Access to cyclic *gem*-difluoroacyl scaffolds *via* electrochemical and visible light photocatalytic radical tandem cyclization of heteroaryl chlorodifluoromethyl ketones

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Supporting information

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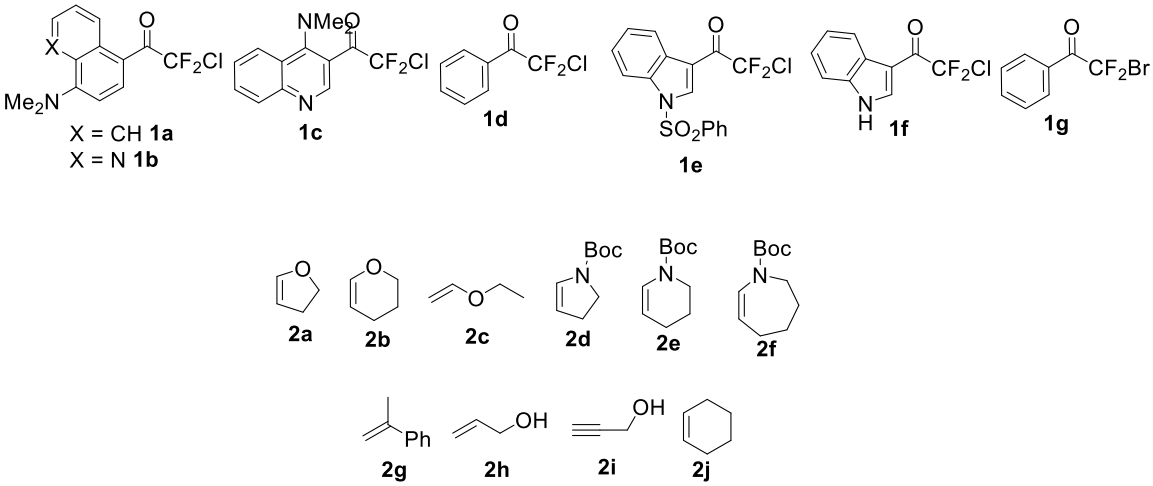
General Methods

Solvents and Et_3N were distilled before use. Reagents were obtained commercially and used without further purification. ^1H, ^{19}F and ^{13}C NMR were recorded with a Bruker Avance 300 (in $CDCl_3$ unless otherwise mentioned) at 300 MHz, 282 MHz and 75 MHz, respectively or a Bruker Avance 400 at 101 MHz (^{13}C NMR). Chemical shifts are given in ppm (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet, br = broad) relative to residual peak of solvent (δ_H = 7.26 ppm for $CHCl_3$, δ_C = 77.0 ppm for $CDCl_3$) or $CFCl_3$ as external reference for ^{19}F spectra. Coupling constants (J) are given in Hertz. TLC was performed on Merck silica Gel 60 F254 plates with detection by UV light. Silica gel chromatography was performed on Macherey-Nagel Silica gel 60M (0.04-0.063 mm). Mass spectra were recorded using a micrOTOF-Q [EI or ESI^+]. Melting points (uncorrected) were determined in capillary tubes on a Büchi apparatus. Solvents for chromatography: DCM = CH_2Cl_2, PE = Petroleum ether, EtOAc = Ethyl acetate). 2-Chloro-1-(4-dimethylamino-naphthalen-1-yl)-2,2-difluoro-ethanone **1a** and *N*,*N*-dimethyl-5-chlorodifluoro-acetyl-8-quinolylamine **1b** were prepared following our published procedures.[1,2] Olefins **2a-j** were commercially available as well as $Ru(bpy)_3Cl_2.6H_2O$ and $Ir(ppy)_3$.

Structure of the substrates and olefins used in this study

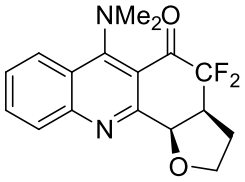


General procedure for photocatalytic radical cyclizations

In an oven-dried flask containing a magnetic stirring bar were added under argon the substrate (1 equiv., 0.55 mmol) and dry DMF (2.5 mL). The mixture was degassed during 15 minutes; the olefin (4.5 equiv., 2.5 mmol) followed by freshly distilled triethylamine (2.5 equiv., 1.4 mmol) were added and the flask was degassed during 10 minutes. Then, *the catalyst* was added and the mixture was degassed again for 15 minutes. The flask was placed at a fixed distance (app. 10 cm) from a 15W fluorescent compact bulb and was stirred at room temperature under visible-light irradiation during 24h. Afterward, the resulting solution was quenched with a NH_4Cl saturated aqueous solution (20 mL) and the aqueous layer was extracted with EtOAc (3 x 20 mL). Organic layers were combined and washed with water (3 x 20 mL), saturated aqueous solution of NaCl (1 x 20 mL), and dried over Na_2SO_4. Solvents and volatiles were removed by evaporation under reduced pressure and the crude residue was purified by silica gel chromatography to provide the desired product.

[1] Philippe Hapiot and M. Médebielle, *Journal of Fluorine Chemistry*, **2001**, *107*, 285-300.
[2] Maurice Médebielle*, Robert Keirouz, Etsuji Okada and Takuro Ashida, *Synlett*, **2001**, *6*, 821-823.

Preparation of 2-Chloro-1-(4-(dimethylamino)quinolin-3-yl)-2,2-difluoroethanone **1c**



The procedure was adapted from the synthesis of the trifluoroacetyl analogue[3] using chlorodifluoroacetic anhydride. Product was obtained in 32% isolated yield.

Preparation of 3-chlorodifluoroacetyl indole **1e** [4]

In an oven-dried flask at 0°C, indole (1 equiv., 8.5 mmol) was dissolved in dry diethylether (5 mL) under argon. Then a mixture of chlorodifluoroacetic anhydride (2,5 equiv., 21.3 mmol) in dry diethylether (27 mL) was added dropwise and the reaction mixture was stirred at 0°C during 6 h. Solvent and volatiles were removed by evaporation under reduced pressure and the crude residue was dissolved in EtOAc (25 mL). The organic layer was washed with an aqueous saturated solution of $NaHCO_3$ (1 x 25 mL) and then dried over Na_2SO_4. After evaporation of solvent, the resulting crude residue was recrystallized in EtOH to give the pure desired product.

Preparation of 1-phenylsulphonyl-3-chlorodifluoroacetyl indole **1f**

In a flask was dissolved NaH at 0°C (1,5 equiv., 2.61 mmol) in dry THF (10 mL). Then, a solution of 3-chlorodifluoroacetyl indole **1e** (1 equiv., 1,74 mmol) in THF (10 mL) was added dropwise. After 30 min stirring at 0°C phenylsulfonyl chloride was added dropwise to the mixture and the medium was allowed to warm to room temperature and was stirred during 17h. Afterward, the mixture was hydrolysed with water (15 mL) at 0°C and extraction was made with EtOAc (3 x 15 mL). Organic layers were combined and washed with water (3 x 15 mL) and with a saturated solution of NaCl (1 x 15 mL) and then dry over Na_2SO_4. After filtration, solvents were eliminated by evaporation under reduced pressure. The crude residue was purified on chromatography column (PE /EtOAc: 95/5) to give the desired product.

Optimization of the Reaction Conditions of the radical annulation for 1e and 1f in the presence of 2a

	1-phenylsulphonyl-3-chlorodifluoroacetyl indole **1e**[a]			
Entry	Photocatalyst	Solvent	Additive	Yield[b] (%)
1	$Ru(bpy)_3Cl_2.6H_2O$	DMF	Et_3N	73
2	/	DMF	Et_3N	11[c,d]
3	$Ru(bpy)_3Cl_2.6H_2O$	DMF	/	N.R
4[e]	$Ru(bpy)_3Cl_2.6H_2O$	DMF	Et_3N	N.R
5	$Ru(bpy)_3Cl_2.6H_2O$	DMF	2,6-lutidine	N.R[c,f]
6	$Ru(bpy)_3Cl_2.6H_2O$	DMF	K_2HPO4	N.R[c,f]

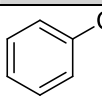
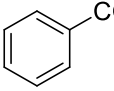
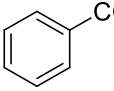
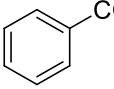
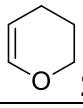
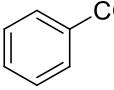
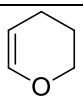
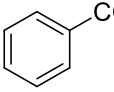
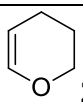
[a] Reaction conditions : **1e** (0.55 mmol), **2a** (2.5 mmol), additive (1.4 mmol), photocatalyst (5.5 mol%), solvent (2.5 mL), 15 W fluorescent light bulb, 24h, rt. [b] Isolated yield. [c] ^{19}F-NMR analysis with $PhOCF_3$ as internal standard. [d] **1e** was detected in 36%. [e] Reaction performed in dark. [f] **1e** was detected in 5-8%

[3] (a) E. Okada, T. Sakaemura, and N. Shimomura, *Chem. Lett*., **2000**, 29, 50; (b) E. Okada, M. Hatakenaka, T. Sakaemura, N. Shimomura, and T. Ashida, *Heterocycles*, **2012**, 86, 1177.
[4] Shun-Jiang Yao, Zhi-Hui Ren, Yao-Yu Wang, and Zheng-Hui Gua, *J. Org. Chem.*, **2016**, *81*, 4226-4234.

	3-chlorodifluoroacetyl indole **1f**[a]			
Entry	Photocatalyst	Solvent	Additive	Yield[b] (%)
1	$Ir(ppy)_3$	DMF	Et_3N	83
2	$Ir(ppy)_3$	DMSO	Et_3N	56
3	$Ir(ppy)_3$	DCM	Et_3N	15[c]
4	$Ir(ppy)_3$	CH_3CN	Et_3N	13[c]
5	/	DMF	Et_3N	Traces
6	$Ir(ppy)_3$	DMF	/	8[c]
7[d]	$Ir(ppy)_3$	DMF	Et_3N	N.R
8	$Ir(ppy)_3$	DMF	2,6-lutidine	68[c]
9	$Ir(ppy)_3$	DMF	K_2HPO4	9[c]
10	$Ir(ppy)_3$[e]	DMF	Et_3N	27[c]
11	$Ru(bpy)_3Cl_2.6H_2O$	DMF	Et_3N	9[c]

[a] Reaction conditions : **1f** (0.55 mmol), **2a** (2.5 mmol), additive (1.4 mmol), photocatalyst (5.5 mol%), solvent (2.5 mL), 15 W fluorescent light bulb, 24h, rt. [b] Isolated yield. [c] ^{19}F-NMR analysis with $PhOCF_3$ as internal standard. [d] Reaction performed in dark. [e] Photocatalyst 1 mol%.

Effect of the light source on the reaction of 1a and 1g with 2a and 2b[a]

Substrate	Olefin	Lamp	Yield
 **1a**	 **2a**	15W	53%[b]
		28W	55%[b]
		Blue LED	36%[b]
	 **2b**	15W	16%[b]
		28W	16%[b]
		Blue LED	13%[c]
 **1g**	 **2a**	15W	13%[c]
	 **2b**	15W	11%[c]

[a]Reaction conditions : **1** (0.55 mmol), **2** (2.5 mmol), Et_3N (1.4 mmol), $Ir(ppy)_3$ (5.5 mol%), solvent (2.5 mL), 24h, rt. [b] Isolated yield. [c] ^{19}F-NMR analysis with $PhOCF_3$ as internal standard.

Cyclic voltammetry

Electrochemical measurements were performed using an EG & G-Princeton Applied Research 263A all-in-one potentiostat, using a standard three-electrode setup with a glassy carbon electrode (working electrode, diameter = 3 mm), platinum wire auxiliary electrode and a non-aqueous Ag/Ag^+ (0.01 M $AgNO_3$ + 0.1 M *n*-Bu_4NClO_4) system in acetonitrile as the reference electrode. All solutions under the study were 0.1 M in the supporting electrolyte *n*-Bu_4NPF_6 (Fluka puriss electrochemical grade) with the

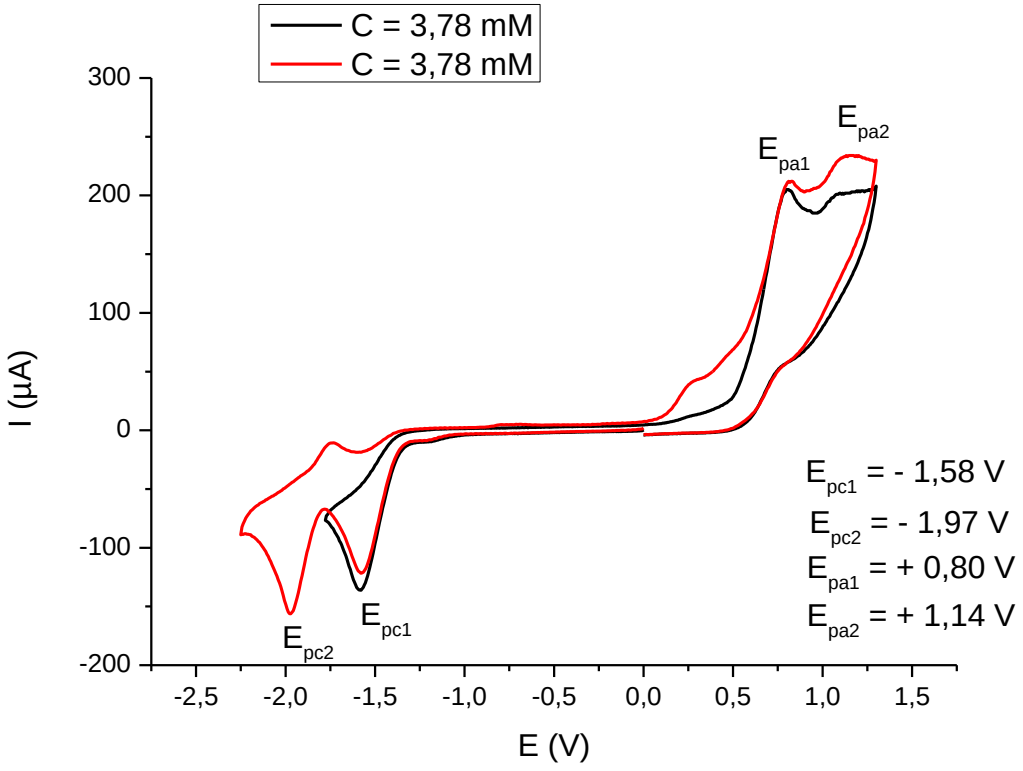
voltage scan rate of 0.2 V s^{-1}. Anhydrous DMF was obtained from Fisher Scientific. Solutions were thoroughly bubbled with dry argon for 15 minutes to remove oxygen before any experiment and kept under positive pressure of argon. Under these experimental conditions the ferrocene/ferricinium couple, used as internal reference for potential measurements, was located at $E_{1/2}$ = + 0.05 V in DMF.

Electrochemical data for substrates **1a-f** and olefins **2a-j.** Glassy carbon electrode (3 mm) in DMF + 0.1 M *n*-Bu_4NPF_6 at 0.2 V s^{-1}.

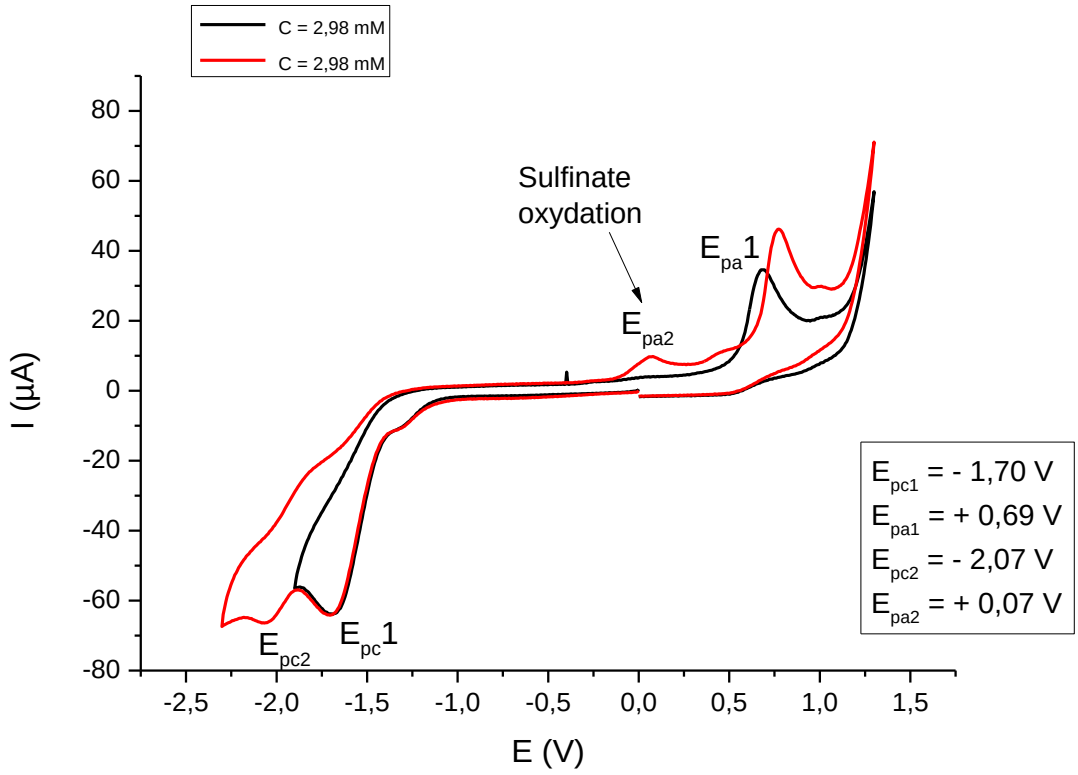
Compound	E_{pc1} (V)[a]	Compound	E_{pa1} (V)[b]
1a	-1.58 (- 1.27)[c]	**2a**	-
1b	-1.45 (-1.14)[c]	**2b**	-
1c	-1.58 (- 1.27)[c]	**2c**	-
1d	-1.84 (- 1.53)[c]	**2d**	+0.98 (+1.29)[c]
1e	-1.70 (- 1.39)[c]	**2e**	+1.11 (+1.42)[c]
1f	-2.00 (- 1.80)[c]	**2f-j**	-
1g	-1.50 (-1.19)[c]		

[a] First cathodic peak potential at 293 K with a glassy carbon electrode in DMF and 0.1 M *n*-Bu_4NPF_6 as the supporting electrolyte; all potentials are quoted *vs*. Ag/Ag^+ 0.01 M in acetonitrile, scan rate: 0.2 V s^{-1}. [b] Anodic peak potential at 293 K with a glassy carbon electrode in DMF and 0.1 M *n*-Bu_4NPF_6 as the supporting electrolyte; all potentials are quoted *vs*. Ag/Ag^+ 0.01 M in acetonitrile, scan rate: 0.2 V s^{-1}. [c] Peak potential quoted *vs* SCE. E (V *vs* SCE) = E (Ag/Ag^+ 0.01 M) + 0.31

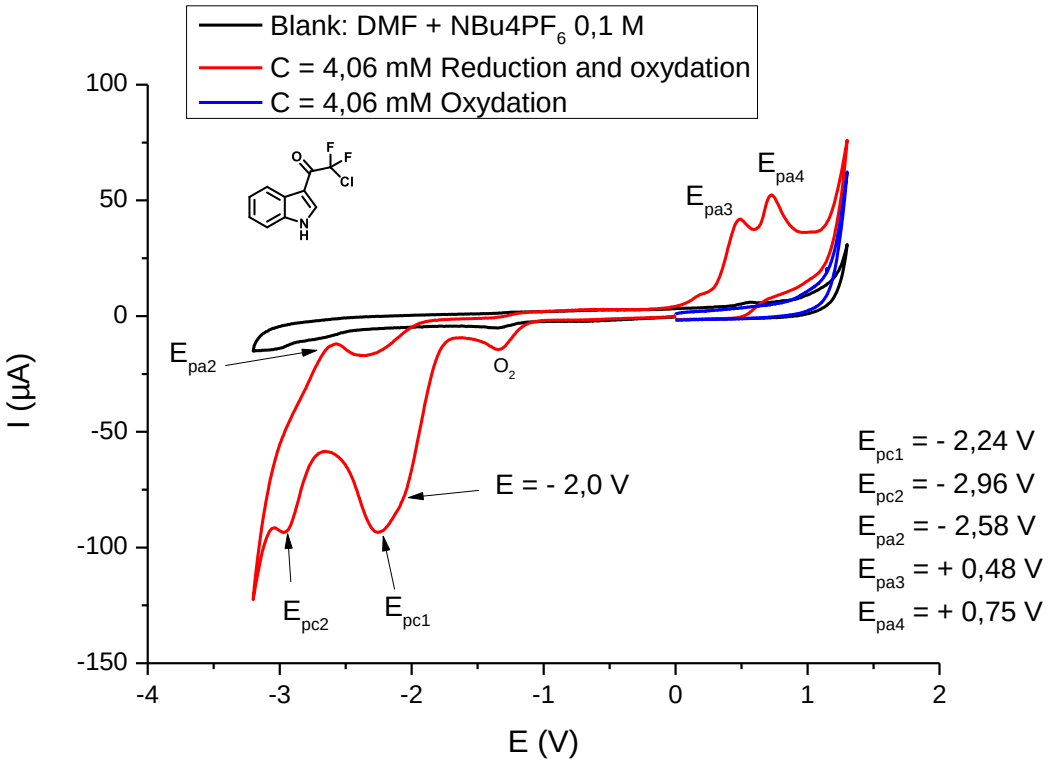
No anodic peak potential could be observed up to oxidation of solvent/electrolyte (onset at + 1.40 V *vs* Ag/Ag^+ 0.01 M (+ 1.71 V *vs* SCE) for olefins **2a-c**, **2f-j**. Only for **2d** and **2e** oxidation peak potentials could be measured. Based on the electrochemical data, none of the olefinic acceptors can be oxidized under the photo-redox reactions either under Ruthenium or Iridium catalysis. Et_3N is irreversibly oxidized at + 0.70 V *vs* Ag/Ag+ (+ 1.01V *vs* SCE). 2,6-lutidine gives rise to no oxidation step up to + 1.40 V *vs* Ag/Ag+ 0.01M (+ 1.71 V *vs* SCE).



Cyclic voltammetry of **1a** *C* = 3.78 mM in DMF + 0.1 M *n*-Bu_4NPF_6

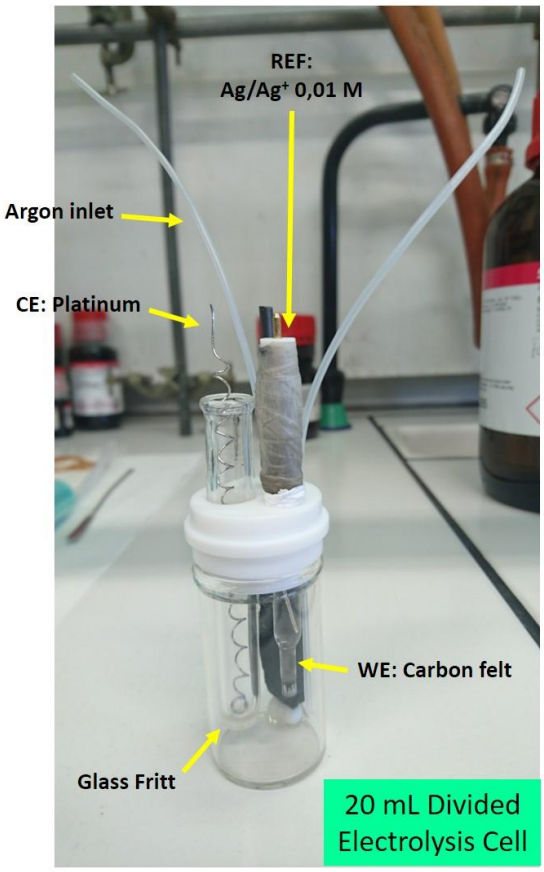


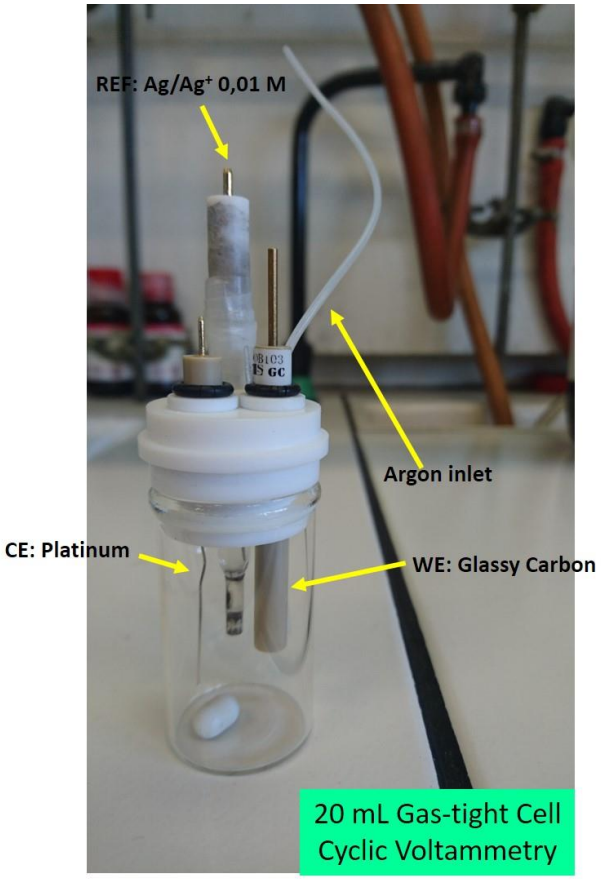
Cyclic voltammetry of *N*-sulfonyl indole **1e**. *C* = 2.98 mM in DMF + 0.1 M *n*-Bu_4NPF_6



Cyclic voltammetry of indole **1f**. *C* = 4.06 mM in DMF + 0.1 M *n*-Bu_4NPF_6

Cells for electrolysis and cyclic voltammetry





Electrolysis

Controlled-potential electrolyses were run in a cylindrical divided cell (see Figure) using a carbon felt electrode (S ~ 2.5 cm^2) as working electrode, a platinum wire as counter electrode separated from the cathodic compartment with a frit glass (porosity 4) and Ag/Ag^+ 0.01M as reference.

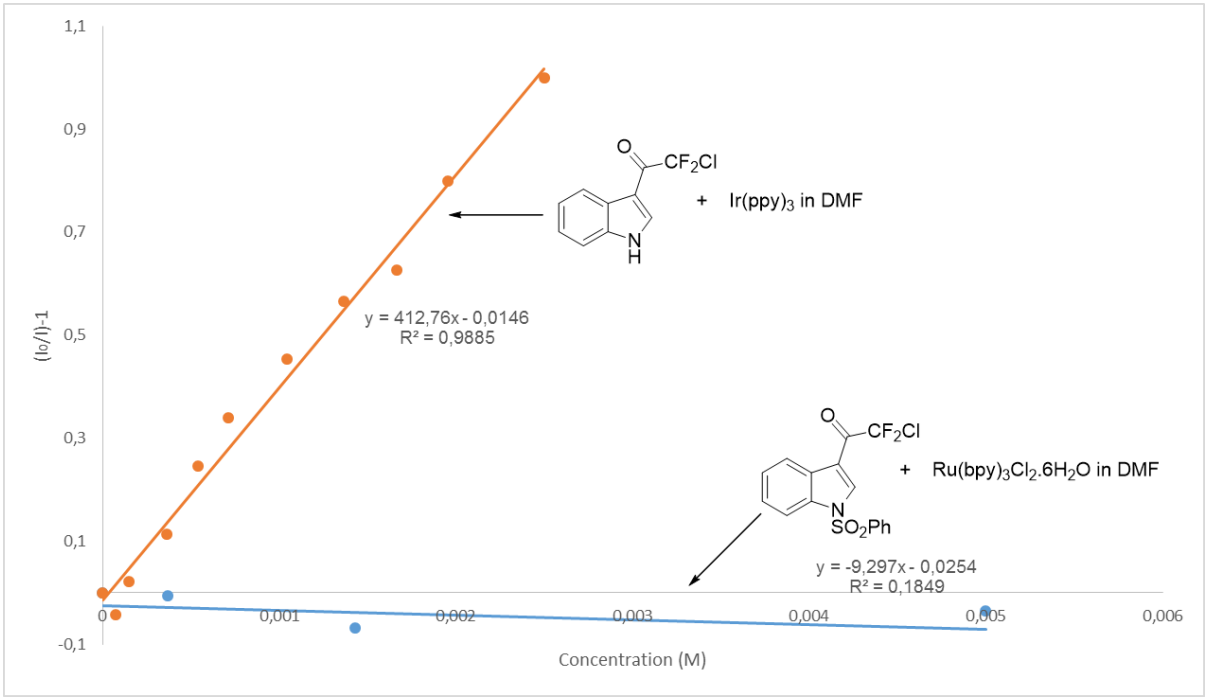
Under argon was introduced in the cathodic compartment, 15 mL of an anhydrous DMF solution containing *n*-Et_4NBF_4 0.1M and 2.5 mL of the same solution in the anodic compartment. The cathodic solution was deoxygenated with argon bubbling for 15 minutes and then was introduced $PhNO_2$ (25 mol%). Solution was stirred and deoxygenated further for 10 minutes. Then substrate and olefin were introduced. A constant potential of - 1.51 V (-1.20 V *vs* SCE) was then applied at room temperature, with an initial current close to 15-20 mA. The progress of the electrolysis was followed by TLC and ^{19}F NMR. After 1.5-1.8 F/mole of starting material (2 h), the electrolysis was stopped and quenched with an aqueous NH_4Cl solution (40 mL) and extracted with EtOAc (3 x 20 mL), the combined organic phases were washed with H_2O (4 x 20 mL), dried over Na_2SO_4 and filtered. Concentration under vacuo left a residue that was co-evaporated several times with toluene and purified by silica gel chromatography (PE/EtOAc: 95/5 → 80/20).

Luminescence quenching experiments

Emission spectra used in the Stern-Volmer experiments were recorded at room temperature using a 10^{-5}M deaerated DMF solution of the $Ir(ppy)_3$ or $Ru(bpy)_3Cl_2.6H_2O$ catalyst. The excitation wavelength [400 nm for $Ir(ppy)_3$, 450 nm for $Ru(bpy)_3Cl_2.6H_2O$] was chosen so that the absorbance did not exceed 0.1.

UV-Visible spectra were recorded with a double beam Jasco 670 UV-Visible spectrophotometer. Luminescence spectra were recorded on a Horiba-Jobin Yvon Fluorolog-3® spectrofluorimeter equipped with a three-slit double-grating excitation and emission monochromator with dispersions of 2.1 $nm.mm^{-1}$ (1200 $grooves.mm^{-1}$). The excitation source was a 450W xenon CW lamp and emission was detected at an angle of 90° by a red-sensitive Hamamatsu R928 photomultiplier tube. Spectra were referenced corrected for both the excitation source light intensity variation (lamp and grating) and the emission spectral response (detector and grating).

A 10^{-5}M stock solution of the $Ir(ppy)_3$ or $Ru(bpy)_3Cl_2.6H_2O$ catalyst was prepared, and split in two batches. 2 mL were put in a sealable 10 mm quartz cuvette equipped with a high-vacuum PTFE young valve and intensively degassed by a minimum of three freeze-pump-thaw cycles on a secondary vacuum line (until no bubble was seen during the thawing process). The rest of the solution was used to prepare a 1.5 10^{-2}M solution of the appropriate quencher. Then, the latter solution was added by aliquots into the solution of pure $Ir(ppy)_3$ or $Ru(bpy)_3Cl_26H_2O$ complex in the sealable cuvette; after each addition, the cuvette was submitted to three additional freeze-pump-thaw cycles, and an emission spectrum was recorded. Emission intensity was calculated by integration of the emission signal, and I_0/I_t-1 (with I_0: the emission intensity of the pure $Ir(ppy)_3$ or $Ru(bpy)_3Cl_26H_2O$ catalyst solution; I_t : the emission of the same solution after addition of the quencher) was plotted against the quencher concentration.



Stern-Volmer plots - Quenching experiments for substrates **1e** and **1f**

Quantum yield determination for the reaction of 1e and 1f

Quantum yield for the photochemical reactions were measured using the xenon lamp of the same Horiba-Jobin Yvon Fluorolog-3® spectrofluorimeter as used for the Stern-Volmer experiments. Sample cavity was equipped with a Thorlabs PM100D photometer. The Ruthenium or Iridium catalyst (1.5 x 10^{-7} mol), 3-Chlorodifluoroacetyl indole **1e** or 1-Phenylsulphonyl-3-chlorodifluoroacetyl indole **1f** (2.7 x 10^{-6} mol), 2,3-Dihyhydrofuran **2a** (1.2x10^{-5} mol) and in the case of Ru catalyst Et_3N (6.8 x 10^{-6} mol) were placed in the same sealable quartz cuvette (3mL) as for the Stern-Volmer experiment, and

thoroughly degassed by three freeze-pump-thaw cycles. The cuvette was stirred (100 rpm) throughout the whole photochemical reaction using a Hellma 300 electronic stirrer.

Excitation was performed at 380 nm and 440 nm for Iridium and Ruthenium respectively, excitation slits were opened at a 10 nm bandwith. Fluorescence of the catalyst were monitored in time (at their maximal emission wavelength), and it was confirmed that no photobleaching occured for the Ir compound in the course of the reaction, while only a minor degradation (ca 10%) was observed for the Ruthenium compound.

Incident light power (3.7×10^{-3} W with Iridium and 6.0×10^{-3} W with Ruthenium) was measured in the absence and in the presence of a sample, enabling determination of the absorbed power P_{abs} (2.9×10^{-3} W with Iridium 5.0×10^{-3} W with Ruthenium). The energy E_{abs} (J) absorbed during the irradiation time t_{irr} (s) was calculated using the following relation:

$$E_{abs} = P_{abs} \cdot t_{irr}$$

and converted into an absorbed photon flux n_{photon} (mol) considering

$$n_{photon} = E_{abs} / E_{photon}$$

where E_{photon} (J/mol) corresponds to the energy of 1 mole of photons given by

$$E_{photon} = N_a \cdot h \cdot c / \lambda_{irr}$$

with N_a the Avogadro number, h the Planck constant, c the light velocity ($m.s^{-1}$) and λ_{irr} (m)the irradiation wavelength.

Reactant to product conversion yield was determined by injection of the cuvette mixture GC/MS using an Agilent 7820 A GC/5977 E MS spectrometer, equiped with a double HP-5ms Ultra Inert, 30 m, 0,25 mm, 0,25 µm capilary column. For the MS part, ions were produced using an Electronic Impact source and separated using a double quadrupole analyzer. For the GC part, reactant and products were quantified by integrating the FID signal ; integration were corrected using the product/reactant response factor, initially determined upon injection of an equimola amount of the limiting reactant and product, enabling calculation of teh conversion rate X_r for the photochemical reaction. The amount of product formed during the reaction n_{prod} (mol) was calculated using equation

$$n_{prod} = n_{react} . X_r$$

with n_{react} (mol) corresponding to the amount of limiting reactant introduced into the reaction mixtures

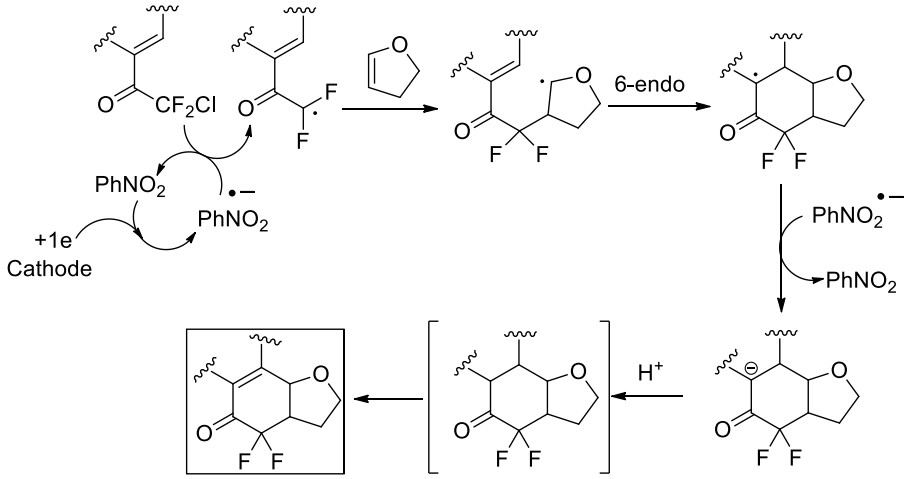
From these values, the photochemical quantum yield of the reaction could be calculated using equation

$$\Phi_r = n_{prod} / n_{photon}$$

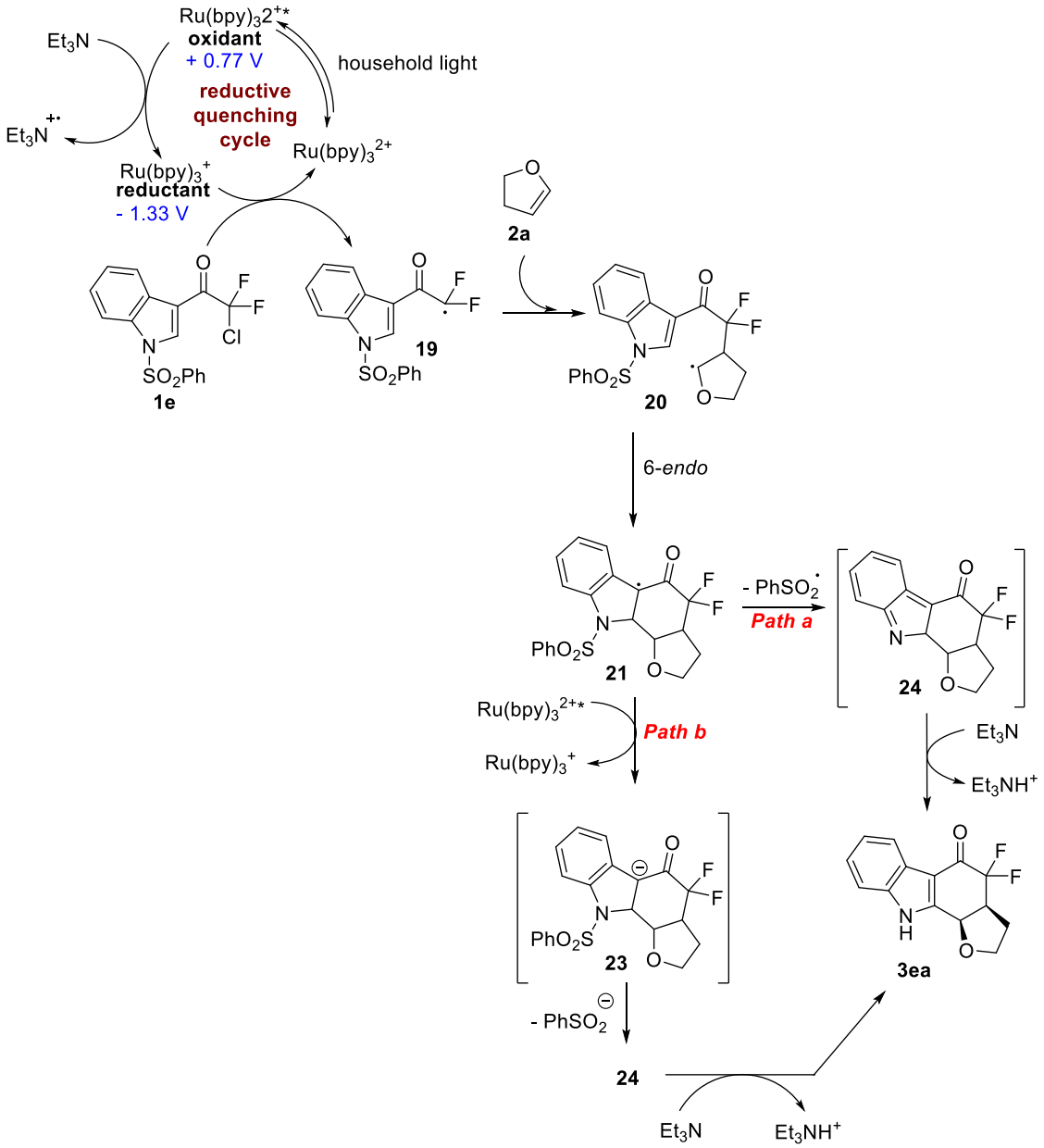
$$\Phi_r^{Iridium} = 0.063$$

$$\Phi_r^{Ruthenium} = 0.021$$

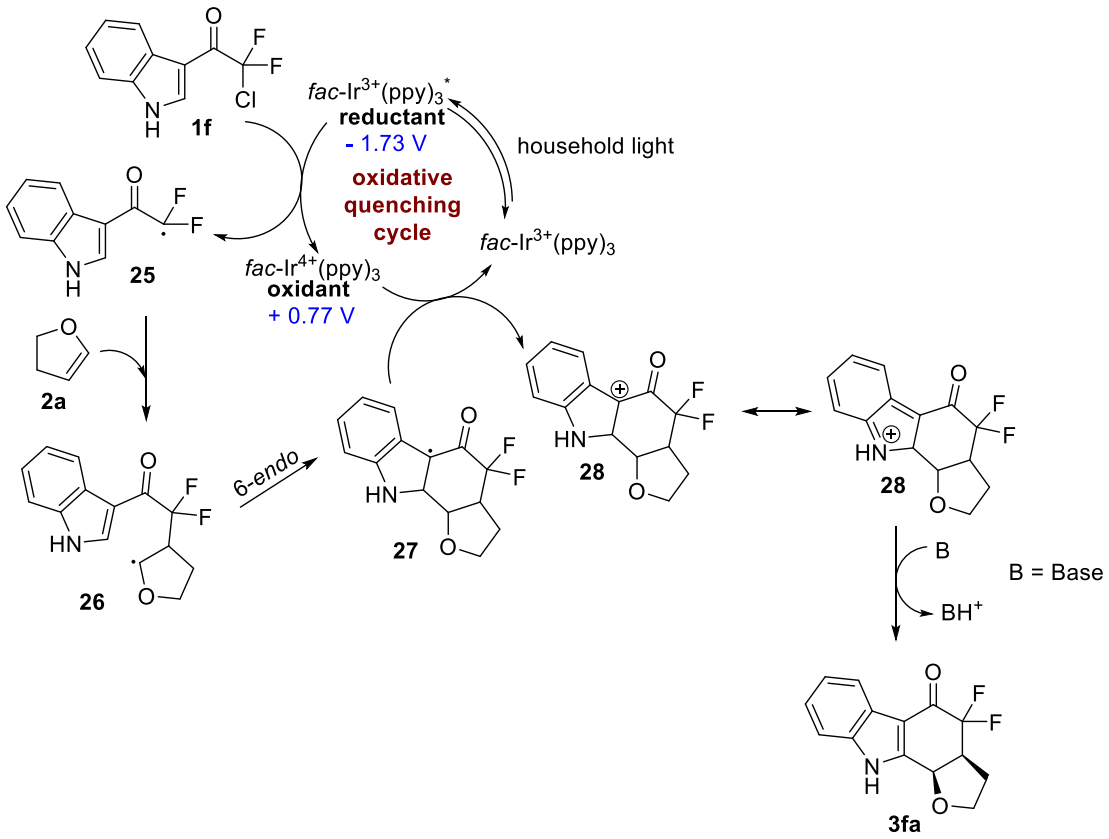
Proposed mechanisms



Proposed electrochemical redox catalyzed mechanism

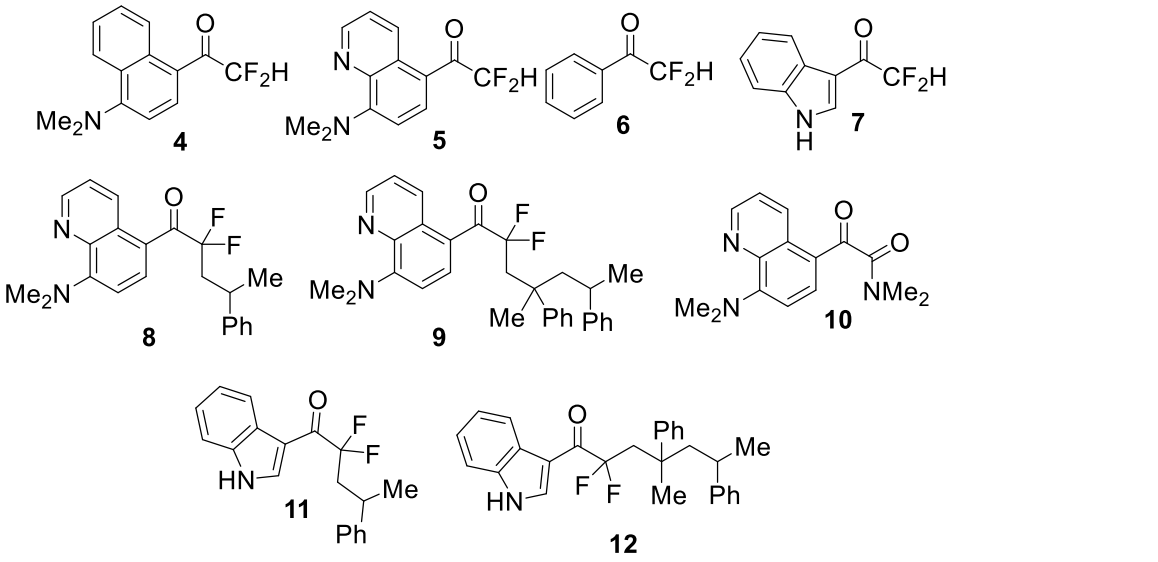


Mechanistic scenarios for the formation of **3ea** from *N*-sulfonyl indole **1e**



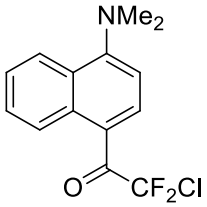
Mechanistic scenarios for the formation of **3ea** under Iridium catalysis from **1f**

Additional products under electrochemical or photoredox catalysis



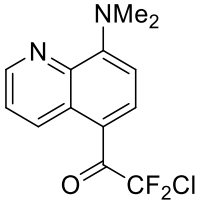
Characterization data of compounds

2-chloro-1-(4-(dimethylamino)naphthalen-1-yl)-2,2-difluoroethanone **1a.**



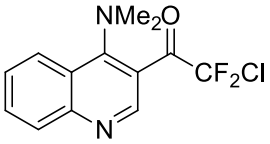
Mp: 80-81°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.97 (d, *J* = 8.7 Hz, 1H), 8.26 (dt, *J* = 8.4, 1.9 Hz, 1H), 8.22 (dd, *J* = 8.5, 0.9 Hz, 1H), 7.65 (ddd, *J* = 8.6, 6.8, 1.4 Hz, 1H), 7.54 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 3.10 (s, 6H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -57.78. ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.29 (t, *J* = 26.8 Hz), 157.91, 134.29 (t, *J* = 5.3 Hz), 129.22, 127.55, 126.26, 125.67, 125.51, 121.05 (t, *J* = 305.0 Hz), 117.90, 110.30, 44.51.

2-chloro-1-(8-(dimethylamino)quinolin-5-yl)-2,2-difluoroethanone **1b.**



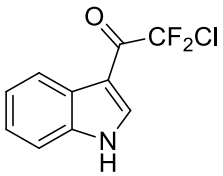
Mp : 37-39°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (dd, *J* = 8.8, 1.5 Hz, 1H), 8.82 (dd, *J* = 3.9, 1.6 Hz, 1H), 8.30 (d, *J* = 8.8 Hz, 1H), 7.59 – 7.49 (m, 1H), 6.87 (d, *J* = 8.9 Hz, 1H), 3.43 (s, 6H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -57.05. ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.64 (t, *J* = 26.5 Hz), 155.44, 146.32, 140.92, 135.72 (t, *J* = 5.1 Hz), 134.57, 130.78, 123.65, 121.02 (t, *J* = 304.7 Hz), 113.06, 109.75, 44.33.

2-Chloro-1-(4-(dimethylamino)quinolin-3-yl)-2,2-difluoroethanone **1c.**



Yield: 32%. Yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.18 (d, *J* = 8.7 Hz, 2H), 7.84 – 7.74 (m, 1H), 7.56 (dd, *J* = 11.9, 4.8 Hz, 1H), 3.21 (s, 6H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -59.92. ^{13}C NMR (75 MHz, Acetone-d_6) δ 160.12, 151.74, 149.99, 149.92, 132.41, 130.87, 130.43, 127.17, 126.78, 124.80 (t, *J* = 236.3 Hz), 115.36, 45.68. HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{13}H_{12}ClF_2N_2O$) requires m/z 285.0601, found m/z 285.0600.

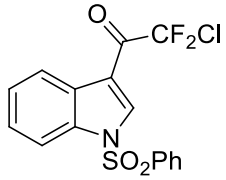
3-Chlorodifluoroacetyl indole **1e.**



Yield: 83%. White solid. Mp: 207-208°C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.66 (s, 1H), 8.49 – 8.45 (m, 1H), 8.22 – 8.15 (m, 1H), 7.62-7.55 (m, 1H), 7.38 – 7.29 (m, 2H). ^{19}F NMR (282 MHz, DMSO-d_6)

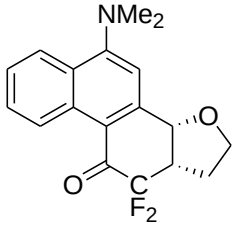
δ -59.98. ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.75 (t, *J* = 28.5 Hz), 137.14, 136.60, 126.20, 124.18, 123.31, 121.19, 120.67 (t, CF_2, *J* = 303.8 Hz), 113.00, 107.36. LRMS (ESI) $[M+H]^+$ = 230.0.

1-Phenylsulphonyl-3-chlorodifluoroacetyl indole **1f.**



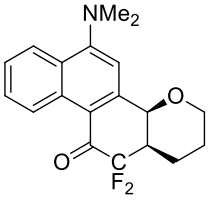
Yield : 87%. White solid. Mp: 131-132°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (t, *J* = 1.9 Hz, 1H), 8.37 – 8.31 (m, 1H), 7.95-8.02 (m, *J* = 5.4, 3.8, 2.4, 1.5 Hz, 3H), 7.69 – 7.62 (m, 1H), 7.59 – 7.51 (m, 2H), 7.49 – 7.38 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -61.77. ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.19 (t, *J* = 30.2 Hz), 136.99, 135.12, 134.82 (t, *J* = 7.0 Hz), 134.43, 129.92, 127.80, 127.36, 126.72, 125.67, 124.21, 120.17 (t, *J* = 302.6 Hz), 113.32, 112.69. HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{16}H_{11}ClF_2NO_3S$) requires m/z 370.0111, found m/z 370.0108.

5-(Dimethylamino)-11,11-difluoro-1,2,11,11a-tetrahydrophenanthro[1,2-b]furan-10(3aH)-one **3aa.**



PE/ETOAc : 90/10. Yield: 71%. Brown solid. Mp : 97-99°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.32 (dd, *J* = 8.7, 0.7 Hz, 1H), 8.14 (dd, *J* = 8.5, 0.9 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.57 – 7.50 (m, 1H), 7.05 (s, 1H), 5.33 (d, *J* = 7.1 Hz, 1H), 4.04 – 3.93 (m, 1H), 3.92 – 3.82 (m, 1H), 3.52 – 3.32 (m, 1H), 3.08 (s, 6H), 2.41 – 2.25 (m, 1H), 2.16 – 1.92 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -99.58 (dd, *J* = 261.9, 12.2 Hz), -111.60 (dd, *J* = 261.9, 10.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.43 (t, *J* = 26.3 Hz), 158.06, 144.57, 132.84, 129.34, 127.19, 126.76, 125.90, 125.18, 117.68 (d, *J* = 1.5 Hz), 114.7 (dd, *J* = 250.5, 241.5 Hz), 111.89, 76.89 (dd, *J* = 6.8, 2.3 Hz), 67.32, 45.22, 44.91 (dd, *J* = 24.0, 21.0 Hz), 26.03 (d, 5.3 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{18}H_{18}F_2NO_2$) requires m/z 318.1300, found m/z 318.1293.

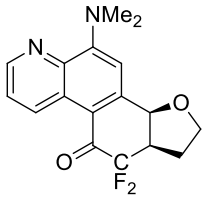
6-(Dimethylamino)-12,12-difluoro-2,3,12,12a-tetrahydro-1H-naphtho[1,2-h]chromen-11(4aH)-one **3ab.**



PE/EtOAc : 95/5. Yield: 44%. Brown solid. Mp : 132-134°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.36 (dd, *J* = 8.7, 0.6 Hz, 1H), 8.16 (dd, *J* = 8.5, 0.9 Hz, 1H), 7.74 – 7.67 (m, 1H), 7.62 – 7.56 (m, 1H), 7.10 (s, 1H), 5.20 (d, *J* = 4.9 Hz, 1H), 3.74 (dt, *J* = 11.3, 3.7 Hz, 1H), 3.49 – 3.38 (m, 1H), 3.11-3.04 (m, 7H), 1.88 – 1.76 (m, 1H), 1.69 – 1.56 (m, 2H), 1.55 – 1.39 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ -104.36 (dd, *J* = 265.2, 9.8 Hz), -113.15 (d, *J* = 263.7 Hz). ^{13}C NMR (101 MHz, DMSO-d_6) δ 183.01 (t, *J* = 25.9 Hz), 158.01, 146.00, 133.24, 129.50, 126.05, 125.98, 125.59, 125.49, 115.53 (d, *J* = 2.4 Hz),

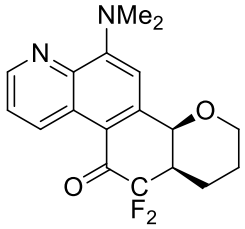
115.28 (dd, *J* = 254.1, 234.6 Hz), 109.68, 70.38 (dd, *J* = 6.7, 3.8 Hz) 62.54, 44.00, 40.92 (t, *J* = 21.0 Hz), 22.68, 19.25 (d, *J* = 5.2 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{19}H_{20}F_2NO_2$) requires m/z 332.1457, found m/z 322.1447.

11-(dimethylamino)-6,6-difluoro-6a,7,8,9a-tetrahydrobenzofuro[6,7-f]quinolin-5(6H)-one **3ba**.



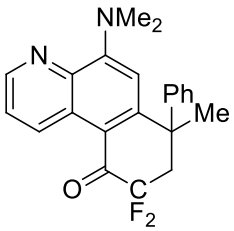
PE/EtOAc : 90/10. Yield: 62%. Brown solid. Mp : 148-150°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (dd, *J* = 8.8, 1.7 Hz, 1H), 8.82 (dd, *J* = 4.1, 1.7 Hz, 1H), 7.53 (dd, *J* = 8.8, 4.1 Hz, 1H), 6.99 (s, 1H), 5.30 (d, *J* = 7.2 Hz, 1H), 3.98 (dd, *J* = 15.8, 7.9 Hz, 1H), 3.92 – 3.82 (m, 1H), 3.45 – 3.30 (m, 1H), 2.38 – 2.25 (m, 1H), 2.14 – 1.98 (dd, *J* = 13.1, 7.9 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -98.55 (dd, *J* = 265.8, 12.4 Hz), -111.33 (dd, *J* = 265.8, 10.3 Hz). ^{13}C NMR (75 MHz, DMSO-d_6) δ 182.11 (t, *J* = 27 Hz), 154.26, 146.68, 145.57, 139.72, 133.79, 128.48, 124.01, 114.81 (dd, *J* = 249.0, 241.5 Hz), 111.73, 110.95, 75.93, 75.90, 66.83, 43.93, 43.53 (dd, *J* = 24.0, 21.8 Hz), 25.47 (d, *J* = 3.0 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{17}H_{17}F_2N_2O_2$) requires m/z 319.1253, found m/z 319.1242.

(12-(Dimethylamino)-6,6-difluoro-6a,8,9,10a-tetrahydro-6H-chromeno[7,8-f]quinolin-5(7H)-one **3bb**.



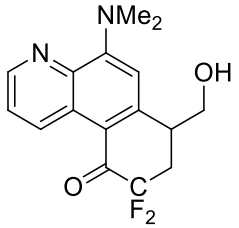
PE/EtOAc : 97/3. Yield: 25%. Orange solid. Mp : 140-142°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (dd, *J* = 8.8, 1.7 Hz, 1H), 8.80 (dd, *J* = 4.1, 1.7 Hz, 1H), 7.52 (dd, *J* = 8.8, 4.1 Hz, 1H), 7.12 (s, 1H), 5.29 (d, *J* = 5.2 Hz, 1H), 3.81 – 3.75 (m, 1H), 3.50 – 3.37 (m, 7H), 3.08 – 2.97 (m, 1H), 1.98 – 1.87 (m, 1H), 1.81 – 1.67 (m, 1H), 1.64 – 1.54 (m, 1H), 1.53 – 1.39 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -104.75 (dd, *J* = 269.9, 10.3 Hz), -117.20 (d, *J* = 270.4 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.97 (t, *J* = 25.3 Hz), 155.90, 146.70, 146.16, 140.70, 135.34, 130.05 (d, *J* = 1.7 Hz) 123.83, 115.04 (dd, *J* = 255.5, 244.4 Hz), 113.85 (d, *J* = 3.0 Hz), 109.28, 70.66 (dd, *J* = 8.1, 2.0 Hz), 62.31, 44.38, 42.84 (t, *J* = 21.2 Hz), 23.59, 19.58 (d, *J* = 6.1 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{18}H_{19}F_2N_2O_2$) requires m/z 333.1409, found m/z 333.1406.

5-(Dimethylamino)-9,9-difluoro-7-methyl-7-phenyl-8,9-dihydrobenzo[f]quinolin-10(7H)-one **3bg**



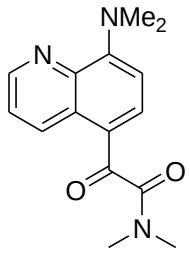
PE/EOAc: 90/10. Yield: 10%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (dd, *J* = 8.8, 1.6 Hz, 4H), 8.86 (d, *J* = 2.7 Hz, 5H), 7.60 (dd, *J* = 8.8, 4.1 Hz, 1H), 7.33 – 7.30 (m, 3H), 7.25 – 7.21 (dd, *J* = 8.3, 1.3 Hz, 2H), 6.38 (s, 1H), 3.20 (s, 6H), 3.00 – 2.85 (m, 1H), 2.77 – 2.65 (m, 1H), 1.99 (d, *J* = 1.6 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -98.58 (ddd, *J* = 274.9, 29.6, 13.0 Hz), -103.03 (dt, *J* = 274.9, 9.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.09 (t, *J* = 25.4 Hz), 156.40, 148.08, 146.67, 136.43, 129.88, 129.03, 128.69, 127.31, 127.13, 125.39, 123.98, 123.89, 112.67 (t, *J* = 2.4 Hz), 47.23 (t, *J* = 21.2 Hz), 44.14, 29.80 (d, *J* = 3.8 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{22}H_{21}F_2N_2O$) requires m/z 367.1616, found m/z 367.1601

5-(Dimethylamino)-9,9-difluoro-7-(hydroxymethyl)-8,9-dihydrobenzo[f]quinolin-10(7H)-one **3bh**



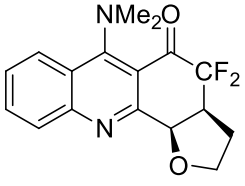
PE/EtOAc: 7/3. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.83 (dd, *J* = 8.8, 1.8 Hz, 1H), 8.77 (dd, *J* = 4.1, 1.7 Hz, 1H), 7.51 (dd, *J* = 8.8, 4.1 Hz, 1H), 6.78 (s, 1H), 4.07 – 3.90 (m, 2H), 3.39 (s, 7H), 2.82 – 2.47 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -99.53 (ddd, *J* = 274.1, 27.3, 12.2 Hz), -101.51 – -103.79 (m). ^{13}C NMR (101 MHz, DMSO) δ 182.36 (t, *J* = 25.3 Hz), 153.74, 149.67, 146.07, 139.35, 133.90, 129.51, 123.79, 114.31 (t, *J* = 245.4 Hz), 112.54, 111.24, 64.89 (d, *J* = 2.3 Hz), 43.93, 39.79, 32.36 (t, *J* = 22.2 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{16}H_{16}F_2N_2O_2$) requires m/z 307.1253, found m/z 307.1253.

2-(8-(Dimethylamino)quinolin-5-yl)-N,N-dimethyl-2-oxoacetamide **8.**



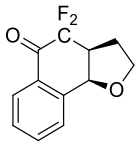
PE/EtOAc : 7/3. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.79 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.84 (dd, *J* = 4.1, 1.8 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.53 (dd, *J* = 8.7, 4.1 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 1H), 3.38 (d, *J* = 7.3 Hz, 6H), 3.13 (s, 3H), 3.00 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.83, 168.23, 155.37, 146.64, 146.41, 140.99, 137.36, 134.81, 129.52, 123.52, 117.44, 110.80, 44.25, 37.39, 34.11. HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{15}H_{18}N_3O_2$) requires m/z 272.1394, found m/z 272.1392.

6-(Dimethylamino)-4,4-difluoro-2,3,3a,4-tetrahydrofuro[3,2-c]acridin-5(11bH)-one **3ca.**



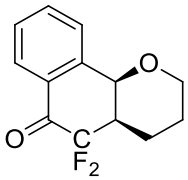
PE/EtOAc : 80/20. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 8.6, 1.0 Hz, 1H), 8.09 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.72 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.52 – 7.44 (m, 1H), 5.17 (d, *J* = 6.7 Hz, 1H), 4.02 (ddd, *J* = 23.8, 12.2, 6.6 Hz, 2H), 3.20 (s, 6H), 2.44 – 2.20 (m, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -111.95 (dd, *J* = 256.0, 15.1 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{17}H_{17}F_2N_2O_2$) requires m/z 319.1253, found m/z 319.1243.

4,4-Difluoro-2,3,3a,4-tetrahydronaphtho[1,2-b]furan-5(9bH)-one **3da.**



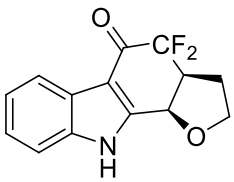
PE/EtOAc: 90/10. Yield: 53%. Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.77 – 7.70 (m, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 5.31 (d, *J* = 7.4 Hz, 1H), 3.99 (dd, *J* = 15.9, 7.9 Hz, 1H), 3.86-3.77 (m, 1H), 3.49 – 3.30 (m, 1H), 2.35-2.26 (m, 1H), 2.03 – 1.86 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -100.46 (dd, *J* = 273.8, 12.1 Hz), -112.78 (dd, *J* = 273.8, 10.9 Hz). ^{13}C NMR (75 MHz, DMSO-d_6) δ 184.80 (t, *J* = 26.6 Hz), 140.74, 136.06, 130.29, 129.41, 128.55 (d, *J* = 3.8 Hz), 126.82, 114.63 (dd, *J* = 249.1, 244.0 Hz), 75.17 (t, *J* = 4.4 Hz), 67.03, 43.77 (dd, *J* = 23.0, 20.4 Hz), 24.95 (dd, *J* = 3.8, 1.8 Hz). HRMS (ESI): exact mass calculated for $[M+Na]^+$ ($C_{12}H_{10}F_2NaO_2$) requires m/z 247.0541, found m/z 247.0545.

5,5-Difluoro-3,4,4a,10b-tetrahydro-2H-benzo[h]chromen-6(5H)-one **3db**.



PE/EtOAc : 97/3. Yield : 16%. White solid. Mp : 58-60°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 – 8.10 (m, 1H), 7.79 – 7.68 (m, 2H), 7.54 – 7.46 (m, 1H), 5.33 (d, *J* = 5.1 Hz, 1H), 3.80 – 3.70 (m, 1H), 3.40 (td, *J* = 11.5, 2.7 Hz, 1H), 3.14 – 2.97 (m, 1H), 1.97 – 1.84 (m, 1H), 1.81 – 1.67 (m, 1H), 1.66 – 1.55 (m, 1H), 1.45 – 1.29 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -107.28 (dd, *J* = 274.9, 7.9 Hz), -118.16 – -119.76 (m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.85 (t, *J* = 26.3 Hz), 141.36, 135.95, 129.54 (d, *J* = 3.0 Hz), 128.88, 128.40 (d, *J* = 2.0 Hz), 127.90, 115.0 (dd, *J* = 258.6, 243.4 Hz), 70.10 (dd, *J* = 7.1, 3.0 Hz), 61.91, 43.09 (t, *J* = 21.2 Hz), 23.89, 19.09 (d, *J* = 8.1 Hz). HRMS (ESI): exact mass calculated for $[M+Na]^+$ ($C_{13}H_{12}F_2NaO_2$) requires m/z 261.0698, found m/z 261.0694.

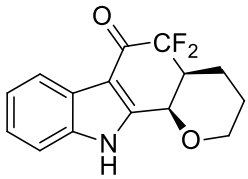
4*,4-Difluoro-3a,4,10,10b-tetrahydro-2H-furo[2,3-a]carbazol-5(3H)-one* **3ea.**



DCM/PE: 90/10. Yield: 83%. White solid. Mp > 210°C. ^{1}H NMR (300 MHz, CD_3OD) δ 8.09 – 8.03 (m, 1H), 7.51 – 7.45 (m, 1H), 7.30 (pd, *J* = 7.2, 1.4 Hz, 2H), 5.49 (d, *J* = 6.7 Hz, 1H), 4.00-4.08 (m, 1H),

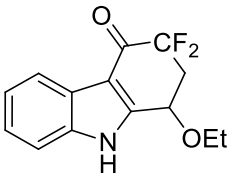
3.78-3.85 (m, 1H), 3.48-3.58 (m, 1H), 2.39 – 2.23 (m, 1H), 2.05 – 1.89 (m, 1H). ^{19}F NMR (282 MHz, CD_3OD) δ -95.24 (dd, *J* = 280.6, 13.5 Hz), -113.36 (dd, *J* = 280.5, 7.6 Hz). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.93 (t, *J* = 26.1 Hz), 148.83 (s), 137.7 (s), 124.51 (s), 123.49 (d, *J* = 1.6 Hz), 122.90 (s), 120.75 (s), 115.78 (dd, *J* = 252.4, 243.3 Hz), 112.74 (s), 109.27 (s), 70.91 (d, *J* = 6.9 Hz), 67.75 (s), 46.25 (dd, *J* = 25.5, 22.2 Hz), 25.50 (d, *J* = 5.8 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{14}H_{12}F_2NO_2$) requires m/z 264.0831, found m/z 264.0840.

5,5-Difluoro-3,4,4a,5,11,11b-hexahydropyrano[2,3-a]carbazol-6(2H)-one **3eb.**



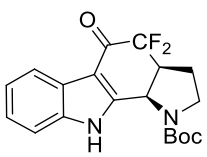
DCM/PE: 90/10. Yield : 67 %. White solid. Mp > 210°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.88 (br. s, 1H), 8.23 (dd, *J* = 6.3, 2.9 Hz, 1H), 7.50 – 7.41 (m, 1H), 7.40 – 7.31 (m, 2H), 5.51 (d, *J* = 5.5 Hz, 1H), 3.88 (ddt, *J* = 11.4, 4.0, 1.9 Hz, 1H), 3.38 (td, *J* = 11.7, 2.4 Hz, 1H), 3.14-3.04 (m, 1H), 2.02 (d, *J* = 16.3 Hz, 1H), 1.84 – 1.66 (m, 1H), 1.57 – 1.48 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -102.58 (dd, J_{AB} = 278.2, 10.6 Hz), -119.51 (d, *J* = 277.8 Hz). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.07 (t, *J* = 25.9 Hz), 149.45, 137.37, 124.24, 124.00, 122.88, 120.60, 116.51 (dd, *J* = 256.5, 242.4 Hz), 112.76, 109.30 (d, *J* = 5.2 Hz), 66.46, 63.39, 41.86 (t, *J* = 22.2 Hz), 22.61, 19.59. HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{15}H_{14}F_2NO_2$) requires m/z 278.0987, found m/z 278.0991.

1-Ethoxy-3,3-difluoro-2,3-dihydro-1H-carbazol-4(9H)-one **3ec.**



DCM/PE: 90/10. Yield: 75%. Pale brown solid. Mp : 194-196 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.07 (br. s, 1H), 8.27 – 8.20 (m, 1H), 7.41-7.47 (m, 1H), 7.38 – 7.30 (m, 2H), 5.08 (dd, *J* = 9.6, 5.2 Hz, 1H), 3.82-3.94 (m, 1H), 3,67-3.78 (m, 1H), 3.13-3.26 (m, 1H), 2.34-2.56 (m, 1H), 1.37 (t, *J* = 7.0 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -102.43 (ddd, *J* = 281.5, 35.0, 10.5 Hz), -108.41 (ddd, *J* = 281.4, 6.5, 4.0 Hz). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.55 (t, *J* = 25.7 Hz), 151.28 (s), 137.17 (s), 124.30 (s), 123.92 (s), 122.87 (s), 120.66 (s), 114.93 (dd, *J* = 250.0 Hz, 244 Hz), 112.79 (s), 108.92 (s), 67.61 (dd, *J* = 7.5, 3.8 Hz), 64.62 (s), 38.23 (t, *J* = 22.2 Hz), 15.29 (s). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{14}H_{14}F_2NO_2$) requires m/z 266.0987, found m/z 266.0985.

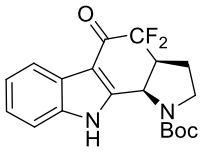
tert-Butyl 4,4-difluoro-5-oxo-3,3a,4,5,10,10b-hexahydropyrrolo[2,3-a]carbazole-1(2H)-carboxylate **3ed.**



PE/DCM: 60/40. Yield: 44%. Pale yellow solid. Mp : 178-180°C. ^{1}H NMR (400 MHz, DMSO-D6) δ 11.37 (br. s, 1H), 8.02 (d, *J* = 7.0 Hz, 1H), 7.72 (d, *J* = 7.7 Hz, 1H), 7.34 – 7.24 (m, 2H), 5.49 (d, *J* = 7.1

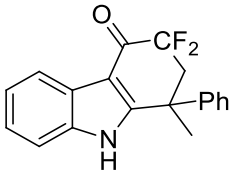
Hz, 1H), 3.67 – 3.48 (m, 2H), 3.23 – 3.16 (m, 1H), 2.25 – 2.12 (m, 1H), 1.91 – 1.83 (m, 1H), 1.53 (s, 9H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -92.72 (ddd, *J* = 280.5, 14.0, 1.3 Hz), -117.86 (dd, *J* = 280.5, 4.4 Hz). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.24 (t, *J* = 25.3 Hz), 149.06, 137.44, 123.96, 123.27, 122.60, 120.25, 115.03 (dd, *J* = 252.5, 243.4 Hz), 113.28, 108.35 (d, *J* = 3.0 Hz), 80.13, 45.93, 45.24, 27.95, 27.77 (t, *J* = 11.1 Hz), 24.67, 23.99. HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{19}H_{21}F_2N_2O_3$) requires m/z 363.1515, found m/z 363.1503.

tert-Butyl 5,5-difluoro-6-oxo-2,3,4,4a,5,6,11,11b-octahydro-1H-pyrido[2,3-a]carbazole-1-carboxylate **3ee.**



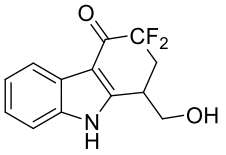
DCM/PE: 70/30. Yield: 33%. Pale yellow solid. Mp > 210 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.69 (s, 1H), 11.53 (s, 1H), 8.12 – 8.04 (m, 2H), 7.50 (ddd, *J* = 10.1, 8.1, 3.9 Hz, 2H), 7.35 – 7.26 (m, 4H), 6.17 (d, *J* = 4.9 Hz, 1H), 6.04 (d, *J* = 4.7 Hz, 1H), 4.19 (d, *J* = 13.8 Hz, 1H), 4.10 (d, *J* = 14.0 Hz, 1H), 3.09 – 2.91 (m, 4H), 2.71 (dd, *J* = 18.7, 7.3 Hz, 1H), 2.55 (dd, *J* = 19.1, 8.1 Hz, 1H), 1.91 (d, *J* = 10.5 Hz, 2H), 1.67 – 1.40 (m, 20H). ^{19}F NMR (282 MHz, Acetone-d_6) δ -102.71 – -104.67 (m), -121.06 (dd, *J* = 276.0, 81.0 Hz). ^{13}C NMR (101 MHz, Acetone-d_6) δ, 178.74 (t, *J* = 25.3 Hz, CO), 178.65 (t, *J* = 25.3 Hz, CO), 155.41, 154.27, 149.72, 149.63, 138.17, 125.72, 124.94, 123.73, 121.69, 117.22 (dd, *J* = 257.6, 244.4 Hz), 113.28, 113.24, 110.95 (d, *J* = 5.1 Hz), 110.64 (d, *J* = 5.1 Hz), 81.26, 81.10, 60.50, 49.27 (d, *J* = 9.1 Hz), 47.98 (d, *J* = 9.1 Hz), 45.12 (t, *J* = 22.2 Hz), 44.74 (t, *J* = 22.2 Hz), 41.72, 40.13, 28.36, 23.91, 23.65, 21.33, 20.80, 14.43. HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{20}H_{23}F_2N_2O_3$) requires m/z 377.1671, found m/z 377.1656.

3,3-Difluoro-1-methyl-1-phenyl-2,3-dihydro-1H-carbazol-4(9H)-one **3eg**.



PE/DCM: 70/30. Yield: 42%. Greenish solid. Mp > 210°C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.43 (br s, 1H), 8.10-8.06 (m, 1H), 7.55 – 7.48 (m, 1H), 7.37 – 7.24 (m, 5H), 7.15 – 7.07 (m, 2H), 3.13 – 2.97 (m, 1H), 2.95-2.82 (m, 1H), 1.90 (s, 3H). ^{19}F NMR (282 MHz, DMSO-d_6) δ -100.68 (ddd, *J* = 276.3, 27.3, 11.2 Hz), -103.62 (*J* = 276.3, 12.8, 8.8 Hz). ^{13}C NMR (75 MHz, DMSO-d_6) δ 179.08 (t, *J* = 25.4 Hz), 156.61, 145.82, 137.21, 128.40, 126.84, 126.14, 124.17, 124.10, 122.88, 120.64, 114.54 (t, *J* = 246.4 Hz), 111.26, 110.01, 46.80 (t, *J* = 21.3 Hz), 40.61 (d, *J* = 7.4 Hz), 27.76. HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{19}H_{16}F_2NO$) requires m/z 312.1194, found m/z 312.1184.

3,3-Difluoro-1-(hydroxymethyl)-2,3-dihydro-1H-carbazol-4(9H)-one **3eh.**

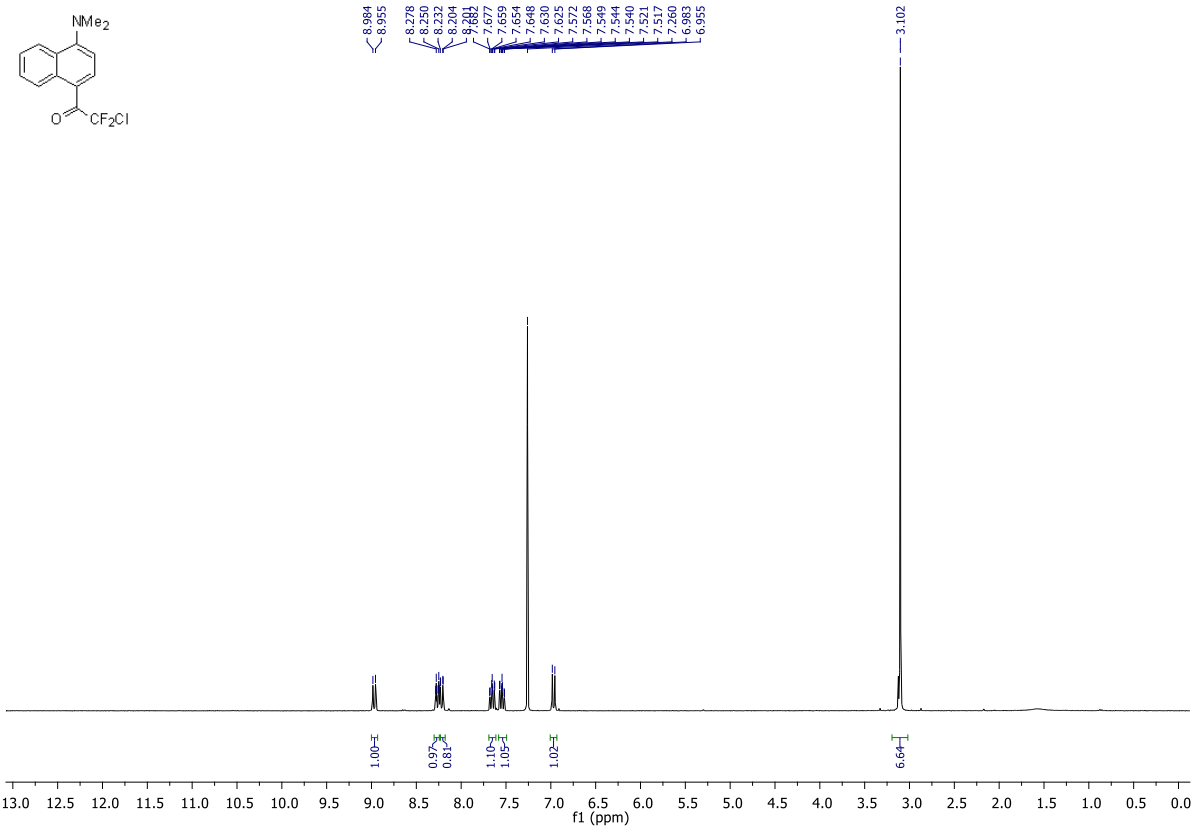


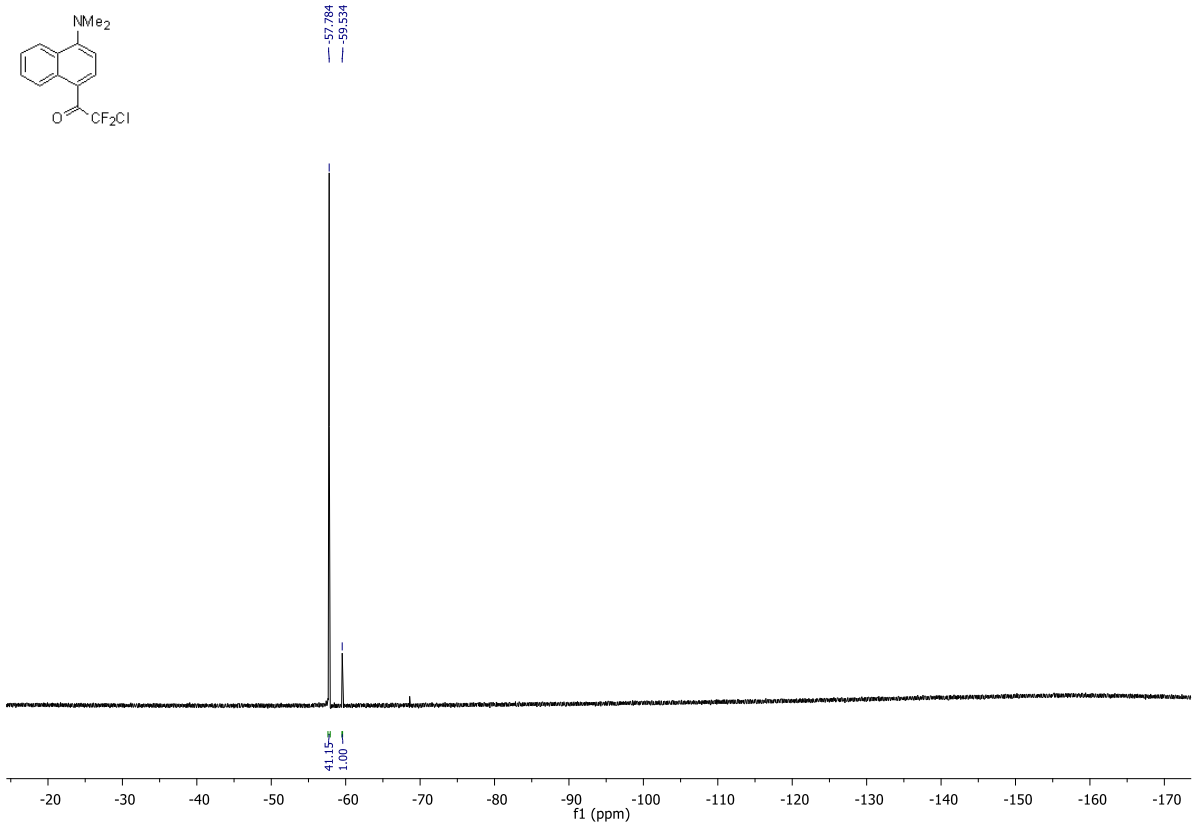
PE/EtOAc: 50/50. Yield: 38%. Brown-orange solid. Mp : 151-153°C. ^{1}H NMR (300 MHz, CD_3OD) δ 8.08-8.02 (m, 1H), 7.50 – 7.45 (m, 1H), 7.31 – 7.20 (m, 2H), 4.05 – 3.87 (m, 2H), 3.59-3.48 (m, 1H),

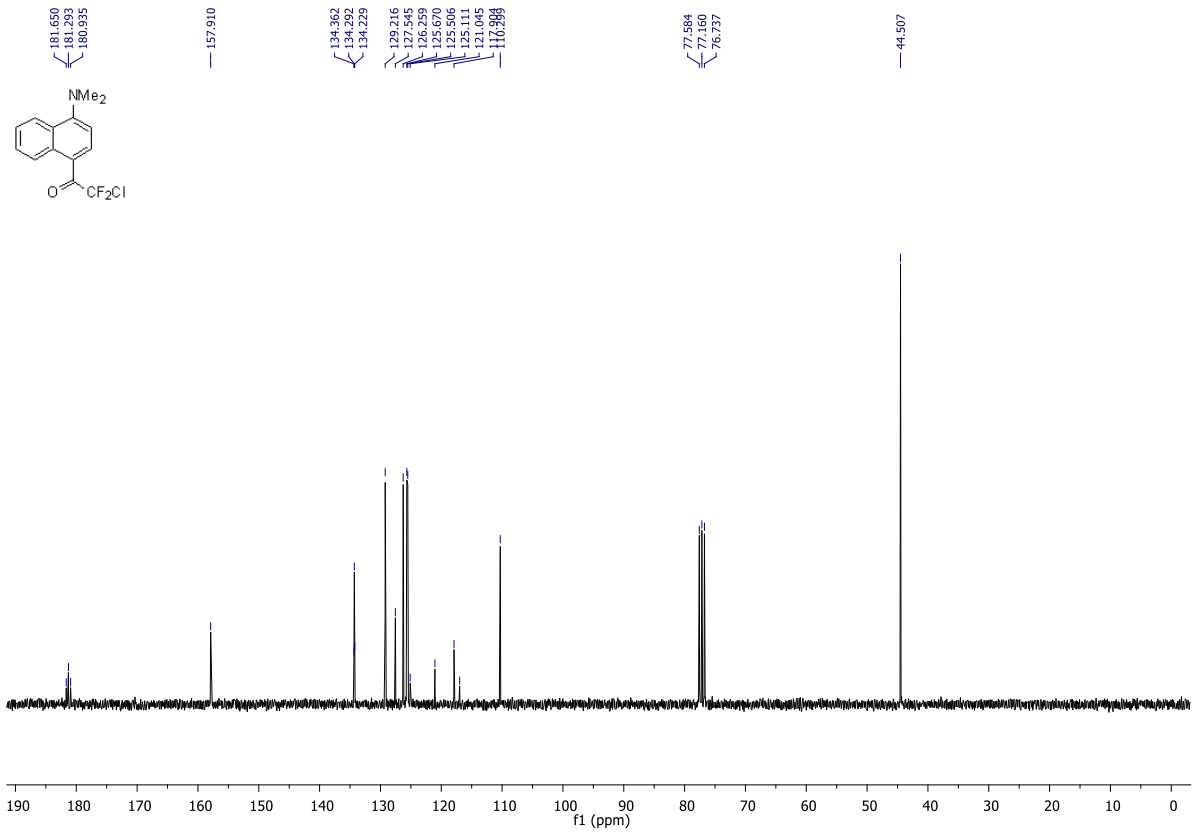
2.76 – 2.62 (m, 1H), 2.62-2.42 (m, 1H). ^{19}F NMR (282 MHz, CD_3OD) δ -106.46 (ddd, *J* = 275.1, 27.0, 10.9 Hz), -108.73 (ddd, *J* = 275.1, 14.5, 8.1 Hz). ^{13}C NMR (101 MHz, CD_3OD) δ 181.60 (t, *J* = 26.3 Hz), 154.68, 138.91, 125.80, 125.27, 123.98, 121.98, 116.57 (dd, *J* = 249.5, 246.44 Hz), 113.19, 111.85, 63.97, 36.17 (dd, *J* = 6.1, 3.0 Hz), 35.81 (t, *J* = 24.2 Hz). HRMS (ESI): exact mass calculated for $[M+H]^+$ ($C_{13}H_{12}F_2NO_2$) requires m/z 252.0831, found m/z 252.0837.

^{1}H, ^{19}F and ^{13}C Spectra

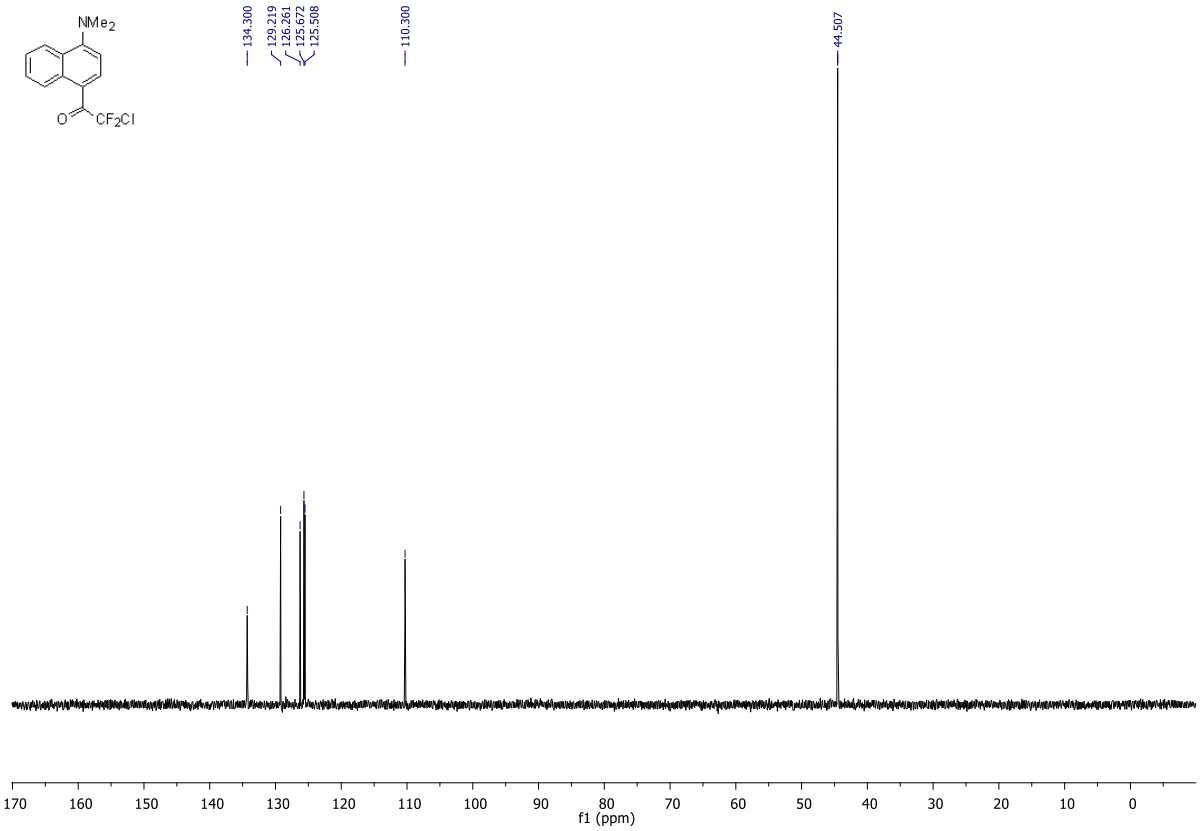
1a



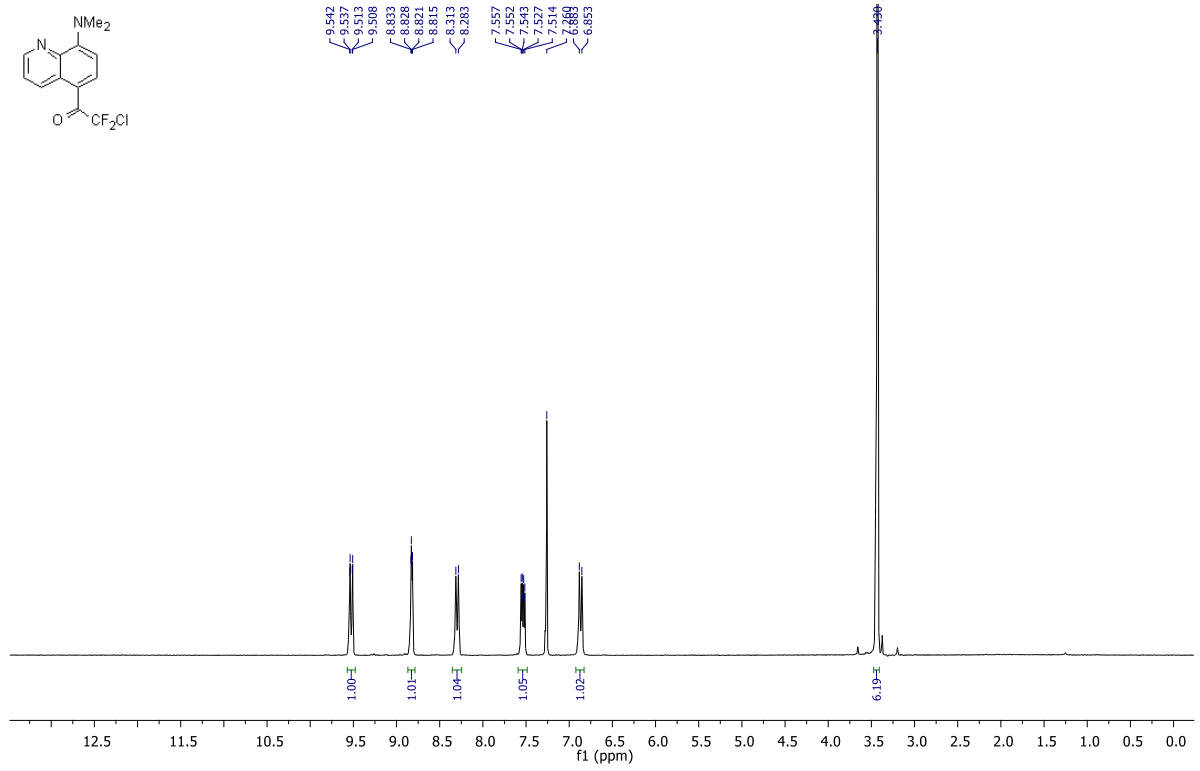

NMe2
O
CF2Cl
-57.784
-59.534
41.15
1.00
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170
f1 (ppm)

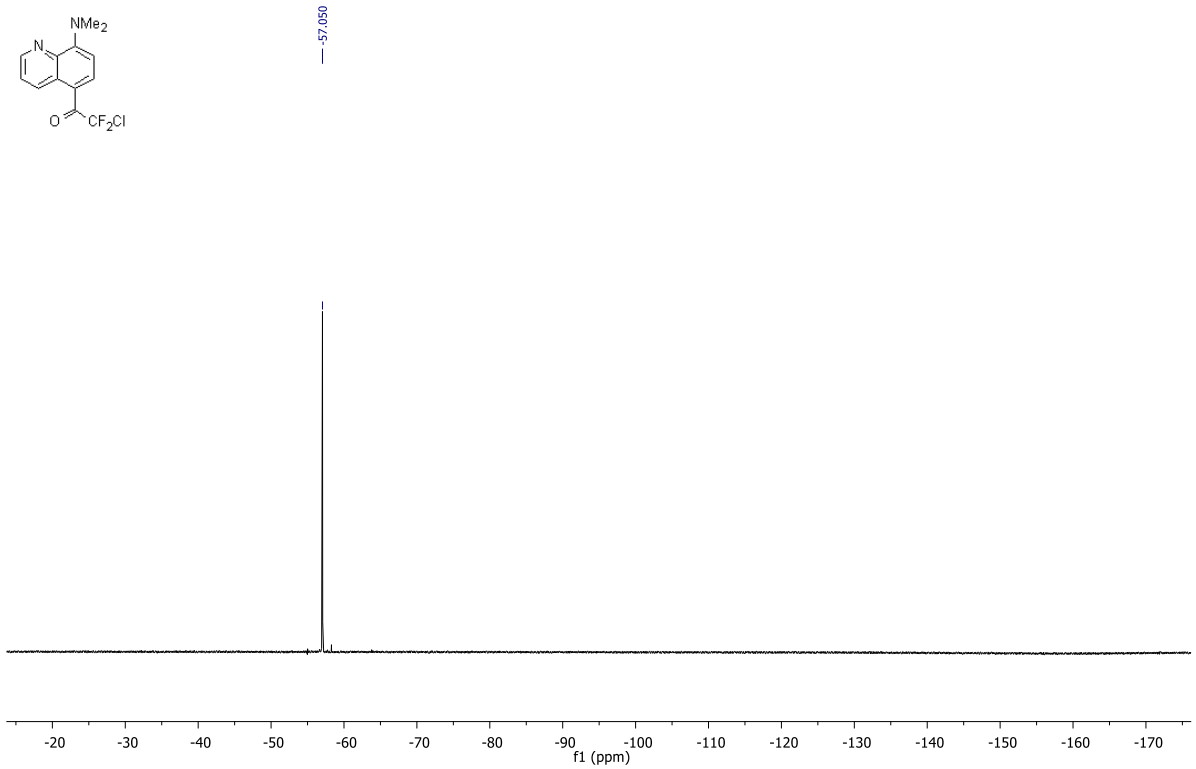

181.650
181.293
180.935
157.910
134.362
134.292
134.229
129.216
127.545
126.259
125.670
125.506
125.111
121.045
77.584
77.160
76.737
44.507
NMe2
O
CF2Cl
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

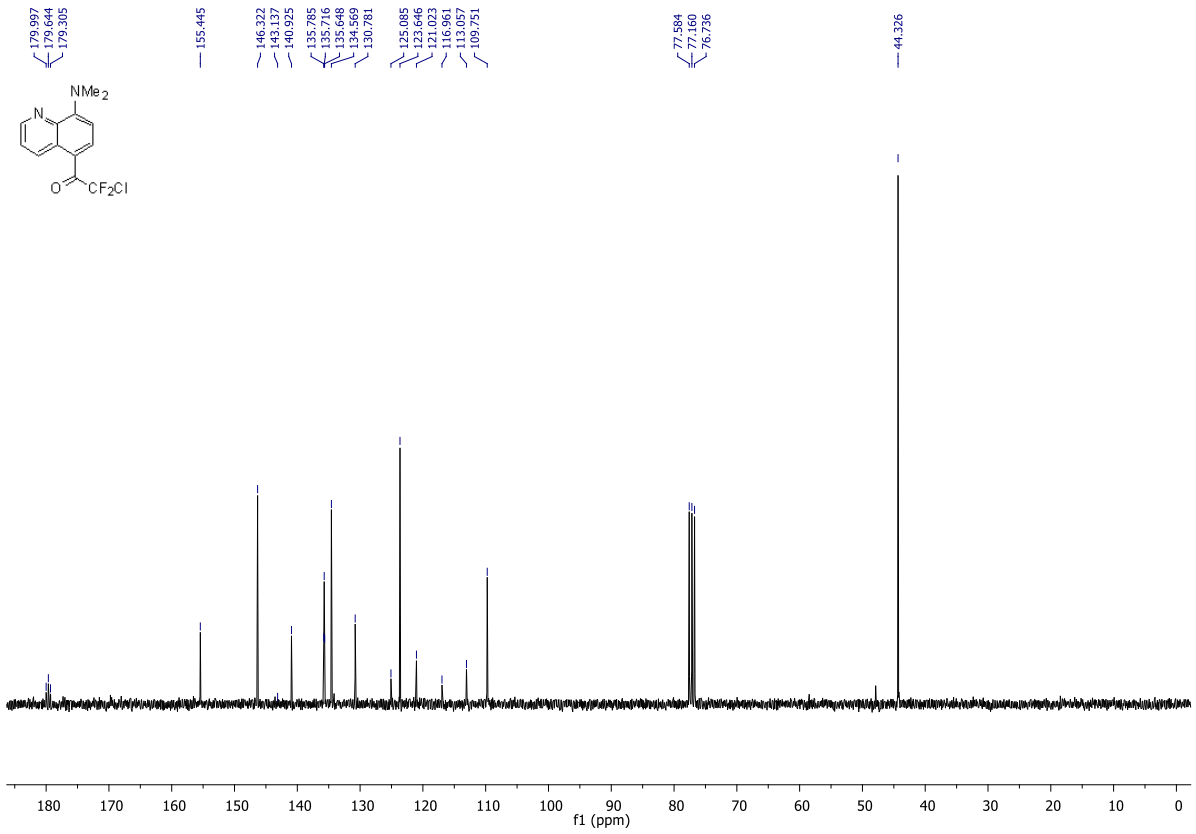
DEPT


NMe2
O
CF2Cl
134.300
129.219
126.261
125.672
125.508
110.300
44.507
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

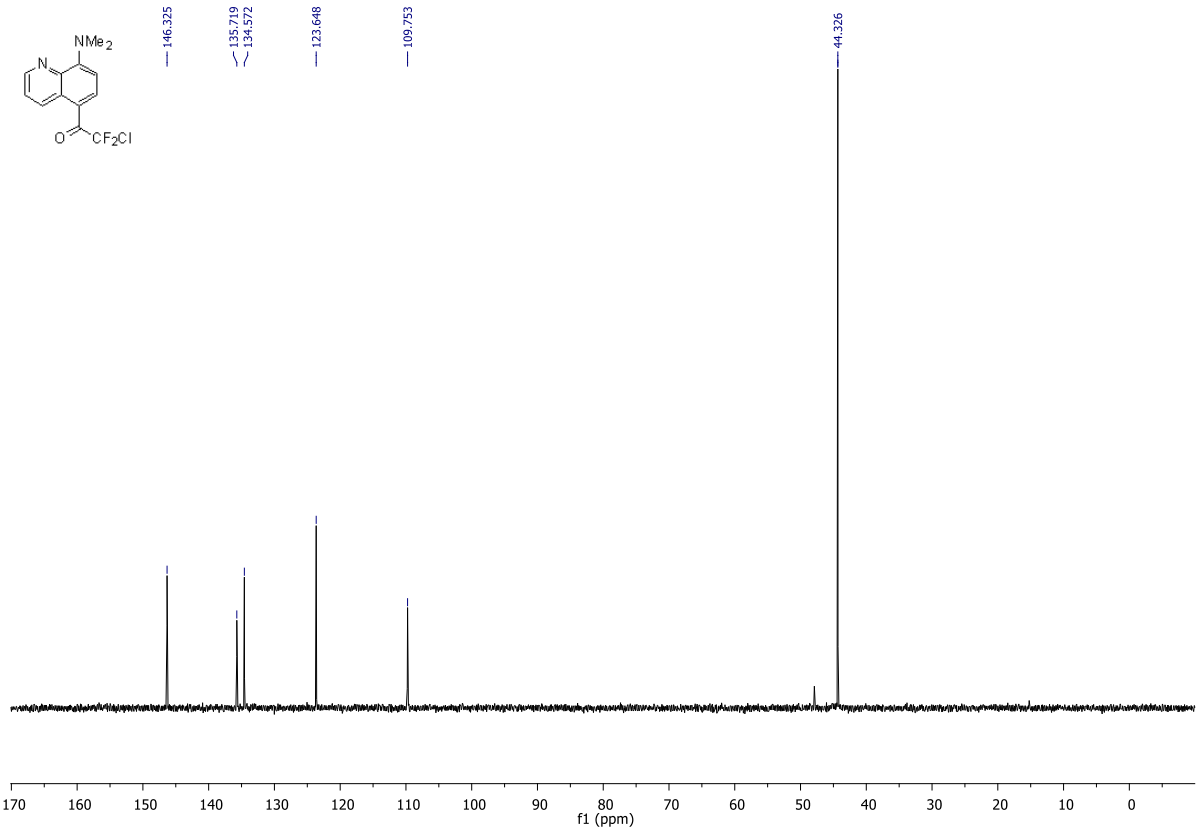
1b


NMe2
N
O
CF2Cl
9.542
9.537
9.513
9.508
8.833
8.828
8.821
8.815
8.313
8.283
7.557
7.552
7.543
7.527
7.514
6.853
3.490
1.00
1.01
1.04
1.05
1.02
6.19
12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

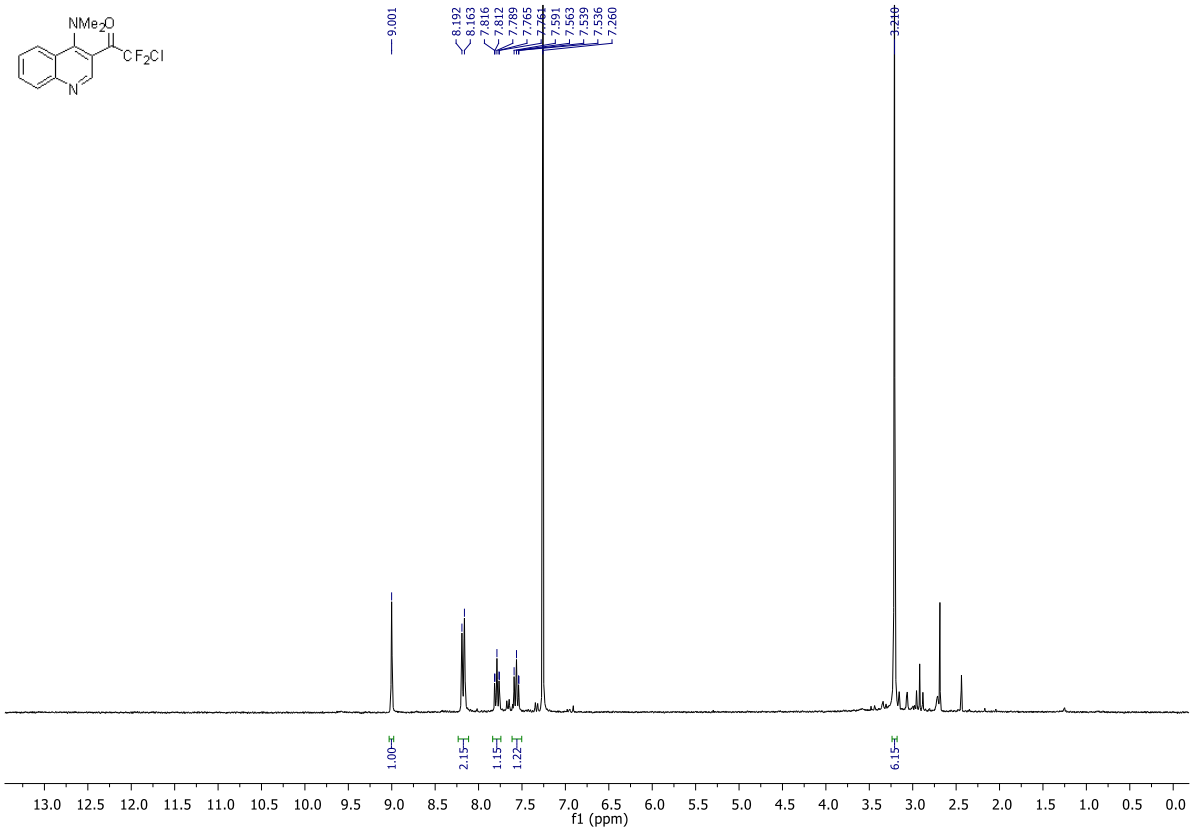

NMe2
N
O
CF2Cl
-57.050
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)


179.997
179.644
179.305
155.445
146.322
143.137
140.925
135.785
135.716
135.648
134.569
130.781
125.085
123.646
121.023
116.961
113.057
109.751
77.584
77.160
76.736
44.326
NMe2
N
O
CF2Cl
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

DEPT


NMe2
O
CF2Cl
146.325
135.719
134.572
123.648
109.753
44.326
f1 (ppm)

1c


NMe2
O
CF2Cl
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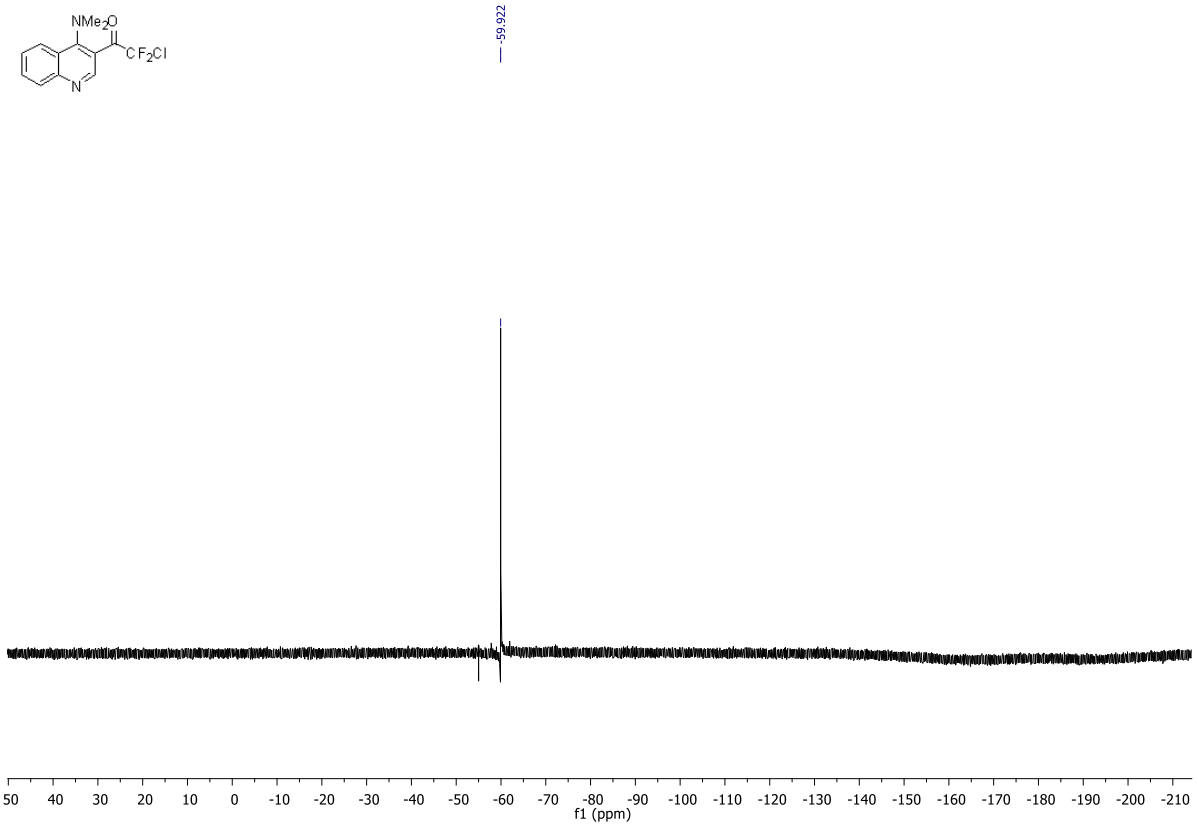
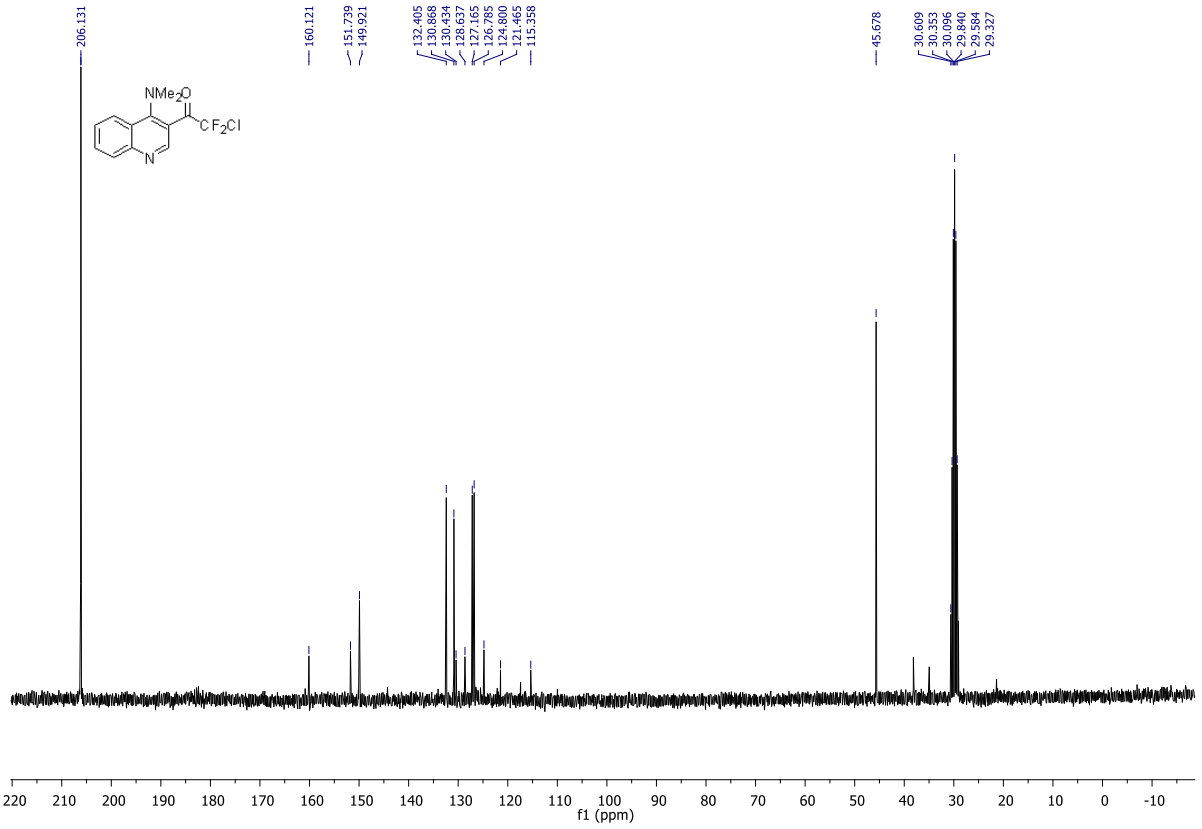
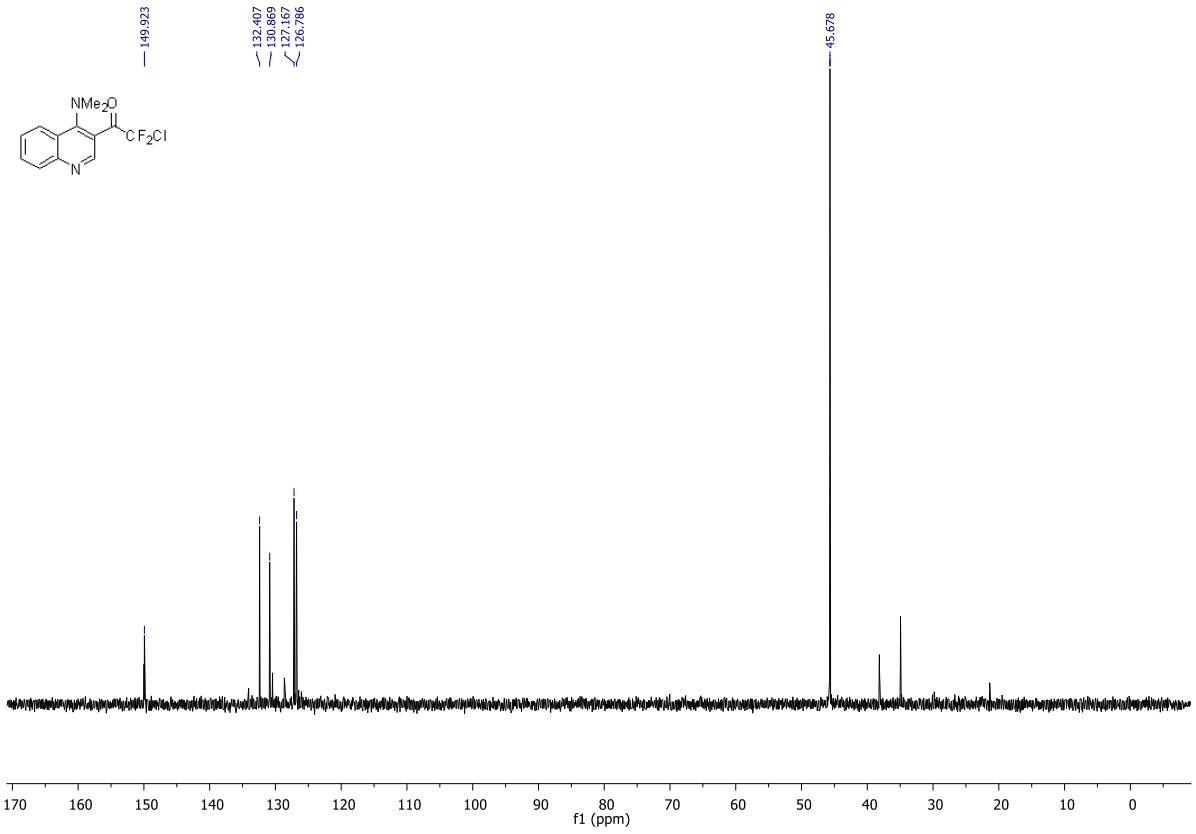
8.192
8.163
7.816
7.812
7.789
7.765
7.761
7.591
7.563
7.539
7.536
7.260
3.210
1.00
2.15
1.15
1.22
6.15
f1 (ppm)

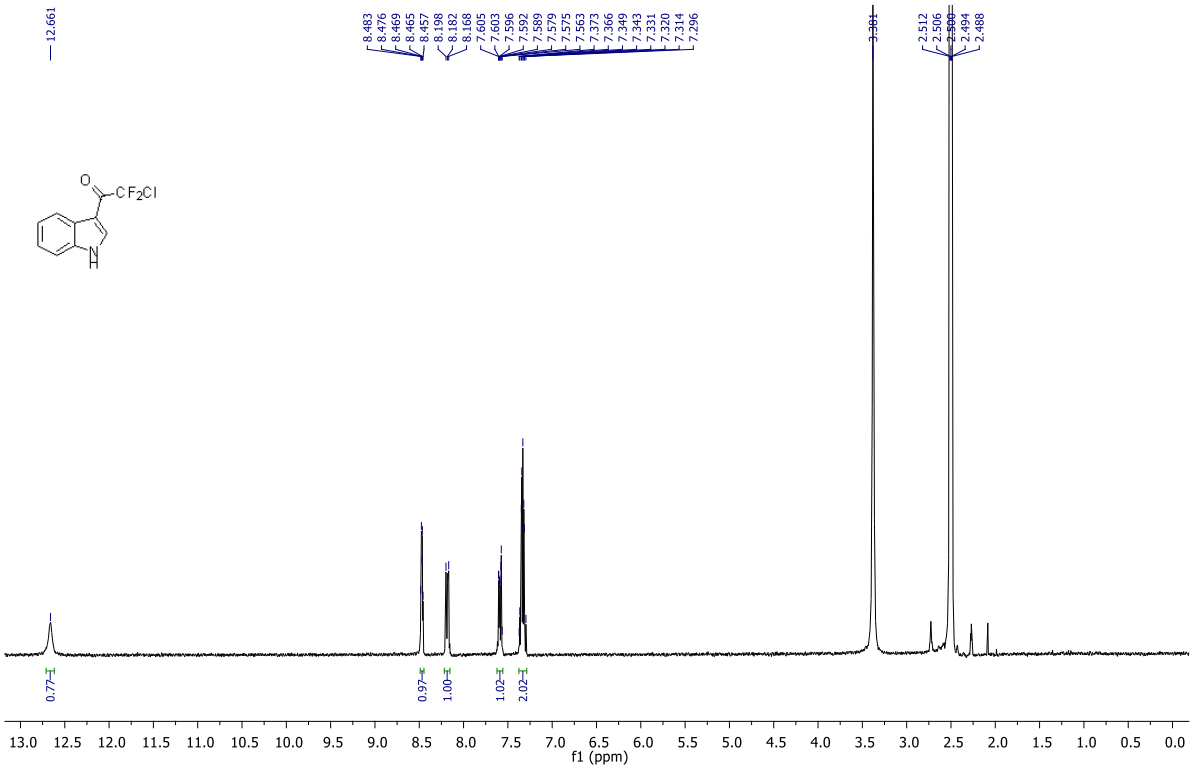

NMe2O
CF2Cl
N
-59.922
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

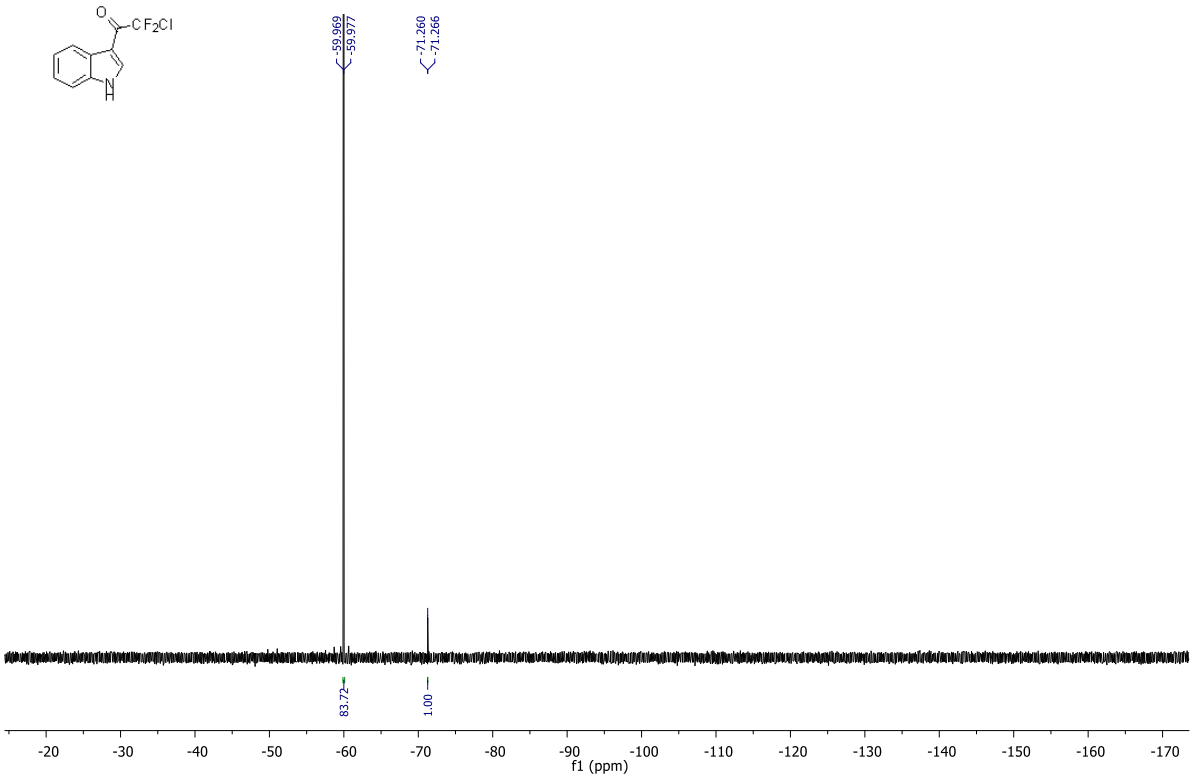

206.131
160.121
151.739
149.921
132.405
130.868
130.434
128.637
127.165
126.785
124.800
121.465
115.358
45.678
30.609
30.353
30.096
29.840
29.584
29.327
NMe2O
CF2Cl
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

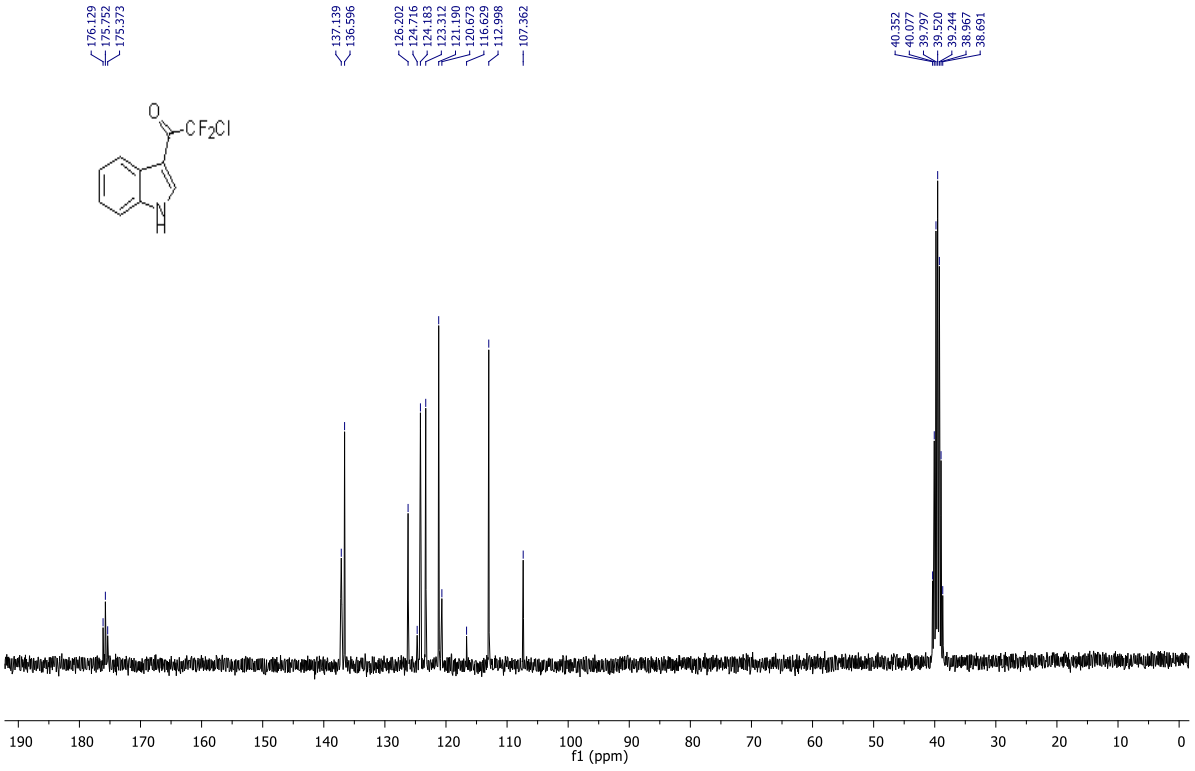
DEPT


149.923
132.407
130.869
127.167
126.786
45.678
NMe2
O
CF2Cl
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

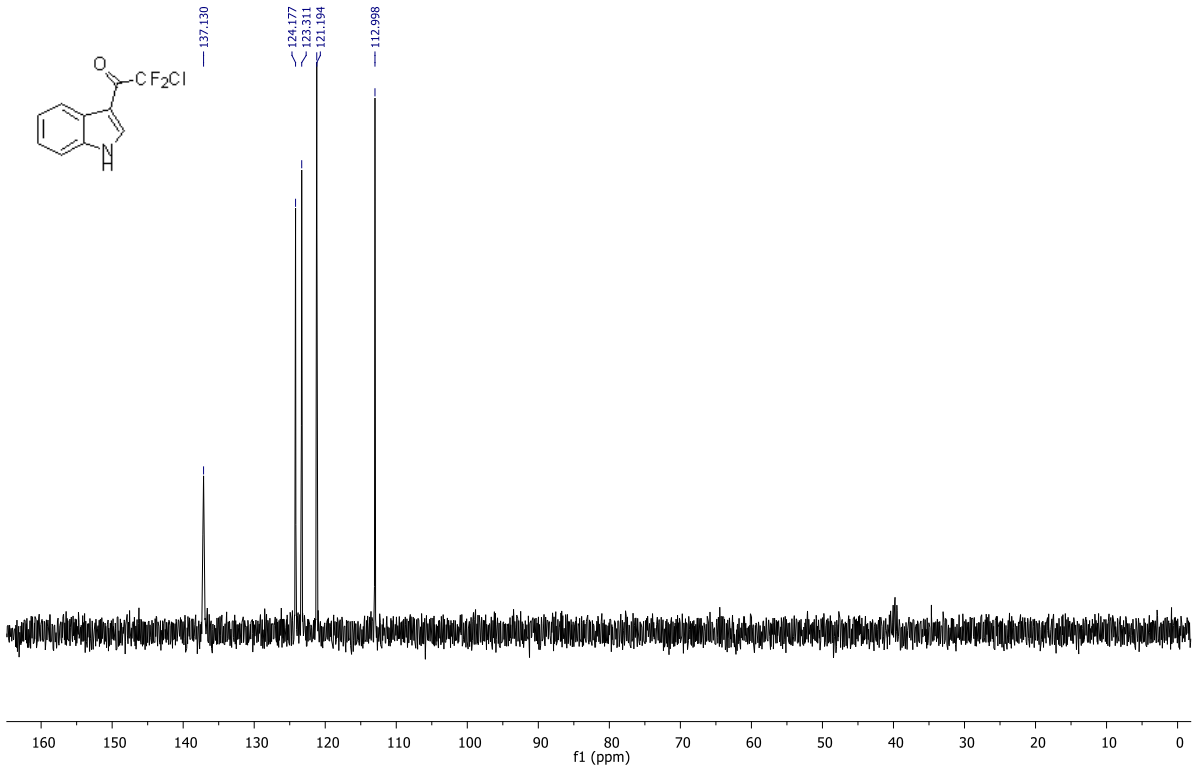
1e


12.661
8.483
8.476
8.469
8.465
8.457
8.198
8.182
8.168
7.605
7.603
7.596
7.592
7.589
7.579
7.575
7.563
7.373
7.366
7.349
7.343
7.331
7.320
7.314
7.296
3.381
2.512
2.506
2.500
2.494
2.488
O
CF2Cl
N
H
0.77
0.97
1.00
1.02
2.02
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

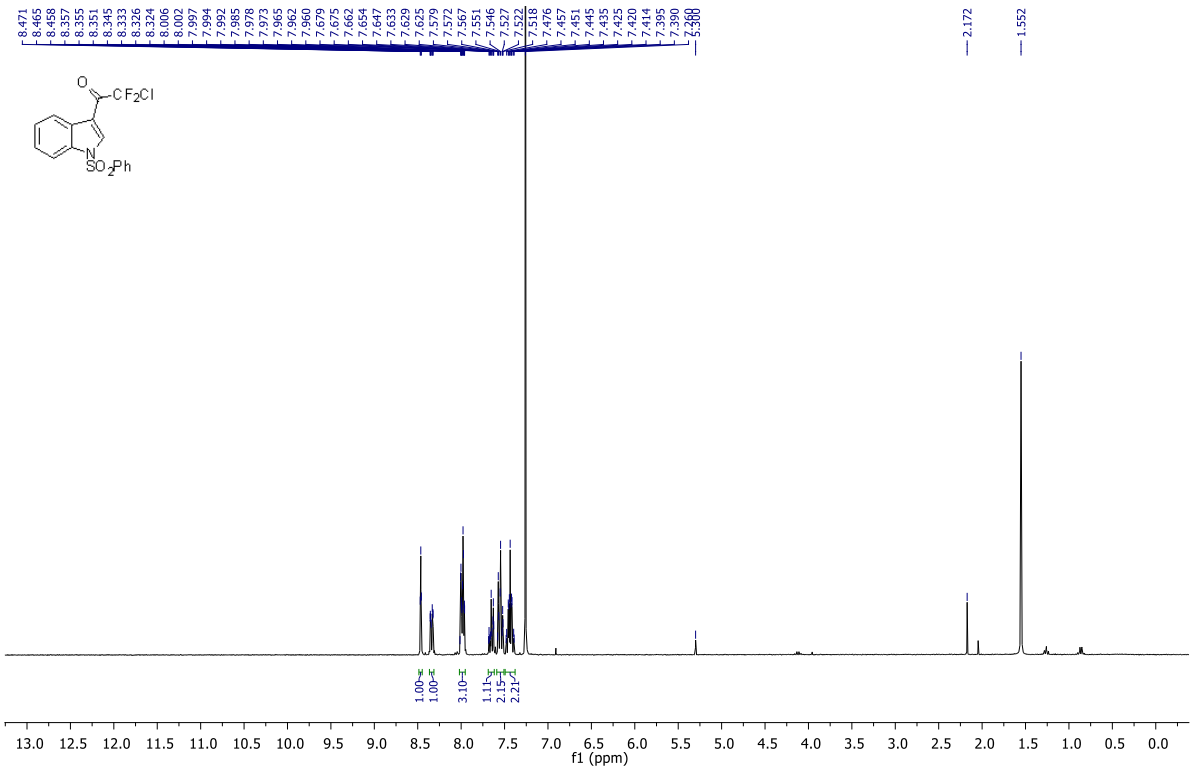

O
CF2Cl
N
H
-59.969
-59.977
-71.260
-71.266
83.72
1.00
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)

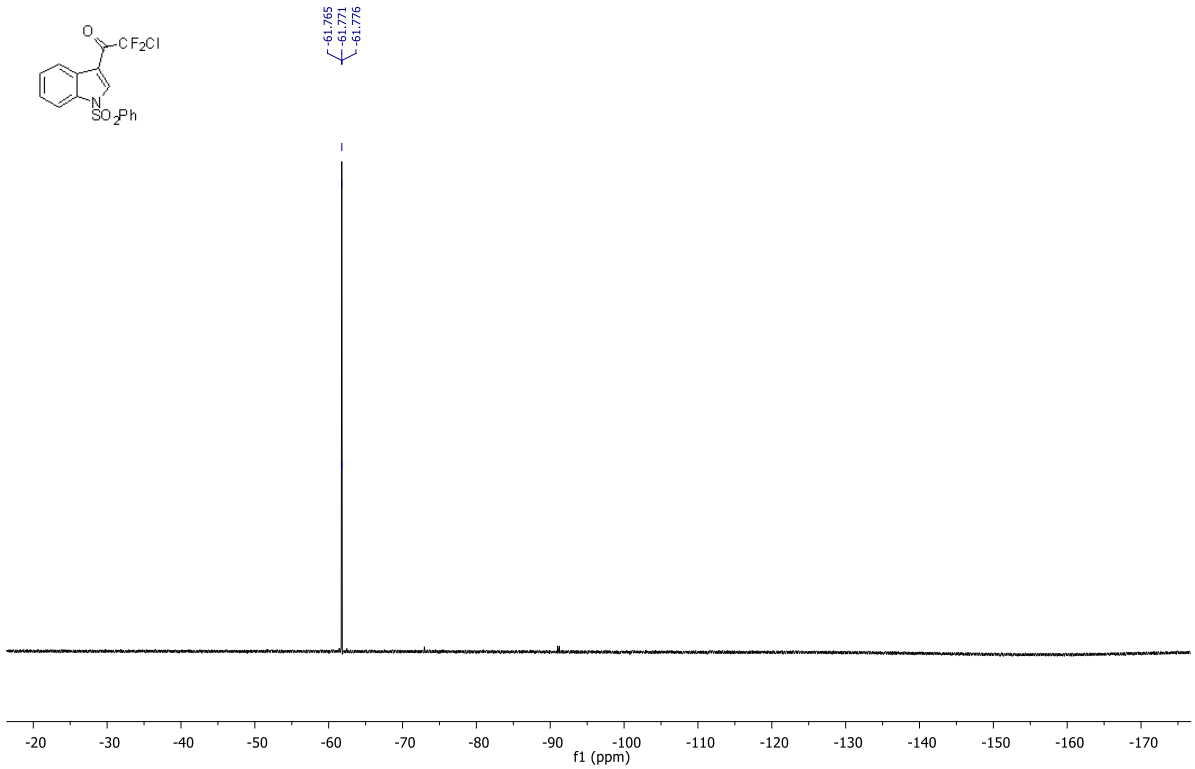

176.129
175.752
175.373
137.139
136.596
126.202
124.716
124.183
123.312
121.190
120.673
116.629
112.998
107.362
40.352
40.077
39.797
39.520
39.244
38.967
38.691
O
CF2Cl
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

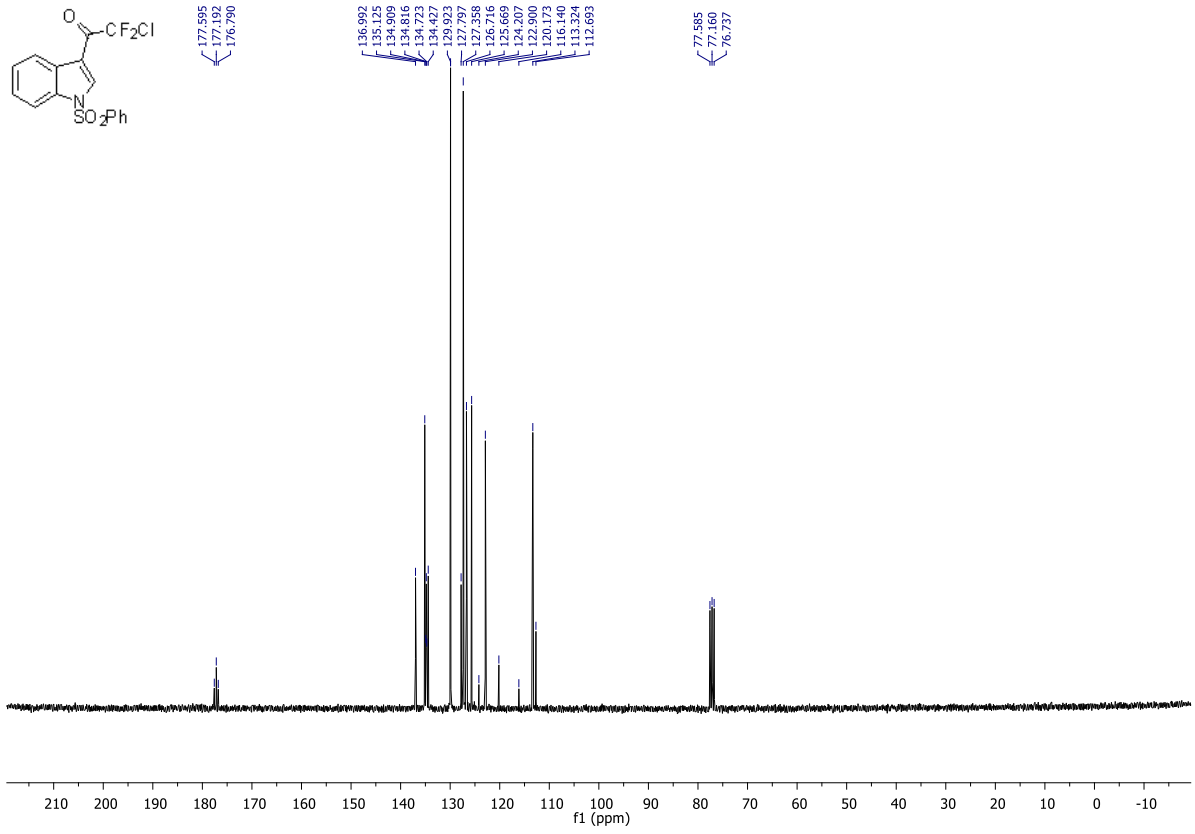
DEPT


137.130
124.177
123.311
121.194
112.998
O
CF2Cl
N
H
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

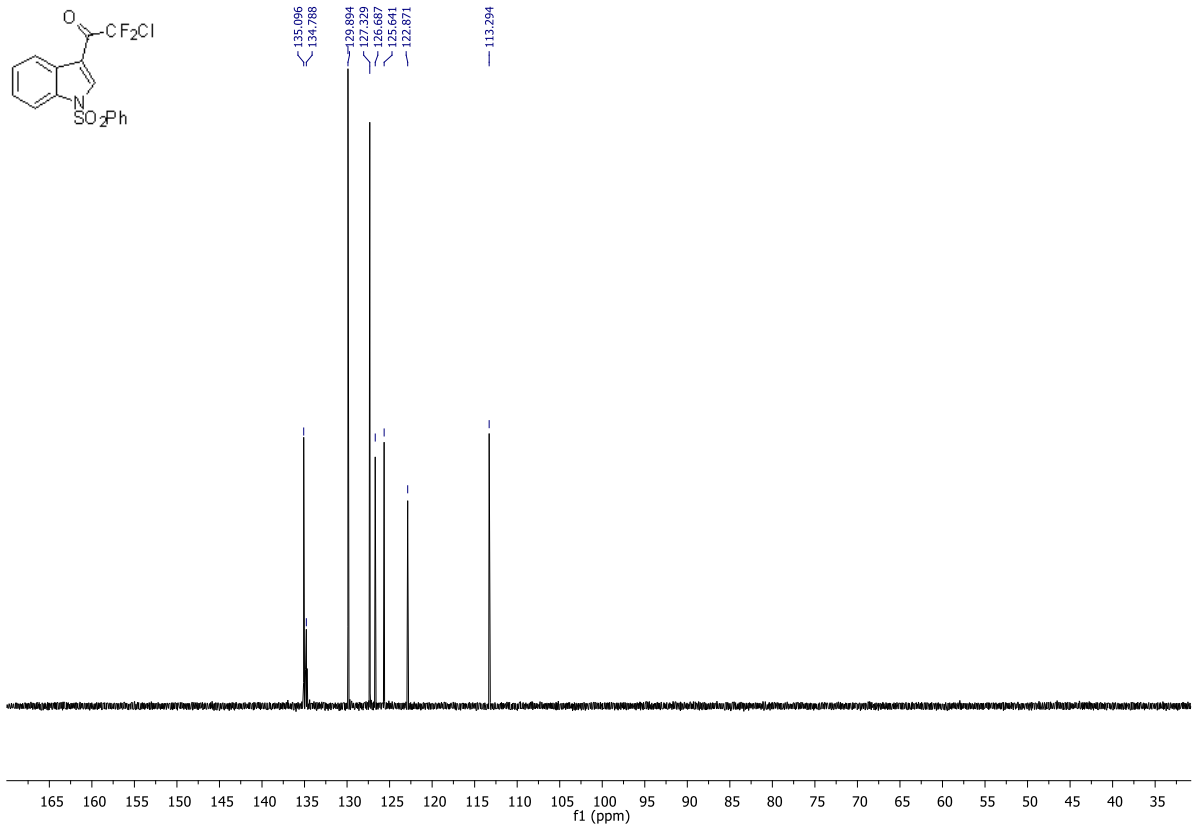
1f


8.471
8.465
8.458
8.357
8.355
8.351
8.345
8.333
8.326
8.324
8.006
8.002
7.997
7.994
7.992
7.985
7.978
7.973
7.965
7.962
7.960
7.679
7.675
7.662
7.654
7.647
7.633
7.629
7.625
7.579
7.572
7.567
7.551
7.546
7.527
7.522
7.518
7.476
7.457
7.451
7.445
7.435
7.425
7.420
7.414
7.395
7.390
7.380
2.172
1.552
O
CF2Cl
N
SO2Ph
1.00
1.00
3.10
1.11
2.15
2.21
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

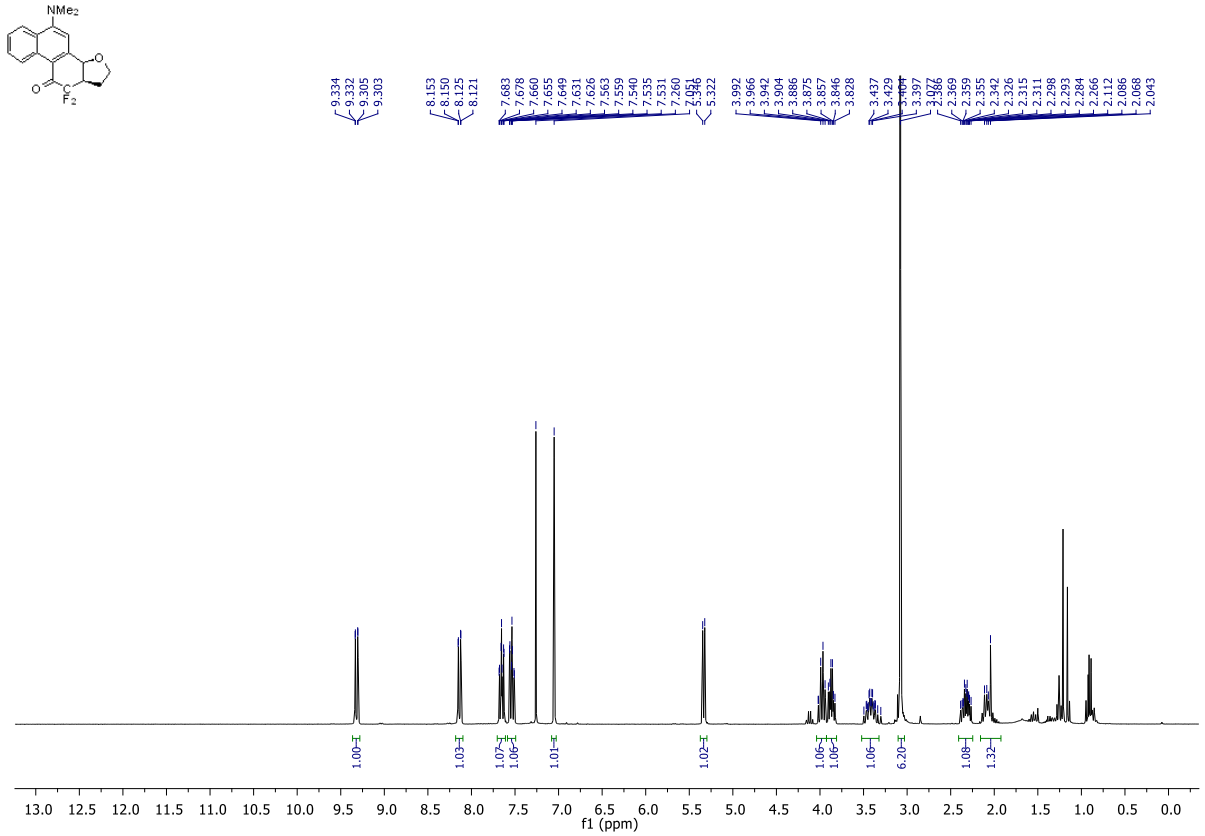

-61.765
-61.771
-61.776
O
CF2Cl
N
SO2Ph
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170
f1 (ppm)

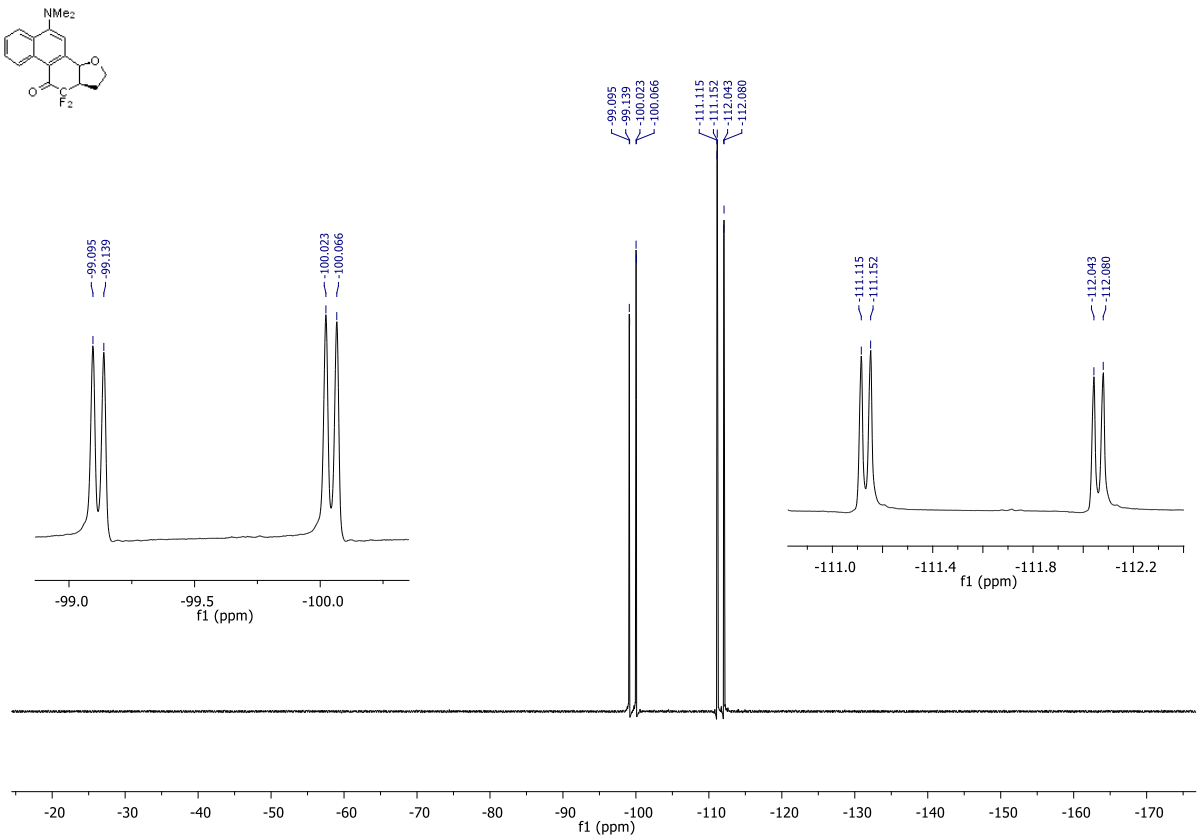

177.595
177.192
176.790
136.992
135.125
134.909
134.816
134.723
134.427
129.923
127.797
127.358
126.716
125.669
124.207
123.900
120.173
116.140
113.324
112.693
77.585
77.160
76.737
O
CF2Cl
N
SO2Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

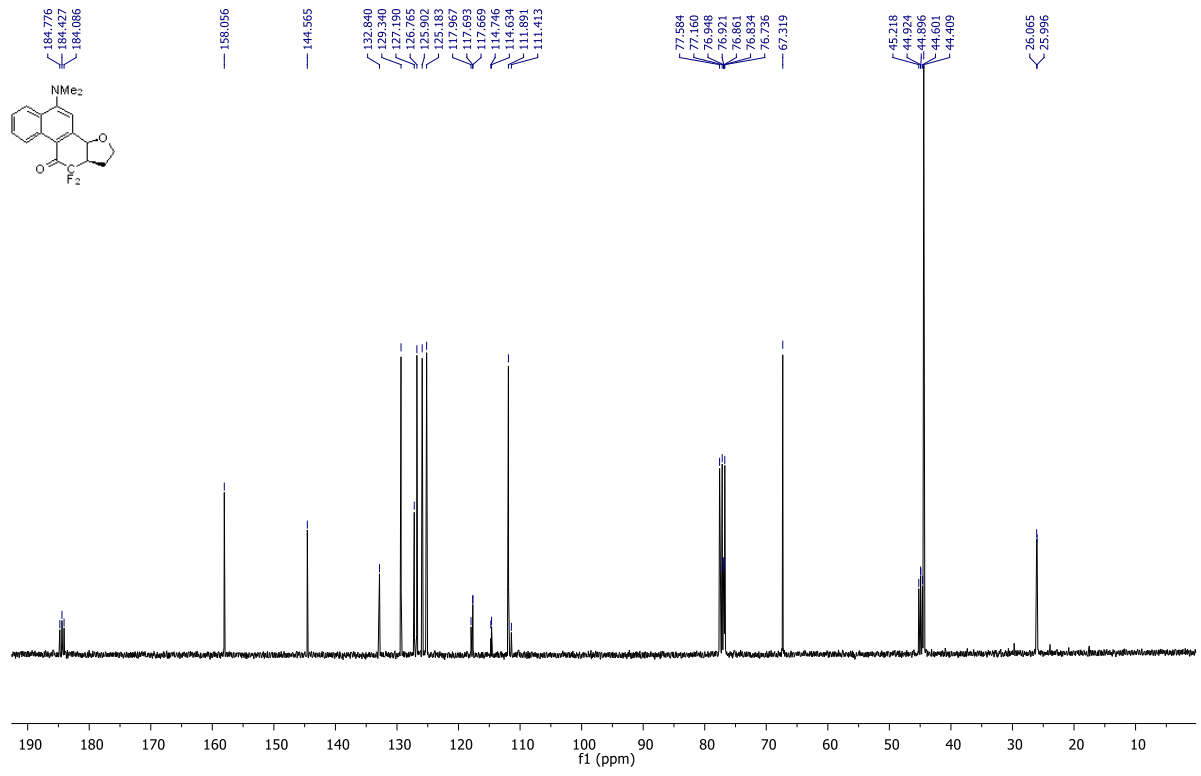
DEPT


O
CF2Cl
N
SO2Ph
135.096
134.788
129.894
127.329
126.687
125.641
122.871
113.294
f1 (ppm)

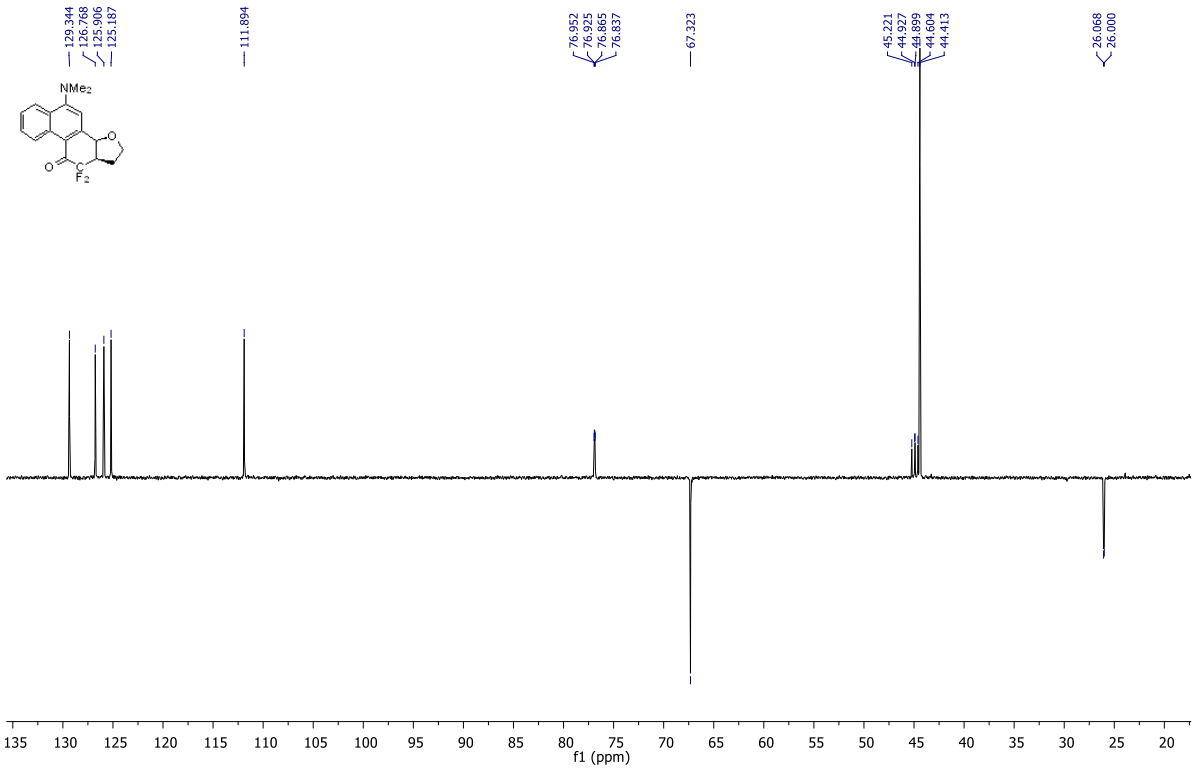
3aa


NMe2
O
O
F2
9.334
9.332
9.305
9.303
8.153
8.150
8.125
8.121
7.683
7.678
7.660
7.655
7.649
7.631
7.626
7.563
7.559
7.540
7.535
7.531
7.260
5.346
5.322
3.992
3.966
3.942
3.904
3.886
3.875
3.857
3.846
3.828
3.437
3.429
3.407
3.397
3.077
2.386
2.369
2.359
2.355
2.342
2.326
2.315
2.311
2.298
2.293
2.284
2.266
2.112
2.086
2.068
2.043
1.00
1.03
1.07
1.06
1.01
1.02
1.06
1.06
1.06
6.20
1.08
1.32
f1 (ppm)

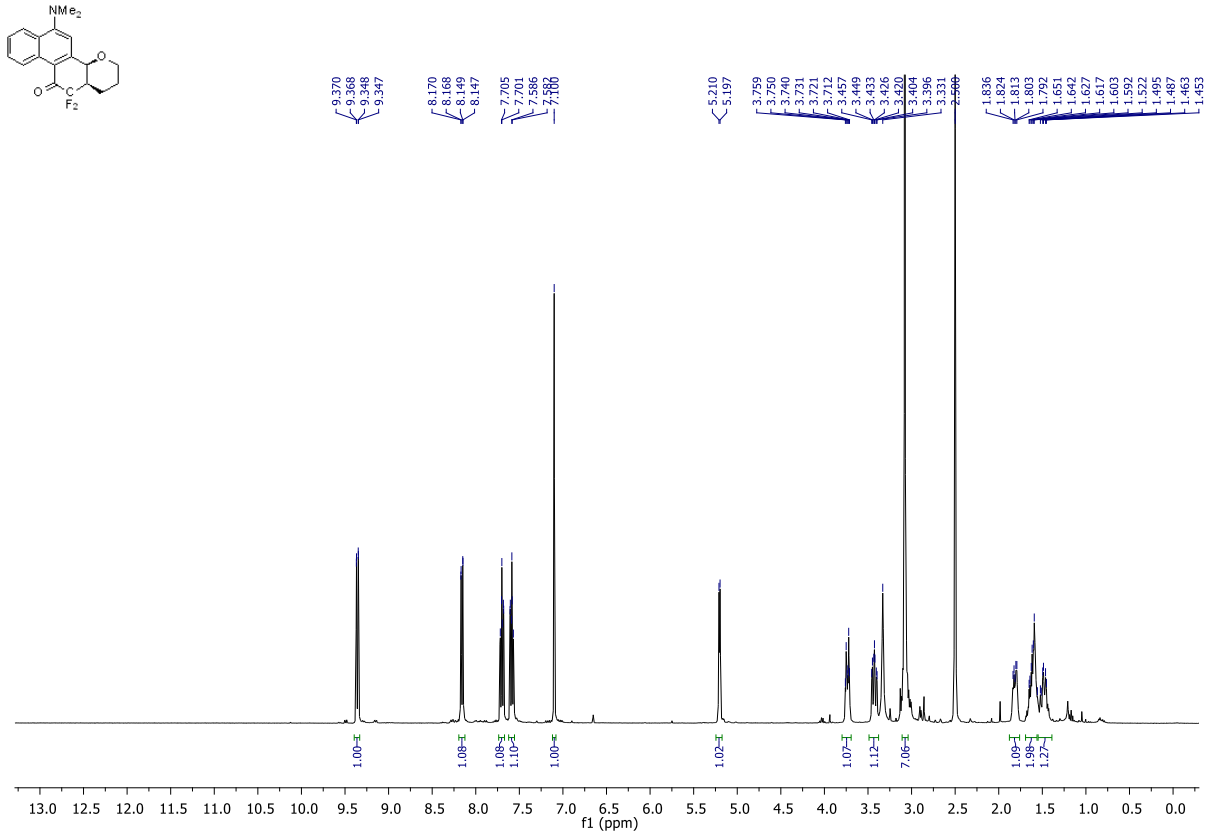

NMe2
O
O
F2
-99.095
-99.139
-100.023
-100.066
-111.115
-111.152
-112.043
-112.080
-99.0
-99.5
-100.0
f1 (ppm)
-111.0
-111.4
-111.8
-112.2
f1 (ppm)
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)

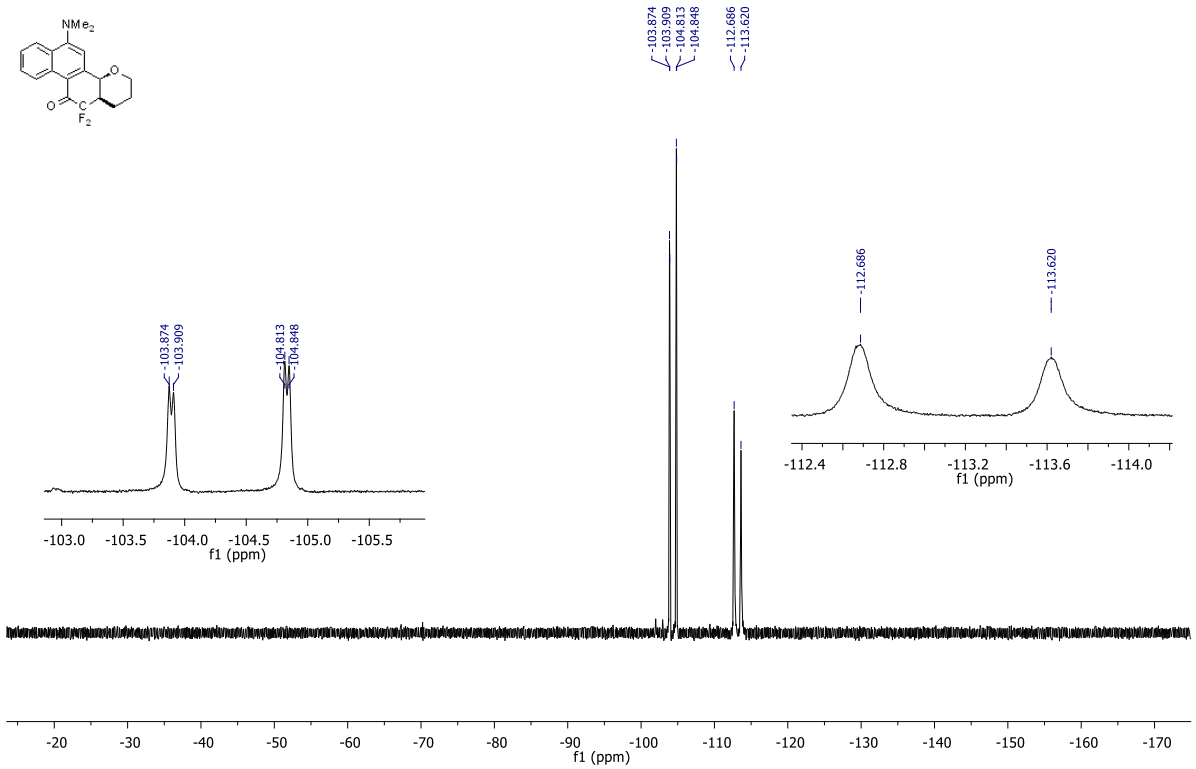

184.776
184.427
184.086
158.056
144.565
132.840
129.340
127.190
126.765
125.902
125.183
117.967
117.693
117.669
114.746
114.634
111.891
111.413
77.584
77.160
76.948
76.921
76.861
76.834
76.736
67.319
45.218
44.924
44.896
44.601
44.409
26.065
25.996
NMe2
O
O
F2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

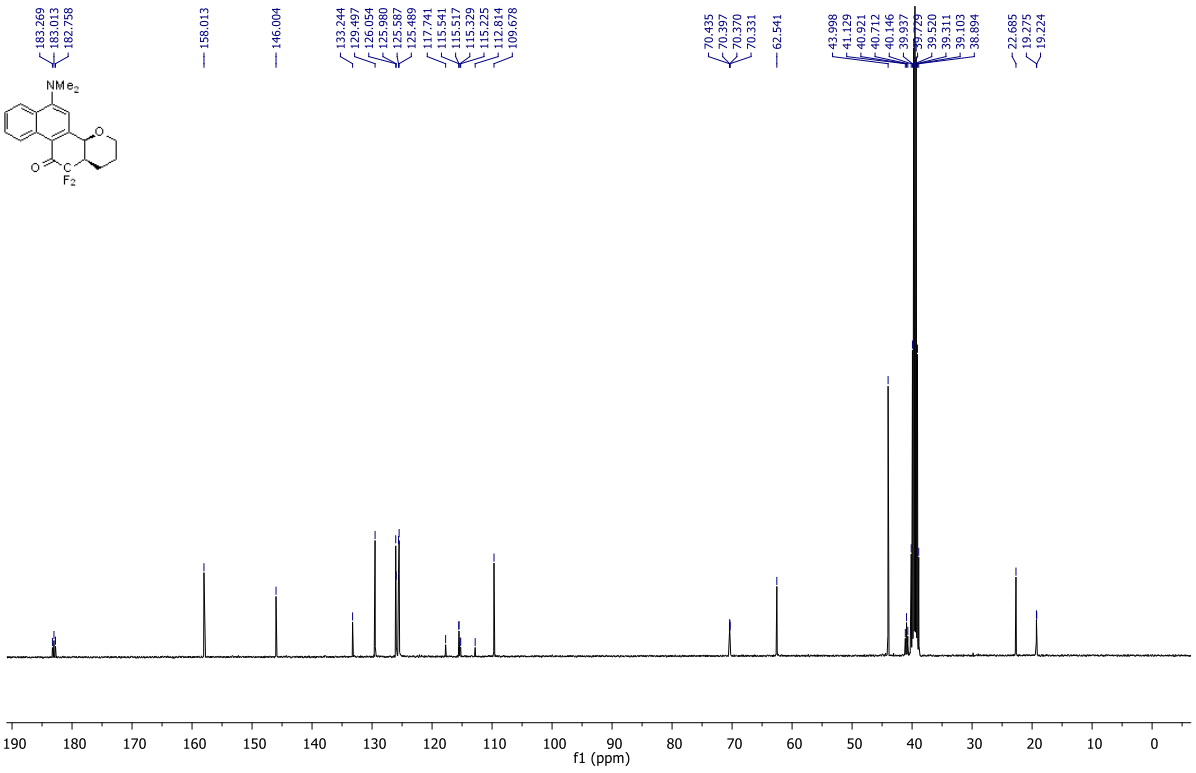
DEPT


129.344
126.768
125.906
125.187
111.894
76.952
76.925
76.865
76.837
67.323
45.221
44.927
44.899
44.604
44.413
26.068
26.000
NMe2
O
O
F2
f1 (ppm)

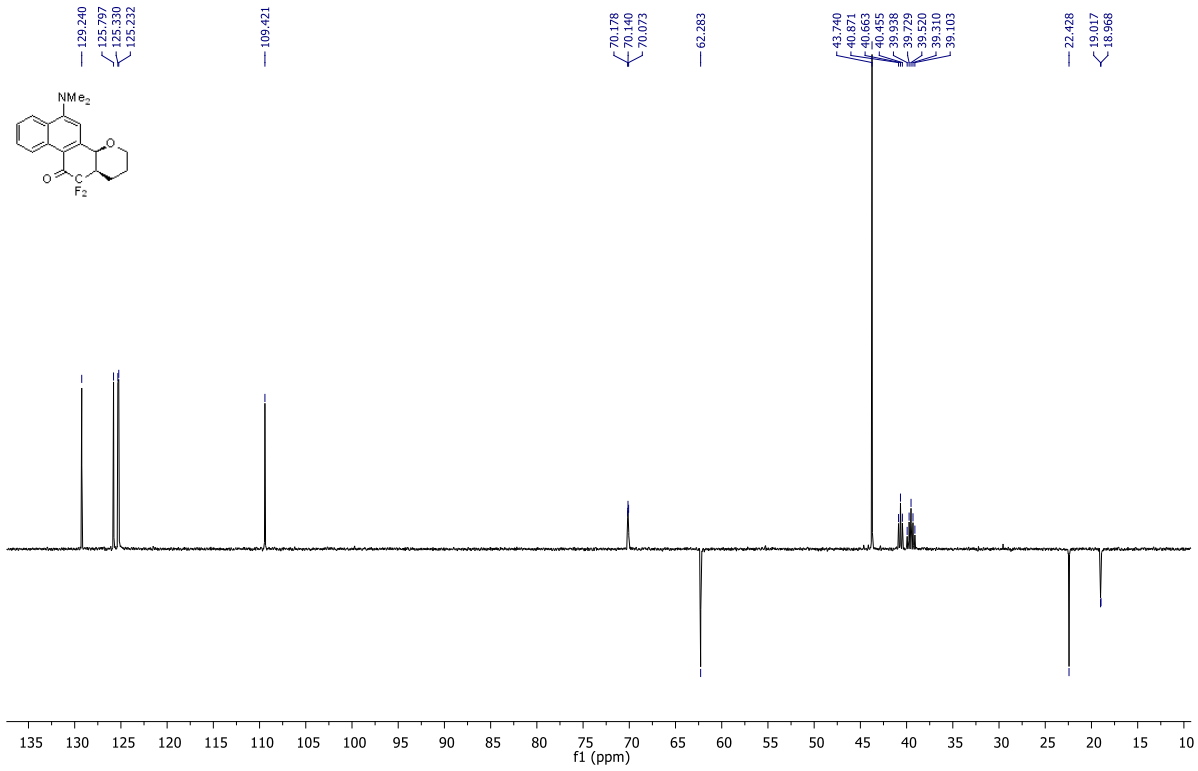
3ab

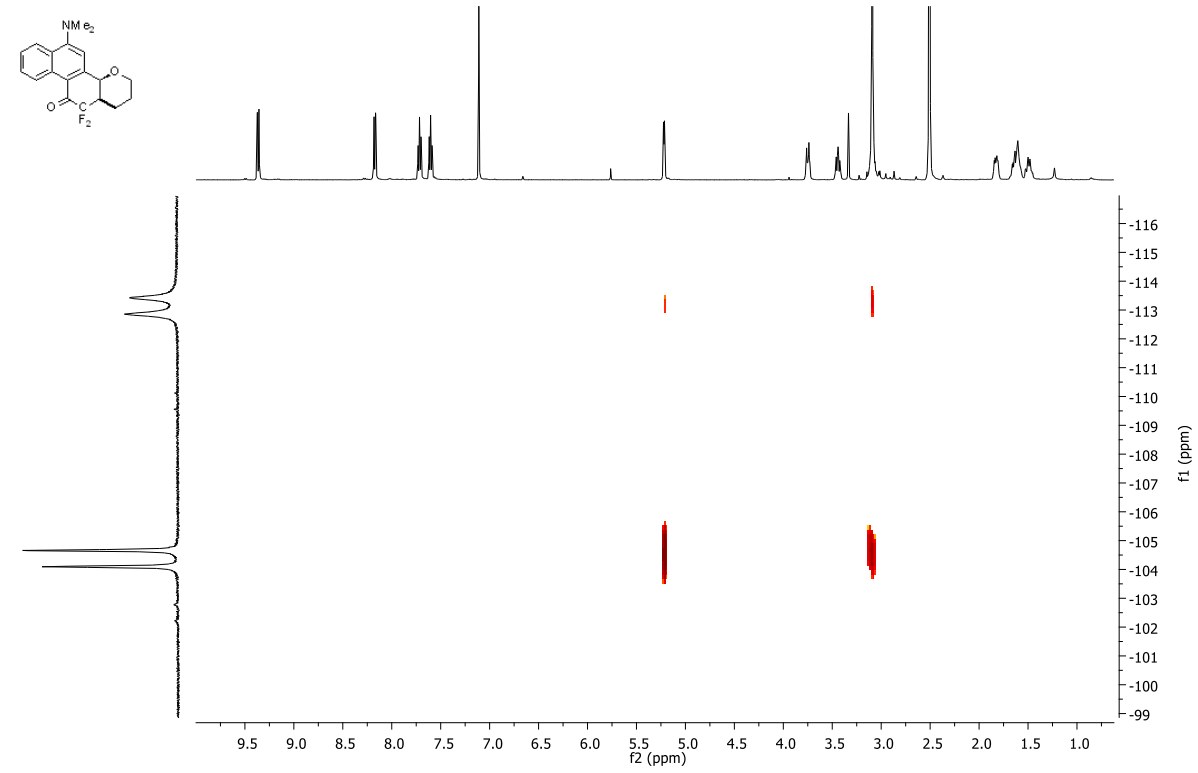

NMe2
O
O
F2
9.370
9.368
9.348
9.347
8.170
8.168
8.149
8.147
7.705
7.701
7.586
7.582
7.188
5.210
5.197
3.759
3.750
3.740
3.731
3.721
3.712
3.457
3.449
3.433
3.426
3.420
3.404
3.396
3.331
2.500
1.836
1.824
1.813
1.803
1.792
1.651
1.642
1.627
1.617
1.603
1.592
1.522
1.495
1.487
1.463
1.453
1.00
1.08
1.08
1.10
1.00
1.02
1.07
1.12
7.06
1.09
1.98
1.27
f1 (ppm)


-103.874
-103.909
-104.813
-104.848
-112.686
-113.620
-103.0
-103.5
-104.0
-104.5
-105.0
-105.5
f1 (ppm)
-112.4
-112.8
-113.2
-113.6
-114.0
f1 (ppm)
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)

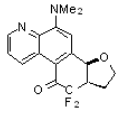

183.269
183.013
182.758
158.013
146.004
133.244
129.497
126.054
125.980
125.587
125.489
117.741
115.541
115.517
115.329
115.225
112.814
109.678
70.435
70.397
70.370
70.331
62.541
43.998
41.129
40.921
40.712
40.146
39.937
39.729
39.520
39.311
39.103
38.894
22.685
19.275
19.224
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

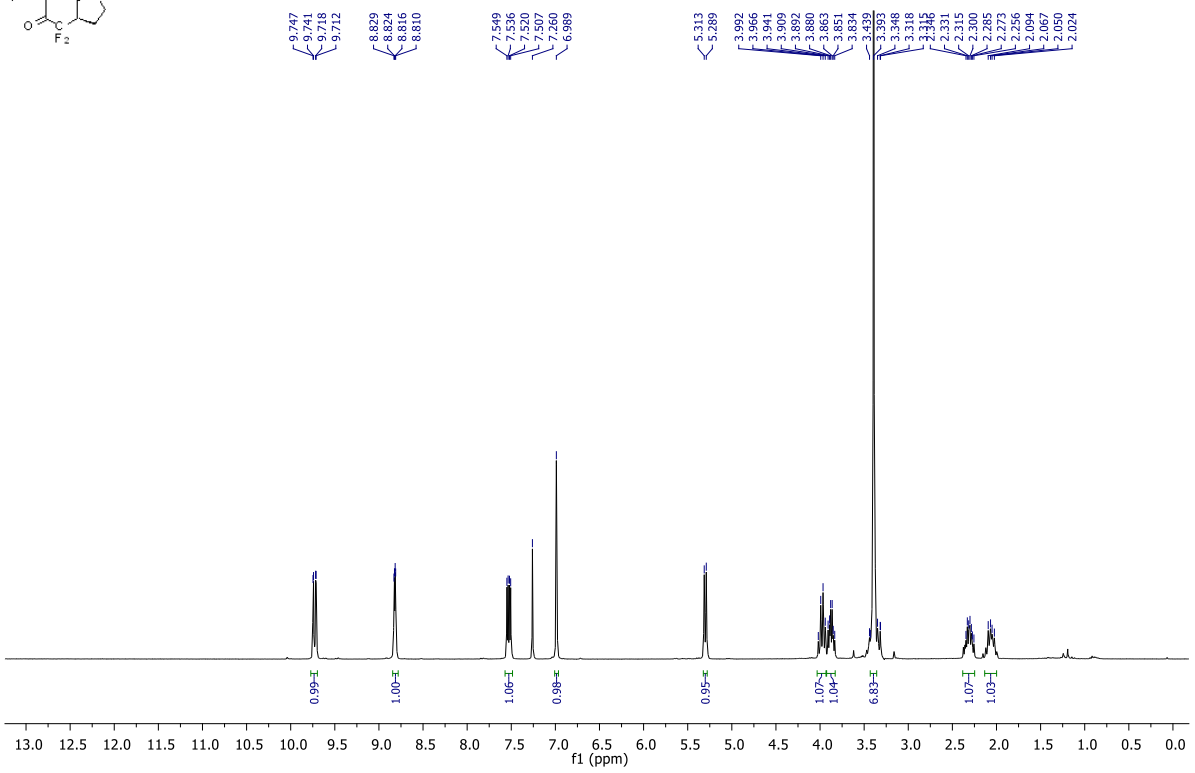
DEPT

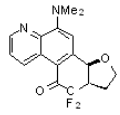

129.240
125.797
125.330
125.232
109.421
70.178
70.140
70.073
62.283
43.740
40.871
40.663
40.455
39.938
39.729
39.520
39.310
39.103
22.428
19.017
18.968
NMe2
O
O
C
F2
135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10
f1 (ppm)

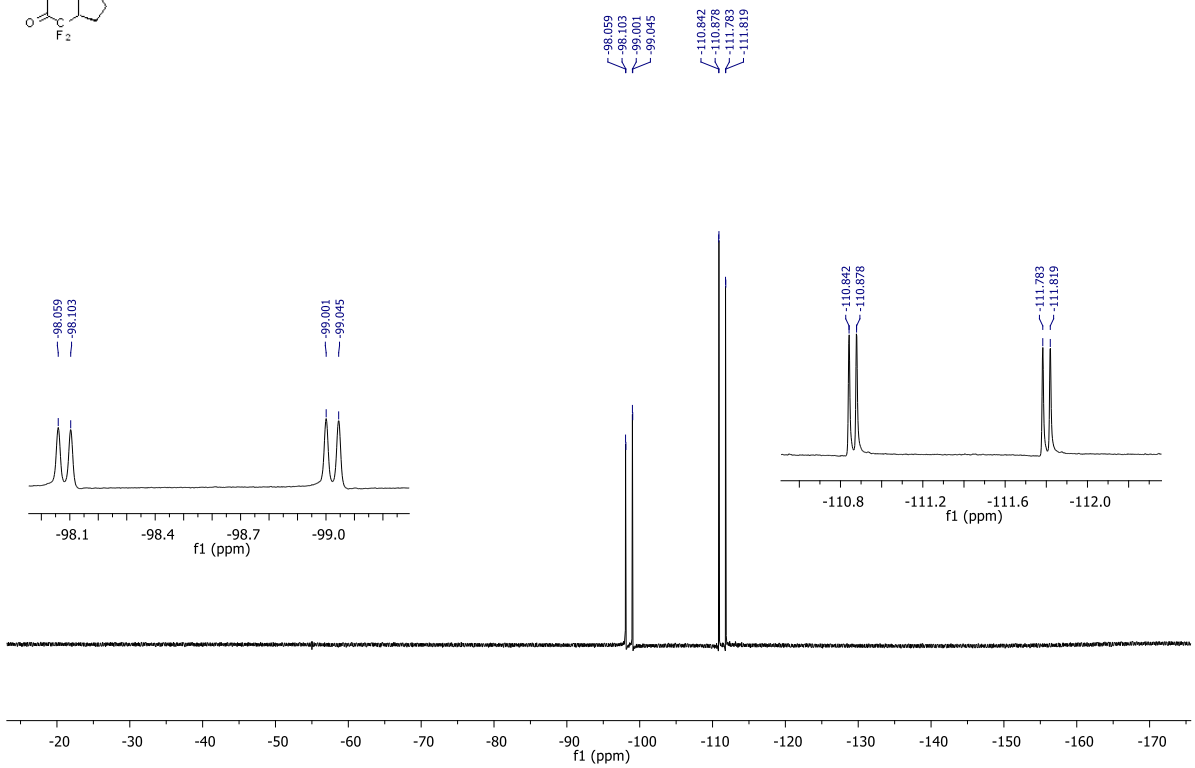

NMe2
O
O
C
F2
-116
-115
-114
-113
-112
-111
-110
-109
-108
-107
-106
-105
-104
-103
-102
-101
-100
-99
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f2 (ppm)

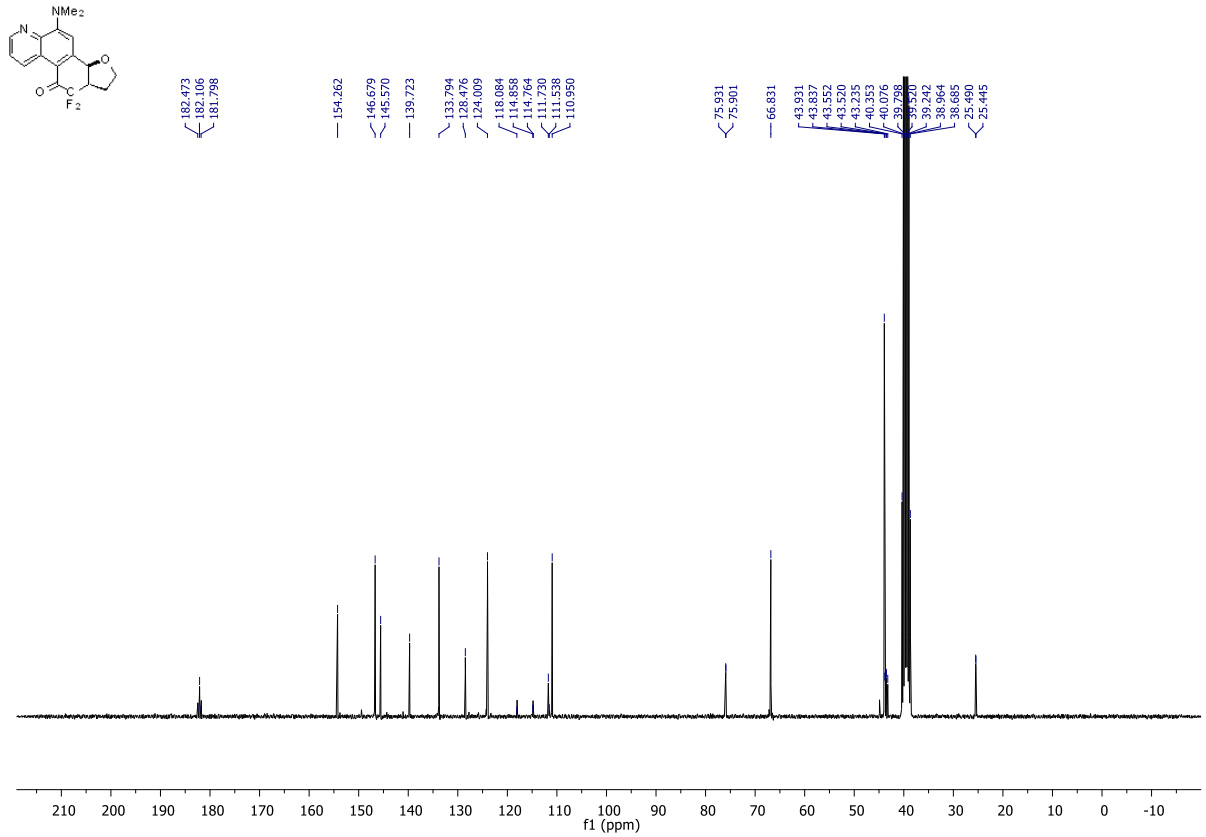
3ba


NMe2
N
O
O
F2

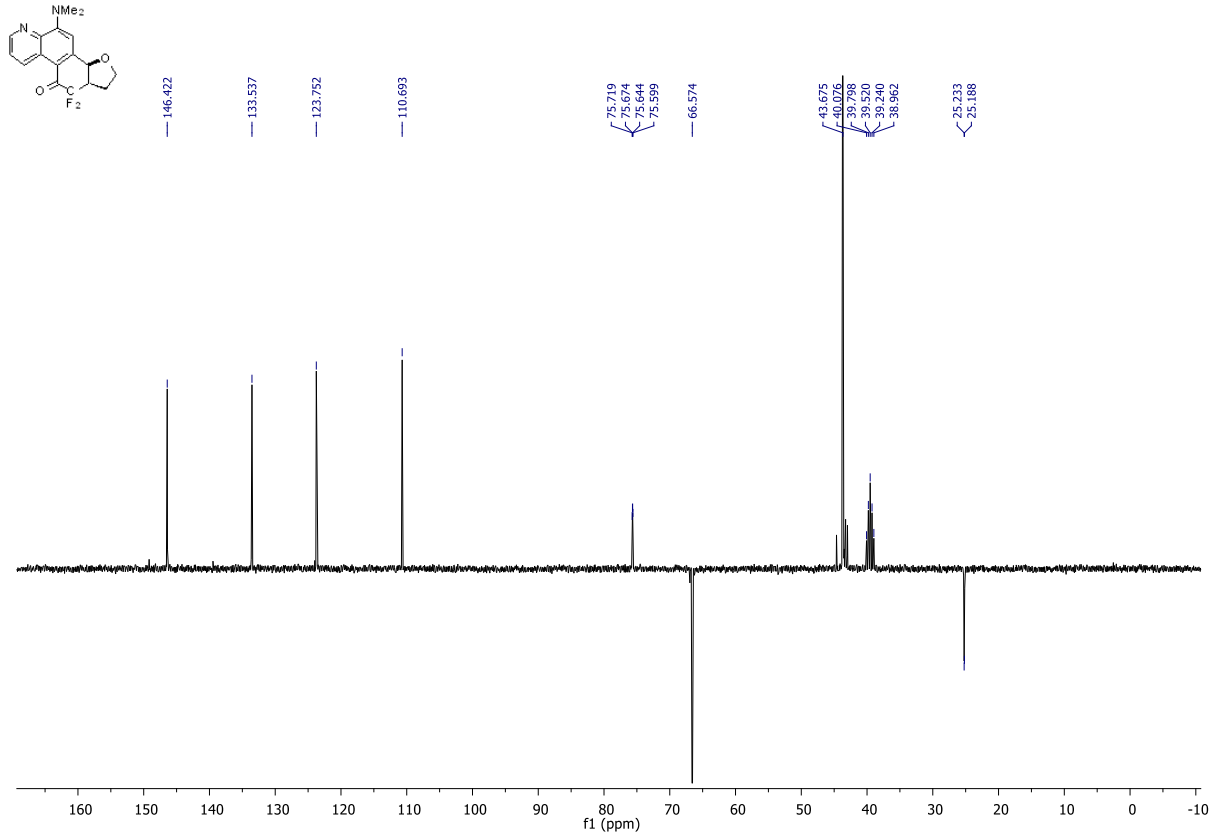

9.747
9.741
9.718
9.712
8.829
8.824
8.816
8.810
7.549
7.536
7.520
7.507
7.260
6.989
5.313
5.289
3.992
3.966
3.941
3.909
3.892
3.880
3.863
3.851
3.834
3.439
3.393
3.348
3.318
2.331
2.315
2.300
2.285
2.273
2.256
2.094
2.067
2.050
2.024
0.99
1.00
1.06
0.98
0.95
1.07
1.04
6.83
1.07
1.03
f1 (ppm)


NMe2
N
O
O
F2

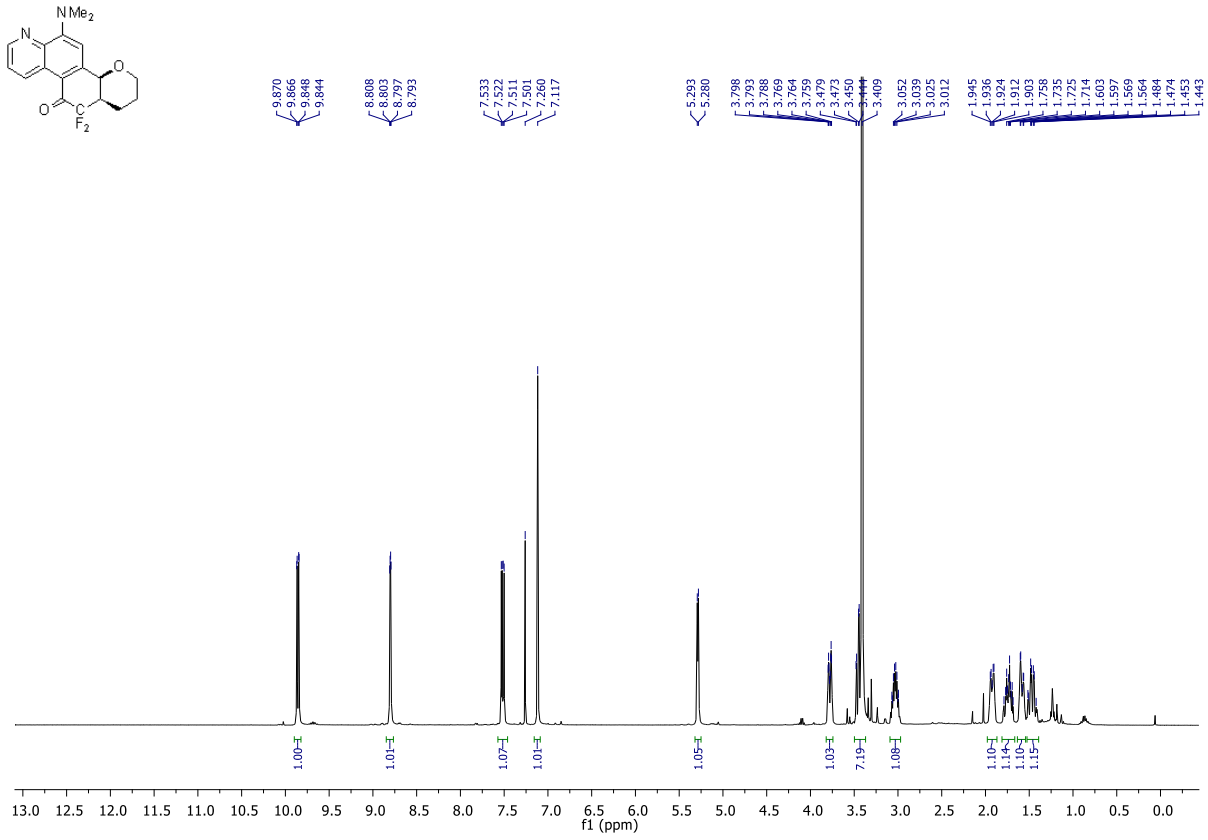

-98.059
-98.103
-99.001
-99.045
-110.842
-110.878
-111.783
-111.819
-98.1
-98.4
-98.7
-99.0
-110.8
-111.2
-111.6
-112.0
f1 (ppm)

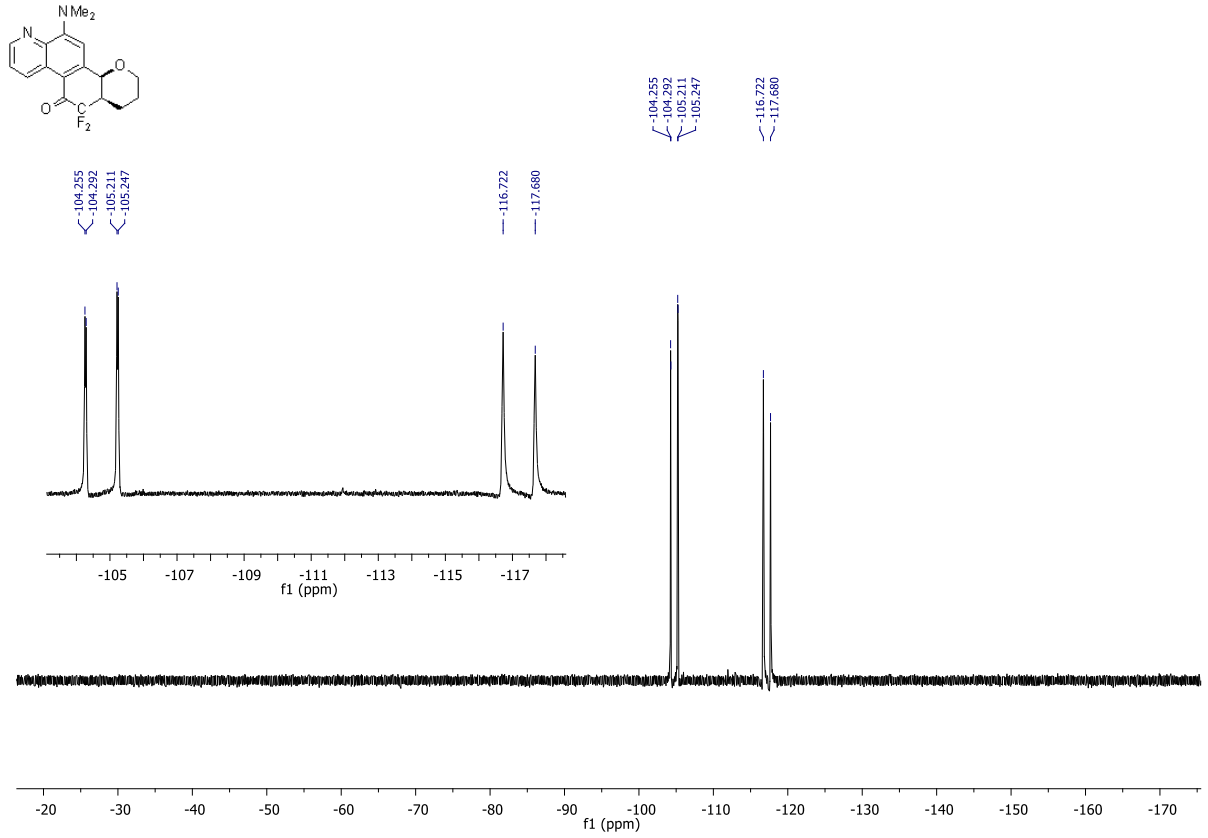

NMe2
N
O
O
F2
182.473
182.106
181.798
154.262
146.679
145.570
139.723
133.794
128.476
124.009
118.084
114.858
114.764
111.730
111.538
110.950
75.931
75.901
66.831
43.931
43.837
43.552
43.520
43.235
40.353
40.076
39.798
39.520
39.242
38.964
38.685
25.490
25.445
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

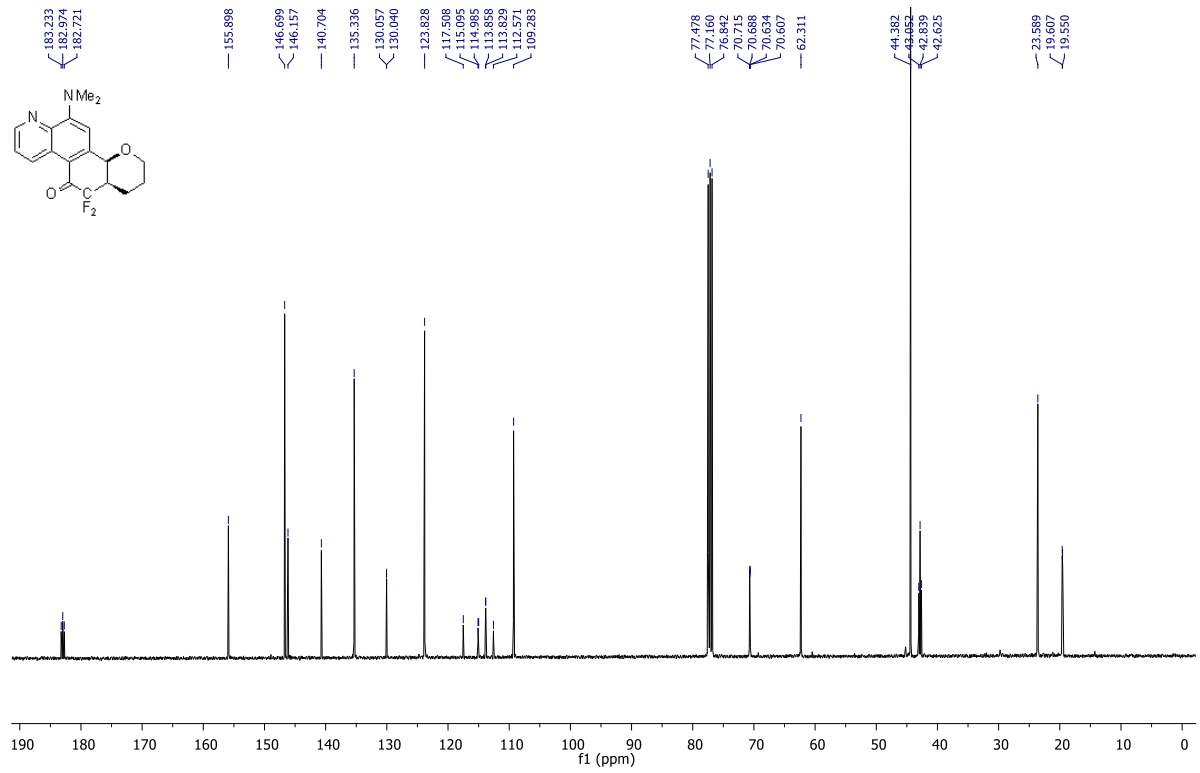
DEPT


NMe2
N
O
O
F2
146.422
133.537
123.752
110.693
75.719
75.674
75.644
75.599
66.574
43.675
40.076
39.798
39.520
39.240
38.962
25.233
25.188
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

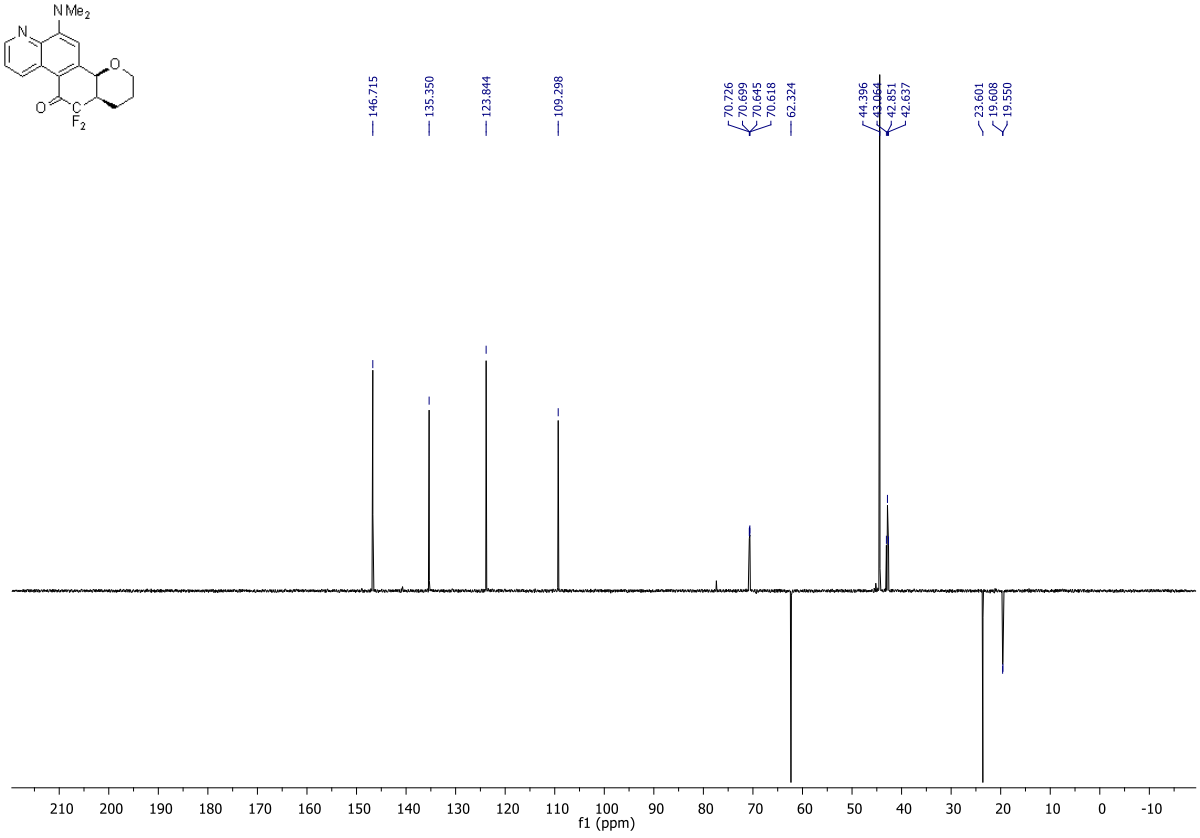
3bb

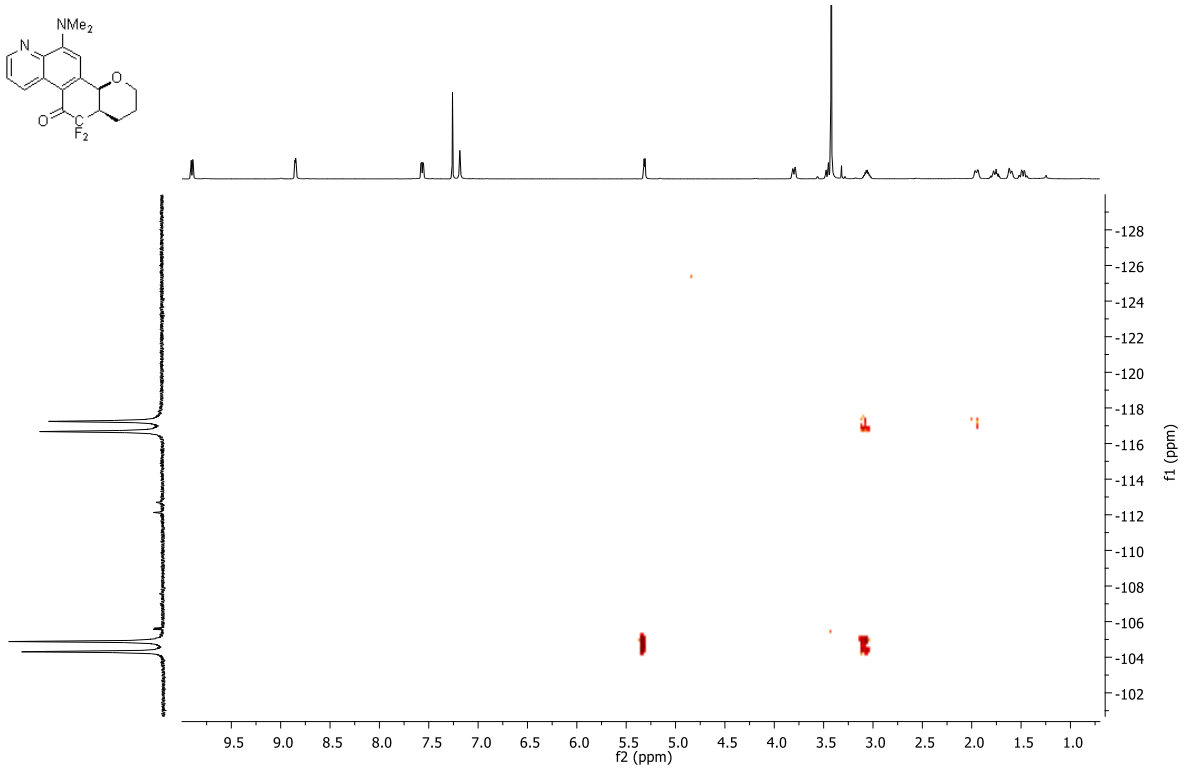

NMe2
N
O
O
F2
9.870
9.866
9.848
9.844
8.808
8.803
8.797
8.793
7.533
7.522
7.511
7.501
7.260
7.117
5.293
5.280
3.798
3.793
3.788
3.769
3.764
3.759
3.479
3.473
3.450
3.444
3.409
3.052
3.039
3.025
3.012
1.945
1.936
1.924
1.912
1.903
1.758
1.735
1.725
1.714
1.603
1.597
1.569
1.564
1.484
1.474
1.453
1.443
1.00
1.01
1.07
1.01
1.05
1.03
7.19
1.08
1.10
1.14
1.10
1.15
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


NMe2
N
O
O
F2
-104.255
-104.292
-105.211
-105.247
-116.722
-117.680
-105 -107 -109 -111 -113 -115 -117
f1 (ppm)
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170
f1 (ppm)

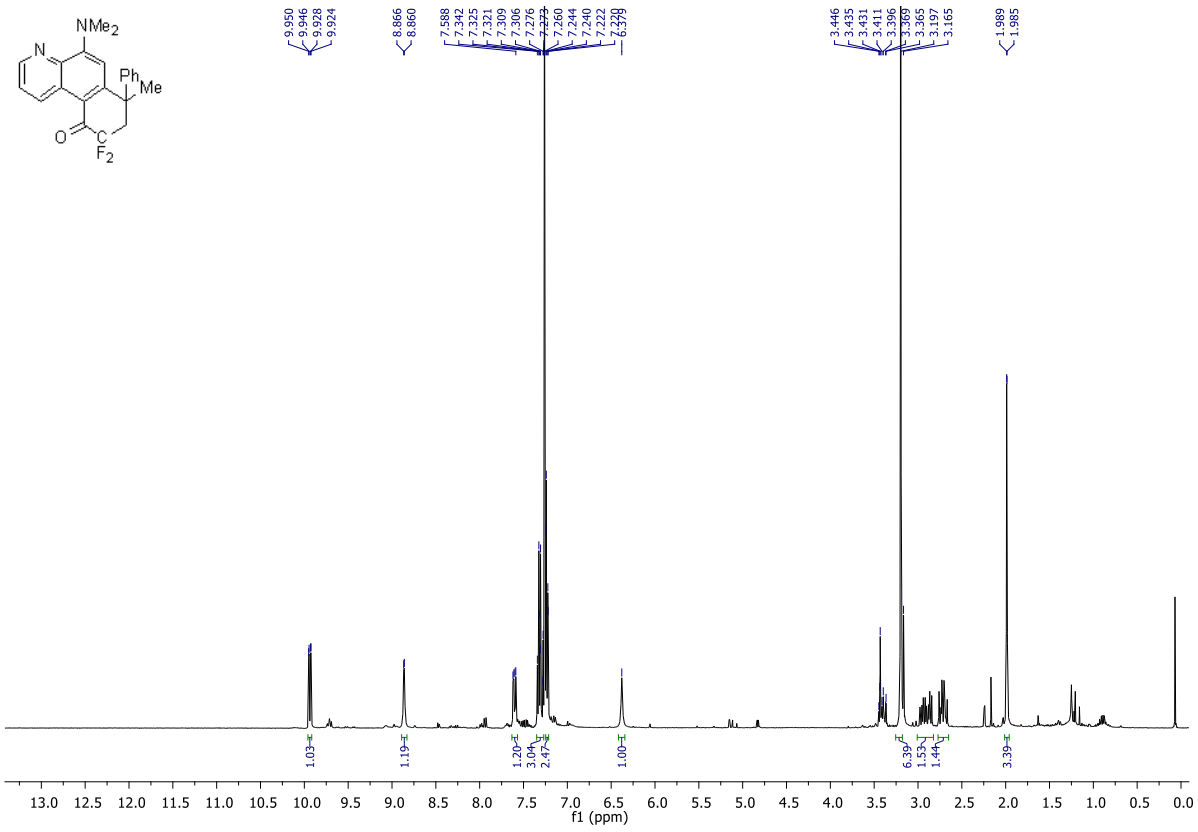

183.233
182.974
182.721
155.898
146.699
146.157
140.704
135.336
130.057
130.040
123.828
117.508
115.095
114.985
113.858
113.829
112.571
109.283
77.478
77.160
76.842
70.715
70.688
70.634
70.607
62.311
44.382
43.052
42.839
42.625
23.589
19.607
19.550
NMe2
N
O
O
C
F2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

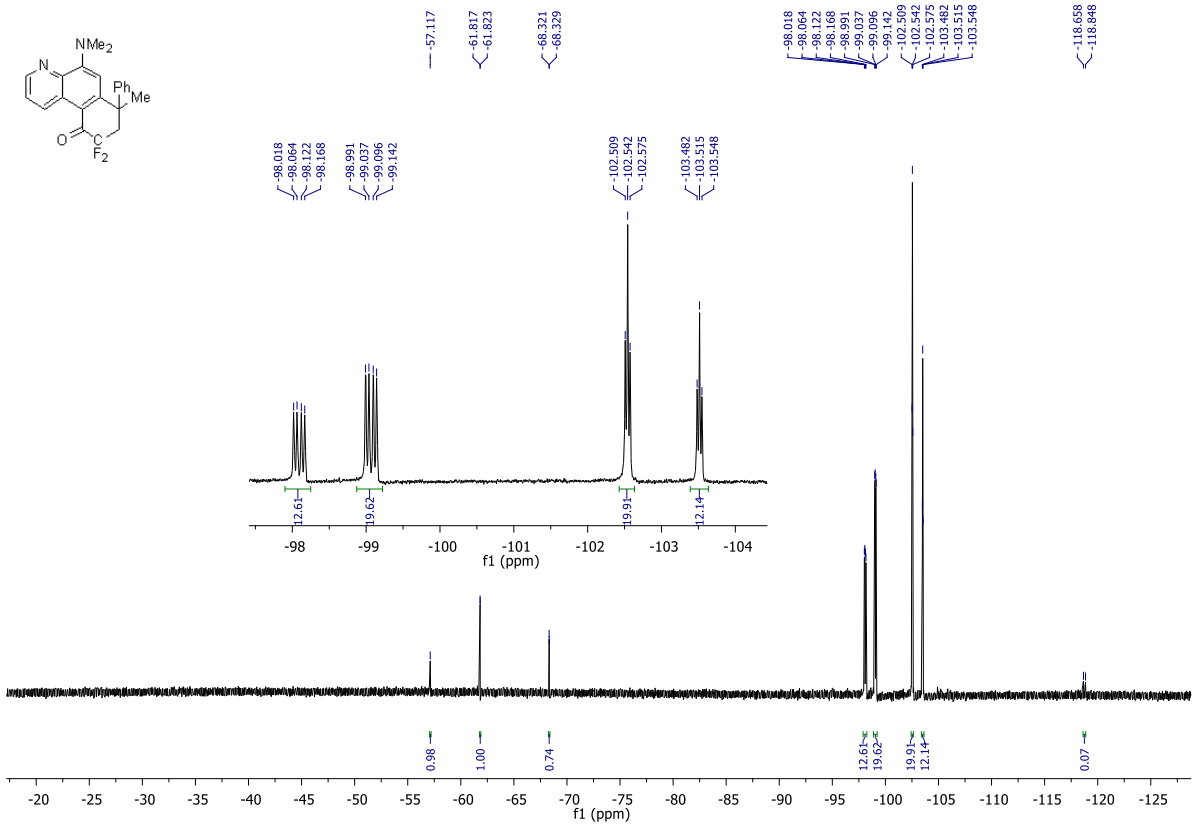
DEPT

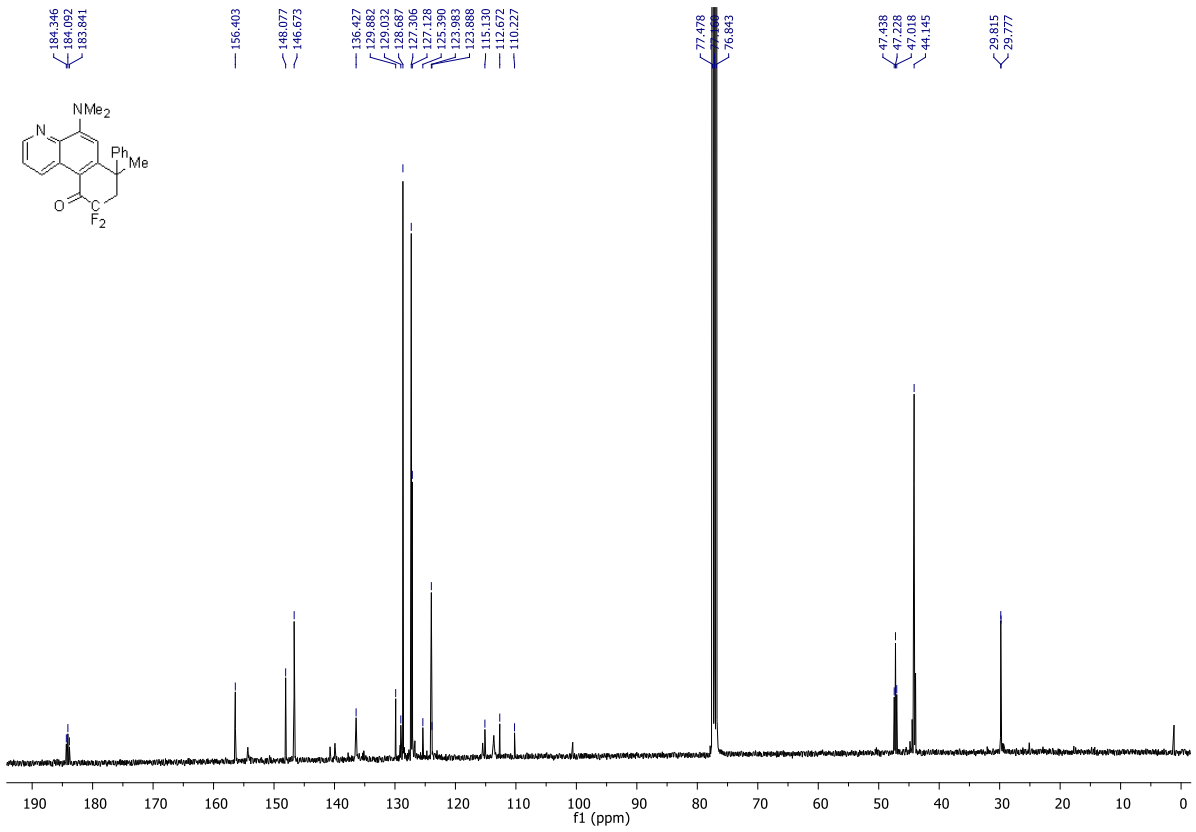

NMe2
N
O
O
C
F2
146.715
135.350
123.844
109.298
70.726
70.699
70.645
70.618
62.324
44.396
43.064
42.851
42.637
23.601
19.608
19.550
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


NMe2
N
O
O
C
F2
-128
-126
-124
-122
-120
-118
-116
-114
-112
-110
-108
-106
-104
-102
f1 (ppm)
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
f2 (ppm)

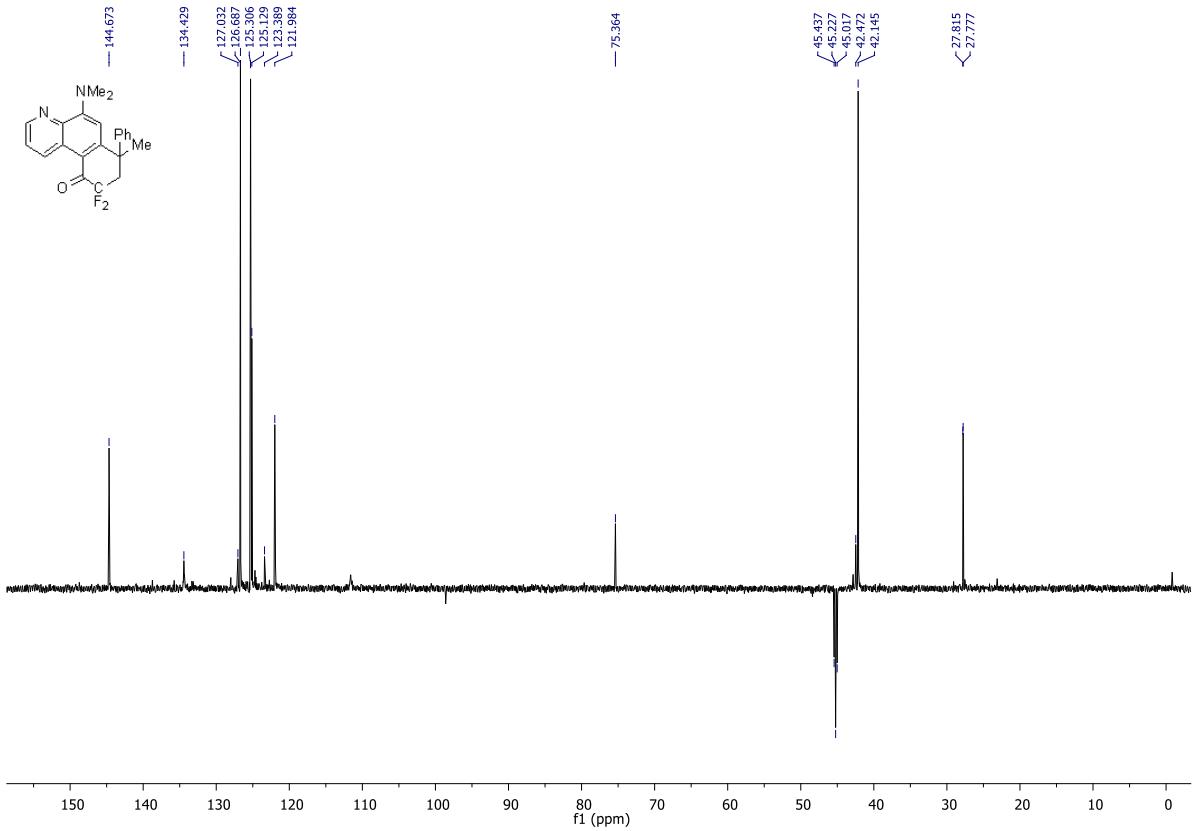
3bg


NMe2
N
Ph
Me
O
C
F2
9.950
9.946
9.928
9.924
8.866
8.860
7.588
7.342
7.325
7.321
7.309
7.306
7.276
7.273
7.260
7.244
7.240
7.222
7.220
6.379
3.446
3.435
3.431
3.411
3.396
3.369
3.365
3.197
3.165
1.989
1.985
1.03
1.19
1.20
3.04
2.47
1.00
6.39
1.53
1.44
3.39
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

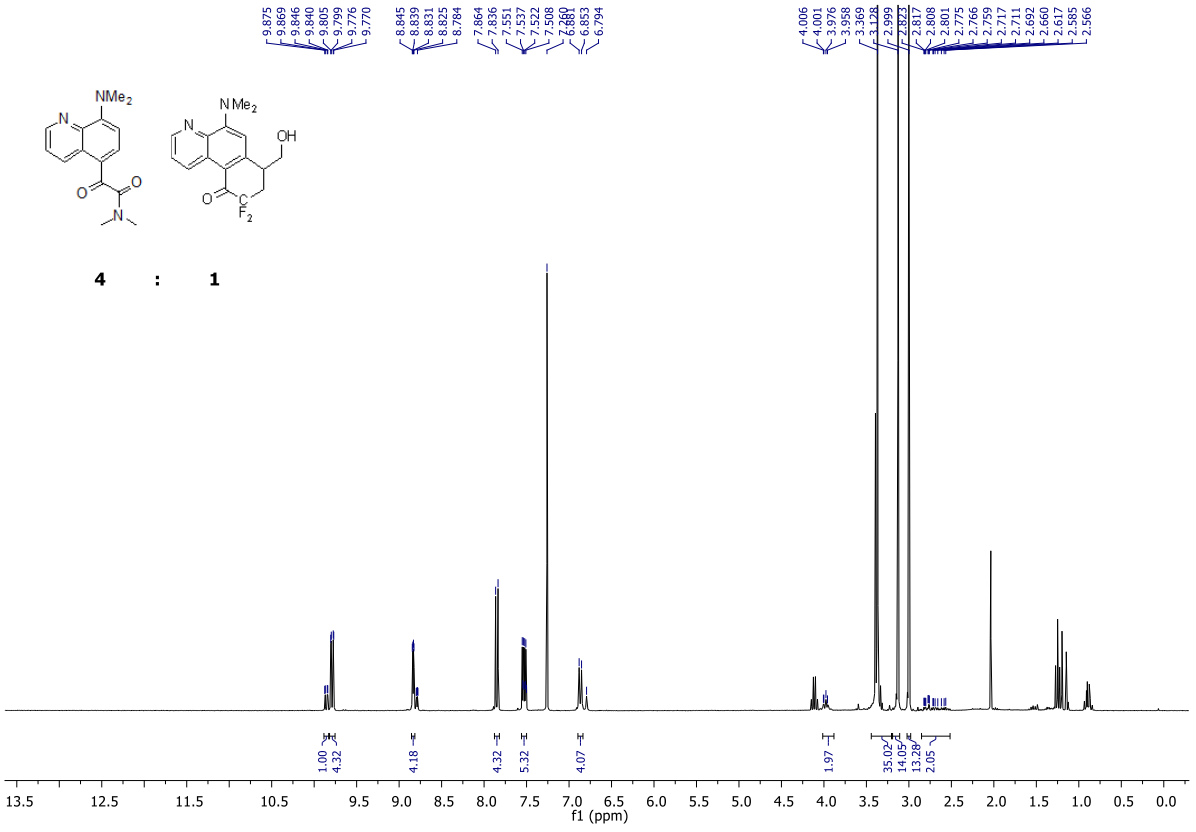

NMe2
Ph
Me
O
F2
-57.117
-61.817
-61.823
-68.321
-68.329
-98.018
-98.064
-98.122
-98.168
-98.991
-99.037
-99.096
-99.142
-102.509
-102.542
-102.575
-103.482
-103.515
-103.548
-118.658
-118.848
12.61
19.62
19.91
12.14
f1 (ppm)
0.98
1.00
0.74
0.07
f1 (ppm)

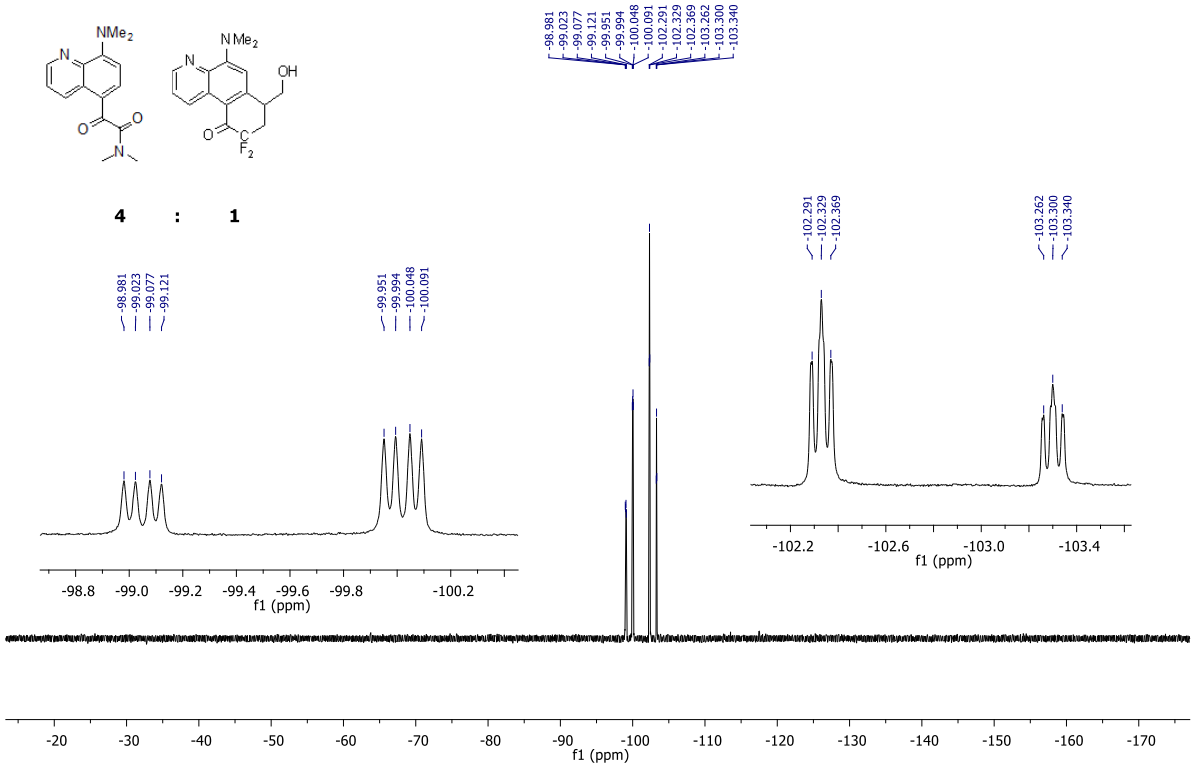

NMe2
Ph
Me
O
F2
184.346
184.092
183.841
156.403
148.077
146.673
136.427
129.882
129.032
128.687
127.306
127.128
125.390
123.983
123.888
115.130
112.672
110.227
77.478
77.160
76.843
47.438
47.228
47.018
44.145
29.815
29.777
f1 (ppm)

DEPT

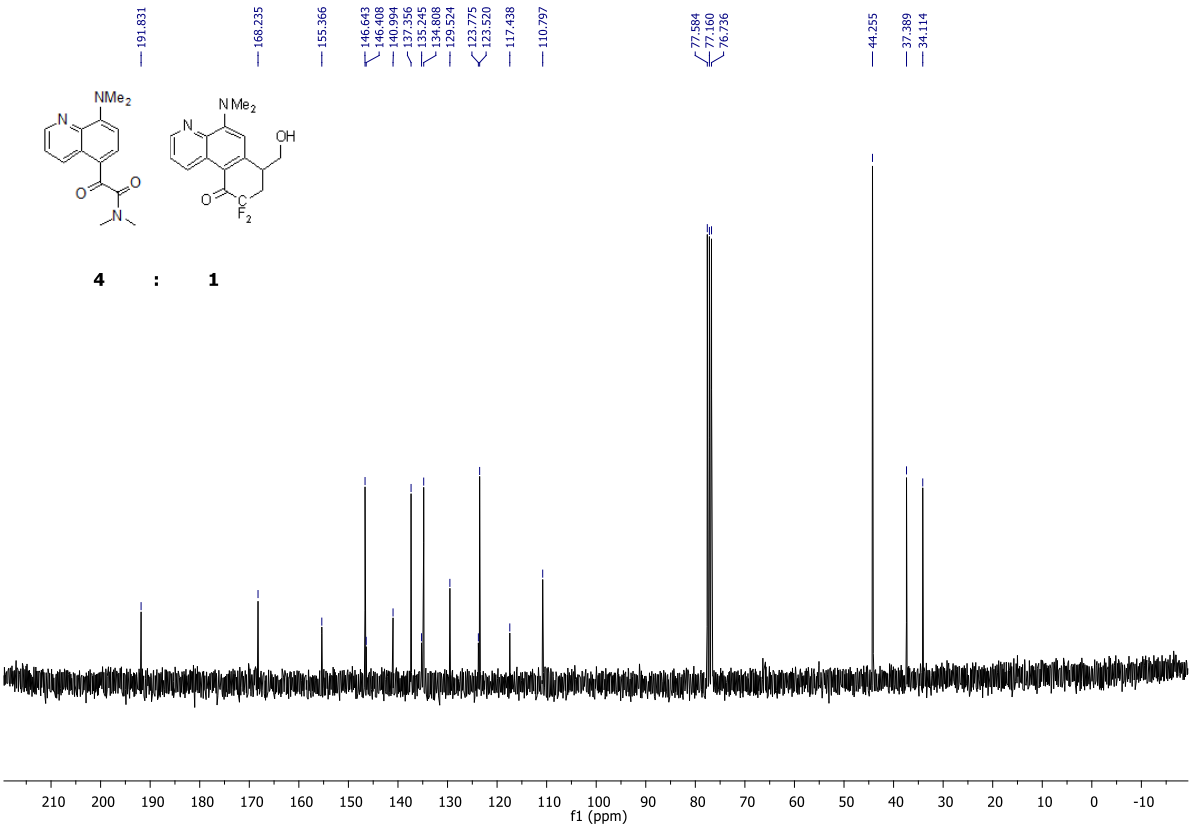

144.673
134.429
127.032
126.687
125.306
125.129
123.389
121.984
75.364
45.437
45.227
45.017
42.472
42.145
27.815
27.777
NMe2
Ph
Me
O
C
F2
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3bh

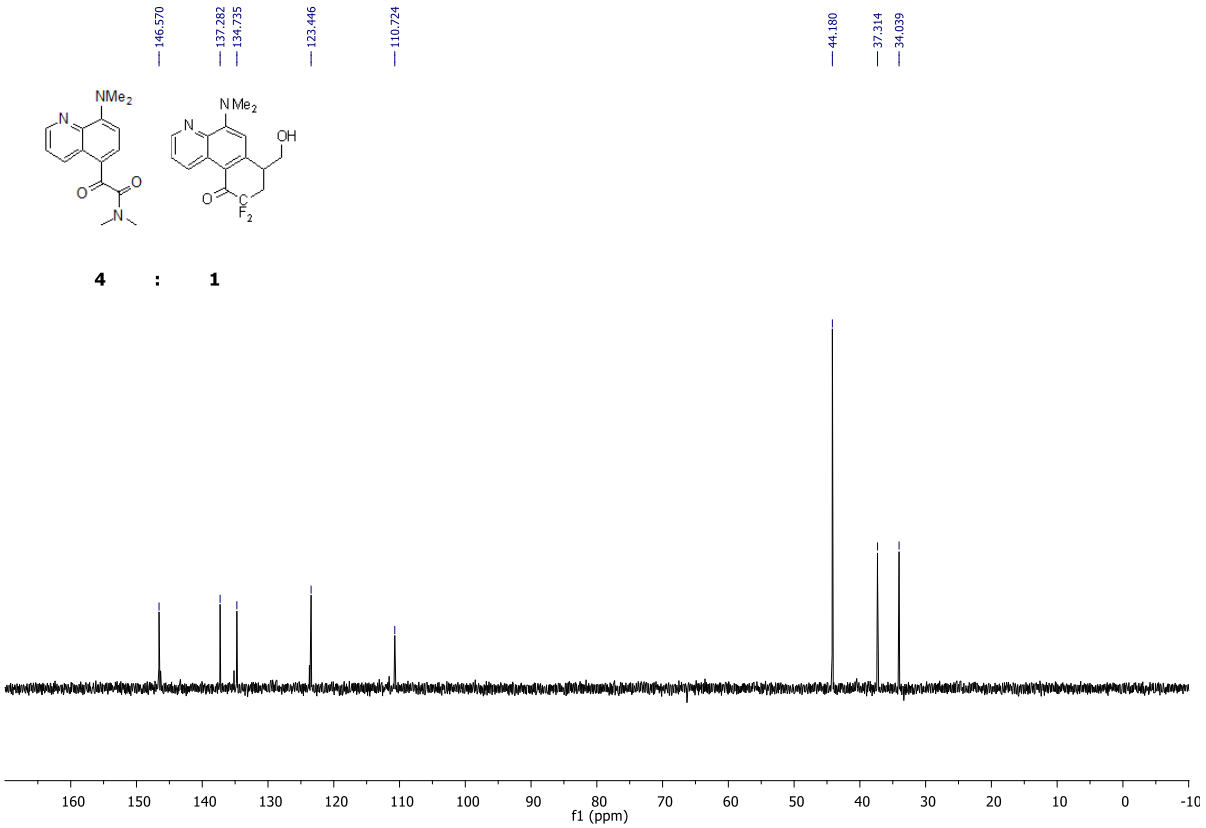

9.875
9.869
9.846
9.840
9.805
9.799
9.776
9.770
8.845
8.839
8.831
8.825
8.784
7.864
7.836
7.551
7.537
7.522
7.508
6.853
6.794
4.006
4.001
3.976
3.958
3.369
3.128
2.999
2.823
2.817
2.808
2.801
2.775
2.766
2.759
2.717
2.711
2.692
2.660
2.617
2.585
2.566
NMe2
N
O
O
N
NMe2
N
OH
O
C
F2
4 : 1
1.00
4.32
4.18
4.32
5.32
4.07
1.97
35.02
14.05
13.28
2.05
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

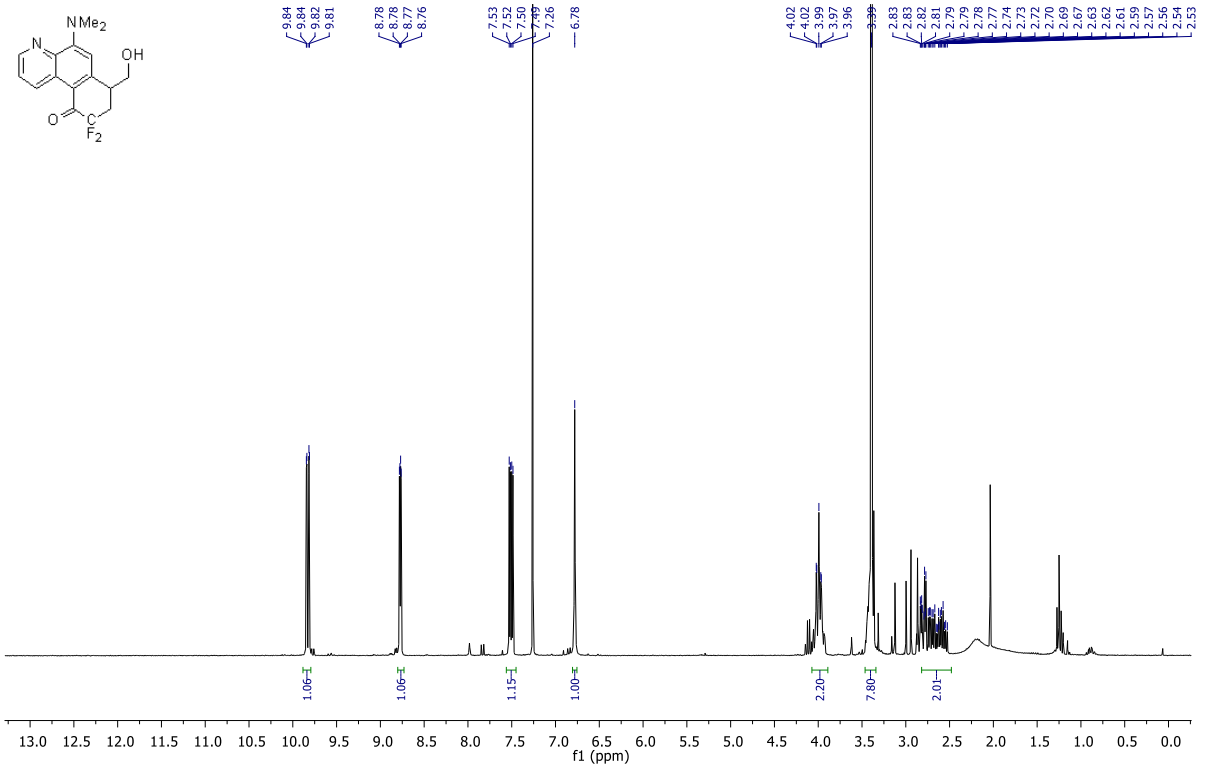

-98.981
-99.023
-99.077
-99.121
-99.951
-99.994
-100.048
-100.091
-102.291
-102.329
-102.369
-103.262
-103.300
-103.340
f1 (ppm)

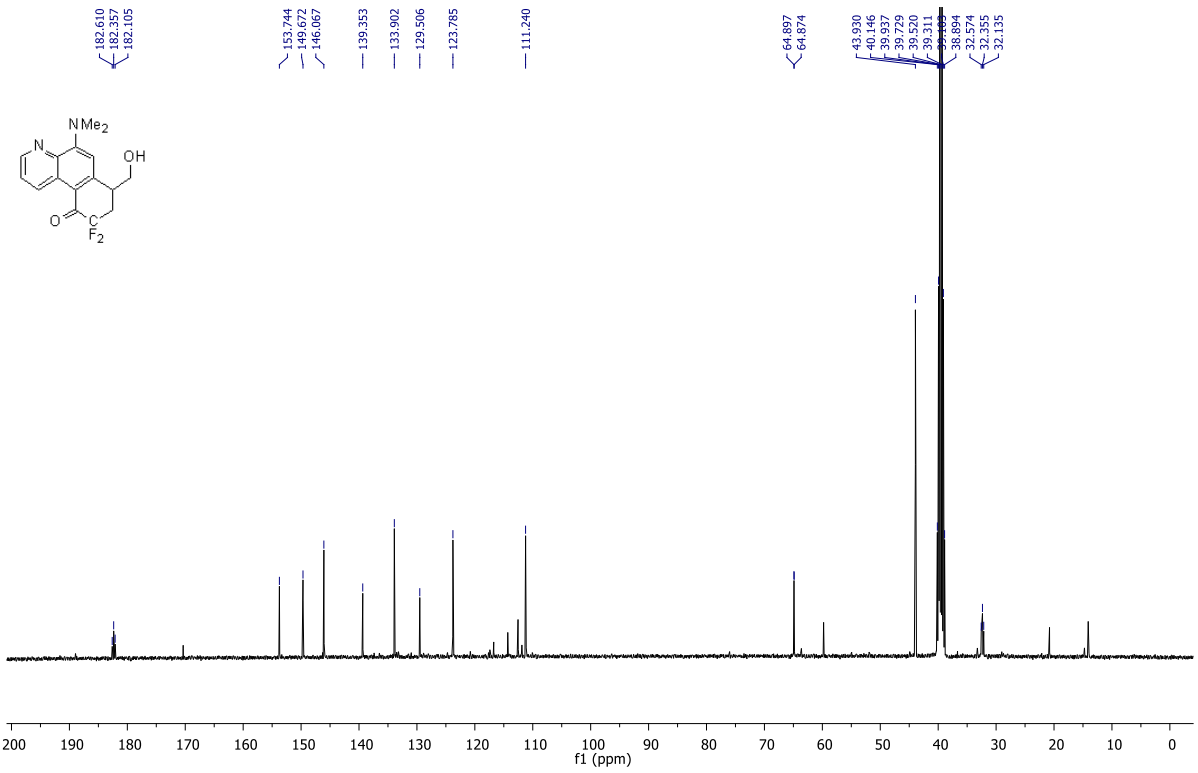
4 : 1


191.831
168.235
155.366
146.643
146.408
140.994
137.356
135.245
134.808
129.524
123.775
123.520
117.438
110.797
77.584
77.160
76.736
44.255
37.389
34.114
f1 (ppm)

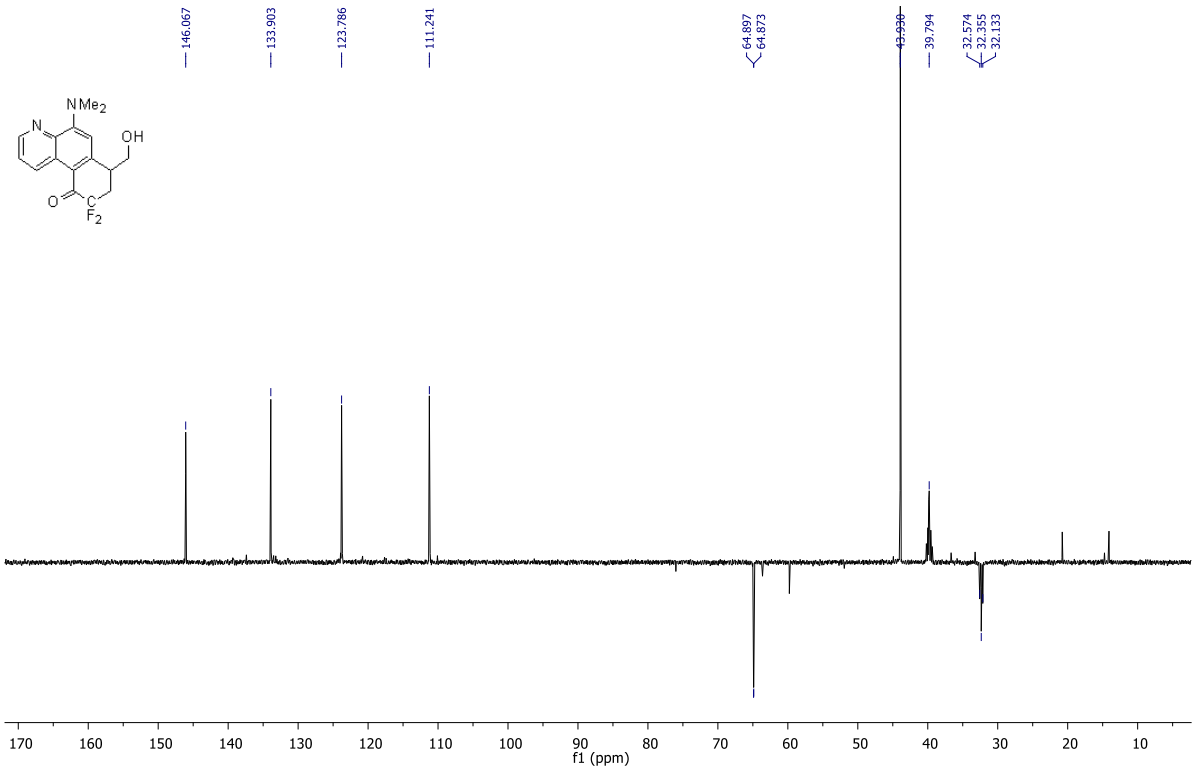
4 : 1


146.570
137.282
134.735
123.446
110.724
44.180
37.314
34.039
NMe2
N
O
O
N
NMe2
N
OH
O
F2
C
4 : 1
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

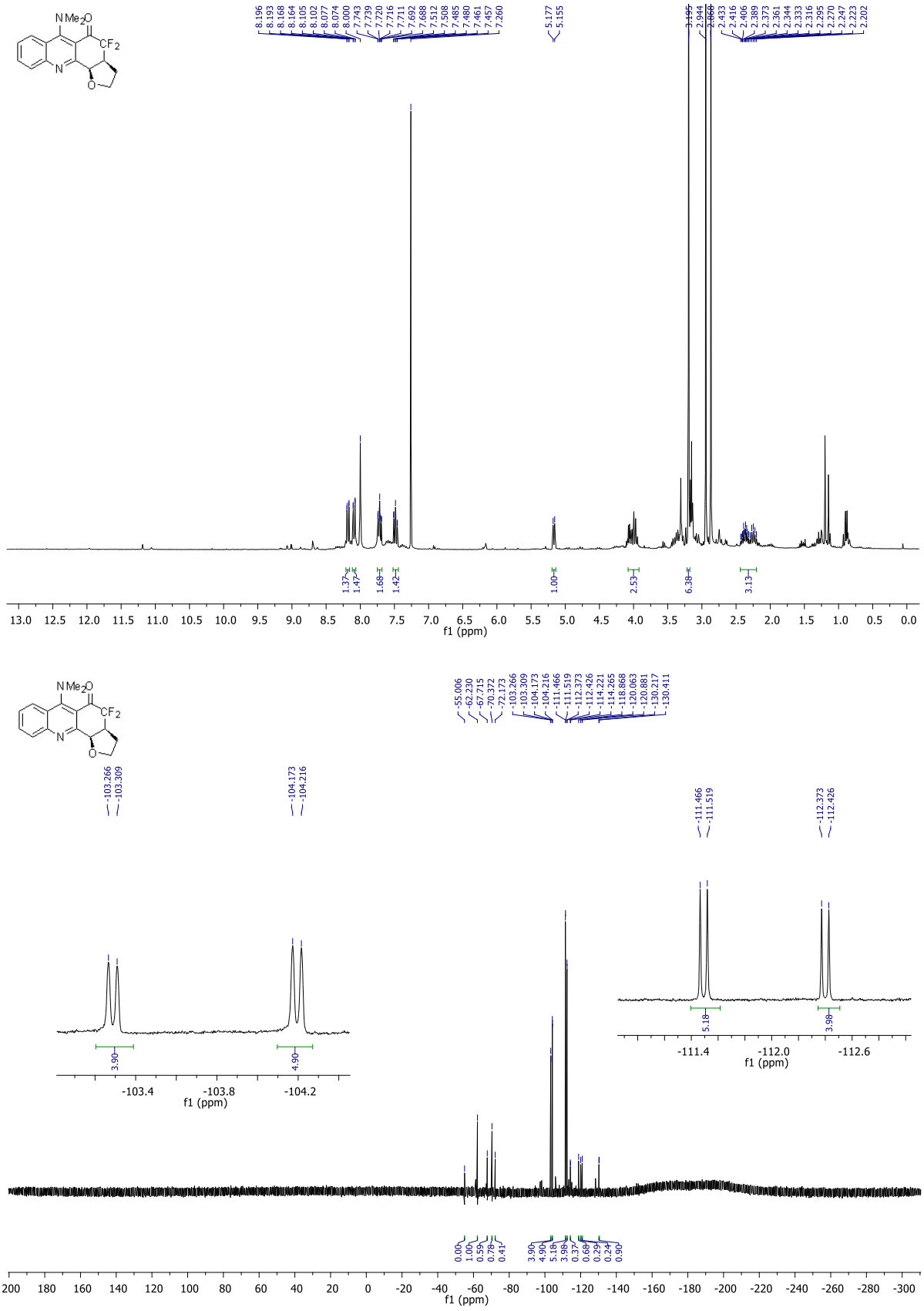

NMe2
N
OH
O
F2
C
9.84
9.84
9.82
9.81
8.78
8.78
8.77
8.76
7.53
7.52
7.50
7.26
6.78
4.02
4.02
3.99
3.97
3.96
2.83
2.83
2.82
2.81
2.79
2.79
2.78
2.78
2.77
2.74
2.73
2.72
2.70
2.69
2.67
2.63
2.62
2.61
2.59
2.57
2.56
2.54
2.53
1.06
1.06
1.15
1.00
2.20
7.80
2.01
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


182.610
182.357
182.105
153.744
149.672
146.067
139.353
133.902
129.506
123.785
111.240
64.897
64.874
43.930
40.146
39.937
39.729
39.520
39.311
38.894
32.574
32.355
32.135
NMe2
N
OH
O
C
F2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

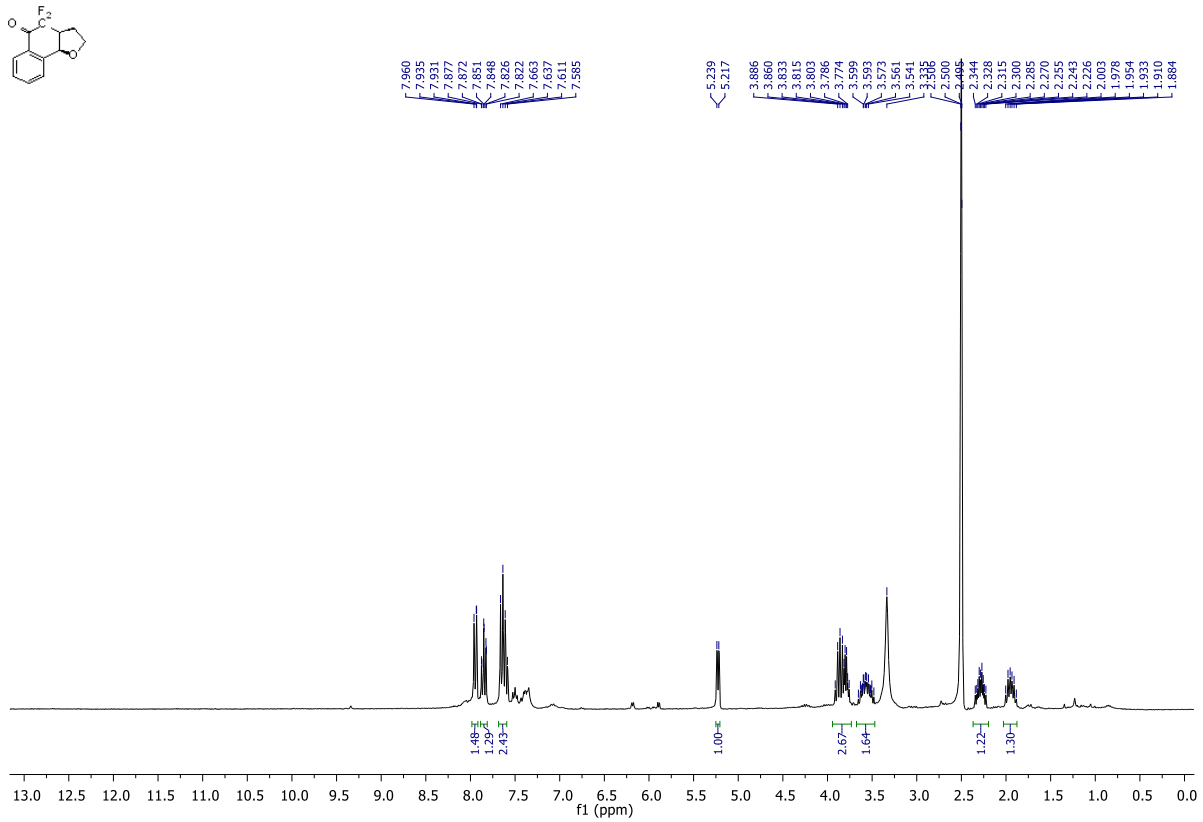
DEPT

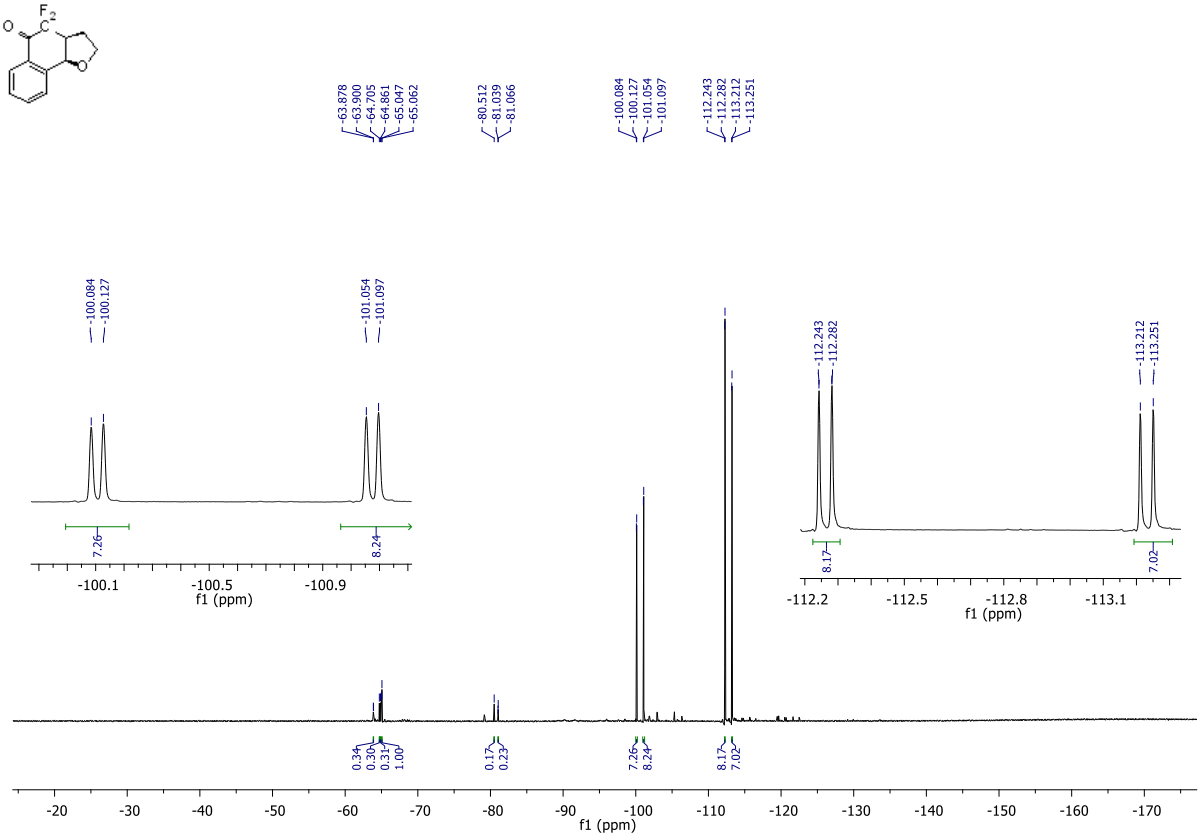

146.067
133.903
123.786
111.241
64.897
64.873
43.930
39.794
32.574
32.355
32.133
NMe2
N
OH
O
C
F2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

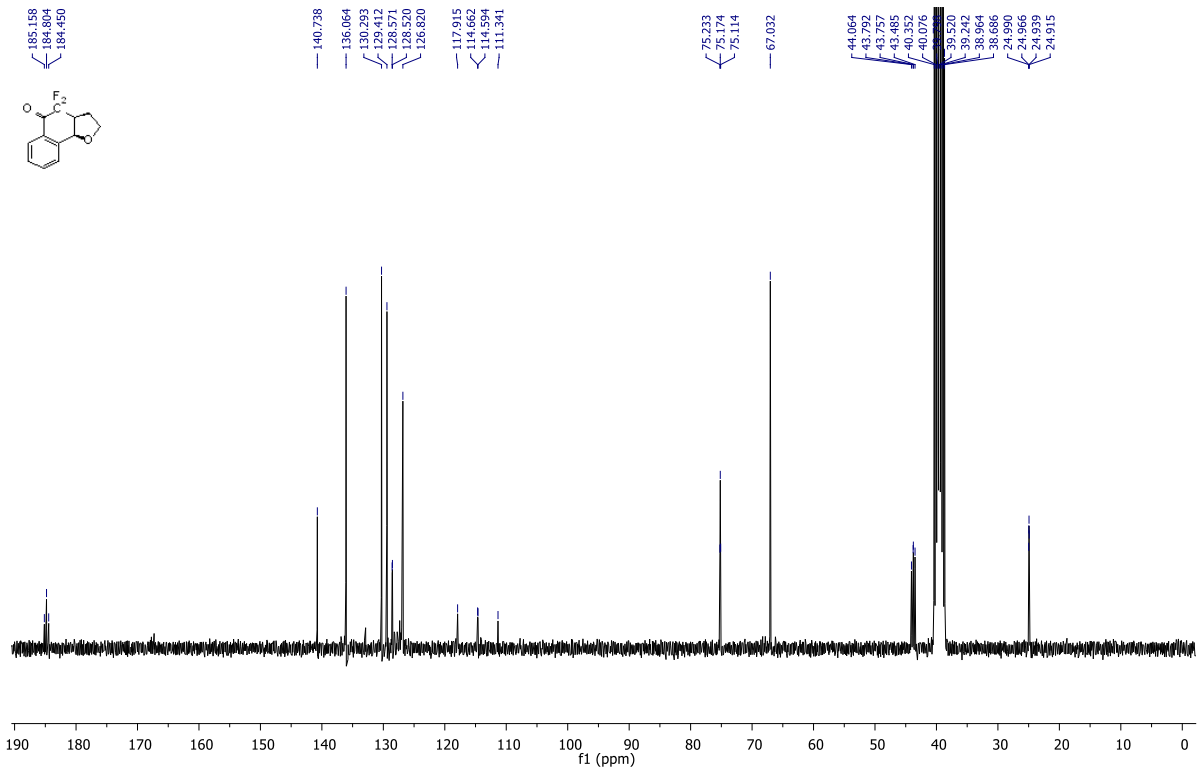
3ca



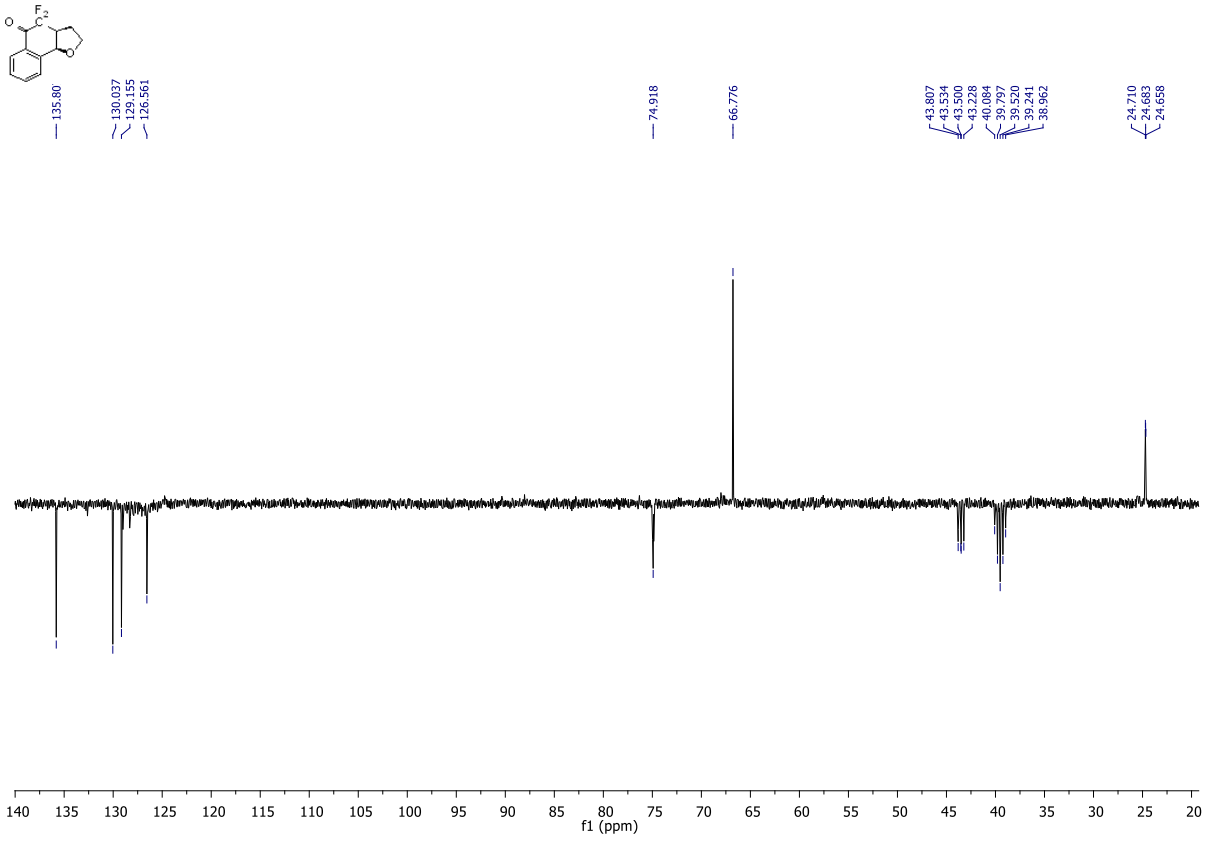
3da


7.960
7.935
7.931
7.877
7.872
7.851
7.848
7.826
7.822
7.663
7.637
7.611
7.585
5.239
5.217
3.886
3.860
3.833
3.815
3.803
3.786
3.774
3.599
3.593
3.573
3.561
3.541
2.500
2.344
2.328
2.315
2.300
2.285
2.270
2.255
2.243
2.226
2.003
1.978
1.954
1.933
1.910
1.884
1.48
1.29
2.43
1.00
2.67
1.64
1.22
1.30
f1 (ppm)

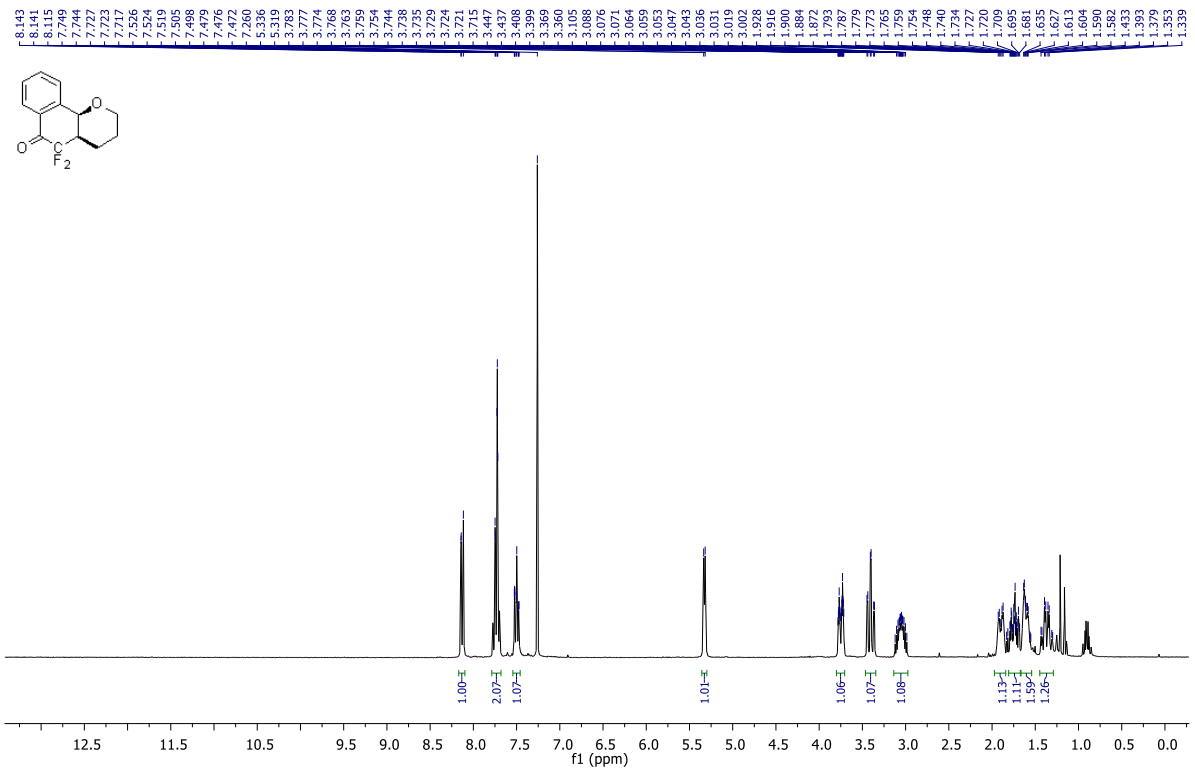

-63.878
-63.900
-64.795
-64.861
-65.047
-65.062
-80.512
-81.039
-81.066
-100.084
-100.127
-101.054
-101.097
-112.243
-112.282
-113.212
-113.251
7.26
8.24
8.17
7.02
f1 (ppm)

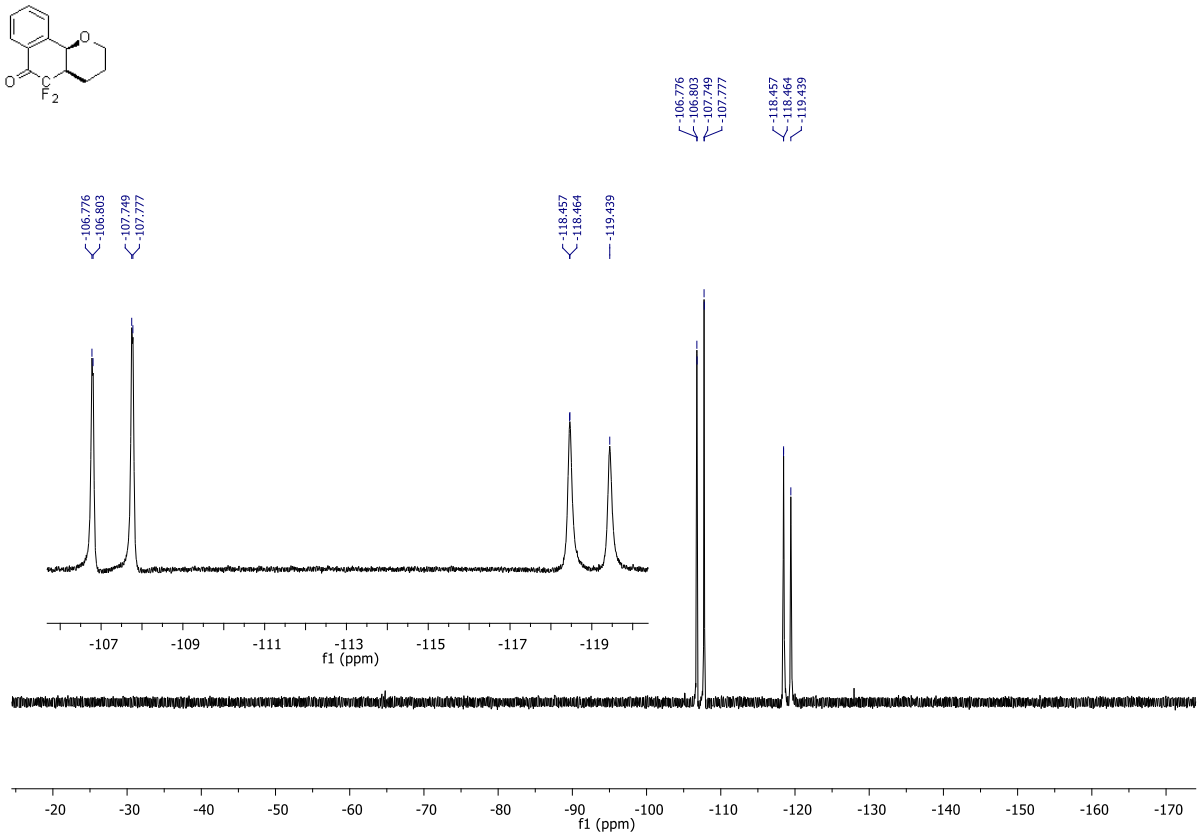

185.158
184.804
184.450
140.738
136.064
130.293
129.412
128.571
128.520
126.820
117.915
114.662
114.594
111.341
75.233
75.174
75.114
67.032
44.064
43.792
43.757
43.485
40.352
40.076
39.520
39.242
38.964
38.686
24.990
24.966
24.939
24.915
F2
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

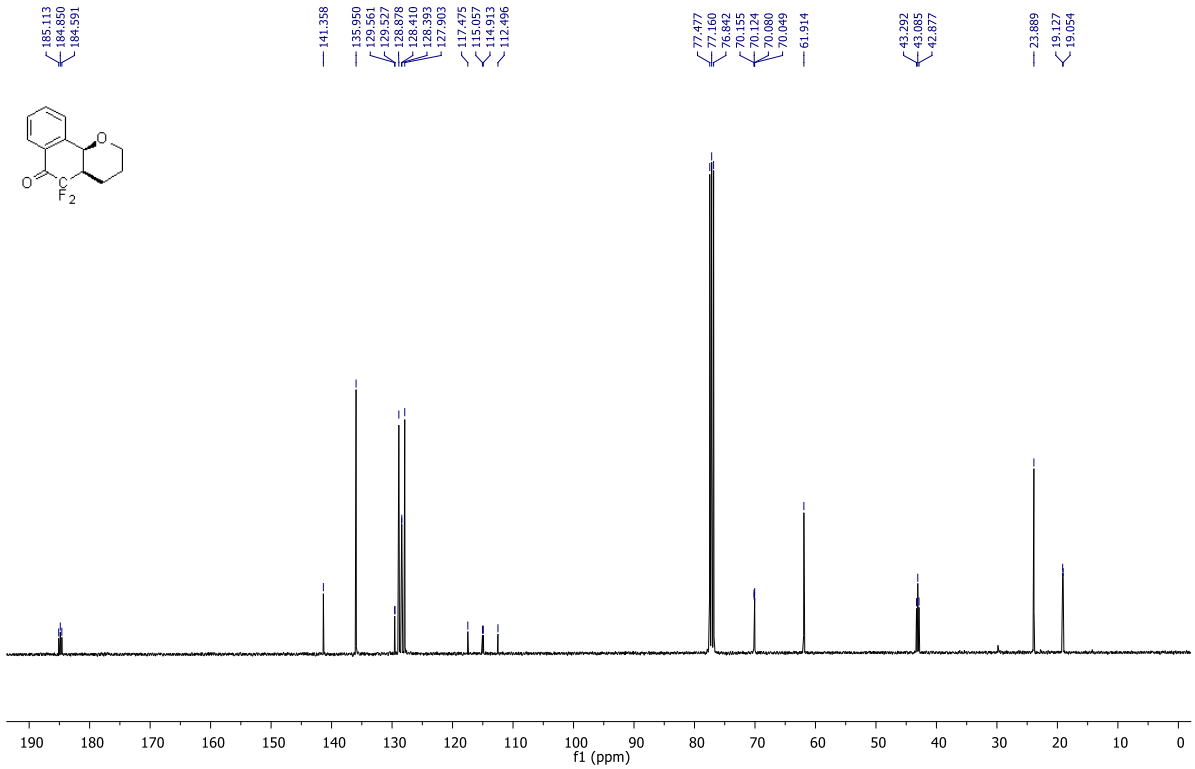
DEPT


F2
O
O
135.80
130.037
129.155
126.561
74.918
66.776
43.807
43.534
43.500
43.228
40.084
39.797
39.520
39.241
38.962
24.710
24.683
24.658
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

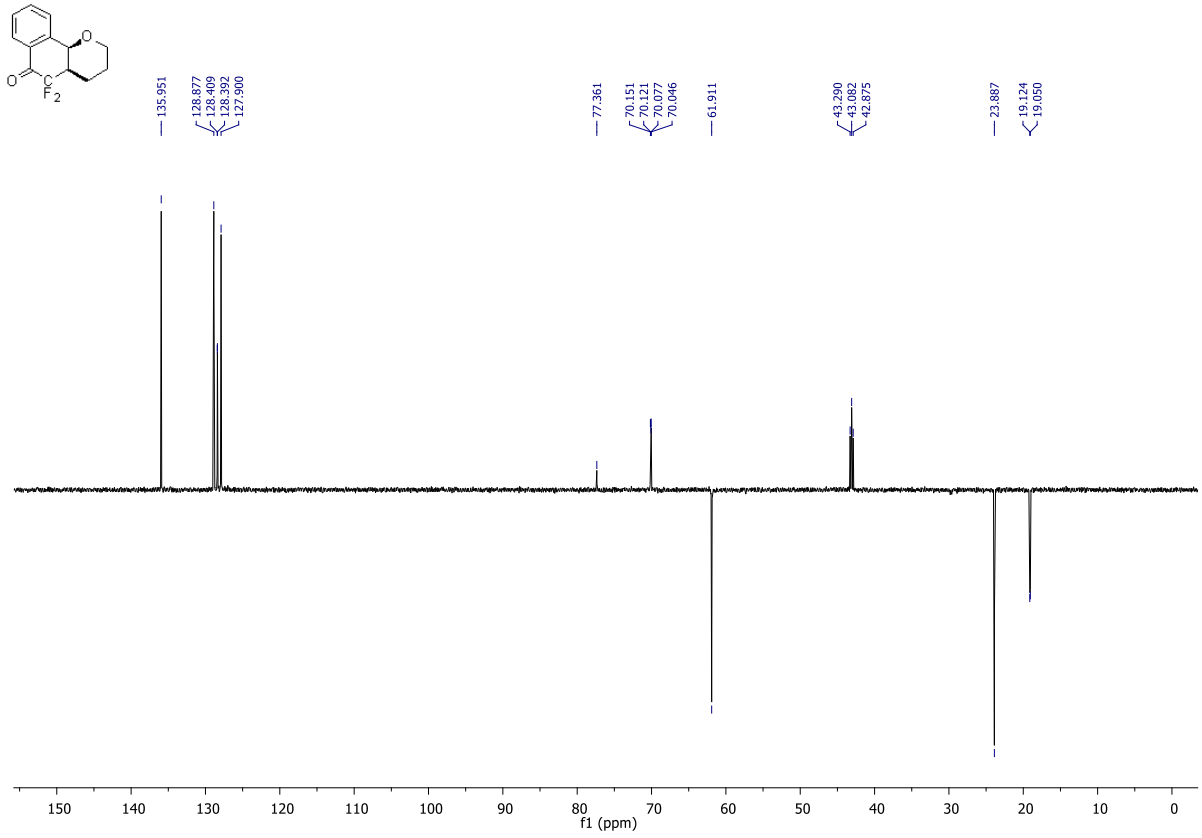
3db

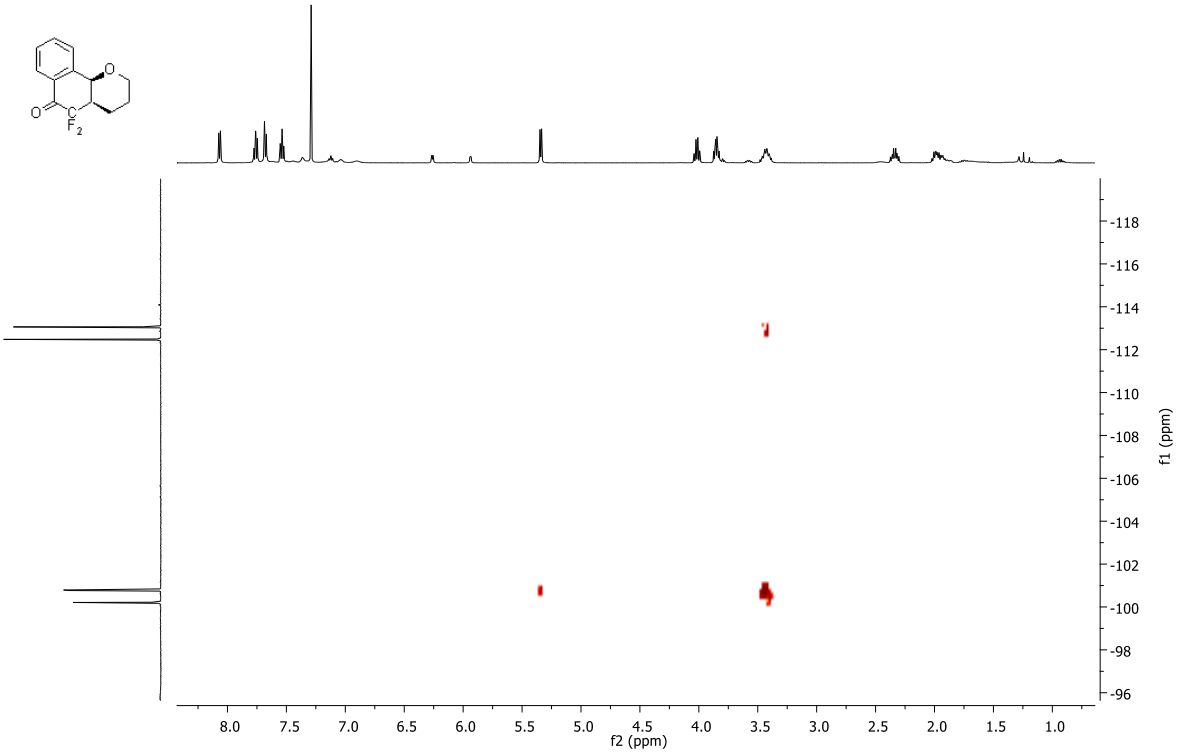

8.143
8.141
8.115
7.749
7.744
7.727
7.723
7.717
7.526
7.524
7.519
7.505
7.498
7.479
7.476
7.472
7.260
5.336
5.319
3.783
3.777
3.774
3.768
3.763
3.759
3.754
3.744
3.738
3.735
3.729
3.724
3.721
3.715
3.447
3.437
3.408
3.399
3.369
3.360
3.105
3.088
3.076
3.071
3.064
3.059
3.053
3.047
3.043
3.036
3.031
3.019
3.002
1.928
1.916
1.900
1.884
1.872
1.793
1.787
1.779
1.773
1.765
1.759
1.754
1.748
1.740
1.734
1.727
1.720
1.709
1.695
1.681
1.635
1.627
1.613
1.604
1.590
1.582
1.433
1.393
1.379
1.353
1.339
O
O
F2
1.00
2.07
1.07
1.01
1.06
1.07
1.08
1.13
1.11
1.59
1.26
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


O
O
F2
-106.776
-106.803
-107.749
-107.777
-118.457
-118.464
-119.439
-107
-109
-111
-113
-115
-117
-119
f1 (ppm)
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)

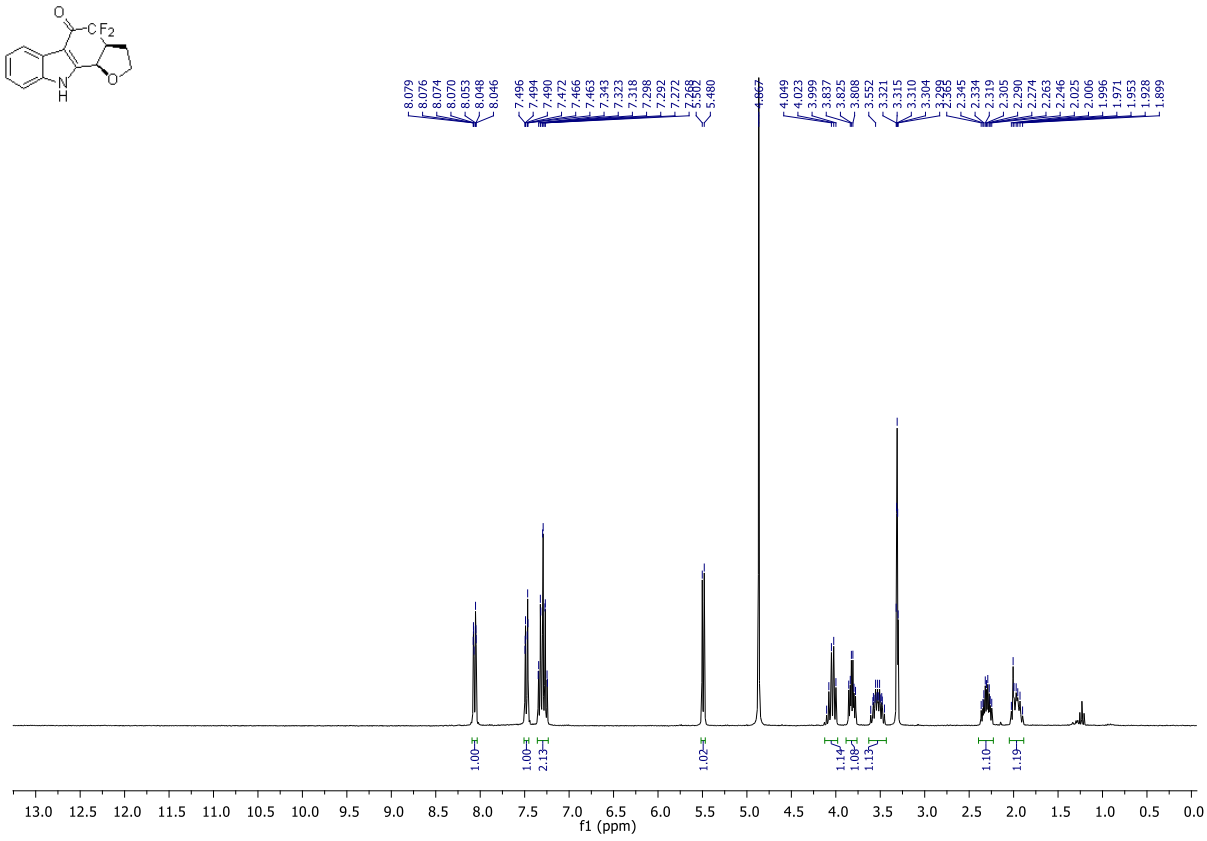

185.113
184.850
184.591
141.358
135.950
129.561
129.527
128.878
128.410
128.393
127.903
117.475
115.057
114.913
112.496
77.477
77.160
76.842
70.155
70.124
70.080
70.049
61.914
43.292
43.085
42.877
23.889
19.127
19.054
O
O
F2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

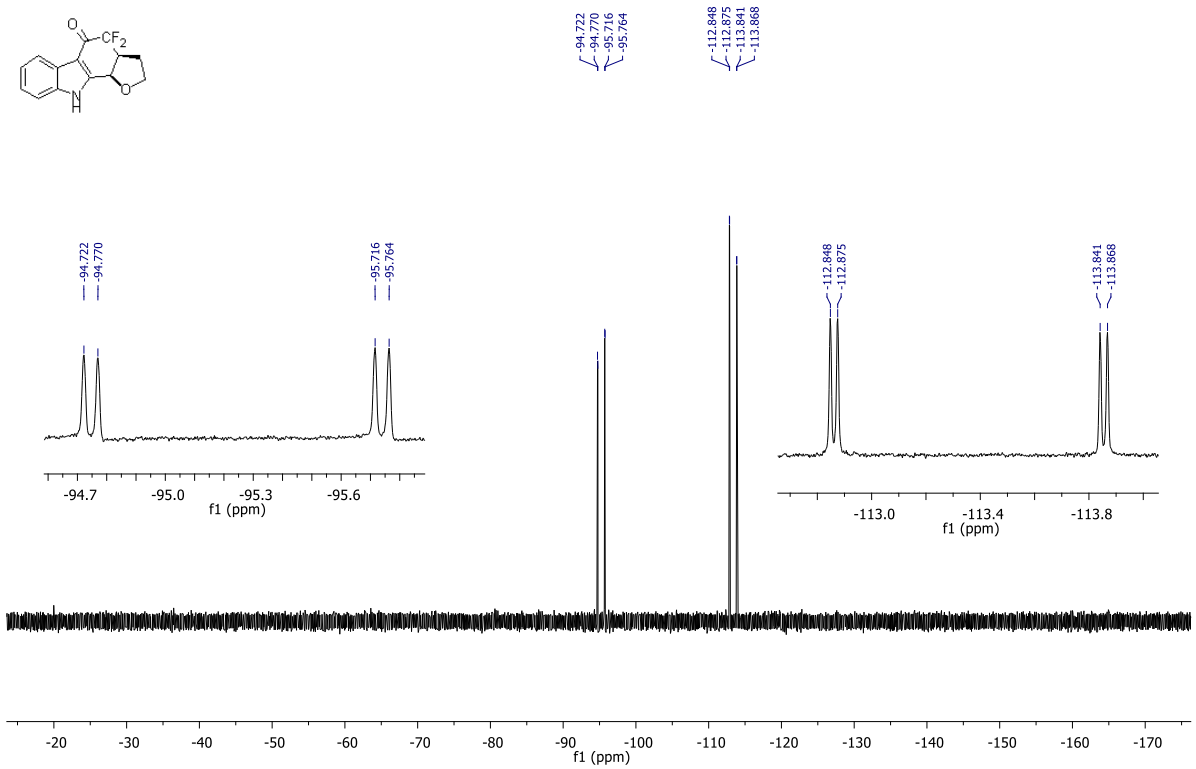
DEPT


O
O
F2
135.951
128.877
128.409
128.392
127.900
77.361
70.151
70.121
70.077
70.046
61.911
43.290
43.082
42.875
23.887
19.124
19.050
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
F2
-118
-116
-114
-112
-110
-108
-106
-104
-102
-100
-98
-96
f1 (ppm)
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
f2 (ppm)

3ea


O
CF2
N
H
O
8.079
8.076
8.074
8.070
8.053
8.048
8.046
7.496
7.494
7.490
7.472
7.466
7.463
7.343
7.323
7.318
7.298
7.292
7.272
5.502
5.480
4.867
4.049
4.023
3.999
3.837
3.825
3.808
3.552
3.321
3.315
3.310
3.304
2.345
2.334
2.319
2.305
2.290
2.274
2.263
2.246
2.025
2.006
1.996
1.971
1.953
1.928
1.899
1.00
1.00
2.13
1.02
1.14
1.08
1.13
1.10
1.19
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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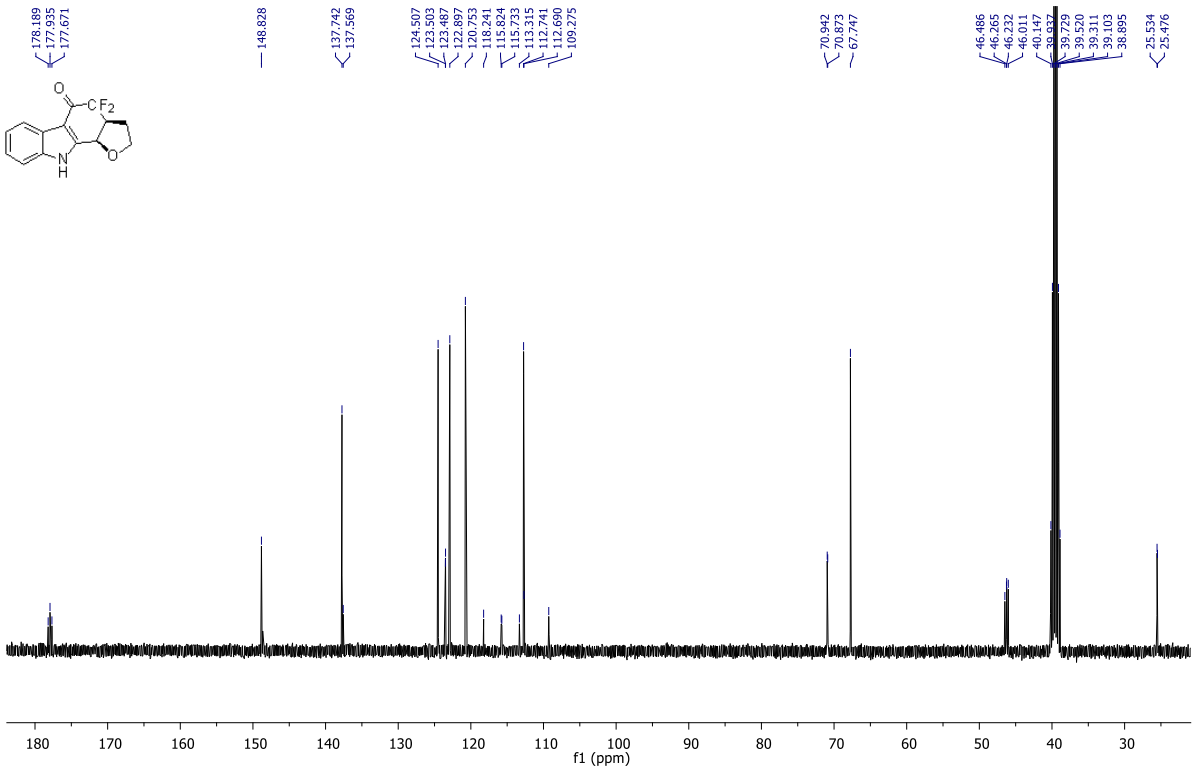
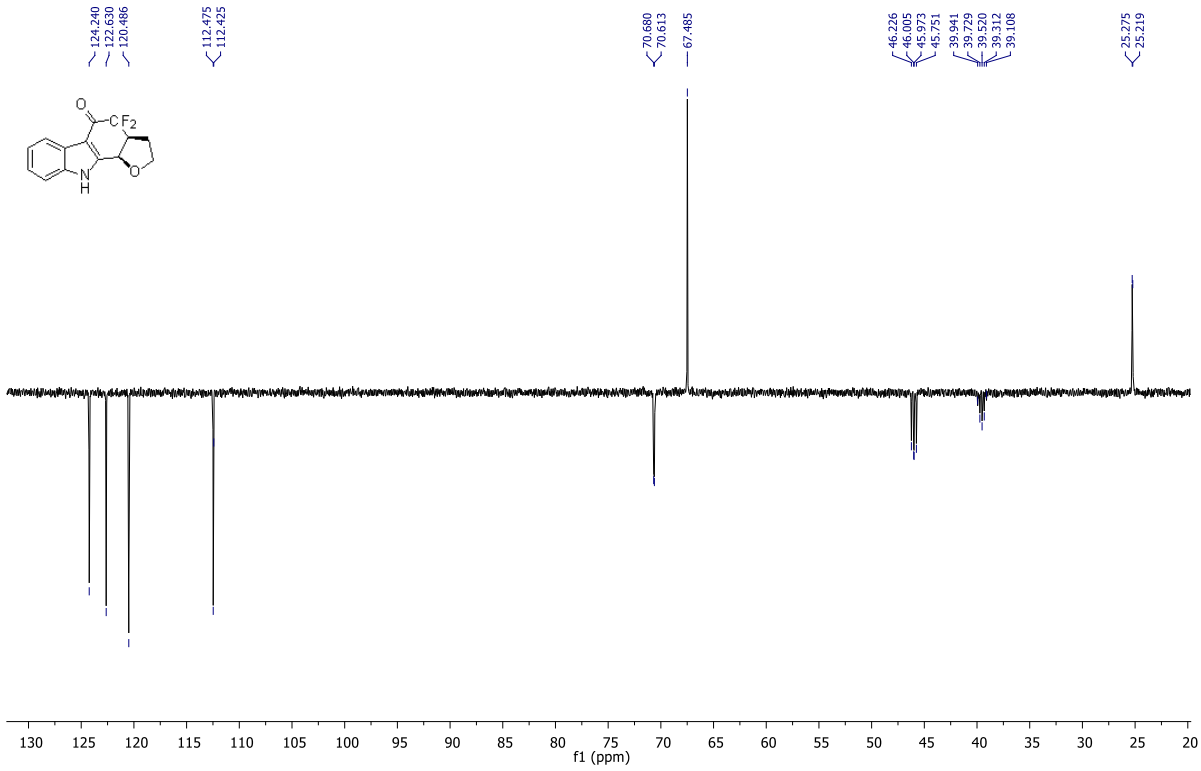
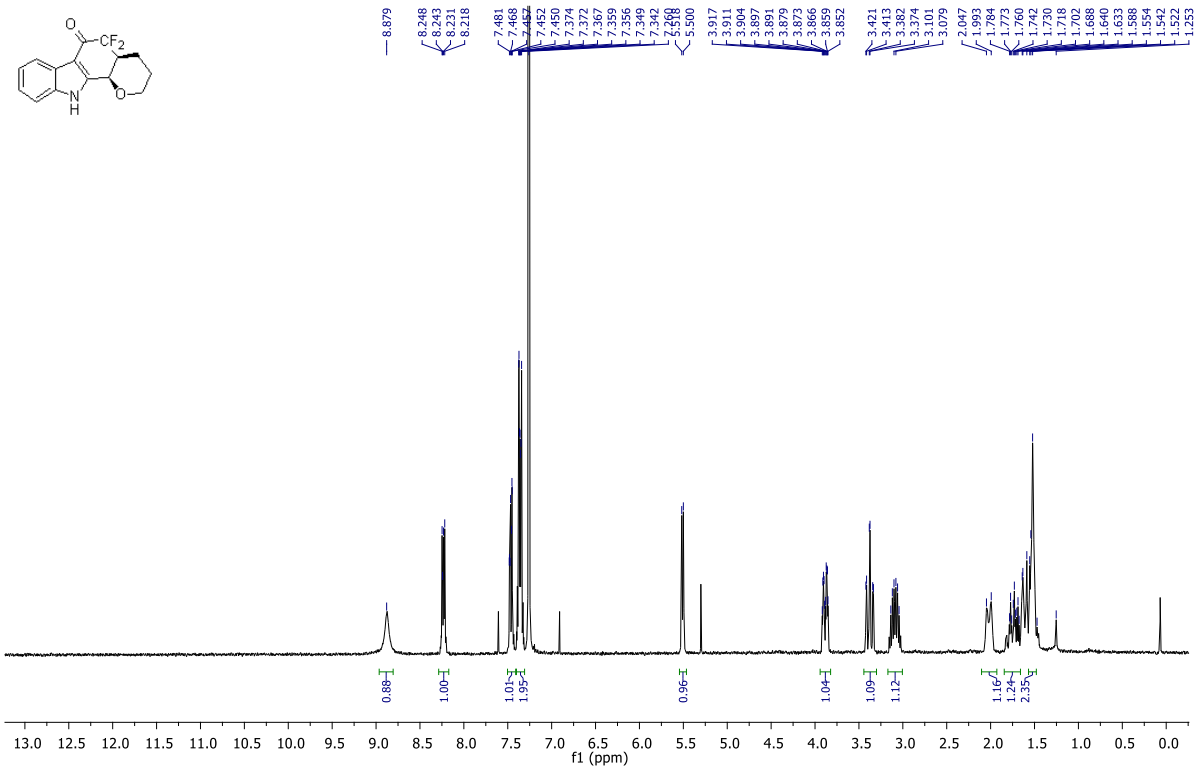
-94.770
-95.716
-95.764
-112.848
-112.875
-113.841
-113.868
f1 (ppm)

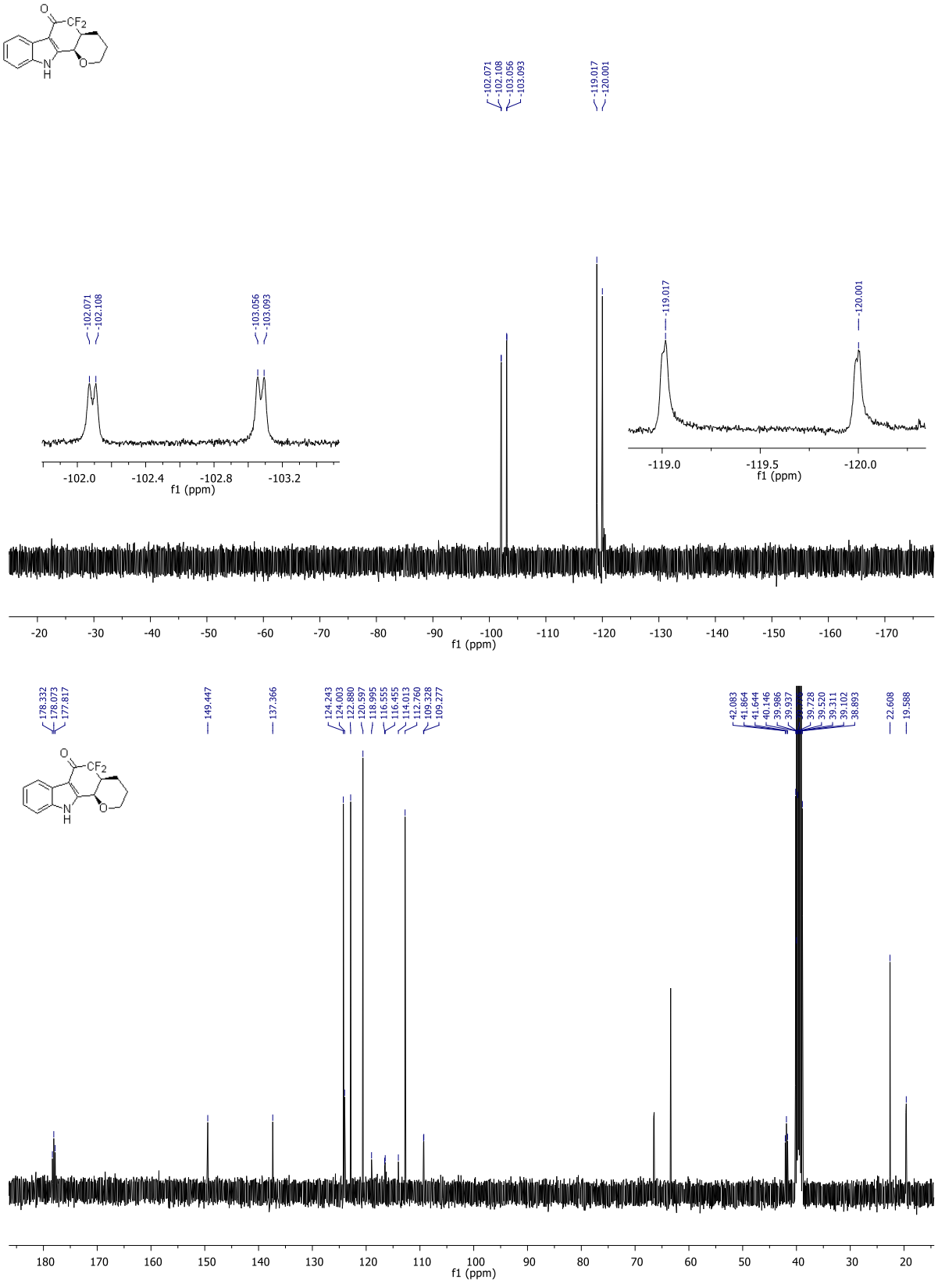

178.189
177.935
177.671
148.828
137.742
137.569
124.507
123.503
123.487
122.897
120.753
118.241
115.824
115.733
113.315
112.741
112.690
109.275
70.942
70.873
67.747
46.486
46.265
46.232
46.011
40.447
39.729
39.520
39.311
39.103
38.895
25.534
25.476
f1 (ppm)

DEPT


124.240
122.630
120.486
112.475
112.425
70.680
70.613
67.485
46.226
46.005
45.973
45.751
39.941
39.729
39.520
39.312
39.108
25.275
25.219
O
CF2
N
H
O
130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

3eb


8.879
8.248
8.243
8.231
8.218
7.481
7.468
7.457
7.452
7.450
7.374
7.372
7.367
7.359
7.356
7.349
7.342
7.260
5.518
5.500
3.917
3.911
3.904
3.897
3.891
3.879
3.873
3.866
3.859
3.852
3.421
3.413
3.382
3.374
3.101
3.079
2.047
1.993
1.784
1.773
1.760
1.742
1.730
1.718
1.702
1.688
1.640
1.633
1.588
1.554
1.542
1.522
1.253
0.88
1.00
1.01
1.95
0.96
1.04
1.09
1.12
1.16
1.24
2.35
O
CF2
N
H
O
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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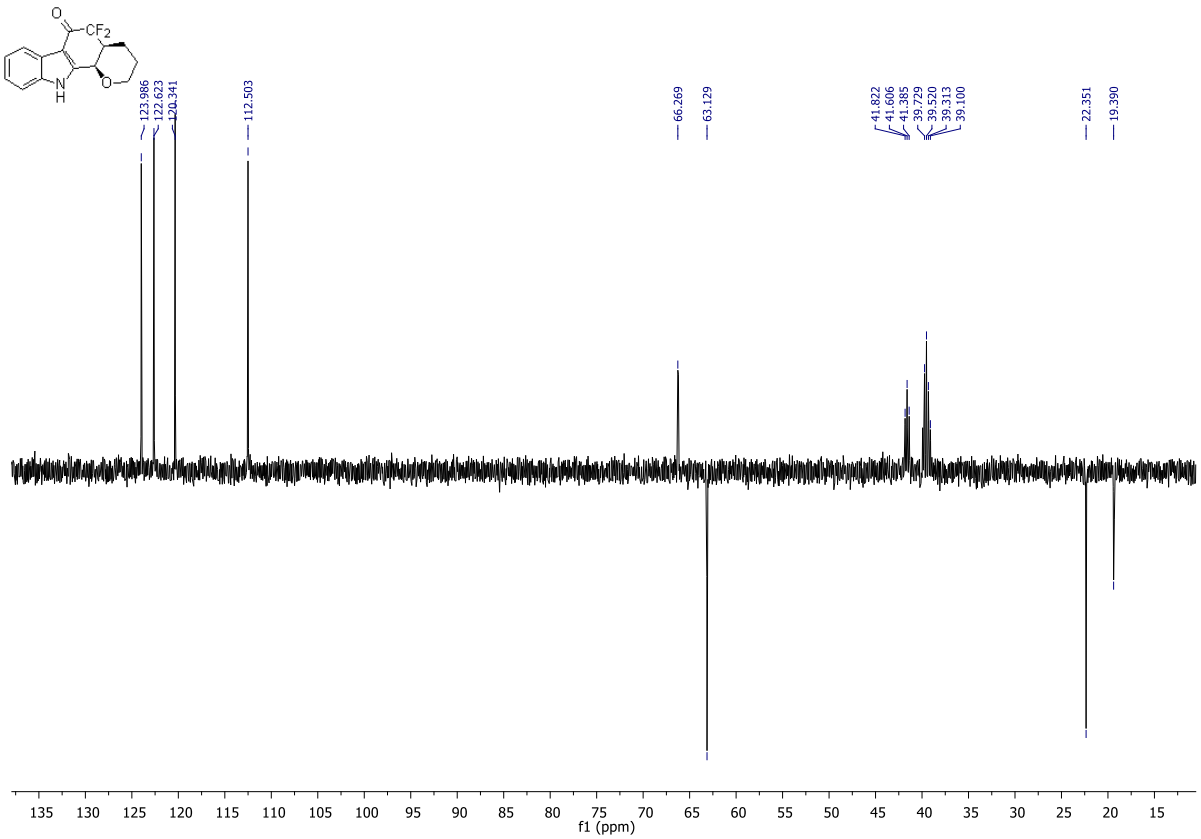
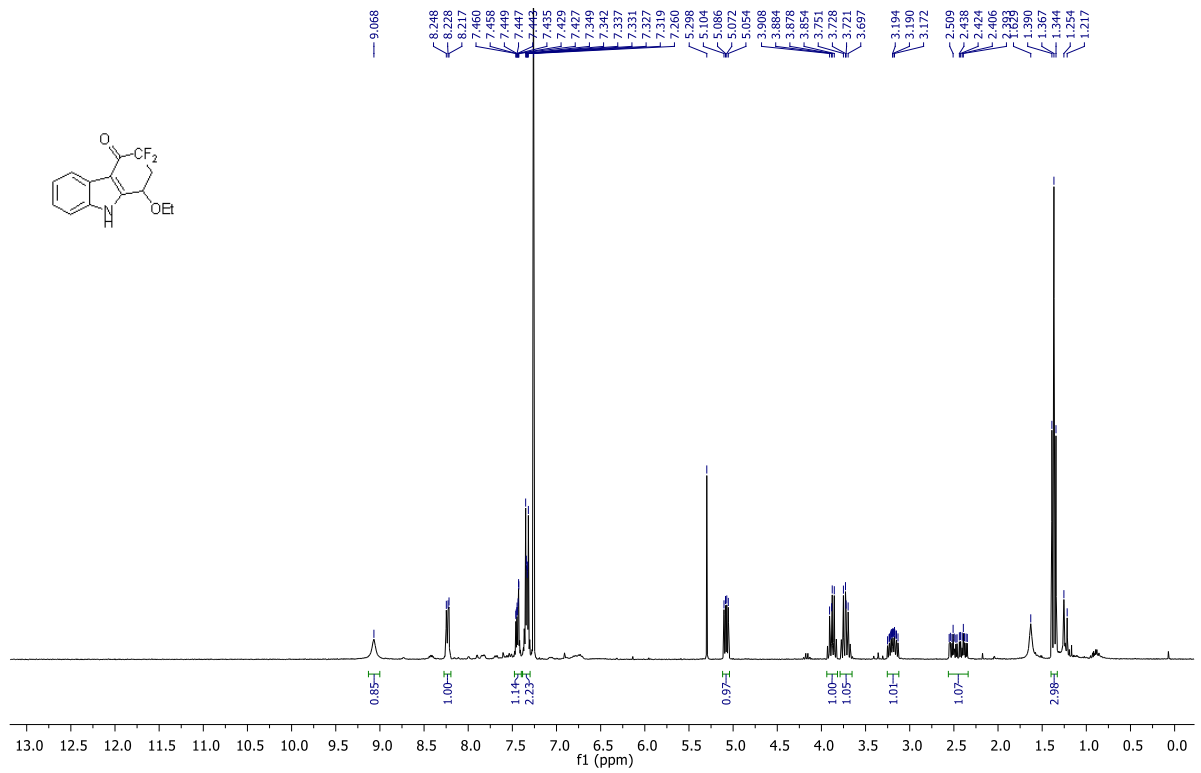
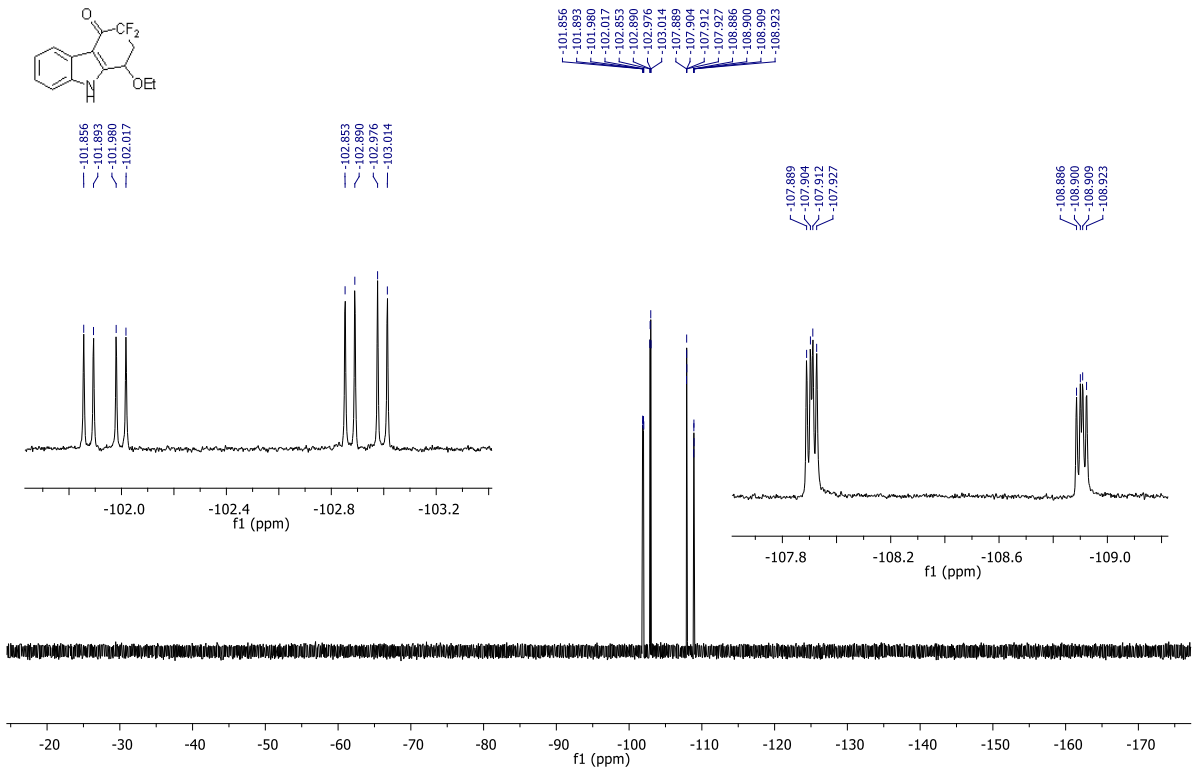
-102.108
-103.056
-103.093
-119.017
-120.001
f1 (ppm)
178.332
178.073
177.817
149.447
137.366
124.243
124.003
122.880
120.597
118.995
116.555
116.455
114.013
112.760
109.328
109.277
42.083
41.864
41.644
40.146
39.986
39.937
39.728
39.520
39.311
39.102
38.893
22.608
19.588
f1 (ppm)

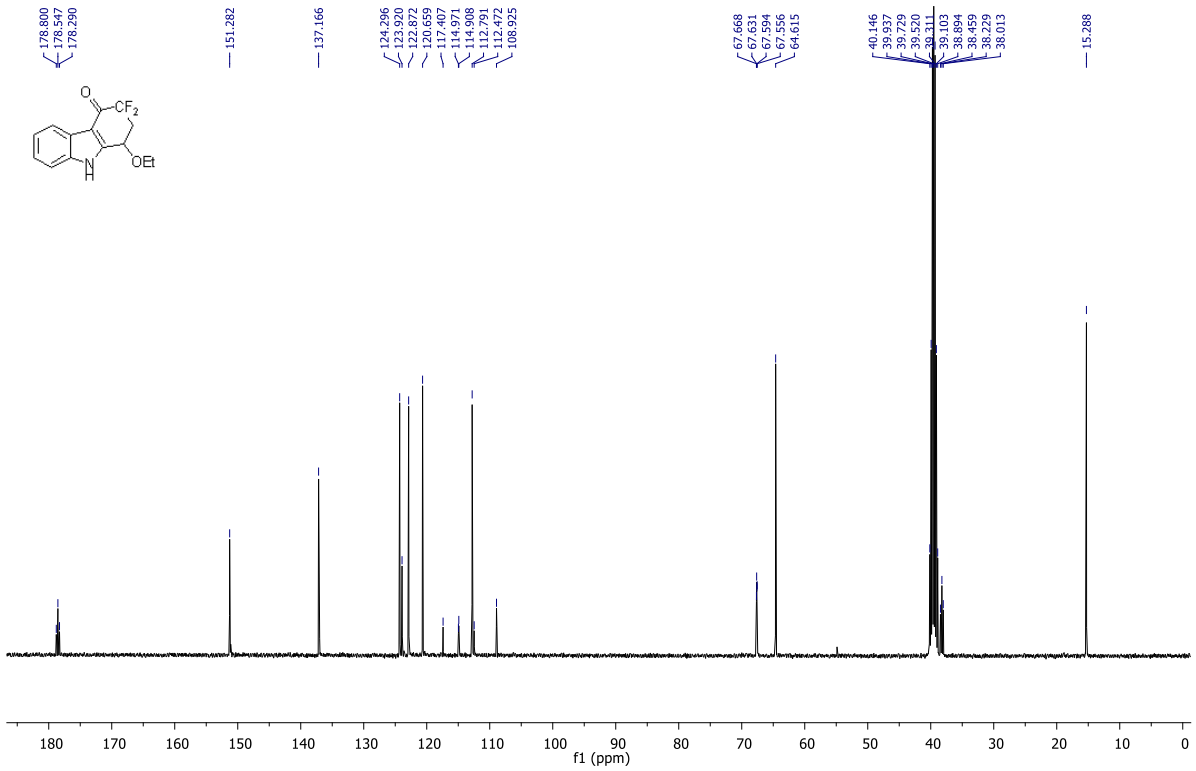
DEPT


123.986
122.623
120.341
112.503
66.269
63.129
41.822
41.606
41.385
39.729
39.520
39.313
39.100
22.351
19.390
f1 (ppm)

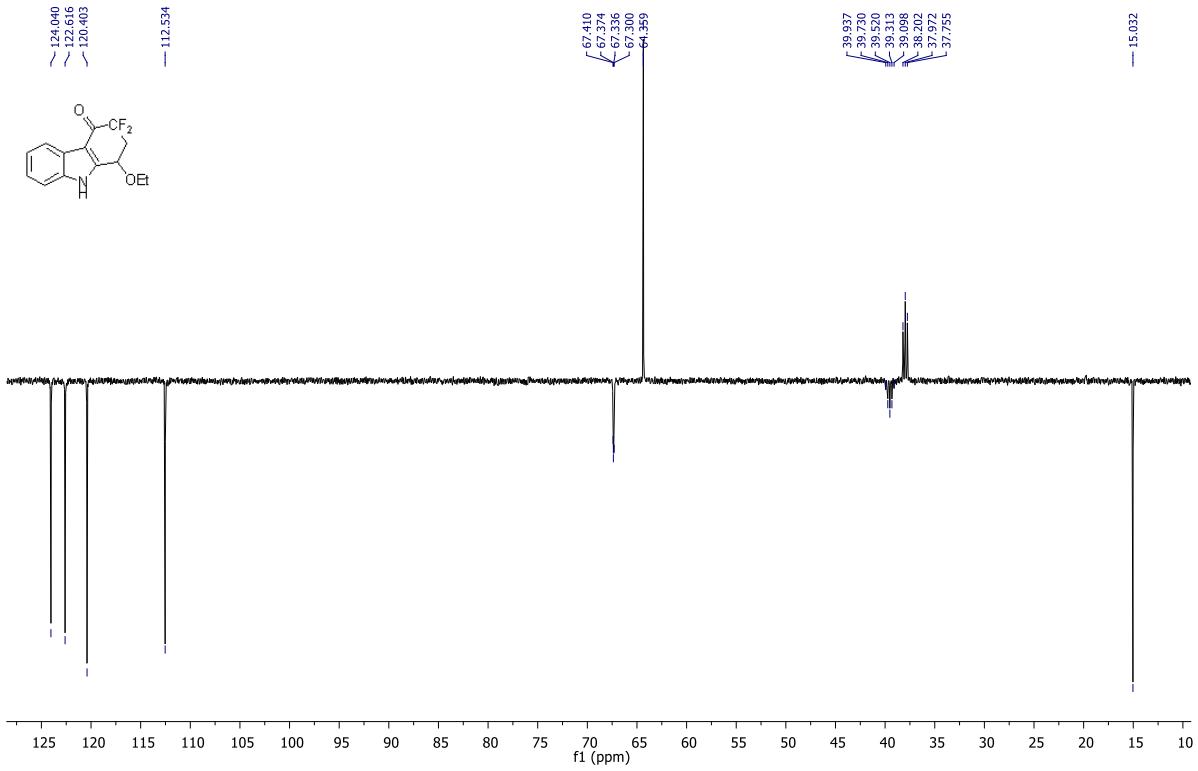
3ec


9.068
8.248
8.228
8.217
7.460
7.458
7.449
7.447
7.443
7.435
7.429
7.427
7.349
7.342
7.337
7.331
7.327
7.319
7.260
5.298
5.104
5.086
5.072
5.054
3.908
3.894
3.878
3.854
3.751
3.728
3.721
3.697
3.194
3.190
3.172
2.509
2.438
2.424
2.406
1.390
1.367
1.344
1.254
1.217
0.85
1.00
1.14
2.23
0.97
1.00
1.05
1.01
1.07
2.98
f1 (ppm)

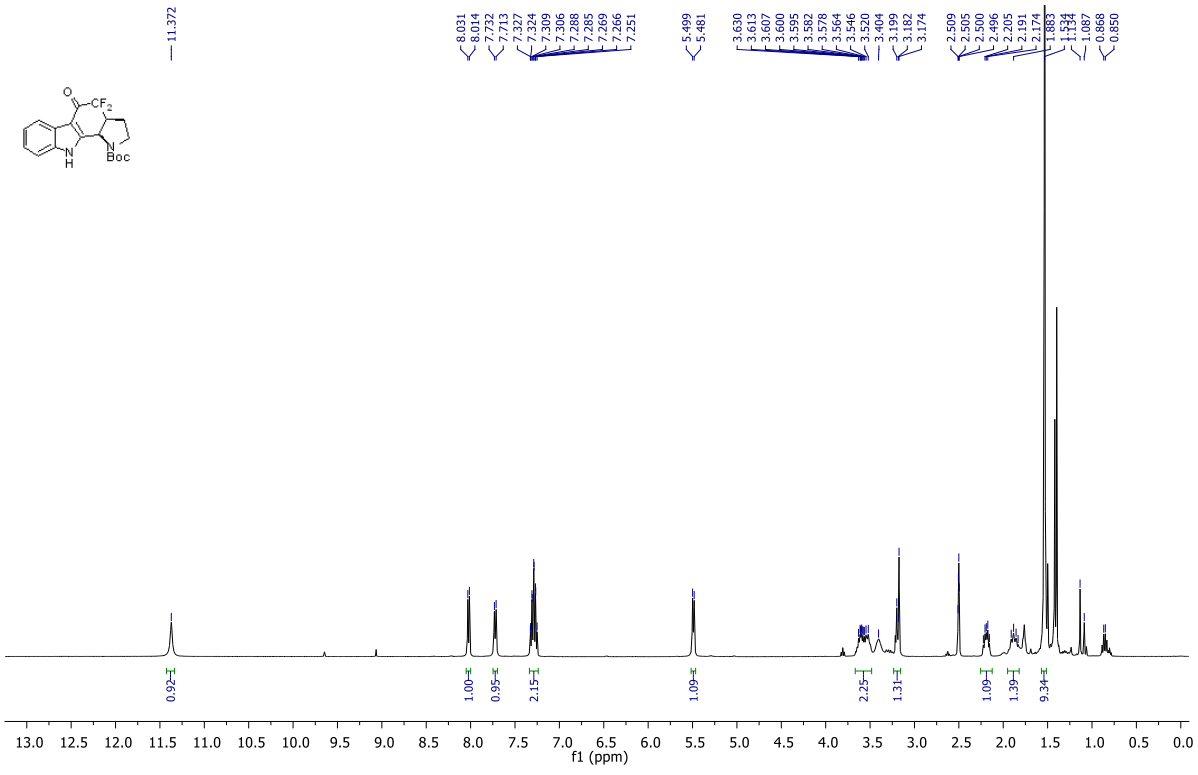

-101.856
-101.893
-101.980
-102.017
-102.853
-102.890
-102.976
-103.014
-107.889
-107.904
-107.912
-107.927
-108.886
-108.900
-108.909
-108.923
-102.0
-102.4
-102.8
-103.2
f1 (ppm)
-107.8
-108.2
-108.6
-109.0
f1 (ppm)
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)

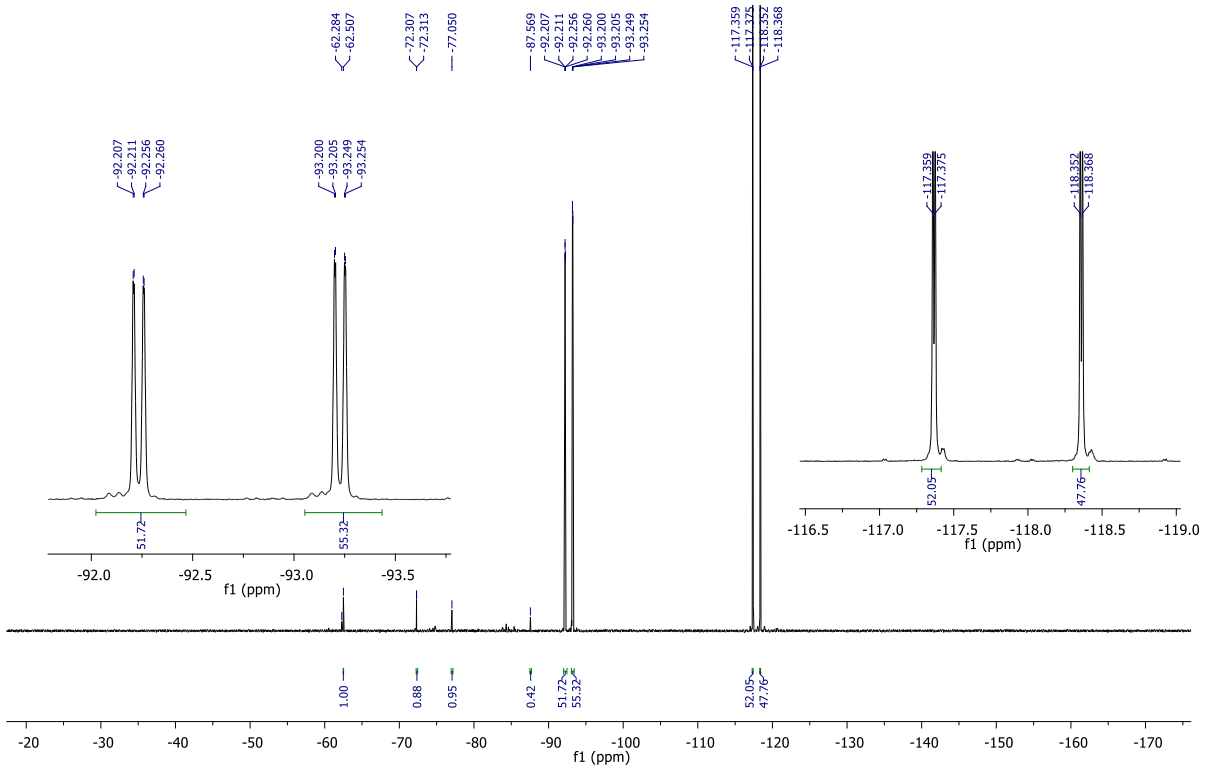

178.800
176.547
178.290
151.282
137.166
124.296
123.920
122.872
120.659
117.407
114.971
114.908
112.791
112.472
108.925
67.668
67.631
67.594
67.556
64.615
40.146
39.937
39.729
39.520
39.311
39.103
38.894
38.459
38.229
38.013
15.288
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

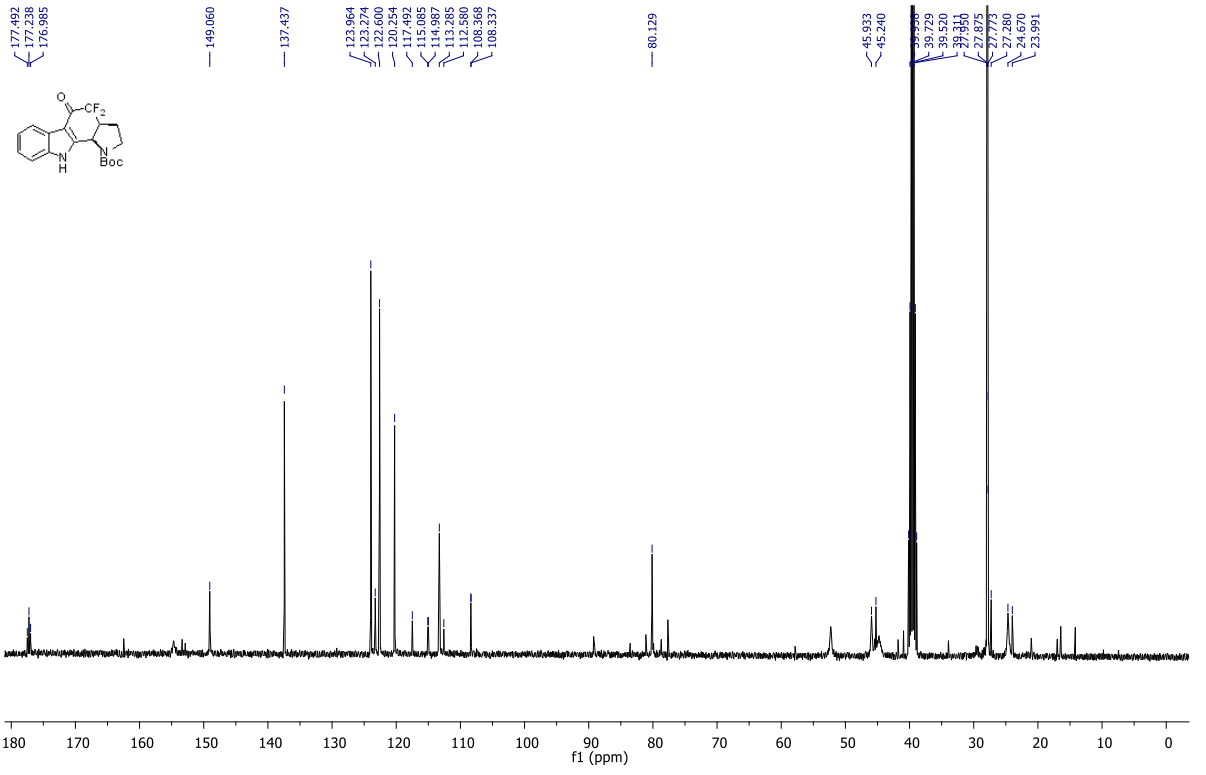
DEPT


124.040
122.616
120.403
112.534
67.410
67.374
67.336
67.300
64.359
39.937
39.730
39.520
39.313
39.098
38.202
37.972
37.755
15.032
O
CF2
OEt
N
H
125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10
f1 (ppm)

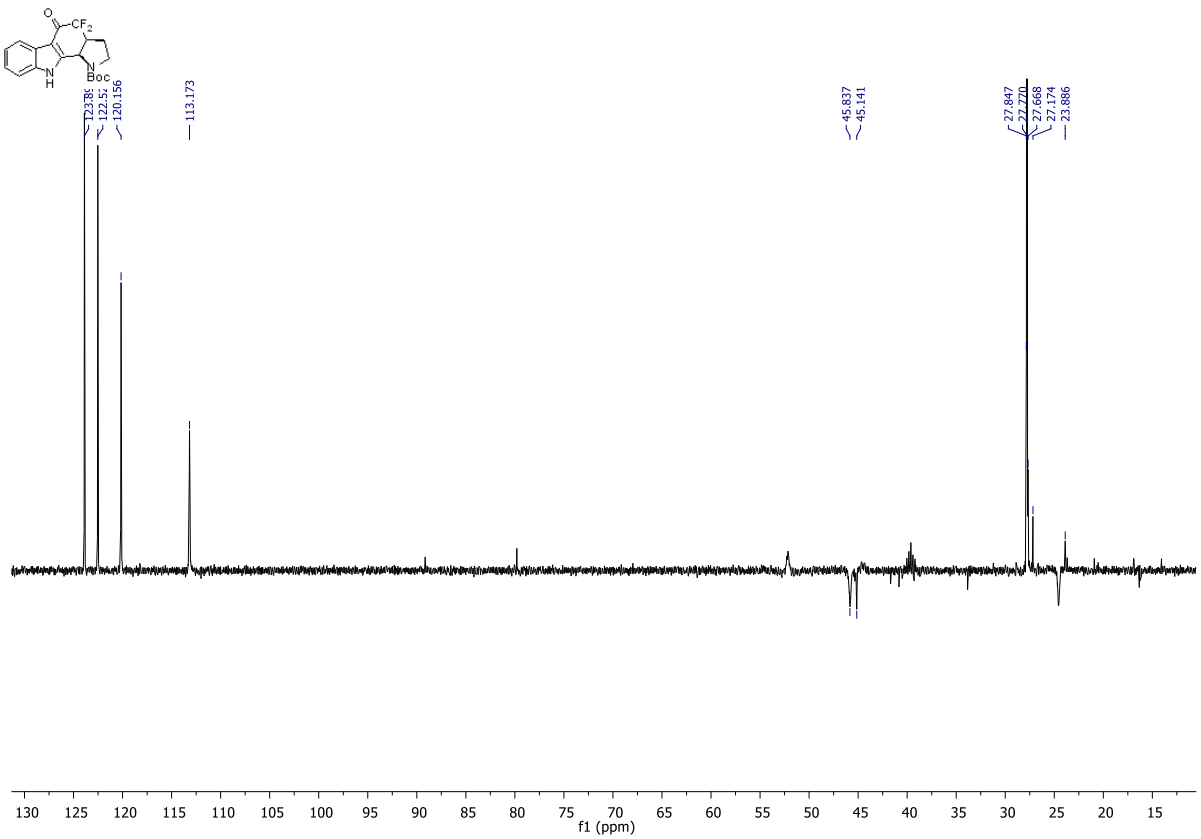
3ed


11.372
8.031
8.014
7.732
7.713
7.327
7.324
7.309
7.306
7.288
7.285
7.269
7.266
7.251
5.499
5.481
3.630
3.613
3.607
3.600
3.595
3.582
3.578
3.564
3.546
3.520
3.404
3.199
3.182
3.174
2.509
2.505
2.500
2.496
2.205
2.191
2.174
1.883
1.534
1.134
1.087
0.868
0.850
O
CF2
N
H
N
Boc
0.92
1.00
0.95
2.15
1.09
2.25
1.31
1.09
1.39
9.34
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

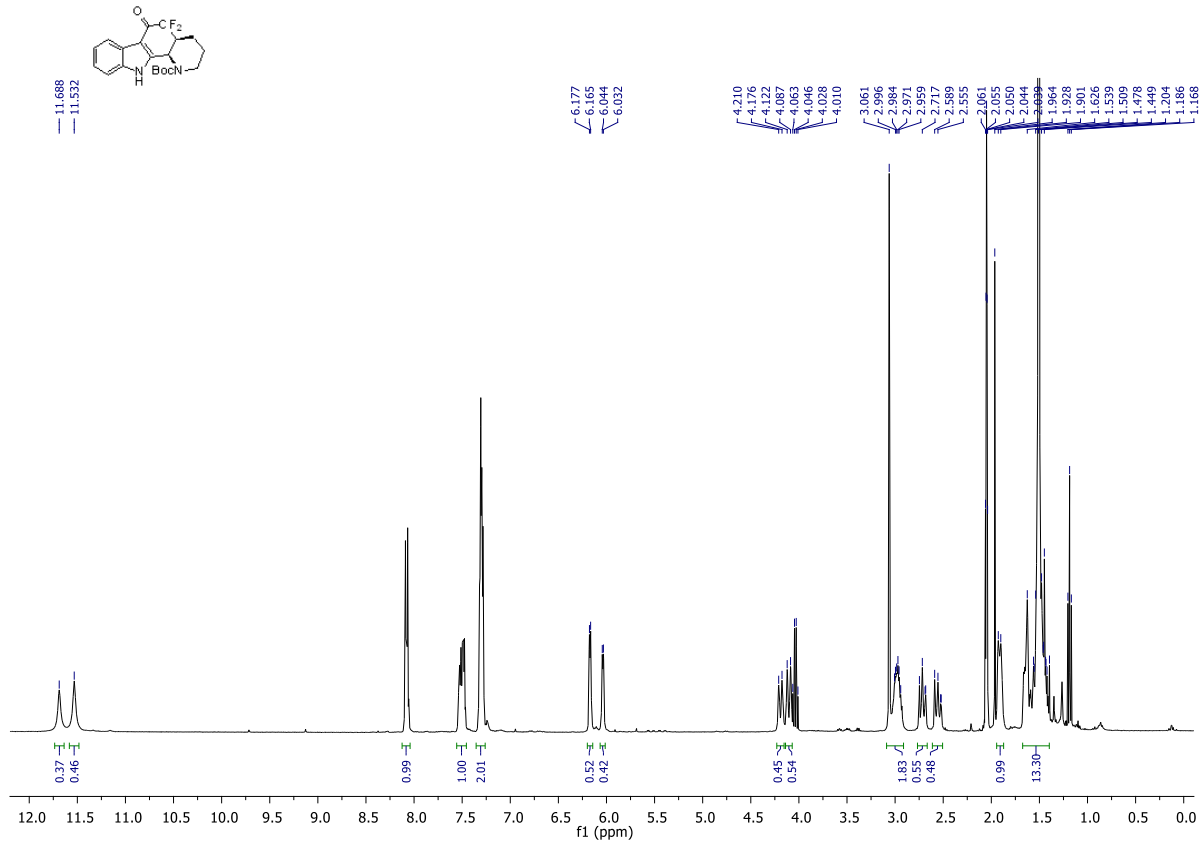

-62.284
-62.507
-72.307
-72.313
-77.050
-87.569
-92.207
-92.211
-92.256
-92.260
-93.200
-93.205
-93.249
-93.254
-117.359
-117.375
-118.352
-118.368
51.72
55.32
52.05
47.76
1.00
0.88
0.95
0.42
f1 (ppm)

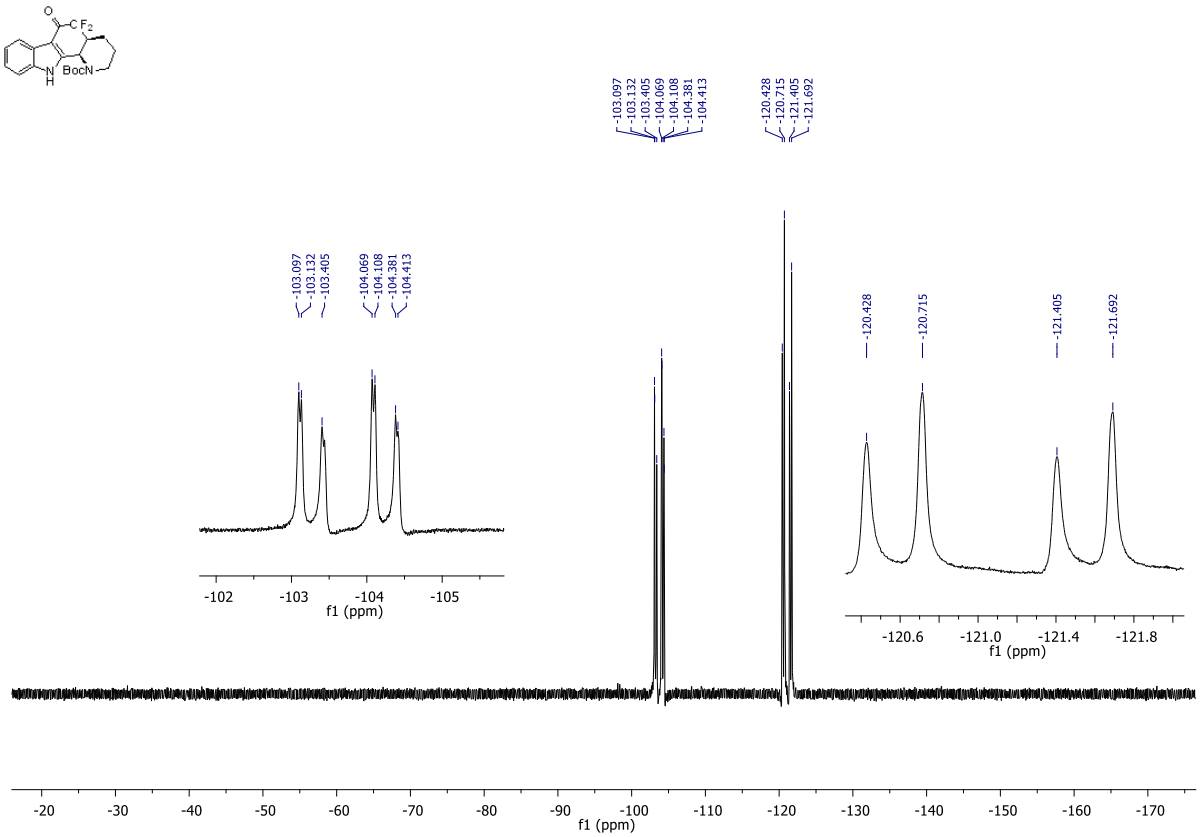

177.492
177.238
176.985
149.060
137.437
123.964
123.274
122.600
120.454
117.492
115.085
114.987
113.285
112.580
108.368
108.337
80.129
45.933
45.240
39.729
39.520
27.875
27.773
27.280
24.670
23.991
f1 (ppm)

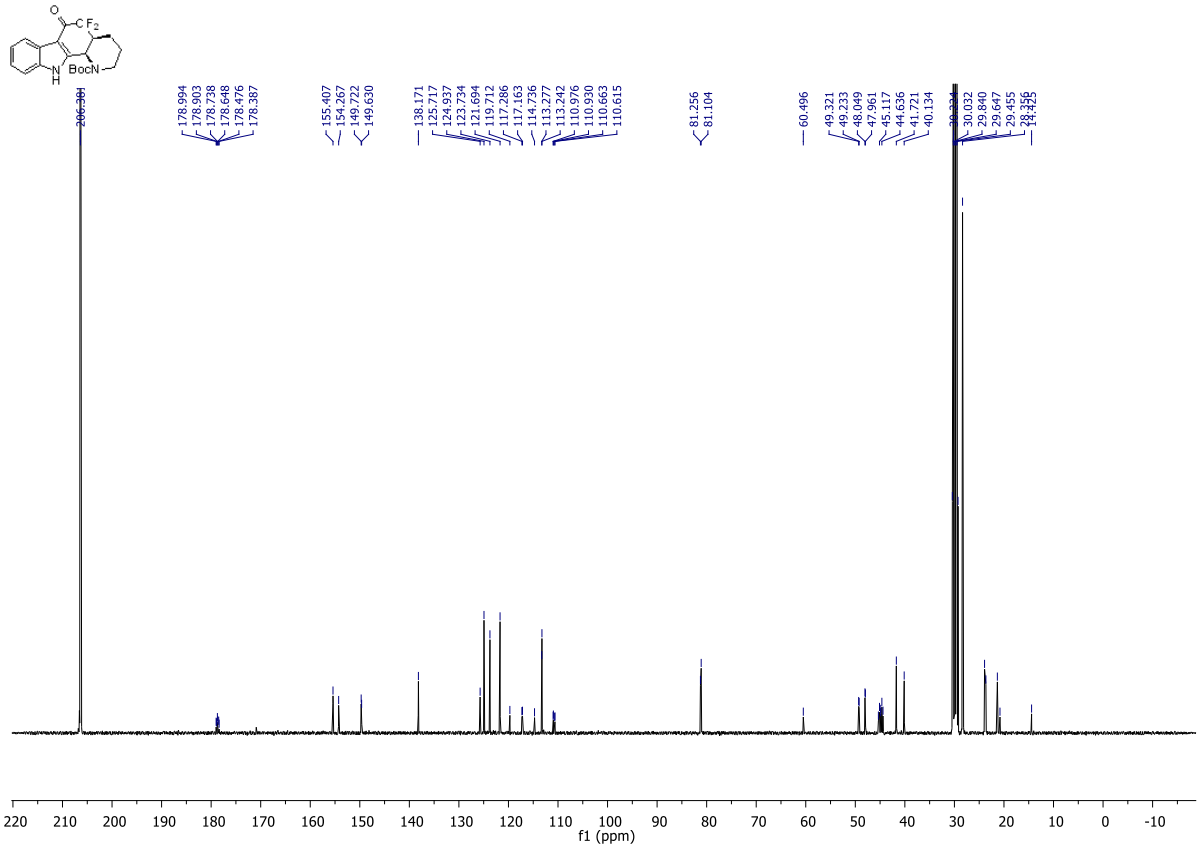
DEPT


123.86
122.51
120.156
113.173
45.837
45.141
27.847
27.720
27.668
27.174
23.886
f1 (ppm)

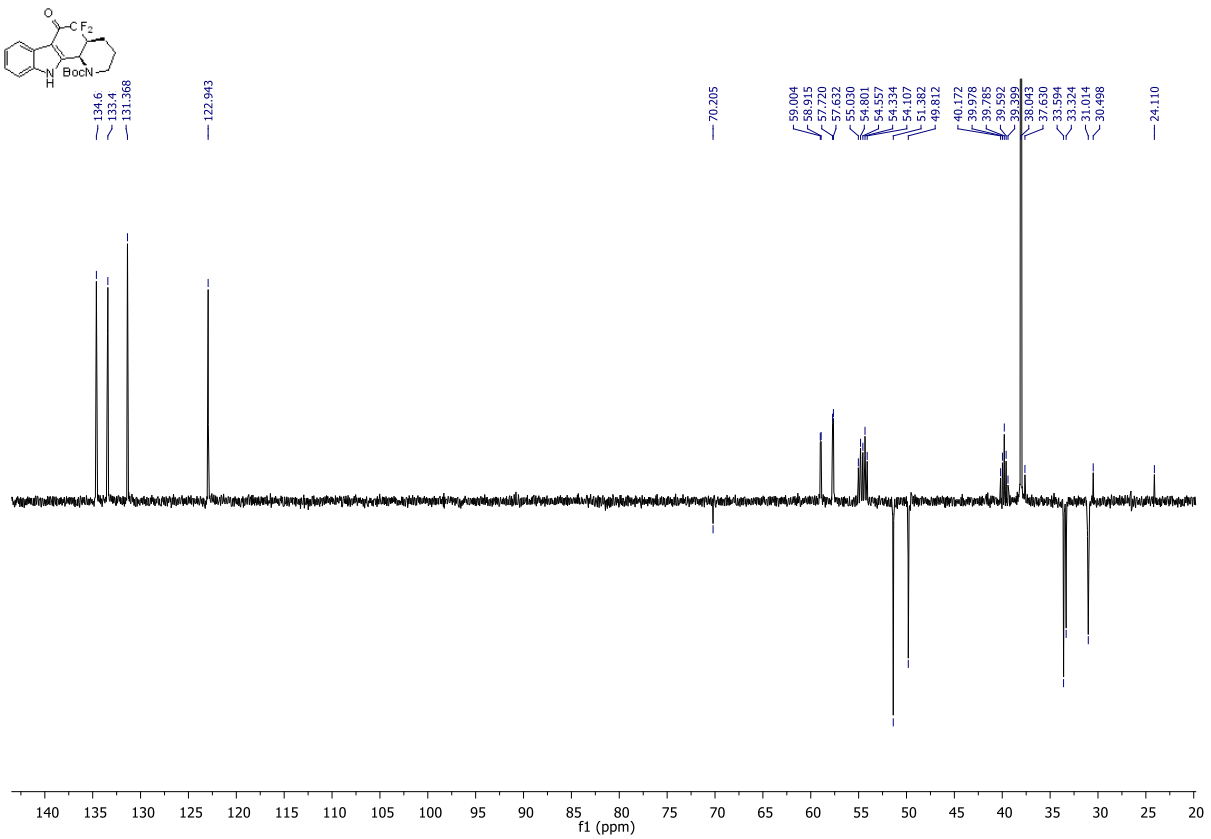
3ee

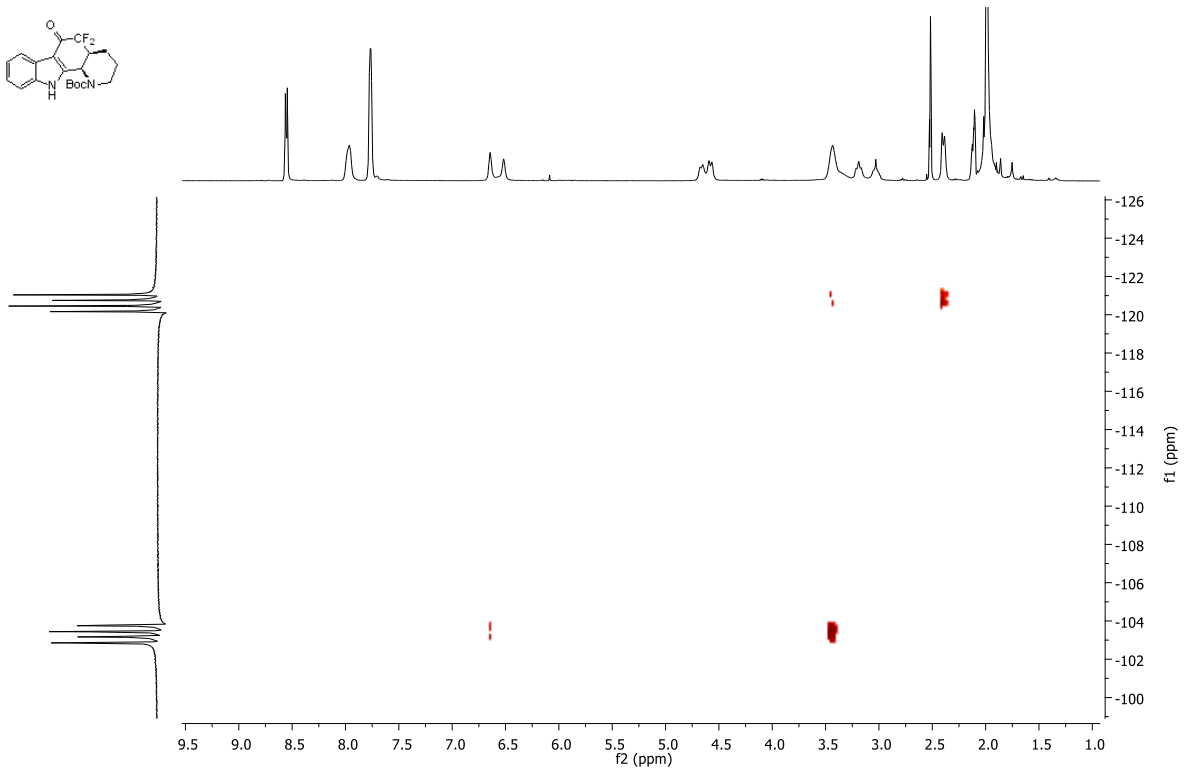

11.688
11.532
6.177
6.165
6.044
6.032
4.210
4.176
4.122
4.087
4.063
4.046
4.028
4.010
3.061
2.996
2.984
2.971
2.959
2.717
2.589
2.555
2.061
2.055
2.050
2.044
1.964
1.928
1.901
1.626
1.539
1.509
1.478
1.449
1.204
1.186
1.168
0.37
0.46
0.99
1.00
2.01
0.52
0.42
0.45
0.54
1.83
0.55
0.48
0.99
13.30
f1 (ppm)


-103.097
-103.132
-103.405
-104.069
-104.108
-104.381
-104.413
-120.428
-120.715
-121.405
-121.692
f1 (ppm)

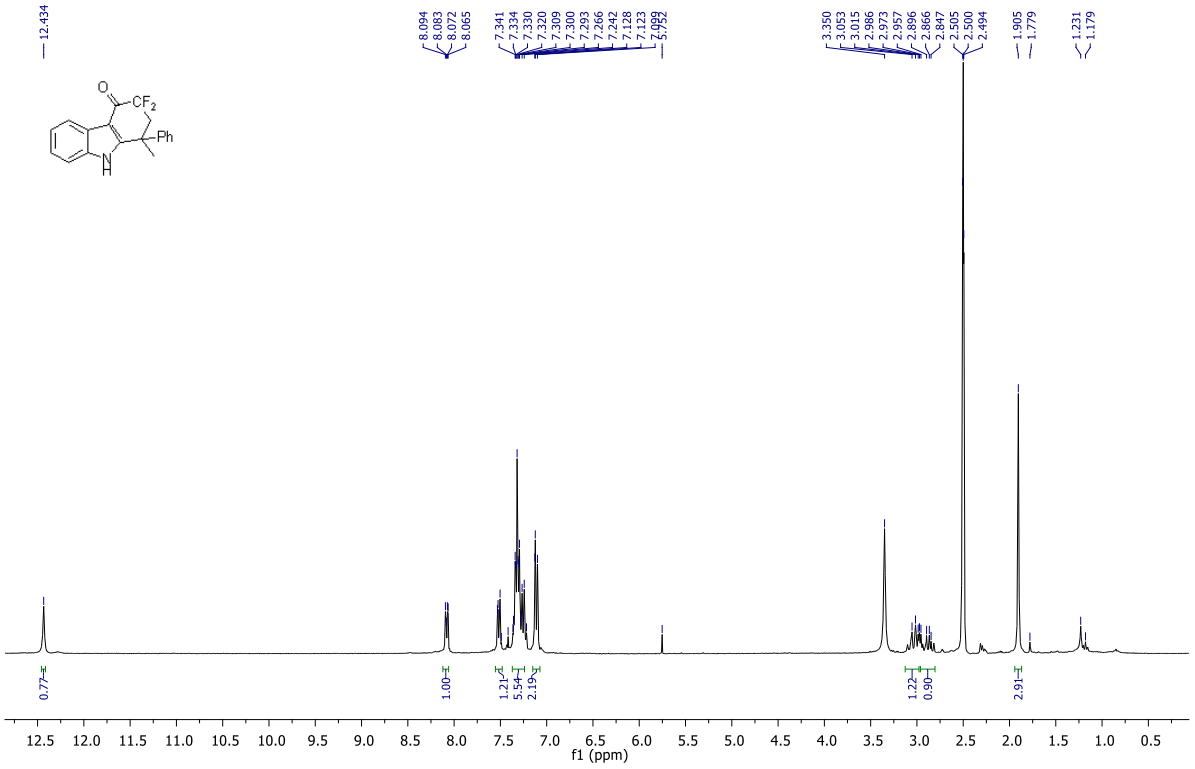

178.994
178.903
178.738
178.648
178.476
178.387
155.407
154.267
149.722
149.630
138.171
125.717
124.937
123.734
121.694
119.712
117.286
117.163
114.736
113.277
113.242
110.976
110.930
110.663
110.615
81.256
81.104
60.496
49.321
49.233
48.049
47.961
45.117
44.636
41.721
40.134
30.032
29.840
29.647
29.455
28.356
14.425
f1 (ppm)

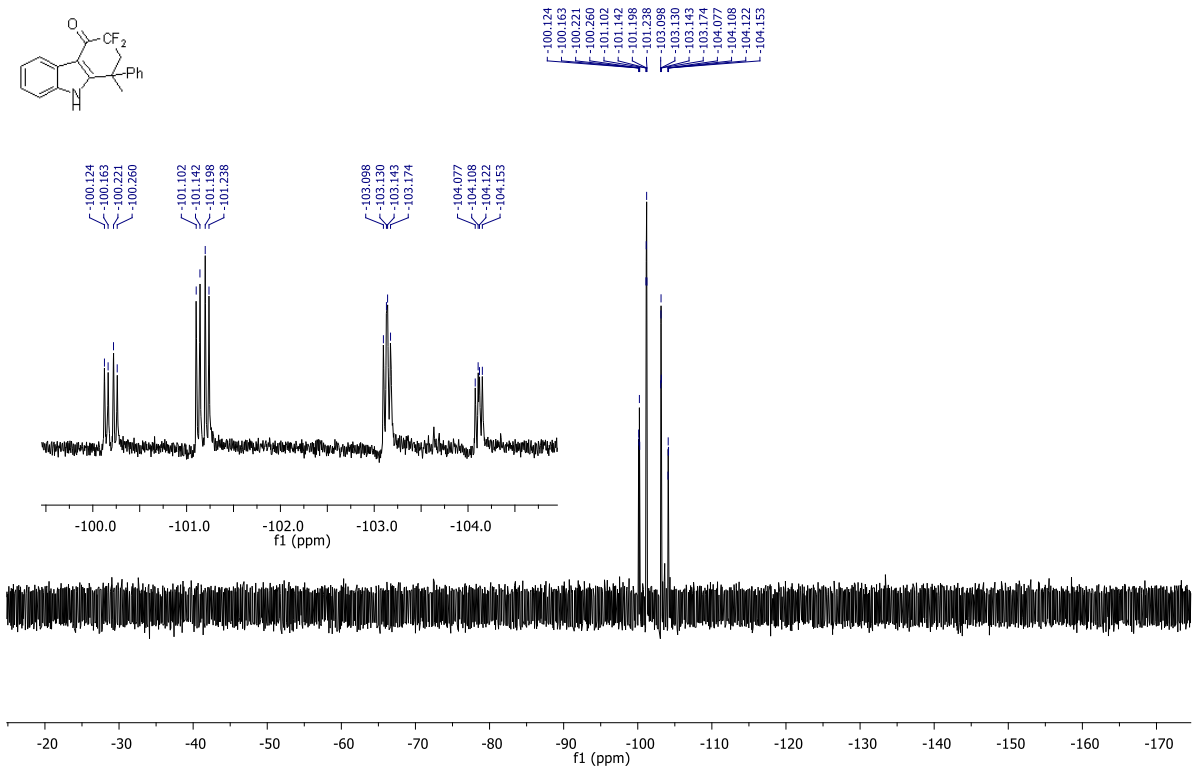
DEPT

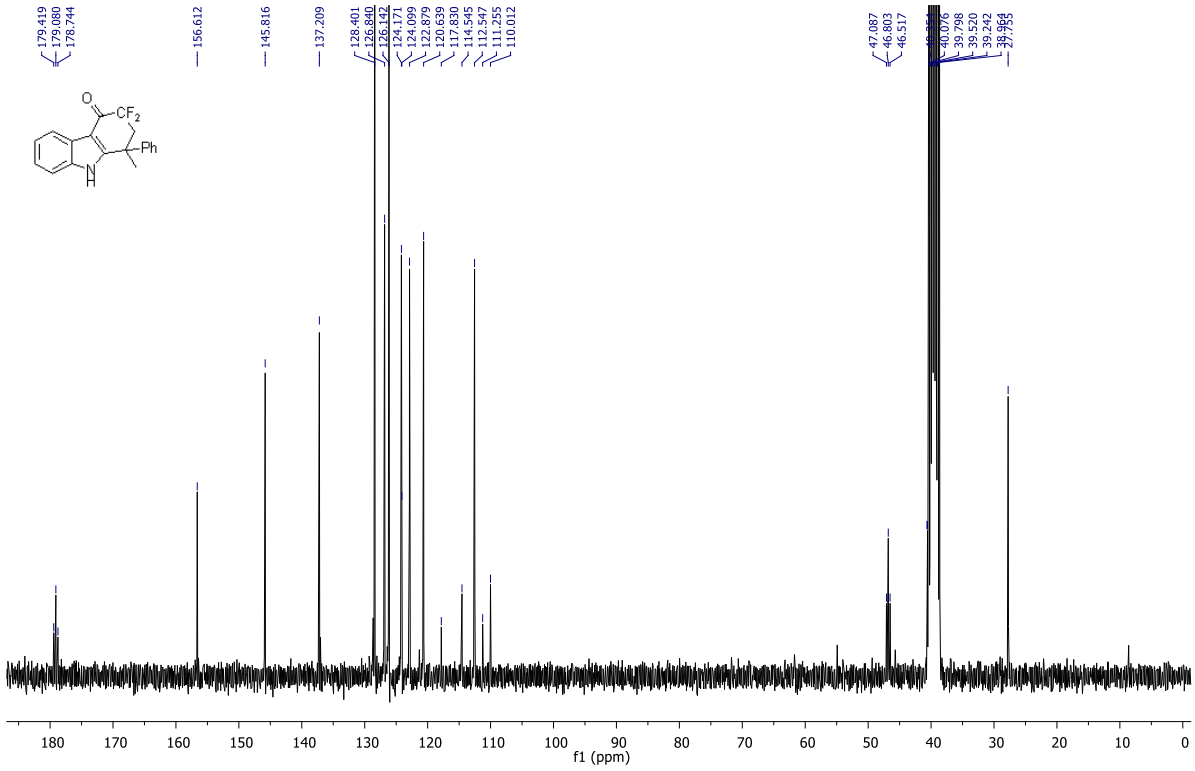

O
CF2
BocN
H
134.6
133.4
131.368
122.943
70.205
59.004
58.915
57.720
57.632
55.030
54.801
54.557
54.334
54.107
51.382
49.812
40.172
39.978
39.785
39.592
39.399
38.043
37.630
33.594
33.324
31.014
30.498
24.110
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)


O
CF2
BocN
H
-126
-124
-122
-120
-118
-116
-114
-112
-110
-108
-106
-104
-102
-100
f1 (ppm)
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
f2 (ppm)

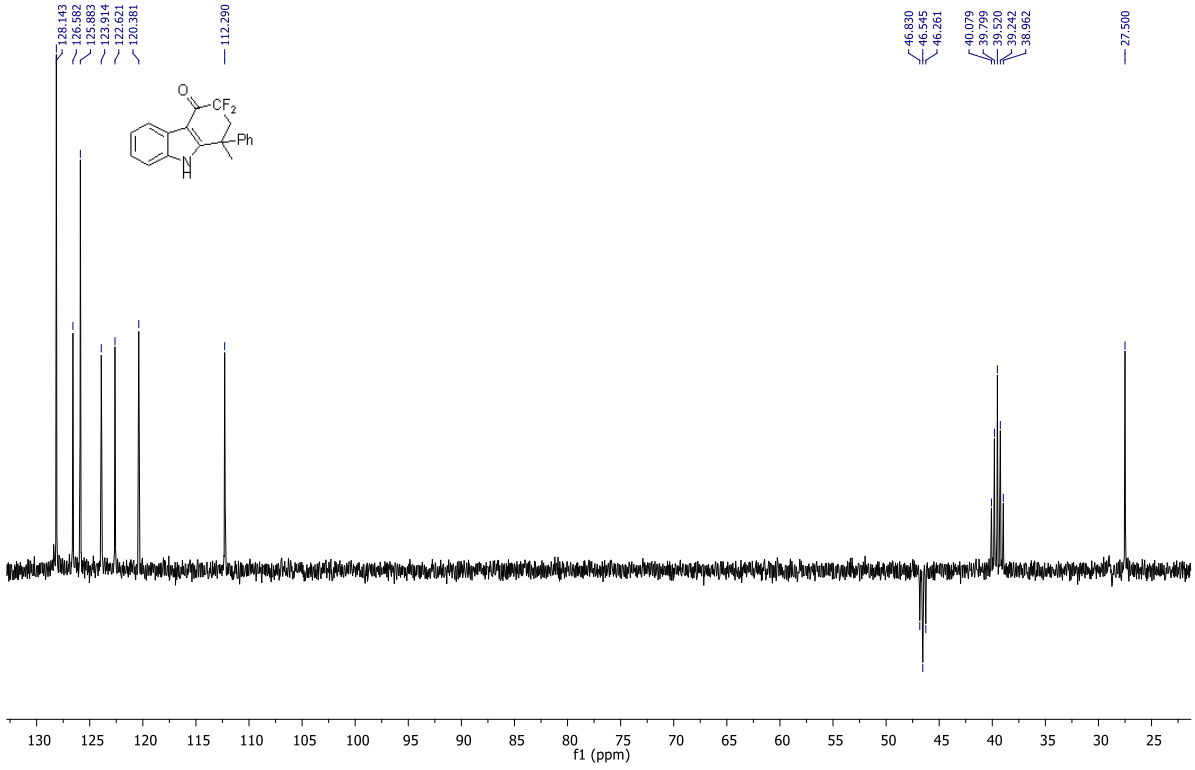
3eg


12.434
8.094
8.083
8.072
8.065
7.341
7.334
7.330
7.320
7.309
7.300
7.293
7.266
7.242
7.128
7.123
7.099
5.752
3.350
3.055
3.015
2.986
2.973
2.957
2.896
2.866
2.847
2.505
2.500
2.494
1.905
1.779
1.231
1.179
O
CF2
Ph
N
H
0.77
1.00
1.21
5.54
2.19
1.22
0.90
2.91
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

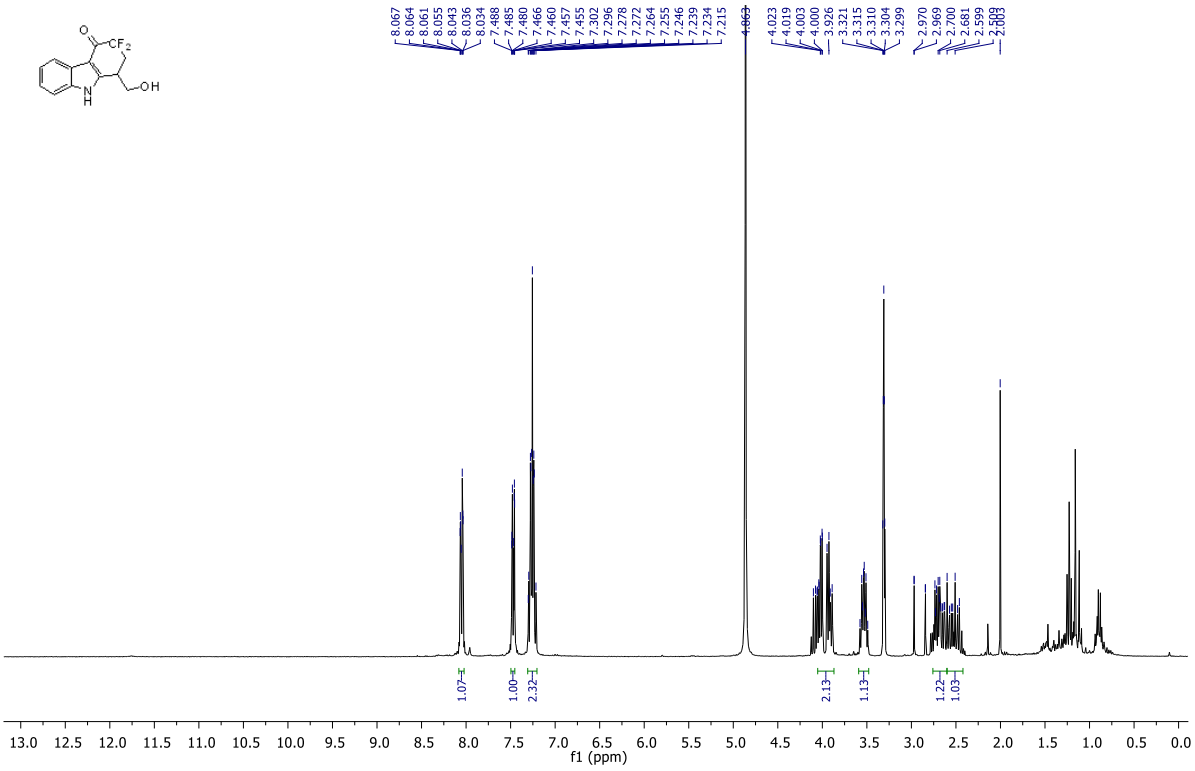

O
CF2
Ph
N
H
-100.124
-100.163
-100.221
-100.260
-101.102
-101.142
-101.198
-101.238
-103.098
-103.130
-103.143
-103.174
-104.077
-104.108
-104.122
-104.153
-100.0 -101.0 -102.0 -103.0 -104.0
f1 (ppm)
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170
f1 (ppm)

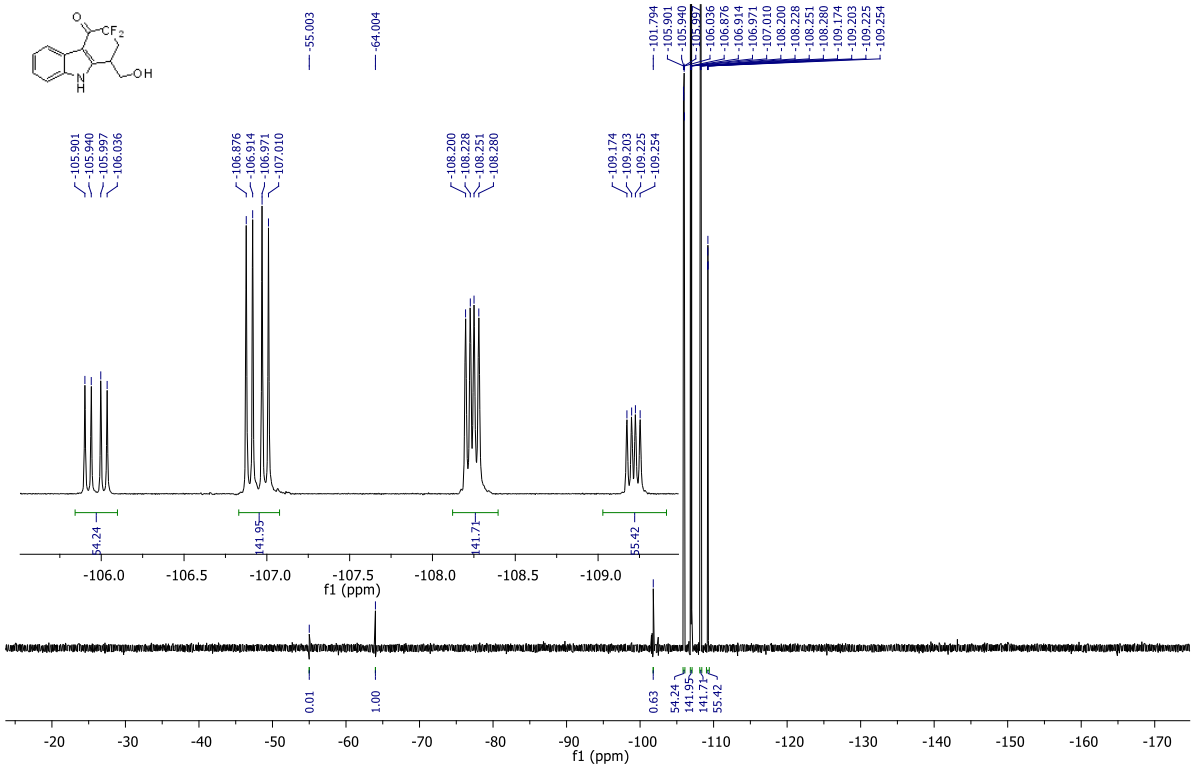

179.419
179.080
178.744
156.612
145.816
137.209
128.401
126.840
126.142
124.171
124.099
122.879
120.639
117.830
114.545
112.547
111.255
110.012
47.087
46.803
46.517
40.076
39.798
39.520
39.242
38.964
27.755
O
CF2
Ph
N
H
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

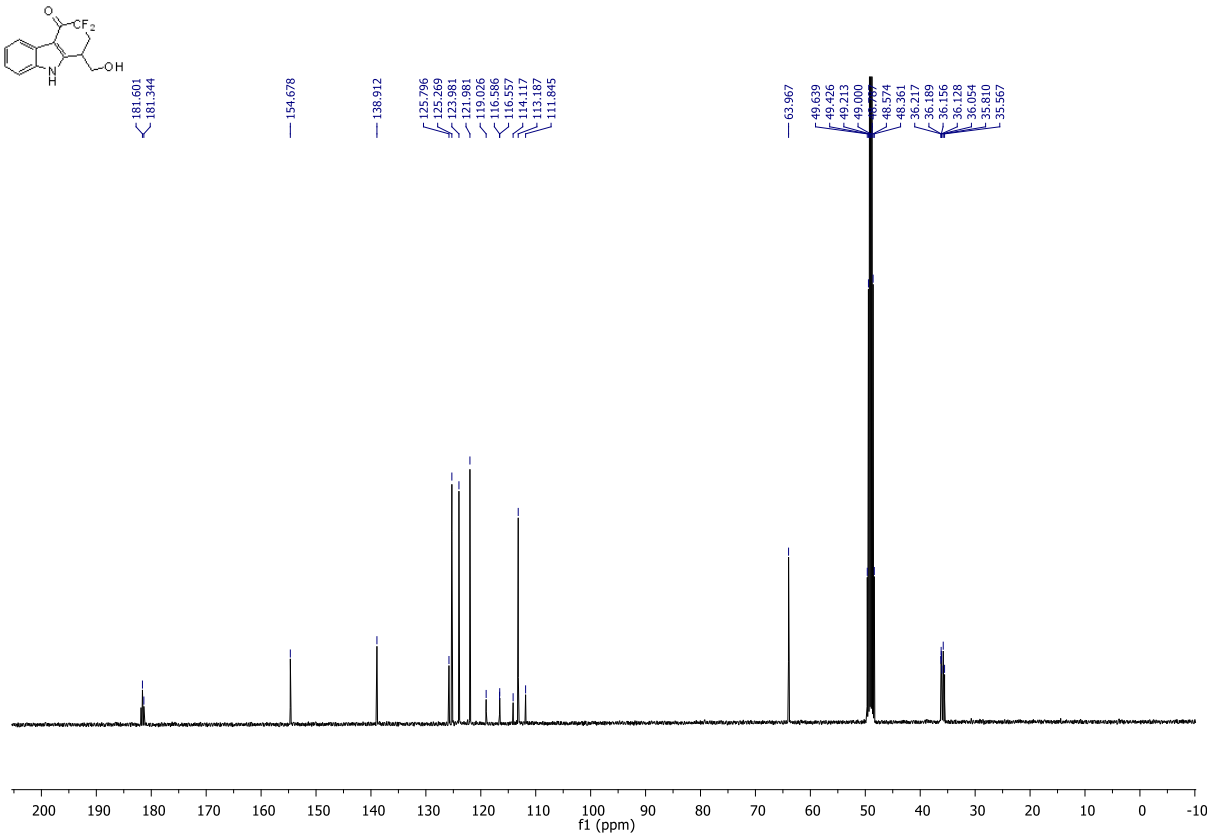
DEPT


128.143
126.582
125.883
123.914
122.621
120.381
112.290
46.830
46.545
46.261
40.079
39.799
39.520
39.242
38.962
27.500
O
CF2
Ph
N
H
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
f1 (ppm)

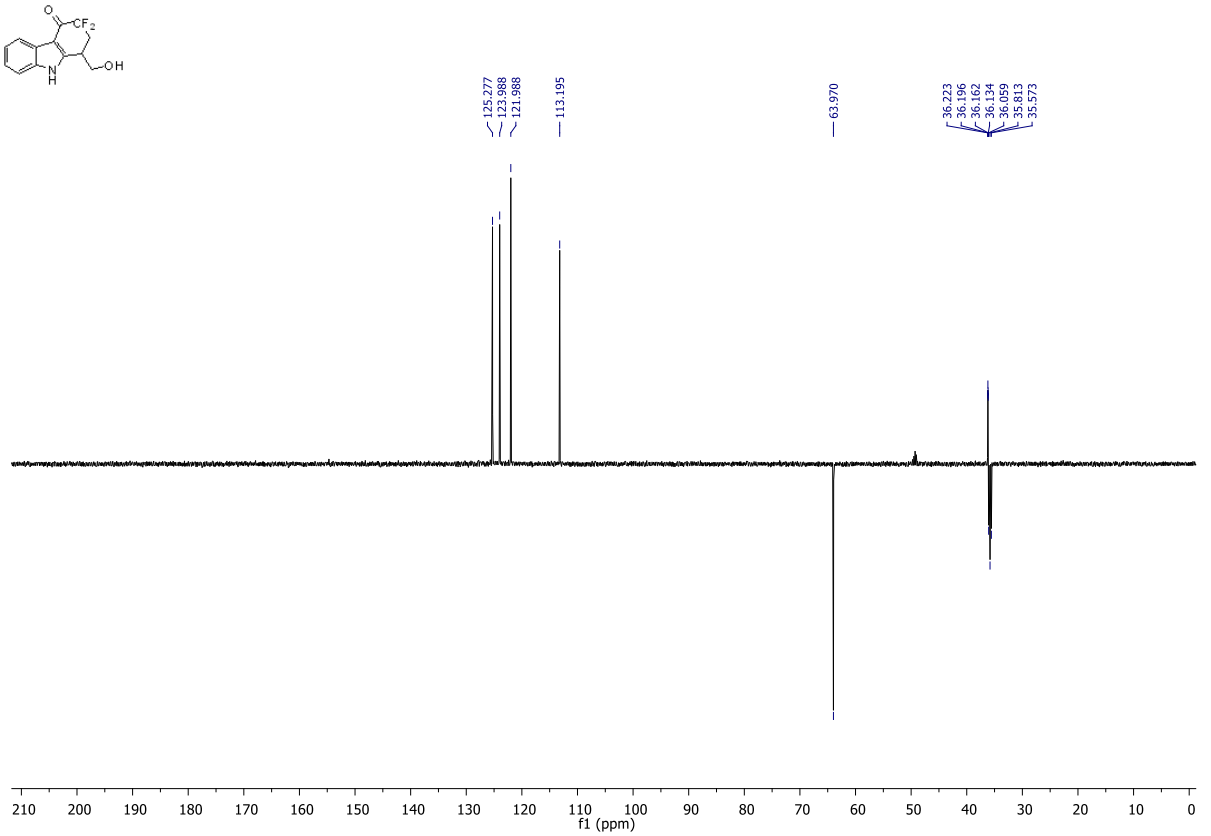
3eh


f1 (ppm)


f1 (ppm)


O
CF2
OH
N
H
181.601
181.344
154.678
138.912
125.796
125.269
123.981
121.981
119.026
116.586
116.557
114.117
113.187
111.845
63.967
49.639
49.426
49.213
49.000
48.787
48.574
48.361
36.217
36.189
36.156
36.128
36.054
35.810
35.567
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

DEPT


O
CF2
OH
N
H
125.277
123.988
121.988
113.195
63.970
36.223
36.196
36.162
36.134
36.059
35.813
35.573
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

X-Ray Diffraction Characterizations

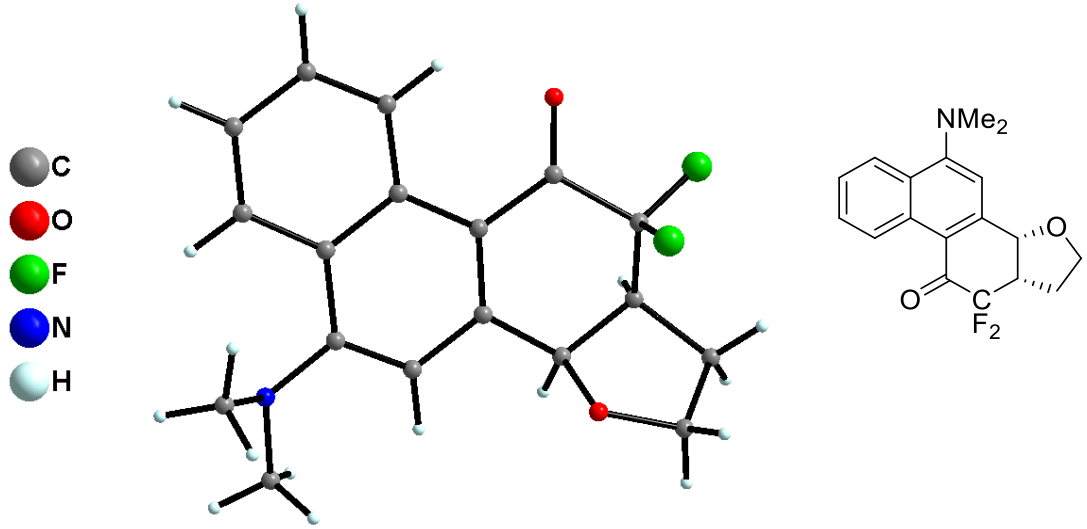
The single-crystal XRD studies of **3aa** and **3eb** were performed with a Gemini diffractometer and the related analysis software.[5] An absorption correction based on the crystal faces was applied to the data set analytical.[6] The structures were solved by direct methods with the SIR97 program[7] combined with Fourier difference syntheses and refined against *F* for reflections with [$I/\sigma(I) > 3$] with the CRYSTALS program.[8] All atomic displacement parameters for non-hydrogen atoms were refined with anisotropic terms. The hydrogen atoms were located theoretically based on the conformation of the supporting atom and refined by using a riding model.

CCDC 1522232 and 1522233 for **3aa** and **3eb**, respectively, contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

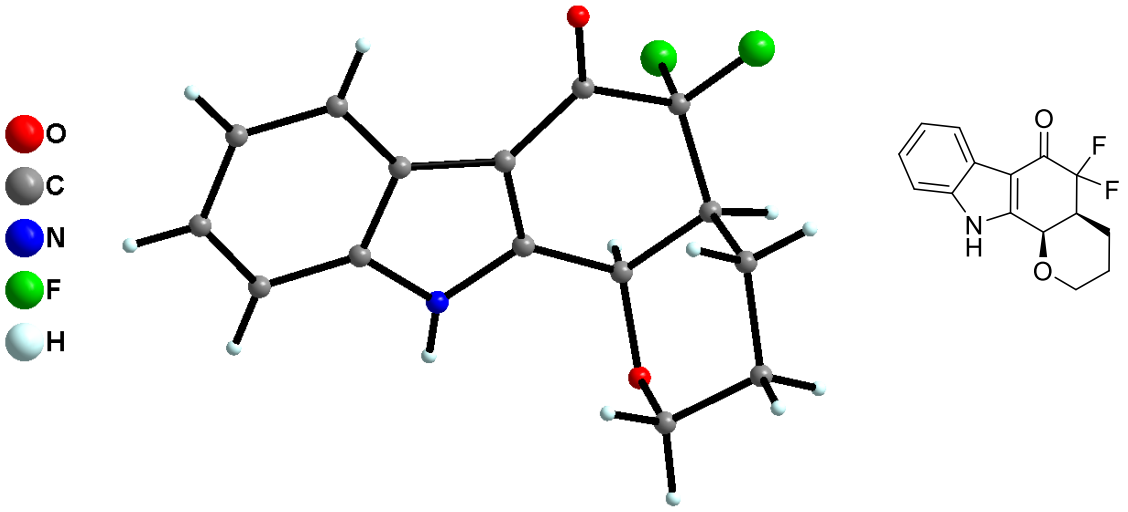
	3aa	**3eb**
CCDC	1522232	1522233
Empirical formula	$C_{18}H_{17}F_2N_1O_2$	$C_{15}H_{13}F_2N_1O_2$
Formula weight ($g.mol^{-1}$)	317.3	277.3
T (K)	293	293
Cyrstal system	monoclinic	triclinic
Space group	$P2_1/c$	P-1
a (Å)	16.129(2)	7.4538(9)
b (Å)	11.1367(9)	9.224(2)
c (Å)	8.7194(9)	10.116(2)
α (°)	90	72.85(2)
β (°)	104.776(8)	78.35(2)
γ (°)	90	73.76(2)
V ($Å^3$)	1514.4(2)	632.6(2)
Z	4	2
Crystal shape	needle	needle
Crystal colour	colorless	colorless
Crystal size (mm^3)	0.048×0.075×0.544	0.034×0.061×0.403
Density (calculated)	1.403	1.455
μ (mm^{-1})	0.108	0.116
F(000)	664	288
θ range (°)	3.04- 29.38	2.76-29.33
Index range	$-21 \le h \le 20$	$-9 \le h \le 9$
	$0 \le k \le 14$	$-11 \le k \le 11$
	$0 \le l \le 12$	$0 \le l \le 13$
Reflns collected / unique [R_{int}]	7530 / 3512 [0.035]	5792 / 2928 [0.069]
Data / restraints / parameters	1474 / 0 / 208	960 / 0 / 181
R / R_w	0.0470 / 0.0532	0.0562 / 0.0475
S	1.12	1.12

[5] CrysAlisPro, v. 1.171.33.46 (rel. 27-08-2009 CrysAlis171.NET), Oxford Diffraction Ltd., **2009**
[6] J. de Meulenaar, H. Tompa, *Acta Crystallogr*. **1965**, 19, 1014–1018.
[7] G. Cascarano, A. Altomare, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, D. Siliqi, M. C. Burla, G. Polidori, M. Camalli, *Acta Crystallogr., Sect. A* **1996**, 52, C-79.
[8] D. J. Watkin, C. K. Prout, J. R. Carruthers, P. W. Betteridge, CRYSTALS Issue 11, Chemical Crystallography Laboratory, Oxford, UK, **1999**.

$\Delta\rho_{max}$ / $\Delta\rho_{min}$ ($e^{-}.Å^{-3}$)	0.22 / -0.24	0.26 / -0.32
Absorption correction	analytical	analytical



Crystal structure of **3aa** molecule.



Crystal structure of **3eb** molecule.