Supporting Information

Photoredox-catalysed radical difluoromethylation/cyclization of *N*-acryloyl-2-arylbenzimidazole to access CF_2H-substituted benzimidazo[2,1-*a*]isoquinolin-6(5*H*)-ones

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1. Experimental section

1.1 General information

All chemicals were commercially available and used as received without further purification. Column chromatography was performed using 300-400 mesh silica. Nuclear magnetic resonance spectra were recorded on Bruker Avance 400 MHz and 500 MHz spectrometer. ^{1}H NMR spectra are recorded in parts per million from tetramethylsilane. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and br = broad), coupling constant in Hz and integration. ^{13}C NMR spectra were recorded in parts per million from tetramethylsilane. ^{19}F NMR spectra were recorded in parts per million with fluorobenzene as external standard. High resolution mass spectra (HR MS) were performed using an Agilent 6546 LC/Q-TOF mass spectrometer operated in positive ion mode. IR spectra were recorded on WQF-510 Fourier transform infrared spectrophotometer.

1.2 The spectrum of our lamp and the visible-light irradiation instrument

Photochemical reaction was carried out under visible light irradiation by a blue LED at 25 ^{o}C. RLH-18 8-position Photo Reaction System manufactured by Beijing Roger Tech Ltd. was used in this system. Eight 10 W blue LEDs were equipped in this Photo reactor. The blue LED's energy peak wavelength is 429 nm, peak width at half-height is 18.4 nm, irradiance@10 W is 236.28 mW/cm^{2}. The reaction vessel is a borosilicate glass test tube and the distance between it and the lamp is 15 mm, no filter applied.

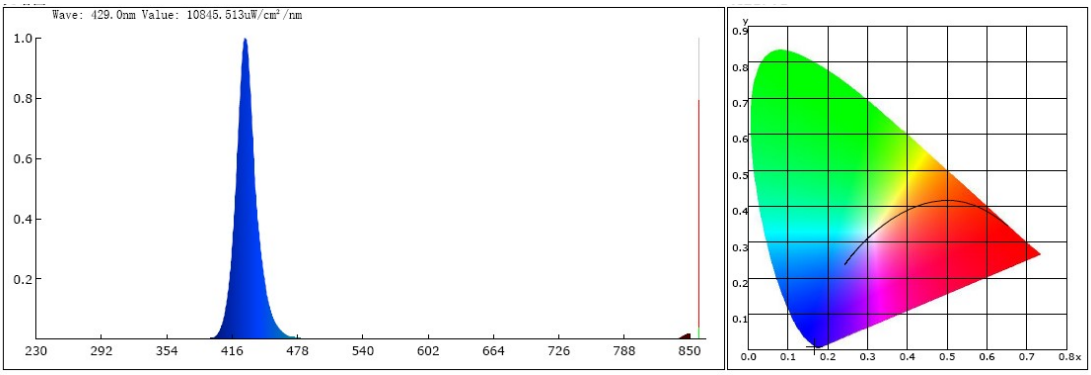
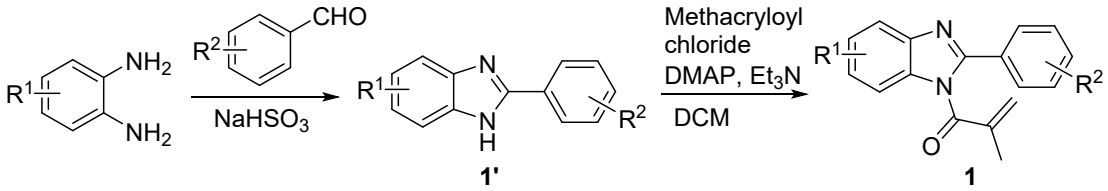


Figure S1 The spectrum of our lamp (blue LED)

Figure S2 The visible-light irradiation instrument

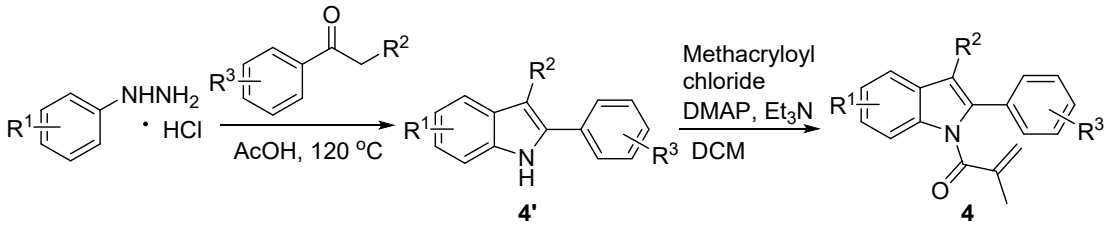
1.3 Synthesis *N*-methacryloyl-2-arylbenzo[*d*]imidazole derivatives 1[1]



In a round-bottomed flask (50 mL) equipped with a magnetic stirrer, a mixture of benzaldehyde (5.0 mmol, 578 µL) and $NaHSO_3$ (11.0 eq, 5.73 g) in H_2O (20.0 mL) was prepared. When the mixture reached refluxing temperature, substituted *o*-phenylenediamine (5.0 mmol, 541 mg) was added. The resulting mixture was stirred for appropriate time. After completion of the reaction, the reaction mixture was vacuum filtered after cooling to room temperature by a glass funnel. The residues were washed by water (20 mL × 2), dried in air dry oven to give the corresponding products **1′**.

To the solution of substituted 2-aryl-benzo[d]imidazoles (3 mmol) and DMAP (0.6 mmol, 73 mg) in DCM (0.5 M) was added Et_3N (6 mmol, 834 µL) at 0 °C. Then methacryloyl chloride (6 mmol, 624 mg) was added dropwise to the solution. The solution was warmed up to room temperature and stirred for 24-30 h. The reaction was complete according to TLC analysis, and water (20 mL) was added to the mixture, which was extracted with CH_2Cl_2 (15 mL × 3). The organic solvent was concentrated in vacuo. The residue was purified by flash column chromatography with Ethyl acetate and petroleum ether as eluent to give the products **1**.

1.4 Synthesis *N*-methacryloyl-2-aryl-1*H*-indole derivatives 4[2]

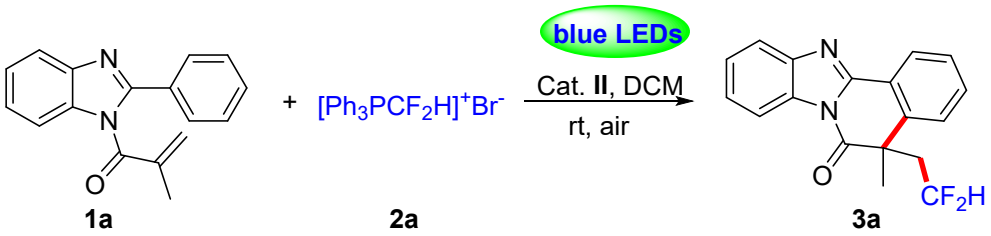


In a 100 mL flask was charged with phenylhydrazine or substituted phenylhydrazine hydrochloride (11.0 mmol, 1.1 equiv), ketone (10.0 mmol, 1.0 equiv) and acetic acid (10 mL, 1.0 M). After stirring for 12-24 h at 120 °C, AcOH was removed by rotory evaporation and the residue was portioned between saturated NaCl solution (50 mL) and EtOAc (20 mL). The aqueous layer was extracted with EtOAc (20 mL x 3), and the combined organic phase was washed with a saturated solution of brine (20 mL), the combined organic layer was dried over anhydrous Na_2SO_4, concentrated to afford the residue. The crude product was purified by column chromatography to afford the substituted indoles **4'**.

In a 100 mL flask was charged with substituted indole **4'** (5 mmol, 1.0 equiv) and DMAP (1.0 mmol, 0.2 equiv) in DCM (0.5 M). The solution was stirred at 0 °C, triethylamine (10 mmol, 2.0 equiv) and methacryloyl chloride (10 mmol, 2.0 equiv) was added. Then acyl chloride (10 mmol) was added dropwise to the solution. The solution was warmed up to room temperature and stirred for 24-30 h. The mixture was diluted with DCM (20 mL) and saturated NH_4Cl solution (20 mL). The organic and aqueous layers were separated. The aqueous layer was extracted with DCM (20 mL x 3). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by flash chromatography and then recrystallized from PE/EtOAc to afford the products **4**.

2. Mechanism study

2.1 Light on/off experiment



1a **2a** **3a**

To a mixture of *N*-acryloyl-2-arylbenzimidazole **1a** (0.2 mmol, 26.2 mg), N^1,N^1,N^4,N^4-tetraphenylnaphthalene-1,4-diamine (Cat. **II**, 0.01 mmol, 4.62 mg) in DCM (2.0 mL) was added $[Ph_3PCF_2H]^+Br^-$ **2a** (0.4 mmol, 156.8 mg). The reaction mixture was stirred under the irradiation of 10 W blue LEDs in air at room temperature and the reaction was placed in light and dark in every alternative 2 h. After the completion of the reaction, ethyl acetate (10 mL) was added to the reaction mixture, washed with saturated sodium chloride solution (10 mL × 2). The organic phase was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by flash column chromatography using ethyl acetate/ petroleum ether as eluent to give the desired product **3a**.

Entry	Time (h)	Light source	Yield (%)
1	2	on	32
2	2	off	32
3	2	on	60
4	2	off	60
5	2	on	92
6	2	off	92

2.2 The Stern-Volmer luminescence-quenching experiment

The fluorescence emission intensities were recorded on a F-7000 FL Spectrophotometer. The excitation wavelength was fixed at 456 nm, and the emission wavelength was measured at 400

nm (emission maximum). In a typical experiment, the emission spectrum of a 2.5 × 10^{-4} M solution of Cat. **II** with different concentration of **1a** and **2a** in degassed anhydrous CH_2Cl_2 and the linear relationship between I_0/I and the increasing concentration of **1a** and **2a** from 0 M to 2.5 × 10^{-2} M**.**

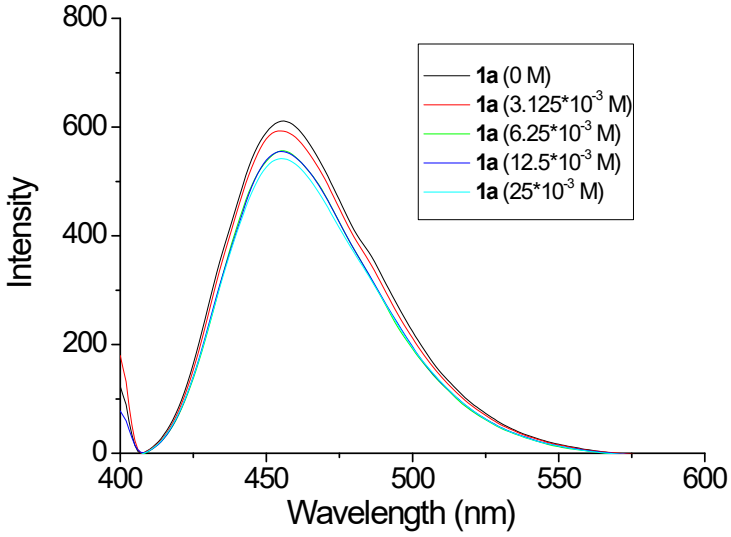


Fig. S3 The fluorescein with the difference concentration of **1a**

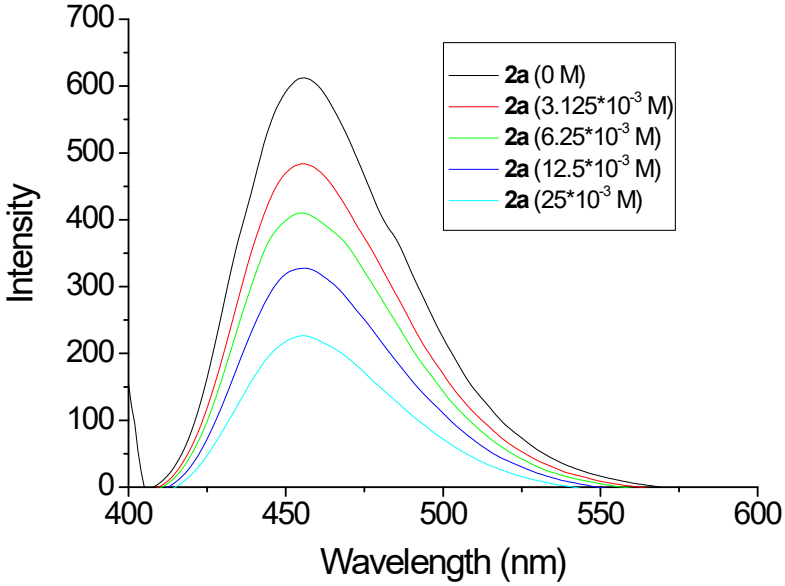


Fig. S4 The fluorescein with the difference concentration of **2a**

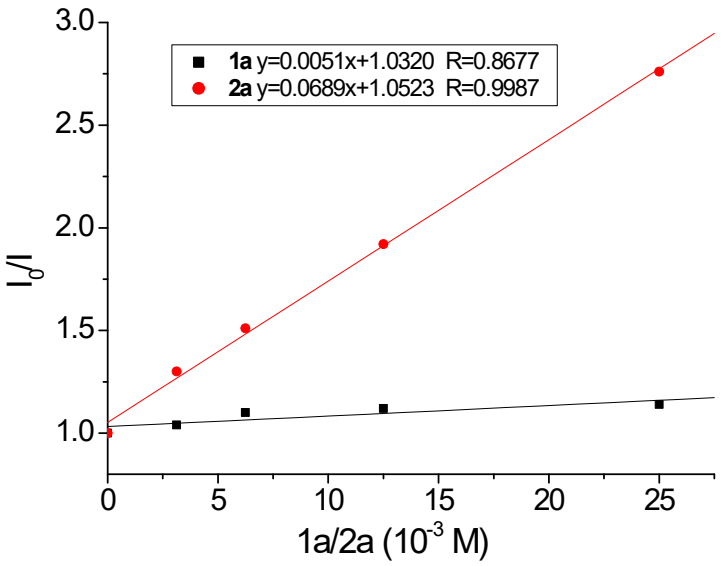


Fig. S5 Stern-Volmer luminescence-quenching experiment

2.2 HR MS spectrum of the adduct 6

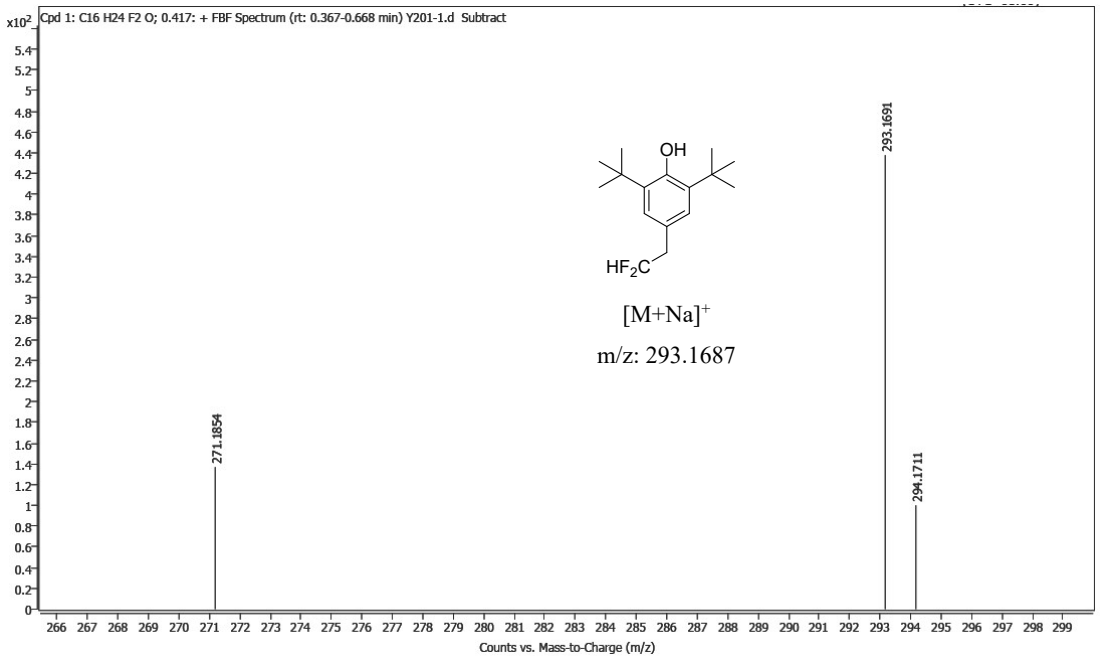


Fig. S6 HR MS spectrum of the BHT-CF_2H adduct **6**

2.3 HR MS spectrum of the adduct 7

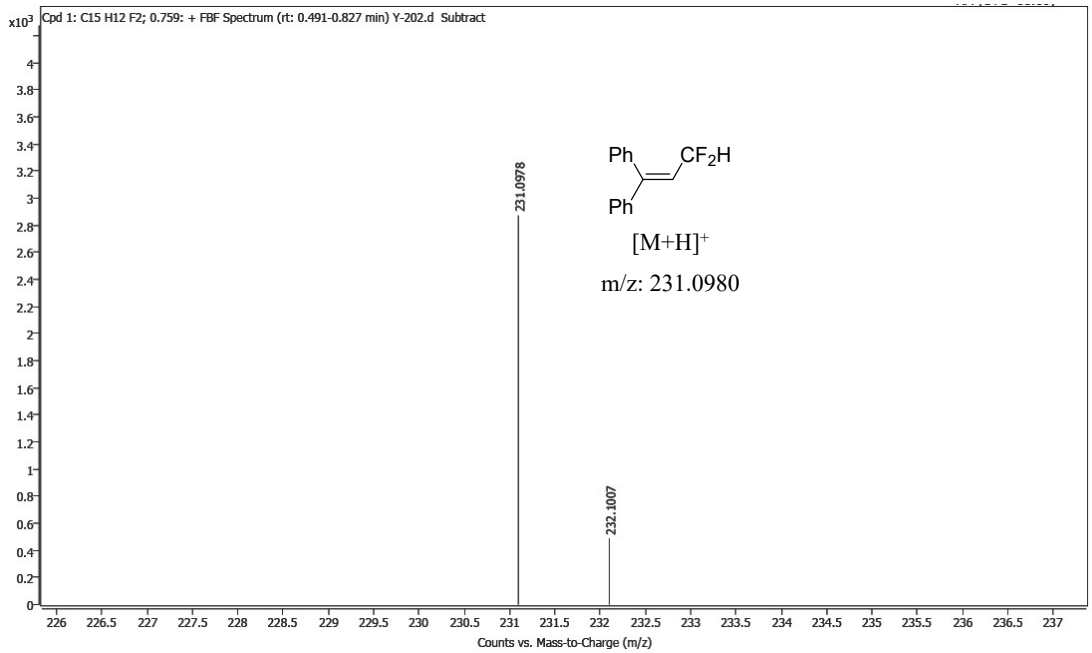


Fig. S7 HR MS spectrum of the DPE-CF_2H adduct **7**

3. Copies of spectra of products

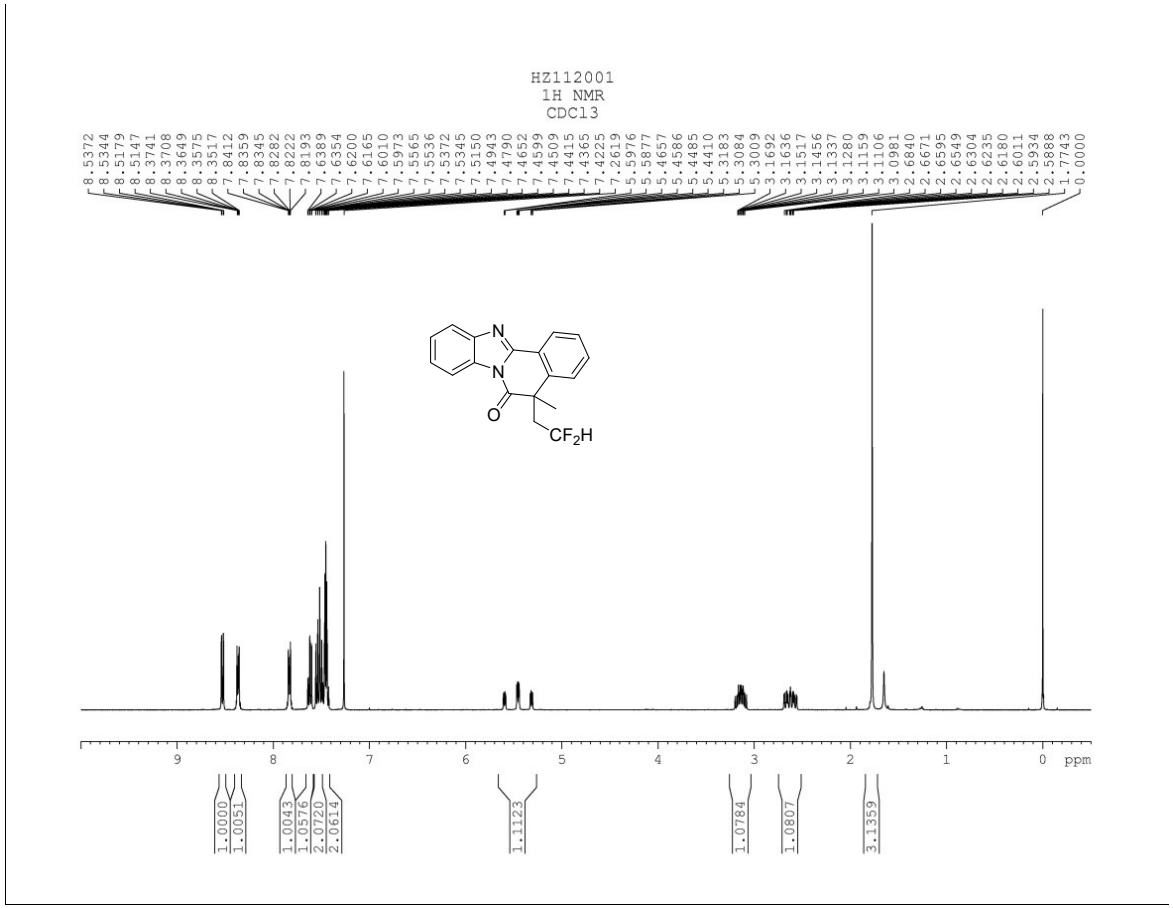


Fig. S8 ^{1}H NMR (400 MHz) spectrum of compound **3a**

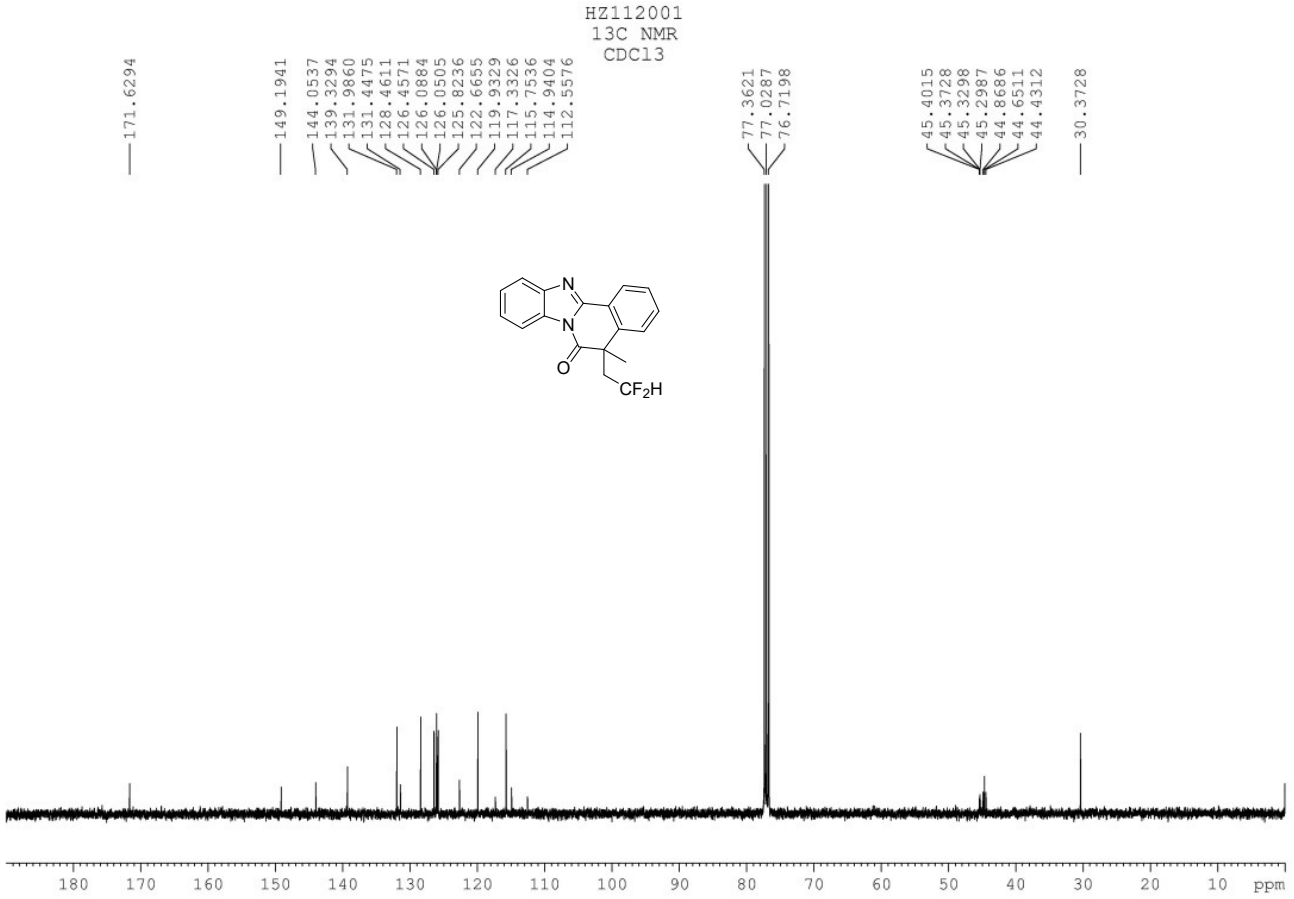


Fig. S9 ^{13}C NMR (101 MHz) spectrum of compound **3a**

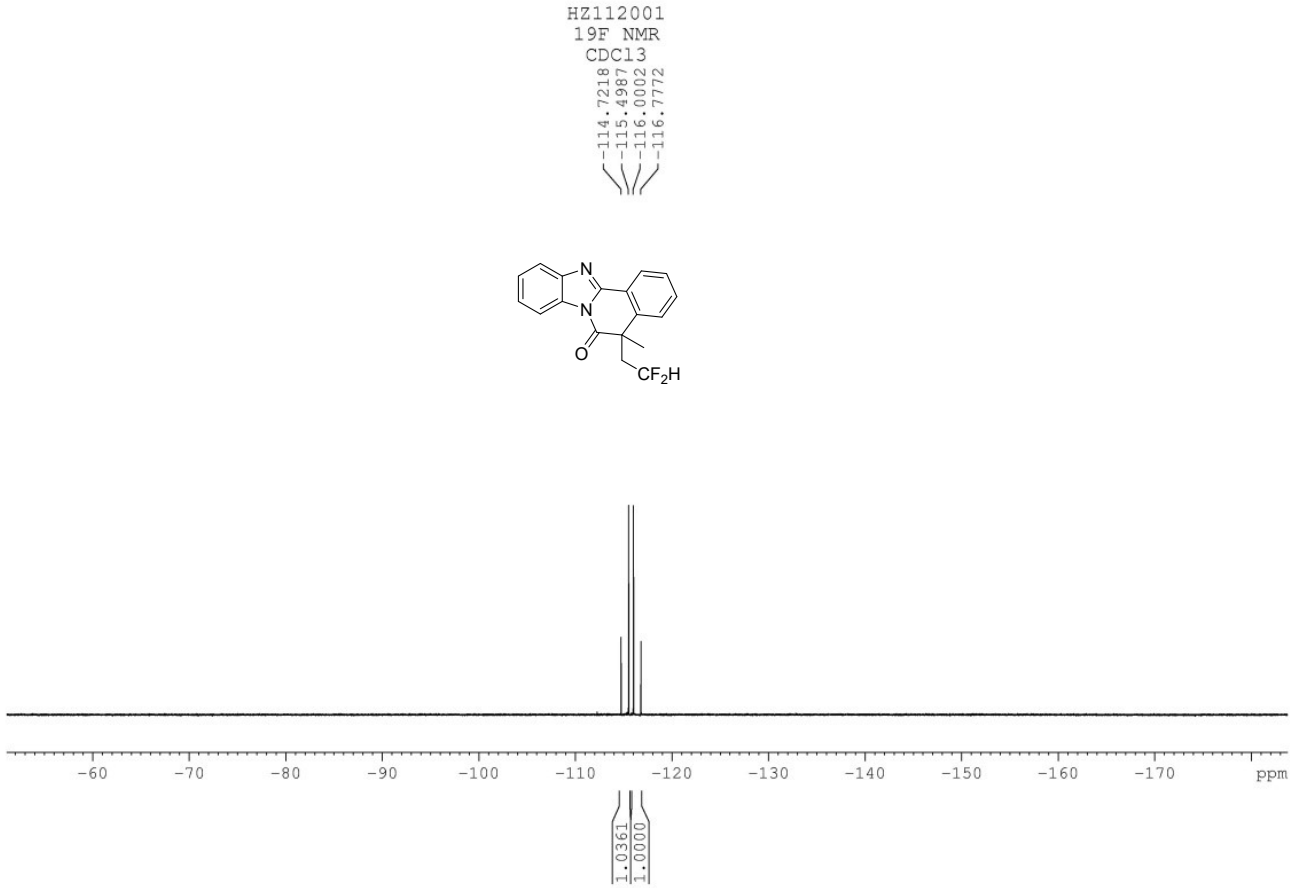


Fig. S10 ^{19}F NMR (376 MHz) spectrum of compound **3a**

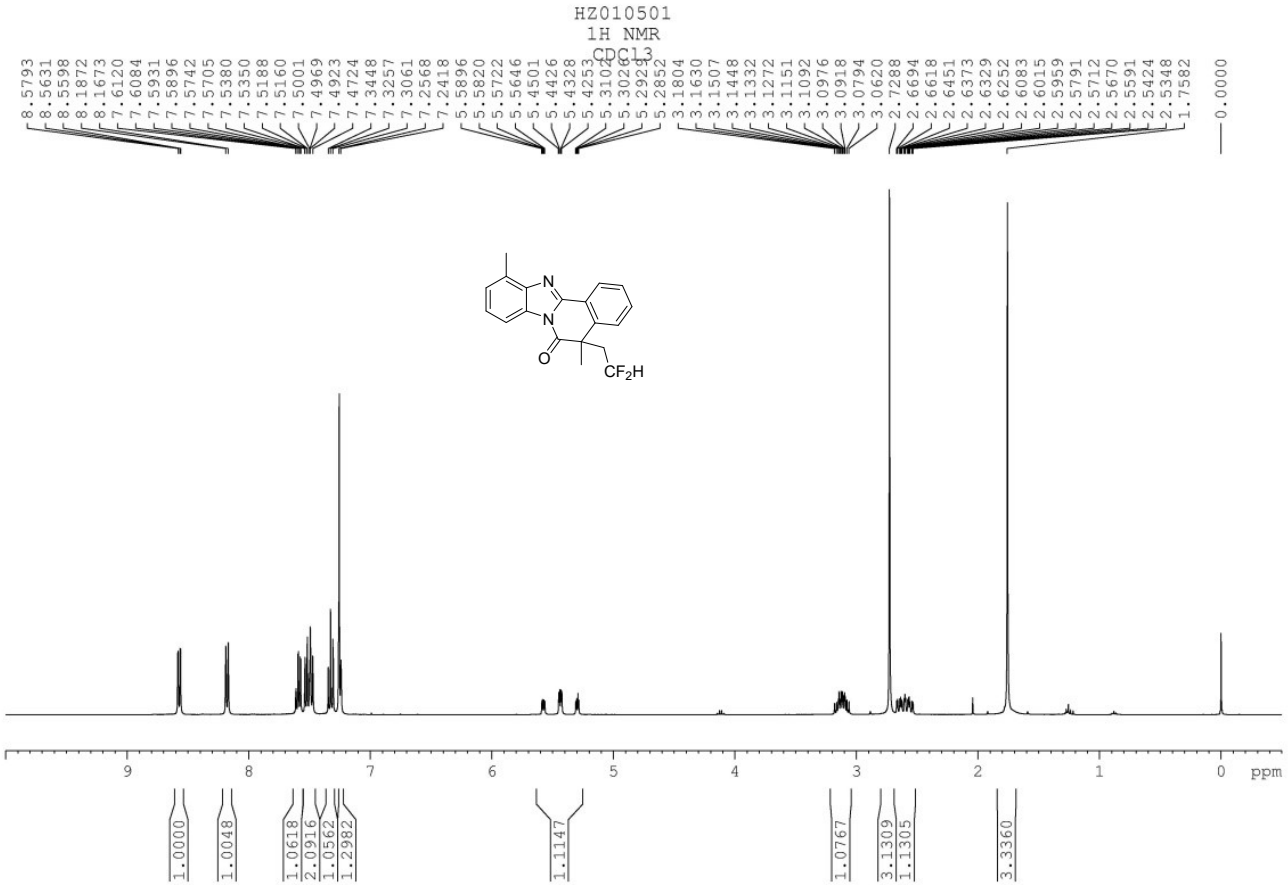


Fig. S11 ^{1}H NMR (400 MHz) spectrum of compound **3b**

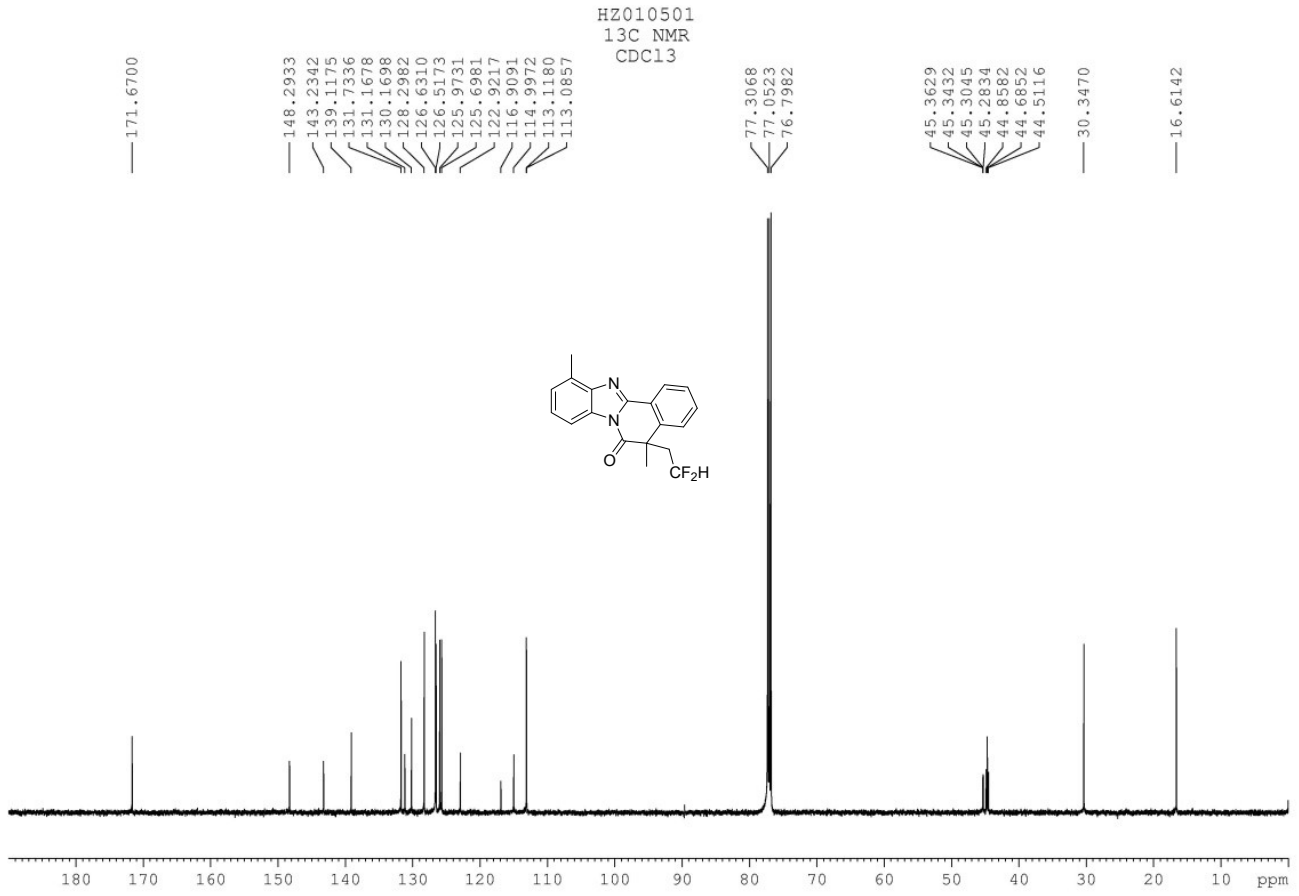


Fig. S12 ^{13}C NMR (125 MHz) spectrum of compound **3b**

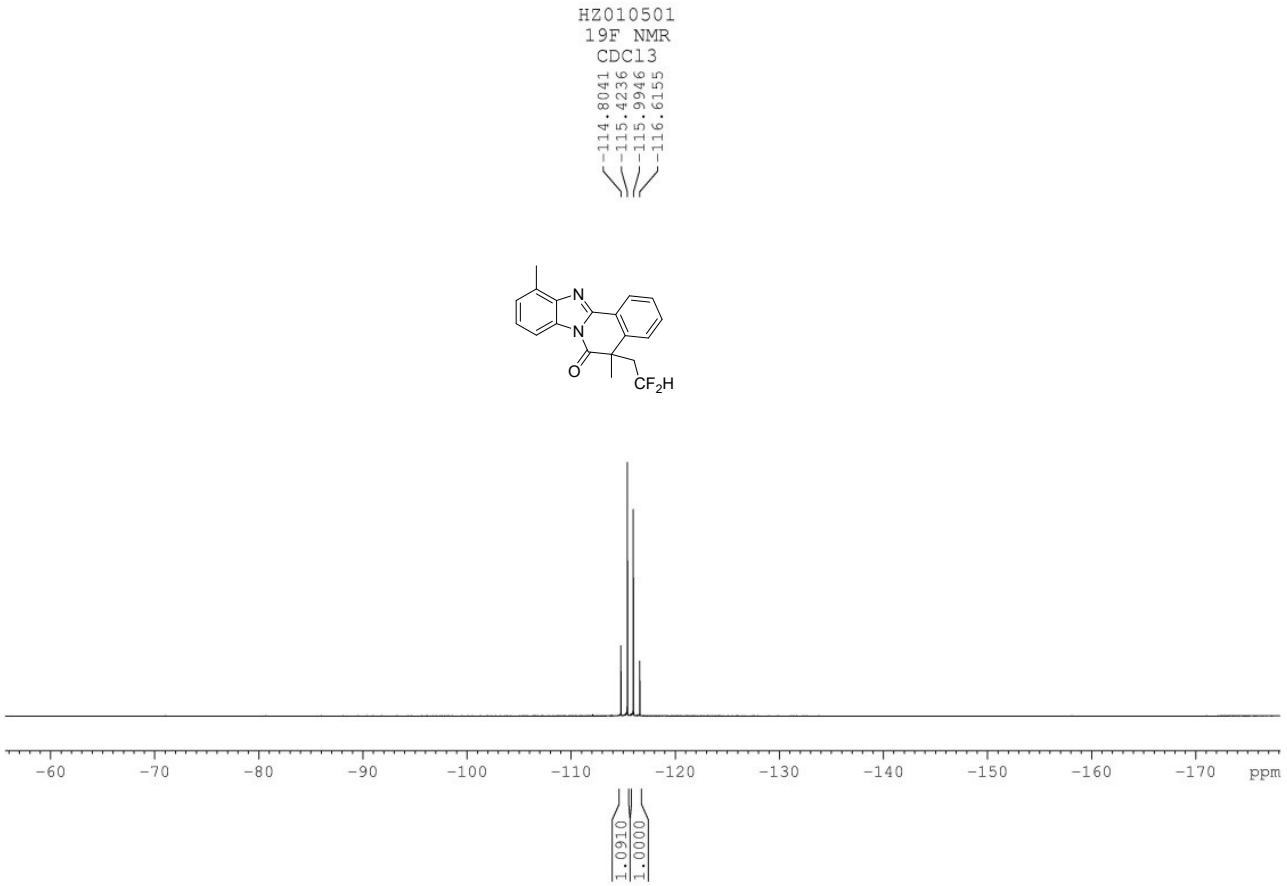


Fig. S13 ^{19}F NMR (470 MHz) spectrum of compound **3b**

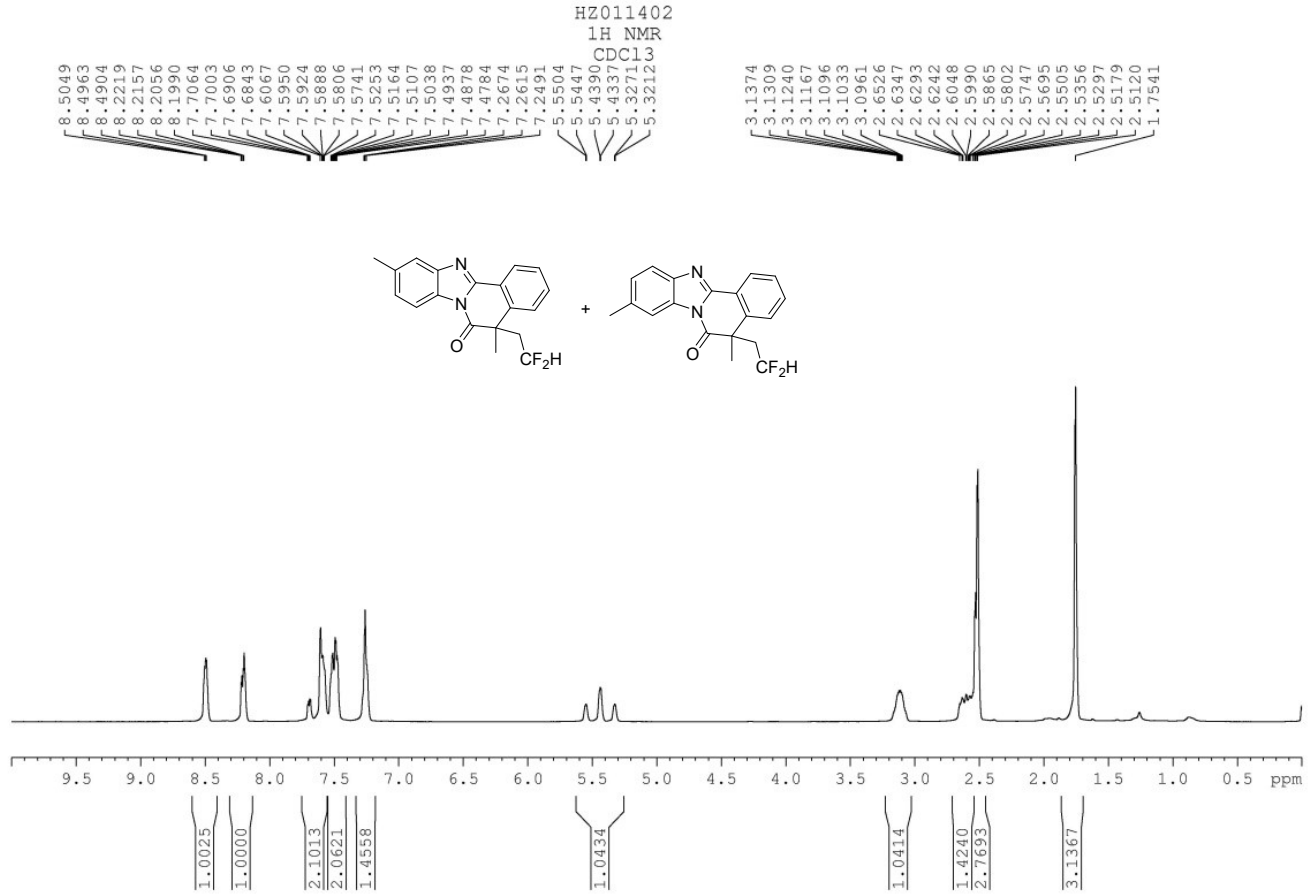


Fig. S14 ^{1}H NMR (500 MHz) spectrum of compound **3c**

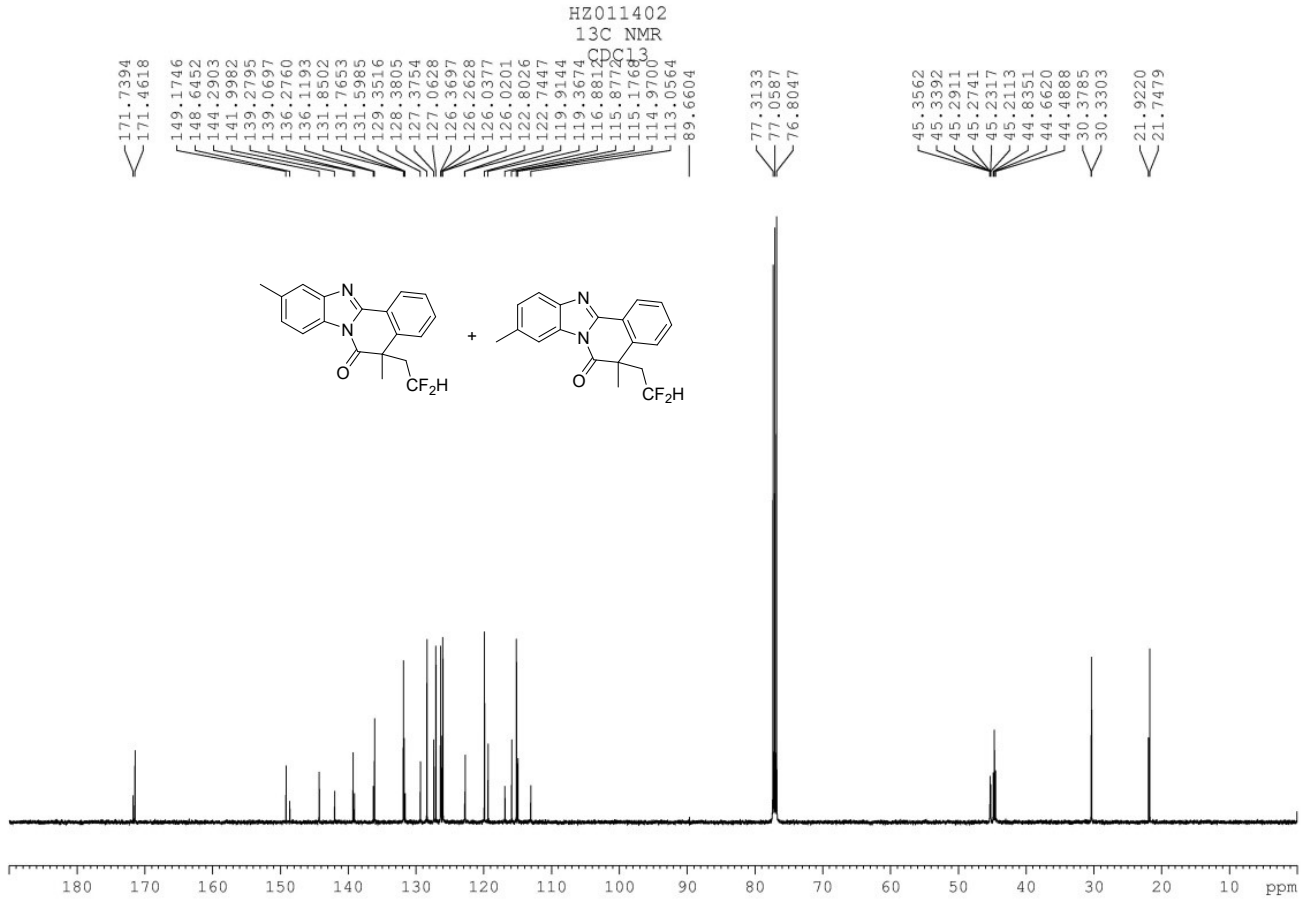


Fig. S15 ^{13}C NMR (125 MHz) spectrum of compound **3c**

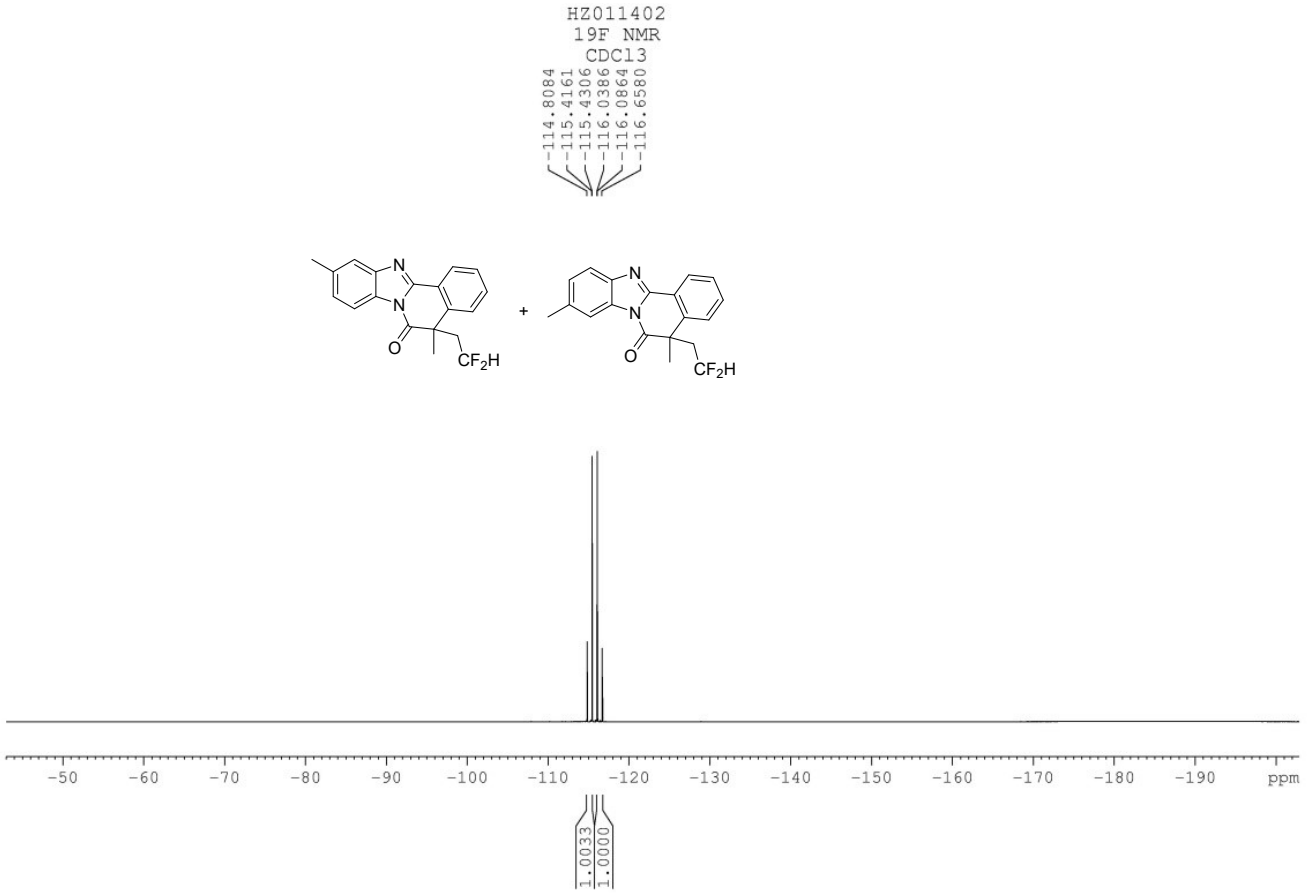


Fig. S16 ^{19}F NMR (470 MHz) spectrum of compound **3c**

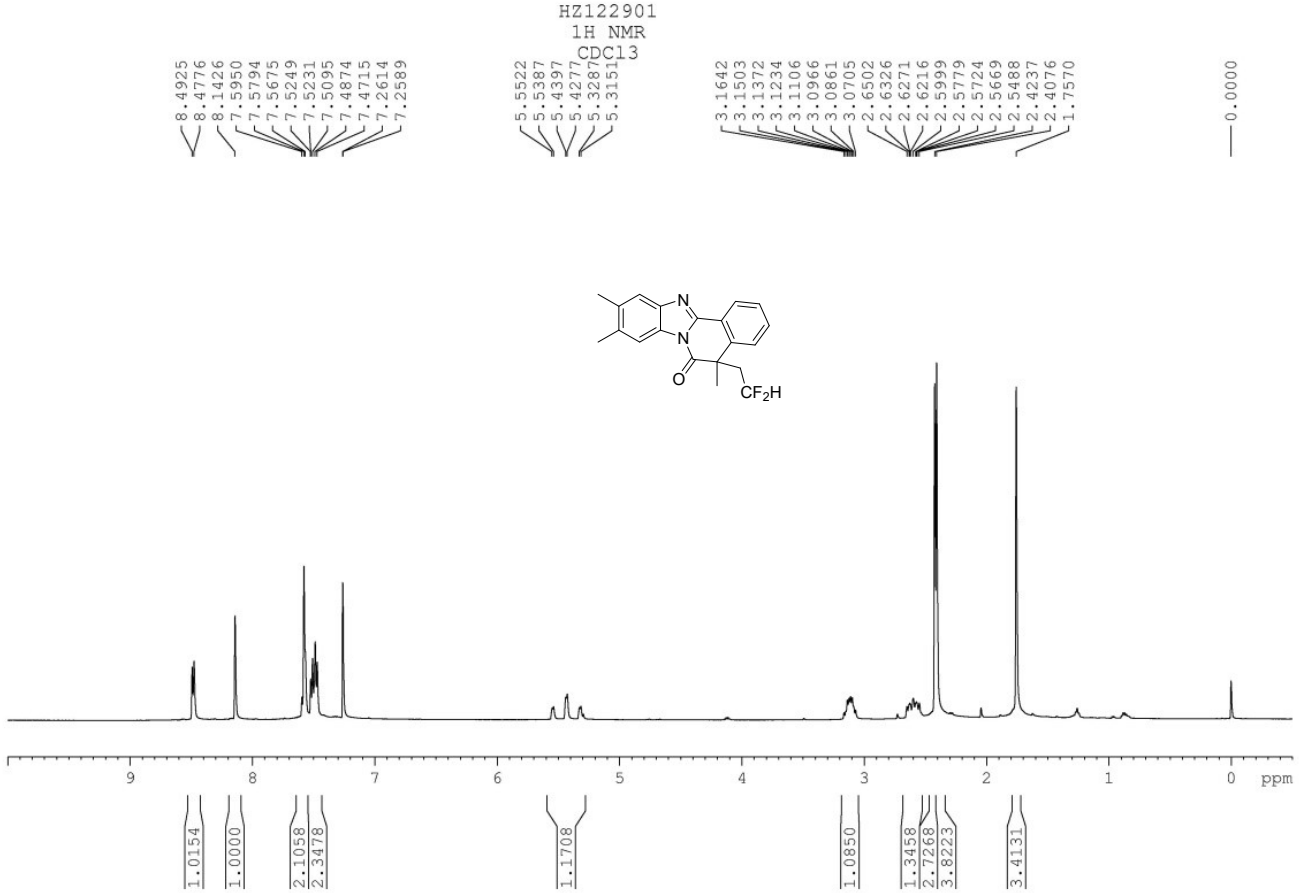


Fig. S17 ^{1}H NMR (500 MHz) spectrum of compound **3d**

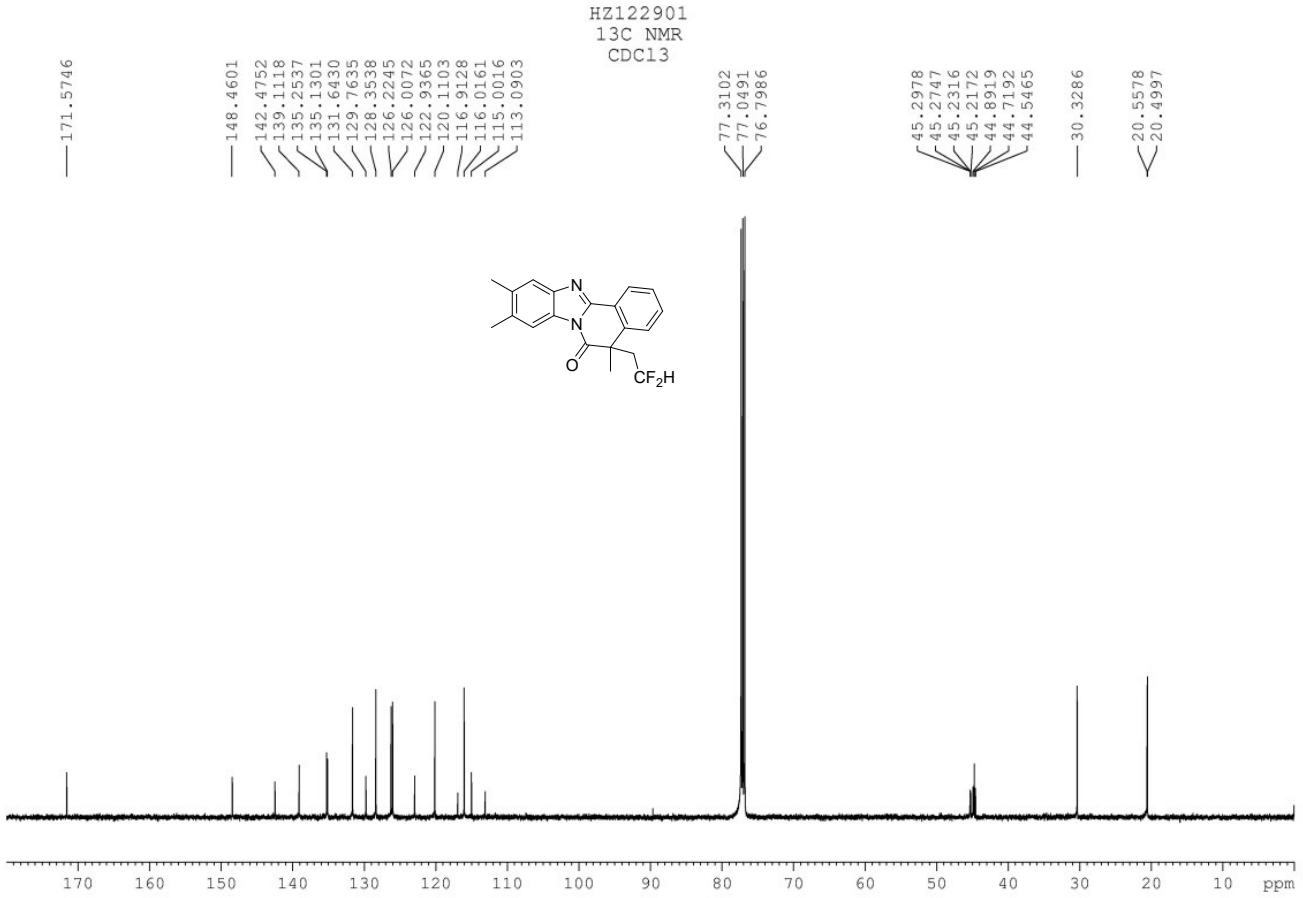


Fig. S18 ^{13}C NMR (125 MHz) spectrum of compound **3d**

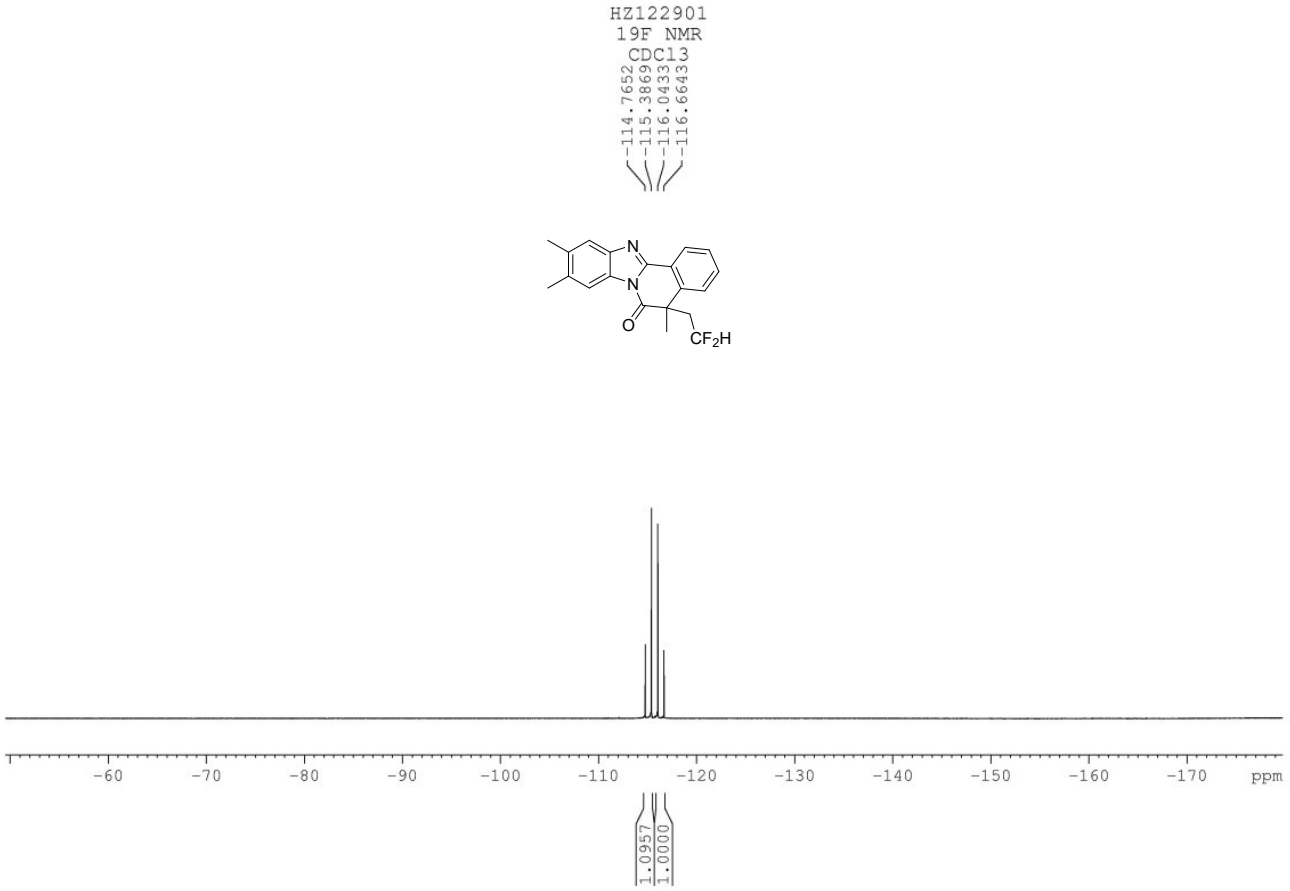


Fig. S19 ^{19}F NMR (470 MHz) spectrum of compound **3d**

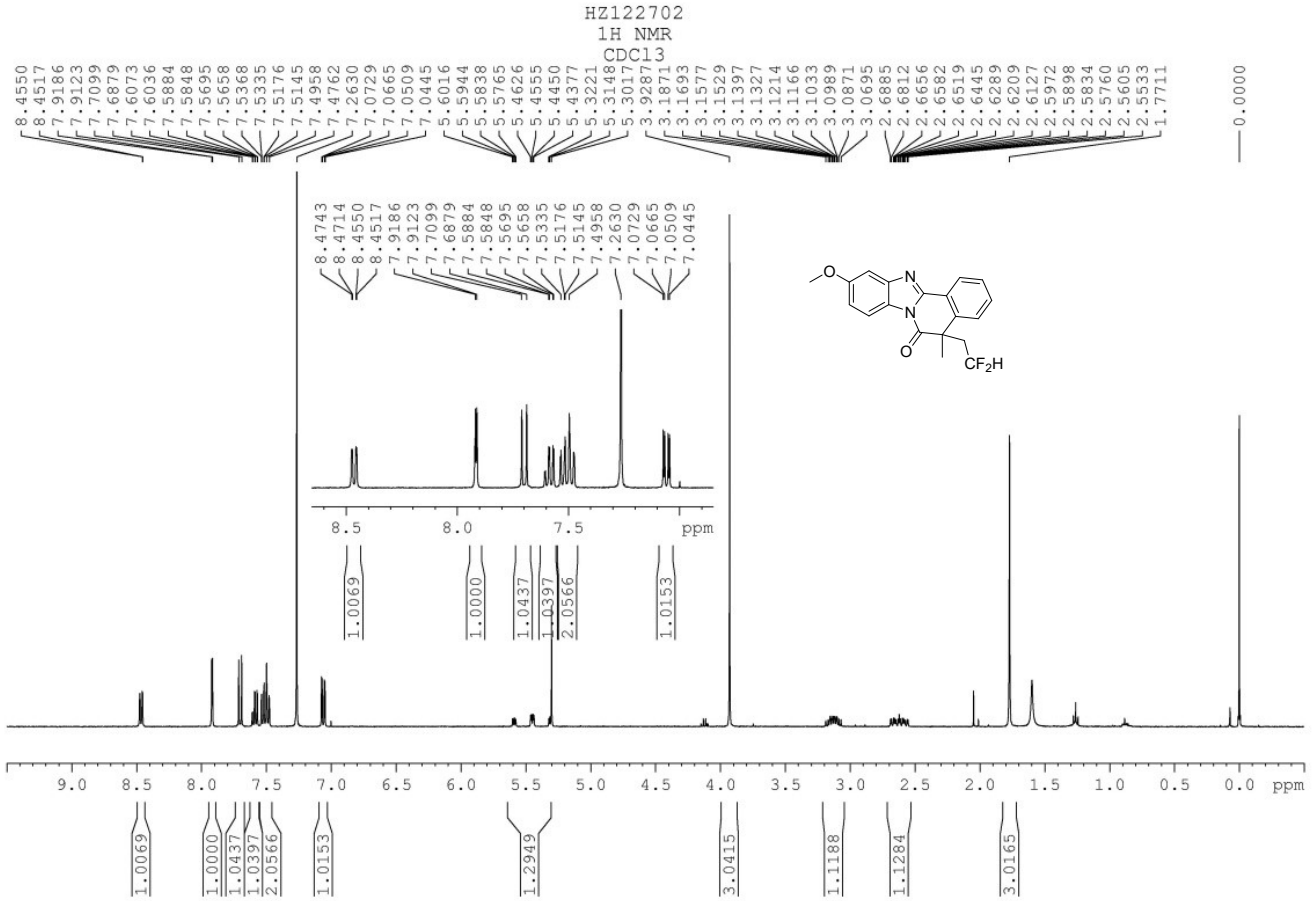


Fig. S20 ^{1}H NMR (400 MHz) spectrum of compound **3e**

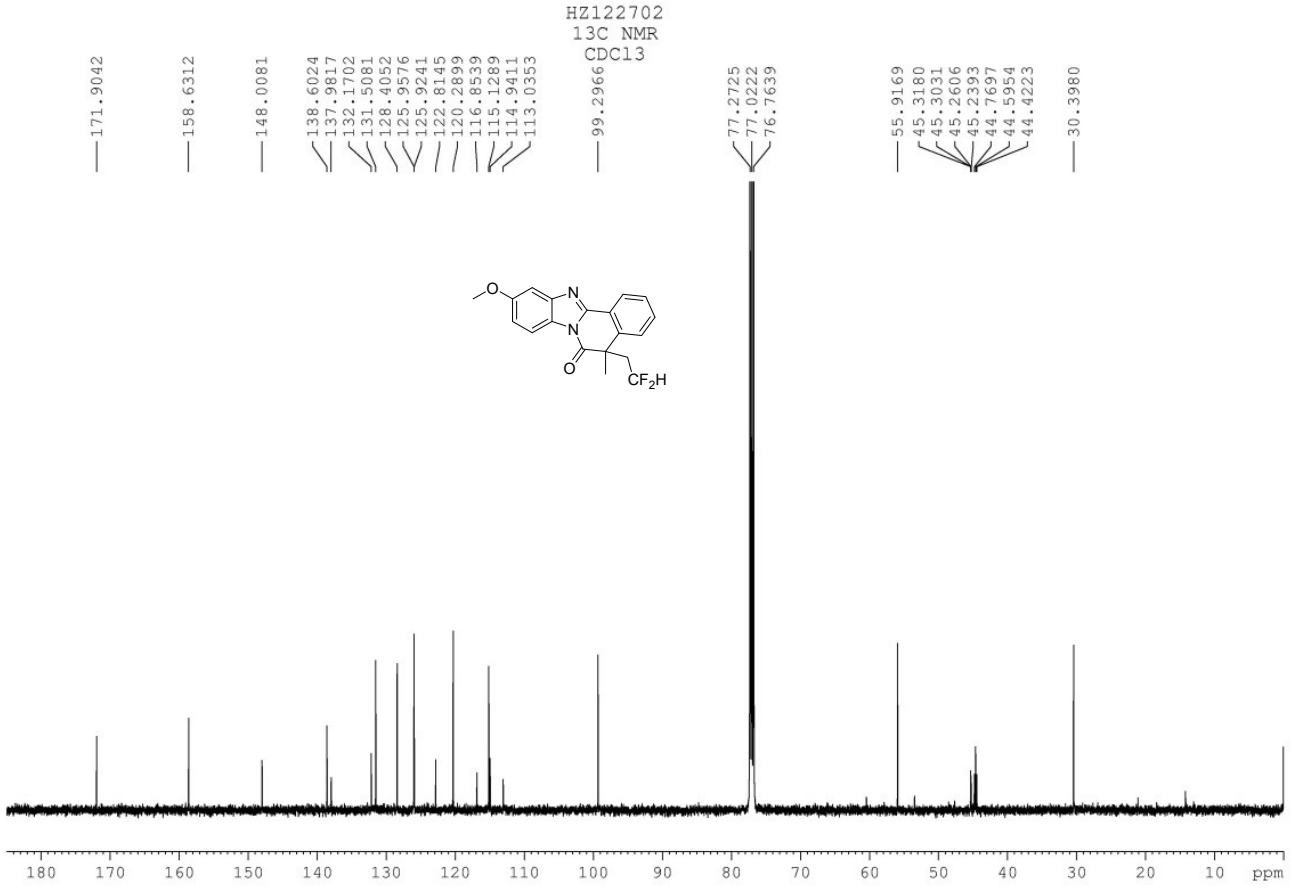


Fig. S21 ^{13}C NMR (125 MHz) spectrum of compound **3e**

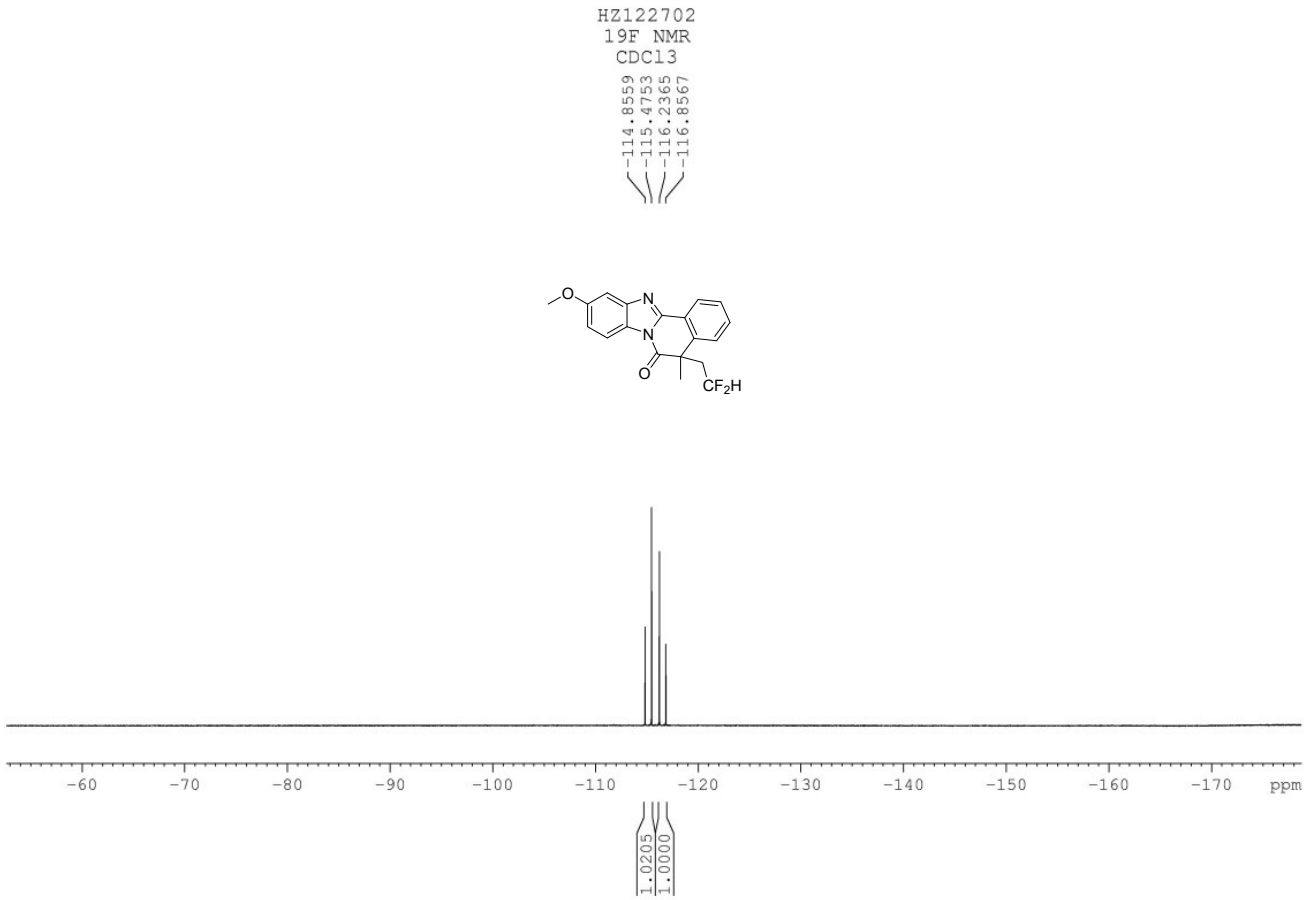


Fig. S22 ^{19}F NMR (470 MHz) spectrum of compound **3e**

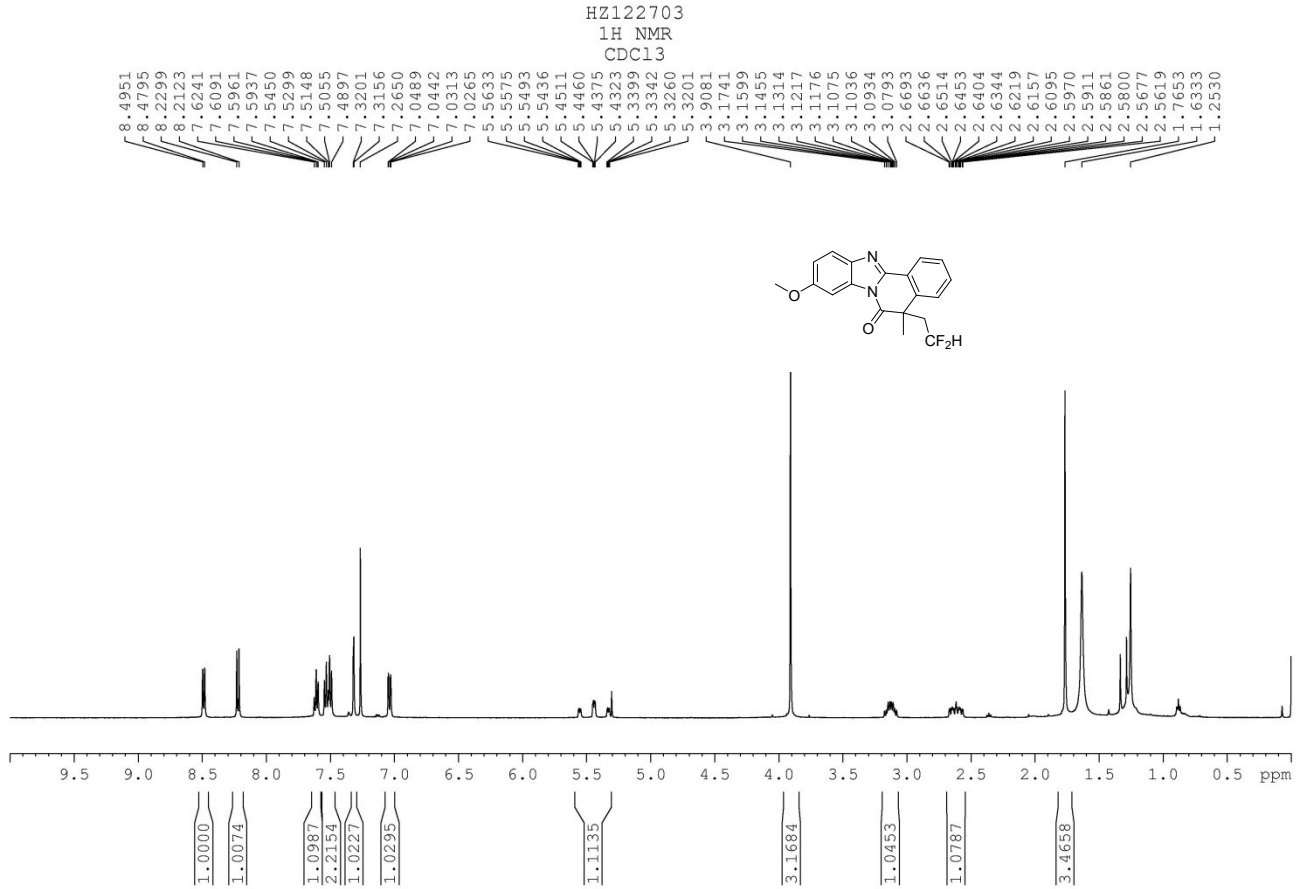


Fig. S23 ^{1}H NMR (400 MHz) spectrum of compound **3f**

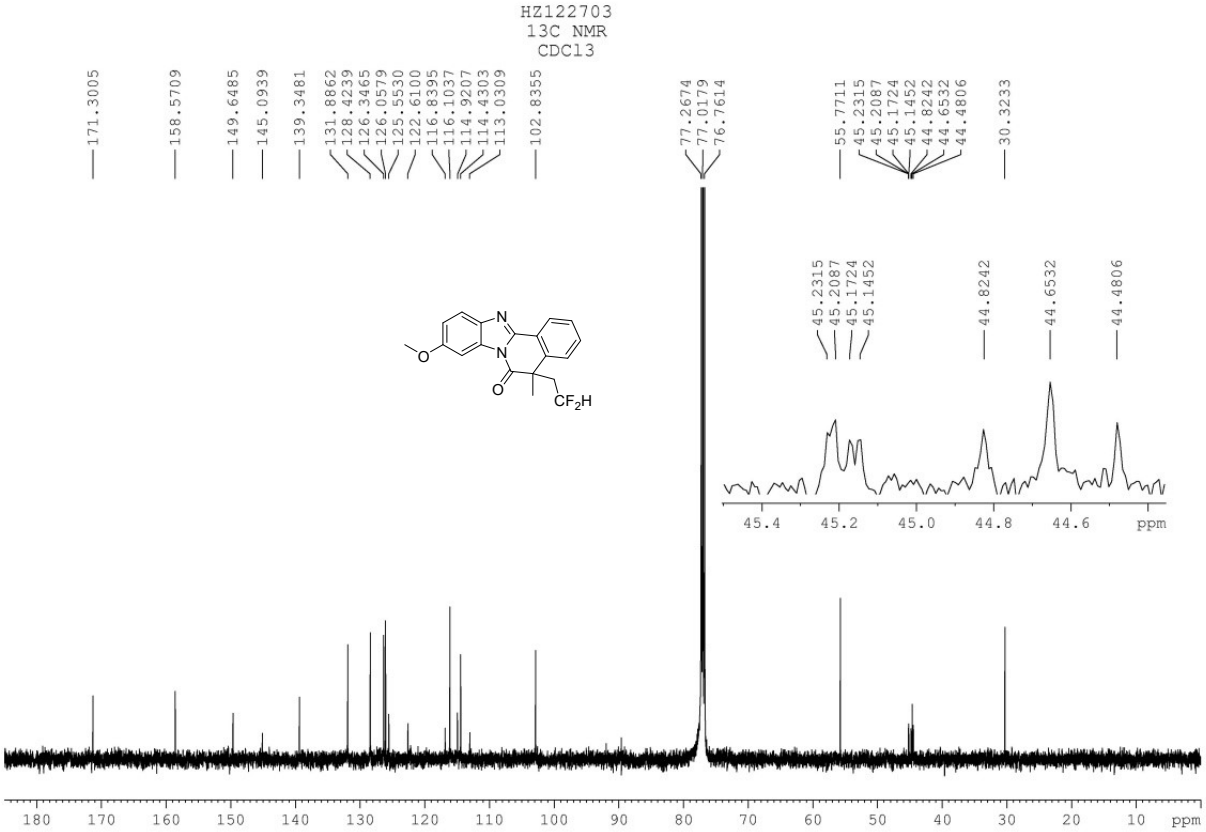


Fig. S24 ^{13}C NMR (125 MHz) spectrum of compound **3f**

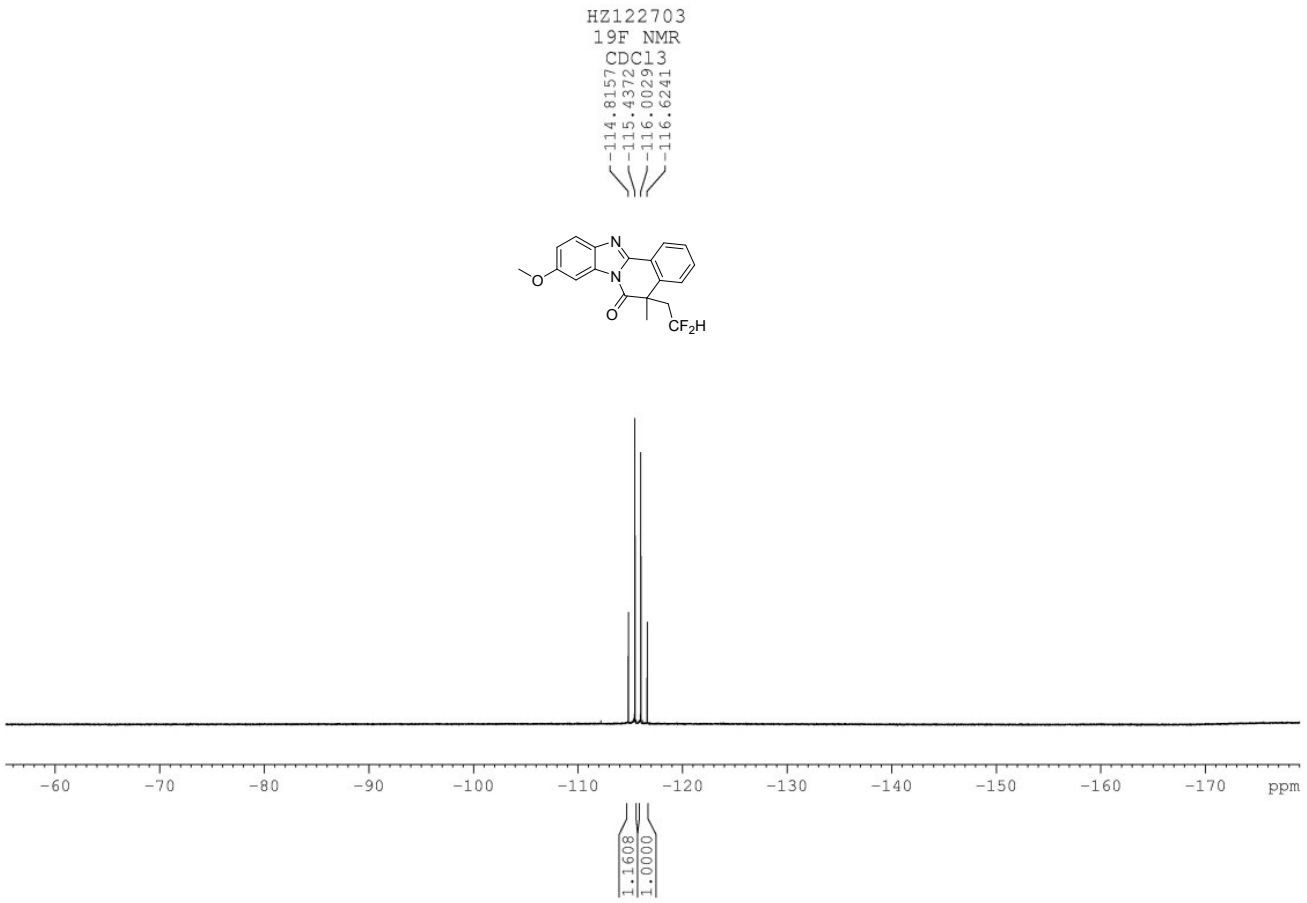


Fig. S25 ^{19}F NMR (470 MHz) spectrum of compound **3f**

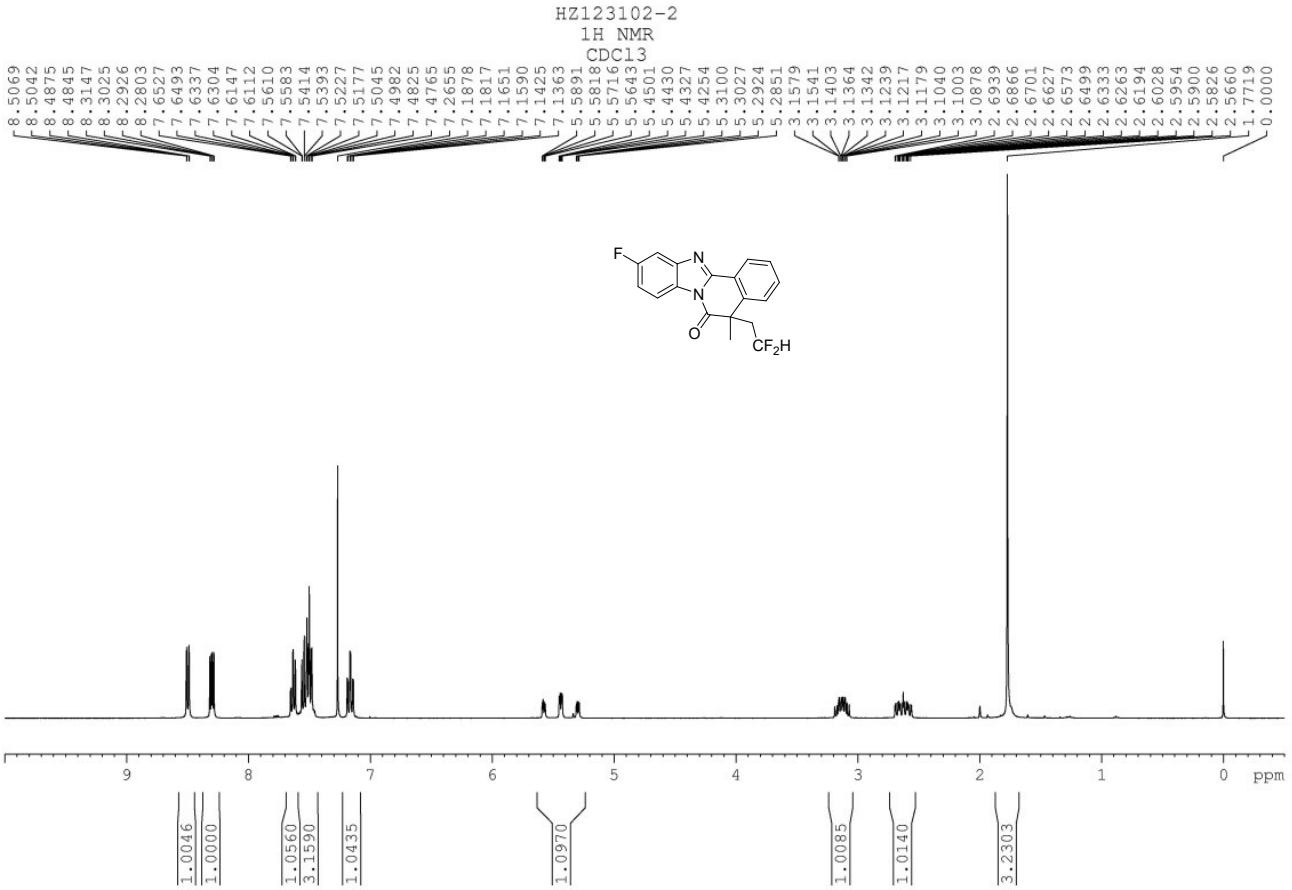


Fig. S26 ^{1}H NMR (400 MHz) spectrum of compound **3g**

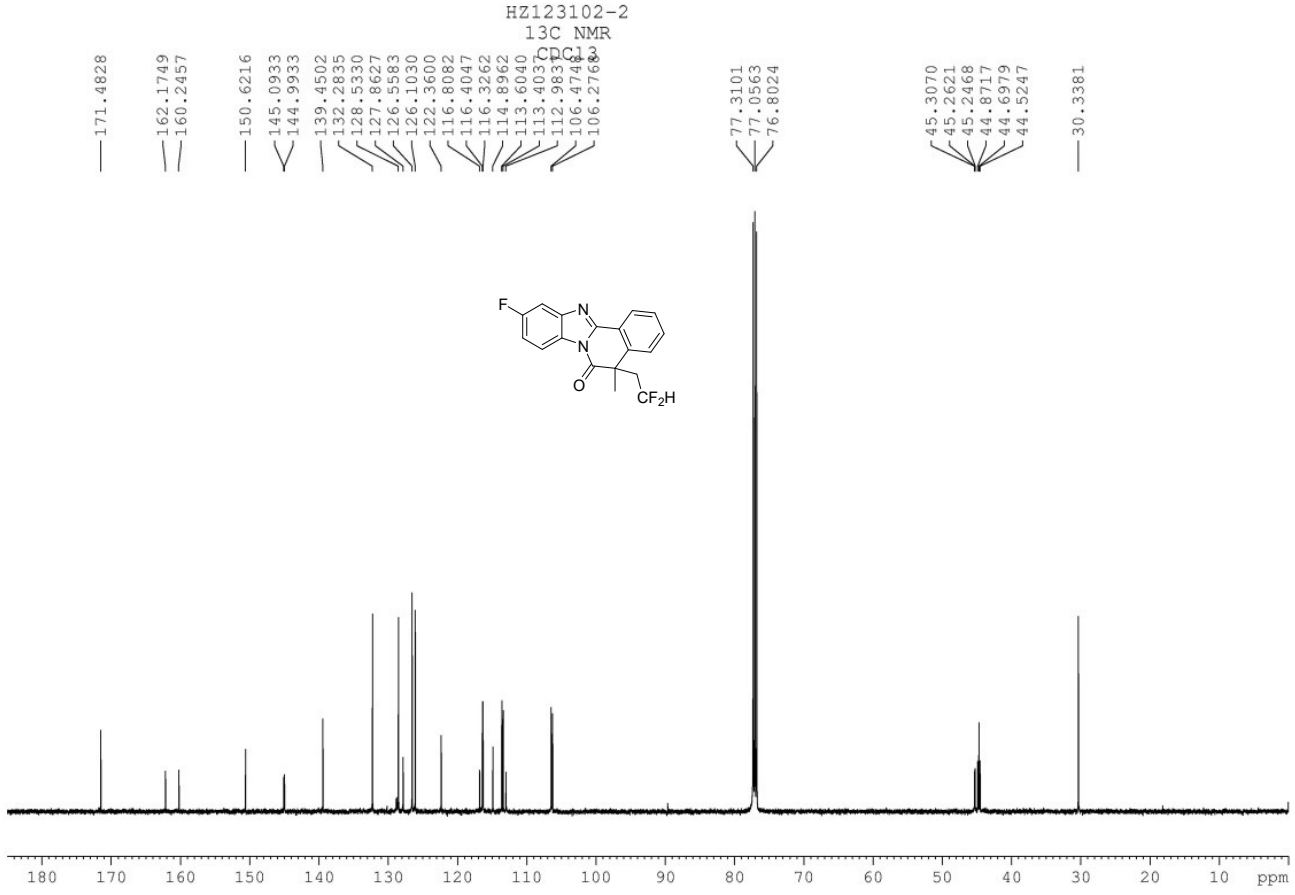


Fig. S27 ^{13}C NMR (125 MHz) spectrum of compound **3g**

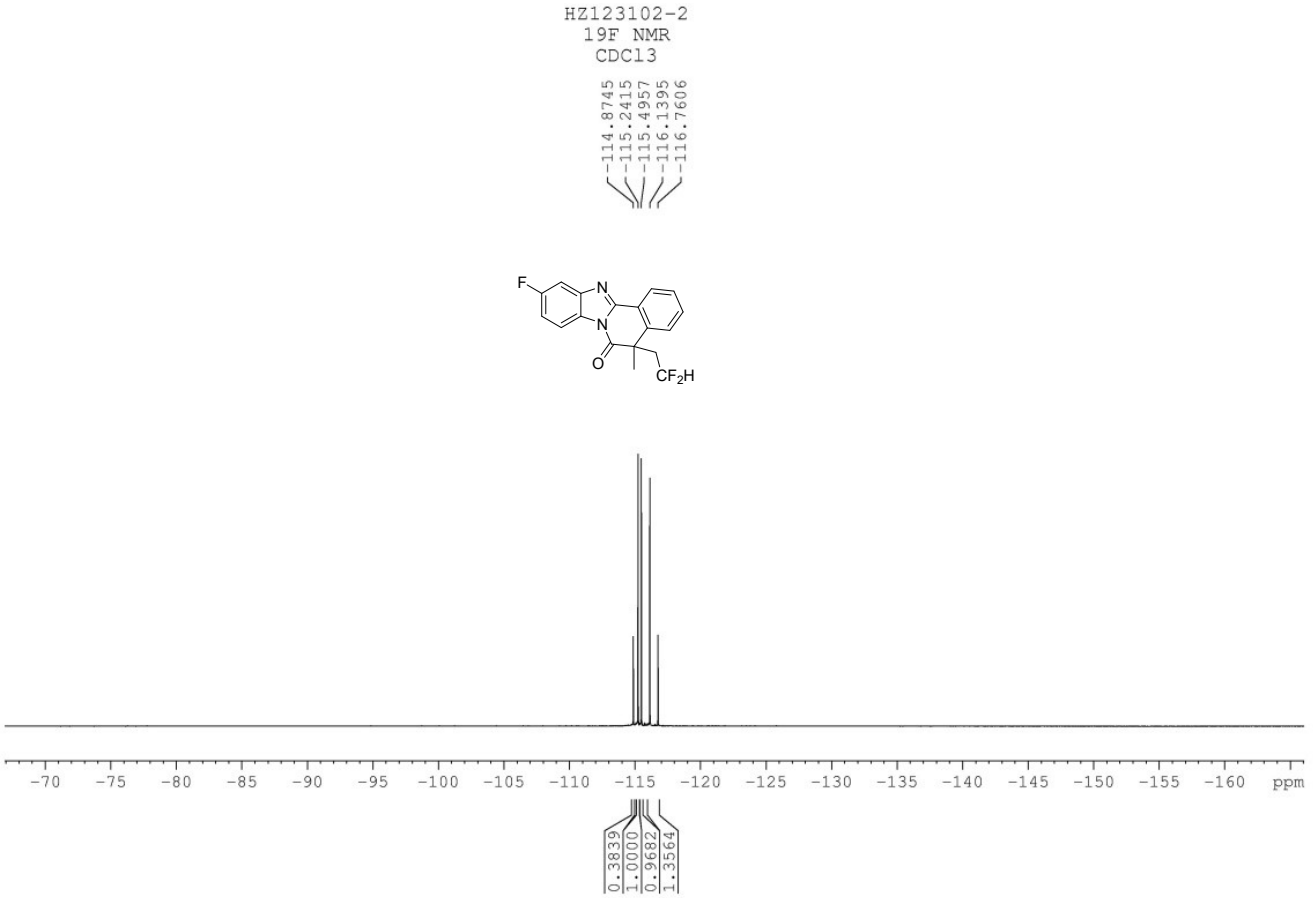


Fig. S28 ^{19}F NMR (470 MHz) spectrum of compound **3g**

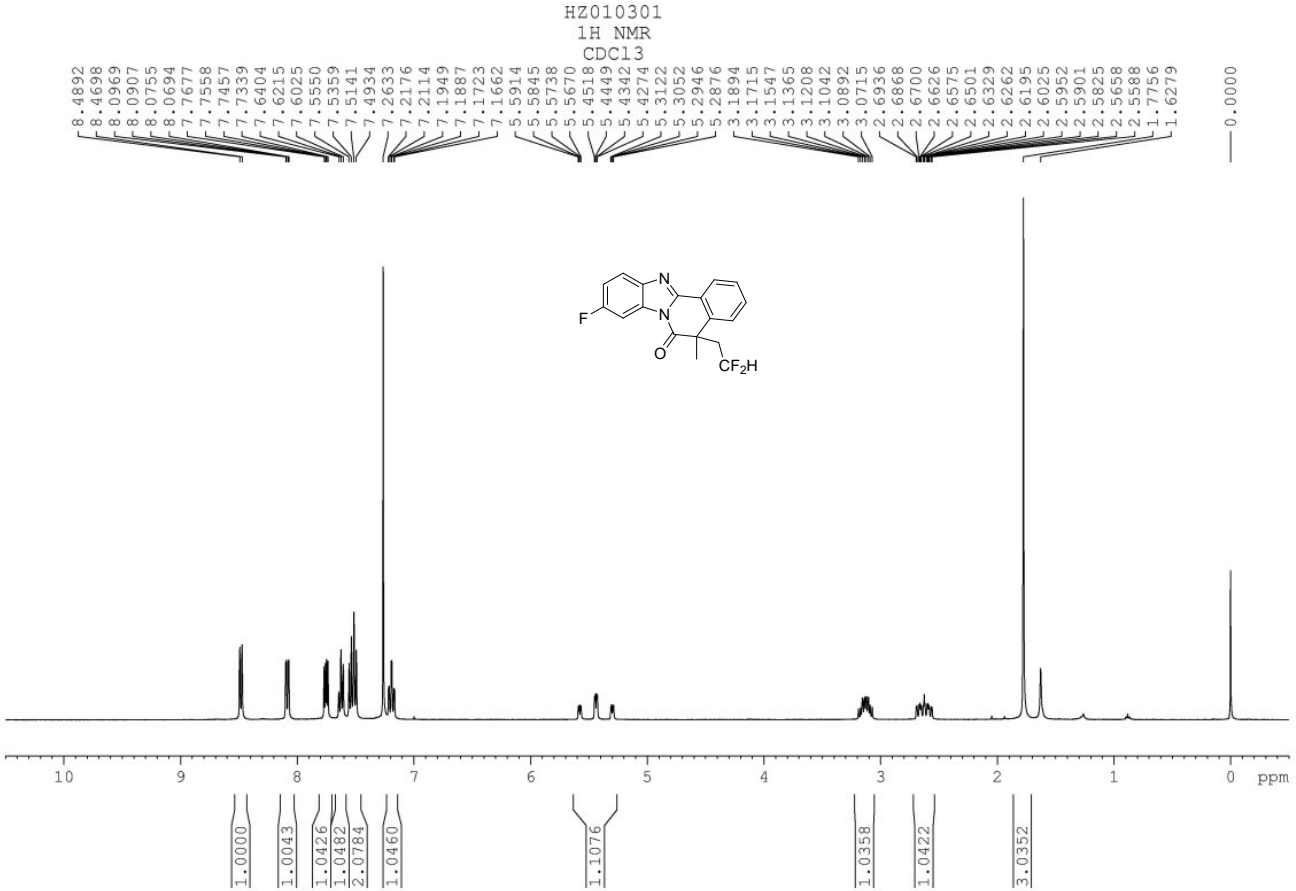


Fig. S29 ^{1}H NMR (400 MHz) spectrum of compound **3h**

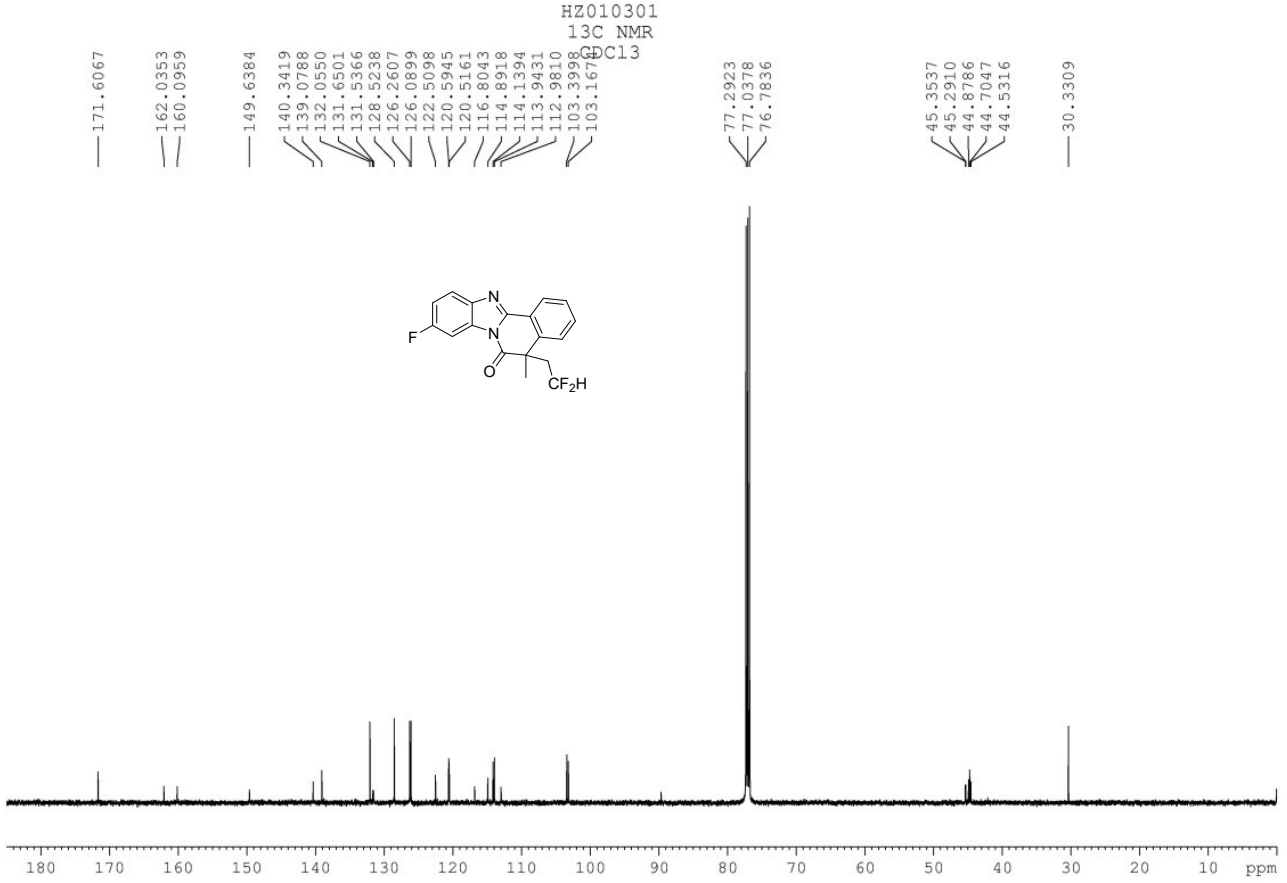


Fig. S30 ^{13}C NMR (125 MHz) spectrum of compound **3h**

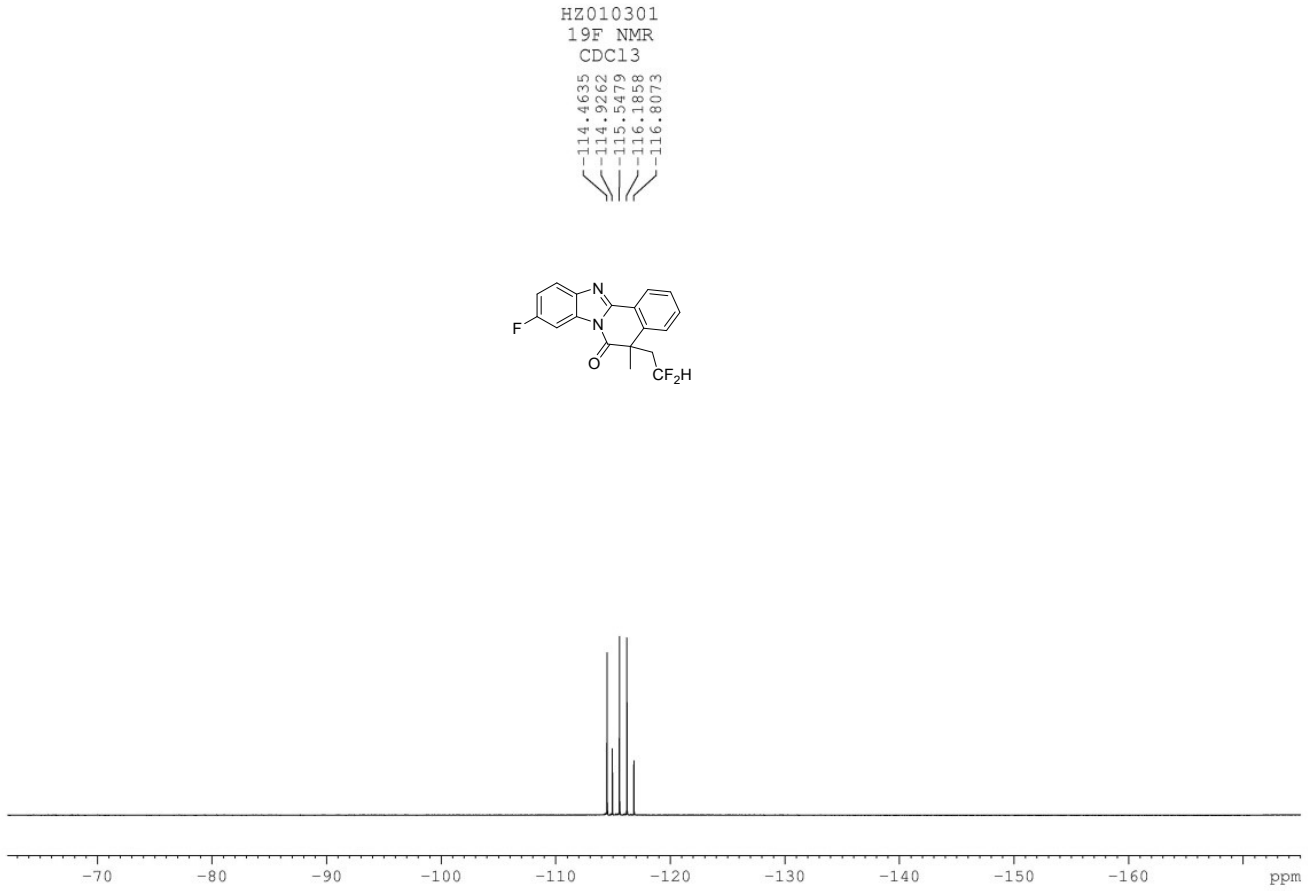


Fig. S31 ^{19}F NMR (470 MHz) spectrum of compound **3h**

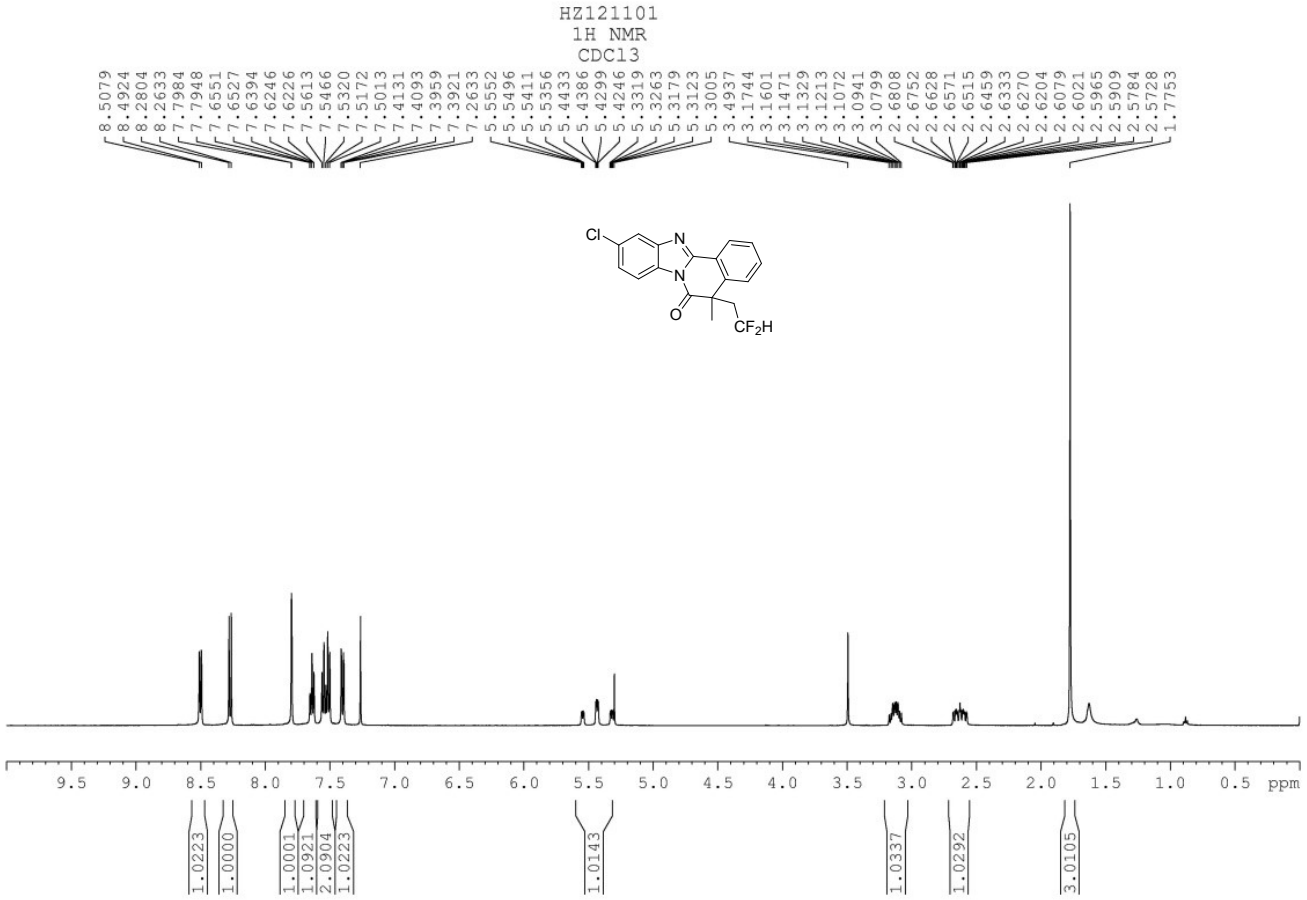


Fig. S32 ^{1}H NMR (500 MHz) spectrum of compound **3i**

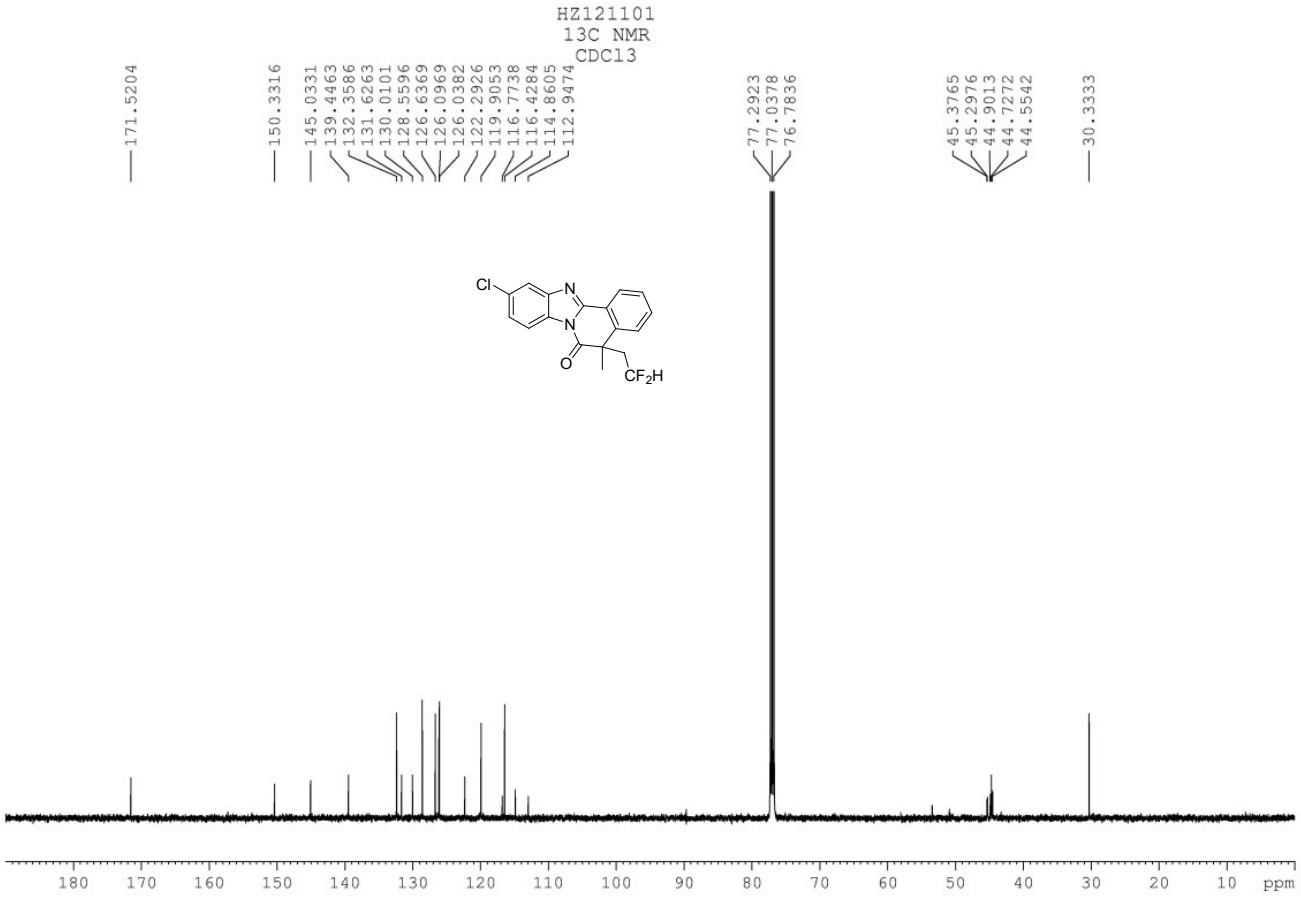


Fig. S33 ^{13}C NMR (125 MHz) spectrum of compound **3i**

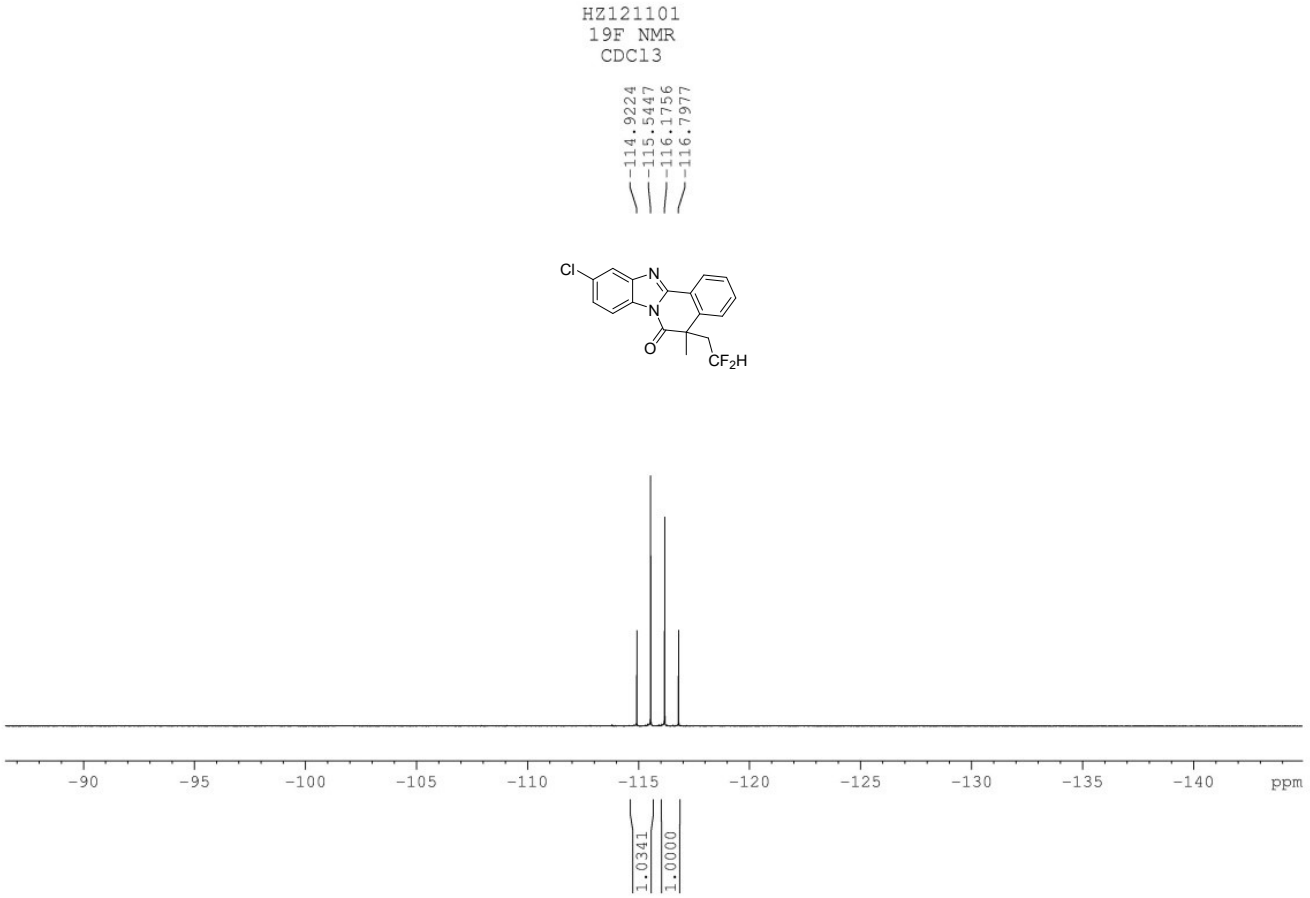


Fig. S34 ^{19}F NMR (470 MHz) spectrum of compound **3i**

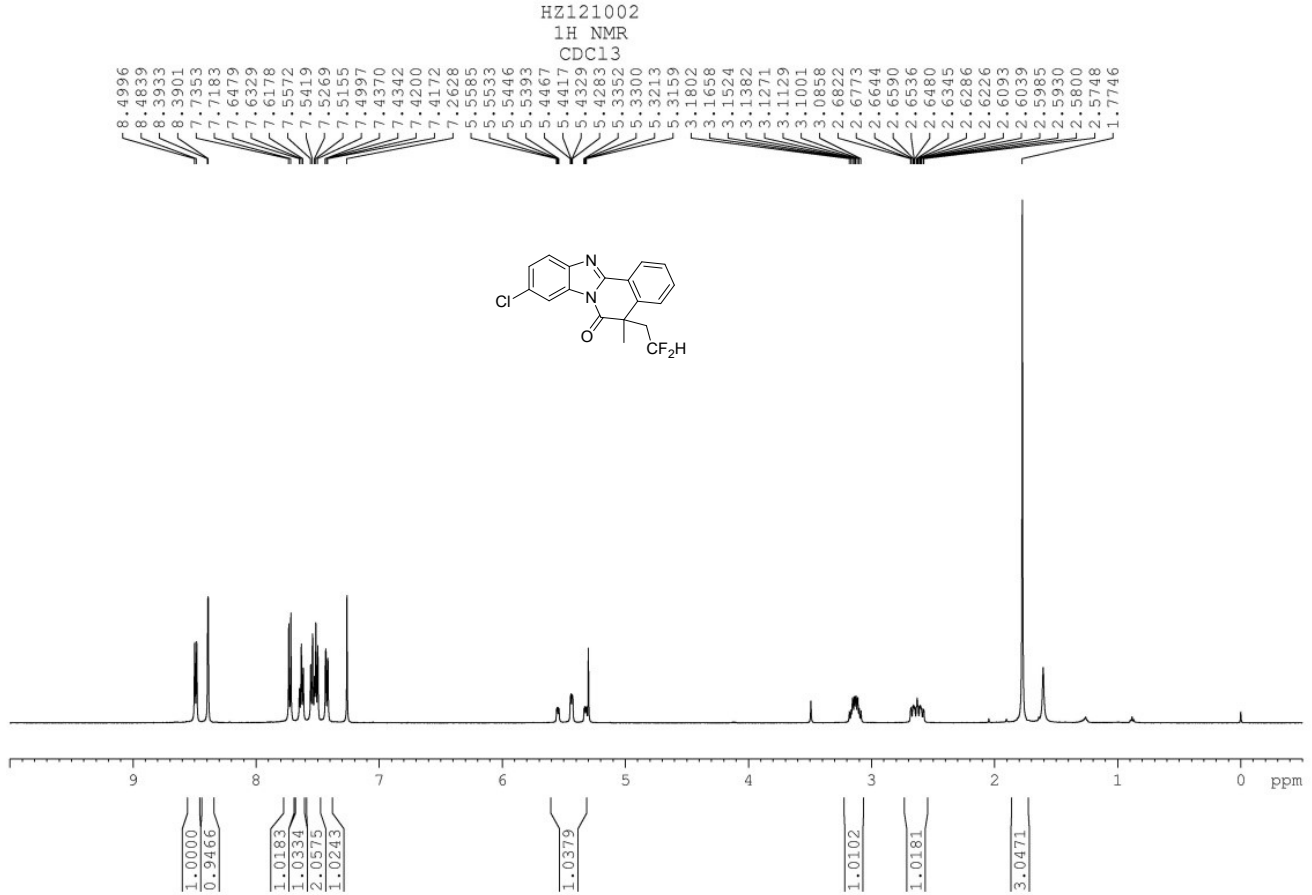


Fig. S35 ^{1}H NMR (500 MHz) spectrum of compound **3j**

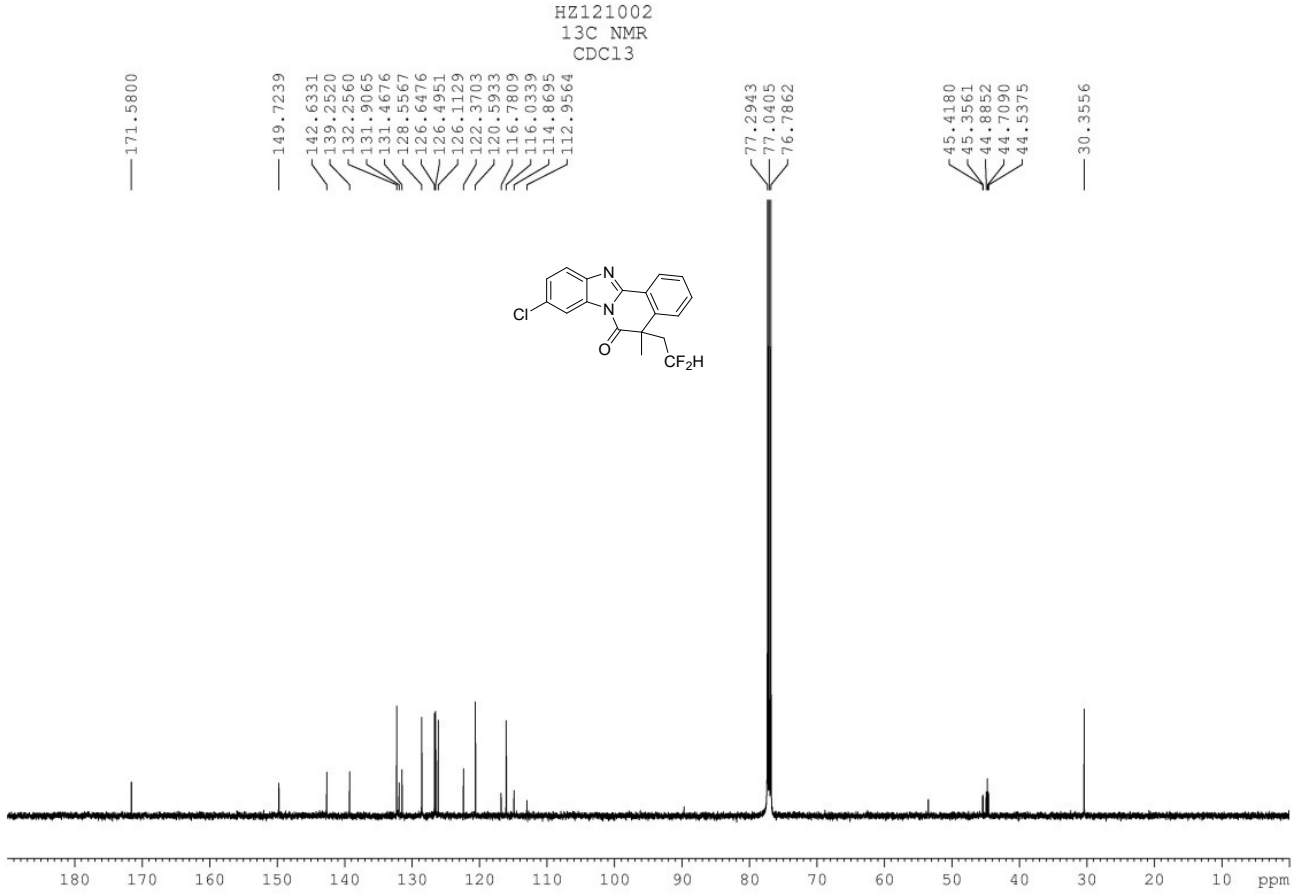


Fig. S36 ^{13}C NMR (125 MHz) spectrum of compound **3j**

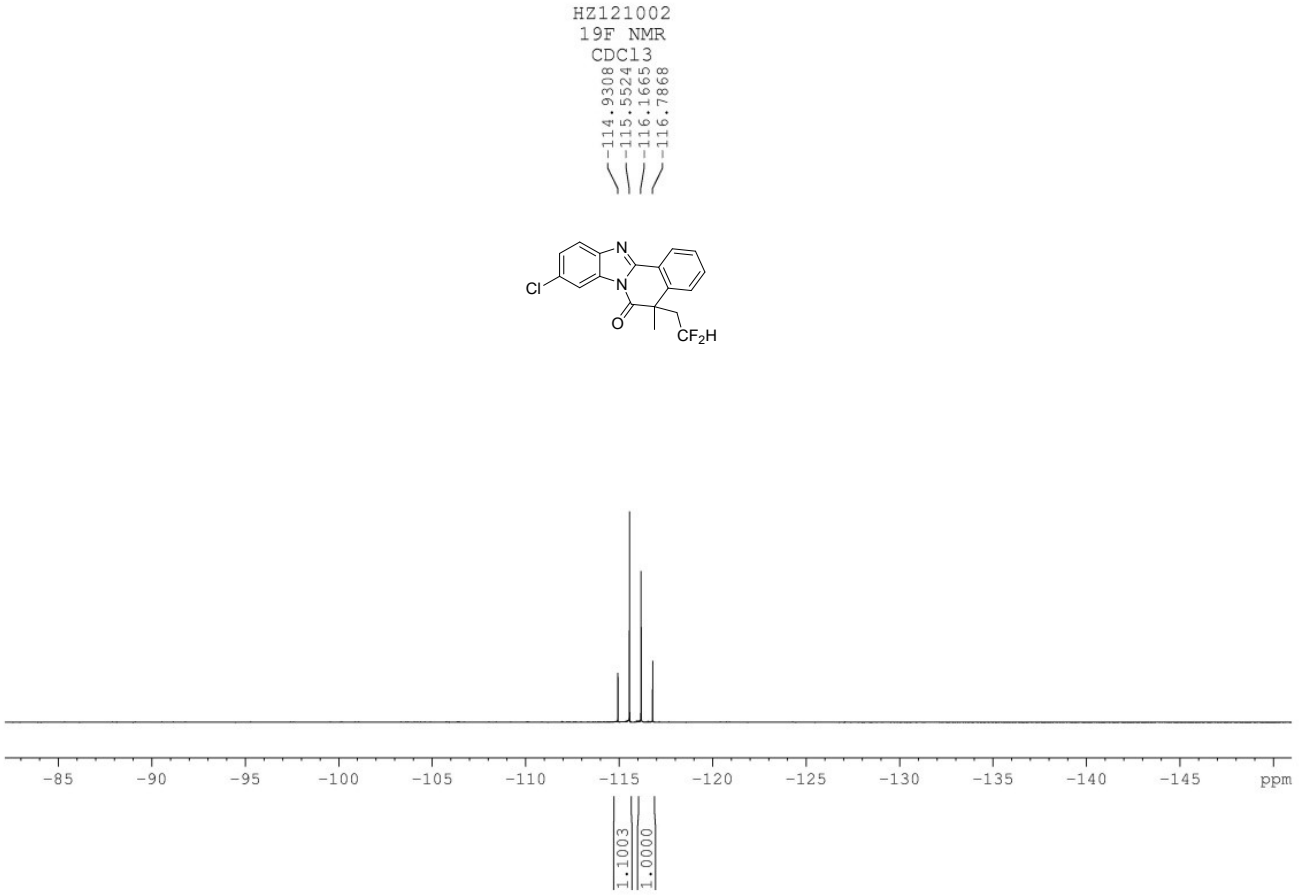


Fig. S37 ^{19}F NMR (470 MHz) spectrum of compound **3j**

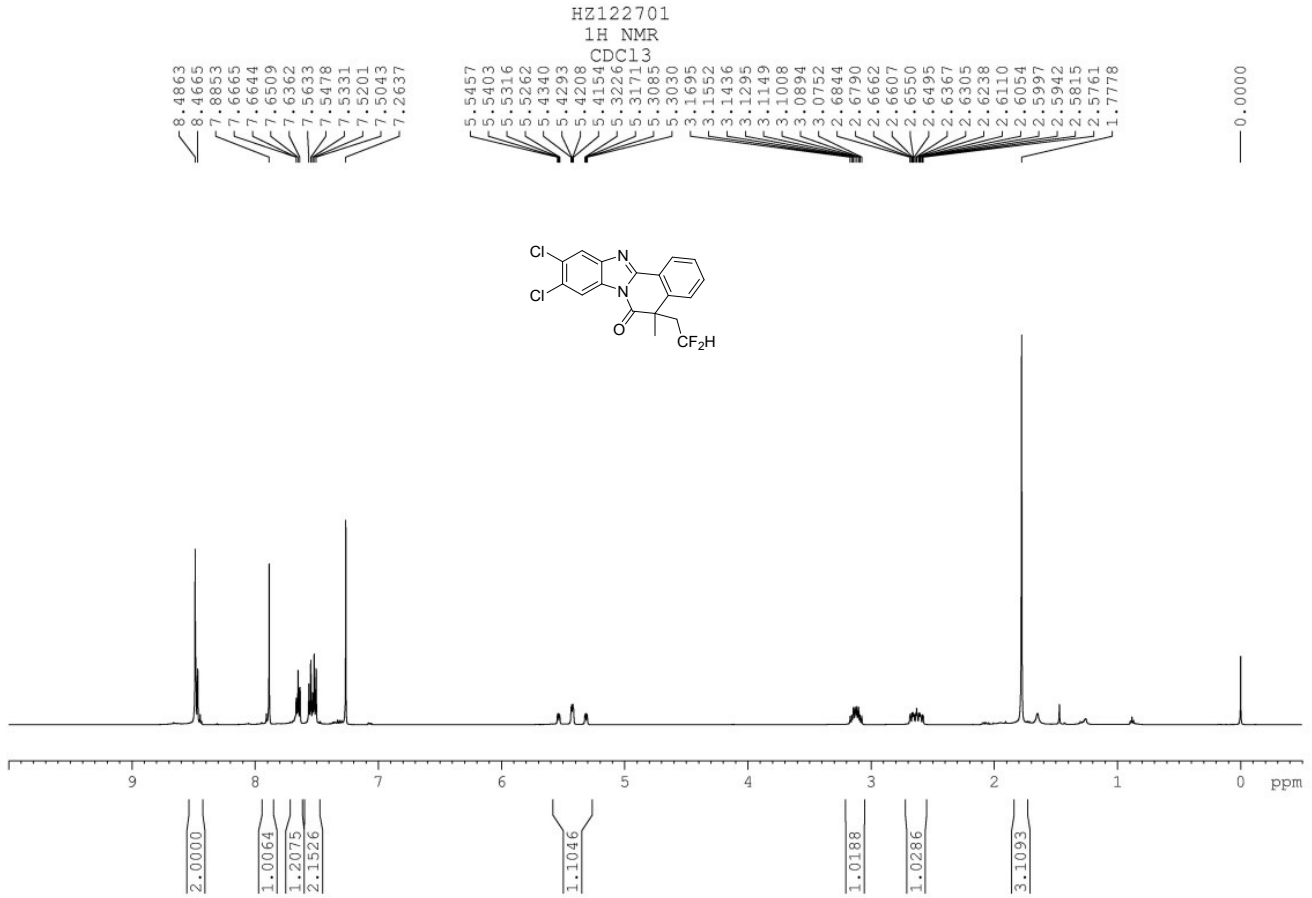


Fig. S38 ^{1}H NMR (500 MHz) spectrum of compound **3k**

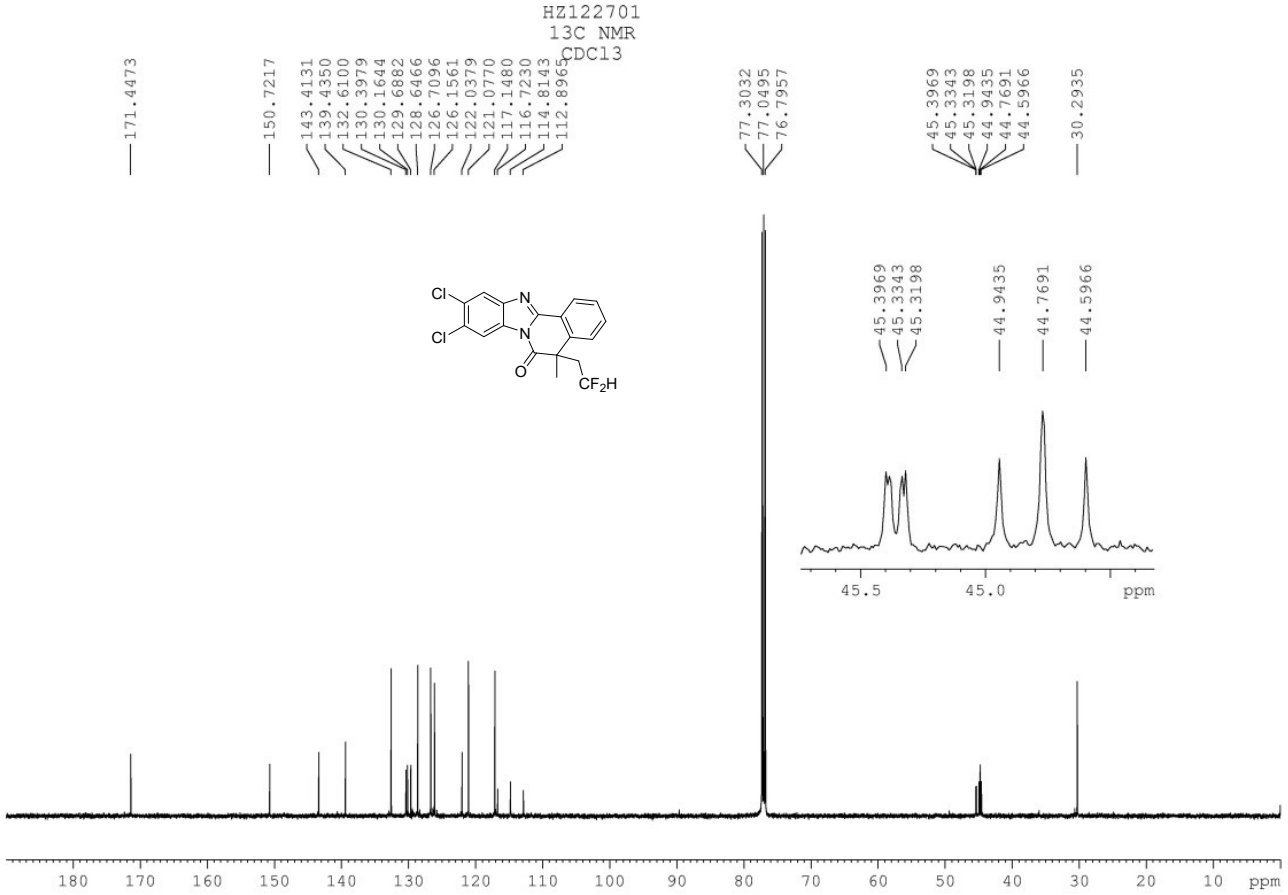


Fig. S39 ^{13}C NMR (125 MHz) spectrum of compound **3k**

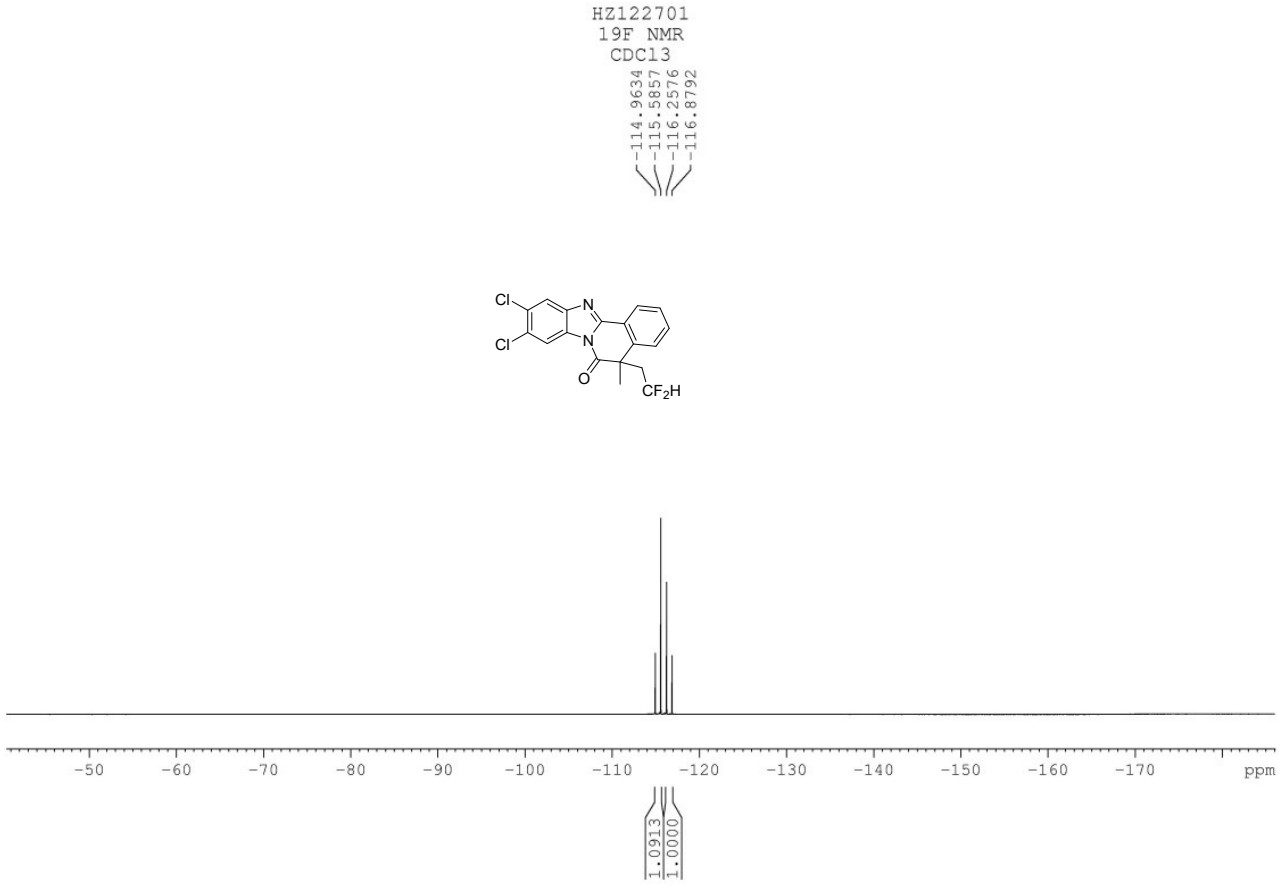


Fig. S40 ^{19}F NMR (470 MHz) spectrum of compound **3k**

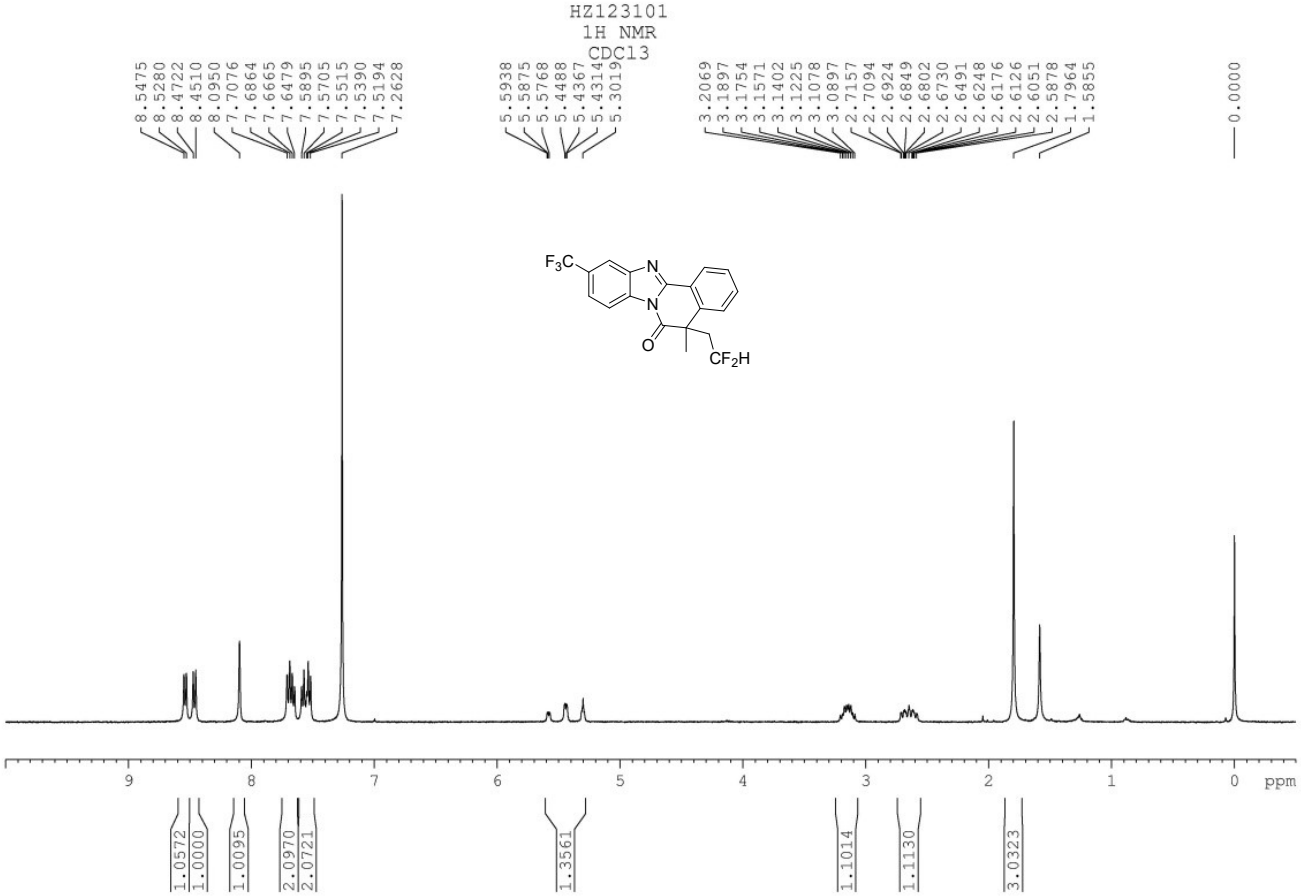


Fig. S41 ^{1}H NMR (400 MHz) spectrum of compound **3l**

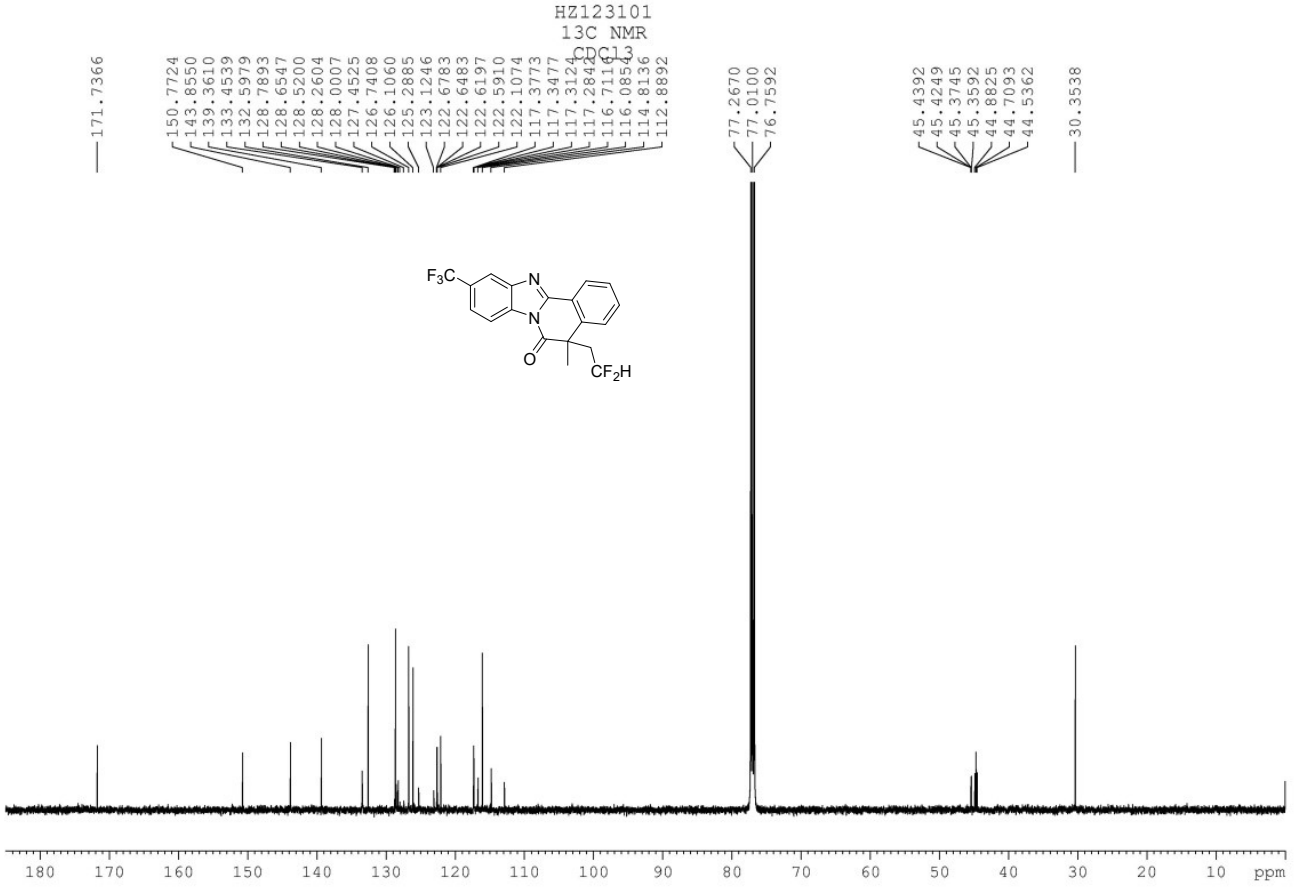


Fig. S42 ^{13}C NMR (125 MHz) spectrum of compound **3l**

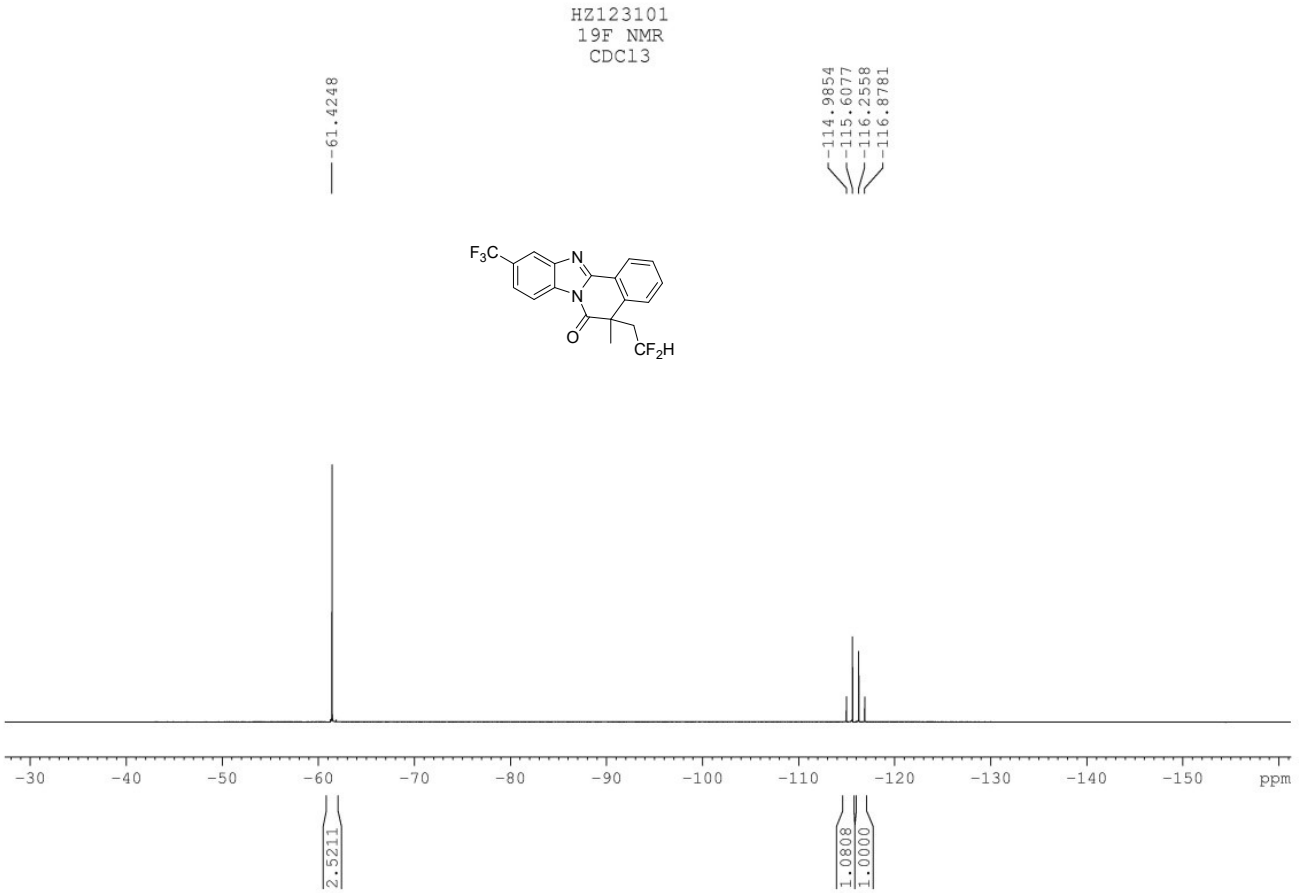


Fig. S43 ^{19}F NMR (470 MHz) spectrum of compound **3l**

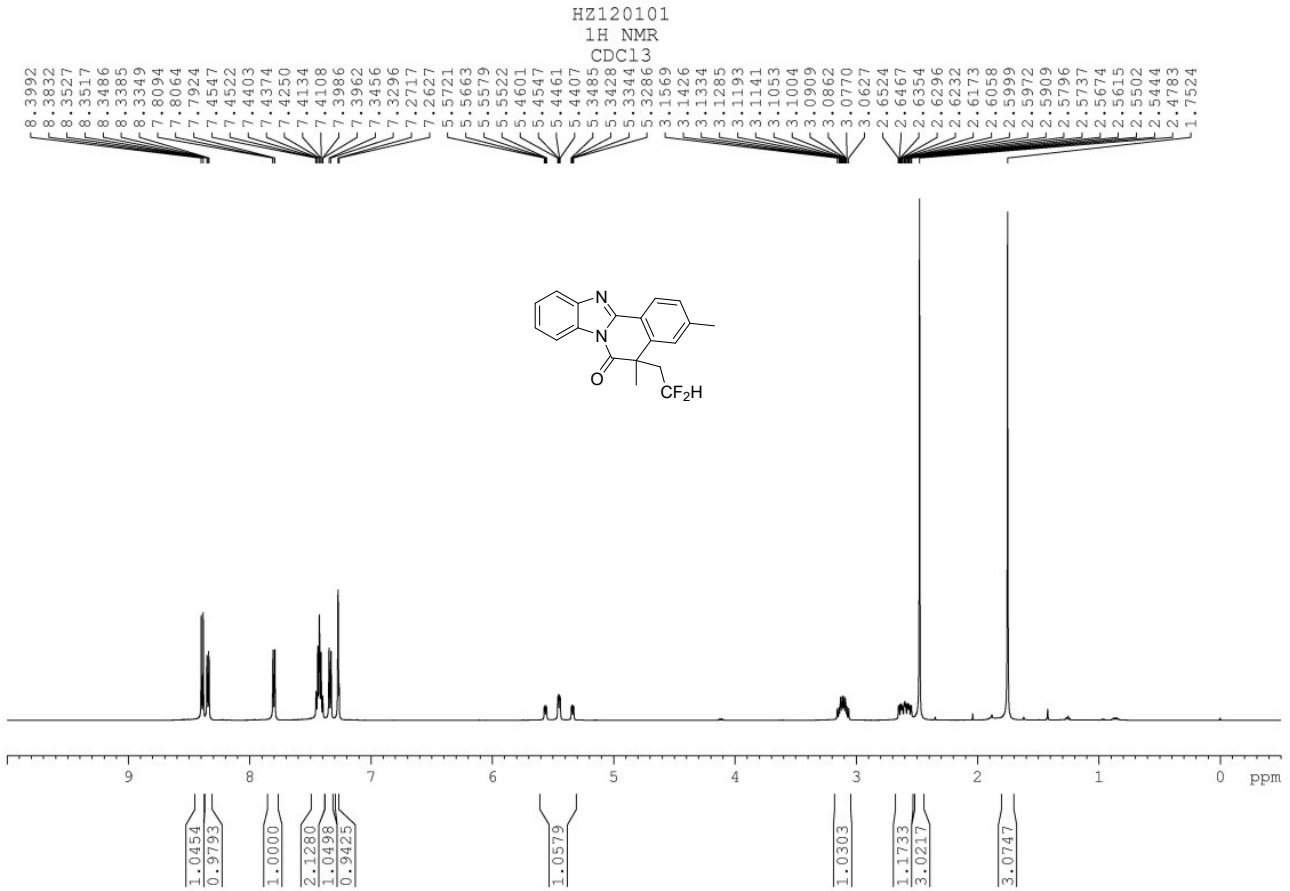


Fig. S44 ^{1}H NMR (500 MHz) spectrum of compound **3m**

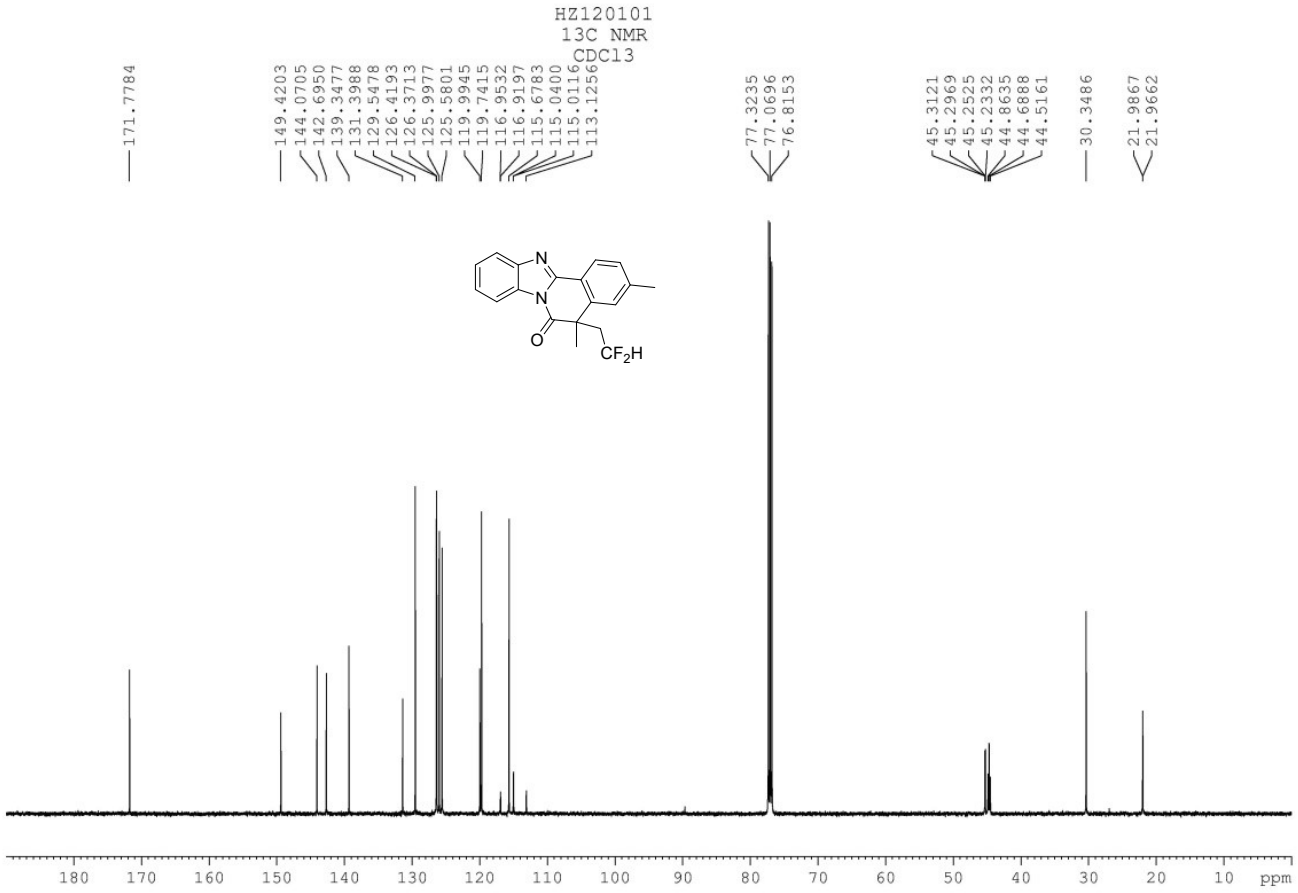


Fig. S45 ^{13}C NMR (125 MHz) spectrum of compound **3m**

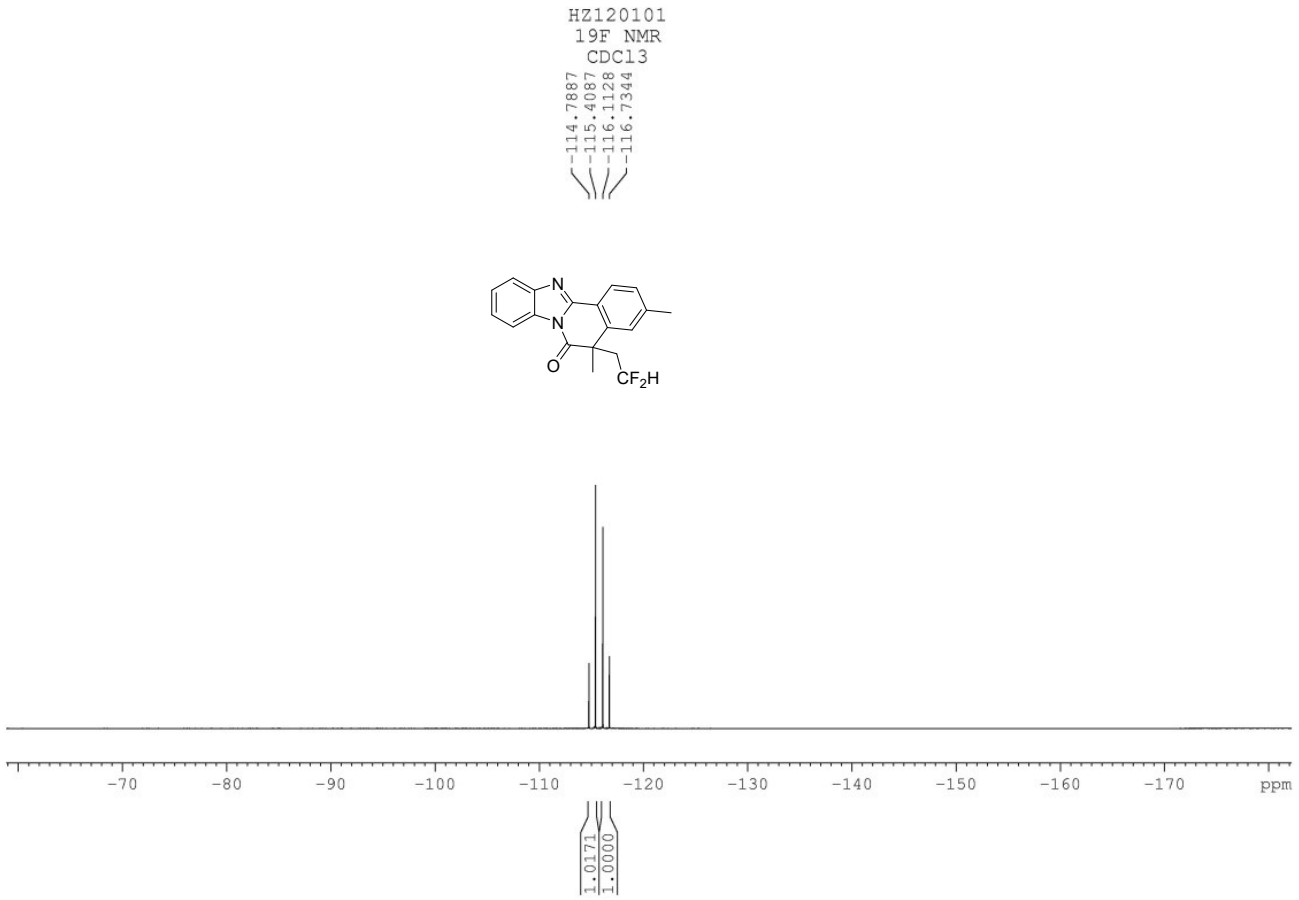


Fig. S46 ^{19}F NMR (470 MHz) spectrum of compound **3m**

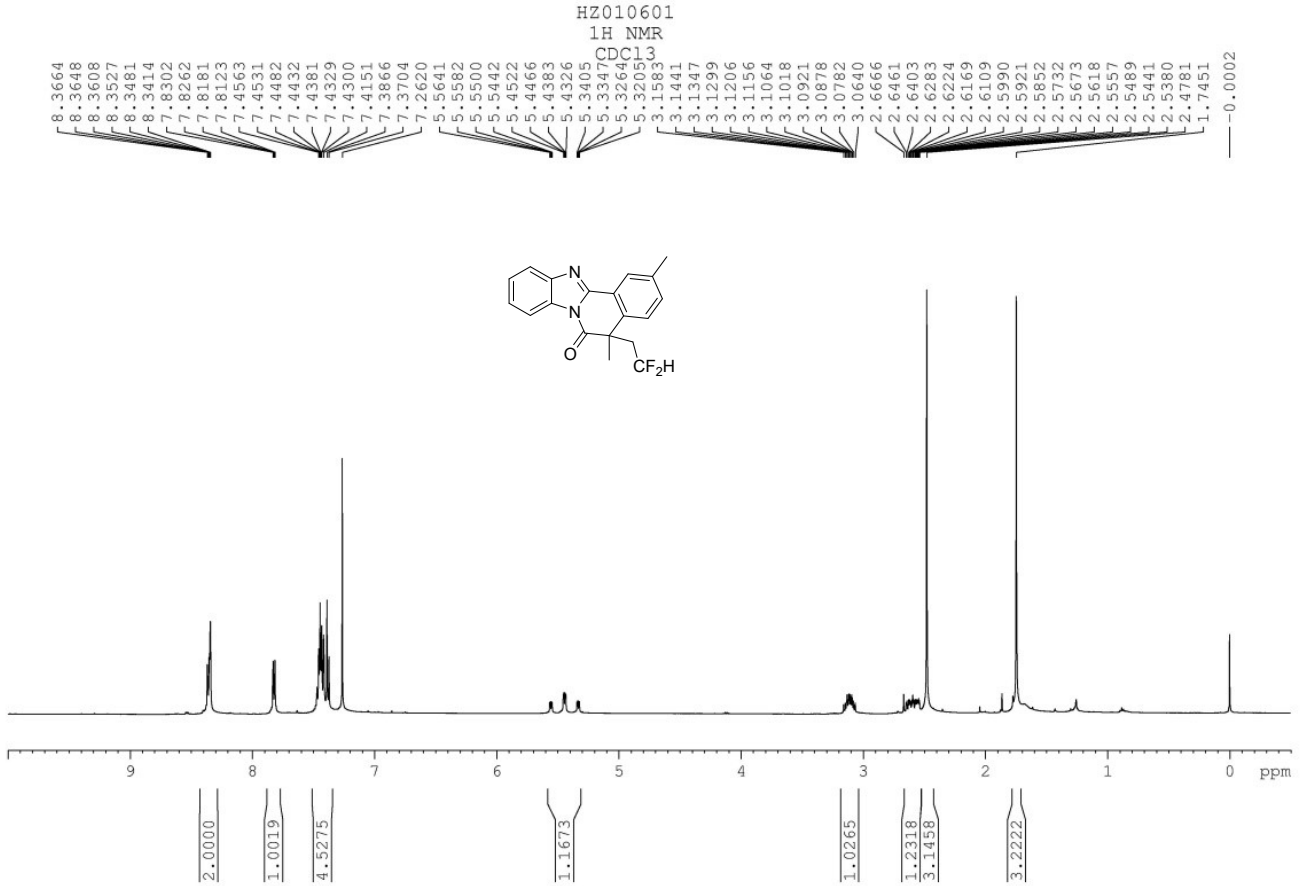


Fig. S47 ^{1}H NMR (500 MHz) spectrum of compound **3n**

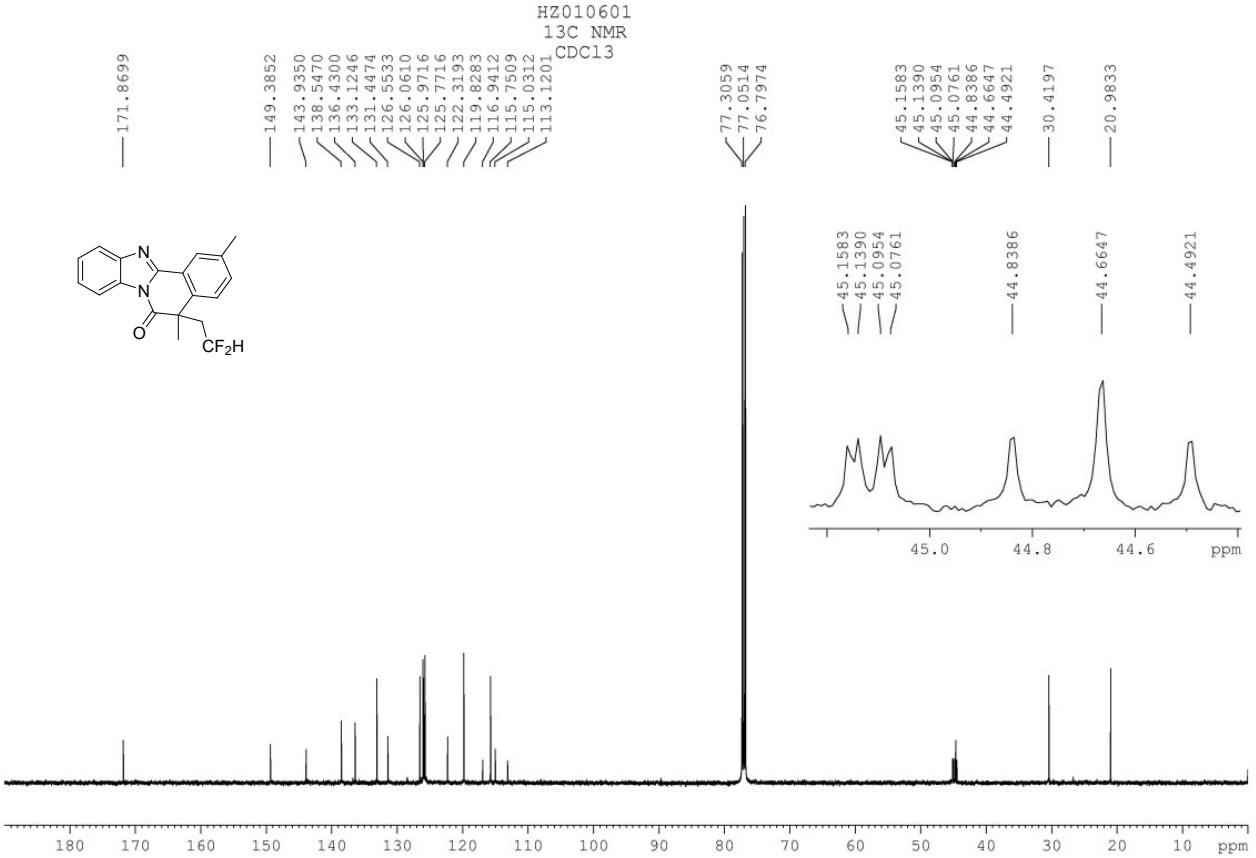


Fig. S48 ^{13}C NMR (125 MHz) spectrum of compound **3n**

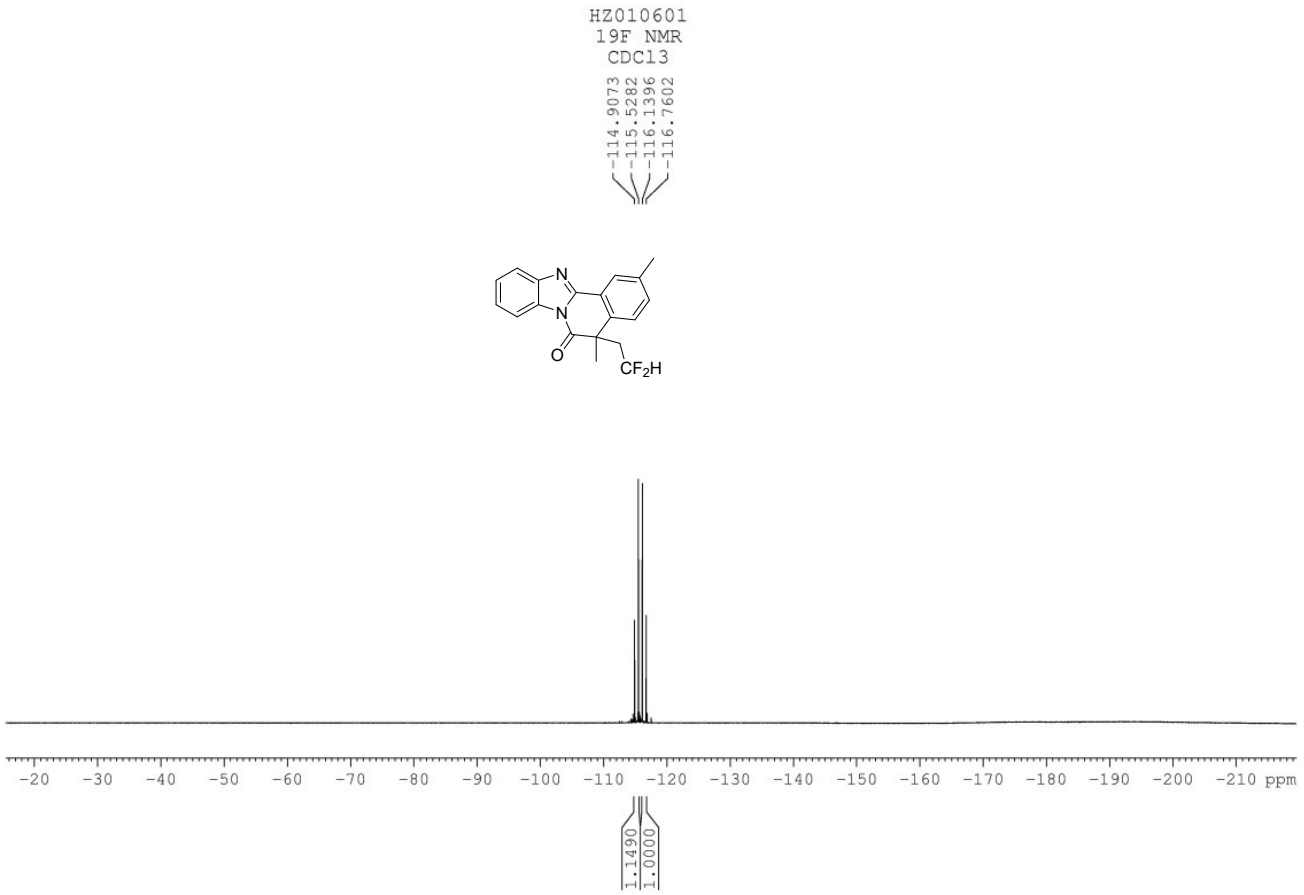


Fig. S49 ^{19}F NMR (470 MHz) spectrum of compound **3n**

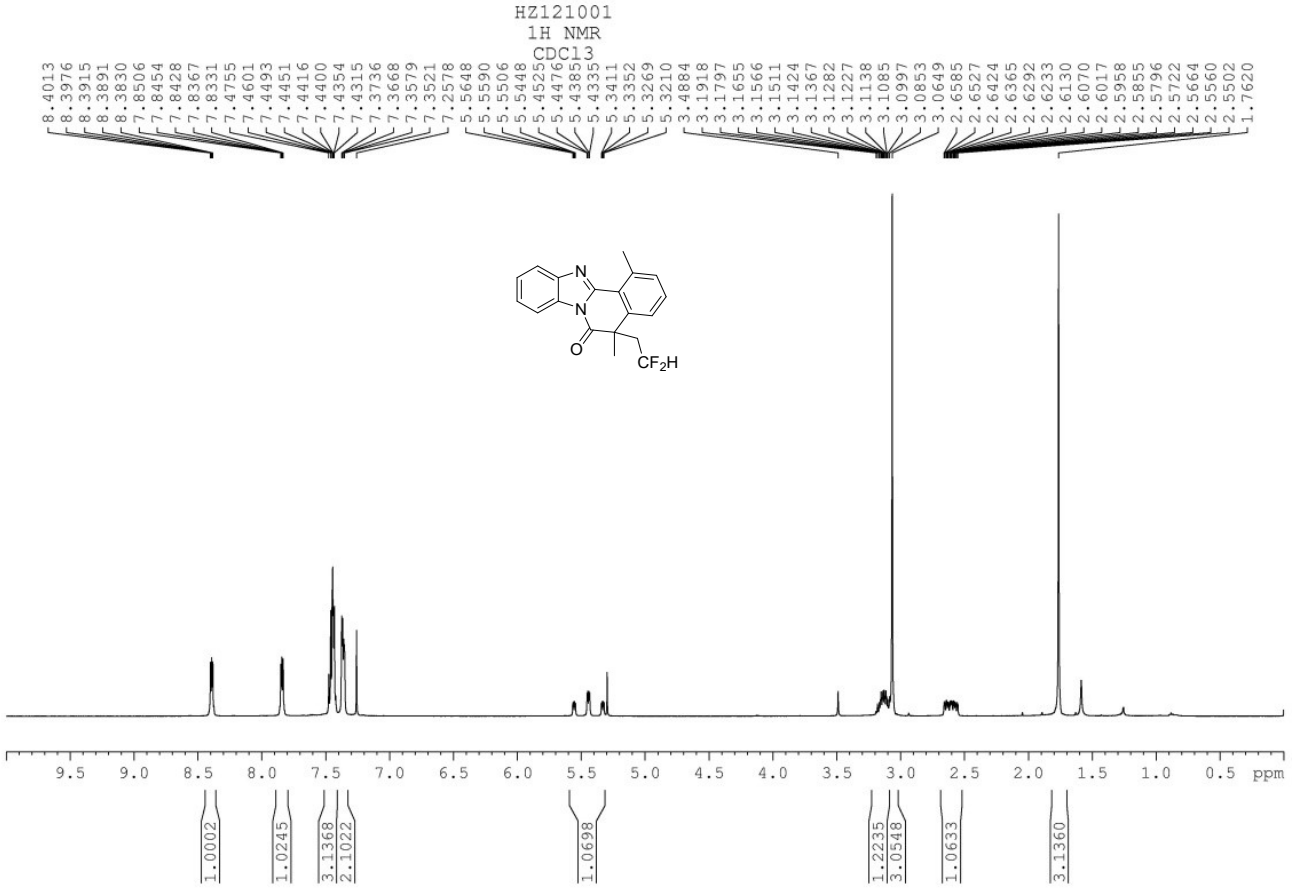


Fig. S50 ^{1}H NMR (500 MHz) spectrum of compound **3o**

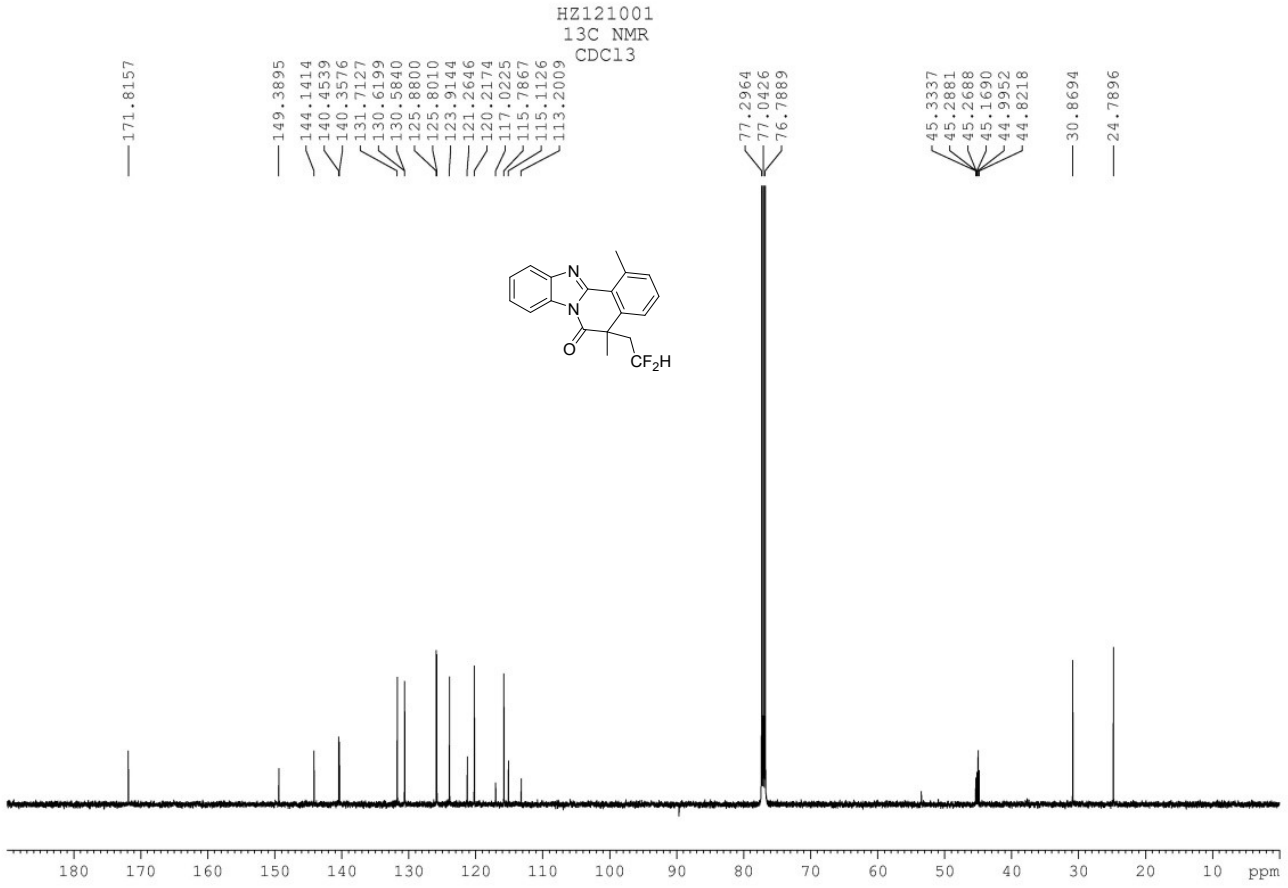


Fig. S51 ^{13}C NMR (125 MHz) spectrum of compound **3o**

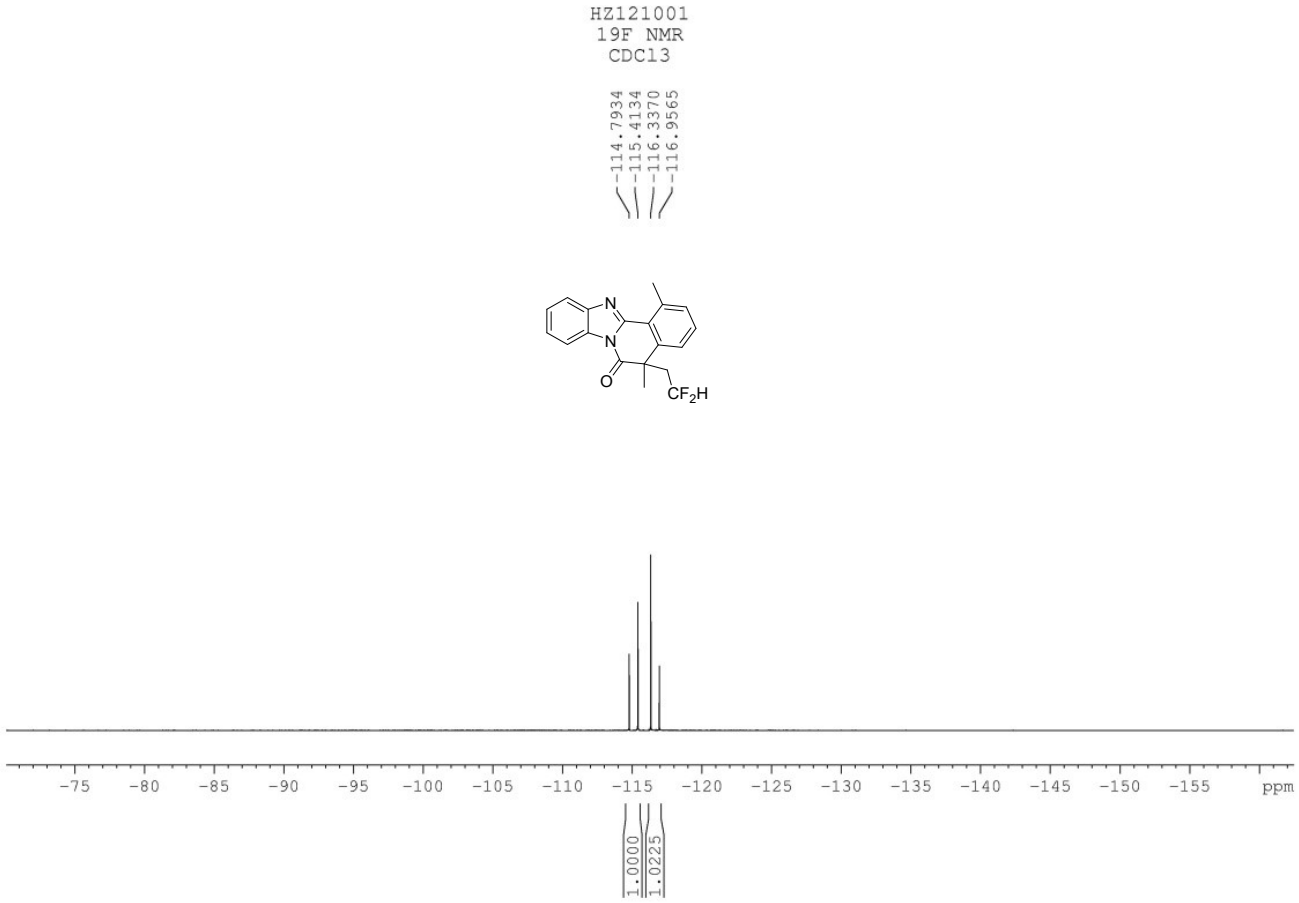


Fig. S52 ^{19}F NMR (470 MHz) spectrum of compound **3o**

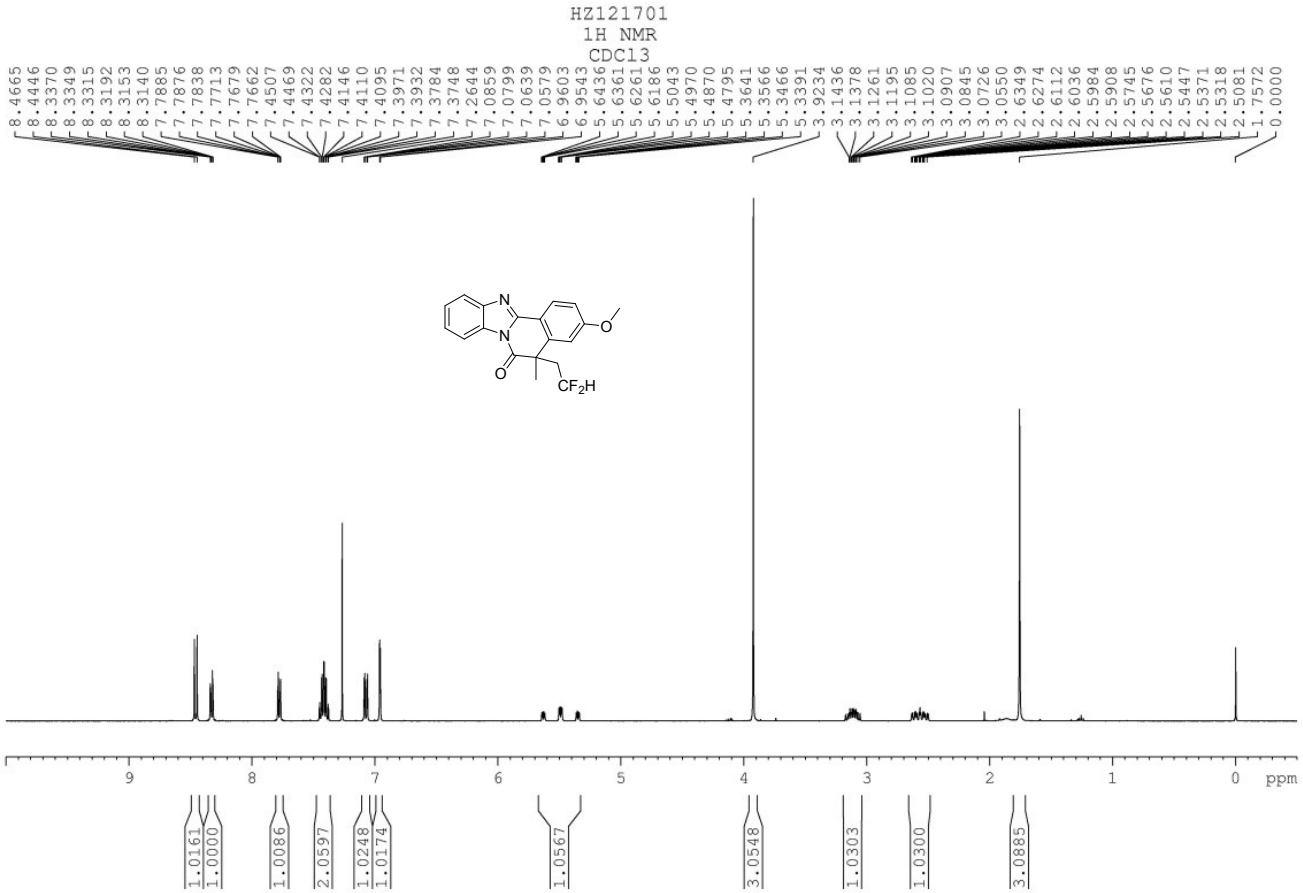


Fig. S53 ^{1}H NMR (400 MHz) spectrum of compound **3p**

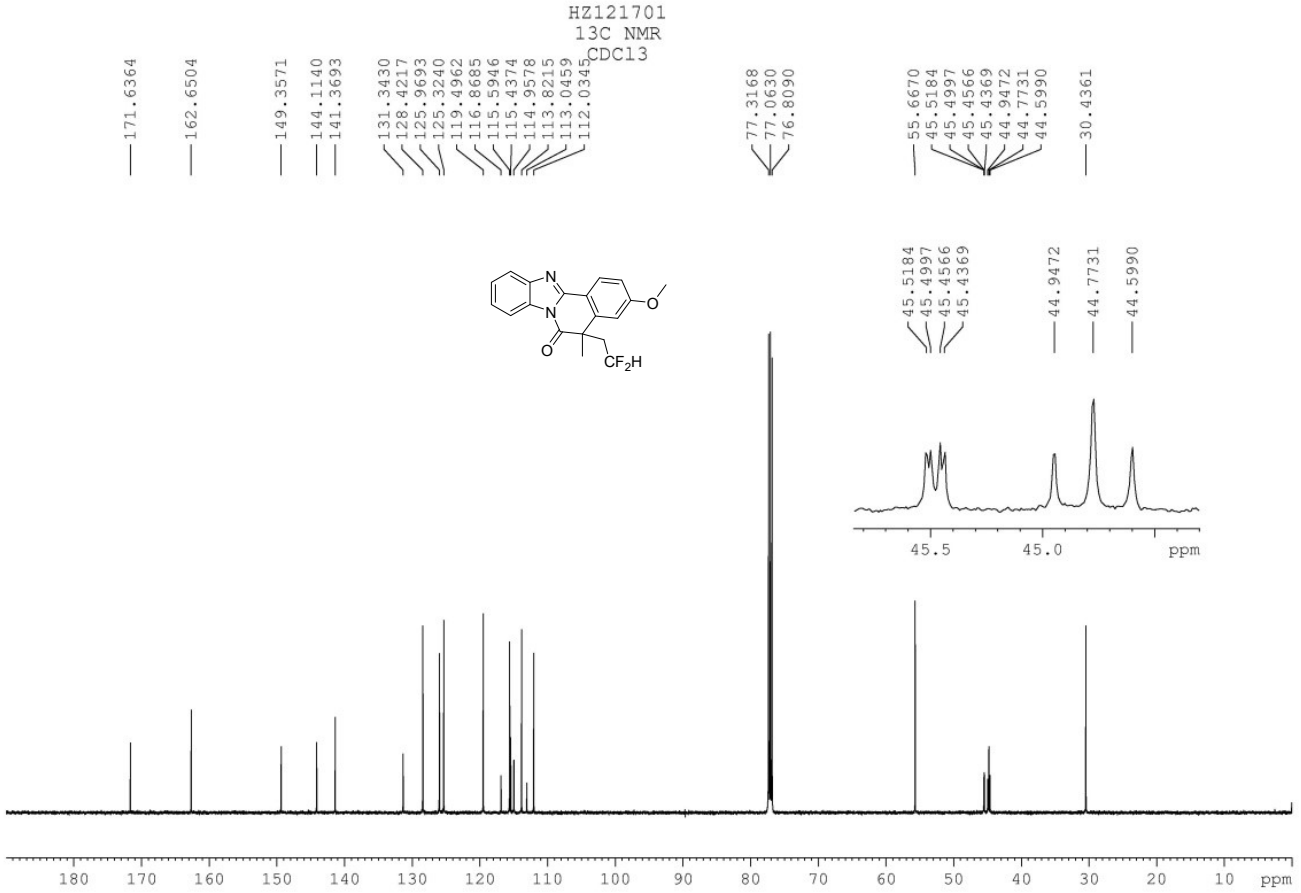


Fig. S54 ^{13}C NMR (125 MHz) spectrum of compound **3p**

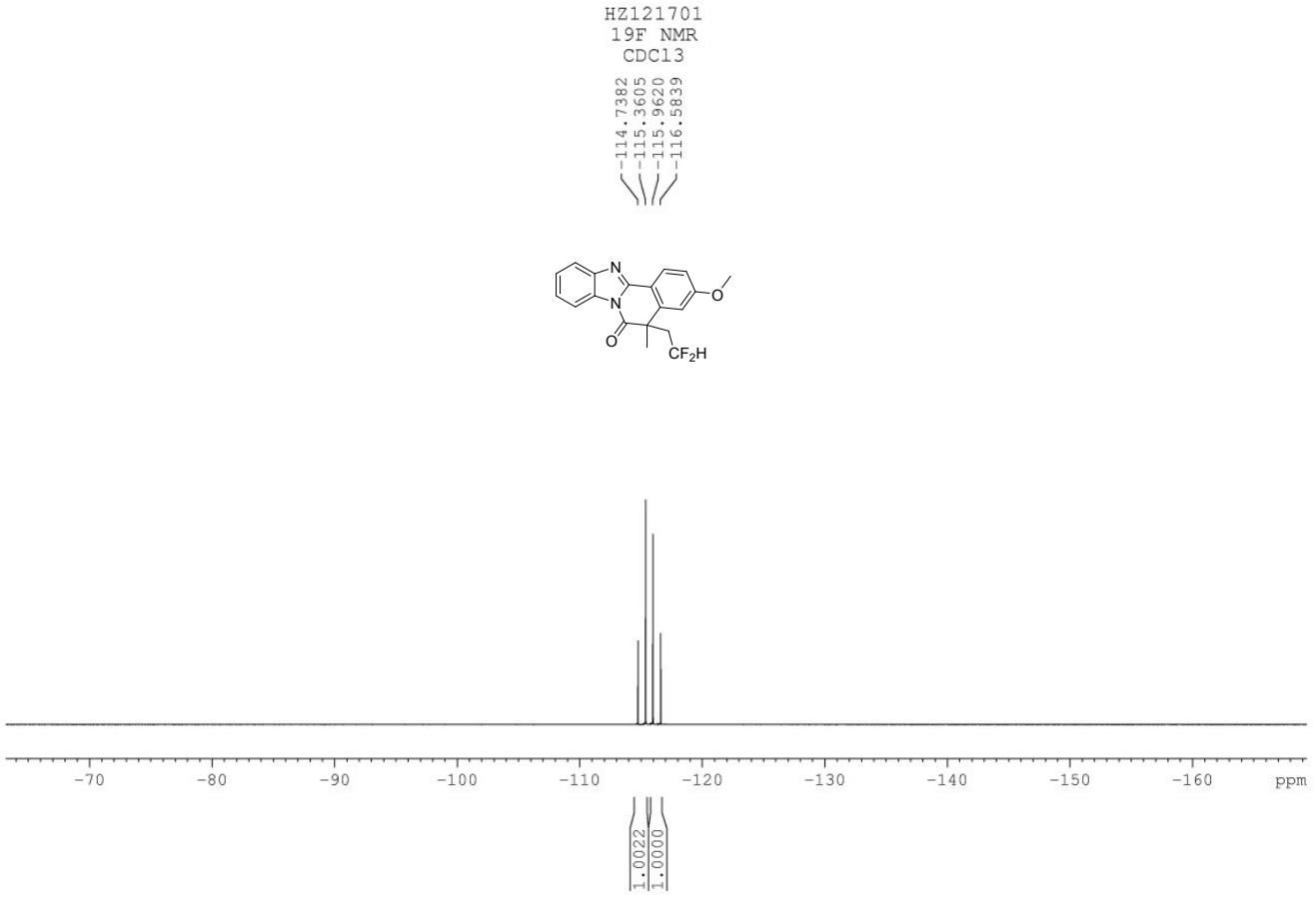


Fig. S55 ^{19}F NMR (470 MHz) spectrum of compound **3p**

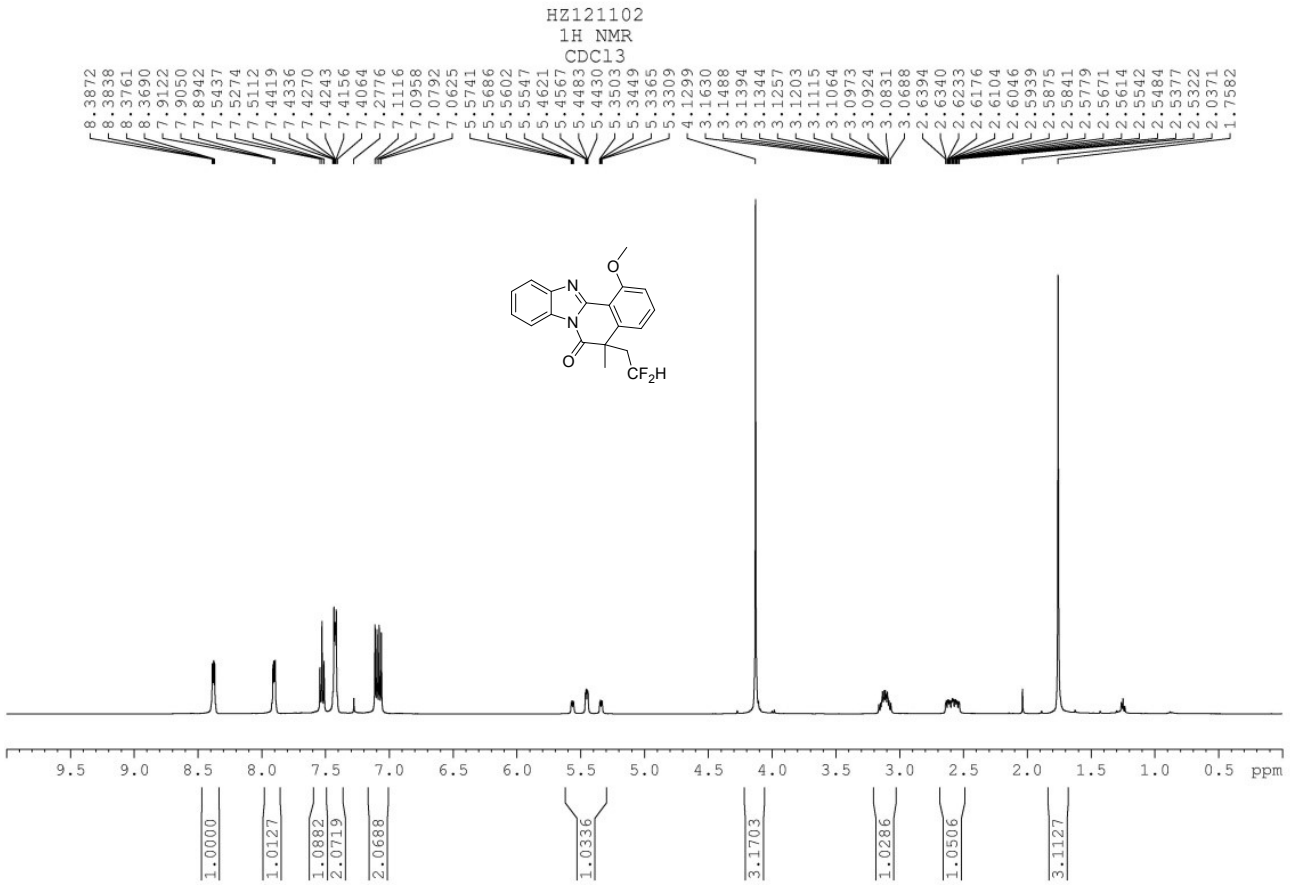


Fig. S56 ^{1}H NMR (500 MHz) spectrum of compound **3q**

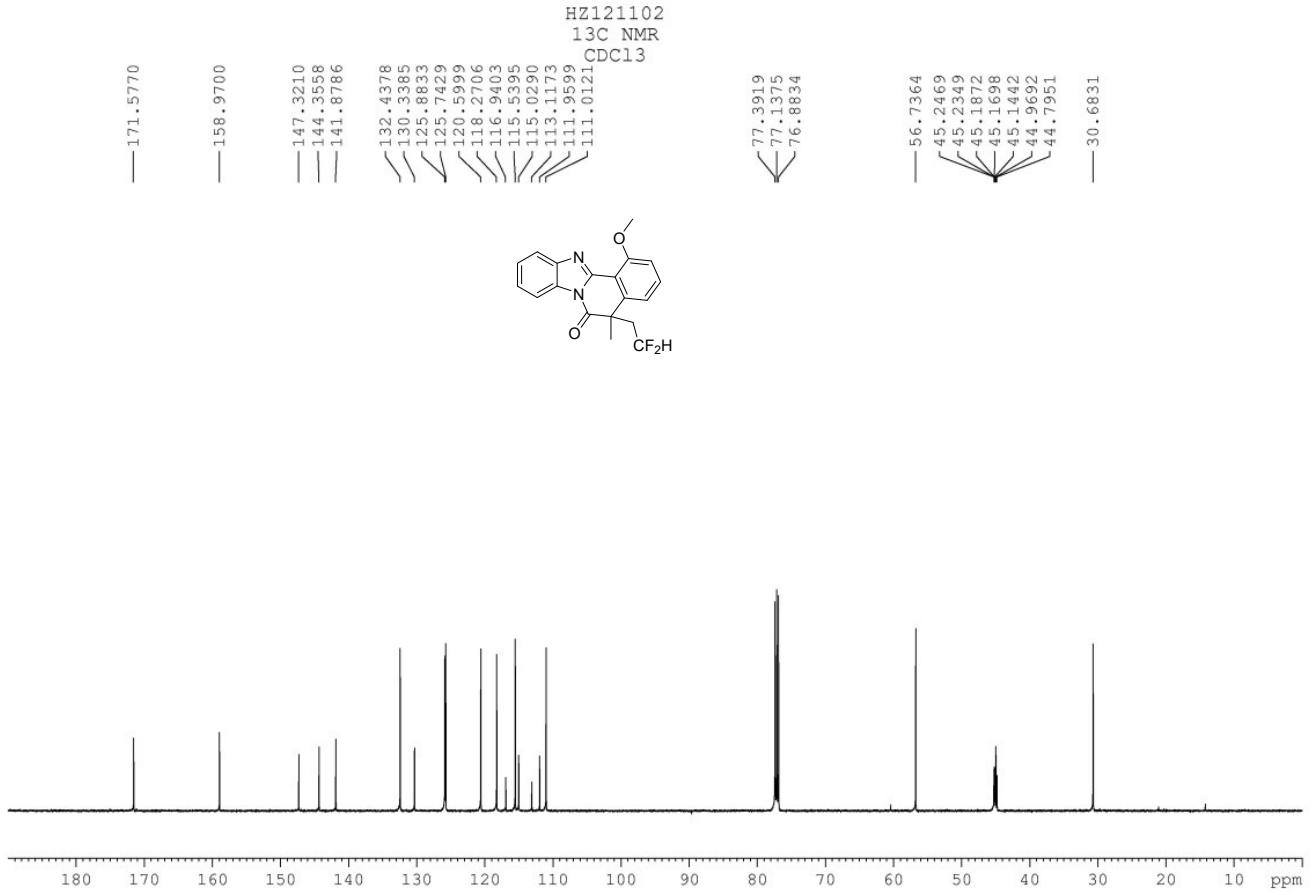


Fig. S57 ^{13}C NMR (125 MHz) spectrum of compound **3q**

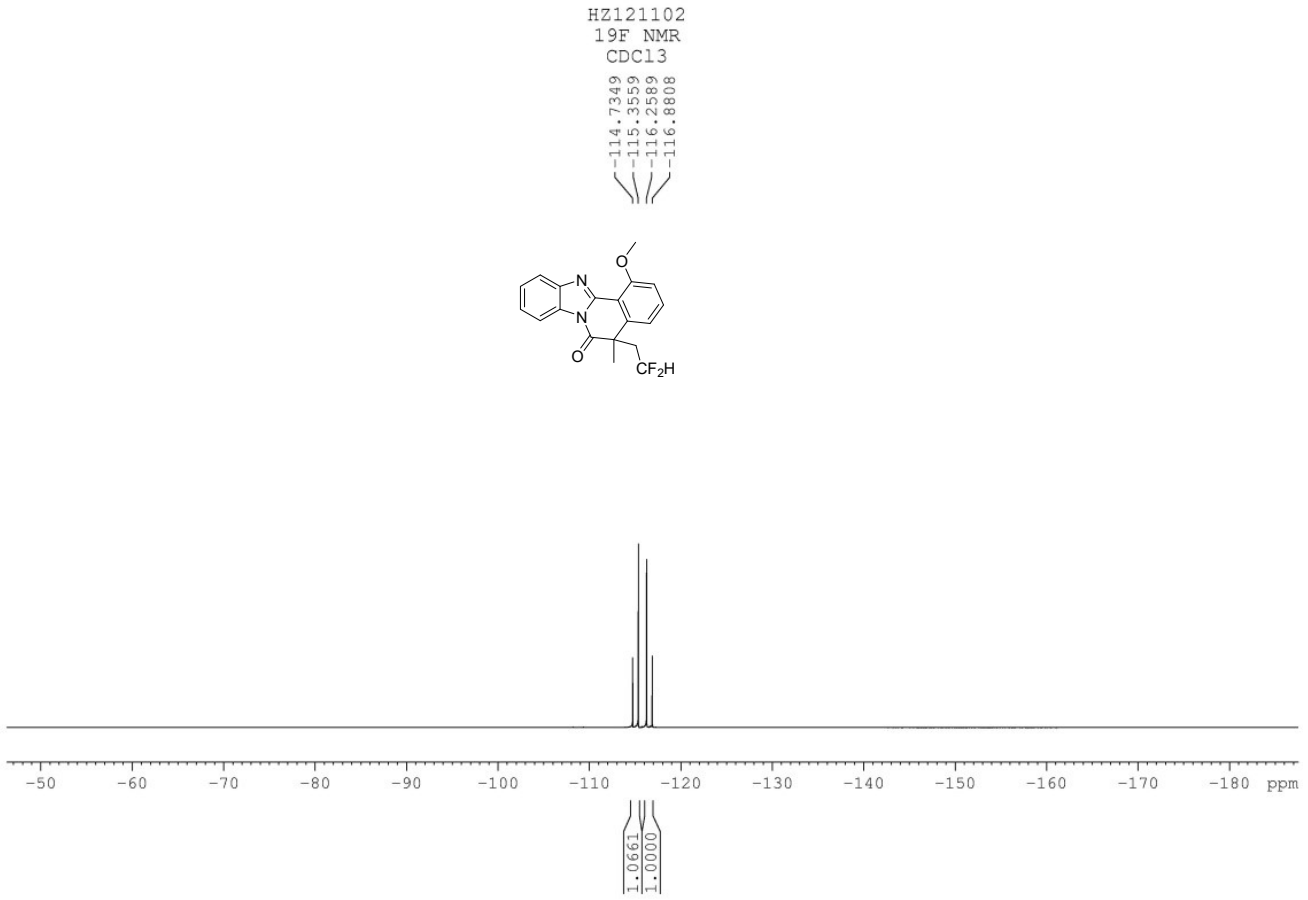


Fig. S58 ^{19}F NMR (470 MHz) spectrum of compound **3q**

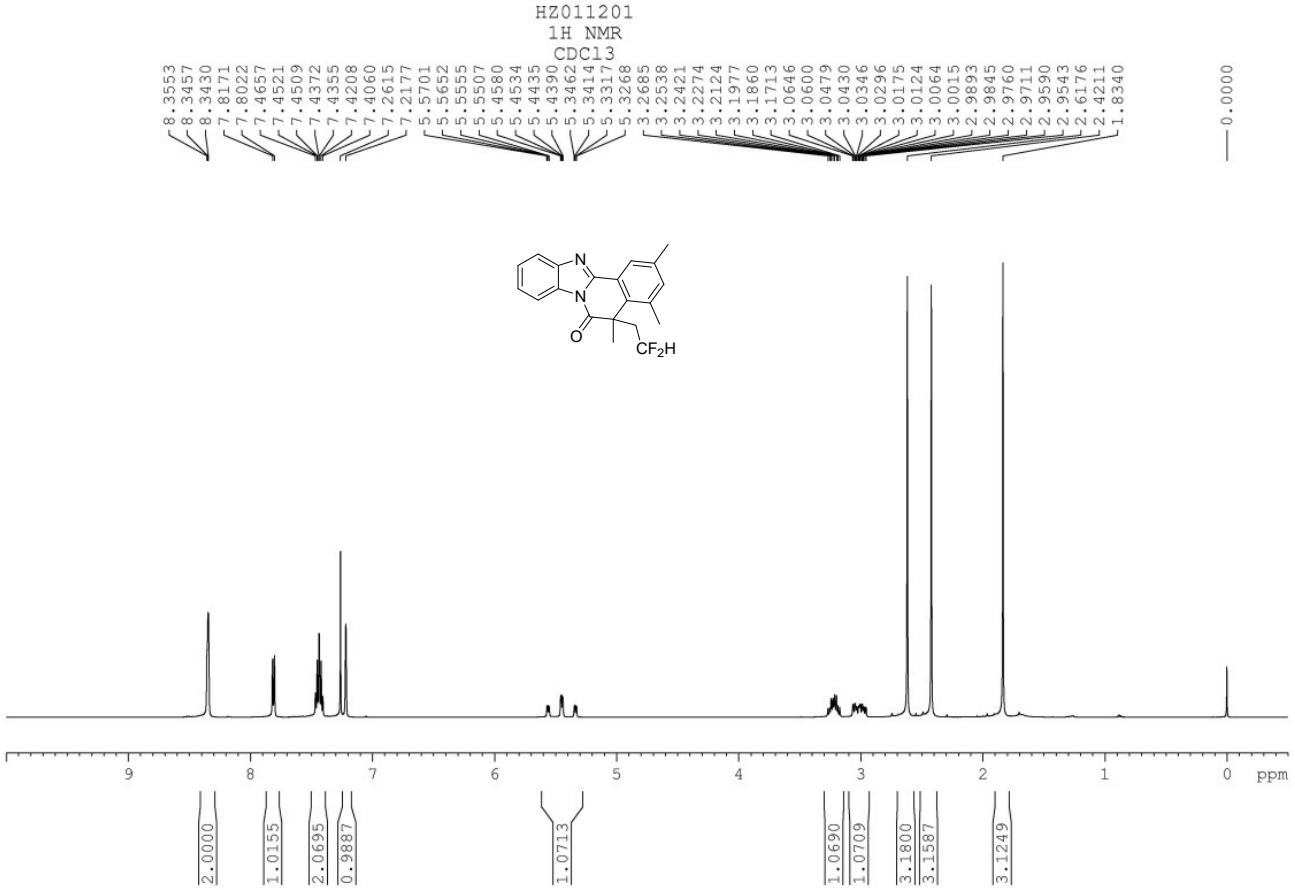


Fig. S59 ^{1}H NMR (500 MHz) spectrum of compound **3r**

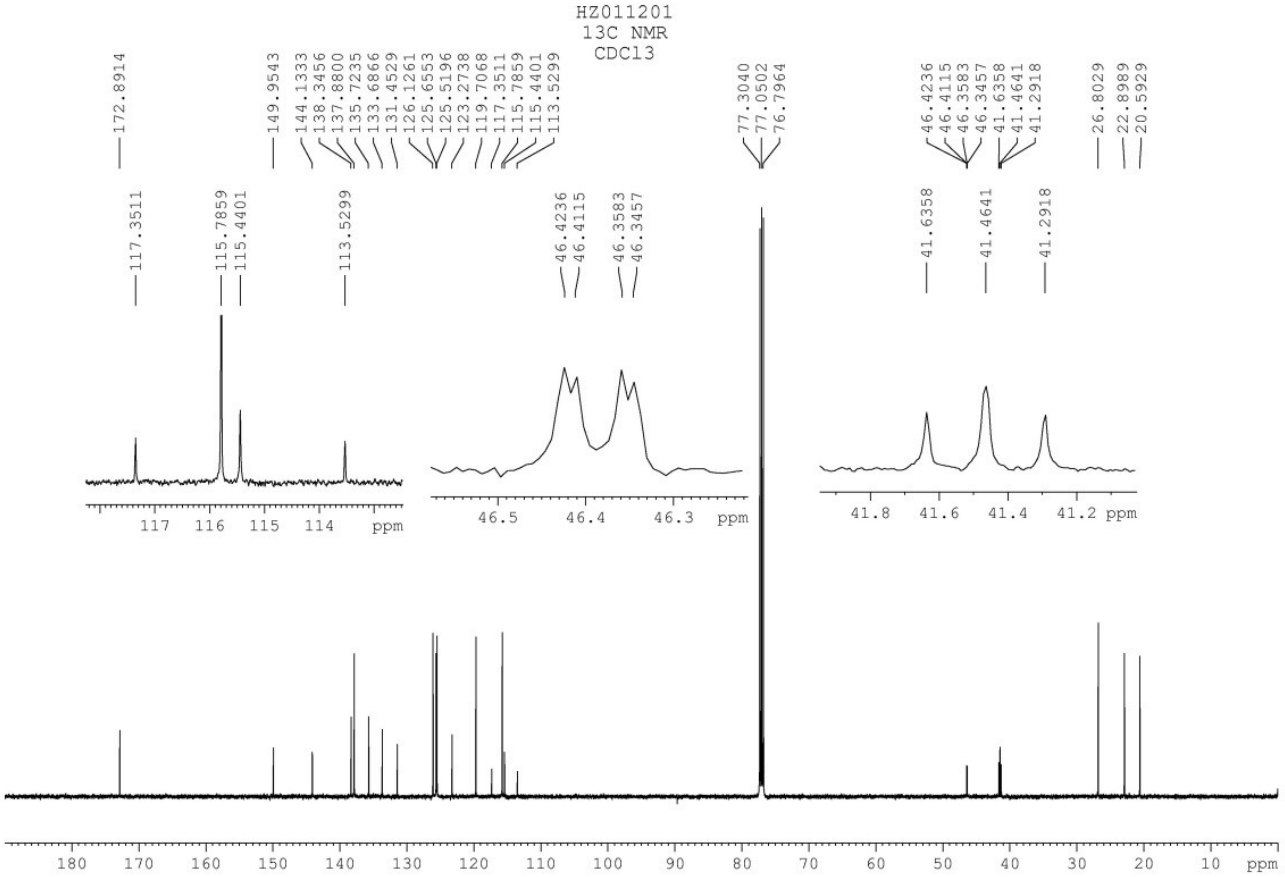


Fig. S60 ^{13}C NMR (125 MHz) spectrum of compound **3r**

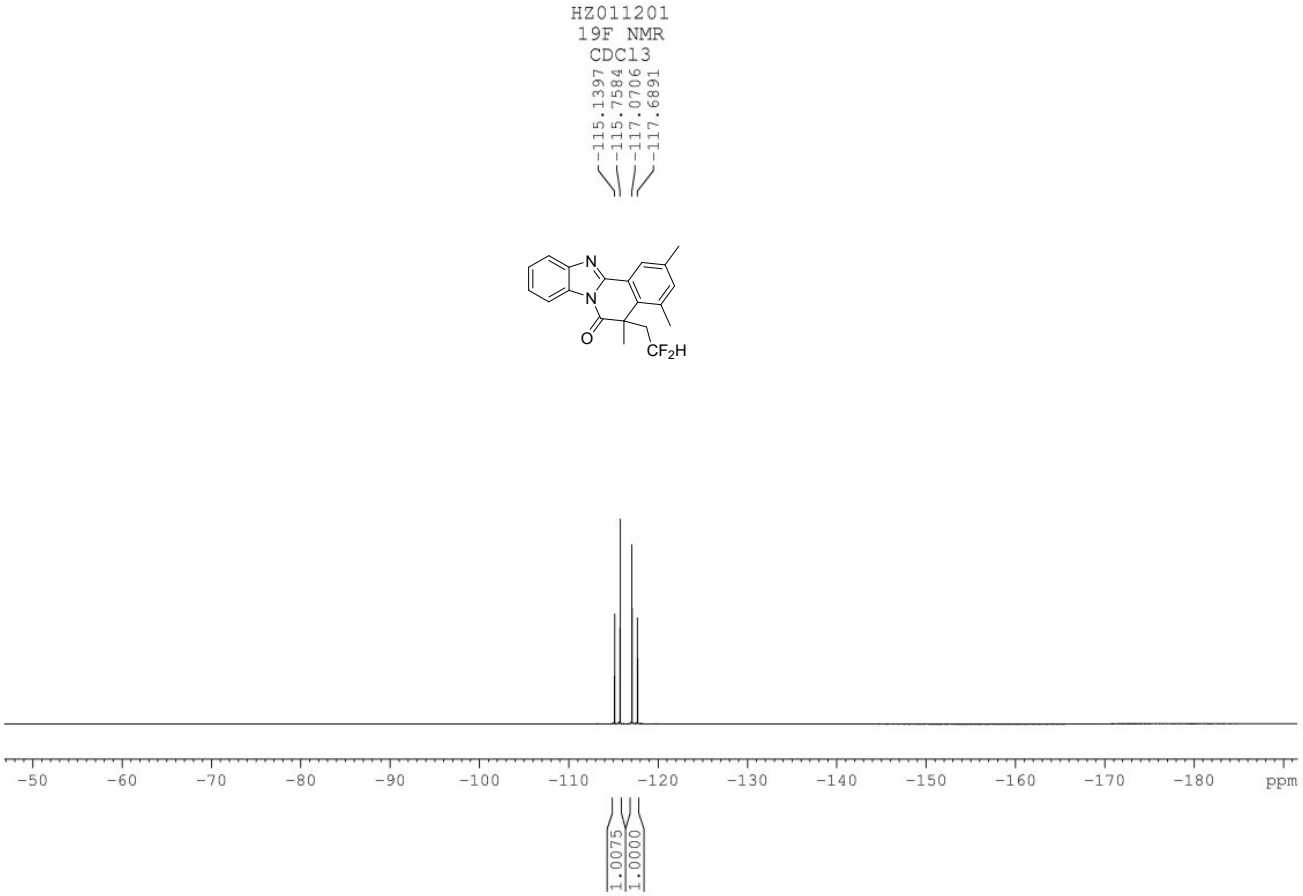


Fig. S61 ^{19}F NMR (470 MHz) spectrum of compound **3r**

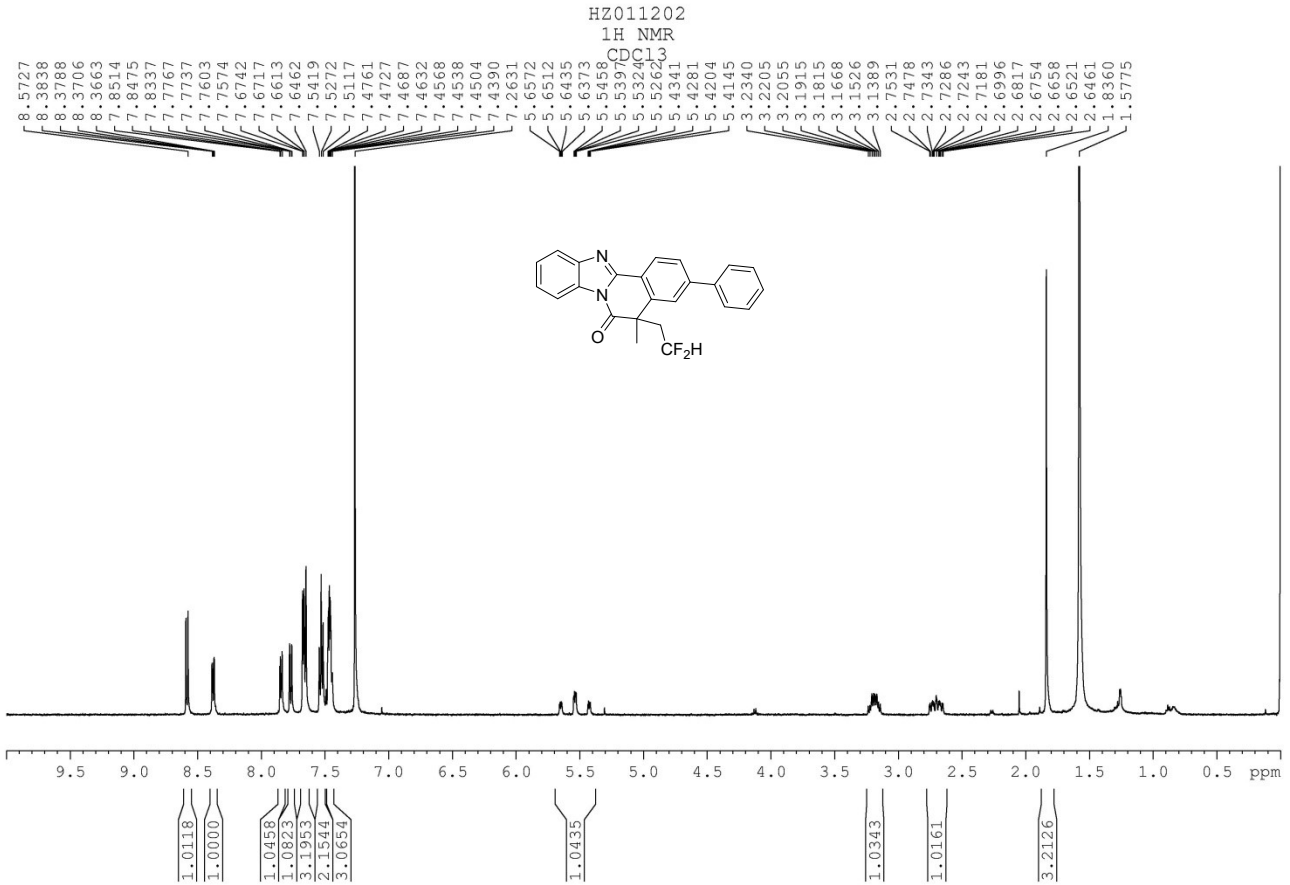


Fig. S62 ^{1}H NMR (500 MHz) spectrum of compound **3s**

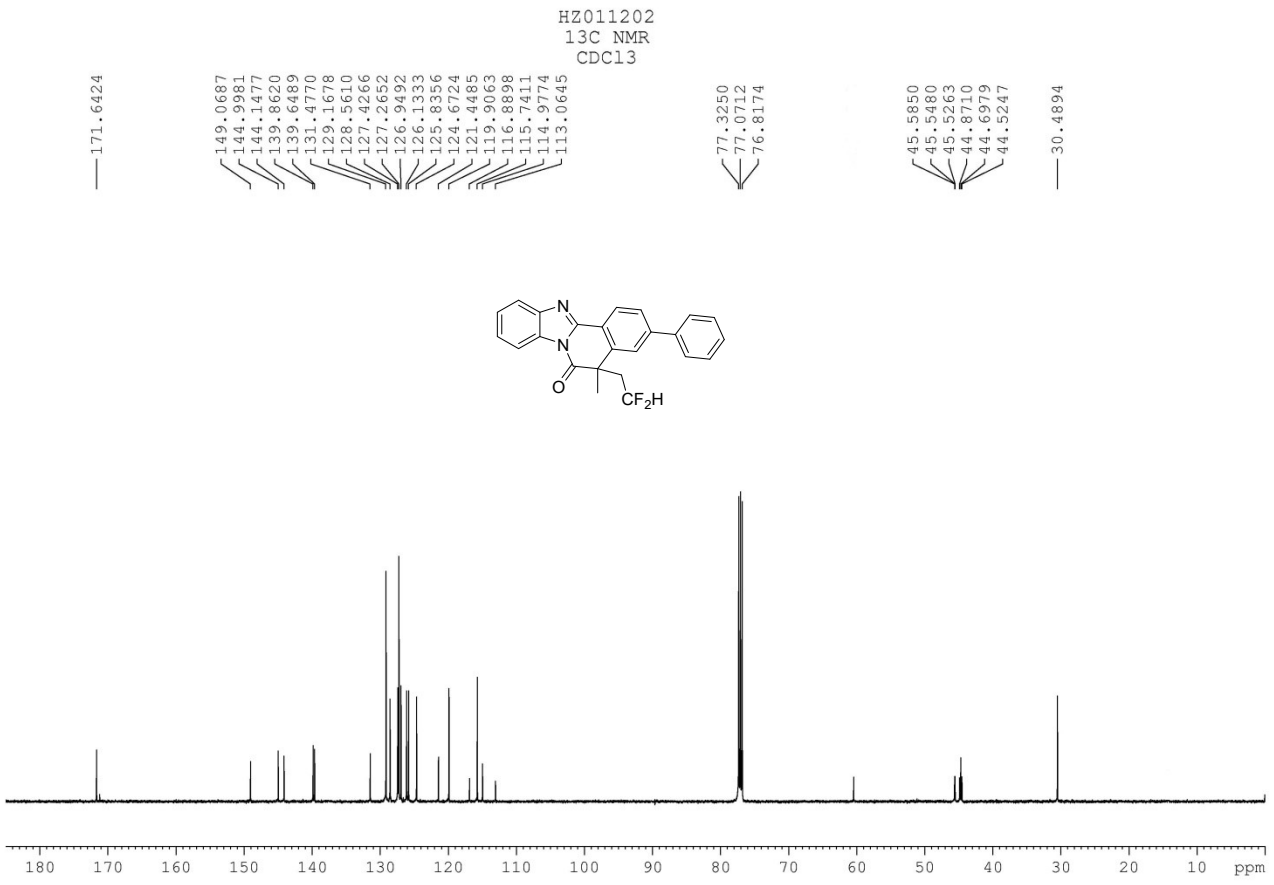


Fig. S63 ^{13}C NMR (125 MHz) spectrum of compound **3s**

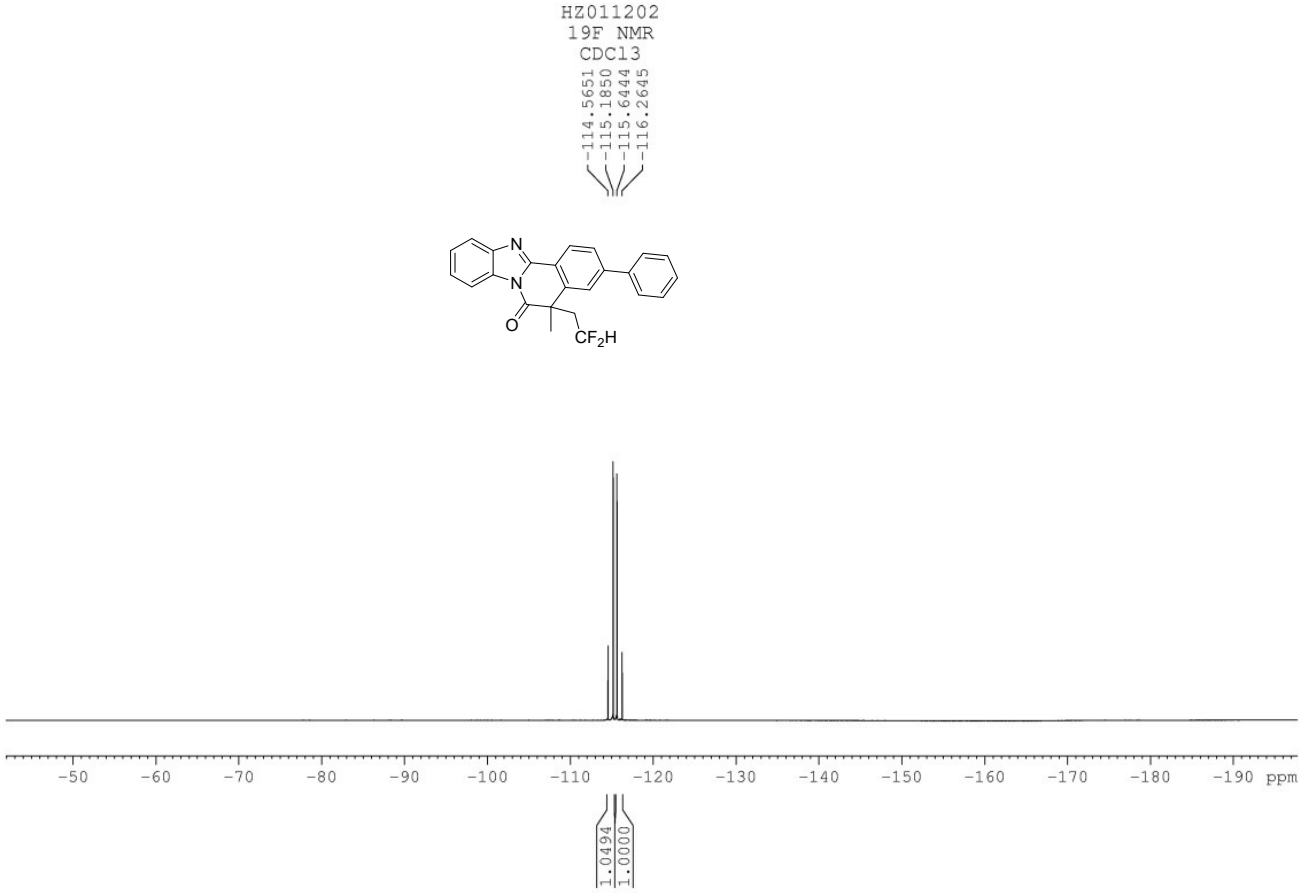


Fig. S64 ^{19}F NMR (470 MHz) spectrum of compound **3s**

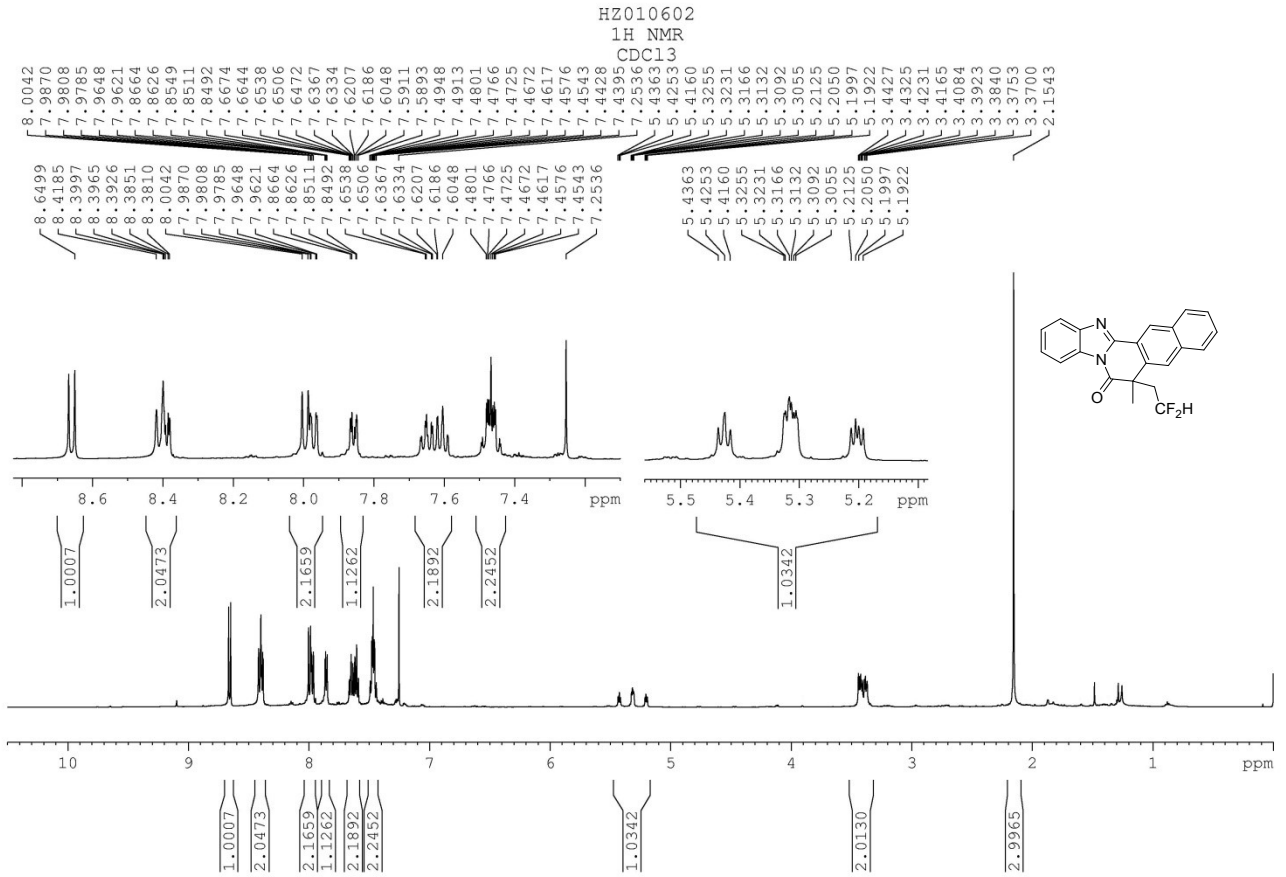


Fig. S65 ^{1}H NMR (500 MHz) spectrum of compound **3t**

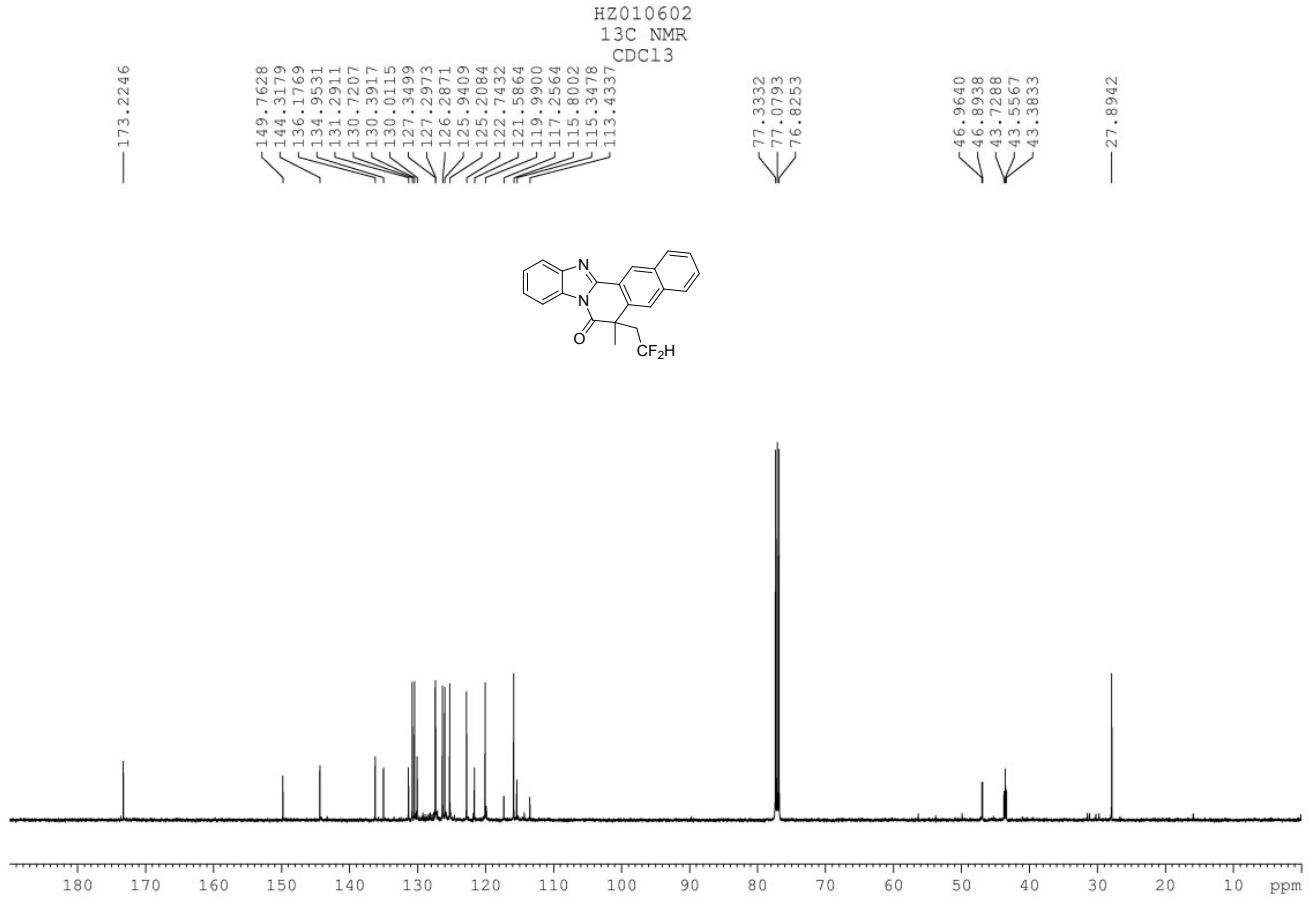


Fig. S66 ^{13}C NMR (125 MHz) spectrum of compound **3t**

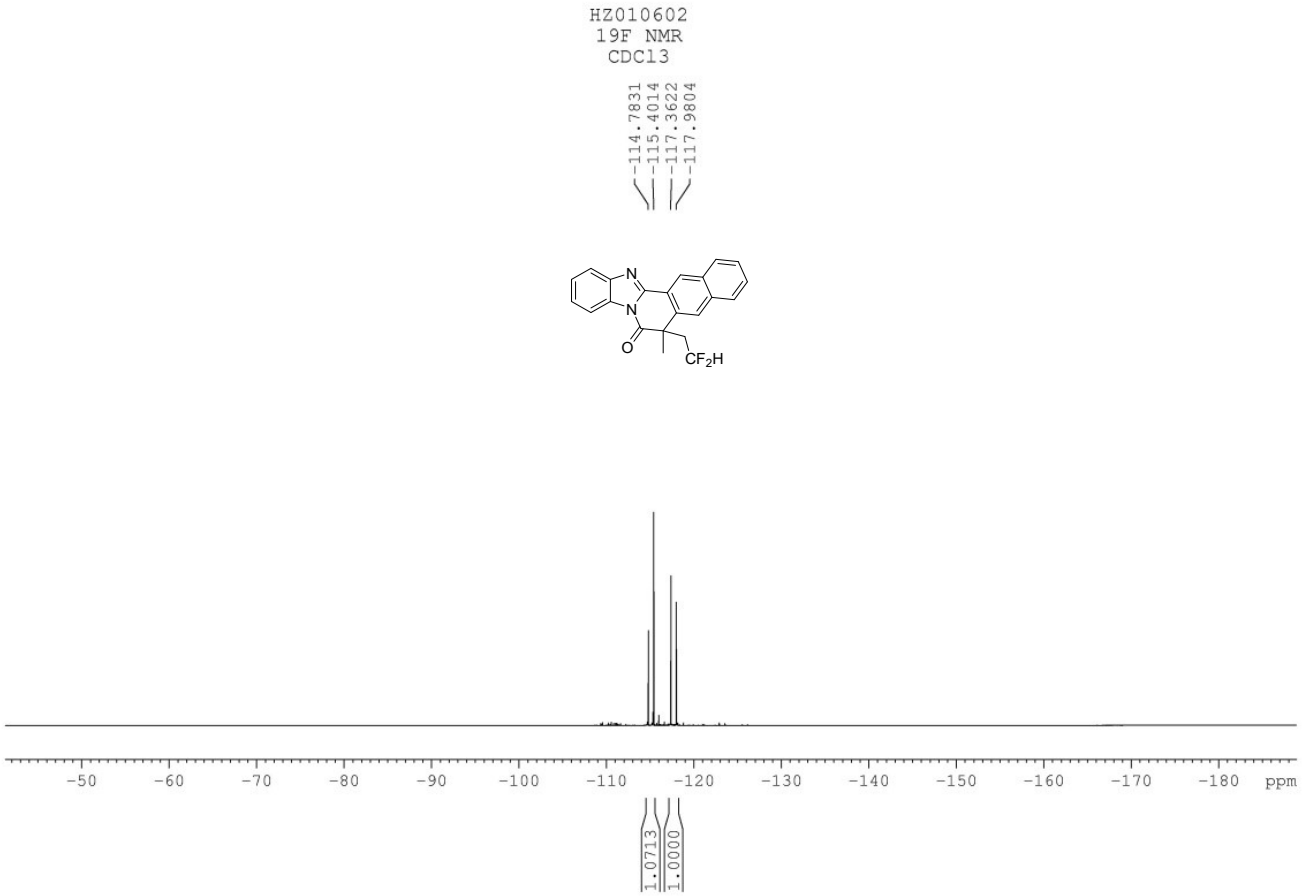


Fig. S67 ^{19}F NMR (470 MHz) spectrum of compound **3t**

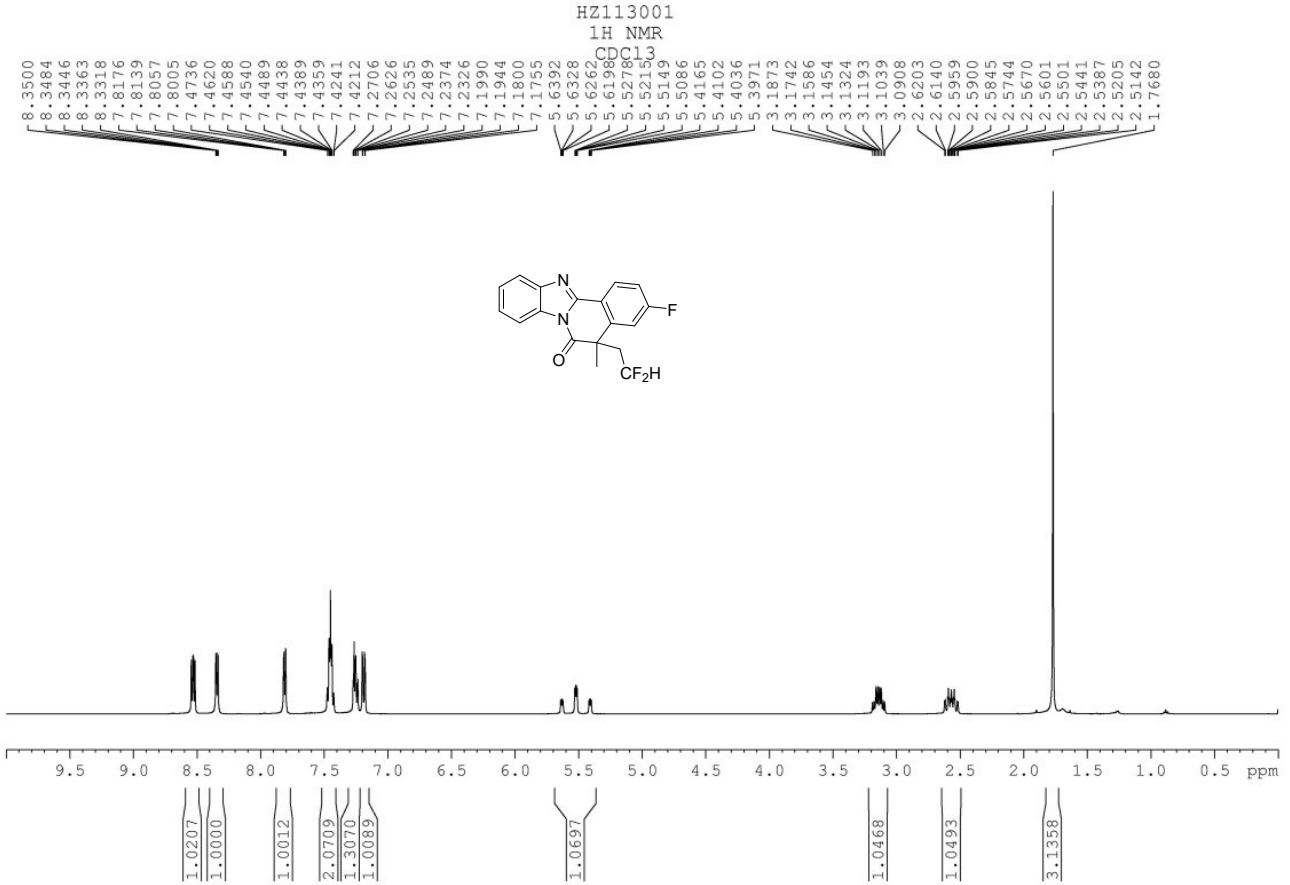


Fig. S68 ^{1}H NMR (500 MHz) spectrum of compound **3u**

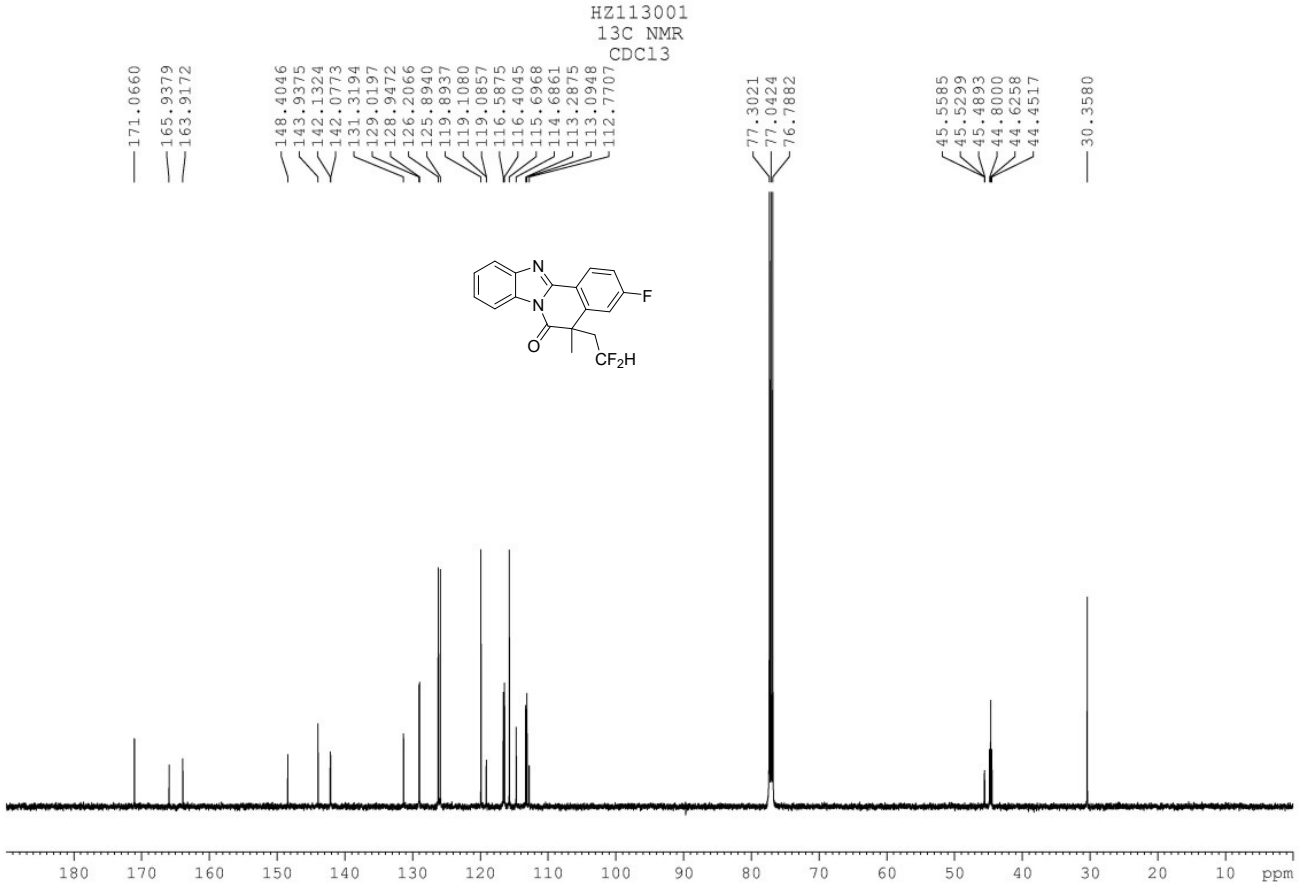


Fig. S69 ^{13}C NMR (125 MHz) spectrum of compound **3u**

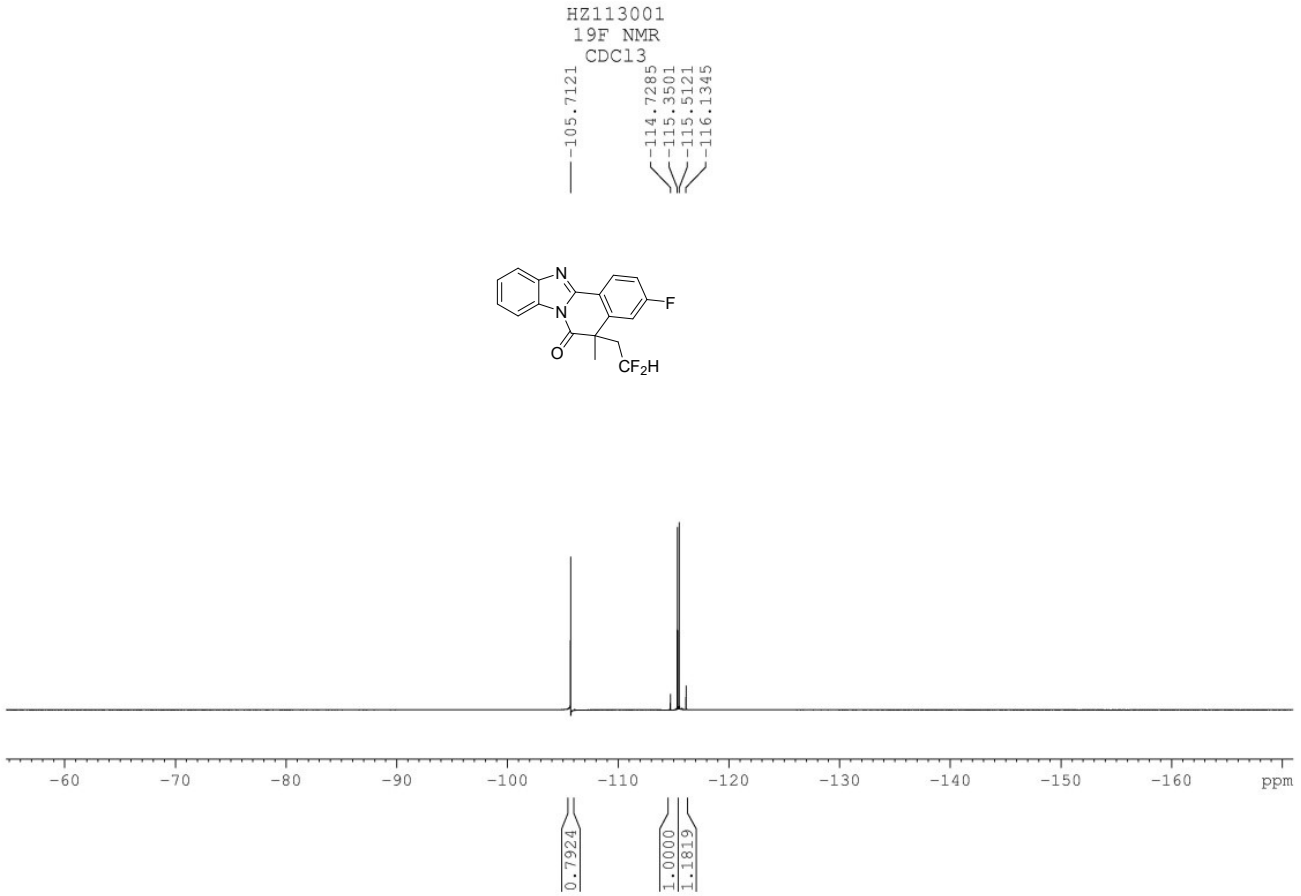


Fig. S70 ^{19}F NMR (470 MHz) spectrum of compound **3u**

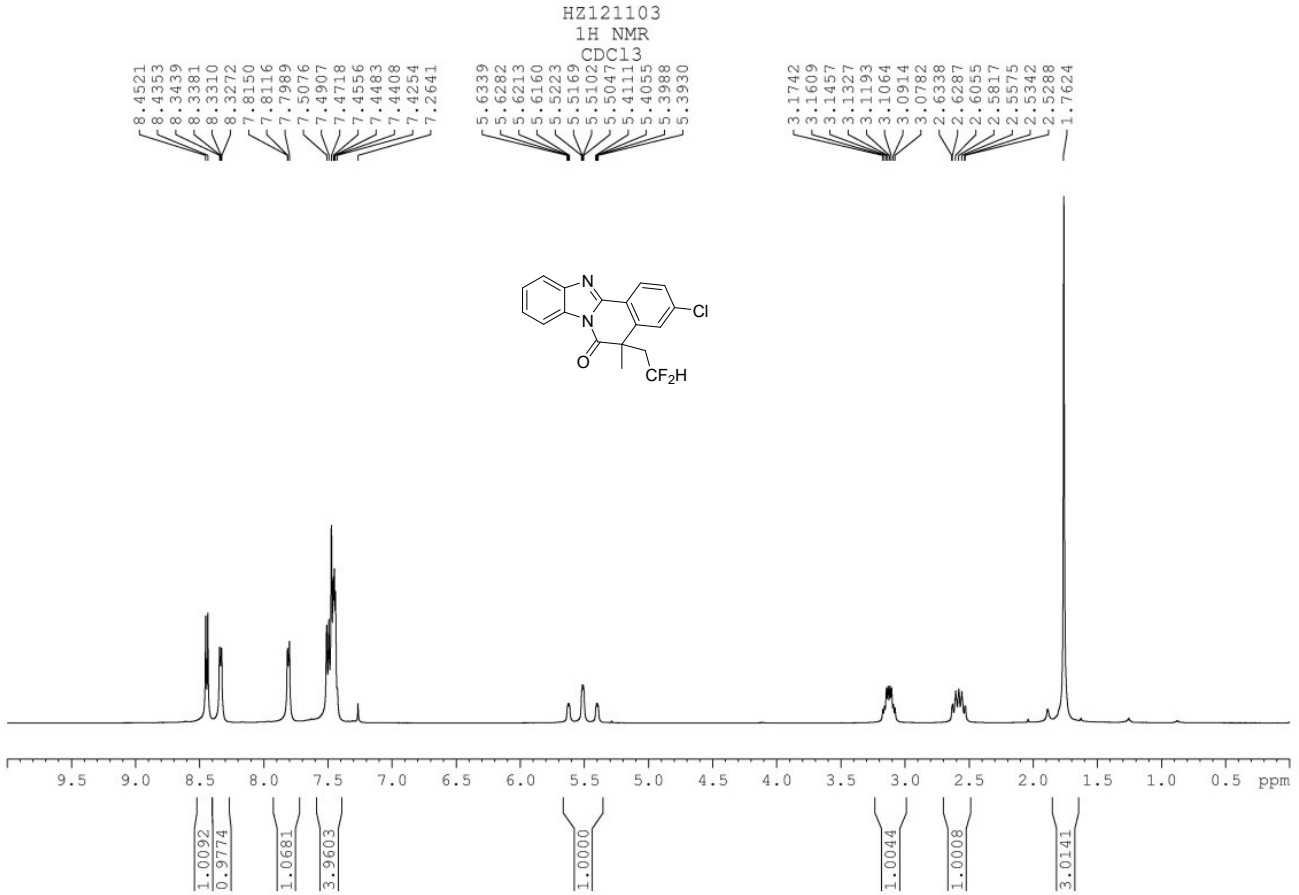


Fig. S71 ^{1}H NMR (500 MHz) spectrum of compound **3v**

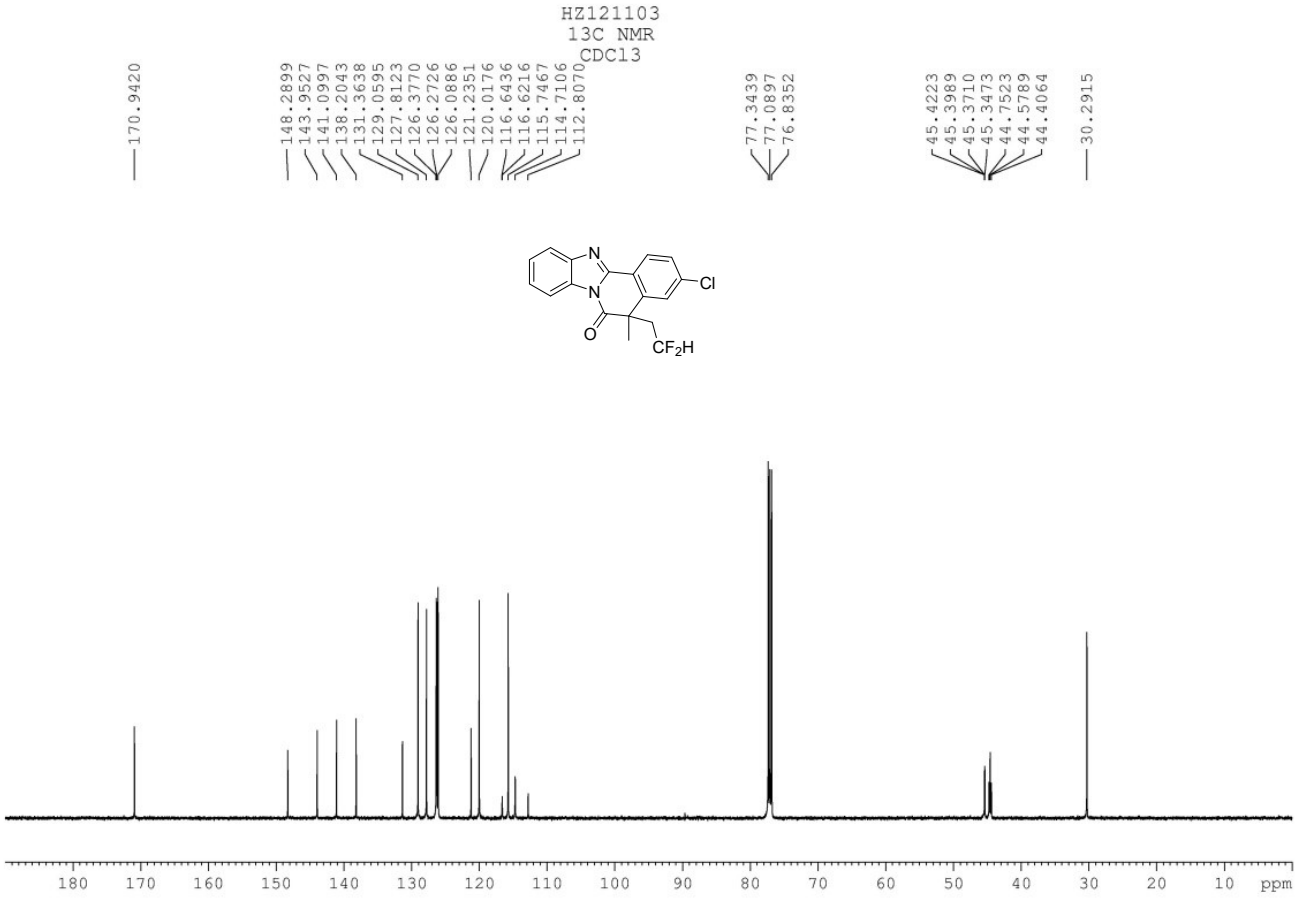


Fig. S72 ^{13}C NMR (125 MHz) spectrum of compound **3v**

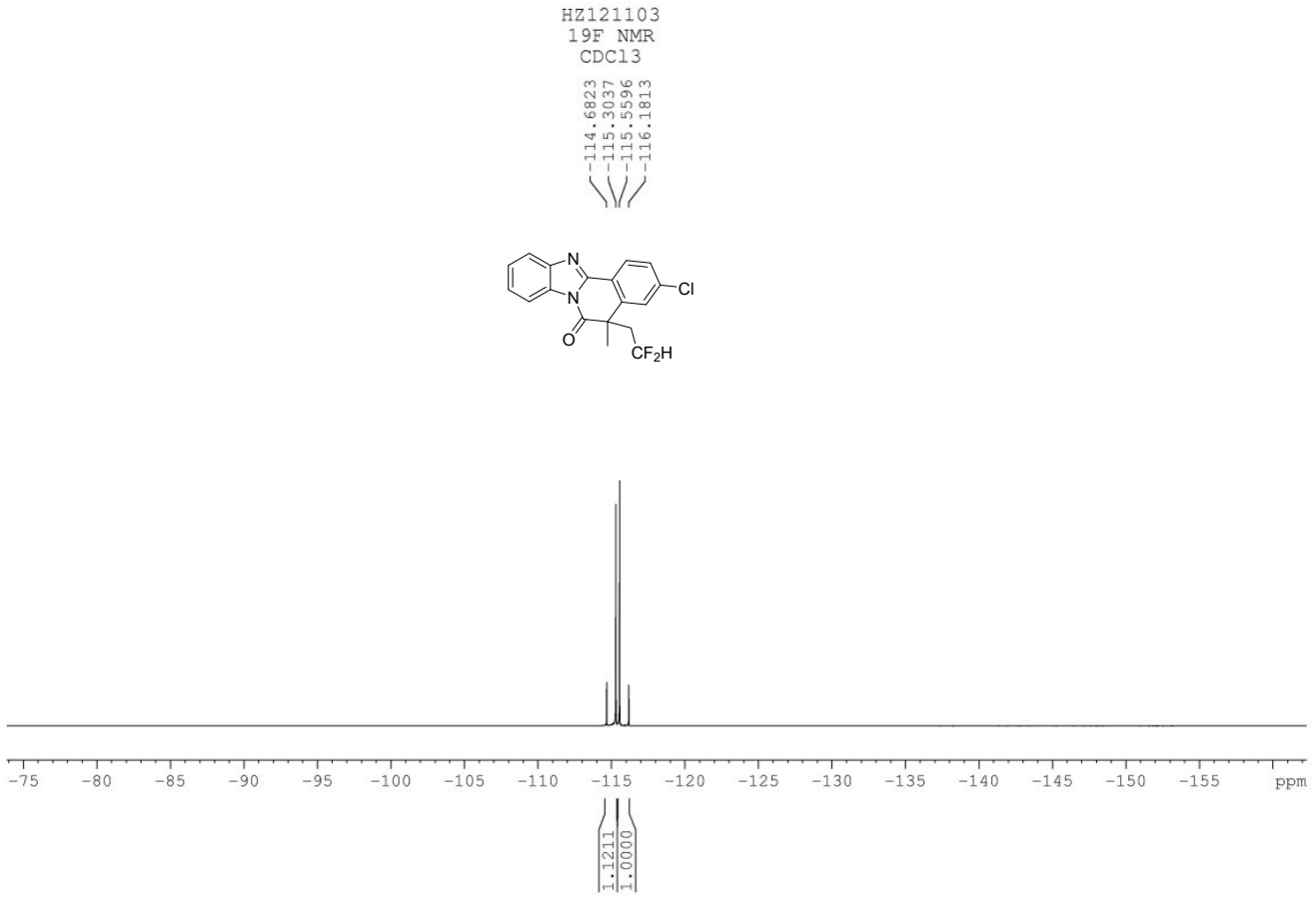


Fig. S73 ^{19}F NMR (470 MHz) spectrum of compound **3v**

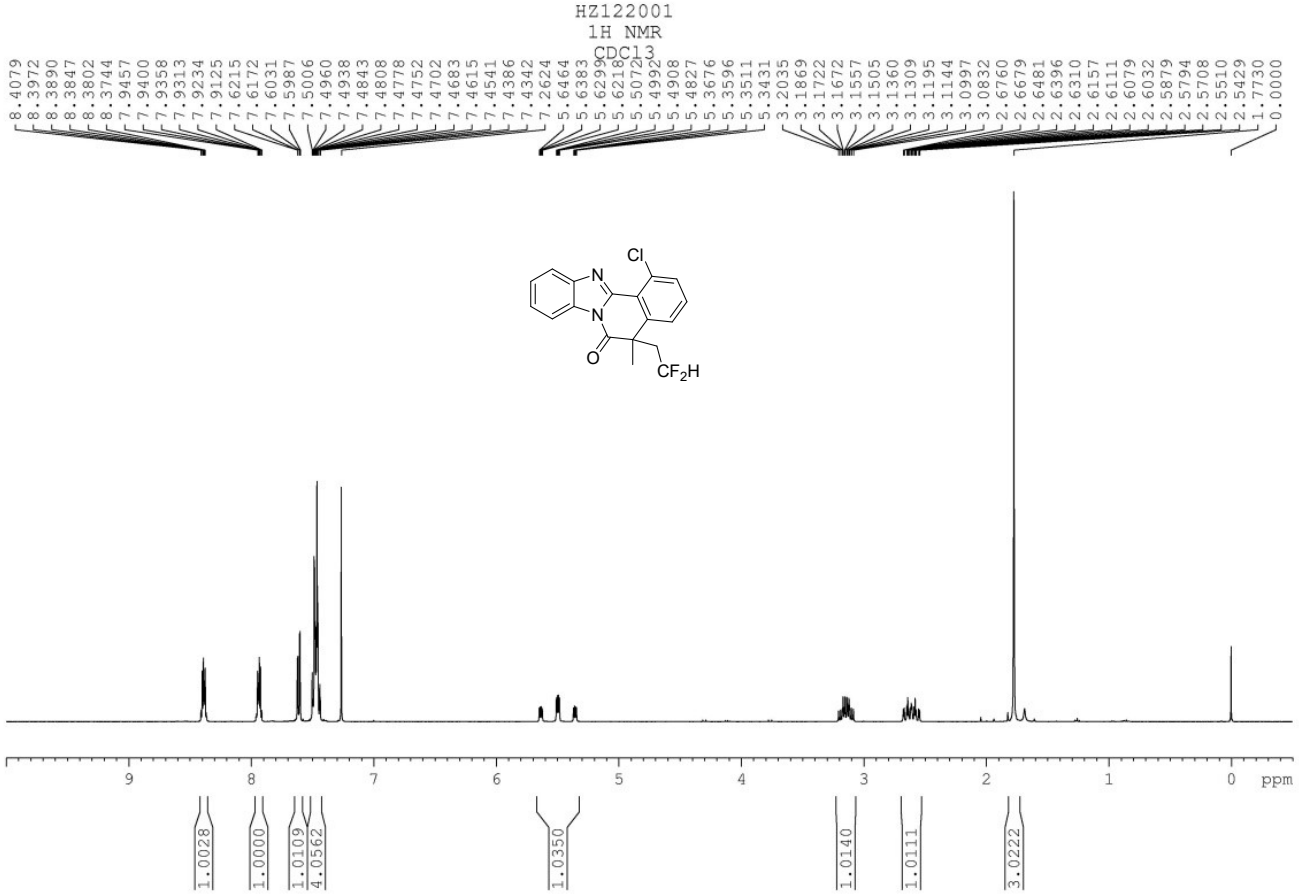


Fig. S74 ^{1}H NMR (400 MHz) spectrum of compound **3w**

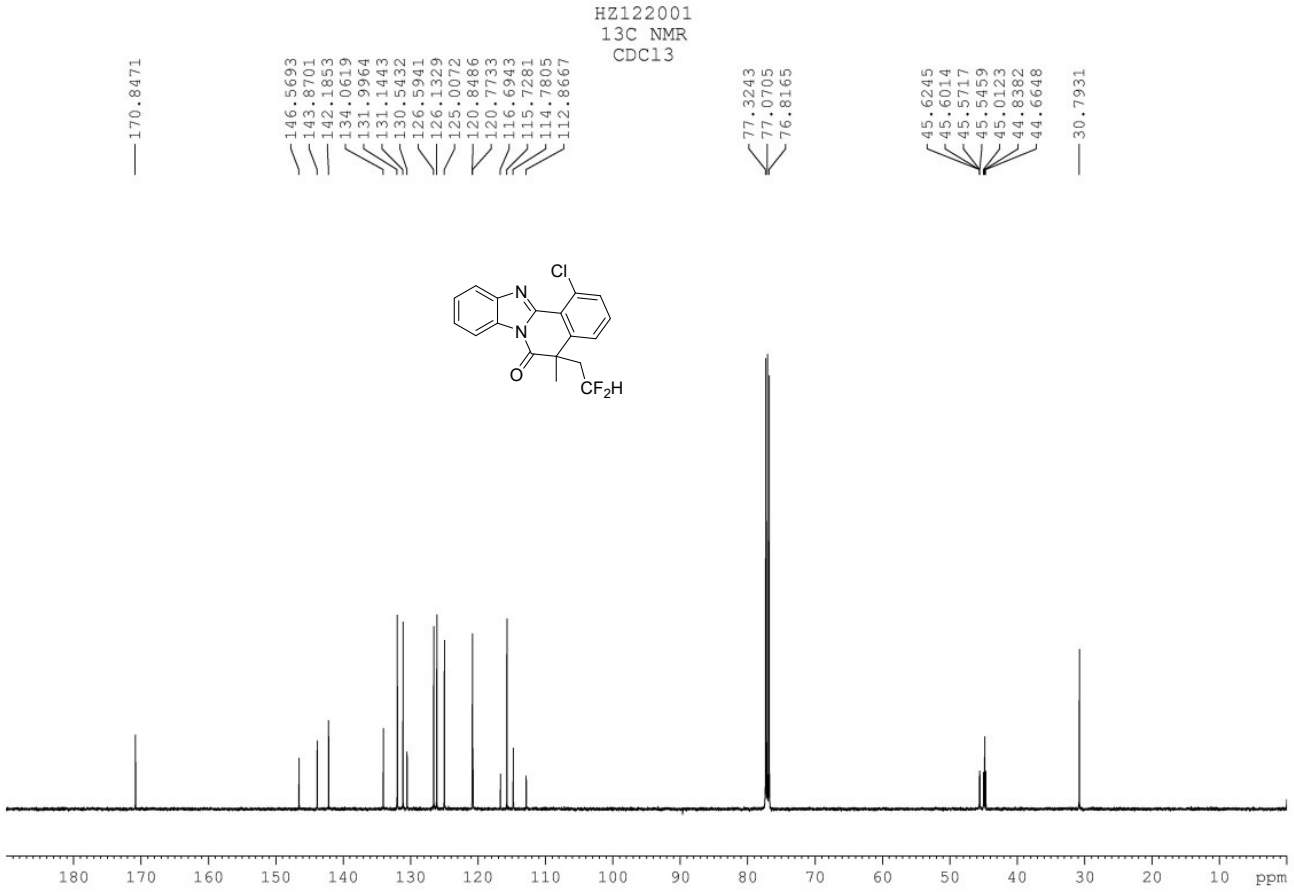


Fig. S75 ^{13}C NMR (125 MHz) spectrum of compound **3w**

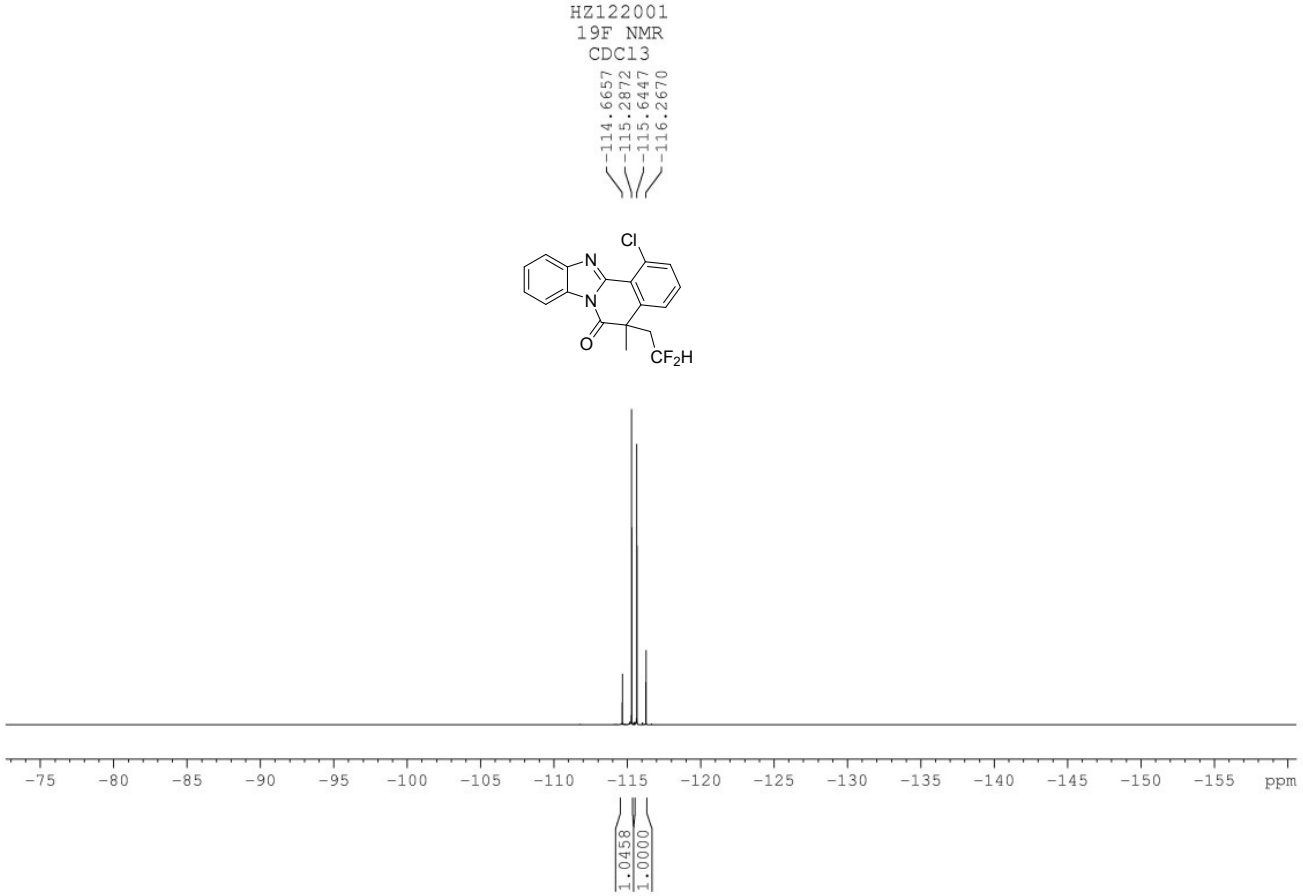


Fig. S76 ^{19}F NMR (470 MHz) spectrum of compound **3w**

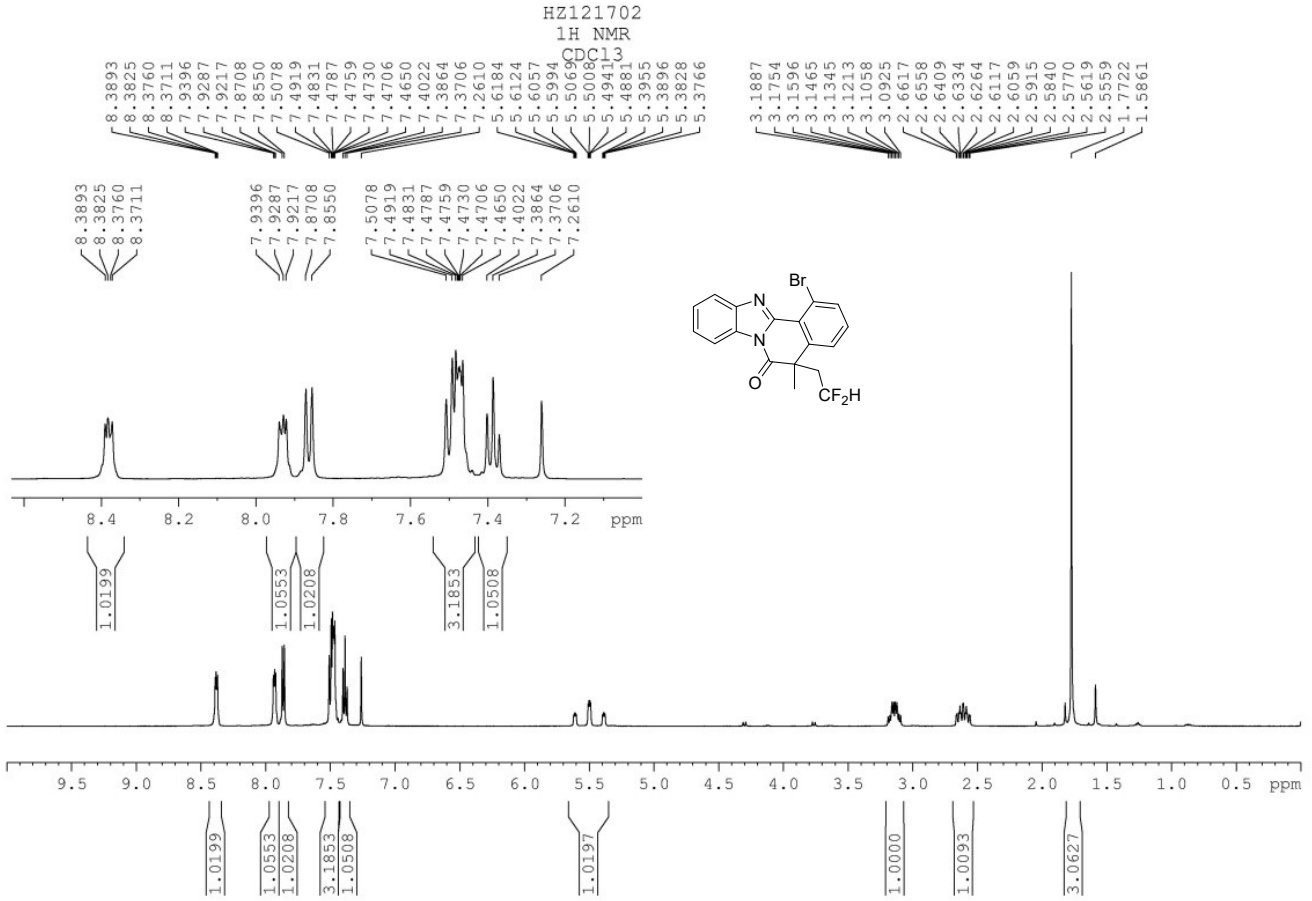


Fig. S77 ^{1}H NMR (500 MHz) spectrum of compound **3x**

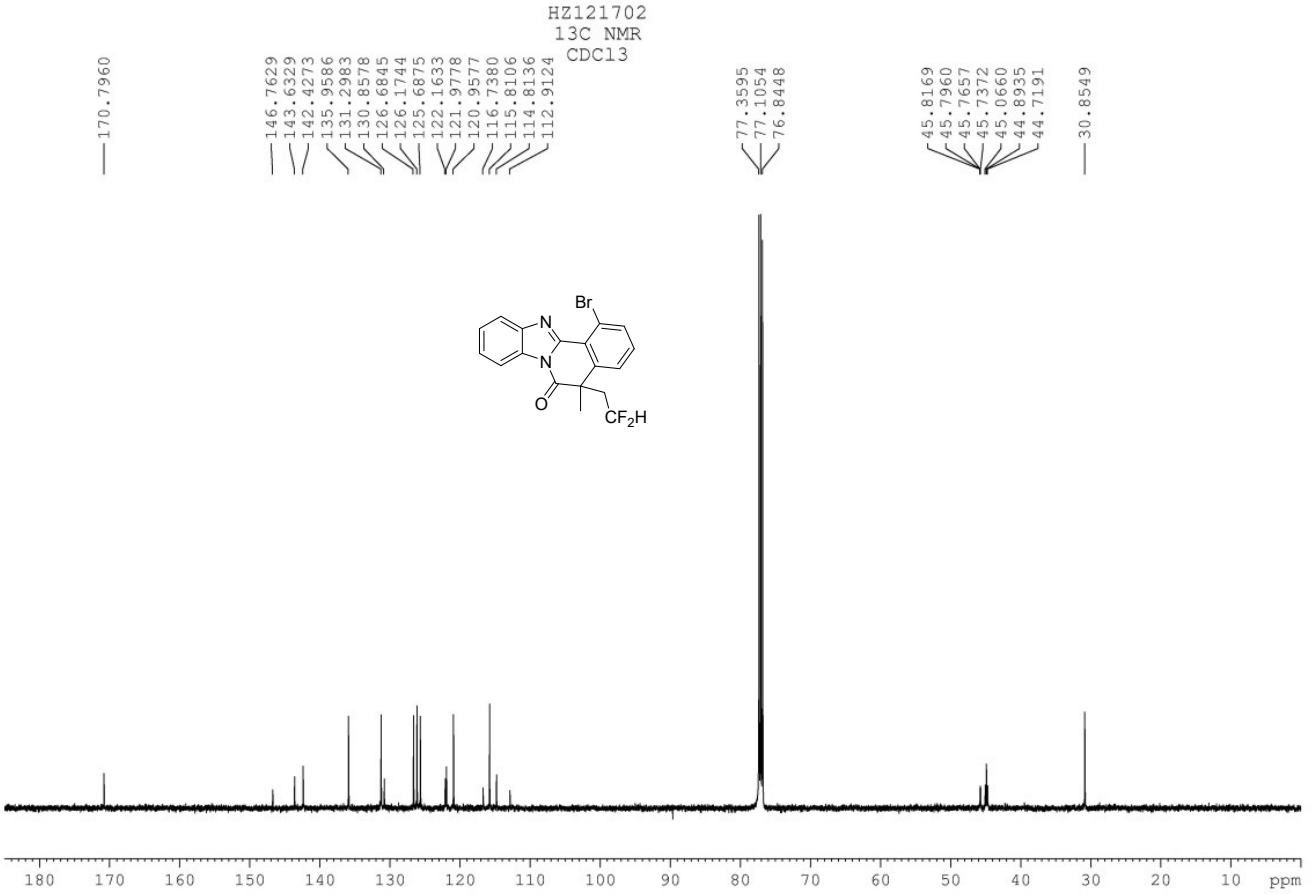


Fig. S78 ^{13}C NMR (125 MHz) spectrum of compound **3x**

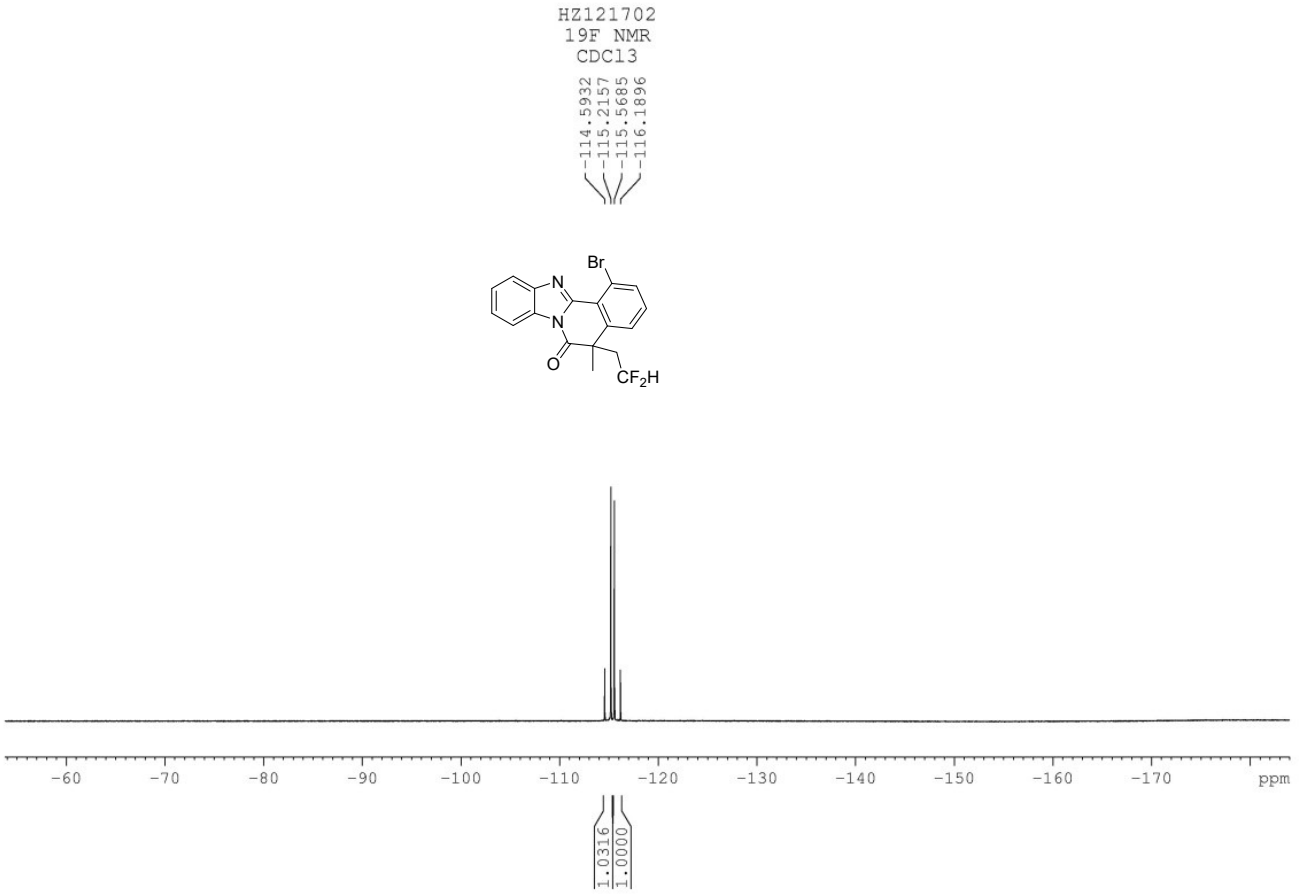


Fig. S79 ^{19}F NMR (470 MHz) spectrum of compound **3x**

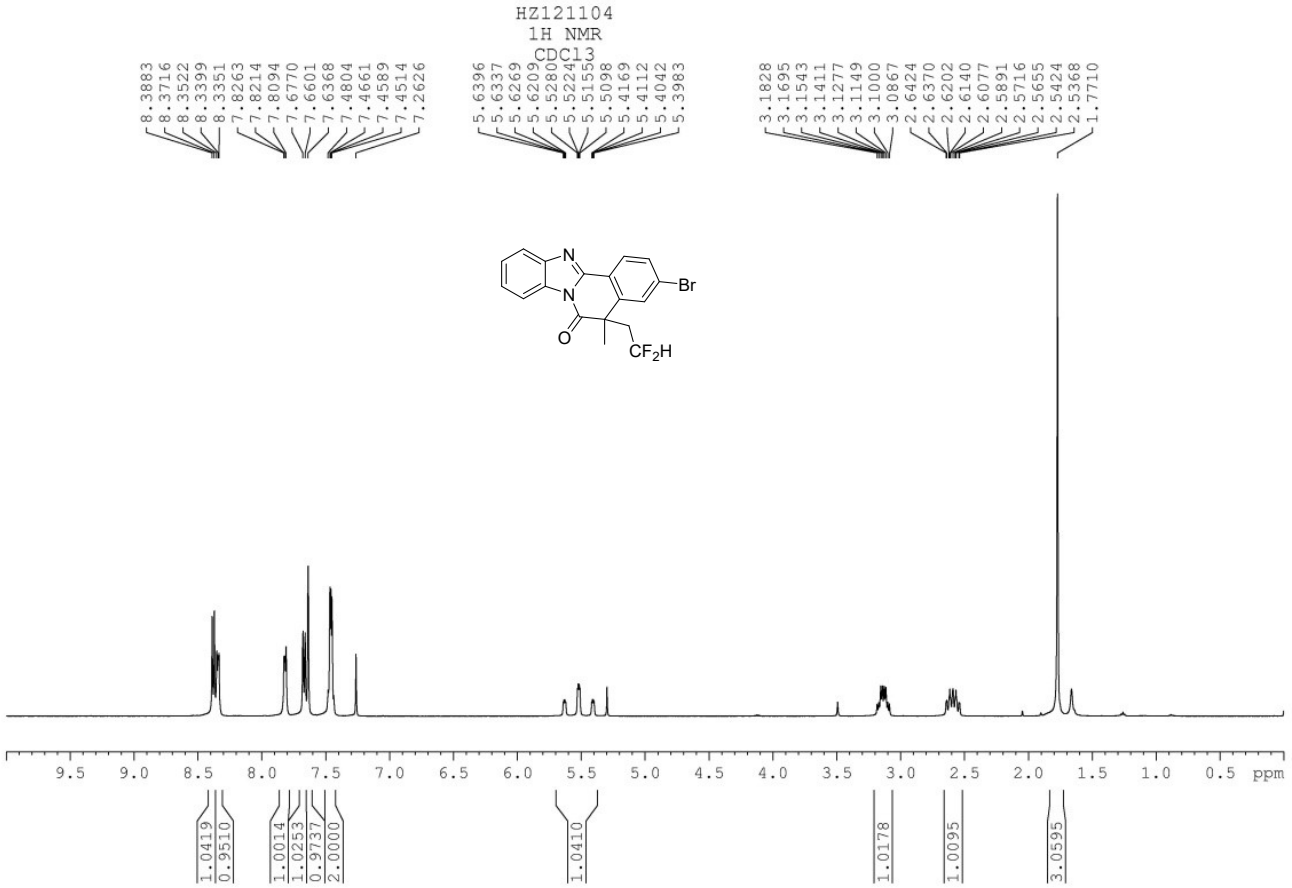


Fig. S80 ^{1}H NMR (500 MHz) spectrum of compound **3y**

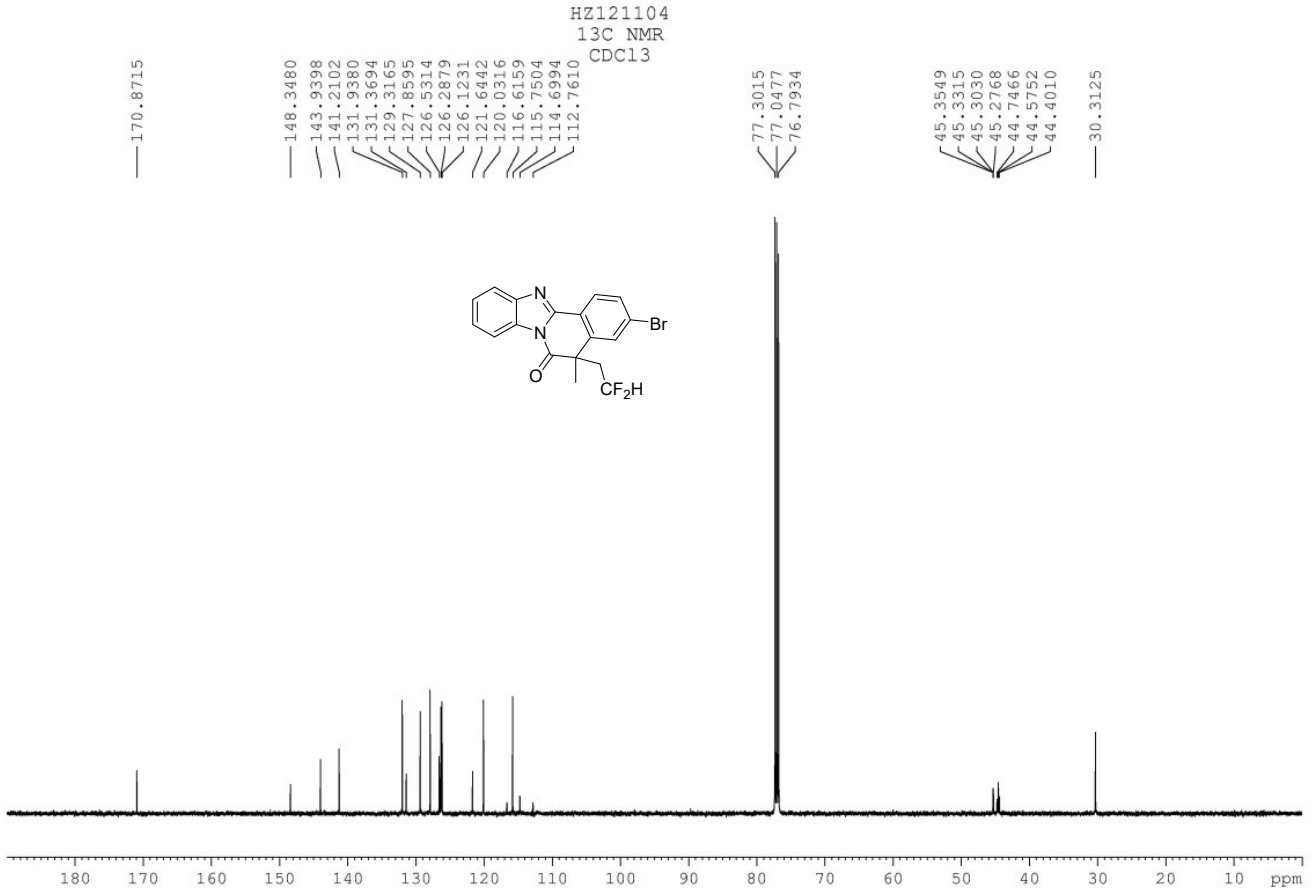


Fig. S81 ^{13}C NMR (125 MHz) spectrum of compound **3y**

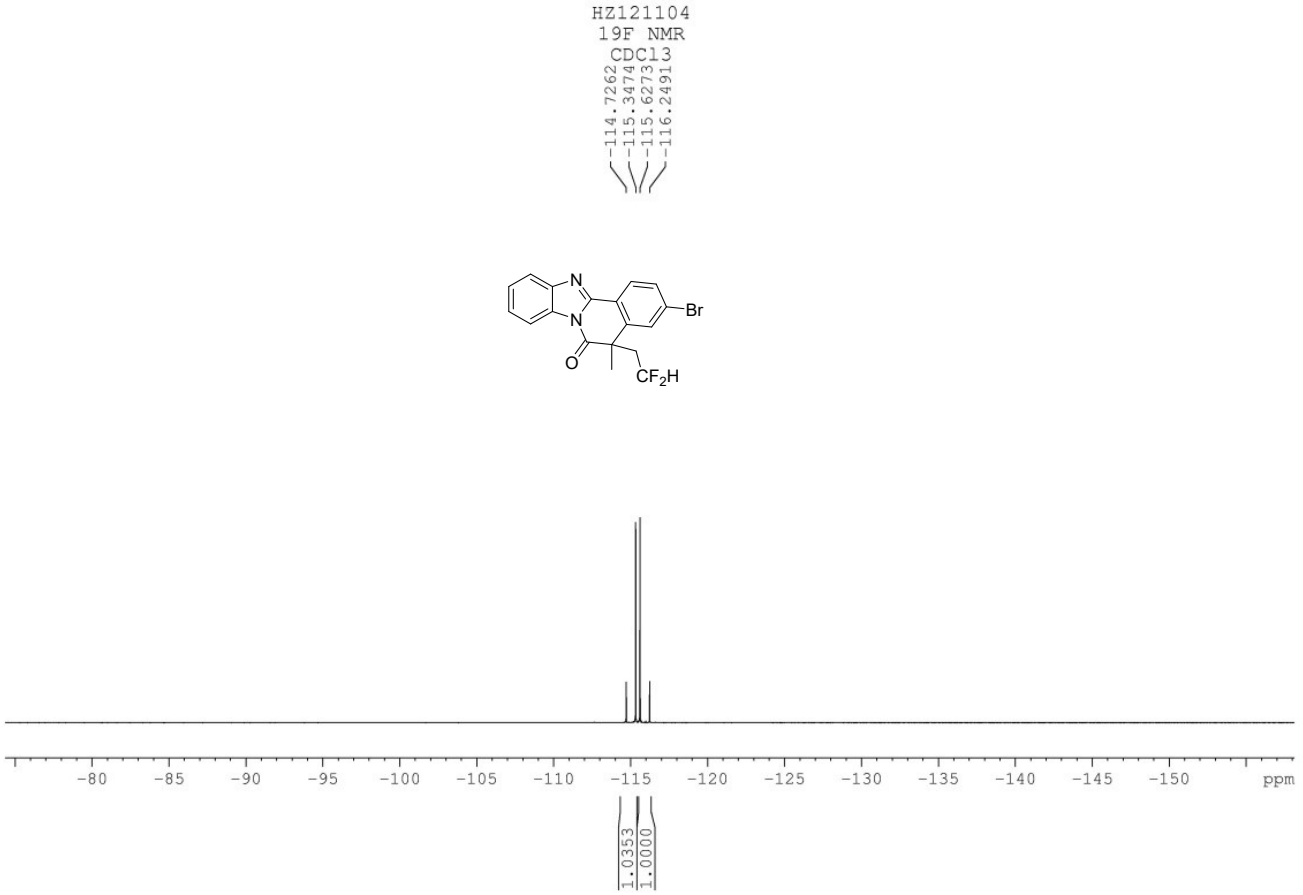


Fig. S82 ^{19}F NMR (470 MHz) spectrum of compound **3y**

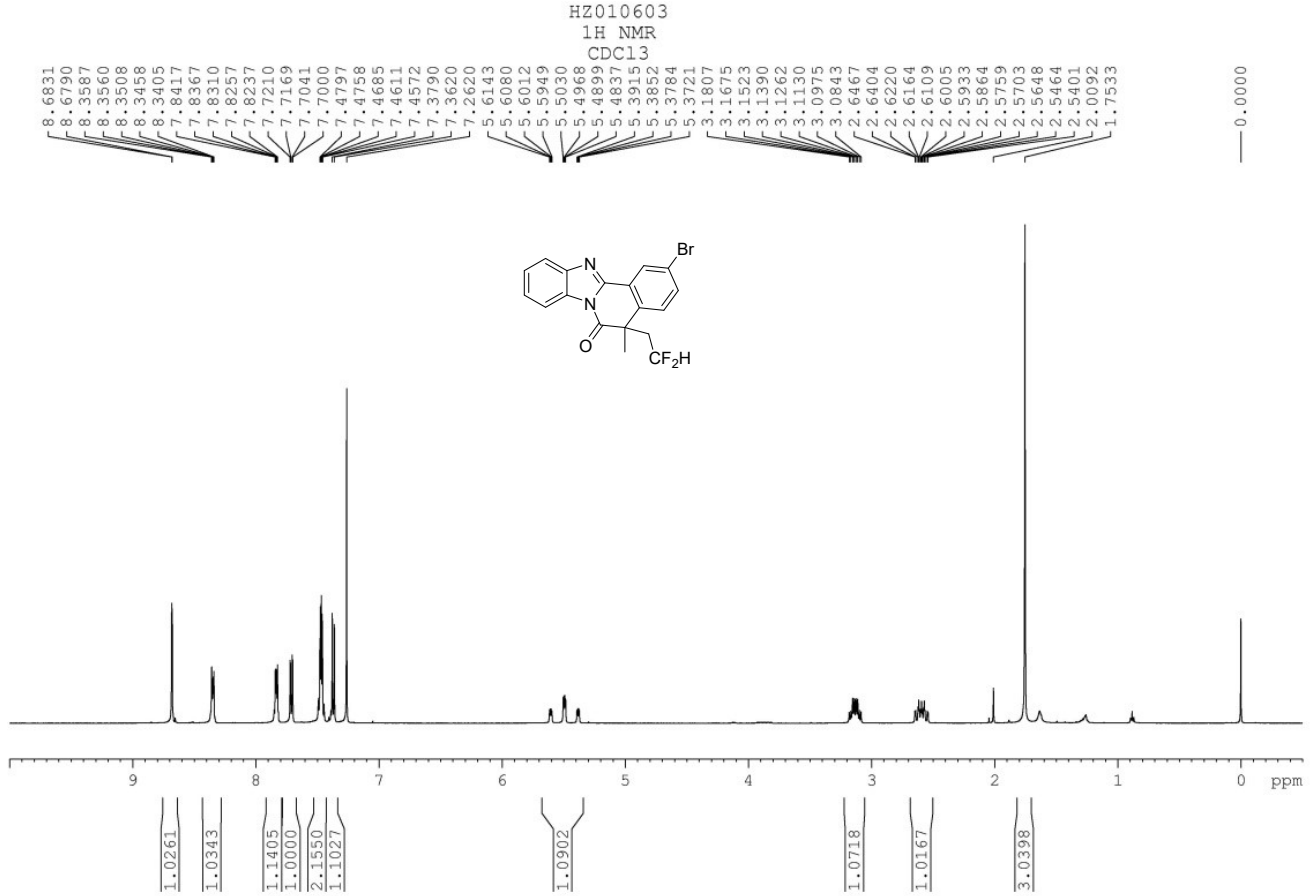


Fig. S83 ^{1}H NMR (500 MHz) spectrum of compound **3z**

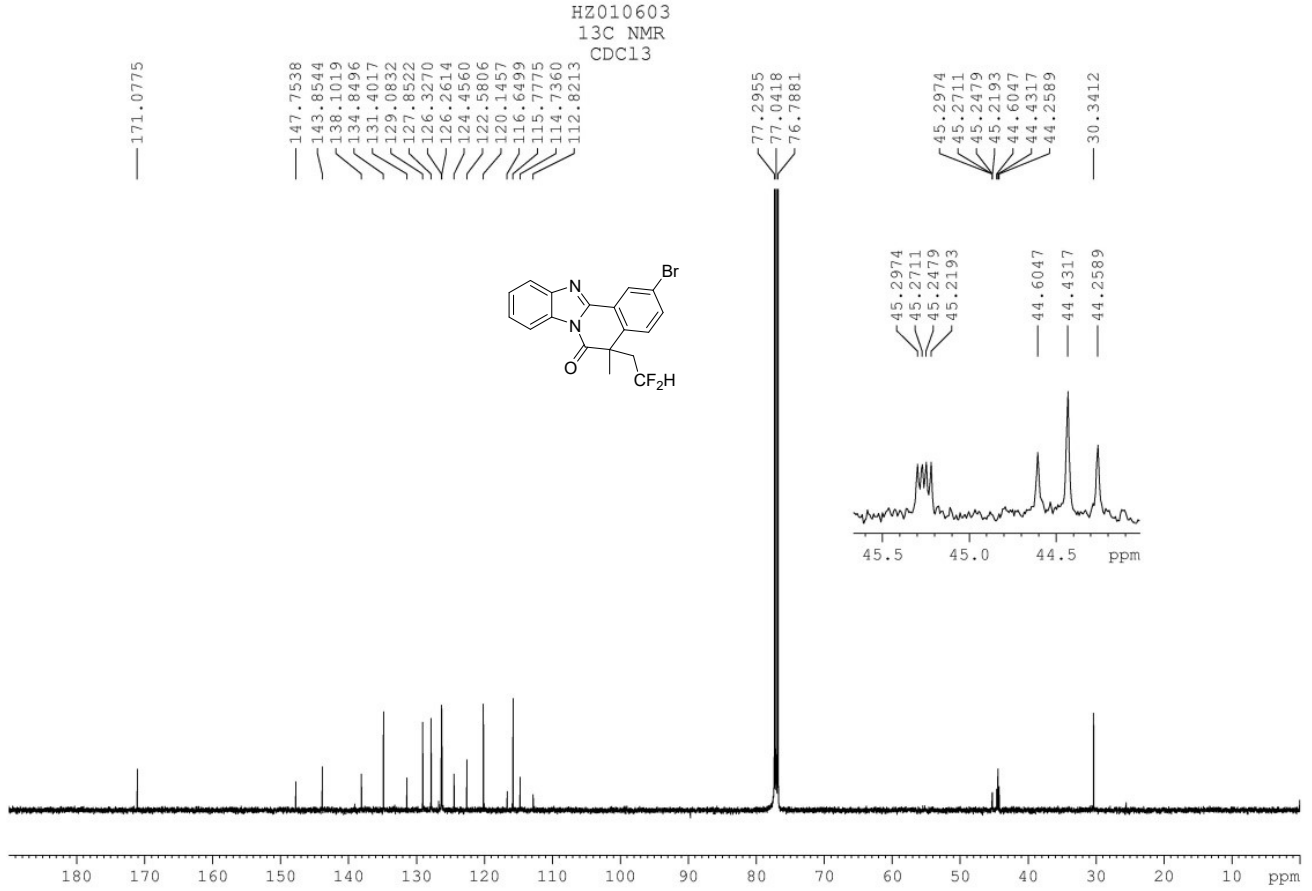


Fig. S84 ^{13}C NMR (125 MHz) spectrum of compound **3z**

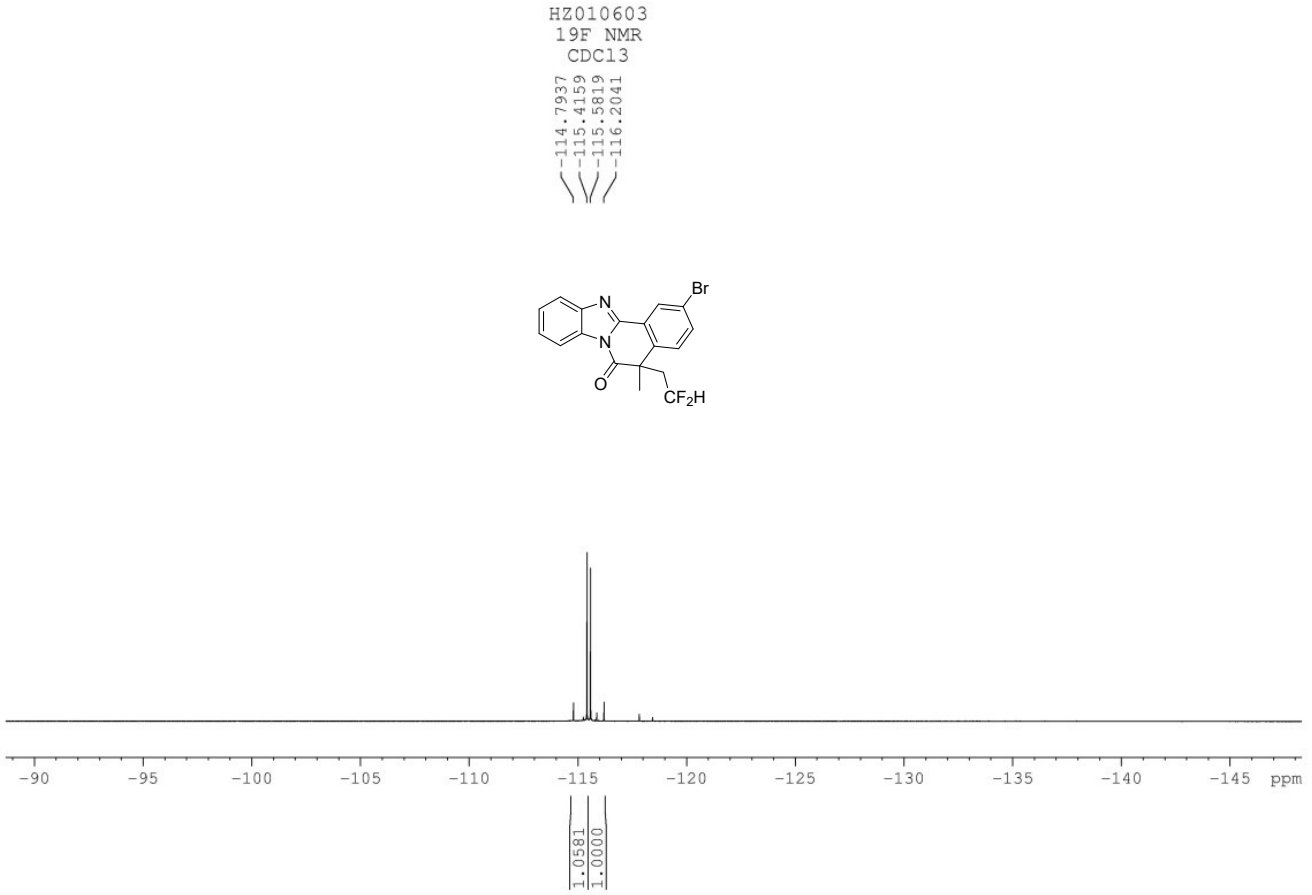


Fig. S85 ^{19}F NMR (470 MHz) spectrum of compound **3z**

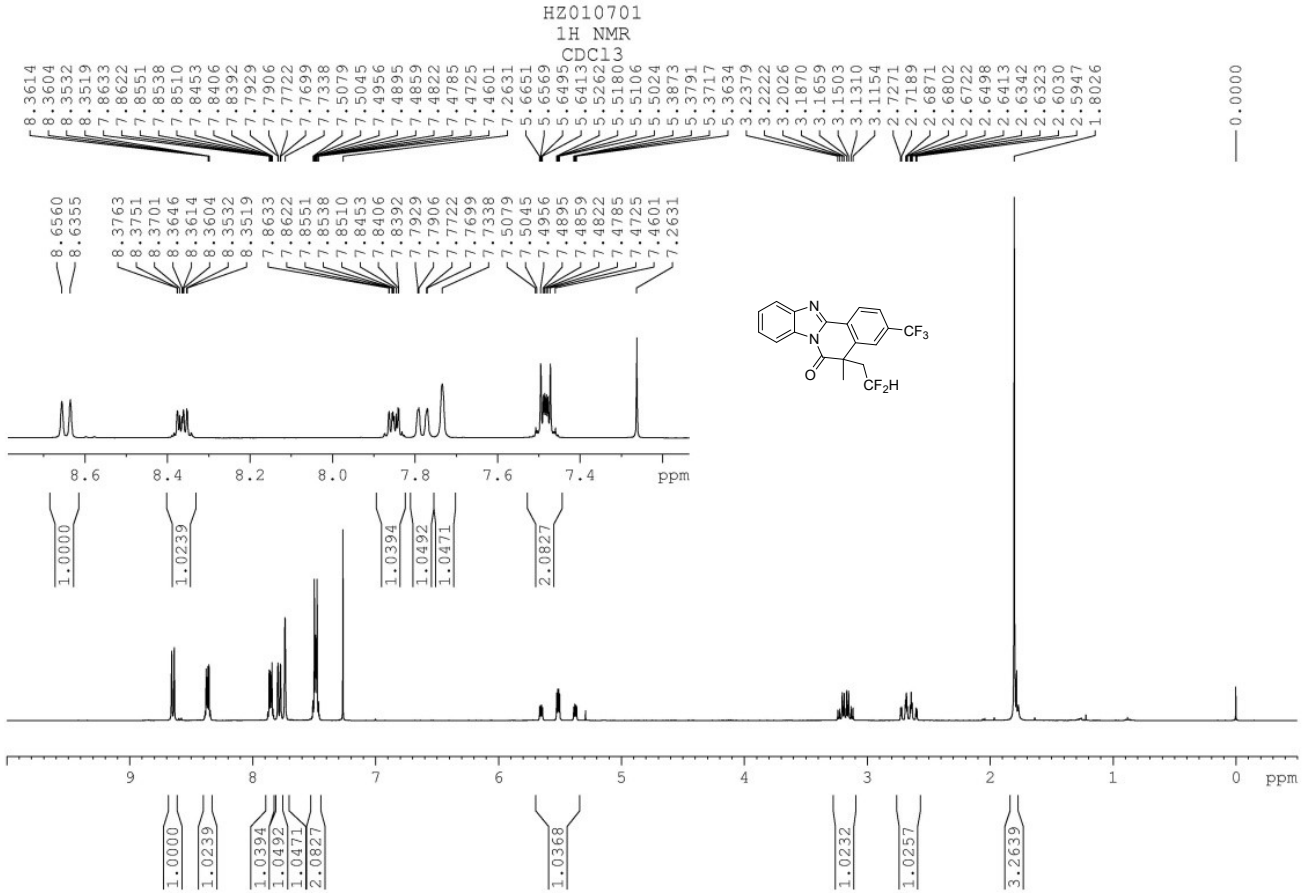


Fig. S86 ^{1}H NMR (400 MHz) spectrum of compound **3aa**

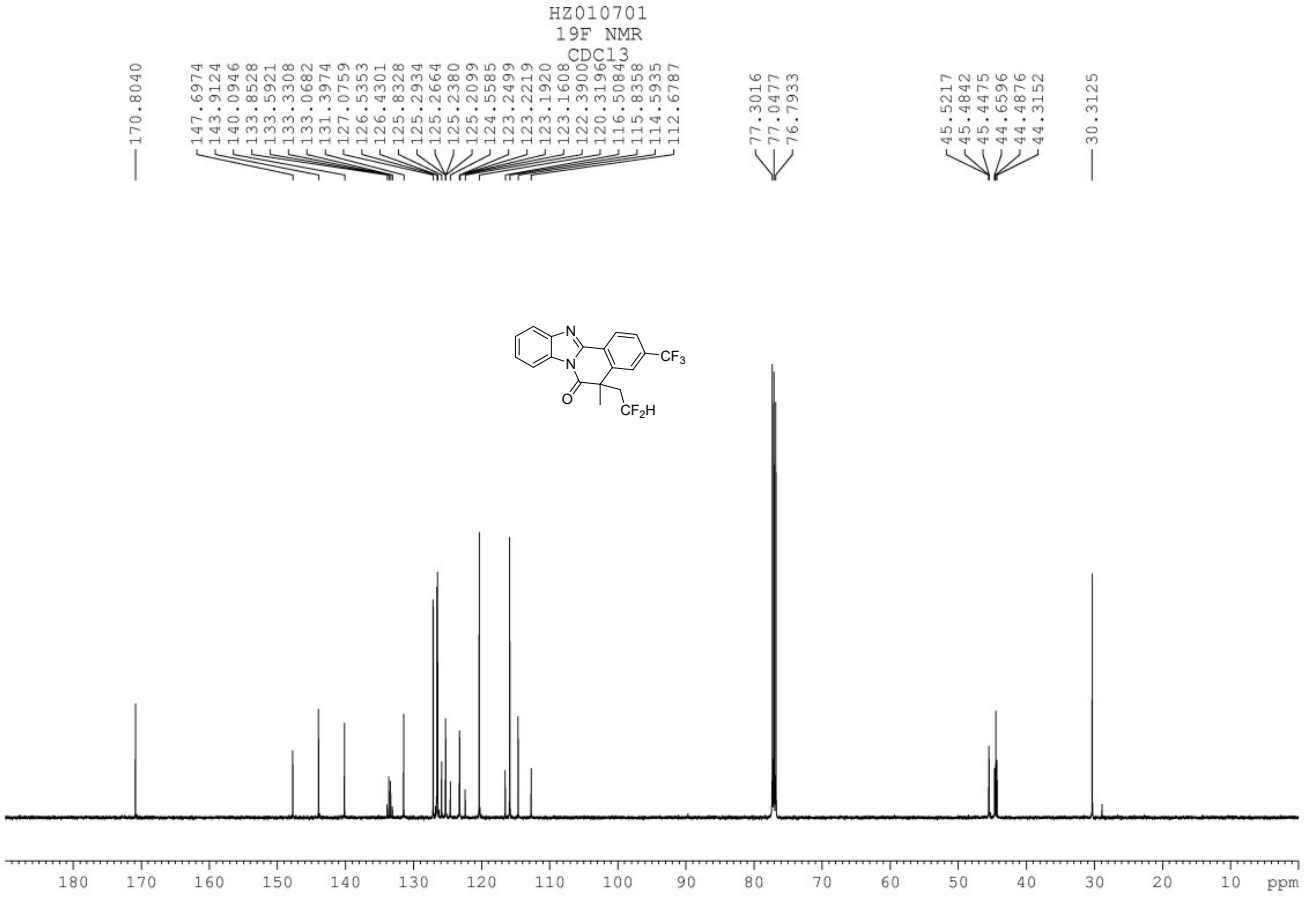


Fig. S87 ^{13}C NMR (125 MHz) spectrum of compound **3aa**

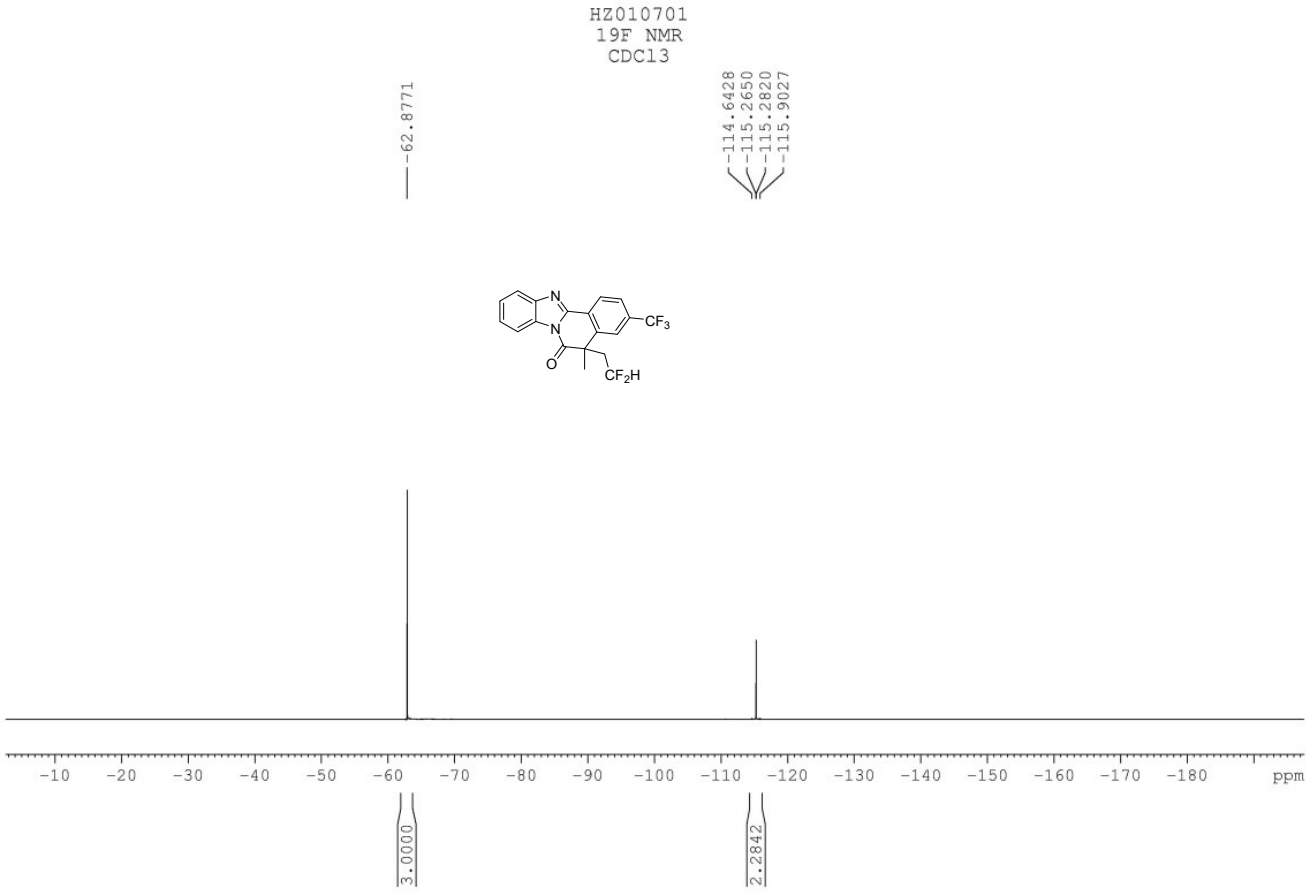


Fig. S88 ^{19}F NMR (470 MHz) spectrum of compound **3aa**

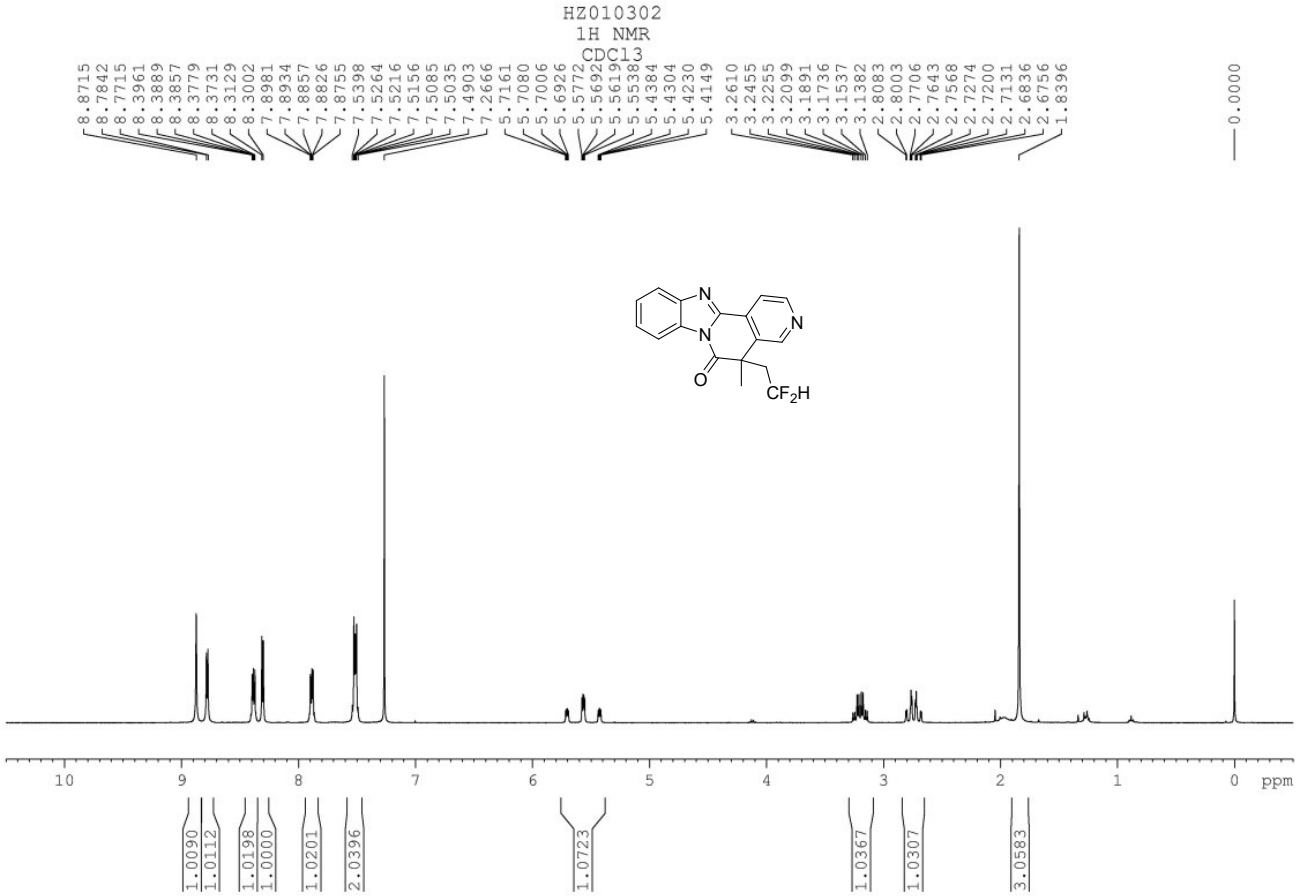


Fig. S89 ^{1}H NMR (400 MHz) spectrum of compound **3ab**

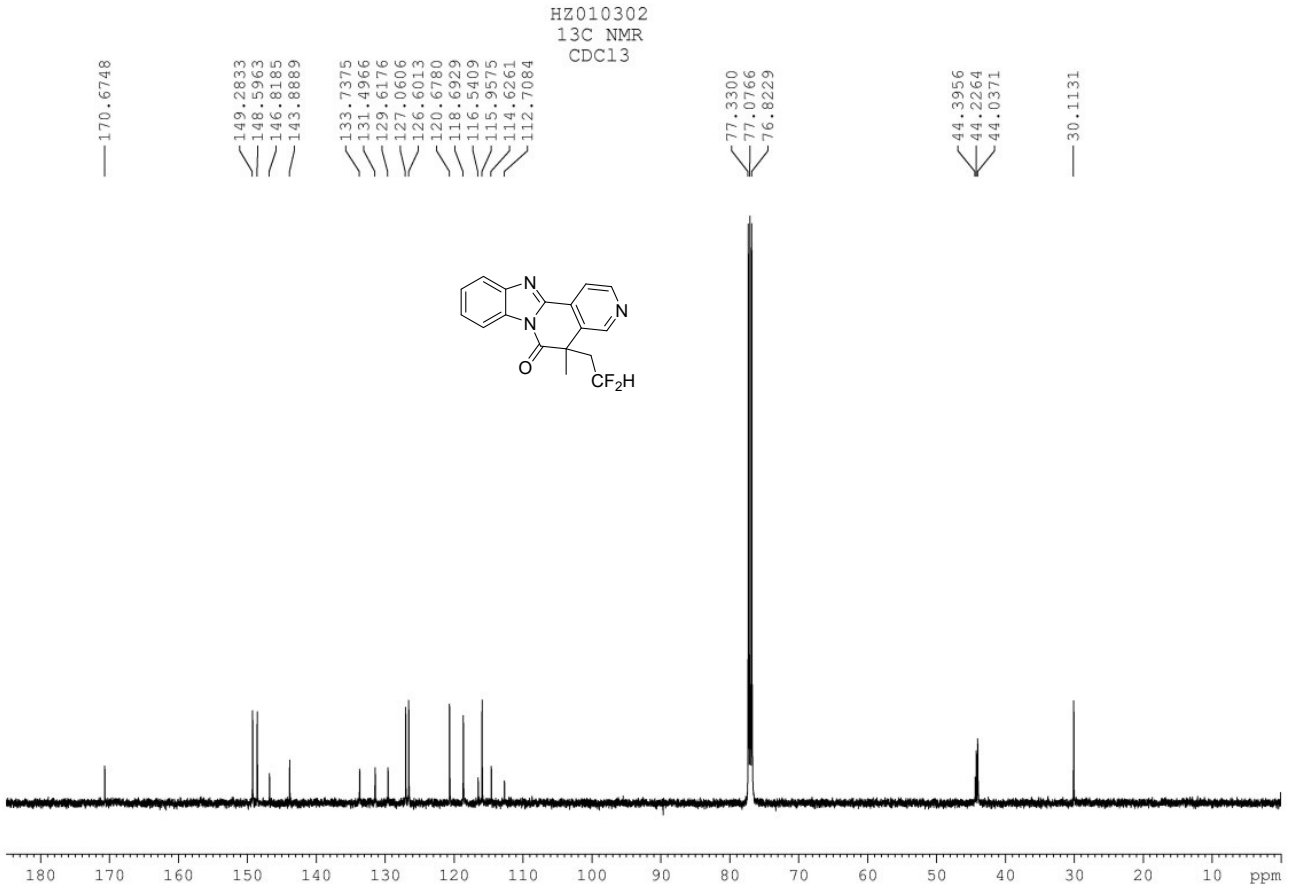


Fig. S90 ^{13}C NMR (125 MHz) spectrum of compound **3ab**

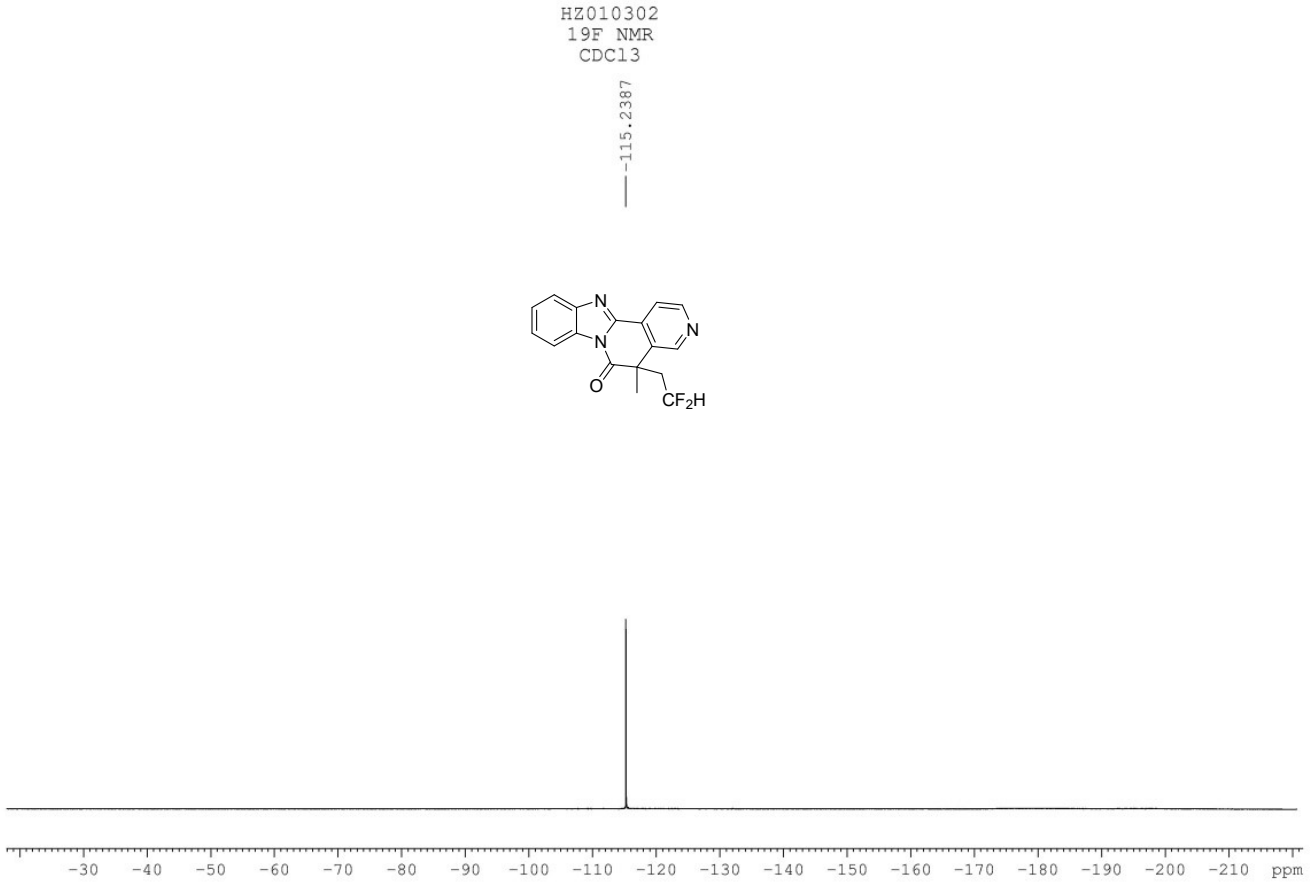


Fig. S91 ^{19}F NMR (470 MHz) spectrum of compound **3ab**

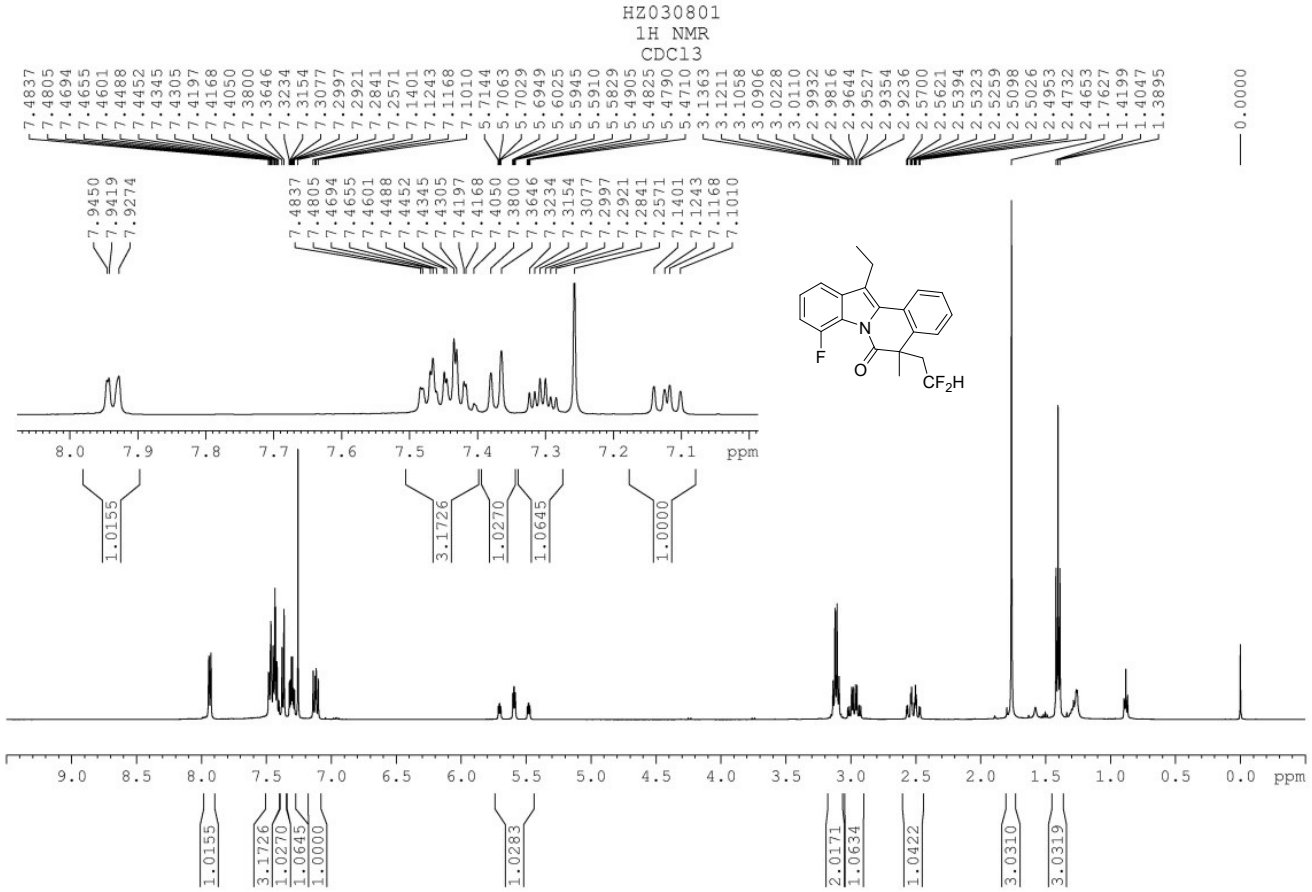


Fig. S92 ^{1}H NMR (500 MHz) spectrum of compound **5a**

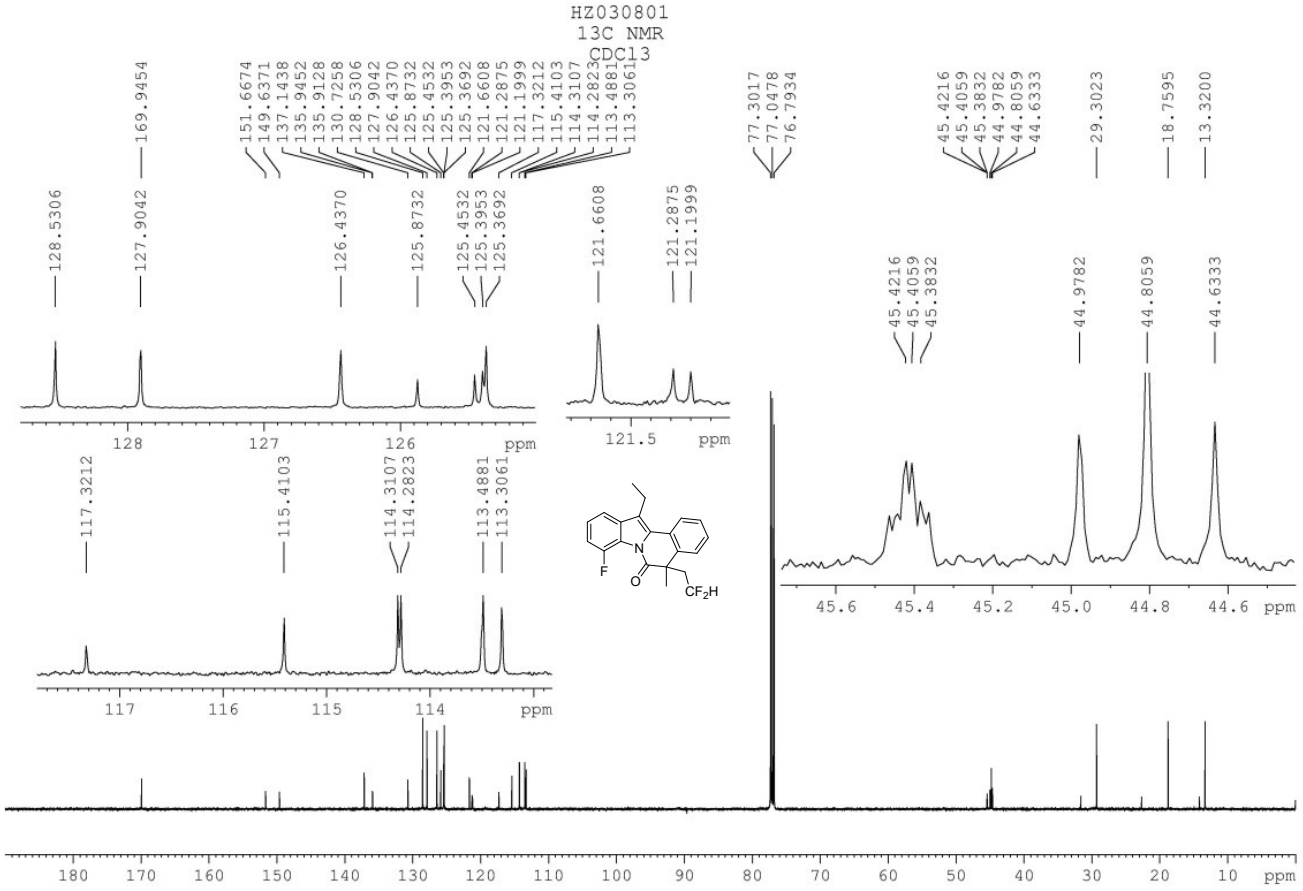


Fig. S93 ^{13}C NMR (125 MHz) spectrum of compound **5a**

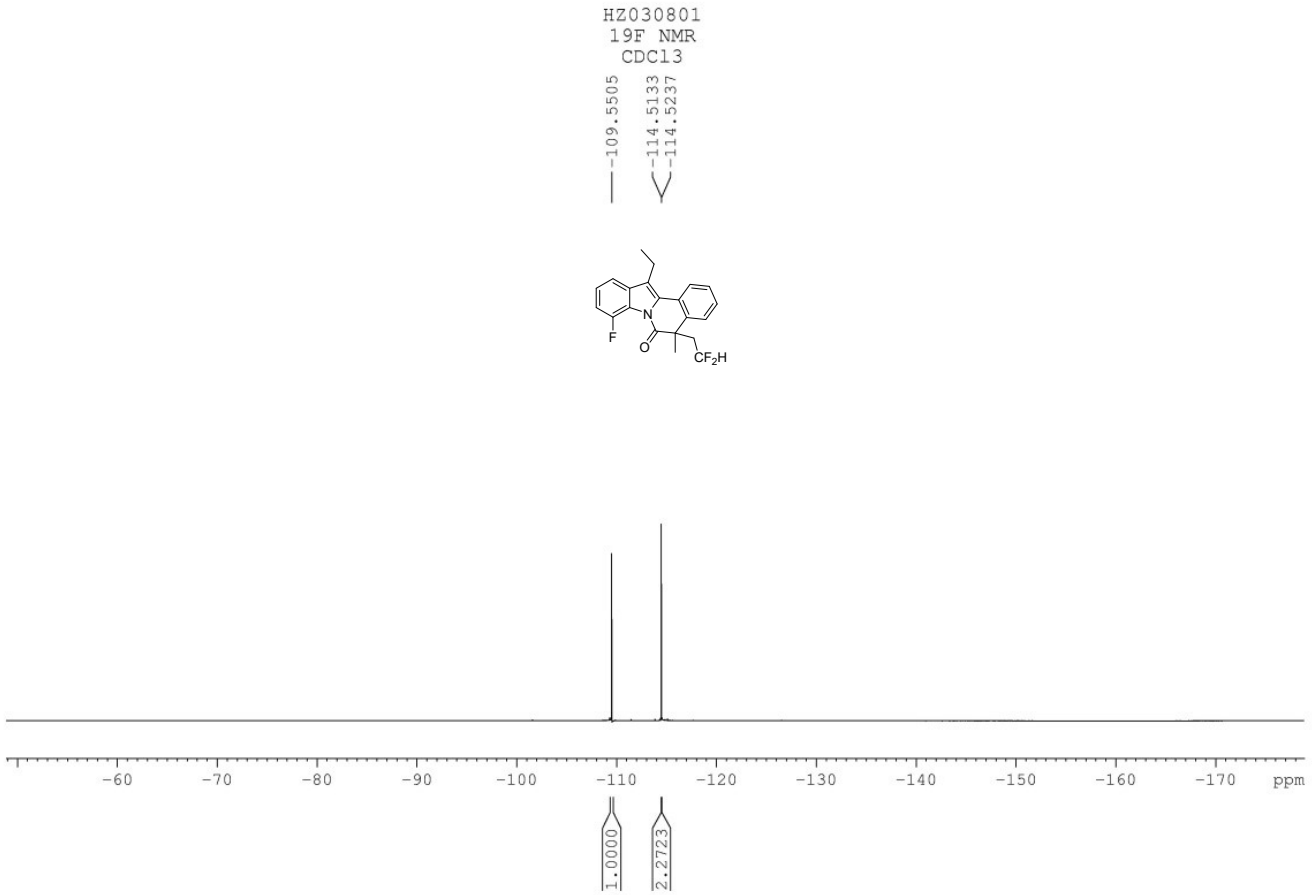


Fig. S94 ^{19}F NMR (470 MHz) spectrum of compound **5a**

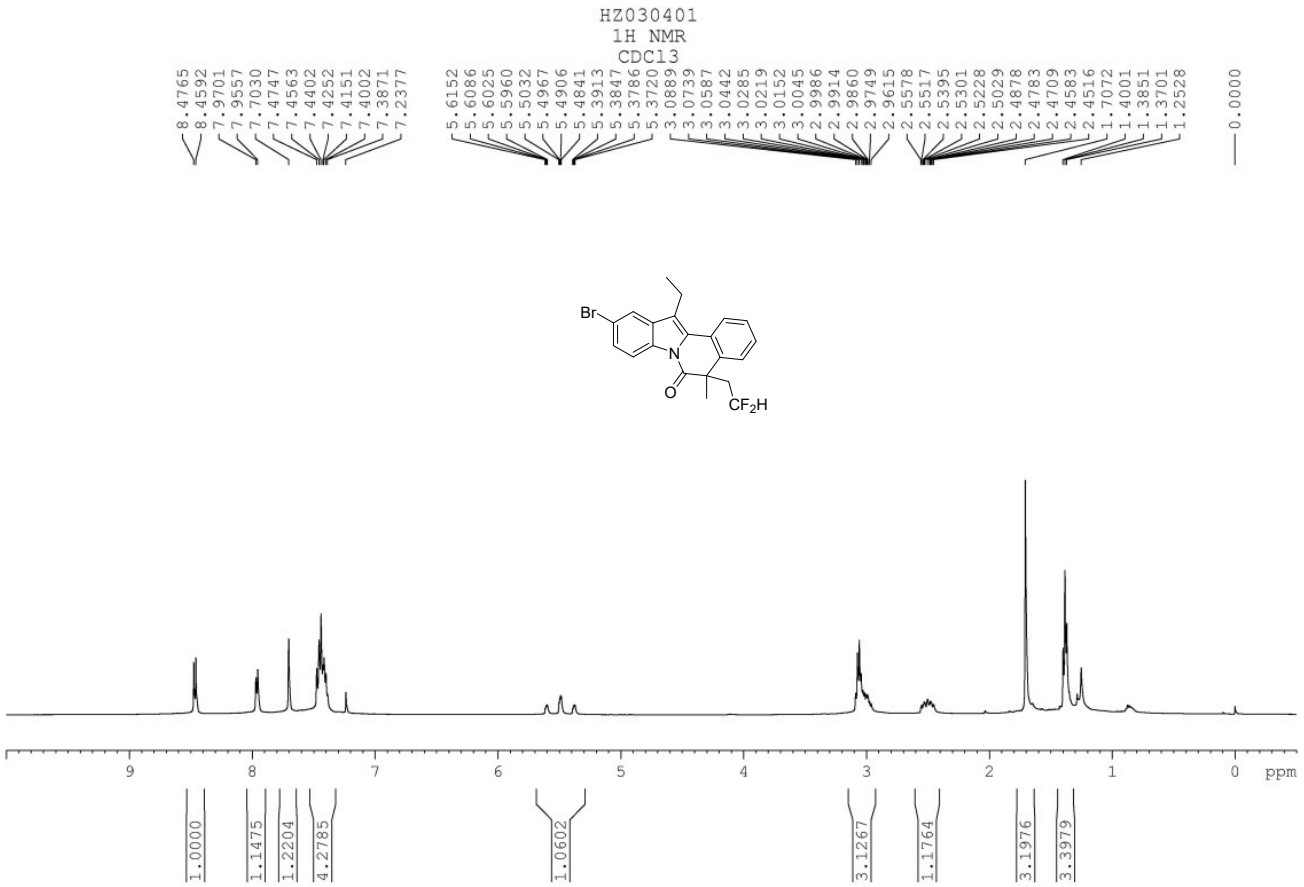


Fig. S95 ^{1}H NMR (500 MHz) spectrum of compound **5b**

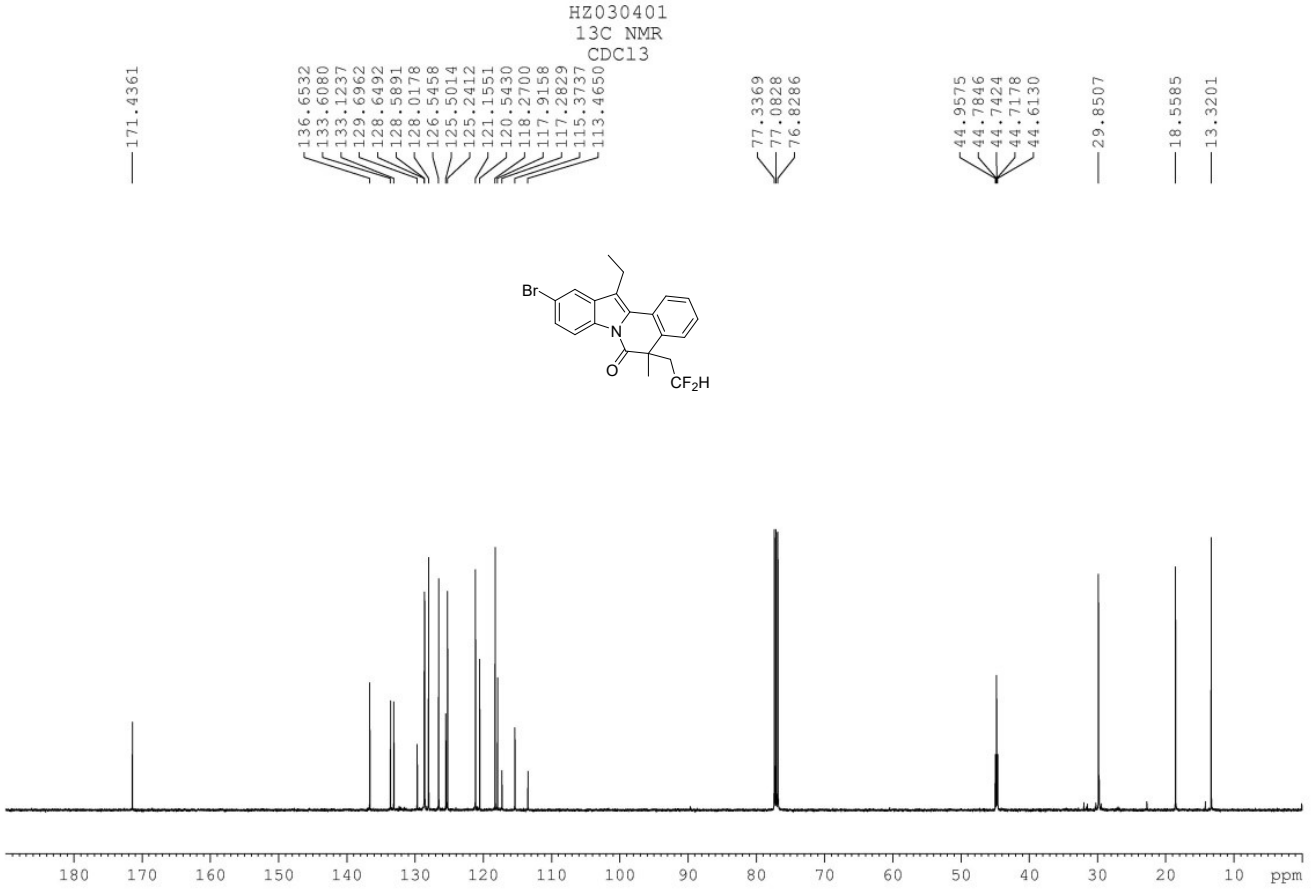


Fig. S96 ^{13}C NMR (125 MHz) spectrum of compound **5b**

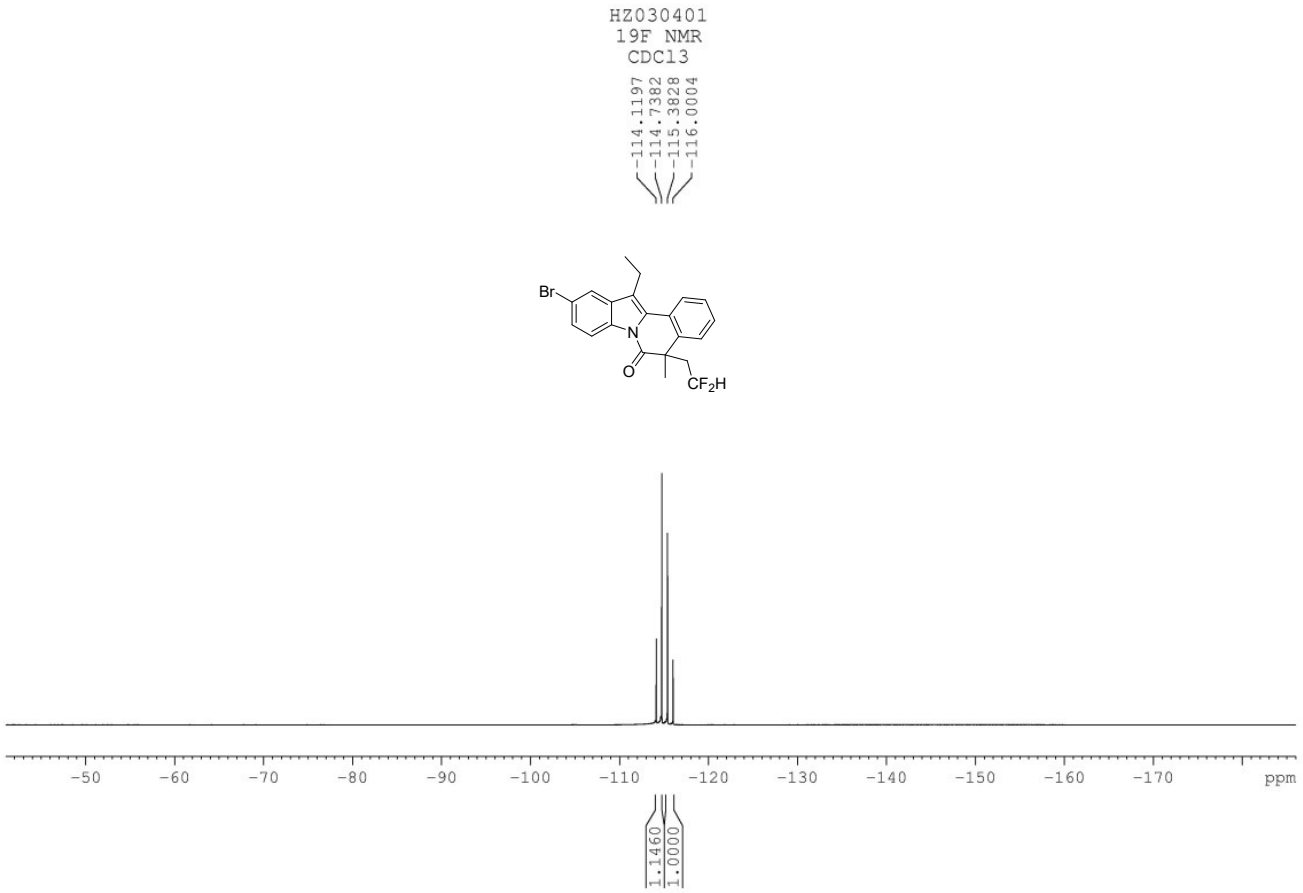


Fig. S97 ^{19}F NMR (470 MHz) spectrum of compound **5b**

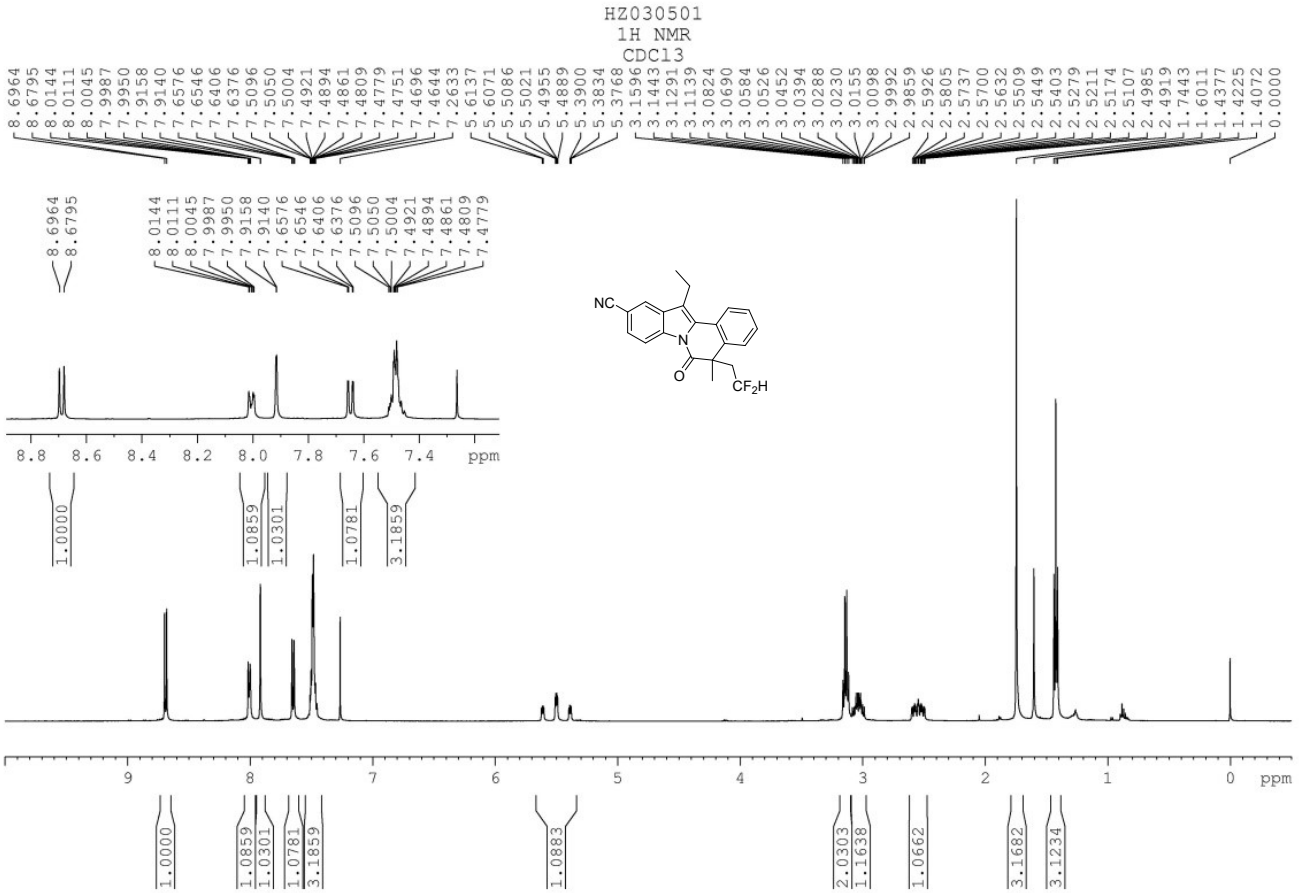


Fig. S98 ^{1}H NMR (500 MHz) spectrum of compound **5c**

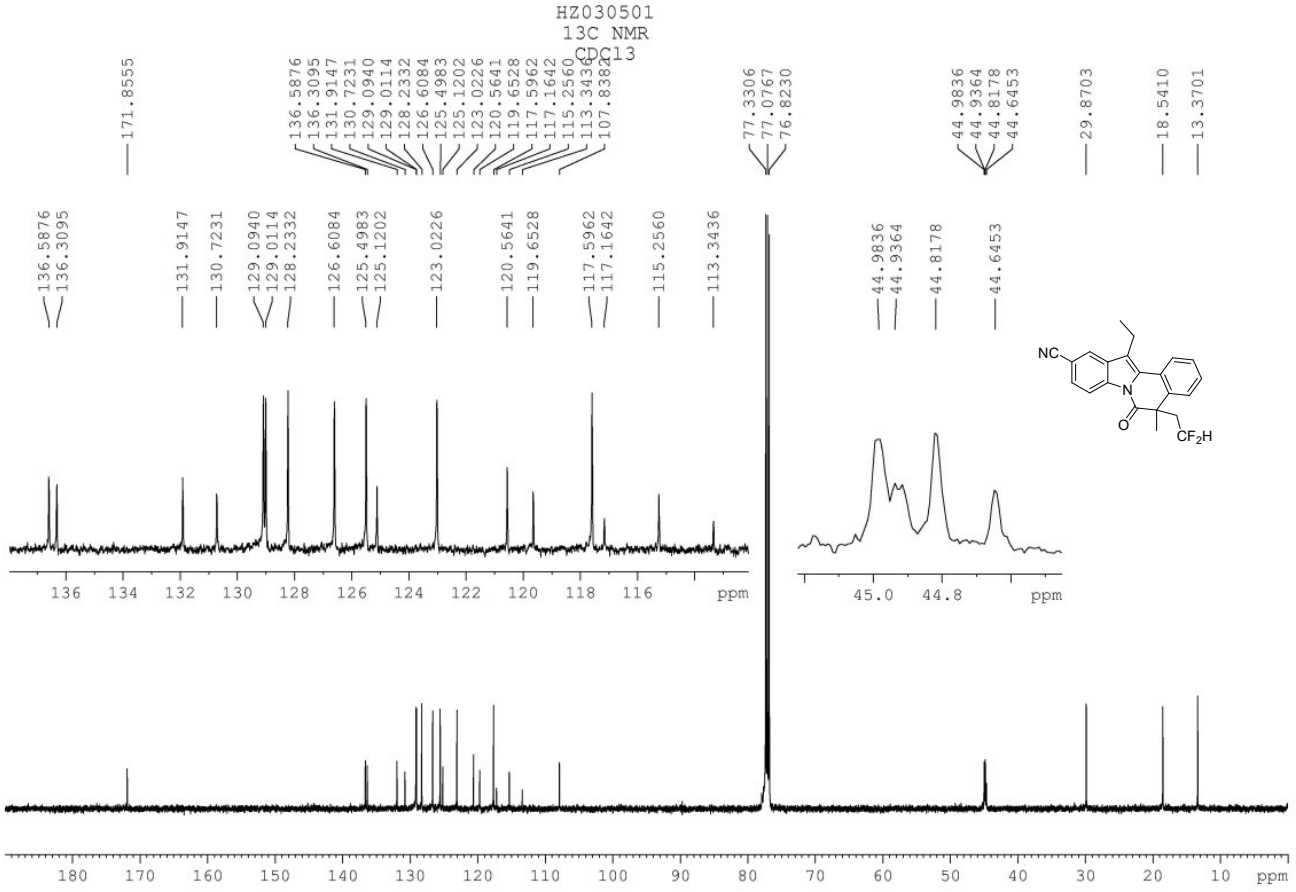


Fig. S99 ^{13}C NMR (125 MHz) spectrum of compound **5c**

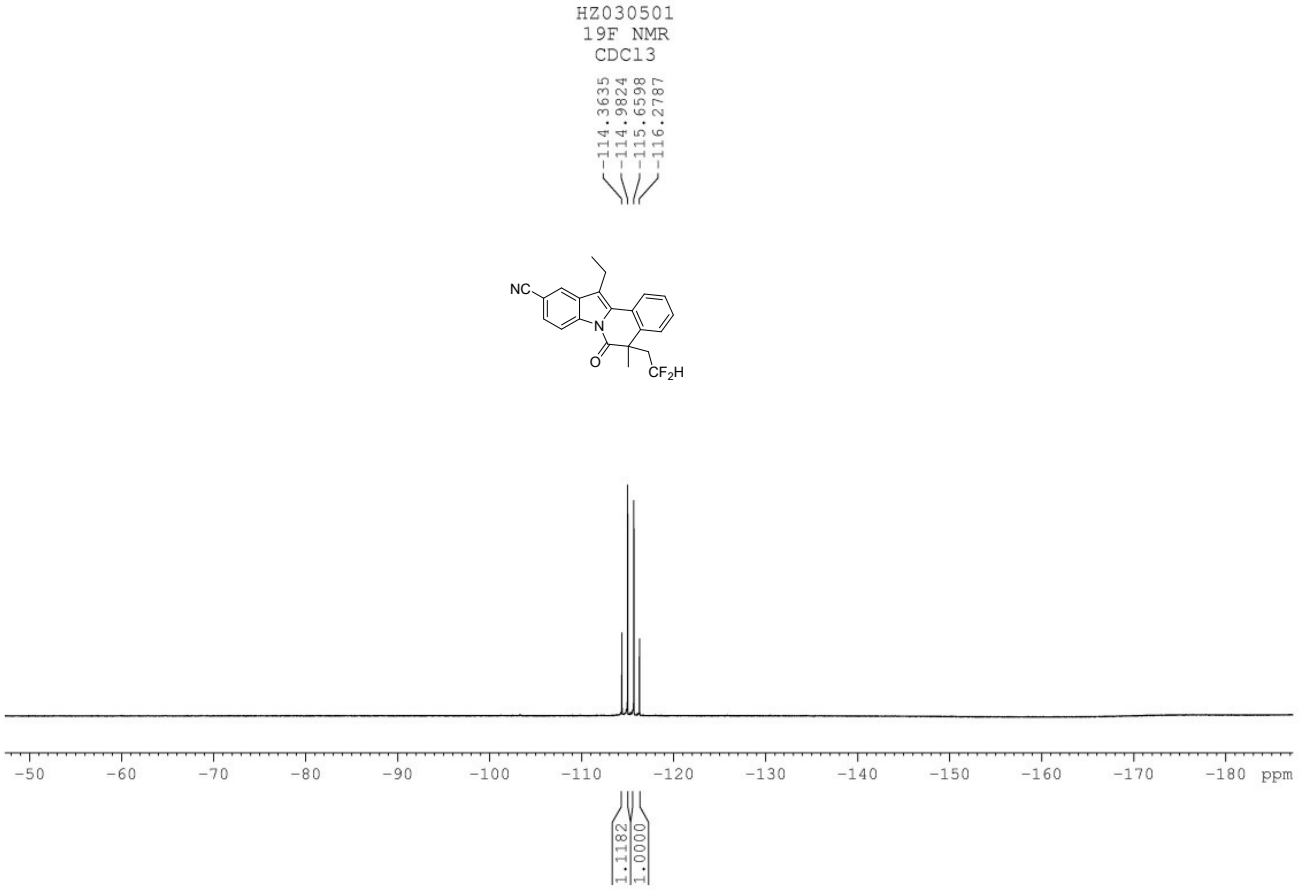


Fig. S100 ^{19}F NMR (470 MHz) spectrum of compound **5c**

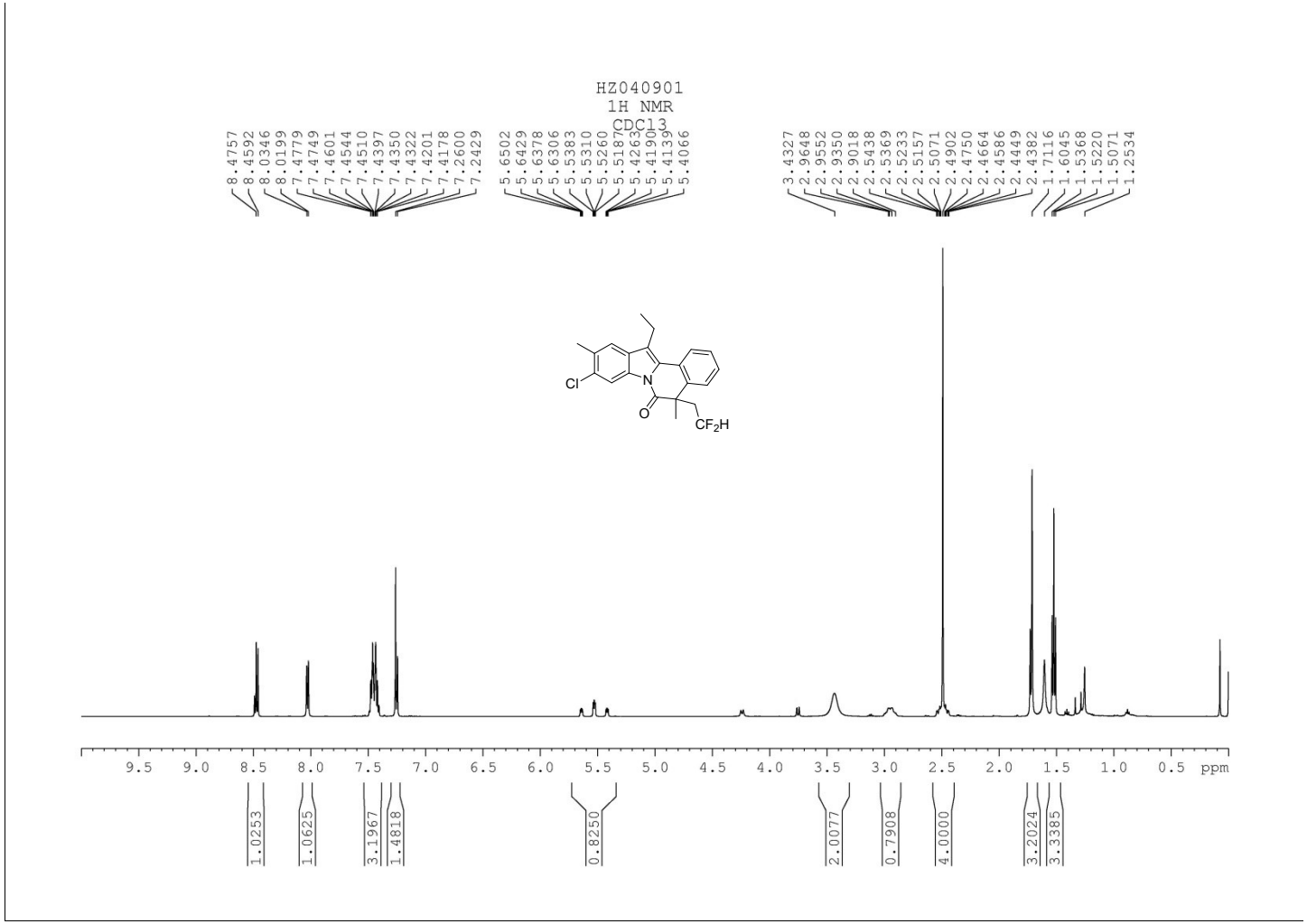


Fig. S101 ^{1}H NMR (500 MHz) spectrum of compound **5d**

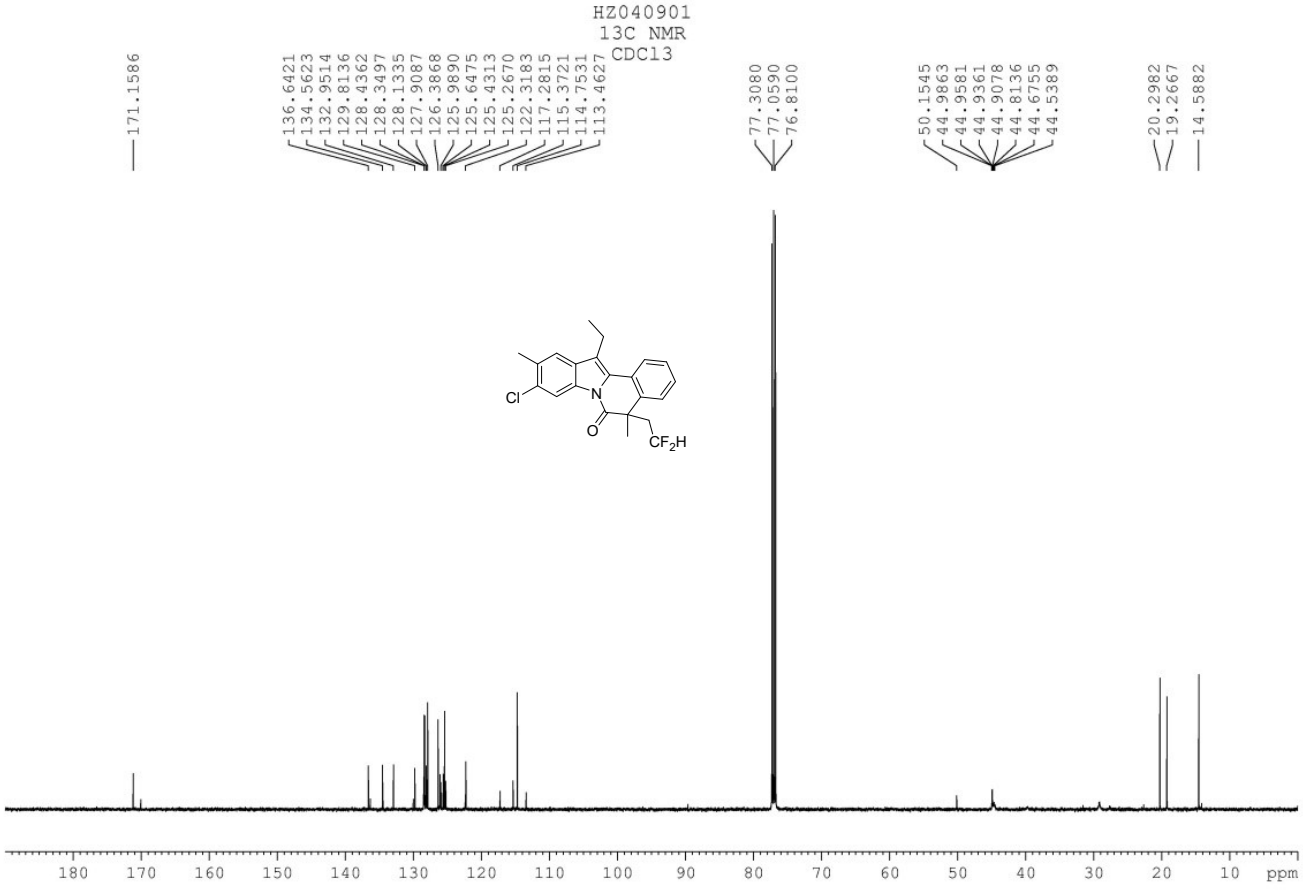


Fig. S102 ^{13}C NMR (125 MHz) spectrum of compound **5d**

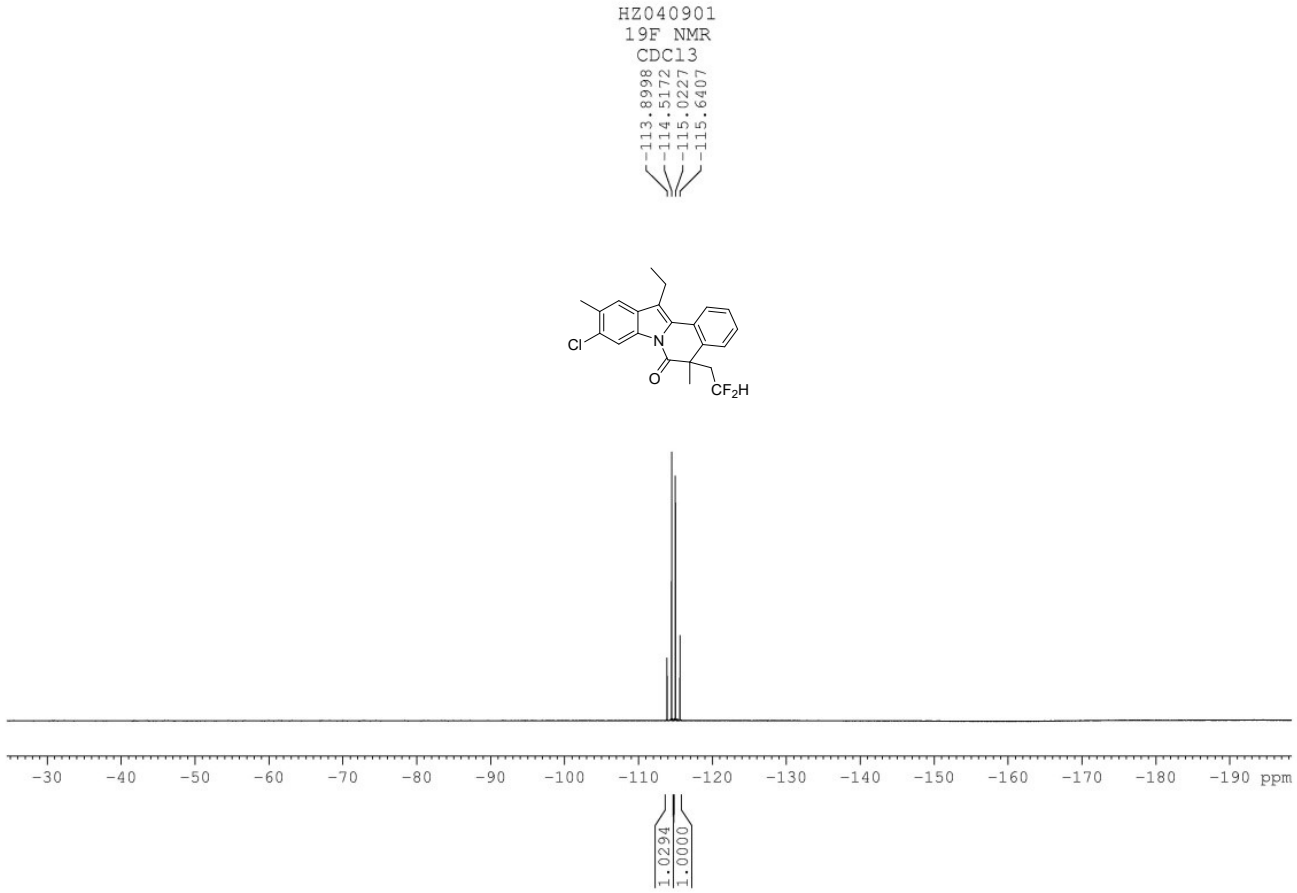


Fig. S103 ^{19}F NMR (470 MHz) spectrum of compound **5d**

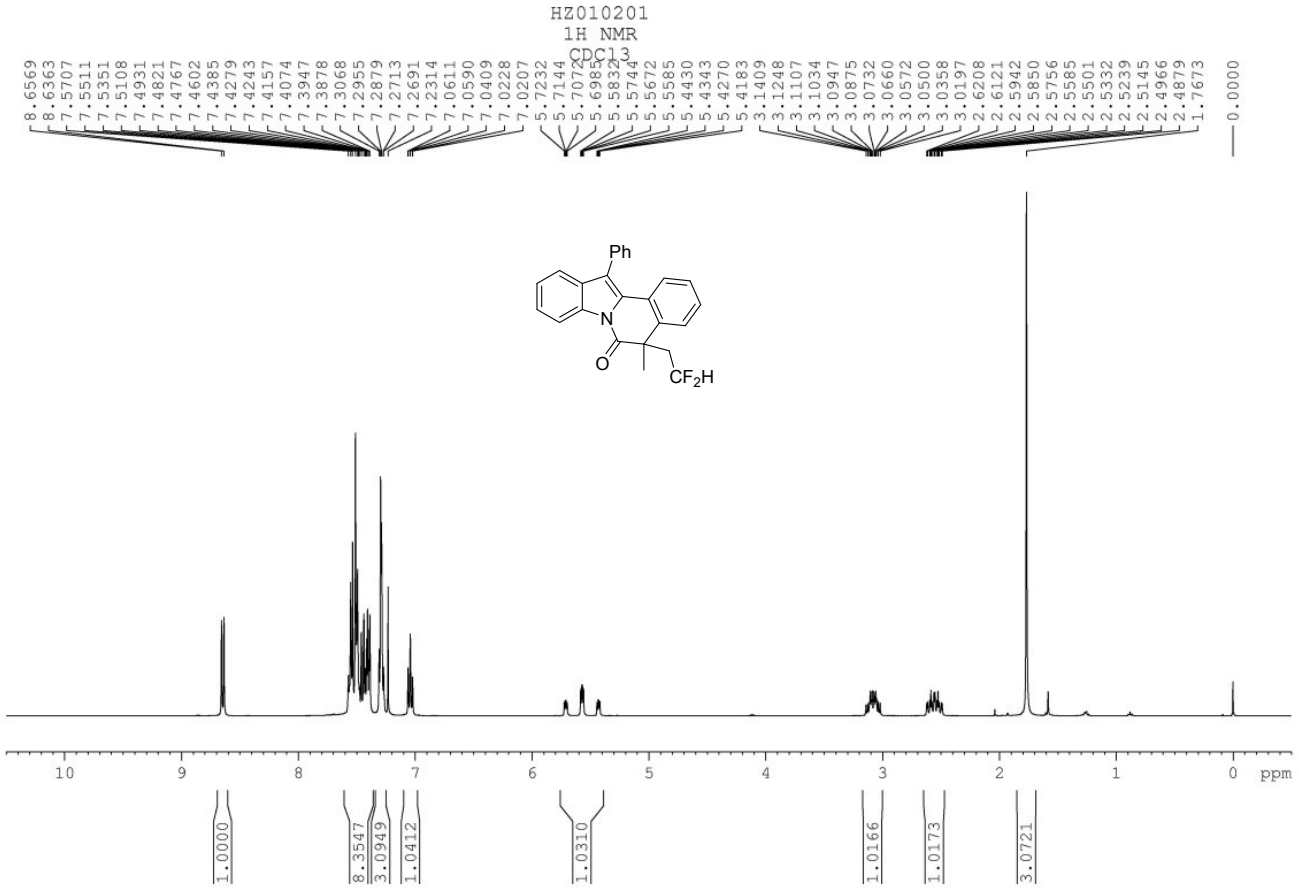


Fig. S104 ^{1}H NMR (400 MHz) spectrum of compound **5e**

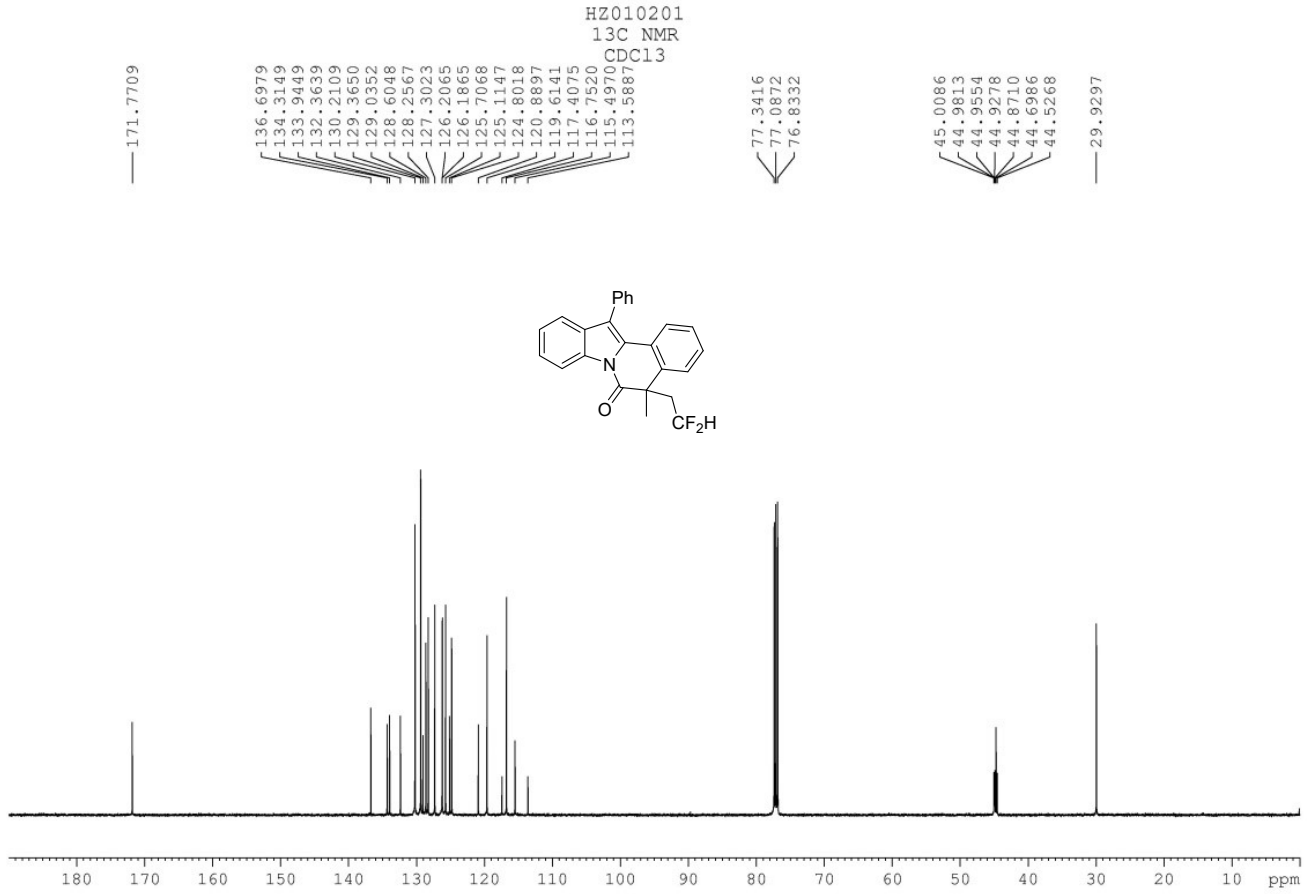


Fig. S105 ^{13}C NMR (125 MHz) spectrum of compound **5e**

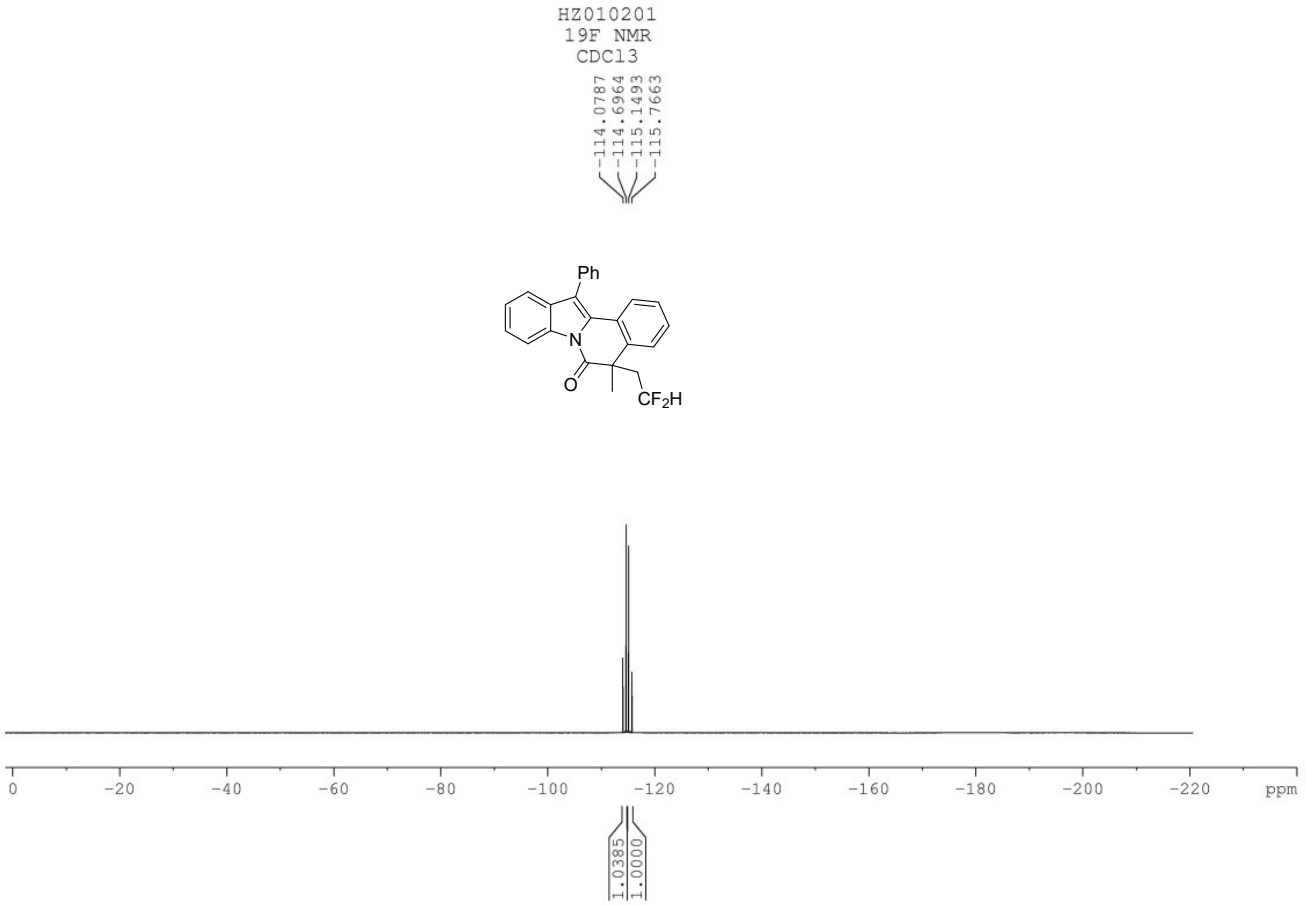


Fig. S106 ^{19}F NMR (470 MHz) spectrum of compound **5e**

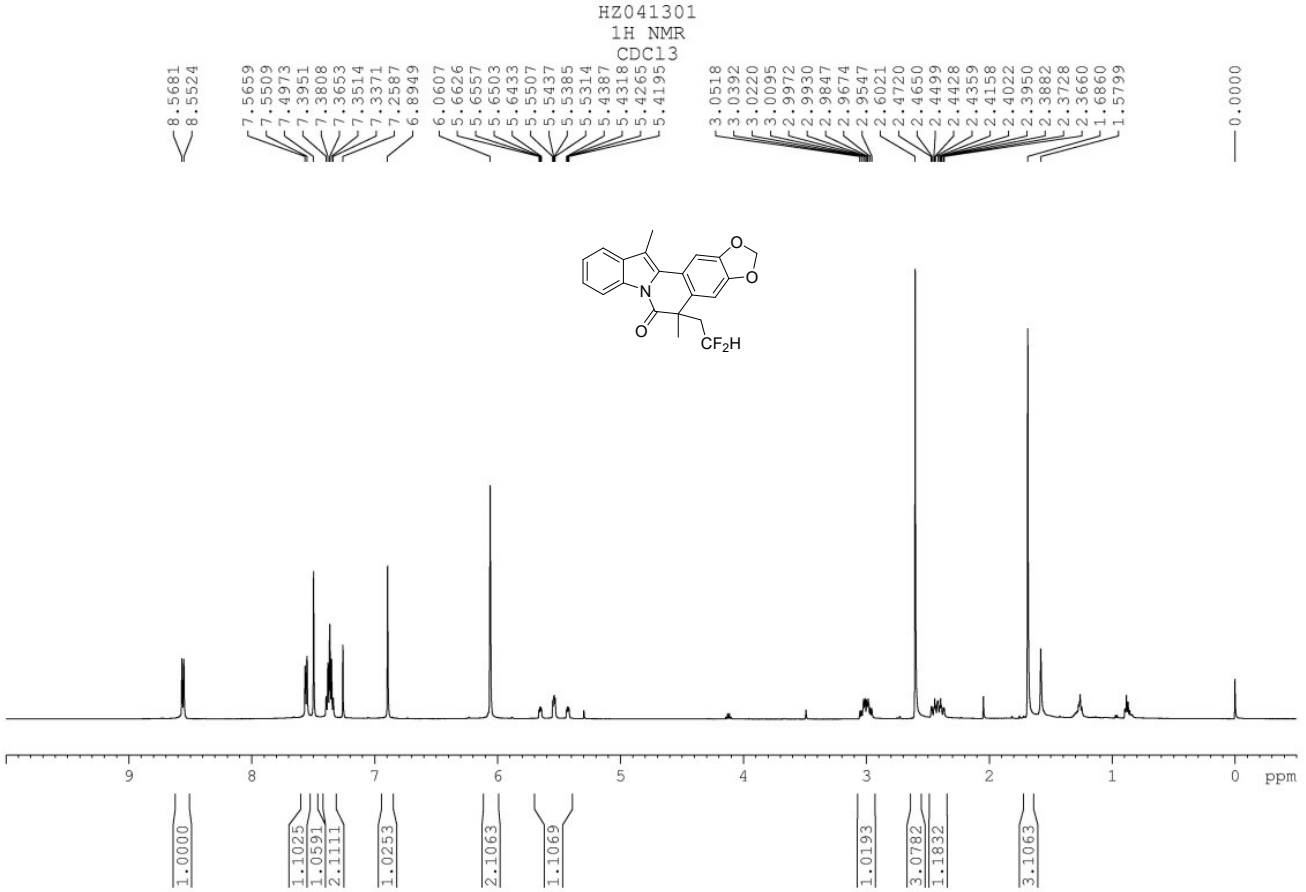


Fig. S107 ^{1}H NMR (500 MHz) spectrum of compound **5f**

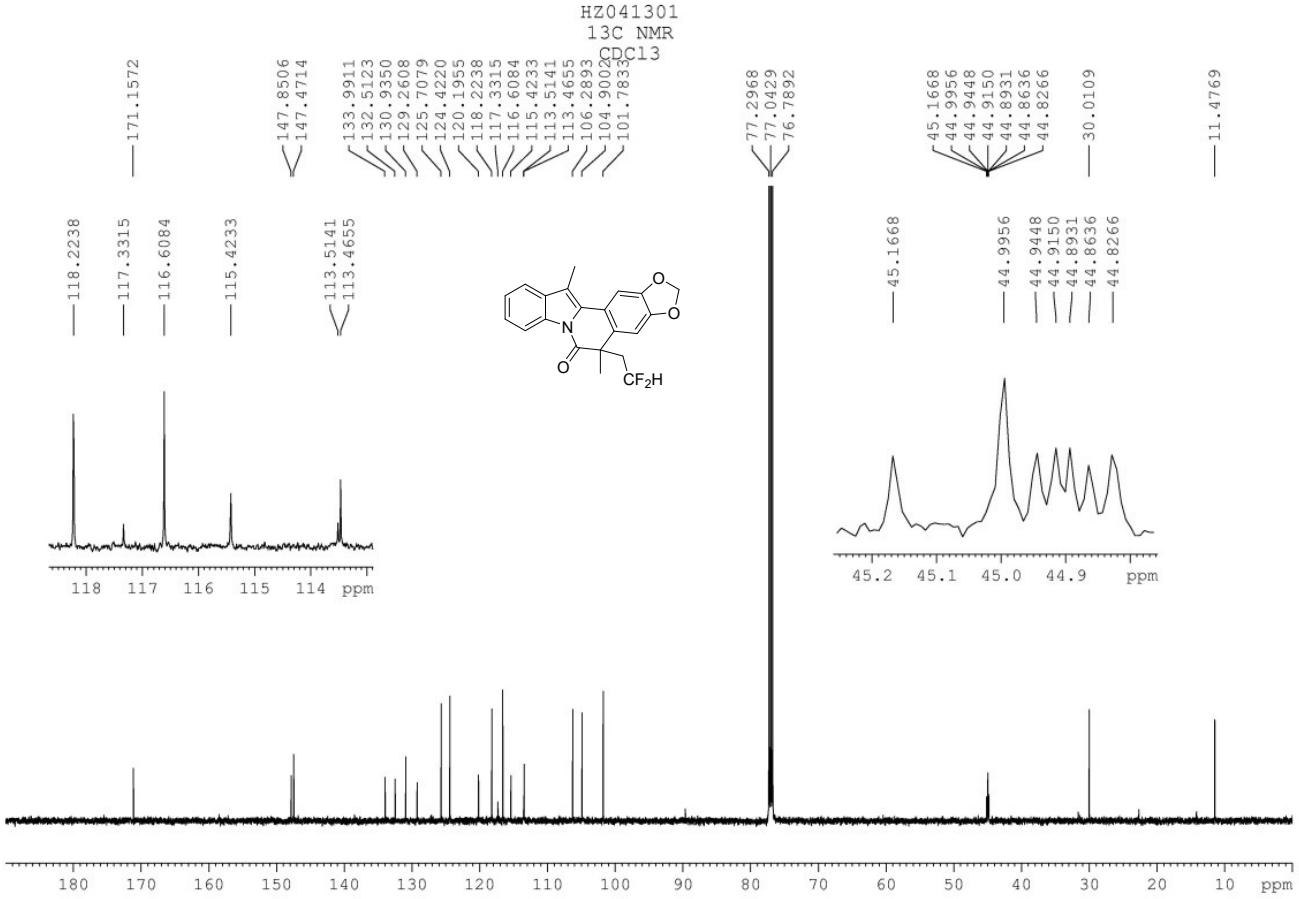


Fig. S108 ^{13}C NMR (125 MHz) spectrum of compound **5f**

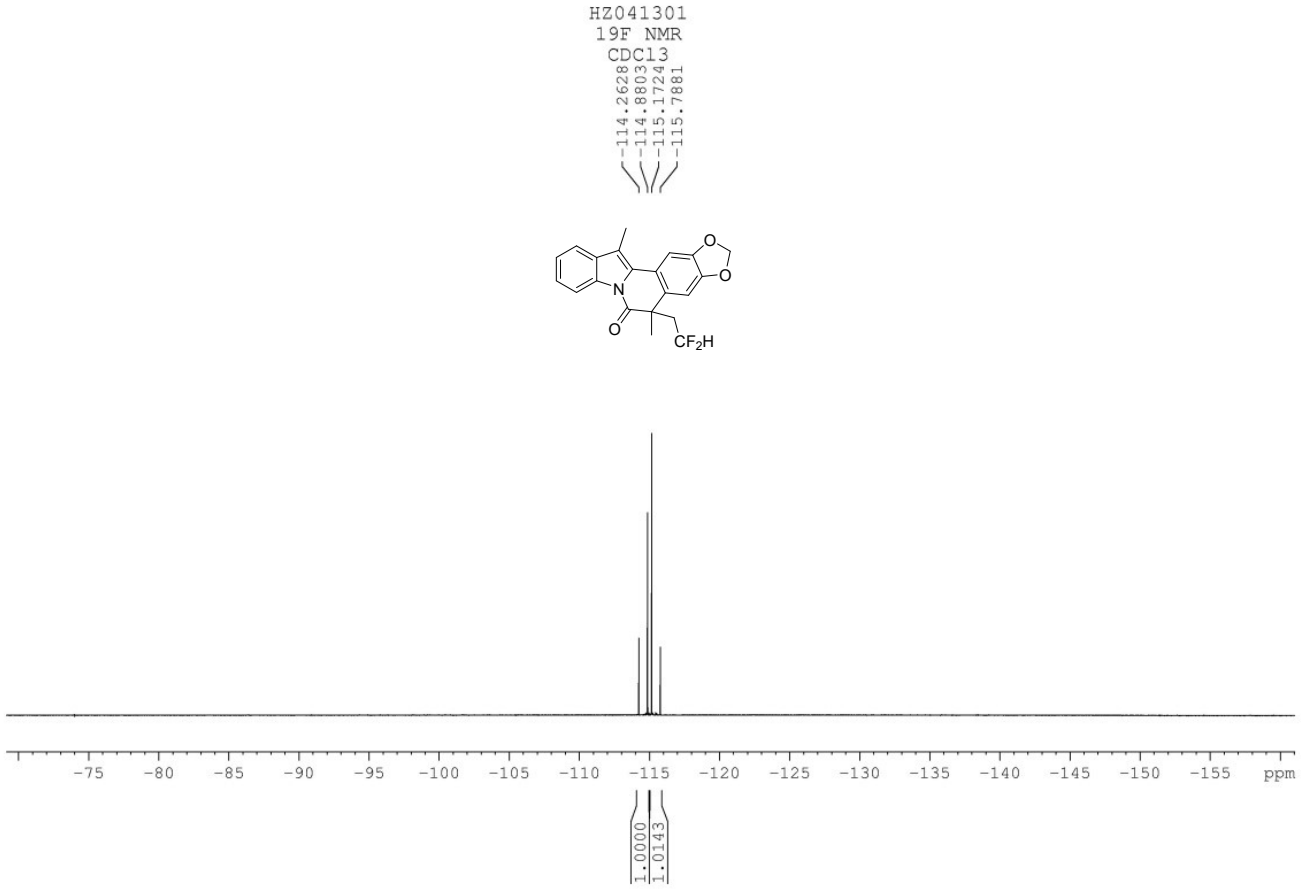


Fig. S109 ^{19}F NMR (470 MHz) spectrum of compound **5f**

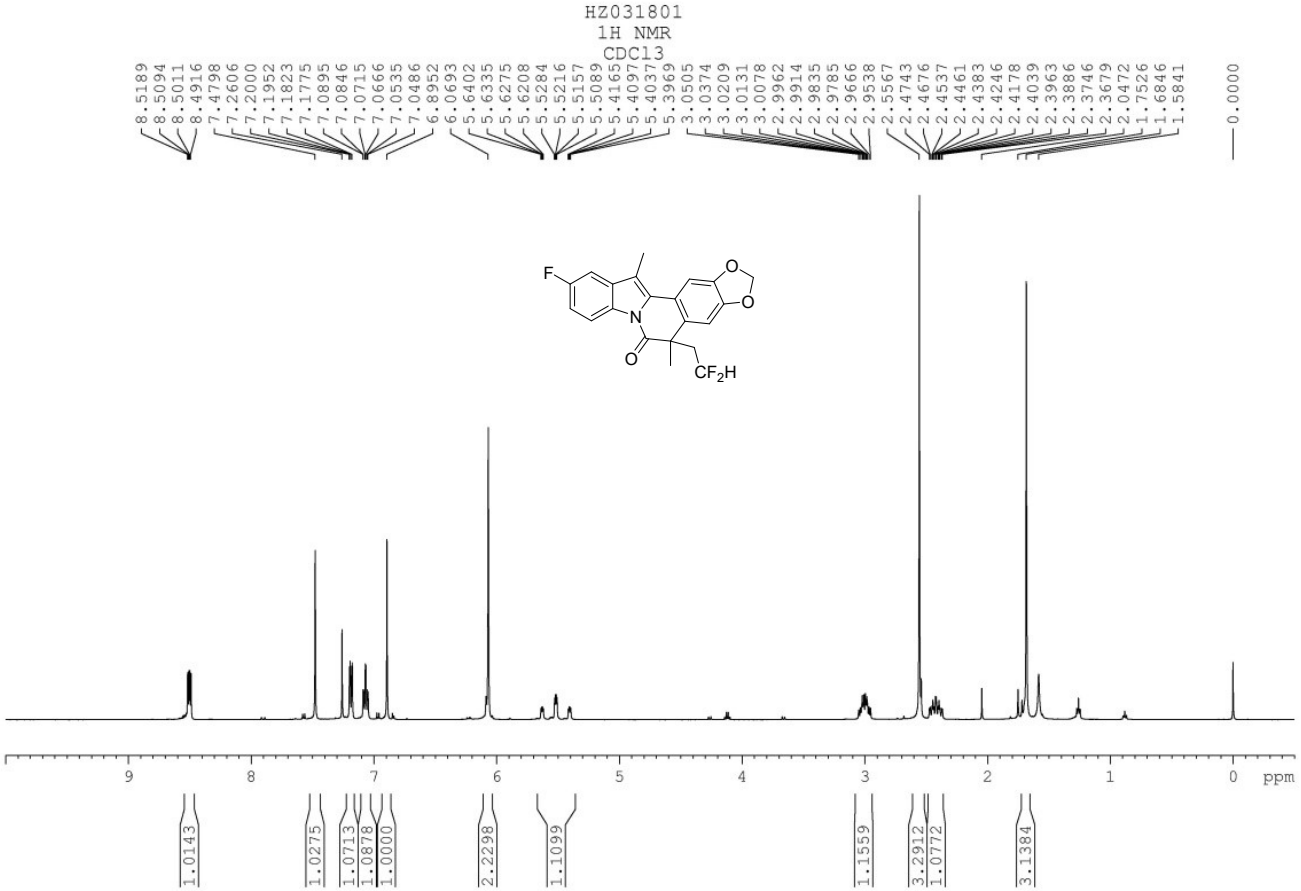


Fig. S110 ^{1}H NMR (500 MHz) spectrum of compound **5g**

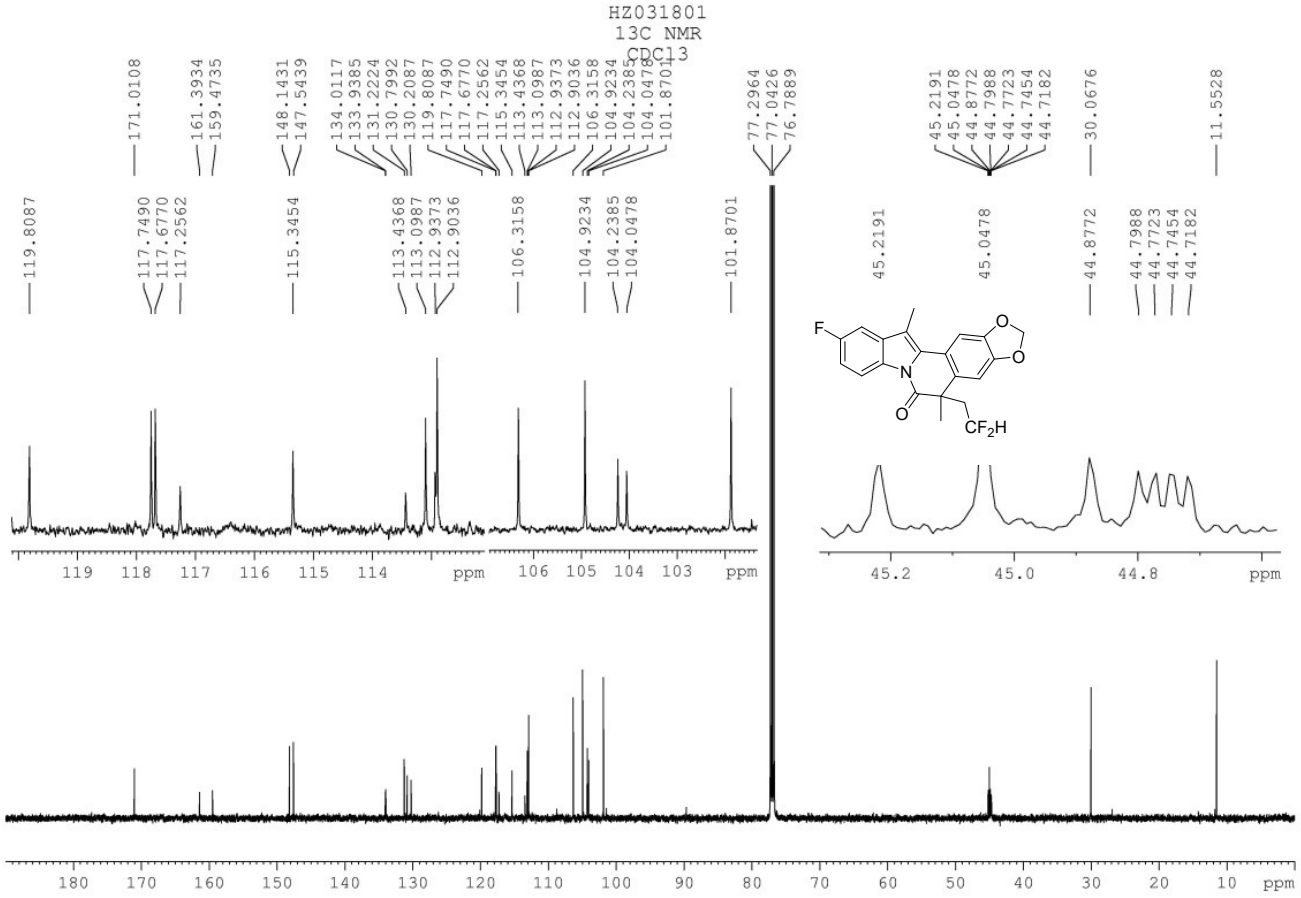


Fig. S111 ^{13}C NMR (125 MHz) spectrum of compound **5g**

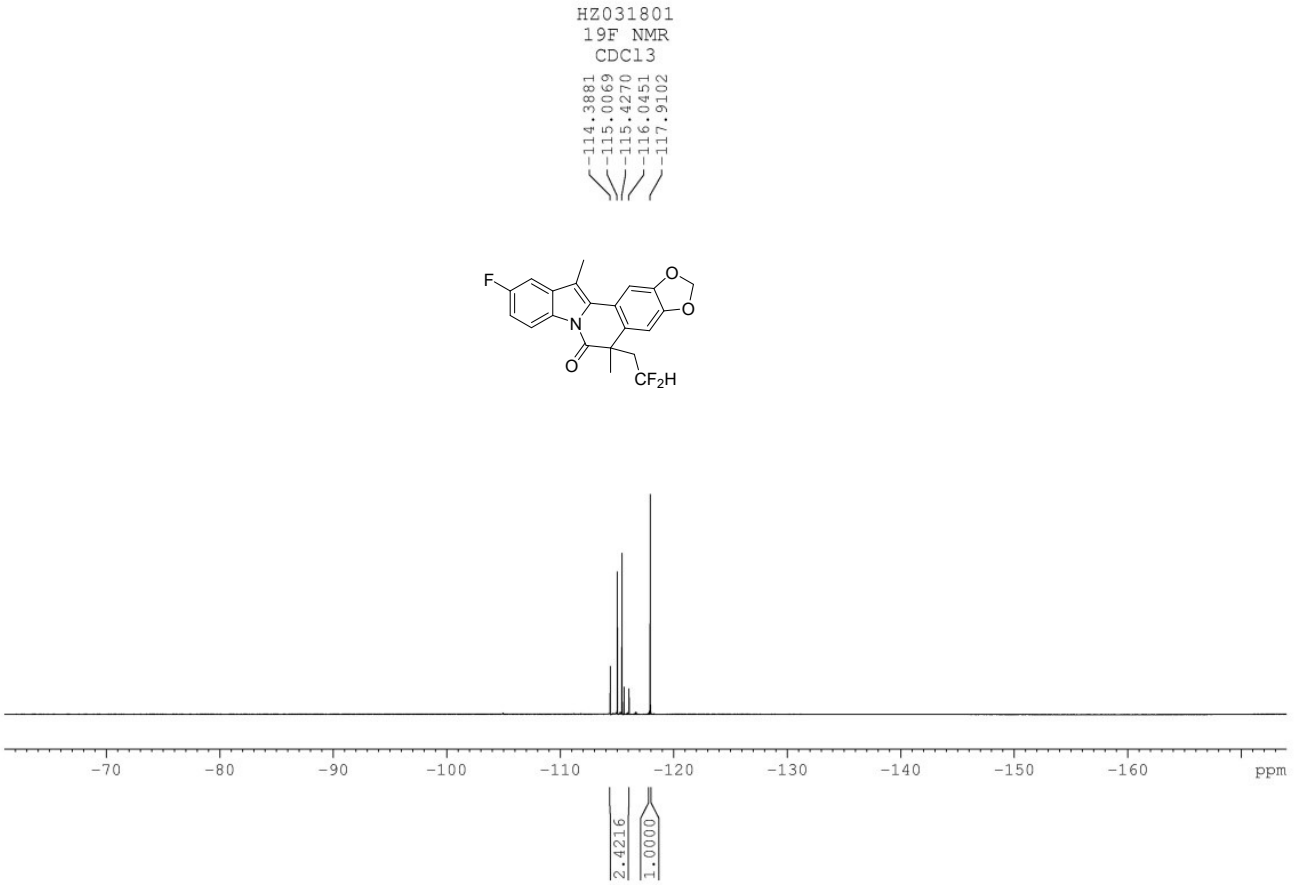


Fig. S1112 ^{19}F NMR (470 MHz) spectrum of compound **5g**

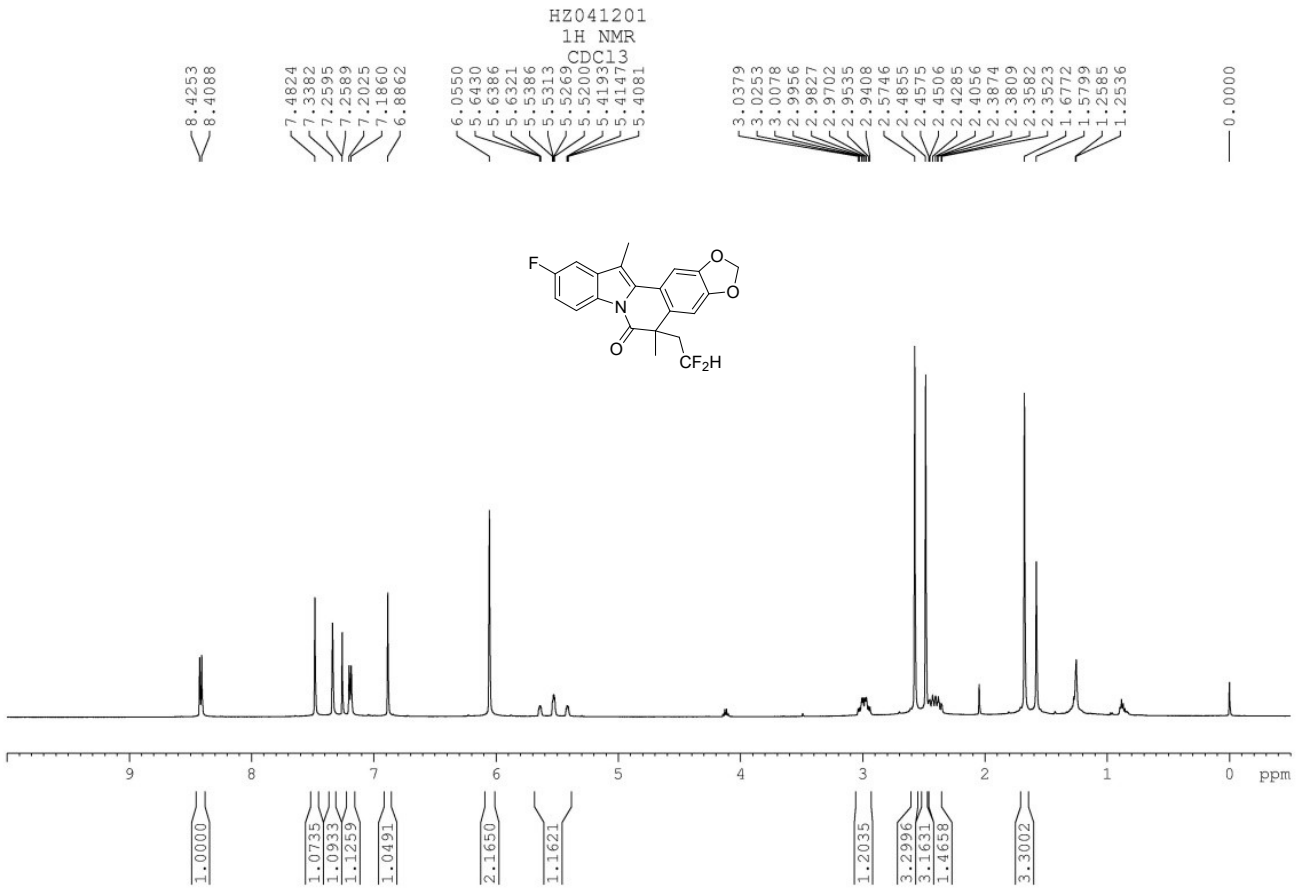


Fig. S113 ^{1}H NMR (500 MHz) spectrum of compound **5h**

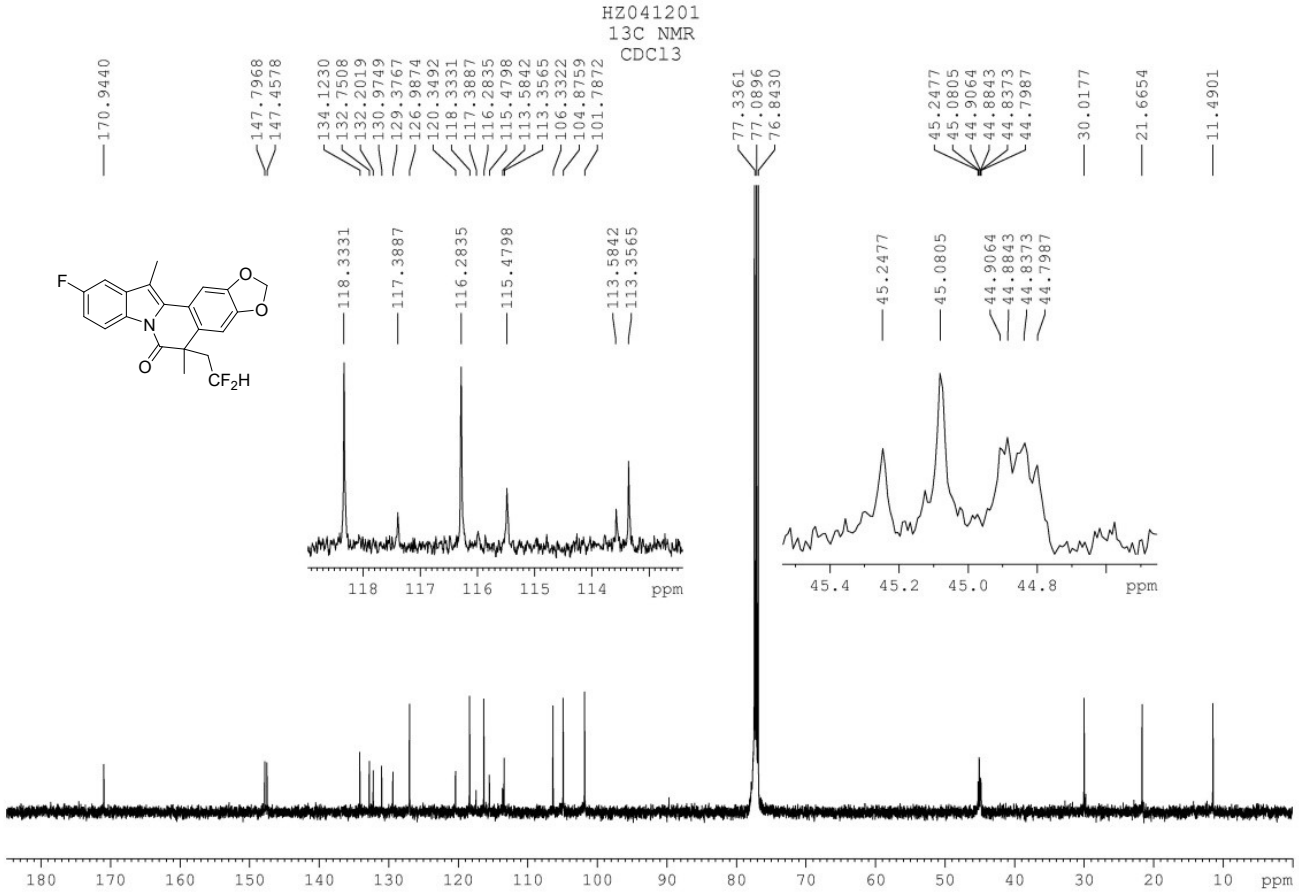


Fig. S114 ^{13}C NMR (125 MHz) spectrum of compound **5h**

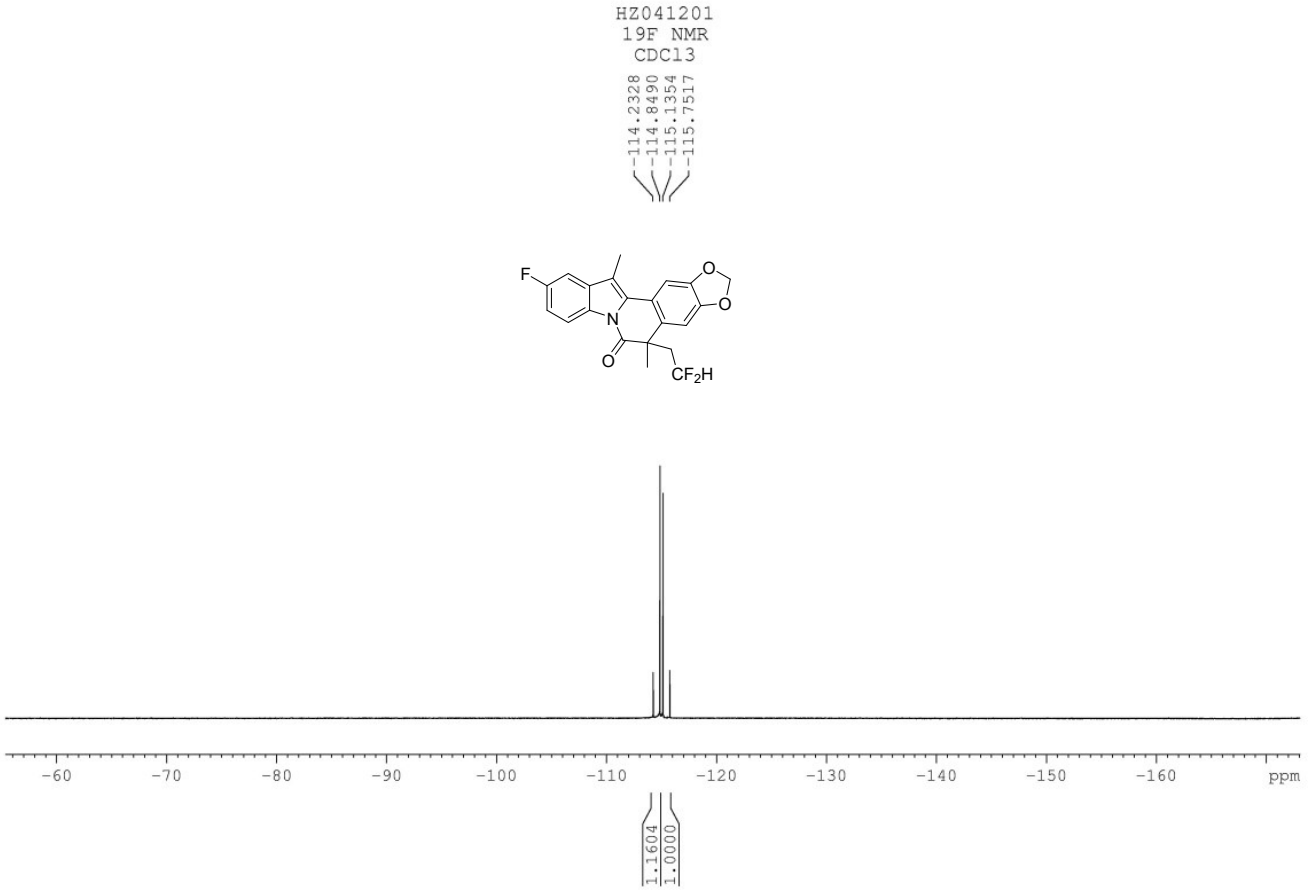


Fig. S115 ^{19}F NMR (470 MHz) spectrum of compound **5h**

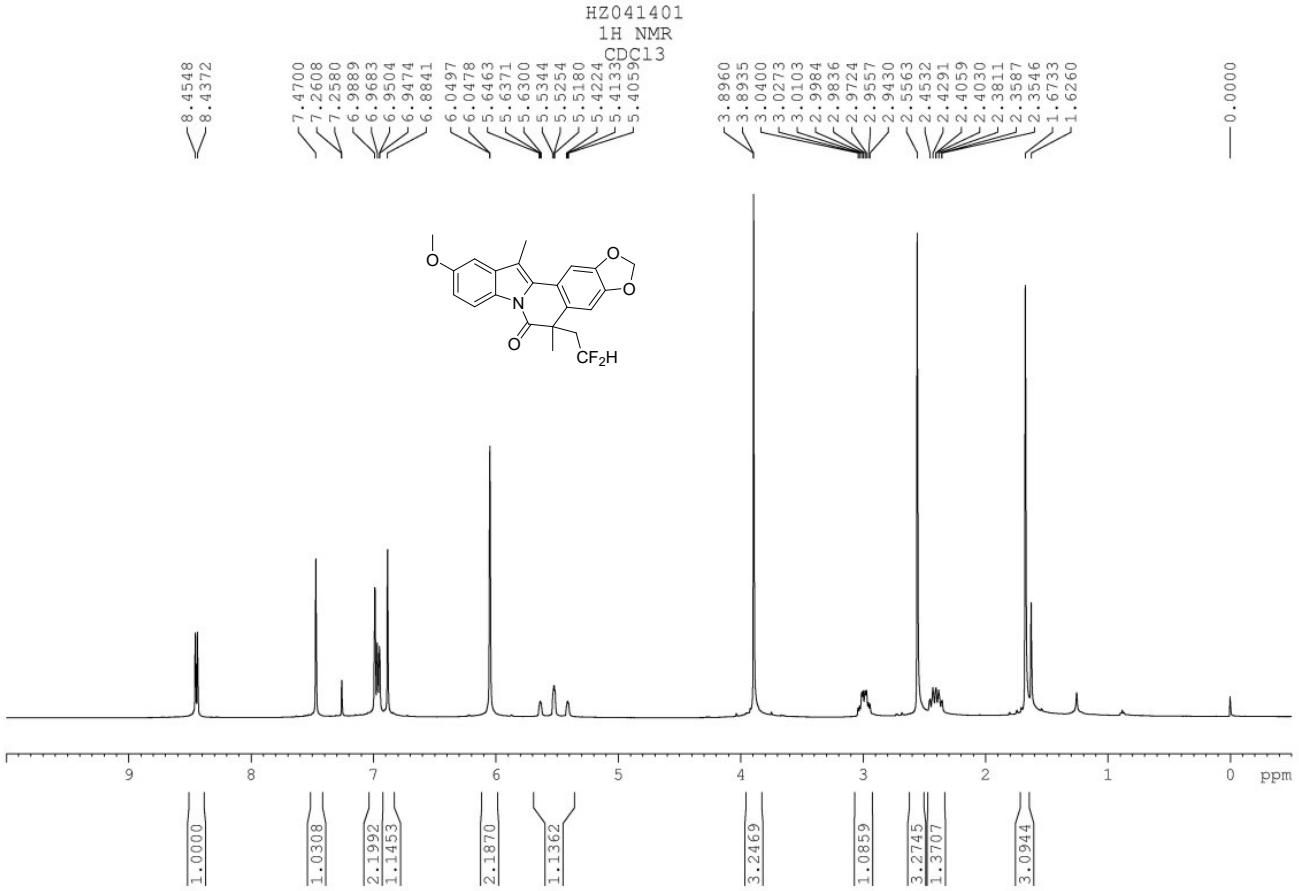


Fig. S116 ^{1}H NMR (500 MHz) spectrum of compound **5i**

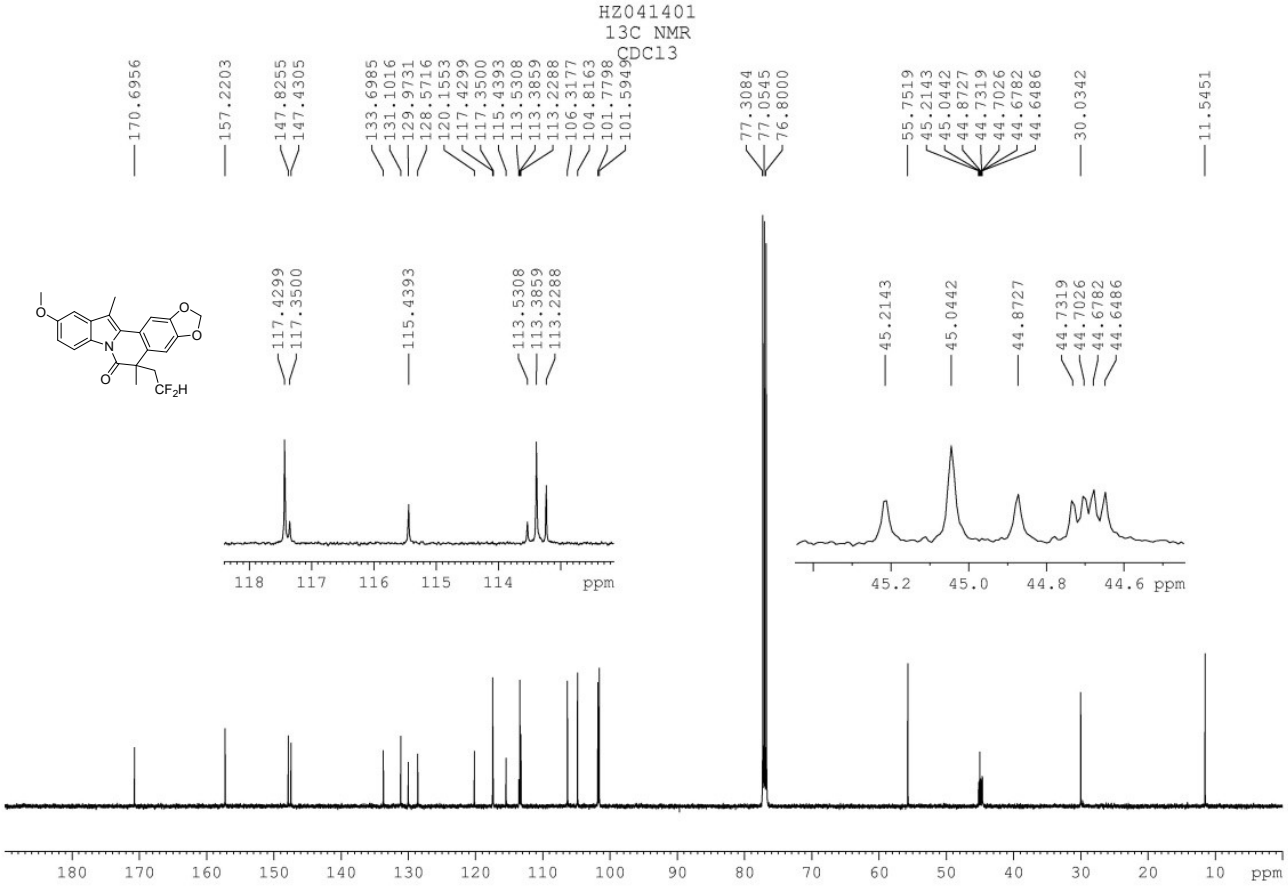


Fig. S117 ^{13}C NMR (125 MHz) spectrum of compound **5i**

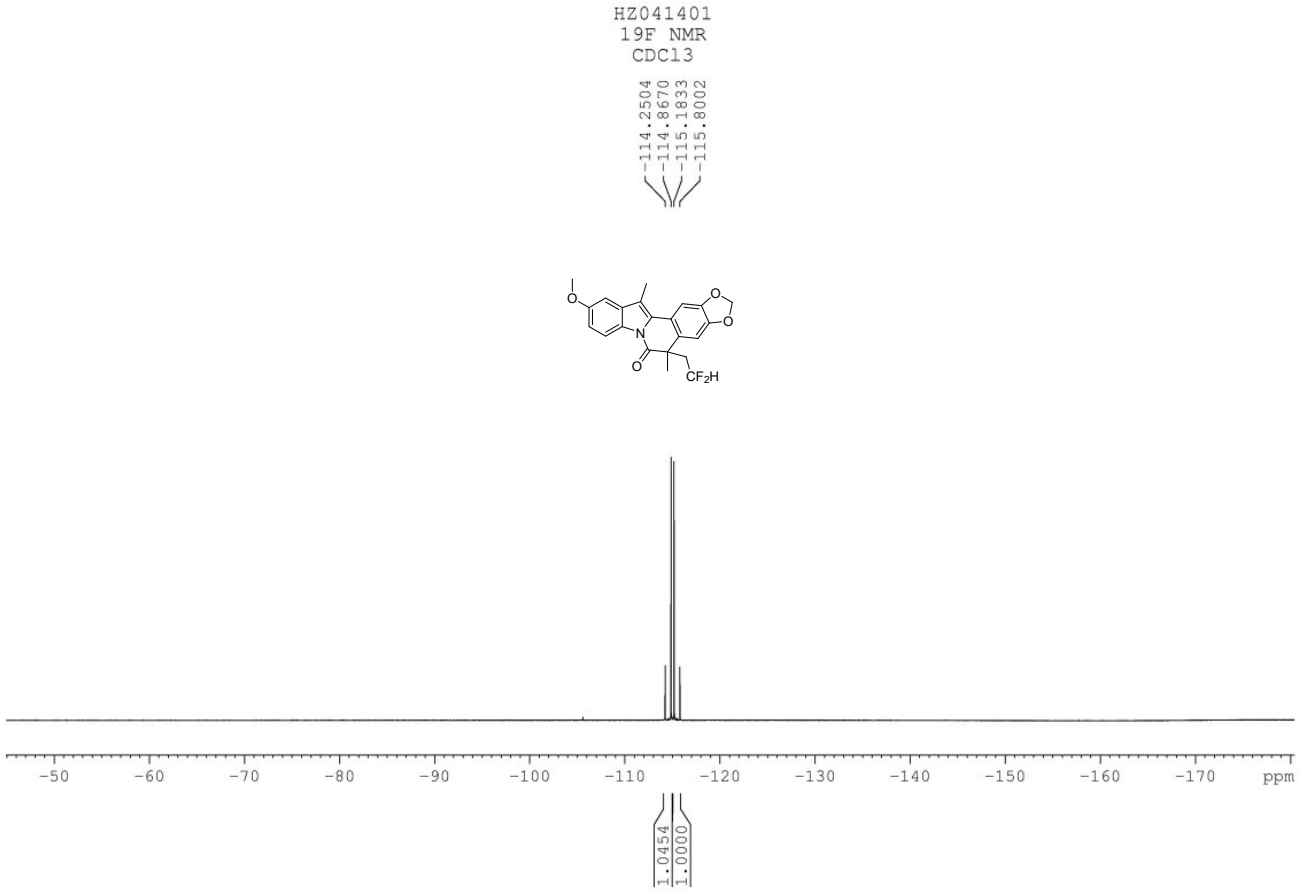


Fig. S118 ^{19}F NMR (470 MHz) spectrum of compound **5i**

References

[1] (a) Zhang, C.; Yu, Z.; Ding, Y.; Shi, Y.; Xie, Y. Metal-free electrochemistry promoted radical cascade cyclization to access CF_3-containing benzimidazo[2,1-*a*]isoquinolin-6(5*H*)-ones. *Org. Biomol. Chem*. **2023**, *21*, 6715-6718; (b) Sun, K.; Li, G.; Guo, S.; Zhang, Z.; Zhang, G. Copper-catalyzed radical cascade cyclization for synthesis of CF_3-containing tetracyclic benzimidazo[2,1-*a*]iso-quinolin-6(5*H*)-ones. *Org. Biomol. Chem*. **2021**, *19*, 375-378.

[2] (a) Wei, Y. L.; Chen, J. Q.; Sun, B.; Xu, P. F. Synthesis of indolo[2,1-*a*]isoquinoline derivatives via visible-light-induced radical cascade cyclization reactions. *Chem. Commun*. **2019**, *55*, 5922-5925; (b) Yuan, X.; Duan, X.; Cui, Y. S.; Sun, Q.; Qin, L. Z.; Zhang, X. P.; Liu, J.; Wu, M. Y.; Qiu, J. K.; Guo, K. Visible-light photocatalytic tri- and difluoroalkylation cyclizations: Access to a series of indole[2,1-a]isoquinoline derivatives in continuous flow. *Org. Lett*. **2021**, *23*, 1950-1954.