Supporting Information

Highly Diastereoselective Oxa-[3+3] Cyclization with C,N-cyclic azomethine imines via Copper-Catalyzed Aerobic Oxygenated C=C bond of Indoles

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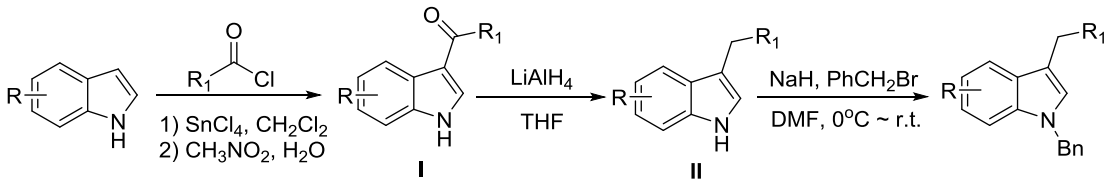
1. General Information

All reactions were performed under oxygen atmosphere using glassware unless otherwise noted, and all reagents were commercially available and used without further purification unless specified otherwise. Organic solutions were concentrated under reduced pressure on a rotary evaporator or an oil pump. Reactions were monitored by thin layer chromatography (TLC), which carried out on GF254 plates. Visualization was performed by fluorescence quenching with UV light at 254 nm, phosphormolybdic acid or $KMnO_4$ straining solution followed by heating. Flash chromatography was performed with 200-300 mesh silica gels. ^{1}H NMR spectra were measured on a Bruker 400 (400 MHz) spectrometer and Bruker 500 (500 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from the residual solvent as an internal standard (δ 7.26 for $CDCl_3$ and δ 0.00 for TMS), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, AB q = AB quartet, m = multiplet, br = broad, and app = apparent), and coupling constants (Hz). ^{13}C NMR spectra were measured on a Bruker 400 and 500 (101 and 126 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard (δ 77.16 for $CDCl_3$). HRMS were recorded on a LCMS-IT-TOF.

2. Synthesis and Characterization of 3-substituted Indoles

The *N*-substituted indoles **1a-1d**, **1f-1g**, **1i**, **1j**, **1l**, **ln**, **1r-1u**[1] and **3v-3z**[2] were prepared according to known procedures. **1e**, **1h**, **lk**, **lm**, **lo-1q** were afforded as follow procedures.

2.1 General procedure for the synthesis of 1e and 1h[3]



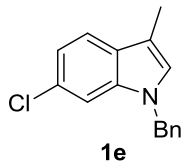
Step 1: To a stirring solution of indole (1.17 g, 10 mmol) in CH_2Cl_2 (20 mL) under argon at 0 ℃ was added $SnCl_4$ (1.44 mL, 12 mmol) in a single portion via syringe. After the ice bath was removed, the mixture was stirred at room temperature for 30 min, and then corresponding acyl chloride (10 mmol) was added in small portions to the suspension, followed by nitro methane (15 mL). The mixture was stirred for 2 h at room temperature. After being quenched with ice and water (30 mL), the mixture was filtered to remove inorganic precipitates, and the organic material was extracted with ethyl acetate (50 mL). The organic phase was dried over Na_2SO_4 and concentrated at reduced pressure, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (PE: EtOAc = 5:1 as the eluent) to give the corresponding immediate **I**.

Step 2: In a dry Shlenk tube, $LiAlH_4$ (15 mmol) in anhydrous THF (40 mL) was cooled at 0 ℃, a solution of the above ketone or aldehyde in THF (20 mL) was added dropwise in 15 min. The mixture was stirred overnight at room temperature. After the reaction was completed, H_2O (2 mL) was added carefully followed by 12 N NaOH (5 mL). The mixture was stirred for 15 min, then the water solid was removed by filtration and was washed with diethyl ether (3 x 20 mL). The combined organic phase was dried over Na_2SO_4, filtrated, and evaporated under reduced pressure.

The residue was purified by flash chromatography (PE:EtOAc = 20:1 as the eluent) to afford the corresponding immediate **II**.

Step 3: To a stirring solution of corresponding immediate **II** (1.41 g, 10 mmol) in DMF (20 ml) at 0 ℃ was added NaH (0.6 g, 1.5 equiv) in small portions. After 30 min, The $PhCH_2Br$ was added and then the ice bath was removed, the mixture was stirred for 1h at room temperature, and then H_2O (100 mL) was added, the suspension was extracted with ethyl acetate (3 x 20 mL), The combined organic phase was dried over Na_2SO_4, filtrated, and evaporated under reduced pressure. The residue was purified by flash chromatography (PE:EtOAc = 100:1 as the eluent) to afford corresponding *N*-protected-3-substitued-1*H*-indole.

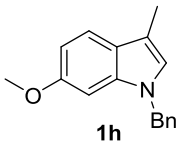
1-Benzyl-6-chloro-3-methyl-1H-indole (1e)



1e

Compound **1e** was prepared according to **step 2**, **step 3** with 6-chloro-1*H*-indole-3-carbaldehyde as starting material, white solid, 60% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 1H), 7.33-7.23 (m, 3H), 7.21 (s, 1H), 7.06 (t, *J* = 6.9 Hz, 3H), 6.84 (s, 1H), 5.16 (s, 2H), 2.29 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.36, 137.04, 128.86, 127.78, 127.74, 127.56, 126.78, 126.55, 120.00, 119.54, 111.19, 109.47, 49.86, 9.60; **HRMS** (ESI) calcd. for $C_{16}H_{15}NCl^+$ $[M+H]^+$ 256.0888, found 256.0882.

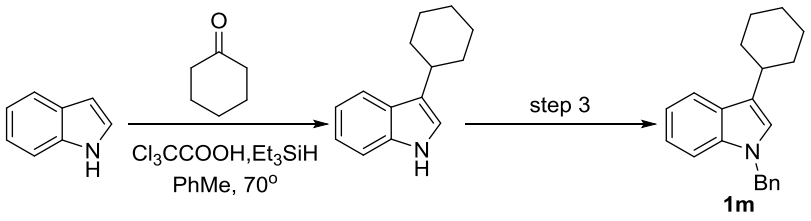
1-Benzyl-6-methoxy-3-methyl-1H-indole (1h)



1h

Compound **1h** was prepared according to **step 2**, **step 3** with 6-methoxy-1*H*-indole-3-carbaldehyde as starting material, PE:EtOAc = 40:1 as the eluent, white solid, 63% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.26 (m, 3H), 7.22-7.13 (m, 3H), 7.09 (d, *J* = 2.4 Hz, 1H), 6.92 (s, 1H), 6.89 (dd, *J* = 8.8, 2.4 Hz, 1H), 5.26 (s, 2H), 3.93 (s, 3H), 2.37 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.82, 138.03, 132.05, 129.25, 128.72, 127.50, 126.79, 126.61, 111.82, 110.31, 101.02, 55.99, 50.01, 9.70; **HRMS** (ESI) calcd. for $C_{17}H_{18}NO^+$ $[M+H]^+$ 252.1383, found 252.1372.

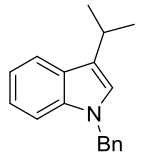
2.2 Synthesis of 3-substituted indole 1k and 1m[4]



1m

Into a 100 mL three-neck flask equipped with a magnetic stir bar, glass stopper, dry toluene (8 mL), Et_3SiH (4.5 g, 39 mmol) and Cl_3CCOOH(3.2 g, 19 mmol) were added under N_2 atmosphere. The mixture was heated to 70 ℃ and treated with a solution of cyclohexanone (1.38 g, 14 mmol) and indole (1.5 g, 13 mmol) in toluene (5 mL) dropwise by syringe. The reaction mixture was then stirred for additional 3 h at this temperature. After cooling to room temperature, the mixture was quenched with saturated Na_2CO_3, extracted with EtOAc. The combined organic layer was dried over anhydrous Na_2SO_4, filtrated, concentrated under vacuum, and the residue was purified by flash column chromatography (PE/EtOAc = 30:1) to give an immediate. Next obtained immediate

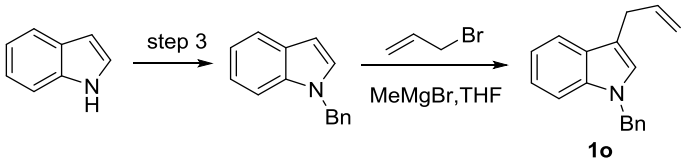
was conducted **step 3** to give compound **1m**, white solid in 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.35 – 7.20 (m, 4H), 7.18 – 7.02 (m, 4H), 6.86 (s, 1H), 5.26 (s, 2H), 2.85 (ddd, *J* = 14.4, 8.9, 5.7 Hz, 1H), 2.11 (d, *J* = 6.4 Hz, 2H), 1.84 (dd, *J* = 5.3, 2.9 Hz, 2H), 1.77 (dd, *J* = 12.6, 1.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.93, 136.78, 128.69, 127.45, 126.78, 123.72, 122.48, 121.51, 119.52, 118.61, 109.62, 49.89, 35.48, 34.19, 26.95, 26.55. These spectra data matched with those previously published.



1k

Compound **1k** was prepared with propan-2-one as substrate, Colorless oil, 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.30 – 7.20 (m, 4H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.11 – 7.07 (m, 3H), 6.86 (s, 1H), 5.24 (s, 2H), 3.30 – 3.12 (m, 1H), 1.35 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.98, 137.02, 128.75, 128.71, 127.51, 126.81, 123.63, 123.31, 121.62, 119.63, 118.73, 109.70, 49.93, 25.57, 23.53. These spectra data matched with those previously published.

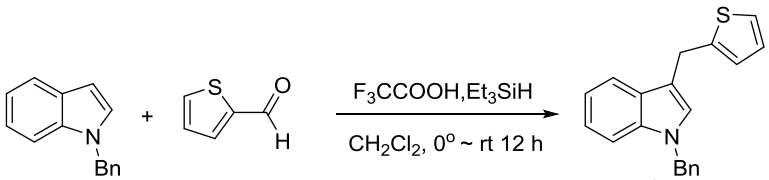
2.3 Synthesis of 3-substituted indole 1o[5]



1o

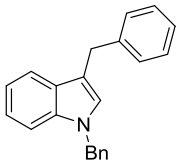
To a solution of *N*-substituted indole (1 equiv) in THF (10 mL) was added the solution of MeMgBr (3.0 N in diethyl ether, 1.2 equiv) at room temperature, the mixture was cooled to -10 ^{o}C after 1 hour, and a solution of allybromide (1.0 equiv in 4 mL THF) was added over 15 minutes. The reaction mixture was warmed to room temperature for 24 h. The reaction was quenched with water (20 mL), extracted with EtOAc (2 x 100 mL), concentrated and purified by column to afford compound **1o**. Yellow oil, 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.47 – 7.35 (m, 4H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 6.8 Hz, 2H), 7.04 (s, 1H), 6.34 – 6.14 (m, 1H), 5.36 (s, 2H), 5.32 (d, *J* = 7.1 Hz, 1H), 5.24 (d, *J* = 10.0 Hz, 1H), 3.69 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.91, 137.54, 136.99, 128.84, 128.27, 127.64, 126.92, 126.01, 121.90, 119.43, 119.11, 115.27, 113.77, 109.77, 49.98, 29.97. These spectra data matched with those previously published.

2.4 General procedure for the synthesis of 1p and 1q[6]



1q

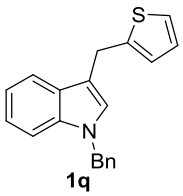
To a solution of *N*-substituted indole (1.0 equiv) in CH_2Cl_2 (25 mL) was added the corresponding aldehyde (2.44 mmol, 1.0 equiv) at room temperature. Triethylsilane (1.08 mL, 6.83 mmol, 2.8 equiv) and trifluoroacetic acid (0.38 mL, 4.88 mmol, 2.0 equiv) were added then at 0 ℃. The solution was allowed to warm to room temperature for 12 h prior to concentration under reduced pressure. The resulting oil was purified by column chromatography (PE:EtOAc = 80:1) to give **1q** as a white solid, 65% yield.



1p

Compound **1k** was prepared with benzaldehyde as substrate, white solid, 65% yield, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.9 Hz, 1H), 7.44 – 7.30 (m, 8H), 7.30 – 7.22 (m, 2H), 7.20 – 7.12 (m, 3H), 5.32 (s, 2H), 4.22 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.36, 137.83, 136.94, 128.83, 128.80, 128.78, 128.75, 128.68, 128.50, 128.44, 128.42, 128.39, 128.25, 127.57, 126.82, 126.78, 126.64, 125.92, 121.86, 119.43, 119.14, 114.99, 109.72, 49.96, 31.66.These spectra data matched with those previously published.

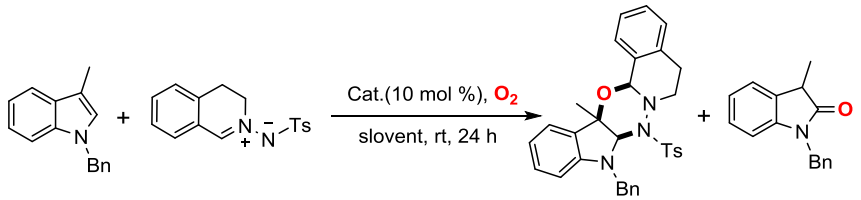
1-Benzyl-3-(thiophen-2-ylmethyl)-1H-indole (1q)



1q

Compound **1q** was prepared with furaldehyde as substrate, brown solid, 54% yield; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.30-7.20 (m, 4H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.11-7.04 (m, 4H), 6.96 (s, 1H), 6.89 (dd, *J* = 8.1, 3.3 Hz, 1H), 6.85 (d, *J* = 10.3 Hz, 1H), 5.24 (s, 2H), 4.30 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.86, 137.70, 136.84, 128.77, 127.86, 127.58, 126.76, 126.71, 126.50, 124.69, 123.41, 121.94, 119.28, 119.23, 114.43, 109.77, 49.98, 25.95; **HRMS** (ESI) calcd. for $C_{20}H_{18}NS^{+}$ $[M+H]^{+}$ 304.1154, found 304.1143.

3 Tables of the Optimization of Reaction Conditions[a]



1a 3a 4a **5**, < 5% yield

entry	cat.	solvent	yield (%)[b]
1[c]	$Cu(CH_3CN)_4BF_4$	CH_2Cl_2	46
2	$Cu(CH_3CN)_4BF_4$	CH_2Cl_2	70
3	$Cu(CH_3CN)_4BF_4$	toluene	50
4	$Cu(CH_3CN)_4BF_4$	Et_2O	trace
5	$Cu(CH_3CN)_4BF_4$	DCE	69
6	$Cu(CH_3CN)_4BF_4$	$CHCl_3$	67
7	$Cu(CH_3CN)_4BF_4$	THF	48
8	$Cu(CH_3CN)_4BF_4$	CH_3CN	45
9	$Cu(CH_3CN)_4BF_4$	$CDCl_3$	67
10[d]	$Cu(CH_3CN)_4BF_4$	CH_2Cl_2	trace
10[e]	$Cu(CH_3CN)_4BF_4$	CH_2Cl_2	71
11	$Cu(CH_3CN)_4PF_6$	CH_2Cl_2	73
12	$Pd(CH_3CN)_4(OTf)_2$	CH_2Cl_2	60
13	$AgSbF_6$	CH_2Cl_2	50
14	$AgN(OTf)_2$	CH_2Cl_2	48
15	CuI	CH_2Cl_2	64
16	$Pd(OAc)_2$	CH_2Cl_2	63
17	$Cu(OAc)_2$	CH_2Cl_2	81
18[f]	$Cu(CH_3CN)_4BF_4$+$CuClO_4$	CH_2Cl_2	45

19[f]	$Cu(CH_3CN)_4PF_4$+$CuClO_4$	CH_2Cl_2	64
20	$CuSO_4{\cdot}5H_2O$	CH_2Cl_2	77
21[g]	$Cu_2(OH)_2CO_3$	CH_2Cl_2	79
22[h]	**$Cu_2(OH)_2CO_3$+$Cu(OAc)_2$**	**CH_2Cl_2**	**88**
23[i]	$Cu_2(OH)_2CO_3$+$Cu(OAc)_2$	CH_2Cl_2	84

[a]Unless otherwise stated, reactions were conducted on a 0.2 mmol scale with **1a** (1.0 equiv), **3a** (1.5 equiv), and catalyst (0.1 equiv) in CH_2Cl_2 (1.0 mL) solvent at room temperature for 24 h. For all of cases, > 99:1 dr values was detected. [b]Isolated yield. [c]air was used as the oxiadant. [d]4Å MS was used. [e]0.5 % H_2O was added. [f] $Cu(CH_3CN)_4BF_4$ (10 mol %) + $CuClO_4$ (5 mol %) or $Cu(CH_3CN)_4PF_4$ (10 mol %) + $CuClO_4$ (5 mol %) was used. [g]**3a** (1.1 equiv) was used. [h]$Cu_2(OH)_2CO_3$ (10 mol %) + $Cu(OAc)_2$ (5 mol %) was used. [i]$Cu_2(OH)_2CO_3$ (5 mol %) + $Cu(OAc)_2$ (2.5 mol %) was used.

4. General Procedure for Indole Oxidation/1, 3-dipolar Cyclization reaction

4.1 Oxidation with Cu/O_2

An oven-dried 10 mL of Schlenk tube was charged with azomethine imine **3** (0.24 mmol), *N*-subsitiuted indoles **1** (0.2 mmol), $Cu_2(OH)_2CO_3$ (0.02 mmol) and $Cu(OAc)_2$ (0.01 mmol), then removed air by vaccum pump and 1 mL of CH_2Cl_2 was added. Subsequently, the mixture was stirred with an O_2 or $^{18}O_2$ balloon at room temperature. After for 24 h, the mixture was crude purified by short column chromatography (CH_2Cl_2, 50 mL), then the organic solvent was removed under reduced pressure. The obtained residue was purified by flash column chromatography to afford the corresponding cyclization product **4**.

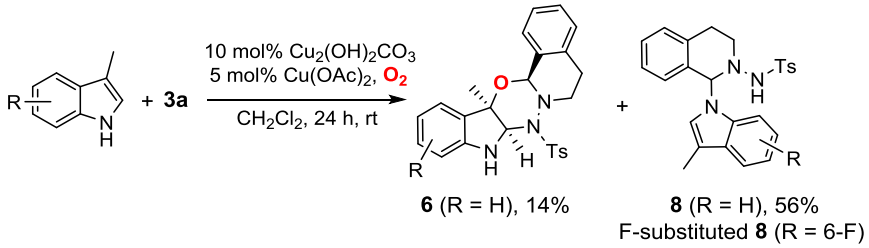
4.2 Oxidation with DMD

An oven-dried 10 mL of Schlenk tube was charged with azomethine imine **3** (0.2 mmol) and *N*-subsitiuted indoles **1** (0.24 mmol), dissolved in 2 mL of DMD at -20 ℃. After 2 h, the organic solvent was removed under reduced pressure. The obtained residue was purified by flash column chromatography to afford the corresponding cyclization product **4**.

4.3 Oxidation with *m*-CPBA

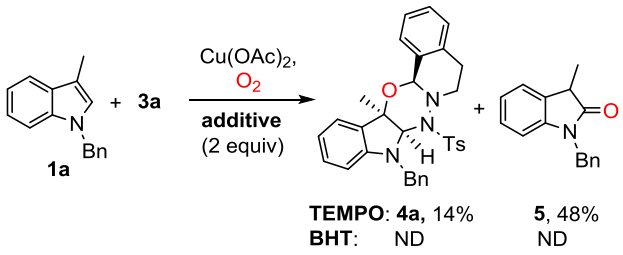
An oven-dried 10 mL of Schlenk tube was charged with azomethine imine **3** (0.24 mmol), *N*-subsitiuted indoles **1** (0.2 mmol), $Cu_2(OH)_2CO_3$ (0.02 mmol) and $Cu(OAc)_2$ (0.01 mmol), dissolved in 1 mL of CH_2Cl_2. Subsequently, *m*-CPBA (2 equiv) was added in small portion at 0 ℃. Then the mixture was stirred at room temperature for 2 h. After finished, the mixture was crude purified by short column chromatography (CH_2Cl_2, 50 mL), then the organic solvent was removed under reduced pressure. The obtained residue was purified by flash column chromatography to afford the corresponding cyclization product **4**.

4.4 Oxidation with Cu/O_2 when *NH*- indoles as the substrate



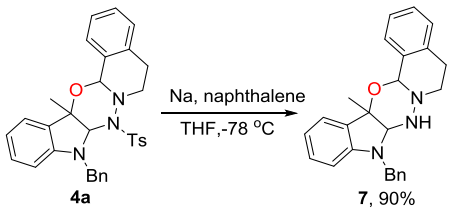
An oven-dried 10 mL of Schlenk tube was charged with azomethine imine **3a** (0.24 mmol), 3-methyl-*NH*-indoles (0.2 mmol), $Cu_2(OH)_2CO_3$ (0.02 mmol) and $Cu(OAc)_2$ (0.01 mmol), then removed air by vaccum pump and 1 mL of CH_2Cl_2 was added. Subsequently, the mixture was stirred with an O_2 balloon at room temperature. After for 24 h, the mixture was crude purified by short column chromatography (CH_2Cl_2, 50 mL), then the organic solvent was removed under reduced pressure. The obtained residue was purified by flash column chromatography to afford the corresponding cyclization product **4** and *N*-1 substituted products.

4.5 The general procedure of control experiments



An oven-dried 10 mL of Schlenk tube was charged with azomethine imine **3** (0.24 mmol), *N*-subsitiuted indoles **1** (0.2 mmol), $Cu_2(OH)_2CO_3$ (0.02 mmol), $Cu(OAc)_2$ (0.01 mmol) and additive (2 equiv), then removed air by vaccum pump and 1 mL of CH_2Cl_2 was added. Subsequently, the mixture was stirred with an oxygen balloon at room temperature. After for 24 h, the mixture was crude purified by short column chromatography (CH_2Cl_2, 50 mL), then the organic solvent was removed under reduced pressure. The obtained residue was purified by flash column chromatography to afford the corresponding cyclization product **4** when TEMPO as the additive. The products were no detected by TLC when BHT as additive.

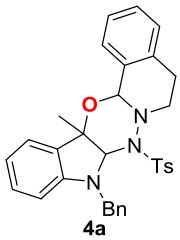
The synthesis of compound 7[7]



To a stirred solution of naphthalene (71 mg, 0.55 mmol) in freshly distilled THF (2.5 mL), sodium (13 mg, 0.53 mmol) was added. After 45 min of stirring at ambient temperature (dark-green color), the mixture was cooled to -78 °C and a solution of compound **4a** (135 mg, 0.25 mmol) in THF (2 mL) was added. The reaction mixture was stirred at that temperature for 30 min, quenched with sat. aqueous NH_4Cl (15 mL) and extracted with $CHCl_3$ (2 x 20 mL). The combined organic layers were dried ($MgSO_4$) and evaporated to give the target compound **7** as white solid (PE:EtOAc = 6 :1, 86 mg, 90 %).

5. Analytic and Characterization Data for Oxygenation/Cyclizaiton Product 4

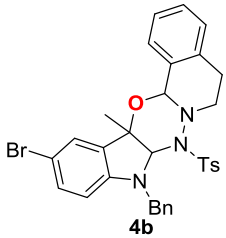
9-Benzyl-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4a)



4a

Afforded according to the general procedure as a white solid in 88% yield, purified by flash chromatography (PE:EtOAc = 10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.25 (t, *J* = 8.2 Hz, 4H), 7.20-7.12 (m, 3H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 3.5 Hz, 1H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.35 (d, *J* = 7.9 Hz, 1H), 5.34 (s, 1H), 5.14 (s, 1H), 4.82 (d, *J* = 16.3 Hz, 1H), 4.30 (d, *J* = 16.3 Hz, 1H), 3.91-3.73 (m, 1H), 2.76-2.63 (m, 1H), 2.53 (dd, *J* = 10.6, 5.8 Hz, 1H), 2.49-2.43 (m, 1H), 2.42 (s, 3H), 1.81 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.11, 144.17, 138.46, 135.31, 134.56, 133.27, 130.91, 130.03, 129.37, 129.07, 128.65, 128.50, 128.48, 128.26, 127.24, 126.88, 126.13, 123.40, 119.46, 109.61, 78.63, 74.60, 73.46, 50.57, 46.81, 30.01, 21.68, 19.26; **HRMS** (ESI) calcd. for $C_{32}H_{32}N_3O_3S^+$ $[M+H]^+$ 538.2159, found 538.2150; **HRMS** (ESI) calcd. for $C_{32}H_{32}N_3O_2{}^{18}OS^+$ $[M+H]^+$ 540.2201, found 540.2199.

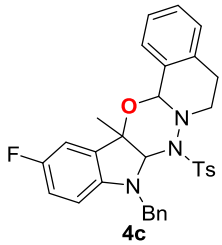
9-Benzyl-12-bromo-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4b)



4b

Afforded according to the general procedure as a white solid in 70% yield, purified by flash chromatography (PE:EtOAc = 12:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.39-7.33 (m, 2H), 7.34-7.29 (m, 2H), 7.29-7.23 (m, 4H), 7.23-7.19 (m, 1H), 7.19-7.14 (m, 2H), 7.12 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.04-6.97 (m, 1H), 6.21 (d, *J* = 8.4 Hz, 1H), 5.31 (s, 1H), 5.16 (s, 1H), 4.79 (d, *J* = 16.3 Hz, 1H), 4.28 (d, *J* = 16.3 Hz, 1H), 3.95-3.69 (m, 1H), 2.79-2.65 (m, 1H), 2.56 (dd, *J* = 10.5, 5.6 Hz, 1H), 2.52-2.45 (m, 1H), 2.42 (s, 3H), 1.78 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.89, 144.34, 137.76, 135.12, 134.48, 132.93, 132.84, 132.66, 129.43, 128.97, 128.68, 128.62, 128.59, 128.34, 127.21, 127.10, 126.64, 126.26, 111.10, 78.68, 74.41, 73.21, 50.15, 46.79, 29.95, 21.68, 19.26; **HRMS** (ESI) calcd. for $C_{32}H_{31}N_3O_3SBr^+$ $[M+H]^+$ 616.1264, found 616.1249.

9-benzyl-12-fluoro-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4c)

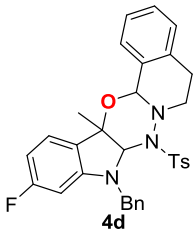


4c

Afforded according to the general procedure as a white solid in 60% yield, purified by flash chromatography (PE:EtOAc=15:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 7.2 Hz, 2H), 7.26 (t, *J* = 8.2 Hz, 2H), 7.29-7.20 (m, 3H), 7.22-7.11 (m, 3H), 7.04-6.98 (m, 1H), 6.95 (dd, *J* = 7.9, 2.6 Hz, 1H), 6.72 (td, *J* = 9.0, 2.6 Hz, 1H), 6.22 (dd, *J* = 8.6, 4.1 Hz, 1H), 5.35 (s, 1H), 5.12 (s, 1H), 4.81 (d, *J* = 16.2 Hz, 1H), 4.22 (d, *J* = 16.2 Hz, 1H), 3.95-3.74 (m, 1H), 2.77-2.65 (m, 1H), 2.57 (dd, *J* = 10.6, 5.7 Hz, 1H), 2.49 (d, *J* = 14.3 Hz, 1H), 2.42 (s, 3H), 1.79 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -124.57; **^{13}C NMR** (101 MHz, $CDCl_3$) δ157.11 ($J_{C\text{-}F}$ = 238.4 Hz), 146.26, 144.25, 138.23, 135.25, 134.52,

133.04, 132.12 ($J_{C\text{-}F}$ = 9.4 Hz), 129.39, 129.01, 128.64, 128.55, 128.31, 127.19, 126.98, 126.21, 116.16 ($J_{C\text{-}F}$ = 23.4 Hz), 111.04 ($J_{C\text{-}F}$ = 23.9 Hz), 110.27 ($J_{C\text{-}F}$ = 8.0 Hz), 78.72, 74.48, 73.75, 51.07, 48.13, 46.91, 30.00, 21.64, 19.27; **HRMS** (ESI) calcd. for $C_{32}H_{31}N_3O_3FS^+$ $[M+H]^+$ 556.2065, found 556.2055.

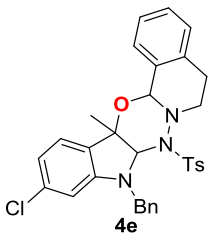
9-benzyl-11-fluoro-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4d)



4d

Afforded according to the general procedure as a white solid in 66% yield, purified by flash chromatography (PE:EtOAc = 16:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.30-7.22 (m, 3H), 7.22-7.10 (m, 4H), 7.10-6.91 (m, 1H), 6.40 (t, *J* = 8.8 Hz, 1H), 6.05 (d, *J* = 10.1 Hz, 1H), 5.32 (s, 1H), 5.19 (s, 1H), 4.78 (d, *J* = 16.3 Hz, 1H), 4.30 (d, *J* = 16.3 Hz, 1H), 3.94-3.63 (m, 1H), 2.69 (tt, *J* = 25.2, 12.6 Hz, 1H), 2.54 (dd, *J* = 10.6, 5.8 Hz, 1H), 2.48 (d, *J* = 15.1 Hz, 1H), 2.42 (s, 3H), 1.78 (s, 3H); **^{19}F NMR** (471 MHz, $CDCl_3$) δ -110.96; **^{13}C NMR** (101 MHz, $CDCl_3$) δ164.61 ($J_{C\text{-}F}$ = 245.4 Hz), 151.65 ($J_{C\text{-}F}$ = 12.2 Hz), 144.30, 137.66, 135.24, 134.49, 133.14, 129.41, 129.01, 128.65, 128.59, 128.32, 127.27, 127.16, 126.74 ($J_{C\text{-}F}$ = 2.0 Hz), 126.19, 124.51 ($J_{C\text{-}F}$ = 11.0 Hz), 105.56 ($J_{C\text{-}F}$ = 23.0 Hz), 97.51 ($J_{C\text{-}F}$ = 27.0 Hz), 78.67, 74.13, 73.52, 50.10, 46.76, 29.98, 21.66, 19.33; **HRMS** (ESI) calcd. for $C_{32}H_{31}N_3O_3FS^+$ $[M+H]^+$ 556.2065, found 556.2069.

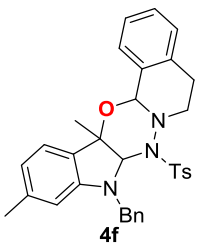
9-Benzyl-11-chloro-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4e)



4e

Afforded according to the general procedure as a white solid in 67% yield, purified by flash chromatography (PE:EtOAc = 15:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.41-7.30 (m, 4H), 7.30-7.22 (m, 3H), 7.21-7.14 (m, 3H), 7.12 (d, *J* = 7.9 Hz, 1H), 7.06-6.93 (m, 1H), 6.70 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.35 (d, *J* = 1.8 Hz, 1H), 5.31 (s, 1H), 5.19 (s, 1H), 4.77 (d, *J* = 16.4 Hz, 1H), 4.32 (d, *J* = 16.4 Hz, 1H), 3.89-3.61 (m, 1H), 2.80-2.61 (m, 1H), 2.57-2.45 (m, 2H), 2.42 (s, 3H), 1.78 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.07, 144.31, 137.59, 135.90, 135.18, 134.47, 133.06, 129.47, 129.40, 129.00, 128.64, 128.61, 128.30, 127.24, 127.17, 126.17, 124.36, 119.21, 109.57, 78.64, 74.16, 73.28, 49.98, 46.70, 29.95, 21.66, 19.24; **HRMS** (ESI) calcd. for $C_{32}H_{31}N_3O_3SCl^+$ $[M+H]^+$ 572.1769, found 572.1759.

9-Benzyl-11,13b-dimethyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4f)

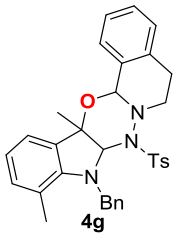


4f

Afforded according to the general procedure as a white solid in 86% yield, purified by flash chromatography (PE:EtOAc = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.26-7.20 (m, 3H), 7.18-7.07 (m, 4H), 7.01-6.93 (m, 1H), 6.57 (d, *J* = 7.5 Hz, 1H), 6.21 (s, 1H), 5.32 (s, 1H), 5.13 (s, 1H), 4.79 (d, *J* = 16.4 Hz, 1H), 4.31 (d, *J* = 16.4 Hz, 1H), 3.89-3.66 (m, 1H), 2.72-2.58 (m, 1H), 2.54-2.46 (m, 2H), 2.41 (s, 3H), 2.16 (s, 3H), 1.78 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.30, 144.07, 140.27, 138.62, 135.42, 134.53, 133.39, 129.31, 129.06, 128.64, 128.42, 128.26,

128.17, 127.25, 126.81, 126.04, 123.13, 120.12, 110.13, 78.62, 74.47, 73.67, 50.52, 46.75, 29.99, 21.84, 21.63, 19.27; **HRMS** (ESI) calcd. for $C_{33}H_{34}N_3O_3S^+$ $[M+H]^+$ 552.2315, found 552.2306.

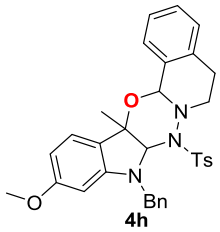
9-Benzyl-10,13b-dimethyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4g)



4g

Afforded according to the general procedure as a white solid in 83% yield, purified by flash chromatography (PE:EtOAc = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.37-7.31 (m, 4H), 7.30-7.26 (m, 1H), 7.20-7.08 (m, 6H), 7.02-6.94 (m, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.71 (t, *J* = 7.5 Hz, 1H), 5.33 (s, 1H), 5.20 (s, 1H), 4.92 (d, *J* = 17.8 Hz, 1H), 4.82 (d, *J* = 17.8 Hz, 1H), 3.75 (td, *J* = 12.2, 3.5 Hz, 1H), 2.74-2.50 (m, 2H), 2.48-2.41 (m, 1H), 2.40 (s, 3H), 2.25 (s, 3H), 1.83 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.07, 143.87, 139.80, 135.23, 134.43, 133.68, 133.44, 131.23, 129.12, 129.05, 128.71, 128.39, 128.36, 128.14, 126.83, 126.79, 126.02, 121.55, 119.55, 119.44, 78.50, 74.62, 73.34, 50.29, 46.12, 29.86, 21.61, 19.63, 19.01; **HRMS** (ESI) calcd. for $C_{33}H_{34}N_3O_3S^+$ $[M+H]^+$ 552.2315, found 552.2302.

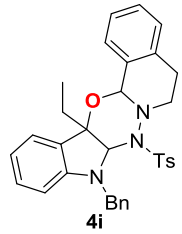
9-Benzyl-11-methoxy-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4h)



4h

Afforded according to the general procedure as a white solid in 64% yield, purified by flash chromatography (PE:EtOAc = 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.29-7.22 (m, 3H), 7.18 (d, *J* = 3.0 Hz, 3H), 7.01 (d, *J* = 2.9 Hz, 1H), 6.85 (d, *J* = 2.6 Hz, 1H), 6.60 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.22 (d, *J* = 8.6 Hz, 1H), 5.38 (s, 1H), 5.06 (s, 1H), 4.81 (d, *J* = 16.1 Hz, 1H), 4.17 (d, *J* = 16.1 Hz, 1H), 3.89 (dt, *J* = 18.1, 4.4 Hz, 1H), 3.70 (s, 3H), 2.75-2.63 (m, 1H), 2.57 (dd, *J* = 10.7, 5.6 Hz, 1H), 2.48 (dd, *J* = 16.0, 2.0 Hz, 1H), 2.42 (s, 3H), 1.81 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.78, 144.26, 144.15, 138.74, 135.30, 134.62, 133.23, 131.91, 129.37, 129.09, 128.66, 128.53, 128.48, 128.28, 127.22, 126.83, 126.13, 115.37, 110.65, 109.99, 78.73, 74.79, 73.97, 55.93, 51.59, 46.92, 30.04, 21.67, 19.25; **HRMS** (ESI) calcd. for $C_{33}H_{34}N_3O_4S^+$ $[M+H]^+$ 568.2265, found 568.2265.

9-benzyl-13b-ethyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4i)

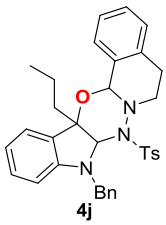


4i

Afforded according to the general procedure as a white solid in 83% yield, purified by flash chromatography (PE:EtOAc=10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.28-7.20 (m, 4H), 7.19-7.12 (m, 3H), 7.04 (t, *J* = 7.8 Hz, 1H), 7.01-6.94 (m, 1H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.36 (d, *J* = 7.9 Hz, 1H), 5.36 (s, 1H), 5.25 (s, 1H), 4.82 (d, *J* = 16.3 Hz, 1H), 4.33 (d, *J* = 16.3 Hz, 1H), 3.91-3.71 (m, 1H), 2.76-2.62 (m, 1H), 2.53 (dd, *J* = 10.6, 5.7 Hz, 1H), 2.46 (dd, *J* = 16.1, 1.7 Hz, 1H), 2.42 (s, 3H), 2.24 (q, *J* = 7.4 Hz, 2H), 1.09 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.68, 144.14, 138.45, 135.43, 134.57, 133.44, 129.90, 129.35, 128.98, 128.90, 128.54, 128.48,

128.29, 127.28, 126.88, 126.12, 124.04, 119.31, 109.50, 78.29, 78.20, 70.46, 50.46, 46.68, 30.00, 23.98, 21.68, 9.78; **HRMS** (ESI) calcd. for $C_{33}H_{34}N_3O_3S^+$ $[M+H]^+$ 552.2315, found 552.2305.

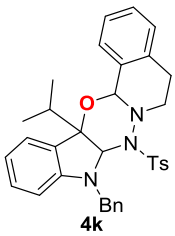
9-Benzyl-13b-propyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4j)



4j

Afforded according to the general procedure as a white solid in 82% yield, purified by flash chromatography (PE:EtOAc = 9:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.32-7.23 (m, 4H), 7.23-7.16 (m, 3H), 7.12-7.00 (m, 2H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.40 (d, *J* = 7.9 Hz, 1H), 5.33 (s, 1H), 5.27 (s, 1H), 4.86 (d, *J* = 16.3 Hz, 1H), 4.37 (d, *J* = 16.3 Hz, 1H), 3.98-3.76 (m, 1H), 2.89-2.72 (m, 1H), 2.65 (dd, *J* = 10.5, 5.6 Hz, 1H), 2.52 (d, *J* = 16.0 Hz, 1H), 2.46 (s, 3H), 2.18-2.09 (m, 2H), 1.63-1.42 (m, 2H), 1.06 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.55, 144.13, 138.44, 135.62, 134.62, 133.40, 129.90, 129.39, 129.13, 128.96, 128.48, 128.46, 128.44, 128.29, 127.27, 126.86, 126.08, 123.95, 119.24, 109.49, 78.24, 77.69, 71.13, 50.32, 46.83, 33.61, 30.00, 21.67, 18.89, 14.65; **HRMS** (ESI) calcd. for $C_{34}H_{36}N_3O_3S^+$ $[M+H]^+$ 566.2472, found 566.2461.

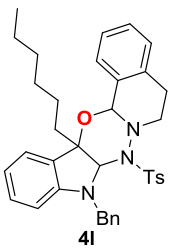
9-Benzyl-13b-isopropyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4k)



4k

Afforded according to the general procedure as a white solid in 81% yield, purified by flash chromatography (PE:EtOAc = 9:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.41-7.28 (m, 6H), 7.28-7.14 (m, 5H), 7.08-6.98 (m, 2H), 6.67 (t, *J* = 7.5 Hz, 1H), 6.38 (d, *J* = 7.9 Hz, 1H), 5.43 (s, 1H), 5.36 (s, 1H), 4.78 (d, *J* = 16.5 Hz, 1H), 4.37 (d, *J* = 16.4 Hz, 1H), 3.86-3.71 (m, 1H), 2.65 (dt, *J* = 14.1, 6.4 Hz, 2H), 2.46 (dd, *J* = 9.3, 6.5 Hz, 2H), 2.41 (s, 3H), 1.52 (d, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.76, 144.03, 138.34, 135.42, 134.53, 133.64, 129.63, 129.23, 128.85, 128.57, 128.48, 128.44, 128.32, 127.61, 127.28, 126.87, 126.09, 125.12, 118.87, 109.26, 80.71, 78.09, 69.94, 50.17, 46.47, 30.00, 28.56, 21.63, 20.01, 16.89; **HRMS** (ESI) calcd. for $C_{34}H_{36}N_3O_3S^+$ $[M+H]^+$ 566.2472, found 566.2471.

9-benzyl-13b-hexyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4l)

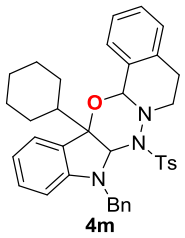


4l

Afforded according to the general procedure as a white solid in 80% yield, purified by flash chromatography (PE:EtOAc=6:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.26 (d, *J* = 6.1 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.21-7.13 (m, 2H), 7.08-6.89 (m, 2H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.36 (d, *J* = 7.9 Hz, 1H), 5.27 (s, 1H), 5.22 (s, 1H), 4.83 (d, *J* = 16.3 Hz, 1H), 4.33 (d, *J* = 16.3 Hz, 1H), 3.90-3.75 (m, 1H), 2.84-2.69 (m, 1H), 2.62 (dd, *J* = 10.5, 5.5 Hz, 1H), 2.49 (d, *J* = 14.5 Hz, 1H), 2.42 (s, 3H), 2.10 (d, *J* = 8.6 Hz, 2H), 1.52-1.20 (m, 8H), 0.93 (t, *J* = 6.5 Hz, 3H);**^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.57, 144.08, 138.46, 135.63, 134.63, 133.40, 129.87, 129.39, 129.19, 128.93, 128.47, 128.45, 128.42, 128.29, 127.26, 126.85, 126.08, 123.96, 119.26, 109.50, 78.23, 77.72,

71.24, 50.37, 46.84, 31.65, 31.38, 29.99, 29.85, 25.33, 22.72, 21.66, 14.11; **HRMS** (ESI) calcd. for $C_{37}H_{41}N_3O_3S^+$ $[M+H]^+$ 608.2941, found 608.2937.

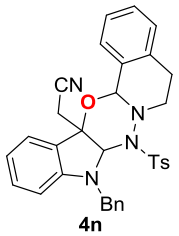
9-benzyl-13b-hexyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino [2,3-a]isoquinoline (4m)



4m

Afforded according to the general procedure as a white solid in 70% yield, purified by flash chromatography (PE:EtOAc=6:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.38-7.31 (m, 3H), 7.31-7.22 (m, 3H), 7.25-7.14 (m, 2H), 7.08-6.99 (m, 2H), 6.69 (t, *J* = 7.5 Hz, 1H), 6.40 (d, *J* = 7.9 Hz, 1H), 5.34 (s, 1H), 5.18 (s, 1H), 4.85 (d, *J* = 16.5 Hz, 1H), 4.41 (d, *J* = 16.4 Hz, 1H), 3.94-3.67 (m, 1H), 2.96-2.78 (m, 1H), 2.73 (dd, *J* = 10.3, 5.6 Hz, 1H), 2.54 (d, *J* = 15.5 Hz, 1H), 2.45 (s, 3H), 2.38 (d, *J* = 12.9 Hz, 1H), 2.10-1.92 (m, 2H), 1.84-1.73 (m, 2H), 1.74-1.65 (m, 1H), 1.61 (d, *J* = 12.7 Hz, 1H), 1.39-1.16 (m, 2H), 1.16-1.00 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.70, 144.04, 138.38, 135.91, 134.73, 133.55, 129.63, 129.40, 128.75, 128.54, 128.45, 128.41, 128.40, 127.86, 127.31, 126.85, 126.04, 125.36, 118.75, 109.23, 80.16, 78.05, 70.53, 49.84, 46.91, 39.23, 30.63, 30.04, 27.06, 26.85, 26.66, 26.58, 21.63; **HRMS** (ESI) calcd. for $C_{37}H_{39}N_3O_3S^+$ $[M+H]^+$ 606.2785, found 606.2779.

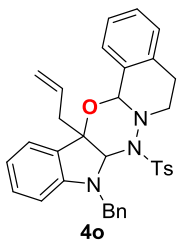
2-(9-Benzyl-8-tosyl-5,8a,9,14a-tetrahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquin olin-13b(8*H*)-yl)acetonitrile (4n)



4n

Afforded according to the general procedure as a white solid in 80% yield, purified by flash chromatography (PE:EtOAc = 10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 7.0 Hz, 1H), 7.46-7.40 (m, 1H), 7.36 (t, *J* = 7.1 Hz, 2H), 7.32 (d, *J* = 7.5 Hz, 2H), 7.30-7.26 (m, 3H), 7.24-7.19 (m, 2H), 7.12 (t, *J* = 7.2 Hz, 1H), 7.00 (d, *J* = 5.9 Hz, 1H), 6.82 (t, *J* = 7.3 Hz, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 5.44 (s, 1H), 5.15 (s, 1H), 4.78 (d, *J* = 16.3 Hz, 1H), 4.33 (d, *J* = 16.3 Hz, 1H), 3.78-3.68 (m, 1H), 3.61 (d, *J* = 17.1 Hz, 1H), 3.01 (d, *J* = 17.2 Hz, 1H), 2.66-2.51 (m, 1H), 2.48-2.35 (m, 5H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.90, 144.84, 137.81, 134.29, 134.13, 132.05, 131.07, 129.56, 129.37, 128.94, 128.79, 128.60, 128.14, 127.75, 127.19, 127.15, 126.60, 123.77, 120.17, 115.85, 110.01, 79.00, 73.46, 70.66, 50.59, 46.81, 29.86, 22.37, 21.70; **HRMS** (ESI) calcd. for $C_{33}H_{31}N_4O_3S^+$ $[M+H]^+$ 563.2111, found 563.2116.

13B-allyl-9-benzyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4o)

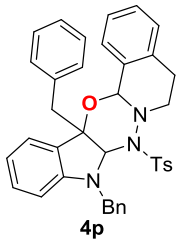


4o

Afforded according to the general procedure as a white solid in 73% yield, purified by flash chromatography (PE:EtOAc = 10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 6.7 Hz, 3H), 7.32-7.23 (m, 4H), 7.24-7.18 (m, 2H), 7.08 (t, *J* = 7.7 Hz, 1H), 7.05-6.98 (m, 1H), 6.77 (t, *J* = 7.4 Hz, 1H), 6.40 (d, *J* = 7.9 Hz, 1H), 5.96 (dt, *J* = 16.6, 9.1 Hz, 1H), 5.49 (s, 1H), 5.36 (d, *J* = 10.4 Hz, 1H), 5.31 (s, 1H), 5.29 (d, *J* = 10.4 Hz, 1H), 4.83 (d, *J* = 16.4 Hz, 1H), 4.37 (d, *J* = 16.3 Hz, 1H), 3.96-3.80 (m, 1H),

3.14 (dd, *J* = 14.5, 5.6 Hz, 1H), 3.03 (dd, *J* = 14.5, 8.3 Hz, 1H), 2.80-2.65 (m, 1H), 2.55 (dd, *J* = 10.8, 5.9 Hz, 1H), 2.51 (m, 1H), 2.46 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.51, 144.15, 138.44, 135.35, 134.50, 133.30, 132.85, 130.01, 129.32, 129.14, 129.00, 128.66, 128.54, 128.46, 128.26, 127.26, 126.88, 126.13, 124.29, 119.59, 119.35, 109.53, 78.47, 76.61, 70.71, 50.50, 46.62, 36.45, 29.98, 21.65; **HRMS** (ESI) calcd. for $C_{34}H_{34}N_3O_3S^+$ $[M+H]^+$ 564.2315, found 564.2322.

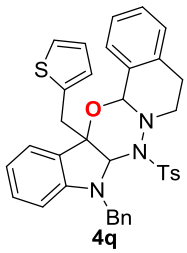
9,13B-dibenzyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4p)



4p

Afforded according to the general procedure as a white solid in 64% yield, purified by flash chromatography (PE:EtOAc = 6:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 5.5 Hz, 3H), 7.29-7.17 (m, 11H), 7.16-7.11 (m, 2H), 7.06-6.93 (m, 2H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.28 (d, *J* = 7.9 Hz, 1H), 5.77 (s, 1H), 5.42 (s, 1H), 4.63 (d, *J* = 16.5 Hz, 1H), 4.27 (d, *J* = 16.6 Hz, 1H), 3.75-3.60 (m, 3H), 2.64-2.52 (m, 1H), 2.46-2.34 (m, 5H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.15, 144.11, 138.01, 135.69, 135.11, 134.41, 133.43, 131.37, 129.97, 129.27, 129.08, 128.82, 128.62, 128.53, 128.39, 128.29, 127.06, 126.76, 126.72, 126.16, 125.02, 118.89, 109.05, 78.71, 78.63, 68.72, 49.64, 46.16, 37.73, 29.95, 21.67; **HRMS** (ESI) calcd. for $C_{38}H_{36}N_3O_3S^+$ $[M+H]^+$ 614.2472, found 614.2466.

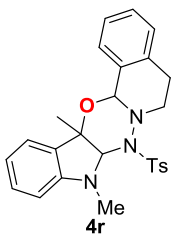
9-Benzyl-13b-(thiophen-2-ylmethyl)-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4q)



4q

Afforded according to the general procedure as a white solid in 42% yield, purified by flash chromatography (PE:EtOAc = 5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.33-7.16 (m, 11H), 7.15 (m, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 7.01-6.96 (m, 2H), 6.94 (d, *J* = 4.0 Hz, 1H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.32 (d, *J* = 7.9 Hz, 1H), 5.59 (s, 1H), 5.41 (s, 1H), 4.68 (d, *J* = 16.5 Hz, 1H), 4.30 (d, *J* = 16.5 Hz, 1H), 3.90 (d, *J* = 15.1 Hz, 1H), 3.82-3.64 (m, 2H), 2.70-2.57 (m, 1H), 2.54-2.48 (m, 1H), 2.48-2.38 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.40, 144.15, 138.09, 137.72, 135.17, 134.45, 133.19, 130.30, 129.32, 129.16, 128.73, 128.59, 128.50, 128.42, 128.40, 128.29, 127.15, 126.78, 126.66, 126.14, 125.48, 124.72, 119.05, 109.11, 78.81, 77.87, 69.20, 49.79, 46.38, 32.57, 29.93, 21.64; **HRMS** (ESI) calcd. for $C_{36}H_{34}N_3O_3S_2^+$ $[M+H]^+$ 620.2036, found 620.2027.

9,13B-dimethyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4r)

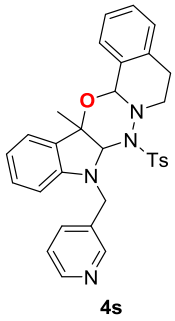


4r

Afforded according to the general procedure as a white solid in 90% yield, purified by flash chromatography (PE:EtOAc = 15:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 7.4 Hz, 2H), 7.25-7.16 (m, 1H), 7.19-7.10 (m, 4H), 7.05-6.93 (m, 1H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.55 (d, *J* = 7.9 Hz, 1H), 5.23 (s, 1H), 4.84 (s, 1H), 3.95-3.73 (m, 1H), 2.91 (s, 3H), 2.89-2.72 (m, 2H), 2.50 (dd, *J* = 14.9, 3.4 Hz, 1H), 2.44 (s, 3H), 1.73 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.27, 144.11, 135.79, 134.56, 133.33, 130.66, 130.17,

129.45, 129.03, 128.47, 128.29, 126.07, 123.38, 119.04, 108.25, 78.77, 74.66, 74.56, 46.29, 31.95, 29.90, 21.71, 18.82; **HRMS** (ESI) calcd. for $C_{26}H_{28}N_3O_3S^+$ $[M+H]^+$ 462.1846, found 462.1850.

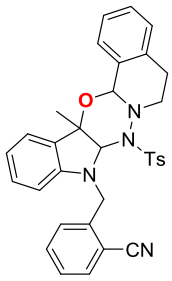
13B-methyl-9-(pyridin-3-ylmethyl)-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4s)



4s

Afforded according to the general procedure as a white solid in 45% yield, purified by flash chromatography (PE:EtOAc = 5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.69 (s, 1H)，8.53 (d, *J* =4.8, 1H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.26 (t, *J* = 6.7 Hz, 4H), 7.22-7.12 (m, 3H), 7.07 (t, *J* = 7.7 Hz, 1H), 7.03-6.97 (m, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 6.35 (d, *J* = 7.9 Hz, 1H), 5.28 (s, 1H), 5.13 (s, 1H), 4.84 (d, *J* = 16.5 Hz, 1H), 4.34 (d, *J* = 16.5 Hz, 1H), 3.92-3.70 (m, 1H), 2.82-2.68 (m, 1H), 2.60-2.53 (m, 1H), 2.49 (d, *J* = 14.8 Hz, 1H), 2.43 (s, 3H), 1.78 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.57, 149.05, 148.55, 144.39, 135.21, 135.08, 134.48, 133.91, 133.08, 130.96, 130.16, 129.46, 129.00, 128.59, 128.54, 128.29, 126.17, 123.65, 123.45, 119.90, 109.25, 78.66, 74.59, 73.49, 48.14, 47.00, 29.98, 21.69, 19.35; **HRMS** (ESI) calcd. for $C_{31}H_{31}N_4O_3S^+$ $[M+H]^+$ 561.1931, found 561.1919.

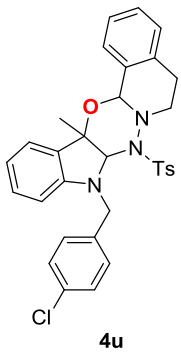
2-((13B-methyl-8-Tosyl-5,8a,13b,14a-tetrahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinolin-9(8*H*)-yl)methyl)benzonitrile (4t)



4t

Afforded according to the general procedure as a white solid in 83% yield, purified by flash chromatography (PE:EtOAc=10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.51-7.41 (m, 2H), 7.39-7.32 (m, 1H), 7.28 (d, *J* = 7.9 Hz, 3H), 7.22-7.16 (m, 3H), 7.07 (td, *J* = 7.8, 1.1 Hz, 1H), 7.01 (d, *J* = 3.1 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.25 (d, *J* = 7.9 Hz, 1H), 5.38 (s, 1H), 5.25 (s, 1H), 4.96 (d, *J* = 17.5 Hz, 1H), 4.61 (d, *J* = 17.5 Hz, 1H), 3.83-3.70 (m, 1H), 2.81-2.66 (m, 1H), 2.54-2.44 (m, 2H), 2.42 (s, 3H), 1.83 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.14, 144.34, 141.99, 135.15, 134.38, 133.15, 132.92, 130.82, 130.19, 129.67, 129.47, 129.07, 128.68, 128.58, 128.26, 127.73, 127.40, 126.21, 123.72, 119.92, 117.31, 110.97, 108.89, 78.67, 74.59, 72.76, 47.72, 46.83, 29.99, 21.67, 19.28; **HRMS** (ESI) calcd. for $C_{33}H_{31}N_4O_3S^+$ $[M+H]^+$ 563.2111, found 563.2104.

9-(4-Chlorobenzyl)-13B-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (4u)

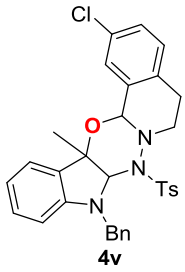


4u

Afforded according to the general procedure as a white solid in 81% yield, purified by flash chromatography (PE:EtOAc=15:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.30-7.26 (m, 2H), 7.26-7.23 (m, 3H), 7.20-7.13 (m, 3H), 7.05 (td, *J* = 7.8, 1.2 Hz, 1H), 7.02-6.97 (m, 1H), 6.79-6.71 (m, 1H), 6.32 (d, *J* = 7.9 Hz, 1H), 5.30 (s, 1H), 5.12 (s, 1H), 4.78 (d, *J* = 16.4 Hz, 1H), 4.26 (d, *J* = 16.4 Hz, 1H), 3.86-3.71 (m, 1H), 2.85-2.65 (m, 1H), 2.54 (dd, *J* = 10.4, 5.7 Hz, 1H), 2.48 (dd, *J* = 16.2, 1.6 Hz, 1H), 2.41 (s, 3H), 1.78 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 149.83, 144.33, 136.99, 135.30, 134.51, 133.18, 132.63, 130.96, 130.11, 129.46, 129.06,

128.67, 128.62, 128.59, 128.31, 126.19, 123.56, 119.73, 109.46, 78.67, 74.60, 73.50, 49.92, 46.97, 30.03, 21.71, 19.32; **HRMS** (ESI) calcd. for $C_{32}H_{30}N_3O_3SCl^+$ $[M+H]^+$572.1769, found 572.1764.

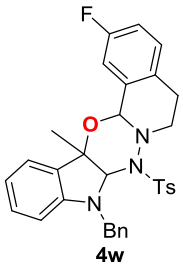
9-Benzyl-2-chloro-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4] oxadiazino[2,3-a]isoquinoline (4v)



4v

Afforded according to the general procedure as a white solid in 78% yield, purified by flash chromatography (PE:EtOAc = 15:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 7.1 Hz, 2H), 7.34-7.28 (m, 2H), 7.28-7.21 (m, 4H), 7.14 (dd, *J* = 6.1, 2.3 Hz, 2H), 7.06 (td, *J* = 7.8, 1.3 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 6.76 (td, *J* = 7.5, 0.8 Hz, 1H), 6.37 (d, *J* = 7.9 Hz, 1H), 5.24 (s, 1H), 5.13 (s, 1H), 4.81 (d, *J* = 16.3 Hz, 1H), 4.30 (d, *J* = 16.3 Hz, 1H), 3.79 (td, *J* = 12.4, 3.4 Hz, 1H), 2.77-2.59 (m, 1H), 2.55 (dd, *J* = 10.5, 5.5 Hz, 1H), 2.50-2.31 (m, 4H), 1.78(s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.06, 144.27, 138.37, 135.34, 134.90, 133.09, 131.76, 130.63, 130.13, 129.65, 129.41, 128.89, 128.68, 128.54, 128.46, 127.25, 126.89, 123.38, 119.54, 109.61, 78.12, 74.80, 73.62, 50.53, 46.61, 29.51, 21.65, 19.17; **HRMS** (ESI) calcd. for $C_{32}H_{31}N_3O_3SCl^+$ $[M+H]^+$ 572.1769, found 572.1760.

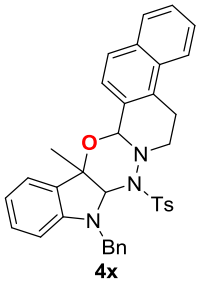
9-Benzyl-2-fluoro-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4] oxadiazino[2,3-a]isoquinoline (4w)



4w

Afforded according to the general procedure as a white solid in 73% yield, purified by flash chromatography (PE:EtOAc = 15:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.25-7.18 (m, 4H), 7.09-7.01 (m, 1H), 7.00-6.92 (m, 1H), 6.92-6.80 (m, 2H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.36 (d, *J* = 7.9 Hz, 1H), 5.27 (s, 1H), 5.14 (s, 1H), 4.81 (d, *J* = 16.2 Hz, 1H), 4.30 (d, *J* = 16.3 Hz, 1H), 3.88-3.71 (m, 1H), 2.68-2.60 (m, 1H), 2.53 (dd, *J* = 10.6, 5.6 Hz, 1H), 2.44 (d, *J* = 7.4 Hz, 1H), 2.43 (s, 3H), 1.79 (s, 3H); **^{19}F NMR** (471 MHz, $CDCl_3$) δ -116.94; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.18 ($J_{C\text{-}F}$ = 245.4 Hz), 150.08, 144.26, 138.39, 135.32, 134.95 ($J_{C\text{-}F}$ = 8.0 Hz), 130.69, 130.22 ($J_{C\text{-}F}$ = 3.0 Hz), 130.13, 129.77 ($J_{C\text{-}F}$ = 8.0 Hz), 129.40, 128.60, 128.48, 127.26, 126.91, 123.37, 119.55, 115.71($J_{C\text{-}F}$ = 42.0, 21.0 Hz), 109.63, 78.24, 77.34, 74.74, 73.56, 50.55, 46.78, 29.36, 21.65, 19.18; **HRMS** (ESI) calcd. for $C_{32}H_{31}N_3O_3FS^+$ $[M+H]^+$ 556.2065, found 556.2089.

9-Benzyl-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-benzo[f]indolo[2',3':5,6][1,3,4]o xadiazino[2,3-a]isoquinoline (4x)

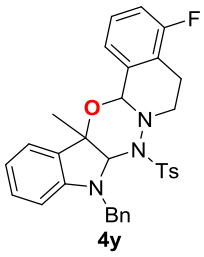


4x

Afforded according to the general procedure as a white solid in 85% yield, purified by flash chromatography (PE:EtOAc = 8:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.9 Hz, 3H), 7.80-7.71 (m, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.52-7.44 (m, 2H), 7.42 (d, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.30-7.19 (m, 5H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.36 (d, *J* = 7.9 Hz, 1H), 5.43 (s, 1H), 5.19 (s, 1H), 4.86 (d, *J* = 16.2 Hz, 1H), 4.33 (d, *J* = 16.2 Hz, 1H), 3.96 (td, *J* = 11.7, 3.5 Hz, 1H), 3.02 (d, *J* = 13.8 Hz, 1H), 2.90-2.78 (m, 1H), 2.73 (dd, *J* = 10.4, 5.9 Hz, 1H), 2.41 (s, 3H), 1.86 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.13, 144.19, 138.53, 135.32, 133.31, 131.37, 130.86, 130.27,

130.08, 129.38, 128.68, 128.50, 127.29, 126.91, 126.77, 126.24, 126.22, 126.17, 123.44, 123.20, 119.48, 109.58, 78.78, 74.83, 73.60, 50.64, 46.40, 26.69, 21.68, 19.32; **HRMS** (ESI) calcd. for $C_{29}H_{25}N_3O^+$ $[M\text{-}Ts]^+$ 432.2070, found 432.2070.

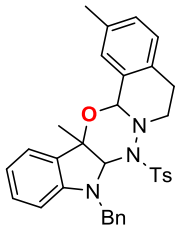
9-Benzyl-4-fluoro-13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4] oxadiazino[2,3-a]isoquinoline (4y)



4y

Afforded according to the general procedure as a white solid in 66% yield, purified by flash chromatography (PE:EtOAc = 15:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 7.4 Hz, 2H), 7.36 (q, *J* = 7.5 Hz, 2H), 7.33-7.22 (m, 4H), 7.23-7.14 (m, 1H), 7.10 (t, *J* = 7.7 Hz, 1H), 7.03 (d, *J* = 7.7 Hz, 1H), 6.95 (t, *J* = 8.7 Hz, 1H), 6.80 (t, *J* = 7.5 Hz, 1H), 6.42 (d, *J* = 7.9 Hz, 1H), 5.45 (s, 1H), 5.21 (s, 1H), 4.85 (d, *J* = 16.3 Hz, 1H), 4.36 (d, *J* = 16.3 Hz, 1H), 3.91-3.68 (m, 1H), 2.67 (d, *J* = 13.6 Hz, 1H), 2.56 (dd, *J* = 10.7, 6.0 Hz, 1H), 2.51-2.38 (m, 4H), 1.88 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -119.28; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.10 ($J_{C\text{-}F}$ = 245.4 Hz), 150.09, 144.30, 138.37, 135.62 ($J_{C\text{-}F}$ = 5.0 Hz), 135.18, 130.72, 130.15, 129.40, 128.68, 128.52, 127.37 ($J_{C\text{-}F}$ = 8.0 Hz), 127.27, 126.96, 124.56 ($J_{C\text{-}F}$ = 4.0 Hz), 123.39, 122.43 ($J_{C\text{-}F}$ = 20.0 Hz), 119.53, 114.65 ($J_{C\text{-}F}$ = 22.0 Hz), 109.63, 78.12 ($J_{C\text{-}F}$ = 2.0 Hz), 74.84, 73.39, 50.63, 45.75, 23.27, 23.23, 21.66, 19.25; **HRMS** (ESI) calcd. for $C_{32}H_{31}N_3O_3FS^+$ $[M+H]^+$ 556.2065, found 556.2095.

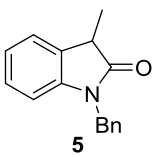
9-Benzyl-2,13b-dimethyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadi azino[2,3-a]isoquinoline



4z

Afforded according to the general procedure as a white solid in 86% yield, purified by flash chromatography (PE:EtOAc = 15:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.3 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 2H), 7.33-7.26 (m, 3H), 7.08-6.98 (m, 3H), 6.92 (d, *J* = 7.8 Hz, 1H), 6.78 (t, *J* = 7.4 Hz, 1H), 6.38 (d, *J* = 7.9 Hz, 1H), 5.35 (s, 1H), 5.17 (d, *J* = 4.2 Hz, 1H), 4.85 (d, *J* = 16.3 Hz, 1H), 4.32 (d, *J* = 16.3 Hz, 1H), 3.84 (dd, *J* = 16.0, 7.1 Hz, 1H), 2.74-2.60 (m, 1H), 2.55 (dd, *J* = 10.3, 5.3 Hz, 1H), 2.47-2.43 (m, 4H), 2.32 (s, 3H), 1.85 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 150.19, 144.18, 138.52, 135.70, 135.40, 133.11, 131.52, 131.02, 130.03, 129.52, 129.48, 129.41, 128.69, 128.53, 128.18, 127.29, 126.92, 123.51, 119.47, 109.61, 78.72, 74.61, 73.52, 50.60, 47.04, 29.67, 21.72, 21.01, 19.30. **HRMS** (ESI) calcd. for $C_{33}H_{34}N_3O_3FS^+$ $[M+H]^+$ 552.2243, found 552.2245.

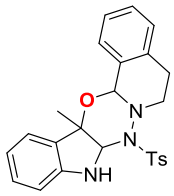
1-Benzyl-3-methylindolin-2-one (5)



5

White solid, < 5% yield; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.18 (m, 6H), 7.15 (t, *J* = 7.7 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 4.91 (s, 2H), 3.53 (q, *J* = 7.6 Hz, 1H), 1.53 (d, *J* = 7.6 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.75, 143.10, 136.02, 130.67, 128.76, 127.79, 127.56, 127.29, 123.57, 122.41, 108.97, 43.68, 40.57, 15.62; **HRMS** (ESI) calcd. for $C_{16}H_{15}NO^+$ $[M+H]^+$ 238.1226, found 238.1224; **HRMS** (ESI) calcd. for $C_{16}H_{15}N^{18}ONa^+$ $[M+Na]^+$ 262.1088, found 262.1086.

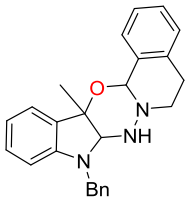
13b-methyl-8-tosyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (6)



6

Afforded according to the general procedure as a white solid in 14% yield, purified by flash chromatography (PE:EtOAc = 3:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.91 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.39-7.27 (m, 5H), 7.16 (d, *J* = 7.5 Hz, 1H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.67 (t, *J* = 7.7 Hz, 1H), 5.21 (d, *J* = 6.9 Hz, 1H), 4.91 (s, 1H), 4.54 (s, 1H), 3.33 (s, 1H), 3.12-2.96 (m, 1H), 2.95-2.82 (m, 1H), 2.61- 2.48 (m, 1H), 2.44 (s, 3H), 2.43-2.31 (m, 1H), 1.67 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 148.03, 144.87, 135.66, 135.26, 132.62, 129.74, 129.49, 129.33, 129.13, 128.79, 128.76, 128.44, 126.46, 124.25, 122.33, 114.01, 89.55, 78.26, 76.00, 49.34, 29.38, 29.25, 21.73. **HRMS** (ESI) calcd for $C_{25}H_{25}N_3O_3SNa^+$ $[M+Na]^+$ 470.1509, found 470.1512.

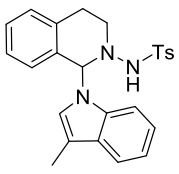
9-benzyl-13b-methyl-5,8,8a,9,13b,14a-hexahydro-6*H*-indolo[2',3':5,6][1,3,4]oxadiazino[2,3-a]isoquinoline (7)



7

White solid, 90% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33 (d, *J* = 7.3 Hz, 2H), 7.31 -7.21 (m, 5H), 7.18-7.12 (m, 2H), 7.09- 6.98 (m, 2H), 6.68 (t, *J* = 7.4 Hz, 1H), 6.46 (d, *J* = 7.9 Hz, 1H), 5.43 (s, 1H), 4.75 (d, *J* = 15.8 Hz, 1H), 4.39 (d, *J* = 15.8 Hz, 1H), 4.26 (s, 1H), 3.85 (td, *J* = 11.2, 3.8 Hz, 1H), 3.71 (d, *J* = 2.6 Hz, 1H), 3.09 - 3.00 (m, 1H), 2.92 (ddd, *J* = 16.9, 11.4, 5.7 Hz, 1H), 2.69 (d, *J* = 16.1 Hz, 1H), 1.82 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 150.05, 138.19, 135.11, 134.45, 131.64, 129.71, 128.69, 128.43, 128.31, 128.17, 127.83, 126.84, 125.95, 123.62, 118.27, 108.41, 81.17, 76.11, 73.76, 48.37, 47.18, 30.23, 19.10; **HRMS** (ESI) calcd for $C_{25}H_{25}N_3O^+$ $[M+H]^+$384.2070, found 384.2080.

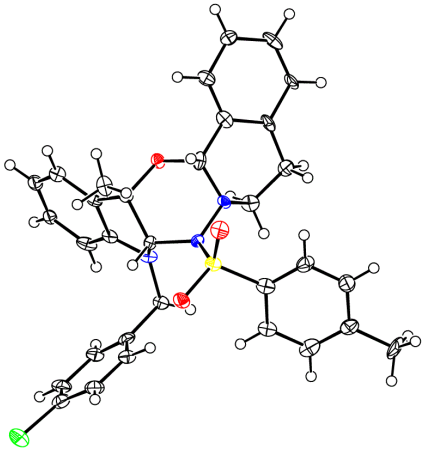
4-Methyl-*N*-(1-(3-methyl-1*H*-indol-1-yl)-3,4-dihydroisoquinolin-2(1*H*)-yl)benzenesulfonamide (8)



8

White solid, 56% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.31- 7.15 (m, 5H), 7.15- 7.03 (m, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.37 (s, 1H), 6.30 (s, 1H), 5.62 (s, 1H), 3.50-3.24 (m, 1H), 3.04 (ddd, *J* = 16.3, 10.0, 6.0 Hz, 1H), 2.91 (d, *J* = 16.7 Hz, 1H), 2.80- 2.68 (m, 1H), 2.41 (s, 3H), 2.15 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.94, 137.91, 135.30, 134.01, 132.81, 129.38, 128.93, 128.61, 128.49, 128.43, 128.11, 126.84, 124.79, 122.23, 119.56, 118.81, 111.73, 110.71, 72.70, 48.28, 28.61, 21.73, 9.67. **HRMS** (ESI) calcd for $C_{25}H_{25}N_3O_2SNa^+$ $[M+Na]^+$ 454.1560, found 454.1564.

6. 1) X-Ray Crystallographic Data of 4u (CCDC number: 1567024)



Bond precision:	C-C = 0.0090 A		Wavelength = 1.54184
Cell:	a = 8.6912 (5)	b = 27.8849 (16)	c = 11. 4280 (8)
	alpha = 90	beta = 94.876 (5)	gamma = 90
Temperature:	100 K		
	Calculated		Reported
Volume	2759.6 (3)		2759.6(3)
Space group	P 21		P 1 21 1
Hall group	P 2yb		P 2yb
Moiety formula	C32 H30 Cl N3 O3 S		C32 H30 Cl N3 O3 S
Sum formula	C32 H30 Cl N3 O3 S		C32 H30 Cl N3 O3 S
Mr	572.10		572.10
Dx,g cm-3	1.377		1.377
Z	4		4
Mu (mm-1)	2.252		2.252
F000	1200.0		1200.0
F000'	1205.91		
h,k,lmax	10, 33, 13		10, 33, 13
Nref	9854 [5038]		7260
Tmin,Tmax	0.612, 0.798		0.516, 1.000
Tmin'	0.485		

Correction method= # Reported T Limits: Tmin = 0.006 Tmax = 1.000

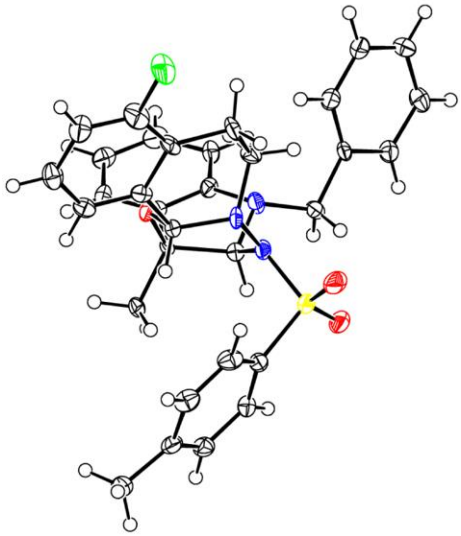
AbsCorr = MULTI-SCAN

Data completeness = 1.44/0.74 Theta(max) = 67.080

R(reflections) = 0.0427(6616) wR2(reflections) = 0.1370 (7260)

S = 1.105 Npar = 725

2) X-Ray Crystallographic Data of 4y (CCDC number: 1567023)



Bond precision:	C-C = 0.0067 A		Wavelength = 1.54184
Cell:	a = 9.27904 (5)	b = 18.37857 (9)	c = 16.77742 (8)
	alpha = 90	beta = 104.2756 (5)	gamma = 90
Temperature:	100 K		
	Calculated		Reported
Volume	2772.80 (2)		2772.80 (3)
Space group	P 21		P 1 21 1
Hall group	P 2yb		P 2yb
Moiety formula	C32 H30 F N3 O3 S		C32 H30 F N3 O3 S
Sum formula	C32 H30 F N3 O3 S		C32 H30 F N3 O3 S
Mr	555.65		555.65
Dx,g cm-3	1.331		1.331
Z	4		4
Mu (mm-1)	1.413		1.413
F000	1168.0		1168.0
F000'	1172.73		
h,k,lmax	11, 22, 20		11, 22, 20
Nref	10924 [5643]		10869
Tmin,Tmax	0.748, 0.868		0.006, 1.000
Tmin'	0.623		

Correction method= # Reported T Limits: Tmin = 0.006 Tmax = 1.000

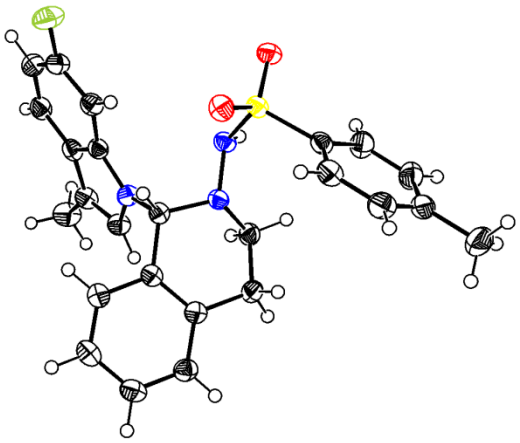
AbsCorr = MULTI-SCAN

Data completeness = 1.93/0.99 Theta(max) = 72.115

R(reflections) = 0.0328(10130) wR2(reflections) = 0.0882 (10869)

S = 1.049 Npar = 725

3) X-Ray Crystallographic Data of F-substituted 8 (CCDC number: 1817477)



Bond precision:	C-C = 0.0020 A		Wavelength = 1.54184
Cell:	a = 8.9433 (1)	b = 19.2152 (3)	c = 13.0237 (2)
	alpha = 90	beta = 96.049 (5)	gamma = 90
Temperature:	100 K		
	Calculated		Reported
Volume	2225.63 (5)		2225.63 (5)
Space group	P 21/c		P 1 21/c 1
Hall group	-P 2yb		-P 2yb
Moiety formula	C25 H24 F N3 O2 S		C25 H24 F N3 O2 S
Sum formula	C25 H24 F N3 O2 S		C25 H24 F N3 O2 S
Mr	449.53		449.53
Dx,g cm-3	1.342		1.342
Z	4		4
Mu (mm-1)	1.592		1.592
F000	944.0		944.0
F000'	948.05		
h,k,lmax	11, 23, 16		11, 23, 16
Nref	4412		4360
Tmin,Tmax	0.717, 0.853		0.277, 1.000
Tmin'	0.591		

Correction method= # Reported T Limits: Tmin = 0.277 Tmax = 1.000
AbsCorr = MULTI-SCAN

Data completeness = 0.988 Theta(max) = 72.599

R(reflections) = 0.0353(4077) wR2(reflections) = 0.0953 (4360)

S = 1.075 Npar = 292

7. References

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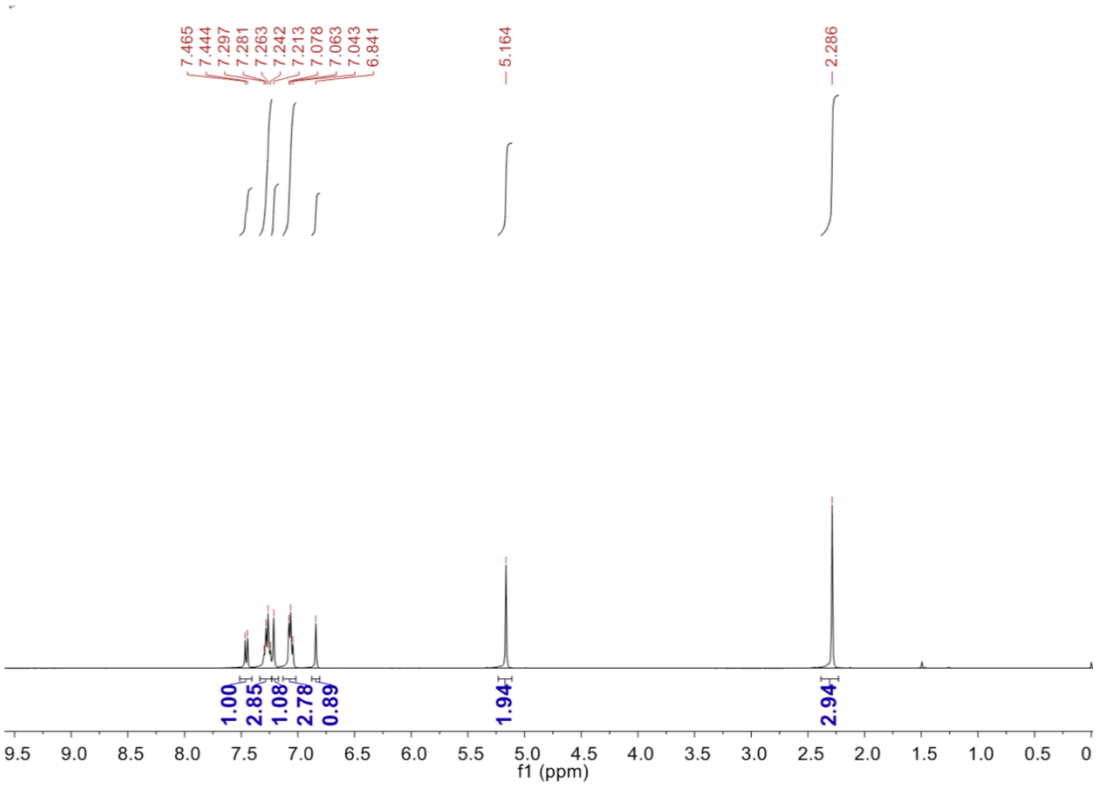
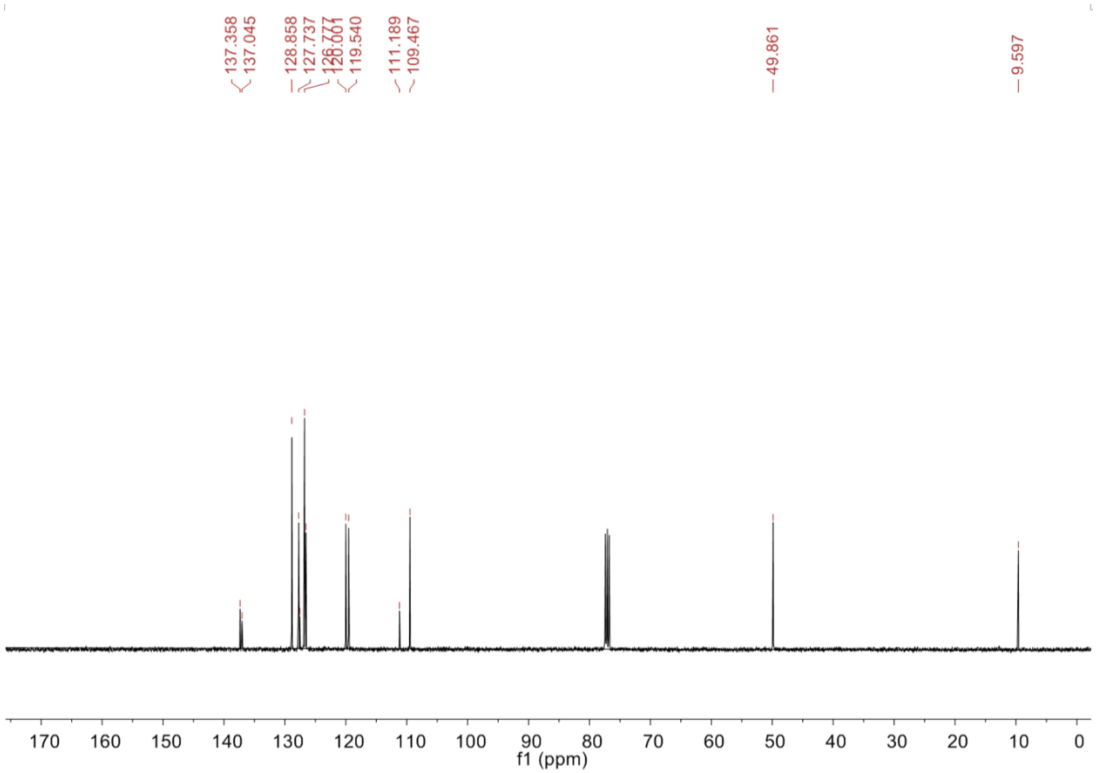
8. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR Spectra of All Products

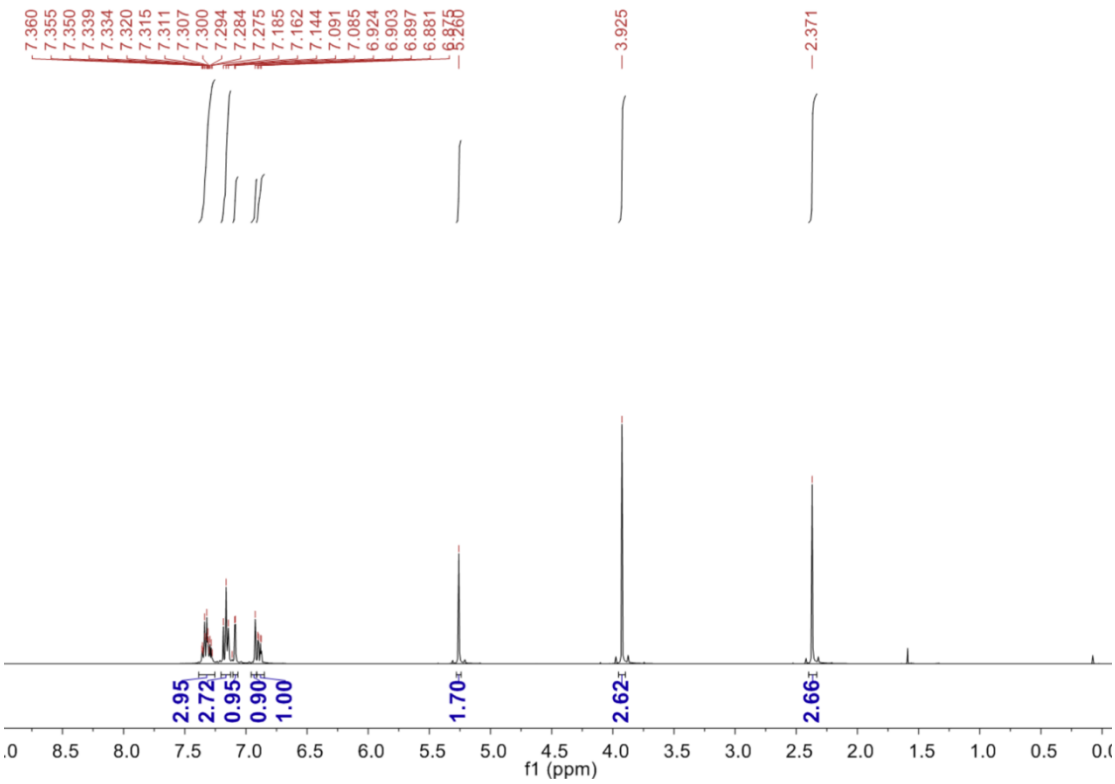
^{1}H NMR of **1e**



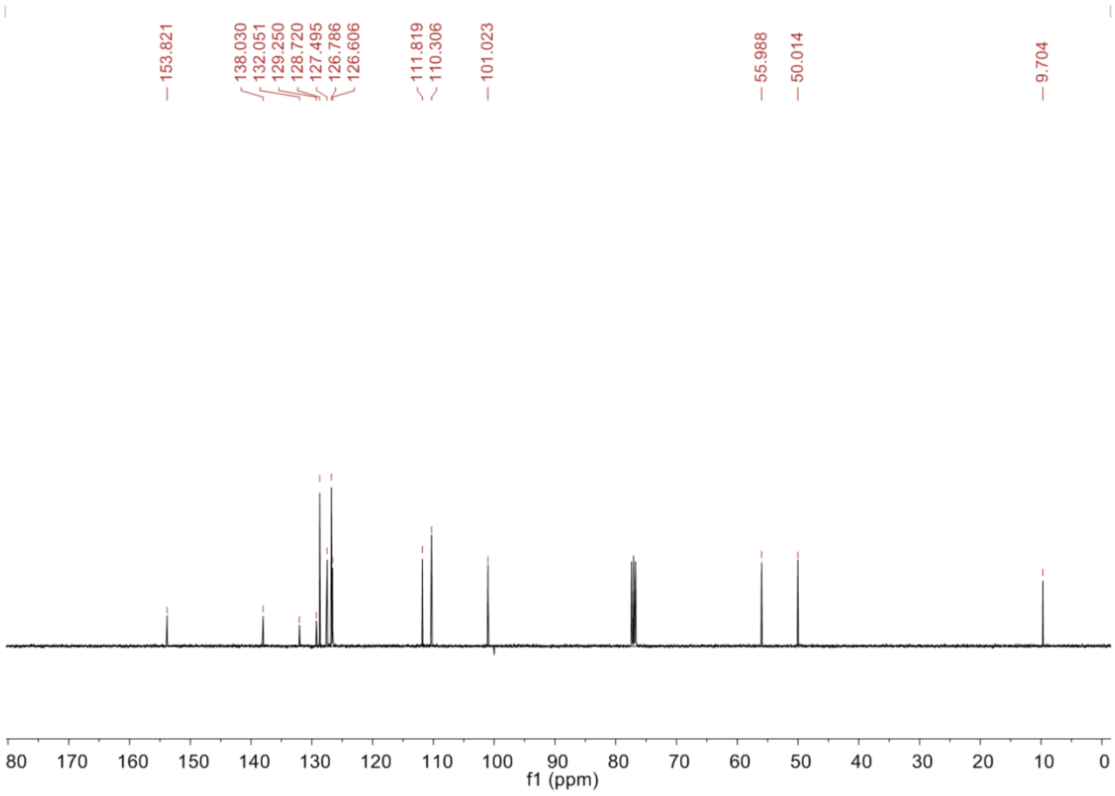
^{13}C NMR of **1e**



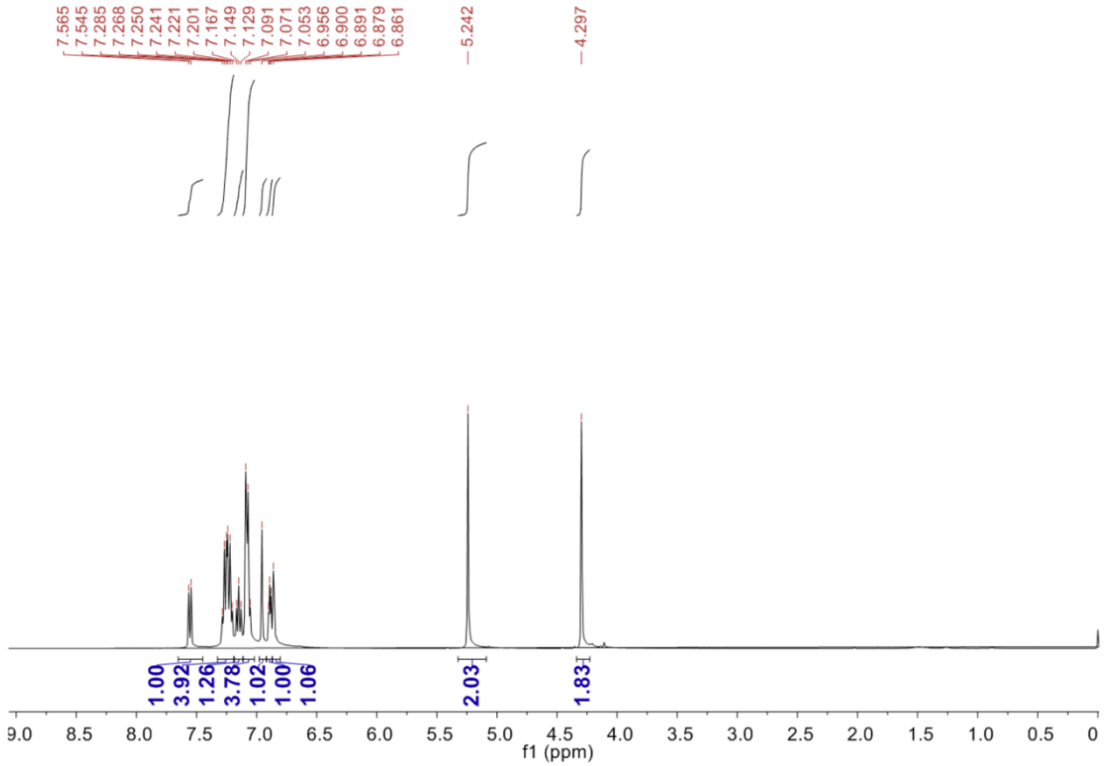
^{1}H NMR of **1h**



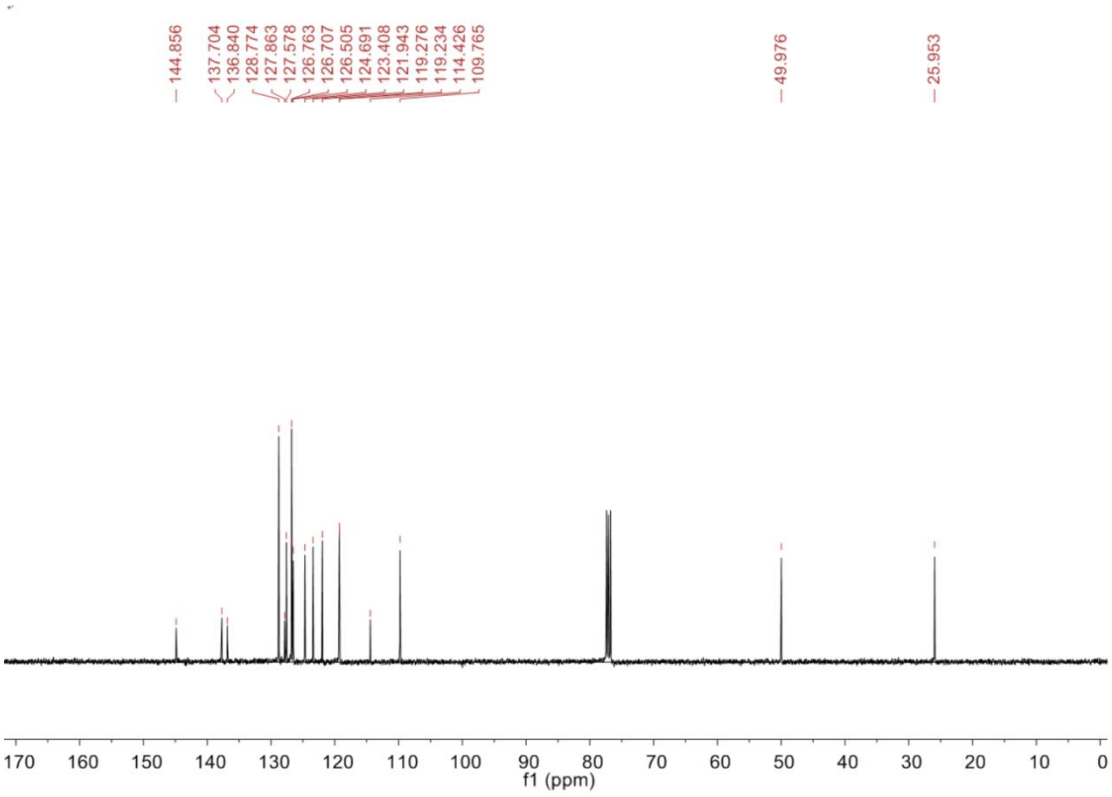
^{13}C NMR of **1h**



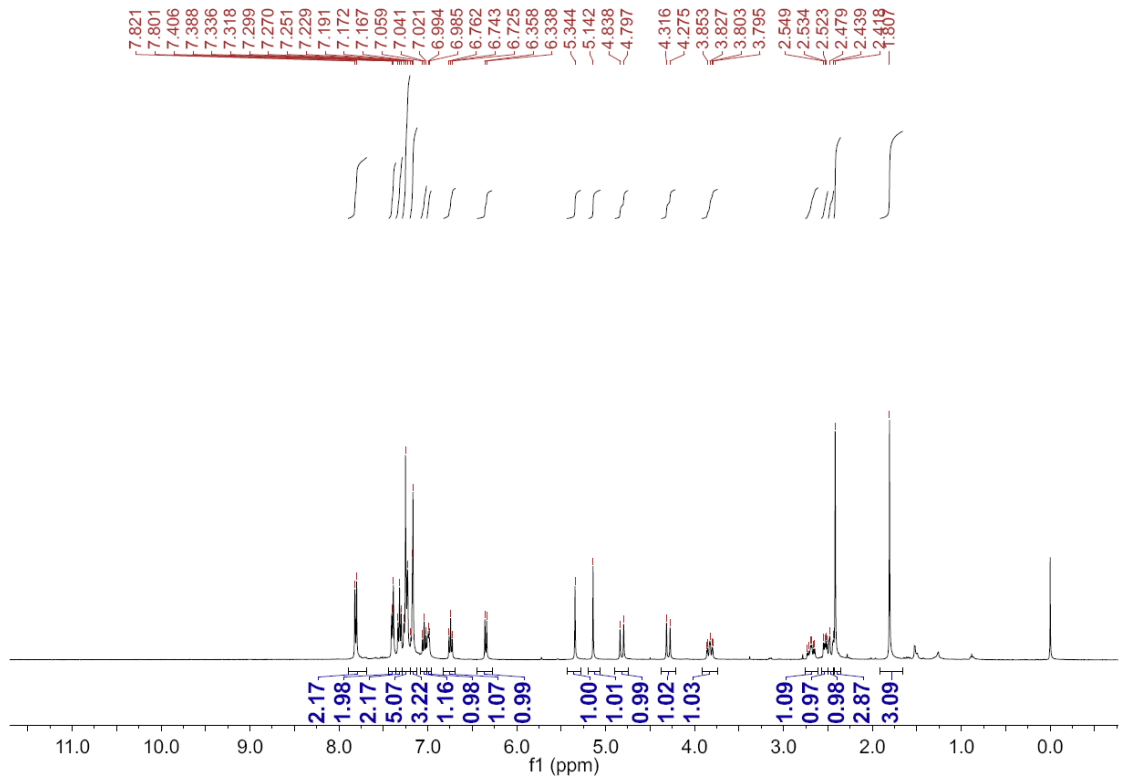
^{1}H NMR of **1q**



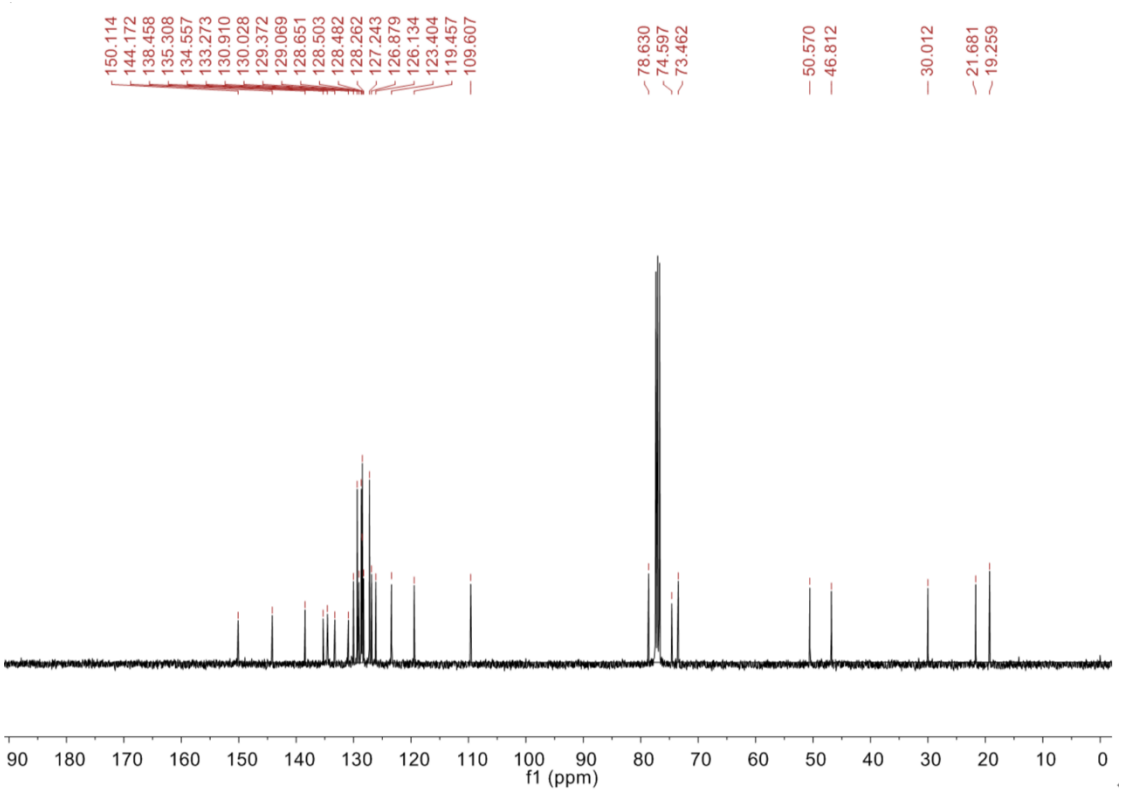
^{13}C NMR of **1q**



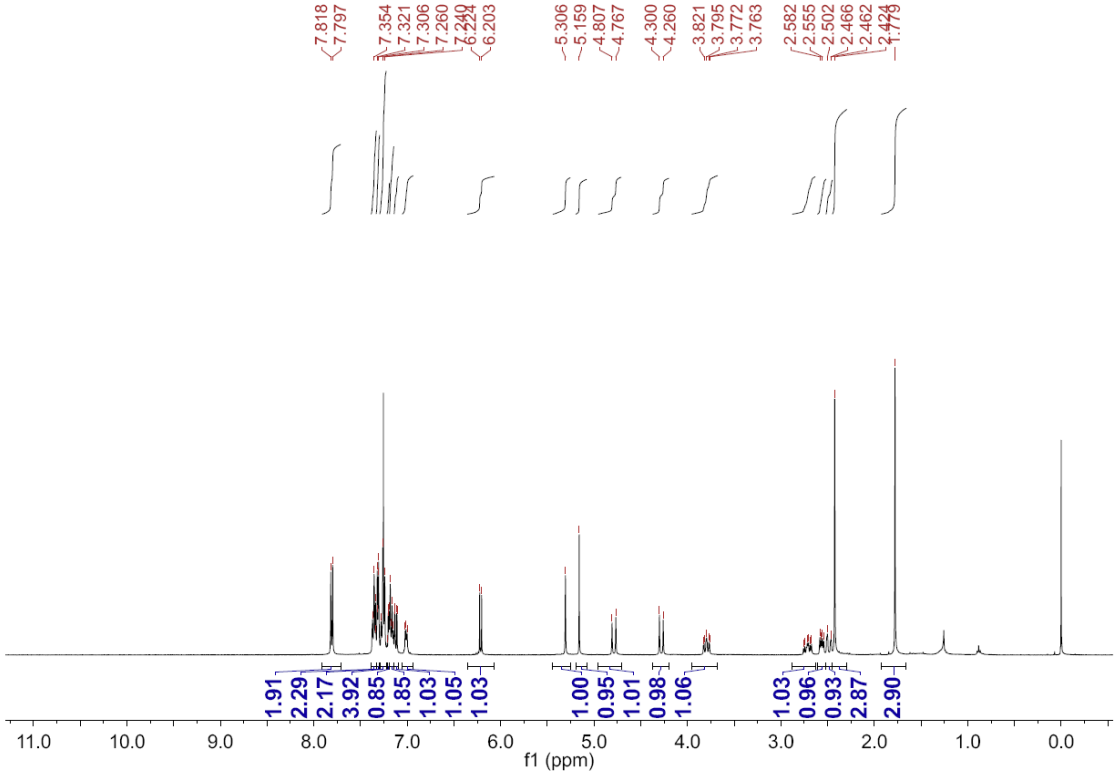
^{1}H NMR of **4a**



^{13}C NMR of **4a**



^{1}H NMR of **4b**



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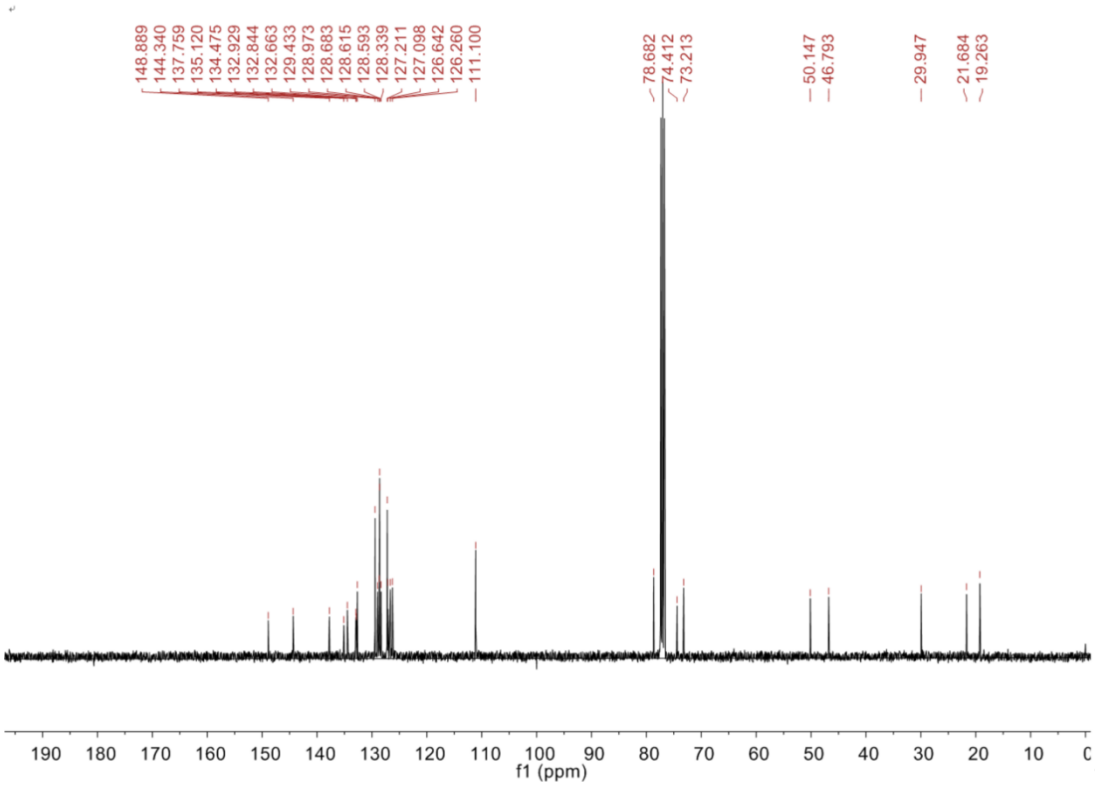
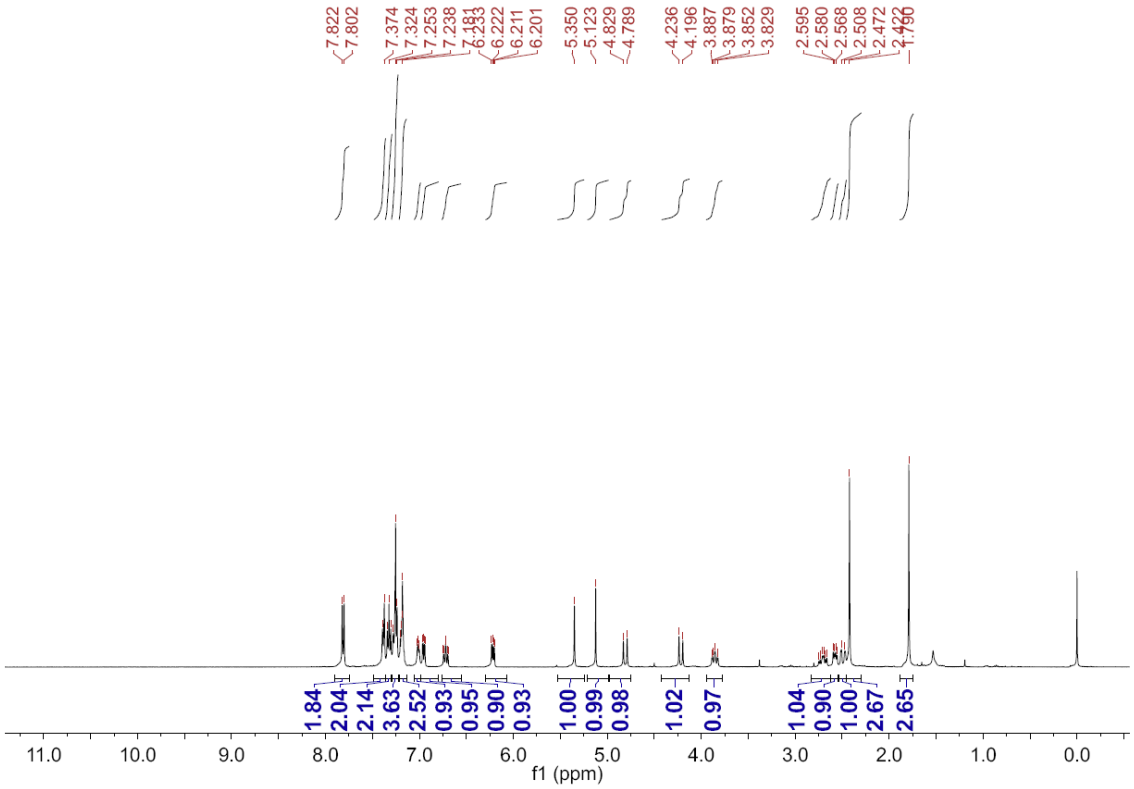


^{1}H NMR of **4c**



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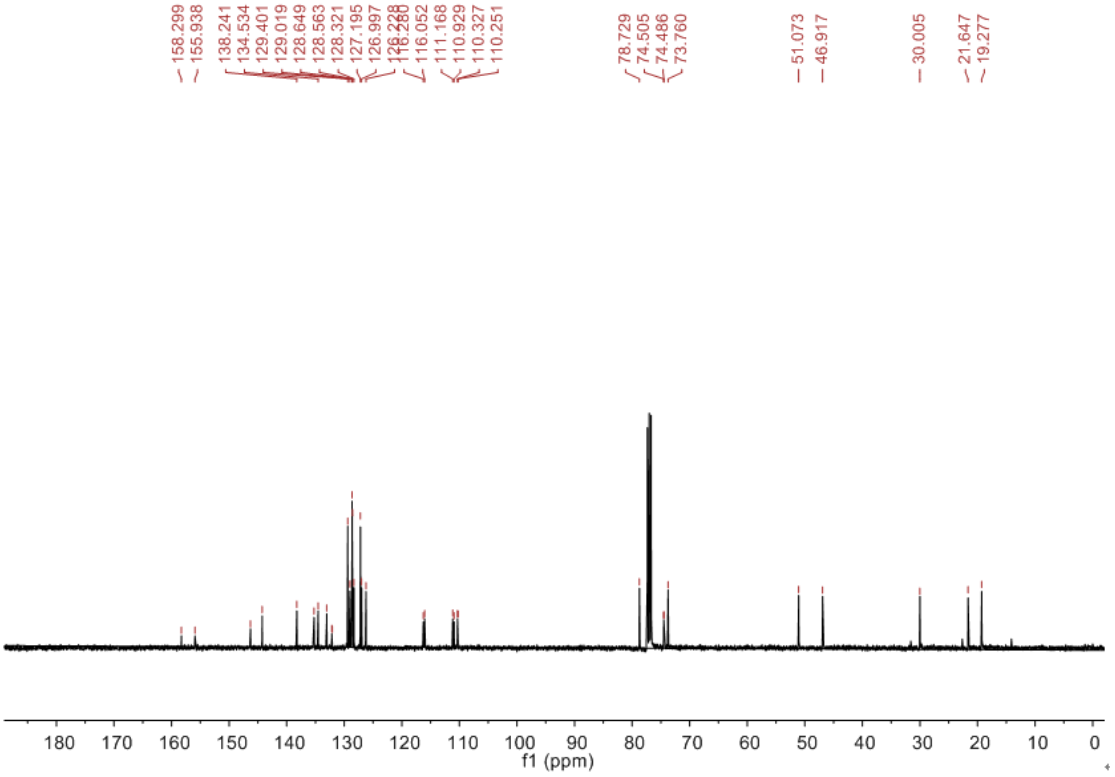
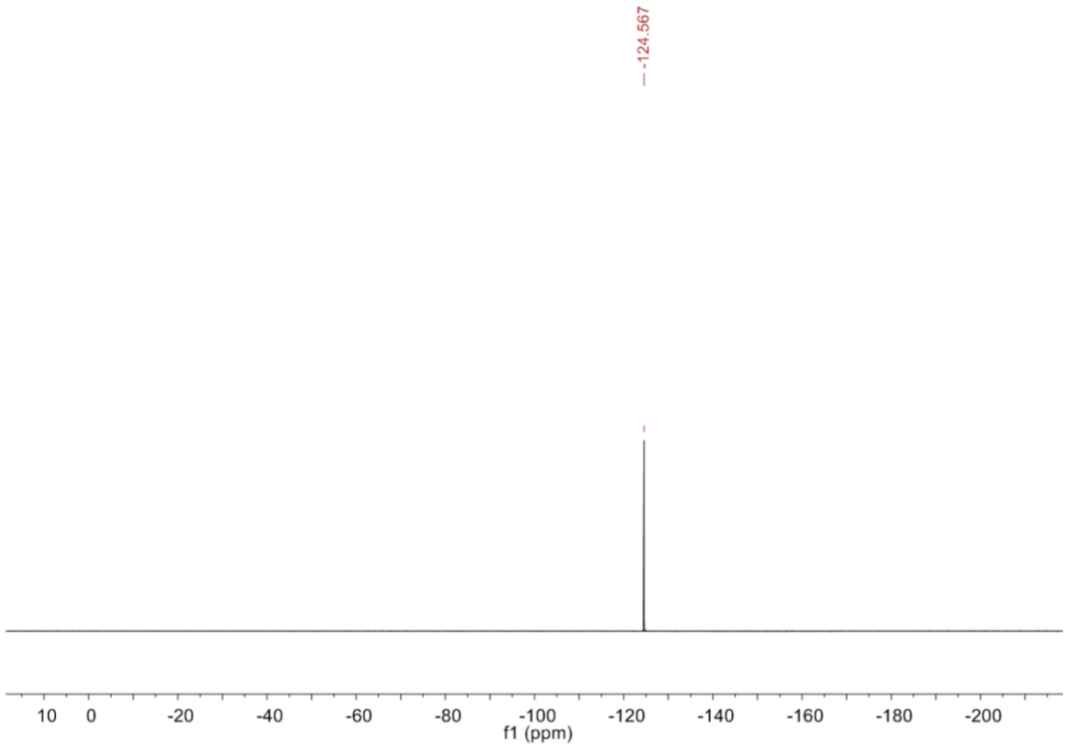
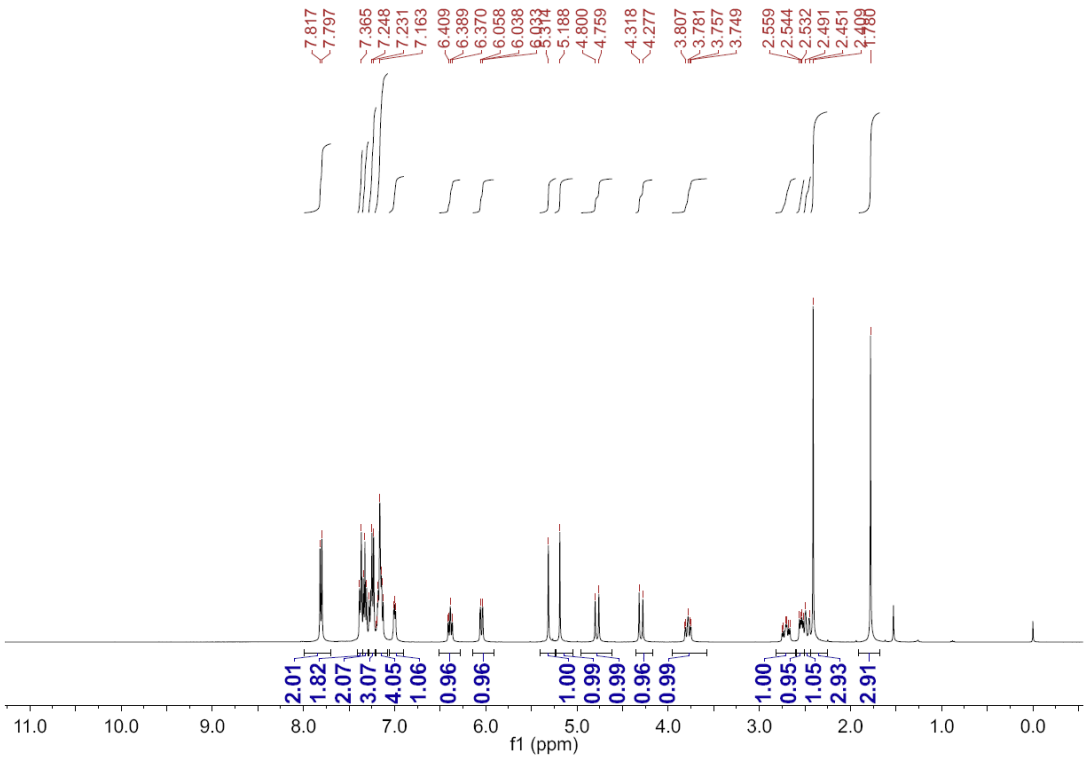


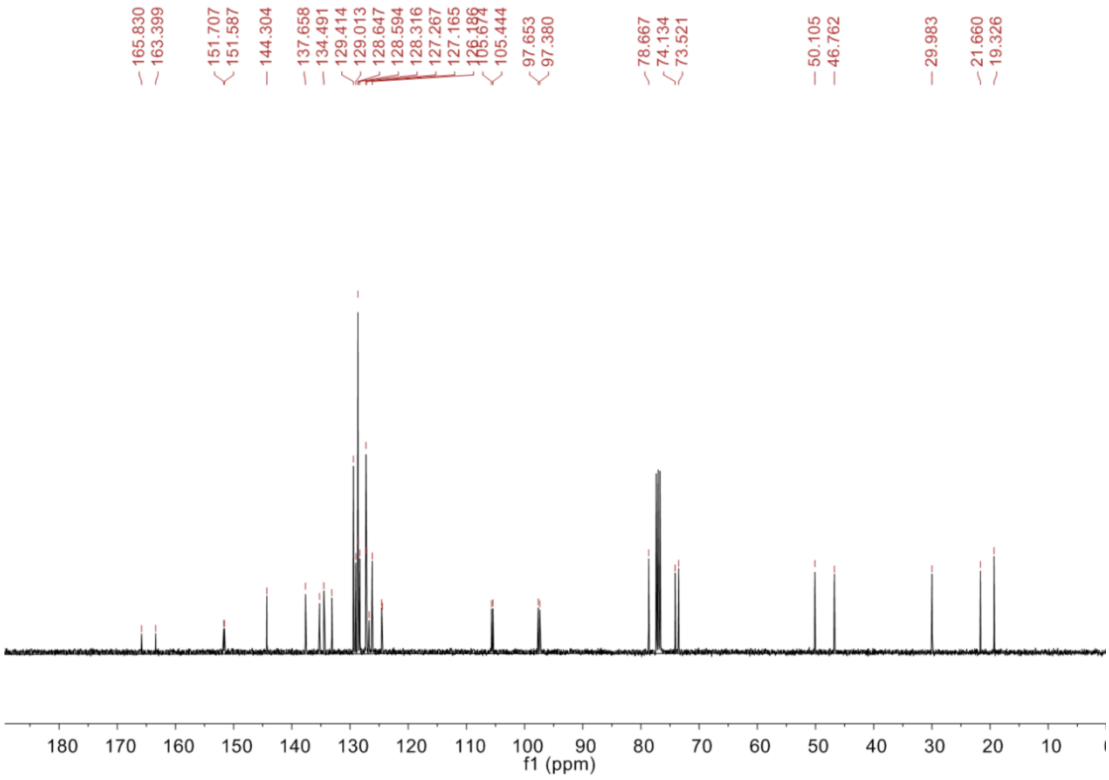
^{19}F NMR of **4c**



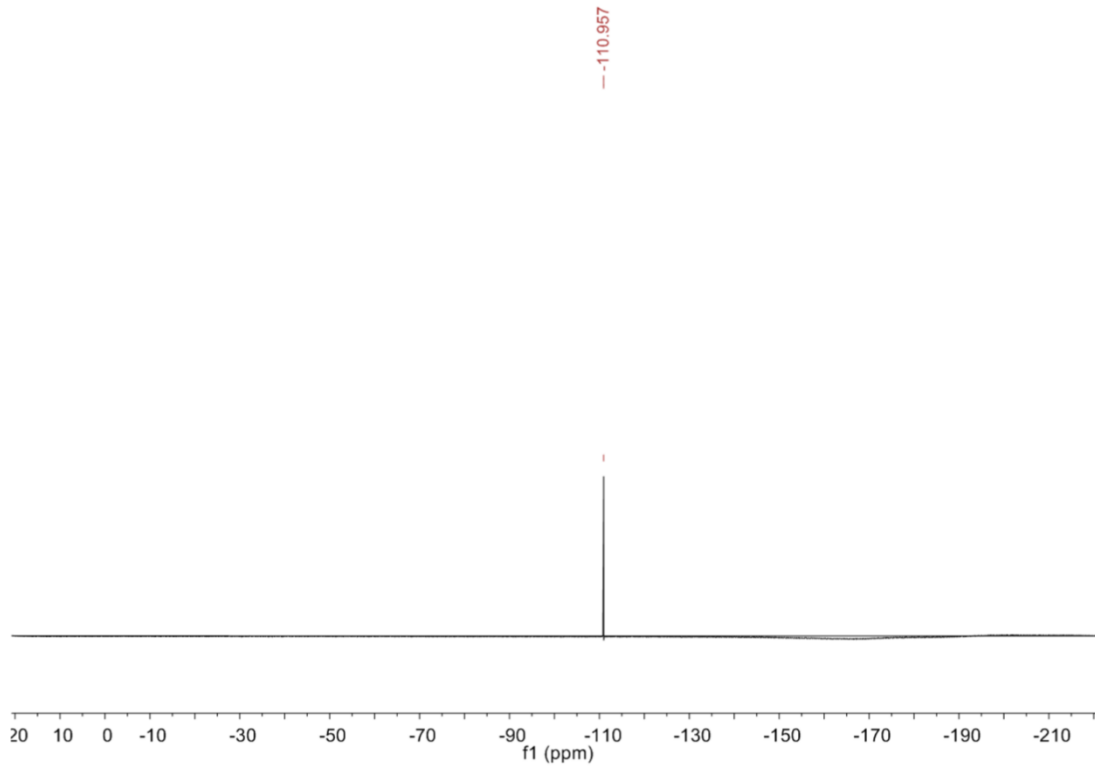
^{1}H NMR of **4d**



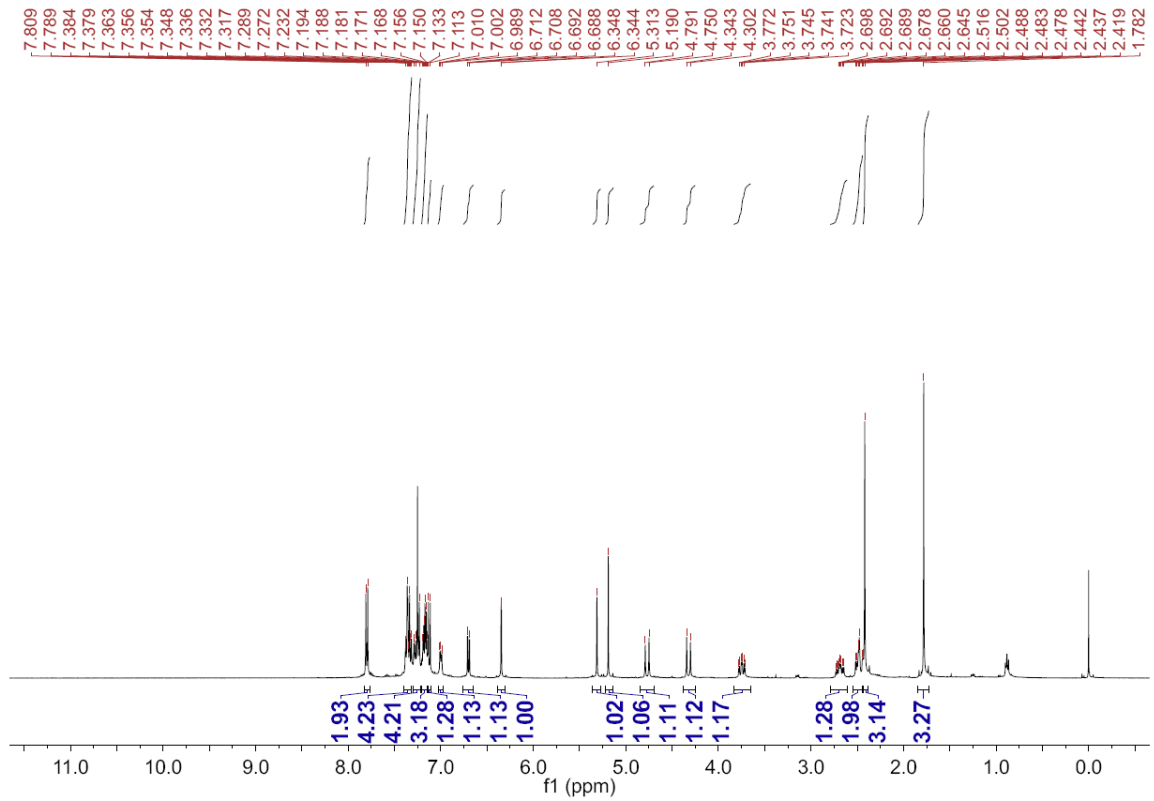
^{13}C NMR of **4d**



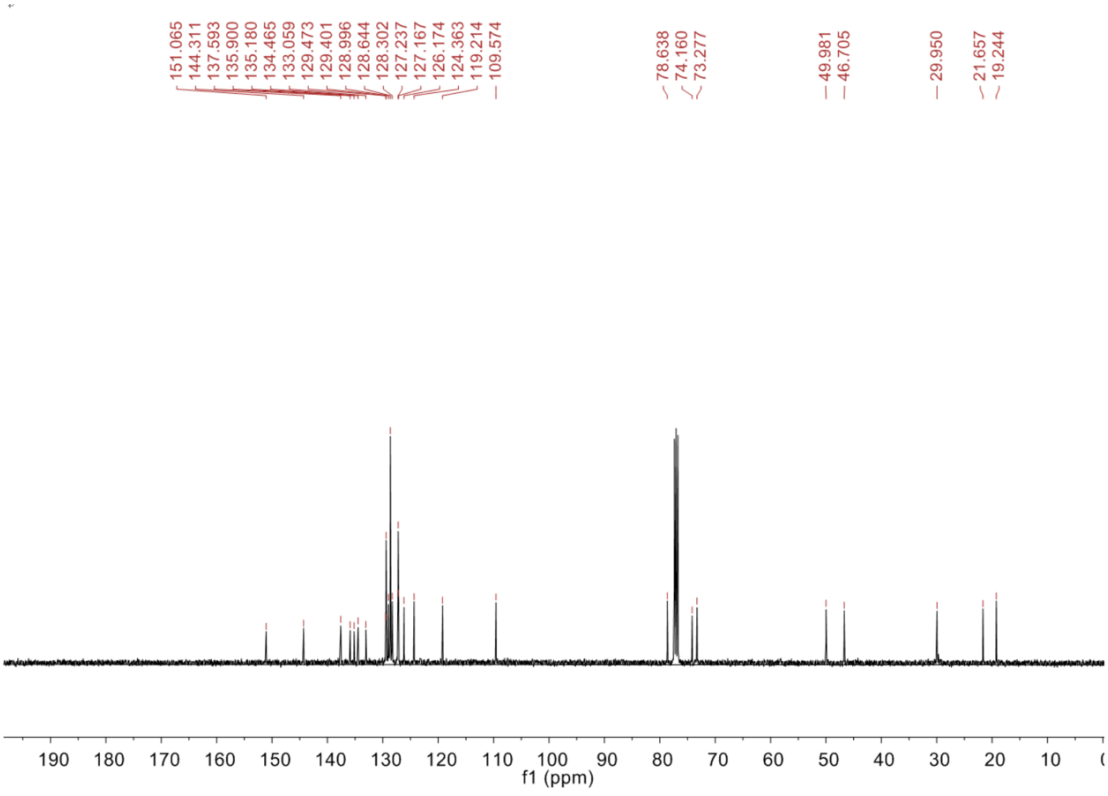
^{19}F NMR of **4d**



^{1}H NMR of **4e**



^{13}C NMR of **4e**



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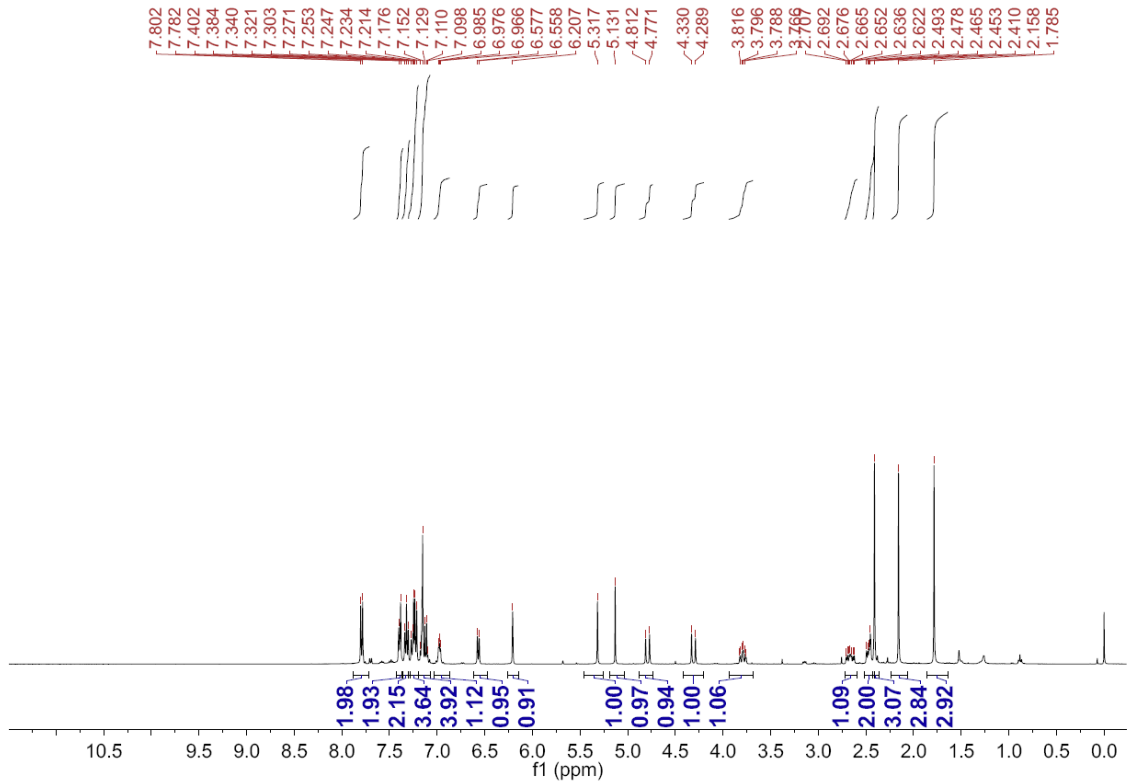
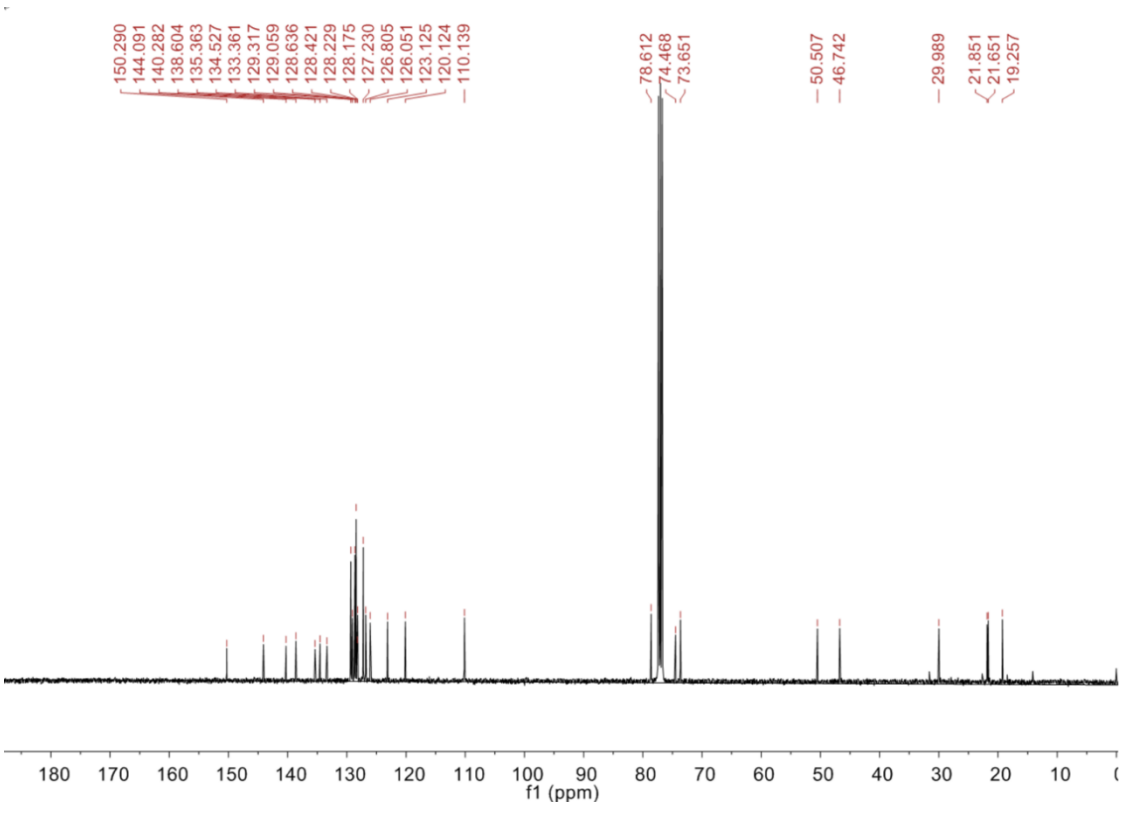
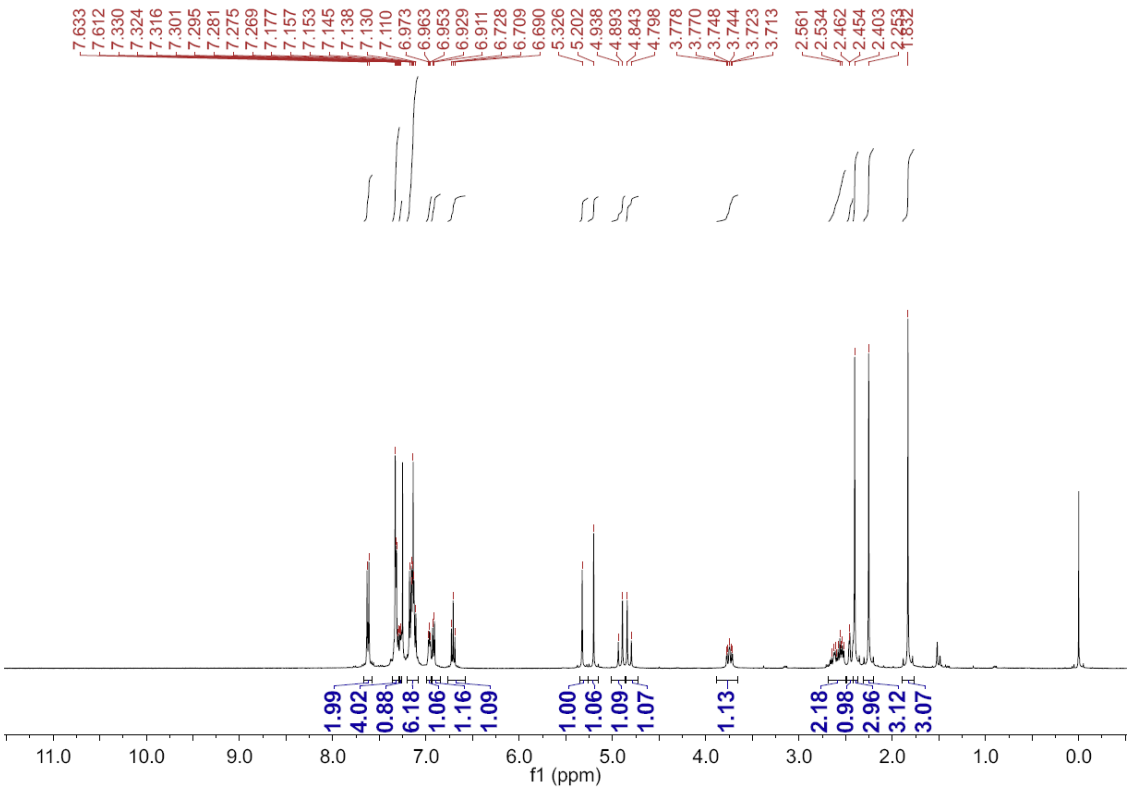


^{13}C NMR of **4f**



^{1}H NMR of **4g**



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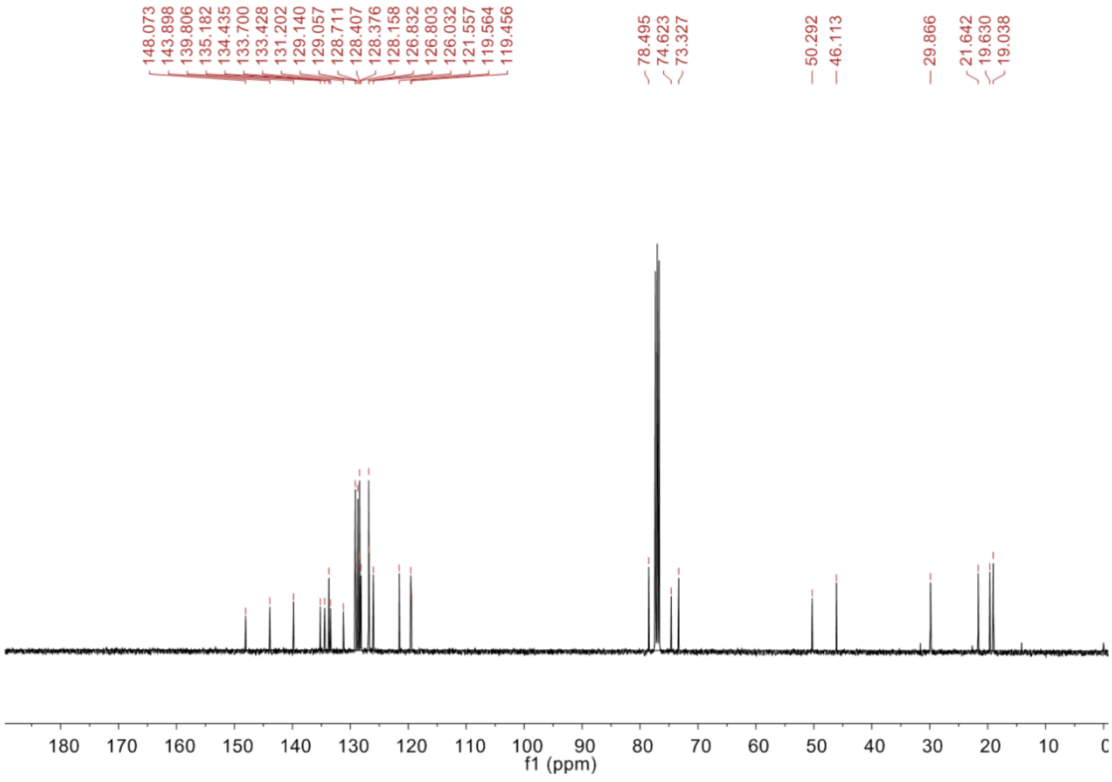

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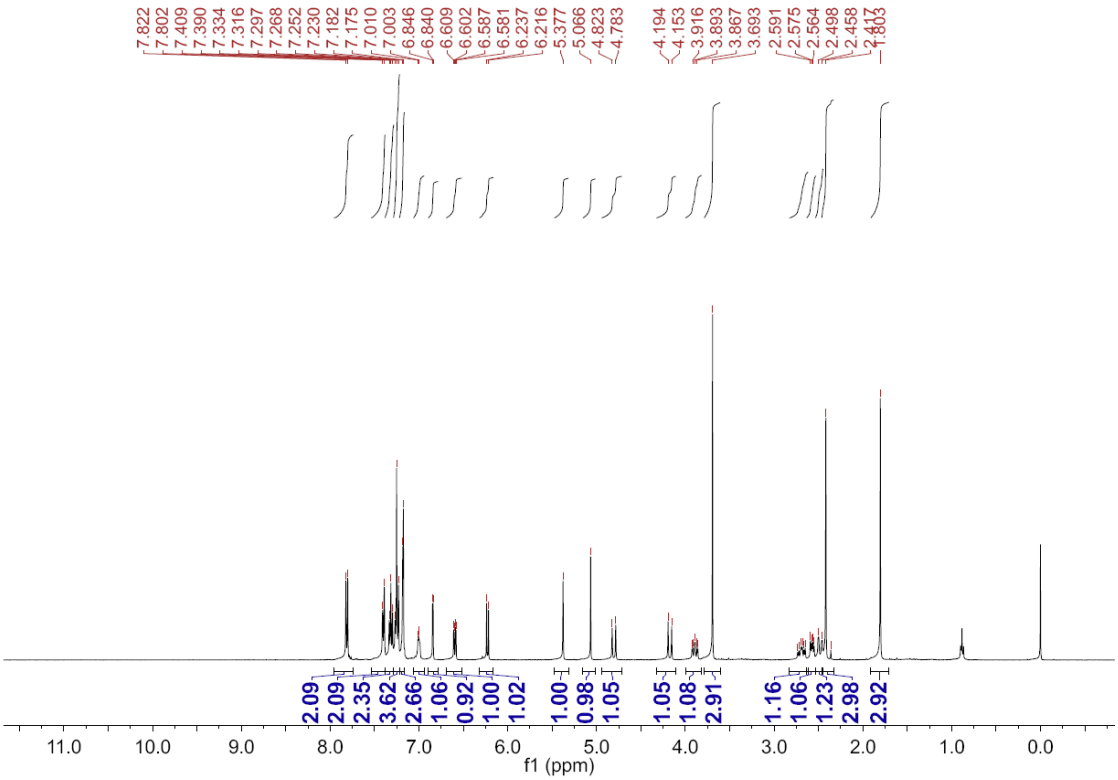

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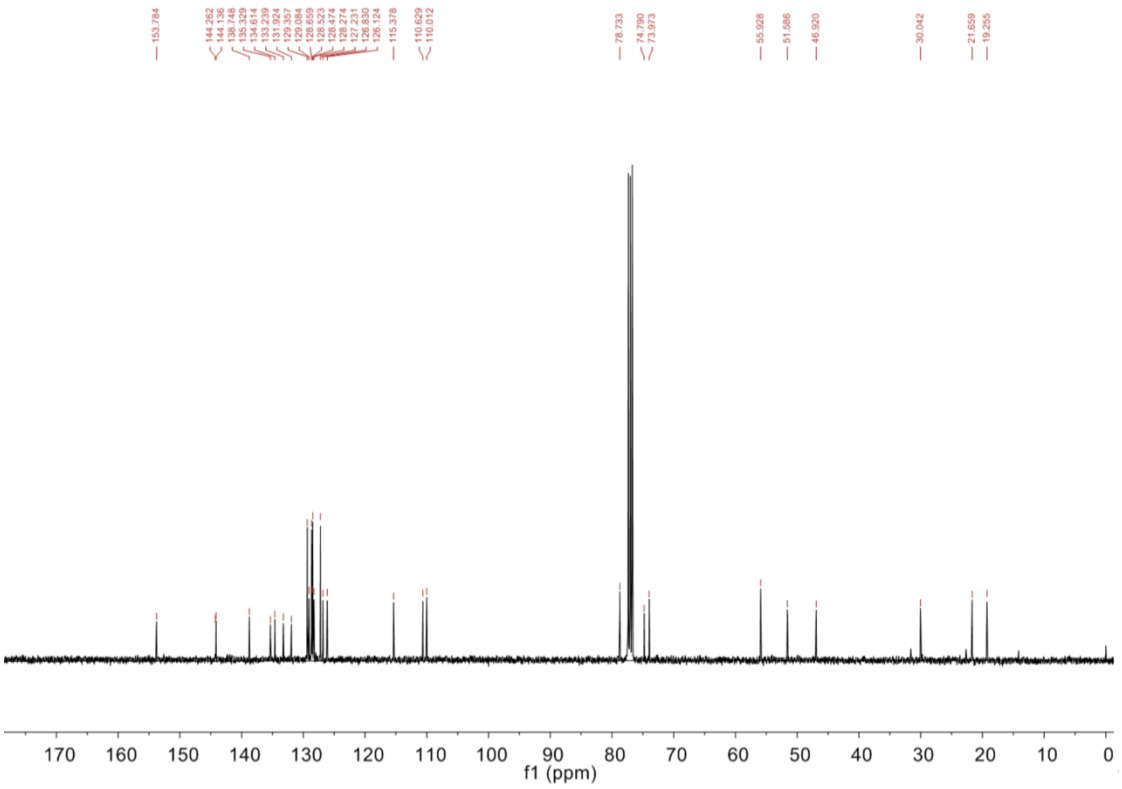

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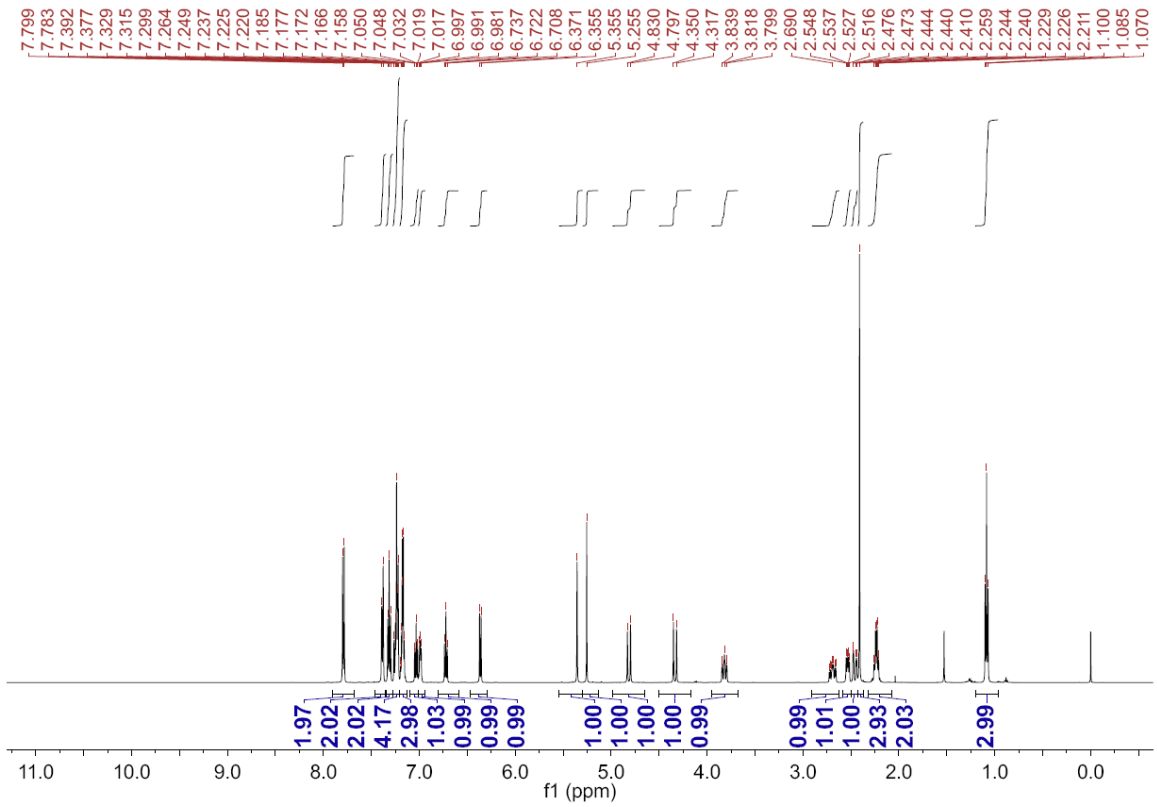
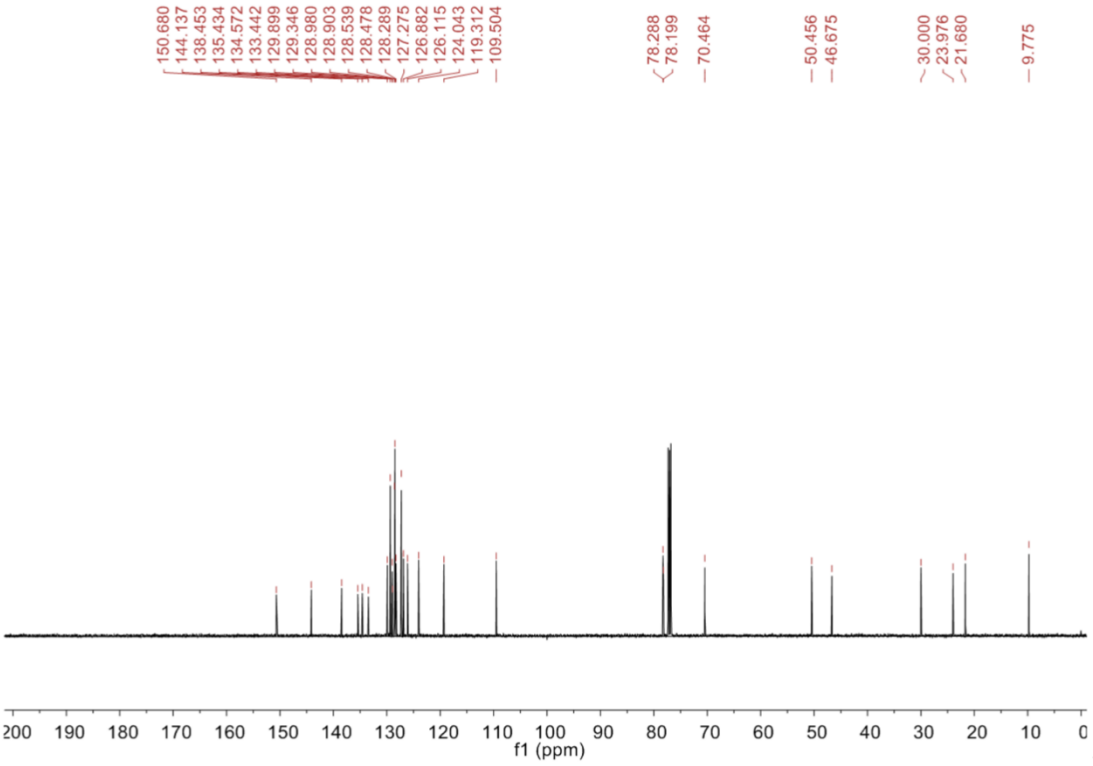


^{13}C NMR of **4i**



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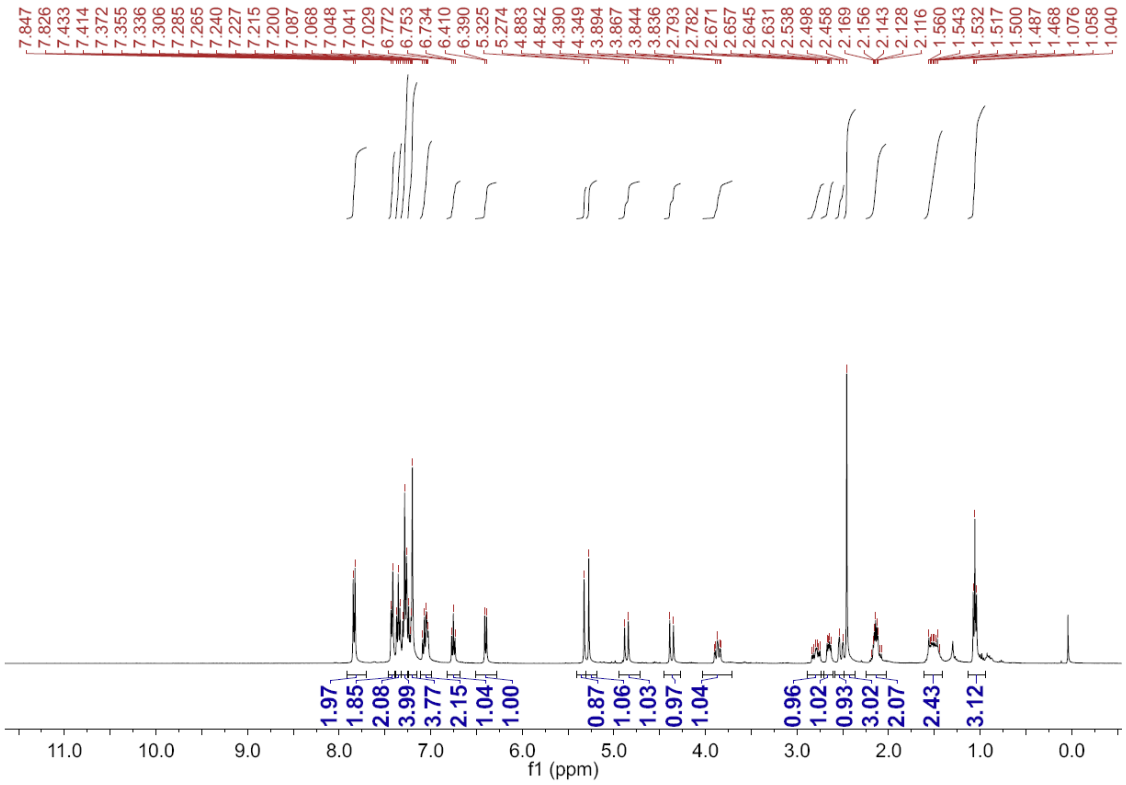

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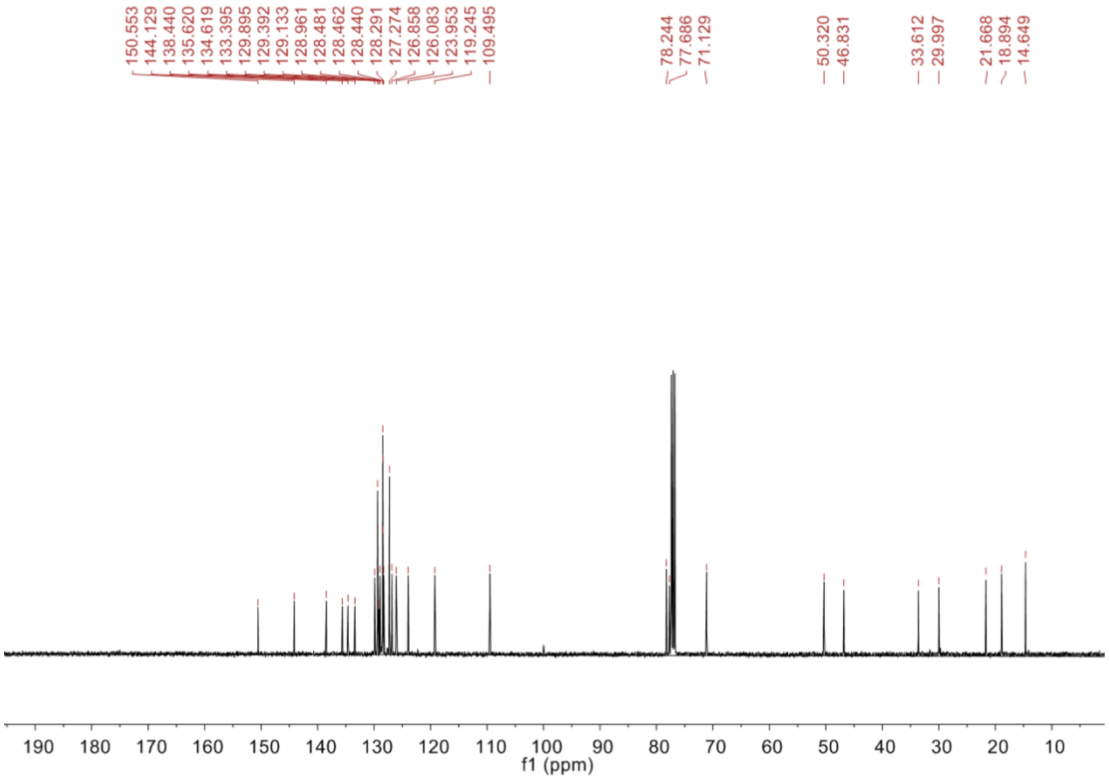

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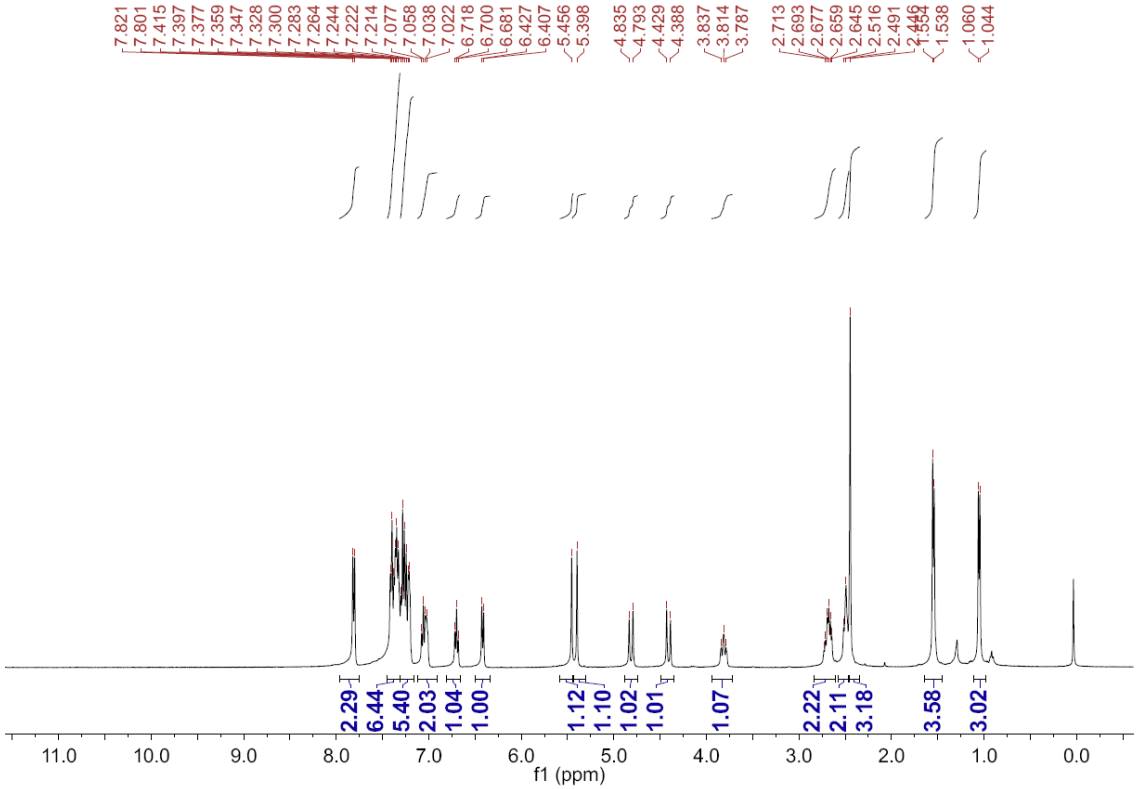
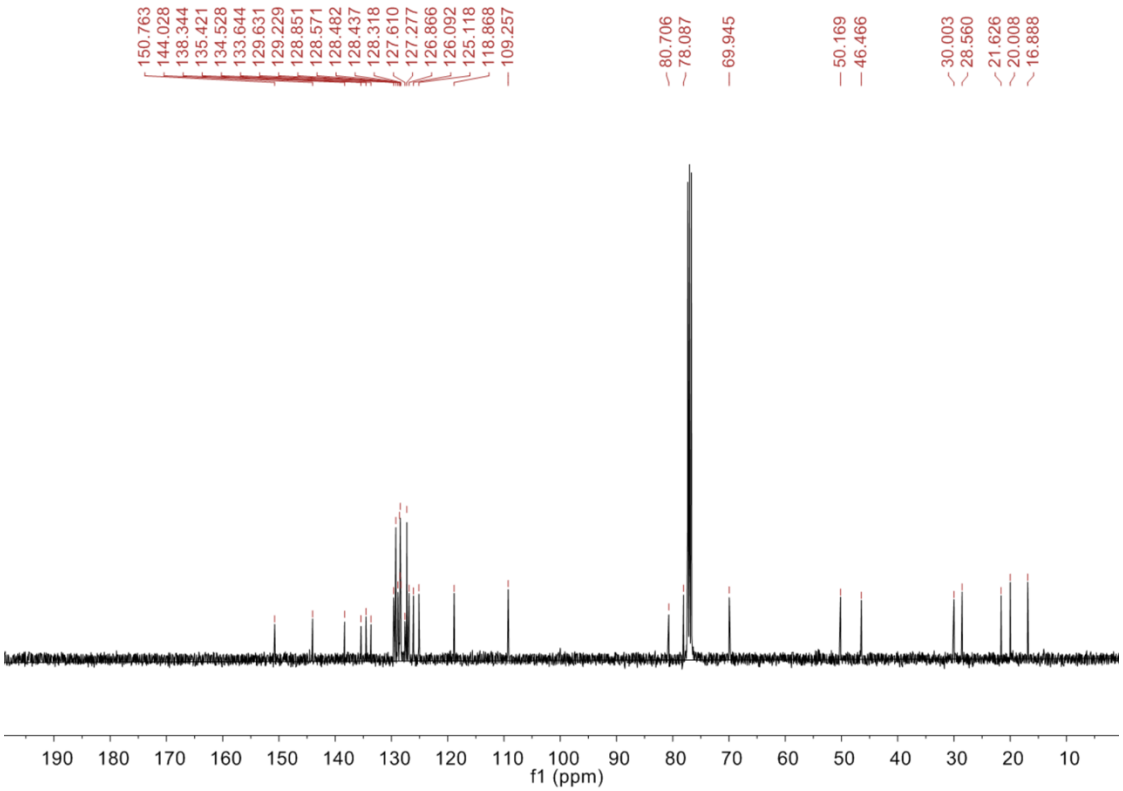


^{13}C NMR of **4k**



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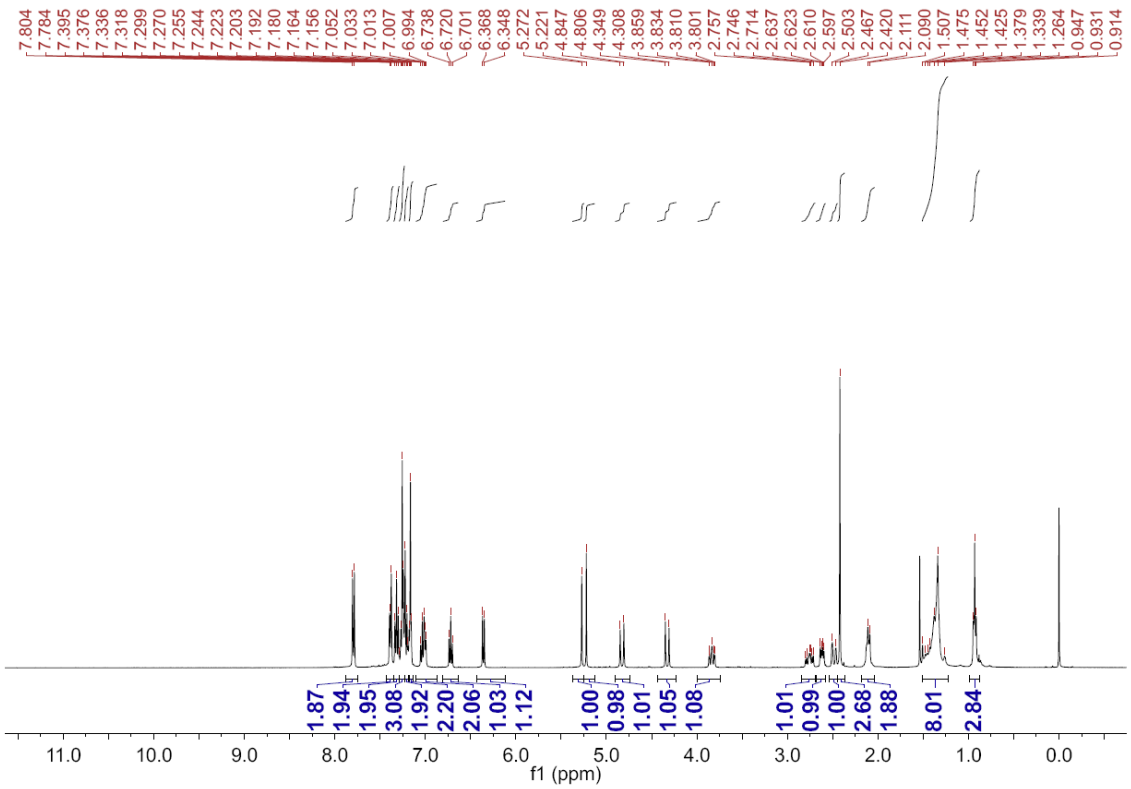

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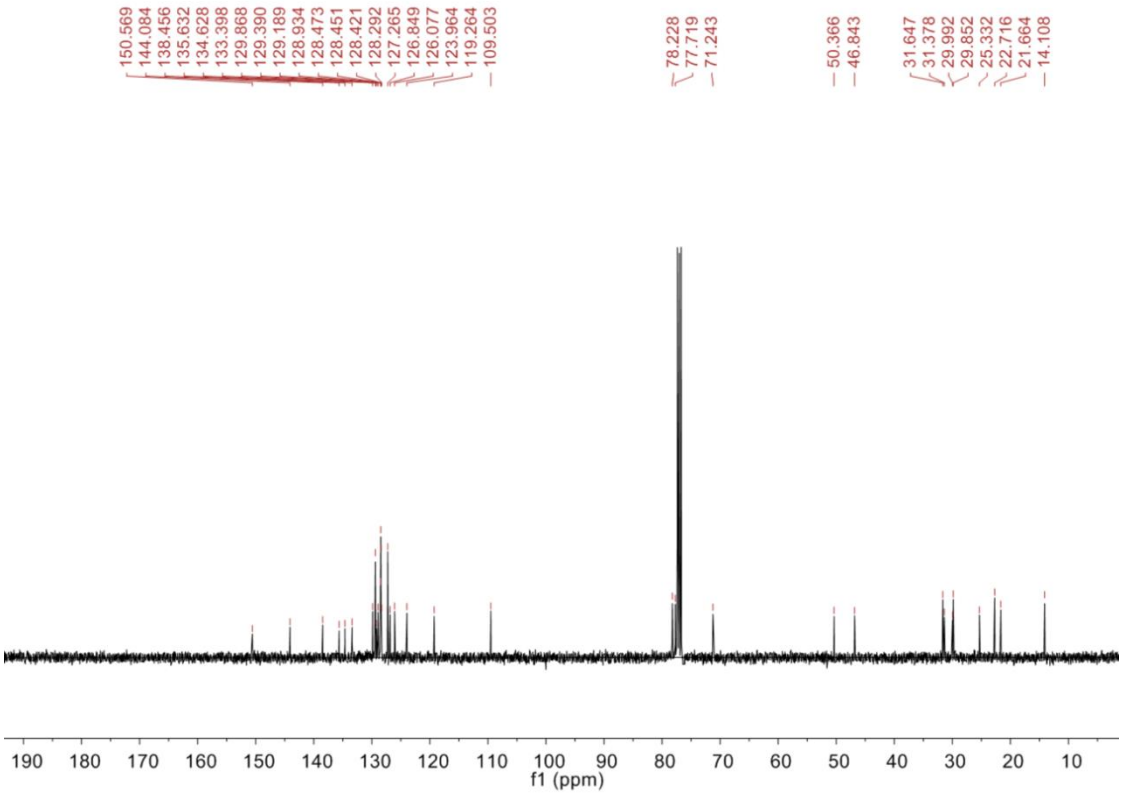

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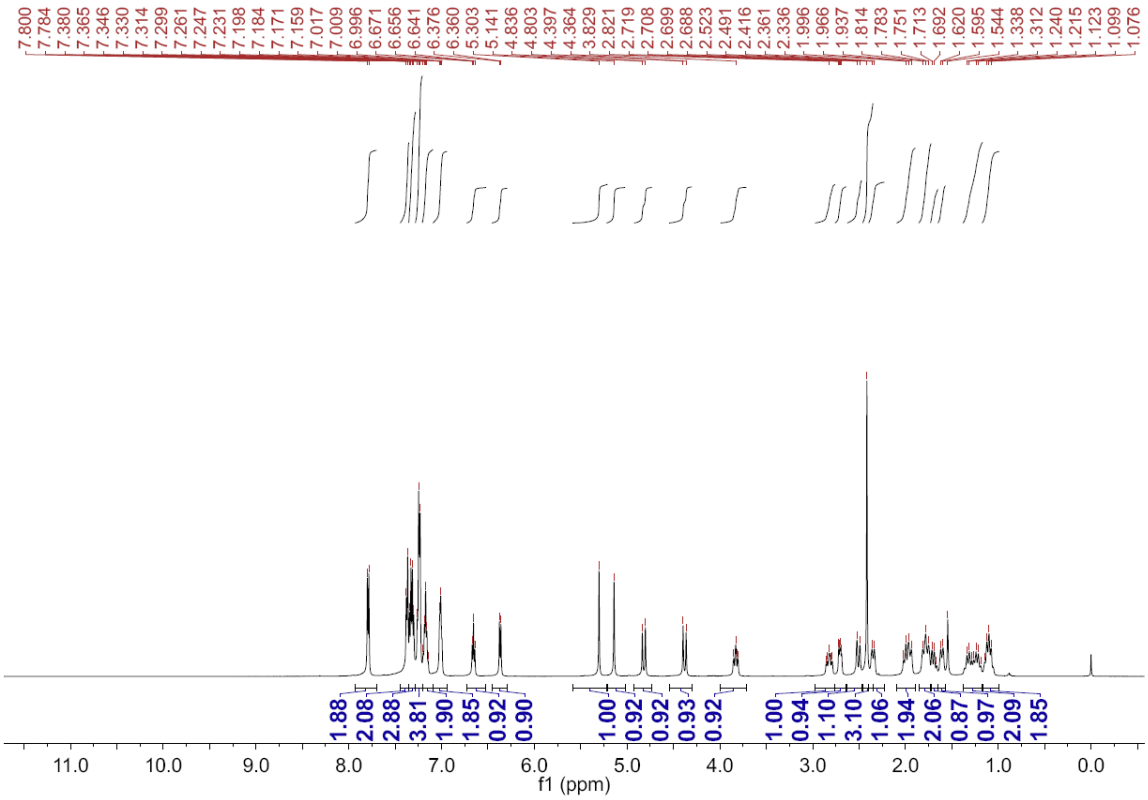
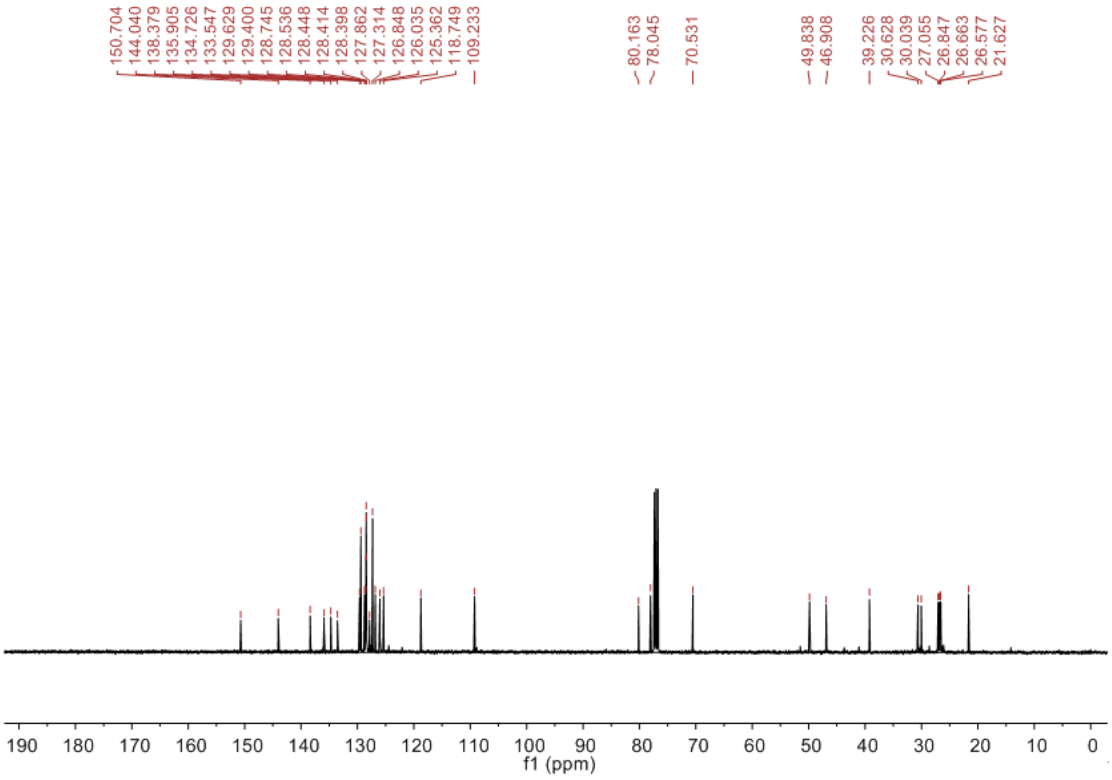


^{13}C NMR of **4m**



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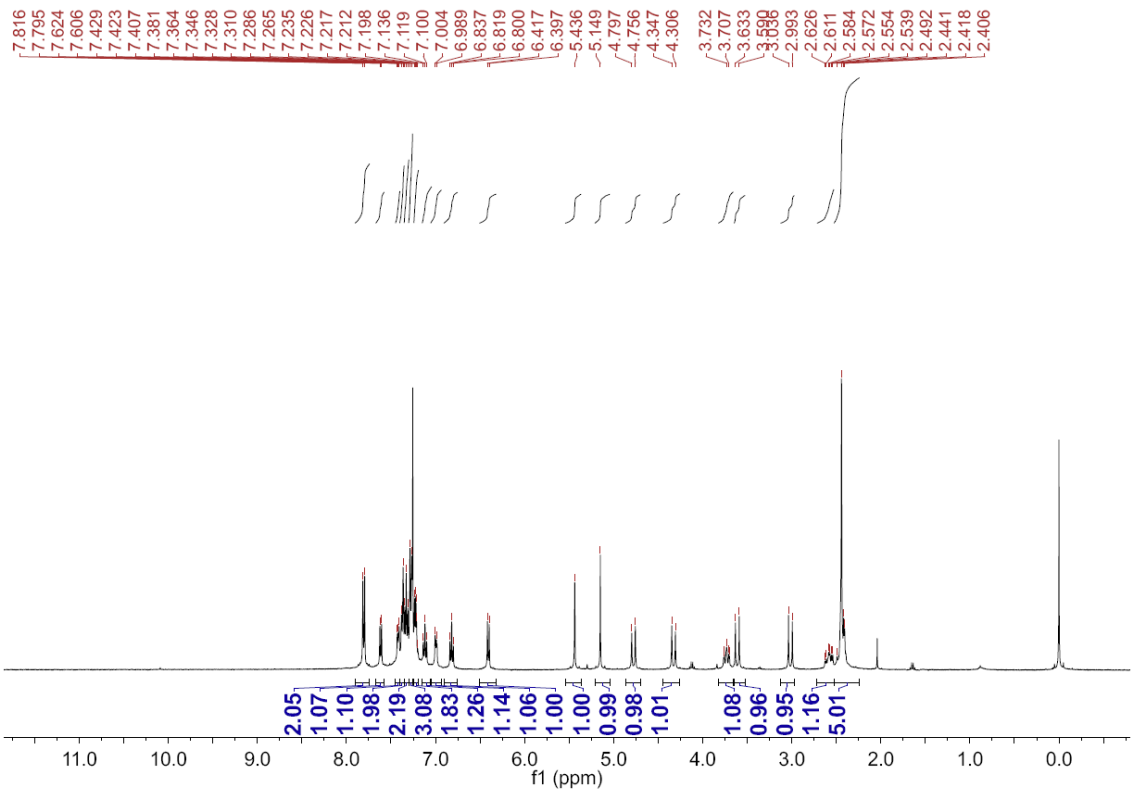

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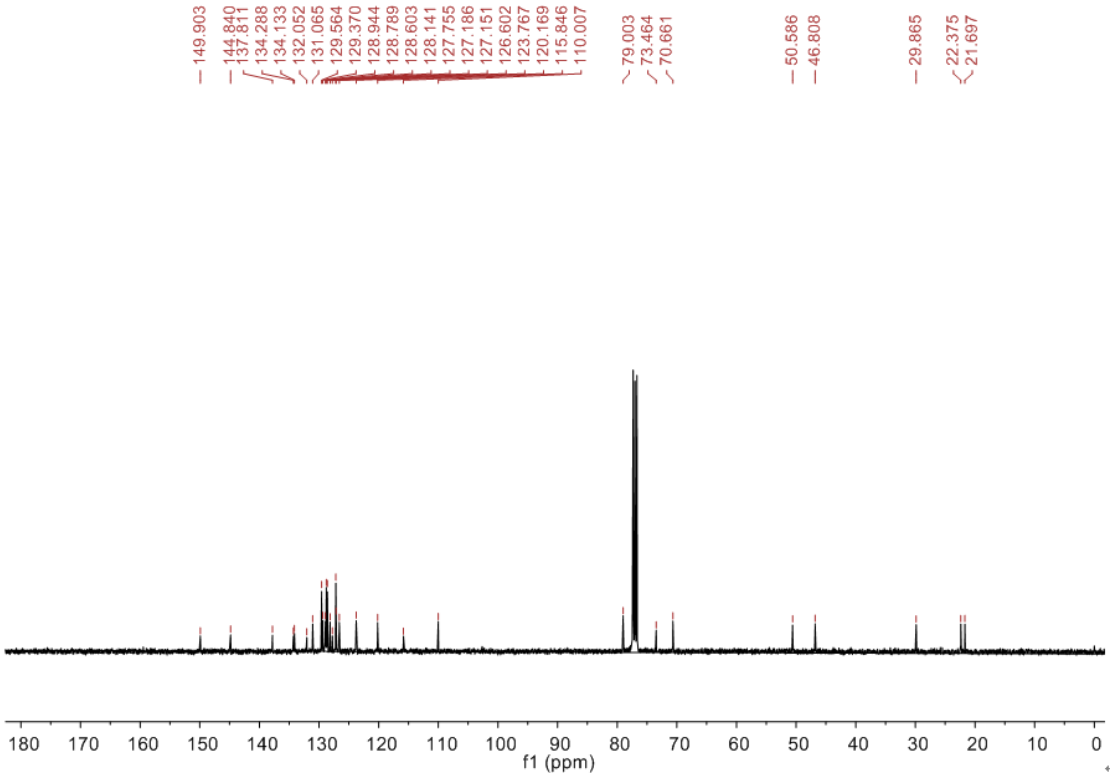

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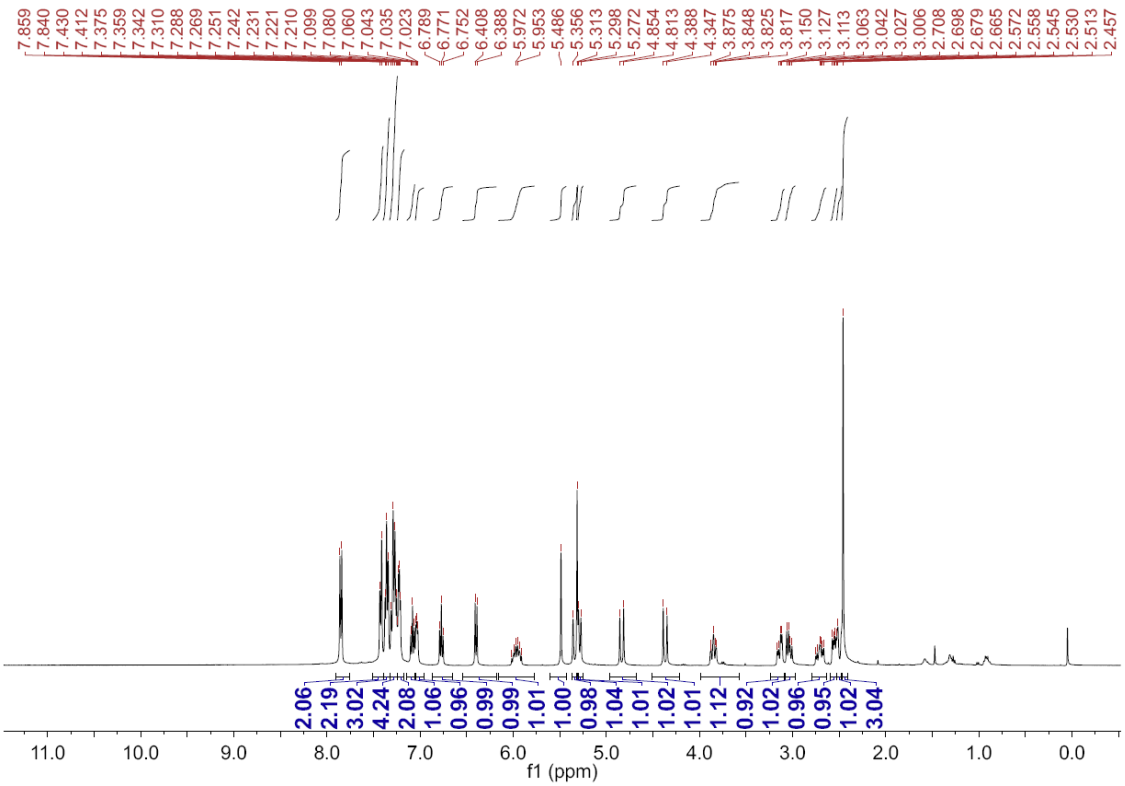

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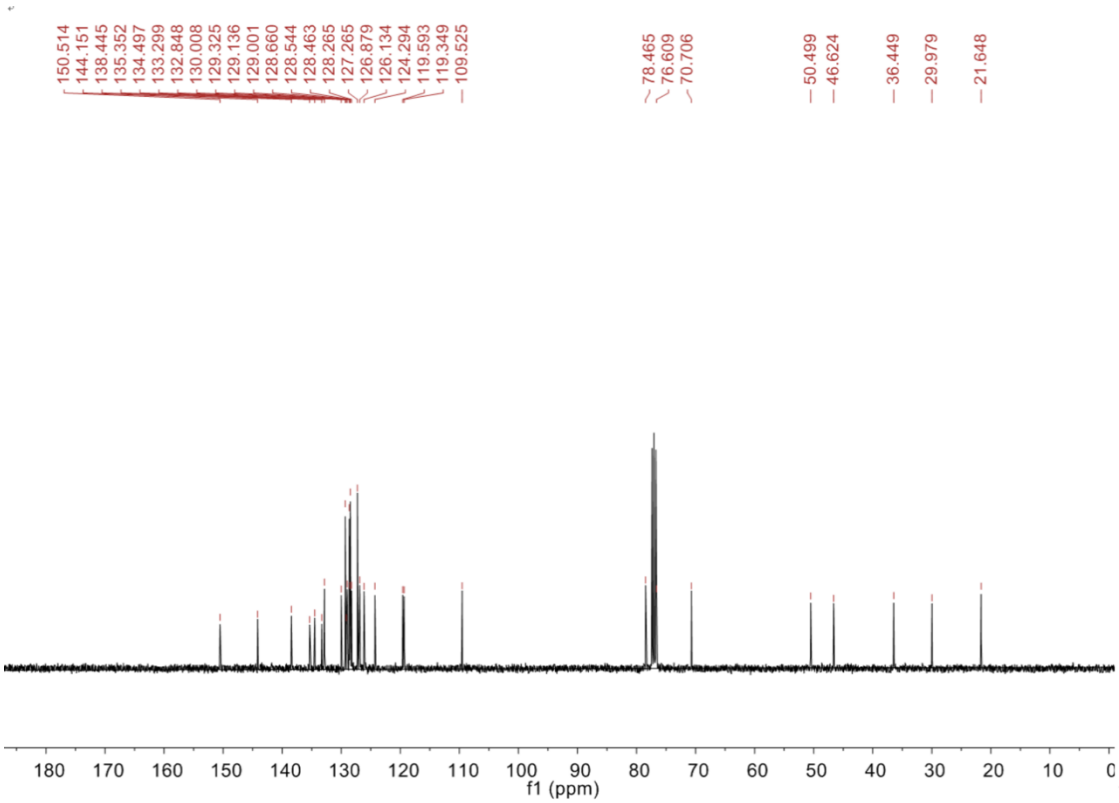

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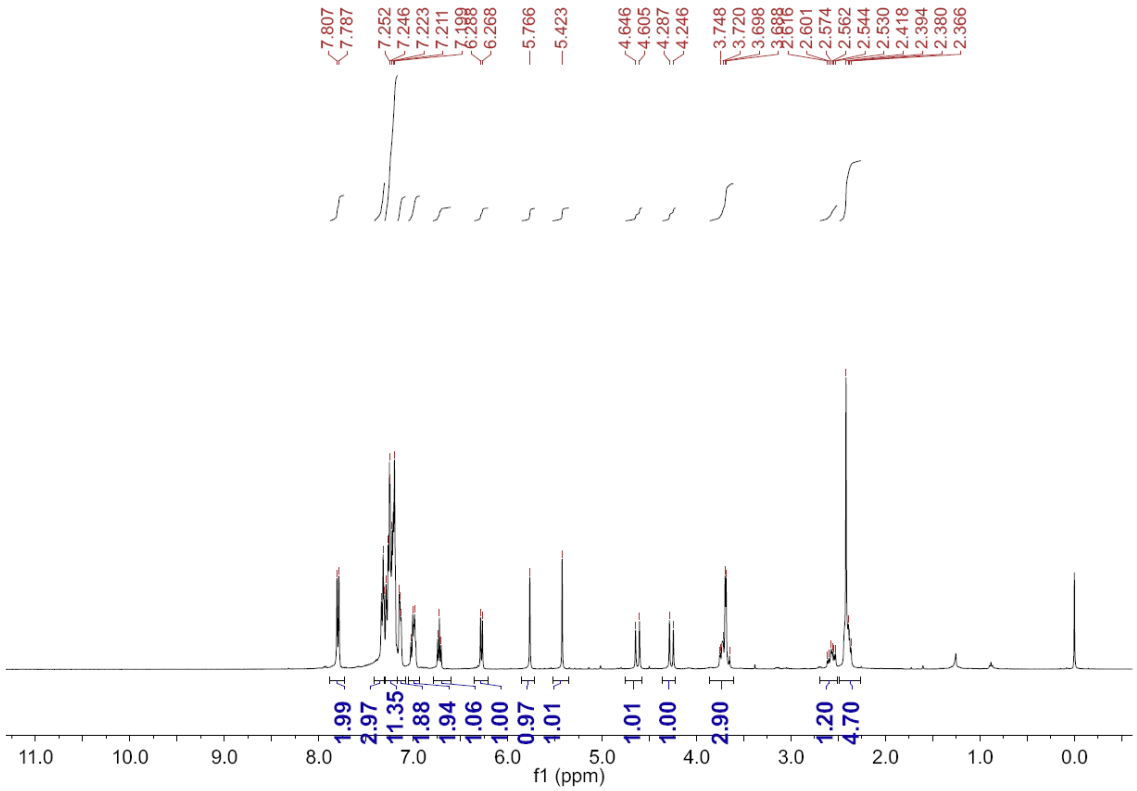

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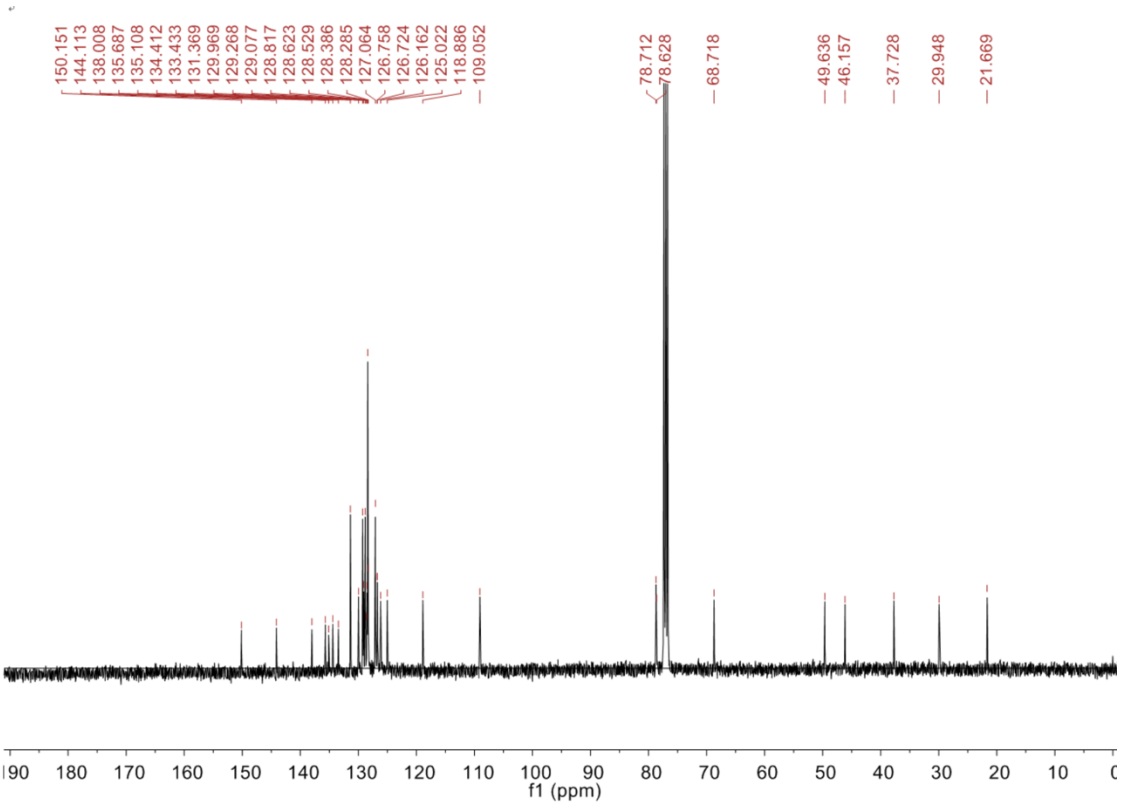

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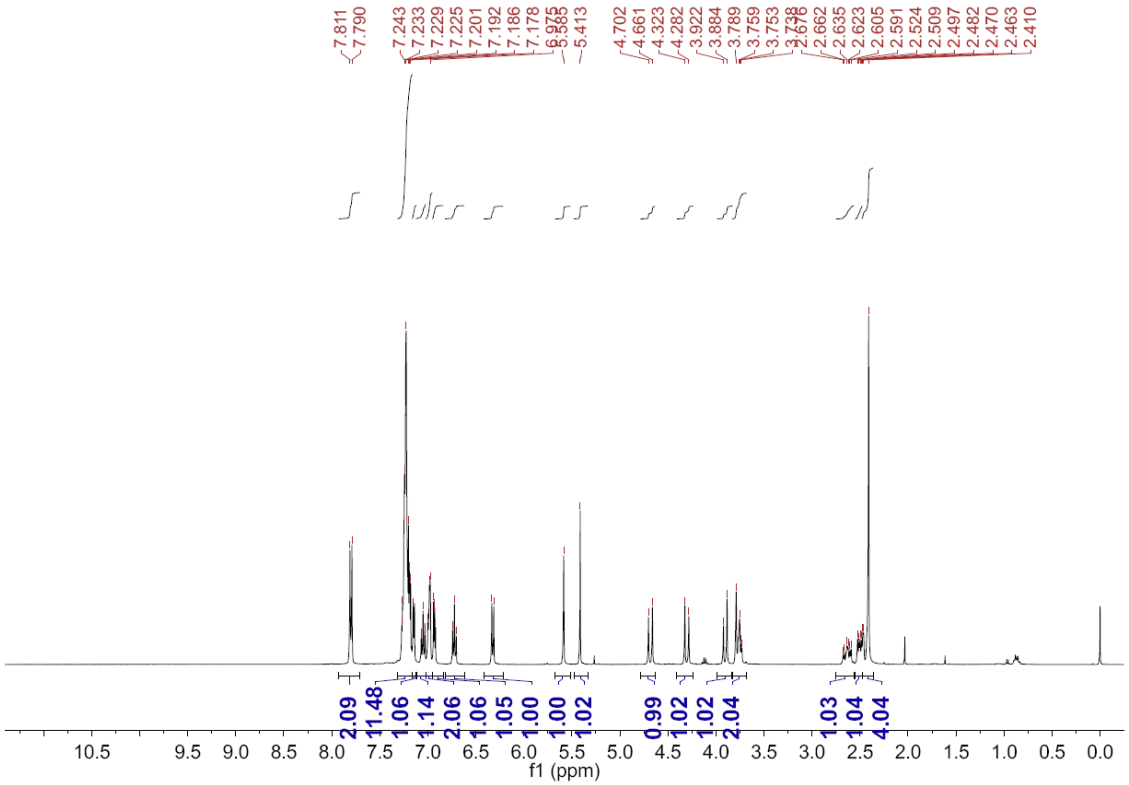

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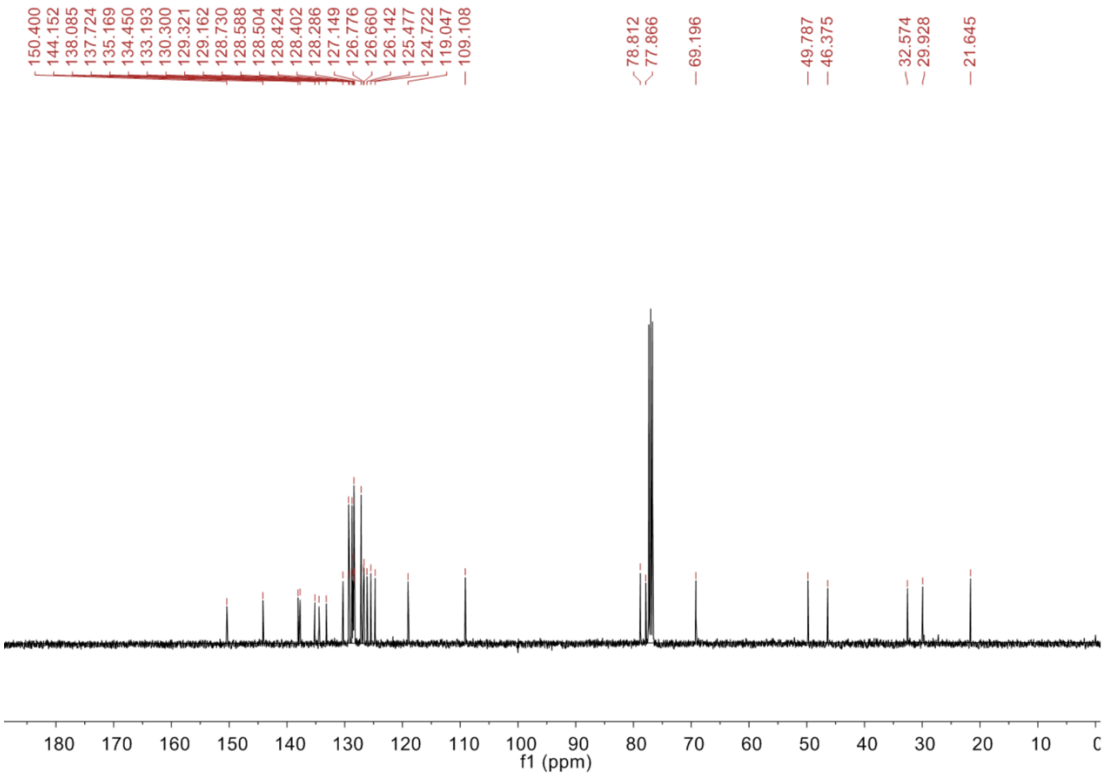
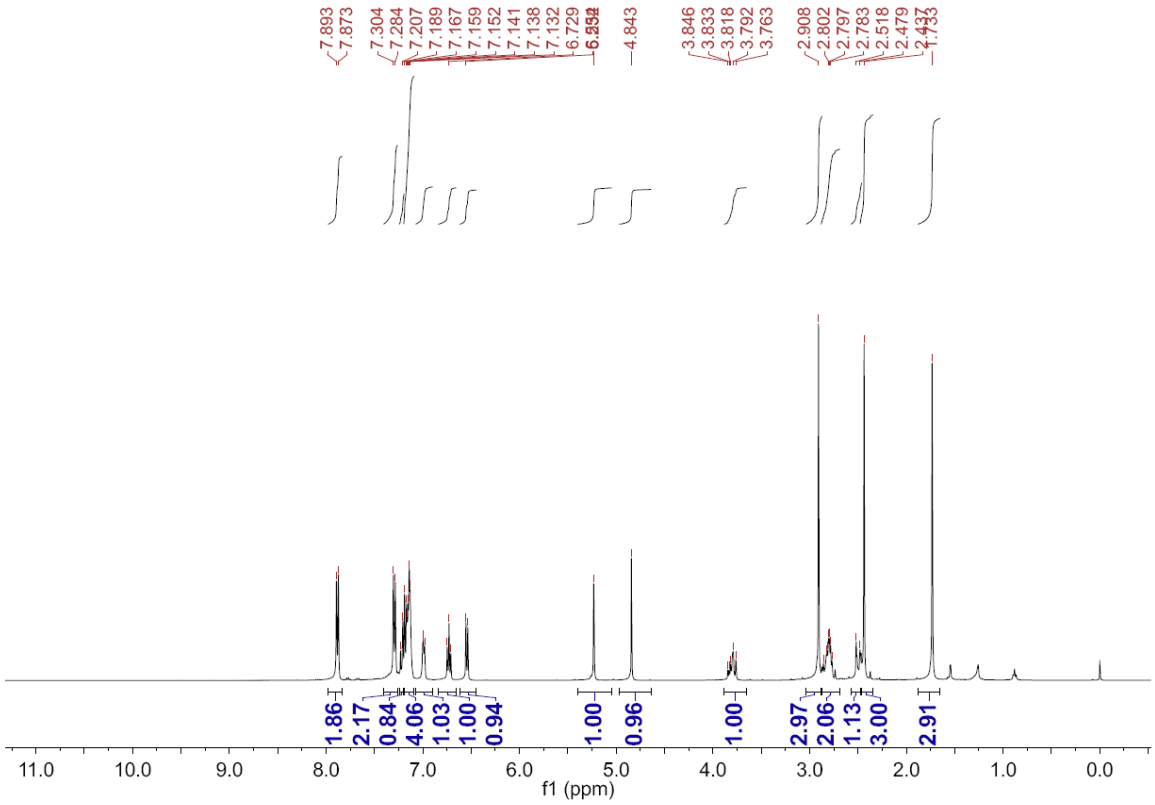


^{1}H NMR of **4r**



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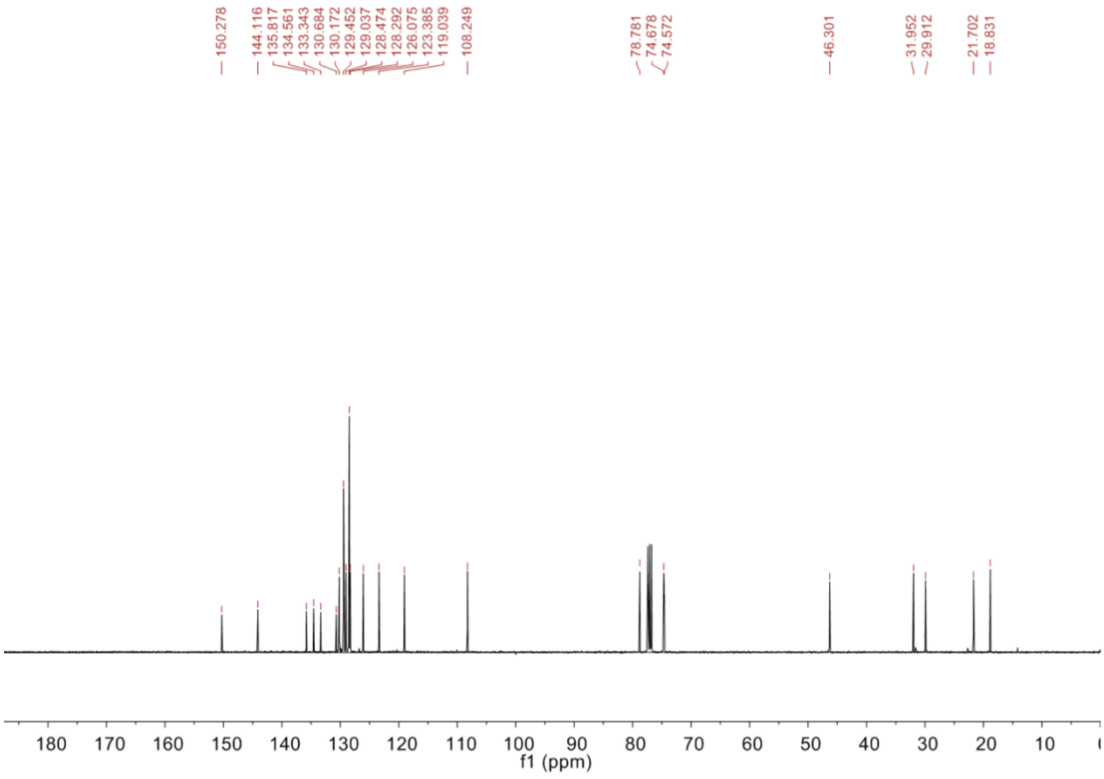
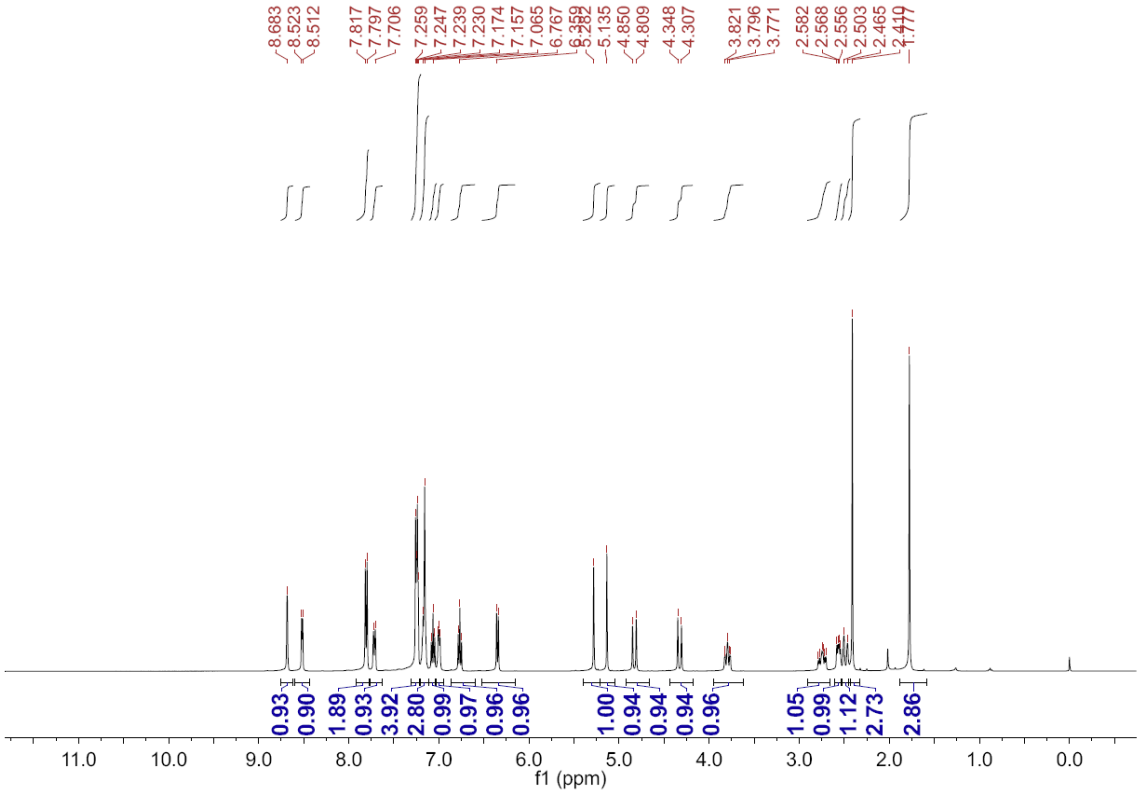


^{1}H NMR of **4s**



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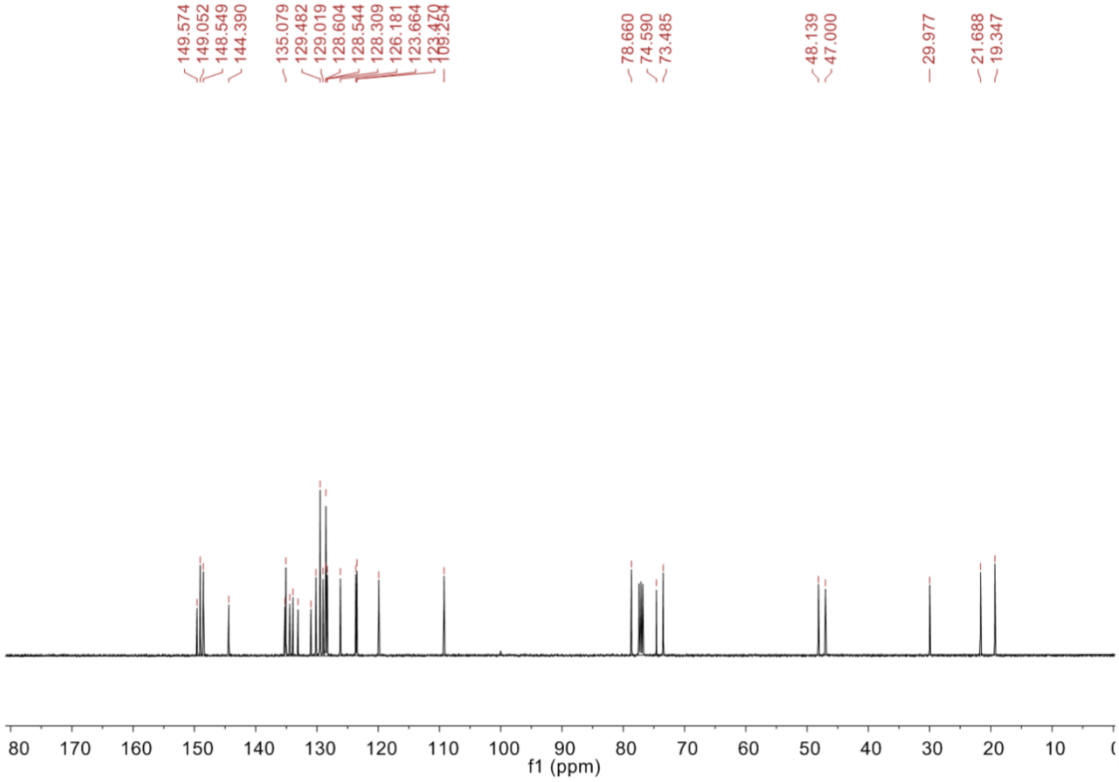
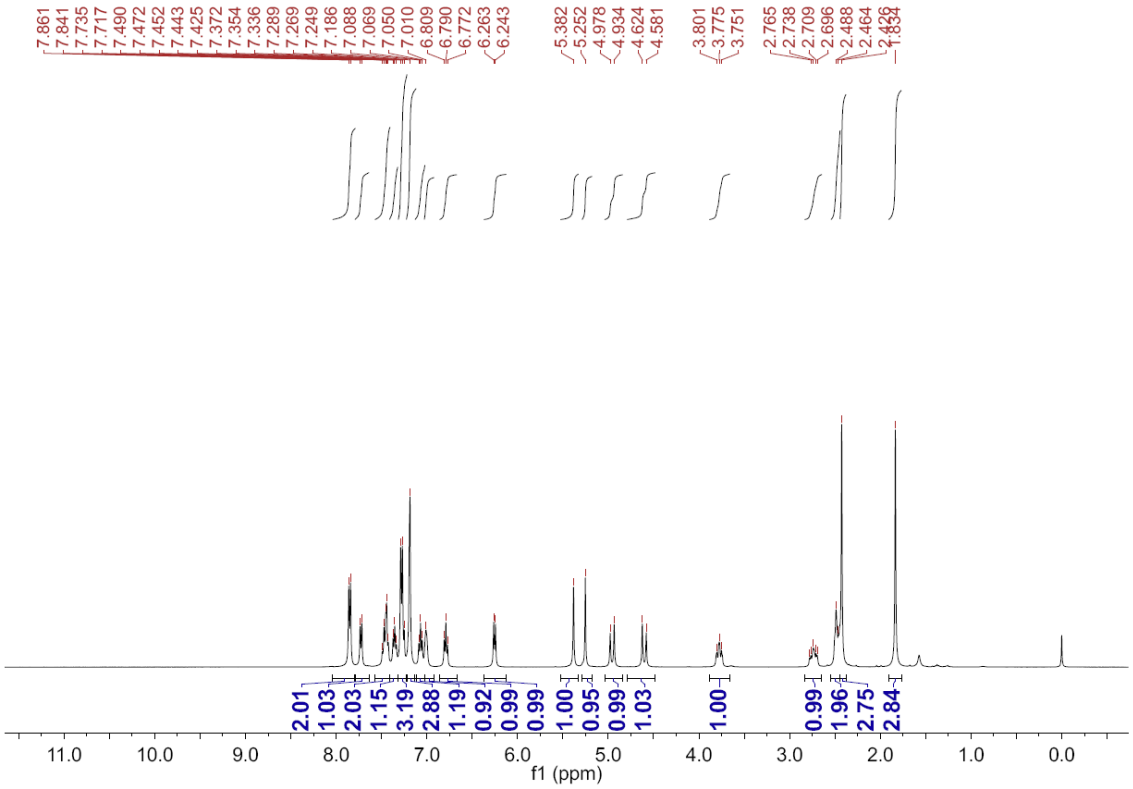
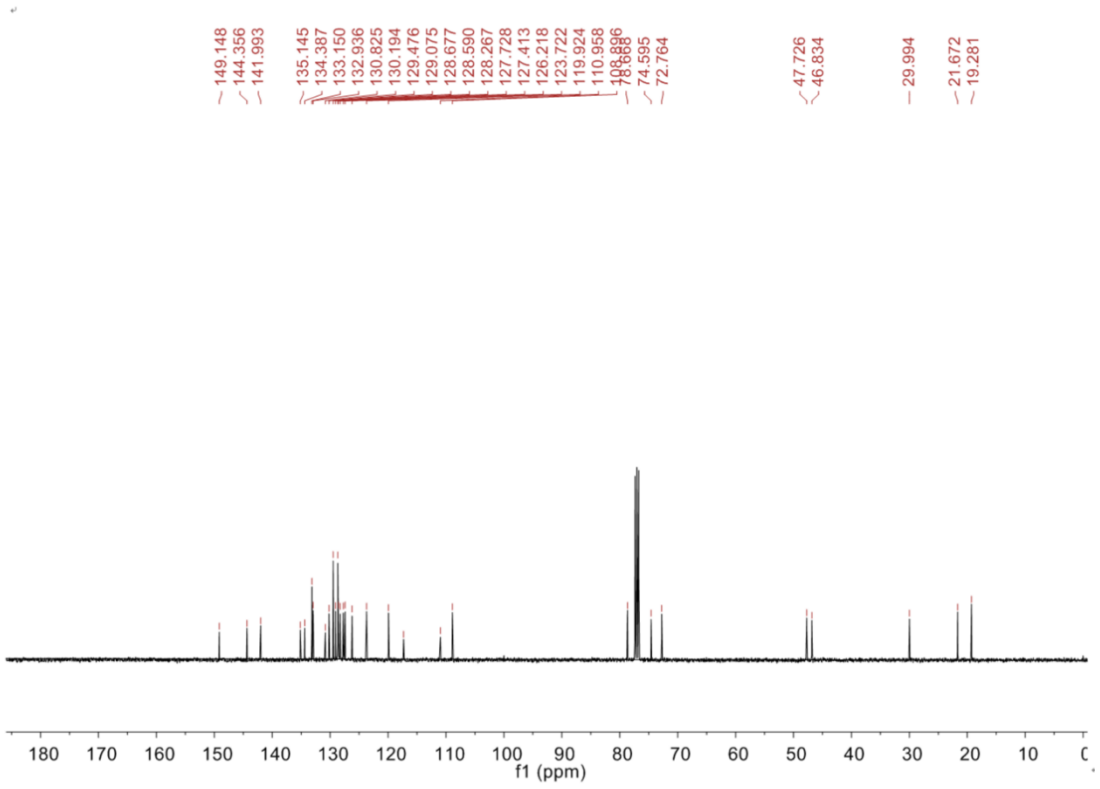


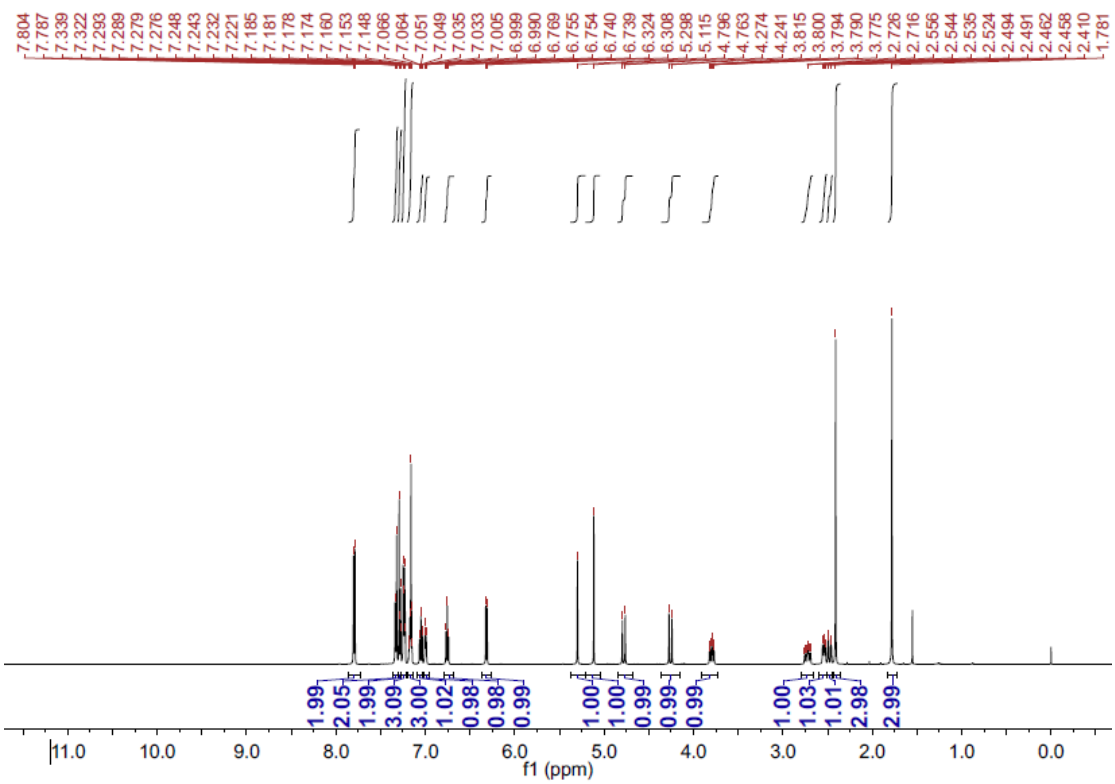
^{1}H NMR of **4t**



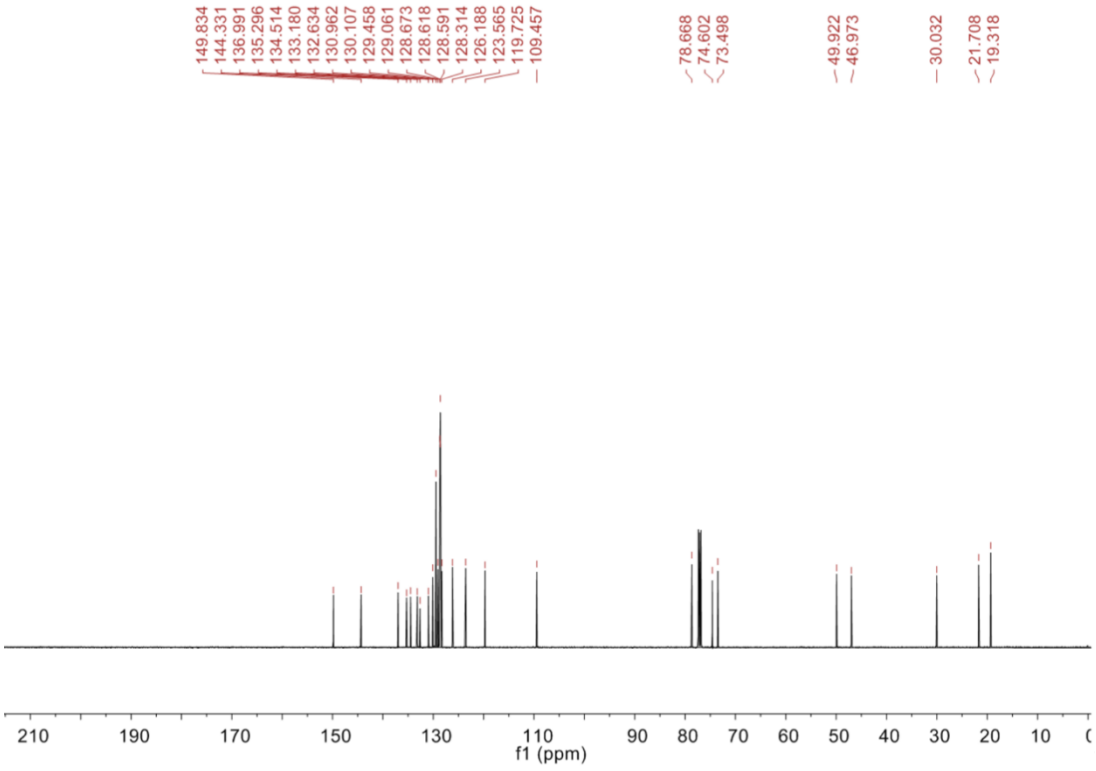
^{13}C NMR of **4t**



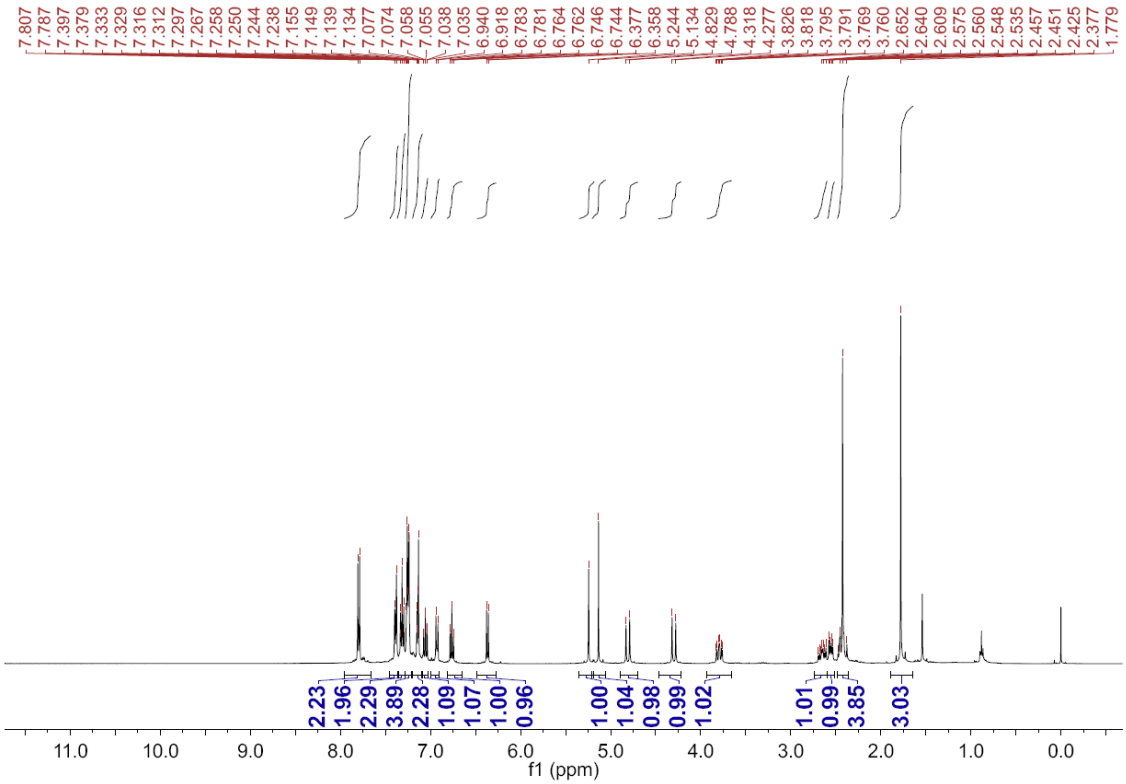
^{1}H NMR of **4u**



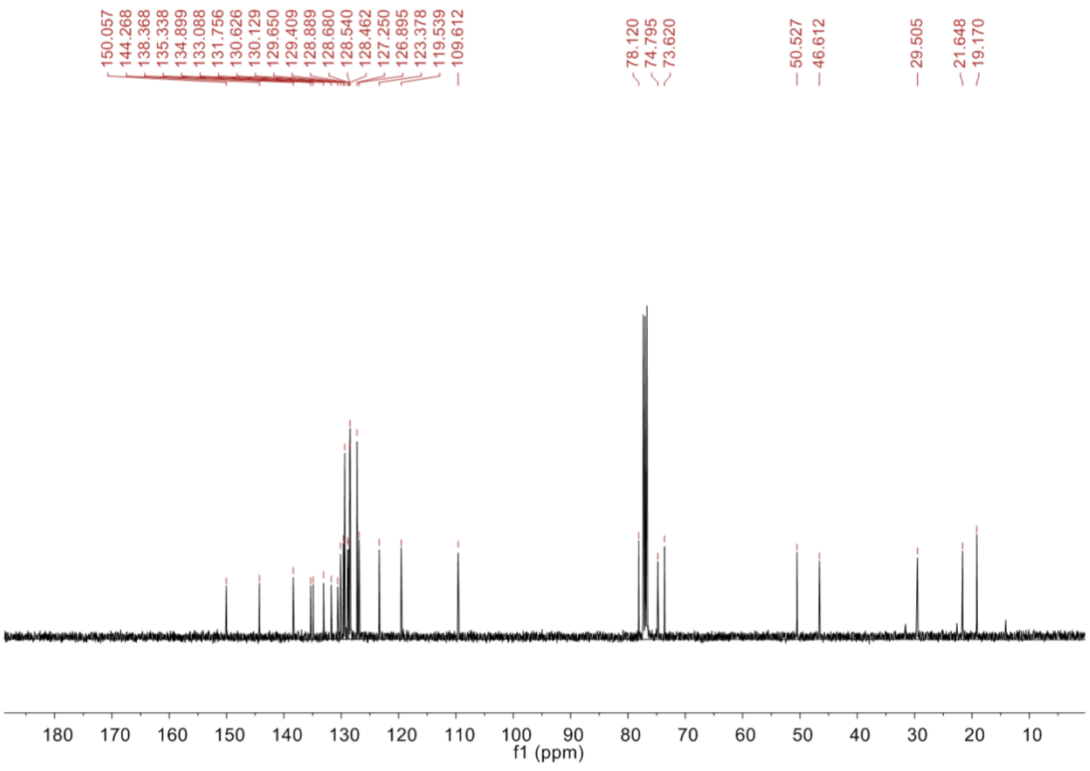
^{13}C NMR of **4u**



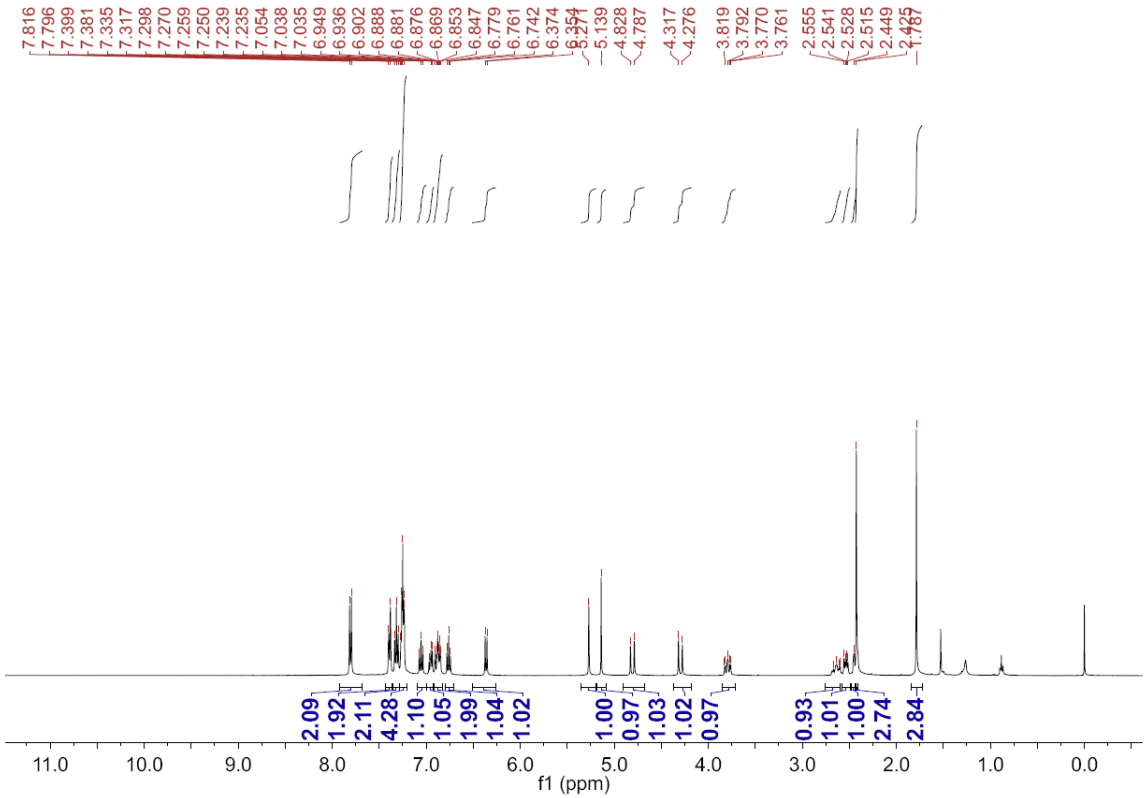
^{1}H NMR of **4v**



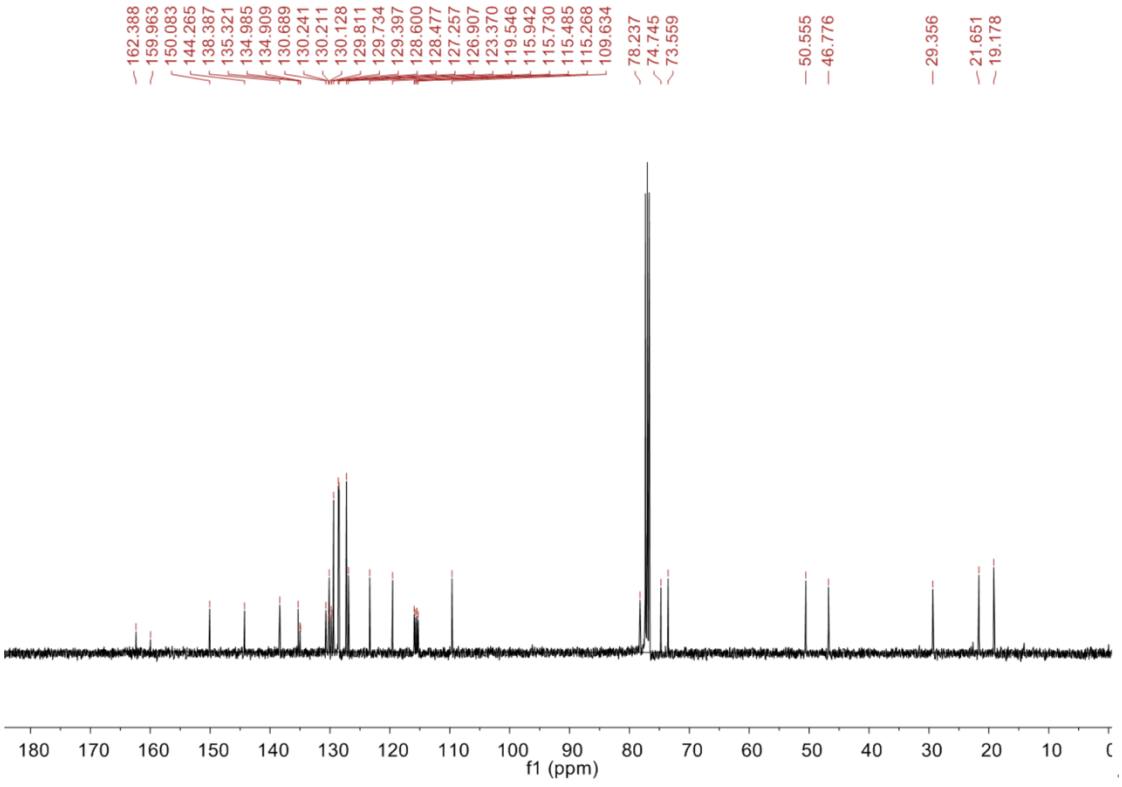
^{13}C NMR of **4v**



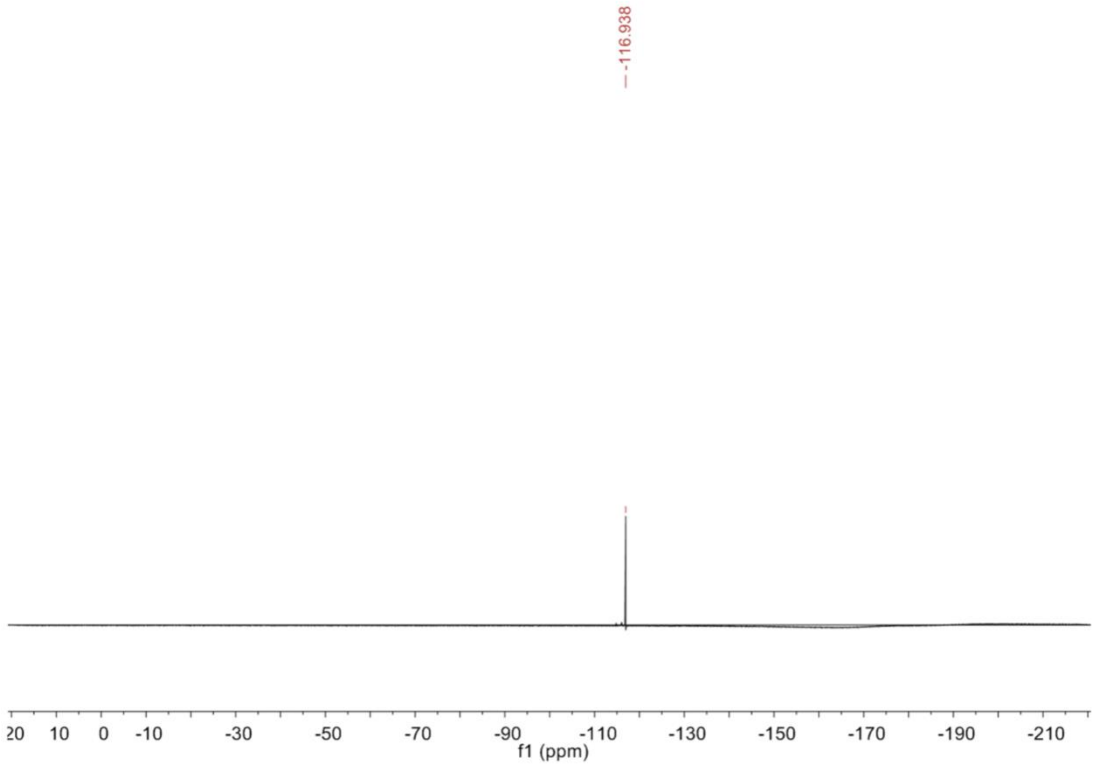
^{1}H NMR of **4w**



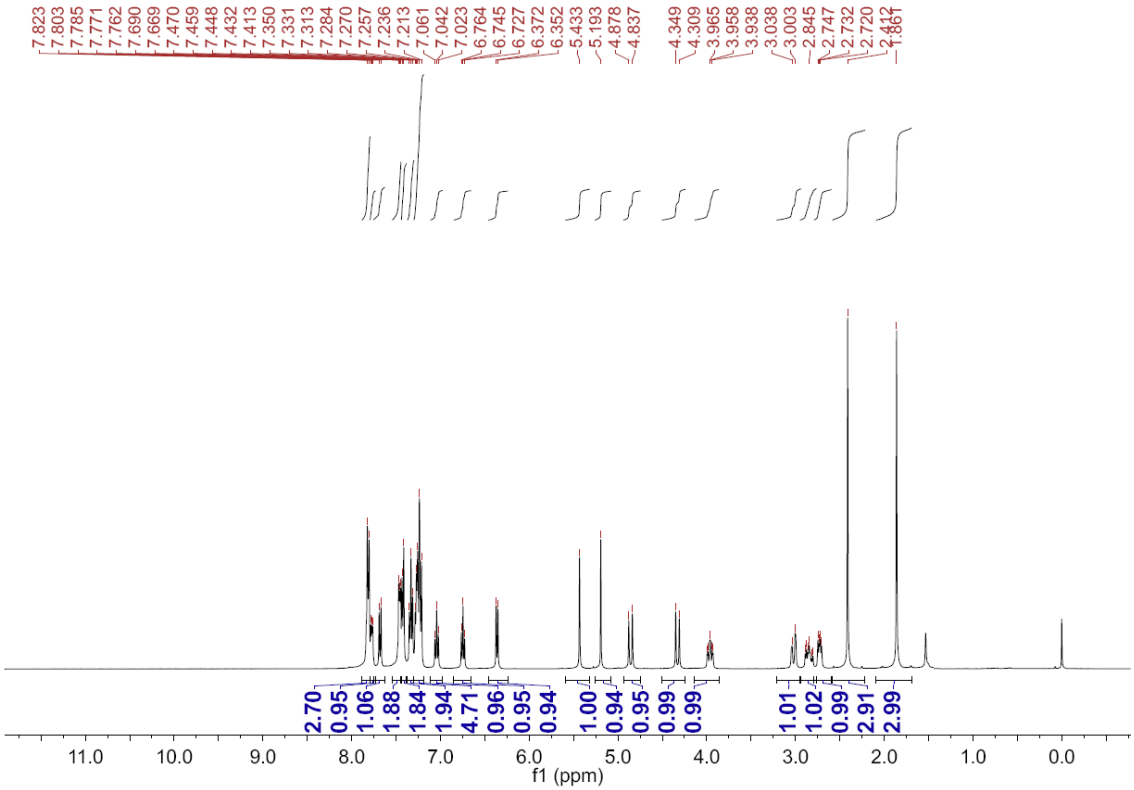
^{13}C NMR of **4w**



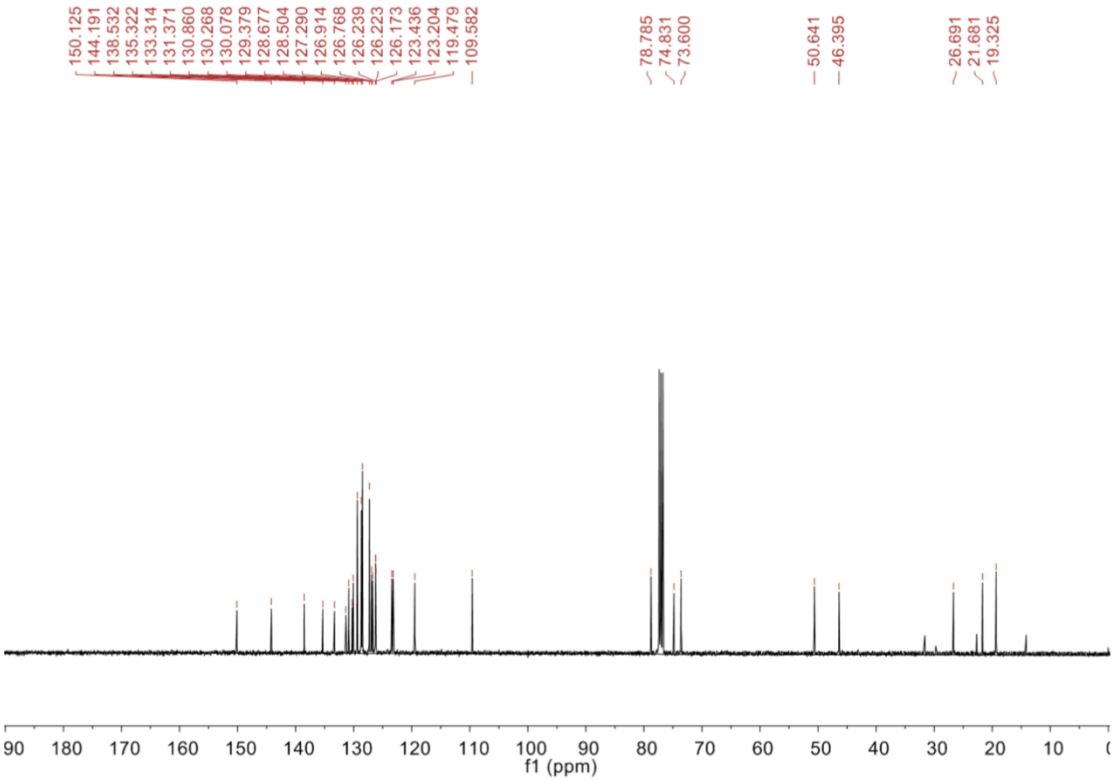
^{19}F NMR of **4w**



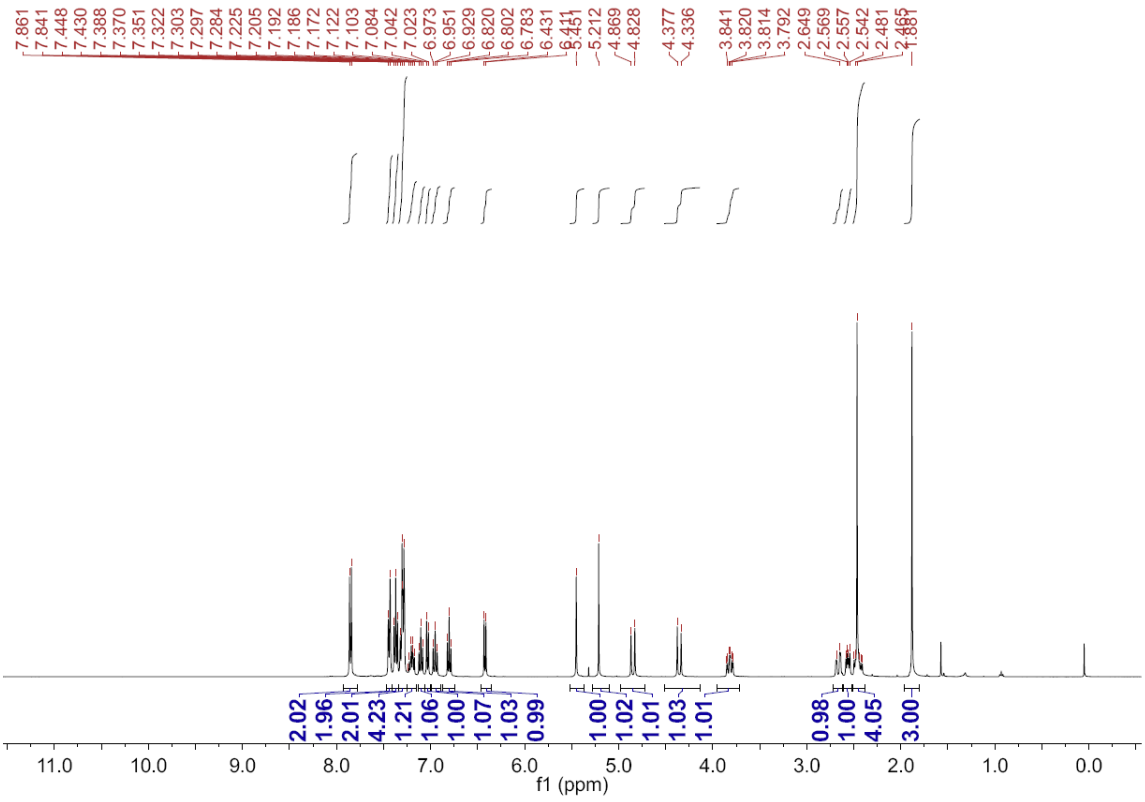
^{1}H NMR of **4x**



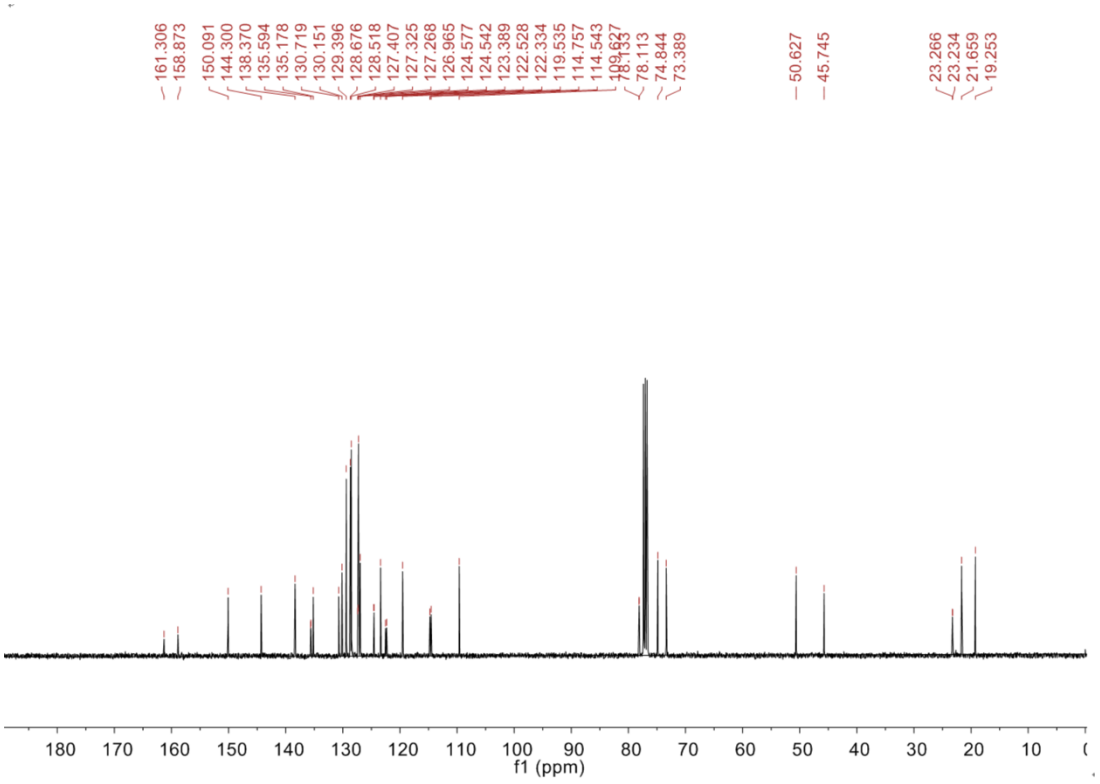
^{13}C NMR of **4x**



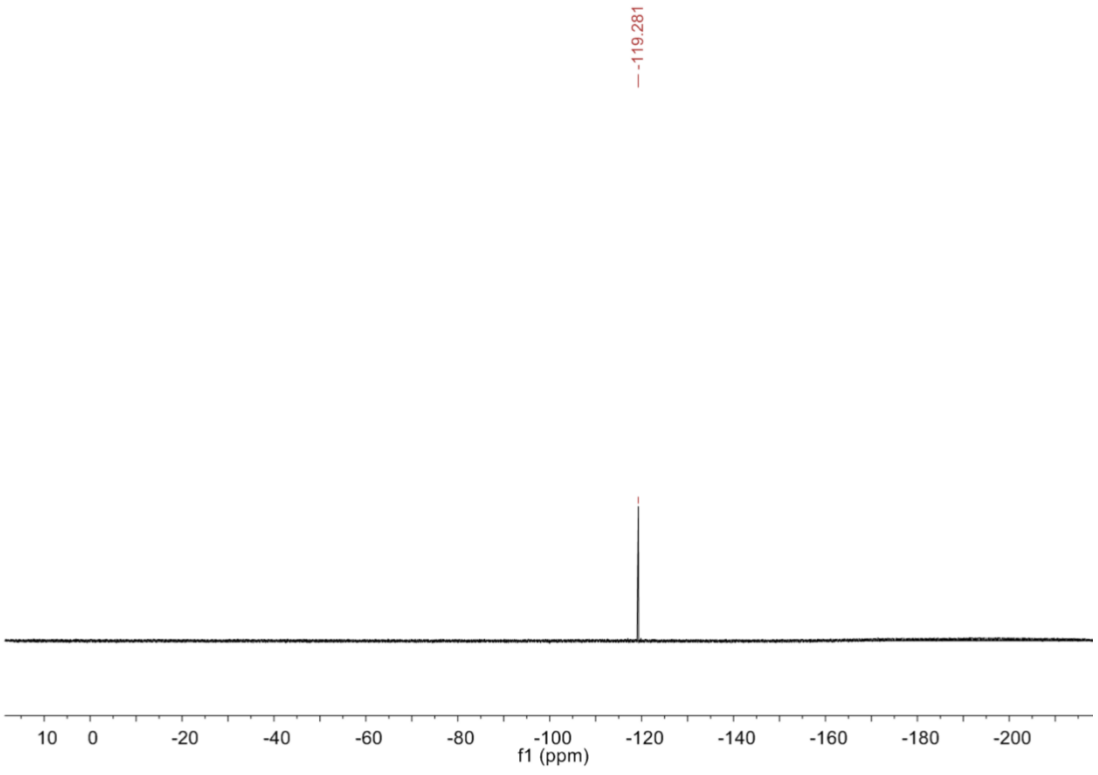
^{1}H NMR of **4y**



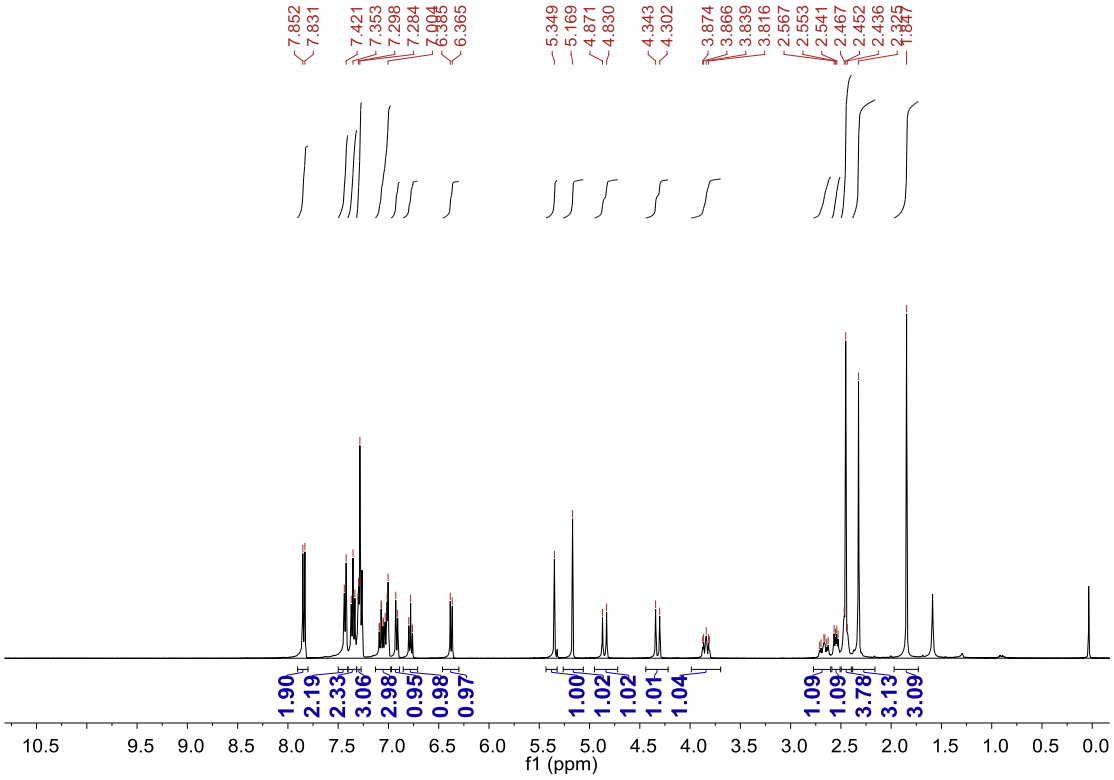
^{13}C NMR of **4y**



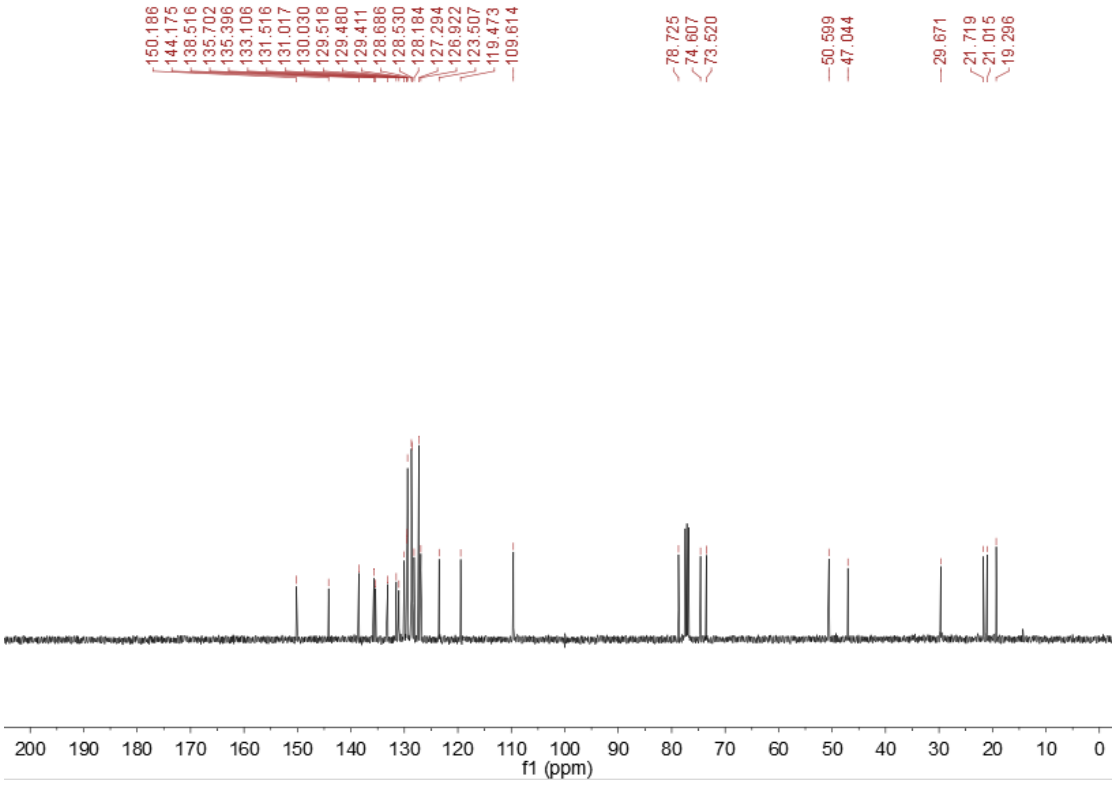
^{19}F NMR of **4y**



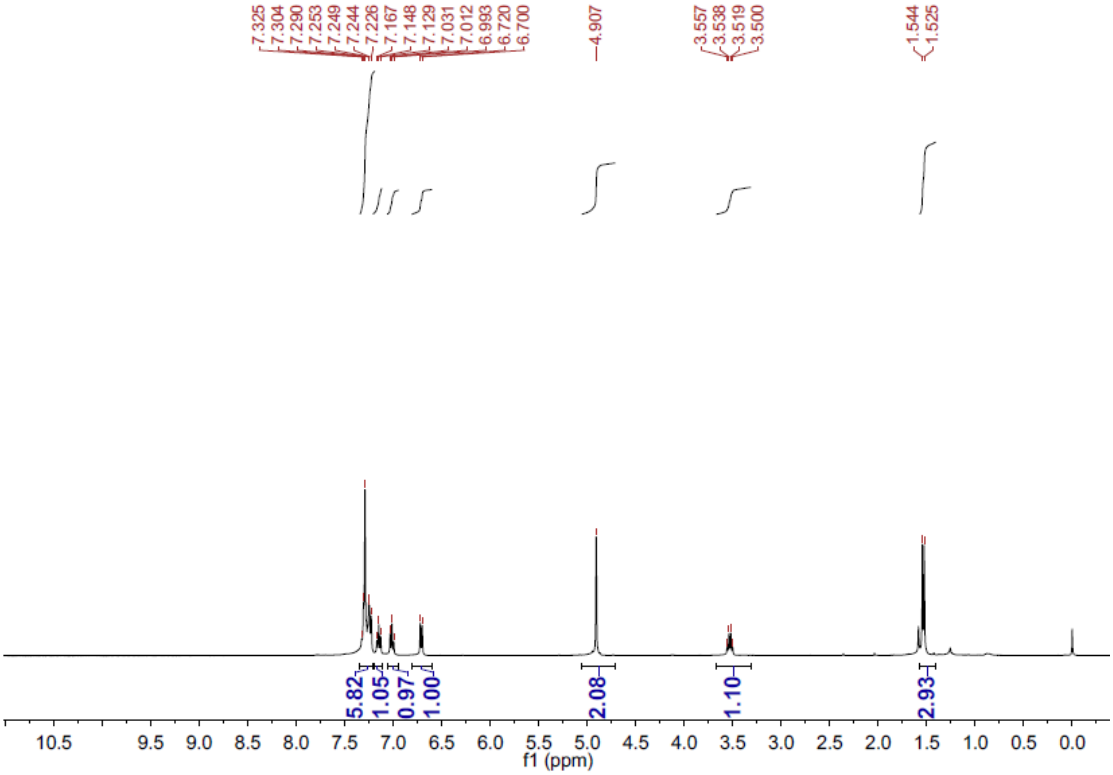
^{1}H NMR of **4z**



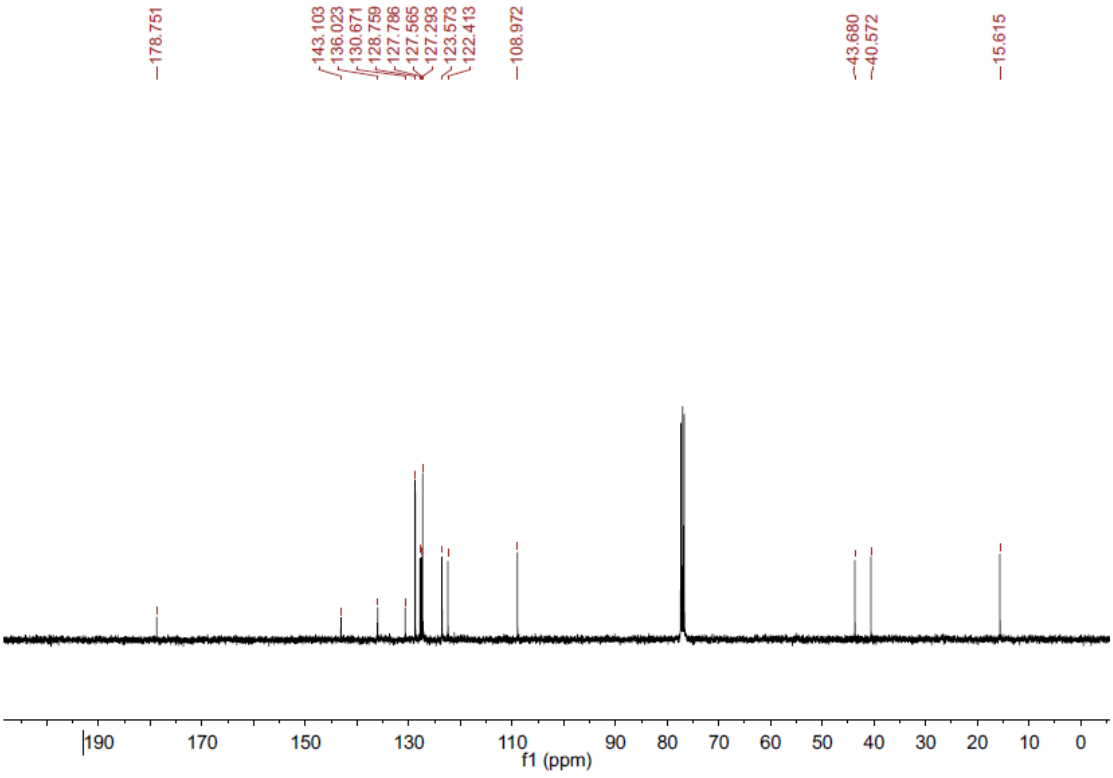
^{13}C NMR of **4z**



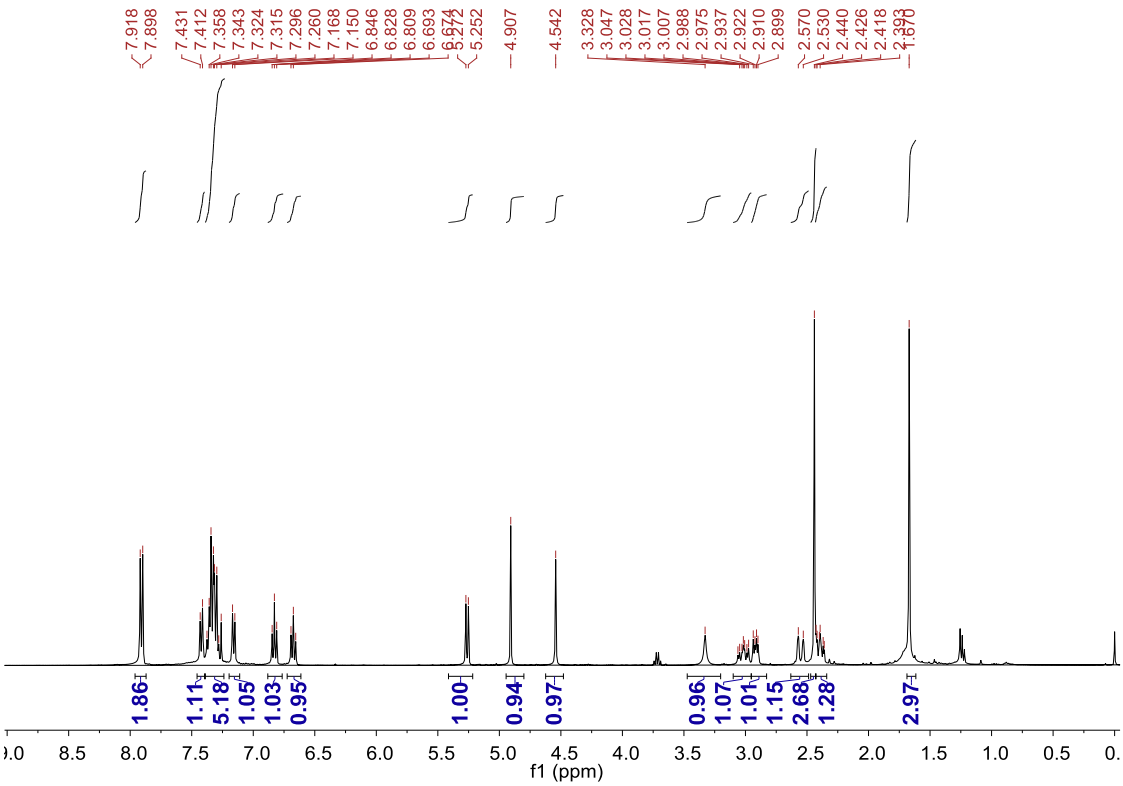
^{1}H NMR of **5**



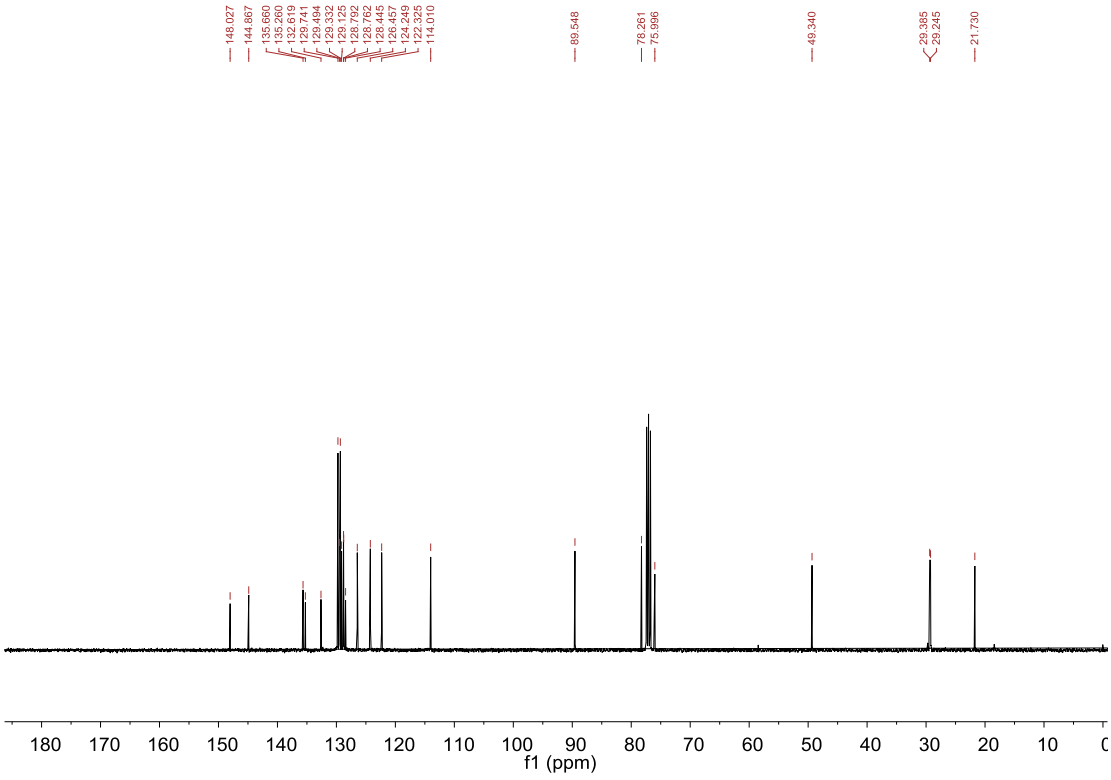
^{13}C NMR of **5**



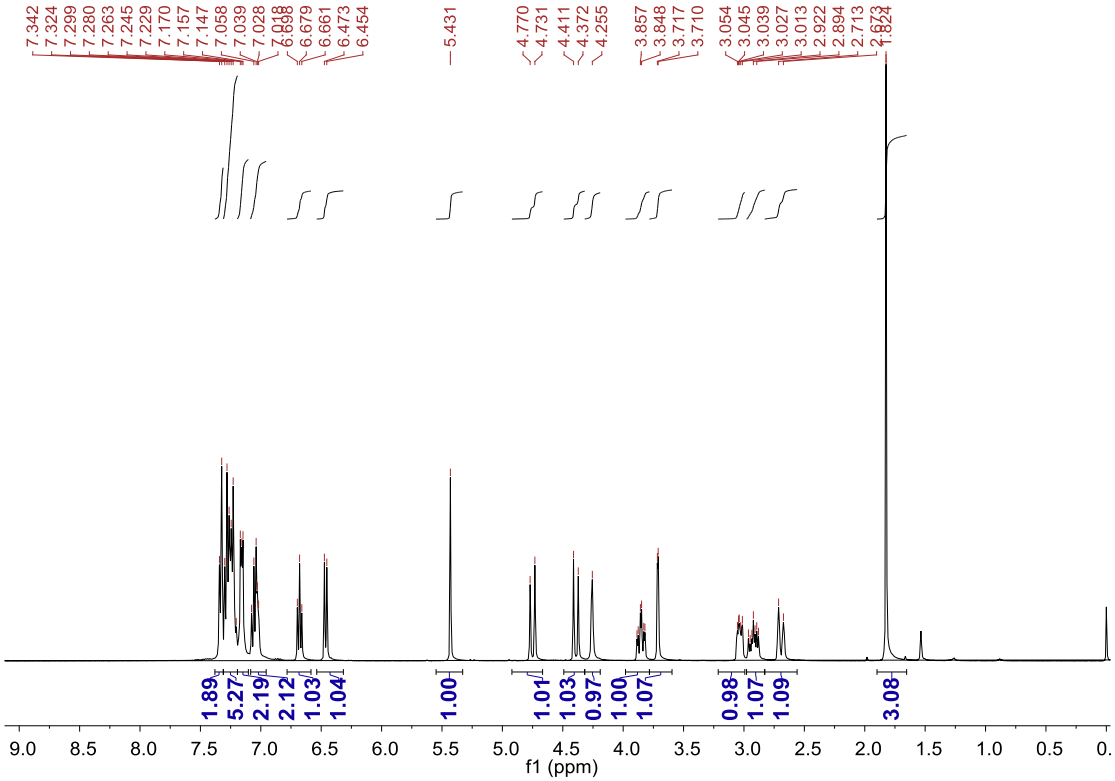
^{1}H NMR of **6**



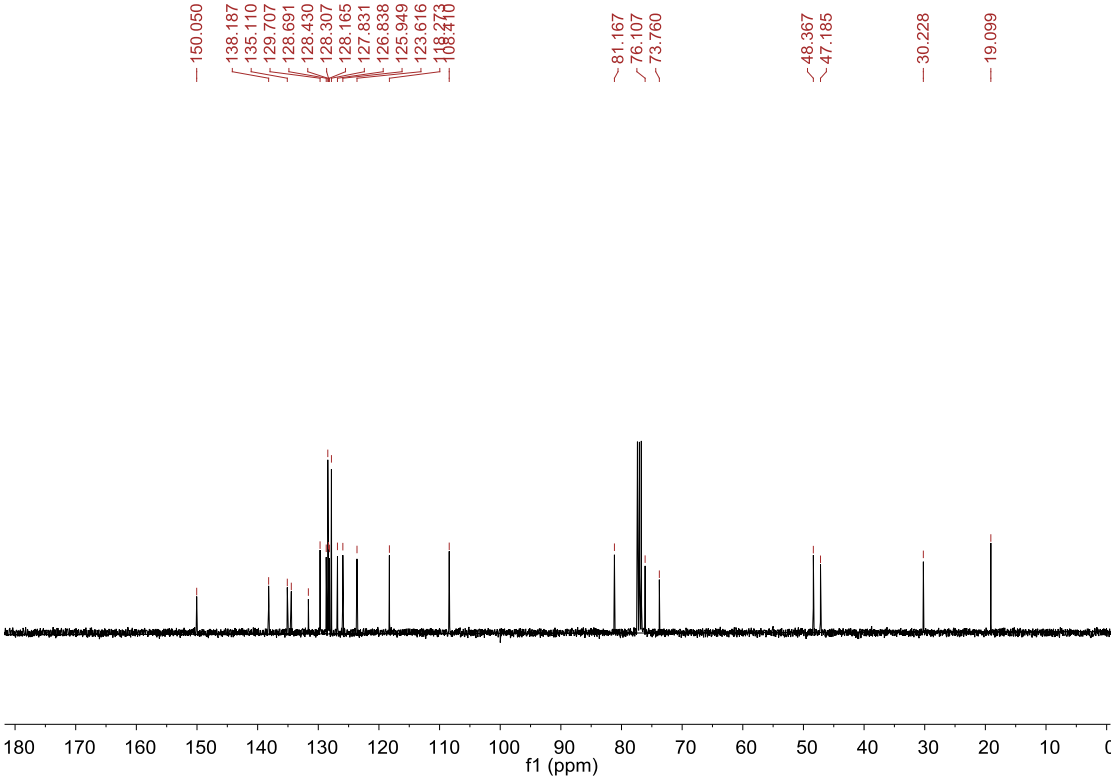
^{13}C NMR of **6**



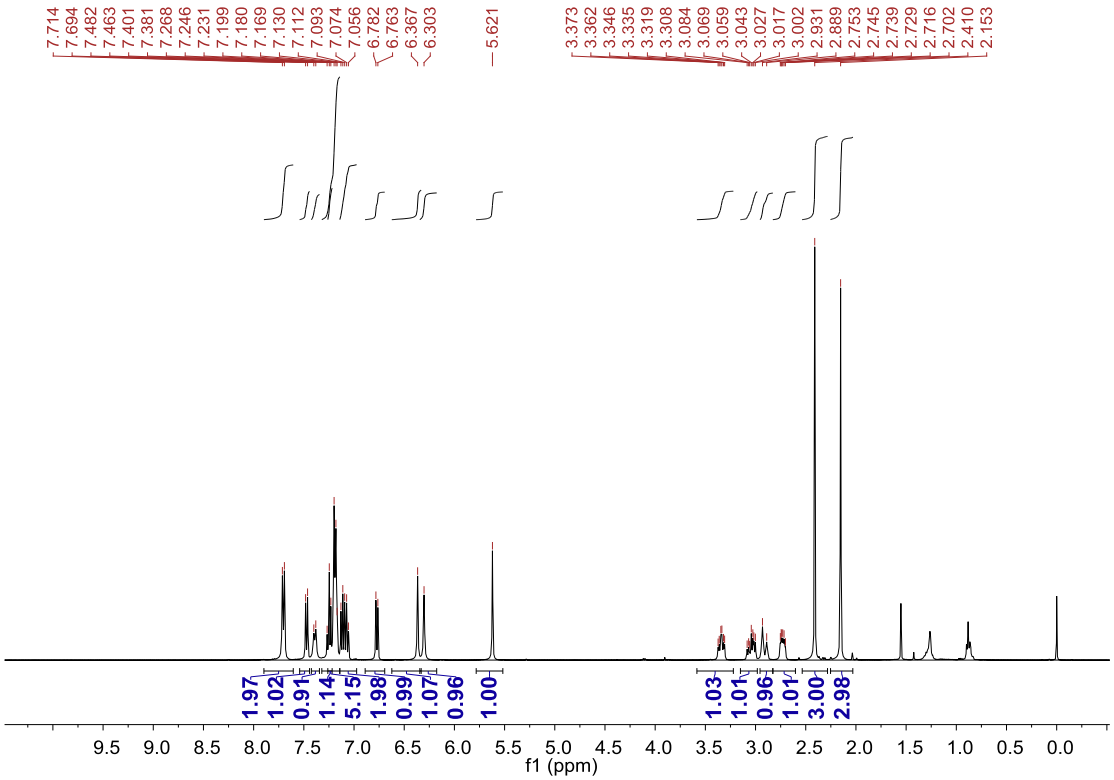
^{1}H NMR of **7**



^{13}C NMR of **7**



^{1}H NMR of **8**



^{13}C NMR of **8**