Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

NHC-catalyzed [12 + 2] reaction of polycyclic arylaldehydes for access to indole derivatives

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Content

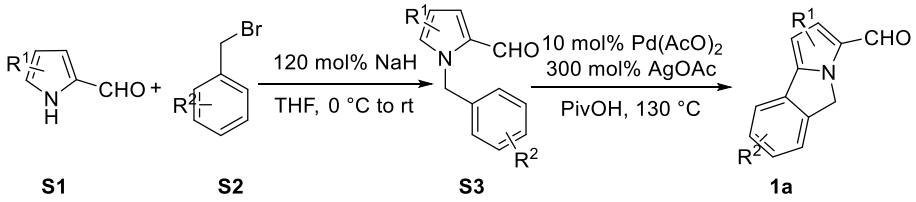
1. General information

Commercially available materials purchased from Energy Chemical and J&K were used as received. Unless otherwise specified, all reactions were carried out in 4.0 mL vial. NMR spectra were measured either on a Bruker ASCEND 400 (400 MHz) Spectrometer. The chemical shift values were corrected to 7.26 ppm (^{1}H NMR), and 77.16 ppm (^{13}C NMR) for $CDCl_3$. The chemical shift values were corrected to 5.32 ppm (^{1}H NMR), and 54.00 ppm (^{13}C NMR) for CD_2Cl_2. ^{1}H NMR splitting patterns are designated as singlet (s), double (d), triplet (t), quartet (q), doublet of doublets (dd), multiplets (m), and etc. All first-order splitting patterns were assigned on the base of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). High resolution mass spectrometer analysis (HRMS) was performed on Waters Xevo G2-S QTof. Infrared spectra (IR) were obtained on a Thermo Fisher FT/IR-Nicolet iS50 spectrometer, and the absorptions have been reported in wavenumbers (cm^{-1}). Chiral HPLC analysis was performed on a Shimadzu LC-20AD instrument using Daicel Chiracelcolumns at 25°C and a mixture of HPLC-grade hexanes and isopropanol as eluent. Optical rotation w8measured using a JASCO P-1030 Polarimeter equipped with a sodium vapor lamp at 589 nm and theconcentration of samples was denoted as c. Chiralcel brand chiral columns from Daicel Chemical Industries were used with models IF, IA, IC, IE, AD-H, OD-H in 4.6 × 250 mm size. The racemic products used to determine the er values were synthesized using achiral catalyst. Optical rotations were measured on an Insmark IP-digi Polarimeter in a 1 dm cuvette. The concentration (*c*) is given in g/100 mL. Melting points (m.p.) were measured on a Beijing Tech Instrument X-4 digital display micro melting point apparatus and are uncorrected. Analytical thin-layer chromatography (TLC) was carried out on pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

2. Synthesis of substrates

Procedure A:

5H-benzo[a]pyrrolizine-3-carbaldehydes**(1a)** were synthesized according to the reported method[1 - 2].

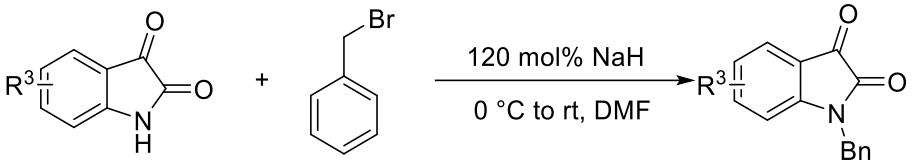


Step 1. sodium hydride (60% dispersion in mineral oil, 1.32 g, 33 mmol) was added to anhydrous DMF (30 mL) in a nitrogen purged two-neck round-bottom flask. The solution was cooled to 0 °C and pyrrole **S1** (2.08 mL, 30 mmol) in anhydrous DMF (8 mL) was added dropwise. The solution was allowed to warm to room temperature and was stirred for 30 minutes before being cooled back to 0 °C when benzyl bromide **S2**(3.57 mL, 30 mmol) was added dropwise. The solution was again allowed to warm to room temperature and was stirred for one hour. The solution was then added to H_2O and extracted with EA. The combined organic layers were washed with H_2O before drying over $MgSO_4$, filtering, and concentrating under reduced pressure. The crude product was purified by flash column chromatography.

Step 2. The appropriate N-benzyl-2-carboxaldehyde **S3** was stirred with $Pd(OAc)_2$ (10 mol%) and AgOAc (3 equiv.) in PivOH (75 equiv.) under an argon atmosphere at 130 ℃ overnight. After cooling, sat. aq. Na_2CO_3 was carefully added until gas formation ceased. The reaction mixture was extracted with EA (3 times), dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by FC (silica gel) to afford the corresponding 5H-benzo[a]pyrrolizine-3-carbaldehydes **1a**.

Procedure B:

1-Benzylindoline-2,3-dione**(2a)** were synthesized according to the reported method.

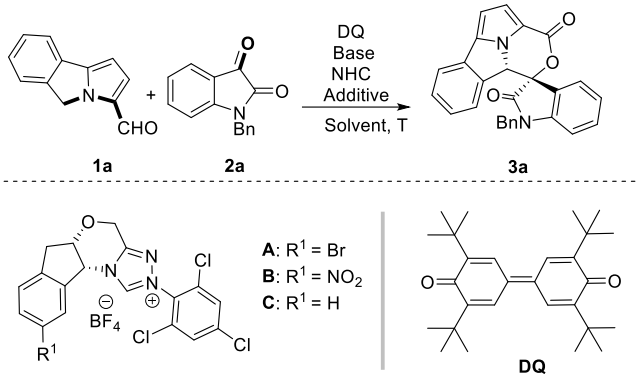


S4 **S5** **2a**

Add DMF (20 ml, 0.25 M), isatin **S4** (736 mg, 5.00 mmol), NaH (60% dispersion in mineral oil, 260 mg, 6.50 mmol) at 0 °C into a 250 ml round bottomed flask under N_2. Stir the reaction mixture at 0 °C for 0.5 hours. Add BnBr **S5** (713 µl, 6.00 mmol) to the reaction mixture. Stir the reaction mixture at room temperature for 2 hours. Add water (100 ml) and filter the resulting precipitate. Dissolve the precipitate in CH_2Cl_2.Wash the precipitate with brine. Dry the combined organic layers over $MgSO_4$ anhydrous. Filter and concentrate the combined organic layers in vacuo. Purification the combined organic layers by recrystallize from EA (evaporation or precipitation with hexane) to obtain N-benzylisatin[3].

3. Condition optimization

Table 1. Condition optimization for the synthesis of **3a**[a]

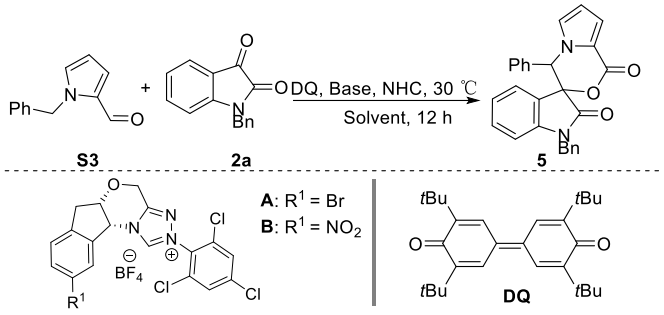


The effects of NHCs, bases, solvents, additive and temperature.[a]

Entry	NHC	Solvent	Base	additive	Yield[b]	er[f]	dr[g]
1	**A**	$CHCl_3$	DIEA		82%	66:34	10:1
2	**B**	$CHCl_3$	DIEA		86%	65:35	8:1
3	**C**	$CHCl_3$	DIEA		81%	65:35	8:1
4	**A**	$PhCF_3$	DIEA		56%	66:34	14:1
5	**A**	THF	DIEA		62%	70:30	>20:1
6	**A**	THF	$NaHCO_3$		43%	67:32	13:1
7	**A**	THF	DABCO		41%	74:26	2:1
8	**A**	THF	$(t\text{-BuO})_2Mg$		56%	85:15	16:1
9	**A**	THF[c]	$(t\text{-BuO})_2Mg$		55%	86:14	8:1
10	**A**	THF[c]	$(t\text{-BuO})_2Mg$[d]		53%	89:11	6:1
11	**A**	THF[c]	$(t\text{-BuO})_2Mg$[d]	DIEA	64%	84:16	15:1
12	**A**	THF[c]	$(t\text{-BuO})_2Mg$[d]	Et_3N	75%	89:11	>20:1
13	**A**	THF[c]	$(t\text{-BuO})_2Mg$[d]	TMEDA	78%	88:12	16:1
14[e]	**A**	THF[c]	$(t\text{-BuO})_2Mg$[d]	Et_3N	79%	91:9	>20:1

[a]General conditions: **1a** (0.12 mmol), **2a** (0.10 mmol), NHC (0.02 mmol), base (0.12 mmol), DQ (0.20 mmol) and additive (0.01 mmol) in solvent (1.0 mL) at 30 °C for 24 h. Yields were determined by ^1H NMR. [c]THF (3 ml) was used. [d]MTB(0.20 mmol)was used, MTB = $(t\text{-BuO})_2Mg$. [e]At -5 °C. [f]e.r. was determined by chiral HPLC analysis of the purified products. [g]d.r. was determined by ^1H NMR analysis of the crude products.

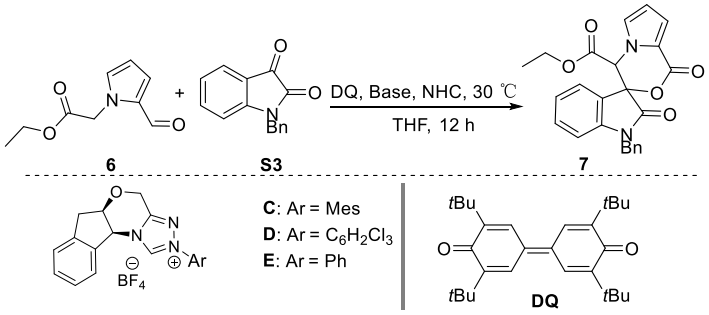
Table 2. Condition optimization for the synthesis of **5**[h]



Entry	NHC	Solvent	Base	Yield%
1	**A**	THF	DMAP	N.R.
2	**A**	THF	$NaHCO_3$	N.R.
3	**A**	THF	Na_2CO_3	N.R.
4	**A**	THF	Et_3N	N.R.
5	**A**	1,4-Dioxane	DMAP	N.R.
6	**B**	THF	DMAP	N.R.

[h]General conditions: **S3** (0.12 mmol), **2a** (0.10 mmol), NHC (0.02 mmol), base (0.12 mmol), DQ (0.20 mmol) in solvent (1.0 mL) at 30 °C for 12 h.

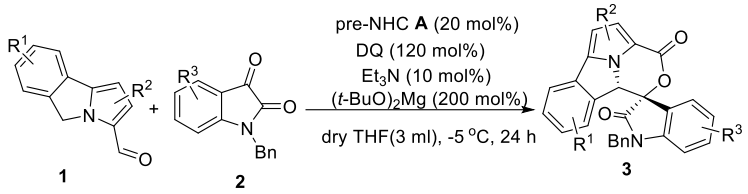
Table 3. Condition optimization for the synthesis of **7**[i]



Entry	NHC	Solvent	Base	Yield%
1	**C**	THF	Et_3N	N.R.
2	**C**	THF	K_2CO_3	N.R.
3	**C**	THF	DBU	N.R.
4	**D**	THF	Et_3N	N.R.
5	**D**	THF	K_2CO_3	N.R.
6	**D**	THF	DBU	N.R.
7	**E**	THF	Et_3N	N.R.
8	**E**	THF	K_2CO_3	N.R.
9	**E**	THF	DBU	N.R.

[i]General conditions: **6** (0.12 mmol), **S3** (0.10 mmol), NHC (0.02 mmol), base (0.12 mmol), DQ (0.20 mmol) in THF (1.0 mL) at 30 °C for 12 h.

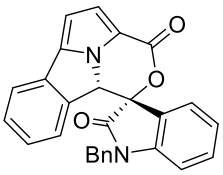
4 Genera procedures for the catalytic reactions



To a 4 mL vial equipped with a magnetic stir bar were added **1** (0.12 mmol), **2** (0.10 mmol), DQ (0.20 mmol), Et_3N (0.01 mmol), *pre*-NHC **A** (0.02 mmol) and (*t*-BuO)$_2$Mg (0.20 mmol) in dry THF (3.0 mL) and the reaction was stirred in ice bath at -5 ℃ for 24 h. Then the mixture was concentrated under reduced pressure. The resulting crude residue was purified by column chromatography on silica gel (petroleum ether/ ethyl acetate = 100 / 1 to 10 / 1) to afford the desired product **3**.

5 Characterization of products

(1S,9bS)-1'-benzylspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione (3a)



3a

The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3a** as a white solid in 79% yield (32.6 mg), m.p. 216–218 °C; **$[\alpha]^{25}D$** = -140.590 (c = 0.2, $CHCl_3$); > 20:1 dr; 91:9 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 48.80 min (minor), t_R = 33.72 min (major);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 7.7 Hz, 1H), 7.41 – 7.33 (m, 5H), 7.27 (s, 1H), 7.25 (d, J = 7.7 Hz, 1H), 7.20 (d, J = 3.9 Hz, 1H), 7.06 (td, J = 7.8, 1.1 Hz, 1H), 6.95 (td, J = 7.6, 0.9 Hz, 1H), 6.80 (d, J = 7.6 Hz, 1H), 6.71 (d, J = 7.9 Hz, 1H), 6.64 – 6.58 (m, 2H), 5.86 (s, 1H), 5.25 (d, J = 7.1 Hz, 1H), 5.01 (dd, J = 44.6, 15.4 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 157.0, 142.7, 142.7, 139.8, 134.9, 134.1, 131.1, 129.5, 129.0, 128.2, 127.8, 127.1, 124.2, 123.8, 123.5, 122.8, 121.0, 121.0, 115.4, 109.7, 105.0, 85.6, 59.6, 44.3.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{19}N_2O_3^+$, $[M+H]^+$: 419.1390, found: 419.1387.

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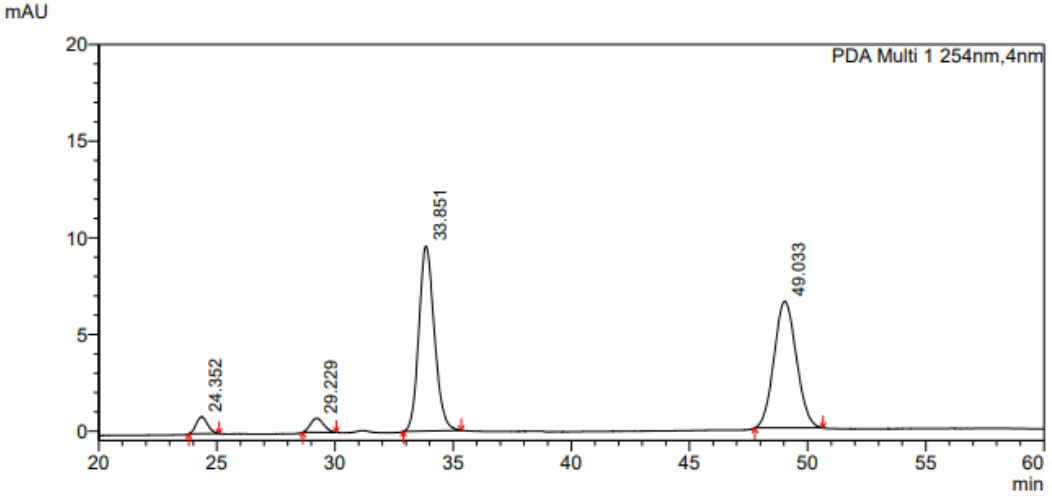

<Peak Table>

PDA Ch1 254nm

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2	29.229	27974	721	3.020
3	33.851	437669	9563	47.243
4	49.033	431728	6550	46.601
Total		926426	17704	100.000

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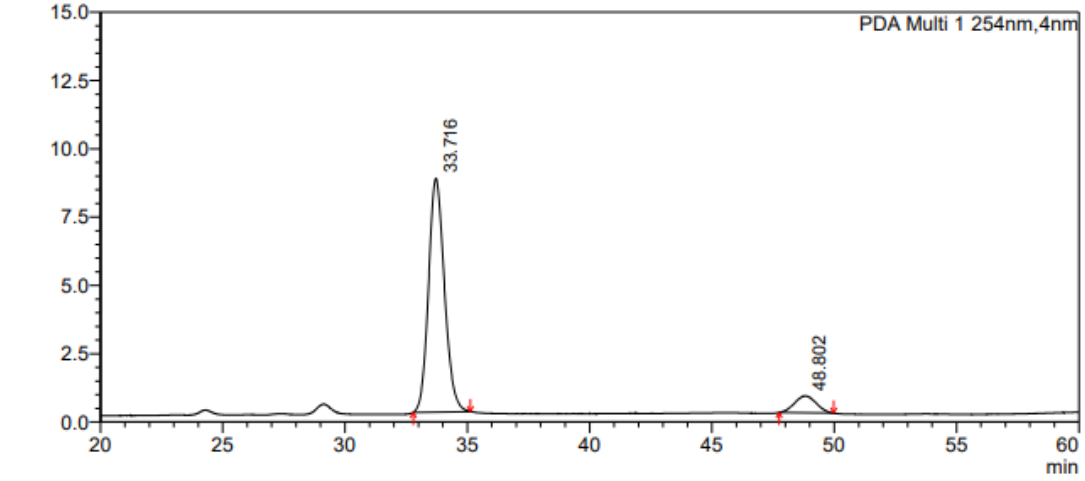

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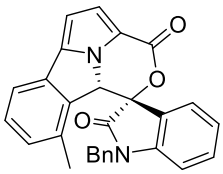
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	33.716	386967	8554	91.027
2	48.802	38147	618	8.973
Total		425115	9172	100.000

(1S,9bS)-1'-benzyl-9-methylspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione (3b)



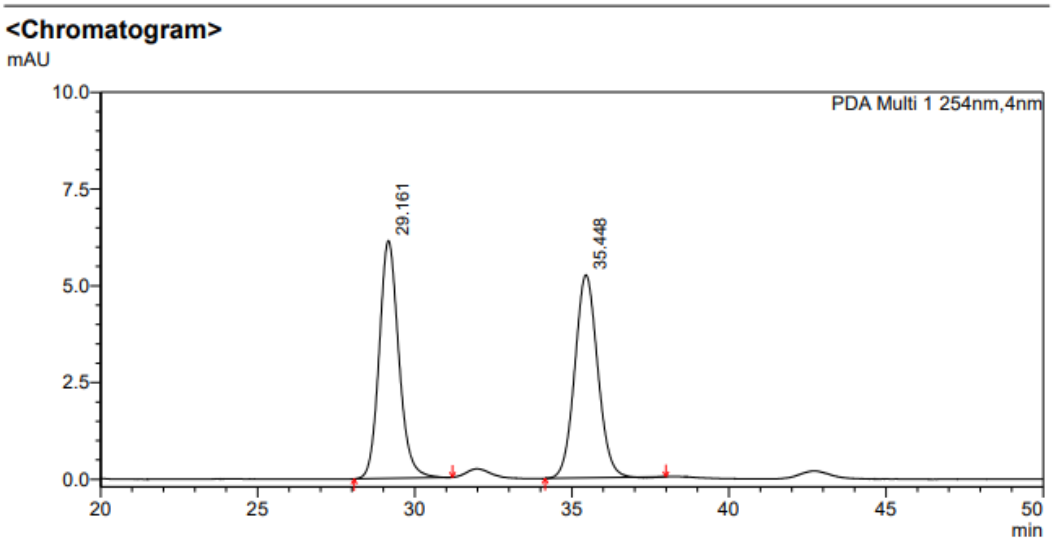
3b

The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3b** as a yellow solid in 80% yield (34.6 mg), m.p. 202-204 °C; **[α]^{25}D** = -228.722 (c = 0.25, $CHCl_3$); 10:1 dr; 98:2 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 34.30 min (minor), t_R = 28.35 min (major)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.35 – 7.20 (m, 6H), 7.14 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 3.9 Hz, 1H), 7.04 (td, J = 7.8, 1.2 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 6.70 (d, J = 7.9 Hz, 1H), 6.60 – 6.52 (m, 2H), 5.82 (s, 1H), 5.15 – 5.07 (m, 2H), 4.61 (d, J = 15.4 Hz, 1H), 1.96 (s, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.7, 156.5, 143.1, 142.8, 138.9, 135.4, 134.5, 134.3, 131.2, 129.6, 129.3, 128.9, 128.1, 127.9 124.1, 123.7, 122.9, 120.6, 118.4, 115.3, 110.1, 104.4, 86.0, 59.7, 44.4, 19.1

HRMS (ESI, m/z) Calcd. for $C_{28}H_{20}N_2NaO_3^+$, $[M+Na]^+$: 455.1366, found: 455.1349



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Peak#	Ret. Time	Area	Height	Area%
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2	35.448	265846	5242	50.006
Total		531623	11381	100.000

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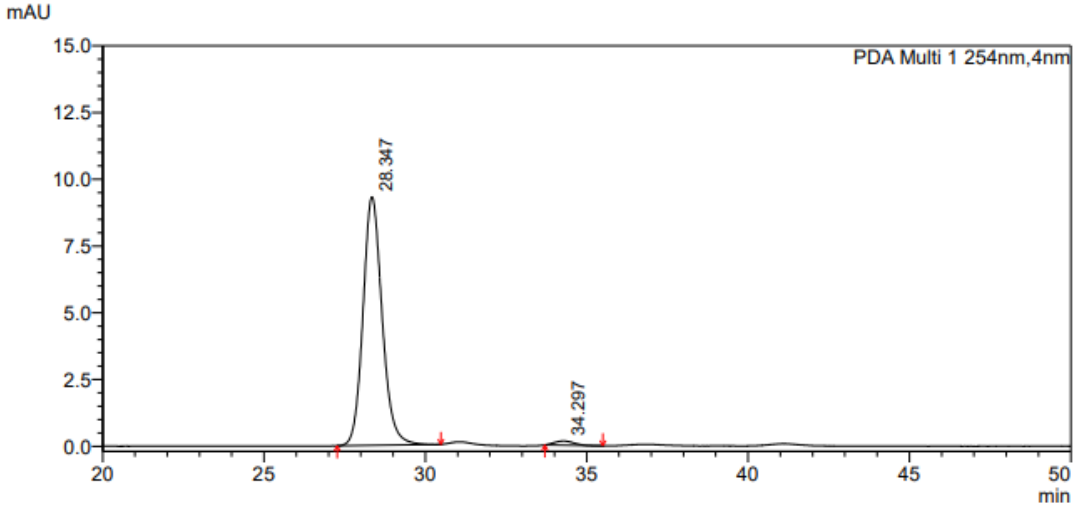

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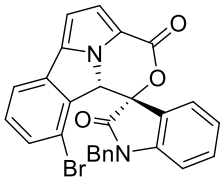
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	28.347	384303	9314	98.345
2	34.297	6467	159	1.655
Total		390771	9473	100.000

(1S,9bS)-1'-benzyl-9-bromospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3c)



3c

The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3c** as a yellow solid in 64% yield (32.0 mg), m.p. 215–217 °C; **[α]^{25}D** = - 154.412 (c = 0.25, $CHCl_3$); 10:1 dr; 98:2 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 48.10 min (minor), t_R = 35.96 min (major)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.44 (dd, J = 6.9, 1.5 Hz, 1H), 7.35 – 7.17 (m, 6H), 7.15 – 7.08 (m, 3H), 7.06 – 7.00 (m, 1H), 6.67 (d, J = 7.9 Hz, 1H), 5.84 (s, 1H), 5.16 (dd, J = 15.6, 11.5 Hz, 2H), 4.51 (d, J = 15.6 Hz, 1H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.4, 156.2, 143.2, 141.7, 140.5, 136.4, 134.7, 131.4, 131.3, 131.2, 128.9, 128.0, 127.8, 123.8, 123.4, 122.5, 120.6, 119.7, 118.3, 115.9, 110.1, 105.3, 85.7, 60.8, 44.6.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}BrN_2NaO_3^+$, $[M+Na]^+$: 519.0315, found: 519.0310.

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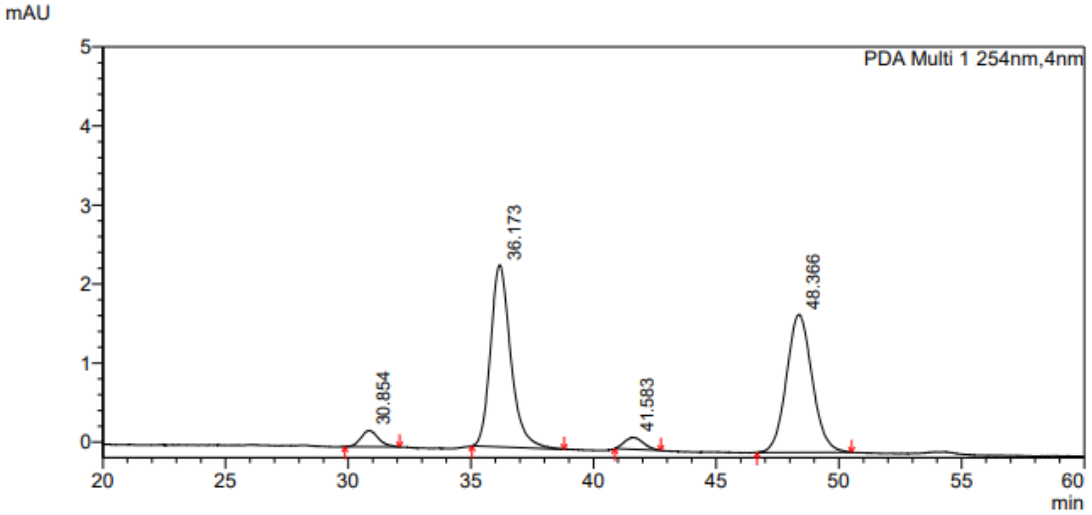

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PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	30.854	10076	203	3.634
2	36.173	131773	2300	47.522
3	41.583	8079	149	2.914
4	48.366	127358	1742	45.930
Total		277287	4394	100.000

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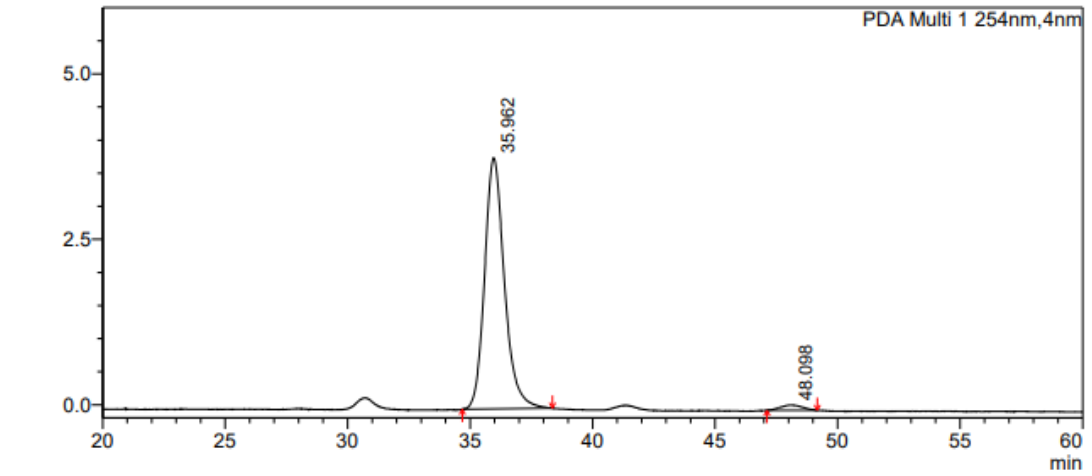

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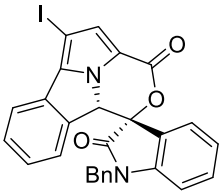
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	35.962	213187	3793	97.767
2	48.098	4869	79	2.233
Total		218056	3872	100.000

(1S,9bS)-1'-benzyl-5-iodospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione (3d)



3d

The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3d** as a orange solid in 37% yield (20.1 mg), m.p. 217–219 °C; **[α]^{25}D** = -101.698 (c = 0.5, $CHCl_3$); 3:1 dr; 92:8 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 36.92 min (minor), t_R = 54.86 min (major);

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.48 – 7.43 (m, 1H), 7.35 – 7.27 (m, 4H), 7.19 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 3.9 Hz, 1H), 7.02 (ddd, J = 7.8, 6.6, 1.2 Hz, 1H), 6.89 (td, J = 7.6, 1.0 Hz, 1H), 6.74 – 6.65 (m, 2H), 6.59 – 6.52 (m, 2H), 5.76 (d, J = 8.1 Hz, 1H), 5.16 (m, J = 13.2, 6.6 Hz, 1H), 4.92 (dd, J = 37.5, 15.5 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2 157.0, 142.8, 142.7, 139.8, 134.9, 134.1, 131.1, 129.5, 129.0, 128.2, 127.8, 127.2, 124.2, 123.8, 123.5, 122.7, 121.0, 121.0, 115.4, 109.8, 105.1, 85.6, 59.6, 44.3.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}N_2IO_3^+$, $[M+Na]^+$: 567.0176, found: 567.0104.

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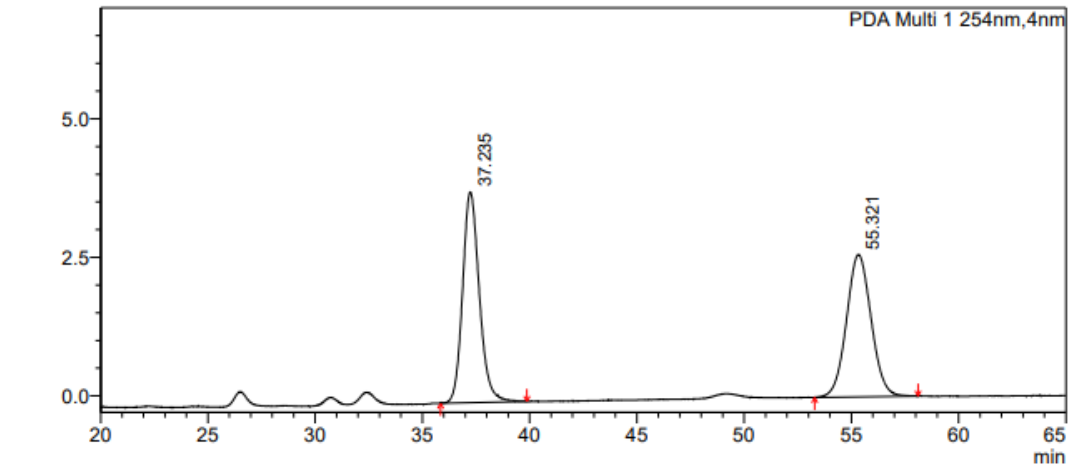

<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
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2	55.321	204945	2563	49.856
Total		411078	6364	100.000

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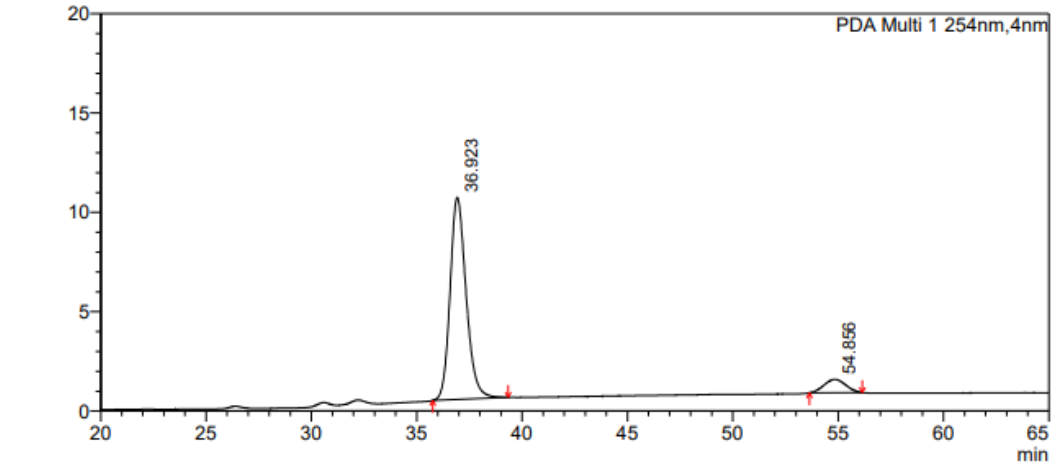
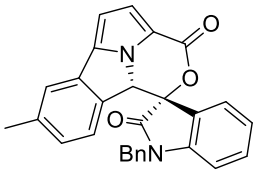


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	36.923	539755	10173	91.883
2	54.856	47685	667	8.117
Total		587440	10840	100.000

(1S,9bS)-1'-benzyl-7-methylspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3e)



3e

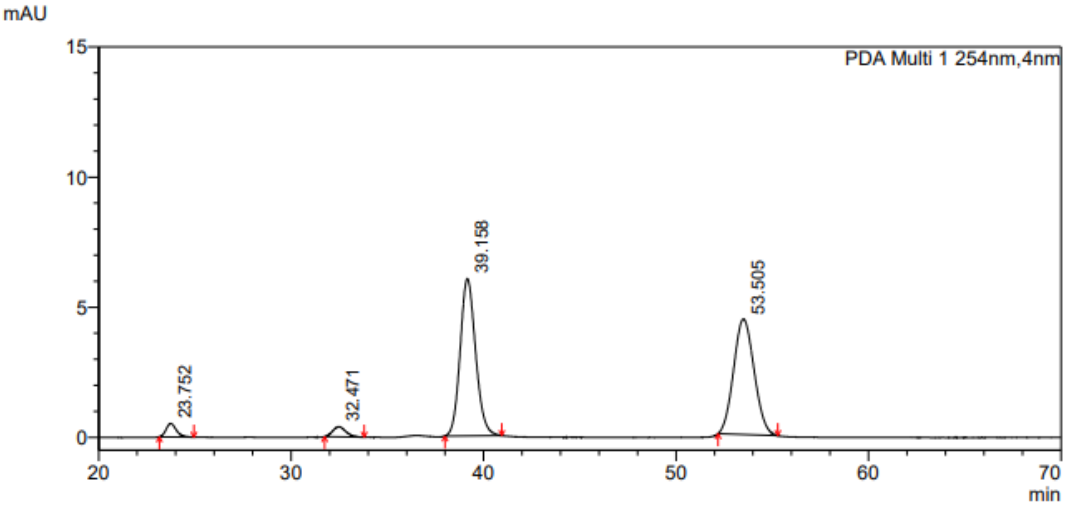
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3e** as a yellow solid in 89% yield (38.6 mg), m.p. 206-208 °C; **[α]^{25}D** = -94.234 (c = 0.25, $CHCl_3$); 10:1 dr; 85:15 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 53.44 min (minor), t_R = 39.04 min (major)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.47 – 7.36 (m, 6H), 7.21 (t, J = 6.7 Hz, 1H), 7.14 (td, J = 7.8, 0.9 Hz, 1H), 6.83 (t, J = 8.1 Hz, 2H), 6.75 – 6.63 (m, 3H), 5.83 (s, 1H), 5.29 (d, J = 7.5 Hz, 1H), 5.04 (dd, J = 49.8, 15.5 Hz, 2H), 2.33 (s, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.1, 156.8, 142.9, 142.8, 139.9, 136.9, 135.2 134.2 131.0, 129.0, 128.2, 127.9, 127.8, 124.1, 123.6, 123.1, 122.9, 121.7, 120.6, 115.3, 109.8, 104.9, 85.5, 59.4, 44.2, 21.2.

HRMS (ESI, m/z) Calcd. for $C_{28}H_{20}N_2NaO_3^+$, $[M+Na]^+$: 455.1366, found: 455.1359.

<Chromatogram>

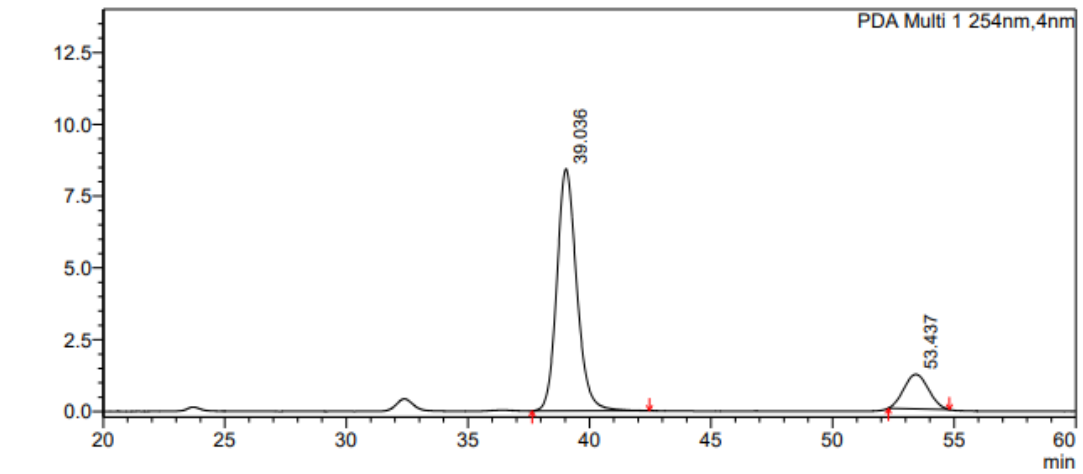


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	23.752	18916	516	2.682
2	32.471	18290	386	2.593
3	39.158	338363	6042	47.978
4	53.505	329676	4438	46.746
Total		705245	11382	100.000

<Chromatogram>

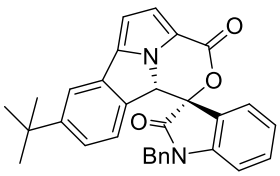


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	39.036	480395	8427	85.027
2	53.437	84599	1202	14.973
Total		564994	9629	100.000

(1S,9bS)-1'-benzyl-7-(tert-butyl)spiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3f)



3f

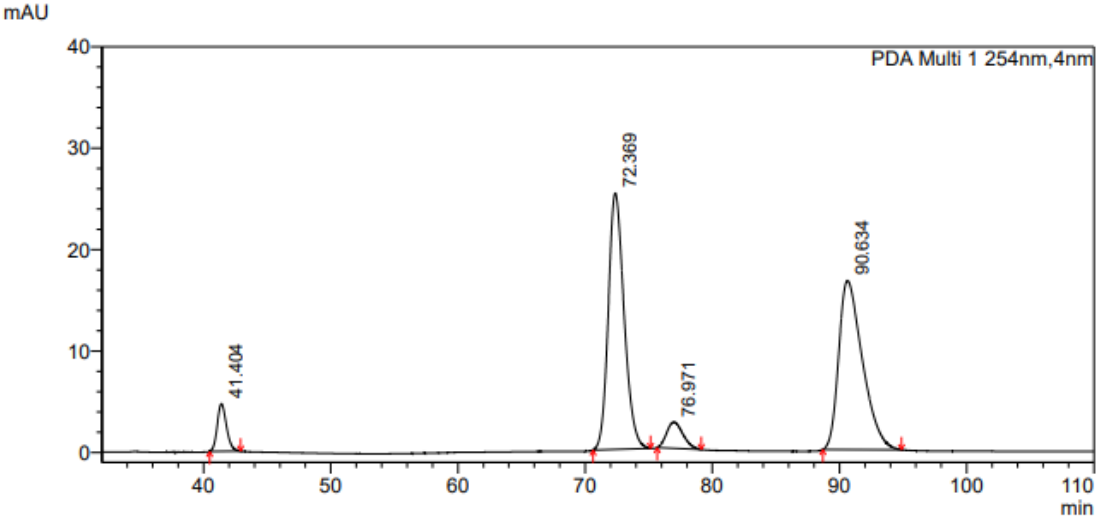
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3f** as a yellow solid in 49% yield (23.4 mg), m.p. 209-211 °C; **$[\alpha]^{25}D$** = -70.810 (c = 0.5, $CHCl_3$); 14:1 dr; 83:17 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 70/30, 0.4 mL/min), t_R = 91.69 min (minor), t_R = 72.48 min(major)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.50 (d, J = 1.5 Hz, 1H), 7.35 – 7.21 (m, 5H), 7.08 (d, J = 3.9 Hz, 1H), 7.06 – 7.00 (m, 1H), 6.99 – 6.94 (m, 1H), 6.70 (dd, J = 12.6, 8.0 Hz, 2H), 6.56 (dd, J = 12.8, 5.7 Hz, 2H), 5.72 (s, 1H), 5.20 (d, J = 7.5 Hz, 1H), 4.90 (dt, J = 17.7, 12.9 Hz, 2H), 1.21 – 1.15 (m, 9H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.2, 156.7, 153.2, 143.0, 142.9, 137.0, 135.2, 134.1, 131.0, 129.0, 128.1, 127.7, 124.3, 124.2, 123.7, 123.0, 123.0, 120.5, 118.3, 115.2, 109.8, 104.7, 85.5, 59.4, 44.2, 34.9, 31.0.

HRMS (ESI, m/z) Calcd. for $C_{31}H_{26}N_2NaO_3^+$, $[M+Na]^+$: 497.1836, found: 497.1832.

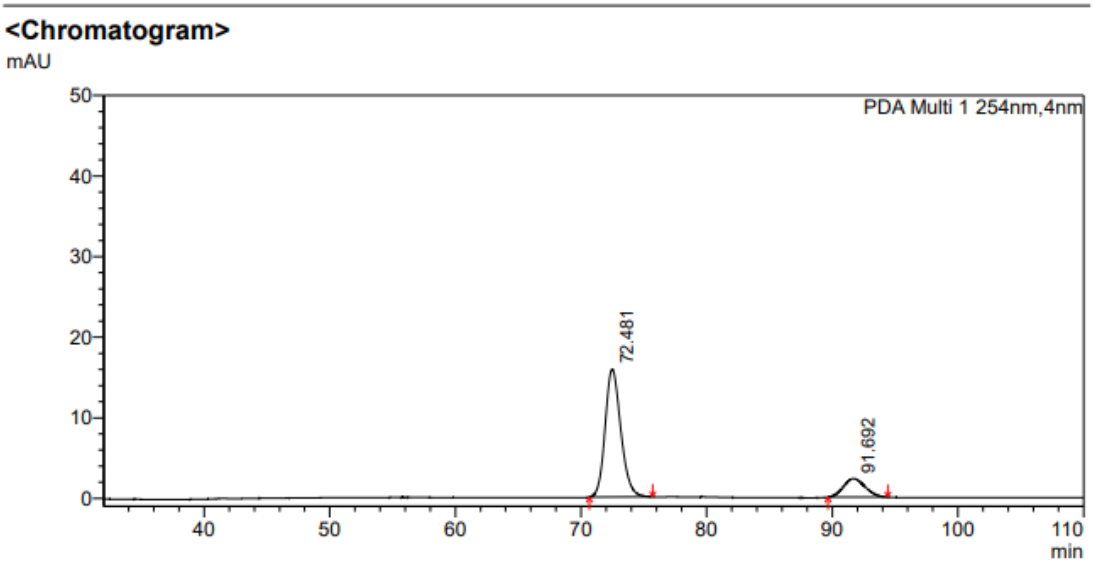
<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	41.404	236883	4683	4.917
2	72.369	2181271	25275	45.279
3	76.971	230668	2577	4.788
4	90.634	2168552	16672	45.015
Total		4817373	49208	100.000

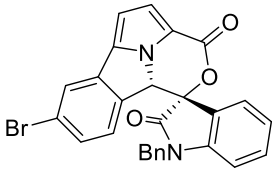


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	72.481	1379417	15871	83.350
2	91.692	275557	2295	16.650
Total		1654974	18166	100.000

(1S,9bS)-1'-benzyl-7-bromospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3g)



3g

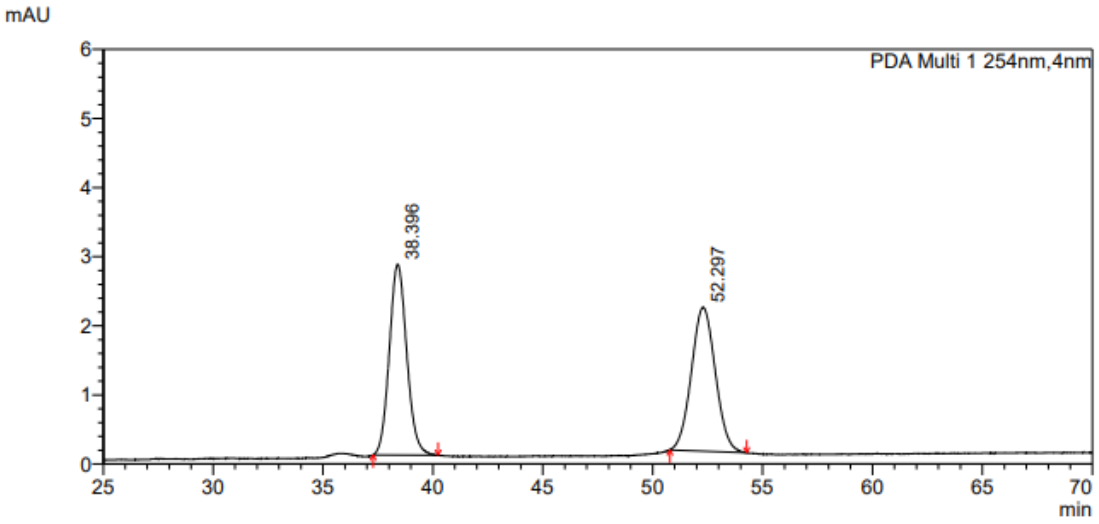
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3g** as a yellow solid in 35% yield (17.3 mg), m.p. 242-244 °C; **[α]^{25}D** = -27.724 (c = 0.25, $CHCl_3$); 10:1 dr; 96:4 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 52.87 min (minor), t_R = 38.66 min(major)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.57 (d, J = 1.7 Hz, 1H), 7.35-7.29 (m, 5H), 7.09 (d, J = 3.9 Hz, 1H), 7.06 (td, J = 7.8, 1.2 Hz, 1H), 6.98 (dd, J = 8.1, 1.8 Hz, 1H), 6.73 (d, J = 7.9 Hz, 1H), 6.60 – 6.55 (m, 2H), 6.50 (d, J = 8.2 Hz, 1H), 5.70 (s, 1H), 5.17 – 5.13 (m, 1H), 4.97 (d, J = 15.4 Hz, 1H), 4.84 (d, J = 15.4 Hz, 1H).

^{13}C NMR(101 MHz, CD_2Cl_2) δ 168.9, 156.4, 142.6, 141.1, 138.6, 136.0, 135.2, 131.3, 129.8, 129.0, 128.3, 127.9, 124.7, 124.2, 124.0, 123.8, 123.6, 122.5, 120.7, 115.8, 109.9, 105.8, 85.2, 59.4, 44.3.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}BrN_2NaO_3^+$, $[M+Na]^+$: 519.0315, found: 519.0303.

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	38.396	152511	2761	49.124
2	52.297	157951	2082	50.876
Total		310462	4843	100.000

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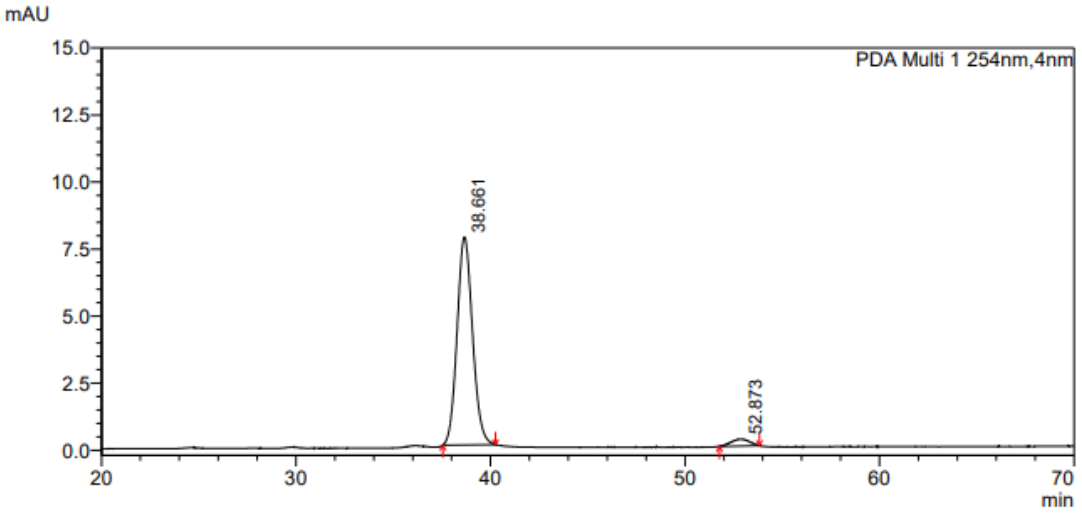
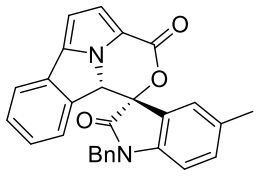


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	38.661	428427	7753	96.243
2	52.873	16722	254	3.757
Total		445149	8007	100.000

(1S,9bS)-1'-benzyl-5'-methylspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3h)



3h

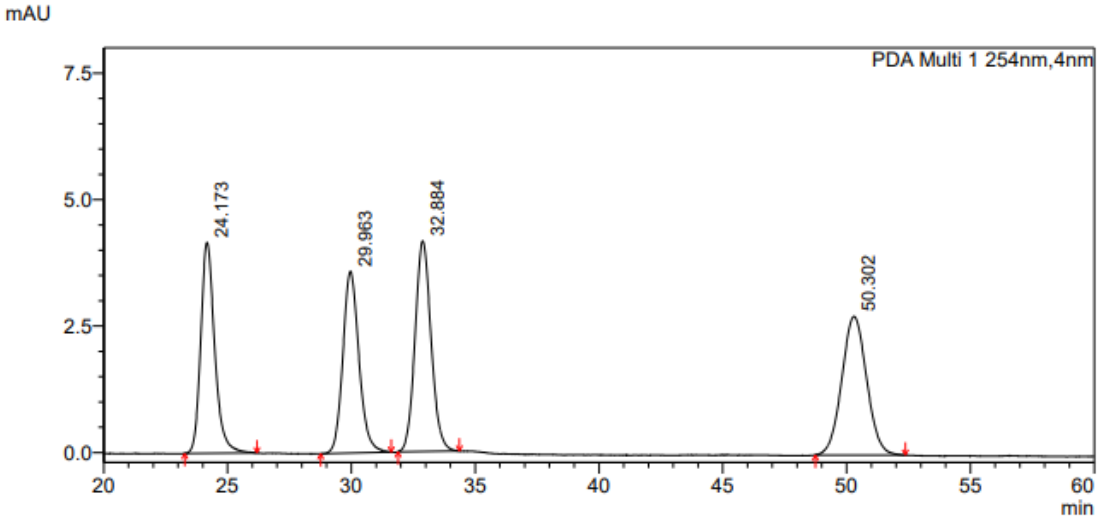
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3h** as a yellow solid in 93% yield (40.3 mg), m.p. 115-117 °C; **$[\alpha]^{25}D$** = -140.217 (c = 0.5, $CHCl_3$); >20:1 dr; 92:8 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 49.43 min (minor), t_R = 32.33 min(major)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.58 (d, J = 7.7 Hz, 1H), 7.48 – 7.36 (m, 5H), 7.32 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 3.9 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 6.74 – 6.65 (m, 2H), 5.85 (s, 1H), 5.02 (dd, J = 45.2, 15.5 Hz, 3H), 1.94 (d, J = 19.8 Hz, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.1, 156.8, 142.7, 140.3, 139.9, 135.3, 134.2, 133.5, 131.2, 129.4, 128.9, 128.1, 127.8, 127.1, 124.9, 123.5, 122.8, 121.0, 120.6, 115.4, 109.5, 104.9, 85.7, 59.6, 44.2, 20.5.

HRMS (ESI, m/z) Calcd. for $C_{28}H_{20}N_2NaO_3^+$, $[M+Na]^+$: 455.1366, found: 455.1362.

<Chromatogram>

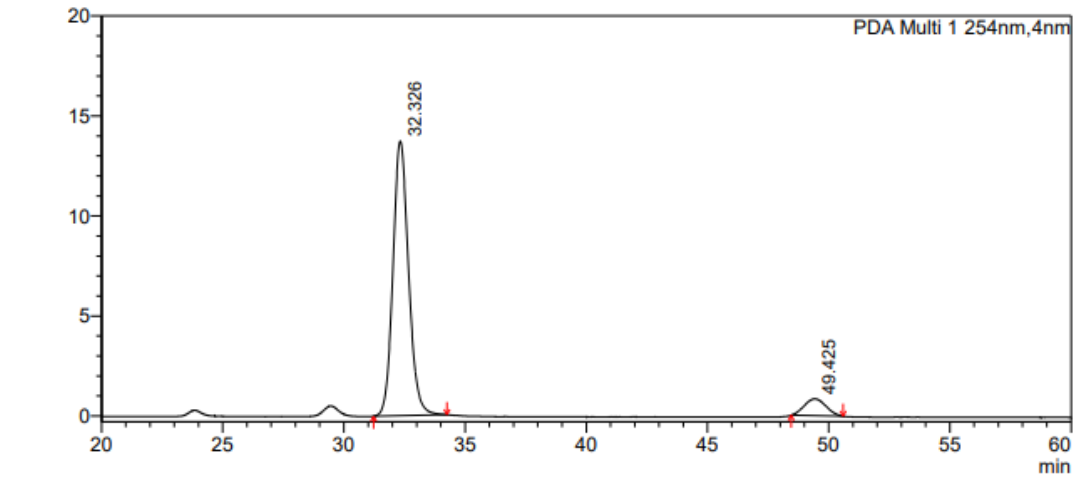


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	24.173	164001	4171	23.219
2	29.963	162923	3593	23.067
3	32.884	187659	4162	26.569
4	50.302	191729	2742	27.145
Total		706312	14668	100.000

<Chromatogram>

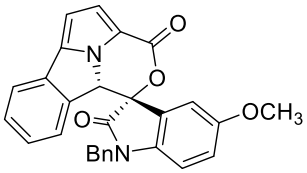


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	32.326	614278	13730	92.169
2	49.425	52194	838	7.831
Total		666472	14568	100.000

(1S,9bS)-1'-benzyl-5'-methoxyspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3i)



3i

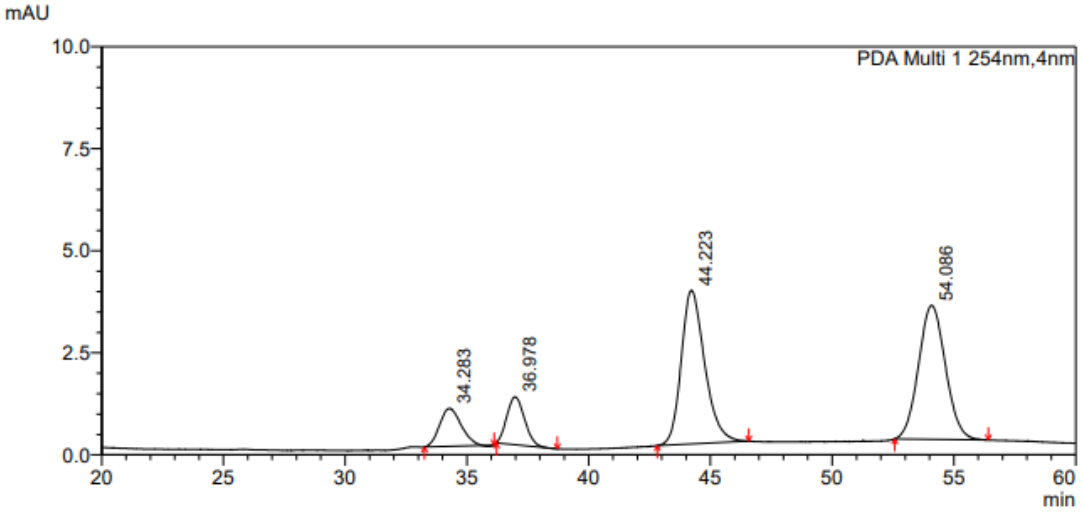
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3i** as a white solid in 96% yield (43.4 mg), m.p. 128-130 °C; **[α]^{25}D** = -119.161 (c = 0.25, $CHCl_3$); 4:1 dr; 88:12 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 54.03 min (minor), t_R = 44.11 min(major);

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.59 (d, J = 7.7 Hz, 1H), 7.48 – 7.38 (m, 5H), 7.34 (t, J = 7.6 Hz, 1H), 7.23 (d, J = 3.9 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.87 (d, J = 7.6 Hz, 1H), 6.73 – 6.61 (m, 3H), 5.87 (s, 1H), 5.14 – 4.92 (m, 2H), 4.84 (d, J = 2.4 Hz, 1H), 3.45 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 156.9, 156.3, 143.0, 139.9, 135.8, 134.9, 134.1, 129.6, 129.0, 128.2, 127.7, 127.2, 123.7, 123.6, 121.0, 120.9, 115.8, 115.6, 110.9, 110.4, 104.9, 85.8, 59.6, 55.5, 44.4.

HRMS (ESI, m/z) Calcd. for $C_{28}H_{20}N_2NaO_4^+$, $[M+Na]^+$: 471.1315, found: 471.1303.

<Chromatogram>

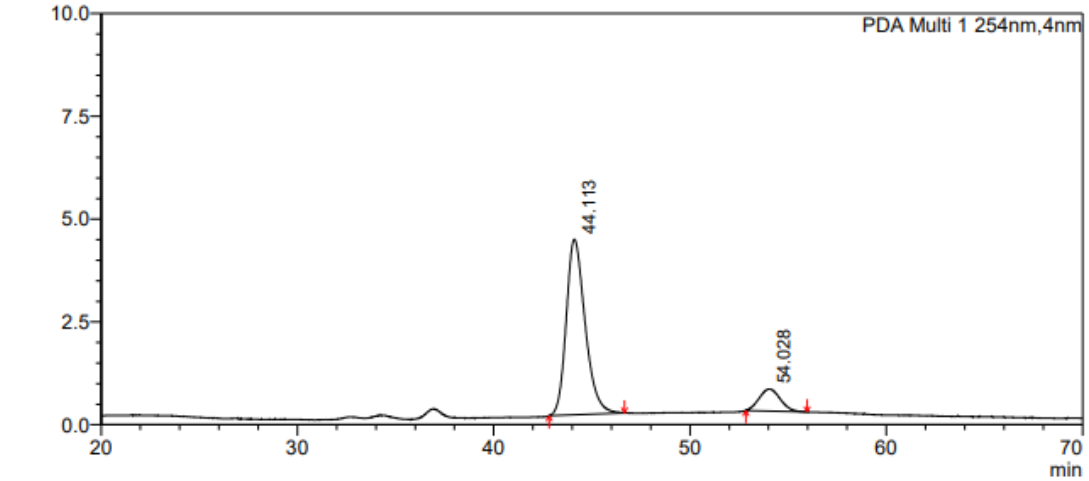


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	34.283	56199	923	9.048
2	36.978	59452	1172	9.571
3	44.223	252745	3761	40.691
4	54.086	252741	3283	40.690
Total		621137	9140	100.000

<Chromatogram>

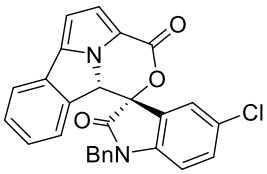


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	44.113	286105	4267	87.735
2	54.028	39997	538	12.265
Total		326102	4805	100.000

(1S,9bS)-1'-benzyl-5'-chlorospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3j)



3j

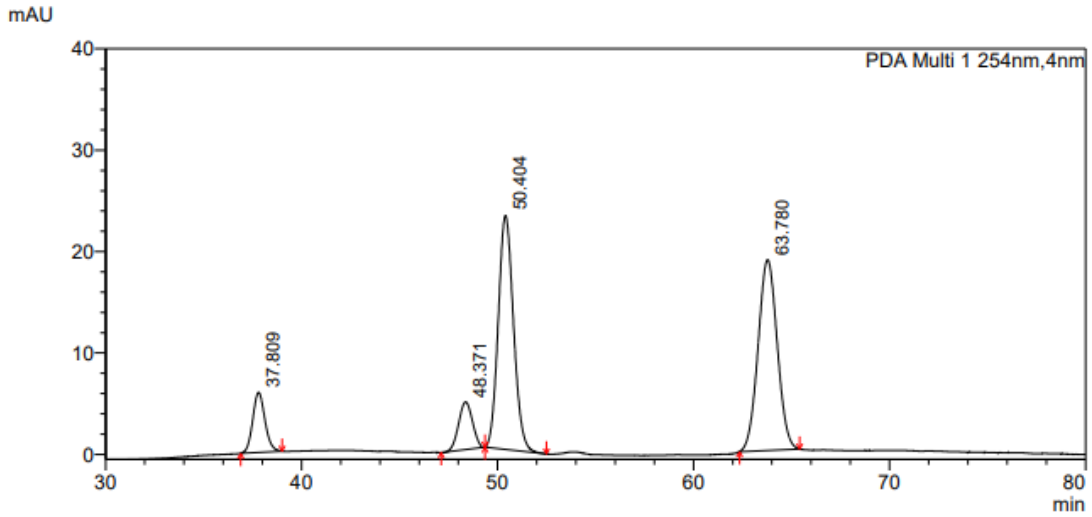
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3j** as a yellow solid in 68% yield (34.0 mg), m.p. 225-227 °C; **[α]^{25}D** = -108.215 (c = 0.2, $CHCl_3$); 7:1 dr; 85:15 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 70/30, 0.4 mL/min), t_R = 64.27 min(minor), t_R = 50.87min(major);

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.61 (d, *J* = 7.7 Hz, 1H), 7.47 – 7.38 (m, 5H), 7.36 (dd, *J* = 13.1, 5.5 Hz, 1H), 7.24 (d, *J* = 3.9 Hz, 1H), 7.11 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.04 (td, *J* = 7.6, 0.8 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.73 (dd, *J* = 10.2, 6.2 Hz, 2H), 5.85 (s, 1H), 5.19 (d, *J* = 2.1 Hz, 1H), 5.03 (dd, *J* = 44.5, 15.5 Hz, 2H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 168.7, 156.2, 142.9, 141.4, 139.4, 134.7, 134.0, 130.9, 129.7, 129.0, 128.9, 128.3, 127.8, 127.3, 124.6, 124.4, 123.5, 121.2, 121.0, 115.1, 110.9, 105.2, 85.2, 59.5, 44.4.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}ClN_2NaO_3^+$, $[M+Na]^+$: 475.0820, found: 475.0817

<Chromatogram>

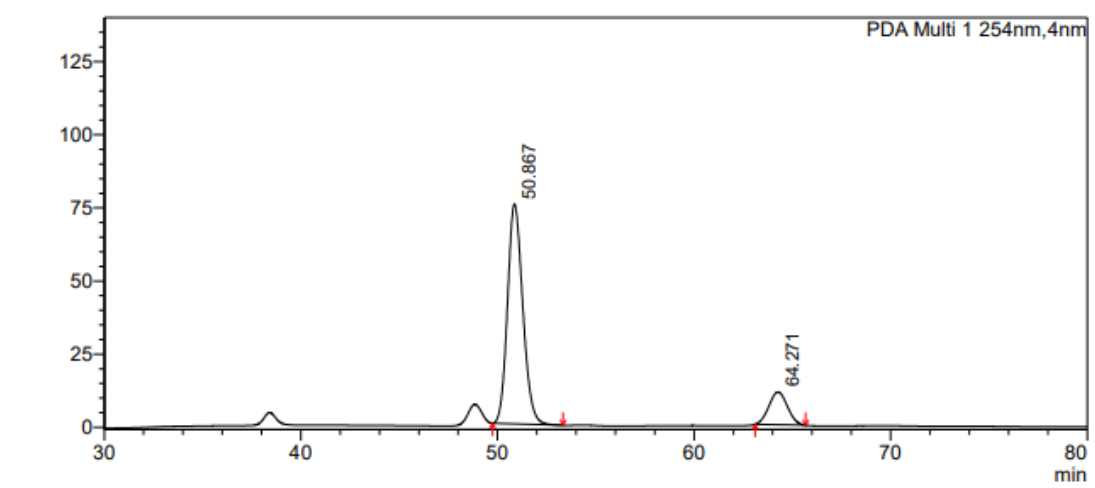


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	37.809	257203	5910	8.538
2	48.371	229942	4692	7.633
3	50.404	1246006	23070	41.360
4	63.780	1279464	18815	42.470
Total		3012615	52486	100.000

<Chromatogram>

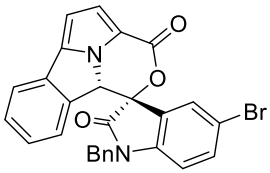


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	50.867	4070128	75210	84.764
2	64.271	731583	11175	15.236
Total		4801711	86385	100.000

(1S,9bS)-1'-benzyl-5'-bromospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3k)



3k

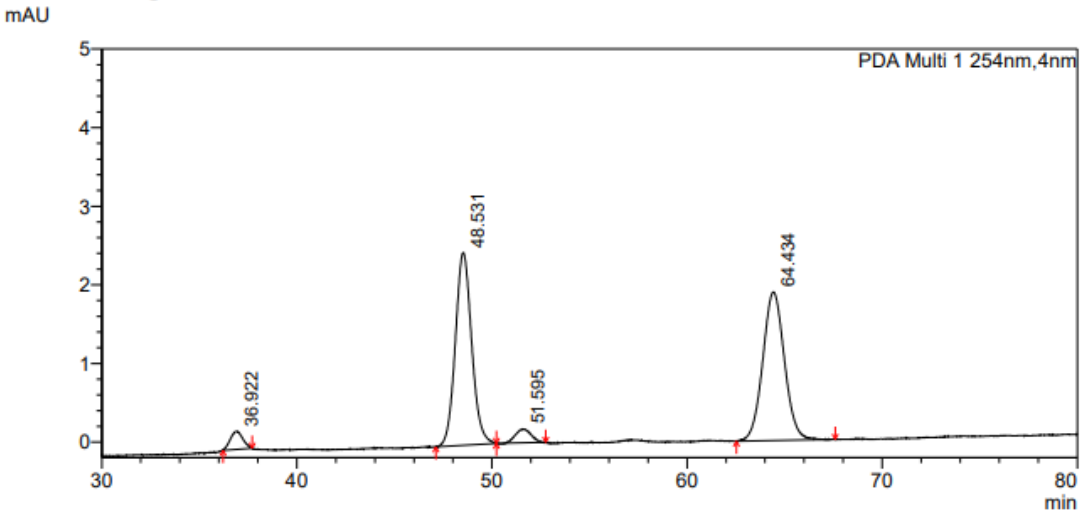
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3k** as a yellow solid in 71% yield (35.2 mg), m.p. 206-208 °C; **[α]^{25}D** = -32.239 (c = 0.2, $CHCl_3$); 6:1 dr; 90:10 er; determined by HPLC on a Chiralpak IF column at 254 nm(n-hexane/2-propanol = 60/40, 0.4 mL/min), t_R = 66.01 min(minor), t_R = 49.45 min(major);

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.61 (d, J = 7.7 Hz, 1H), 7.48 – 7.38 (m, 5H), 7.35 (t, J = 7.6 Hz, 1H), 7.29 – 7.22 (m, 2H), 7.04 (dd, J = 8.3, 7.6 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 6.74 – 6.67 (m, 2H), 5.84 (s, 1H), 5.31 (d, J = 1.9 Hz, 1H), 5.03 (dd, J = 45.6, 15.5 Hz, 2H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 168.6, 156.2, 143.0, 141.8, 139.4, 134.7, 134.0, 133.9, 129.7, 129.0, 128.3, 127.8, 127.4, 127.3, 124.8, 123.5, 121.2, 121.0, 116.2, 115.1, 111.4, 105.1, 85.2, 59.5, 44.4.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}BrN_2NaO_3^+$, $[M+Na]^+$: 519.0315; found: 519.0308.

<Chromatogram>

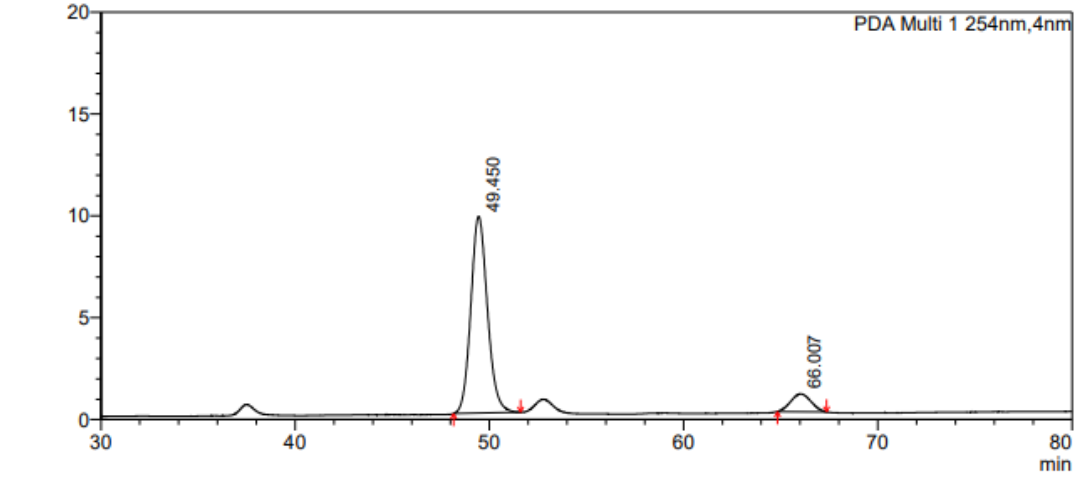


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	36.922	10164	228	3.293
2	48.531	142732	2452	46.247
3	51.595	9767	177	3.165
4	64.434	145966	1887	47.295
Total		308630	4744	100.000

<Chromatogram>

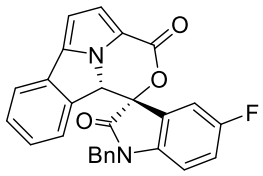


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	49.450	576568	9668	90.104
2	66.007	63325	873	9.896
Total		639893	10541	100.000

(1S,9bS)-1'-benzyl-5'-fluorospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3l)



3l

The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3l** as a yellow solid in 66% yield (28.7 mg), m.p. 230-232 °C; **$[\alpha]^{25}D$** = 64.911 (c = 0.25, $CHCl_3$); 9:1 dr; 84:16 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 49.44 min (minor), t_R = 36.05 min(major);

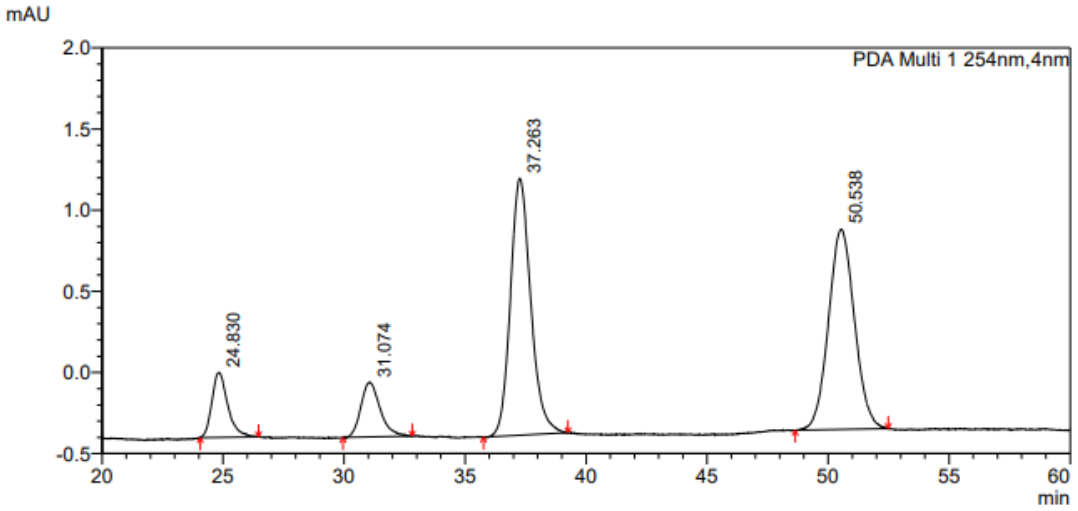
^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.59 (t, *J* = 6.5 Hz, 1H), 7.47 – 7.38 (m, 5H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 3.9 Hz, 1H), 7.04 (td, *J* = 7.6, 1.0 Hz, 1H), 6.90 – 6.80 (m, 2H), 6.77 – 6.69 (m, 2H), 5.87 (s, 1H), 5.12 – 4.94 (m, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.4, 164.3 (d, *J* = 250.5 Hz), 156.4, 144.7 (d, *J* = 12.1 Hz), 142.8, 139.7, 134.7, 134.1, 129.1, 128.4 (d, *J* = 240.4 Hz), 127.8, 127.2, 125.8 (d, *J* = 10.1 Hz), 123.5, 121.0, 120.8, 118.5 (d, *J* = 3.0 Hz), 115.24, 109.8 (d, *J* = 22.2 Hz), 105.1, 99.0, 98.7, 85.0, 59.6, 44.5.

^{19}F NMR (377 MHz, CD_2Cl_2) δ -107.14.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}FN_2NaO_3^+$, $[M+Na]^+$: 459.1115, found: 459.1108.

<Chromatogram>

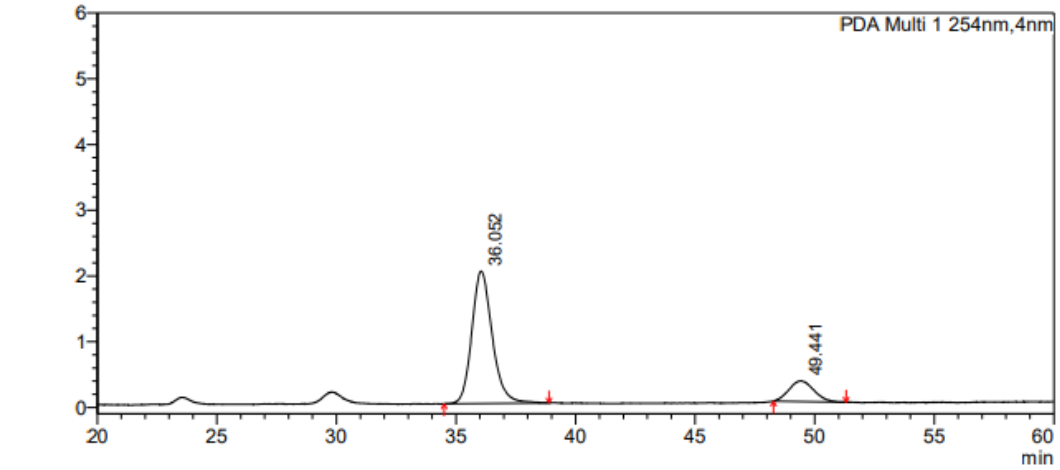


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	24.830	18270	399	8.251
2	31.074	18565	336	8.384
3	37.263	92469	1583	41.761
4	50.538	92119	1234	41.603
Total		221423	3552	100.000

<Chromatogram>

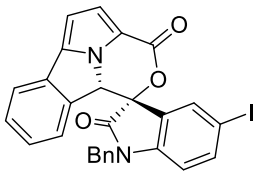


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	36.052	119733	2011	84.057
2	49.441	22709	314	15.943
Total		142442	2325	100.000

(1S,9bS)-1'-benzyl-5'-iodospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3m)



3m

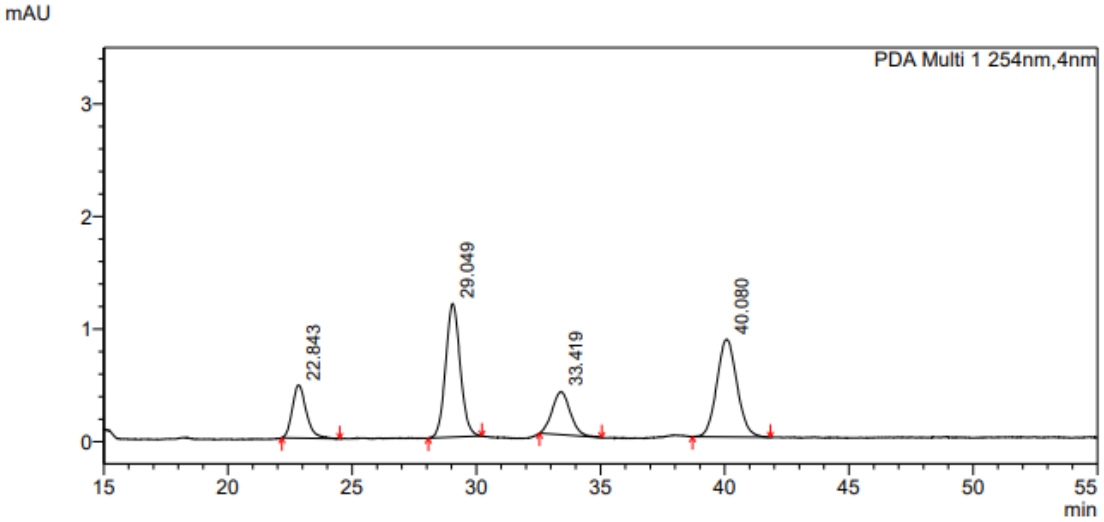
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3m** as a white solid in 58% yield (31.6 mg), m.p. 180–182 °C; **[α]^{25}D** = -175.209 (c = 0.25, $CHCl_3$); 5:1 dr; 82:18 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 40.15 min (minor), t_R = 29.07 min (major);

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.48 (d, J = 7.7 Hz, 1H), 7.39 – 7.25 (m, 6H), 7.22 (t, J = 7.6 Hz, 1H), 7.11 (d, J = 3.9 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 6.70 (d, J = 7.6 Hz, 1H), 6.60 (d, J = 3.9 Hz, 1H), 6.48 (dd, J = 11.7, 6.1 Hz, 1H), 5.69 (s, 1H), 5.31 (t, J = 8.7 Hz, 1H), 5.01 – 4.77 (m, 2H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 168.5, 156.4, 143.1, 142.4, 139.8, 139.4, 134.6, 134.1, 133.1, 129.8, 129.1, 128.3, 127.8, 127.3, 125.0, 123.5, 121.2, 121.1, 115.2, 111.8, 105.1, 86.2, 85.3, 59.5, 44.4.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}IN_2NaO_3^+$, $[M+Na]^+$: 567.0176, found: 567.0162.

<Chromatogram>

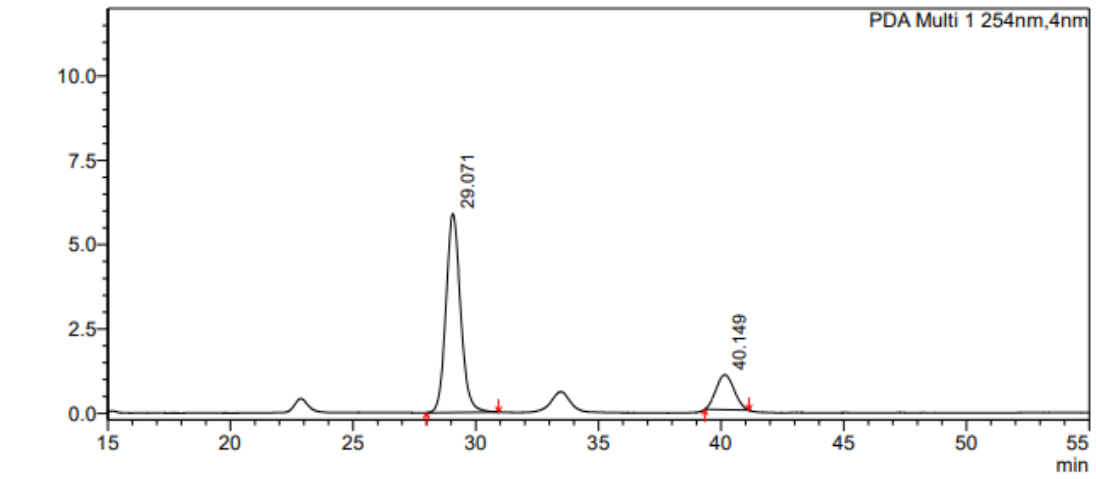


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	22.843	18278	470	13.534
2	29.049	48472	1187	35.890
3	33.419	19289	381	14.282
4	40.080	49019	866	36.295
Total		135058	2904	100.000

<Chromatogram>

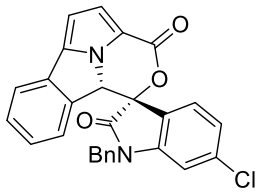


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	29.071	244170	5893	82.115
2	40.149	53180	1037	17.885
Total		297350	6930	100.000

(1S,9bS)-1'-benzyl-6'-chlorospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione (3n)



3n

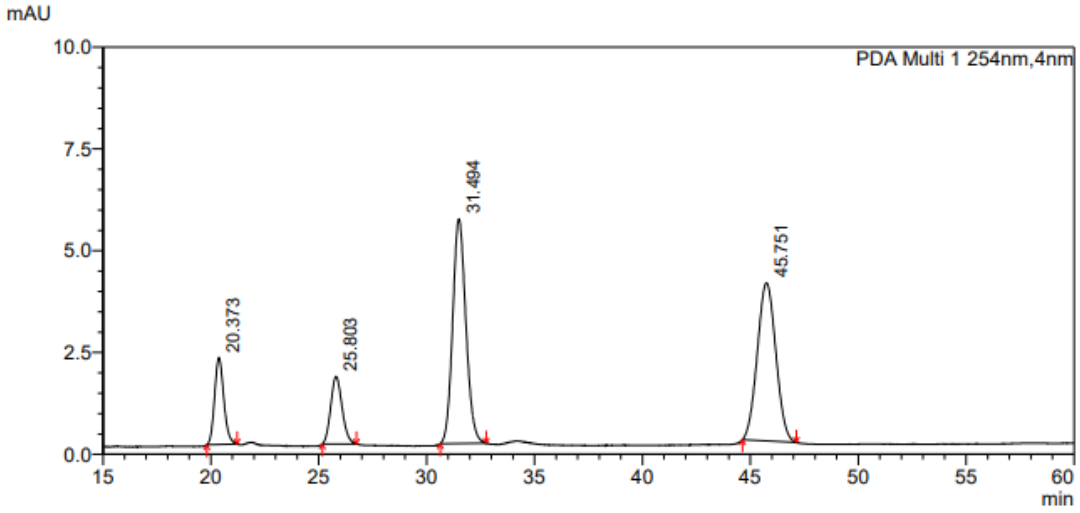
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3n** as a white solid in 71% yield (32.2 mg), m.p. 228-230 °C; **[α]^{25}D** = -123.626 (c = 0.5, $CHCl_3$); 10:1 dr; 96:4 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 45.85 min (minor), t_R = 31.14 min(major)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.44 (d, J = 7.7 Hz, 1H), 7.35 – 7.28 (m, 4H), 7.21 (t, J = 7.6 Hz, 1H), 7.07 (t, J = 7.6 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 6.69 (dd, J = 7.9, 4.7 Hz, 2H), 6.57 – 6.48 (m, 2H), 5.72 (s, 1H), 5.05 (d, J = 8.1 Hz, 1H), 4.89 (dd, J = 47.0, 15.5 Hz, 2H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.1, 156.4, 144.1, 142.9, 139.5, 137.0, 134.7, 134.0, 129.7, 129.1, 128.4, 127.8, 127.3, 125.3, 123.6, 123.5, 121.3, 121.1, 120.9, 115.2, 110.5, 105.2, 84.9, 59.5, 44.4.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}ClN_2NaO_3^+$, $[M+Na]^+$: 475.0820, found: 475.0820.

<Chromatogram>

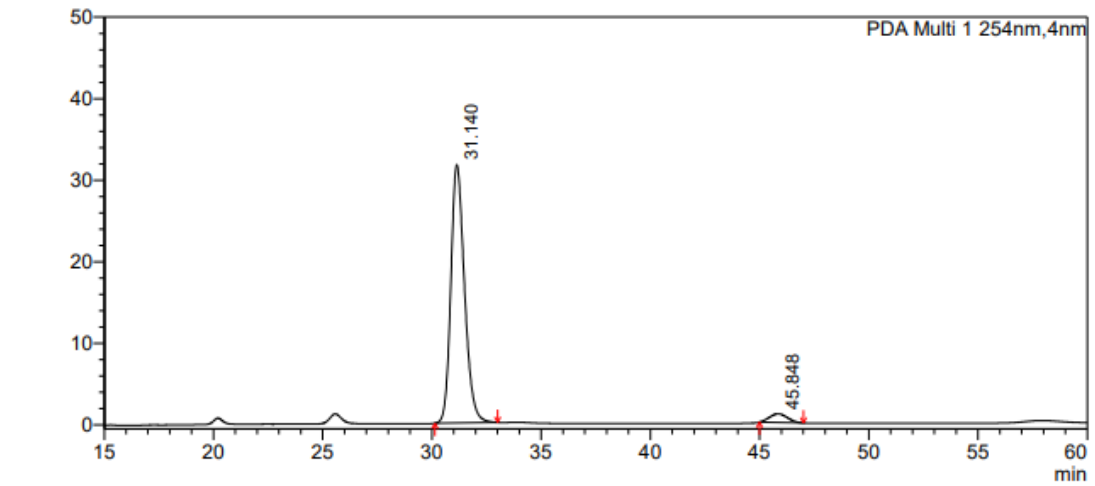


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	20.373	63547	2135	10.752
2	25.803	60662	1651	10.264
3	31.494	234854	5516	39.736
4	45.751	231976	3884	39.249
Total		591039	13186	100.000

<Chromatogram>

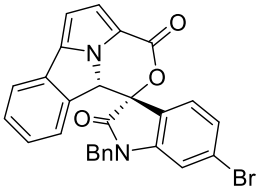


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	31.140	1376695	31648	95.846
2	45.848	59670	1049	4.154
Total		1436364	32697	100.000

(1S,9bS)-1'-benzyl-6'-bromospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3o)



3o

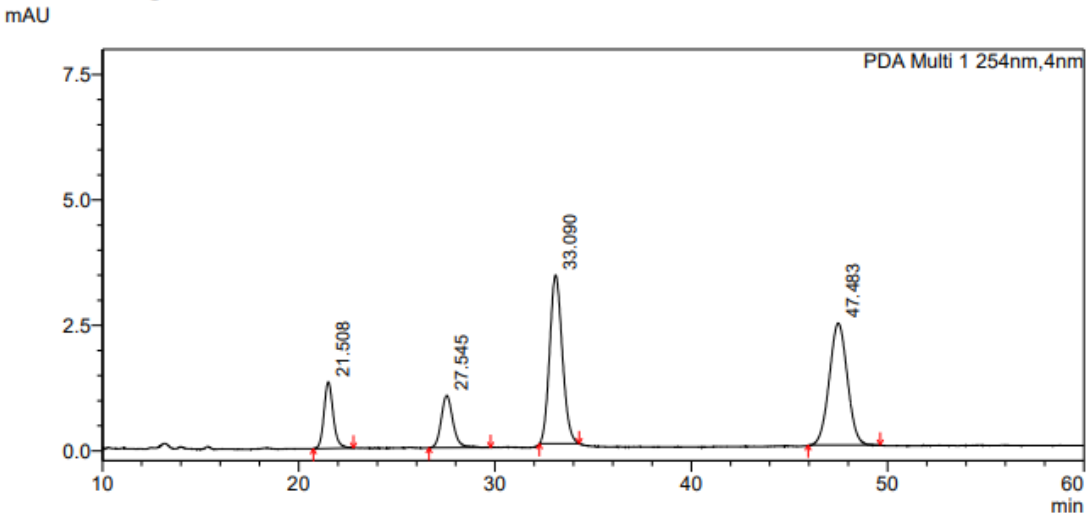
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3o** as a yellow solid in 65% yield (32.1 mg), m.p. 204–206 °C; **[α]^{25}D** = -120.960 (c = 0.5, $CHCl_3$); 16:1 dr; 87:13 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 47.03 min (minor), t_R = 32.84 min(major) ;

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.45 (d, J = 7.7 Hz, 1H), 7.37 – 7.27 (m, 5H), 7.25 – 7.19 (m, 1H), 7.09 (t, J = 5.9 Hz, 1H), 6.95 – 6.89 (m, 1H), 6.84 (d, J = 1.6 Hz, 1H), 6.74 – 6.66 (m, 2H), 6.54 (d, J = 3.9 Hz, 1H), 5.72 (s, 1H), 4.99 (d, J = 8.1 Hz, 1H), 4.89 (dd, J = 46.7, 15.5 Hz, 2H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.0, 156.3, 144.1, 142.9, 139.5, 134.7, 134.1, 129.7, 129.1, 128.3, 127.7, 127.3, 126.6, 125.5, 125.0, 123.5, 121.8, 121.1, 120.9, 115.2, 113.3, 105.2, 85.0, 59.4, 44.4.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}BrN_2NaO_3^+$, [M+Na] $^+$: 519.0315, found: 519.0313.

<Chromatogram>

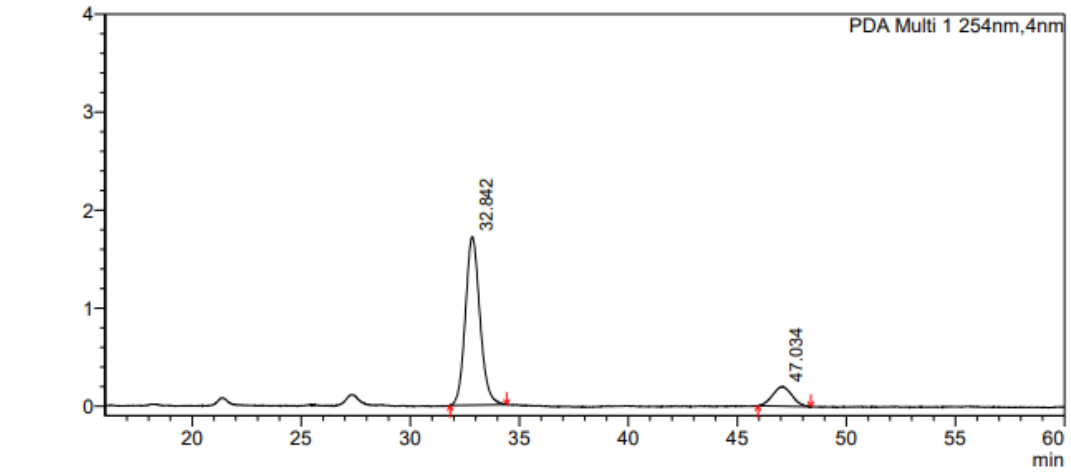


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	21.508	43255	1323	11.028
2	27.545	43224	1040	11.020
3	33.090	150836	3360	38.455
4	47.483	154925	2426	39.497
Total		392241	8149	100.000

<Chromatogram>

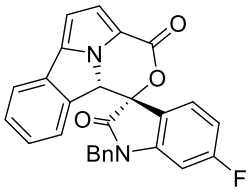


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	32.842	79816	1719	86.824
2	47.034	12112	198	13.176
Total		91928	1917	100.000

(1S,9bS)-1'-benzyl-6'-fluorospiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3p)



3p

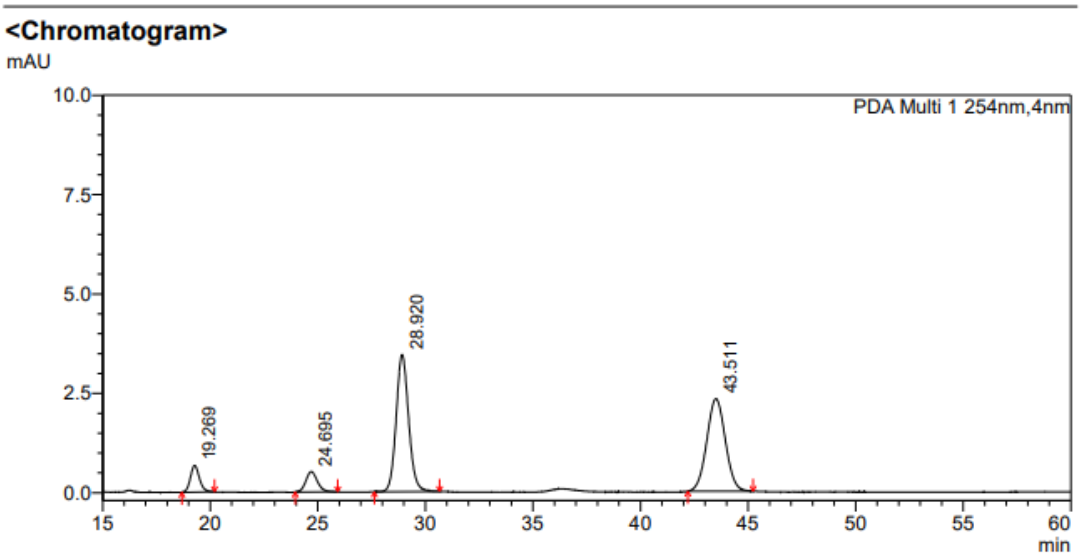
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3p** as a yellow solid in 48% yield (20.9 mg), m.p. 208-210 °C; **[α]^{25}D** = 18.325 (c = 0.2, $CHCl_3$); 3:1 dr; 92:8 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 43.55 min (minor), t_R = 28.90 min(major) ;

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.45 (d, J = 7.7 Hz, 1H), 7.34 – 7.27 (m, 5H), 7.24 – 7.18 (m, 1H), 7.09 (d, J = 3.9 Hz, 1H), 6.94 – 6.88 (m, 1H), 6.72 (dd, J = 7.7, 0.8 Hz, 1H), 6.54 (t, J = 4.0 Hz, 1H), 6.42 (dd, J = 8.8, 2.3 Hz, 1H), 6.26 – 6.19 (m, 1H), 5.73 (s, 1H), 5.10 (dd, J = 8.4, 5.3 Hz, 1H), 4.98 – 4.79 (m, 2H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 168.9, 159.1 (d, J = 243.4 Hz), 156.2, 142.9, 139.5, 138.8, 134.9, 134.1, 129.0, 128.5(d, J = 246.4 Hz), 128.3, 127.8, 124.2 (d, J = 9.1 Hz), 123.5, 121.2, 120.9, 117.4 (d, J = 23.2 Hz), 115.1, 112.5, 112.2, 110.7 (d, J = 8.1 Hz), 105.2, 85.3 (d, J = 1.2 Hz), 59.5, 44.4.

^{19}F NMR (377 MHz, $CDCl_3$) δ -117.82.

HRMS (ESI, m/z) Calcd. for $C_{27}H_{17}FN_2NaO_3^+$, $[M+Na]^+$: 459.1115, found: 459.1106.

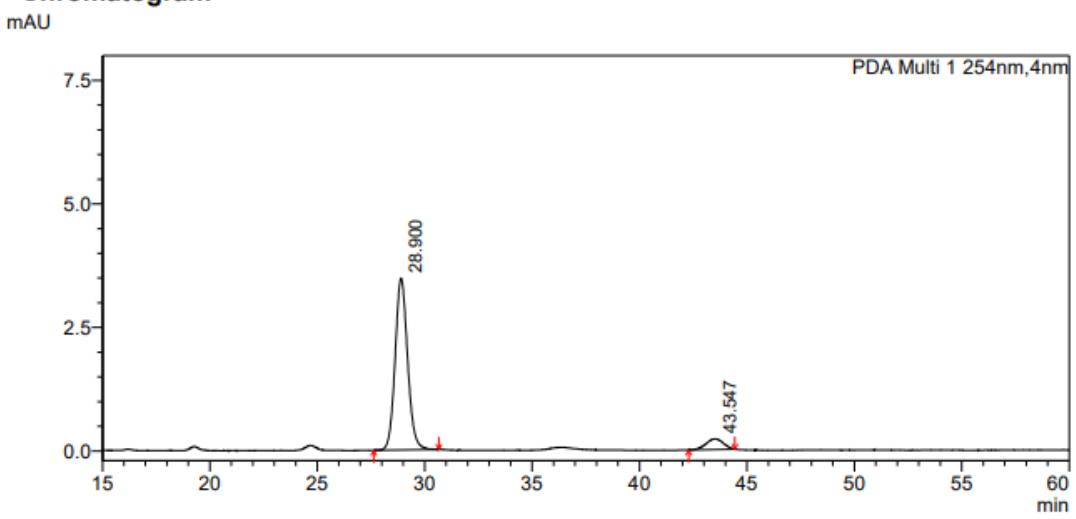


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	19.269	19448	668	6.128
2	24.695	18955	511	5.973
3	28.920	139235	3444	43.874
4	43.511	139716	2325	44.025
Total		317354	6948	100.000

<Chromatogram>

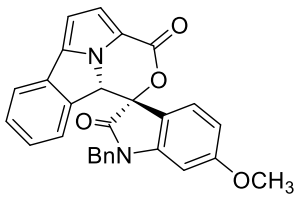


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	28.900	140575	3474	92.115
2	43.547	12033	215	7.885
Total		152608	3689	100.000

(1S,9bS)-1'-benzyl-6'-methoxyspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3q)



3q

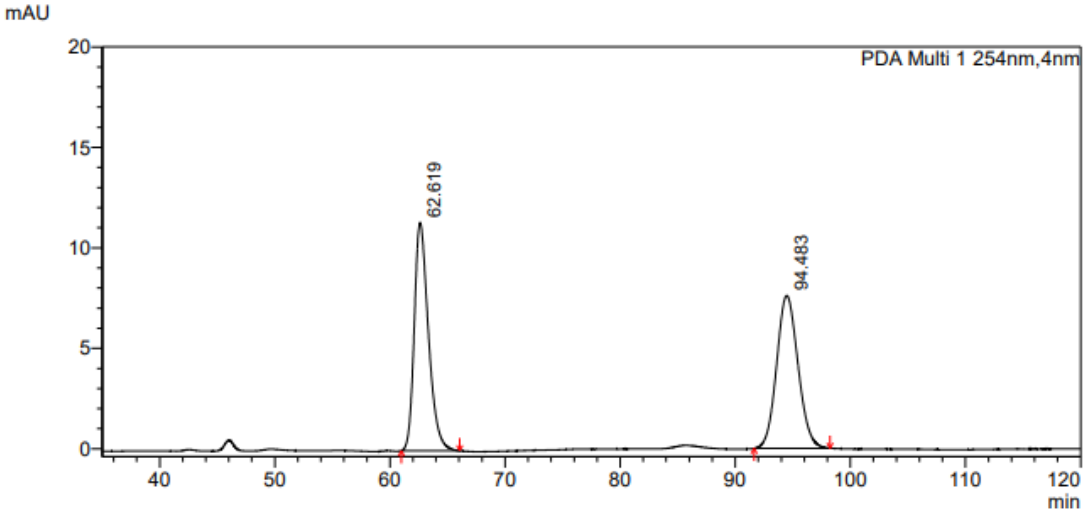
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3q** as a yellow solid in 88% yield (39.7 mg), m.p. 210-212 °C; **[α]^{25}D** = -113.063 (c = 0.5, $CHCl_3$); 6:1 dr; 86:14 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.5 mL/min), t_R = 93.18 min(minor), t_R = 61.40 min(major) ;

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.43 (d, J = 7.7 Hz, 1H), 7.35 – 7.23 (m, 5H), 7.19 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 5.0 Hz, 1H), 6.89 (dd, J = 11.0, 4.2 Hz, 1H), 6.70 (t, J = 10.4 Hz, 1H), 6.52 (d, J = 3.9 Hz, 1H), 6.21 (t, J = 7.8 Hz, 1H), 5.98 (dt, J = 24.8, 12.4 Hz, 1H), 5.71 (s, 1H), 5.07 (d, J = 8.4 Hz, 1H), 4.89 (dt, J = 34.4, 14.7 Hz, 2H), 3.47 (s, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.7, 162.1, 157.0, 144.4, 142.7, 140.1, 135.2, 134.2, 129.5, 129.0, 128.2, 127.8, 127.2, 125.3, 123.6, 121.0, 120.6, 115.5, 114.5, 107.0, 105.0, 98.0, 85.6, 59.8, 55.4, 44.3.

HRMS (ESI, m/z) Calcd. for $C_{28}H_{20}N_2NaO_4^+$, [M+Na] $^+$: 471.1315, found: 471.1310.

<Chromatogram>

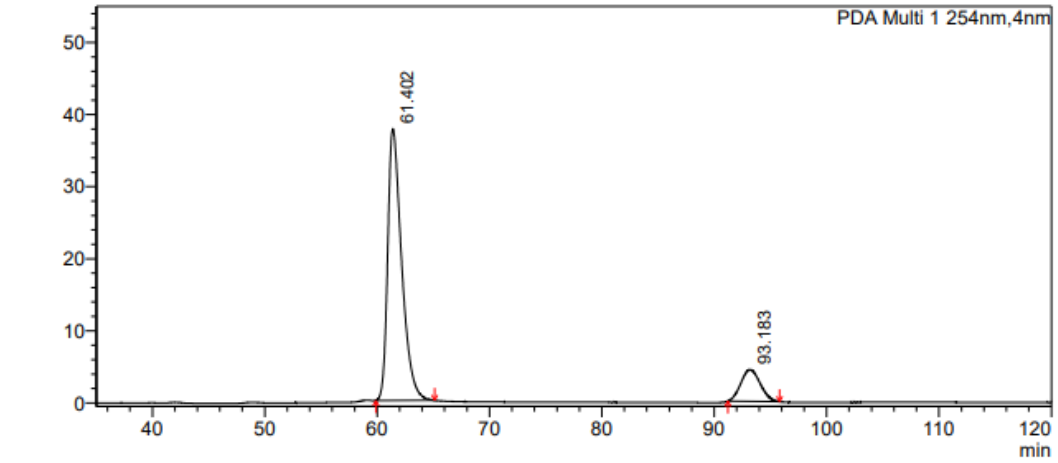


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	62.619	970314	11361	49.668
2	94.483	983294	7600	50.332
Total		1953608	18960	100.000

<Chromatogram>

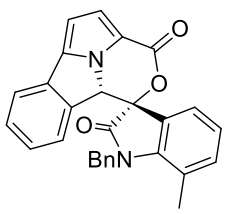


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	61.402	3240730	37692	86.045
2	93.183	525605	4399	13.955
Total		3766335	42091	100.000

(1S,9bS)-1'-benzyl-7'-methylspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3r)



3r

The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3r** as a yellow solid in 76% yield (33.2 mg), m.p. 242-244 °C; **[α]^{25}D** = -113.696 (c = 0.25, $CHCl_3$); 16:1 dr; 89:11 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 67.43 min (minor), t_R = 52.88 min(major);

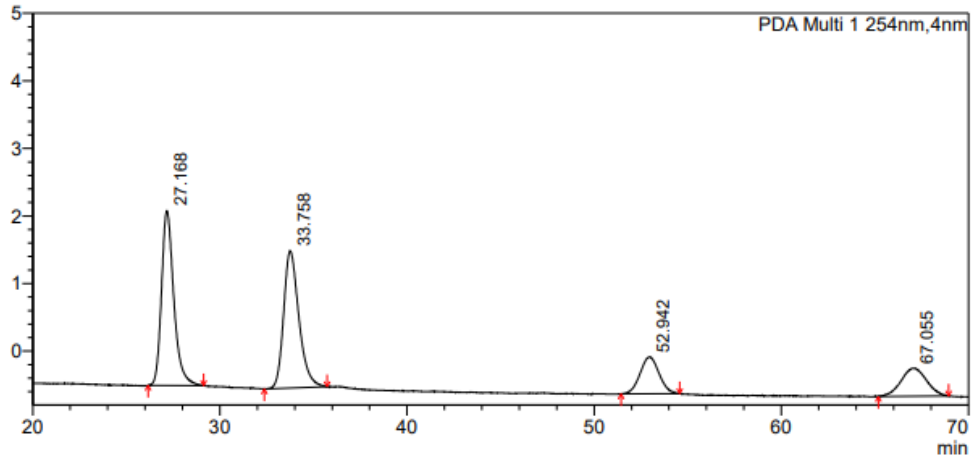
^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.49 (d, J = 7.7 Hz, 1H), 7.36 – 7.22 (m, 4H), 7.18 (d, J = 7.1 Hz, 2H), 7.09 (d, J = 3.9 Hz, 1H), 7.03 (m, 1H), 6.91 (dd, J = 7.6, 0.7 Hz, 1H), 6.79 (d, J = 7.6 Hz, 1H), 6.57 (d, J = 3.9 Hz, 1H), 6.48 (t, J = 7.7 Hz, 1H), 5.78 (s, 1H), 5.28 (d, J = 16.8 Hz, 1H), 5.14 (d, J = 16.8 Hz, 1H), 4.96 (d, J = 7.1 Hz, 1H), 2.13 (s, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 170.3, 156.7, 142.6, 141.0, 140.0, 136.8, 135.2, 134.2, 129.5, 129.0, 127.7, 127.1, 125.9, 123.8, 123.8, 123.4, 121.9, 121.0, 121.0, 120.6, 115.4, 105.1, 84.9, 59.5, 45.6, 18.6.

HRMS (ESI, m/z) Calcd. for $C_{28}H_2N_2NaO_3^+$, $[M+Na]^+$: 455.1366, found: 455.1361.

<Chromatogram>

mAU



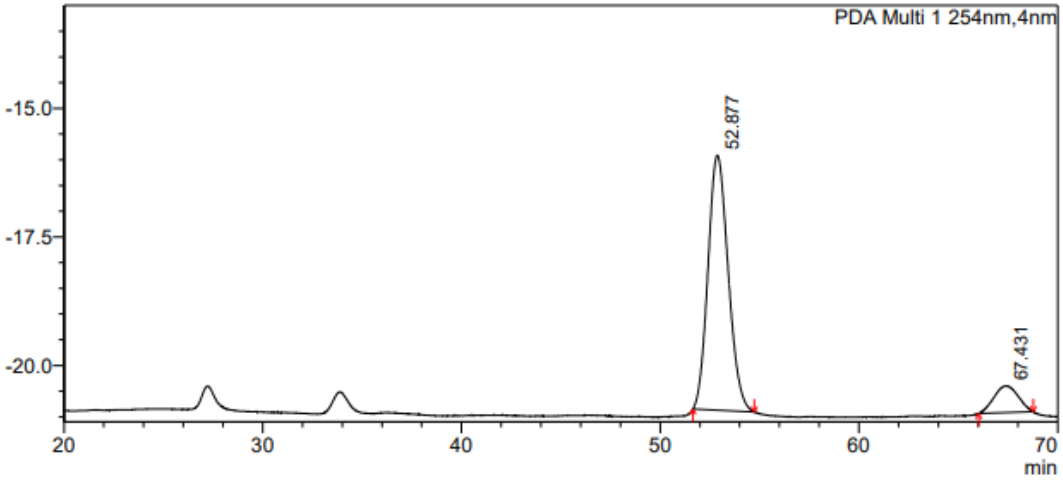
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	27.168	118345	2588	38.053
2	33.758	115210	2026	37.045
3	52.942	38494	545	12.378
4	67.055	38951	414	12.524
Total		310999	5573	100.000

<Chromatogram>

mAU

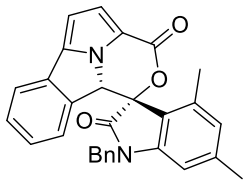


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	52.877	350185	4957	88.785
2	67.431	44233	518	11.215
Total		394418	5475	100.000

(1S,9bS)-1'-benzyl-4',6'-dimethylspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione(3s)



3s

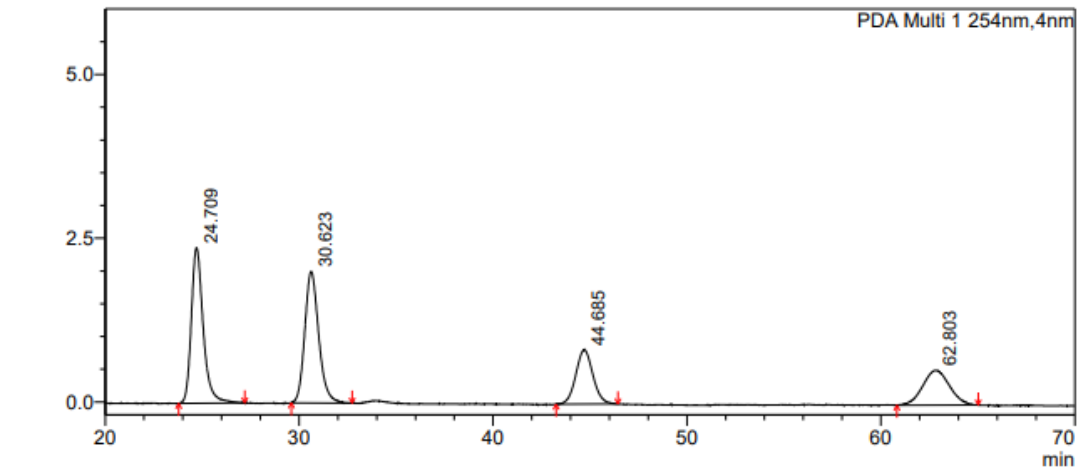
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3s** as a yellow solid in 82% yield (36.5 mg), m.p. 176–178 °C; **[α]^{25}D** = -180.272 (c = 0.2, $CHCl_3$); >20:1 dr; 97:3 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 62.82 min (minor), t_R = 44.61 min(major);

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.48 (d, J = 7.7 Hz, 1H), 7.32 – 7.21 (m, 4H), 7.16 (d, J = 7.1 Hz, 2H), 7.09 (d, J = 3.9 Hz, 1H), 7.02 (td, J = 7.6, 0.8 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.61 – 6.55 (m, 2H), 5.76 (s, 1H), 5.23 (dd, J = 9.3, 5.4 Hz, 1H), 5.11 (d, J = 16.8 Hz, 1H), 4.76 (s, 1H), 2.07 (s, 3H), 1.80 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 157.2, 142.6, 140.0, 138.4, 136.6, 135.6, 134.2, 133.4, 129.5, 129.0, 127.7, 127.2, 126.0, 123.9, 123.4, 122.8, 121.0, 120.9, 120.2, 115.6, 104.8, 85.3, 59.5, 45.5, 20.5, 18.6.

HRMS (ESI, m/z) Calcd. for $C_{29}H_{22}N_2NaO_3^+$, $[M+Na]^+$: 469.1523, found: 469.1517.

<Chromatogram>

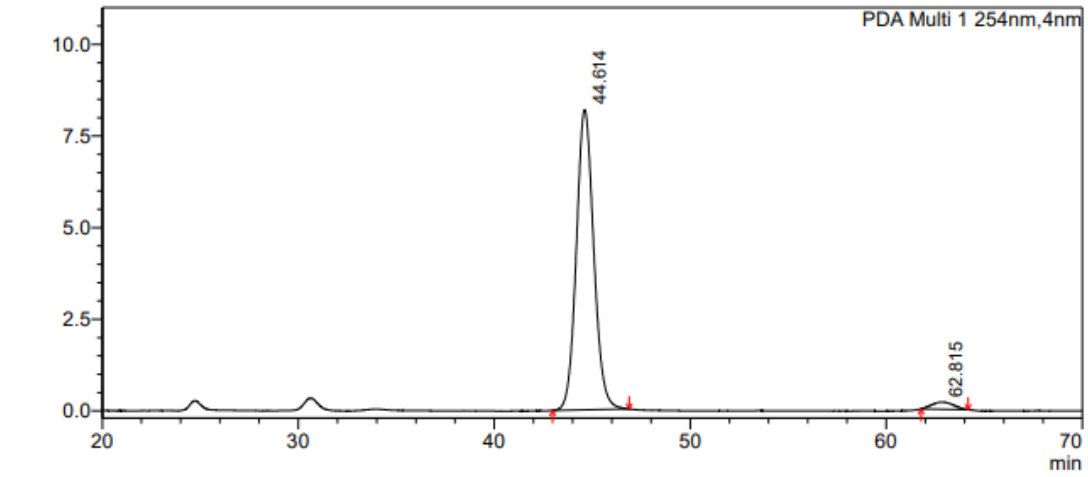


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	24.709	101775	2376	33.470
2	30.623	100528	2005	33.060
3	44.685	50825	827	16.714
4	62.803	50952	530	16.756
Total		304080	5738	100.000

<Chromatogram>

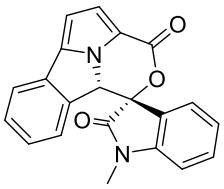


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	44.614	505633	8190	97.104
2	62.815	15080	195	2.896
Total		520712	8385	100.000

(1S,9bS)-1'-methylspiro[benzo[a][1,4]oxazino[3,4,5-cd]pyrrolizine-1,3'-indoline]-2',3(9bH)-dione (3t)



3t

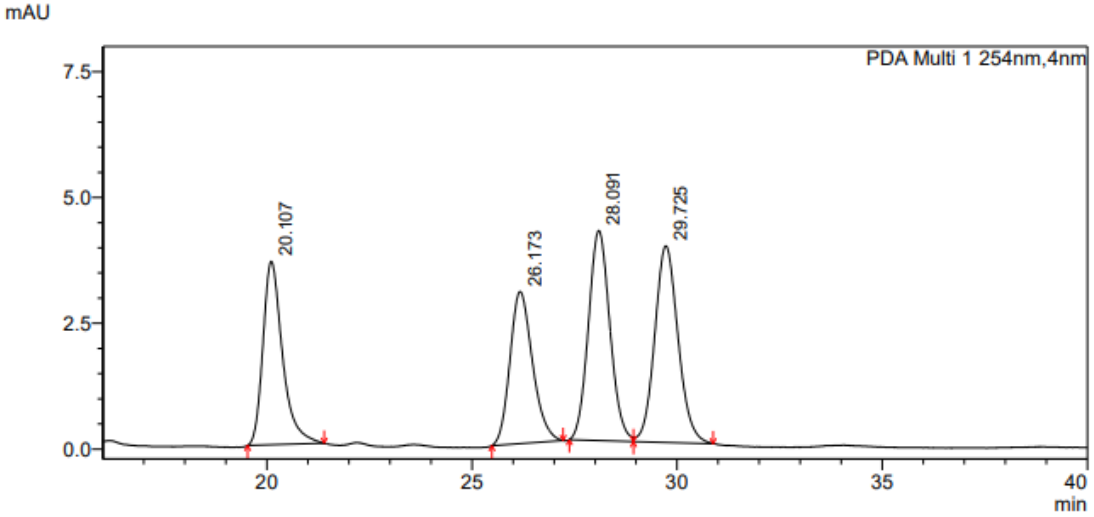
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 100/1 to 10/1) giving the product **3t** as a yellow solid in 72% yield (26.5 mg), m.p. 185-187 °C; **[α]^{25}D** = -123.126 (c = 0.2, $CHCl_3$); >20:1 dr; 82:18 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 28.15 min (minor), t_R = 29.76 min(major);

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.58 (t, J = 6.1 Hz, 1H), 7.35 (t, J = 7.7 Hz, 1H), 7.25 – 7.19 (m, 2H), 7.17 – 7.11 (m, 1H), 7.07 (d, J = 7.4 Hz, 1H), 6.83 (d, J = 7.9 Hz, 1H), 6.69 (dd, J = 8.0, 5.8 Hz, 2H), 5.85 (s, 1H), 5.30 (d, J = 7.5 Hz, 1H), 3.36 (s, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 168.9, 157.5, 156.7, 143.6, 142.7, 140.0, 134.2, 131.1, 129.5, 127.2, 123.9, 123.5, 123.3, 122.7, 121.0, 120.6, 115.4, 109.0, 105.1, 85.5, 59.5, 26.6.

HRMS (ESI, m/z) Calcd. for $C_{21}H_{14}N_2NaO_3^+$, $[M+Na]^+$: 365.0897, found: 365.0888.

<Chromatogram>

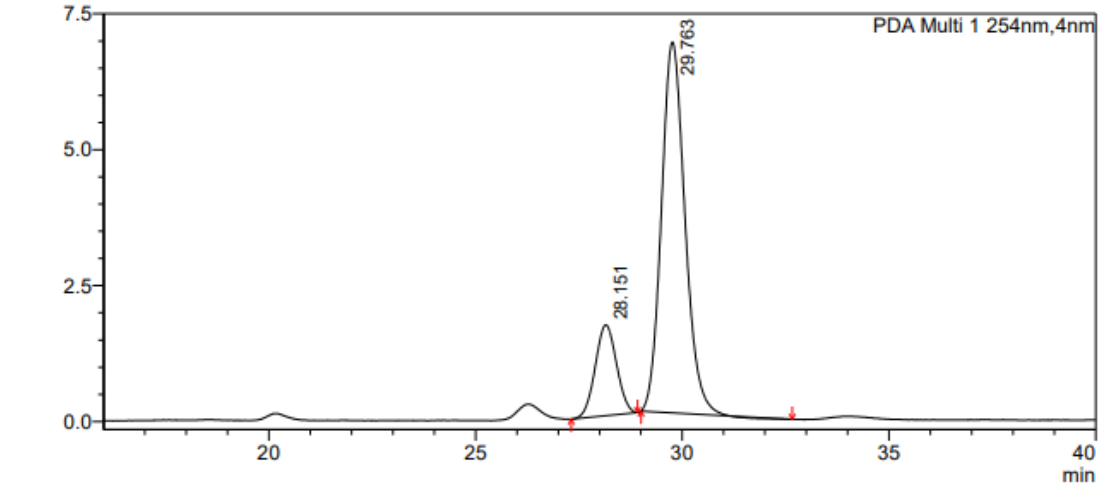


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	20.107	121247	3645	22.292
2	26.173	115768	3022	21.285
3	28.091	152231	4170	27.989
4	29.725	154656	3906	28.435
Total		543902	14742	100.000

<Chromatogram>



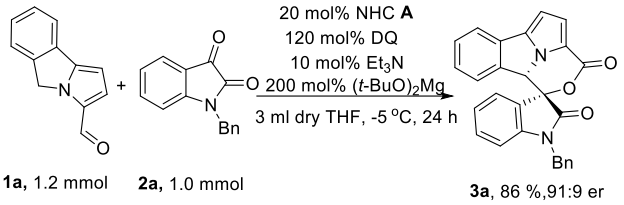
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	28.151	59902	1671	18.228
2	29.763	268732	6818	81.772
Total		328634	8488	100.000

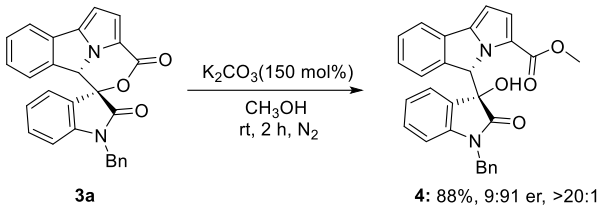
6. Large scale reaction and synthetic transformation of 3a

Large scale reaction for 3a synthesis



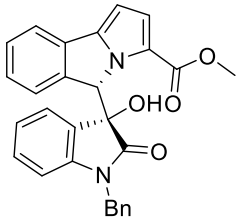
To a 50 mL vial equipped with a magnetic stir bar were added **1a** (1.2 mmol 237.3 mg), **2a** (1.0 mmol 219 mg), DQ (2.0 mmol 490.4 mg), Et_3N (0.1 mmol 15 μL), pre-NHC **A** (0.2 mmol 112 mg) and $(t\text{-BuO})_2Mg$ (2.0 mmol 336 mg) in dry THF (30.0 mL) and the reaction was stirred in ice bath at -5 ℃ for 24 h. Then the mixture was concentrated under reduced pressure. The resulting crude residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 100/1 to 10/1) to afford the desired product **3a**. (White solid, 359 mg, 86 % yield, 91:9 er, >20:1 dr)

synthetic transformation of 3a[4]



To a 10 mL flame-dry Schlenk reaction flask equipped with a magnetic stir bar was added **3a** (41.84 mg, 0.10 mmol), K_2CO_3 (41.46 mg, 0.15 mmol). The flask was then sealed, evacuated, and backfilled with nitrogen three times using standard Schlenk techniques, and anhydrous CH_3OH (2.0 mL) was added as solvent, the reaction mixture was stirred at room temperature for 2 hours and evaporated. The resulting crude residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 100/1 to 10/1) to afford the desired product **4**. (yellow solid, 396 mg, 86% yield, 9:91 er, >20:1 dr)

methyl (S)-5-((R)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-5H-pyrrolo[2,1-a]isoindole-3-carboxylate (4)



4

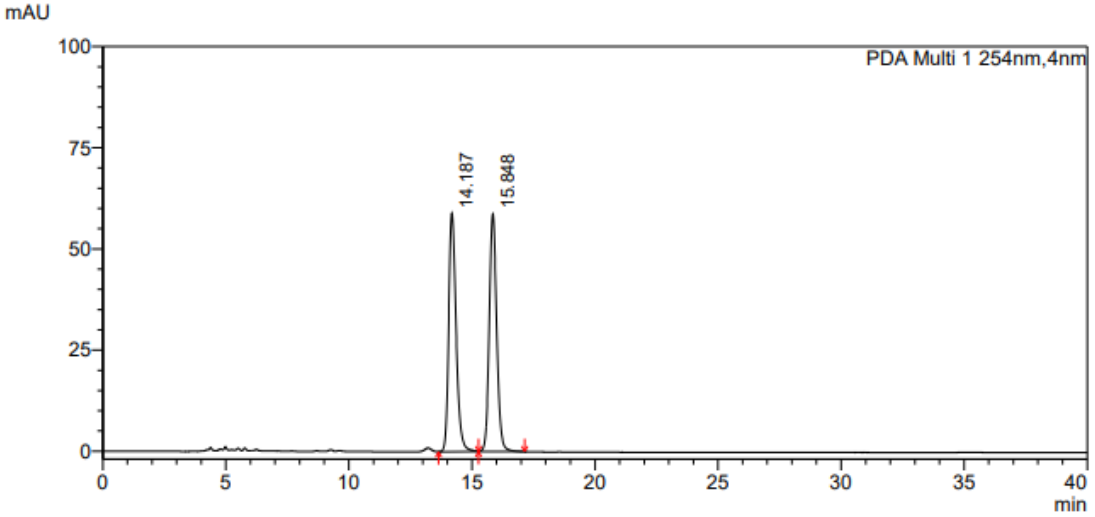
The residue was purified by a silica gel flash chromatography (petroleum ether/ethyl acetate = 10/1) giving the product **4** as a yellow solid in 88% yield (39.6 mg), m.p. 166-168 °C; **[α]^{25}D** = -387.793 (c = 0.2, $CHCl_3$); >20:1 dr; 9:91 er; determined by HPLC on a Chiralpak IF column at 254 nm (n-hexane/2-propanol = 60/40, 0.7 mL/min), t_R = 16.16 min (minor), t_R = 14.48 min(major);

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.30 – 7.16 (m, 7H), 7.08 – 6.94 (m, 2H), 6.86 (td, *J* = 7.8, 1.3 Hz, 1H), 6.76 (td, *J* = 7.6, 1.1 Hz, 1H), 6.55 (td, *J* = 7.6, 0.9 Hz, 1H), 6.36 (dd, *J* = 10.7, 5.9 Hz, 2H), 6.20 (s, 1H), 6.01 (s, 1H), 5.77 (dd, *J* = 7.5, 0.8 Hz, 1H), 4.87 (d, *J* = 15.6 Hz, 1H), 4.63 (d, *J* = 15.5 Hz, 1H).

^{13}C NMR (101 MHz, CD_2Cl_2) δ 175.7, 164.5, 145.4, 142.5, 139.6, 135.5, 132.0, 129.5, 128.7, 128.7, 127.8, 127.8, 126.4, 126.3, 124.1, 123.3, 123.2, 122.7, 121.8, 119.3, 108.6, 100.9, 80.1, 67.1, 52.1, 43.9.

HRMS (ESI, m/z) Calcd. for $C_{28}H_{23}N_2O_4^+$, $[M+H]^+$: 451.1652, found: 451.1652.

<Chromatogram>

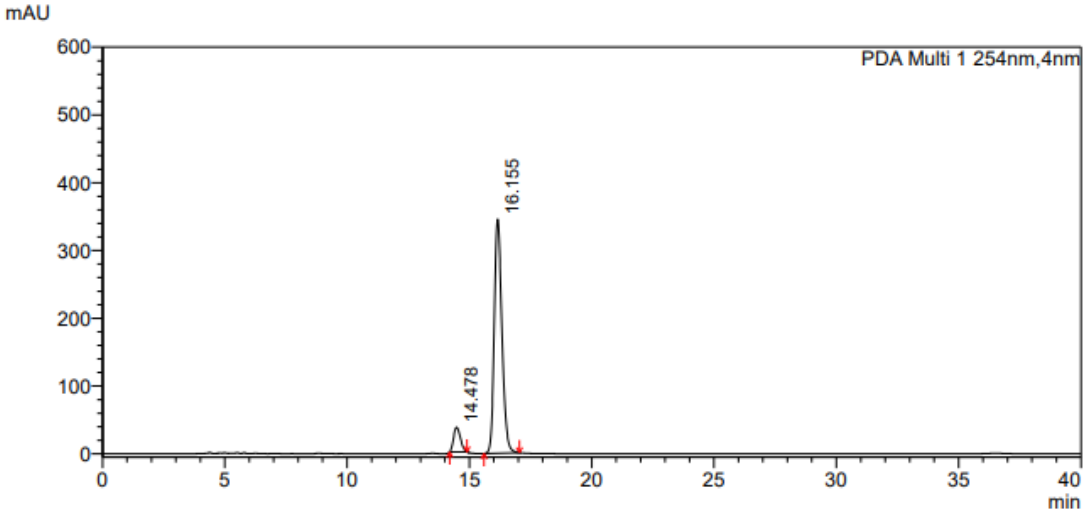


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.187	1232854	58983	49.981
2	15.848	1233815	58753	50.019
Total		2466669	117737	100.000

<Chromatogram>



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.478	706143	36241	8.561
2	16.155	7542065	345261	91.439
Total		8248208	381503	100.000

7. Anti-Xoo and anti-Xac activities of Products in Vitro

Antibacterial activities of the target compounds **3** against Xac(Xanthomonas axonopodis pv. Citri) and Xoo(Xanthomonas oryzae pv.oryzae) in vitro were evaluated by using the turbidimeter test, commercial agricultural antibacterial thiodiazole-copper and Bismerthiazol were used as control. The compoundsto be measured were dissolved in 150 μL of dimethylformamide and diluted with 0.1% (V/V) Tween-20 to prepare two concentrations of 100 μg/mL. 1 mL of the liquid sample was added to the non-toxic nutrient broth (NB: 1.5 g of beef extract, 2.5 g of peptone, 0.5 g of yeast powder, 5.0 g of glucose and 500 mL of distilled water, pH = 7.0 -7.2) liquid medium in 4 mL tubes. Then, 40 μL of NB containing Xac and Xoo was added separately to 5 mL of solvent NB containing the test compounds, thiodiazole-copper. The inoculated test tubes were incubated at (30 ± 1) ℃ under continuous shaking at 180 rpm for 38 h. The culture growth was monitored spectrophotometric ally by measuring the optical density at 595 nm (OD595) and expressed as corrected turbidity. The relative inhibitory rate (I %) compared with a blank assay was calculated as follows:

$$\text{Relative inhibitory rate I (\%)} = (Ctur - Ttur)/Ctur \times 100$$

Ctur: the corrected turbidity value of bacterial growth on untreated NB;

Ttur: the corrected turbidity value of bacterial growth on treated NB；

I: The relative inhibitory rate.

Each experiment was repeated thrice

Table 2. Antibacterial activities[a] of the target compounds **3** against Xac and Xoo.

compound	Inhibition rate(%) of 100 μg/mL	
	Xac	Xoo
3b	41.17±4.25	81.76±1. 65
3c	75.26±1.84	79.05±1.54
3d	77.84±5.25	78.65±12.69
3e	80. 06±8.27	38. 42±2. 3
3f	77.49±2 22	76.67±5.85
3g	30.82±5.97	77.57±5.7
3h	68.71±8.19	52.97±5.15
3i	70.53±3.54	80.05±2. 91
3j	44.39±2.98	77. 75±1.72
3k	35.26±4.67	74. 46±5.79
3l	78. 95±1.11	77.84±5.55
3m	56.14±2.46	82.25±1.89
3n	31.87±2.72	65.23±0.96
3o	56.37±5.4	79.14±1.91
3p	42.51±3.48	54.77±2.56
3q	27.95±2.4	79.86±2.46
3r	27.37±3.75	63.74±3.06
3s	72.11±7.42	67.57±5.03
3t	47.13±6. 02	71.13±4.78
BT[b]	45.73±4.92	53.69±2.8
TC[c]	54.33±3.29	59.73±1.9

[a]All date were average data of three replicates [b]BT = Bismerthiazol [c]TC = Thiodiazole Copper

8. References

1. J. E. Taylor, M. D. Jones, J. M. J. Williams, and S. D. Bull, *Org. Lett*, 2010, **12**, 5740-5743.

2. G. Bertuzzi, V. Corti, J. A. Izzo, S. Ricko, N. I. Jessen, and K. A. Jørgensen, *J. Am. Chem. Soc*. 2022, **144**, 1056-1065.

3. Y. Abdelhamid, K. Kasten, J. Dunne, W. C. Hartley, C. M. Young, D. B. Cordes, A. M. Z. Slawin, S. Ng, A. D. Smith, *Org. Lett*. 2022, **24**, 5444-5449.

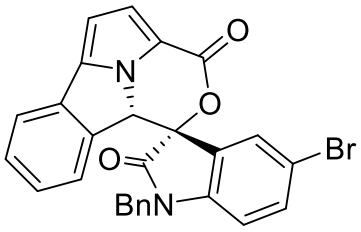
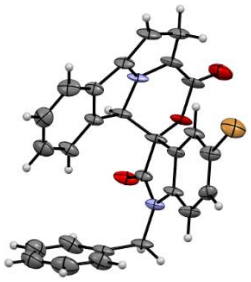
4. X. Q. Yang, J. Sun, X. Huang, and Zh. Ch. Jin. *Org. Lett*. 2022, **24**, 5474-5479.

9. X-ray crystallography of compound 3k.

Good quality crystal of **3k** (colourless needle crystal) was obtained by vaporization of a petroleum ether / dichloromethane solution of cycloaddition compound **3k** (~60 mg). A suitable crystal with dimensions 0.1 × 0.16 × 0.2 mm^3 was selected and mounted on a Bruker APEX-II CCD diffractometer. CCDC:2244403 contains the supplementary crystallographic data for this paper. The crystal was kept at a steady T = 273.15 K during data collection. These data can be obtained free of charge from The Cambridge Crystallographic

Data Centre via https://www.ccdc.cam.ac.uk/.

Supplementary Table 5. X-ray analysis data of compounds **3k**.

 **3k**	 **3k**, CCDC: **2244403**

Crystal Data. $C_{28}H_{20}BrCl_2N_2O_3$, (*M* = 583.27 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 9.824(5) Å, *b* = 14.724(9) Å, *c* = 17.133(10) Å, $\alpha = \beta = \gamma = 90°$, *V* = 2478(2) Å3 , *Z* = 4, *Z'* = 1, *T* = 298 K, μ(CuKα) = 4.530 mm^{-1} , *Dcalc* = 1.563 g/cm^3, 16610 reflections measured, 4705 unique (R_{int} = 0.0675, R_{sigma} = 0.0664) which were used in all calculations. The final R_1 was 0.0911 (I > 2σ(I)) and wR_2 was 0.2399 (all data).

Cartesian coordinates of all the optimized structures

Table 6 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 20221228JH_0m_a. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Br01	8802.8(13)	1724.6(12)	3282.2(8)	52.6(6)
Cl01	8824(6)	4087(6)	4611(4)	110(2)
O004	4890(7)	3236(7)	951(3)	32.6(18)
O005	2528(7)	4173(7)	1631(5)	43(2)
N006	6827(8)	4432(8)	1290(5)	31(2)
O007	6096(10)	2649(8)	-24(5)	53(3)
N008	3234(8)	3256(8)	2637(4)	29.1(19)
C00B	5511(9)	4591(8)	1648(6)	28(2)
C00F	7042(5)	2157(6)	3095(4)	35(3)
C00E	6773(5)	2703(6)	2451(3)	31(3)
C009	5475(6)	3053(5)	2337(3)	26(2)
C00A	4444(5)	2858(6)	2867(4)	29(2)
C00K	4713(6)	2313(6)	3511(3)	35(3)
C00I	6011(7)	1962(5)	3625(3)	33(2)
C00G	7354(6)	5298(6)	2323(4)	32(2)
C00C	5958(6)	5147(5)	2344(3)	29(2)
C00D	5174(5)	5534(6)	2932(4)	37(3)
C00T	5787(7)	6071(6)	3499(4)	45(3)
C00R	7183(8)	6222(6)	3478(4)	45(3)
C00V	7967(6)	5836(6)	2890(4)	44(3)
C00H	1999(9)	3308(10)	3116(6)	34(3)
C00J	8600(11)	3740(10)	779(6)	36(3)
C00L	7924(10)	4783(9)	1666(6)	32(2)
C00M	4893(9)	3657(9)	1720(6)	31(2)
C00O	9066(11)	4384(11)	1331(7)	45(3)
C00Q	7163(10)	3769(10)	769(6)	35(3)
C00S	3381(10)	3734(8)	1963(5)	27(2)
C00U	6088(11)	3189(10)	515(6)	39(3)
C00X	2711(10)	4836(7)	4863(4)	65(5)
C00N	2641(9)	4073(6)	4387(4)	48(4)
C00P	2033(8)	4132(5)	3656(4)	35(3)
C00W	1495(9)	4953(7)	3402(4)	53(4)
C00Y	1565(11)	5716(5)	3879(5)	56(4)
C00Z	2173(11)	5657(6)	4609(5)	57(4)
C010	7034(19)	4125(14)	4570(9)	66(5)
Cl1	6281(5)	3391(3)	5232(2)	69.0(12)

Table 7 Anisotropic Displacement Parameters ($Å^2×10^3$) for 20221228JH_0m_a. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br01	25.0(6)	83.5(12)	49.5(8)	8.8(7)	-11.2(5)	14.2(7)
Cl01	66(3)	165(6)	99(4)	3(4)	32(3)	-6(4)
O004	19(3)	69(6)	9(3)	0(3)	3(2)	1(4)
O005	15(3)	85(7)	30(4)	12(4)	-2(3)	9(4)
N006	9(3)	61(7)	22(4)	5(4)	4(3)	-1(4)
O007	45(5)	86(8)	29(4)	-18(4)	8(4)	-9(5)
N008	17(3)	51(5)	19(3)	0(3)	4(3)	-2(4)
C00B	12(4)	55(7)	17(4)	3(5)	4(3)	1(4)
C00F	24(5)	59(8)	22(5)	0(5)	-4(4)	-4(5)
C00E	12(4)	60(8)	22(4)	4(5)	1(3)	7(5)
C009	17(4)	42(5)	18(3)	2(3)	5(3)	2(4)
C00A	10(4)	57(7)	20(4)	-1(4)	3(3)	-1(4)
C00K	22(5)	60(8)	23(5)	12(5)	4(4)	2(5)
C00I	38(6)	42(7)	19(4)	7(4)	-2(4)	-2(5)
C00G	18(5)	49(7)	29(5)	0(5)	-2(4)	-1(5)
C00C	15(5)	50(7)	23(4)	2(4)	2(3)	3(4)
C00D	24(5)	60(8)	25(5)	-3(5)	0(4)	10(5)
C00T	42(7)	62(9)	30(6)	-7(6)	3(5)	3(6)
C00R	53(8)	51(8)	31(6)	-5(5)	-10(5)	-6(7)
C00V	28(6)	70(10)	34(6)	-4(6)	-10(5)	-14(6)
C00H	12(4)	66(8)	26(5)	4(5)	6(3)	-5(5)
C00J	18(5)	60(8)	31(5)	10(5)	8(4)	2(5)
C00L	12(4)	56(7)	29(5)	0(5)	0(4)	-5(4)
C00M	9(4)	70(8)	14(4)	0(5)	0(3)	0(4)
C00O	14(5)	83(10)	37(6)	6(6)	8(4)	-1(6)
C00Q	17(5)	70(9)	19(4)	2(5)	7(4)	2(5)
C00S	14(4)	43(5)	22(4)	-3(4)	0(3)	-2(4)
C00U	23(5)	74(9)	19(4)	1(5)	11(4)	2(6)
C00X	58(9)	108(15)	30(6)	-4(8)	-1(6)	-8(10)
C00N	43(7)	77(11)	26(6)	-2(6)	-3(5)	5(7)
C00P	15(5)	65(9)	25(5)	-1(5)	7(4)	-3(5)
C00W	38(7)	89(11)	31(6)	-3(7)	3(5)	17(7)
C00Y	57(9)	64(10)	49(8)	7(7)	6(6)	14(8)
C00Z	50(8)	78(11)	43(7)	-12(7)	11(6)	1(8)
C010	72(11)	83(13)	43(8)	12(8)	-3(7)	-2(10)
Cl1	65(2)	99(3)	43.0(16)	2.8(19)	3.6(16)	-10(3)

Table 8 Bond Lengths for 20221228JH_0m_a.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Br01	C00F	1.871(5)	C00G	C00C	1.3900
Cl01	C010	1.76(2)	C00G	C00V	1.3900
O004	C00M	1.456(12)	C00G	C00L	1.469(13)
O004	C00U	1.396(11)	C00C	C00D	1.3900
O005	C00S	1.202(14)	C00D	C00T	1.3900
N006	C00B	1.450(11)	C00T	C00R	1.3900
N006	C00L	1.357(13)	C00R	C00V	1.3900
N006	C00Q	1.363(17)	C00H	C00P	1.526(15)
O007	C00U	1.218(15)	C00J	C00O	1.42(2)
N008	C00A	1.384(10)	C00J	C00Q	1.412(14)
N008	C00H	1.466(11)	C00L	C00O	1.390(16)
N008	C00S	1.360(14)	C00M	C00S	1.547(12)
C00B	C00C	1.512(12)	C00Q	C00U	1.426(18)
C00B	C00M	1.508(17)	C00X	C00N	1.3900
C00F	C00E	1.3900	C00X	C00Z	1.3900
C00F	C00I	1.3900	C00N	C00P	1.3900
C00E	C009	1.3900	C00P	C00W	1.3900
C009	C00A	1.3900	C00W	C00Y	1.3900
C009	C00M	1.495(12)	C00Y	C00Z	1.3900
C00A	C00K	1.3900	C010	Cl1	1.733(17)
C00K	C00I	1.3900			

Table 8 Bond Angles for 20221228JH_0m_a.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C00U	O004	C00M	120.2(8)	C00R	C00V	C00G	120.0
C00L	N006	C00B	116.5(9)	N008	C00H	C00P	111.3(9)
C00L	N006	C00Q	113.0(9)	C00Q	C00J	C00O	108.1(11)
C00Q	N006	C00B	127.5(9)	N006	C00L	C00G	105.0(8)
C00A	N008	C00H	125.0(8)	N006	C00L	C00O	106.5(10)
C00S	N008	C00A	111.7(7)	C00O	C00L	C00G	147.3(10)
C00S	N008	C00H	122.5(9)	O004	C00M	C00B	108.3(8)
N006	C00B	C00C	99.3(7)	O004	C00M	C009	112.8(10)
N006	C00B	C00M	104.2(9)	O004	C00M	C00S	105.8(7)
C00M	C00B	C00C	123.1(8)	C00B	C00M	C00S	110.0(10)
C00E	C00F	Br01	120.5(4)	C009	C00M	C00B	116.5(8)
C00E	C00F	C00I	120.0	C009	C00M	C00S	102.7(7)
C00I	C00F	Br01	119.4(4)	C00L	C00O	C00J	107.3(10)
C009	C00E	C00F	120.0	N006	C00Q	C00J	104.8(11)
C00E	C009	C00A	120.0	N006	C00Q	C00U	116.7(9)
C00E	C009	C00M	132.1(5)	C00J	C00Q	C00U	136.5(13)

Table 8 Bond Angles for 20221228JH_0m_a.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C00A	C009	C00M	107.9(5)	O005	C00S	N008	127.3(9)
N008	C00A	C009	110.6(5)	O005	C00S	C00M	125.6(10)
N008	C00A	C00K	129.4(5)	N008	C00S	C00M	107.0(8)
C009	C00A	C00K	120.0	O004	C00U	C00Q	115.5(10)
C00I	C00K	C00A	120.0	O007	C00U	O004	116.3(11)
C00K	C00I	C00F	120.0	O007	C00U	C00Q	128.2(10)
C00C	C00G	C00V	120.0	C00N	C00X	C00Z	120.0
C00C	C00G	C00L	108.2(6)	C00P	C00N	C00X	120.0
C00V	C00G	C00L	131.7(6)	C00N	C00P	C00H	120.4(7)
C00G	C00C	C00B	110.6(5)	C00N	C00P	C00W	120.0
C00D	C00C	C00B	129.3(5)	C00W	C00P	C00H	119.5(7)
C00D	C00C	C00G	120.0	C00Y	C00W	C00P	120.0
C00T	C00D	C00C	120.0	C00W	C00Y	C00Z	120.0
C00R	C00T	C00D	120.0	C00Y	C00Z	C00X	120.0
C00V	C00R	C00T	120.0	Cl1	C010	Cl01	112.3(10)

Table 9 Torsion Angles for 20221228JH_0m_a.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
Br01	C00F	C00E	C009	-177.1(6)	C00C	C00G	C00L	C00O	-158.2(19)
Br01	C00F	C00I	C00K	177.1(6)	C00C	C00D	C00T	C00R	0.0
O004	C00M	C00S	O005	-62.7(16)	C00D	C00T	C00R	C00V	0.0
O004	C00M	C00S	N008	120.6(10)	C00T	C00R	C00V	C00G	0.0
N006	C00B	C00C	C00G	2.9(9)	C00V	C00G	C00C	C00B	176.7(8)
N006	C00B	C00C	C00D	179.2(7)	C00V	C00G	C00C	C00D	0.0
N006	C00B	C00M	O004	-55.1(9)	C00V	C00G	C00L	N006	-176.7(7)
N006	C00B	C00M	C009	73.4(10)	C00V	C00G	C00L	C00O	19(3)
N006	C00B	C00M	C00S	-170.3(7)	C00H	N008	C00A	C009	-170.1(10)
N006	C00L	C00O	C00J	-3.8(14)	C00H	N008	C00A	C00K	11.3(15)
N006	C00Q	C00U	O004	-13.5(16)	C00H	N008	C00S	O005	-7.8(19)
N006	C00Q	C00U	O007	168.1(13)	C00H	N008	C00S	C00M	168.8(10)
N008	C00A	C00K	C00I	178.5(10)	C00H	C00P	C00W	C00Y	-177.7(8)
N008	C00H	C00P	C00N	-87.3(10)	C00J	C00Q	C00U	O004	147.8(13)
N008	C00H	C00P	C00W	90.4(9)	C00J	C00Q	C00U	O007	-31(2)
C00B	N006	C00L	C00G	-4.3(14)	C00L	N006	C00B	C00C	1.1(13)
C00B	N006	C00L	C00O	166.8(11)	C00L	N006	C00B	C00M	-126.7(11)
C00B	N006	C00Q	C00J	-163.4(10)	C00L	N006	C00Q	C00J	-4.1(14)
C00B	N006	C00Q	C00U	3.3(17)	C00L	N006	C00Q	C00U	162.7(11)
C00B	C00C	C00D	C00T	-176.0(9)	C00L	C00G	C00C	C00B	-5.5(9)
C00B	C00M	C00S	O005	54.1(14)	C00L	C00G	C00C	C00D	177.8(8)

Table 9 Torsion Angles for 20221228JH_0m_a.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C00B	C00M	C00S	N008	-122.6(10)	C00L	C00G	C00V	C00R	-177.1(10)
C00F	C00E	C009	C00A	0.0	C00M	O004	C00U	O007	162.8(12)
C00F	C00E	C009	C00M	179.0(10)	C00M	O004	C00U	C00Q	-15.8(17)
C00E	C00F	C00I	C00K	0.0	C00M	C00B	C00C	C00G	116.7(8)
C00E	C009	C00A	N008	-178.8(8)	C00M	C00B	C00C	C00D	-66.9(12)
C00E	C009	C00A	C00K	0.0	C00M	C009	C00A	N008	2.0(8)
C00E	C009	C00M	O004	65.0(11)	C00M	C009	C00A	C00K	-179.2(7)
C00E	C009	C00M	C00B	-61.3(12)	C00O	C00J	C00Q	N006	1.5(14)
C00E	C009	C00M	C00S	178.4(7)	C00O	C00J	C00Q	C00U	-161.2(13)
C009	C00A	C00K	C00I	0.0	C00Q	N006	C00B	C00C	159.8(10)
C009	C00M	C00S	O005	178.8(11)	C00Q	N006	C00B	C00M	32.1(13)
C009	C00M	C00S	N008	2.2(12)	C00Q	N006	C00L	C00G	-166.1(9)
C00A	N008	C00H	C00P	85.3(14)	C00Q	N006	C00L	C00O	5.0(14)
C00A	N008	C00S	O005	-177.7(11)	C00Q	C00J	C00O	C00L	1.4(15)
C00A	N008	C00S	C00M	-1.1(13)	C00S	N008	C00A	C009	-0.5(11)
C00A	C009	C00M	O004	-115.9(7)	C00S	N008	C00A	C00K	-179.2(7)
C00A	C009	C00M	C00B	117.9(7)	C00S	N008	C00H	C00P	-83.2(12)
C00A	C009	C00M	C00S	-2.5(9)	C00U	O004	C00M	C00B	52.8(13)
C00A	C00K	C00I	C00F	0.0	C00U	O004	C00M	C009	-77.8(13)
C00I	C00F	C00E	C009	0.0	C00U	O004	C00M	C00S	170.7(11)
C00G	C00C	C00D	C00T	0.0	C00X	C00N	C00P	C00H	177.7(8)
C00G	C00L	C00O	C00J	160.2(18)	C00X	C00N	C00P	C00W	0.0
C00C	C00B	C00M	O004	-166.5(8)	C00N	C00X	C00Z	C00Y	0.0
C00C	C00B	C00M	C009	-38.0(12)	C00N	C00P	C00W	C00Y	0.0
C00C	C00B	C00M	C00S	78.3(10)	C00P	C00W	C00Y	C00Z	0.0
C00C	C00G	C00V	C00R	0.0	C00W	C00Y	C00Z	C00X	0.0
C00C	C00G	C00L	N006	5.9(11)	C00Z	C00X	C00N	C00P	0.0

Table 10 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 20221228JH_0m_a.

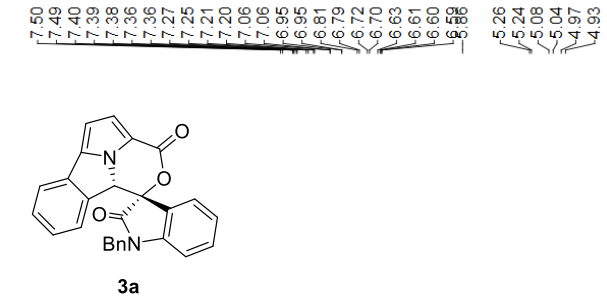
Atom	*x*	*y*	*z*	U(eq)
H00B	4950.08	4965.98	1301.4	33
H00E	7462.7	2832.96	2096.03	38
H00K	4023.4	2182.46	3866.05	42
H00I	6190.99	1597.36	4056.02	39
H00D	4240.25	5432.79	2946.49	44
H00T	5262.46	6330.14	3892.73	54
H00R	7592.86	6582.21	3857.43	54
H00V	8901.06	5936.93	2875.89	53
H00A	1916.89	2759.59	3425.56	41

Table 10 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 20221228JH_0m_a.

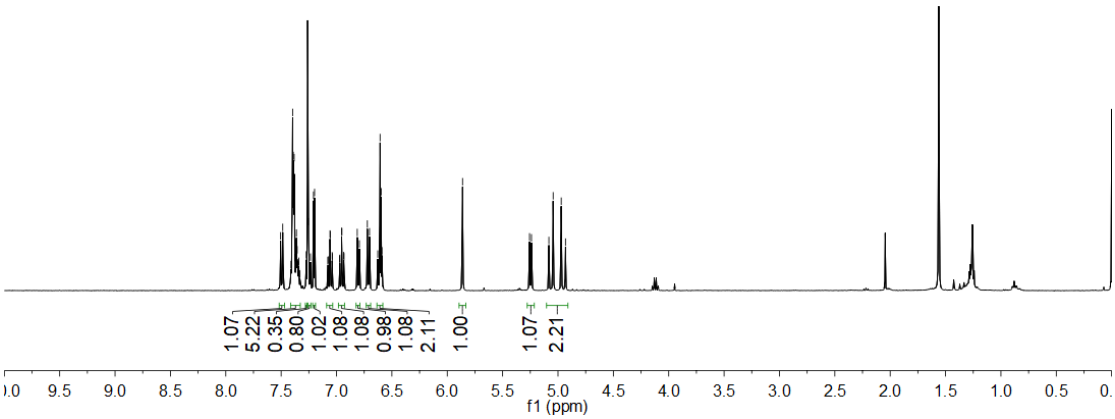
Atom	*x*	*y*	*z*	U(eq)
H00C	1208.46	3347.54	2778.36	41
H00F	8956.41	3883.44	265.63	44
H00G	8909.11	3136.7	922.14	44
H00O	9969.07	4515.72	1448.33	54
H00X	3118.35	4796.23	5352.31	78
H00N	3001.72	3523.46	4556.86	58
H00W	1087.67	4992.65	2913.04	63
H00Y	1204.29	6265.43	3708.48	68
H00Z	2219.63	6167.24	4928.11	68
H01A	6731.77	4739.96	4677.57	79
H01B	6738.63	3967.87	4047.15	79

10. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra.

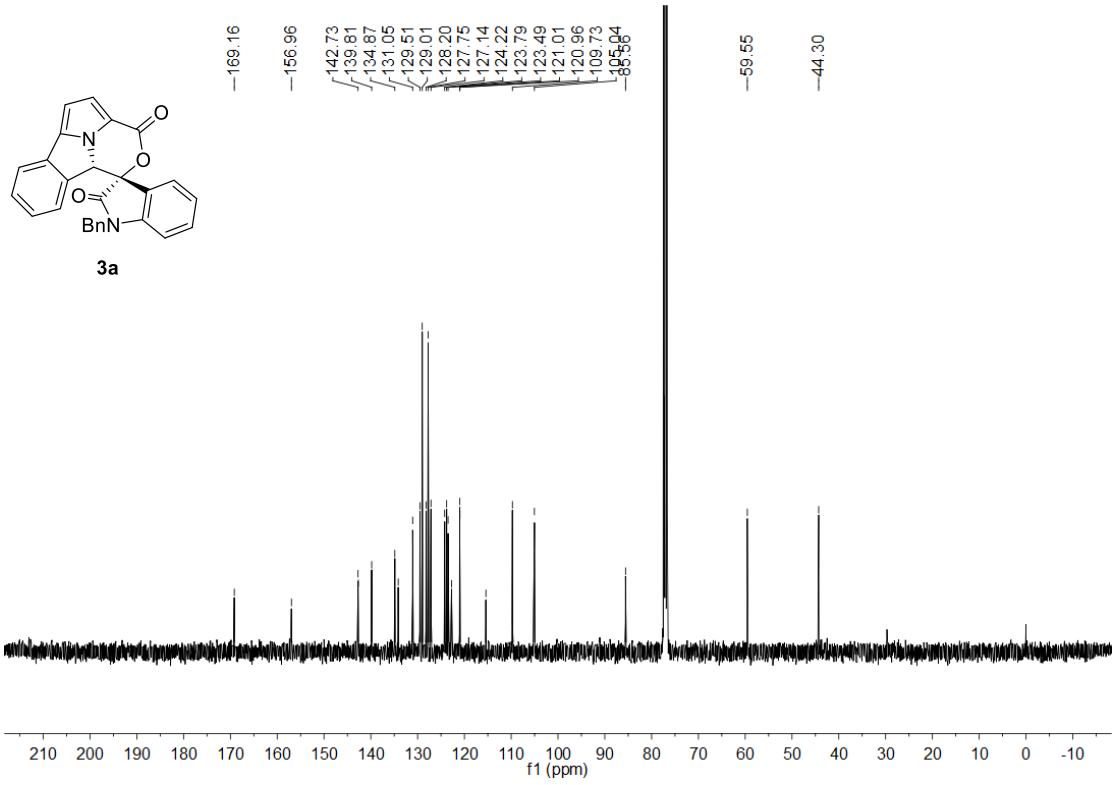
^{1}H NMR spectrum **3a** in $CDCl_3$ (400 MHz)



3a

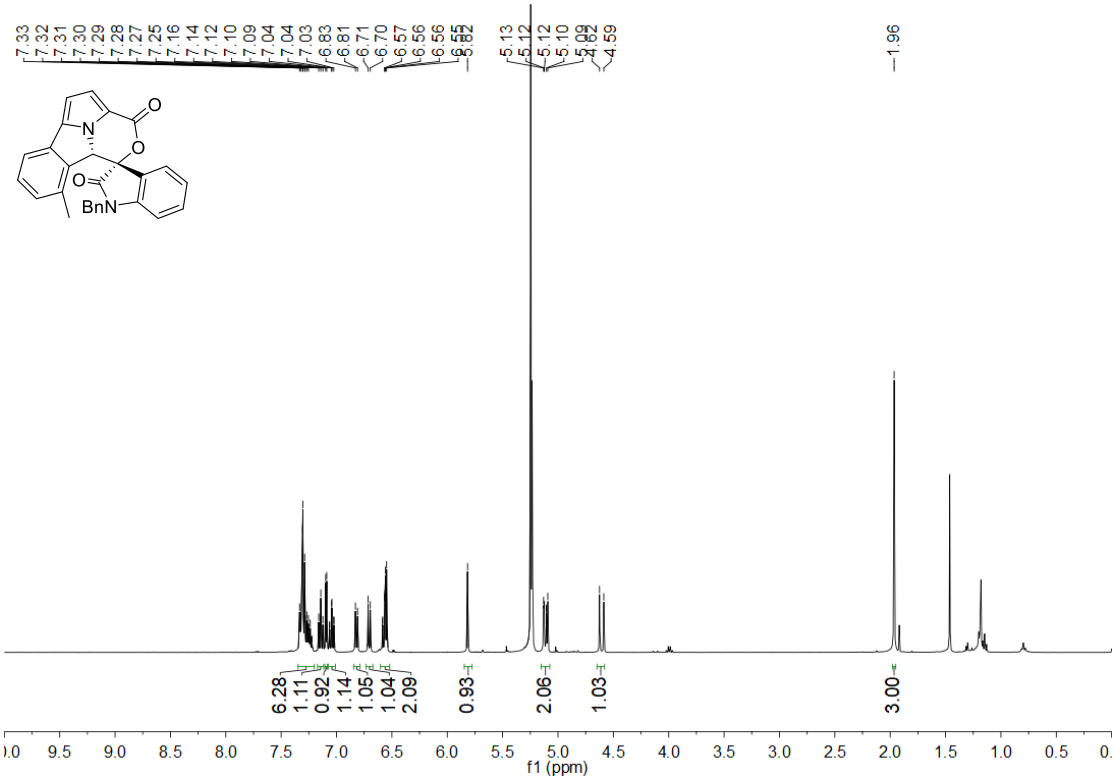


^{13}C NMR spectrum **3a** in $CDCl_3$ (101 MHz)

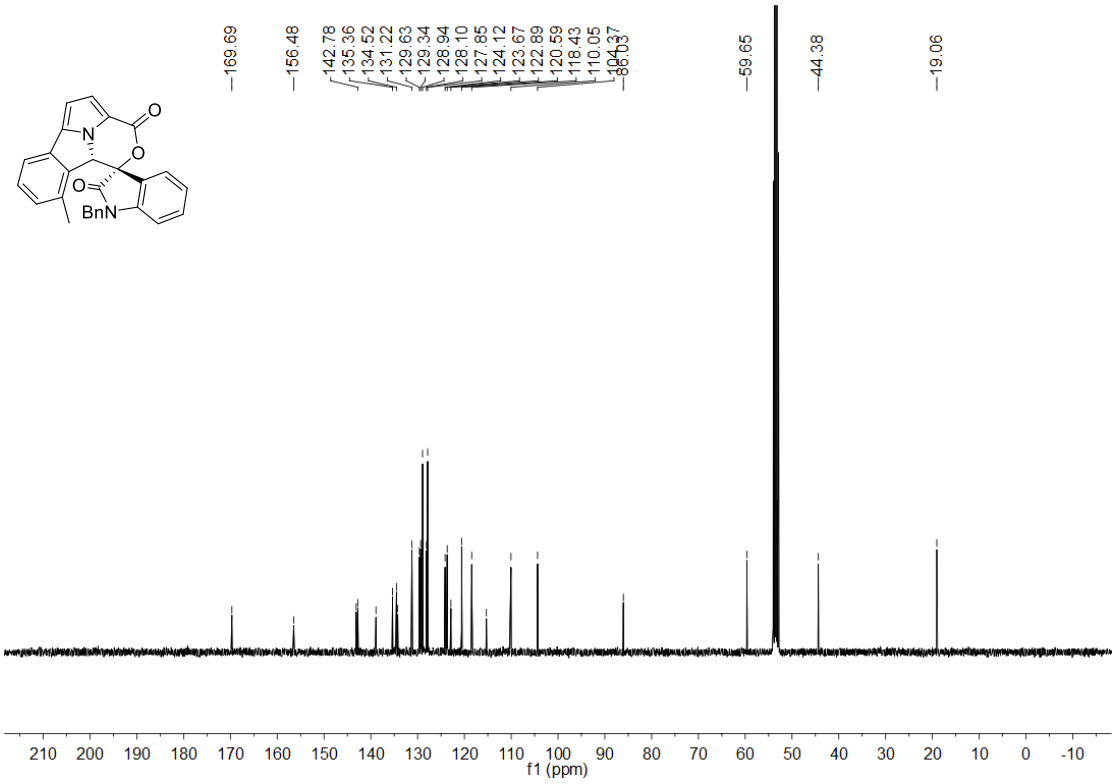


3a

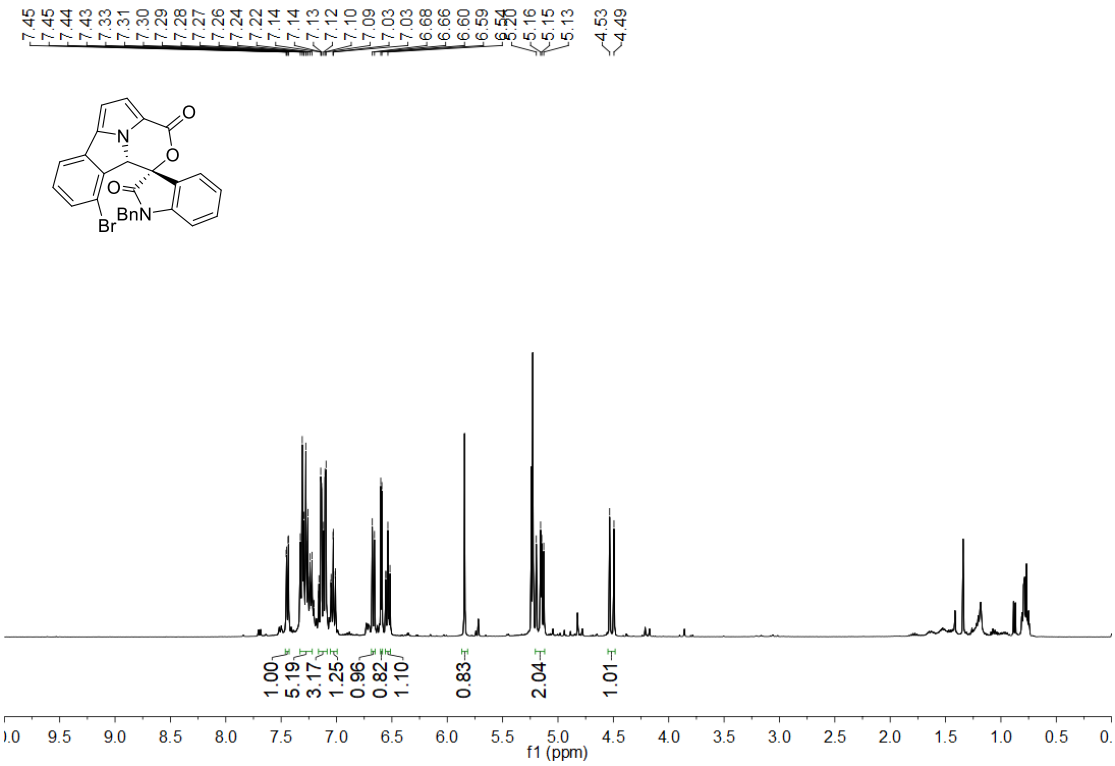
^{1}H NMR spectrum **3b** in CD_2Cl_2 (400 MHz)



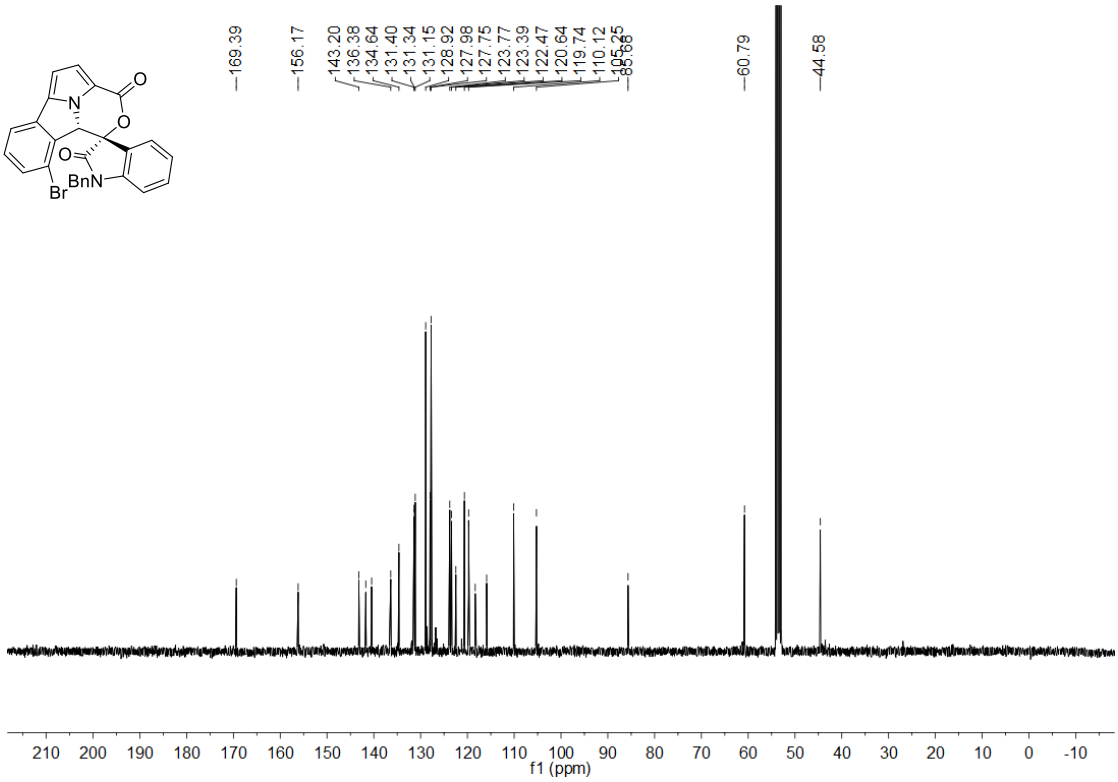
^{13}C NMR spectrum **3b** in CD_2Cl_2 (101 MHz)



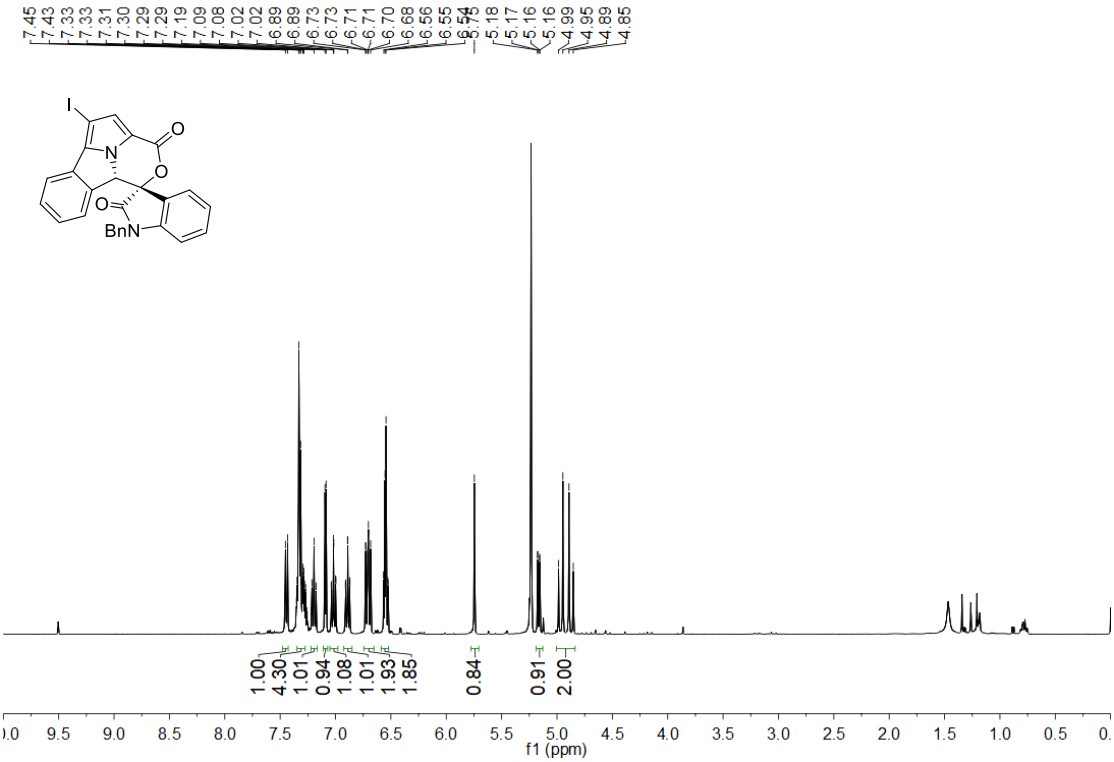
^{1}H NMR spectrum **3c** in CD_2Cl_2 (400 MHz)



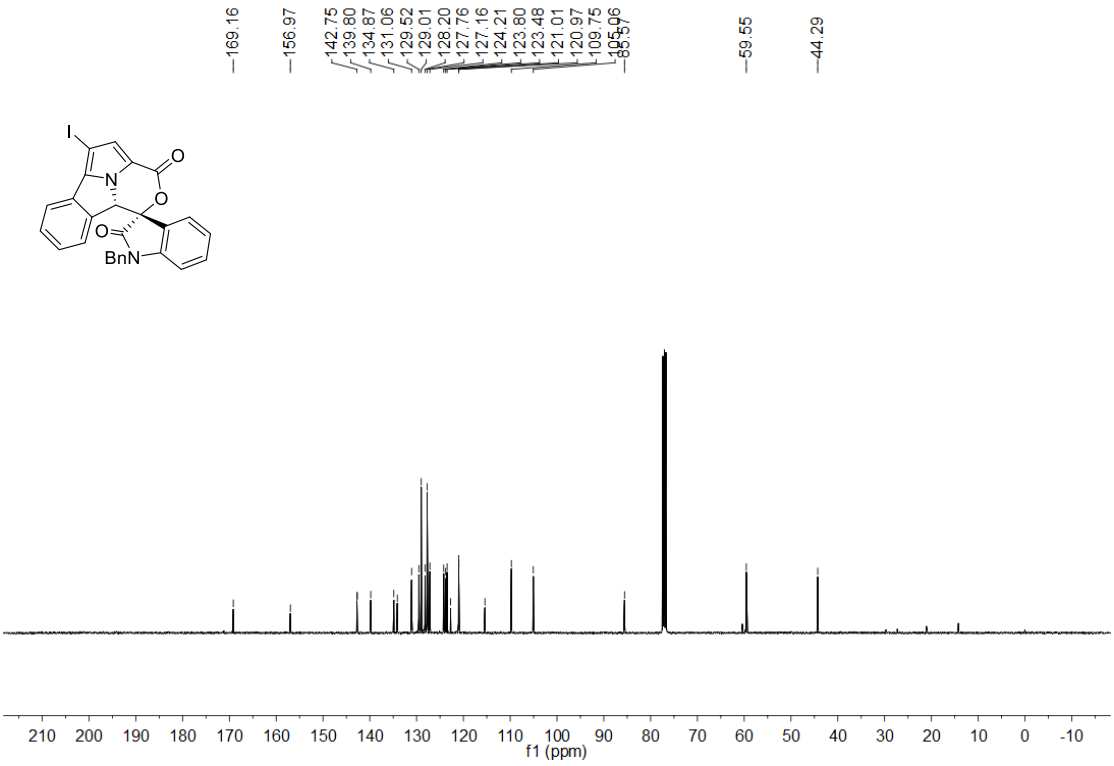
^{13}C NMR spectrum **3c** in CD_2Cl_2 (101 MHz)



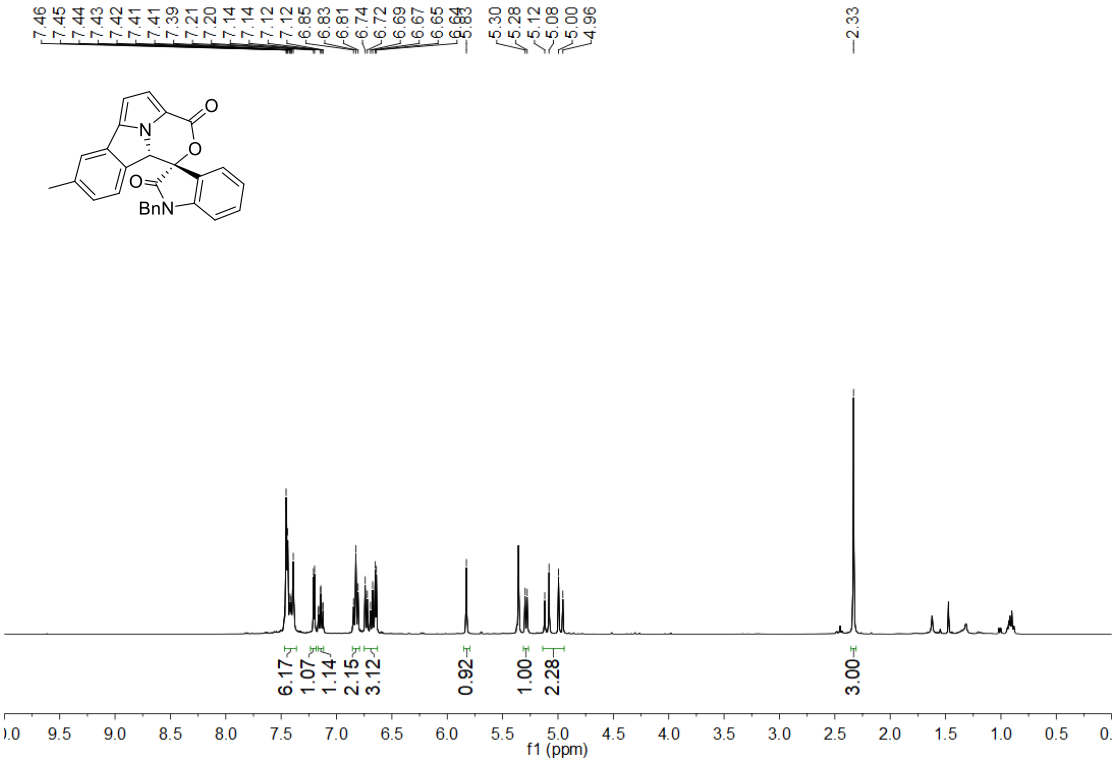
^{1}H NMR spectrum **3d** in CD_2Cl_2 (400 MHz)



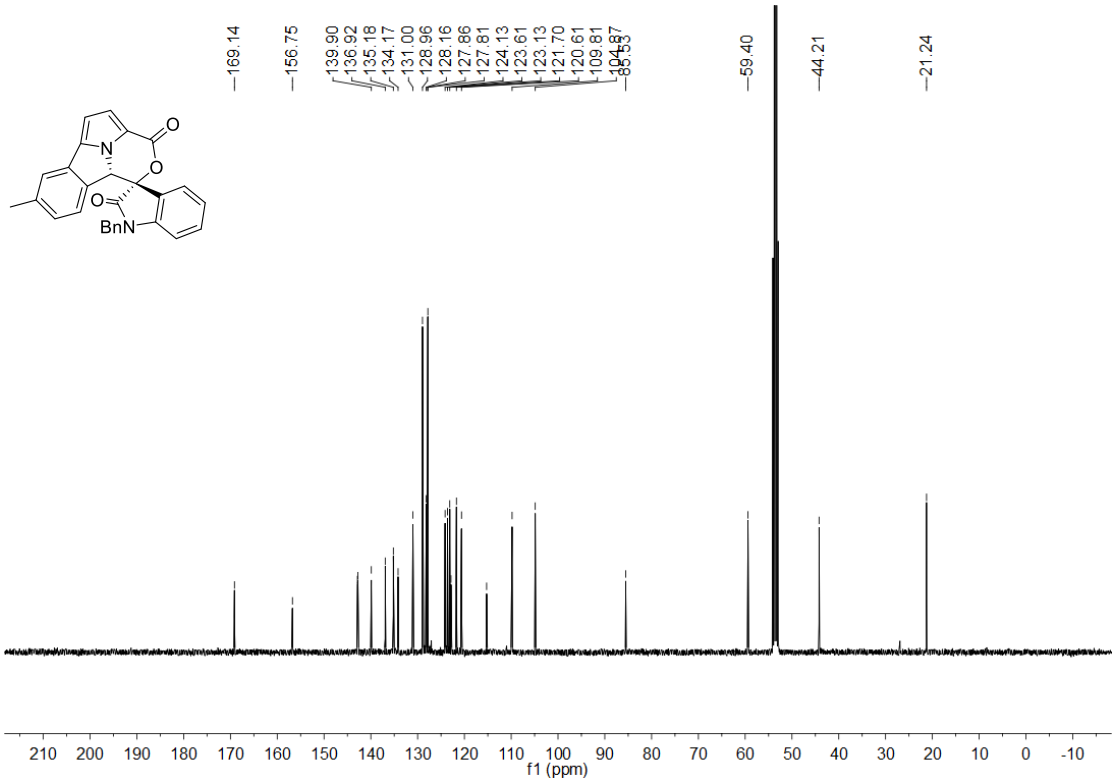
^{13}C NMR spectrum **3d** in $CDCl_3$ (101 MHz)



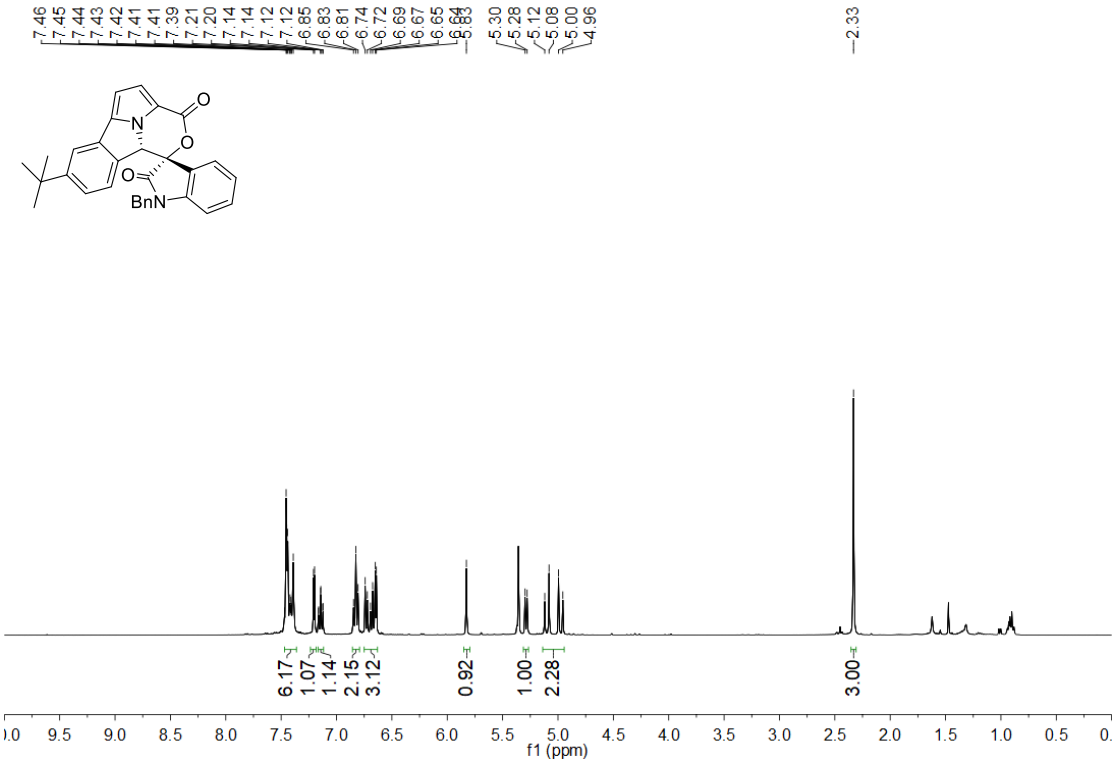
^{1}H NMR spectrum **3e** in CD_2Cl_2 (400 MHz)



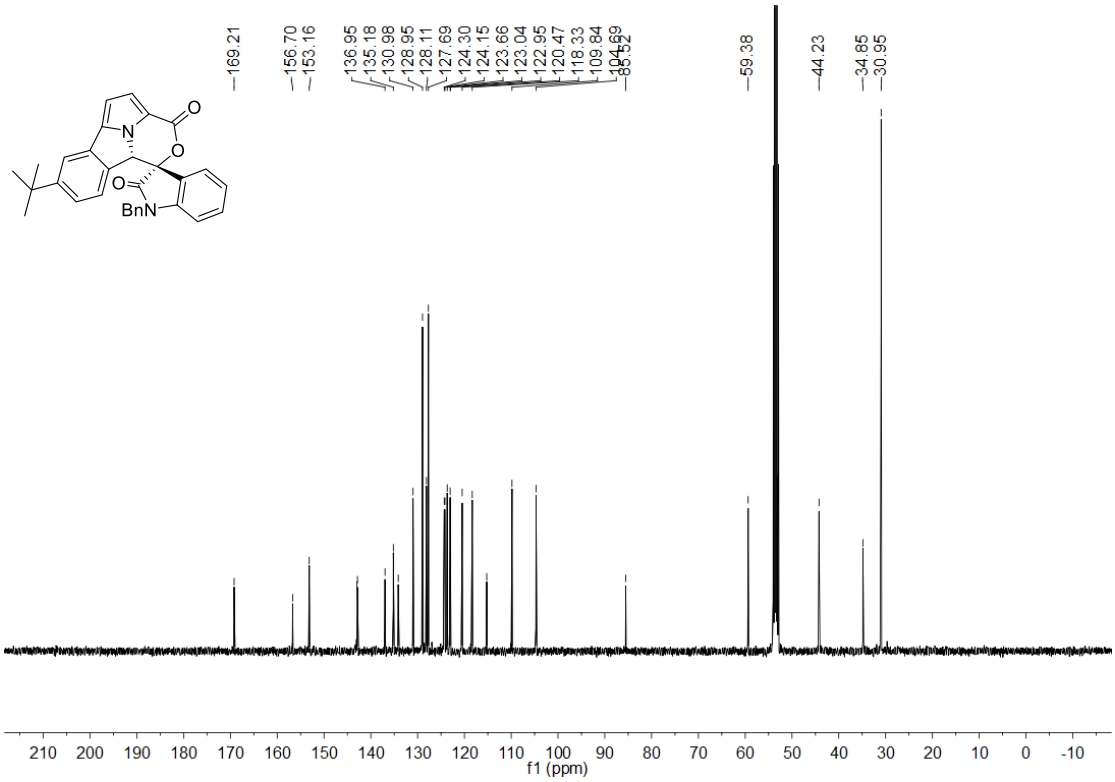
^{13}C NMR spectrum **3e** in CD_2Cl_2 (101 MHz)



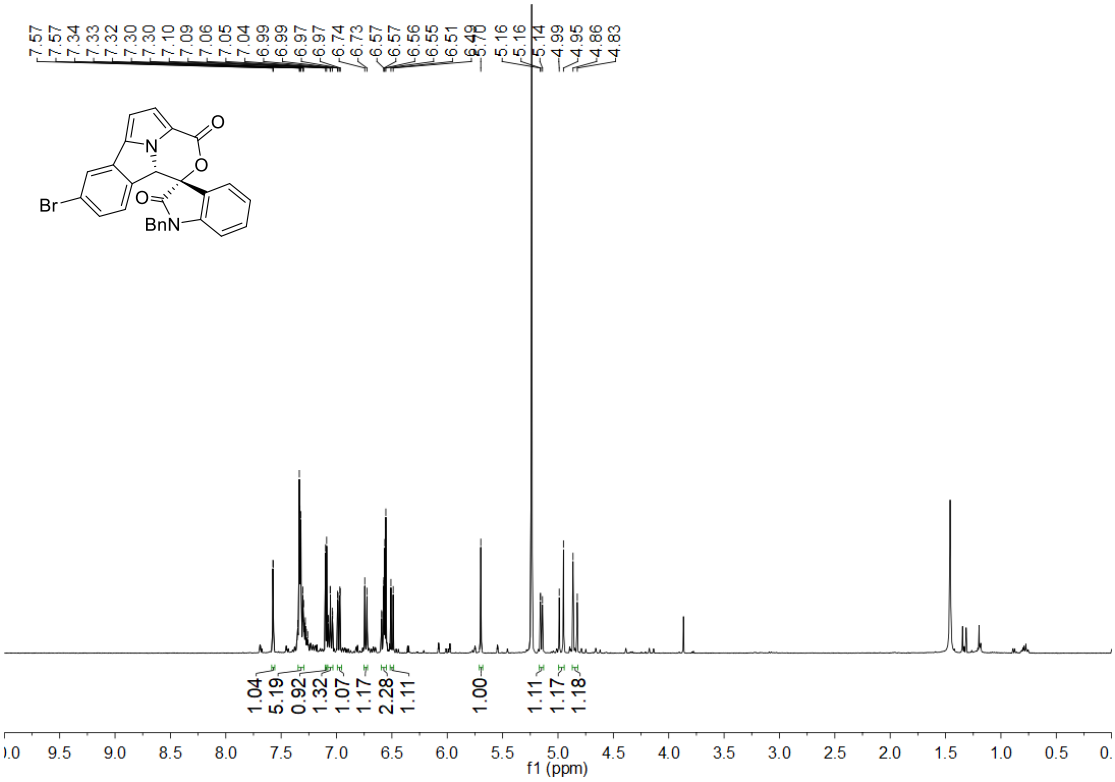
^{1}H NMR spectrum **3f** in CD_2Cl_2 (400 MHz)



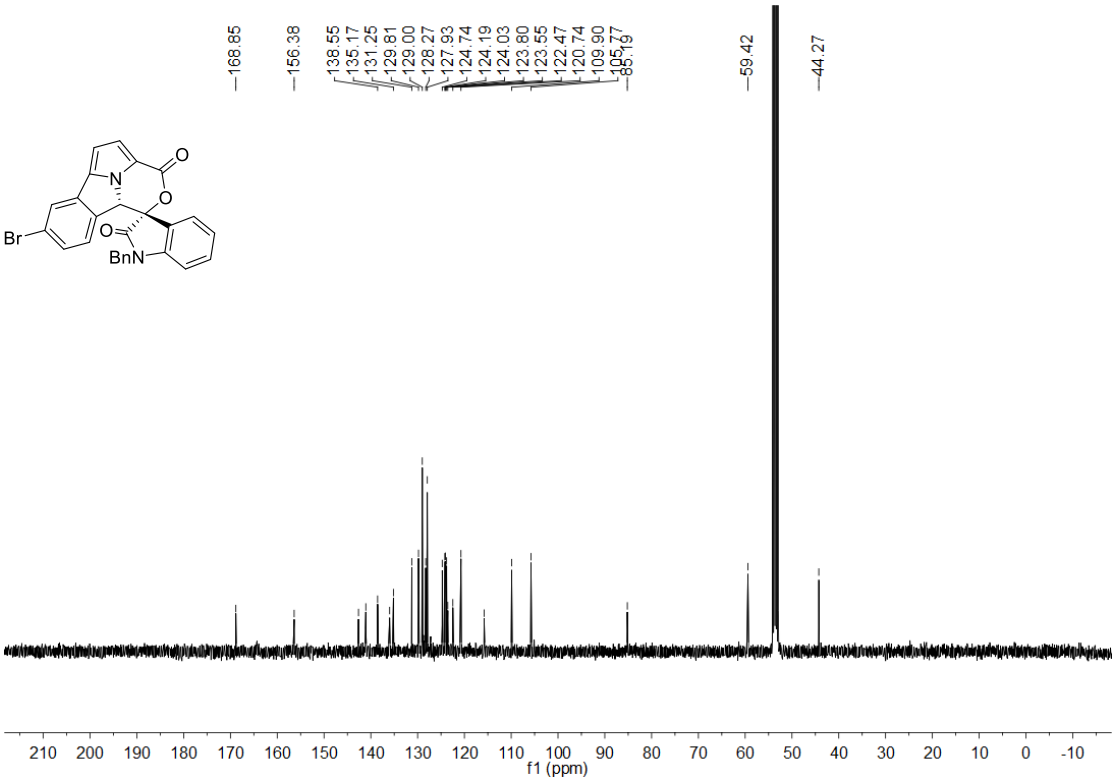
^{13}C NMR spectrum **3f** in CD_2Cl_2 (101 MHz)



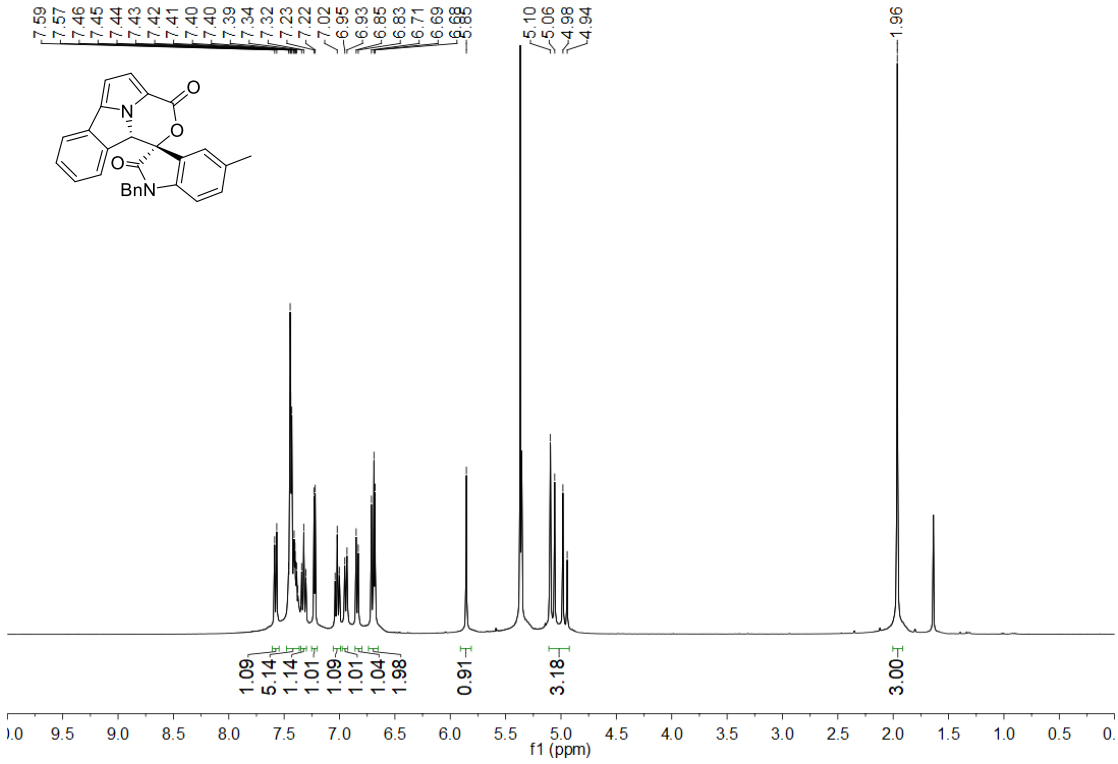
^{1}H NMR spectrum **3g** in CD_2Cl_2 (400 MHz)



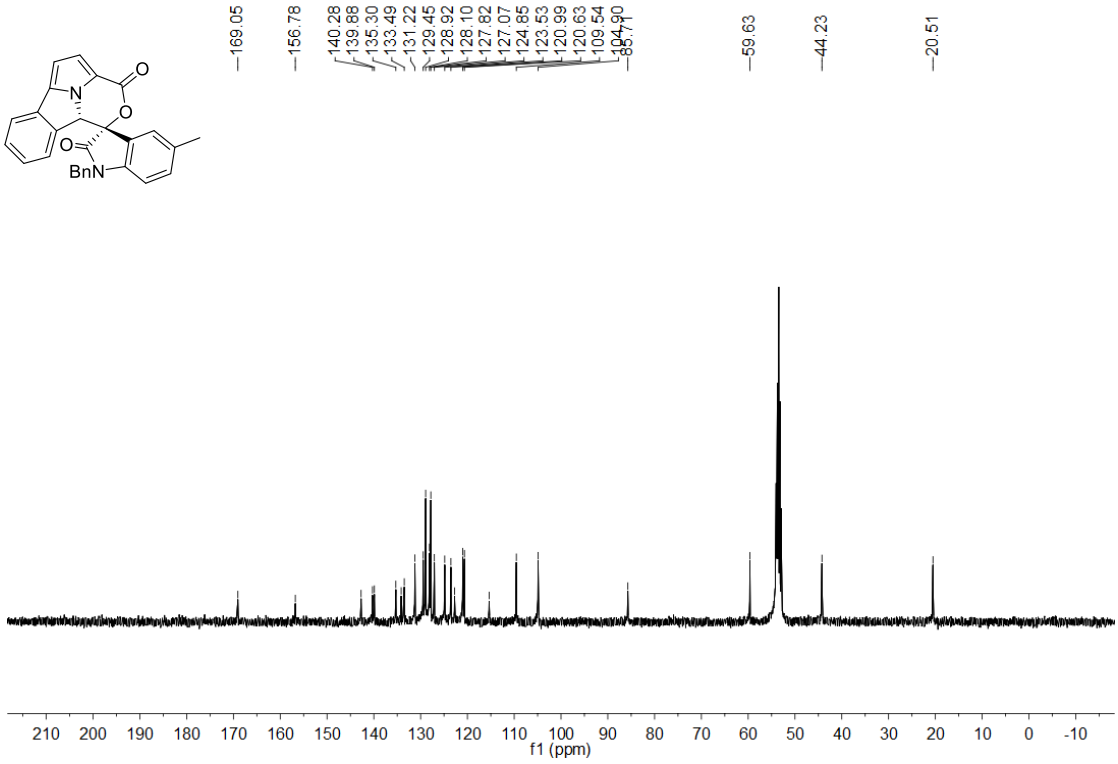
^{13}C NMR spectrum **3g** in CD_2Cl_2 (101 MHz)



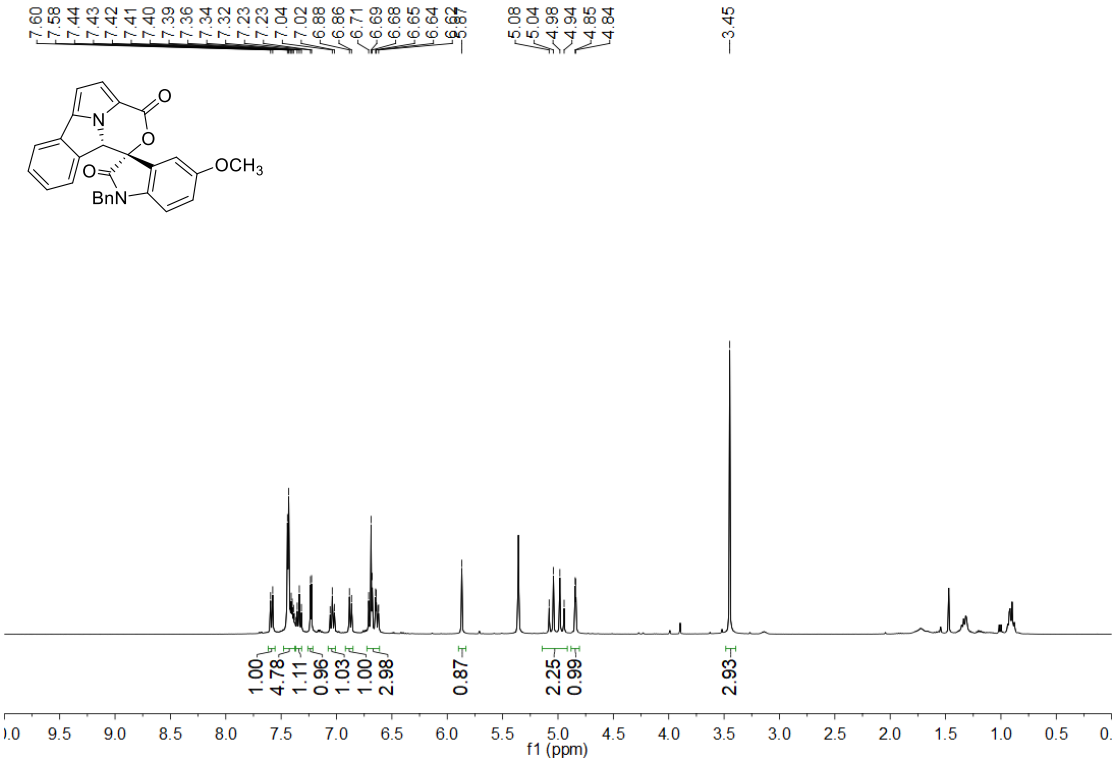
^{1}H NMR spectrum **3h** in CD_2Cl_2 (400 MHz)



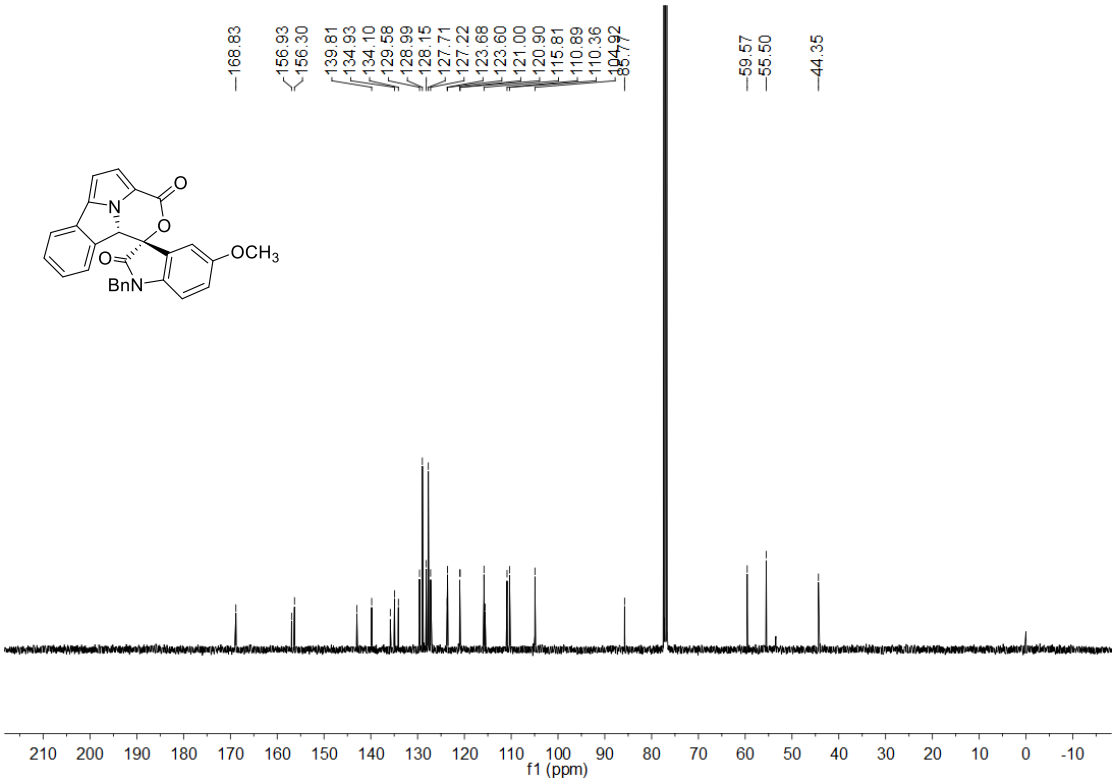
^{13}C NMR spectrum **3h** in CD_2Cl_2 (101 MHz)



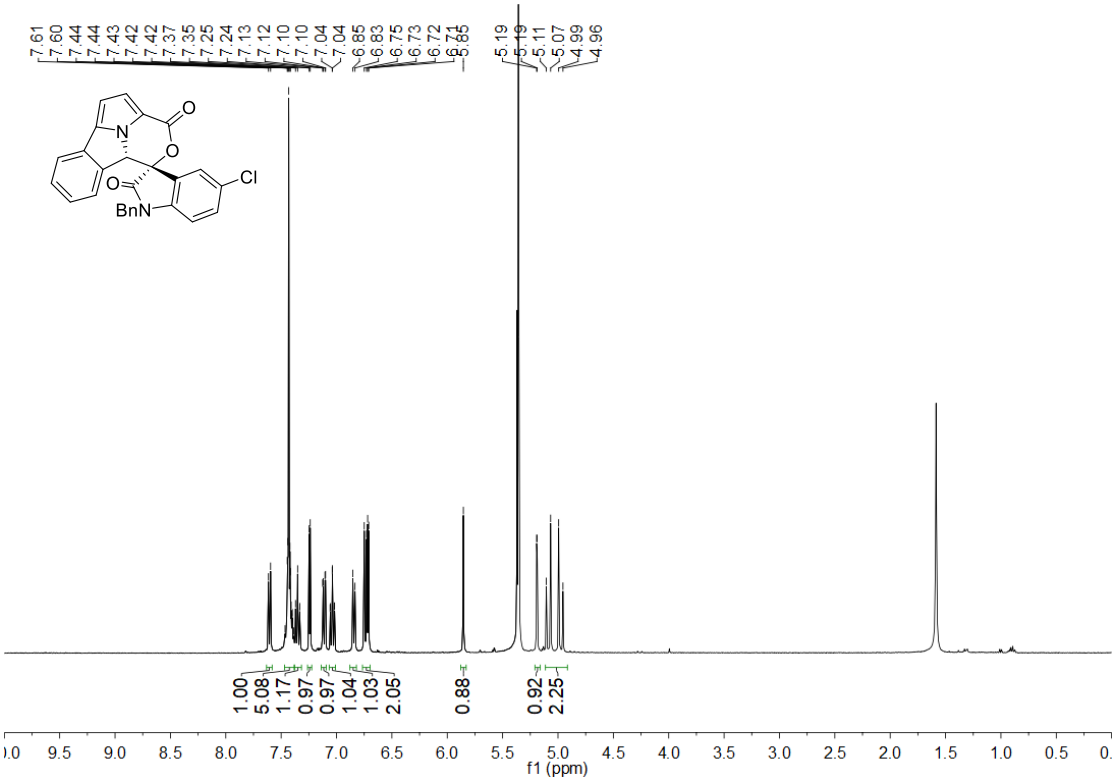
^{1}H NMR spectrum **3i** in CD_2Cl_2 (400 MHz)



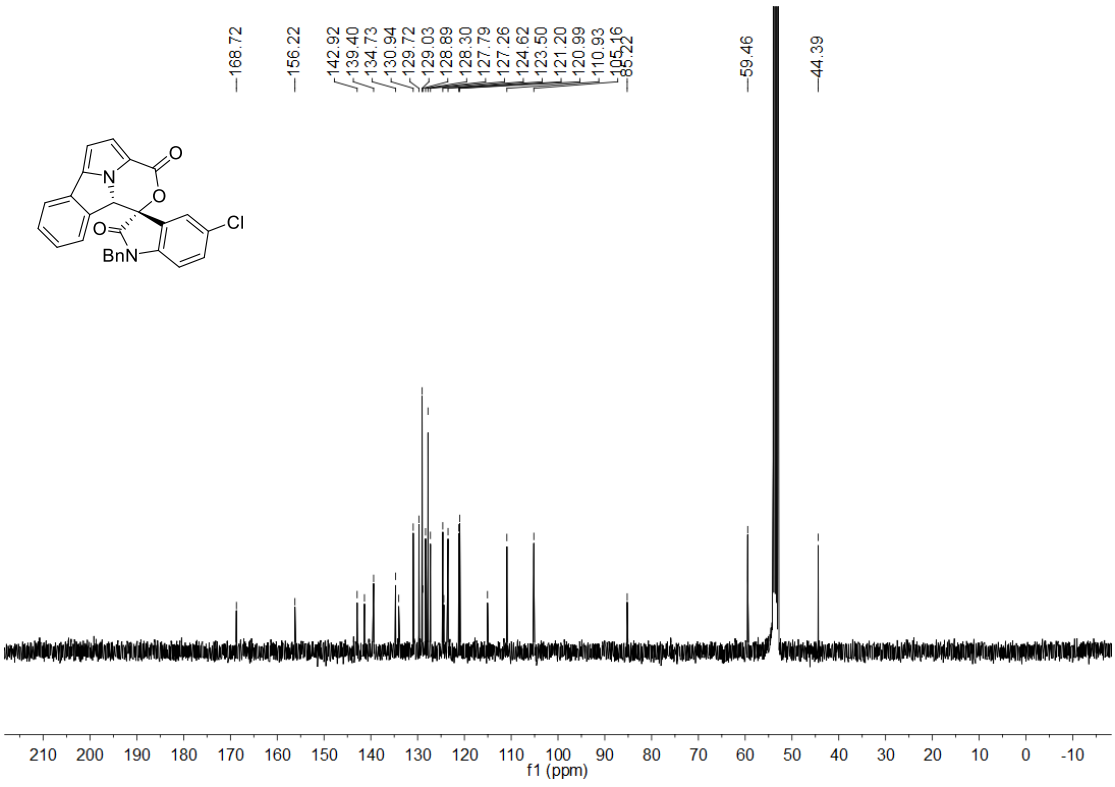
^{13}C NMR spectrum **3i** in $CDCl_3$ (101 MHz)



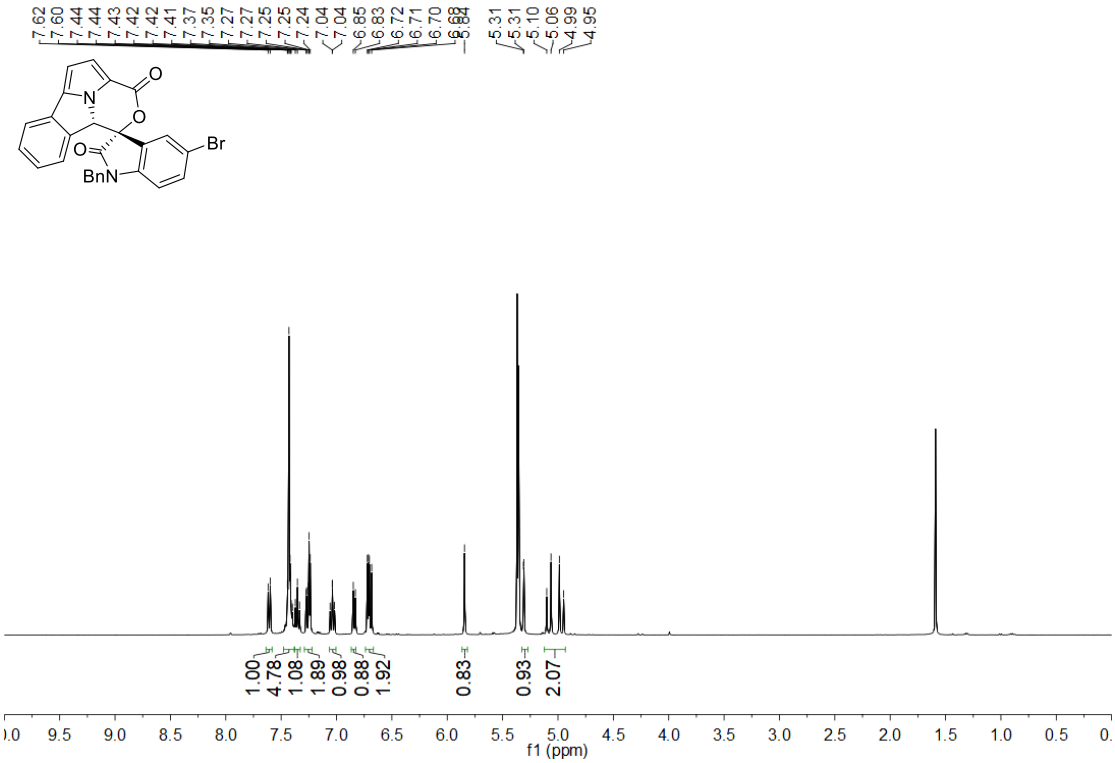
^{1}H NMR spectrum **3j** in CD_2Cl_2 (400 MHz)



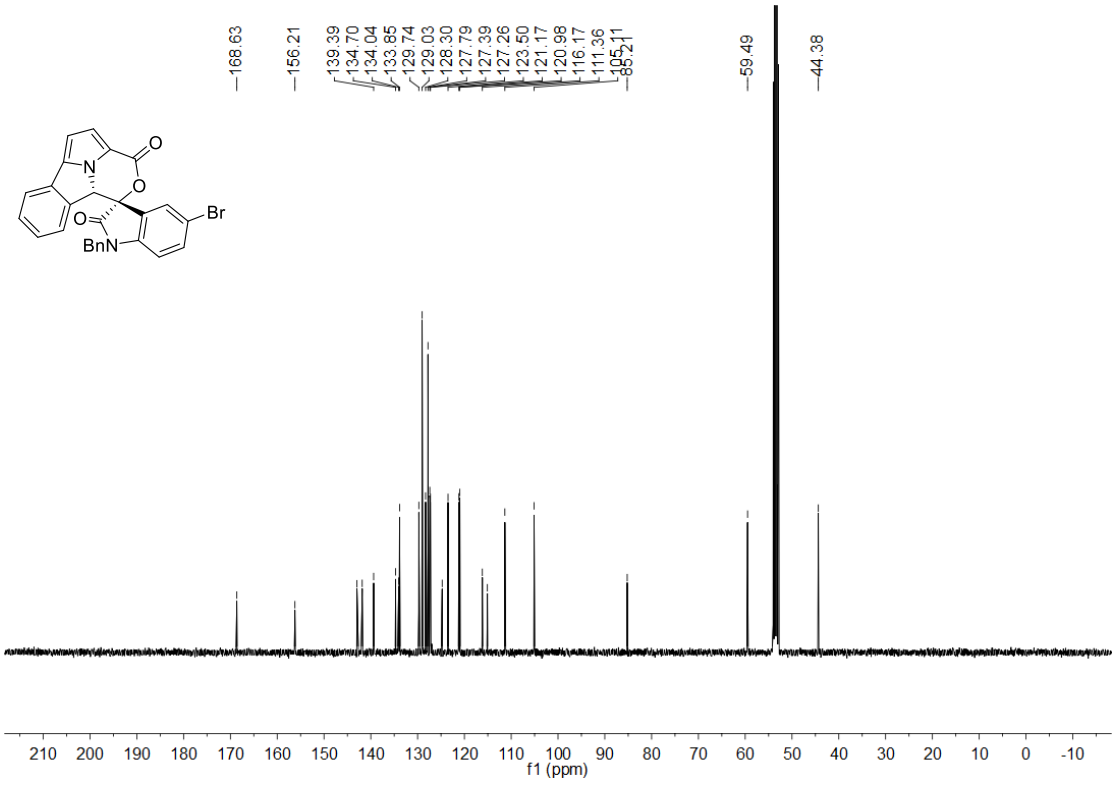
^{13}C NMR spectrum **3j** in CD_2Cl_2 (101 MHz)



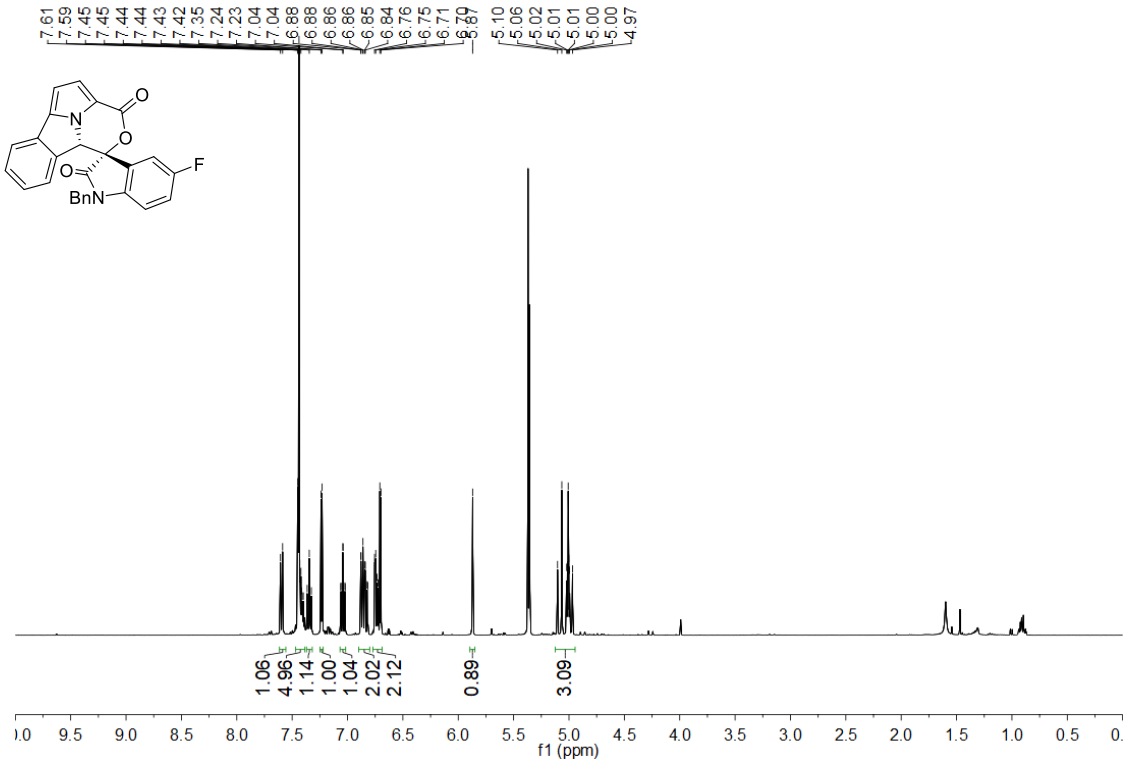
^{1}H NMR spectrum **3k** in CD_2Cl_2 (400 MHz)



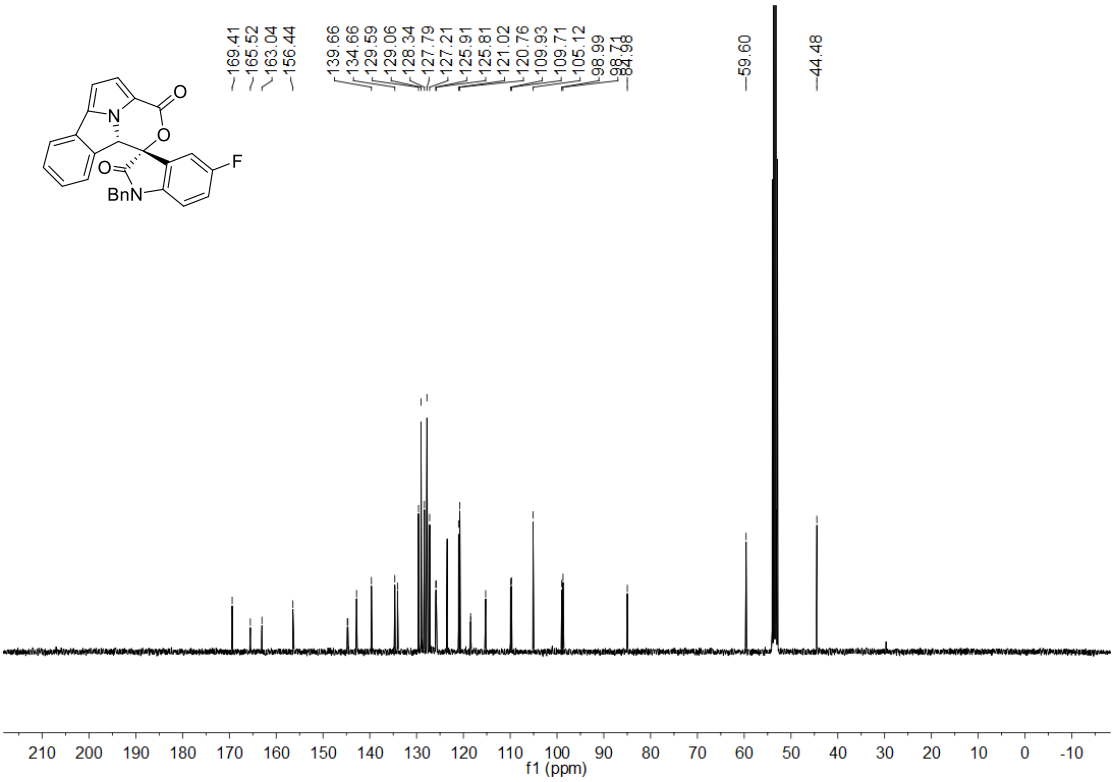
^{13}C NMR spectrum **3k** in CD_2Cl_2 (101 MHz)



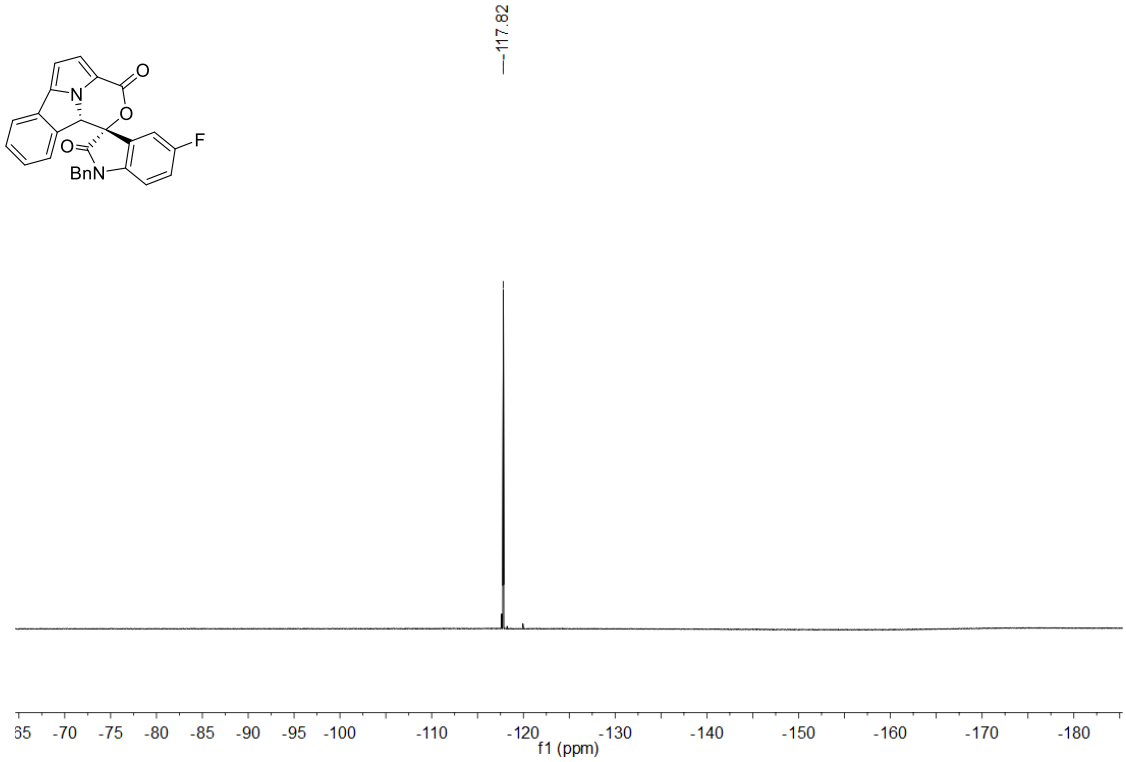
^{1}H NMR spectrum **3l** in CD_2Cl_2 (400 MHz)



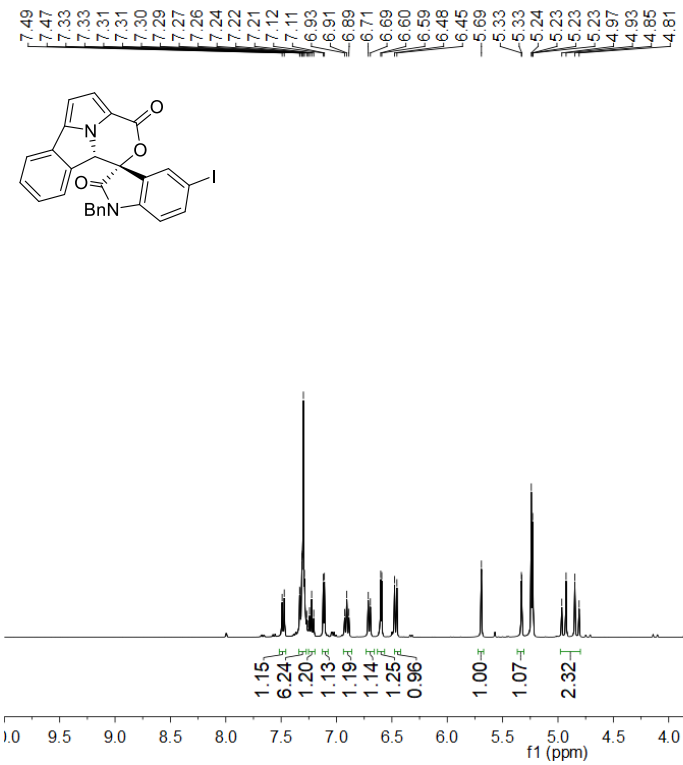
^{13}C NMR spectrum **3l** in CD_2Cl_2 (101 MHz)



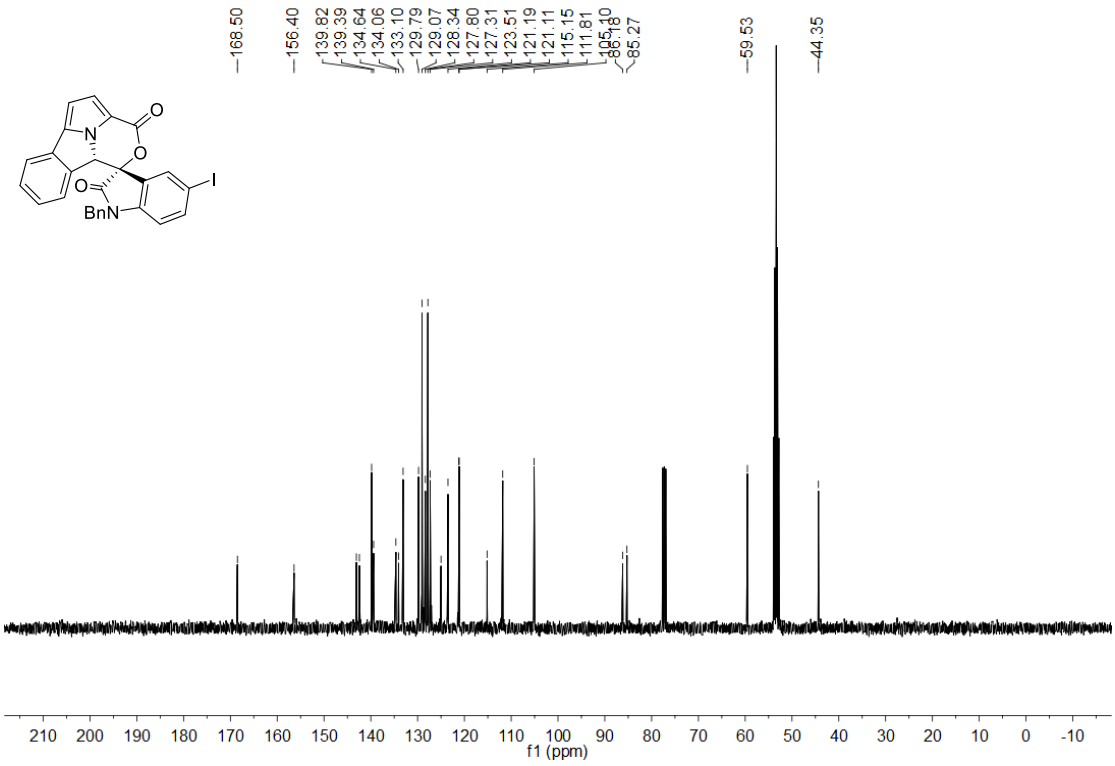
^{19}F NMR spectrum **3l** in CD_2Cl_2 (377 MHz)



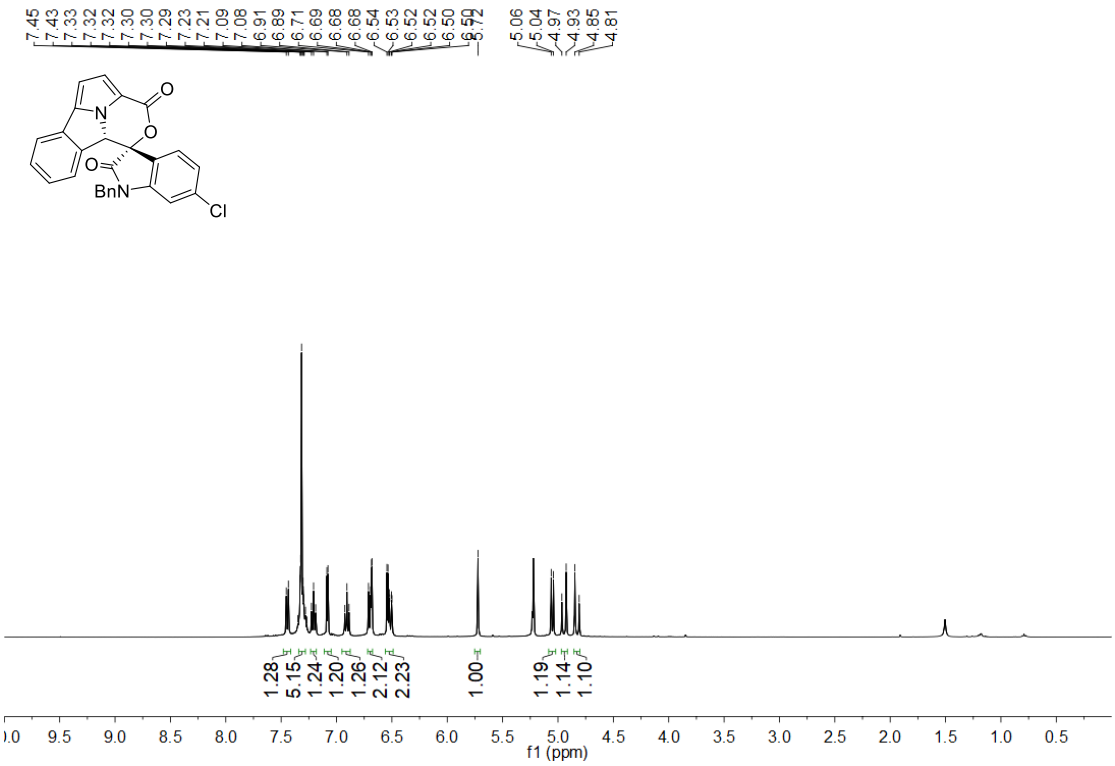
^{1}H NMR spectrum **3m** in CD_2Cl_2 (400 MHz)



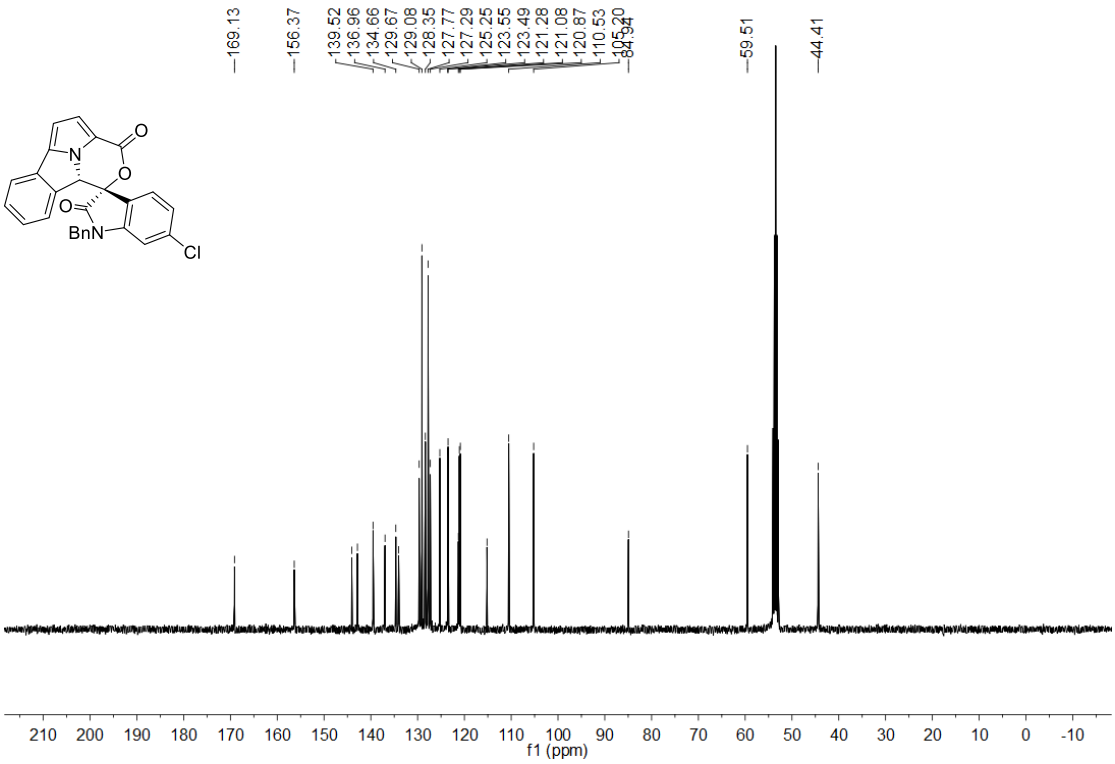
^{13}C NMR spectrum **3m** in CD_2Cl_2 (101 MHz)



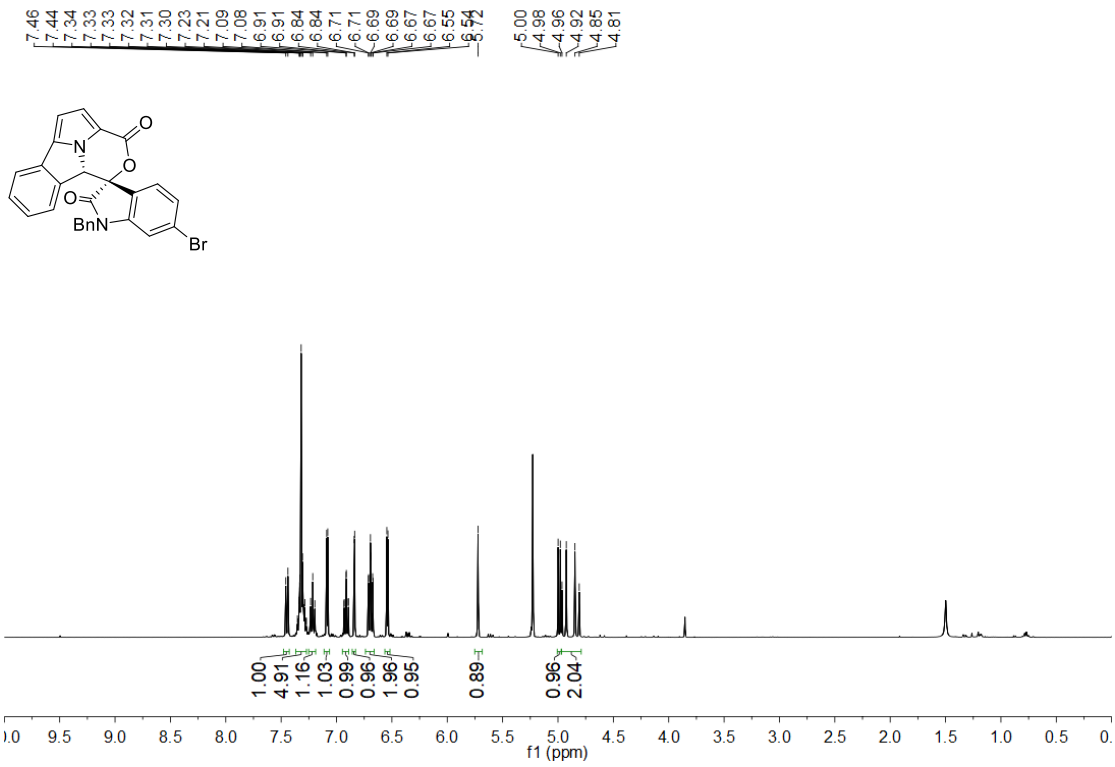
^{1}H NMR spectrum **3n** in CD_2Cl_2 (400 MHz)



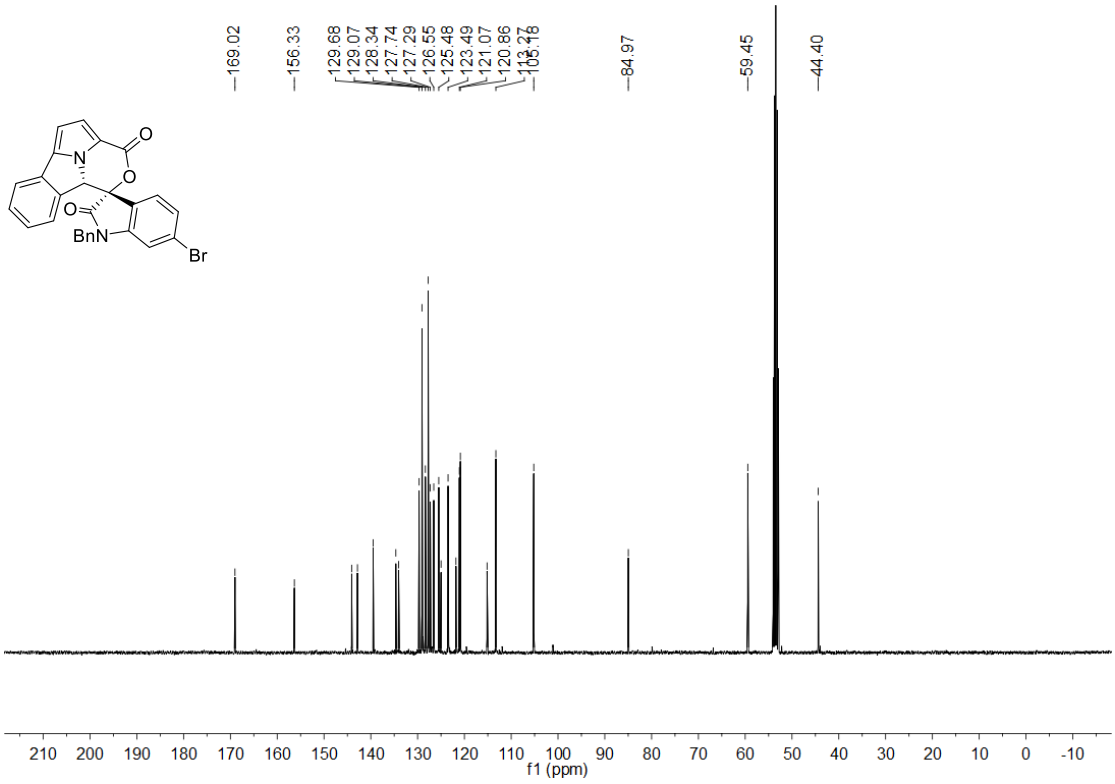
^{13}C NMR spectrum **3n** in CD_2Cl_2 (101 MHz)



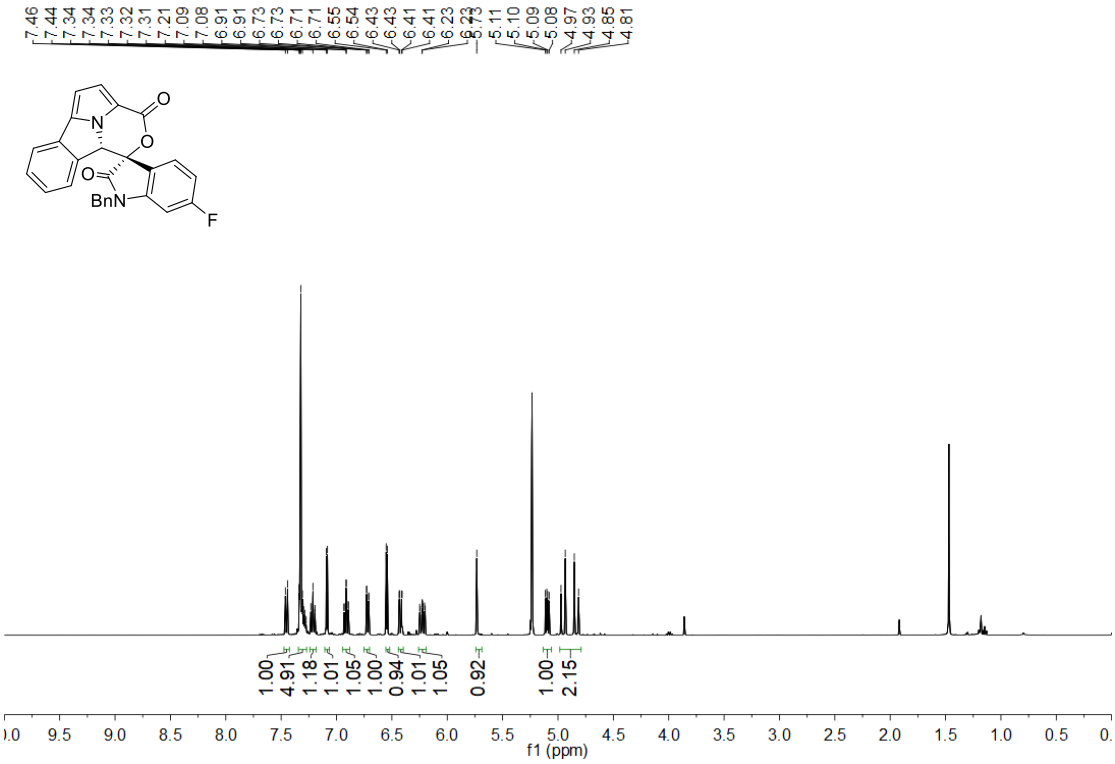
^{1}H NMR spectrum **3o** in CD_2Cl_2 (400 MHz)



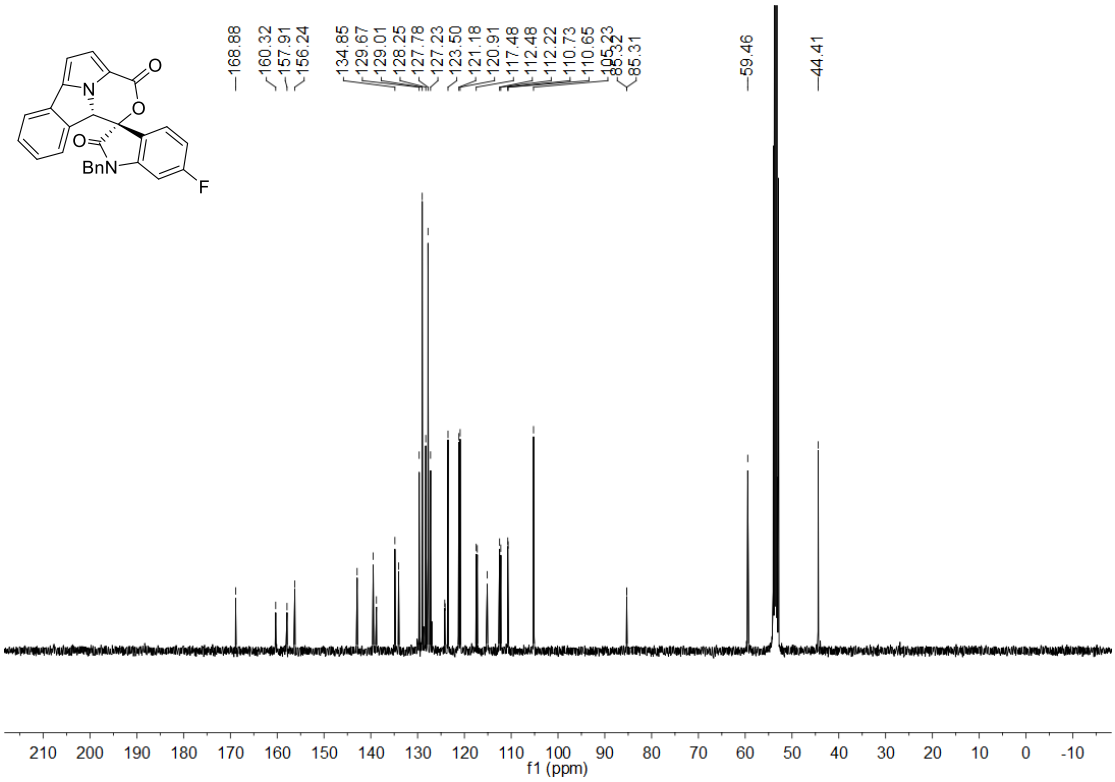
^{13}C NMR spectrum **3o** in CD_2Cl_2 (101 MHz)



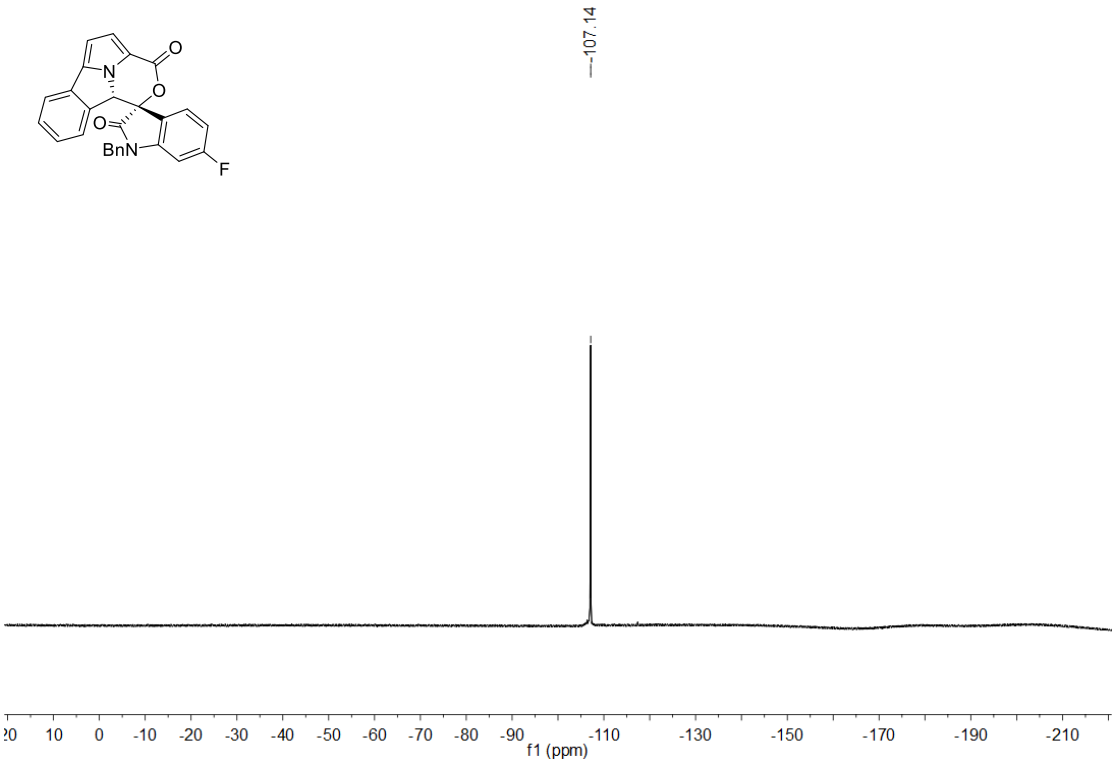
^{1}H NMR spectrum **3p** in CD_2Cl_2 (400 MHz)



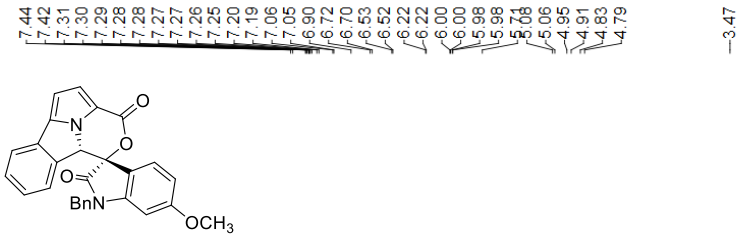
^{13}C NMR spectrum **3p** in CD_2Cl_2 (101 MHz)

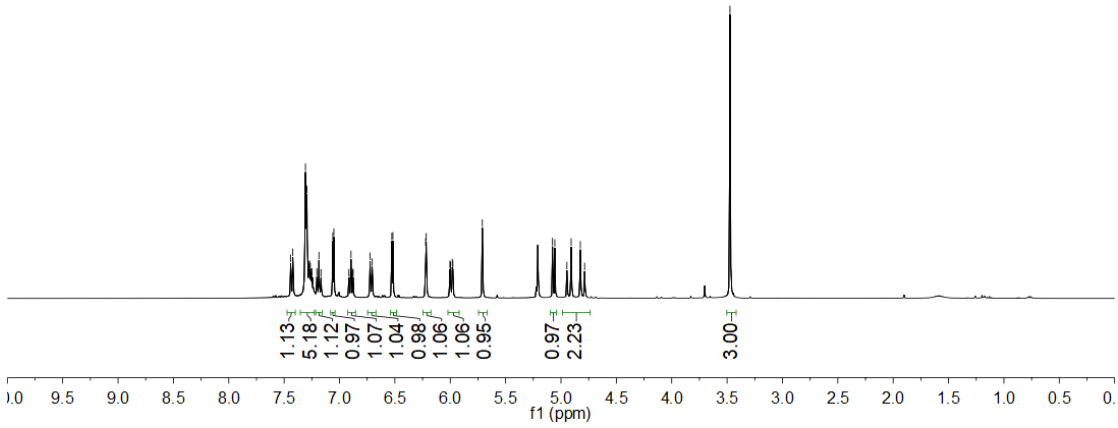


^{19}F NMR spectrum **3p** in $CDCl_3$ (377 MHz)

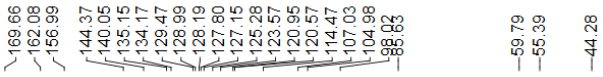


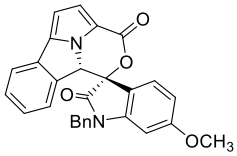
^{1}H NMR spectrum **3q** in CD_2Cl_2 (400 MHz)

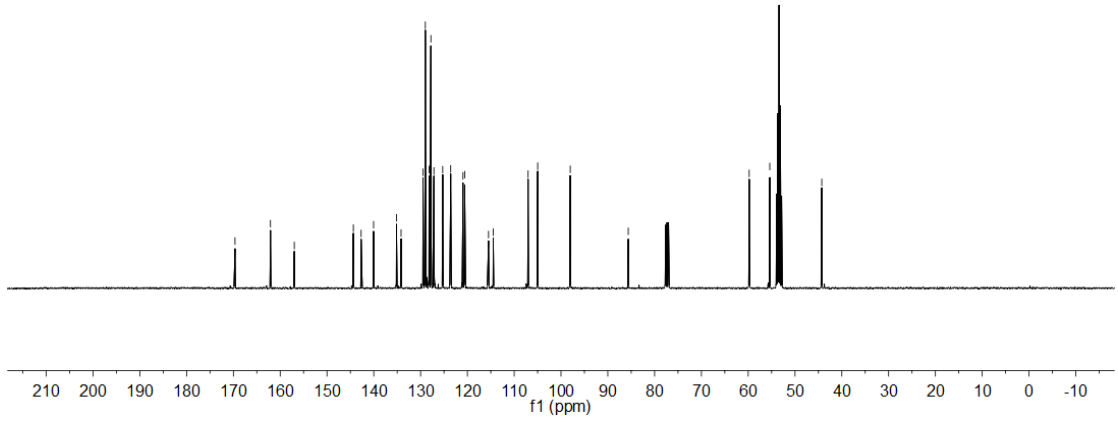




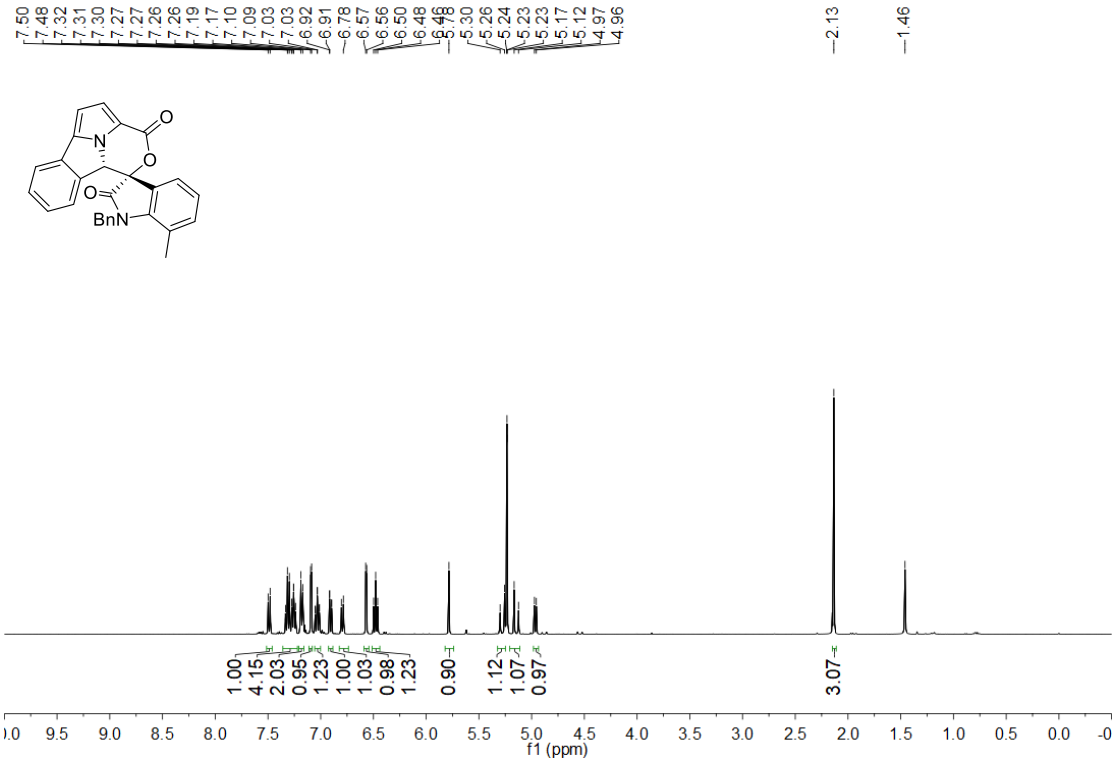
^{13}C NMR spectrum **3q** in CD_2Cl_2 (101 MHz)



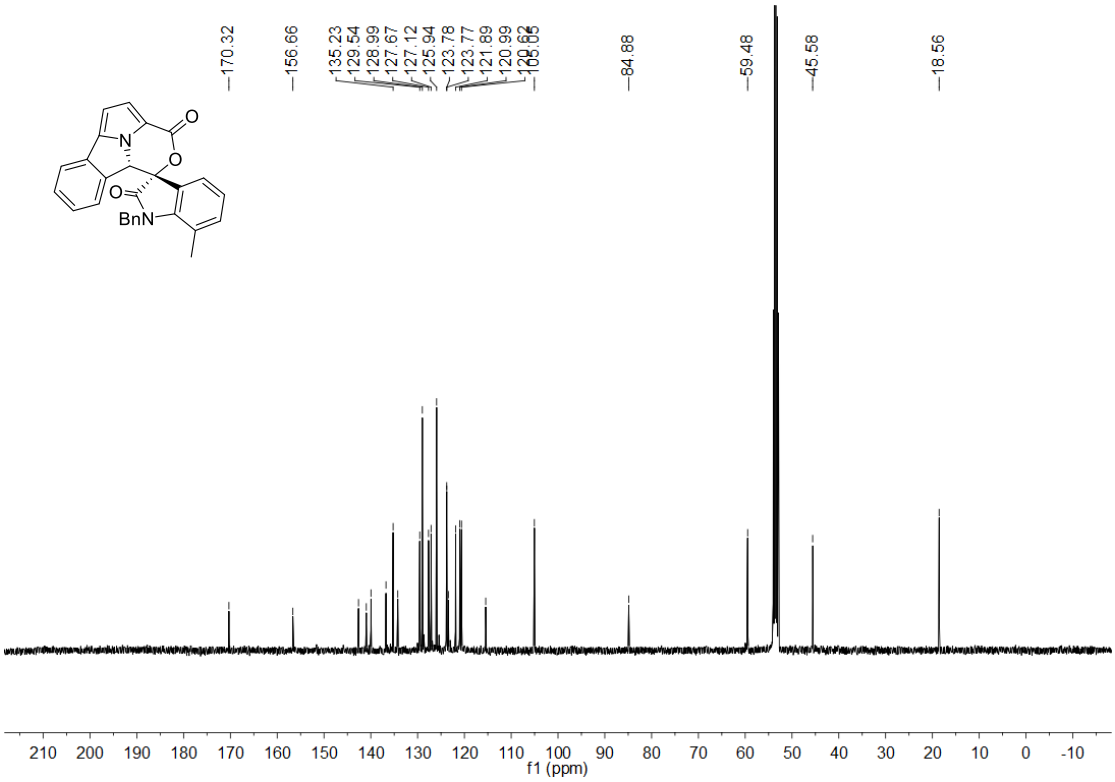




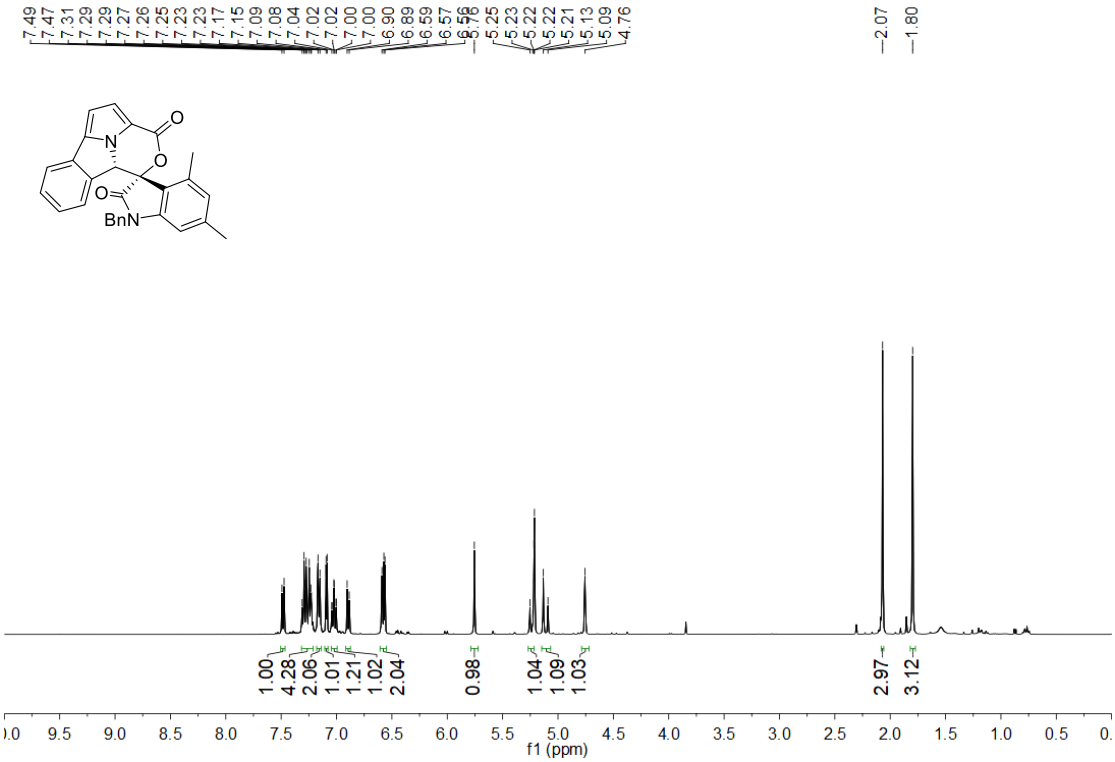
^{1}H NMR spectrum **3r** in CD_2Cl_2 (400 MHz)



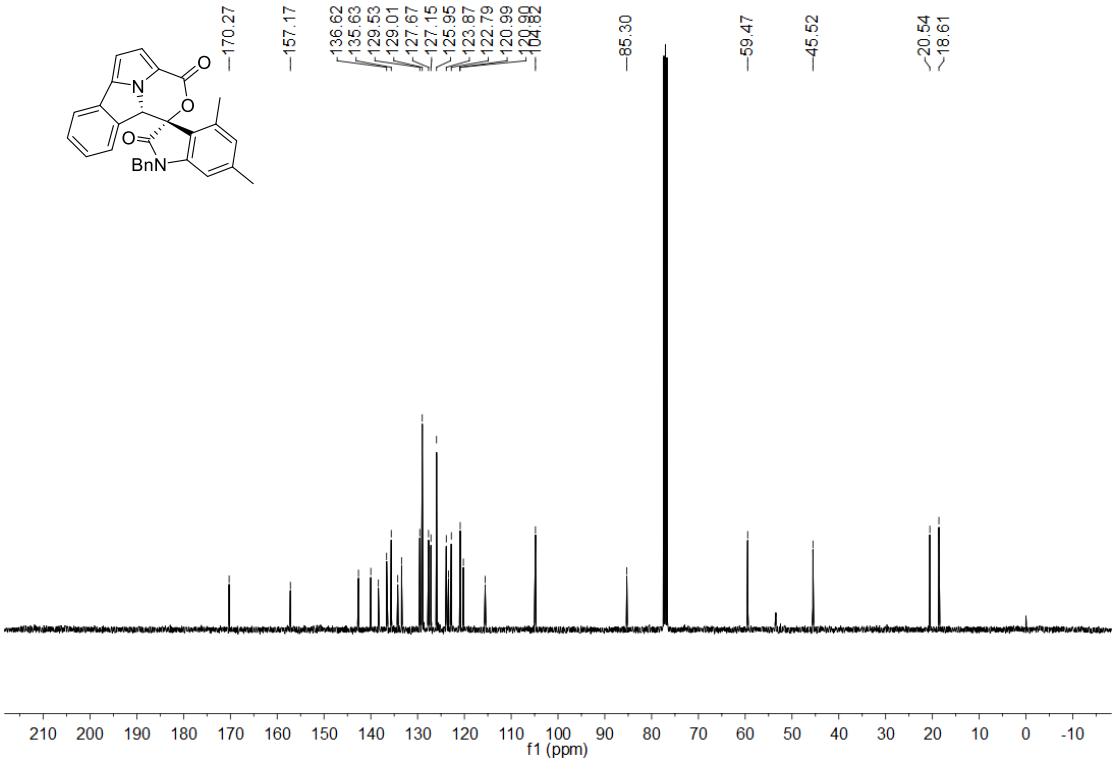
^{13}C NMR spectrum **3r** in CD_2Cl_2 (101 MHz)



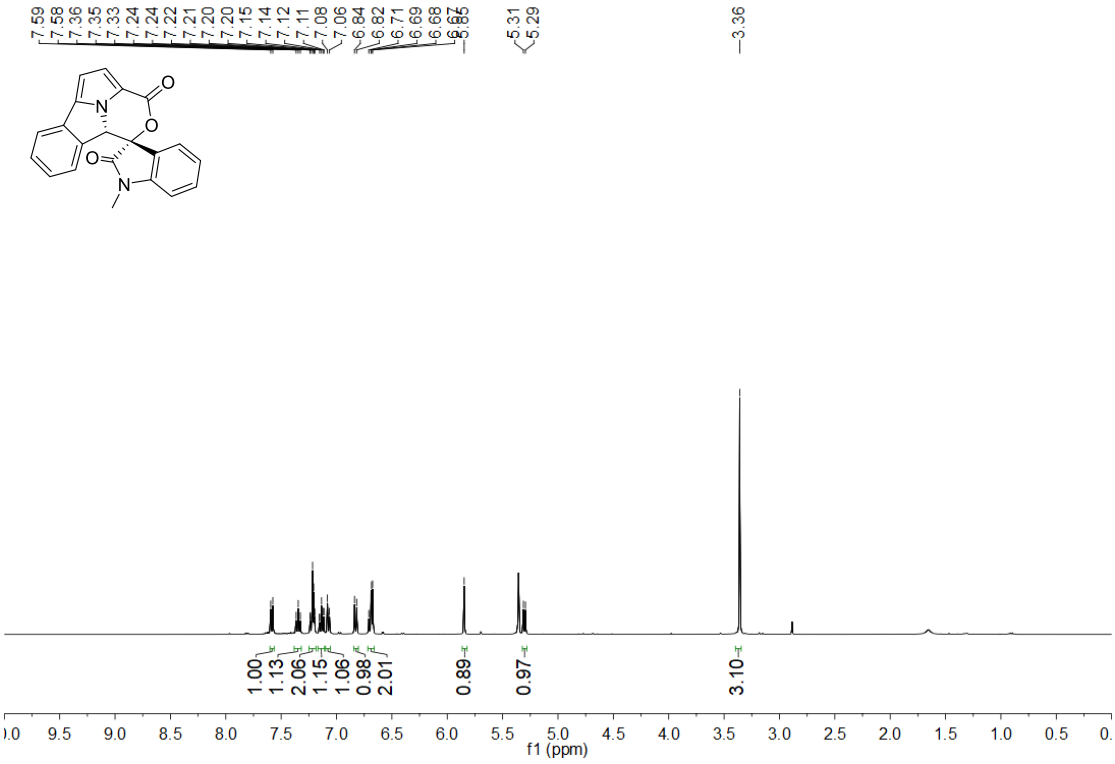
^{1}H NMR spectrum **3s** in CD_2Cl_2 (400 MHz)



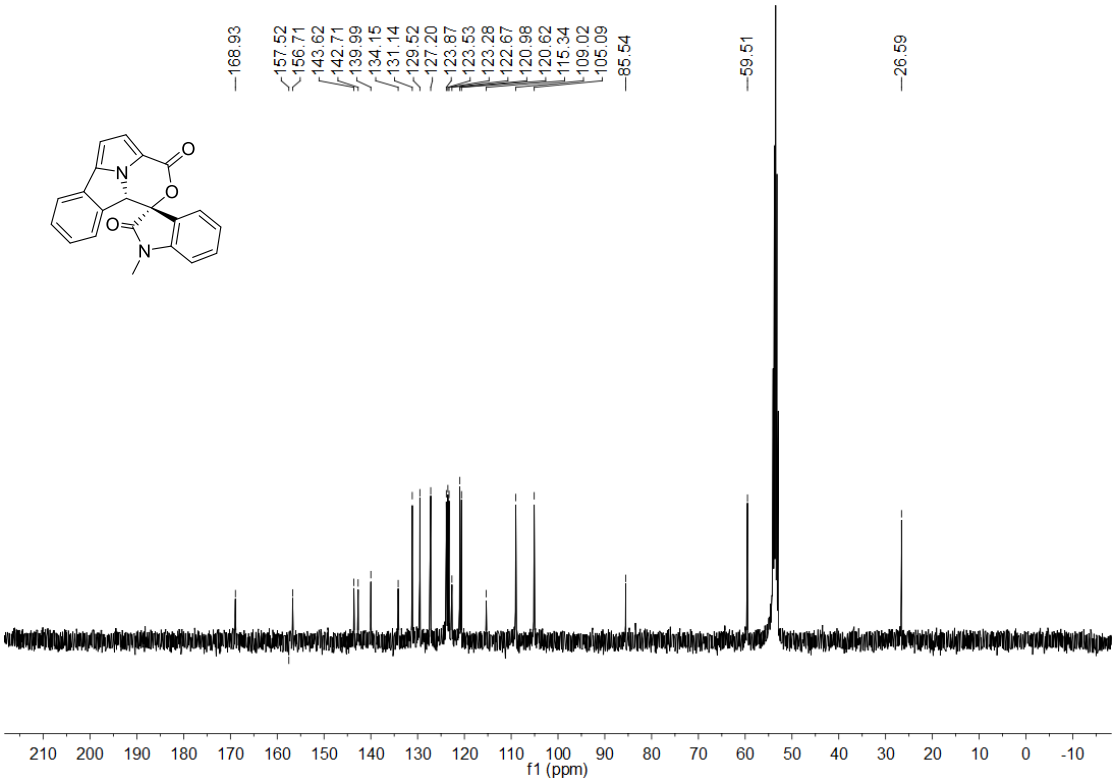
^{13}C NMR spectrum **3s** in $CDCl_3$ (101 MHz)



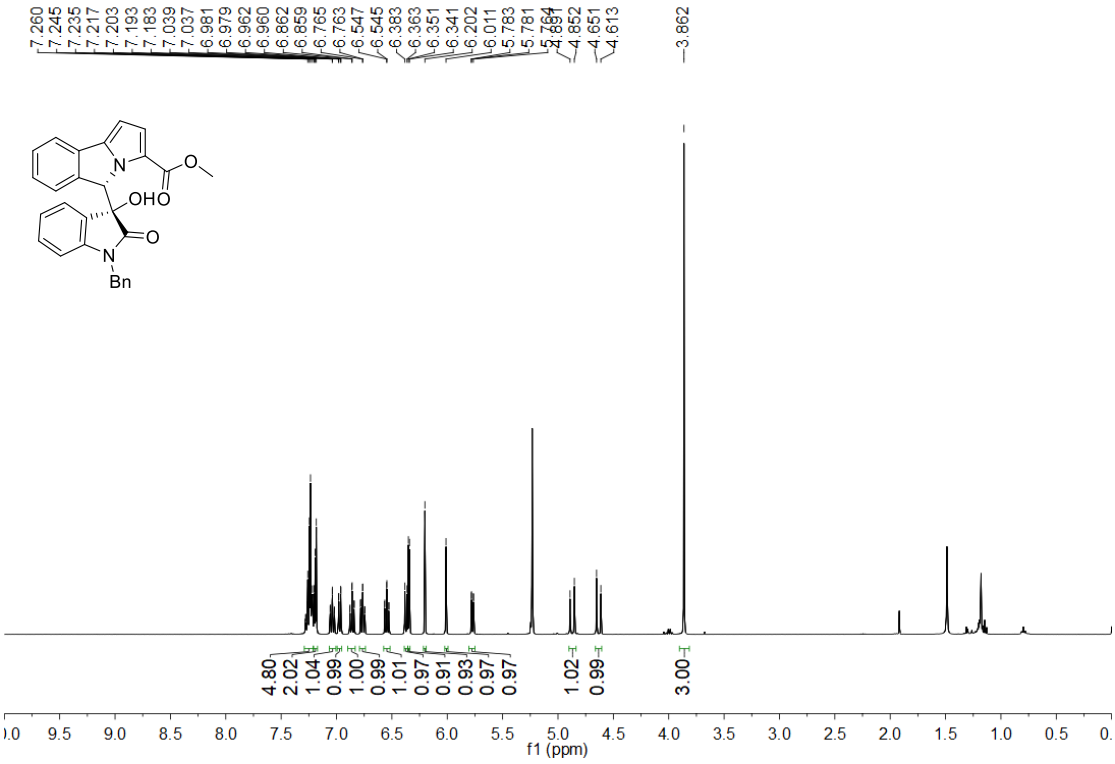
^{1}H NMR spectrum **3t** in CD_2Cl_2 (400 MHz)



^{13}C NMR spectrum **3t** in CD_2Cl_2 (101 MHz)



^{1}H NMR spectrum **4** in CD_2Cl_2 (400 MHz)



^{13}C NMR spectrum **4** in CD_2Cl_2 (101 MHz)