Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Organocatalytic asymmetric [3+3] annulations of 3-carboxamide oxindoles with *β,γ*-unsaturated *α*-keto esters: facile access to chiral spiro-*δ*-lactam oxindoles

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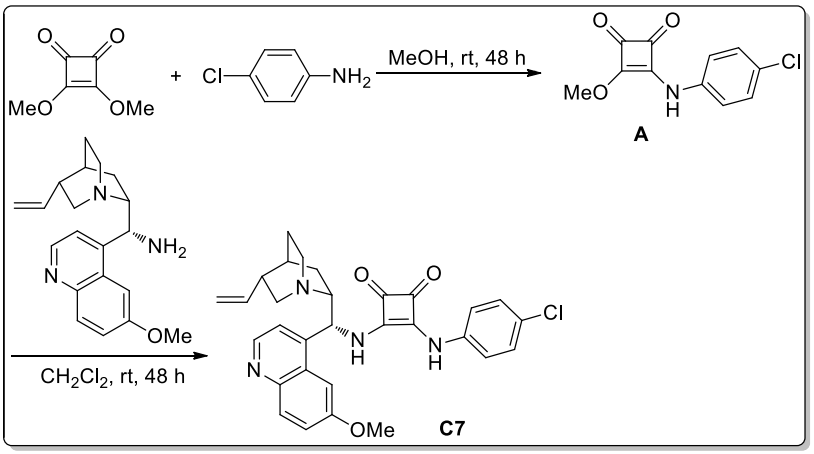
1. General information

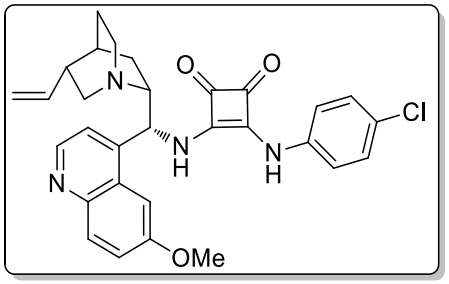
Unless otherwise indicated, all reactions were carried out under an argon atmosphere using standard Schlenk-Lines. Column chromatography was performed on silica gel (200−300 mesh) eluting with ethyl acetate and petroleum ether. ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra were recorded at 100 MHz (Bruker Avance II 400) with $CDCl_3$ or DMSO-d_6 as solvents. Chemical shifts are reported in parts per million (ppm) down field from TMS with the solvent resonance as the internal standard. Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplications. HRMS was recorded on a Bruker micrOTOF-Q II mass spectrometer and a Waters UPLC-QTOT-MS (Xevo G2-XS). Enantiomeric excess (*ee*) were determined by HPLC analysis on a Shimadzu LC-20A. Optical rotation data were examined in CH_2Cl_2 solution at 25 ℃.

All solvents were purified by using standard methods prior to use. 3-Carboxamide oxindoles **1a-1k** were prepared by previously reported method.[1] *β*,*γ*-Unsaturated *α*-keto esters **2** were prepared according to the reported procedure.[2] Catalysts **C1**, **C2**, **C4** and **C12-C14** were purchased from commercial sources. Thiourea catalysts **C3** and **C9-C11** were prepared according to the method reported in the literature.[3] Squaramide catalysts **C5**, **C6**, **C8** and **C15-C18** were prepared according to the method previously described.[4] All other reagents were purchased from commercial sources and used without further purification.

2. Preparation of new squaramide catalyst C7

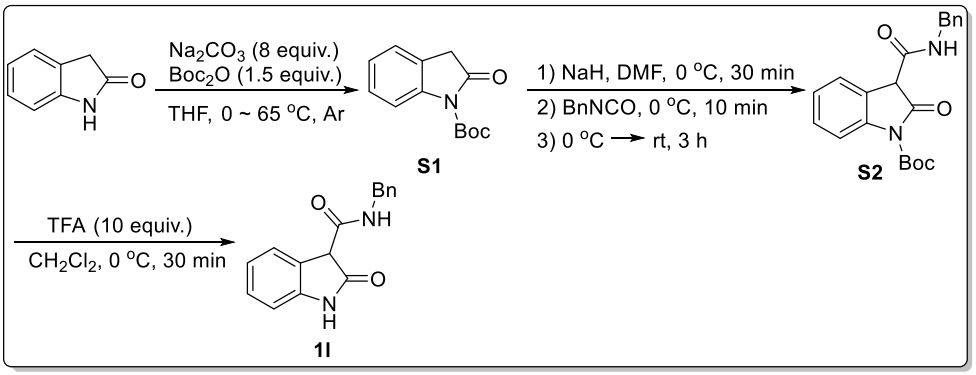


To a solution of 3,4-dimethoxycyclobut-3-ene-1,2-dione (213.2 mg, 1.5 mmol) in MeOH (5 mL) was added *p*-chloroaniline (190.5 mg, 1.5 mmol) in MeOH (2 mL). The reaction mixture was stirred at room temperature for 48 h and then concentrated in vacuo to afford the intermediate **A** as a solid without further purification. To a solution of **A** (71.1 mg, 0.3 mmol) in CH_2Cl_2 (4 mL) was added a solution of quinidine amine (106.7 mg, 0.33 mmol) in CH_2Cl_2 (1 mL). After 48 h, the reaction mixture was concentrated and the residue was subjected to flash chromatograph (DCM/MeOH 20:1) on silica gel to afford the corresponding squaramide catalyst **C7**.



3-((4-chlorophenyl)amino)-4-(((*R*)-(6-methoxyquinolin-4-yl)((*1S*,*2R*,*4S*,*5R*)-5-vinylquinuclidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione (C7): The desired catalyst was obtained as a white solid (96.8 mg, 61% yield); $[\alpha]_D^{25}$ = +0.726 (c 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, DMSO-d_6)** δ 9.74 (s, 1H), 8.83 (s, 1H), 8.17 (s, 1H), 7.98 (d, *J* = 9.2 Hz, 1H), 7.76-7.67 (m, 2H), 7.46-7.34 (m, 5H), 6.11-5.82 (m, 2H), 5.21 (d, *J* = 17.6 Hz, 1H), 5.09 (d, *J* = 10.8 Hz, 1H), 3.95 (s, 3H), 3.20-3.14 (m, 1H), 3.00-2.78 (m, 4H), 2.26-2.22 (m, 1H), 1.57-1.48 (m, 3H), 1.13-1.07 (m, 1H), 0.92-0.83 (m, 1H). **^{13}C NMR (100 MHz, DMSO-d_6)** δ 184.66, 180.25, 168.70, 163.61, 158.35, 148.21, 144.75, 143.74, 141.25, 138.21, 131.97, 129.60, 127.94, 127.13, 122.56, 120.24, 119.91, 114.89, 101.64, 59.26, 56.07, 56.00, 49.45, 46.09, 38.97, 27.68, 26.63, 25.69. **HRMS *m/z* (ESI):** calcd for $C_{30}H_{30}ClN_4O_3^+$ $[M+H]^+$: 529.2006, found 529.1977.

3. Preparation of substrates 1l and 1m

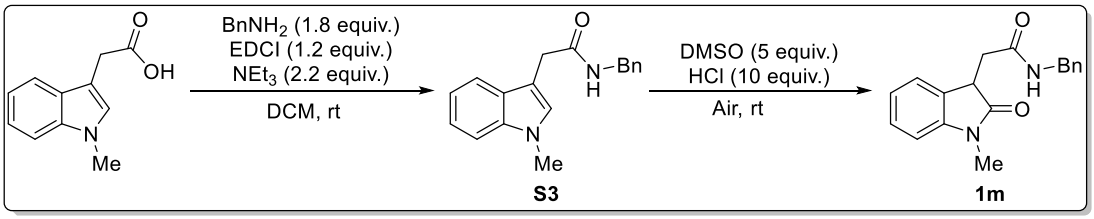


An over-dried round-bottom flask was charged with 2-oxindole (1.33 g, 10.0 mmol, 1.0 equiv.) in dry THF (40 mL) under argon atmosphere. After the resultant solution was cooled to 0 ℃, Na_2CO_3 (8.48 g, 80 mmol, 8.0 equiv.) and Boc_2O (3.27 g, 15.0 mmol, 1.5 equiv.) were added and the resulted mixture was stirred at 65 ℃ for 8 hours. The reaction was quenched with ice-water and diluted with 40 mL of EtOAc. The organic layer was dried by Na_2SO_4 and concentrated after the filtration in a rotary evaporator under vacuum. The residue was purified by flash chromatography to afford the corresponding **S1** as a white solid**.**

To a stirred suspension of sodium hydride (0.24 g, 6.0 mmol, 1.2 equiv., 60% dispersion in mineral oil) in dry DMF (5 mL) at 0 ℃ under argon atmosphere was added **S1** (1.17 g, 5.0 mmol, 1.0 equiv.) in small portions. The mixture was stirred for 30 minutes at 0 ℃. Isocyanatobenzene (0.80 g, 6.0 mmol, 1.2 equiv.) was slowly added, and this reaction was maintained at 0 ℃ for 10 minutes and further stirred at room temperature for 3 h (monitored by TLC). The reaction mixture was then poured into ice-cooled water (100 mL) and was acidized with HCl (1 M) to pH 4-6. The desired products **S2** were obtained after filtration and washed with ether.

The **S2** (1.09 g, 3 mmol, 1.0 equiv.) was dissolved in **10 mL** CH_2Cl_2 and cooled to 0 ℃. TFA (2.3 mL, 30 mmol, 10.0 equiv) was added dropwise and the resulting mixture was stirred at 0 ℃ for 30 min. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography to afford the **ll** as white solid (0.34g, 42% yield). ^{1}H NMR (**400 MHz, DMSO-*d*$_6$**) δ 10.55 (s, 1H), 8.87 (dd, *J* = 6.0, 6.0 Hz, 1H), 7.37-7.30 (m, 4H), 7.27 (dd, *J* = 9.6, 6.8 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.95 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 4.46 (s, 1H), 4.35 (d, *J* = 6.0 Hz, 2H). ^{13}C NMR (**100 MHz, DMSO-*d*$_6$**) δ 174.44, 166.63, 143.88, 139.45, 128.82, 127.65, 127.37, 126.93, 124.77, 121.96, 109.90, 53.84, 42.89.

HRMS *m/z* **(ESI):** calcd for $C_{16}H_{14}N_2O_2Na^+$ $[M+Na]^+$: 289.0947, found 289.0957.

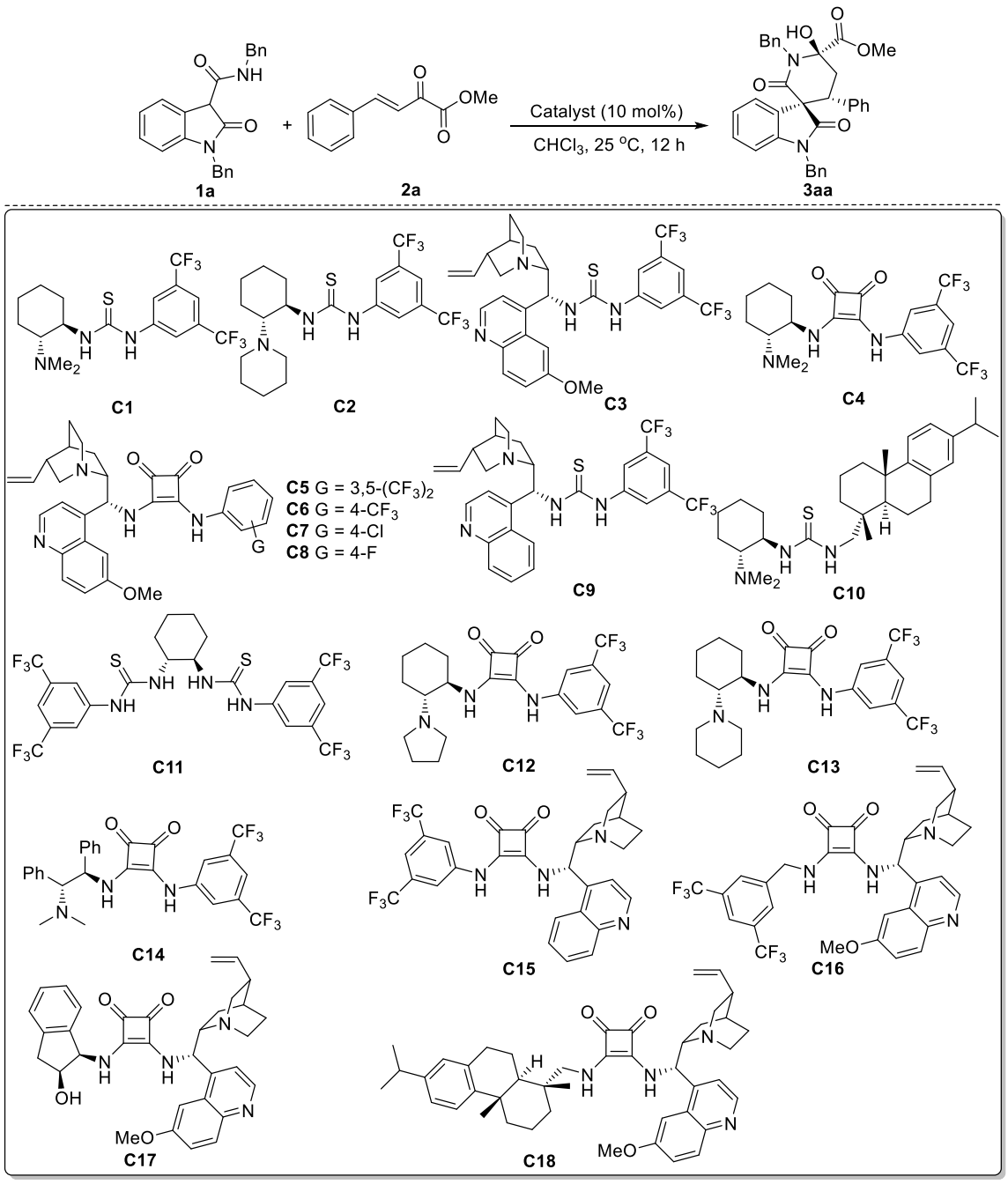


To a 50 mL round bottom flask was added *N*-Me-indole acetic acid (1.89 g, 10 mmol, 1.0 equiv.) and CH_2Cl_2 (30 mL). Then, Et_3N (3 mL, 22 mmol; 2.2 equiv.) was added, followed by EDCI (2.16 g, 12 mmol; 1.2 equiv.). The mixture was allowed to stir for a few minutes, and then the benzylamine (2 mL, 18 mmol, 1.8 equiv.) was added. Upon consumption of starting material, the reaction was diluted with water. The mixture was poured into a separatory funnel and washed with 1.0 M NaOH several times and brine and dried over Na_2SO_4. The residue was purified by flash column chromatography to give **S3**.

To a solution of **S3** (1.06 g, 3.8 mmol, 1.0 equiv.) in DMSO (1.3 mL, 19 mmol, 5.0 equiv.) at ambient temperature was added dropwise 12.1 M HCl (10.5 mL, 38 mmol, 10.0 equiv.). After the oxidation was completed, the reaction mixture was neutralized with saturated $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography to give **1m** as a white solid (0.90g, 82% yield). ^{1}H NMR (**400 MHz, $CDCl_3$**) δ 7.32-7.22 (m, 7H), 7.06-7.00 (m, 2H), 6.80 (d, *J* = 7.6 Hz, 1H), 4.51-4.35 (m, 2H), 3.82 (t, *J* = 6.8 Hz, 1H), 3.14 (s, 3H), 2.91 (dd, *J* = 15.2, 5.6 Hz, 1H), 2.57 (dd, *J* = 15.2, 7.6 Hz, 1H). ^{13}C NMR (**100 MHz, $CDCl_3$**) δ 177.60, 170.12, 143.93, 138.28, 128.65, 128.30, 128.28, 127.77, 127.39, 124.27, 122.76, 108.17, 43.66, 42.31, 37.07, 26.30. **HRMS** *m/z* **(ESI):** calcd for $C_{18}H_{19}N_2O_2^+$ $[M+H]^+$: 295.1441, found 295.1439.

4. Reaction optimization

Table S1. Reaction optimization[a]

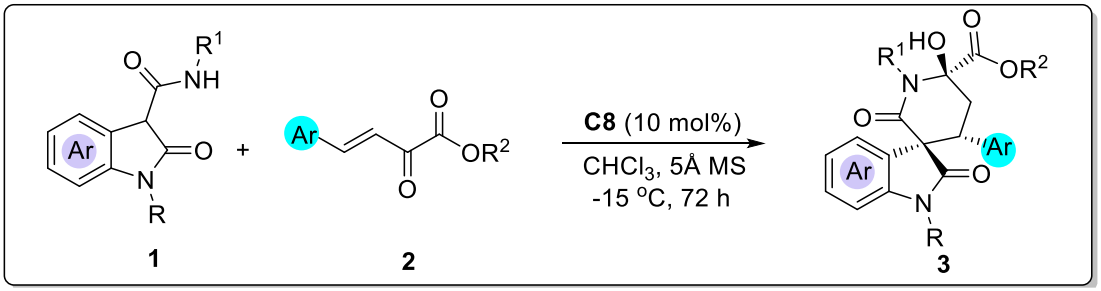


Entry	Catalyst	Solvent	temperature	Time	Yield(%)[b]	*dr*[c]	*ee*(%)[d]
1	**C1**	$CHCl_3$	25	12	78	>95:5	24
2	**C2**	$CHCl_3$	25	12	71	>95:5	6
3	**C3**	$CHCl_3$	25	12	73	>95:5	54

4	**C4**	$CHCl_3$	25	12	67	>95:5	40
5	**C5**	$CHCl_3$	25	12	71	>95:5	46
6	**C6**	$CHCl_3$	25	12	68	>95:5	61
7	**C7**	$CHCl_3$	25	12	75	>95:5	78
8	**C8**	$CHCl_3$	25	12	80	>95:5	80
9	**C9**	$CHCl_3$	25	12	73	>95:5	52
10	**C10**	$CHCl_3$	25	12	66	>95:5	8
11	**C11**	$CHCl_3$	25	12	trace	-	-
12	**C12**	$CHCl_3$	25	12	64	>95:5	16
13	**C13**	$CHCl_3$	25	12	75	>95:5	40
14	**C14**	$CHCl_3$	25	12	70	>95:5	52
15	**C15**	$CHCl_3$	25	12	77	>95:5	-56
16	**C16**	$CHCl_3$	25	12	69	>95:5	-58
17	**C17**	$CHCl_3$	25	12	68	>95:5	-50
18	**C18**	$CHCl_3$	25	12	71	>95:5	-35
19	**C8**	CH_2Cl_2	25	12	77	>95:5	60
20	**C8**	THF	25	12	79	>95:5	49
21	**C8**	CH_3CN	25	12	76	>95:5	18
22	**C8**	CH_3OH	25	12	71	>95:5	12
23	**C8**	$CHCl_3$	0	24	77	>95:5	86
24	**C8**	$CHCl_3$	-15	72	73	>95:5	89
25	**C8**	$CHCl_3$	-40	72	56	>95:5	77
26[e]	**C8**	$CHCl_3$	-15	72	trace	-	-
27[f]	**C8**	$CHCl_3$	-15	72	76	>95:5	65
28[g]	**C8**	**$CHCl_3$**	**-15**	**72**	**79**	**>95:5**	**91**

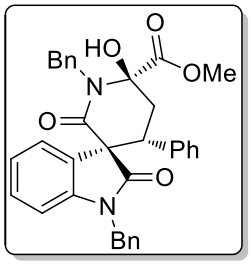
[a]Unless otherwise specified, reactions were carried out with **1a** (0.1 mmol), **2a** (0.14 mmol), and catalyst (10 mol%) in solvent (1 mL) at the specified temperature for the indicated time. [b]Yields of isolated products. [c]The diastereomeric ratio (*dr*) value was determined by ^{1}H NMR analysis of the crude products. [d]The enantiomeric excess (*ee*) value was determined by HPLC analysis. [e]3Å molecular sieve (50 mg) was used. [f]4Å molecular sieve (50 mg) was used. [g]5Å molecular sieve (50 mg) was used.

5. Chiral squaramide-catalyzed asymmetric [3+3] annulation



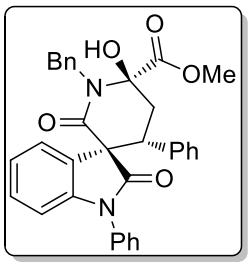
An argon purged reaction tube was charged with 3-carboxamide oxindoles **1** (0.1 mmol), *β*,*γ*-unsaturated *α*-keto esters **2** (0.14 mmol), catalyst **C8** (0.01 mmol) and 5Å molecular sieve (50 mg). Then, freshly distilled $CHCl_3$ (1 mL) was added and the reaction mixture was stirred at -15 ^oC for 72 h. After completion of the reaction, the crude product was purified by flash column chromatography on silica gel to afford the corresponding products **3**. The diastereomeric ratio was determined by crude ^1H NMR analysis and the enantiomeric excess was determined by chiral-phase HPLC analysis.

(*3R,4'R,6'R*)-methyl1,1'-dibenzyl-6'-hydroxy-2,2'-dioxo-4'-phenylspiro[indoline-3, 3'-piperidine]-6'-carboxylate (3aa)



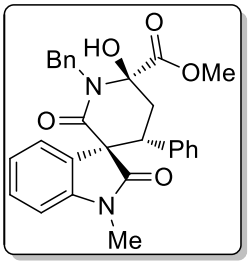
White solid; 43.1 mg, 79% yield; *dr* > 95:5; *ee* = 91%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, t_r(major) = 20.16 min, t_r(minor) = 14.72 min]; $[\alpha]_D^{25}$ = -92.4 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (d, *J* = 7.2 Hz, 1H), 7.29-7.04 (m, 13H), 6.91 (d, *J* = 7.6 Hz, 2H), 6.55 (d, *J* = 7.2 Hz, 2H), 6.39 (d, *J* = 7.6 Hz, 1H), 5.25 (d, *J* = 16.0 Hz, 1H), 5.04 (d, *J* = 16.0 Hz, 1H), 4.74 (s, 1H), 4.48 (d, *J* = 16.4 Hz, 1H), 4.42 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.13 (d, *J* = 15.6 Hz, 1H), 3.39 (t, *J* = 14.0 Hz, 1H), 3.31 (s, 3H), 2.21 (dd, *J* = 14.0, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.27, 172.06, 168.50, 144.23, 137.13, 136.89, 134.76, 129.34, 128.55, 128.52, 128.22, 128.19, 128.07, 127.87, 127.64, 127.20, 127.03, 126.42, 124.02, 122.33, 110.20, 84.84, 62.30, 53.62, 45.77, 43.74, 41.31, 36.22; **HRMS** *m/z* **(ESI):** calcd for $C_{34}H_{30}N_2O_5Na^+$ $[M+Na]^+$: 569.2052, found 569.2035.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6'-hydroxy-2,2'-dioxo-1,4'-diphenylspiro[indoline-3,3'-piperidine]-6'-carboxylate (3ba)



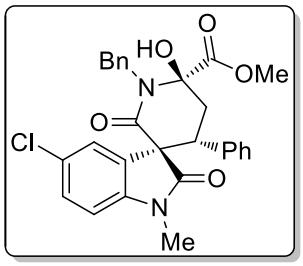
White solid; 39.4 mg, 74% yield; *dr* > 95:5; *ee* = 84%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 92/8, 1.0 mL/min, λ = 254 nm, t_r(major) = 33.30 min, t_r(minor) = 18.03 min]; $[\alpha]_D^{25}$ = -47.4 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 (d, *J* = 7.2 Hz, 1H), 7.40-7.04 (m, 13H), 6.88 (d, *J* = 7.6 Hz, 4H), 6.45 (d, *J* = 8.0 Hz, 1H), 5.28 (d, *J* = 16.0 Hz, 1H), 4.76 (s, 1H), 4.38 (d, *J* = 14.2 Hz, 1H), 4.15 (d, *J*= 15.6 Hz, 1H), 3.39-3.32 (m, 4H), 2.22 (d, *J* = 12.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.48, 172.05, 168.38, 145.18, 137.17, 136.36, 133.83, 129.46, 129.24, 128.26, 128.22, 128.10, 127.86, 127.65, 127.57, 127.24, 126.80, 124.06, 122.69, 109.98, 84.86, 62.50, 53.65, 45.82, 41.82, 35.46; **HRMS** *m/z* **(ESI):** calcd for $C_{33}H_{28}N_2O_5Na^+$ $[M+Na]^+$: 555.1896, found 555.1893.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6'-hydroxy-1-methyl-2,2'-dioxo-4'-phenylspiro[indoline-3,3'-piperidine]-6'-carboxylate (3ca)



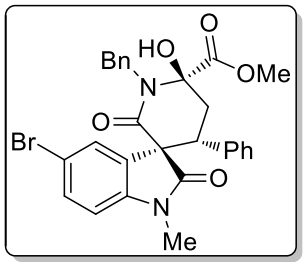
White solid; 35.3 mg, 75% yield; *dr* > 95:5; *ee* = 99%, determined by HPLC analysis [Chiralpak OD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 13.22 min, t_r(minor) = 17.18 min]; $[\alpha]_D^{25}$ = -68.3 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.60 (d, *J* = 7.2 Hz, 1H), 7.28-7.16 (m, 6H), 7.11-6.98 (m, 4H), 6.83 (d, *J* = 7.6 Hz, 2H), 6.56 (d, *J* = 8.0 Hz, 1H), 5.22 (d, *J* = 15.6 Hz, 1H), 4.80 (s, 1H), 4.34 (dd, *J* = 14.0, 2.8 Hz, 1H), 4.14 (d, *J* = 16.0 Hz, 1H), 3.37-3.30 (m, 4H), 2.91 (s, 3H), 2.18 (dd, *J* = 13.6, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.25, 172.04, 168.35, 144.84, 137.20, 136.36, 129.30, 128.20, 128.09, 127.92, 127.82, 127.60, 127.45, 127.18, 123.76, 122.26, 108.68, 84.85, 62.38, 53.60, 45.87, 41.22, 35.43, 26.09; **HRMS** *m/z* **(ESI):** calcd for $C_{28}H_{26}N_2O_5Na^+$ $[M+Na]^+$: 493.1793, found 493.1781.

(*3R,4'R,6'R*)-methyl 1'-benzyl-5-chloro-6'-hydroxy-1-methyl-2,2'-dioxo-4'-phenyl spiro[indoline-3,3'-piperidine]-6'-carboxylate (3da)



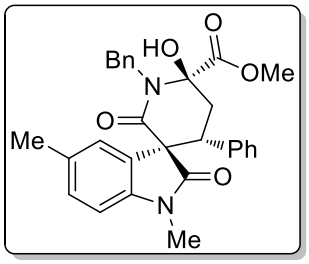
White solid; 38.8 mg, 77% yield; *dr* > 95:5; *ee* = 96%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 18.09 min, t_r(minor) = 12.73 min]; $[\alpha]_D^{25}$ = -58.5 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (d, *J* = 2.0 Hz, 1H), 7.29-7.23 (m, 4H), 7.17 (d, *J* = 7.6 Hz, 2H), 7.09-7.04 (m, 3H), 6.85 (d, *J* = 7.6 Hz, 2H), 6.50 (d, *J* = 8.4 Hz, 1H), 5.18 (d, *J* = 16.0 Hz, 1H), 4.79 (s, 1H), 4.32 (dd, *J* = 14.0, 2.8 Hz, 1H), 4.16 (d, *J* = 16.0 Hz, 1H), 3.33 (s, 3H), 3.27 (t, *J* = 14.0 Hz, 1H), 2.89 (s, 3H), 2.21 (dd, *J* = 14.0, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.77, 171.82, 167.71, 143.52, 136.94, 135.98, 129.31, 129.16, 128.29, 128.06, 127.85, 127.83, 127.70, 127.47, 127.33, 124.62, 109.51, 84.79, 62.42, 53.61, 45.85, 41.12, 35.46, 26.20; **HRMS** *m/z* **(ESI):** calcd for $C_{28}H_{25}ClN_2O_5Na^+$ $[M+Na]^+$: 527.1350, found 527.1347.

(*3R,4'R,6'R*)-methyl 1'-benzyl-5-bromo-6'-hydroxy-1-methyl-2,2'-dioxo-4'-phenyl spiro[indoline-3,3'-piperidine]-6'-carboxylate (3ea)



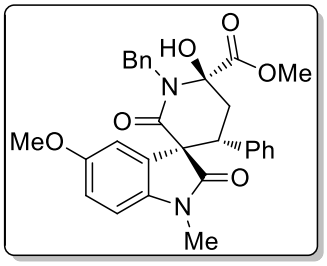
White solid; 40.6 mg, 74% yield; *dr* > 95:5; *ee* = 90%, determined by HPLC analysis [Chiralpak OD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 14.83 min, t_r(minor) = 10.93 min]; $[\alpha]_D^{25}$ = -57.1 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.32-7.23 (m, 4H), 7.16 (d, *J* = 7.6 Hz, 2H), 7.10-7.03 (m, 3H), 6.85 (d, *J* = 7.2 Hz, 2H), 6.46 (d, *J* = 8.0 Hz, 1H), 5.21 (d, *J* = 15.6 Hz, 1H), 4.75 (s, 1H), 4.30 (dd, *J* = 14.4, 3.2 Hz, 1H), 4.13 (d, *J* = 15.6 Hz, 1H), 3.32 (s, 3H), 3.27 (t, *J* = 14.0 Hz, 1H), 2.88 (s, 3H), 2.21 (dd, *J* = 14.0, 3.2 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.60, 171.87, 167.71, 144.02, 136.94, 135.98, 132.04, 129.67, 128.32, 128.07, 127.93, 127.87, 127.74, 127.49, 127.34, 114.67, 110.03, 84.72, 62.31, 53.63, 45.71, 41.13, 35.47, 26.17; **HRMS** *m/z* **(ESI):** calcd for $C_{28}H_{25}BrN_2O_5Na^+$ $[M+Na]^+$: 571.0845, found 571.0836.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6'-hydroxy-1,5-dimethyl-2,2'-dioxo-4'-phenylspiro [indoline-3,3'-piperidine]-6'-carboxylate (3fa)



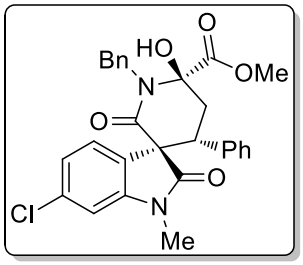
White solid; 36.3 mg, 75% yield; *dr* > 95:5; *ee* = 99%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t_r(major) = 49.49 min, t_r(minor) = 25.67 min]; $[\alpha]_D^{25}$ = -60.1 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 (s, 1H), 7.28-7.17 (m, 5H), 7.09-7.05 (m, 2H), 7.01 (dd, *J* = 7.6, 7.2 Hz, 2H), 6.83 (d, *J* = 7.6 Hz, 2H), 6.46 (d, *J* = 8.0 Hz, 1H), 5.21 (d, *J* = 15.6 Hz, 1H), 4.90 (s, 1H), 4.31 (dd, *J* = 14.4, 3.2 Hz, 1H), 4.15 (d, *J* = 15.6 Hz, 1H), 3.37-3.31 (m, 4H), 2.88 (s, 3H), 2.38 (s, 3H), 2.18 (dd, *J* = 14.0, 3.2 Hz, 1H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.18, 171.93, 168.46, 142.46, 137.26, 136.48, 131.54, 129.51, 128.13, 128.11, 127.96, 127.78, 127.63, 127.44, 127.19, 124.93, 108.42, 84.96, 62.39, 53.42, 45.77, 41.13, 35.56, 26.11, 21.44; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{28}N_2O_5Na^+$ $[M+Na]^+$: 507.1896, found 507.1883.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6'-hydroxy-5-methoxy-1-methyl-2,2'-dioxo-4'-phenylspiro[indoline-3,3'-piperidine]-6'-carboxylate (3ga)



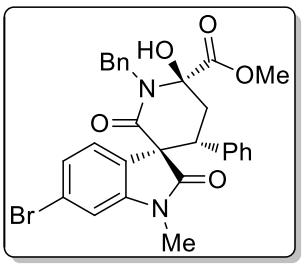
White solid; 39.0 mg, 78% yield; *dr* = 93:7; *ee* = 99%, determined by HPLC analysis [Chiralpak OD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 27.66 min, t_r(minor) = 14.53 min]; $[\alpha]_D^{25}$ = -72.7 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 (d, *J* = 2.4 Hz, 1H), 7.27-7.18 (m, 5H), 7.09-7.00 (m, 3H), 6.87-6.85 (m, 2H), 6.80 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.47 (d, *J* = 8.8 Hz, 1H), 5.25 (d, *J* = 15.6 Hz, 1H), 4.77 (s, 1H), 4.32 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.12 (d, *J* = 15.6 Hz, 1H), 3.81 (s, 3H), 3.36-3.29 (m, 4H), 2.88 (s, 3H), 2.18 (dd, *J* = 14.0, 3.2 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.92, 171.88, 168.25, 155.60, 138.43, 137.29, 136.38, 128.82, 128.16, 128.13, 127.93, 127.65, 127.47, 127.19, 113.81, 111.47, 108.98, 84.88, 62.68, 55.78, 53.51, 45.74, 41.14, 35.41, 26.16; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{28}N_2O_6Na^+$ $[M+Na]^+$: 523.1845, found 523.1826.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6-chloro-6'-hydroxy-1-methyl-2,2'-dioxo-4'-phenyl spiro[indoline-3,3'-piperidine]-6'-carboxylate (3ha)



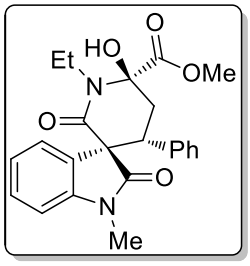
White solid; 39.3 mg, 78% yield; *dr* = 93:7; *ee* = 92%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 18.34 min, t_r(minor) = 11.41 min]; $[\alpha]_D^{25}$ = -47.0 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49 (d, *J* = 8.0 Hz, 1H), 7.30-7.22 (m, 4H), 7.16 (d, *J* = 7.2 Hz, 2H), 7.10-7.02 (m, 3H), 6.84 (d, *J* = 7.2 Hz, 2H), 6.57 (d, *J* = 2.0 Hz, 1H), 5.17 (d, *J* = 16.0 Hz, 1H), 4.70 (s, 1H), 4.31 (dd, *J* = 14.0, 2.8 Hz, 1H), 4.14 (d, *J* = 15.6 Hz, 1H), 3.33 (s, 3H), 3.25 (t, *J* = 14.0 Hz, 1H), 2.90 (s, 3H), 2.19 (dd, *J* = 14.0, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.17, 171.94, 167.92, 146.12, 137.03, 136.04, 135.23, 128.66, 128.27, 128.06, 127.83, 127.69, 127.31, 126.23, 124.57, 122.08, 109.40, 84.72, 62.10, 53.72, 45.90, 41.09, 35.40, 26.21; **HRMS** *m/z* **(ESI):** calcd for $C_{28}H_{25}ClN_2O_5Na^+$ $[M+Na]^+$: 527.1350, found 527.1375.

(*3R,4'R,6'R*)-methyl1'-benzyl-6-bromo-6'-hydroxy-1-methyl-2,2'-dioxo-4'-phenyl spiro[indoline-3,3'-piperidine]-6'-carboxylate (3ia)



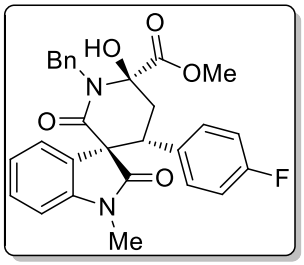
White solid; 41.1mg, 75% yield; *dr* > 95:5; *ee* = 92%, determined by HPLC analysis [Chiralpak OD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 37.25 min, t_r(minor) = 22.82 min]; $[\alpha]_D^{25}$ = -49.6 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 (d, *J* = 8.0 Hz, 1H), 7.29-7.22 (m, 4H), 7.16 (d, *J* = 7.2 Hz, 2H), 7.10-7.03 (m, 3H), 6.82 (d, *J* = 7.2 Hz, 2H), 6.72 (d, *J* = 2.0 Hz, 1H), 5.17 (d, *J* = 16.0 Hz, 1H), 4.66 (s, 1H), 4.31 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.13 (d, *J* = 15.6 Hz, 1H), 3.32 (s, 3H), 3.24 (t, *J* = 14.0 Hz, 1H), 2.90 (s, 3H), 2.18 (dd, *J* = 13.6, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.18, 171.79, 167.82, 146.18, 137.03, 136.03, 128.26, 128.04, 127.84, 127.83, 127.70, 127.28, 126.82, 125.09, 124.95, 123.06, 112.20, 84.83, 62.20, 53.65, 45.97, 41.01, 35.42, 26.21; **HRMS** *m/z* **(ESI):** calcd for $C_{28}H_{25}BrN_2O_5Na^+$ $[M+Na]^+$: 571.0845, found 571.0838.

(*3R,4'R,6'R*)-methyl 1'-ethyl-6'-hydroxy-1-methyl-2,2'-dioxo-4'-phenylspiro[indoline-3,3'-piperidine]-6'-carboxylate (3ja)



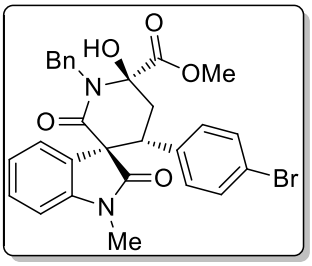
White solid; 29.4mg, 72% yield; *dr* > 95:5; *ee* = 96%, determined by HPLC analysis [Chiralpak OD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 13.60 min, t_r(minor) = 12.28 min]; $[\alpha]_D^{25}$ = -77.6 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.22 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.05 (dd, *J* = 7.6, 7.6 Hz, 2H), 6.99 (dd, *J* = 7.6, 7.2 Hz, 2H), 6.80 (d, *J* = 7.6 Hz, 2H), 6.52 (d, *J* = 8.0 Hz, 1H), 4.53 (s, 1H), 4.25 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.07 (s, 3H), 3.35-3.23 (m, 3H), 2.89 (s, 3H), 2.17 (dd, *J* = 13.6, 2.8 Hz, 1H), 1.19 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.37, 172.83, 167.29, 144.74, 136.37, 129.15, 127.88, 127.67, 127.57, 127.40, 123.80, 122.20, 108.50, 86.36, 62.32, 54.35, 41.17, 40.58, 35.96, 26.04, 13.45; **HRMS** *m/z* **(ESI):** calcd for $C_{23}H_{24}N_2O_5Na^+$ $[M+Na]^+$: 431.1583, found 431.1560.

(*3R,4'R,6'R*)-methyl 1'-benzyl-4'-(4-fluorophenyl)-6'-hydroxy-1-methyl-2,2'-dioxospiro[indoline-3,3'-piperidine]-6'-carboxylate (3cb)



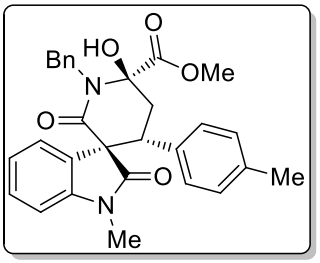
White solid; 36.6 mg, 75% yield; *dr* > 95:5; *ee* = 95%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, t_r(major) = 23.13 min, t_r(minor) = 19.60 min]; $[\alpha]_D^{25}$ = -92.4 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59 (d, *J* = 7.2 Hz, 1H), 7.28-7.21 (m, 4H), 7.16 (d, *J* = 7.2 Hz, 2H), 7.10 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.80 (dd, *J* = 8.4, 5.6 Hz, 2H), 6.69 (dd, *J* = 8.8, 8.8 Hz, 2H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.21 (d, *J* = 16.0 Hz, 1H), 4.89 (s, 1H), 4.32 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.13 (d, *J* = 15.6 Hz, 1H), 3.32-3.25 (m, 4H), 2.94 (s, 3H), 2.16 (dd, *J* = 14.0, 3.2 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.20, 171.86, 168.17, 161.99 (d, *J* = 246.3 Hz), 144.79, 137.11, 132.21 (d, *J* = 3.4 Hz), 129.55, 129.47, 128.22, 128.06, 127.56, 127.21, 123.73, 122.39, 114.51 (d, *J* = 21.2 Hz), 108.86, 84.79, 62.32, 53.62, 45.88, 40.52, 35.58, 26.14; **HRMS** *m/z* **(ESI):** calcd for $C_{28}H_{25}FN_2O_5Na^+$ $[M+Na]^+$: 511.1645, found 511.1636.

(*3R,4'R,6'R*)-methyl1'-benzyl-4'-(4-bromophenyl)-6'-hydroxy-1-methyl-2,2'-dioxospiro[indoline-3,3'-piperidine]-6'-carboxylate (3cc)



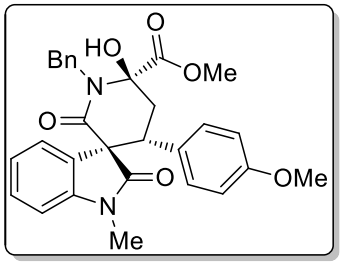
White solid; 42.2 mg, 77% yield; *dr* > 95:5; *ee* = 99%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 19.24 min, t_r(minor) = 9.25 min]; $[\alpha]_D^{25}$ = -55.4 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (d, *J* = 7.2 Hz, 1H), 7.31-7.21 (m, 4H), 7.17-7.08 (m, 5H), 6.71 (d, *J* = 8.4 Hz, 2H), 6.63 (d, *J* = 7.6 Hz, 1H), 5.20 (d, *J* = 16.0 Hz, 1H), 4.86 (s, 1H), 4.29 (dd, *J* = 14.0, 2.8 Hz, 1H), 4.12 (d, *J* = 15.6 Hz, 1H), 3.32-3.25 (m, 4H), 2.96 (s, 3H), 2.14 (dd, *J* = 14.0, 3.2 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.10, 171.81, 168.08, 144.78, 137.06, 135.51, 130.78, 129.65, 129.57, 128.23, 128.06, 127.41, 127.24, 123.71, 122.44, 121.55, 109.01, 84.71, 62.08, 53.66, 45.87, 40.67, 35.35, 26.22; **HRMS** *m/z* **(ESI):** calcd for $C_{28}H_{25}BrN_2O_5Na^+$ $[M+Na]^+$: 571.0845, found 571.0850.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6'-hydroxy-1-methyl-2,2'-dioxo-4'-(p-tolyl)spiro[indoline-3,3'-piperidine]-6'-carboxylate (3cd)



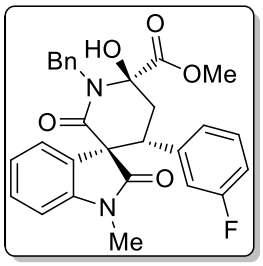
White solid; 37.3 mg, 77% yield; *dr* > 95:5; *ee* = 92%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 33.23 min, t_r(minor) = 17.93 min]; $[\alpha]_D^{25}$ = -60.2 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ: 7.59 (d, *J* = 7.6 Hz, 1H), 7.28-7.16 (m, 6H), 7.09 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 6.58 (d, *J* = 8.0 Hz, 1H), 5.20 (d, *J* = 15.6 Hz, 1H), 4.83 (s, 1H), 4.29 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.13 (d, *J* = 16.0 Hz, 1H), 3.34-3.27 (m, 4H), 2.93 (s, 3H), 2.16-2.13 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ:174.41, 172.03, 168.46, 144.87, 137.21, 136.99, 133.35, 129.23, 128.30, 128.19, 128.07, 127.95, 127.75, 127.15, 123.76, 122.23, 108.73, 84.90, 62.42, 53.56, 45.89, 40.82, 35.64, 26.13, 20.98; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{28}N_2O_5Na^+$ $[M+Na]^+$: 507.1896, found 507.1883.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6'-hydroxy-4'-(4-methoxyphenyl)-1-methyl-2,2'-dioxospiro[indoline-3,3'-piperidine]-6'-carboxylate (3ce)



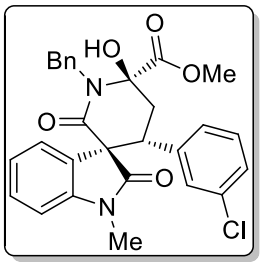
White solid; 37.0 mg, 74% yield; *dr* > 95:5; *ee* = 97%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 40.66 min, t_r(minor) = 23.79 min]; $[\alpha]_D^{25}$ = -61.7 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz,$CDCl_3$)** δ 7.58 (d, *J* = 7.2 Hz, 1H), 7.28-7.21 (m, 4H), 7.18 (d, *J* = 7.2 Hz, 2H), 7.09 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.74 (d, *J* = 8.8 Hz, 2H), 6.59 (d, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 8.4 Hz, 2H), 5.21 (d, *J* = 15.6 Hz, 1H), 4.73 (s, 1H), 4.28 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.12 (d, *J* = 16.0 Hz, 1H), 3.67 (s, 3H), 3.31-3.24 (m, 4H), 2.94 (s, 3H), 2.14 (dd, *J* = 13.6, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.32, 172.12, 168.45, 158.69, 144.91, 137.22, 129.27, 128.96, 128.56, 128.20, 128.09, 127.89, 127.17, 123.72, 122.20, 112.93, 108.77, 84.83, 62.48, 55.08, 53.59, 45.82, 40.51, 35.77, 26.14; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{28}N_2O_6Na^+$ $[M+Na]^+$: 523.1845, found 523.1836.

(*3R,4'R,6'R*)-methyl 1'-benzyl-4'-(3-fluorophenyl)-6'-hydroxy-1-methyl-2,2'-dioxospiro[indoline-3,3'-piperidine]-6'-carboxylate (3cf)



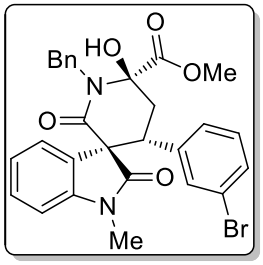
White solid; 38.1 mg, 78% yield; *dr* > 95:5; *ee* = 98%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 92/8, 1.0 mL/min, λ = 254 nm, t_r(major) = 36.80 min, t_r(minor) = 29.42 min]; $[\alpha]_D^{25}$ = -58.9 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, DMSO-d_6)** δ 7.66 (d, *J* = 7.6 Hz, 1H), 7.41 (s, 1H), 7.32-7.10 (m, 8H), 6.92 (dd, *J* = 8.8, 8.0 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 10.4 Hz, 1H), 4.70 (d, *J* = 16.0 Hz, 1H), 4.30 (d, *J* = 16.0 Hz, 1H), 4.17 (d, *J* = 14.0 Hz, 1H), 3.43-3.25 (m, 4H), 2.87 (s, 3H), 2.17 (dd, *J* = 14.0, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ 174.14, 171.20, 167.54, 163.06, 160.64, 144.78, 140.02 (d, *J* = 7.4 Hz), 137.80, 129.97 (d, *J* = 8.1 Hz), 129.77, 128.26, 127.55, 127.05, 124.49, 124.27, 122.77, 114.70 (d, *J* = 22.7 Hz), 109.38, 86.11, 62.04, 53.11, 47.05, 40.65, 35.11, 26.32; **HRMS** *m/z* **(ESI):** calcd for $C_{28}H_{25}FN_2O_5Na^+$ $[M+Na]^+$: 511.1645, found 511.1664.

(*3R,4'R,6'R*)-methyl 1'-benzyl-4'-(3-chlorophenyl)-6'-hydroxy-1-methyl-2,2'-dioxospiro[indoline-3,3'-piperidine]-6'-carboxylate (3cg)



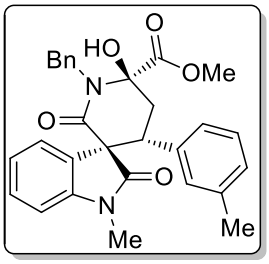
White solid; 37.3 mg, 74% yield; *dr* > 95:5; *ee* = 90%, determined by HPLC analysis [Chiralpak OD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 10.77 min, t_r(minor) = 7.53 min]; $[\alpha]_D^{25}$ = -78.1 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57 (d, *J* = 7.6 Hz, 1H), 7.31-7.21 (m, 4H), 7.17 (d, *J* = 7.2 Hz, 2H), 7.11 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.96 (dd, *J* = 8.0, 7.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 2H), 6.62 (d, *J* = 7.6 Hz, 1H), 5.20 (d, *J* = 16.0 Hz, 1H), 4.88 (s, 1H), 4.30 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.13 (d, *J* = 15.6 Hz, 1H), 3.32-3.25 (m, 4H), 2.96 (s, 3H), 2.17 (dd, *J* = 13.6, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.13, 171.72, 168.02, 144.70, 138.47, 137.07, 133.49, 129.60, 128.88, 128.22, 128.04, 127.87, 127.66, 127.42, 127.22, 126.38, 123.71, 122.51, 108.91, 84.75, 62.10, 53.64, 45.93, 40.90, 35.27, 26.18; **HRMS *m/z* (ESI):** calcd for $C_{28}H_{25}ClN_2O_5Na^+$ $[M+Na]^+$: 527.1530, found 527.1333.

(*3R,4'R,6'R*)-methyl 1'-benzyl-4'-(3-bromophenyl)-6'-hydroxy-1-methyl-2,2'-dioxospiro[indoline-3,3'-piperidine]-6'-carboxylate (3ch)



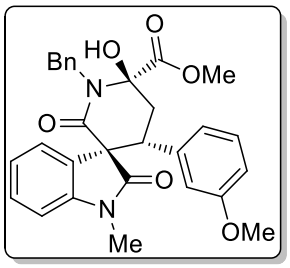
White solid; 41.1 mg, 75% yield; *dr* > 95:5; *ee* = 99%, determined by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 26.75 min, t_r(minor) = 29.00 min]; $[\alpha]_D^{25}$ = -73.6 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, DMSO-d_6)** δ 7.64 (d, *J* = 7.2 Hz, 1H), 7.41 (s, 1H), 7.31-7.12 (m, 8H), 7.03 (dd, *J* = 8.0, 7.6 Hz, 1H), 6.91 (s, 1H), 6.84-6.81 (m, 2H), 4.71 (d, *J* = 16.0 Hz, 1H), 4.30 (d, *J* = 16.0 Hz, 1H), 4.13 (dd, *J* = 14.0, 2.8 Hz, 1H), 3.39-3.31 (m, 4H), 2.87 (s, 3H), 2.18 (dd, *J* = 14.4, 3.2 Hz, 1H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ 178.87, 175.90, 172.22, 149.49, 144.48, 142.54, 135.51, 135.47, 134.96, 134.57, 133.02, 132.30, 132.20, 132.08, 131.81, 128.98, 127.53, 126.08, 114.19, 90.84, 66.77, 57.89, 51.79, 45.49, 39.71, 31.07; **HRMS *m/z* (ESI):** calcd for $C_{28}H_{25}BrN_2O_5Na^+$ $[M+Na]^+$: 571.0845, found 571.0851.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6'-hydroxy-1-methyl-2,2'-dioxo-4'-(m-tolyl)spiro[indoline-3,3'-piperidine]-6'-carboxylate (3ci)



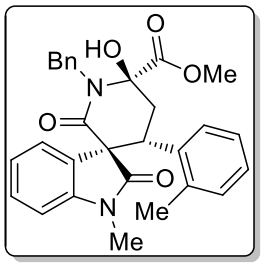
White solid; 36.8mg, 76% yield; *dr* > 95:5; *ee* = 98%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 12.37 min, t_r(minor) = 16.48 min]; $[\alpha]_D^{25}$ = -67.2 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.60 (d, *J* = 7.2 Hz, 1H), 7.27-7.16 (m, 6H), 7.09 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.89-6.86 (m, 2H), 6.63-6.60 (m, 2H), 6.56 (d, *J* = 7.6 Hz, 1H), 5.20 (d, *J* = 16.0 Hz, 1H), 4.86 (br, 1H), 4.29 (dd, *J* = 14.4, 2.8 Hz, 1H), 4.14 (d, *J* = 15.6 Hz, 1H), 3.34-3.27 (m, 4H), 2.90 (s, 3H), 2.17 (dd, *J* = 13.6, 2.8 Hz, 1H), 2.09 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.36, 172.00, 168.42, 144.85, 137.23, 137.20, 136.30, 129.24, 128.67, 128.19, 128.10, 128.06, 127.97, 127.41, 127.15, 124.95, 123.77, 122.21, 108.66, 84.93, 62.39, 53.56, 45.92, 41.17, 35.55, 26.07, 21.16; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{28}N_2O_5Na^+$ $[M+Na]^+$: 507.1896, found 507.1883.

(*3R,4'R,6'R*)-methyl 1'-benzyl-6'-hydroxy-4'-(3-methoxyphenyl)-1-methyl-2,2'-dioxospiro[indoline-3,3'-piperidine]-6'-carboxylate (3cj)



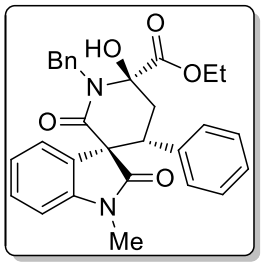
White solid; 37.0mg, 74% yield; *dr* = 91:9; *ee* = 93%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 23.42 min, t_r(minor) = 14.37 min]; $[\alpha]_D^{25}$ = -83.6 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62 (d, *J* = 7.6 Hz, 1H), 7.39-7.16 (m, 6H), 7.12 (dd, *J* = 7.6, 7.2 Hz, 1H), 6.96 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.65-6.61 (m, 2H), 6.52 (d, *J* = 7.6 Hz, 1H), 6.30 (s, 1H), 5.21 (d, *J* = 15.6 Hz, 1H), 4.84 (s, 1H), 4.33 (dd, *J* = 14.4, 3.2 Hz, 1H), 4.17 (d, *J* = 16.0 Hz, 1H), 3.55 (s, 3H), 3.35 (s, 3H), 3.29 (d, *J* = 13.6 Hz, 1H), 2.96 (s, 3H), 2.20 (dd, *J* = 13.6, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.21, 171.97, 168.30, 158.85, 144.95, 137.95, 137.18, 129.33, 128.61, 128.20, 128.07, 127.97, 127.18, 123.71, 122.24, 120.69, 113.77, 112.60, 108.79, 84.85, 62.28, 55.12, 53.60, 45.90, 41.20, 35.63, 26.14; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{28}N_2O_6Na^+$ $[M+Na]^+$: 523.1845, found 523.1857.

(3*R*,4'*R*,6'*R*)-methyl 1'-benzyl-6'-hydroxy-1-methyl-2,2'-dioxo-4'-(*o*-tolyl)spiro[indoline-3,3'-piperidine]-6'-carboxylate (3ck)



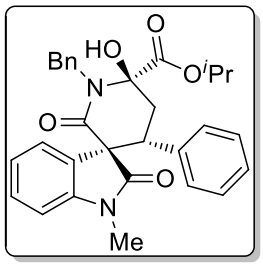
White solid; 31.0 mg, 64% yeild; *dr* > 95:5; *ee* = 98%, determined by HPLC analysis [Chiralpak IB, *n*-hexane/*i*-PrOH = 93/7, 1.0 mL/min, λ = 254 nm, t_r(major) = 38.79 min, t_r(minor) = 26.95 min]; $[\alpha]_D^{25}$ = -53.4 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70 (d, *J* = 7.6 Hz, 1H), 7.36 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.30-7.11 (m, 6H), 7.06 (d, *J* = 7.6 Hz, 1H), 6.94 (dd, *J* = 7.6, 7.2, Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.62 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.21 (d, *J* = 8.0 Hz, 1H), 5.28 (d, *J* = 16.0 Hz, 1H), 4.85-4.54 (m, 2H), 4.08 (d, *J* = 16.0 Hz, 1H), 3.32-3.14 (m, 4H), 2.91 (s, 3H), 2.48 (s, 3H), 2.03 (dd, *J* = 14.0, 2.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.22, 172.12, 168.80, 145.35, 137.27, 137.15, 135.39, 130.53, 129.50, 128.30, 128.18, 128.16, 127.18, 127.04, 126.39, 124.83, 124.21, 122.28, 108.89, 84.82, 61.75, 53.55, 45.67, 37.54, 35.63, 26.17, 20.17; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{28}N_2O_5Na^+$ $[M+Na]^+$: 507.1896, found 507.1883.

(*3R,4'R,6'R*)-ethyl 1'-benzyl-6'-hydroxy-1-methyl-2,2'-dioxo-4'-phenylspiro[indoline-3,3'-piperidine]-6'-carboxylate (3cl)



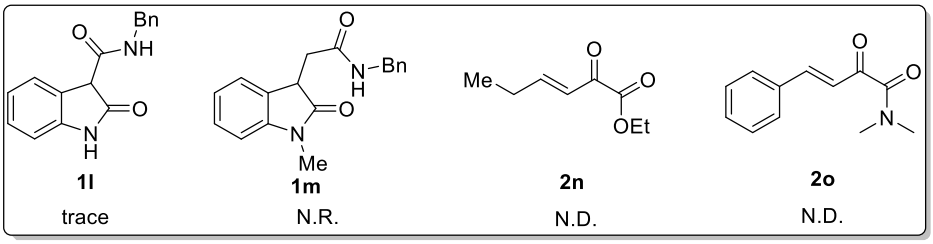
White solid; 33.4 mg, 69% yield; *dr* > 95:5; *ee* = 94%, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 22.64 min, t_r(minor) = 25.61 min]; $[\alpha]_D^{25}$ = -92.4 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (d, *J* = 7.6, 1H), 7.29-7.26 (m, 2H), 7.24-7.17 (m, 4H), 7.09-7.04 (m, 2H), 7.02-6.98 (m, 2H), 6.82 (d, *J* = 7.2 Hz, 2H), 6.57 (d, *J* = 8.0 Hz, 1H), 5.19 (d, *J* = 16.0 Hz, 1H), 4.75 (s, 1H), 4.32 (dd, *J* = 14.4, 3.2 Hz, 1H), 4.14 (d, *J* = 16.0 Hz, 1H), 4.12-3.98 (m, 1H), 3.46-3.21 (m, 2H), 2.90 (s, 3H), 2.18 (dd, *J* = 13.6, 2.8 Hz, 1H), 1.09 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.14, 171.72, 168.36, 144.94, 137.39, 136.36, 129.31, 128.19, 128.14, 127.91, 127.71, 127.61, 127.47, 127.19, 123.83, 122.02, 108.69, 84.88, 63.66, 62.34, 45.95, 41.25, 35.61, 26.06, 13.51; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{28}N_2O_5Na^+$ $[M+Na]^+$: 507.1896, found 507.1895.

(*3R,4'R,6'R*)-isopropyl 1'-benzyl-6'-hydroxy-1-methyl-2,2'-dioxo-4'-phenylspiro[indoline-3,3'-piperidine]-6'-carboxylate (3cm)



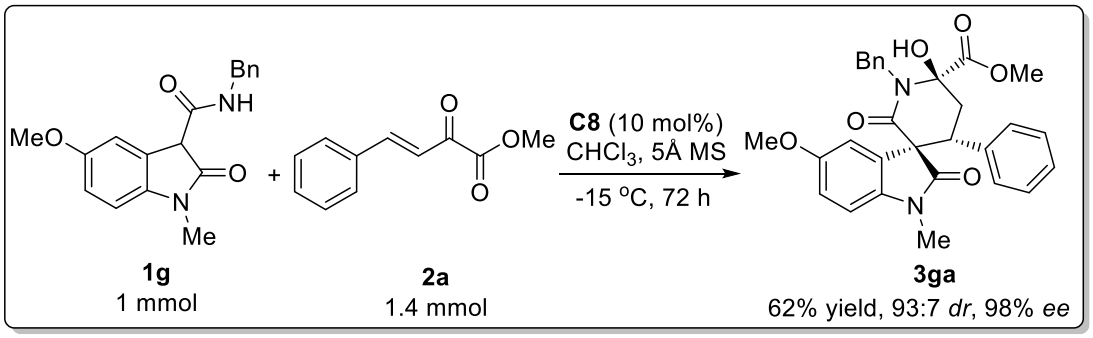
White solid; 32.9 mg, 66% yield; *dr* > 95:5; *ee* = 87%, determined by HPLC analysis [Chiralpak OD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 21.19 min, t_r(minor) = 13.77 min]; $[\alpha]_D^{25}$ = -71.3 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.67 (d, *J* = 7.6 Hz, 1H), 7.28-7.20 (m, 6H), 7.08-6.98 (m, 4H), 6.82 (d, *J* = 7.2 Hz, 2H), 6.56 (d, *J* = 8.0 Hz, 1H), 4.95 (d, *J* = 15.6 Hz, 1H), 4.73-4.67 (m, 2H), 4.34-4.27 (m, 2H), 3.33 (t, *J* = 14.0 Hz, 1H), 2.88 (s, 3H), 2.18 (dd, *J* = 14.0, 3.2 Hz, 1H), 1.34 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.13, 171.30, 168.38, 144.94, 137.45, 136.40, 129.30, 128.27, 127.94, 127.91, 127.62, 127.48, 127.15, 123.89, 121.97, 108.69, 85.47, 72.74, 62.37, 46.59, 41.24, 35.70, 26.04, 21.57, 20.88; **HRMS *m/z* (ESI):** calcd for $C_{30}H_{30}N_2O_5Na^+$ $[M+Na]^+$: 521.2052, found 521.2059.

Unsuccessful Examples



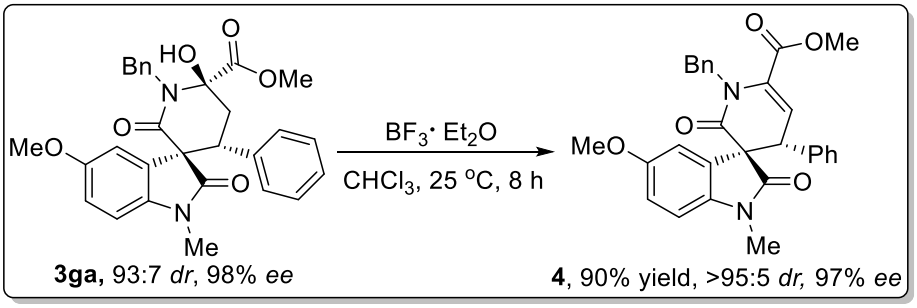
6. Scale-up and transformation of product 3

(a) Scale-up reaction of 3ga



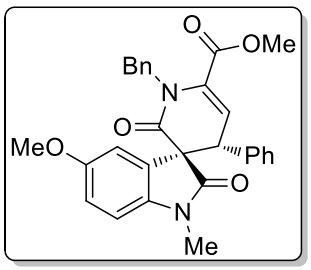
3-Carboxamide oxindole **1g** (1.0 mmol), *β*,*γ*-unsaturated *α*-keto ester **2a** (1.4 mmol), catalyst **C8** (0.1 mmol) and 5Å molecular sieve (500 mg) was added to an argon purged vial. Then, freshly distilled $CHCl_3$ (10 mL) was added and the reaction mixture was stirred at -15 ^oC for 72 h. After completion of the reaction, the crude product was purified by flash column chromatography on silica gel to afford the desired product **3ga** as a white solid in 62% yield with 93:7 dr and 98% *ee*.

(b) Transformation of 3ga



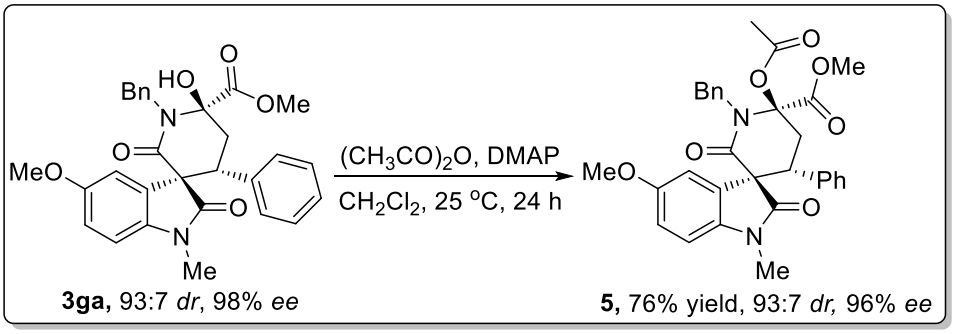
To an argon purged reaction tube containing **3ga** (0.1 mmol) and BF_3 ·Et_2O (0.12 mmol) was added freshly distilled $CHCl_3$ (1 mL). After the reaction was stirred for 8 hours at room temperature, the resulted mixture was purified by flash column chromatography on silica gel to afford the desired product **4**.

(*3R,4'R*)-methyl 1'-benzyl-5-methoxy-1-methyl-2,2'-dioxo-4'-phenyl-2',4'-dihydro -1'H-spiro[indoline-3,3'-pyridine]-6'-carboxylate (4)



White solid; 43.4 mg, 90% yield; *dr* > 95:5; *ee* = 97%, determined by HPLC analysis [Chiralpak OD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 13.25 min, t_r(minor) = 15.63 min]; $[\alpha]_D^{25}$ = +20.0 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33-7.31 (m, 2H),

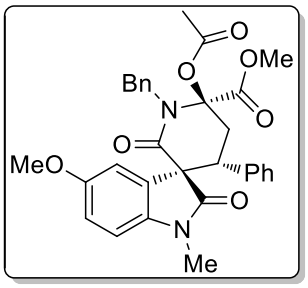
7.28-7.25 (m, 3H), 7.12-7.02 (m, 1H), 7.06-7.02 (m, 2H), 6.95 (d, *J* = 2.4 Hz, 1H), 6.93-6.90 (m, 2H), 6.74 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.45 (d, *J* = 8.4 Hz, 1H), 6.41 (d, *J* = 3.2 Hz, 1H), 5.62 (d, *J* = 14.8 Hz, 1H), 4.82 (d, *J* = 14.8 Hz, 1H), 4.69 (d, *J* = 2.8 Hz, 1H), 3.75 (d, *J* = 2.0 Hz, 6H), 2.90 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.11, 166.77, 162.83, 155.54, 137.66, 136.62, 135.31, 133.91, 128.76, 128.65, 128.15, 127.85, 127.71, 127.65, 126.01, 122.13, 113.59, 112.12, 108.73, 60.43, 55.85, 52.66, 46.23, 45.72, 26.27; **HRMS** *m/z* **(ESI):** calcd for $C_{29}H_{26}N_2O_5Na^+$ $[M+Na]^+$: 505.1739, found 505.1735.



3ga, 93:7 *dr*, 98% *ee* — **5**, 76% yield, 93:7 *dr*, 96% *ee*

To an argon purged reaction tube containing **3ga** (0.1 mmol), $(CH_3CO)_2O$ (0.25 mmol) and DMAP (0.1 mmol) was added freshly distilled CH_2Cl_2 (1 mL). After the reaction was stirred for 24 h at room temperature, the resulted mixture was purified by flash column chromatography on silica gel to afford the desired product **5**.

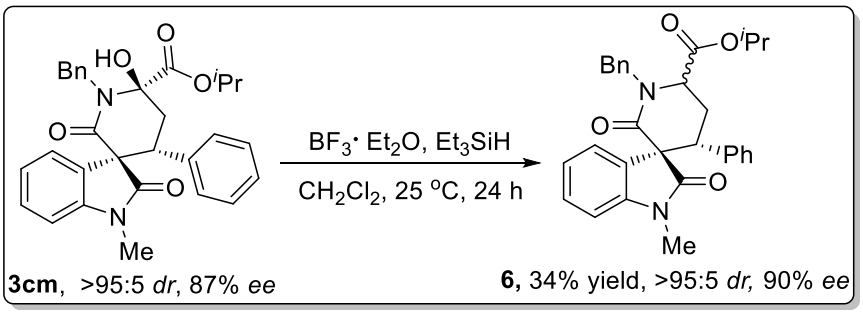
(*3R,4'R,6'R*)-methyl 6'-acetoxy-1'-benzyl-5-methoxy-1-methyl-2,2'-dioxo-4'-phenylspiro[indoline-3,3'-piperidine]-6'-carboxylate (5)



White solid; 41.2 mg, 76% yield; *dr* = 93:7; *ee* = 96%, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 20.16 min, t_r(minor) = 12.40 min]; $[\alpha]_D^{25}$ = -92.1 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36 (d, *J* = 2.4 Hz, 1H), 7.26-7.17 (m, 3H), 7.10-7.01 (m, 5H), 6.88 (d, *J* = 7.2 Hz, 2H), 6.81 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.48 (d, *J* = 8.4 Hz, 1H), 5.39 (d, *J* = 16.0 Hz, 1H), 4.40 (d, *J* = 16.0 Hz, 1H), 4.04 (dd, *J* = 14.8, 2.8 Hz, 1H), 3.83 (s, 3H), 3.62 (t, *J* = 15.2 Hz, 1H), 3.25 (s, 3H), 3.18 (dd, *J* = 15.6, 2.8 Hz, 1H), 2.89 (s, 3H), 2.21 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.60, 170.11, 168.56, 165.80, 155.72, 138.23, 136.79, 135.87, 128.33, 128.12, 127.89, 127.72, 127.62, 127.22, 127.04, 114.30, 111.16, 109.16, 90.48, 62.68, 55.84, 53.24, 45.95, 40.52, 29.54, 26.20, 21.61; **HRMS**

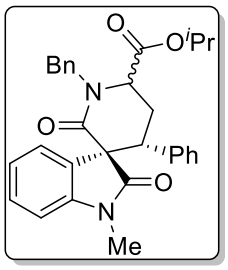
m/z **(ESI):** calcd for $C_{31}H_{30}N_2O_7Na^+$ $[M+Na]^+$: 565.1951, found 565.1945.

(c) Transformation of 3cm



3cm, >95:5 *dr*, 87% *ee* — **6,** 34% yield, >95:5 *dr,* 90% *ee*

To an argon purged reaction tube containing **3cm** (0.1 mmol), $BF_3·Et_2O$ (0.22 mmol) and Et_3SiH (0.2 mmol) was added freshly distilled CH_2Cl_2 (1 mL). After the reaction was stirred for 24 h at room temperature, the resulted mixture was purified by flash column chromatography on silica gel to afford the desired product **6**.



(*3S,4′R*)-isopropyl 1'-benzyl-1-methyl-2,2'-dioxo-4'-phenylspiro[indoline-3,3'-piperidine]-6'-carboxylate (6)

White solid; 16.4 mg, 34% yield; *dr* > 95:5; *ee* = 90%, determined by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, λ = 254 nm, t_r(major) = 39.50 min, t_r(minor) = 15.23 min]; $[\alpha]_D^{25}$ = -77.4 (*c* 0.01, CH_2Cl_2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 (d, *J* = 7.2 Hz, 1H), 7.40-7.32 (m, 5H), 7.23 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.11-7.04 (m, 2H), 7.00-6.97 (m, 2H), 6.79-6.72 (m, 2H), 6.54 (d, *J* = 7.2 Hz, 1H), 5.58 (d, *J* = 14.8 Hz, 1H), 5.15 (p, *J* = 6.4 Hz, 1H), 4.26 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.90 (d, *J* = 14.2 Hz, 1H), 3.74 (dd, *J* = 14.0, 3.2 Hz, 1H), 2.91-2.81 (m, 4H), 2.37-2.31 (m, 1H), 1.37 (d, *J* = 6.4 Hz, 3H), 1.28 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.60, 171.05, 144.90, 136.48, 135.75, 129.18, 128.83, 128.61, 127.80, 127.70, 127.65, 127.63, 127.48, 124.63, 122.29, 108.37, 69.86, 61.99, 59.09, 48.53, 44.15, 27.82, 25.99, 21.81, 21.65; **HRMS** *m/z* **(ESI):** calcd for $C_{30}H_{30}N_2O_4Na^+$ $[M+Na]^+$: 505.2103, found 505.2100.

7. X-ray structures of 1c, 3ca and 3cf

The absolute configurations of **1c**, **3ca** and **3cf** were determined by X-ray crystallography. The stereochemistry of **3aa**, **3ba**, **3da-3ja**, **3cb-3ce**, **3cg-3cm**, and **4-6** were assigned by analogy.

(a) X-ray structure of substrate 1c

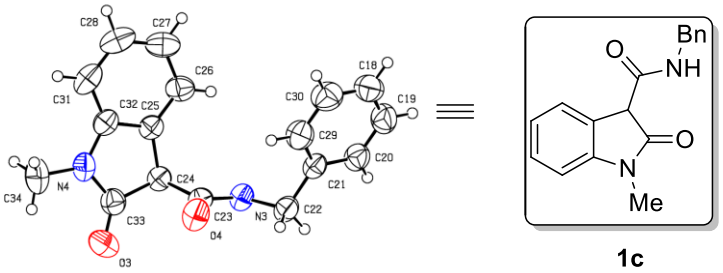


Figure S1. ORTEP diagram (50% probability) of **1c**

A single crystal of **1c** [$C_{17}H_{16}N_2O_2$] was obtained from diffusion of hexane into a solution of **1c** in DCM at room temperature. A suitable crystal of **1c** was selected and analyzed by an Agilent Gemini X-ray Single Crystal Diffractometer. Using Olex2[4], the structure was solved with the ShelXT[5] structure solution program using Direct Methods and refined with the ShelXL[6] refinement package using Least Squares minimization. Details of the crystal, data collection, and structure refinement parameters for crystallographic analysis of **1c** are summarized in **Table S2**. Crystallographic data (CCDC 1963639) for **1c** can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S2. Parameters for crystallographic analysis of **1c**

Identification code	cu_20180303_sanxianan_0ma-auto
Empirical formula	$C_{34}H_{32}N_4O_4$
Formula weight	560.63
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	22.2717(14)
b/Å	14.1714(9)
c/Å	9.3683(5)
α/°	90
β/°	96.922(3)
γ/°	90
Volume/Å^3	2935.3(3)
Z	4

ρ_{calc}g/cm^3	1.269
μ/mm^{-1}	0.679
F(000)	1184
Radiation	CuKα (λ = 1.54178)
Theta range for data collection/ °	7.41 to 120.274
Index ranges	-25 ≤ h ≤ 25, -15 ≤ k ≤ 15, -10 ≤ l ≤ 10
Reflections collected	37447
Independent reflections	4369 [R_{int} = 0.0723, R_{sigma} = 0.0459]
Data/restraints/parameters	4369/0/321
Goodness-of-fit on F^2	1.010
Final R indexes [I>=2σ (I)]	R_1 = 0.0467, wR_2 = 0.1111
Final R indexes [all data]	R_1 = 0.0731, wR_2 = 0.1260
Largest diff. peak/hole / e Å^{-3}	0.15/-0.20

(b) X-ray structure of product 3ca

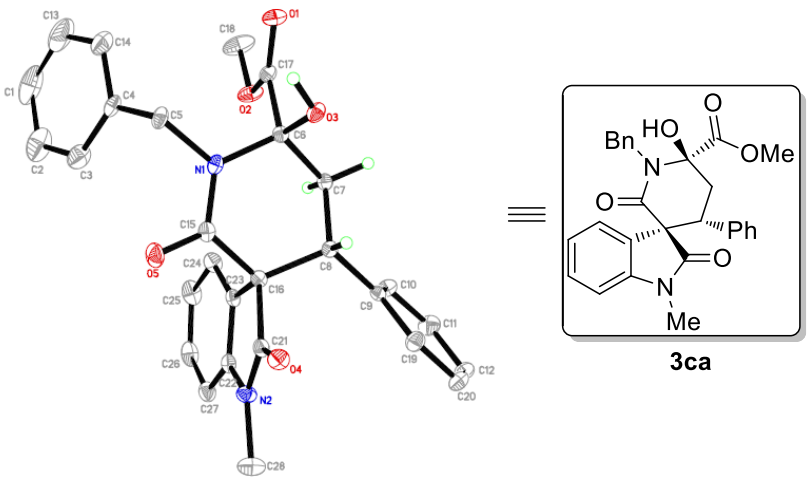


Figure S2. ORTEP diagram (30% probability) of **3ca**

A single crystal of **3ca** [$C_{28}H_{26}N_2O_5$] was obtained from diffusion of hexane into a solution of **3ca** in DCM at room temperature. A suitable crystal of **3ca** was selected and analyzed by an Agilent Gemini X-ray Single Crystal Diffractometer. Using Olex2[4], the structure was solved with the ShelXT[5] structure solution program using Direct Methods and refined with the ShelXL[6] refinement package using Least Squares minimization.

Refinement of the Flack parameter[7] for **3ca** was refined to the value of 0.00(8), which clearly suggests that the absolute configuration of the major isomer of **3ca** is (3*R*,4'*R*,6'*R*). Details of the crystal, data collection, and structure refinement parameters for crystallographic analysis of **3ca** are summarized in **Table S3**. Crystallographic data (CCDC 1963638) for **3ca** can be obtained free of charge from

the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S3. Parameters for crystallographic analysis of **3ca**

Identification code	Cu_20170607nch3_0m-auto
Empirical formula	$C_{28}H_{26}N_2O_5$
Formula weight	470.51
Temperature/K	149(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	11.1247(17)
b/Å	11.7728(18)
c/Å	18.015(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2359.4(6)
Z	4
ρ_{calc}g/cm^3	1.325
μ/mm^{-1}	0.746
F(000)	992.0
Radiation	CuKα (λ = 1.54178)
Theta range for data collection/ °	8.972 to 127.732
Index ranges	$-12 \leq h \leq 12$, $-13 \leq k \leq 13$, $-20 \leq l \leq 20$
Reflections collected	34236
Independent reflections	3889 [R_{int} = 0.0541, R_{sigma} = 0.0242]
Data/restraints/parameters	3889/0/321
Goodness-of-fit on F^2	1.095
Final R indexes [I>=2σ (I)]	R_1 = 0.0293, wR_2 = 0.0702
Final R indexes [all data]	R_1 = 0.0320, wR_2 = 0.0717
Largest diff. peak/hole / e Å^{-3}	0.14/-0.22
Flack parameter	0.00(8)

(c) X-ray structure of product 3cf

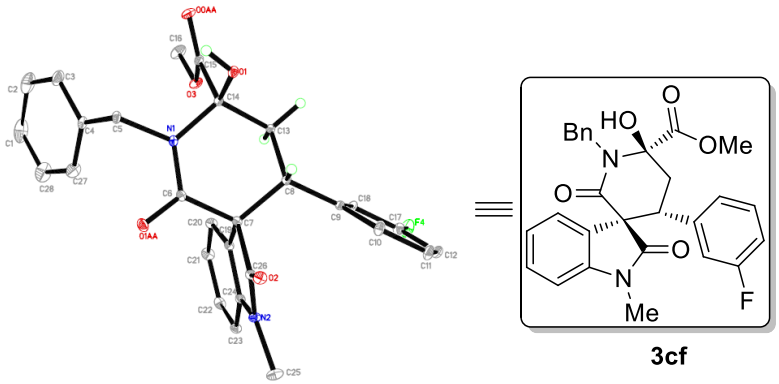


Figure S3. ORTEP diagram (30% probability) of **3cf**

A single crystal of **3cf** [$C_{28}H_{25}FN_2O_5$] was obtained from diffusion of hexane into a solution of **3cf** in DCM at room temperature. A suitable crystal of **3cf** was selected and analyzed by an Agilent Gemini X-ray Single Crystal Diffractometer. Using Olex2[4], the structure was solved with the ShelXT[5] structure solution program using Direct Methods and refined with the ShelXL[6] refinement package using Least Squares minimization.

Refinement of the Flack parameter[7] for **3cf** was refined to the value of 0.11(7), which clearly suggests that the absolute configuration of the major isomer of **3cf** is (3*R*,4'*R*,6'*R*). Details of the crystal, data collection, and structure refinement parameters for crystallographic analysis of **3cf** are summarized in **Table S4**. Crystallographic data (CCDC 1963637) for **3cf** can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S4. Parameters for crystallographic analysis of **3cf**

Identification code	cu_20170324mf_0m-auto
Empirical formula	$C_{28}H_{25}FN_2O_5$
Formula weight	488.50
Temperature/K	273(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	11.316(4)
b/Å	11.859(4)
c/Å	18.168(3)
α/°	90
β/°	90
γ/°	90

Volume/Å^3	2438.0(11)
Z	4
ρ_{calc}g/cm^3	1.331
μ/mm^{-1}	0.804
F(000)	1024
Radiation	Cu Kα (λ = 1.54178)
theta range for data collection/ °	8.904 to 127.56
Index ranges	$-13 \leq h \leq 13$, $-12 \leq k \leq 13$, $-21 \leq l \leq 21$
Reflections collected	14025
Independent reflections	3990 [R_{int} = 0.0282, R_{sigma} = 0.0257]
Data/restraints/parameters	3990/0/328
Goodness-of-fit on F^2	1.152
Final R indexes [I>=2σ (I)]	R_1 = 0.0362, wR_2 = 0.0983
Final R indexes [all data]	R_1 = 0.0421, wR_2 = 0.1076
Largest diff. peak/hole / e Å^{-3}	0.37/-0.33
Flack parameter	0.11(7)

8. References

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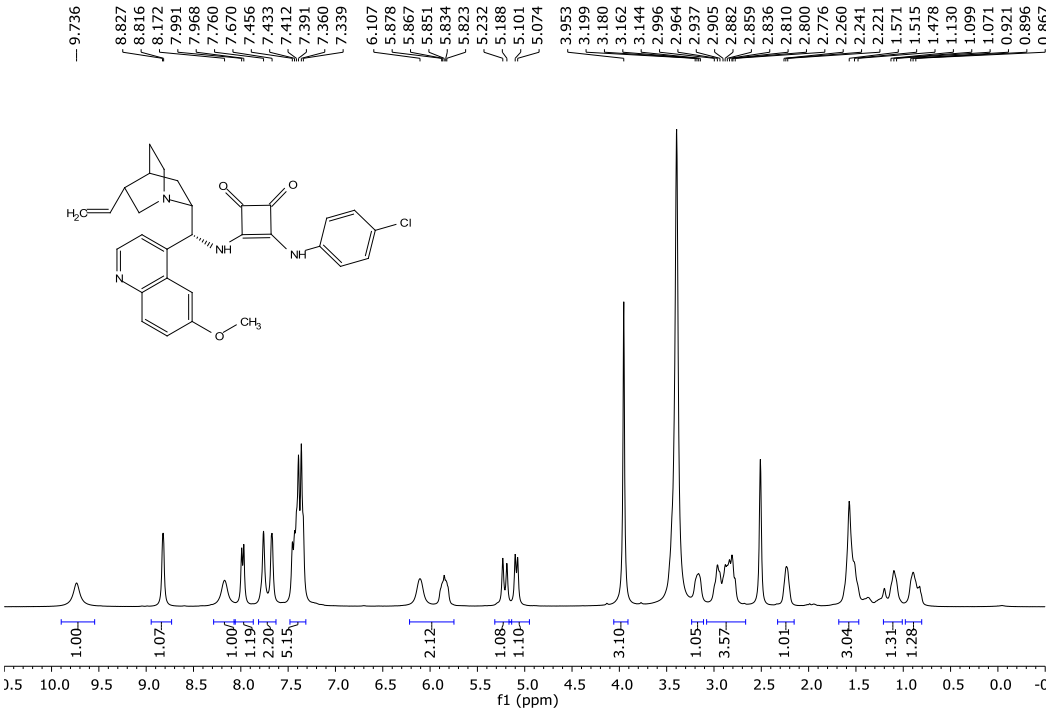
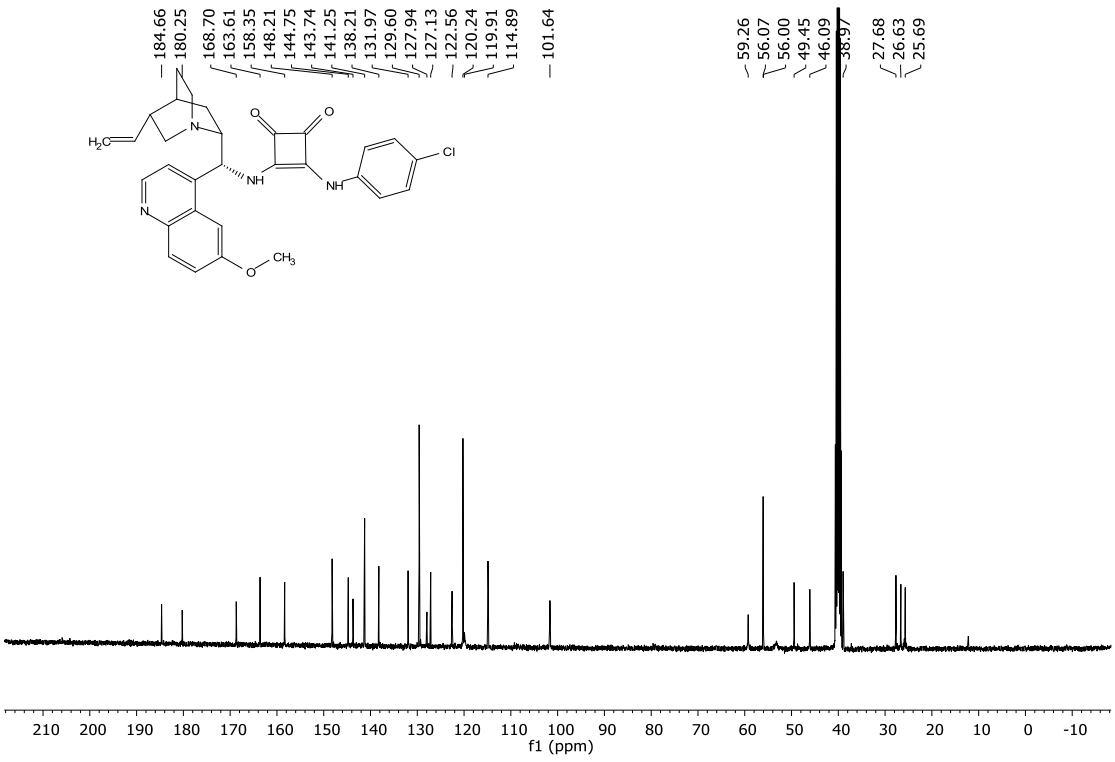
9. NMR spectra

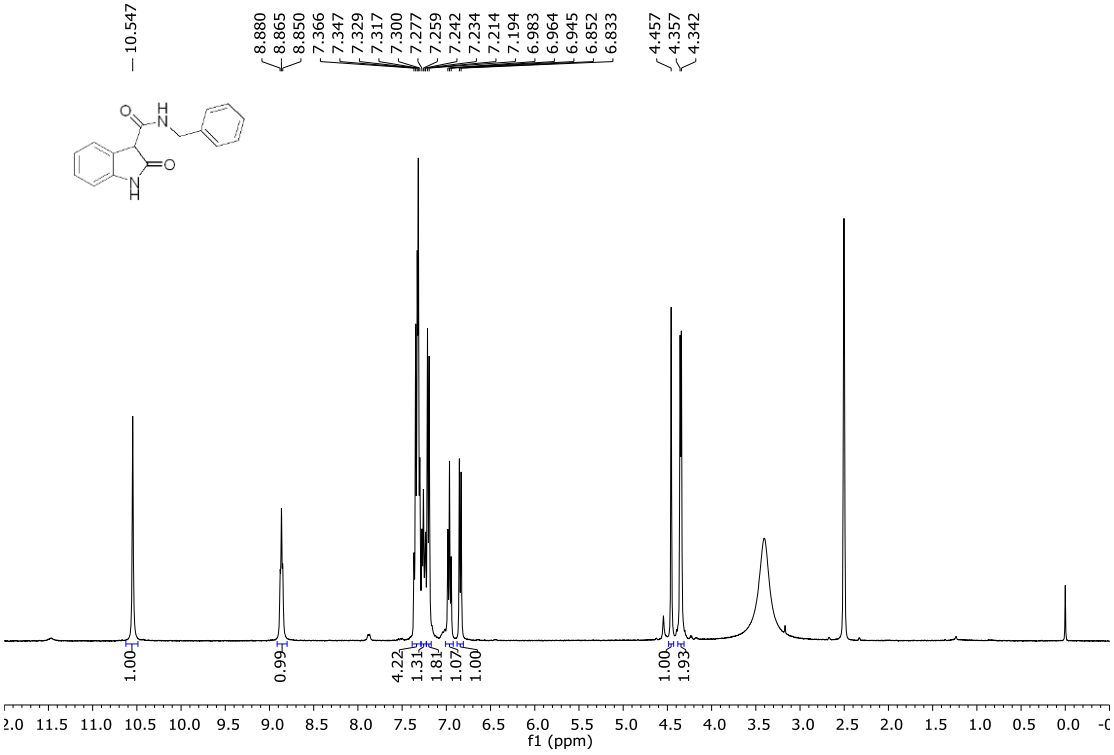
C7, ^{1}H NMR (400 MHz, DMSO-d_6):



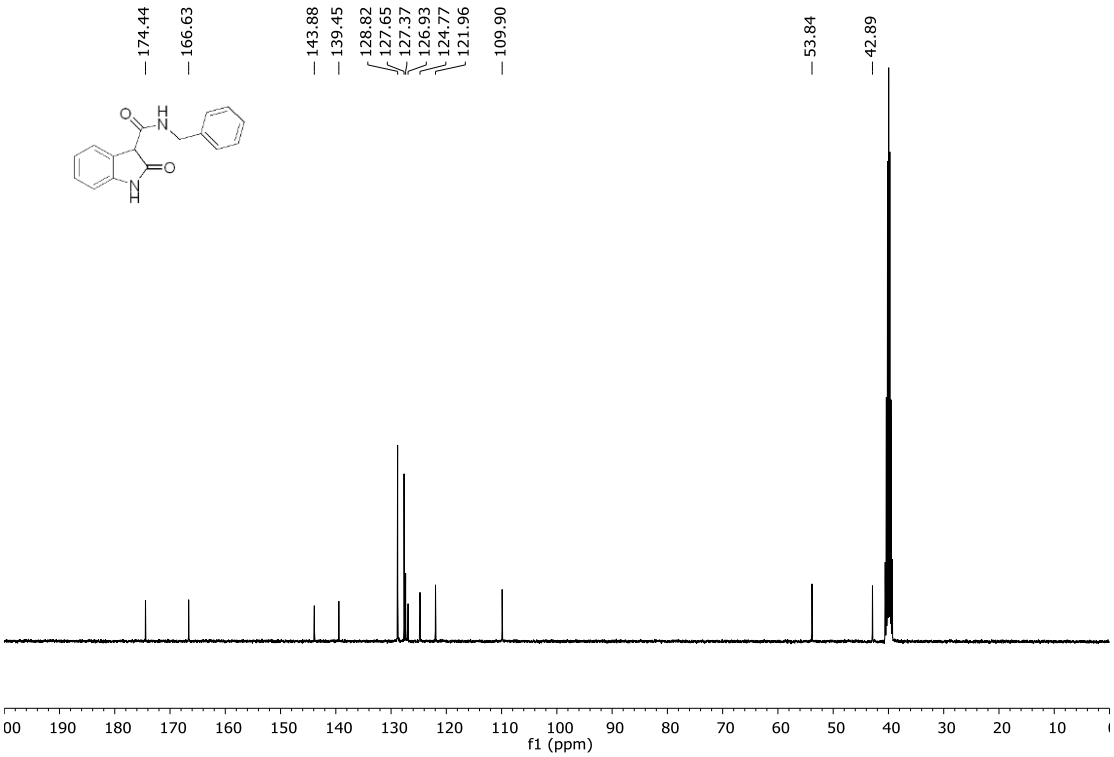
C7, ^{13}C NMR (100 MHz, DMSO-d_6):



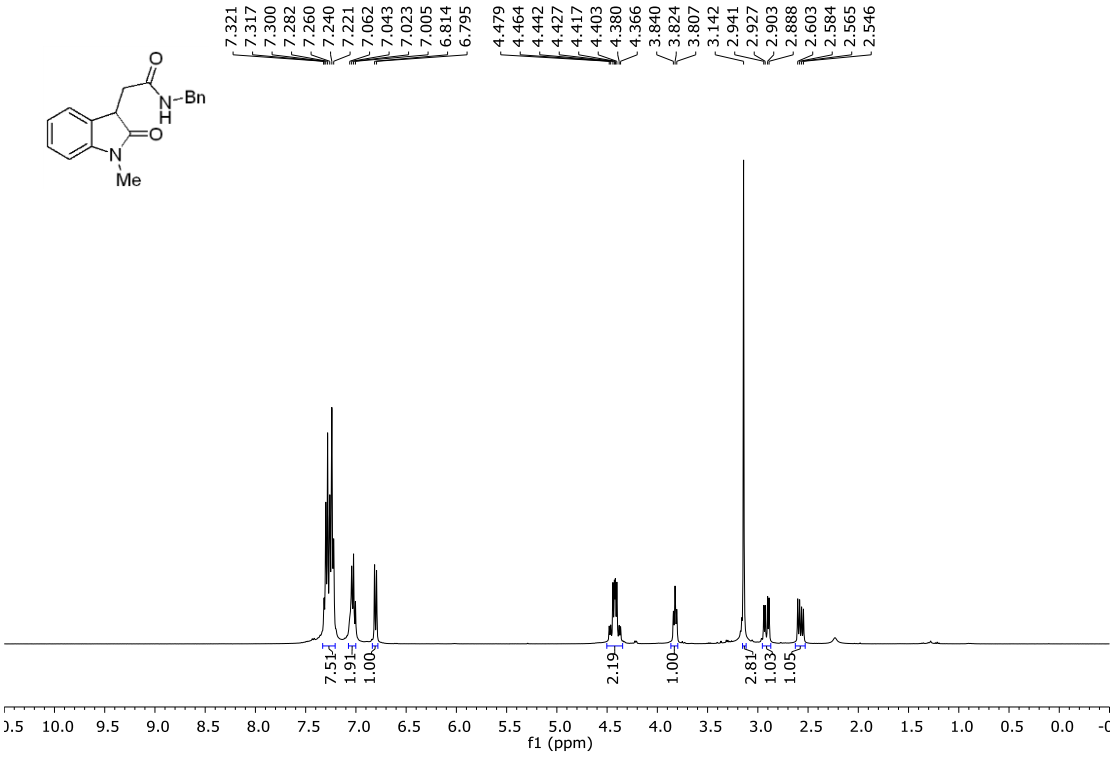
1l, ^{1}H NMR (400 MHz, DMSO-d_6)



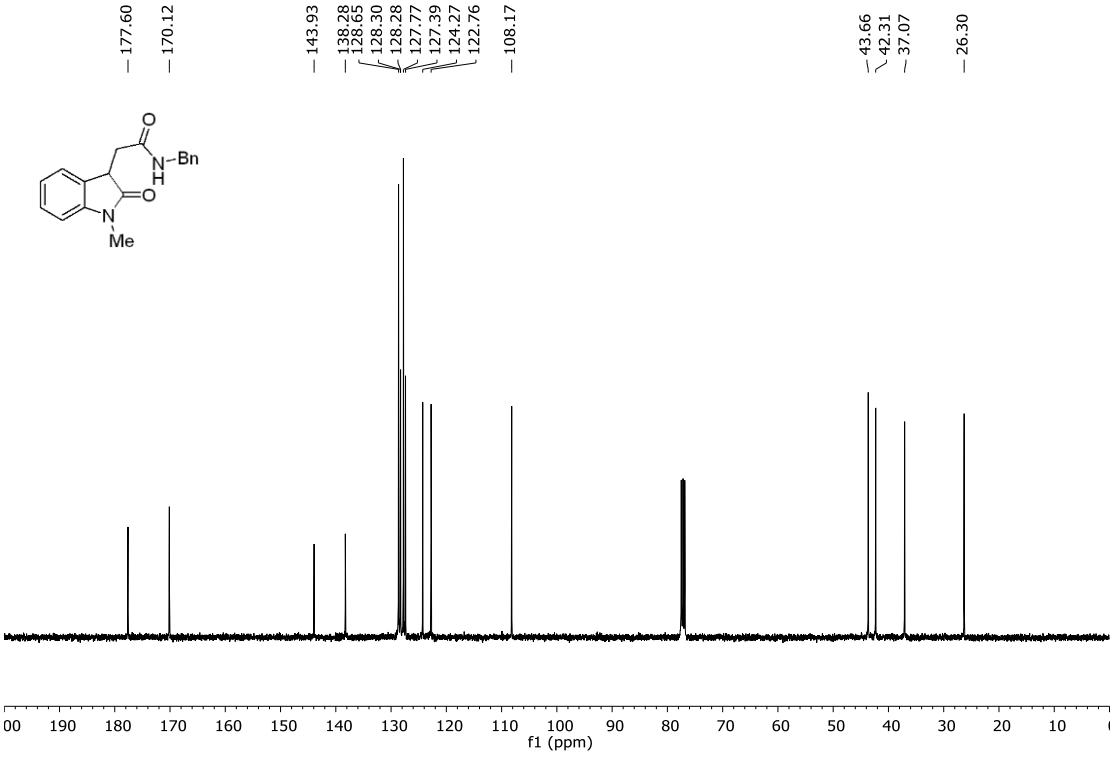
1l, ^{13}C NMR (100 MHz, DMSO-d_6):



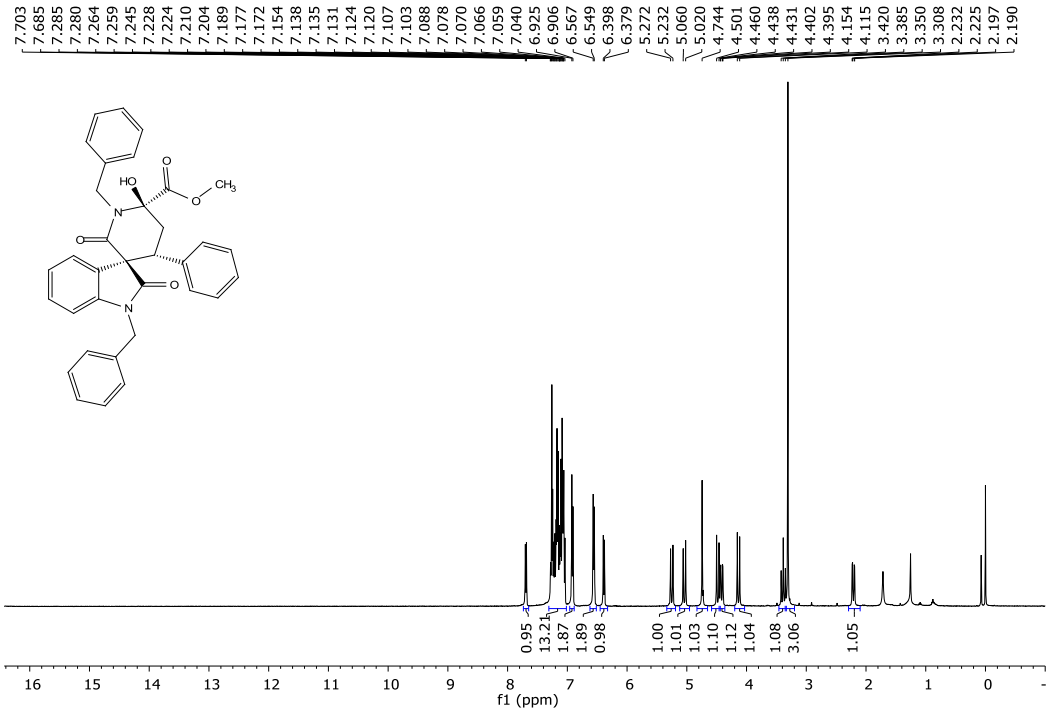
1m, ^{1}H NMR (400 MHz, $CDCl_3$):



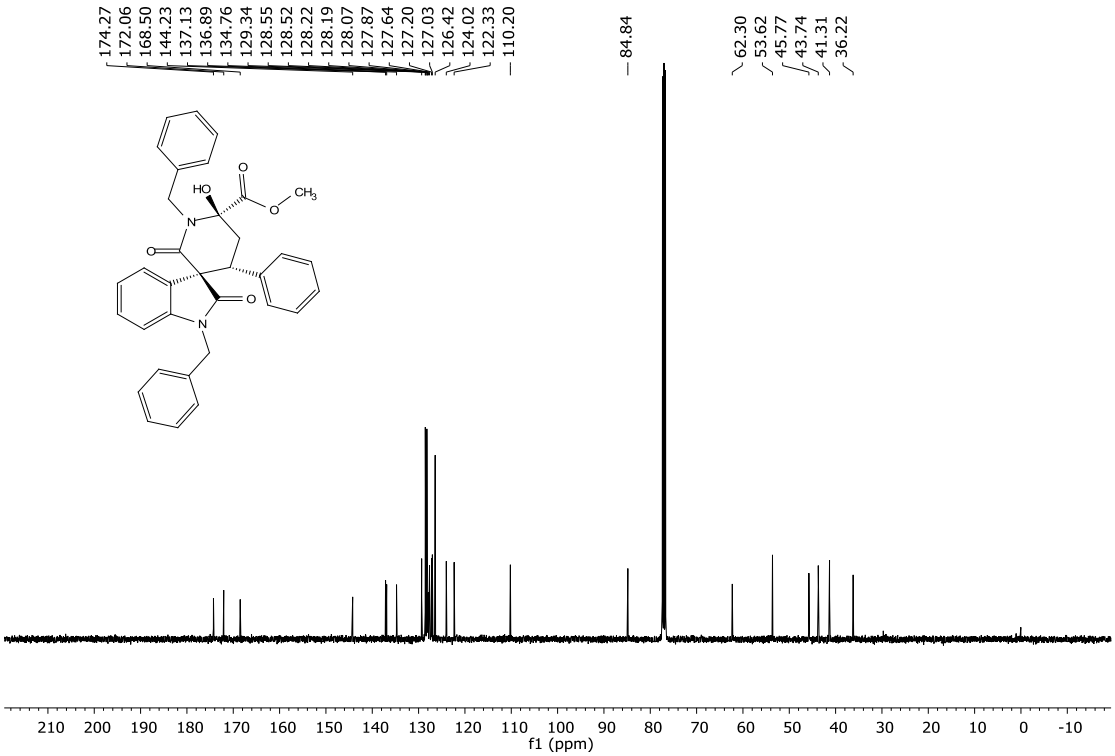
1m, ^{13}C NMR (100 MHz, $CDCl_3$):



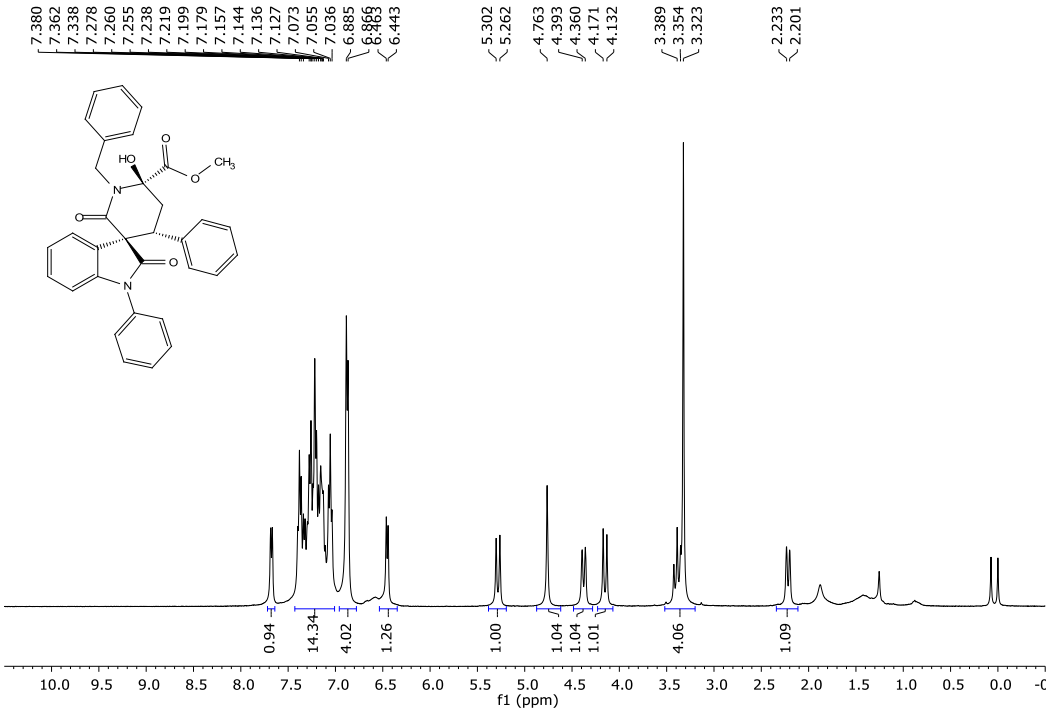
3aa, ^{1}H NMR (400 MHz, $CDCl_3$):



3aa, ^{13}C NMR (100 MHz, $CDCl_3$):



3ba, ^{1}H NMR (400 MHz, $CDCl_3$):



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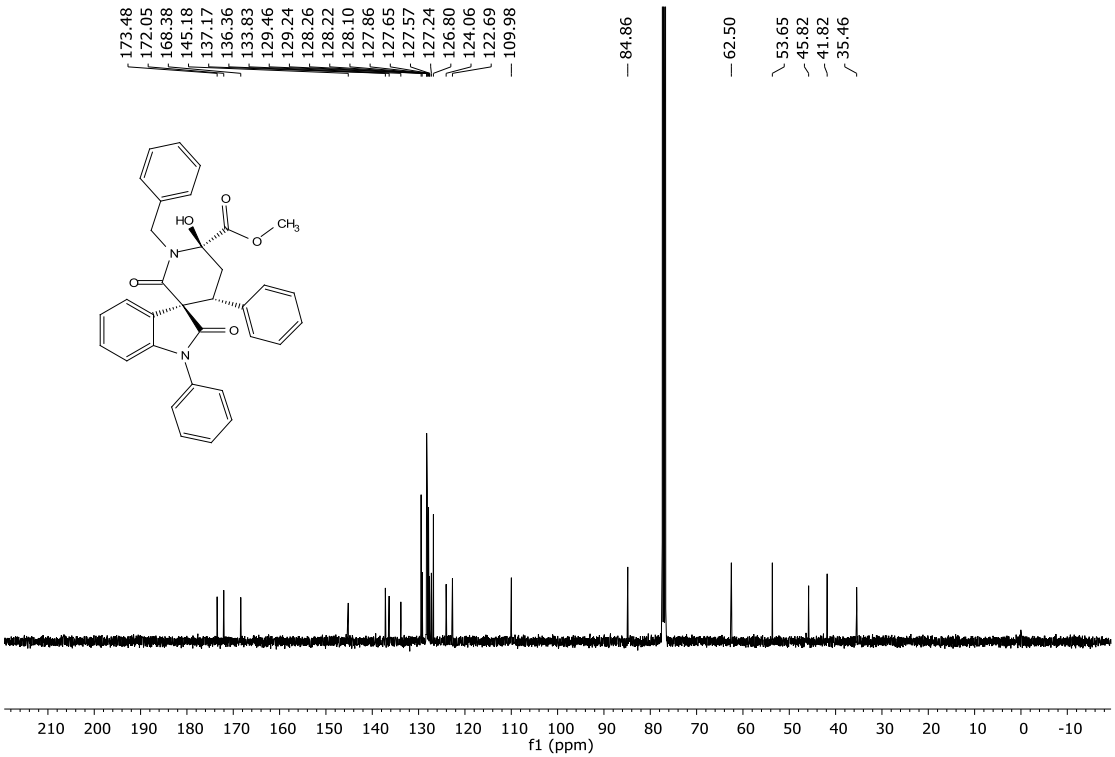
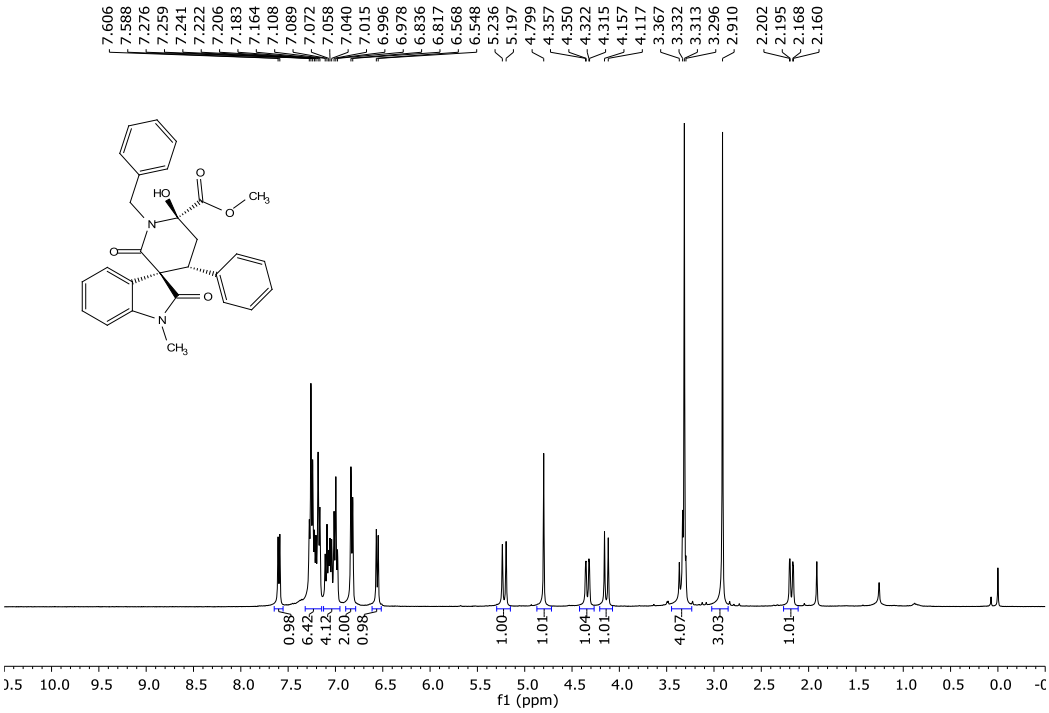
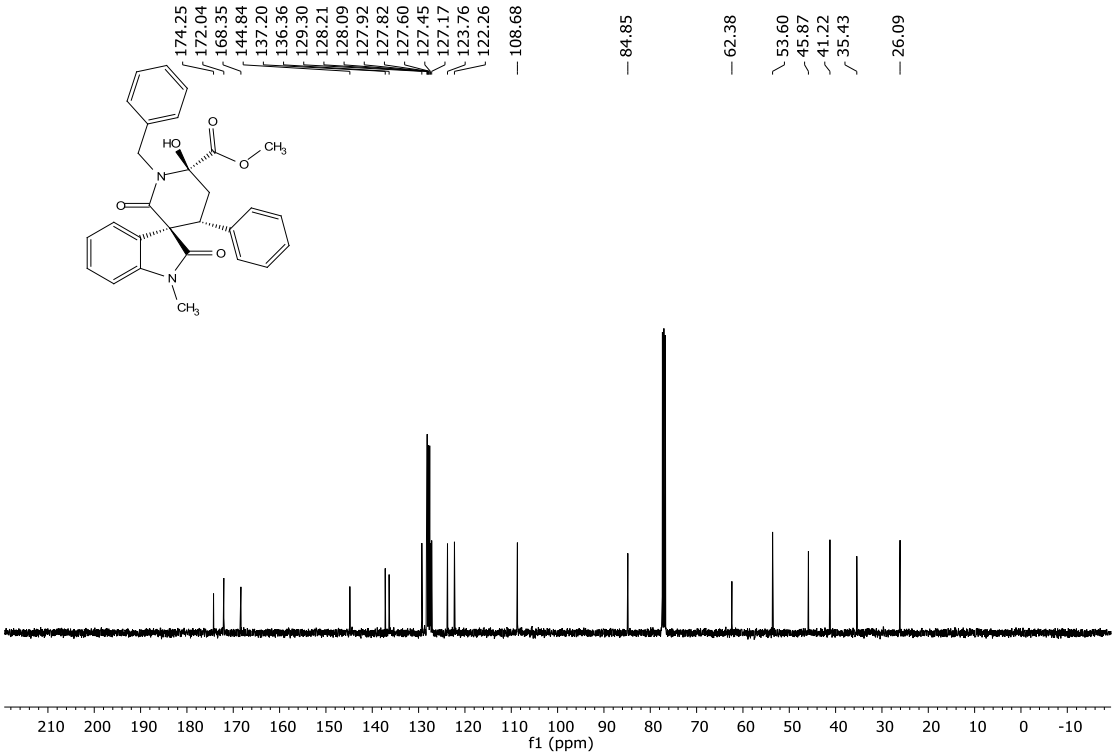


3ca, ^{1}H NMR (400 MHz, $CDCl_3$):



3ca, ^{13}C NMR (100 MHz, $CDCl_3$):



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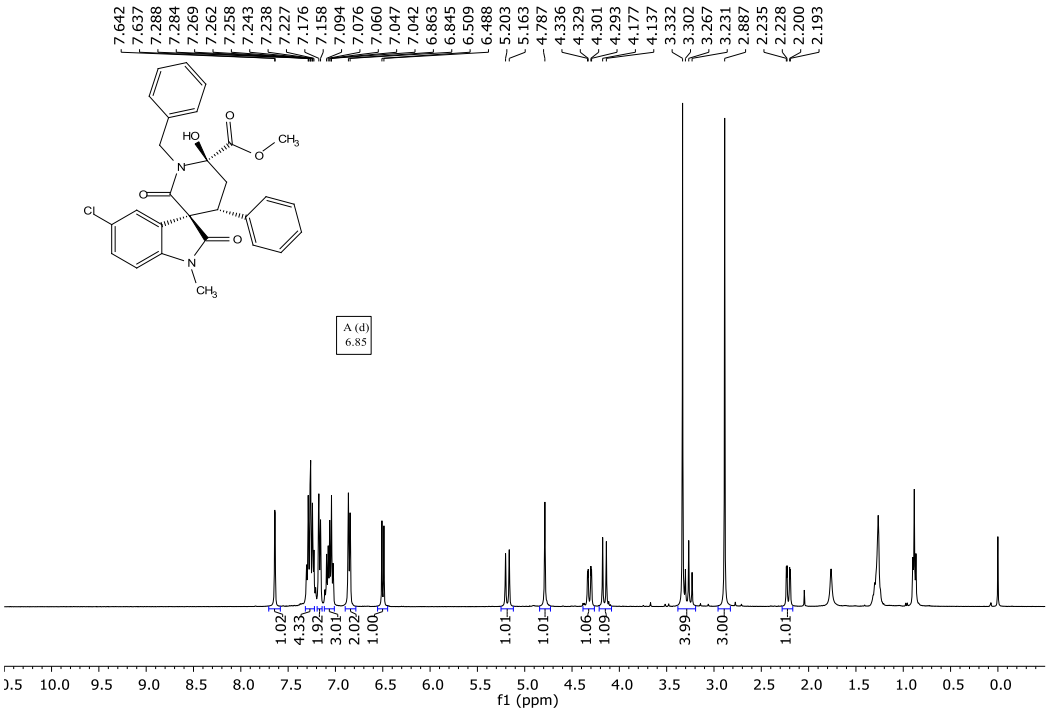

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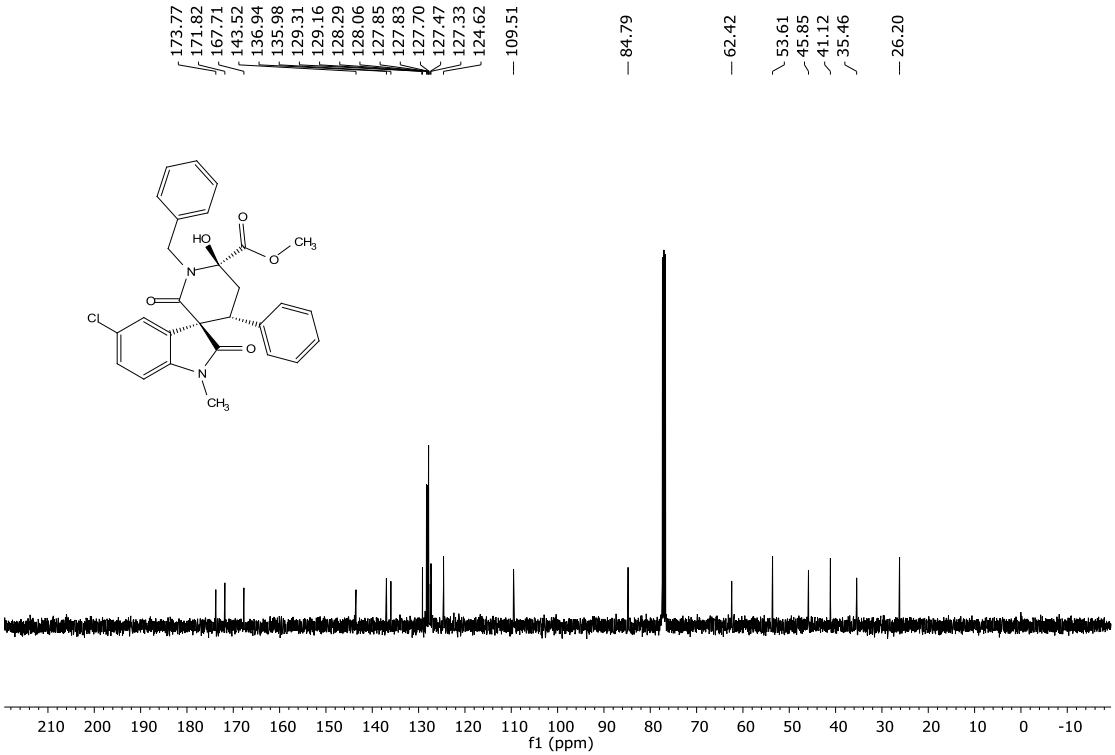

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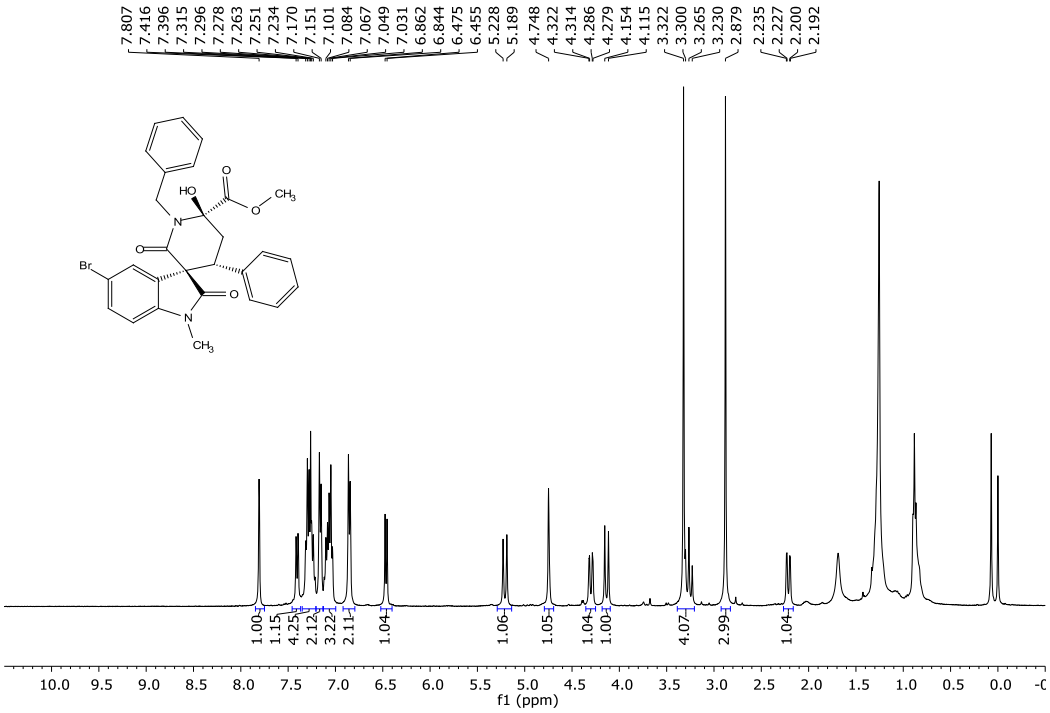
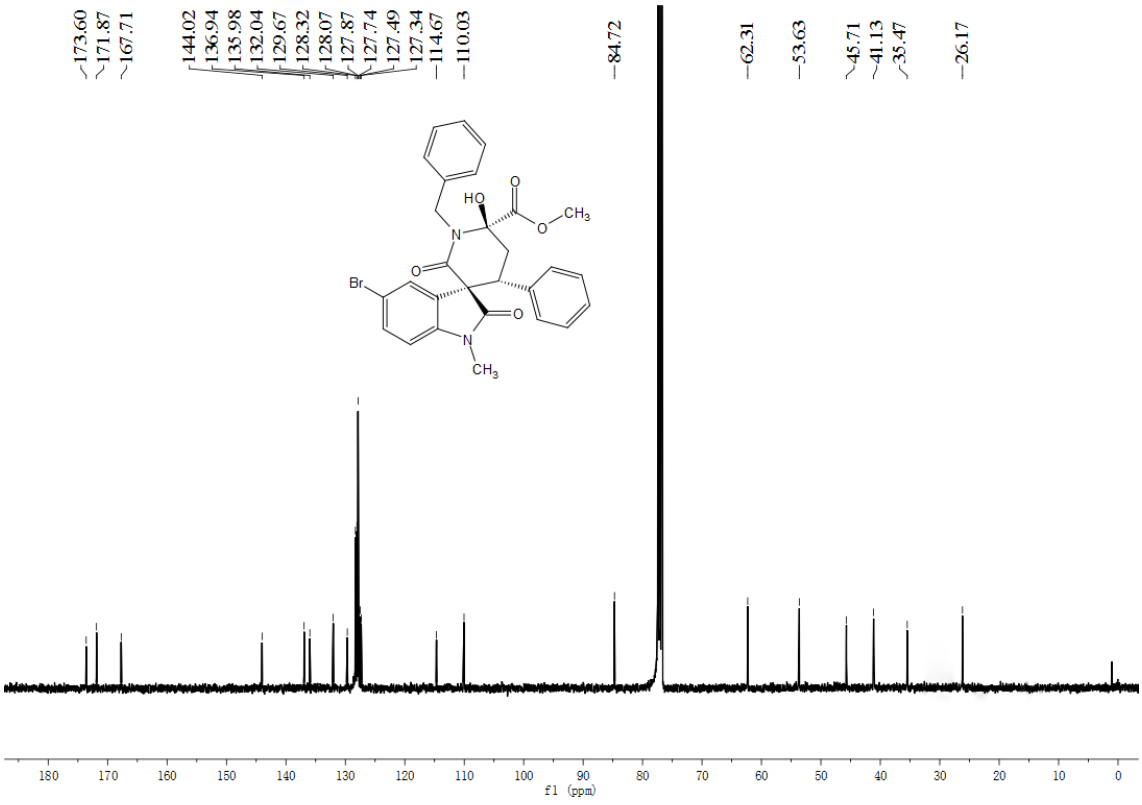


3ea, ^{13}C NMR (100 MHz, $CDCl_3$):



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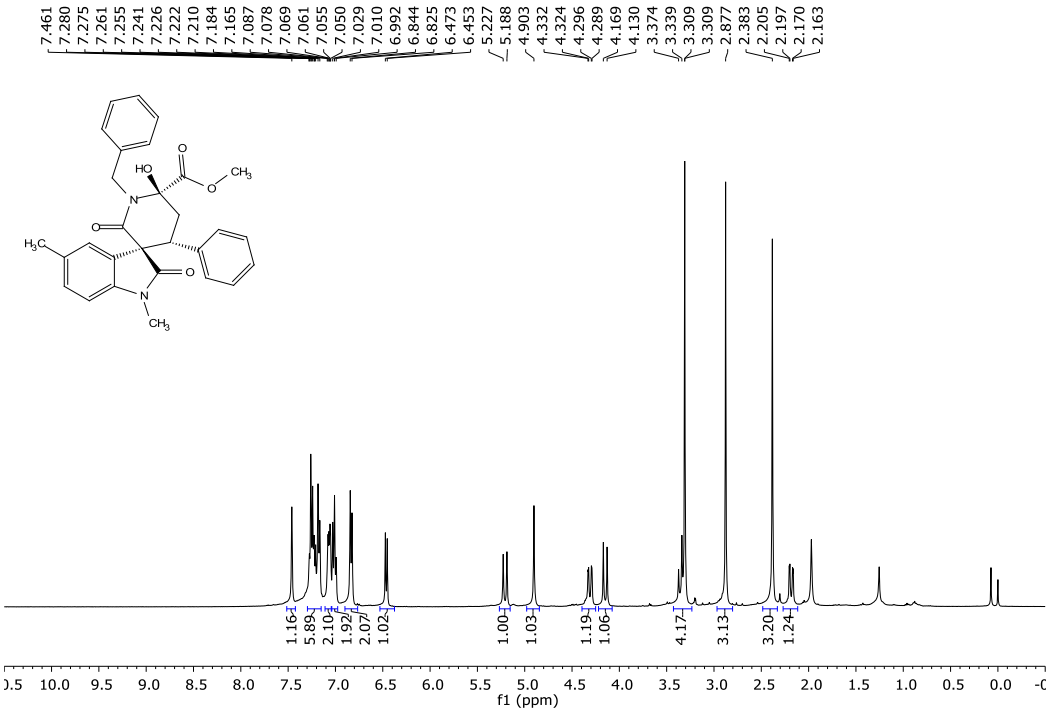

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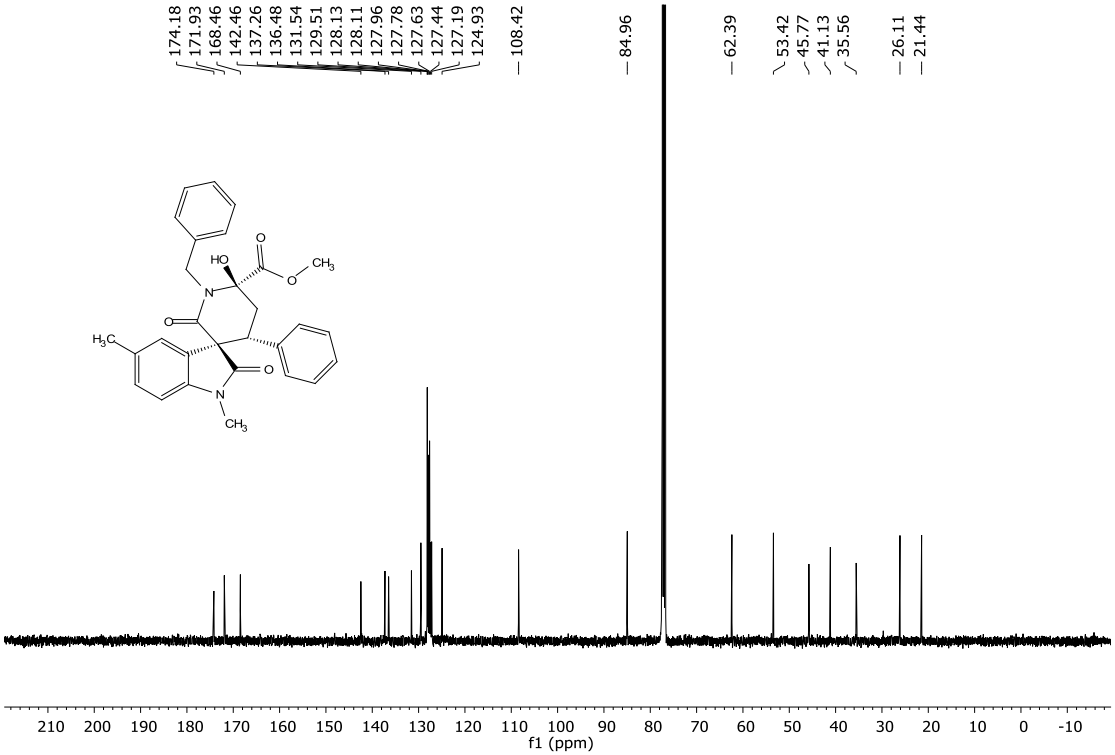
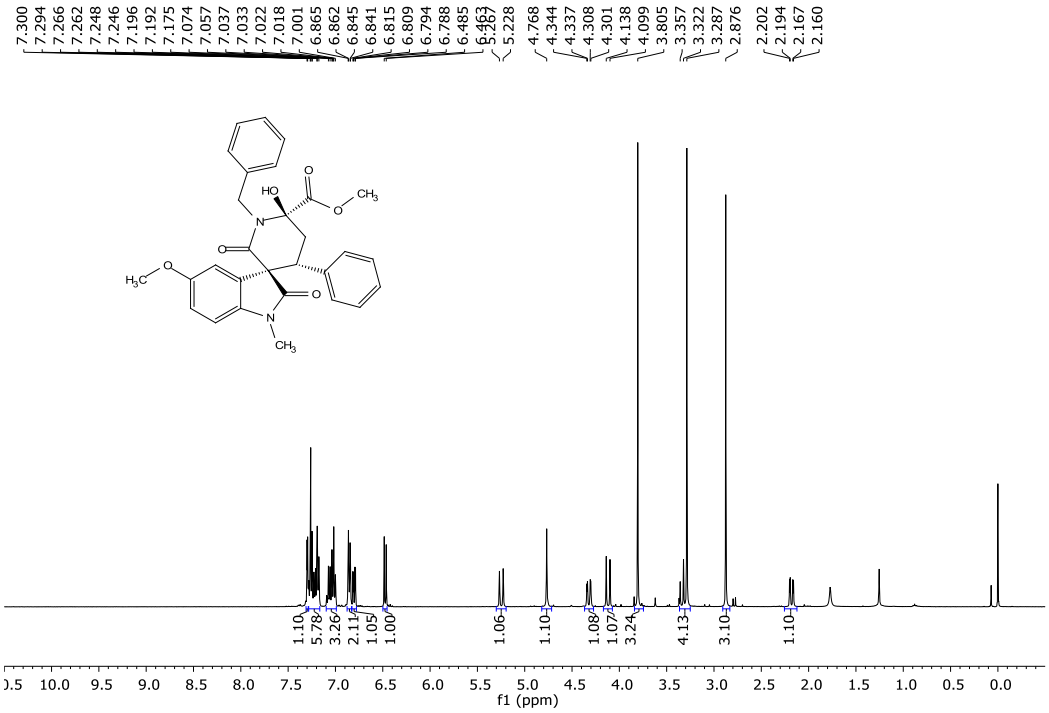


3ga, ^{1}H NMR (400 MHz, $CDCl_3$):



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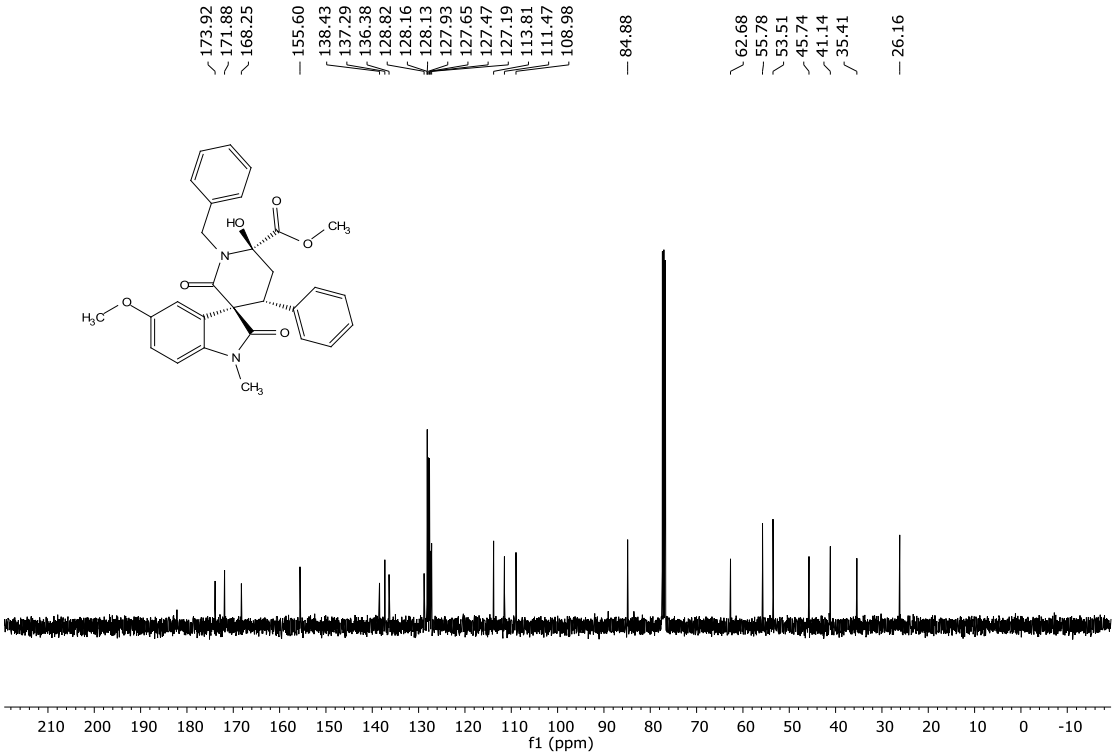

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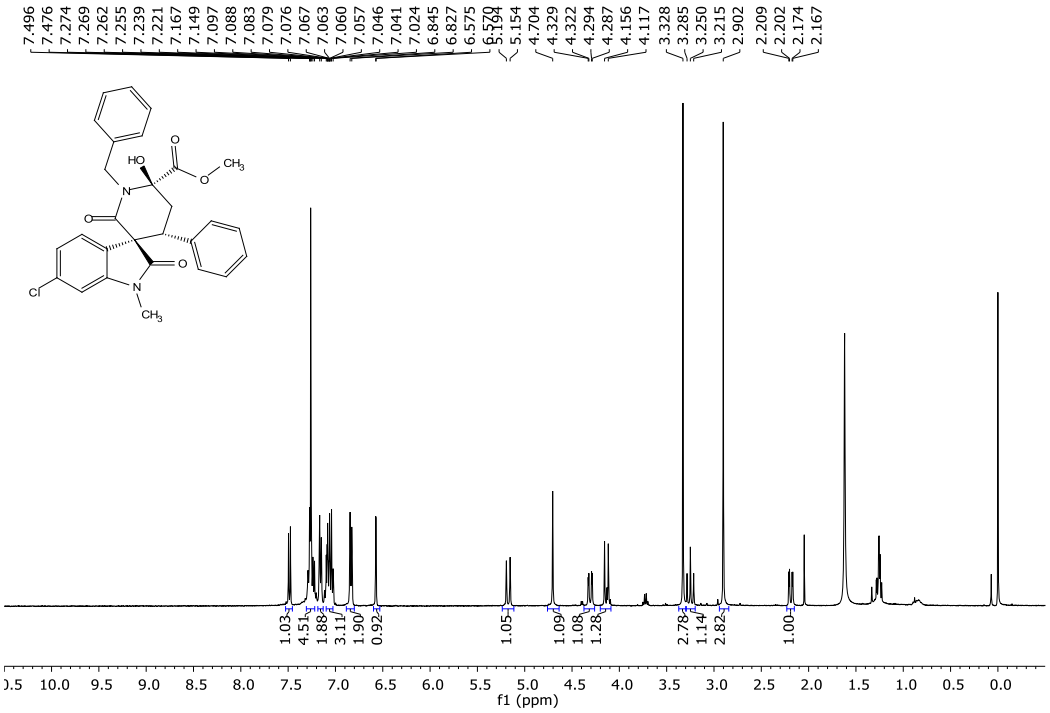
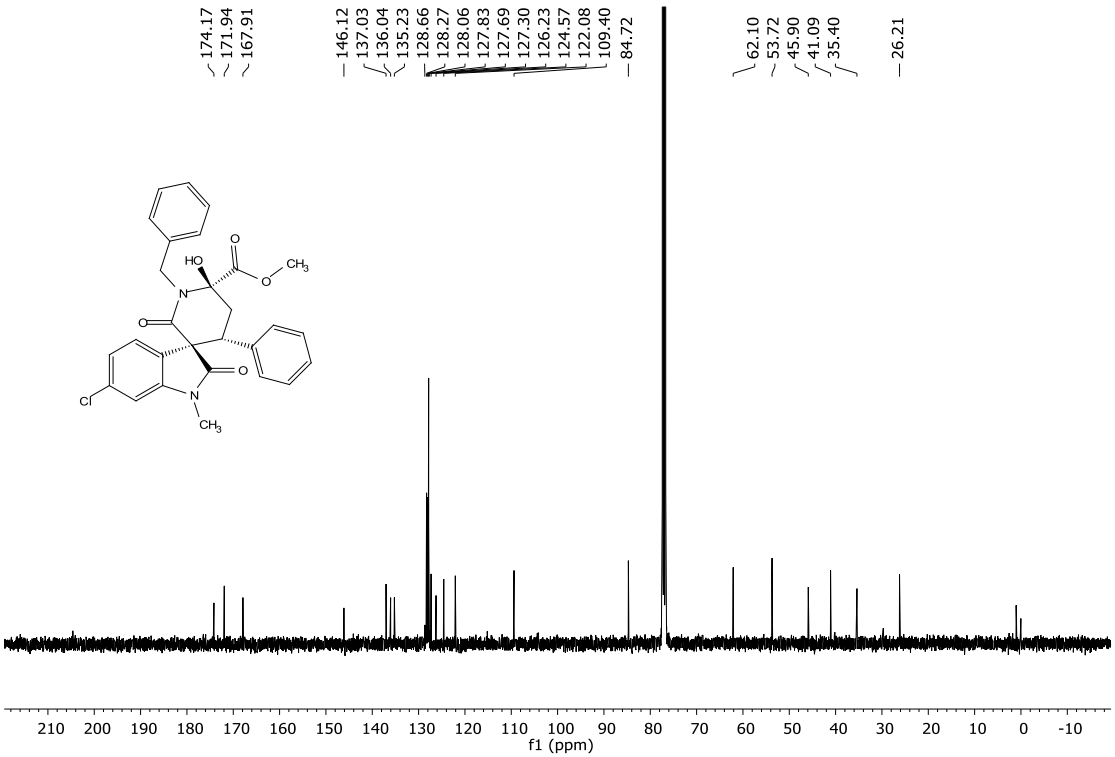


3ha, ^{13}C NMR (100 MHz, $CDCl_3$):



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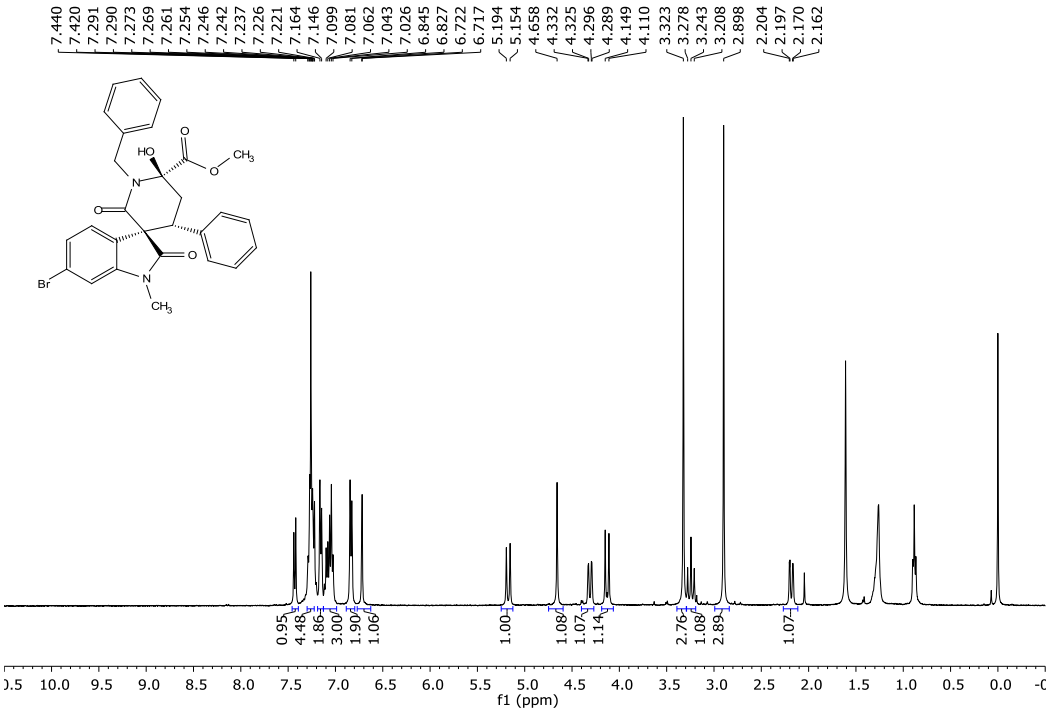
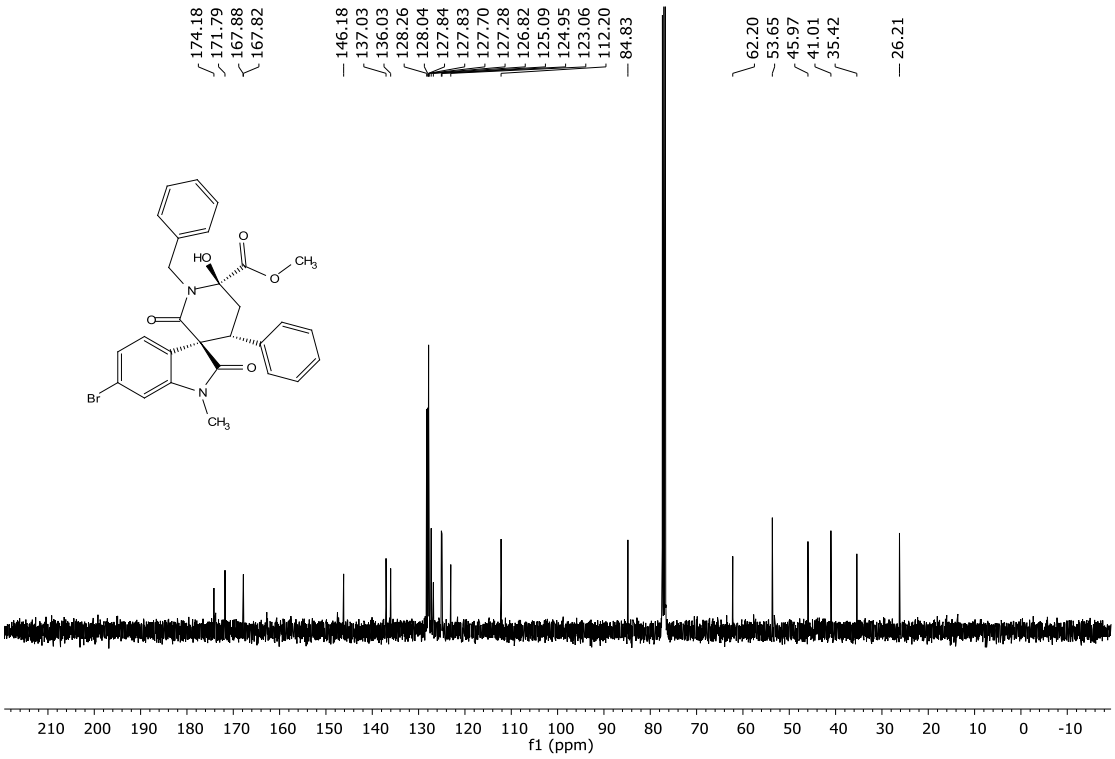


3ia, ^{13}C NMR (100 MHz, $CDCl_3$):



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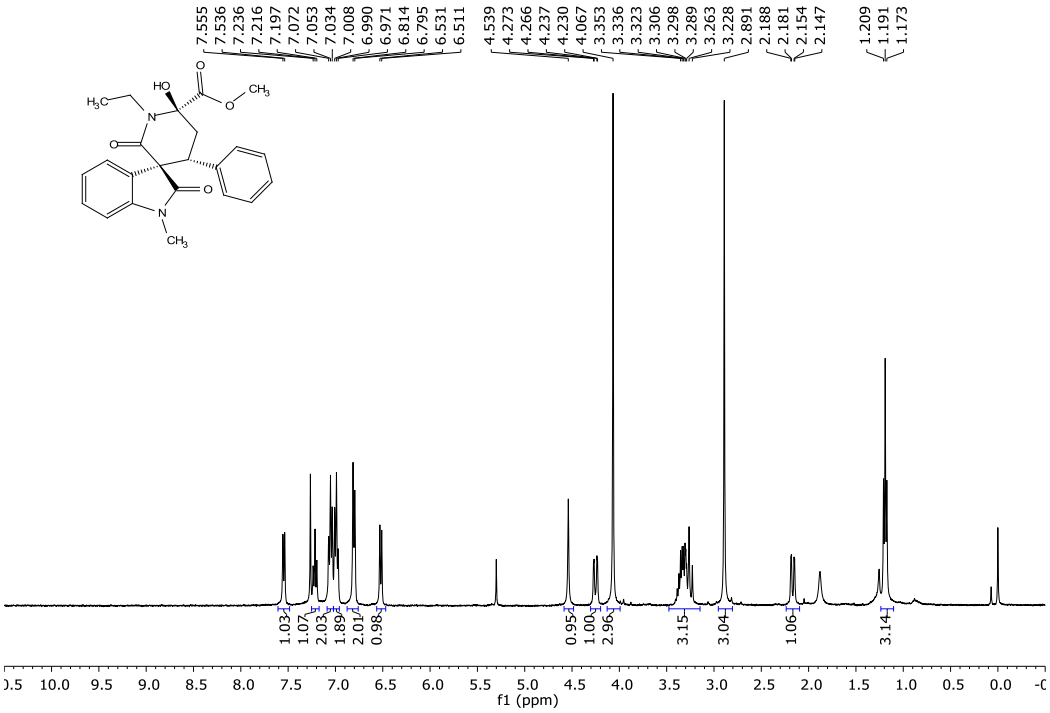

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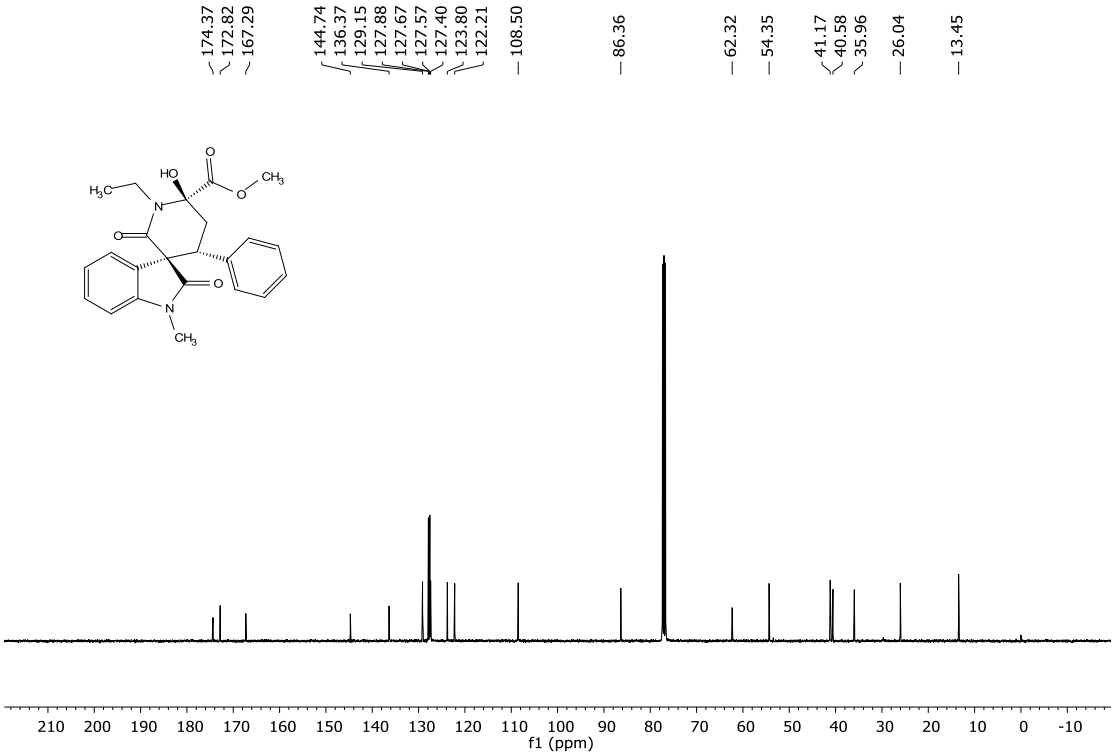
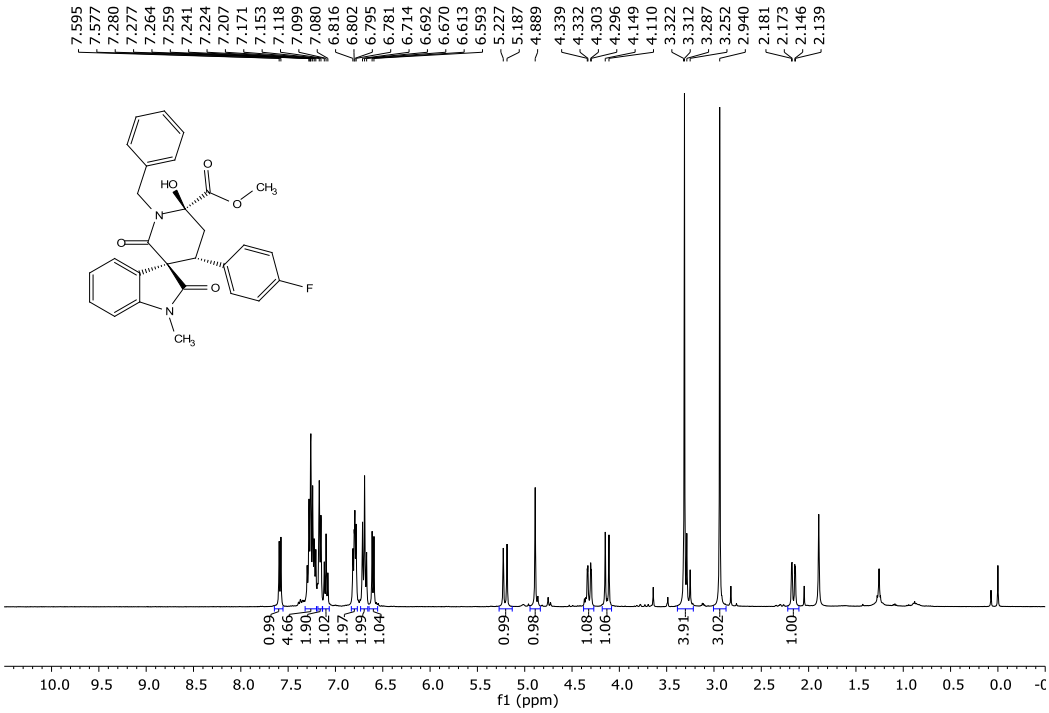
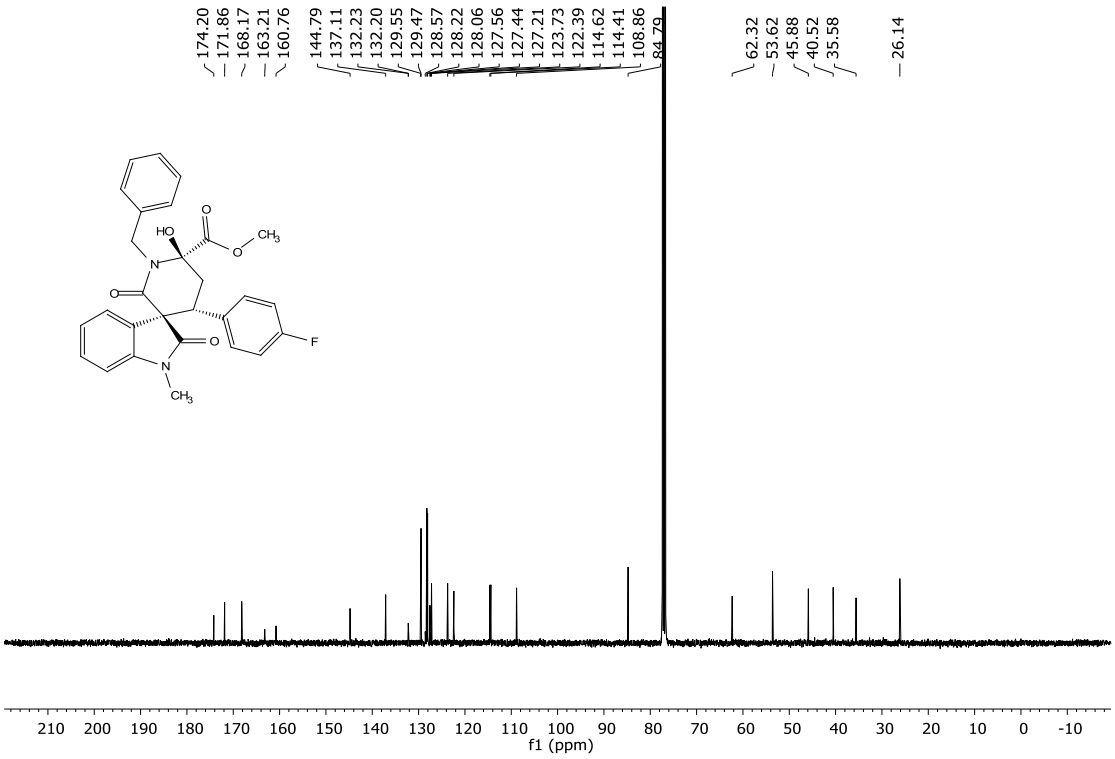


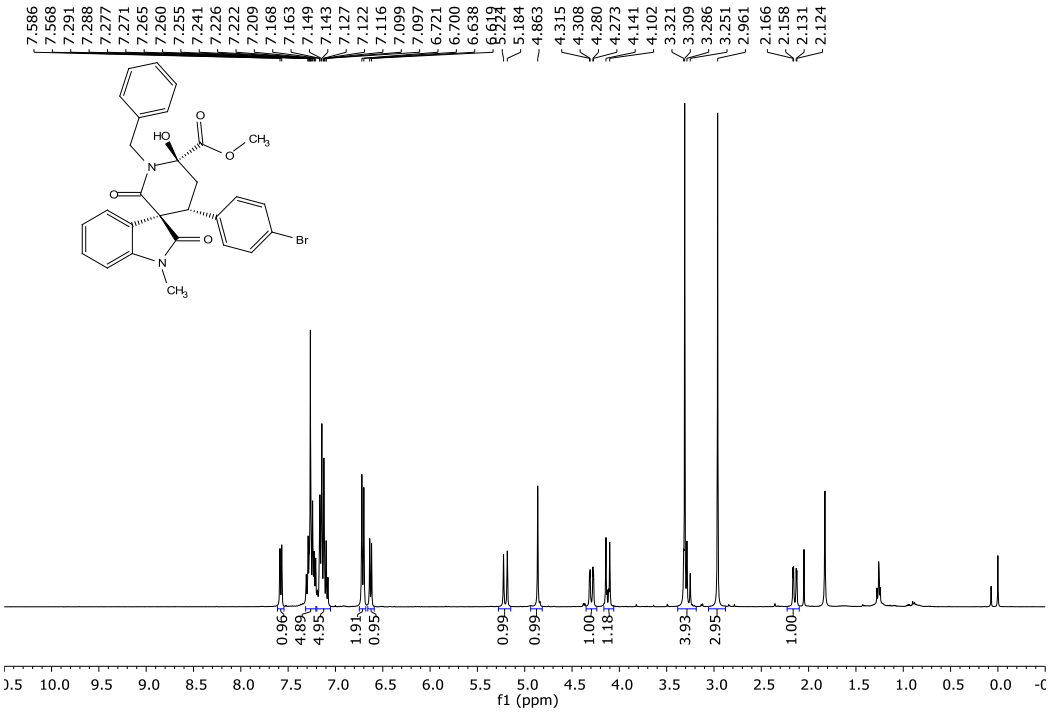
3cb, ^{1}H NMR (400 MHz, $CDCl_3$):



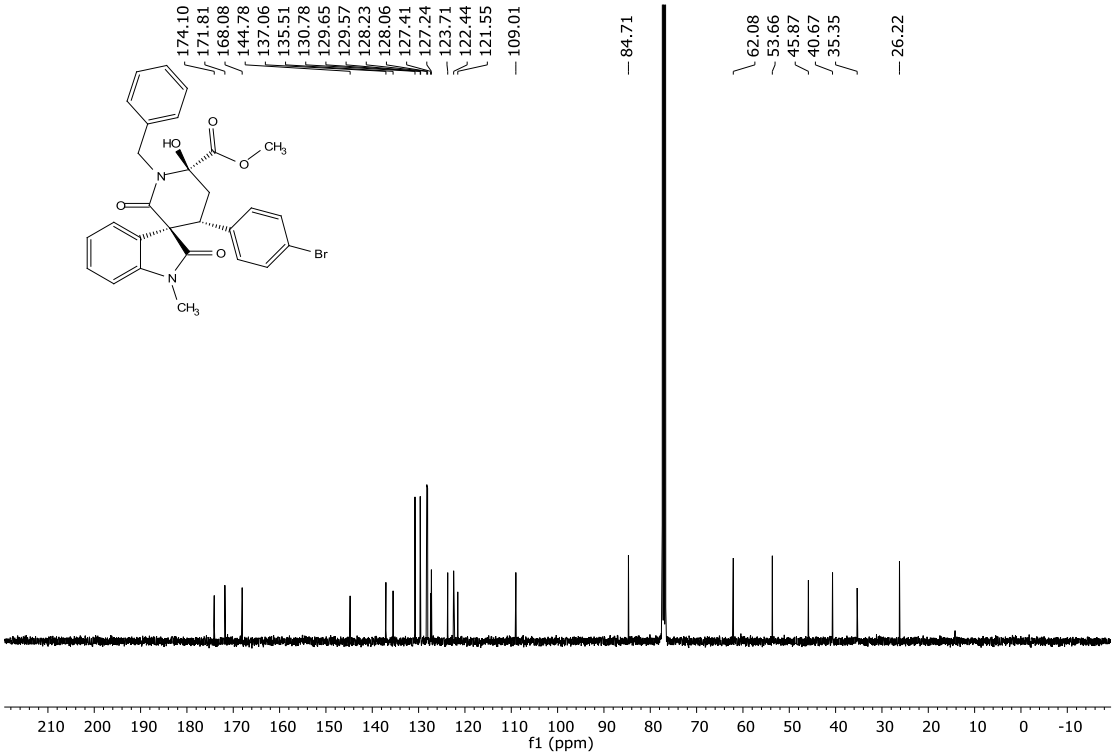
3cb, ^{13}C NMR (100 MHz, $CDCl_3$):



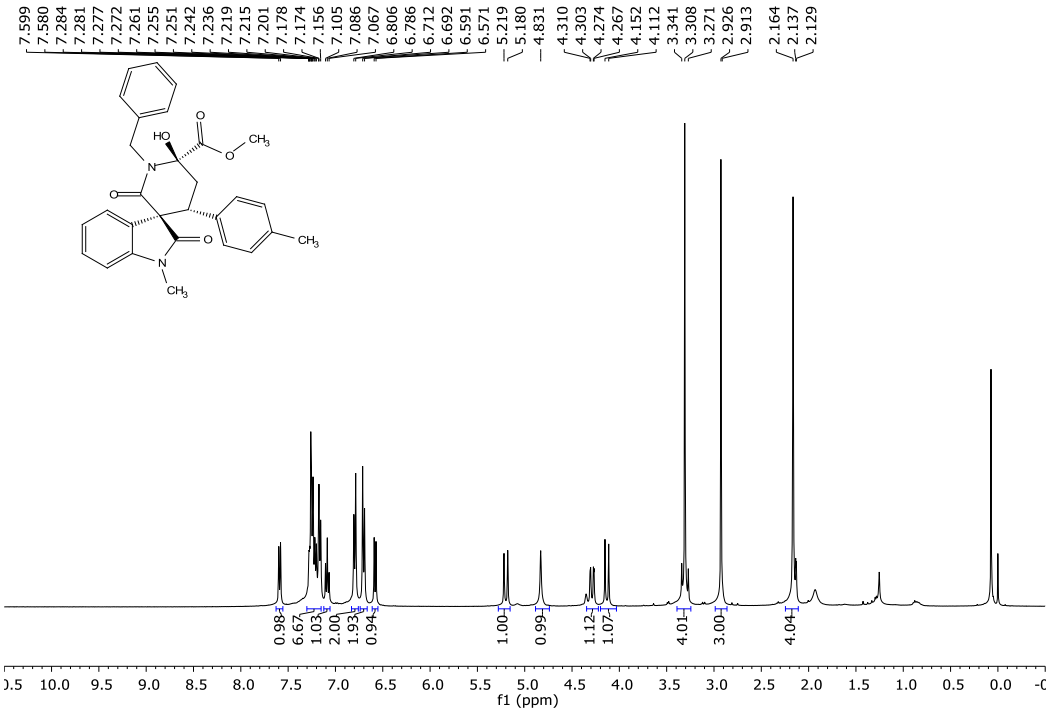
3cc, ^{1}H NMR (400 MHz, $CDCl_3$):



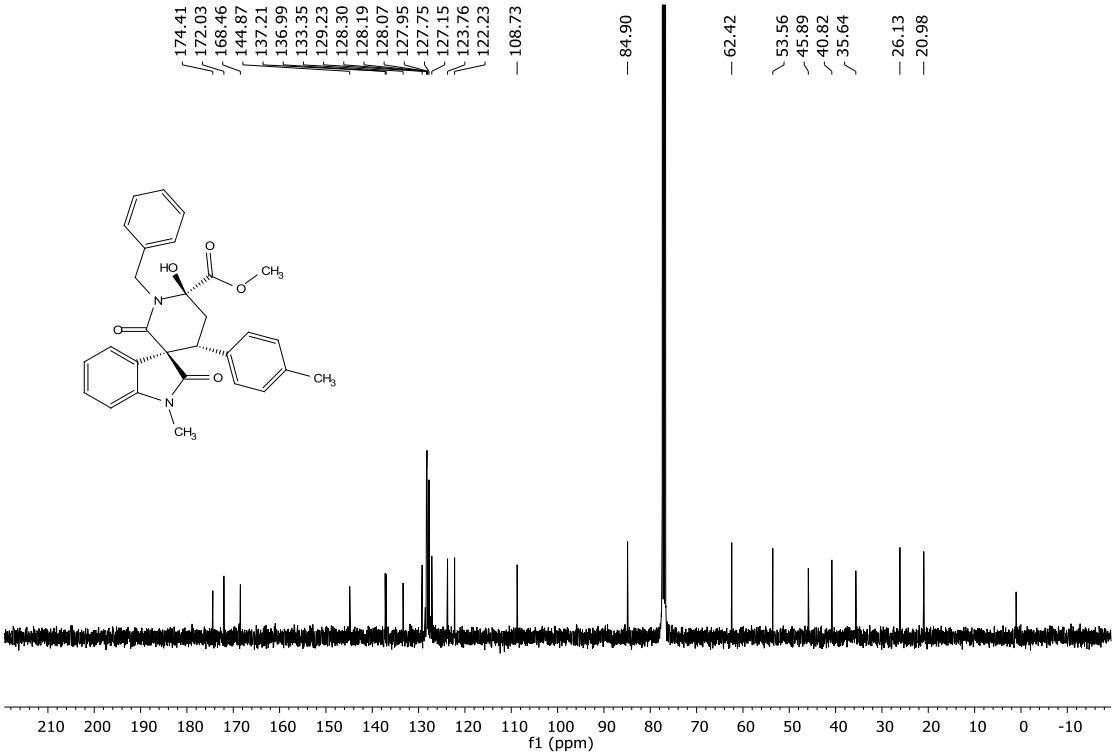
3cc, ^{13}C NMR (100 MHz, $CDCl_3$):



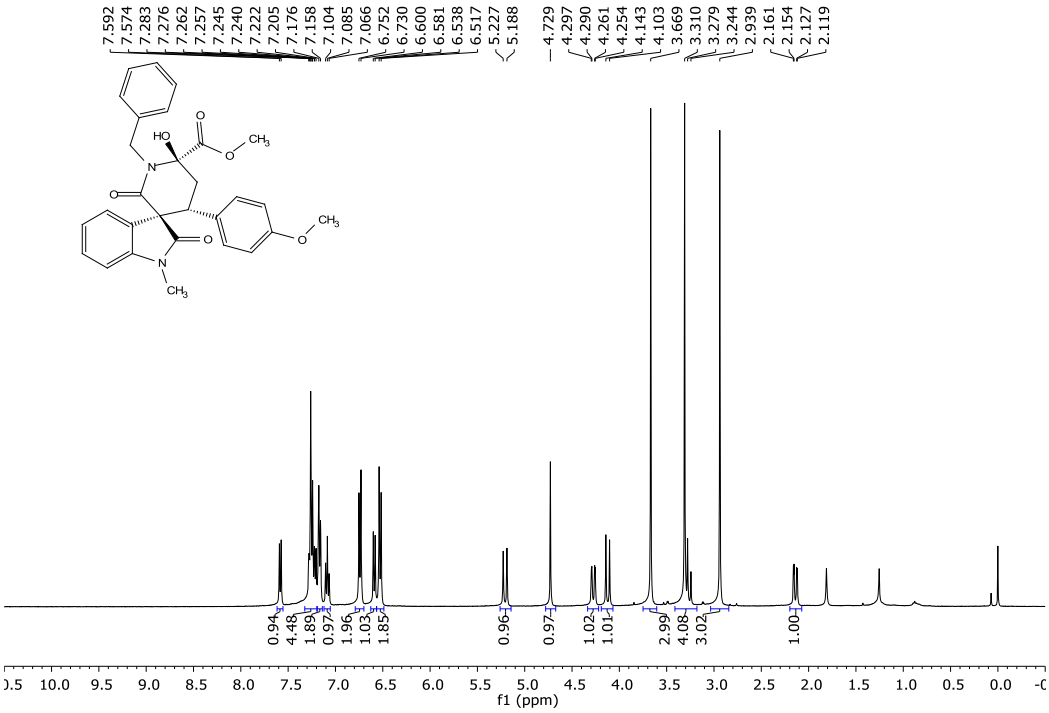
3cd, ^{1}H NMR (400 MHz, $CDCl_3$):



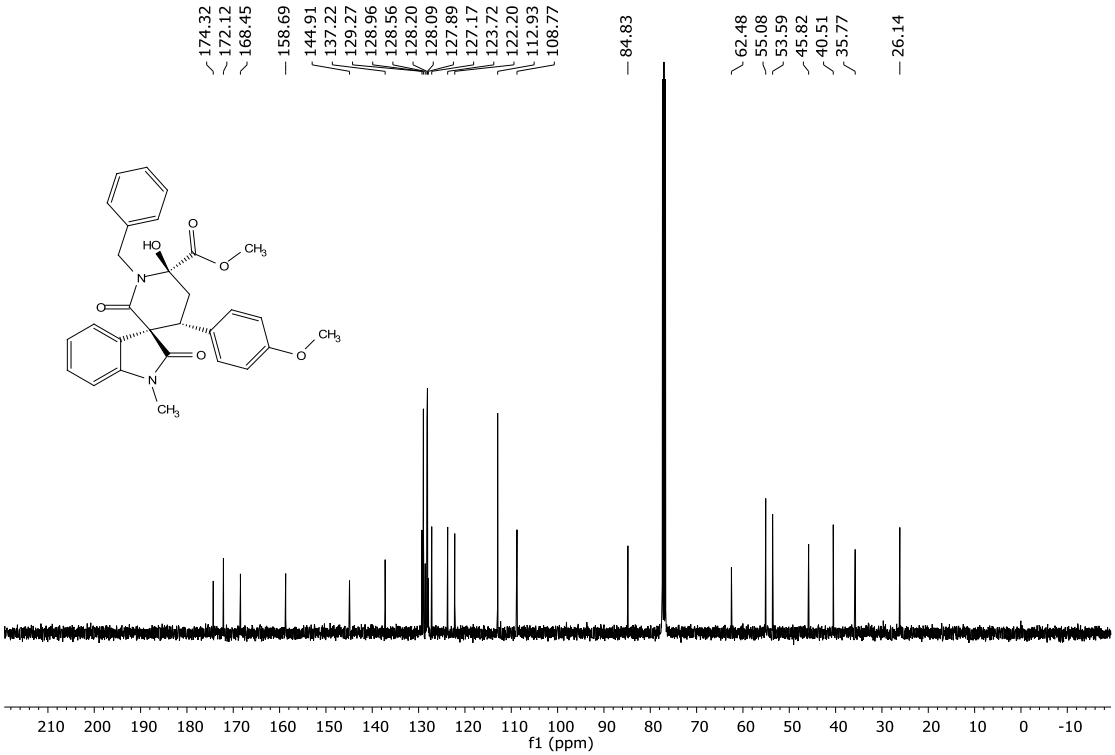
3cd, ^{13}C NMR (100 MHz, $CDCl_3$):



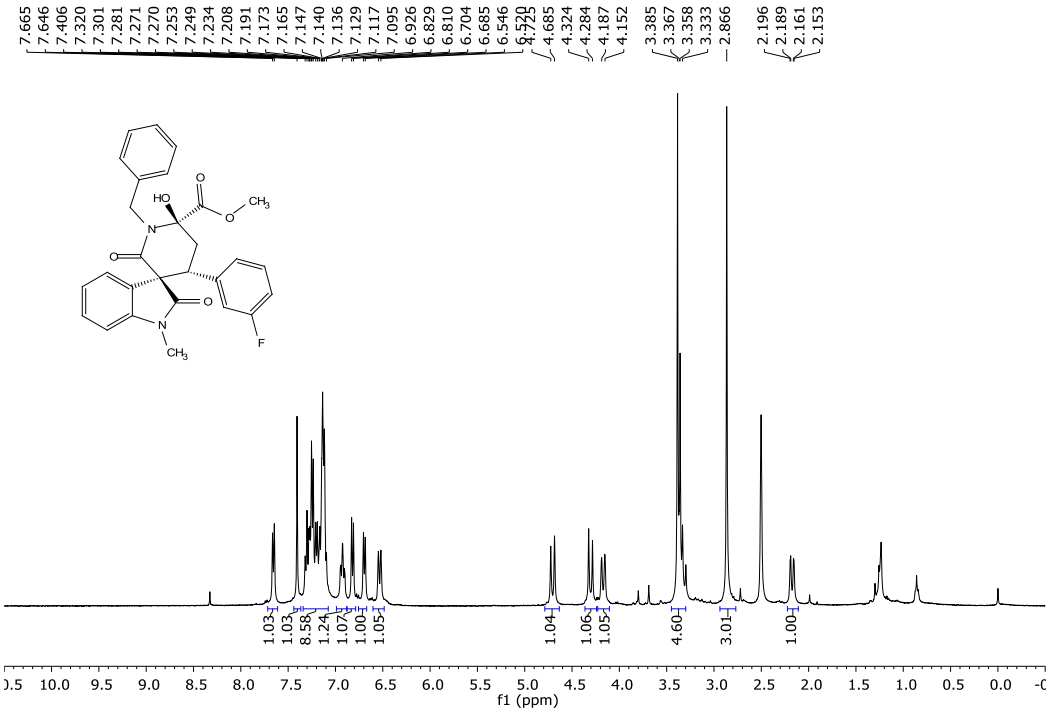
3ce, ^{1}H NMR (400 MHz,$CDCl_3$):



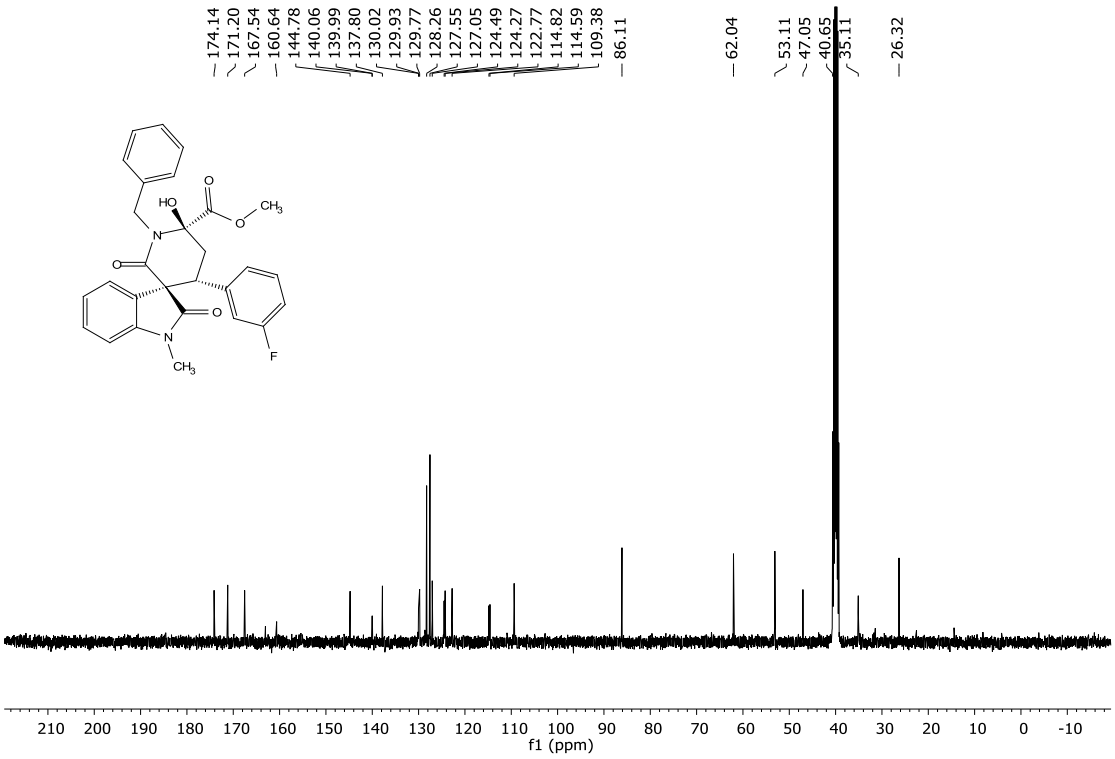
3ce, ^{13}C NMR (100 MHz, $CDCl_3$):



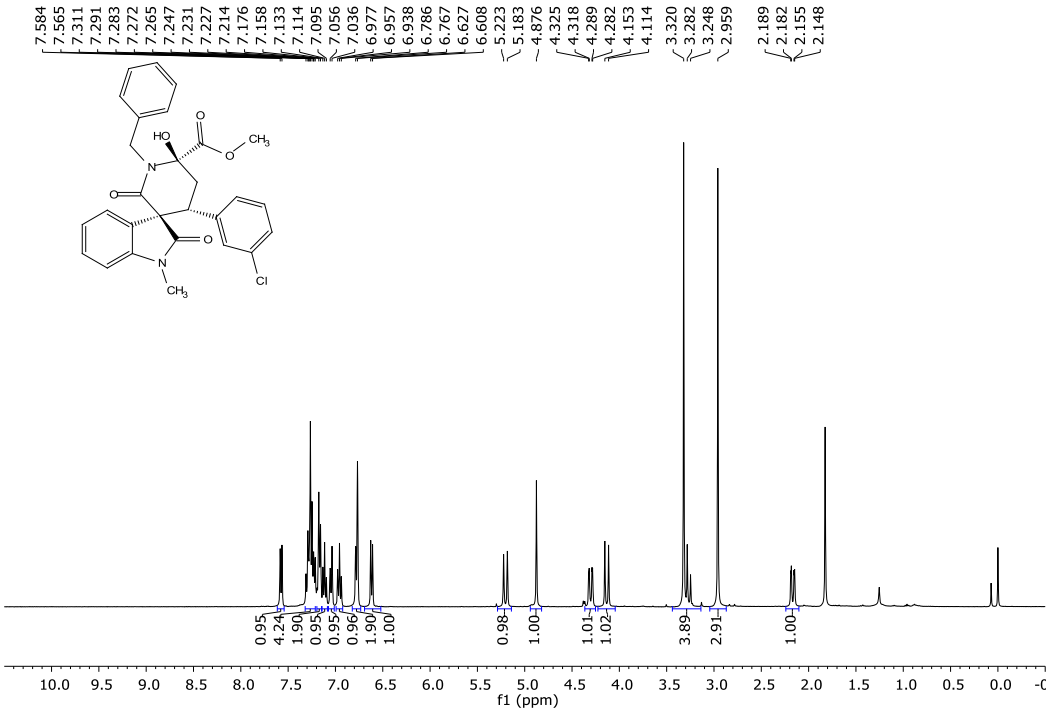
3cf, ^{1}H NMR (400 MHz, DMSO-d_6):



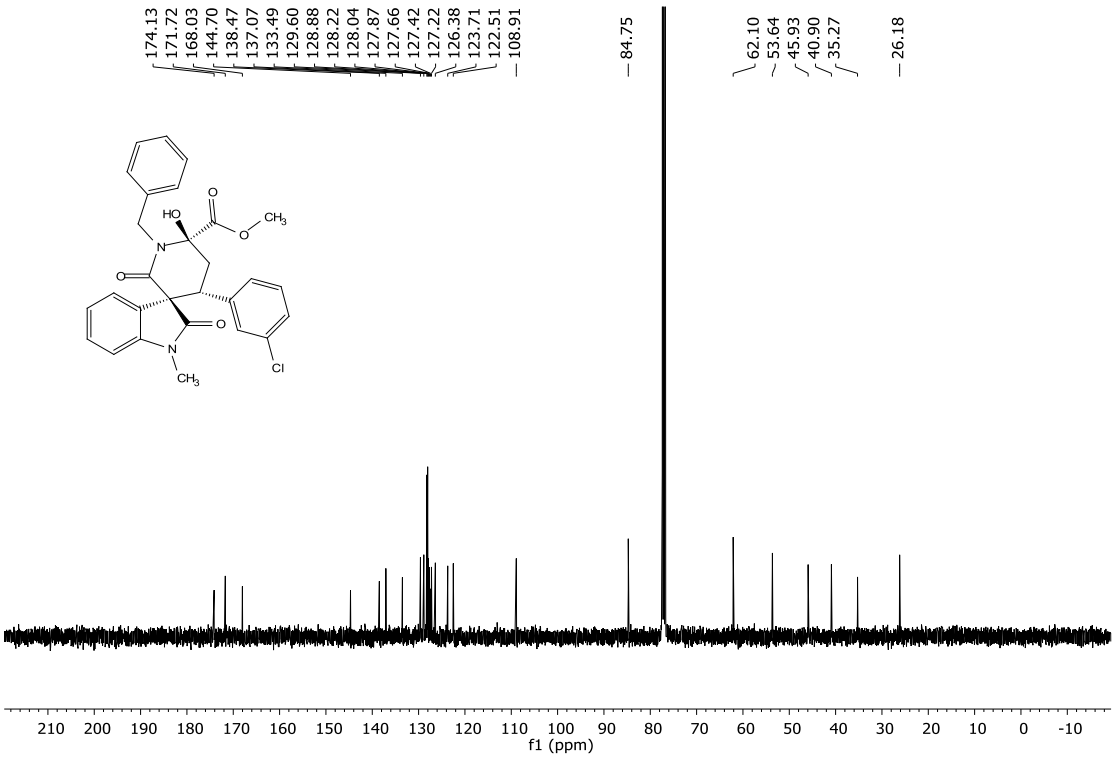
3cf, ^{13}C NMR (100 MHz, DMSO-d_6):



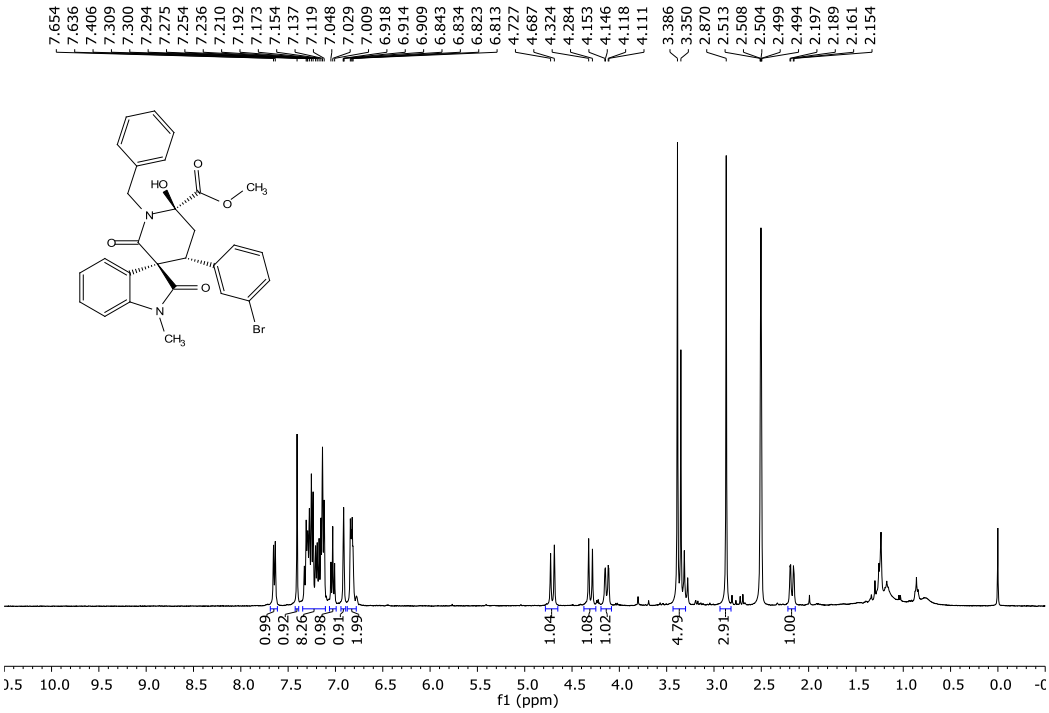
3cg, ^{1}H NMR (400 MHz, $CDCl_3$):



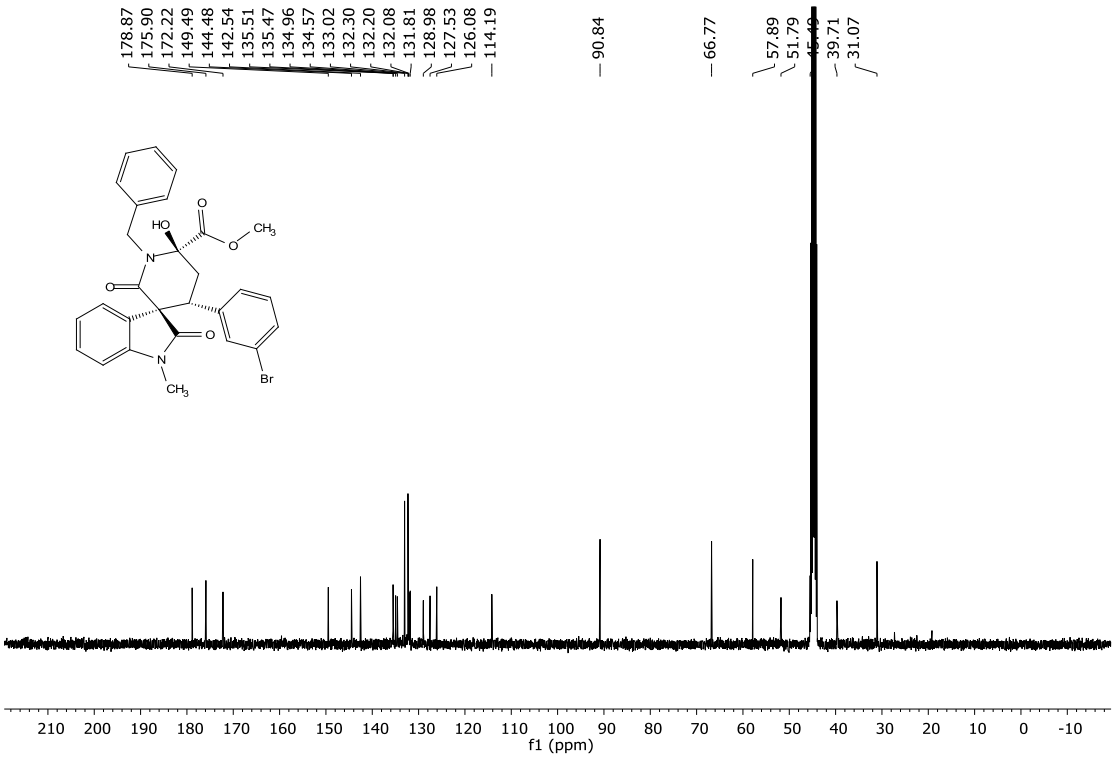
3cg, ^{13}C NMR (100 MHz, $CDCl_3$):



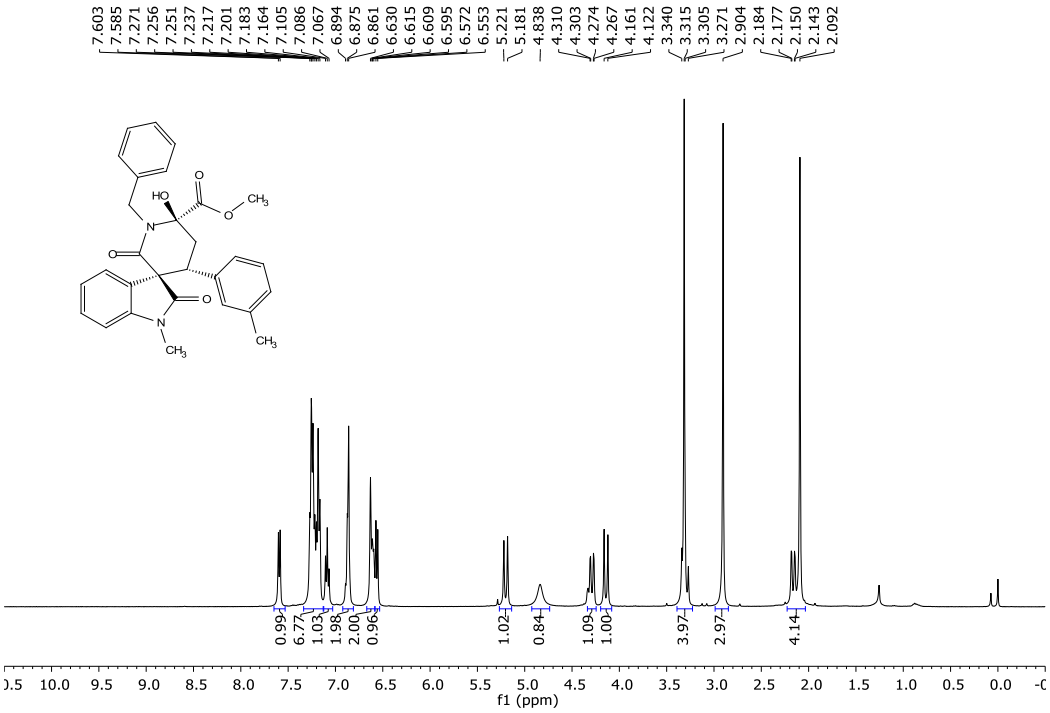
3ch, ^{1}H NMR (400 MHz, DMSO-d_6):



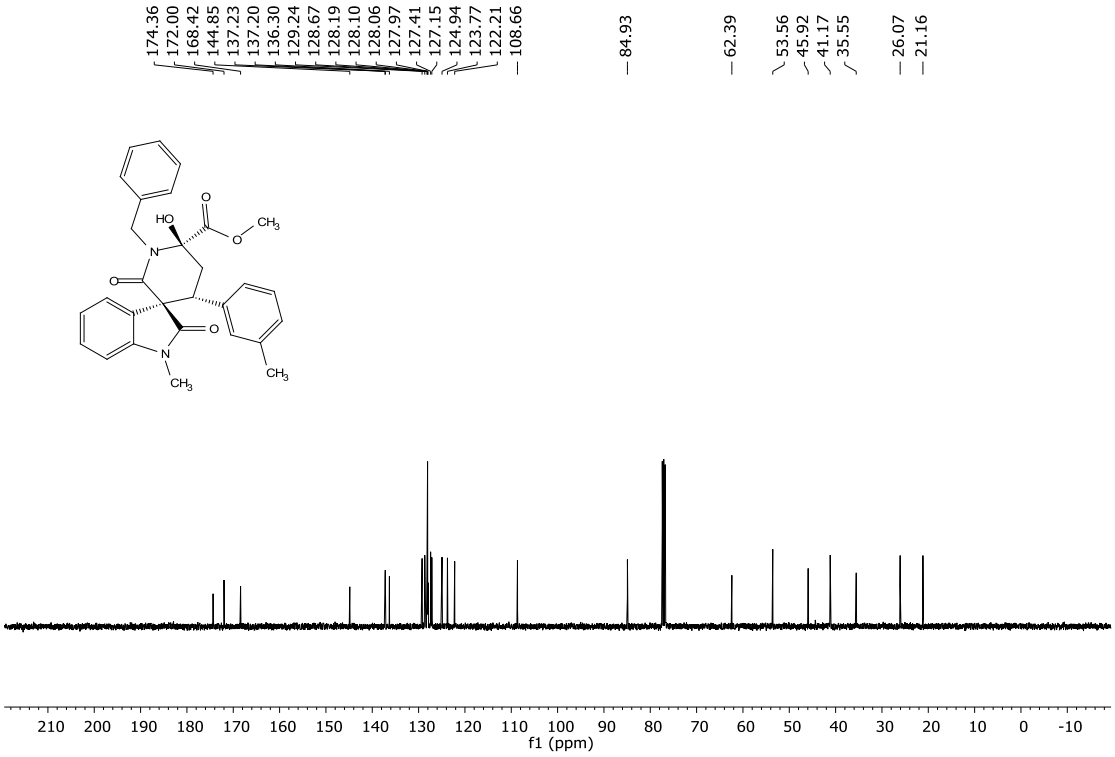
3ch, ^{13}C NMR (100 MHz, DMSO-d_6):



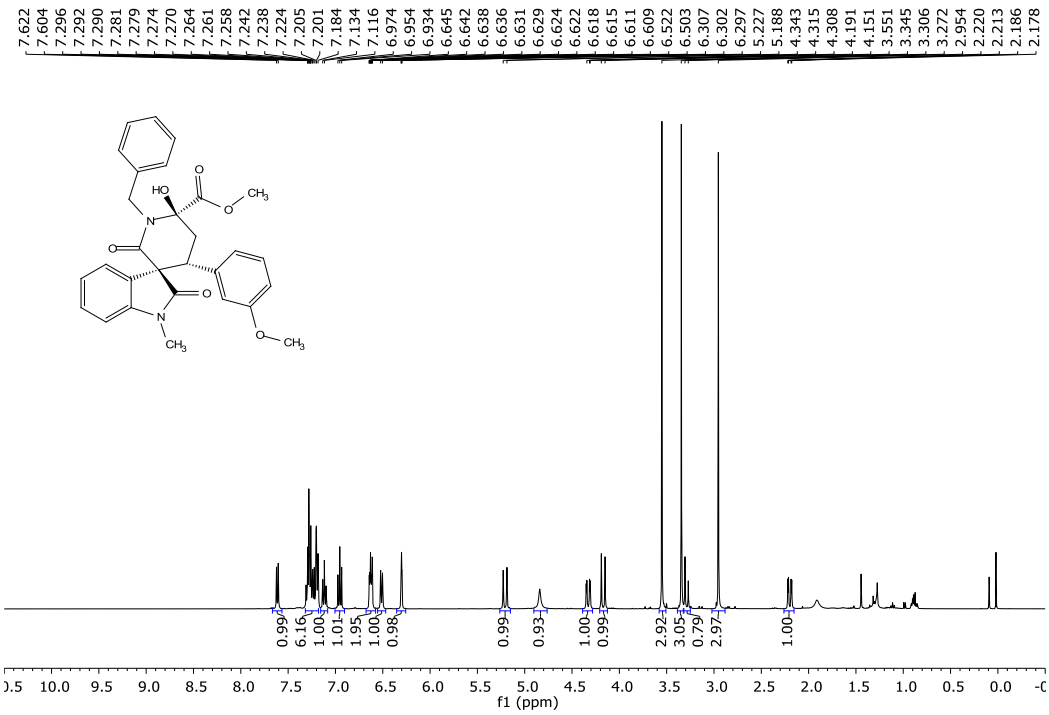
3ci, ^{1}H NMR (400 MHz, $CDCl_3$):



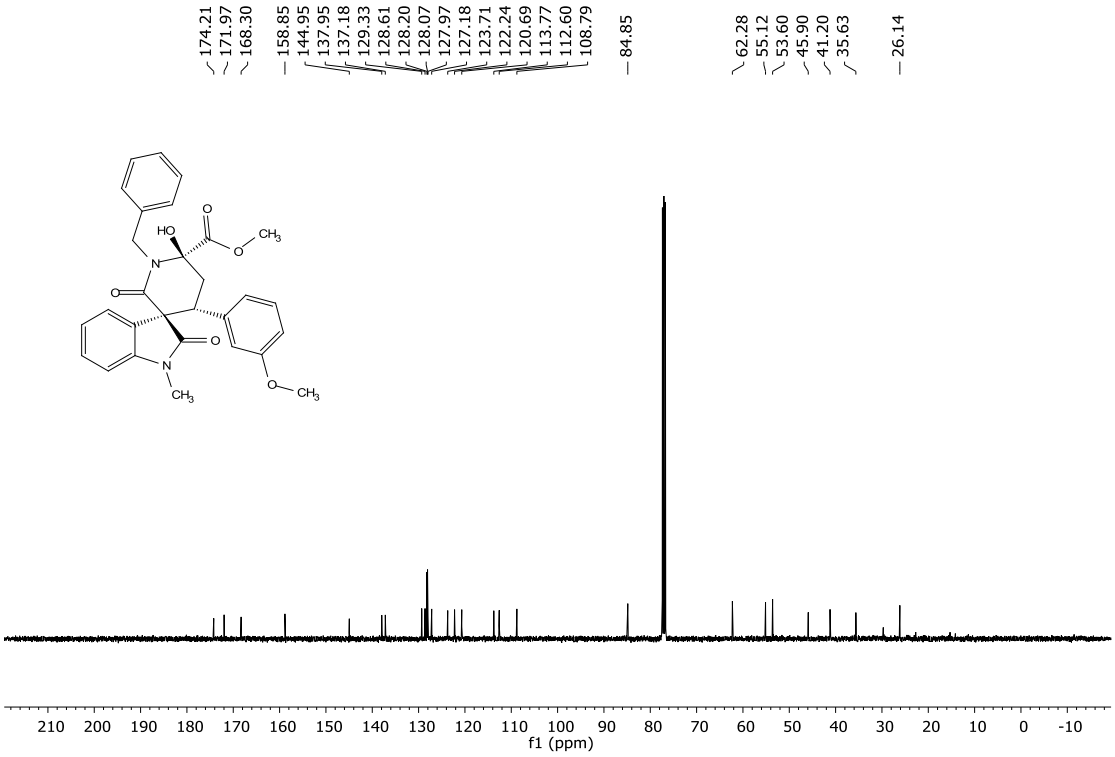
3ci, ^{13}C NMR (100 MHz, $CDCl_3$):



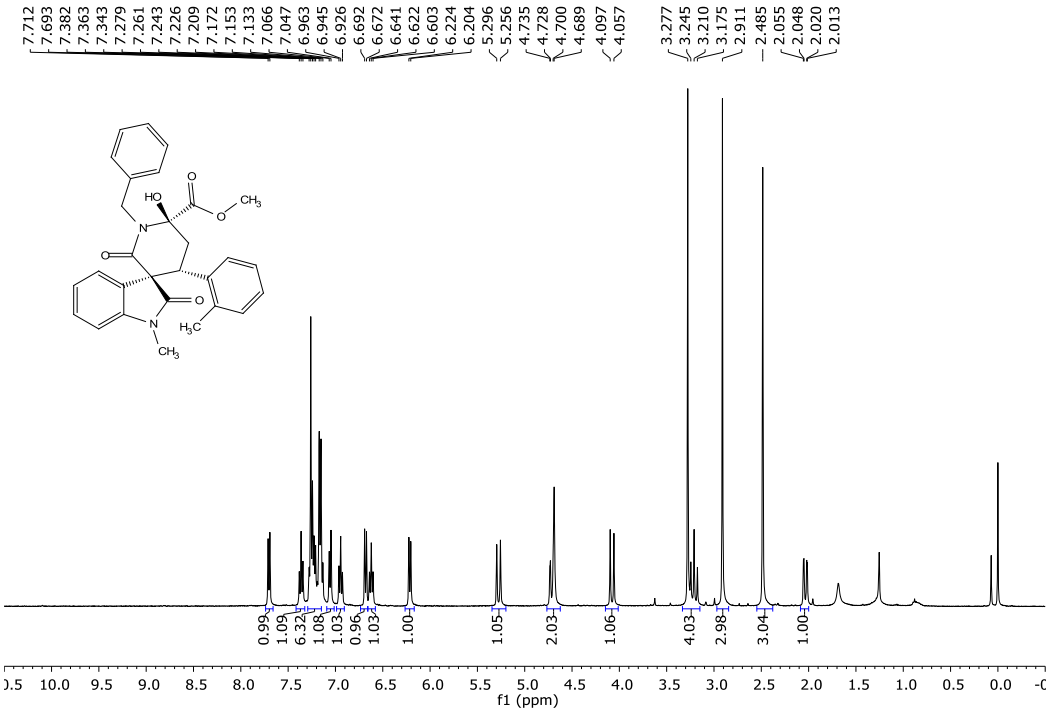
3cj, ^{1}H NMR (400 MHz, $CDCl_3$):



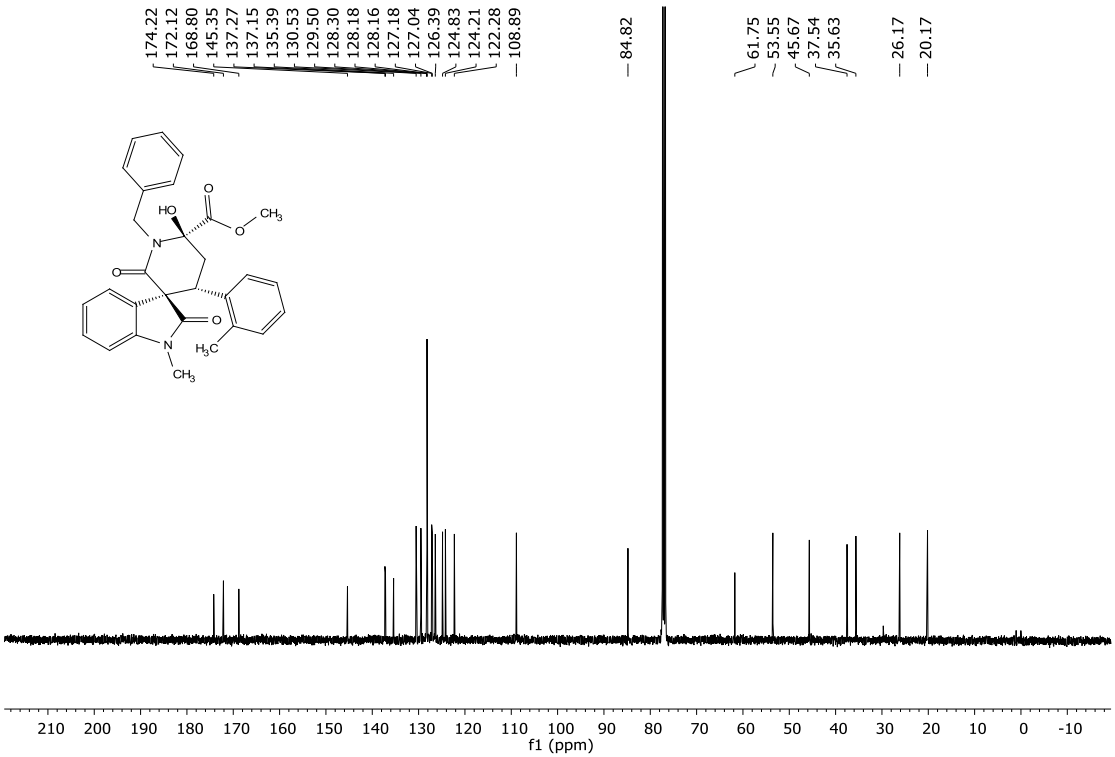
3cj, ^{13}C NMR (100 MHz, $CDCl_3$):



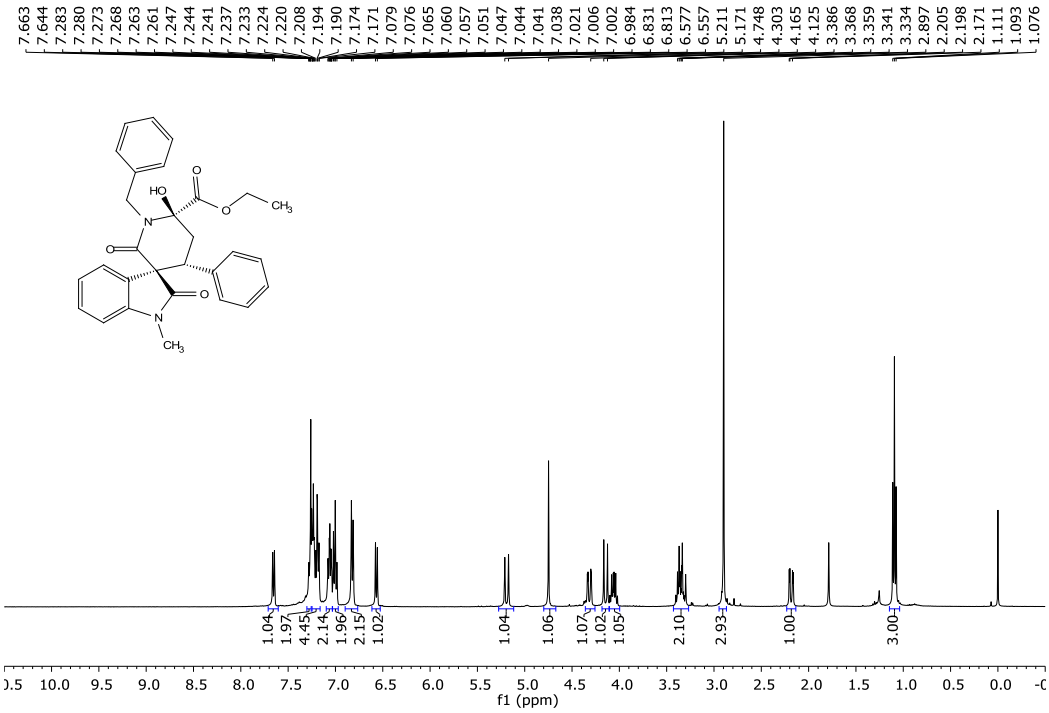
3ck, ^{1}H NMR (400 MHz, $CDCl_3$):



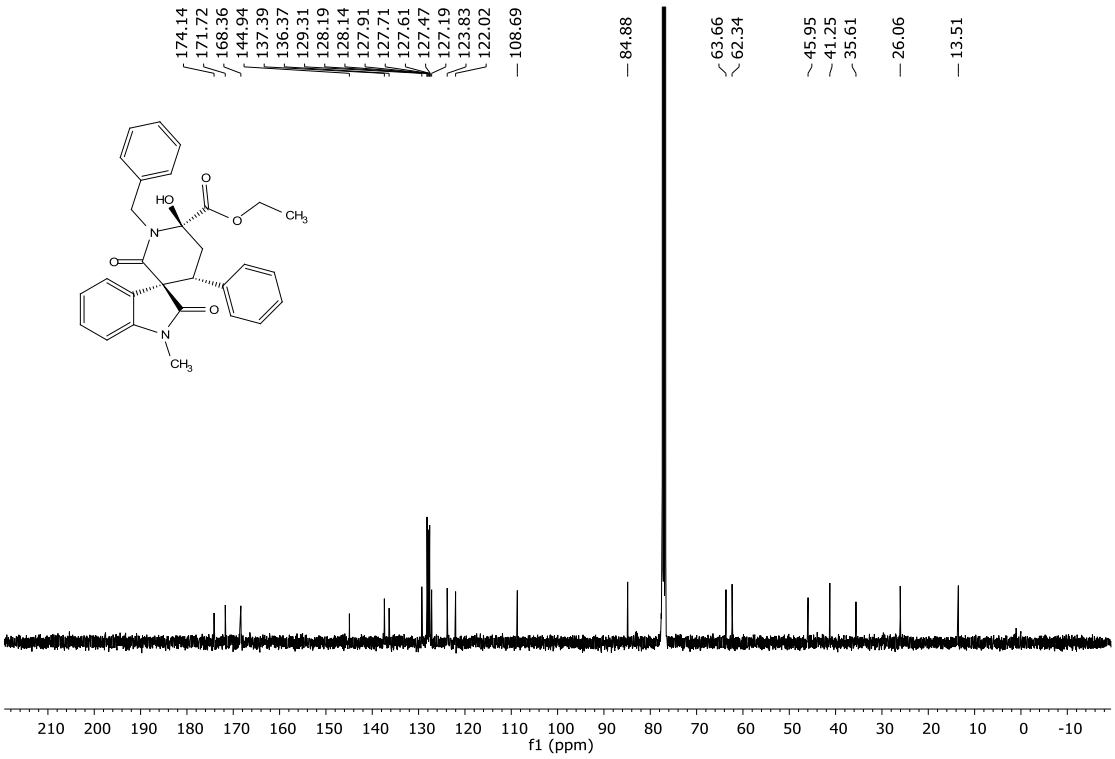
3ck, ^{13}C NMR (100 MHz, $CDCl_3$)



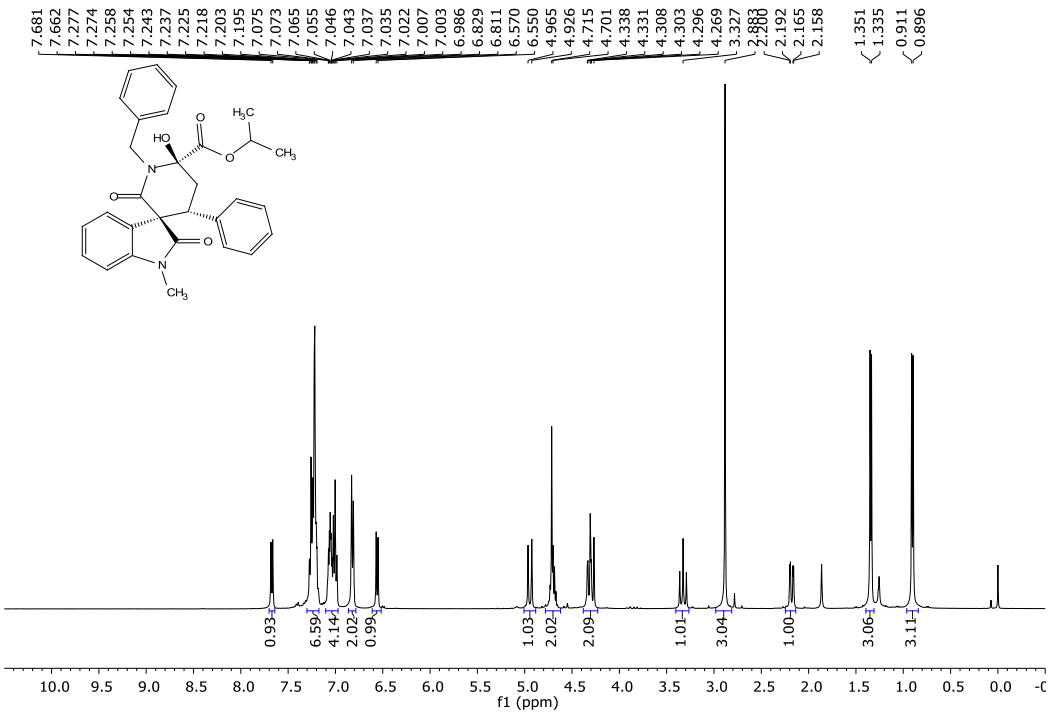
3cl, ^{1}H NMR (400 MHz, $CDCl_3$):



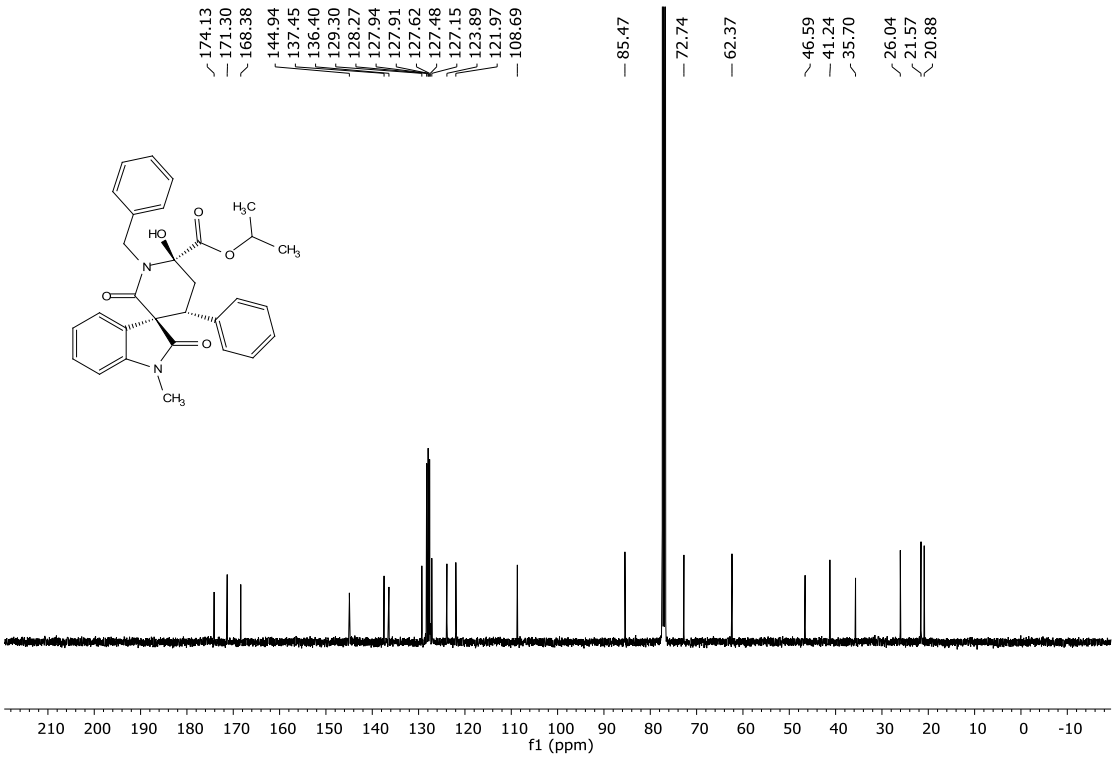
3cl, ^{13}C NMR (100 MHz, $CDCl_3$):



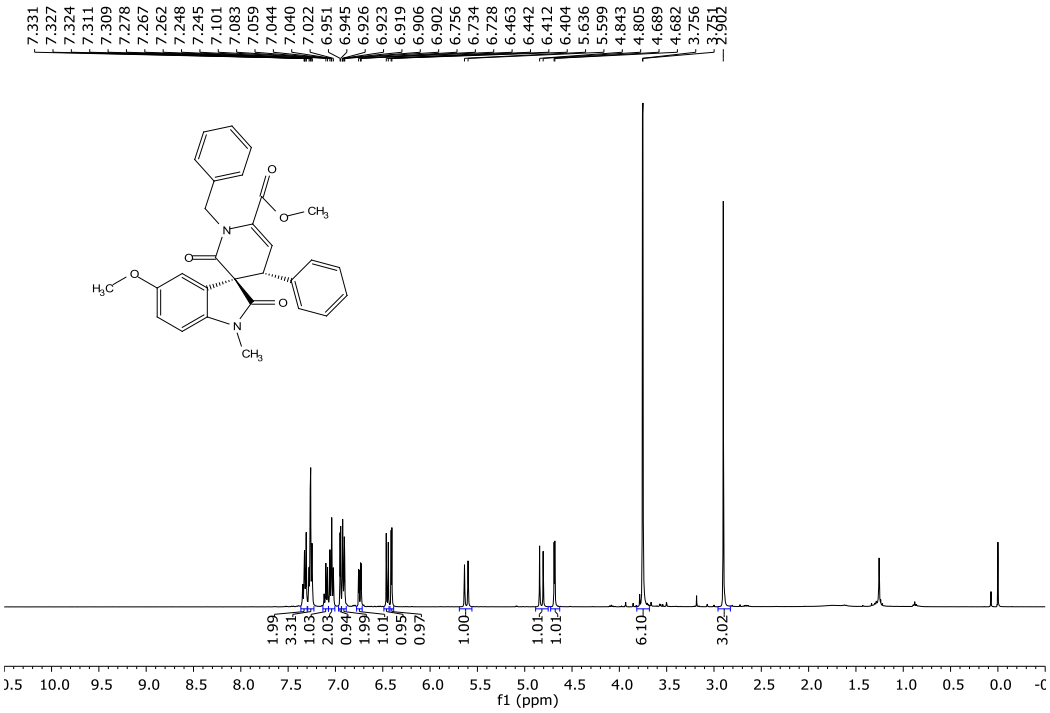
3cm, ^{1}H NMR (400 MHz, $CDCl_3$):



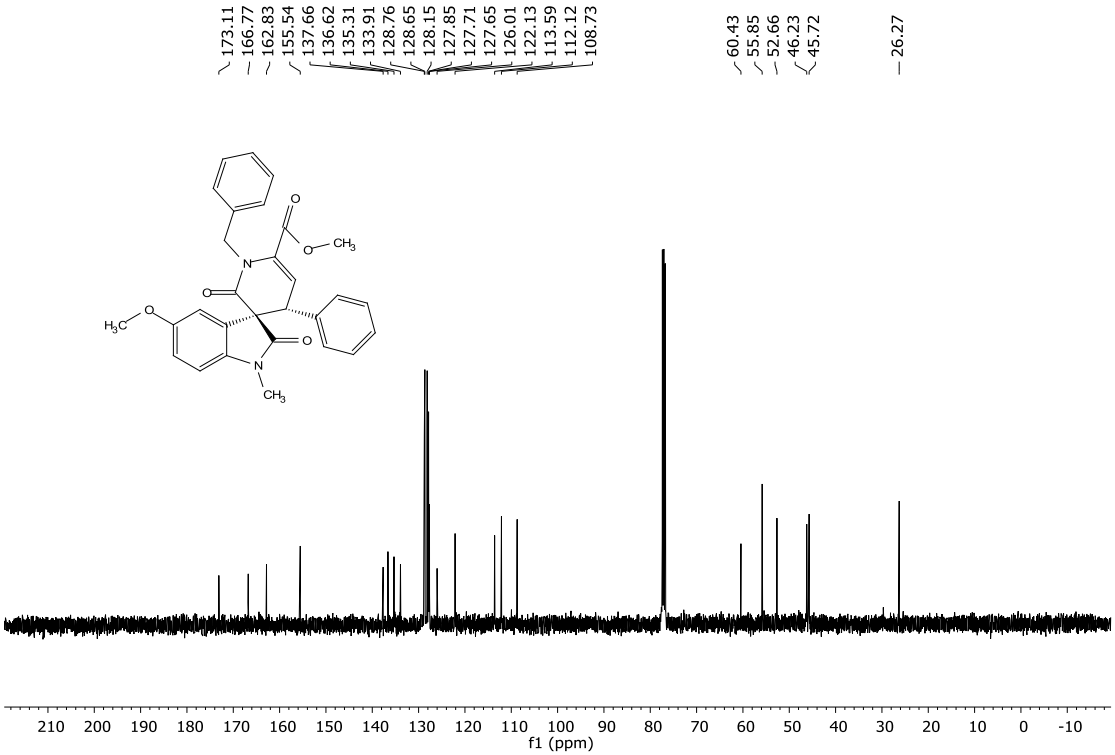
3cm, ^{13}C NMR (100 MHz, $CDCl_3$)



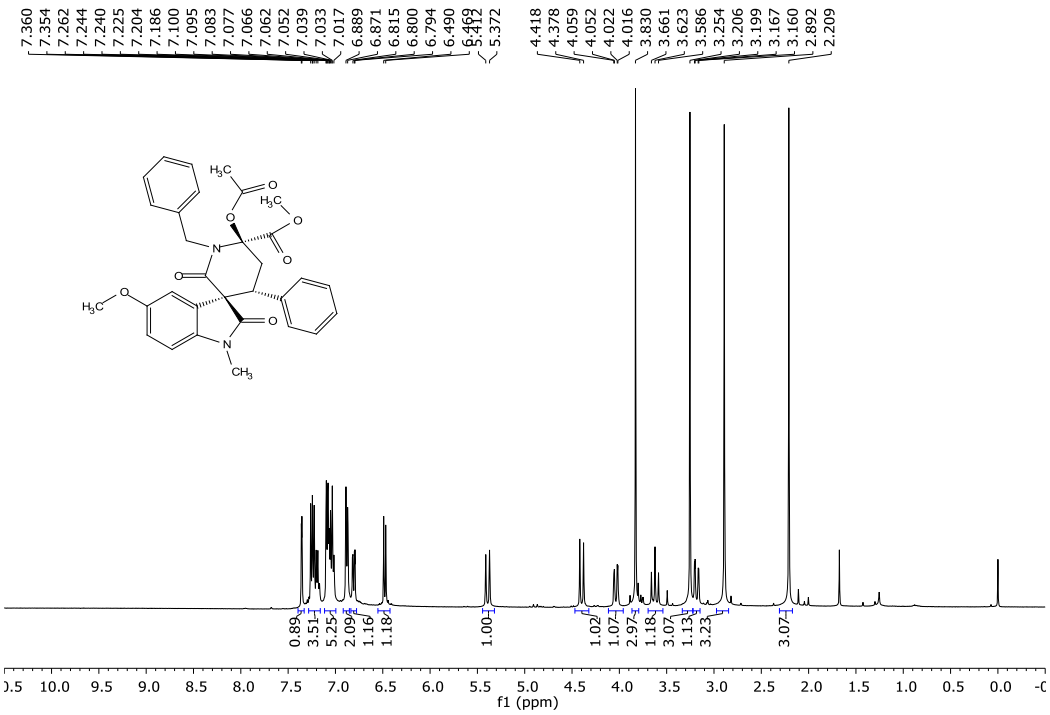
4, ^{1}H NMR (400 MHz, $CDCl_3$):



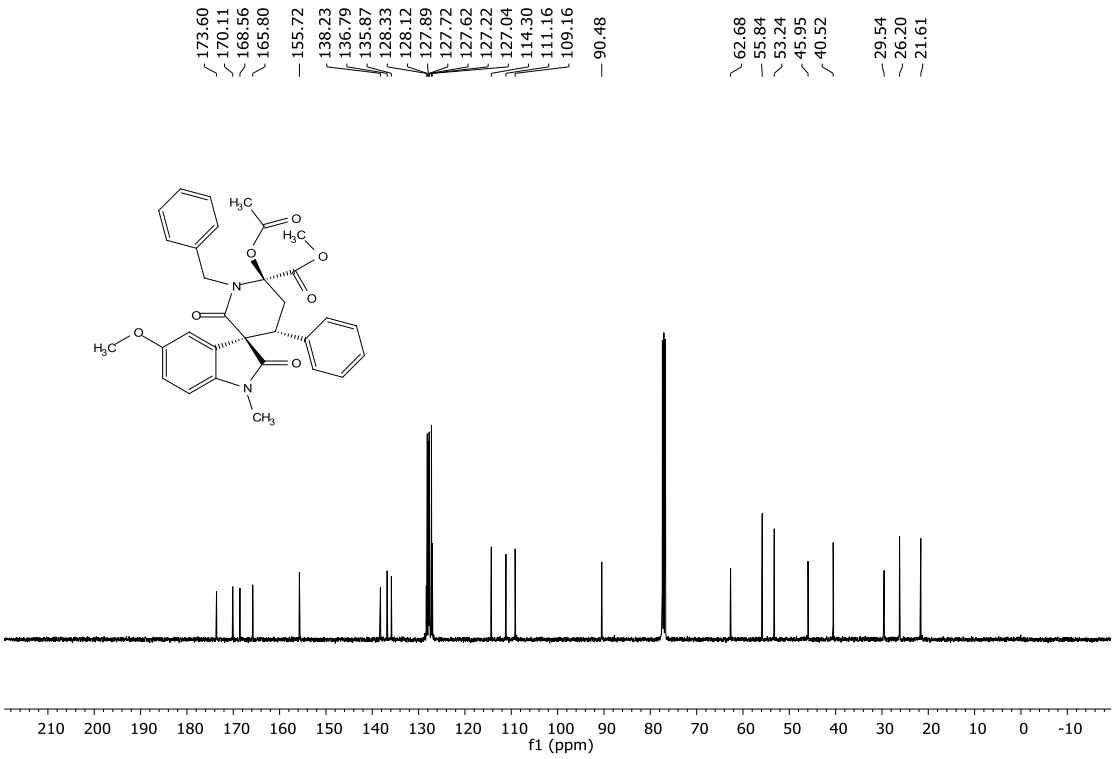
4, ^{13}C NMR (100 MHz, $CDCl_3$):



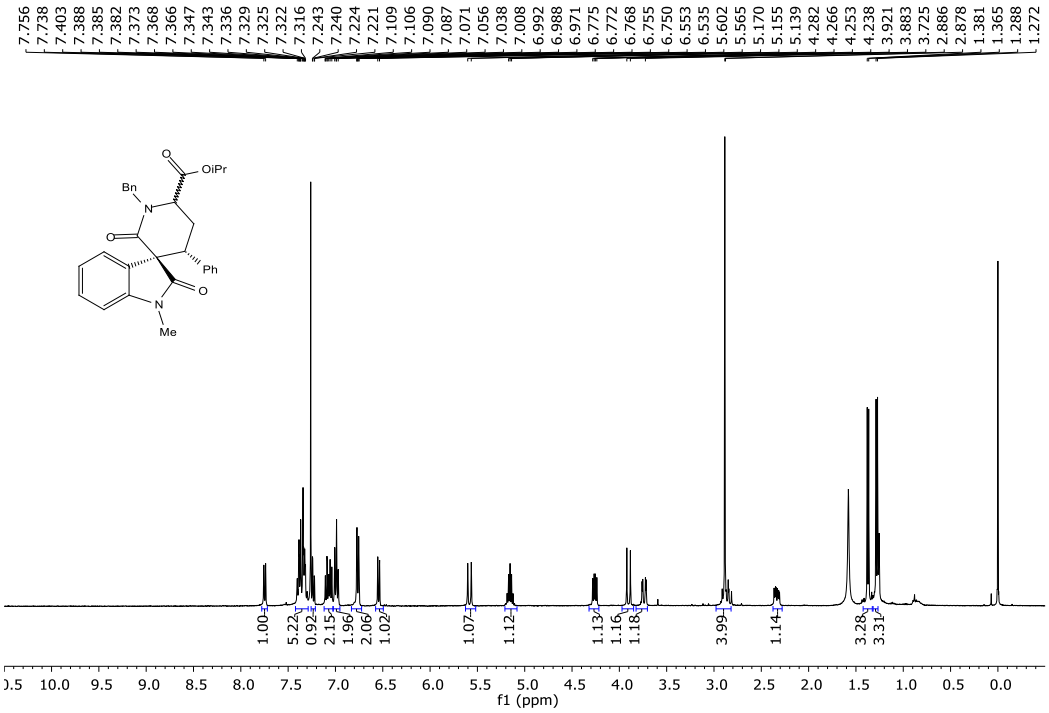
5, ^{1}H NMR (400 MHz, $CDCl_3$):



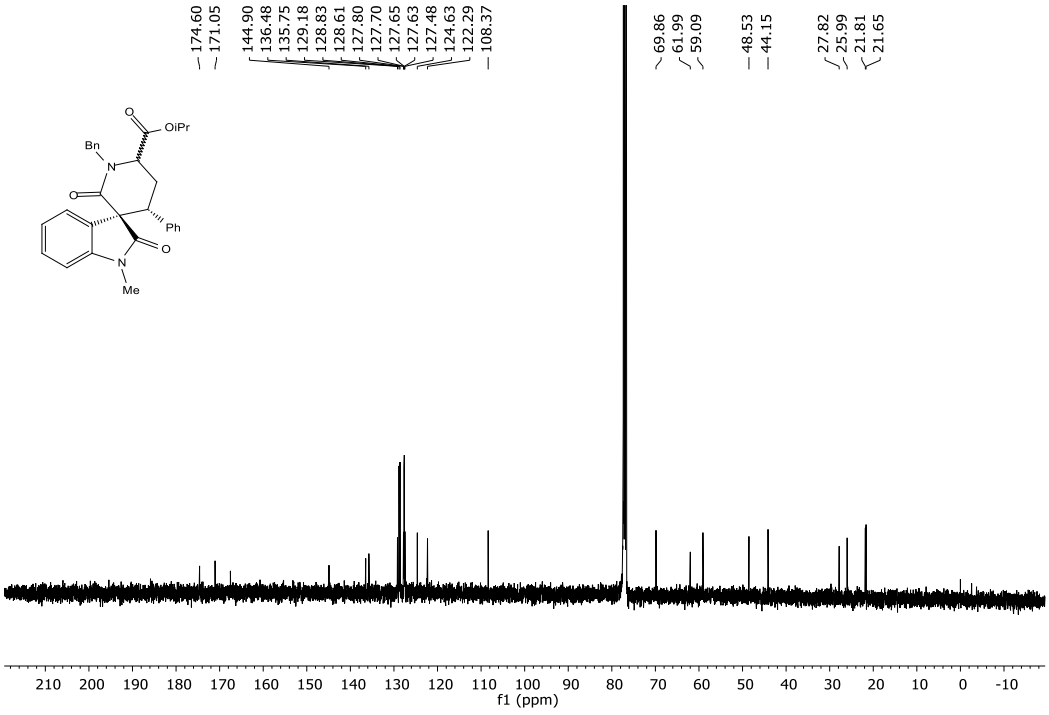
5, ^{13}C NMR (100 MHz, $CDCl_3$):



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

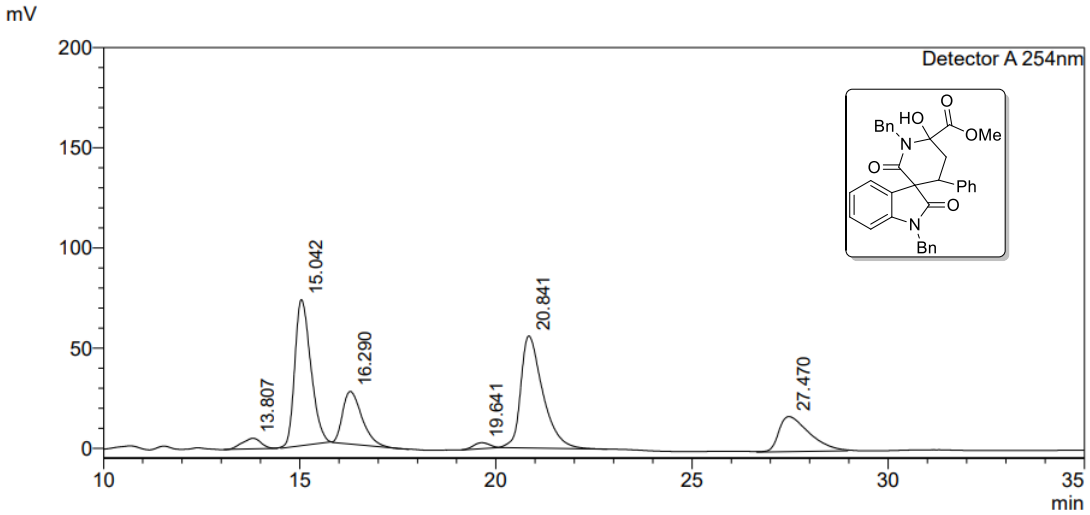


6, ^{13}C NMR (100 MHz, $CDCl_3$)



10. HPLC spectra

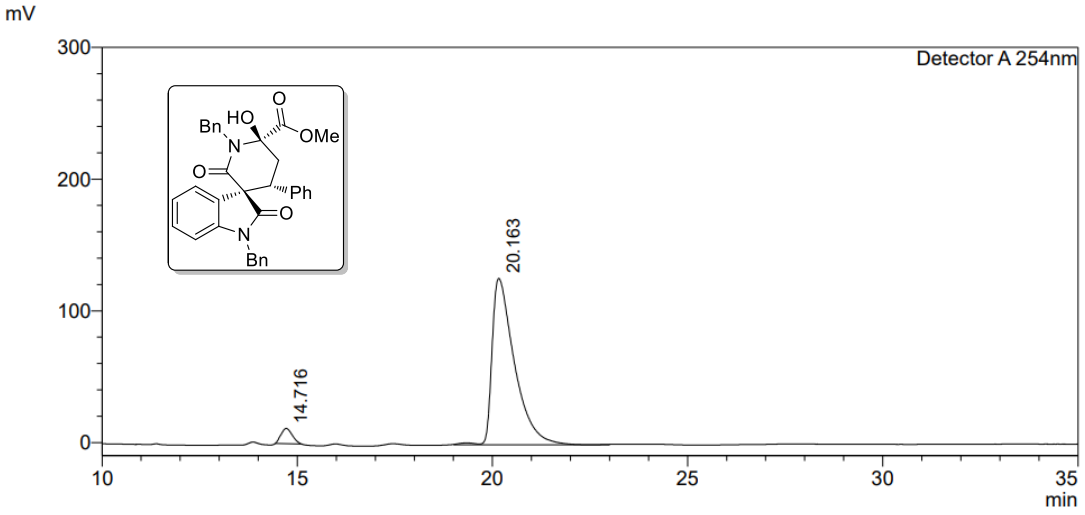
3aa:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	13.807	180740	5355	2.828
2	15.042	2074076	72903	32.454
3	16.290	904430	26287	14.152
4	19.641	88573	3035	1.386
5	20.841	2194903	55995	34.344
6	27.470	948162	17551	14.836
Total		6390885	181126	100.000

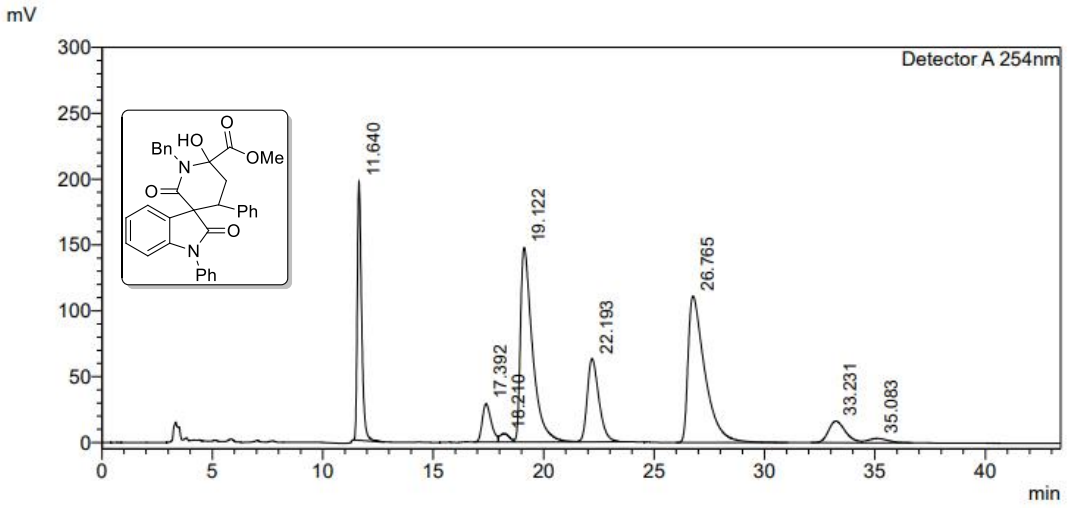


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.716	232575	11602	4.408
2	20.163	5043880	126362	95.592
Total		5276455	137963	100.000

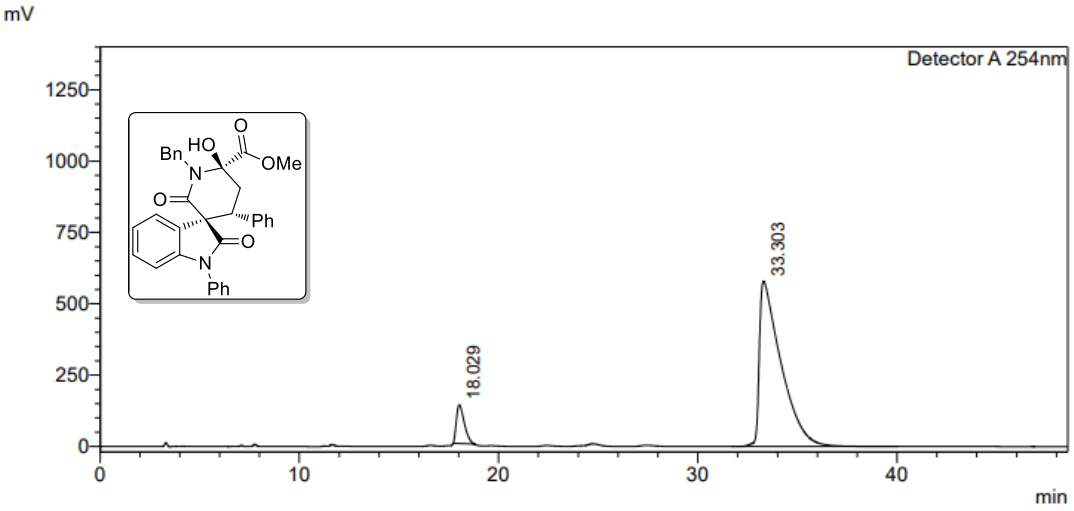
3ba:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	11.640	2670766	196488	14.362
2	17.392	827247	29048	4.449
3	18.210	193766	6509	1.042
4	19.122	5621234	147674	30.228
5	22.193	2321491	63277	12.484
6	26.765	5886607	111282	31.655
7	33.231	868690	16366	4.671
8	35.083	206255	3302	1.109
Total		18596056	573946	100.000

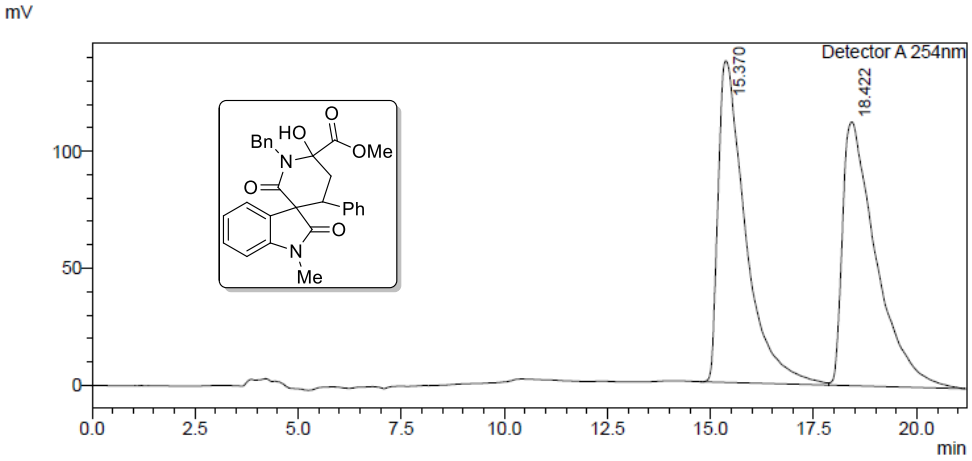


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	18.029	3737119	135616	7.829
2	33.303	43994795	579635	92.171
Total		47731914	715251	100.000

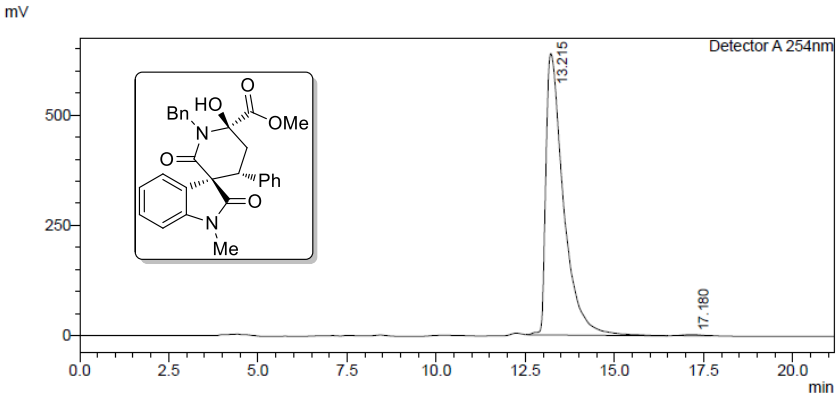
3ca:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	15.370	6343838	137358	49.842
2	18.422	6384155	112728	50.158
Total		12727994	250086	100.000

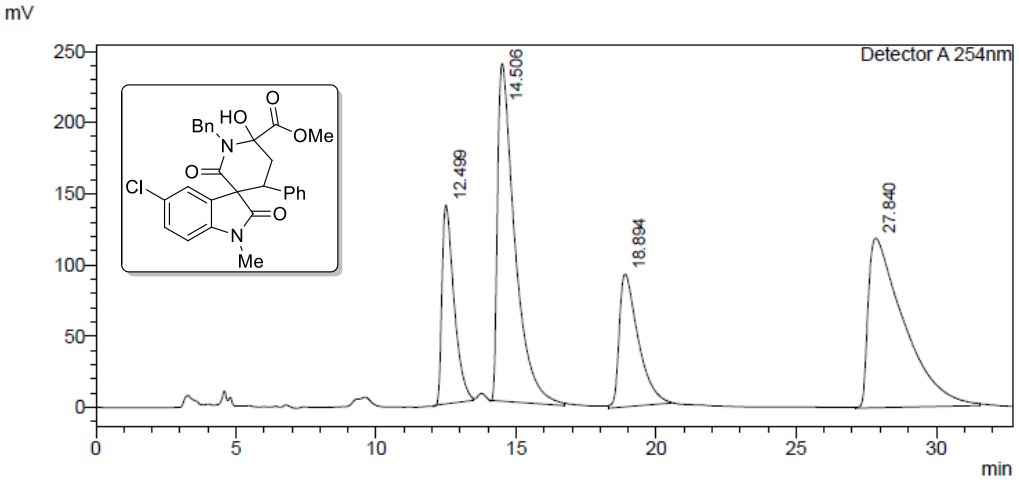


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	13.215	21991475	638147	99.658
2	17.180	75425	2133	0.342
Total		22066900	640280	100.000

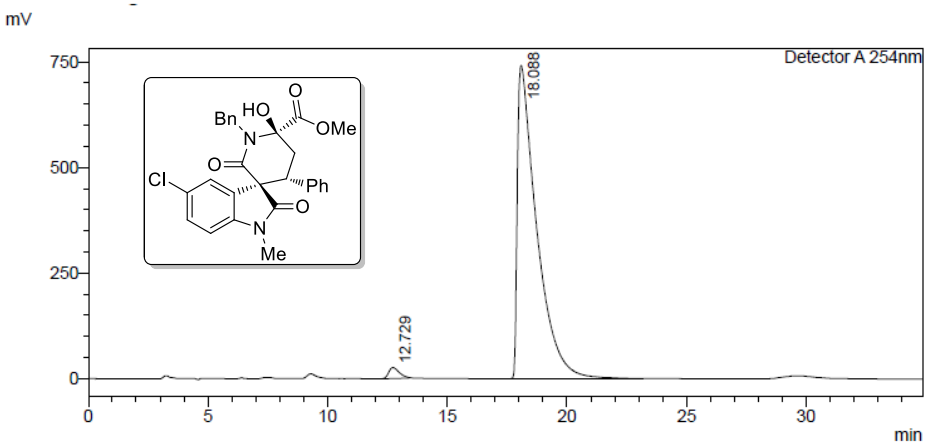
3da:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.499	4187706	139493	14.293
2	14.506	10151156	236859	34.647
3	18.894	4395988	93242	15.004
4	27.840	10564339	118932	36.057
Total		29299190	588525	100.000

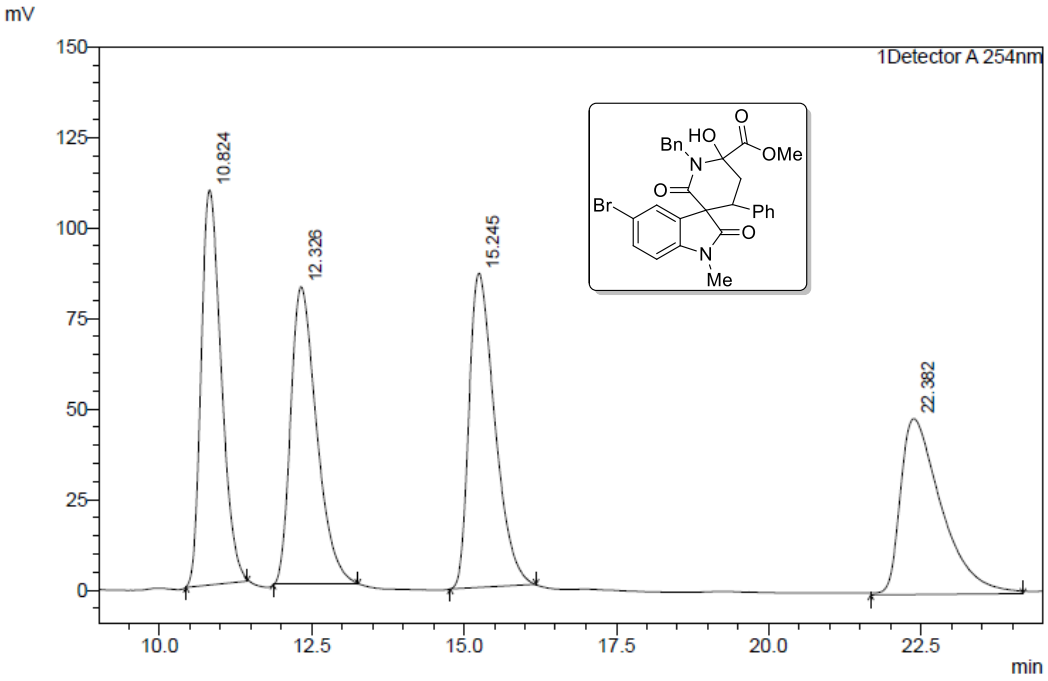


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.729	810682	26138	1.898
2	18.088	41909090	742036	98.102
Total		42719772	768174	100.000

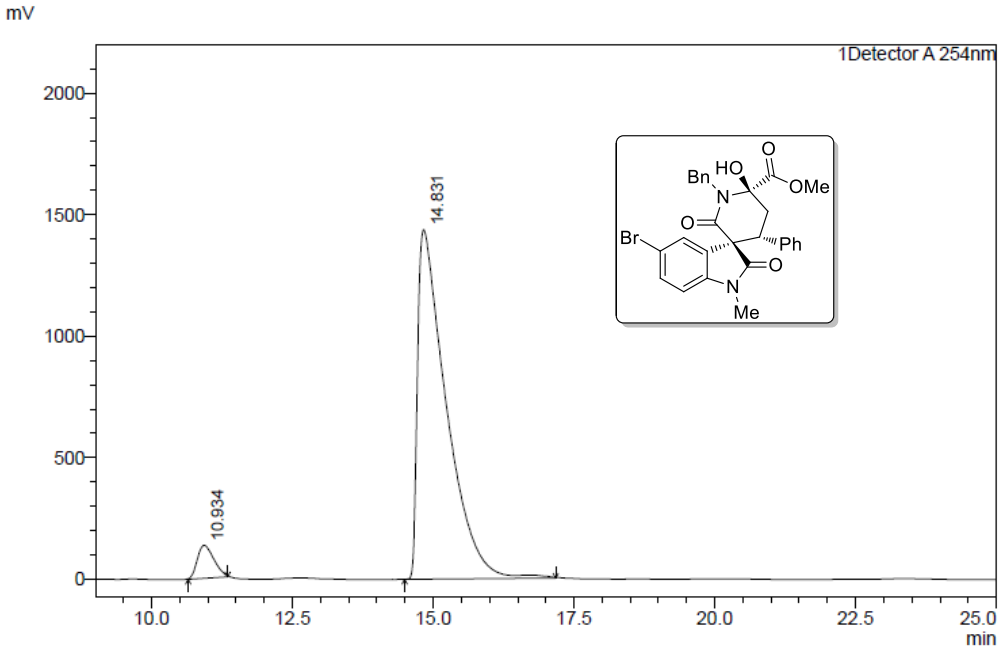
3ea:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	10.824	2504790	109031	25.698
2	12.326	2413784	82158	24.764
3	15.245	2550650	86708	26.168
4	22.382	2277980	48563	23.371
Total		9747205	326460	100.000

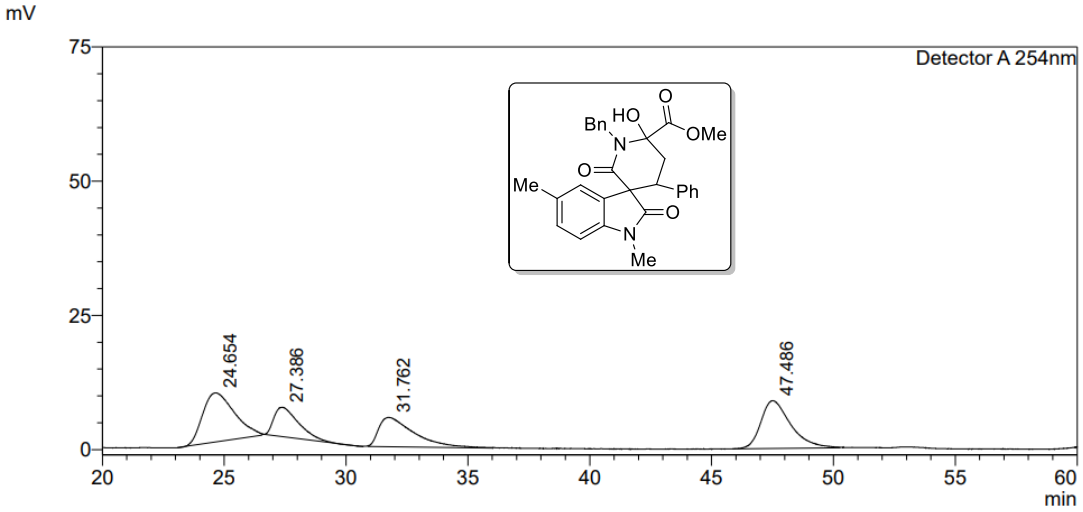


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	10.934	2791620	136013	5.186
2	14.831	51040421	1438028	94.814
Total		53832041	1574041	100.000

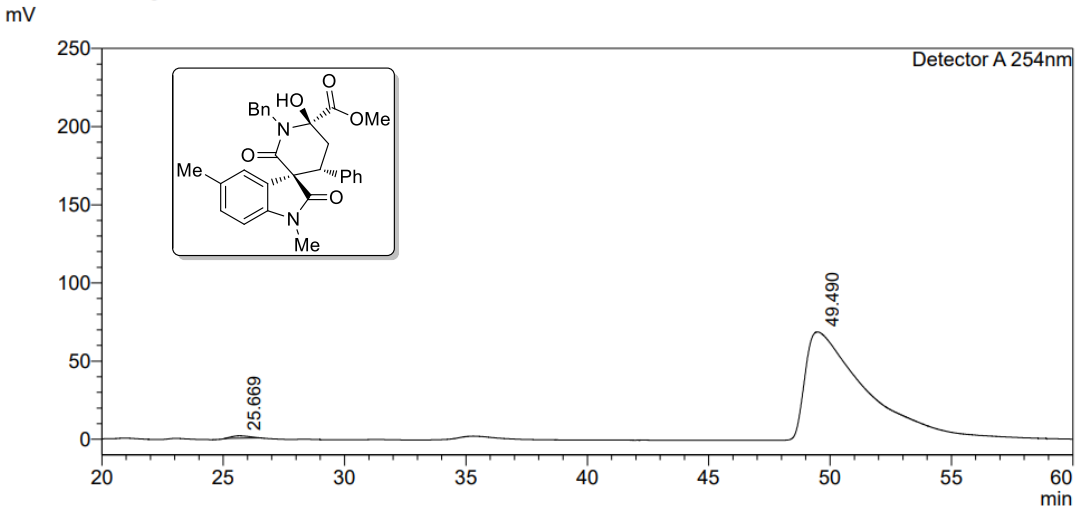
3fa:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	24.654	825442	9145	32.648
2	27.386	383551	5446	15.170
3	31.762	558329	5476	22.083
4	47.486	761011	8910	30.099
Total		2528333	28977	100.000

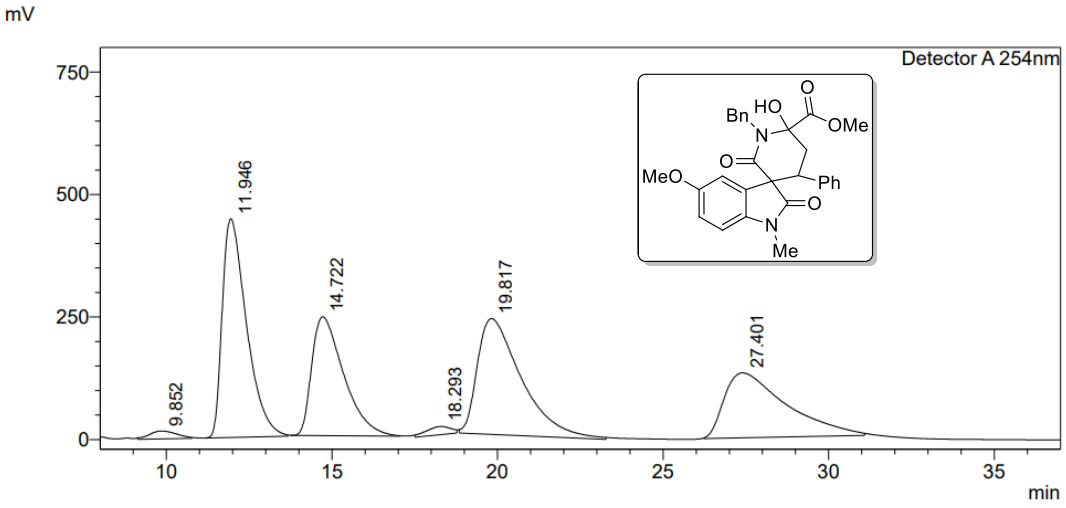


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	25.669	77223	1536	0.614
2	49.490	12489729	69476	99.386
Total		12566953	71012	100.000

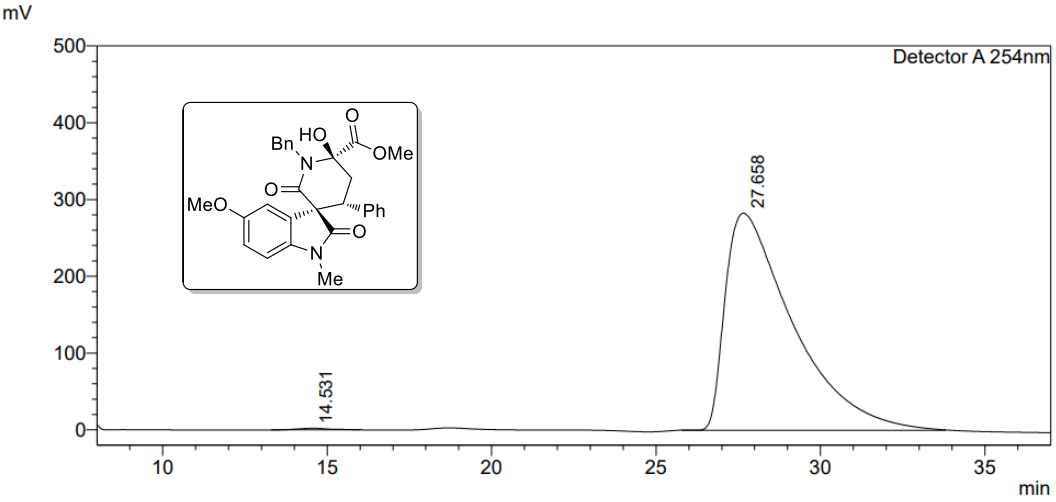
3ga:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.852	930961	16156	1.165
2	11.946	22727160	446349	28.441
3	14.722	16295081	242199	20.392
4	18.293	867200	16462	1.085
5	19.817	21824229	236308	27.311
6	27.401	17265307	132411	21.606
Total		79909938	1089885	100.000

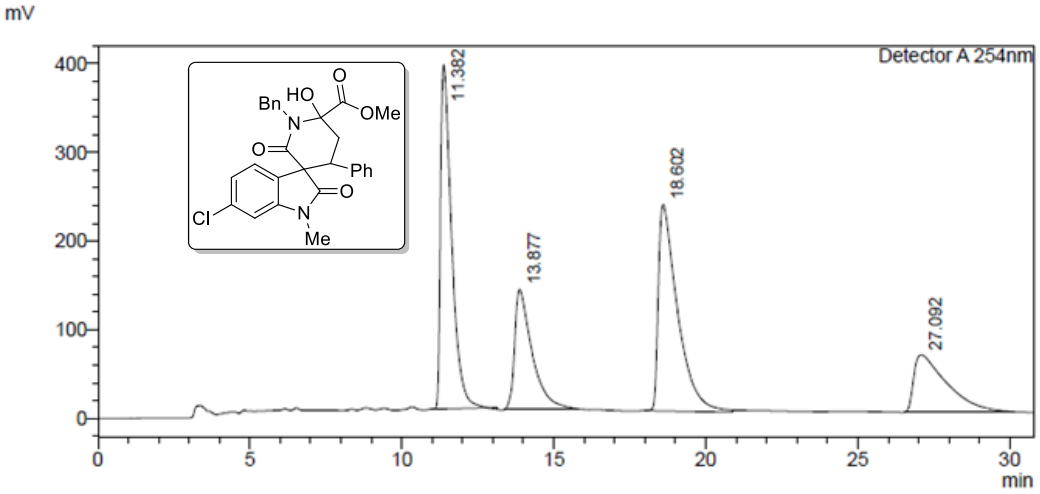


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.531	117930	2066	0.291
2	27.658	40414366	282578	99.709
Total		40532297	284644	100.000

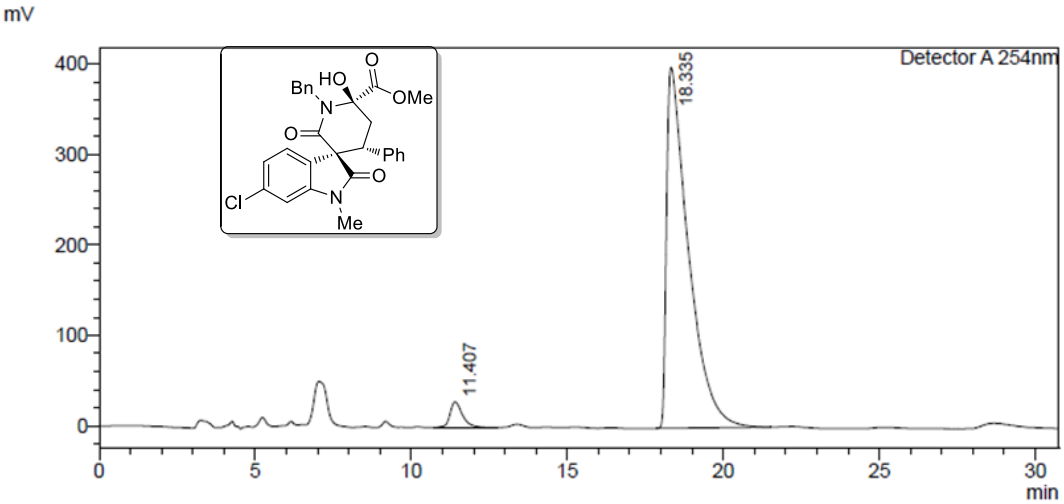
3ha:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	11.382	9799804	387368	32.210
2	13.877	5390020	135073	17.716
3	18.602	10275881	233070	33.774
4	27.092	4959402	64913	16.300
Total		30425107	820425	100.000

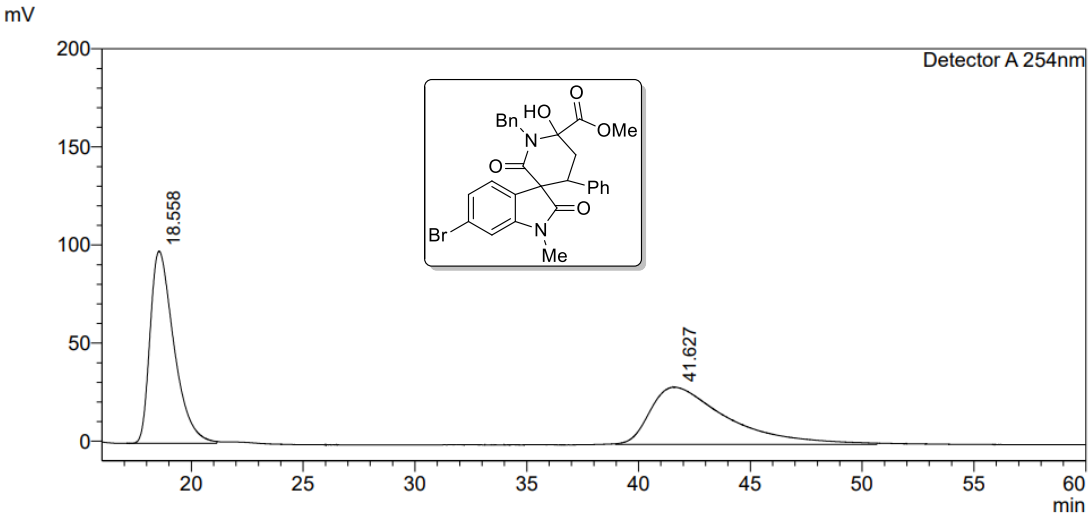


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	11.407	777371	28052	3.849
2	18.335	19419110	398356	96.151
Total		20196481	426408	100.000

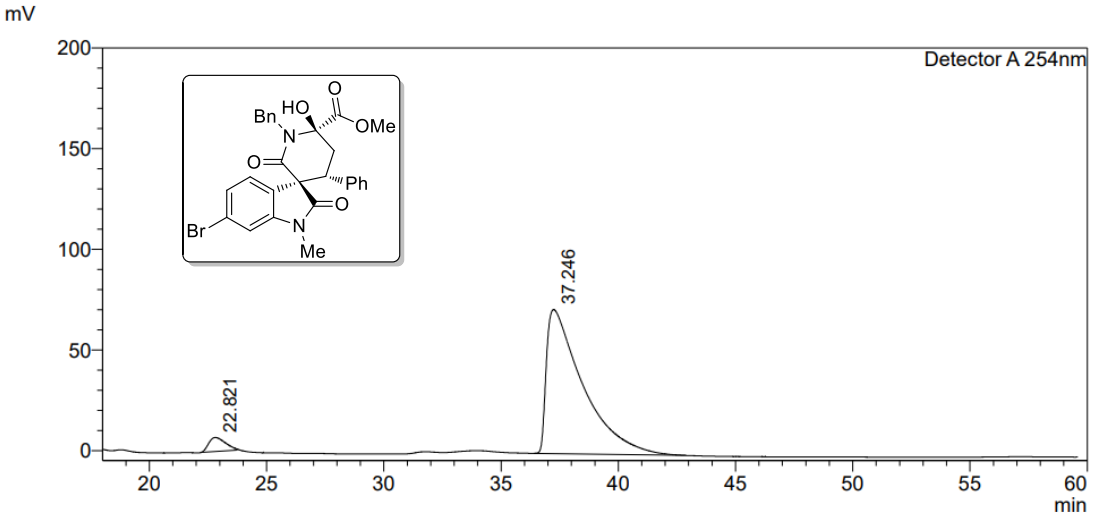
3ia:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	18.558	7270581	97918	50.988
2	41.627	6988761	29179	49.012
Total		14259343	127098	100.000

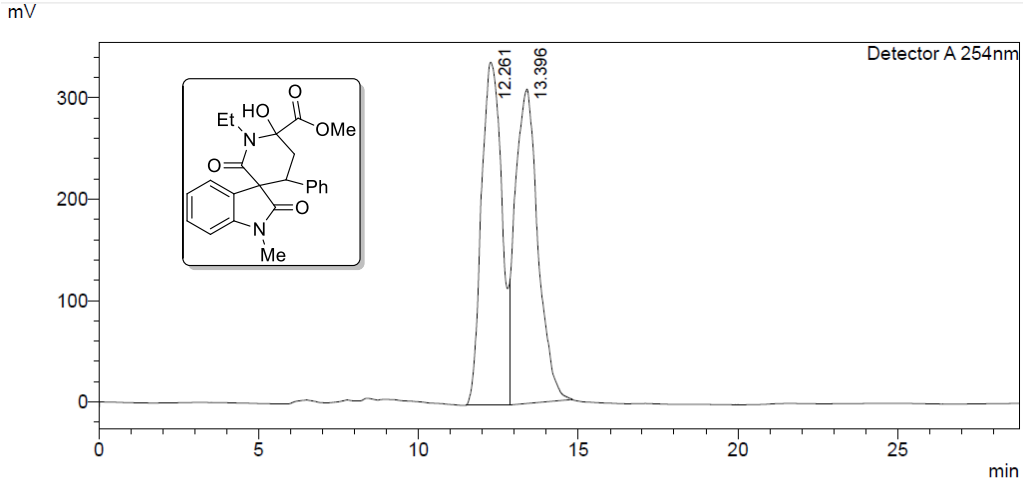


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	22.821	343047	6956	4.242
2	37.246	7743630	71610	95.758
Total		8086677	78566	100.000

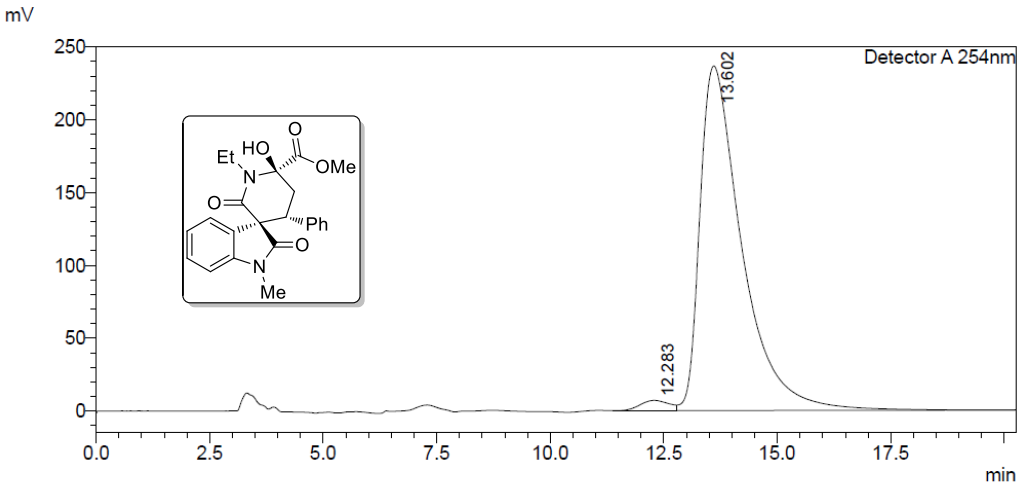
3ja:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.261	14981131	338223	49.414
2	13.396	15336357	310325	50.586
Total		30317488	648548	100.000

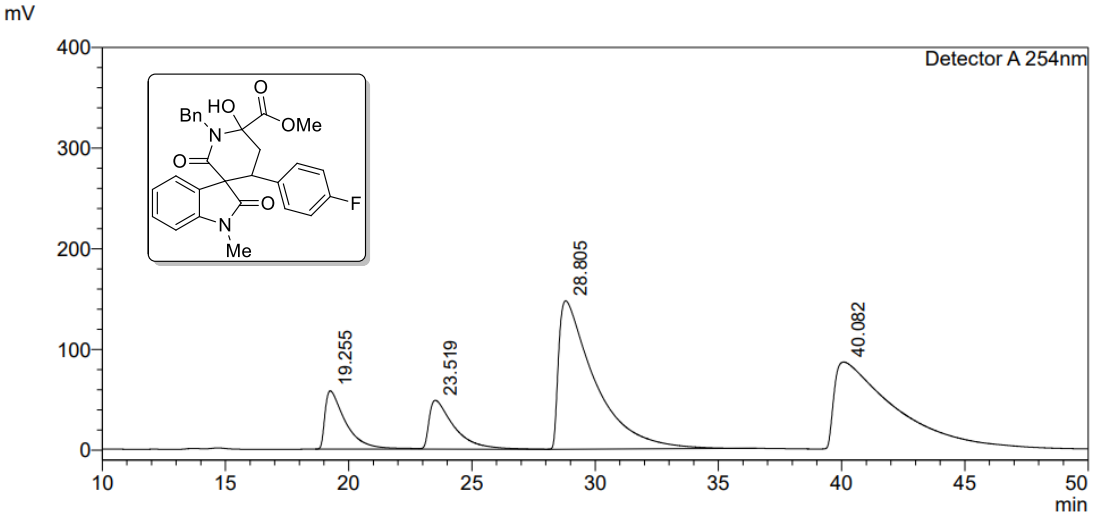


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.283	308209	6996	1.985
2	13.602	15220942	236625	98.015
Total		15529151	243621	100.000

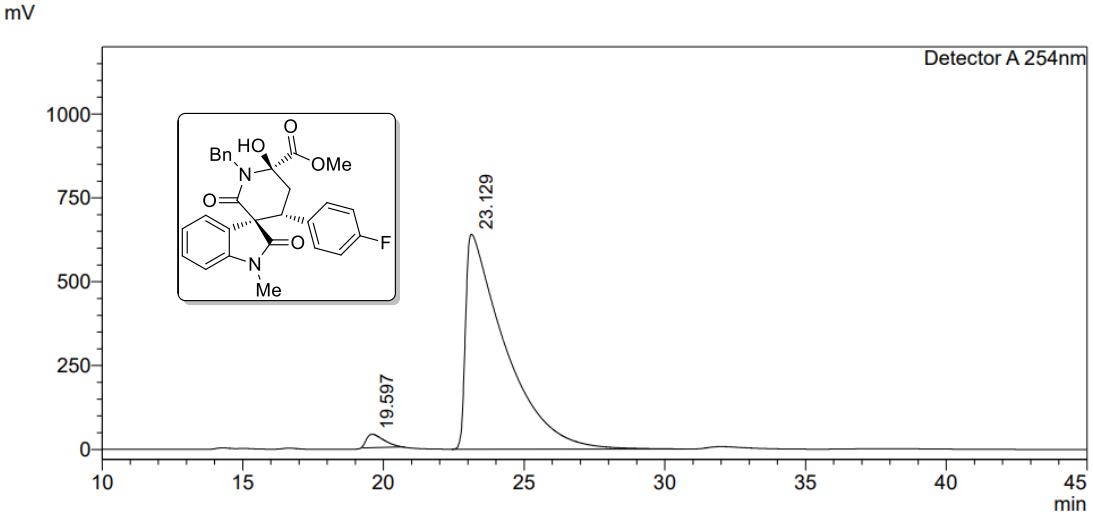
3cb:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	19.255	3380148	57953	9.160
2	23.519	3409593	48638	9.239
3	28.805	15112751	147470	40.953
4	40.082	15000621	86408	40.649
Total		36903113	340469	100.000

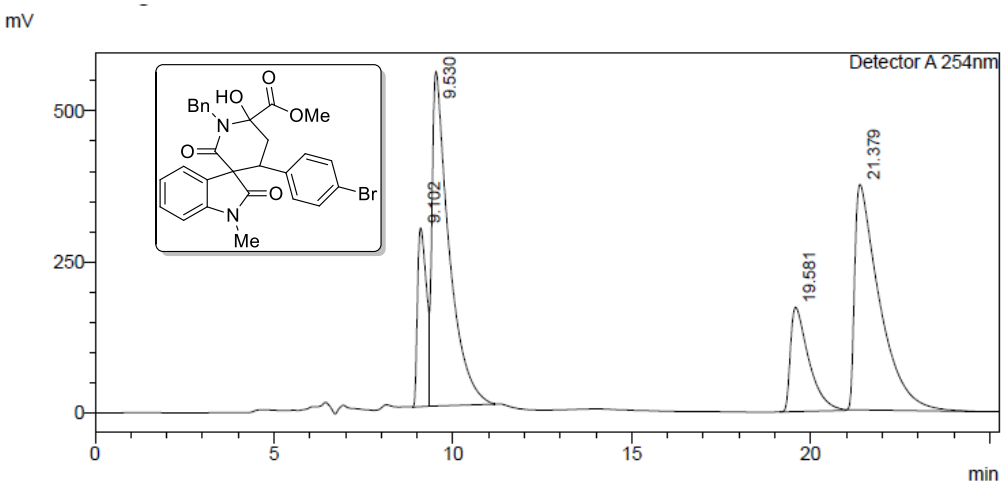


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	19.597	1675989	39878	2.600
2	23.129	62792622	641258	97.400
Total		64468611	681135	100.000

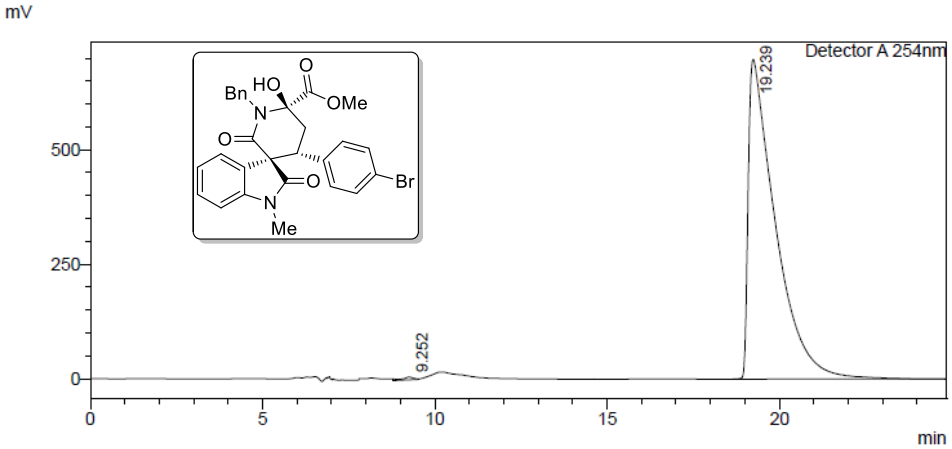
3cc:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.102	5141299	296143	10.788
2	9.530	18334411	554076	38.469
3	19.581	6153513	172497	12.911
4	21.379	18030545	373098	37.832
Total		47659769	1395815	100.000

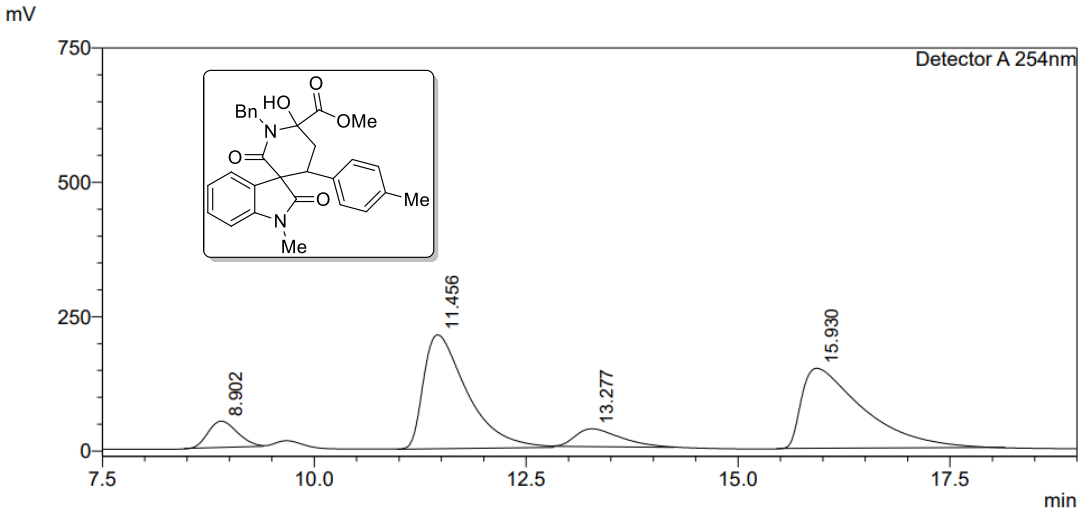


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height%	Area%
1	9.252	148135	0.874	0.386
2	19.239	38268499	99.126	99.614
Total		38416634	100.000	100.000

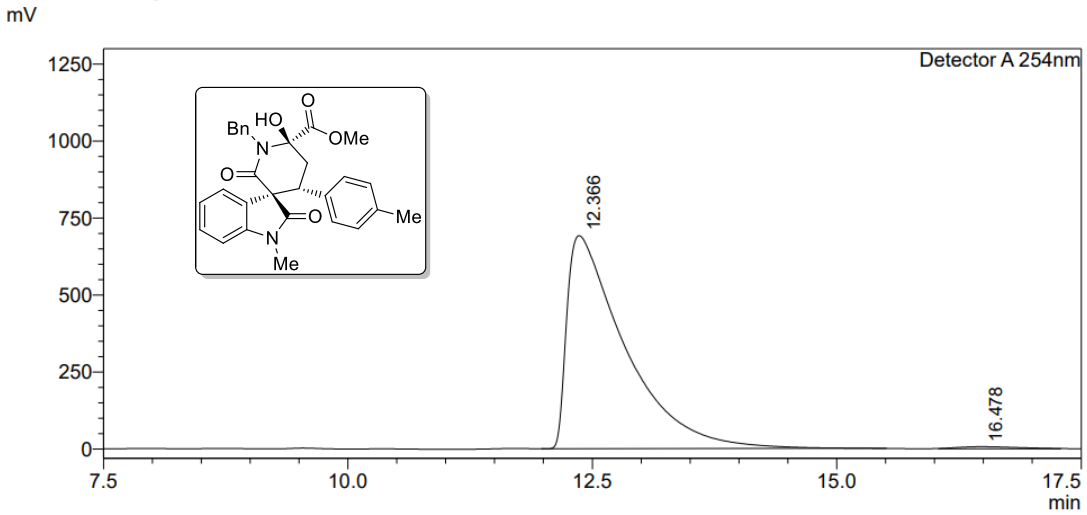
3cd:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.902	1175611	48909	6.688
2	11.456	7640532	212223	43.464
3	13.277	1251899	33318	7.122
4	15.930	7510969	148785	42.727
Total		17579011	443235	100.000

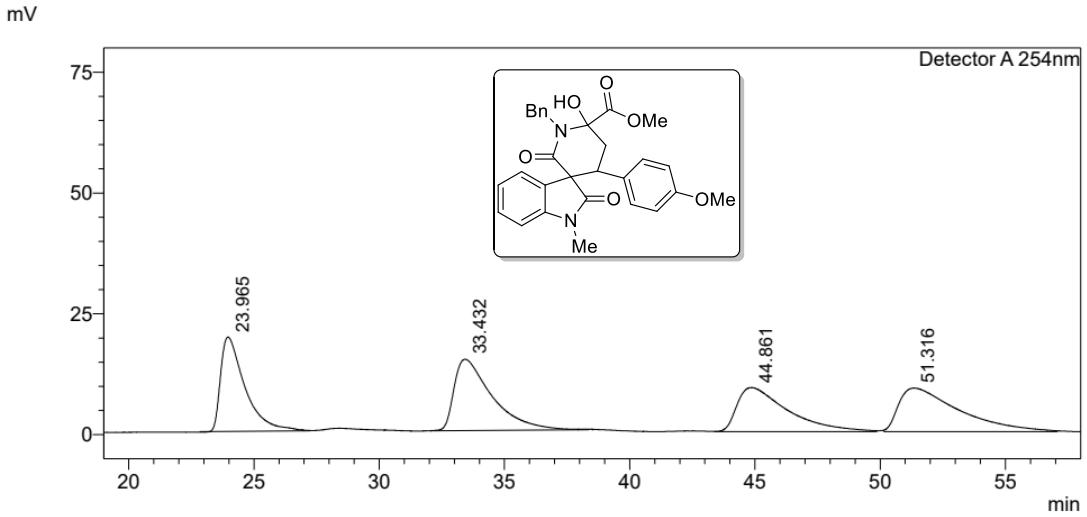


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.366	28641600	691798	99.017
2	16.478	284436	6555	0.983
Total		28926036	698353	100.000

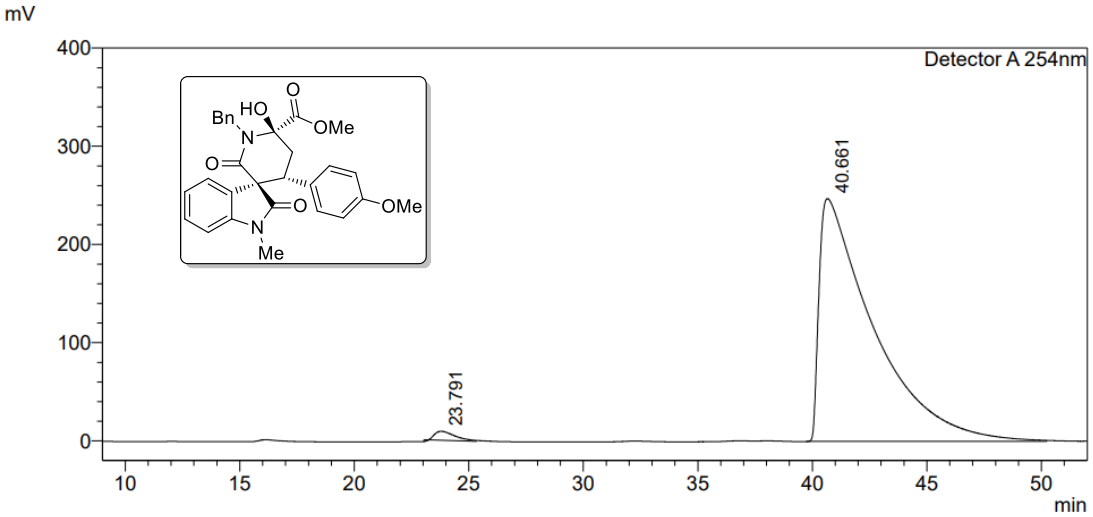
3ce:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	23.965	1319387	19535	23.200
2	33.432	1562184	14760	27.470
3	44.861	1289532	9144	22.675
4	51.316	1515852	9038	26.655
Total		5686954	52478	100.000

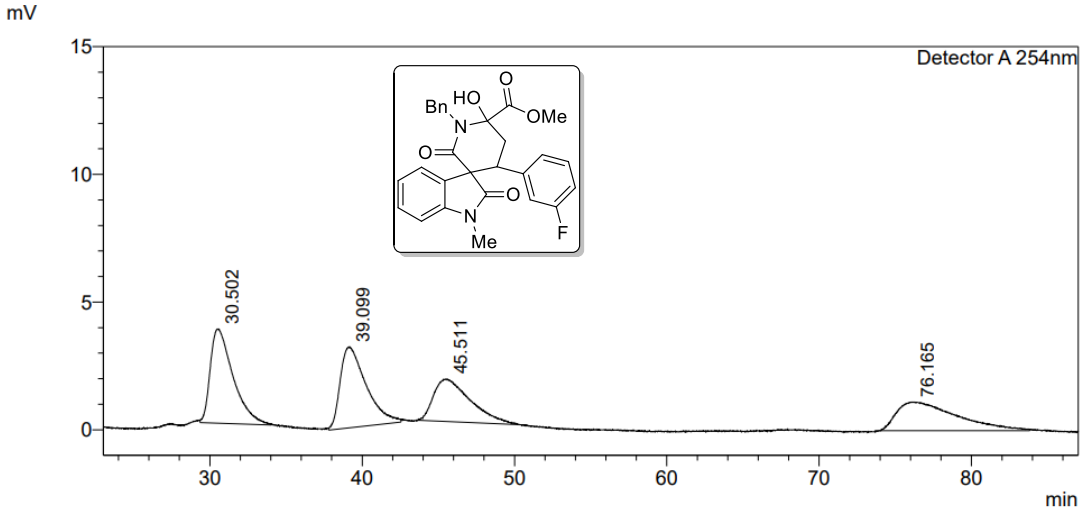


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	23.791	553294	9080	1.342
2	40.661	40664865	247186	98.658
Total		41218159	256266	100.000

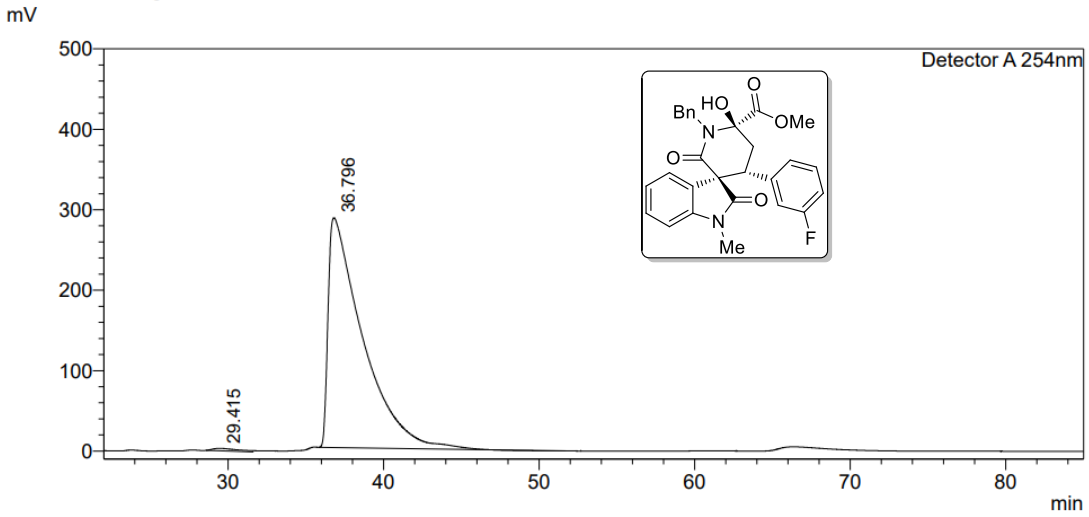
3cf:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	30.502	383528	3684	28.557
2	39.099	374127	3158	27.857
3	45.511	278739	1654	20.754
4	76.165	306649	1120	22.832
Total		1343043	9616	100.000

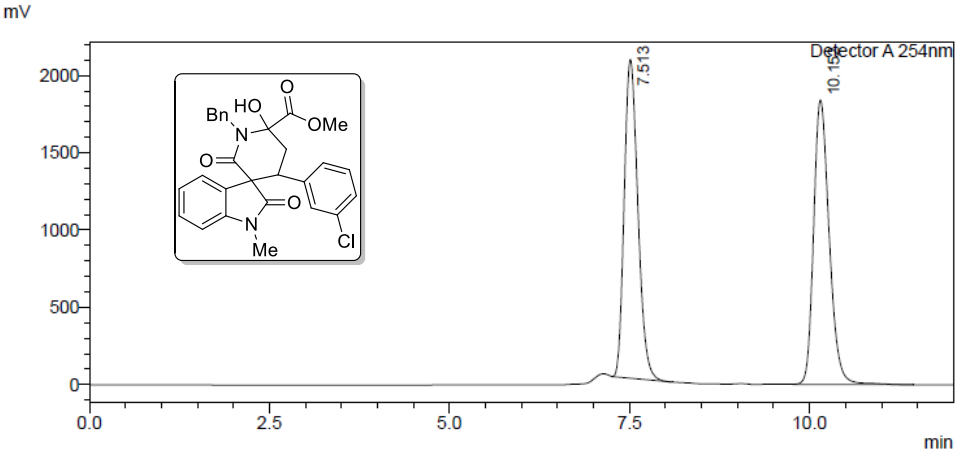


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	29.415	378063	3023	0.849
2	36.796	44130210	285744	99.151
Total		44508273	288767	100.000

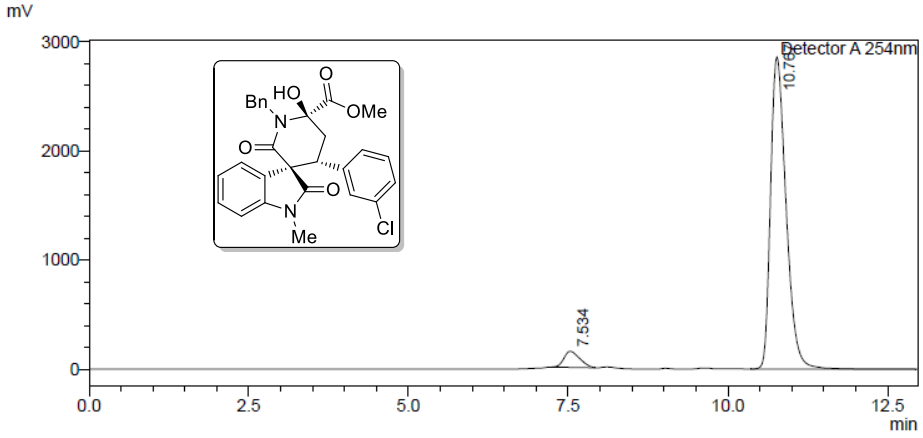
3cg:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.513	27209395	2058693	49.507
2	10.152	27751301	1838571	50.493
Total		54960696	3897265	100.000

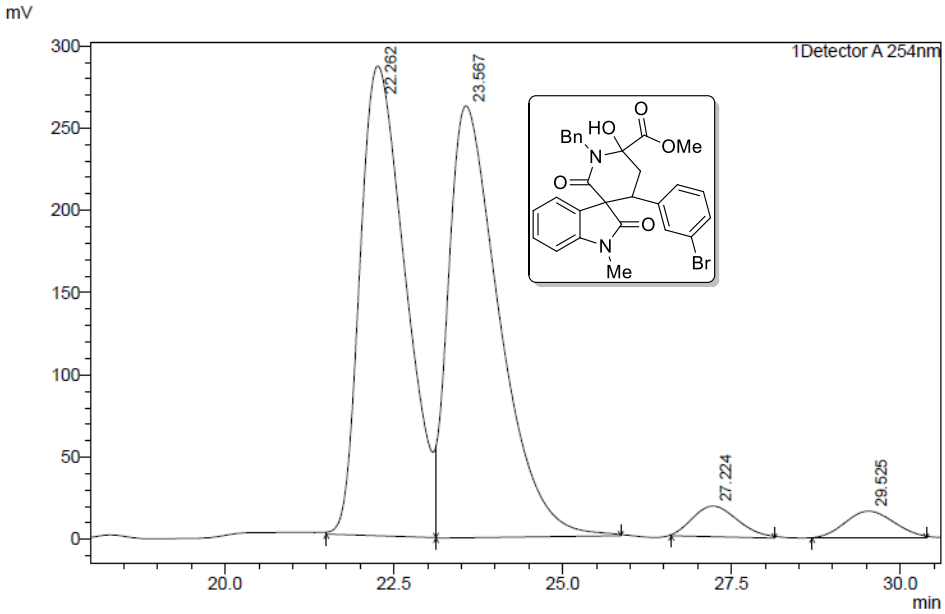


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.534	2546675	147845	5.010
2	10.767	48288364	2859295	94.990
Total		50835038	3007141	100.000

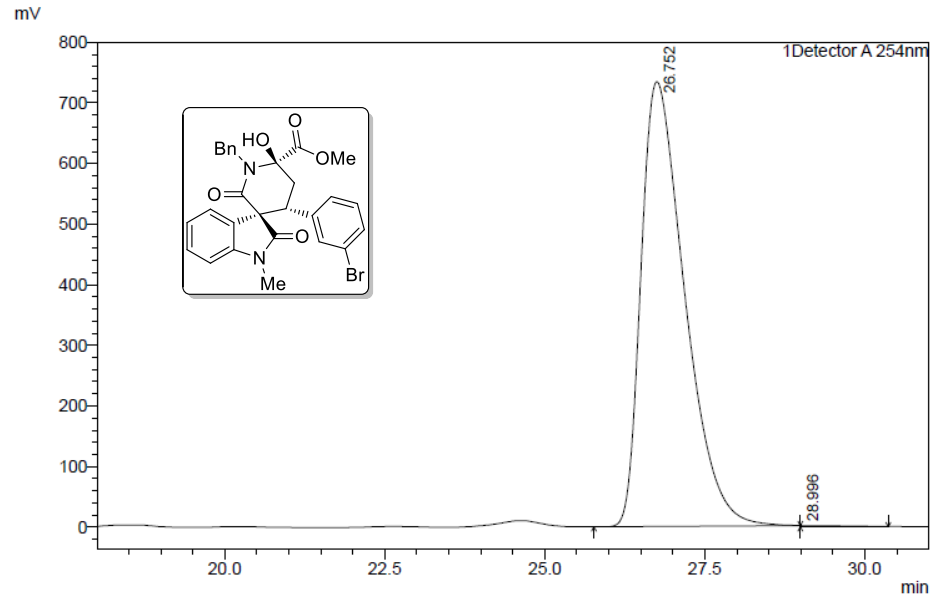
3ch:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	22.262	13211657	285656	46.077
2	23.567	13758889	262602	47.985
3	27.224	868120	18612	3.028
4	29.525	834635	16337	2.911
Total		28673301	583207	100.000

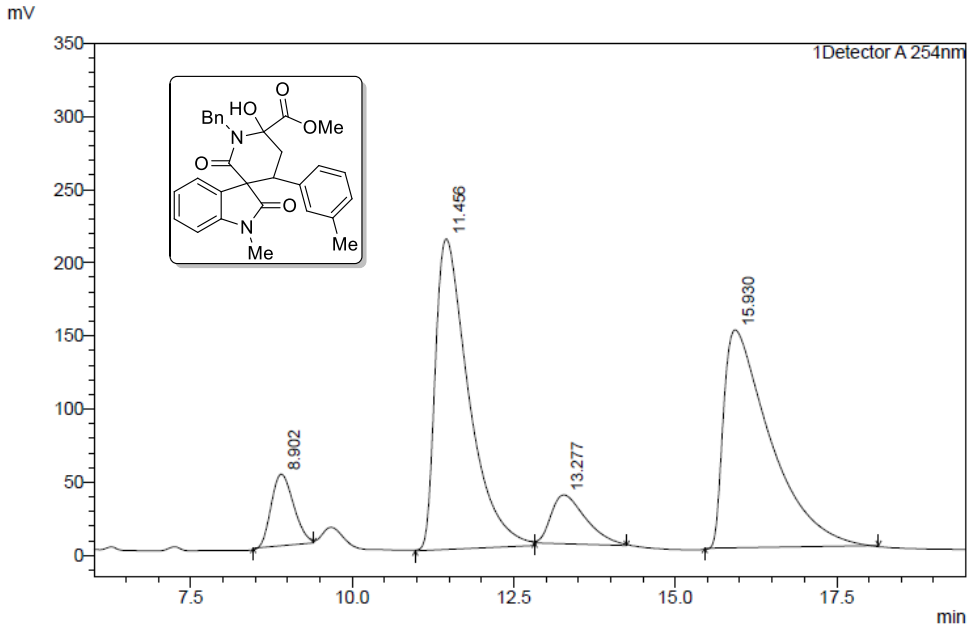


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	26.752	34742312	733746	99.682
2	28.996	110856	2129	0.318
Total		34853168	735875	100.000

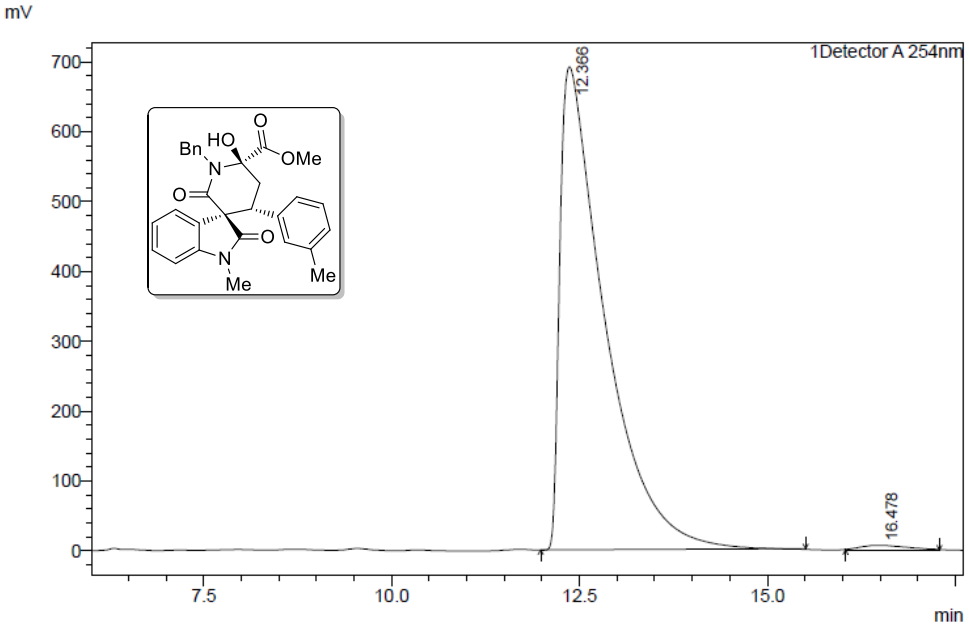
3ci:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.902	1175611	48909	6.688
2	11.456	7640532	212223	43.464
3	13.277	1251899	33318	7.122
4	15.930	7510969	148785	42.727
Total		17579011	443235	100.000

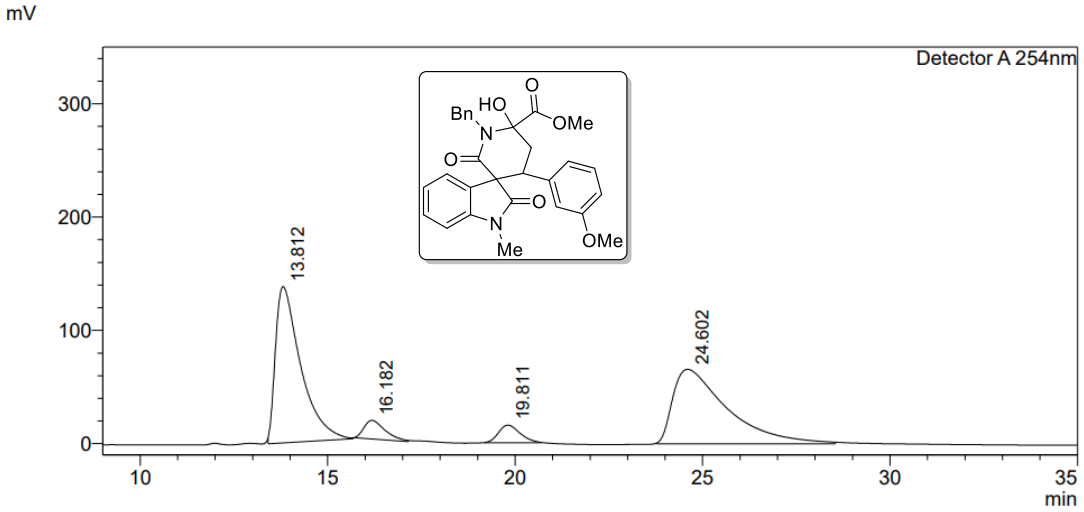


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.366	28641600	691798	99.017
2	16.478	284436	6555	0.983
Total		28926036	698353	100.000

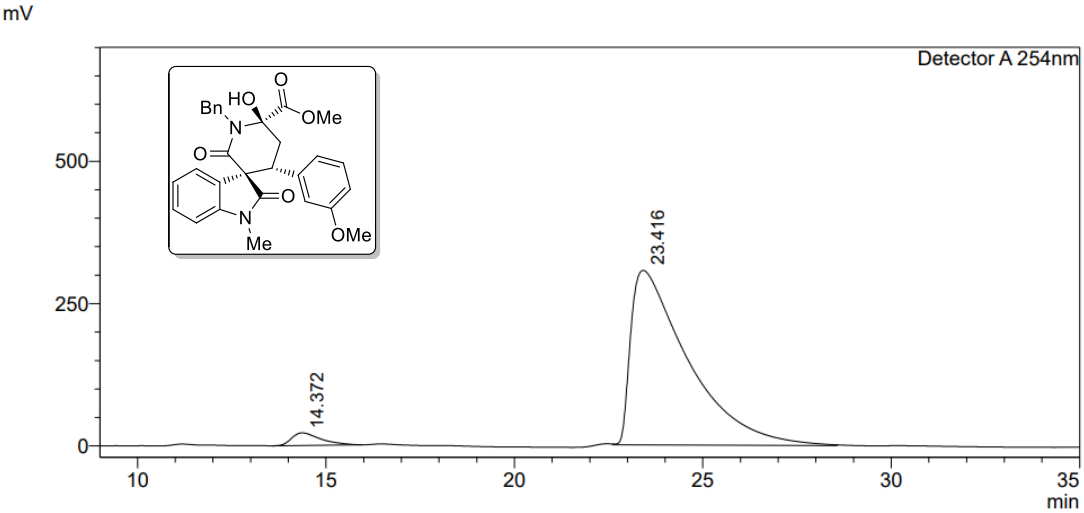
3cj:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	13.812	6472617	138025	44.948
2	16.182	652915	16503	4.534
3	19.811	631294	15640	4.384
4	24.602	6643562	65749	46.135
Total		14400388	235917	100.000

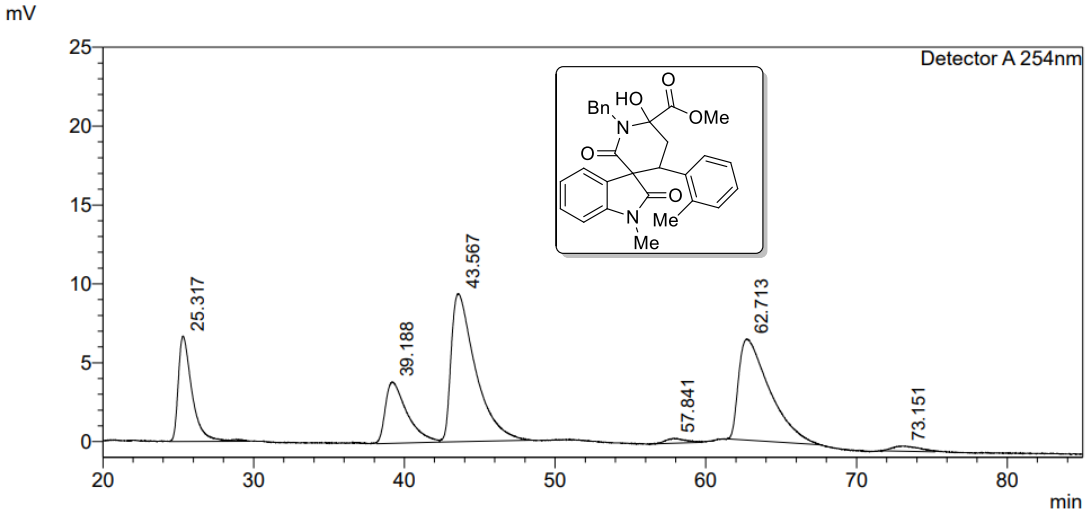


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.372	1178301	22043	3.495
2	23.416	32531497	306667	96.505
Total		33709798	328710	100.000

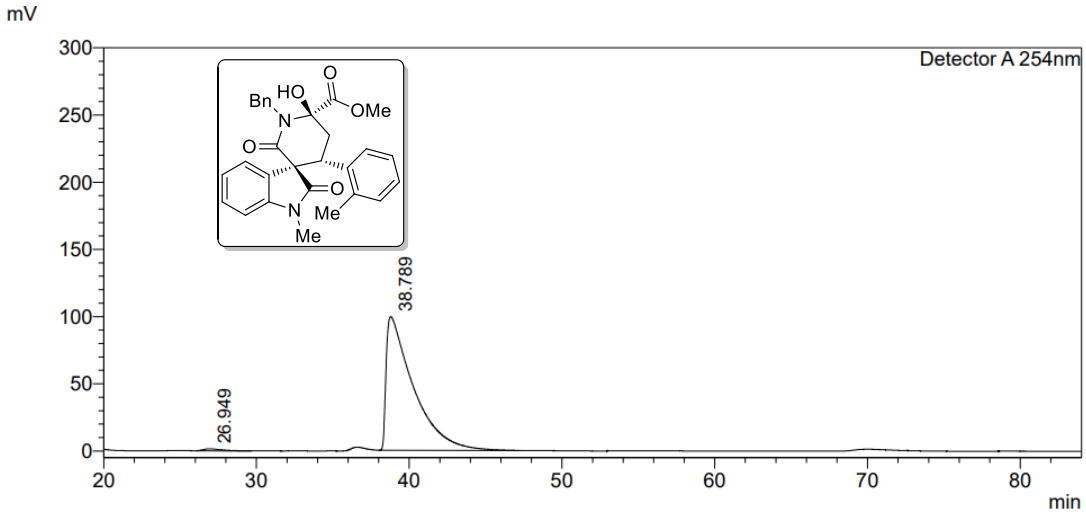
3ck:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	25.317	418326	6672	14.646
2	39.188	387694	3879	13.574
3	43.567	1060782	9390	37.140
4	57.841	28600	316	1.001
5	62.713	919237	6410	32.184
6	73.151	41534	330	1.454
Total		2856174	26997	100.000

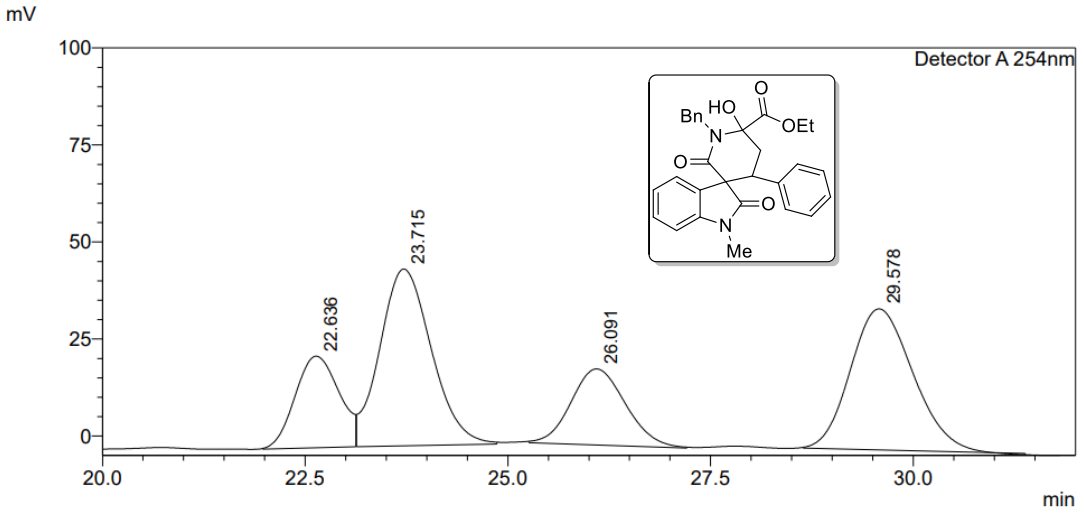


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	26.949	121323	1456	0.974
2	38.789	12340406	99468	99.026
Total		12461728	100924	100.000

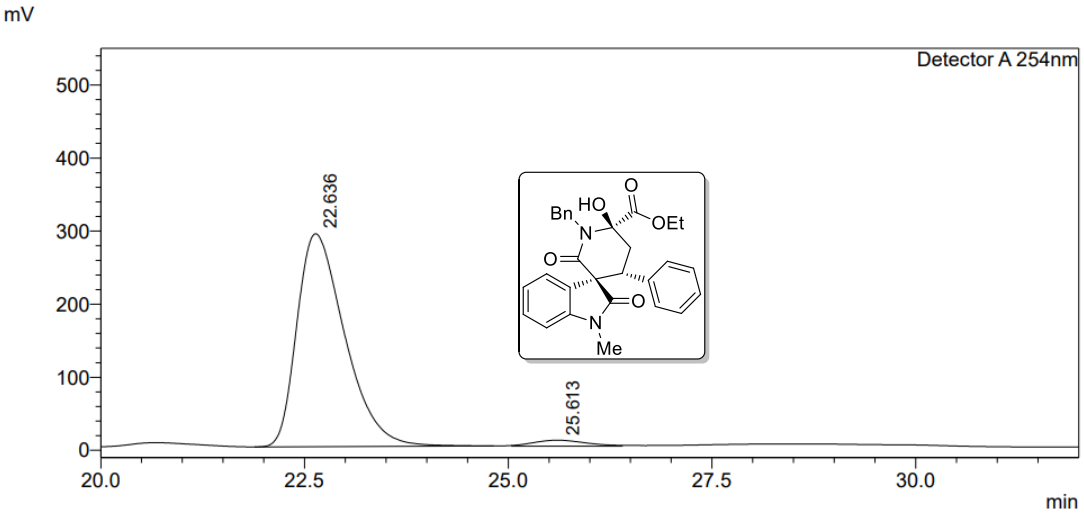
3cl:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	22.636	893946	23613	15.494
2	23.715	2020190	45579	35.014
3	26.091	912645	19584	15.818
4	29.578	1942879	36314	33.674
Total		5769659	125091	100.000

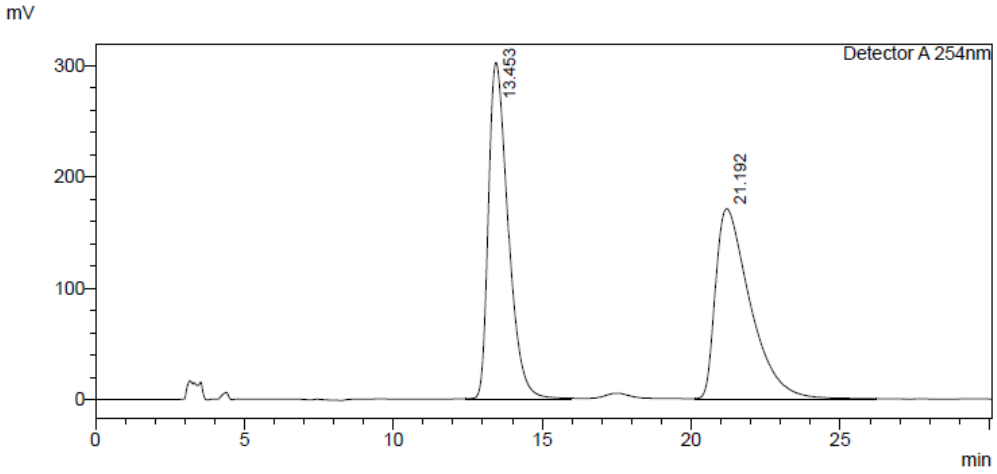


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	22.636	11935092	291391	96.969
2	25.613	373026	8226	3.031
Total		12308117	299617	100.000

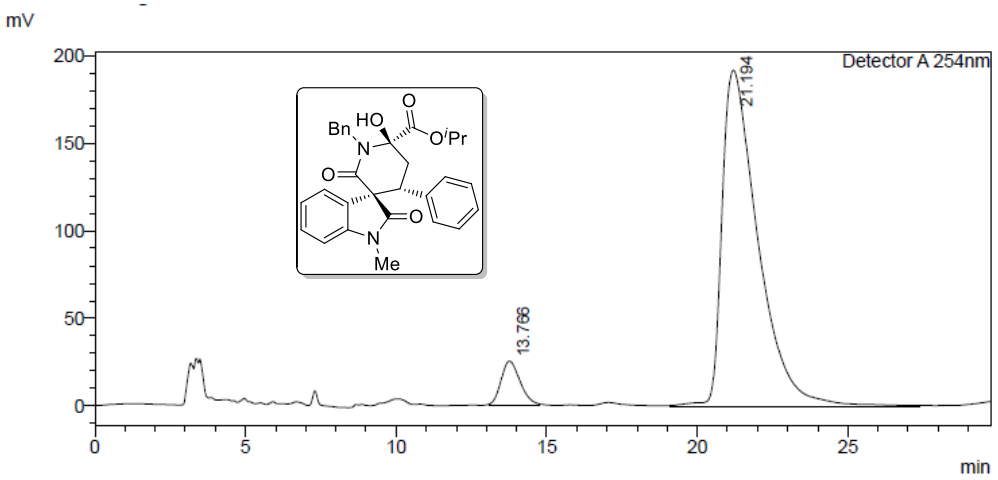
3cm:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	13.453	13887586	302047	50.010
2	21.192	13882287	170868	49.990
Total		27769873	472915	100.000

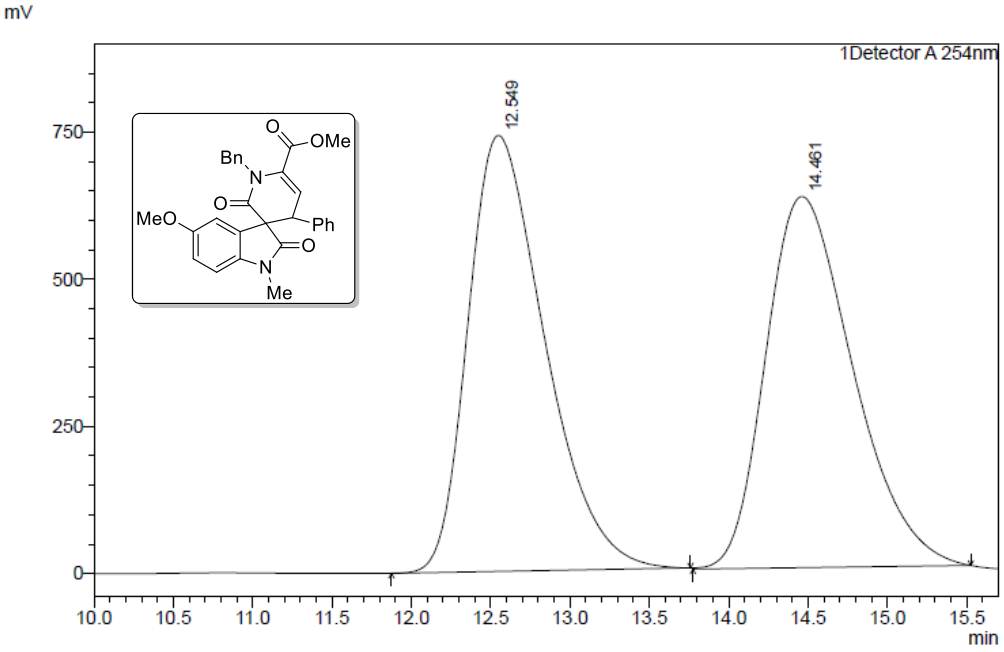


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	13.766	1096206	25070	6.419
2	21.194	15981615	192199	93.581
Total		17077821	217268	100.000

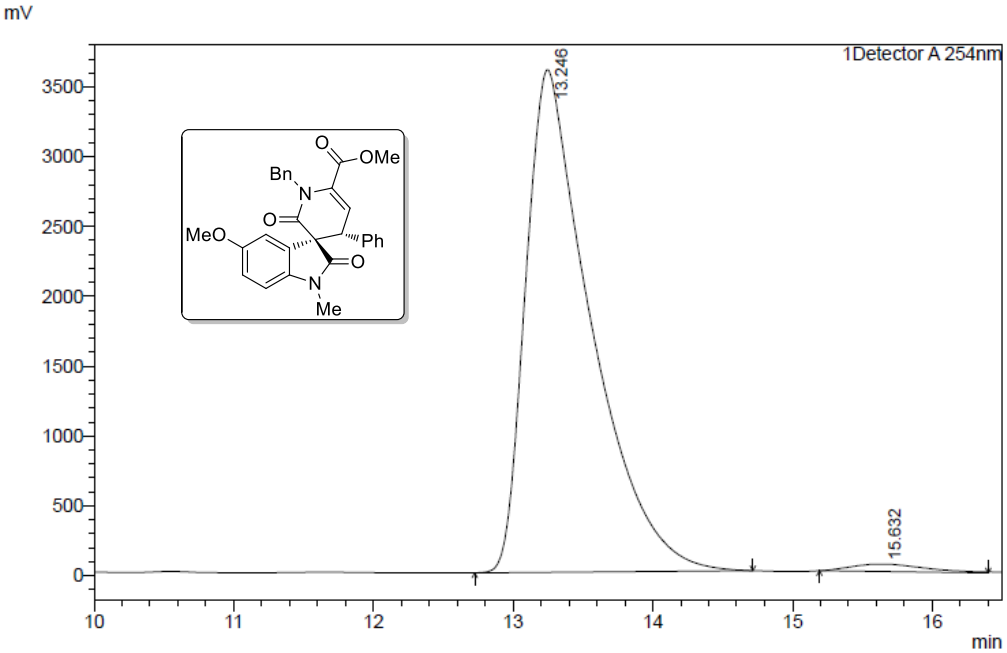
4:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.549	25282163	742498	50.609
2	14.461	24674099	635269	49.391
Total		49956262	1377768	100.000

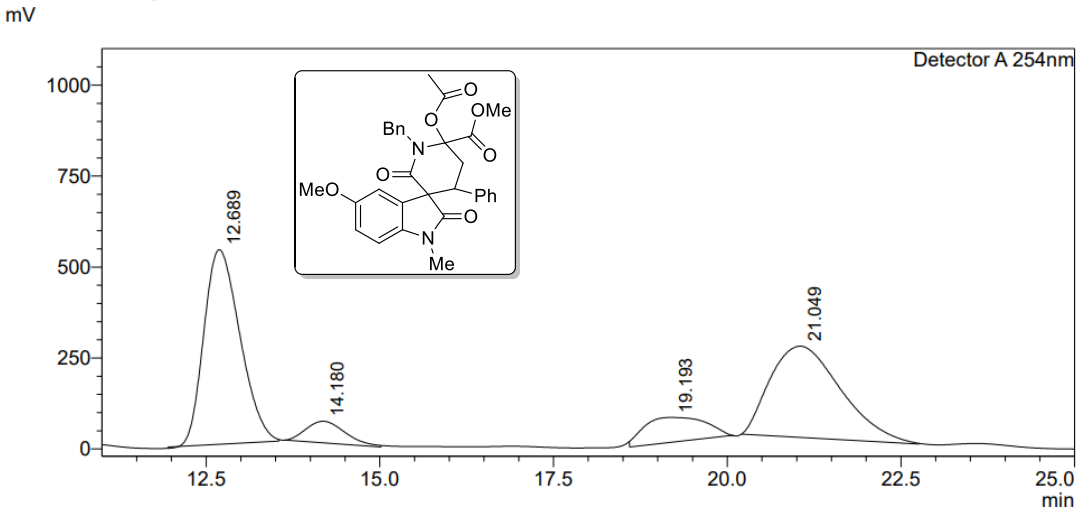


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	13.246	116923684	3601457	98.331
2	15.632	1984605	53470	1.669
Total		118908290	3654927	100.000

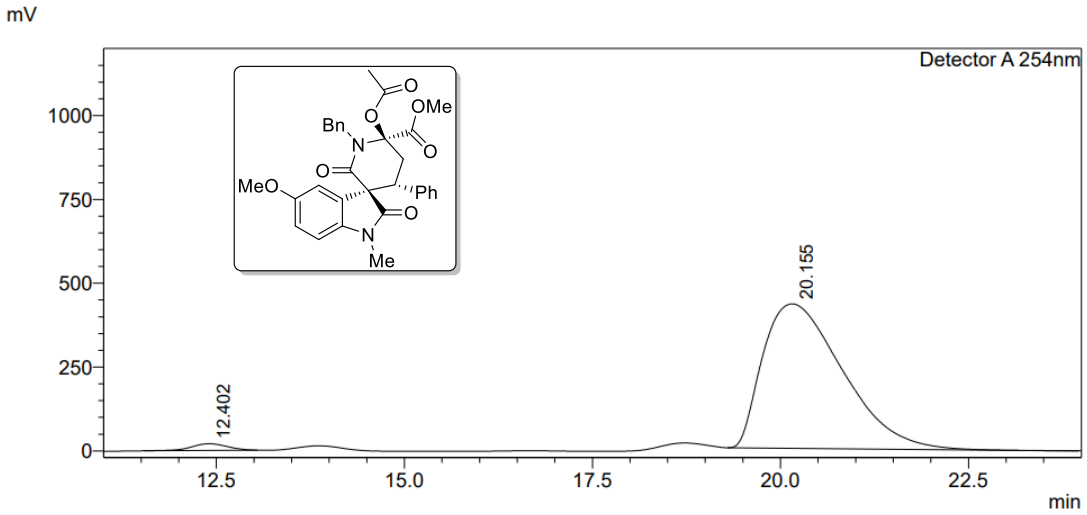
5:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.689	19314050	534598	44.317
2	14.180	2330849	59224	5.348
3	19.193	4170095	67792	9.568
4	21.049	17766572	250728	40.766
Total		43581566	912342	100.000

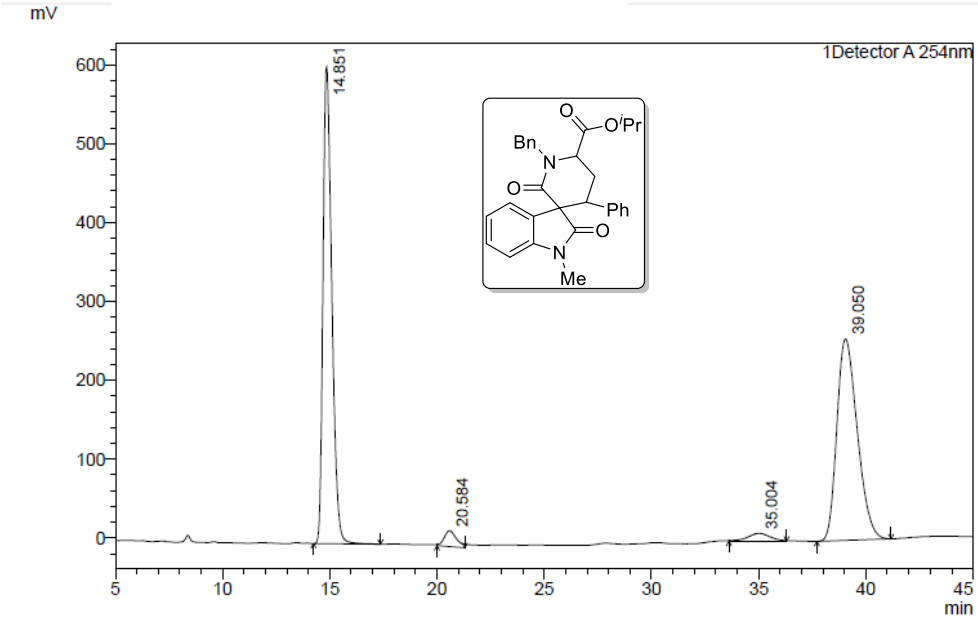


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.402	679670	20242	2.082
2	20.155	31963694	431117	97.918
Total		32643364	451359	100.000

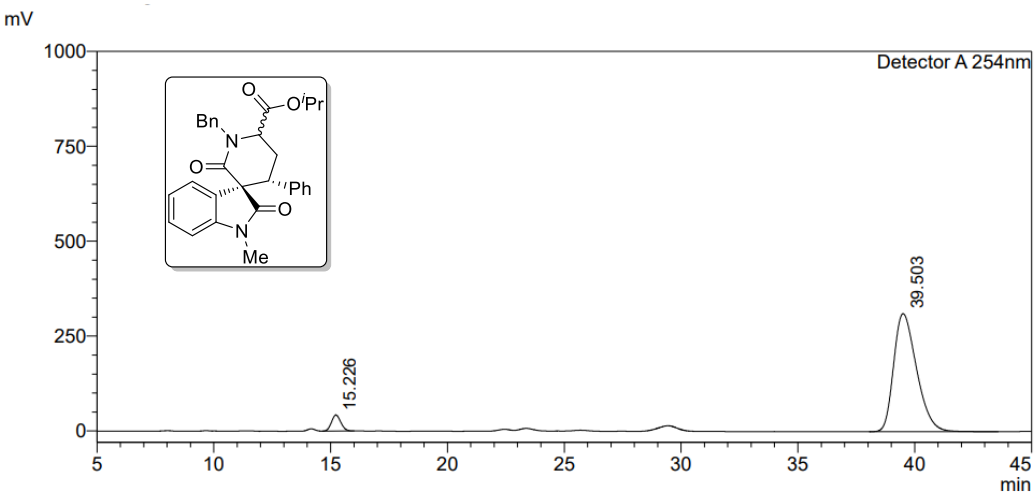
6:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.851	17281534	604570	48.350
2	20.584	802095	20185	2.244
3	35.004	737510	9898	2.063
4	39.050	16921103	255483	47.342
Total		35742242	890135	100.000



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	15.226	1171588	42234	5.229
2	39.503	21235384	310945	94.771
Total		22406972	353179	100.000