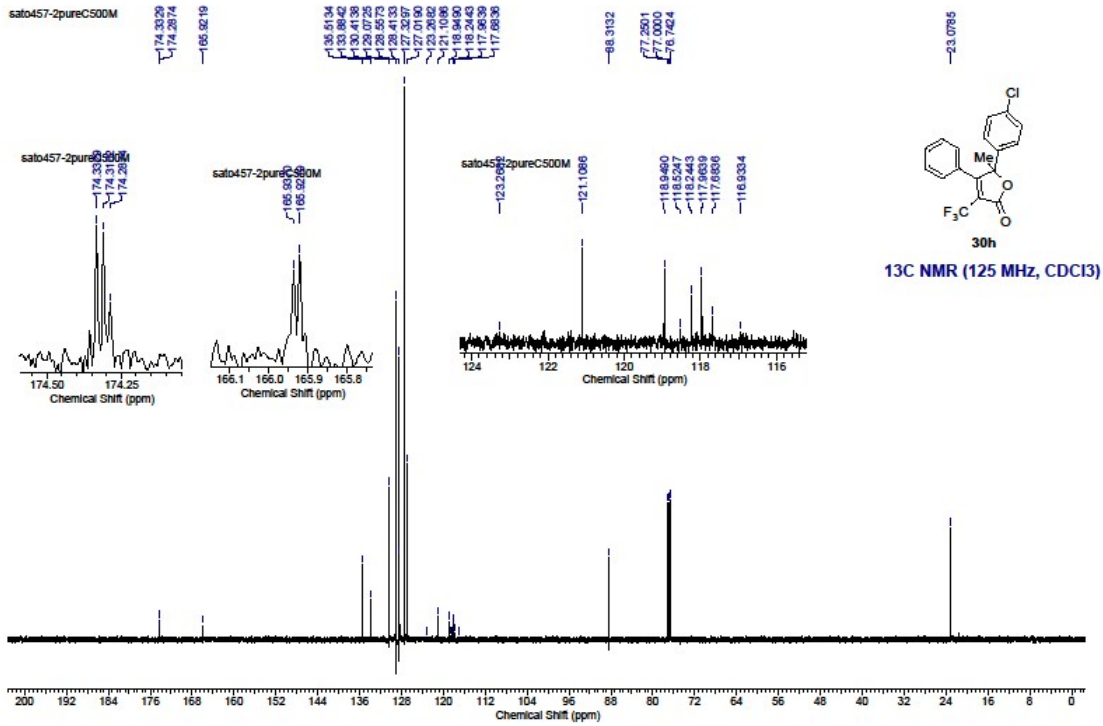

sato424F500M
-60.6276
Me
O
F3C
O
30f
19F NMR (470 MHz, CDCl3)
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125
Chemical Shift (ppm)

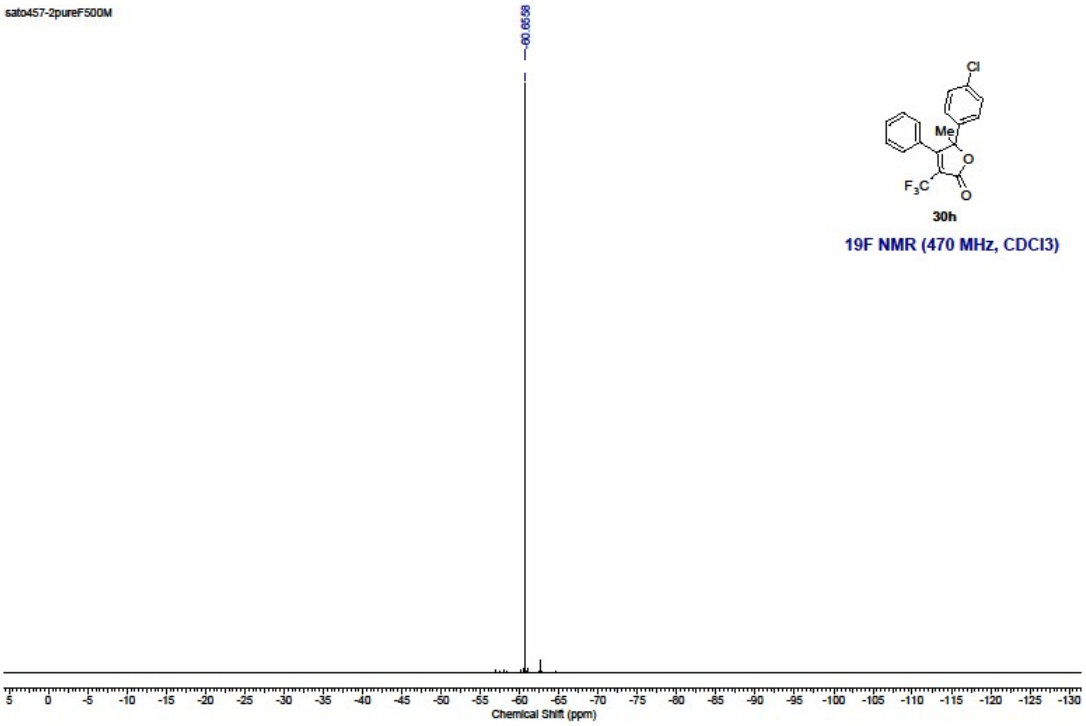

sato457pureH500M
7.4224
7.3311
7.3150
7.2998
7.2060
7.1899
7.1034
7.0863
6.7702
6.7532
6.7540
6.7511
2.3898
1.8899
0.0127
Me
Me
O
F3C
O
30g
1H NMR (500 MHz, CDCl3)
0.99 1.99 1.94 1.91 1.94
2.87 3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

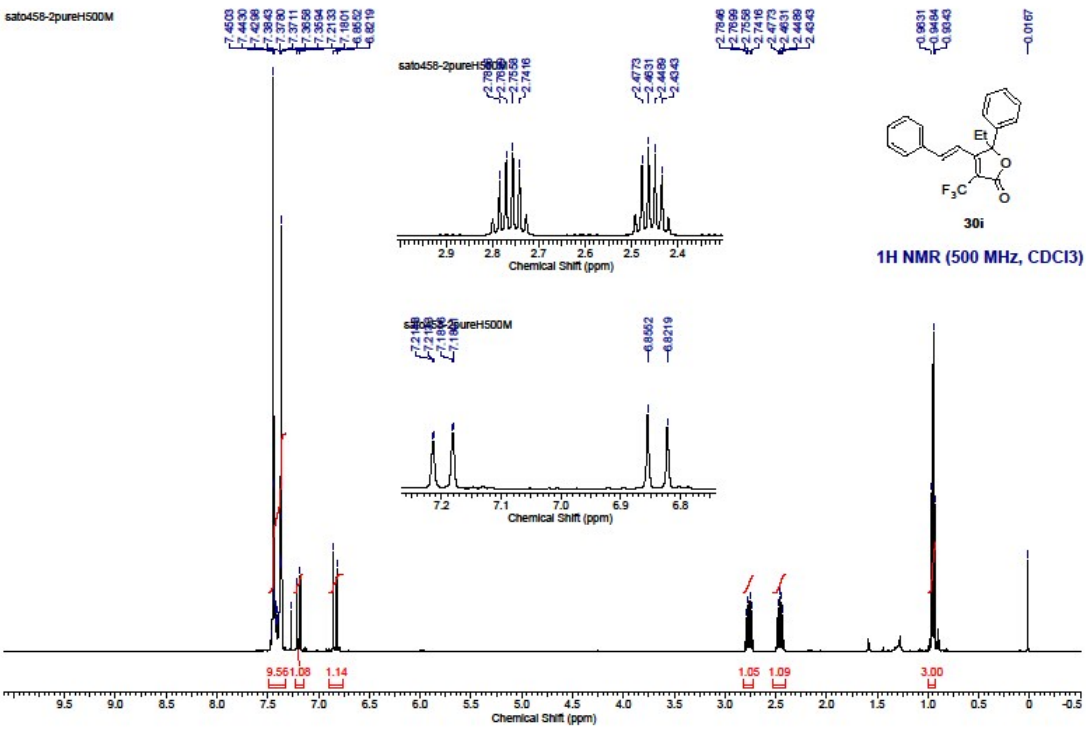

sato457pureC500M
Chemical Shift (ppm)
Me
Me
O
O
F3C
30g
13C NMR (125 MHz, CDCl3)

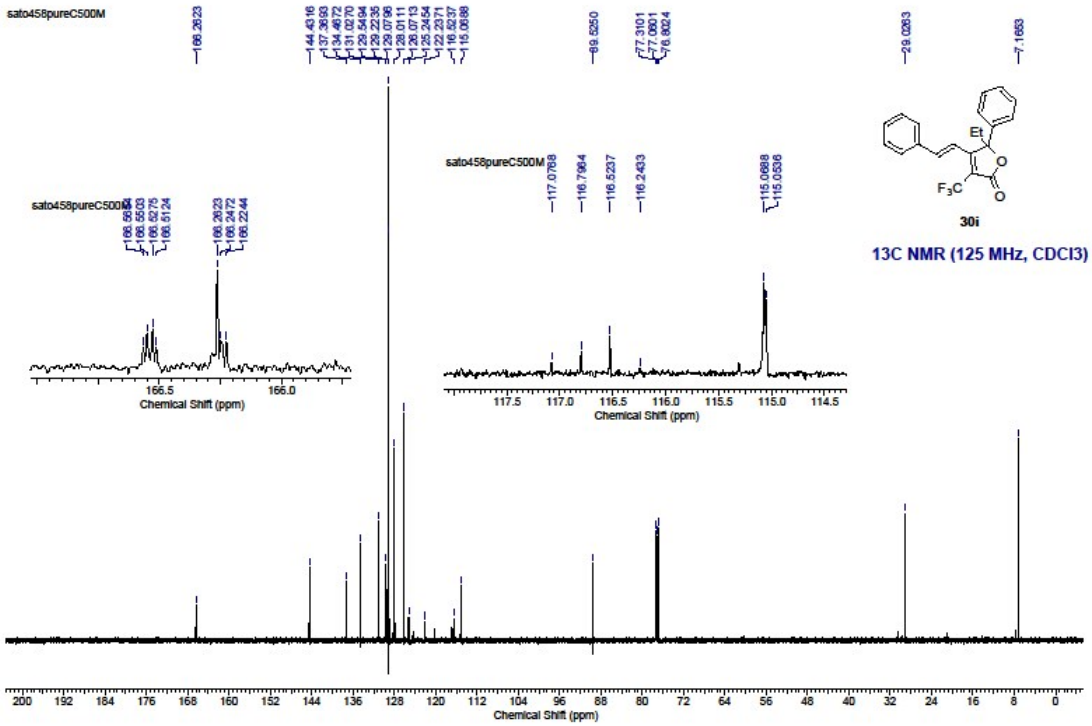

sato457pureF500M
Chemical Shift (ppm)
Me
Me
O
O
F3C
30g
19F NMR (470 MHz, CDCl3)

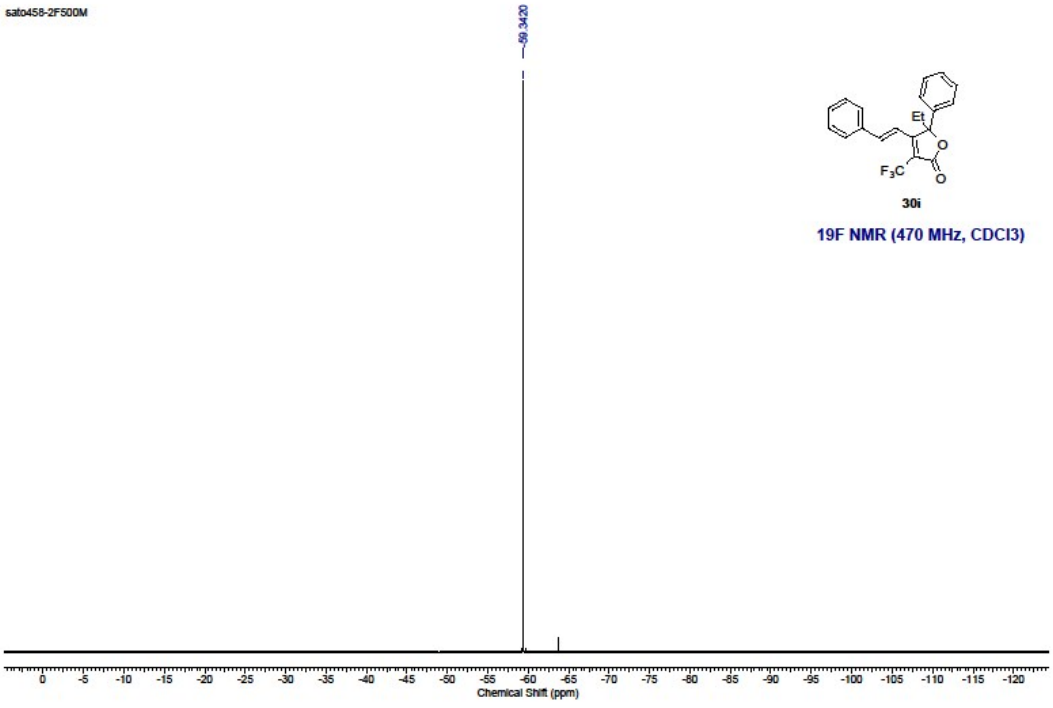

sato457-2pureH500M
1.09
4.01
2.03
2.00
3.09
Chemical Shift (ppm)
30h
1H NMR (500 MHz, CDCl3)

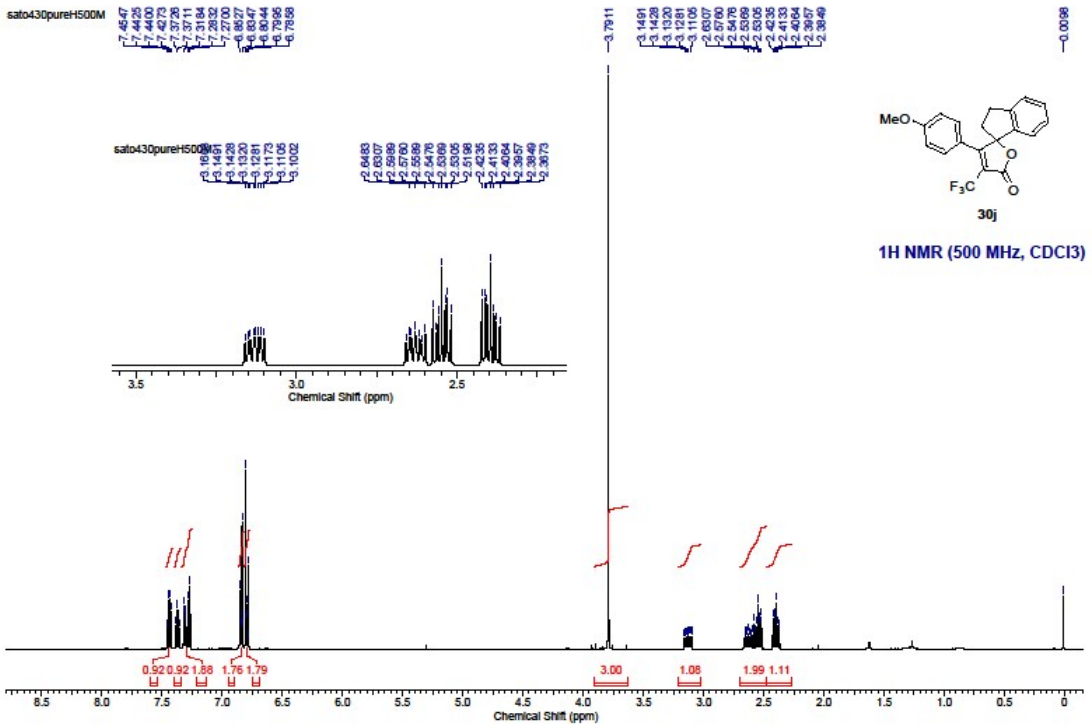

sato457-2pureC500M
Chemical Shift (ppm)
30h
13C NMR (125 MHz, CDCl3)

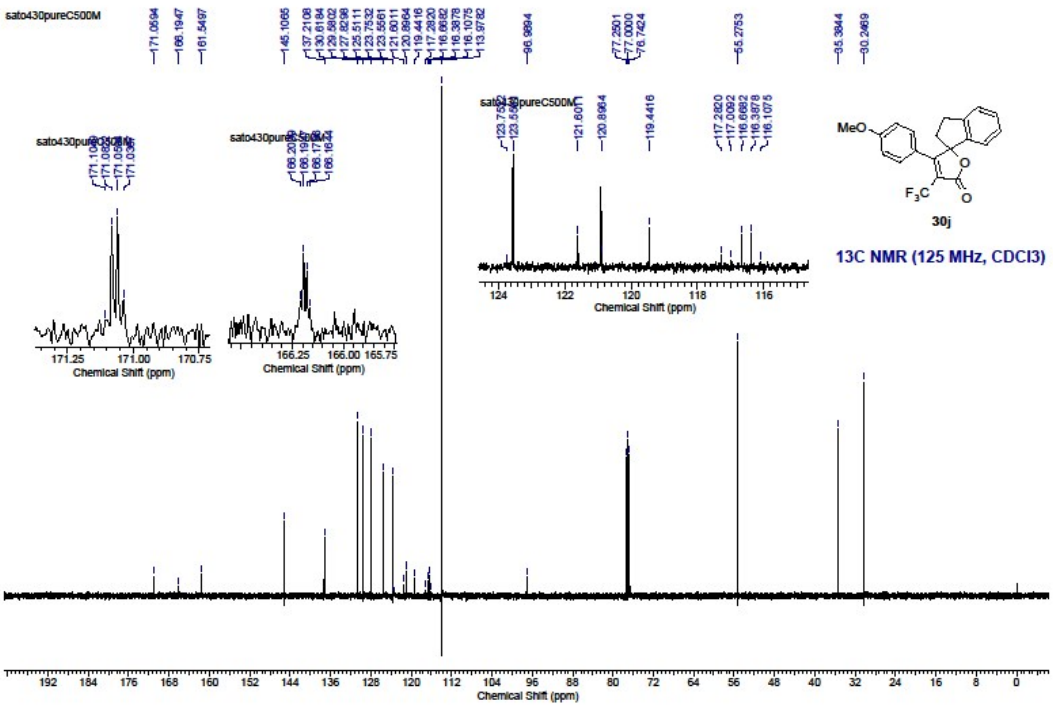

sato457-2pureF500M
-60.6558
Cl
Me
O
F_3C
O
30h
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

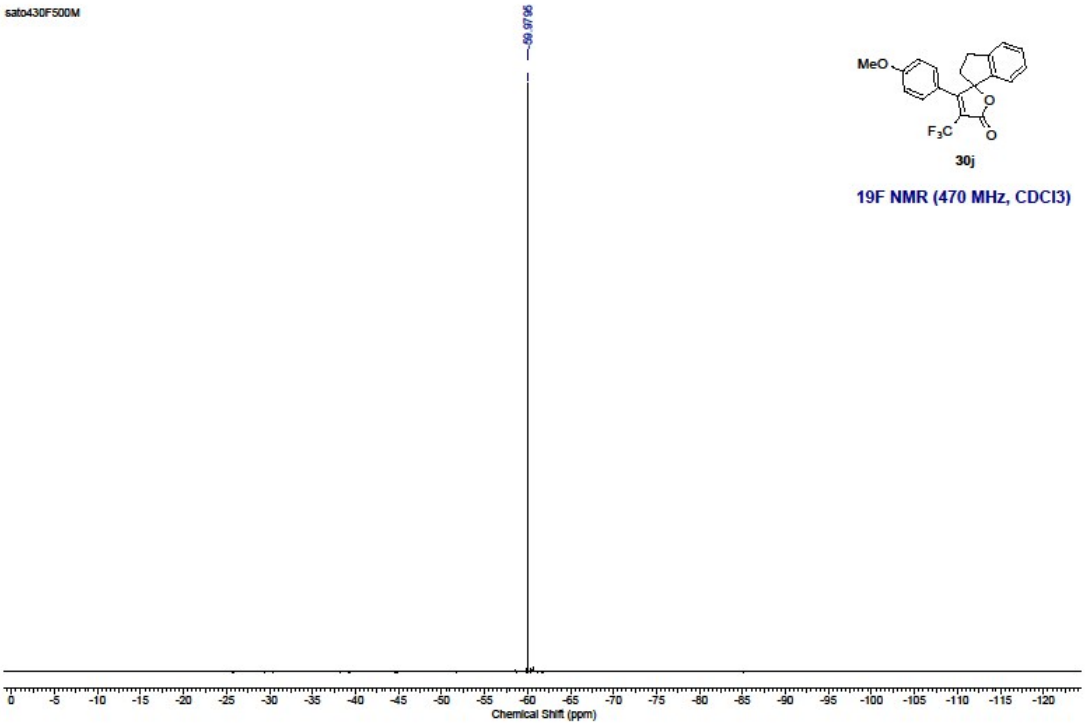

sato458-2pureH500M
7.4503
7.4430
7.4298
7.3843
7.3780
7.3711
7.3658
7.3594
7.2133
7.1901
6.8552
6.8219
2.7846
2.7699
2.7558
2.7416
2.4773
2.4631
2.4489
2.4343
0.9831
0.9484
0.9343
-0.0167
Et
O
F_3C
O
30i
1H NMR (500 MHz, CDCl3)
9.56
1.08
1.14
1.05
1.09
3.00
Chemical Shift (ppm)

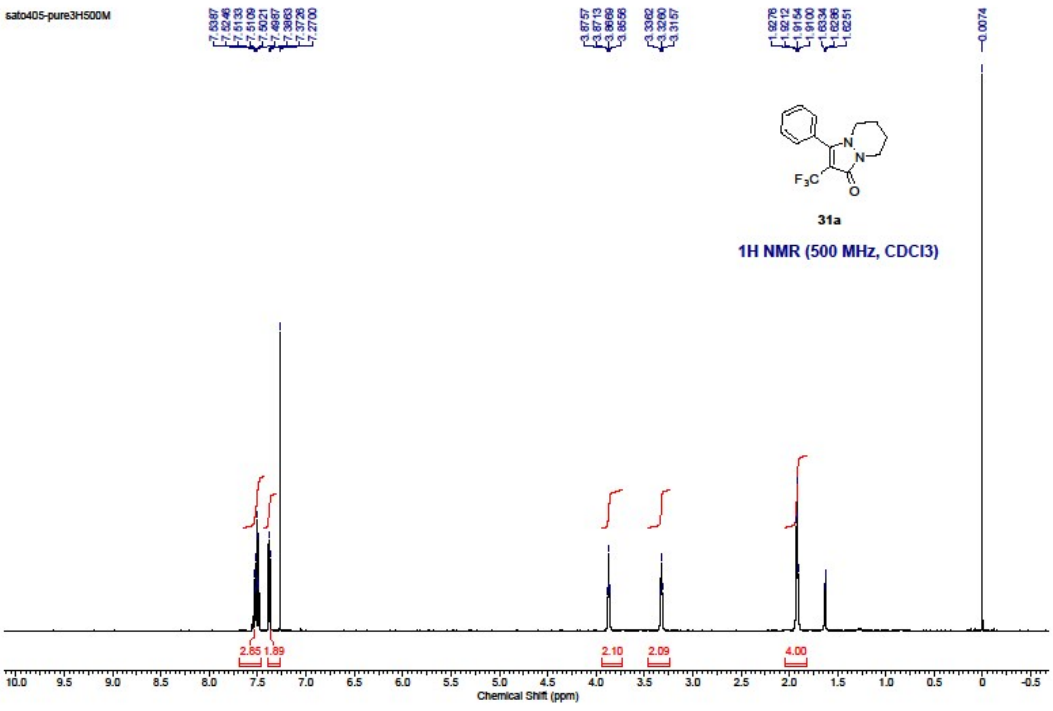

sato458pureC500M
166.2623
144.4316
137.3693
134.4672
131.0270
129.5494
129.2235
128.0796
128.0711
128.0713
125.2454
122.2371
116.5237
115.0688
89.5250
77.3101
77.0001
76.6824
29.0263
7.1663
sato458pureC500M
117.0788
116.7964
116.5237
116.2433
115.0688
115.0536
sato458pureC500M
166.5603
166.5275
166.5124
166.2623
166.2472
166.2244
166.5 166.0
Chemical Shift (ppm)
117.5 117.0 116.5 116.0 115.5 115.0 114.5
Chemical Shift (ppm)
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)
Et
O
F3C
O
30i
13C NMR (125 MHz, CDCl3)

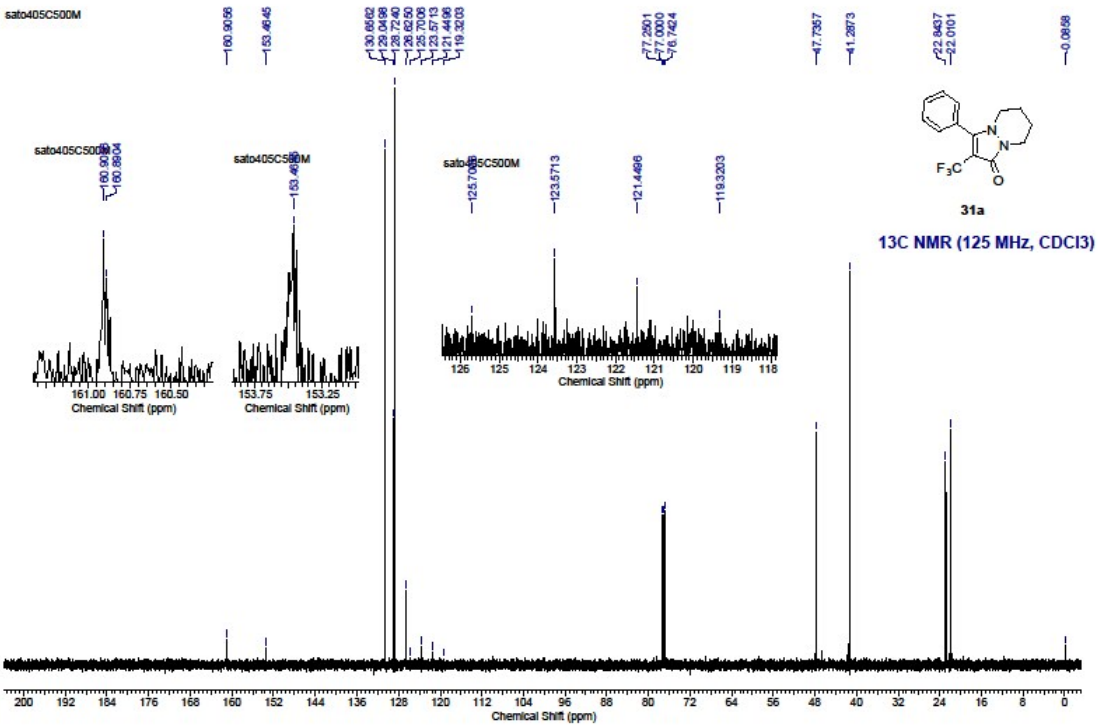

sato458-2F500M
-59.3420
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120
Chemical Shift (ppm)
Et
O
F3C
O
30i
19F NMR (470 MHz, CDCl3)

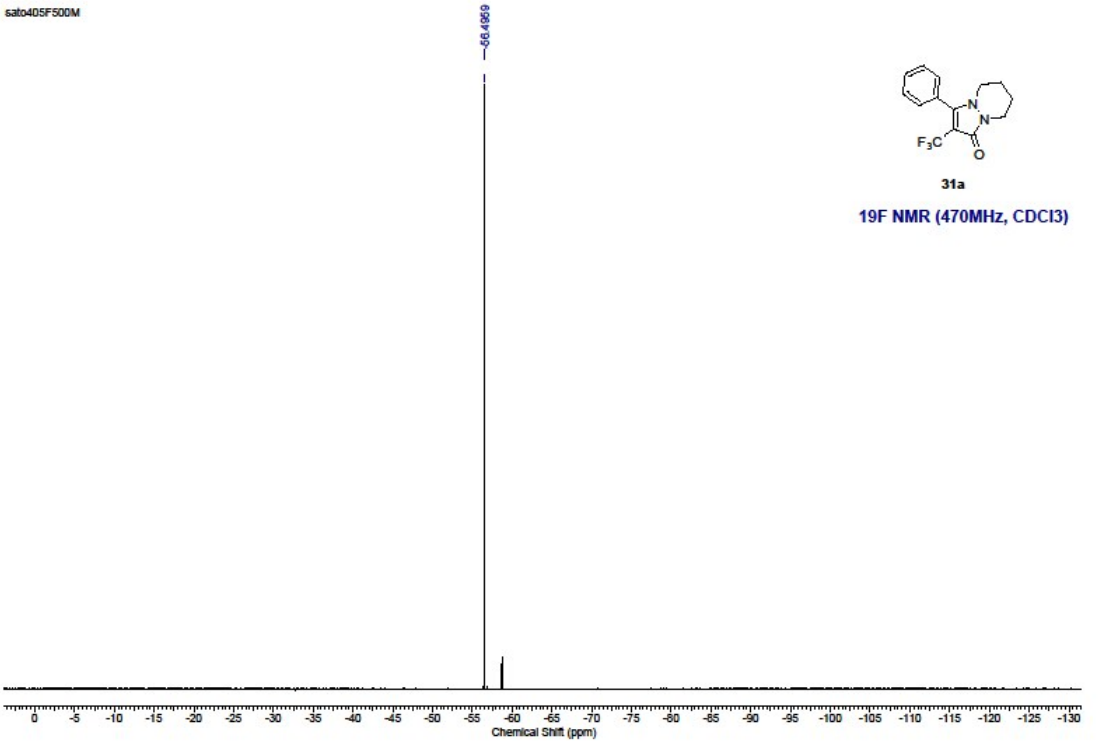

sato430pureH500M
MeO
F3C
O
30j
1H NMR (500 MHz, CDCl3)
Chemical Shift (ppm)

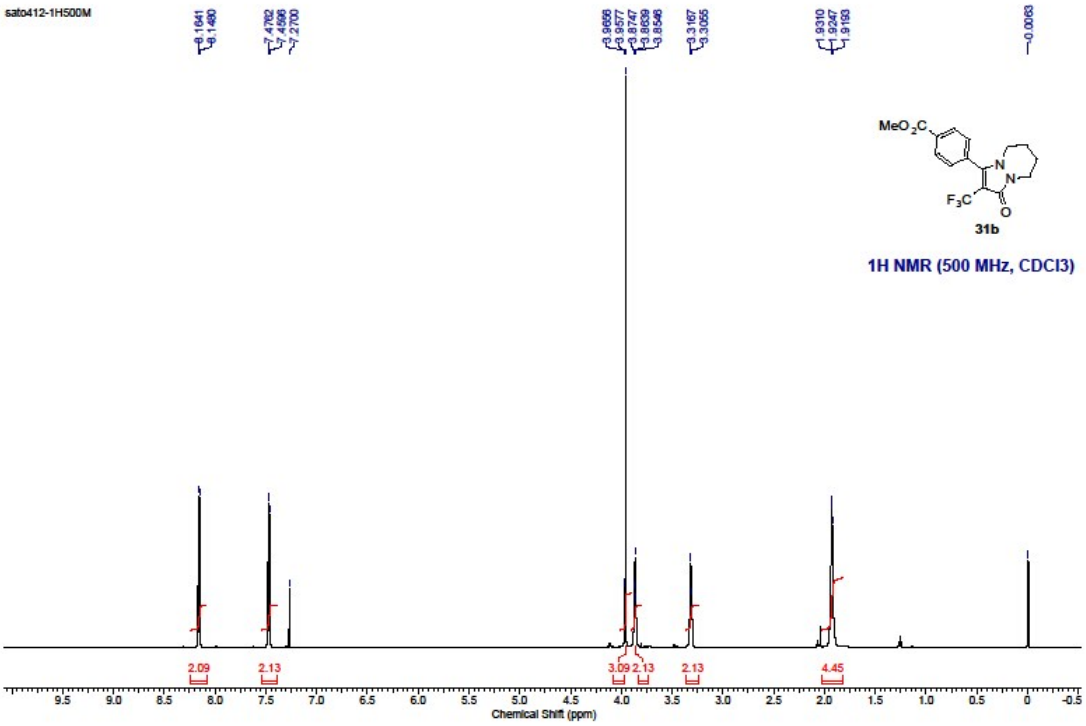

sato430pureC500M
MeO
F3C
O
30j
13C NMR (125 MHz, CDCl3)
Chemical Shift (ppm)

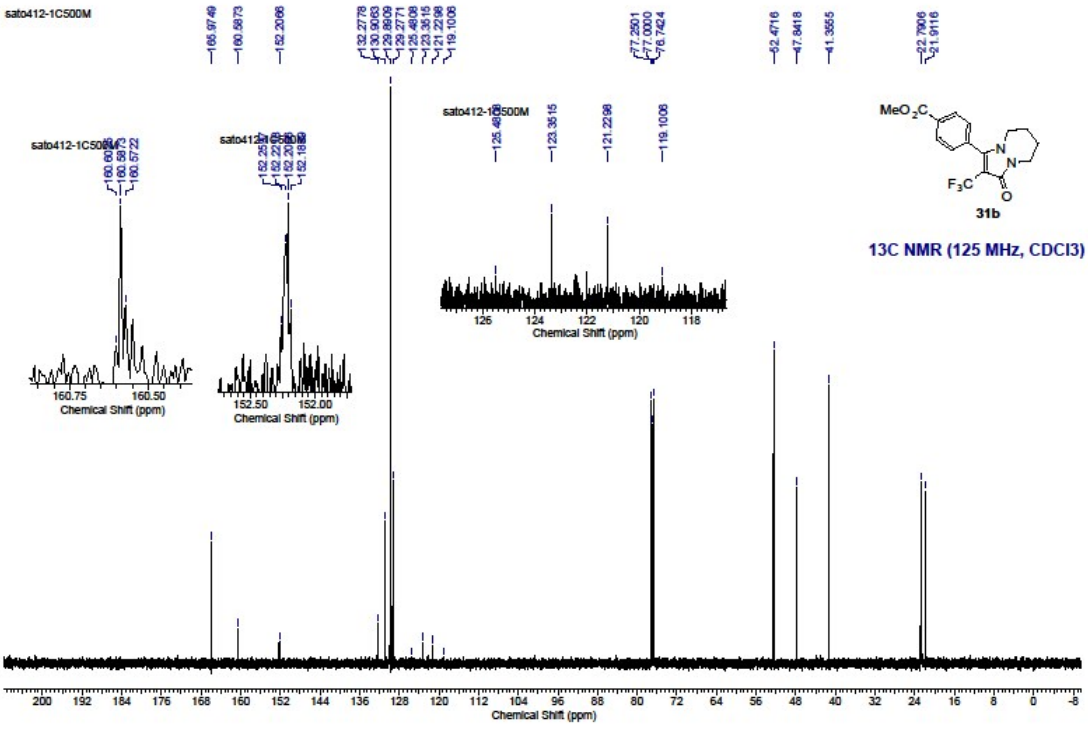

sato430F500M
-59.9795
MeO
O
F3C
O
30j
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

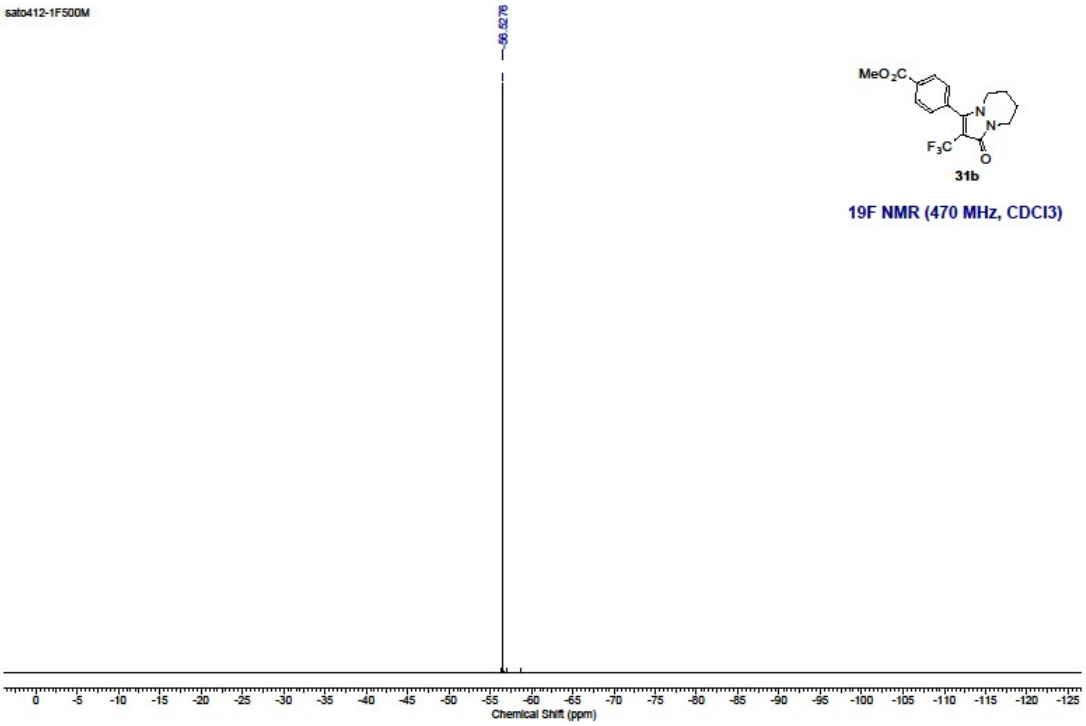

sato405-pure3H500M
7.5387
7.5246
7.5133
7.5109
7.5021
7.4987
7.3963
7.3726
7.2700
3.8757
3.8713
3.8669
3.8626
3.3282
3.3260
3.3157
1.9276
1.9212
1.9154
1.9100
1.6334
1.6286
1.6251
0.0074
N
N
F3C
O
31a
1H NMR (500 MHz, CDCl3)
2.85
1.89
2.10
2.09
4.00
Chemical Shift (ppm)

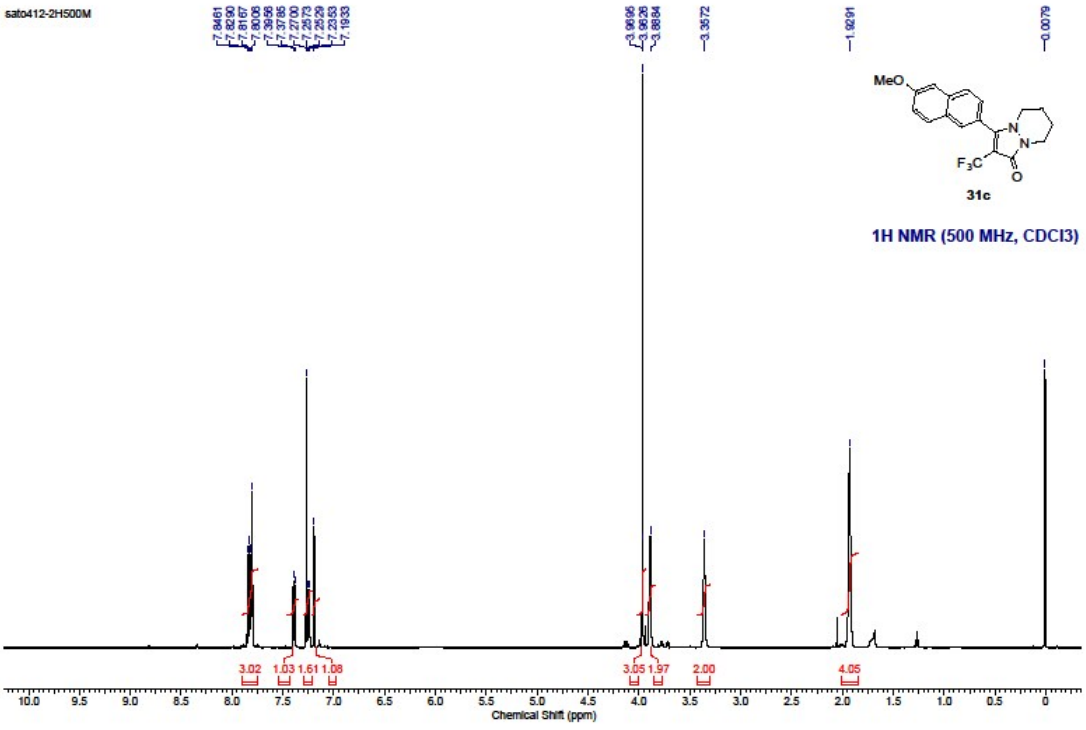

sato405C500M
160.9056
153.4645
30.6662
29.0498
28.7240
26.6250
25.7006
23.5713
21.4496
19.3203
77.2501
77.0000
76.7424
47.7357
41.2873
22.8437
22.0101
0.0898
sato405C500M
160.9056
160.8804
sato405C500M
153.4645
sato405C500M
123.7006
123.5713
121.4496
119.3203
161.00 160.75 160.50
Chemical Shift (ppm)
153.75 153.25
Chemical Shift (ppm)
126 125 124 123 122 121 120 119 118
Chemical Shift (ppm)
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)
31a
13C NMR (125 MHz, CDCl3)

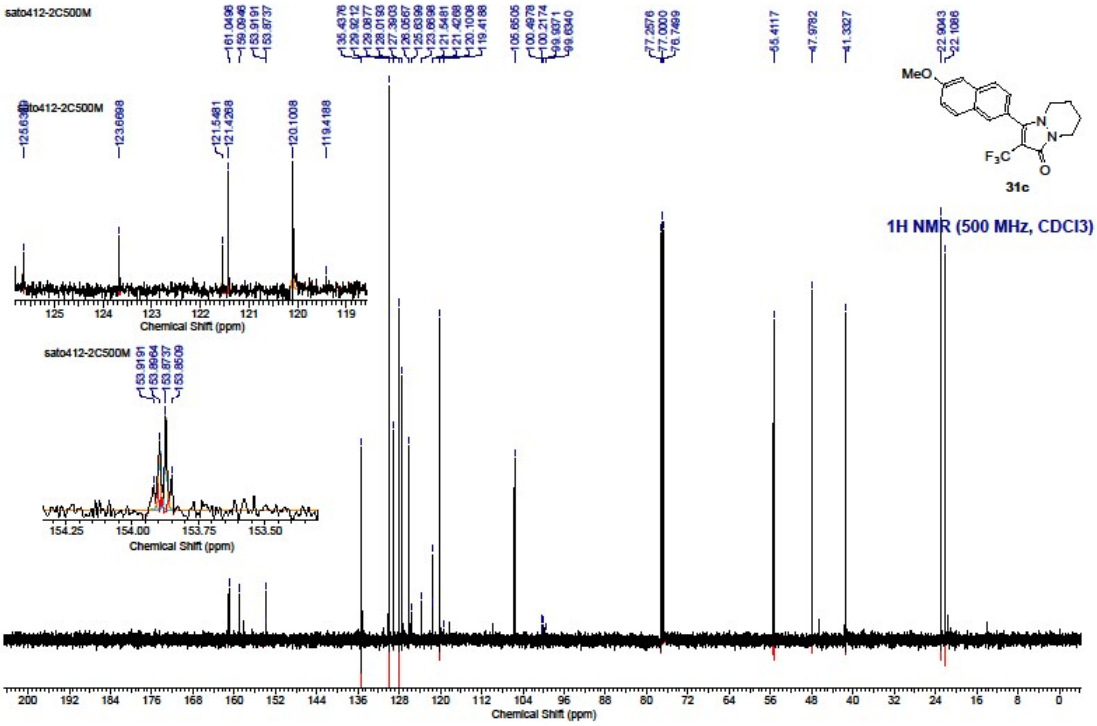

sato405F500M
-56.4969
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130
Chemical Shift (ppm)
31a
19F NMR (470MHz, CDCl3)

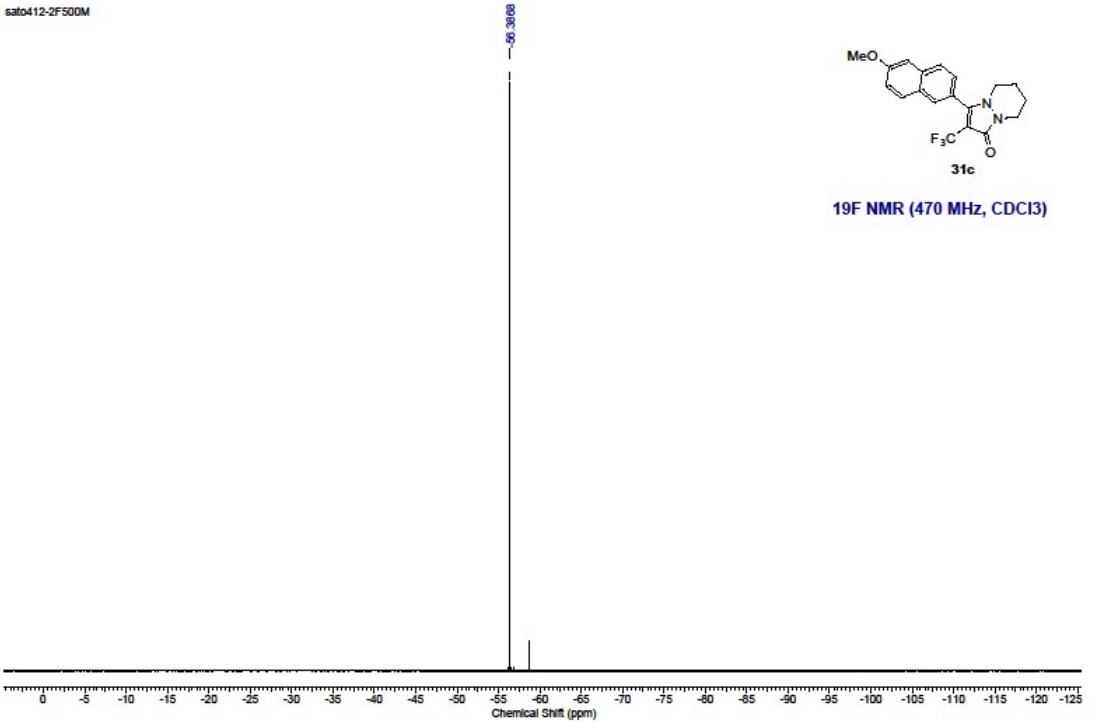

sato412-1H500M
8.1641
8.1480
7.4762
7.4596
7.2700
3.9656
3.9577
3.8747
3.8639
3.8546
3.3167
3.3055
1.9310
1.9207
1.9193
0.0063
MeO2C
F3C
N
N
O
31b
1H NMR (500 MHz, CDCl3)
2.09
2.13
3.09
2.13
2.13
4.45
Chemical Shift (ppm)

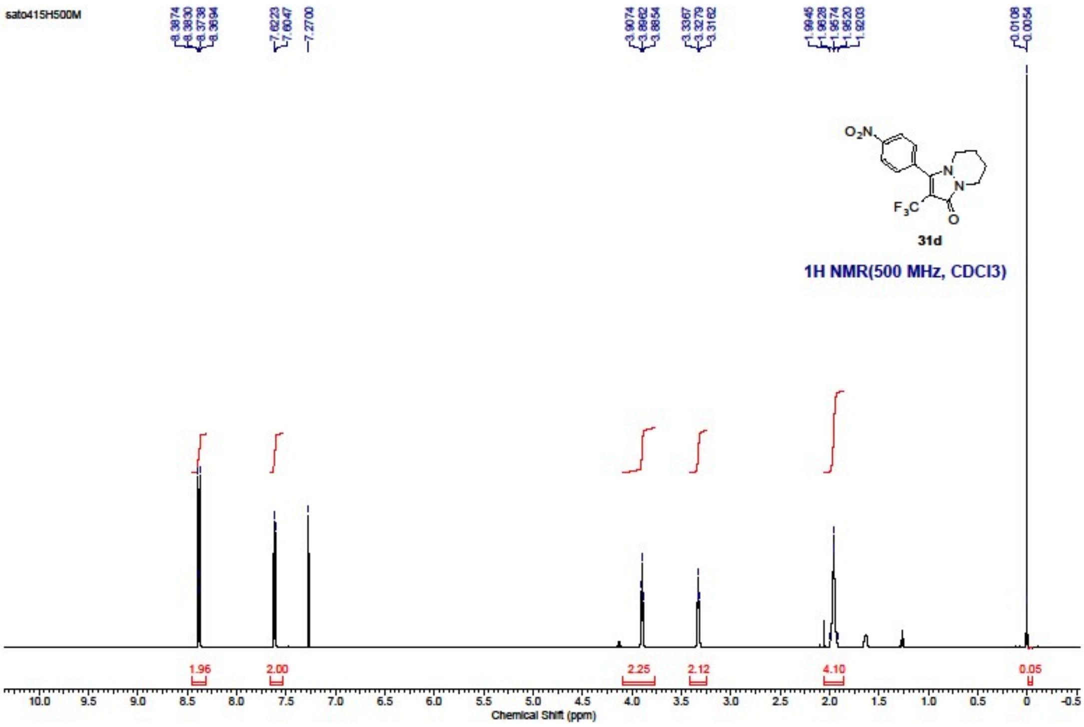

sato412-1C500M
165.9749
160.5973
152.2066
132.2778
130.9063
129.8609
129.2771
123.4608
123.3515
121.2298
119.1006
77.2501
77.0000
76.7424
52.4716
47.8418
41.3555
22.7906
21.9116
MeO2C
F3C
N
N
O
31b
13C NMR (125 MHz, CDCl3)
sato412-1C500M
sato412-1C500M
sato412-1C500M
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)

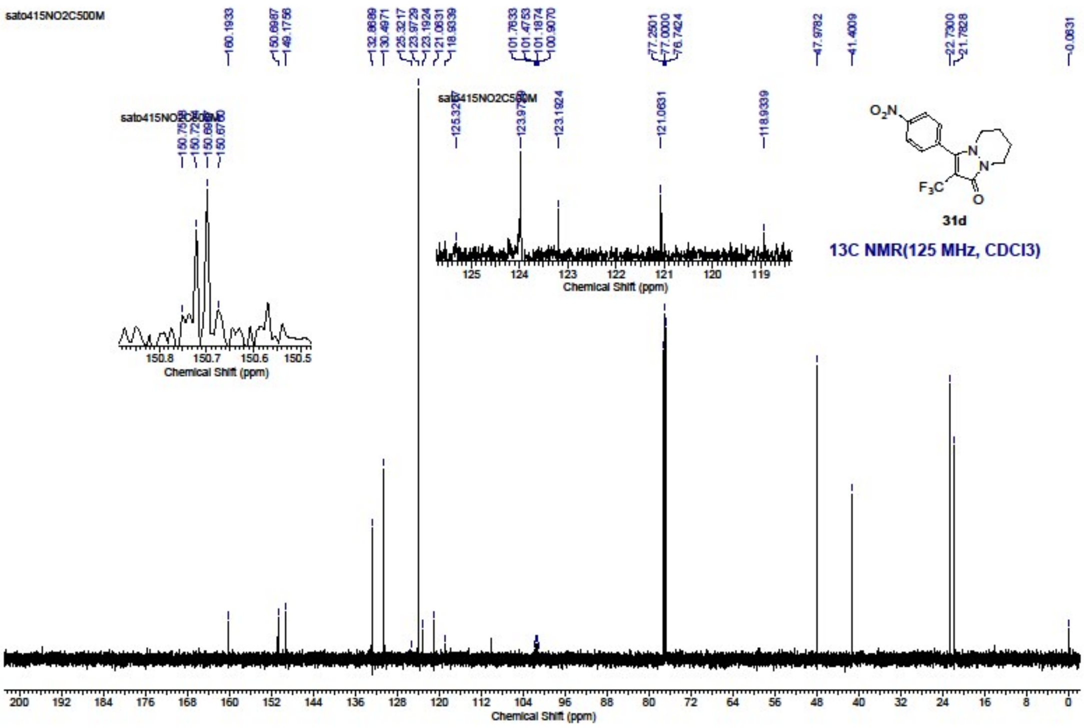

sato412-1F500M
-55.5276
MeO2C
F3C
O
N
N
31b
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

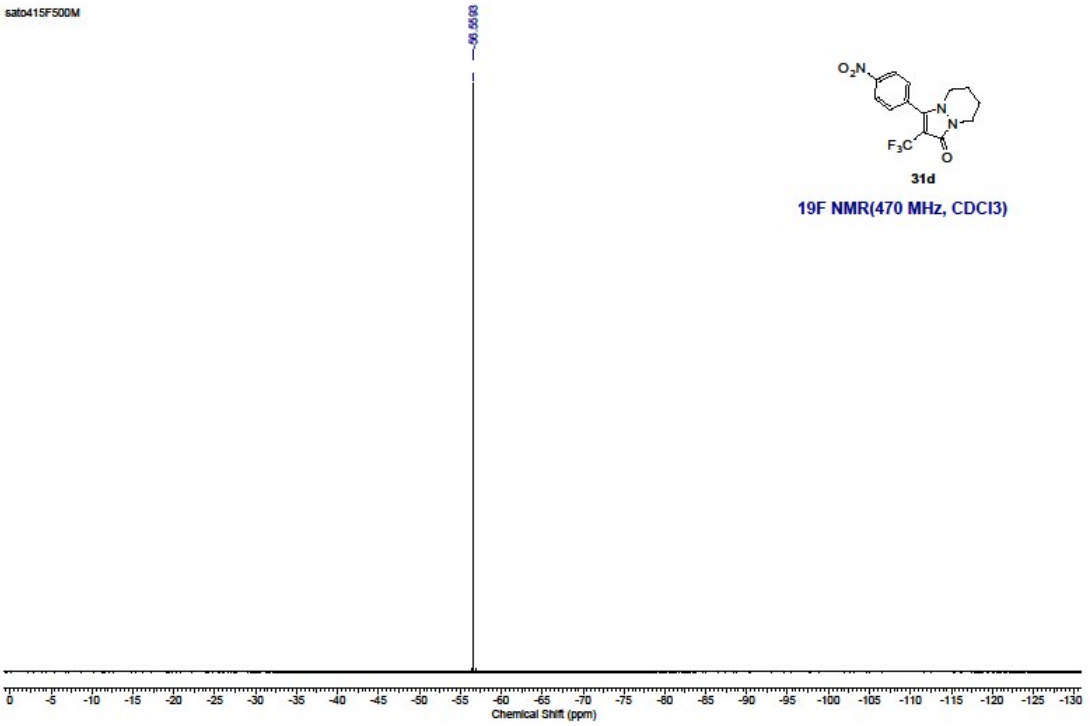

sato412-2H500M
7.8461
7.8190
7.8167
7.8006
7.3956
7.3785
7.2700
7.2573
7.2529
7.2353
7.1933
3.9995
3.9926
3.8884
3.3572
1.9291
0.0079
MeO
F3C
O
N
N
31c
1H NMR (500 MHz, CDCl3)
3.02
1.03
1.61
1.08
3.05
1.97
2.00
4.05
Chemical Shift (ppm)


sato412-2C500M
sato412-2C500M
sato412-2C500M
MeO
F3C
O
N
N
31c
1H NMR (500 MHz, CDCl3)
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)


sato412-2F500M
MeO
F3C
O
N
N
31c
19F NMR (470 MHz, CDCl3)
Chemical Shift (ppm)

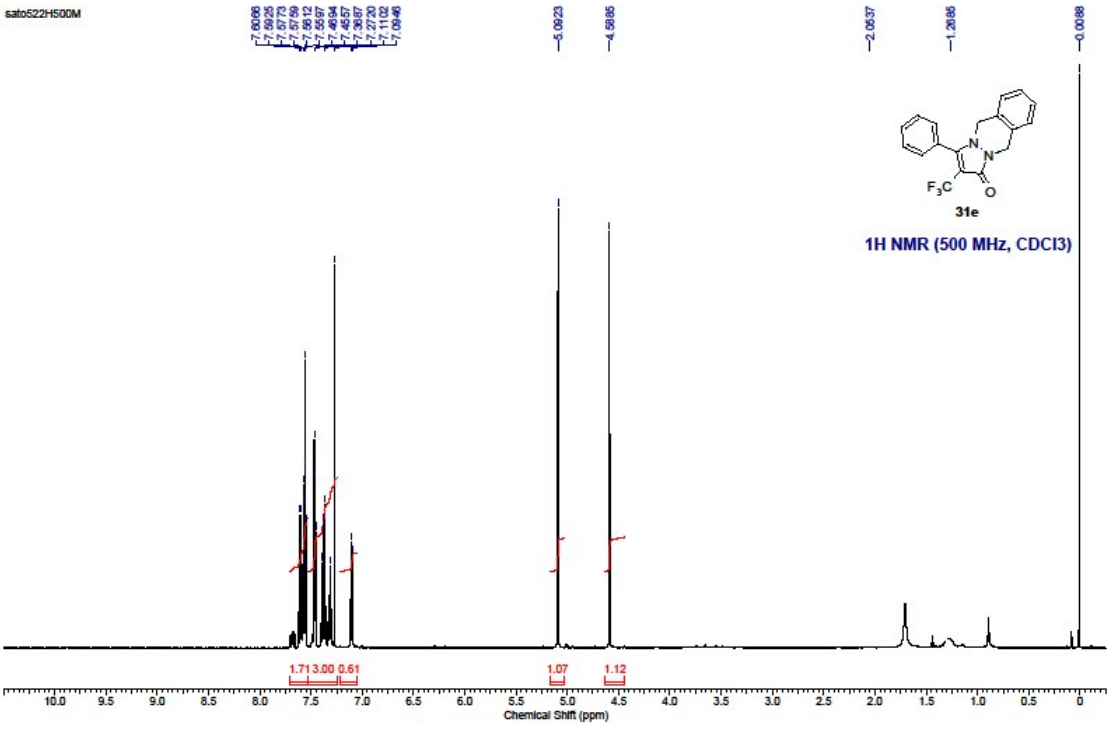

sato415H500M
O_2N
F_3C
O
31d
1H NMR(500 MHz, CDCl3)
Chemical Shift (ppm)


sato415NO2C500M
O_2N
F_3C
O
31d
13C NMR(125 MHz, CDCl3)
Chemical Shift (ppm)



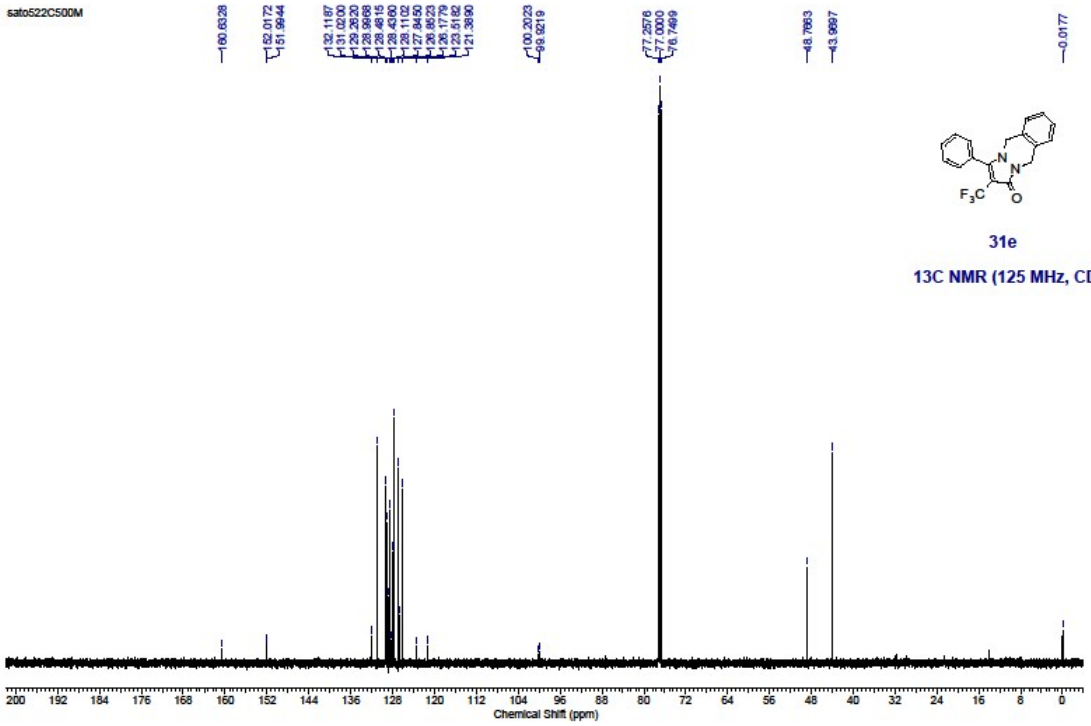
31d

19F NMR(470 MHz, CDCl3)



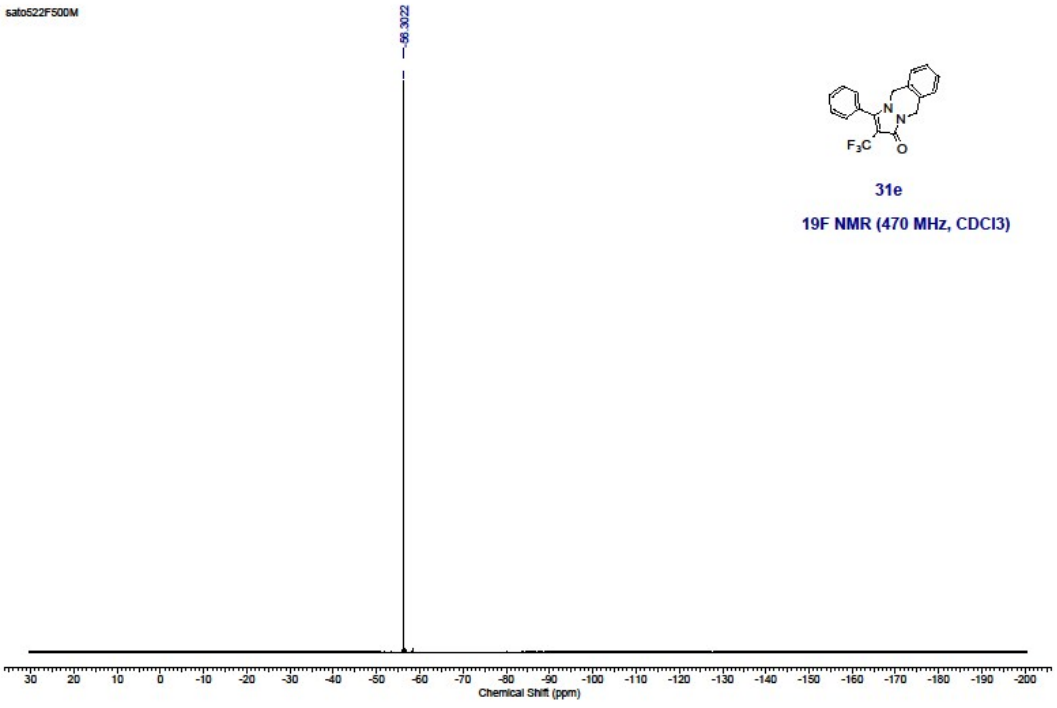
31e

1H NMR (500 MHz, CDCl3)



31e

13C NMR (125 MHz, CDCl3)



31e

19F NMR (470 MHz, CDCl3)