Direct N-H/α, α, β, β-C(sp^3)-H functionalization of Piperidine via an Azomethine Ylide Route：Synthesis of Spirooxindoles Bearing 3-Substituted Oxindoles

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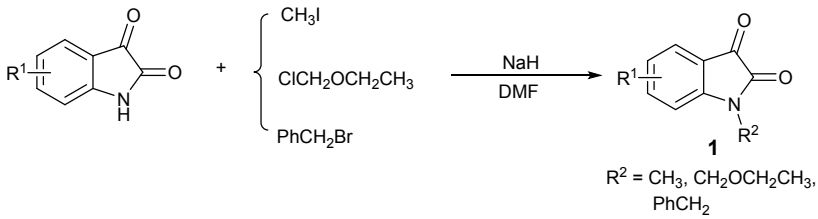
Contents

1. General information and materials

All reactions were performed under Ar atmospheres in oven-dried glassware with magnetic stirring. Unless otherwise stated, all reagents including isatins, **1w**, **3d**, 3-bromoprop-1-ene, sodium benzenesulfinate, sodium 4-methylbenzenesulfinate, sodium 4-chlorobenzenesulfinate, 1H-indene-1,2,3-trione, phenanthrene-9,10-dione and 9H-fluoren-9-one were purchased from commercial suppliers (Aldrich, TCI or Alfa Aesar) and used without further purification. All solvents were purified and dried according to standard methods prior to use. TLC monitored all reactions with silica gel-coated plates. Flash column chromatography was performed using 200-300 mesh silica gel. ^{1}H- and ^{13}C-NMR spectrum was recorded at ambient temperature on Bruker 400 instruments. All spectra were referenced to $CDCl_3$ (^{1}H δ 7.26 ppm and ^{13}C NMR δ 77.00 ppm). HRMS were obtained on Waters Xevo Q-TOF MS with ESI resource. Melting points were measured on a RY-I apparatus and are reported uncorrected. Compound **1x** was synthesized according to literature.[1] Compounds **3e** [2], **3f** [3] were synthesized according to literatures.

1. J. H. Yao, C. Chi, J. Wu and K.-P. Loh *Chem. Eur. J.*, 2009, **15**, 9299-9302.
2. F. Caturla and C. Nájera, Tetrahedron, 1996, **52**, 15243-15256.
3. T. Llamas, R. Gómez, Arrayás and J. C. Carretero, *Org. Lett.*, 2006, **8**, 1795-1798.

2. Synthesis of N-protected isatins 1



Under Ar atmosphere, to a solution of isatin (10 mmol, 1.0 eq) in DMF 45 ml was added NaH (12 mmol, 1.2 eq.) in portions at 0 °C. After stirring for 5 min, MeI (12 mmol, 1.2 eq.), $ClCH_2OCH_2CH_3$ (12 mmol, 1.2 eq.) or BnBr (12 mmol, 1.2 eq.) was added to the above mixture slowly. After warming to room temperature, the reaction mixture was stirred for 12-20 h. The reaction was then quenched by water and extracted with EtOAc. The organic layer was separated and washed with water, then the ethyl acetate layer was dried over $MgSO_4$, filtered and concentrated in vacuum. The crude product was purified by chromatography (SiO_2, ethyl acetate : petroleum ether = 1:2). The spectral data consist with the data reported in the literatures.

Entry	R^1	R^2	Time (h)	Yield (%)
1	5-CH_3 (**1a**) [4]	CH_3	16	82
2	H (**1b**) [4]	CH_3	16	89
3	5-CH_3O (**1c**) [4]	CH_3	12	98
4	5-^{t}Bu (**1d**) [5]	CH_3	16	90
5	5-F (**1e**) [4]	CH_3	20	69
6	5-Cl (**1f**)	CH_3	16	78
7	5-Br (**1g**)[6]	CH_3	16	75
8	5-OCF_3 (**1h**)[7]	CH_3	16	58
9	5-NO_2 (**1i**)[6]	CH_3	16	46
10	5,6-F_2 (**1j**)	CH_3	12	64
11	6-Br (**1k**)[8]	CH_3	16	77
12	7-CH_3 (**1l**) [4]	CH_3	12	86
13	7-Cl (**1m**)[9]	CH_3	16	76
14	7-Br (**1n**)[10]	CH_3	16	70
15	4-Br (**1o**)[8]	CH_3	16	66
16	H (**1p**)	CH_2OEt	12	80
17	5-CH_3 (**1q**)	CH_2OEt	12	83
18	5-Br (**1r**)	CH_2OEt	12	67
19	H (**1s**) [4]	CH_2Ph	12	88
20	5-CH_3 (**1t**)[11]	CH_2Ph	12	86
21	5-Cl (**1u**)[11]	CH_2Ph	12	90
22	5-Br (**1v**)[12]	CH_2Ph	12	71

The spectral data of known N-methyl isatins as below:

4. B.-X. Tang, R.-J. Song, C.-Y. Wu, Y. Liu, M.-B. Zhou, W.-T. Wei, G.-B. Deng, D.-L. Yin, and J.-H. Li, *J. Am. Chem. Soc.*, 2010, **132**, 8900-8902.

5. W. Li, Z. Duan, X. Zhang, H. Zhang, M. Wang, R. Jiang, H. Zeng, C. Liu and A. Lei, *Angew. Chem. Int. Ed.*, 2015, **54**, 1893-1896.

6. A. Beauchard, Y. Ferandin, S. Frère, O. Lozach, M. Blairvacq, L. Meijer, V. Thiéry and T. Besson, *Bioorg. Med. Chem.*, 2006, **14**, 6434-6443.

7. A. D. Mamuye, S. Monticelli, L. Castoldi, W. Holzer and V. Pace, *Green Chem.*, 2015, **17**, 4194-4197

8. Y. Wang, W. Li, X. Cheng, Z. Zhan, X. Ma, L. Guo, H. Jin and Y. Wu, *Tetrahedron*, 2016, **72**, 3193-3197.

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10. K. Engen, J. Sävmarker, U. Rosenström, J. Wannberg, T. Lundbäck, A. Jenmalm-Jensen and M. Larhed, *Org. Process Res. Dev.*, 2014, **18**, 1582-1588.

11. G. Satish, A. Polu, T. Ramar and A. Ilangovan, *J. Org. Chem.*, 2015, **80**, 5167-5175.

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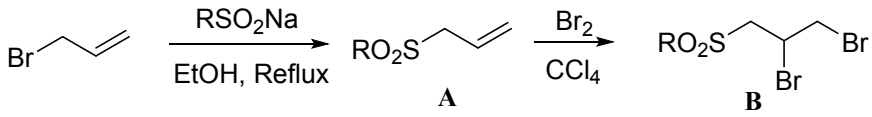
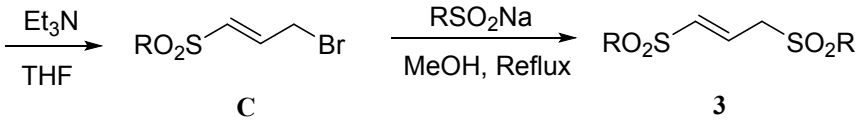
3. Synthesis of 3





R = Ph, **3a**
R = p-ClPh, **3b**
R = p-CH_3Ph, **3c**

Entry	R	**A**	**B**	**C**	3
1	Ph	89%	85%	65%	**3a**, 87%
2	p-ClC_6H_4	75%	80%	62%	**3b**, 94%
3	p-$CH_3C_6H_4$	88%	89%	90%	**3c**, 84%

3a as an example

Under Ar atmosphere, to a well stirred ethanol (60 mL) solution of sodium benzenesulfinate (10.00 g, 82.60 mmol) was added 3-bromoprop-1-ene (13.57 g, 82.66 mmol). The reaction mixture was refluxed for 4 h. After cooling to room temperature, the reaction mixture was filtrated and removed the white solid. The filtrate was concentrated under vacuum and the crude product **A** (13.4 g, 89%) was taken for the next reaction.

To a well stirred CCl_4 (26 mL) solution of **A** (13 g, 71.34 mmol) was added a CCl_4 (10 mL) solution of Br_2 (11.96 g, 74.90 mmol) dropwise. After completion of the reaction (monitored by TLC), the reaction was quenched by addition of saturated aqueous $NaHSO_3$ solution and extracted by CH_2Cl_2 (50

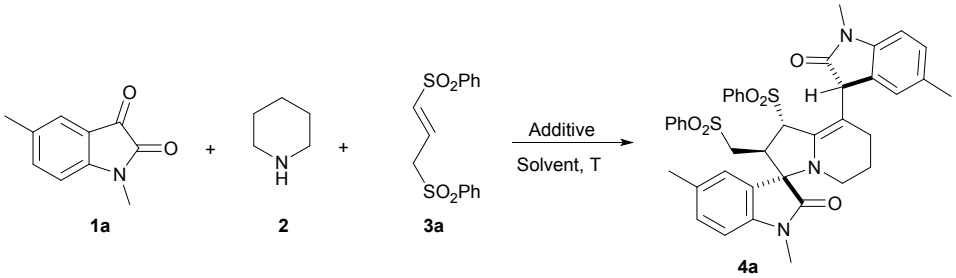
mL × 3). The organic layer was separated and dried over anhydrous Na_2SO_4. The organic layer was concentrated under vacuum, and the crude product **B** (20.82 g, 85%) was taken for the next reaction.

To a THF (55 mL) solution of **B** (20 g, 58.47 mmol) was added Et_3N (6.21 g, 61.39 mmol) dropwise at 0 ^oC, and the reaction mixture was stirred under the same temperature for 1 h. After completion of the reaction (monitored by TLC), the reaction was acidified by addition of HCl (1M) and extracted by CH_2Cl_2 (50 mL × 3). The combined organic extract was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was recrystallized (ethanol) to afford the pure product **C** (10.34 g, 65%).

To a CH_3OH (25 mL) solution of **C** (5.00 g, 19.15 mmol) was added sodium benzenesulfinate (6.29 g, 38.30 mmol), and the reaction mixture was refluxed for 3 h. After completion of the reaction (monitored by TLC), the reaction was quenched by addition of 30 mL saturated aqueous ammonium chloride solution. The organic layer was extracted with CH_2Cl_2 (30 mL×3), and then washed with a saturated aqueous sodium bicarbonate solution. The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product (**3a**, 5.4 g, 87%) was used in the next step without further purification. The spectral data (**3a**, **3b**) consist with the data reported in the literatures.[13]

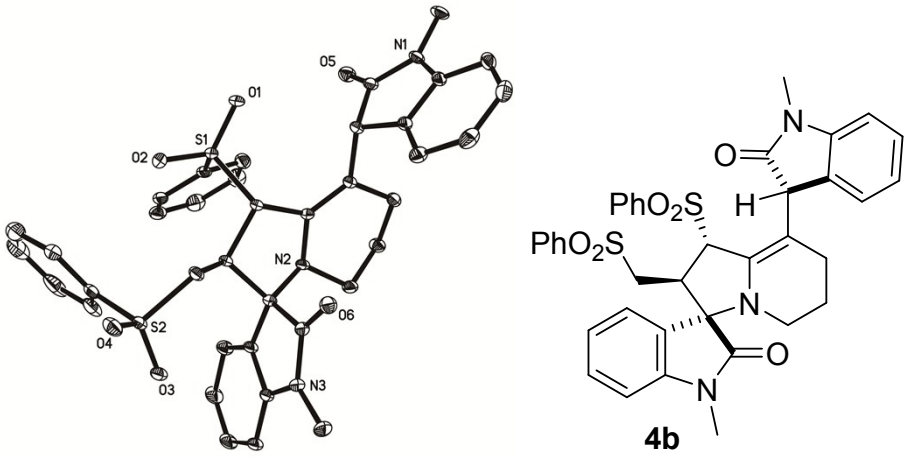
13. (a) P. R. Joshi, S. Undeela, D. D. Reddy, K. K. Singarapu and R. S. Menon, *Org. Lett.*, 2015, **17**, 1449-1452. (b) C. Nájera, A. Pérez-Pinar and J. M. Sansano, *Tetrahedron*, 1991, **47**, 6337-6352.

4. Optimization of the domino reaction

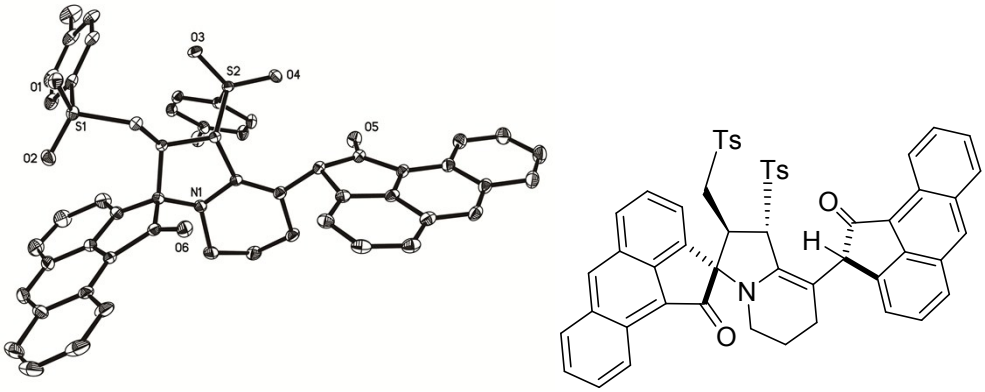


Entry	Ratio	Additive	Solvent	T (°C)	Yield (%)
1	1.2:1.2:1	4-TFBA (0.1)	toluene	110	42
2	1.2:1.2:1	4-TFBA (0.3)	toluene	110	51
3	1.2:1.2:1	4-TFBA (0.5)	toluene	110	54
4	1.2:1.2:1	4-TFBA (0.7)	toluene	110	50
5	1.2:1.2:1	4-TFBA (1.2)	toluene	110	68
6	1.2:1.2:1	4-TFBA	toluene	90	40
7	1.2:1.2:1	4-TFBA	toluene	70	trace
8	1.2:1.2:1	4-TFBA	toluene	50	trace
9	1.4:1.2:1	4-TFBA	toluene	110	70
10	1.6:1.2:1	4-TFBA	toluene	110	64
11	1.8:1.2:1	4-TFBA	toluene	110	62
12	2.4:1.2:1	4-TFBA	toluene	110	66

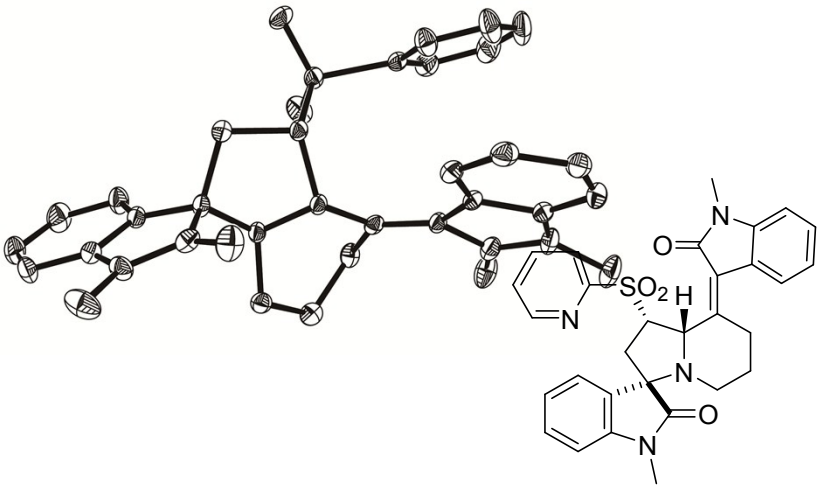
5. Crystal structures of 4b, 5f and 7



Crystal structure of **4b**



Crystal structure of **5f**



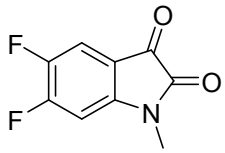
Crystal structure of **7**

6. General procedure for the synthesis of 4

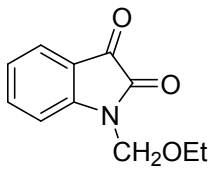
4a as an example

To a stirred solution of **3a** (100 mg, 0.31 mmol) in toluene (2 mL), 4-(trifluoromethyl)benzoic acid (59 mg, 0.31 mmol), piperidine (32 mg, 0.37 mmol), and **1a** (65 mg, 0.37 mmol) were added under argon atmosphere, and the reaction mixture was stirred for 1 h at 110 °C. After the reaction complete (monitored by TLC), the reaction was quenched by the addition of water (5 mL), extracted by CH_2Cl_2 (10 mL×3). Combined the organic phase and washed with saturated $NaHCO_3$ solution (10 mL×3), and dried with Na_2SO_4. The solvent was evaporated and the reside was purified by silica-gel column chromatography (ethyl acetate : petroleum ether = 1:1) to give **4a** (93 mg, 70%) as colorless solid.

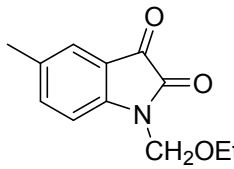
7. NMR spectra data



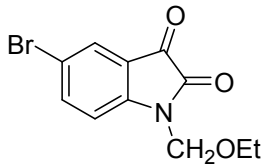
5,6-difluoro-1-methylindoline-2,3-dione (1j): 64%, red solid; R_f (ethyl acetate : petroleum ether = 1:2) = 0.60; m.p. 138-139 °C; IR(KBr): 3063, 1738, 1627, 1615, 1498, 1474, 1434, 1388 1247, 1104 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.47 (t, *J* = 7.8 Hz, 1H), 6.75 (dd, *J* = 9.2, 5.6 Hz, 1H), 3.24 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 180.88, 157.75, 156.93 (dd, *J* = 260.7, 14.2 Hz), 149.08 (dd, *J* = 10.0, 1.6 Hz), 147.30 (dd, *J* = 246.2, 13.6 Hz), 114.72 (dd, *J* = 19.3, 2.9 Hz), 112.65 (t, *J* = 4.5 Hz), 100.59 (d, *J* = 23.3 Hz), 26.41 ppm; ESI-HRMS: calcd. For $C_9H_5F_2NO_2$+H 198.0367, found 198.0371.



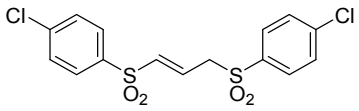
1-(ethoxymethyl)indoline-2,3-dione (1p): 80%, yellow solid; R_f (ethyl acetate : petroleum ether = 1:2) = 0.50; m.p. 81-82 °C; IR(KBr): 2975, 1741, 1727, 1605, 1470, 1343, 1287, 1222, 1191, 1095, 1077 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.52 – 7.77 (m, 2H), 7.02 – 7.21 (m, 2H), 5.18 (s, 2H), 3.56 (q, *J* = 7.0 Hz, 2H), 1.18 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 182.91, 158.22, 150.22, 138.53, 125.30, 124.16, 117.46, 111.59, 70.08, 64.63, 14.76 ppm; ESI-HRMS: calcd. For $C_{11}H_{11}NO_3$+H 206.0817, found 206.0815.



1-(ethoxymethyl)-5-methylindoline-2,3-dione (1q): 83%, orange solid; R_f (ethyl acetate : petroleum ether = 1:2) = 0.55; m.p. 94-95 °C; IR(KBr): 2970, 1745, 1735, 1619, 1598, 1491, 1456, 1355, 1331, 1298, 1220, 1096 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.34 – 7.51 (m, 2H), 7.02 (d, *J* = 8.0 Hz, 1H), 5.15 (s, 2H), 3.55 (q, *J* = 6.8 Hz, 2H), 2.33 (s, 3H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 183.14, 158.39, 148.08, 139.03, 134.03, 125.52, 117.49, 111.39, 70.06, 64.54, 20.63, 14.76 ppm; ESI-HRMS: calcd. For $C_{12}H_{13}NO_3$+H 220.0974, found 220.0977.

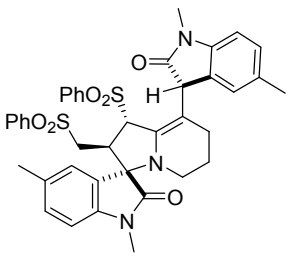


5-bromo-1-(ethoxymethyl)indoline-2,3-dione (1r): 67%, orange solid; R_f (ethyl acetate : petroleum ether = 1:2) = 0.48; m.p. 103-104 °C; IR(KBr): 2968, 1746, 1607, 1473, 1441, 1348, 1320, 1284, 1223, 1093, 1077 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.87 – 7.63 (m, 2H), 7.07 (dd, *J* = 8.2, 0.6 Hz, 1H), 5.18 (s, 2H), 3.56 (q, *J* = 7.0 Hz, 2H), 1.19 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 181.81, 157.44, 148.89, 140.80, 128.05, 118.63, 117.16, 113.43, 70.18, 64.75, 14.75 ppm; ESI-HRMS: calcd. For $C_{11}H_{10}BrNO_3$+H 283.9922, found 283.9915.



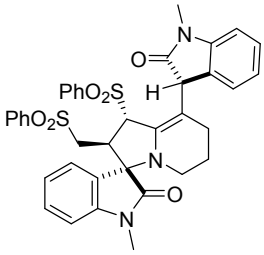
(E)-4,4'-(prop-1-ene-1,3-diyldisulfonyl)bis(chlorobenzene) (3b): white solid; R_f (ethyl acetate : petroleum ether = 1:2) = 0.47; m.p. 135-136 °C; IR(KBr): 2361, 2342, 1577, 1559, 1473, 1396, 1320, 1279, 1150, 1086, 1012 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.65 – 7.85 (m, 4H), 7.49 – 7.65 (m, 2H), 7.40 – 7.49 (m, 2H), 6.81 (dt, *J* = 15.4, 7.8 Hz, 1H), 6.37 (d, *J* = 15.2 Hz, 1H), 3.95 (d, *J* = 7.6 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.37, 140.93, 138.51, 137.60, 135.96, 131.49, 129.86, 129.78, 129.71, 129.33, 57.73 ppm; ESI-HRMS: calcd. For $C_{15}H_{12}Cl_2S_2O_4$+H 390.9632, found 390.9626.

Following the general procedure, treatment of **1a** (65 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a**(100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4a:**



8'-(1,5-dimethyl-2-oxoindolin-3-yl)-1,5-dimethyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4a); 93 mg; white solid; R_f (ethyl acetate :

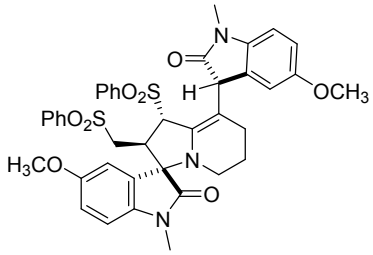
petroleum ether = 1:1) = 0.45; m.p. 215-216 °C; IR(KBr): 3059, 2926, 2841, 2356, 2343, 1700, 1621, 1499, 1447, 1363, 1353, 1324, 1312, 1282, 1204, 1169, 1144, 1084 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.10 (d, *J* = 7.6 Hz, 2H), 7.69-7.77 (m, 2H), 7.56 (t, *J* = 8.0 Hz, 4H), 7.45 – 7.51 (m, 2H), 7.23 (s, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.71 (dd, *J* = 8.0, 2.0 Hz, 2H), 5.74 (s, 1H), 5.35 (s, 1H), 4.36 (d, *J* = 7.6 Hz, 1H), 4.03 (dd, *J* = 14.8, 2.4 Hz, 1H), 3.80 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.23 (s, 3H), 3.20 (s, 3H), 2.88 (ddd, *J* = 11.6, 7.4, 2.2 Hz, 1H), 2.40 (s, 3H), 2.28 (s, 3H), 2.12 (dd, *J* = 7.2, 3.6 Hz, 2H), 1.60 – 1.72 (m, 2H), 1.30 – 1.48 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.20, 174.18, 143.38, 141.80, 137.94, 134.62, 134.26, 133.70, 133.55, 132.30, 131.87, 131.28, 130.50, 130.33, 128.89, 128.70, 128.58, 128.56, 128.26, 128.12, 125.68, 125.51, 125.47, 124.95, 124.59, 108.46, 108.28, 107.36, 71.87, 69.86, 56.75, 49.83, 42.14, 41.33, 26.31, 26.21, 22.64, 21.27, 21.03, 20.76 ppm; ESI-HRMS: calcd. For $C_{40}H_{39}N_3O_6S_2$+H 722.2359, found 722.2358.



Following the general procedure, treatment of **1b** (60 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4b:**

1-methyl-8'-(1-methyl-2-oxoindolin-3-yl)-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4b); 94 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.42; m.p. 205-206 °C; IR (KBr): 3055, 2925, 2841, 1709, 1613, 1493, 1470, 1447, 1422, 1374, 1346, 1310, 1279, 1209, 1184, 1145, 1134, 1084 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.20 (d, *J* = 7.6 Hz, 2H), 7.67 – 7.76 (m, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.55 (d, *J* = 4.4 Hz, 4H), 7.45 (d, *J* = 7.2 Hz, 1H), 7.36 (td, *J* = 8.3, 1.2 Hz, 1H), 7.26 – 7.31 (m, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.82 (dd, *J* = 8.0, 4.0 Hz, 2H), 6.16 (d, *J* = 7.2 Hz, 1H), 5.41 (s, 1H), 4.40 (d, *J* = 7.6 Hz, 1H), 4.02 (dd, *J* = 14.6, 2.2 Hz, 1H), 3.71 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.26 (s, 3H), 3.23 (s, 3H), 3.07 (ddd, *J* = 11.6, 7.6, 2.4 Hz, 1H), 2.04 – 2.17 (m, 2H), 1.54 – 1.74 (m, 2H), 1.26 – 1.47 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.18, 174.34, 145.68, 144.13, 138.23, 134.76, 134.42, 133.66, 133.50, 131.27, 130.52, 130.31, 129.04, 128.59, 128.49, 127.88, 125.40, 124.09, 123.84, 122.89, 122.69, 108.81, 108.57, 107.64, 71.98, 69.58, 56.78, 49.71, 42.26, 41.15, 26.28, 26.17, 22.61, 20.72 ppm; ESI-HRMS: calcd. For $C_{38}H_{35}N_3O_6S_2$+Na 716.1865, found 716.1875.

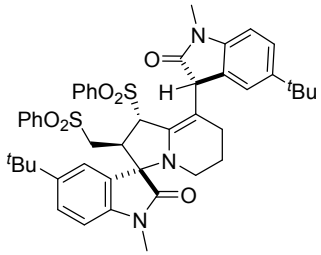
Following the general procedure, treatment of **1c** (71 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a**(100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4c:**



5-methoxy-8'-(5-methoxy-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one

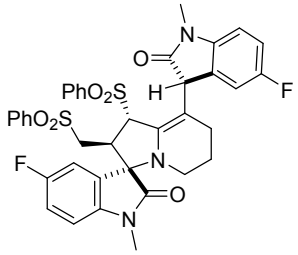
(4c); 110 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.30; m.p. 218-219 °C; IR(KBr): 3003, 2926, 2841, 2357, 2343, 1699, 1671, 1542, 1521, 1507, 1498, 1473, 1447, 1363, 1313, 1288, 1142, 1084 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.15 (d, *J* = 7.2 Hz, 2H), 7.67 – 7.75 (m, 2H), 7.51 – 7.64 (m, 6H), 7.20 – 7.22 (m, 1H), 6.86 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.77 – 6.82 (m, 1H), 6.71 (dd, *J* = 8.4, 4.8 Hz, 2H), 5.77 (d, *J* = 2.4 Hz, 1H), 5.38 (s, 1H), 4.39 (d, *J* = 7.6 Hz, 1H), 4.04 (dd, *J* = 14.6, 2.2 Hz, 1H), 3.87 (s, 3H), 3.75 (s, 3H), 3.68 – 3.75 (m, 1H), 3.23 (s, 3H), 3.18 (s, 3H), 2.98 (ddd, *J* = 11.6, 7.6, 2.2 Hz, 1H), 2.00 – 2.15 (m, 2H), 1.67 – 1.78 (m, 1H), 1.21 – 1.56 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.68, 173.69, 156.35, 156.01, 139.17, 138.16, 137.61, 134.79, 134.34, 133.63, 133.53, 131.28, 130.05, 129.01, 128.53, 128.50, 126.45, 114.42, 112.67, 111.07, 111.05, 109.18, 108.91, 107.95, 72.22, 69.55, 56.73, 55.87, 55.71, 50.04, 42.27, 41.26, 26.33, 26.16, 22.50, 20.75 ppm; ESI-HRMS: calcd. For $C_{40}H_{39}N_3O_8S_2$+H 754.2257, found 754.2244.

Following the general procedure, treatment of **1d** (81 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4d:**



5-(tert-butyl)-8'-(5-(tert-butyl)-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4d); 127 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.65; m.p. 213-214 °C; IR(KBr): 3059, 2954, 2908, 2358, 2342, 1710, 1622, 1500, 1472, 1459, 1447, 1369, 1348, 1311, 1279, 1209, 1143, 1082 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.15 (d, *J* = 7.2 Hz, 2H), 7.68 – 7.75 (m, 2H), 7.53 – 7.67 (m, 7H), 7.34 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.27 – 7.31 (m, 1H), 6.73 (d, *J* = 8.0 Hz, 2H), 6.36 (d, *J* = 2.0 Hz, 1H), 5.39 (s, 1H), 4.44 (d, *J* = 8.0 Hz, 1H), 4.03 (dd, *J* = 14.8, 2.0 Hz, 1H), 3.73 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.24 (s, 3H), 3.18 (s, 3H), 3.09 (ddd, *J* = 11.6, 7.6, 2.0 Hz, 1H), 1.96 – 2.14 (m, 2H), 1.49 – 1.77 (m, 3H), 1.38 (s, 9H), 1.33 – 1.36 (m, 1H), 1.31 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.27, 173.92, 146.22, 145.60, 143.31, 141.71, 138.63, 134.75, 134.11, 133.71, 133.59, 131.24, 129.02, 128.52, 128.51 128.49, 126.70, 124.90, 124.08, 121.80, 120.84, 109.25, 107.74, 106.83, 72.33, 69.50, 56.77, 49.91, 42.36, 41.00, 34.72, 34.61, 31.65, 31.61, 26.23, 25.93, 22.63, 20.77 ppm; ESI-HRMS: calcd. For $C_{46}H_{51}N_3O_6S_2$+H 806.3298, found 806.3295.

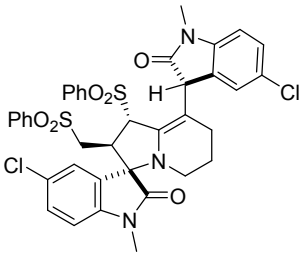
Following the general procedure, treatment of **1e** (67 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4e:**



5-fluoro-8'-(5-fluoro-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-

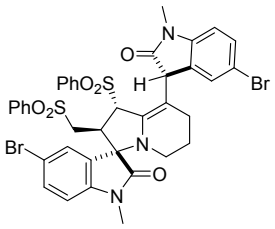
2'H-spiro[indoline-3,3'-indolizin]-2-one (4e); 71 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.51; m.p. 210-211°C; IR(KBr): 3048, 2950, 2902, 2351, 2340, 1710, 1612, 1510, 1479, 1459, 1437, 1368, 1348, 1301, 1249, 1209, 1113, 1081 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.16 (d, *J* = 7.6 Hz, 2H), 7.71 – 7.78 (m, 2H), 7.57 – 7.64 (m, 6H), 7.22 – 7.25 (m, 1H), 7.05 (td, *J* = 8.8, 2.8 Hz, 1H), 6.98 (td, *J* = 8.6, 2.4 Hz, 1H), 6.74 (td, *J* = 8.8, 4.0 Hz, 2H), 5.86 (dd, *J* = 7.8, 2.6 Hz, 1H), 5.39 (s, 1H), 4.35 (d, *J* = 7.6 Hz, 1H), 4.01 (dd, *J* = 14.6, 2.2 Hz, 1H), 3.70 (dd, *J* = 14.6, 11.6 Hz, 1H), 3.25 (s, 3H), 3.22 (s, 3H), 3.00 (ddd, *J* = 11.8, 7.6, 2.2 Hz, 1H), 2.02 – 2.20 (m, 2H), 1.59 – 1.77 (m, 2H), 1.23 – 1.50 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.63, 173.89, 160.60 (d, *J* = 31.0 Hz), 158.20 (d, *J* = 33.0 Hz), 141.68 (d, *J* = 1.8 Hz), 140.11 (d, *J* = 1.6 Hz), 138.12, 135.01, 134.67, 133.83, 133.31, 131.22, 130.20 (d, *J* = 8.1 Hz), 129.14, 128.71, 128.39, 126.99 (d, *J* = 7.7 Hz), 116.46 (d, *J* = 23.3 Hz), 114.16 (d, *J* = 23.4 Hz), 112.40, 112.14 (d, *J* = 2.0 Hz), 111.88, 109.21 (d, *J* = 7.8 Hz), 108.60, 108.05 (d, *J* = 8.0 Hz), 72.05, 69.44, 56.61, 49.99, 42.29, 41.16, 26.43, 26.31, 22.53, 20.66 ppm; ESI-HRMS: calcd. For $C_{38}H_{33}N_3O_6S_2F_2$+H 730.1857, found 730.1836.

Following the general procedure, treatment of **1f** (73 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4f:**



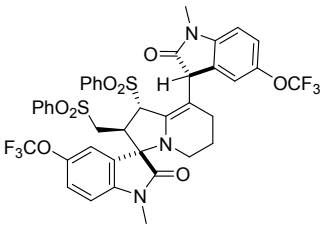
5-chloro-8'-(5-chloro-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4f); 107 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.55; m.p. 190-191 °C; IR(KBr): 3056; 2953, 2913, 2358, 2343, 1716, 1685, 1558, 1542, 1490, 1436, 1339, 1320, 1309, 1281, 1216, 1145, 1082 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.21 (d, *J* = 7.6 Hz, 2H), 7.67 – 7.78 (m, 2H), 7.52 – 7.65 (m, 6H), 7.31 – 7.36 (m, 1H), 7.24 – 7.28 (m, 1H), 7.17 – 7.22 (m, 1H), 6.99 – 7.05 (m, 1H), 6.86 – 6.93 (m, 1H), 6.05 (d, *J* = 7.2 Hz, 1H), 5.39 (s, 1H), 4.35 (d, *J* = 7.6 Hz, 1H), 3.99 (dd, *J* = 14.4, 2.0 Hz, 1H), 3.61 – 3.66 (m, 4H), 3.57 (s, 3H), 3.07 (ddd, *J* = 11.6, 7.8, 2.2 Hz, 1H), 2.02 – 2.20 (m, 2H), 1.65 – 1.77 (m, 1H), 1.28 – 1.59 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.11, 174.67, 141.51, 139.88, 138.38, 134.96, 134.56, 133.78, 132.55, 133.40, 131.27, 131.19, 130.25, 129.10, 128.67, 128.34, 128.23, 123.63, 123.49, 122.62, 122.34, 116.15, 115.06, 108.96, 71.59, 69.32, 56.58, 49.56, 42.33, 41.38, 29.62, 29.59, 22.53, 20.67 ppm; $C_{38}H_{33}N_3O_6S_2Cl_2$+H 762.1266, found 762.1245.

Following the general procedure, treatment of **1g** (89 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4g:**



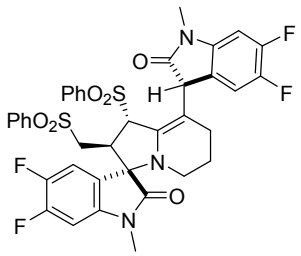
5-bromo-8'-(5-bromo-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4g); 102 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.55; m.p. 198-199 °C; IR(KBr): 3057, 2913, 1840, 2358, 2342, 1715, 1609, 1488, 1474, 1447, 1434, 1362, 1340, 1319, 1278, 1214, 1182, 1140, 1084 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.94 (d, *J* = 7.6 Hz, 2H), 7.72 – 7.85 (m, 2H), 7.68 (t, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.8 Hz, 2H), 7.45 – 7.53 (m, 4H), 7.42 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.71 (dd, *J* = 8.4, 6.4 Hz, 2H), 5.96 (d, *J* = 2.0 Hz, 1H), 5.36 (s, 1H), 4.31 (d, *J* = 7.2 Hz, 1H), 4.03 (dd, *J* = 14.8, 2.2 Hz, 1H), 3.79 (dd, *J* = 14.8, 11.8 Hz, 1H), 3.24 (s, 3H), 3.21 (s, 3H), 2.74 (ddd, *J* = 11.8, 7.6, 2.0 Hz, 1H), 2.08 – 2.18 (m, 2H), 1.59 – 1.73 (m, 2H), 1.34 – 1.51 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.39, 173.46, 144.92, 143.23, 137.32, 134.95, 134.72, 133.80, 133.17, 132.93, 131.05, 130.93, 130.47, 129.23, 128.79, 128.73, 127.84, 127.21, 126.98, 115.54, 115.16, 110.10, 109.15, 107.99, 71.64, 69.61, 56.50, 49.71, 42.12, 41.37, 26.39, 26.34, 22.52, 20.65 ppm; ESI-HRMS: calcd. For $C_{38}H_{33}N_3O_6S_2Br_2$+H 850.0256, found 850.0240.

Following the general procedure, treatment of **1h** (91 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1.5 h followed by column chromatography afforded the product **4h:**



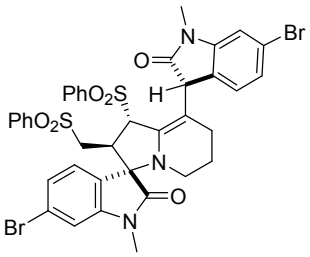
1-methyl-8'-(1-methyl-2-oxo-5-(trifluoromethoxy)indolin-3-yl)-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-5-(trifluoromethoxy)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4h); 84 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.55; m.p. 169-170 °C; IR(KBr): 3064, 2936, 2844, 2358, 2342, 1747, 1649, 1623, 1541, 1507, 1497, 1473, 1313, 1261, 1217, 1168, 1146, 1086 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.10 (d, *J* = 7.6 Hz, 2H), 7.70 – 7.79 (m, 2H), 7.52 – 7.67 (m, 6H), 7.35 (d, *J* = 2.4 Hz, 1H), 7.13 – 7.24 (m, 2H), 6.80 (dd, *J* = 8.4, 6.0 Hz, 2H), 6.03 (s, 1H), 5.39 (s, 1H), 4.36 (d, *J* = 7.6 Hz, 1H), 4.00 (dd, *J* = 14.8, 2.0 Hz, 1H), 3.71 (dd, *J* = 14.4, 11.6 Hz, 1H), 3.26 (s, 3H), 3.23 (s, 3H), 3.00 (ddd, *J* = 11.6, 7.6, 2.9 Hz, 1H), 2.02 – 2.16 (m, 2H), 1.60 – 1.76 (m, 1H), 1.23 – 1.55 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.71, 173.86, 145.07, 144.79, 144.33, 142.79, 137.99, 135.10, 134.66, 133.91, 133.13, 131.09, 129.97, 129.20, 128.74, 128.38, 127.01, 123.33, 120.99, 118.08, 117.26, 109.15, 108.34, 108.02, 72.00, 69.30, 56.50, 49.87, 42.30, 41.07, 26.46, 26.29, 22.55, 20.62 ppm; ESI-HRMS: calcd. For $C_{40}H_{33}N_3O_8S_2F_6$+H 863.1692, found 863.1666.

Following the general procedure, treatment of **1j** (73 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4j:**



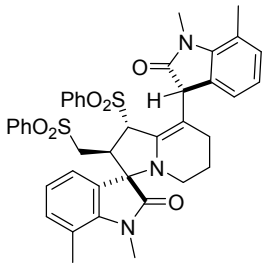
8'-(5,6-difluoro-1-methyl-2-oxoindolin-3-yl)-5,6-difluoro-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4j); 58 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.48; m.p. 198-199 ^{o}C; IR(KBr): 3063, 2930, 2842, 2358, 2342, 1717, 1626, 1508, 1471, 1448, 1427, 1395, 1310, 1253, 1206, 1144, 1132, 1083 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 8.21 (d, *J* = 7.6 Hz, 2H), 7.70-7.82 (m, 2H), 7.46 – 7.70 (m, 6H), 7.30 (t, *J* = 8.4 Hz, 1H), 6.66 (ddd, *J* = 8.6, 6.2, 2.0 Hz, 2H), 6.02 (t, *J* = 8.2 Hz, 1H), 5.34 (s, 1H), 4.32 (d, *J* = 7.6 Hz, 1H), 3.99 (dd, *J* = 14.8, 2.4 Hz, 1H), 3.62 (dd, *J* = 14.4, 11.6 Hz, 1H), 3.22 (s, 3H), 3.19 (s, 3H), 3.02 – 3.13 (m, 1H), 1.99 – 2.18 (m, 2H), 1.64 – 1.78 (m, 1H), 1.15 – 1.56 (m, 3H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.63, 174.00, 138.35, 138.32, 135.03, 134.80, 134.66, 134.34 (d, *J* = 1.4 Hz), 134.03 (d, *J* = 1.7 Hz), 133.97, 133.92, 133.28, 131.24, 129.59, 129.49, 129.37, 129.35, 129.25, 128.77, 128.26, 128.20, 128.10, 128.06, 113.82 (d, *J* = 18.6 Hz), 113.62 (d, *J* = 16.9 Hz), 108.68, 99.15 (d, *J* = 22.7 Hz), 98.41 (d, *J* = 60.0 Hz), 71.83, 69.17, 56.49, 49.41, 42.27, 40.98, 26.54, 26.41, 22.43, 20.61 ppm; $C_{38}H_{31}N_3O_6S_2F_4$+H 766.1669, found 766.1675.

Following the general procedure, treatment of **1k** (89 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 ^{o}C for 1.5 h followed by column chromatography afforded the product **4k:**

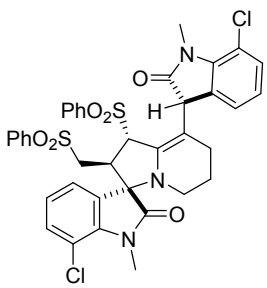


6-bromo-8'-(6-bromo-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4k); 80 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.52; m.p. 195-196 ^{o}C; IR(KBr): 3068, 2929, 2839, 2358, 2342, 1714, 1649, 1607, 1491, 1447, 1368, 1313, 1278, 1245, 1207, 1182, 1145, 1085 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 8.23 (d, *J* = 7.2 Hz, 2H), 7.71 – 7.79 (m, 2H), 7.52 – 7.69 (m, 6H), 7.29 – 7.32 (m, 1H), 7.26 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.16 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.99 (s, 2H), 6.07 (d, *J* = 8.0 Hz, 1H), 5.35 (s, 1H), 4.38 (d, *J* = 7.6 Hz, 1H), 4.01 (dd, *J* = 14.6, 2.2 Hz, 1H), 3.66 (dd, *J* = 14.4, 11.6 Hz, 1H), 3.26 (s, 3H), 3.22 (s, 3H), 3.13 (ddd, *J* = 11.8, 7.6, 2.4 Hz, 1H), 2.02 – 2.19 (m, 2H), 1.59 – 1.82 (m, 2H), 1.25 – 1.51 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.78, 174.11, 146.81, 145.45, 138.26, 134.82, 134.57, 133.83, 133.34, 131.21, 129.16, 128.64, 128.26, 127.32, 125.67, 125.60, 125.38, 124.99, 124.17, 124.04, 121.39, 112.24, 111.19, 108.62, 71.67, 69.28, 56.51, 49.30, 42.22, 40.77, 26.39, 26.25, 22.48, 20.60 ppm; ESI-HRMS: calcd. For $C_{38}H_{33}N_3O_6S_2Br_2$+H 850.0256, found 850.0223.

Following the general procedure, treatment of **1l** (65 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4l:**



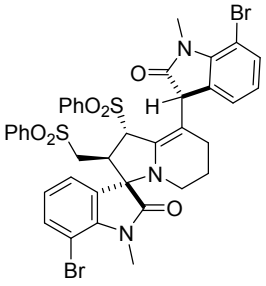
8'-(1,7-dimethyl-2-oxoindolin-3-yl)-1,7-dimethyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4l); 100 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.39; m.p. 213-214 °C; IR(KBr): 3058, 2939, 2842, 2358, 2342, 1705, 1604, 1458, 1447, 1363, 1339, 1312, 1278, 1185, 1150, 1134, 1113, 1084 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.15 (d, *J* = 7.6 Hz, 2H), 7.66 – 7.76 (m, 2H), 7.49 – 7.64 (m, 6H), 7.28 – 7.33 (m, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 6.95 – 7.03 (m, 2H), 6.85 (t, *J* = 7.6 Hz, 1H), 5.91 (d, *J* = 7.2 Hz, 1H), 5.34 (s, 1H), 4.35 (d, *J* = 7.6 Hz, 1H), 4.01 (dd, *J* = 14.8, 2.0 Hz, 1H), 3.69 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.54 (s, 3H), 3.49 (s, 3H), 2.94 (ddd, *J* = 11.6, 7.6, 2.2 Hz, 1H), 2.58 (s, 3H), 2.55 (s, 3H), 2.02 – 2.15 (m, 2H), 1.57 – 1.74 (m, 2H), 1.27 – 1.46 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.80, 175.02, 143.43, 141.80, 138.15, 134.74, 134.34, 133.91, 133.56, 133.49, 131.57, 131.23, 129.12, 128.96, 128.59, 128.53, 126.01, 122.73, 122.51, 122.04, 121.72, 120.23, 119.12, 108.91, 71.39, 69.61, 56.86, 49.39, 42.25, 41.64, 29.57, 22.61, 20.75, 18.97, 18.94, 14.17 ppm; ESI-HRMS: calcd. For $C_{40}H_{39}N_3O_6S_2$+Na 744.2178, found 744.2169.



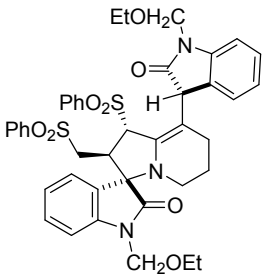
Following the general procedure, treatment of **1m** (73 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4m:**

7-chloro-8'-(7-chloro-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4m); 86 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.63; m.p. 187-188 °C; IR(KBr): 3065, 2940, 2842, 2360, 2342, 1715, 1684, 1558, 1541, 1521, 1507, 1473, 1458, 1363, 1339, 1311, 1239, 1107, 1083 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.21 (d, *J* = 7.6 Hz, 2H), 7.67 – 7.77 (m, 2H), 7.50 – 7.66 (m, 6H), 7.31 – 7.36 (m, 1H), 7.24 – 7.30 (m, 1H), 7.19 (d, *J* = 8.2 Hz, 1H), 7.02 (t, *J* = 7.8 Hz, 1H), 6.90 (t, *J* = 7.8 Hz, 1H), 6.05 (d, *J* = 7.2 Hz, 1H), 5.39 (s, 1H), 4.35 (d, *J* = 7.6 Hz, 1H), 3.99 (dd, *J* = 14.6, 2.2 Hz, 1H), 3.63 (s, 4H), 3.58 (s, 3H), 3.07 (ddd, *J* = 11.6, 7.6, 2.2 Hz, 1H), 2.02 – 2.18 (m, 2H), 1.59 – 1.80 (m, 2H), 1.32 – 1.55 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.10, 174.63, 141.47, 139.84, 138.29, 134.93, 134.57, 133.79, 133.32, 132.54, 131.23, 131.15, 130.23, 129.09, 128.66, 128.33, 128.18, 123.62, 123.48, 122.59, 122.31, 116.12, 115.04, 108.93, 71.56, 69.25, 56.53, 49.55, 42.31, 41.35, 29.61, 29.59, 22.51, 20.66 ppm; ESI-HRMS: calcd. For $C_{38}H_{33}N_3O_6S_2Cl_2$+H 762.1266, found 762.1233.

Following the general procedure, treatment of **1n** (89 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4n:**



7-bromo-8'-(7-bromo-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4n); 91 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.63; m.p. 198-199 °C; IR(KBr): 3063, 2944, 2841, 2344, 2307, 1710, 1607, 1578, 1460, 1447, 1364, 1339, 1313, 1198, 1177, 1152, 1132, 1104, 1055 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.21 (d, *J* = 7.2 Hz, 2H), 7.67 – 7.78 (m, 2H), 7.49 – 7.67 (m, 6H), 7.44 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.37 (dd, *J* = 7.6, 1.2 Hz, 2H), 6.96 (t, *J* = 7.8 Hz, 1H), 6.83 (t, *J* = 7.8 Hz, 1H), 6.08 (d, *J* = 7.2 Hz, 1H), 5.40 (s, 1H), 4.34 (d, *J* = 7.6 Hz, 1H), 3.99 (dd, *J* = 14.8, 2.2 Hz, 1H), 3.64 (s, 3H), 3.56 – 3.62 (m, 4H), 3.06 (ddd, *J* = 11.8, 7.6, 2.4 Hz, 1H), 1.98 – 2.20 (m, 2H), 1.63 – 1.78 (m, 1H), 1.41 – 1.57 (m, 2H), 1.17 – 1.40 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.26, 174.80, 142.95, 141.26, 138.26, 135.85, 134.95, 134.57, 133.79, 133.55, 133.30, 131.49, 131.22, 129.08, 128.66, 128.51, 128.33, 124.05, 123.85, 123.12, 122.85, 108.92, 103.01, 102.01, 71.48, 69.25, 56.53, 49.55, 42.30, 41.38, 29.83, 29.79, 22.51, 20.64 ppm; ESI-HRMS: calcd. For $C_{38}H_{33}N_3O_6S_2Br_2$+Na 872.0075, found 872.0051.

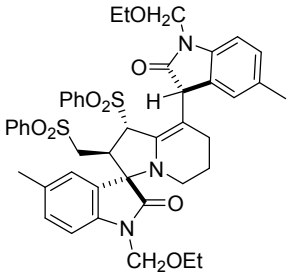


Following the general procedure, treatment of **1p** (76 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4p:**

1-(ethoxymethyl)-8'-(1-(ethoxymethyl)-2-oxoindolin-3-yl)-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4p) ; 130 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.58; m.p. 187-188 °C; IR(KBr): 3055, 2977, 2927, 2354, 2338, 1715, 1614, 1505, 1470, 1455, 1346, 1308, 1210, 1181, 1147, 1133, 1084, 1019 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.14 (d, *J* = 7.6 Hz, 2H), 7.69 – 7.78 (m, 2H), 7.61 (t, *J* = 7.8 Hz, 2H), 7.54 – 7.58 (m, 4H), 7.45 (d, *J* = 7.2 Hz, 1H), 7.36 (td, *J* = 7.8, 1.2 Hz, 1H), 7.28 (t, *J* = 6.6 Hz, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 2H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.17 (d, *J* = 6.8 Hz, 1H), 5.51 (s, 1H), 5.17 – 5.28 (m, 3H), 5.10 (d, *J* = 11.2 Hz, 1H), 4.39 (d, *J* = 7.6 Hz, 1H), 4.03 (dd, *J* = 14.8, 2.2 Hz, 1H), 3.52 – 3.70 (m, 5H), 3.04 – 3.12 (m, 1H), 2.06 – 2.21 (m, 2H), 1.59 – 1.79 (m, 2H), 1.26 – 1.49 (m, 2H), 1.20 (q, *J* = 7.0 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.39, 174.62, 144.37, 142.50, 138.10, 134.71, 134.47, 133.73, 133.39, 131.15, 130.48, 129.06, 128.64, 128.50, 128.05, 128.00, 124.84, 124.15, 123.84, 123.24,

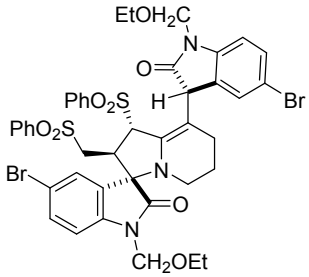
123.05, 110.06, 109.23, 108.80, 72.21, 70.57, 70.06, 69.45, 64.48, 64.24, 56.66, 49.87, 42.26, 41.01, 22.62, 20.58, 14.96, 14.90 ppm; ESI-HRMS: calcd. For $C_{42}H_{43}N_3O_8S_2$+H 782.2570, found 782.2560.

Following the general procedure, treatment of **1q** (82 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4q:**



1-(ethoxymethyl)-8'-(1-(ethoxymethyl)-5-methyl-2-oxoindolin-3-yl)-5-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4q); 99 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.51; m.p. 179-180 °C; IR(KBr): 3056, 2976, 2355, 2339, 1715, 1603, 1496, 1447, 1394, 1367, 1330, 1311, 1281, 1214, 1145, 1133, 1086 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.04 (d, *J* = 7.6 Hz, 2H), 7.71 – 7.78 (m, 2H), 7.54 – 7.60 (m, 4H), 7.49 – 7.53 (m, 2H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.95 (dd, *J* = 8.0, 5.2 Hz, 2H), 5.78 (s, 1H), 5.45 (s, 1H), 5.15 – 5.27 (m, 3H), 5.06 (d, *J* = 11.2 Hz, 1H), 4.36 (d, *J* = 7.6 Hz, 1H), 4.04 (dd, *J* = 14.8, 2.0 Hz, 1H), 3.74 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.48 – 3.64 (m, 5H), 2.91 (ddd, *J* = 11.8, 7.6, 2.2 Hz, 1H), 2.40 (s, 3H), 2.29 (s, 3H), 2.08 – 2.20 (m, 2H), 1.59 – 1.78 (m, 2H), 1.26 – 1.52 (m, 2H), 1.14 – 1.23 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.42, 174.46, 142.03, 140.09, 137.75, 134.56, 134.33, 133.64, 133.49, 132.68, 132.24, 131.12, 130.60, 128.91, 128.69, 128.61, 128.30, 128.03, 125.01, 124.92, 124.50, 109.74, 108.92, 108.57, 72.07, 70.55, 70.07, 69.62, 64.33, 64.14, 56.60, 49.93, 42.14, 41.14, 22.60, 21.23, 21.03, 20.59, 14.95, 14.84 ppm; ESI-HRMS: calcd. For $C_{44}H_{47}N_3O_8S_2$+H 810.2883, found 810.2867.

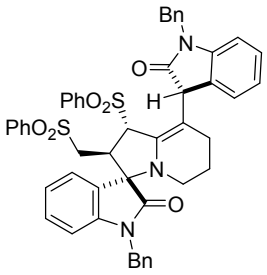
Following the general procedure, treatment of **1r** (106 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4r:**



5-bromo-8'-(5-bromo-1-(ethoxymethyl)-2-oxoindolin-3-yl)-1-(ethoxymethyl)-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4r); 106 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.58; m.p. 162-163 °C; IR(KBr): 3058, 2977, 2930, 2356, 2329, 1722, 1608, 1584, 1480, 1446, 1428, 1357, 1323, 1312, 1262, 1207, 1148, 1084 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.88 (d, *J* = 7.6 Hz, 2H), 7.74 – 7.83 (m, 2H), 7.69 (t, *J* = 7.8 Hz, 2H), 7.44 – 7.63 (m, 6H), 7.39 – 7.44 (m, 1H), 6.96 (dd, *J* = 13.2, 8.2 Hz, 2H), 5.99 (d, *J* = 2.0 Hz, 1H), 5.45 (s, 1H), 5.13 – 5.28 (m, 3H), 5.06 (d, *J* = 11.2 Hz, 1H), 4.31 (d, *J* = 7.2 Hz, 1H), 4.05 (dd, *J* = 14.8, 2.0 Hz, 1H), 3.74 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.47 – 3.66 (m, 4H), 2.76 (ddd, *J* = 12.0, 7.6, 2.2

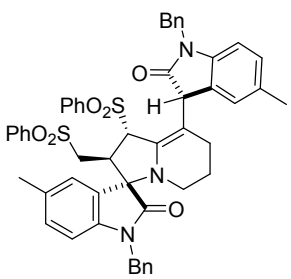
Hz, 1H), 2.08 – 2.23 (m, 2H), 1.62 – 1.78 (m, 2H), 1.29 – 1.54 (m, 2H), 1.14 – 1.25 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.59, 173.75, 143.54, 141.54, 137.15, 134.94, 134.79, 133.89, 133.17, 133.01, 131.09, 130.93, 130.03, 129.26, 128.83, 128.78, 127.32, 127.28, 126.96, 116.07, 115.70, 111.79, 110.89, 108.06, 71.91, 70.73, 70.13, 69.41, 64.62, 64.33, 56.39, 49.87, 42.15, 41.28, 22.52, 20.55, 14.92, 14.82 ppm; ESI-HRMS: calcd. For $C_{42}H_{41}N_3O_8S_2Br_2$+H 938.0780, found 938.0742.

Following the general procedure, treatment of **1s** (88 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4s:**



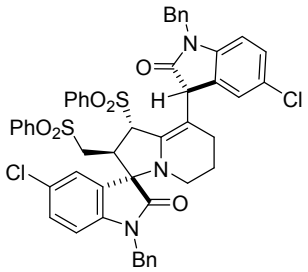
1-benzyl-8'-(1-benzyl-2-oxoindolin-3-yl)-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4s); 122 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.61; m.p. 144-145 °C; IR(KBr): 3014, 2946, 2838, 2353, 2321, 1713, 1613, 1486, 1454, 1447, 1359, 1311, 1210, 1181, 1145, 1132, 1083 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 8.24 (d, *J* = 7.6 Hz, 2H), 7.68 – 7.79 (m, 2H), 7.50 – 7.68 (m, 6H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.27 – 7.35 (m, 9H), 7.20 – 7.25 (m, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.69 (t, *J* = 8.0 Hz, 2H), 6.23 (d, *J* = 7.2 Hz, 1H), 5.56 (s, 1H), 5.24 (d, *J* = 15.6 Hz, 1H), 5.07 (d, *J* = 16.0 Hz, 1H), 4.91 (d, *J* = 15.6 Hz, 1H), 4.66 (d, *J* = 15.6 Hz, 1H), 4.47 (d, *J* = 7.6 Hz, 1H), 4.05 (dd, *J* = 14.4, 2.0 Hz, 1H), 3.72 (dd, *J* = 14.6, 11.4 Hz, 1H), 3.17 (ddd, *J* = 11.6, 7.6, 2.0 Hz, 1H), 2.12 – 2.30 (m, 2H), 1.62 – 1.90 (m, 2H), 1.29 – 1.53 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.03, 174.42, 145.06, 145.04, 143.29, 138.40, 136.10, 136.07, 135.70, 135.68, 134.81, 134.44, 133.69, 133.55, 133.53, 131.29, 130.23, 129.06, 128.76, 128.70, 128.63, 128.48, 127.79, 127.59, 127.43, 127.20, 125.36, 124.24, 123.92, 122.87, 122.75, 109.65, 109.14, 108.73, 71.95, 69.59, 56.77, 49.64, 44.25, 43.87, 42.37, 41.10, 22.70, 20.66 ppm; ESI-HRMS: calcd. For $C_{50}H_{43}N_3O_6S_2$+H 846.2672, found 846.2654.

Following the general procedure, treatment of **1t** (94 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4t:**



1-benzyl-8'-(1-benzyl-5-methyl-2-oxoindolin-3-yl)-5-methyl-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4t); 113 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.60; m.p.165-166 °C; IR(KBr): 3028, 2918, 2840, 2356, 2339, 1709, 1602, 1584, 1514, 1446, 1346, 1324, 1311, 1281, 1203, 1185, 1144, 1084 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 8.12 (d, *J* = 7.8 Hz, 2H), 7.74 (t, *J* = 7.2 Hz, 2H), 7.42 – 7.66 (m, 6H), 7.25 – 7.37

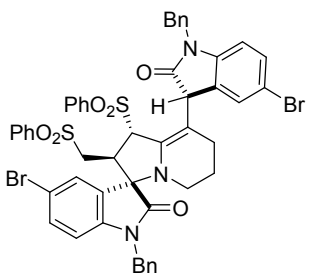
(m, 10H), 7.21 – 7.24 (m, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.56 (dd, *J* = 8.0, 4.0 Hz, 2H), 5.82 (s, 1H), 5.50 (s, 1H), 5.25 (d, *J* = 16.0 Hz, 1H), 5.05 (d, *J* = 16.0 Hz, 1H), 4.89 (d, *J* = 15.6 Hz, 1H), 4.61 (d, *J* = 16.0 Hz, 1H), 4.43 (d, *J* = 7.6 Hz, 1H), 4.06 (d, *J* = 16.0 Hz, 1H), 3.81 (dd, *J* = 14.8, 11.6 Hz, 1H), 2.93 – 3.04 (m, 1H), 2.34 (s, 3H), 2.25 (s, 3H), 2.20 (t, *J* = 5.6 Hz, 2H), 1.62 – 1.88 (m, 2H), 1.31 – 1.54 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.03, 174.18, 142.71, 140.89, 138.05, 136.19, 135.95, 134.66, 134.29, 133.66, 133.60, 132.31, 131.91, 131.27, 130.30, 128.93, 128.71, 128.69, 128.66, 128.61, 128.04, 127.51, 127.36, 127.24, 127.16, 125.59, 125.08, 124.65, 109.37, 108.89, 108.46, 71.81, 69.79, 56.73, 49.72, 44.27, 43.87, 42.25, 41.23, 22.71, 21.20, 21.01, 20.68. ppm; ESI-HRMS: calcd. For $C_{52}H_{47}N_3O_6S_2$+H 874.2985, found 874.2976.



Following the general procedure, treatment of **1u** (101 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4u:**

1-benzyl-8'-(1-benzyl-5-chloro-2-oxoindolin-3-yl)-5-chloro-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4u); 133 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.61; m.p. 195-196 °C; IR(KBr): 3029, 2918, 2840, 2356, 2329, 1710, 1602, 1584, 1496, 1446, 1346, 1324, 1311, 1281, 1185, 1144, 1130, 1084 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 8.02 (d, *J* = 7.6 Hz, 2H), 7.73 – 7.81 (m, 2H), 7.63 – 7.68 (m, 2H), 7.59 (t, *J* = 7.8 Hz, 2H), 7.52 – 7.56 (m, 2H), 7.43 – 7.46 (m, 1H), 7.26 – 7.37 (m, 10H), 7.20 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.10 – 7.14 (m, 1H), 6.59 (t, *J* = 8.4 Hz, 2H), 5.94 (d, *J* = 2.0 Hz, 1H), 5.51 (s, 1H), 5.26 (d, *J* = 16.0 Hz, 1H), 5.06 (d, *J* = 15.6 Hz, 1H), 4.87 (d, *J* = 15.6 Hz, 1H), 4.61 (d, *J* = 16.0 Hz, 1H), 4.39 (d, *J* = 7.2 Hz, 1H), 4.07 (dd, *J* = 14.8, 2.0 Hz, 1H), 3.79 (dd, *J* = 14.8, 11.6 Hz, 1H), 2.85 – 2.94 (m, 2H), 2.15 – 2.25 (m, 2H), 1.64 – 1.86 (m, 2H), 1.22 – 1.45 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.45, 173.73, 143.67, 141.80, 137.51, 135.56, 135.22, 135.02, 134.75, 133.87, 133.14, 131.09, 130.16, 130.01, 129.20, 128.86, 128.81, 128.69, 128.27, 128.06, 127.93, 127.78, 127.64, 127.36, 127.30, 127.30, 127.14, 127.14, 124.65, 124.36, 110.79, 109.76, 108.46, 71.69, 69.48, 56.50, 49.69, 44.46, 43.98, 42.24, 41.28, 22.60, 20.61 ppm; ESI-HRMS: calcd. For $C_{50}H_{41}N_3O_6S_2Cl_2$+H 914.1892, found 914.1880.

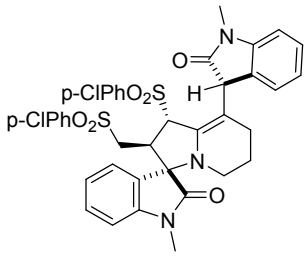
Following the general procedure, treatment of **1v** (118 mg, 0.37 mmol) with **2** (32 mg, 0.37 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4v:**



1-benzyl-8'-(1-benzyl-5-bromo-2-oxoindolin-3-yl)-5-bromo-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4v); 126 mg; white solid; R_f

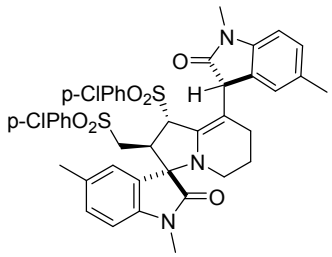
(ethyl acetate : petroleum ether = 1:1) = 0.61; m.p. 206-207 °C; IR(KBr): 3059, 3030, 2917, 2359, 2341, 1717, 1608, 1583, 1483, 1447, 1429, 1379, 1343, 1315, 1278, 1211, 1143, 1082 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.96 (d, *J* = 7.6 Hz, 2H), 7.73 – 7.83 (m, 2H), 7.68 (t, *J* = 7.8 Hz, 2H), 7.47 – 7.63 (m, 5H), 7.26 – 7.38 (m, 12H), 6.55 (t, *J* = 8.8 Hz, 2H), 6.03 (d, *J* = 2.0 Hz, 1H), 5.51 (s, 1H), 5.27 (d, *J* = 15.6 Hz, 1H), 5.06 (d, *J* = 16.0 Hz, 1H), 4.87 (d, *J* = 16.0 Hz, 1H), 4.59 (d, *J* = 16.0 Hz, 1H), 4.38 (d, *J* = 7.6 Hz, 1H), 4.07 (dd, *J* = 14.8, 2.0 Hz, 1H), 3.82 (dd, *J* = 14.8, 11.6 Hz, 1H), 2.83 (ddd, *J* = 11.8, 7.6, 2.0 Hz, 1H), 2.12 – 2.28 (m, 2H), 1.64 – 1.88 (m, 2H), 1.31 – 1.56 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.33, 173.57, 155.01, 152.52, 144.19, 142.30, 137.38, 135.52, 135.21, 135.01, 134.76, 133.86, 133.11, 132.87, 131.05, 130.85, 130.53, 129.26, 128.87, 128.82, 128.79, 127.82, 127.79, 127.65, 127.37, 127.33, 127.13, 127.04, 115.66, 115.30, 115.21, 111.27, 110.29, 108.37, 71.62, 69.53, 56.50, 49.64, 44.46, 43.97, 42.23, 41.34, 22.60, 20.63 ppm；ESI-HRMS: calcd. For $C_{50}H_{41}N_3O_6S_2Br_2$+H 1002.0882, found 1002.0860.

Following the general procedure, treatment of **1b** (49 mg, 0.31 mmol) with **2** (26 mg, 0.31 mmol), **3b** (100 mg, 0.26 mmol) and 4-TFBA (49 mg, 0.26 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4w:**



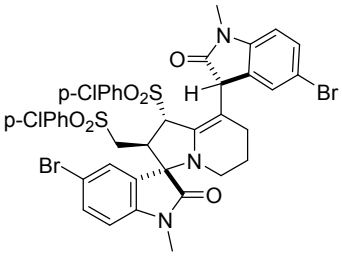
1'-((4-chlorophenyl)sulfonyl)-2'-(((4-chlorophenyl)sulfonyl)methyl)-1-methyl-8'-(1-methyl-2-oxoindolin-3-yl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4w); 91 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.41; m.p. 196-197 °C; IR(KBr): 3055, 2930, 2839, 2355, 2329, 1705, 1613, 1524, 1494, 1471, 1373, 1346, 1318, 1278, 1210, 1183, 1146, 1089 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.24 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.46 – 7.57 (m, 4H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.38 (d, *J* = 7.6, Hz, 1H), 7.24 – 7.33 (m, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.83 (t, *J* = 7.4 Hz, 2H), 6.27 (d, *J* = 7.6 Hz, 1H), 5.35 (s, 1H), 4.42 (d, *J* = 7.6 Hz, 1H), 3.96 (dd, *J* = 14.6, 2.2 Hz, 1H), 3.67 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.26 (s, 3H), 3.23 (s, 3H), 3.04 (ddd, *J* = 11.2, 7.6, 2.2 Hz, 1H), 2.15 – 2.24 (m, 1H), 2.10 (td, *J* = 10.8, 2.8 Hz, 1H), 1.60 – 1.77 (m, 2H), 1.41 – 1.53 (m, 1H), 1.23 – 1.36 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.06, 174.15, 145.65, 144.14, 141.50, 140.57, 136.76, 134.56, 132.74, 132.16, 130.54, 129.96, 129.35, 128.94, 128.39, 127.97, 125.02, 124.09, 123.75, 122.91, 122.87, 109.40, 108.73, 107.72, 71.95, 69.58, 56.82, 49.67, 42.36, 41.30, 26.29, 26.17, 22.58, 20.79 ppm; ESI-HRMS: calcd. For $C_{38}H_{33}N_3O_6S_2Cl_2$+H 762.1266, found 762.1252.

Following the general procedure, treatment of **1a** (60 mg, 0.31 mmol) with **2** (26 mg, 0.31 mmol), **3b** (100 mg, 0.26 mmol) and 4-TFBA (49 mg, 0.26 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4x:**



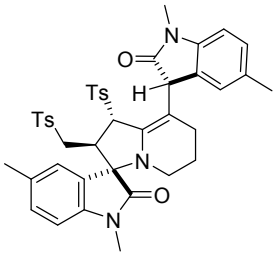
1'-((4-chlorophenyl)sulfonyl)-2'-(((4-chlorophenyl)sulfonyl)methyl)-8'-(1,5-dimethyl-2-oxoindolin-3-yl)-1,5-dimethyl-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4x); 95 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.47; m.p. 199-200 °C; IR(KBr): 3051, 2937, 2839, 2355, 2329, 1700, 1611, 1524, 1484, 1461, 1373, 1336, 1318, 1294, 1210, 1183, 1146, 1085 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.13 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.20 (s, 1H), 7.16 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.72 (dd, *J* = 7.8, 4.2 Hz, 2H), 5.73 (d, *J* = 1.6 Hz, 1H), 5.29 (s, 1H), 4.37 (d, *J* = 7.6 Hz, 1H), 3.96 (dd, *J* = 14.8, 2.4 Hz, 1H), 3.79 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.23 (s, 3H), 3.20 (s, 3H), 2.80 (ddd, *J* = 11.6, 7.6, 2.4 Hz, 1H), 2.39 (s, 3H), 2.32 (s, 3H), 2.10 – 2.22 (m, 2H), 1.64 (d, *J* = 9.2 Hz, 2H), 1.35 – 1.53 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.10, 173.94, 143.29, 141.77, 141.42, 140.45, 136.24, 134.35, 132.65, 132.31, 132.11, 130.54, 130.18, 130.07, 129.41, 129.31, 129.18, 128.97, 128.29, 128.21, 127.63, 108.80, 108.45, 107.46, 71.74, 69.78, 56.75, 49.81, 42.17, 41.43, 26.32, 26.22, 22.61, 21.26, 21.10, 20.79 ppm; ESI-HRMS: calcd. For $C_{40}H_{37}N_3O_6S_2Cl_2$+H 790.1579, found 790.1570.

Following the general procedure, treatment of **1g** (74 mg, 0.31 mmol) with **2** (26 mg, 0.31 mmol), **3b** (100 mg, 0.26 mmol) and 4-TFBA (49 mg, 0.26 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4y:**



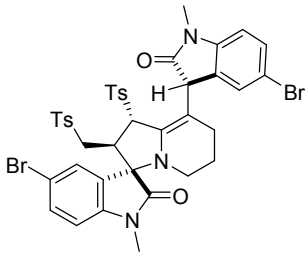
5-bromo-8'-(5-bromo-1-methyl-2-oxoindolin-3-yl)-1'-((4-chlorophenyl)sulfonyl)-2'-(((4-chlorophenyl)sulfonyl)methyl)-1-methyl-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4y); 87 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.48; m.p. 184-85 °C; IR(KBr): 3084, 2925, 2839, 2355, 2320, 1712, 1609, 1574, 1487, 1475, 1360, 1345, 1325, 1278, 1209, 1184, 1141, 1092 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.97 (d, *J* = 7.8 Hz, 2H), 7.75 – 7.84 (m, 2H), 7.70 (t, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.8 Hz, 2H), 7.49 – 7.52 (m, 3H), 7.42 – 7.46 (m, 1H), 6.73 (dd, *J* = 8.0, 6.4 Hz, 2H), 5.99 (d, *J* = 2.0 Hz, 1H), 5.38 (s, 1H), 4.34 (d, *J* = 7.4 Hz, 1H), 4.05 (dd, *J* = 14.8, 2.2 Hz, 1H), 3.81 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.26 (s, 3H), 3.24 (s, 3H), 2.77 (ddd, *J* = 11.8, 7.4, 2.2 Hz, 1H), 2.08 – 2.21 (m, 2H), 1.63 – 1.76 (m, 1H), 1.30 – 1.56 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.83, 174.16, 146.86, 145.50, 138.31, 134.87, 134.62, 133.88, 133.39, 131.26, 129.21, 128.69, 128.31, 127.37, 125.72, 125.65, 125.43, 125.04, 124.23, 124.09, 121.44, 112.29, 111.24, 108.67, 71.72, 69.33, 56.56, 49.35, 42.27, 40.82, 26.44, 26.30, 22.53, 20.65 ppm; ESI-HRMS: calcd. For $C_{38}H_{31}N_3O_6S_2Cl_2Br_2$+H 917.9476, found 917.9488.

Following the general procedure, treatment of **1a** (60 mg, 0.34 mmol) with **2** (29 mg, 0.34 mmol), **3c** (100 mg, 0.29 mmol) and 4-TFBA (54 mg, 0.29 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4z:**



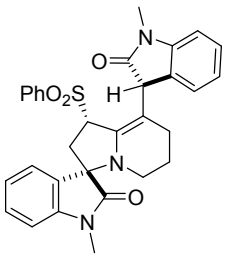
8'-(1,5-dimethyl-2-oxoindolin-3-yl)-1,5-dimethyl-1'-tosyl-2'-(tosylmethyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4z); 65 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.62; m.p. 218-219 °C; IR(KBr): 3045, 2926, 2840, 2354, 2321, 1712, 1621, 1598, 1499, 1446, 1363, 1352, 1322, 1309, 1280, 1203, 1142, 1086 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.87 – 7.99 (m, 2H), 7.28 – 7.40 (m, 6H), 7.22 (s, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 2H), 5.70 (s, 1H), 5.35 (s, 1H), 4.32 (d, *J* = 7.2 Hz, 1H), 3.92 – 4.01 (m, 1H), 3.78 (t, *J* = 13.2 Hz, 1H), 3.22 (s, 3H), 3.20 (s, 3H), 2.79 – 2.88 (m, 1H), 2.53 (s, 3H), 2.51 (s, 3H), 2.39 (s, 3H), 2.28 (s, 3H), 2.09 – 2.19 (m, 2H), 1.60 – 1.74 (m, 2H), 1.34 – 1.49 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.15, 174.18, 145.21, 144.55, 143.39, 141.81, 134.90, 134.70, 132.21, 131.63, 131.27, 130.90, 130.21, 129.42, 129.20, 128.81, 128.59, 128.07, 125.97, 124.90, 124.63, 108.17, 108.03, 107.30, 71.85, 69.84, 56.86, 49.83, 42.10, 41.34, 26.27, 26.19, 22.65, 21.87, 21.70, 21.28, 21.02, 20.81 ppm; ESI-HRMS: calcd. For $C_{42}H_{43}N_3O_6S_2$+H 750.2672, found 750.2666.

Following the general procedure, treatment of **1g** (60 mg, 0.34 mmol) with **2** (29 mg, 0.34 mmol), **3c** (100 mg, 0.29 mmol) and 4-TFBA (54 mg, 0.29 mmol) in toluene (2 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4aa:**



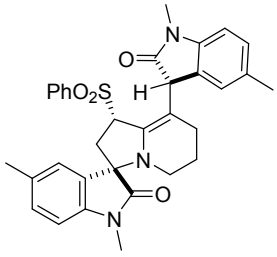
5-bromo-8'-(5-bromo-1-methyl-2-oxoindolin-3-yl)-1-methyl-1'-tosyl-2'-(tosylmethyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4aa); 72 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.69; m.p. 190-191 °C; IR(KBr): 3048, 2981, 2838, 2355, 2328, 1713, 1682, 1593, 1495, 1434, 1359, 1318, 1284, 1221, 1187, 1154, 1144, 1084 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 7.76 (d, *J* = 7.6 Hz, 2H), 7.43 – 7.50 (m, 4H), 7.38 – 7.44 (m, 1H), 7.28 – 7.36 (m, 4H), 6.70 (dd, *J* = 8.0, 5.2 Hz, 2H), 5.84 (d, *J* = 2.0 Hz, 1H), 5.35 (s, 1H), 4.27 (d, *J* = 7.2 Hz, 1H), 3.98 (dd, *J* = 14.8, 2.4 Hz, 1H), 3.79 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.23 (s, 3H), 3.21 (s, 3H), 2.67 (ddd, *J* = 11.8, 7.2, 2.2 Hz, 1H), 2.58 (s, 3H), 2.53 (s, 3H), 2.10 – 2.19 (m, 2H), 1.60 – 1.69 (m, 2H), 1.45 – 1.52 (m, 1H), 1.36 – 1.44 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.43, 173.57, 145.88, 144.96, 144.89, 143.28, 135.07, 134.33, 132.78, 131.08, 130.92, 130.56, 130.40, 130.05, 130.01, 129.78, 129.48, 128.83, 128.35, 128.25, 128.03, 127.20, 127.07, 115.11, 110.04, 109.11, 107.55, 76.68, 71.66, 69.70, 56.65, 49.76, 42.11, 41.44, 26.38, 26.34, 22.58, 21.96, 21.75, 20.72 ppm; ESI-HRMS: calcd. For $C_{40}H_{37}N_3O_6S_2Br_2$+H 878.0569, found 878.0580.

Following the general procedure, treatment of **1b** (115 mg, 0.71 mmol) with **2** (61 mg, 0.71 mmol), **3d** (100 mg, 0.59 mmol) and 4-TFBA (113 mg, 0.59 mmol) in toluene (4 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4ab:**



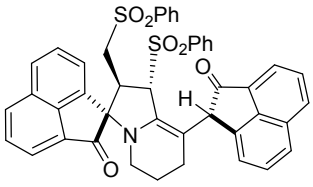
1-methyl-8'-(1-methyl-2-oxoindolin-3-yl)-1'-(phenylsulfonyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4ab); 118 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.51; m.p. 170-171 °C; IR(KBr): 3043, 2931, 2838, 2353, 2321, 1713, 1613, 1494, 1470, 1446, 1372, 1346, 1308, 1258, 1204, 1132, 1085 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.56 (d, *J* = 7.2 Hz, 2H), 7.76 (t, *J* = 7.4 Hz, 1H), 7.69 (t, *J* = 7.4 Hz, 2H), 7.52 (d, *J* = 7.2 Hz, 1H), 7.29 (t, *J* = 8.0 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 7.2 Hz, 1H), 5.53 (s, 1H), 4.95 (dd, *J* = 9.8, 6.6 Hz, 1H), 3.28 (s, 3H), 3.15 (s, 3H), 2.73 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.51 (dd, *J* = 14.8, 6.8 Hz, 1H), 2.17 – 2.28 (m, 1H), 2.11 (td, *J* = 10.4, 3.2 Hz, 1H), 1.70 – 1.82 (m, 1H), 1.59 – 1.68 (m, 1H), 1.31 – 1.54 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.35, 177.32, 144.18, 144.13, 137.18, 134.80, 134.10, 131.33, 129.88, 128.95, 128.49, 127.75, 126.69, 125.97, 124.19, 123.67, 123.20, 122.85, 108.31, 108.23, 107.52, 69.33, 64.96, 49.80, 42.49, 35.38, 26.27, 25.95, 22.46, 20.92 ppm; ESI-HRMS: calcd. For $C_{31}H_{29}N_3O_4S$+H 540.1957, found 540.1965.

Following the general procedure, treatment of **1a** (125 mg, 0.71 mmol) with **2** (61 mg, 0.71 mmol), **3d** (100 mg, 0.59 mmol) and 4-TFBA (113 mg, 0.59 mmol) in toluene (4 mL) at 110 °C for 1 h followed by column chromatography afforded the product **4ac:**



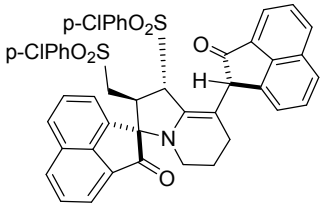
8'-(1,5-dimethyl-2-oxoindolin-3-yl)-1,5-dimethyl-1'-(phenylsulfonyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (4ac); 119 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.53; m.p. 170-171; IR(KBr): 3032, 2921, 2836, 2351, 2311, 1714, 1612, 1493, 1471, 1445, 1373, 1345, 1309, 1254, 1200, 1132, 1088 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.55 – 8.61 (m, 2H), 7.74 – 7.80 (m, 1H), 7.65 – 7.74 (m, 2H), 7.32 (s, 1H), 6.98 – 7.10 (m, 2H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.15 (s, 1H), 5.49 (s, 1H), 4.92 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.26 (s, 3H), 3.12 (s, 3H), 2.73 (dd, *J* = 14.6, 10.2 Hz, 1H), 2.48 (dd, *J* = 14.8, 6.4 Hz, 1H), 2.40 (s, 3H), 2.26 (s, 3H), 2.09 – 2.24 (m, 2H), 1.70 – 1.82 (m, 1H), 1.60 – 1.70 (m, 1H), 1.35 – 1.55 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.36, 177.34, 141.87, 141.71, 137.10, 133.98, 132.72, 132.18, 131.41, 129.98, 128.96, 128.50, 127.96, 126.93, 125.08, 124.48, 108.02, 107.21, 69.39, 65.12, 49.89, 42.41, 35.42, 26.27, 25.94, 22.49, 21.25, 20.95, 20.94 ppm; ESI-HRMS: calcd. For $C_{33}H_{33}N_3O_4S$+H 568.2270, found 568.2272.

Following the general procedure, treatment of **1w** (68 mg, 0.37 mmol) with **2** (32 mg, 0.27 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1.5 h followed by column chromatography afforded the product **5a:**



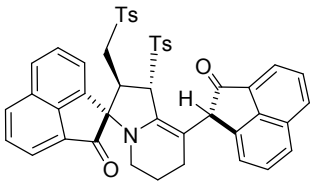
8'-(2-oxo-1,2-dihydroacenaphthylen-1-yl)-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-2H,2'H-spiro[acenaphthylene-1,3'-indolizin]-2-one (5a); 79 mg; yellow solid; R_f (e ethyl acetate : petroleum ether = 1:1) = 0.44; m.p. 214-215 °C; IR(KBr): 3054, 2929, 2839, 2353, 2321, 1716, 1605, 1583, 1494, 1464, 1434, 1310, 1276, 1196, 1164, 1138, 1083 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.39 (d, *J* = 7.6 Hz, 2H), 8.14 (dd, *J* = 11.2, 8.0 Hz, 2H), 7.90 – 8.02 (m, 3H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.79 – 7.84 (m, 1H), 7.67 – 7.79 (m, 5H), 7.59 – 7.67 (m, 2H), 7.44 – 7.55 (m, 4H), 6.68 (d, *J* = 6.8 Hz, 1H), 5.78 (s, 1H), 4.63 (d, *J* = 7.6 Hz, 1H), 4.05 (dd, *J* = 14.2, 1.8 Hz, 1H), 3.58 (dd, *J* = 14.2, 11.4 Hz, 1H), 3.44 – 3.52 (m, 1H), 2.07 (t, *J* = 5.4 Hz, 2H), 1.56 – 1.80 (m, 2H), 1.14 – 1.35 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.76, 205.16, 143.58, 141.47, 138.36, 137.80, 135.29, 134.48, 133.88, 133.18, 133.06, 131.46, 130.83, 130.81, 130.17, 129.69, 128.43, 128.36, 128.04, 127.69, 127.61, 127.40, 125.49, 123.33, 120.60, 120.46, 120.14, 120.08, 109.82, 74.75, 69.12, 55.77, 55.13, 41.88, 40.37, 22.40, 20.19 ppm; $C_{44}H_{33}NO_6S_2$+H 736.1828, found 736.1816.

Following the general procedure, treatment of **1w** (56 mg, 0.31 mmol) with **2** (26 mg, 0.31 mmol), **3b** (100 mg, 0.26 mmol) and 4-TFBA (49 mg, 0.26 mmol) in toluene (2 mL) at 110 °C for 1.5 h followed by column chromatography afforded the product **5b:**

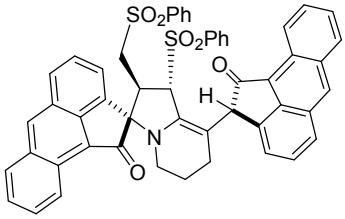


1'-((4-chlorophenyl)sulfonyl)-2'-(((4-chlorophenyl)sulfonyl)methyl)-8'-(2-oxo-1,2-dihydroacenaphthylen-1-yl)-1',5',6',7'-tetrahydro-2H,2'H-spiro[acenaphthylene-1,3'-indolizin]-2-one (5b); 97 mg; yellow solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.44; m.p. 200-201°C; IR(KBr): 3086, 2948, 2837, 2353, 2321, 1713, 1604, 1581, 1494, 1477, 1464, 1433, 1396, 1365, 1316, 1178, 1144, 1089 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.46 (d, *J* = 8.4 Hz, 2H), 8.15 (dd, *J* = 14.4, 8.0 Hz, 2H), 7.89 – 8.01 (m, 3H), 7.83 – 7.89 (m, 2H), 7.64 – 7.81 (m, 6H), 7.42 (s, 4H), 6.80 (d, *J* = 6.8 Hz, 1H), 5.74 (s, 1H), 4.67 (d, *J* = 7.2 Hz, 1H), 4.00 (d, *J* = 12.4 Hz, 1H), 3.40 – 3.63 (m, 2H), 1.95 – 2.24 (m, 2H), 1.55 – 1.74 (m, 2H), 1.08 – 1.43 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 206.13, 205.69, 144.12, 142.13, 141.53, 140.44, 138.78, 137.08, 135.43, 134.94, 134.43, 132.95, 132.67, 132.51, 131.85, 131.50, 130.82, 130.42, 129.53, 129.26, 129.02, 128.40, 128.05, 126.30, 124.03, 121.30, 121.15, 120.77, 111.04, 75.36, 69.75, 56.44, 55.72, 42.60, 41.17, 22.99, 20.88 ppm; ESI-HRMS: calcd. For $C_{44}H_{31}NO_6S_2Cl_2$+H 804.1048, found 804.1034.

Following the general procedure, treatment of **1w** (62 mg, 0.34 mmol) with **2** (29 mg, 0.34 mmol), **3c** (100 mg, 0.29 mmol) and 4-TFBA (54 mg, 0.29 mmol) in toluene (2 mL) at 110 °C for 2 h followed by column chromatography afforded the product **5c:**



8'-(2-oxo-1,2-dihydroacenaphthylen-1-yl)-1'-tosyl-2'-(tosylmethyl)-1',5',6',7'-tetrahydro-2H,2'H-spiro[acenaphthylene-1,3'-indolizin]-2-one (5c); 96 mg; yellow solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.45; m.p. 190-191 °C; IR(KBr): 3043, 2946, 2838, 2353, 2320, 1722, 1682, 1594, 1574, 1487, 1434, 1416, 1318, 1305, 1218, 1196, 1135, 1085 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 8.23 (d, *J* = 8.0 Hz, 2H), 8.13 (dd, *J* = 11.6, 8.0 Hz, 2H), 7.93 – 8.02 (m, 2H), 7.92 (s, 1H), 7.86 (dd, *J* = 7.6, 2.8 Hz, 2H), 7.68 – 7.79 (m, 3H), 7.64 (dd, *J* = 8.4, 6.8 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.34 – 7.41 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 6.8 Hz, 1H), 5.79 (s, 1H), 4.60 (d, *J* = 7.6 Hz, 1H), 4.01 (dd, *J* = 14.0, 1.2 Hz, 1H), 3.42 – 3.60 (m, 2H), 2.57 (s, 3H), 2.46 (s, 3H), 2.03 – 2.12 (m, 2H), 1.69-1.81 (m, 1H), 1.59-1.68 (m, 1H), 1.27-1.41 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 206.42, 205.72, 145.44, 144.61, 144.18, 142.05, 139.07, 138.72, 136.07, 135.52, 135.20, 134.54, 132.43, 132.11, 131.47, 131.35, 131.10, 130.88, 130.77, 130.04, 129.99, 129.50, 129.25, 129.03, 128.32, 128.24, 128.17, 128.01, 127.97, 126.02, 123.88, 121.15, 121.01, 120.73, 110.22, 75.41, 69.74, 57.85, 56.51, 55.74, 42.49, 41.03, 23.00, 21.97, 21.64, 20.86 ppm; ESI-HRMS: calcd. For $C_{46}H_{37}NO_6S_2$+H 764.2141, found 764.2178.

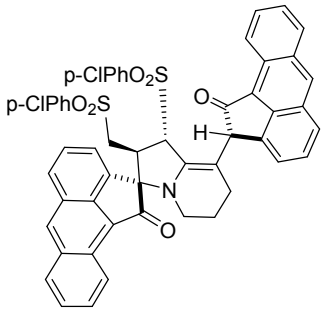


Following the general procedure, treatment of **1x** (86 mg, 0.37 mmol) with **2** (32 mg, 0.27 mmol), **3a** (100 mg, 0.31 mmol) and 4-TFBA (59 mg, 0.31 mmol) in toluene (2 mL) at 110 °C for 1.5 h followed by column chromatography afforded the product **5d:**

8'-(1-oxo-1,2-dihydroaceanthrylen-2-yl)-1'-(phenylsulfonyl)-2'-((phenylsulfonyl)methyl)-1',5',6',7'-tetrahydro-1H,2'H-spiro[aceanthrylene-2,3'-indolizin]-1-one (5d); 113 mg; yellow solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.53; m.p. 227-228 °C; IR(KBr): 3048, 2924, 2839, 2403, 2307, 1691, 1626, 1595, 1579, 1532, 1458, 1403, 1318, 1305, 1221, 1154, 1143, 1085 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 9.27 (d, *J* = 8.4 Hz, 1H), 9.19 (d, *J* = 8.8 Hz, 1H), 8.73 (d, *J* = 9.6 Hz, 2H), 8.39 – 8.49 (m, 2H), 8.17 (dd, *J* = 8.4, 5.2 Hz, 2H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.99 (dd, *J* = 7.6, 6.0 Hz, 2H), 7.71 – 7.88 (m, 6H), 7.56 – 7.68 (m, 4H), 7.44 – 7.53 (m, 4H), 6.67 (d, *J* = 6.4 Hz, 1H), 5.94 (s, 1H), 4.77 (d, *J* = 8.0 Hz, 1H), 4.10 (dd, *J* = 14.4, 1.2 Hz, 1H), 3.69 (dd, *J* = 14.4, 11.2 Hz, 1H), 3.49 – 3.59 (m, 1H), 2.08 – 2.21 (m, 2H), 1.74 – 1.86 (m, 1H), 1.54 – 1.68 (m, 1H), 1.20 – 1.35 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.76, 205.73, 146.41, 144.20, 139.27, 138.48, 136.36, 135.36, 134.41, 133.89, 133.73, 133.51, 133.48, 133.40, 132.28, 131.49, 130.44, 129.51, 129.19, 128.86, 128.64, 128.46, 128.27, 128.09, 128.01, 127.66, 127.55,

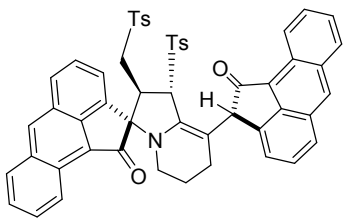
127.23, 126.56, 126.26, 125.42, 125.38, 125.09, 124.77, 124.65, 124.12, 120.23, 120.17, 110.32, 75.54, 69.86, 56.49, 55.99, 42.47, 40.89, 22.87, 20.85 ppm; ESI-HRMS: calcd. For $C_{52}H_{37}NO_6S_2$+H 836.2141, found 836.2114.

Following the general procedure, treatment of **1x** (71 mg, 0.31 mmol) with **2** (26 mg, 0.31 mmol), **3b** (100 mg, 0.26 mmol) and 4-TFBA (49 mg, 0.26 mmol) in toluene (2 mL) at 110 °C for 1.5 h followed by column chromatography afforded the product **5e:**



1'-((4-chlorophenyl)sulfonyl)-2'-(((4-chlorophenyl)sulfonyl)methyl)-8'-(1-oxo-1,2-dihydroaceanthrylen-2-yl)-1',5',6',7'-tetrahydro-1H,2'H-spiro[aceanthrylene-2,3'-indolizin]-1-one (5e)：99 mg; yellow solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.52; m.p. 217-218 °C; IR(KBr): 3045, 2911, 2839, 2397, 2307, 1710, 1624, 1592, 1570, 1530, 1448, 1413, 1315, 1305, 1211, 1162, 1144, 1080 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 9.25 (d, *J* = 8.4 Hz, 1H), 9.16 (d, *J* = 8.4 Hz, 1H), 8.74 (d, *J* = 12.0 Hz, 2H), 8.55 (d, *J* = 8.4 Hz, 2H), 8.18 (d, *J* = 8.4 Hz, 2H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.98 (dd, *J* = 10.8, 7.6 Hz, 2H), 7.73 – 7.88 (m, 5H), 7.58 – 7.82 (m, 3H), 7.35 – 7.42 (m, 2H), 7.31 – 7.34 (m, 2H), 6.80 (d, *J* = 6.6 Hz, 1H), 5.90 (s, 1H), 4.81 (d, *J* = 7.6 Hz, 1H), 4.05 (d, *J* = 14.0 Hz, 1H), 3.52 – 3.72 (m, 2H), 2.12 – 2.22 (m, 2H), 1.72 – 1.83 (m, 1H), 1.58 – 1.70 (m, 1H), 1.25 – 1.32 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.75, 205.55, 146.33, 144.30, 141.46, 140.26, 139.11, 137.09, 135.84, 135.20, 133.98, 133.50, 133.45, 133.03, 132.55, 132.43, 129.71, 129.64, 129.43, 129.24, 129.11, 129.03, 128.99, 128.48, 128.26, 128.17, 128.03, 127.54, 127.38, 126.70, 126.48, 126.35, 124.87, 124.76, 124.57, 124.23, 120.36, 120.27, 110.95, 75.52, 69.79, 56.47, 55.96, 42.58, 41.08, 22.87, 20.95 ppm; ESI-HRMS: calcd. For $C_{52}H_{35}NO_6S_2Cl_2$+H 904.1361, found 904.1328.

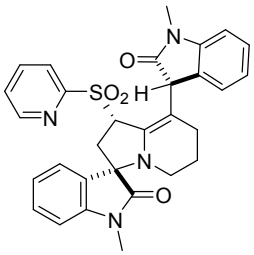
Following the general procedure, treatment of **1x** (80 mg, 0.34 mmol) with **2** (29 mg, 0.34 mmol), **3c** (100 mg, 0.29 mmol) and 4-TFBA (54 mg, 0.29 mmol) in toluene (2 mL) at 110 °C for 2 h followed by column chromatography afforded the product **5f:**



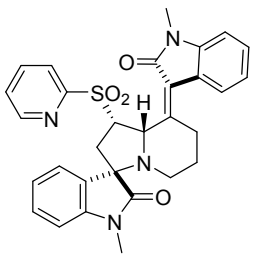
8'-(1-oxo-1,2-dihydroaceanthrylen-2-yl)-1'-tosyl-2'-(tosylmethyl)-1',5',6',7'-tetrahydro-1H,2'H-spiro[aceanthrylene-2,3'-indolizin]-1-one (5f): 123 mg; yellow solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.50; m.p. 245-246 °C; IR(KBr): 3044, 2901, 2811, 2388, 2317, 1716, 1614, 1591, 1561, 1524, 1449, 1411, 1324, 1311, 1231, 1154, 1114, 1076 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ = 9.26 (d, *J* = 8.8 Hz, 1H), 9.18 (d, *J* = 8.8 Hz, 1H), 8.72 (d, *J* = 11.6 Hz, 2H), 8.29 (d, *J* = 7.6 Hz, 2H), 8.12 – 8.20 (m, 2H), 8.04 (d, *J* = 8.8 Hz, 1H), 7.95 – 8.01 (m, 2H), 7.77 – 7.84 (m, 2H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.57 – 7.68 (m, 3H), 7.52 (d, *J* = 8.0

Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 6.8 Hz, 1H), 5.94 (s, 1H), 4.75 (d, *J* = 8.0 Hz, 1H), 4.00 – 4.13 (m, 1H), 3.70 (dd, *J* = 14.8, 11.6 Hz, 1H), 3.41 – 3.58 (m, 2H), 3.09 (s, 1H), 2.60 (s, 3H), 2.41 (s, 3H), 2.11 – 2.19 (m, 2H)., 1.74 – 1.84 (m, 1H), 1.52 – 1.69 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.80, 205.75, 146.38, 144.45, 144.18, 139.39, 136.53, 135.57, 133.62, 133.46, 133.41, 132.22, 131.54, 131.19, 129.49, 129.46, 129.39, 129.26, 129.18, 128.81, 128.47, 128.29, 128.27, 128.09, 128.02, 127.71, 127.54, 127.23, 126.54, 126.24, 126.20, 125.11, 124.80, 124.66, 124.08, 120.21, 110.14, 75.58, 69.85, 56.61, 55.99, 42.48, 40.95, 22.89, 21.98, 21.57, 20.92. ppm; ESI-HRMS: calcd. For $C_{54}H_{41}NO_6S_2$+H 864.2454, found 864.2438.

Following the general procedure, treatment of **1b** (114 mg, 0.71 mmol) with **2** (61 mg, 0.71 mmol), **3f** (100 mg, 0.59 mmol) and 4-TFBA (113 mg, 0.59 mmol) in toluene (4 mL) at 110 °C for 2 h followed by column chromatography afforded the product **6** and **7:**

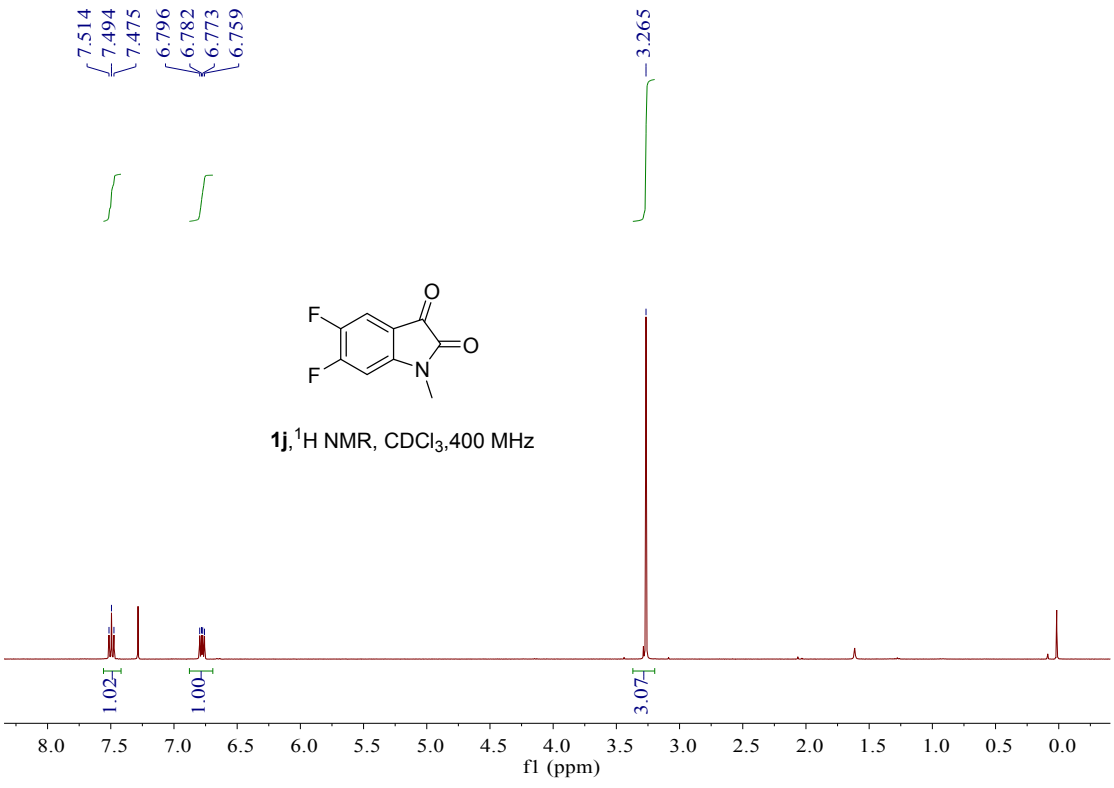


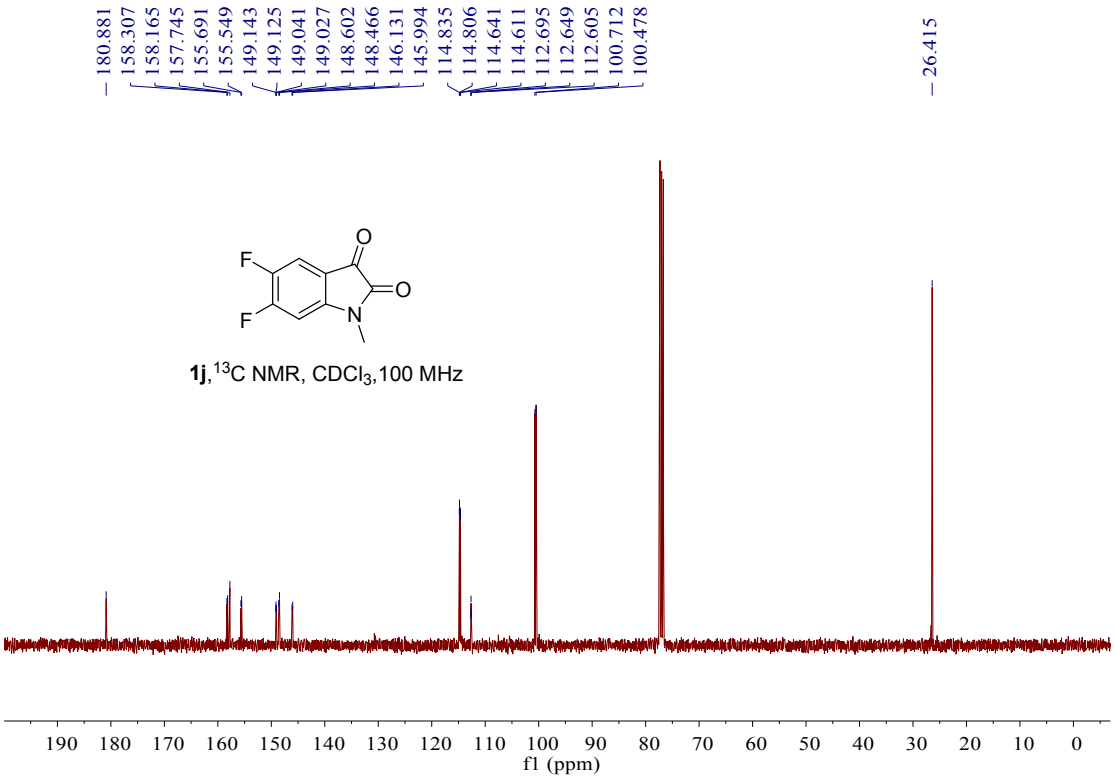
1-methyl-8'-(1-methyl-2-oxoindolin-3-yl)-1'-(pyridin-2-ylsulfonyl)-1',5',6',7'-tetrahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (6): 46 mg; white solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.38; m.p. 170-171 °C; IR(KBr): 3035, 2928, 2833, 2348, 2311, 1714, 1611, 1492, 1469, 1444, 1377, 1349, 1306, 1251, 1210, 1122, 1087 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 9.15 (d, *J* = 8.0 Hz, 1H), 8.89 (d, *J* = 4.8 Hz, 1H), 8.07 (td, *J* = 7.6, 2.0 Hz, 1H), 7.59 – 7.64 (m, 1H), 7.54 (d, *J* = 7.2 Hz, 1H), 7.27 – 7.34 (m, 2H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.07 – 7.15 (m, 2H), 6.80 (t, *J* = 8.4 Hz, 2H), 5.38 (s, 1H), 5.02 (dd, *J* = 10.0, 6.4 Hz, 1H), 3.32 (dd, *J* = 14.4, 6.4 Hz, 1H), 3.26 (s, 3H), 3.16 (s, 3H), 2.74 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.16 – 2.24 (m, 1H), 2.06 – 2.14 (m, 1H), 1.60 – 1.68 (m, 1H), 1.49 – 1.58 (m, 1H), 1.35 – 1.45 (m, 1H), 0.99 – 1.15 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.27, 177.10, 154.83, 149.22, 144.18, 144.04, 137.53, 136.90, 129.91, 128.90, 128.15, 127.78, 127.61, 126.56, 124.78, 124.23, 123.26, 122.97, 108.38, 108.18, 107.51, 69.68, 64.68, 49.68, 42.33, 34.72, 26.25, 25.93, 22.29, 20.96. ppm; ESI-HRMS: calcd. For $C_{30}H_{28}N_4O_4S$+H 541.1910, found 541.1932.



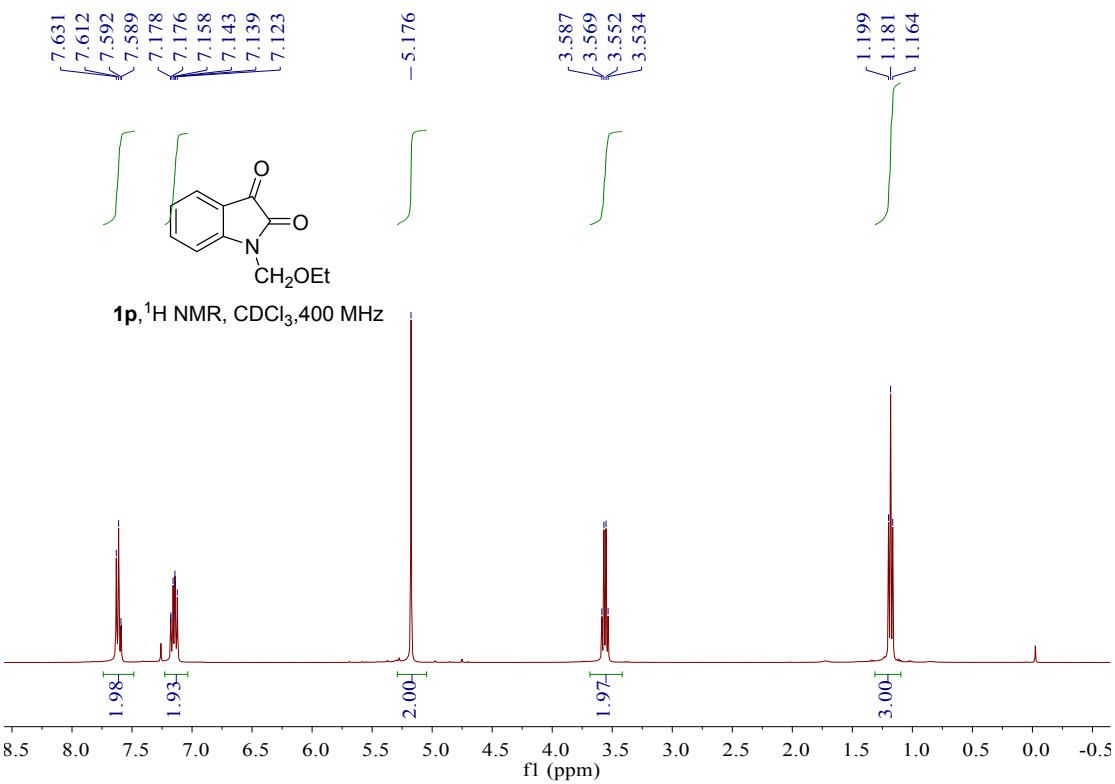
(Z)-1-methyl-8'-(1-methyl-2-oxoindolin-3-ylidene)-1'-(pyridin-2-ylsulfonyl)-1',5',6',7',8',8a'-hexahydro-2'H-spiro[indoline-3,3'-indolizin]-2-one (7); 92 mg; yellow solid; R_f (ethyl acetate : petroleum ether = 1:1) = 0.32; m.p. 165-166 °C; IR(KBr): 2924, 2854, 2361, 2343, 1734, 1717, 1686, 1654, 1611, 1472, 1459, 1375, 1319, 1261, 1164, 1090 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.92 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 4.8 Hz, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.67 (td, *J* = 7.8, 1.6 Hz, 1H), 7.36 (td, *J* = 7.8, 1.2 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.17 – 7.25 (m, 2H), 7.06 (td, *J* = 7.6, 1.2 Hz, 1H), 7.00 (ddd, *J* = 7.6, 4.6, 1.2 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.59 (dd, *J* = 7.8, 1.2 Hz, 1H), 5.40 – 5.45 (m, 1H), 5.24 – 5.32 (m, 1H), 4.38 (ddd,

J = 12.8, 5.6, 1.6 Hz, 1H), 3.24 (dd, *J* = 15.4, 3.6 Hz, 1H), 3.18 (s, 3H), 3.05 (s, 3H), 2.96 – 3.04 (m, 1H), 2.92 (dd, *J* = 15.4, 9.8 Hz, 1H), 2.49 (td, *J* = 11.2, 3.6 Hz, 1H), 2.22 – 2.33 (m, 1H), 2.02 – 2.15 (m, 1H), 1.33 – 1.49 (m, 1H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 178.48, 166.65, 157.15, 149.22, 143.99, 141.54, 136.87, 129.61, 128.49, 128.30, 125.95, 125.34, 124.06, 123.81, 123.37, 122.98, 122.37, 122.20, 121.21, 107.92, 107.09, 66.53, 62.84, 56.31, 40.06, 33.94, 25.78, 25.45, 23.29, 22.67 ppm; ESI-HRMS: calcd. For $C_{30}H_{28}N_4O_4S$+H 541.1910, found 541.1917.

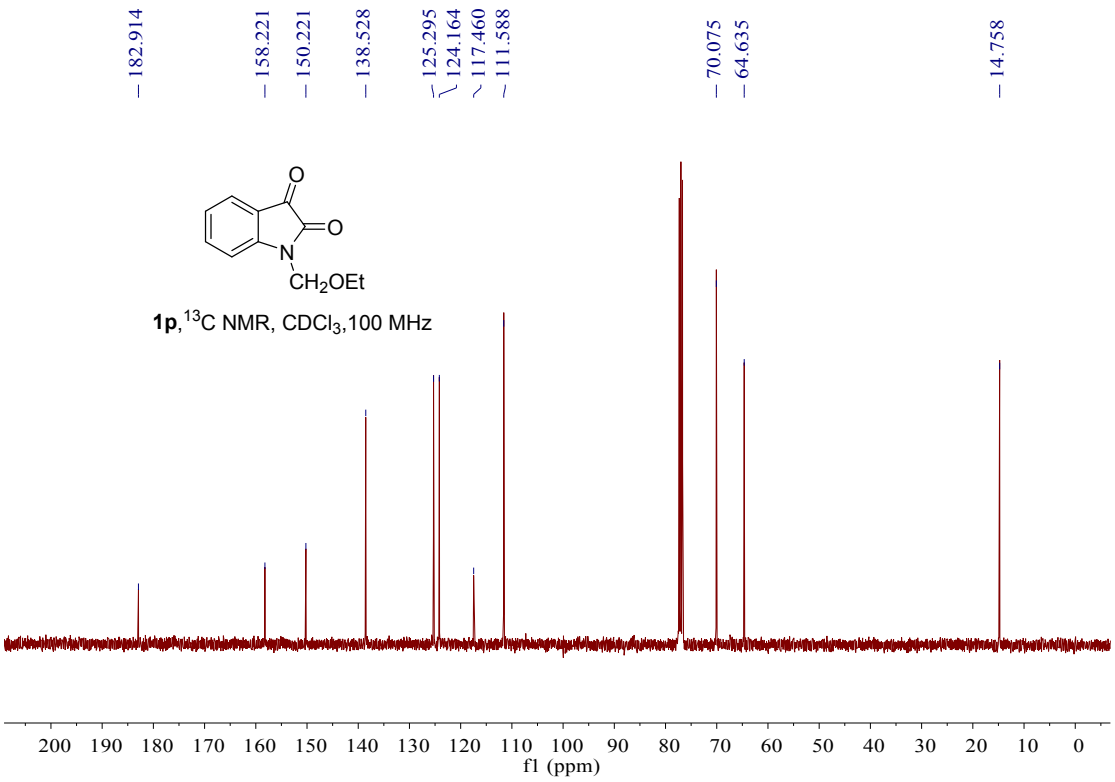




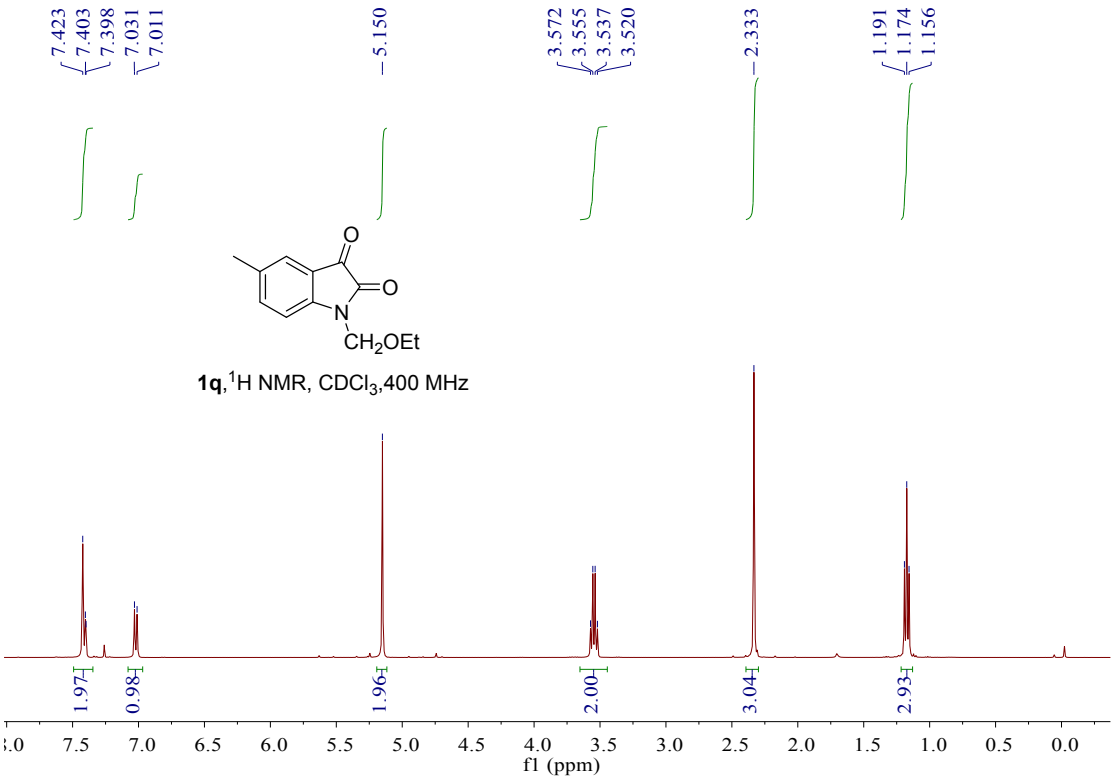
1j,^{13}C NMR, $CDCl_3$,100 MHz



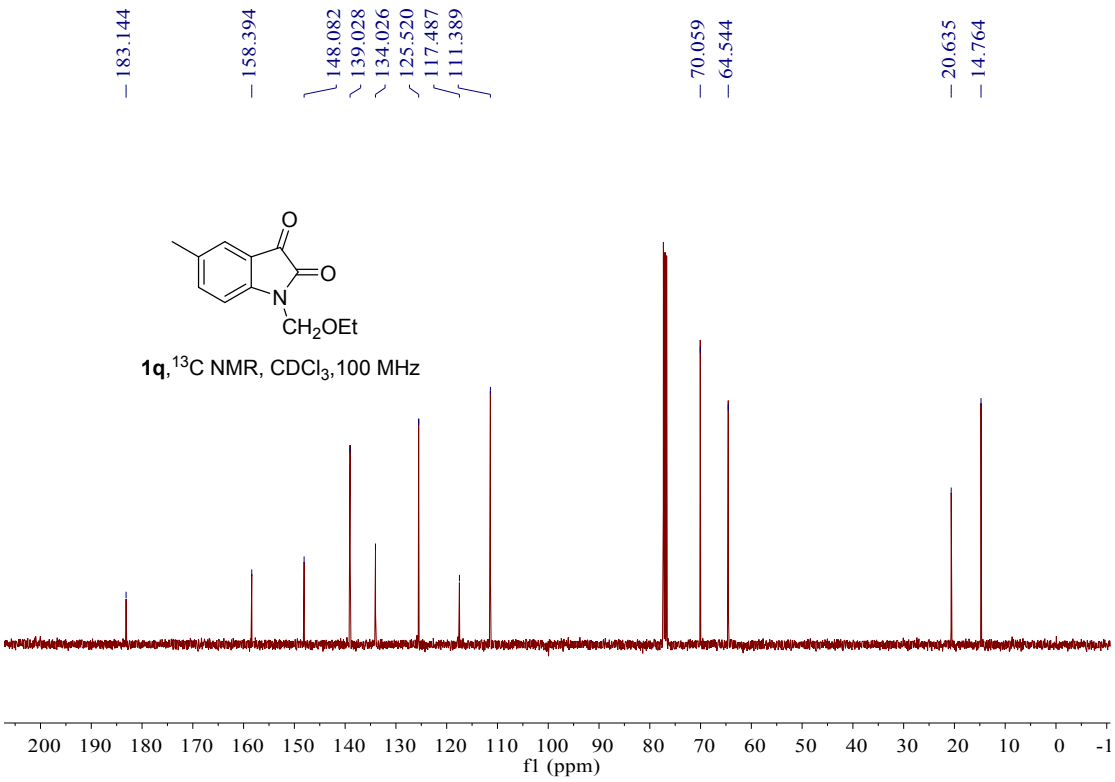
1p,^{1}H NMR, $CDCl_3$,400 MHz

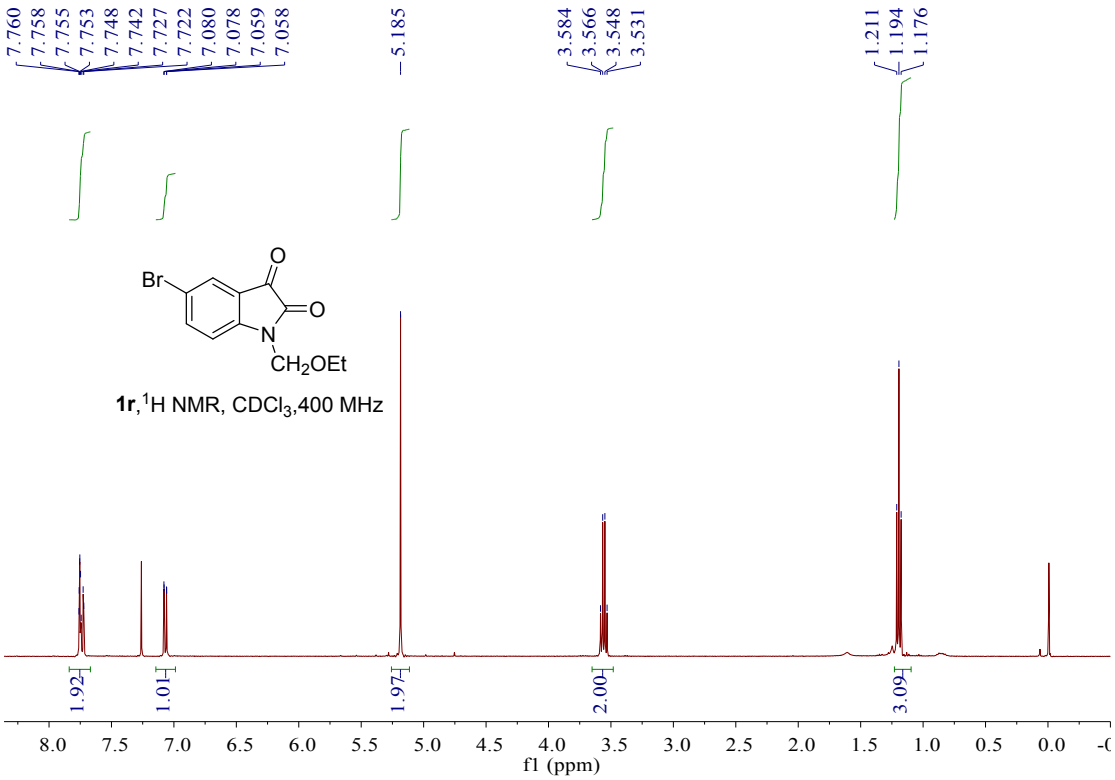


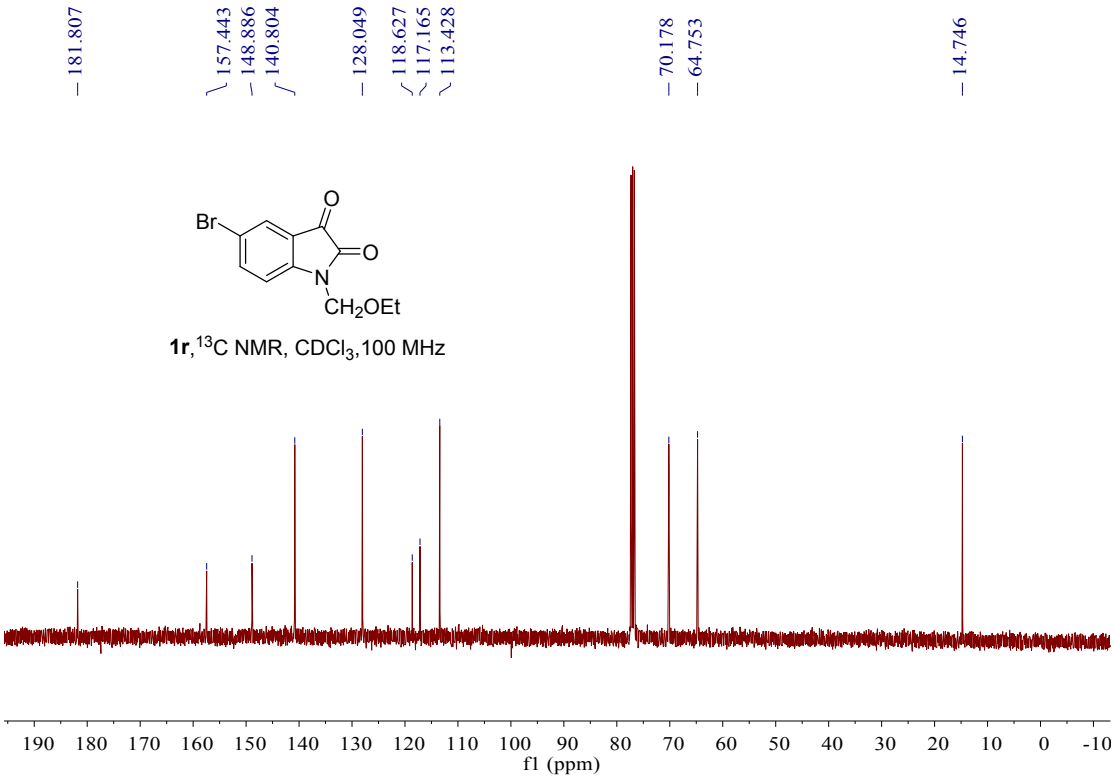
1p,^{13}C NMR, $CDCl_3$,100 MHz



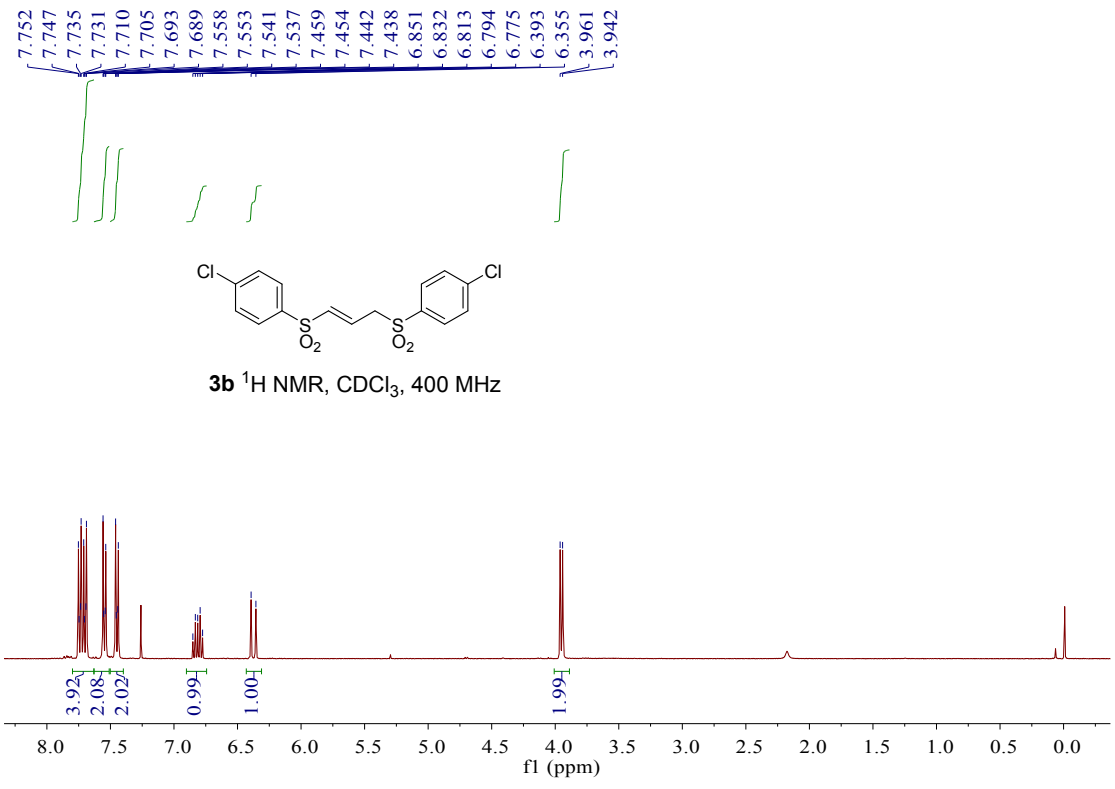
1q,^{1}H NMR, $CDCl_3$,400 MHz


183.144
158.394
148.082
139.028
134.026
125.520
117.487
111.389
70.059
64.544
20.635
14.764
O
O
N
CH2OEt
1q,13C NMR, CDCl3,100 MHz
f1 (ppm)

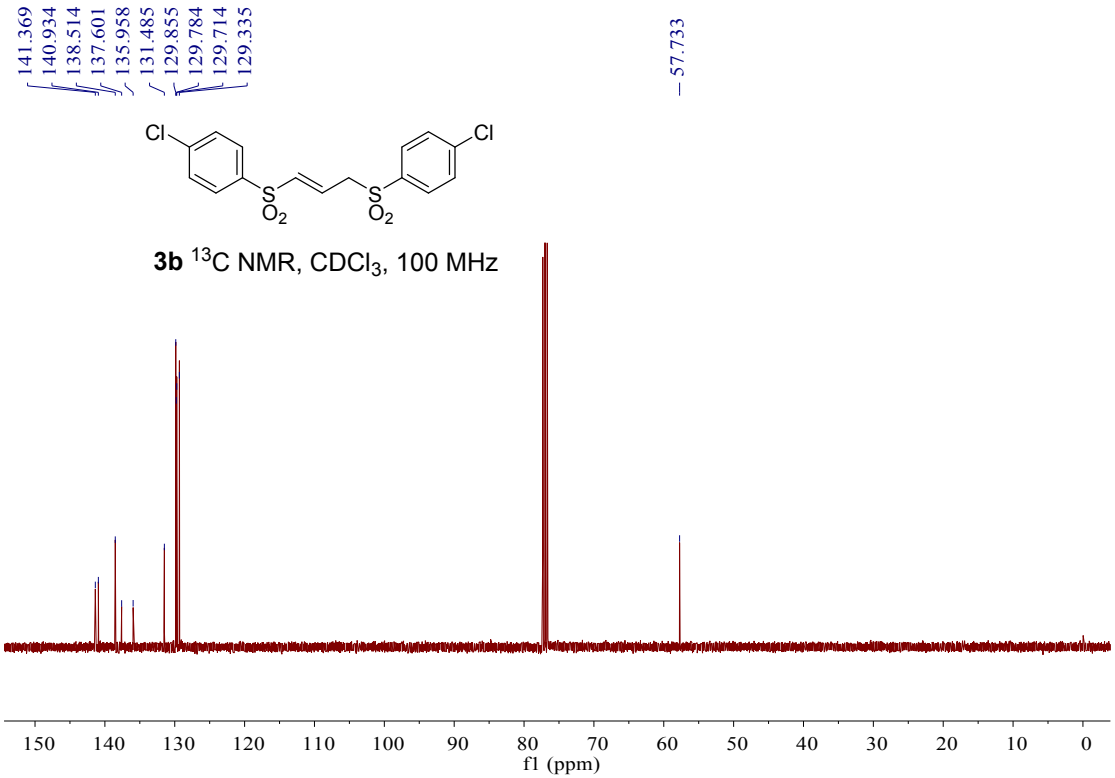

7.760
7.758
7.755
7.753
7.748
7.742
7.727
7.722
7.080
7.078
7.059
7.058
5.185
3.584
3.566
3.548
3.531
1.211
1.194
1.176
Br
O
O
N
CH2OEt
1r,1H NMR, CDCl3,400 MHz
1.92
1.01
1.97
2.00
3.09
f1 (ppm)



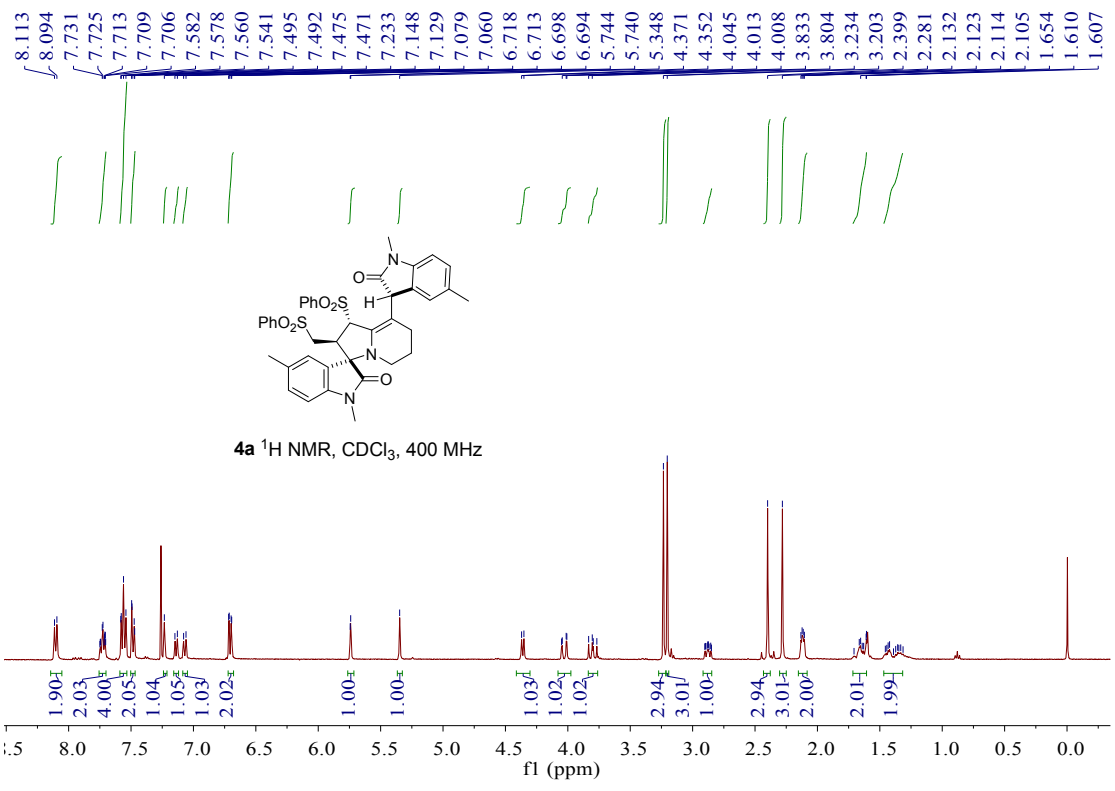
1r,^{13}C NMR, $CDCl_3$,100 MHz



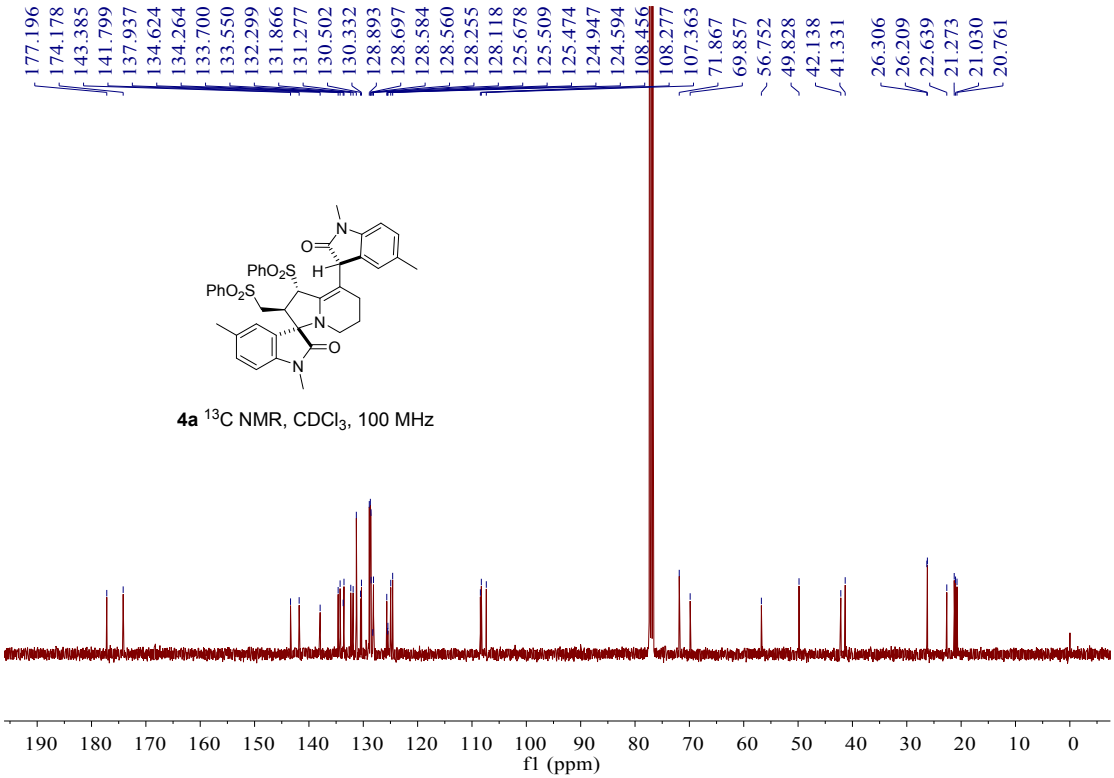
3b ^{1}H NMR, $CDCl_3$, 400 MHz



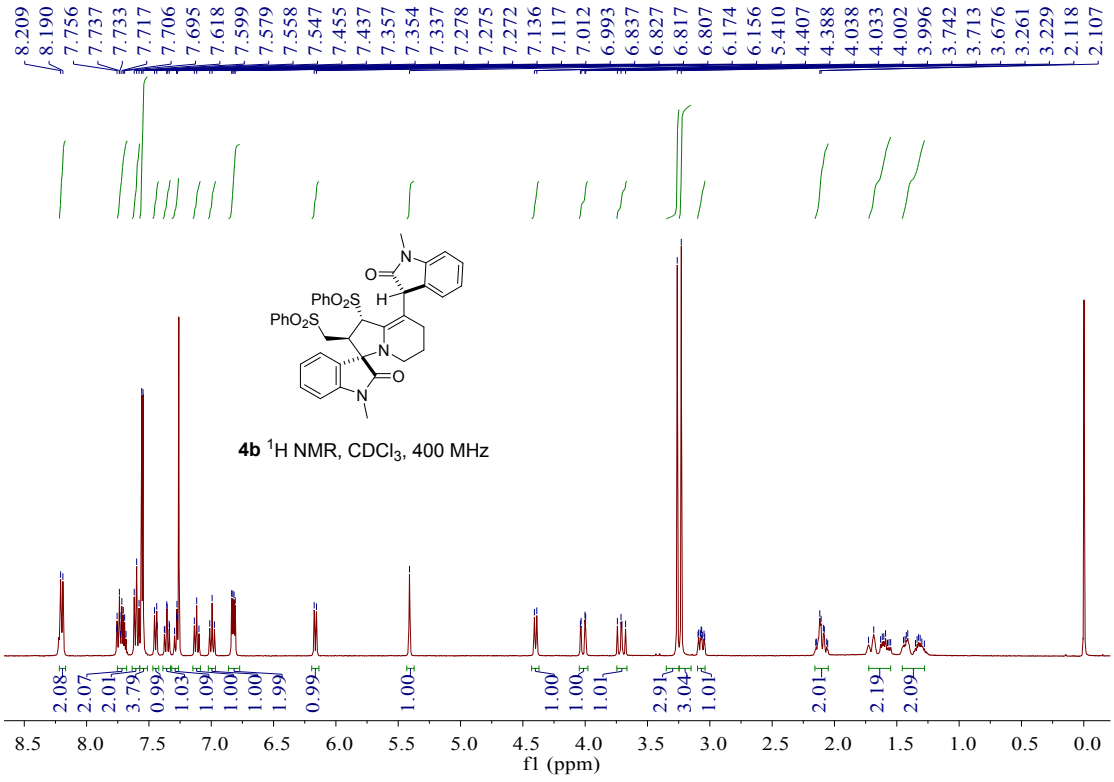
3b ^{13}C NMR, $CDCl_3$, 100 MHz



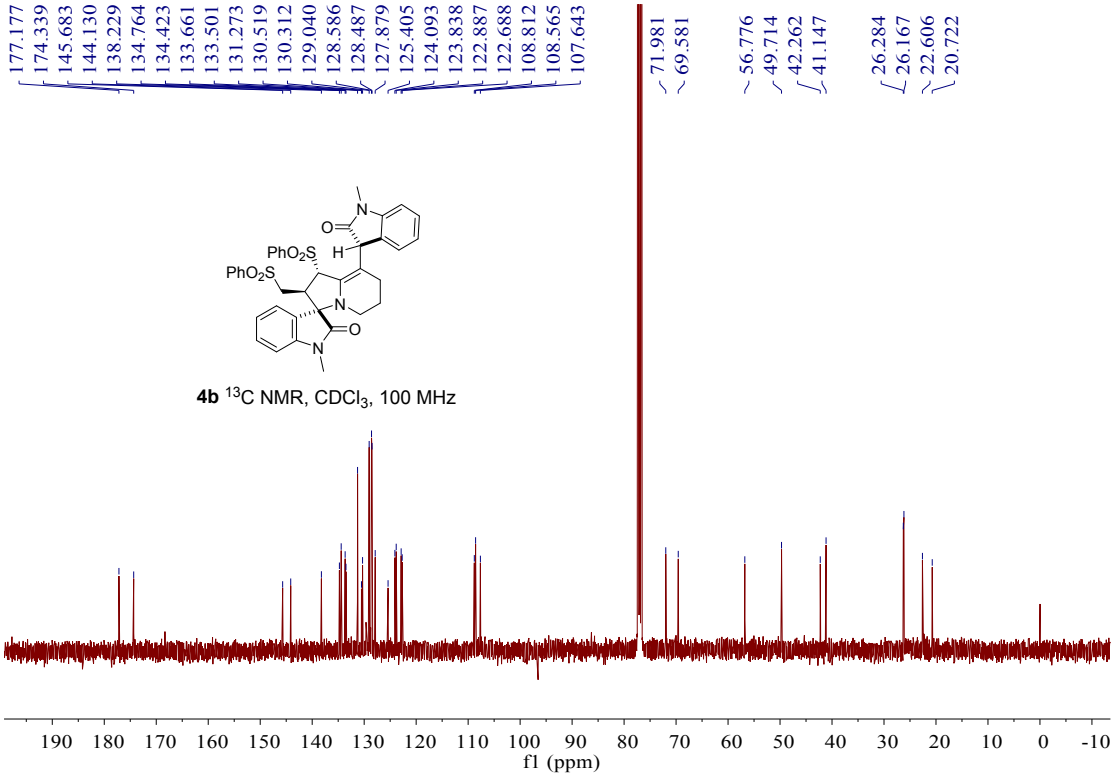
4a ^{1}H NMR, $CDCl_3$, 400 MHz



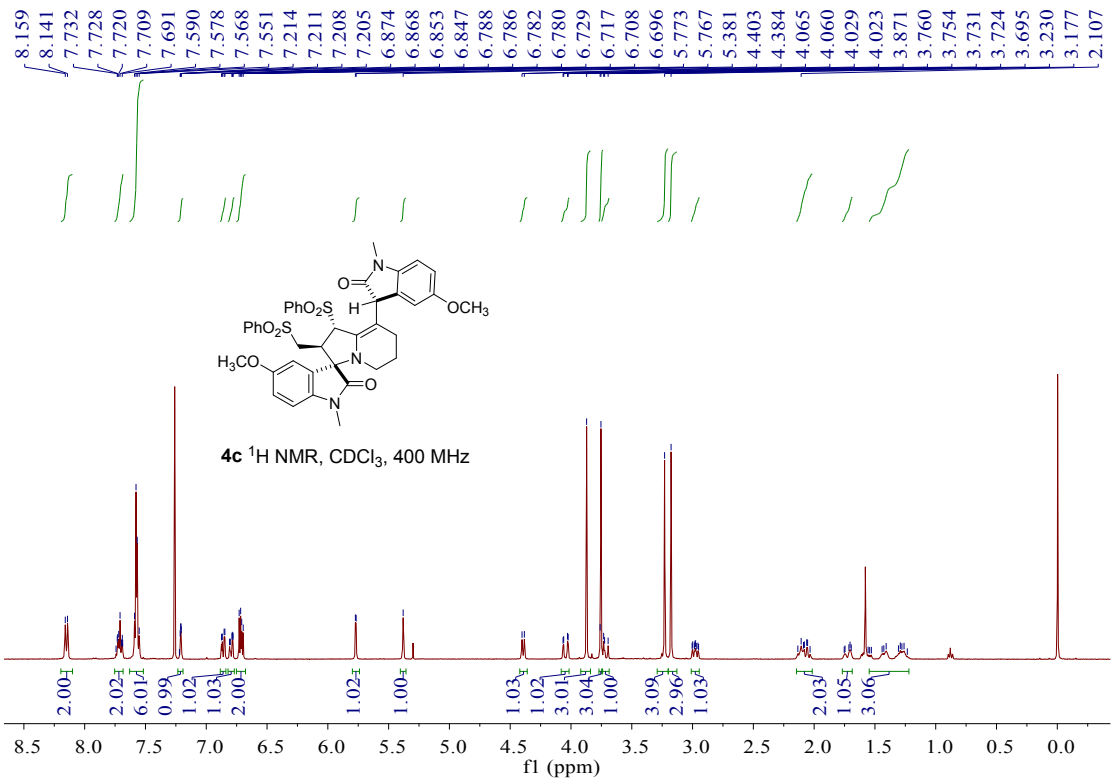
4a ^{13}C NMR, $CDCl_3$, 100 MHz



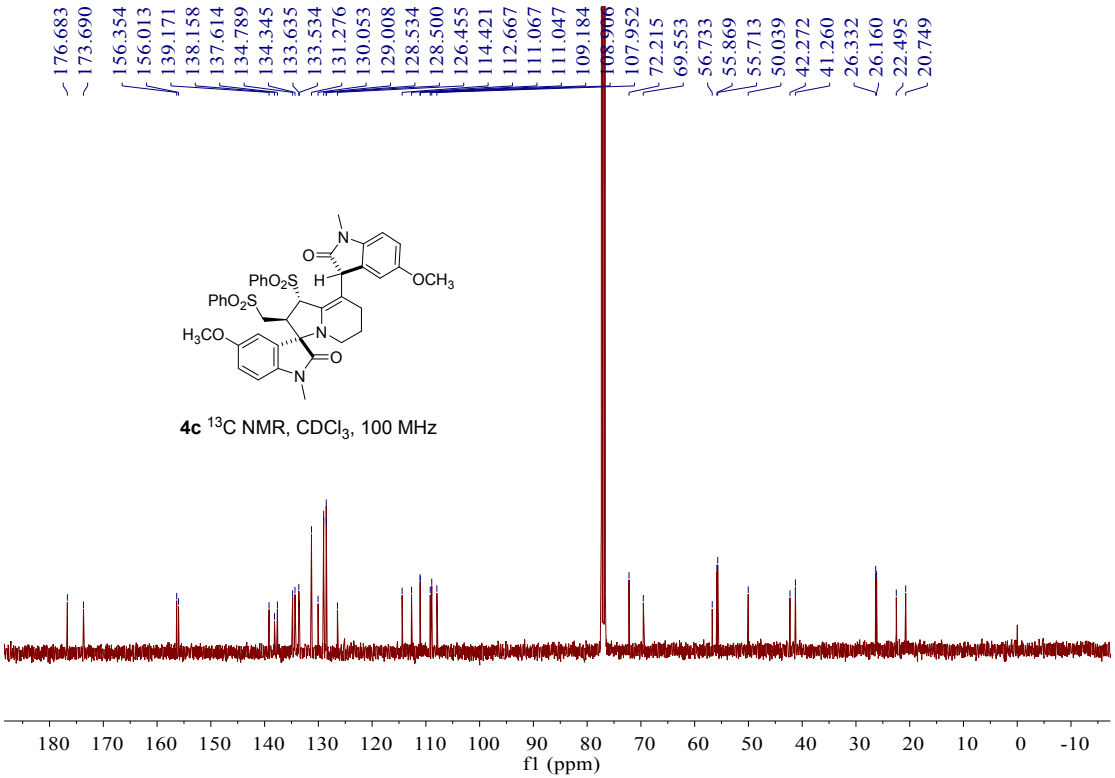
4b ^{1}H NMR, $CDCl_3$, 400 MHz



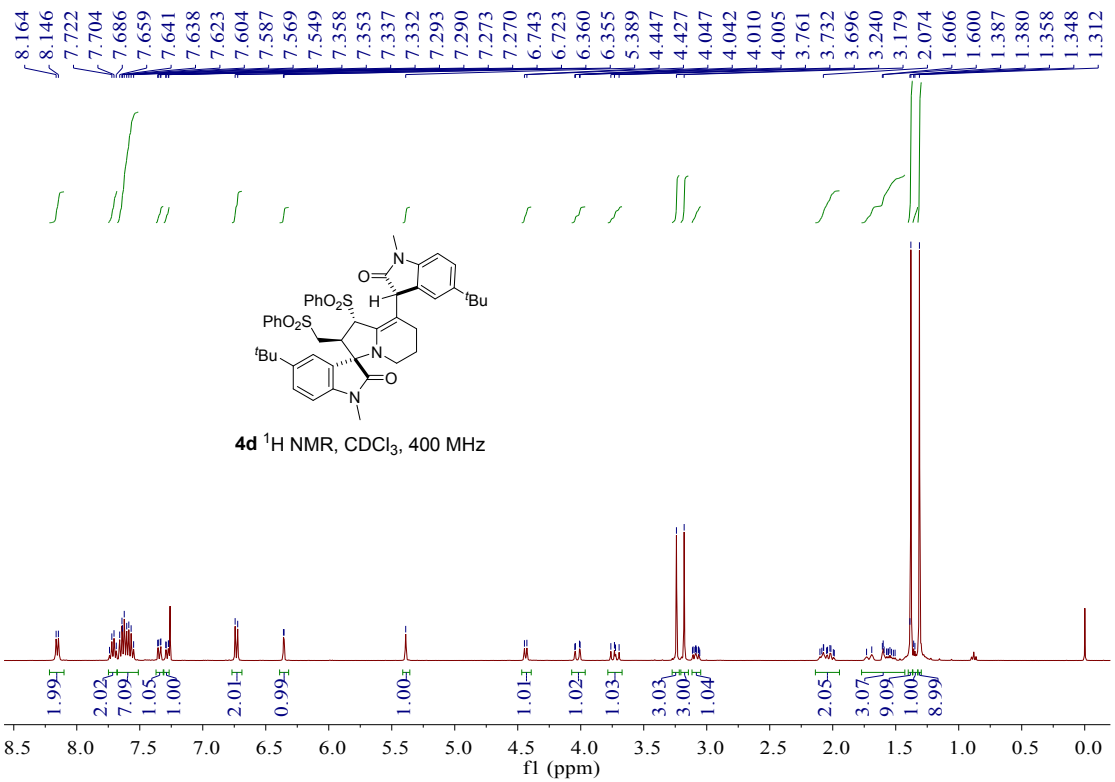
4b ^{13}C NMR, $CDCl_3$, 100 MHz



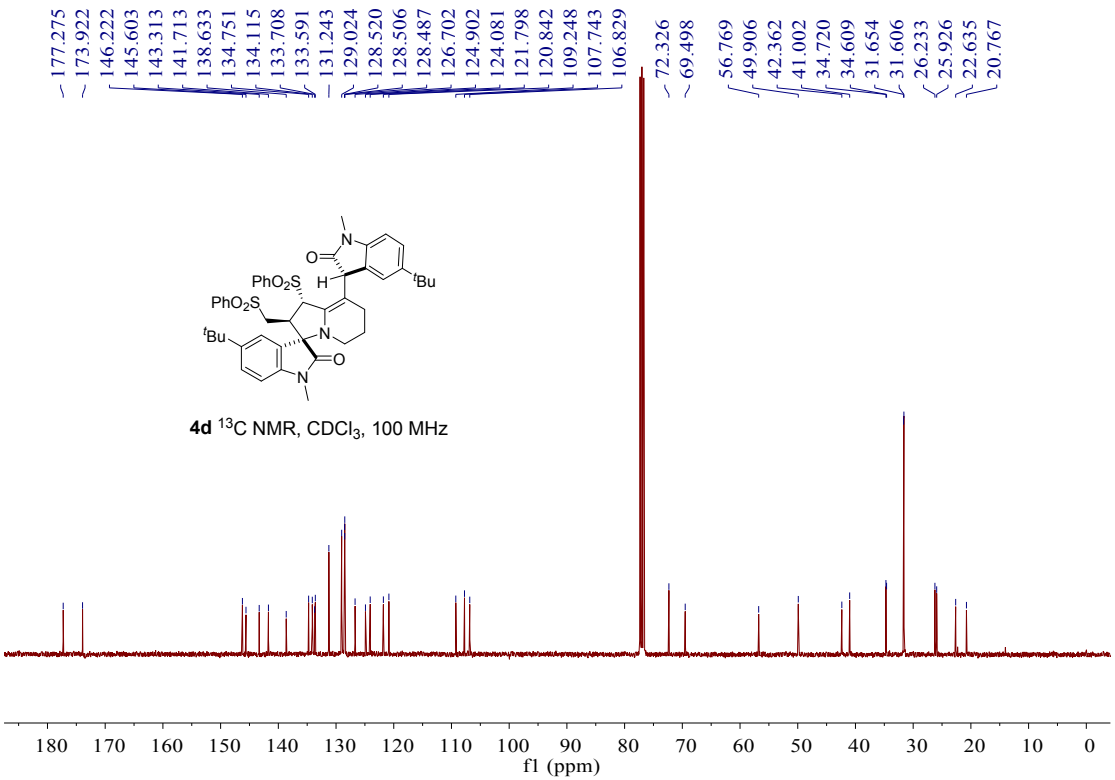
4c ^{1}H NMR, $CDCl_3$, 400 MHz



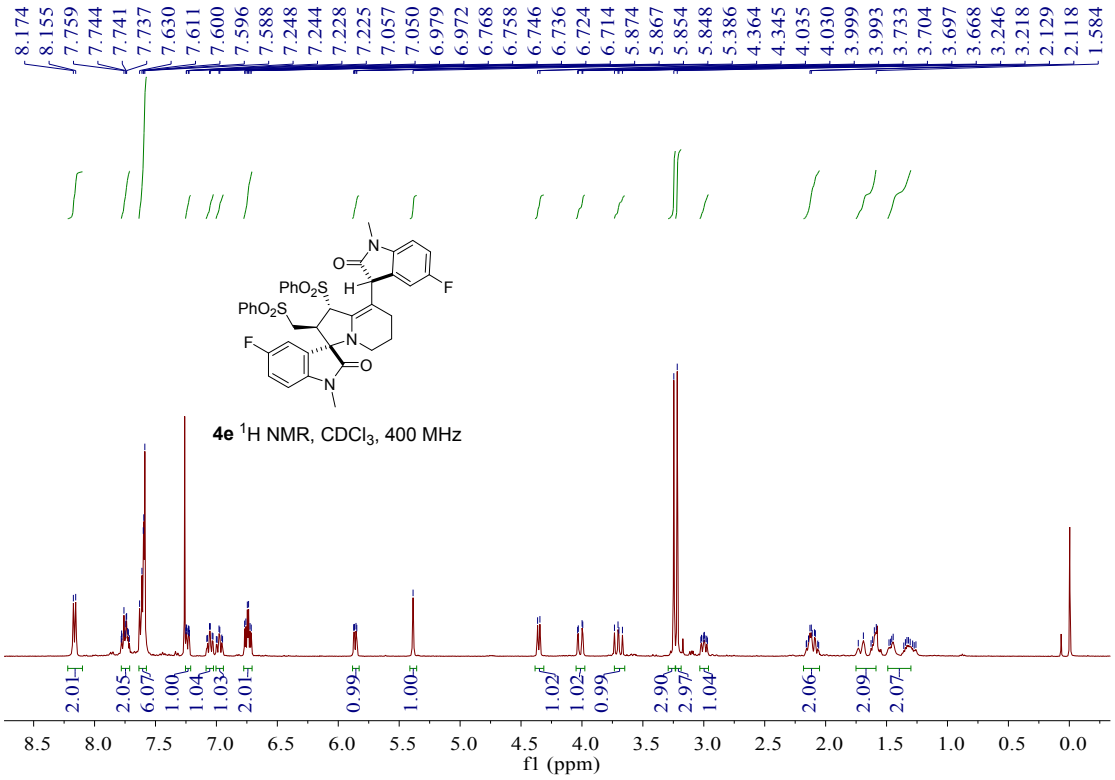
4c ^{13}C NMR, $CDCl_3$, 100 MHz



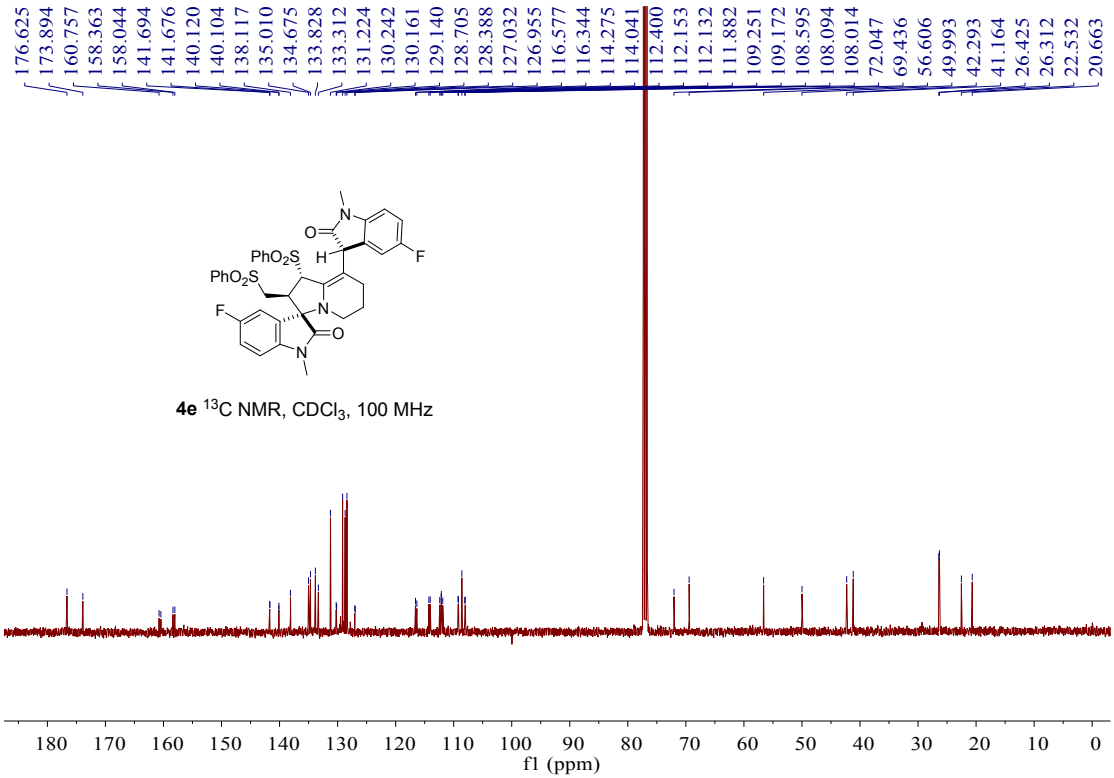
4d ^{1}H NMR, $CDCl_3$, 400 MHz



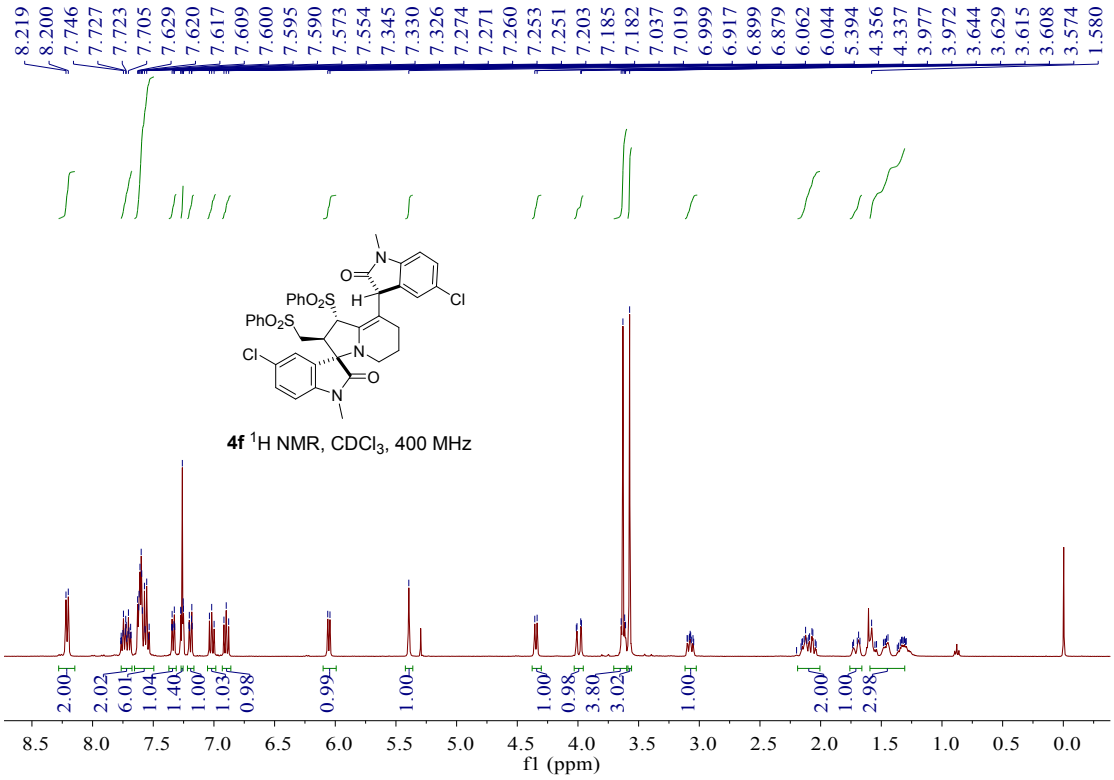
4d ^{13}C NMR, $CDCl_3$, 100 MHz



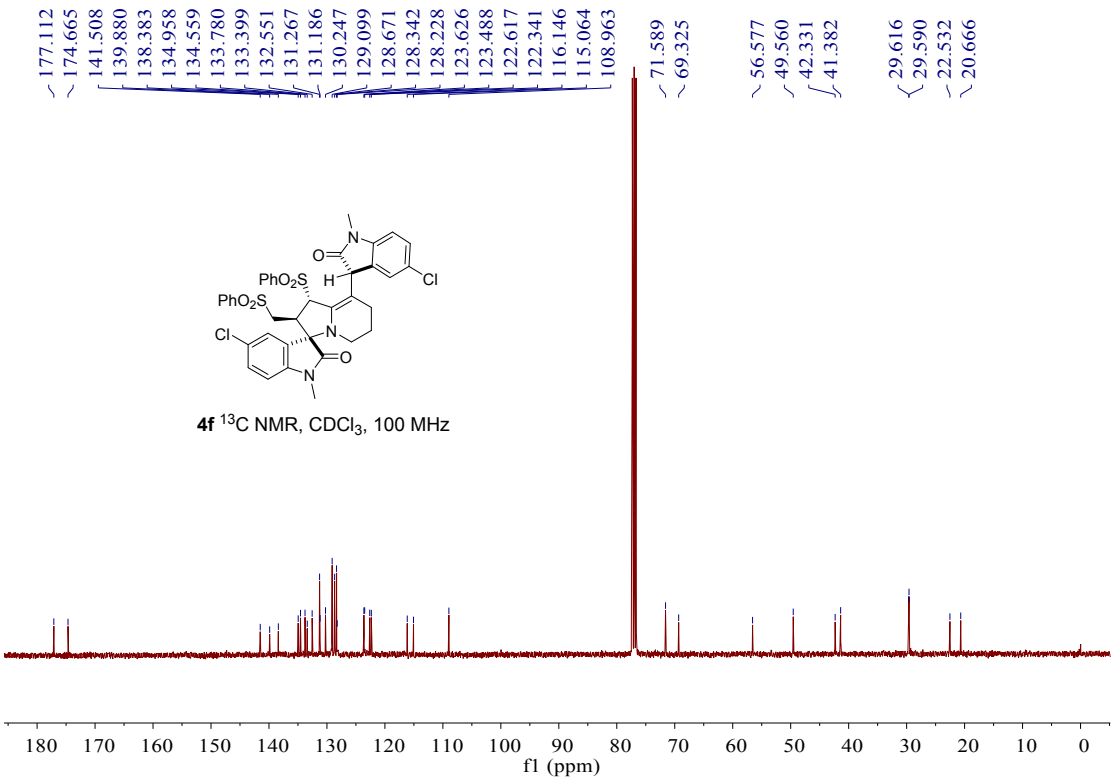
4e ^{1}H NMR, $CDCl_3$, 400 MHz



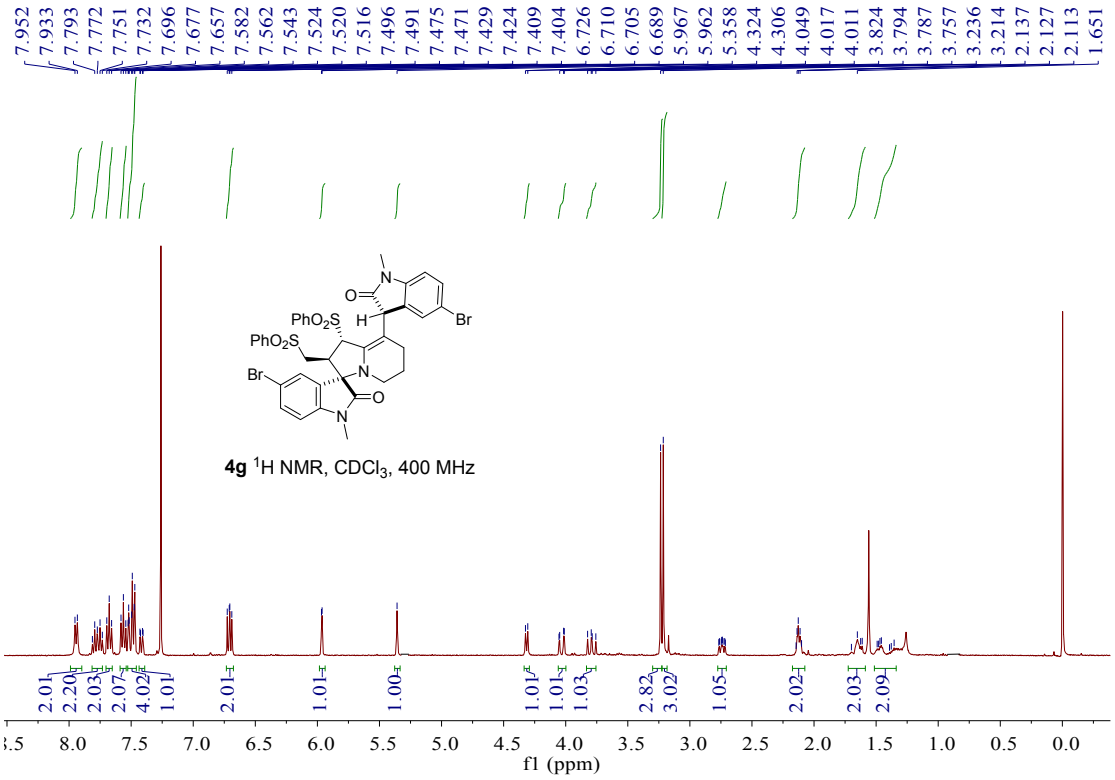
4e ^{13}C NMR, $CDCl_3$, 100 MHz



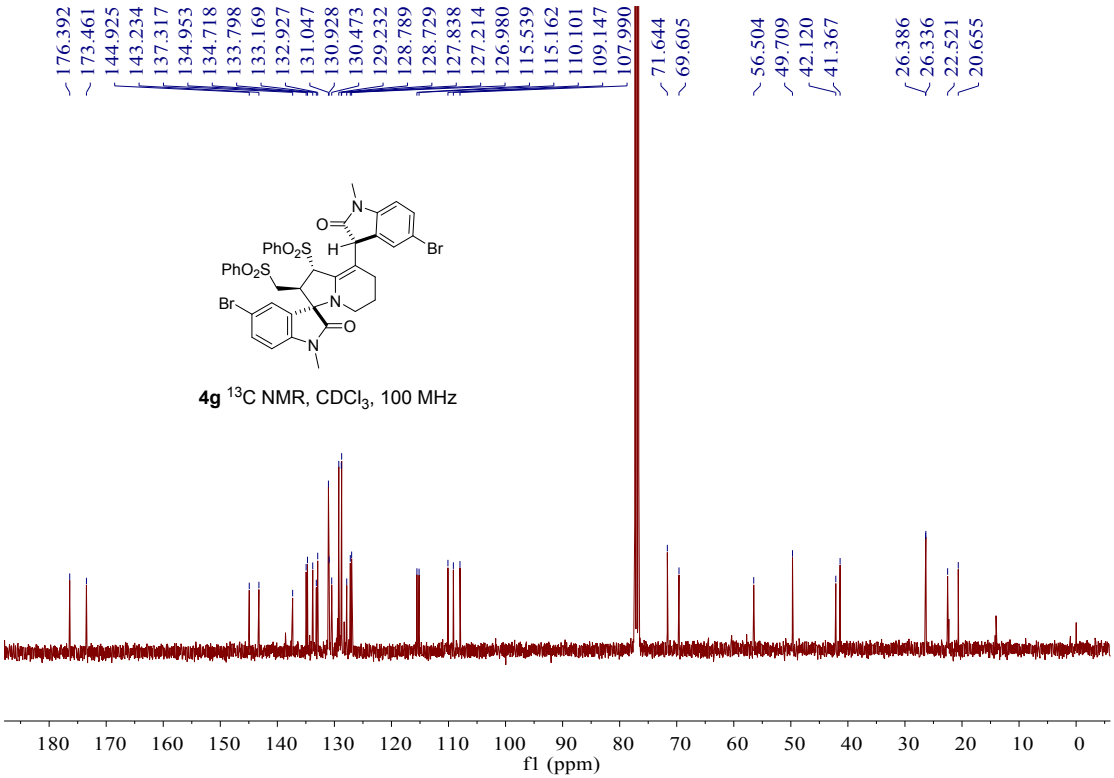
4f ^{1}H NMR, $CDCl_3$, 400 MHz



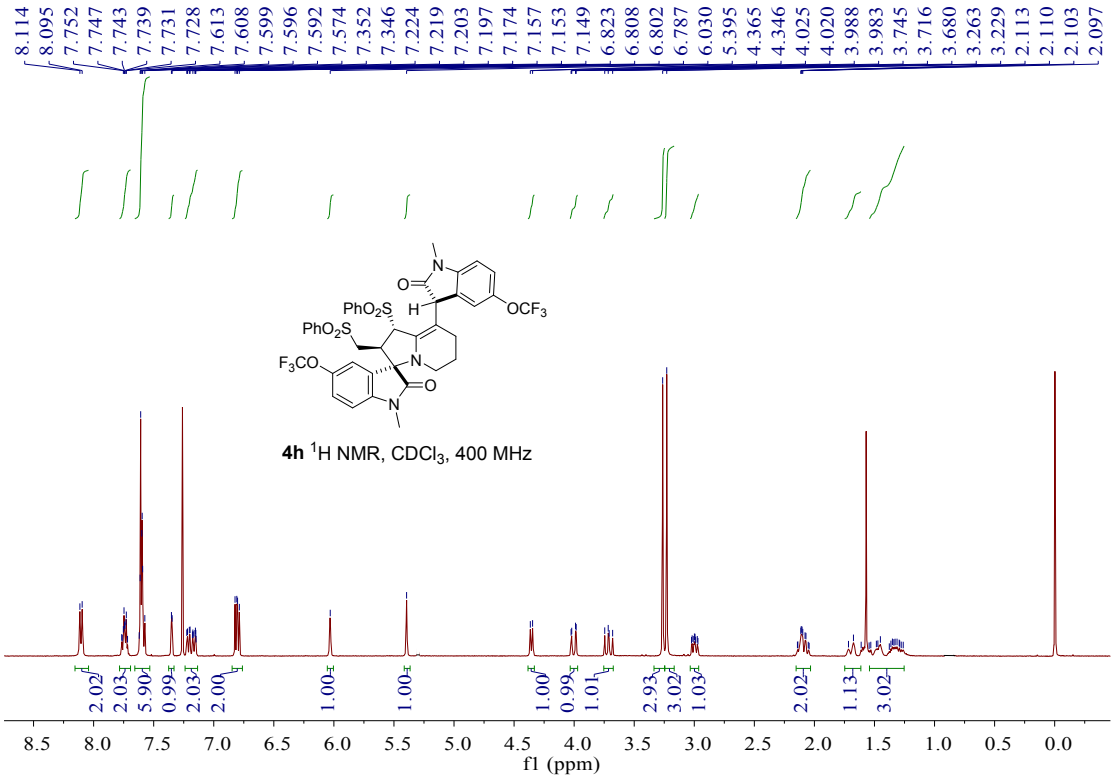
4f ^{13}C NMR, $CDCl_3$, 100 MHz



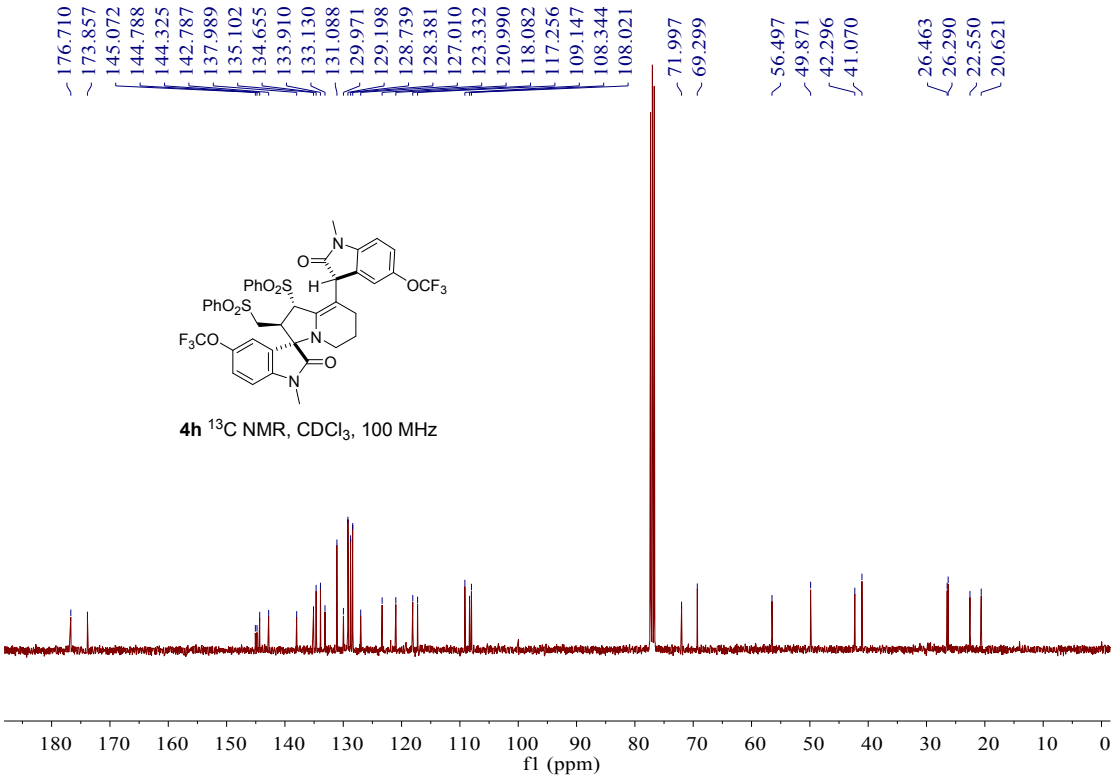
4g ^{1}H NMR, $CDCl_3$, 400 MHz



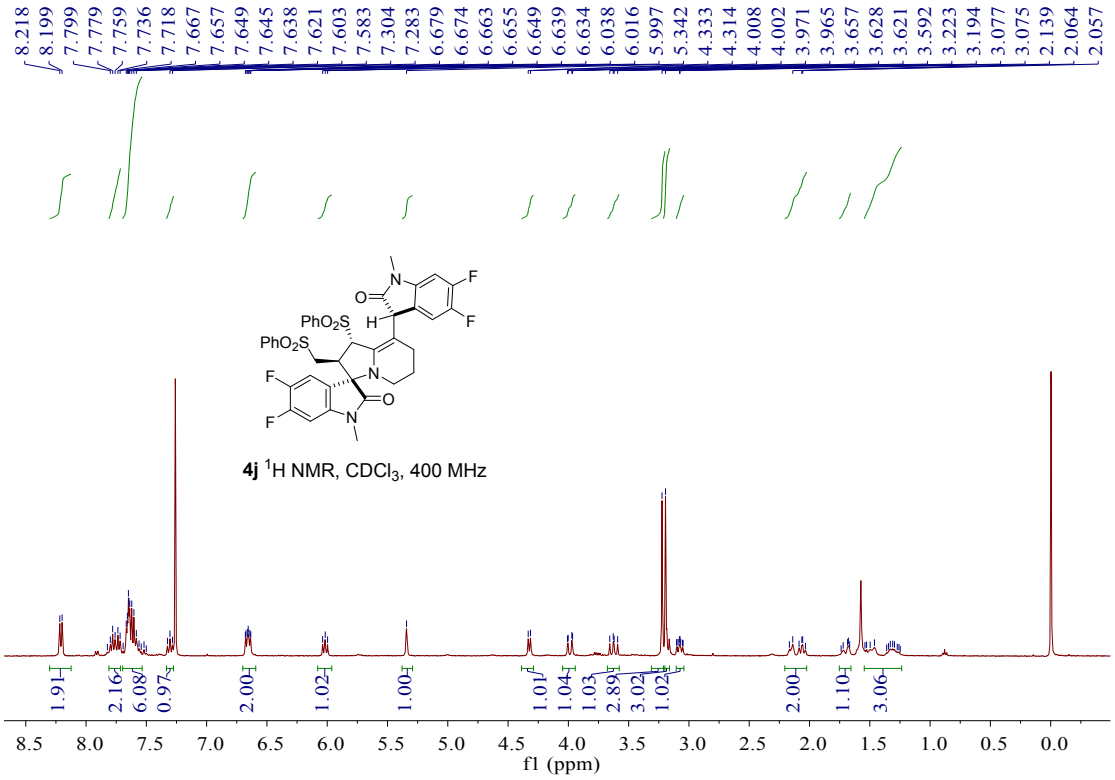
4g ^{13}C NMR, $CDCl_3$, 100 MHz



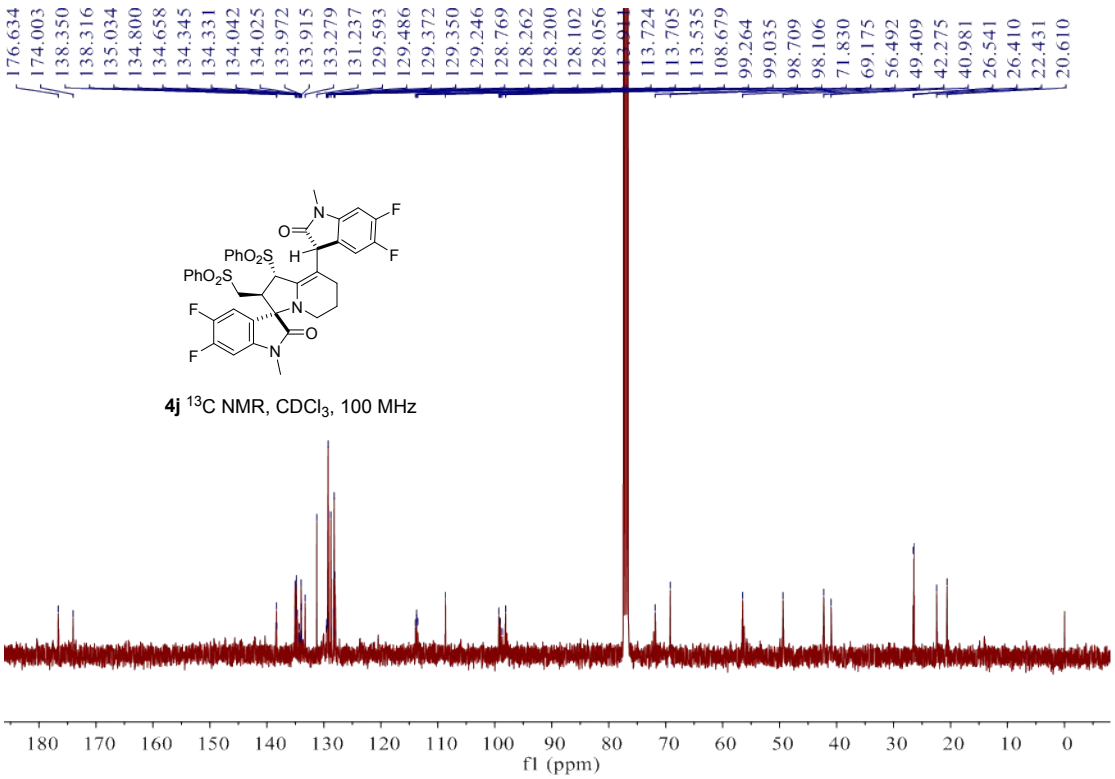
4h ^{1}H NMR, $CDCl_3$, 400 MHz



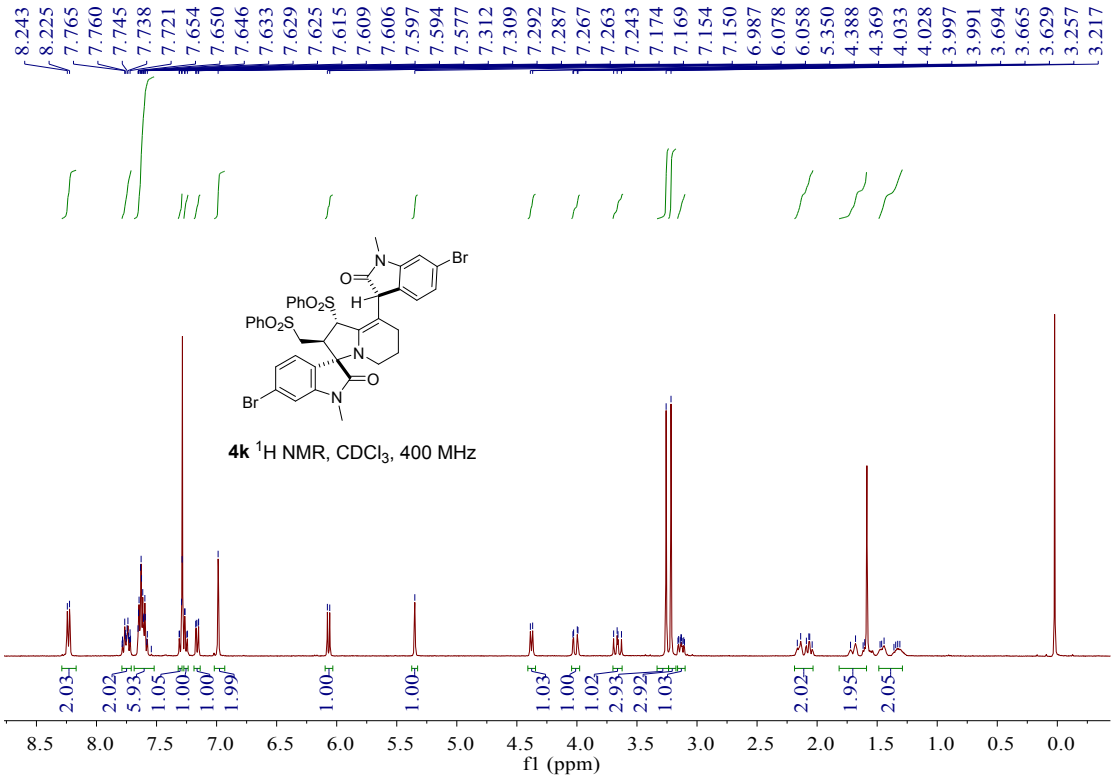
4h ^{13}C NMR, $CDCl_3$, 100 MHz



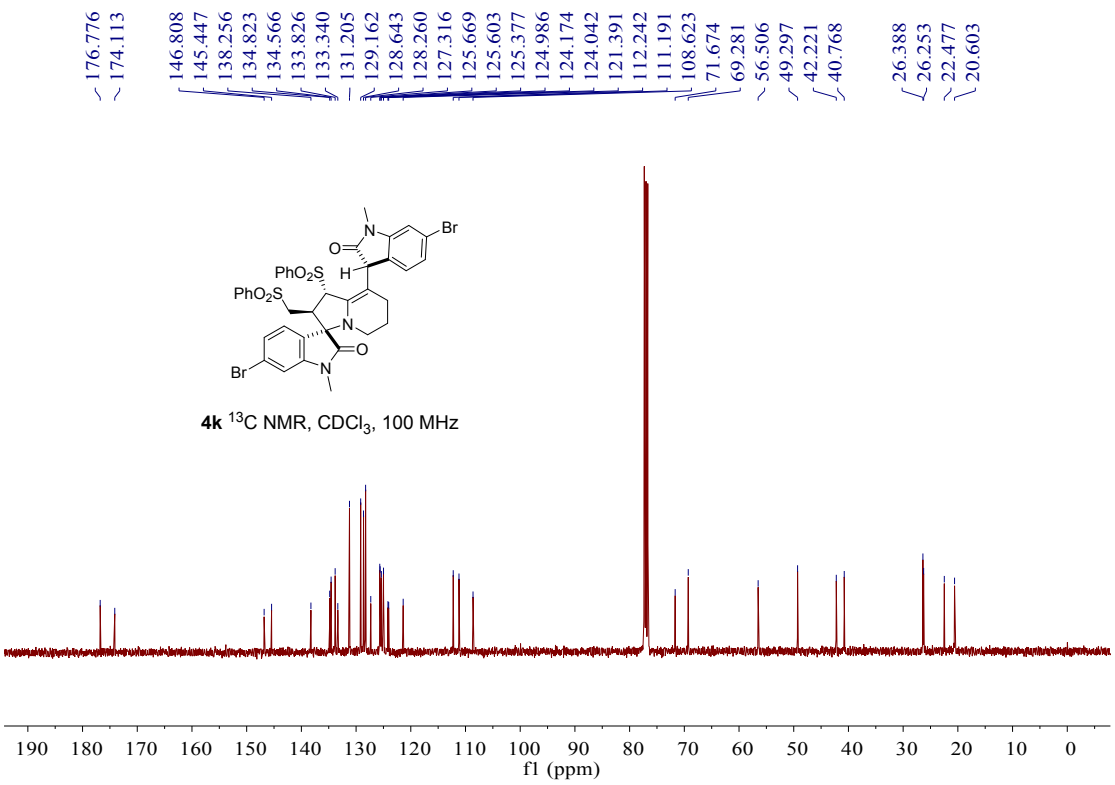
4j ^{1}H NMR, $CDCl_3$, 400 MHz



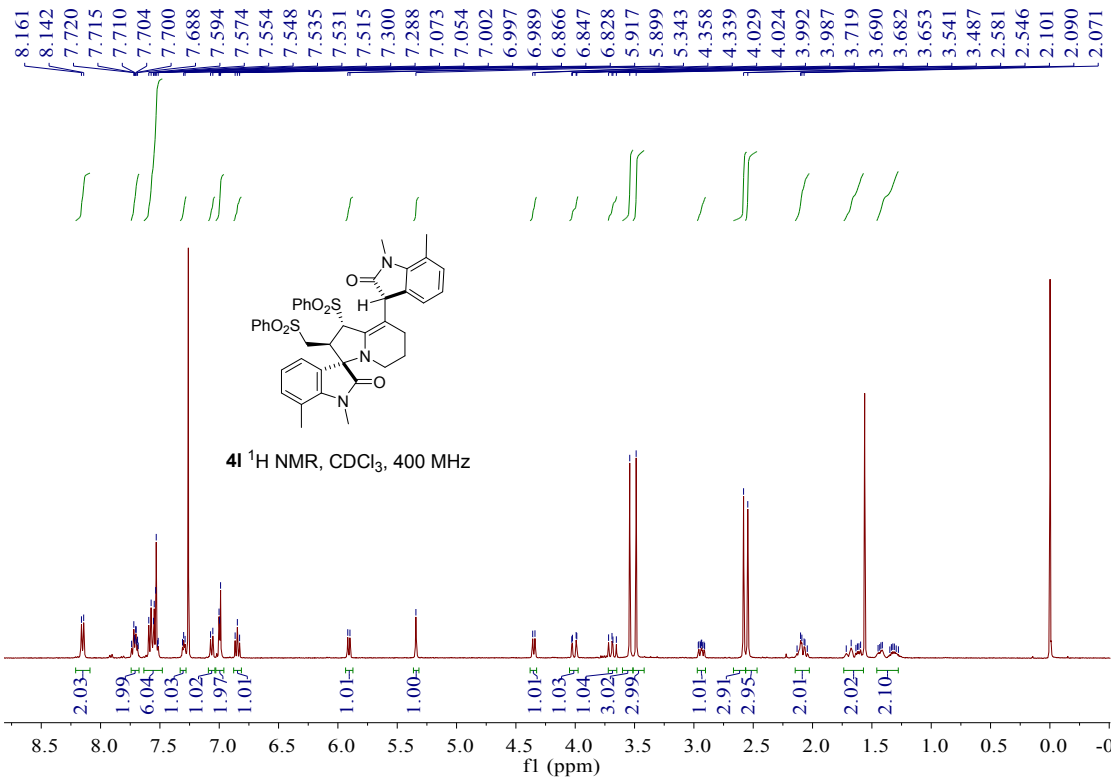
4j ^{13}C NMR, $CDCl_3$, 100 MHz



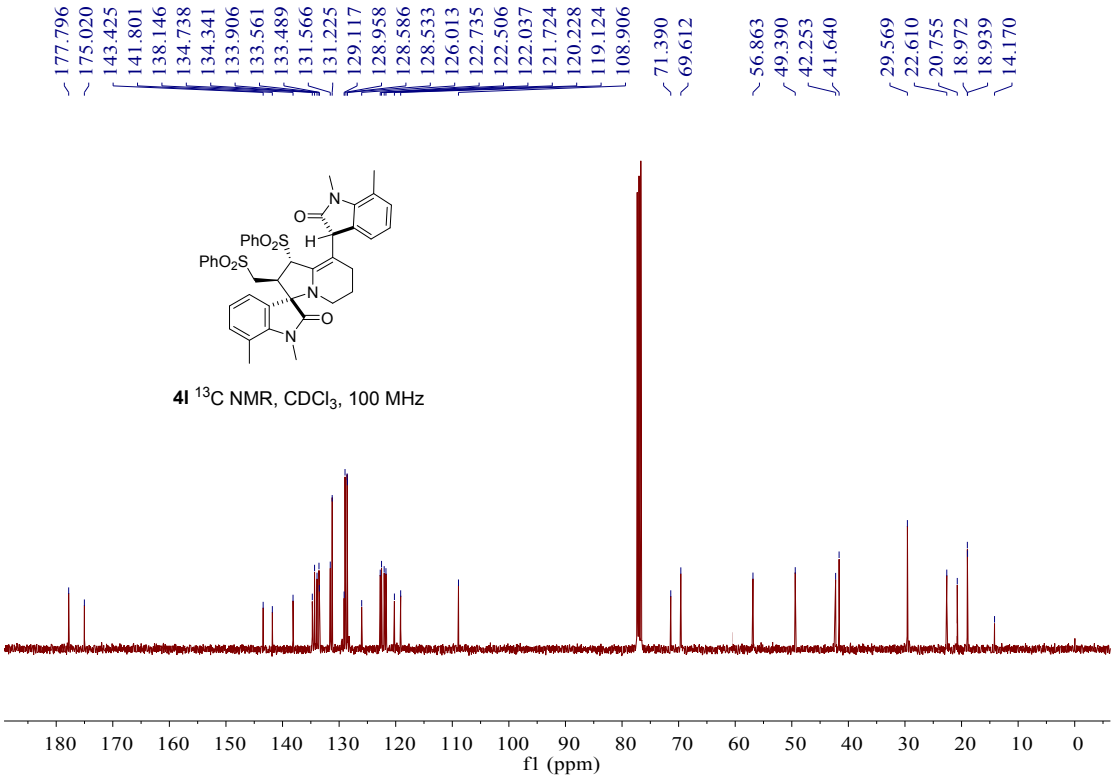
4k ^{1}H NMR, $CDCl_3$, 400 MHz



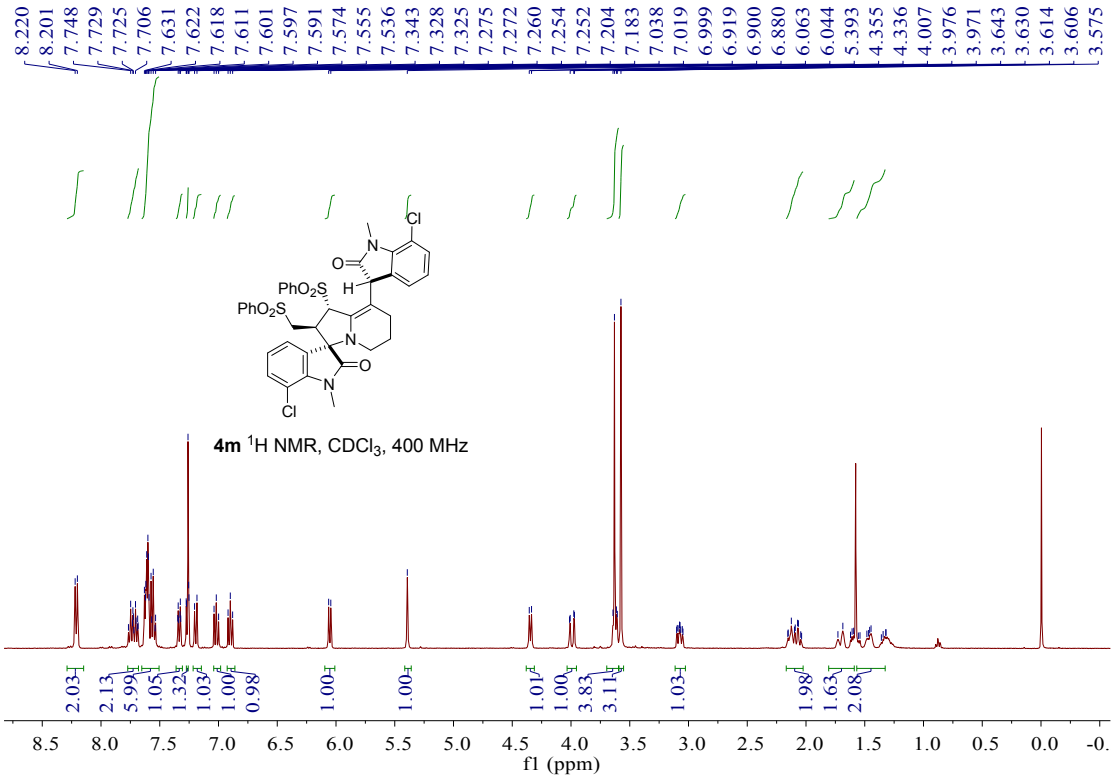
4k ^{13}C NMR, $CDCl_3$, 100 MHz



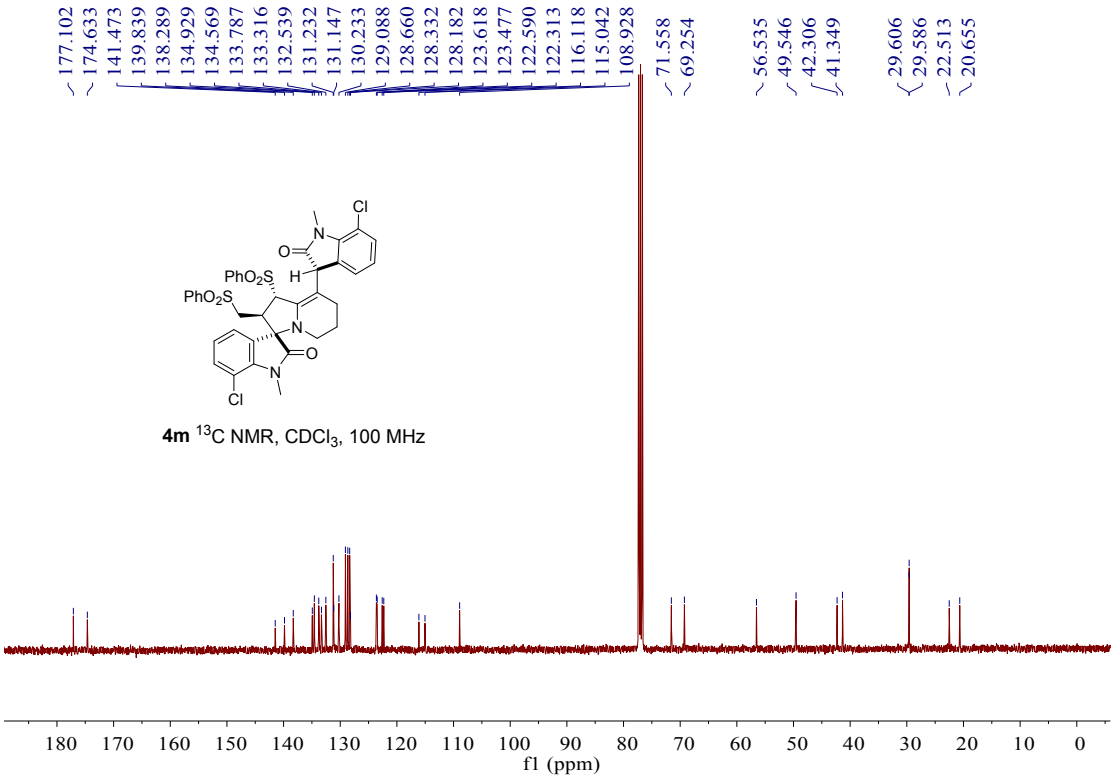
4l ^{1}H NMR, $CDCl_3$, 400 MHz



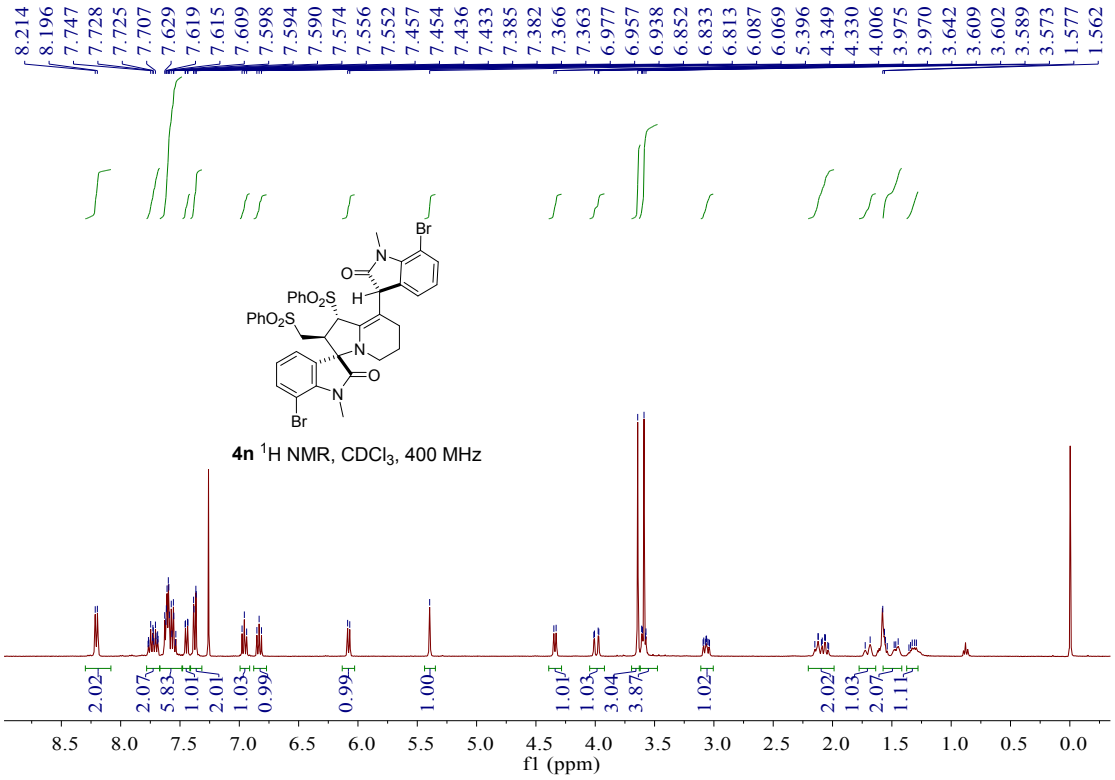
4l ^{13}C NMR, $CDCl_3$, 100 MHz



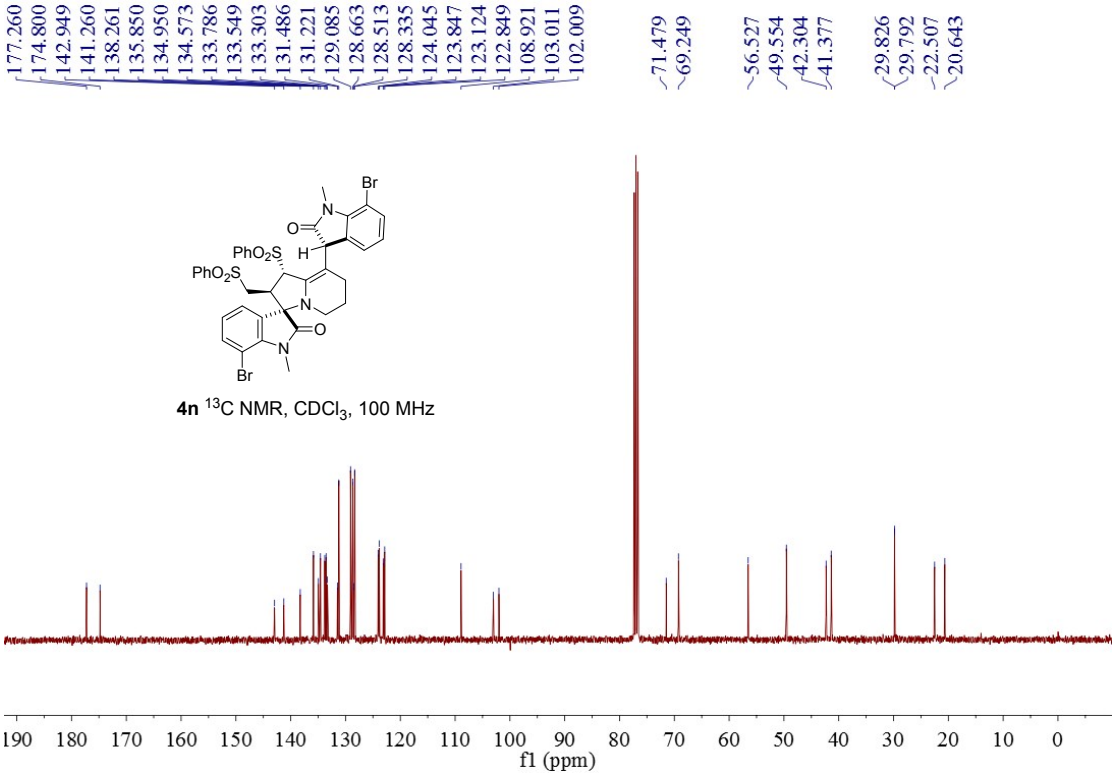
4m ^{1}H NMR, $CDCl_3$, 400 MHz



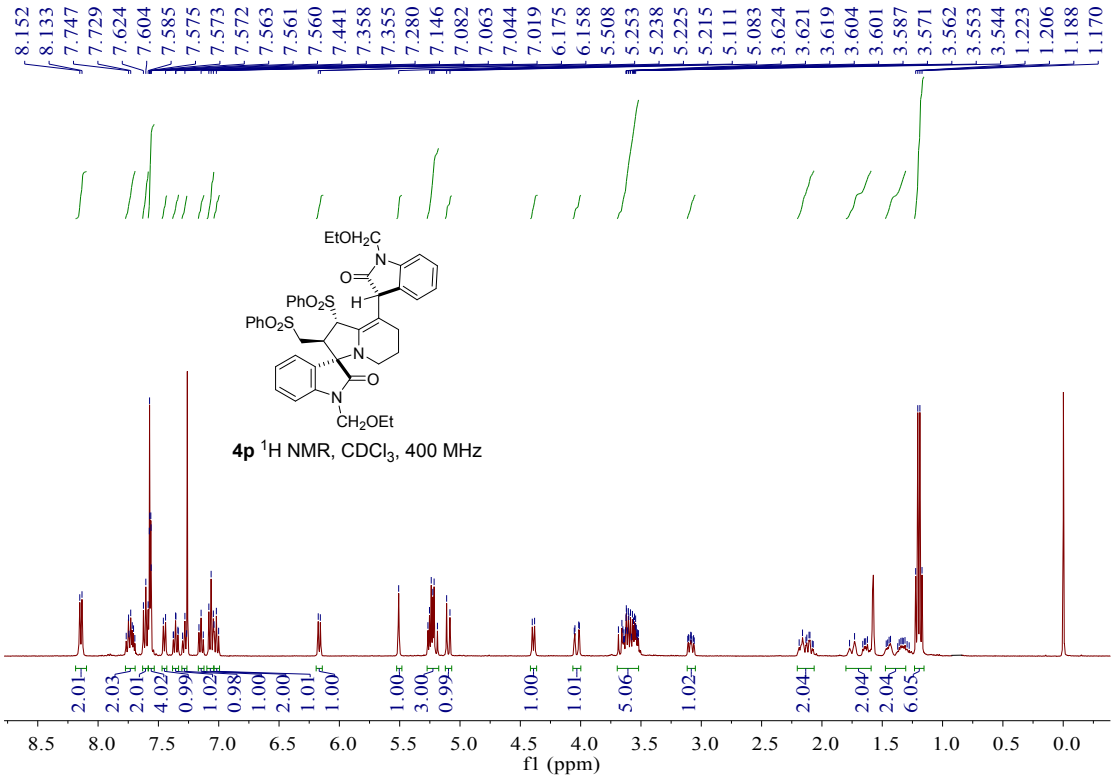
4m ^{13}C NMR, $CDCl_3$, 100 MHz



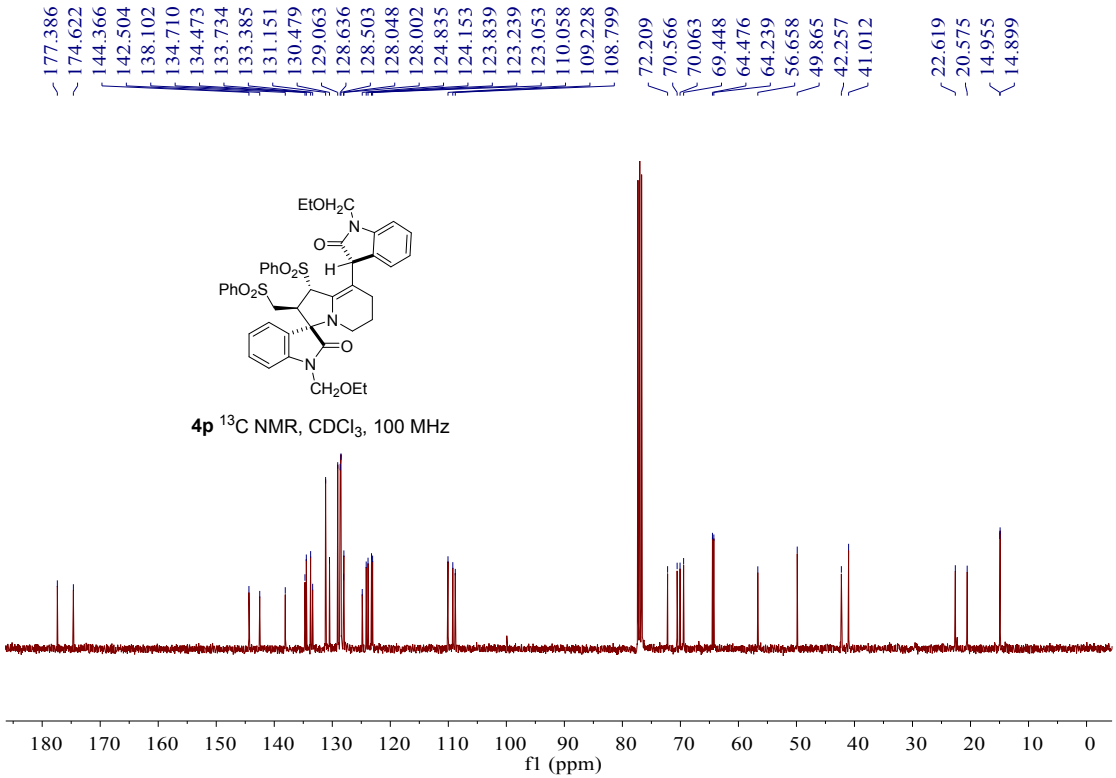
4n ^{1}H NMR, $CDCl_3$, 400 MHz



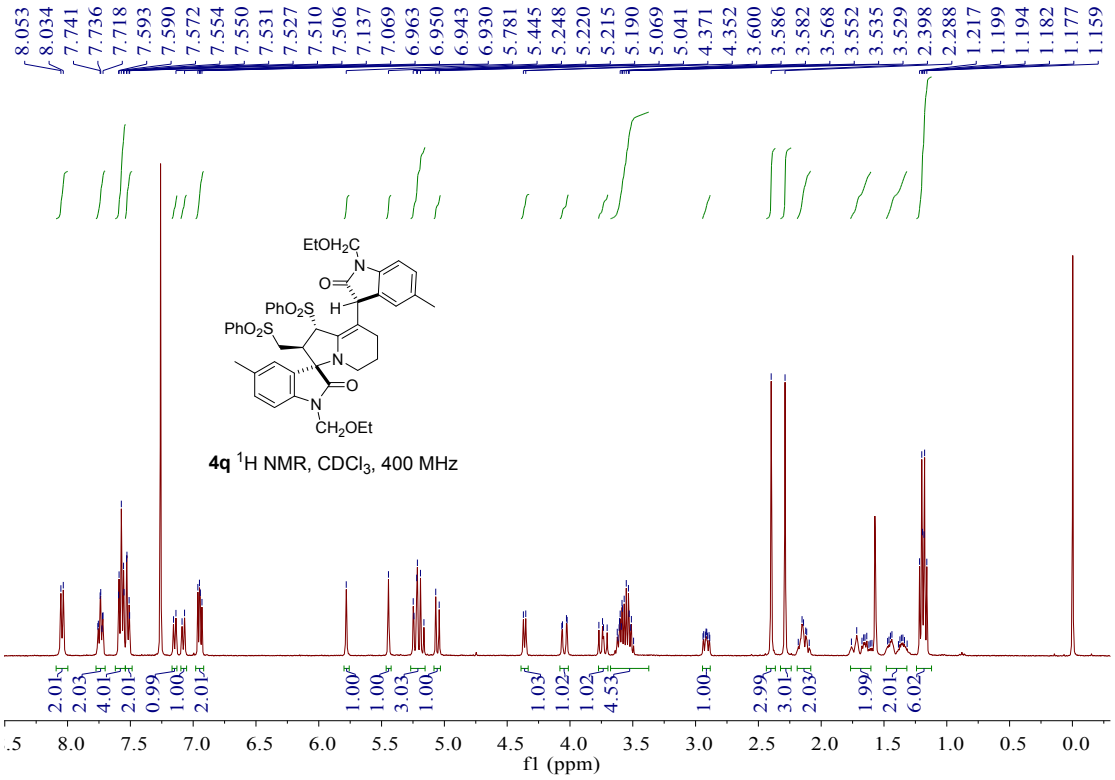
4n ^{13}C NMR, $CDCl_3$, 100 MHz



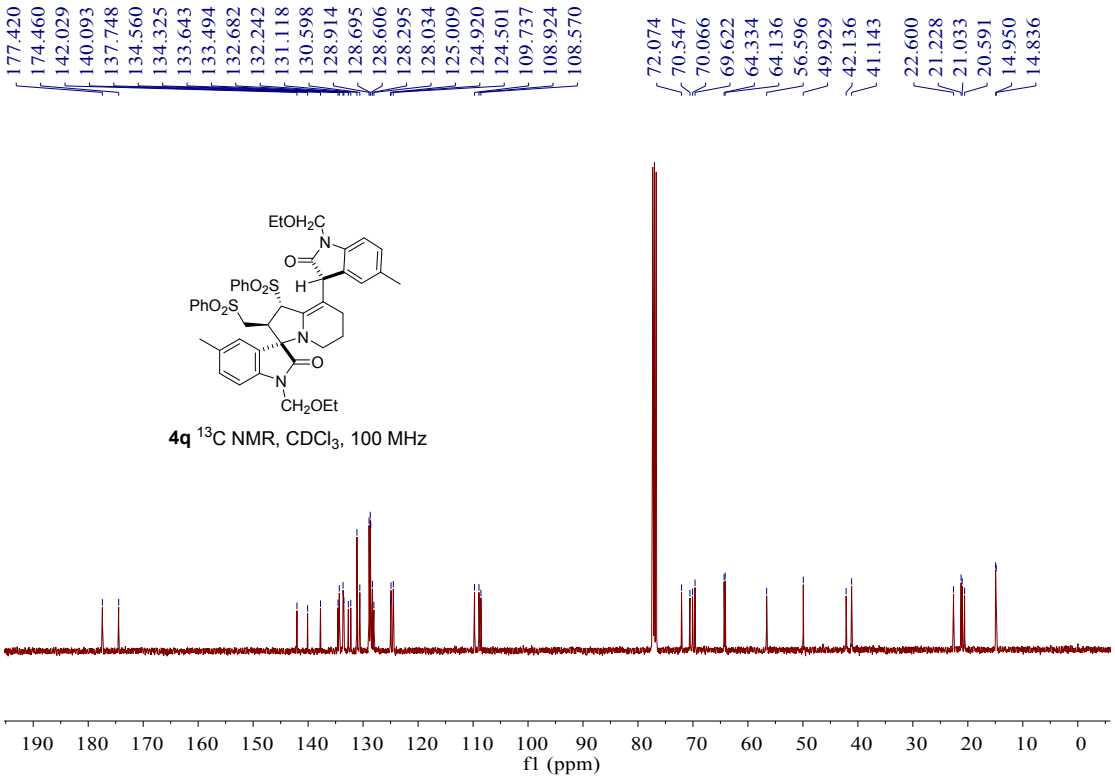
4p ^{1}H NMR, $CDCl_3$, 400 MHz



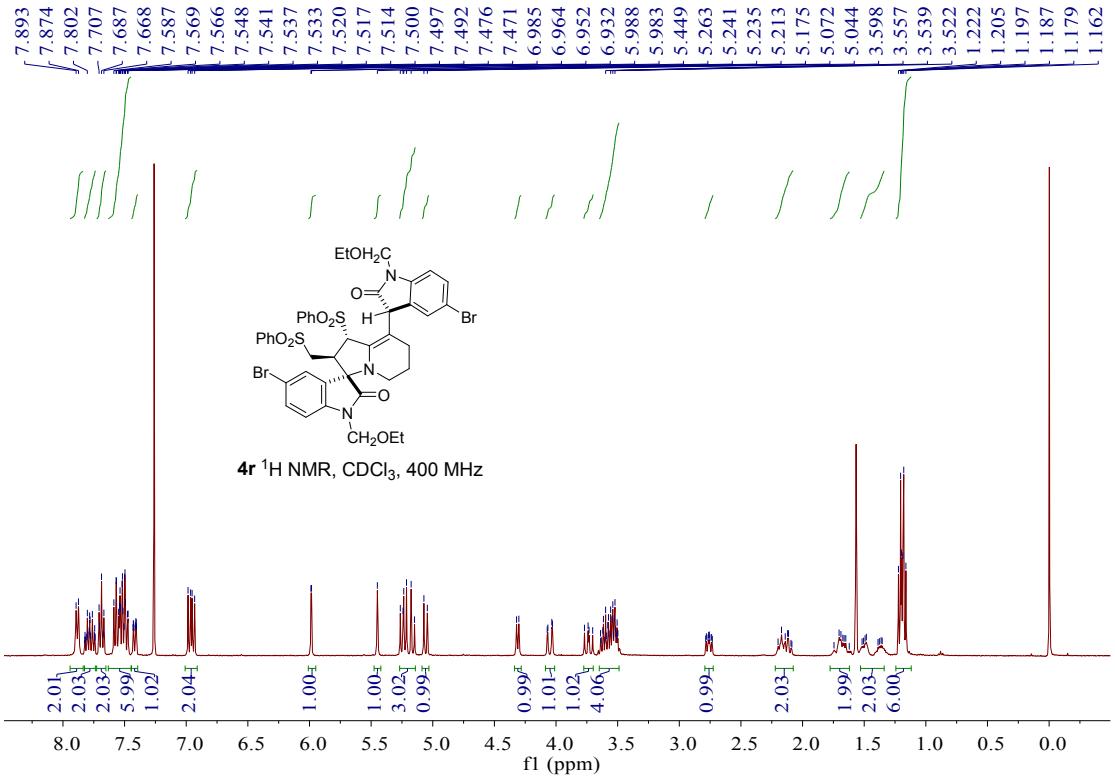
4p ^{13}C NMR, $CDCl_3$, 100 MHz



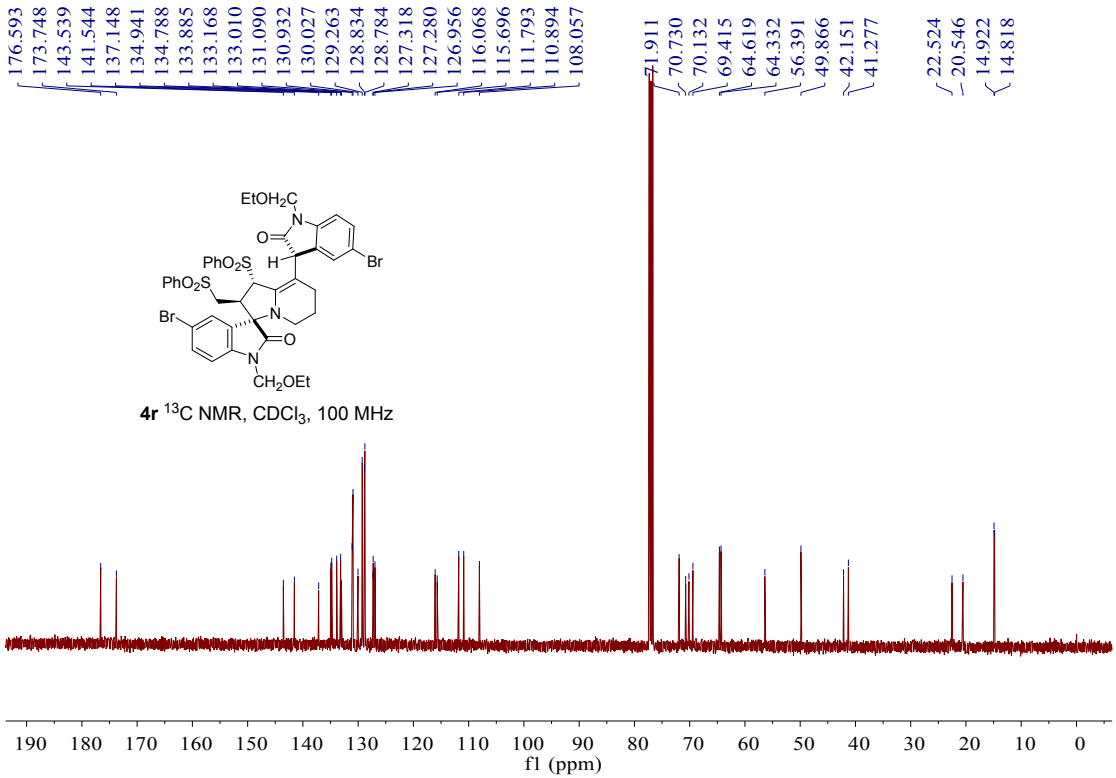
4q ^{1}H NMR, $CDCl_3$, 400 MHz



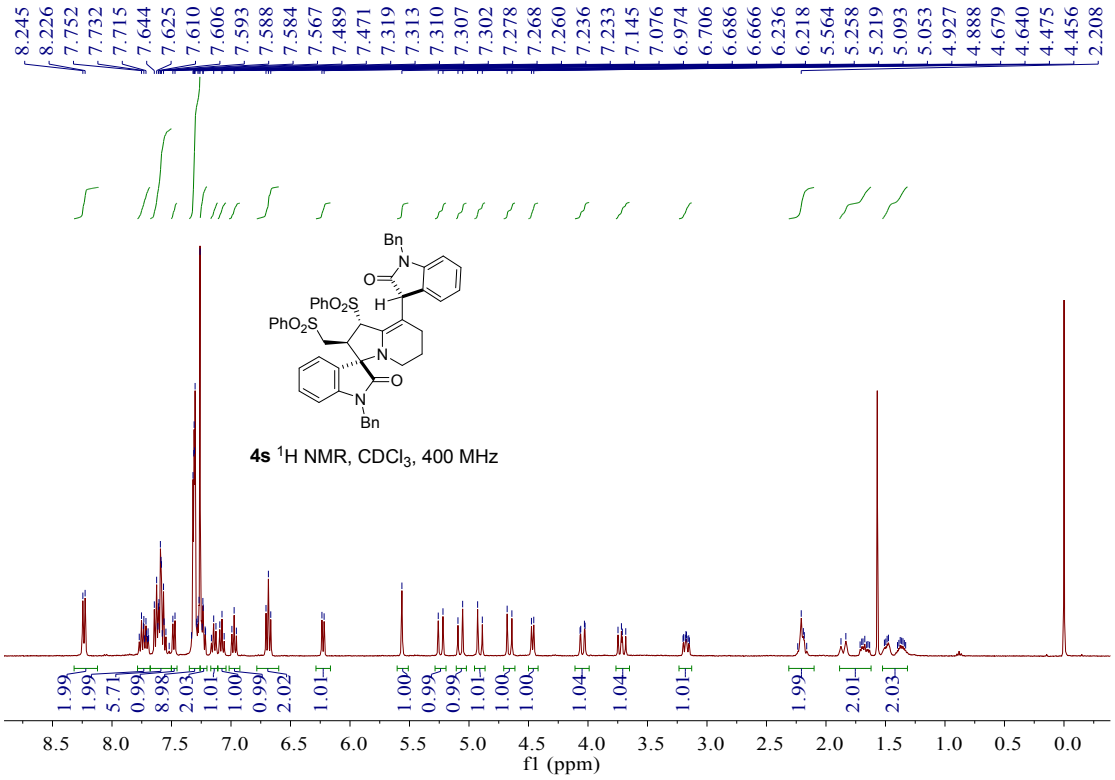
4q ^{13}C NMR, $CDCl_3$, 100 MHz



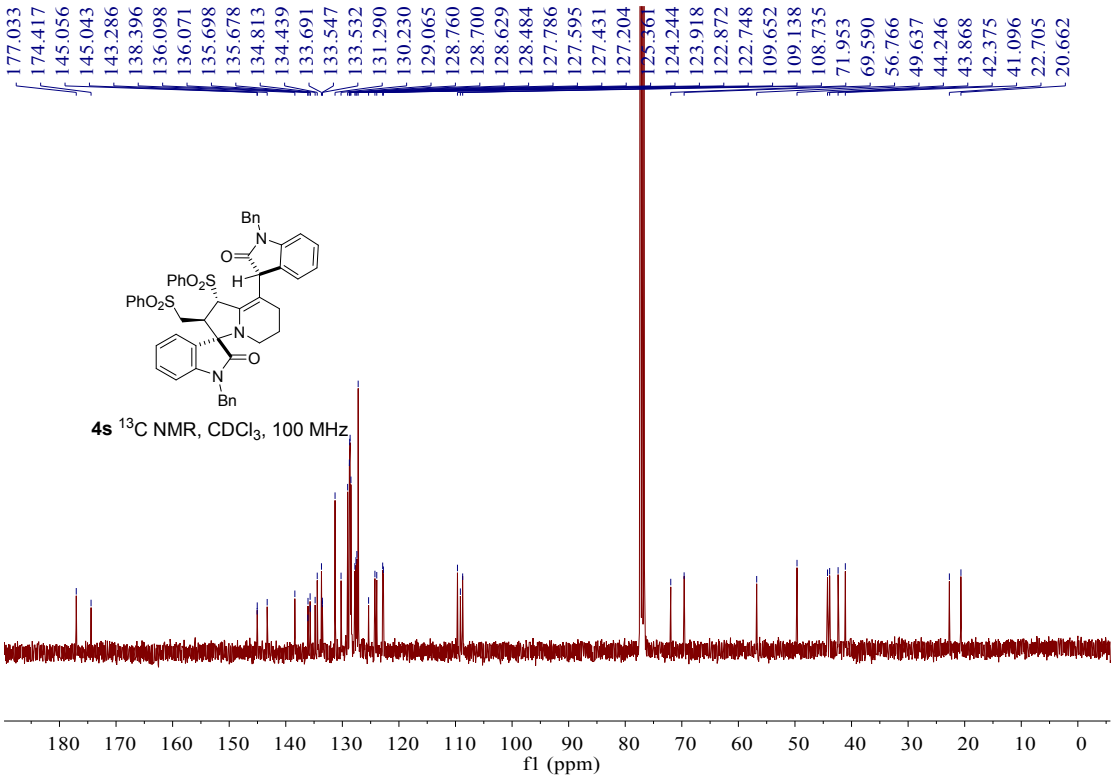
4r ^{1}H NMR, $CDCl_3$, 400 MHz



4r ^{13}C NMR, $CDCl_3$, 100 MHz



4s ^{1}H NMR, $CDCl_3$, 400 MHz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133.532
131.290
130.230
129.065
128.760
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128.629
128.484
127.786
127.595
127.431
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125.361
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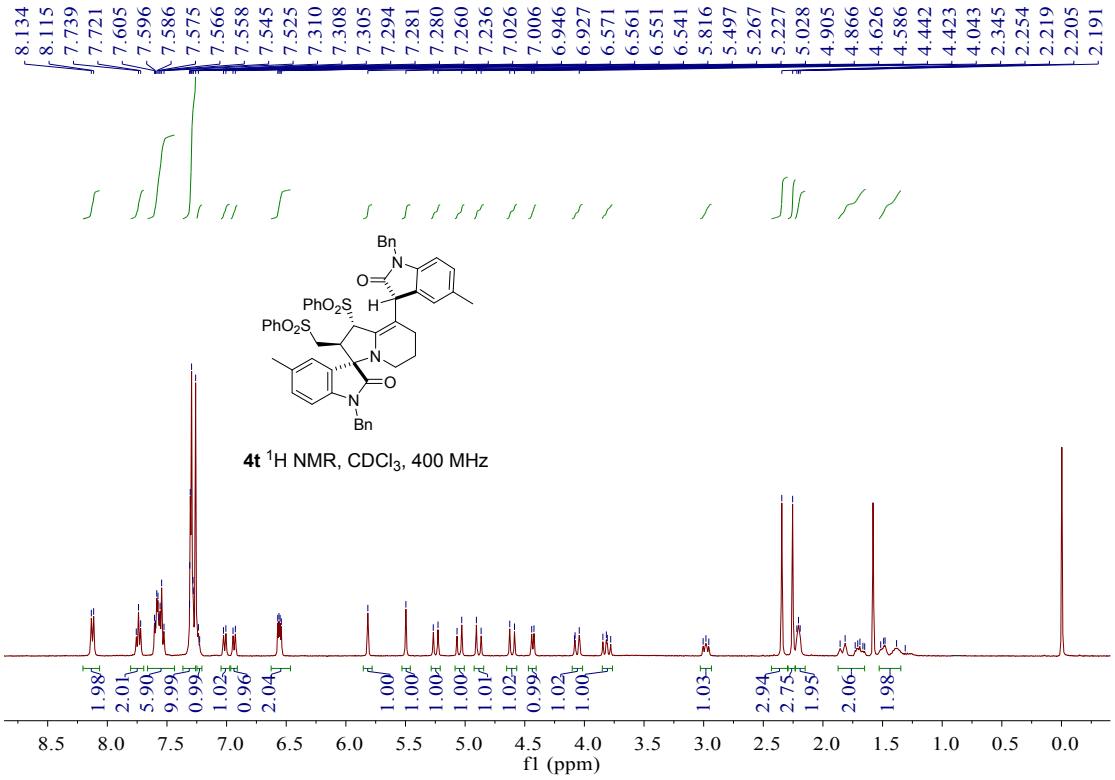
123.918
122.872
122.748
109.652
109.138
108.735
71.953
69.590
56.766
49.637
44.246
43.868
42.375
41.096
22.705
20.662
Bn
PhO2S
PhO2S
H
4s 13C NMR, CDCl3, 100 MHz
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.115
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7.721
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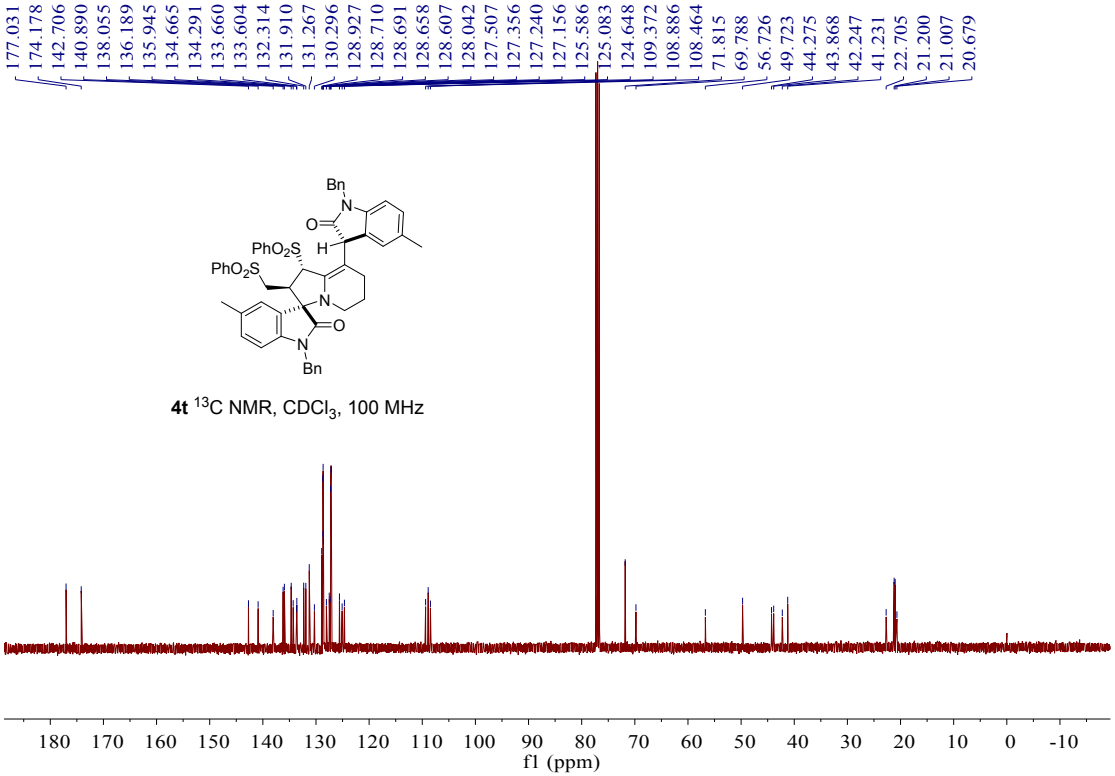
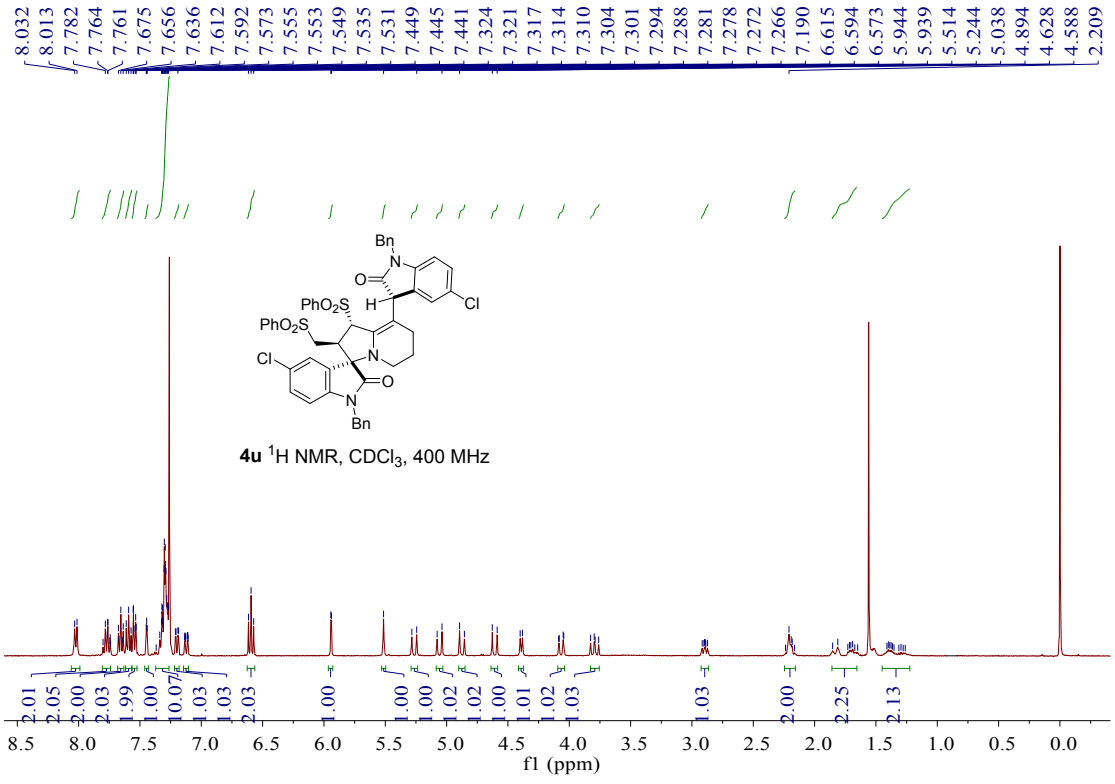
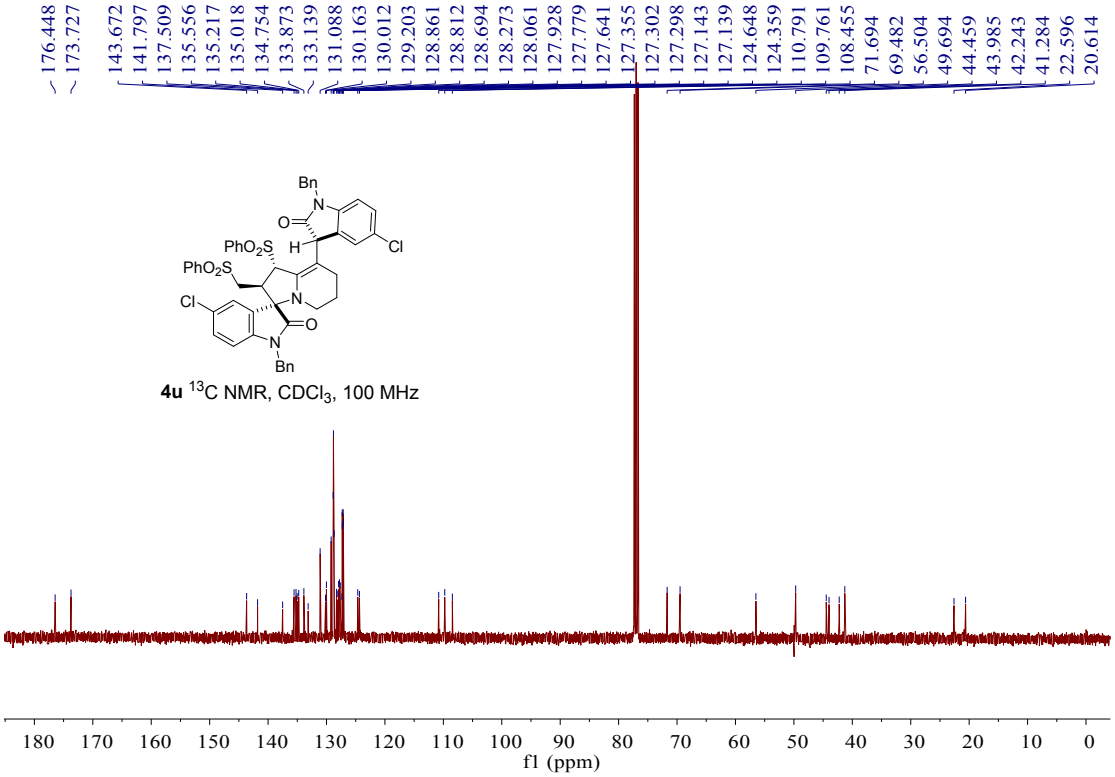
7.558
7.545
7.525
7.310
7.308
7.305
7.294
7.281
7.280
7.260
7.236
7.026
7.006
6.946
6.927
6.571
6.561
6.551
6.541
5.816
5.497
5.267
5.227
5.028
4.905
4.866
4.626
4.586
4.442
4.423
4.043
2.345
2.254
2.219
2.205
2.191
Bn
PhO2S
PhO2S
H
4t 1H NMR, CDCl3, 400 MHz
1.98
2.01
5.90
9.99
0.99
1.02
0.96
2.04
1.00
1.00
1.00
1.00
1.01
1.02
0.99
1.02
1.00
1.03
2.94
2.75
1.95
2.06
1.98
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



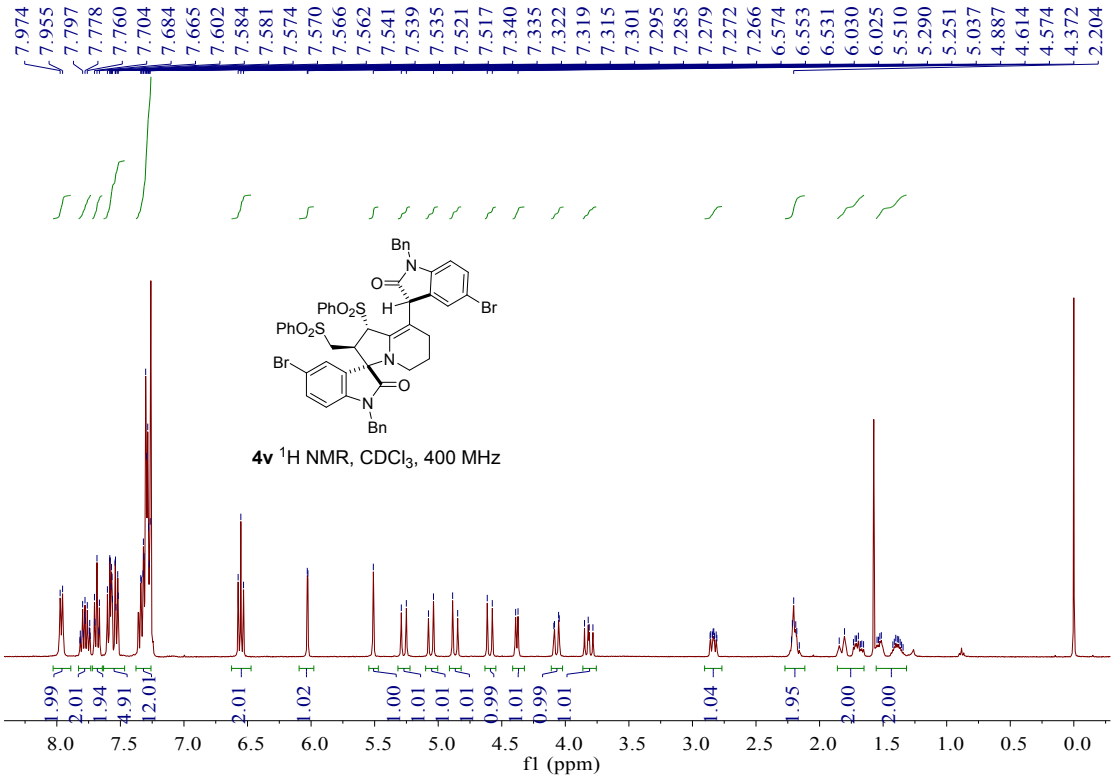
4t ^{13}C NMR, $CDCl_3$, 100 MHz



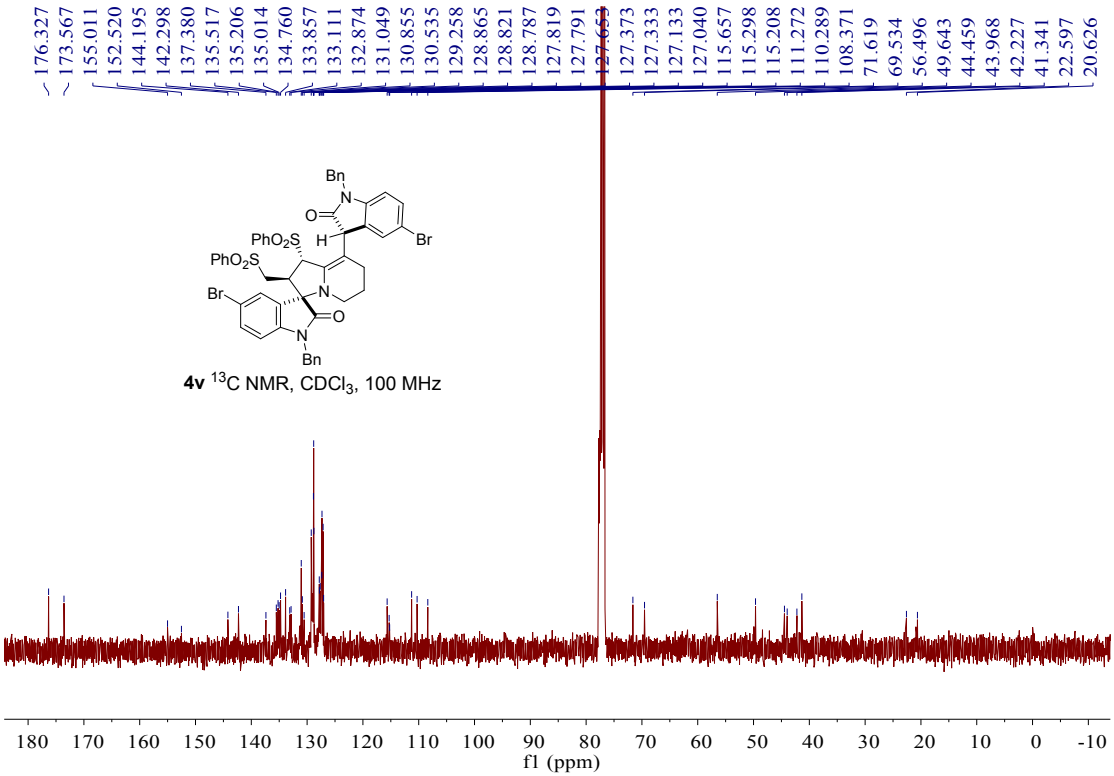
4u ^{1}H NMR, $CDCl_3$, 400 MHz



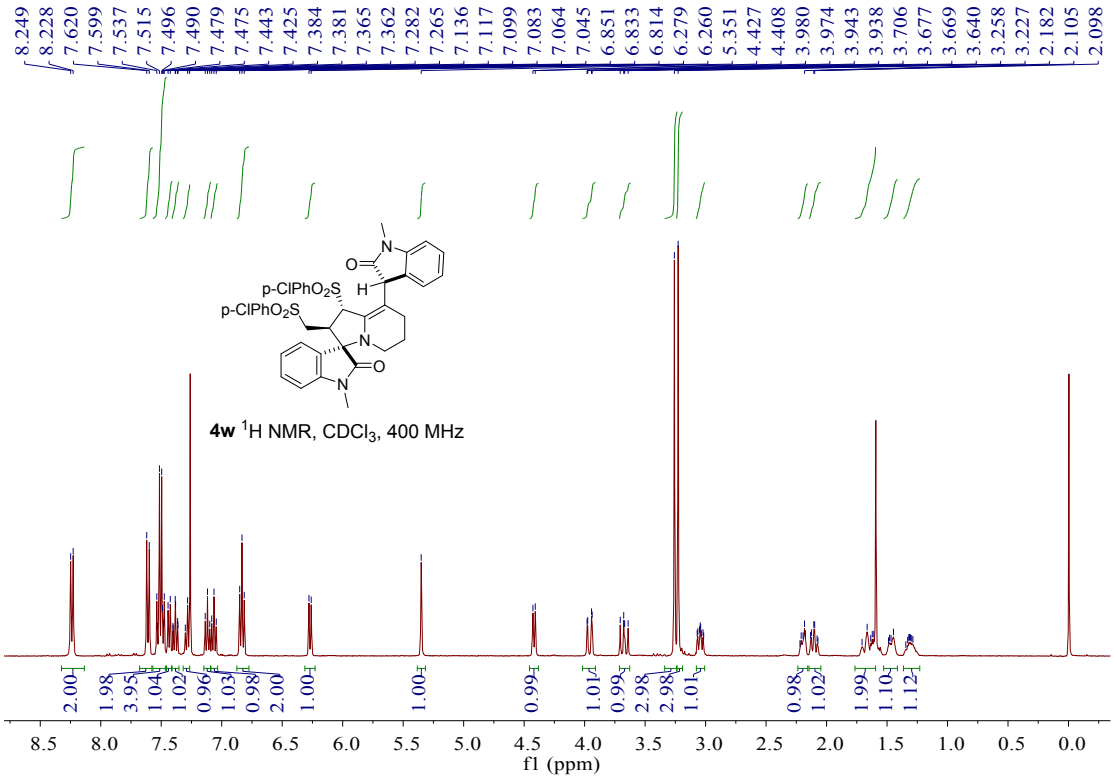
4u ^{13}C NMR, $CDCl_3$, 100 MHz



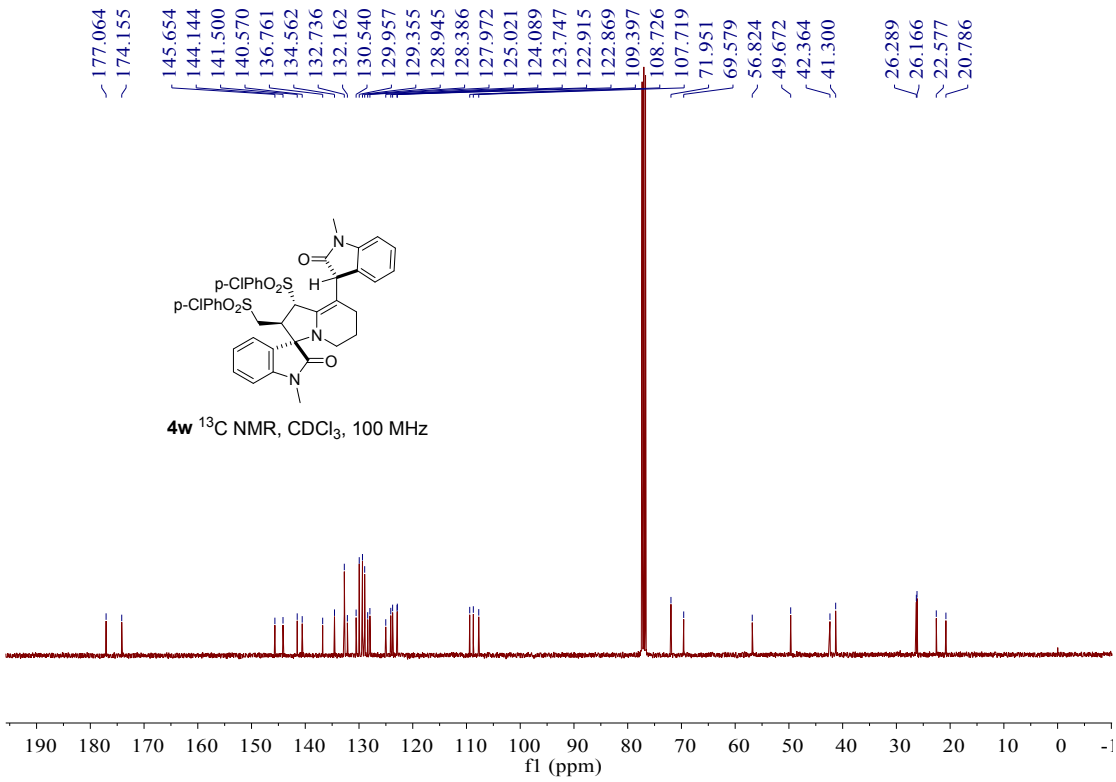
4v ^{1}H NMR, $CDCl_3$, 400 MHz



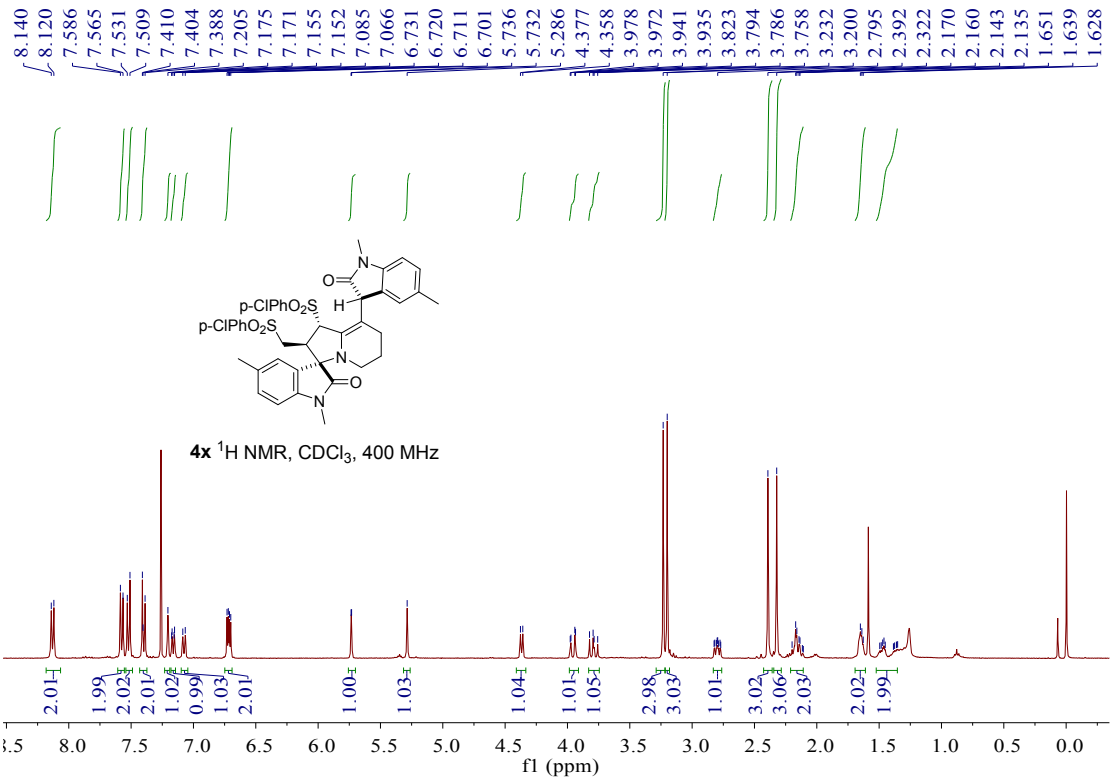
4v ^{13}C NMR, $CDCl_3$, 100 MHz



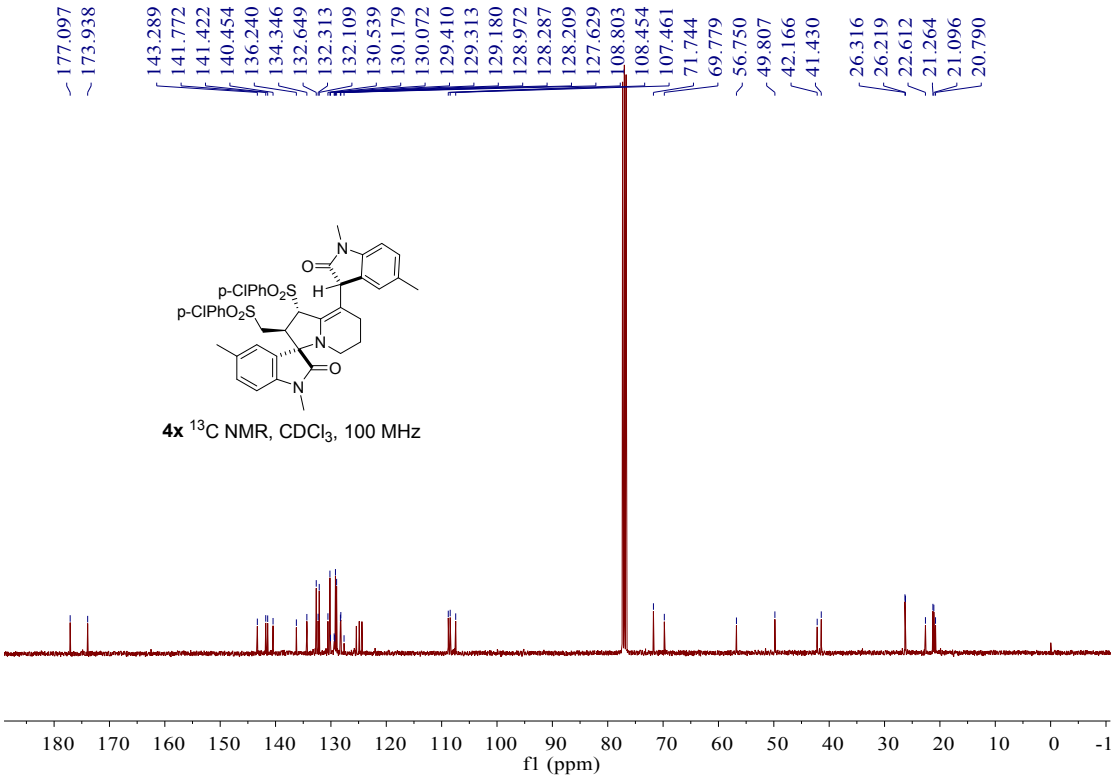
4w ^{1}H NMR, $CDCl_3$, 400 MHz



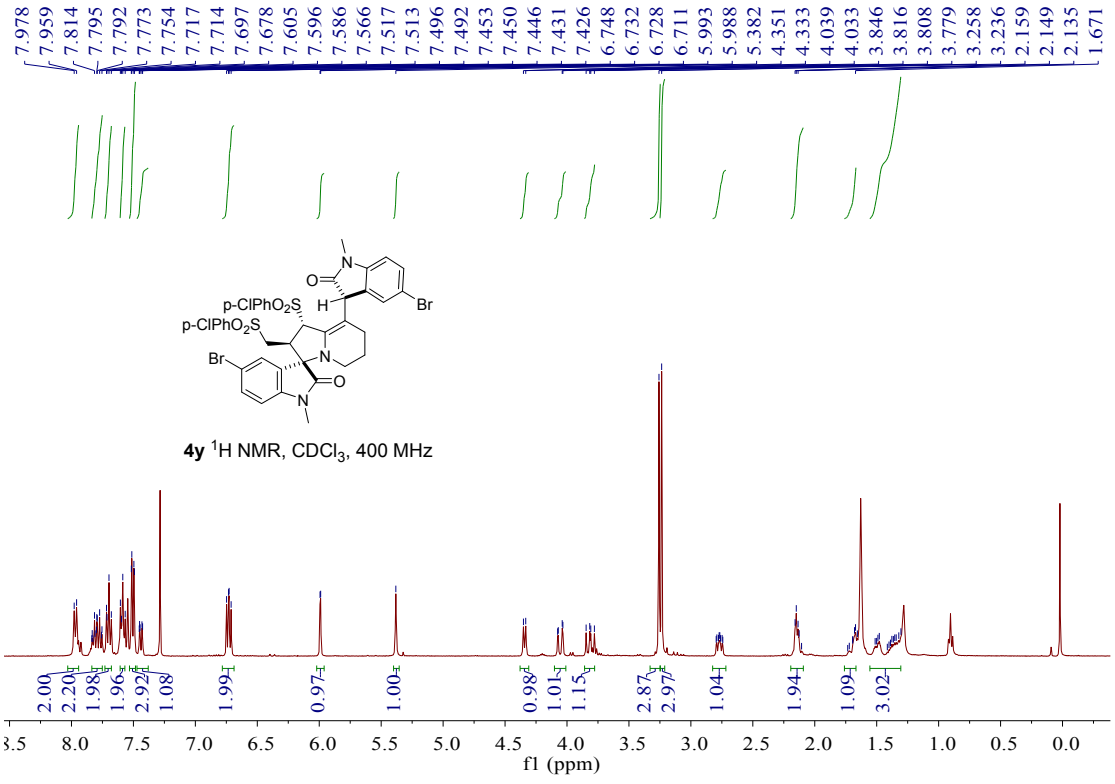
4w ^{13}C NMR, $CDCl_3$, 100 MHz



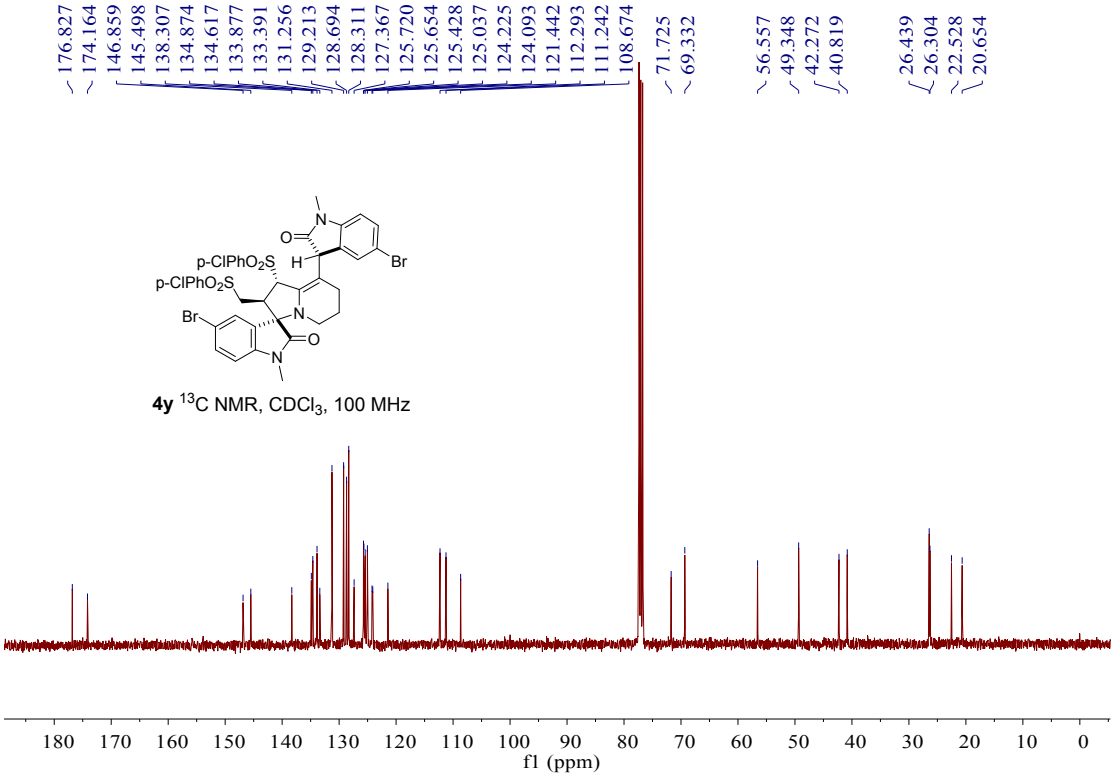
4x ^{1}H NMR, $CDCl_3$, 400 MHz



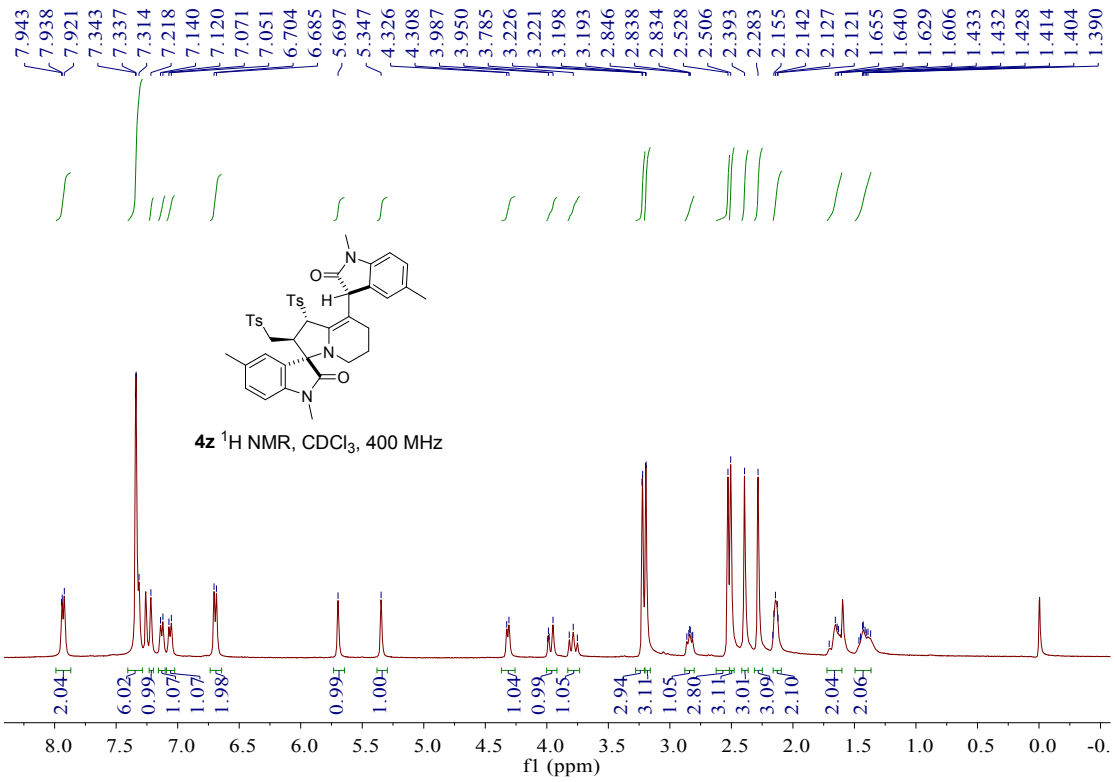
4x ^{13}C NMR, $CDCl_3$, 100 MHz



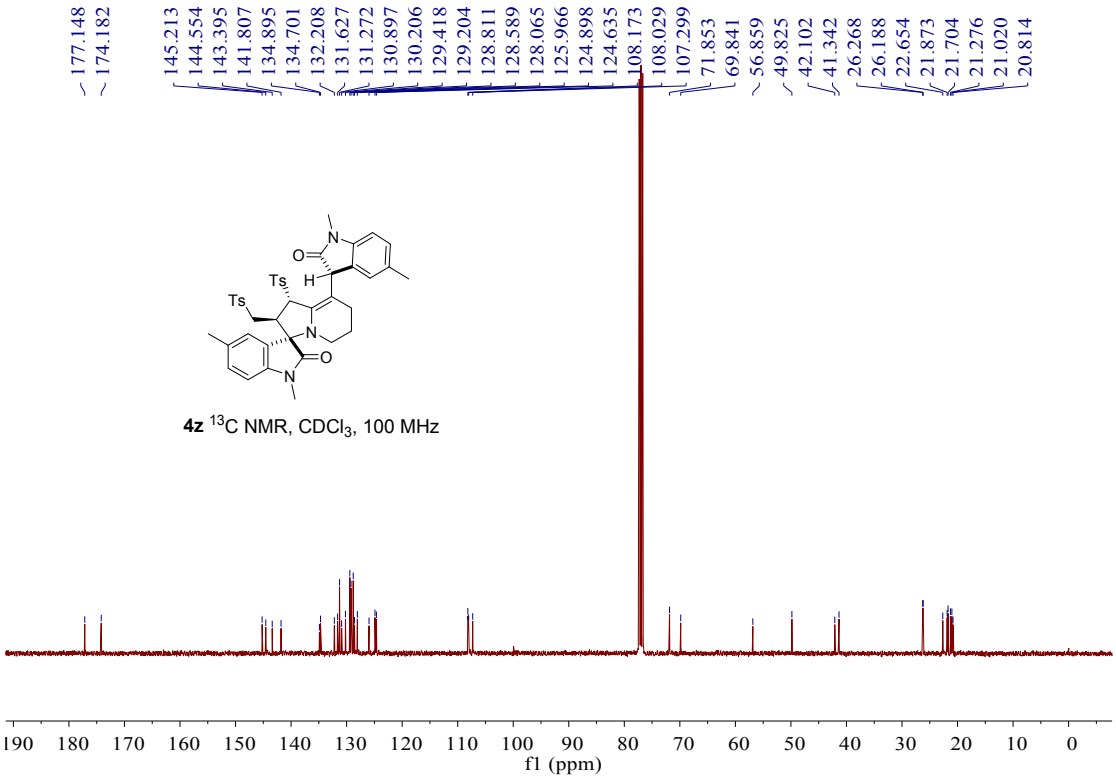
4y ^{1}H NMR, $CDCl_3$, 400 MHz



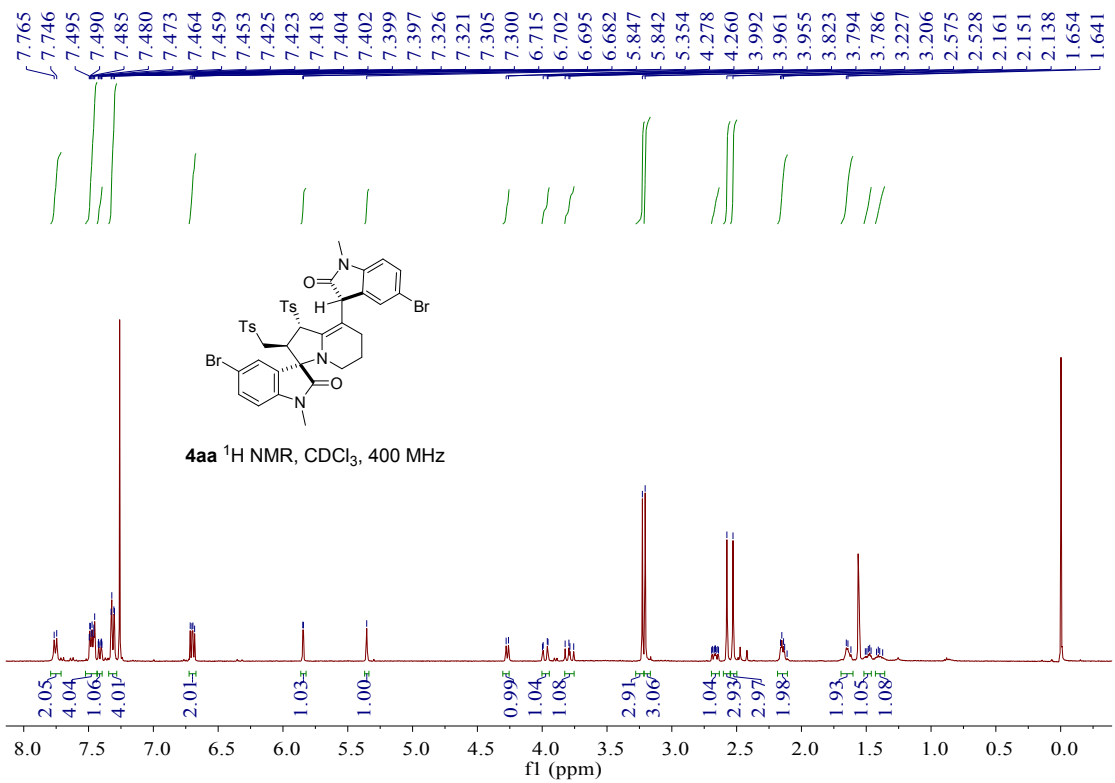
4y ^{13}C NMR, $CDCl_3$, 100 MHz



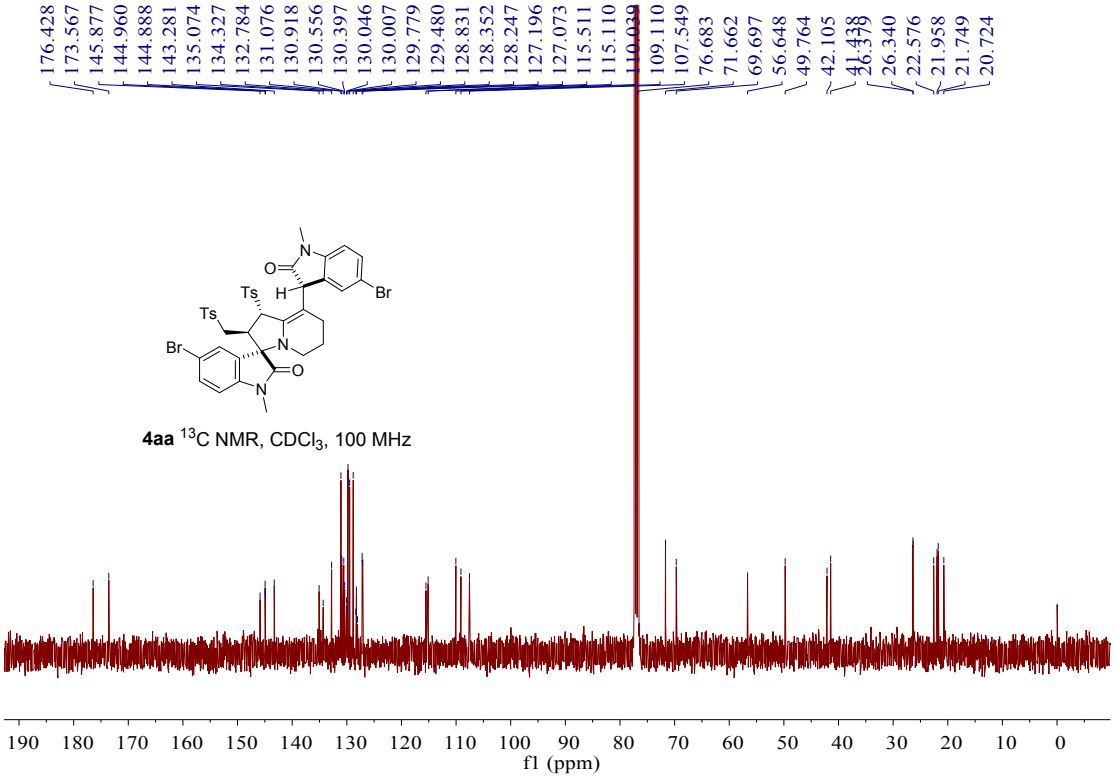
4z ^{1}H NMR, $CDCl_3$, 400 MHz



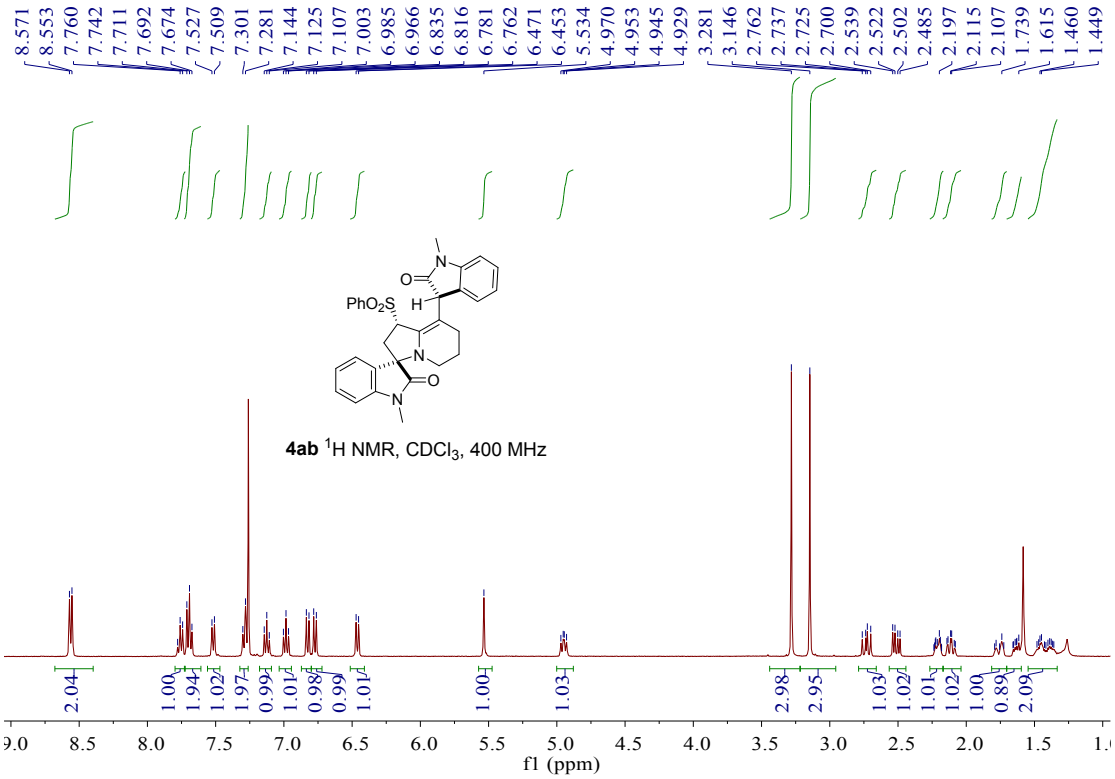
4z ^{13}C NMR, $CDCl_3$, 100 MHz



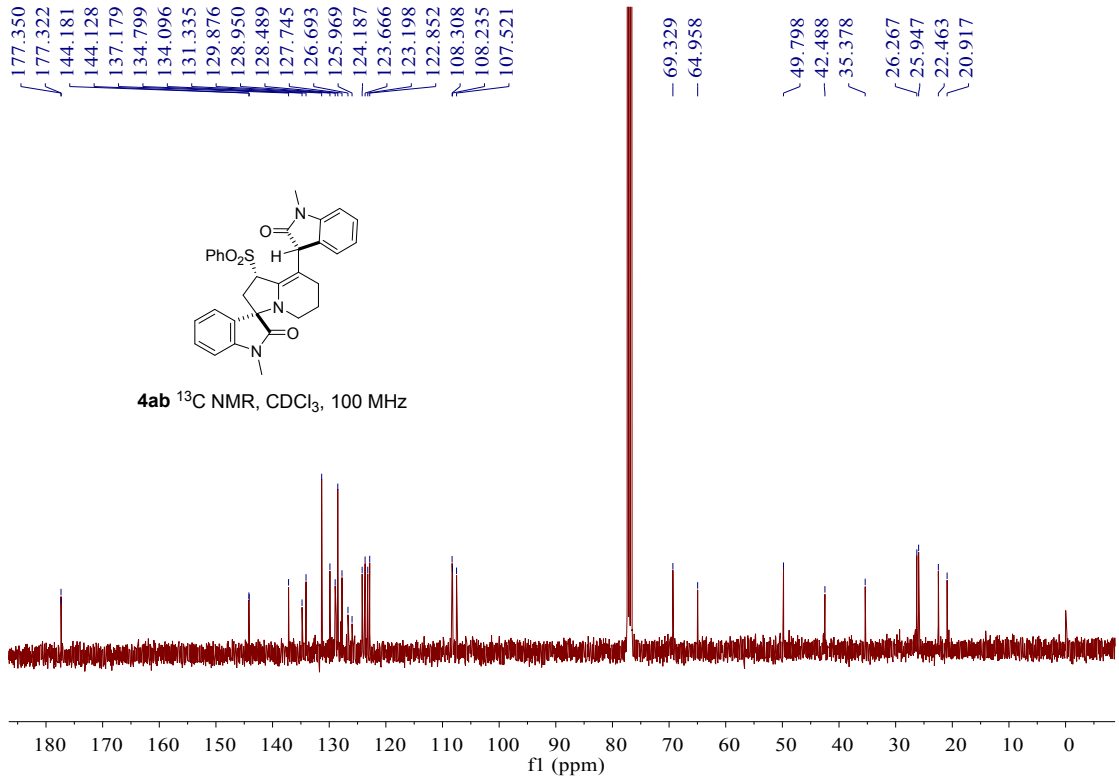
4aa ^{1}H NMR, $CDCl_3$, 400 MHz



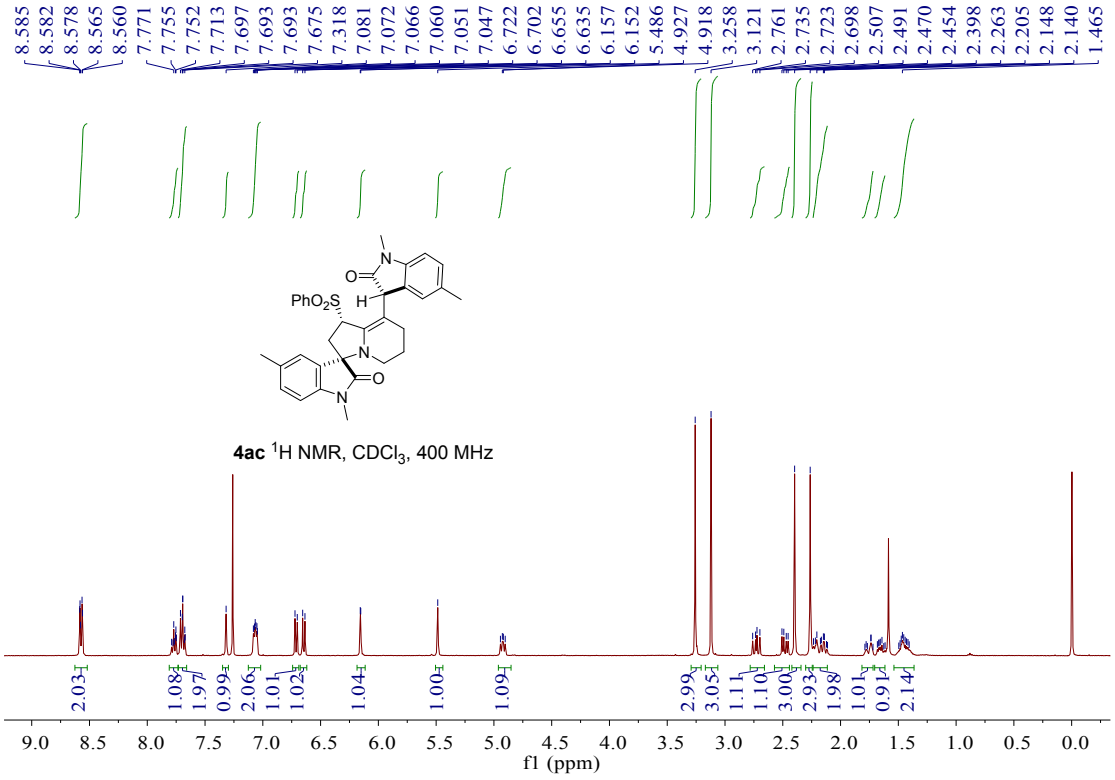
4aa ^{13}C NMR, $CDCl_3$, 100 MHz



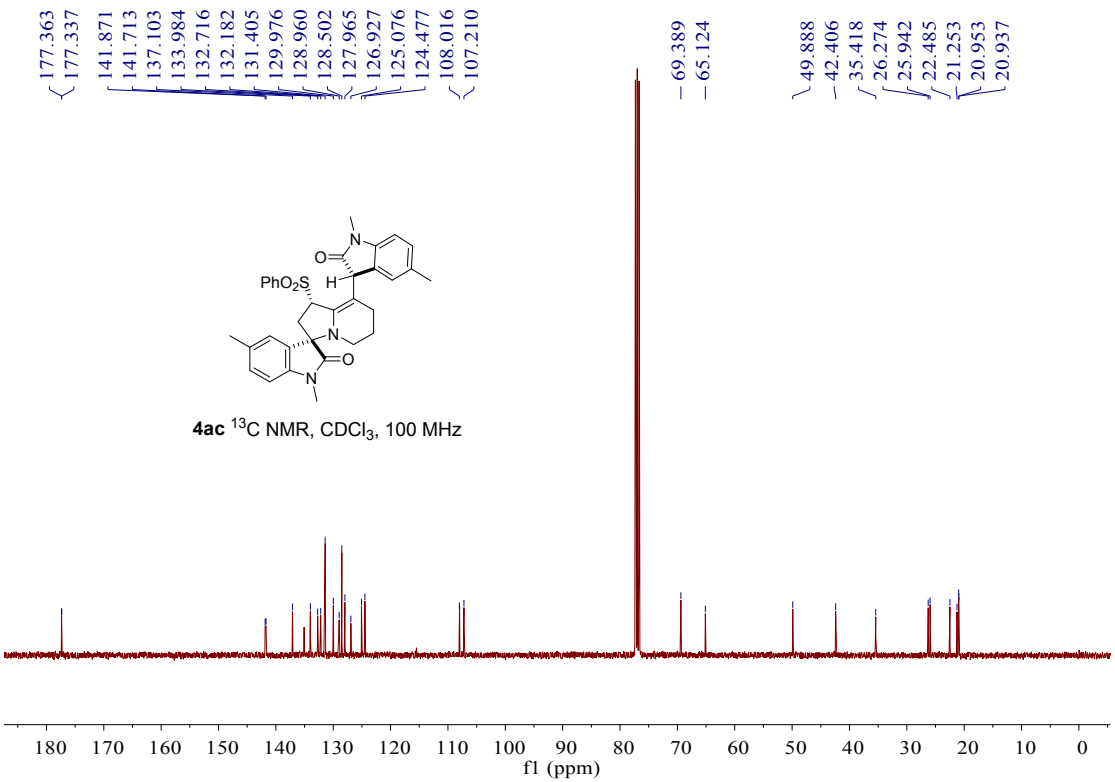
4ab ^{1}H NMR, $CDCl_3$, 400 MHz



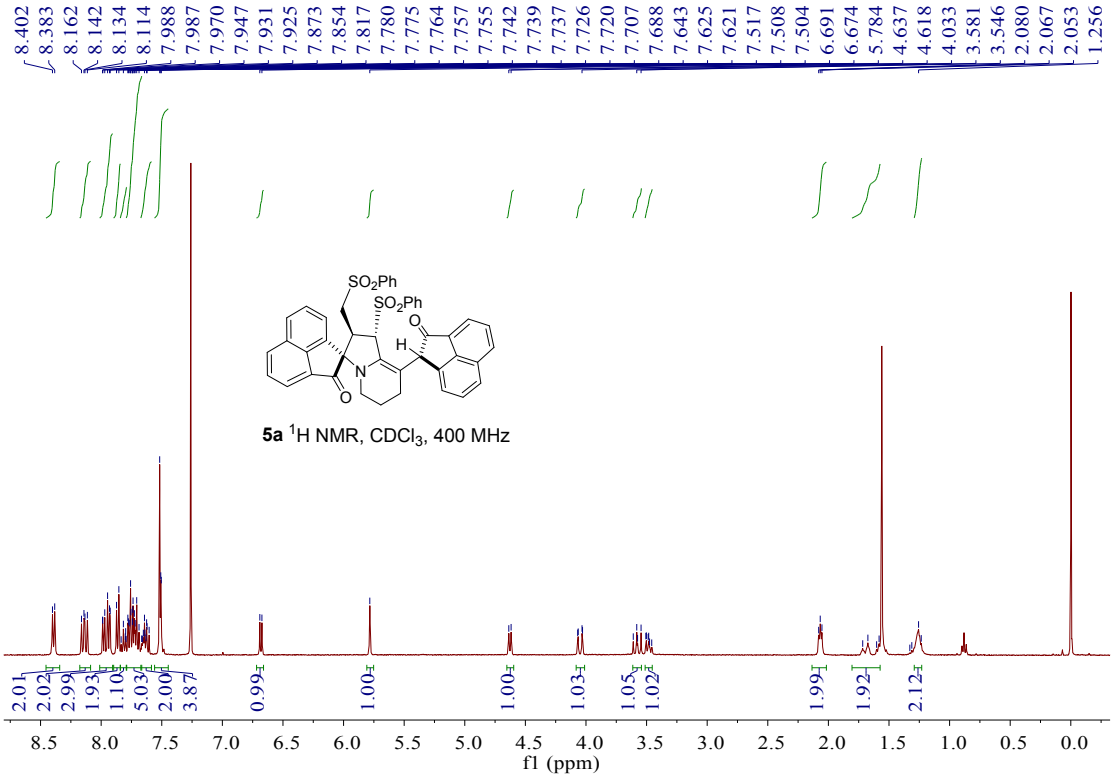
4ab ^{13}C NMR, $CDCl_3$, 100 MHz



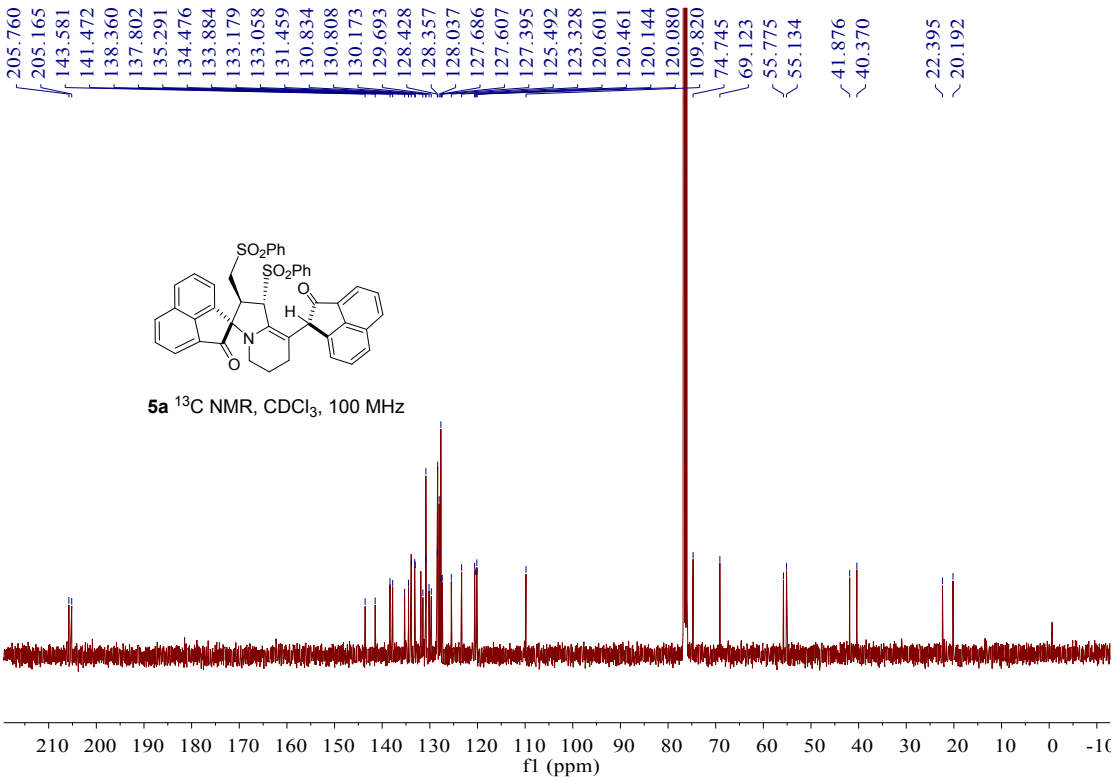
4ac ^{1}H NMR, $CDCl_3$, 400 MHz



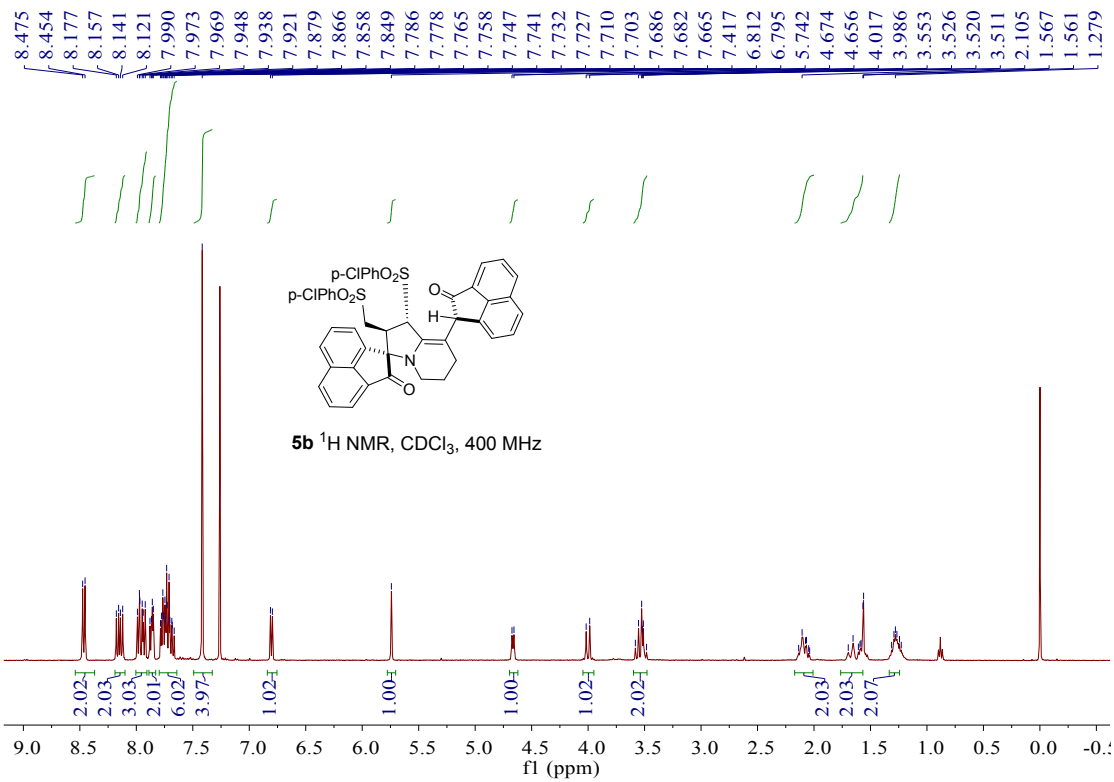
4ac ^{13}C NMR, $CDCl_3$, 100 MHz



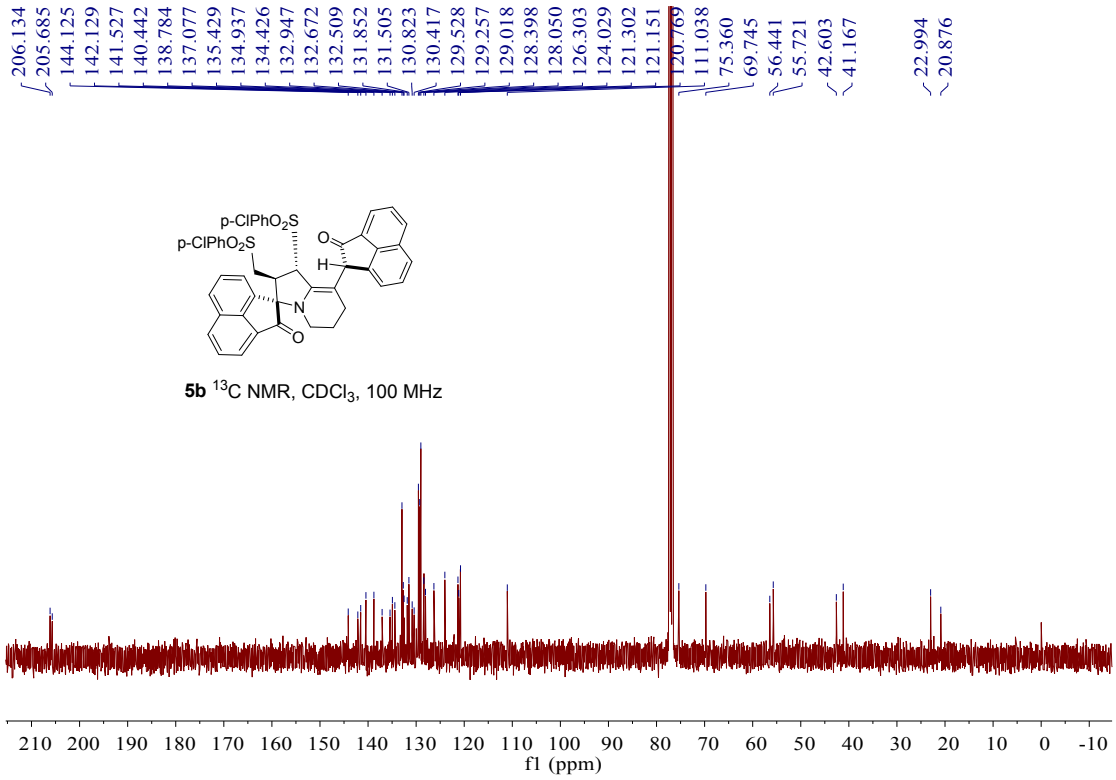
5a ^{1}H NMR, $CDCl_3$, 400 MHz



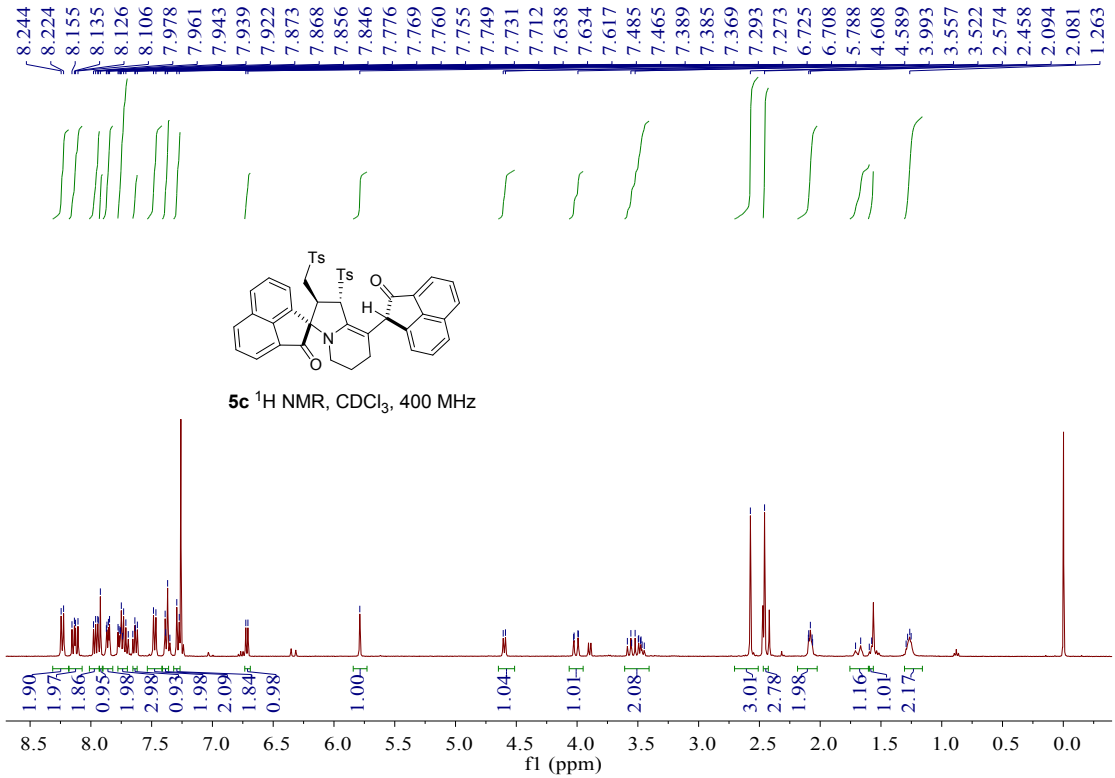
5a ^{13}C NMR, $CDCl_3$, 100 MHz



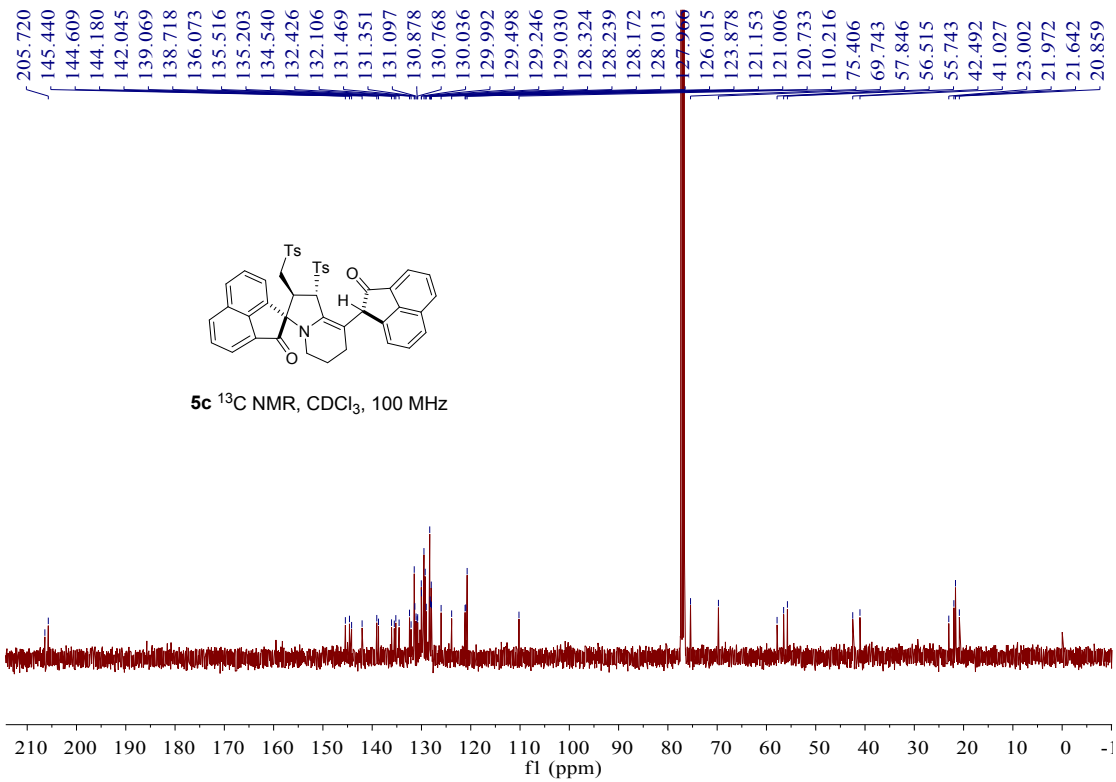
5b ^{1}H NMR, $CDCl_3$, 400 MHz



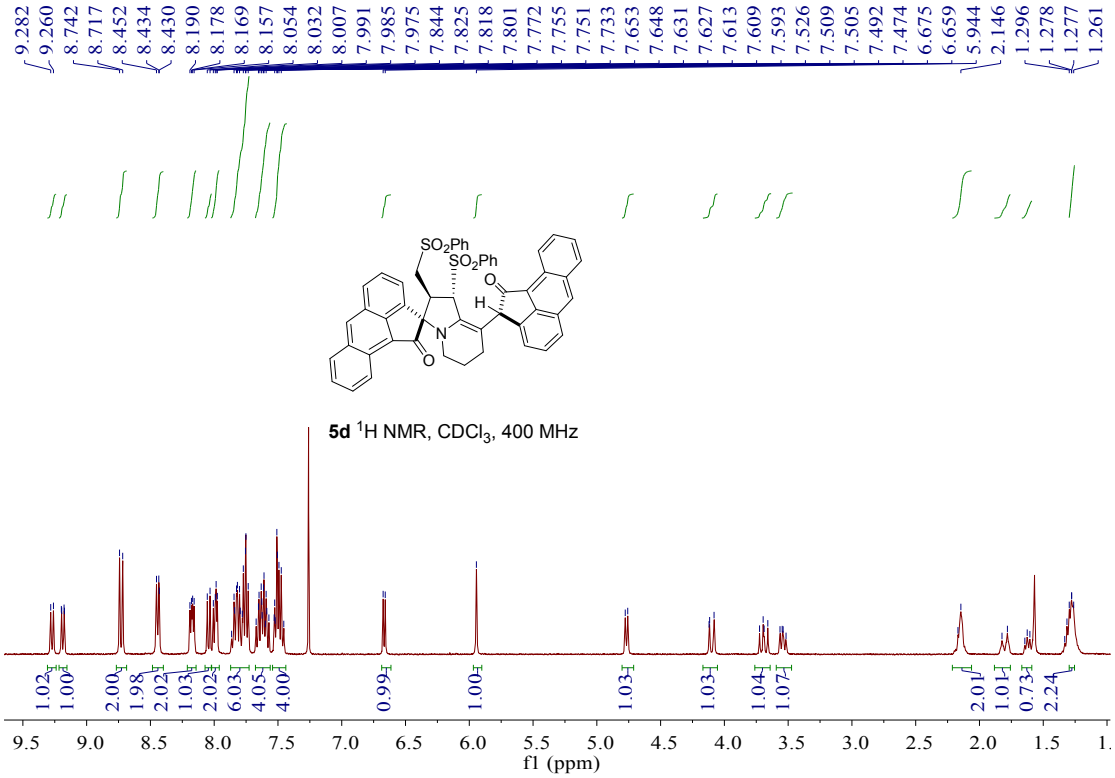
5b ^{13}C NMR, $CDCl_3$, 100 MHz



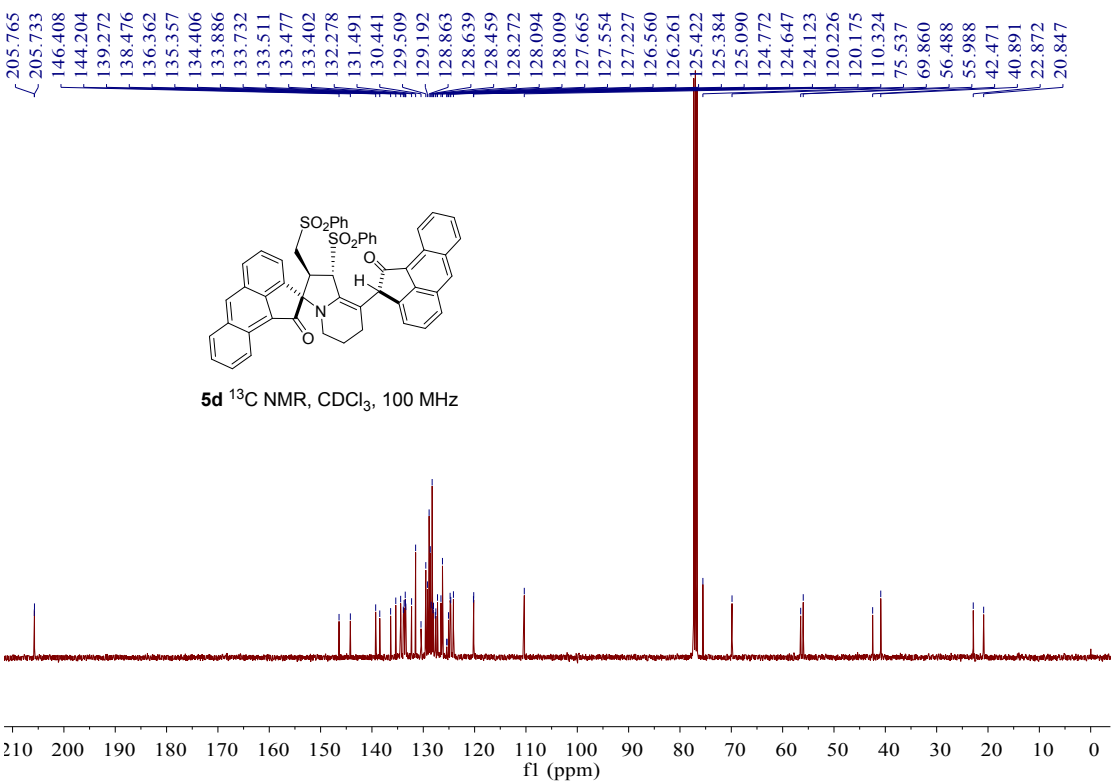
5c ^{1}H NMR, $CDCl_3$, 400 MHz



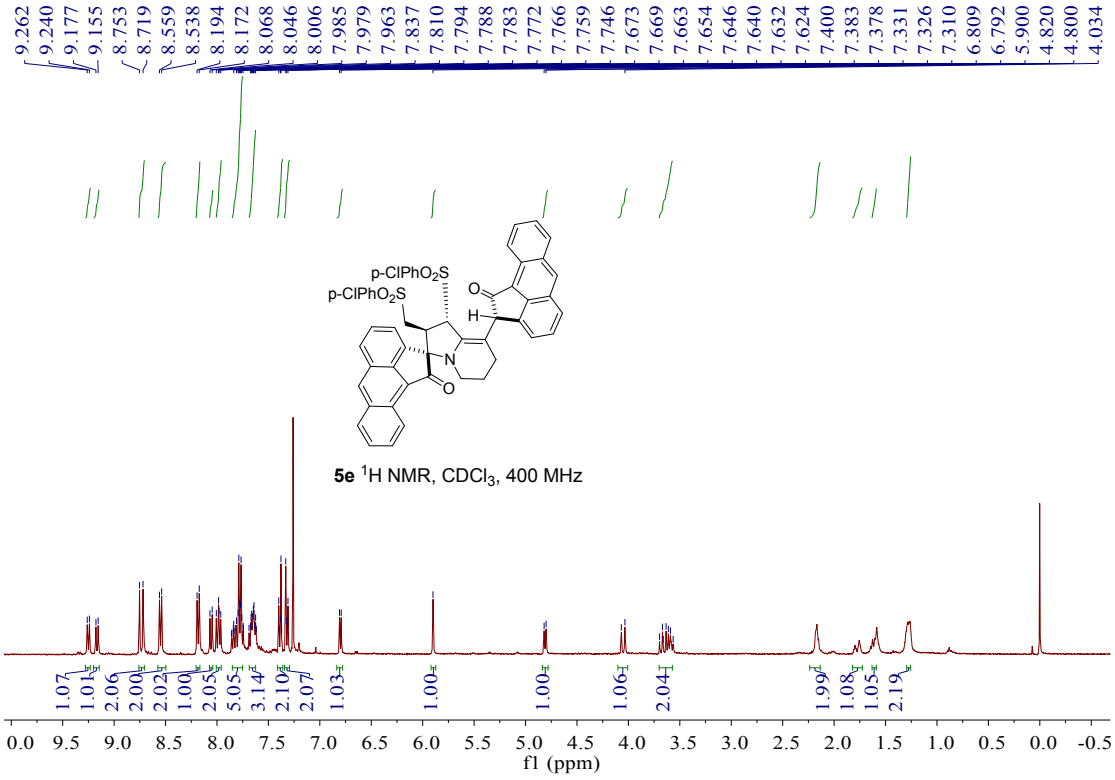
5c ^{13}C NMR, $CDCl_3$, 100 MHz



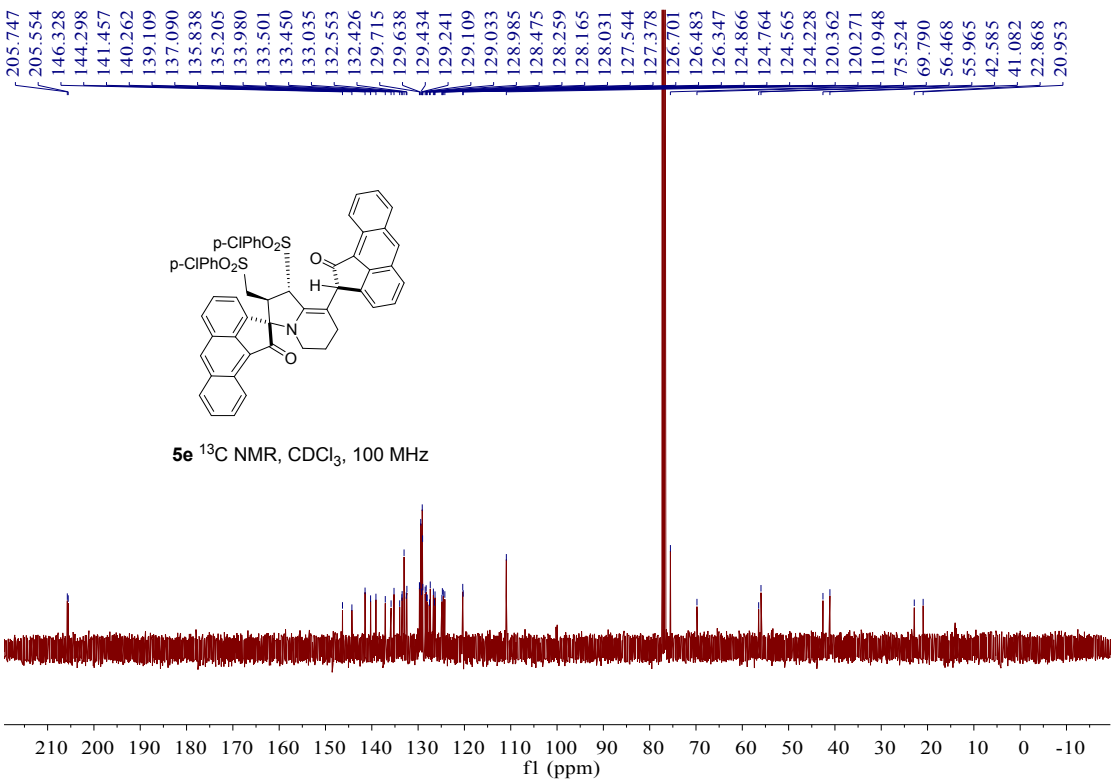
5d ^{1}H NMR, $CDCl_3$, 400 MHz



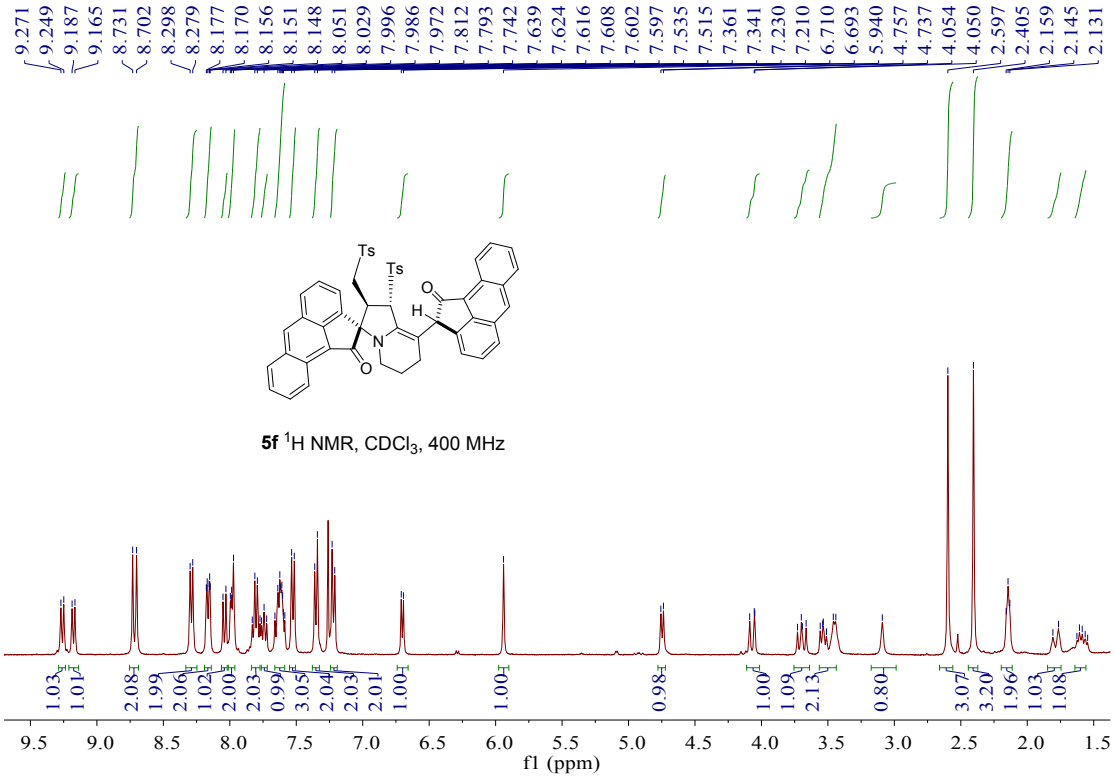
5d ^{13}C NMR, $CDCl_3$, 100 MHz



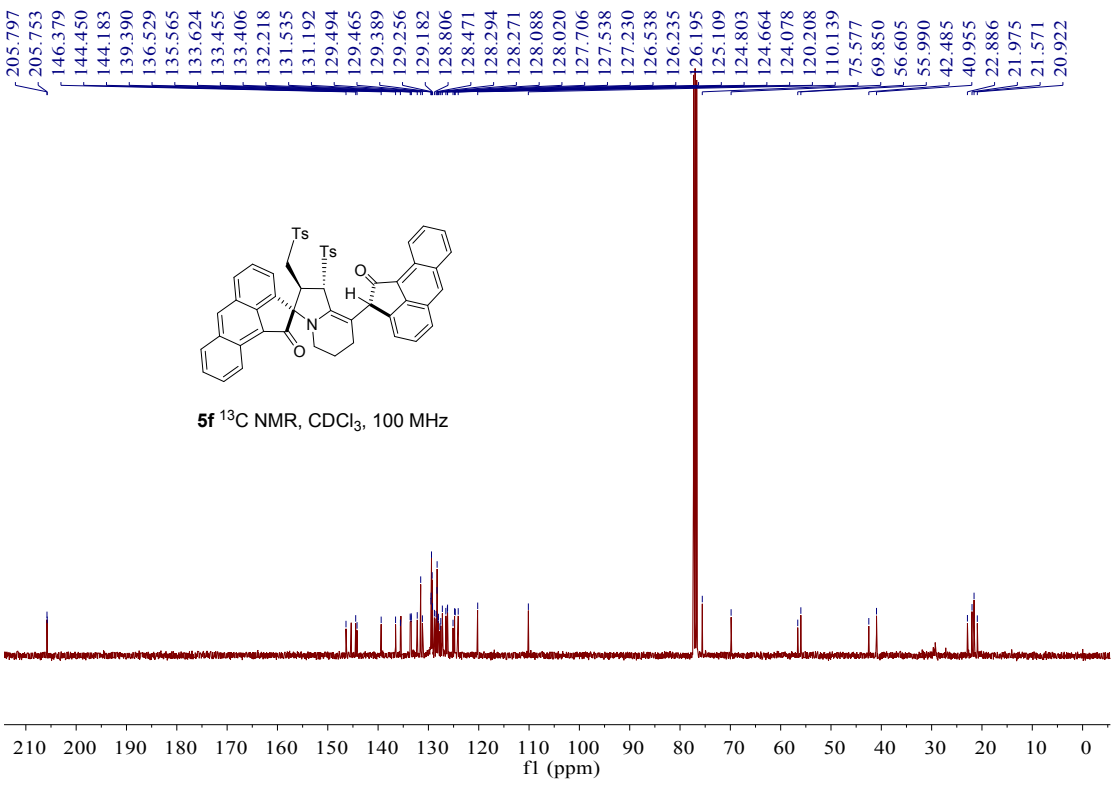
5e ^{1}H NMR, $CDCl_3$, 400 MHz



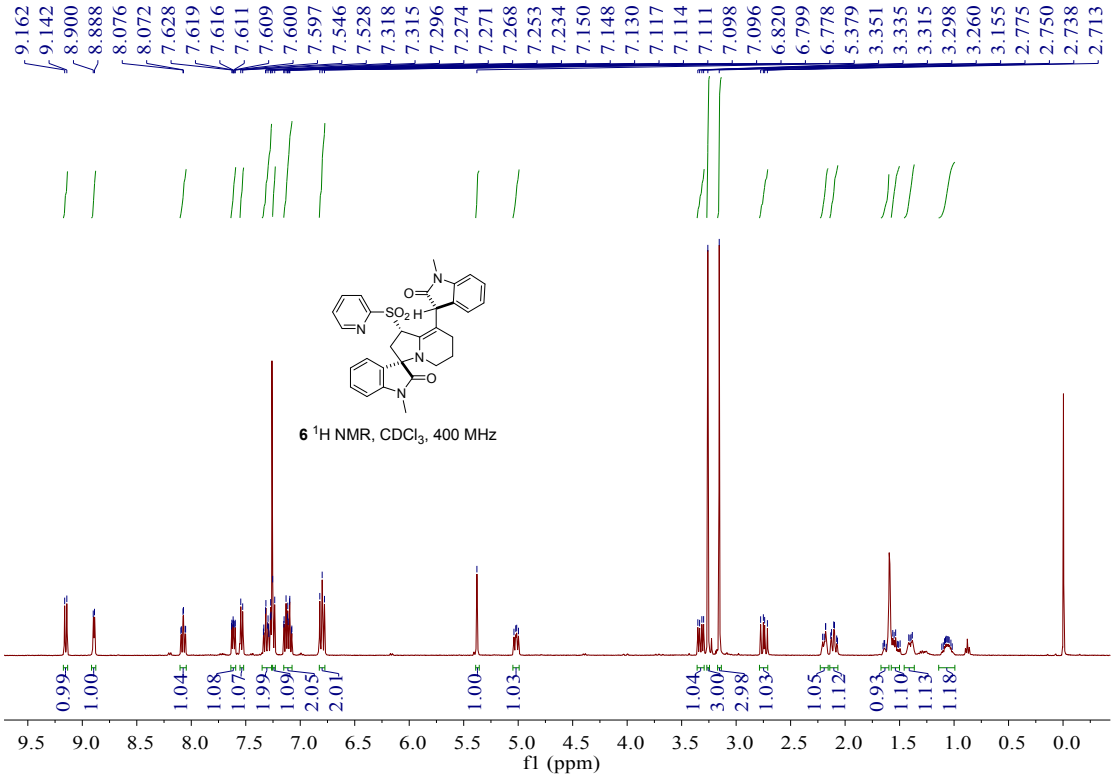
5e ^{13}C NMR, $CDCl_3$, 100 MHz



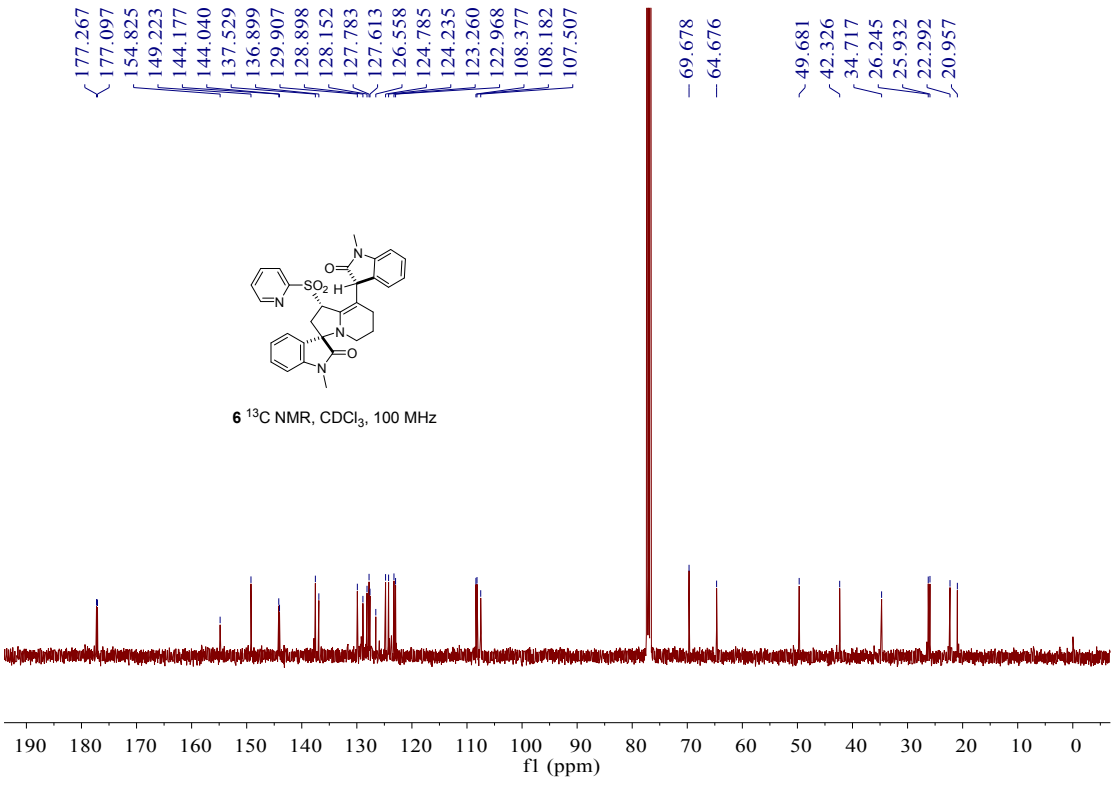
5f ^{1}H NMR, $CDCl_3$, 400 MHz



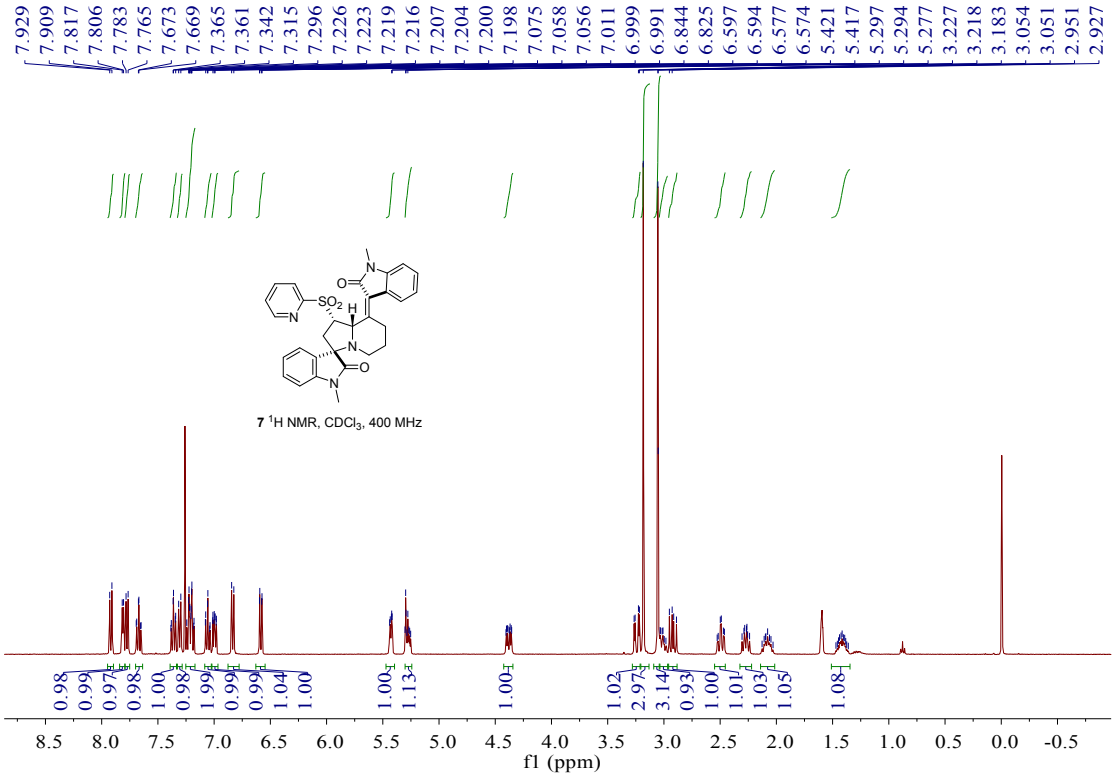
5f ^{13}C NMR, $CDCl_3$, 100 MHz



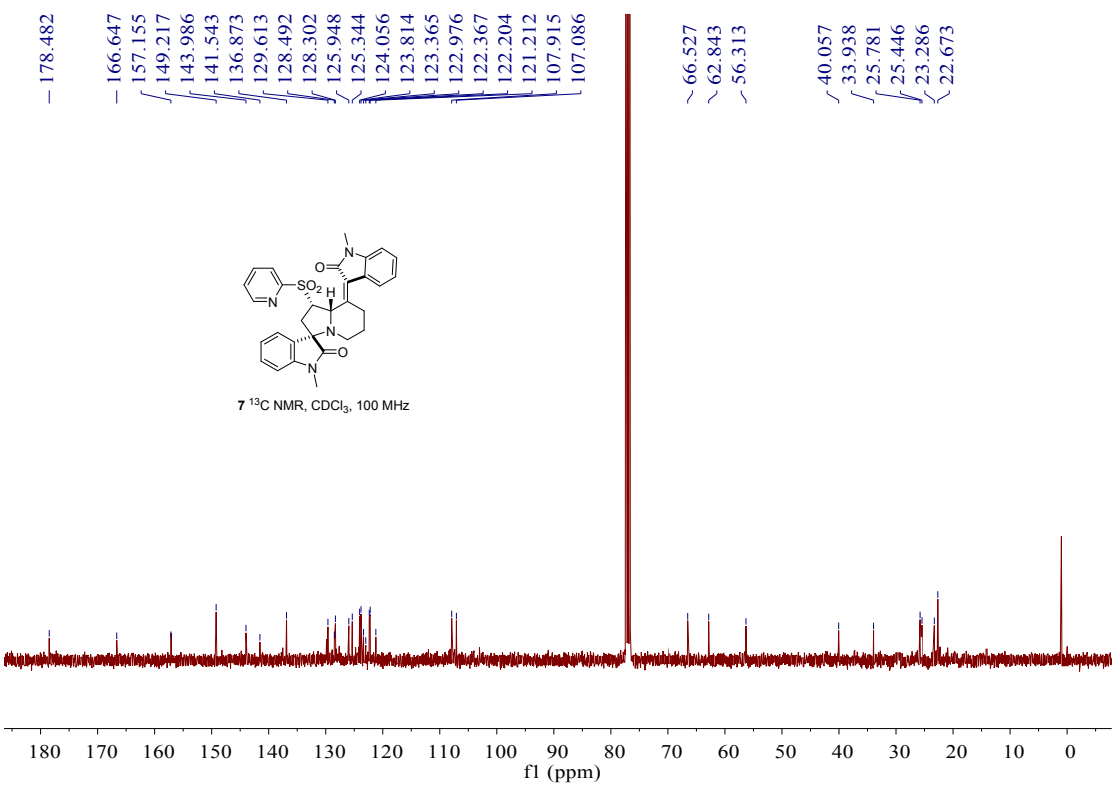
6 ^{1}H NMR, $CDCl_3$, 400 MHz



6 ^{13}C NMR, $CDCl_3$, 100 MHz



7 ^{1}H NMR, $CDCl_3$, 400 MHz



7 ^{13}C NMR, $CDCl_3$, 100 MHz