Catalytic Stereoselective Synthesis of Diverse Oxindoles and Spirooxindoles from Isatins

Jacob P. MacDonald, Joseph J. Badillo, Gary E. Arevalo, Abel Silva-Garcia, Annaliese K. Franz*

University of California, Department of Chemistry, One Shields Ave, Davis, CA 95616 USA

akfranz@ucdavis.edu

Supporting Information

I. General Information

Materials. Commercially available reagents were obtained from (Aldrich, Acros, AKSci) and used without further purification. Indole-2,3-dione (isatin) reagents were purchased from commercial sources or prepared in one step by alkylation. Dry CH_2Cl_2 was dispensed from a solvent purification system that passes CH_2Cl_2 through two columns of dry neutral alumina. Anhydrous acetonitrile was purchased from EMD (drisolv® bottle). The following abbreviations are used throughout: ethyl acetate (EtOAc), dichloromethane (DCM), dimethylformamide (DMF), *N,N*-Dimethylethylenediamine (DMEDA), diastereomeric ratio (dr), triethylamine (Et_3N), *para*-methoxyphenyl (PMP), *para*-methoxybenzyl (PMB), benzyl (Bn), trimethoxyphenyl (TMP), percent enantiomeric excess (% ee), isopropyl alcohol (IPA).

Synthesis, Purification, and Analysis. All reactions were performed in oven-dried and argon-purged glassware (including 4-8 mL vials fitted with PTFE caps). All ^1H and ^{13}C spectra were recorded at ambient temperature at 400 (or 300, 600) and 100 (or 75, 150) MHz, respectively, using a Varian Mercury 300 (300 MHz), or Varian Inova 400 (400 MHz) or Varian 600 (600 MHz) spectrometer. The ^1H spectral data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane on the δ scale, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; sep, septet; m, multiplet; dd, doublet of doublets; dt, doublets of triplets; td, triplet of doublets, and b, broadened), coupling constant (Hz), and integration. Carbon NMR chemical shifts are reported in ppm from tetramethylsilane with the solvent reference employed as the internal standard (deuterochloroform ($CDCl_3$) at 77.16 ppm).

Compounds were analyzed for HRMS on a Thermo Fisher Orbitrap (San Jose, CA) using electrospray in the positive ion mode at >60,000 resolution and using typical ESI source values. These settings result in mass accuracies <5ppm. Compounds were analyzed for MS (ESI) by an Applied Biosystems Qtrap (Foster City, CA) in the positive ion mode. Source parameters were 5kV spray voltage, with a curtain plate temperature of 275 ˚C and sheath gas setting of 15. Samples were analyzed via flow injection analysis by injecting 20 μL samples into a stream of 80% MeOH/20% aqueous solution of 0.1% formic acid, flowing at 200 μL/min. When indicated, the progress of reactions was monitored by analytical thin layer chromatography using glass or aluminum backed plates pre-coated with EMD silica gel 60 F254 and visualized with UV light. Flash chromatography was performed either on Acros silica gel 60 Å (0.035-0.070 mm), Aldrich silica gel 150 Å grade 62 (60-200 mesh), or using a CombiFlash Companion system (Teledyne ISCO, Inc.) with pre-packed FLASH silica columns (RediSep, Rf®). All HPLC analyses were performed on a Shimadzu LC-20AB system with a Daicel CHIRALPAK® AD-H column (4.6 x 250 mm, 5 μm), CHIRALPAK® AS-H column (4.6 x 250 mm, 5 μm) or CHIRALPAK® OD-H

column (4.6 x 250 mm, 5 μm), each attached to a guard column, at a flow rate of 1 mL/min (isopropanol/hexanes isocratic system) using a Shimadzu SPD-M20A photodiode array detector and 40 °C column oven temperature. Optical rotations were obtained on a Rudolph AUTOPOL IV polarimeter at a wavelength of 589 nm (sodium D line) using a 1.0 dm cell. Specific rotations are reported in degrees per decimeter at 23 °C and the concentrations are given in grams per 100 mL of solvent. Solvents used for optical rotations were MeOH (reagent grade), and $CHCl_3$ (stabilized with 0.5% - 1% EtOH, and filtered through basic alumina).

II. Experimental Procedures

a. General Procedures

General Procedure for the Preparation of 5-methoxyoxazoles[1-2]

To a solution of benzoic acid (4.48 mmol) in EtOAc (30 mL) was added the methyl ester hydrochloride (6.72 mmol), NEt_3 (19.3 mmol), HOBt (4.93 mmol), and HBTU (5.38 mmol). The reaction was stirred for 24 h until the reaction was complete as visualized by TLC (10% EtOAc/CH_2Cl_2). The reaction was diluted with 20 mL of EtOAc, washed with 100 mL of $NaHCO_3$ (sat. aq.), brine (100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting residue was purified using flash chromatography (gradient of EtOAc/CH_2Cl_2 ending with 10% EtOAc/CH_2Cl_2) to give the amide.

To a mixture of PPh_3 (13.3 mmol) and I_2 (13.3 mmol) in dry CH_2Cl_2 (25 mL), Et_3N (26.5 mmol) was added dropwise and stirred for 10 min to give a dark red solution. The amide (6.63 mmol) was added as a solution in CH_2Cl_2 (25 mL) by cannula and the reaction mixture was stirred for 24 h until complete as determined by TLC (10% EtOAc/CH_2Cl_2). The reaction mixture was diluted with 50 mL of CH_2Cl_2, washed with 100 mL of $NaHCO_3$ (sat. aq.), brine (100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo.* The resulting residue was purified by flash chromatography (gradient of 20-40% hexanes/EtOAc) to give the 5-methoxyoxazoles **11e**,**f**.

General Procedures for Preparation of Core Spirocyclic Oxazoline Scaffolds[1]

A solution of isatin (0.18 mmol) and 5-methoxyoxazole (0.12 mmol) was prepared in dry CH_2Cl_2 (0.12 M) at 25 ˚C in an oven-dried and Ar-purged 8 mL vial fitted with a magnetic stir bar. To this mixture, 24 μL of a 1.0 M solution of $TiCl_4$ (0.024 mmol, 1.0 M solution in CH_2Cl_2) was added. The reaction was stirred until it was complete as judged by TLC (10% EtOAc/CH_2Cl_2).

---

[1] Badillo, J. J.; Arevalo, G. E.; Fettinger, J. C.; Franz, A. K. *Org. Lett.* **2010,** *13*, 418-421.
[2] Mitchell, J. M.; Shaw, J. T. *Angew. Chem. Int. Ed.* **2006,** *45*, 1722-1726.

Upon completion of the reaction, the reaction mixture was diluted with 5 mL of CH_2Cl_2. The organic layer was washed with 20 mL of sodium potassium tartrate (sat. aq,), brine (20 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Before purification the diastereomeric ratio (dr) was determined by ^1H NMR spectroscopy. The resulting residue was loaded onto a flash silica gel column (gradient of EtOAc/CH_2Cl_2 ending with 10% EtOAc/CH_2Cl_2) to afford the spirooxindole oxazoline. Note that purification of NH substrates required a gradient of EtOAc/CH_2Cl_2 ending with 40 to 60% EtOAc/CH_2Cl_2.

General Procedure for Preparation of Hydroxy-oxindole Core Scaffolds[3]

To an oven dried, argon-purged 4 mL vial equipped with a stir bar and 4 Å molecular sieves (100 mg/mmol) was added $Sc(OTf)_3$ (0.028 mmol) and 2,6-Bis[(3a*S*,8a*R*)-3a,8a-dihydro-8H-indeno[1,2-d]oxazolin-2-yl]pyridine ((*S*,*R*)-indapybox) ligand (0.030 mmol) in dry CH_2Cl_2 (0.24 M). This solution was stirred at room temperature for 1-2 h. The appropriate isatin (0.300 mmol) was then added to the scandium-pybox complex at room temperature. The corresponding nucleophile (0.900 mmol) was added at the appropriate temperature (-20 °C or 23 °C). The reaction was monitored by TLC and when complete, the reaction mixture was loaded directly onto a flash silica gel column and eluted using a gradient of DCM/EtOAc.

General Procedures for Preparation of Spiroindolone Core Scaffolds

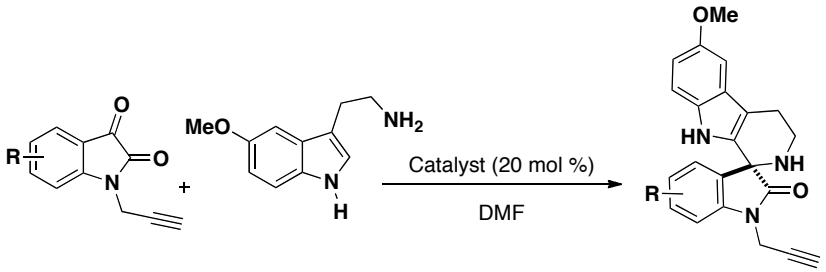
Method A.[4] A solution of isatin (0.05 mmol), tryptamine (0.05 mmol) and (*S*)-3,3′-bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate (0.005 mmol, 10 mol %) was prepared in dry DMF (0.2 M) at 40 °C in an oven-dried and Ar-purged 4 mL vial containing a magnetic stir bar. The reaction was stirred until it was complete as judged by TLC (80% EtOAc/hexanes). The reaction was then concentrated and loaded onto a flash silica gel column (gradient of EtOAc/hexanes ending in 80% EtOAc/hexanes) to afford the spiroindolone product.

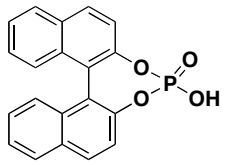
Method B.[5] A solution of isatin (1.0 mmol), tryptamine (1.0 mmol) and 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea or $Sc(OTf)_3$ (0.1 mmol, 20 mol %) was prepared in dry CH_2Cl_2 (0.06 M) at 25 °C in an oven-dried and Ar-purged 4 mL vial containing a magnetic stir bar. The reaction was stirred until it was complete as judged by TLC (80% EtOAc/hexanes). The

[3] Hanhan, N. V.; Sahin, A. H.; Chang, T. W.; Fettinger, J. C.; Franz, A. K. *Angew. Chem. Int. Ed.* **2010,** *49*, 744-747.
[4] Duce, S.; Pesciaioli, F.; Gramigna, L.; Bernardi, L.; Mazzanti, A.; Ricci, A.; Bartoli, G.; Bencivenni, G. *Adv. Synth. Catal.* **2011,** *353*, 860-864.
[5] Badillo, J. J.; Silva-Garcia, A.; Shupe, B. H.; Fettinger, J. C.; Franz, A. K. *Tetrahedron Lett.* **2011,** *52*, 5550-5553.

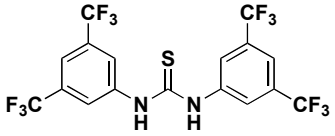
reaction was then concentrated and loaded onto a flash silica gel column (gradient of EtOAc/hexanes ending in 80% EtOAc/hexanes) to afford the spiroindolone product.

During the course of this investigation, optimization of catalysts for the racemic synthesis was performed. The results are summarized below:





Phosphoric Acid

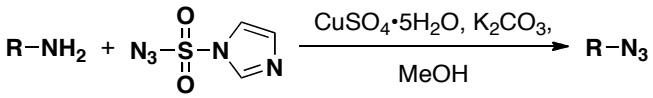


Thiourea

Table S1.

entry	R	catalyst	time (days)	yield (%)
1	H	phosphoric acid	4	18
2	H	$Sc(OTf)_3$	2	89
3	5-F	$Sc(OTf)_3$	1	93
4	7-F	thiourea	3	92

General Procedure for the Preparation of Azides, Method A:

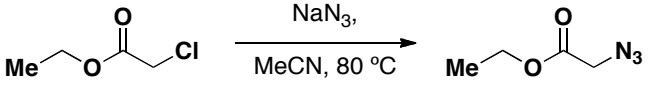


Following the procedure outlined by Stick and coworkers,[6] the appropriate amine (1.00 mmol) and 5 mL of methanol was added to a 20 mL scintillation vial containing a magnetic stir bar, followed by the addition of $CuSO_4•5H_2O$ (0.01 mmol), K_2CO_3 (1.7 mmol), and imidazole-1-sulfonyl azide hydrochloride (1.2 mmol). The reaction was stirred at room temperature until complete (as judged by TLC, 10% EtOAc/DCM). The reaction mixture was concentrated *in vacuo*, diluted with H_2O (10 mL), and acidified with concentrated HCl (5-10 drops). The aqueous layer was extracted with 3 × 20 mL of EtOAc. Then the combined organic layers were

[6] Goddard-Borger, E. D.; Stick, R. V. *Org. Lett.* **2007,** *9*, 3797-3800.

dried with $MgSO_4$, filtered and concentrated *in vacuo*. The compound was then purified by flash chromatography using a gradient of EtOAc/DCM (100% DCM to 10% EtOAc/DCM) to give the corresponding azide. Spectral data matches reports from the literature. [6,7,8,9,10]

General Procedure for the Preparation of Azides, Method B:[11]



To a dry 250 mL round-bottom flask with magnetic stir bar, acetonitrile (75 mL) was added, followed by ethyl chloroacetate (1.6 mL, 0.015 mol), and sodium azide (1.17 g, 0.018 mol). The mixture was refluxed at 80 °C for 4 h under argon, than cooled to room temperature and stirred for 18 h under argon atmosphere. The reaction mixture was then filtered over diatomaceous earth (celite®) and concentrated in *vacuo*. The crude product was purified by flash chromatography (gradient from 100% DCM to 10:90 EtOAc/DCM) to afford the ethyl azidoacetate **12f** as a colorless oil (1.45 g, 75%). Spectral data matches reports in the literature.[11]

General Procedure for Triazole Synthesis from Azides[12]

A solution of azide (0.16 mmol) in THF (0.24 M) was prepared in a 4 mL vial containing a magnetic stir bar at room temperature that had been dried under vacuum and flushed with argon. To this solution was added copper(I) iodide (0.016 mmol, *N,N*-diisopropylethylamine (0.024 mmol), and the alkyne (0.18 mmol). The reaction was stirred at room temperature until complete as judged by TLC. The crude mixture was concentrated *in vacuo* and the resulting residue was loaded onto a flash silica gel column and was eluted with a gradient of DCM/EtOAc.

General Procedure for Triazole Synthesis from Aryl-Iodides[13]

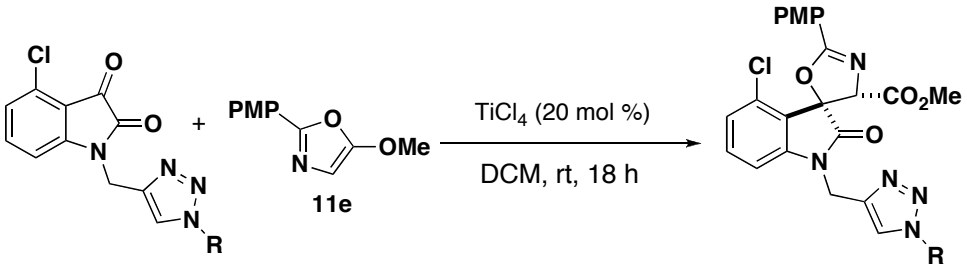
A solution of alkyne (0.041 mmol) in DMF (0.33 M) was prepared in an 8 mL vial fitted with a magnetic stir bar at room temperature. No precautions were taken to exclude air and moisture. To this mixture was added the aryl iodide (0.049 mmol), sodium azide (0.043 mmol, 1.05 equiv)

---

[7] Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *Eur. J. Org. Chem.* **2010,**1875-1884.
[8] Pal, B.; Jaisankar, P.; Giri, V. S. *Synth. Commun.* **2004,** 1317-1323.
[9] Pietruszka, J.; Solduga, G. *Eur. J. Org. Chem.* **2009,** 5998-6008.
[10] Katritzky, A. R.; El, K. M.; Bol'shakov, O.; Khelashvili, L.; Steel, P. J. *J. Org. Chem.* **2010,** *75* ,6532-6539.
[11] Nguyen, D. M.; Miles, D. H.. *Synth. Commun.* **2011,** *41*, 1759-1771.
[12] Dales, N.; Zhang, Z.; Fonarev, J.; Fu, J.; Kamboj, R.; Kodumuru, V.; Pokrovskaia, N.; Sun, S. Preparation of thiazole derivatives as stearoyl-CoA desaturase (SCD) inhibitors. WO2008074835A1, 2008.
[13] Ackermann, L.; Potukuchi, H. K.; Landsberg, D.; Vicente, R. *Org. Lett.* **2008,** *10*, 3081-3084.

and copper(I) iodide (0.0041 mmol, 0.10 equiv). Next was added DMEDA (0.0062 mmol, 0.15 equiv) and the reaction was stirred overnight. The crude mixture was diluted with diethyl ether (10 mL) and washed with water (10 mL), ammonium chloride (10 mL, sat. aq.), and brine (10 mL). The aqueous layers were combined and washed with diethyl ether (2 x 10 mL). Organic layers were combined, dried over sodium sulfate and concentrated *in vacuo*. The resulting residue was loaded onto a flash silica gel column (gradient of hexanes/acetone ending with 50% hexanes/acetone).

b. Alternate Synthesis of 9ca:



8ca, R = *p*-methoxyphenyl
8cb, R = 3-ethylene-indole

9ca, R = PMP: 71% yield, 97:3 dr
9cb, R = 3-ethylene-indole: NO REACTIO

Instead of starting directly with the isatin, the triazole-isatin **8cx** was subjected to the general method for the addition of 5-methoxyoxazoles with oxazole **11e**. Using **8ca**, the reaction afforded 71% yield with a 97:3 dr of product **9ca**, while no reaction was observed using **8cb**.

III. Characterization Data

a. Characterization Data for oxindole scaffolds:

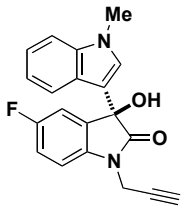
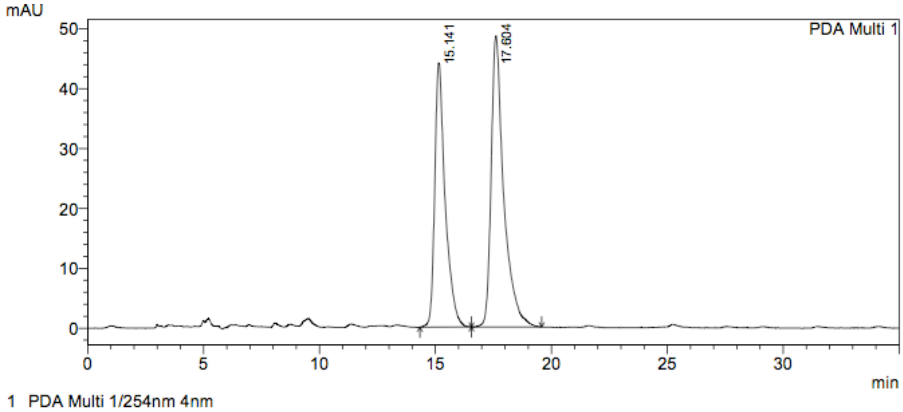


Table 1, entry 1: (*R*)-5-fluoro-3-hydroxy-3-(1-methyl-1H-indol-3-yl)-1-(prop-2-yn-1-yl)indolin-2-one (13b): The general procedure for the preparation of hydroxy oxindoles was followed, and the reaction was completed in 45 min. White foam (0.0747 g, 97%). $[\alpha]_D^{23}$ 7.4° (*c* 0.34, $CHCl_3$). Enantiomeric excess was determined using HPLC with a Daicel CHIRALPAK® AD-H column (30% IPA/hexanes), 1.0 mL/min. t_R (major) = 7.9 min, t_R (minor) = 4.0 min. 92% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0, 1H), 7.32 – 7.18 (m, 3H), 7.13 – 7.04 (m, 4H), 6.96 (s, 1H), 4.63 (dd, *J* = 17.7, 2.6, 1H), 4.43 (dd, *J* = 17.7, 2.5, 1H), 3.72 (s, 3H), 3.11 (s, 1H), 2.27 (dd, *J* = 2.6, 2.5, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.3, 159.8 (d, J_{FC} = 242.4), 137.8, 137.2, 133.0 (d, J_{FCCC} = 7.6), 127.9, 125.2, 122.3, 120.6, 120.0, 116.1 (d, J_{FCC} = 23.7), 113.3, 113.2, 110.5 (d, J_{FCCC} = 8.0), 109.8, 76.6, 75.9 (d, J_{FCCCC} = 1.5), 73.1, 32.9, 29.8; FT IR (neat): 3451, 3306, 3061, 2172, 1720, 1479, 1159, 738 cm^{-1}; HRMS (ESI) *m/z* $[M - H_2O + H]^+$ calcd for $C_{20}H_{15}FN_2O$, 317.1012; found 317.1085; XLogP = 2.58.

Unoptimized reaction conditions **13b** (14% *ee*):



1 PDA Multi 1/254nm 4nm

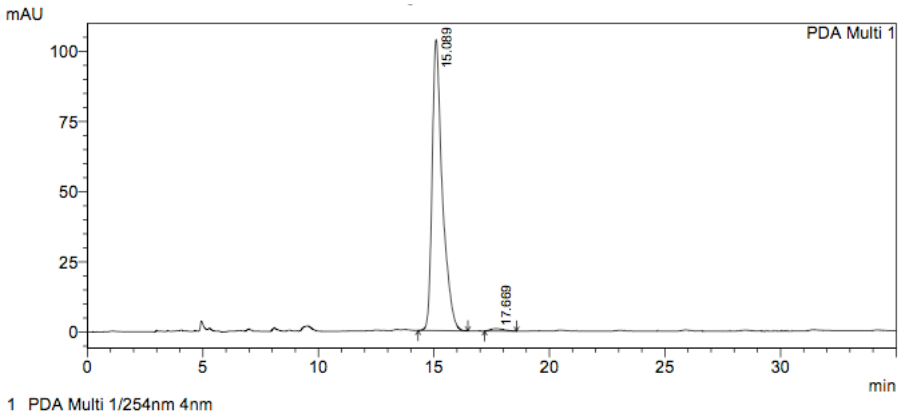
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-15-S2-AD_85_15.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.141	1384450	44153	43.017	47.583
2	17.604	1833896	48639	56.983	52.417
Total		3218346	92792	100.000	100.000

Enantiomerically enriched **13b** (98% *ee*):



1 PDA Multi 1/254nm 4nm

< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-92-AD-85-15.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.089	3188833	103647	98.989	99.176
2	17.669	32583	861	1.011	0.824
Total		3221417	104508	100.000	100.000

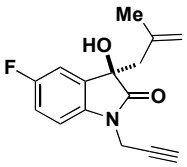
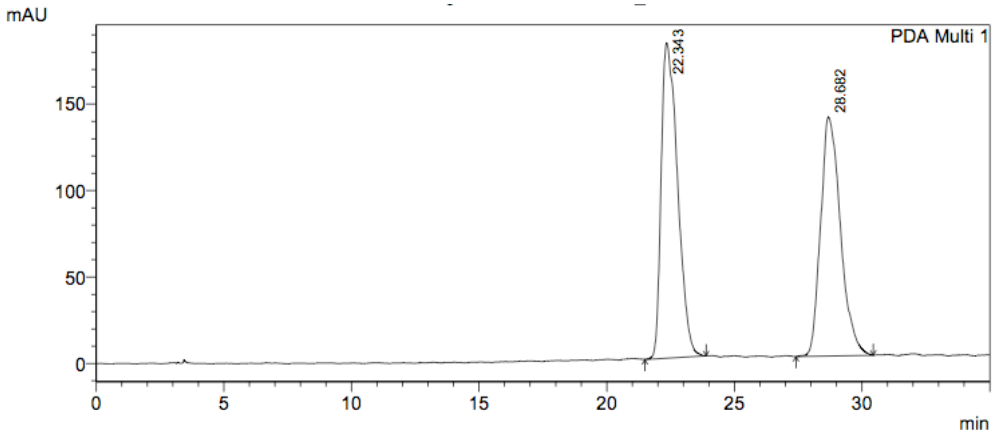


Table 1, entry 2: (*R*)-5-fluoro-3-hydroxy-3-(2-methylallyl)-1-(prop-2-yn-1-yl)indolin-2-one (14b):

To an oven dried, argon purged 4 mL vial equipped with a stir bar and 4 Å molecular sieves (100mg/mmol) was added $Sc(OTf)_3$ (0.098 mmol) and 2,6-Bis[(3a*S*,8a*R*)-3a,8a-dihydro-8H-indeno[1,2-d]oxazolin-2-yl]pyridine (0.098 mmol) and $NaSbF_6$ (0.098 mmol). This was dissolved in 4.1 mL of acetonitrile, and stirred for 2 h. Then isatin (0.98 mmol), TMSCl (2.90 mmol), and 3 equiv of methyallylsilane (2.9 mmol) were added and the reaction was complete in 2 h. Yellow oil (0.202 g, 79%). $[\alpha]_D^{23}$ 26.5° (*c* 0.712, $CHCl_3$). Enantiomeric excess was determined using HPLC with a Daicel CHIRALPAK® OD-H column (2% IPA/hexanes), 1.0 mL/min. t_R (major) = 21.8 min, t_R (minor) = 29.0 min. 88% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dd, *J* = 7.7, 2.5, 1H), 6.98 (td, *J* = 8.8, 2.5, 1H), 6.91 (dd, *J* = 8.8, 4.1, 1H), 4.69 (s, 1H), 4.53 (s, 1H), 4.48 (dd, *J* = 17.8, 2.5, 1H), 4.28 (s, 1H), 4.24 (dd, *J* = 17.8, 2.4, 1H), 2.67 (s, 2H), 2.20 (dd, *J* = 2.5, 2.4, 1H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 159.8 (d, J_{FC} = 242.3), 138.6, 137.5 (d, J_{FCCC} = 2.1), 131.7 (d, J_{FCCC} = 7.9), 116.7, 116.0 (d, J_{FCC} = 23.6), 112.9 (d, J_{FCC} = 24.9), 110.3 (d, J_{FCCC} = 8.0), 76.8 (d, J_{FCCCC} = 1.7), 76.4, 73.0, 46.3, 29.6, 24.0; FT IR (neat) 3535, 3026, 2092, 1721, 1070 cm^{-1}; HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{15}H_{14}FNNaO_2$,

282.0901; found 282.0902; XLogP = 1.53.

Unoptimized reaction conditions **14b** (4% *ee*):



1 PDA Multi 1/254nm 4nm

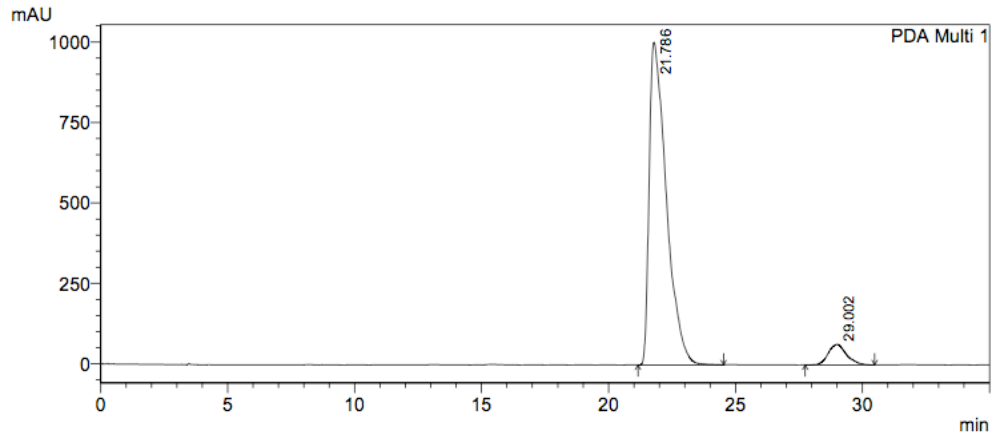
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-112_OD-98-2.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.343	8144868	182311	52.016	56.853
2	28.682	7513589	138362	47.984	43.147
Total		15658457	320673	100.000	100.000

Enantiomerically enriched **14b** (87% *ee*):



1 PDA Multi 1/254nm 4nm

< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-110_OD-98-2.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.786	47035823	1001691	93.618	94.000
2	29.002	3206334	63936	6.382	6.000
Total		50242157	1065627	100.000	100.000

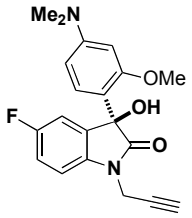
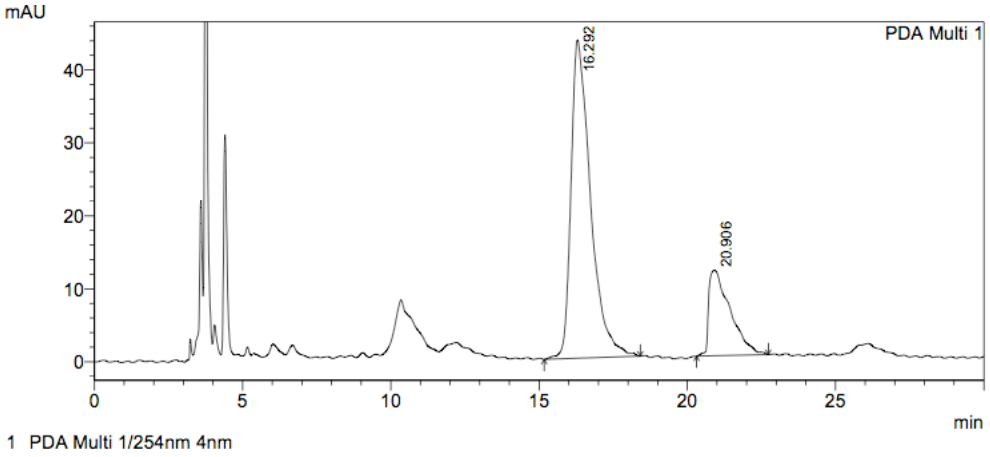


Table 1, entry 3: (*S*)-3-(4-(dimethylamino)-2-methoxyphenyl)-5-fluoro-3-hydroxy-1-(prop-2-yn-1-yl)indolin-2-one (15b): The general procedure for the preparation of hydroxy-oxindoles was followed and the reaction was complete in 1 h. White foam (0.207 g, 97%). Enantiomeric excess was determined using HPLC with a Daicel CHIRALPAK® AS-H column (5% IPA/hexanes), 1.0 mL/min. t_R (major) = 15.8 min, t_R (minor) = 20.8 min. 96% *ee*. $[\alpha]_D^{23}$ 43.4° (*c* 0.1.12, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.6, 1H), 7.06 – 6.94 (m, 2H), 6.93 – 6.81 (m, 1H), 6.34 (dd, *J* = 8.6, 2.4, 1H), 6.15 (d, *J* = 2.4, 1H), 4.75 (dd, *J* = 17.7, 2.6, 1H), 4.27 (dd, *J* = 17.7, 2.5, 1H), 3.79 (s, 1H), 3.64 (s, 3H), 2.93 (s, 6H), 2.28 (dd, *J* = 2.6, 2.5 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 161.0, 158.6, 157.3, 152.4, 138.3, 133.0 (d, J_{FCCC} = 7.5), 127.2, 116.1, 115.7 (d, J_{FCC} = 23.6), 112.8 (d, J_{FCC} = 24.8), 109.8 (d, J_{FCCC} = 7.9), 105.0, 96.9, 76.7, 72.6, 55.8, 40.8, 29.6; FT IR (neat) 3348, 2915, 2127, 1869, 1706, 1485, 1239, 1124 cm^{-1}; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{20}FN_2O_3$, 355.1380; found 355.1453; XLogP = 2.33.

Unoptimized reaction conditions **15b** (54% *ee*):



1 PDA Multi 1/254nm 4nm

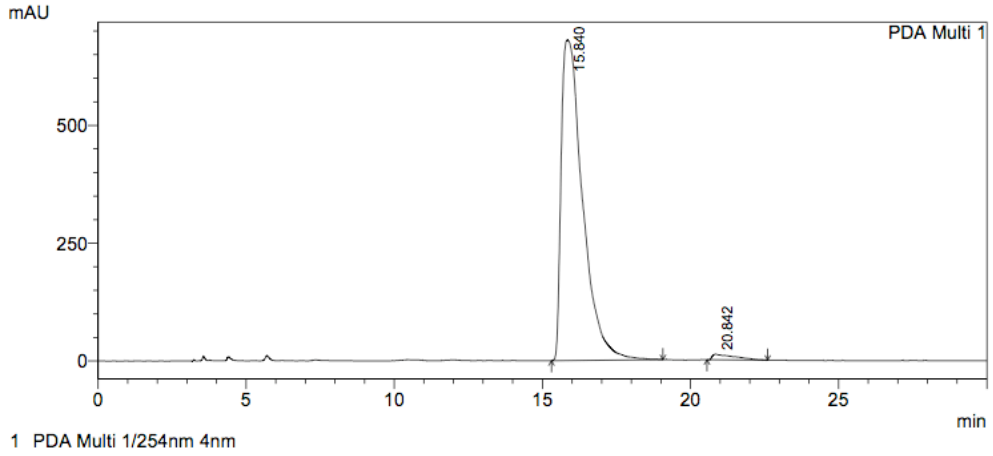
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-60_AS_95_5.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.292	2003372	43639	77.162	78.843
2	20.906	592942	11710	22.838	21.157
Total		2596314	55349	100.000	100.000

Enantiomerically enriched **15b** (96% *ee*):



< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-53_AS_95_5.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.840	34191929	680003	98.190	98.298
2	20.842	630279	11775	1.810	1.702
Total		34822208	691777	100.000	100.000

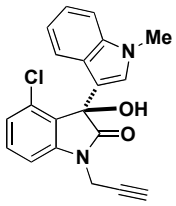
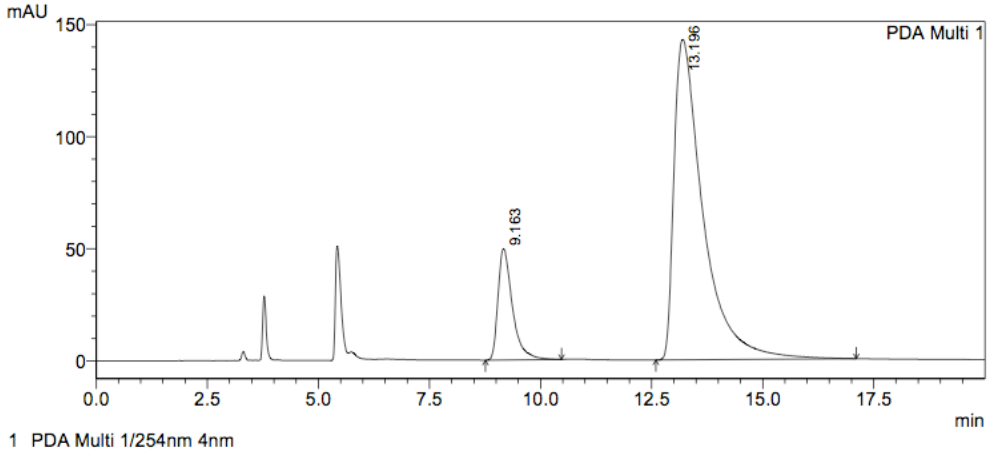


Table 1, entry 4: (*R*)-4-chloro-3-hydroxy-3-(1-methyl-1H-indol-3-yl)-1-(prop-2-yn-1-yl)indolin-2-one (13c): The general procedure for the preparation of hydroxy-oxindoles was followed, and the reaction was complete in 15 h. Off white powder (0.164 g, 78%). Enantiomeric excess was determined using HPLC with a Daicel CHIRALPAK® AS-H column (20% IPA/hexanes), 1.0 mL/min. t_R (major) = 9.1 min, t_R (minor) = 13.4 min. 86% *ee*. $[\alpha]_D^{23}$ 261.5° (*c* 1.29, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 2H), 7.34 – 7.30 (m, 1H), 7.26 – 7.22 (m, 2H), 7.12 (dd, *J* = 7.9, 3.9, 2H), 7.06 (t, *J* = 7.9, 1H), 4.63 (d, *J* = 17.8, 1H), 4.45 (d, *J* = 17.8, 1H), 3.46 (s, 3H), 2.36 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.2, 143.3, 137.6, 132.2, 131.1, 128.8, 127.6, 124.9, 124.7, 122.0, 121.5, 120.9, 120.1, 119.8, 119.3, 111.1, 109.6, 108.2, 73.1, 33.0, 29.8; FT IR (neat) 3391, 3273, 2921, 2116, 1714, 1596, 1326, 741 cm^{-1}; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{16}ClN_2O_2$, 351.0822; found 351.0888; XLogP = 3.07.

Unoptimized reaction conditions **13c** (71% *ee*):



1 PDA Multi 1/254nm 4nm

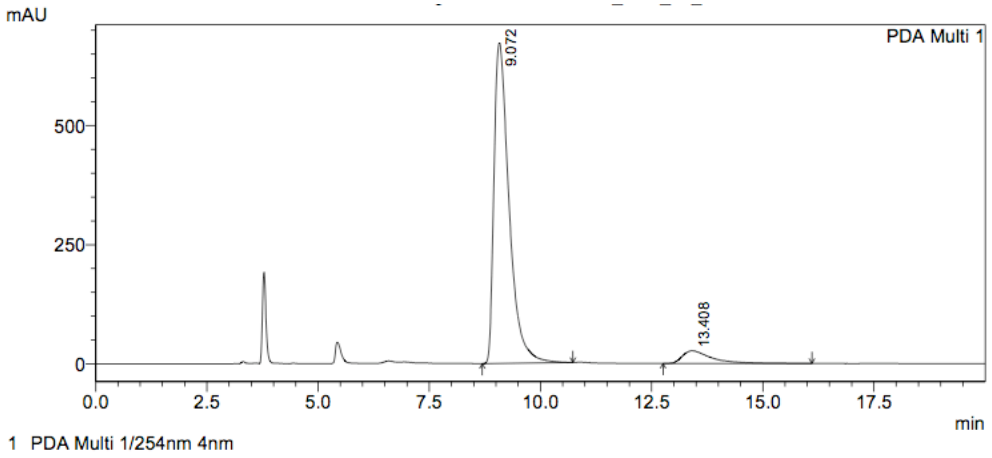
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-91_ASS_80_20.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.163	1121696	49672	14.698	25.786
2	13.196	6509893	142963	85.302	74.214
Total		7631589	192635	100.000	100.000

Enantiomerically enriched **13c** (86% *ee*):



1 PDA Multi 1/254nm 4nm

< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-76_ASS_80_20.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.072	15886865	672716	92.891	96.202
2	13.408	1215788	26562	7.109	3.798
Total		17102653	699278	100.000	100.000

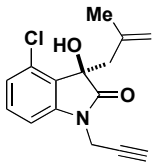
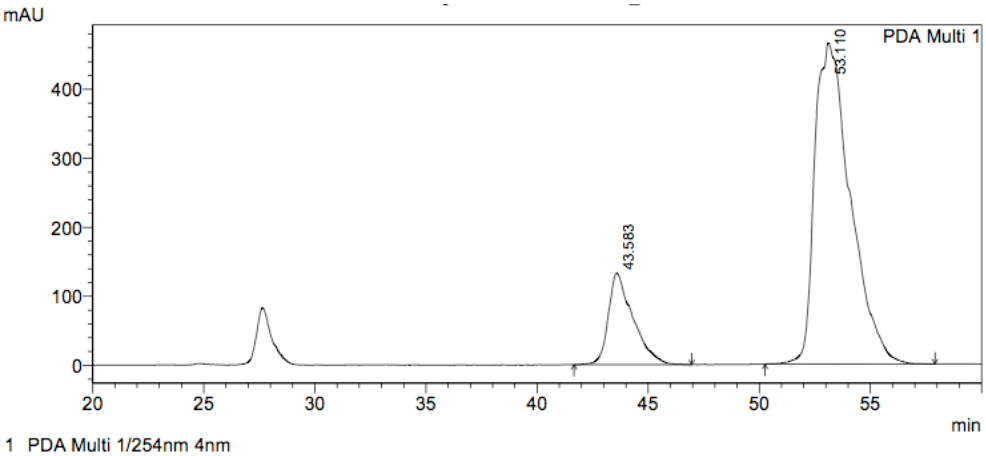


Table 1, entry 5: (*R*)-4-chloro-3-hydroxy-3-(2-methylallyl)-1-(prop-2-yn-1-yl)indolin-2-one (14c):

To an oven dried, argon purged 4 mL vial equipped with a stir bar and 4 Å molecular sieves (100mg/mmol) was added $Sc(OTf)_3$ (0.023 mmol) and 2,6-Bis[(3a*S*,8a*R*)-3a,8a-dihydro-8H-indeno[1,2-d]oxazolin-2-yl]pyridine (0.023 mmol) and $NaSbF_6$ (0.023 mmol). This was dissolved in 0.96 mL of acetonitrile, and stirred for 2. Then isatin (0.023 mmol), TMSCl (0.69 mmol), and methyallylsilane (0.69 mmol) were added and the reaction was complete in 2 h. White solid (0.057 g, 90%). $[\alpha]_D^{23}$ 0.25˚ (*c* 6.5, $CHCl_3$). Enantiomeric excess was determined using HPLC with a Daicel CHIRALPAK® AD-H column (5% IPA/hexanes), 1.0 mL/min. t_R (major) = 43.8 min, t_R (minor) = 54.4 min. 94% *ee*. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (t, *J* = 8.2, 1H), 7.02 (d, *J* = 8.2, 1H), 6.89 (d, *J* = 8.2, 1H), 4.63 (s, 2H), 4.51 (dd, *J* = 17.7, 2.4, 1H), 4.28 (dd, *J* = 17.7, 2.2, 1H), 3.16 (d, *J* = 12.6, 1H), 2.83 (d, *J* = 12.6, 1H), 2.19 (dd, *J* = 2.4, 2.2, 1H), 1.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.7, 143.5, 138.1, 131.8, 130.9, 126.0, 124.4, 116.1, 107.9, 77.4, 75.9, 72.7, 43.7, 29.4, 23.0; FT IR (neat) 3290, 3073, 2127, 1702, 1595 cm^{-1}; HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{15}H_{14}ClNNaO_2$, 298.0605; found 298.0605; XLogP = 2.02.

Unoptimized reaction conditions **14c** (68% *ee*):



1 PDA Multi 1/254nm 4nm

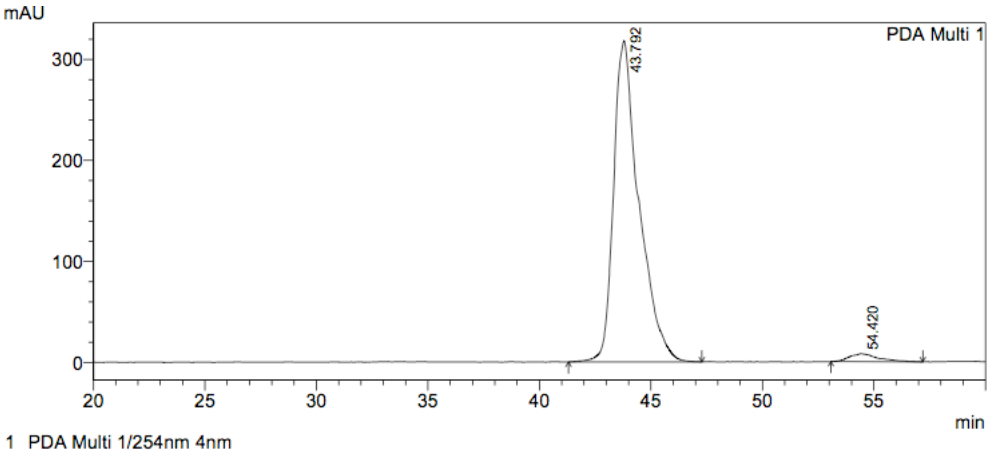
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-105_AD-98-2.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	43.583	10271061	132651	16.449	22.180
2	53.110	52169135	465419	83.551	77.820
Total		62440197	598070	100.000	100.000

Enantiomerically enriched sample **14c** (94% *ee*):



1 PDA Multi 1/254nm 4nm

< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-107_AD-98-2.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	43.792	25234747	317869	97.273	97.600
2	54.420	707351	7818	2.727	2.400
Total		25942098	325687	100.000	100.000

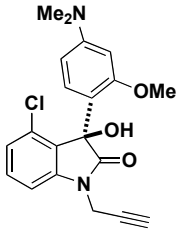
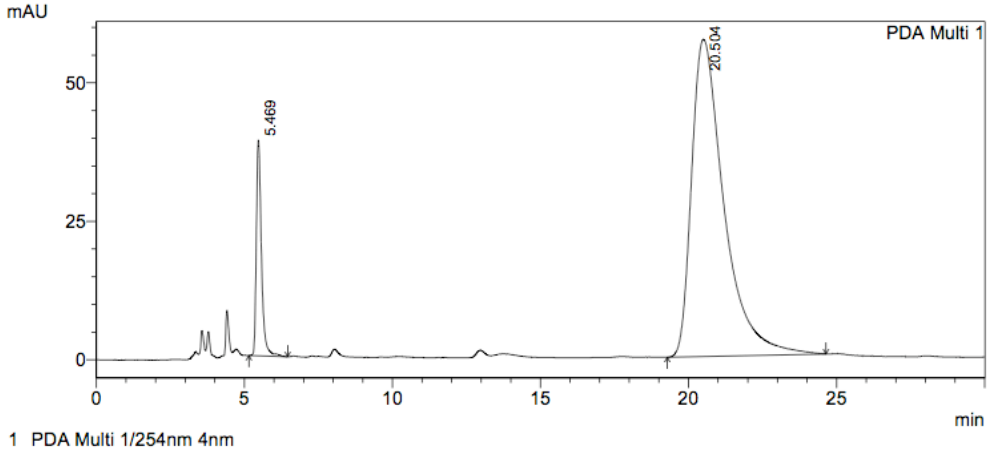


Table 1, entry 6: (*R*)-4-chloro-3-(4-(dimethylamino)-2-methoxyphenyl)-3-hydroxy-1-(prop-2-yn-1-yl)indolin-2-one (15c): The general procedure for the preparation of hydroxy-oxindoles was followed, and the reaction was complete in 22 h. Green powder (0.277 g, 97%). Enantiomeric excess was determined using HPLC with a Daicel CHIRALPAK® AS-H column (30% IPA/hexanes), 1.0 mL/min. t_R (major) = 5.8 min, t_R (minor) = 20.5 min. >99% *ee*. $[\alpha]_D^{23}$ -19.4° (*c* 0.392, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.7, 1H), 7.25 (t, *J* = 8.1, 1H), 7.00 – 6.92 (m, 2H), 6.36 (dd, *J* = 8.7, 2.4, 1H), 6.15 (d, *J* = 2.4, 1H), 4.74 (dd, *J* = 17.7, 2.6, 1H), 4.30 (dd, *J* = 17.7, 2.5, 1H), 3.63 (s, 3H), 2.94 (s, 6H), 2.28 (dd, *J* = 2.5, 2.6, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 157.3, 152.2, 144.3, 131.9, 130.6, 129.0, 127.4, 124.5, 114.0, 107.6, 104.7, 96.6, 72.7, 55.8, 40.7, 29.7; FT IR (neat) 3495, 3350, 3087, 2114, 1711, 1599, 1339, 1131, cm^{-1}; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{20}ClN_2O_3$, 371.1084; found 371.1160; XLogP = 2.81.

Unoptimized reaction conditions **15c** (81% *ee*):



1 PDA Multi 1/254nm 4nm

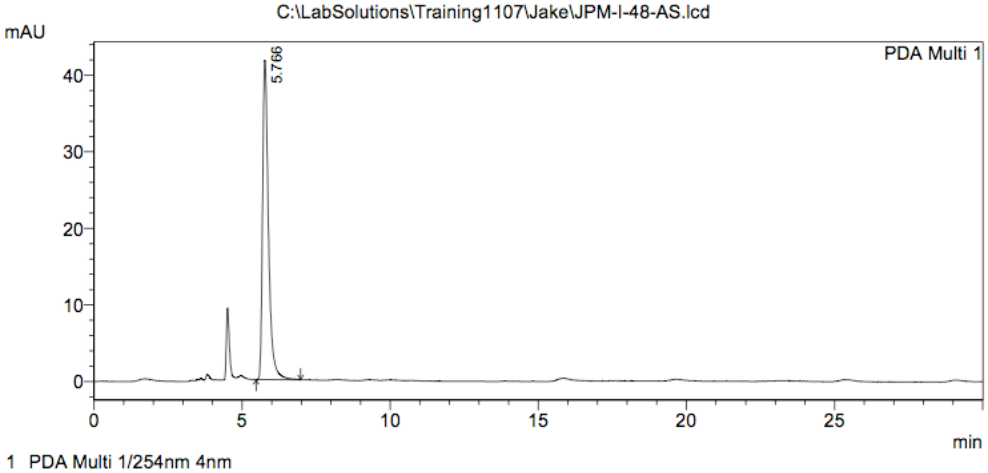
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-27-AS.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.469	466285	38978	9.665	40.509
2	20.504	4358249	57243	90.335	59.491
Total		4824534	96221	100.000	100.000

Enantiomerically enriched **15c** (>99% *ee*):



1 PDA Multi 1/254nm 4nm

< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-48-AS.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.766	576119	41762	100.000	100.000
Total		576119	41762	100.000	100.000

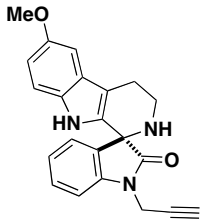


Table 2, entry 1: 6'-methoxy-1-(prop-2-ynyl)-2',3',4',9'-tetrahydrospiro[indoline-3,1'-pyrido[3,4-*b*]indol]-2-one (16a): The general method B for the addition of 5-methoxytryptamines was used with $Sc(OTf)_3$. Beige solid (yield 86 mg, 89% yield). ^{1}H NMR (400 MHz, DMSO) δ 9.36 (s, 1H), 6.54 (m, 1H), 6.35 (m, 1H), 6.30 (m, 1H), 6.24 – 6.14 (m, 2H), 6.11 (s, 1H), 5.84 – 5.80 (m, 1H), 3.78 (dd, *J* = 17.8, 1.3, 1H), 3.58 (dd, *J* = 17.8, *J* = 1.1, 1H), 2.90 (s, 3H), 2.72 (m, 1H), 2.27 (m, 1H), 2.16, (s, 1H), 2.00 – 1.83 (m, 2H), 1.65 (dd, *J* = 1.3, *J* = 1.1, 1H); LRMS (ESI) m/z [M + H]+ calcd for $C_{22}H_{20}N_3O_2$, 358.15 ; found 358.3; XlogP = 2.73.

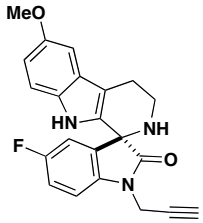
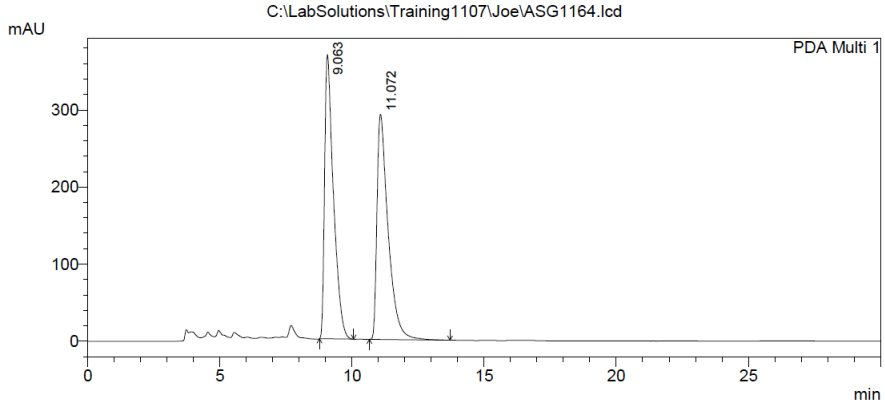


Table 2, entry 2: (*S*)-5-fluoro-1-propargyl-6'-methoxy-2',3',4',9'-tetrahydrospiro[indoline-3,1'-pyrido[3,4-*b*]indol]-2-one (16b): The general method A for the addition of 5-methoxytryptamines was used. White foamy solid (0.016 g, 86%). Enantiomeric ratio was determined by HPLC with a Daicel CHIRALPAK® AD-H column (30% IPA/hexanes), 0.8 mL/min. t_R (major) = 9.0 min, t_R (minor) = 11.1 min. 84% *ee*. $[\alpha]_D^{24}$ -12.2° (*c* = 0.27, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.12 – 6.93 (m, 6H), 6.78 (dd, *J* = 8.8, 1.8, 1H), 4.57 (dd, *J* = 17.7, 2.3, 1H), 4.45 (dd, *J* = 17.7, 2.5, 1H), 3.90 – 3.78 (m, 4H), 3.30 (m, 1H), 2.92 (m, 2H), 2.31 (dd, *J* = 2.5, 2.3, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 160.0 (d, J_{FC} = 243.3), 154.4, 137.6, 133.1 (d, J_{FCCC} = 7.5), 131.5, 130.1, 127.7, 116.4 (d, J_{FCC} = 23.7), 113.2 (d, J_{FCC} = 25.0), 112.9, 112.8, 112.0, 110.7 (d, J_{FCCC} = 7.9) ,100.9, 76.7, 73.3, 62.0, 56.2, 40.2, 29.9, 22.2; IR (neat) 3296, 3193, 1977, 1696, 1485, 1173, 1028 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{22}H_{19}FN_3O_2$, 376.1461, LRMS Found 376.2; XLogP = 2.87. The spectral data matches those of the literature.[5]

Racemic standard **16b**:



1 PDA Multi 1/254nm 4nm

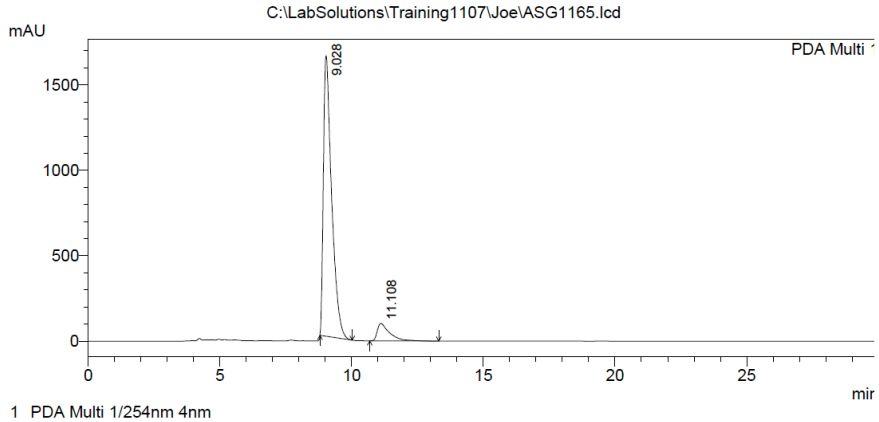
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Joe\ASG1164.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.063	8555398	368613	49.966	55.805
2	11.072	8566928	291925	50.034	44.195
Total		17122326	660538	100.000	100.000

Enantiomerically enriched **16b** (84% *ee*).



1 PDA Multi 1/254nm 4nm

< Peak Table >

PeakTable C:\LabSolutions\Training1107\Joe\ASG1165.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.028	35654086	1642103	91.522	94.150
2	11.108	3302569	102040	8.478	5.850
Total		38956655	1744142	100.000	100.000

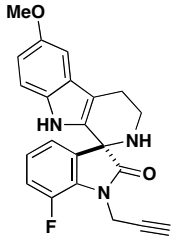


Table 2, entry 3: 7-fluoro-1-propargyl-6'-methoxy-2',3',4',9'-tetrahydrospiro[indoline-3,1'-pyrido[3,4-*b*]indol]-2-one (16f): The general method B for the addition of 5-methoxytryptamines was used with 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea. Pink solid (0.345 g, 92%). ^{1}H NMR (400 MHz, DMSO) δ 9.41 (s, 1H), 6.41 (m, 1H), 6.22 – 6.09 (m, 4H), 5.82 (m, 1H), 3.81 (dd, J = 17.9, 2.2, 1H), 3.59 (dd, J = 17.9, 1.9, 1H), 2.89 (s, 3H), 2.74 (m, 1H), 2.47 (m, 1H), 2.33 (m, 1H), 2.27 (m, 1H), 1.88 (m, 2H); ^{13}C NMR (100 MHz, DMSO) δ 176.4, 153.8, 147.6 (d, J_{FC} = 242.6), 135.6, 131.8 (d, J_{FCC} = 17.3), 129.3 (d, J_{FCCC} = 9.0), 127.4, 124.5 (d, J_{FCCC} = 6.2), 121.4, 117.7 (d, J_{FCC} = 19.1), 112.4, 112.0, 111.1, 106.1, 105.0, 100.7, 79.4, 75.1, 61.7, 56.1, 31.8, 22.3. FTIR (neat) 3254, 2936, 1723, 1485, 1216, 744 cm^{-1}; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{22}H_{19}FN_3O_2$, 376.1461; found 376.1451; XLogP = 2.87.

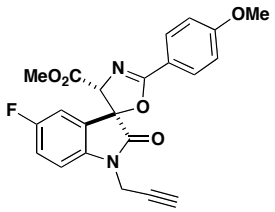


Table 3, entry 1: Methyl 5-fluoro-2'-(4-methoxyphenyl)-2-oxo-1-(prop-2-ynyl)-4'*H* spiro[indoline-3,5'-oxazole]-4'-carboxylate (17b): The general method for the addition of 5-methoxyoxazoles was followed. The diastereomers are inseparable by column chromatography. Yellow foam (0.031 g, 55%), 90:10 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.9, 2H), 7.16 (m, 2H), 7.08 (m, 1H), 6.92 (d, J = 8.9, 2H), 5.27 (s, 1H), 4.62 (dd, J = 17.8, 2.6, 1H), 4.41 (dd, J = 17.8, 2.5, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 2.32 (dd, J = 2.5, 2.6, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 168.7, 164.9, 162.9, 159.7 (d, J_{FC} = 243.7), 138.3, 130.9, 128.7 (d, J_{FCCC} = 7.8), 118.3, 117.6 (d, J_{FCC} = 23.5), 113.8, 112.4 (d, J_{FCC} = 25.2), 110.8 (d, J_{FCCC} = 7.9), 84.1, 78.3, 76.0, 73.0, 55.4, 52.8, 29.6. Peaks corresponding to the minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (s, 1H), 4.53 (dd, J = 17.7, 2.5, 1H), 3.86 (s, 3H), 3.42 (s, 3H). HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{22}H_{18}FN_2O_5$, 409.1194; found 409.1191; XLogP = 2.28. The spectral data matches that of the literature.[1]

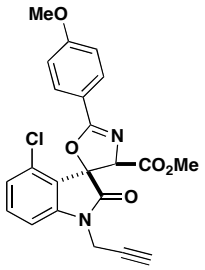


Table 3, entry 2: Methyl 4-chloro-2'-(4-methoxyphenyl)-2-oxo-1-(prop-2-ynyl)-4'*H*-spiro[indoline-3,5'-oxazole]-4'-carboxylate (17c): The general method for the addition of 5-methoxyoxazoles was followed. Yellow powder (0.372 g, 74%), >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.95 (m, 2H), 7.40 (t, *J* = 8.1, 1H), 7.12 (dd, *J* = 8.1, 0.7, 1H), 7.05 (dd, *J* = 8.1, 0.7, 1H), 6.95 – 6.88 (m, 2H), 5.58 (s, 1H), 4.63 (dd, *J* = 17.8, 2.6, 1H), 4.40 (dd, *J* = 17.8, 2.5, 1H), 3.85 (s, 3H), 3.75 (s, 3H), 2.32 (dd, *J* = 2.6, 2.5 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 169.4, 164.9, 163.0, 144.3, 132.5, 132.2, 131.1, 124.8, 123.9, 118.7, 114.0, 108.6, 84.3, 76.2, 76.0, 73.3, 55.7, 53.0, 29.9. IR (neat) 3294, 2951, 2146, 1763, 1737, 1257, 1165 cm^{-1}; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{22}H_{18}ClN_2O_5$, 425.0899; found 425.0895; XLogP = 2.76.

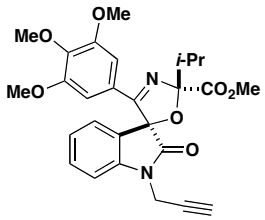


Table 3, entry 3: Methyl 2'-isopropyl-2-oxo-1-(prop-2-ynyl)-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (18a): The general method for the addition of 5-methoxyoxazoles was used with minor variation: A solution of isatin (0.12 mmol) and 5-methoxyoxazole (0.18 mmol) was prepared in dry CH_2Cl_2 (0.12 M) at 25 ˚C in an oven-dried and Ar-purged 8 mL vial fitted with a magnetic stir bar. To this mixture, 12 µL (10 mol %) of a 1.0 M solution of $TiCl_4$ (0.012 mmol, 1.0 M solution in CH_2Cl_2) was added. The remaining procedure follows the details described for general method. White powder (0.265 g, 77%), 90:10 dr. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (m, 1H), 7.32 (m, 1H), 7.22 – 6.96 (m, 2H), 6.76 (s, 2H), 4.78 (dd, *J* = 17.7, 2.4, 1H), 4.21 (dd, *J* = 17.7, 2.3, 1H), 3.88 (s, 3H), 3.79 (s, 3H), 3.63 (s, 6H), 2.63 (m, 1H), 2.31 (dd, *J* = 2.4, 2.3, 1H), 1.18 (d, *J* = 6.9, 3H), 1.12 (d, *J* = 6.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 170.4, 165.2, 153.2, 143.0, 141.3, 131.4, 126.5, 125.9, 124.5, 124.4, 113.9, 110.2, 105.8, 105.7, 104.7, 90.7, 76.7, 73.2, 61.1, 56.2, 52.8, 35.7, 30.0, 17.2, 16.7; FT IR (neat) 2973, 2007, 1732, 1351, 1254, 1001 cm^{-1}; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{27}H_{29}FN_2O_7$ 493.1970; 493.1967; XLogP = 3.92.

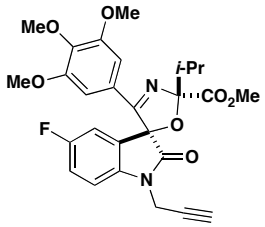


Table 3, entry 4: Methyl 5-fluoro-2'-isopropyl-2-oxo-1-(prop-2-ynyl)-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (18b): The general method for the addition of 5-methoxyoxazoles was used. Off-white foam (0.213 g, 87%), 93:7 dr. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 – 7.10 (m, 2H), 7.03 (m, 1H), 6.73 (s, 2H), 4.80 (dd, *J* = 17.8, 2.6, 1H), 4.17 (dd, *J* = 17.8, 2.5, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.65 (s, 6H), 2.61 (m, 1H), 2.26 (dd, *J* = 2.6, 2.5 1H), 1.16 (d, *J* = 6.8, 3H), 1.10 (d, *J* = 6.8, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.7, 170.0, 164.5, 159.7 (J_{FC} = 244.3), 153.1, 141.3, 138.7, 138.7, 127.8 (J_{FCCC} = 7.8), 124.0, 117.60 (J_{FCC} = 23.6), 114.1, 113.7 (J_{FCC} = 25.0), 110.8 (J_{FCCC} = 7.9), 105.5, 90.3, 76.2, 73.3, 60.8, 56.1, 52.7, 35.5, 30.0, 17.0, 16.5. IR (neat) 3262, 2963, 1727, 2107, 1494, 1124, 993, 833 cm^{-1}; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{27}H_{28}FN_2O_7$ 511.1875; found 511.1872; XLogP = 4.06.

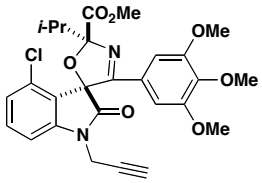


Table 3, entry 5: Methyl 4-chloro-2'-isopropyl-2-oxo-1-(prop-2-ynyl)-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (18c): The general method for the addition of 5-methoxyoxazoles was used. White foam (0.129 g, 51%) >99:1 dr. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (t, *J* = 8.1, 1H), 7.07 (d, *J* = 8.1, 1H), 7.05 (d, *J* = 8.1, 1H), 4.81 (dd, *J* = 17.8, 2.6, 1H), 4.16 (dd, *J* = 17.8, 2.5, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.65 (s, 6H), 2.53 (m, 1H), 2.26 (dd, *J* = 2.6, 2.5, 1H), 1.31 (d, *J* = 7.0, 3H), 1.21 (d, *J* = 7.0, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.3, 169.1, 163.3, 153.2, 144.6, 141.3, 132.9, 132.5, 125.1, 124.7, 122.8, 114.5, 108.5, 105.0, 90.1, 76.2, 73.4, 61.0, 56.1, 52.4, 37.2, 30.1, 18.8, 17.1; FT IR (neat) 2942, 1736, 1454, 1249, 998 cm^{-1}; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{27}H_{28}ClN_2O_7$ 527.1580; 527.1577; XLogP = 4.54.

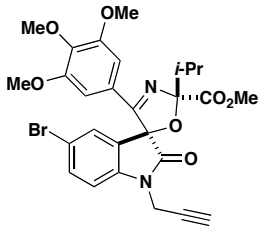


Table 3, entry 6: Methyl 5-bromo-2'-isopropyl-2-oxo-1-(prop-2-ynyl)-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (18d): The general method for the addition of 5-methoxyoxazoles was used. Orange foam (0.262 g, 95%), >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.4, 1.9, 1H), 7.38 (d, *J* = 1.9, 1H), 7.08 (d, *J* = 8.4, 1H), 6.81 – 6.71 (m, 2H), 4.81 (dd, *J* = 17.8, 2.5, 1H), 4.19 (dd, *J* = 17.8, 2.5, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 3.67 (s, 6H), 2.72 – 2.56 (m, 1H), 2.29 (dd, *J* = 2.5, 2.5, 1H), 1.17 (d, *J* = 6.9, 3H), 1.12 (d, *J* = 6.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.1, 164.6, 153.4, 142.0, 141.6, 134.3, 128.9, 128.4, 124.2, 116.9, 114.3, 111.7, 105.7, 90.2, 76.2, 73.7, 61.1, 56.3, 52.9, 35.7, 30.2, 17.2, 16.8; FT IR (neat) 3264, 2941, 1732, 11414, 252,996 cm^{-1}; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{27}H_{28}BrN_2O_7$, 571.1075; Found 571.1078; XLogP = 4.72.

b. Characterization Data for Triazole isatins and oxindoles

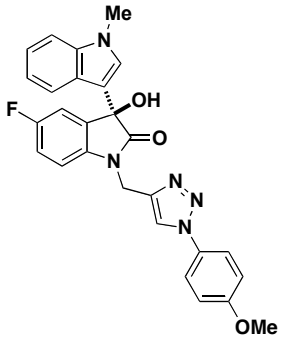
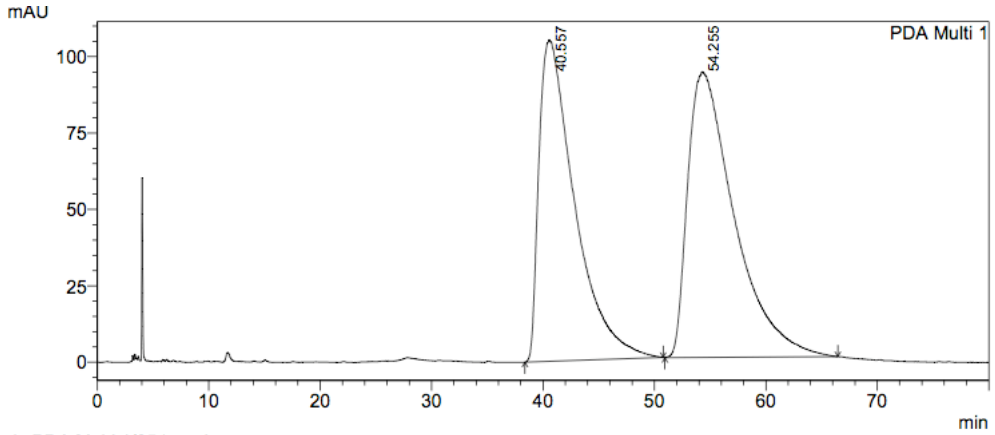


Table 4, entry 1: (*R*)-5-fluoro-3-hydroxy-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)-3-(1-methyl-1H-indol-3-yl)indolin-2-one (4ba): General method for the formation of triazoles from azides was used. Pink foam (0.0505 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.47 – 7.41 (m, 2H), 7.37 (d, *J* = 8.0, 1H), 7.25 (d, *J* = 8.7, 1H), 7.21 (dd, *J* = 8.7, 4.2, 1H), 7.17 – 7.13 (m, 2H), 7.05 – 6.99 (m, 2H), 6.94 (ddd, *J* = 8.0, 7.1, 0.9, 1H), 6.90 – 6.84 (m, 2H), 5.03 (s, 2H), 4.25 (bs, 1H), 3.81 (s, 3H), 3.66 (s, 3H); LRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{27}H_{23}FN_5O_3$, 484.49; found 484.0; XLogP = 3.07.

Unoptimized reaction conditions **4ba** (7% *ee*):



1 PDA Multi 1/254nm 4nm

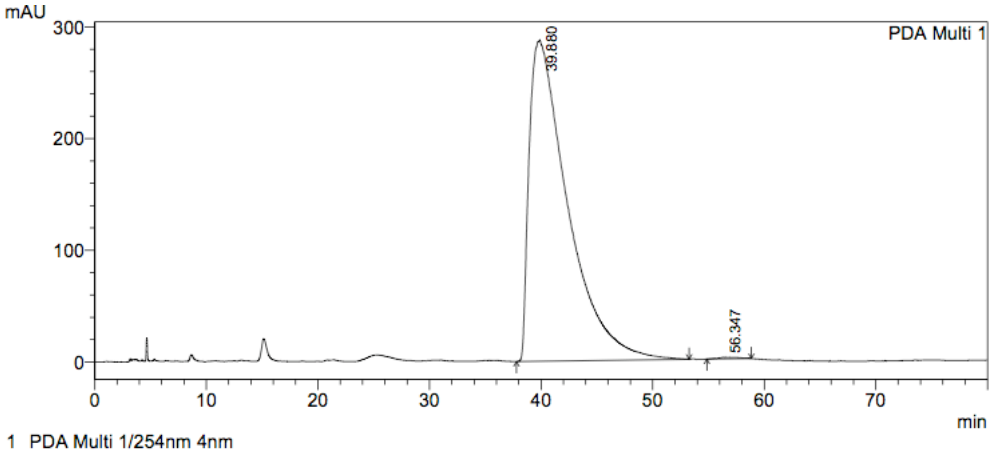
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-142A-AS_90_10-80M.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.557	23466494	105297	46.384	52.974
2	54.255	27125423	93475	53.616	47.026
Total		50591917	198772	100.000	100.000

Enantiomerically enriched **4ba** (99% *ee*):



1 PDA Multi 1/254nm 4nm

< Peak Table >

PeakTable C:\LabSolutions\Training1107\Jake\JPM-I-94-AS_90_10-80m.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	39.880	68878395	287676	99.731	99.516
2	56.347	185783	1398	0.269	0.484
Total		69064178	289074	100.000	100.000

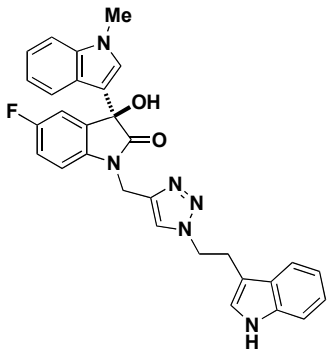


Table 4, entry 2: (*R*)-1-((1-(2-(1H-indol-2-yl)ethyl)-1H-1,2,3-triazol-4-yl)methyl)-5-fluoro-3-hydroxy-3-(1-methyl-1H-indol-3-yl)indolin-2-one (4bb): General method for the formation of triazoles from azides was used. Yellow foam (0.067 g, 80%). $[\alpha]_D^{23}$ -31.7° (*c* 1.20 ,MeOH). ^{1}H NMR (600 MHz, 3:1$CDCl_3$:MeOH) δ 8.15 (s, 1H), 7.50 (d, *J* = 8.0, 1H), 7.40 (d, *J* = 8.0, 1H), 7.30 – 7.23 (m, 1H), 7.23 – 7.15 (m, 3H), 7.15 – 7.07 (m, 2H), 7.03 (dt, *J* = 11.4, 7.6, 2H), 7.00 – 6.91 (m, 2H), 6.22 (s, 1H), 4.89 (d, *J* = 15.5, 1H), 4.80 (d, *J* = 15.5, 1H), 4.62 (s, 1H), 4.51-4.28 (m, 2H), 3.58 (s, 3H), 3.16 – 2.93 (m, 2H); ^{13}C NMR (150 MHz, 3:1$CDCl_3$:MeOH) δ 176.8, 160.5, 158.9, 141.8, 137.8, 137.1 (d, J_{FC} = 233.5), 132.9 (d, J_{FCCCC} = 7.6), 128.2, 126.6, 125.2, 123.6, 123.1, 122.4, 122.2, 120.7, 120.0, 119.6, 118.1, 116.3 (d, J_{FCCC} = 23.6), 113.1, 113.0, 111.7, 110.9 (d, J_{FCCCC} = 7.9), 110.5, 109.9, 75.8, 50.9, 35.7, 32.9, 26.5; FT IR (neat): 3328, 2923, 1709, 1470, 1335, 1157, 733 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{30}H_{26}FN_6O_2$, 521.56; found 521.2; XLogP = 3.43.

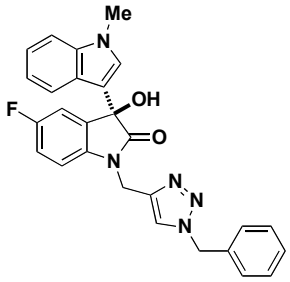


Table 4, entry 3: (*R*)-1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-fluoro-3-hydroxy-3-(1-methyl-1H-indol-3-yl)indolin-2-one (4bc): General method for the formation of triazoles from azides was used. Orange foam (0.037 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.35 (d, *J* = 8.2, 1H), 7.32-7.27 (m, 2H), 7.25 (d, *J* = 8.2, 1H), 7.20 – 7.11 (m, 6H), 7.00 – 6.94 (m, 2H), 6.94-6.88 (m, 1H), 5.37 (d, *J* = 14.8, 1H), 5.31 (d, *J* = 14.8, 1H), 4.94 (s, 2H), 3.87 (s, 1H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 159.8 (d, J_{FC} = 242.3), 137.9, 137.8 (d, J_{FCCCC} = 2.1), 134.4, 132.8 (d, J_{FCCC} = 7.6), 129.3, 129.0, 128.3, 128.0, 125.2, 122.4, 120.5, 120.0, 116.3 (d, J_{FCC} = 23.5), 113.3, 113.0, 110.9 (d, J_{FCCC} = 7.9), 109.9, 75.9, 54.4, 35.9, 33.1; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{27}H_{23}FN_5O_2$, 468.49; found 468.1; XLogP = 3.27.

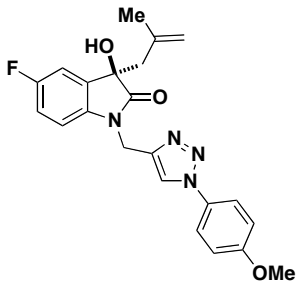


Table 4, entry 4: (*R*)-5-fluoro-3-hydroxy-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)-3-(2-methylallyl)indolin-2-one (5ba): General method for the formation of triazoles from azides was used. Faint brown oil (0.039 g, 64%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.57 – 7.43 (m, 2H), 7.09 (ddd, *J* = 12.7, 8.1, 2.6, 2H), 6.96 (td, *J* = 8.9, 2.6, 1H), 6.93 – 6.86 (m, 2H), 4.95 (s, 2H), 4.71 (s, 1H), 4.60 (s, 1H), 3.81 (s, 3H), 2.73 (d, *J* = 13.0, 1H), 2.69 (d, *J* = 13.0, 1H), 1.47 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{22}H_{22}FN_4O_2$, 409.43; found 409.1; XLogP = 2.02.

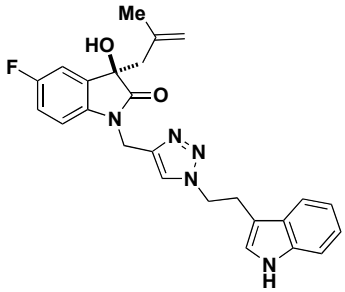


Table 4, entry 5: (*R*)-1-((1-(2-(1H-indol-2-yl)ethyl)-1H-1,2,3-triazol-4-yl)methyl)-5-fluoro-3-hydroxy-3-(2-methylallyl)indolin-2-one (5bb): General method for the formation of triazoles from azides was used. Off-white foam (0.044 g, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.41 (d, *J* = 8.1, 1H), 7.27 (d, *J* = 8.1, 1H), 7.12 (dd, *J* = 8.4, 7.6 2H), 7.02 (t, *J* = 7.6, 1H), 6.98-6.87 (m, 2H), 6.45 (s, 1H), 4.89 (d, *J* = 15.7, 1H), 4.74 (d, *J* = 15.7, 1H), 4.66 (s, 1H), 4.62 – 4.51 (m, 2H), 4.47 – 4.38 (m, 1H), 3.90 (s, 1H), 3.28 – 3.20 (m, 1H), 3.19 – 3.11 (m, 1H), 2.66 (s, 2H), 1.44 (s, 3H). LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{25}H_{25}FN_5O_2$, 446.5; found 446.3; XLogP = 2.38.

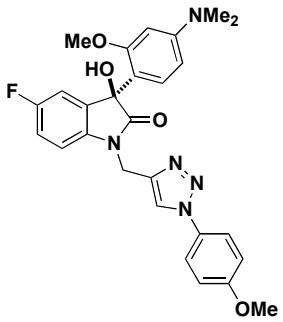


Table 4, entry 6: (*S*)-3-(4-(dimethylamino)-2-methoxyphenyl)-5-fluoro-3-hydroxy-1-((1-(4-methoxyphenyl)- 1H-1,2,3-triazol-4-yl)methyl)indolin-2-one (6ba): General method for the formation of triazoles from azides was used. White solid (0.0284 g, 56%). $[\alpha]_D^{23}$ 58.1˚ (*c* 0.57, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.54 (dd, *J* = 9.0, 1.2, 2H), 7.34 (d, *J* = 8.6, 1H), 7.13 (dd, *J* = 8.6, 3.5, 1H), 7.02 – 6.88 (m, 5H), 6.88 – 6.81 (m, 1H), 6.11 (s, 1H), 5.08 – 4.99 (m, 2H), 3.82 (s, 3H), 3.37 (s, 3H), 2.90 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.8, 160.0, 158.9, 157.5, 152.2, 143.5, 138.7, 133.10 (d, J_{FCC} = 6.6), 130.5, 127.5, 122.1, 121.4, 115.8 (d, J_{FC} = 23.2), 114.9, 112.7 (d, J_{FC} = 24.9), 110.1 (d, J_{FCC} = 8.0), 105.0, 97.0, 55.8, 55.7, 40.7, 35.8; FT IR ($CHCl_3$): 3375, 2934, 1717, 1614, 1501, 1244, 749 cm^{-1}; LRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{27}H_{27}FN_5O_4$, 504.52; found 503.9; XLogP = 2.81.

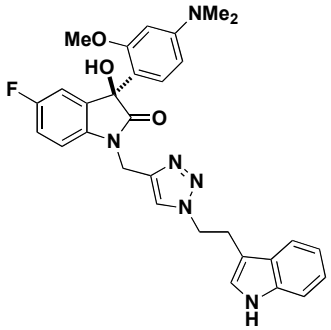


Table 4, entry 7: (*S*)-1-((1-(2-(1H-indol-2-yl)ethyl)-1H-1,2,3-triazol-4-yl)methyl)-3-(4-(dimethylamino)-2-methoxyphenyl)-5-fluoro-3-hydroxyindolin-2-one (6bb): General method for the formation of triazoles from azides was used. Off-white powder (0.0812 g, 99%). $[\alpha]_D^{23}$ 51.8˚ (*c* .67 ,MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.7, 1H), 7.44 (d, *J* = 7.9, 1H), 7.30 (d, *J* = 8.7, 1H), 7.14 – 7.08 (m, 1H), 7.02 (ddd, *J* = 7.9, 7.0, 0.8, 1H), 6.89 – 6.83 (m, 3H), 6.66 (s, 1H), 6.78 – 6.72 (m, 1H), 6.35 (dd, *J* = 8.7, 2.3, 1H), 6.03 (d, *J* = 2.3, 1H), 4.98 (d, *J* = 15.7, 1H), 4.78 (d, *J* = 15.7, 1H), 4.55 (ddq, J = 20.3, 13.6, 6.9, 2H), 3.83 (s, 3H), 3.25 (dd, *J* = 13.6, 6.9, 2H), 3.17 (s, 3H), 2.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 159.5 (d, J_{FC} = 241.2), 156.7, 152.1, 142.1, 138.3, 136.4, 133.9, 133.8, 127.2, 126.6, 123.6, 123.2, 121.8, 119.2, 117.8, 116.1, 115.2 (d, J_{FCC} = 23.9), 112.1 (d, J_{FCC} = 25.1), 111.6, 109.9, 109.5 (d, J_{FCCC} = 7.9), 104.9, 96.8, 75.8, 55.2, 51.1, 40.5, 35.3, 26.5; FT IR (neat): 3133, 3080, 2928, 1704, 1610, 1451,

1135, 754 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{30}H_{30}FN_6O_3$, 541.59; found 541.1; XLogP = 3.17.

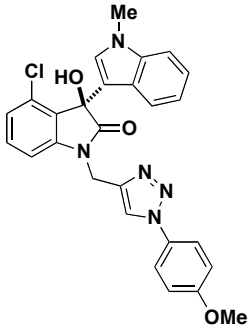


Table 4, entry 8: (*R*)-4-chloro-3-hydroxy-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)-3-(1-methyl-1H-indol-3-yl)indolin-2-one (4ca): General method for the formation of triazoles from azides was used. Off-white solid (0.014 g, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.47 – 7.42 (m, 2H), 7.29 (t, *J* = 8.3, 1H), 7.23 (d, *J* = 8.3, 2H), 7.10 (dd, *J* = 7.9, 1.2, 1H), 7.05 (ddd, *J* = 8.2, 7.0, 1.2, 1H), 6.99 (dd, *J* = 8.2, 0.7, 1H), 6.97 – 6.92 (m, 2H), 6.81 (d, *J* = 7.9, 1H), 6.74 (ddd, *J* = 8.0, 7.0, 0.7, 1H), 5.08 (s, 2H), 3.86 (s, 3H), 3.79 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{27}H_{23}ClN_5O_3$, 500.95; found 500.2; XLogP = 3.55.

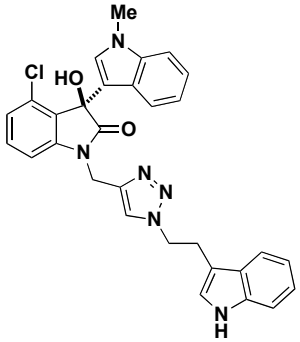


Table 4, entry 9: (*R*)-1-((1-(2-(1H-indol-2-yl)ethyl)-1H-1,2,3-triazol-4-yl)methyl)-4-chloro-3-hydroxy-3-(1-methyl-1H-indol-3-yl)indolin-2-one (4cb): General method for the formation of triazoles from azides was used.. White powder (0.0491 g, 70%). $[\alpha]_D^{23}$ -139.9° (*c* 0.491, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.42 (d, *J* = 7.9, 1H), 7.36 (d, *J* = 7.9, 1H), 7.34 – 7.11 (m, 5H), 7.07 (s, 1H), 7.07 – 6.98 (m, 3H), 6.88 (s, 1H), 6.14 (s, 1H), 4.86 (d, *J* = 15.5, 1H), 4.79 (d, *J* = 15.5, 1H), 4.45 (t, *J* = 6.6, 2H), 3.91 (s, 1H), 3.68 (s, 3H), 3.17 – 3.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 144.0, 141.7, 137.8, 136.4, 132.0, 131.5, 128.7, 127.4, 126.6, 125.1, 124.4, 123.8, 123.2, 122.3, 122.3, 120.6, 120.0, 119.6, 118.1, 111.8, 111.2, 110.5, 109.9, 108.8, 76.3, 51.0, 35.7, 33.2, 26.7; FT IR (neat): 3286, 1709, 1596, 1448, 1329,

1141, 1054, 732 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{30}H_{26}ClN_6O_2$, 538.01; found 537.1; XLogP = 3.85.

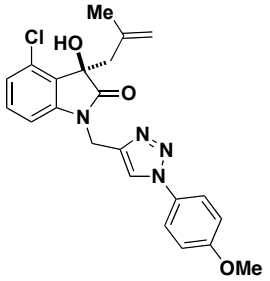


Table 4, entry 10: (*R*)-4-chloro-3-hydroxy-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)-3-(2-methylallyl)indolin-2-one (5ca): General method for the formation of triazoles from azides was used. White foam (0.053 g, 94%). ^1H NMR (600 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.51 (d, *J* = 9.0, 2H), 7.21 (t, *J* = 8.1, 1H), 7.06 (d, *J* = 8.1, 1H), 6.99 (d, *J* = 8.1, 1H), 6.94 (d, *J* = 9.0, 2H), 5.00 (d, *J* = 15.6, 1H), 4.94 (d, *J* = 15.6, 1H), 4.68-4.54 (m, 2H), 3.82 (s, 3H), 3.23 (s, 1H), 3.20 (d, *J* = 12.6, 1H), 2.88 (d, *J* = 12.6, 1H), 1.33 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{22}H_{22}ClN_4O_2$, 425.88; found 425.1; XLogP = 2.50.

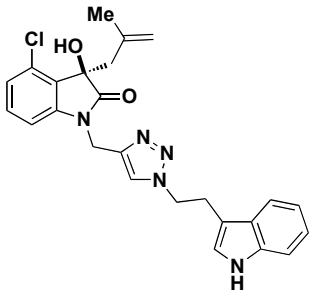


Table 4, entry 11: (*R*)-1-((1-(2-(1H-indol-2-yl)ethyl)-1H-1,2,3-triazol-4-yl)methyl)-4-chloro-3-hydroxy-3-(2-methylallyl)indolin-2-one (5cb): General method for the formation of triazoles from azides was used.. Yellow foam (0.018 g, 58%). ^1H NMR (600 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.42 (d, *J* = 7.9, 1H), 7.31 (d, *J* = 8.1, 1H), 7.20 (dd, *J* = 8.1, 7.9, 1H), 7.15 (t, *J* = 7.6, 1H), 7.05 – 6.92 (m, 4H), 6.49 (s, 1H), 4.91 (d, *J* = 15.7, 1H), 4.77 (d, *J* = 15.7, 1H), 4.65 – 4.55 (m, 3H), 4.49 – 4.38 (m, 1H), 3.56 (s, 1H), 3.34 – 3.22 (m, 1H), 3.22 – 3.09 (m, 2H), 2.90 – 2.82 (m, 1H), 1.32 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{24}H_{23}ClN_5O_2$, 462.94; found 462.3; XLogP = 2.86.

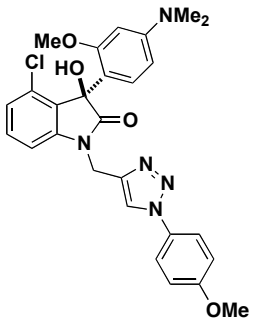


Table 4, entry 12: (*R*)-4-chloro-3-(4-(dimethylamino)-2-methoxyphenyl)-3-hydroxy-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)indolin-2-one (6ca): General method for the formation of triazoles from azides was used. White foam (0.0695 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.57 – 7.51 (m, 2H), 7.51 – 7.45 (m, 1H), 7.19 (t, *J* = 7.8, 1H), 7.14 (dd, *J* = 7.8, 1.0, 1H), 6.95 – 6.91 (m, 2H), 6.89 (dd, *J* = 7.8, 1.0, 1H), 6.30 (dd, *J* = 8.7, 2.3, 1H), 6.07 (d, *J* = 2.3, 1H), 5.03 (s, 2H), 4.42 (s, 1H), 3.82 (s, 3H), 3.28 (s, 3H), 2.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 159.9, 157.2, 152.0, 144.7, 143.3, 131.5, 130.7, 130.4, 129.0, 127.8, 124.2, 122.0, 121.5, 114.9, 114.0, 107.8, 104.7, 96.6, 64.5, 55.7, 55.5, 40.6; LRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{27}H_{27}ClN_5O_4$, 520.28; found 520.1; XLogP = 3.30.

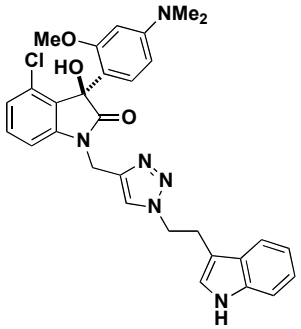


Table 4, entry 13: (*R*)-1-((1-(2-(1H-indol-3-yl)ethyl)-1H-1,2,3-triazol-4-yl)methyl)-4-chloro-3-(4-(dimethylamino)-2-methoxyphenyl)-3-hydroxyindolin-2-one (6cb): General method for the formation of triazoles from azides was used. Off white powder (0.0224 g, 94%). $[\alpha]_D^{23}$ 3.3° (*c* 5.59 ,MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.48 (d, *J* = 8.1, 1H), 7.32 (d, *J* = 8.1, 1H), 7.25 – 7.13 (m, 3H), 7.11 – 7.04 (m, 2H), 6.97 (s, 1H), 6.95 (s, 1H), 6.37 (d, *J* = 2.2, 1H), 6.28 (dd, *J* = 8.7, 2.4, 1H), 6.14 (d, *J* = 2.4, 1H), 5.02 (d, *J* = 15.5, 1H), 4.81 (d, *J* = 15.5, 1H), 4.68 – 4.44 (m, 2H), 4.24 (bs, 1H), 3.47 (s, 3H), 33.32 – 3.15 (m, 2H), 2.93 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 152.2, 144.8, 136.5, 131.9, 131.0, 129.1, 128.7, 127.7, 127.4, 126.7, 124.3, 123.8, 123.3, 122.4, 119.8, 118.2, 111.8, 110.7, 108.1, 106.1, 104.9, 97.0, 55.9, 51.1, 40.7, 35.8, 26.8; FT IR (neat): 3318, 3133, 2920, 1709, 1603, 1448, 1127, 742 cm^{-1}; LRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{30}H_{30}ClN_6O_3$, 558.04; found 557.1; XLogP = 3.65.

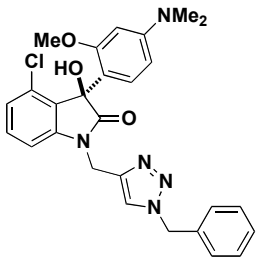


Table 4, entry 14: (*R*)-1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-4-chloro-3-(4-(dimethylamino)-2-methoxyphenyl)-3-hydroxyindolin-2-one (6cc): General method for the formation of triazoles from azides was used. White solid (0.0417 g, 58% yield). $[\alpha]_D^{23}$ 6.0° (*c* 0.74, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.39 (d, *J* = 8.7, 1H), 7.35 – 7.30 (m, 3H), 7.23 (dd, *J* = 6.5, 3.0, 2H), 7.18 (dd, *J* = 8.1, 7.8 1H), 7.09 (dd, *J* = 7.8, 0.8, 1H), 6.89 (dd, *J* = 8.1, 0.8, 1H), 6.31 (dd, *J* = 8.7, 2.4, 1H), 6.06 (d, *J* = 2.4, 1H), 5.49 (d, *J* = 14.8, 1H), 5.38 (d, *J* = 14.8, 1H), 4.96 (s, 2H), 3.19 (s, 3H), 2.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 157.4, 152.1, 144.8, 143.3, 134.5, 131.6, 130.8, 129.3, 129.0, 128.8, 128.4, 127.6, 124.28, 123.1, 114.0, 107.9, 104.9, 96.9, 77.4, 64.6, 55.6, 54.5, 40.7, 35.9, 30.9, 19.3; FT IR (neat): 3227, 3142, 2925, 1720, 1600, 1449, 1130, 711 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{27}H_{27}ClN_5O_3$, 504.98; found 503.9; XLogP = 3.50.

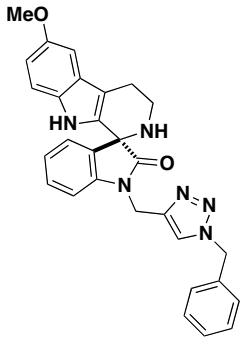


Table 4, entry 15: 1-((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)-6'-methoxy-2',3',4',9'-tetrahydrospiro[indoline-3,1'-pyrido[3,4-*b*]indol]-2-one (7ac): General method for the formation of triazoles from azides was used**.** Brown oil **(**26 mg, 95% yield**);** ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.46 (s, 1H), 7.39 -7.19 (m, 7H), 7.06 (m, 2H), 7.03 – 6.97 (m, 2H), 6.77 (dd, *J* = 8.7, 2.4, 1H), 5.45 (d, *J* = 4.3, 2H), 5.12 (d, *J* = 15.8, 1H), 4.86 (d, *J* = 15.8 1H), 3.85 (s, 3H), 3.91 – 3.73 (m, 1H), 3.45 – 3.31 (m, 1H), 2.92 (m, 3H); LRMS (ESI) m/z $[M + H]^+$ calcd for $C_{29}H_{27}N_6O_2$, 491.21; found 491.4; XlogP = 3.42.

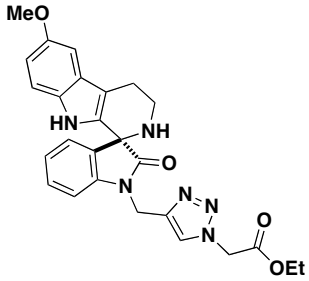


Table 4, entry 16: Ethyl 2-(4-((6'-methoxy-2-oxo-2',3',4',9'-tetrahydrospiro[indoline-3,1'-pyrido[3,4-*b*]indole]-1-yl)methyl)-1*H*-1,2,3-triazol-1-yl)acetate (7af): General method for the formation of triazoles from azides was used**.** light brown foam (26 mg, 95% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.18 (s, 1H), 7.63 (s, 1H), 7.35 – 7.16 (m, 2H), 7.12 – 6.96 (m, 4H), 6.73 (d, *J* = 2.0, 1H), 6.71 (d, *J* = 2.0, 1H), 5.11 (d, *J* = 15.7, 1H), 5.06 (d, *J* = 17.8, 1H), 4.99 (d, *J* = 17.8, 1H), 4.89 (d, *J* = 15.7, 1H), 4.22 (q, *J* = 7.2, 2H), 3.83 (s, 3H), 3.81 – 3.70 (m, 1H), 3.41 – 3.28 (m, 1H), 2.90 (t, *J* = 5.8, 2H), 1.27 (t, *J* = 7.2, 3H); LRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{27}N_6O_4$, 487.20; found 487.4; XlogP = 1.70.

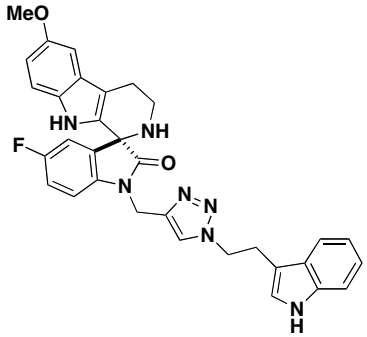
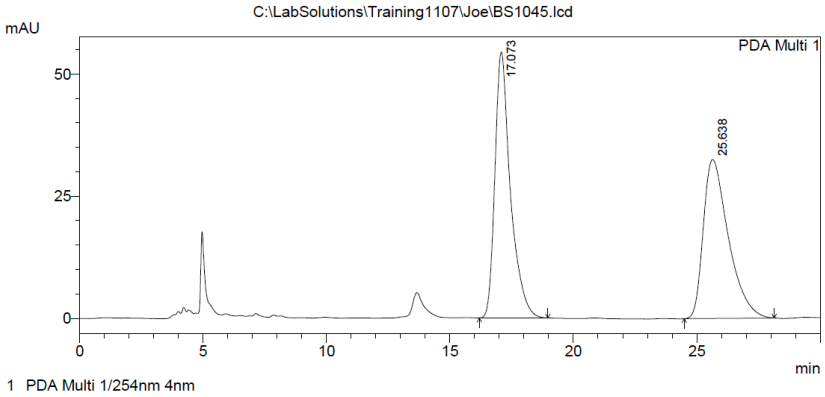


Table 4, entry 17: (*S*)-1-((1-(2-(1*H*-indol-3-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)-5-fluoro-6'-methoxy-2',3',4',9'-tetrahydrospiro[indoline-3,1'-pyrido[3,4-*b*]indol]-2-one (7bb): General method for the formation of triazoles from azides was used. Pink foam (0.0205 g, 62%). Enantiomeric excess was determined using HPLC with a Daicel CHIRALPAK® AD-H column (30% IPA/hexanes), 0.8 mL/min. t_R (major) = 15.0 min, t_R (minor) = 24.6 min. 86% ee. $[\alpha]_D^{23}$ +4.1° (*c* = 0.32, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.22 (s, 1H), 7.46 (d, *J* = 7.8, 1H), 7.31 (m, 1H), 7.18 (m, 1H), 7.11 – 6.92 (m, 7H), 6.78 (m, 1H), 6.32 (m, 1H), 4.96 (d, *J* = 15.7, 1H), 4.83 (d, *J* = 15.7, 1H), 4.61 (m, 1H), 4.50 (m, 1H), 3.83 (s, 3H), 3.88 – 3.78 (m, 1H), 3.48 – 3.38 (m, 2H), 3.24 (m, 2H), 2.95 (m, 2H), 1.91 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 159.8 (d, J_{FC} = 242.9), 154.3, 141.3, 138.0, 136.5, 131.6, 130.8, 127.5, 126.8, 123.3, 123.2, 122.4, 119.8, 118.3, 116.2 (d, J_{FCC} = 23.4), 112.8 (d, J_{FCC} = 25.0), 112.8, 112.3, 111.8, 111.7, 110.9 (d, J_{FCCC} = 7.8), 110.7, 100.8, 64.6, 62.3, 56.2, 51.2, 40.7, 35.9, 26.8, 22.3.

IR (neat) 3304, 2924, 1708, 1488, 1337, 1164, 740 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{32}H_{29}FN_7O_2$, 562.24; found 562.1; XLogP = 3.71.

Racemic Standard **7bb**.



1 PDA Multi 1/254nm 4nm

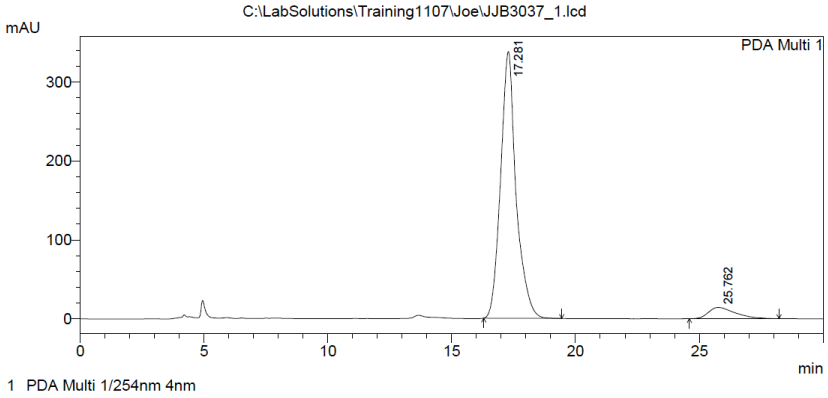
< Peak Table >

PeakTable C:\LabSolutions\Training1107\Joe\BS1045.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.073	2379362	54414	50.857	62.590
2	25.638	2299155	32523	49.143	37.410
Total		4678517	86937	100.000	100.000

Enantiomerically enriched **7bb** (86% *ee*).



1 PDA Multi 1/254nm 4nm

< Peak Table >

PeakTable C:\LabSolutions\Training1107\Joe\JJB3037_1.lcd

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.281	14675209	337523	93.240	95.955
2	25.762	1063968	14228	6.760	4.045
Total		15739177	351750	100.000	100.000

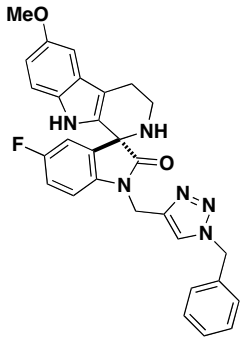


Table 4, entry 18: 1-((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)-5-fluoro-6'-methoxy-2',3',4',9'-tetrahydrospiro[indoline-3,1'-pyrido[3,4-*b*]indol]-2-one (7bc): General method for the formation of triazoles from azides was used**.** Green-brown foam (55.0 mg, 97% yield),. ^{1}H NMR (400 MHz, CDCl3) δ 8.49 (s, 1H), 7.44 (s, 1H), 7.39 – 7.30 (m, 3H), 7.23-7.19 (m, 2H), 7.07 (m, 1H), 7.02 – 6.88 (m, 4H), 6.77 (m, 1H), 5.43 (s, 2H), 5.10 (d, *J* = 15.6, 1H), 4.80 (d, *J* = 15.6, 1H), 3.84 (s, 3H), 3.78 – 3.68 (m, 1H), 3.40 – 3.31 (m, 1H), 2.90 (m, 2H), 2.22 (bs, 1H); LRMS (ESI) m/z $[M + H]^+$ calcd for $C_{29}H_{26}FN_6O_2$, 509.20 ; found 509.3; XLogP = 3.55.

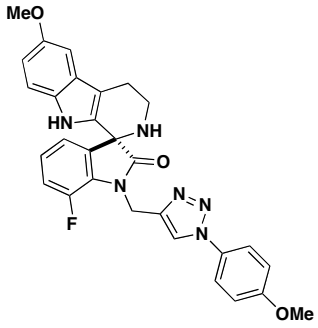


Table 4, entry 19: 7-fluoro-6'-methoxy-1-((1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)-2',3',4',9'-tetrahydrospiro[indoline-3,1'-pyrido[3,4-*b*]indol]-2-one (7fa): General method for the formation of triazoles from azides was used. Yellowish solid (0.1098 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.83 (s, 1H), 7.53 (d, *J* = 9.0, 2H), 7.12 (d, *J* = 8.8, 1H), 7.06 (m, 1H), 7.00 – 6.85 (m, 6H), 6.74 (dd, *J* = 8.8, 2.4, 1H), 5.35 (d, *J* = 16.0, 1H), 5.05 (d, *J* = 16.0, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.72 (m, 1H), 3.49 – 3.37 (m, 1H), 2.91 (m, 2H), 2.47 (bs, 1H); FTIR (neat) 2937, 1721, 1517, 1160, 831, 732 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{29}H_{26}FN_6O_3$ 525.2050, found 525.2048; XLogP = 3.35.

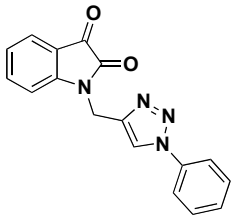


Table 4, entry 20: 1-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (8ad): General method for the formation of triazoles from azides was used. Orange powder (0.025 g, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.70 (d, *J* = 8.0, 2H), 7.61 (t, *J* = 8.0, 2H), 7.51 (t, *J* = 7.7, 2H), 7.44 (t, *J* = 7.5, 1H), 7.37 (d, *J* = 7.7, 1H), 7.13 (t, *J* = 7.5, 1H), 5.12 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 158.2, 150.3, 142.6, 138.8, 136.8, 129.9, 129.2, 125.5, 124.2, 121.3, 120.6, 117.7, 111.6, 35.5; FT IR (neat): 3153, 2927, 1731, 1604, 1468 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{17}H_{13}N_4O_2$ 305.3; found 305.0; XLogP = 1.60.

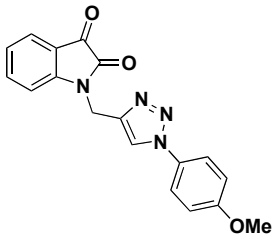


Table 4, entry 21: 1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (8aa): General method for the formation of triazoles from azides was used. Orange solid (0.072 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.64 – 7.56 (m, 4H), 7.38 (m, 1H), 7.12 (m, 1H), 7.00 (m, 2H), 5.10 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.2, 160.1, 158.1, 150.3, 142.4, 138.8, 130.3, 125.5, 124.2, 122.3, 121.4, 117.7, 114.9, 111.7, 55.8, 35.5; FT IR (neat): 3155, 2924, 1738, 1610, 1515, 1465 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{18}H_{15}N_4O_3$ 335.3; found 335.0; XLogP = 1.46.

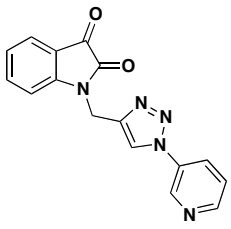


Table 4, entry 22: 1-((1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (8ae): General method for the formation of triazoles from azides was used. Orange-yellow solid (0.0202 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.71 (s, 1H), 8.22 (s, 1H), 8.10 (m, 1H), 7.62 (m, 2H), 7.55 – 7.45 (m, 1H), 7.36 (d, *J* = 7.9, 1H), 7.14 (t, *J* = 7.5, 1H), 5.14 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 158.3, 150.5, 150.2, 143.2, 141.9, 138.9, 128.2, 125.7,

124.4, 121.6, 117.8, 111.6, 35.5; LRMS (ESI) m/z [M + H] calculated for $C_{16}H_{12}N_5O_2$ 306.09; found 306.3; XLogP = 0.62.

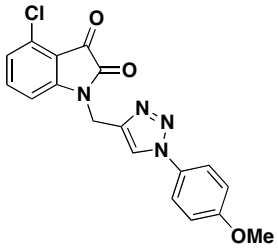


Table 4, entry 23: 4-chloro-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (**8ca**): When the general method for the formation of triazoles from azides was used. Orange solid (0.015 g, 55%). When the general method for the formation of triazoles from aryl-iodides was used. Orange solid (0.0154 g, 23%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.58 (d, *J* = 9.1, 2H), 7.50 (t, *J* = 8.1, 1H), 7.31 (d, *J* = 8.1, 1H), 7.05 (d, *J* = 8.1, 1H), 6.99 (d, *J* = 9.1, 2H), 5.09 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.9, 160.0, 157.1, 151.2, 138.8, 133.8, 130.1, 125.6, 122.1, 121.3, 114.8, 109.9, 55.6, 35.5; LRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{14}ClN_4O_3$, 369.1; Found 369.2; XLogP = 2.07.

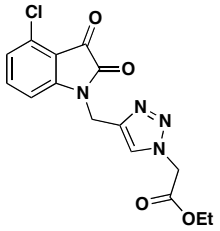


Table 4, entry 24: 4-chloro-1-((1-ethyl acetate-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (8cf): General method for the formation of triazoles from azides was used Yellow solid (0.064 g, 99%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.48 (t, *J* = 8.1, 1H), 7.23 (dd, *J* = 8.1, 0.6, 1H), 7.03 (dd, *J* = 8.1, 0.6, 1H), 5.14 (s, 2H), 5.04 (s, 2H), 4.24 (q, *J* = 7.1, 2H), 1.27 (t, *J* = 7.1, 3H); LRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{14}ClN_4O_4$, 349.1; found 348.9; XLogP = 0.56.

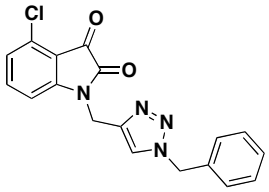


Table 4, entry 25: 4-chloro-1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (8cc): General method for the formation of triazoles from azides was used. Yellow solid (0.062 g, 97%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.49 (t, *J* = 8.1, 1H), 7.39 – 7.35 (m, 2H),

7.31 – 7.24 (m, 4H), 7.05 (dd, J = 8.1, 0.6, 1H), 5.48 (s, 2H), 4.99 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.9, 157.0, 151.2, 138.7, 133.9, 133.7, 129.2, 129.0, 128.3, 125.5, 122.9, 114.6, 109.8, 54.4, 35.5; LRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{14}ClN_4O_2$; 353.1, found 353.2; XLogP = 2.28.

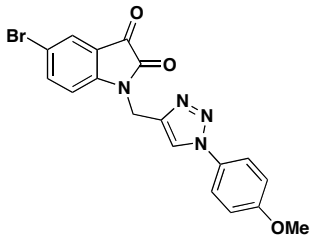


Table 4, entry 26: 5-bromo-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (8da): General method for the formation of triazoles from azides was used. Orange solid (0.058 g, 74% yield). ^{1}H NMR (300 MHz, CD_2Cl_2) 7.98 (s, 1H), 7.72 (dd, J = 8.4, 2.0, 1H), 7.69 (d, J = 2.0, 1H), 7.58 (d, J = 9.0, 2H), 7.34 (d, J = 8.4, 1H), 7.00 (d, J = 9.0, 2H), 5.08 (s, 2H), 3.86 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{18}H_{14}BrN_4NaO_3$ 435.01; found 435.3; XLogP = 2.26.

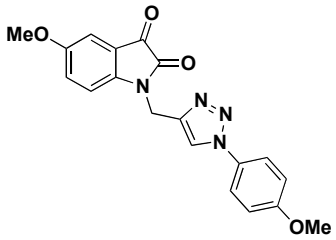


Table 4, entry 27: 5-methoxy-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (8ea): General method for the formation of triazoles from azides was used. Red foam (0.067 g, 99%). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.97 (s, 1H), 7.59 (d, J = 9.1, 2H), 7.24 – 7.11 (m, 3H), 7.02 (d, J = 9.1, 2H), 5.05 (s, 2H), 3.85 (s, 3H), 3.79 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{19}H_{17}N_4O_4$ 365.1; found 365.3; XLogP = 1.31.

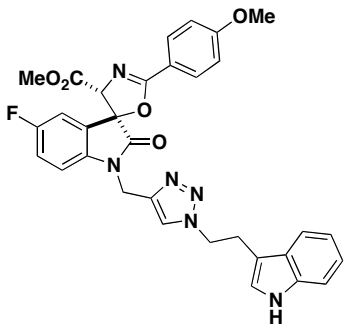


Table 4, entry 28: (3*R*,4'*S*)-methyl 1-((1-(2-(1*H*-indol-3-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)-5-fluoro-2'-(4-methoxyphenyl)-2-oxo-4'*H*-spiro[indoline-3,5'-oxazole]-4'-carboxylate (9bb): General method for the formation of triazoles from azides was used. White yellow foam (0.014 g, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.95 (d, J = 8.9, 2H), 7.50 (m, 1H), 7.39 (s, 1H), 7.31 (m, 1H), 7.18 (m, 1H), 7.13 – 6.99 (m, 4H), 6.91 (d, J = 8.9, 2H), 6.72 (d, J = 2.3, 1H), 5.23 (s, 1H), 5.13 (d, J = 15.8, 1H), 4.79 (d, J = 15.8, 1H), 4.61 (m, 2H), 3.85 (s, 3H), 3.63 (s, 3H), 3.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 169.5, 165.1, 163.2, 159.8 (d, J_{FC} = 243.5), 141.9, 139.0, 136.4, 131.1, 128.9 (d, J_{FCCC} = 7.8), 126.9, 123.5, 122.9, 122.5, 119.9, 118.5, 118.3, 117.9 (d, J_{FCC} = 23.4), 114.08, 112.4 (d, J_{FCC} = 25.3), 111.6, 111.5 (d, J_{FCCC} = 7.9), 111.1, 84.5, 78.6, 55.7, 53.1, 51.1, 36.3; LRMS (ESI) *m/z* [M + H]$^{+}$ calcd for $C_{32}H_{28}FN_6O_5$, 595.21; found 595.0; XLogP = 3.12.

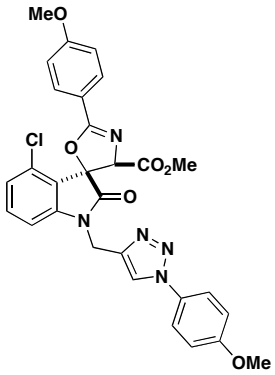


Table 4, entry 29: Methyl 4-chloro-2'-(4-methoxyphenyl)-1-((1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)-2-oxo-4'*H*-spiro[indoline-3,5'-oxazole]-4'-carboxylate (9ca): General method for the formation of triazoles from azides was used. Yellow foam (0.0081 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.99 (d, J = 8.9, 2H), 7.63 (d, J = 9.0, 2H), 7.31 (t, J = 8.1, 1H), 7.05 (m, 2H), 7.00 (d, J = 9.0, 2H), 6.93 (d, J = 8.9, 2H), 5.61 (s, 1H), 5.32 (d, J = 16.0, 1H), 4.90 (d, J = 16.0, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 170.6, 163.1, 160.3, 160.1, 144.7, 132.7, 132.1, 131.0, 124.6, 122.1, 118.7, 115.0, 114.0, 108.9, 76.2, 55.8, 55.7, 53.1, 36.4, 29.9; FT IR (neat): 2955, 2923, 1728, 1608, 1515, 1457, 1167, 1025, 781 cm^{-1}; LRMS (ESI) *m/z* [M + H]$^{+}$ calcd for $C_{29}H_{25}ClN_5O_6$,

574.15; found 574.1; XLogP = 3.25.

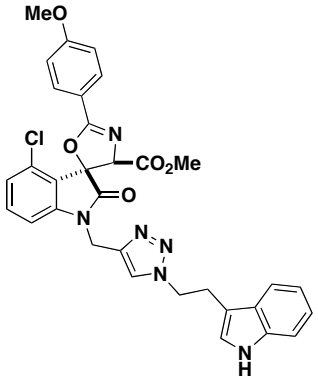


Table 4, entry 30: Methyl 1-((1-(2-(1*H*-indol-3-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)-4-chloro-2'-(4-methoxyphenyl)-2-oxo-4'*H*-spiro[indoline-3,5'-oxazole]-4'-carboxylate (9cb): General method for the formation of triazoles from azides was used. Yellow foam (0.0184 g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (m, 2H), 7.50 (d, *J* = 7.9, 1H), 7.40 (s, 1H), 7.32 – 7.25 (m, 2H), 7.17 (m, 1H), 7.08 (m, 2H), 6.98 (d, *J* = 7.9, 1H), 6.91 (m, 2H), 6.67 (m, 1H), 5.55 (s, 1H), 5.14 (d, *J* = 15.8, 1H), 4.80 (d, *J* = 15.8, 1H), 4.61 (t, *J* = 6.9, 2H), 3.85 (s, 3H), 3.63 (s, 3H), 3.32 (t, *J* = 6.9, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 170.1, 164.9, 163.1, 144.9, 136.5, 132.6, 132.0, 131.0, 126.8, 124.4, 123.9, 123.7, 122.9, 122.5, 119.8, 118.7, 118.3, 114.0, 111.6, 111.1, 109.1, 84.6, 76.1, 55.7, 53.0, 51.1, 36.4; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{32}H_{28}ClN_6O_5$, 611.1810; found 610.9; XLogP = 3.60.

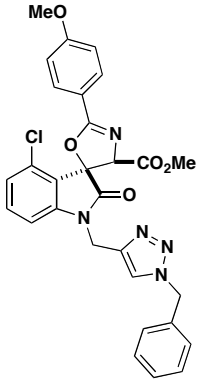


Table 4, entry 31: Methyl 4-chloro-2'-benzyl-2-oxo-1-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl)-4'*H*-spiro[indoline-3,5'-oxazole]-4'-carboxylate (9cc): General method for the formation of triazoles from azides was used using 3 equiv azide**.** White foam (0.061 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.9, 2H), 7.67 (s, 1H), 7.37 – 7.24 (m, 6H), 7.04 (m, 1H), 6.91 (d, *J* = 8.9, 2H), 5.56 (s, 1H), 5.51 (d, *J* = 14.8, 1H), 5.47 (d, *J* = 14.8, 1H), 5.19 (d, *J* = 15.8, 1H), 4.81 (d, *J* = 15.8, 1H), 3.84 (s, 3H), 3.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 170.2, 164.9, 163.0, 144.8, 142.6, 134.5, 132.6, 132.0, 131.0, 129.3, 129.0, 128.5, 124.6,

123.8, 123.2, 118.7, 114.0, 109.0, 84.6, 76.0, 55.6, 54.6, 52.9, 36.4. LRMS (ESI) *m/z* Exact mass calculated for $[M + H]^+$ $C_{29}H_{25}ClN_5O_5$,558.1544; 558.2; XLogP = 3.45.

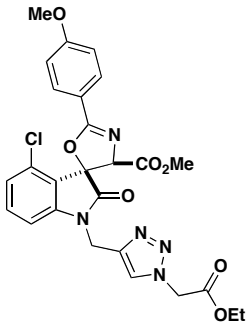


Table 4, entry 32: Methyl 4-chloro-2'-(4-methoxyphenyl)-2-oxo-1-((1-ethylacetate-1*H*-1,2,3-triazol-4-yl)methyl)-4'*H*-spiro[indoline-3,5'-oxazole]-4'-carboxylate (9cf): General method for the formation of triazoles from azides was used. Yellow foam (0.0387 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.9, 2H), 7.86 (s, 1H), 7.30 (m, 1H), 7.03 (m, 2H), 6.92 (d, *J* = 8.9, 2H), 5.58 (s, 1H), 5.26 (d, *J* = 15.8, 1H), 5.13 (d, *J* = 1.7, 1H), 5.13 (d, *J* = 1.7, 1H), 4.87 (d, *J* = 15.8, 1H), 4.24 (q, *J* = 7.1, 2H), 3.85 (s, 3H), 3.76 (s, 3H), 1.26 (t, *J* = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 170.4, 166.2, 165.0 163.0, 144.7, 142.7, 132.6, 132.0, 131.0, 124.7, 124.6, 123.8, 118.7, 114.0, 109.0, 84.6, 76.1, 62.7, 55.6, 53.1, 51.2, 36.3, 14.2; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{26}H_{25}ClN_5O_7$, 554.1; found 554.2; XLogP = 1.73.

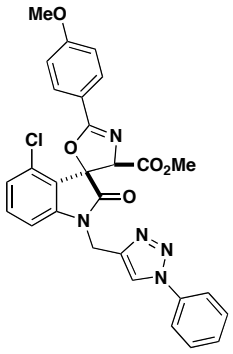


Table 4, entry 33: Methyl 4-chloro-2'-phenyl-2-oxo-1-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl)-4'*H*-spiro[indoline-3,5'-oxazole]-4'-carboxylate (9cd): General method for the formation of triazoles from azides was used. Yellow foam (0.044 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.99 (d, *J* = 8.7, 2H), 7.74 (m, 2H), 7.50 (m, 2H), 7.42 (m, 1H), 7.32 (m, 1H), 7.05 (m, 2H), 6.93 (d, *J* = 8.7, 2H), 5.63 (s, 1H), 5.35 (d, *J* = 15.9, 1H), 4.91 (d, *J* = 15.9, 1H), 3.85 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 170.6, 165.0, 163.1, 144.7, 137.1, 132.7, 132.1, 131.0, 130.0, 129.1, 124.7, 123.8, 121.5, 120.5, 118.7, 114.0, 108.9, 84.7, 76.2, 55.7, 53.2, 36.4.; FT IR (neat): 2923, 2852, 1760, 1722, 1606, 1455, 1255, 1100 838 cm^{-1};

LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{28}H_{23}ClN_5O_5$, 544.14; found 544.1; XLogP = 3.39.

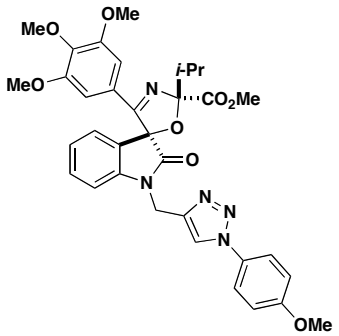


Table 4, entry 34: Methyl 2'-isopropyl-1-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)-2-oxo-4'-(3,4,5-trimethoxyphenyl)-2'H-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10aa): General method for the formation of triazoles from azides was used. Yellow powder (0.053 g, 92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.56 – 7.35 (m, 4H), 7.30 (d, *J* = 7.4, 1H), 7.16 – 7.03 (m, 1H), 6.96 (d, *J* = 8.7, 2H), 6.62 (s, 2H), 5.23 (d, *J* = 15.5, 1H), 4.89 (d, *J* = 15.5, 1H), 3.91 (s, 3H), 3.83 (s, 3H), 3.65 (s, 3H), 3.35 (s, 6H), 2.71 – 2.55 (m, 1H), 1.18 (d, *J* = 6.7, 3H), 1.13 (d, *J* = 6.7, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{34}H_{36}N_5O_8$ 642.7; found 642.9; XLogP = 4.41.

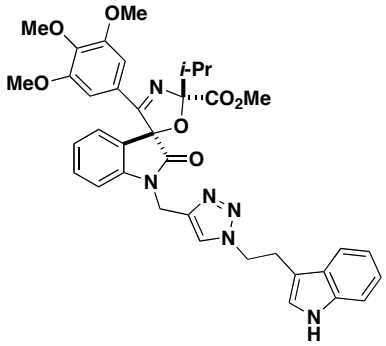


Table 4, entry 35: Methyl 2'-isopropyl-1-((1-(2-(1*H*-indol-3-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)-2-oxo-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10ab): General method for the formation of triazoles from azides was used. White foam (0.052 g, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.50 (m, 1H), 7.46 (m, 1H), 7.39-7.34 (m, 1H), 7.35 (s, 1H), 7.17 (m, 1H), 7.09 (m, 1H), 7.03 (m, 1H), 6.80 (s, 1H), 6.66 (s, 2H), 6.24 (m, 1H), 4.85 (d, *J* = 15.4, 1H), 4.77 (d, *J* = 15.4, 1H), 4.62 – 4.56 (m, 1H), 4.45 (m, 1H), 3.91 (s, 3H), 3.77 (s, 3H), 3.48 (s, 6H), 3.18 – 3.06 (m, 2H), 2.56 (m, 1H), 1.33 (d, *J* = 7.0, 3H), 1.26 (d, *J* = 7.0, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.8, 169.7, 163.2, 153.1, 145.0, 141.2, 140.6, 136.6, 132.7, 132.6, 126.3, 124.8, 124.4, 123.9, 123.5, 122.4, 122.0, 119.3, 117.8, 114.5, 112.0, 110.0, 109.0, 104.8, 90.1, 60.8, 55.8, 53.0, 50.8, 37.1, 35.6, 26.6, 18.7, 17.0. FT IR

(neat) 2934, 1729, 1454, 1251, 997cm^{-1}; LRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{37}H_{39}N_6O_7$, 679.29; found 679.5; XLogP = 4.76.

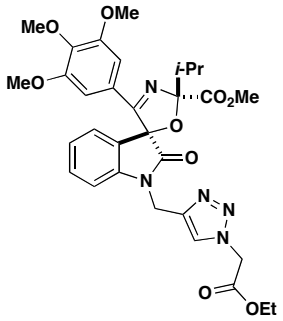


Table 4, entry 36: Methyl -2'-isopropyl-1-((1-(ethylacetate)-1*H*-1,2,3-triazol-4-yl)methyl)-2-oxo-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10af): General method for the formation of triazoles from azides was used. White foam (0.035 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.28 (m, 4H), 7.10 (m, 1H), 6.57 (s, 2H), 5.17 (d, *J* = 15.5, 1H), 5.11 (d, *J* = 17.6, 1H), 4.94 (d, *J* = 17.6, 1H), 4.82 (d, *J* = 15.5, 1H), 4.20 (q, *J* = 7.1, 3H), 3.90 (s, 3H), 3.77 (s, 3H), 3.38 (s, 6H), 2.64 (m, 1H), 1.25 (t, *J* = 7.1, 3H), 1.18 (d, *J* = 6.9, 3H), 1.13 (d, *J* = 6.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 170.5, 166.1, 153.1, 143.4, 142.7, 131.6, 126.3, 125.7, 124.7, 124.2, 114.0, 110.6, 105.7, 62.7, 61.0, 56.0, 52.9, 51.0, 35.9, 35.7, 17.2, 16.7, 14.2; LRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{31}H_{36}N_5O_9$, 622.3; found 622.4; XLogP = 2.89.

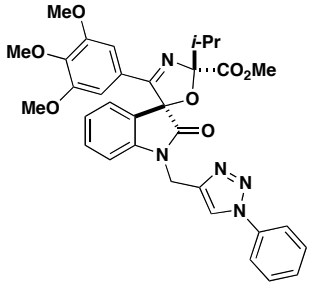


Table 4, entry 37: Methyl-2'-isopropyl-2-oxo-1-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)-4'-(3,4,5-trimethoxyphenyl)-2'H-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10ad): General method for the formation of triazoles from azides was used. White powder (0.044 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.56 (m, 2H), 7.44 (m, 5H), 7.30 (d, *J* = 7.4, 1H), 7.13 – 7.07 (m, 1H), 6.61 (s, 2H), 5.23 (d, *J* = 15.5, 1H), 4.90 (d, *J* = 15.5, 1H), 3.90 (s, 3H), 3.61 (s, 3H), 3.35 (s, 6H), 2.68 – 2.59 (m, 1H), 1.18 (d, *J* = 6.9, 3H), 1.13 (d, *J* = 6.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 170.2, 164.9, 152.9, 143.1, 142.9, 141.1, 136.6, 131.4, 129.8, 129.0, 126.2, 125.6, 124.2, 124.1, 121.2, 120.5, 113.7, 110.3, 105.4, 90.5, 60.6, 55.6, 52.6, 35.7, 35.5, 16.9, 16.5; LRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{33}H_{34}N_5O_7$ 612.7; found 612.4; XLogP = 4.55.

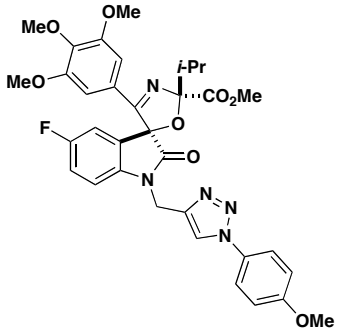


Table 4, entry 38: Methyl 5-fluoro-2'-isopropyl-1-((1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)-2-oxo-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10ba): General method for the formation of triazoles from azides was used. White foam (0.0137 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.47 (d, *J* = 9.0, 1H), 7.45 (m, 1H), 7.14 (m, 1H), 7.02 (m, 1H), 6.96 (d, *J* = 9.0, 2H), 6.60 (s, 2H), 5.23 (d, *J* = 15.5, 1H), 4.86 (d, *J* = 15.5, 1H), 3.90 (s, 3H), 3.84 (s, 3H), 3.67 (s, 3H), 3.37 (s, 6H), 2.72 – 2.55 (m, 1H), 1.17 (d, *J* = 6.8, 3H), 1.12 (d, *J* = 6.8, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{34}H_{35}FN_5O_8$, 660.2; found 660.5; XLogP = 4.54.

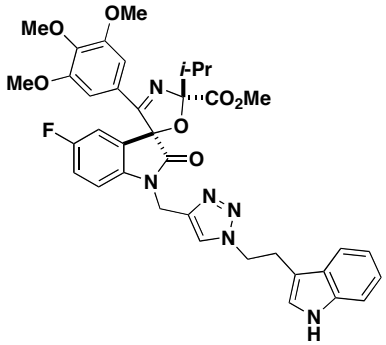


Table 4, entry 39: Methyl 5-fluoro-2'-isopropyl-1-((1-(2-(1*H*-indol-3-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)-2-oxo-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10bb): General method for the formation of triazoles from azides was used. White foam (0.0513 g, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 7.54 – 7.43 (m, 3H), 7.23 – 7.08 (m, 3H), 7.03 (m, 1H), 6.81 (s, 1H), 6.65 (s, 2H), 6.28 (d, *J* = 2.3, 1H), 4.90 (d, *J* = 15.3, 1H), 4.79 (d, *J* = 15.3, 1H), 4.71 – 4.61 (m, 1H), 4.50 – 4.38 (m, 1H), 3.94 (s, 3H), 3.78 (s, 3H), 3.51 (s, 6H), 3.25-3.17 (m, 1H), 3.16 – 3.07 (m, 1H), 2.70 – 2.58 (m, 1H), 1.21 (d, *J* = 6.8, 3H), 1.15 (d, *J* = 6.8, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 170.8, 164.9, 159.9 (d, J_{FC} = 244.2), 153.3, 141.6, 139.4, 136.8, 127.8 (d, J_{FCCC} = 7.8), 126.5, 124.1, 123.7, 122.3, 119.6, 118.1 (d, J_{FCC}= 23.5), 118.1, 114.3, 113.7 (d, J_{FCC} = 25.0), 112.2, 111.8 (d, J_{FCCC} = 7.7), 110.3, 105.6, 61.1, 56.1, 53.1, 51.1, 35.9, 35.8, 26.8, 17.4, 16.7; IR (neat): 2950, 1729, 1488, 1454, 1252, 743 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{37}H_{38}FN_6O_7$, 697.28; found 697.2; XLogP = 4.90.

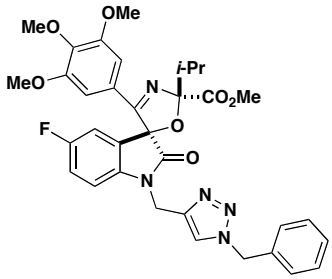


Table 4, entry 40: (2'*S*,3*S*)-methyl 1-((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)-5-fluoro-2'-isopropyl-2-oxo-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10bc): General method for the formation of triazoles from azides was used. (0.036 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (m, 1H), 7.34 – 7.30 (m, 3H), 7.25 (bs, 1H), 7.20 – 7.09 (m, 3H), 7.02 (m, 1H), 6.56 (s, 2H), 5.49 (d, *J* = 14.7, 1H), 5.30 (d, *J* = 14.7, 1H), 5.10 (d, *J* = 15.3, 1H), 4.75 (d, *J* = 15.3, 1H), 3.87 (s, 3H), 3.81 (s, 3H), 3.38 (s, 6H), 2.62 (m, 1H), 1.16 (d, *J* = 6.9, 3H), 1.11 (d, *J* = 6.9, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.57, 170.20, 164.74, 159.85 (J_{FC} = 244.1), 153.19, 141.40, 139.43, 139.40, 134.04, 129.39, 129.17, 128.43, 127.86 (J_{FCCC} = 7.8), 124.18, 123.14, 117.93 (J_{FCC} = 23.4), 113.71 (J_{FCC} = 25.1), 113.59, 111.62 (J_{FCCC} = 7.5), 105.70, 105.65, 90.66, 61.05, 55.98, 55.95, 54.54, 52.92, 52.88, 35.68, 17.18, 16.72; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{34}H_{35}FN_5O_7$ 644.3; found 644.0; XLogP = 4.74.

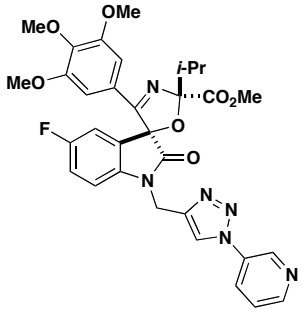


Table 4, entry 41: Methyl 5-fluoro-2'-isopropyl-2-oxo-1-((1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)methyl)-4'-(3,4,5-trimethoxyphenyl)-2'H-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10be): General method for the formation of triazoles from azides was used White powder (0.024 g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.70 (m, 1H), 7.96 (s, 2H), 7.52 – 7.38 (m, 2H), 7.22 – 7.11 (m, 1H), 7.07 – 7.02 (m, 1H), 6.61 (s, 2H), 5.22 (d, *J* = 15.5, 1H), 4.93 (d, *J* = 15.5, 1H), 3.90 (s, 3H), 3.68 (s, 3H), 3.41 (s, 6H), 2.63 (m, 1H), 1.17 (d, *J* = 6.8, 3H), 1.12 (d, *J* = 6.8, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{32}H_{32}FN_6O_7$ 631.6; found 631.3; XLogP = 3.70.

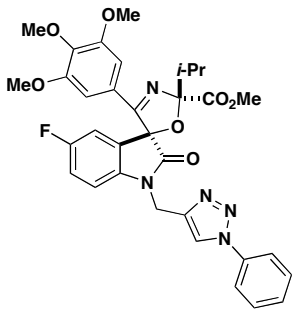


Table 4, entry 42: Methyl 5-fluoro-2'-isopropyl-2-oxo-1-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)-4'-(3,4,5-trimethoxyphenyl)-2'H-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10bd): General method for the formation of triazoles from azides was used. Off-white powder (0.037 g, 74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 8.2, 2H), 7.52 – 7.34 (m, 4H), 7.15 (td, J = 8.2, 2.4, 1H), 7.03 (dd, J = 7.3, 2.4, 1H), 6.61 (s, 2H), 5.24 (d, J = 15.5, 1H), 4.88 (d, J = 15.5, 1H), 3.91 (s, 3H), 3.65 (s, 3H), 3.38 (s, 6H), 2.76 – 2.49 (m, 1H), 1.17 (d, J = 6.8, 3H), 1.12 (d, J = 6.8, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 170.0, 164.4, 159.7 (J_{FC} = 243), 153.0, 142.6, 141.3, 139.1 (J_{FCCCC} = 3), 136.5, 129.8, 129.1, 127.7 (J_{FCCC} = 8), 123.9, 121.3, 120.4, 117.7 (J_{FCC} = 23), 114.1, 113.6 (J_{FCC} = 25), 111.3 (J_{FCC} = 8), 105.5, 90.3, 60.7, 55.7, 52.7, 35.7, 35.4, 16.9, 16.5; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{33}H_{33}FN_5O_7$ 630.6; found 630.3; XLogP = 4.69.

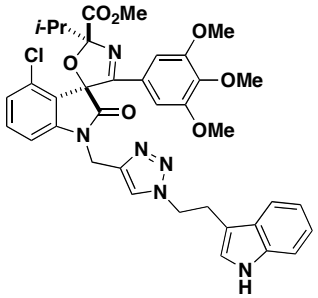


Table 4, entry 43: Methyl 4-chloro-2'-isopropyl-1-((1-(2-(1*H*-indol-3-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)-2-oxo-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10cb): General method for the formation of triazoles from azides was used. White foam (0.0427 g, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 7.50 (d, J = 7.9, 1H), 7.47 – 7.40 (m, 1H), 7.31 (d, J = 7.4, 1H), 7.20 – 7.05 (m, 3H), 6.80 (s, 1H), 6.65 (s, 2H), 6.28 (d, J = 2.2, 1H), 4.89 (d, J = 15.3, 1H), 4.80 (d, J = 15.3, 1H), 4.63 – 4.54 (m, 1H), 4.47 – 4.35 (m, 1H), 3.93 (s, 3H), 3.76 (s, 3H), 3.46 (s, 6H), 3.22 – 3.04 (m, 2H), 2.70 – 2.61 (m, 1H),1.22 (d, J = 6.8, 1H), 1.16 (d, J = 6.8, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 171.0, 165.5, 153.2, 143.5, 141.3, 136.8, 131.7, 126.5, 126.3, 125.7, 124.4, 124.3, 124.0, 123.7, 122.2, 119.5, 118.1, 114.0, 112.2, 110.8, 110.3, 105.7, 90.9, 61.0, 56.0, 53.1, 51.0, 35.9, 35.7, 6.8, 17.4, 16.8; FT IR (neat):

2937, 1727, 1463, 1349, 1253, 997 cm^{-1}; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{37}H_{38}ClN_6O_7$, 713.25; found 713.2; XLogP = 5.38.

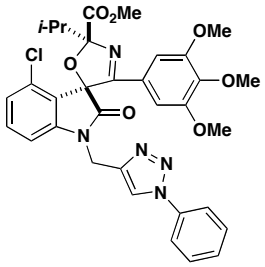


Table 4, entry 44: Methyl 4-chloro-2'-isopropyl-2-oxo-1-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)-4'-(3,4,5-trimethoxyphenyl)-2'H-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10cd): General method for the formation of triazoles from azides was used. Off white foam (0.024 g, 93%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.59 – 7.56 (m, 2H), 7.47 (m, 2H), 7.43 – 7.34 (m, 4H), 7.02 (m, 1H), 6.62 (s, 2H), 5.23 (d, *J* = 15.6, 1H), 4.85 (d, *J* = 15.6, 1H), 3.88 (s, 3H), 3.65 (s, 3H), 3.36 (s, 6H), 2.58 – 2.47 (m, 1H), 1.30 (d, *J* = 7.0, 3H), 1.21 (d, *J* = 7.0, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.1, 169.1, 163.0, 153.0, 144.9, 141.1, 136.5, 132.7, 132.5, 129.8, 129.1, 124.8, 124.5, 122.6, 121.3, 120.4, 114.4, 108.8, 104.8, 90.0, 60.7, 55.6, 52.3, 37.1, 35.9, 18.6, 17.0. ;LRMS (ESI) m/z $[M + H]^+$ calcd for $C_{33}H_{33}ClN_5O_7$ 647.1; found 646.3; XLogP = 5.17.

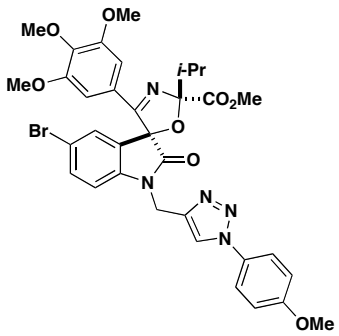


Table 4, entry 45: Methyl 5-bromo-2'-isopropyl-1-((1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)-2-oxo-4'-(3,4,5-trimethoxyphenyl)-2'*H*-spiro[indoline-3,5'-oxazole]-2'-carboxylate (10da): General method for the formation of triazoles from azides was used. White foam (0.0244 g, >99%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.57 (dd, *J* = 8.4, 1.9, 1H), 7.47 (d, *J* = 9.0, 2H), 7.40 (d, *J* = 8.4, 1H), 7.36 (d, *J* = 1.9, 1H), 6.97 (d, *J* = 9.0, 2H), 6.60 (s, 2H), 5.23 (d, *J* = 15.5, 1H), 4.87 (d, *J* = 15.5, 1H), 3.90 (s, 3H), 3.84 (s, 3H), 3.68 (s, 3H), 3.38 (s, 6H), 2.70 – 2.56 (m, 2H), 1.16 (d, *J* = 6.8, 3H), 1.14 (d, *J* = 6.8, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 170.2, 164.6, 160.3, 153.2, 142.4, 134.4, 130.1, 128.8, 128.3, 124.1, 122.3, 121.6, 116.9, 115.0, 114.3, 112.2, 106.0, 105.6, 90.3, 61.0 56.0, 55.9, 52.9, 36.0, 35.7, 17.2,

16.8; LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{34}H_{35}BrN_5O_8$, 722.16; found 722.2; XLogP = 5.20.

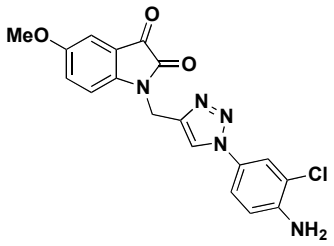


Table 5, entry 2: 1-((1-(4-amino-3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-5-methoxyindoline-2,3-dione. (8eh): General method for the formation of triazoles from aryl-iodides was used. Red powder (0.036 g, 35%). ^{1}H NMR (600 MHz, 3:1 $CDCl_3$:CD_3OD) δ 8.10 (s, 1H), 7.62 (d, *J* = 2.4, 1H), 7.44 (s, 2H), 7.39 (dd, *J* = 8.7, 2.4, 1H), 7.26 – 7.14 (m, 3H), 6.90 (d, *J* = 8.7, 1H), 5.07 (s, 3H), 3.82 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{18}H_{15}ClN_5O_3$ 384.1; found 384.3; XLogP = 1.30.

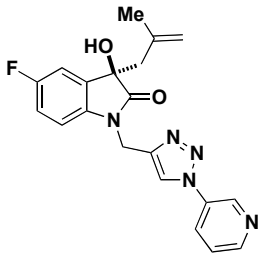


Table 5, entry 3: (*R*)-5-fluoro-3-hydroxy-3-(2-methylallyl)-1-((1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)methyl)indolin-2-one (5bi): General method for the formation of triazoles from azides was used. White solid (0.011 g, 28%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.54 (d, *J* = 4.1, 1H), 8.02 (s, 2H), 7.41 (dd, *J* = 8.0, 4.8, 1H), 7.12 (dd, *J* = 8.0, 2.5, 1H), 7.09 (dd, *J* = 8.7, 4.1, 1H), 6.98 (ddd, *J* = 8.7, 2.5, 1H), 5.02 (d, *J* = 15.7, 1H), 4.96 (d, *J* = 15.7, 1H), 4.72 (s, 1H), 4.61 (s, 1H), 2.70 (s, 2H), 1.80 (s, 1H), 1.48 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{19}FN_5O_2$, 380.4; found 380.1; XLogP = 1.18.

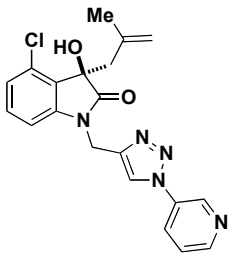


Table 5, entry 4: (*R*)-4-chloro-3-hydroxy-3-(2-methylallyl)-1-((1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)methyl)indolin-2-one (5ci): General method for the formation of triazoles from azides was used. Off-white solid (0.016 g, 40%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.89 (d, *J* = 2.3, 1H), 8.67 (d, *J* = 4.7, 1H), 8.05 (ddd, *J* = 8.3, 2.3, 1.5, 1H), 8.00 (s, 1H), 7.47 (dd, *J* = 8.3, 4.7, 1H), 7.33 – 7.16 (m, 2H), 7.08 (d, *J* = 7.9, 1H), 7.03 (d, *J* = 7.9, 1H), 5.06 (d, *J* = 15.7, 1H), 5.03 (d, *J* = 15.7, 1H), 4.68 (s, 1H), 4.64 (s, 1H), 3.22 (d, *J* = 12.6, 1H), 2.91 (d, *J* = 12.6, 1H), 1.38 (s, 3H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{20}H_{19}ClN_5O_2$, 396.84; found 396.1; XLogP = 1.66.

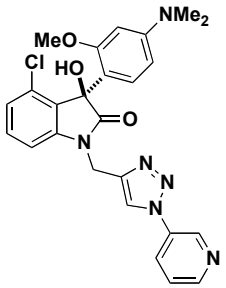
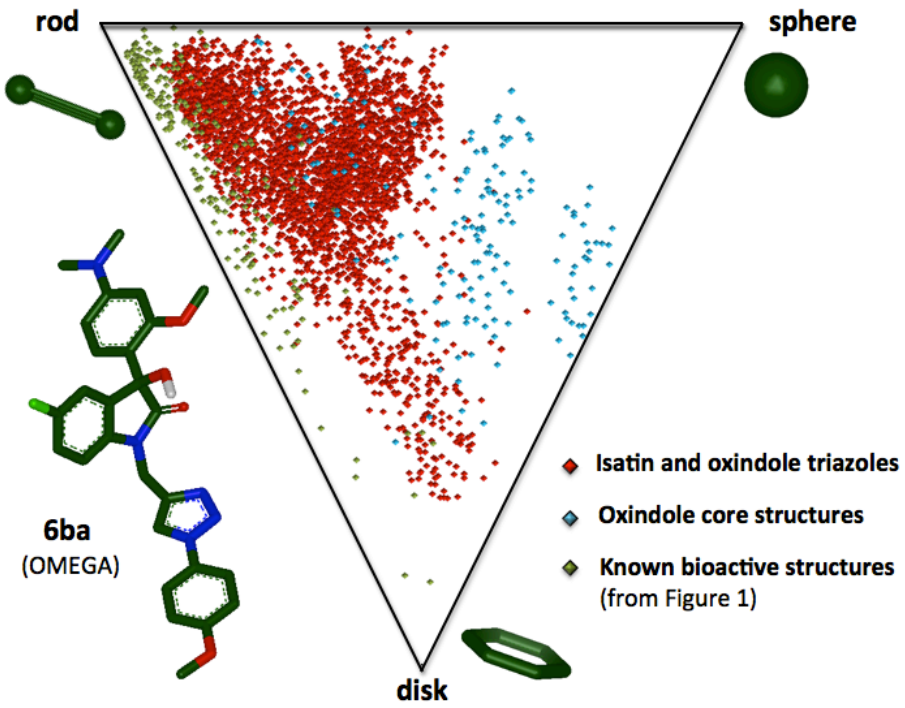


Table 5, entry 5: (*R*)-4-chloro-3-(4-(dimethylamino)-2-methoxyphenyl)-3-hydroxy-1-((1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)methyl)indolin-2-one (6ci): The general procedure for the formation of triazoles from aryl-iodides was followed, White solid (0.0205 g, 19%). ^{1}H NMR (400 MHz, 3:1 $CDCl_3$:MeOD) δ 8.99 (d, *J* = 2.1, 1H), 8.62 (d, *J* = 5.2, 1H), 8.38 (s, 1H), 8.17 (ddd, *J* = 8.3, 2.6, 1.4, 1H), 7.70 (d, *J* = 8.7, 1H), 7.54 (dd, *J* = 8.0, 5.2, 1H), 7.40 (s, 1H), 7.17 (t, *J* = 8.0, 2H), 7.10 – 6.95 (m, 2H), 6.87 (dd, *J* = 8.3, 0.8, 1H), 6.39 (dd, *J* = 8.7, 2.6, 1H), 6.06 (d, *J* = 2.1, 1H), 5.17 (d, *J* = 15.9, 1H), 5.01 (d, *J* = 15.9, 1H), 3.20 (s, 3H), 2.89 (s, 6H); LRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{25}H_{24}ClN_6O_3$, 491.98; found 491.2; XLogP = 2.46.

IIIc. Diversity Analysis

Procedure for generation of Ternary Plot: [14,15]

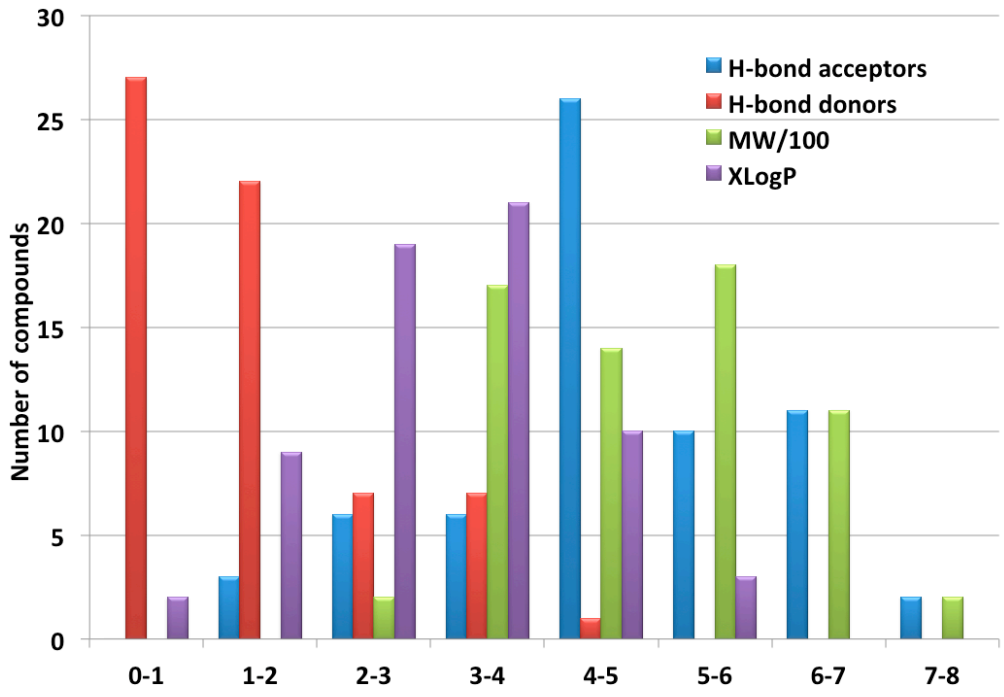
2D Simplified Molecular Input Line Entry Specification (SMILES) strings were generated using CambridgeSoft ® ChemDraw ®.[16] The strings were imported into Windows XP ® Notepad and saved as a .smi files. The .smi files were converted to 3D structures using OpenEye Scientific Software, Inc., OMEGA-V2.4.3;(-ewindow 3.0 kcal/mol).[17] OMEGA was used to directly generate .xyz (Cartesian coordinates). Conformers >3 kcal/mol from the lowest energy conformer and duplicates were discarded. Conformers were estimated using Merks Molecular Force Field 94, MMFF94.[18] The Principal Moments of Inertia (PMI)[14] were calculated using the Perl module Math::MatrixReal.[19] Values at (1,1) correspond to spherical shapes (methane or adamantane), (0.5,0.5) disk shaped (benzene), and (0,1) rod shaped (acetylene).



[14] Sauer, W. H. B.; Schwarz, M. K. *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 987-1003.
[15] Guggenheim, K. G.; Butler, J. D.; Painter, P. P.; Lorsbach, B. A.; Tantillo, D. J.; Kurth, M. J. *J. Org. Chem.* **2011**, *76*, 5803-5812.
[16] http://www.cambridgesoft.com/
[17] For more information on OpenEye and OMEGA: http://www.eyesopen.com/
[18] Halgren, T. A. *J. Comput. Chem.* **1996**, *17*, 520-552.
[19] http://www.cpan.org/modules/index.html

Graph of Diversity Analysis:

Data for molecular weights, XLogP, # of H-bond donors, and # of H-bond acceptors obtained from FILTER[17]. XLogP determination based on the Wang method.[20]



Summary of Average Properties of the Library:

Table data generated using FILTER.[14] Topological Polar Surface Area based on Ertl method.[21] XLogP based on Wang method.[20]

Table S2.

property	oxindole cores (n = 15)	isatin triazoles (n = 9)	oxindole triazoles (n = 40)
MW	399	353	551
XLogP	3	2	3
TPSA	67	81	109
rotatable bonds	4	4	8
HBA	3	4	5
HBD	1	0	1
# of rings	2	3	4

[20] Wang, R.; Fu, Y.; Lai, L. *J. Chem. Inf. Comput. Sci.* **1997**, *37*, 615-621.

[21] Ertl, P.; Rohde, B.; Selzer, P. *J. Med. Chem.* **2000**, *43*, 3714-3717.

Table S3. Summary of all compound properties (using FILTER: http://www.eyesopen.com/filter)

#	Chiral Centers	HBA	HBD	MW	FC	# Rings	Rotatable Bonds	Rigid Bonds	XLogP	TPSA
4ba	1	4	1	483.49	0	4	5	36	3.07	85.41
4bb	1	4	2	520.56	0	4	6	39	3.43	91.97
4bc	1	4	1	467.49	0	4	5	35	3.27	76.18
4ca	1	4	1	499.95	0	4	5	36	3.55	85.41
4cb	1	4	2	537.01	0	4	6	39	3.85	91.97
5ba	1	4	1	408.43	0	3	6	27	2.02	80.48
5bb	1	4	2	445.49	0	3	7	30	2.38	87.04
5bi	1	5	1	379.39	0	3	5	26	1.18	84.14
5ca	1	4	1	424.88	0	3	6	27	2.5	80.48
5cb	1	4	2	461.94	0	3	7	30	2.86	87.04
5ci	1	5	1	395.84	0	3	5	26	1.66	84.14
6ba	1	4	1	503.53	0	4	7	34	2.81	92.95
6bb	1	4	2	540.59	0	4	8	37	3.17	99.51
6ca	1	4	1	519.98	0	4	7	34	3.3	92.95
6cb	1	4	2	557.04	0	4	8	37	3.65	99.51
6cc	1	4	1	503.98	0	4	7	33	3.5	83.72
6ci	1	5	1	490.94	0	4	6	33	2.46	96.61
7ac	1	3	3	491.56	1	3	5	38	3.42	92.65
7af	1	4	3	487.53	1	2	7	34	1.7	118.95
7bb	1	3	4	562.62	1	3	6	43	3.71	108.44
7bc	1	3	3	509.55	1	3	5	39	3.55	92.65
7fa	1	3	3	525.55	1	3	5	40	3.35	101.88
8aa	0	4	0	334.33	0	3	4	24	1.46	77.32
8ad	0	4	0	304.3	0	3	3	23	1.6	68.09
8ae	0	5	0	305.29	0	3	3	23	0.62	80.98
8ca	0	4	0	368.77	0	3	4	25	2.07	77.32
8cc	0	4	0	352.77	0	3	4	24	2.28	68.09
8cf	0	5	0	348.74	0	2	6	20	0.56	94.39
8da	0	4	0	413.22	0	3	4	25	2.26	77.32
8ea	0	4	0	364.35	0	3	5	25	1.31	86.55
8eh	0	4	2	383.79	0	3	4	26	1.3	103.34
9bb	2	5	1	594.59	0	4	9	41	3.12	123.93
9ca	2	5	0	573.98	0	4	8	38	3.25	117.37
9cb	2	5	1	611.05	0	4	9	41	3.6	123.93
9cc	2	5	0	557.98	0	4	8	37	3.45	108.14
9cd	2	5	0	543.96	0	4	7	37	3.39	108.14
9cf	2	6	0	553.95	0	3	10	33	1.73	134.44
10aa	2	6	0	641.67	0	4	11	41	4.41	135.83
10ab	2	6	1	678.73	0	4	12	44	4.76	142.39
10ad	2	6	0	611.64	0	4	10	40	4.55	126.6
10af	2	7	0	621.64	0	3	13	36	2.89	152.9

#	Chiral Centers	HBA	HBD	MW	FC	# Rings	Rotatable Bonds	Rigid Bonds	XLogP	TPSA
10ba	2	6	0	659.66	0	4	11	42	4.54	135.83
10bb	2	6	1	696.72	0	4	12	45	4.9	142.39
10bc	2	6	0	643.66	0	4	11	41	4.74	126.6
10bd	2	6	0	629.64	0	4	10	41	4.69	126.6
10be	2	7	0	630.62	0	4	10	41	3.7	139.49
10cb	2	6	1	713.18	0	4	12	45	5.38	142.39
10cd	2	6	0	646.09	0	4	10	41	5.17	126.6
10da	2	6	0	720.57	0	4	11	42	5.2	135.83
13b	1	2	1	334.34	0	2	2	26	2.58	45.47
13c	1	2	1	350.8	0	2	2	26	3.07	45.47
14b	1	2	1	259.28	0	1	3	17	1.53	40.54
14c	1	2	1	275.73	0	1	3	17	2.02	40.54
15b	1	2	1	354.37	0	2	4	24	2.33	53.01
15c	1	2	1	370.83	0	2	4	24	2.81	53.01
16a	1	1	3	358.41	1	1	2	29	2.73	61.94
16b	1	1	3	376.4	1	1	2	30	2.87	61.94
16f	1	1	3	376.4	1	1	2	30	2.87	61.94
17b	2	3	0	408.38	0	2	5	28	2.28	77.43
17c	2	3	0	424.83	0	2	5	28	2.76	77.43
18a	2	4	0	492.52	0	2	8	31	3.92	95.89
18b	2	4	0	510.51	0	2	8	32	4.06	95.89
18c	2	4	0	526.97	0	2	8	32	4.54	95.89
18d	2	4	0	571.42	0	2	8	32	4.72	95.89

MW = Molecular Weight

FC = Formal Charge at physiological pH

HBD = Hydrogen Bond Donors

HBA = Hydrogen Bond Acceptors

TPSA = Topological Polar Surface Area based on the Ertl method[21]

XLogP based on Wang method[20]

SMILES STRINGS used for FILTER generated compound properties and ternary plot:

Bioactive compounds from Figure 1

FC(C(Cl)=C1)=CC2=C1NC3=C2C[C@@H](C)N[C@@](C4=C(N5)C=CC(Cl)=C4)3C5=O

O=C1NC2=C(Br)C=C(Br)C=C2[C@@]1(CC(C)=O)O

O=C1N(CC2=CC=C(C=CC=C3)C3=C2)C4=CC=C(C(N)=O)C=C4C1=O

O=C(C1=CC2=C(O[C@H](CN3N=NC(CCCCCC)=C3)C2)C=C1)[H]

Oxindole Core Structures

O=C1N(CC#C)C2=CC=C(F)C=C2[C@@]1(C3=CN(C4=C3C=CC=C4)C)O

O=C1N(CC#C)C2=CC=C(F)C=C2[C@@]1(CC(C)=C)O

O=C1N(CC#C)C2=CC=C(F)C=C2[C@@]1(C3=C(OC)C=C(N(C)C)C=C3)O

O=C1N(CC#C)C2=CC=CC(Cl)=C2[C@@]1(C(C3=C4C=CC=C3)=CN4C)O

O=C1N(CC#C)C2=CC=CC(Cl)=C2[C@@]1(CC(C)=C)O

O=C1N(CC#C)C2=CC=CC(Cl)=C2[C@@]1(C3=C(OC)C=C(N(C)C)C=C3)O

O=C1N(CC#C)C2=C(C=CC=C2)[C@@](NCC3)1C4=C3C5=CC(OC)=CC=C5N4

C#CCN1C2=CC=C(F)C=C2[C@@]3(NCCC4=C3NC5=C4C=C(OC)C=C5)C1=O

C#CCN1C2=C(F)C=CC=C2[C@@]3(NCCC4=C3NC5=C4C=C(OC)C=C5)C1=O

C#CCN1C2=CC=C(F)C=C2[C@@]3(OC(C4=CC=C(OC)C=C4)=N[C@H]3C(OC)=O)C1=O

C#CCN1C2=CC=CC(Cl)=C2[C@@]3([C@@H](C(OC)=O)N=C(C4=CC=C(OC)C=C4)O3)C1=O

C#CCN1C2=CC=CC=C2[C@@]3(O[C@](C(OC)=O)(C(C)C)N=C3C4=CC(OC)=C(OC)C(OC)=C4)C1=O

C#CCN1C2=CC=C(F)C=C2[C@@]3(O[C@](C(OC)=O)(C(C)C)N=C3C4=CC(OC)=C(OC)C(OC)=C4)C1=O

C#CCN1C2=CC=CC(Cl)=C2[C@@]3(C(C4=CC(OC)=C(OC)C(OC)=C4)=N[C@@](C(C)C)(C(OC)=O)O3)C1=O

C#CCN1C2=CC=C(Br)C=C2[C@@]3(O[C@@](C(C)C)(C(OC)=O)N=C3C4=CC(OC)=C(OC)C(OC)=C4)C1=O

Oxindole Triazole Structures

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=C(F)C=C4[C@@]1(C5=CN(C6=C5C=CC=C6)C)O

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=C(F)C=C5[C@@]1(C6=CN(C7=C6C=CC=C7)C)O

O=C1N(CC2=CN(CC3=CC=CC=C3)N=N2)C4=CC=C(F)C=C4[C@@]1(C5=CN(C6=C5C=CC=C6)C)O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=C(F)C=C4[C@@]1(CC(C)=C)O

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=C(F)C=C5[C@@]1(CC(C)=C)O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=C(F)C=C4[C@@]1(C5=C(OC)C=C(N(C)C)C=C5)O

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=C(F)C=C5[C@@]1(C6=C(OC)C=C(N(C)C)C=C6)O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]1(C(C5=C6C=CC=C5)=CN6C)O

O=C1N(CC2=CN(CCC3=CC(C=CC=C4)=C4N3)N=N2)C5=CC=CC(Cl)=C5[C@@]1(C(C6=C7C=CC=C6)=CN7C)O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]1(CC(C)=C)O

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=CC(Cl)=C5[C@@]1(CC(C)=C)O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]1(C5=C(OC)C=C(N(C)C)C=C5)O

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=CC(Cl)=C5[C@@]1(C6=C(OC)C=C(N(C)C)C=C6)O

O=C1N(CC2=CN(CC3=CC=CC=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]1(C5=C(OC)C=C(N(C)C)C=C5)O

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=C(F)C=C5[C@@]16NCCC7=C6NC8=C7C=C(OC)C=C8

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=C(F)C=CC=C4[C@@]15NCCC6=C5NC7=C6C=C(OC)C=C7

O=C1N(CC2=CN(CC(OCC)=O)N=N2)C3=C(C=CC=C3)[C@@](NCC4)1C5=C4C6=CC(OC)=CC=C6N5

O=C1N(CC2=CN(CC3=CC=CC=C3)N=N2)C4=C(C=CC=C4)[C@@](NCC5)1C6=C5C7=CC(OC)=CC=C7N6

O=C1N(CC2=CN(CC3=CC=CC=C3)N=N2)C4=C(C=C(F)C=C4)[C@@](NCC5)1C6=C5C7=CC(OC)=CC=C7N6

O=C1N(CC2=CN(C3=CC=CC=C3)N=N2)C4=CC=CC=C4C1=O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=CC=C4C1=O

O=C1N(CC2=CN(C3=CC=CN=C3)N=N2)C4=CC=CC=C4C1=O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=CC(Cl)=C4C1=O

O=C1N(CC2=CN(CC(OCC)=O)N=N2)C3=CC=CC(Cl)=C3C1=O

O=C1N(CC2=CN(CC3=CC=CC=C3)N=N2)C4=CC=CC(Cl)=C4C1=O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=C(Br)C=C4C1=O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=C(OC)C=C4C1=O

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=C(F)C=C5[C@@]16OC(C7=CC=C(OC)C=C7)=N[C@H]6C(OC)=O

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]15[C@@H](C(OC)=O)N=C(C6=CC=C(OC)C=C6)O5

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=CC(Cl)=C5[C@@]16[C@@H](C(OC)=O)N=C(C7=CC=C(OC)C=C7)O6

O=C1N(CC2=CN(CC3=CC=CC=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]15[C@@H](C(OC)=O)N=C(C6=CC=C(OC)C=C6)O5

O=C1N(CC2=CN(CC(OCC)=O)N=N2)C3=CC=CC(Cl)=C3[C@@]14[C@@H](C(OC)=O)N=C(C5=CC=C(OC)C=C5)O4

O=C1N(CC2=CN(C3=CC=CC=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]15[C@@H](C(OC)=O)N=C(C6=CC=C(OC)C=C6)O5

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=CC=C4[C@@]15O[C@@](C(C)C)(C(OC)=O)N=C5C6=CC(OC)=C(OC)C(OC)=C6

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=CC=C5[C@@]16O[C@@](C(C)C)(C(OC)=O)N=C6C7=CC(OC)=C(OC)C(OC)=C7

O=C1N(CC2=CN(CC(OCC)=O)N=N2)C3=CC=CC=C3[C@@]14O[C@@](C(C)C)(C(OC)=O)N=C4C5=CC(OC)=C(OC)C(OC)=C5

O=C1N(CC2=CN(C3=CC=CC=C3)N=N2)C4=CC=CC=C4[C@@]15O[C@@](C(C)C)(C(OC)=O)N=C5C6=CC(OC)=C(OC)C(OC)=C6

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=C(F)C=C4[C@@]15O[C@@](C(C)C)(C(OC)=O)N=C5C6=CC(OC)=C(OC)C(OC)=C6

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=C(F)C=C5[C@@]16O[C@@](C(C)C)(C(OC)=O)N=C6C7=CC(OC)=C(OC)C(OC)=C7

O=C1N(CC2=CN(CC3=CC=CC=C3)N=N2)C4=CC=C(F)C=C4[C@@]15O[C@](C(OC)=O)(C(C)C)N=C5C6=CC(OC)=C(OC)C(OC)=C6

O=C1N(CC2=CN(C3=CC=CN=C3)N=N2)C4=CC=C(F)C=C4[C@@]15O[C@](C(OC)=O)(C(C)C)N=C5C6=CC(OC)=C(OC)C(OC)=C6

O=C1N(CC2=CN(C3=CC=CC=C3)N=N2)C4=CC=C(F)C=C4[C@@]15O[C@](C(OC)=O)(C(C)C)N=C5C6=CC(OC)=C(OC)C(OC)=C6

O=C1N(CC2=CN(CCC3=CNC4=C3C=CC=C4)N=N2)C5=CC=CC(Cl)=C5[C@@]16C(C7=CC(OC)=C(OC)C(OC)=C7)=N[C@@](C(C)C)(C(OC)=O)O6

O=C1N(CC2=CN(C3=CC=CC=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]15C(C6=CC(OC)=C(OC)C(OC)=C6)=N[C@](C(OC)=O)(C(C)C)O5

O=C1N(CC2=CN(C3=CC=C(OC)C=C3)N=N2)C4=CC=C(Br)C=C4[C@@]15O[C@](C(OC)=O)(C(C)C)N=C5C6=CC(OC)=C(OC)C(OC)=C6

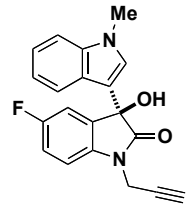
O=C1N(CC2=CN(C3=CC=C(N)C(Cl)=C3)N=N2)C4=CC=C(OC)C=C4C1=O

O=C1N(CC2=CN(C3=CC=CN=C3)N=N2)C4=CC=C(F)C=C4[C@@]1(CC(C)=C)O

O=C1N(CC2=CN(C3=CC=CN=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]1(CC(C)=C)O

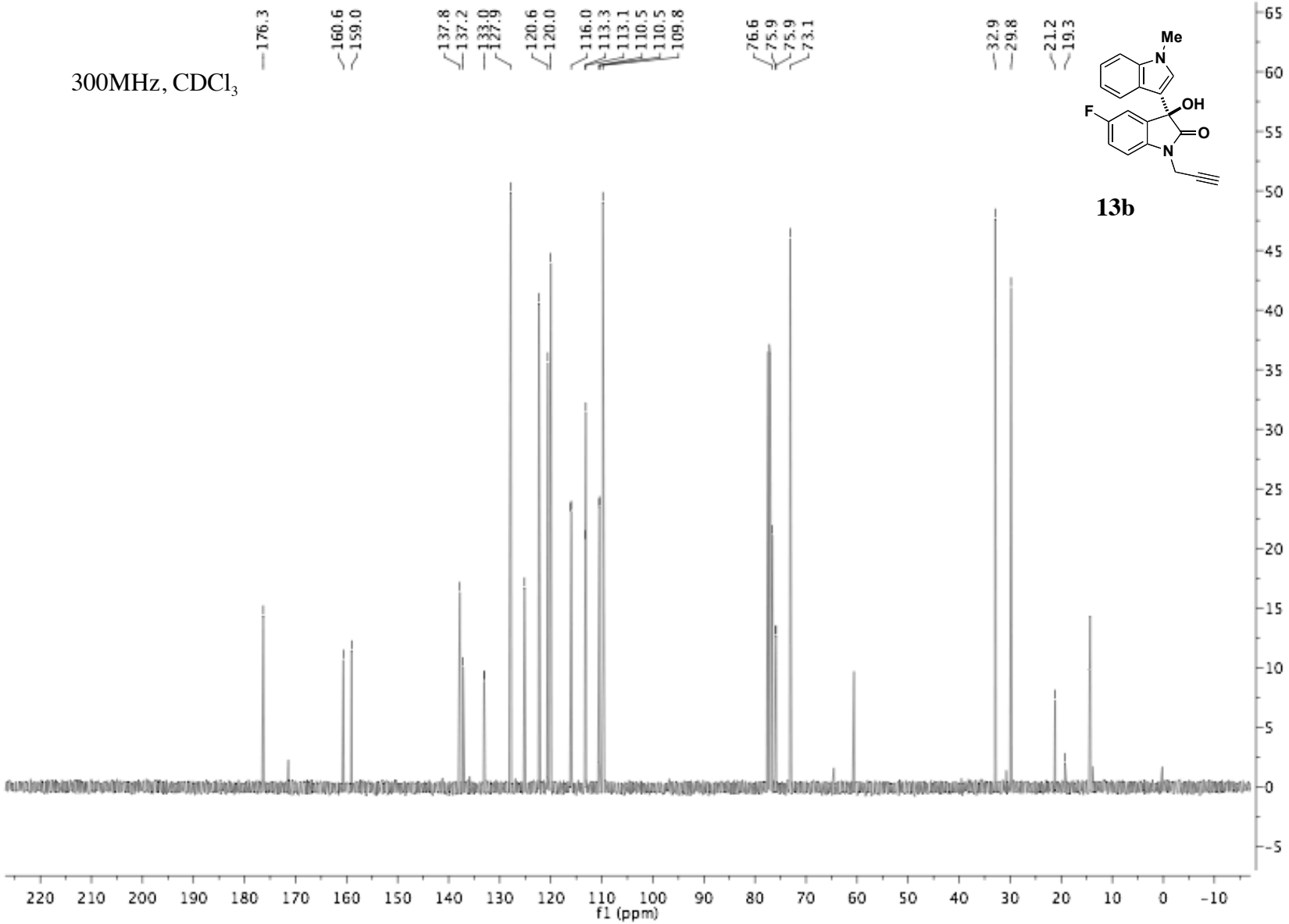
O=C1N(CC2=CN(C3=CC=CN=C3)N=N2)C4=CC=CC(Cl)=C4[C@@]1(C5=C(OC)C=C(N(C)C)C=C5)O

300MHz, $CDCl_3$



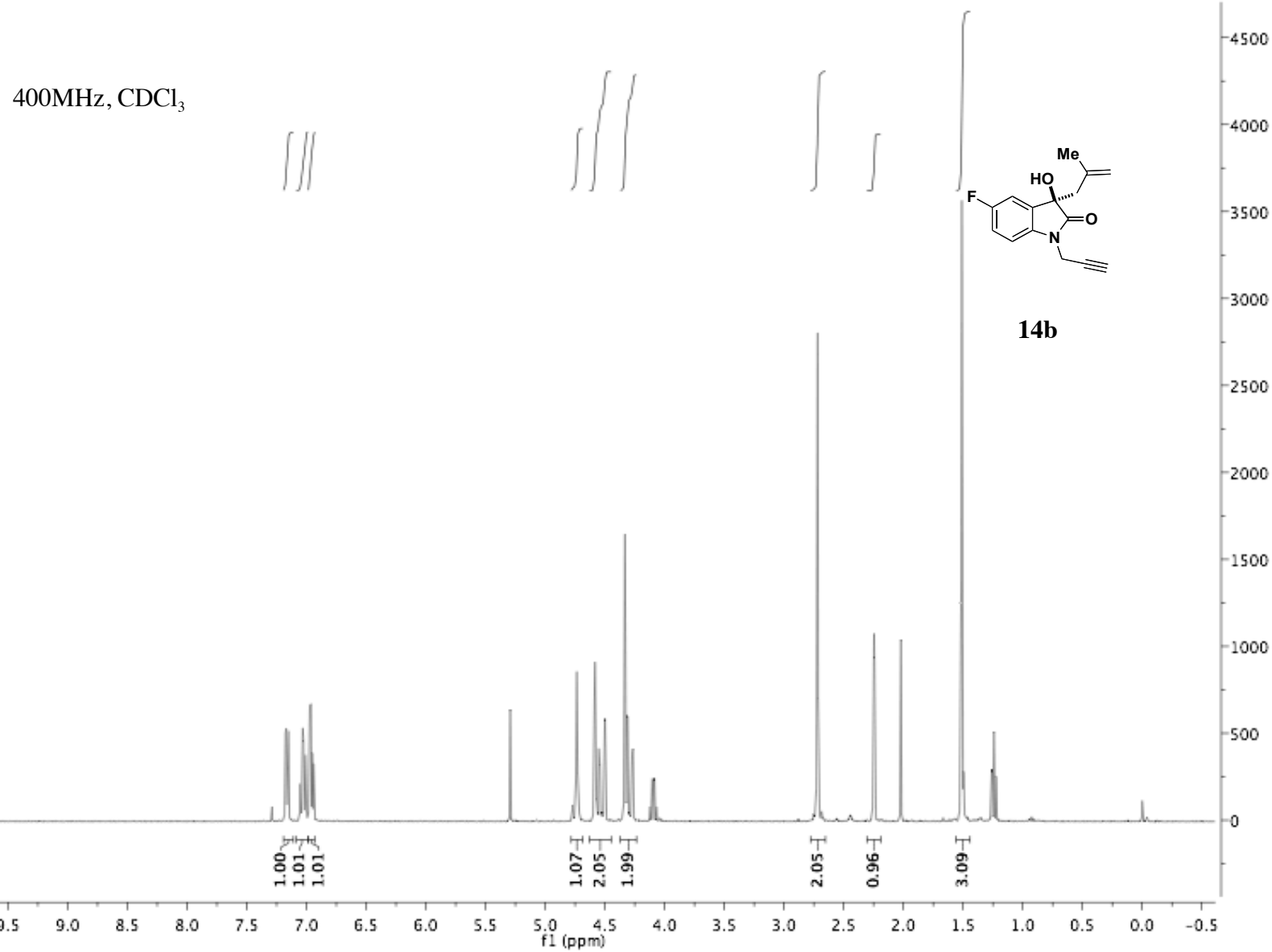
13b

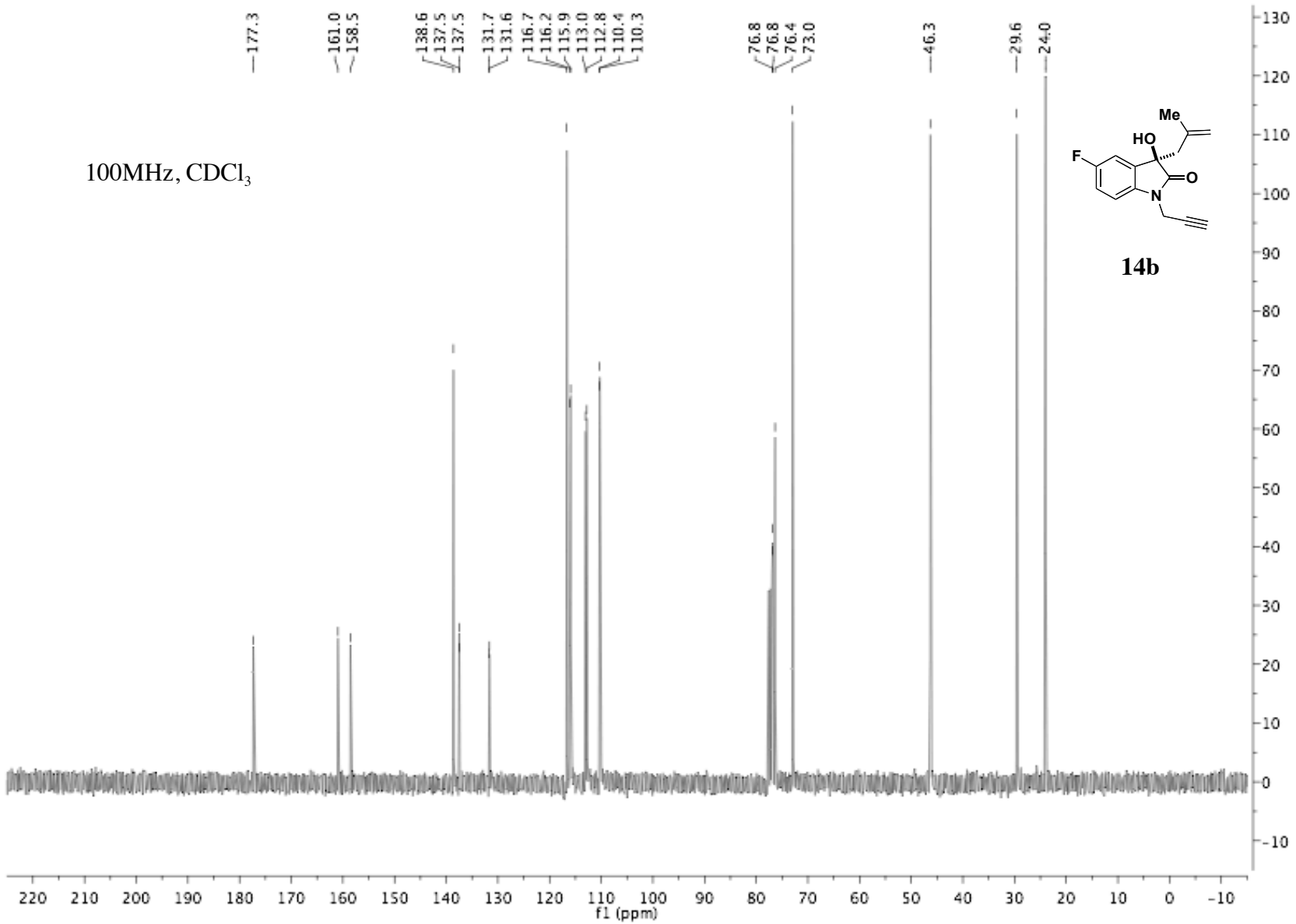
300MHz, $CDCl_3$



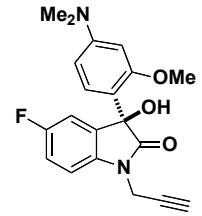
13b

400MHz, $CDCl_3$



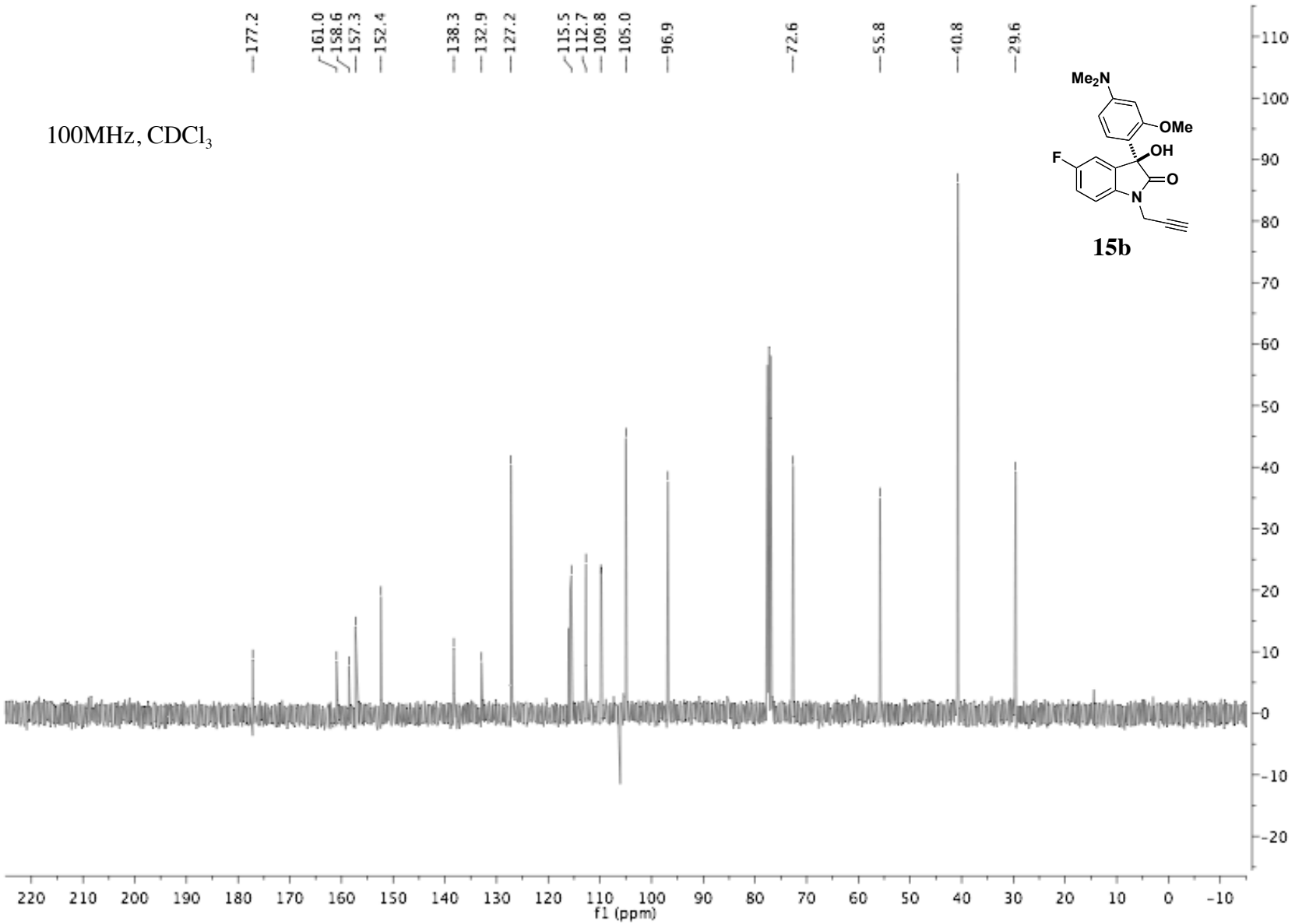

177.3
161.0
158.5
138.6
137.5
137.5
131.7
131.6
116.7
116.2
115.9
113.0
112.8
110.4
110.3
76.8
76.8
76.4
73.0
46.3
29.6
24.0
100MHz, CDCl3
Me
HO
F
O
N
14b
f1 (ppm)

400MHz, $CDCl_3$

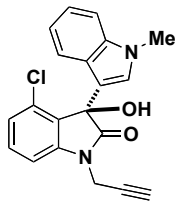


15b

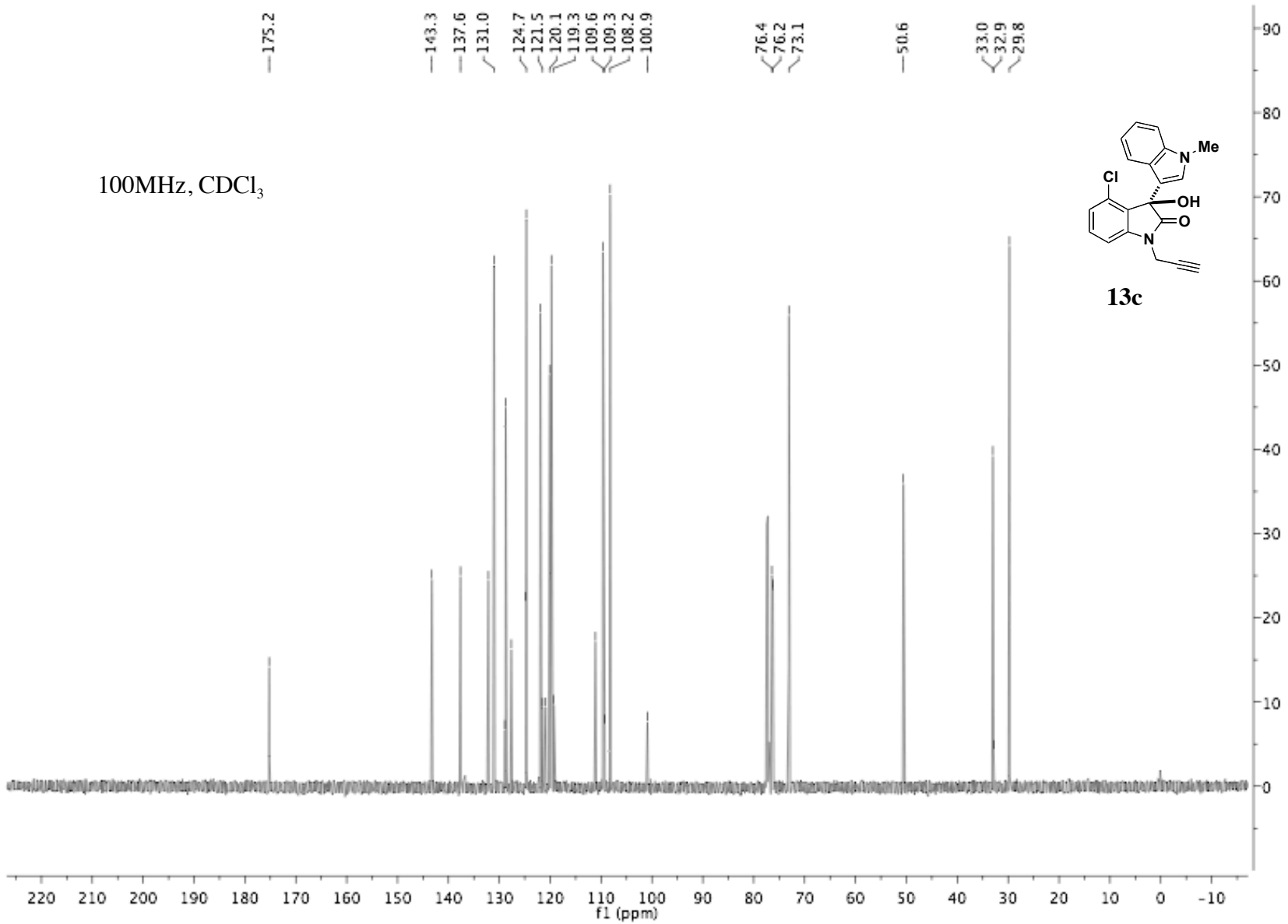
100MHz, $CDCl_3$



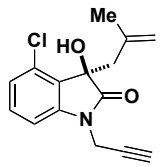
100MHz, $CDCl_3$



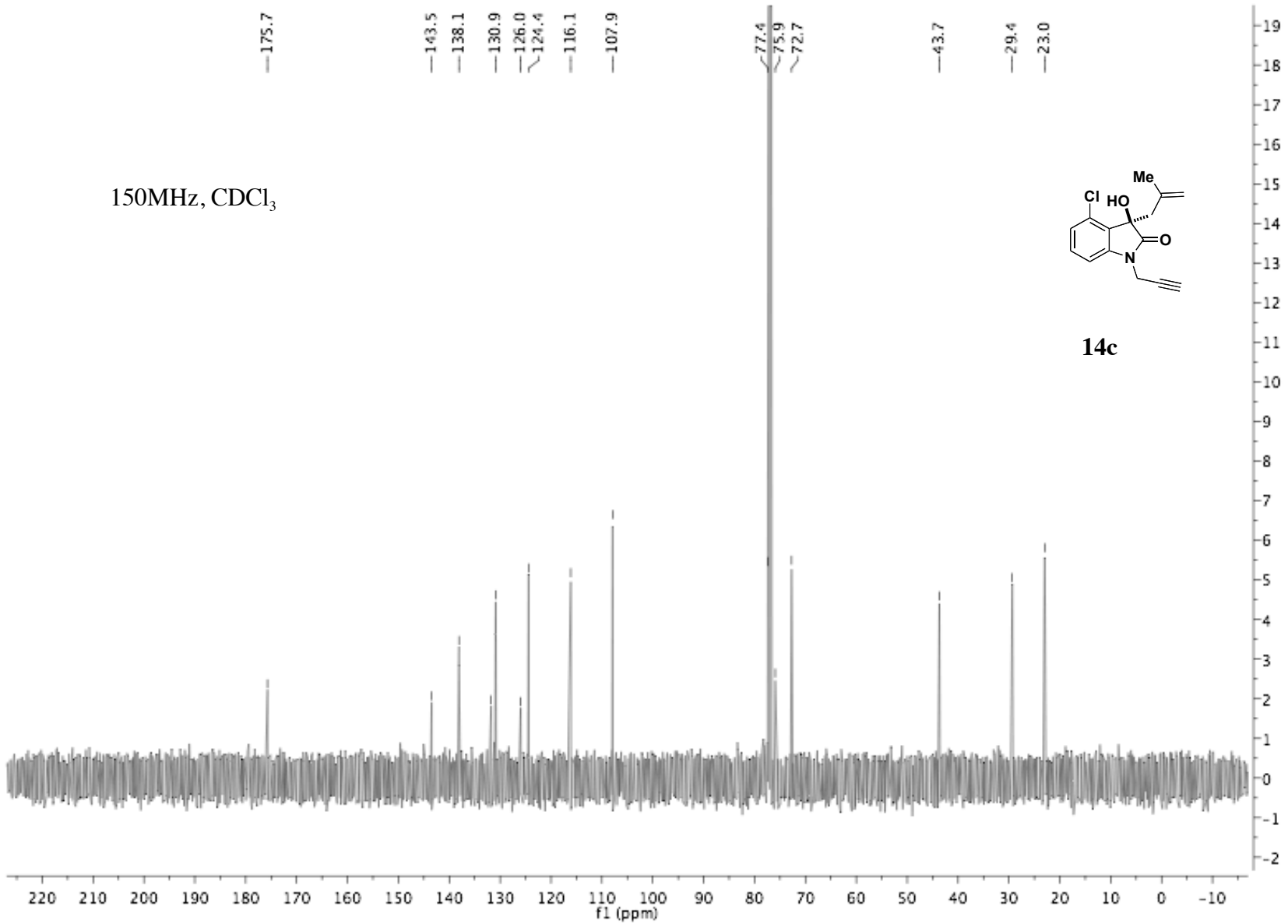
13c


175.2
143.3
137.6
131.0
124.7
121.5
120.1
119.3
109.6
109.3
108.2
100.9
76.4
76.2
73.1
50.6
33.0
32.9
29.8
100MHz, CDCl3
Me
N
Cl
OH
O
N
13c
f1 (ppm)

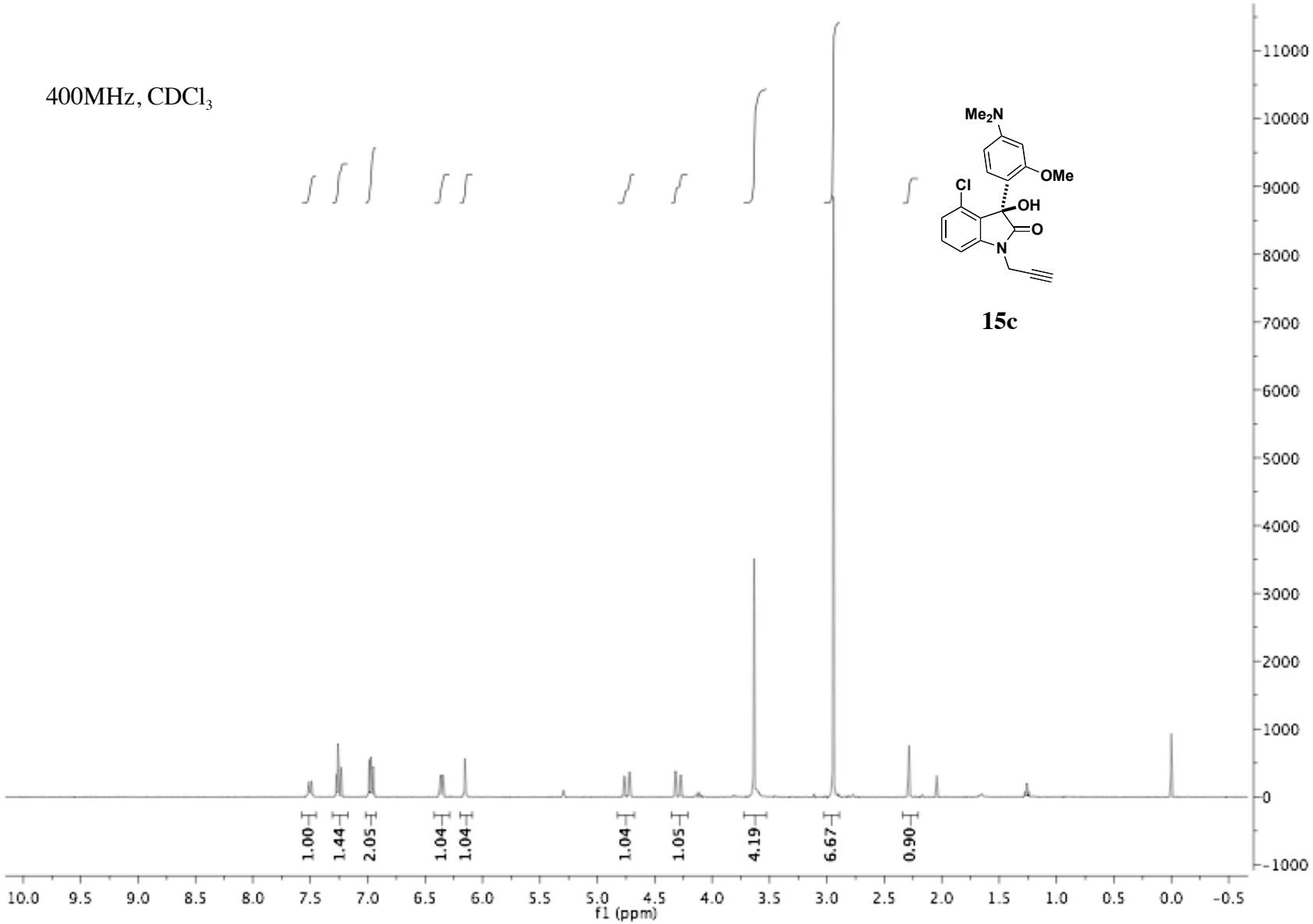
600MHz, $CDCl_3$



14c

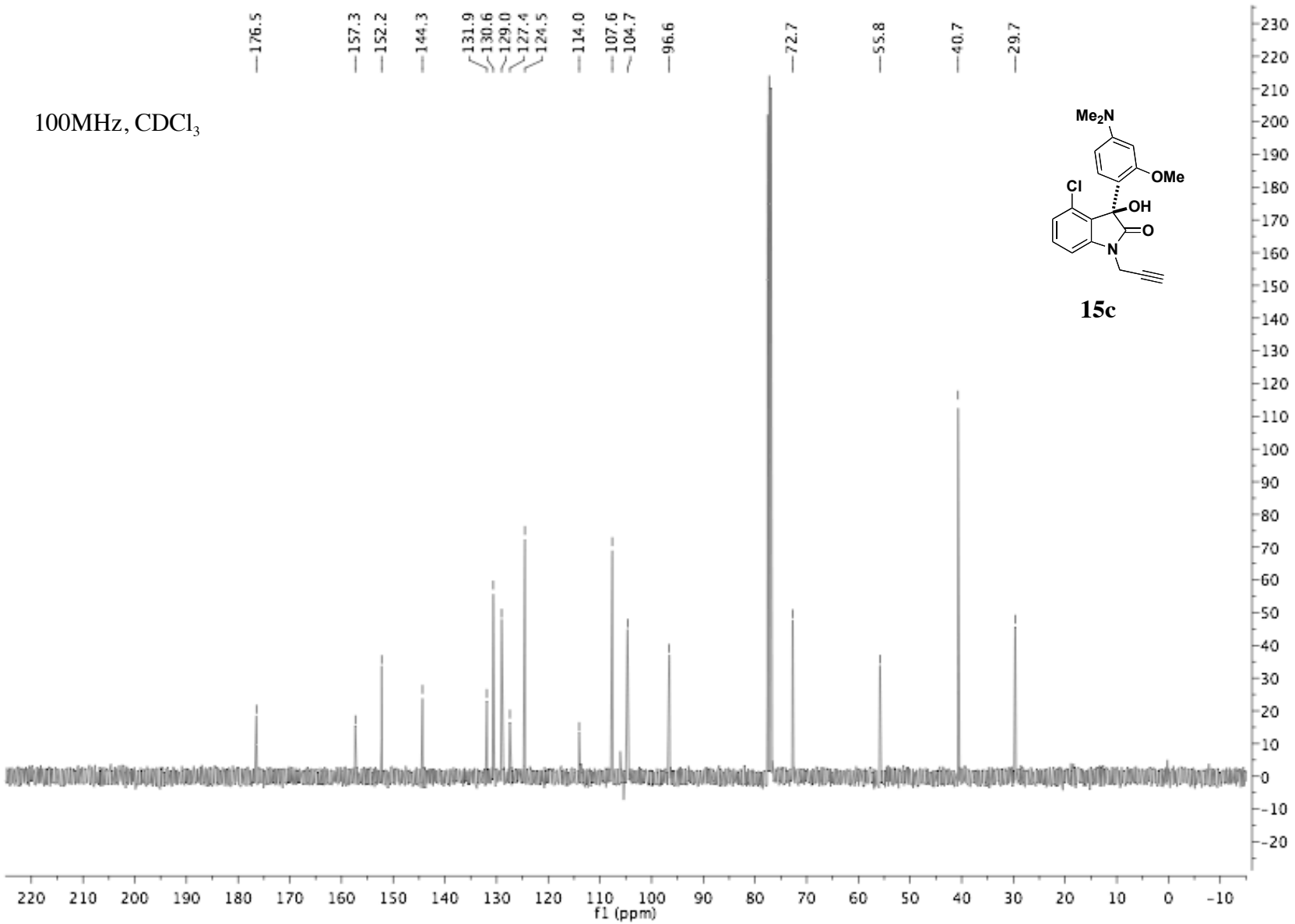

175.7
143.5
138.1
130.9
126.0
124.4
116.1
107.9
77.4
75.9
72.7
43.7
29.4
23.0
150MHz, CDCl3
Cl
HO
Me
O
N
14c
f1 (ppm)

400MHz, $CDCl_3$



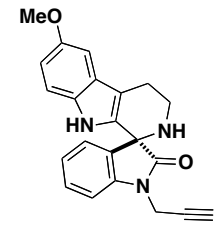
15c

100MHz, $CDCl_3$



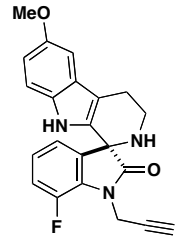
15c

400MHz, $(CD_3)_2SO$

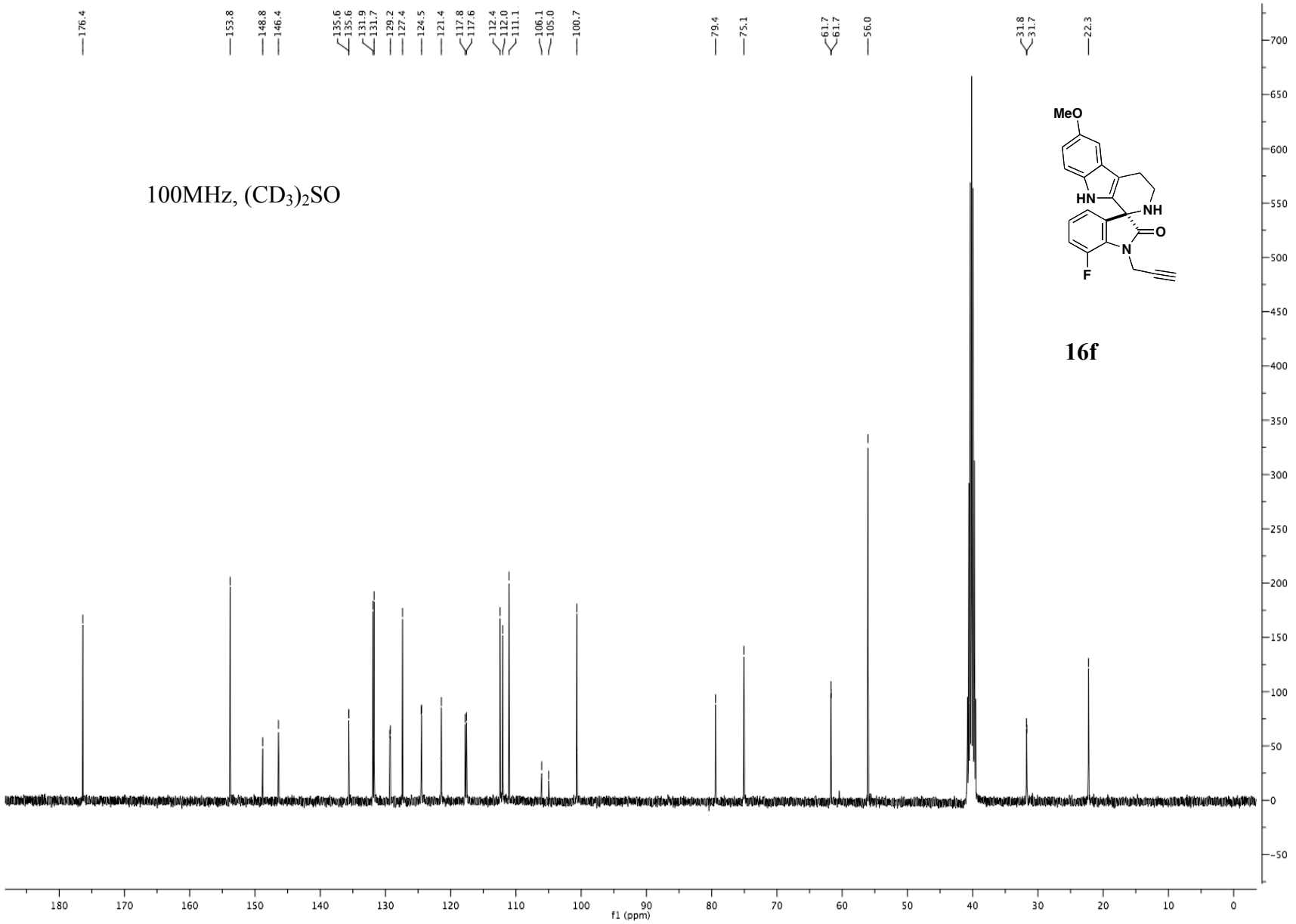


16a

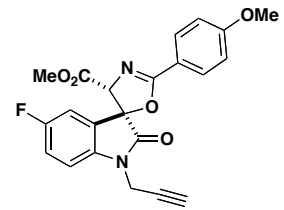
400MHz, $(CD_3)_2SO$



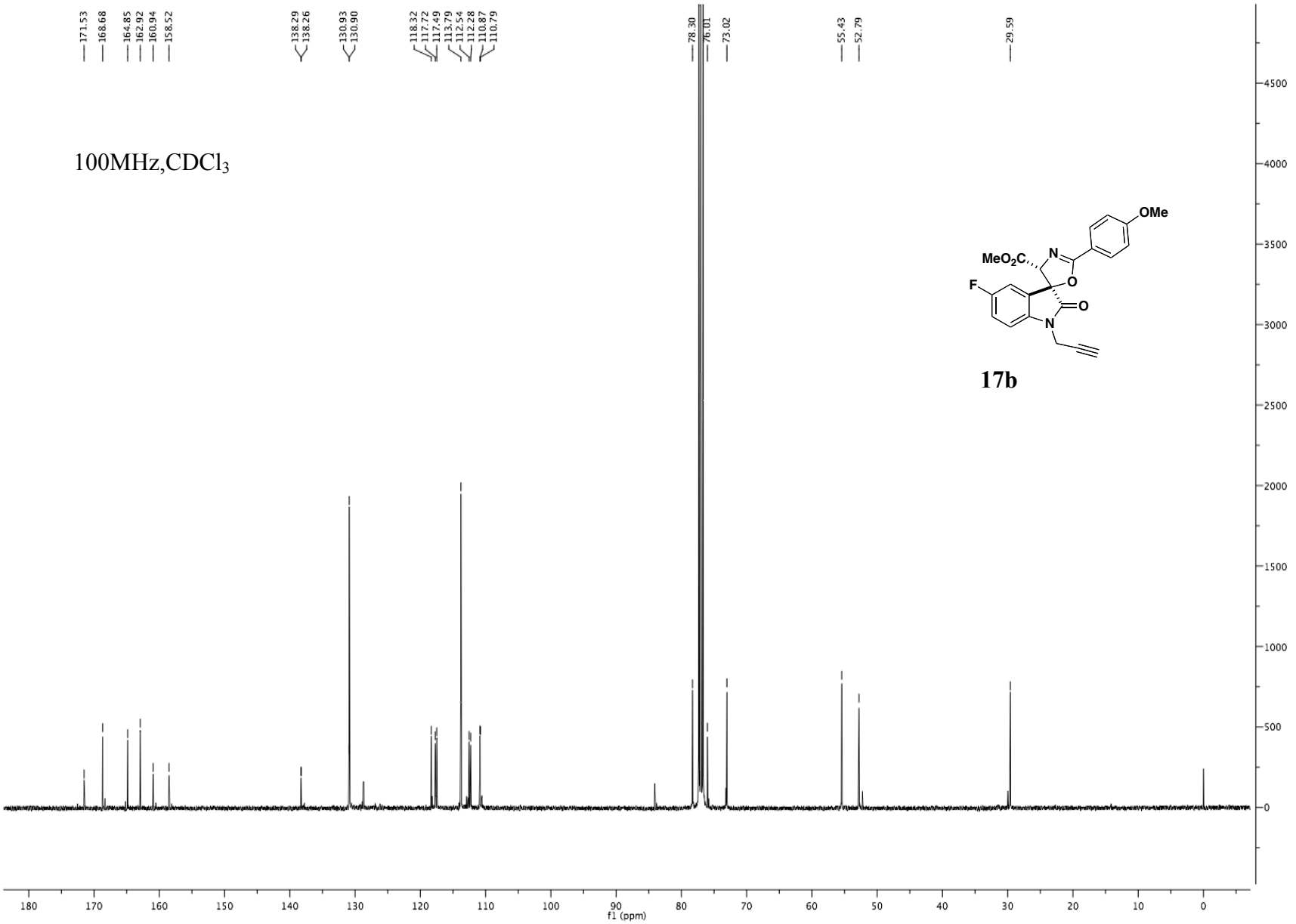
16f


176.4
153.8
148.8
146.4
135.6
135.6
131.9
131.7
129.2
127.4
124.5
121.4
117.8
117.6
112.4
112.0
111.1
106.1
105.0
100.7
79.4
75.1
61.7
61.7
56.0
31.8
31.7
22.3
100MHz, (CD3)2SO
MeO
HN
NH
O
N
F
16f
f1 (ppm)

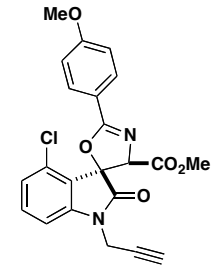
400MHz,$CDCl_3$



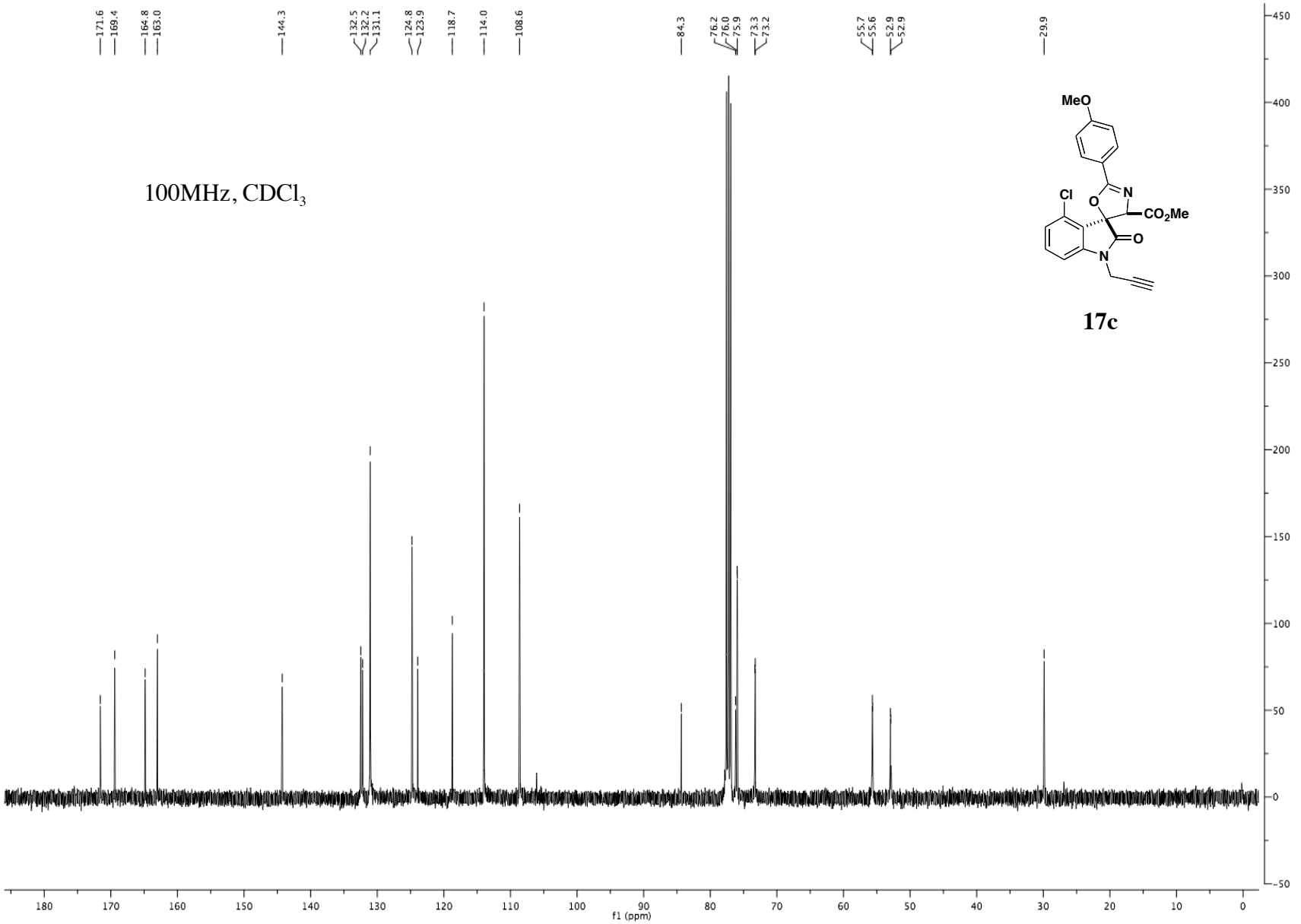
17b


171.53
168.68
164.85
162.92
160.94
158.52
138.29
138.26
130.93
130.90
118.32
117.72
117.49
113.79
112.54
112.28
110.87
110.79
78.30
76.01
73.02
55.43
52.79
29.59
100MHz,CDCl3
OMe
MeO2C
N
O
F
O
N
17b
4500
4000
3500
3000
2500
2000
1500
1000
500
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

400MHz, $CDCl_3$

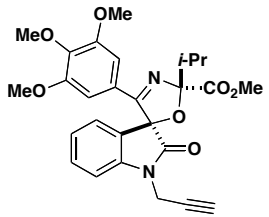


17c

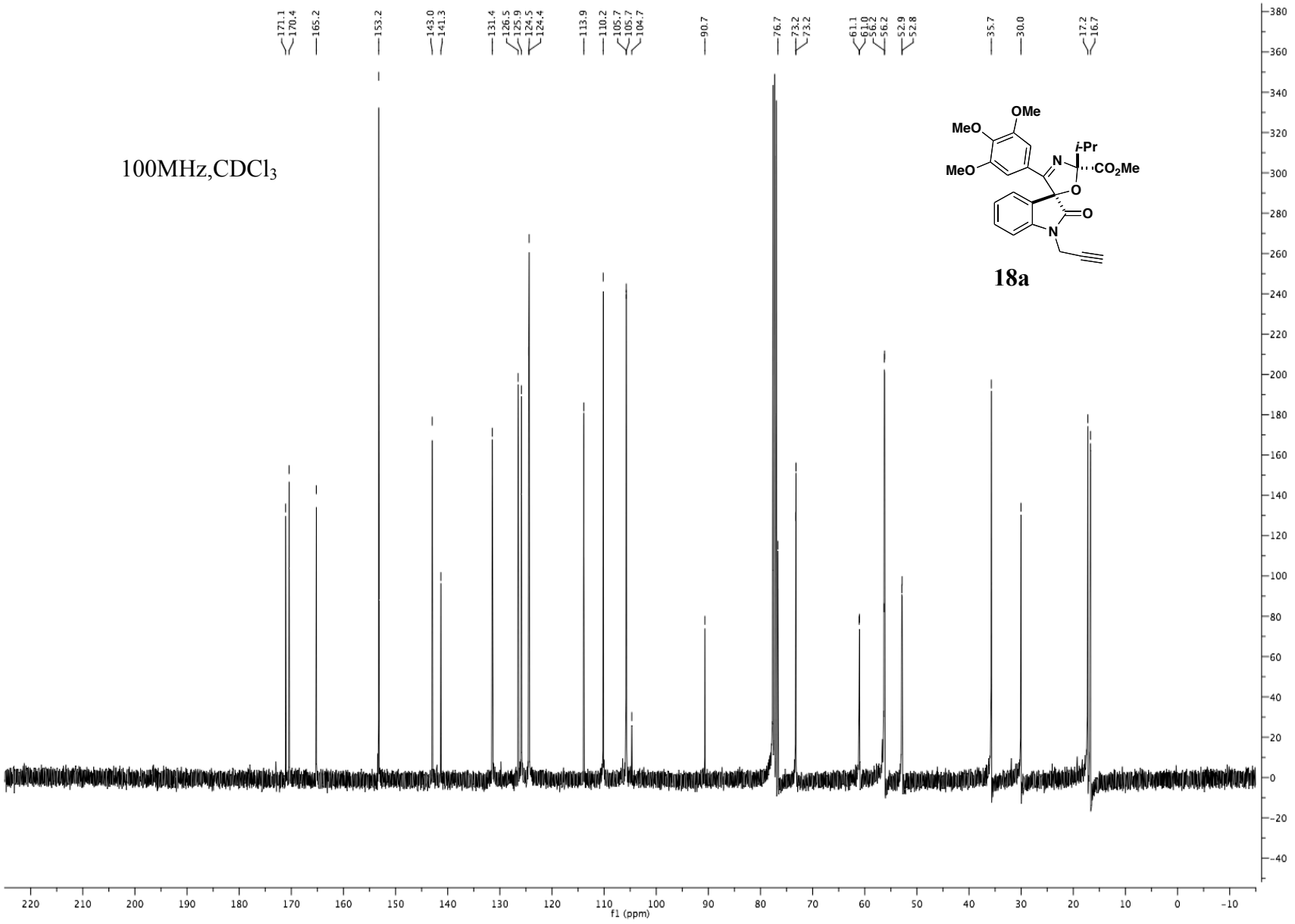

171.6
169.4
164.8
163.0
144.3
132.5
132.2
131.1
124.8
123.9
118.7
114.0
108.6
84.3
76.2
76.0
75.9
73.3
73.2
55.7
55.6
52.9
52.9
29.9
100MHz, CDCl3
MeO
Cl
O
N
CO2Me
O
N
f1 (ppm)

17c

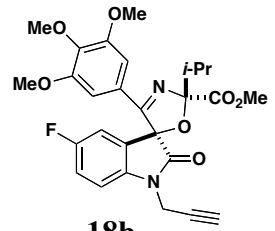
400MHz,$CDCl_3$



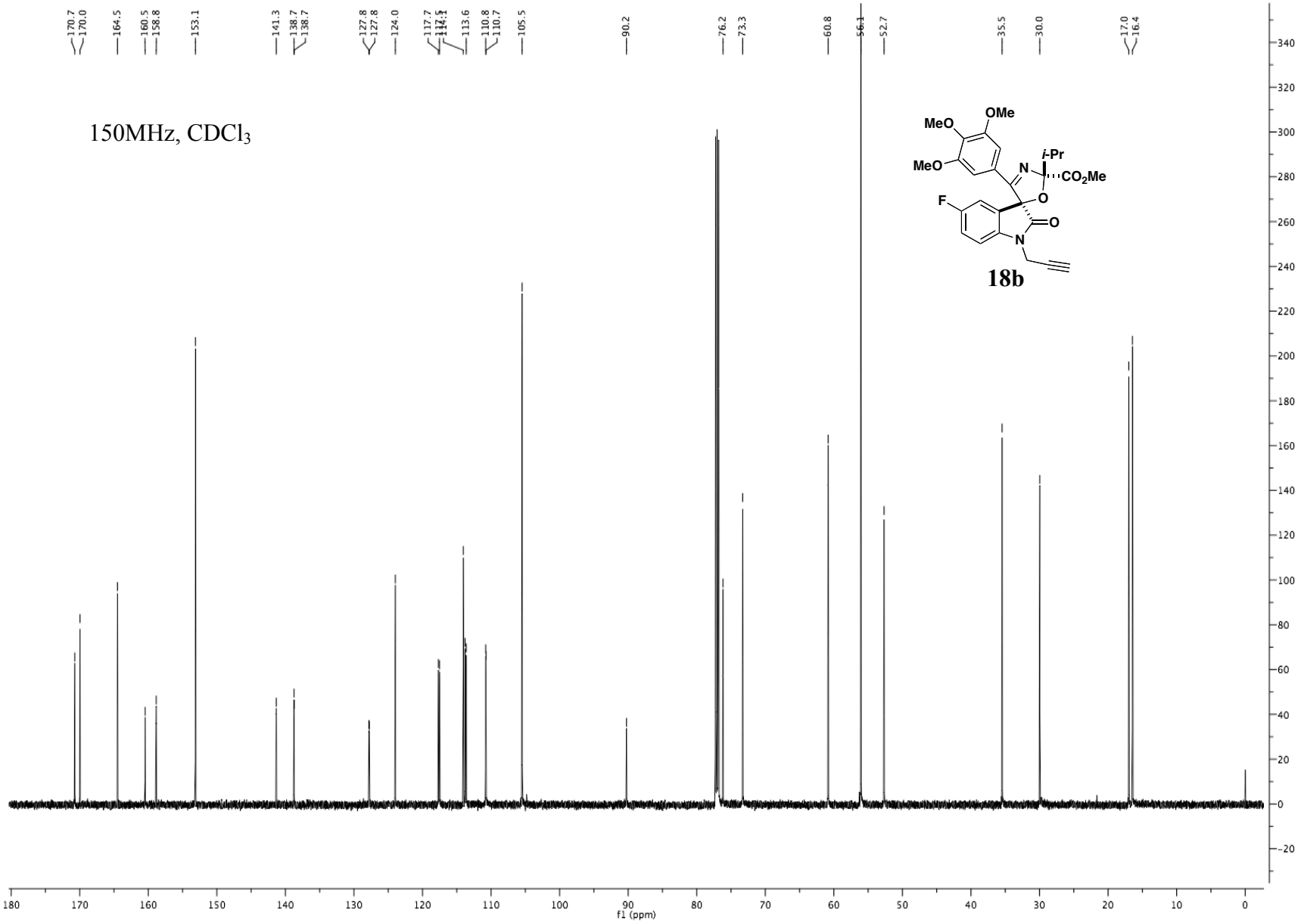
18a

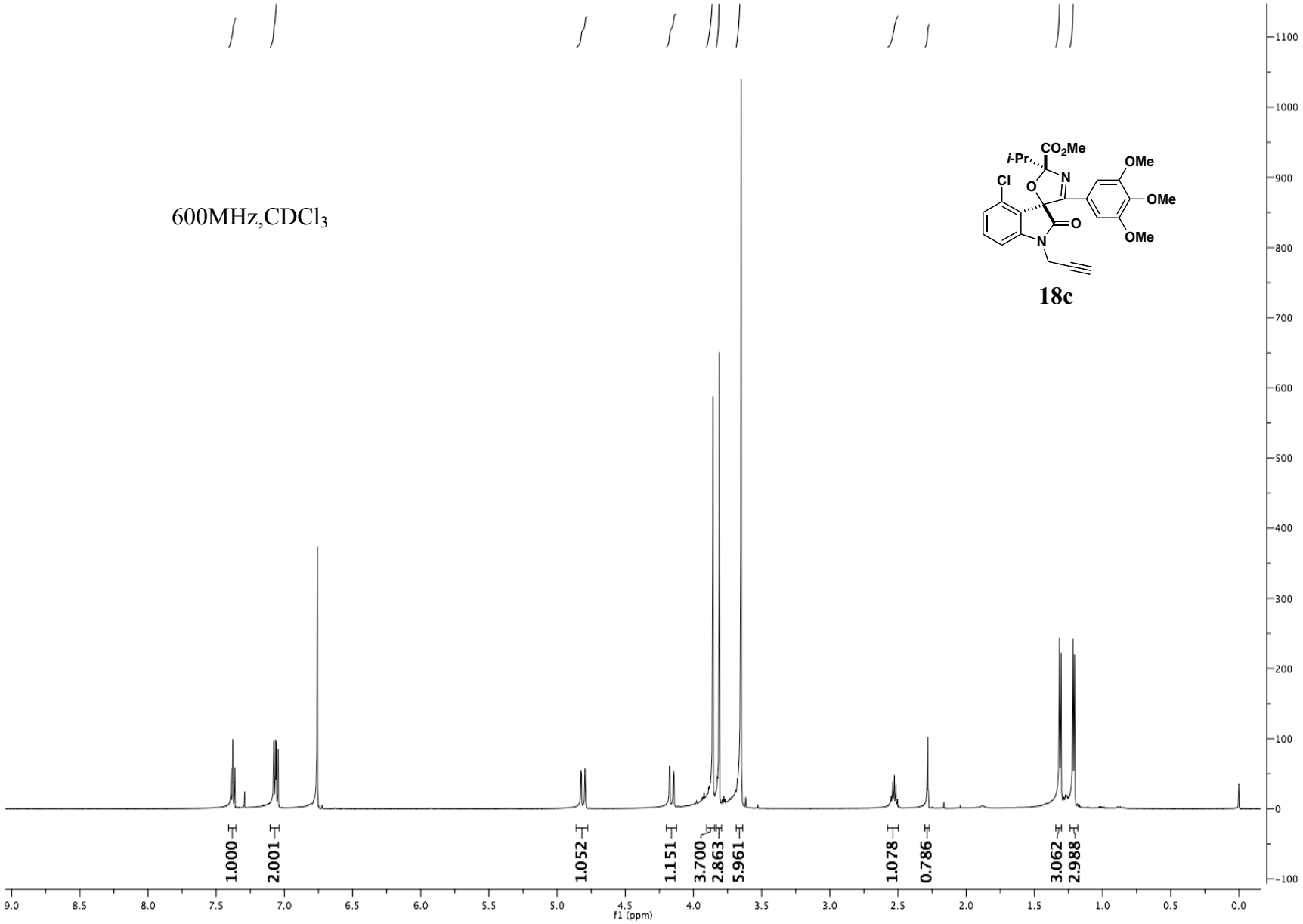

100MHz,CDCl3
171.1
170.4
165.2
153.2
143.0
141.3
131.4
126.5
125.9
124.5
124.4
113.9
110.2
105.7
105.7
104.7
90.7
76.7
73.2
73.2
61.1
61.0
56.2
56.2
52.9
52.8
35.7
30.0
17.2
16.7
OMe
MeO
MeO
i-Pr
N
CO2Me
O
O
N
18a
f1 (ppm)

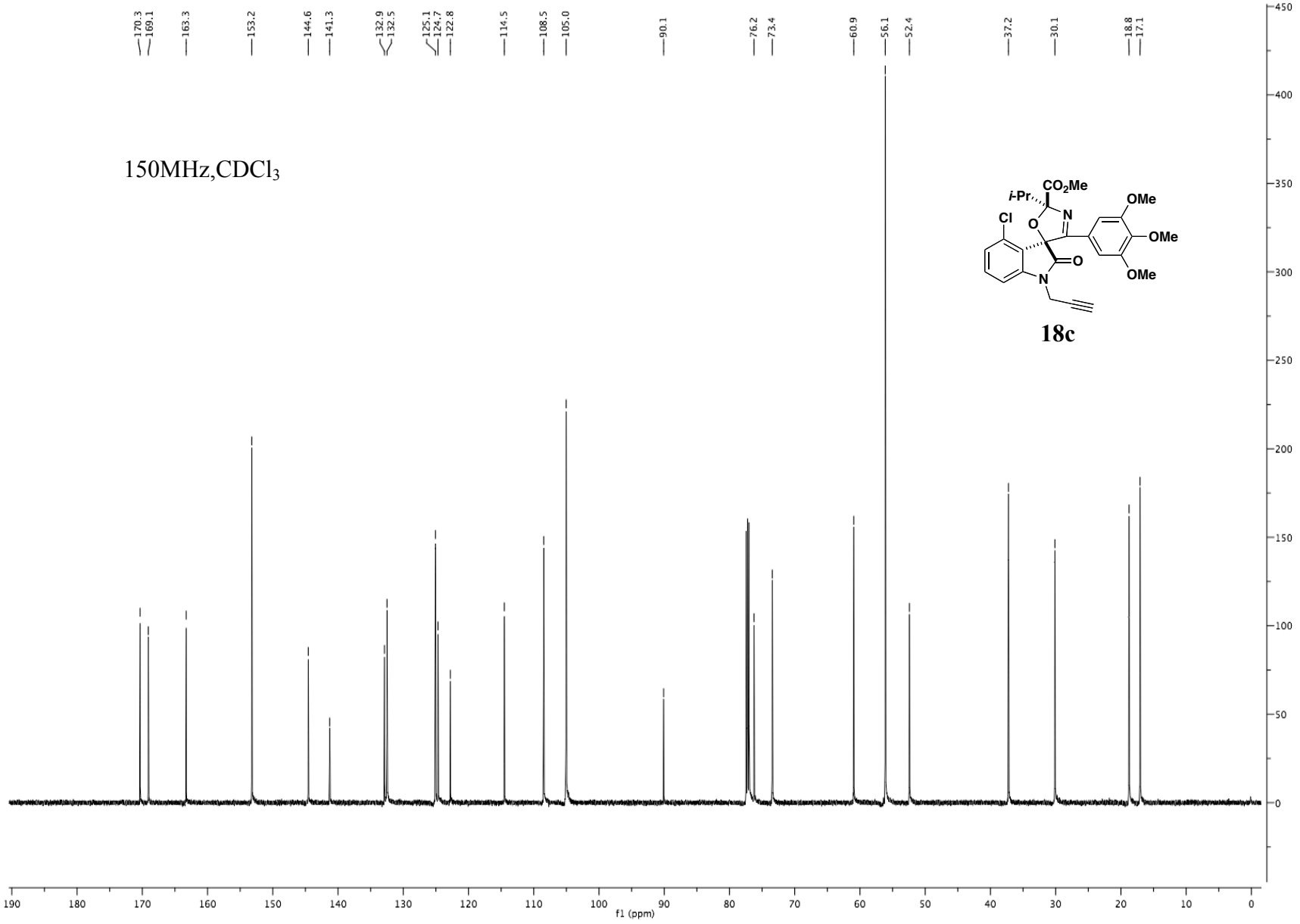
600MHz, $CDCl_3$



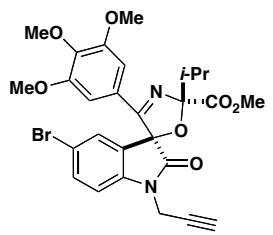
18b


170.7
170.0
164.5
160.5
158.8
153.1
141.3
138.7
138.7
127.8
127.8
124.0
117.7
113.6
110.8
110.7
105.5
90.2
76.2
73.3
60.8
56.1
52.7
35.5
30.0
17.0
16.4
150MHz, CDCl3
MeO
OMe
MeO
i-Pr
N
CO2Me
O
F
O
N
18b
f1 (ppm)

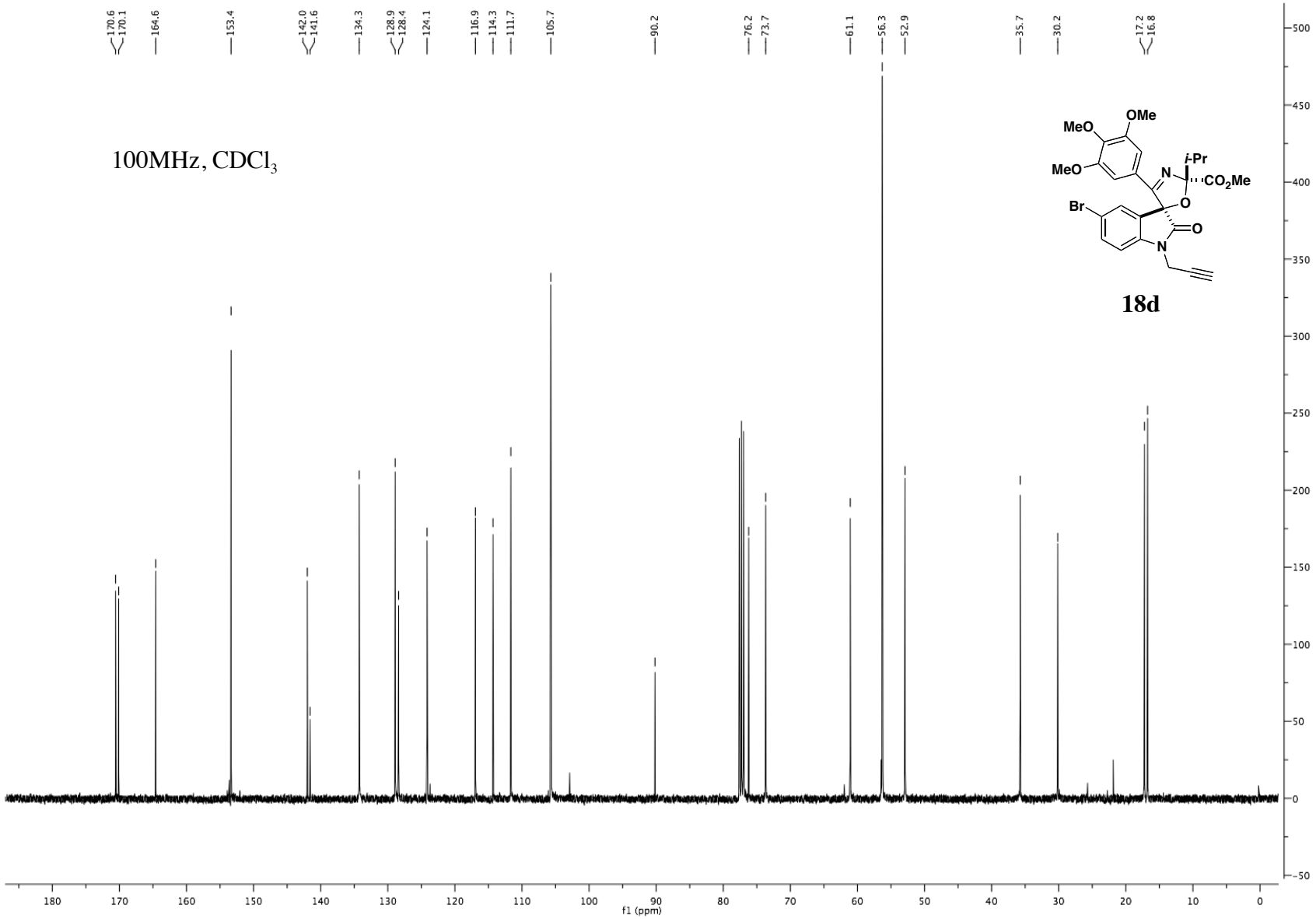

600MHz,CDCl3
CO2Me
i-Pr
Cl
O
N
OMe
OMe
OMe
O
N
18c
1.000
2.001
1.052
1.151
3.700
2.863
5.961
1.078
0.786
3.062
2.988
f1 (ppm)


170.3
169.1
163.3
153.2
144.6
141.3
132.9
132.5
125.1
124.7
122.8
114.5
108.5
105.0
90.1
76.2
73.4
60.9
56.1
52.4
37.2
30.1
18.8
17.1
150MHz,CDCl3
CO2Me
i-Pr
Cl
O
N
OMe
OMe
OMe
O
N
18c
f1 (ppm)

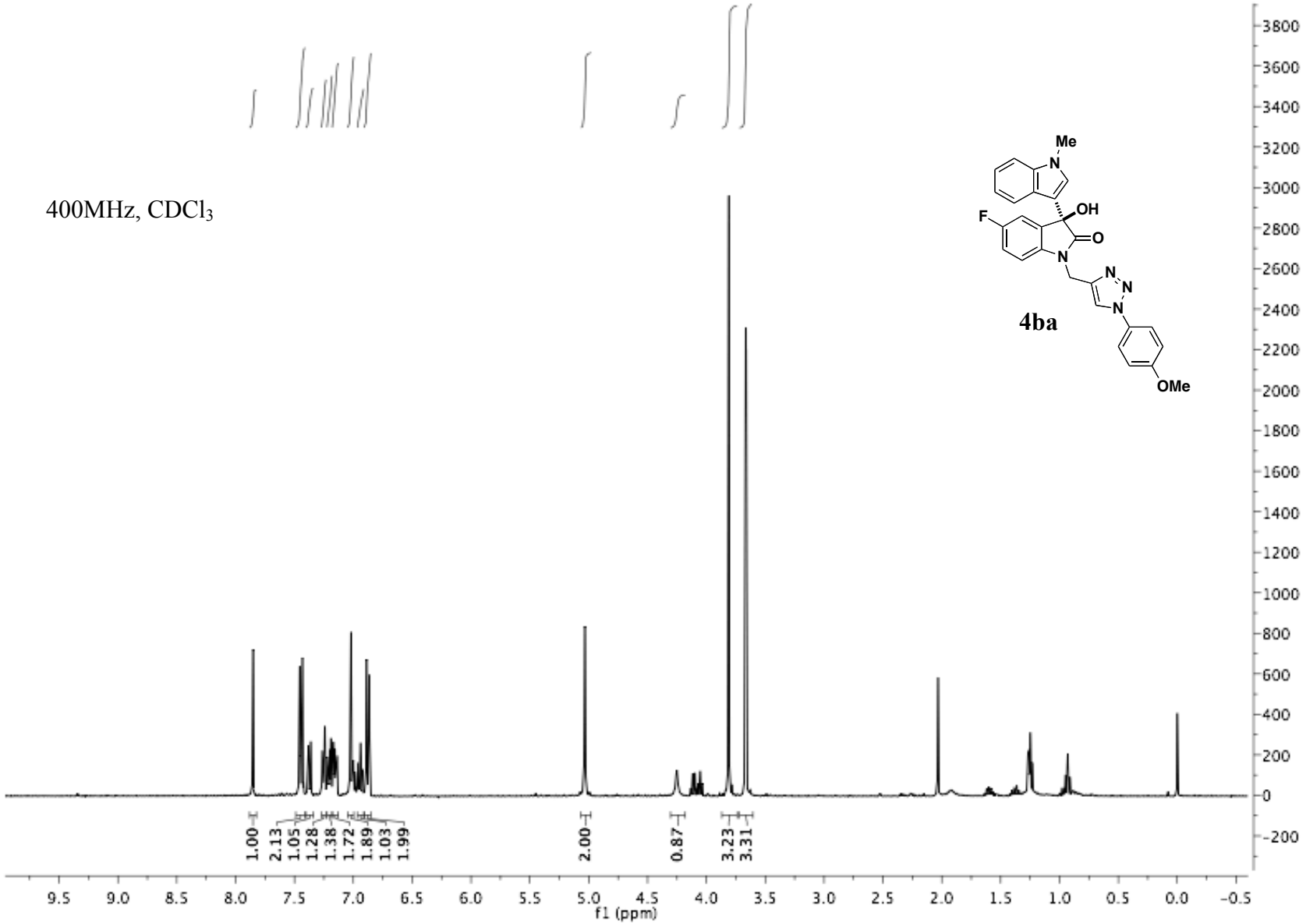
400MHz, $CDCl_3$



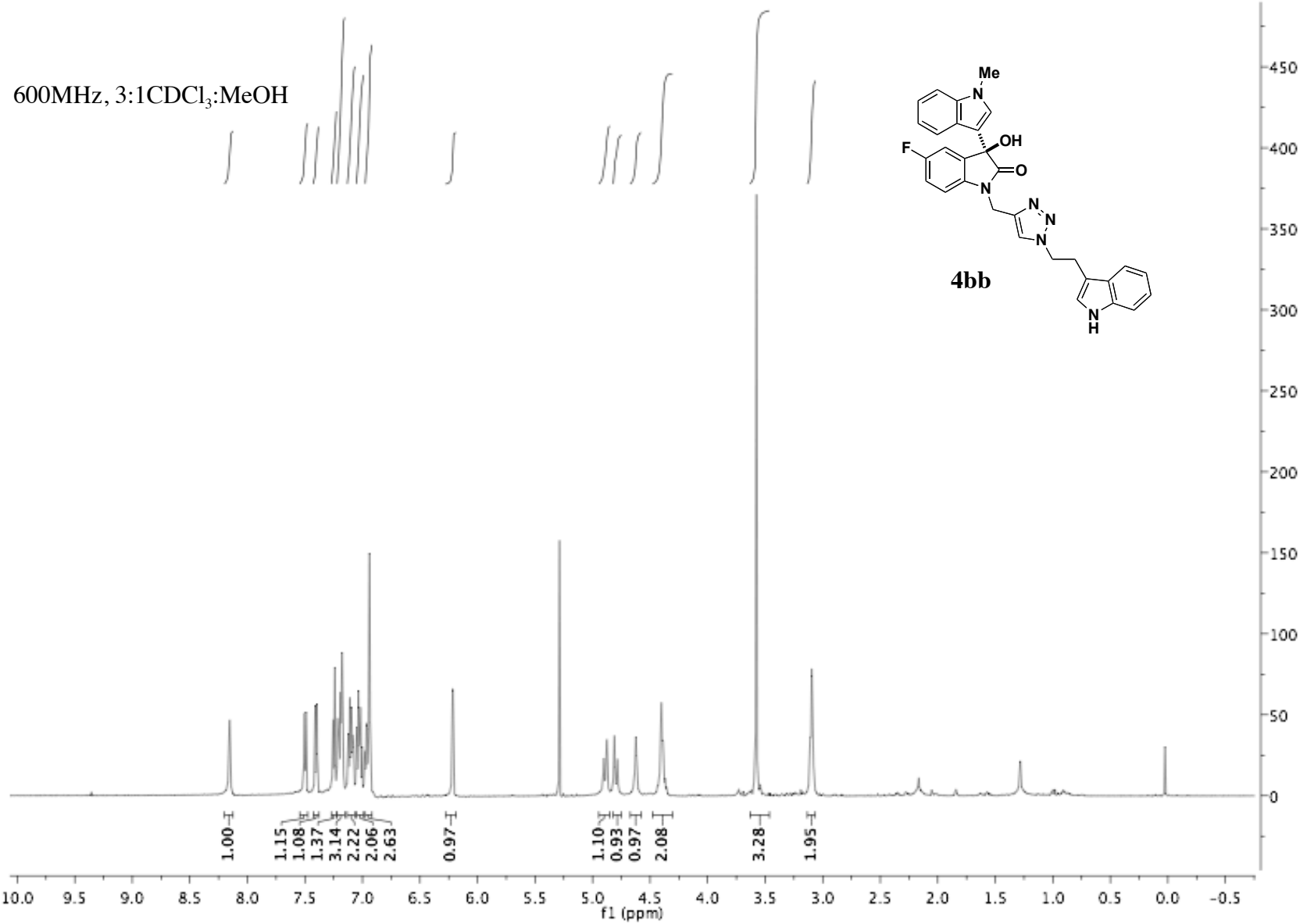
18d

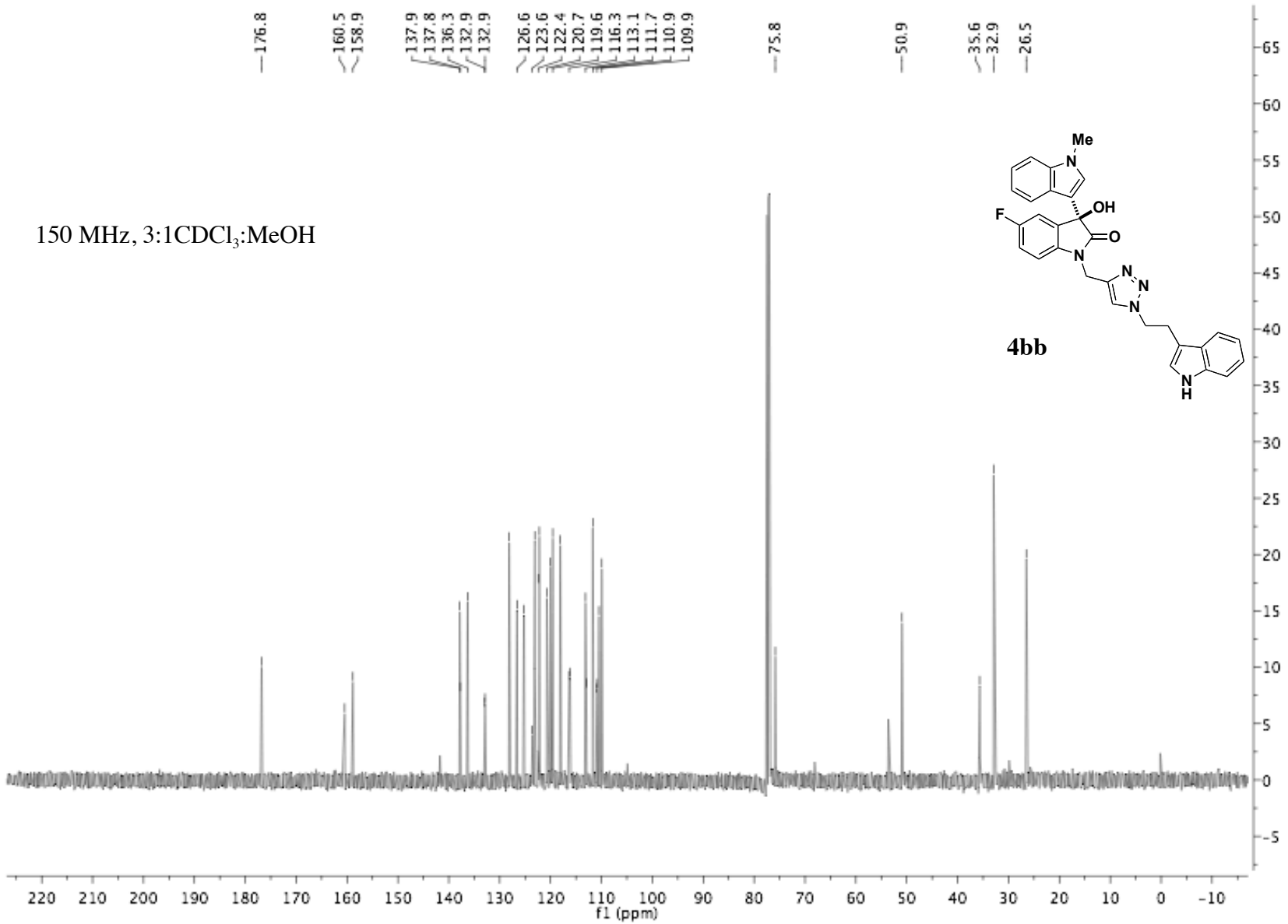

170.6
170.1
164.6
153.4
142.0
141.6
134.3
128.9
128.4
124.1
116.9
114.3
111.7
105.7
90.2
76.2
73.7
61.1
56.3
52.9
35.7
30.2
17.2
16.8
100MHz, CDCl3
MeO
OMe
MeO
i-Pr
CO2Me
Br
N
O
O
N
18d
f1 (ppm)

400MHz, $CDCl_3$

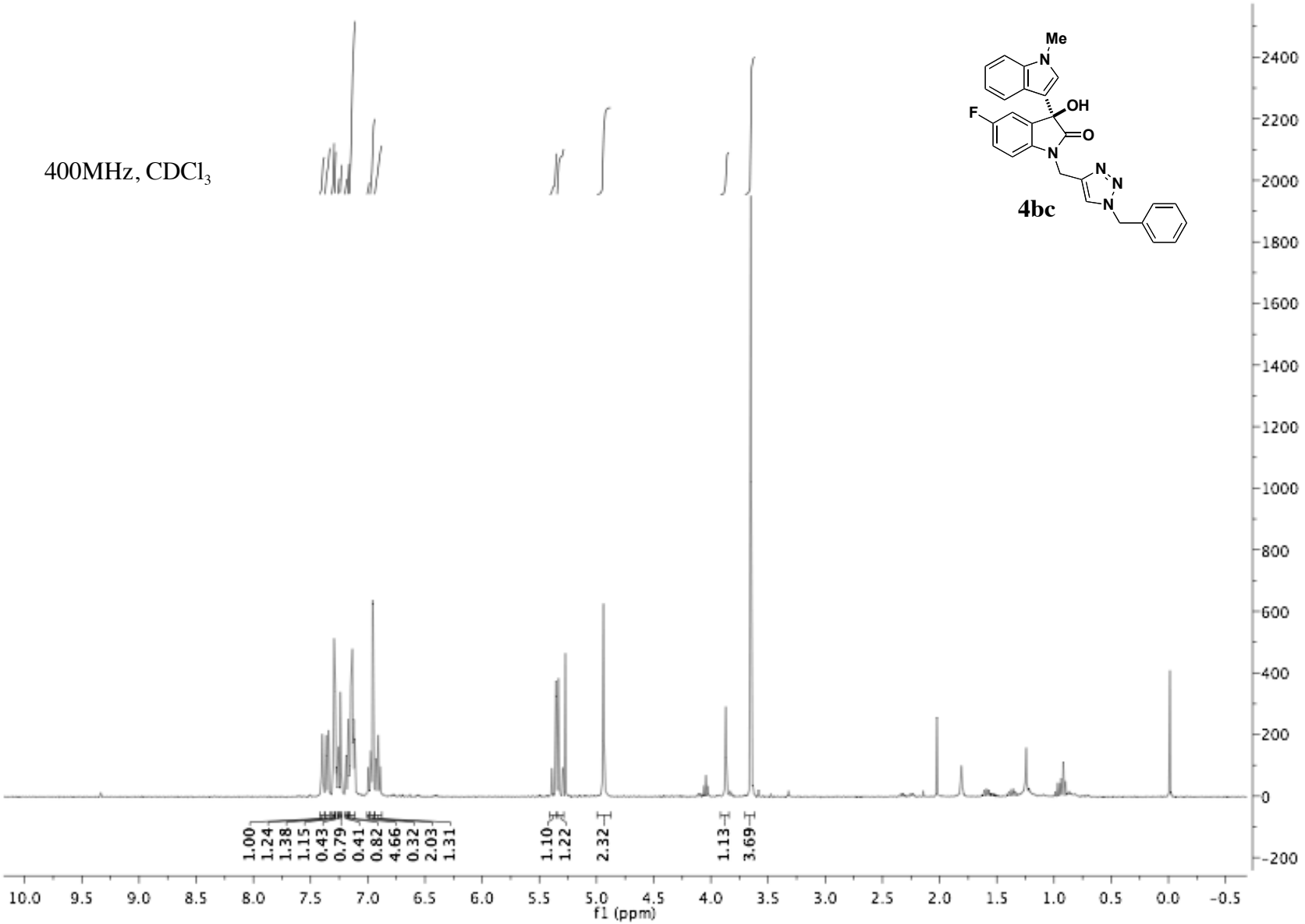


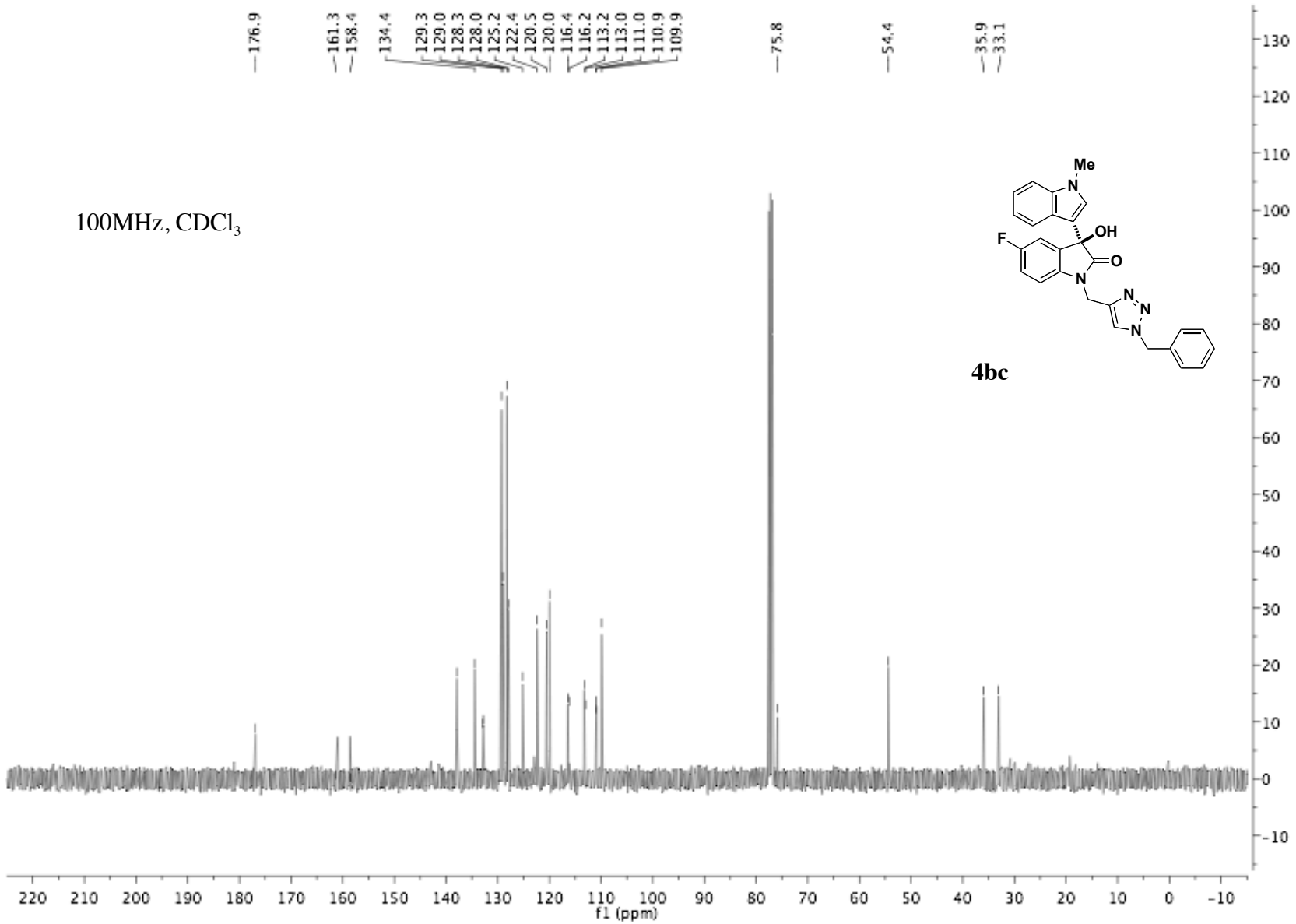
600MHz, 3:1$CDCl_3$:MeOH

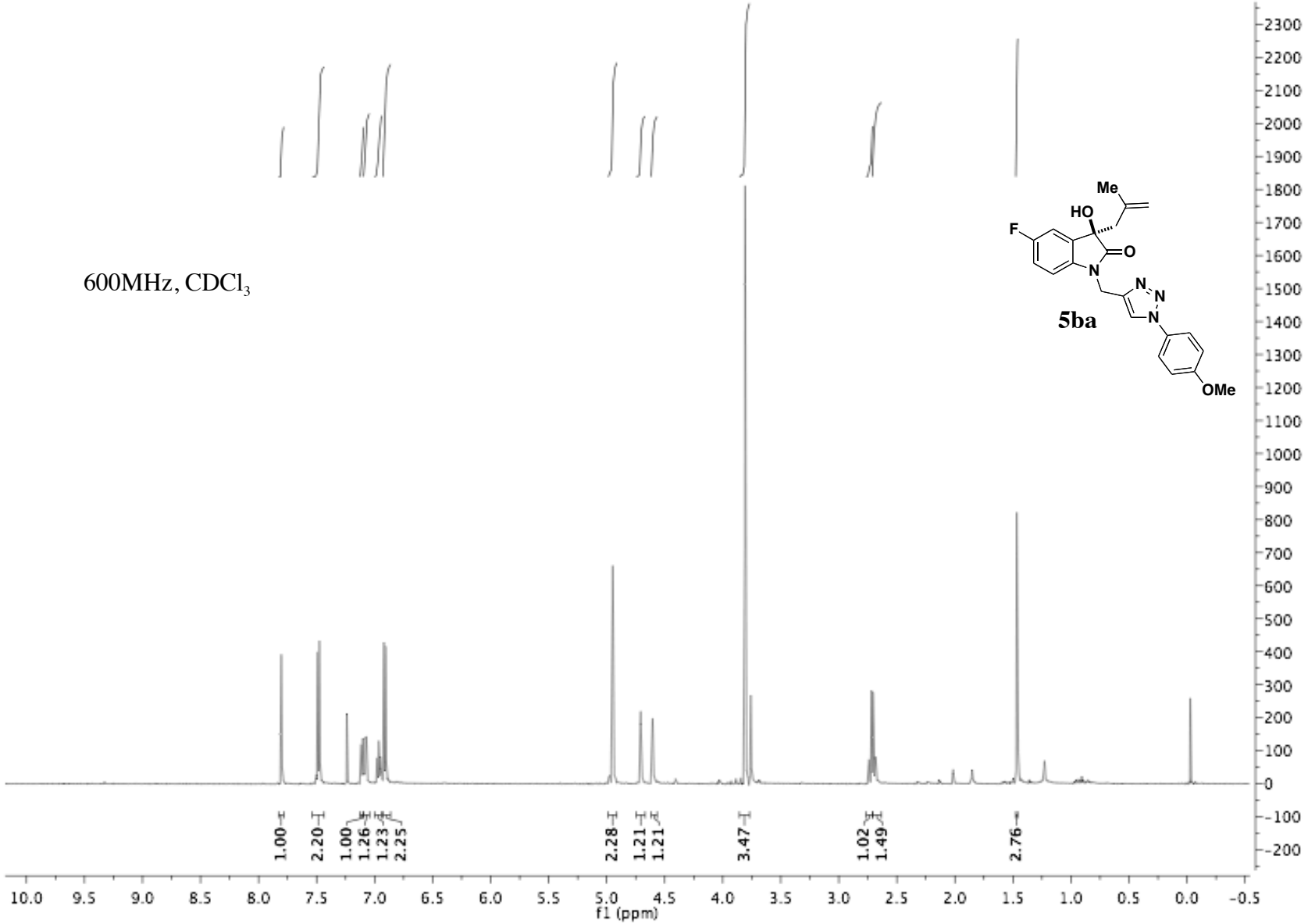



176.8
160.5
158.9
137.9
137.8
136.3
132.9
132.9
126.6
123.6
122.4
120.7
119.6
116.3
113.1
111.7
110.9
109.9
75.8
50.9
35.6
32.9
26.5
150 MHz, 3:1CDCl3:MeOH
Me
N
OH
F
O
N
N
N
N
H
4bb
f1 (ppm)

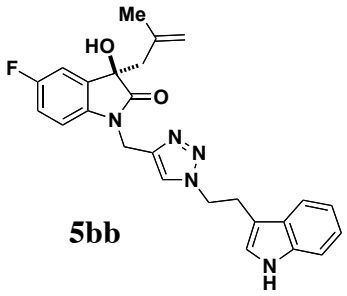
400MHz, $CDCl_3$




176.9
161.3
158.4
134.4
129.3
129.0
128.3
128.0
125.2
122.4
120.5
120.0
116.4
116.2
113.2
113.0
111.0
110.9
109.9
75.8
54.4
35.9
33.1
100MHz, CDCl3
Me
N
OH
F
O
N
N
N
N
4bc
f1 (ppm)

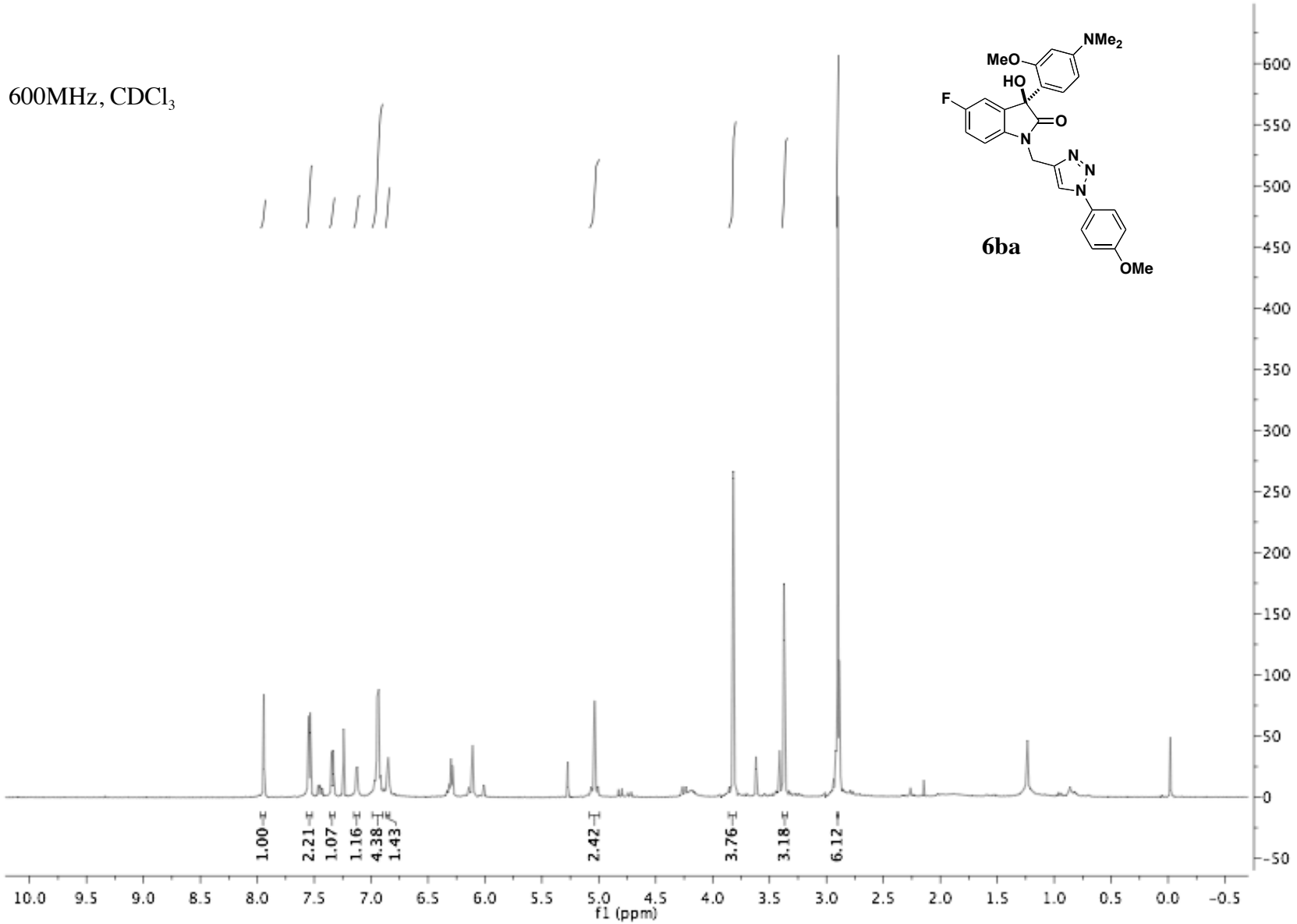

600MHz, $CDCl_3$
Me
HO
F
O
N
N
N
N
OMe
5ba
1.00
2.20
1.00
1.26
1.23
2.25
2.28
1.21
1.21
3.47
1.02
1.49
2.76
f1 (ppm)

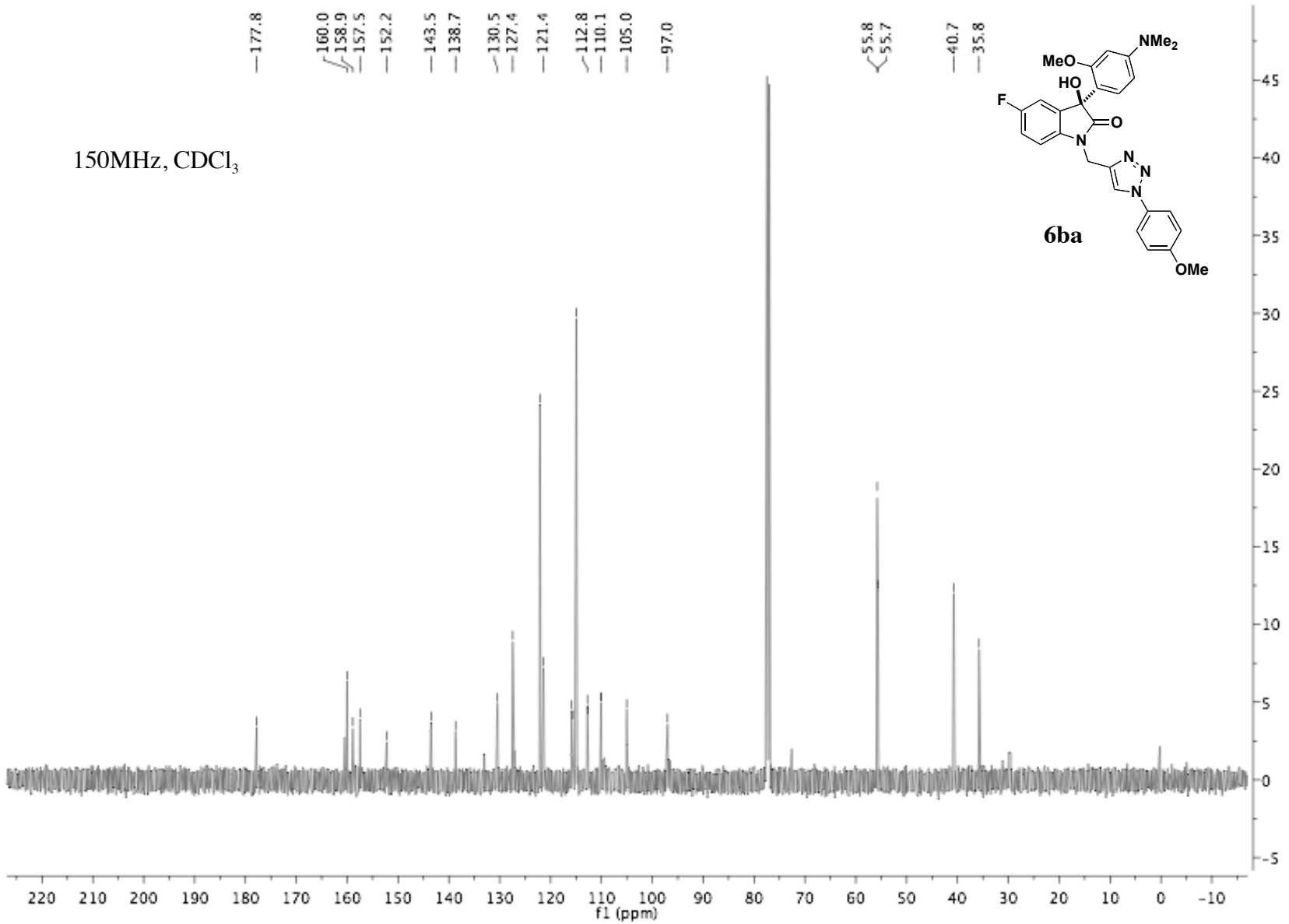
600MHz, $CDCl_3$



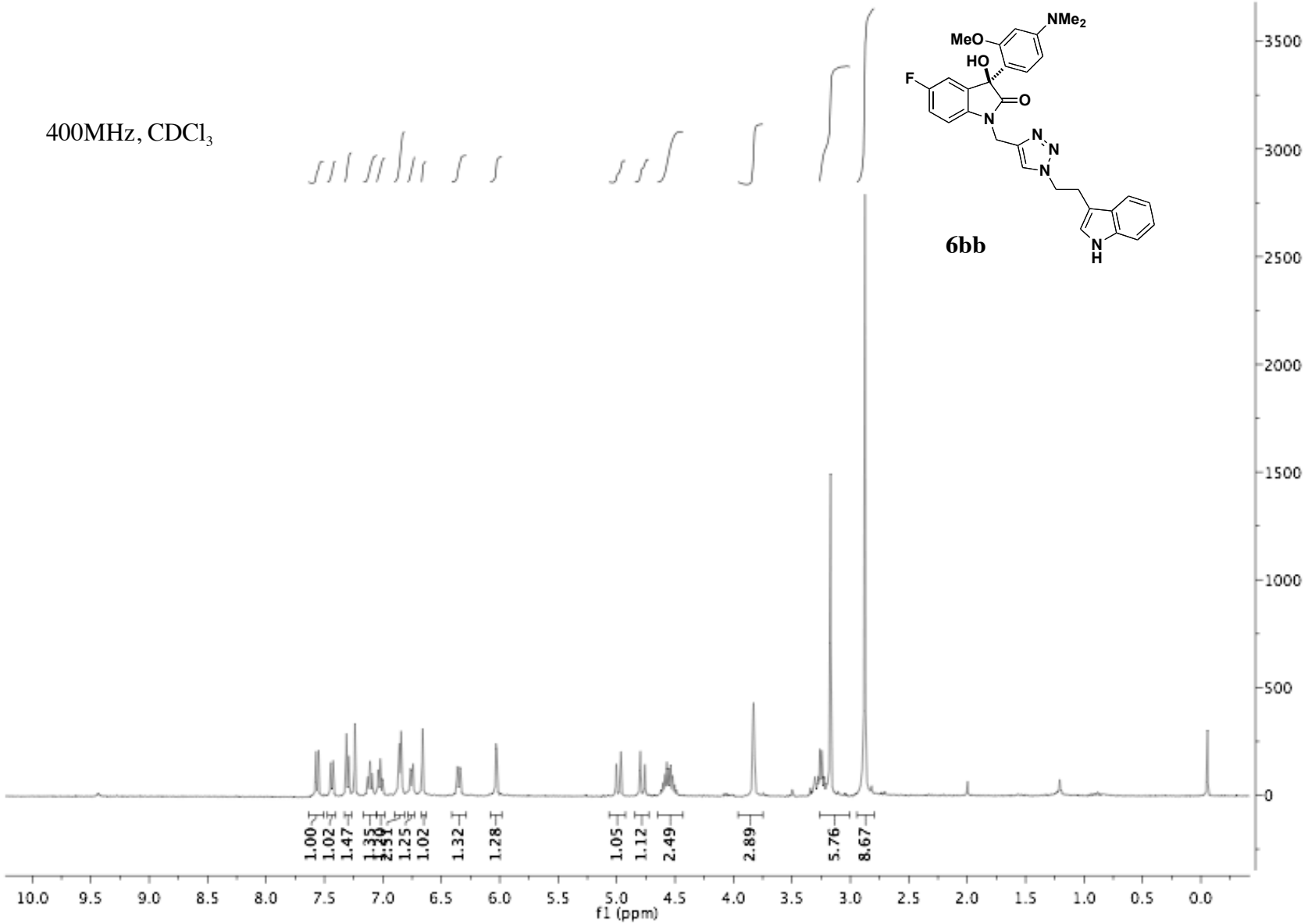
5bb

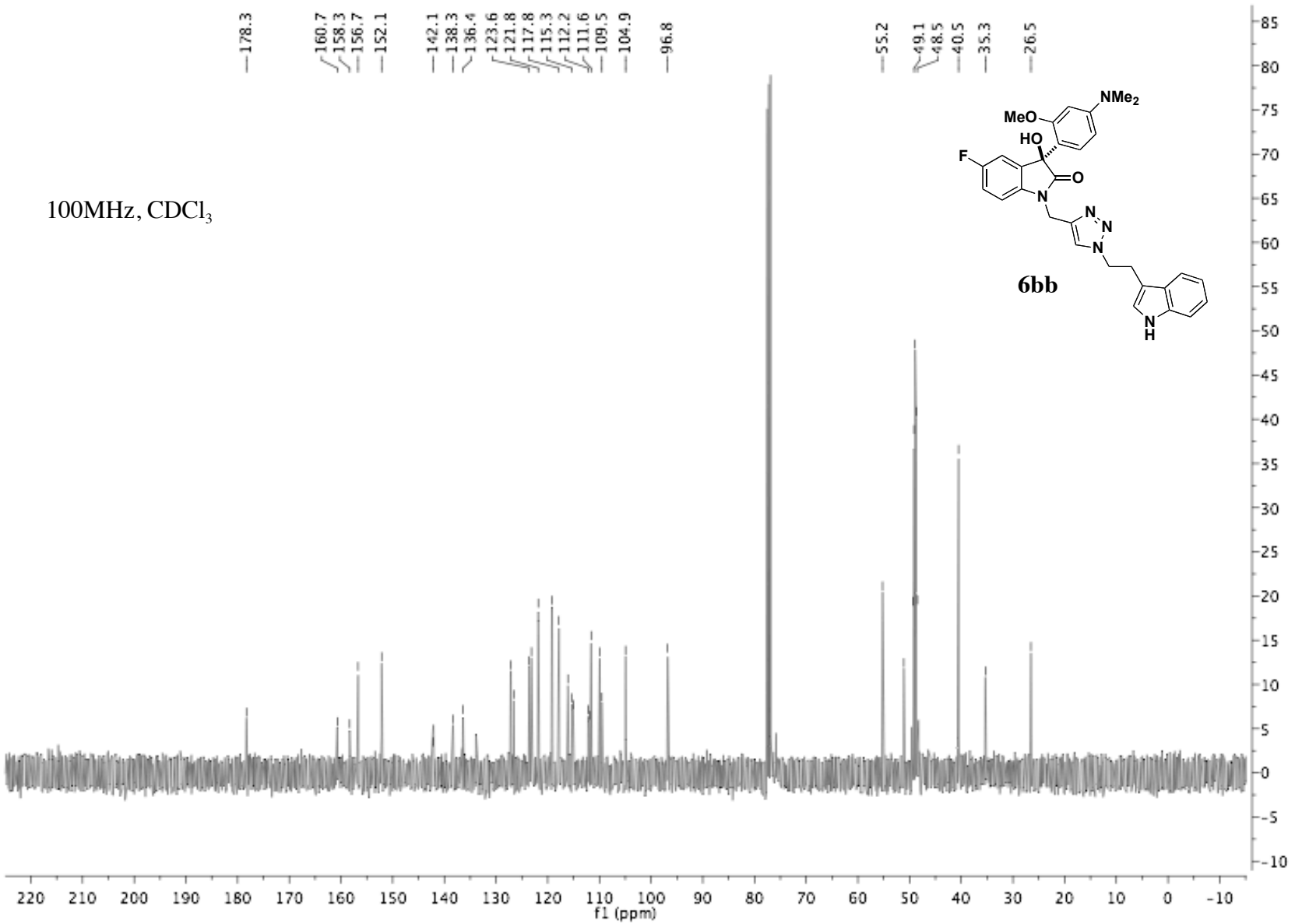
600MHz, $CDCl_3$




177.8
160.0
158.9
157.5
152.2
143.5
138.7
130.5
127.4
121.4
112.8
110.1
105.0
97.0
55.8
55.7
40.7
35.8
150MHz, CDCl3
NMe2
MeO
HO
F
O
N
N
N
N
OMe
6ba
f1 (ppm)

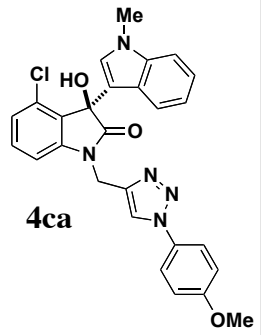
400MHz, $CDCl_3$





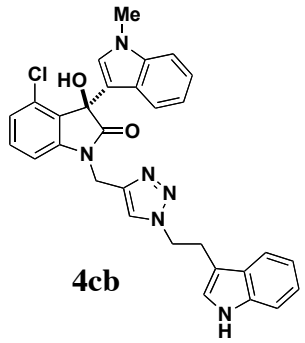
100MHz, $CDCl_3$

400MHz, $CDCl_3$



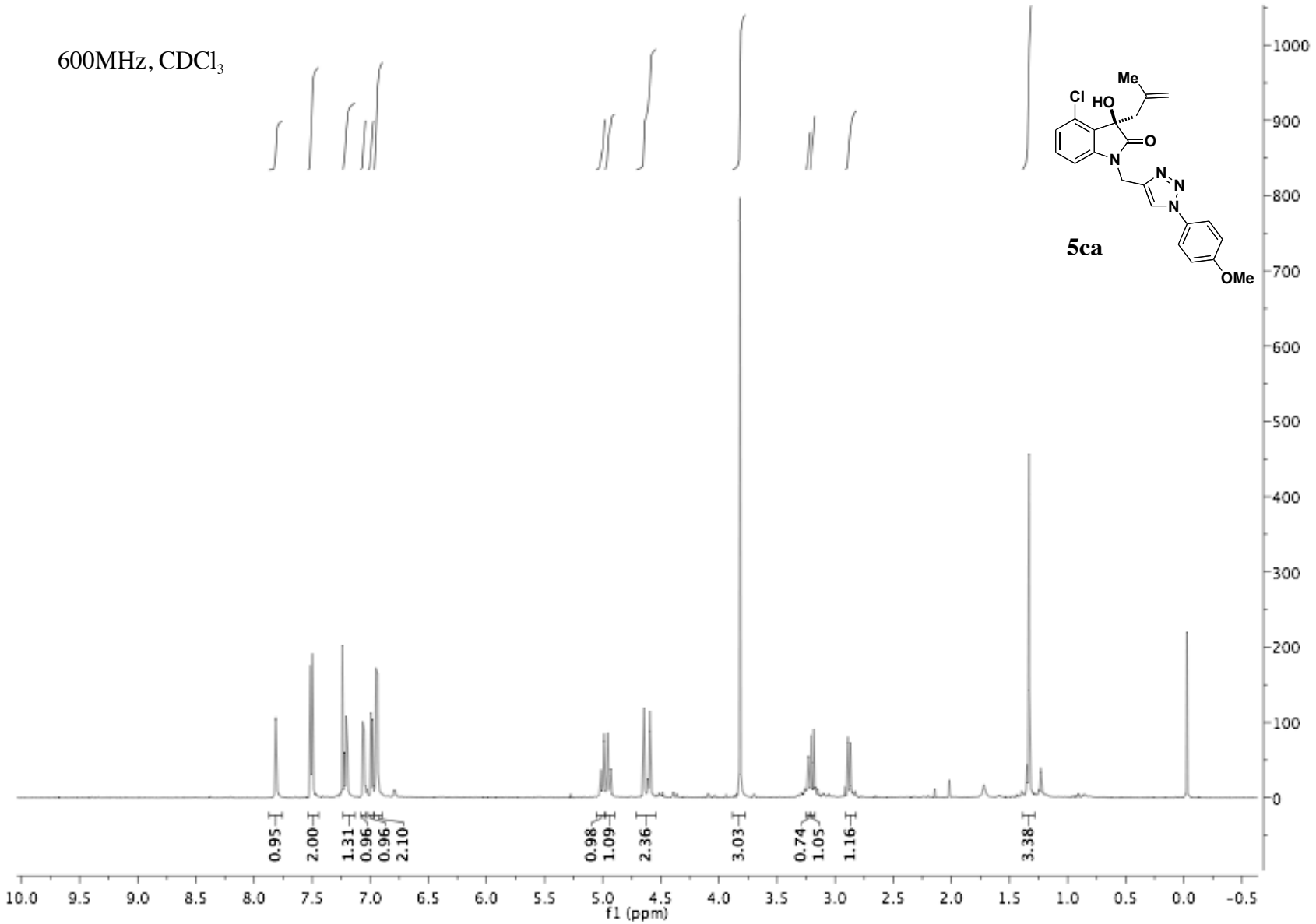
4ca

400MHz, $CDCl_3$

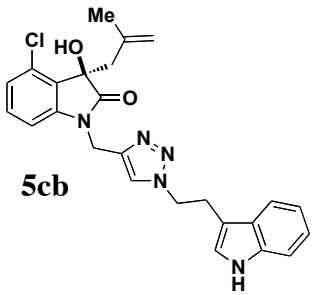


4cb

600MHz, $CDCl_3$

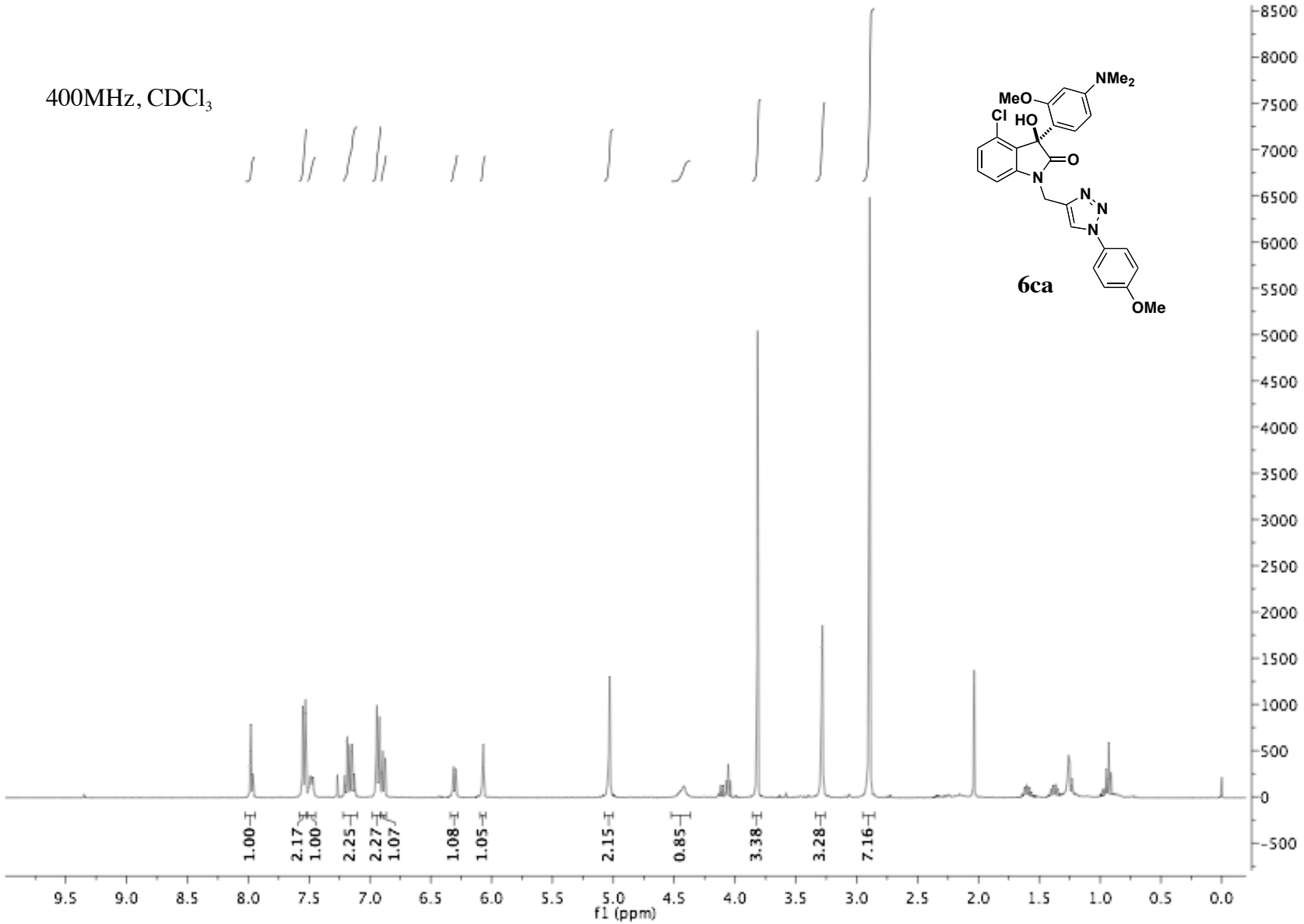


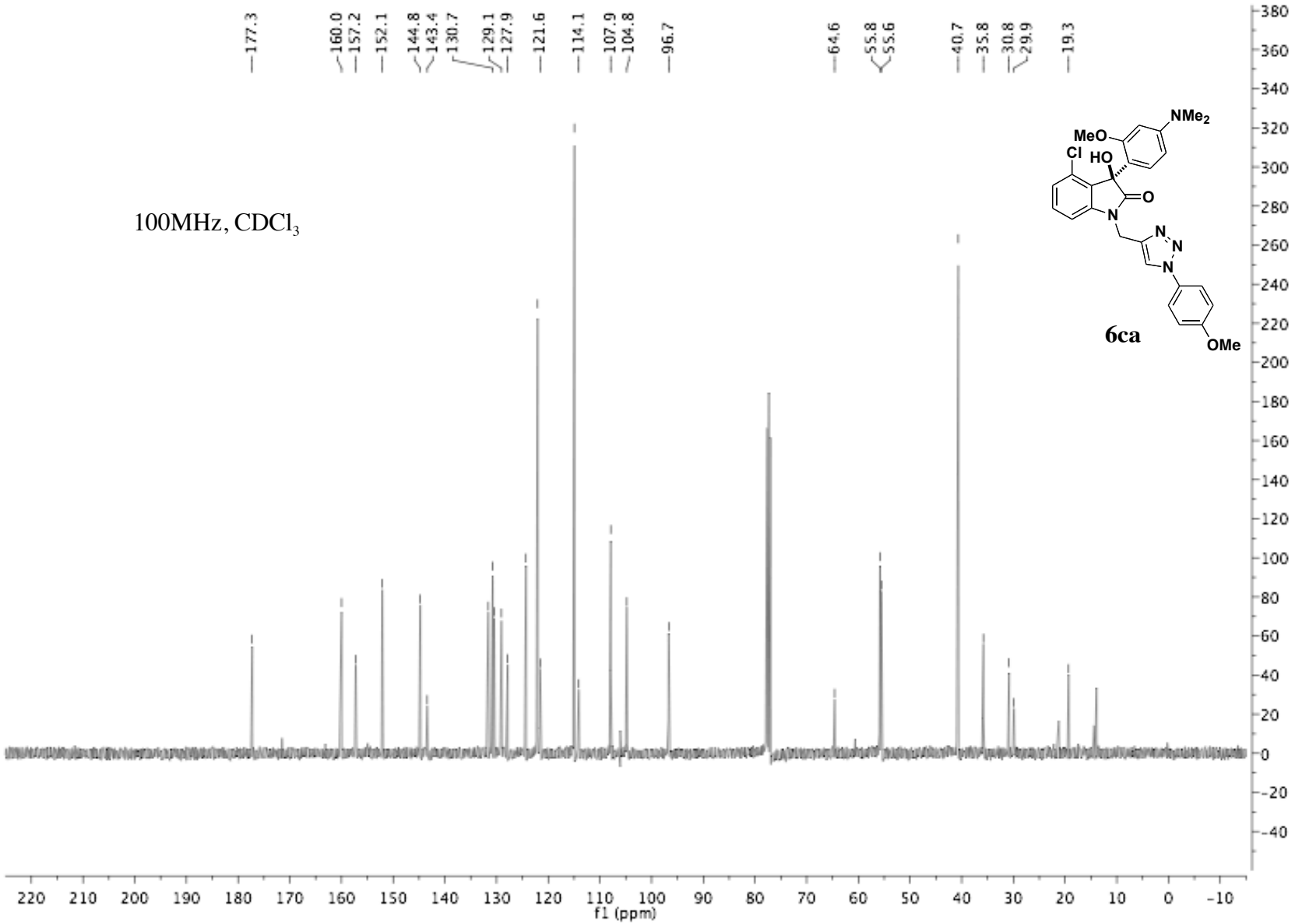
600MHz, $CDCl_3$



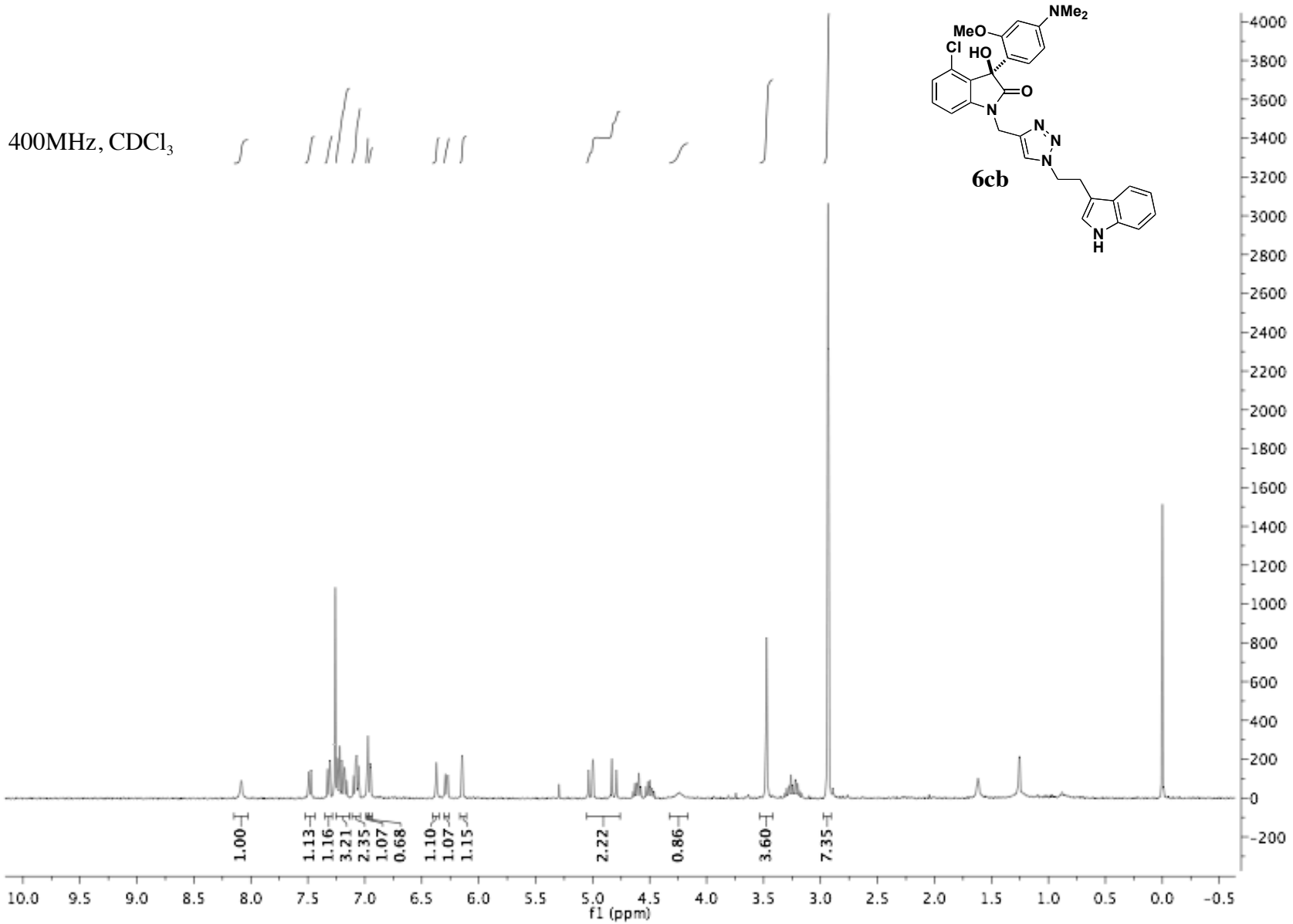
5cb

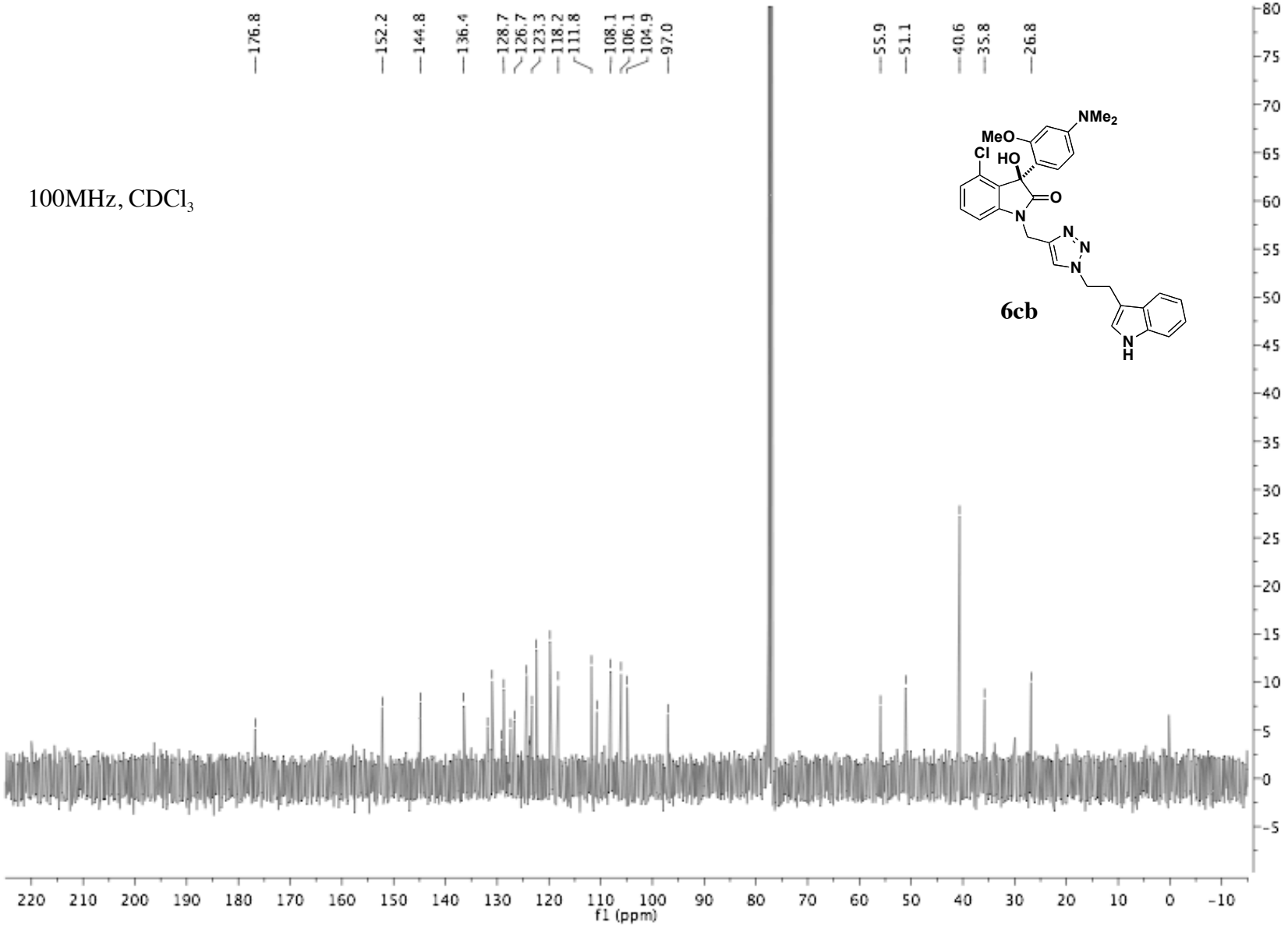
400MHz, $CDCl_3$




177.3
160.0
157.2
152.1
144.8
143.4
130.7
129.1
127.9
121.6
114.1
107.9
104.8
96.7
64.6
55.8
55.6
40.7
35.8
30.8
29.9
19.3
100MHz, CDCl3
NMe2
MeO
Cl
HO
O
N
N
N
N
OMe
6ca
f1 (ppm)

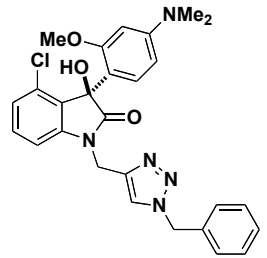
400MHz, $CDCl_3$





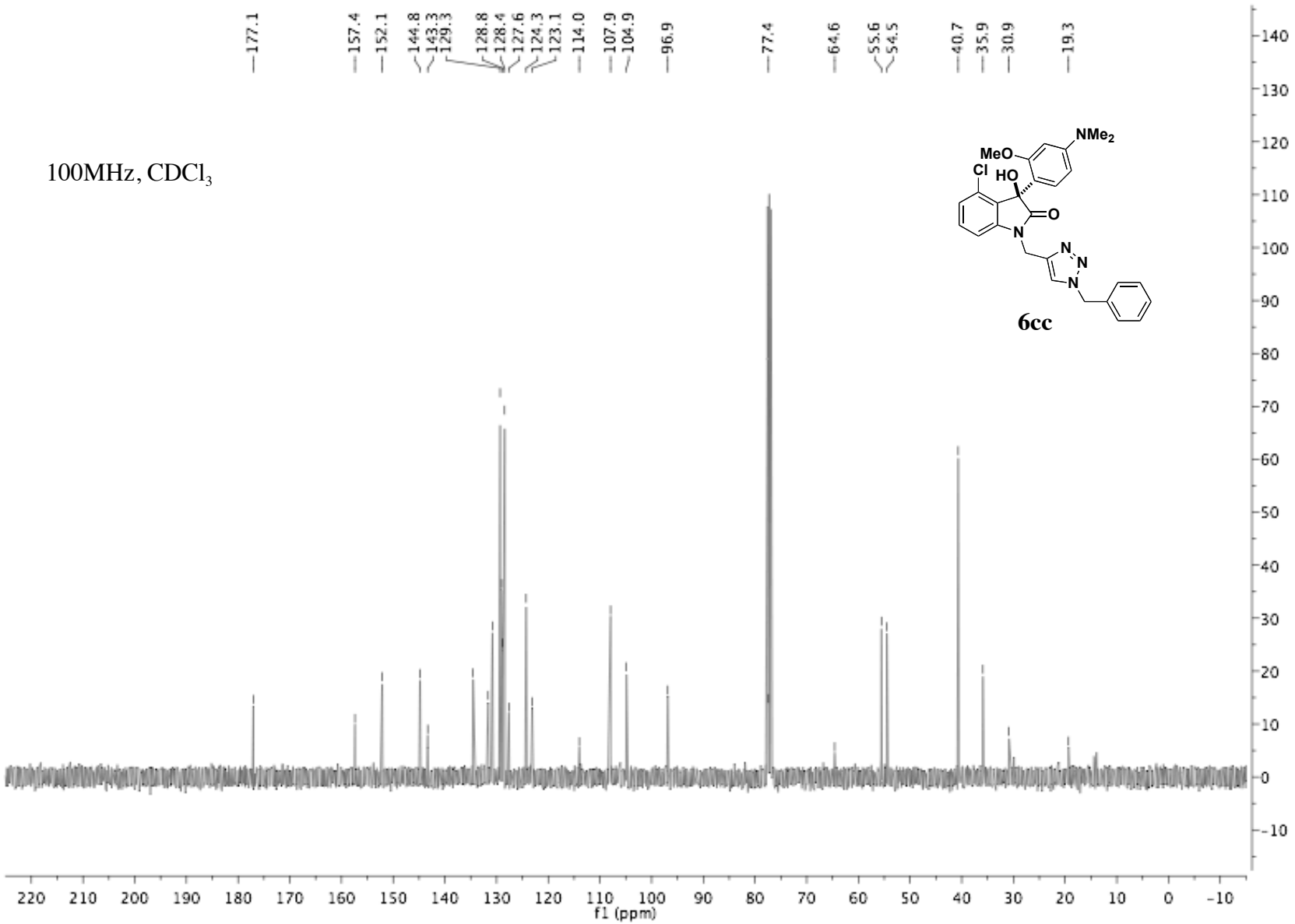
100MHz, $CDCl_3$

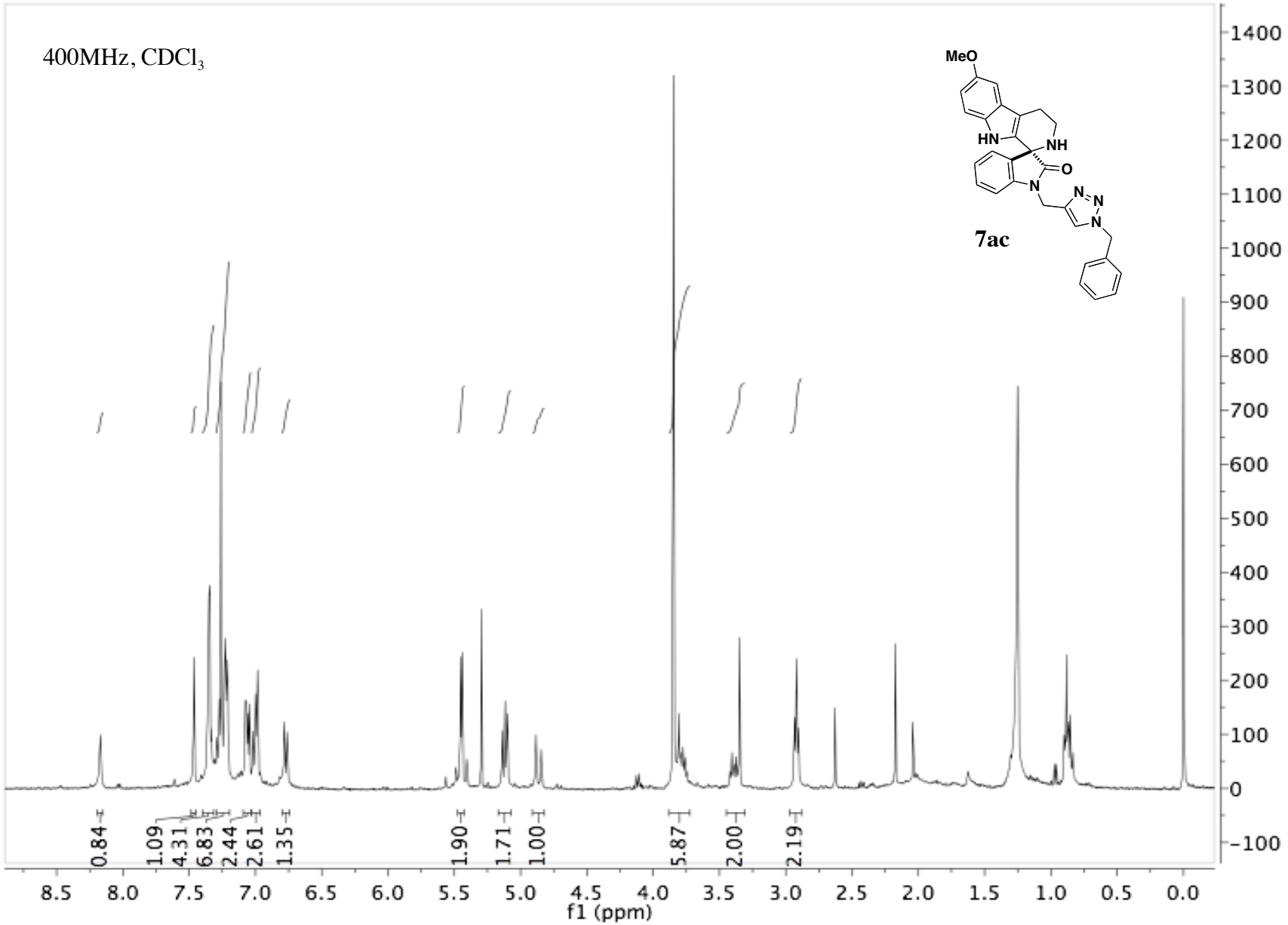
400MHz, $CDCl_3$

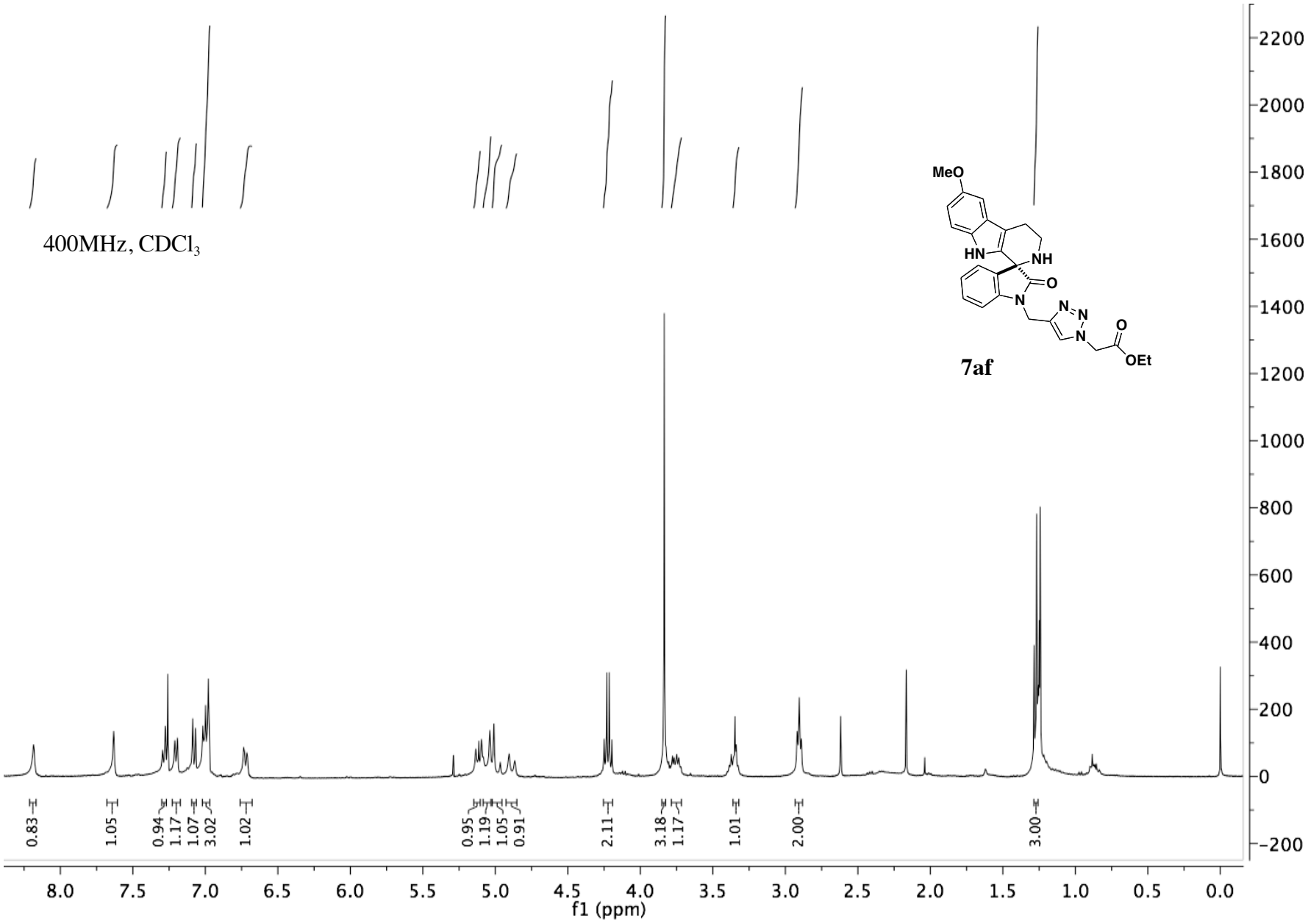


6cc

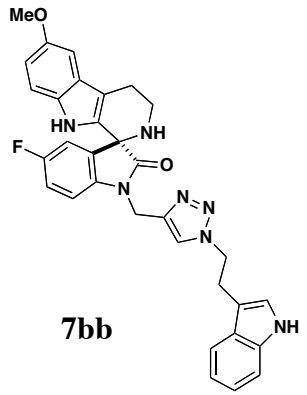
100MHz, $CDCl_3$



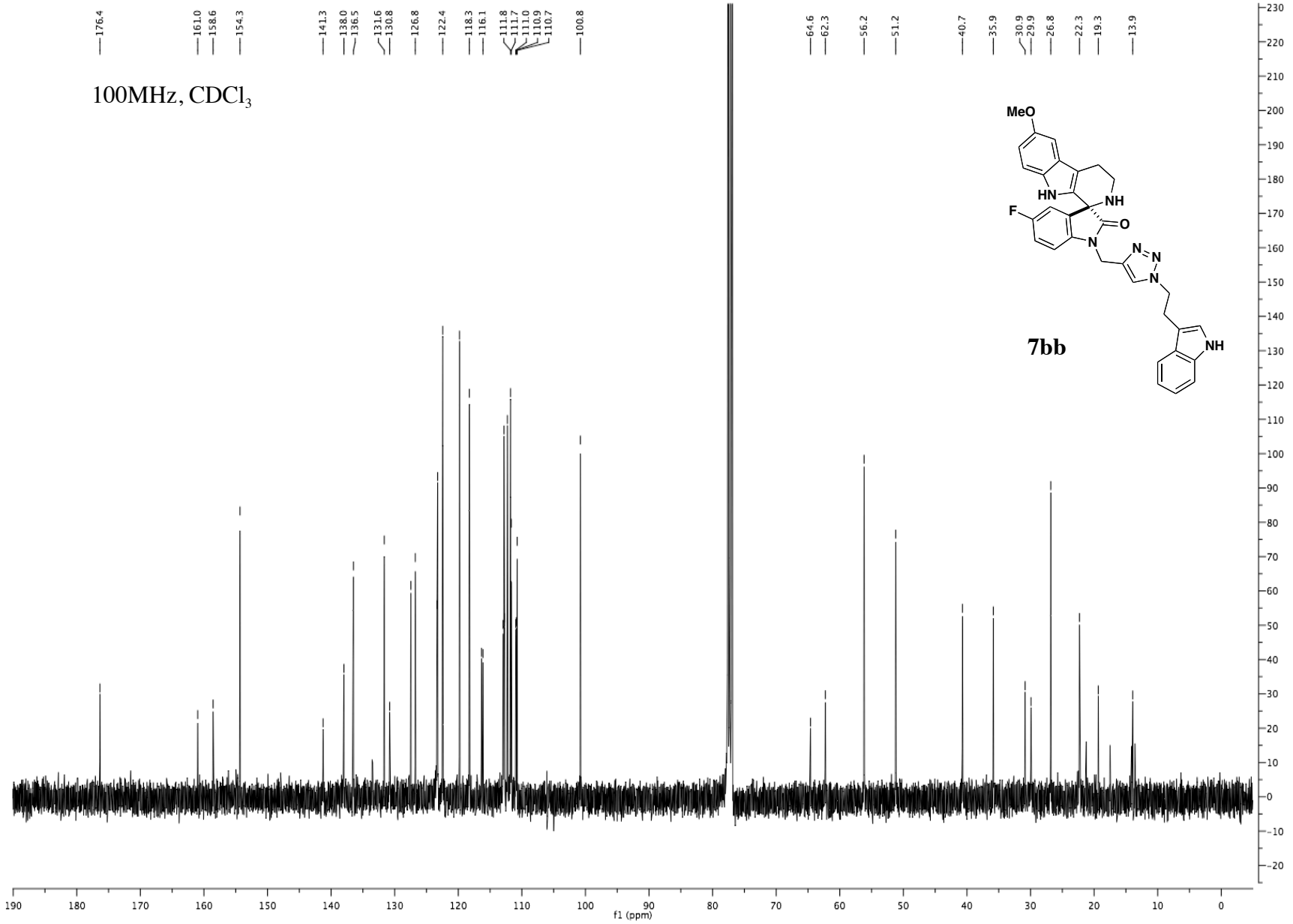

400MHz, $CDCl_3$
MeO
HN
NH
O
N
N
N
N
7ac
0.84
1.09
4.31
6.83
2.44
2.61
1.35
1.90
1.71
1.00
5.87
2.00
2.19
f1 (ppm)


400MHz, $CDCl_3$
MeO
HN
NH
O
N
N
N
O
OEt
7af
0.83
1.05
0.94
1.17
1.07
3.02
1.02
0.95
1.19
1.05
0.91
2.11
3.18
1.17
1.01
2.00
3.00
f1 (ppm)

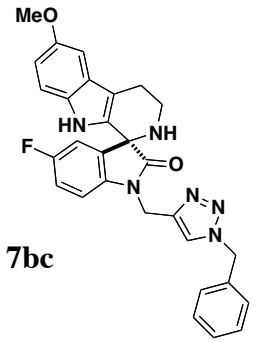
400MHz, $CDCl_3$



7bb

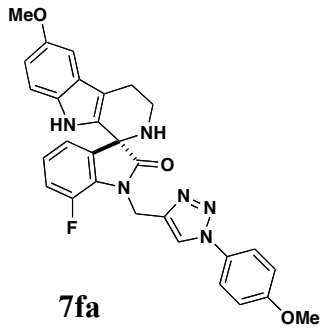

176.4
161.0
158.6
154.3
141.3
138.0
136.5
131.6
130.8
126.8
122.4
118.3
116.1
111.8
111.7
111.0
110.9
110.7
100.8
64.6
62.3
56.2
51.2
40.7
35.9
30.9
29.9
26.8
22.3
19.3
13.9
100MHz, CDCl3
MeO
HN
NH
F
O
N
N
N
N
NH
7bb
f1 (ppm)

400MHz, $CDCl_3$



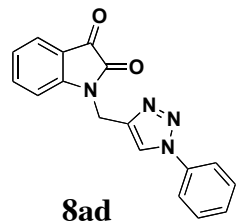
7bc

400MHz, $CDCl_3$

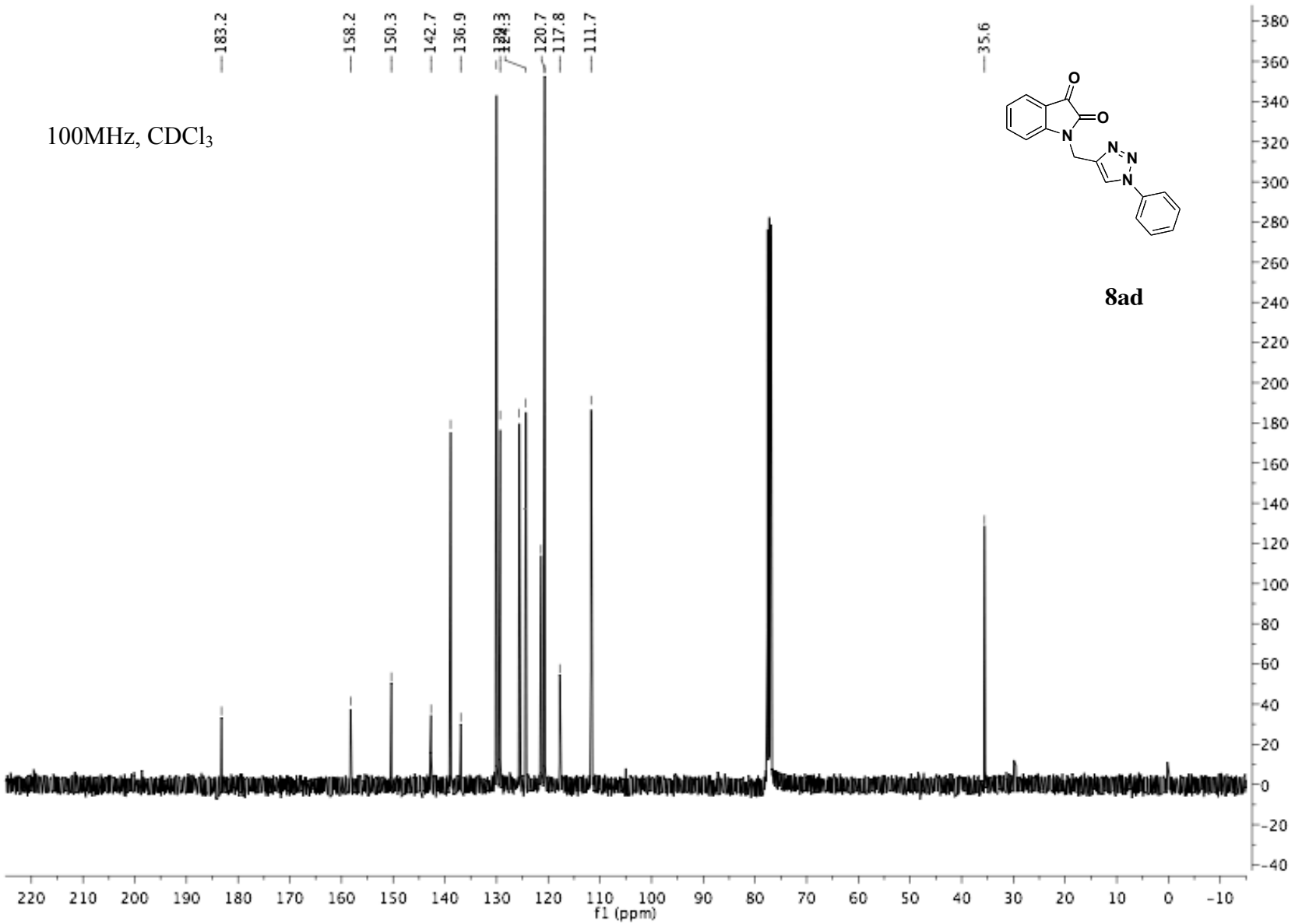


7fa

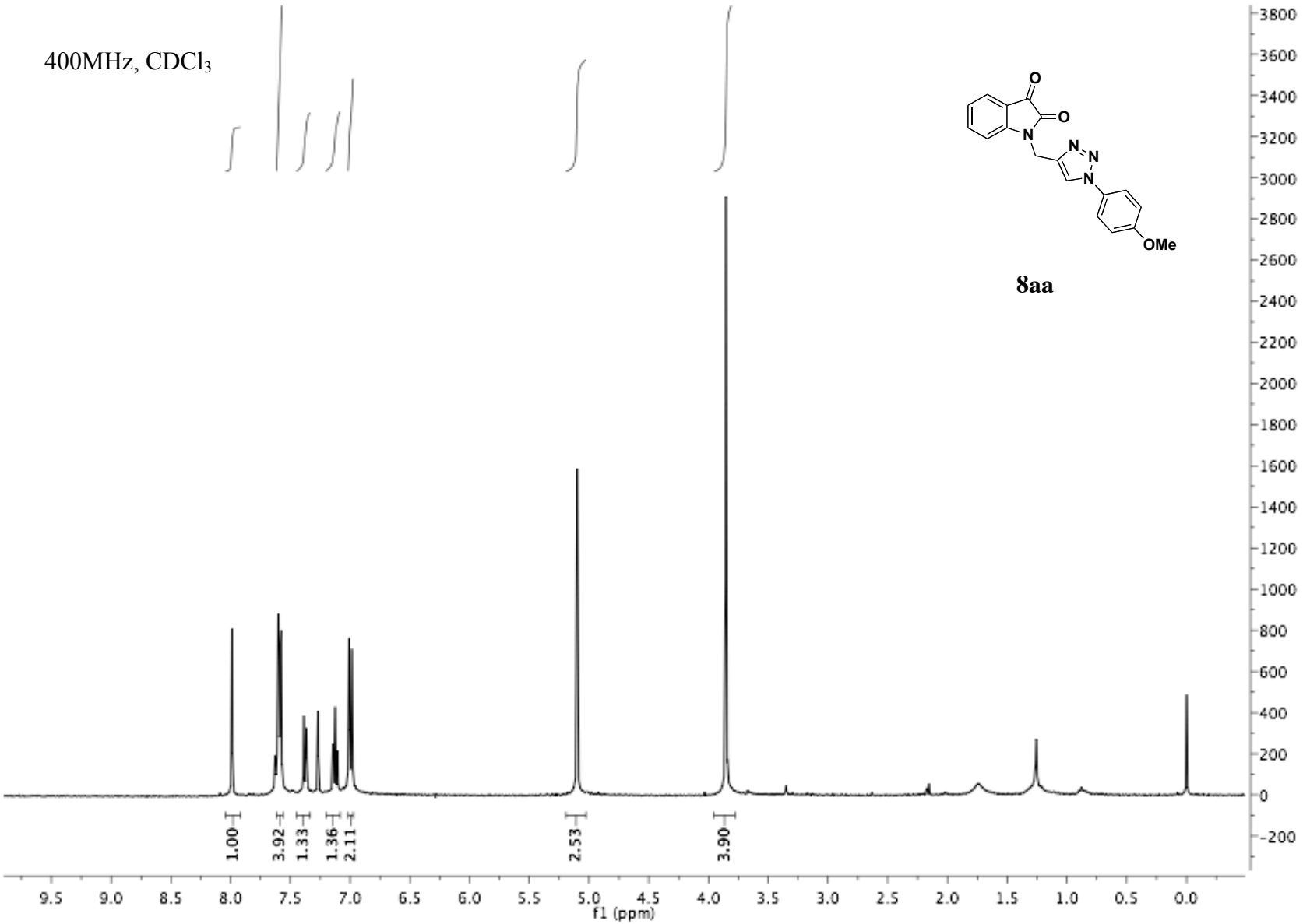
400MHz, $CDCl_3$



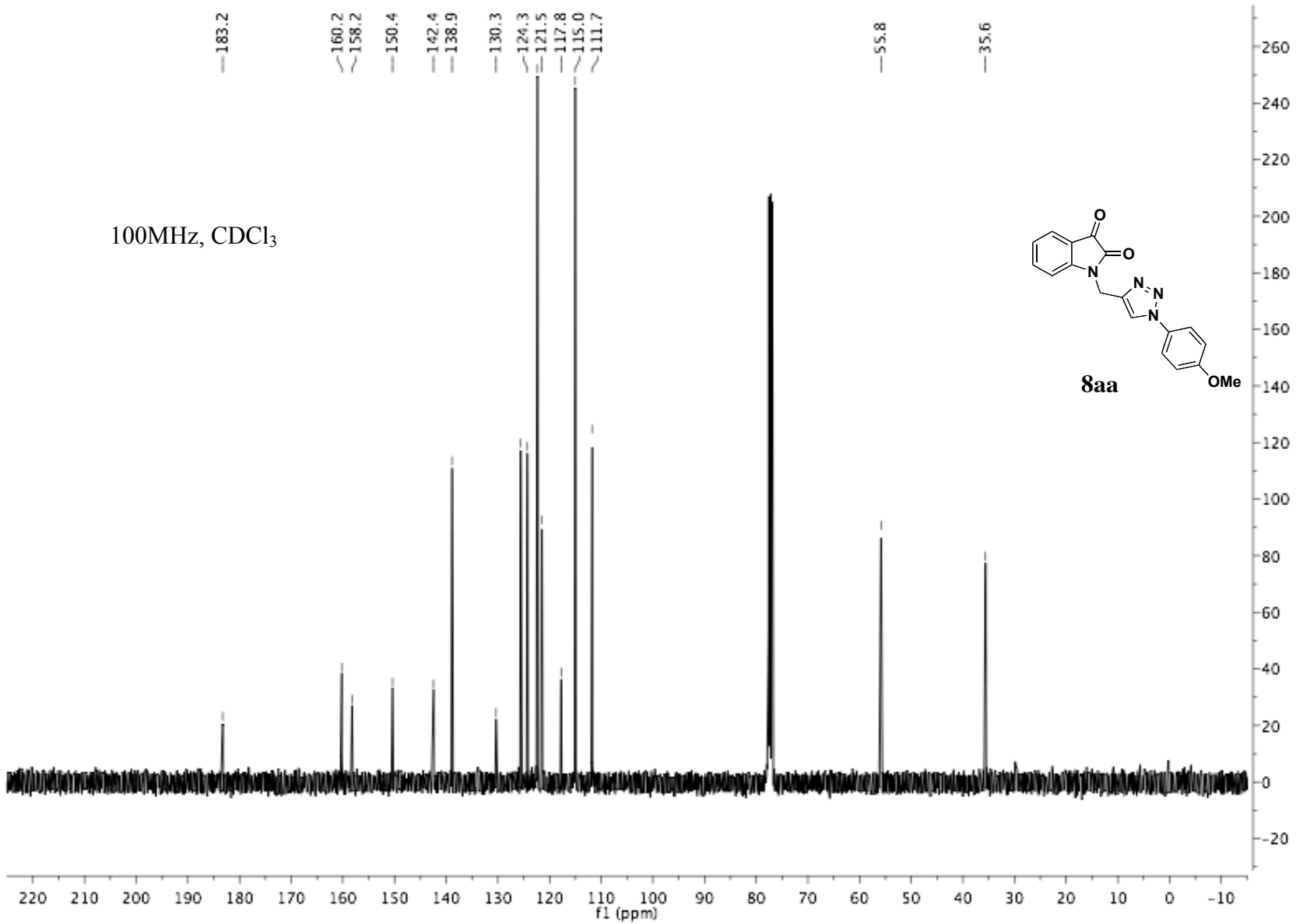
8ad

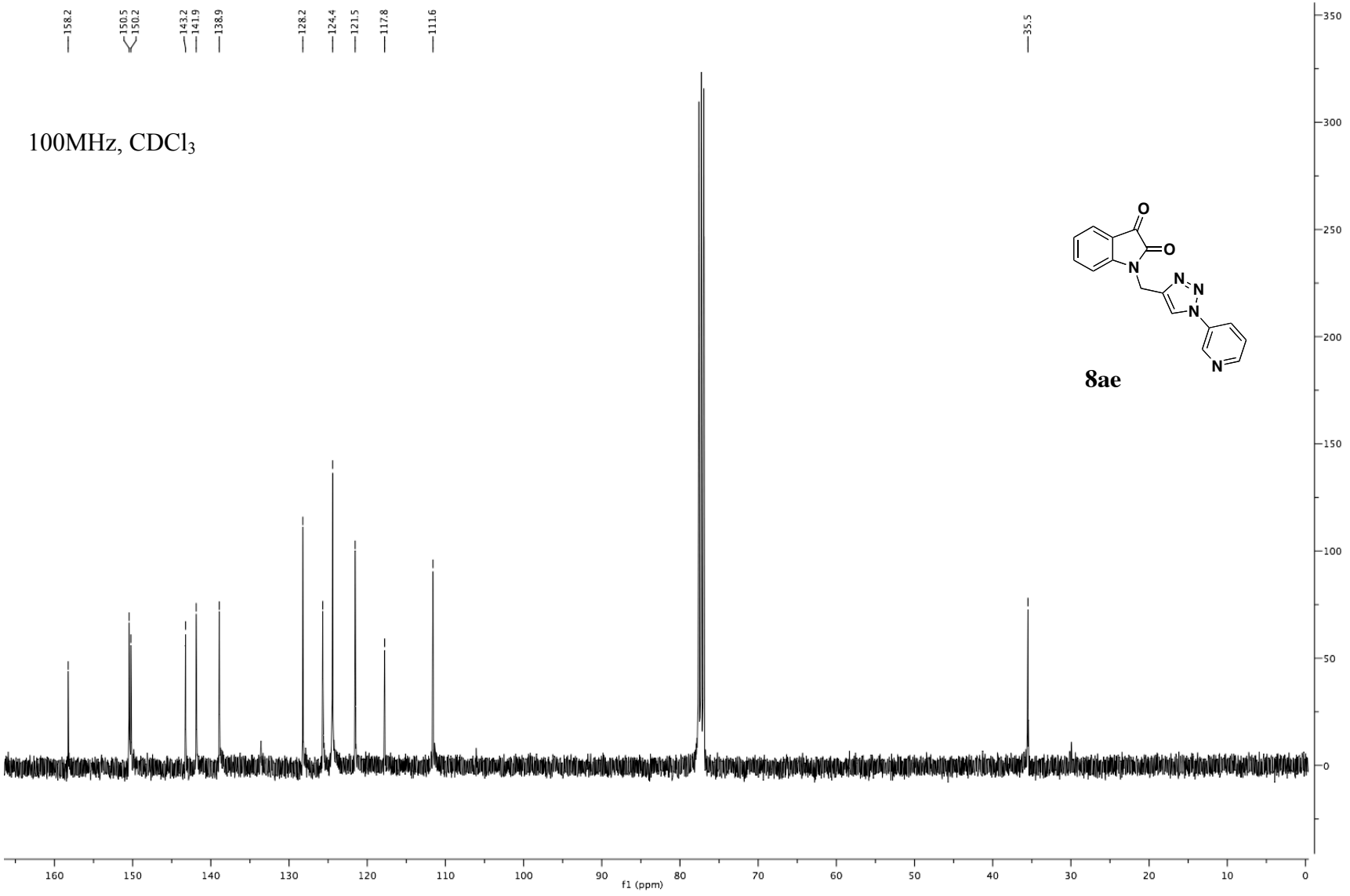

100MHz, CDCl3
183.2
158.2
150.3
142.7
136.9
129.3
124.3
120.7
117.8
111.7
35.6
8ad
f1 (ppm)

400MHz, $CDCl_3$

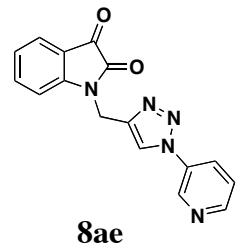


8aa

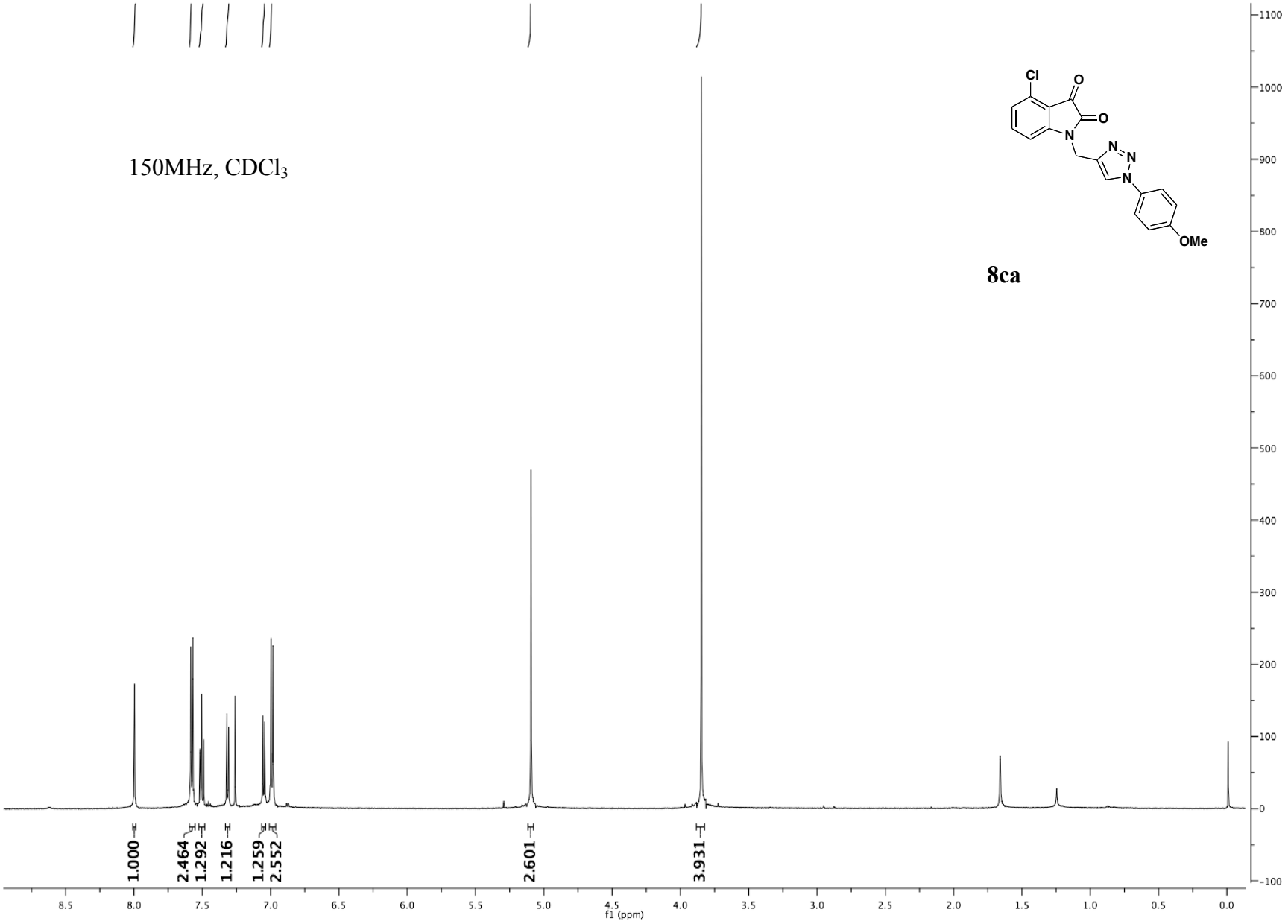

183.2
160.2
158.2
150.4
142.4
138.9
130.3
124.3
121.5
117.8
115.0
111.7
55.8
35.6
100MHz, CDCl3
8aa
OMe
f1 (ppm)

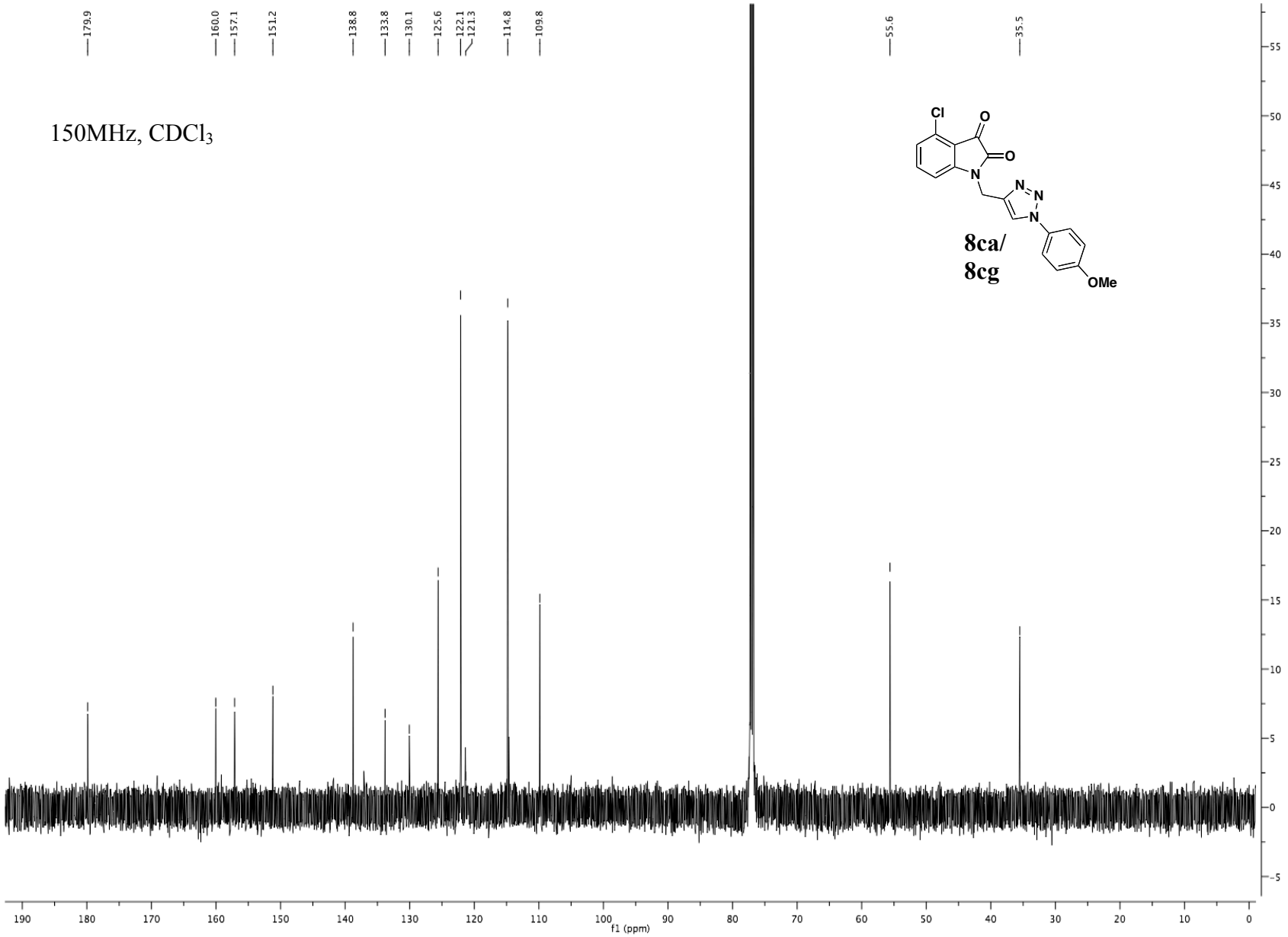

158.2
150.5
150.2
143.2
141.9
138.9
128.2
124.4
121.5
117.8
111.6
35.5
100MHz, CDCl3
8ae
f1 (ppm)

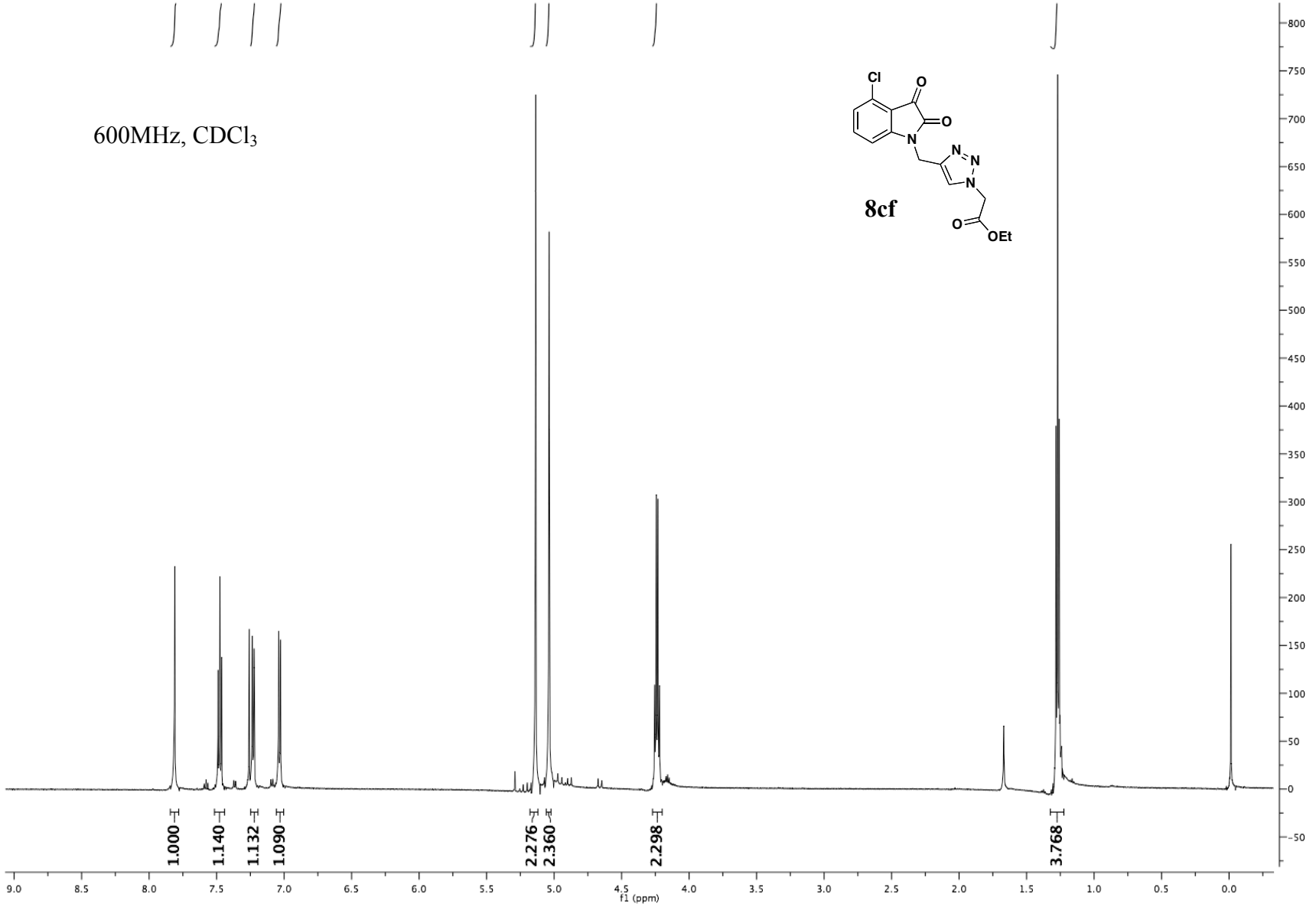
150MHz, $CDCl_3$

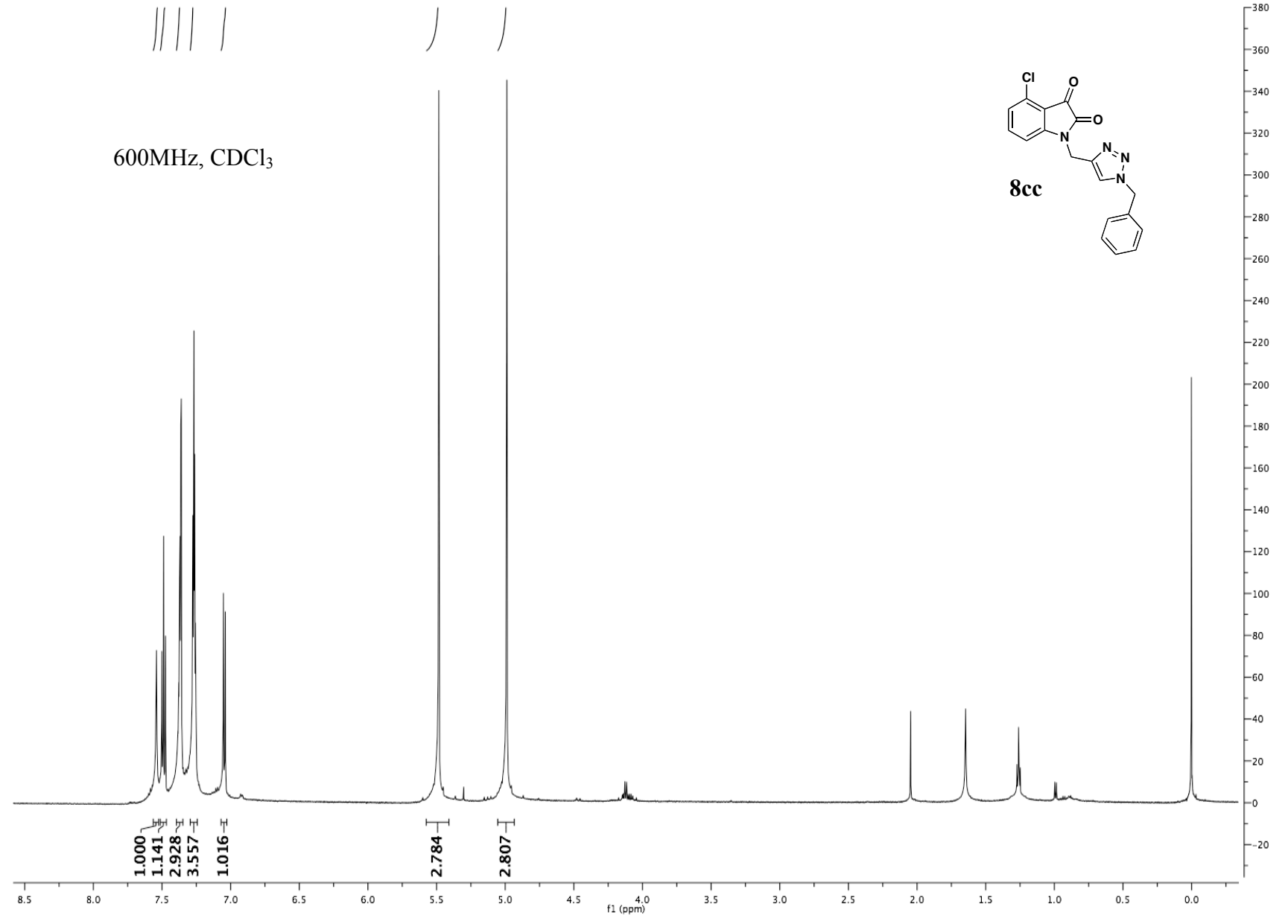


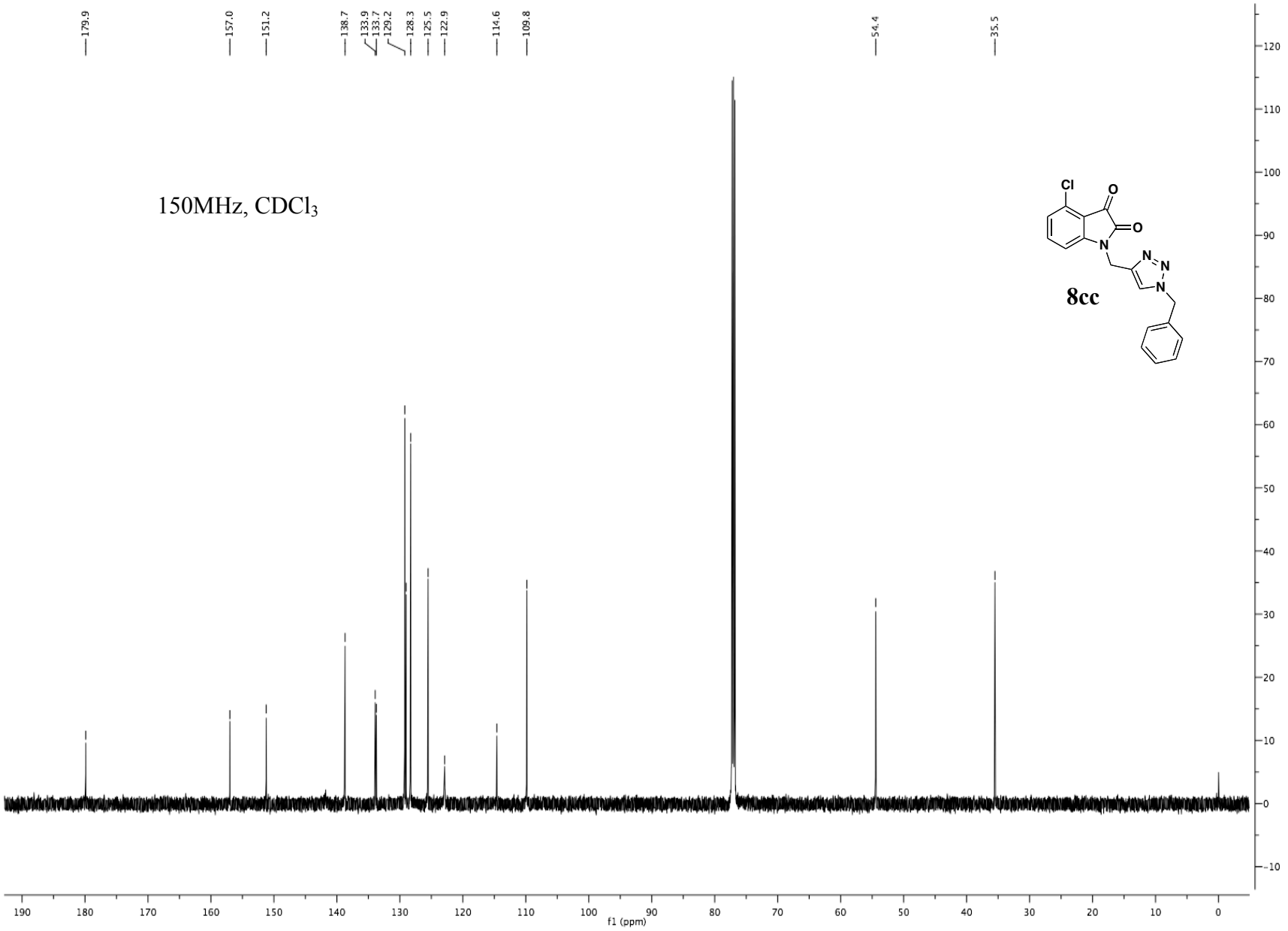
8ae

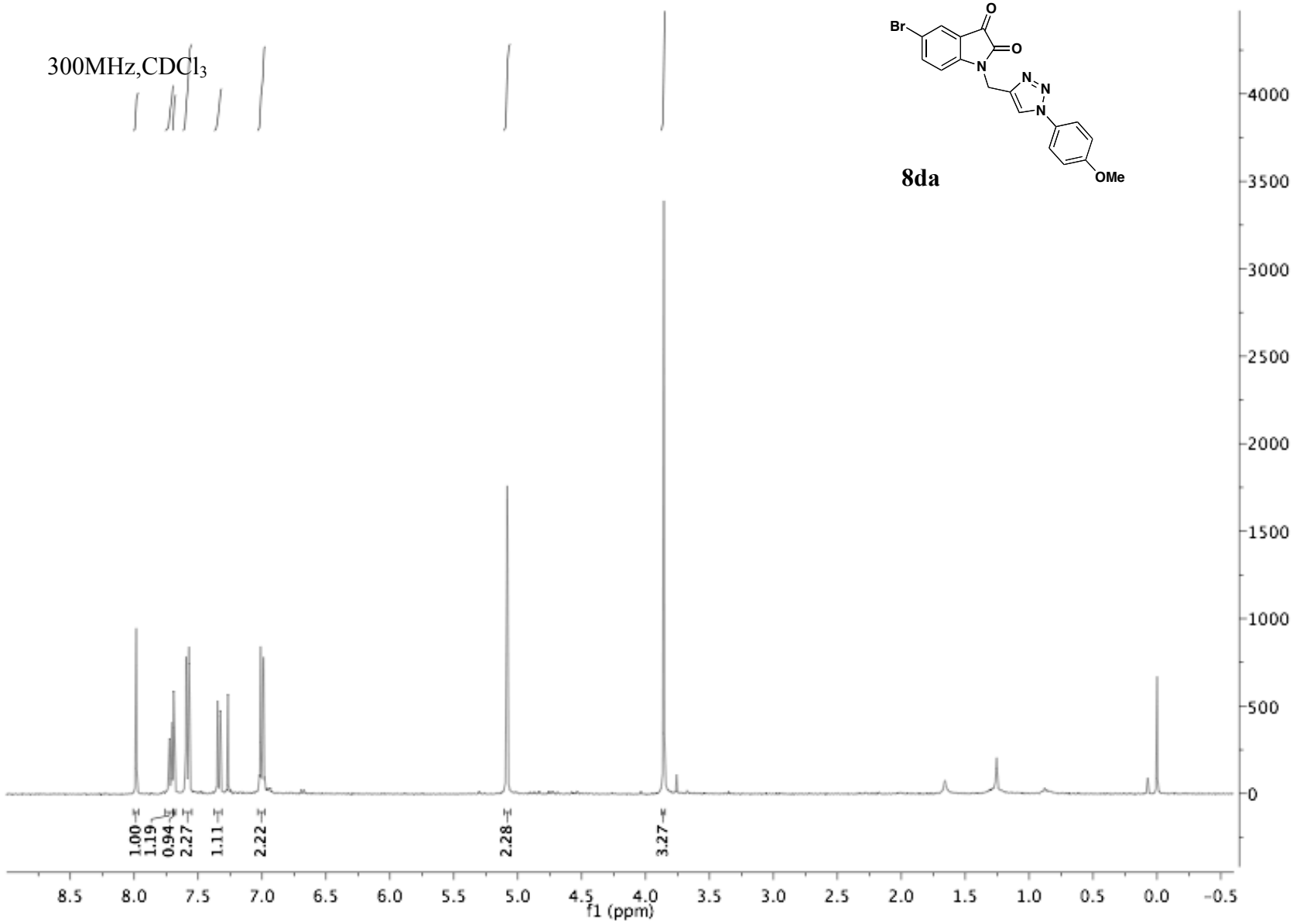

150MHz, CDCl3
Cl
O
O
N
N
N
N
OMe
8ca
1.000
2.464
1.292
1.216
1.259
2.552
2.601
3.931
f1 (ppm)


179.9
160.0
157.1
151.2
138.8
133.8
130.1
125.6
122.1
121.3
114.8
109.8
55.6
35.5
150MHz, CDCl3
Cl
O
O
N
N
N
N
OMe
8ca/
8cg
f1 (ppm)

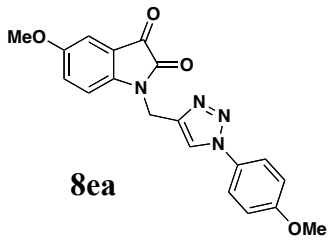

600MHz, CDCl3
8cf
Cl
O
O
N
N
N
N
O
OEt
1.000
1.140
1.132
1.090
2.276
2.360
2.298
3.768
f1 (ppm)


600MHz, CDCl3
8cc
Cl
O
O
N
N
N
N
1.000
1.141
2.928
3.557
1.016
2.784
2.807
f1 (ppm)


179.9
157.0
151.2
138.7
133.9
133.7
129.2
128.3
125.5
122.9
114.6
109.8
54.4
35.5
150MHz, CDCl3
Cl
O
O
N
N
N
N
8cc
f1 (ppm)

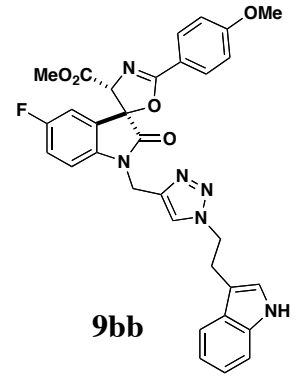

300MHz,CDCl3
Br
O
O
N
N
N
N
OMe
8da
4000
3500
3000
2500
2000
1500
1000
500
0
1.00
1.19
0.94
2.27
1.11
2.22
2.28
3.27
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

400 MHz, CD_2Cl_2

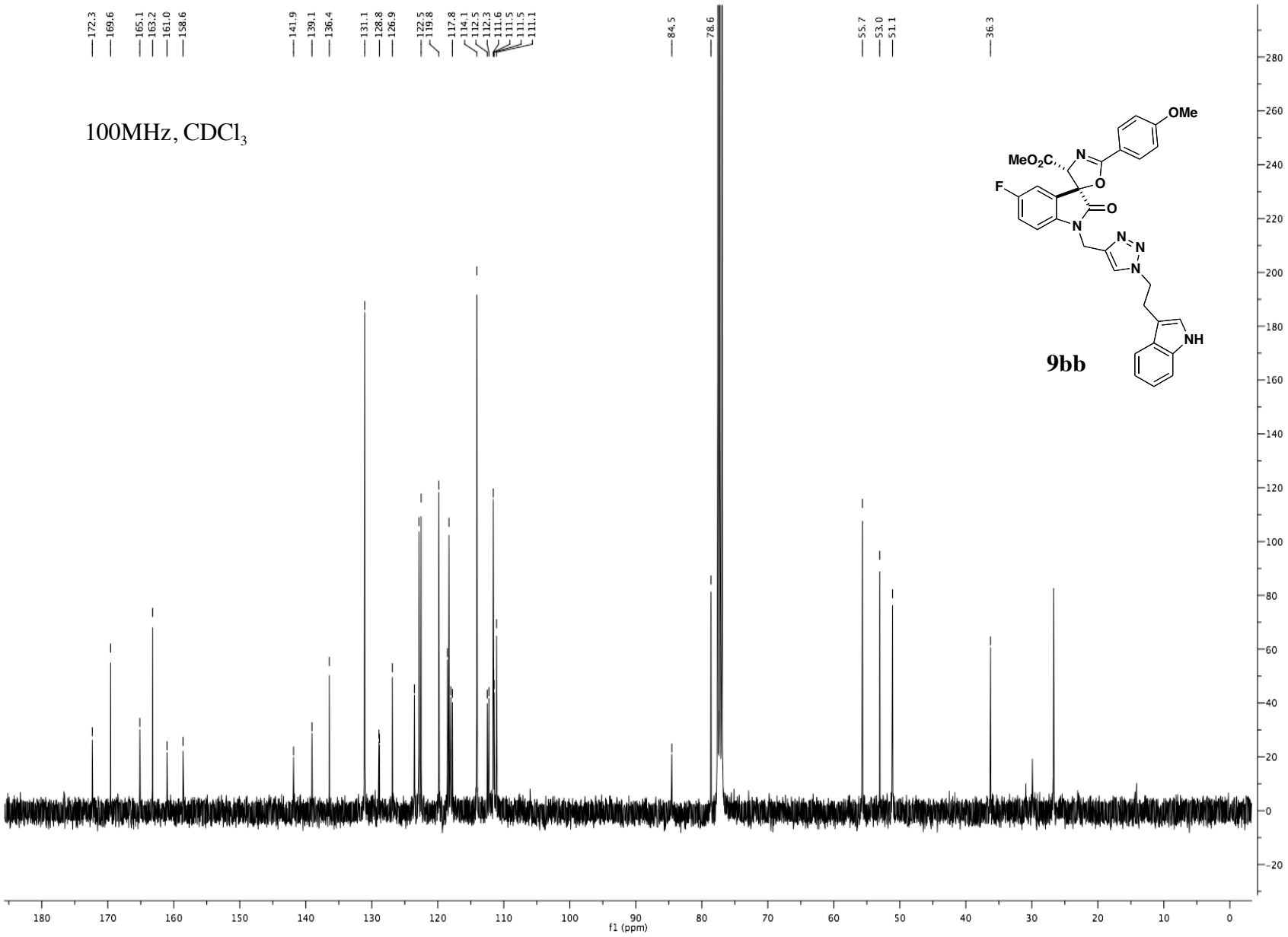


8ea

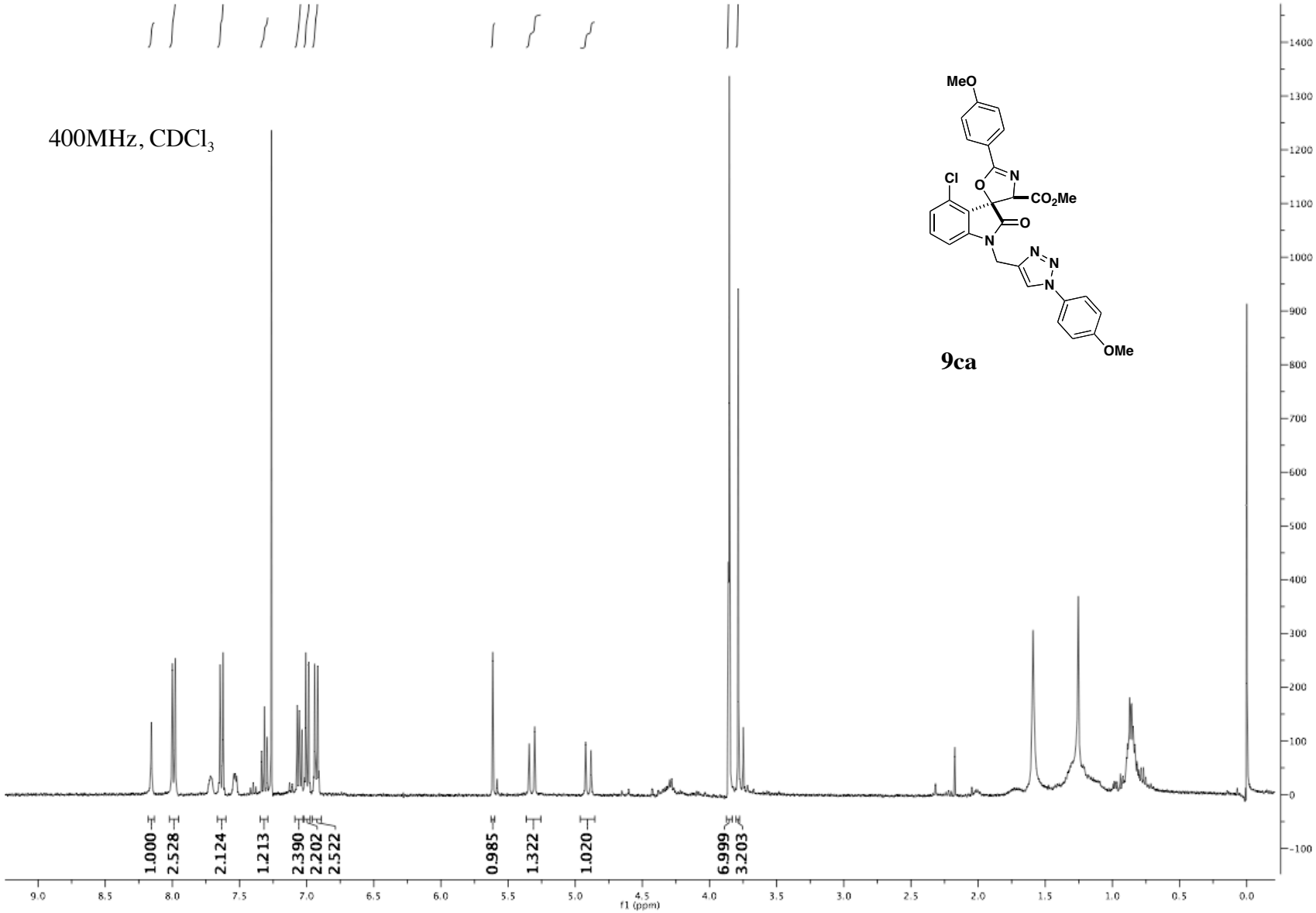
400MHz, $CDCl_3$



9bb

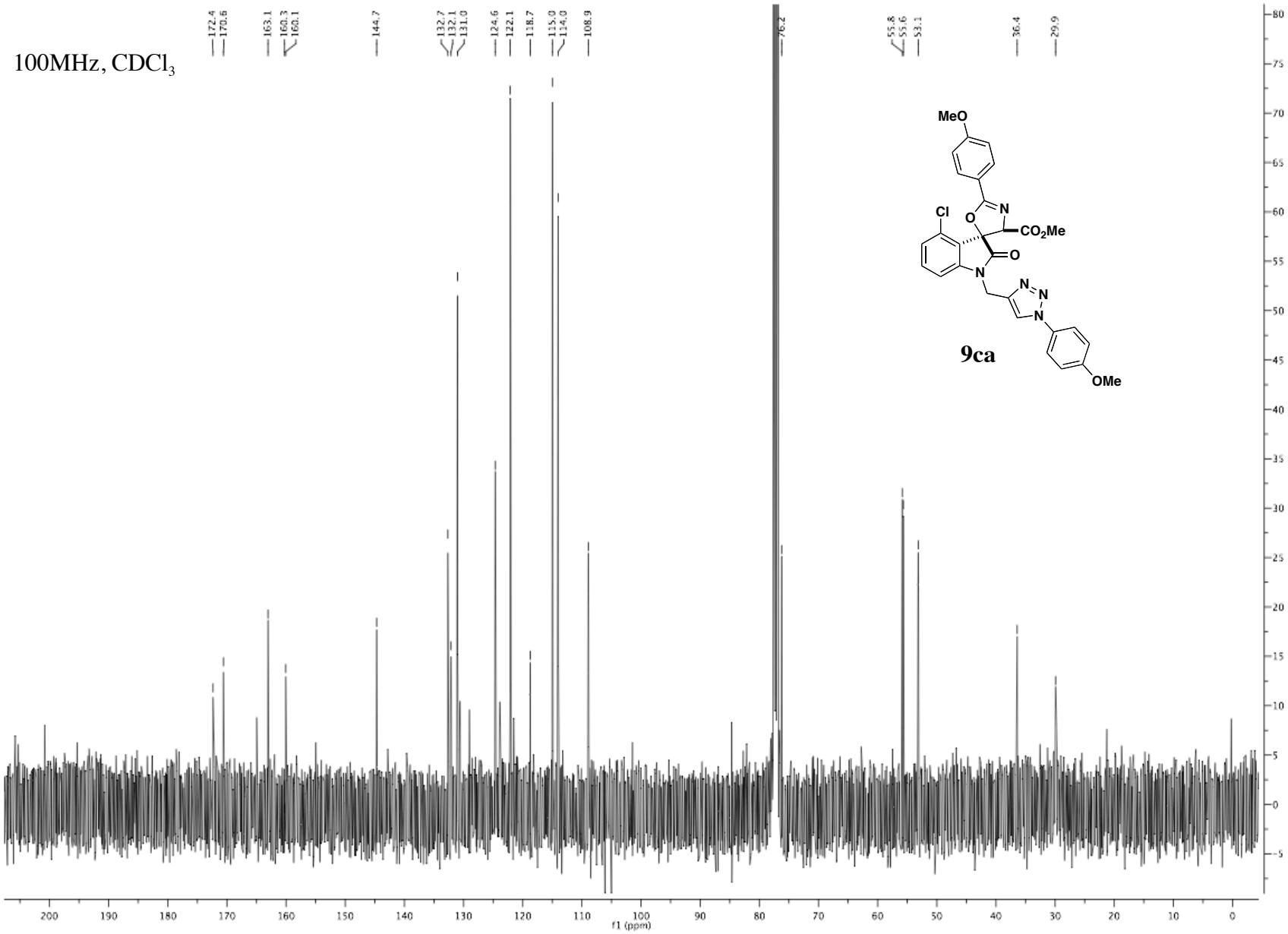

172.3
169.6
165.1
163.2
161.0
158.6
141.9
139.1
136.4
131.1
128.8
126.9
122.5
119.8
117.8
114.1
112.5
112.3
111.6
111.5
111.5
111.1
84.5
78.6
55.7
53.0
51.1
36.3
100MHz, CDCl3
OMe
MeO2C
N
O
F
O
N
N
N
N
NH
9bb
f1 (ppm)

400MHz, $CDCl_3$

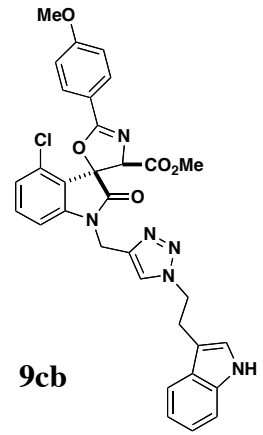


9ca

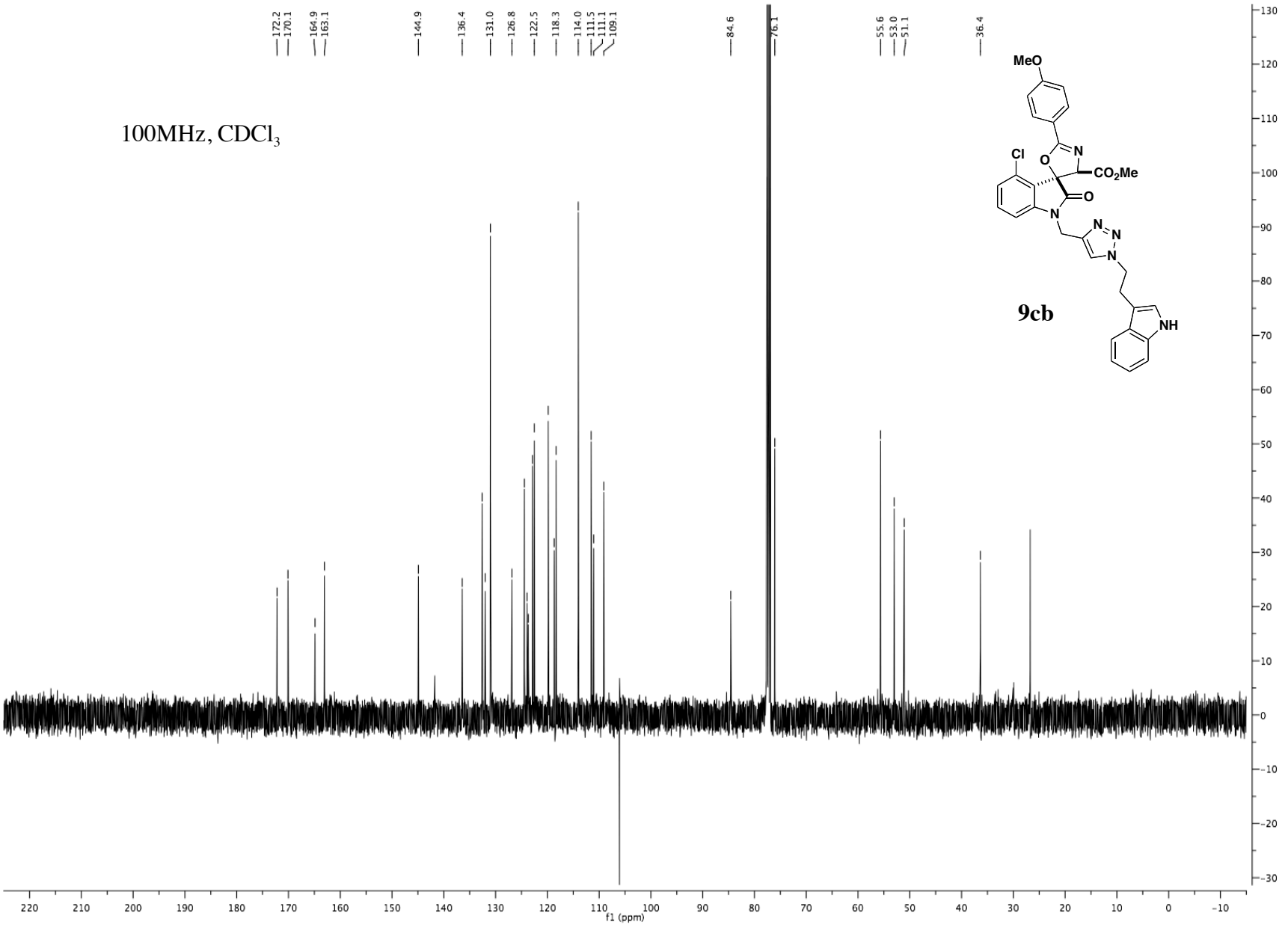
100MHz, $CDCl_3$



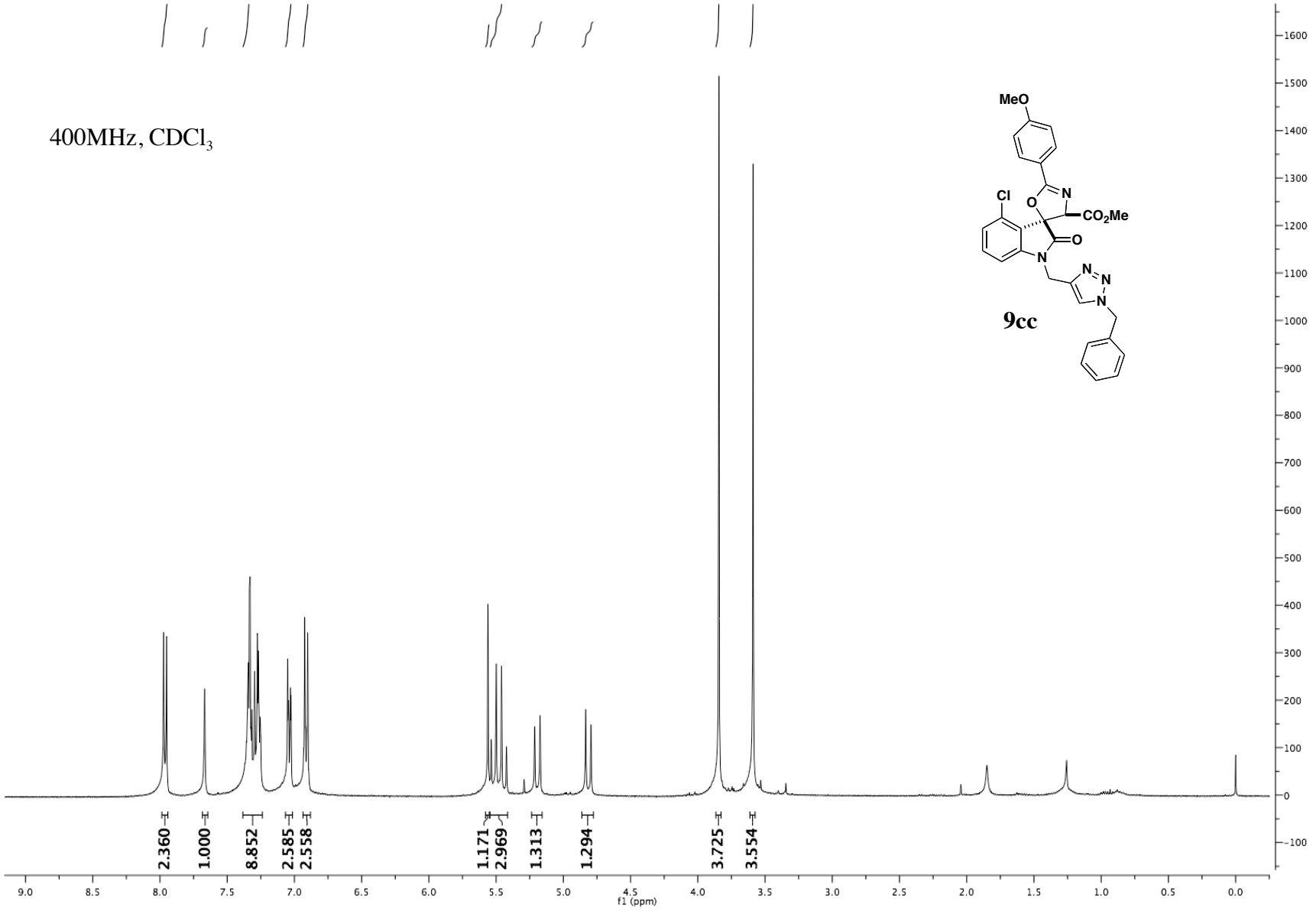
400MHz, $CDCl_3$

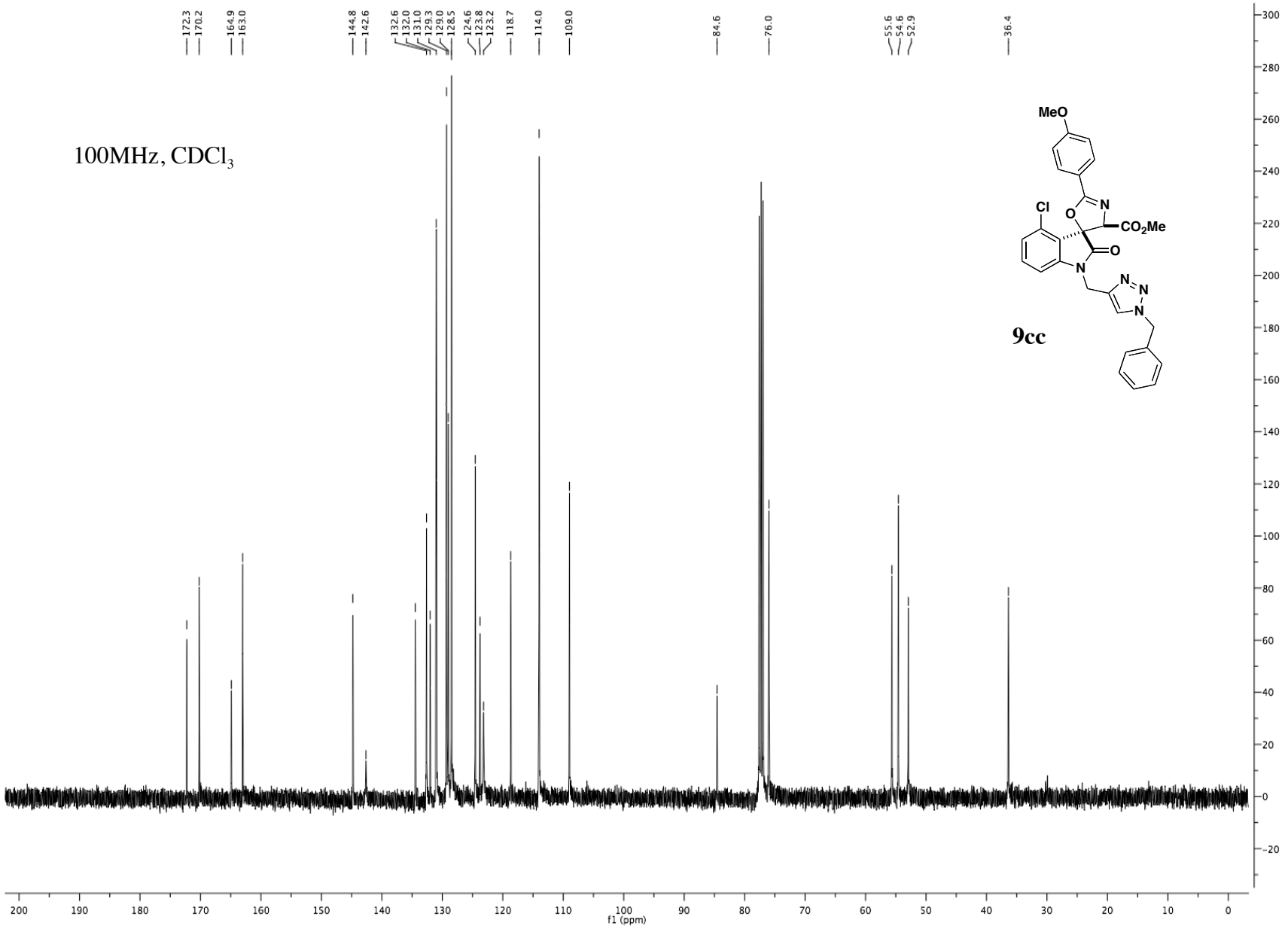


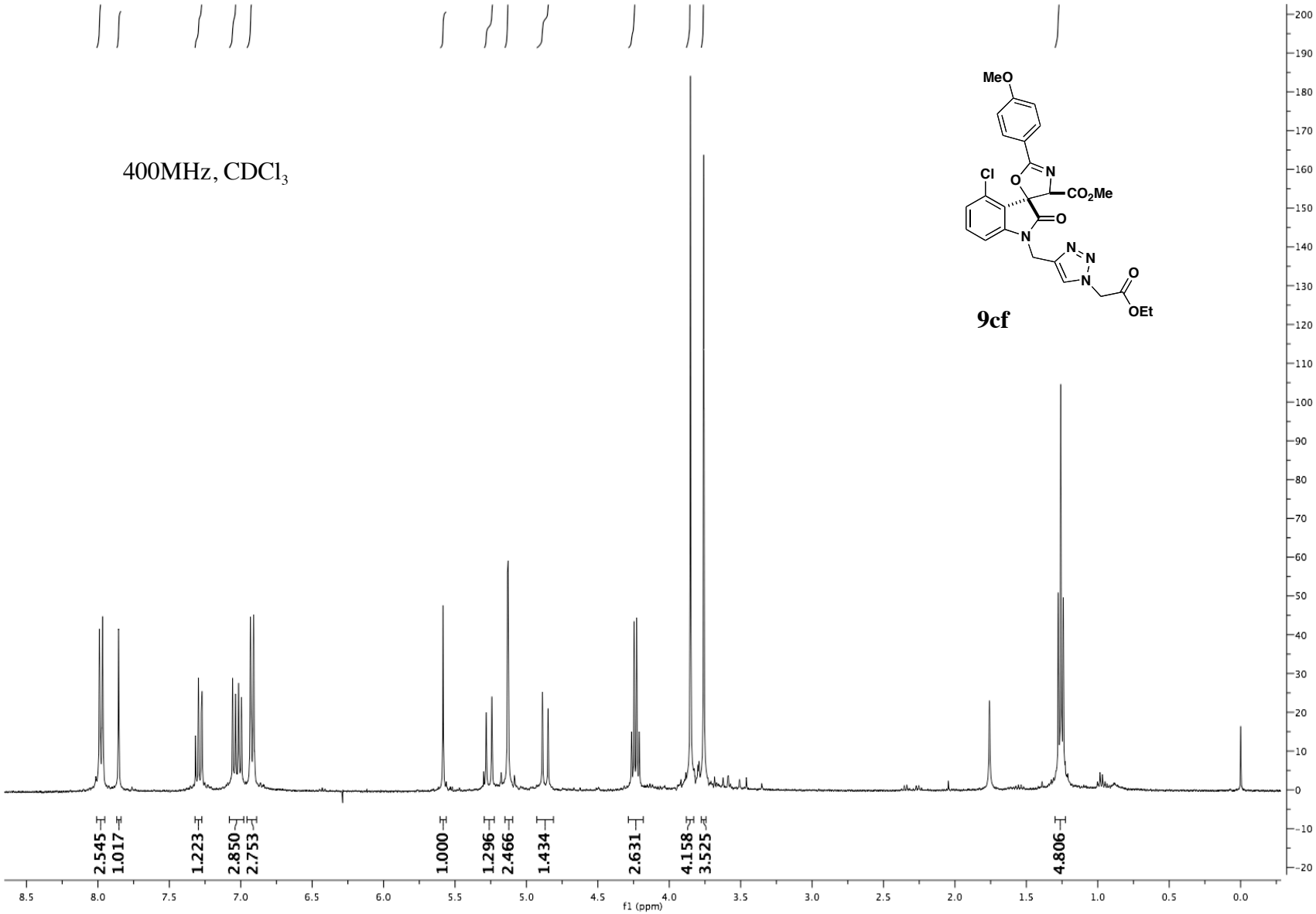
9cb

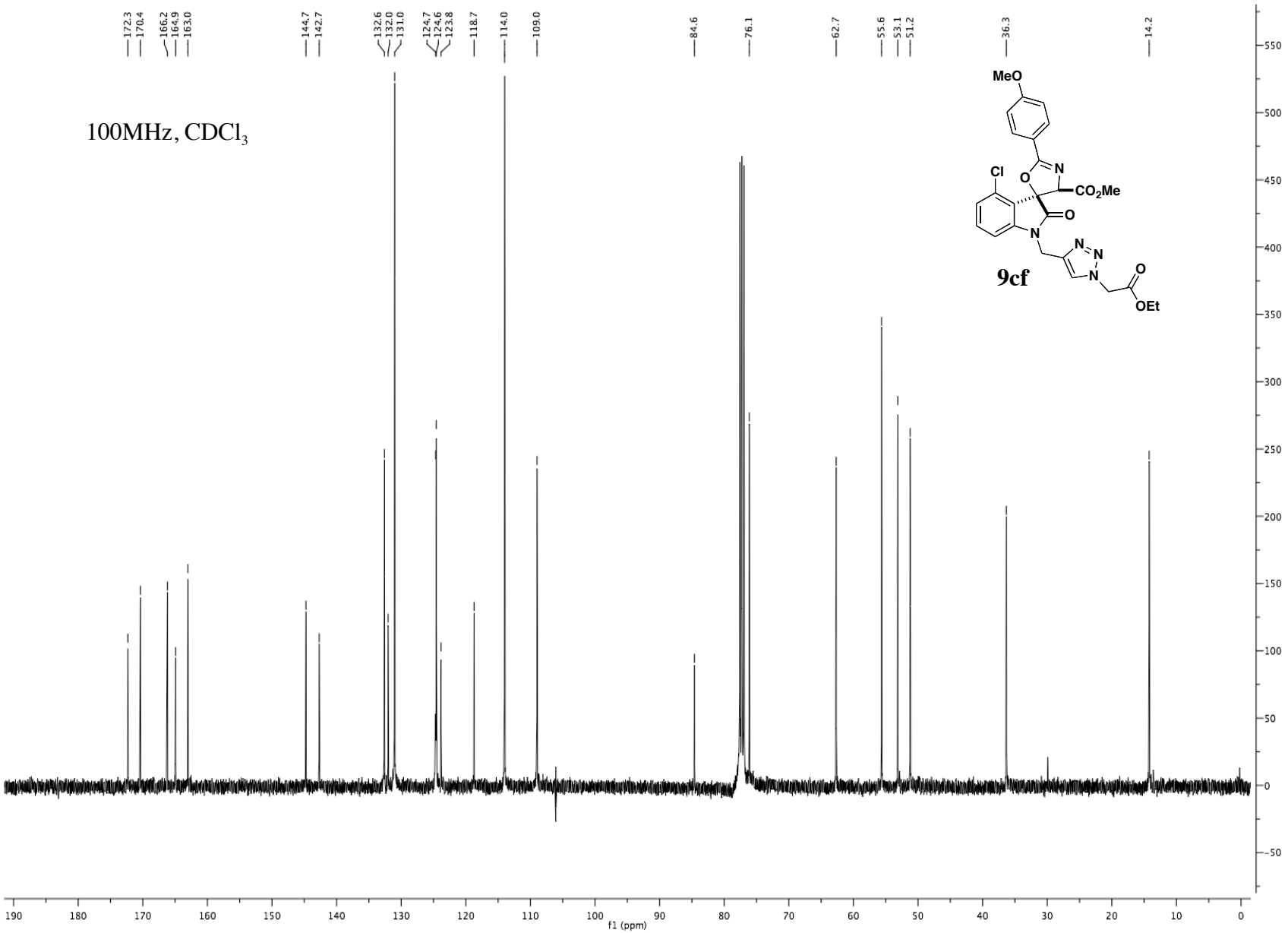

100MHz, CDCl3
172.2
170.1
164.9
163.1
144.9
136.4
131.0
126.8
122.5
118.3
114.0
111.5
111.1
109.1
84.6
76.1
55.6
53.0
51.1
36.4
MeO
Cl
O
N
CO2Me
O
N
N
N
N
NH
9cb
f1 (ppm)

400MHz, $CDCl_3$

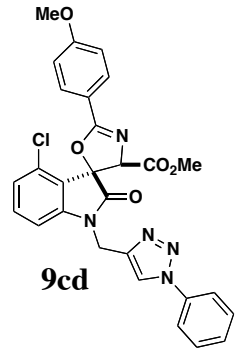



172.3
170.2
164.9
163.0
144.8
142.6
132.6
132.0
131.0
129.3
129.0
128.5
124.6
123.8
123.2
118.7
114.0
109.0
84.6
76.0
55.6
54.6
52.9
36.4
100MHz, CDCl3
MeO
Cl
O
N
CO2Me
O
N
N
N
N
9cc
f1 (ppm)

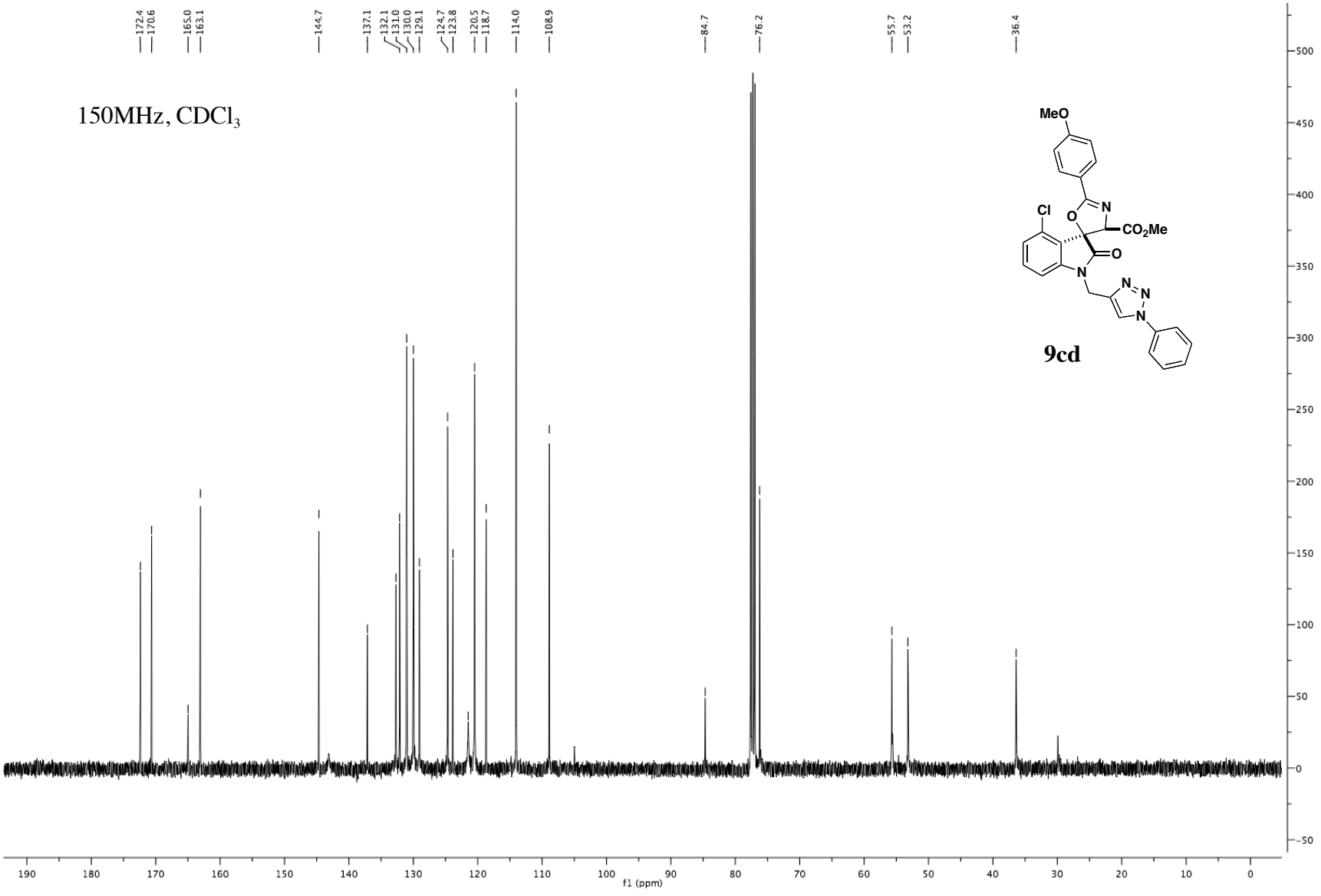

400MHz, CDCl3
MeO
Cl
O
N
CO2Me
O
N
N
N
N
O
OEt
9cf
2.545
1.017
1.223
2.850
2.753
1.000
1.296
2.466
1.434
2.631
4.158
3.525
4.806
f1 (ppm)

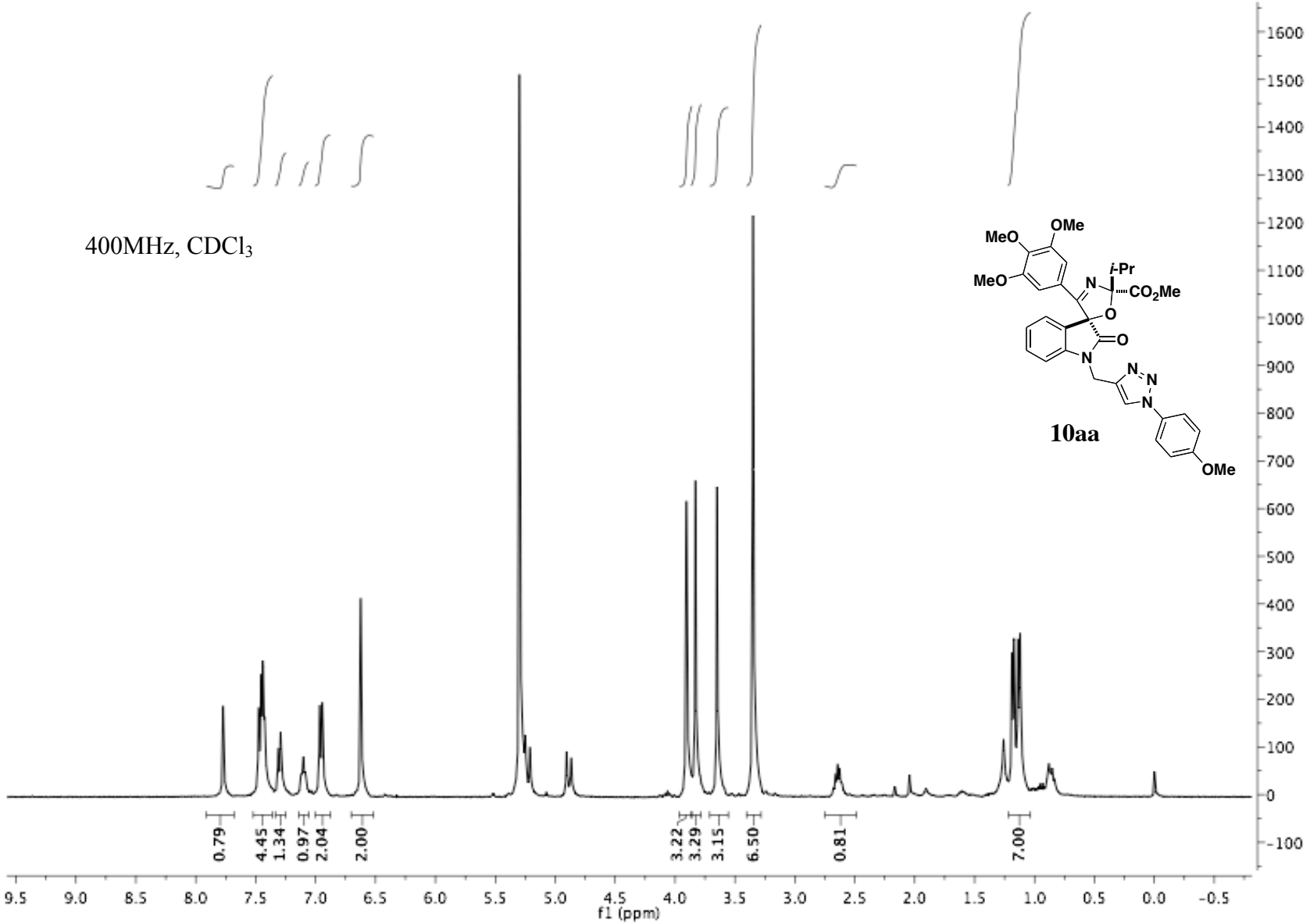

172.3
170.4
166.2
164.9
163.0
144.7
142.7
132.6
132.0
131.0
124.7
124.6
123.8
118.7
114.0
109.0
84.6
76.1
62.7
55.6
53.1
51.2
36.3
14.2
100MHz, CDCl3
MeO
Cl
CO2Me
9cf
OEt
f1 (ppm)

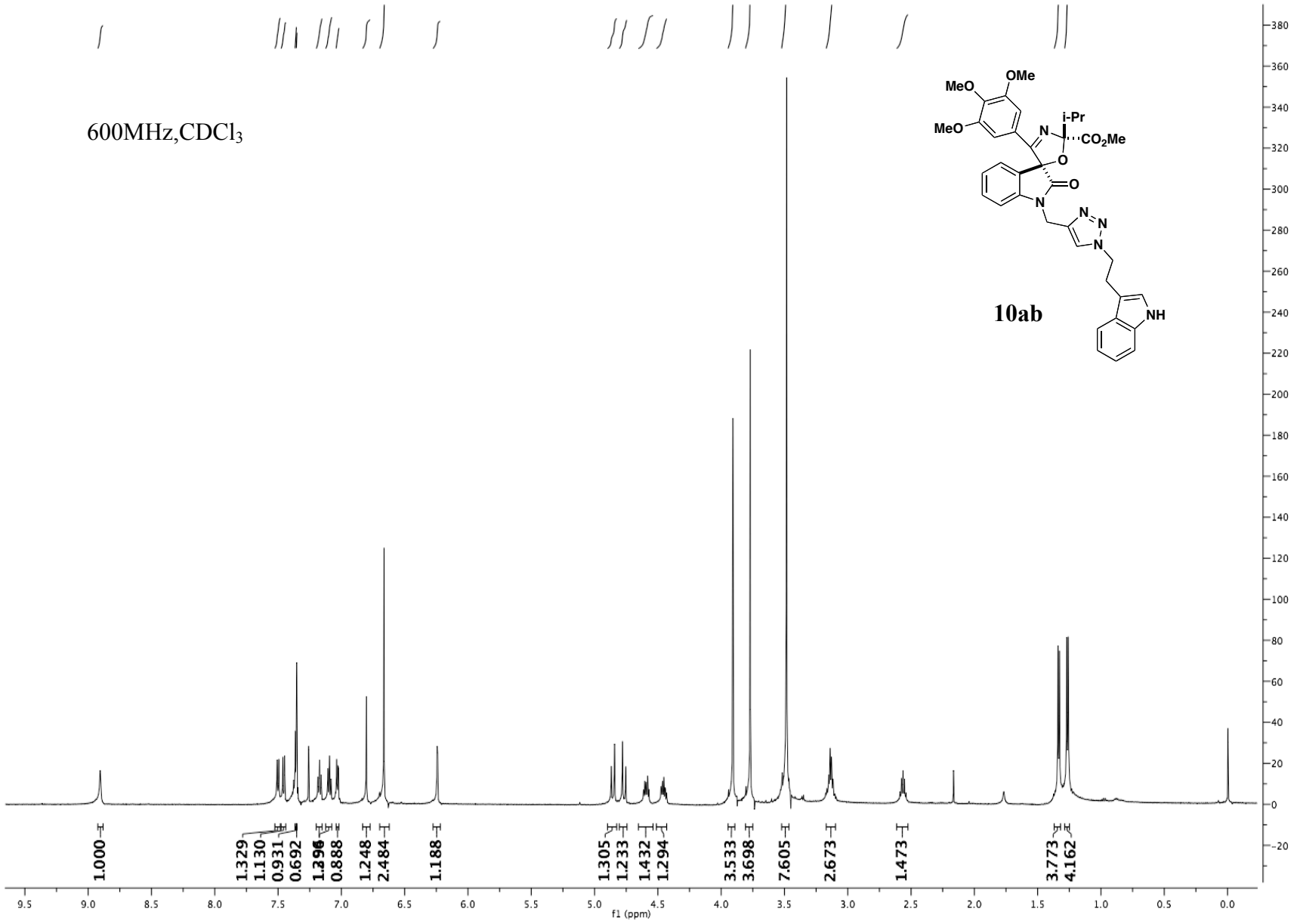
600MHz, $CDCl_3$

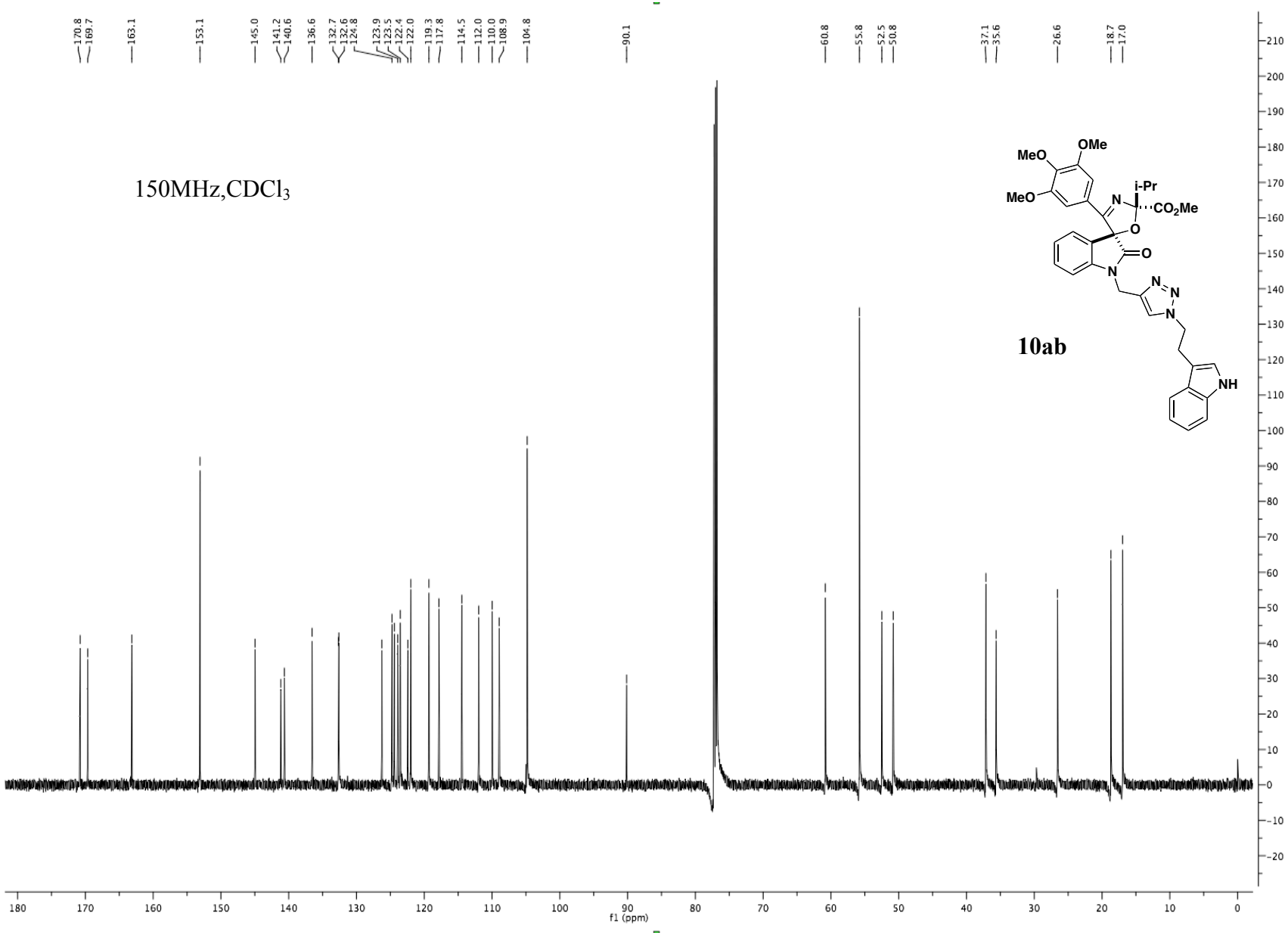


9cd

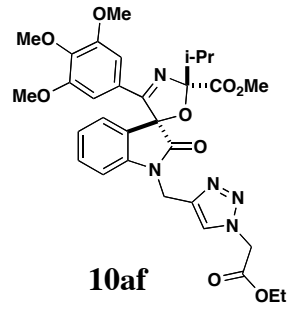

172.4
170.6
165.0
163.1
144.7
137.1
132.1
131.0
130.0
129.1
124.7
123.8
120.5
118.7
114.0
108.9
84.7
76.2
55.7
53.2
36.4
150MHz, CDCl3
MeO
Cl
O
N
CO2Me
O
N
N
N
N
9cd
f1 (ppm)


400MHz, CDCl3
MeO
OMe
MeO
i-Pr
CO2Me
N
O
O
N
N
N
N
OMe
10aa
0.79
4.45
1.34
0.97
2.04
2.00
3.22
3.29
3.15
6.50
0.81
7.00
f1 (ppm)

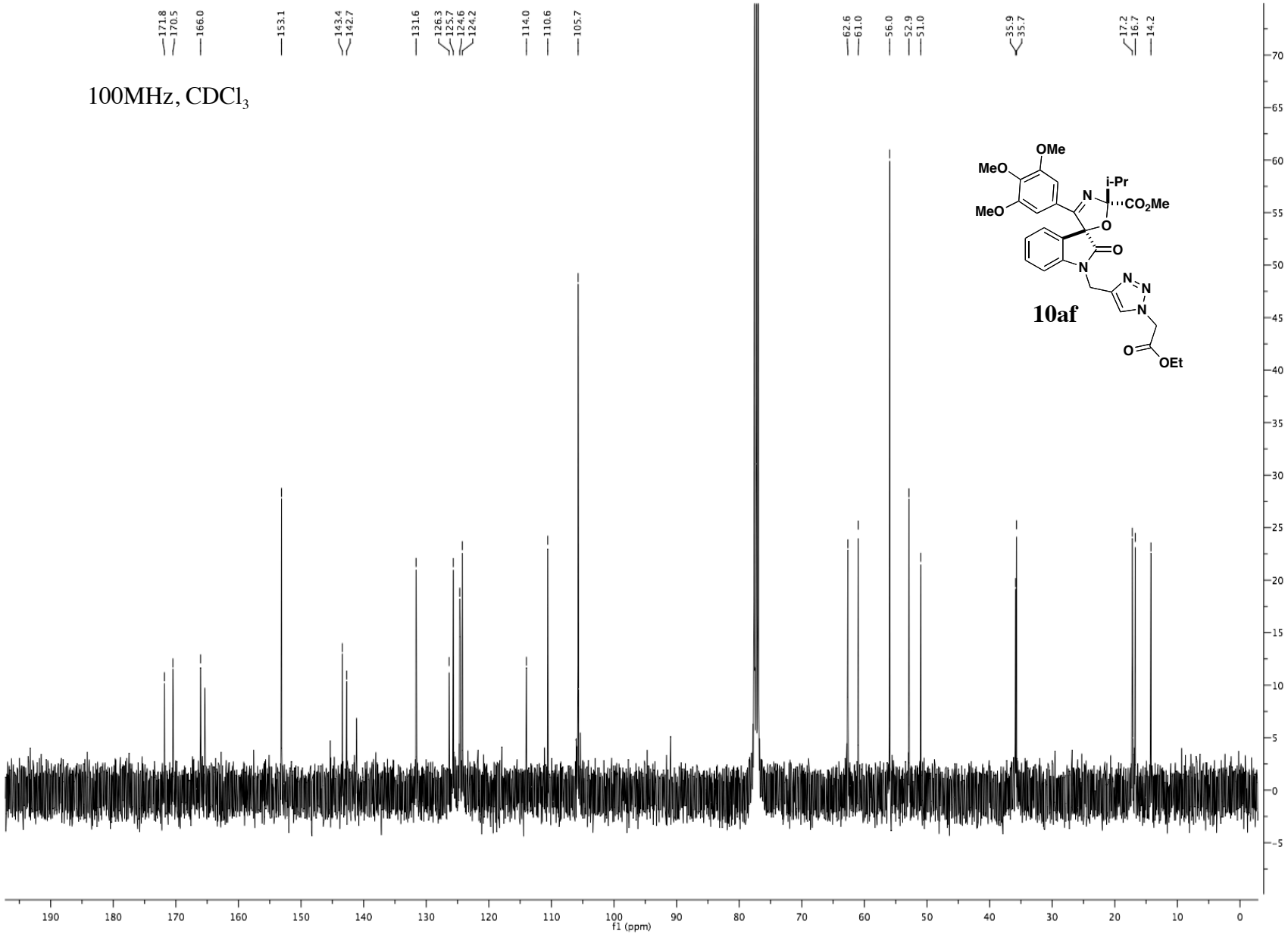

600MHz,CDCl3
MeO
OMe
MeO
i-Pr
CO2Me
10ab
NH
1.000
1.329
1.130
0.931
0.692
0.888
1.248
2.484
1.188
1.305
1.233
1.432
1.294
3.533
3.698
7.605
2.673
1.473
3.773
4.162
f1 (ppm)


170.8
169.7
163.1
153.1
145.0
141.2
140.6
136.6
132.7
132.6
124.8
123.9
123.5
122.4
122.0
119.3
117.8
114.5
112.0
110.0
108.9
104.8
90.1
60.8
55.8
52.5
50.8
37.1
35.6
26.6
18.7
17.0
150MHz,CDCl3
MeO
OMe
MeO
i-Pr
CO2Me
N
O
O
N
N
N
N
NH
10ab
f1 (ppm)

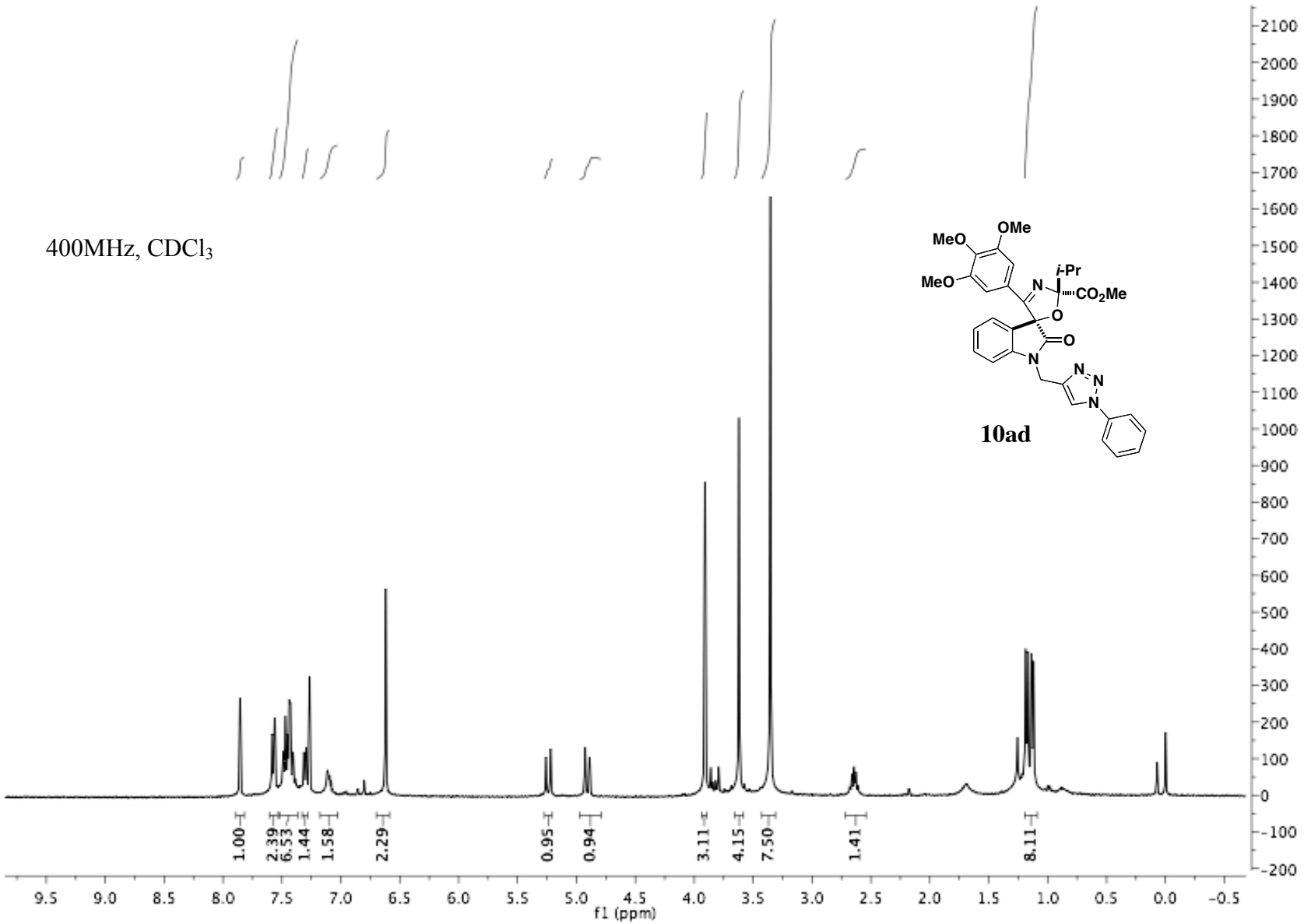
400MHz, $CDCl_3$

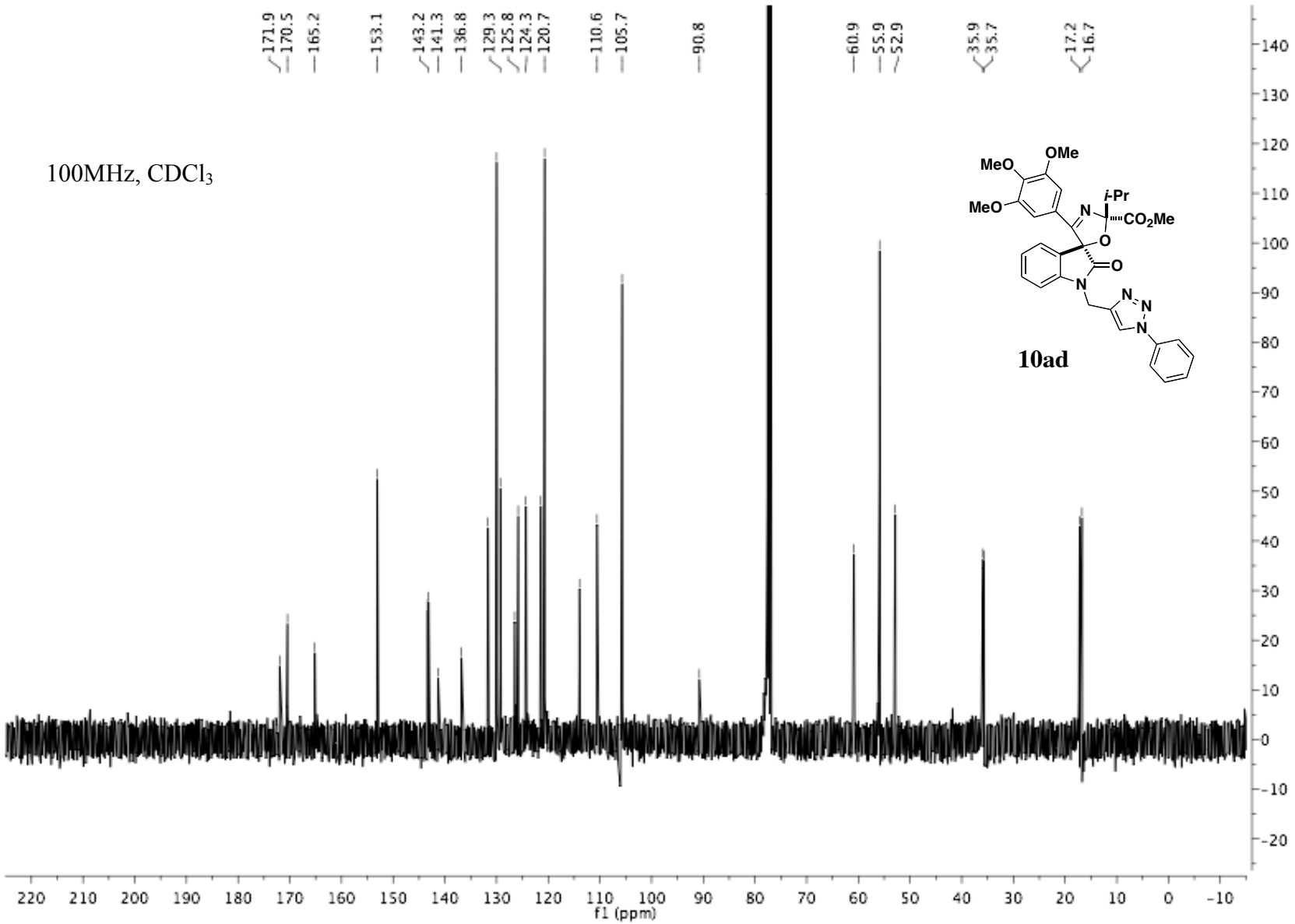


10af

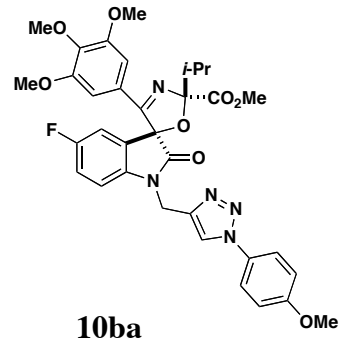

171.8
170.5
166.0
153.1
143.4
142.7
131.6
126.3
125.7
124.6
124.2
114.0
110.6
105.7
62.6
61.0
56.0
52.9
51.0
35.9
35.7
17.2
16.7
14.2
100MHz, CDCl3
OMe
MeO
MeO
i-Pr
CO2Me
10af
OEt
f1 (ppm)

400MHz, $CDCl_3$



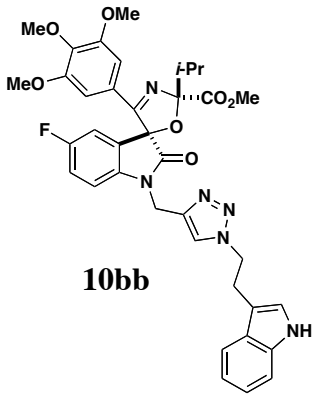

100MHz, CDCl3
171.9
170.5
165.2
153.1
143.2
141.3
136.8
129.3
125.8
124.3
120.7
110.6
105.7
90.8
60.9
55.9
52.9
35.9
35.7
17.2
16.7
MeO
OMe
MeO
i-Pr
CO2Me
N
O
O
N
N
N
N
10ad
f1 (ppm)

400MHz, $CDCl_3$



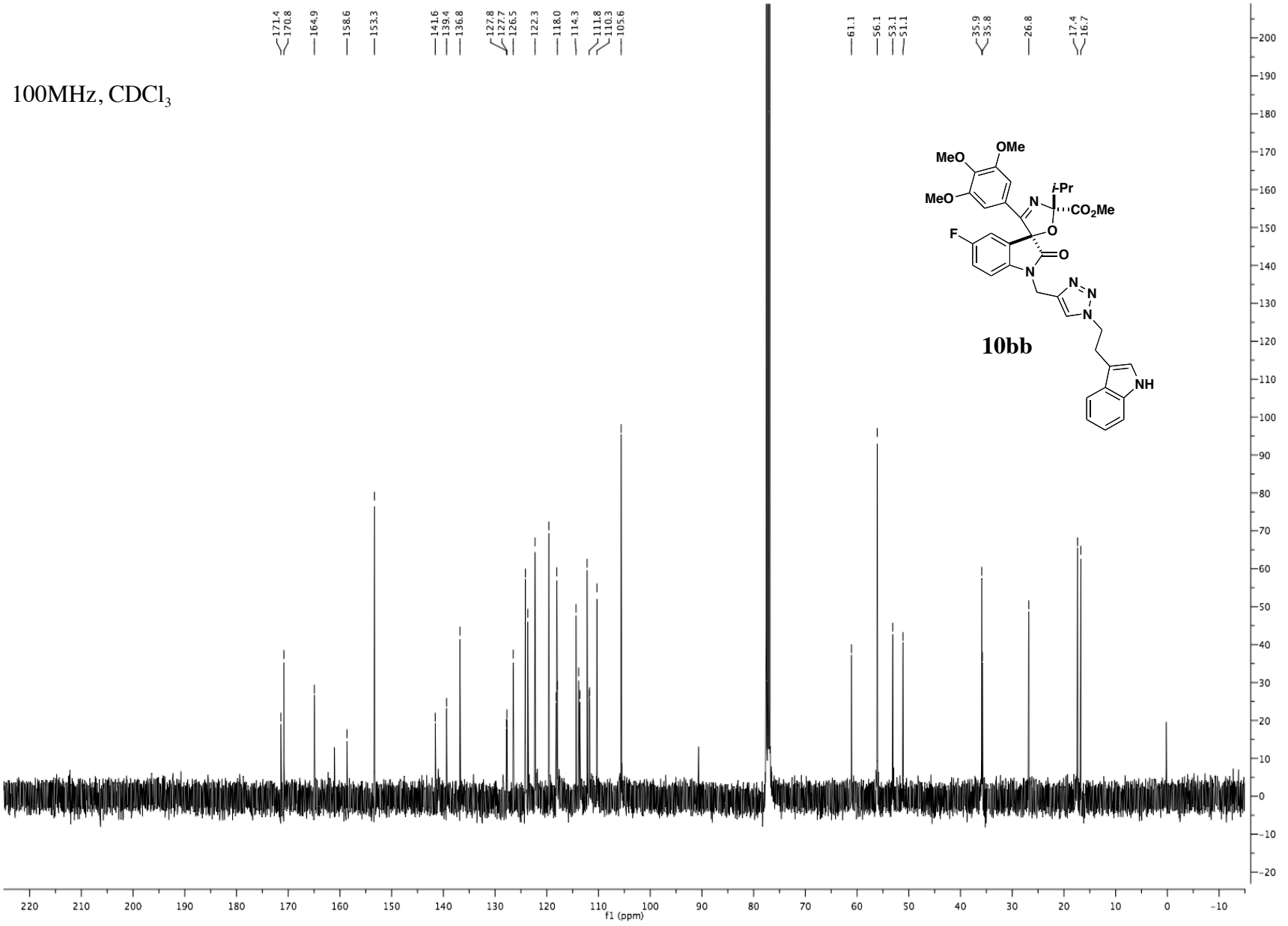
10ba

400MHz, $CDCl_3$

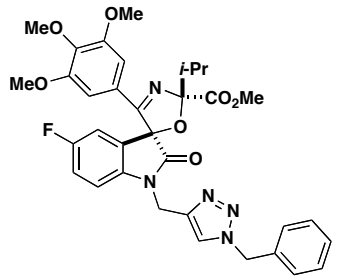


10bb

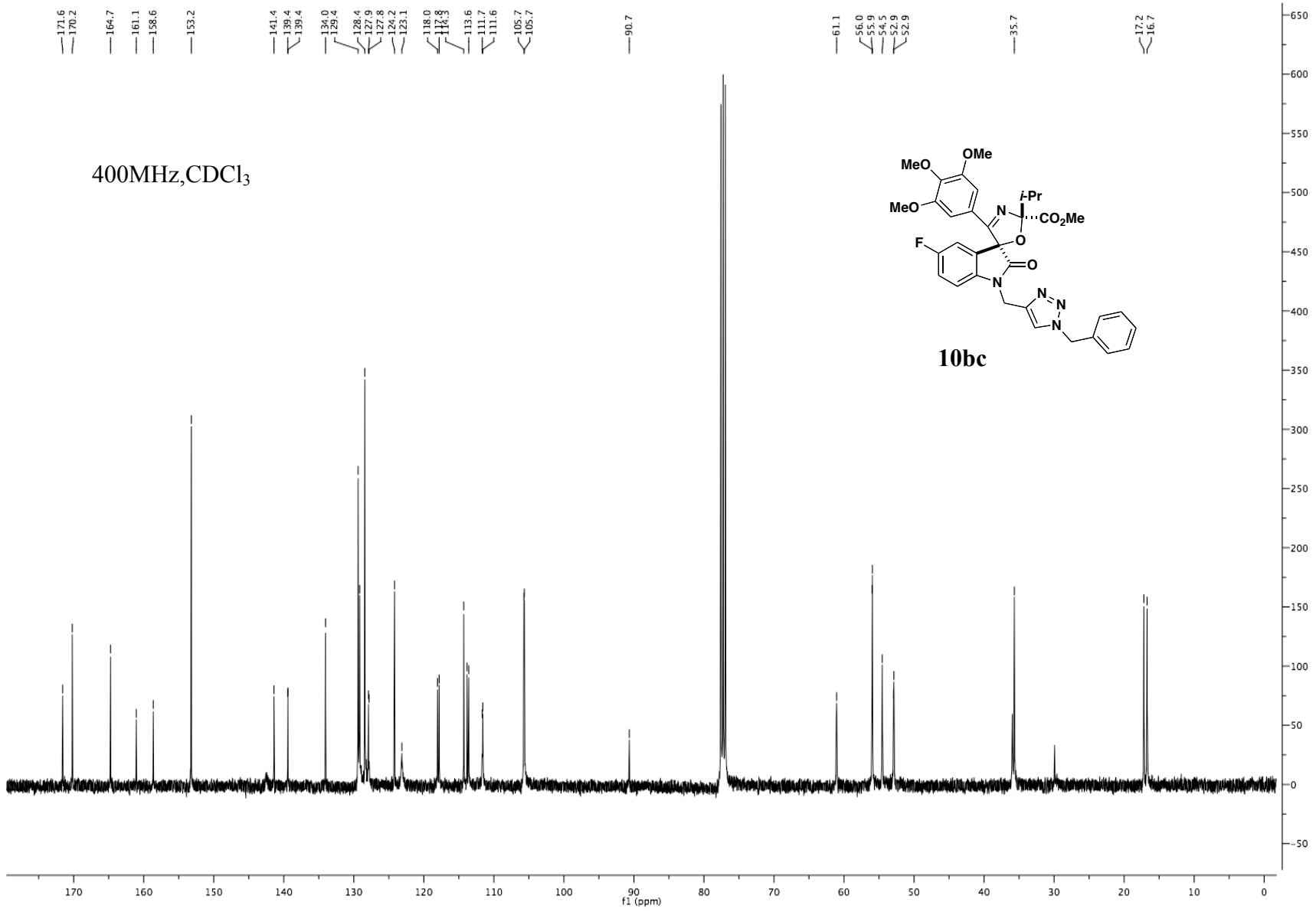
100MHz, $CDCl_3$



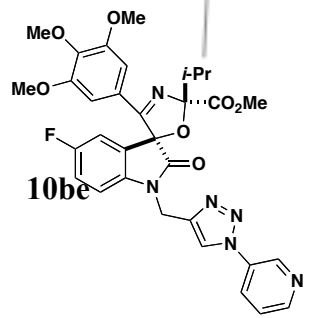
400MHz,$CDCl_3$



10bc

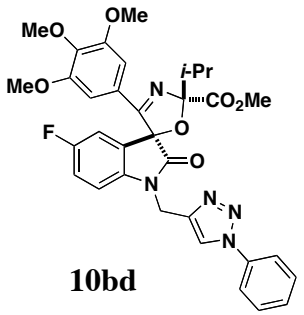

400MHz,CDCl3
10bc
171.6
170.2
164.7
161.1
158.6
153.2
141.4
139.4
139.4
134.0
129.4
128.4
127.9
127.8
124.2
123.1
118.0
113.6
111.7
111.6
105.7
105.7
90.7
61.1
56.0
55.9
54.5
52.9
52.9
35.7
17.2
16.7
f1 (ppm)

400 MHz, $CDCl_3$

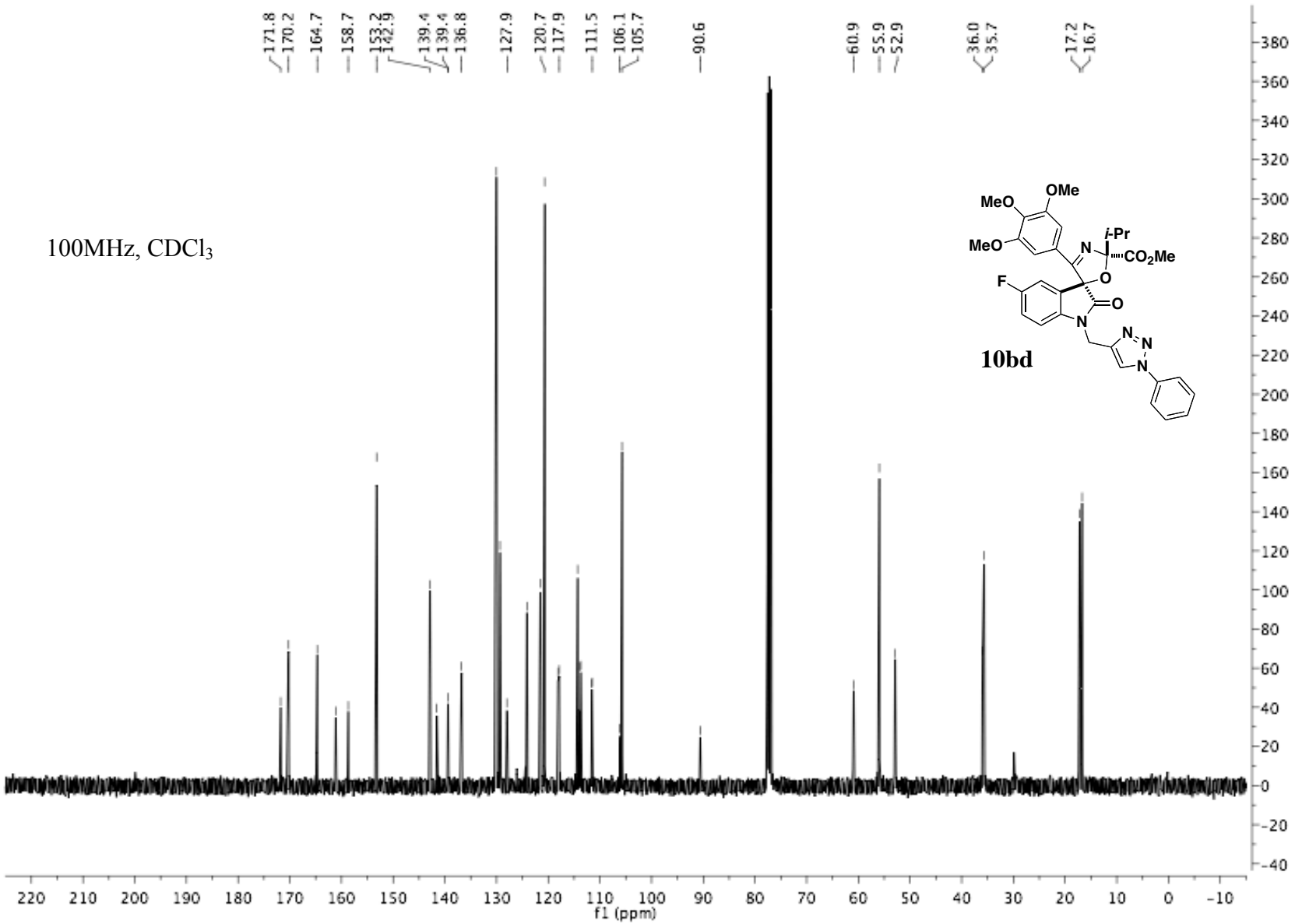


10be

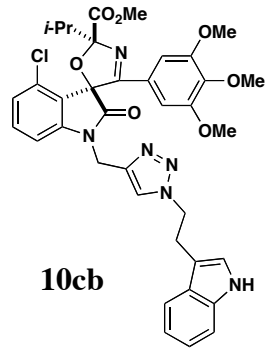
300MHz, $CDCl_3$



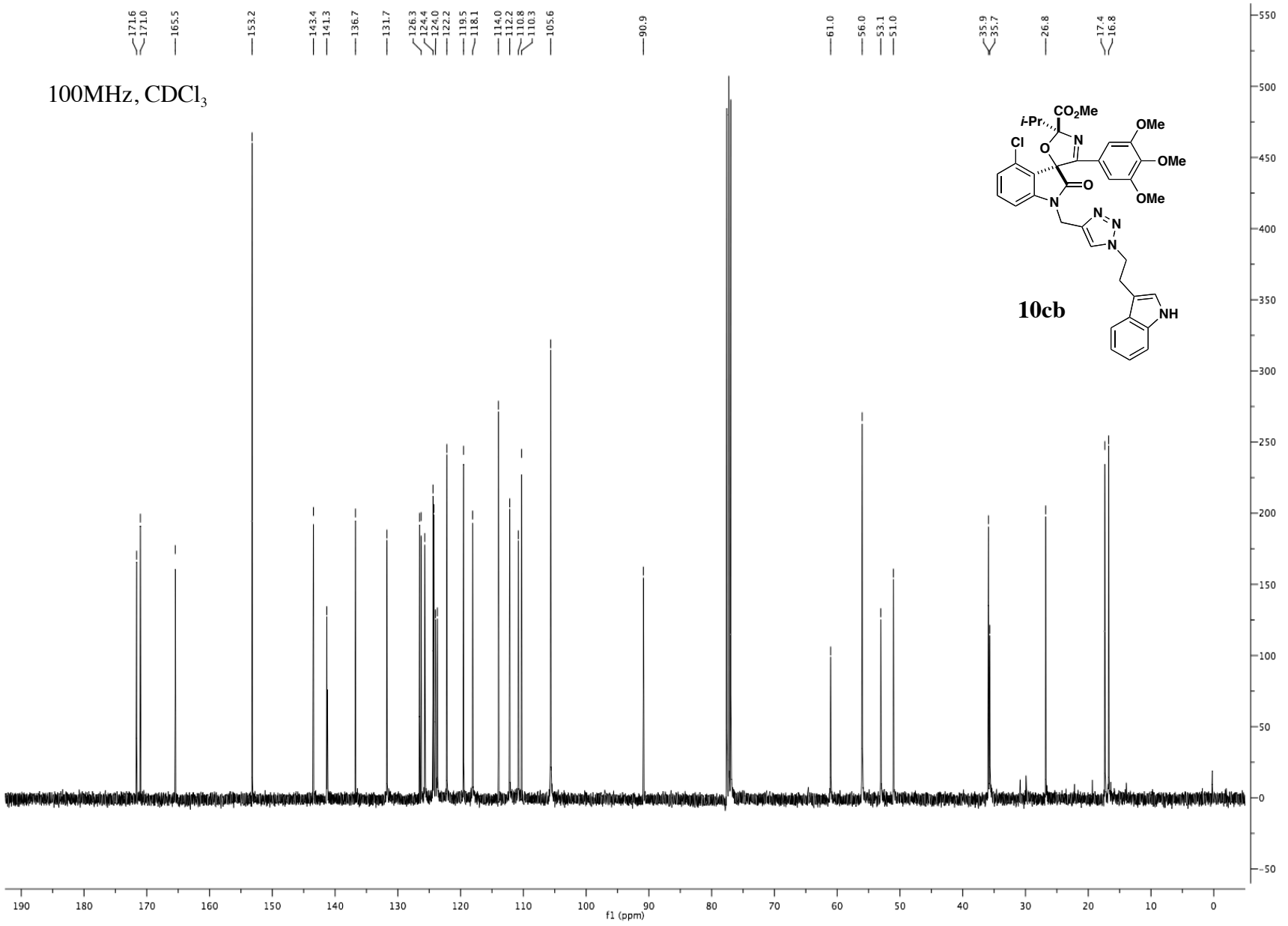
10bd


171.8
170.2
164.7
158.7
153.2
142.9
139.4
139.4
136.8
127.9
120.7
117.9
111.5
106.1
105.7
90.6
60.9
55.9
52.9
36.0
35.7
17.2
16.7
f1 (ppm)
100MHz, CDCl3
MeO
OMe
MeO
i-Pr
CO2Me
F
O
N
10bd

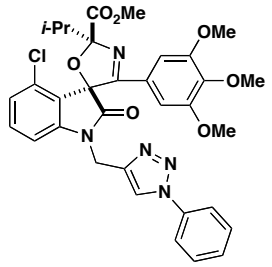
400MHz, $CDCl_3$



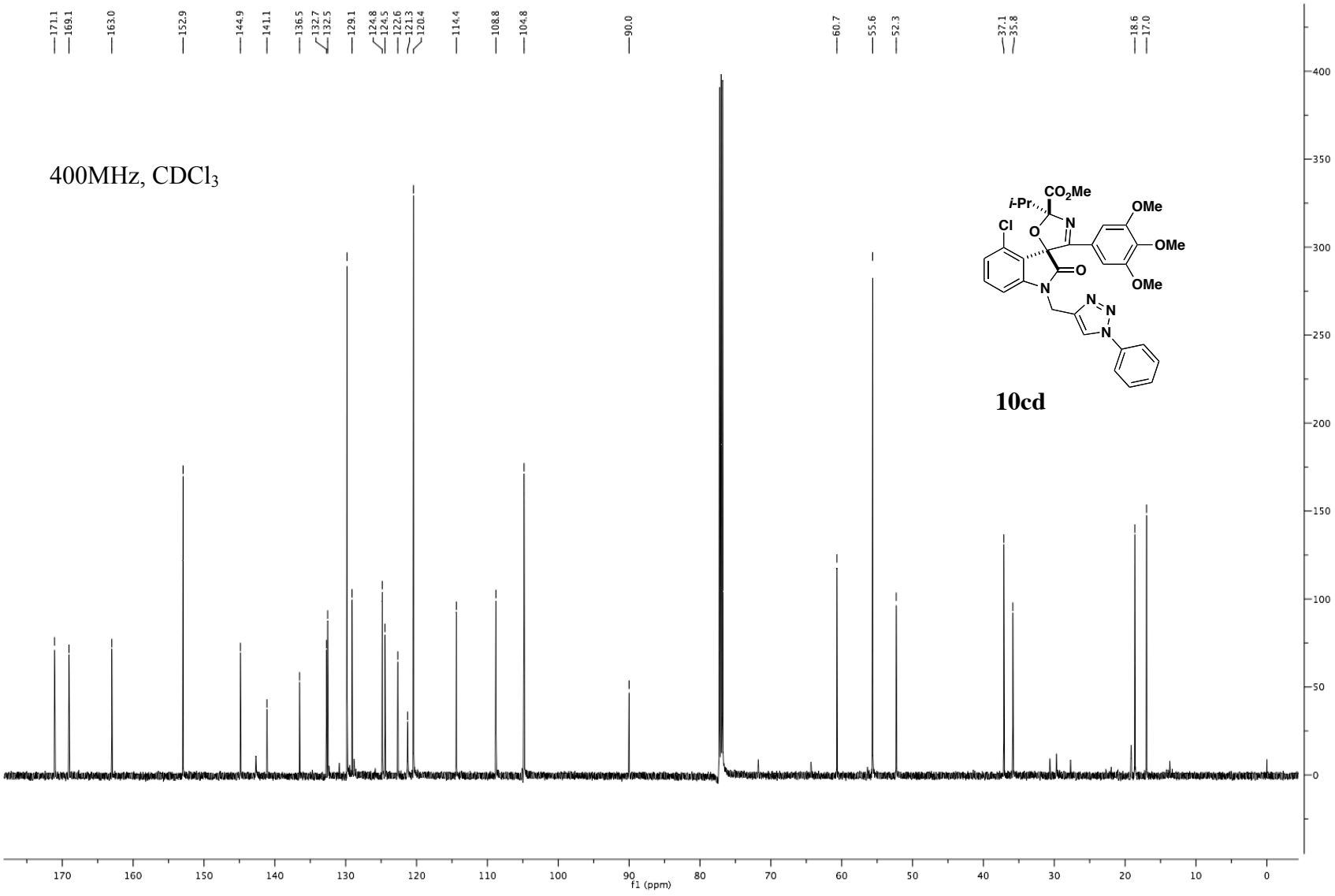
10cb


100MHz, CDCl3
171.6
171.0
165.5
153.2
143.4
141.3
136.7
131.7
126.3
124.4
124.0
122.2
119.5
118.1
114.0
112.2
110.8
110.3
105.6
90.9
61.0
56.0
53.1
51.0
35.9
35.7
26.8
17.4
16.8
i-Pr
CO2Me
Cl
O
N
OMe
OMe
OMe
O
N
N
N
N
NH
10cb
f1 (ppm)

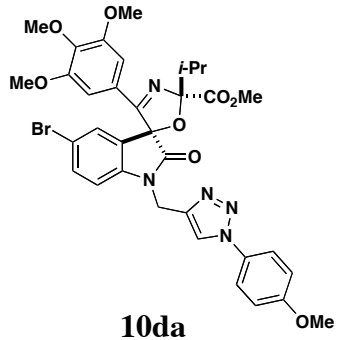
400MHz, $CDCl_3$



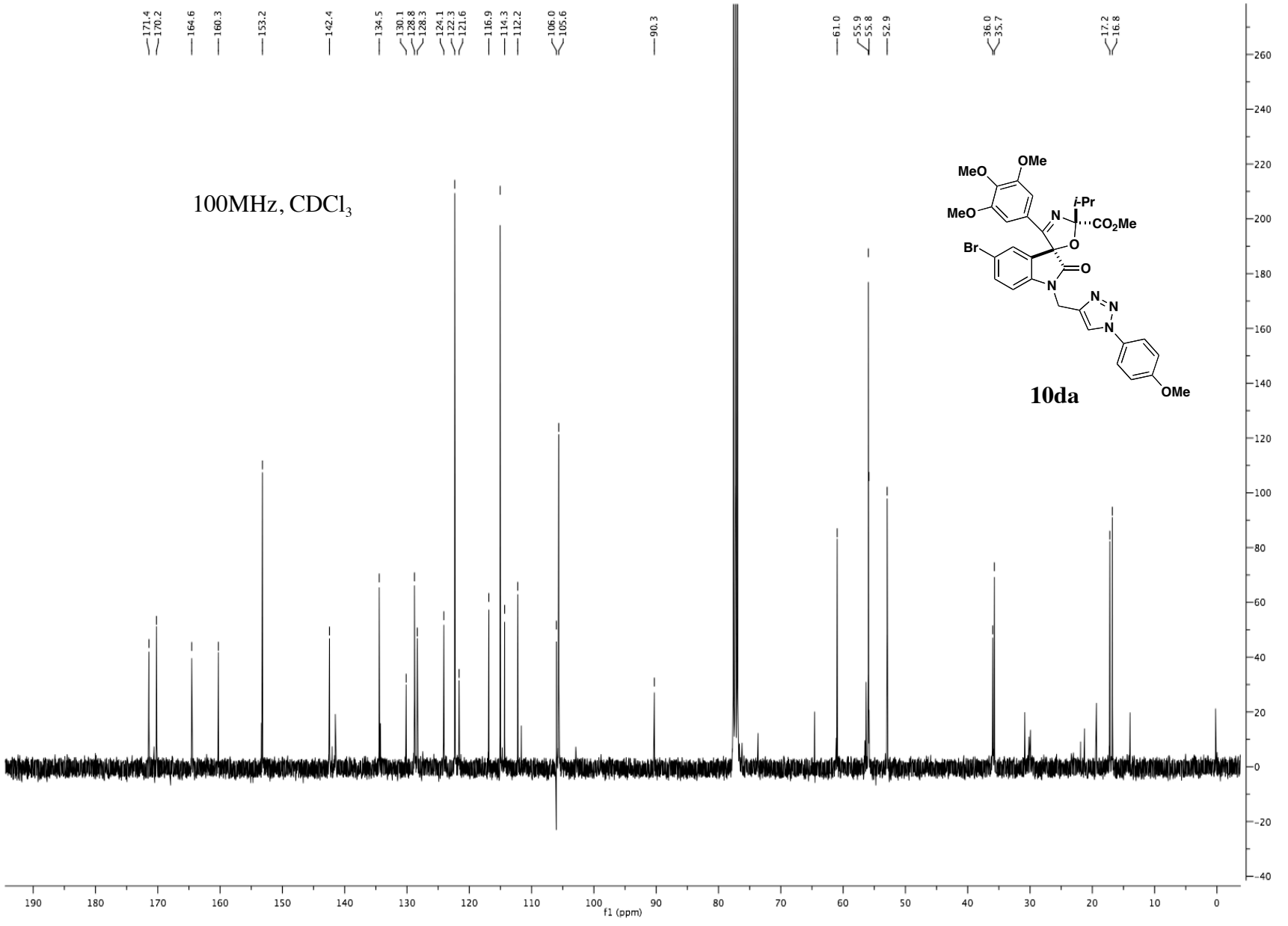
10cd


171.1
169.1
163.0
152.9
144.9
141.1
136.5
132.7
132.5
129.1
124.8
124.5
122.6
121.3
120.4
114.4
108.8
104.8
90.0
60.7
55.6
52.3
37.1
35.8
18.6
17.0
400MHz, CDCl3
CO2Me
i-Pr
Cl
O
N
OMe
OMe
OMe
O
N
N
N
N
10cd
f1 (ppm)

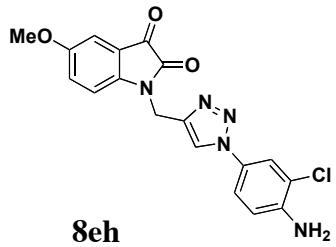
400MHz, $CDCl_3$



10da

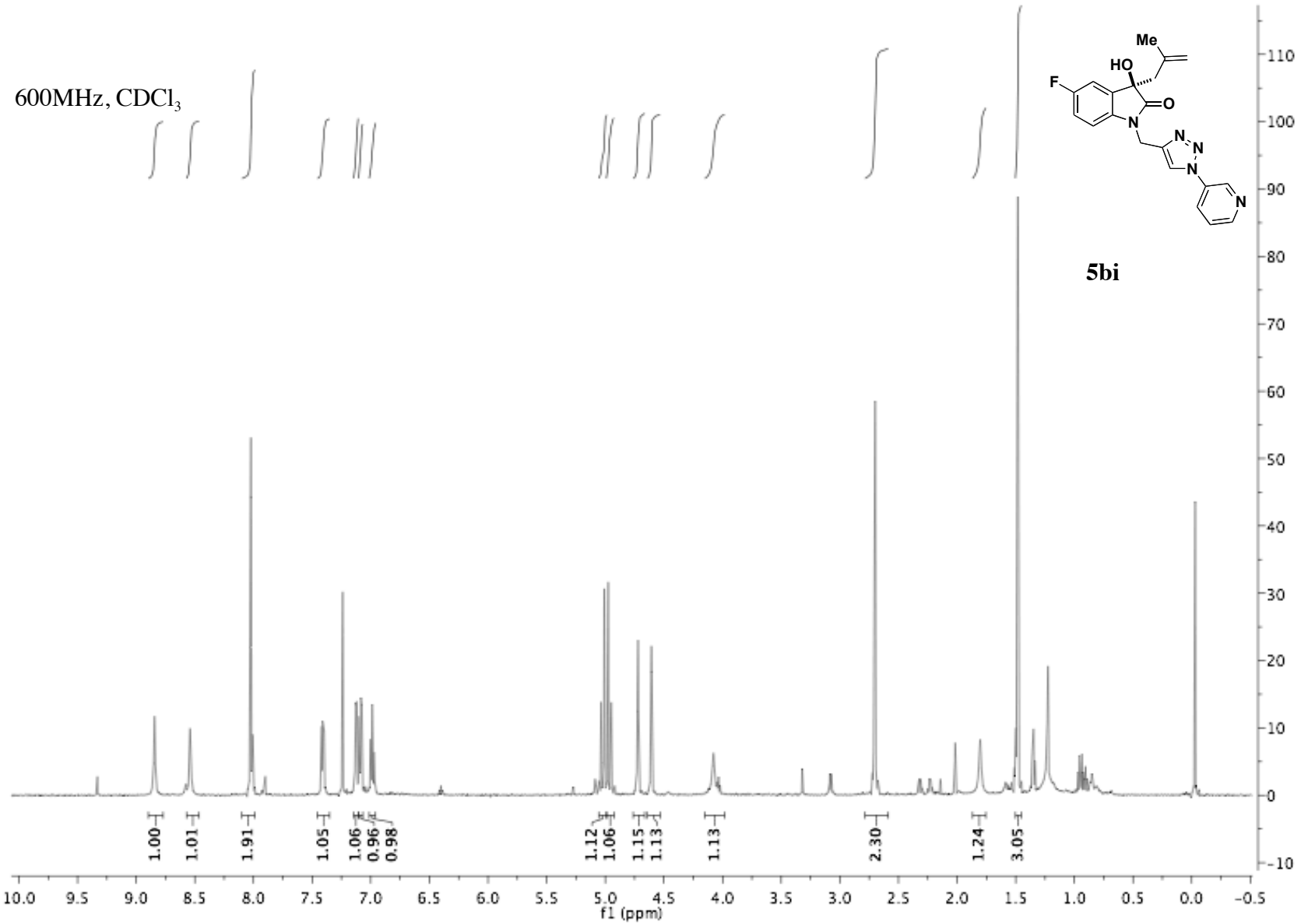

171.4
170.2
164.6
160.3
153.2
142.4
134.5
130.1
128.8
128.3
124.1
122.3
121.6
116.9
114.3
112.2
106.0
105.6
90.3
61.0
55.9
55.8
52.9
36.0
35.7
17.2
16.8
100MHz, CDCl3
MeO
OMe
MeO
i-Pr
CO2Me
Br
O
O
N
N
N
N
OMe
10da
f1 (ppm)

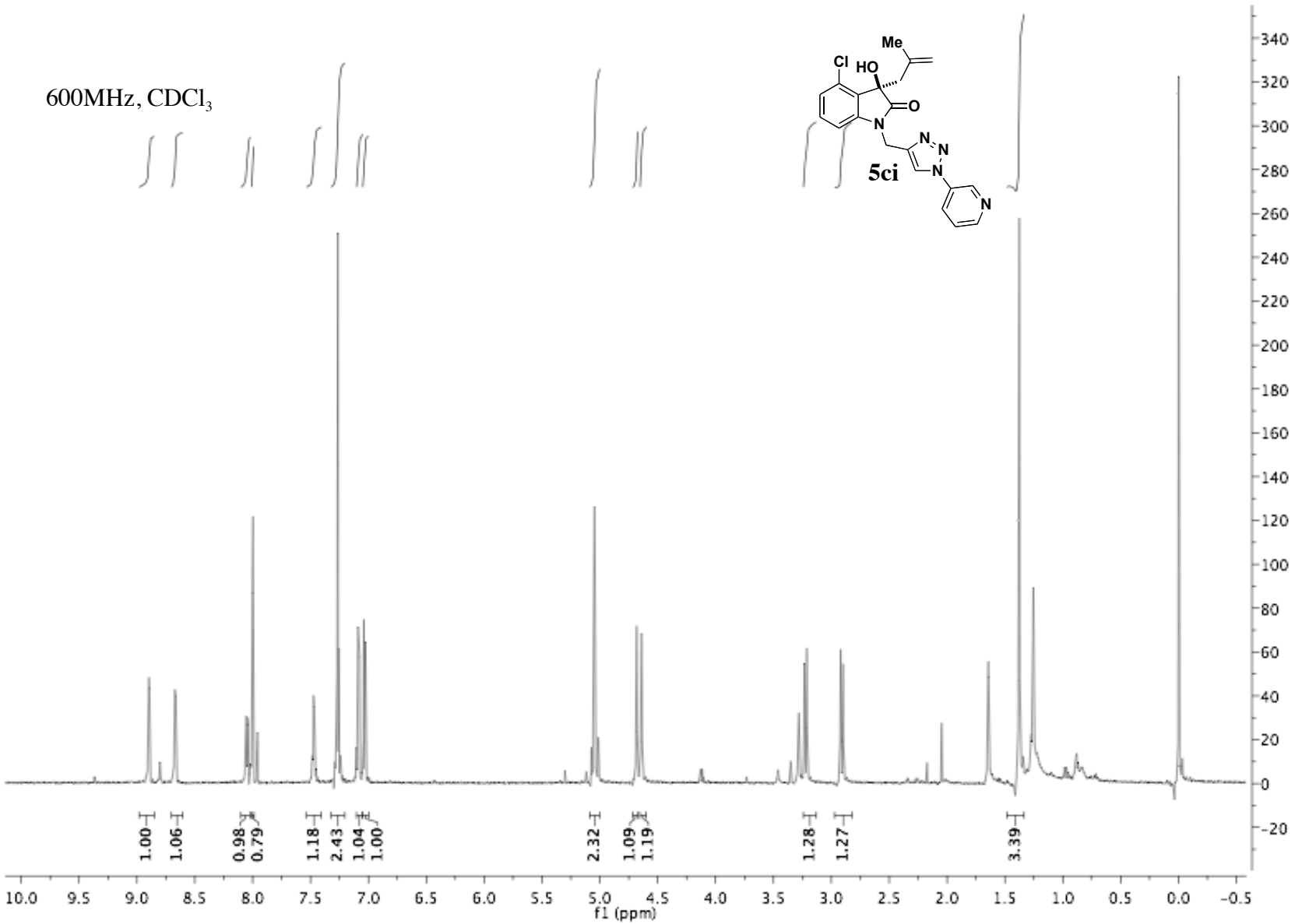
600MHz, 3:1 $CDCl_3$:CD_3OD



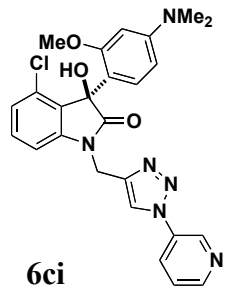
8eh

600MHz, $CDCl_3$




600MHz, CDCl3
Me
Cl
HO
O
N
N
N
N
N
5ci
1.00
1.06
0.98
0.79
1.18
2.43
1.04
1.00
2.32
1.09
1.19
1.28
1.27
3.39
f1 (ppm)

400MHz, CD_3OD



6ci