Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Phosphine-Catalyzed Enantioselective [4 + 1] Annulation of Oxindoles and Allenic Ketones: Constructing Five-Membered Rings with Weak Dinucleophiles

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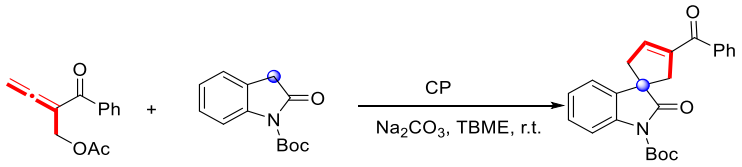
A. General Information

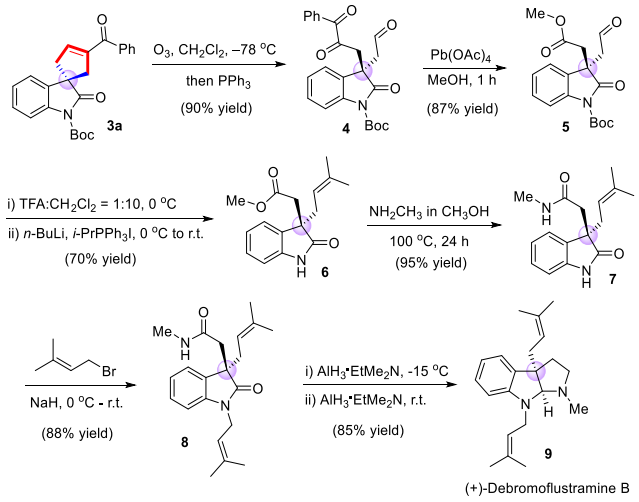
Unless otherwise specified, all reactions were conducted under an inert atmosphere and anhydrous conditions. All the solvents were purified according to the standard procedures. All chemicals which are commercially available were employed without further purification. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash chromatography was conducted on silica gel (200–300 mesh). ^{1}H and ^{13}C NMR spectra were recorded at ambient temperature in $CDCl_3$ on a Bruker AMX500 (500 MHz) or AMX400 (400 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm). The data are reported as follows: for ^{1}H NMR, chemical shift in ppm from tetramethylsilane with the solvent as internal standard ($CDCl_3$ δ 7.26 ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of non-equivalent resonances), integration; for ^{13}C NMR, chemical shift in ppm from tetramethylsilane with the solvent as internal indicator ($CDCl_3$ δ 77.1 ppm), multiplicity with respect to protons. All high-resolution mass spectra were performed by the MS service at the chemistry department, National University of Singapore, and were obtained on a Finnigan/MAT 95XL-T spectrometer to be given in m/z. Optical rotations were measured using an Anton Paar MCP-100 digital polarimeter using a 1 cm glass cell. Enantiomeric excesses were determined by HPLC analysis on a chiral stationary phase using CHIRALPAK® columns (IA and ID) eluting with hexane/isopropanol mixtures as indicated. Allenic ketones and catalysts were synthesized by following our previously reported procedures[1,3]. *N*-Protected oxindoles **2** were synthesized according to the literature-reported procedures[2].

B. Representative procedure for enantioselective [4 + 1] Annulation



To a 4 mL reaction vial, sodium carbonate (0.1 mmol) and chiral phosphine catalyst (0.02 mmol) and Boc-protected oxindole (0.1 mmol) were added to 2.0 mL of *t*-Butyl methyl ether, then 2-benzoylbuta-2,3-dien-1-yl acetate (0.12 mmol) was injected slowly into the stirring solution using a micro-syringe. The reaction vial was left to stir at -35 °C until the allene has been fully consumed. The solution was then purified using a column chromatography (Hexane:Ethyl acetate = 20:1) to yield a yellow solid as the cyclized product.

C. Procedure of total synthesis of (+)-Debromoflustramie B



To a 50 mL round-bottle flask, sodium carbonate (424 mg, 4 mmol) and chiral phosphine catalyst (532 mg, 0.8 mmol) and Boc-protected oxindole (932 mg, 4 mmol) were added to 20.0 mL of *t*-Butyl methyl ether, then 2-benzoylbuta-2,3-dien-1-yl acetate (768 mg, 4.8 mmol) was injected slowly into the stirring solution using a micro-syringe under -35°C. The reaction vial was left to stir at -35 °C until the allene has been fully consumed. The solution was then purified using a column chromatography

(Hexane:Ethyl acetate = 20:1) to yield a yellow solid as the cyclized product 1.1 g, 71% yield, 92% *ee*.

To a solution of **3a** (389 mg, 1 mmol) in CH_2Cl_2 (10 mL), ozone was bubbled into the solution under -78 ºC (dry ice - acetone bath). Ozone was stopped after the solution turned to light blue, and oxygen was bubbled into the reaction until the blue color disappeared. The reaction was allowed to warm to room temperature, and triphenyl phosphine (262 mg, 1 mmol) was added into the reaction. The reaction mixture was stirred for one hour, then removed the solvent, and the residue was purified by silica gel column (Hexane:Ethyl acetate = 4:1), yielding product **4** in 379 mg (90%).

To a solution of **4** in methanol (10 mL), lead tetraacetate (443 mg, 1 mmol) was added under 0 ºC. The reaction was complete in one hour then filtered with celite pad and washed the pad with ethyl acetate. The organic solvent was removed in vacuum, and the residue was purified with silica gel column (Hexane:Ethyl acetate = 2:1). **5** was obtained in 272 mg, 87% yield.

To a solution of **5** in dichloromethane (3 mL), trifluoro acid (0.3 mL) was added under 0 ºC. The reaction mixture was stirred for 1 hour, then the reaction mixture was evaporated to dryness, the residue used directly without further purification.

To a witting precursor (743 mg, 1.7 mmol) in THF solution, *n*-butyl lithium (0.85 mL, 1.7 mmol) was added in dropwise with ice bath. An Aldehyde **5** solution in THF was added after 40 mins. Stirring for 3 hours, the reaction was quenched by water and extracted by ethyl acetate, brine and dried over sodium sulphate. After remove the solvent, the residue was purified by silica gel column (Hexane:Ethyl acetate = 4:1). **6** was obtained in 150 mg, 70% yield.

To a seal tube, intermediate **6** (150 mg, 0.55 mmol) was dissolved in methanol solution containing methyl amine (33 % w/w). Heating the solution to 100 ^{o}C for 24h, the solvent was removed in vacuum, and the residue purified with silica gel column (CH_2Cl_2: MeOH = 95:5). **7** was obtained in 142 mg, 95% yield.

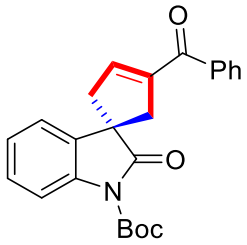
To a solution of **7** (0.52 mmol) in THF 5 mL, sodium hydride (51.2 mg, 1.28 mmol 60% in mineral oil) was added under 0 ^{o}C. After stirred 30 mins, 1-bromo-3-methylbut-2-ene (0.52 mmol) was added to the reaction mixture, then warm to room temperature. The reaction completed in one hour and was quenched with water. Removing the solvent in vacuum, the residue was purified with silica gel column (Hexane:Ethyl acetate = 2 :1). **8** was obtained in 156 mg, 88% yield.

An oven-dried round-bottomed flask containing a stirring bar was charged with **8** (156 mg, 0.458 mmol), and placed under a protective argon atmosphere. Anhydrous THF (10 mL) was added and the mixture was cooled to -15 ^{o}C followed by the addition of $AlH_3{\cdot}EtMe_2N$ (0.5 M in THF, 5 mL, 2.2 mmol) via syringe. The mixture was stirred for 5 min then treated with THF:H_2O = 1:1 (50 mL) at the same temperature and stirred for 15 min, filtered through celite and concentrated in vaccuo to give a residue that was dissolved in EtOAc washed with sat. aq. Na_2CO_3, dried over $MgSO_4$ and concentrated in vaccuo to yield an oily residue. Anhydrous THF (10 mL) was added and the mixture was let stir at room temperature for 5 min followed by the addition of $AlH_3{\cdot}EtMe_2N$ (0.5 M in THF, 2.5 mL, 1.1 mmol) via syringe. The mixture was stirred for 5 min then treated with THF : H_2O = 1:1 (25 mL) and stirred for 15 min, filtered through celite and concentrated in vaccuo to give a residue that was dissolved in EtOAc washed with sat.

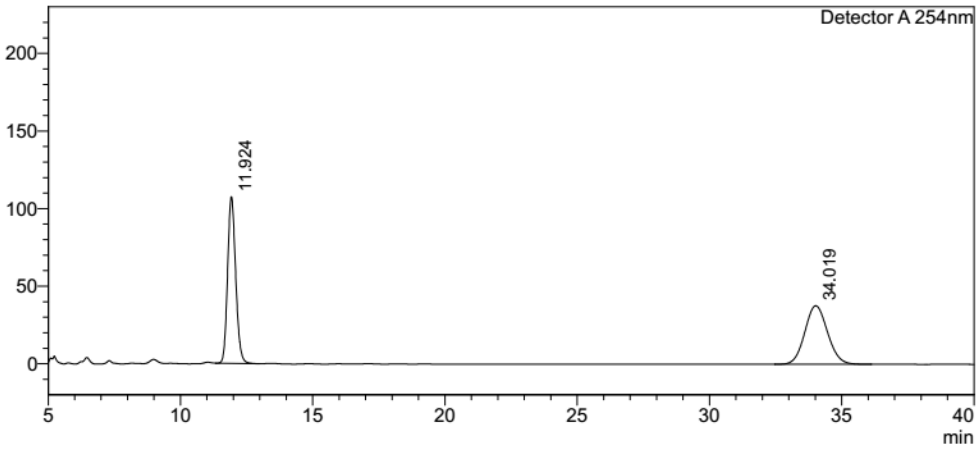
aq. Na_2CO_3 dried over $MgSO_4$ and concentrated in vaccuo to yield an oily residue which was purified via column chromatography CH_2Cl_2:MeOH = 95:5, (+)-Debromoflustramine B was obtained in 120 mg 85%.[4]

D. Analytical Data and HPLC Chromatograms of the Products

tert-Butyl (*R*)-3-benzoyl-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3a**



According to general [4 + 1] annulation procedure, **3a** was obtained in 95% yield (37.0 mg) as a white solid and 92% *ee*. $[\alpha]_D^{25}$ = 1.7 (*c* 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 32.6 min, t_R (minor) = 11.8 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (m, 3H), 7.59 (m, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.33 (m, 2H), 7.19 (m, 1H), 6.59 (m, 1H), 3.48 (dd, *J* = 16.7, 2.2 Hz, 1H), 3.39 (m, 1H), 3.15 (dd, *J* = 16.7, 1.2 Hz, 1H), 2.95 (m, 1H), 1.69 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.6, 179.2, 149.2, 142.1, 142.0, 138.4, 138.3, 134.4, 132.2, 128.9, 128.4, 128.3, 125.0, 121.8, 115.0, 84.5, 52.1, 47.0, 45.4, 28.1. HRMS (ESI) m/z calcd for $C_{24}H_{22}NO_4$ $[M + Na]^+$ = 412.1519, found: 412.1524.



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Detector A 254nm

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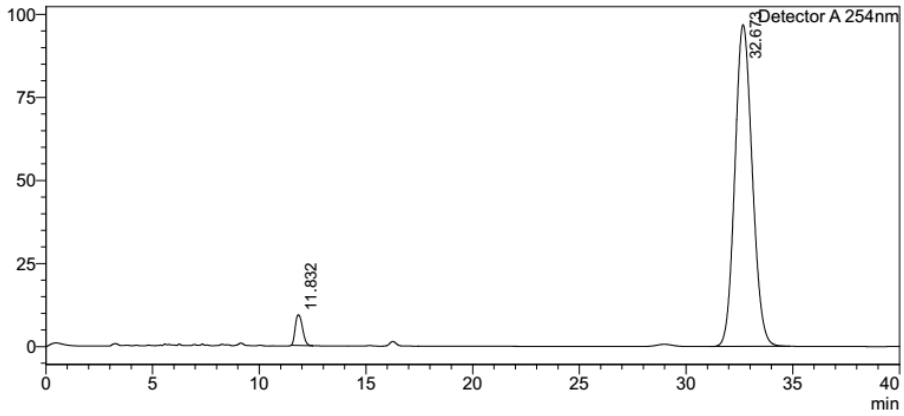
1	11.924	2280057	107464	50.294		M	
2	34.019	2253363	37722	49.706			
Total		4533420	145186				



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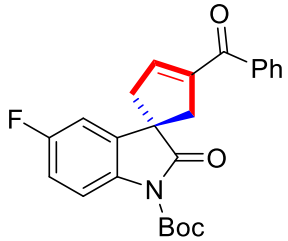
Detector A 254nm

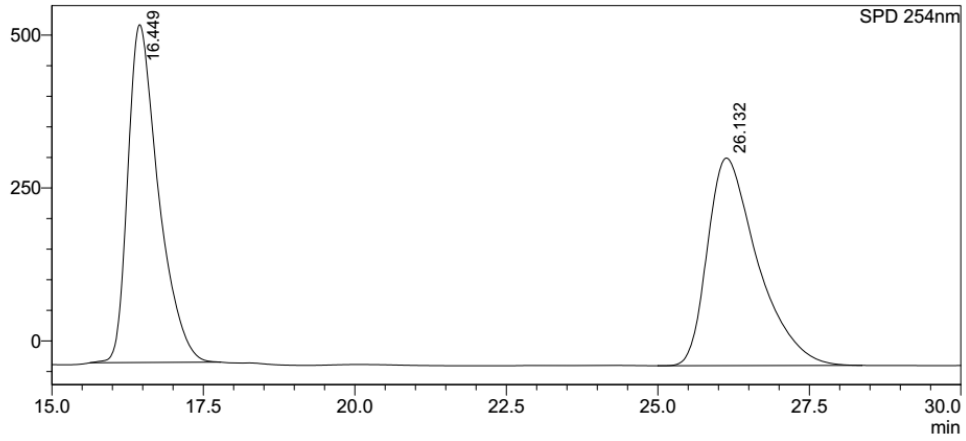
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.832	217597	9241	3.810		M	
2	32.673	5492888	96858	96.190			
Total		5710485	106099				

tert-Butyl (*R*)-3-benzoyl-5'-fluoro-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3b**



According to general [4 + 1] annulation procedure, **3b** was obtained in 94% yield (38.3 mg) as a white solid and 93% *ee*. $[\alpha]_D^{25}$ = -3.7 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane =

20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 26.3 min, t_R (minor) = 16.5 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.81 (m, 3H), 7.63 – 7.58 (m, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.03 (d, *J* = 8.3 Hz, 2H), 6.59 (d, *J* = 2.1 Hz, 1H), 3.44 (ddd, *J* = 21.1, 17.8, 2.2 Hz, 2H), 3.14 (dd, *J* = 16.8, 1.1 Hz, 1H), 2.99 – 2.90 (m, 1H), 1.68 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.4, 178.7, 178.7, 161.4, 161.2, 160.0, 159.3, 154.7, 149.1, 141.9, 141.8, 138.1, 136.0, 135.9, 134.3, 132.3, 128.9, 128.4, 116.5, 116.4, 115.0, 114.8, 109.4, 109.2, 84.7, 52.3, 46.9, 45.3, 28.1. HRMS (ESI) m/z calcd for $C_{24}H_{22}FNO_4$ $[M + Na]^+$ = 430.1425, found: 430.1431.



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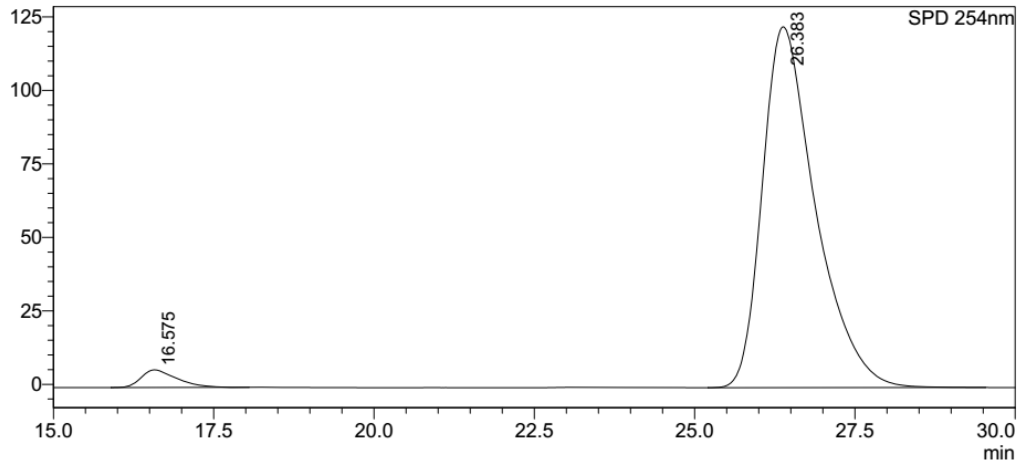
SPD 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.449	19436416	552561	49.878		M	
2	26.132	19531632	339376	50.122		M	
Total		38968048	891937				



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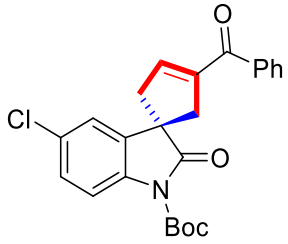
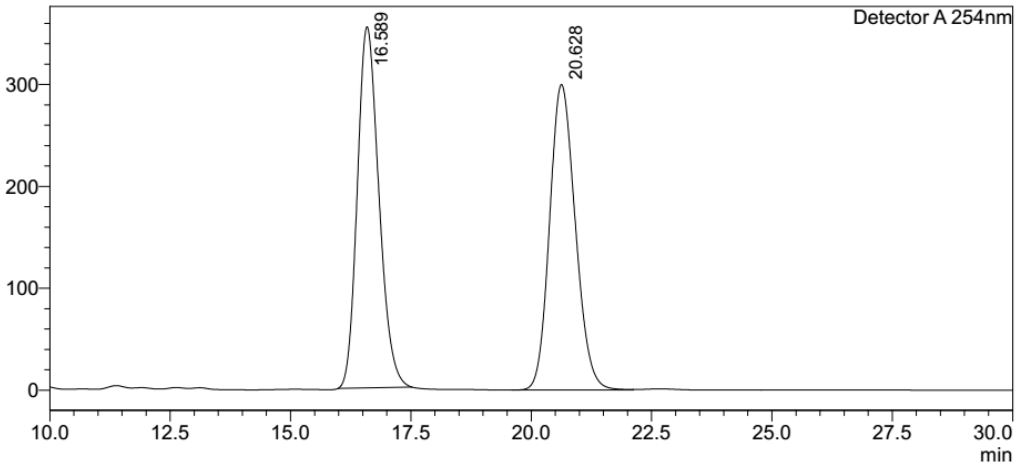
SPD 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.575	229426	5987	3.141			
2	26.383	7075262	122769	96.859			
Total		7304688	128756				

tert-Butyl (*R*)-3-benzoyl-5'-chloro-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3c**



According to general [4 + 1] annulation procedure, **3c** was obtained in 90% yield (38.2 mg) as a white solid and 91% *ee*. $[\alpha]_D^{25}$ = 11.8 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 16.8 min, t_R (minor) = 13.9 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 1.8 Hz, 1H), 7.84 (m, 2H), 7.59 (m, 3.7 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.17 (m, 1H), 6.58 (m, 1H), 3.46 (m, 1H), 3.37 (m, 1H), 3.12 (dd, *J* = 16.7, 1.0 Hz, 1H), 2.92 (d, *J* = 18.9 Hz, 1H), 1.69 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.4, 178.6, 148.9, 142.0, 141.7, 139.4, 138.2, 134.1, 132.7, 132.3, 128.9, 128.4, 125.0, 122.6, 115.8, 85.0, 51.9, 47.0, 45.3, 28.0. HRMS (ESI) m/z calcd for $C_{24}H_{22}ClNO_4$ $[M + Na]^+$ = 446.1130, found:446.1143.



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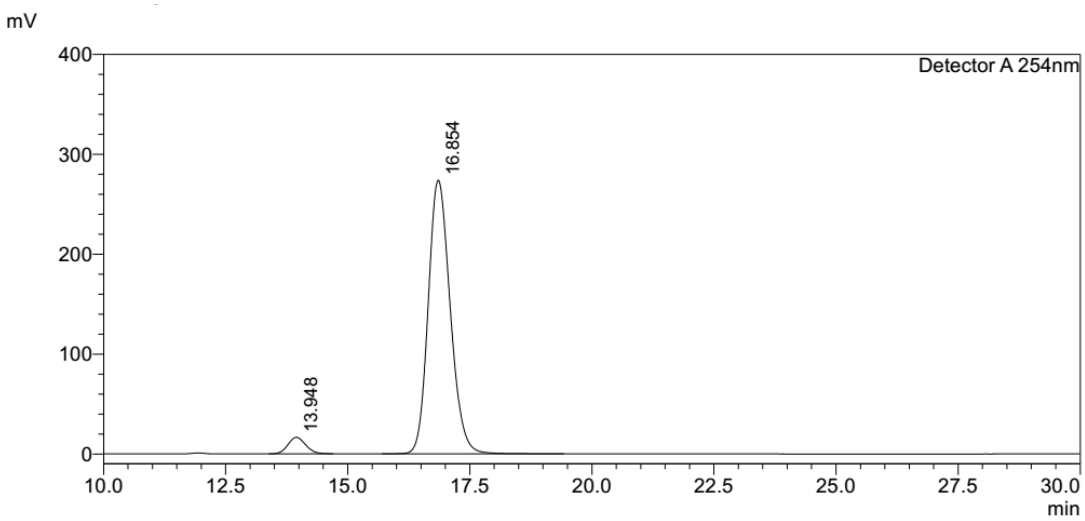
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.589	11056170	354263	49.738		M	
2	20.628	11172492	299887	50.262			
Total		22228662	654151				



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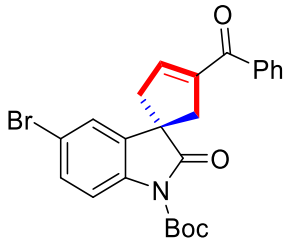
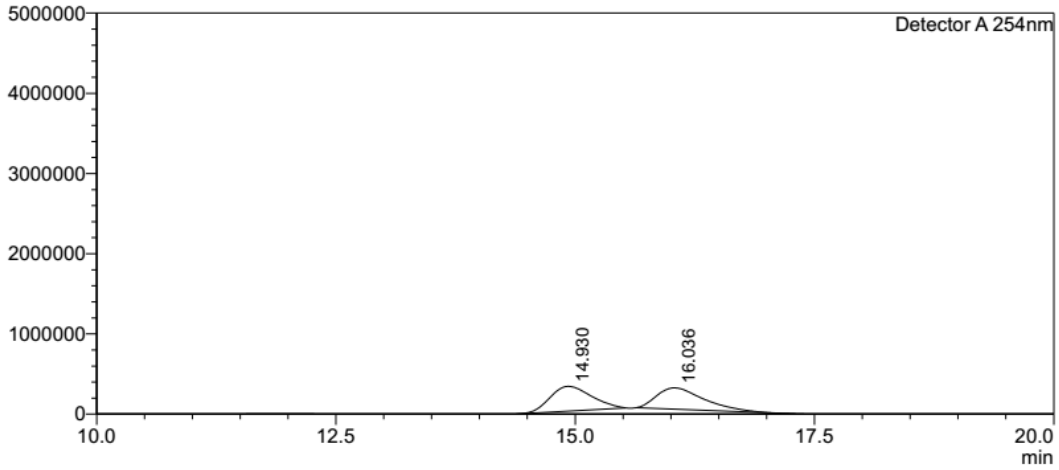
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.948	417873	16509	4.636		M	
2	16.854	8595046	274096	95.364			
Total		9012919	290606				

tert-Butyl (*R*)-3-benzoyl-5'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3d**



According to general [4 + 1] annulation procedure, **3d** was obtained in 85% yield (39.8 mg) as a white solid and 90% *ee*. $[\alpha]_D^{25}$ = 1.7 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 17.0 min, t_R (minor) = 15.5 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.60 (m, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.46 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.41 (d, *J* = 1.9 Hz, 1H), 6.59 (s, 1H), 3.47 (dd, *J* = 16.8, 2.1 Hz, 1H), 3.39 (dd, *J* = 18.9, 2.1 Hz, 1H), 3.14 (dd, *J* = 16.8, 1.0 Hz, 1H), 2.94 (d, *J* = 18.9 Hz, 1H), 1.67 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.4, 178.3, 148.9, 141.9, 141.8, 138.1, 137.5, 136.4, 132.4, 131.4, 128.9, 128.4, 125.0, 117.9, 116.8, 84.9, 52.0, 47.0, 45.4, 28.0. HRMS (ESI) m/z calcd for $C_{24}H_{22}BrNO_4$ $[M + Na]^+$ = 490.0624, found:490.0625.



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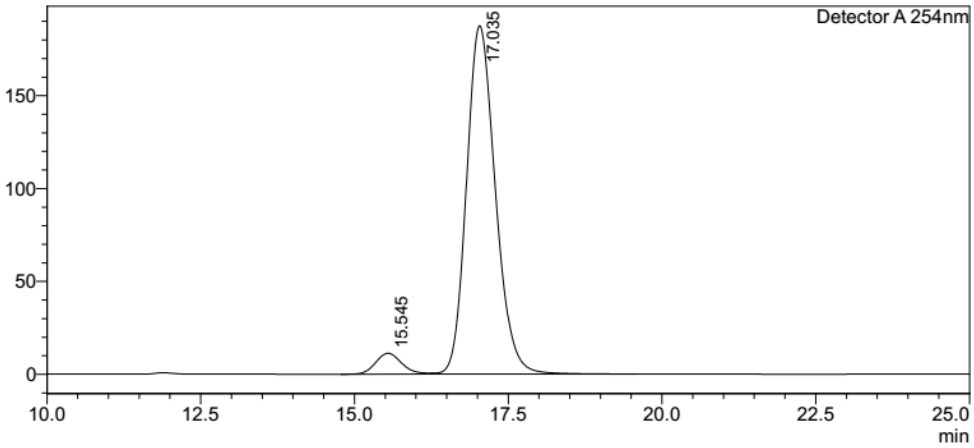
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.930	9250727	307599	50.032		M	
2	16.036	9238912	266388	49.968		M	
Total		18489639	573988				



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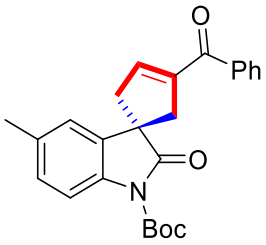
Detector A 254nm

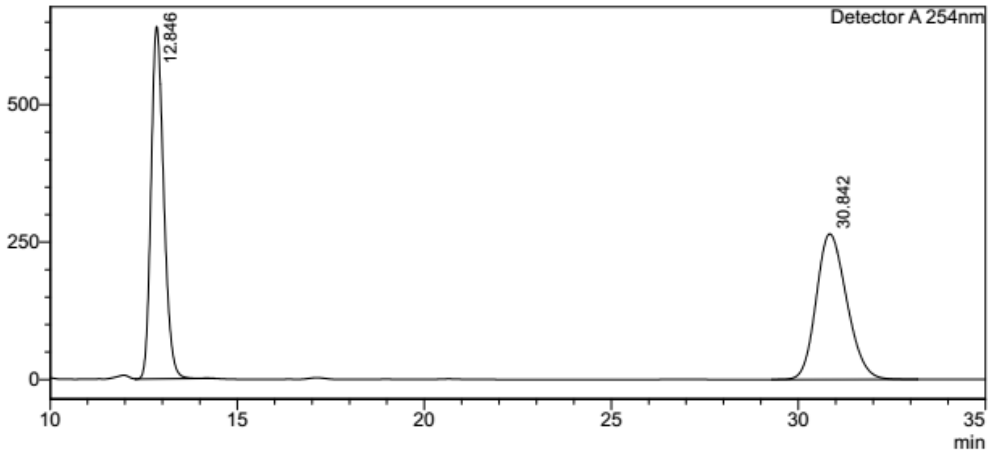
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	15.545	335019	11287	5.182			
2	17.035	6129529	187570	94.818		V	
Total		6464548	198857				

tert-Butyl (*R*)-3-benzoyl-5'-methyl-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3e**



According to general [4 + 1] annulation procedure, **3e** was obtained in 80% yield (32.3 mg) as a white solid and 92% *ee*. $[\alpha]_D^{25}$ = -5.1 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane =

20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 30.8 min, t_R (minor) = 12.9 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (m, 2H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.51 (m, 2H), 7.13 (d, *J* = 8.3 Hz, 1H), 7.10 (s, 1H), 6.60 (m, 1H), 3.45 (m, 1H), 3.38 (m, 1H), 3.15 (m, 1H), 2.94 (ddd, *J* = 18.9, 2.5, 1.4 Hz, 1H), 2.36 (s, 3H), 1.68 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.7, 179.5, 149.2, 145.5, 142.2, 142.1, 138.3, 136.0, 134.8, 134.4, 132.2, 129.0, 128.9, 128.3, 122.4, 114.8, 84.3, 52.1, 47.1, 45.4, 28.1, 21.0. HRMS (ESI) m/z calcd for $C_{25}H_{25}NO_4$ $[M + Na]^+$ = 426.1676, found:426.1680.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
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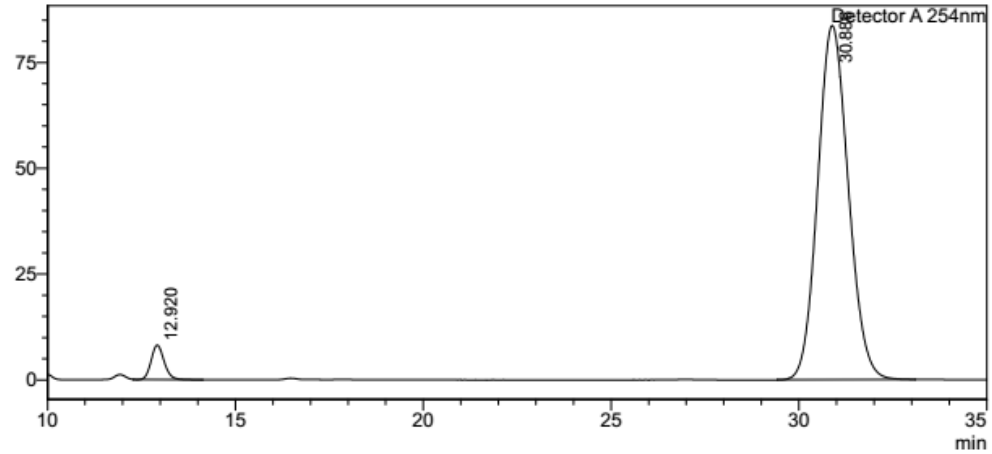
2	30.842	15044450	264817	49.936			
Total		30127643	905450				



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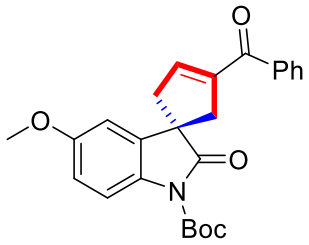
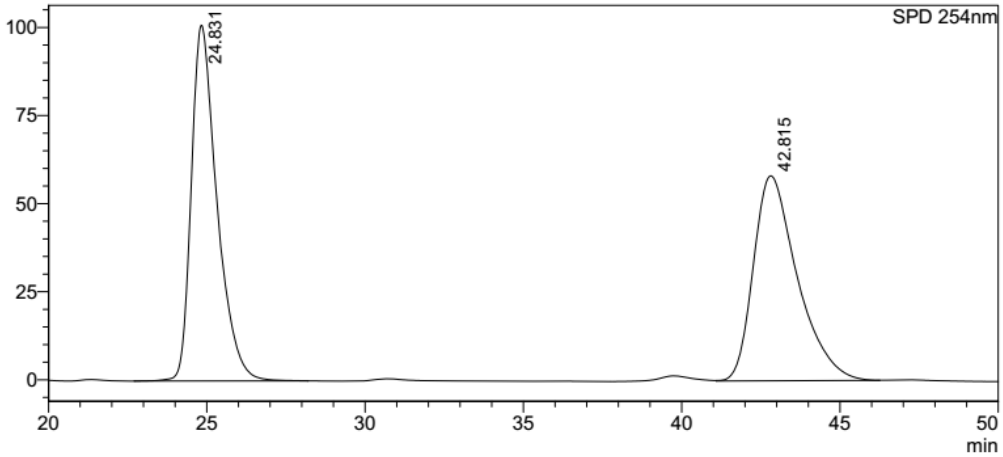
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.920	194425	8120	3.935		M	
2	30.886	4746039	83680	96.065			
Total		4940464	91800				

tert-Butyl (*R*)-3-benzoyl-5'-methoxy-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3f**



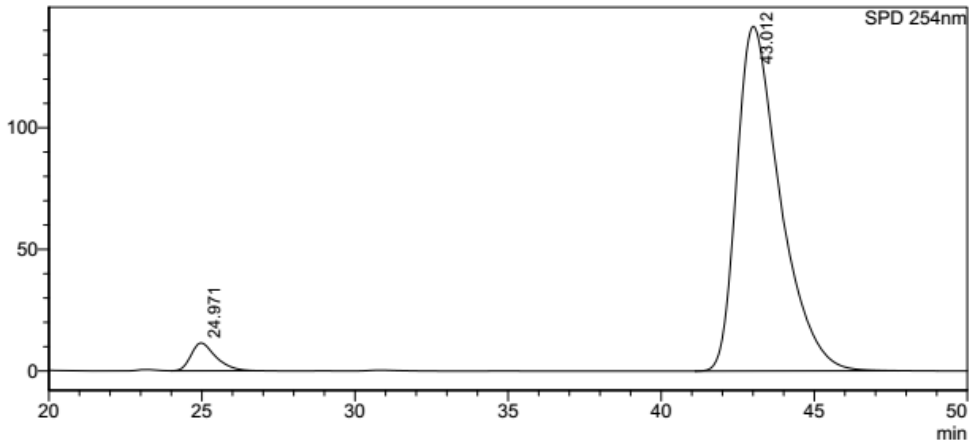
According to general [4 + 1] annulation procedure, **3f** was obtained in 95% yield (40 mg) as a white solid and 91% *ee*. $[\alpha]_D^{25}$ = 7.9 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 43.0 min, t_R (minor) = 24.9 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.58 (m, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 6.86 (s, 1H), 6.84 (d, *J* = 2.3 Hz, 1H), 6.59 (s, 1H), 3.82 (s, 3H), 3.47 (d, *J* = 16.8 Hz, 1H), 3.38 (d, *J* = 18.9 Hz, 1H), 3.15 (d, *J* = 16.8 Hz, 1H), 2.94 (d, *J* = 18.9 Hz, 1H), 1.68 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.6, 179.3, 157.3, 149.2, 142.1, 142.0, 138.3, 135.7, 132.3, 131.8, 128.9, 128.4, 116.0, 112.8, 108.3, 84.3, 55.7, 52.4, 47.1, 45.4, 28.1. HRMS (ESI) m/z calcd for $C_{25}H_{25}NO_5$ $[M + Na]^+$ = 442.1625, found:442.1638.



<Peak Table>

SPD 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	24.831	5699014	100962	50.430		S	
2	42.815	5601865	58147	49.570			
Total		11300879	159109				

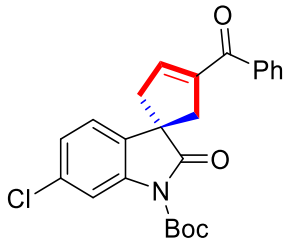


<Peak Table>

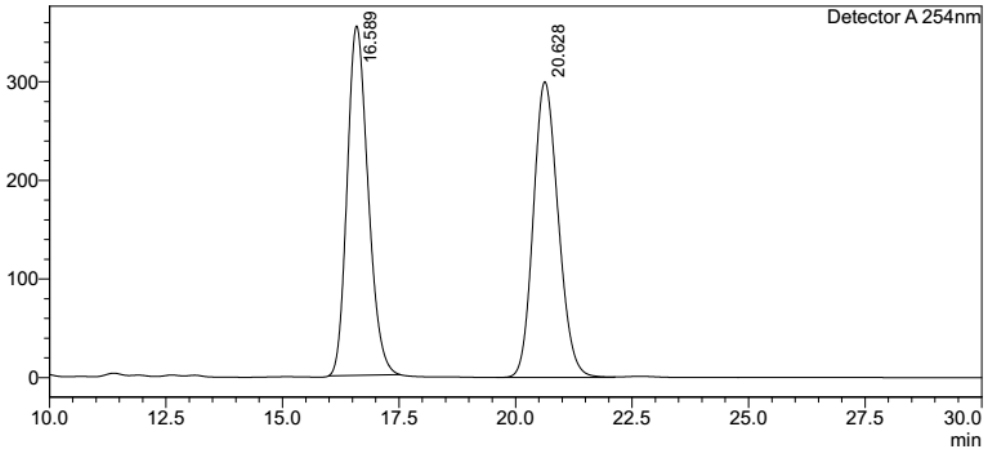
SPD 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	24.971	647404	11457	4.430			
2	43.012	13967672	141665	95.570			
Total		14615076	153121				

tert-Butyl (*R*)-3-benzoyl-6'-chloro-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3g**



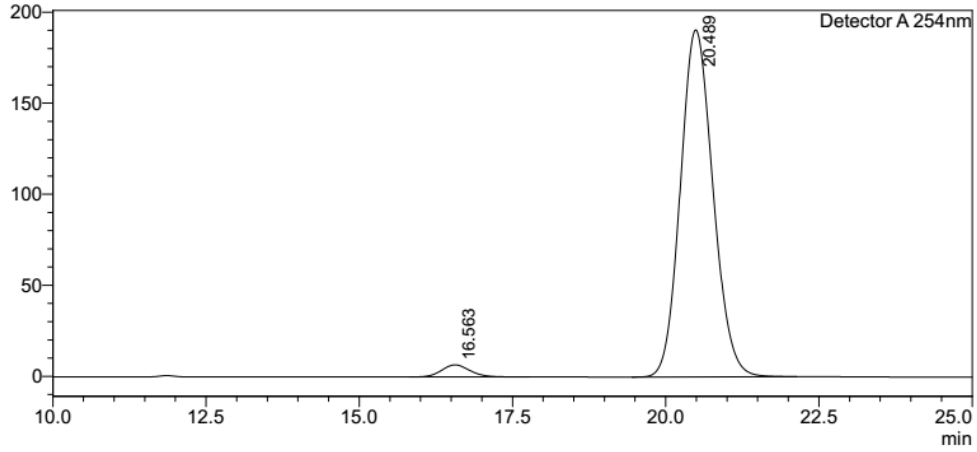
According to general [4 + 1] annulation procedure, **3g** was obtained in 95% yield (40.3 mg) as a white solid and 94% *ee*. $[\alpha]_D^{25}$ = 1.6 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 20.4 min, t_R (minor) = 16.5 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (m, 3H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.31 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.27 (d, *J* = 2.1 Hz, 1H), 6.59 (s, 1H), 3.47 (dd, *J* = 16.8, 2.1 Hz, 1H), 3.39 (dd, *J* = 18.9, 2.2 Hz, 1H), 3.14 (d, *J* = 16.8 Hz, 1H), 2.94 (d, *J* = 18.8 Hz, 1H), 1.68 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.4, 178.4, 149.0, 141.9, 141.8, 138.1, 137.0, 136.1, 132.4, 130.4, 128.9, 128.5, 128.4, 122.1, 116.4, 84.9, 52.1, 46.9, 45.3, 28.0. HRMS (ESI) m/z calcd for $C_{24}H_{22}ClNO_4$ $[M + Na]^+$ = 446.1130, found:446.1142.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.589	11056170	354263	49.738		M	
2	20.628	11172492	299887	50.262			
Total		22228662	654151				

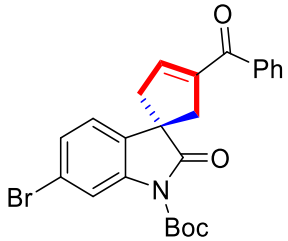


<Peak Table>

Detector A 254nm

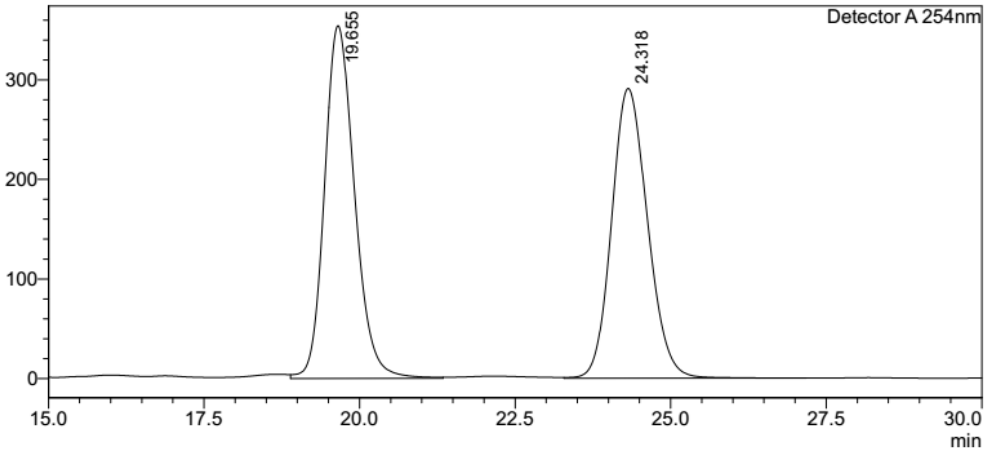
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.563	213530	6627	2.934		S	
2	20.489	7063702	190602	97.066			
Total		7277232	197229				

tert-Butyl (*R*)-3-benzoyl-6'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3h**



According to general [4 + 1] annulation procedure, **3h** was obtained in 85% yield (39.8 mg) as a white solid and 95% *ee*. $[\alpha]_D^{25}$ = 1.6 (c 1.0, $CHCl_3$). The *ee* was determined by

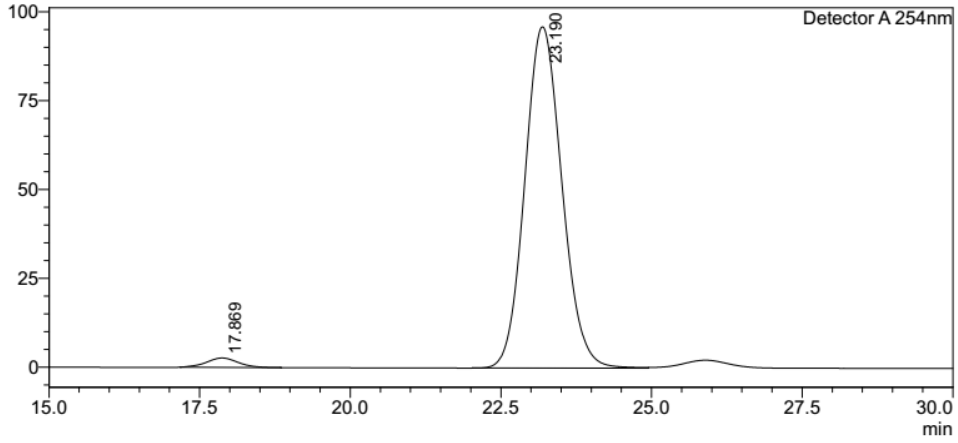
chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 30/70, 1.0 mL/min, λ = 254 nm, t_R (major) = 23.1 min, t_R (minor) = 17.8 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 1.7 Hz, 1H), 7.84 (m, 2H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.34 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 6.58 (m, 1H), 3.46 (m, 1H), 3.38 (dd, *J* = 18.9, 2.3 Hz, 1H), 3.12 (d, *J* = 16.8 Hz, 1H), 2.92 (d, *J* = 18.8 Hz, 1H), 1.69 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.5, 178.5, 148.9, 142.0, 141.7, 139.5, 138.1, 133.3, 132.4, 128.9, 128.4, 128.0, 123.0, 121.9, 118.6, 85.1, 51.9, 46.9, 45.3, 28.0. HRMS (ESI) m/z calcd for $C_{24}H_{22}BrNO_4$ $[M + Na]^+$ = 490.0624, found:490.0619.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	19.655	11942682	354378	50.517			
2	24.318	11698414	291137	49.483			
Total		23641096	645515				

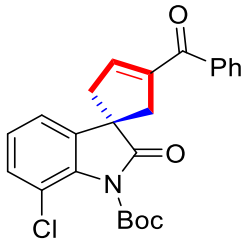


<Peak Table>

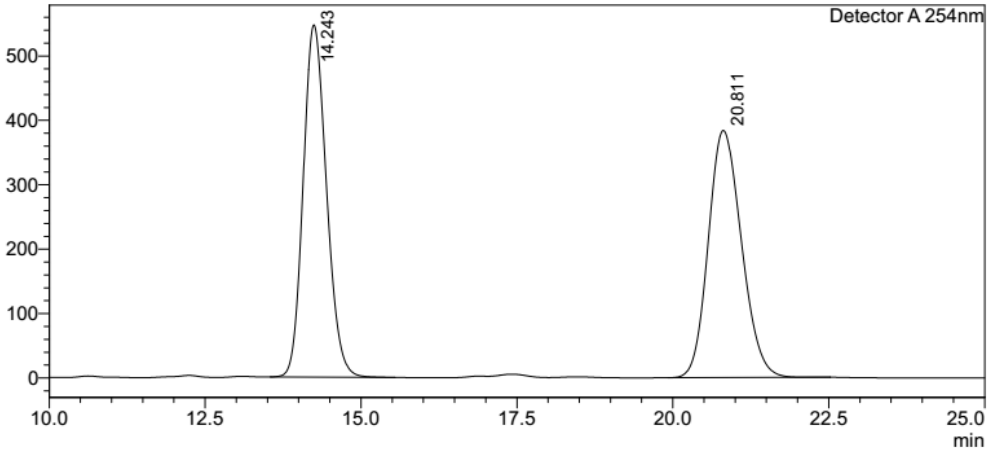
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	17.869	96323	2629	2.290		M	
2	23.190	4110597	96022	97.710			
Total		4206921	98651				

tert-Butyl (*R*)-3-benzoyl-7'-chloro-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3i**



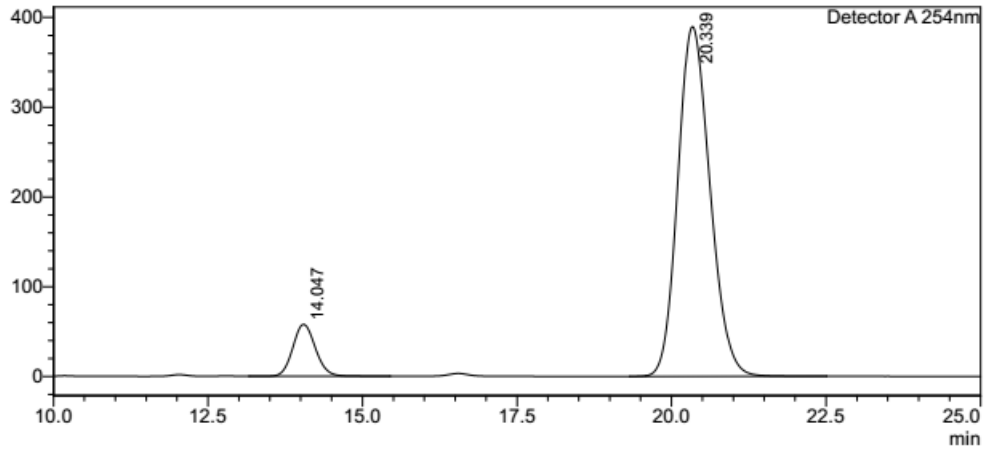
According to general [4 + 1] annulation procedure, **3i** was obtained in 80% yield (34 mg) as a white solid and 81% *ee*. $[\alpha]_D^{25}$ = -4.9 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 20.3 min, t_R (minor) = 14.0 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.4 Hz, 2H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.12 (t, *J* = 7.9 Hz, 1H), 6.59 (s, 1H), 3.47 (dd, *J* = 16.8, 2.1 Hz, 1H), 3.39 (dd, *J* = 18.9, 2.2 Hz, 1H), 3.16 (d, *J* = 18.1 Hz, 1H), 2.96 (d, *J* = 18.9 Hz, 1H), 1.68 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.5, 178.9, 148.1, 142.0, 142.0, 141.8, 138.1, 137.6, 137.5, 135.8, 132.4, 130.3, 130.1, 128.9, 128.4, 127.7, 125.6, 120.3, 118.3, 85.7, 52.6, 46.6, 44.9, 27.7. HRMS (ESI) m/z calcd for $C_{24}H_{22}ClNO_4$ $[M + Na]^+$ = 446.1130, found:446.1143.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.243	14201946	547026	49.989		M	
2	20.811	14208352	383743	50.011		M	
Total		28410298	930768				

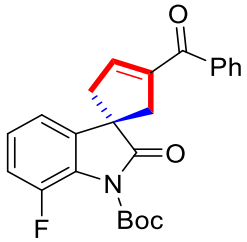


<Peak Table>

Detector A 254nm

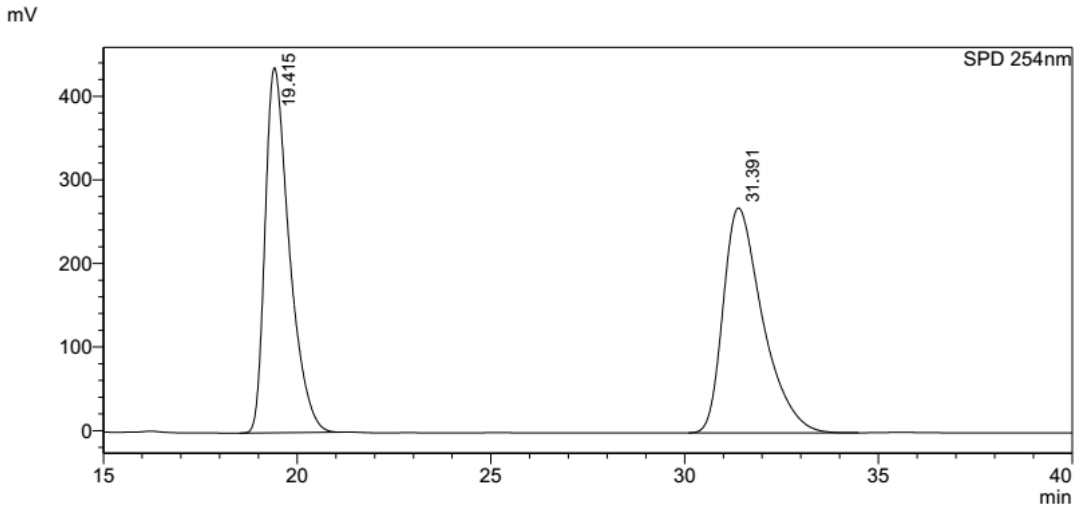
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.047	1474551	57821	9.456			
2	20.339	14118638	389651	90.544			
Total		15593188	447473				

tert-Butyl (*R*)-3-benzoyl-7'-fluoro-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3j**



According to general [4 + 1] annulation procedure, **3j** was obtained in 83% yield (33.8 mg) as a white solid and 76% *ee*. $[\alpha]_D^{25}$ = 13.6 (c 1.0, $CHCl_3$). The *ee* was determined

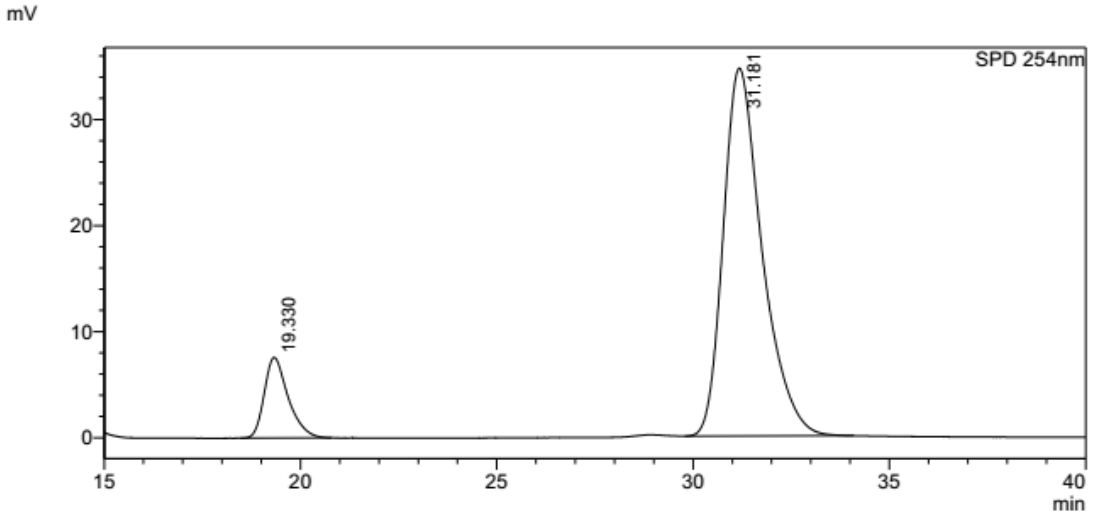
by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 31.1 min, t_R (minor) = 19.3 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (m, 2H), 7.59 (m, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.16 (m, 1H), 7.11 (m, 2H), 6.59 (s, 1H), 3.49 (dd, *J* = 16.8, 2.1 Hz, 1H), 3.41 (dd, *J* = 18.9, 2.1 Hz, 1H), 3.17 (dd, *J* = 16.9, 1.0 Hz, 1H), 2.96 (d, *J* = 18.9 Hz, 1H), 1.66 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.5, 178.4, 147.5, 142.0, 141.7, 138.2, 137.6, 132.4, 128.9, 128.4, 126.1, 126.2, 117.6, 116.8, 116.6, 85.2, 52.6, 46.9, 45.3, 27.7. HRMS (ESI) m/z calcd for $C_{24}H_{22}FNO_4$ $[M + Na]^+$ = 430.1425, found:430.1421.



<Peak Table>

SPD 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	19.415	18947056	436517	49.854		M	
2	31.391	19058149	268882	50.146		M	
Total		38005205	705399				

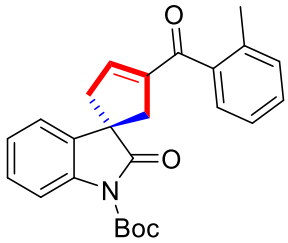


<Peak Table>

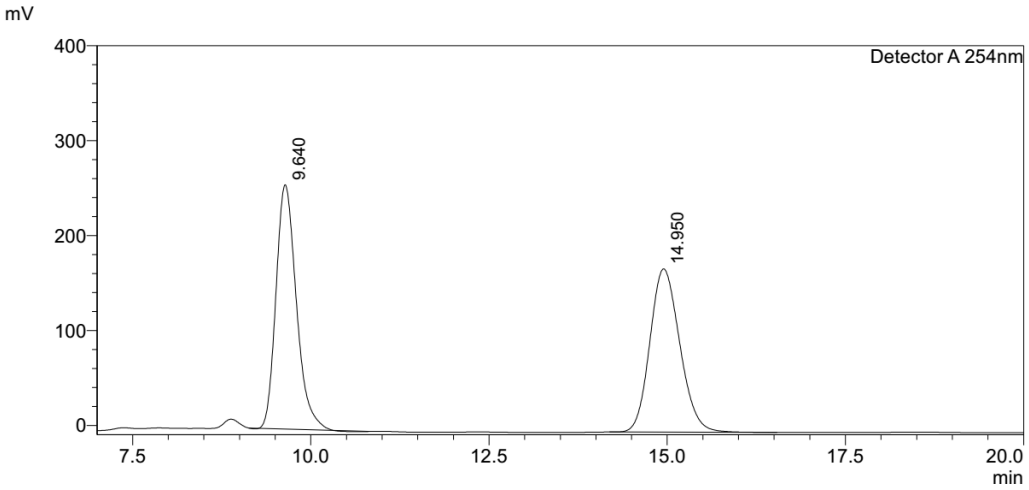
SPD 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	19.330	321973	7594	11.889			
2	31.181	2386120	34688	88.111		S	
Total		2708092	42282				

tert-Butyl (*R*)-3-(2-methylbenzoyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3k**



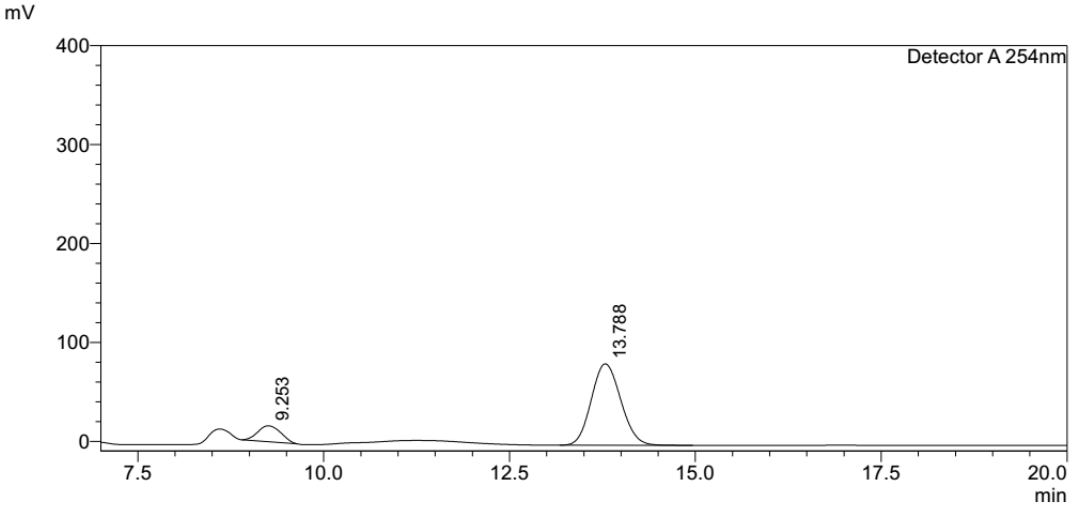
According to general [4 + 1] annulation procedure, **3k** was obtained in 85% yield (34.3 mg) as a white solid and 67% *ee*. $[\alpha]_D^{25}$ = 13.6 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 20/80, 1.0 mL/min, λ = 254 nm, t_R (major) = 13.7 min, t_R (minor) = 9.2 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.2 Hz, 1H), 7.44 (d, *J* = 7.4 Hz, 1H), 7.35 (m, 3H), 7.27 (t, *J* = 5.7 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 6.43 (s, 1H), 3.44 (dd, *J* = 16.8, 2.2 Hz, 1H), 3.33 (dd, *J* = 19.1, 2.3 Hz, 1H), 3.11 (dd, *J* = 16.8, 1.1 Hz, 1H), 2.89 (d, *J* = 19.1 Hz, 1H), 2.42 (s, 3H), 1.69 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.2, 179.2, 149.1, 144.3, 143.9, 138.9, 138.4, 136.2, 134.5, 131.0, 130.1, 128.4, 128.0, 128.0, 125.1, 124.2, 121.7, 115.1, 84.6, 52.3, 46.9, 44.4, 28.1, 19.8. HRMS (ESI) m/z calcd for $C_{25}H_{25}NO_4$ $[M + Na]^+$ = 426.1676, found:426.1682.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.640	5107919	257445	50.432		M	
2	14.950	5020385	172065	49.568		M	
Total		10128304	429511				

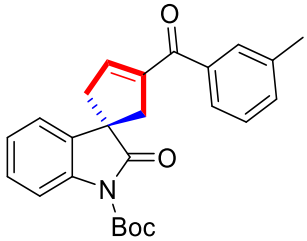


<Peak Table>

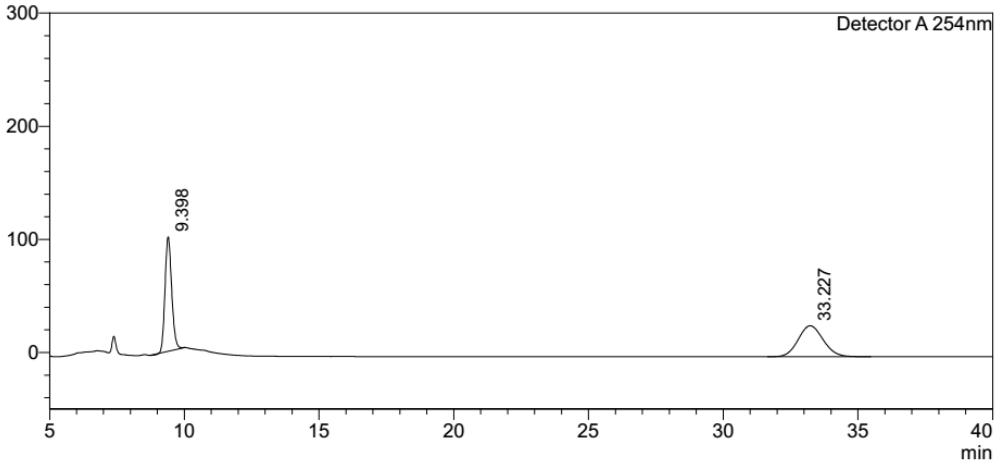
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.253	348782	16149	13.276		M	
2	13.788	2278465	82370	86.724		M	
Total		2627247	98519				

tert-Butyl (*R*)-3-(3-methylbenzoyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3l**



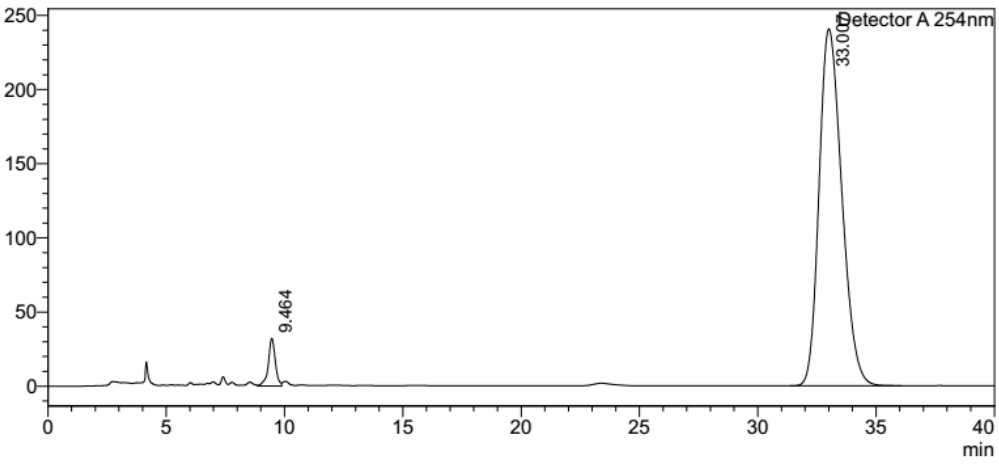
According to general [4 + 1] annulation procedure, **3l** was obtained in 95% yield (38.3 mg) as a white solid and 92% *ee*. $[\alpha]_D^{25}$ = 13.6 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 30/70, 1.0 mL/min, λ = 254 nm, t_R (major) = 33.0 min, t_R (minor) = 9.4 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (m, 2H), 7.59 (m, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.16 (m, 1H), 7.11 (m, 2H), 6.59 (s, 1H), 3.49 (dd, *J* = 16.8, 2.1 Hz, 1H), 3.41 (dd, *J* = 18.9, 2.1 Hz, 1H), 3.17 (dd, *J* = 16.9, 1.0 Hz, 1H), 2.96 (d, *J* = 18.9 Hz, 1H), 1.66 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.8, 179.2, 149.2, 142.2, 141.8, 138.4, 138.2, 134.5, 133.0, 129.3, 128.4, 128.1, 126.2, 125.0, 121.8, 115.0, 84.5, 52.1, 47.0, 45.4, 28.1, 21.3. HRMS (ESI) m/z calcd for $C_{25}H_{25}NO_4$ $[M + Na]^+$ = 426.1676, found:426.1672.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.398	1738212	101131	49.573		M	
2	33.227	1768154	27374	50.427			
Total		3506365	128504				

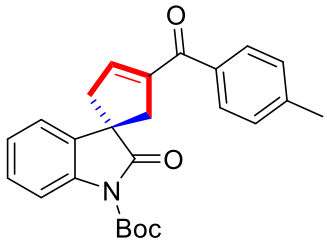


<Peak Table>

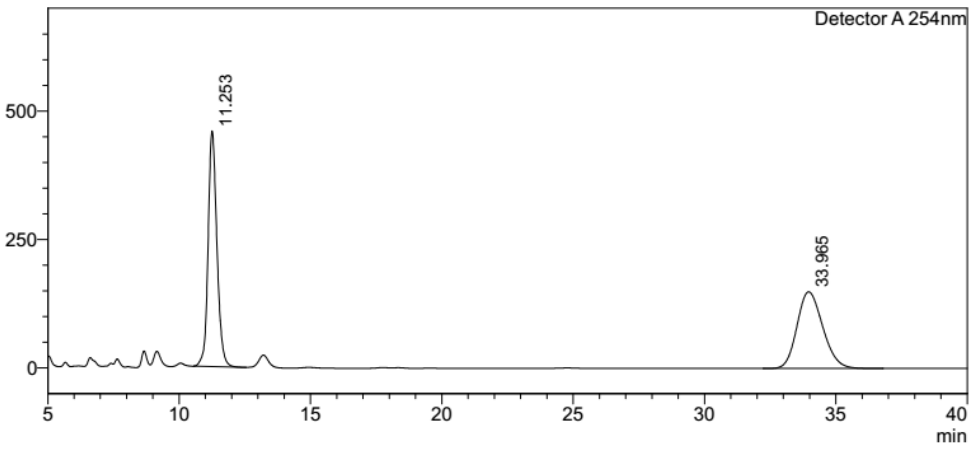
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.464	659442	32166	3.942			
2	33.007	16067158	240700	96.058		S	
Total		16726600	272866				

tert-Butyl (*R*)-3-(4-methylbenzoyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3m**



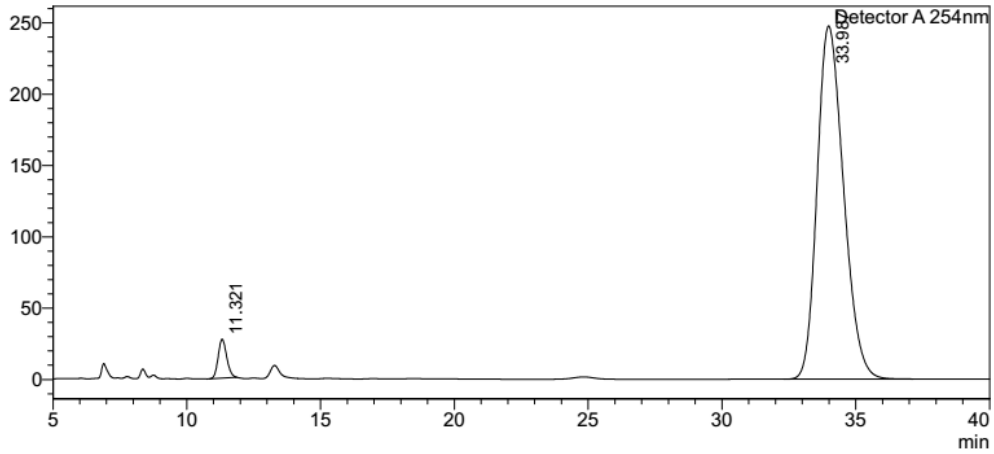
According to general [4 + 1] annulation procedure, **3m** was obtained in 95% yield (38.3 mg) as a white solid and 93% *ee*. $[\alpha]_D^{25}$ = - 0.8 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 30/70, 1.0 mL/min, λ = 254 nm, t_R (major) = 33.9 min, t_R (minor) = 11.3 min]. ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.32 (m, 4H), 7.20 (m, 1H), 6.57 (m, 1H), 3.46 (m, 1H), 3.38 (dt, *J* = 4.7, 2.3 Hz, 1H), 3.14 (m, 1H), 2.94 (m, 1H), 2.46 (s, 3H), 1.69 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.3, 179.3, 149.2, 143.0, 142.1, 141.3, 138.4, 135.6, 134.5, 129.2, 129.0, 128.4, 125.1, 121.8, 115.0, 84.5, 52.1, 47.0, 45.5, 28.1, 21.6. HRMS (ESI) m/z calcd for $C_{25}H_{25}NO_4$ $[M + Na]^+$ = 426.1676, found:426.1682.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.253	10693222	458798	51.262		M	
2	33.965	10166892	149206	48.738			
Total		20860114	608004				

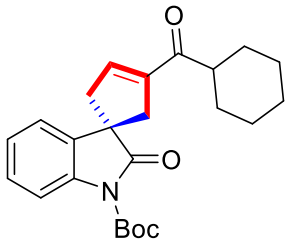


<Peak Table>

Detector A 254nm

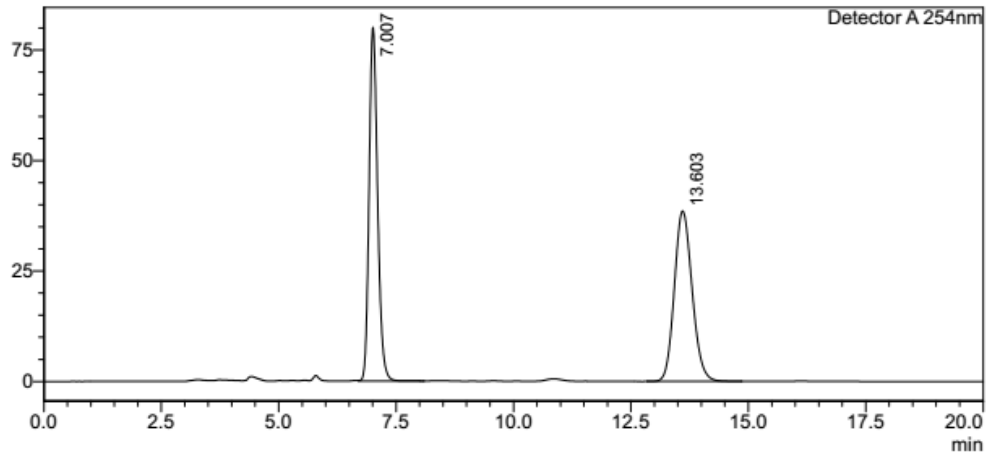
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.321	604308	27271	3.431		M	
2	33.987	17008244	247566	96.569			
Total		17612552	274838				

tert-Butyl (*R*)-3-(cyclohexanecarbonyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3n**



According to general [4 + 1] annulation procedure, **3n** was obtained in 96% yield (38 mg) as a white solid and 94% *ee*. $[\alpha]_D^{25}$ = - 0.8 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane =

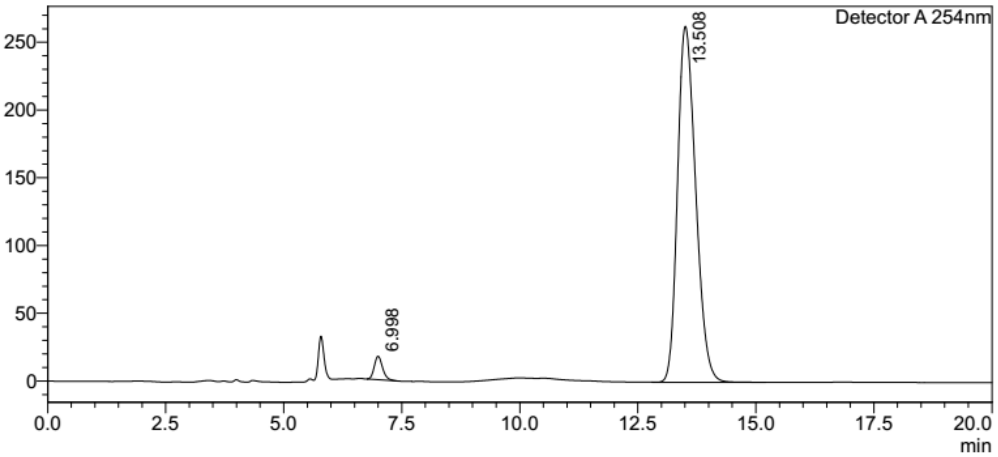
30/70, 1.0 mL/min, λ = 254 nm, t_R (major) = 13.5 min, t_R (minor) = 6.9 min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 1H), 7.31 (m, 1H), 7.21 (m, 1H), 7.15 (m, 1H), 6.77 (d, *J* = 2.2 Hz, 1H), 3.30 (m, 2H), 2.93 (m, 3H), 1.86 (d, *J* = 12.6 Hz, 4H), 1.74 (dd, *J* = 22.1, 8.3 Hz, 1H), 1.67 (s, 9H), 1.46 (m, 2H), 1.33 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.4, 179.3, 149.2, 142.3, 138.5, 138.3, 134.7, 128.3, 125.0, 121.6, 115.0, 84.5, 52.1, 46.9, 46.7, 44.7, 29.5, 29.3, 28.1, 25.8, 25.7. HRMS (ESI) m/z calcd for $C_{24}H_{29}NO_4$ $[M + Na]^+$ = 418.1989, found:418.1993.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.007	1014090	80073	49.945		S	
2	13.603	1016320	38563	50.055			
Total		2030410	118636				

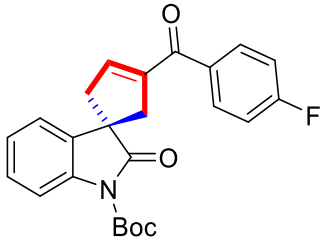


<Peak Table>

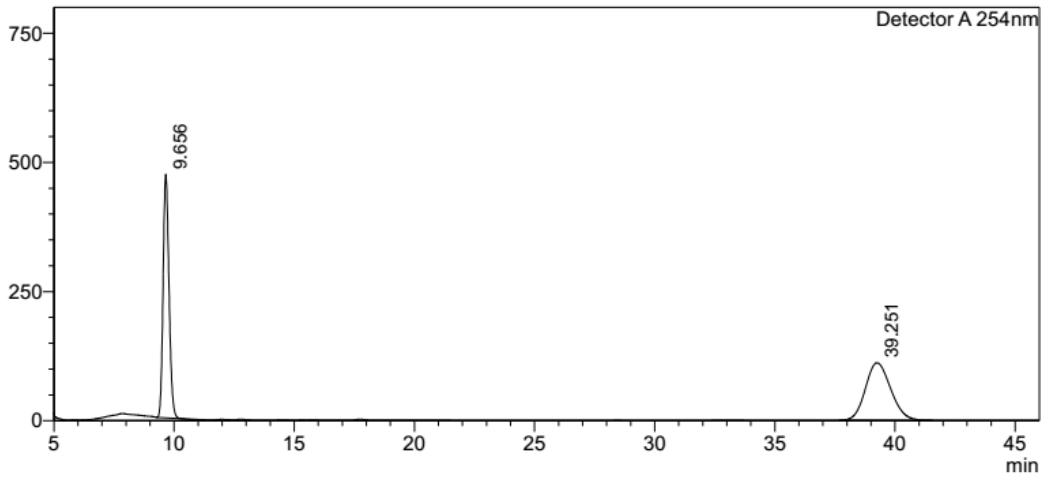
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.998	213198	17321	2.939		M	
2	13.508	7041444	262724	97.061			
Total		7254642	280044				

tert-Butyl (*R*)-3-(4-fluorobenzoyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3o**



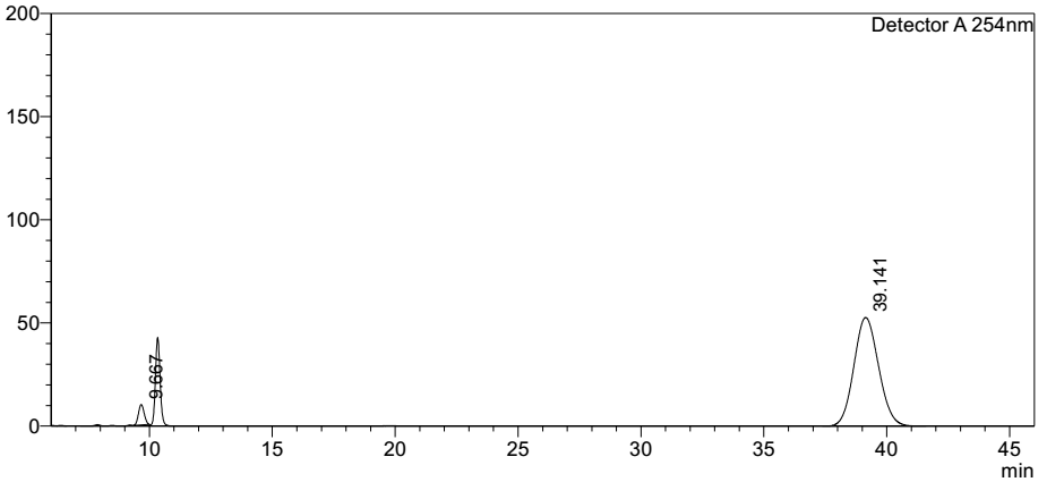
According to general [4 + 1] annulation procedure, **3o** was obtained in 94% yield (38.3 mg) as a white solid and 92% *ee*. $[\alpha]_D^{25}$ = - 0.8 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 30/70, 1.0 mL/min, λ = 254 nm, t_R (major) = 39.1 min, t_R (minor) = 9.6 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (m, 3H), 7.30 (m, 2H), 7.17 (m, 3H), 6.54 (m, 1H), 3.42 (m, 1H), 3.36 (dd, *J* = 18.8, 2.3 Hz, 1H), 3.12 (m, 1H), 2.94 (m, 1H), 1.66 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.1, 179.2, 166.6, 164.0, 149.1, 141.9, 141.8, 138.5, 134.4, 134.5, 134.2, 131.6, 131.5, 128.5, 125.1, 121.8, 115.6, 115.4, 115.1, 84.6, 52.1, 47.0, 45.4, 28.1. HRMS (ESI) m/z calcd for $C_{24}H_{22}FNO_4$ $[M + Na]^+$ = 430.1425, found:430.1429.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.656	8007526	471018	49.703		M	
2	39.251	8103186	111226	50.297		M	
Total		16110712	582244				

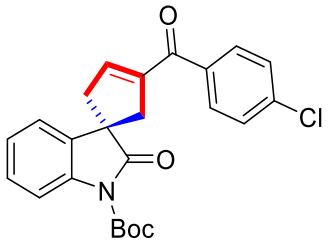


<Peak Table>

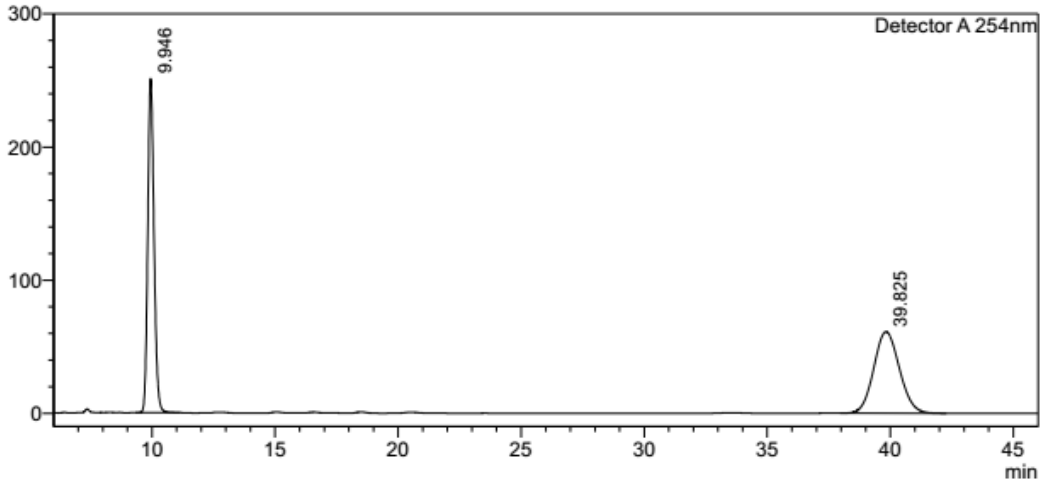
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.667	159385	9882	4.128		M	
2	39.141	3701814	52739	95.872			
Total		3861199	62621				

tert-Butyl (*R*)-3-(4-chlorobenzoyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3p**



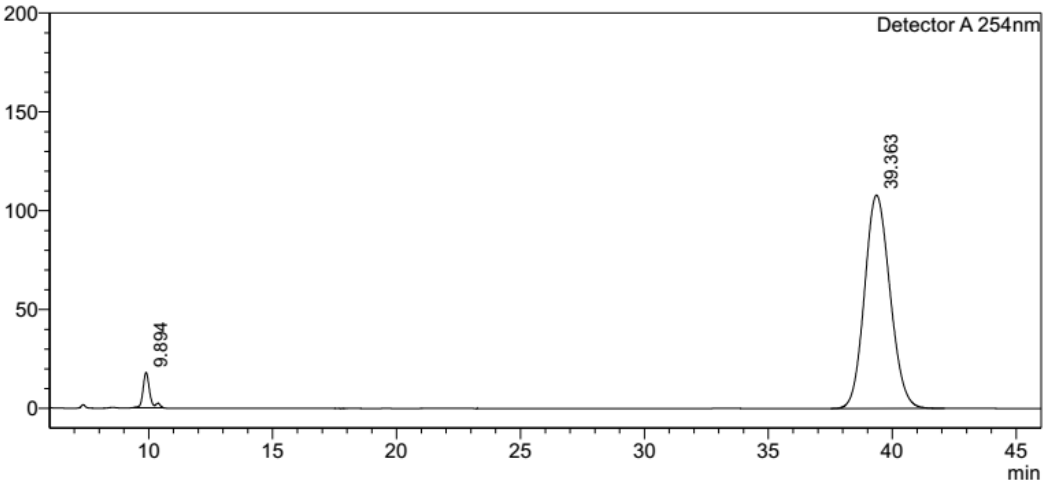
According to general [4 + 1] annulation procedure, **3p** was obtained in 95% yield (40.3 mg) as a white solid and 91% *ee*. $[\alpha]_D^{25}$ = - 0.8 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 30/70, 1.0 mL/min, λ = 254 nm, t_R (major) = 39.3 min, t_R (minor) = 9.9 min]. ^{1}H NMR (400 MHz, CDCl3) δ 7.77 (d, *J* = 8.1 Hz, 1H), 7.71 (m, 2H), 7.39 (m, 2H), 7.24 (m, 2H), 7.19 (s, 1H), 7.10 (m, 1H), 6.48 (m, 1H), 3.32 (m, 2H), 3.04 (m, 1H), 2.86 (m, 1H), 1.59 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 191.3, 179.2, 149.1, 142.2, 141.9, 138.7, 138.5, 136.5, 134.2, 130.4, 128.7, 128.5, 125.1, 121.8, 115.1, 84.6, 52.0, 47.0, 45.3, 29.7, 28.1. HRMS (ESI) m/z calcd for $C_{24}H_{22}ClNO_4$ $[M + Na]^+$ = 446.1130, found:446.1131.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.946	4430214	250699	49.923		M	
2	39.825	4443849	61256	50.077			
Total		8874063	311955				

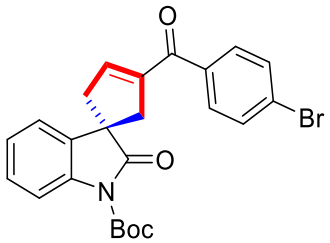


<Peak Table>

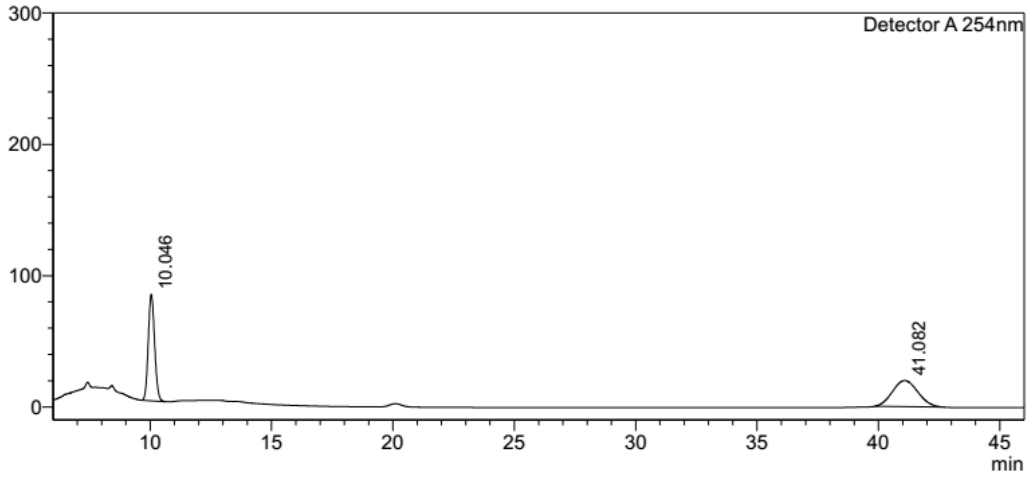
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.894	341811	17855	4.244		M	
2	39.363	7712527	107919	95.756			
Total		8054339	125774				

tert-Butyl (*R*)-3-(4-bromobenzoyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-3-ene-1'-carboxylate **3q**



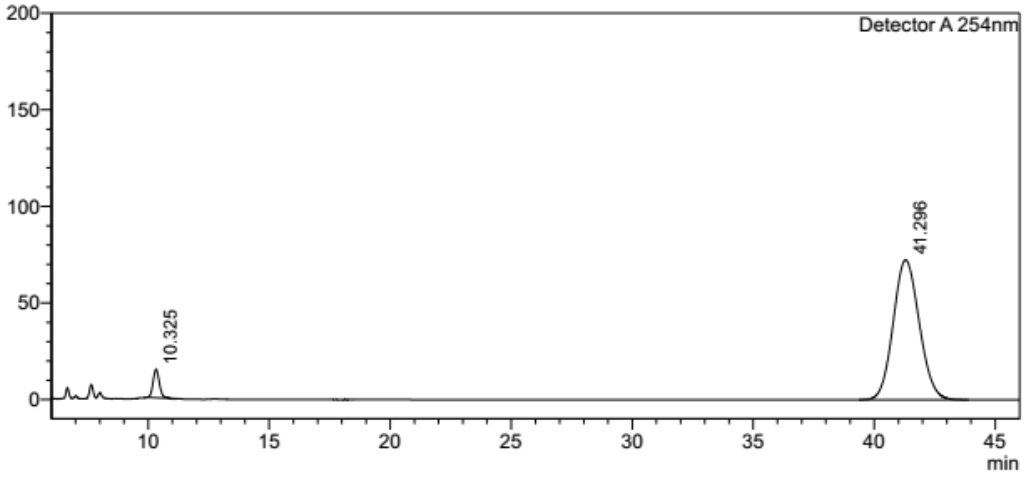
According to general [4 + 1] annulation procedure, **3q** was obtained in 93% yield (43.6 mg) as a white solid and 91% *ee*. $[\alpha]_D^{25}$ = - 0.8 (c 1.0, $CHCl_3$). The *ee* was determined by chiral stationary phase HPLC analysis [Daicel Chiralpak IC, isopropanol/hexane = 30/70, 1.0 mL/min, λ = 254 nm, t_R (major) = 41.2 min, t_R (minor) = 10.3 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.1 Hz, 1H), 7.64 (m, 2H), 7.55 (m, 2H), 7.24 (m, 2H), 7.19 (s, 1H), 7.10 (m, 1H), 6.48 (m, 1H), 3.32 (m, 2H), 3.04 (m, 1H), 2.86 (m, 1H), 1.59 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.5, 179.2, 149.1, 142.3, 141.9, 138.5, 136.9, 134.2, 131.7, 130.5, 128.5, 127.3, 125.1, 121.8, 115.1, 84.6, 52.0, 47.0, 45.3, 28.1. HRMS (ESI) m/z calcd for $C_{24}H_{22}BrO_4$ $[M + Na]^+$ = 490.0624, found:490.0621.



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.046	1467745	81015	50.415		M	
2	41.082	1443587	19894	49.585		M	
Total		2911332	100909				

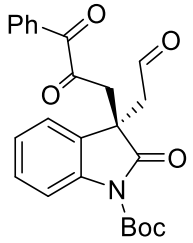


<Peak Table>

Detector A 254nm

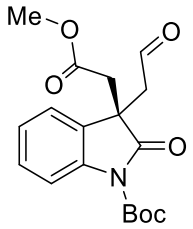
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.325	261536	14662	4.596		M	
2	41.296	5428835	72377	95.404			
Total		5690371	87038				

tert-Butyl (*R*)-3-(2,3-dioxo-3-phenylpropyl)-2-oxo-3-(2-oxoethyl)indoline-1-carboxylate **4**



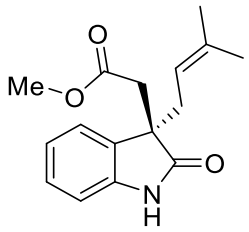
According to the procedure showed above, **4** was obtained in 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.76 (m, 2H), 7.58 (dd, *J* = 10.6, 4.3 Hz, 1H), 7.40 (m, 2H), 7.29 (m, 2H), 7.11 (m, 1H), 3.94 (d, *J* = 18.1 Hz, 1H), 3.42 (d, *J* = 18.0 Hz, 1H), 3.19 (dd, *J* = 17.6, 1.3 Hz, 1H), 3.03 (d, *J* = 17.7 Hz, 1H), 1.67 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 197.2, 189.8, 177.0, 149.0, 140.3, 134.7, 131.3, 130.3, 129.1, 128.7, 128.6, 124.6, 122.9, 115.6, 84.6, 50.5, 46.7, 44.9, 28.1. HRMS (ESI) m/z calcd for $C_{24}H_{23}NO_6$ $[M + Na]^+$ = 444.1418, found:444.1451.

tert-Butyl (*R*)-3-(2-methoxy-2-oxoethyl)-2-oxo-3-(2-oxoethyl)indoline-1-carboxylate **5**



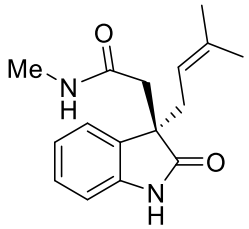
According to the procedure showed above, **5** was obtained in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (d, *J* = 1.1 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.24 (m, 1H), 7.17 (m, 1H), 7.04 (td, *J* = 7.5, 1.0 Hz, 1H), 3.43 (s, 3H), 3.14 (dd, *J* = 17.8, 1.4 Hz, 1H), 2.95 (m, 1H), 2.88 (m, 2H), 1.58 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4, 176.9, 169.4, 149.1, 140.2, 128.9, 128.7, 124.4, 122.8, 115.4, 84.4, 51.8, 50.2, 46.8, 41.3, 28.1. HRMS (ESI) m/z calcd for $C_{18}H_{21}NO_6$ $[M + Na]^+$ = 370.1216, found:370.1220.

Methyl (*R*)-2-(3-(3-methylbut-2-en-1-yl)-2-oxoindolin-3-yl)acetate **6**



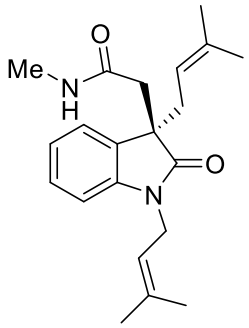
According to the procedure showed above, **6** was obtained in 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.10 (ddd, *J* = 12.3, 9.4, 4.3 Hz, 2H), 6.90 (td, *J* = 7.5, 0.9 Hz, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 4.87 (m, 1H), 3.37 (s, 3H), 2.97 (d, *J* = 16.3 Hz, 1H), 2.85 (d, *J* = 16.3 Hz, 1H), 2.39 (ddd, *J* = 33.8, 14.0, 7.6 Hz, 2H), 1.53 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.7, 170.5, 141.3, 136.3, 131.5, 128.0, 123.1, 121.9, 116.9, 109.8, 51.5, 50.3, 39.7, 36.3, 29.6, 25.8, 17.9. HRMS (ESI) m/z calcd for $C_{16}H_{19}NO_3$ $[M + Na]^+$ = 296.1257, found:296.1260.

(*R*)-*N*-Methyl-2-(3-(3-methylbut-2-en-1-yl)-2-oxoindolin-3-yl)acetamide **7**



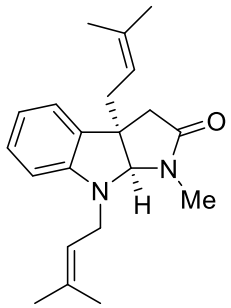
According to the procedure showed above, **7** was obtained in 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.10 (ddd, *J* = 8.9, 6.0, 2.2 Hz, 2H), 6.92 (td, *J* = 7.6, 1.0 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.20 (d, *J* = 4.3 Hz, 1H), 4.82 (m, 1H), 2.79 (d, *J* = 14.9 Hz, 1H), 2.66 (d, *J* = 14.9 Hz, 1H), 2.56 (d, *J* = 4.8 Hz, 3H), 2.45 (m, 2H), 1.51 (s, 3H), 1.41 (d, *J* = 0.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.1, 169.9, 140.9, 136.0, 132.0, 127.9, 123.4, 122.2, 117.0, 109.9, 51.0, 42.2, 36.0, 26.2, 25.8, 17.9. HRMS (ESI) m/z calcd for $C_{16}H_{20}N_2O_2$ $[M + Na]^+$ = 295.1417, found:295.1421.

(*R*)-2-(1,3-Bis(3-methylbut-2-en-1-yl)-2-oxoindolin-3-yl)-N-methylacetamide **8**



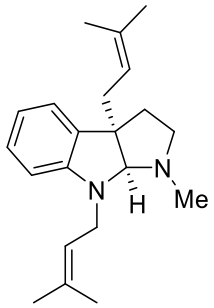
According to the procedure showed above, **8** was obtained in 88% yield. $[\alpha]_D^{25}$ = 32 (c 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (m, 2H), 7.01 (td, *J* = 7.7, 1.0 Hz, 1H), 6.76 (d, *J* = 7.7 Hz, 1H), 6.46 (d, *J* = 3.9 Hz, 1H), 5.06 (m, 1H), 4.74 (m, 1H), 4.39 (dd, *J* = 15.5, 6.4 Hz, 1H), 4.20 (dd, *J* = 15.5, 6.7 Hz, 1H), 2.93 (s, 1H), 2.86 (d, *J* = 0.4 Hz, 1H), 2.73 (dd, *J* = 43.4, 14.7 Hz, 2H), 2.62 (d, *J* = 4.8 Hz, 3H), 2.50 (d, *J* = 7.6 Hz, 2H), 1.80 (s, 3H), 1.69 (d, *J* = 1.1 Hz, 3H), 1.52 (d, *J* = 0.7 Hz, 3H), 1.43 (d, *J* = 0.7 Hz, 3H). HRMS (ESI) m/z calcd for $C_{21}H_{28}N_2O_2$ $[M + Na]^+$ = 363.2043, found:363.2050. HNMR is identical to the literature report.[4]

(3a*R*,8a*S*)-1-Methyl-3a,8-bis(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-*b*] indol-2(1H)-one **9**



According to the procedure showed above, the cyclization product was obtained in 94% yield. ^{1}H NMR (500 MHz, CD_3OD) δ 7.10 (m, 2H), 6.76 (td, *J* = 7.4, 0.9 Hz, 1H), 6.60 (d, *J* = 7.9 Hz, 1H), 5.29 (m, 1H), 5.03 (m, 1H), 4.02 (ddd, *J* = 55.6, 15.7, 6.8 Hz, 2H), 2.88 (s, 3H), 2.69 (dt, *J* = 40.6, 9.0 Hz, 2H), 2.47 (dd, *J* = 14.4, 8.4 Hz, 1H), 2.39 (dd, *J* = 14.4, 6.6 Hz, 1H), 1.77 (m, 6H), 1.71 (s, 3H), 1.57 (s, 3H). HRMS (ESI) m/z calcd for $C_{21}H_{28}N_2O$ $[M + Na]^+$ = 347.2094, found:347.2097. HNMR is identical to the literature report.[4]

(+)-Debromoflustramine B

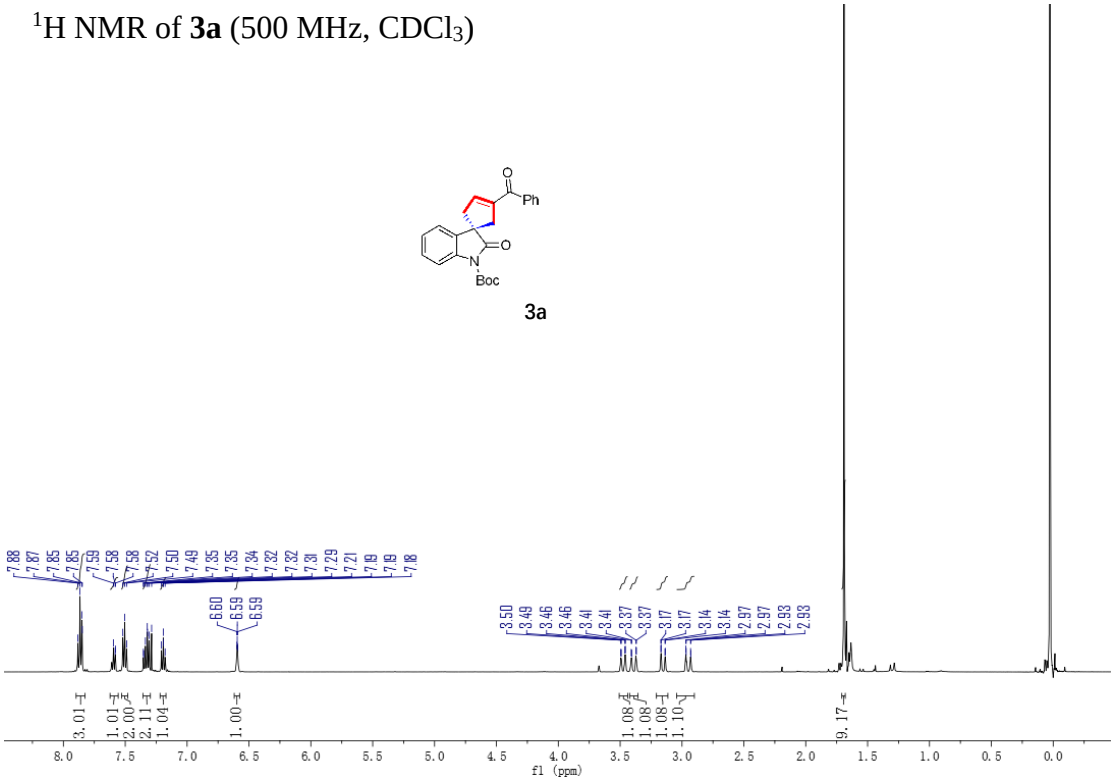


According to the procedure showed above, the reduction product was obtained in 91% yield. $[\alpha]_D^{25}$ = 56 (c 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (m, 1H), 6.90 (dd, *J* = 7.3, 1.0 Hz, 1H), 6.58 (td, *J* = 7.4, 1.0 Hz, 1H), 6.34 (d, *J* = 7.8 Hz, 1H), 5.10 (tdd, *J* = 5.7, 2.8, 1.4 Hz, 1H), 4.90 (m, 1H), 4.19 (s, 1H), 3.85 (dd, *J* = 16.1, 5.7 Hz, 1H), 3.73 (dd, *J* = 16.1, 7.2 Hz, 1H), 2.60 (ddd, *J* = 10.0, 6.7, 3.4 Hz, 1H), 2.49 (td, *J* = 9.2, 5.8 Hz, 1H), 2.41 (s, 3H), 2.35 (d, *J* = 7.1 Hz, 2H), 1.99 (m, 1H), 1.85 (m, 1H), 1.63

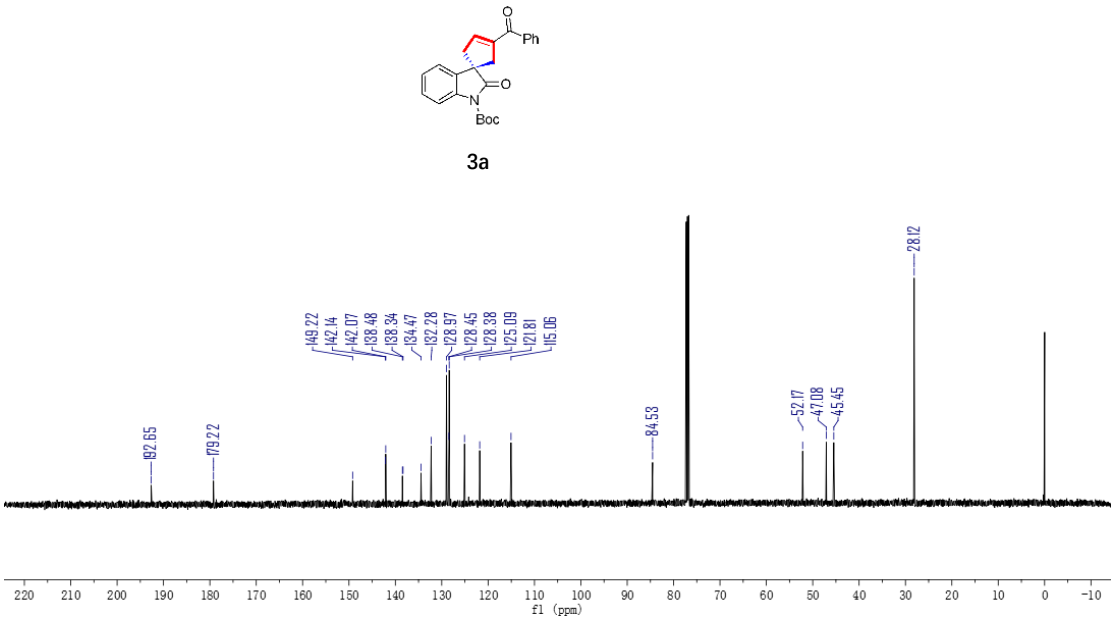
(m, 6H), 1.58 (d, *J* = 1.0 Hz, 3H), 1.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 135.6, 134.3, 133.7, 127.6, 122.9, 121.5, 120.7, 117.6, 107.5, 91.3, 57.1, 52.8, 46.9, 39.0, 38.4, 37.8, 26.0, 25.8, 18.2, 18.1. HRMS (ESI) m/z calcd for $C_{21}H_{30}N_2$ $[M + Na]^+$ = 333.2301, found:333.2308. HNMR is identical to the literature report.[4]

E. ^{1}H and ^{13}C NMR spectra

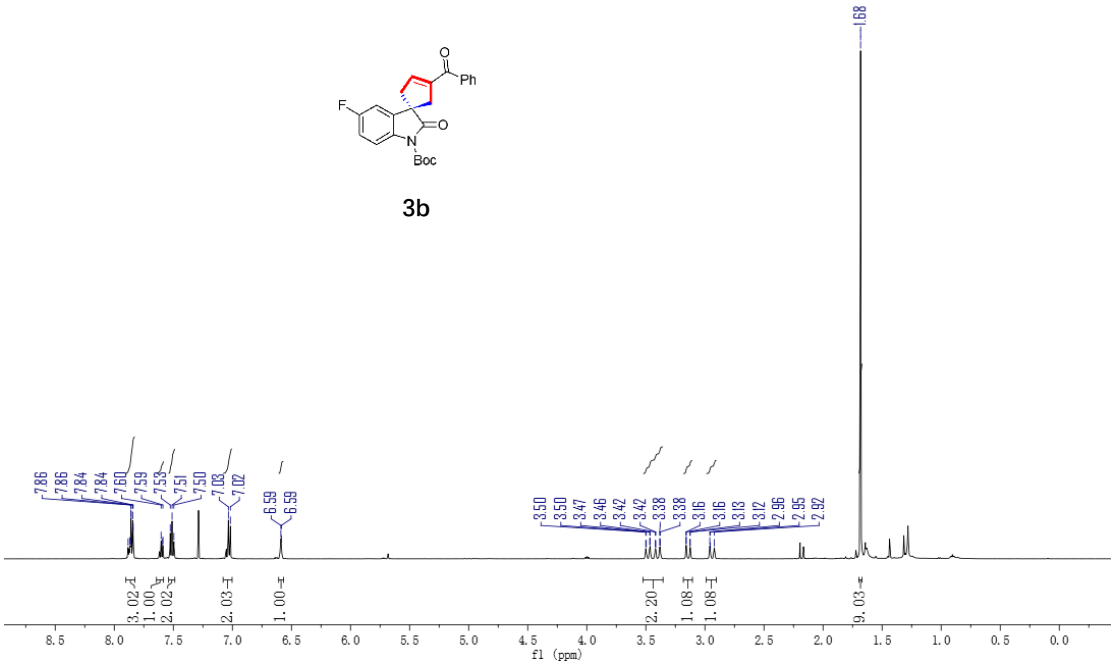
^{1}H NMR of **3a** (500 MHz, $CDCl_3$)



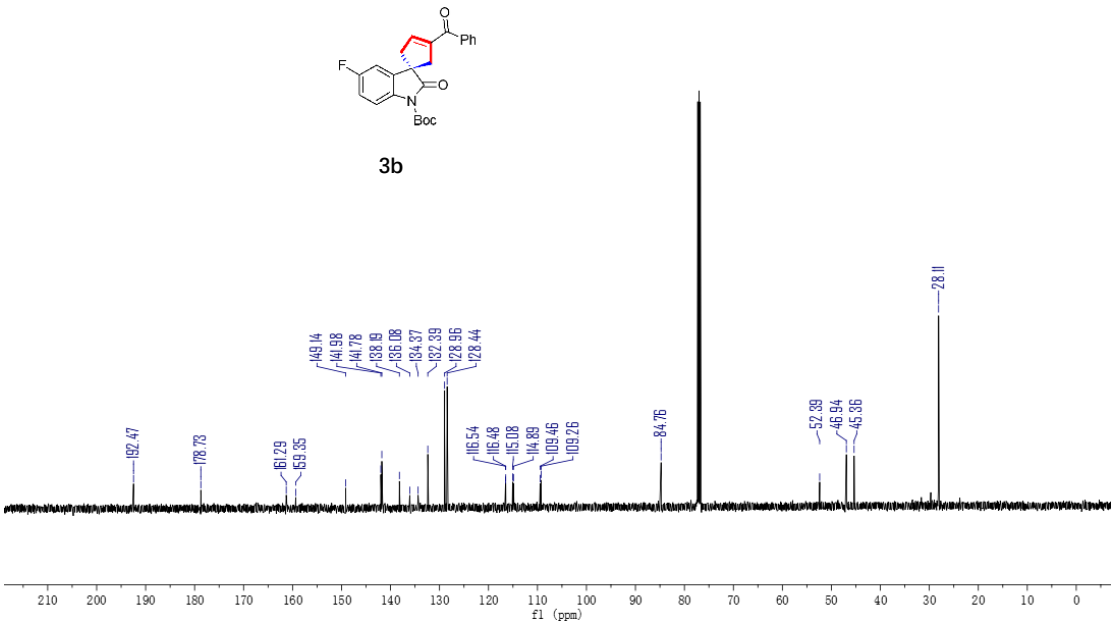
^{13}C NMR of **3a** (126 MHz, $CDCl_3$)



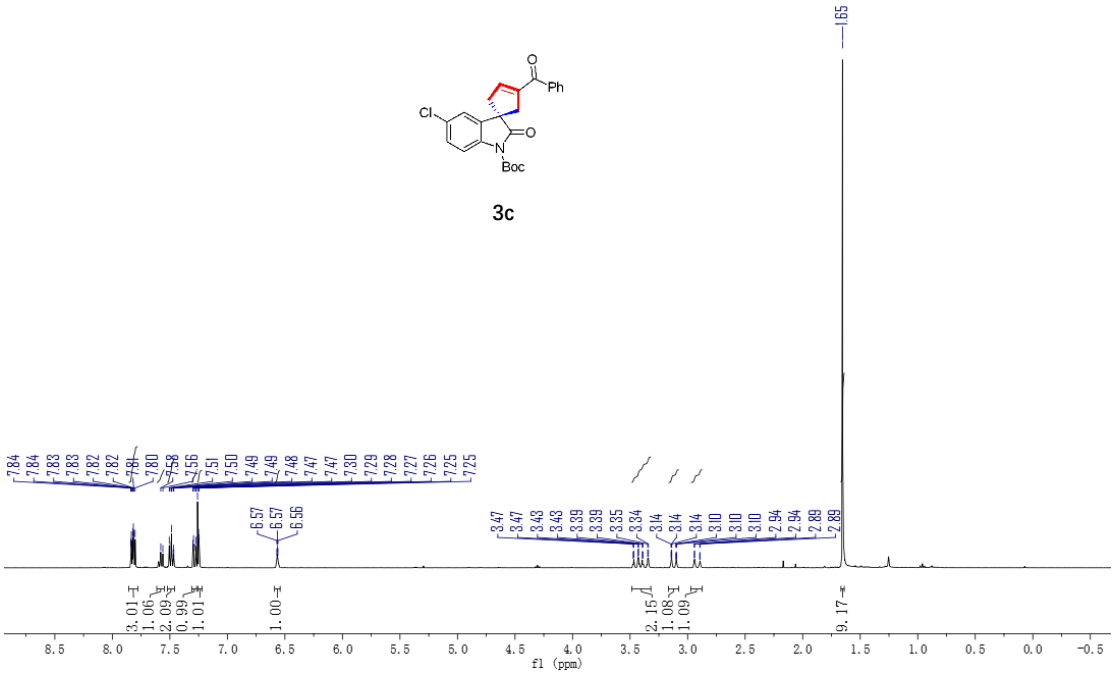
^{1}H NMR of **3b** (500 MHz, $CDCl_3$)



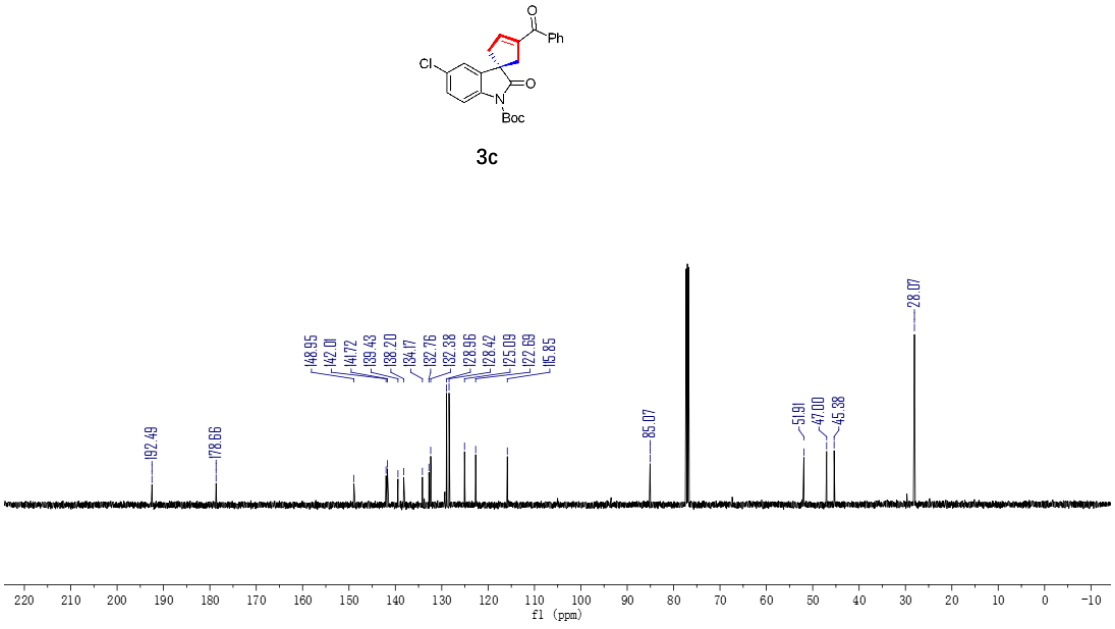
^{13}C NMR of **3b** (126 MHz, $CDCl_3$)



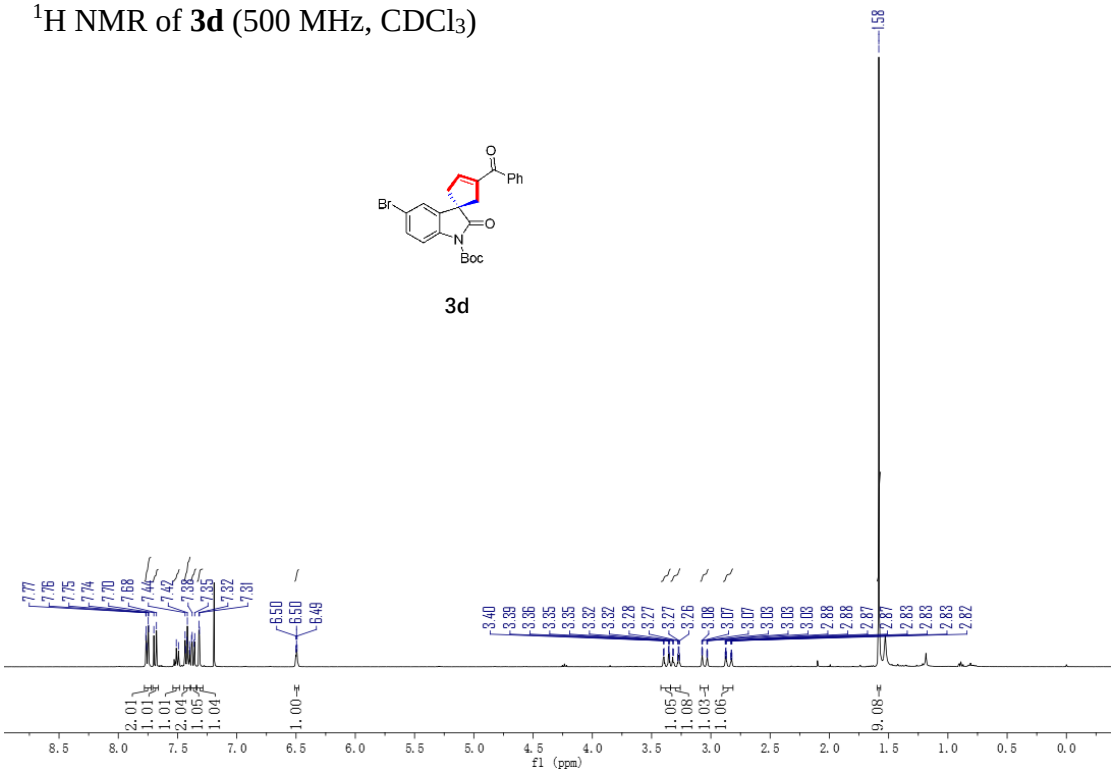
^{1}H NMR of **3c** (500 MHz, $CDCl_3$)



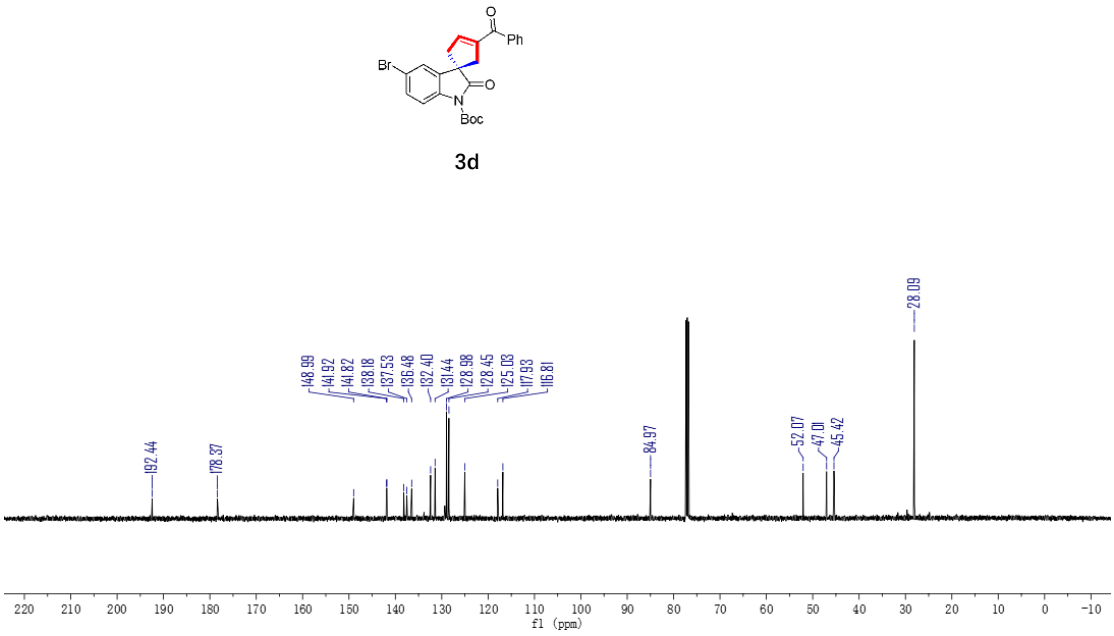
^{13}C NMR of **3c** (126 MHz, $CDCl_3$)



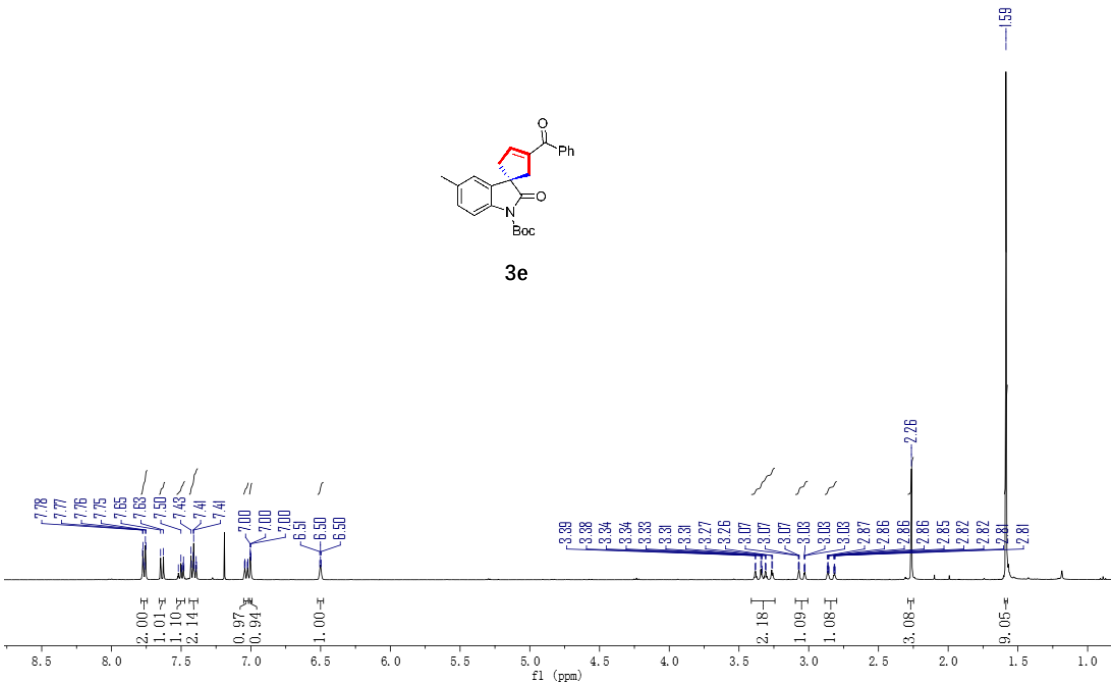
^{1}H NMR of **3d** (500 MHz, $CDCl_3$)



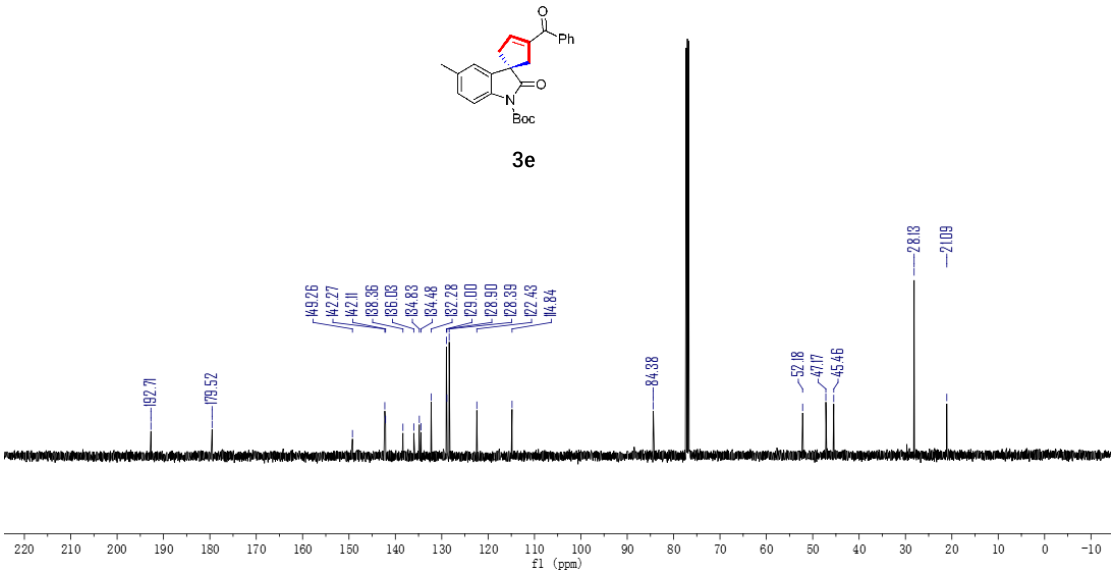
^{13}C NMR of **3d** (126 MHz, $CDCl_3$)



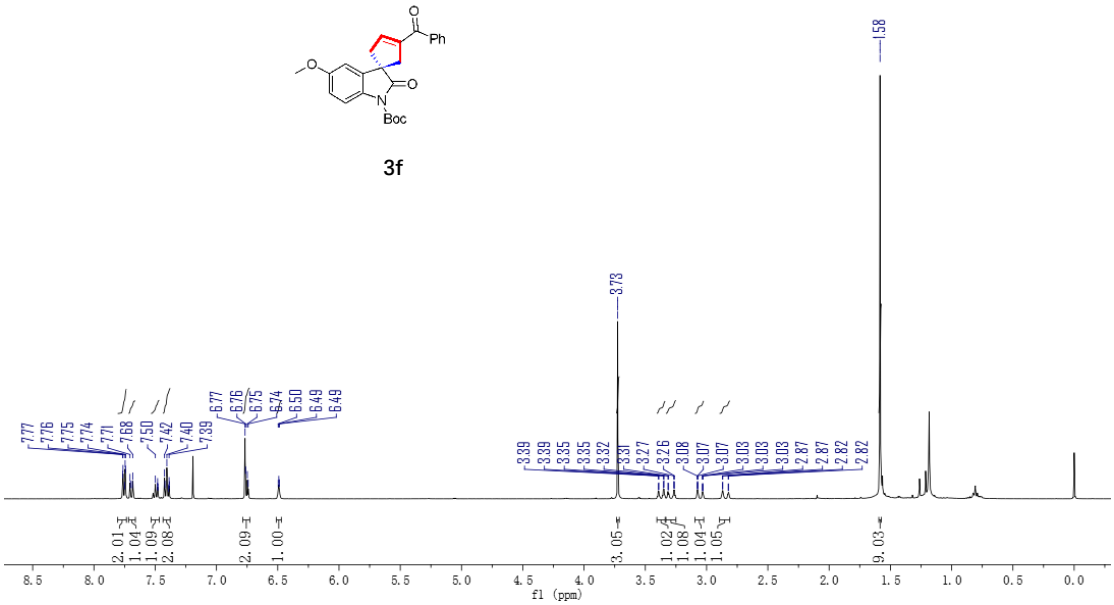
^{1}H NMR of **3e** (500 MHz, $CDCl_3$)



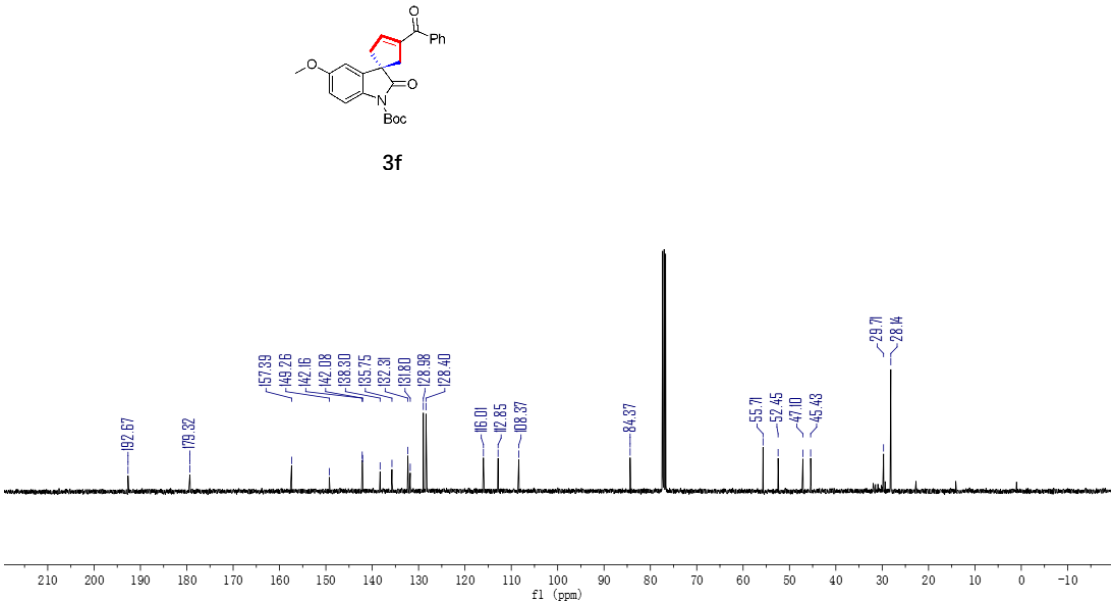
^{13}C NMR of **3e** (126 MHz, $CDCl_3$)



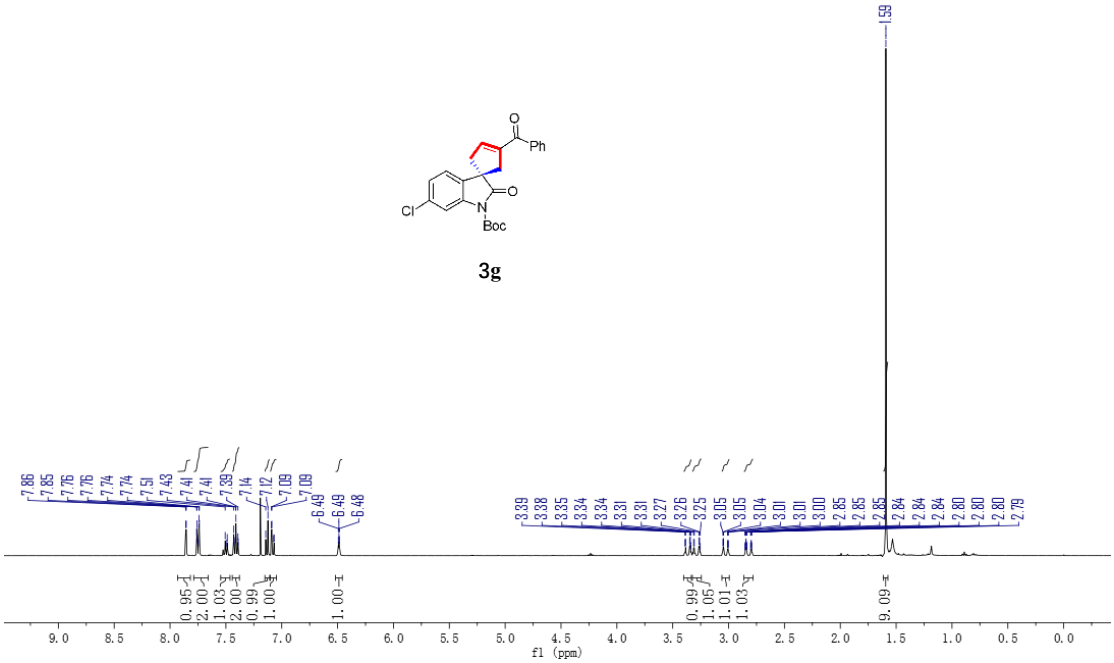
^{1}H NMR of **3f** (500 MHz, $CDCl_3$)



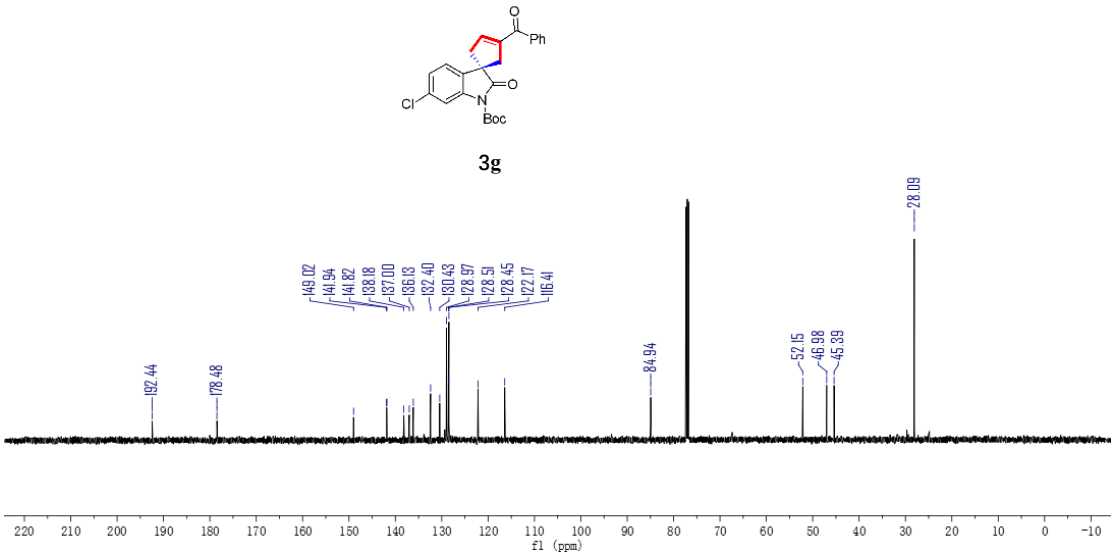
^{13}C NMR of **3f** (126 MHz, $CDCl_3$)



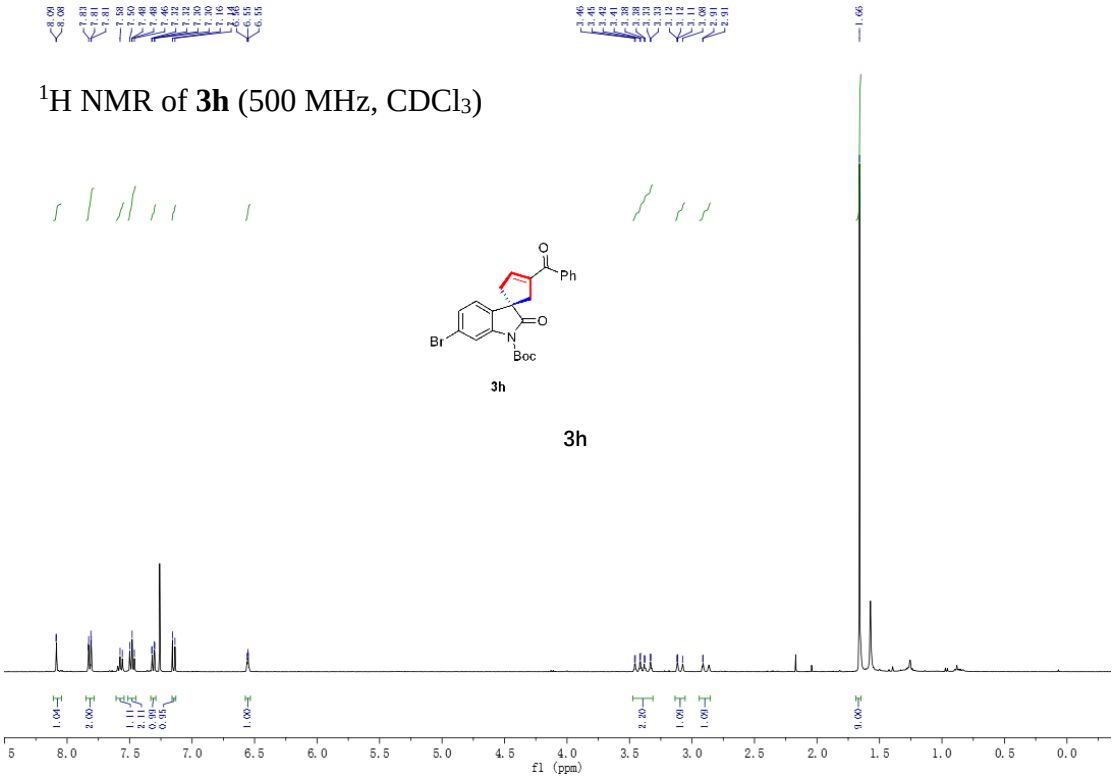
^{1}H NMR of **3g** (500 MHz, $CDCl_3$)



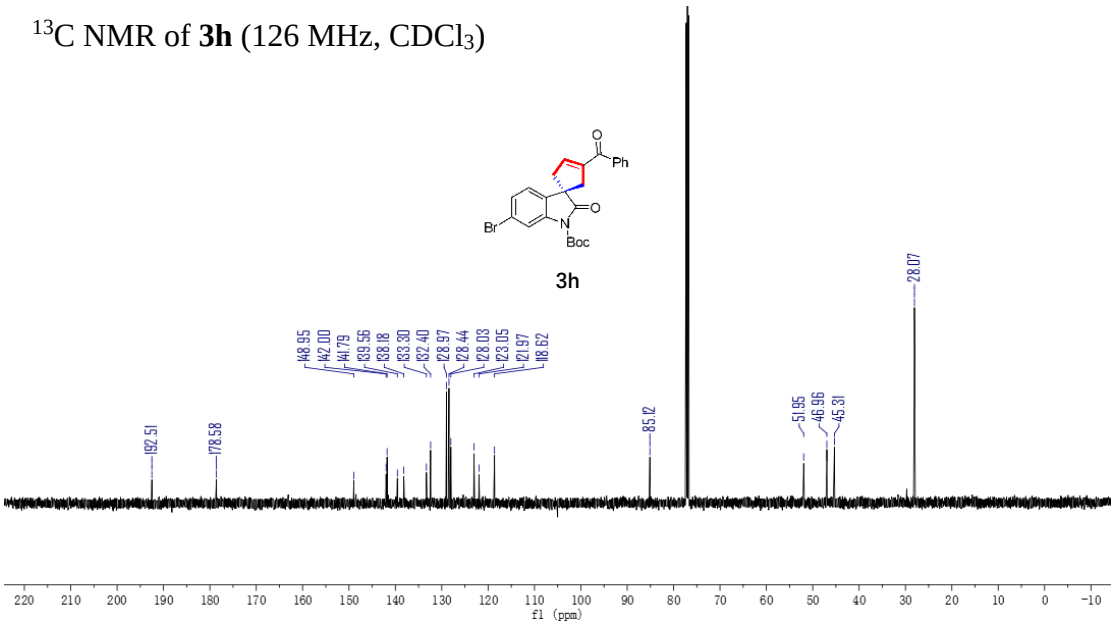
^{13}C NMR of **3g** (126 MHz, $CDCl_3$)



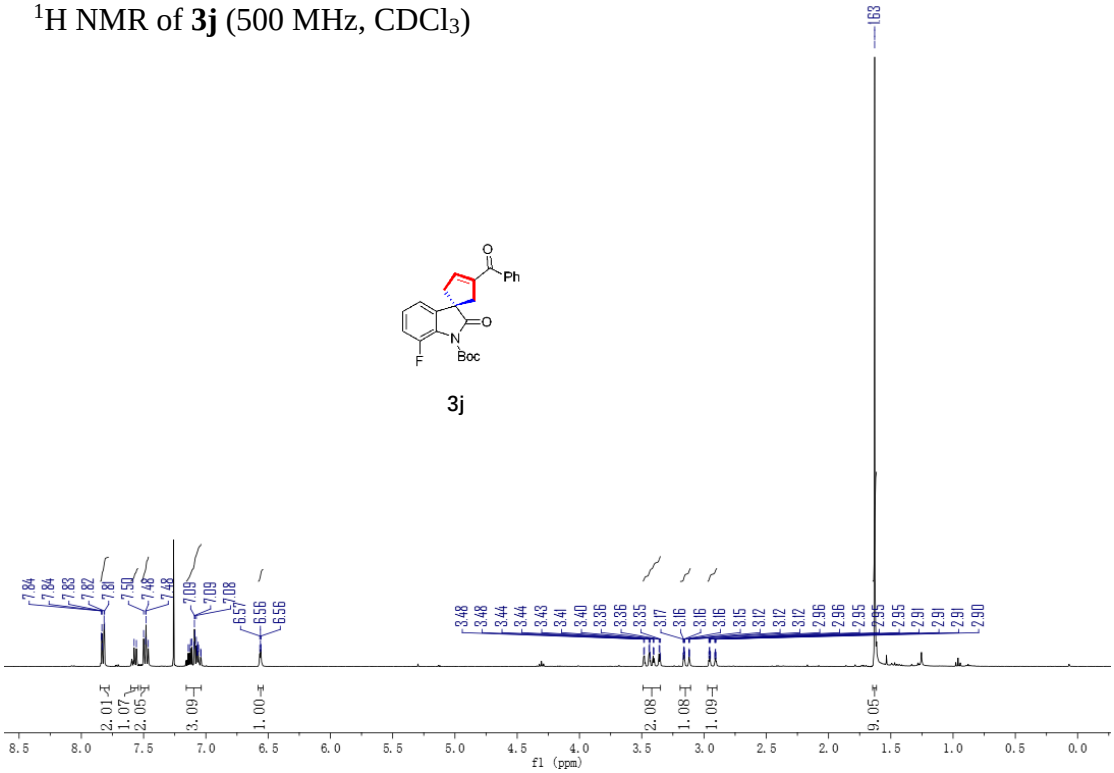
^{1}H NMR of **3h** (500 MHz, $CDCl_3$)



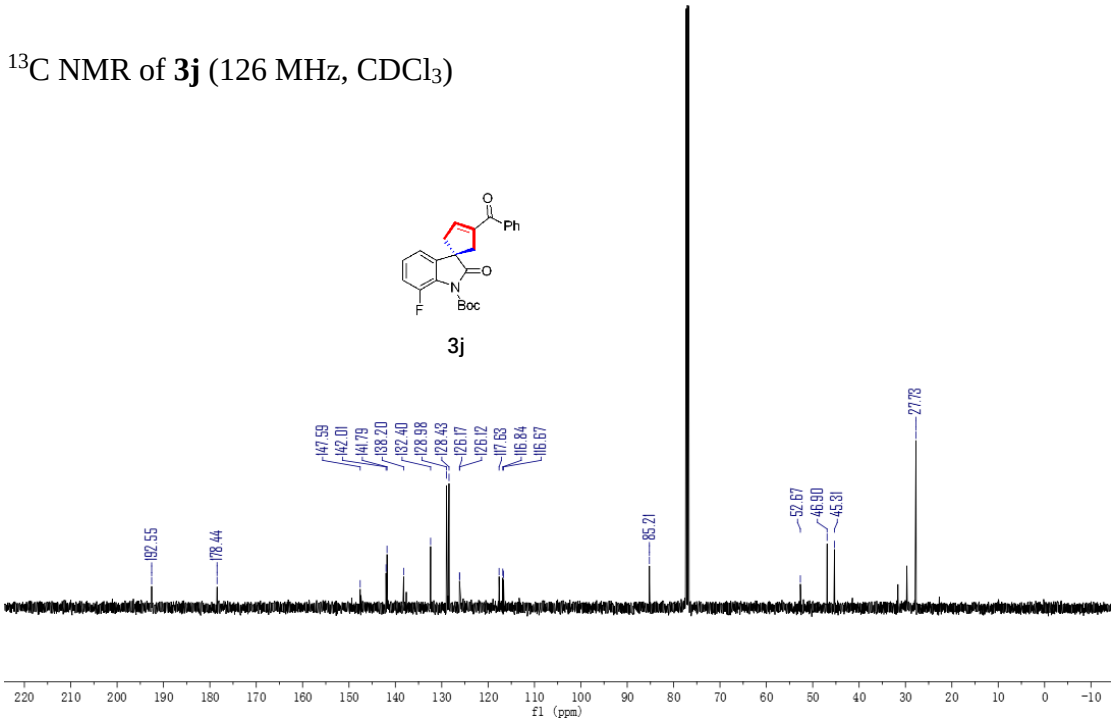
^{13}C NMR of **3h** (126 MHz, $CDCl_3$)



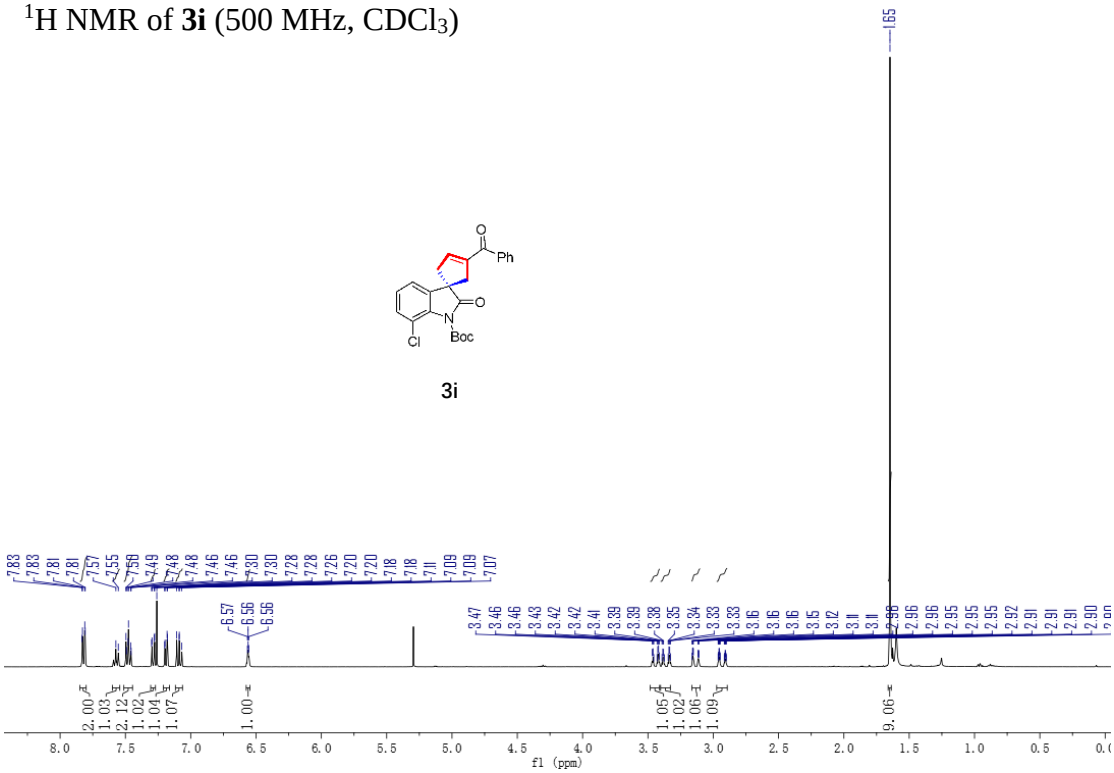
^{1}H NMR of **3j** (500 MHz, $CDCl_3$)

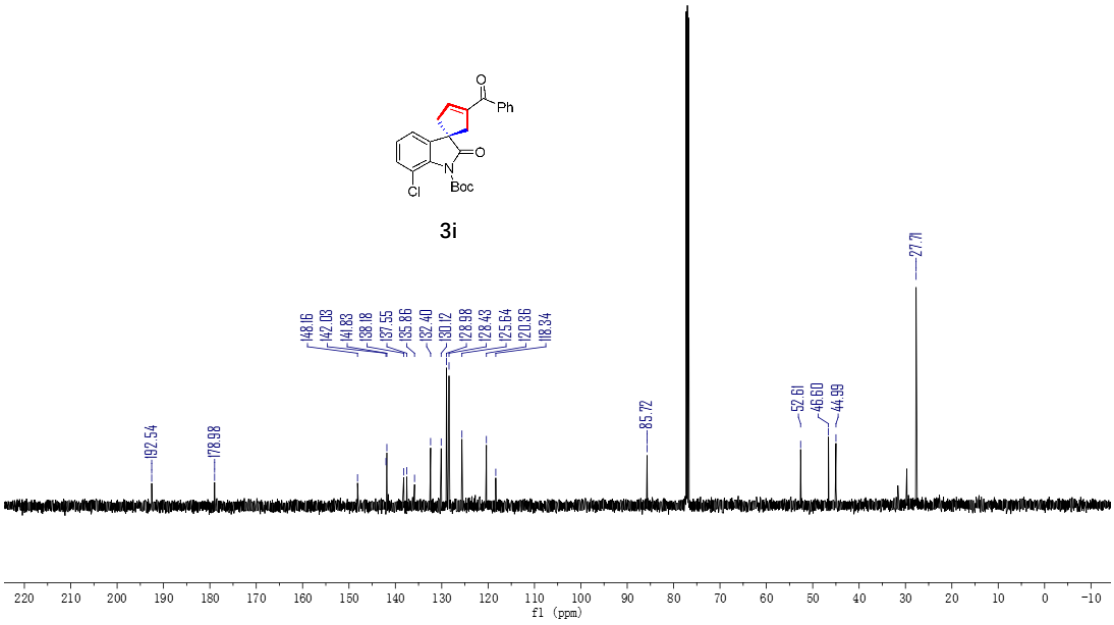


^{13}C NMR of **3j** (126 MHz, $CDCl_3$)

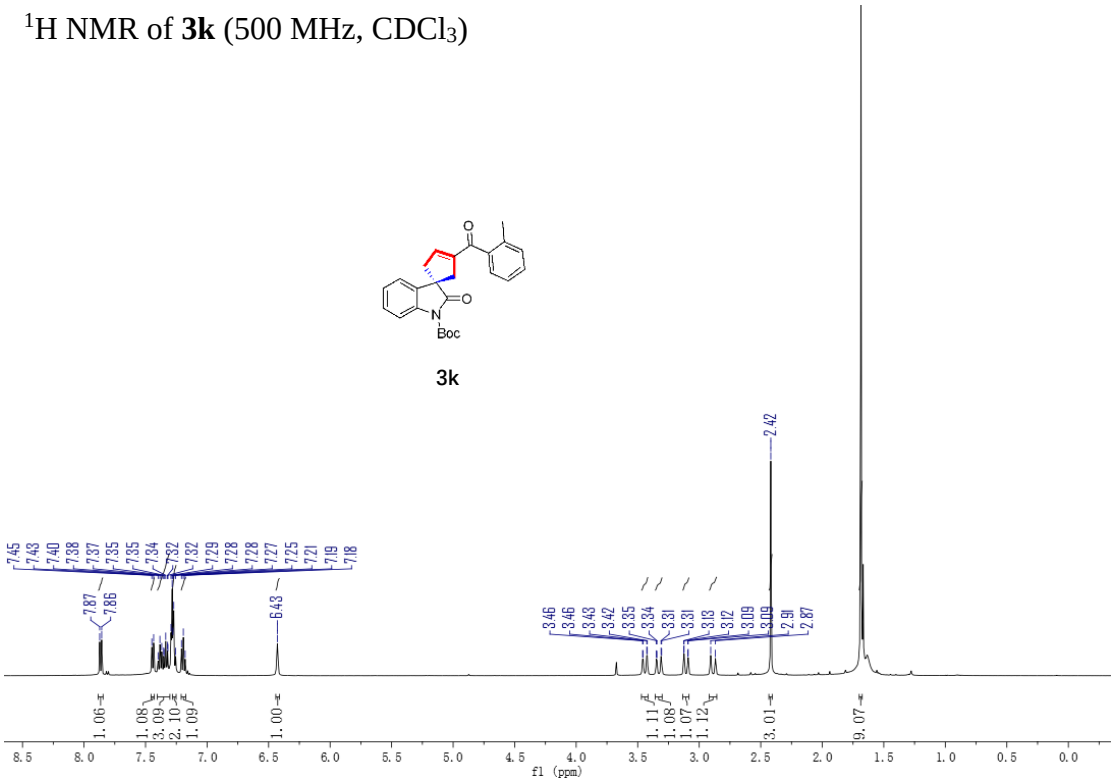


^{1}H NMR of **3i** (500 MHz, $CDCl_3$)

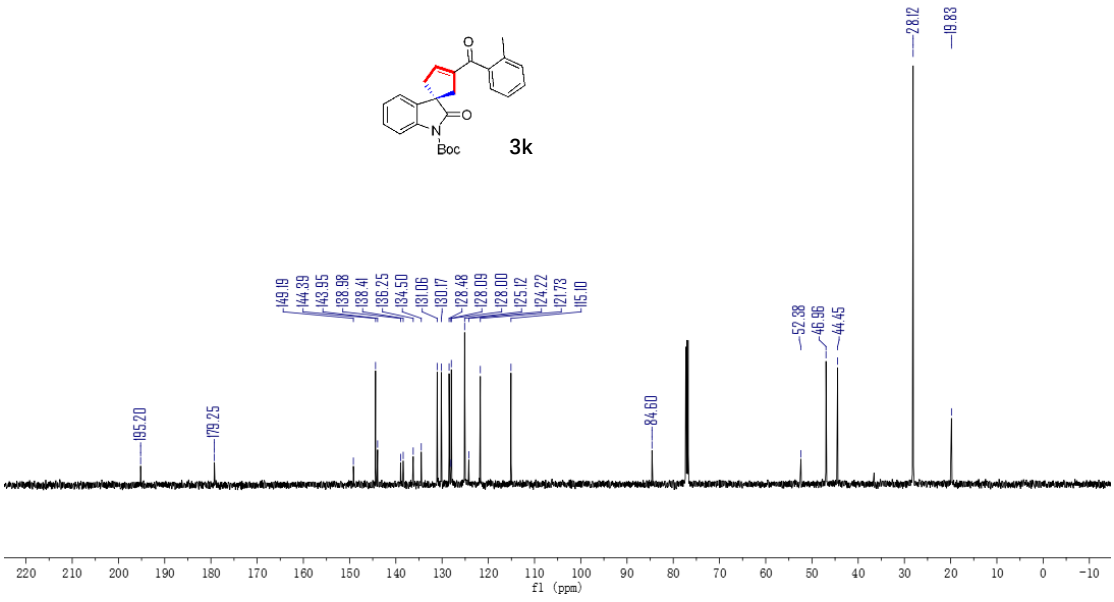




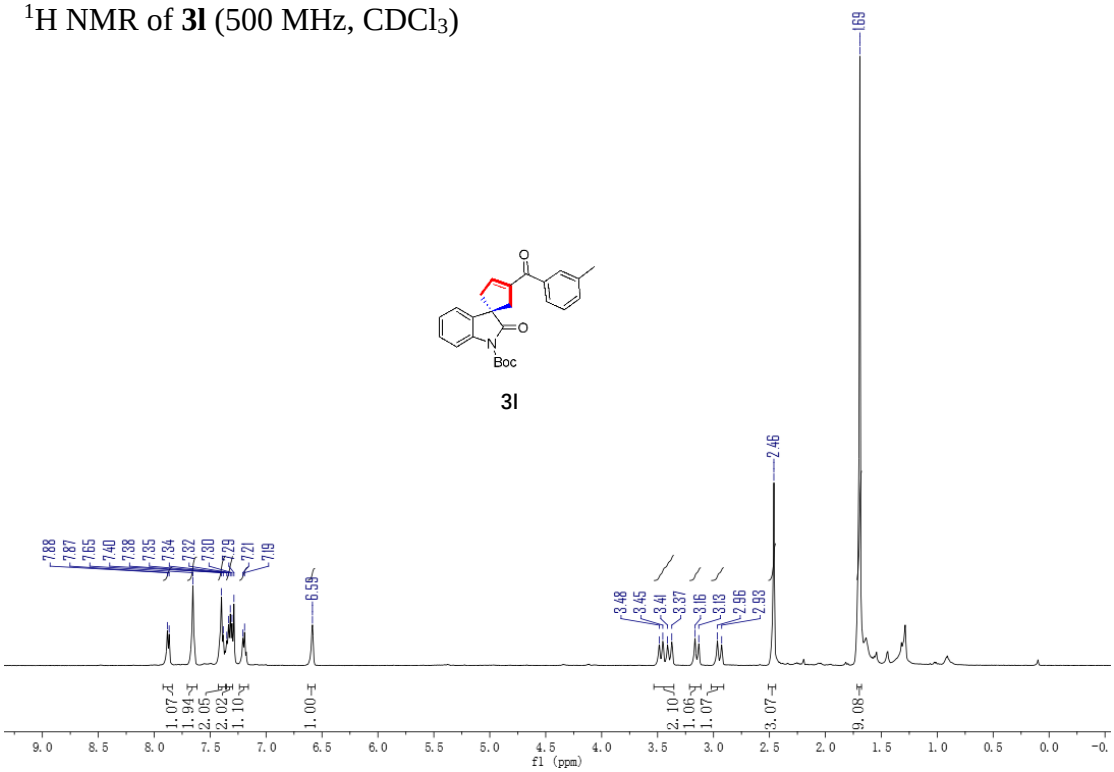
^{1}H NMR of **3k** (500 MHz, $CDCl_3$)



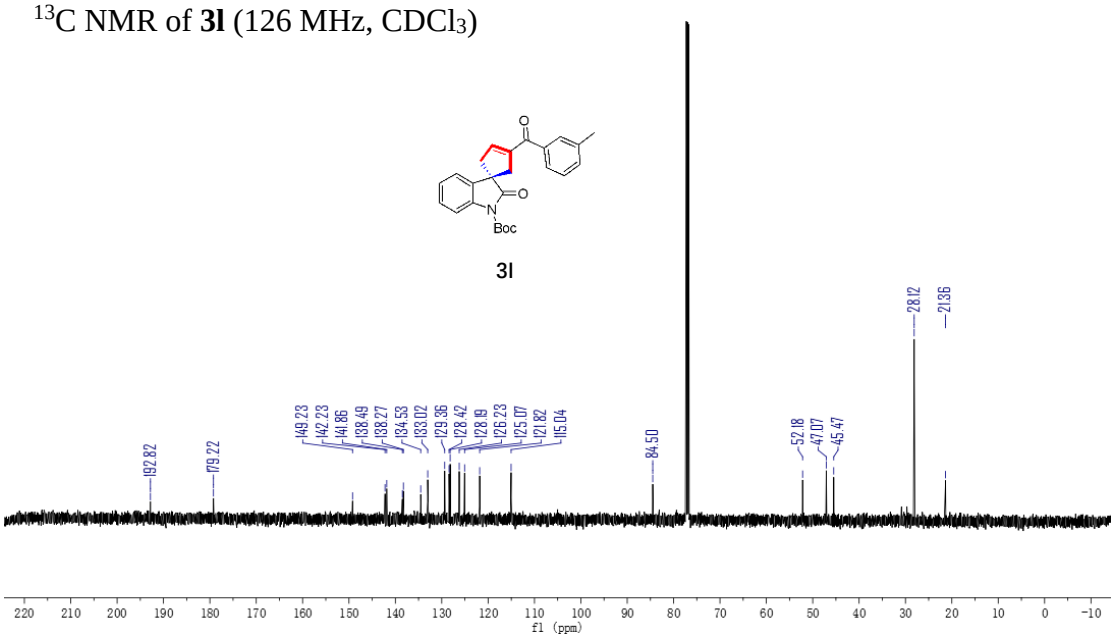
^{13}C NMR of **3k** (126 MHz, $CDCl_3$)



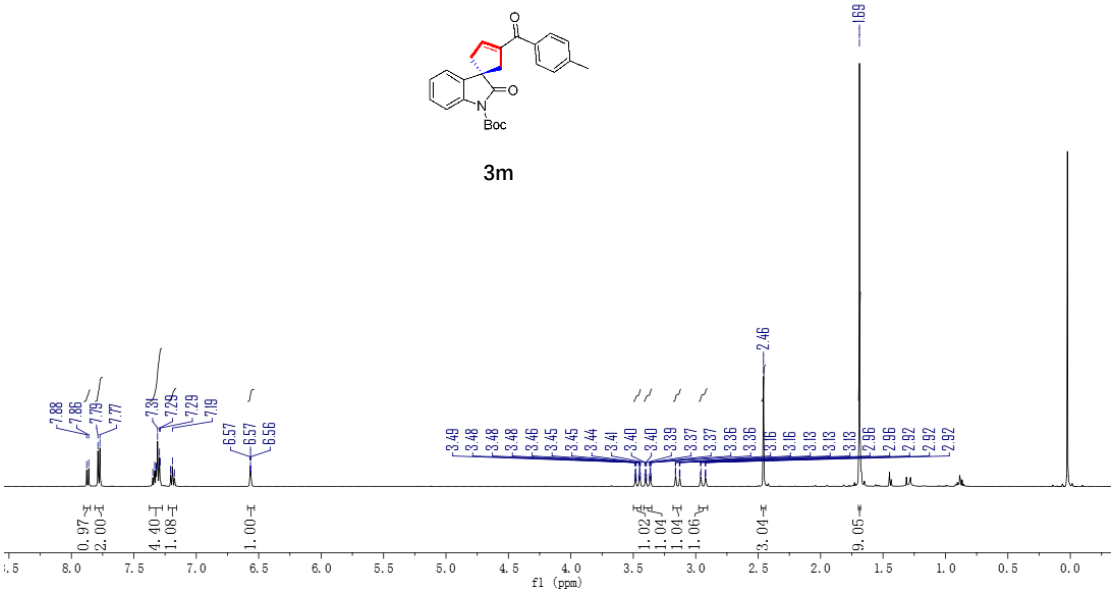
^{1}H NMR of **3l** (500 MHz, $CDCl_3$)



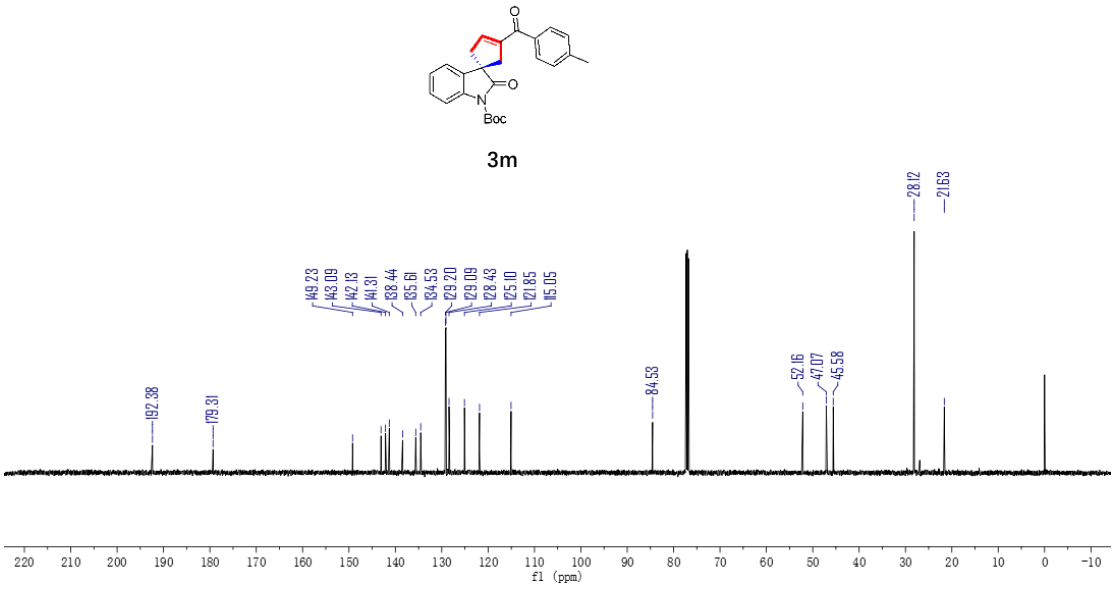
^{13}C NMR of **3l** (126 MHz, $CDCl_3$)



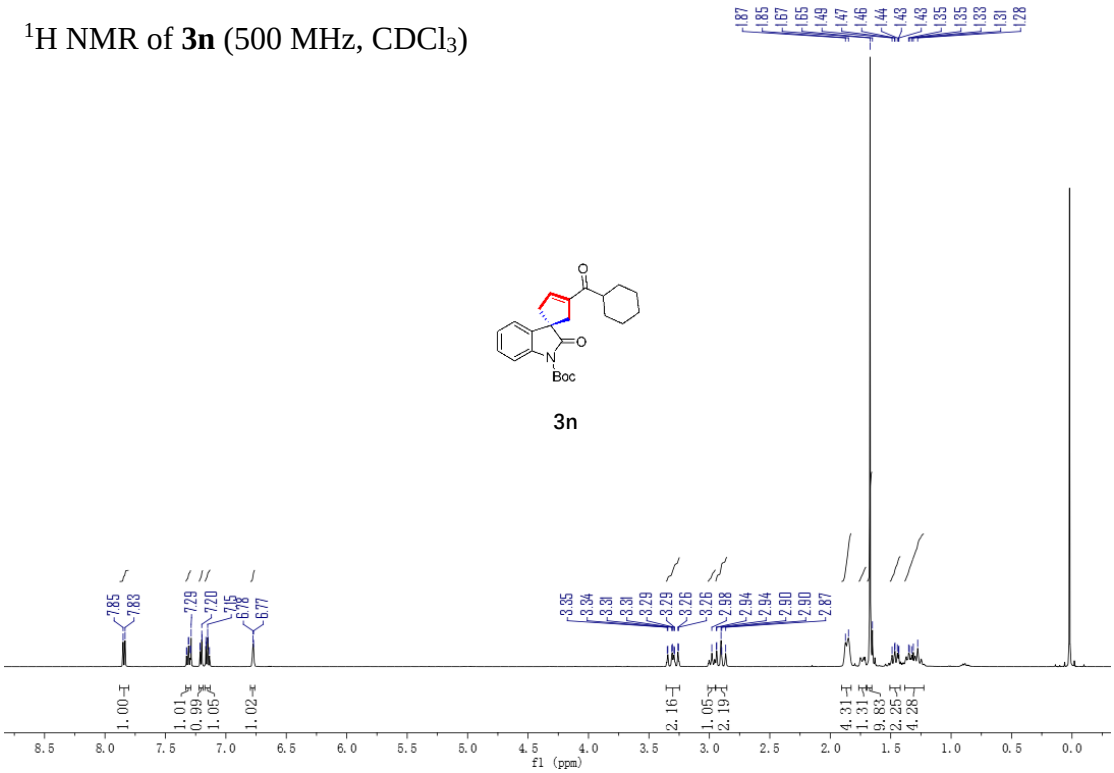
^{1}H NMR of **3m** (500 MHz, $CDCl_3$)



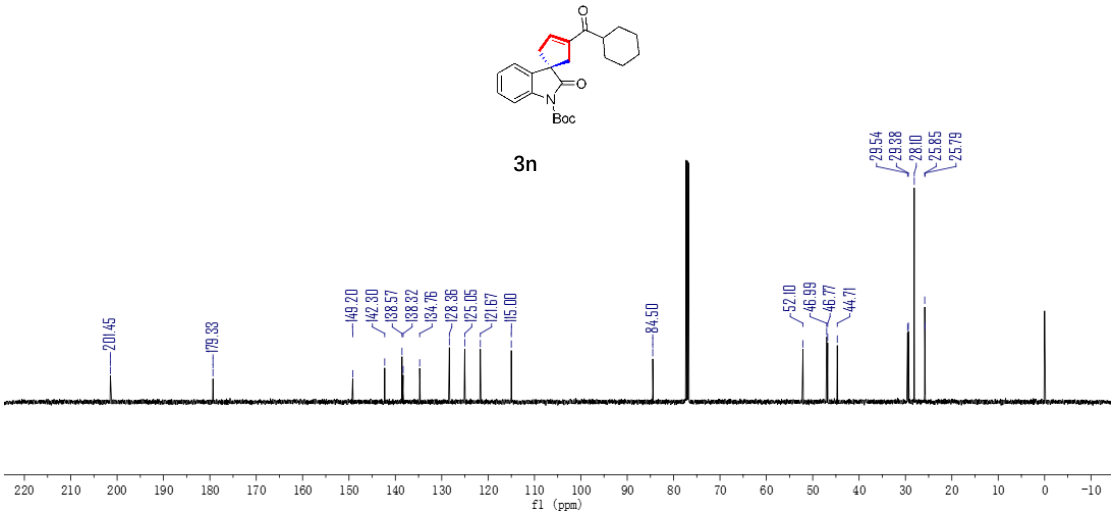
^{13}C NMR of **3m** (126 MHz, $CDCl_3$)



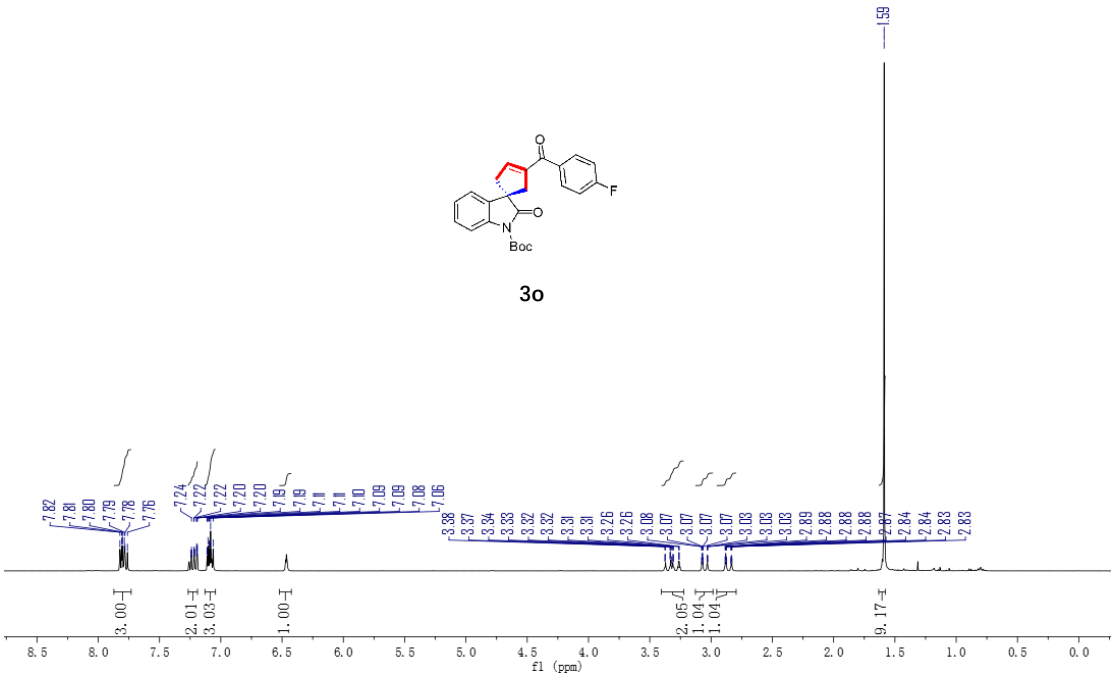
^{1}H NMR of **3n** (500 MHz, $CDCl_3$)



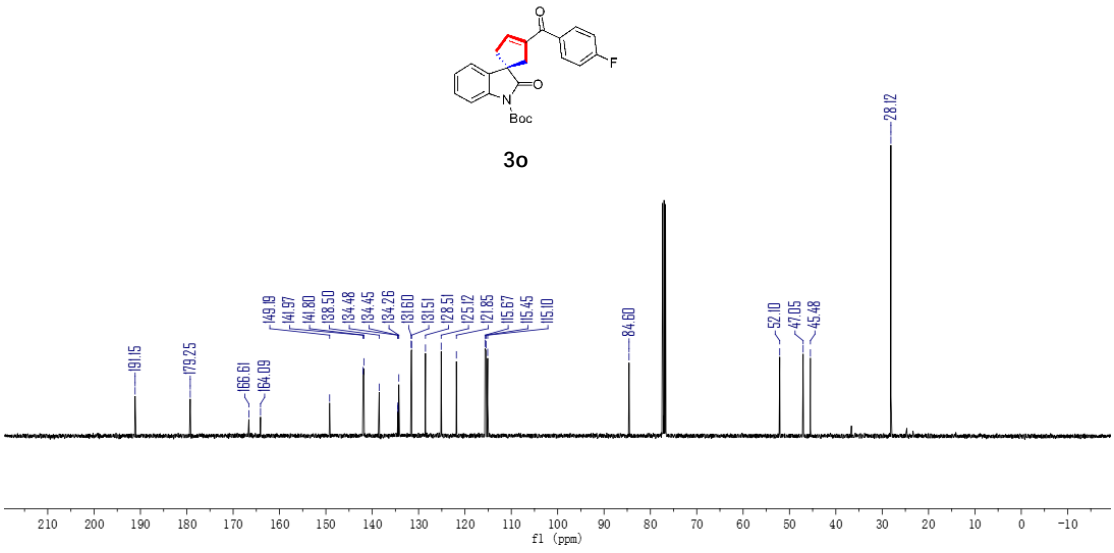
^{13}C NMR of **3n** (126 MHz, $CDCl_3$)



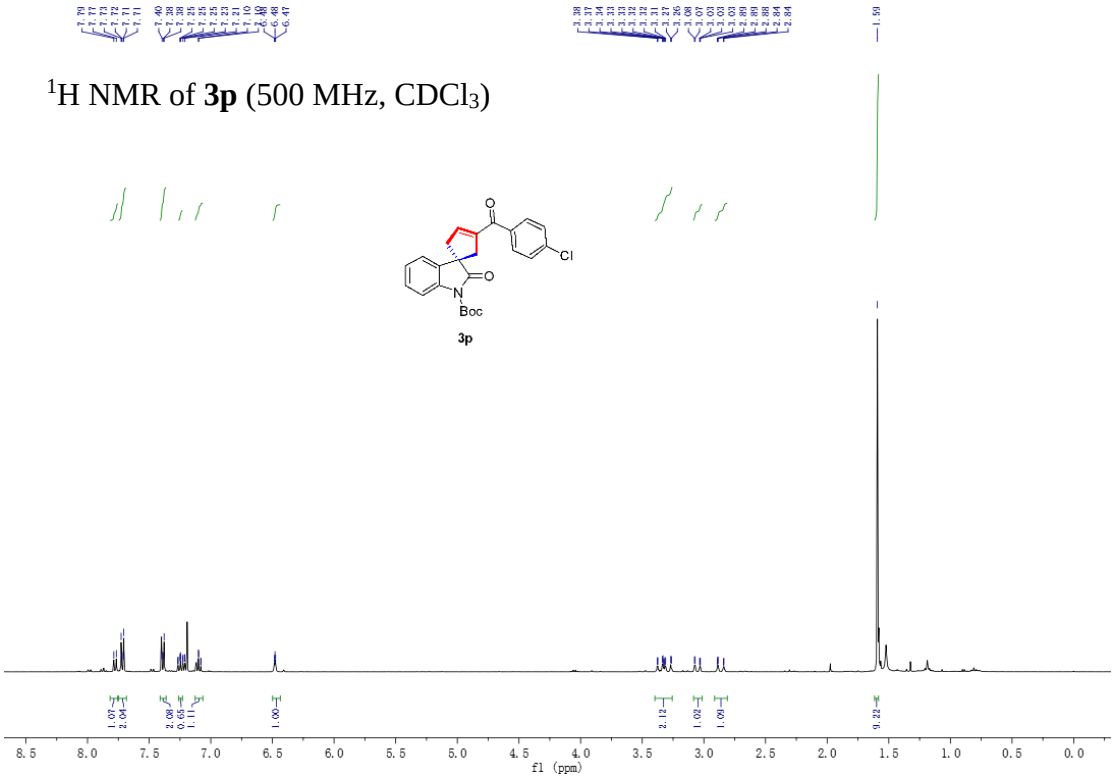
^{1}H NMR of **3o** (500 MHz, $CDCl_3$)



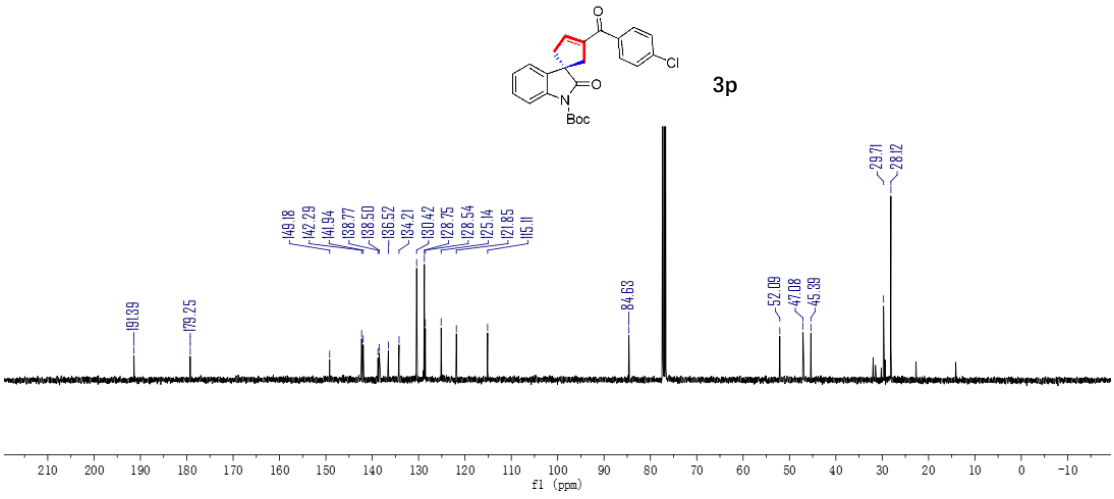
^{13}C NMR of **3o** (126 MHz, $CDCl_3$)



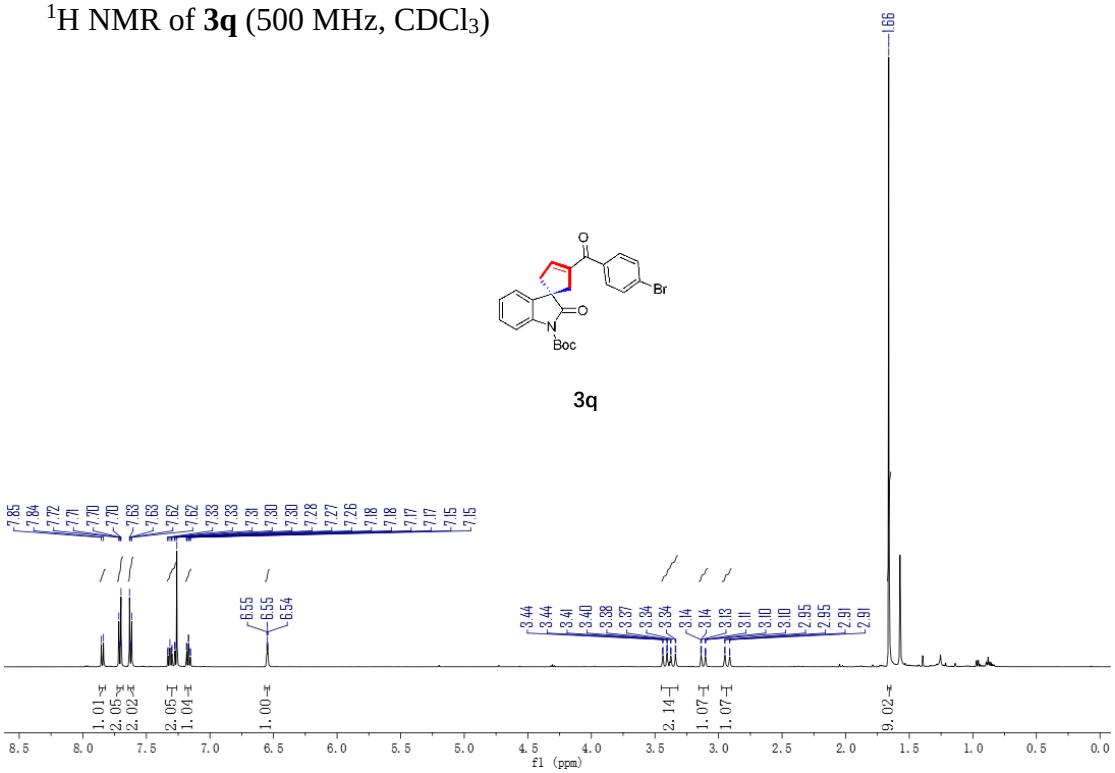
^{1}H NMR of **3p** (500 MHz, $CDCl_3$)



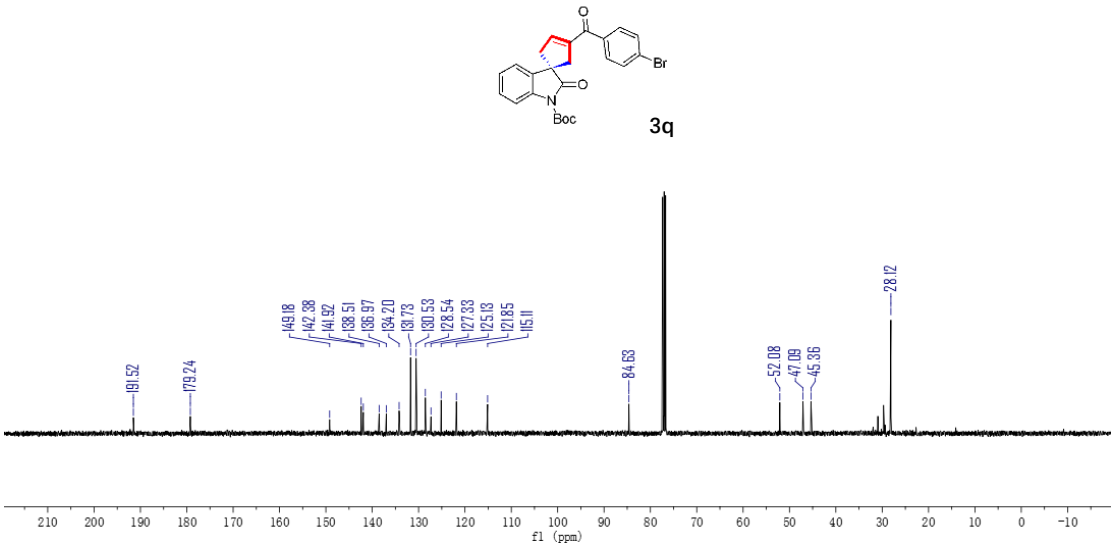
^{13}C NMR of **3p** (126 MHz, $CDCl_3$)



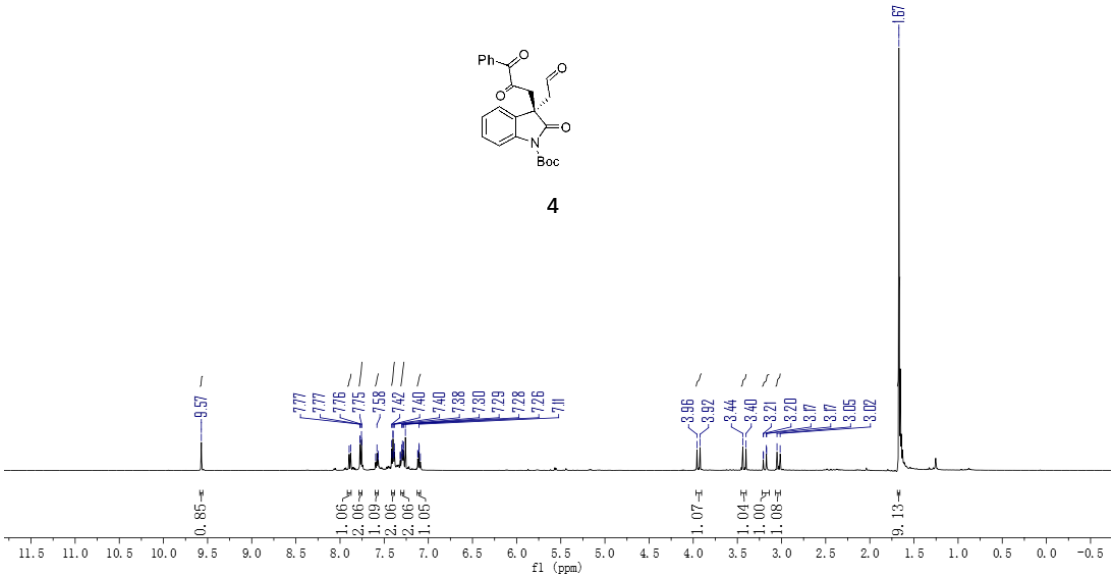
^{1}H NMR of **3q** (500 MHz, $CDCl_3$)



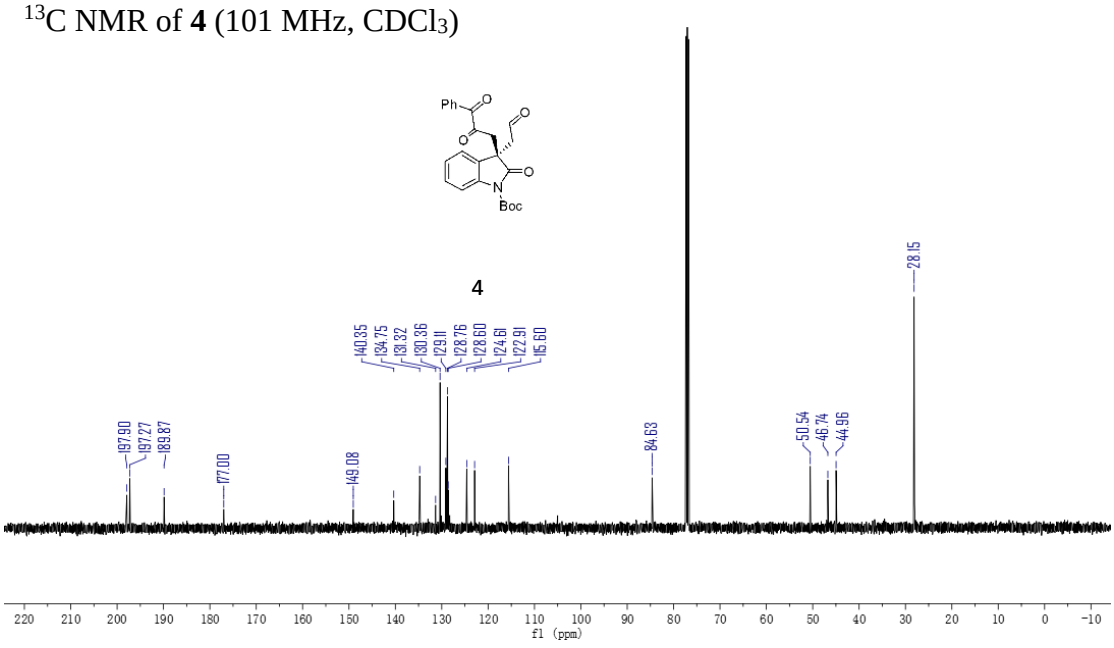
^{13}C NMR of **3q** (126 MHz, $CDCl_3$)



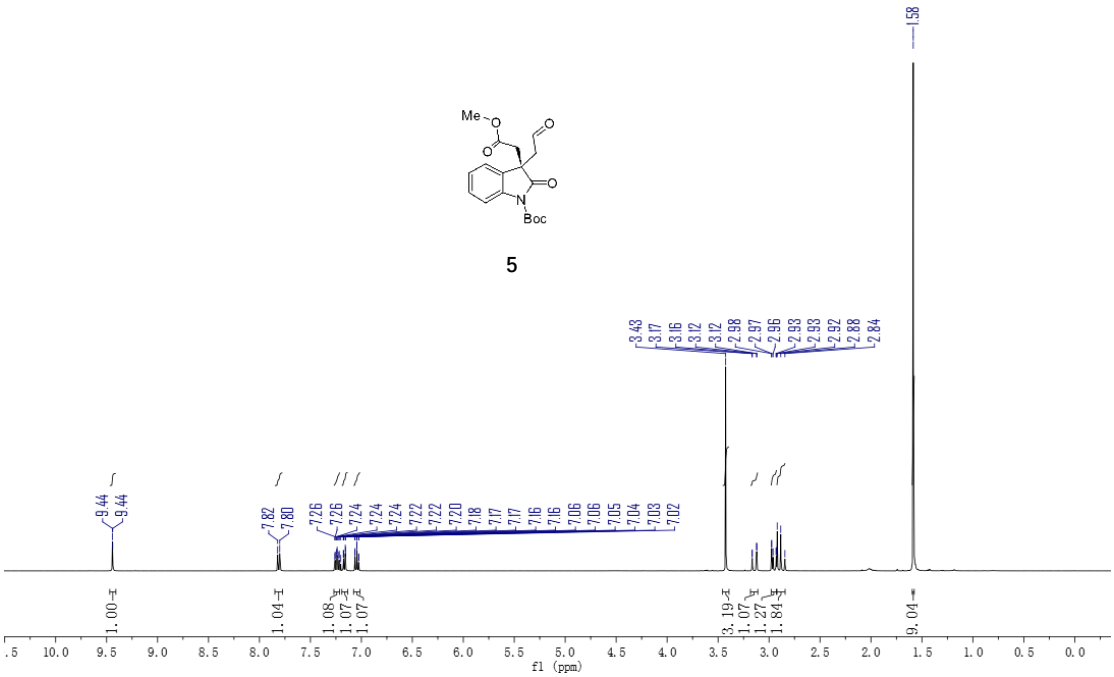
^{1}H NMR of **4** (400 MHz, $CDCl_3$)



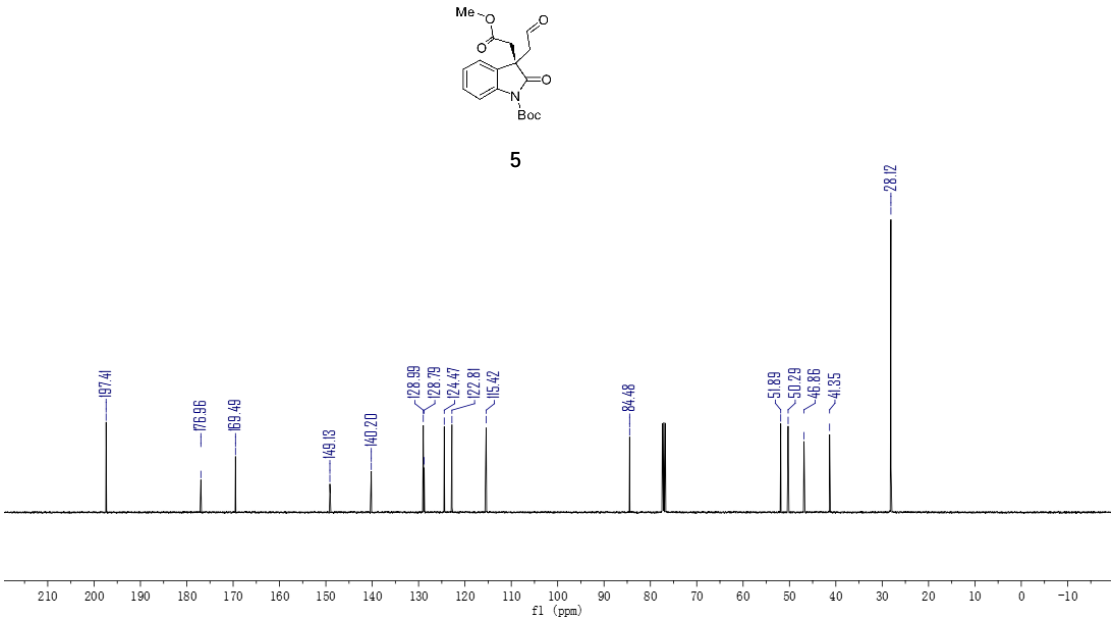
^{13}C NMR of **4** (101 MHz, $CDCl_3$)



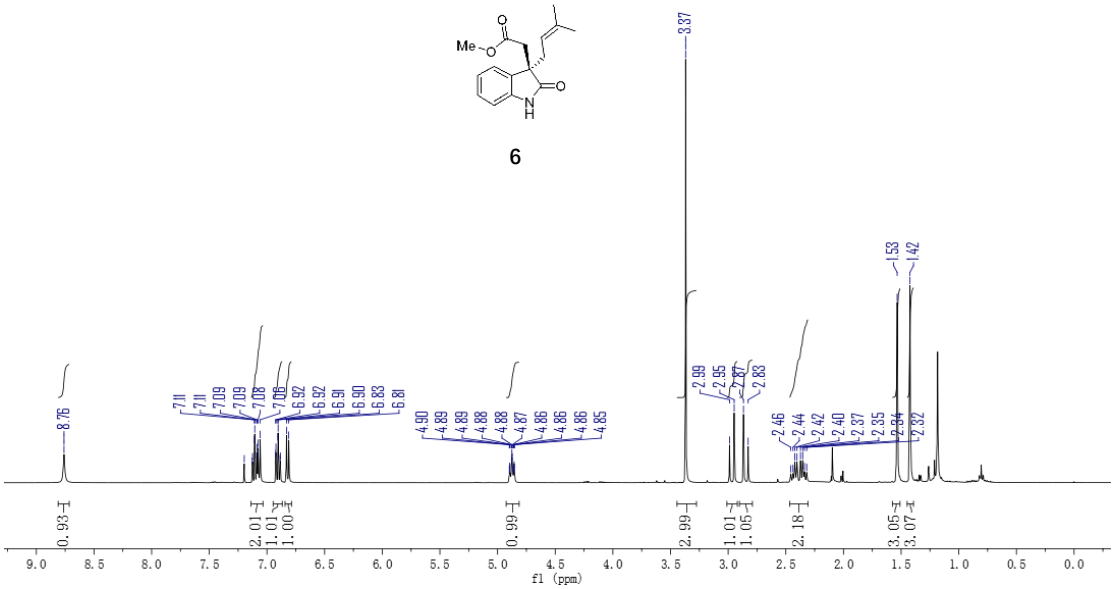
^{1}H NMR of **5** (400 MHz, $CDCl_3$)



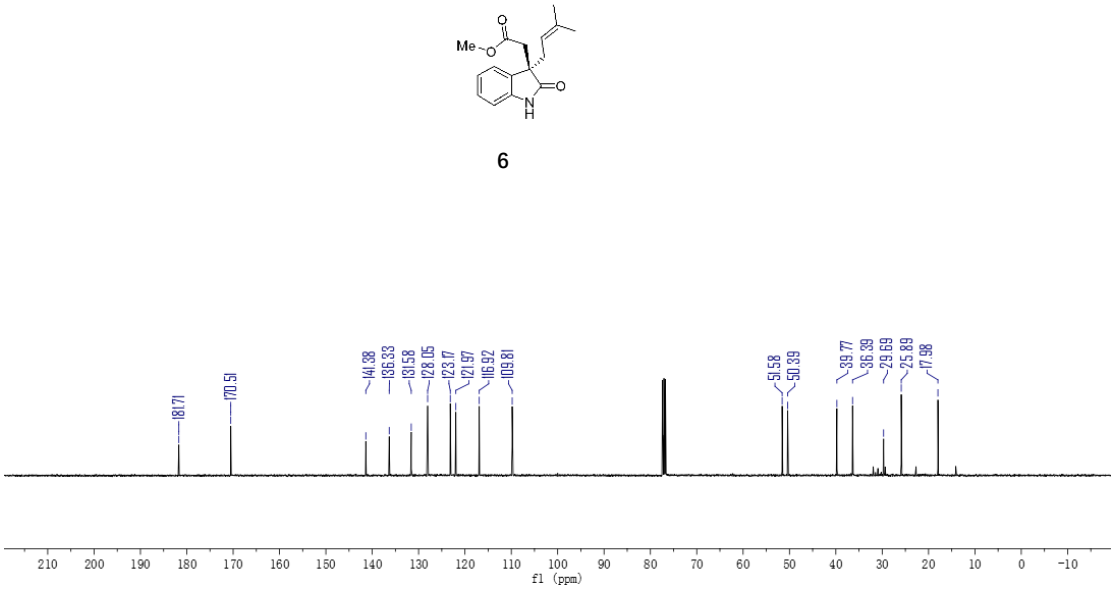
^{13}C NMR of **5** (101 MHz, $CDCl_3$)



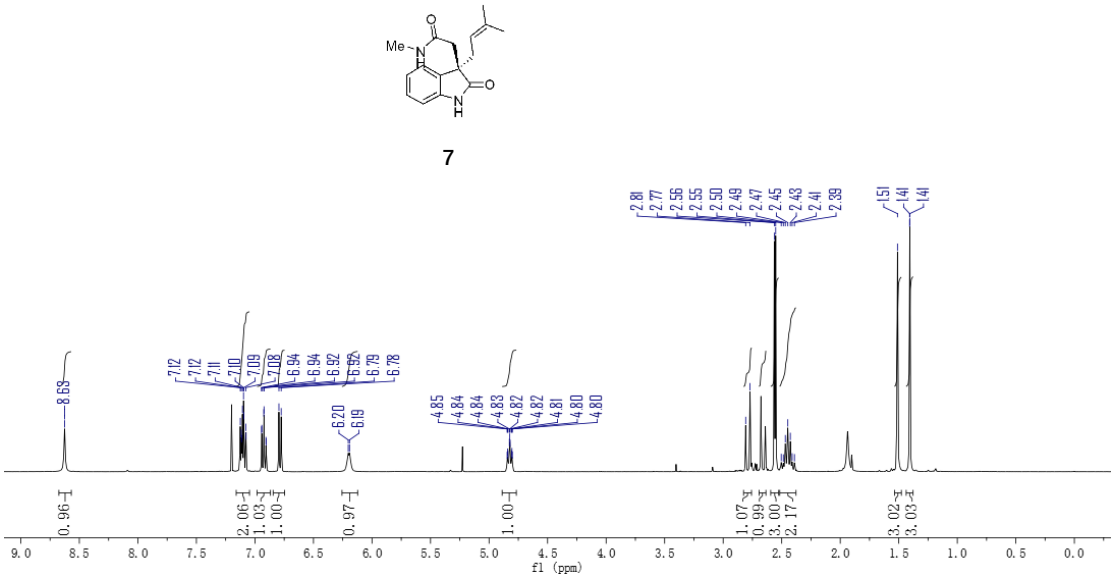
^{1}H NMR of **6** (400 MHz, $CDCl_3$)



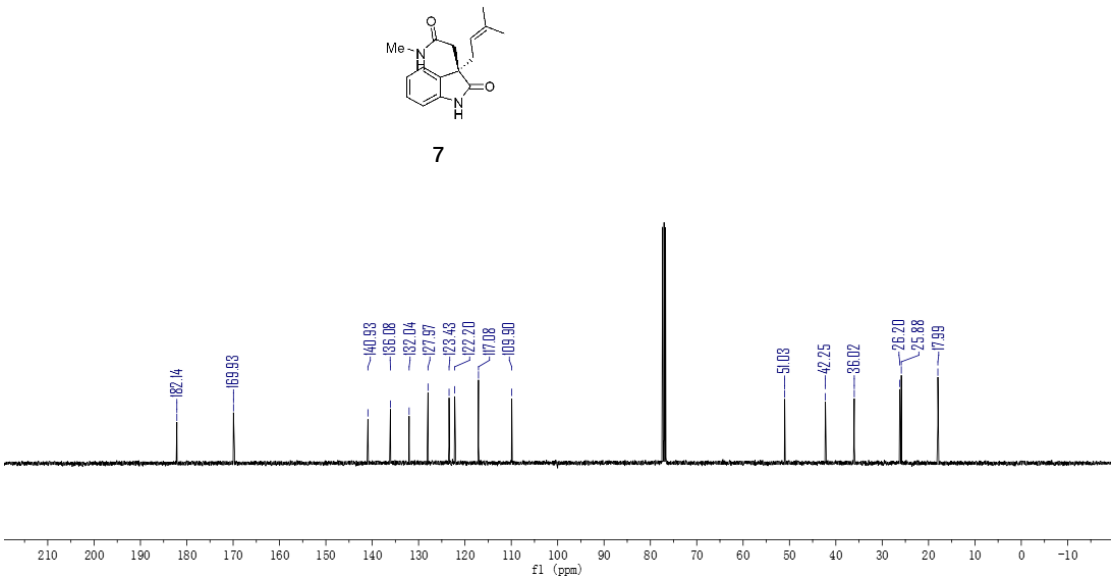
^{13}C NMR of **6** (101 MHz, $CDCl_3$)



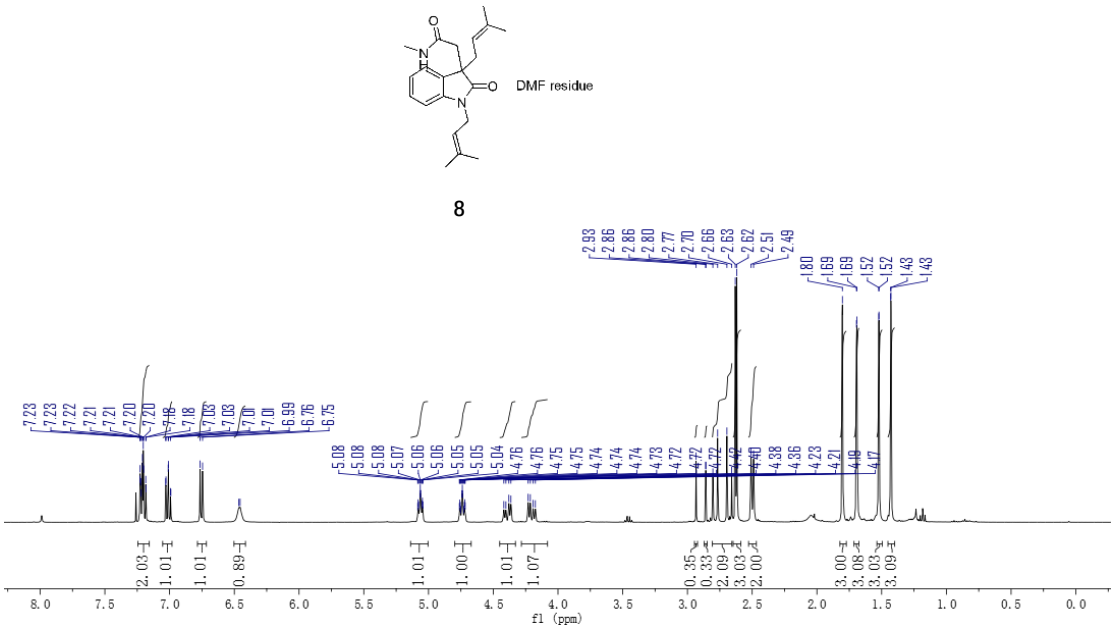
^{1}H NMR of **7** (400 MHz, $CDCl_3$)



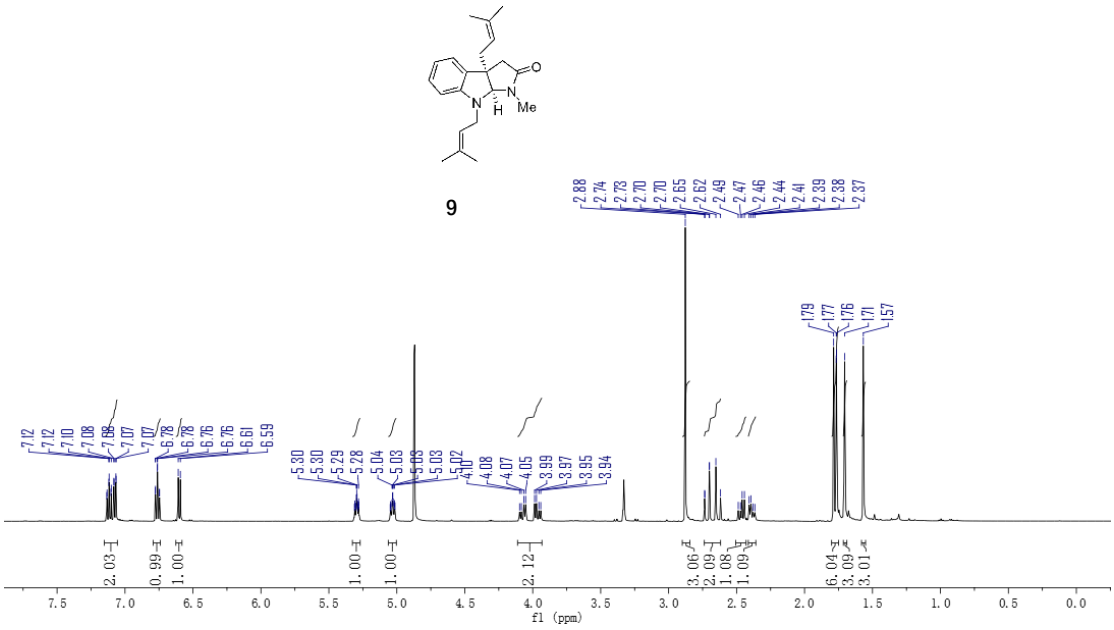
^{13}C NMR of **7** (101 MHz, $CDCl_3$)



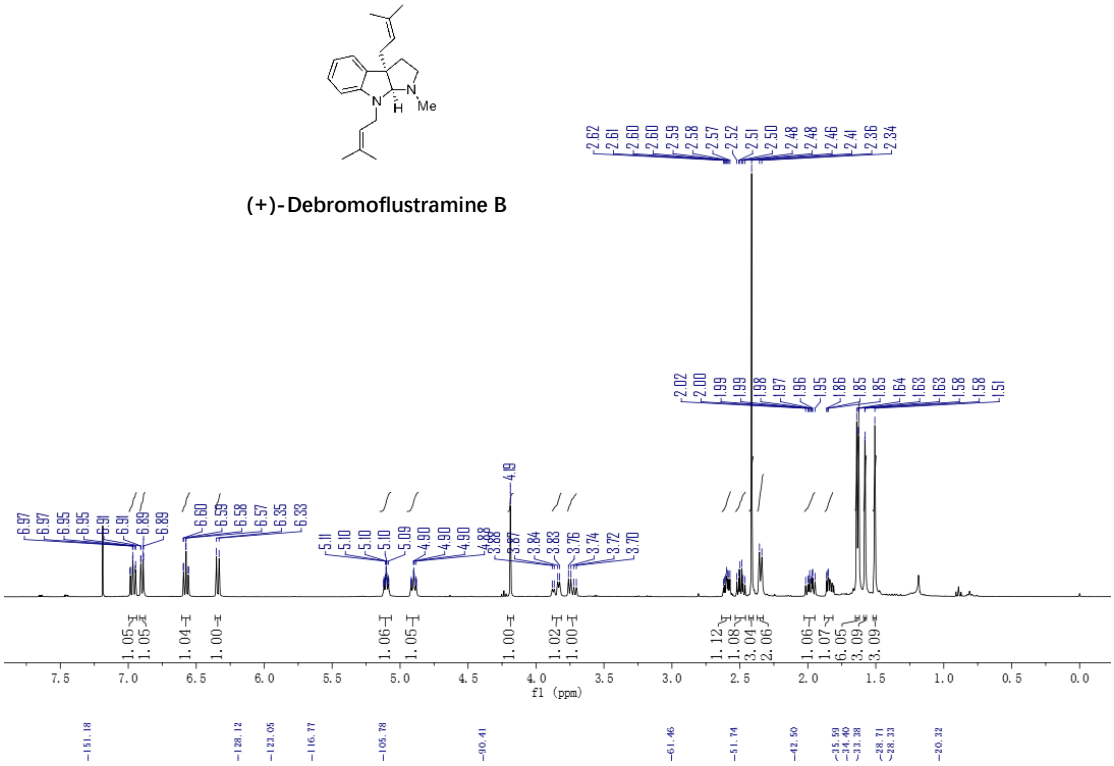
^{1}H NMR of **8** (400 MHz, $CDCl_3$)



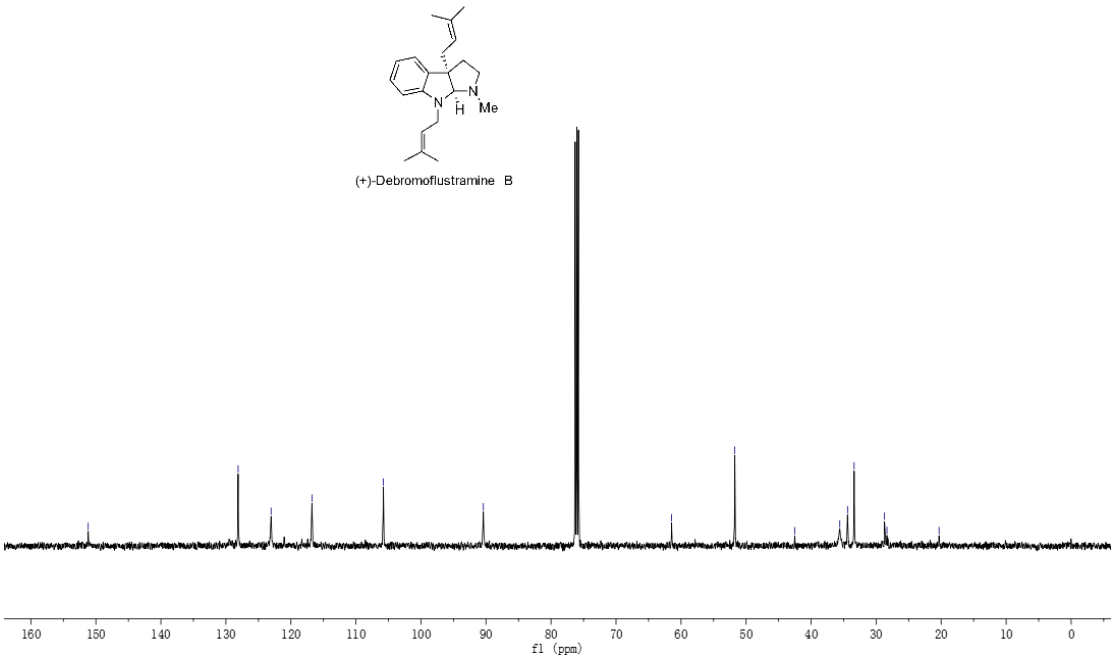
^{1}H NMR of **9** (500 MHz, CD_3OD)



^{1}H NMR of **(+) - Debromoflustramine B** (400 MHz, $CDCl_3$)



^{13}C NMR of **(+) – Debromoflustramine B** (101 MHz, $CDCl_3$)



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