SUPPORTING INFORMATION

Radical-Promoted Cyclization of 3-Allyl-2-arylquinazolinones Mediated by Silver(I) Salts to Access SCF_3/SCN-Enriched Dihydroisoquinolino[1,2-b]quinazolinones

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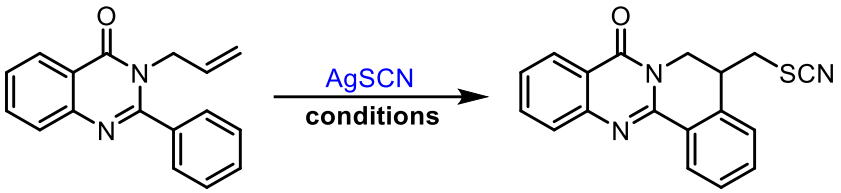
1. General Information:

Most of the reagents and starting materials used were purchased from commercial sources and used as such. Commercially available dry Dimethyl sulfoxide and dry Acetonitrile were used without further distillation. Melting points are uncorrected and recorded using a digital Buchi Melting Point Apparatus B-540. ^{1}H, ^{13}C, DEPT, and 19F NMR spectra were recorded on Bruker AV 400/500, AV 100/125 & AV 376 MHz spectrometers, respectively, in CDCl3 /DMSO-d6 using TMS as internal standard, and the chemical shifts are shown in δ scale. Multiplicities of ^{1}H NMR signals are designated as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), quin (quintet), spt (septet) br.s.(broad signal), m (multiplet) etc. Thin layer chromatography was performed on Merck silica gel 60 F254 TLC plates using EtOAc/ pet ether as an eluent. Column chromatography was carried out through silica gel (100-200 mesh) using ethyl acetate/pet ether as an eluent. High-resolution mass spectra (HRMS) were recorded on a Q-Exactive Hybrid Quadrupole Orbitrap Mass Spectrometer, where the mass analyzer used for analysis is an Orbitrap. Chemical nomenclature was generated using ChemDraw Ultra 20.0.

Note: Compounds 2g, 2h, 2i, 2j, and 3j are a mixture of regioisomers and cannot be separated by normal column chromatography. The ratios of regioisomers (r : r') are calculated based on ^{1}H NMR analysis.

2. Optimization Studies:

Table S1. Optimization of reaction conditions[a]

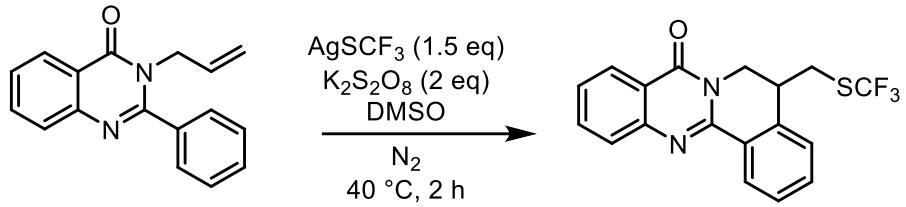


entry	oxidant	solvent	base	temp. (°C)	time (h)	yield (%)[e]
1	$K_2S_2O_8$	DMSO	-	rt	8	-
2	$K_2S_2O_8$	DMSO	-	40	8	63
3	$Na_2S_2O_8$	DMSO	-	40	8	Trace
4	CAN	DMSO	-	40	8	34
5	Oxone	DMSO	-	40	8	27
6	TBHP	DMSO	-	40	8	24
7	$PhI(OAc)_2$	DMSO	-	40	8	Trace
8	$K_2S_2O_8$	THF	-	40	8	-
9	$K_2S_2O_8$	Ethylacetate	-	40	8	-
10	$K_2S_2O_8$	CH_3CN	-	40	8	68
11	$K_2S_2O_8$	DCE	-	40	8	42
12	$K_2S_2O_8$	DMSO	-	40	8	Trace
13	$K_2S_2O_8$	CH_3CN	DBU	40	8	51
14	$K_2S_2O_8$	CH_3CN	Pyridine	40	8	86
15	$K_2S_2O_8$	CH_3CN	Et_3N	40	8	-
16	$K_2S_2O_8$	CH_3CN	Cs_2CO_3	40	8	74
17	$K_2S_2O_8$	CH_3CN	K_2CO_3	40	8	-
18	$K_2S_2O_8$	CH_3CN	Pyridine	60	8	84
19	$K_2S_2O_8$	CH_3CN	Pyridine	75	8	88
20	$K_2S_2O_8$	CH_3CN	Pyridine	75	4	88
21	$K_2S_2O_8$	CH_3CN	Pyridine	75	2	88
22	$K_2S_2O_8$	CH_3CN	Pyridine	75	1.5	60
23		CH_3CN	Pyridine	75	2	-

[a]Reaction conditions: 3-Allyl-2-arylquinazolinones **1a** (0.2 mmol, 1equiv), AgSCN (0.3 mmol, 1.5 equiv), oxidant (0.4 mmol, 2 equiv) and base (0.04, 0.2 equiv) in CH_3CN (2 mL) solvent in a reaction vial, isolated yields, N.D.: not detected

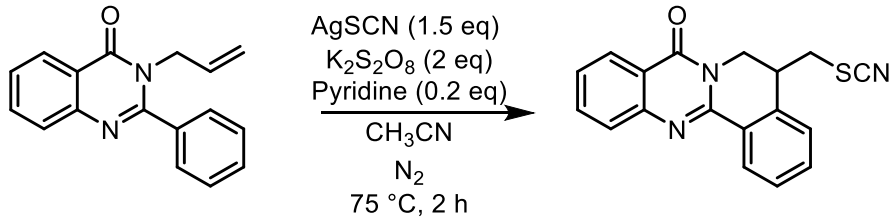
3. Experimental Procedures:

3.1 General procedure for the synthesis of 2a.



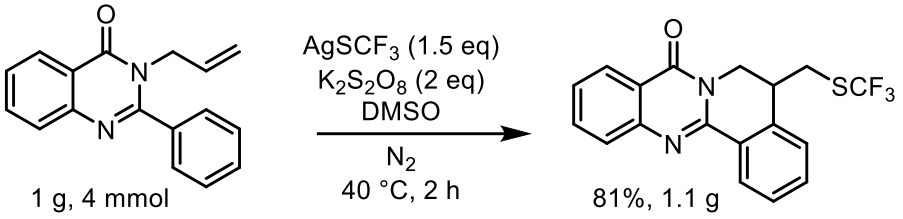
Allylquinazolinones (0.2 mmol, 1 equiv), Silver trifluoromethanethiolate (0.3 mmol, 1.5 equiv), and $K_2S_2O_8$ (0.4 mmol, 2 equiv) were taken in a 10 mL two-neck round-bottom reaction flask. Then DMSO (2 mL) was added with a syringe under a N_2 atmosphere. The reaction mixture was stirred at 40 °C (oil bath temperature) for 2 hrs. After completion of the reaction (monitored by TLC), water was added to the mixture, and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to get the crude product, which was purified by column chromatography on silica gel using ethyl acetate and hexane as eluents to afford the desired product.

3.2 General procedure for the synthesis of 3a.



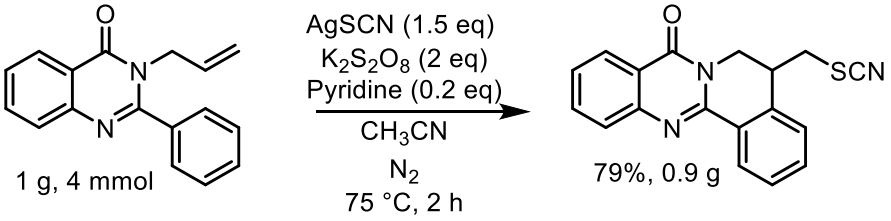
Allylquinazolinones (0.2 mmol, 1 equiv), Silver thiocyanate (0.3 mmol, 1.5 equiv), $K_2S_2O_8$ (0.4 mmol, 2 equiv), and Pyridine (0.04 mmol, 0.2 equiv) were taken in a 10 mL two-neck round-bottom reaction flask. Then CH_3CN (2 mL) was added with a syringe under a N_2 atmosphere. The reaction mixture was stirred at 75 °C (oil bath temperature) for 2 hrs. After completion of the reaction (monitored by TLC), water was added to the mixture, and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to get the crude product, which was purified by column chromatography on silica gel using ethyl acetate and hexane as eluents to afford the desired product.

3.3 General procedure for the gram scale synthesis of 2a.



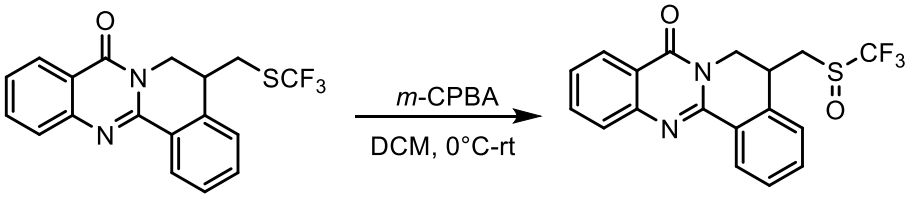
Allylquinazolinones (4 mmol, 1 equiv), Silver trifluoromethanethiolate (6 mmol, 1.5 equiv), and $K_2S_2O_8$ (8 mmol, 2 equiv) were taken in a 50 mL two-neck round-bottom reaction flask. Then DMSO (10 mL) was added with a syringe under a N_2 atmosphere. The reaction mixture was stirred at 40 °C (oil bath temperature) for 2 hrs. After completion of the reaction (monitored by TLC), water was added to the mixture, and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to get the crude product, which was purified by column chromatography on silica gel using ethyl acetate and hexane as eluents to afford the desired product.

3.4 General procedure for the gram scale synthesis of 3a.



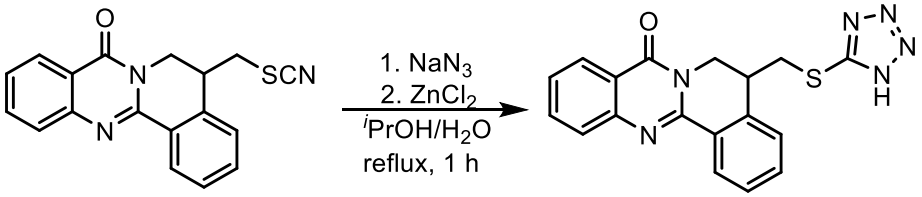
Allylquinazolinones (4 mmol, 1 equiv), Silver thiocyanate (6 mmol, 1.5 equiv), $K_2S_2O_8$ (8 mmol, 2 equiv), and Pyridine (0.4 mmol, 0.2 equiv) were taken in a 50 mL two-neck round-bottom reaction flask. Then CH_3CN (10 mL) was added with a syringe under a N_2 atmosphere. The reaction mixture was stirred at 75 °C (oil bath temperature) for 2 hrs. After completion of the reaction (monitored by TLC), water was added to the mixture, and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to get the crude product, which was purified by column chromatography on silica gel using ethyl acetate and hexane as eluents to afford the desired product.

3.5 General procedure for the synthesis of 4.



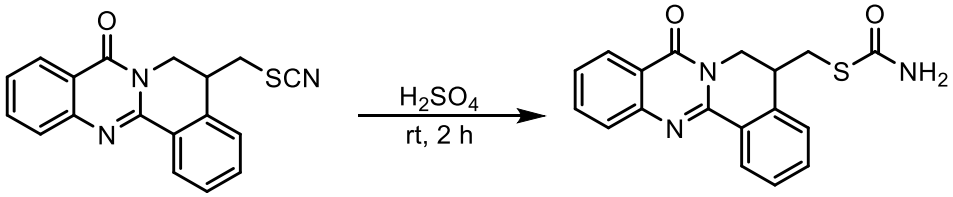
An oven-dried 10 mL round-bottom flask fitted with a stirring bar was charged with compound **2a** (0.2 mmol, 1 equiv) in DCM (4 mL) under a N_2 atmosphere. *m*-CPBA (0.3 mmol, 1.5 equiv) was added portion-wise to the solution at 0°C and stirred at room temperature for 2 h until TLC indicated the consumption of starting materials. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel (hexane:ethyl acetate, 15%) to give the corresponding products **4**.

3.6 General procedure for the synthesis of 5.



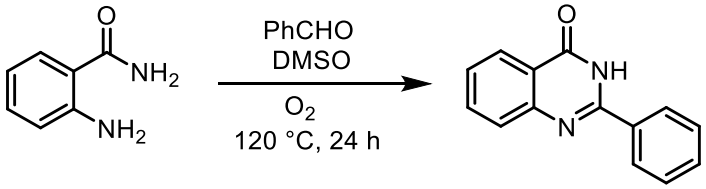
Compound **2g** (0.2 mmol, 1 equiv), $ZnBr_2$ (0.2 mmol, 1 equiv) and NaN_3 (0.5 mmol, 2.5 equiv) were combined in a mixed solvent [H_2O/^{i}PrOH (1:1, 3 mL)] and refluxed for 1 h. Upon completion of the reaction, the mixture was diluted with EtOAc. The solvent was then removed under vacuo. Column chromatography of the residue (DCM/Methanol, 5%) provided tetrazole **5**.

3.7 General procedure for the synthesis of 6.



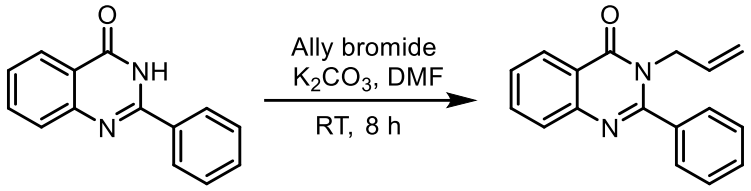
Compound **2g** (0.2 mmol, 1 equiv) and 1 mL 95% sulfuric acid were stirred for 2 h at room temperature. Upon completion of the reaction, the mixture was diluted with EtOAc and cooled water. The solvent was then removed under vacuo. The residue was purified by column chromatography on silica gel (hexane:ethyl acetate, 25%) to give the corresponding products **6**.

3.8.1 General procedure for the synthesis of Quinazolinones[1-3]



A mixture of anthranilamide (1.0 mmol, 1.0 equiv) and benzaldehyde (1.2 mmol, 1.2 equiv) was charged into a dry flask equipped with a stir bar, to which DMSO was added under O_2. The mixture was stirred for 24 h at 120 °C. After cooling to rt, ice-cold water (100 mL) was added to the reaction mixture, and the precipitate was formed and collected by filtration. The crude product was recrystallized in ethanol to afford a pure product (quinazolinones).

3.8.2 General procedure for the synthesis of 2-Phenyl-3-allylquinazolinones

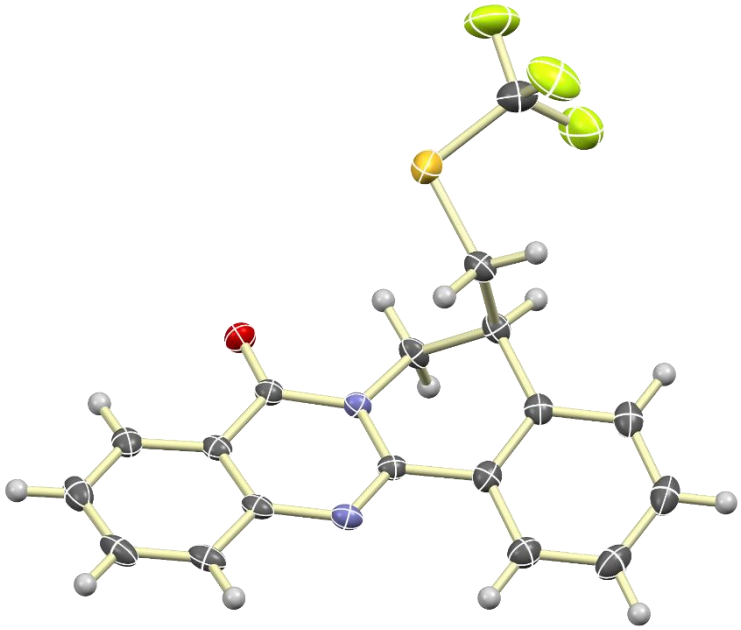


To a mixture of quinazolinones (1.0 mmol, 1.0 equiv) in DMF, allyl bromide (1.2 mmol, 1.2 equiv) and potassium carbonate (3.0 mmol, 3.0 equiv) were added, and the reaction mixture was stirred at room temperature for 8 h. After completion of the reaction, the reaction mixture was washed with water and extracted with chloroform. The combined organic layers were dried over Na_2SO_4 and concentrated to get the crude product, which was purified by column chromatography on silica gel using ethyl acetate and hexane as eluents to afford the desired allylquinazolinones product.

4. X-ray Analysis:

The single crystals of component **2a** were obtained from the Chloroform solvent by the slow evaporation method. The single crystal X-ray diffraction measurements were performed to determine the crystal structure of all three components at 100 K using APEX3 (Bruker,2016; Bruker D8 VENTURE Kappa Duo PHOTON II CPAD) diffractometer having graphite-monochromatized (MoKα (0.71073)). The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of unit cell parameters and an orientation matrix were calculated from 36 frames, and the cell refinement was performed by SAINT-Plus (Bruker,2016). An optimised strategy used for data collection consisted of different sets of φ and ω scans with 0.5^{o} steps φ/ω. The data were collected with a time frame of 10 sec by setting the sample to detector distance fixed at 40 cm. All the data points were corrected for Lorentzian, polarisation, and absorption effects using SAINT-Plus and SADABS programs (Bruker,2016). SHELXS-97 (Sheldrick,2008) was used for structure solution, and full-matrix least-squares refinement on F^{2}.[1, 2] The molecular graphics of ORTEP diagrams were performed by Mercury software. The crystal symmetry of the components was cross-checked by running the cif files through PLATON (Spek, 2020) software and notified that no additional symmetry was observed. The Encifer software was used to correct the cif files.

Figure S1. ORTEP drawing of **2a** with 50% thermal ellipsoids.



Sample and crystal data for 2a.

Identification code	2s_scf3	
Chemical formula	$C_{18}H_{13}F_3N_2OS$	
Formula weight	362.36 g/mol	
Temperature	179(2) K	
Wavelength	0.71073 Å	
Crystal size	0.160 x 0.200 x 0.220 mm	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 18.4664(18) Å	α = 90°
	b = 8.2112(10) Å	β = 111.933(3)°
	c = 23.118(3) Å	γ = 90°
Volume	3251.7(6) $Å^3$	
Z	8	
Density (calculated)	1.480 g/cm^3	
Absorption coefficient	0.239 mm^{-1}	
F(000)	1488	
CCDC number	2487002	

Data collection and structure refinement for 2a.

Theta range for data collection	2.43 to 28.73°	
Index ranges	-24<=h<=24, -10<=k<=10, -30<=l<=30	
Reflections collected	45447	
Independent reflections	8170 [R(int) = 0.0867]	
Max. and min. transmission	0.9630 and 0.9490	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)	
Function minimized	$\Sigma\ w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	8170 / 0 / 451	
Goodness-of-fit on F^2	1.043	
Δ/σ_{max}	0.001	
Final R indices	6358 data; I>2σ(I)	R1 = 0.0576, wR2 = 0.1428
	all data	R1 = 0.0793, wR2 = 0.1611

Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0664P)^2+3.4690P]$ where $P=(F_o^2+2F_c^2)/3$
Largest diff. peak and hole	0.572 and -0.701 eÅ^{-3}
R.M.S. deviation from mean	0.078 eÅ^{-3}

Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for 2a.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
F1A	0.70943(11)	0.1184(2)	0.47025(8)	0.0436(4)
O1	0.68051(9)	0.6386(2)	0.63029(7)	0.0251(4)
O1A	0.79985(9)	0.1771(2)	0.69520(7)	0.0233(3)
N1	0.78597(10)	0.7359(2)	0.71108(8)	0.0177(4)
N1A	0.66963(10)	0.2334(2)	0.65523(8)	0.0160(3)
C1	0.91234(12)	0.7354(3)	0.69726(11)	0.0212(4)
C1A	0.59952(12)	0.2105(3)	0.54112(10)	0.0179(4)
F2	0.96385(12)	0.9932(2)	0.55345(10)	0.0561(5)
F2A	0.76970(12)	0.3059(2)	0.44129(10)	0.0579(5)
N2	0.77447(11)	0.9094(2)	0.78910(8)	0.0204(4)
N2A	0.60713(10)	0.3864(2)	0.71015(8)	0.0173(4)
C2	0.94983(12)	0.7824(3)	0.76516(11)	0.0220(4)
C2A	0.52424(12)	0.2248(3)	0.55241(10)	0.0180(4)
F3	0.90943(13)	0.7970(3)	0.49184(8)	0.0633(6)
F3A	0.64413(11)	0.3033(2)	0.40794(7)	0.0473(4)
C3	0.03102(13)	0.7832(3)	0.79658(12)	0.0260(5)
C3A	0.45147(12)	0.2007(3)	0.50483(10)	0.0209(4)
C4	0.06338(14)	0.8242(3)	0.85905(13)	0.0321(6)
C4A	0.38374(13)	0.2173(3)	0.51696(11)	0.0240(5)
C5	0.01601(15)	0.8683(3)	0.89104(12)	0.0322(6)
C5A	0.38773(13)	0.2592(3)	0.57618(11)	0.0239(5)
C6	0.93545(14)	0.8708(3)	0.86044(11)	0.0270(5)
C6A	0.45978(12)	0.2853(3)	0.62382(10)	0.0205(4)
C7	0.90228(13)	0.8268(3)	0.79759(11)	0.0220(4)
C7A	0.52812(12)	0.2691(3)	0.61178(10)	0.0176(4)
C8	0.81649(12)	0.8264(3)	0.76557(10)	0.0185(4)
C8A	0.60453(12)	0.2997(3)	0.66248(10)	0.0169(4)
C9	0.69399(13)	0.9055(3)	0.75769(10)	0.0204(4)
C9A	0.67950(12)	0.4105(3)	0.75731(9)	0.0174(4)

	x/a	y/b	z/c	U(eq)
C10	0.64704(14)	0.9984(3)	0.78141(11)	0.0253(5)
C10A	0.68446(13)	0.5104(3)	0.80829(10)	0.0205(4)
C11	0.56720(15)	0.9951(3)	0.75210(12)	0.0298(5)
C11A	0.75581(13)	0.5354(3)	0.85585(10)	0.0238(5)
C12	0.53101(14)	0.8978(3)	0.69947(12)	0.0302(5)
C12A	0.82348(13)	0.4612(3)	0.85468(11)	0.0257(5)
C16	0.83820(13)	0.6414(3)	0.68848(11)	0.0217(4)
S1	0.84936(4)	0.84765(12)	0.57316(3)	0.0427(2)
S1A	0.71727(3)	0.40531(7)	0.52277(3)	0.02453(14)
F1	0.98992(11)	0.7542(3)	0.58624(9)	0.0534(5)
C13	0.57616(13)	0.8063(3)	0.67524(11)	0.0242(5)
C13A	0.81963(12)	0.3630(3)	0.80539(10)	0.0223(4)
C14	0.65783(12)	0.8122(3)	0.70376(10)	0.0195(4)
C14A	0.74790(12)	0.3397(3)	0.75568(9)	0.0176(4)
C15	0.70608(12)	0.7213(3)	0.67777(10)	0.0191(4)
C15A	0.74390(12)	0.2438(3)	0.70153(10)	0.0175(4)
C17	0.89695(14)	0.8885(3)	0.65658(11)	0.0253(5)
C16A	0.66155(12)	0.1380(3)	0.59916(10)	0.0187(4)
C18	0.93160(16)	0.8478(4)	0.55073(12)	0.0347(6)
C17A	0.62041(12)	0.3803(3)	0.52376(10)	0.0187(4)
C18A	0.70961(16)	0.2775(3)	0.45819(13)	0.0334(6)

Bond lengths (Å) for 2a.

F1A-C18A	1.336(3)	O1-C15	1.225(3)
O1A-C15A	1.226(3)	N1-C8	1.388(3)
N1-C15	1.391(3)	N1-C16	1.477(3)
N1A-C8A	1.386(3)	N1A-C15A	1.392(3)
N1A-C16A	1.474(3)	C1-C2	1.510(3)
C1-C16	1.518(3)	C1-C17	1.532(3)
C1A-C2A	1.512(3)	C1A-C16A	1.523(3)
C1A-C17A	1.539(3)	F2-C18	1.325(3)
F2A-C18A	1.328(3)	N2-C8	1.295(3)
N2-C9	1.390(3)	N2A-C8A	1.298(3)
N2A-C9A	1.387(3)	C2-C7	1.399(3)
C2-C3	1.401(3)	C2A-C7A	1.395(3)
C2A-C3A	1.397(3)	F3-C18	1.334(3)
F3A-C18A	1.344(3)	C3-C4	1.383(4)

C3A-C4A	1.387(3)	C4-C5	1.388(4)
C4A-C5A	1.387(3)	C5-C6	1.389(3)
C5A-C6A	1.391(3)	C6-C7	1.397(3)
C6A-C7A	1.397(3)	C7-C8	1.477(3)
C7A-C8A	1.481(3)	C9-C14	1.402(3)
C9-C10	1.410(3)	C9A-C14A	1.403(3)
C9A-C10A	1.411(3)	C10-C11	1.374(4)
C10A-C11A	1.380(3)	C11-C12	1.400(4)
C11A-C12A	1.400(3)	C12-C13	1.386(3)
C12A-C13A	1.376(3)	S1-C18	1.779(3)
S1-C17	1.827(3)	S1A-C18A	1.787(3)
S1A-C17A	1.809(2)	F1-C18	1.328(3)
C13-C14	1.403(3)	C13A-C14A	1.405(3)
C14-C15	1.454(3)	C14A-C15A	1.457(3)

Bond angles (°) for 2a.

C8-N1-C15	122.39(18)	C8-N1-C16	120.33(17)
C15-N1-C16	117.15(17)	C8A-N1A-C15A	122.20(17)
C8A-N1A-C16A	120.52(17)	C15A-N1A-C16A	117.14(16)
C2-C1-C16	108.02(18)	C2-C1-C17	109.67(19)
C16-C1-C17	112.58(19)	C2A-C1A-C16A	108.41(17)
C2A-C1A-C17A	108.11(17)	C16A-C1A-C17A	113.86(17)
C8-N2-C9	117.38(19)	C8A-N2A-C9A	117.69(18)
C7-C2-C3	119.0(2)	C7-C2-C1	119.20(19)
C3-C2-C1	121.8(2)	C7A-C2A-C3A	119.49(19)
C7A-C2A-C1A	118.51(18)	C3A-C2A-C1A	121.96(19)
C4-C3-C2	120.3(2)	C4A-C3A-C2A	120.1(2)
C3-C4-C5	120.5(2)	C5A-C4A-C3A	120.3(2)
C4-C5-C6	120.1(2)	C4A-C5A-C6A	120.2(2)
C5-C6-C7	119.8(2)	C5A-C6A-C7A	119.7(2)
C6-C7-C2	120.4(2)	C6-C7-C8	119.6(2)
C2-C7-C8	120.1(2)	C2A-C7A-C6A	120.17(19)
C2A-C7A-C8A	120.42(18)	C6A-C7A-C8A	119.40(19)
N2-C8-N1	124.0(2)	N2-C8-C7	119.1(2)
N1-C8-C7	116.86(19)	N2A-C8A-N1A	124.03(19)
N2A-C8A-C7A	119.18(18)	N1A-C8A-C7A	116.80(18)
N2-C9-C14	122.59(19)	N2-C9-C10	118.5(2)
C14-C9-C10	118.9(2)	N2A-C9A-C14A	122.16(19)

N2A-C9A-C10A	118.83(19)	C14A-C9A-C10A	119.01(19)
C11-C10-C9	120.0(2)	C11A-C10A-C9A	119.8(2)
C10-C11-C12	121.1(2)	C10A-C11A-C12A	120.9(2)
C13-C12-C11	119.8(2)	C13A-C12A-C11A	120.1(2)
N1-C16-C1	111.17(18)	C18-S1-C17	100.44(12)
C18A-S1A-C17A	100.00(11)	C12-C13-C14	119.6(2)
C12A-C13A-C14A	119.9(2)	C9-C14-C13	120.5(2)
C9-C14-C15	119.11(19)	C13-C14-C15	120.3(2)
C9A-C14A-C13A	120.3(2)	C9A-C14A-C15A	119.30(19)
C13A-C14A-C15A	120.38(19)	O1-C15-N1	121.19(19)
O1-C15-C14	124.4(2)	N1-C15-C14	114.44(19)
O1A-C15A-N1A	120.87(19)	O1A-C15A-C14A	124.73(19)
N1A-C15A-C14A	114.40(17)	C1-C17-S1	113.77(17)
N1A-C16A-C1A	111.27(17)	F2-C18-F1	104.2(2)
F2-C18-F3	107.0(2)	F1-C18-F3	108.6(2)
F2-C18-S1	113.9(2)	F1-C18-S1	113.75(19)
F3-C18-S1	109.1(2)	C1A-C17A-S1A	116.84(15)
F2A-C18A-F1A	107.5(2)	F2A-C18A-F3A	107.4(2)
F1A-C18A-F3A	105.2(2)	F2A-C18A-S1A	109.2(2)
F1A-C18A-S1A	113.94(18)	F3A-C18A-S1A	113.24(19)

Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$) for 2a.

	x/a	y/b	z/c	U(eq)
H1	0.9489	0.6628	0.6864	0.025000
H1A	0.5910	0.1350	0.5052	0.021000
H3	1.0640	0.7554	0.7749	0.031000
H3A	0.4484	0.1728	0.4641	0.025000
H4	1.1185	0.8221	0.8803	0.038000
H4A	0.3344	0.1999	0.4845	0.029000
H5	1.0387	0.8969	0.9339	0.039000
H5A	0.3411	0.2701	0.5842	0.029000
H6	0.9030	0.9022	0.8822	0.032000
H6A	0.4625	0.3140	0.6644	0.025000
H10	0.6706	1.0632	0.8177	0.030000
H10A	0.6388	0.5604	0.8099	0.025000
H11	0.5361	1.0600	0.7678	0.036000
H11A	0.7590	0.6040	0.8898	0.029000
H12	0.4757	0.8944	0.6804	0.036000

H12A	0.8721	0.4786	0.8879	0.031000
H16A	0.8107	0.6161	0.6437	0.026000
H16B	0.8518	0.5372	0.7115	0.026000
H13	0.5519	0.7399	0.6395	0.029000
H13A	0.8654	0.3110	0.8050	0.027000
H17A	0.9473	0.9441	0.6642	0.030000
H17B	0.8637	0.9637	0.6694	0.030000
H16C	0.6472	0.0245	0.6047	0.022000
H16D	0.7122	0.1357	0.5937	0.022000
H17C	0.6140	0.4601	0.5536	0.022000
H17D	0.5821	0.4086	0.4819	0.022000

Hydrogen bond distances (Å) and angles (°) for 2a.

	Donor-H	**Acceptor-H**	**Donor-Acceptor**	**Angle**
C1A-H1A···F1A	1.00	2.60	3.140(3)	113.6
C10-H10···F3A#2	0.95	2.56	3.366(3)	142.6
C17-H17B···O1A#1	0.99	2.31	3.290(3)	169.3
C17A-H17C···O1	0.99	2.27	3.123(3)	143.0

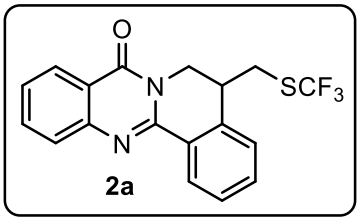
*Symmetry transformations used to generate equivalent atoms:

#1 x, y+1, z

#2 x, -y+3/2, z+1/2

5. Characterization Data:

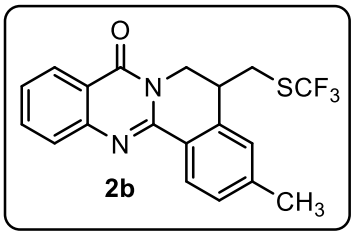
1. 5-(((Trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2a)



2a

The product **2a** was obtained in 89% yield (61 mg, white solid); mp = 133-135°C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.54 (d, *J* = 7.4 Hz, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 3.7 Hz, 2H), 7.61 – 7.44 (m, 3H), 7.36 (d, *J* = 7.3 Hz, 1H), 5.33 (dd, *J* = 14.0, 2.1 Hz, 1H), 3.86 (dd, *J* = 14.0, 3.9 Hz, 1H), 3.43-3.32 (m, 1H), 3.05 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.94 (dd, *J* = 14.3, 8.9 Hz, 1H); **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 162.0, 148.5, 147.7, 137.7, 134.6, 132.3, 128.9, 128.7, 128.6, 128.1, 127.8, 127.1, 127.1, 120.8, 42.1, 37.6, 32.7; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.83; **HRMS (ESI^+)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{14}ON_2F_3S$ 363.0773; found 363.0774.

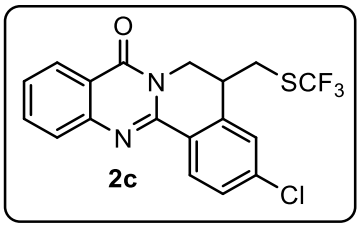
2. 3-Methyl-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2b)



2b

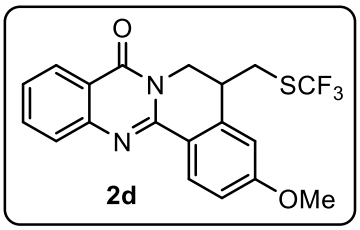
The product **2b** was obtained in 85% yield (58 mg, white solid); mp = 134-136 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.42 (d, *J* = 8.0 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 7.83 – 7.71 (m, 2H), 7.52 – 7.41 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.14 (s, 1H), 5.32 (dd, *J* = 14.0, 2.4 Hz, 1H), 3.81 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.42 – 3.32 (m, 1H), 3.05 (dd, *J* = 14.3, 6.2 Hz, 1H), 2.90 (dd, *J* = 14.3, 9.2 Hz, 1H), 2.45 (s, 3H); **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.9, 148.8, 147.5, 143.2, 137.8, 134.6, 132.4, 129.8, 129.4, 128.7, 128.5, 127.5, 127.1, 126.8, 125.8, 120.6, 42.05, 37.5, 32.6, 21.7; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.81; **HRMS (ESI^+)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}ON_2F_3S$ 377.0930; found 377.0933.

3. 3-Chloro-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2c)



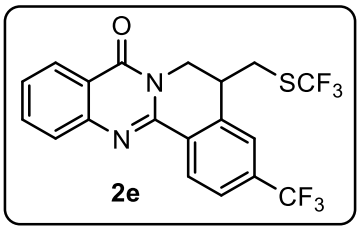
The product **2c** was obtained in 81% yield (54 mg, white solid); mp = 147-149 °C; R_f = 0.3 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.49 (d, *J* = 8.5 Hz, 1H), 8.30 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 3.6 Hz, 2H), 7.56 – 7.45 (m, 2H), 7.36 (d, *J* = 1.7 Hz, 1H), 5.32 (dd, *J* = 14.1, 2.3 Hz, 1H), 3.84 (dd, *J* = 14.1, 3.9 Hz, 1H), 3.39-3.31 (m, 1H), 3.05 (dd, *J* = 14.4, 6.5 Hz, 1H), 2.94 (dd, *J* = 14.4, 8.9 Hz, 1H); **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.7, 147.8, 147.4, 139.3, 138.5, 135.7, 134.8, 132.3, 132.0, 130.2, 129.7, 129.3, 128.0, 127.8, 127.3, 127.2, 120.8, 41.9, 37.4, 32.4; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.75; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{13}OClN_2F_3S$ 397.0384; found 397.0388.

4. 3-Methoxy-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2d)



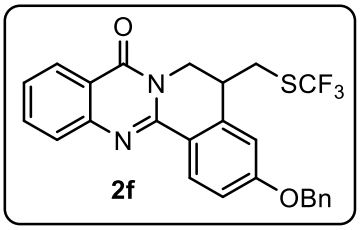
The product **2d** was obtained in 82% yield (55 mg, white solid); mp = 118-120 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.42 (d, *J* = 8.8 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 7.77 – 7.64 (m, 2H), 7.47 – 7.37 (m, 1H), 6.98 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.79 (d, *J* = 2.4 Hz, 1H), 3.88 (s, 3H), 3.81 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.38 – 3.30 (m, 1H), 3.04 (dd, *J* = 14.3, 6.4 Hz, 1H), 2.93 (dd, *J* = 14.3, 8.9 Hz, 1H); **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 162.7, 161.9, 148.5, 147.9, 139.6, 135.4, 134.5, 132.4, 130.6, 129.3, 127.4, 127.0, 126.4, 126.3, 121.1, 120.4, 114.7, 112.7, 55.7, 42.0, 37.7, 32.5, 32.5; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.81; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}O_2N_2F_3S$ 393.0879; found 393.0887.

5. 3-(Trifluoromethyl)-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2e)



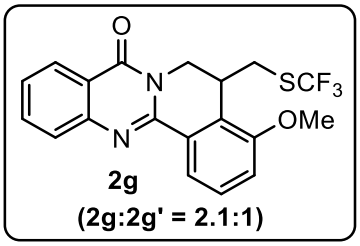
The product **2e** was obtained in 86% yield (58 mg, white solid); mp = 161-163°C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.67 (d, *J* = 8.2 Hz, 1H), 8.31 (d, *J* = 7.9 Hz, 1H), 7.78 (dd, *J* = 13.5, 6.1 Hz, 3H), 7.62 (s, 1H), 7.54 – 7.49 (m, 1H), 5.36 (dd, *J* = 14.1, 1.9 Hz, 1H), 3.87 (dd, *J* = 14.1, 3.8 Hz, 1H), 3.50-3.32 (m, 1H), 3.07 (dd, *J* = 14.4, 6.6 Hz, 1H), 2.97 (dd, *J* = 14.4, 8.7 Hz, 1H); **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.7, 147.4, 147.2, 138.3, 134.8, 133.7 (q, J = 32.9 Hz), 133.5, 132.3, 132.1, 129.3, 129.3, 129.2, 128.1, 127.7, 127.2, 125.6 (q, J = 3.4 Hz), 125.1 (q, J = 3.6 Hz), 124.9, 122.3, 121.0, 41.9, 37.5, 32.5; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.7, -63.0; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{13}ON_2F_6S$ 431.0647; found 431.0651.

6. 3-(Benzyloxy)-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2f)



The product **2f** was obtained in 84% yield (54 mg, white solid); mp = 144-146 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.45 (d, *J* = 8.8 Hz, 1H), 8.28 (d, *J* = 7.7 Hz, 1H), 7.79 – 7.69 (m, 2H), 7.48 – 7.33 (m, 6H), 7.08 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.89 (d, *J* = 2.5 Hz, 1H), 5.28 (dd, *J* = 14.0, 2.5 Hz, 1H), 5.16 (s, 2H), 3.82 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.43-3.31 (m, 1H), 3.02 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.93 (dd, *J* = 14.3, 8.8 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 162.0, 161.8, 148.5, 147.9, 139.6, 136.1, 134.5, 132.4, 130.6, 129.3, 128.8, 128.4, 127.6, 127.5, 127.0, 126.5, 121.4, 120.4, 115.5, 113.8, 70.4, 42.0, 37.8, 32.5; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.78; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{25}H_{20}O_2N_2F_3S$ 469.1192; found 469.1202.

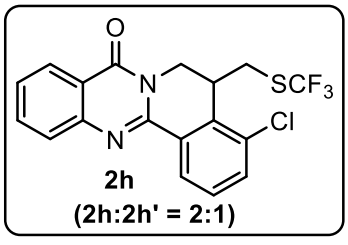
7. 4-Methoxy-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2g)



2g
(2g:2g' = 2.1:1)

The product **2g** was obtained in 69% yield (46 mg, white solid); mp = 146-148 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.29 (d, *J* = 8.0 Hz, 3H), 8.14 (d, *J* = 7.9 Hz, 2H), 8.05 (d, *J* = 2.2 Hz, 1H), 7.85 – 7.72 (m, 7H), 7.50 – 7.41 (m, 6H), 7.24 (s, 1H), 7.10 – 7.04 (m, 3H), 5.52 (d, *J* = 14.2 Hz, 2H), 5.29 (dd, *J* = 14.0, 2.1 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 6H), 3.82 (dd, *J* = 6.7, 3.2 Hz, 3H), 3.58 (dd, *J* = 14.2, 4.0 Hz, 2H), 3.36-3.33 (m, 1H), 3.12 (dd, *J* = 14.1, 4.0 Hz, 2H), 2.99 (dd, *J* = 14.2, 6.5 Hz, 1H), 2.89 (dd, *J* = 14.2, 8.8 Hz, 1H), 2.66 – 2.60 (m, 2H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.9, 161.8, 160.0, 155.8, 148.7, 148.6, 147.4, 134.7, 134.6, 132.5, 130.1, 129.6, 129.4, 129.3, 127.7, 127.6, 127.2, 127.2, 127.1, 127.0, 126.7, 120.8, 120.7, 120.3, 119.9, 113.6, 112.0, 77.4, 55.9, 42.41, 41.1, 36.7, 32.8, 31.0, 30.8; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.79, -40.96; **HRMS (ESI^+)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}O_2N_2F_3S$ 393.0879; found 393.0882.

8. 4-Chloro-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2h)

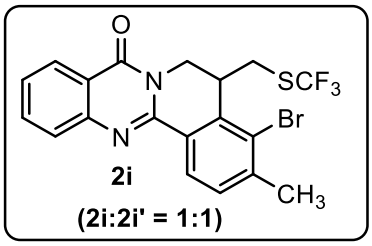


2h
(2h:2h' = 2:1)

The product **2h** was obtained in 73% yield (49 mg, white solid); mp = 116-118 °C; R_f = 0.3 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.51 (dd, *J* = 14.6, 4.8 Hz, 3H), 8.35 – 8.29 (m, 3H), 7.77 (t, *J* = 5.4 Hz, 6H), 7.60 (d, *J* = 7.9 Hz, 2H), 7.53 – 7.43 (m, 6H), 7.31 (d, *J* = 8.1 Hz, 1H), 5.64 (d, *J* = 14.3 Hz, 2H), 5.32 (dd, *J* = 14.1, 2.0 Hz, 1H), 3.92 – 3.81 (m, 3H), 3.64 (dd, *J* = 14.3, 3.4 Hz, 2H), 3.42-3.39 (m, 1H), 3.25 (dd, *J* = 14.6, 3.2 Hz, 2H), 2.98 (qd, *J* = 14.4, 7.7 Hz, 2H), 2.67 – 2.58 (m, 2H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.7, 147.8, 147.4, 139.3, 138.5, 135.7, 134.8, 132.3, 132.0, 130.2, 129.7, 129.3,

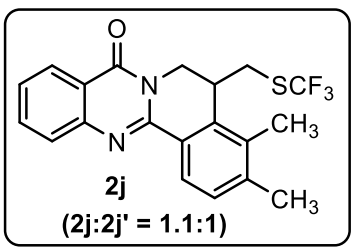
128.1, 127.8, 127.3, 127.2, 120.8, 77.5, 77.1, 76.8, 41.9, 37.5, 32.4; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.6, -40.7; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{13}ON_2ClF_3S$ 397.0384; found 397.0396.

9. 4-Bromo-3-methyl-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2i)



The product **2i** was obtained in 74% yield (47 mg, white solid); mp = 173-175 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.70 (s, 1H), 8.57 (d, *J* = 8.7 Hz, 1H), 8.28 (t, *J* = 8.6 Hz, 2H), 7.82 – 7.72 (m, 4H), 7.51 – 7.42 (m, 2H), 7.04 (d, *J* = 8.8 Hz, 1H), 6.79 (s, 1H), 5.64 (d, *J* = 14.2 Hz, 1H), 5.32 (d, *J* = 14.0 Hz, 1H), 4.01 (s, 6H), 3.89 (d, *J* = 11.3 Hz, 1H), 3.81 (dd, *J* = 14.0, 3.7 Hz, 1H), 3.63 (dd, *J* = 14.3, 3.1 Hz, 1H), 3.36 (s, 1H), 3.28 (dd, *J* = 14.6, 3.1 Hz, 1H), 3.07 – 2.93 (m, 2H), 2.57 (t, *J* = 13.1 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.8, 161.6, 159.3, 158.8, 148.2, 147.6, 147.3, 139.4, 138.7, 135.3, 134.8, 134.7, 133.6, 132.3, 129.7, 129.3, 127.6, 127.2, 127.1, 126.9, 126.9, 123.7, 122.2, 120.5, 120.4, 117.8, 112.7, 112.5, 111.8, 110.5, 56.8, 56.8, 42.1, 40.6, 37.7, 37.4, 32.5, 29.8; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.3, -40.7; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{15}O_2{}^{81}BrN_2F_3S$ 472.9964; found 472.9945.

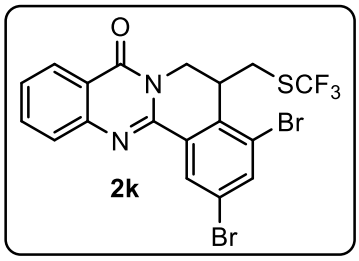
10. 3,4-Dimethyl-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2j)



The product **2j** was obtained in 70% yield (47 mg, white solid); mp = 162-164 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.32 – 8.25 (m, 4H), 7.77 – 7.73 (m, 4H), 7.48 – 7.43 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.09 (s, 1H), 5.60 (d, *J* =

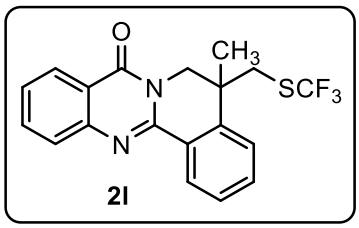
13.3 Hz, 1H), 5.29 (dd, *J* = 14.0, 2.2 Hz, 1H), 3.80 (dd, *J* = 14.0, 3.9 Hz, 1H), 3.64 (d, *J* = 14.9 Hz, 2H), 3.34 (d, *J* = 2.8 Hz, 1H), 3.10 – 3.01 (m, 2H), 2.89 (dd, *J* = 14.1, 9.1 Hz, 1H), 2.64 (d, *J* = 12.4 Hz, 1H), 2.39 (s, 3H), 2.36 (d, *J* = 5.3 Hz, 6H), 2.31 (s, 3H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 162.0, 161.9, 149.3, 148.8, 147.9, 147.8, 142.1, 141.9, 137.7, 136.4, 135.3, 134.5, 134.5, 133.5, 132.6, 132.5, 130.3, 129.5, 129.4, 129.2, 129.0, 127.6, 127.6, 127.1, 127.0, 126.7, 126.6, 126.2, 126.0, 120.7, 120.6, 42.2, 40.9, 37.1, 34.6, 32.7, 30.7, 21.2, 20.1, 19.7, 14.4; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.53 (s), -40.82 (s); **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{20}H_{18}ON_2F_3S$ 391.1086; found 391.1091.

11. 2,4-Dibromo-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2k)



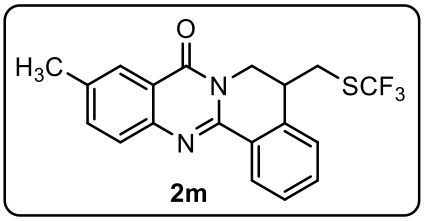
The product **2k** was obtained in 73% yield (46 mg, white solid); mp = 191-193 °C; R_f = 0.3 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** δ 8.69 (d, *J* = 1.4 Hz, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 7.92 (d, *J* = 1.5 Hz, 1H), 7.84 – 7.76 (m, 2H), 7.53 (ddd, *J* = 8.0, 5.3, 2.8 Hz, 1H), 5.68 – 5.60 (m, 1H), 3.80 (d, *J* = 11.1 Hz, 1H), 3.63 (dd, *J* = 14.3, 3.5 Hz, 1H), 3.25 (dd, *J* = 14.5, 3.4 Hz, 1H), 2.57 (t, *J* = 13.0 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.5, 147.2, 146.5, 138.3, 136.3, 134.9, 132.3, 132.2, 130.9, 129.2, 128.0, 127.8, 127.2, 124.0, 123.1, 120.9, 40.4, 36.9, 29.9; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.35 (s); **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{12}ON_2Br^{81}BrF_3S$ 520.8963; found 520.8967.

12. 5-Methyl-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2l)



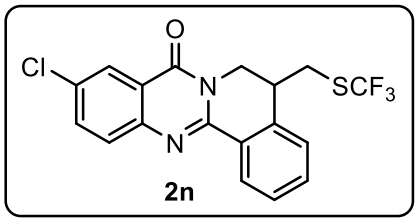
The product **2l** was obtained in 85% yield (58 mg, white solid); mp = 123-125 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.59 (d, *J* = 7.7 Hz, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 7.85 – 7.75 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.50 (dd, *J* = 12.7, 7.0 Hz, 2H), 7.42 (d, *J* = 7.7 Hz, 1H), 4.86 (d, *J* = 13.9 Hz, 1H), 3.83 (d, *J* = 13.9 Hz, 1H), 3.16 – 3.06 (m, 2H), 1.58 (s, 3H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.6, 148.8, 147.6, 141.4, 134.7, 132.4, 132.1, 129.1, 128.9, 128.6, 128.5, 127.8, 127.1, 127.0, 124.7, 120.7, 48.1, 37.9, 37.0, 22.6; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -41.14 (s); **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}ON_2F_3S$ 377.0930; found 377.0931.

13. 10-Methyl-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2m)



The product **2m** was obtained in 86% yield (58 mg, white solid); mp = 139-141 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.56 – 8.50 (m, 1H), 8.10 (s, 1H), 7.70 (d, *J* = 8.3 Hz, 1H), 7.61 – 7.48 (m, 3H), 7.38 – 7.33 (m, 1H), 5.32 (dd, *J* = 14.0, 2.5 Hz, 1H), 3.84 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.42-3.39 (m, 1H), 3.04 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.93 (dd, *J* = 14.3, 8.9 Hz, 1H), 2.50 (s, 3H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.9, 147.8, 145.5, 137.6, 137.4, 136.2, 132.4, 132.1, 129.4, 128.9, 128.7, 128.5, 128.0, 127.5, 126.5, 120.5, 42.1, 37.6, 32.6, 21.5; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.82 (s); **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}ON_2F_3S$ 377.0930; found 377.0941.

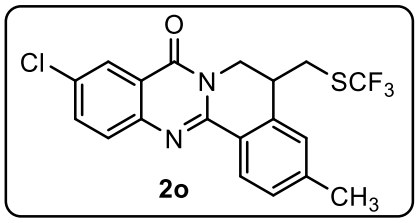
14. 10-Chloro-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2n)



The product **2n** was obtained in 88% yield (59 mg, white solid); mp = 154-156 °C; R_f = 0.3 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** δ 8.51 (d, *J* = 7.5 Hz,

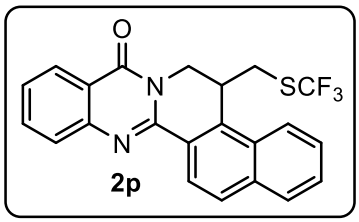
1H), 8.25 (d, *J* = 2.2 Hz, 1H), 7.70 (dt, *J* = 8.7, 5.5 Hz, 2H), 7.54 (dtd, *J* = 13.9, 7.4, 6.3 Hz, 2H), 7.36 (d, *J* = 7.3 Hz, 1H), 5.29 (dd, *J* = 14.1, 2.4 Hz, 1H), 3.86 (dd, *J* = 14.1, 4.0 Hz, 1H), 3.43-3.41 (m, 1H), 3.05 (dd, *J* = 14.3, 6.4 Hz, 1H), 2.93 (dd, *J* = 14.3, 8.9 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 160.9, 148.8, 146.1, 137.7, 135.4, 135.1, 132.8, 132.5, 132.3, 129.4, 129.3, 129.0, 128.7, 128.3, 128.1, 126.4, 121.7, 42.2, 37.4, 32.6; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.81 (s); **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{13}ON_2ClF_3S$ 397.0384; found 397.0397.

15. 10-Chloro-3-methyl-5-(((trifluoromethyl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (2o)



The product **2o** was obtained in 86% yield (57 mg, white solid); mp = 188-190 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.38 (d, *J* = 8.1 Hz, 1H), 8.24 (d, *J* = 2.0 Hz, 1H), 7.73 – 7.65 (m, 2H), 7.31 (d, *J* = 7.9 Hz, 1H), 7.14 (s, 1H), 5.29 (dd, *J* = 14.1, 2.4 Hz, 1H), 3.82 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.37-3.34 (m, 1H), 3.05 (dd, *J* = 14.3, 6.1 Hz, 1H), 2.89 (dd, *J* = 14.3, 9.2 Hz, 1H), 2.46 (s, 3H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.0, 149.0, 146.2, 143.5, 137.7, 135.0, 132.5, 132.4, 129.9, 129.4, 129.2, 128.7, 128.5, 126.4, 125.6, 121.6, 42.2, 37.4, 32.6, 21.8; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.80 (s); **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{15}ON_2ClF_3S$ 411.0540; found 411.0547.

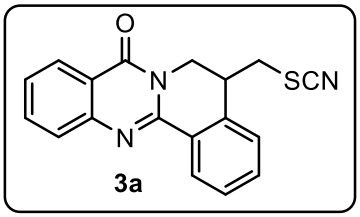
16. 5-(((Trifluoromethyl)thio)methyl)-5,6-dihydro-8H-benzo[5,6]isoquinolino[1,2-b]quinazolin-8-one (2p)



The product **2p** was obtained in 85% yield (61 mg, white solid); mp = 195-197 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 10%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.62 (d, *J* = 8.5 Hz, 1H), 8.34 (d, *J* = 7.5 Hz, 1H), 8.09 (d, *J* = 7.9 Hz, 1H), 7.96 (d, *J* = 7.9 Hz, 2H), 7.82 (dd, *J* =

16.4, 7.0 Hz, 2H), 7.67 (dd, *J* = 16.9, 8.7 Hz, 2H), 7.51 (t, *J* = 6.9 Hz, 1H), 5.75 (d, *J* = 14.0 Hz, 1H), 4.18 (d, *J* = 10.2 Hz, 1H), 3.77 (d, *J* = 13.6 Hz, 1H), 3.29 (d, *J* = 13.1 Hz, 1H), 2.78 (t, *J* = 12.9 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.8, 148.8, 147.7, 135.6, 135.4, 134.6, 132.6, 129.6, 129.4, 129.1, 128.3, 127.9, 127.8, 127.1, 126.4, 124.3, 123.0, 120.8, 40.7, 33.6, 31.1; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -40.29; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{22}H_{16}ON_2F_3S$ 413.0930; found 413.0928.

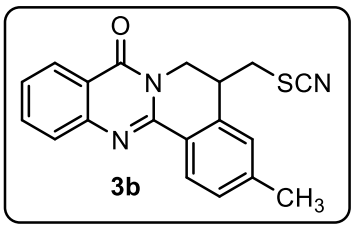
17. 5-(Thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3a)



3a

The product **3a** was obtained in 88% yield (53 mg, white solid); mp = 177-179 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.55 (d, *J* = 7.2 Hz, 1H), 8.27 (d, *J* = 7.8 Hz, 1H), 7.81 – 7.73 (m, 2H), 7.60 – 7.51 (m, 2H), 7.47 (dd, *J* = 10.3, 4.1 Hz, 1H), 7.41 (d, *J* = 7.1 Hz, 1H), 5.41 (d, *J* = 14.1 Hz, 1H), 3.83 (dd, *J* = 14.1, 3.6 Hz, 1H), 3.54-3.49 (m, 1H), 3.08 (dd, *J* = 13.3, 6.3 Hz, 1H), 2.98 (dd, *J* = 13.3, 8.8 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.8, 148.3, 147.4, 136.6, 134.7, 132.5, 129.2, 128.7, 128.6, 128.3, 127.7, 127.2, 127.0, 120.7, 111.5, 41.7, 37.4, 36.4; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{14}ON_3S$ 320.0852; found 320.0852.

18. 3-Methyl-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3b)

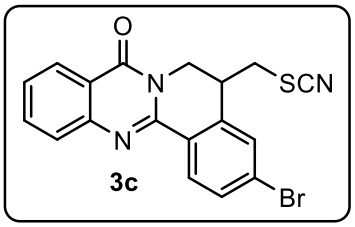


3b

The product **3b** was obtained in 86% yield (52 mg, white solid); mp = 164-166 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.42 (d, *J* = 8.1 Hz, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 4.7 Hz, 2H), 7.48 (ddd, *J* = 8.1, 5.6, 2.7 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.21 (s, 1H), 5.44 (dd, *J* = 14.2, 1.8 Hz, 1H), 3.82 (dd, *J* = 14.1, 3.8 Hz, 1H), 3.52 – 3.46 (m, 1H), 3.10 (dd, *J* = 13.7, 6.2 Hz, 1H), 2.93 (dd, *J* = 13.7, 9.0 Hz, 1H),

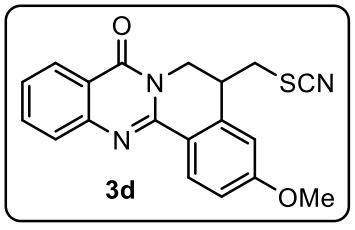
2.47 (s, 3H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 162.1, 148.5, 147.8, 143.4, 136.6, 134.7, 130.2, 128.8, 128.7, 127.8, 127.1, 126.9, 126.2, 120.7, 111.6, 41.7, 37.6, 36.4, 21.8; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}ON_3S$ 334.1009; found 334.1006.

19. 3-Bromo-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3c)



The product **3c** was obtained in 83% yield (48 mg, white solid); mp = 175-177 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.40 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 7.9 Hz, 1H), 7.76 (q, *J* = 7.8 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.58 (s, 1H), 7.49 (t, *J* = 6.8 Hz, 1H), 5.41 (d, *J* = 13.2 Hz, 1H), 3.83 (dd, *J* = 14.2, 3.6 Hz, 1H), 3.50-3.49 (s, 1H), 3.09 (dd, *J* = 13.7, 6.4 Hz, 1H), 2.96 (dd, *J* = 13.7, 8.8 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.7, 147.5, 147.5, 138.3, 134.8, 132.6, 131.2, 130.3, 127.9, 127.8, 127.4, 127.1, 127.1, 120.7, 111.2, 41.6, 37.3, 36.2; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{13}ON_3BrS$ 397.9957; found 397.9959.

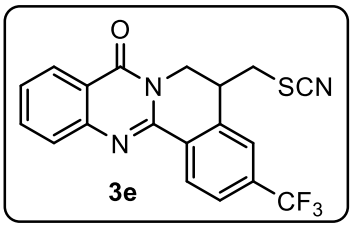
20. 3-Methoxy-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3d)



The product **3d** was obtained in 85% yield (51 mg, white solid); mp = 137-139 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.46 (d, *J* = 8.8 Hz, 1H), 8.26 (d, *J* = 7.6 Hz, 1H), 7.73 (q, *J* = 8.3 Hz, 2H), 7.47 – 7.41 (m, 1H), 7.04 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.87 (d, *J* = 2.2 Hz, 1H), 5.42 (dd, *J* = 14.1, 1.6 Hz, 1H), 3.92 (s, 3H), 3.81 (dd, *J* = 14.2, 3.8 Hz, 1H), 3.49-3.41 (m, 1H), 3.10 (dd, *J* = 13.7, 6.3 Hz, 1H), 2.95 (dd, *J* = 13.7, 8.9 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 162.9, 162.0, 148.3, 147.9, 138.6, 134.6,

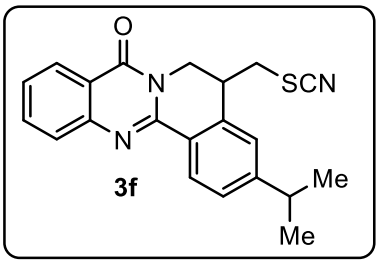
130.7, 127.6, 127.0, 126.6, 121.2, 120.4, 115.4, 112.7, 111.6, 55.8, 41.6, 37.8, 36.3; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}ON_3S$ 350.0958; found 350.0956.

21. 5-(Thiocyanatomethyl)-3-(trifluoromethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3e)



The product **3e** was obtained in 82% yield (48 mg, white solid); mp = 108-110 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.69 (d, *J* = 8.2 Hz, 1H), 8.31 (d, *J* = 7.9 Hz, 1H), 7.85 – 7.76 (m, 3H), 7.69 (s, 1H), 7.57 – 7.50 (m, 1H), 5.47 (d, *J* = 14.3 Hz, 1H), 3.87 (dd, *J* = 14.3, 3.8 Hz, 1H), 3.67 – 3.57 (m, 1H), 3.13 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.99 (dd, *J* = 13.8, 8.8 Hz, 1H); **^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.6, 147.3, 146.9, 137.2, 134.9, 134.1 (q, J = 31.9 Hz), 132.1, 129.4, 128.1, 127.8, 127.1, 125.9, 125.3, 122.1, 120.9, 111.1, 41.5, 37.5, 36.2, 29.8; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -62.93; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{13}ON_3F_3S$ 388.0726; found 388.0726.

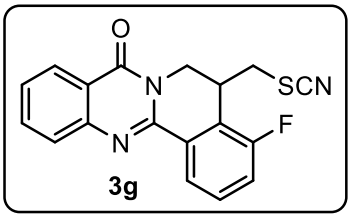
22. 3-Isopropyl-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3f)



The product **3f** was obtained in 85% yield (50 mg, white solid); mp = 128-130 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.50 (d, *J* = 8.1 Hz, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 7.88 – 7.74 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 7.4 Hz, 1H), 7.25 (s, 1H), 5.46 (d, *J* = 14.2 Hz, 1H), 3.84 (dd, *J* = 13.9, 3.4 Hz, 1H), 3.53-3.49 (m, 1H), 3.16 – 2.91 (m, 3H), 1.32 (d, *J* = 6.9 Hz, 6H);**^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 162.0, 154.3, 148.5, 147.8, 136.7, 134.7, 128.9, 127.8, 127.7, 127.1, 126.9, 126.4, 126.2, 120.7, 111.6,

41.7, 37.7, 36.6, 34.4, 29.8, 23.9, 23.8; **HRMS (ESI$^+$)** *m/z*: [M + H]$^+$ calcd for $C_{21}H_{20}ON_3S$ 362.1322; found 362.1325.

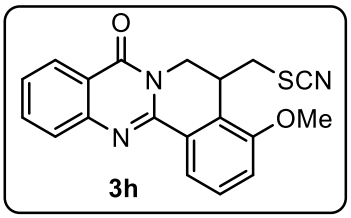
23. 4-Fluoro-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3g)



3g

The product **3g** was obtained in 73% yield (44 mg, white solid); mp = 215-217 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.32 (d, *J* = 7.9 Hz, 1H), 8.25 (dd, *J* = 9.4, 2.2 Hz, 1H), 7.84 – 7.75 (m, 2H), 7.52 (dd, *J* = 9.9, 4.1 Hz, 1H), 7.43 (dd, *J* = 8.2, 5.2 Hz, 1H), 7.30 (dd, *J* = 8.1, 2.4 Hz, 1H), 5.44 (d, *J* = 14.2 Hz, 1H), 3.85 (dd, *J* = 14.2, 3.8 Hz, 1H), 3.56-3.48 (m, 1H), 3.01 (qd, *J* = 13.7, 7.7 Hz, 2H);**^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 164.3 (d, J = 252.6 Hz), 161.8, 147.4, 134.9, 132.4, 130.9, 130.3, 130.2, 128.0, 127.6, 127.2, 120.9, 119.7 (d, J = 22.3 Hz), 115.4 (d, J = 24.4 Hz), 111.4, 41.9, 36.9, 36.5;**^{19}F NMR (376 MHz, $CDCl_3$) δ** = -111.13; **HRMS (ESI$^+$)** *m/z*: [M + H]$^+$ calcd for $C_{18}H_{13}ON_3FS$ 388.0758; found 388.0764.

24. 4-Methoxy-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3h)

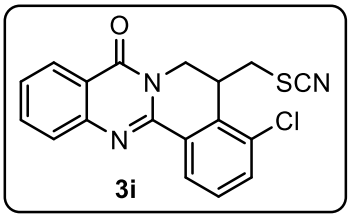


3h

The product **3h** was obtained in 68% yield (40 mg, white solid); mp = 139-141 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.28 (d, *J* = 7.8 Hz, 1H), 8.21 (d, *J* = 7.3 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.77 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 6.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 1H), 5.55 (d, *J* = 14.1 Hz, 1H), 3.96 (s, 3H), 3.65 (d, *J* = 14.1 Hz, 1H), 3.21 (d, *J* = 9.4 Hz, 1H), 2.74 (d, *J* = 9.8 Hz, 1H);**^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.7, 155.9, 148.7, 146.7, 134.8, 129.9, 129.2, 127.4, 127.1, 125.6, 120.6, 120.5, 114.0, 111.5,

55.9, 40.9, 34.6, 31.1; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}O_2N_3S$ 350.0958; found 350.0951.

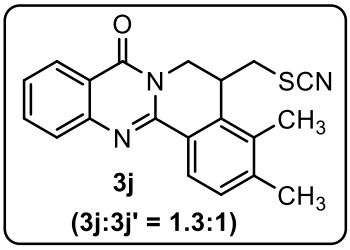
25. 4-Chloro-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3i)



3i

The product **3i** was obtained in 71% yield (42 mg, white solid); mp = 186-188 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.49 (d, *J* = 7.9 Hz, 1H), 8.29 (d, *J* = 7.9 Hz, 1H), 7.84 – 7.71 (m, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.54 – 7.44 (m, 2H), 5.65 (d, *J* = 14.4 Hz, 1H), 4.02 (d, *J* = 10.8 Hz, 1H), 3.70 (dd, *J* = 14.4, 3.3 Hz, 1H), 3.34 (dd, *J* = 13.7, 3.1 Hz, 1H), 2.71 – 2.60 (m, 1H);**^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.7, 147.5, 147.4, 134.8, 134.5, 133.4, 133.0, 131.1, 129.9, 127.9, 127.5, 127.3, 127.1, 120.8, 110.9, 40.2, 34.8, 33.7; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{13}ON_3ClS$ 354.0462; found 354.0462.

26. 3,4-Dimethyl-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3j)

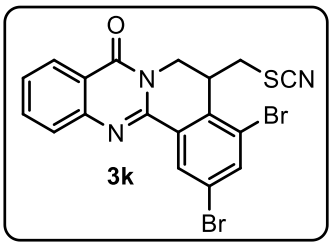


3j
(3j:3j' = 1.3:1)

The product **3j** was obtained in 71% yield (43 mg, white solid); mp = 217-219 °C; R_f = 0.3 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.34 – 8.27 (m, 4H), 7.76 (d, *J* = 3.3 Hz, 4H), 7.47 (dt, *J* = 7.7, 3.7 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 5.64 (d, *J* = 14.1 Hz, 1H), 5.42 (d, *J* = 13.9 Hz, 1H), 3.80 (dd, *J* = 13.6, 3.2 Hz, 2H), 3.66 (dd, *J* = 14.2, 2.9 Hz, 1H), 3.46 (s, 1H), 3.18 (dd, *J* = 13.8, 2.5 Hz, 1H), 3.08 (dd, *J* = 13.6, 6.1 Hz, 1H), 2.91 (dd, *J* = 13.6, 9.0 Hz, 1H), 2.61 (dd, *J* = 13.6, 11.6 Hz, 1H), 2.41 (s, 3H), 2.38 (s, 6H); **^{13}C NMR (100 MHz, $CDCl_3$) δ=** 161.9, 161.9, 148.9, 148.5, 147.9, 147.7, 142.3, 142.1,

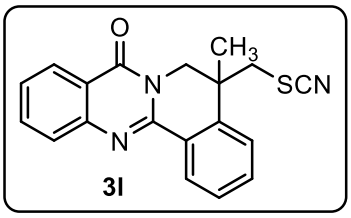
138.0, 135.0, 134.5, 134.5, 134.1, 133.7, 130.6, 129.1, 129.1, 127.7, 127.6, 126.9, 126.9, 126.7, 126.7, 126.2, 126.1, 120.6, 120.5, 111.6, 111.6, 41.7, 40.4, 37.0, 36.4, 34.6, 34.1, 21.2, 20.1, 19.7, 14.6; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{20}H_{18}ON_3S$ 348.1165; found 348.1157.

27. 2,4-Dibromo-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one(3k)



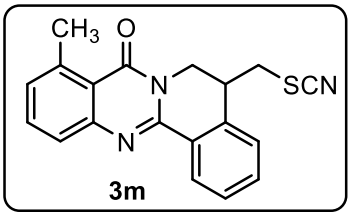
The product **3k** was obtained in 74% yield (42 mg, white solid); mp = 217-219 °C; R_f = 0.3 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =**8.70 (d, *J* = 1.8 Hz, 1H), 8.32 (d, *J* = 7.7 Hz, 1H), 7.94 (d, *J* = 1.9 Hz, 1H), 7.85 – 7.76 (m, 2H), 7.54 (ddd, *J* = 8.1, 6.4, 1.9 Hz, 1H), 5.67 (dd, *J* = 14.4, 1.5 Hz, 1H), 3.99 – 3.89 (m, 1H), 3.74 – 3.65 (m, 1H), 3.41 – 3.31 (m, 1H), 2.57 (dd, *J* = 13.8, 11.3 Hz, 1H); **^{13}C NMR (100 MHz, DMSO-d6) δ=** 160.7, 146.8, 146.4, 137.4, 135.9, 134.5, 132.5, 129.6, 127.6, 127.2, 126.4, 124.3, 122.0, 120.9, 112.3, 79.2, 69.8, 36.2, 33.1; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{12}ON_3Br_2S$ 475.9062; found 475.9063.

28. 5-Methyl-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3l)



The product **3l** was obtained in 84% yield (51 mg, white solid); mp = 124-126 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.34 (d, *J* = 7.9 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.79 (t, *J* = 7.5 Hz, 1H), 7.58 (d, *J* = 6.5 Hz, 2H), 7.55 – 7.45 (m, 4H), 4.88 (s, 1H), 4.49 (d, *J* = 12.5 Hz, 3H), 1.63 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$) δ=** 161.6, 156.9, 139.9, 134.9, 130.5, 128.7, 127.9, 127.5, 127.2, 127.0, 120.5, 110.9, 50.7, 20.5; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}ON_3S$ 334.1009; found 334.1003.

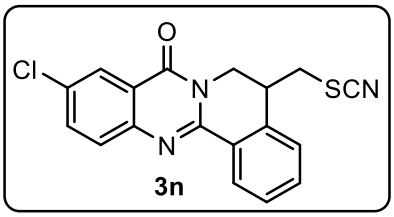
29. 9-Methyl-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3m)



3m

The product **3m** was obtained in 82% yield (50 mg, white solid); mp = 193-195 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.59 (d, *J* = 6.7 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.64 – 7.54 (m, 3H), 7.42 (d, *J* = 6.8 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 5.42 (d, *J* = 14.0 Hz, 1H), 3.84 (dd, *J* = 14.0, 3.1 Hz, 1H), 3.55 (s, 1H), 3.08 (dd, *J* = 13.0, 5.9 Hz, 1H), 3.03 – 2.94 (m, 1H), 2.71 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$) δ=** 162.2, 147.0, 145.9, 136.5, 136.3, 135.3, 132.3, 129.2, 129.0, 128.8, 128.3, 126.8, 124.7, 120.7, 111.6, 41.7, 37.5, 36.6, 17.5; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}ON_3S$ 334.1009; found 334.1011.

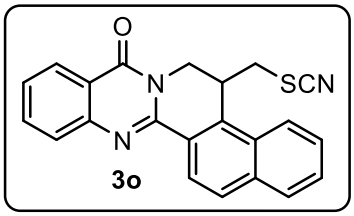
30. 10-Chloro-5-(thiocyanatomethyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3n)



3n

The product **3n** was obtained in 85% yield (51 mg, white solid); mp = 165-167 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.55 (d, *J* = 7.0 Hz, 1H), 8.23 (s, 1H), 7.76 (s, 1H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.64 – 7.52 (m, 2H), 7.43 (d, *J* = 7.0 Hz, 1H), 5.40 (d, *J* = 13.9 Hz, 1H), 3.86 (d, *J* = 12.5 Hz, 1H), 3.56 (s, 1H), 3.09 (s, 1H), 2.99 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$) δ=** 160.8, 148.7, 145.7, 136.6, 135.3, 133.1, 132.9, 129.4, 129.2, 128.9, 128.4, 128.1, 126.4, 121.6, 111.4, 41.9, 37.4, 36.4; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{13}ON_3ClS$ 354.0462; found 354.0462.

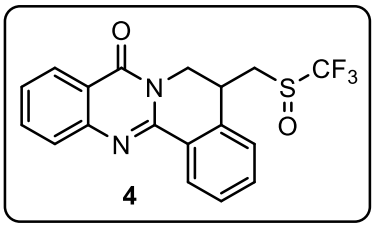
31. 5-(Thiocyanatomethyl)-5,6-dihydro-8H-benzo[5,6]isoquinolino[1,2-b]quinazolin-8-one (3o)



3o

The product **3o** was obtained in 84% yield (49 mg, white solid); mp = 234-236 °C; R_f = 0.2 (petroleum ether:ethyl acetate = 20%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.60 (d, *J* = 8.7 Hz, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 8.20 (d, *J* = 8.3 Hz, 1H), 8.00 – 7.94 (m, 2H), 7.80 (t, *J* = 7.1 Hz, 2H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 6.6 Hz, 1H), 5.77 (d, *J* = 14.2 Hz, 1H), 4.33 (d, *J* = 11.1 Hz, 1H), 3.82 (dd, *J* = 14.2, 2.9 Hz, 1H), 3.43 – 3.36 (m, 1H), 2.79 – 2.69 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$) δ=** 161.9, 148.5, 147.8, 135.4, 134.7, 134.1, 129.5, 129.5, 129.4, 128.4, 128.3, 127.9, 127.2, 127.0, 126.7, 124.2, 122.8, 120.8, 111.7, 40.4, 34.5, 33.6; **HRMS (ESI^+)** *m/z*: $[M + H]^+$ calcd for $C_{22}H_{16}ON_3S$ 370.1009; found 370.1021.

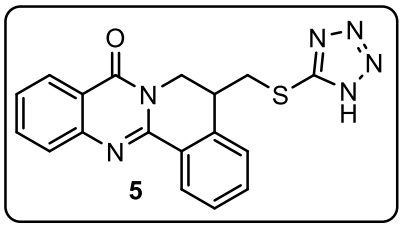
32. 5-(((Trifluoromethyl)sulfinyl)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (4)



4

The product **4** was obtained in 58% yield (30 mg, white solid); mp = 191-193°C; R_f = 0.2 (petroleum ether:ethyl acetate = 15%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.54 (d, *J* = 7.3 Hz, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 7.78 (d, *J* = 3.7 Hz, 2H), 7.62 – 7.44 (m, 3H), 7.37 (d, *J* = 7.3 Hz, 1H), 5.34 (dd, *J* = 14.0, 2.2 Hz, 1H), 3.86 (dd, *J* = 14.0, 3.9 Hz, 1H), 3.49-3.41 (m, 1H), 3.05 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.94 (dd, *J* = 14.3, 8.9 Hz, 1H); **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 162.0, 148.5, 147.8, 137.7, 134.7, 132.3, 128.9, 128.8, 128.6, 128.1, 127.9, 127.1, 127.1, 120.8, 42.1, 37.6, 32.7; **^{19}F NMR (376 MHz, $CDCl_3$) δ** = -72.84; **HRMS (ESI^+)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{14}O_2N_2F_3S$ 379.0723; found 379.0721.

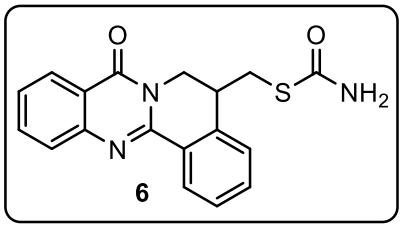
33. 5-(((1H-Tetrazol-5-yl)thio)methyl)-5,6-dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (5)



5

The product **5** was obtained in 83% yield (47 mg, white solid); mp = 286-288°C; R_f = 0.2 (DCM:methanol = 5%); **^{1}H NMR (400 MHz, DMSO-d6) δ =** 8.41 (d, *J* = 7.7 Hz, 1H), 8.16 (d, *J* = 7.7 Hz, 1H), 7.84 (t, *J* = 7.2 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.52 (dd, *J* = 14.0, 7.1 Hz, 3H), 5.08 (dd, *J* = 13.8, 2.3 Hz, 1H), 3.88 (dd, *J* = 13.8, 3.9 Hz, 1H), 3.57 (d, *J* = 3.6 Hz, 1H), 3.34 (dd, *J* = 13.6, 5.1 Hz, 1H), 3.16 (dd, *J* = 13.4, 9.6 Hz, 1H); **^{13}C{^{1}H} NMR (100 MHz, DMSO-d6) δ=** 161.0, 148.7, 147.3, 139.3, 134.4, 132.0, 128.3, 128.2, 127.9, 127.5, 127.4, 126.6, 126.4, 120.6, 41.4, 35.9, 34.8; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{15}ON_6S$ 363.1023; found 363.1025.

34. S-((8-Oxo-5,8-dihydro-6H-isoquinolino[1,2-b]quinazolin-5-yl)methylcarbamothioate (6)



6

The product **6** was obtained in 80% yield (42 mg, white solid); mp = 181-183°C; R_f = 0.2 (petroleum ether:ethyl acetate = 25%); **^{1}H NMR (400 MHz, $CDCl_3$) δ =** 8.56 (d, *J* = 6.4 Hz, 1H), 8.30 (dd, *J* = 6.9, 4.5 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.76 (t, *J* = 7.3 Hz, 1H), 7.55 – 7.45 (m, 3H), 7.33 (dd, *J* = 19.7, 6.6 Hz, 1H), 5.33 (t, *J* = 12.0 Hz, 1H), 3.80 (d, *J* = 13.7 Hz, 1H), 3.48 (s, 1H), 2.78 (dd, *J* = 16.9, 8.5 Hz, 2H); **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ=** 161.8, 161.7, 149.2, 147.0, 138.8, 138.8, 134.7, 132.5, 128.7, 128.6, 128.2, 128.1, 127.4, 127.1, 127.1, 120.6, 42.2, 41.3, 41.2, 36.6, 36.4, 22.4, 14.2; **HRMS (ESI$^+$)** *m/z*: $[M + H]^+$ calcd for $C_{18}H_{16}O_2N_3S$ 338.0958; found 338.0954.

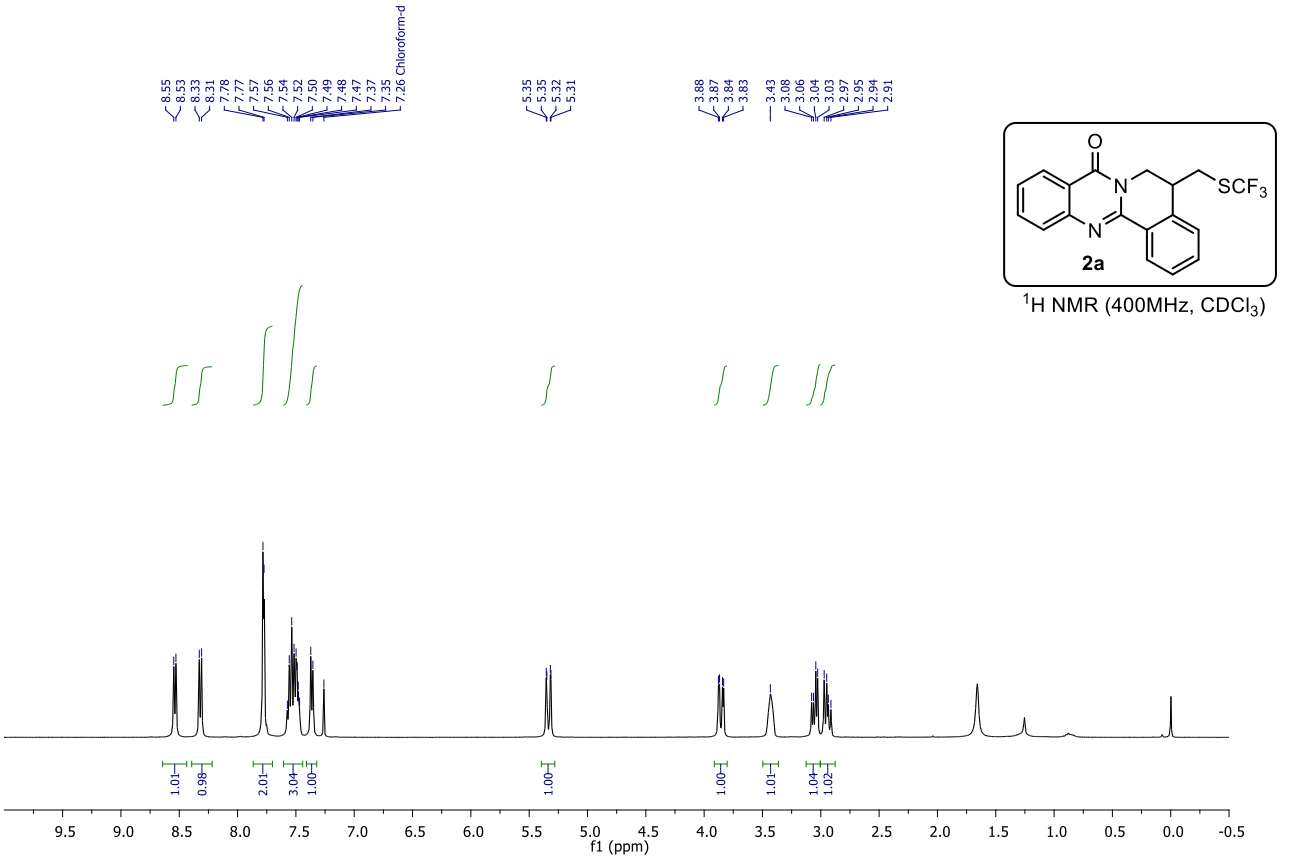
6. References:

1. Huang, J.; Ban, C.; Qin, J.; Xu, J.; Gu, Y.; Wei, L.; Yuan, J.-M.; Huang, G. Visible-Light Promoted Radical Cascade Cyclization of 3-Allyl-2-Arylquinazolinones for the Synthesis of Phosphorylated Dihydroisoquinolino[1,2-b]Quinazolinones. *Chem. Commun.* **2024**, *60* (62), 8119–8122.

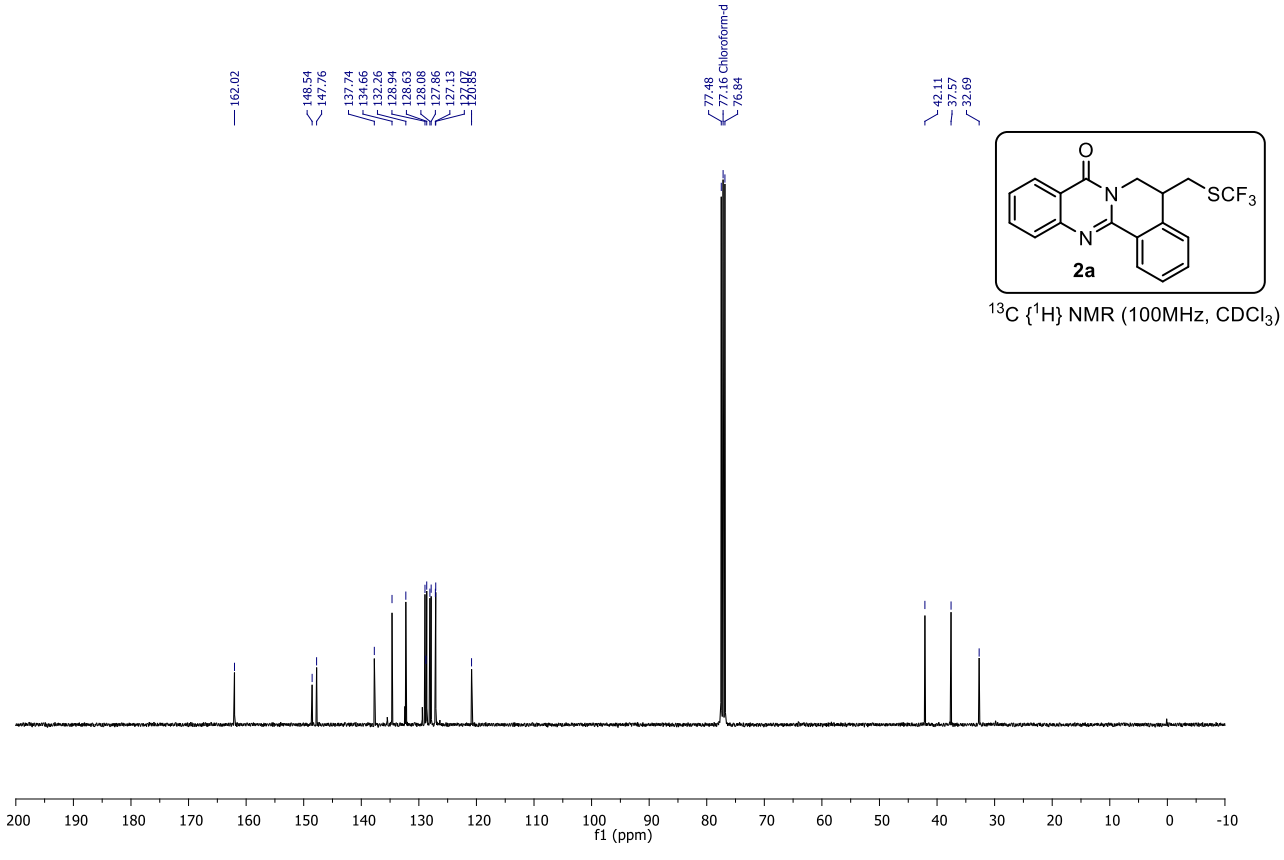
2. Palem, J. D.; Alugubelli, G. R.; Bantu, R.; Nagarapu, L.; Polepalli, S.; Jain, S. N.; Bathini, R.; Manga, V. Quinazolinones–Phenylquinoxaline Hybrids with Unsaturation/Saturation Linkers as Novel Anti-Proliferative Agents. *Bioorg. Med. Chem. Lett.* **2016**, *26* (13), 3014–3018.

3. Bairy, G.; Nandi, A.; Manna, K.; Jana, R. Ruthenium(II)-Catalyzed Migratory C–H Allylation/Hydroamination Cascade for the Synthesis of Rutaecarpine Analogues. *Synthesis* **2019**, *51*, 2523–2531.

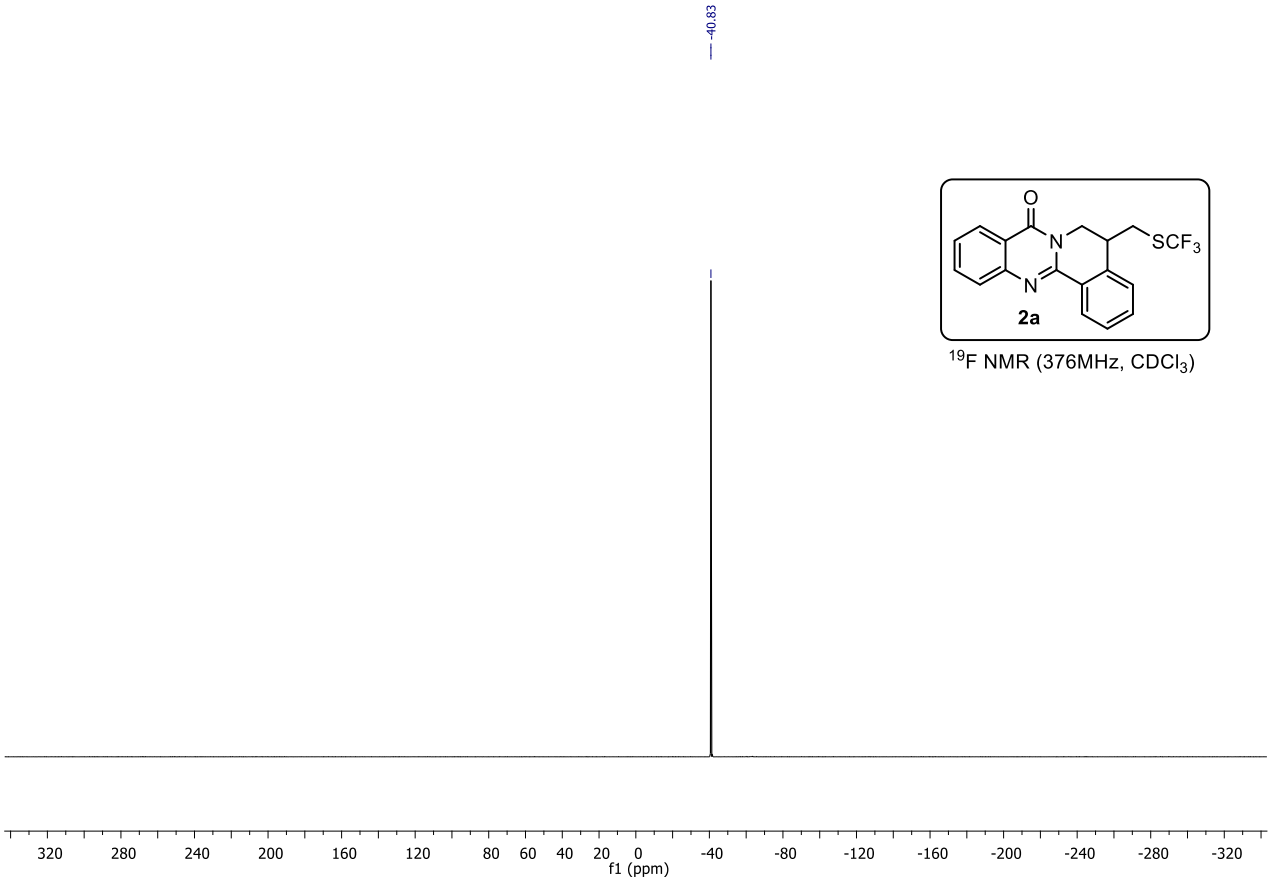
7. Spectrum



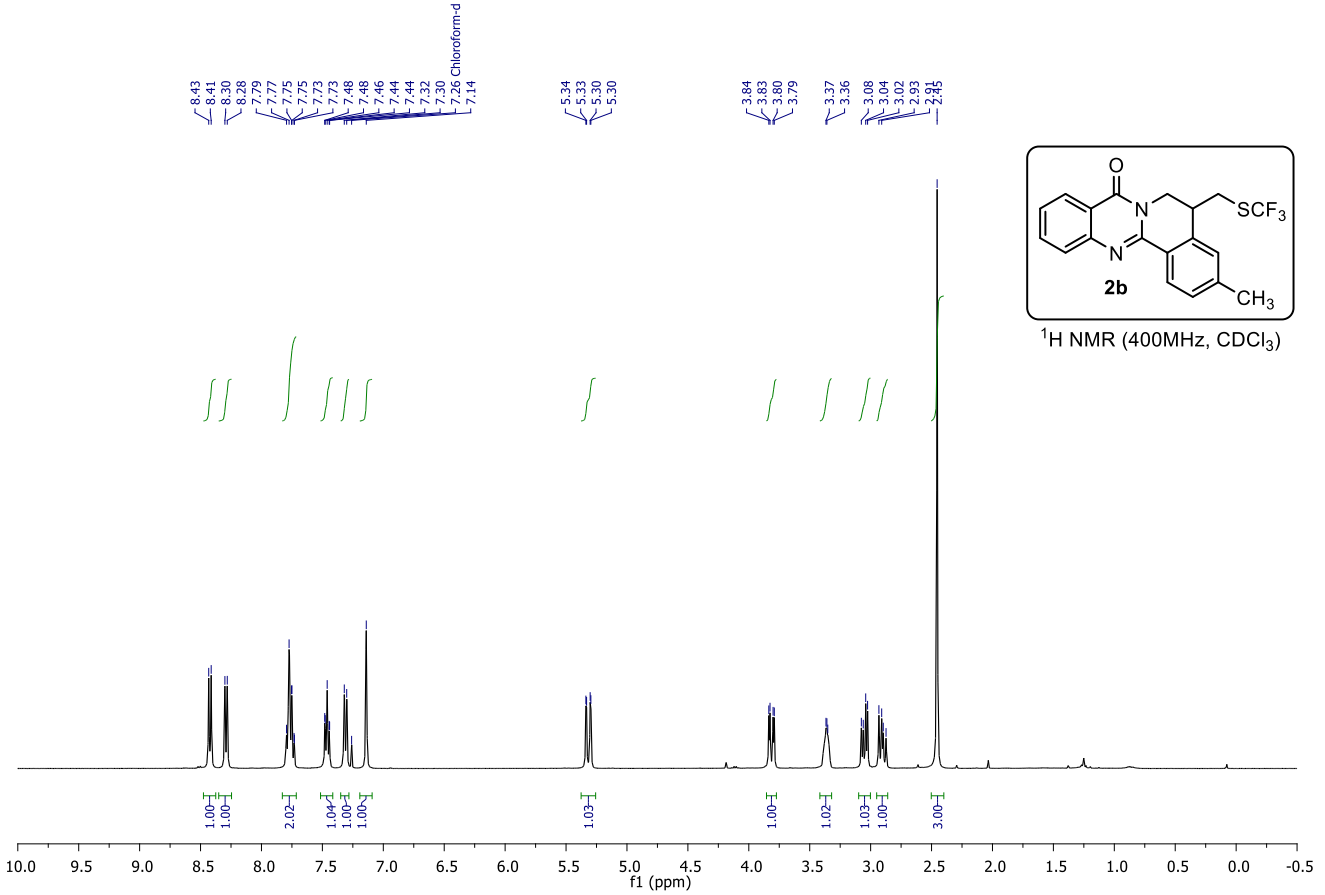
^{1}H NMR (400MHz, $CDCl_3$)



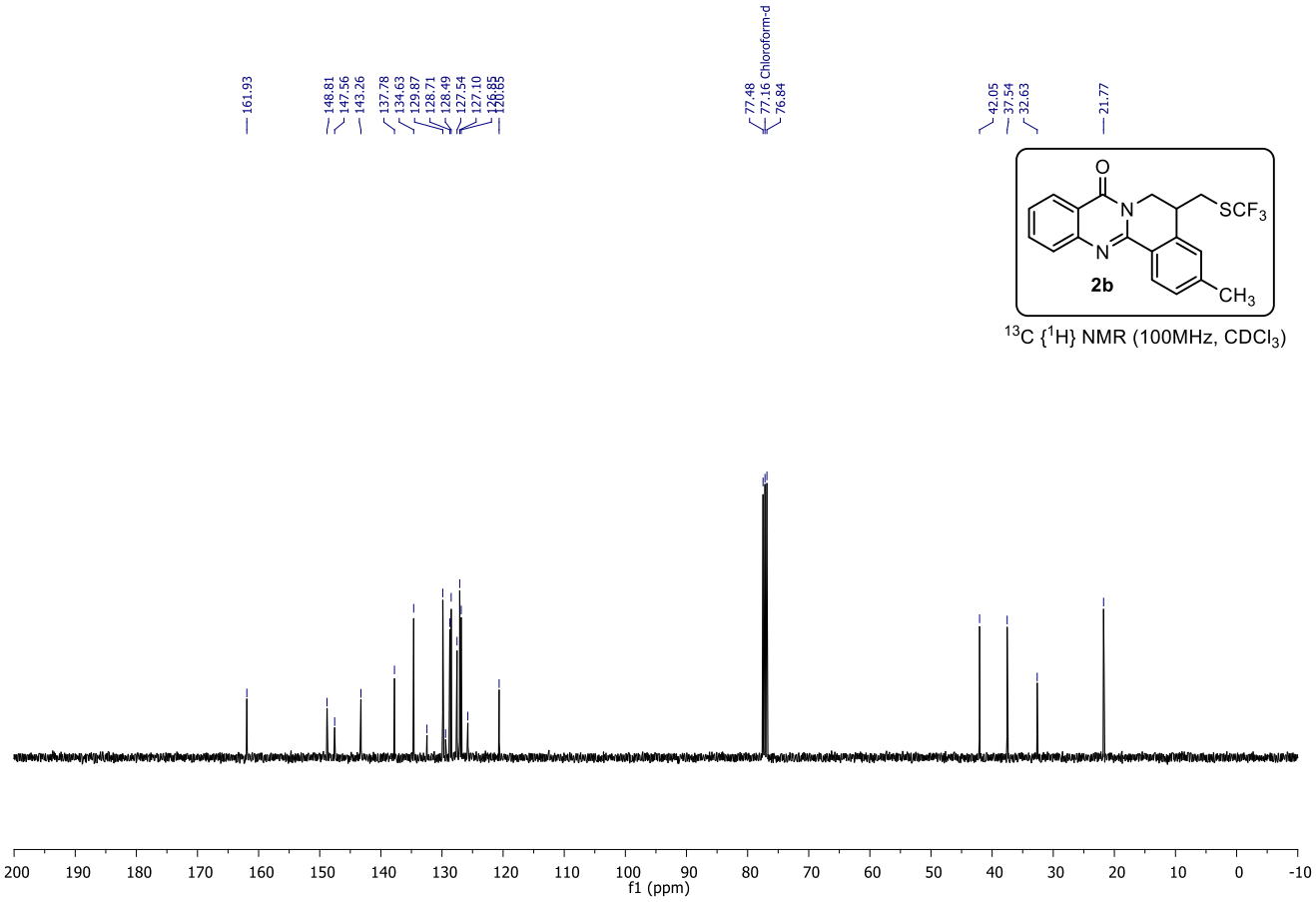
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



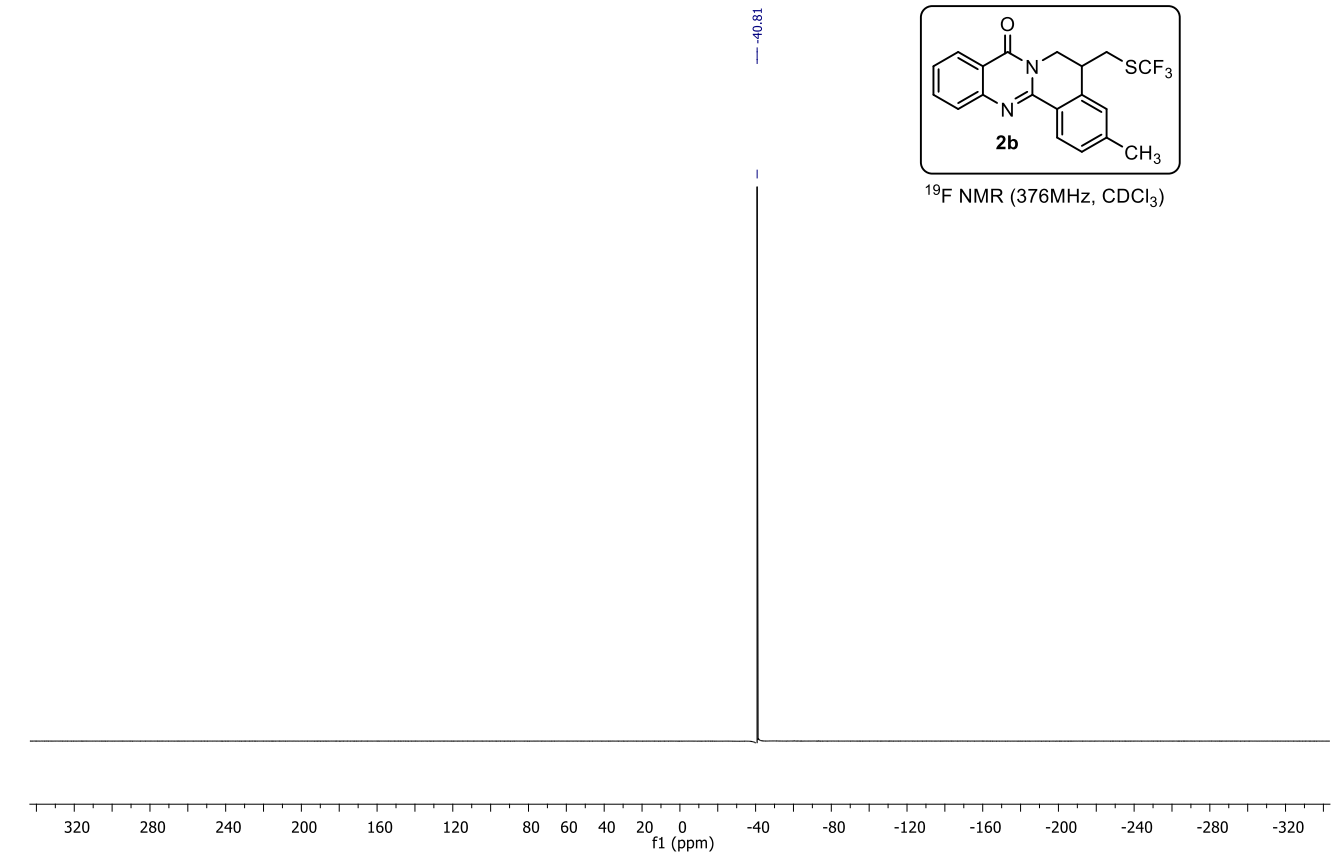
^{19}F NMR (376MHz, $CDCl_3$)



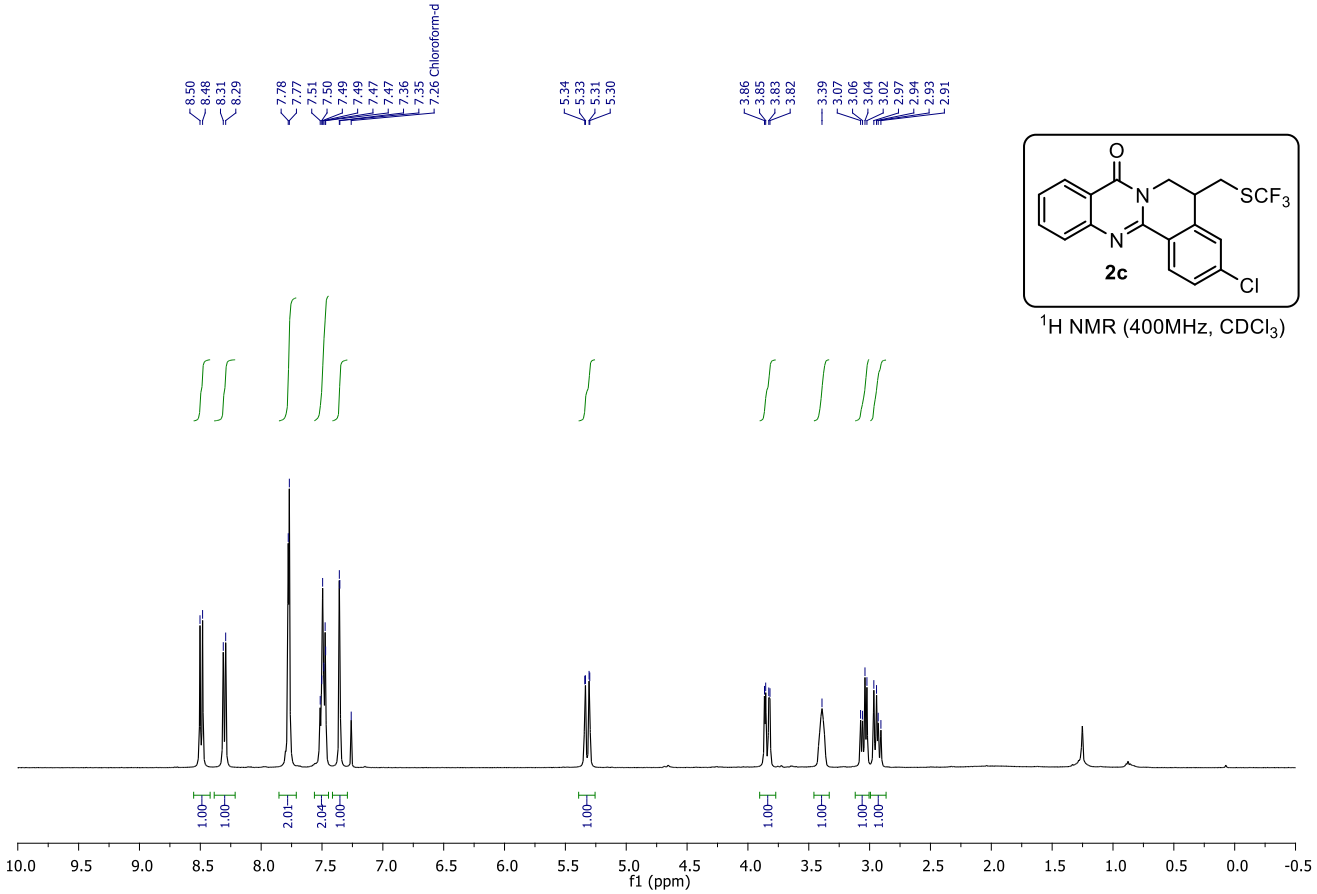
^{1}H NMR (400MHz, $CDCl_3$)



^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)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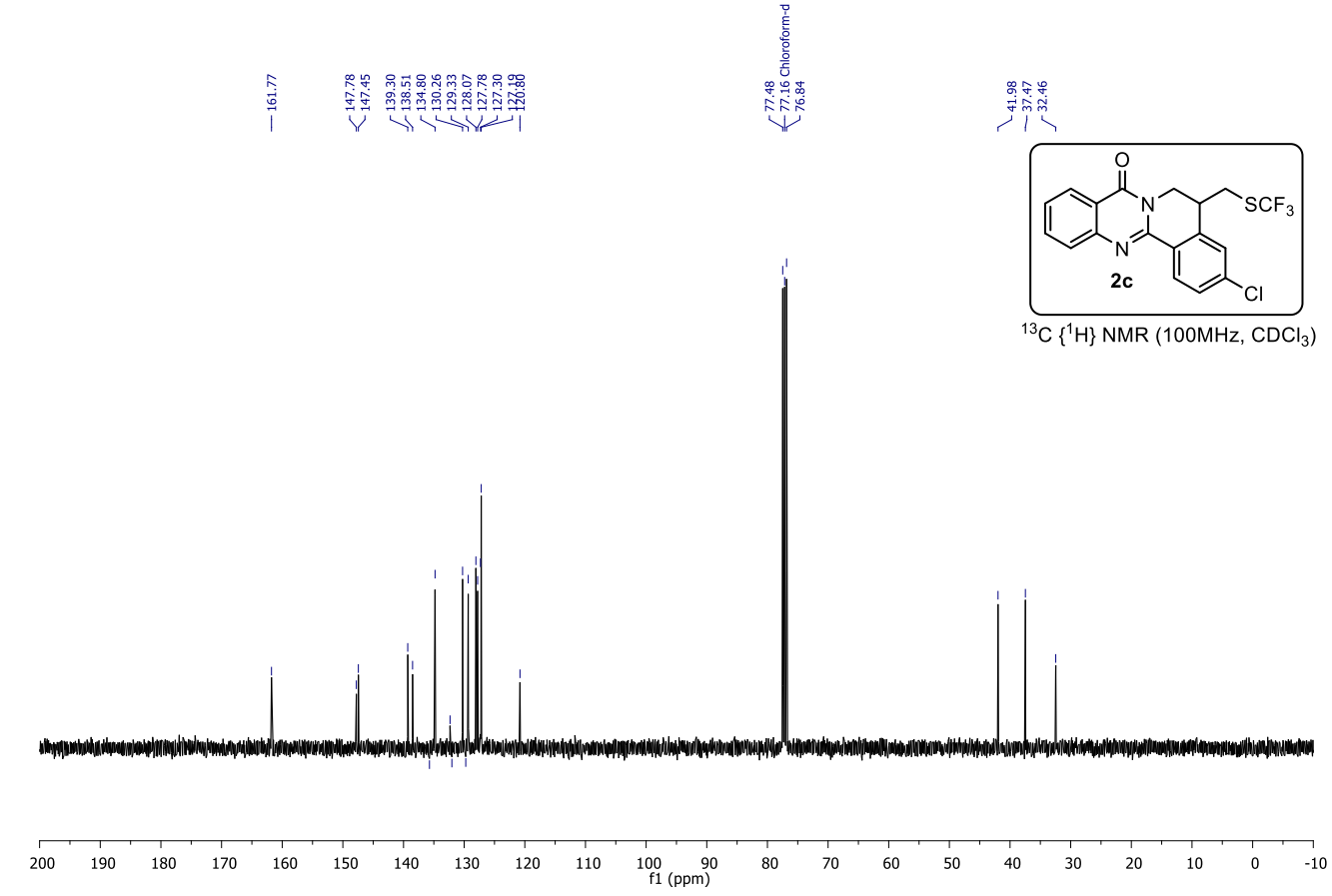
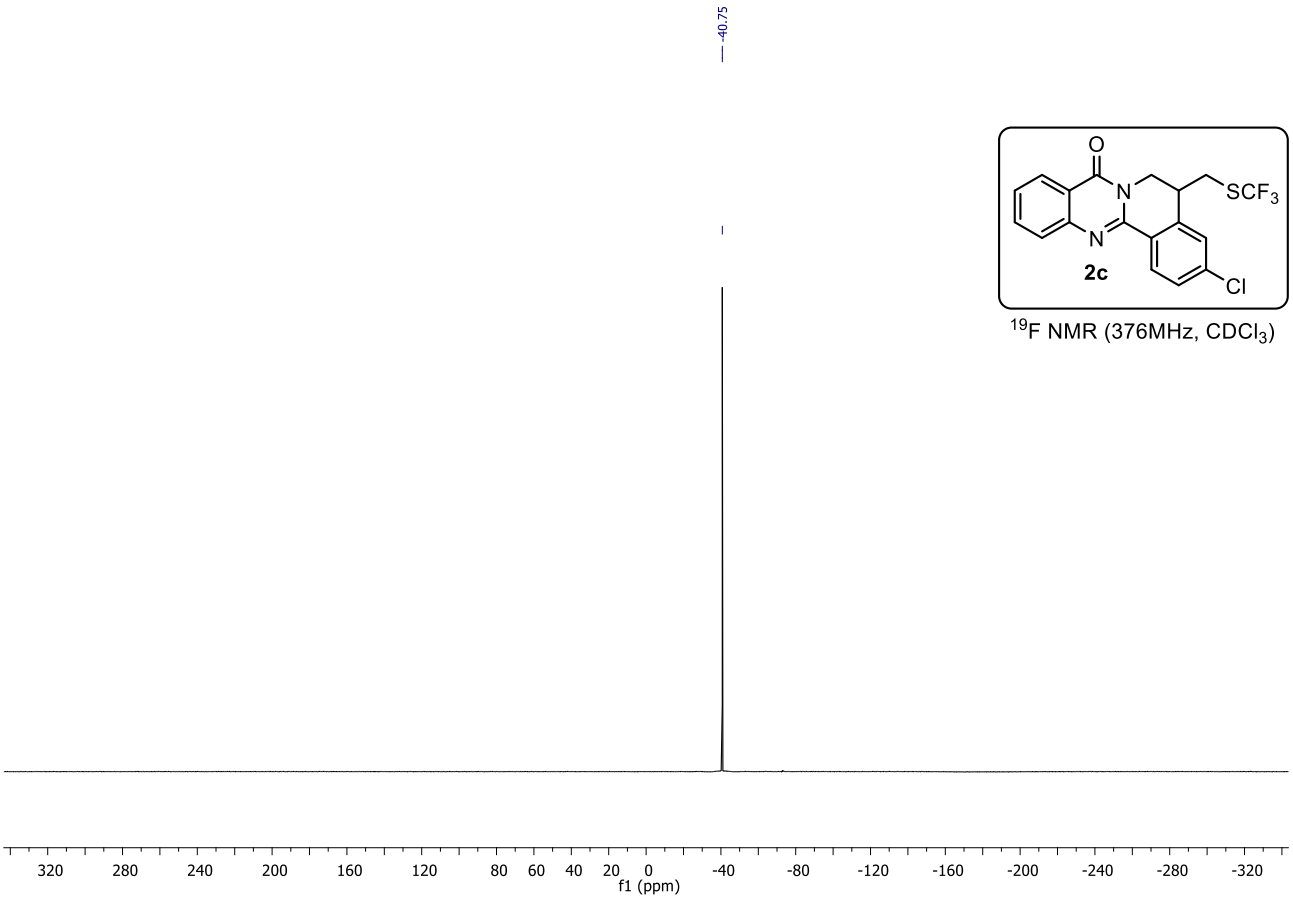
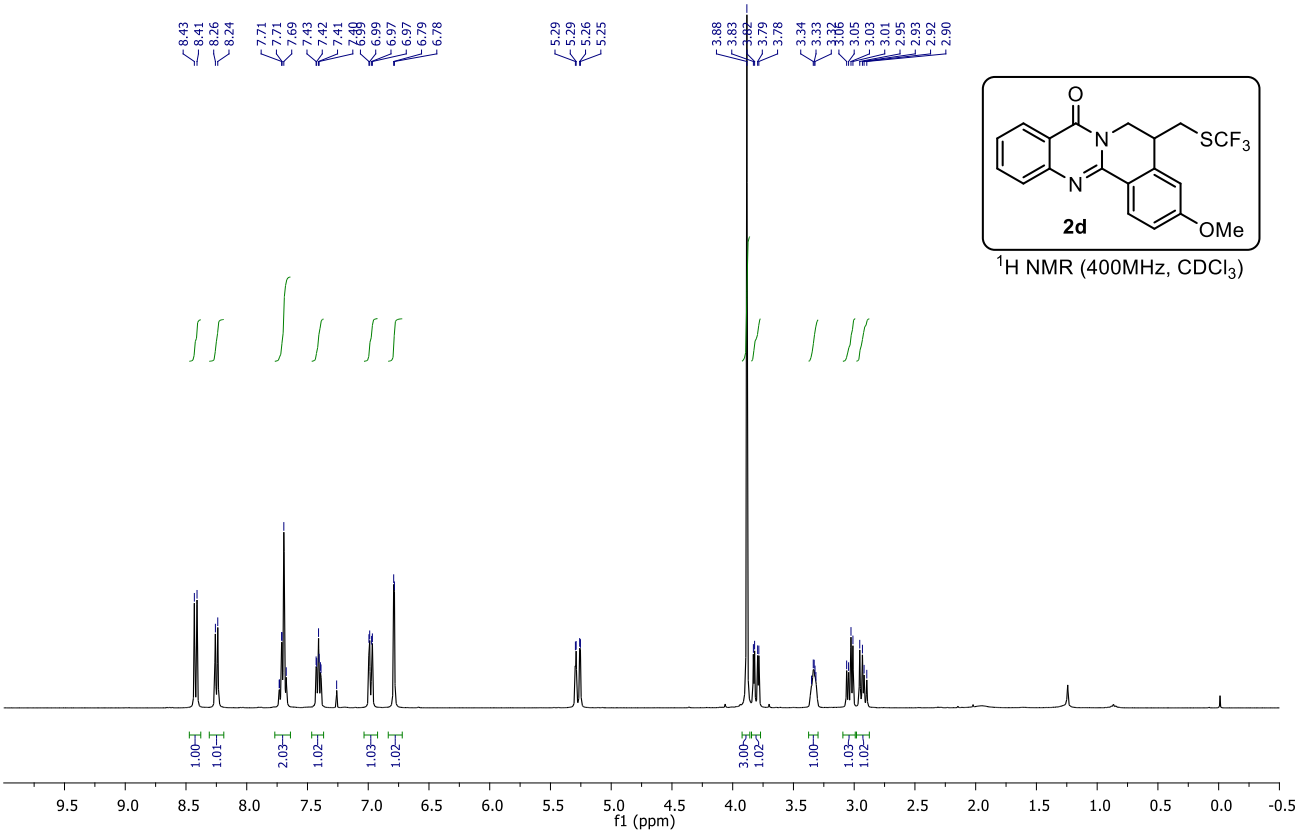
8.48
8.31
8.29
7.78
7.77
7.51
7.50
7.49
7.49
7.47
7.47
7.36
7.35
7.26 Chloroform-d
5.34
5.33
5.31
5.30
3.86
3.85
3.83
3.82
3.39
3.07
3.06
3.04
3.02
2.97
2.94
2.93
2.91
O
N
N
SCF3
Cl
2c
1H NMR (400MHz, CDCl3)
1.00
1.00
2.01
2.04
1.00
1.00
1.00
1.00
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

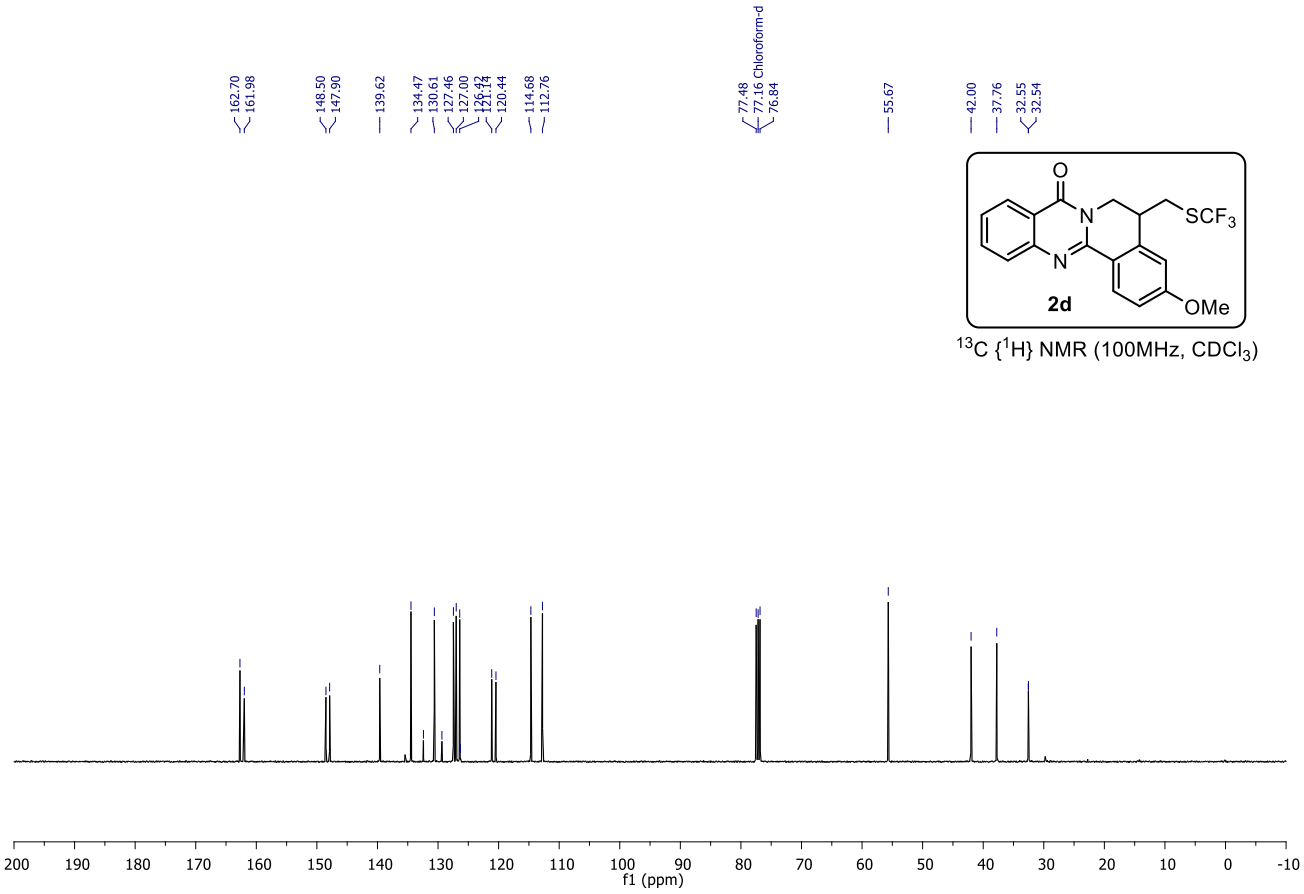

161.77
147.78
147.45
139.30
138.51
134.80
130.26
129.33
128.07
127.78
127.30
77.48
77.16 Chloroform-d
76.84
41.98
37.47
32.46
O
N
N
SCF3
Cl
2c
13C {1H} NMR (100MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



^{19}F NMR (376MHz, $CDCl_3$)



^{1}H NMR (400MHz, $CDCl_3$)



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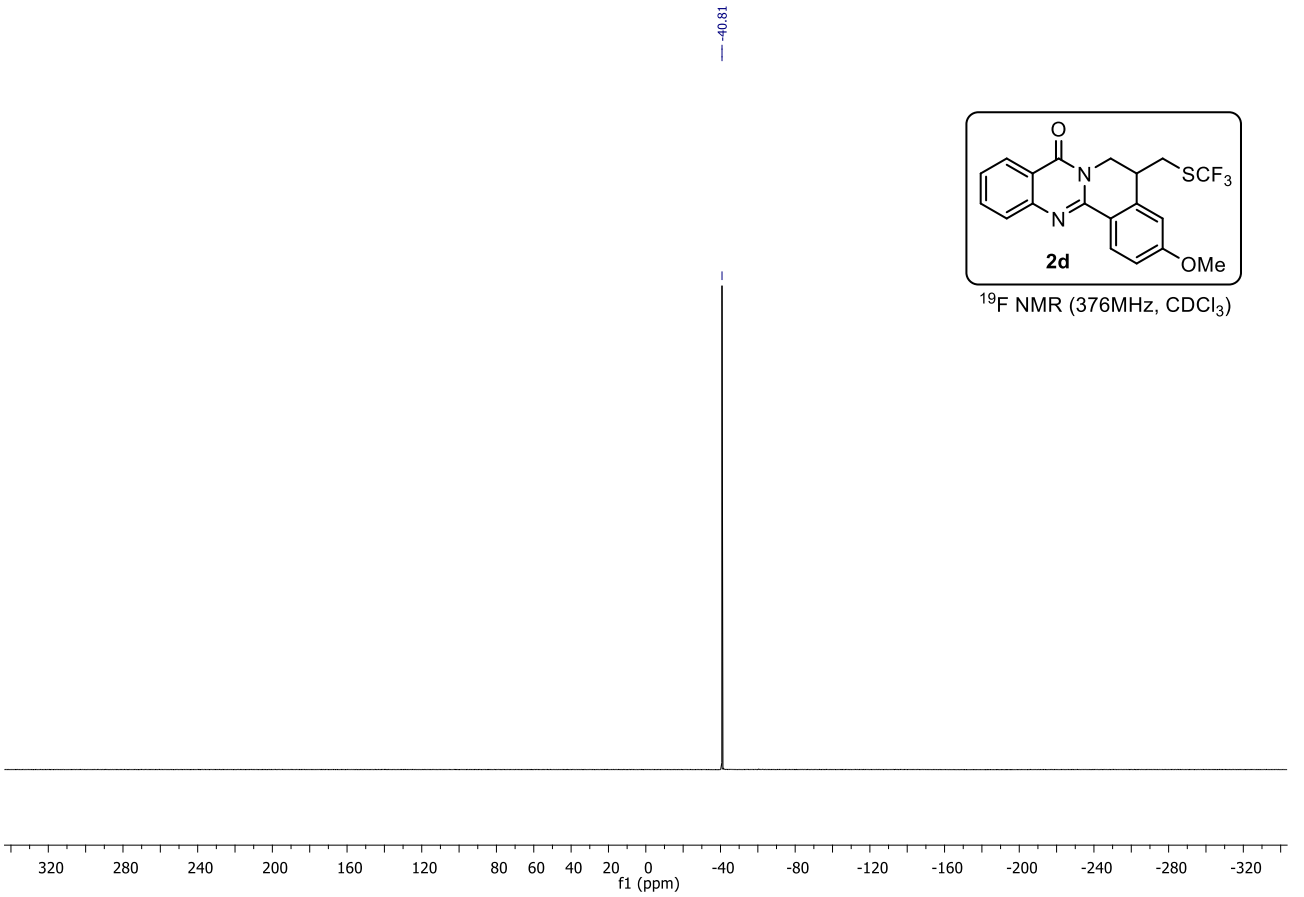
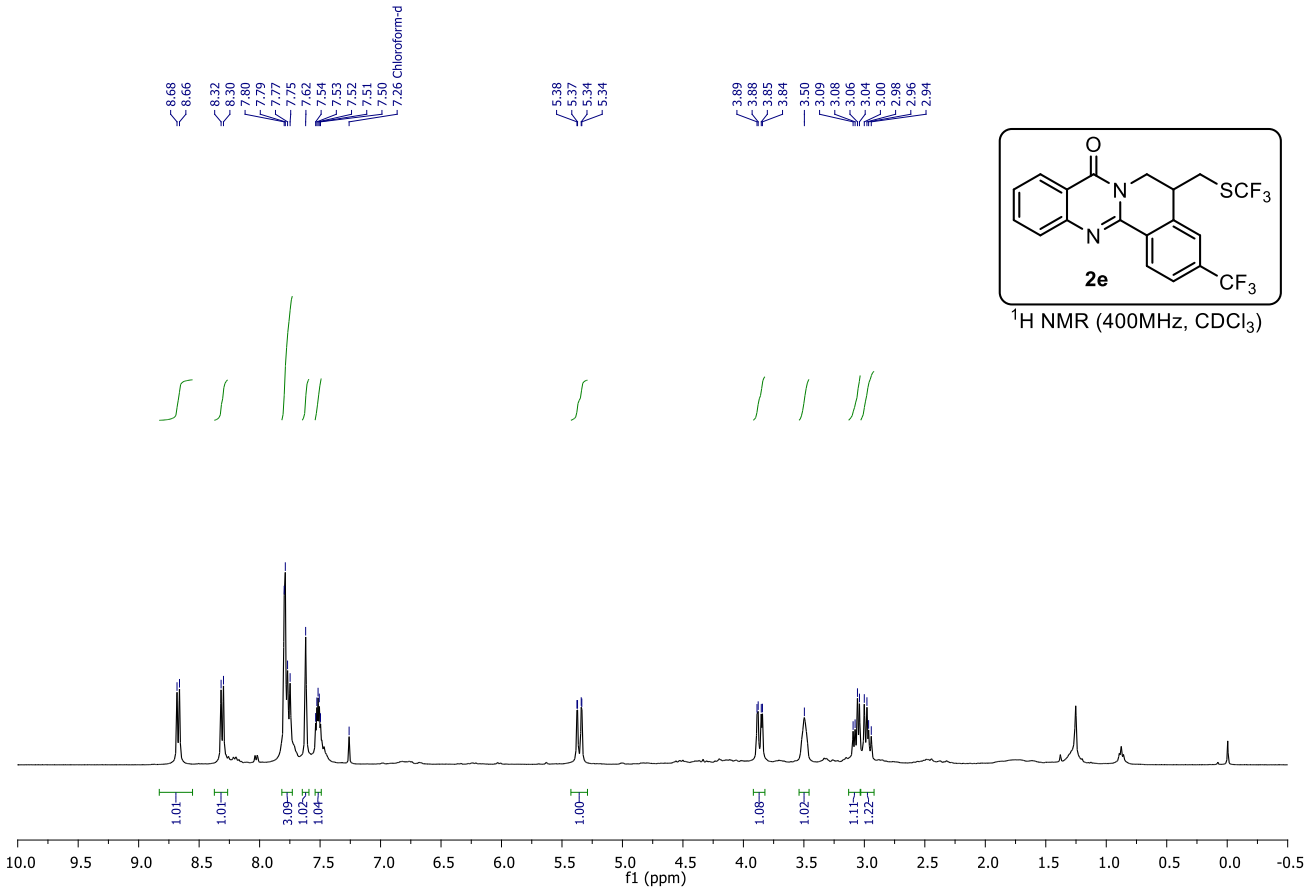


^{19}F NMR (376MHz, $CDCl_3$)


8.68
8.66
8.32
8.30
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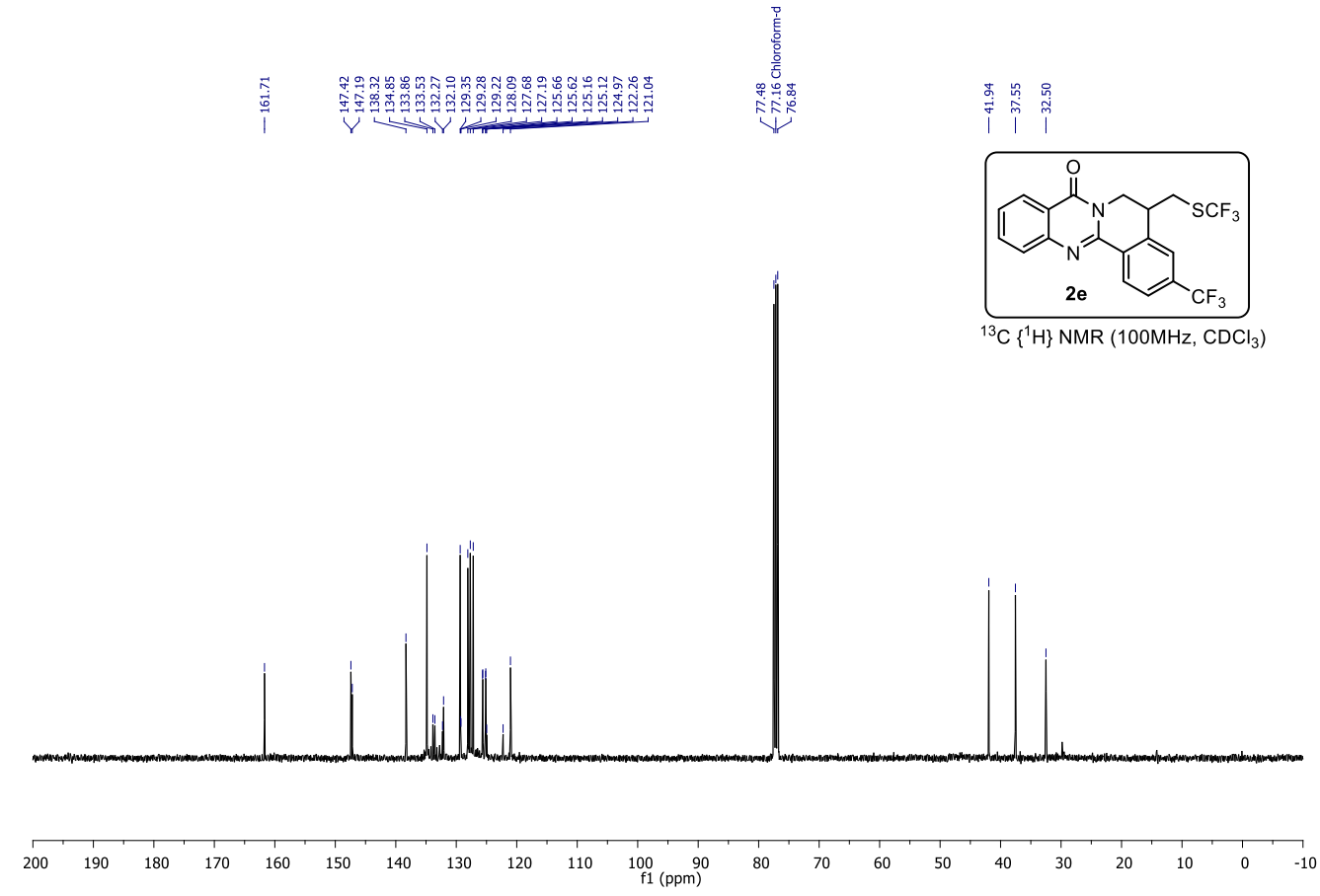
7.79
7.77
7.75
7.62
7.54
7.53
7.52
7.51
7.50
7.26 Chloroform-d
5.38
5.37
5.34
5.34
3.89
3.88
3.85
3.84
3.50
3.09
3.08
3.06
3.04
3.00
2.98
2.96
2.94
O
N
N
SCF3
CF3
2e
1H NMR (400MHz, CDCl3)
1.01
1.01
3.09
1.02
1.04
1.00
1.08
1.02
1.11
1.22
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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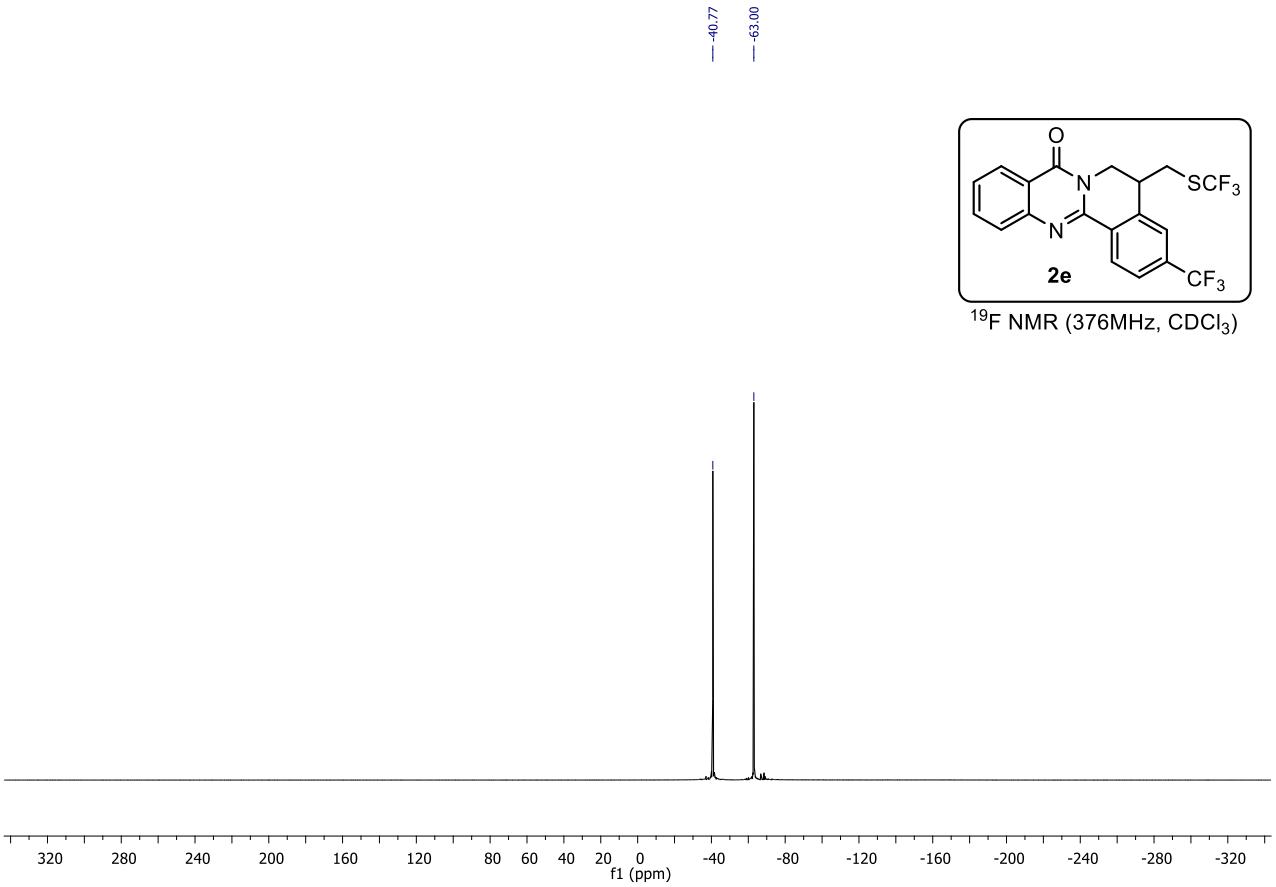
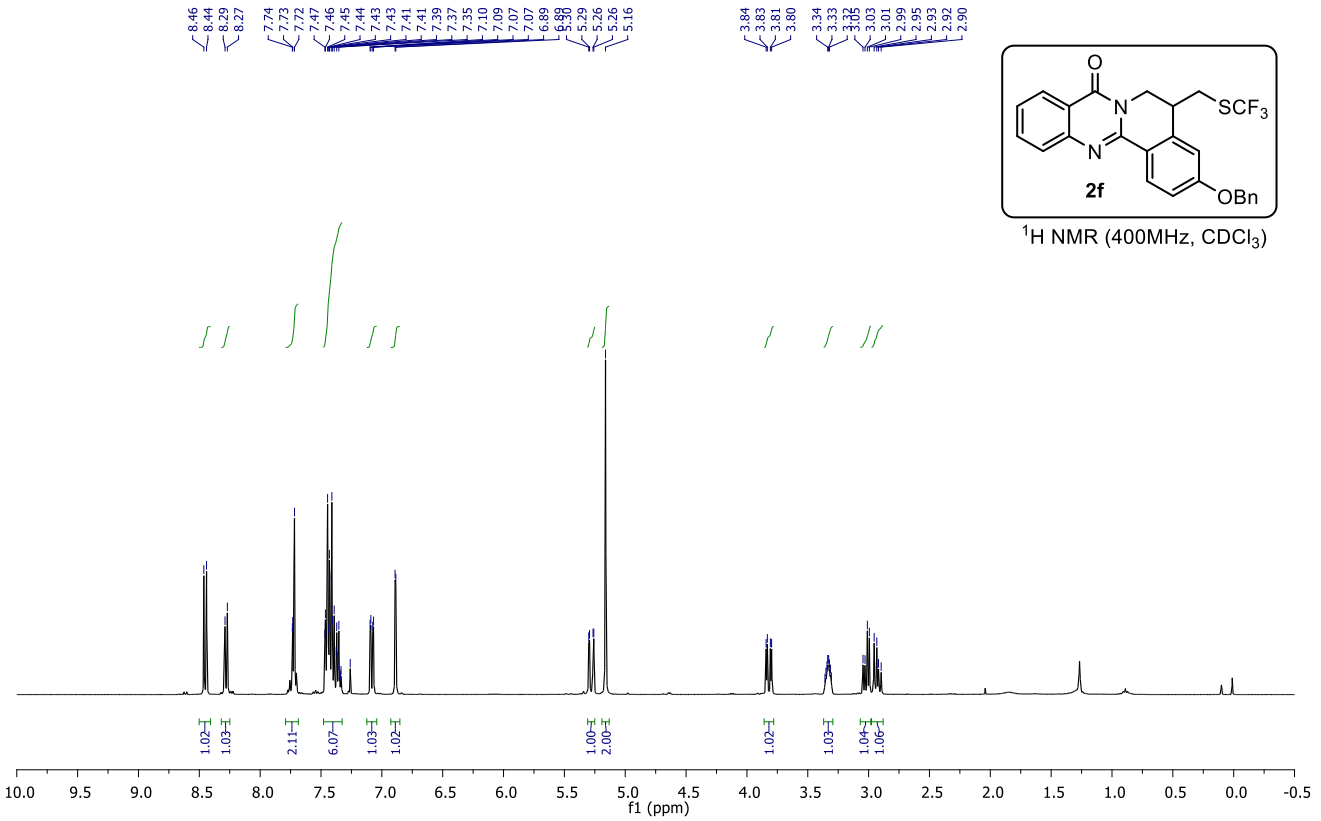
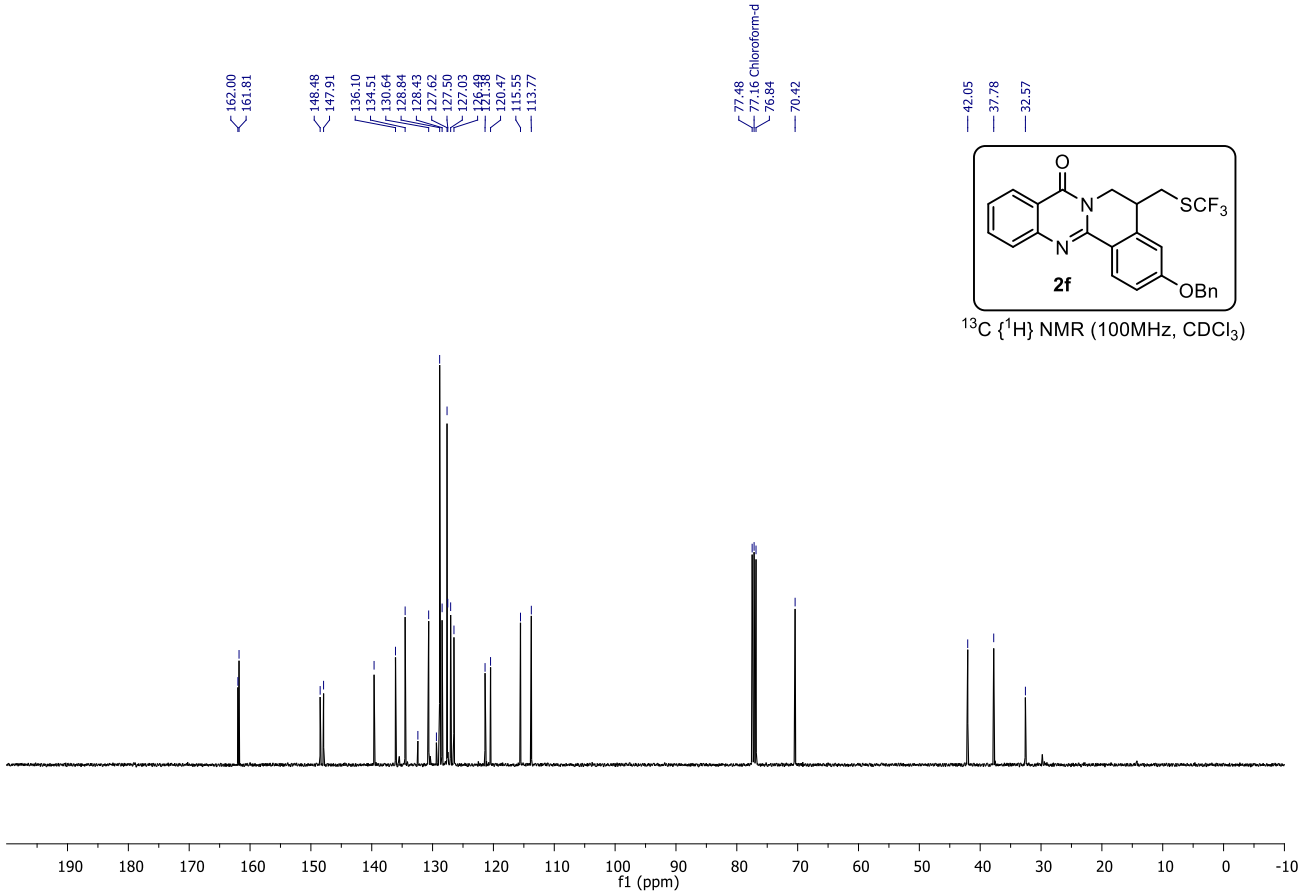
147.19
138.32
134.85
133.86
133.53
132.27
132.10
129.35
129.28
129.22
128.09
127.68
127.19
125.66
125.62
125.16
125.12
124.97
122.26
121.04
77.48
77.16 Chloroform-d
76.84
41.94
37.55
32.50
O
N
N
SCF3
CF3
2e
13C {1H} NMR (100MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



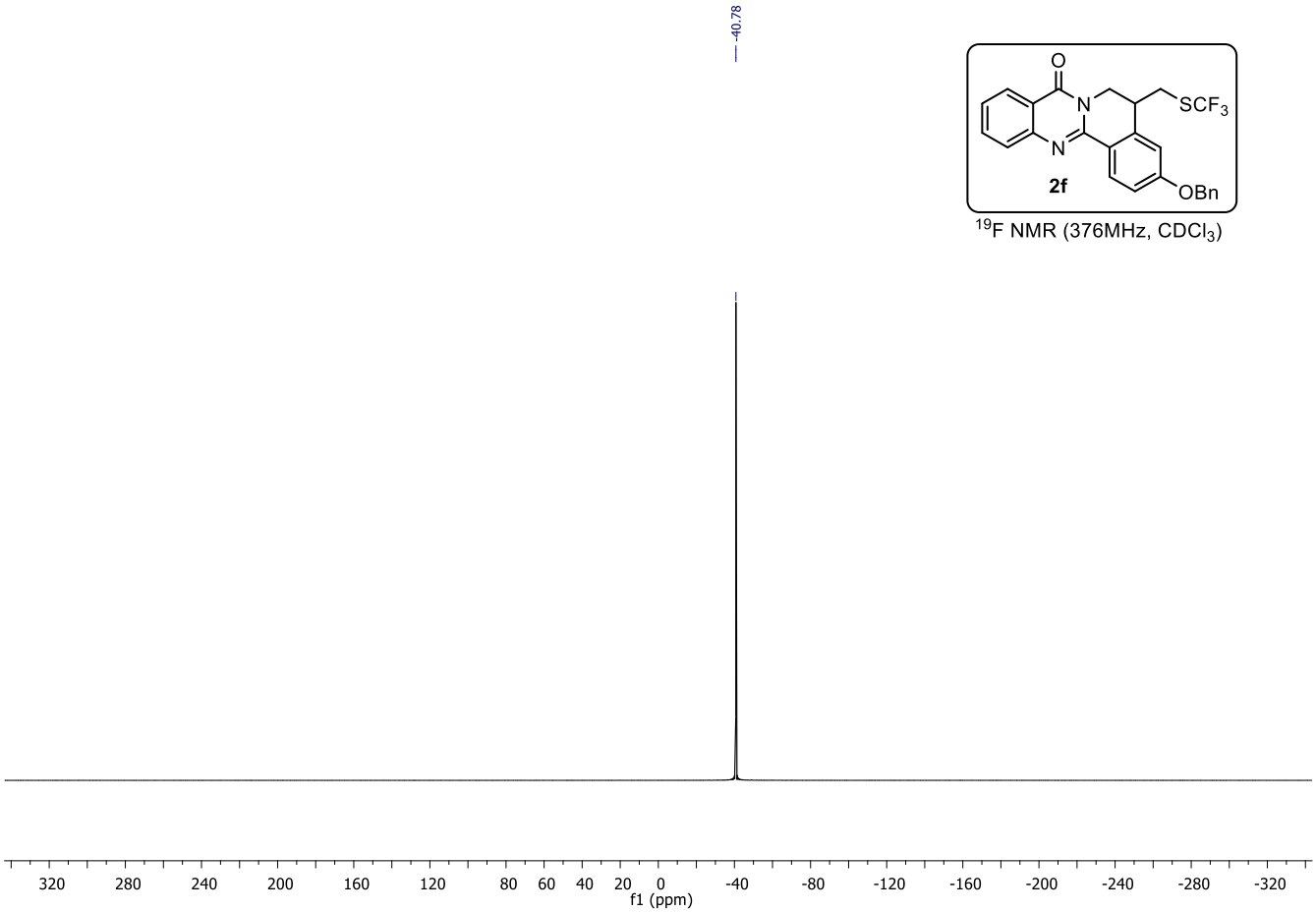
^{19}F NMR (376MHz, $CDCl_3$)



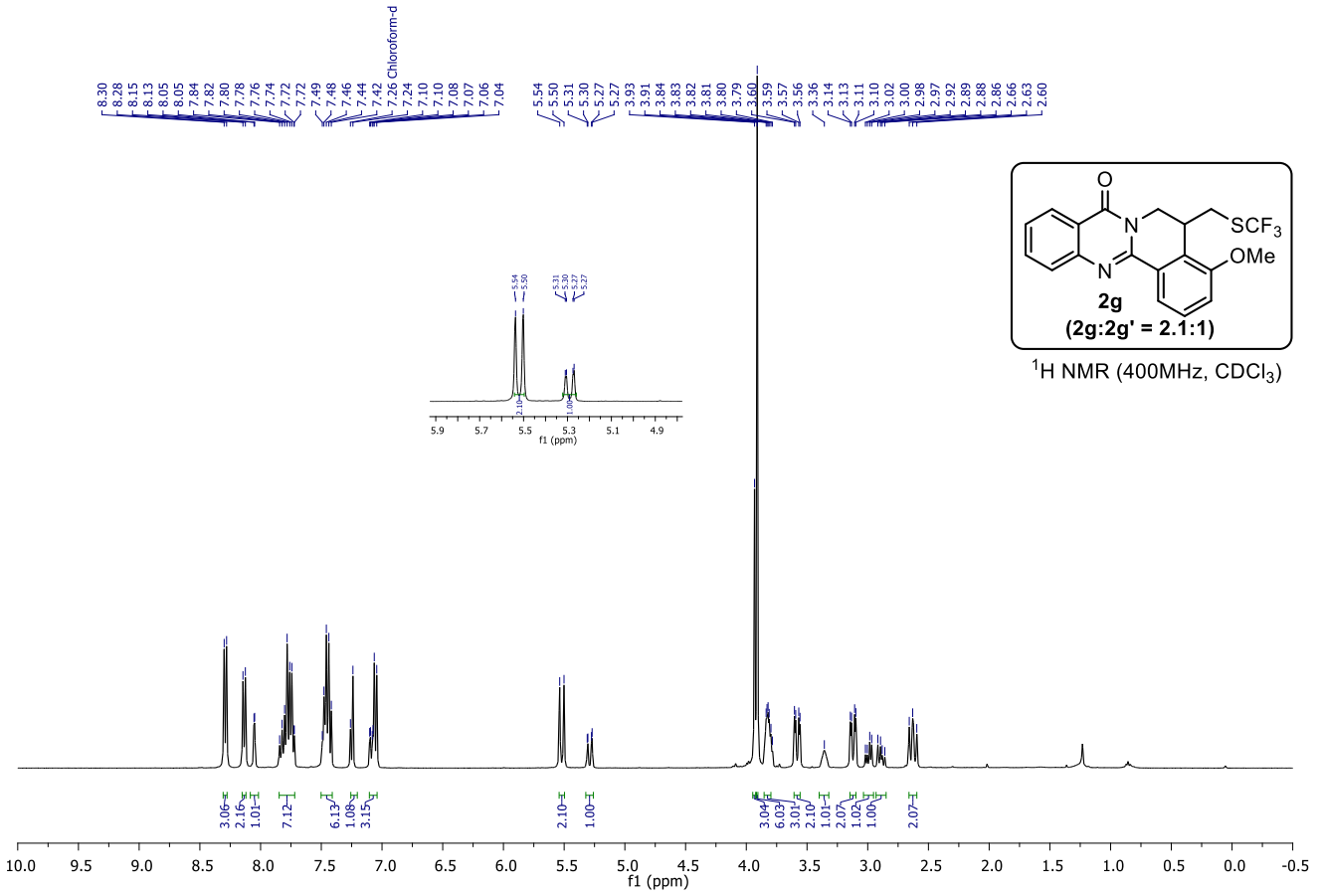
^{1}H NMR (400MHz, $CDCl_3$)



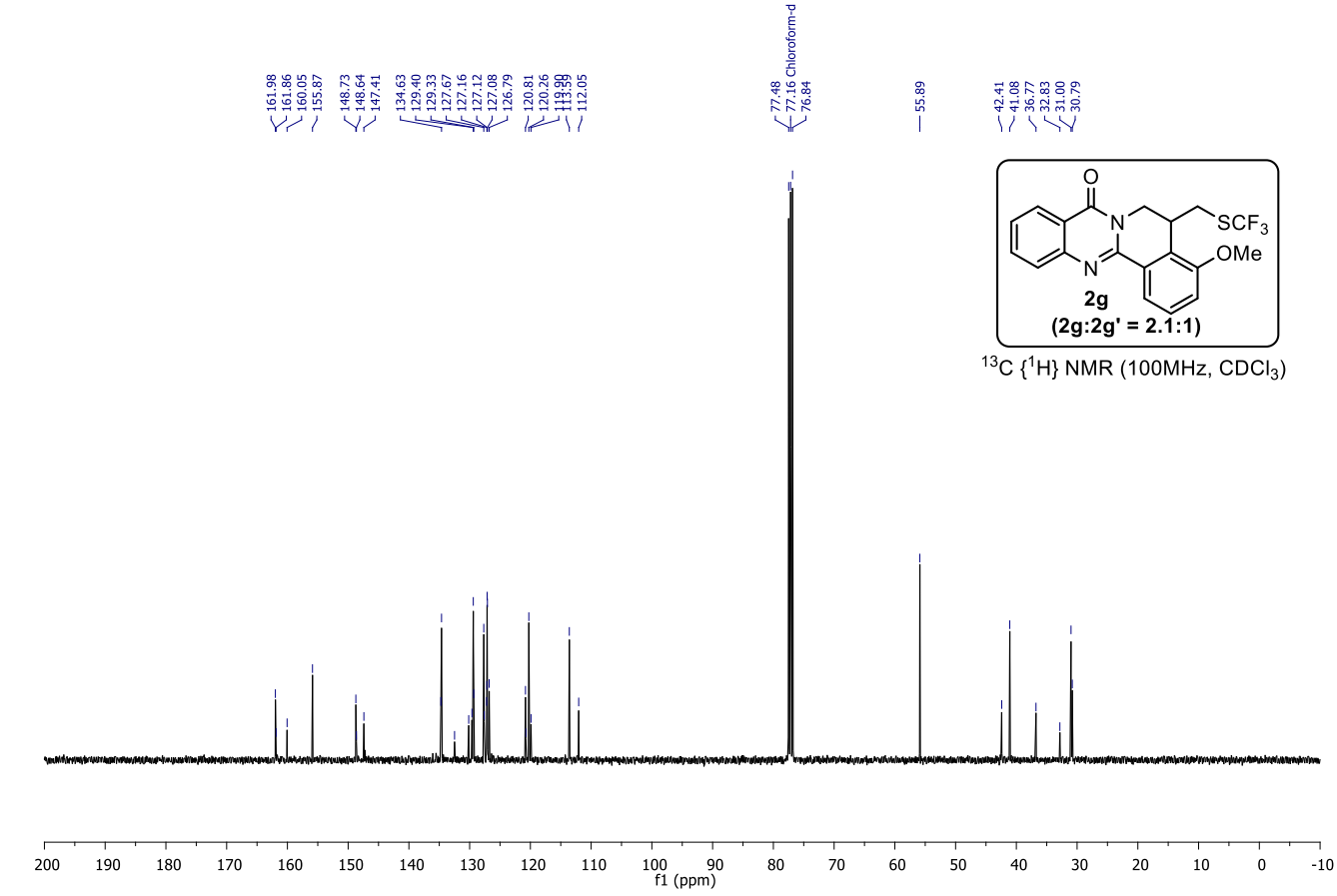
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



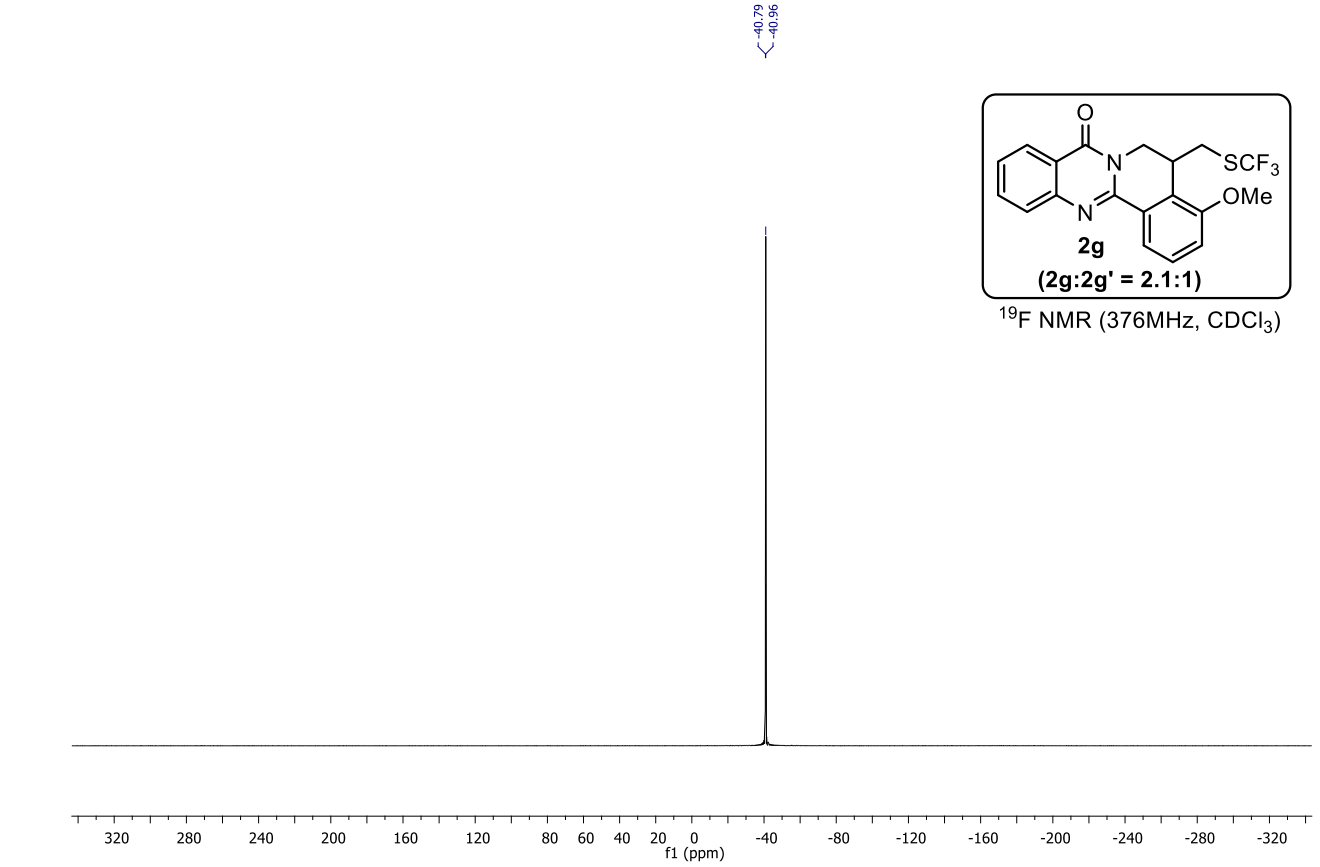
^{19}F NMR (376MHz, $CDCl_3$)

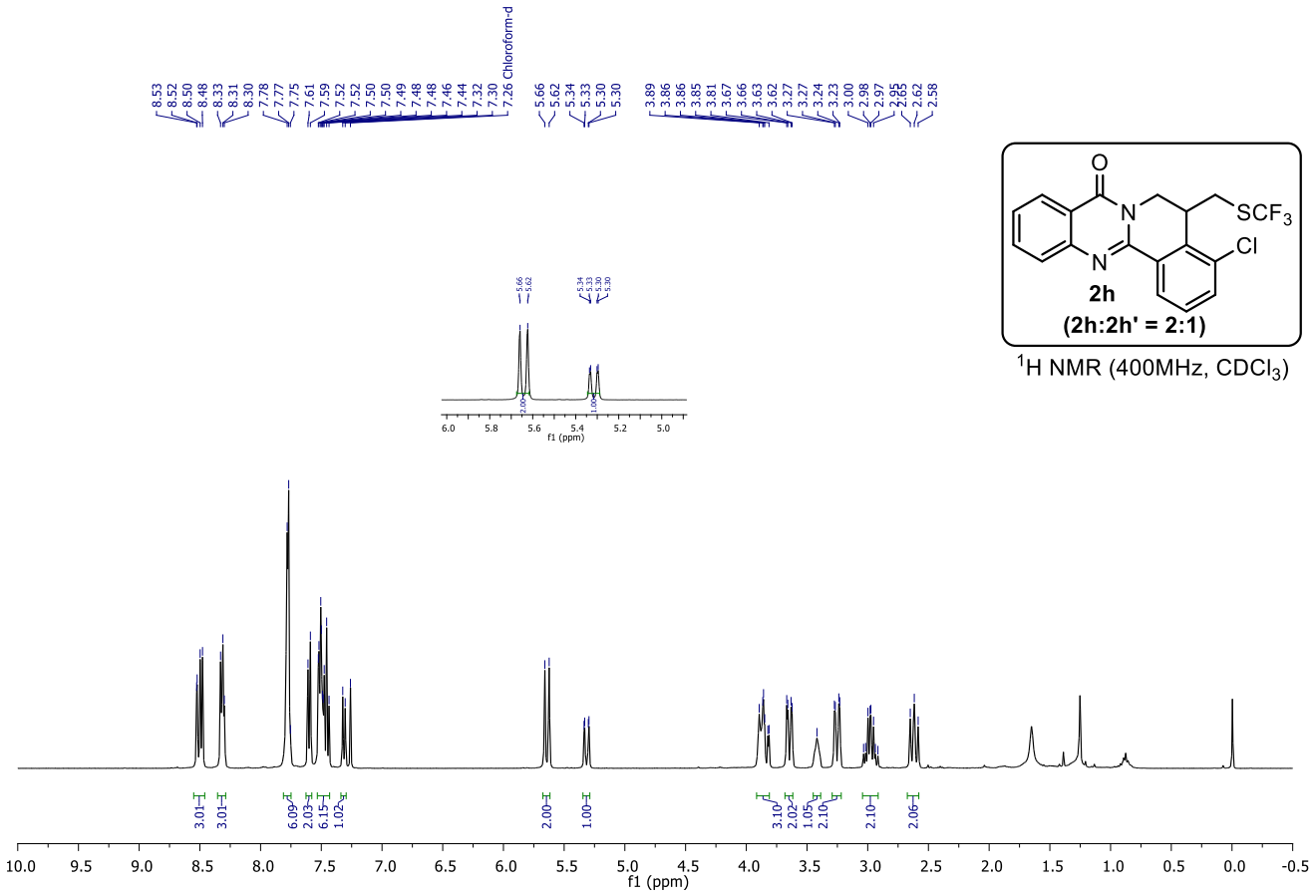


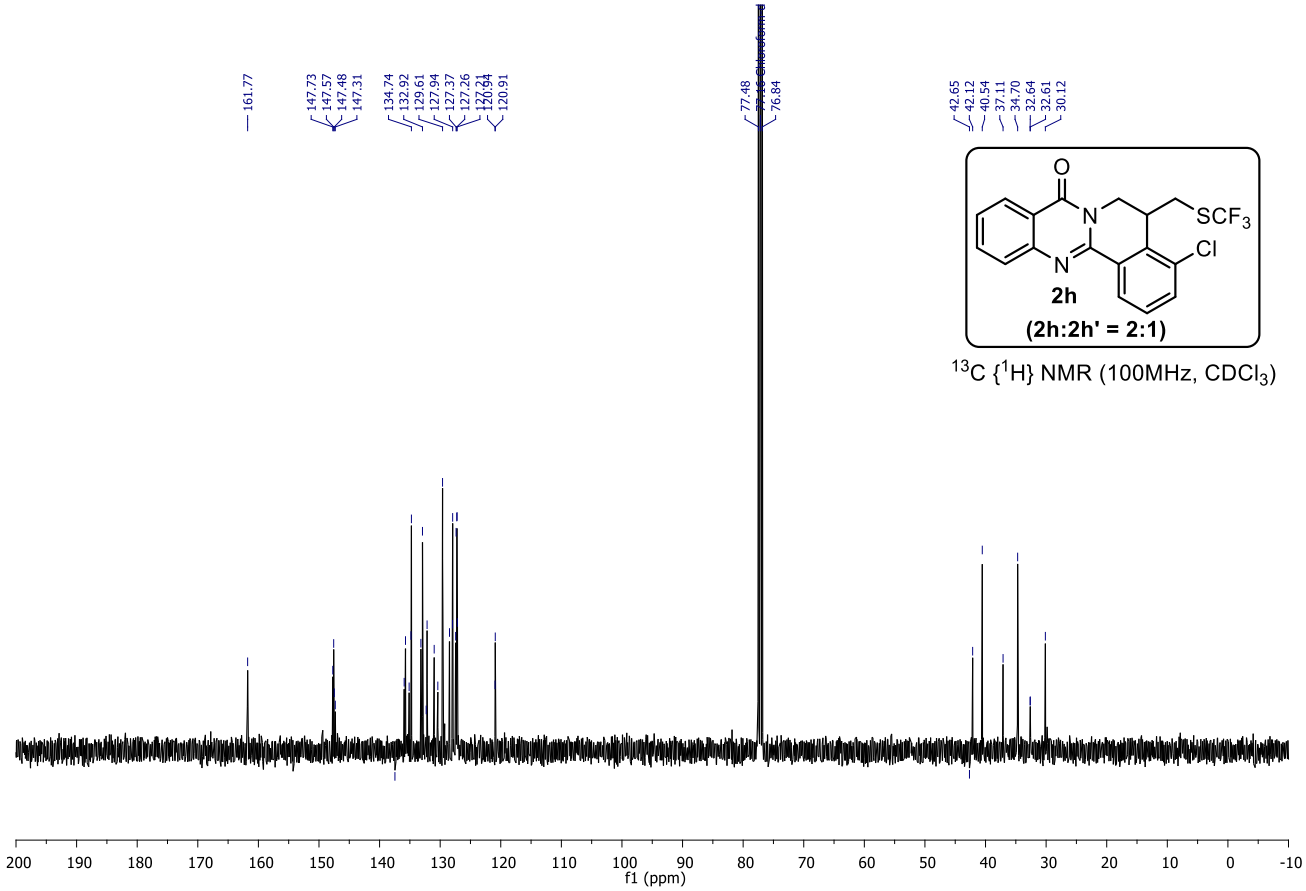
^{1}H NMR (400MHz, $CDCl_3$)



^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)


-40.79
-40.96
O
N
N
SCF3
OMe
2g
(2g:2g' = 2.1:1)
19F NMR (376MHz, CDCl3)
f1 (ppm)


Chloroform-d
O
N
N
SCF3
Cl
2h
(2h:2h' = 2:1)
1H NMR (400MHz, CDCl3)
f1 (ppm)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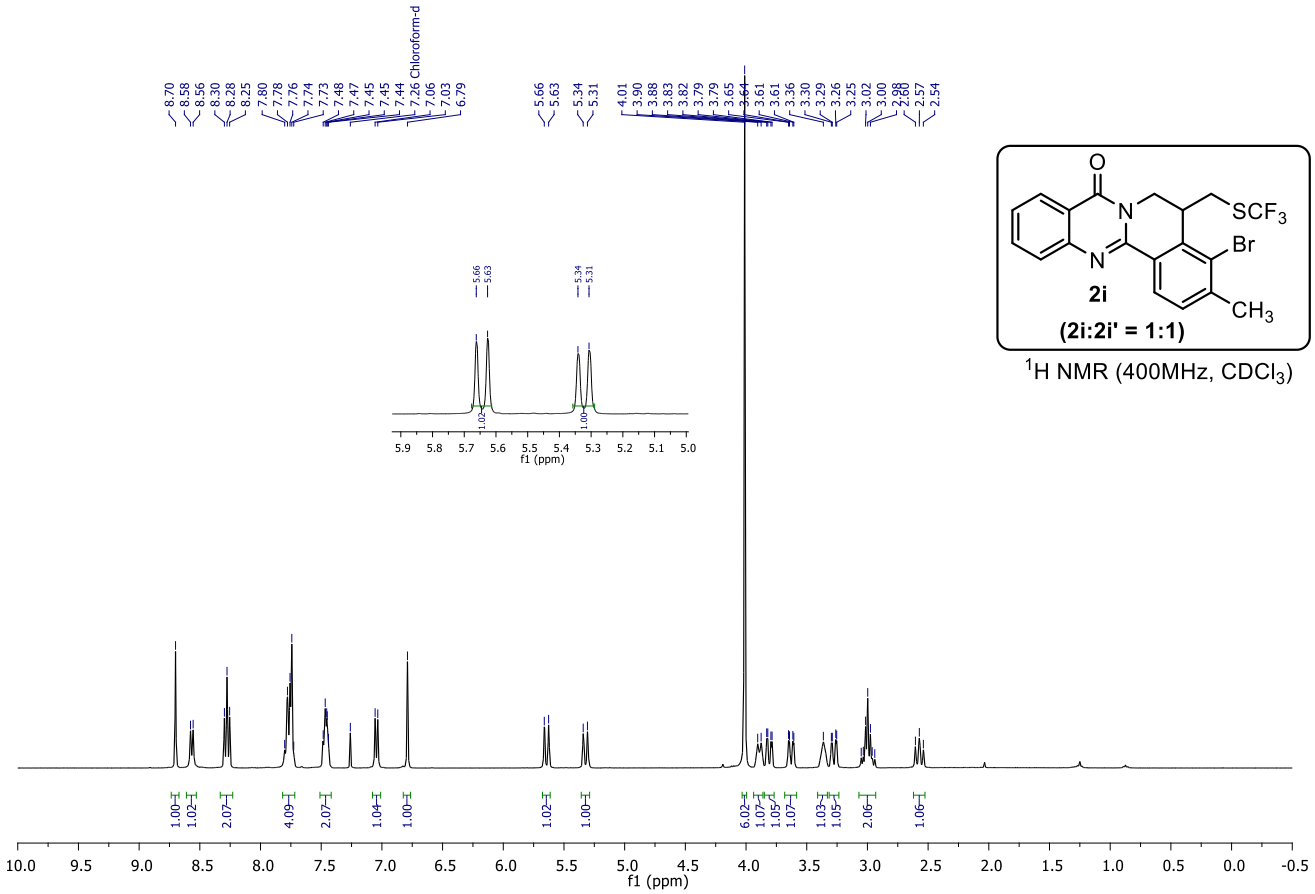
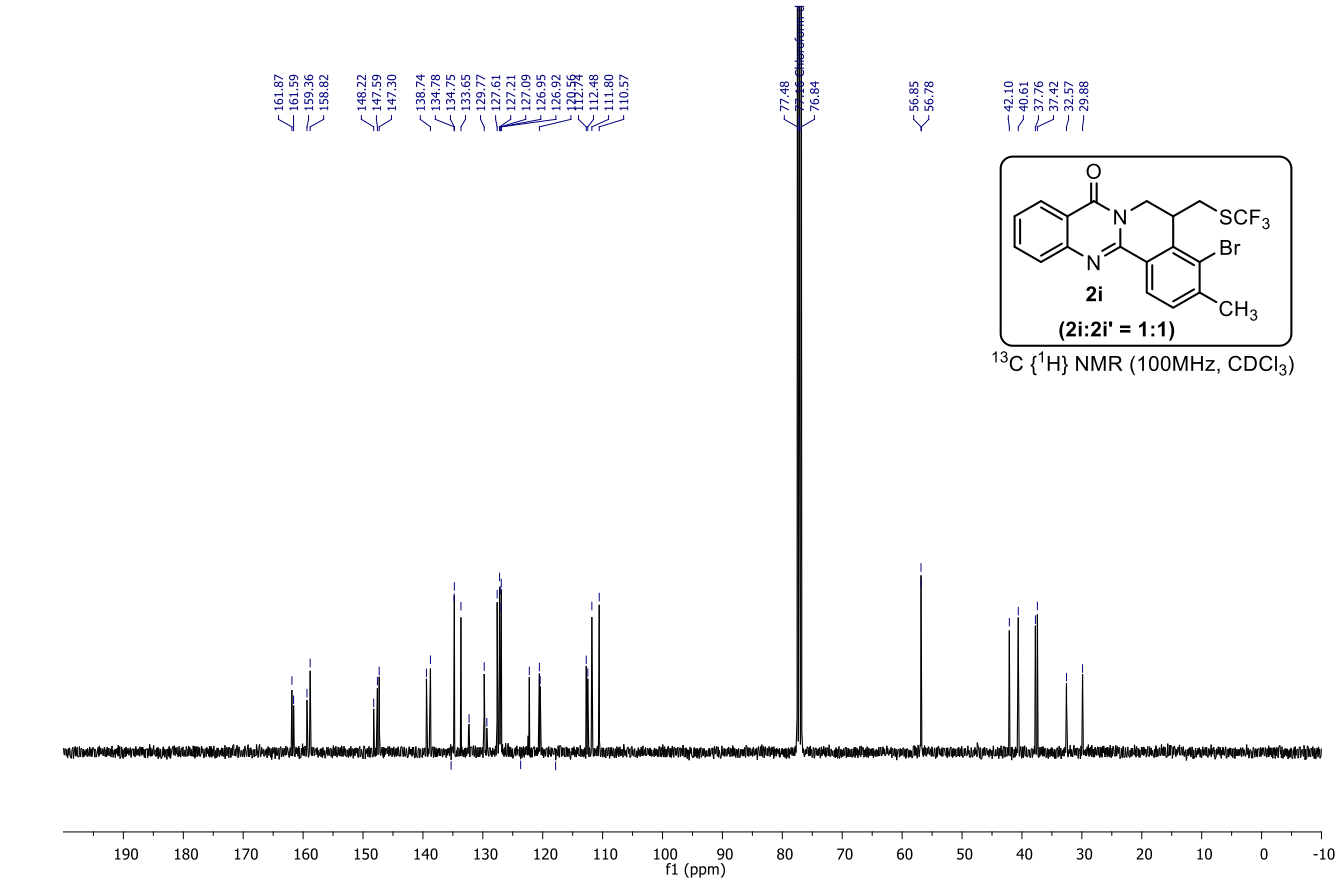
147.57
147.48
147.31
134.74
132.92
129.61
127.94
127.37
127.26
121.21
120.94
120.91
77.48
77.16
76.84
42.65
42.12
40.54
37.11
34.70
32.64
32.61
30.12
O
N
N
SCF3
Cl
2h
(2h:2h' = 2:1)
13C {1H} NMR (100MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

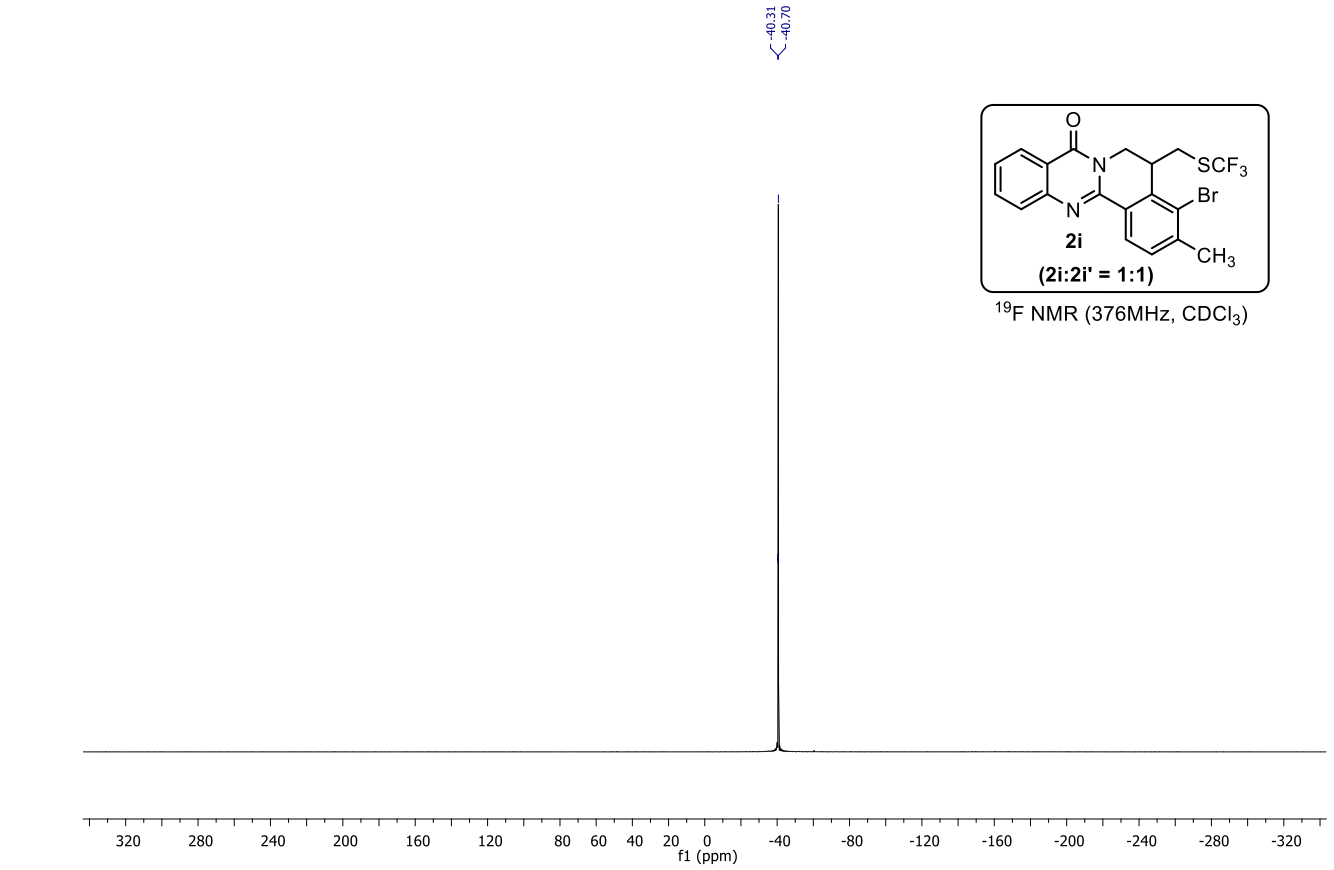

-40.59
-40.78
O
N
N
SCF3
Cl
2h
(2h:2h' = 2:1)
19F NMR (376MHz, CDCl3)
320 280 240 200 160 120 80 60 40 20 0 -40 -80 -120 -160 -200 -240 -280 -320
f1 (ppm)



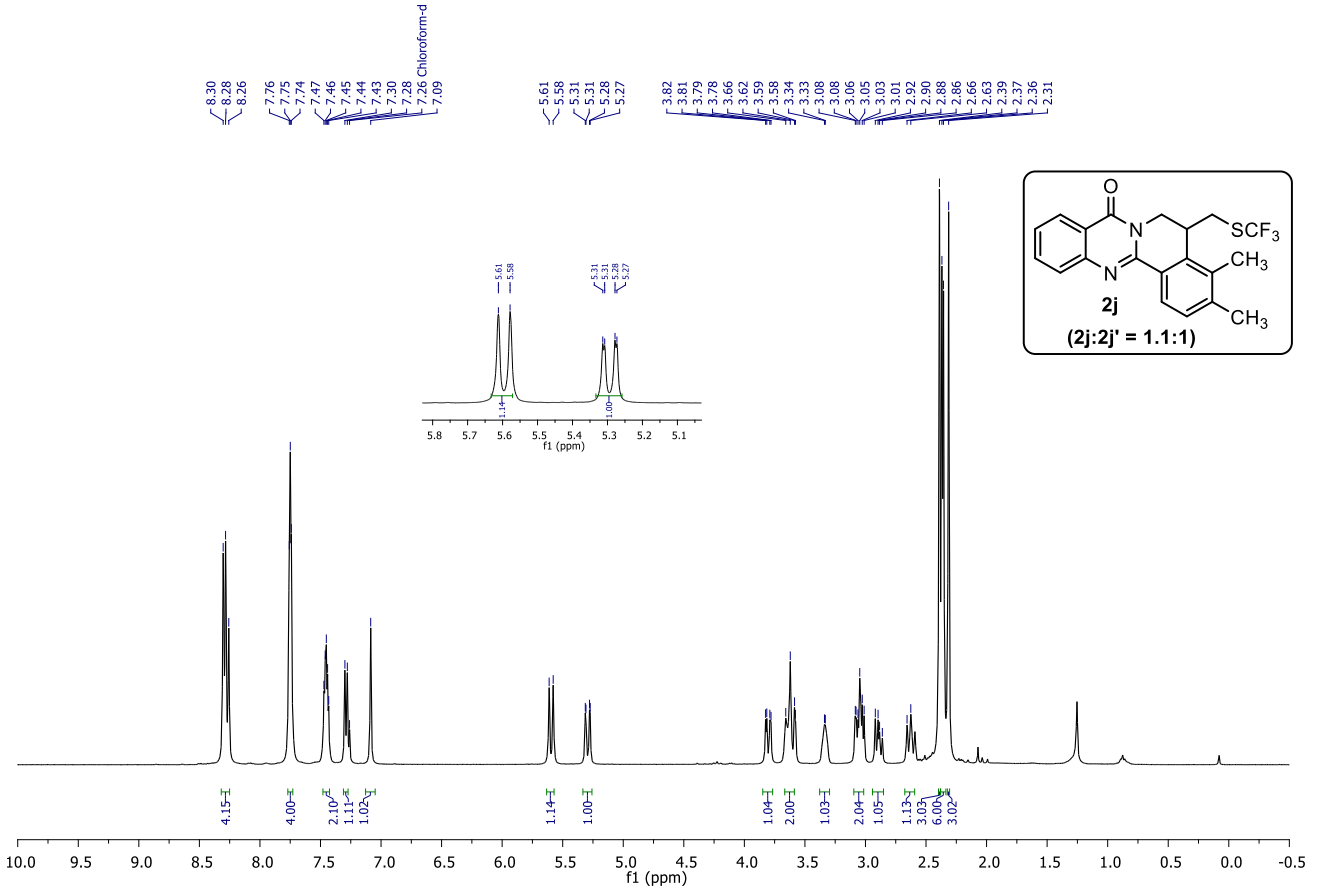
^{1}H NMR (400MHz, $CDCl_3$)

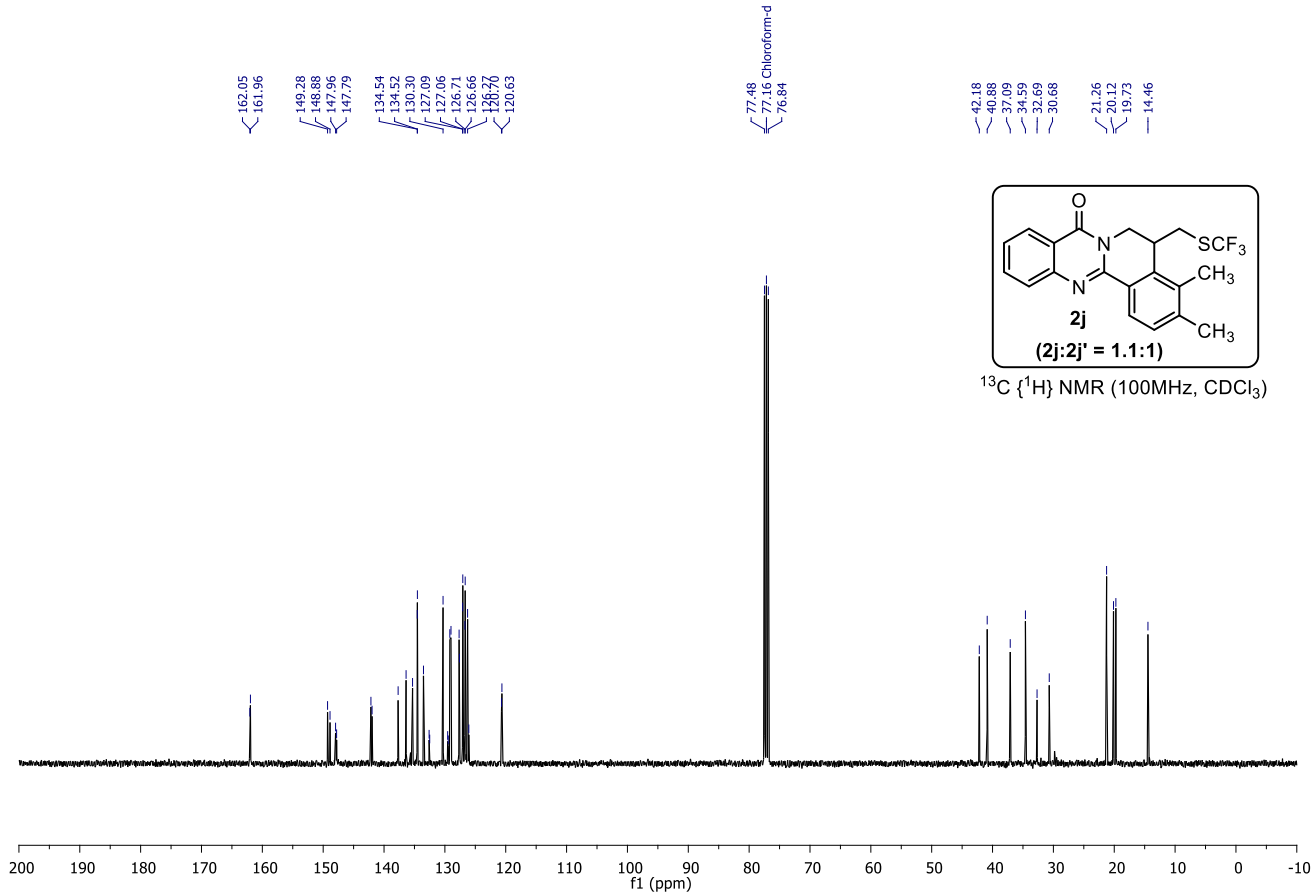


^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)





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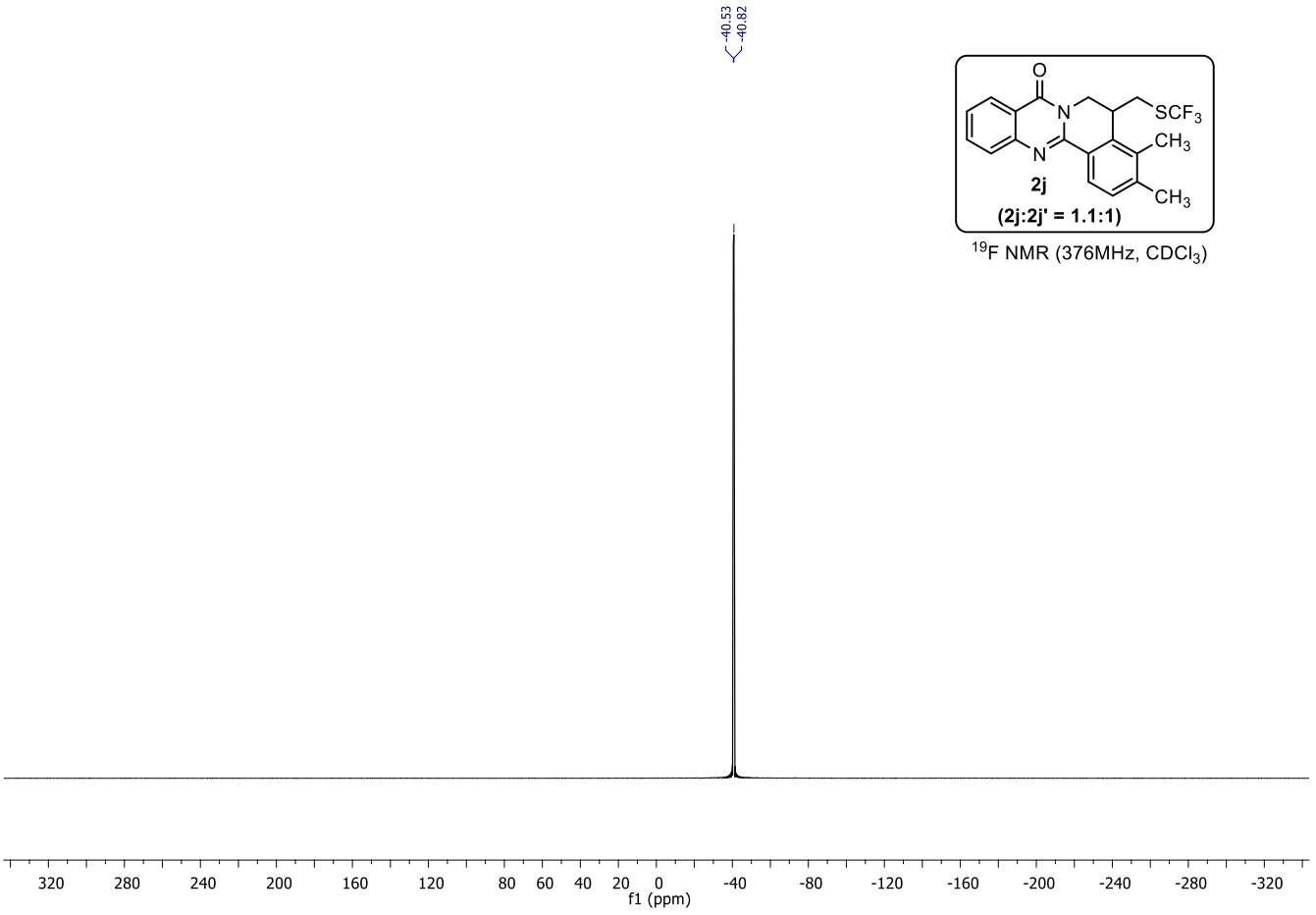
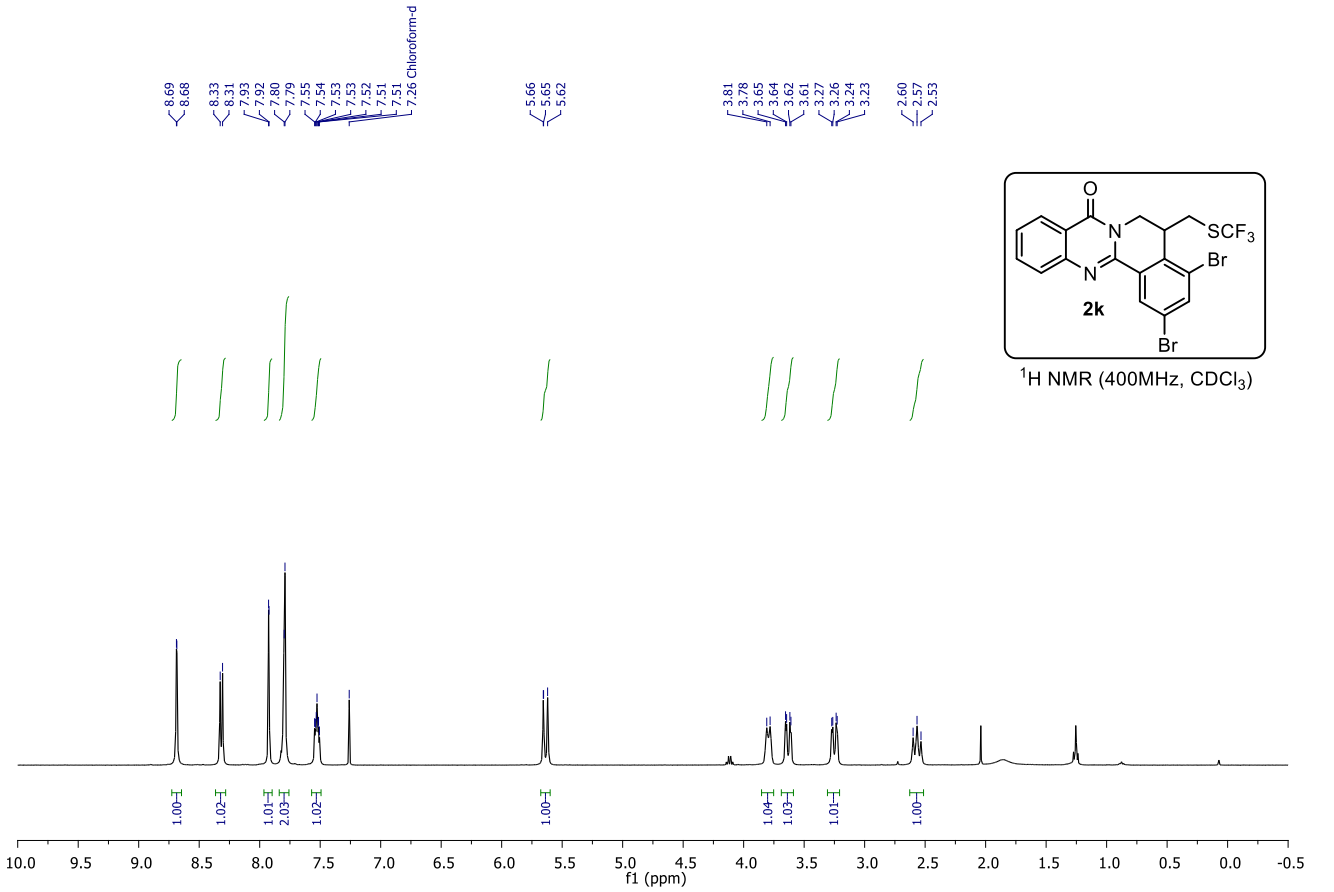
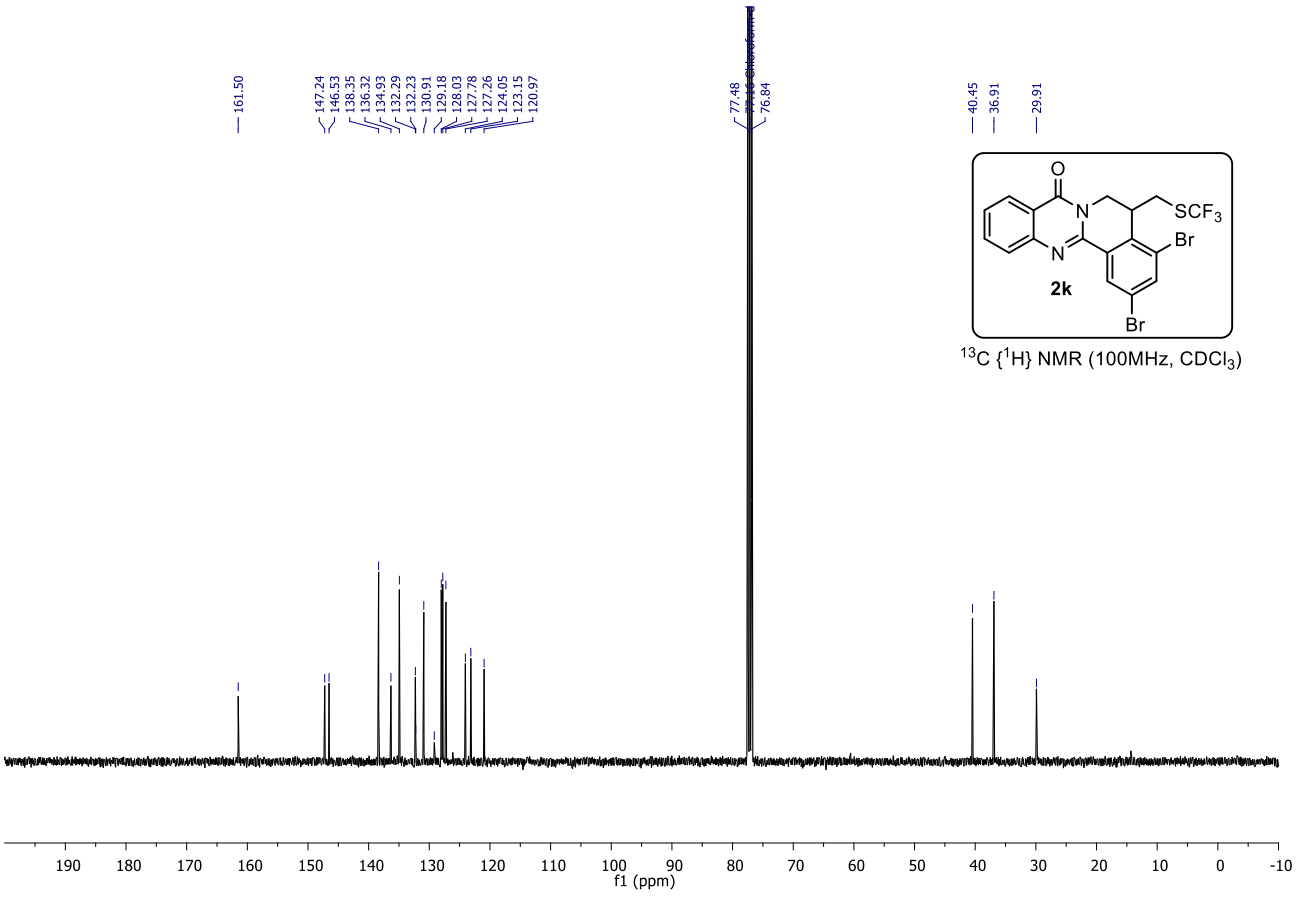


^{19}F NMR (376MHz, $CDCl_3$)



^{1}H NMR (400MHz, $CDCl_3$)



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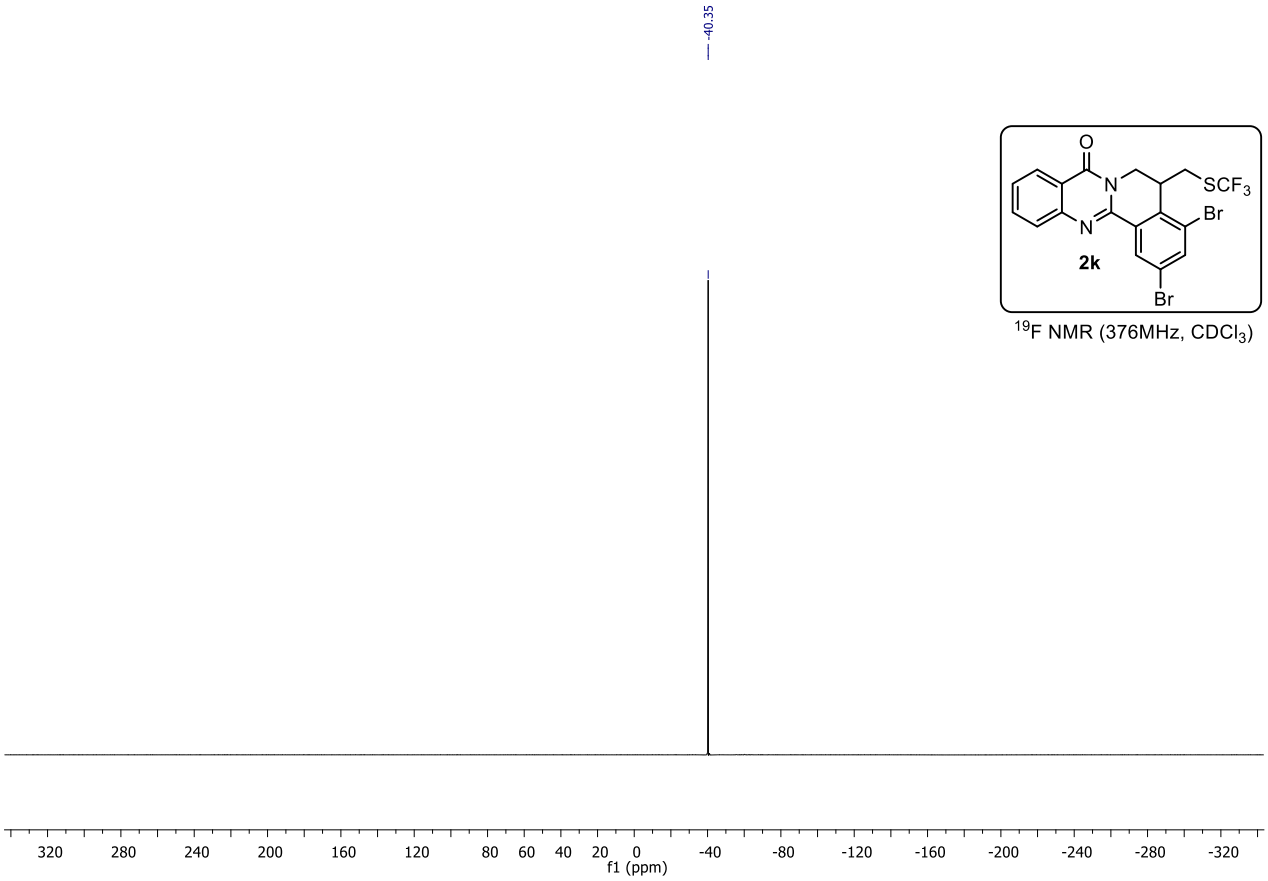
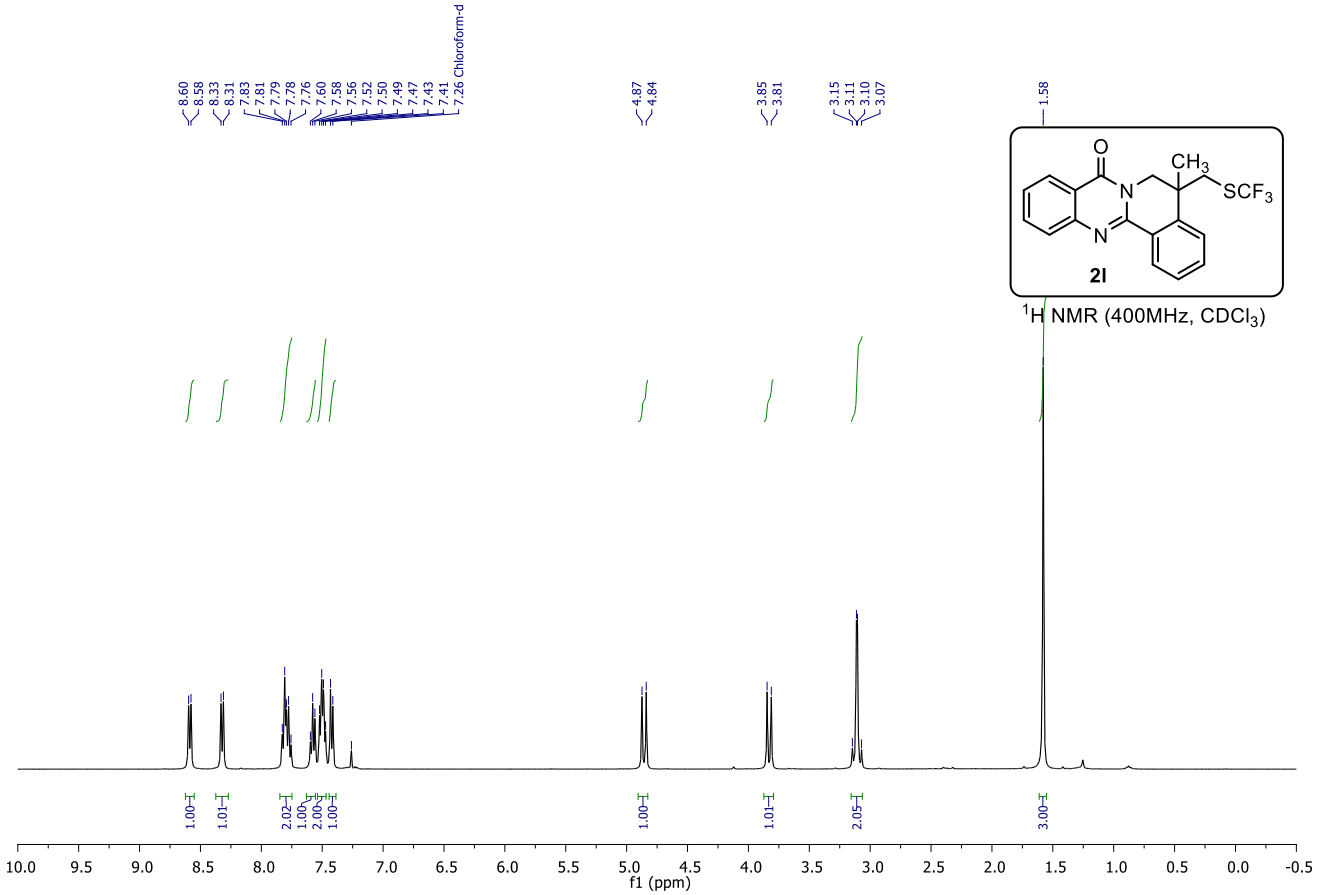
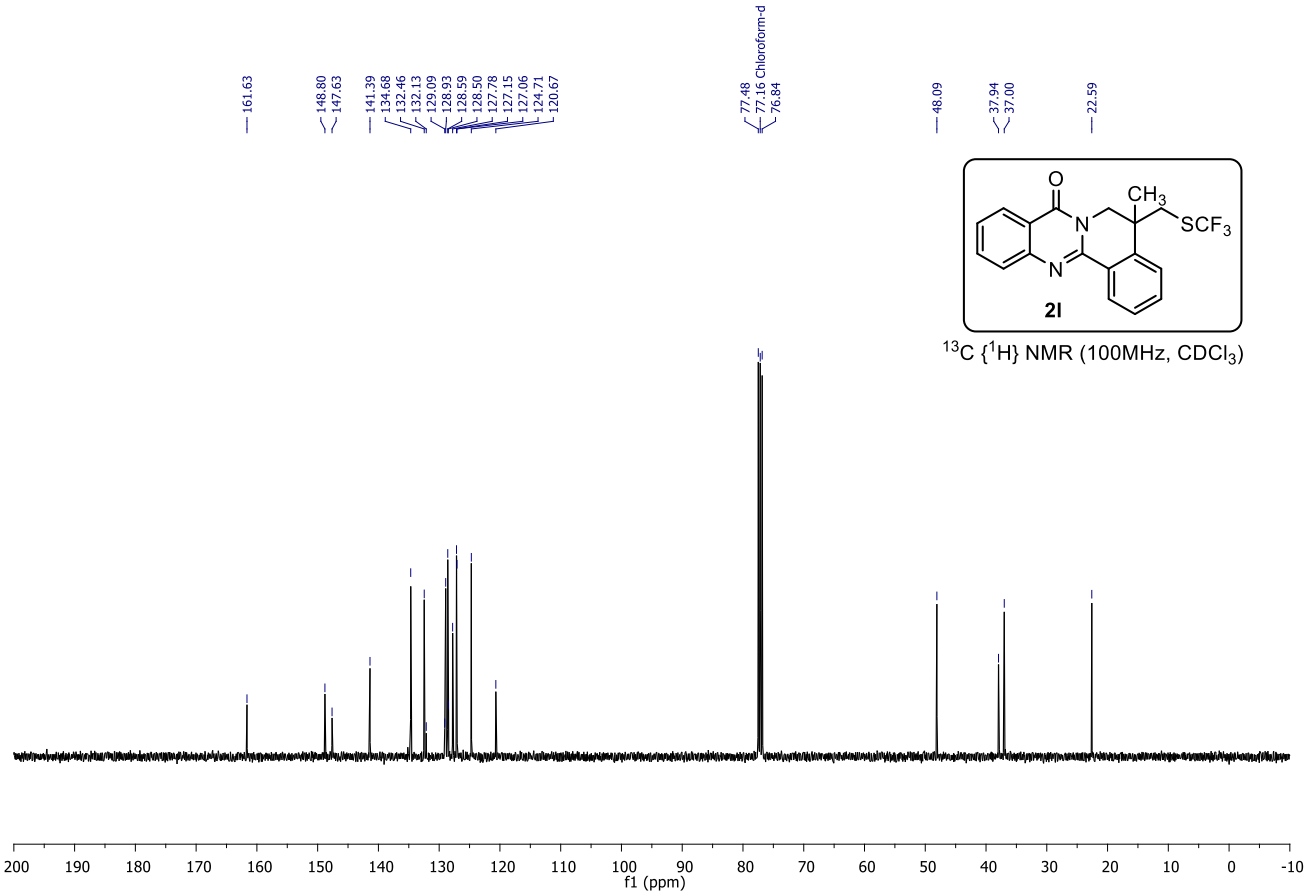


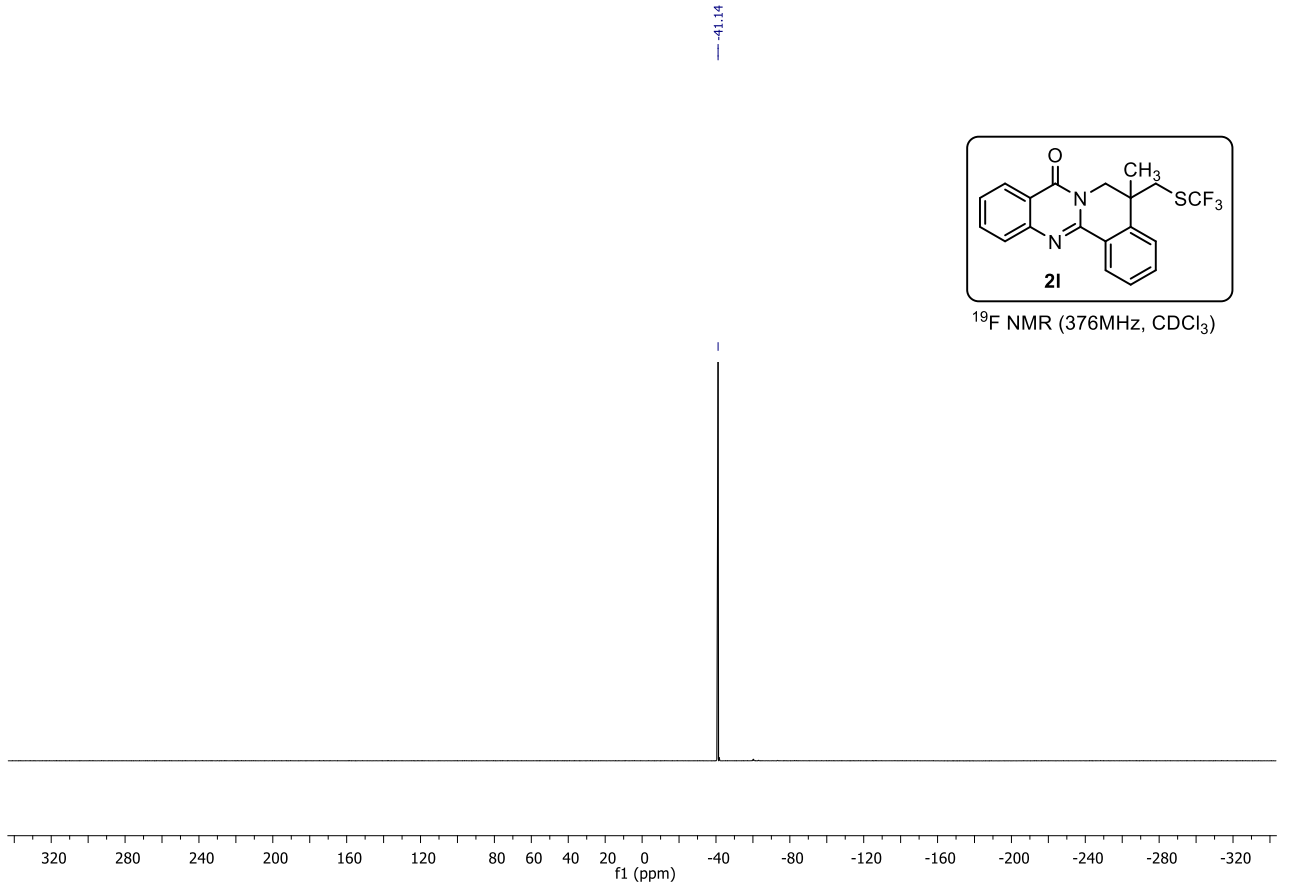
^{19}F NMR (376MHz, $CDCl_3$)



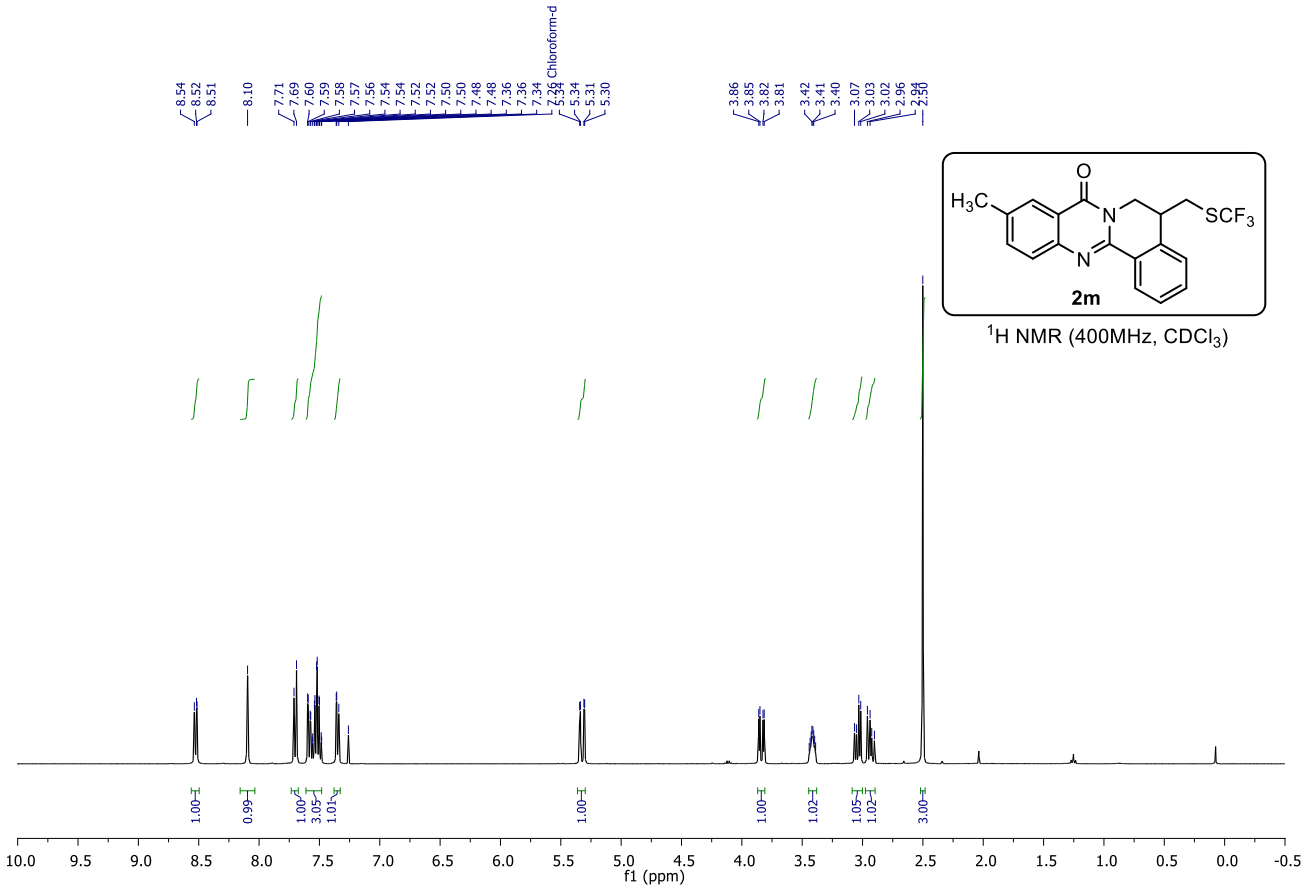
^{1}H NMR (400MHz, $CDCl_3$)

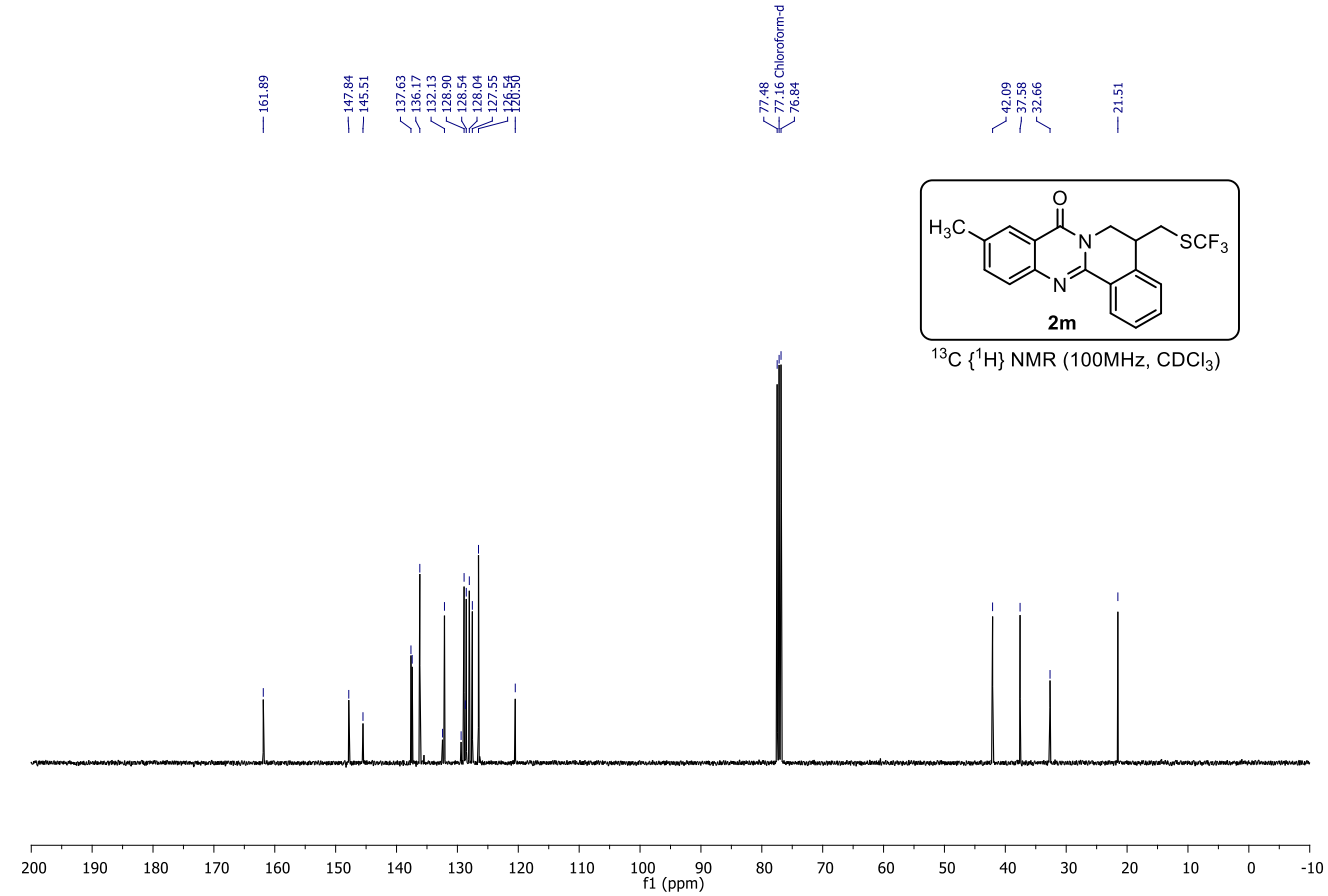


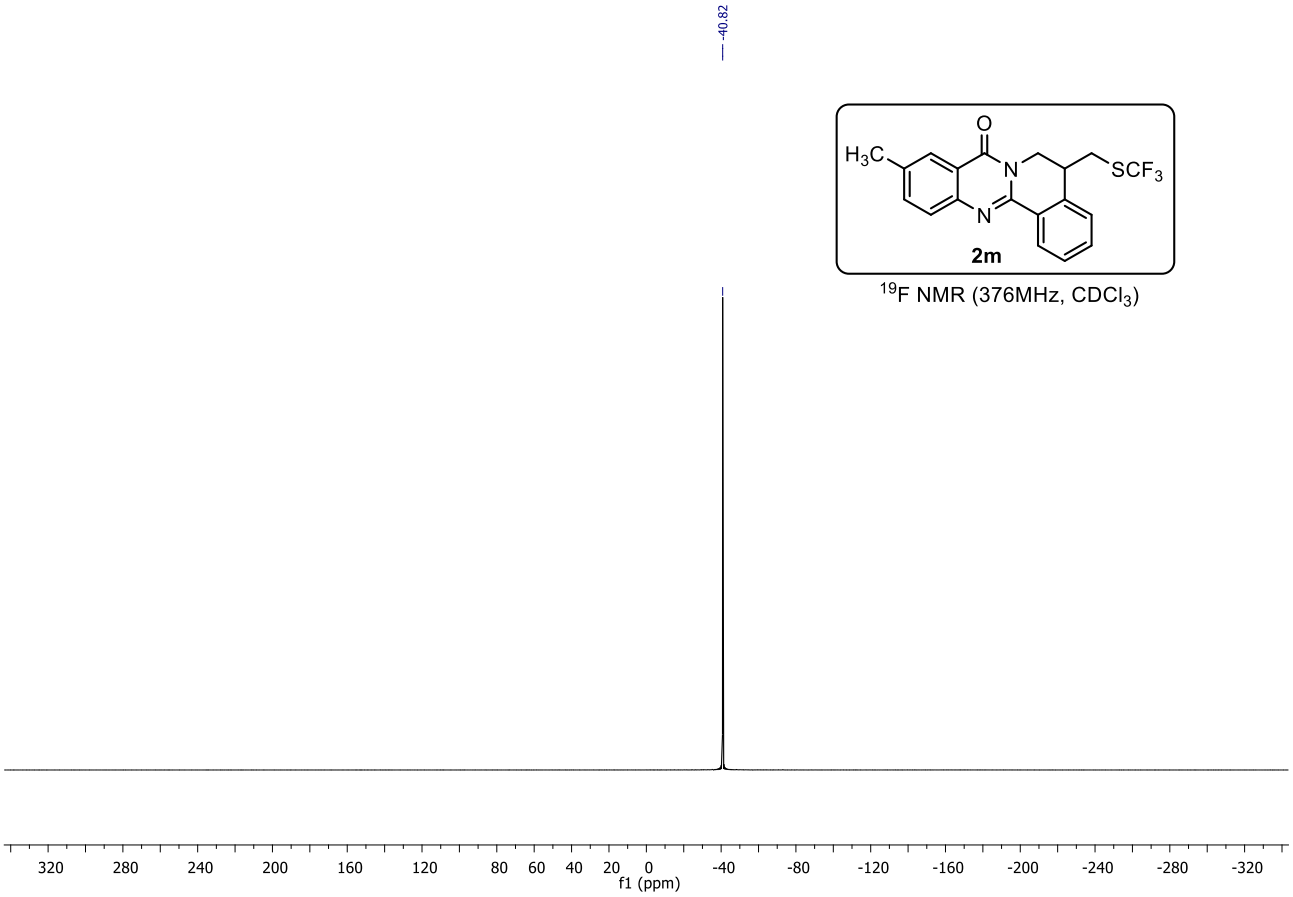
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



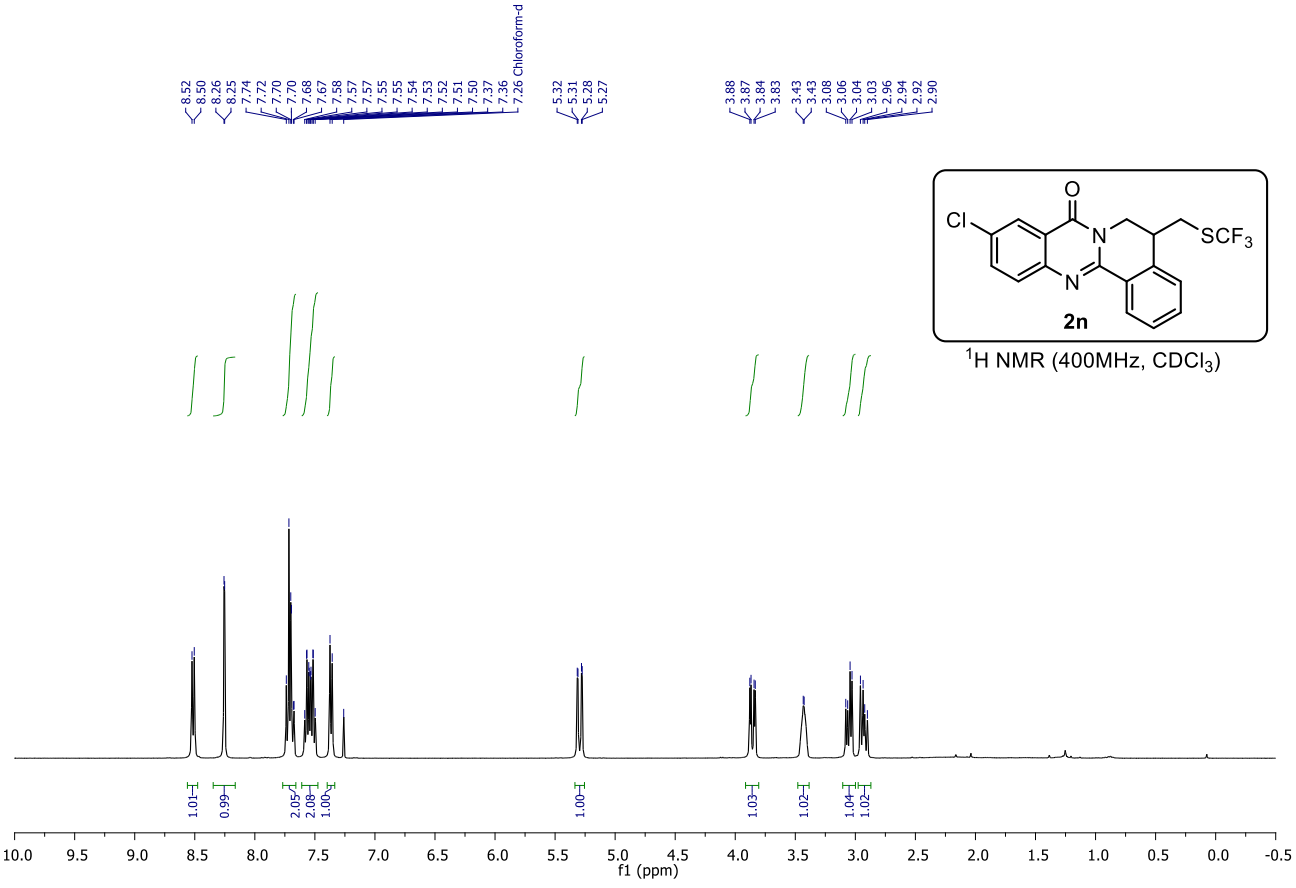
^{19}F NMR (376MHz, $CDCl_3$)


8.54
8.52
8.51
8.10
7.71
7.69
7.60
7.59
7.58
7.57
7.56
7.54
7.54
7.52
7.52
7.50
7.50
7.48
7.36
7.36
7.34
7.26 Chloroform-d
5.32
5.34
5.31
5.30
3.86
3.85
3.82
3.81
3.42
3.41
3.40
3.07
3.03
3.02
2.96
2.94
2.90
1.00
0.99
1.00
3.05
1.01
1.00
1.00
1.02
1.05
1.02
3.00
f1 (ppm)
2m
^{1}H NMR (400MHz, $CDCl_3$)

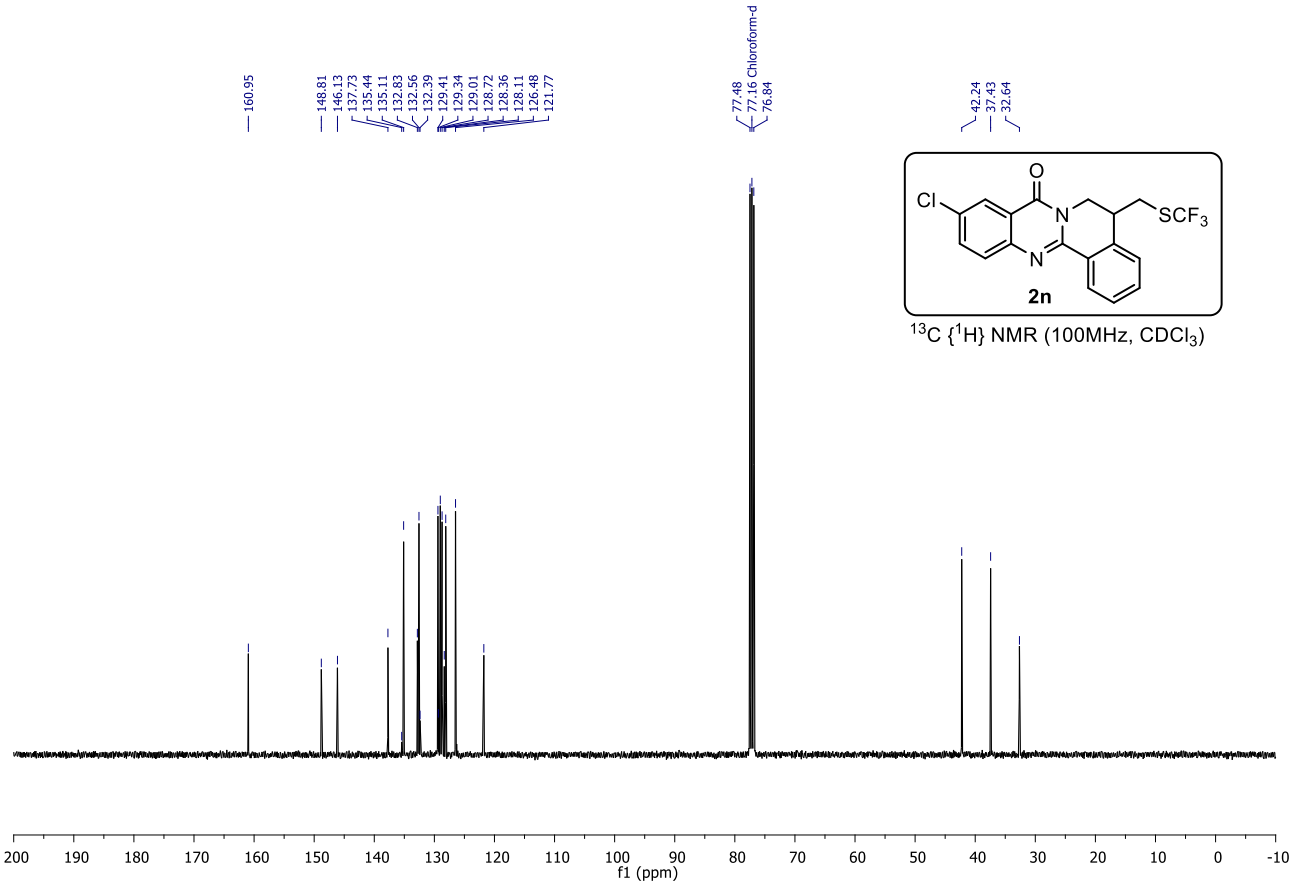

161.89
147.84
145.51
137.63
136.17
132.13
128.90
128.54
128.04
127.55
126.54
120.50
77.48
77.16 Chloroform-d
76.84
42.09
37.58
32.66
21.51
f1 (ppm)
2m
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



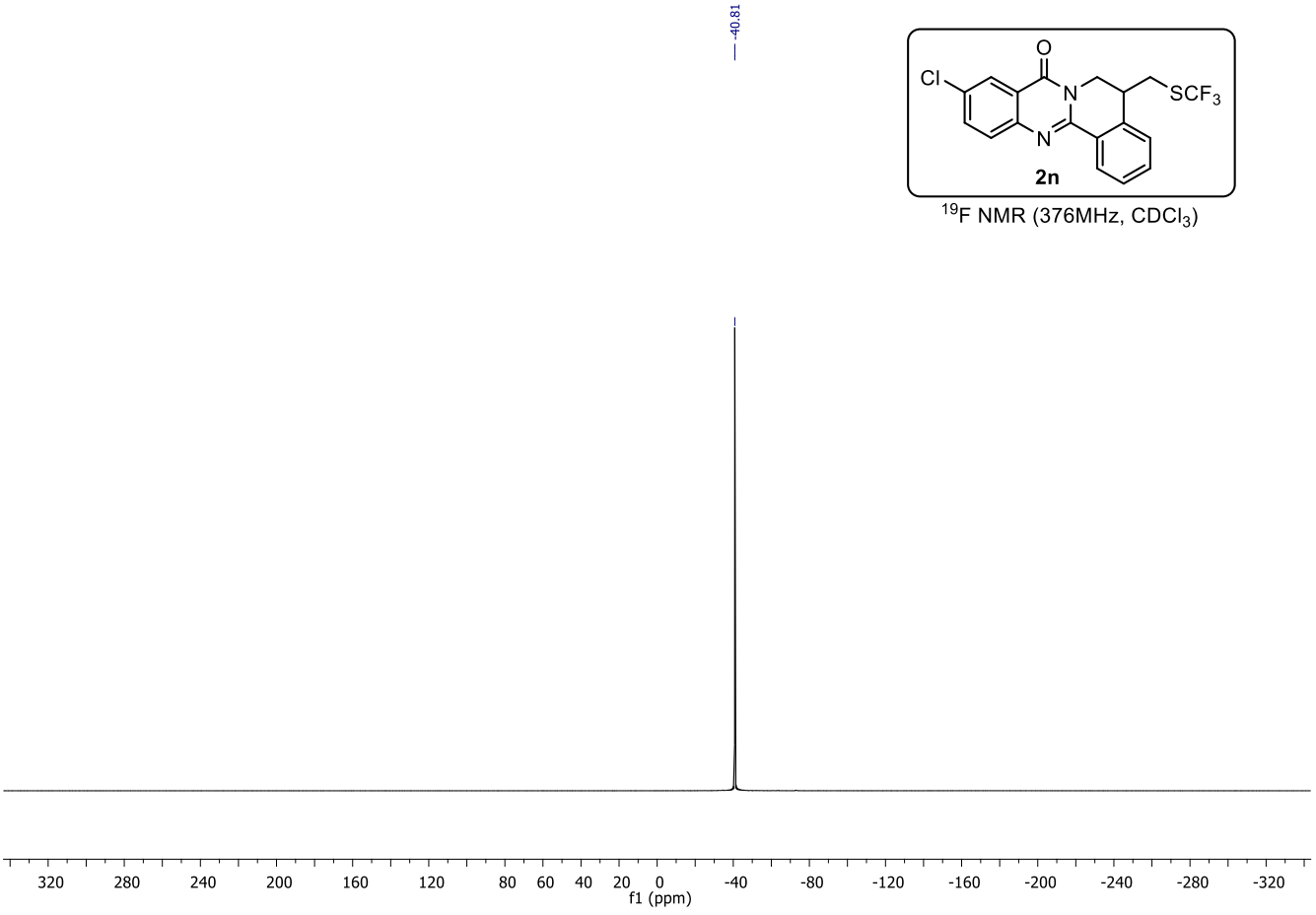
^{19}F NMR (376MHz, $CDCl_3$)



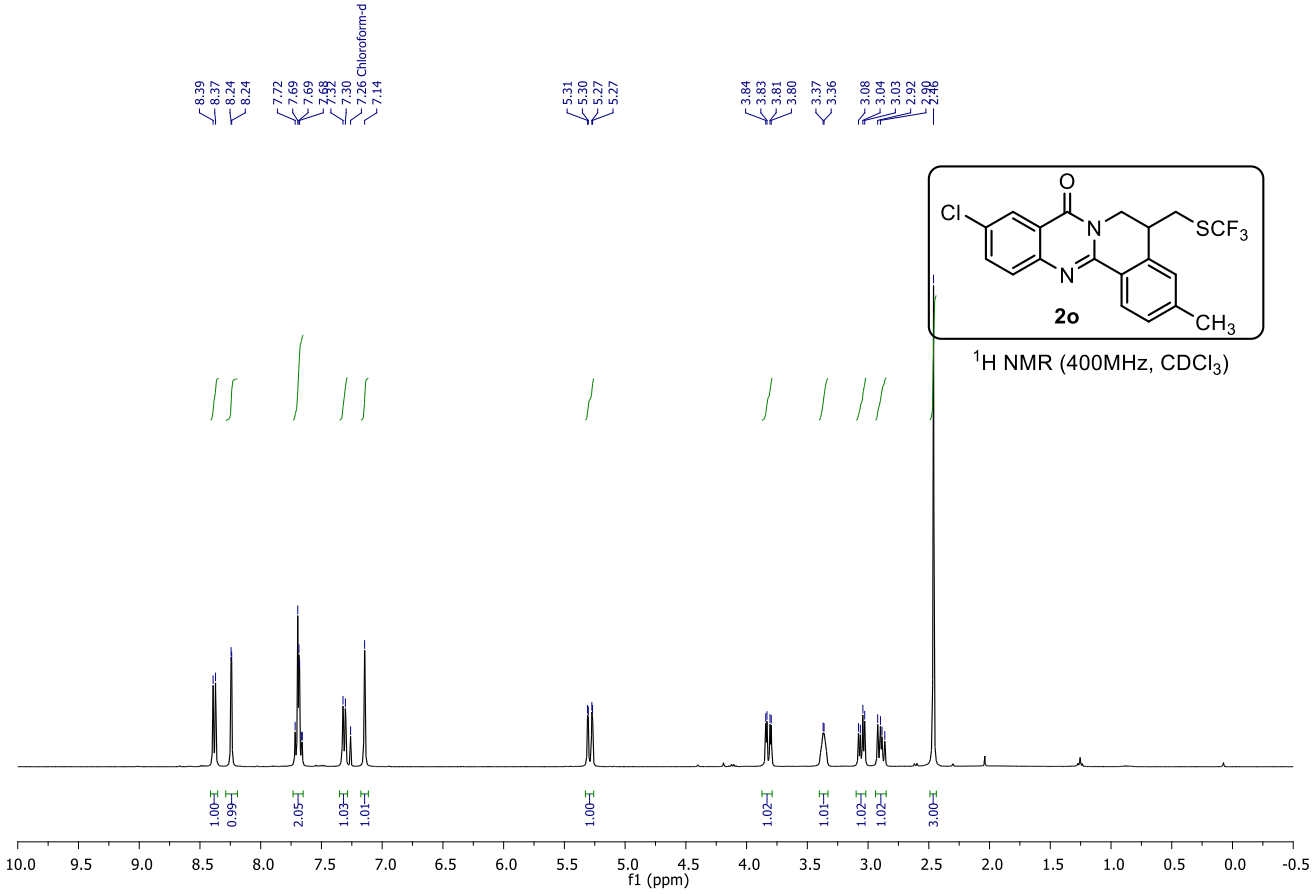
^{1}H NMR (400MHz, $CDCl_3$)



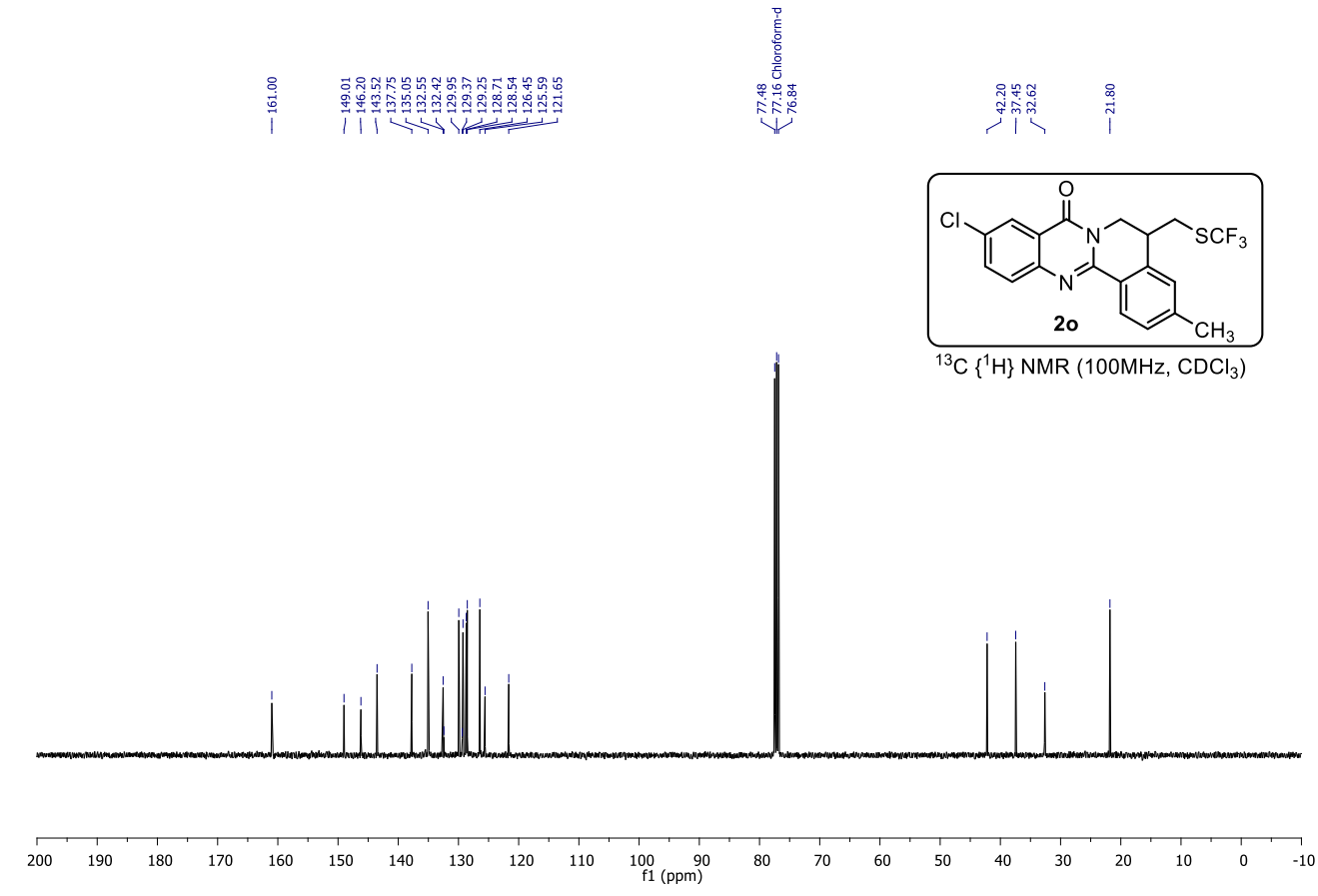
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



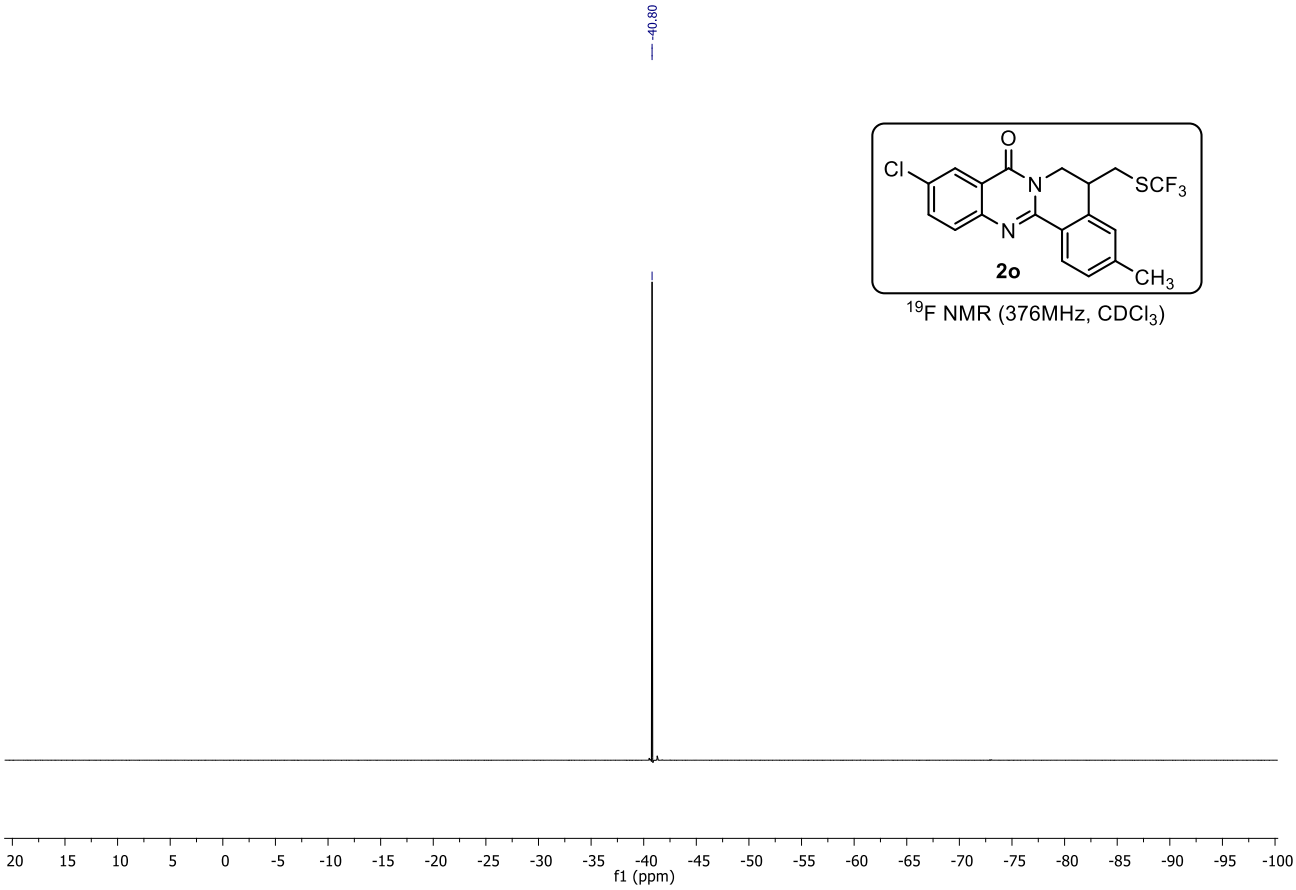
^{19}F NMR (376MHz, $CDCl_3$)



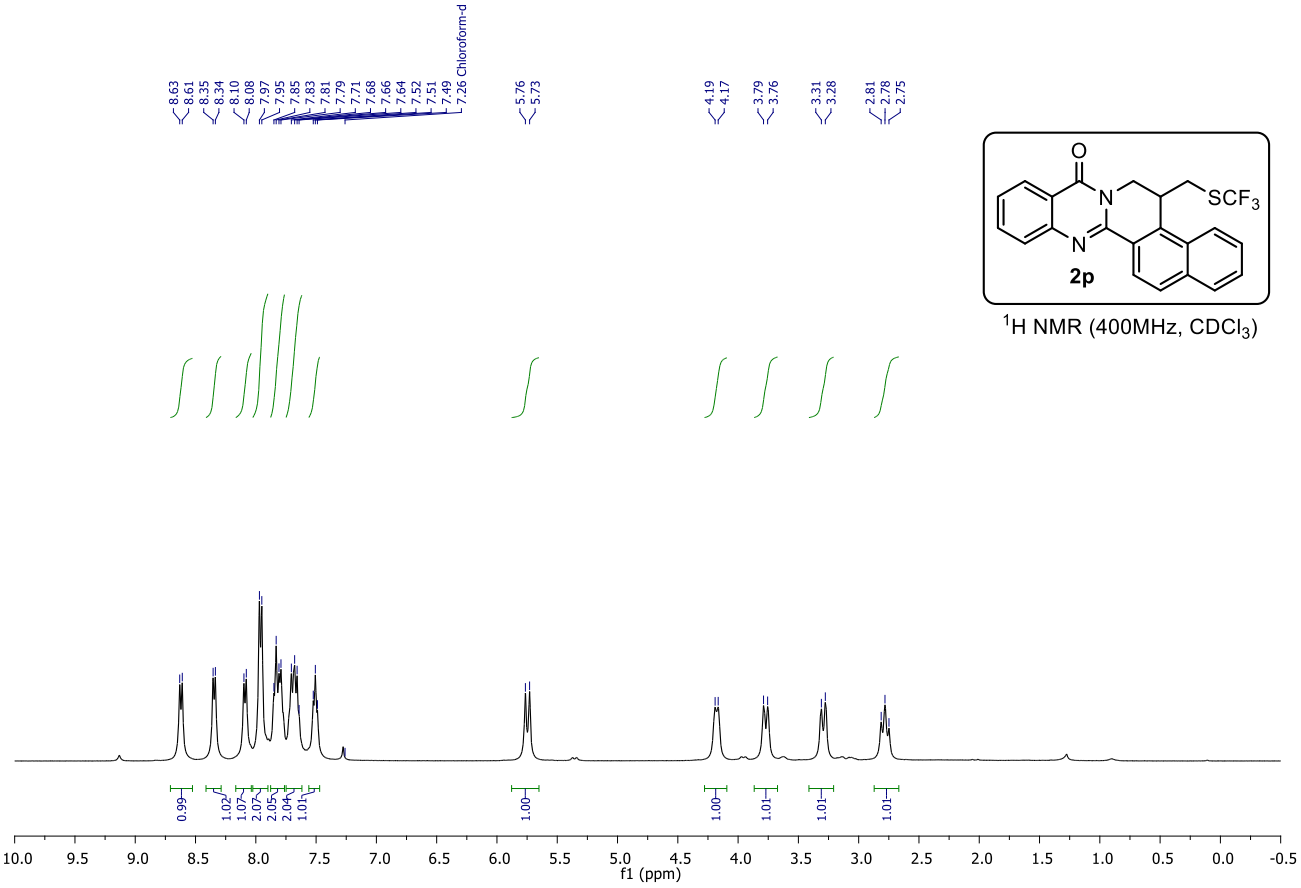
^{1}H NMR (400MHz, $CDCl_3$)



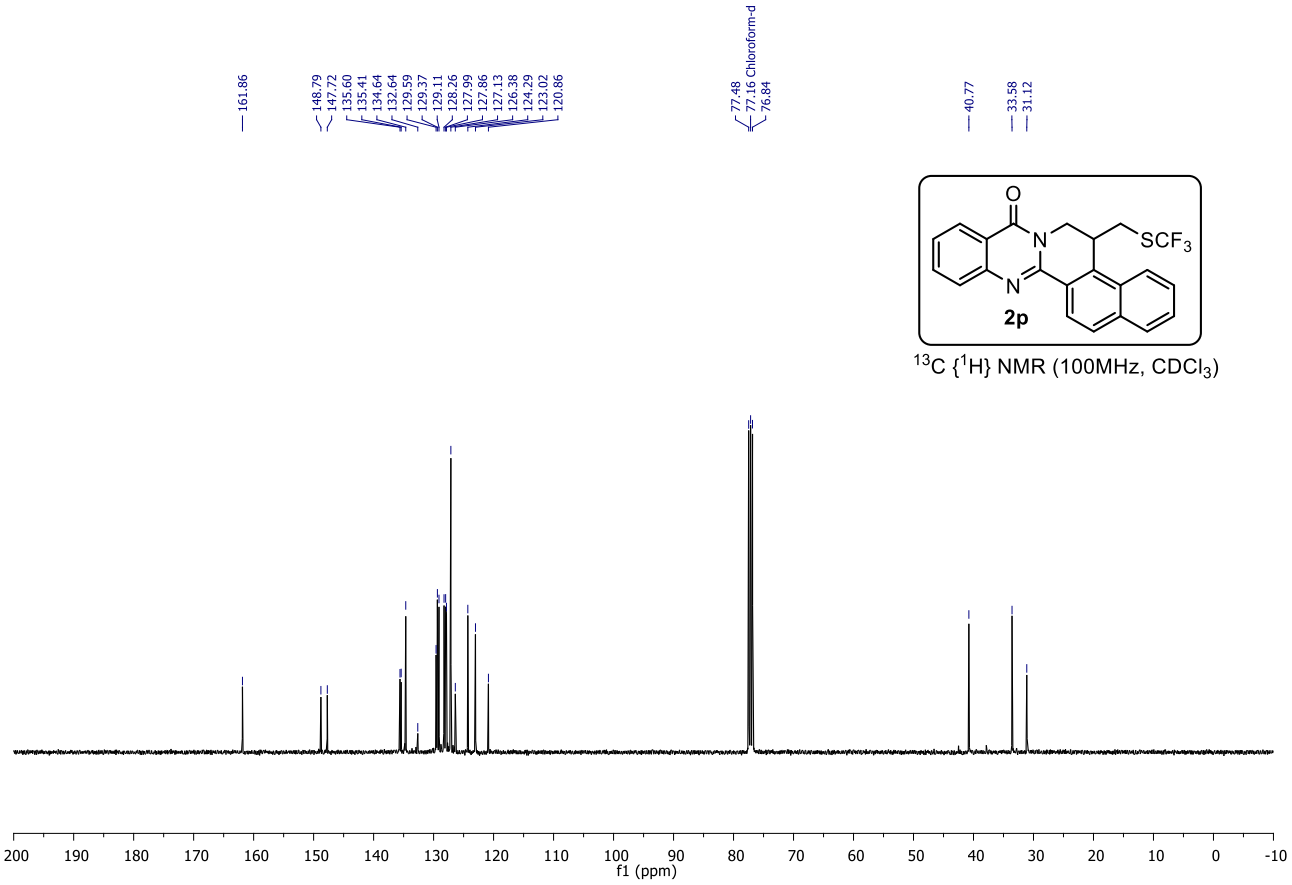
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



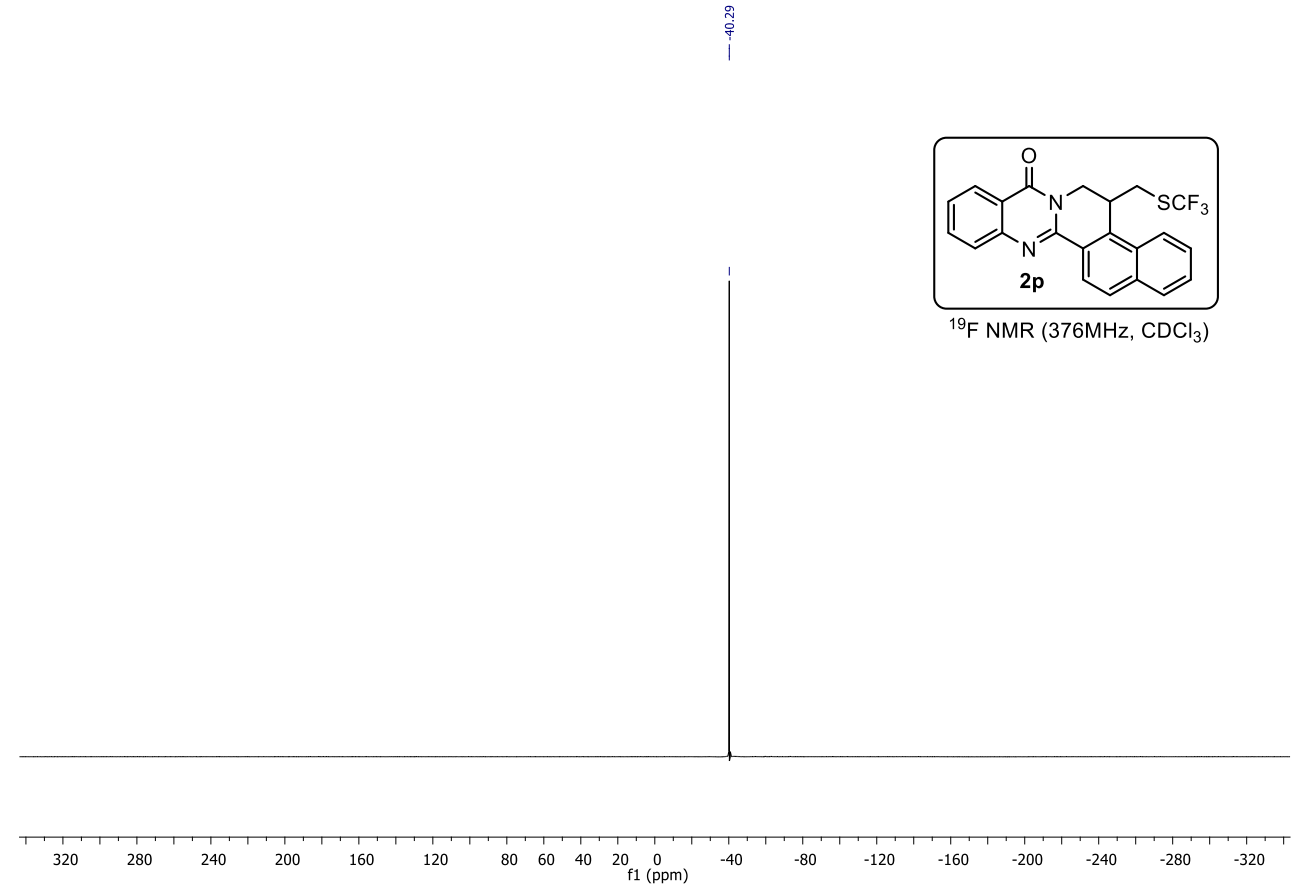
^{19}F NMR (376MHz, $CDCl_3$)



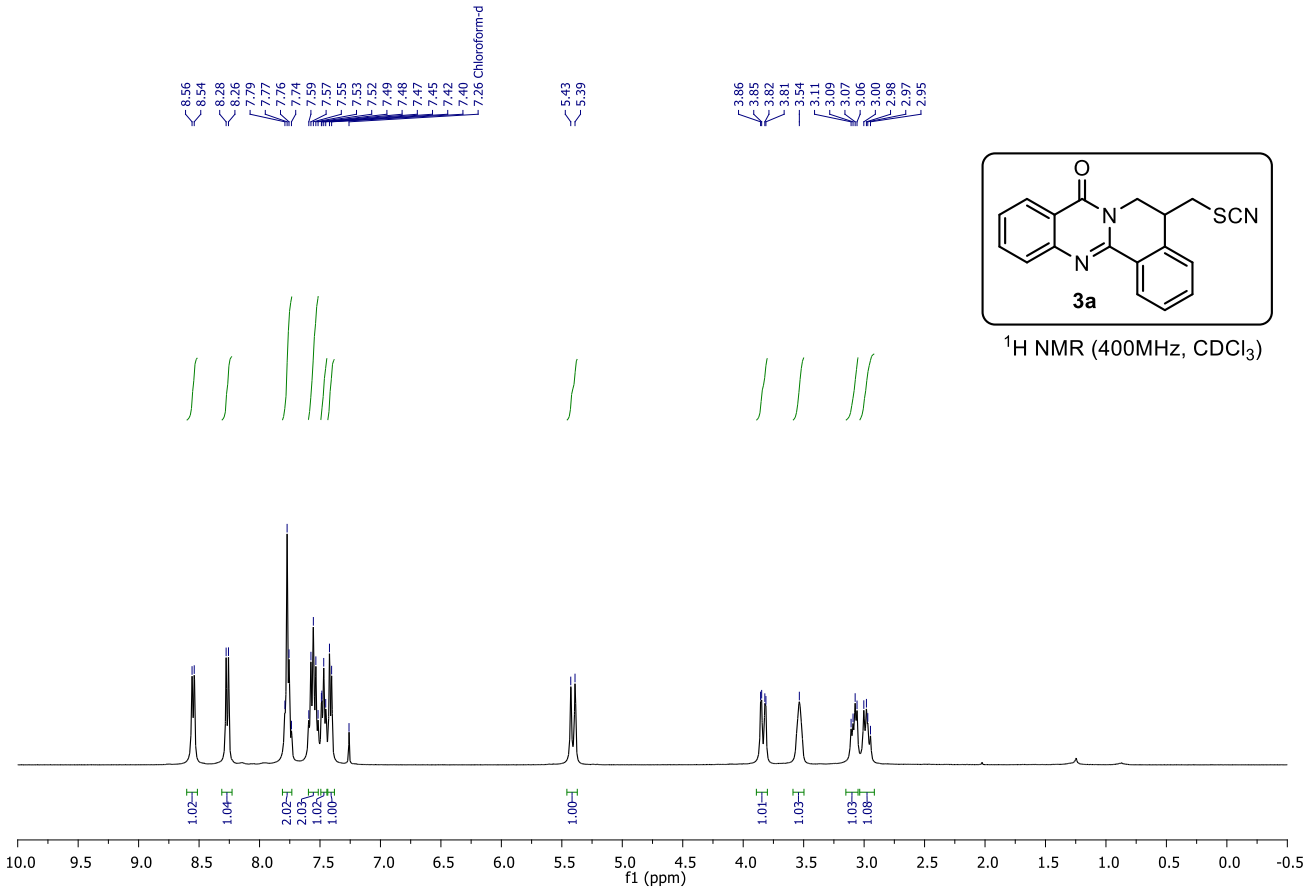
^{1}H NMR (400MHz, $CDCl_3$)



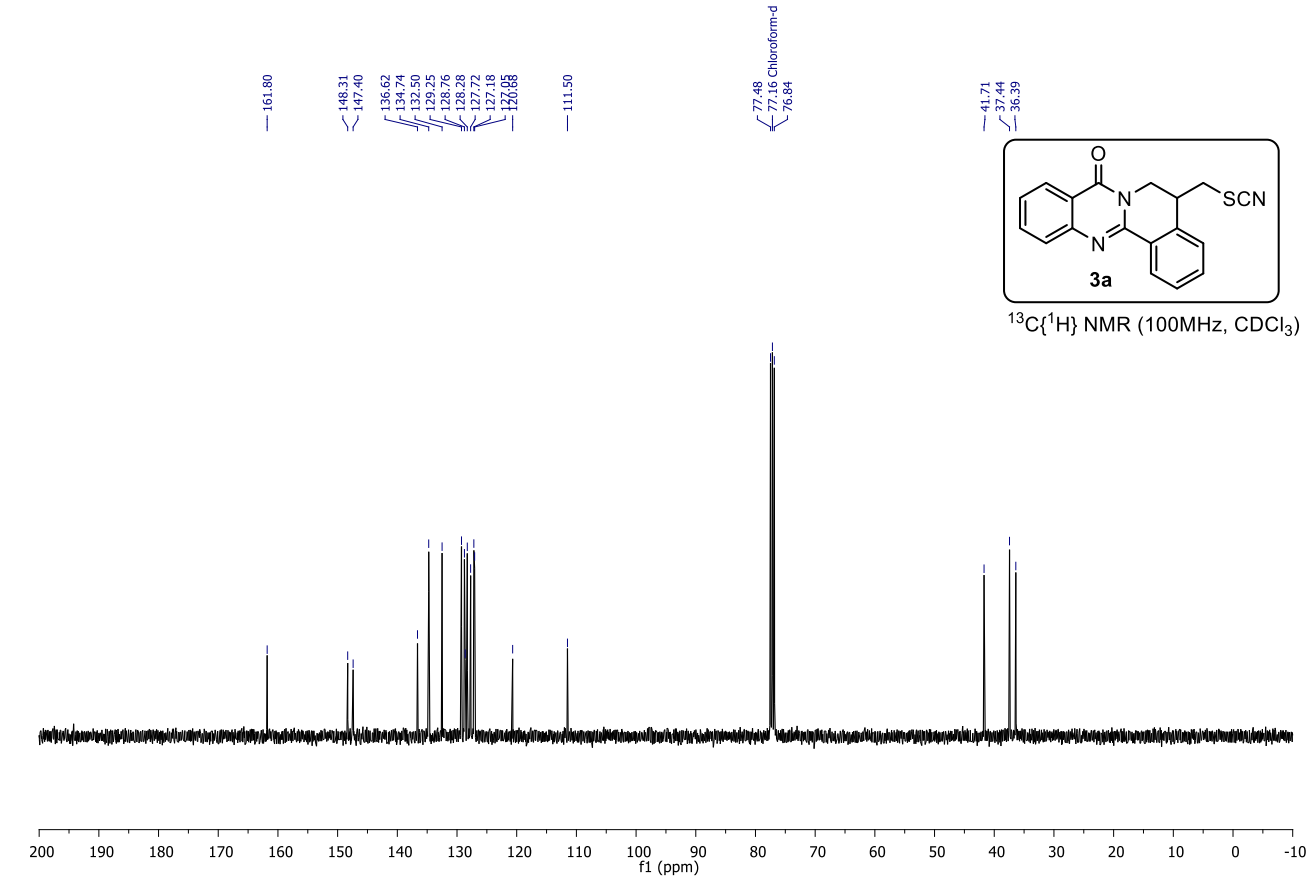
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



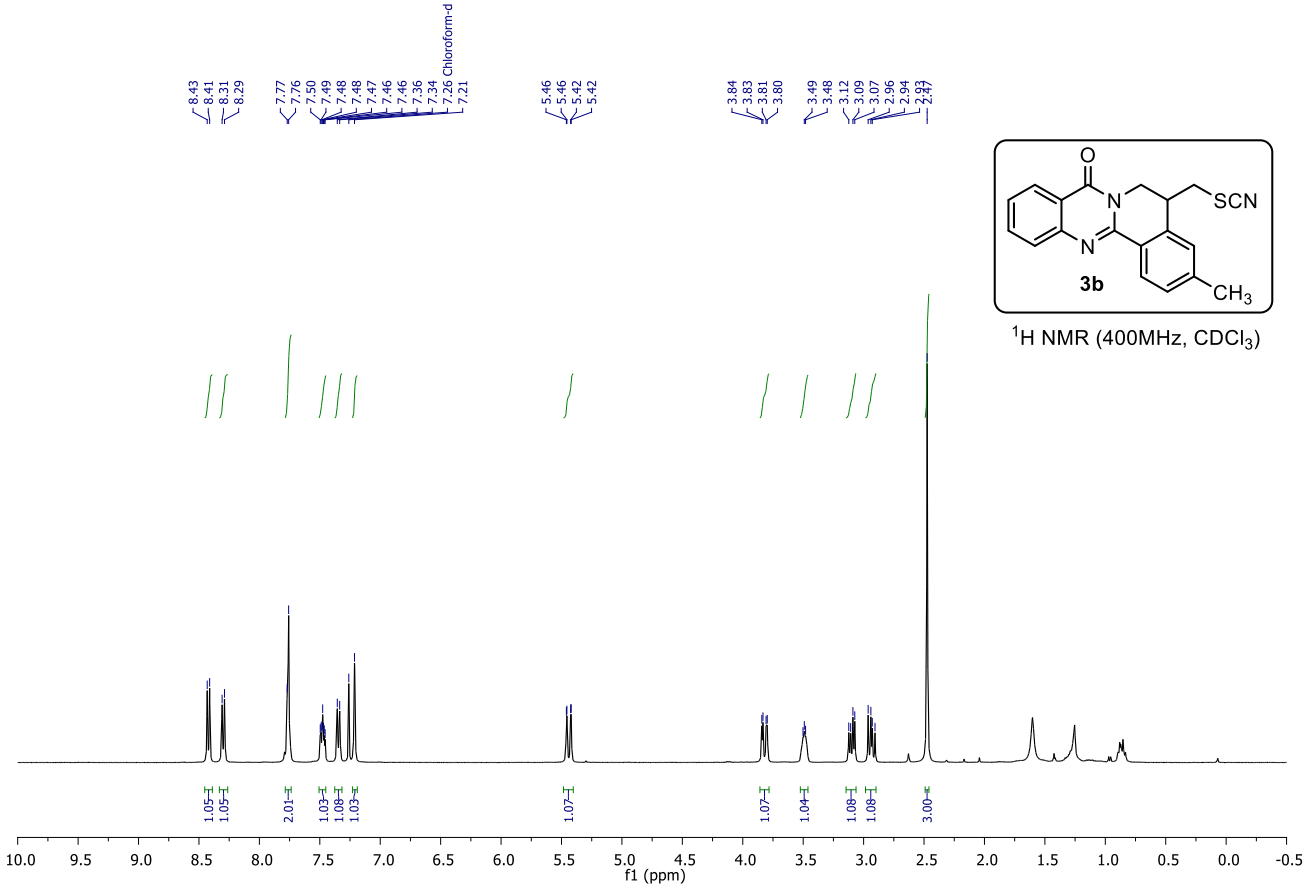
^{19}F NMR (376MHz, $CDCl_3$)



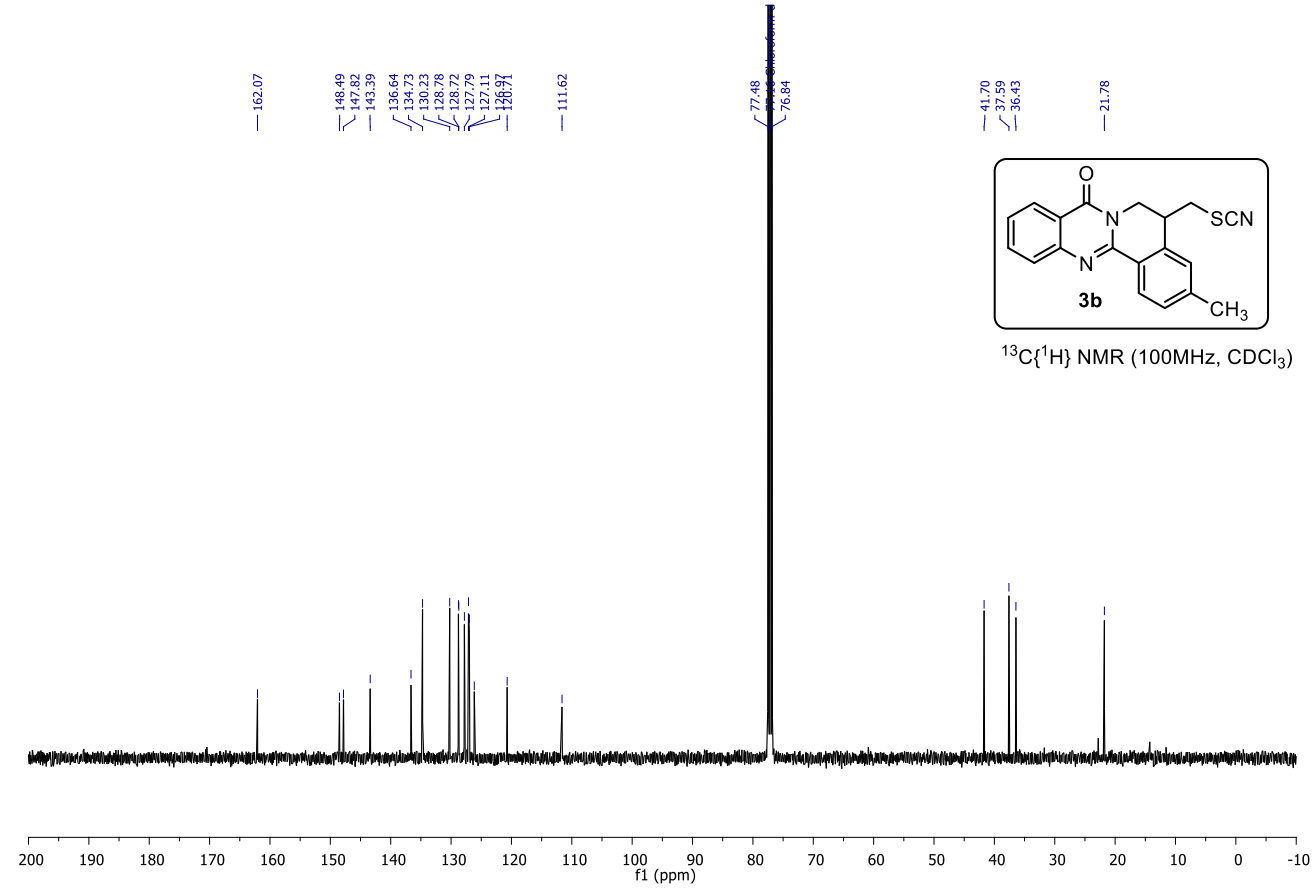
^{1}H NMR (400MHz, $CDCl_3$)



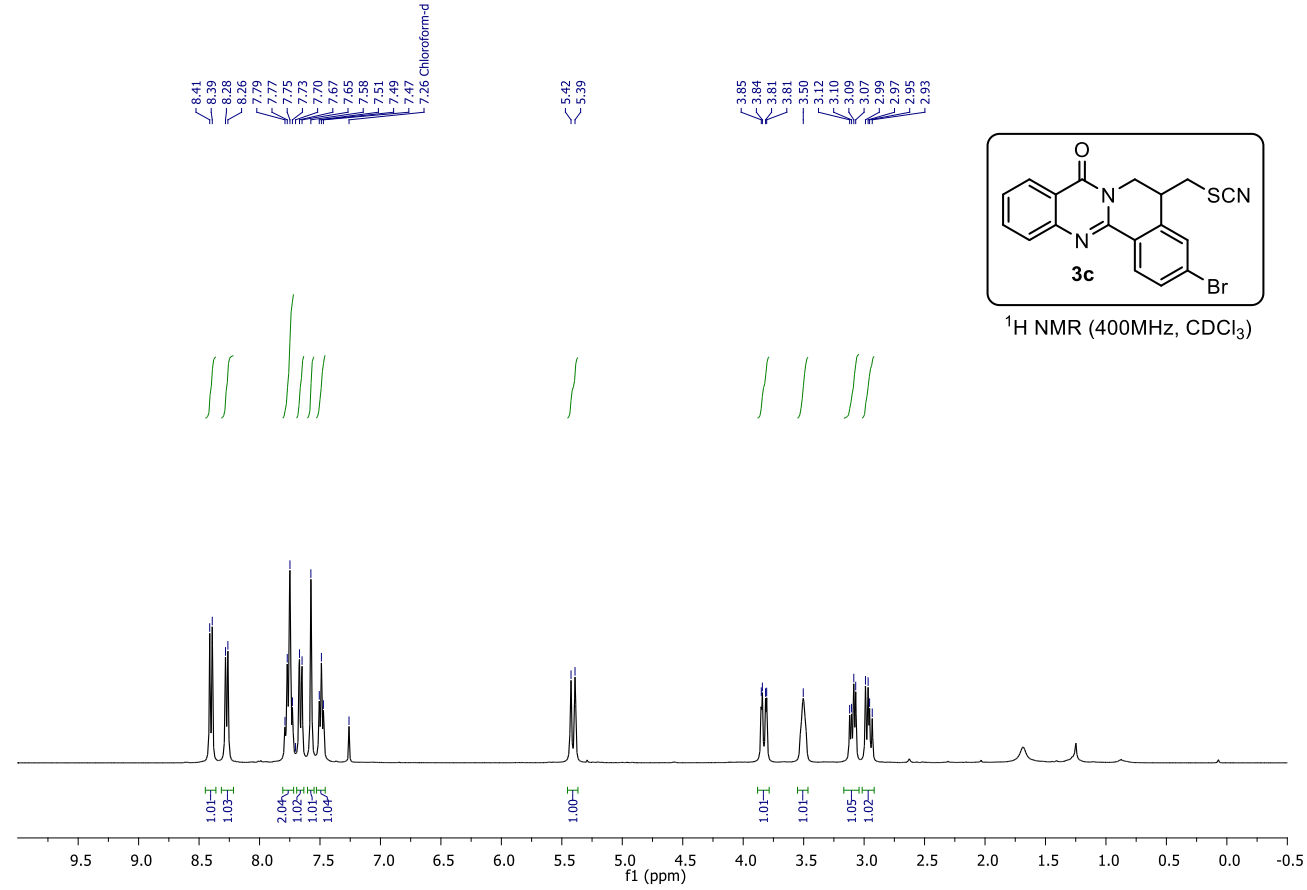
$^{13}C\{^{1}H\}$ NMR (100MHz, $CDCl_3$)



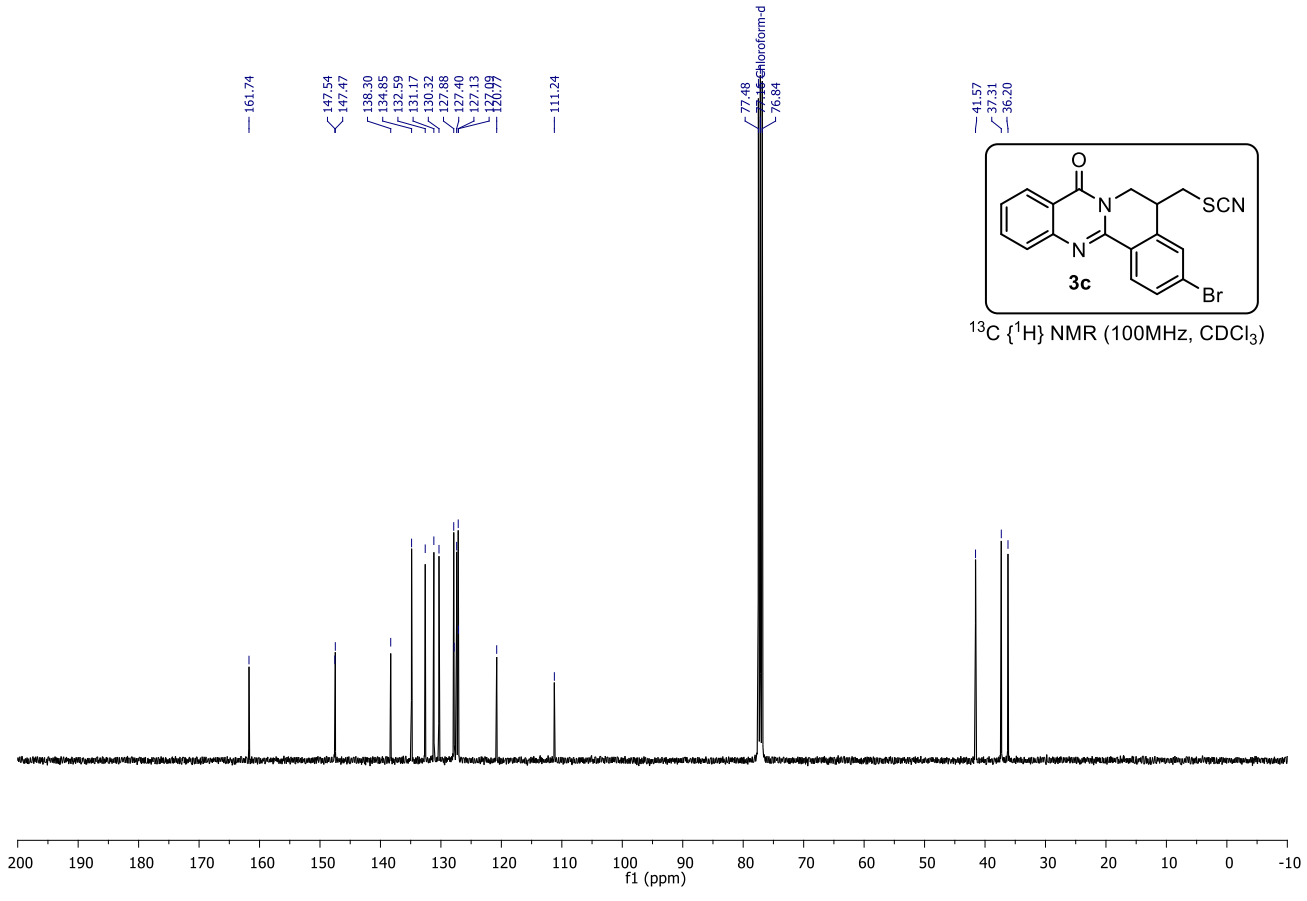
^{1}H NMR (400MHz, $CDCl_3$)



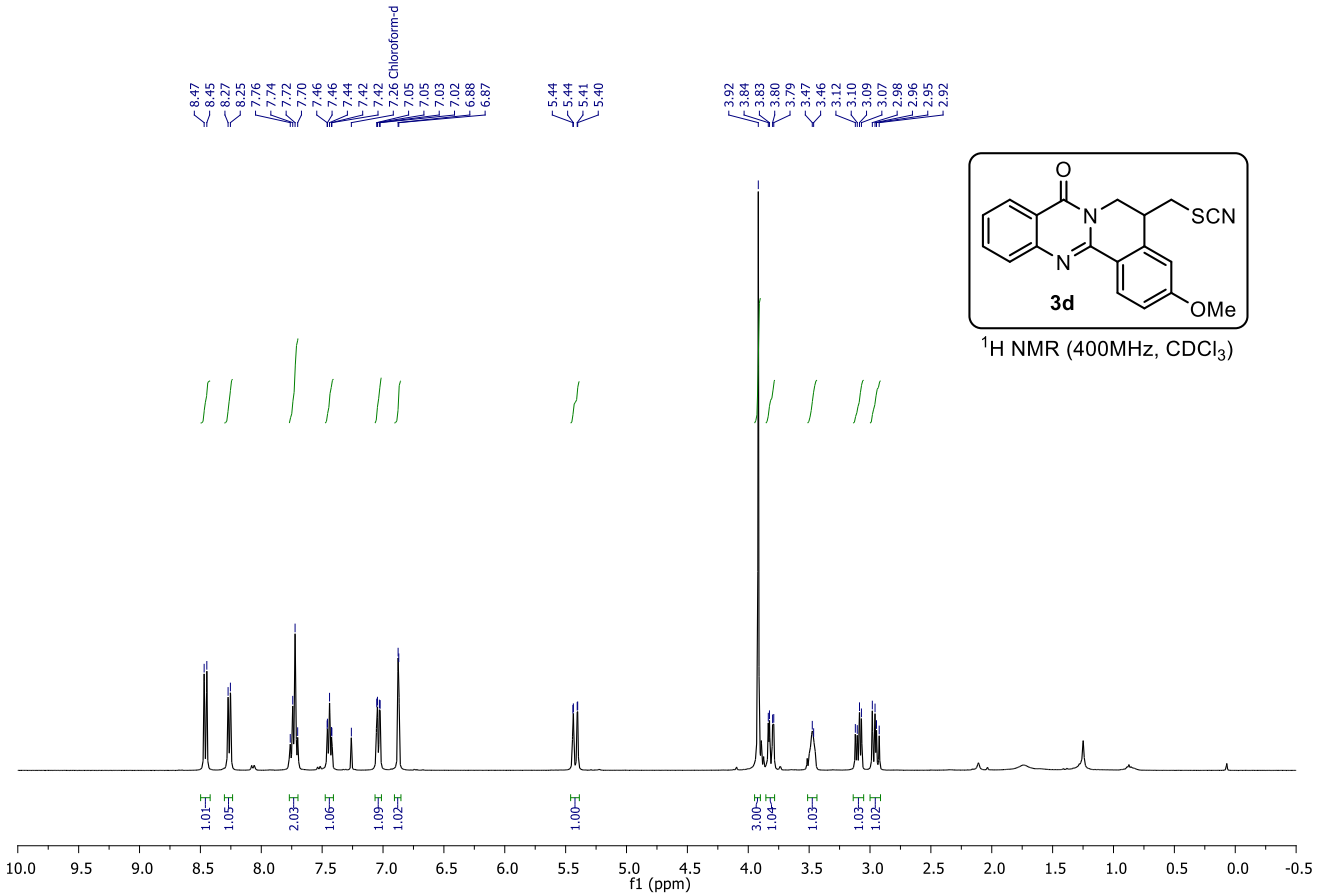
$^{13}C\{^{1}H\}$ NMR (100MHz, $CDCl_3$)



^{1}H NMR (400MHz, $CDCl_3$)



^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



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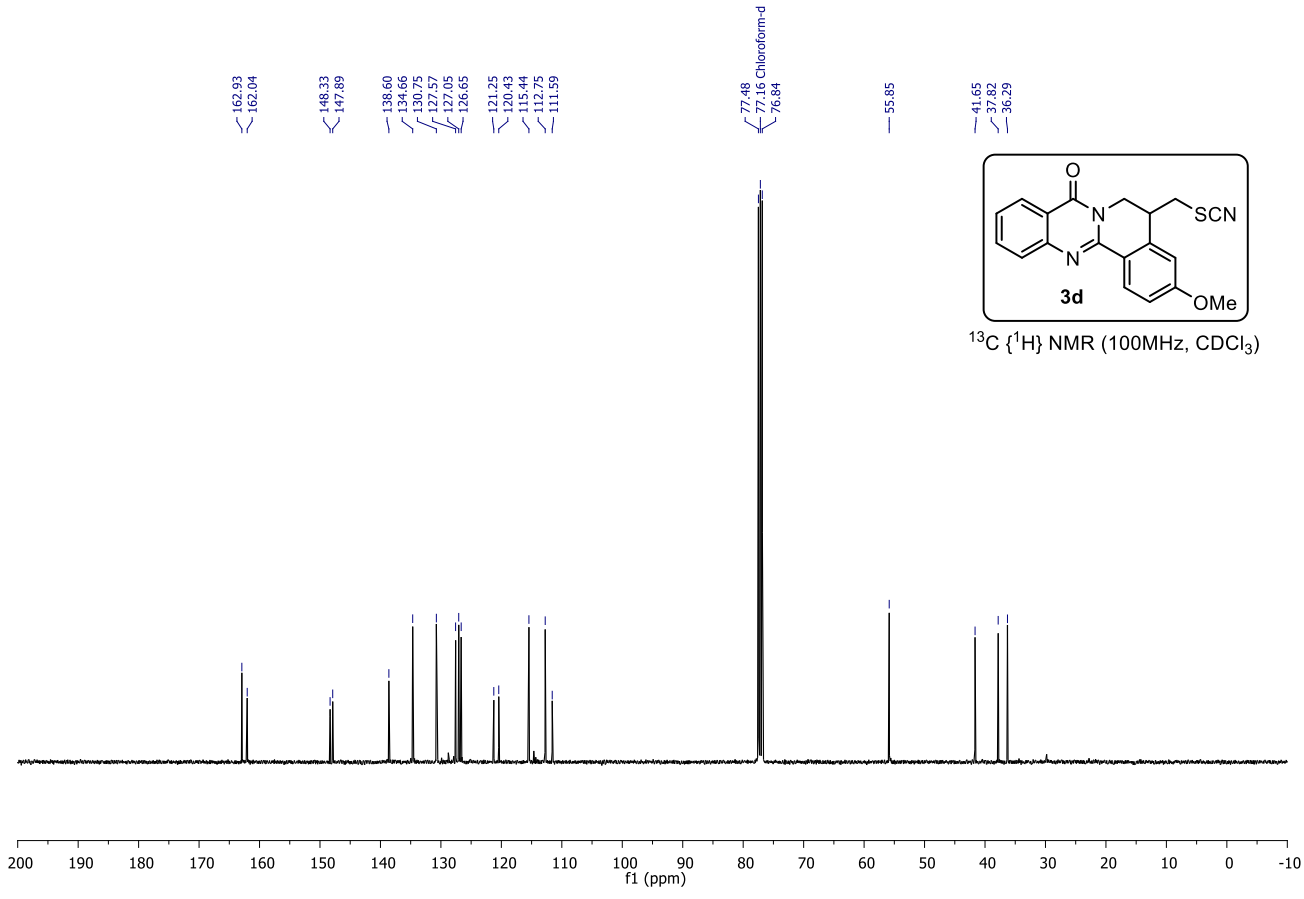
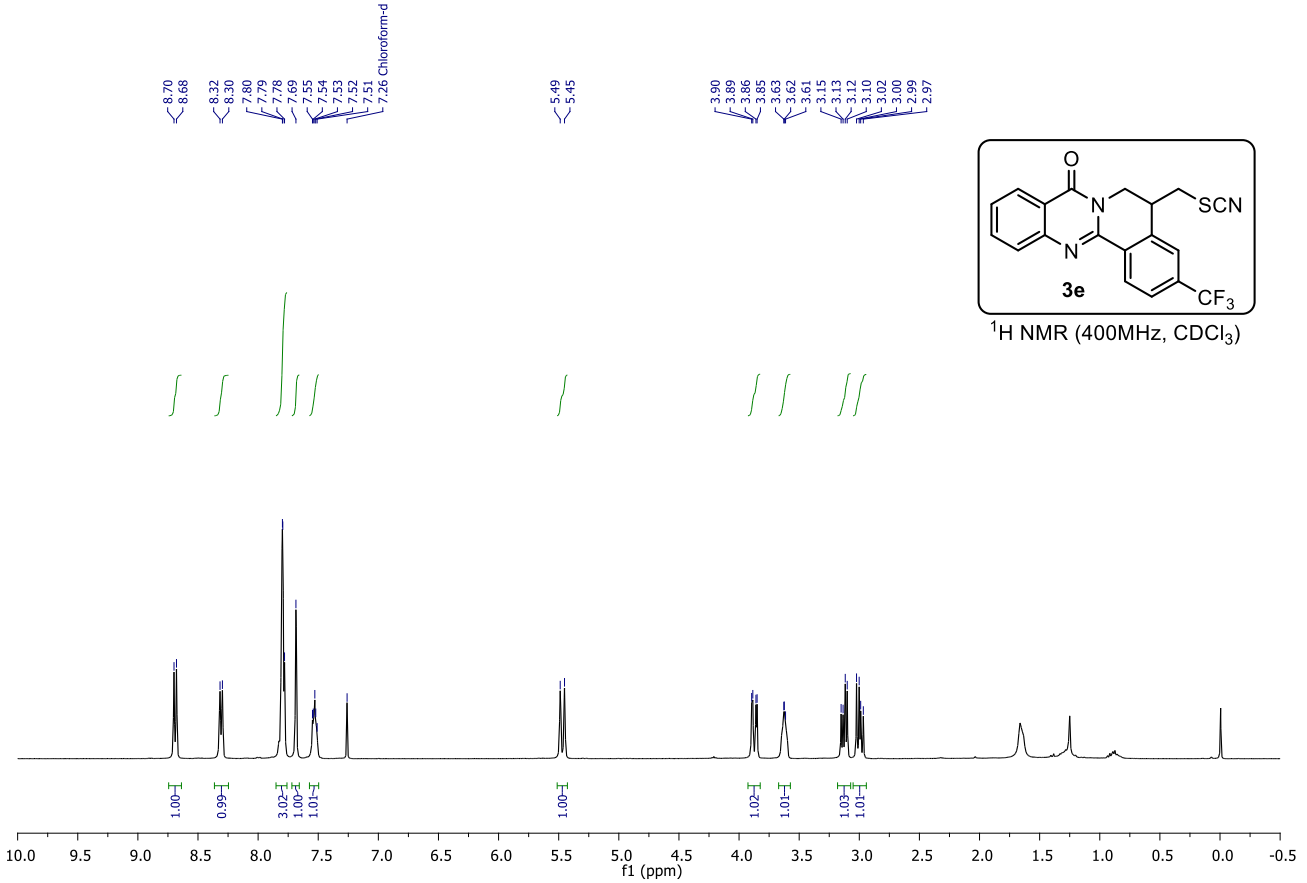
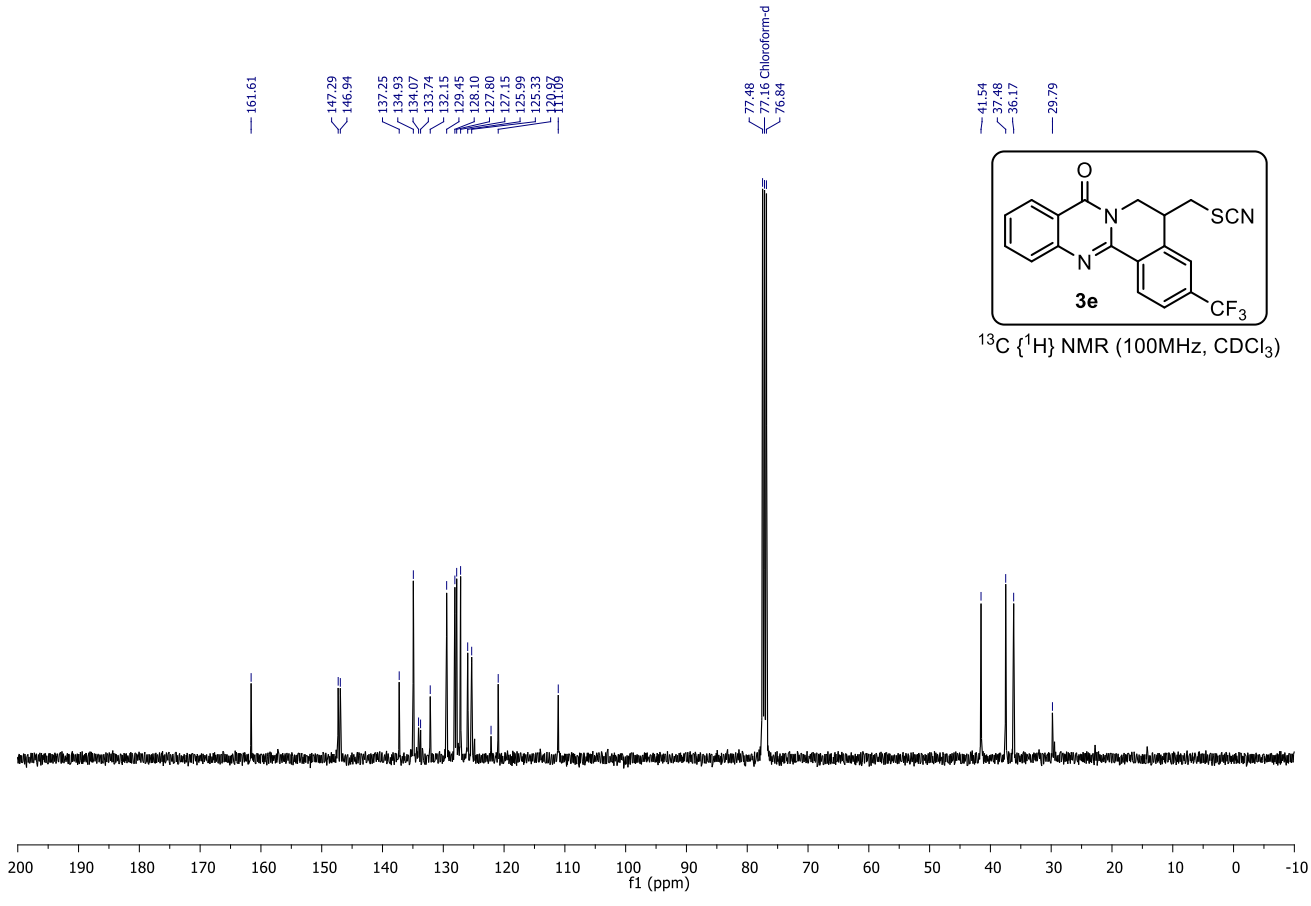


^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



^{1}H NMR (400MHz, $CDCl_3$)



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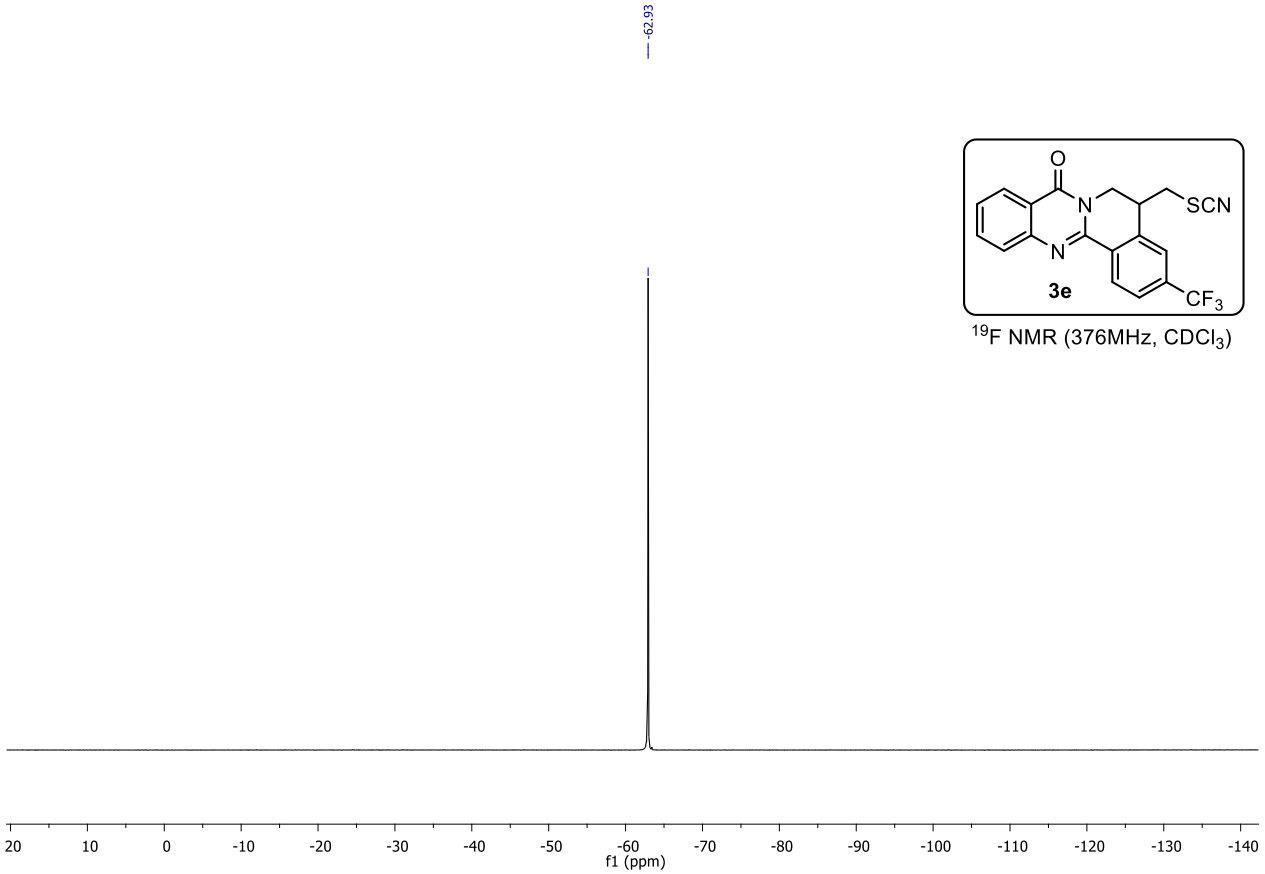
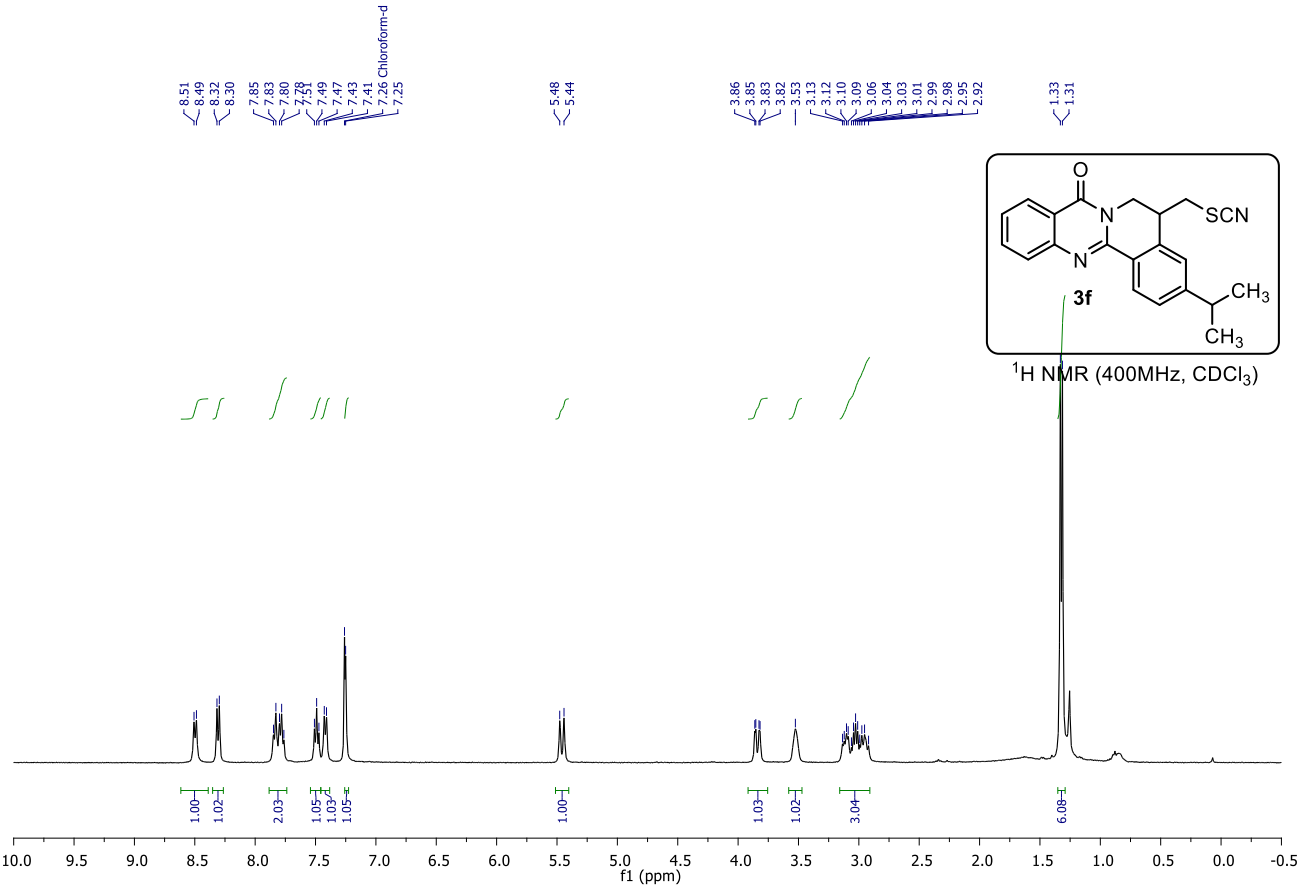
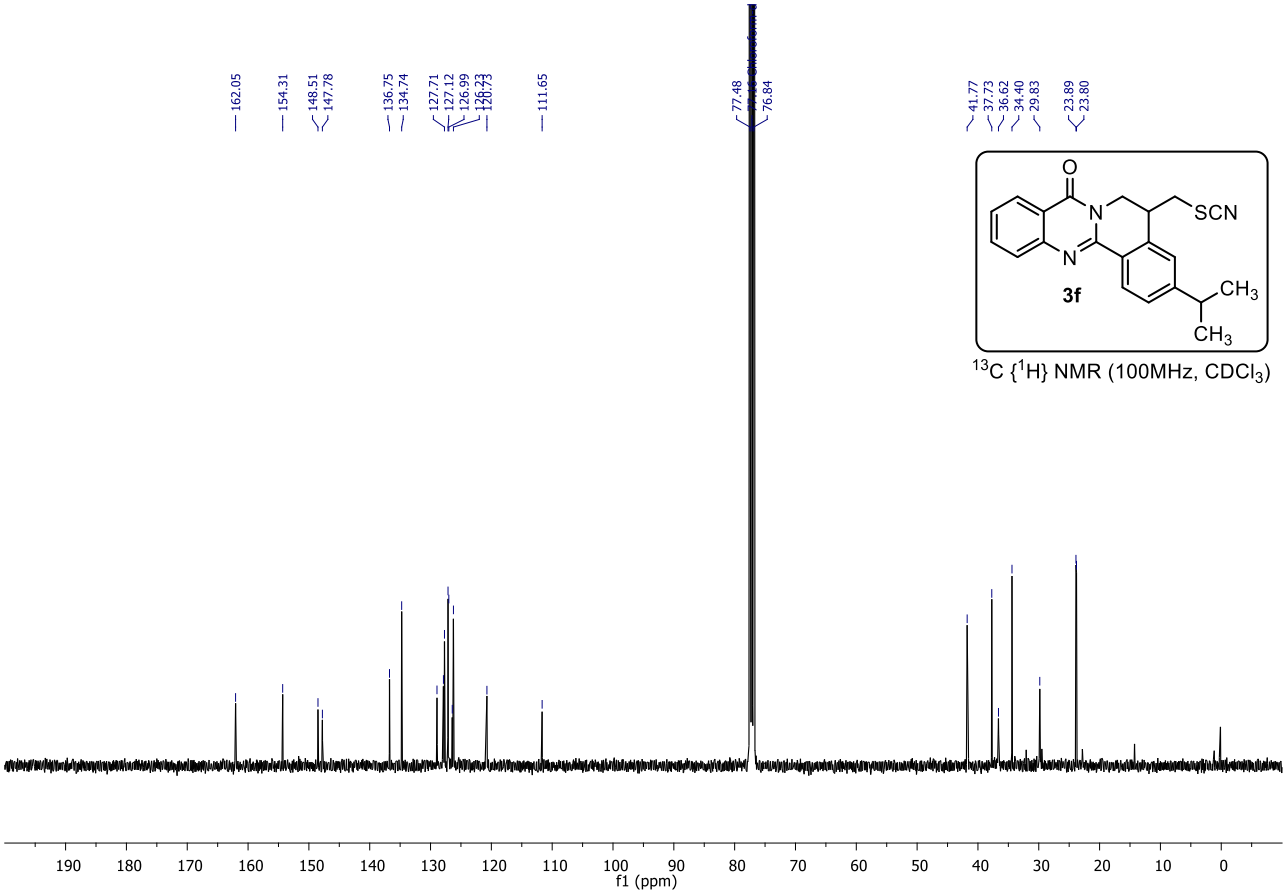


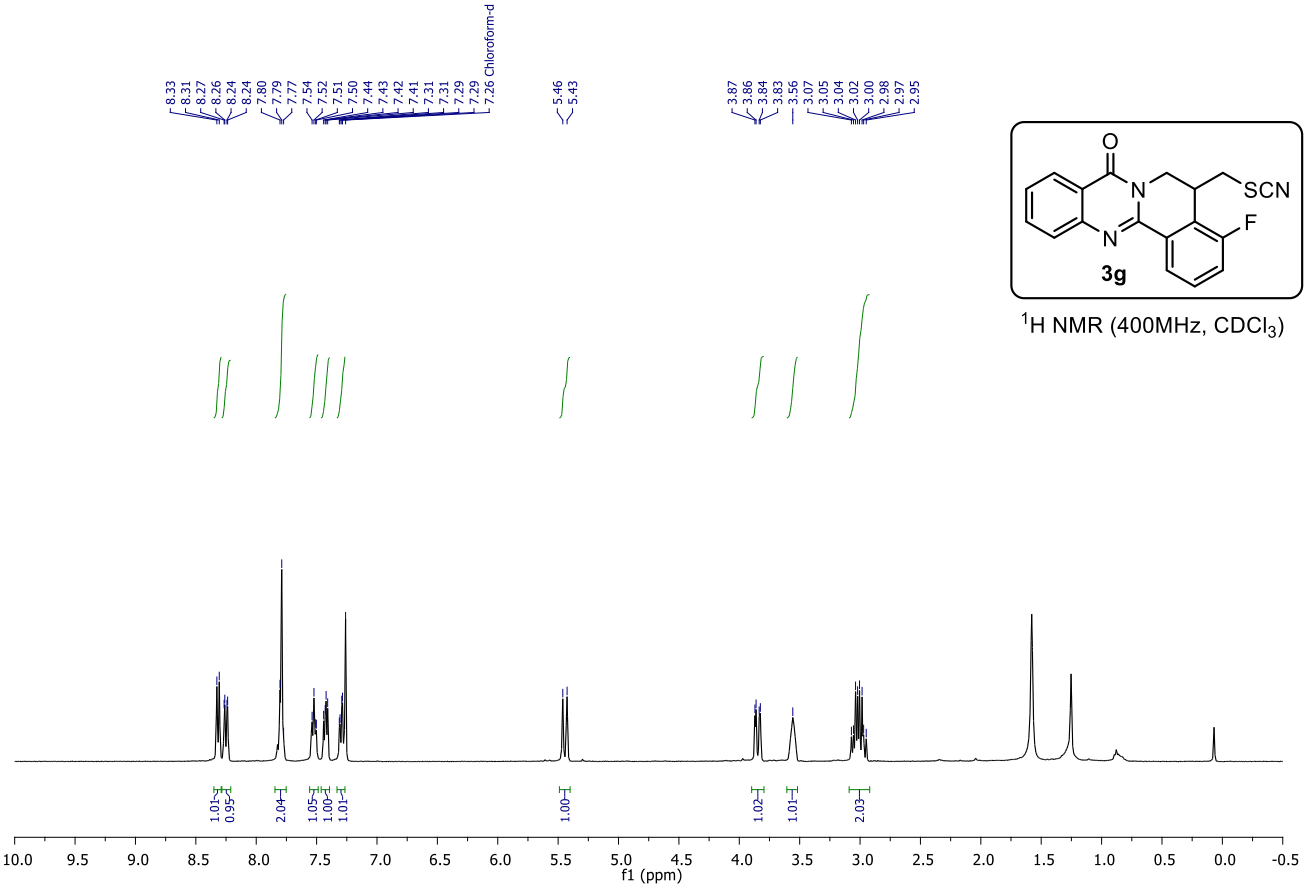
^{19}F NMR (376MHz, $CDCl_3$)



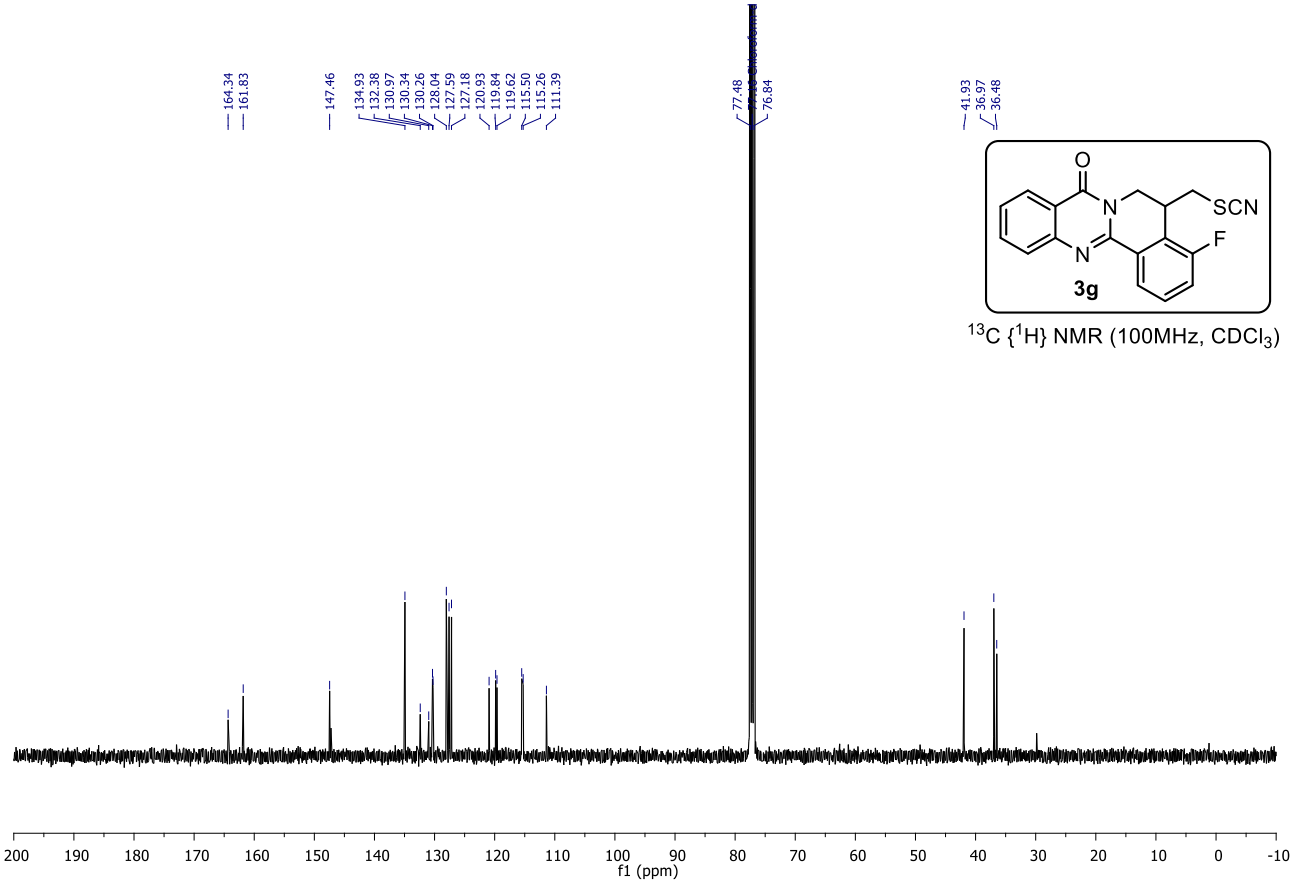
^{1}H NMR (400MHz, $CDCl_3$)



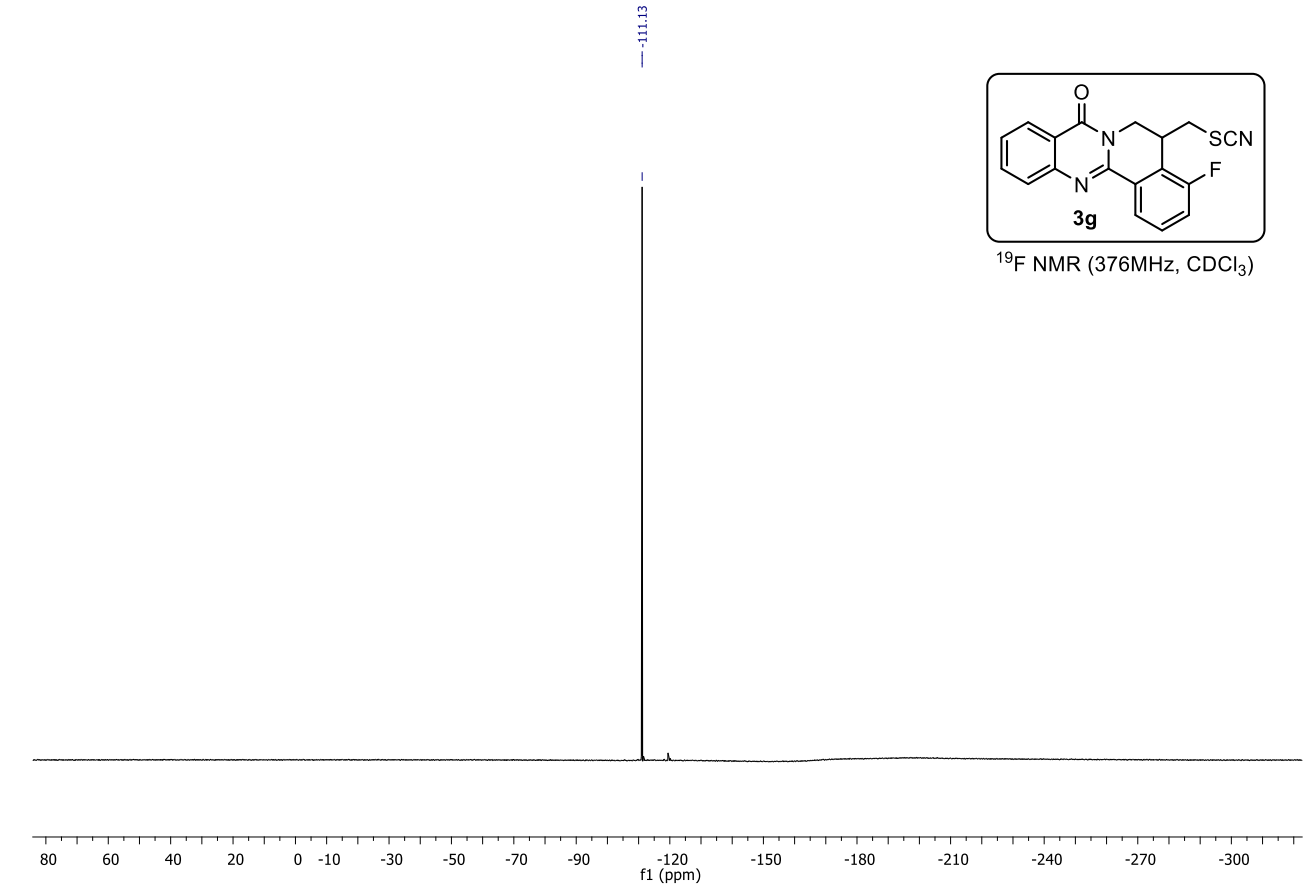
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



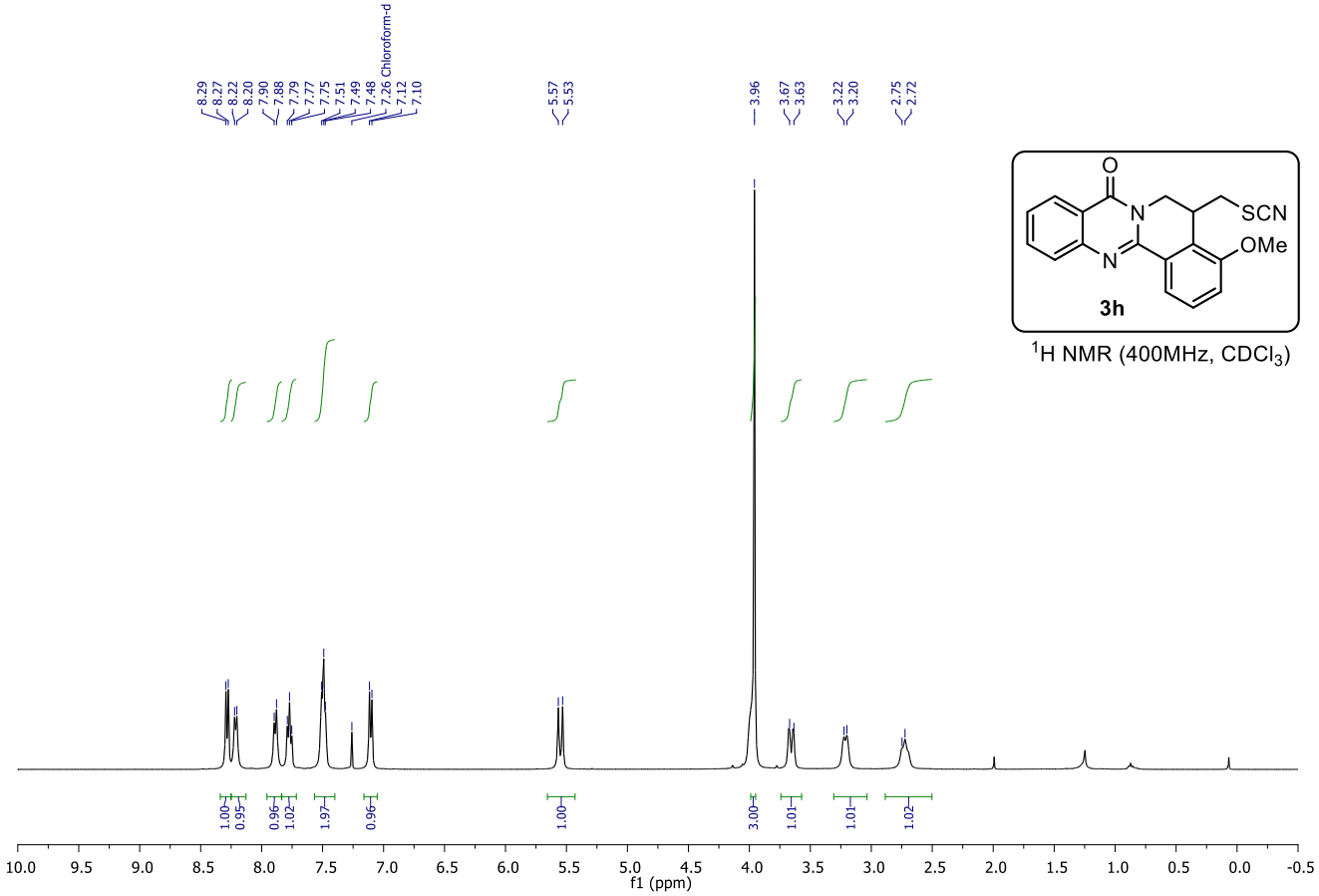
^{1}H NMR (400MHz, $CDCl_3$)



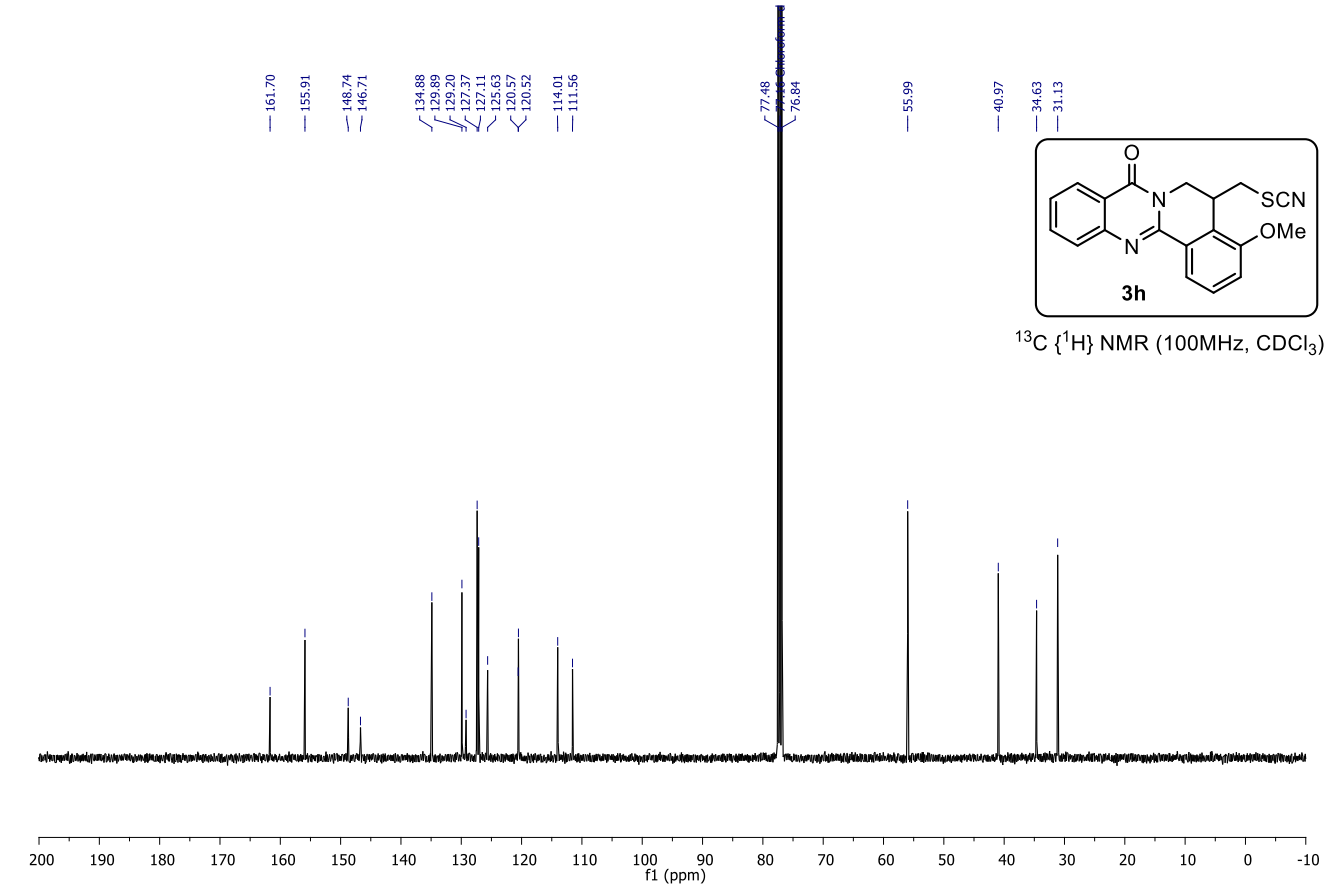
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



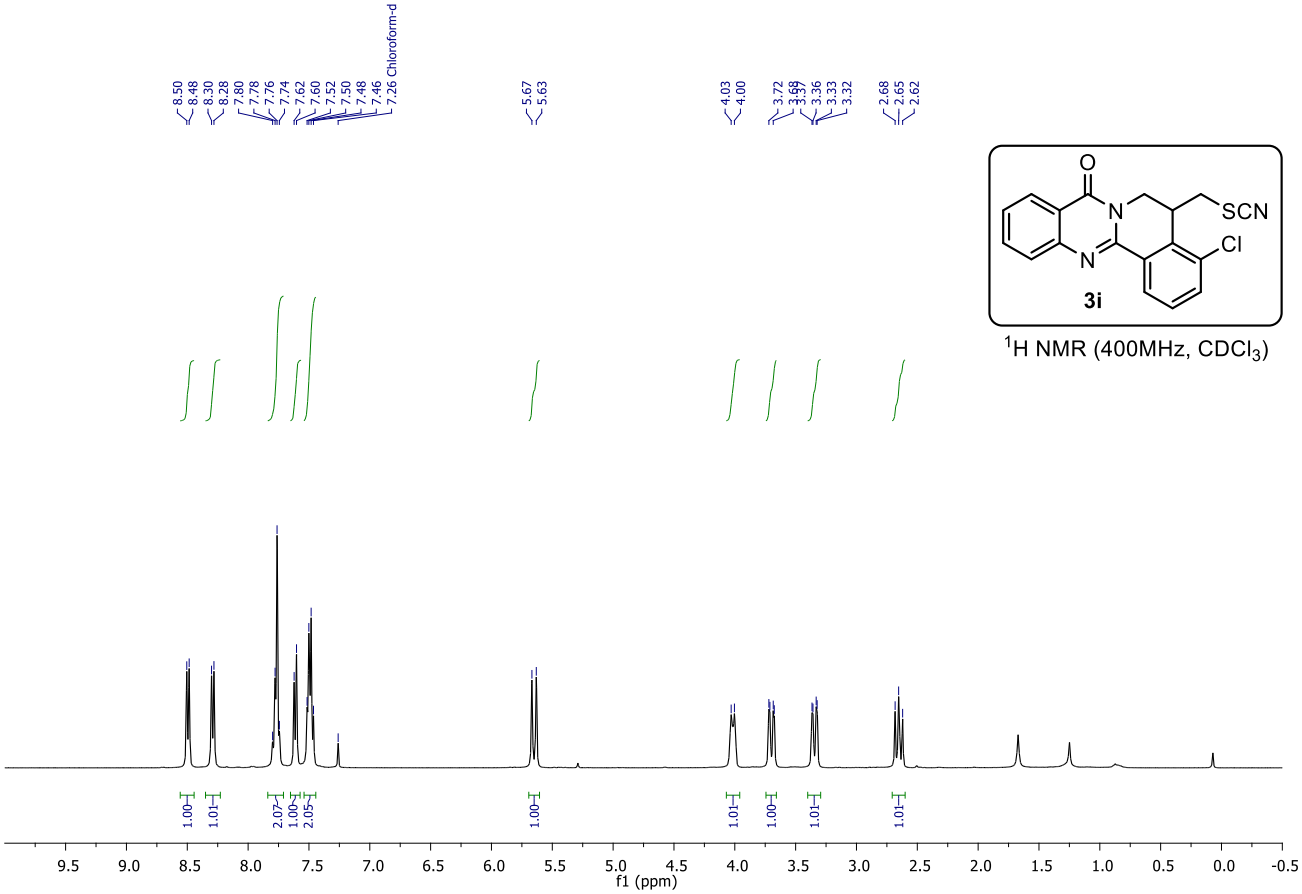
^{19}F NMR (376MHz, $CDCl_3$)



^{1}H NMR (400MHz, $CDCl_3$)



^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



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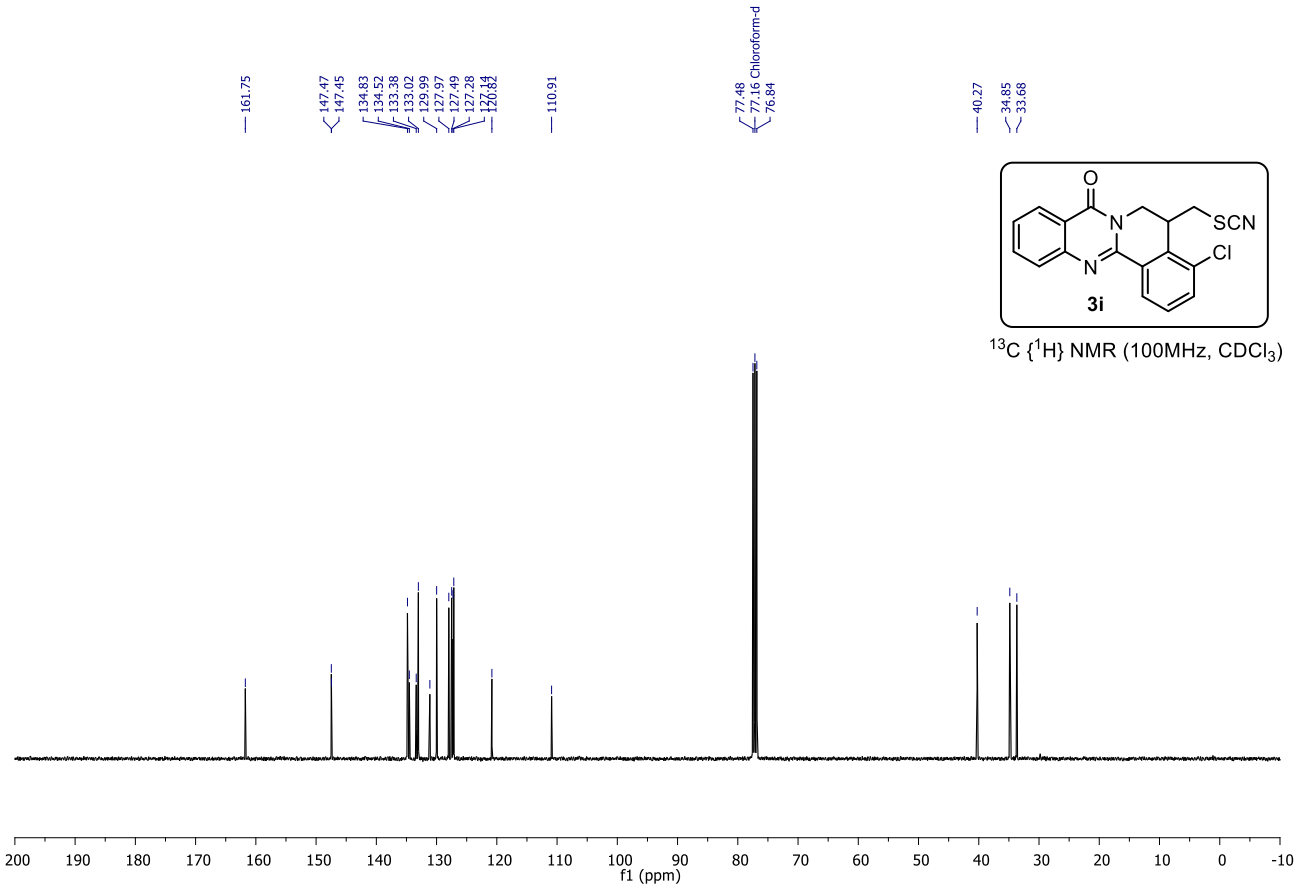
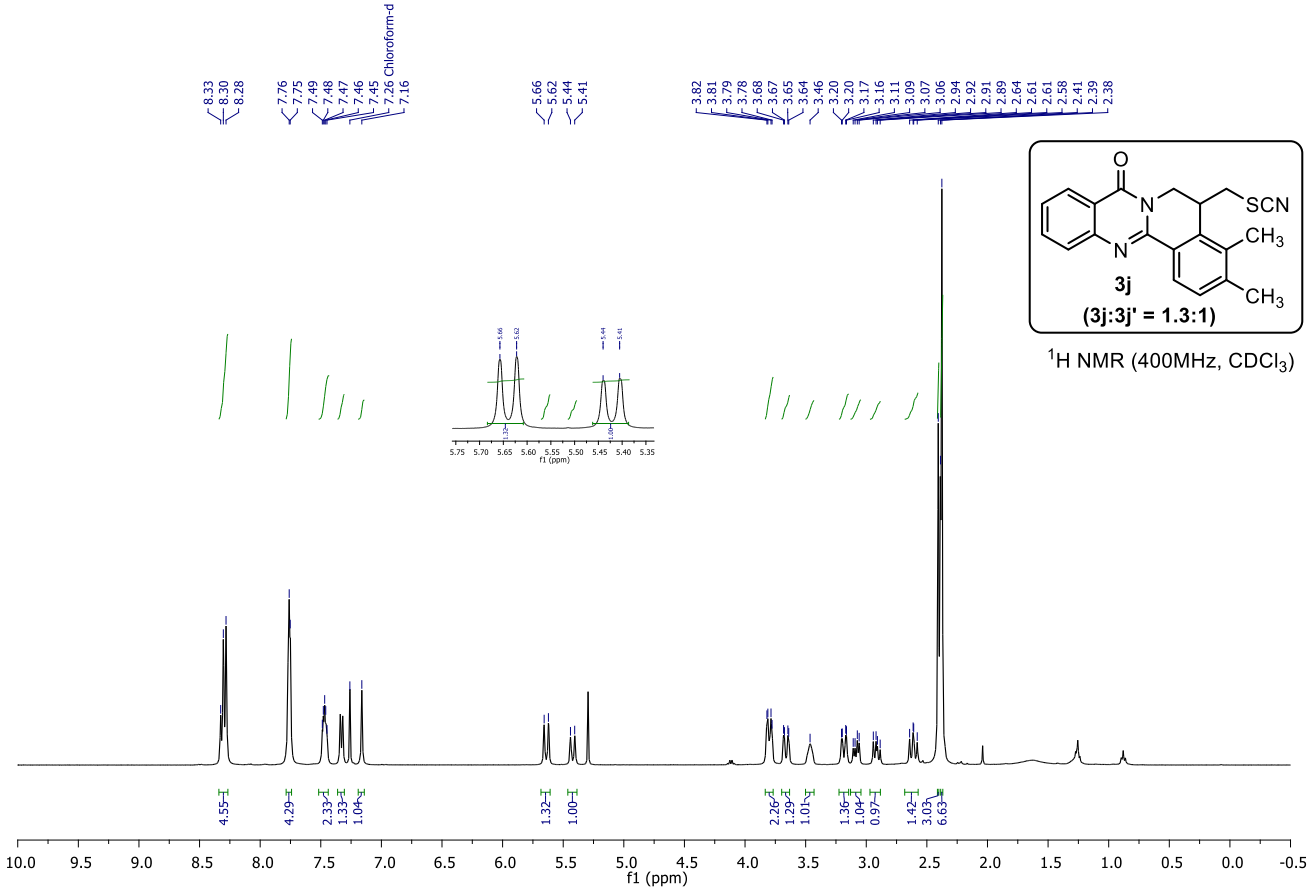
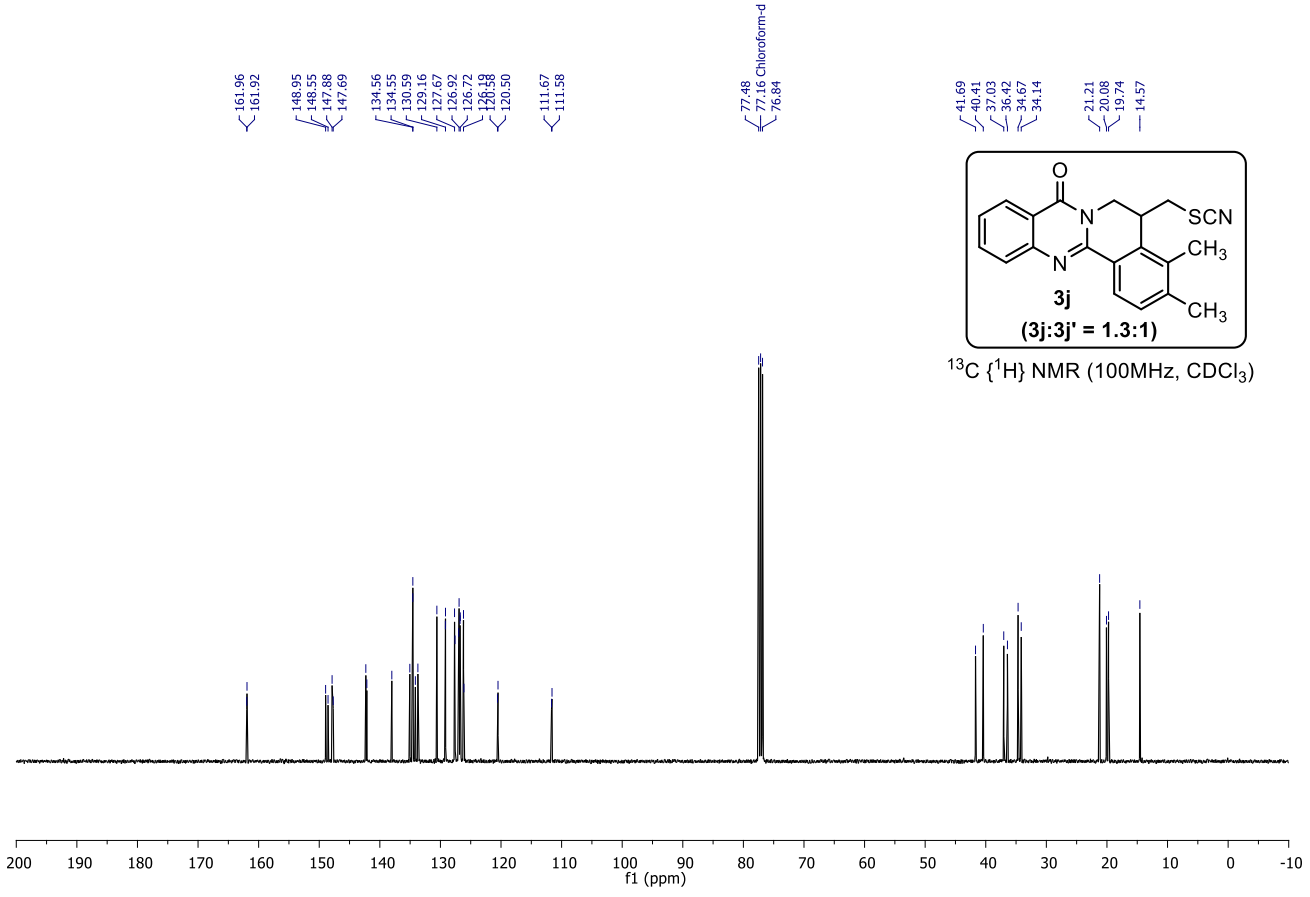
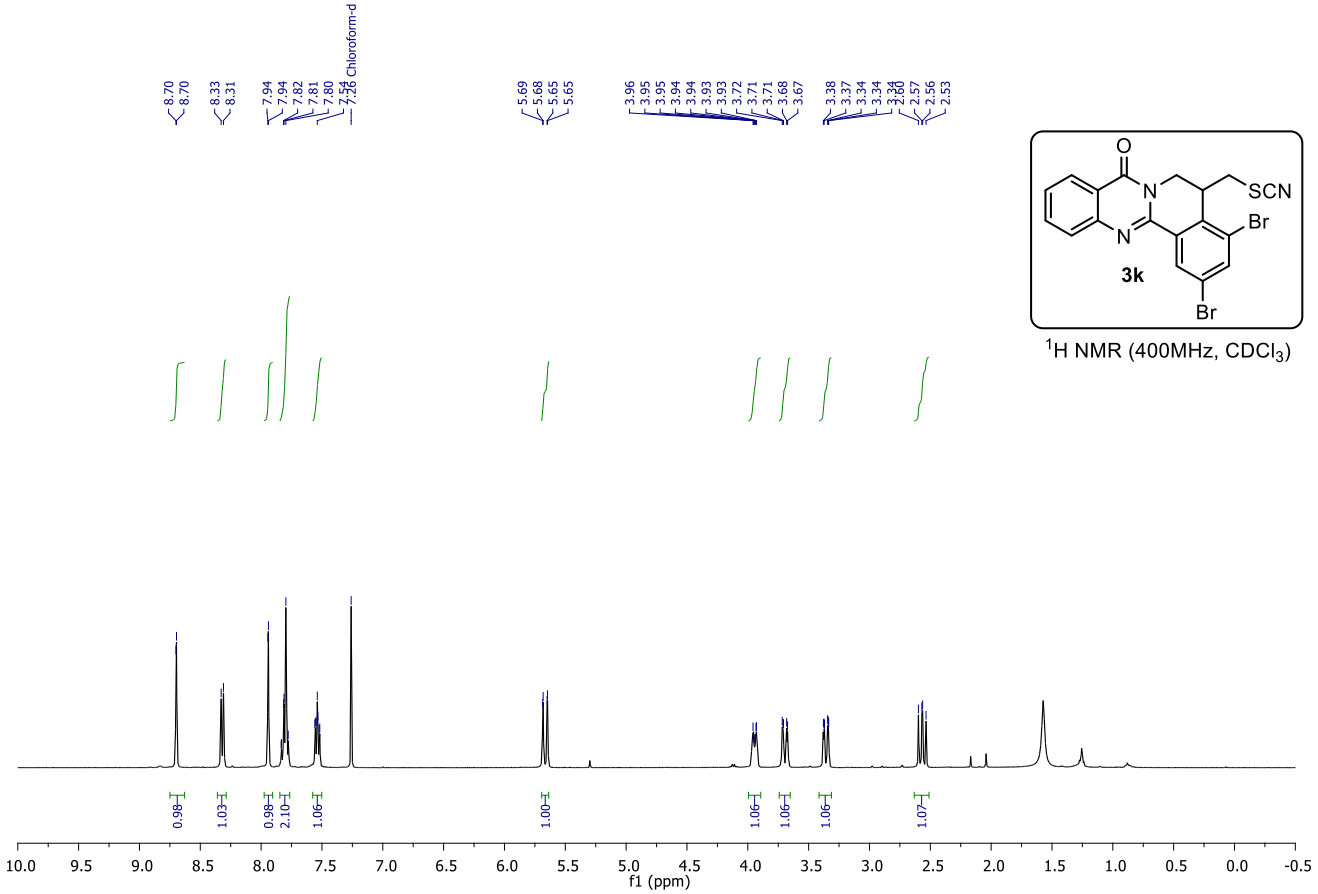


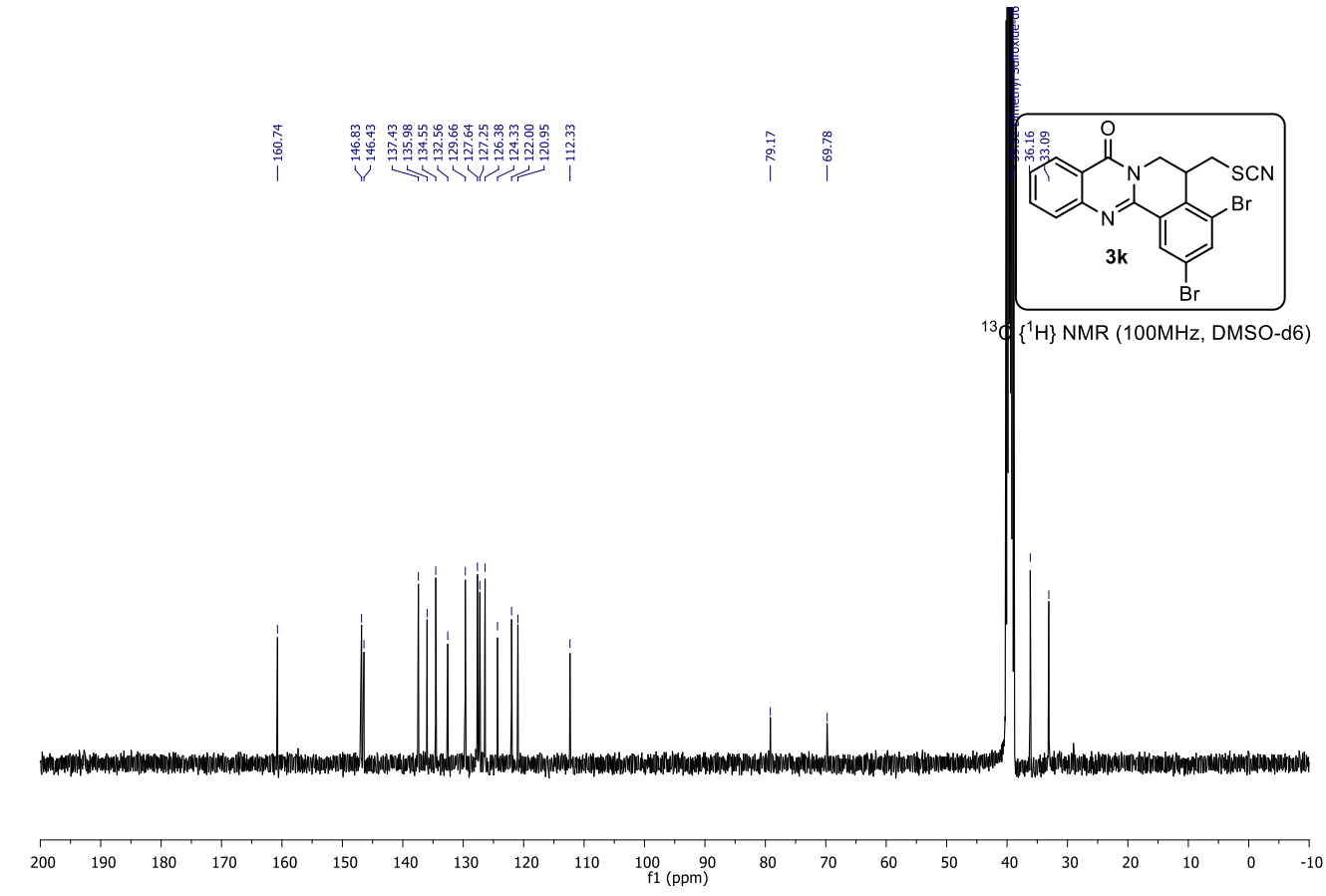
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)


8.33
8.30
8.28
7.76
7.75
7.49
7.48
7.47
7.46
7.45
7.26 Chloroform-d
7.16
5.66
5.62
5.44
5.41
3.82
3.81
3.79
3.78
3.68
3.67
3.65
3.64
3.46
3.20
3.17
3.16
3.11
3.09
3.07
3.06
2.94
2.92
2.91
2.89
2.64
2.61
2.61
2.58
2.41
2.39
2.38
O
N
N
SCN
CH3
CH3
3j
(3j:3j' = 1.3:1)
1H NMR (400MHz, CDCl3)
4.55
4.29
2.33
1.33
1.04
1.32
1.00
2.26
1.29
1.01
1.36
1.04
0.97
1.42
3.03
6.63
f1 (ppm)

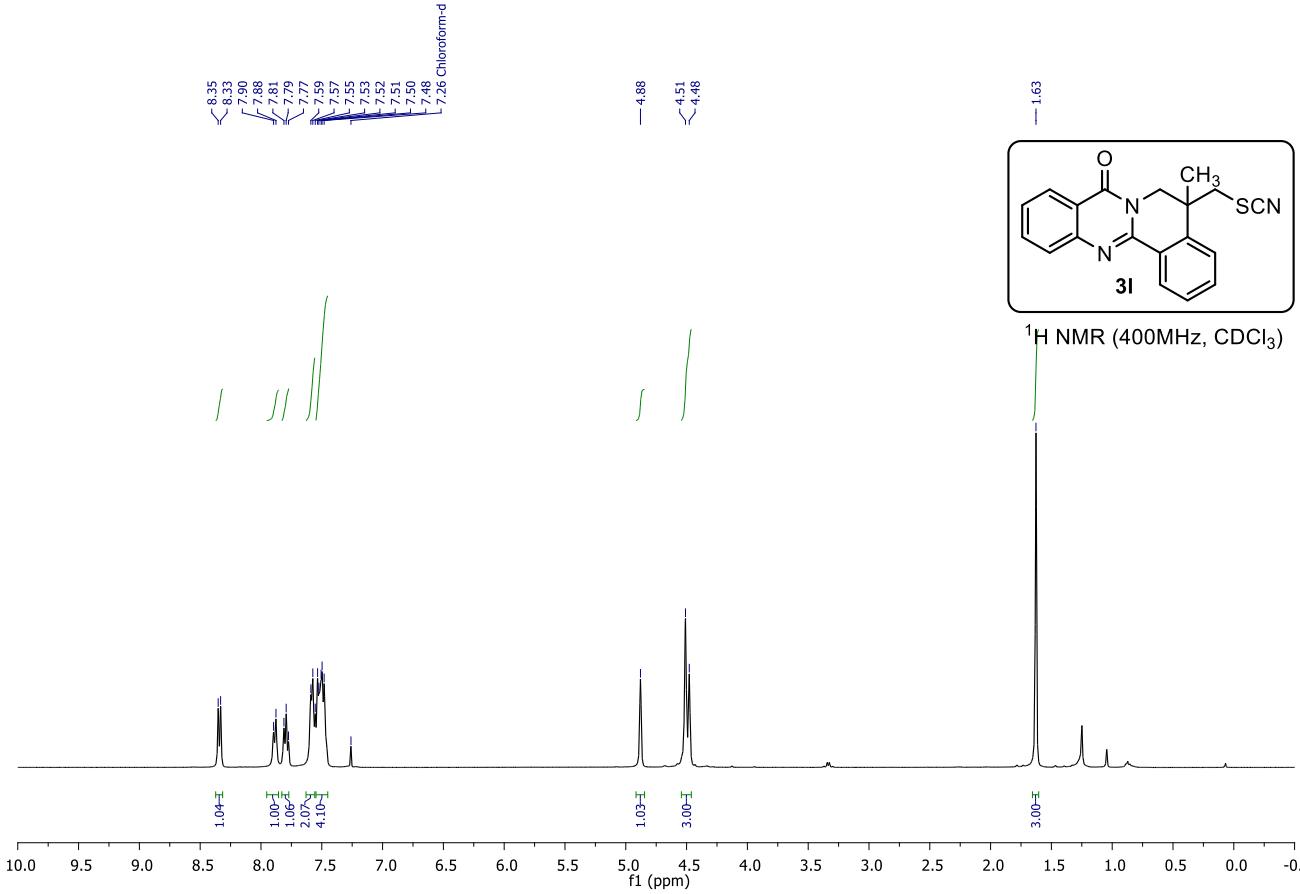

161.96
161.92
148.95
148.55
147.88
147.69
134.56
134.55
130.59
129.16
127.67
126.92
126.72
126.19
120.58
120.50
111.67
111.58
77.48
77.16 Chloroform-d
76.84
41.69
40.41
37.03
36.42
34.67
34.14
21.21
20.08
19.74
14.57
O
N
N
SCN
CH3
CH3
3j
(3j:3j' = 1.3:1)
13C {1H} NMR (100MHz, CDCl3)
f1 (ppm)



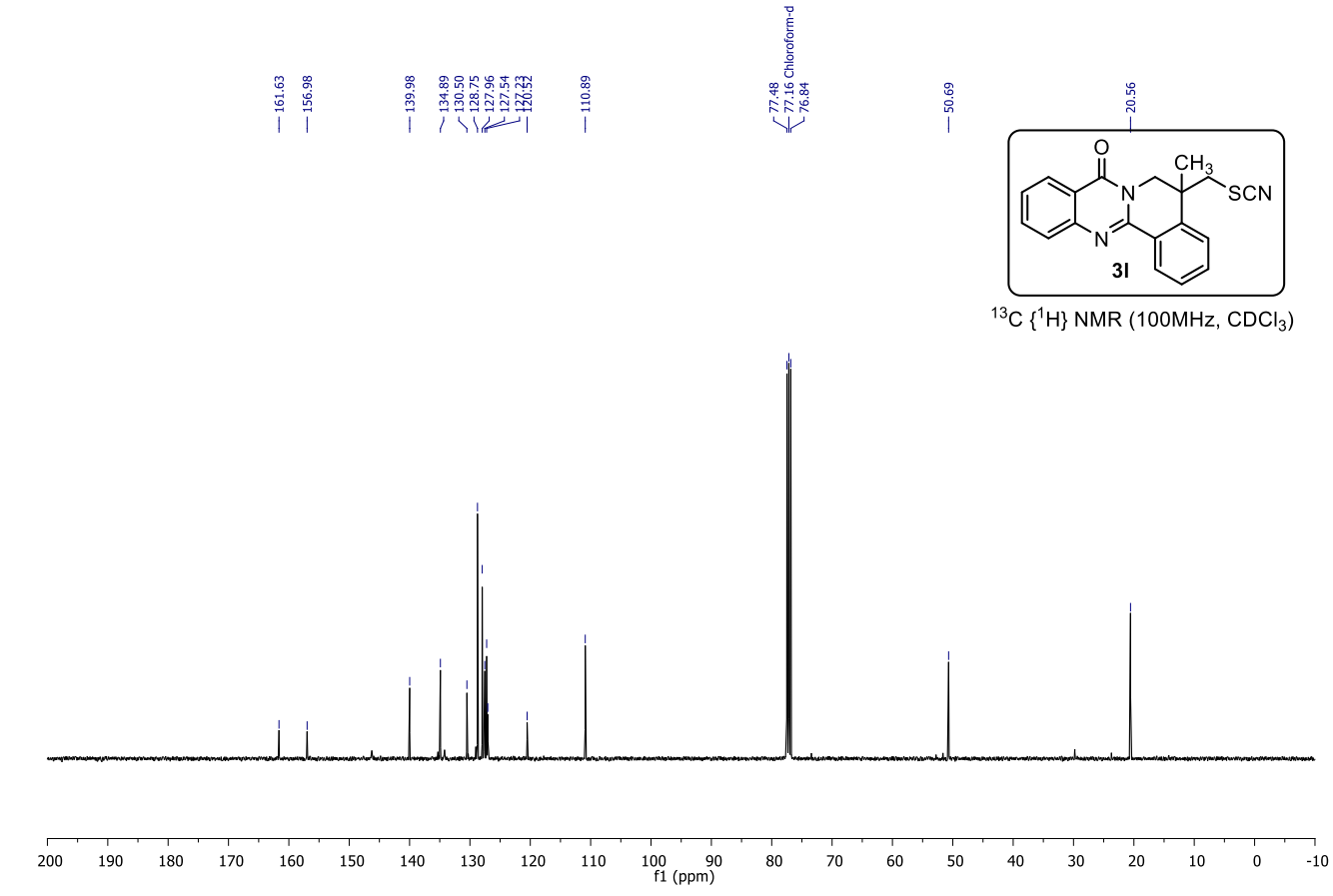
^{1}H NMR (400MHz, $CDCl_3$)



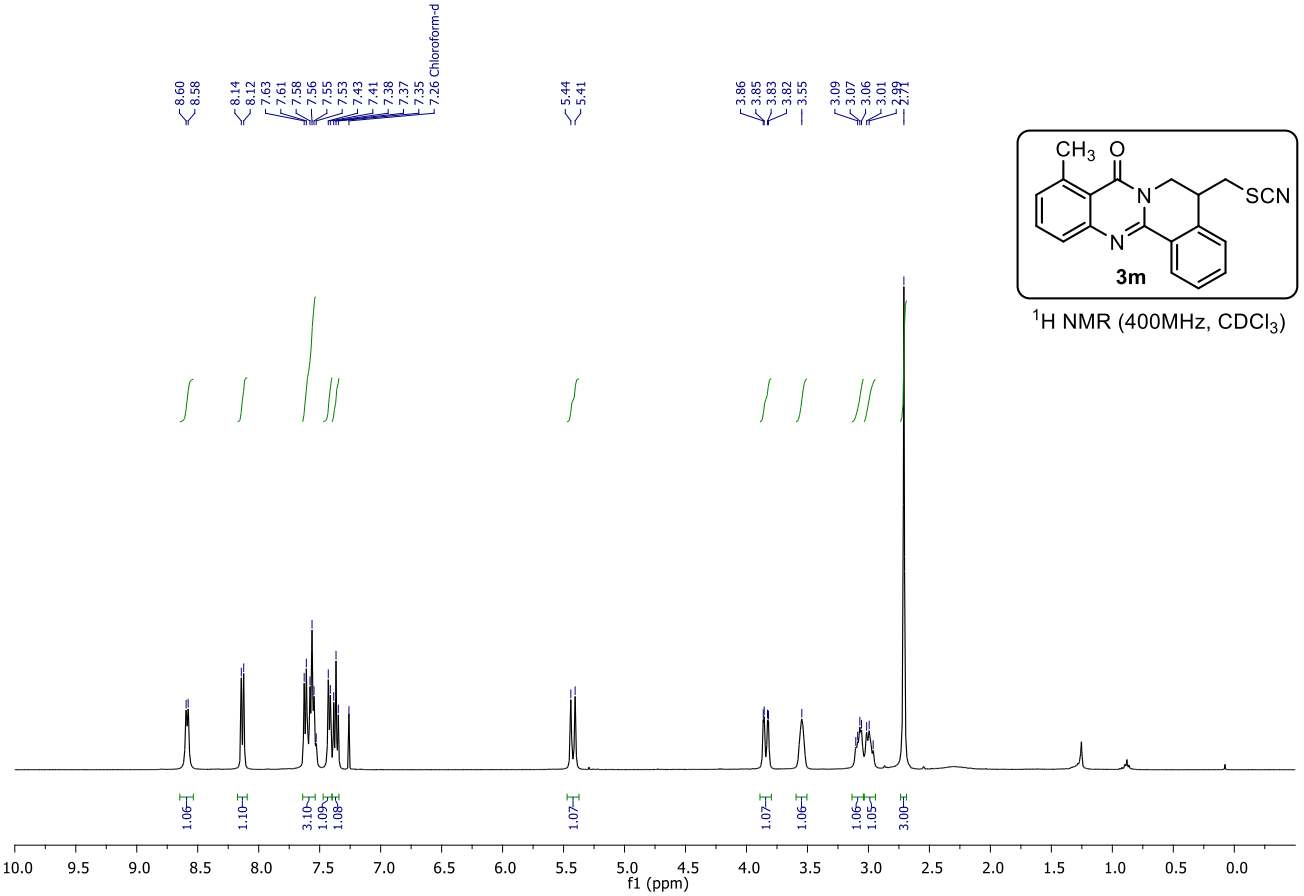
^{13}C {^{1}H} NMR (100MHz, DMSO-d6)



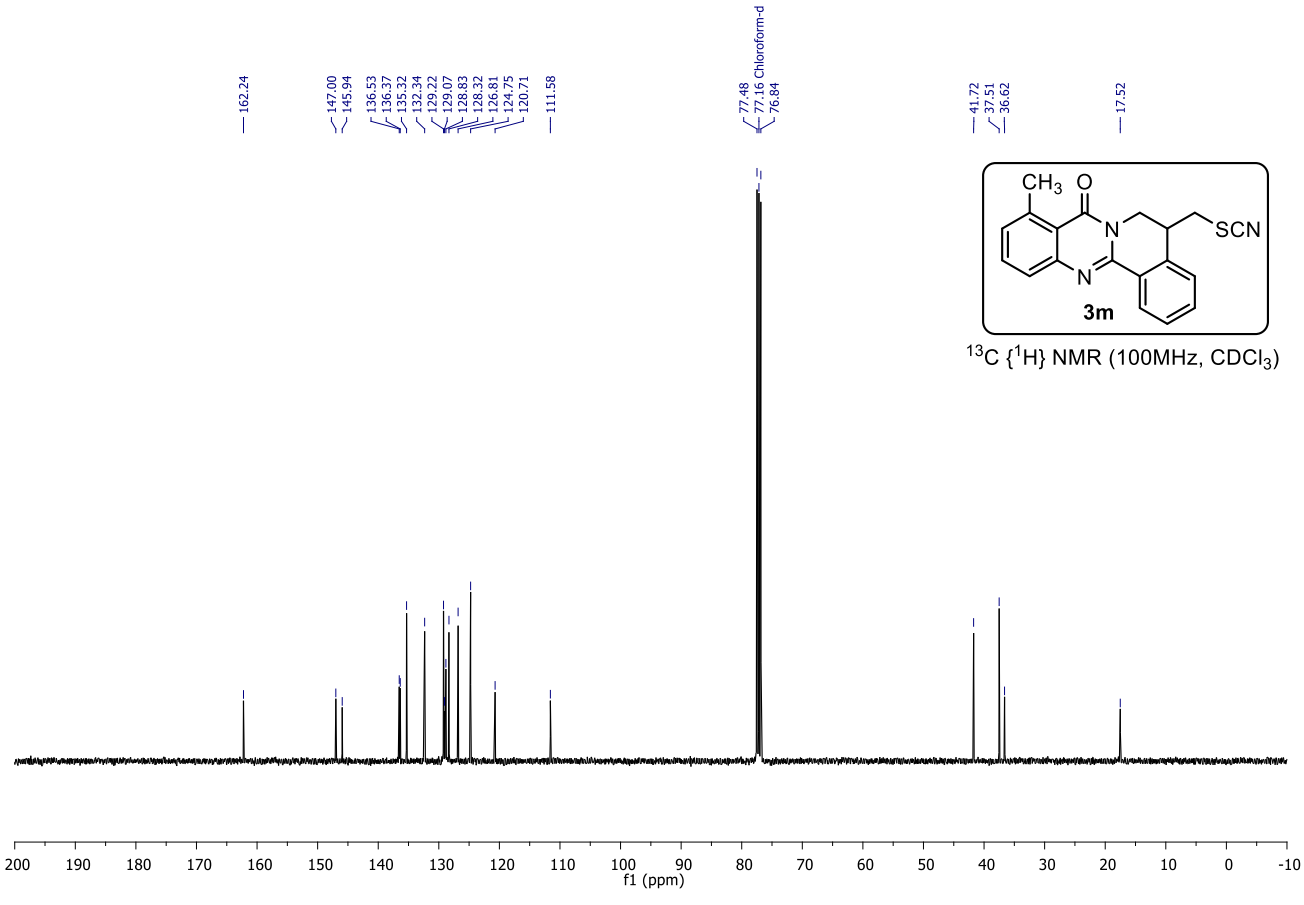
^{1}H NMR (400MHz, $CDCl_3$)



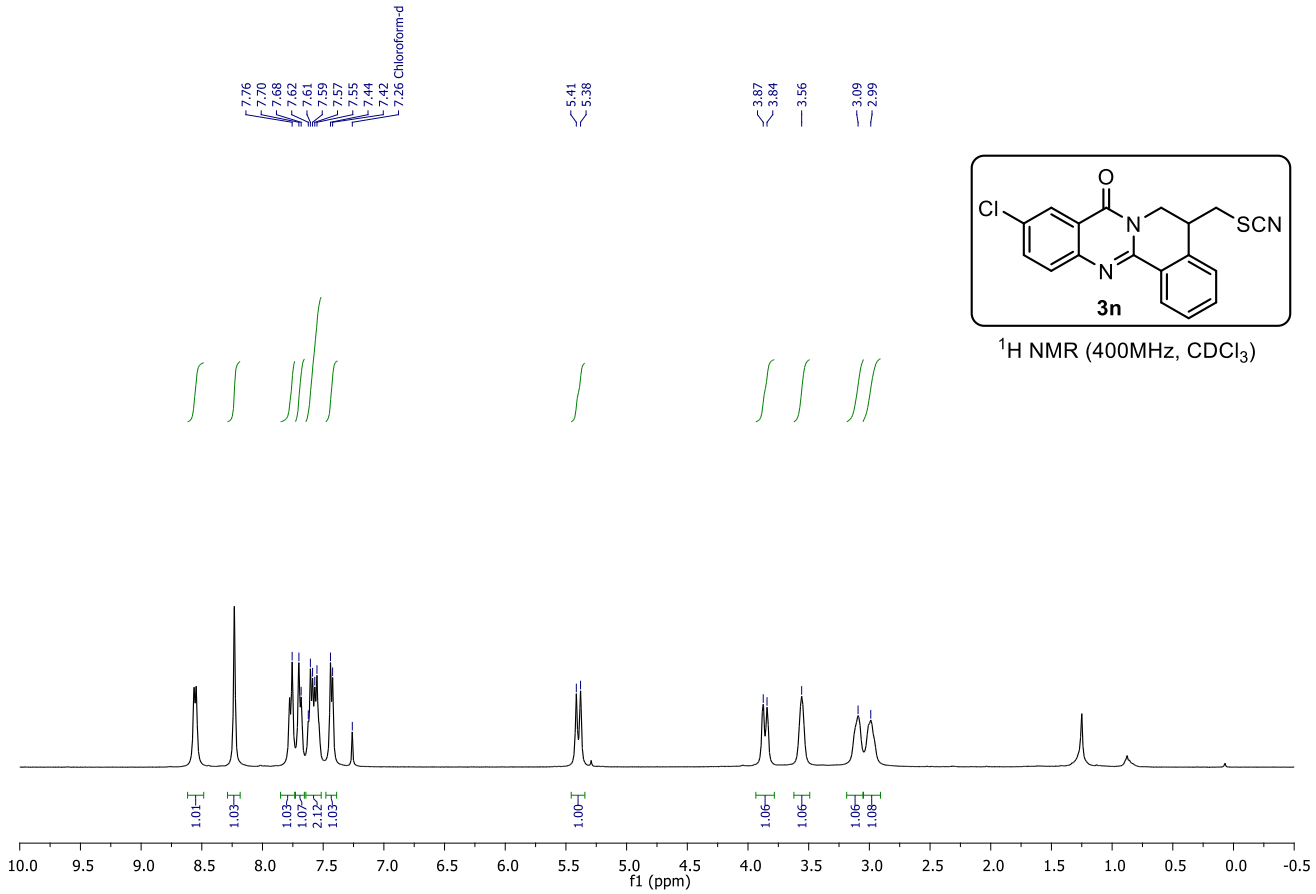
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



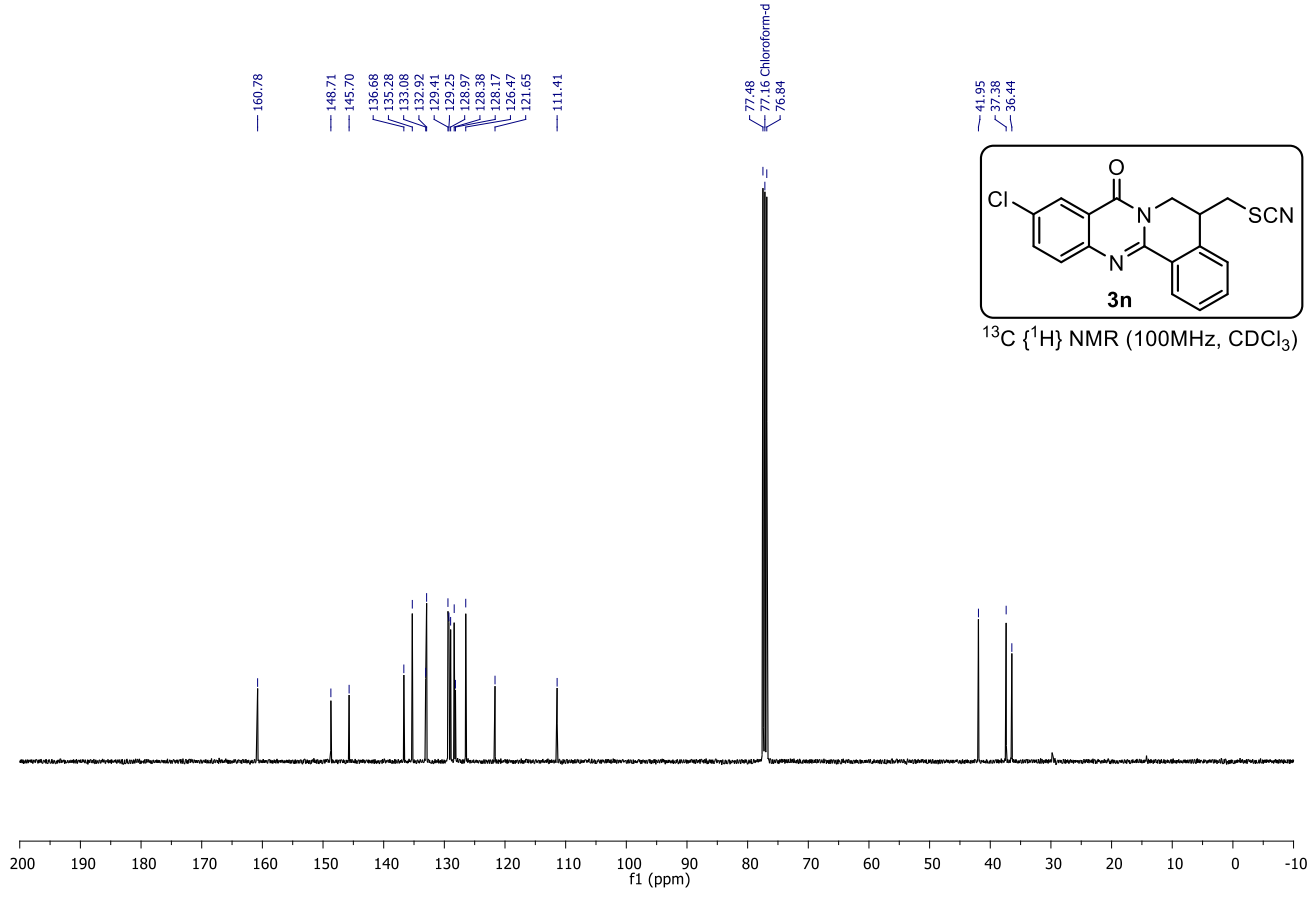
^{1}H NMR (400MHz, $CDCl_3$)



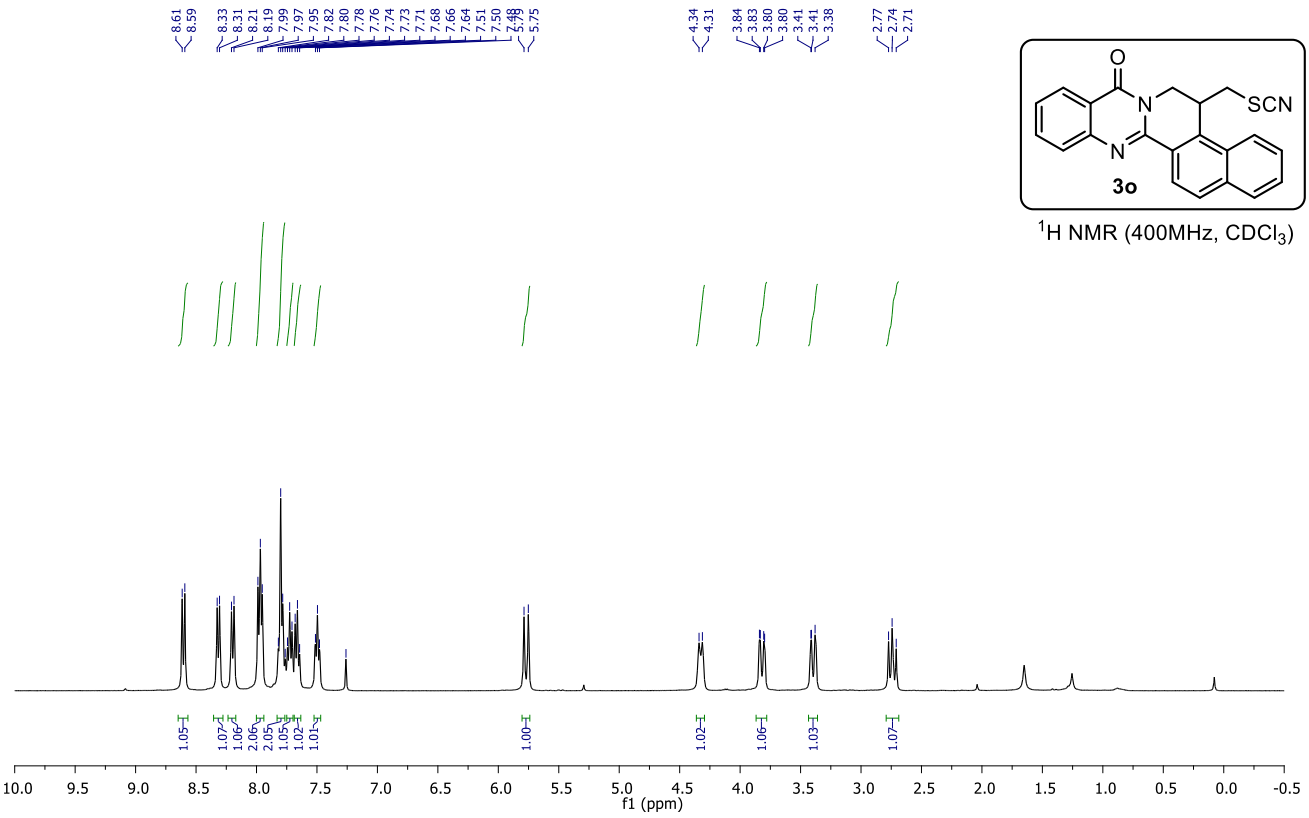
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



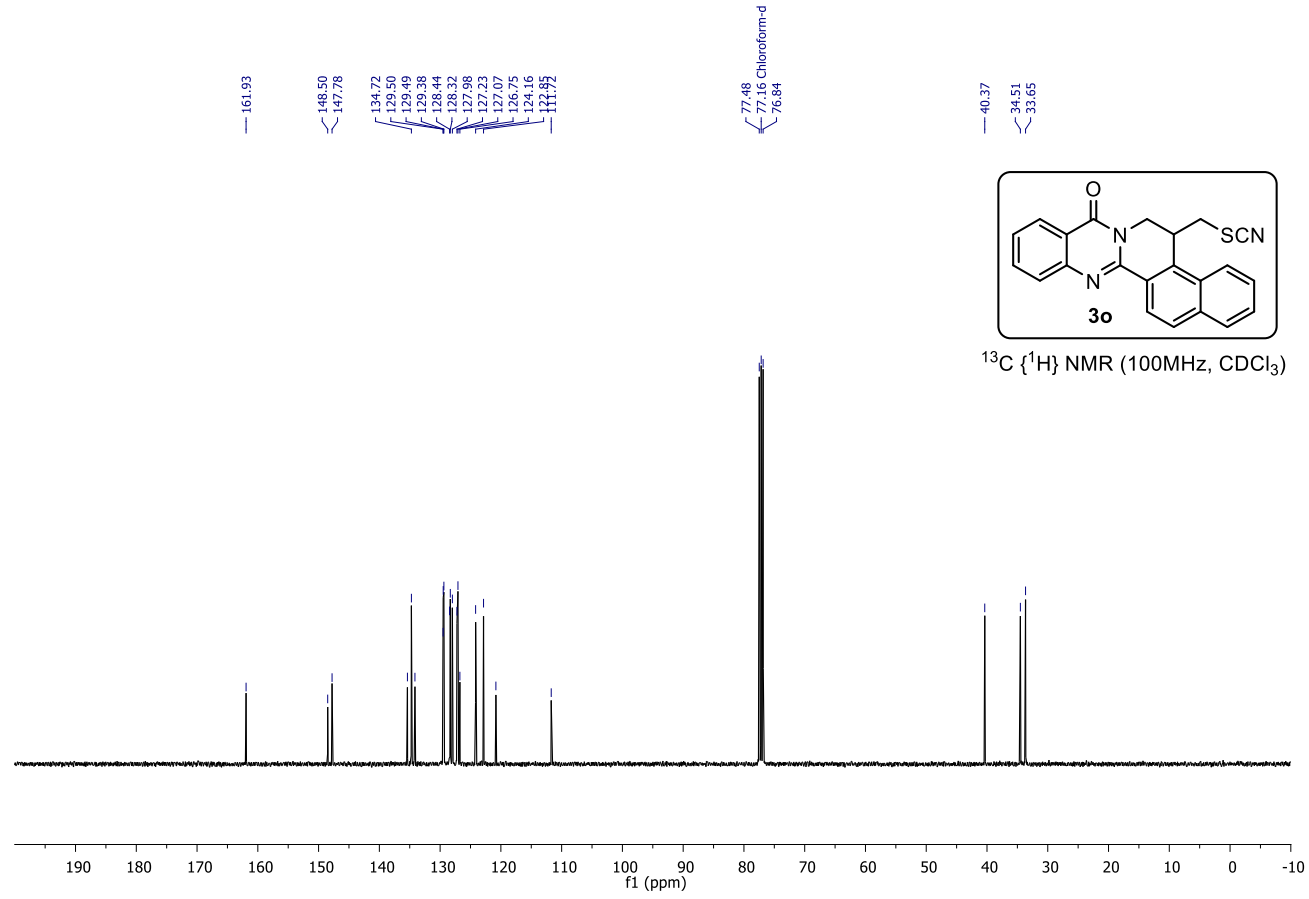
^{1}H NMR (400MHz, $CDCl_3$)



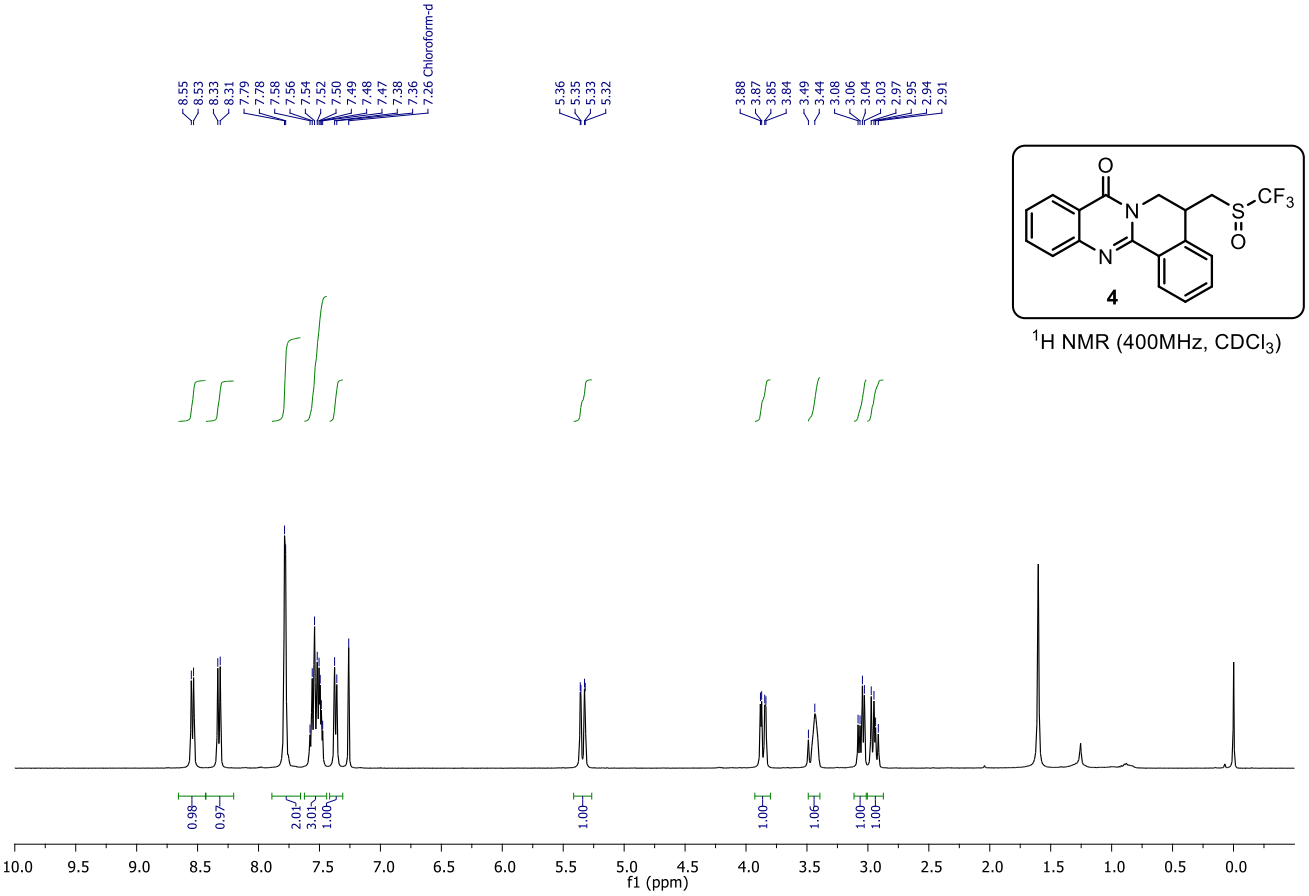
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



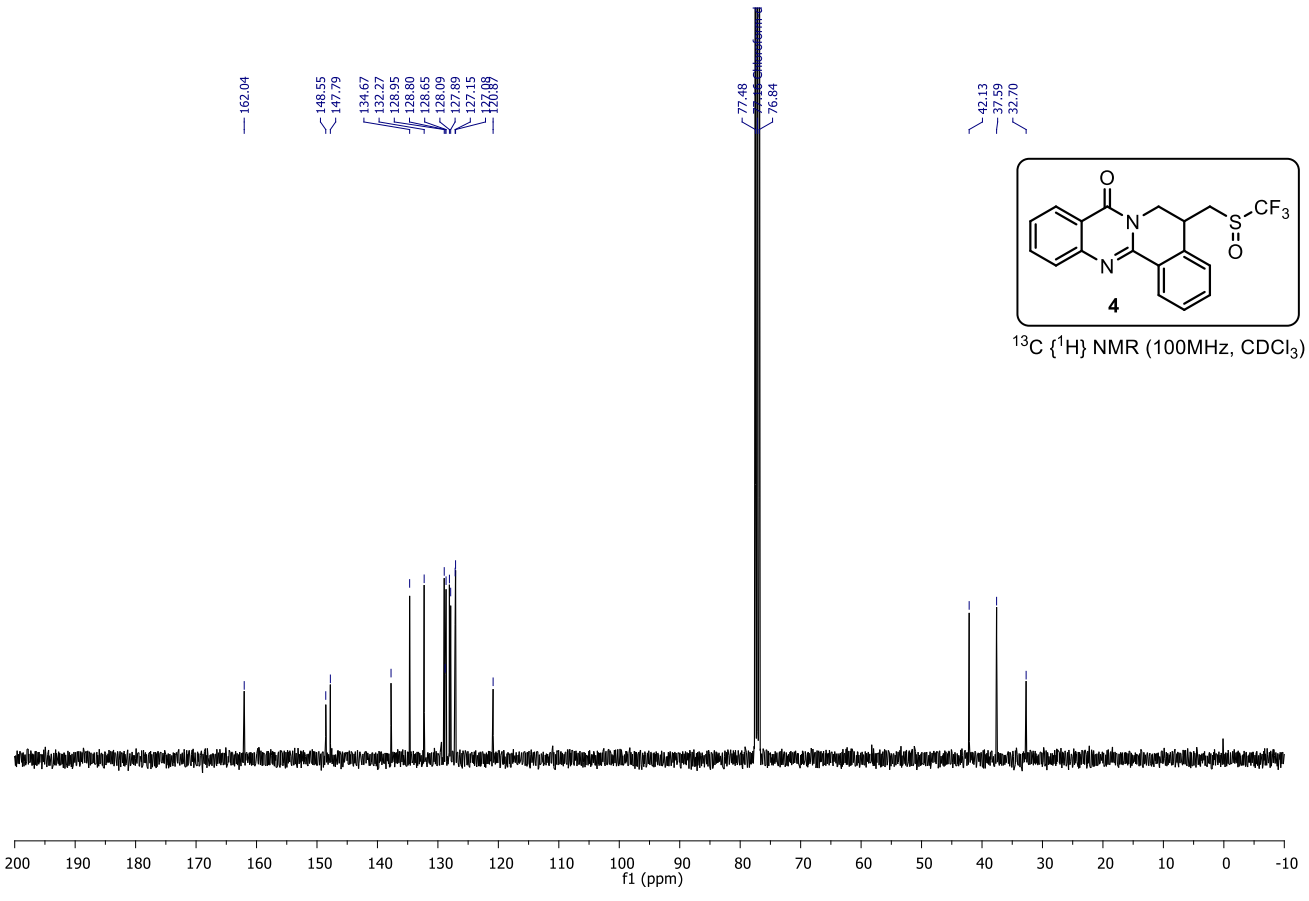
^{1}H NMR (400MHz, $CDCl_3$)



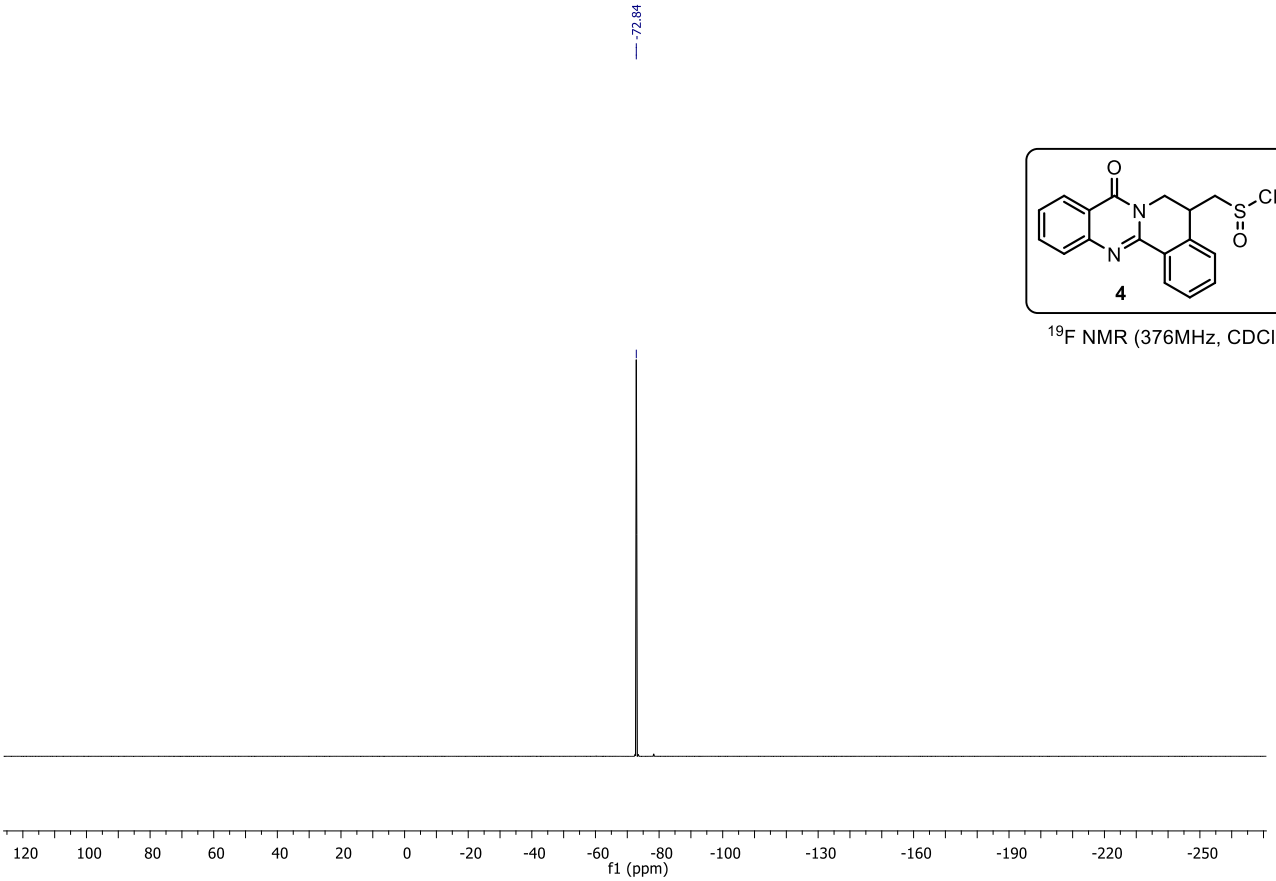
^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



^{1}H NMR (400MHz, $CDCl_3$)

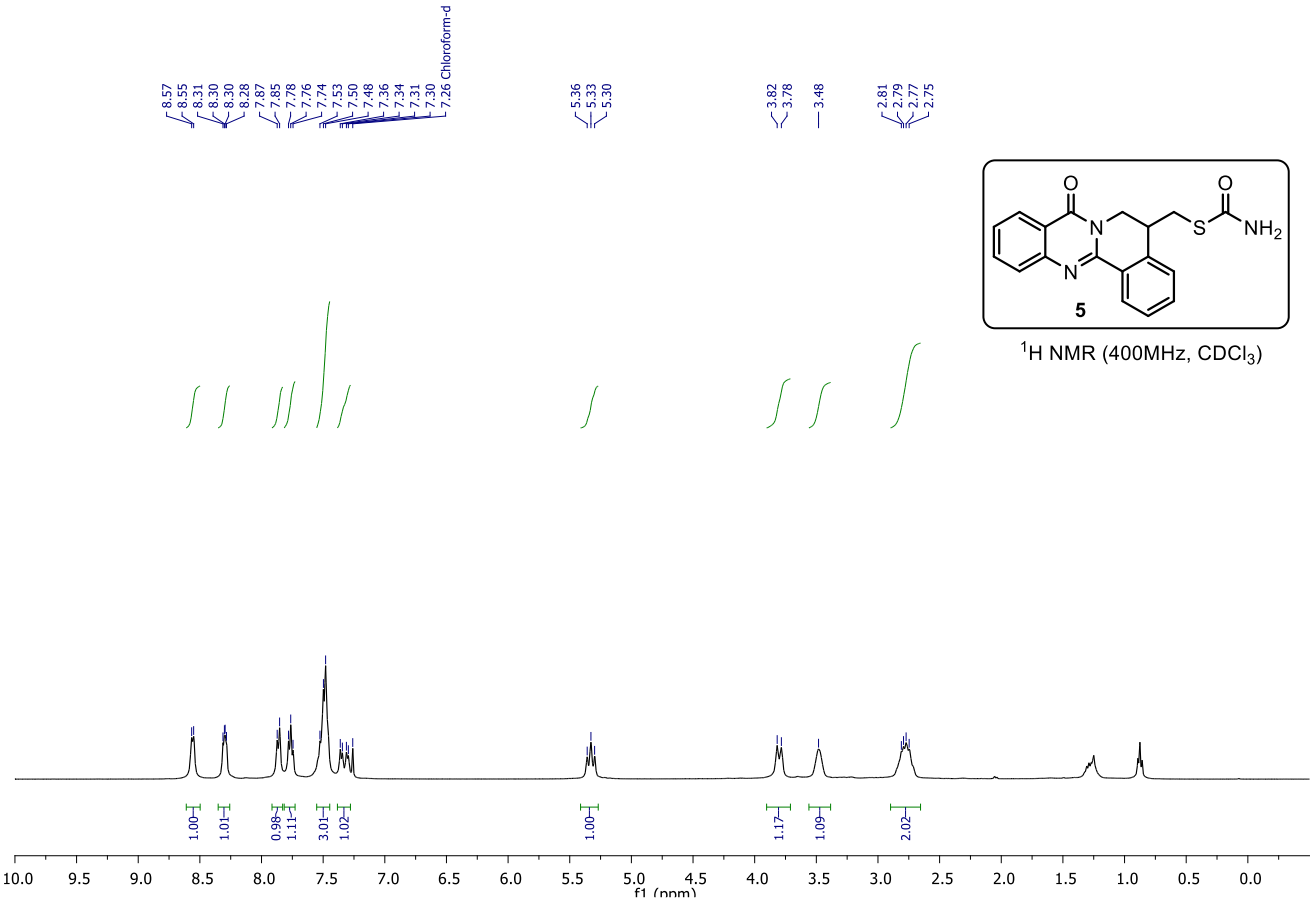


^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



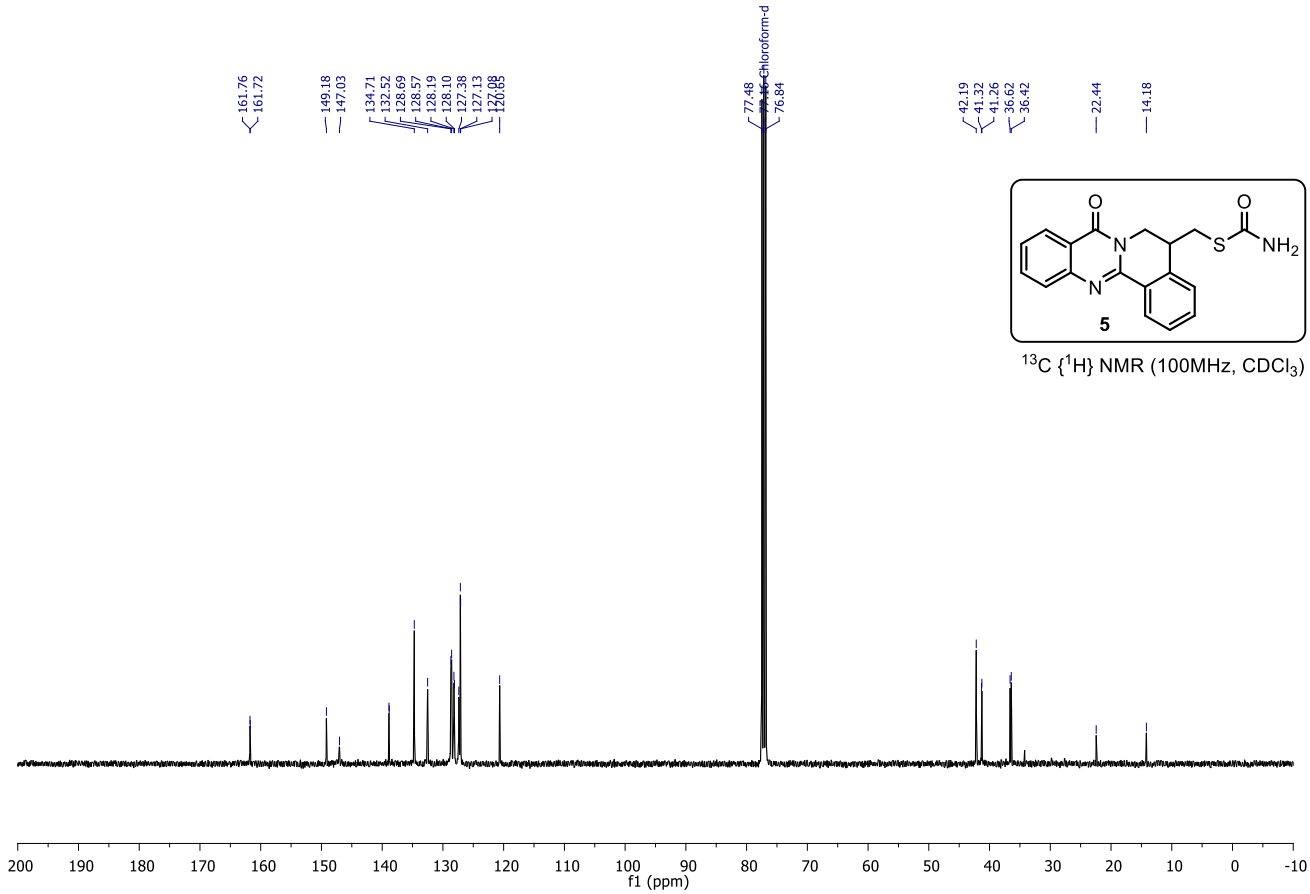
4

^{19}F NMR (376MHz, $CDCl_3$)

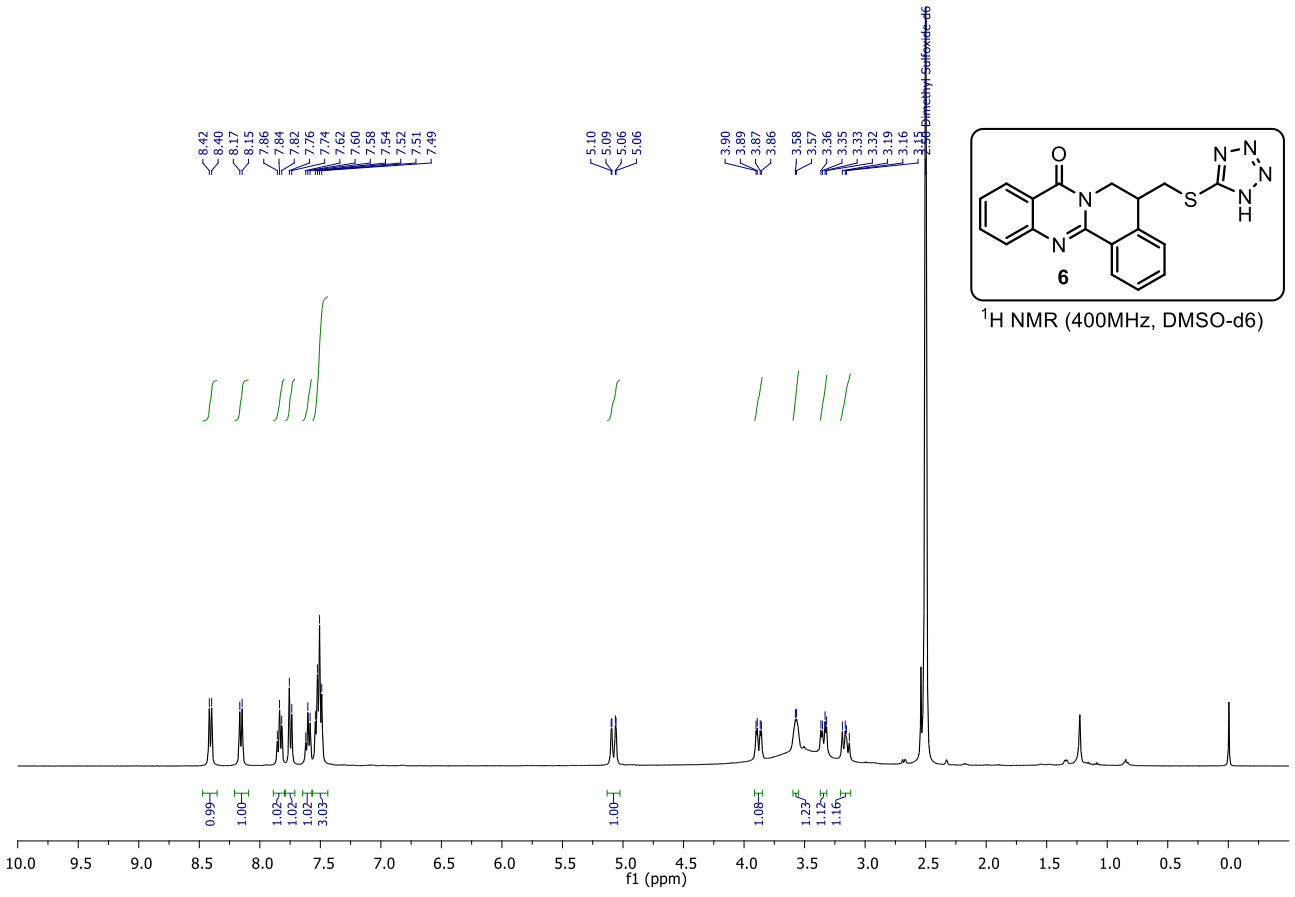


5

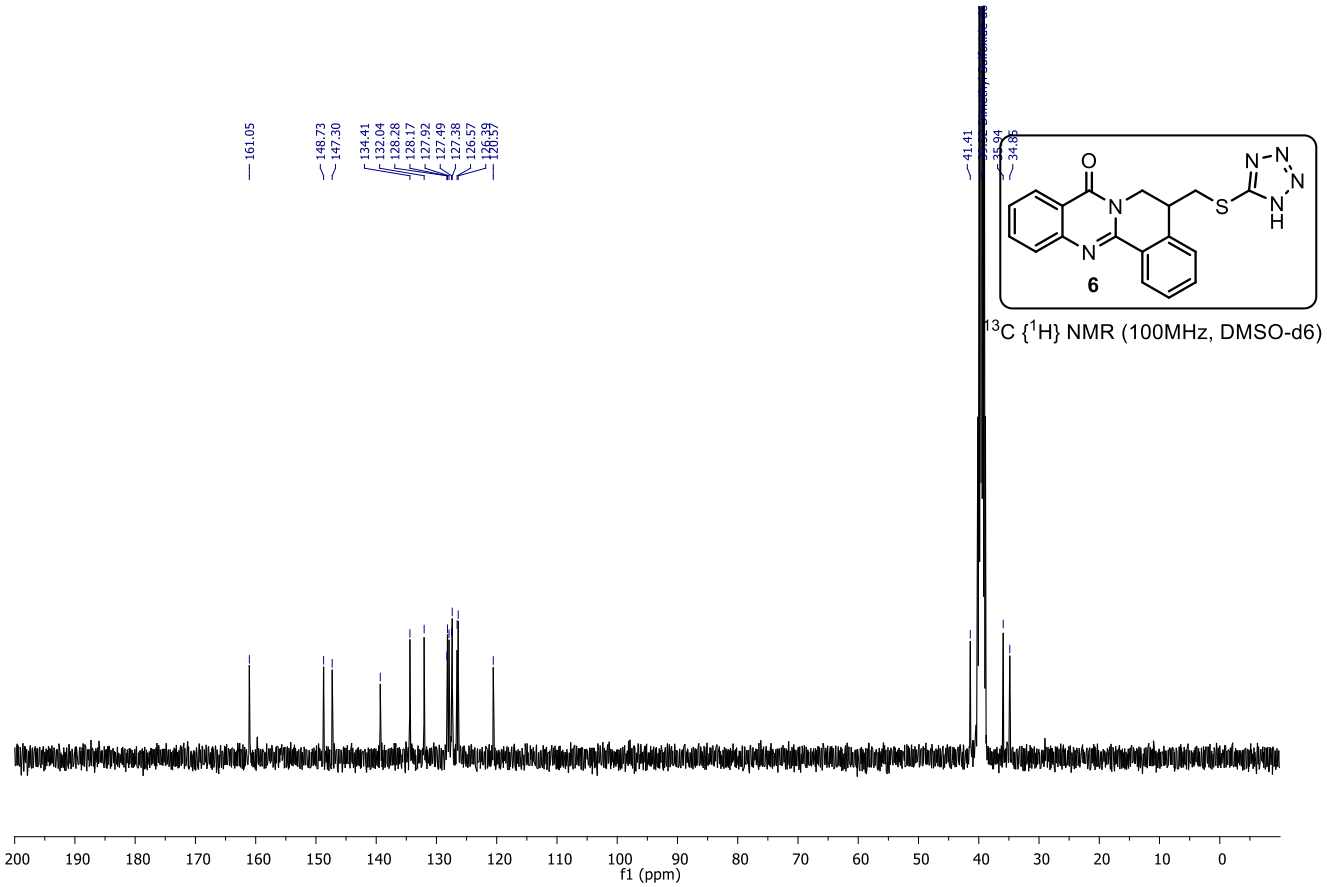
^{1}H NMR (400MHz, $CDCl_3$)



^{13}C {^{1}H} NMR (100MHz, $CDCl_3$)



^{1}H NMR (400MHz, DMSO-d6)



^{13}C {^{1}H} NMR (100MHz, DMSO-d6)