Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Title: Synthesis of CHF_2-substituted 3-azabicyclo[3.1.0]hexanes by photochemical decomposition of CHF_2-pyrazolines

Author(s): Yang Zheng, Xinling Yu, Songyang Lv, Pavel K. Mykhailiuk, Qiang Ma, Li Hai and Yong Wu

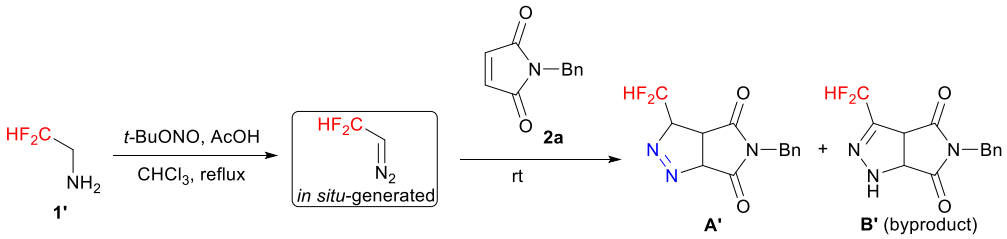
Table of Concents:

1. General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. Except for the specially mentioned dry solvent, all the solvents were treated according to general methods. All the reactions were monitored by thin-layer chromatography (TLC) and were visualized using UV light. The product purification was done using silica gel column chromatography. Thin layer chromatography (TLC) characterization was performed with precoated silica gel GF254 (0.2 mm), while column chromatography characterization was performed with silica gel (100-200 mesh). ^{1}H-NMR, ^{13}C-NMR and ^{19}F-NMR spectra were recorded with tetramethylsilane (TMS, δ = 0.00 ppm) as the internal standard. ^{1}H-NMR spectra were recorded at 400 or 600 MHz (Varian), ^{13}C NMR spectra were recorded at 100 or 150 MHz (Varian) and ^{19}F-NMR spectra were recorded at 376 MHz (Varian). Chemical shifts are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) or DMSO-d_6 (δ = 2.54 ppm) for ^{1}H NMR and chemical shifts for ^{13}C NMR spectra are reported in ppm relative to the central $CDCl_3$ (δ = 77.0 ppm) or DMSO-d_6 (δ = 39.6 ppm). Coupling constants are given in Hz. Melting points were measured with YRT-3 melting point apparatus (Shantou Keyi Instrument & Equipment Co., Ltd., Shantou, China). Photochemical reaction was done using photochemical reaction instrument (Shanghai Bilon Instrument Manufacturing Co., Ltd., model: BL-GHX-V). High resolution mass spectroscopy data of the products were collected on a Waters Micromass GCT or a Bruker Apex IV FTMS instrument.

2. Optimization of the reaction conditions

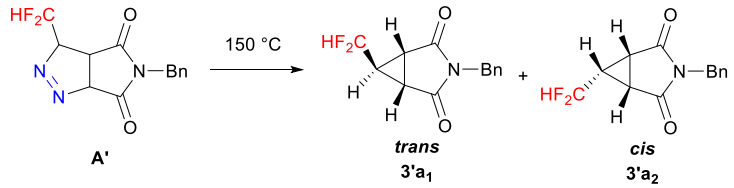
2.1. Synthesis of 3-benzyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione 3'a by thermal decomposition of pyzoline A'.



Scheme S1. Synthesis of pyzoline **A'**

The pyzoline **A'** was synthesized as described in the literature.[1] To a stirred solution of 2,2-difluoroethanamine **1'** (648.5 mg, 8.0 mmol) in dry $CHCl_3$ (75 mL), *t*-BuONO (988.8 mg, 9.6 mmol) and HOAc (96.1 mg, 1.6 mmol) were added dropwisely. Then the reaction mixture was heated at 65 °C. After 10 min heating, the obtained yellow solution was cooled down to a room temperature by external water bath, and 1-benzyl-1*H*-pyrrole-2,5-dione **2a** (750.0 mg, 4.0 mmol, 1.0 equiv.) was added immediately. The reaction mixture was left at room temperature for 2 h stirring. The solvent was evaporated under vacuum. Compound **A'** could be obtained through crystallization (solvent: hexane/EA = 1:2). 592.0 mg, 53% yield, white solid, m.p. 135-136 °C.

3-(difluoromethyl)-5-benzyl-3a,6a-dihydropyrrolo[3,4-*c*]pyrazole-4,6(*3H,5H*)-dione (A'): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (s, 5H), 6.49 (td, *J* = 55.4, 1.6 Hz, 1H), 5.81 (dd, *J* = 7.8, 2.7 Hz, 1H), 5.48 (dd, *J* = 23.8, 4.4 Hz, 1H), 4.59 (d, *J* = 1.9 Hz, 2H), 3.35 (dd, *J* = 7.8, 2.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 167.9, 134.5, 128.9, 128.8, 128.5, 111.1 (t, *J* = 245.7 Hz), 94.6, 93.6 (t, *J* = 22.2 Hz), 43.0, 37.2 (d, *J* = 4.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.7 (dd, *J* = 291.4 Hz), -130.0 (dd, *J* = 291.4 Hz); HRMS (ESI) Calcd for $C_{13}H_{11}F_2N_3O_2$ $[M+Na]^+$ 302.0712; found 302.0713.



Scheme S2. Synthesis of 3-benzyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione **3'a**.

Compound **3'a** was synthesized as described in the literature.[2] Pyzoline **A'** (592.0 mg, 2.1 mmol) was heated in an oil bath under vacuum (20 mmHg) at 150 °C during 1 h; an exothermic evolution of N_2 was observed. The crude product was dissolved in CH_2Cl_2 (10 mL), triturated with 5% aq $KMnO_4$ (10 mL), washed with H_2O (10 mL), dried ($MgSO_4$), and evaporated. The obtained residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 10/1). Yield: **3'a$_1$**: (213.2 mg, 40% yield, white solid, m.p. 72-73 °C), and **3'a$_2$**: (58.9 mg, 11% yield, white solid, m.p. 137-139 °C).

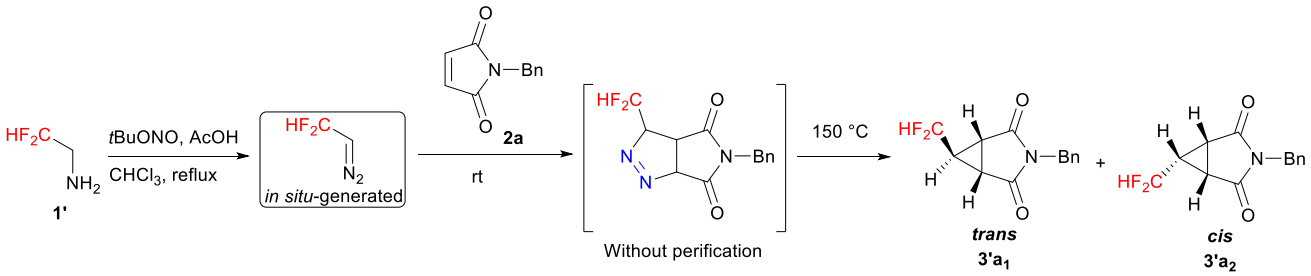
The total yield of **3a'** was obtained only in 27% based on the maleimide **1b**.

***trans*-3-benzyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione (3'a$_1$):** ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43-7.21 (m, 5H), 5.92 (td, *J* = 56.2, 2.2 Hz, 1H), 4.54 (s, 2H), 2.72 (d, *J* = 3.1 Hz, 2H), 2.04 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.2, 135.5, 128.7, 128.5, 128.1, 111.2 (t, *J* = 242.3 Hz), 42.0, 32.9 (t, *J* = 26.5 Hz), 21.5 (t, *J* = 4.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -125.7 (dd, *J* = 291.4, 10.2 Hz); HRMS (ESI) Calcd for $C_{13}H_{11}F_2NO_2$ $[M+H]^+$ 251.0758; found 251.0759.

***cis*-3-benzyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione (3'a$_2$):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.23 (m, 5H), 5.14 (td, *J* = 54.7, 6.6 Hz, 1H), 4.56 (s, 2H), 2.74 (d, *J* = 8.5 Hz, 2H), 2.24 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.6, 135.1, 129.0, 128.8, 128.4, 112.5 (t, *J* = 240.8 Hz), 42.2, 33.2 (t, *J* = 33.5 Hz), 24.0 (t, *J* = 3.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -115.2 (dd, *J* = 54.6 Hz, 6.7 Hz); HRMS (ESI) Calcd for $C_{13}H_{11}F_2NO_2$ $[M+H]^+$ 251.0758; found 251.0759.

2.2. One-pot cascade approach to formation 3a'.

Table S1. The conditions for the one-pot cascade approach.



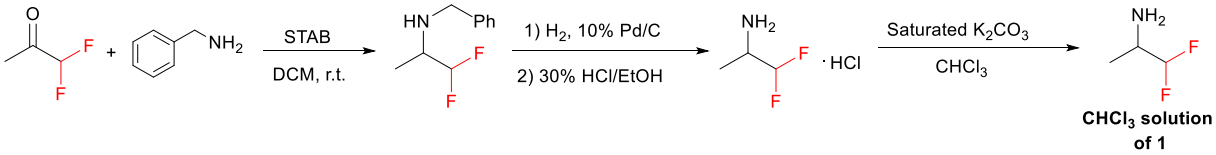
Entry	Conditions of nitrogen removal	T (°C)	Time (h)	Yield(%)[a]	
				3'a$_1$	3'a$_2$
1	Thermal decomposition	150	1	26	6
2	Thermal decomposition	150	5	27	6
3	Thermal decomposition	180	1	27	7
4	Photodecomposition by high-pressure mercury lamp, solvent-free	r.t.	24	25	5
5	Photodecomposition by high-pressure mercury lamp, toluene as the solvent	r.t.	24	31	8
6	Photodecomposition by blue LED	r.t.	24	Trace	Trace

[a] Isolated yield by chromatography on silicagel.

Considering the low yield and the tedious operation, we tried to develop a one-pot cascade approach: CHF2CHN$_2$ was generated *in situ* according to the above procedure. 1-benzyl-1*H*-pyrrole-2,5-dione **2a** (750.0 mg,

4.0 mmol, 1.0 equiv.) was added immediately. The reaction mixture was left at room temperature for 2 h stirring. After evaporating the solvent, the residue was heated in an oil bath under vacuum (20 mmHg) at 150 °C during 1 h. The crude product was purified according to the above procedure. The **3'a$_1$** and **3'a$_2$** were isolated in 26% and 6% yields, respectively (Table S1, entry 1). And we accidentally discovered that photochemical process was more effective than thermal decomposition, and the total yield of **3'a** was up to 39% (entry 5), but it was still less than satisfactory, which might be because of the quantitative formation of the isomeric Δ^2-pyrazoline **B'** (See Scheme S3). Therefore, we decided to block the formation of pyrazoline **B'** by taking the simplest higher homologue - $CF_2HC(CH_3)NH_2$.

2.3. The preparation of the solution of 1-methyl-2,2-difluoroethanamine 1.

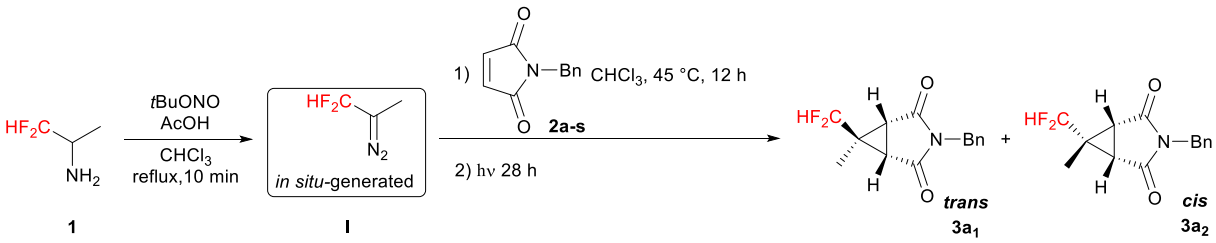


Scheme S3. The preparation of the solution of 1-methyl-2,2-difluoroethanamine **1**.

1-Methyl-2,2-difluoroethanamine was synthesized as described in the literature.[3] 1,1-Difluoroacetone (5.0 g, 53.2 mmol), benzylamine (5.7 g, 53.2 mmol) and $NaBH(OAc)_3$ (STAB, 33.8 g, 159.5 mmol) were dissolved in DCM (200 ml) and stirred for 18 h. The reaction mixture was diluted with DCM (3 × 100 mL), washed with saturated Na_2CO_3 (2 × 100 mL), brine (2 × 100 mL), dried with $MgSO_4$, and concentrated in vacuo. Then the residue was dissolved in MeOH (100 mL), and 10% Pd/C (0.5 g) was added. After stirring for 4 days under an atmosphere of H_2, the reaction mixture was filtered through celite and the filtrate was diluted with 30% HCl/EtOH. After 2 h of stirring, the solvent was evaporated under vacuum to afford 1-methyl-2,2-difluoroethanamine hydrochloride (4.9 g, 70% yield) as a gray solid. M.p. 43-45 °C.

The solid was dispersed in 100 mL $CHCl_3$ and 2 mL saturated K_2CO_3 was added. After stirring for 1 h, the organic layer was separated and dried with $MgSO_4$, Then the solids were filtered, and appropriate amount of anhydrous $CHCl_3$ was added to afford the $CHCl_3$ solution of **1** (*c* = 0.1 M).

2.4. General procedures for the synthesis of 6-methyl-6-difluoromethyl-3-azabicyclo[3.1.0]hexane-2,4-dione derivatives (3a as an example).



Scheme S4. Synthesis of 3-benzyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione **3a.**

To a stirred solution of 1-methyl-2,2-difluooethanamine **1** (285.3 mg, 3.0 mmol) in dry $CHCl_3$ (30 mL), *t*-BuONO (371.2 mg, 3.6 mmol) and HOAc (36.0 mg, 0.6 mmol) were added in turn. Then the reaction mixture was heated at 65 °C. After 10 min heating, the obtained yellow solution was cooled down to a room temperature by external water bath, and 1-benzyl-1*H*-pyrrole-2,5-dione **2a** (187.2 mg, 1.0 mmol) was added immediately. The reaction mixture was stirred at 45 °C for 12 h. After removing $CHCl_3$, the residue was dissolved by acetonitrile (5 ml) and transferred into a quartz tube which was irradiated with a 1000 W high-pressure mercury lamp (250−720 nm) for 28 h. Then the solvent was removed and the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate = 5/1 as an eluent, to afford the desired product **3a$_1$** (169.7 mg, 64% yield, white solid, m.p. 120-121 °C) and **3a$_2$** (42.4 mg, 16% yield, white solid, m.p. 131-132 °C).

2.5. NOESY interaction for $3a_1$ and $3a_2$.

Take diastereoisomer **$3a_1$** for example, the bridgehead protons (δ = 2.67 ppm) were correlated through space to the nearby difluromethyl protons (δ = 5.59 ppm), indicating they were on the same convex side of the bicyclic system (Figure S1); As for **$3a_2$**, the bridgehead protons (δ = 2.55 ppm) were correlated through space to the nearby methyl protons (δ = 1.31 ppm), indicating they were on the same convex side of the bicyclic system (Figure S2).

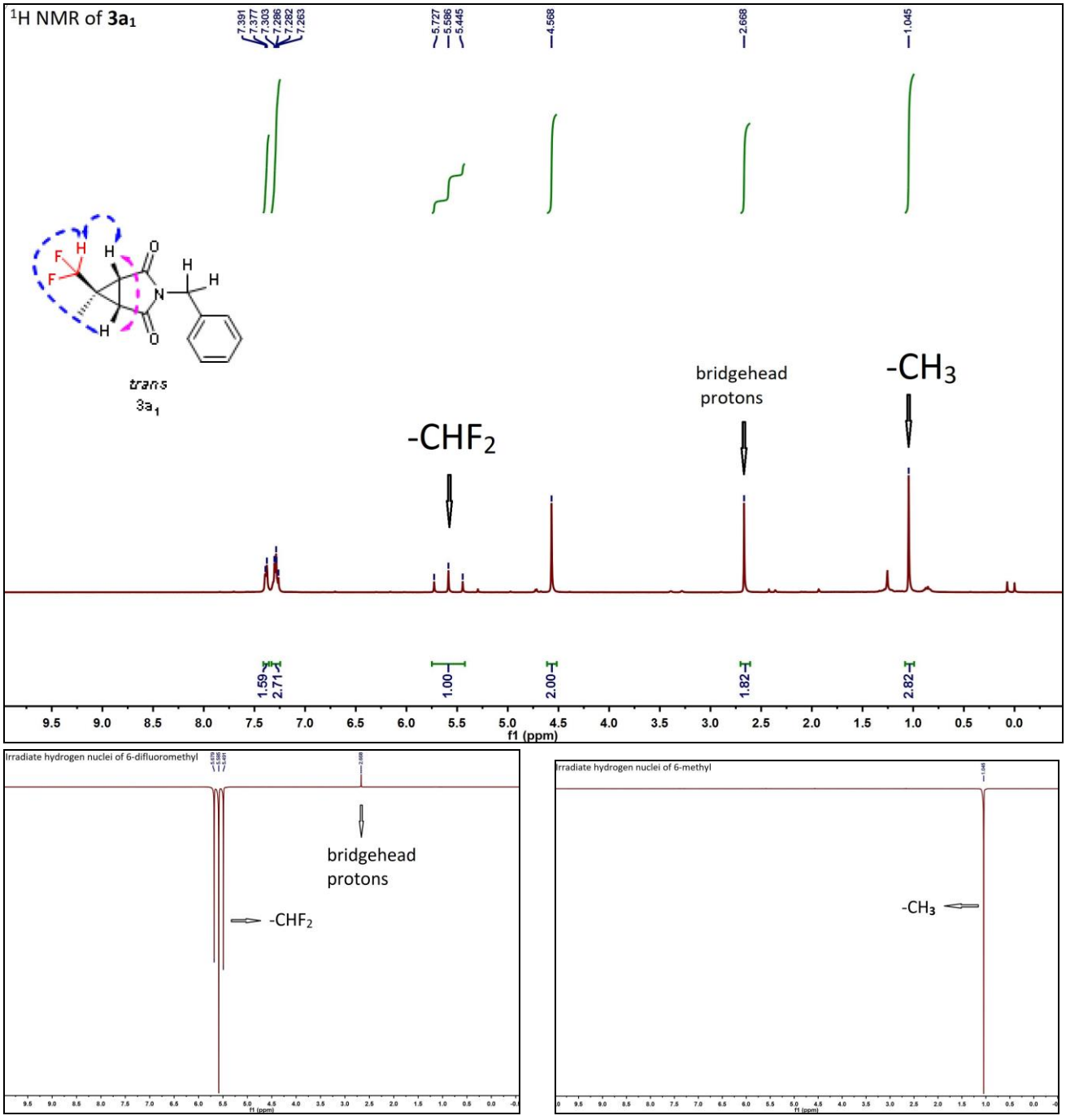


Figure S1. NOESY of **$3a_1$**.

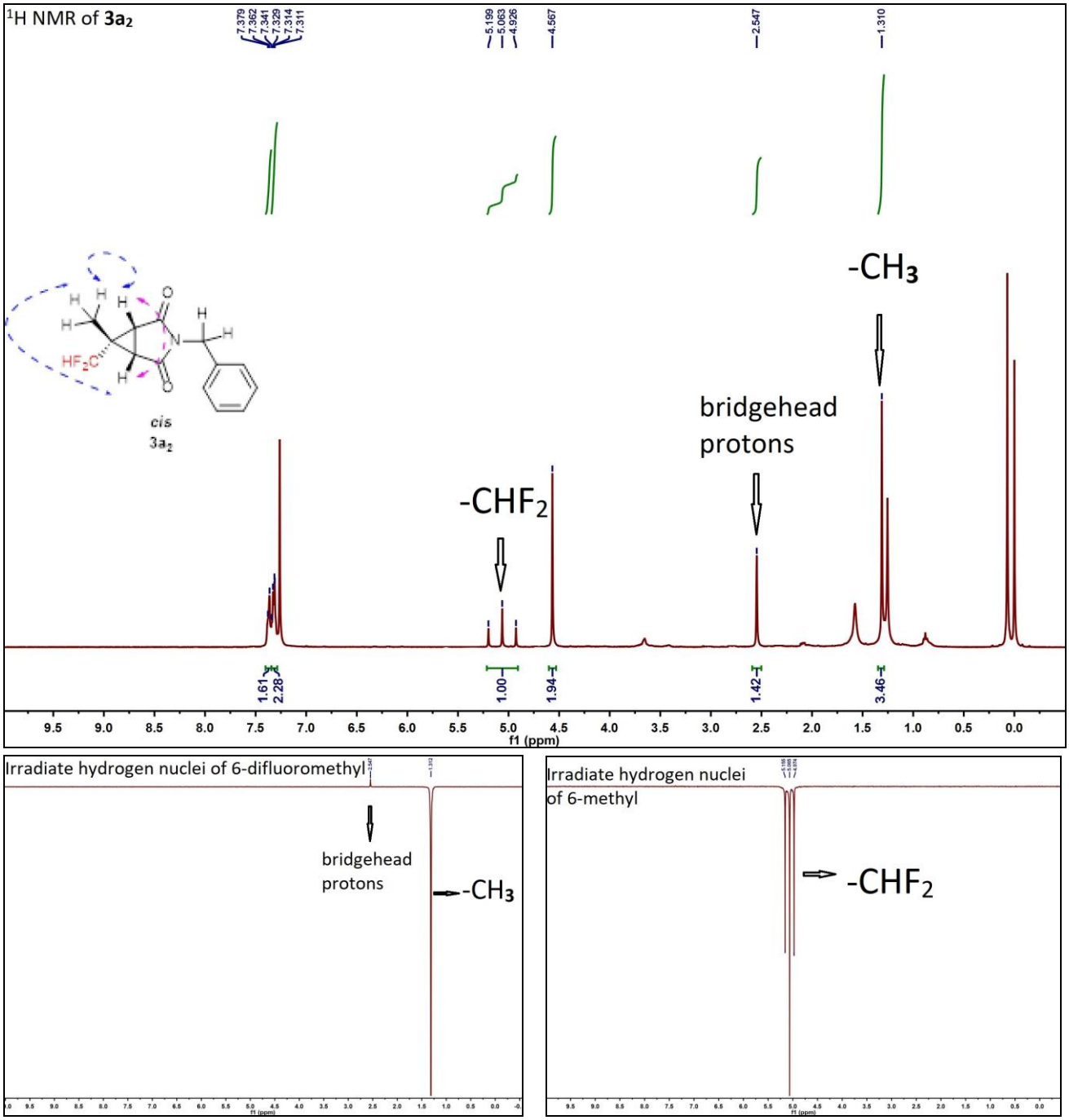
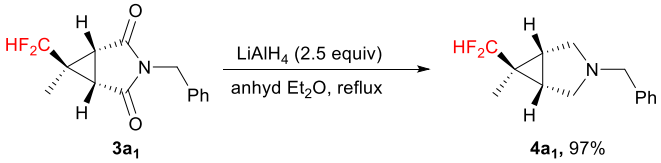


Figure S2. NOESY of **3a$_2$**.

3. Synthesis of *trans*-3-benzyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane (4a$_1$).



Scheme S5. Synthesis of 3-azabicyclo[3.1.0]hexane **4a$_1$**.

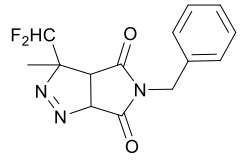
Compound **4a$_1$** was synthesized as described in the literature.[2] A solution of compound **3a$_1$** (132.6 mg, 0.5 mmol) in anhyd Et_2O (3 mL) was added dropwisely to a stirred suspension of $LiAlH_4$ (49.3 mg, 1.3 mmol) in anhydrous Et_2O (2 mL). The formed suspension was heated at reflux for 3 h. The reaction mixture was cooled to room temperature. And H_2O (0.5 mL) was added. The solution was evaporated under vacuum and H_2O (10 mL)

was added. The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and evaporated under vacuum. The residue was purified by column chromatography on silica gel using PE/EtOAc = 15/1 as an eluent, to afford the desired product **4a$_1$** (115.1 mg, 97 % yield, colorless oil).

***trans*-3-benzyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane (4a$_1$):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.16 (m, 5H), 5.24 (t, *J* = 57.4 Hz, 1H), 3.60 (s, 2H), 2.95 (d, *J* = 9.6 Hz, 2H), 2.66 (d, *J* = 9.6 Hz, 2H), 1.58 (s, 2H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 128.2, 128.2, 126.8, 119.4 (t, *J* = 239.2 Hz), 59.6, 52.1, 29.7, 23.0 (t, *J* = 4.9 Hz), 6.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ -119; HRMS (ESI) Calcd for $C_{14}H_{17}F_2N$ $[M+Na]^+$ 260.1221; found 260.1223.

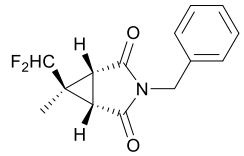
4. Spectroscopic characterization data of products

3-methyl-3-(difluoromethyl)-5-benzyl-3a,6a-dihydropyrrolo[3,4-c]pyrazole-4,6(3H,5H)-dione (A)



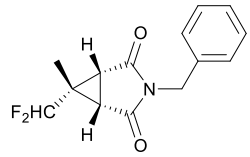
White solid; m.p. 95-96 °C; PE/ EtOAc = 3/1, R_f = 0.61. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (s, 5H), 6.16 (t, *J* = 55.3 Hz, 1H), 5.87 (d, *J* = 8.2 Hz, 1H), 4.61 (s, 2H), 3.27 (d, *J* = 8.2 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 167.9, 134.7, 128.8, 128.7, 128.4, 113.9 (t, *J* = 247.0 Hz), 98.5 (t, *J* = 20.1 Hz), 95.6, 42.9, 39.6, 15.9; ^{19}F NMR (376 MHz, $CDCl_3$): δ -127.9 (d, *J* = 285.8 Hz), -131.3 (d, *J* = 285.8 Hz); HRMS (ESI) Calcd for $C_{14}H_{13}F_2N_3O_2$ $[M+Na]^+$ 316.0868; found 316.0869.

***trans*-3-benzyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione (3a$_1$)**



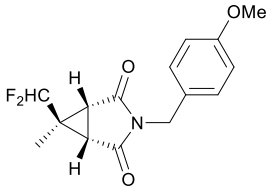
Yield: 63%; white solid; m.p. 120-122 °C; Hexane/ Et_2O = 1/1, R_f = 0.52. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 5.8 Hz, 2H), 7.33-7.25 (m, 3H), 5.59 (t, *J* = 56.4 Hz, 1H), 4.57 (s, 2H), 2.67 (s, 2H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 135.2, 129.2, 128.6, 128.1, 114.1 (t, *J* = 245.0 Hz), 42.1, 29.6, 27.0, 8.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -123.5; HRMS (ESI) Calcd for $C_{14}H_{13}F_2NO_2$ $[M+H]^+$ 265.0914; found 265.0916.

***cis*-3-benzyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione (3a$_2$)**



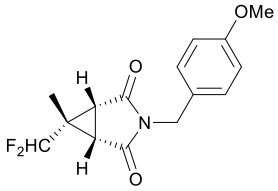
Yield: 16%; white solid; m.p. 131-132 °C; Hexane/ Et_2O = 1/1, R_f = 0.38. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 6.5 Hz, 2H), 7.34-7.29 (m, 3H), 5.06 (t, *J* = 54.5 Hz, 1H), 4.57 (s, 2H), 2.55 (s, 2H), 1.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.3, 135.0, 128.9, 128.7, 128.3, 113.0 (t, *J* = 241.5 Hz), 42.1, 31.6, 29.6, 16.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -117.6; HRMS (ESI) Calcd for $C_{14}H_{13}F_2NO_2$ $[M+H]^+$ 265.0914; found 265.0916.

***trans*-3-(*p*-methoxybenzyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione ($3b_1$)**



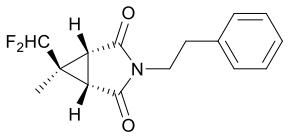
Yield: 66%; white solid; m.p. 135-137 °C; Hexane/ Et_2O = 1/1, R_f = 0.50. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 5.58 (t, *J* = 56.4 Hz, 1H), 4.51 (s, 2H), 3.78 (s, 3H), 2.65 (s, 2H), 1.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.6, 159.3, 134.1, 130.6, 127.6, 114.1 (t, *J* = 244.2 Hz), 113.8, 55.2, 41.5, 26.9, 8.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -123.6; HRMS (ESI) Calcd for $C_{15}H_{15}F_2NO_3$ $[M+H]^+$ 295.1020; found 295.1021.

***cis*-3-(*p*-methoxybenzyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione ($3b_2$)**



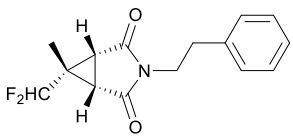
Yield: 15%; white solid; m.p. 139-140 °C; Hexane/ Et_2O = 1/1, R_f = 0.40. ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 5.05 (t, *J* = 54.4 Hz, 1H), 4.50(s, 2H), 3.78 (s, 3H), 2.53 (s, 2H), 1.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.5, 159.6, 130.5, 129.7, 114.1, 113.9 (t, *J* = 244.2 Hz), 55.2, 41.6, 31.7, 29.7, 16.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ -117.6; HRMS (ESI) Calcd for $C_{15}H_{15}F_2NO_3$ $[M+H]^+$ 295.1020; found 295.1021.

***trans*-3-phenethyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3c_1$)**



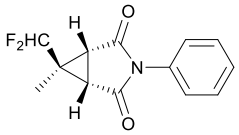
Yield: 56%; white solid; m.p. 99-100 °C; Hexane/ Et_2O = 1/1 , R_f = 0.55. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 2H), 7.25-7.19 (m, 3H), 5.62 (t, *J* = 56.4 Hz, 1H), 3.67 (t, *J* = 8.0 Hz, 2H), 2.87 (t, *J* = 8.0 Hz, 2H), 2.66 (s, 2H), 1.19 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.7, 137.4, 128.7, 128.6, 126.8, 114.2 (t, *J* = 245.4 Hz), 39.6, 36.8 (t, *J* = 23.6 Hz), 33.6, 27.2 (t, *J* = 4.3 Hz), 8.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.6; HRMS (ESI) Calcd for $C_{15}H_{15}F_2NO_2$ $[M+H]^+$ 279.1071; found 279.1073.

***cis*-3-phenethyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3c_2$)**



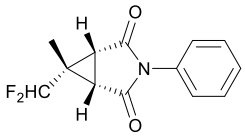
Yield: 18%; white solid; m.p. 105-106 °C; Hexane/ Et_2O = 1/1, R_f = 0.50. ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.2 Hz, 2H), 7.25-7.19 (m, 3H), 5.01 (t, *J* = 54.4 Hz, 1H), 3.71 (t, *J* = 7.6 Hz , 2H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.51 (s, 2H), 1.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.6, 137.1, 128.6, 128.5, 126.9, 113.4 (t, *J* = 242.1 Hz), 39.4, 39.0 (t, *J* = 29.8 Hz), 32.9, 31.9, 16.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.2; HRMS (ESI) Calcd for $C_{15}H_{15}F_2NO_2$ $[M+H]^+$ 279.1071; found 279.1073.

***trans*-3-phenyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3d_1$)**



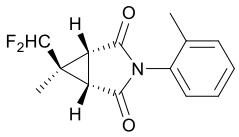
Yield: 54%; white solid; m.p. 139-140 °C; Hexane/ Et_2O = 1/1, R_f = 0.52. ^1H NMR (400 MHz, DMSO-d_6): δ 7.49(t, *J* = 7.2 Hz, 2H), 7.42(t, *J* = 7.2 Hz, 1H), 7.25(d, *J* = 7.2 Hz ,2H), 5.89(t, *J* = 55.6 Hz, 1H), 3.11(s, 2H), 1.37(s, 3H); ^{13}C NMR(150 MHz, DMSO-d_6): δ 171.2, 131.5, 129.2, 128.7, 127.0, 115.8(t, *J* = 240.3 Hz), 36.6, 27.5, 7.4; ^{19}F NMR (376 MHz, DMSO-d_6) δ -121.6; HRMS (ESI) Calcd for $C_{13}H_{11}F_2NO_2$ $[M+H]^+$ 251.0758; found 251.0759.

***cis*-3-phenyl-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3d_2$)**



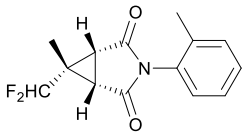
Yield: 18%; white solid; m.p. 147-148 °C; Hexane/ Et_2O = 1/1, R_f = 0.35. ^1H NMR (400 MHz, DMSO-d_6): δ 7.47(t, *J* = 7.8 Hz, 2H), 7.41(t, *J* = 7.8 Hz, 1H), 7.27(d, *J* = 7.8 Hz ,2H), 6.18(t, *J* = 54.2 Hz, 1H), 3.08(s, 2H), 1.33(s, 3H); ^{13}C NMR(150 MHz, DMSO-d_6): δ 170.9, 131.7, 129.3, 128.8, 127.4, 115.4 (t, *J* = 239.1 Hz), 39.4(t, *J* = 27.8 Hz), 32.1, 16.7; ^{19}F NMR (376 MHz, DMSO-d_6) δ -116.2; HRMS (ESI) Calcd for $C_{13}H_{11}F_2NO_2$ $[M+H]^+$ 251.0758; found 251.0759.

***trans*-3-(*o*-methylphenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3e_1$)**



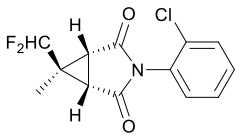
Hexane/ Et_2O = 1/1, R_f = 0.48. ^1H NMR (400 MHz, $CDCl_3$) (mixture) δ 7.35-7.25 (m, 3H), 6.96 (d, *J* = 7.7 Hz, 1H), 5.72 (t, *J* = 56.4 Hz , 1H), 2.88 (s, 2H), 2.18 (s, 3H), 1.58 (s, 3H); HRMS (ESI) Calcd for $C_{14}H_{13}F_2NO_2$ $[M+H]^+$ 265.0914; found 265.0916.

***cis*-3-(*o*-methylphenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3e_2$)**



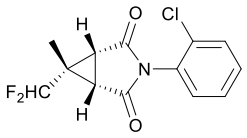
Hexane/ Et_2O = 1/1, R_f = 0.48. ^1H NMR (400 MHz, $CDCl_3$) (mixture) δ 7.35-7.25 (m, 3H), 6.96 (d, *J* = 7.7 Hz, 1H), 5.72 (t, *J* = 56.4Hz , 1H), 2.88 (s, 2H), 2.18 (s, 3H), 1.58 (s, 3H); HRMS (ESI) Calcd for $C_{14}H_{13}F_2NO_2$ $[M+H]^+$ 265.0914; found 265.0916.

***trans*-3-(*o*-chlorophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3f_1$)**



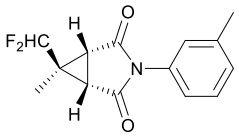
Hexane/ Et_2O = 1/1, R_f = 0.46. ^1H NMR (400 MHz, $CDCl_3$)(mixture) δ 7.56 (d, *J* = 7.9 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 5.73 (t, *J* = 56.4 Hz, 1H), 2.92 (s, 2H), 1.58 (s, 3H); ; HRMS (ESI) Calcd for $C_{13}H_{10}ClF_2NO_2$ $[M+H]^+$ 285.0368; found 285.0369.

***cis*-3-(*o*-chlorophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3f_2$)**



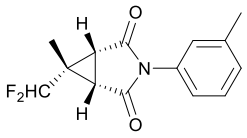
Hexane/ Et_2O = 1/1, R_f = 0.46. ^1H NMR (400 MHz, $CDCl_3$)(mixture) 7.54-7.50 (m, 1H), 7.39 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.25-7.22 (m, 1H), 5.74 (t, *J* = 56.4 Hz, 1H), 2.87 (s, 2H), 1.74 (s, 3H) ; HRMS (ESI) Calcd for $C_{13}H_{10}ClF_2NO_2$ $[M+H]^+$ 285.0368; found 285.0369.

***trans*-3-(*m*-methylphenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3g_1$)**



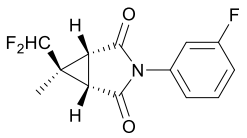
Yield: 50%; white solid; m.p. 120-121 °C; Hexane/ Et_2O = 1/1, R_f = 0.55. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (t, *J* = 8.1 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 5.0 Hz, 2H), 5.71 (t, *J* = 56.4 Hz, 1H), 2.85 (s, 2H), 2.38 (s, 3H), 1.51 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.1, 139.4, 130.8, 129.6, 129.0, 126.7, 123.2, 114.2 (t, *J* = 245.7 Hz), 36.7 (t, *J* = 23.8 Hz), 27.2, 21.3, 8.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.5; HRMS (ESI) Calcd for $C_{14}H_{13}F_2NO_2$ $[M+H]^+$ 265.0914; found 265.0916.

***cis*-3-(*m*-methylphenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3g_2$)**



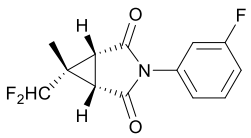
Yield: 1 %; white solid; m.p. 115-116 °C; Hexane/ Et_2O = 1/1, R_f = 0.35. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (t, *J* = 8.1 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.01 (s, 2H), 5.81 (t, *J* = 54.8 Hz, 1H), 2.71 (s, 2H), 2.38 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.8, 139.3, 130.6, 129.6, 129.0, 126.5, 123.0, 113.9 (t, *J* = 243.3 Hz), 39.2 (t, *J* = 29.1 Hz), 32.1, 21.3, 16.9; ^{19}F NMR (376 MHz, CDCl3) δ -116.6; HRMS (ESI) Calcd for $C_{14}H_{13}F_2NO_2$ $[M+H]^+$ 265.0914; found 265.0916.

***trans*-3-(*m*-fluorophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3h_1$)**



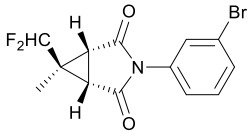
Yield: 58%; white solid; m.p. 107-108 °C; Hexane/ Et_2O = 1/1, R_f=0.55. ^1H NMR (600 MHz, $CDCl_3$) δ 7.44 (q, *J* = 8.1 Hz, 1H), 7.13-7.11 (m, 1H), 7.09 (d, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 9.4 Hz, 1H), 5.74 (t, *J* = 56.3 Hz, 1H), 2.87 (s, 2H), 1.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 162.6 (d, *J* = 246.6 Hz), 132.1 (d, *J* = 9.9 Hz), 130.4 (d, *J* = 8.7 Hz), 121.5, 115.7 (d, *J* = 20.9 Hz), 113.9 (t, *J* = 246.6 Hz), 113.5 (d, *J* = 24.6 Hz), 39.3 (t, *J* = 28.4 Hz), 32.1, 17.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.6, -116.5; HRMS (ESI) Calcd for $C_{13}H_{10}F_3NO_2$ $[M+H]^+$ 269.0664; found 269.0665.

***cis*-3-(*m*-fluorophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3h_2$)**



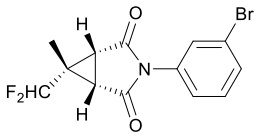
Yield: 18%; white solid; m.p. 113-114 °C; Hexane/ Et_2O = 1/1, R_f = 0.35. ^1H NMR (600 MHz, $CDCl_3$) δ 7.43 (q, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 7.04 (d, *J* = 9.3 Hz, 1H), 5.81 (t, *J* = 54.8 Hz, 1H), 2.74 (s, 2H), 1.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.5, 162.6 (d, *J* = 246.6 Hz), 132.2 (d, *J* = 10.0 Hz), 130.4 (d, *J* = 8.7 Hz), 121.6, 115.7 (d, *J* = 21.2 Hz), 113.7 (t, *J* = 243.8 Hz), 112.4, 36.9 (t, *J* = 23.5 Hz), 27.3, 9.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.6, -123.6; HRMS (ESI) Calcd for $C_{13}H_{10}F_3NO_2$ $[M+H]^+$ 269.0664; found 269.0665.

***trans*-3-(*m*-bromophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3i_1$)**



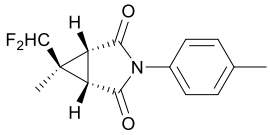
Yield: 50%; yellow solid; m.p. 115-118 °C; Hexane/ Et_2O = 1/1, R_f = 0.55. ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.26 (t, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 6.86 (t, *J* = 56.3 Hz, 1H), 2.87 (s, 2H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 133.3, 131.4, 131.3, 126.5, 126.3, 121.5, 113.1 (t, *J* = 244.5 Hz), 28.7 (t, *J* = 71.7 Hz), 26.3 (t, *J* = 4.4 Hz), 8.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.5; HRMS (ESI) Calcd for $C_{13}H_{10}BrF_2NO_2$ $[M+H]^+$ 328.9863; found 328.9865.

***cis*-3-(*m*-bromophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3i_2$)**



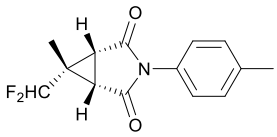
Yield: 16%; yellow solid; m.p. 109-110 °C; Hexane/ Et_2O = 1/1, R_f = 0.50. ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 5.80 (t, *J* = 54.8 Hz, 1H), 2.72 (s, 2H), 1.43 (s, 3H); ^3C NMR (100 MHz, $CDCl_3$) δ 169.5, 133.3, 131.4, 131.3, 126.5, 126.3, 121.5, 113.1 (t, *J* = 244.5 Hz), 28.7 (t, *J* = 71.7 Hz), 26.3 (t, *J* = 4.4 Hz), 8.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.5; HRMS (ESI) Calcd for $C_{13}H_{10}BrF_2NO_2$ $[M+H]^+$ 328.9863; found 328.9865.

***trans*-3-(*p*-methylphenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3j_1$)**



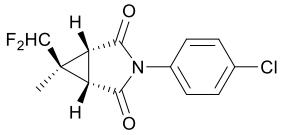
Yield: 49%; white solid; m.p. 129-130 °C; Hexane/ Et_2O = 1/1,R_f = 0.55. ^1H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 5.72 (t, *J* = 56.3 Hz, 1H), 2.85 (s, 2H), 2.38 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.0, 138.9, 129.8, 128.3, 125.9, 114.1 (t, *J* = 244.2 Hz), 29.6, 27.2, 21.17, 8.96; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.7; HRMS (ESI) Calcd for $C_{14}H_{13}F_2NO_2$ $[M+H]^+$ 265.0914; found 265.0916.

***cis*-3-(*p*-methylphenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3j_2$)**



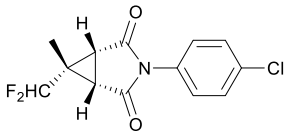
Yield: 17%; white solid; m.p. 136-138 °C; Hexane/ Et_2O = 1/1, R_f = 0.35. ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 5.80 (t, *J* = 54.8 Hz, 1H), 2.72 (s, 2H), 2.37 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.9, 138.9, 129.8, 128.1, 125.7, 113.9 (t, *J* = 241.5), 32.02, 29.6, 21.1, 16.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.6; HRMS (ESI) Calcd for $C_{14}H_{13}F_2NO_2$ $[M+H]^+$ 265.0914; found 265.0916.

***trans*-3-(*p*-chlorophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3k_1$)**



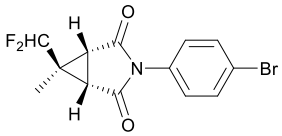
Yield: 55%; yellow solid; m.p. 124-125 °C; Hexane/ Et_2O = 1/1, R_f = 0.50. ^1H NMR (400 MHz, DMSO-d_6) δ 7.56 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 5.89 (t, *J* = 55.4 Hz, 1H), 3.12 (s, 2H), 1.36 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 171.0, 133.1,130.2, 129.3, 128.7, 115.8 (t, *J* = 241.3 Hz), 36.7 (t, *J* = 25.8 Hz), 27.6, 7.4; ^{19}F NMR (376 MHz, DMSO-d_6) δ -121.6; HRMS (ESI) Calcd for $C_{13}H_{10}ClF_2NO_2$ $[M+H]^+$ 285.0368; found 285.0369.

***cis*-3-(*p*-chlorophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3k_2$)**



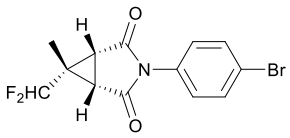
Yield: 18%; yellow solid; m.p. 132-133 °C; Hexane/ Et_2O =1/1, R_f = 0.36. ^1H NMR (400 MHz, DMSO-d_6) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 5.90 (t, *J* = 55.4 Hz, 1H), 3.17 (s, 2H), 1.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 132.4, 129.8, 127.4, 122.5, 114.0 (t, *J* = 244.0 Hz), 39.3 (t, *J* = 29.1 Hz), 32.1, 17.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.5; HRMS (ESI) Calcd for $C_{13}H_{10}ClF_2NO_2$ $[M+H]^+$ 285.0368; found 285.0369.

***trans*-3-(*p*-bromophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3l_1$)**



Yield: 54%; yellow solid; m.p. 127-128 °C; Hexane/ Et_2O = 1/1, R_f = 0.60. ^1H NMR (400 MHz, DMSO-d_6) δ 7.89 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 5.90 (t, *J* = 55.4 Hz, 1H), 3.17 (s, 2H), 1.38 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 171.1, 135.1, 127.9, 126.6, 126.5, 116.0 (t, *J* = 241.4 Hz), 37.0 (t, *J* = 26.0 Hz), 27.9, 7.7; ^{19}F NMR (376 MHz, DMSO-d_6) δ -116.8; HRMS (ESI) Calcd for $C_{13}H_{10}BrF_2NO_2$ $[M+H]^+$ 328.9863; found 328.9865.

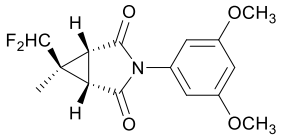
***cis*-3-(*p*-bromophenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3l_2$)**



Yield: 14%; yellow solid; m.p. 138-139 °C; Hexane/ Et_2O = 1/1, R_f = 0.40. ^1H NMR (600 MHz, DMSO-d_6) δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 6.24 (t, *J* = 54.0 Hz, 1H), 3.11 (s, 2H), 1.32 (s, 3H); ^{13}C NMR (150 MHz,

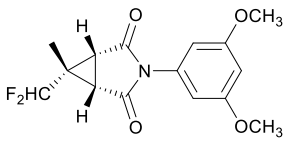
DMSO-d_6) δ 170.3, 135.1, 127.9, 126.1, 126.1, 115.2 (t, *J* = 239.4 Hz), 32.0, 29.2, 16.5; ^{19}F NMR (376 MHz, DMSO-d_6) δ -116.3; HRMS (ESI) Calcd for $C_{13}H_{10}BrF_2NO_2$ $[M+H]^+$ 328.9863; found 328.9865.

trans-3-(3',5'-dimethoxy-1'-phenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3m_1$)



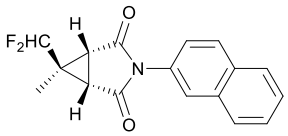
Yield: 56%; white solid; m.p. 140-141 °C; Hexane/ Et_2O = 1/1, R_f = 0.5. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.48 (s, 1H), 6.38 (s, 2H), 5.71 (t, *J* = 56.3 Hz, 1H), 3.79 (s, 6H), 2.84 (s, 2H), 1.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.7, 161.0, 132.4, 114.1 (t, *J* = 242.7 Hz), 104.7 (d, *J* = 6.6 Hz), 100.7, 55.5 (d, *J* = 7.1 Hz), 36.8 (t, *J* = 23.6 Hz), 27.2, 9.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.6; HRMS (ESI) Calcd for $C_{15}H_{15}F_2NO_4$ $[M+H]^+$ 311.0969; found 311.0971.

cis-3-(3',5'-dimethoxy-1'-phenyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3m_2$)



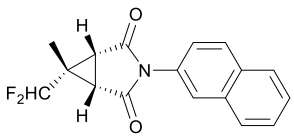
Yield: 19%; white solid; m.p. 147-148 °C; Hexane/ Et_2O = 1/1, R_f = 0.4. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.48 (s, 1H), 6.37 (s, 2H), 5.80 (t, *J* = 54.8 Hz, 1H), 3.79 (s, 6H), 2.71 (s, 2H), 1.42 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.6, 161.0, 132.2, 113.9 (t, *J* = 243.5Hz), 104.5, 100.8, 55.5, 39.1 (t, *J* = 28.9 Hz), 32.0, 17.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.5; HRMS (ESI) Calcd for $C_{15}H_{15}F_2NO_4$ $[M+H]^+$ 311.0969; found 311.0971.

trans-3-(2'-naphthyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3n_1$)



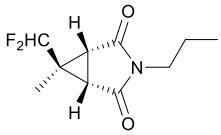
Yield: 60%; white solid; m.p. 152-153 °C; Hexane/ Et_2O = 1/1, R_f = 0.45. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.04-7.98 (m, 3H), 7.86 (d, *J* = 1.9 Hz, 1H), 7.62-7.57 (m, 2H), 7.38 (dd, *J* = 8.8, 1.9 Hz, 1H), 5.92 (t, *J* = 55.4 Hz, 1H), 3.17 (s, 2H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.4, 137.9, 137.5, 134.0, 134.0, 133.1, 132.9, 132.2, 132.0, 130.9, 129.7, 120.9 (t, *J* = 241.0 Hz), 41.8 (t, *J* = 25.9 Hz), 32.7 (t, *J* = 3.9 Hz), 12.6; ^{19}F NMR (376 MHz, DMSO-d_6) δ -121.5; HRMS (ESI) Calcd for $C_{17}H_{13}F_2NO_2$ $[M+H]^+$ 301.0914; found 301.0916.

cis-3-(2'-naphthyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3n_2$)



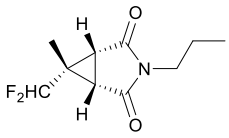
Yield: 18%; white solid; m.p. 163-164 °C; Hexane/ Et_2O = 1/1, R_f = 0.35. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.01 (d, *J* = 8.8 Hz, 1H), 8.00-7.92 (m, 2H), 7.91-7.87 (m, 1H), 7.64-7.54 (m, 2H), 7.40 (dd, *J* = 8.8, 1.9 Hz, 1H), 6.27 (t, *J* = 54.0 Hz, 1H), 3.14 (s, 2H), 1.36 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 171.0, 133.0, 132.7, 129.3, 128.9, 128.4, 128.1, 127.4, 127.1, 126.3, 125.2, 115.4 (t, *J* = 240.7 Hz), 39.3, 32.2, 16.6; ^{19}F NMR (376 MHz, DMSO-d_6) δ -116.2; HRMS (ESI) Calcd for $C_{17}H_{13}F_2NO_2$ $[M+H]^+$ 301.0914; found 301.0916.

***trans*-3-(n-propyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3o_1$)**



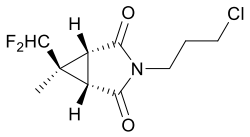
Yield: 48%; colorless oil; Hexane/ Et_2O = 2/1, R_f = 0.5. ^1H NMR (400 MHz, $CDCl_3$) δ 5.64 (t, *J* = 56.4 Hz, 1H), 3.37 (t , *J* = 7.4 Hz, 2H), 2.69 (s, 2H), 1.57 (m, 2H), 1.30 (s, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.9, 114.2 (t, *J* = 245.3 Hz), 40.2, 36.9 (t, *J* = 23.4 Hz), 27.1 (t, *J* = 4.3 Hz), 21.2, 11.3, 8.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.5; HRMS (ESI) Calcd for $C_{10}H_{13}F_2NO_2$ $[M+H]^+$ 217.0914; found 217.0915.

***cis*-3-(n-propyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3o_2$)**



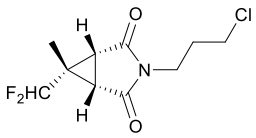
Yield: 23%; colorless oil; Hexane/ Et_2O = 2/1, R_f = 0.35. ^1H NMR (400 MHz, $CDCl_3$) δ 5.50 (t, *J* = 54.7 Hz, 1H), 3.36 (t, *J* = 7.5 Hz, 2H), 2.57 (s, 2H), 1.55 (m, 2H), 1.36 (s, 3H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.8, 113.6 (t, *J* = 242.5 Hz), 40.2, 39.0 (t, *J* = 29.4 Hz), 31.9, 21.1, 16.4, 11.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.4; HRMS (ESI) Calcd for $C_{10}H_{13}F_2NO_2$ $[M+H]^+$ 217.0914; found 217.0915.

***trans*-3-(3-chloropropyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3p_1$)**



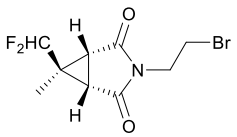
Yield: 45%; colorless oil; Hexane/ Et_2O = 2/1, R_f = 0.5. ^1H NMR (400 MHz, $CDCl_3$) δ 5.65 (t, *J* = 56.3 Hz, 1H), 3.57 (t, *J* = 7.2 Hz, 2H), 3.52 (t, *J* = 7.2 Hz, 2H), 2.71 (s, 2H), 2.03 (m, 2H), 1.28 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.7, 114.1 (t, *J* = 242.7 Hz), 41.8, 36.2, 30.7, 29.6, 27.2 (t, *J* = 4.5 Hz), 8.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.6; HRMS (ESI) Calcd for $C_{10}H_{12}ClF_2NO_2$ $[M+H]^+$ 251.0525; found 251.0526.

***cis*-3-(3-chloropropyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3p_2$)**



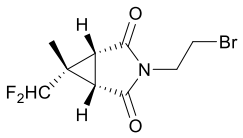
Yield: 23%; colorless oil; Hexane/ Et_2O = 2/1, R_f = 0.35. ^1H NMR (400 MHz, $CDCl_3$) δ 5.53 (t, *J* = 54.8 Hz, 1H), 3.55 (m, 4H), 2.59 (s, 2H), 2.03 (m, 2H), 1.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.8, 113.6 (t, *J* = 242.5 Hz), 40.2, 39.0, 31.8, 21.1, 16.4, 11.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.4; HRMS (ESI) Calcd for $C_{10}H_{12}ClF_2NO_2$ $[M+H]^+$ 251.0525; found 251.0526.

***trans*-3-(2-bromoethyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3q_1$)**



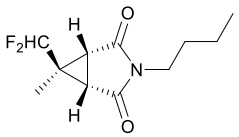
Yield: 45%; yellow oil; Hexane/ Et_2O = 2/1, R_f = 0.6. ^1H NMR (400 MHz, $CDCl_3$) δ 5.81 (t, *J* = 54.4 Hz, 1H), 3.87 (t, *J* = 6.3 Hz, 2H), 3.52 (t, *J* = 6.3 Hz, 2H), 2.61 (s, 2H), 1.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.4, 113.7 (t, *J* = 242.7 Hz), 40.2, 32.1, 29.7, 27.2, 16.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.5; HRMS (ESI) Calcd for $C_9H_{10}BrF_2NO_2$ $[M+H]^+$ 280.9863; found 280.9865.

cis-3-(2-bromoethyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3q_2$)



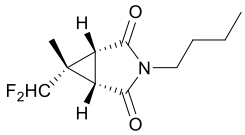
Yield: 23%; yellow oil; Hexane/ Et_2O = 2/1, R_f = 0.5. ^1H NMR (400 MHz, $CDCl_3$) δ 5.68 (t, *J* = 56.4 Hz, 1H), 3.87 (t, *J* = 6.5 Hz, 2H), 3.50 (t, *J* = 6.5 Hz, 2H), 2.74 (s, 2H), 1.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.8, 113.7 (t, *J* = 241.2 Hz), 38.5, 31.9, 29.8, 20.1, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.5; HRMS (ESI) Calcd for $C_9H_{10}BrF_2NO_2$ $[M+H]^+$ 280.9863; found 280.9865.

trans-3-(n-butyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3r_1$)



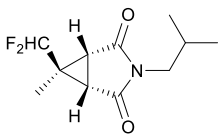
Yield: 42%; colorless oil; Hexane/ Et_2O = 2/1, R_f = 0.6. ^1H NMR (400 MHz, $CDCl_3$) δ 5.64 (t, *J* = 56.4 Hz, 1H), 3.40 (t, *J* = 7.6 Hz, 2H), 2.68 (s, 2H), 1.55-1.47 (m, 2H), 1.35-1.25 (m, 2H), 1.29(s, 3H), 0.92 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.9, 114.3 (t, *J* = 243.2 Hz), 38.4, 36.9 (t, *J* = 23.5 Hz), 29.9, 27.1 (t, *J* = 4.3 Hz), 20.1, 13.5, 8.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.5; HRMS (ESI) Calcd for $C_{11}H_{15}F_2NO_2$ $[M+H]^+$ 231.1071; found 231.1072.

cis-3-(n-butyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3r_2$)



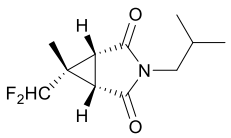
Yield: 22%; colorless oil; Hexane/ Et_2O = 2/1, R_f = 0.45. ^1H NMR (400 MHz, $CDCl_3$) δ 5.48 (t, *J* = 54.4 Hz, 1H), 3.44-3.35 (m, 2H), 2.56 (s, 2H), 1.50 (m, 2H), 1.36 (s, 3H), 1.34-1.27 (m, 2H), 0.93 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.8, 113.7 (t, *J* = 242.6 Hz), 39.1 (t, *J* = 29.4 Hz), 38.5, 31.9 (t, *J* = 2.7 Hz), 29.8, 20.1, 16.4 (t, *J* = 2.8 Hz), 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.3; HRMS (ESI) Calcd for $C_{11}H_{15}F_2NO_2$ $[M+H]^+$ 231.1071; found 231.1072.

trans-3-(1-isobutyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3s_1$)



Yield: 45%; colorless oil; Hexane/ Et_2O = 2/1, R_f = 0.5. ^1H NMR (400 MHz, $CDCl_3$) δ 5.49 (t, *J* = 54.7 Hz, 1H), 3.22 (d, *J* = 7.2 Hz, 2H), 2.58 (s, 2H), 1.95 (m, 1H), 1.36 (s, 3H), 0.89 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 114.3 (t, *J* = 243.2 Hz), 38.4, 29.8, 27.1 (t, *J* = 4.3 Hz), 20.1, 13.5, 8.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.5; HRMS (ESI) Calcd for $C_{11}H_{15}F_2NO_2$ $[M+H]^+$ 231.1071; found 231.1072.

***cis*-3-(1-isobutyl)-6-methyl-6-(difluoromethyl)-3-azabicyclo[3.1.0]hexane-2,4-dione($3s_2$)**



Yield: 21%; colorless oil; Hexane/ Et_2O = 2/1, R_f = 0.38. ^1H NMR (400 MHz, $CDCl_3$) δ 5.42 (t, *J* = 54.7 Hz, 1H), 3.15 (d, *J* = 7.2 Hz, 2H), 2.51 (s, 2H), 1.87 (m, 1H), 1.29 (s, 3H), 0.82 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 114.3 (t, *J* = 242.6 Hz), 40.2, 36.9 (t, *J* = 32.1 Hz), 27.1 (t, *J* = 28.0 Hz), 21.3, 11.4, 8.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.3; HRMS (ESI) Calcd for $C_{11}H_{15}F_2NO_2$ $[M+H]^+$ 231.1071; found 231.1072.

5. References

1 J. Li, X.L. Yu, J. Cossy, S.Y. Lv, H.L. Zhang, F. Su, P. K. Mykhailiuk, Y. Wu, *Eur. J. Org. Chem.,* 2017, **2017**, 266.

2 O. S. Artamonov, E. Y. Slobodyanyuk, O. V. Shishkin, I. V. Komarov, P. K. Mykhailiuk, *Synthesis* 2012, **45**, 225.

3 G. Brown, M. Higginbottom, A. Stewart, L. Patient, A. Carley, I. Simpson, E. D. Savory, K. Oliver, A. G. Cole, WO Patent 2012049277, *Chem. Abs.* 2012, 156, 560431m.

6. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of products

Figure 1. The ^{1}H NMR (400 MHz, $CDCl_3$) of **A'**

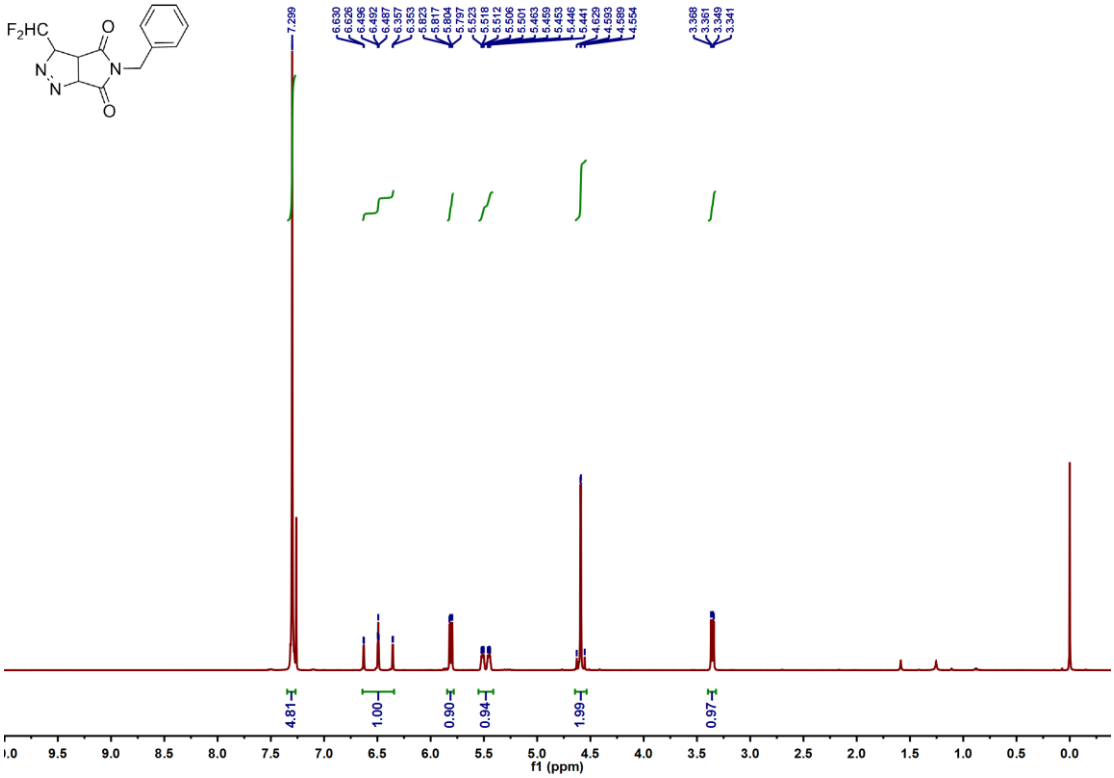


Figure 2. The ^{13}C NMR (100 MHz, $CDCl_3$) of **A'**

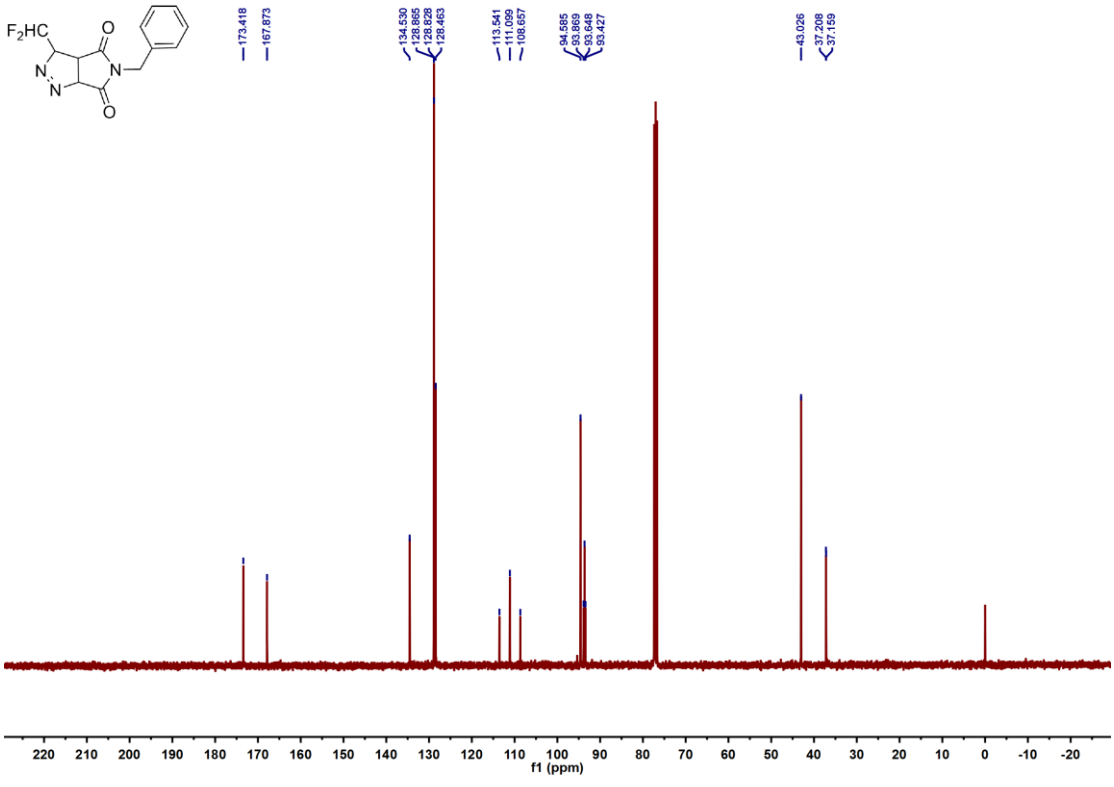


Figure 3. The ^{19}F NMR (376 MHz, $CDCl_3$) of **A'**

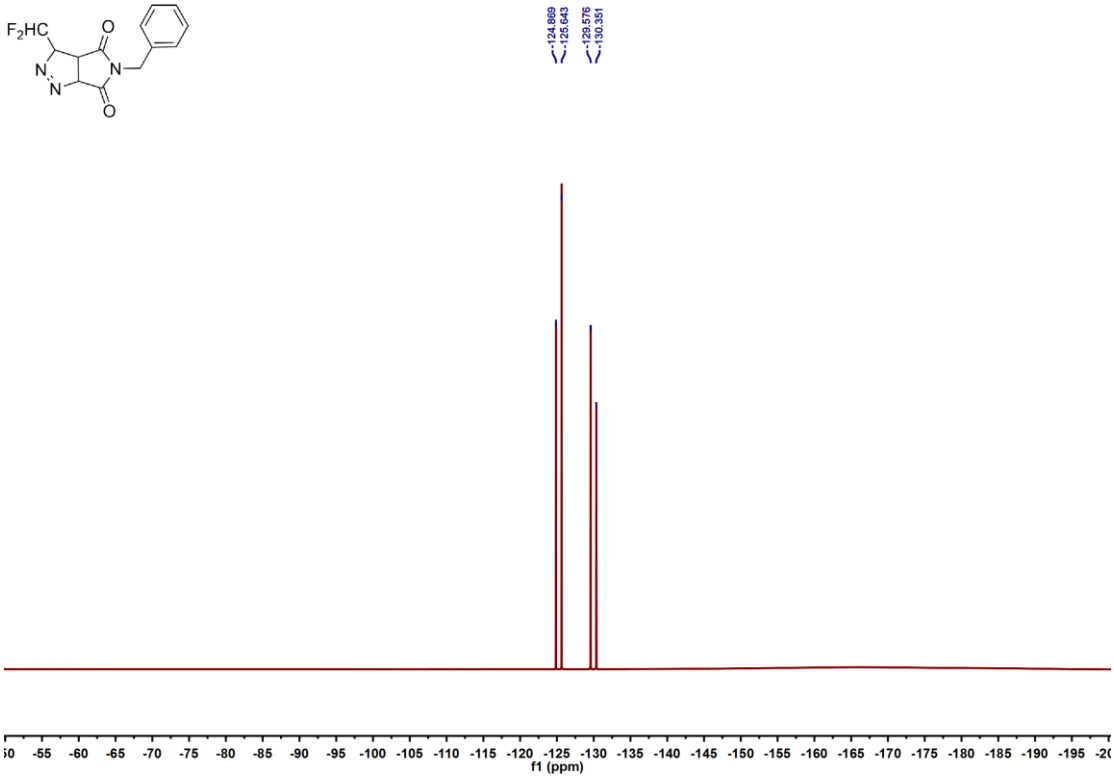


Figure 4. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3'a$_1$**

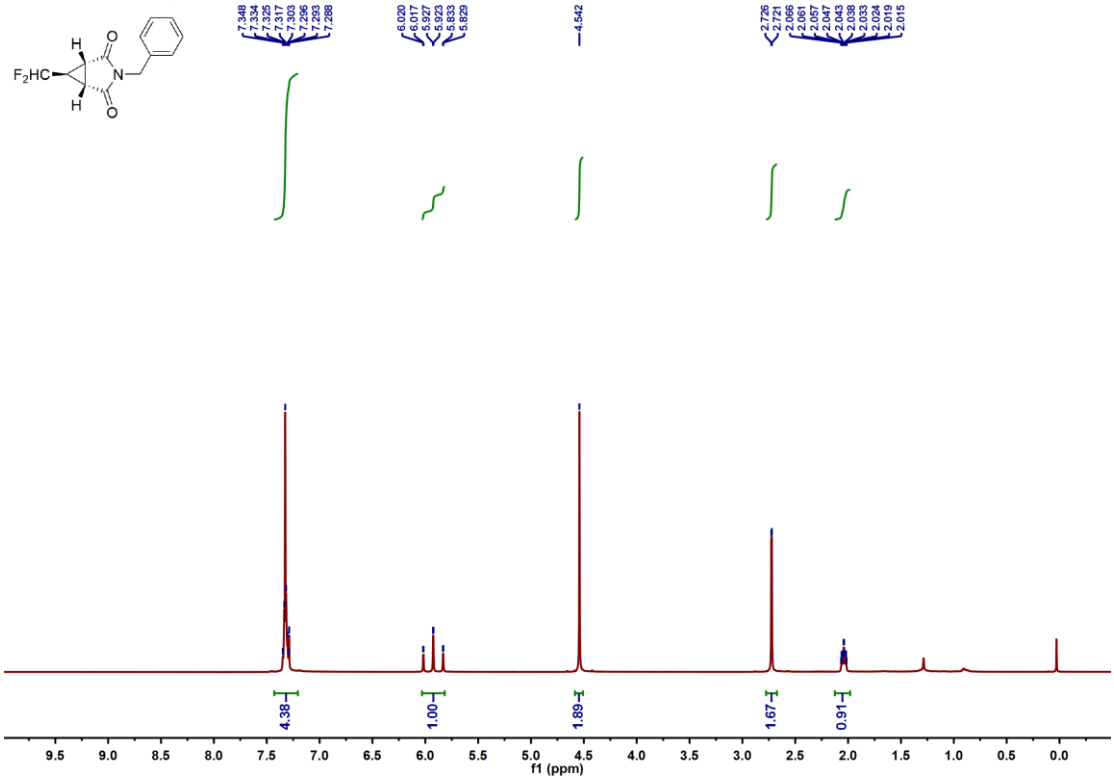


Figure 5. The ^{13}C NMR (100 MHz, $CDCl_3$) of **3'a$_1$**

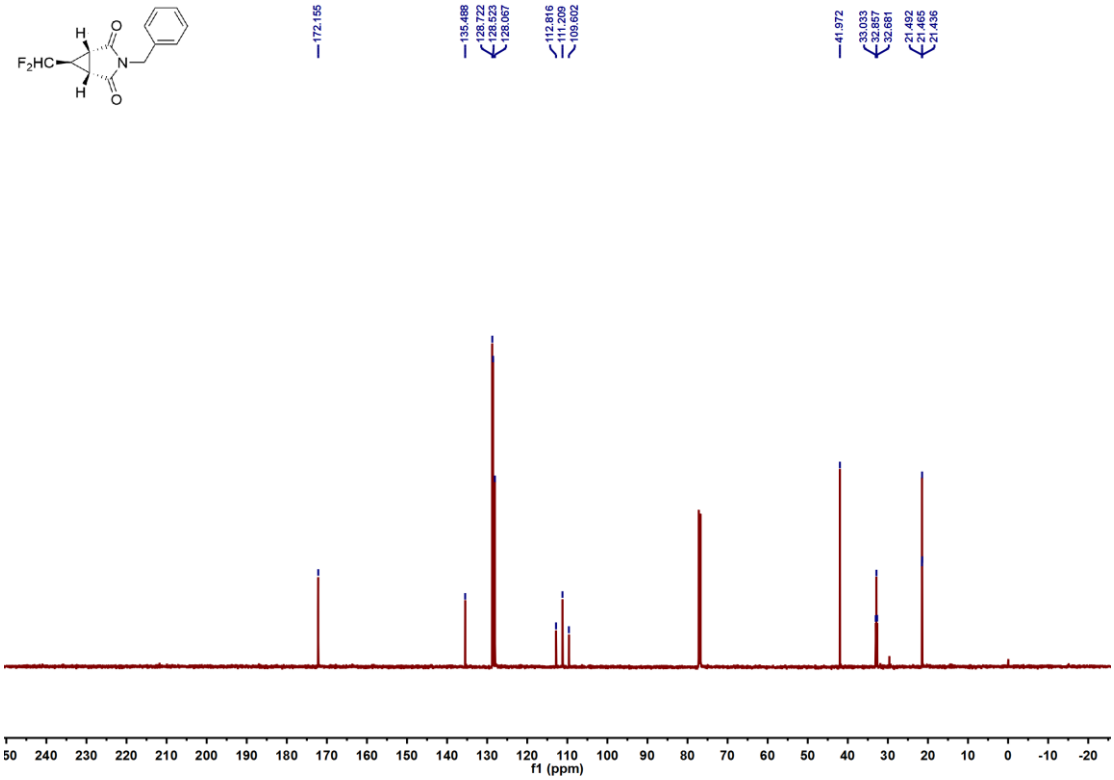


Figure 6. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3'a$_1$**

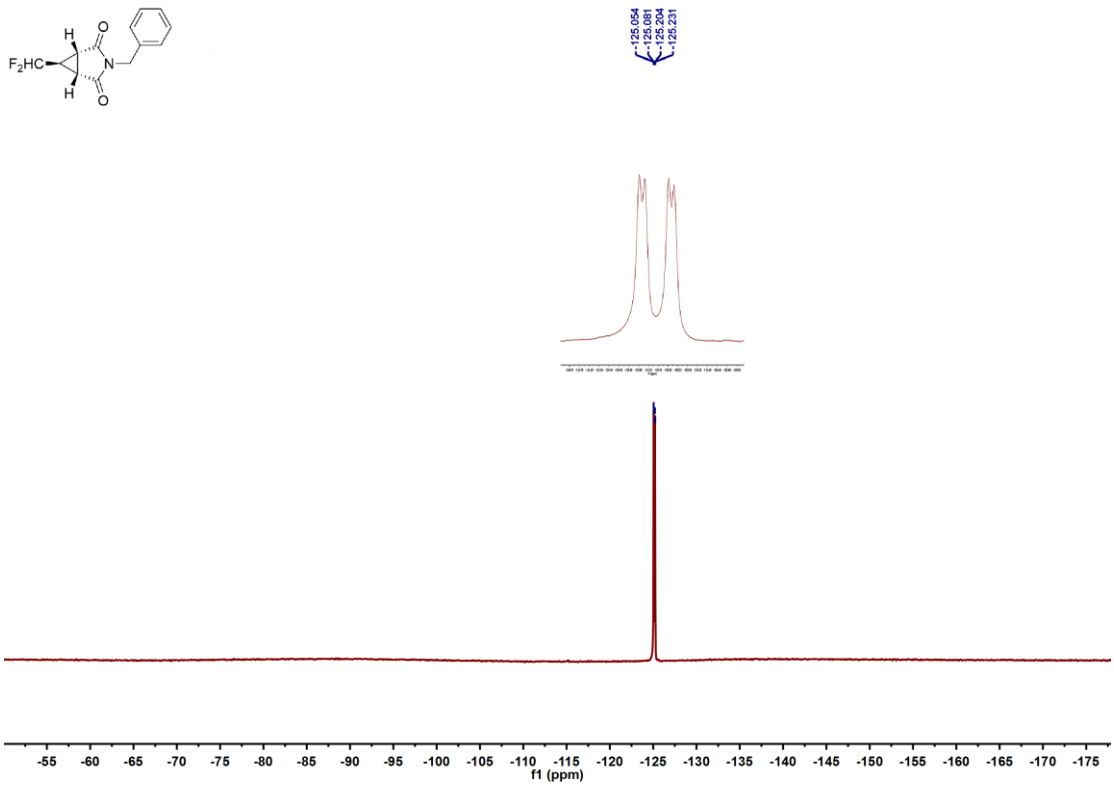


Figure 7. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3'a$_2$**

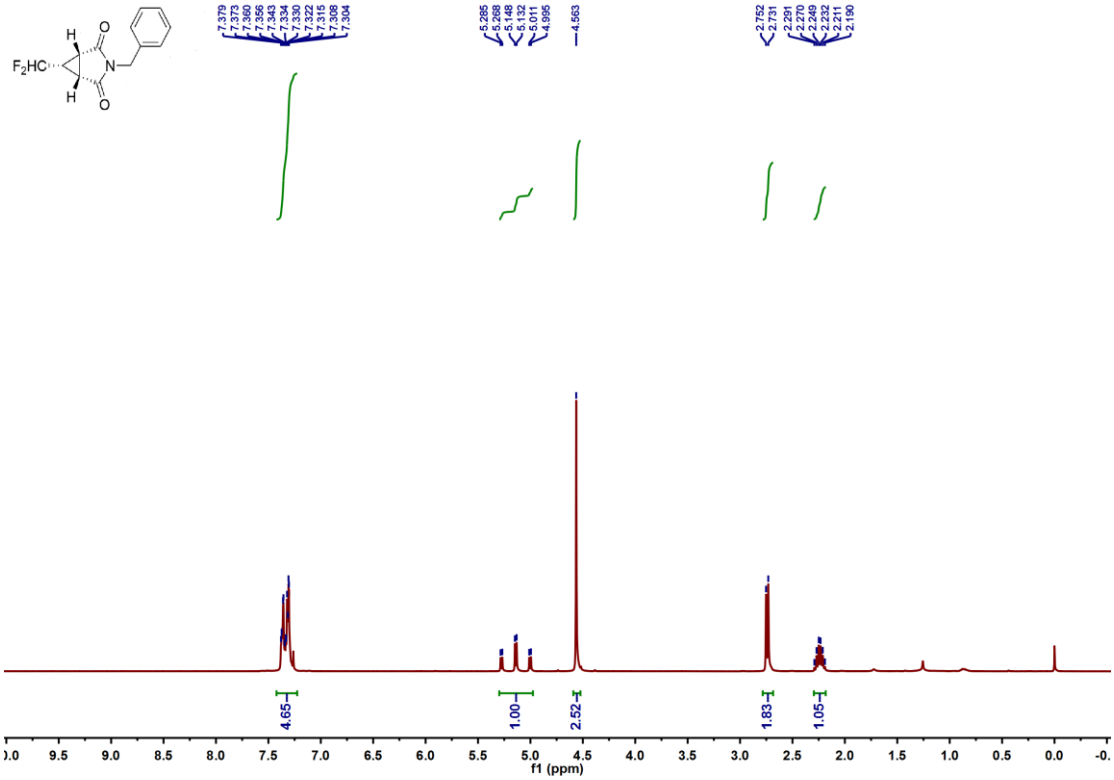


Figure 8. The ^{13}C NMR (100 MHz, $CDCl_3$) of **3'a$_2$**

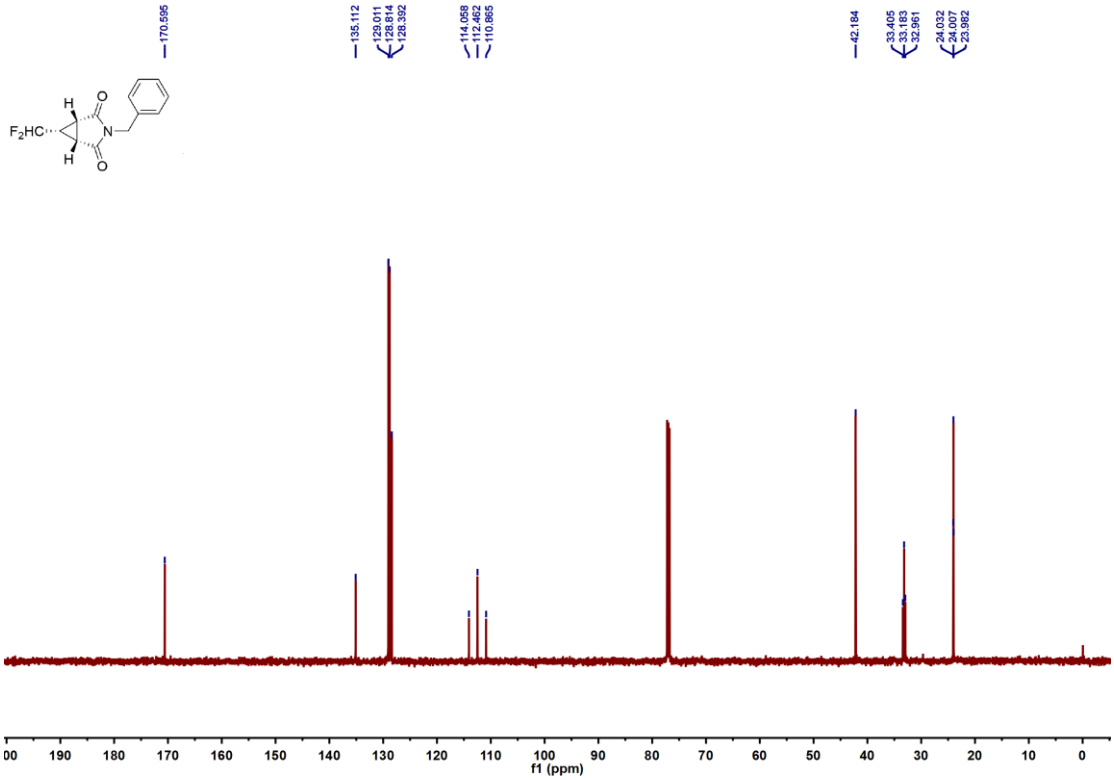


Figure 9. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3'a$_2$**

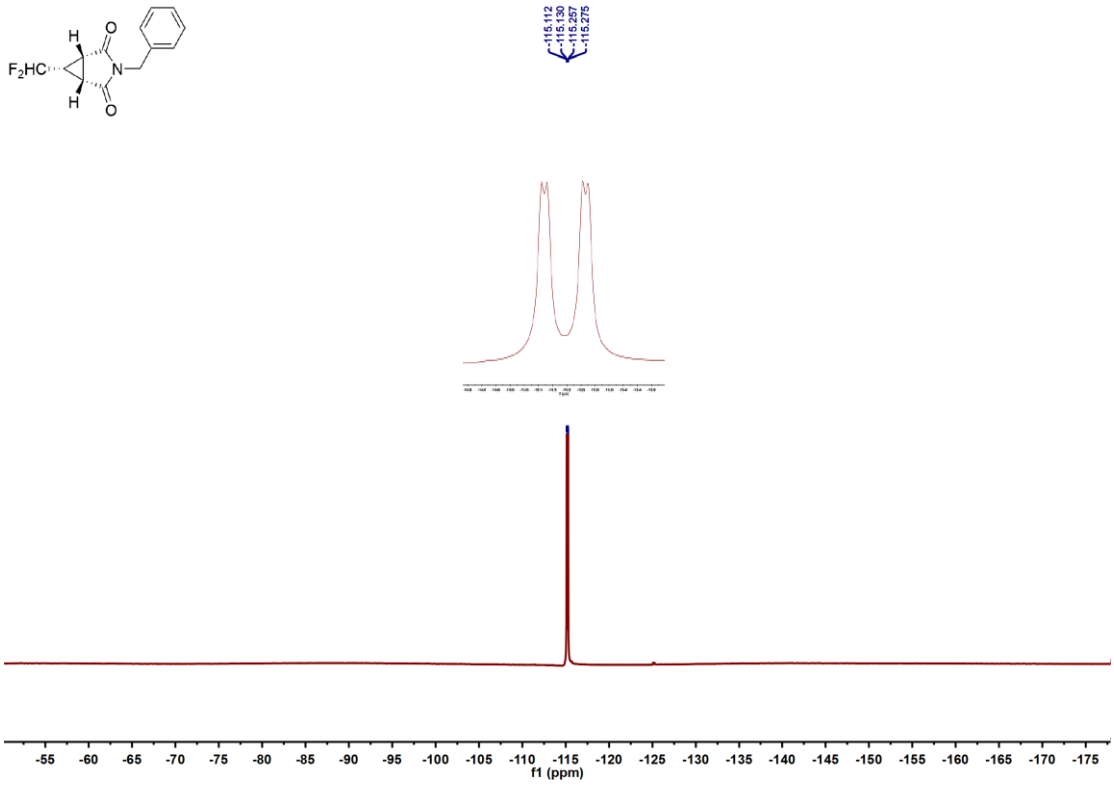


Figure 10. The ^{1}H NMR (400 MHz, $CDCl_3$) of **A**

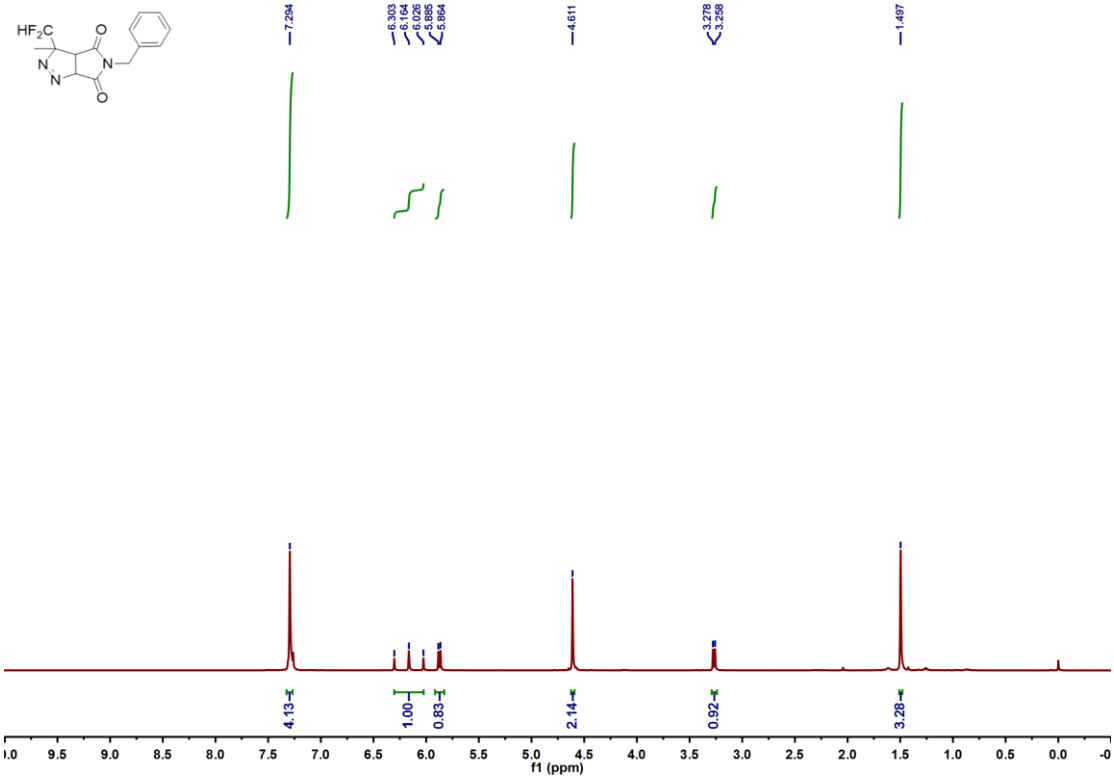


Figure 11. The ^{13}C NMR (100 MHz, $CDCl_3$) of **A**

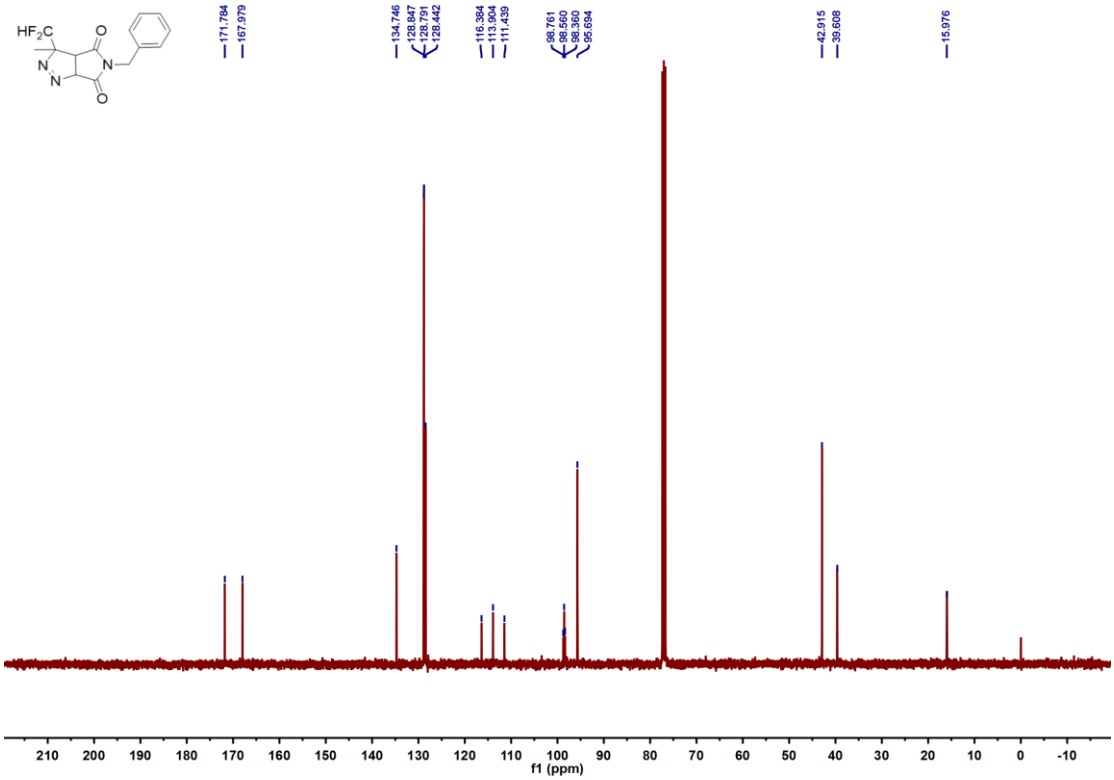


Figure 12. The ^{19}F NMR (376 MHz, $CDCl_3$) of **A**

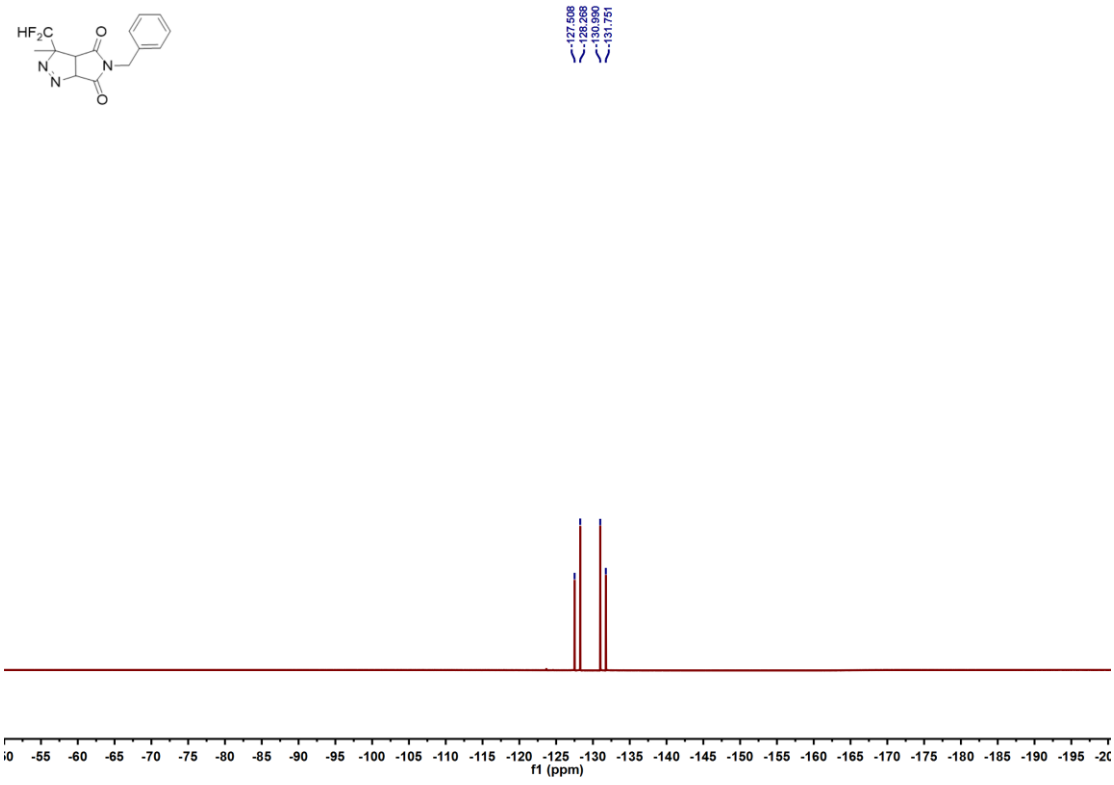


Figure 13. The ^{1}H NMR (400 MHz, $CDCl_3$) of **$3a_1$**

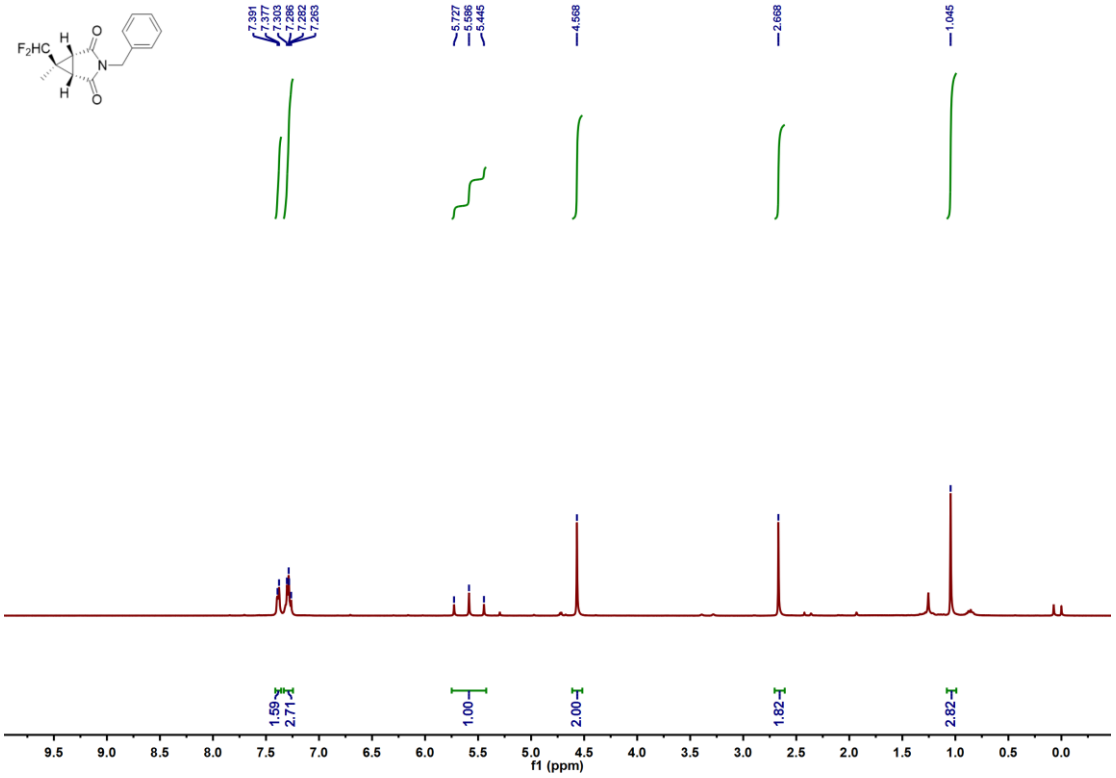


Figure 14. The ^{13}C NMR (100 MHz, $CDCl_3$) of **$3a_1$**

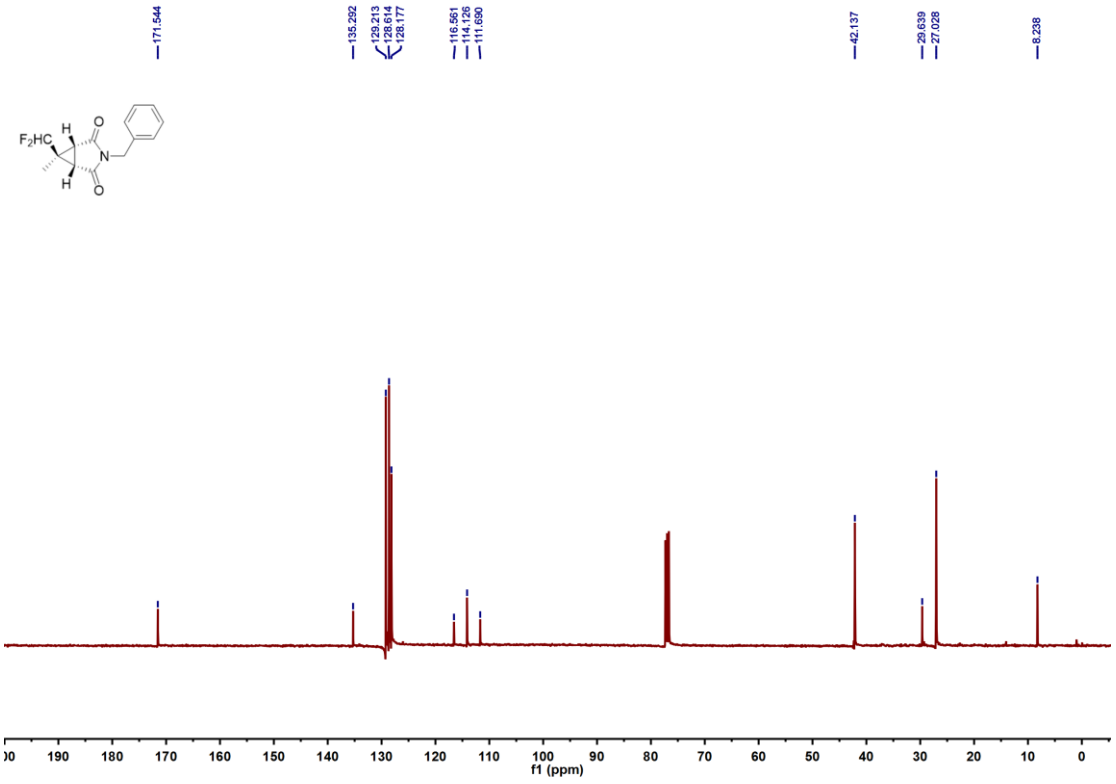


Figure 15. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3a₁**

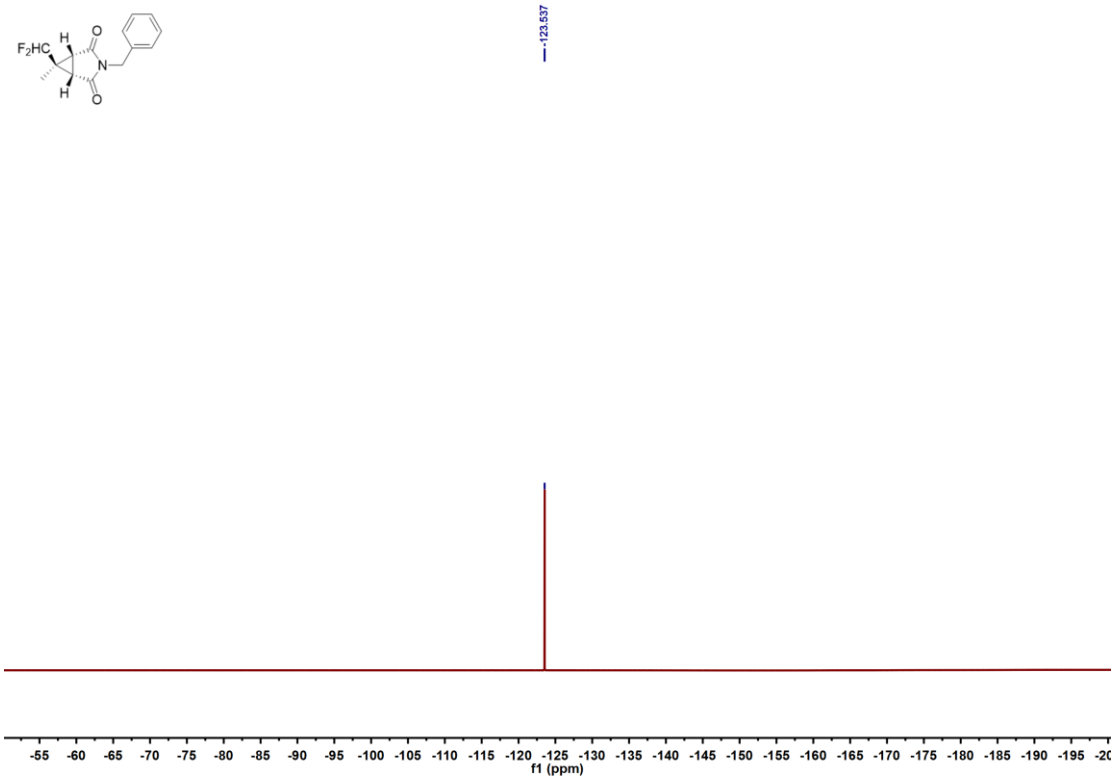


Figure 16. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3a₂**

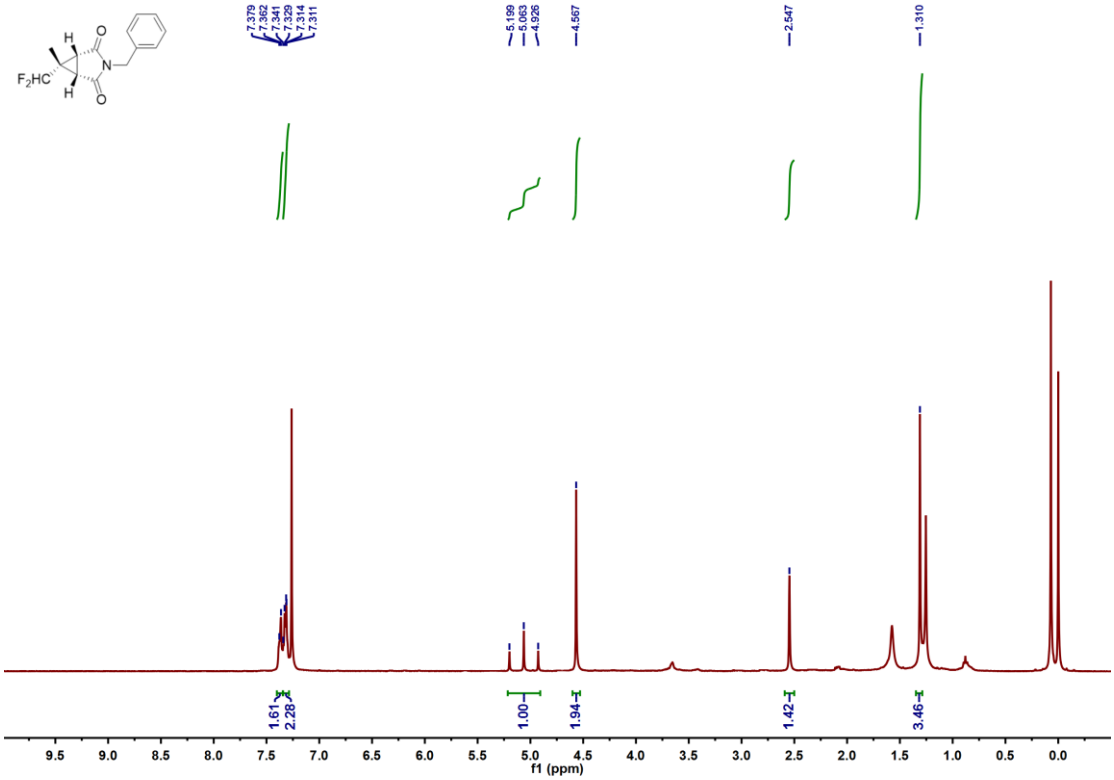


Figure 17. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3a₂**

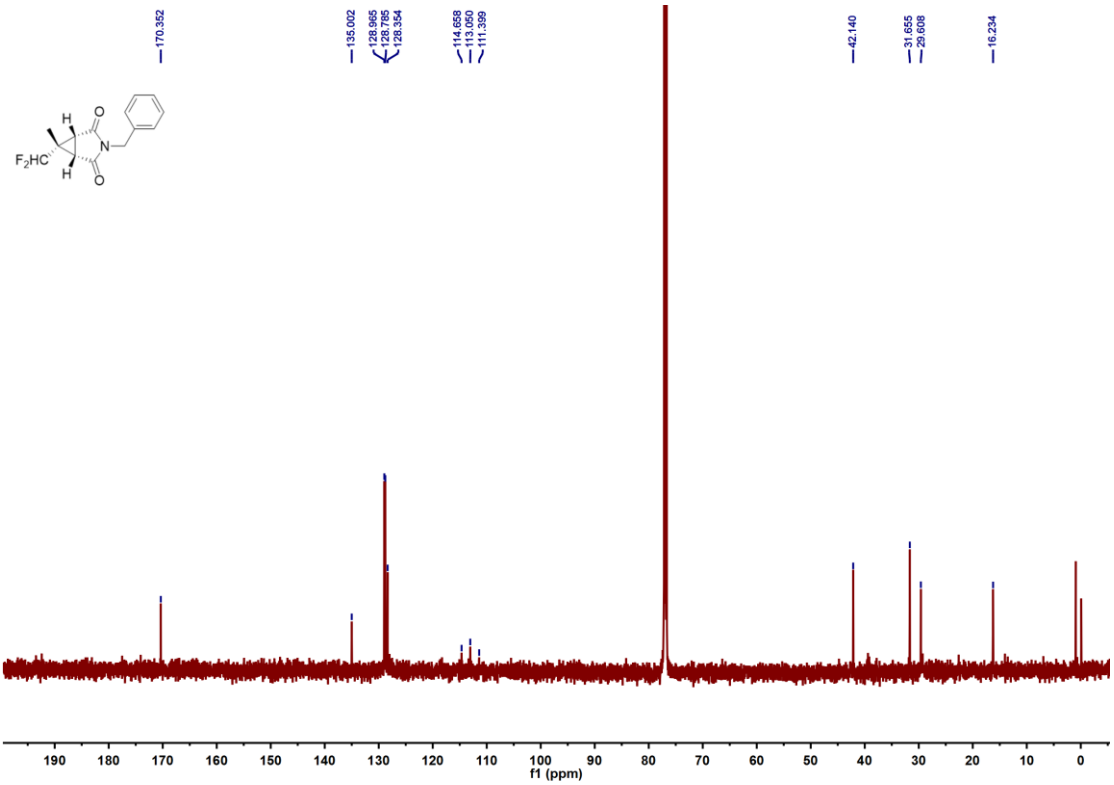


Figure 18. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3a₂**

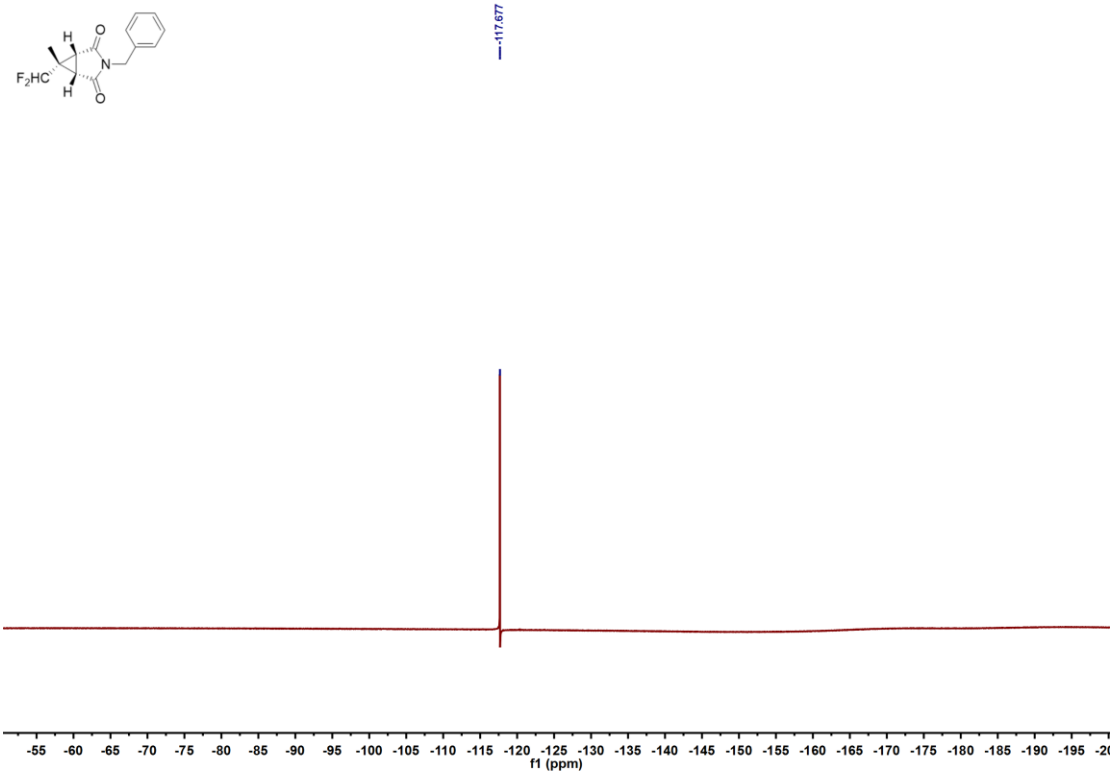


Figure 19. The ^{1}H NMR (400 MHz, $CDCl_3$) of **$3b_1$**

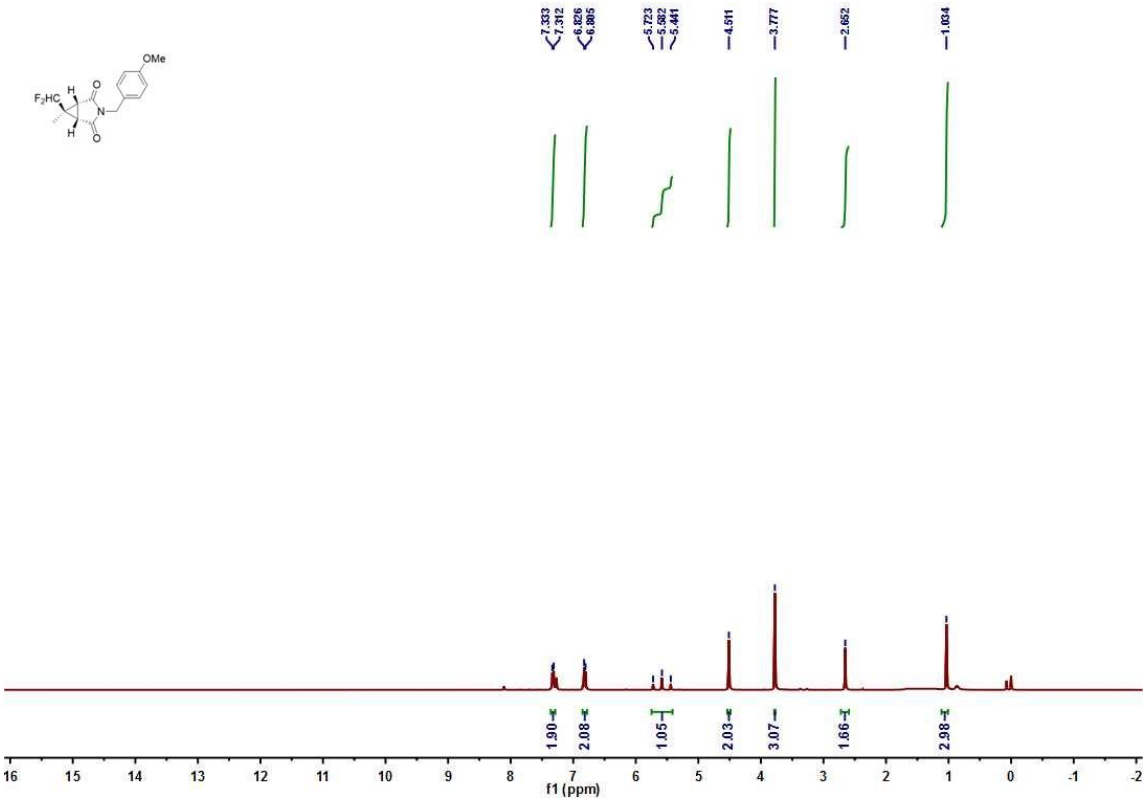


Figure 20. The ^{13}C NMR (150 MHz, $CDCl_3$) of **$3b_1$**

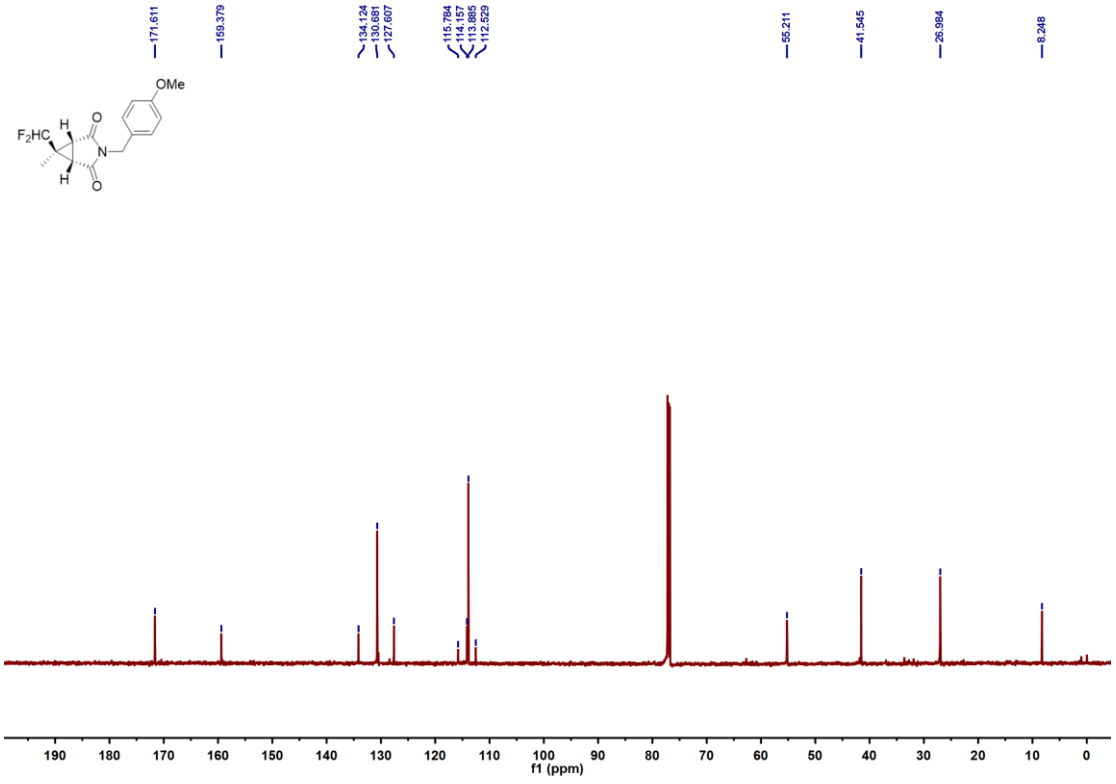


Figure 21. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3b₁**

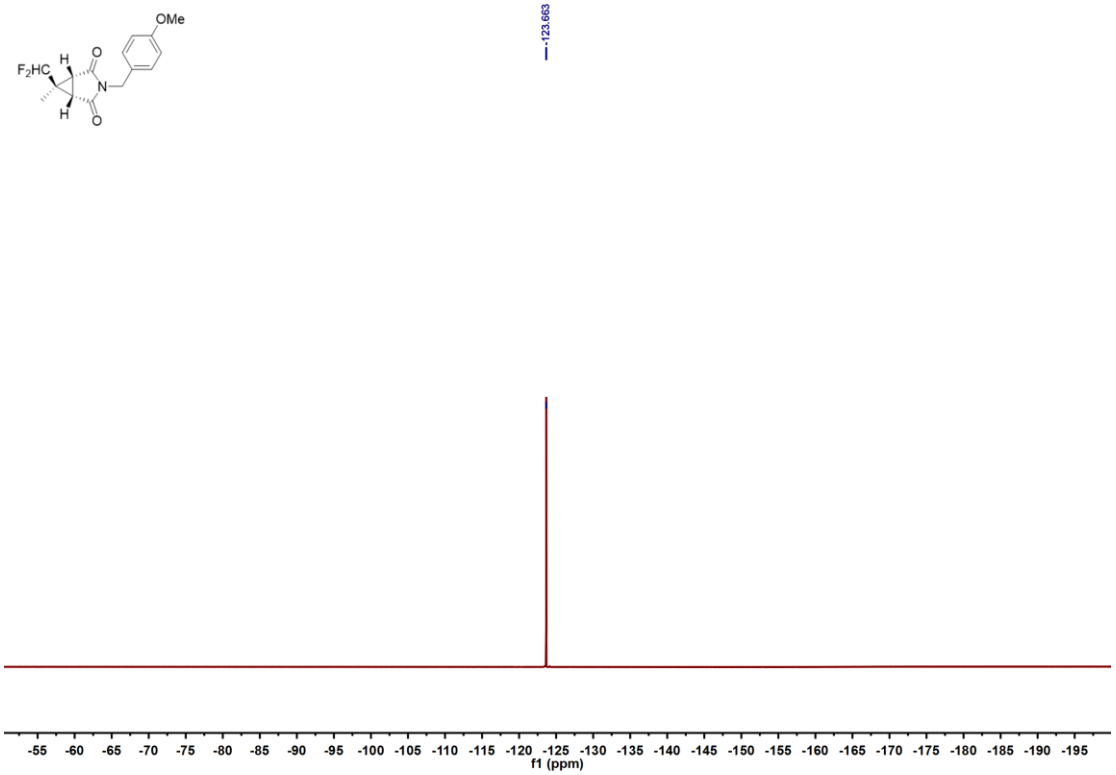


Figure 22. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3b₂**

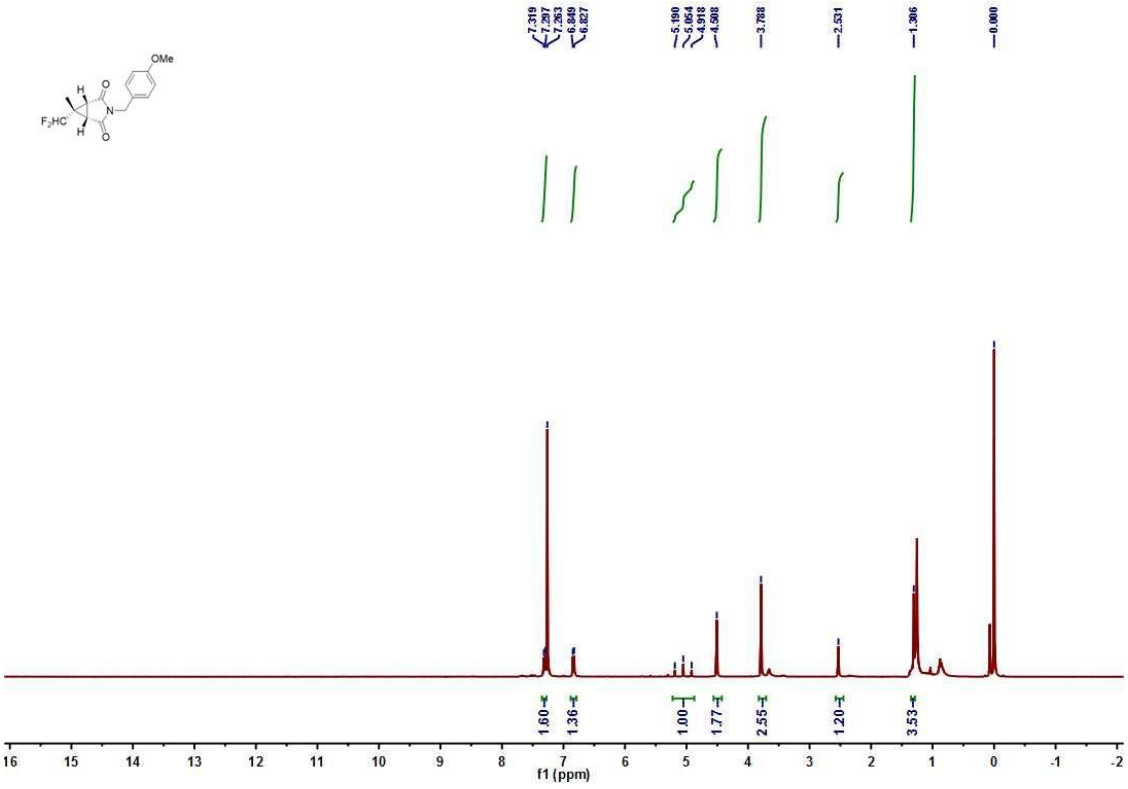


Figure 23. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3b₂**

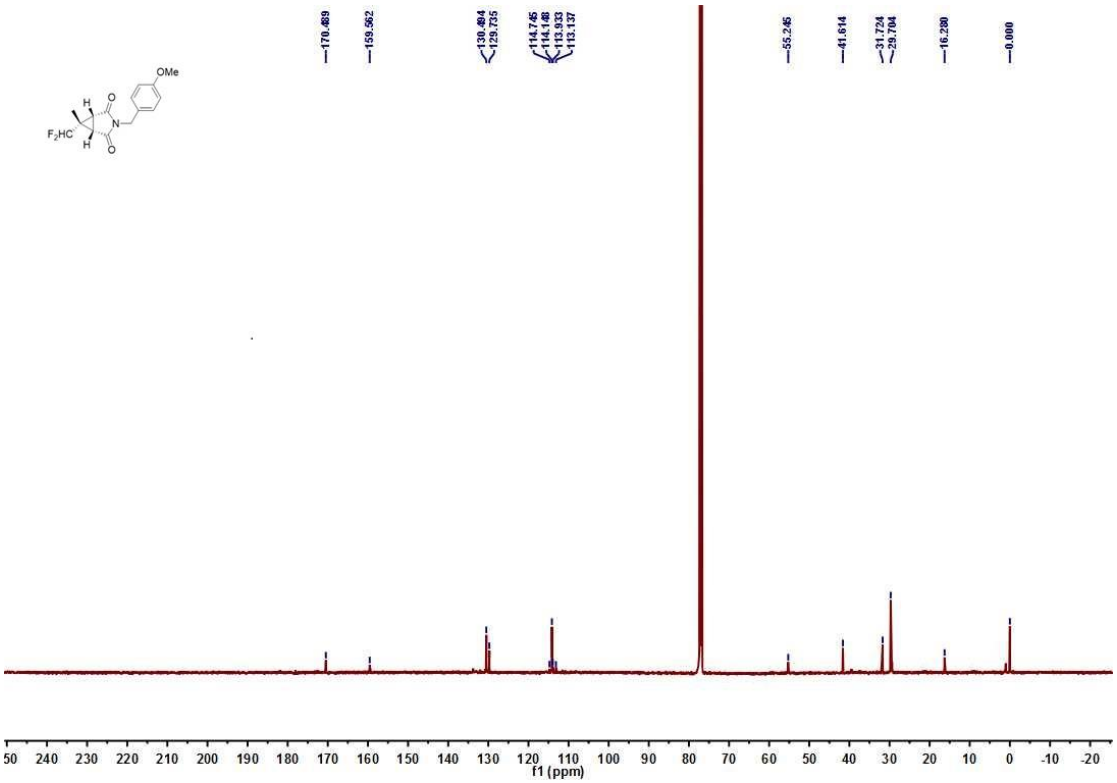


Figure 24. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3b₂**

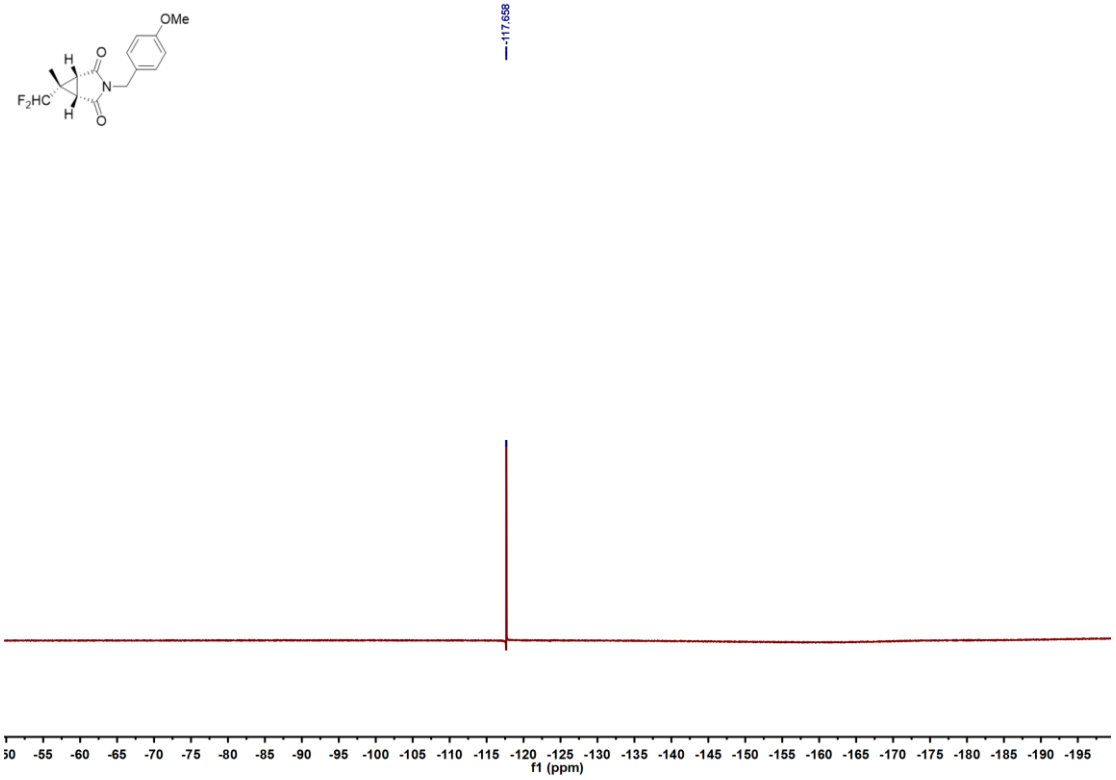


Figure 25. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3c$_1$**

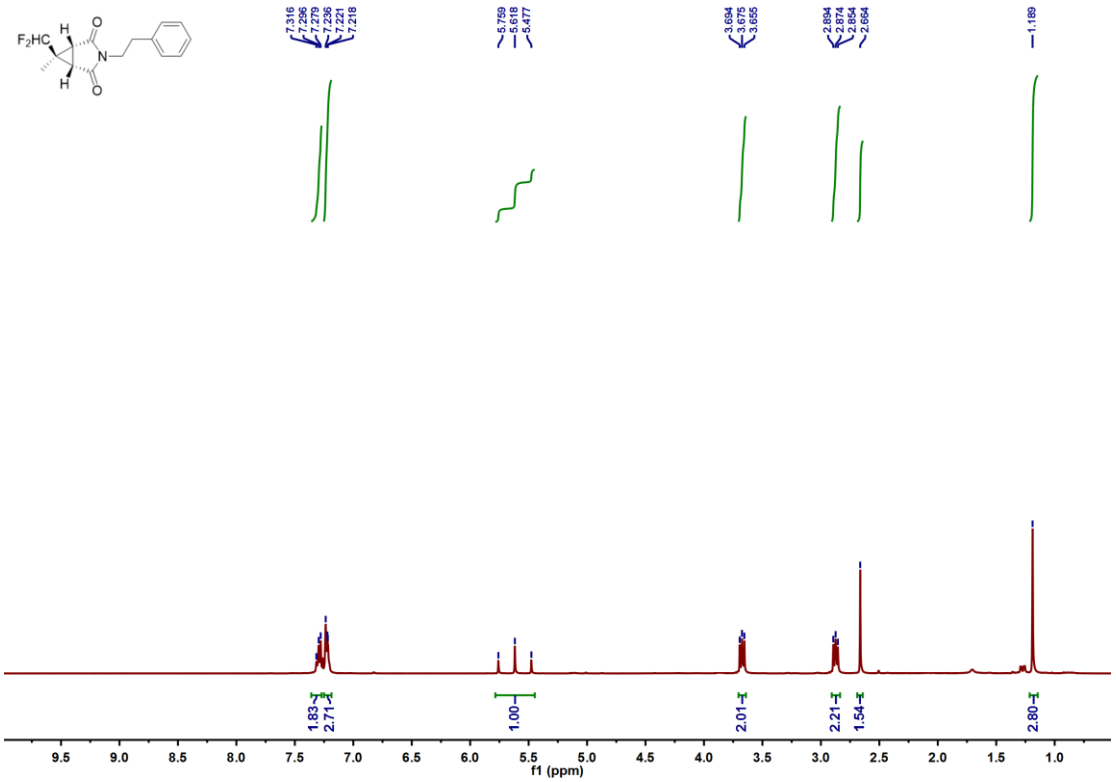


Figure 26. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3c$_1$**

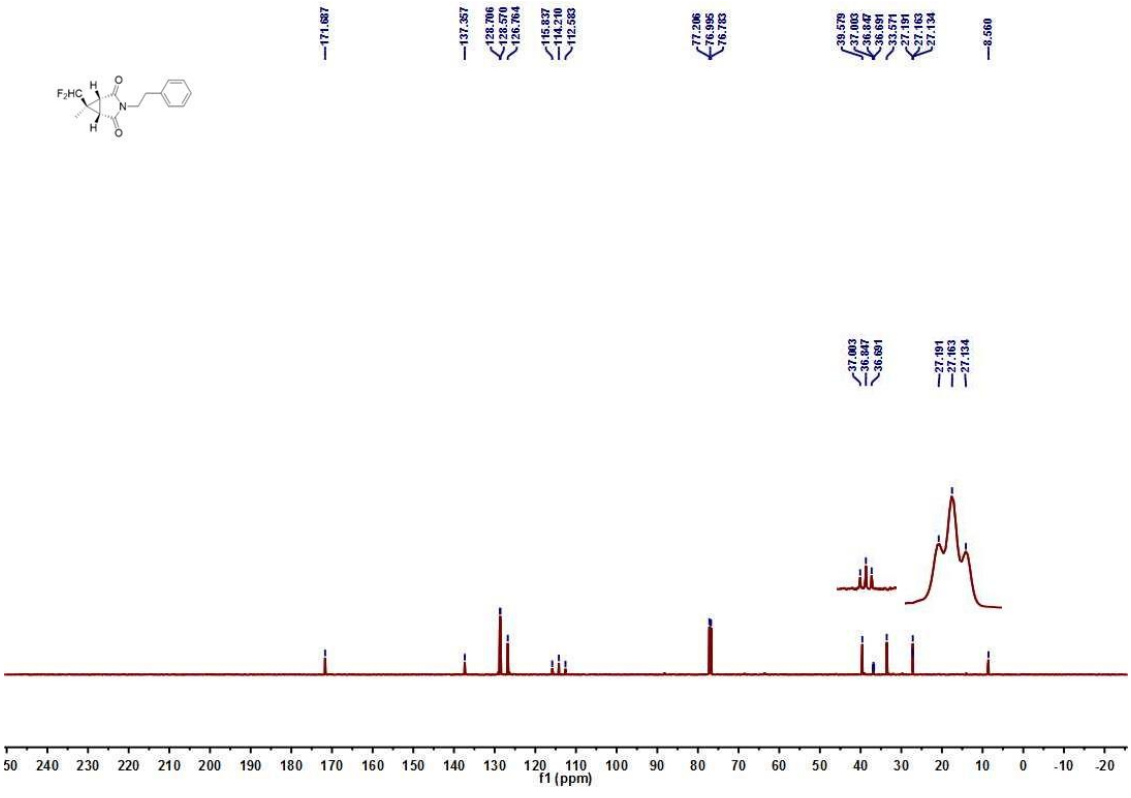


Figure 27. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3c$_1$**

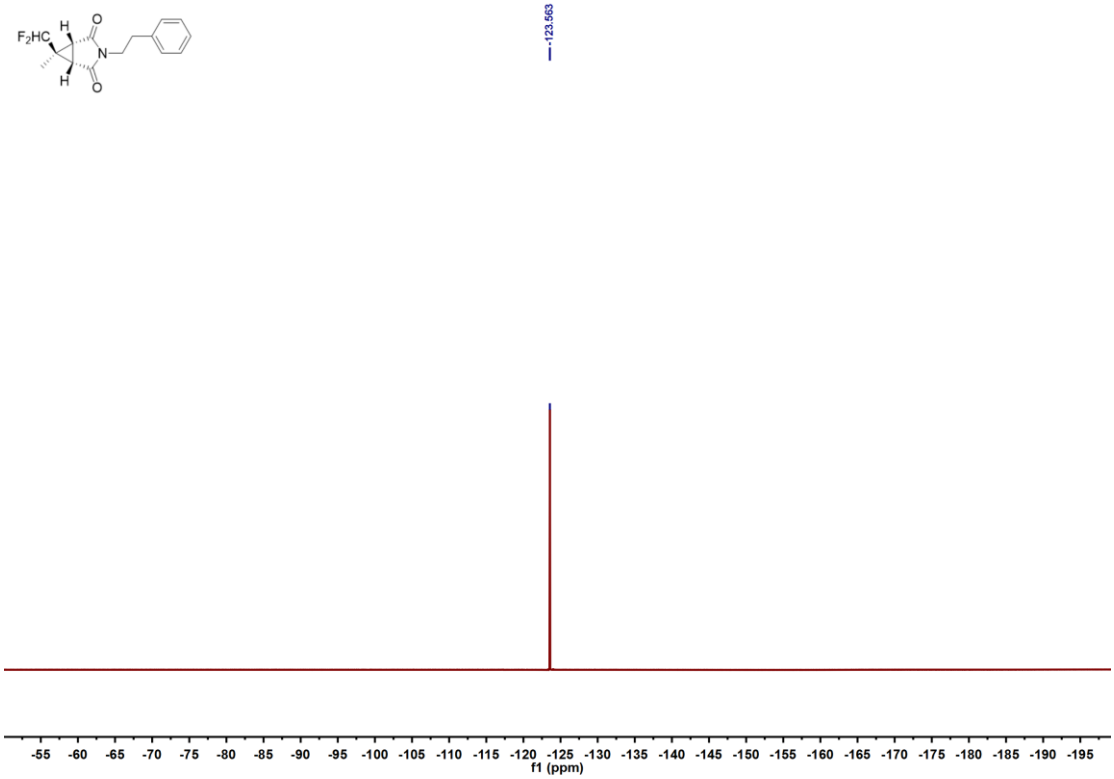


Figure 28. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3c$_2$**

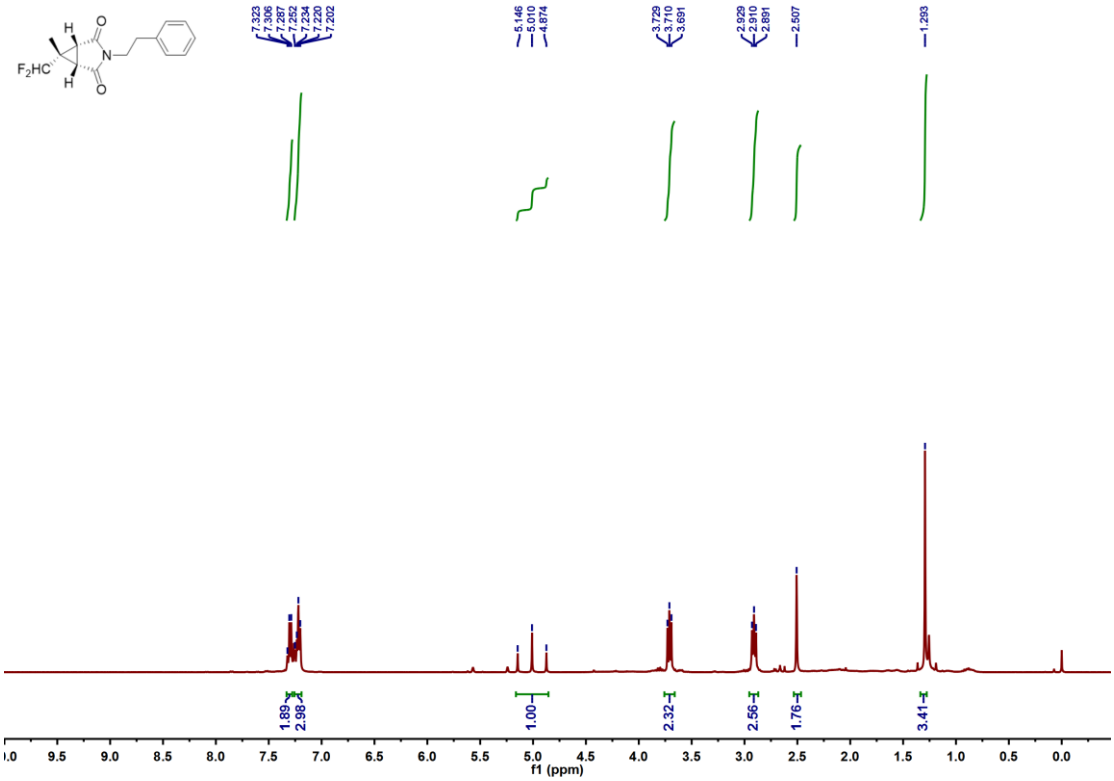


Figure 29. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3c₂**

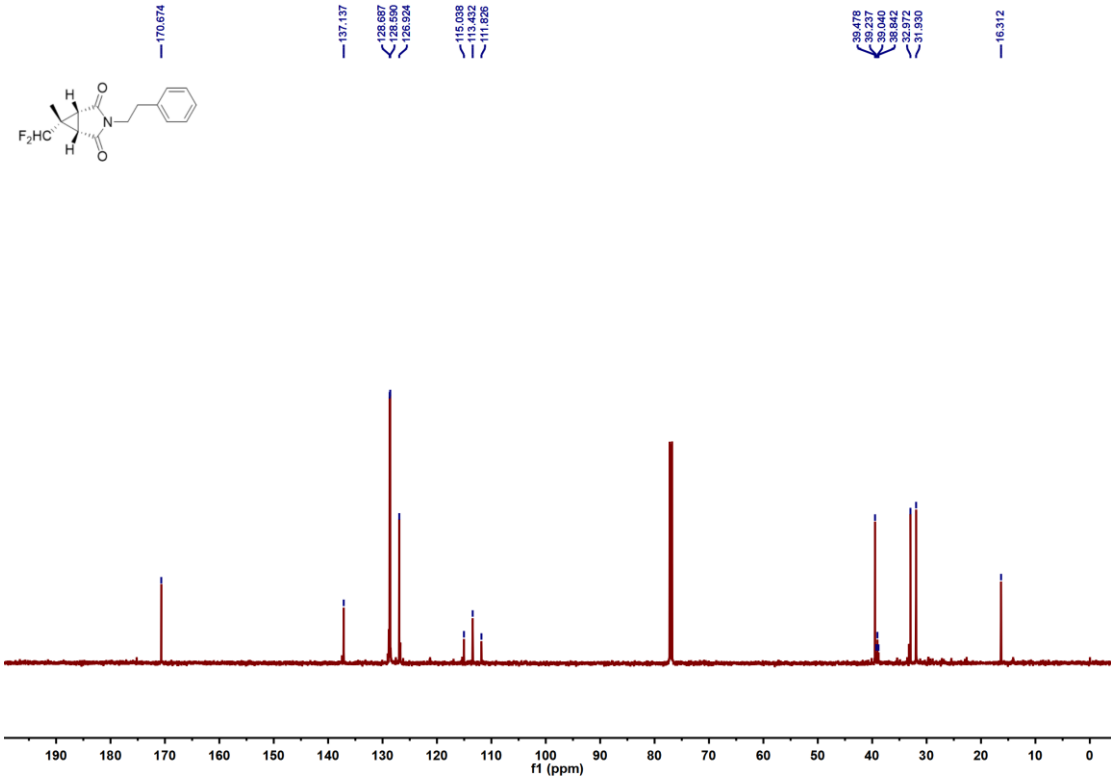


Figure 30. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3c₂**

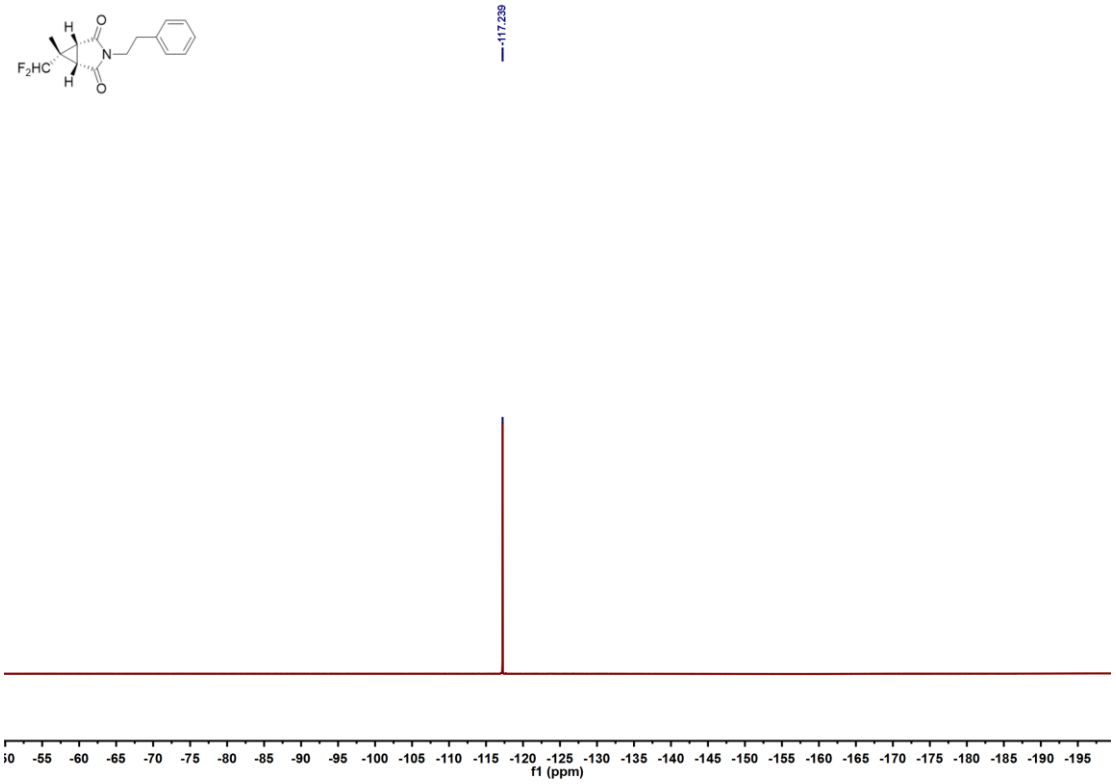


Figure 31. The ^{1}H NMR (400 MHz, DMSO-d_6) of **3d$_1$**

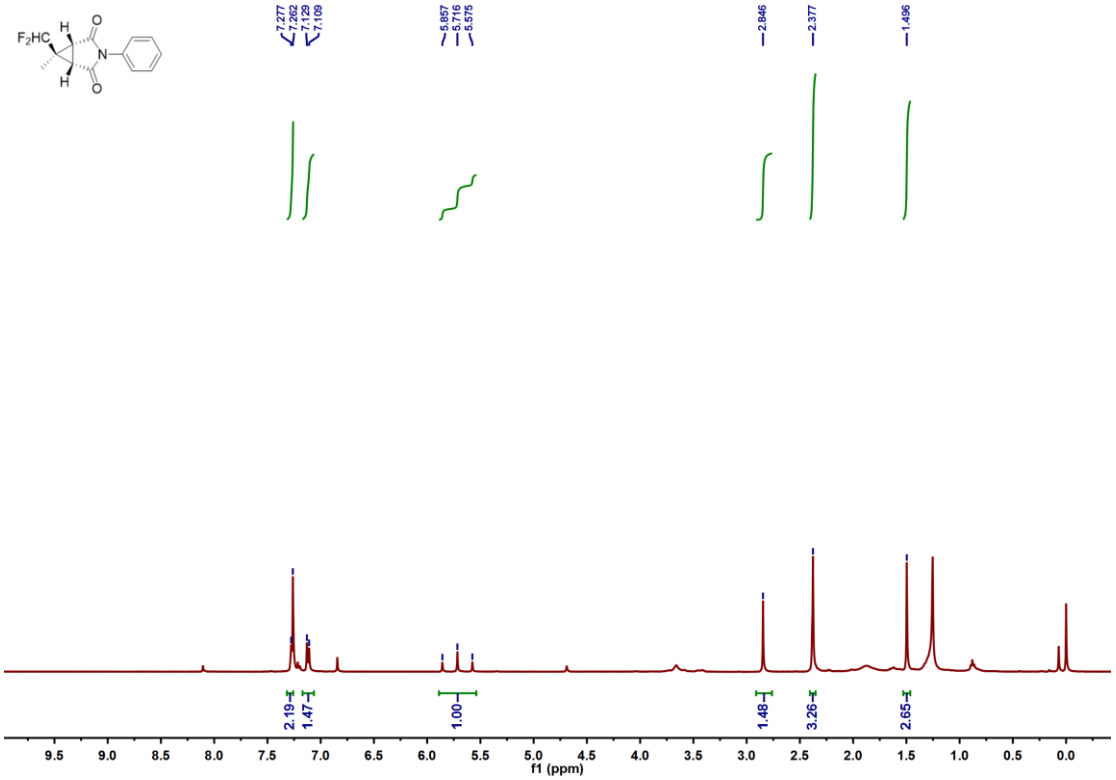


Figure 32. The ^{13}C NMR (150 MHz, DMSO-d_6) of **3d$_1$**

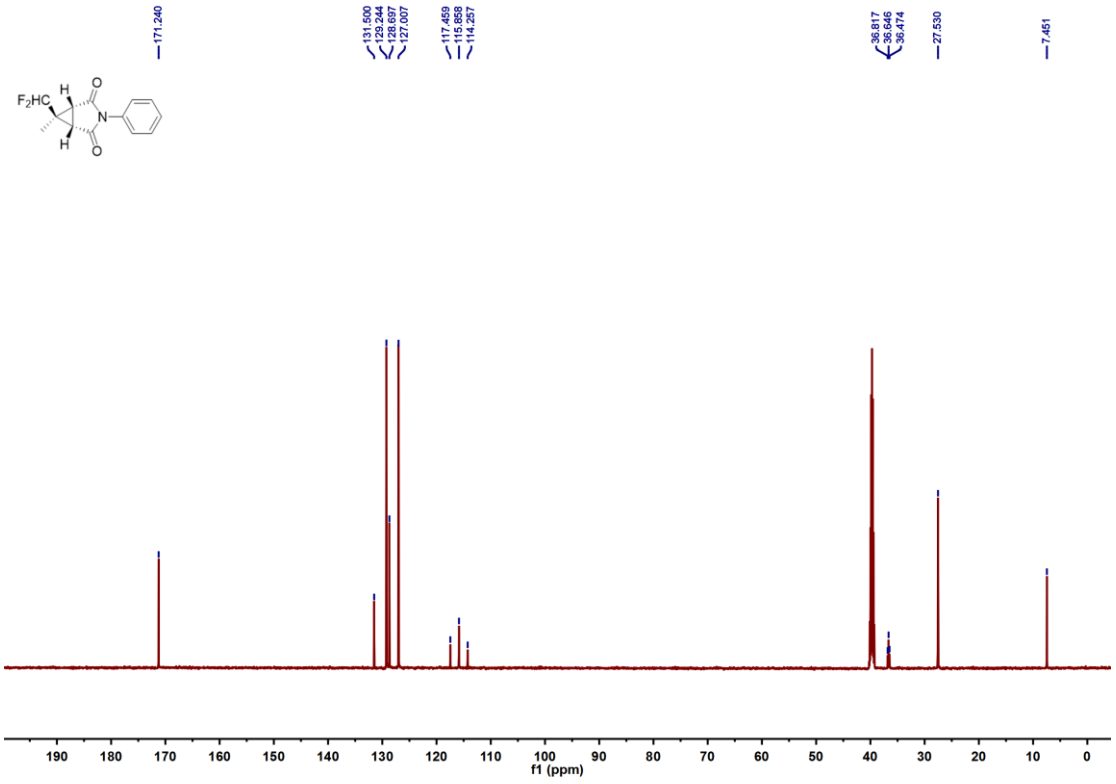


Figure 33. The ^{19}F NMR (376 MHz, DMSO-d_6) of **3d$_1$**

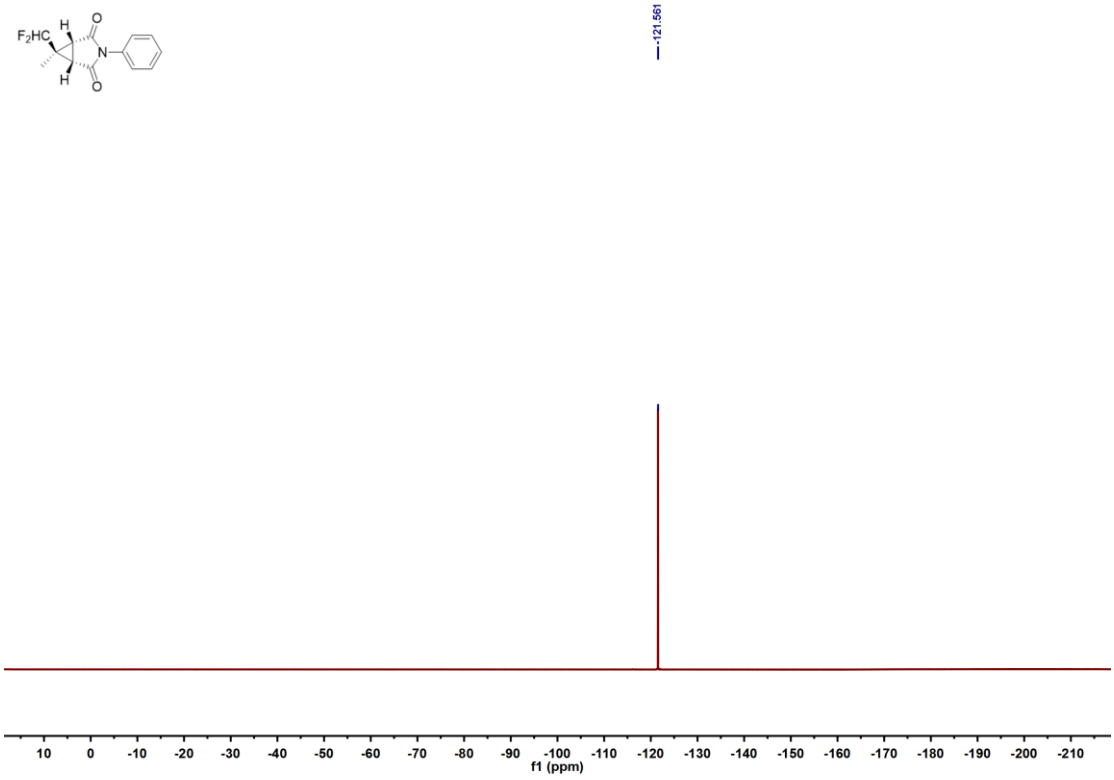


Figure 34. The ^{1}H NMR (400 MHz, DMSO-d_6) of **3d$_2$**

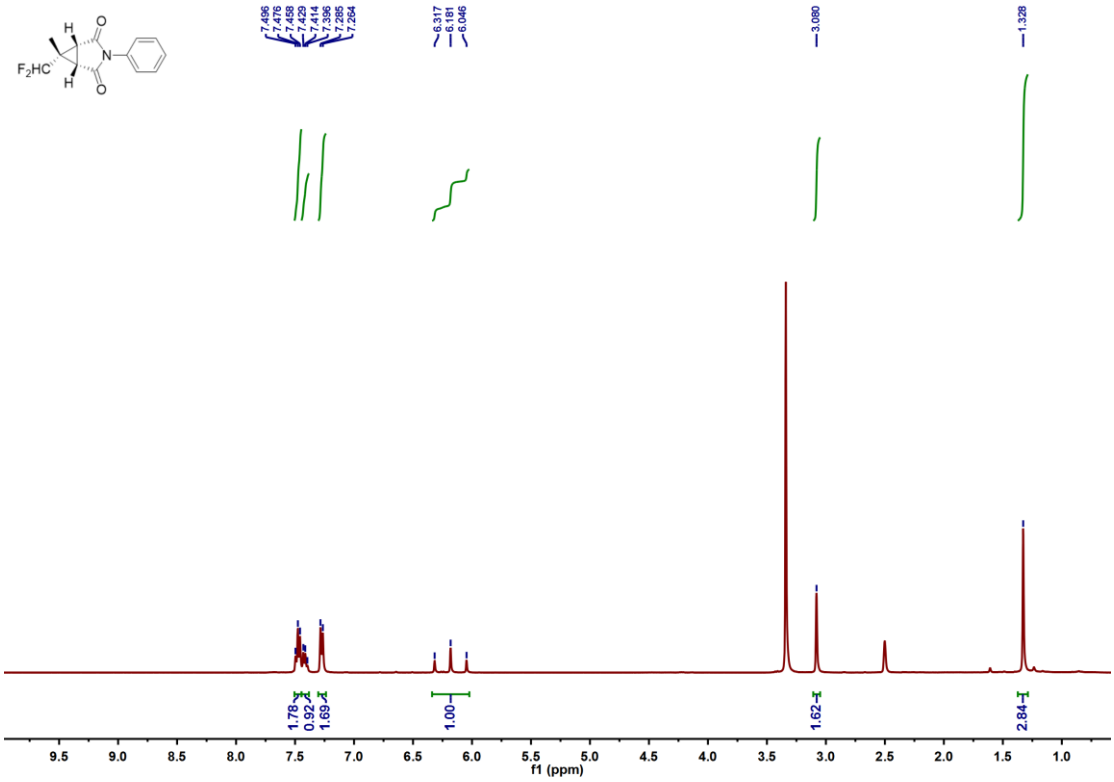


Figure 35. The ^{13}C NMR (150 MHz, DMSO-d_6) of **3d₂**

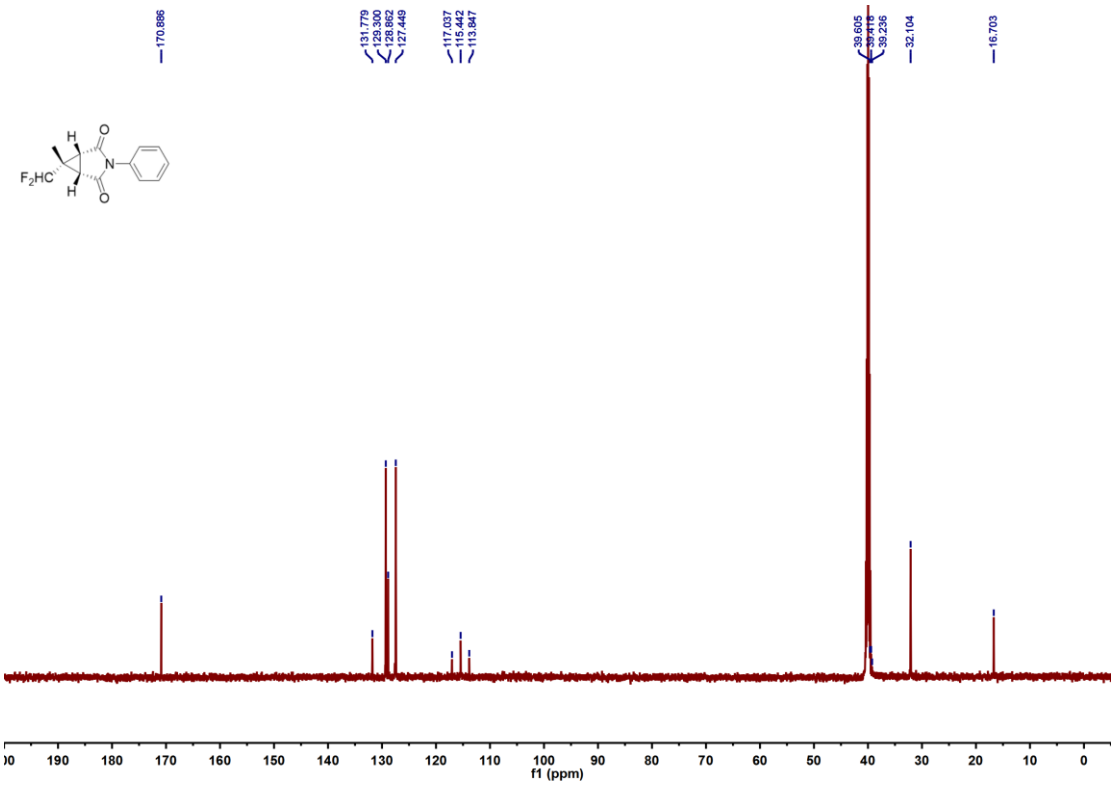


Figure 36. The ^{19}F NMR (376 MHz, DMSO-d_6) of **3d₂**

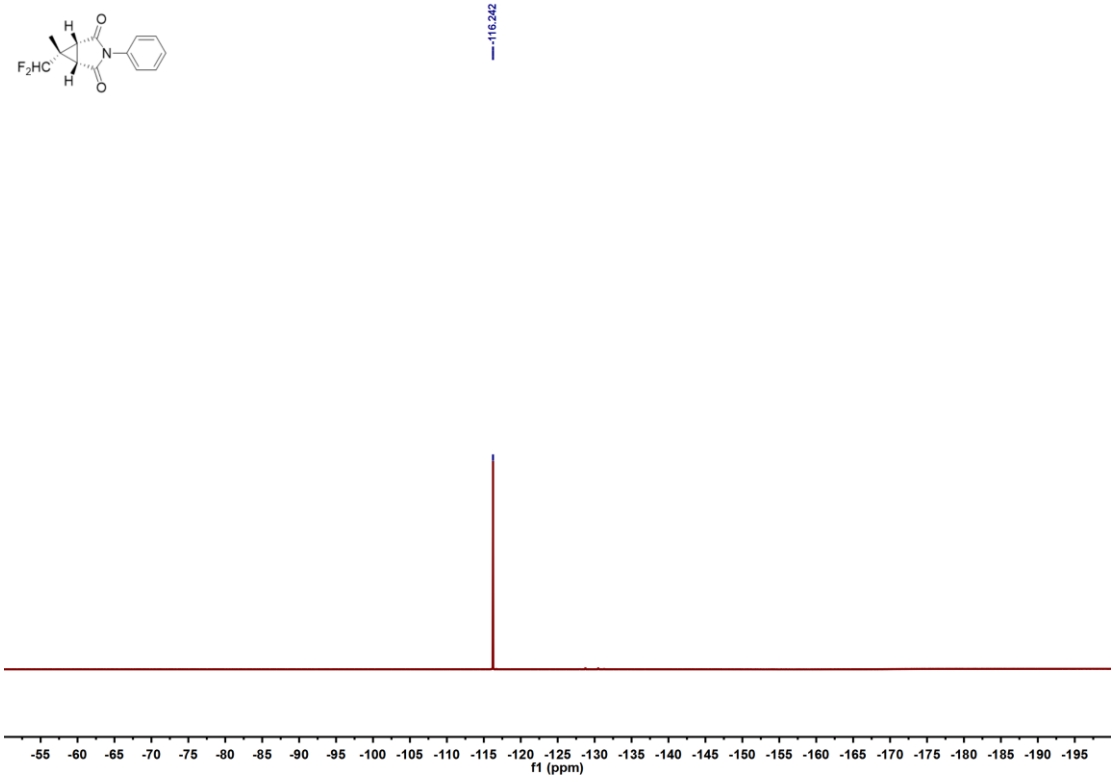


Figure 37. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3e$_1$** and **3e$_2$**

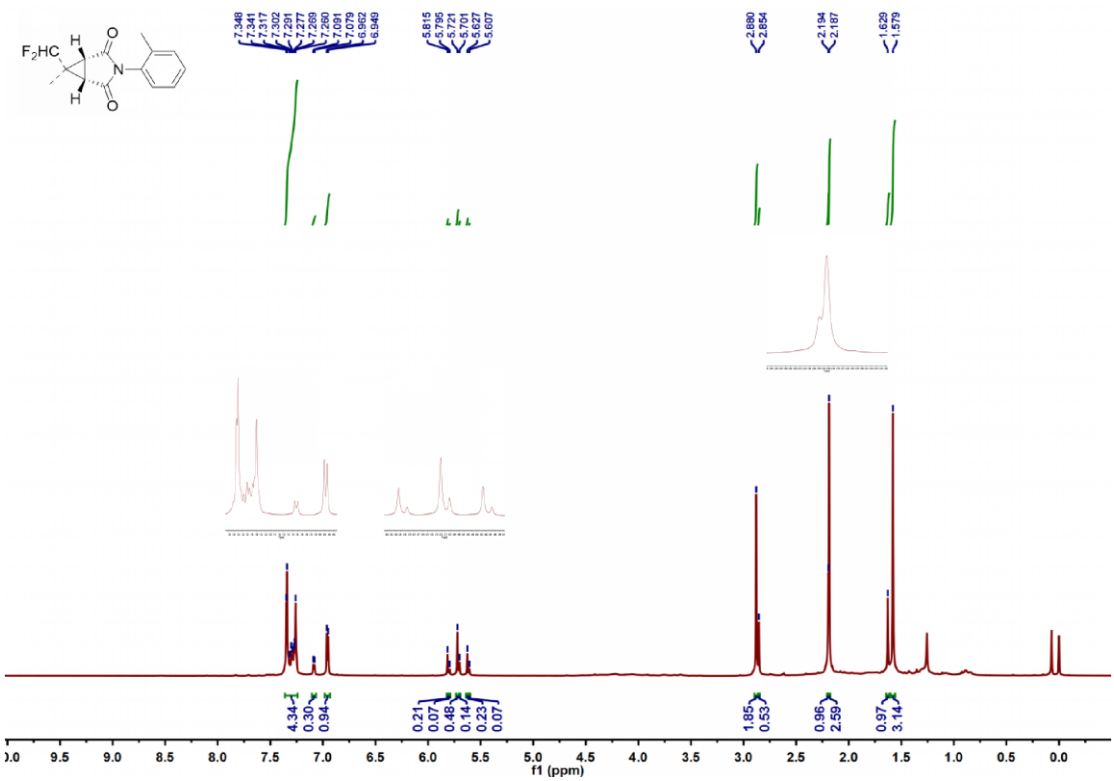


Figure 38. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3f$_1$** and **3f$_2$**

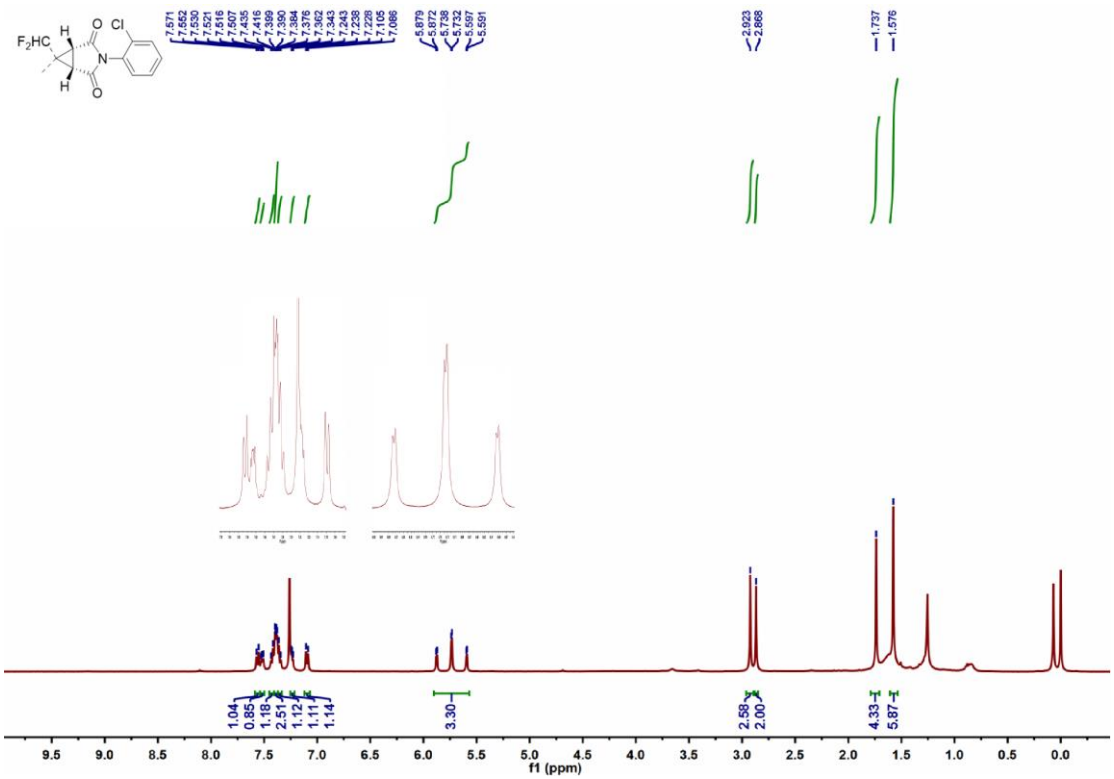


Figure 39. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3g$_1$**

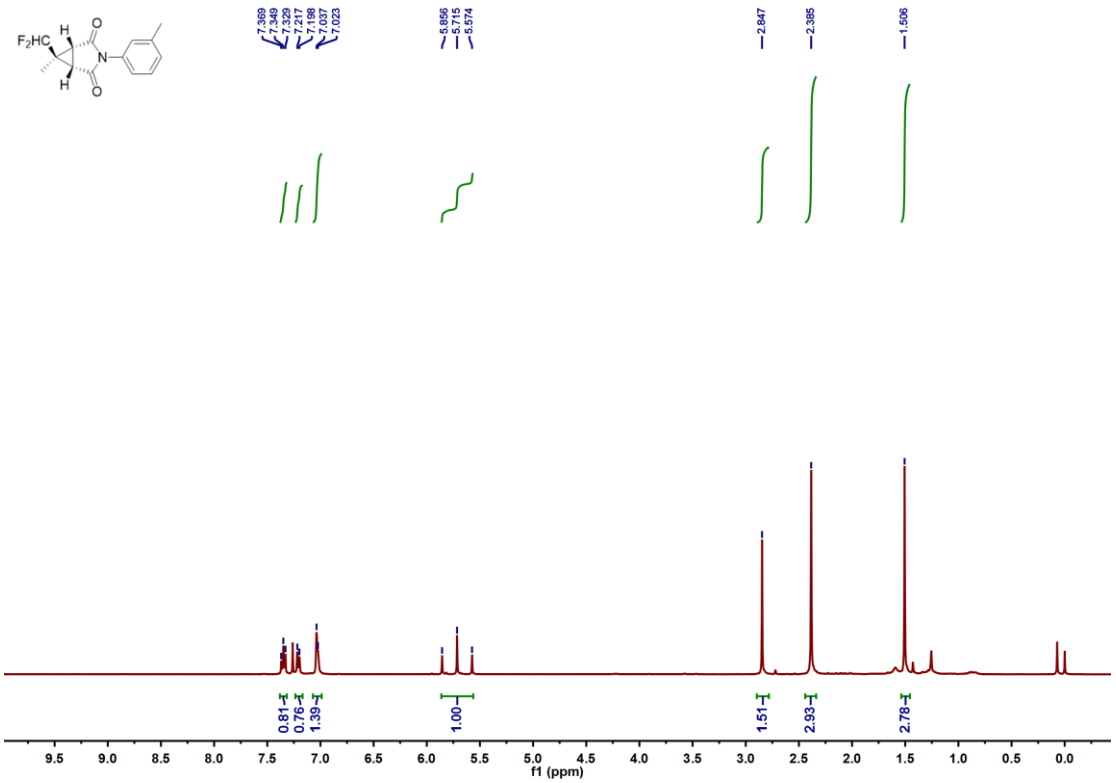


Figure 40. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3g$_1$**

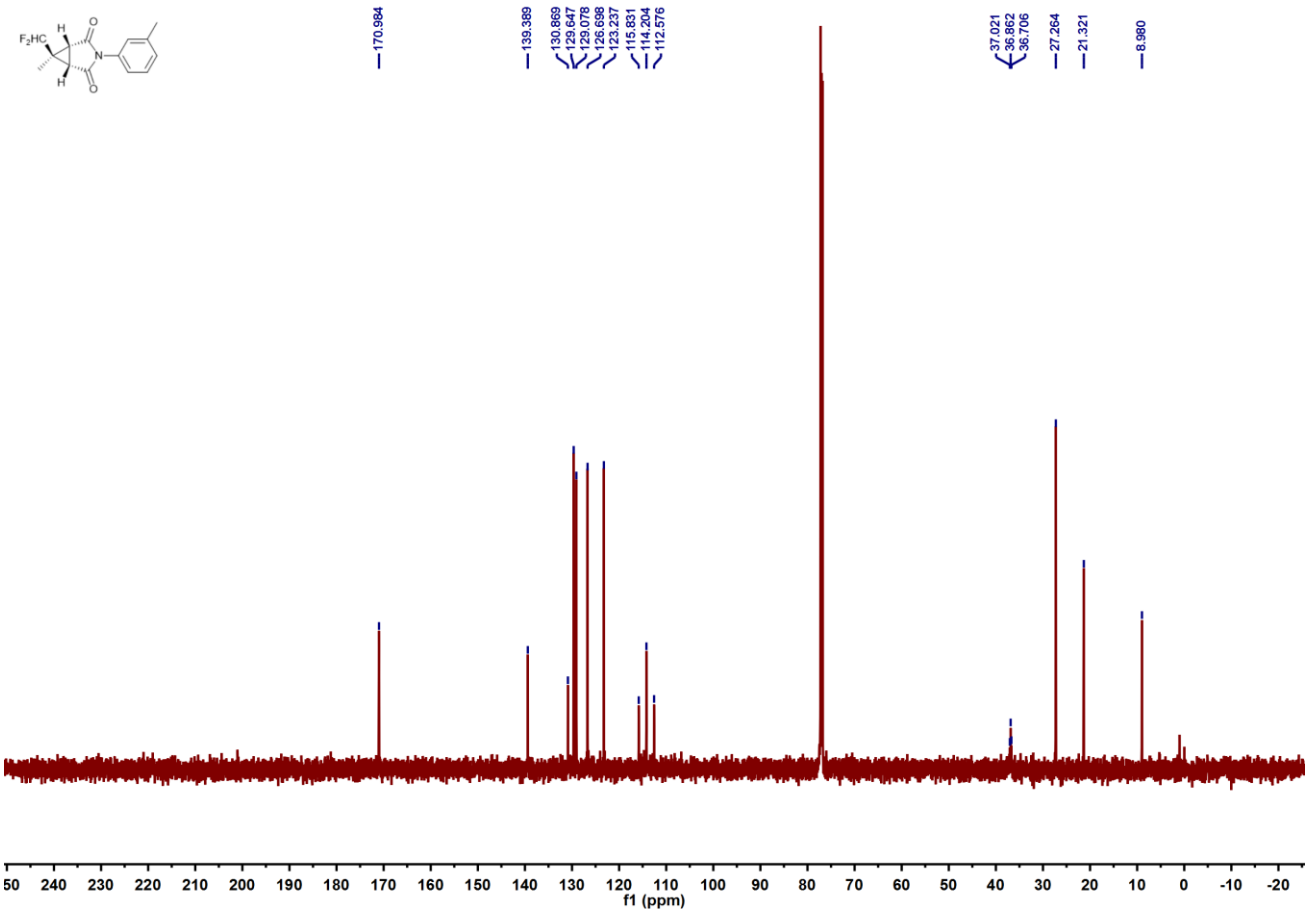


Figure 41. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3g$_1$**

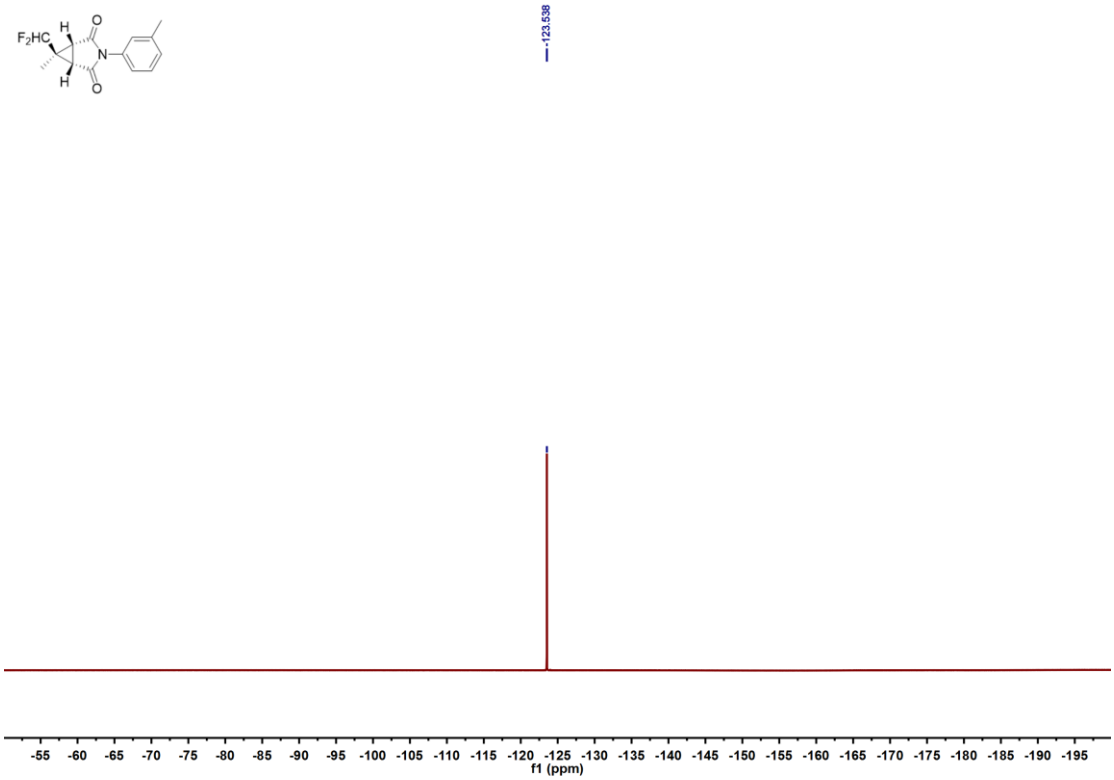


Figure 42. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3g$_2$**

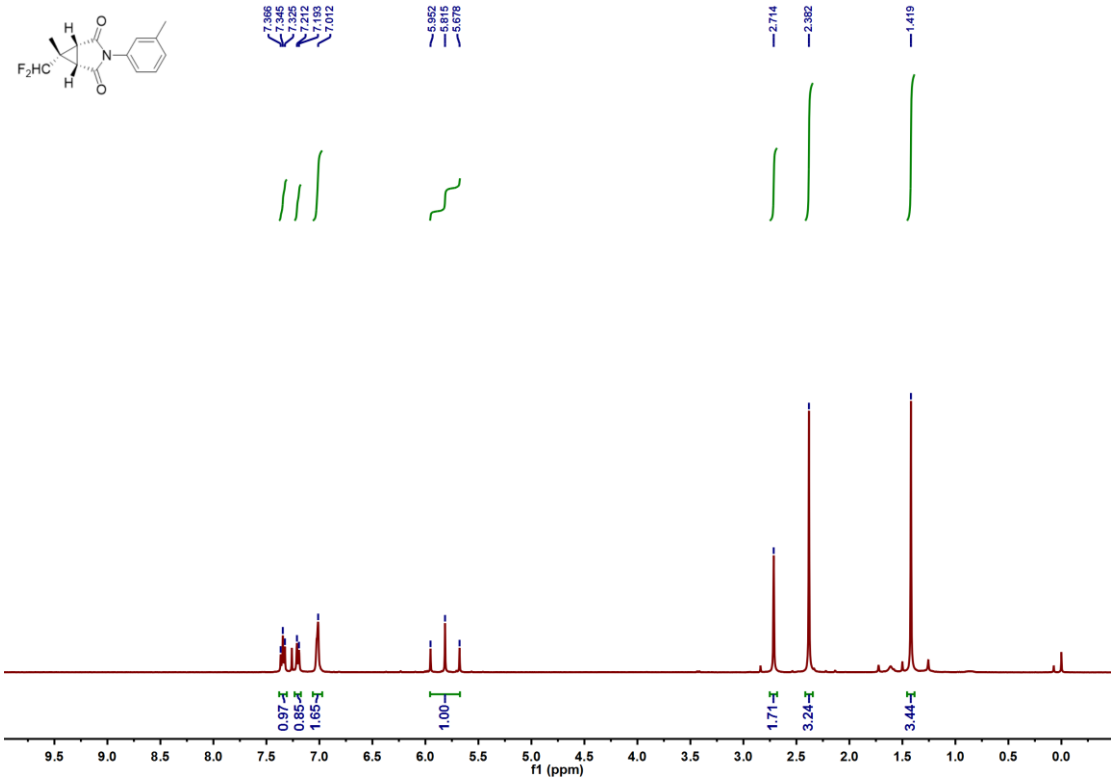


Figure 43. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3g₂**

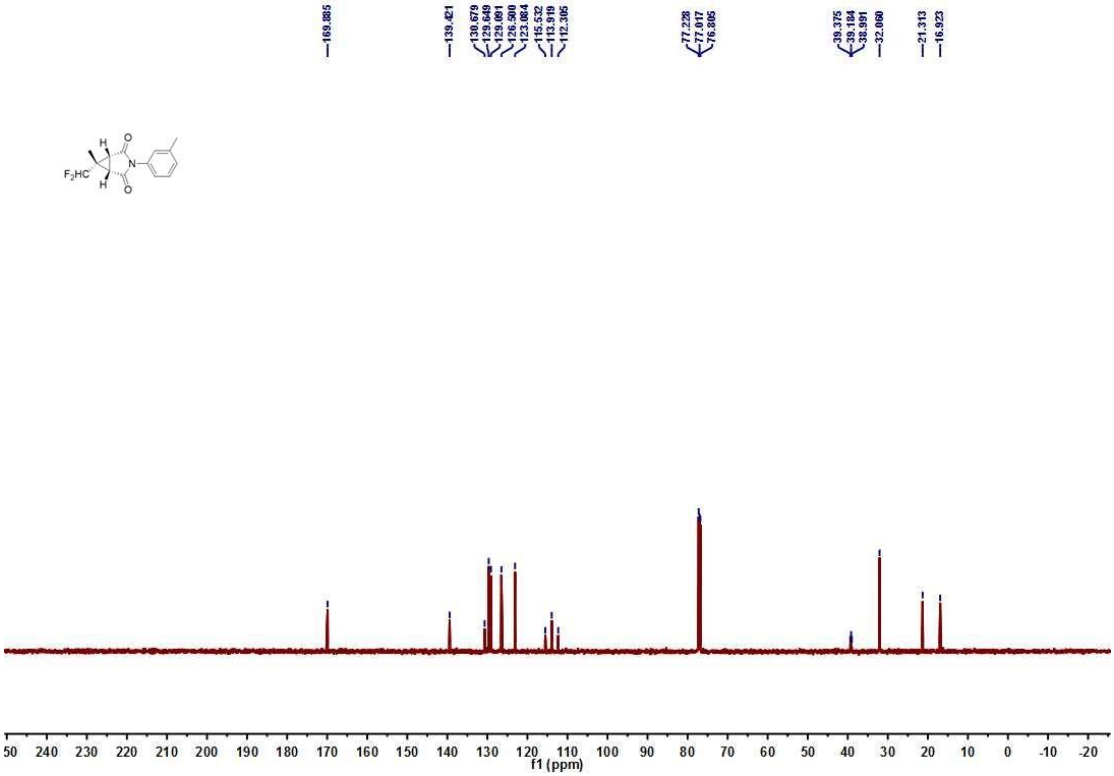


Figure 44. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3g₂**

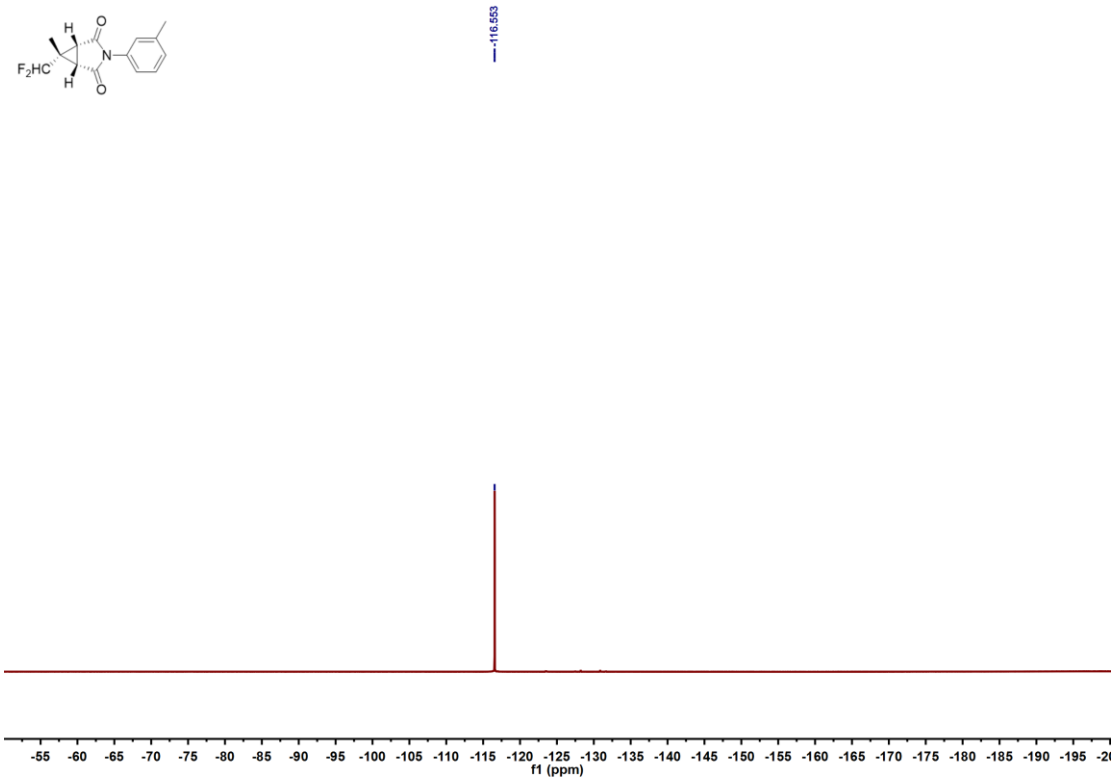


Figure 45. The ^{1}H NMR (600 MHz, $CDCl_3$) of **3h$_1$**

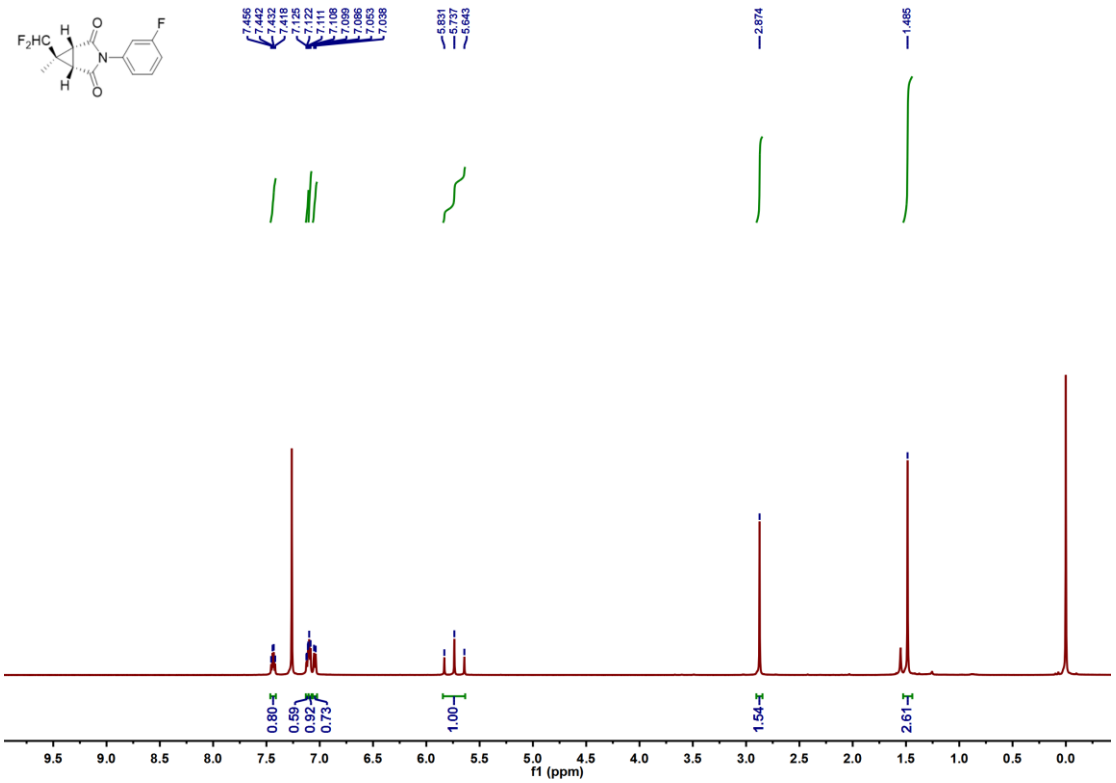


Figure 46. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3h$_1$**

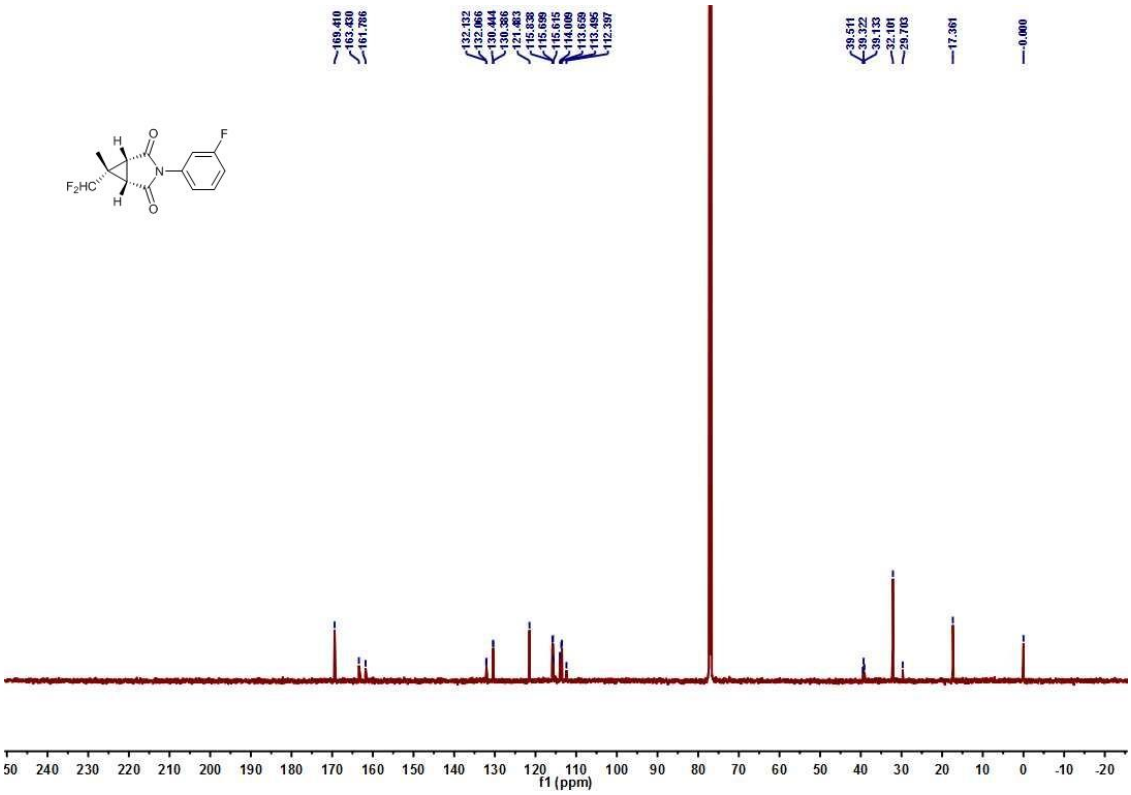


Figure 47. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3h₁**

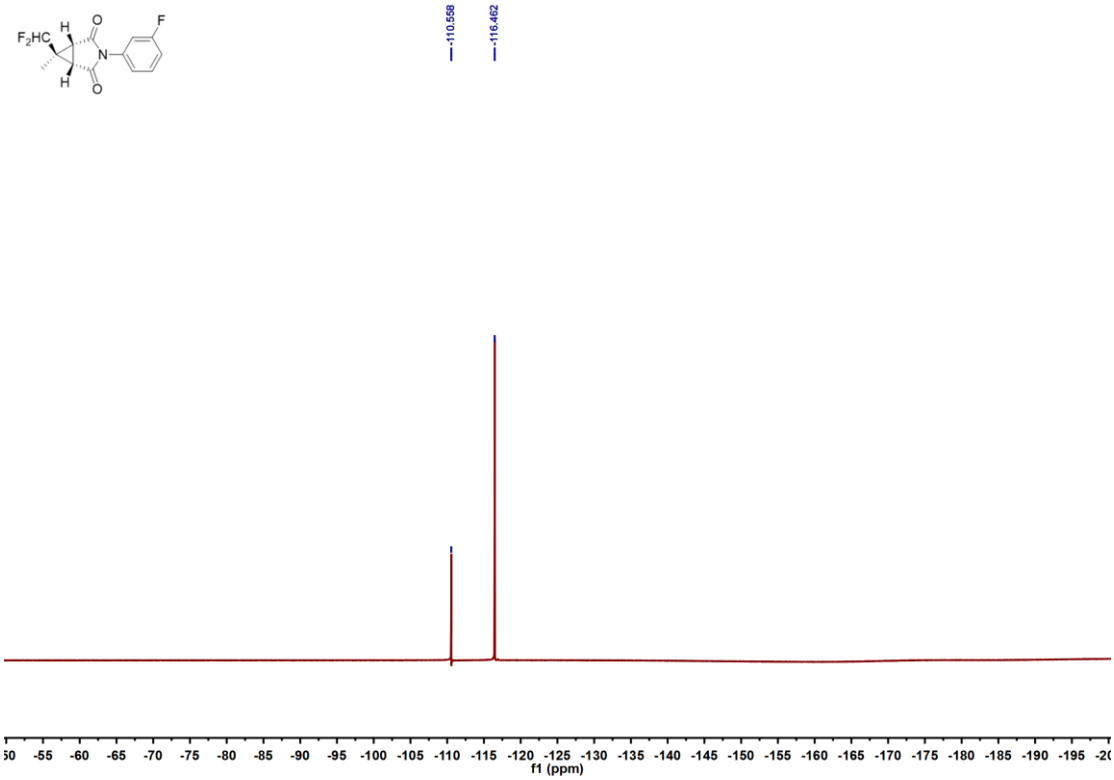


Figure 48. The ^{1}H NMR (600 MHz, $CDCl_3$) of **3h₂**

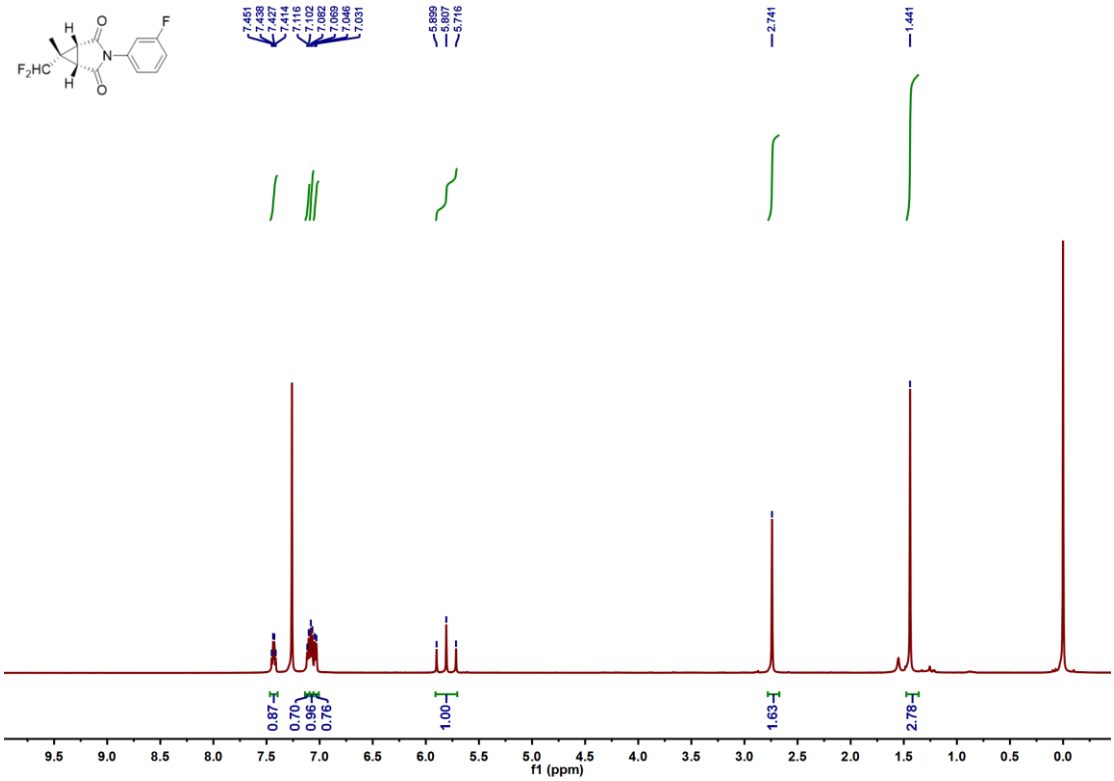


Figure 49. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3h₂**

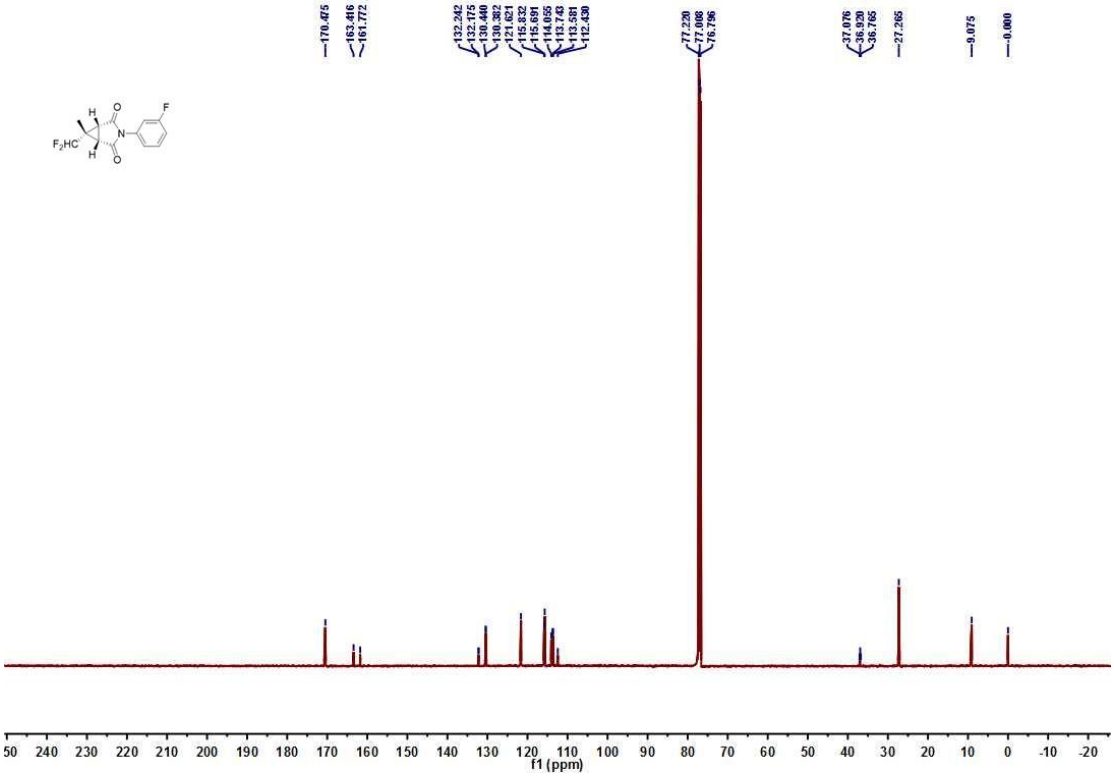


Figure 50. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3h₂**

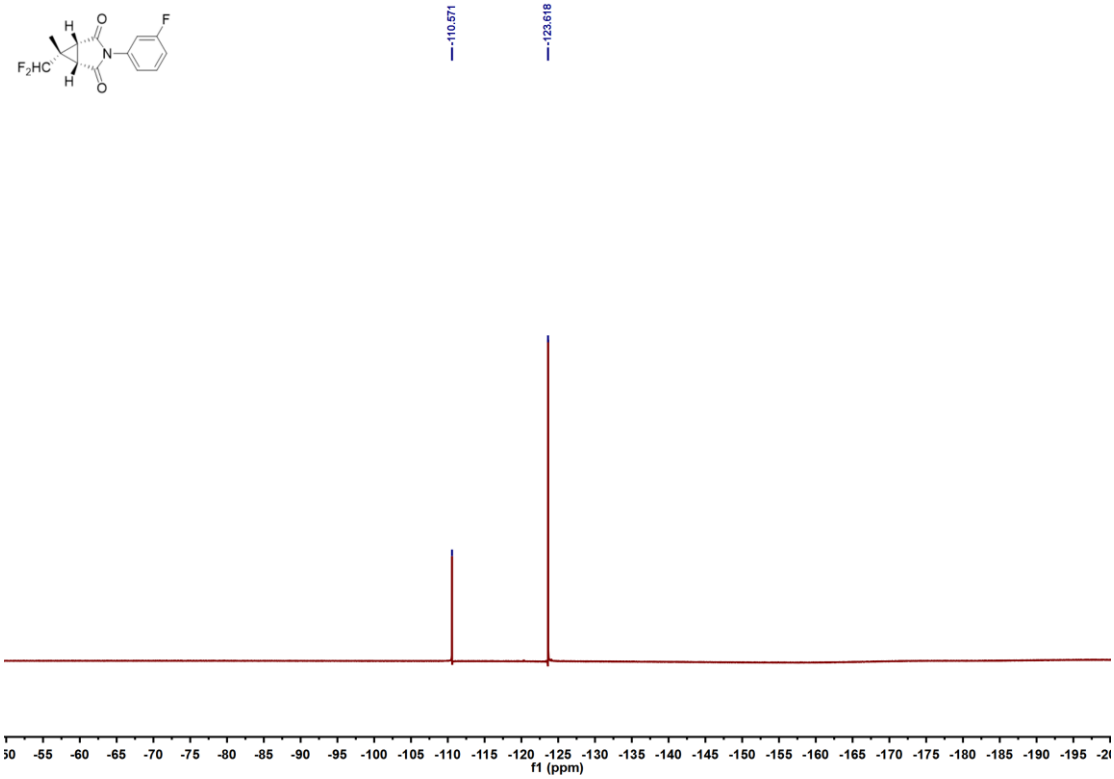


Figure 51. The ^{1}H NMR (400 MHz, DMSO-d_6) of **3i$_1$**

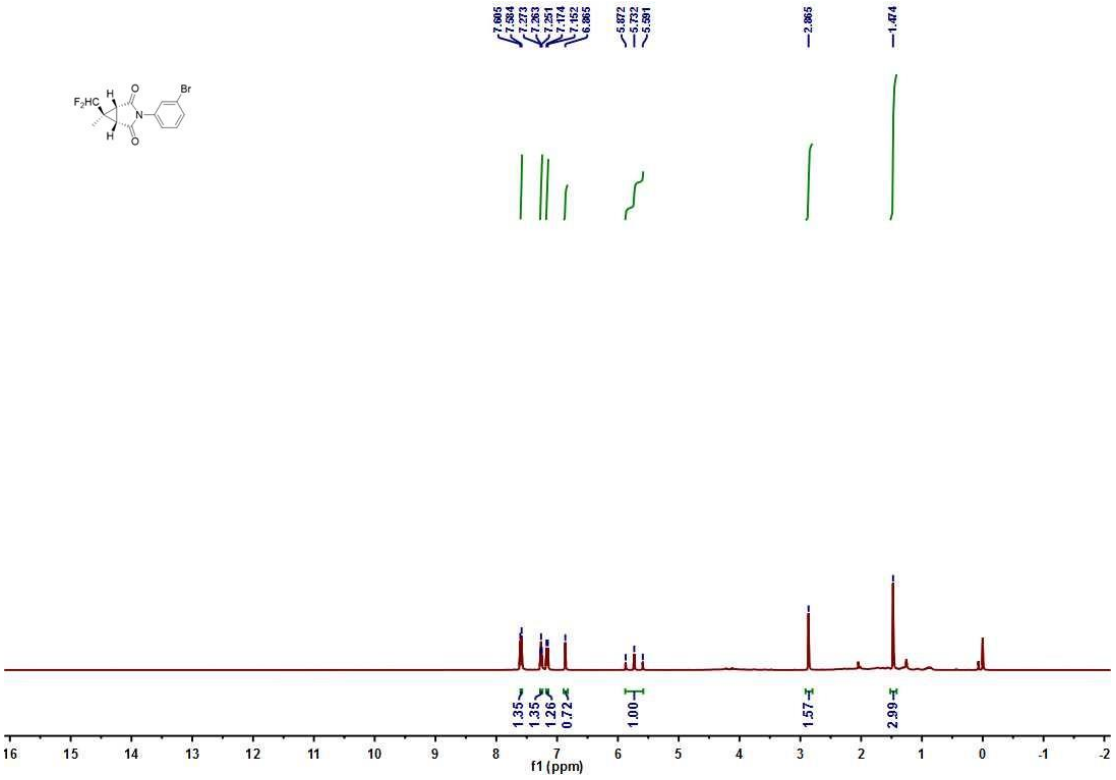


Figure 52. The ^{13}C NMR (150 MHz, DMSO-d_6) of **3i$_1$**

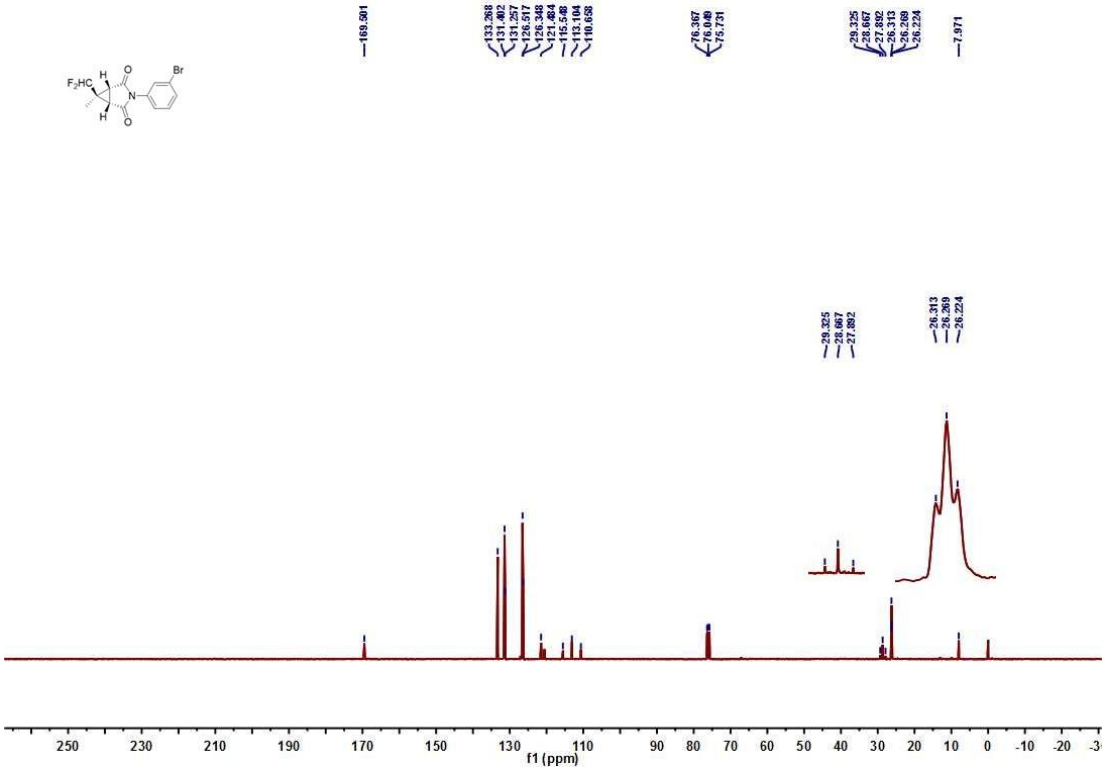


Figure 53. The ^{19}F NMR (376 MHz, DMSO-d_6) of **3i$_1$**

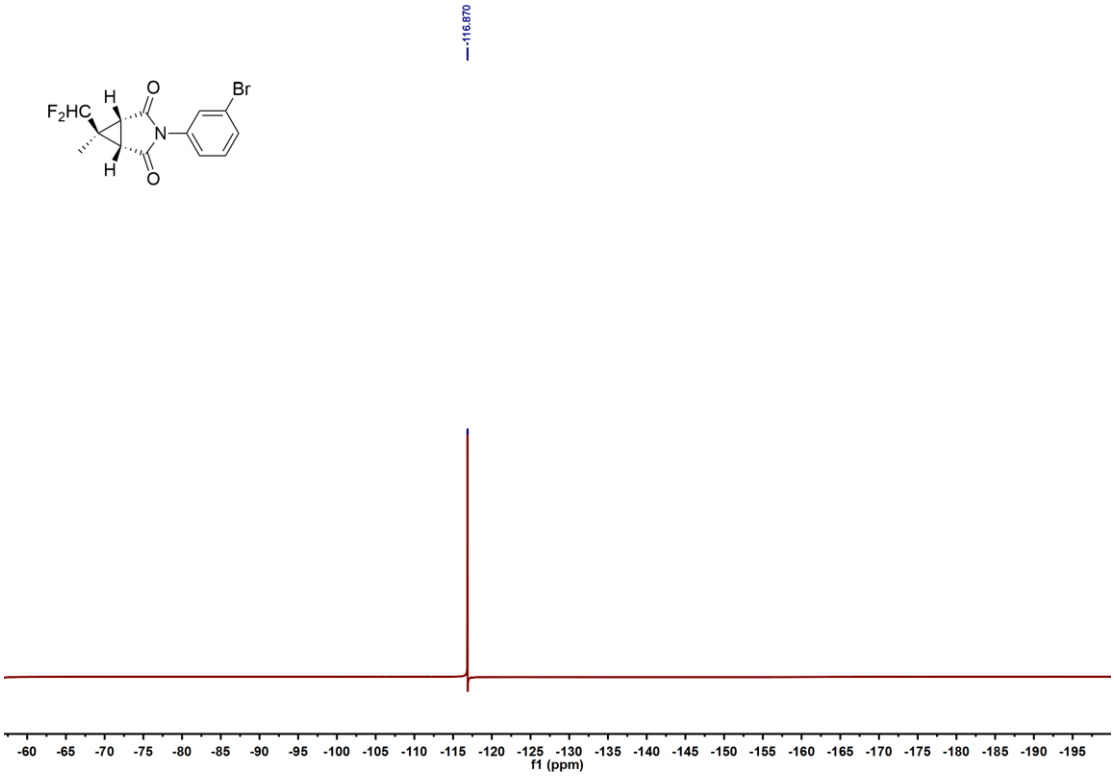


Figure 54. The ^{1}H NMR (600 MHz, DMSO-d_6) of **3i$_2$**

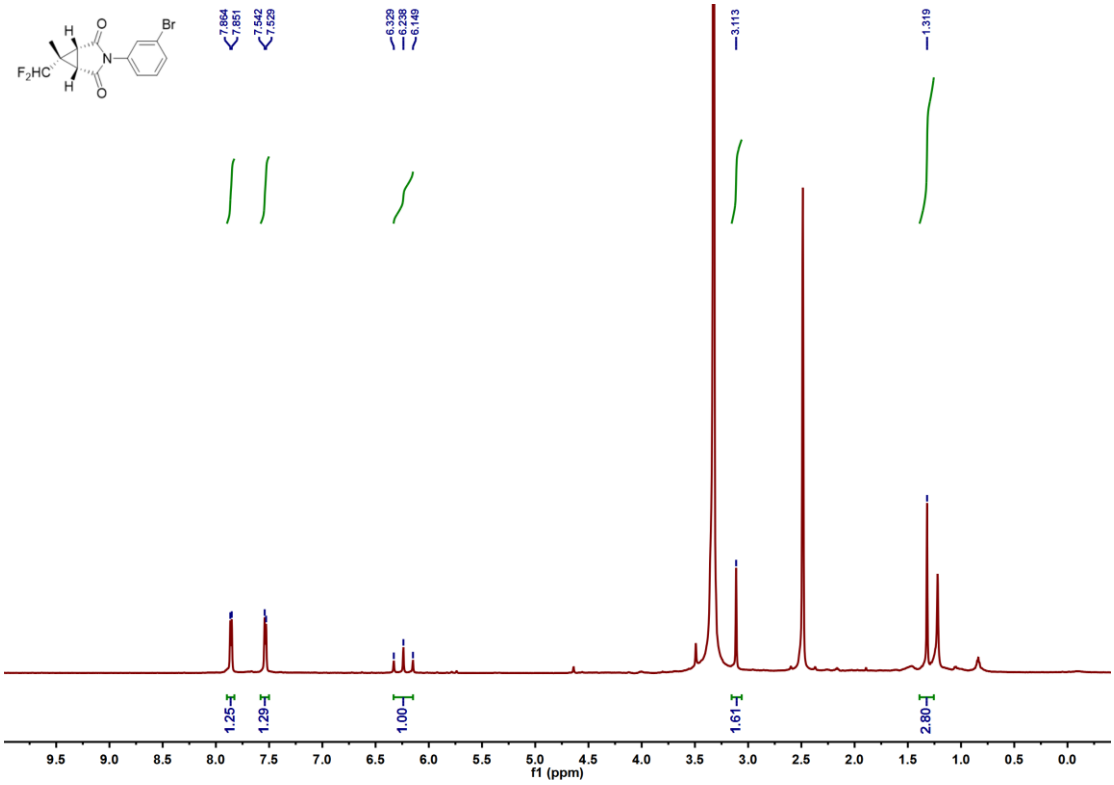


Figure 55. The ^{13}C NMR (150 MHz, DMSO-d_6) of **3i$_2$**

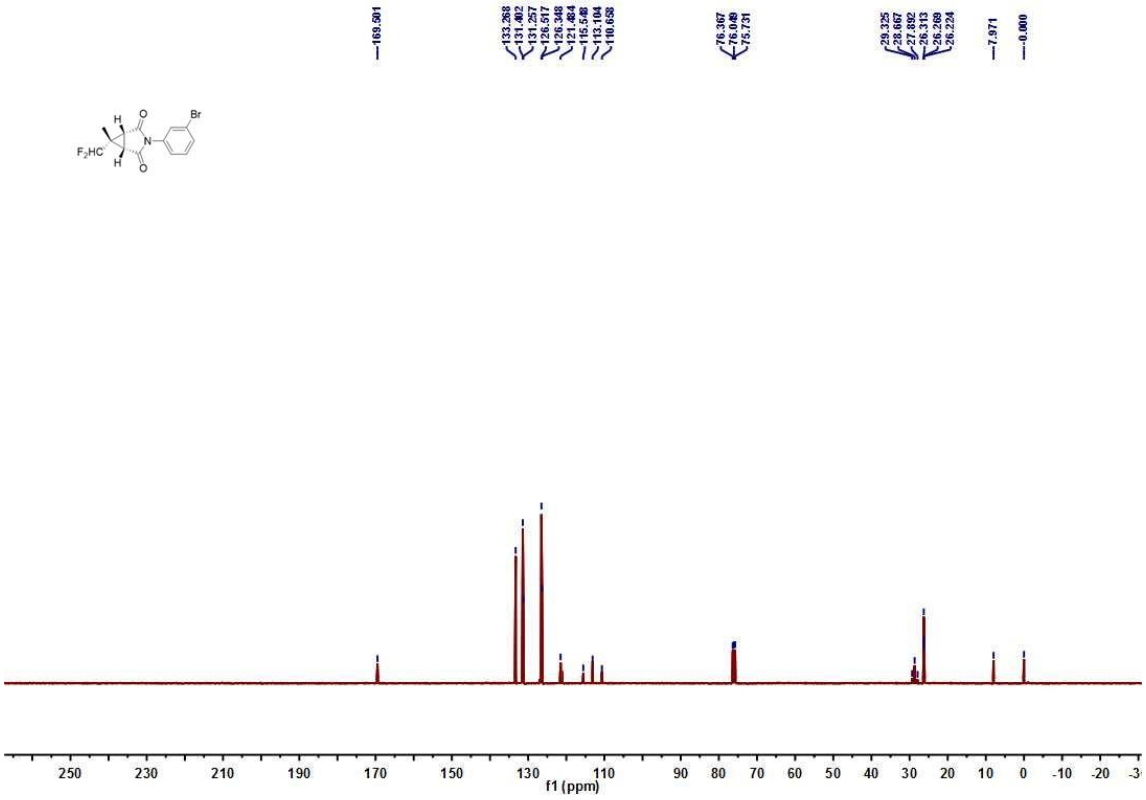


Figure 56. The ^{19}F NMR (376 MHz, DMSO-d_6) of **3i$_2$**

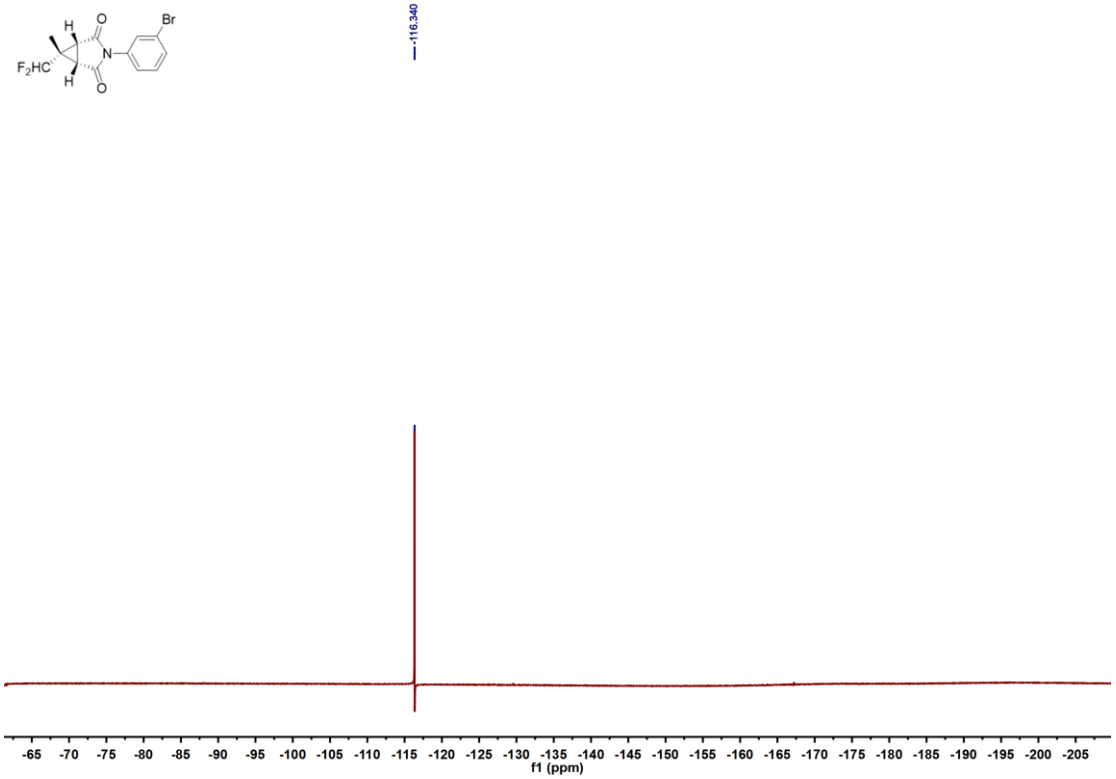


Figure 57. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3j₁**

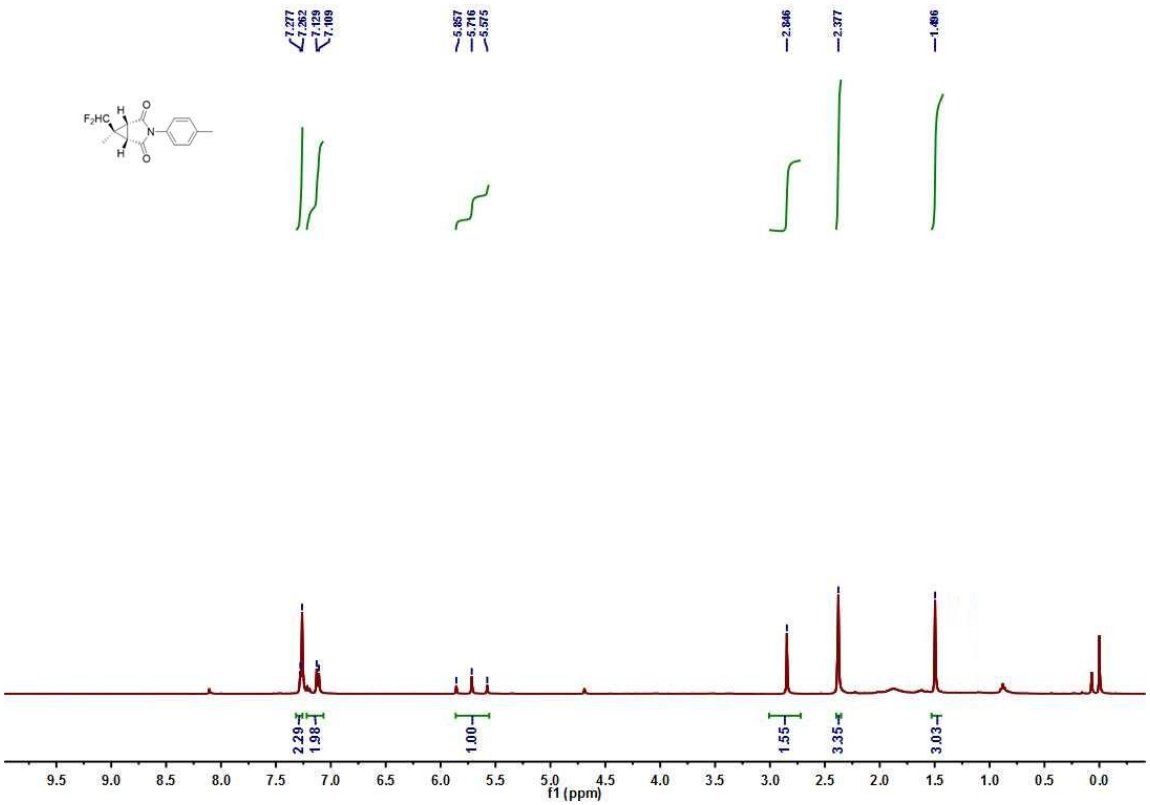


Figure 58. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3j₁**

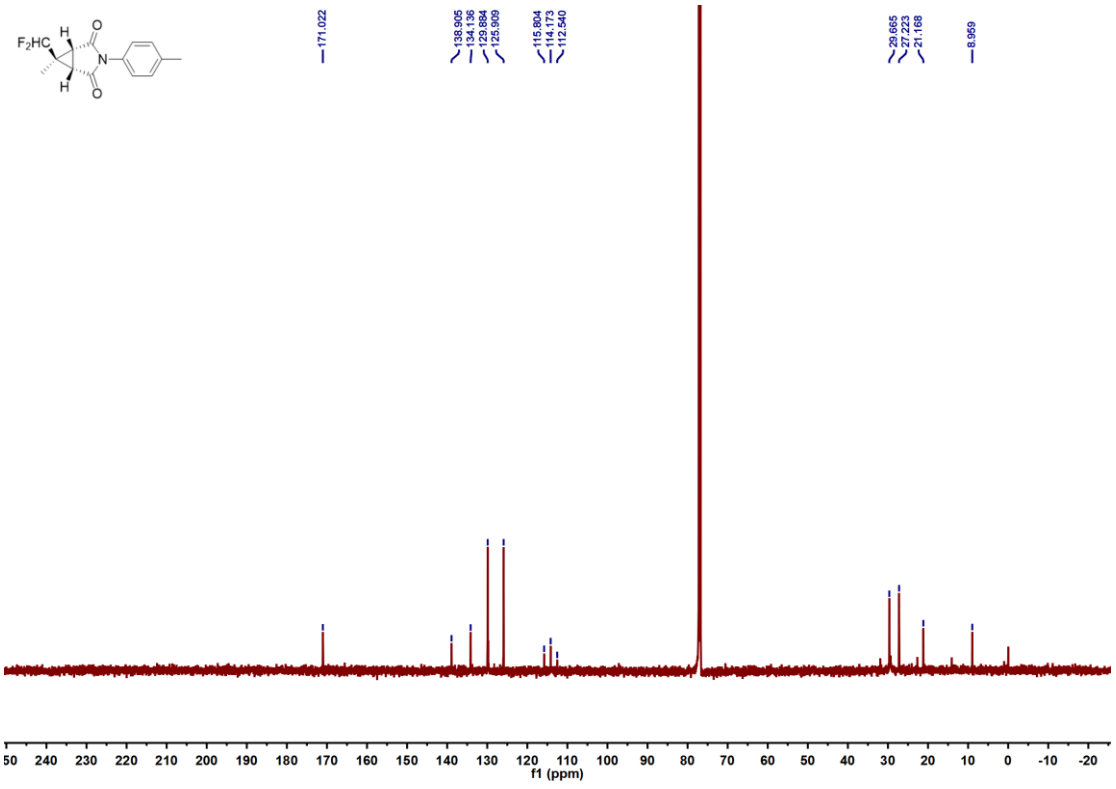


Figure 59. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3j$_1$**

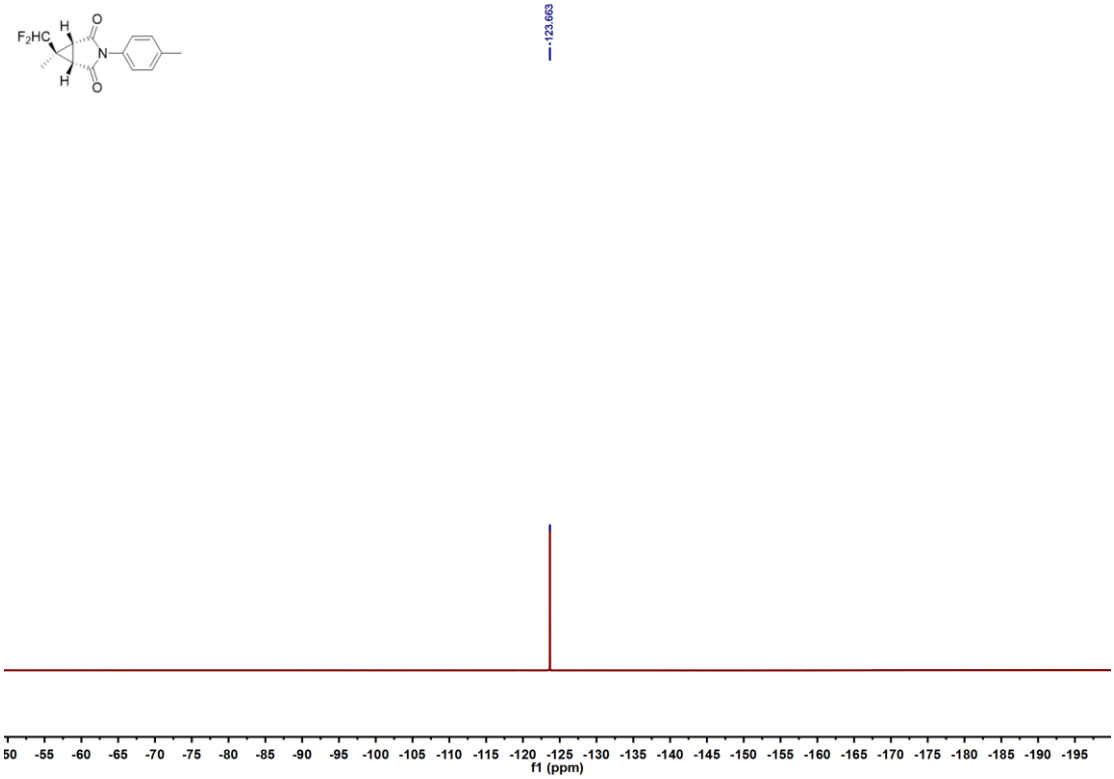


Figure 60. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3j$_2$**

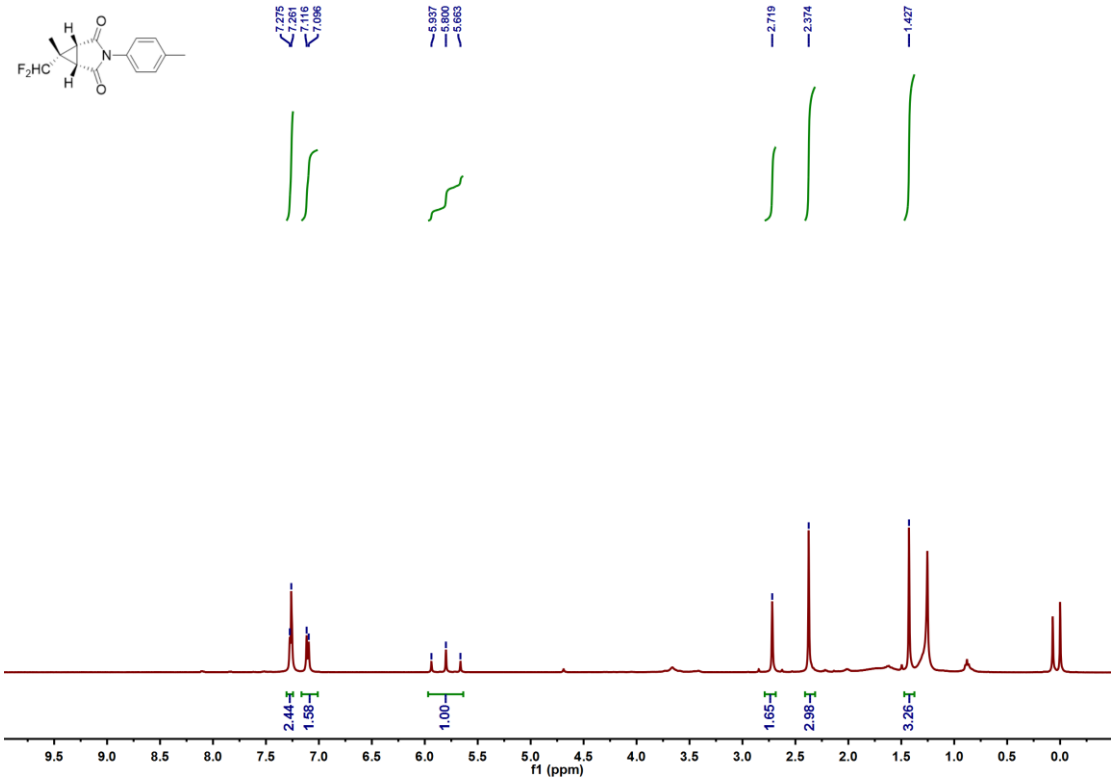


Figure 61. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3j₂**

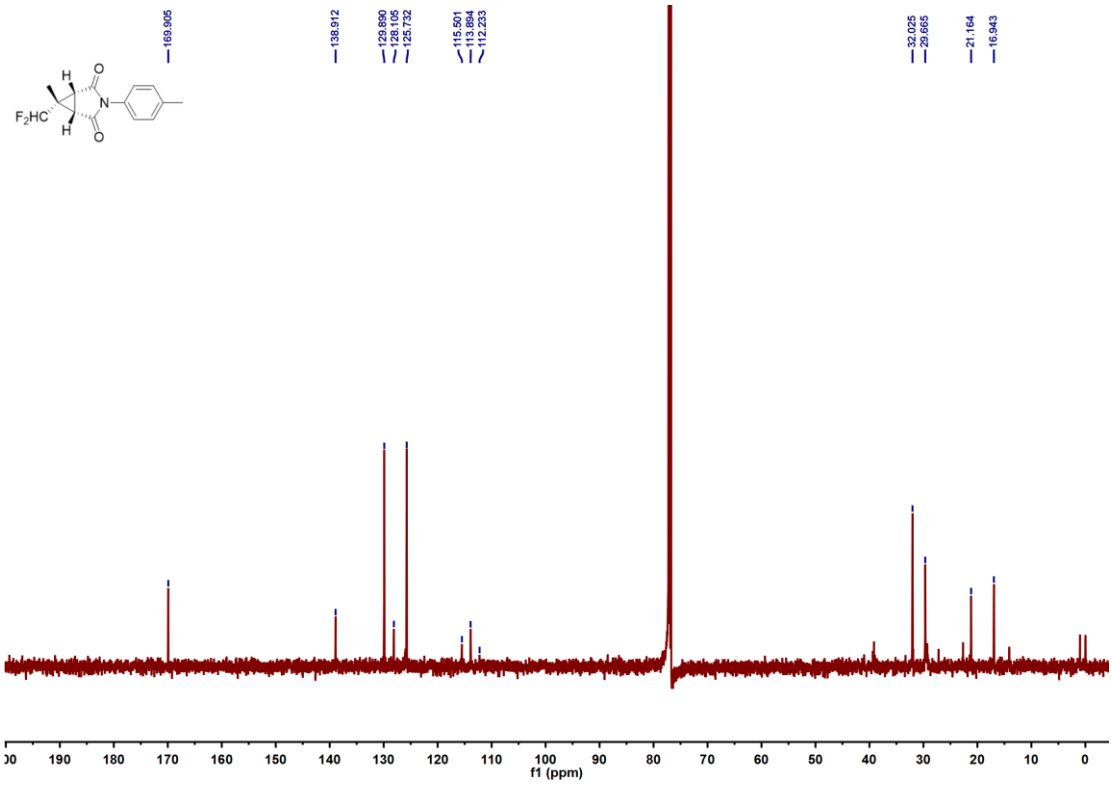


Figure 62. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3j₂**

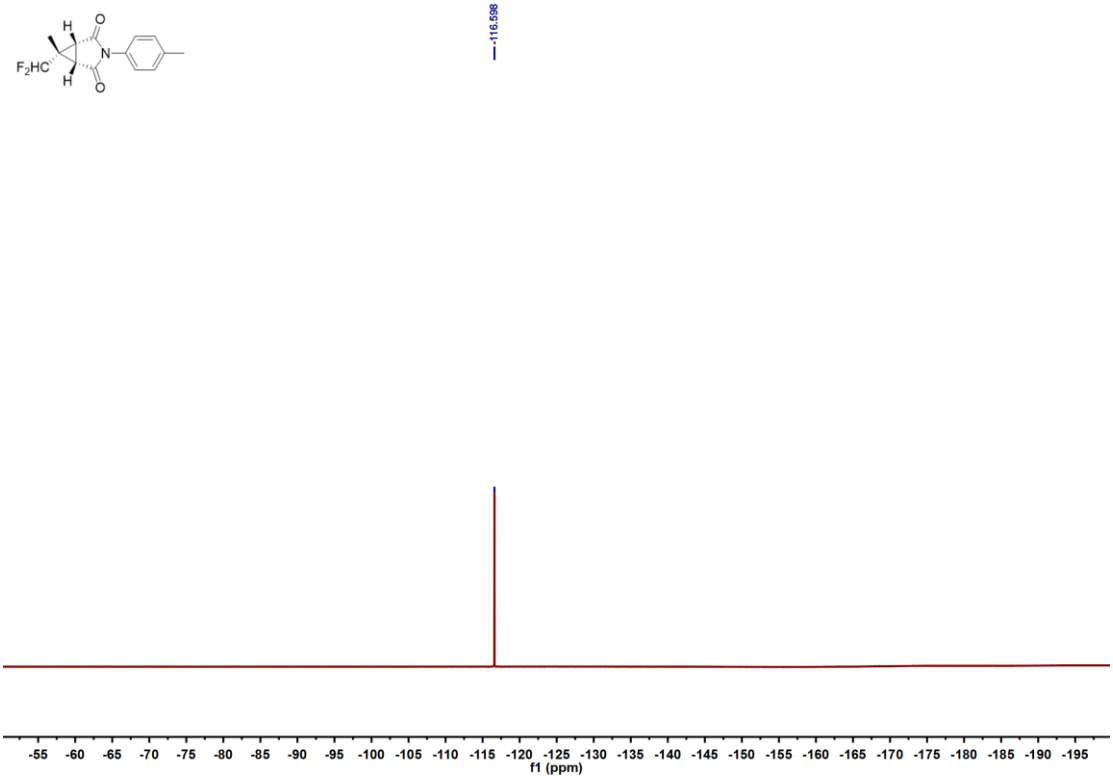


Figure 63. The ^{1}H NMR (400 MHz, DMSO-d_6) of **3k$_1$**

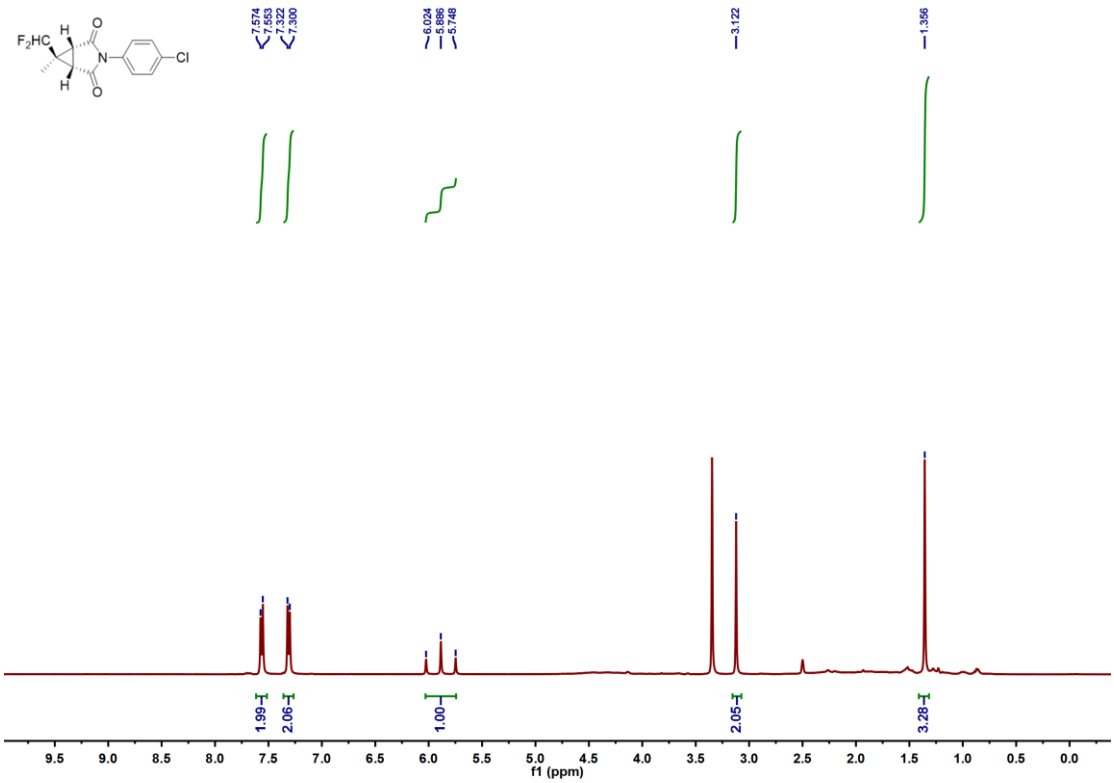


Figure 64. The ^{13}C NMR (150 MHz, DMSO-d_6) of **3k$_1$**

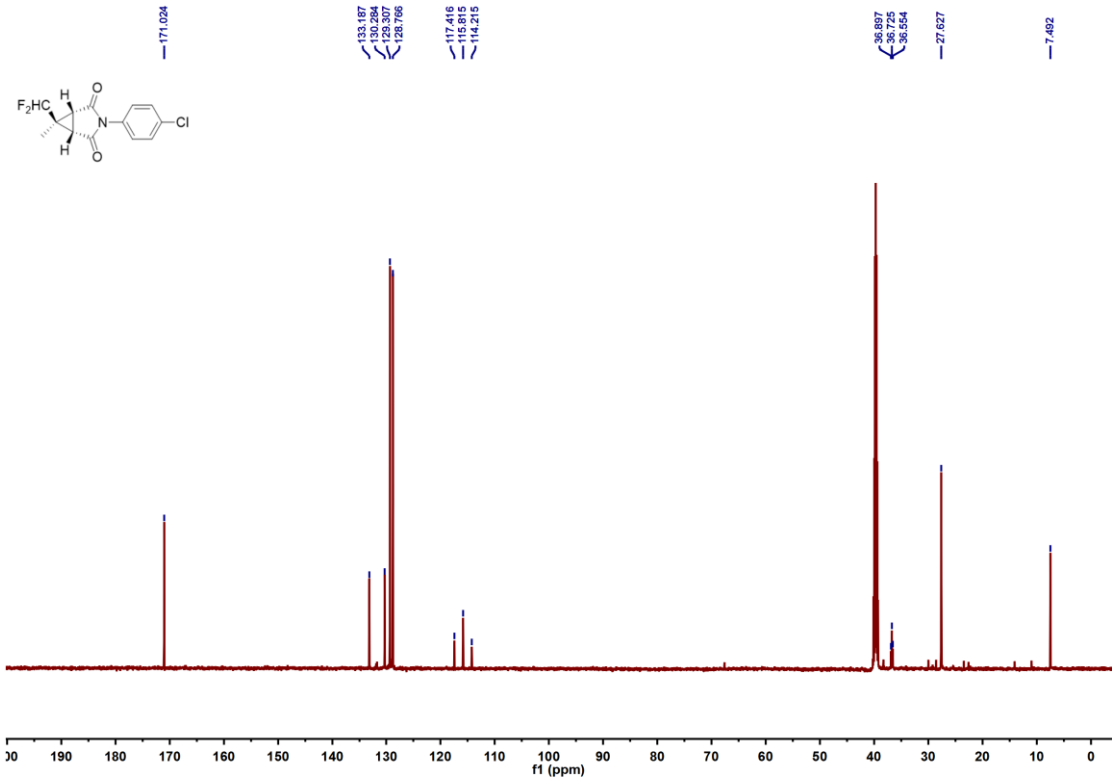


Figure 65. The ^{19}F NMR (376 MHz, DMSO-d_6) of **3k$_1$**

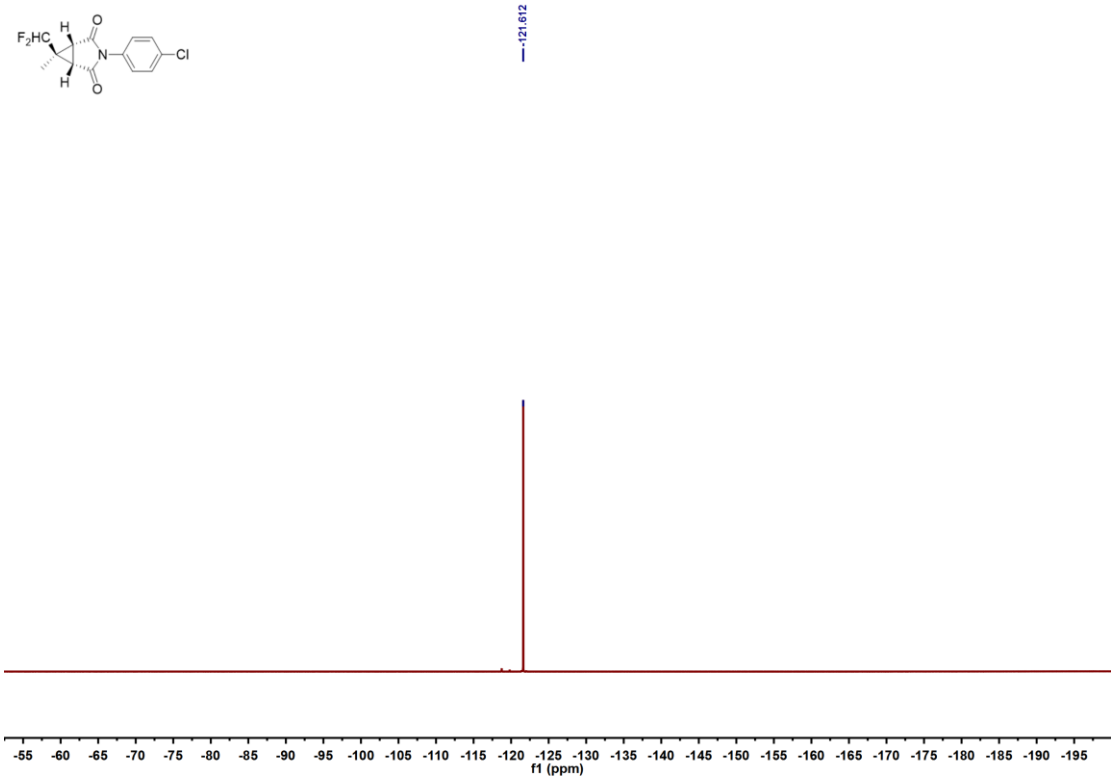


Figure 66. The ^{1}H NMR (400 MHz, DMSO-d_6) of **3k$_2$**

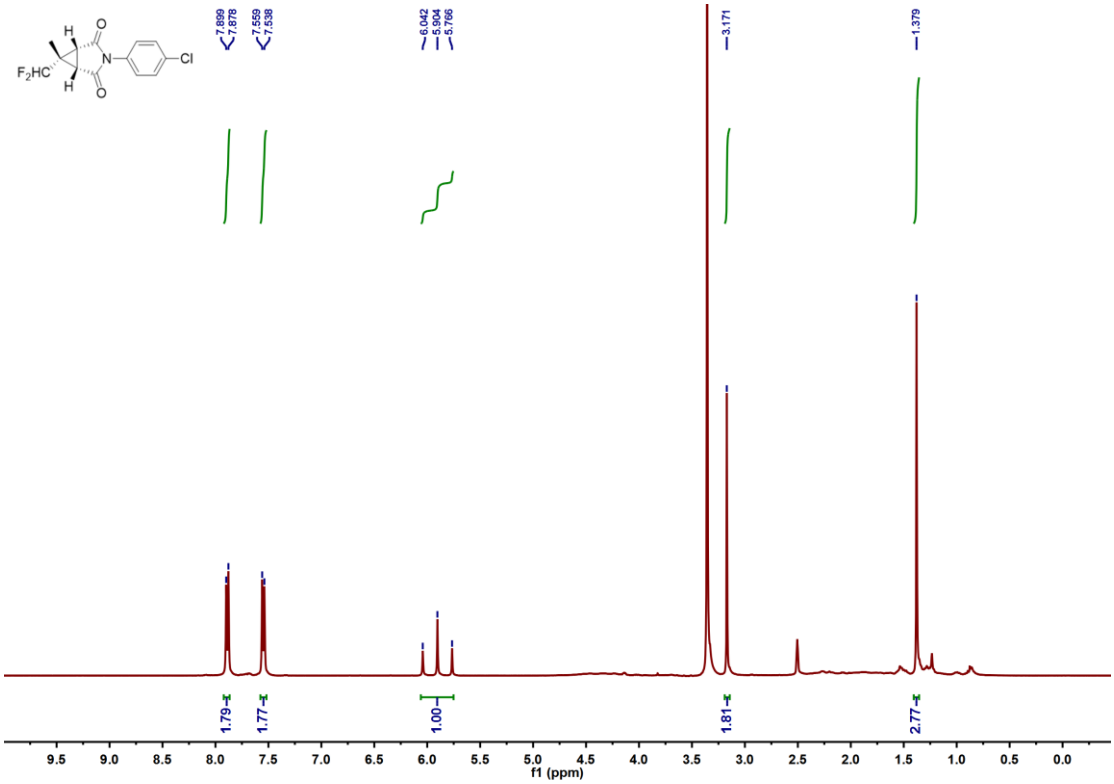


Figure 67. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3k₂**

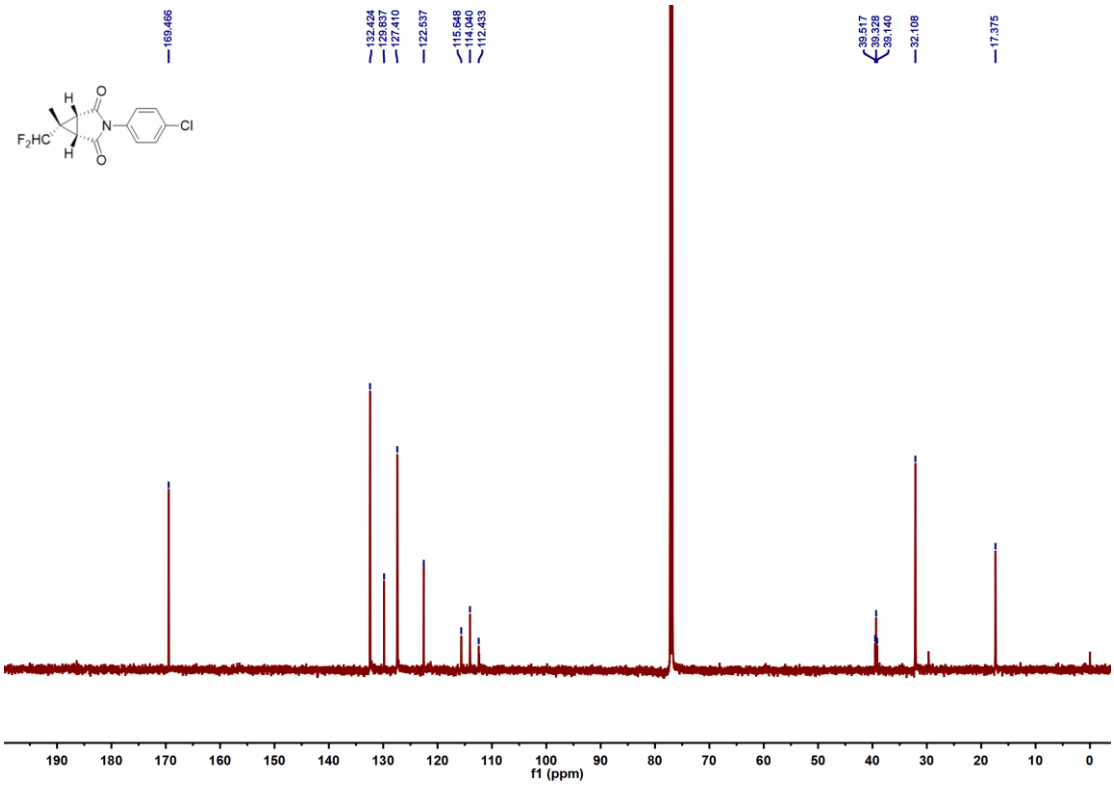


Figure 68. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3k₂**

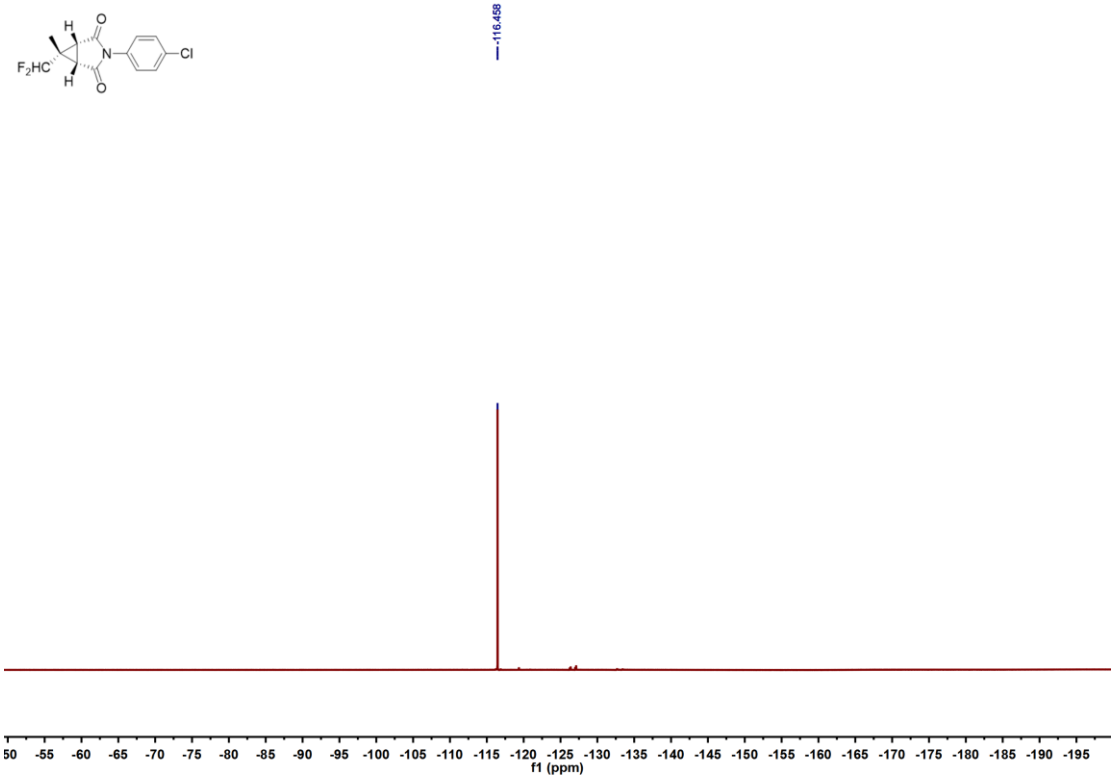


Figure 69. The ^{1}H NMR (400 MHz, $CDCl_3$) of **$3l_1$**

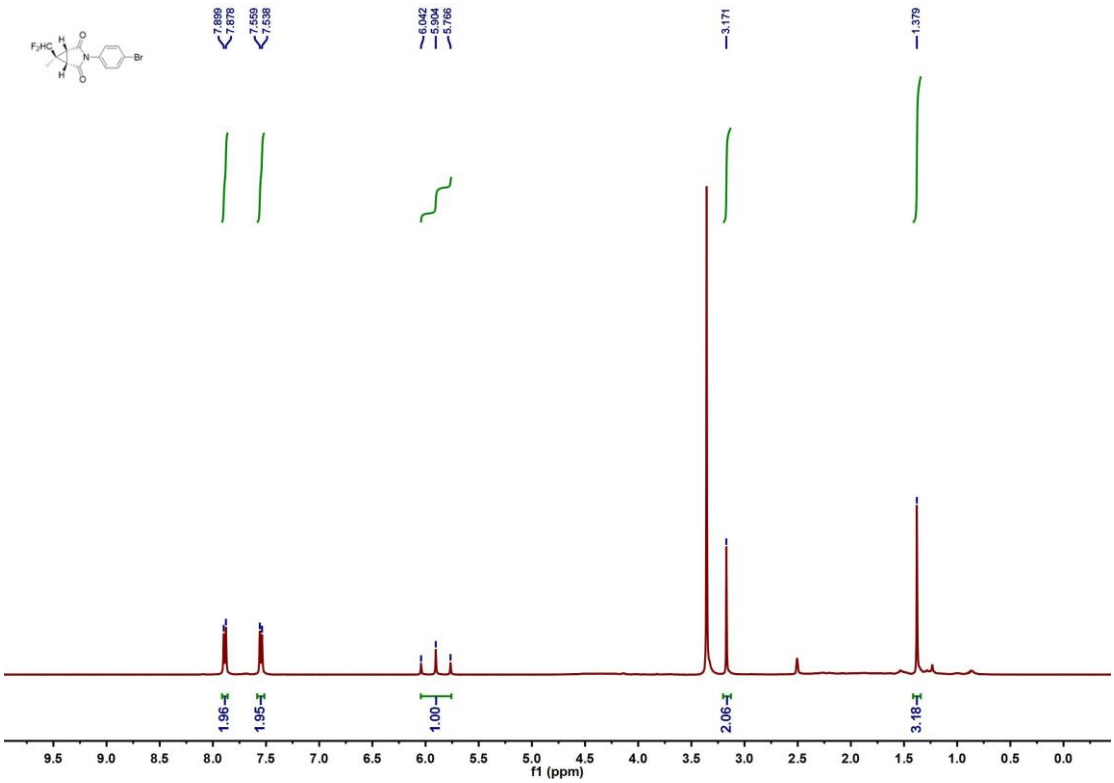


Figure 70. The ^{13}C NMR (100 MHz, $CDCl_3$) of **$3l_1$**

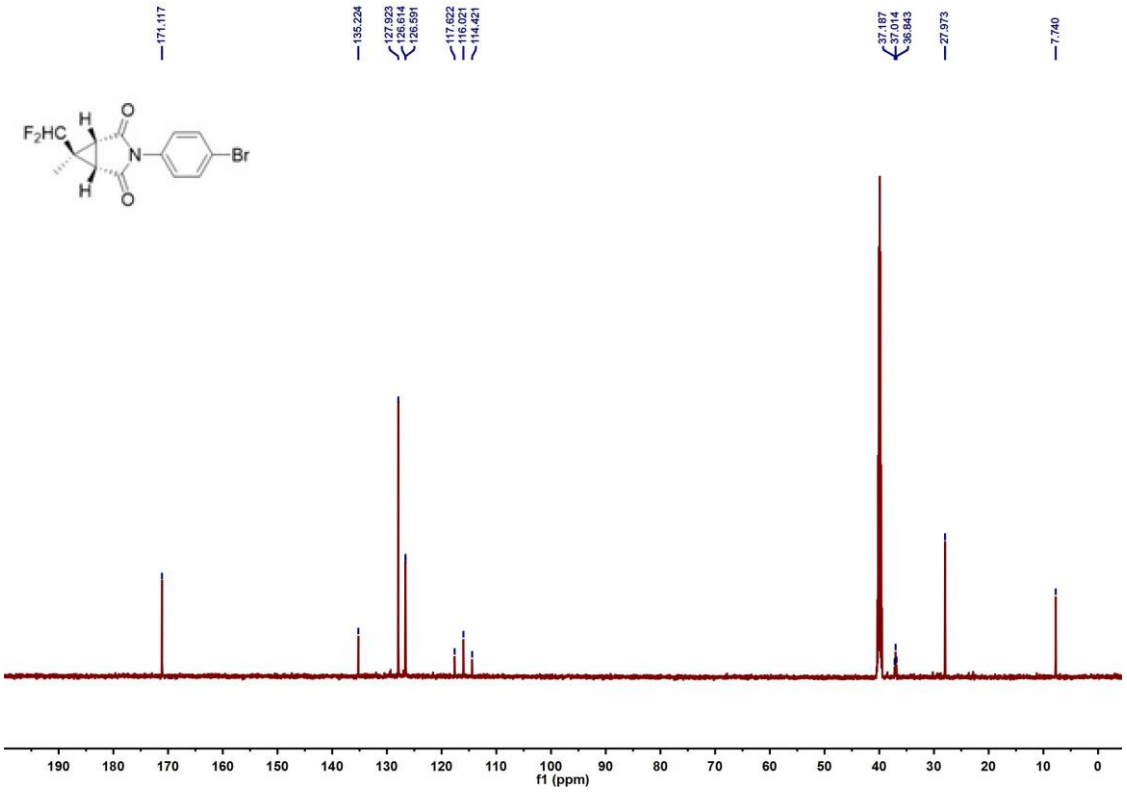


Figure 71. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3l₁**

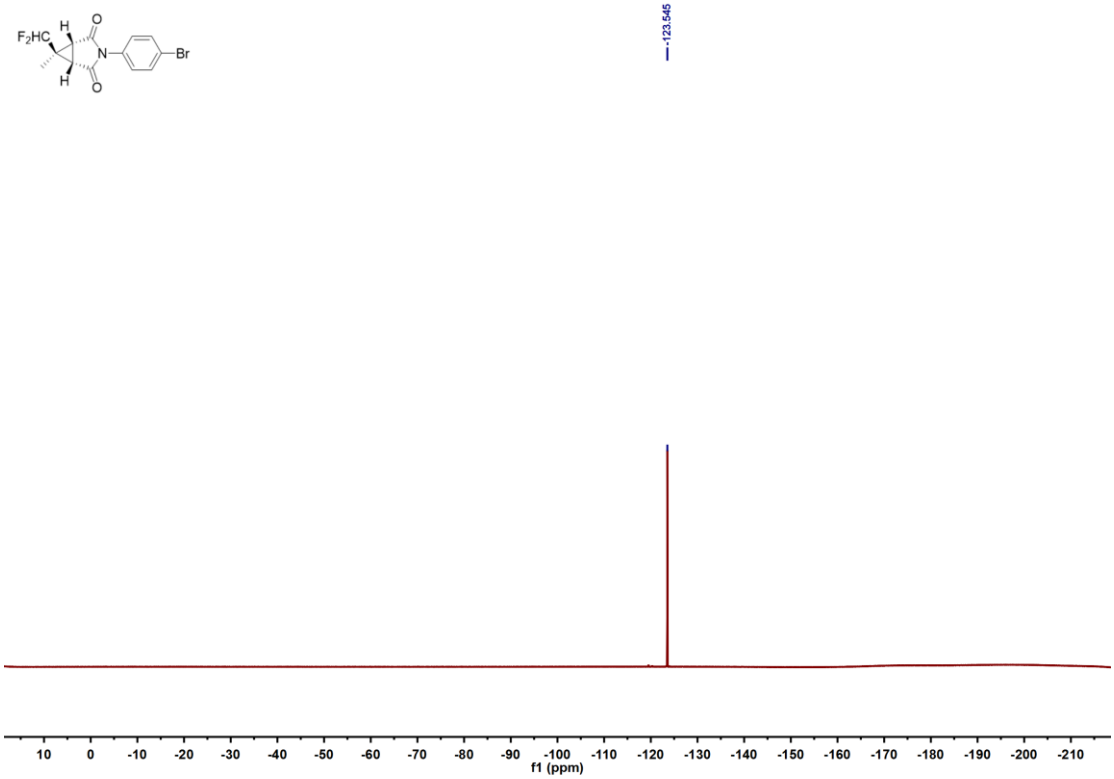


Figure 72. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3l₂**

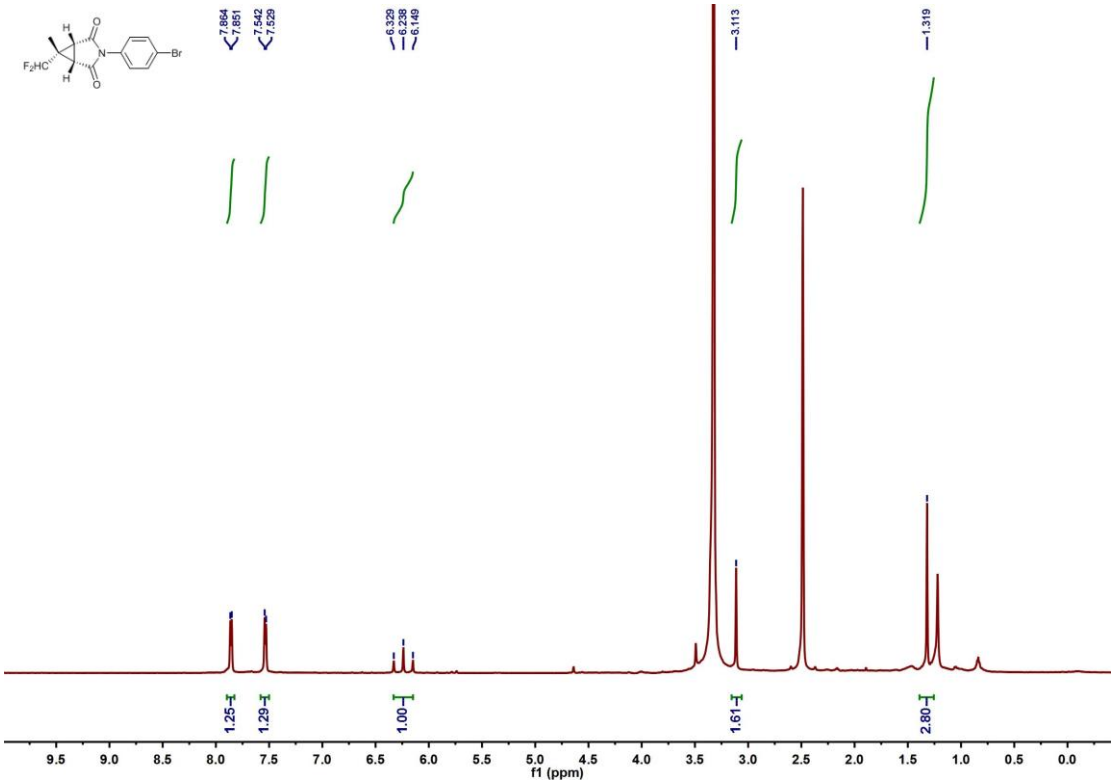


Figure 73. The ^{13}C NMR (100 MHz, $CDCl_3$) of **3l$_2$**

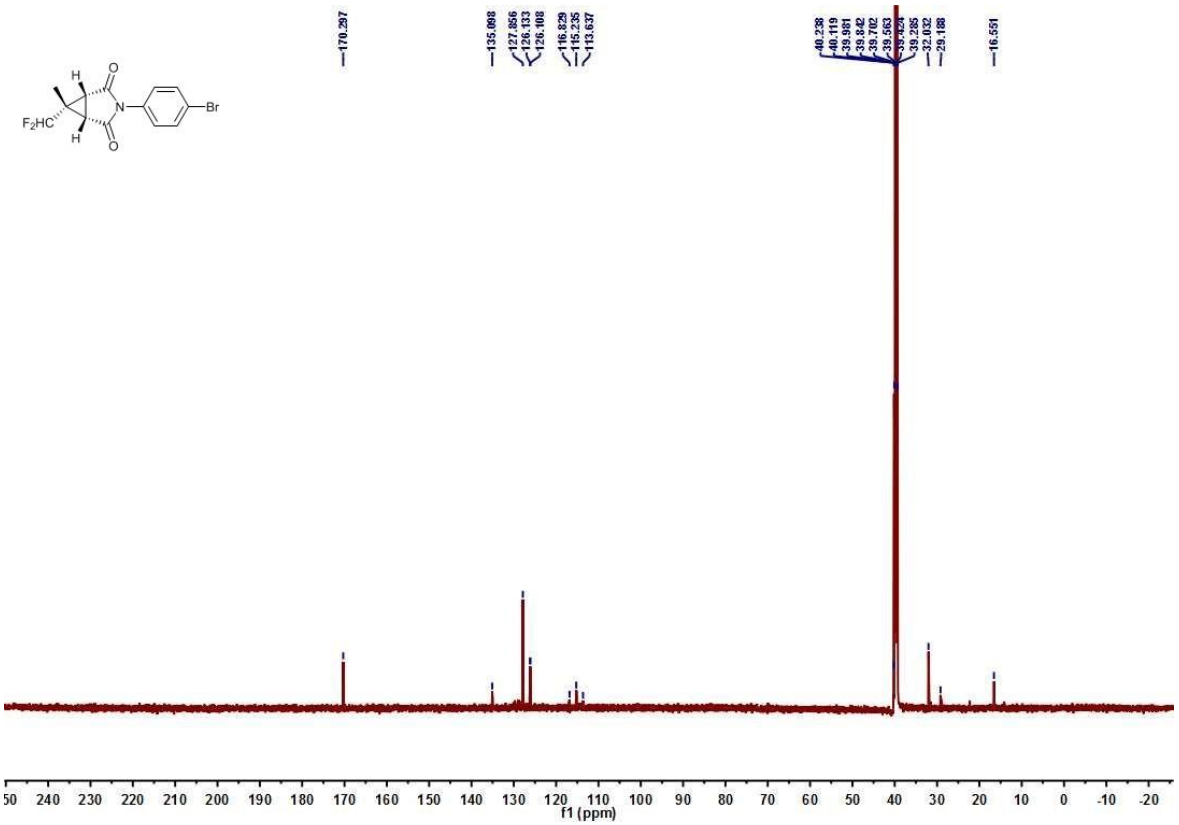


Figure 74. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3l$_2$**

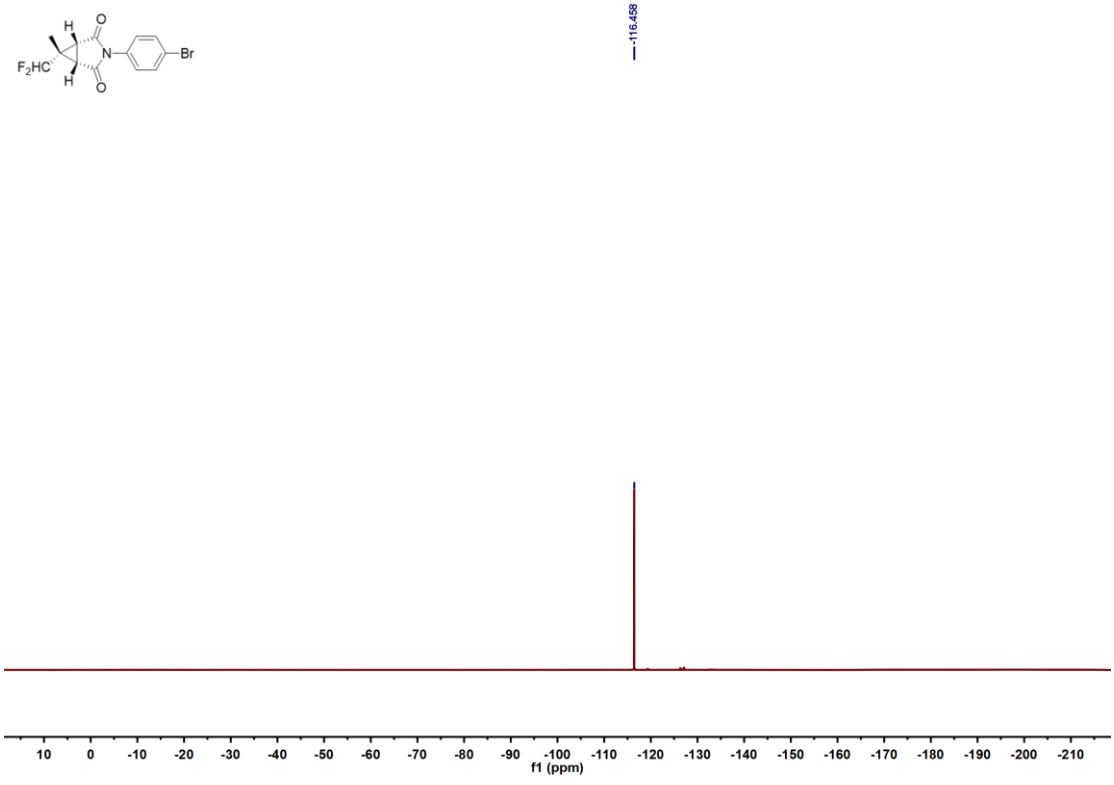


Figure 75. The ^{1}H NMR (600 MHz, $CDCl_3$) of **$3m_1$**

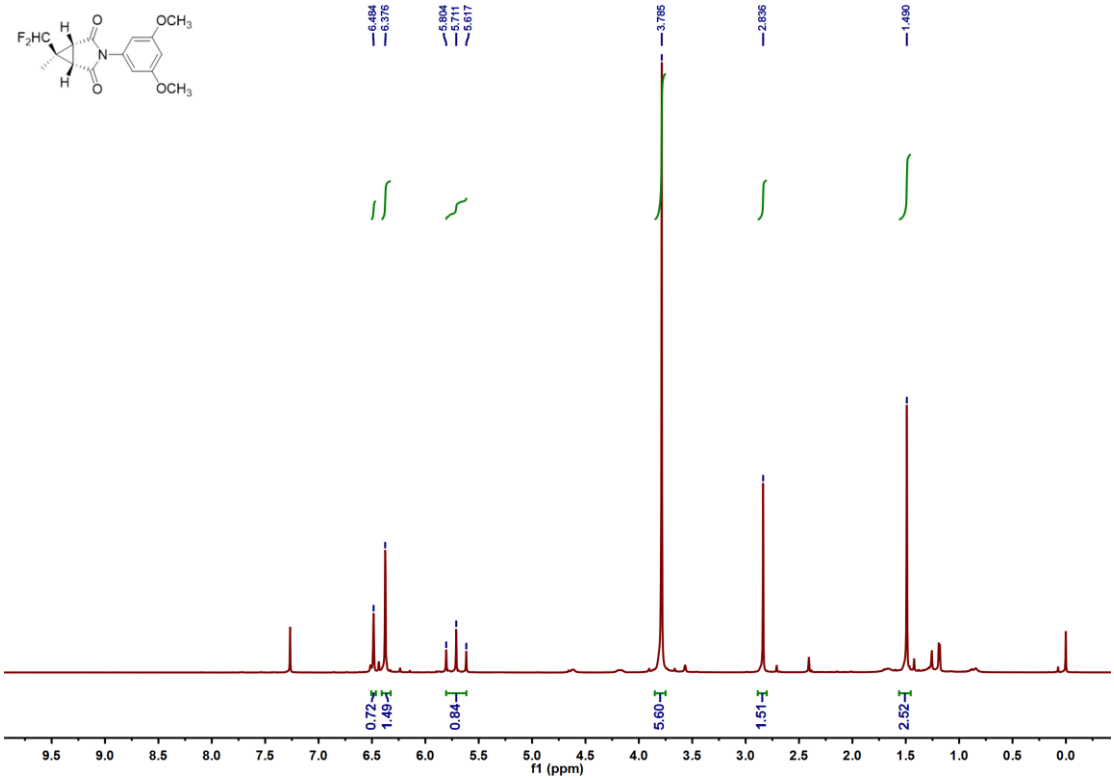


Figure 76. The ^{13}C NMR (150 MHz, $CDCl_3$) of **$3m_1$**

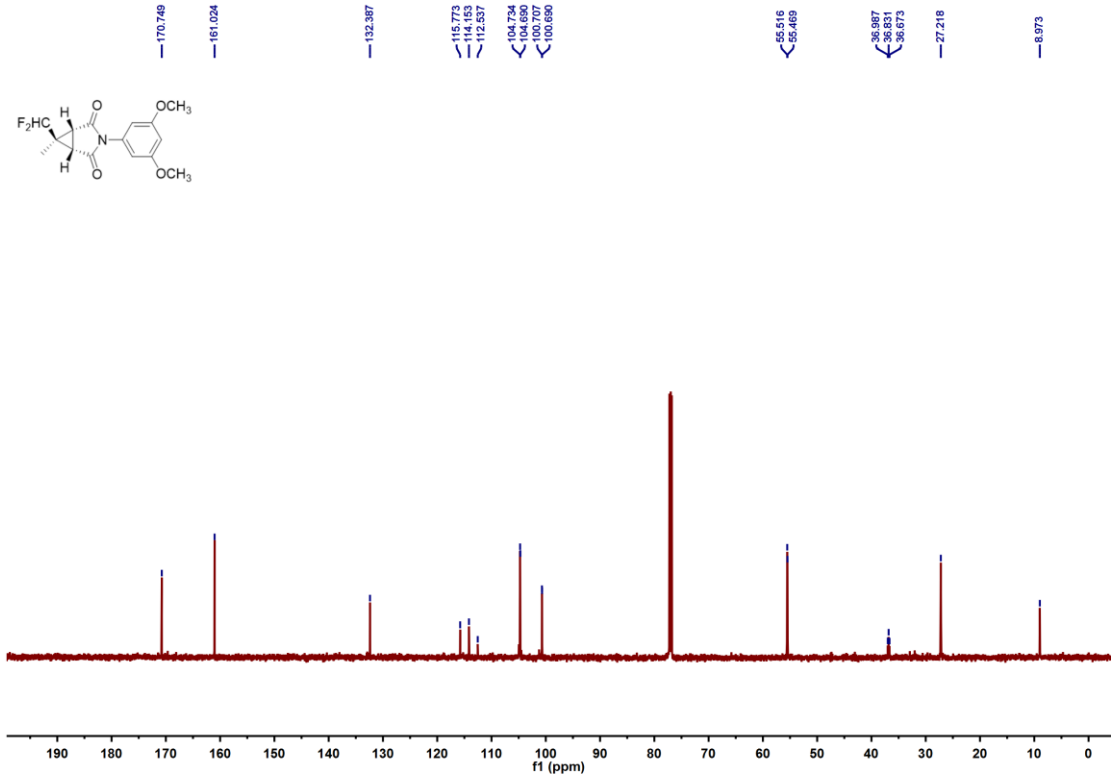


Figure 77. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3m₁**

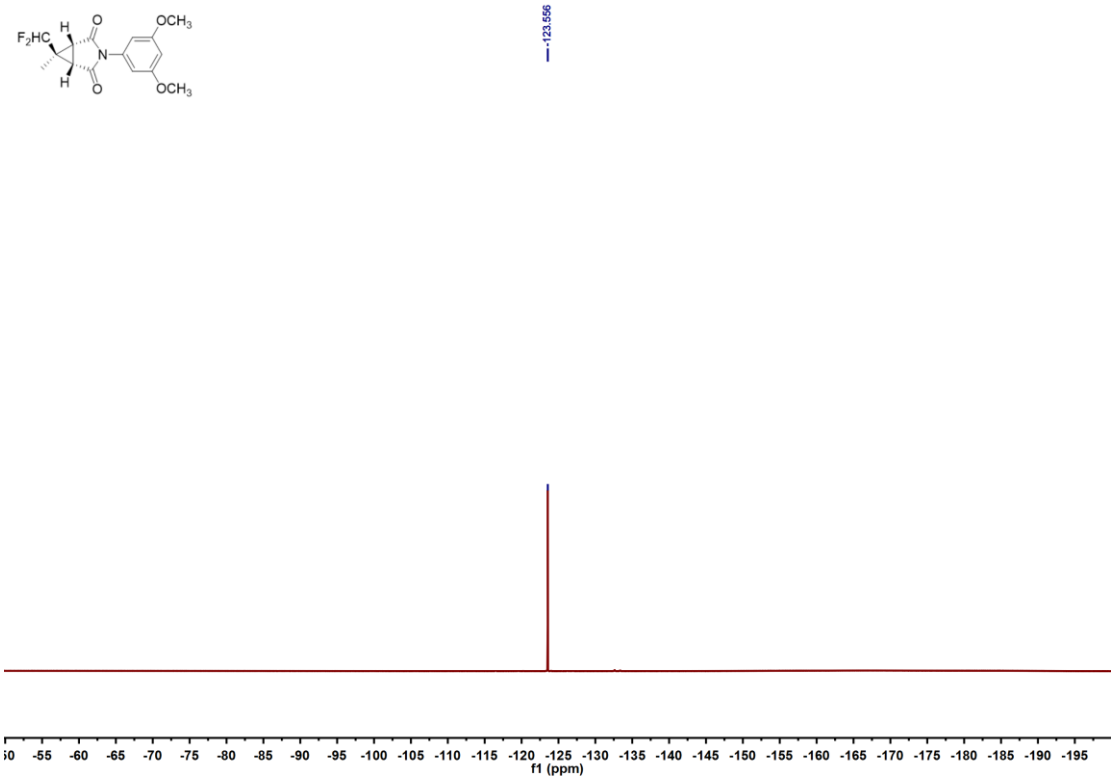


Figure 78. The ^{1}H NMR (600 MHz, $CDCl_3$) of **3m₂**

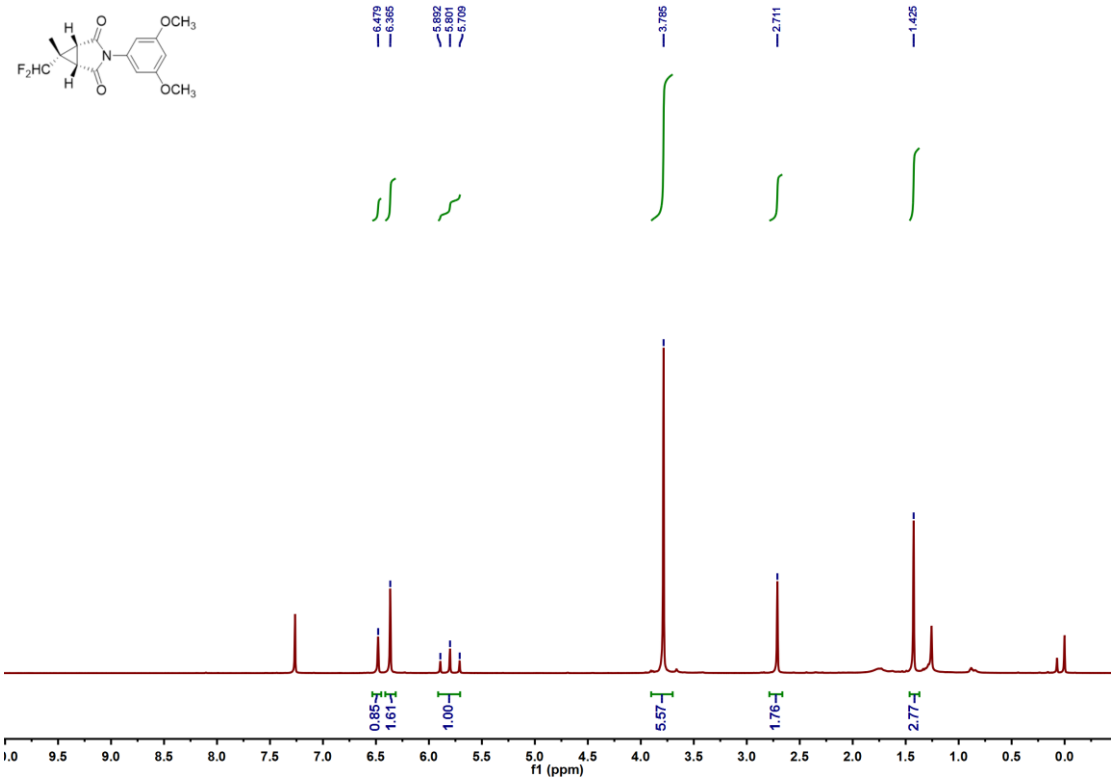


Figure 79. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3m₂**

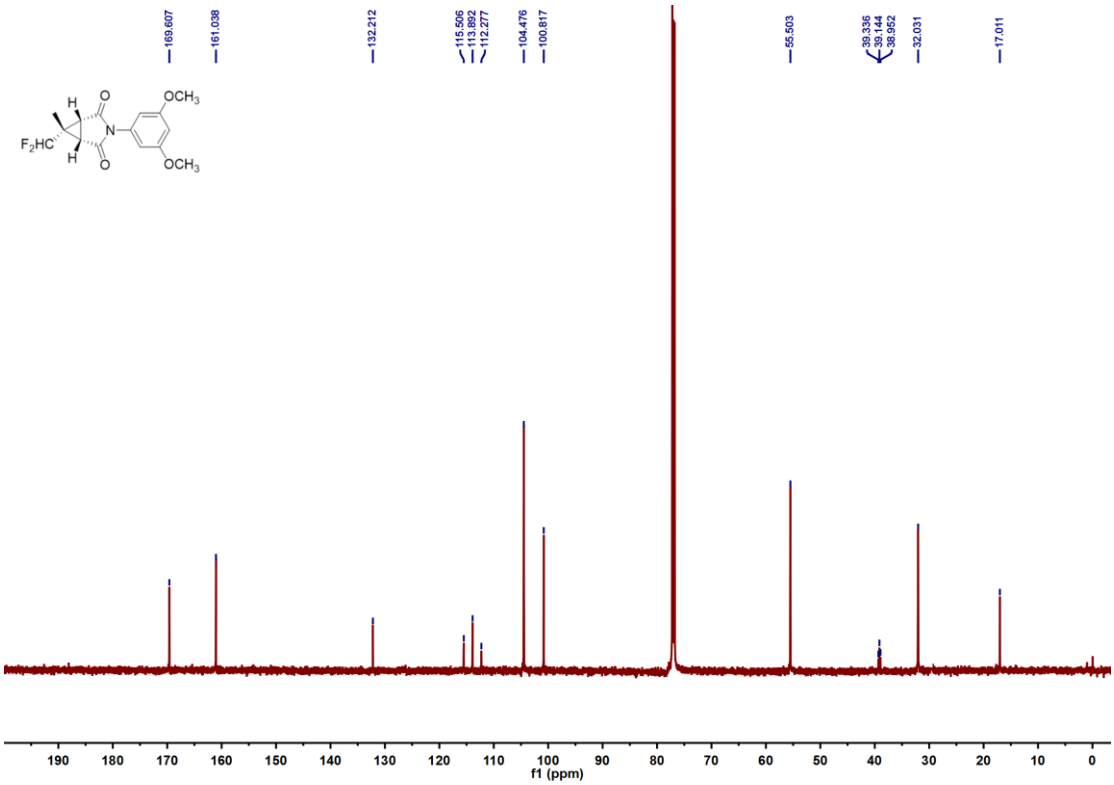


Figure 80. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3m₂**

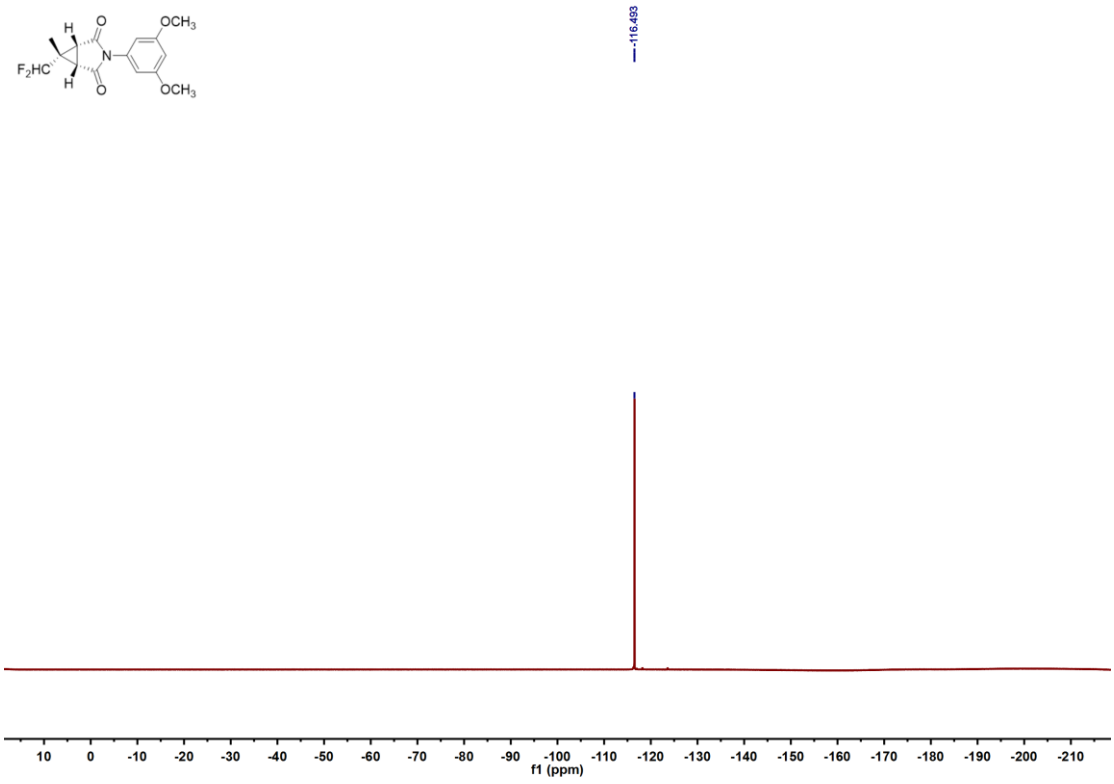


Figure 81. The ^{1}H NMR (400 MHz, DMSO-d_6) of **3n$_1$**

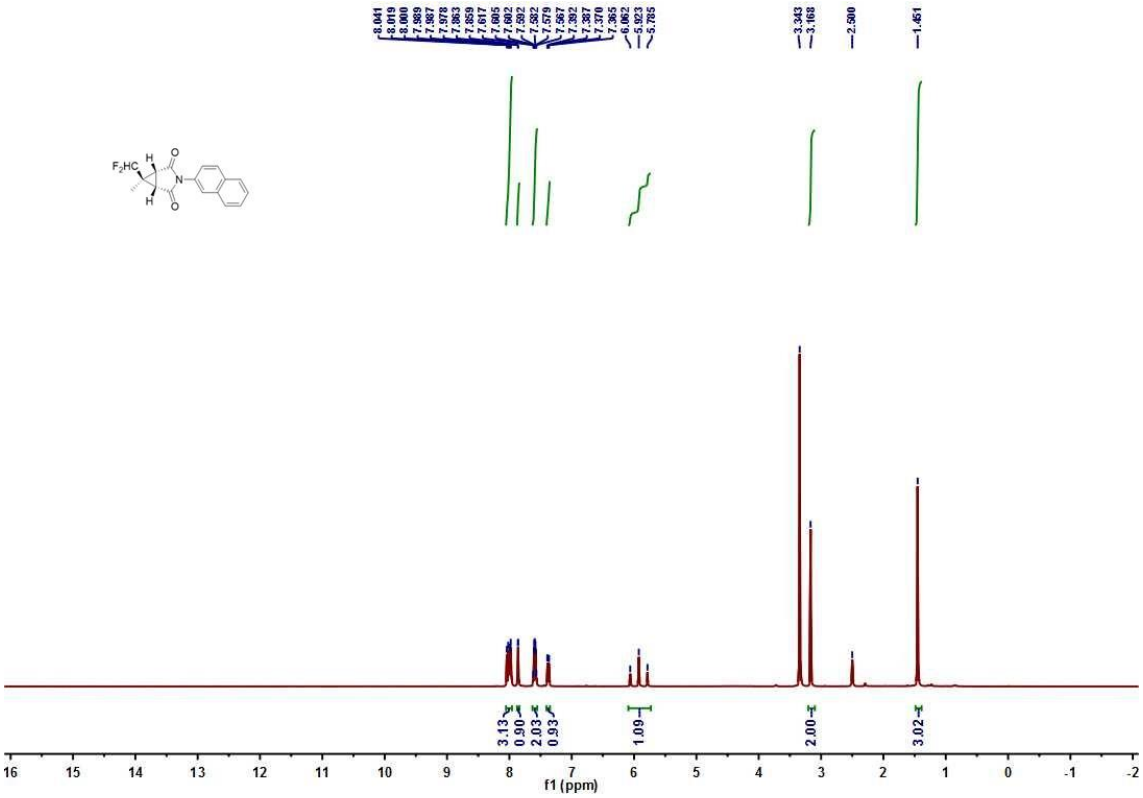


Figure 82. The ^{13}C NMR (100 MHz, DMSO-d_6) of **3n$_1$**

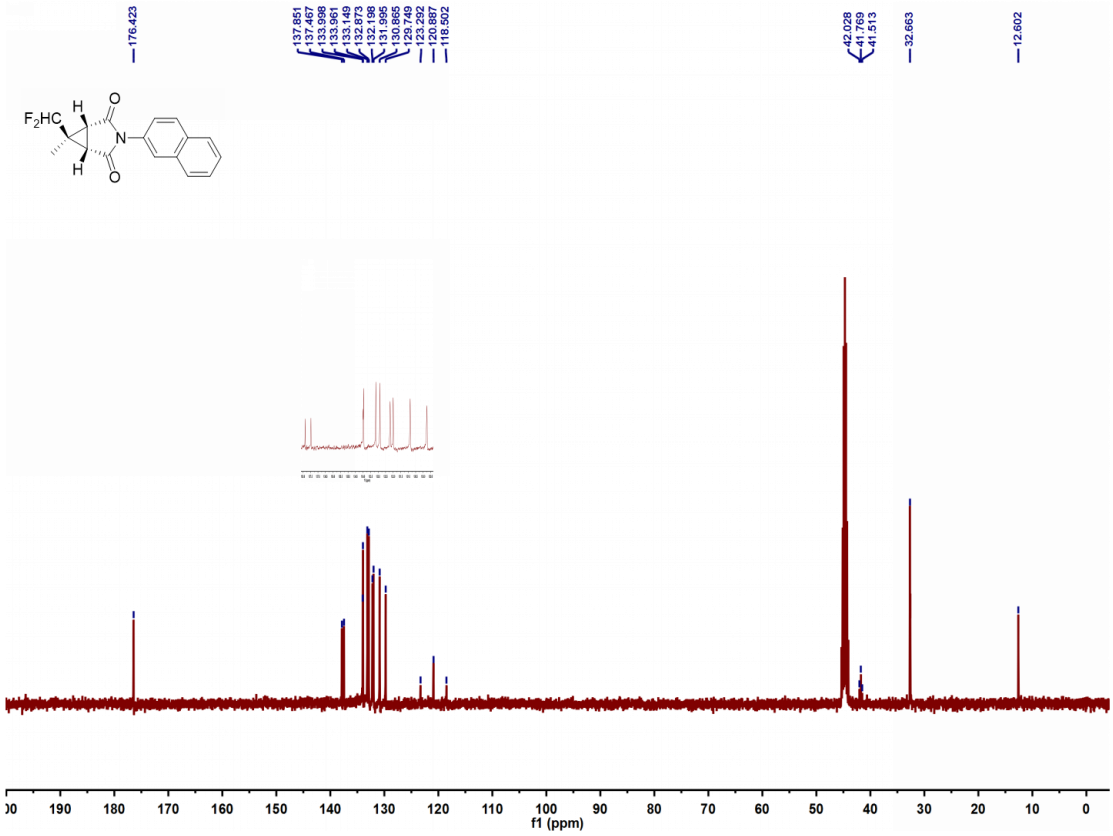


Figure 83. The ^{19}F NMR (376 MHz, DMSO-d_6) of **3n$_1$**

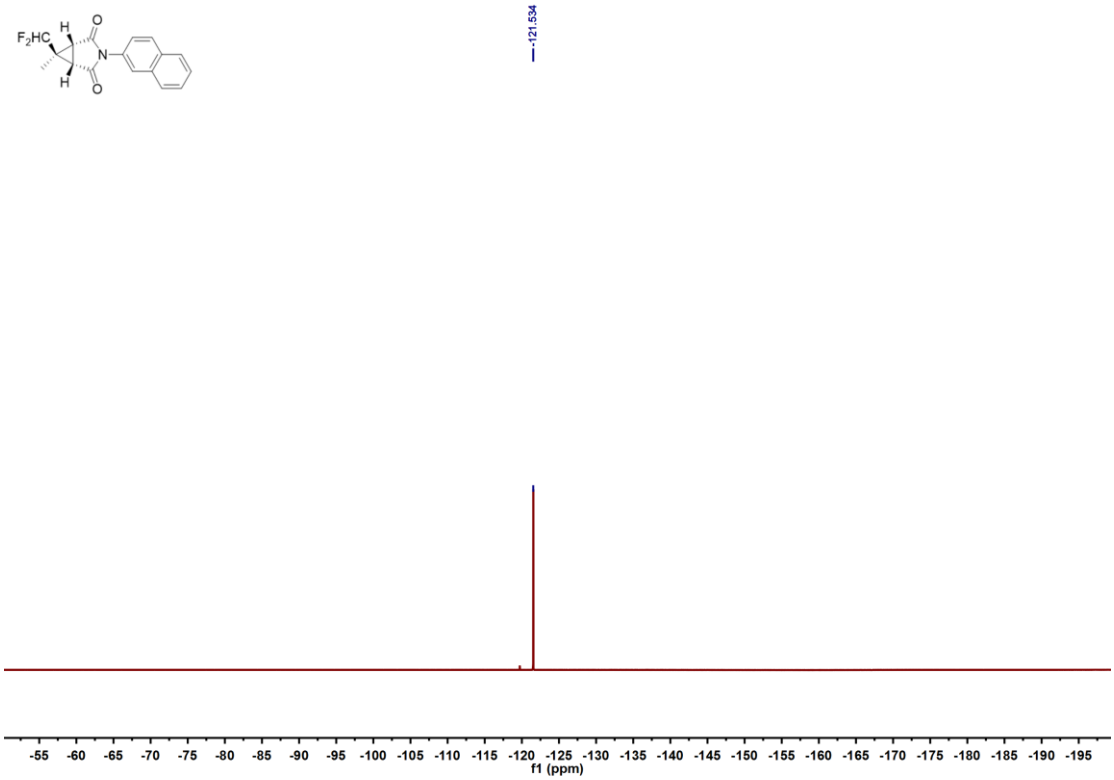


Figure 84. The ^{1}H NMR (400 MHz, DMSO-d_6) of **3n$_2$**

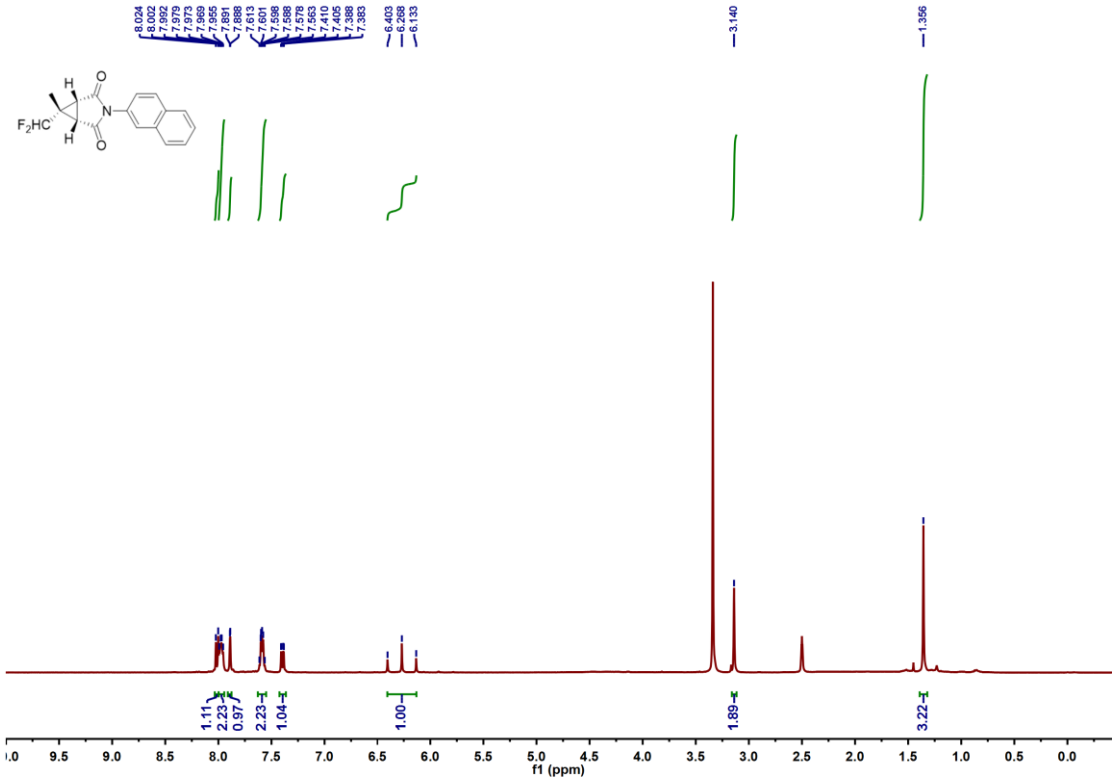


Figure 85. The ^{13}C NMR (150 MHz, DMSO-d_6) of **3n₂**

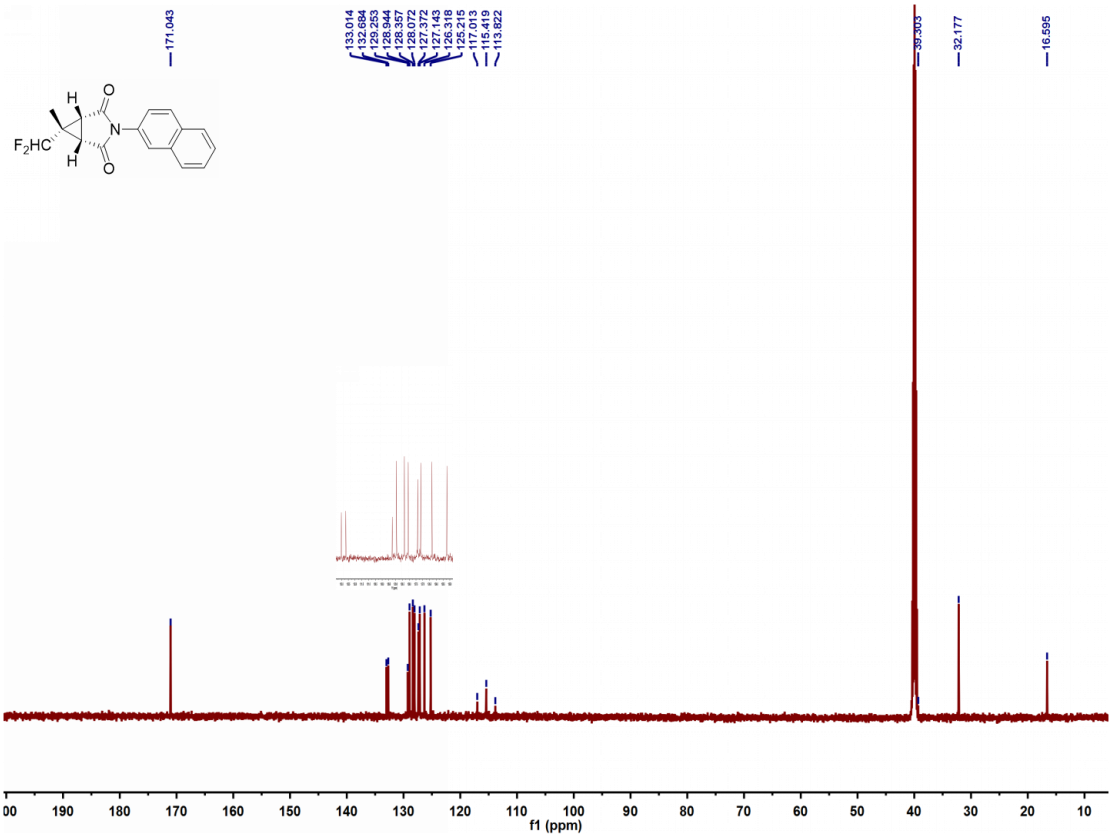


Figure 86. The ^{19}F NMR (376 MHz, DMSO-d_6) of **3n₂**

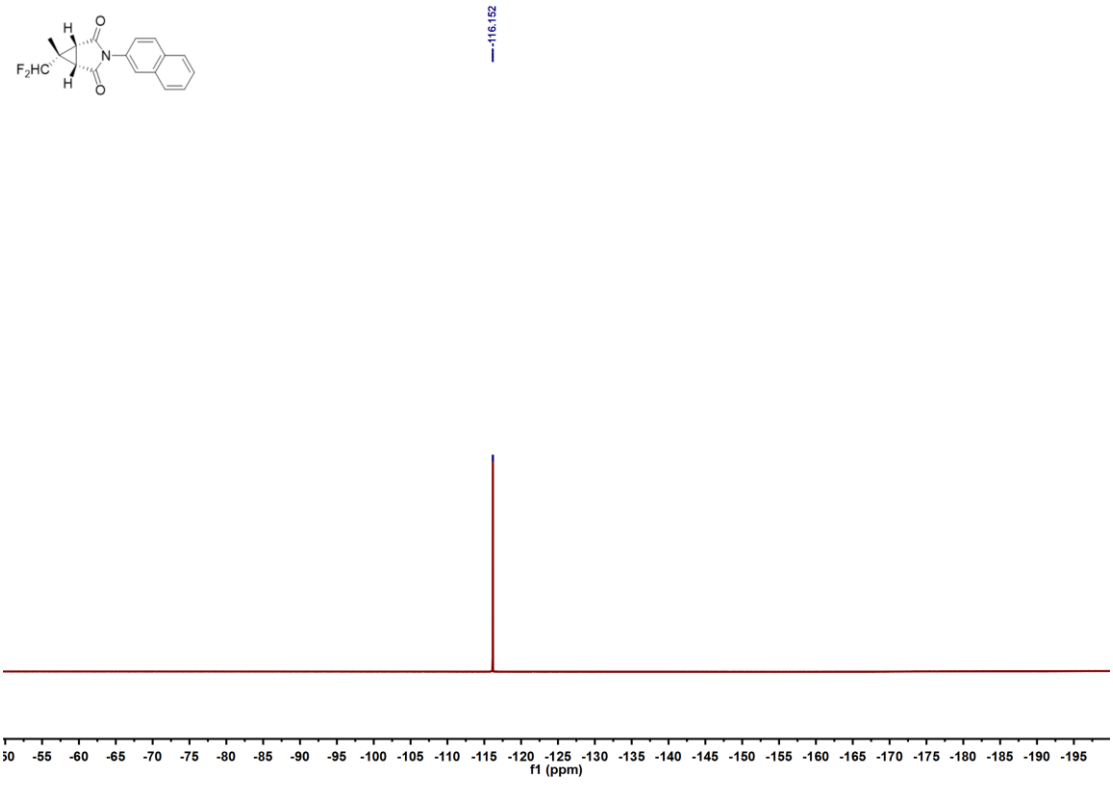


Figure 87. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3o$_1$**

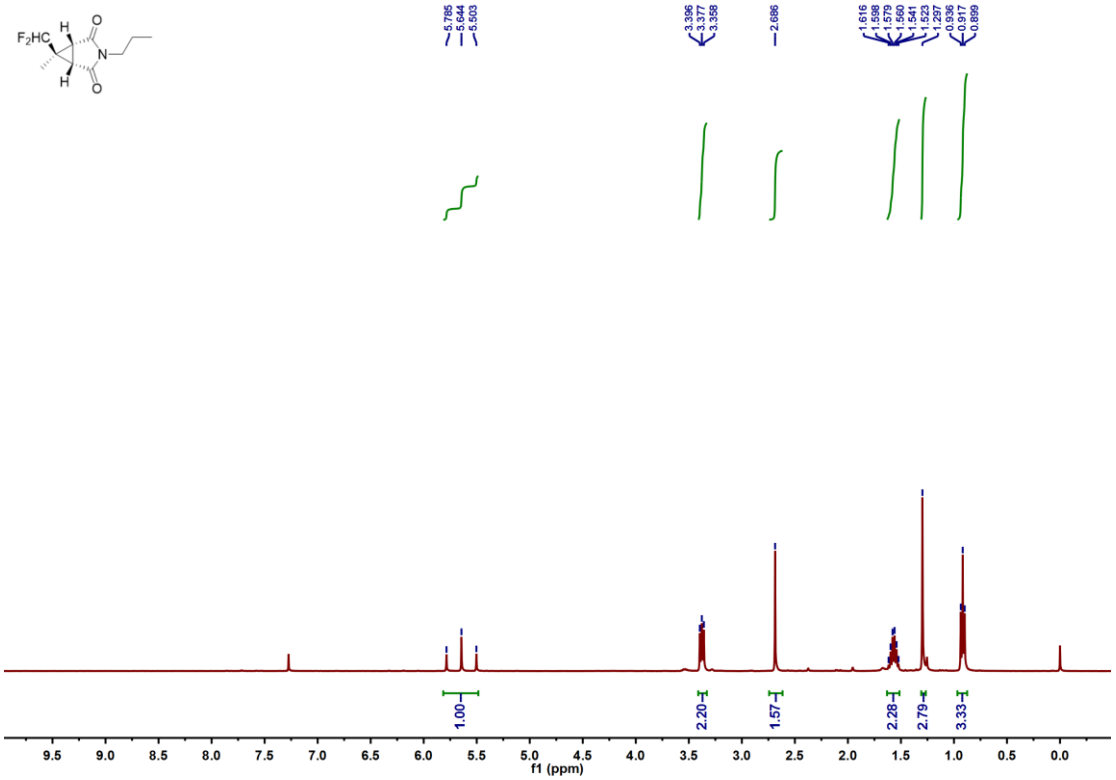


Figure 88. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3o$_1$**

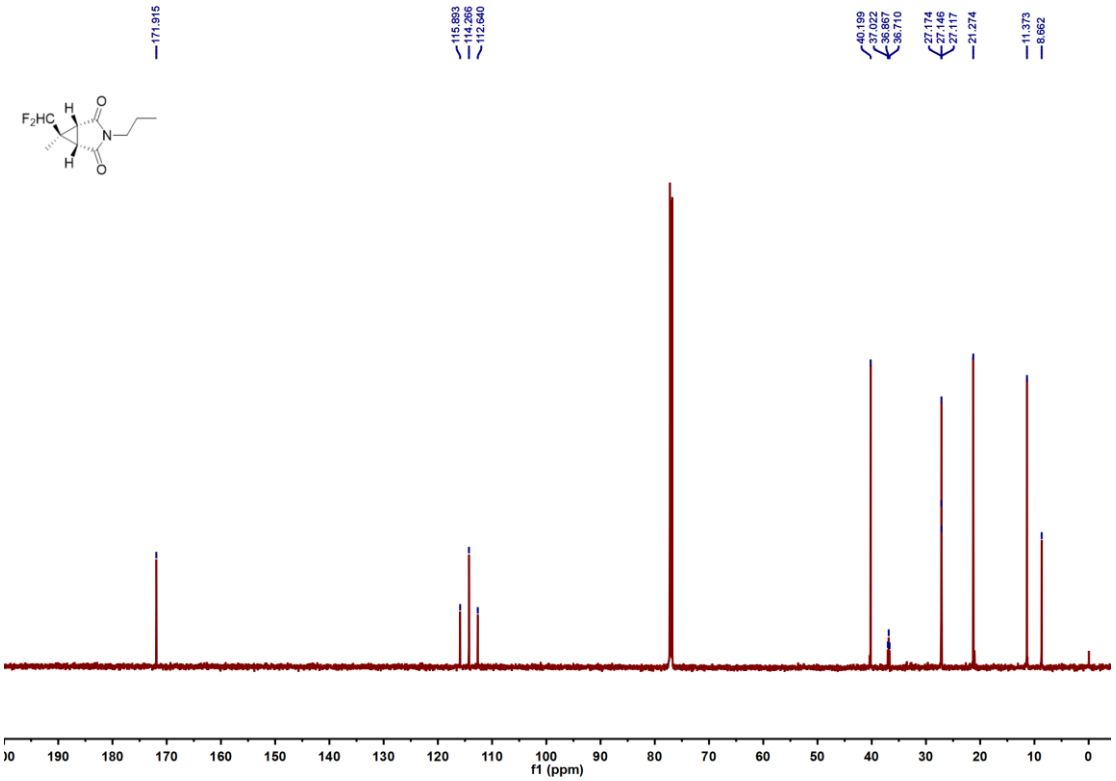


Figure 89. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3o₁**

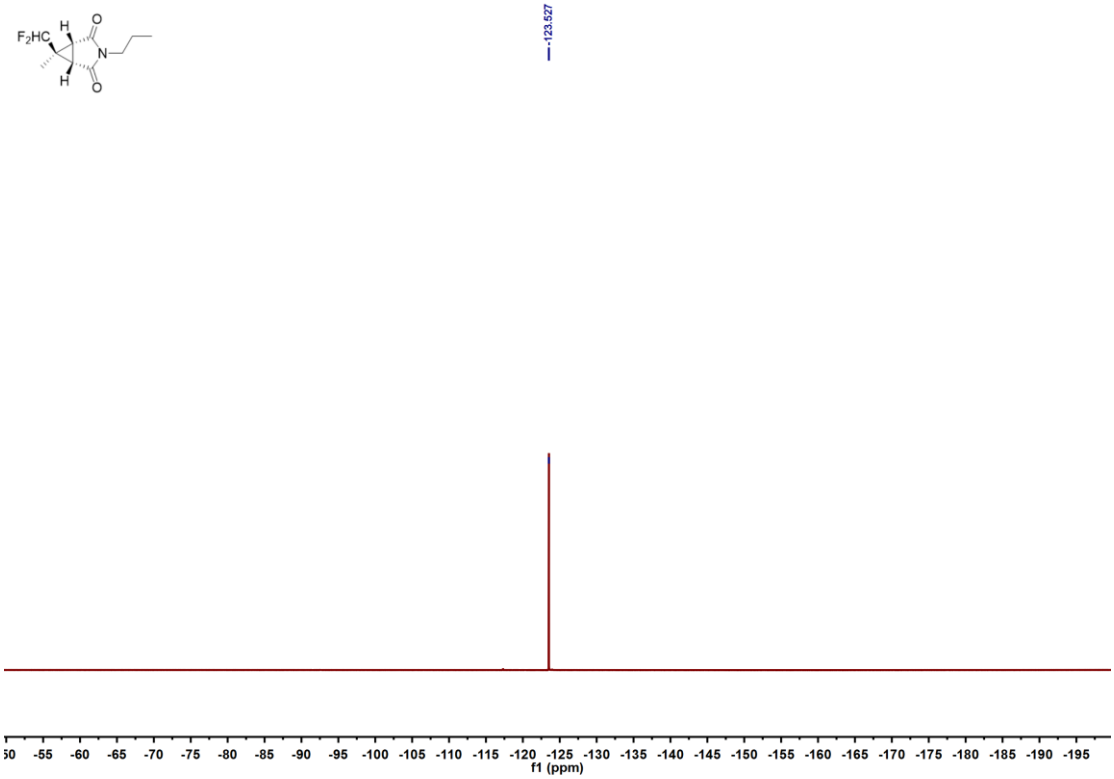


Figure 90. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3o₂**

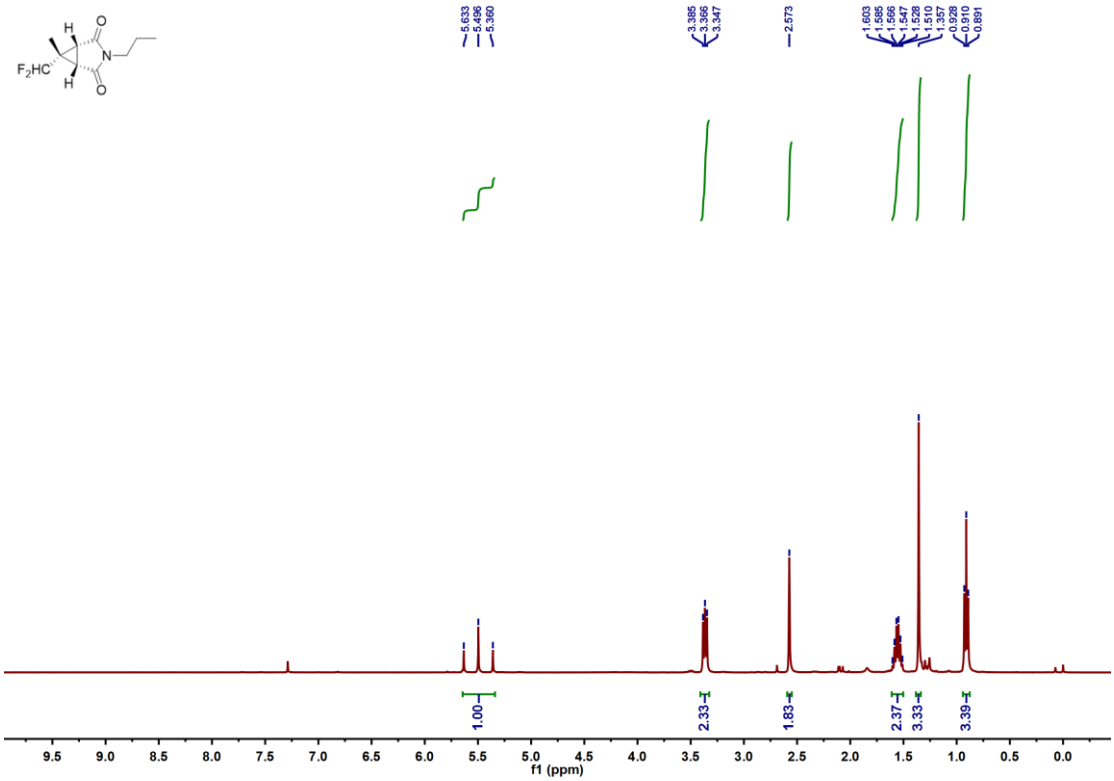


Figure 91. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3o₂**

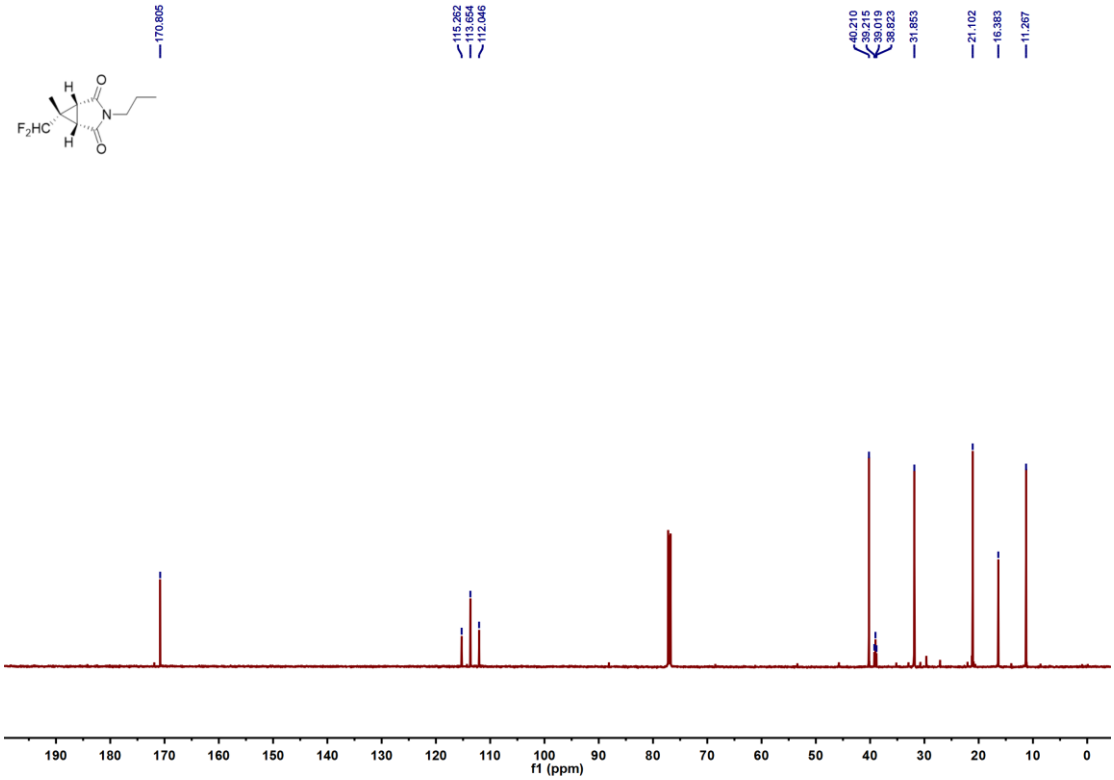


Figure 92. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3o₂**

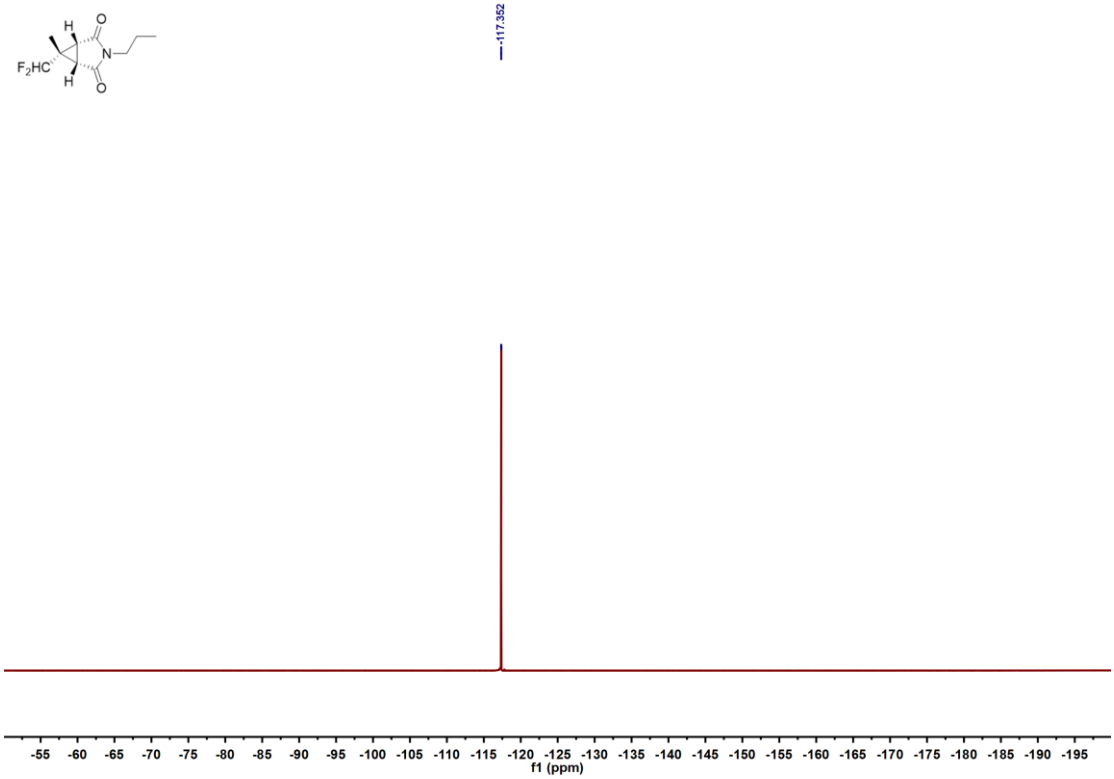


Figure 93. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3p$_1$**

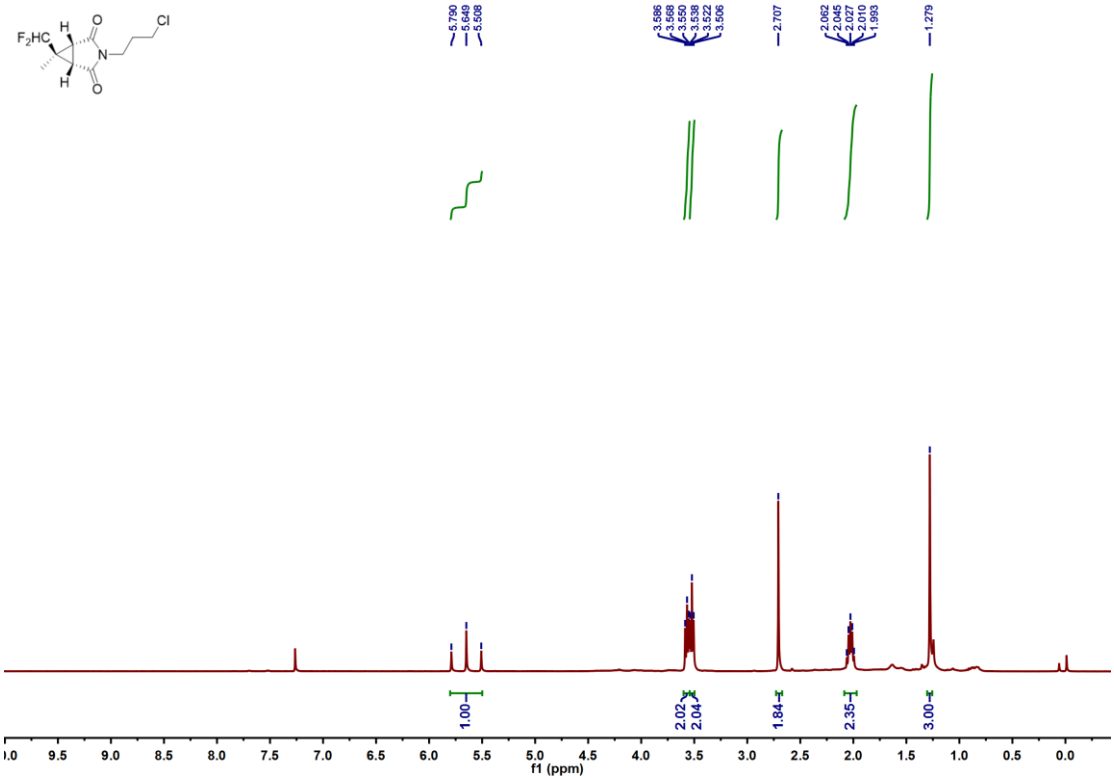


Figure 94. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3p$_1$**

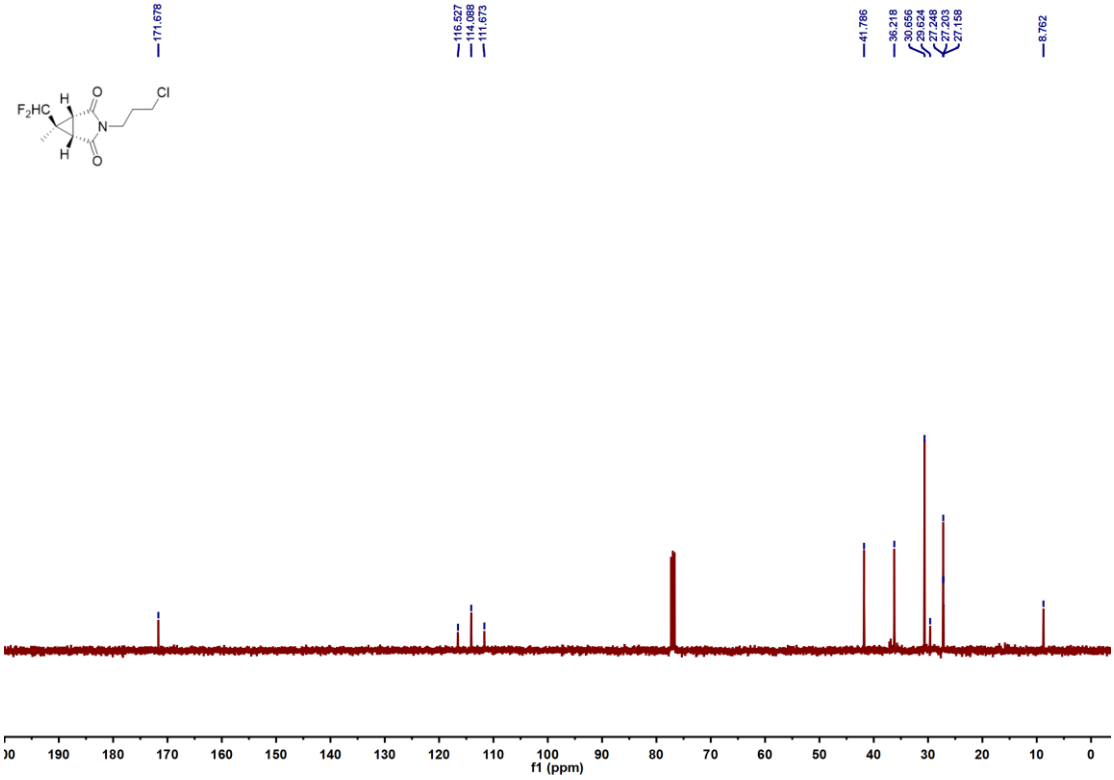


Figure 95. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3p₁**

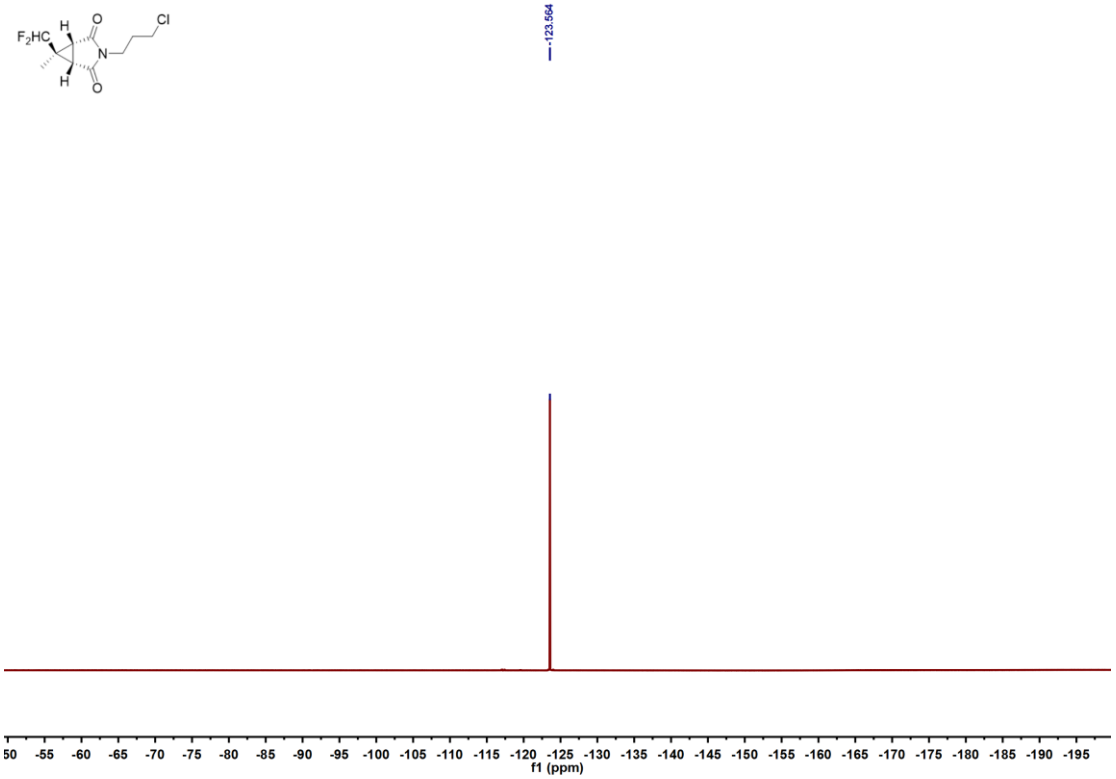


Figure 96. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3p₂**

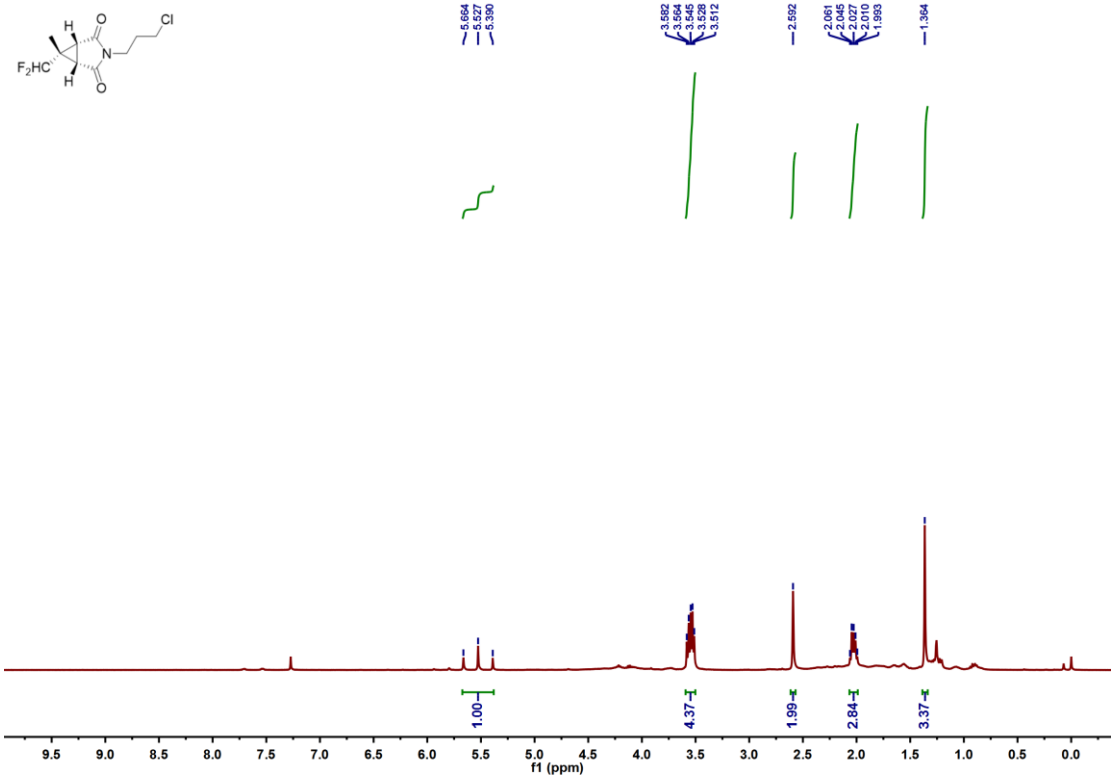


Figure 97. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3p₂**

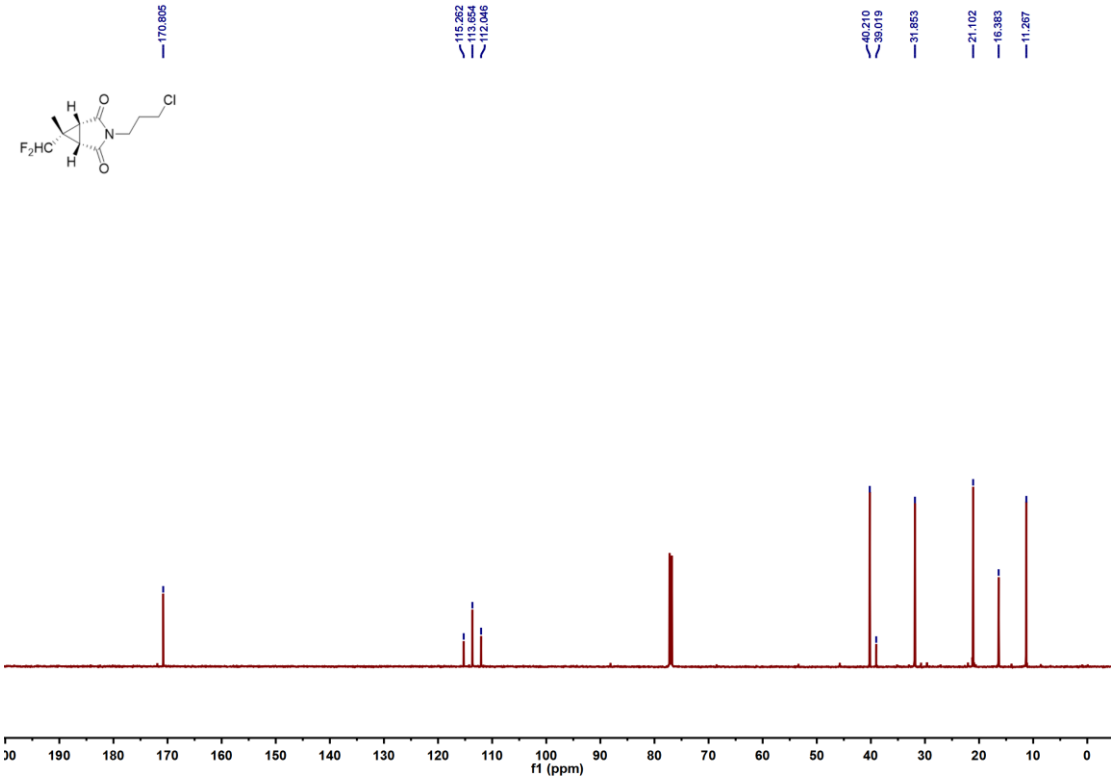


Figure 98. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3p₂**

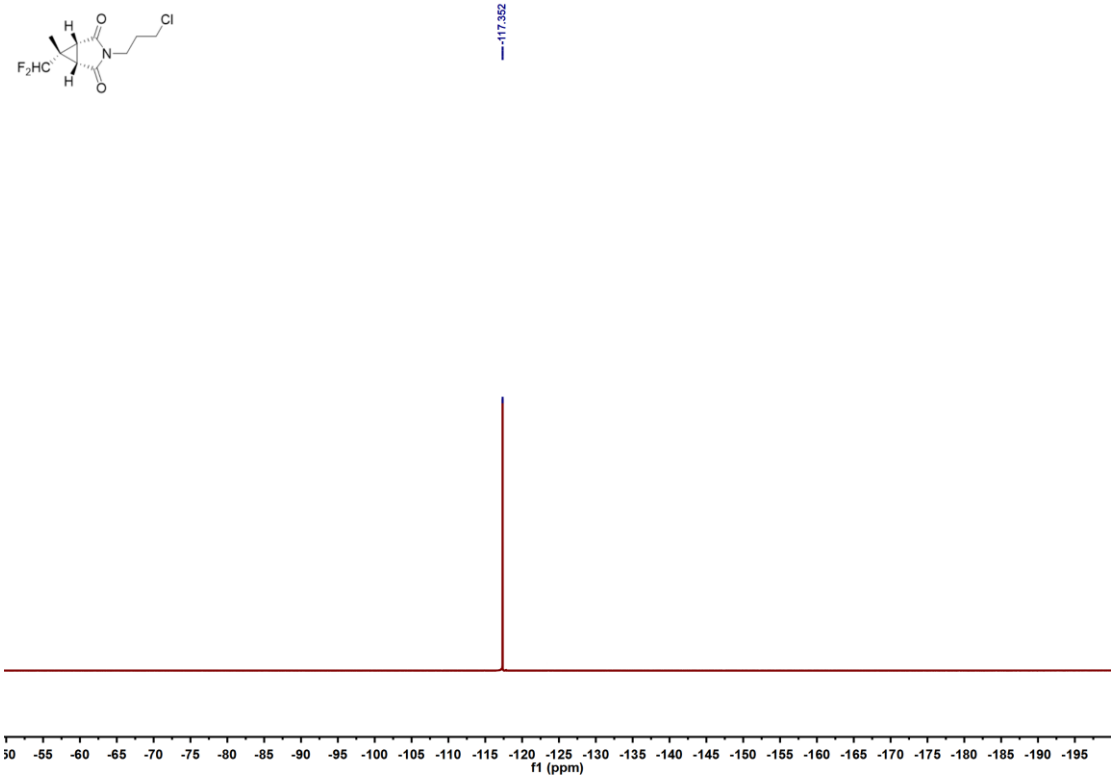


Figure 99. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3q$_1$**

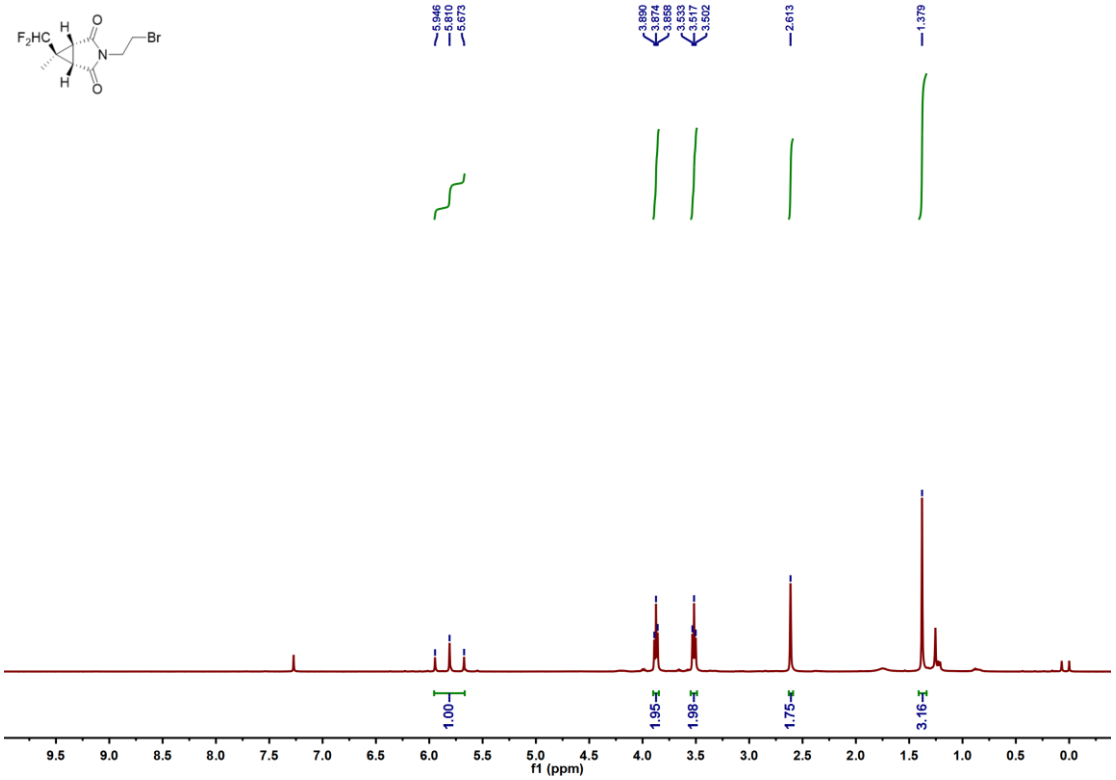


Figure 100. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3q$_1$**

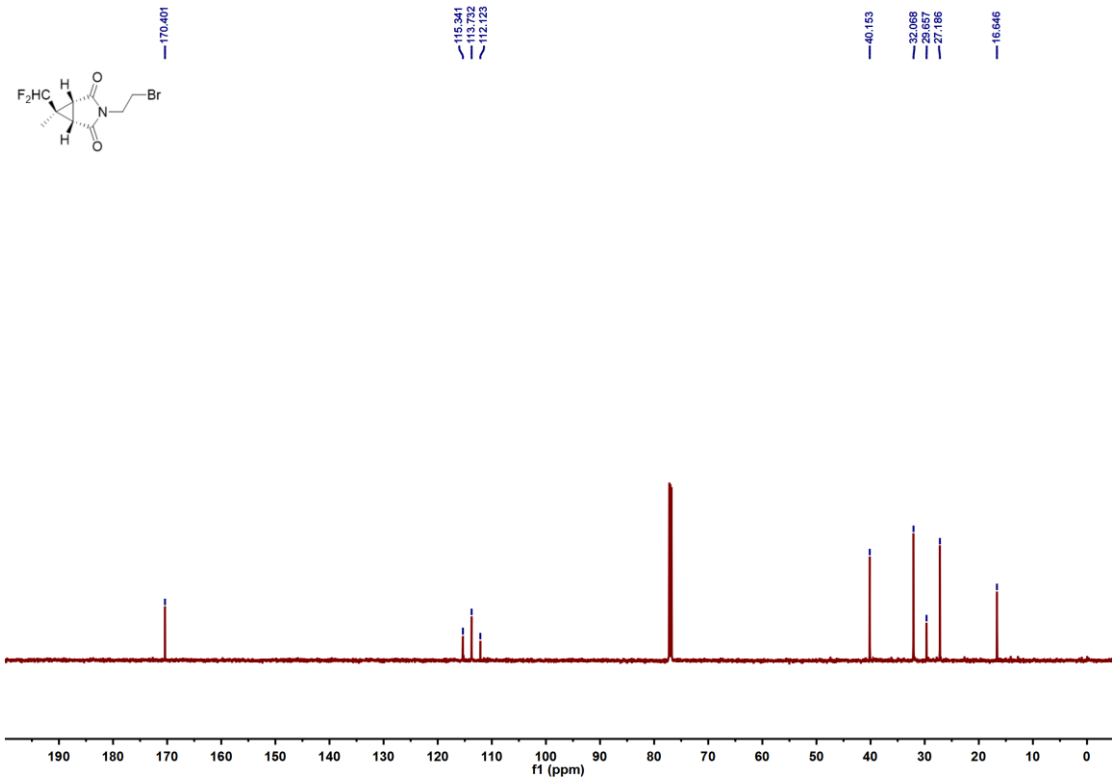


Figure 101. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3q₁**

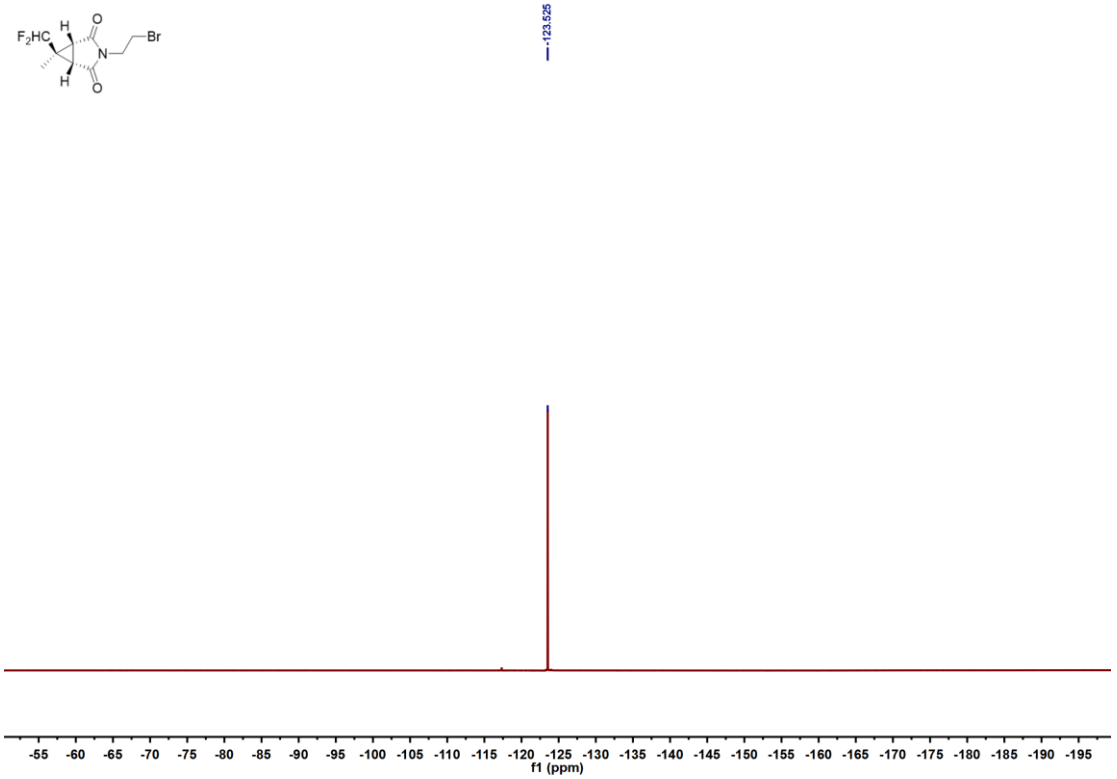


Figure 102. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3q₂**

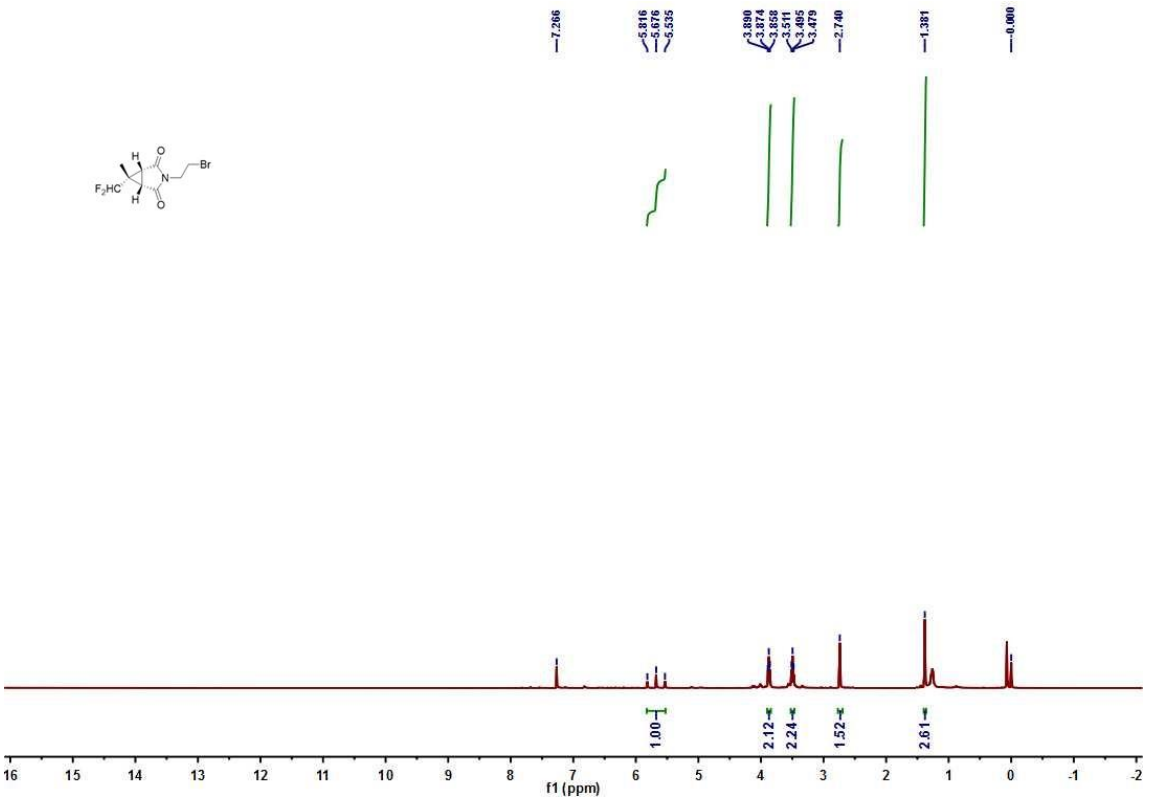


Figure 103. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3q₂**

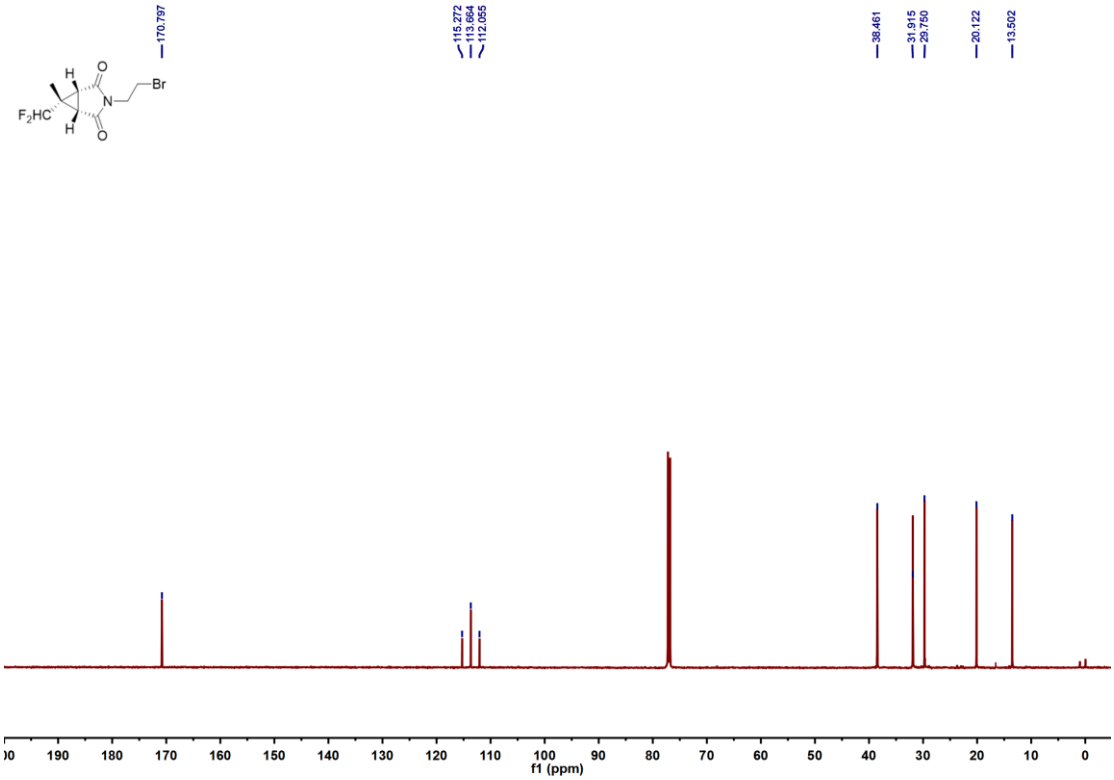


Figure 104. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3q₂**

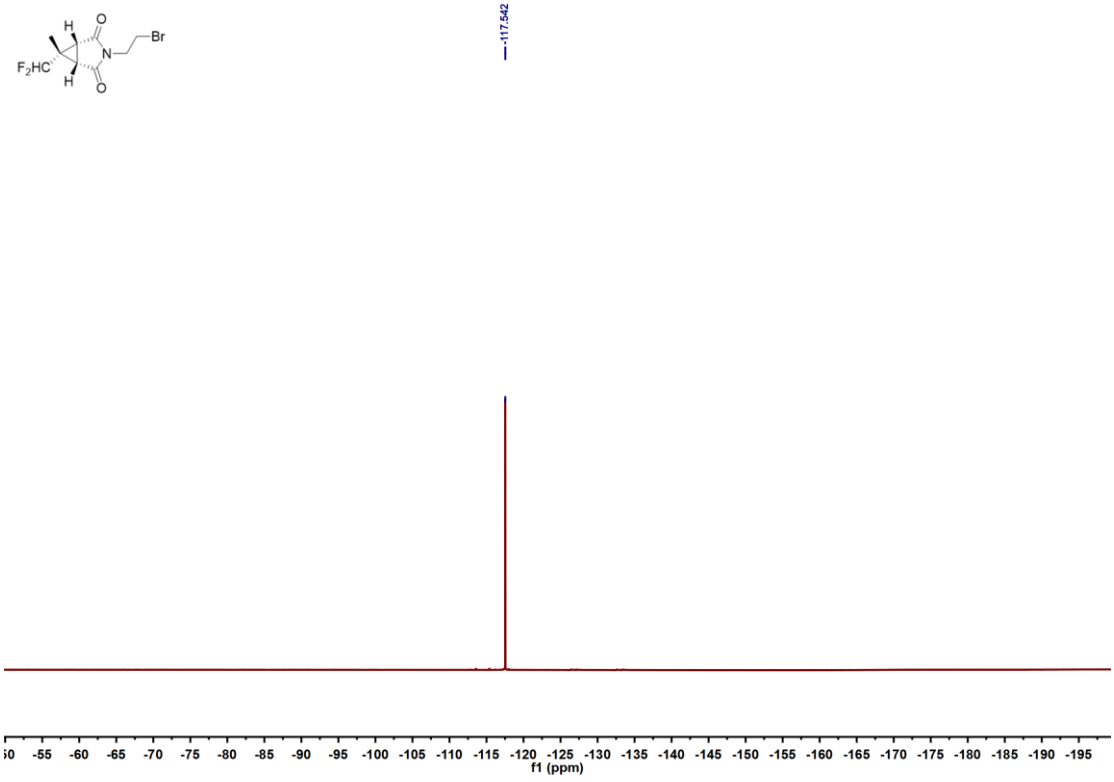


Figure 105. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3r$_1$**

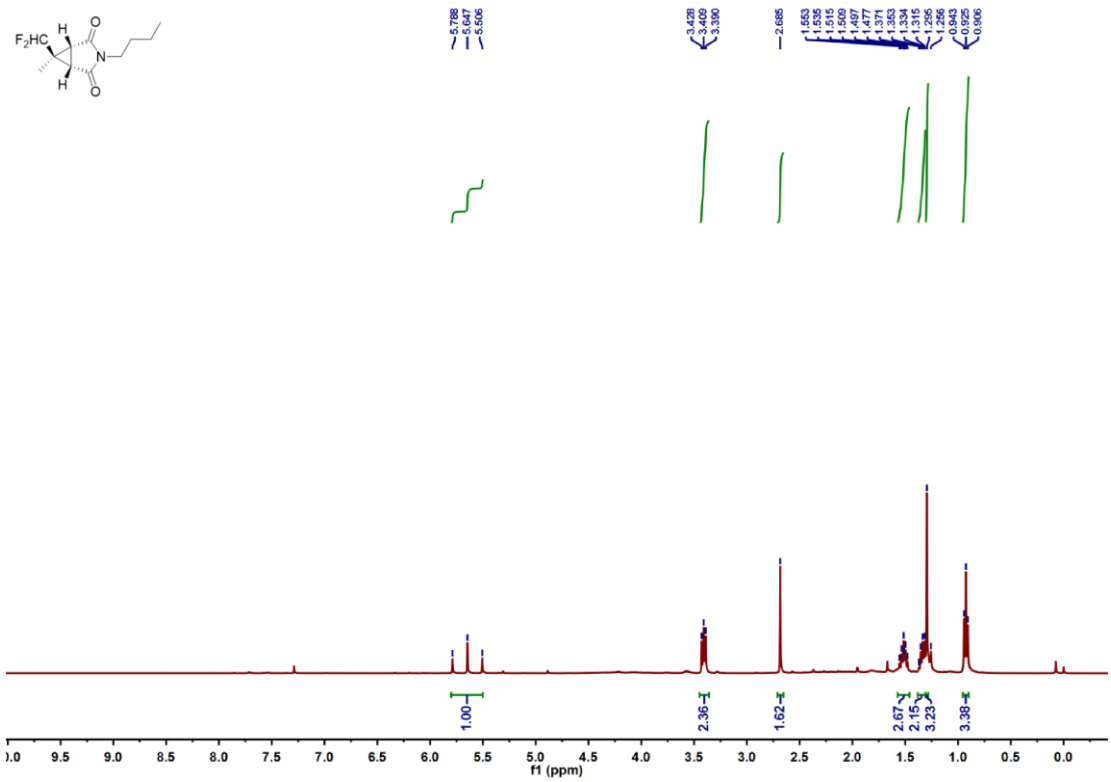


Figure 106. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3r$_1$**

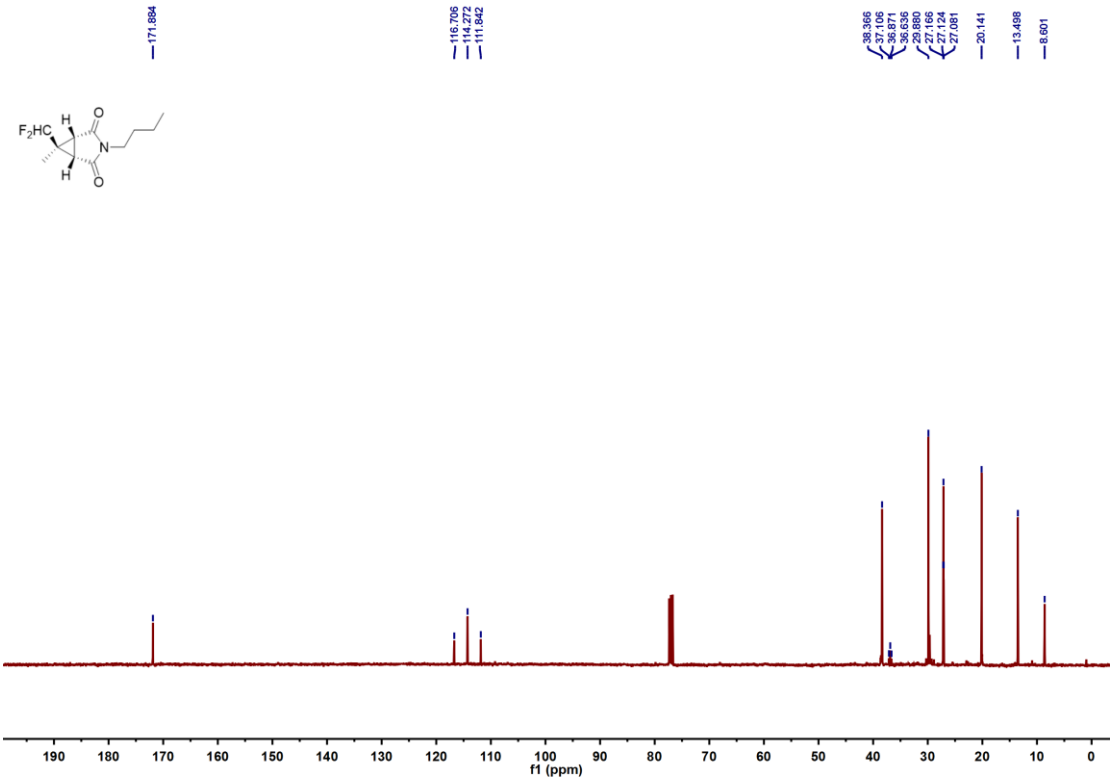


Figure 107. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3r$_1$**

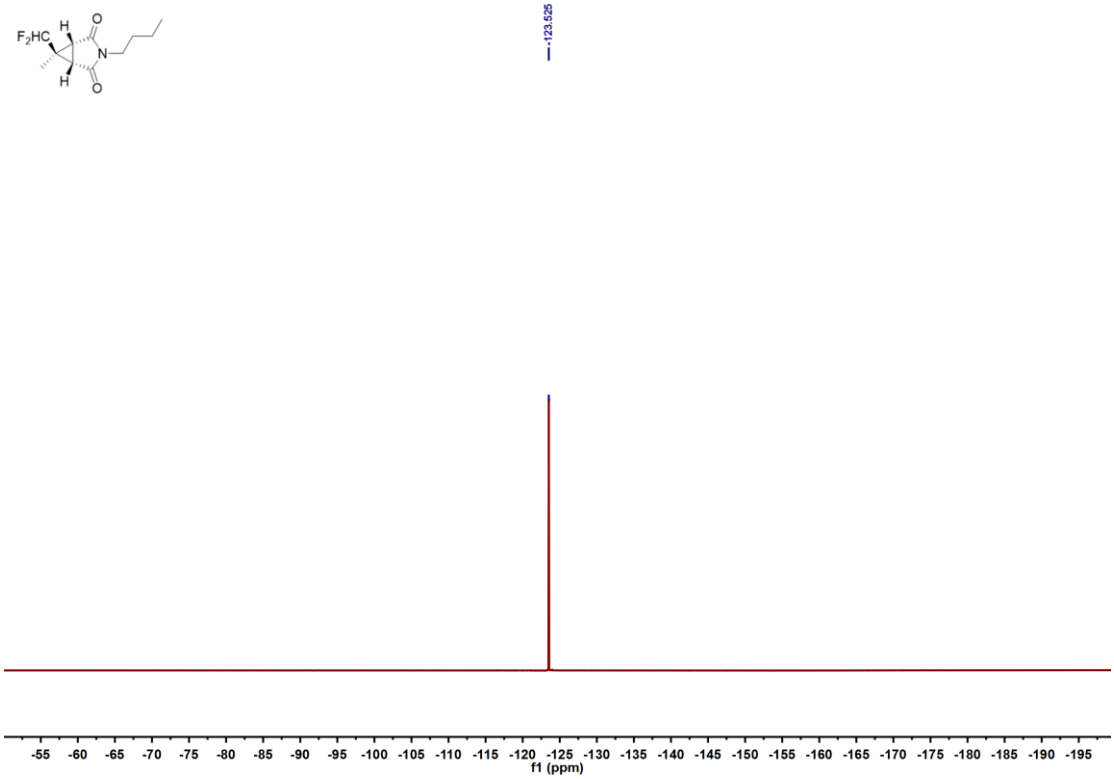


Figure 108. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3r$_2$**

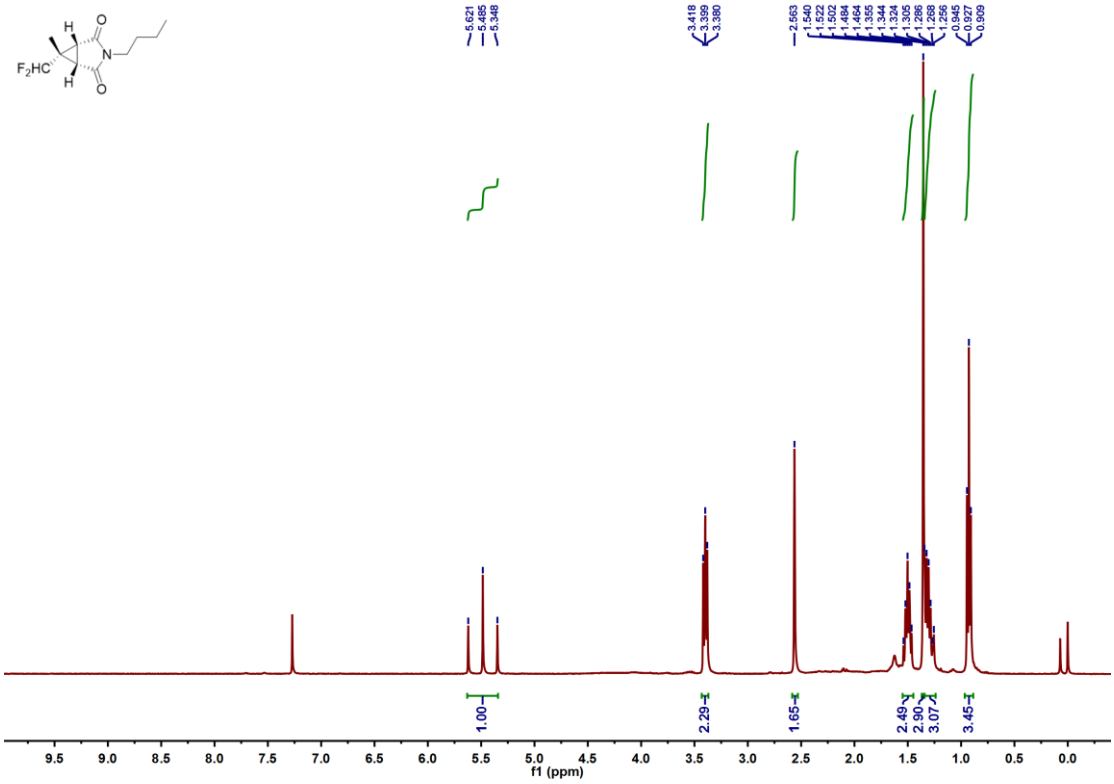


Figure 109. The ^{13}C NMR (150 MHz, $CDCl_3$) of **3r₂**

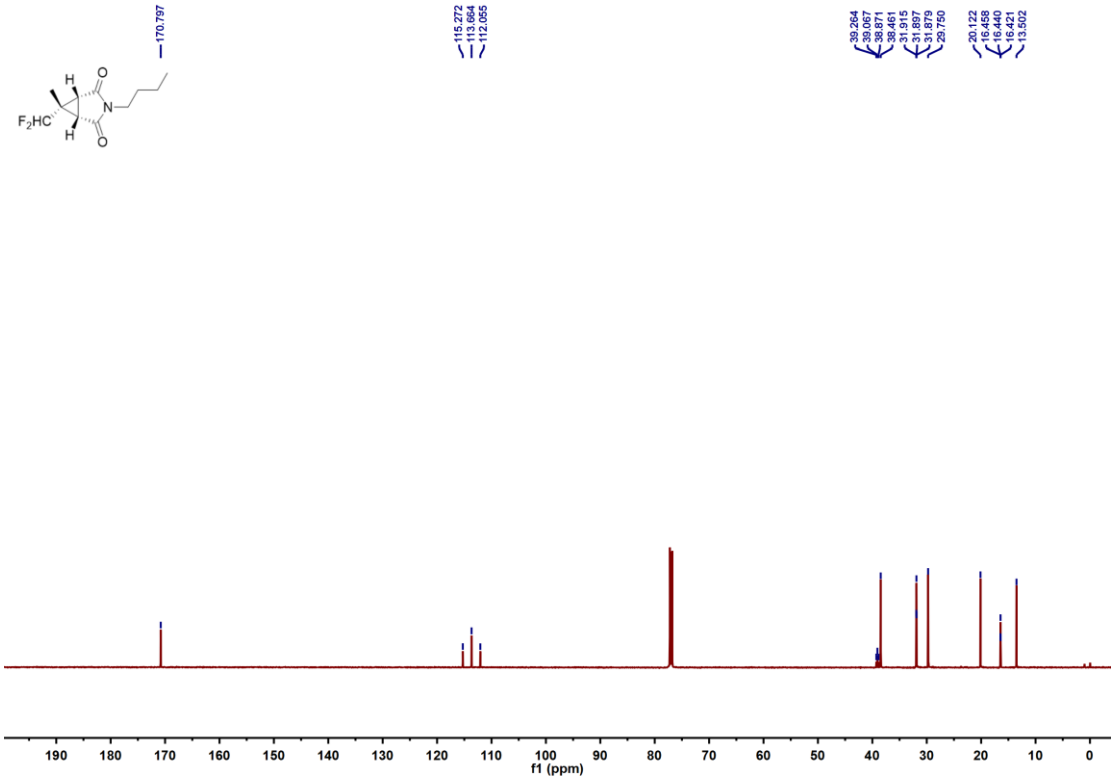


Figure 110. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3r₂**

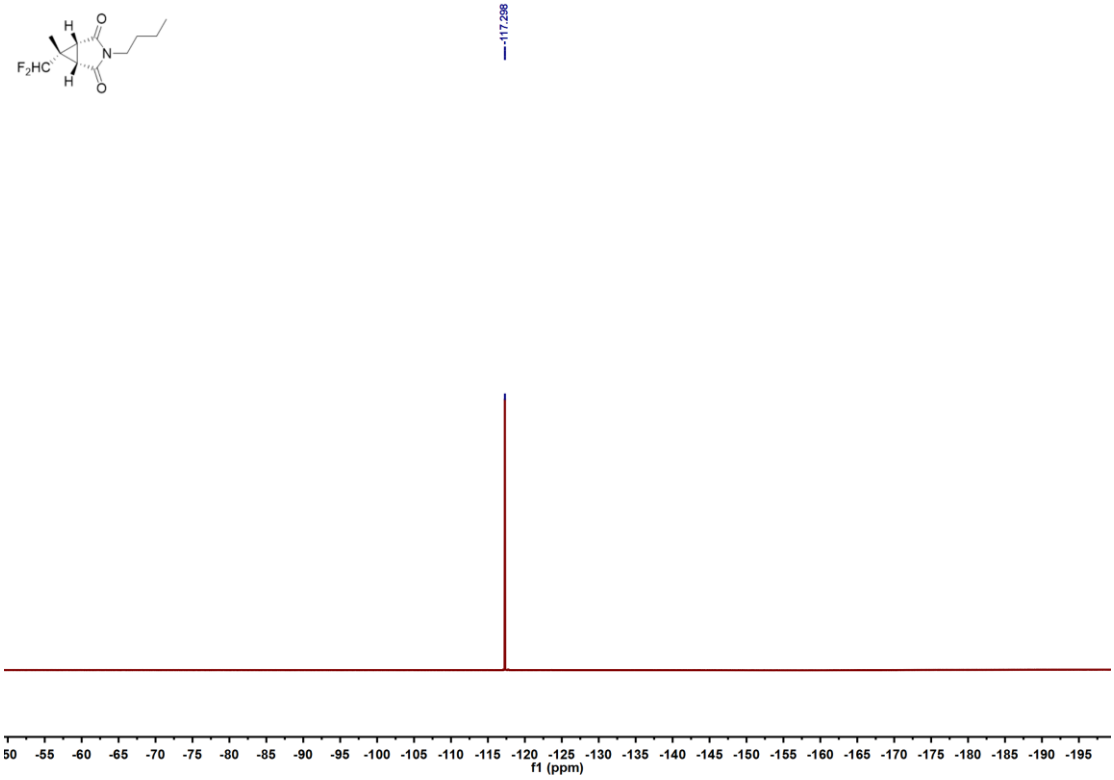


Figure 111. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3s$_1$**

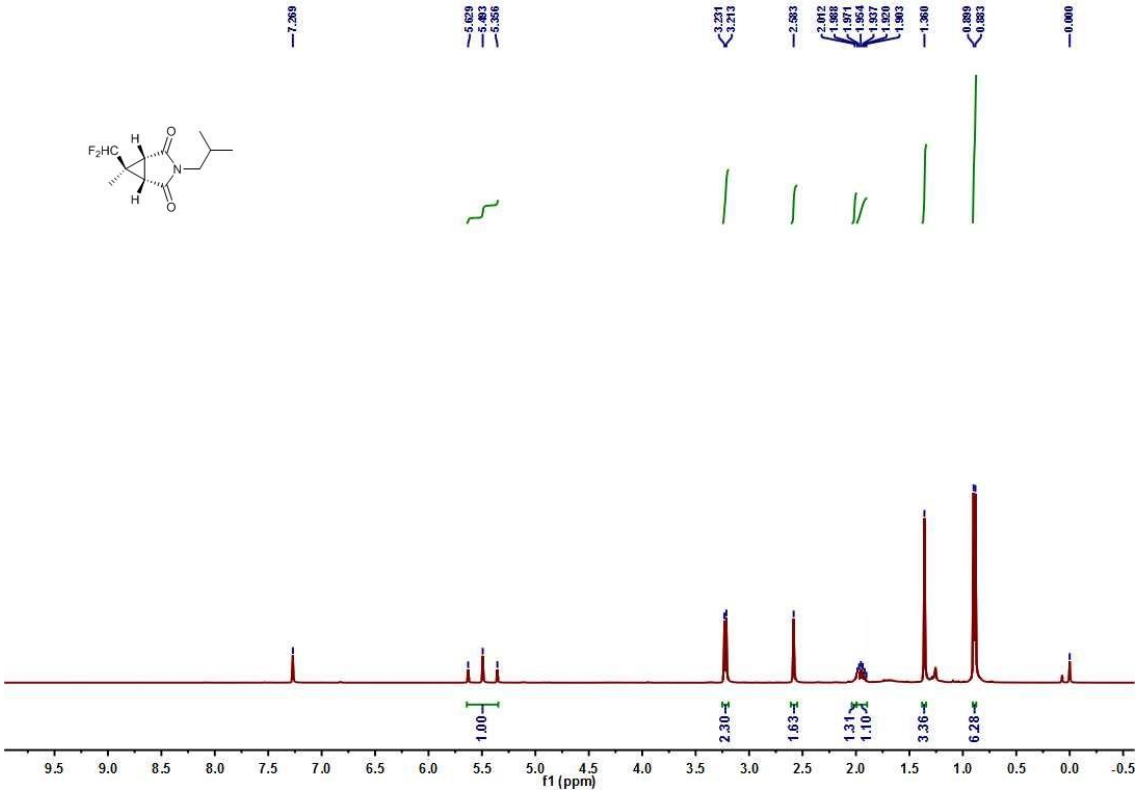


Figure 112. The ^{13}C NMR (100 MHz, $CDCl_3$) of **3s$_1$**

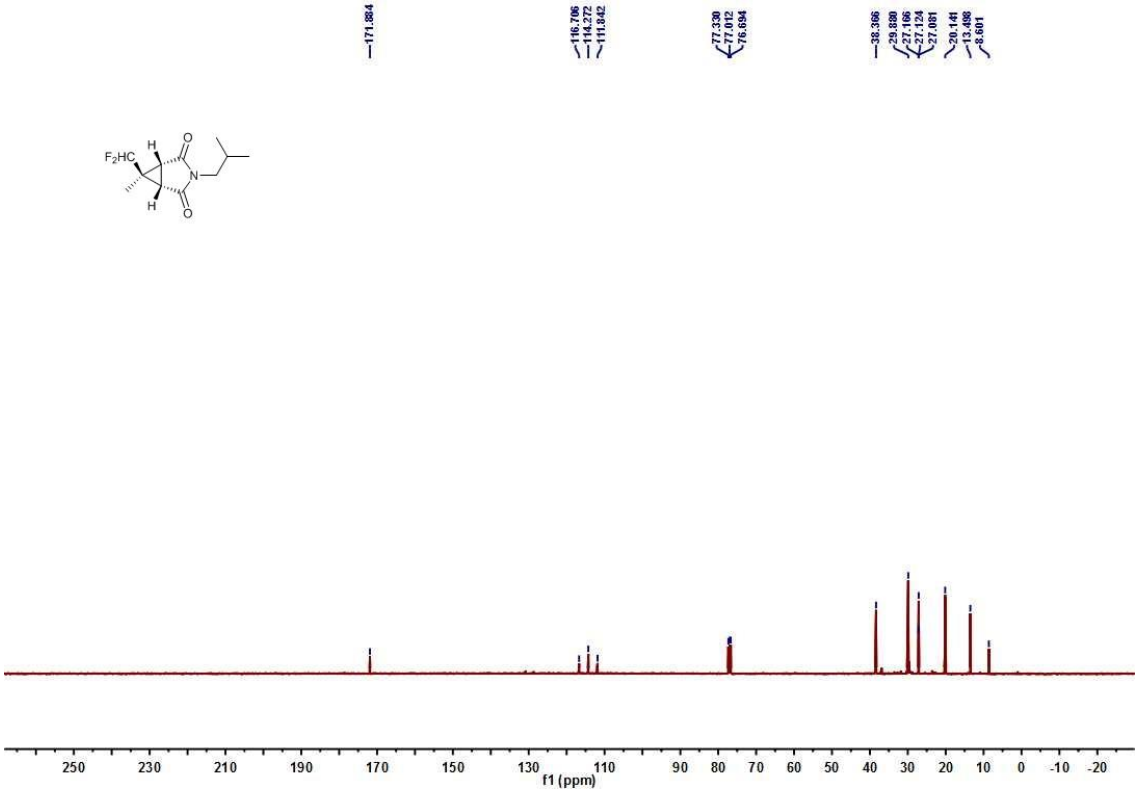


Figure 113. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3s$_1$**

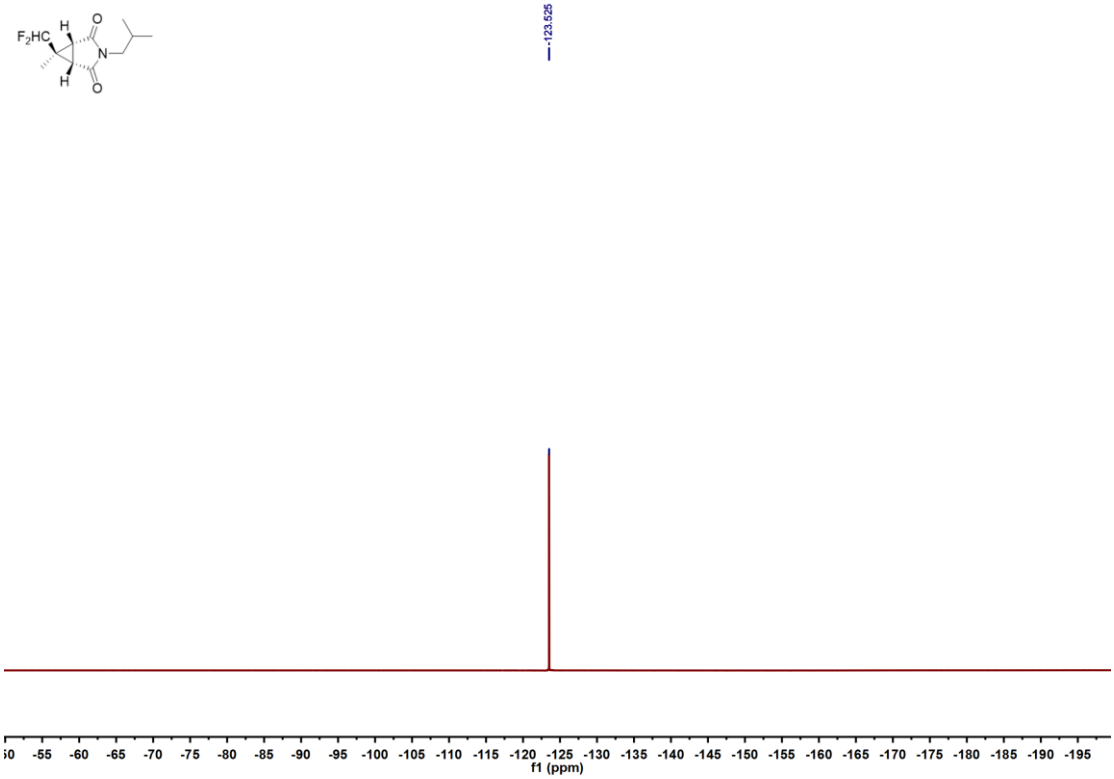


Figure 114. The ^{1}H NMR (400 MHz, $CDCl_3$) of **3s$_2$**

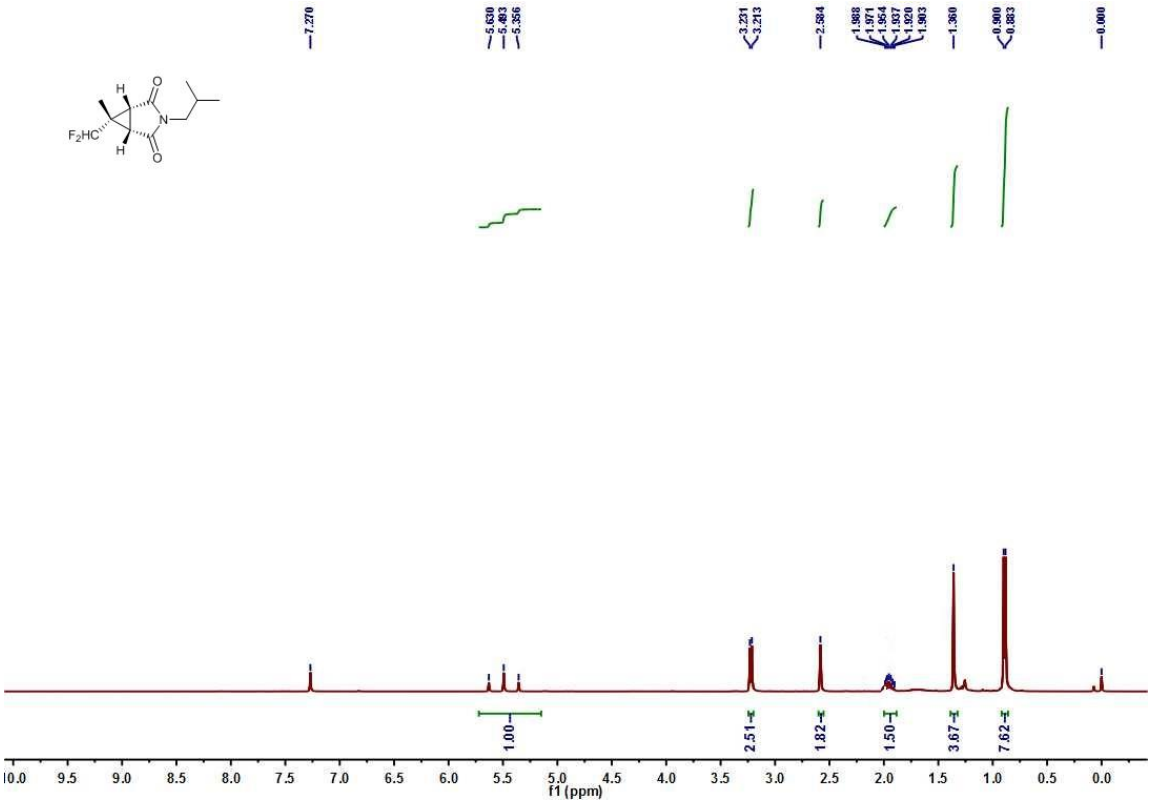


Figure 115. The ^{13}C NMR (100 MHz, $CDCl_3$) of **3s₂**

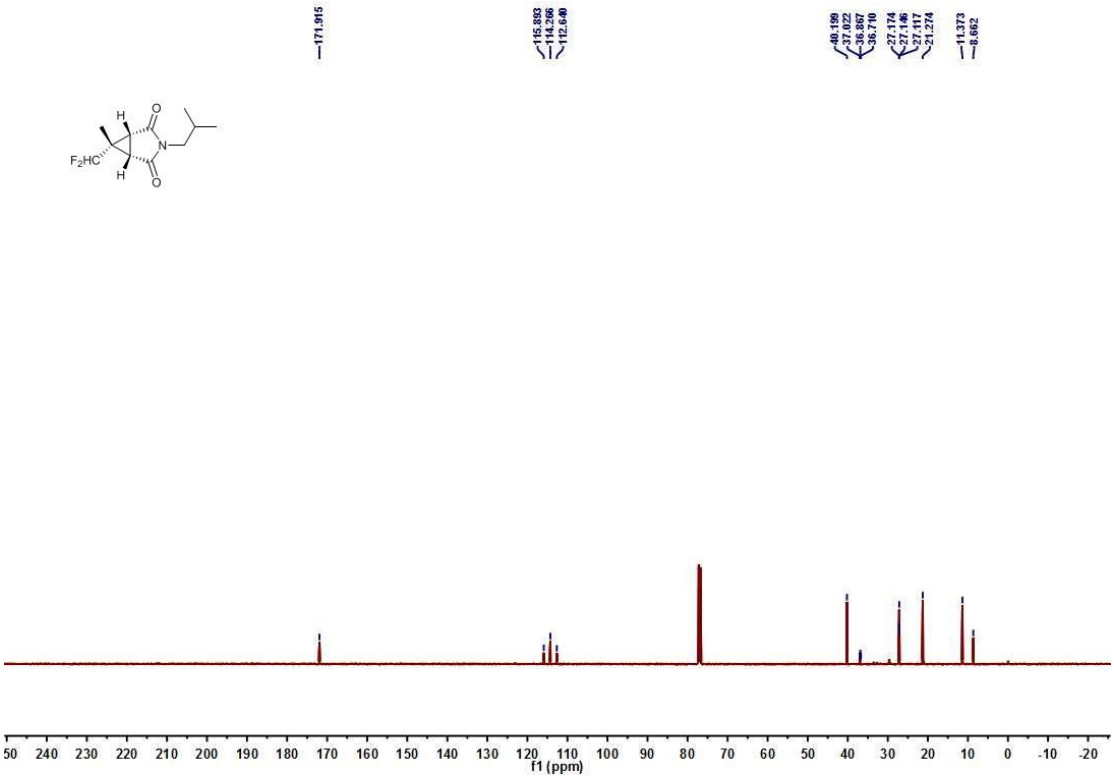


Figure 116. The ^{19}F NMR (376 MHz, $CDCl_3$) of **3s₂**

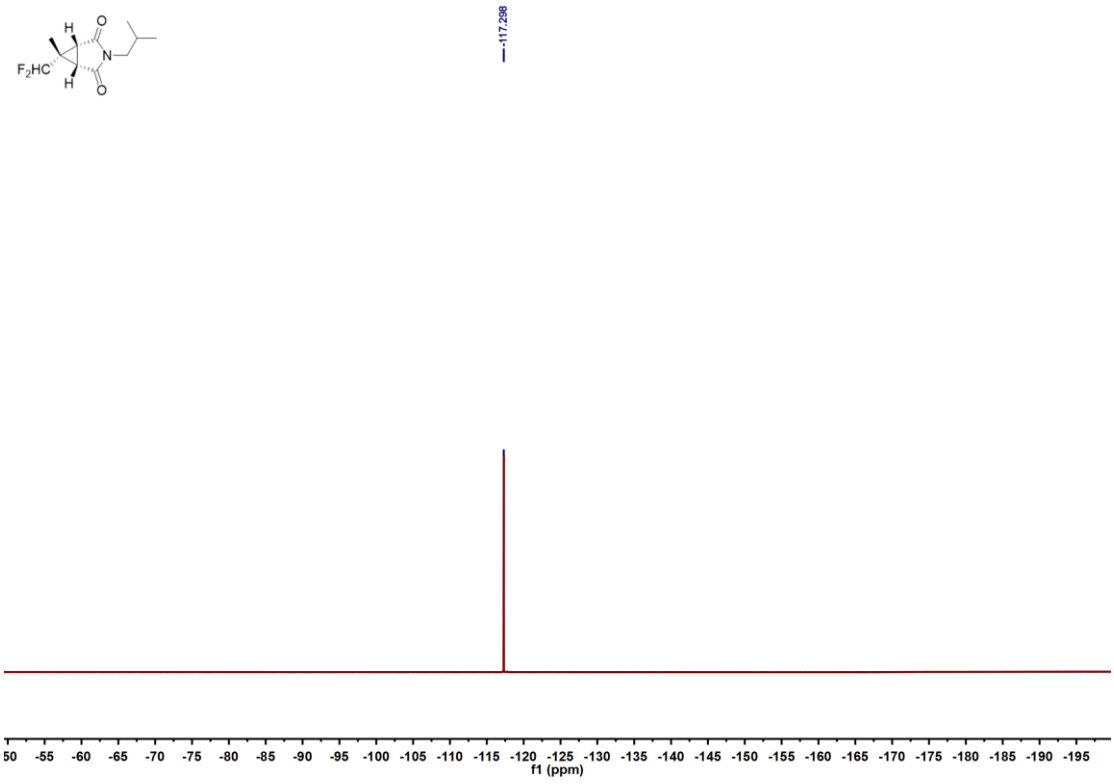


Figure 117. The ^{1}H NMR (400 MHz, $CDCl_3$) of **$4a_1$**

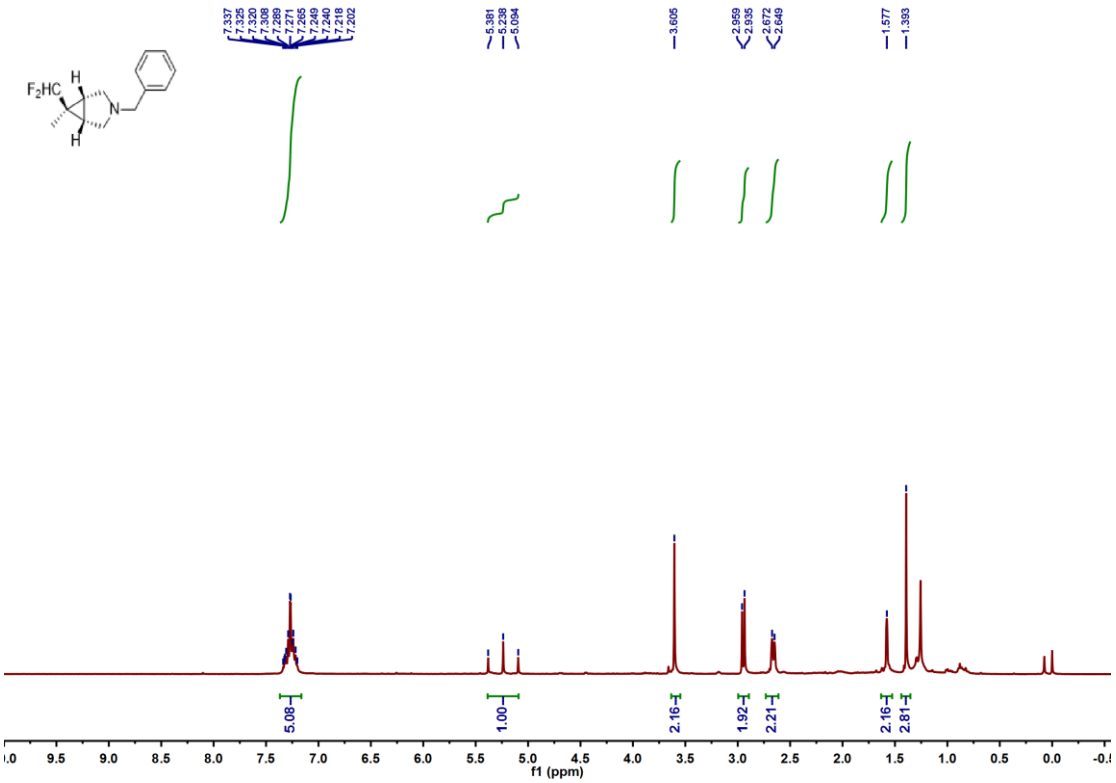


Figure 118. The ^{13}C NMR (100 MHz, $CDCl_3$) of **$4a_1$**

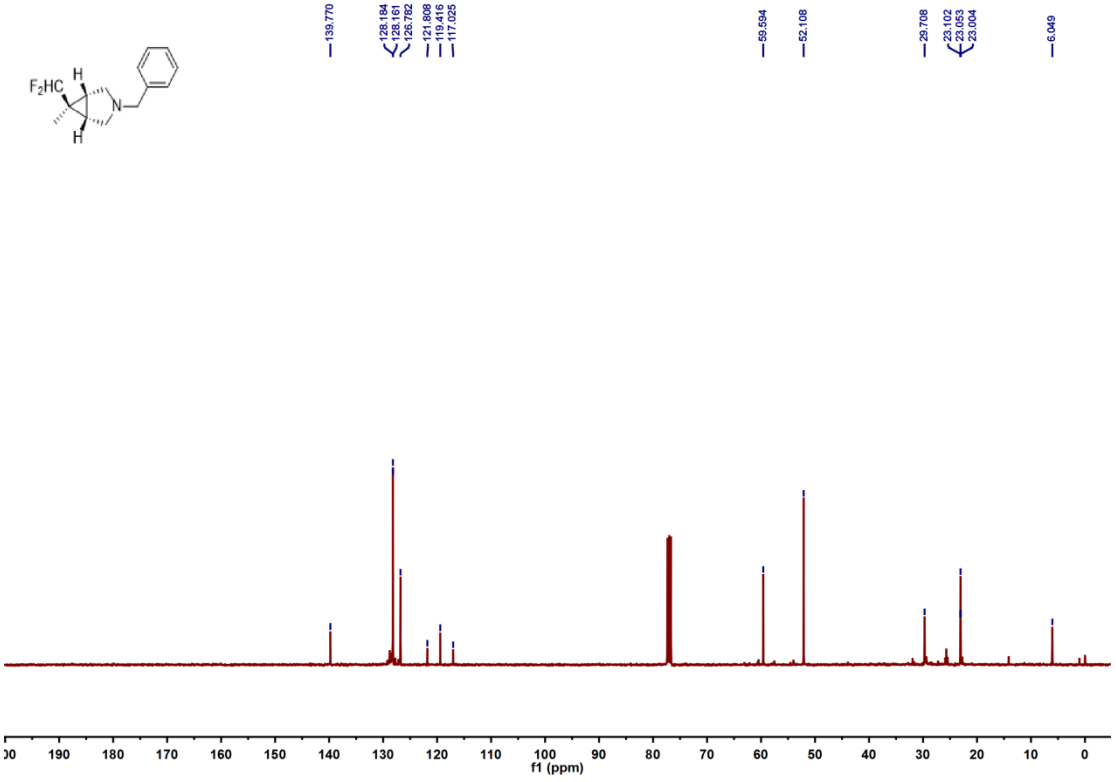


Figure 119. The ^{19}F NMR (376 MHz, $CDCl_3$) of **$4a_1$**