Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Highly Enantio- and Diastereoselective Construction of Spirocyclic Oxindoles *via* a Palladium-Catalyzed Decarboxylative Asymmetric [4 + 2] Annulation Strategy

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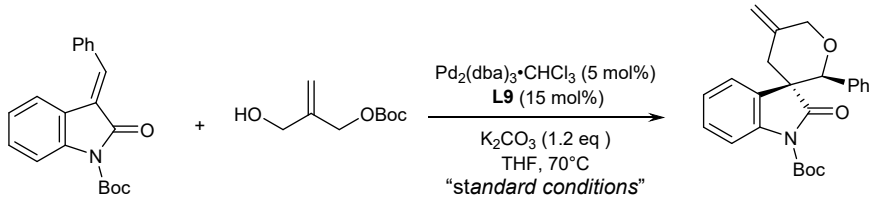
1. Supporting tables and figures

Table S1. Screen of reaction conditions



2a **1b** **3a**

entry	Variation from the "standard conditions"[a]	yield [b]	dr [c]	*ee* (%) [d]
		screen of [Pd]		
1	$Pd(OAc)_2$	53	>20:1	70
		screen of addictive		
2	-	80	>20:1	75
3	Et_3N	82	>20:1	78
4	Pyridine	81	>20:1	76
5	DMAP	40	>20:1	78
6	TsOH	trace	-	-
7	AcOH	trace	-	-

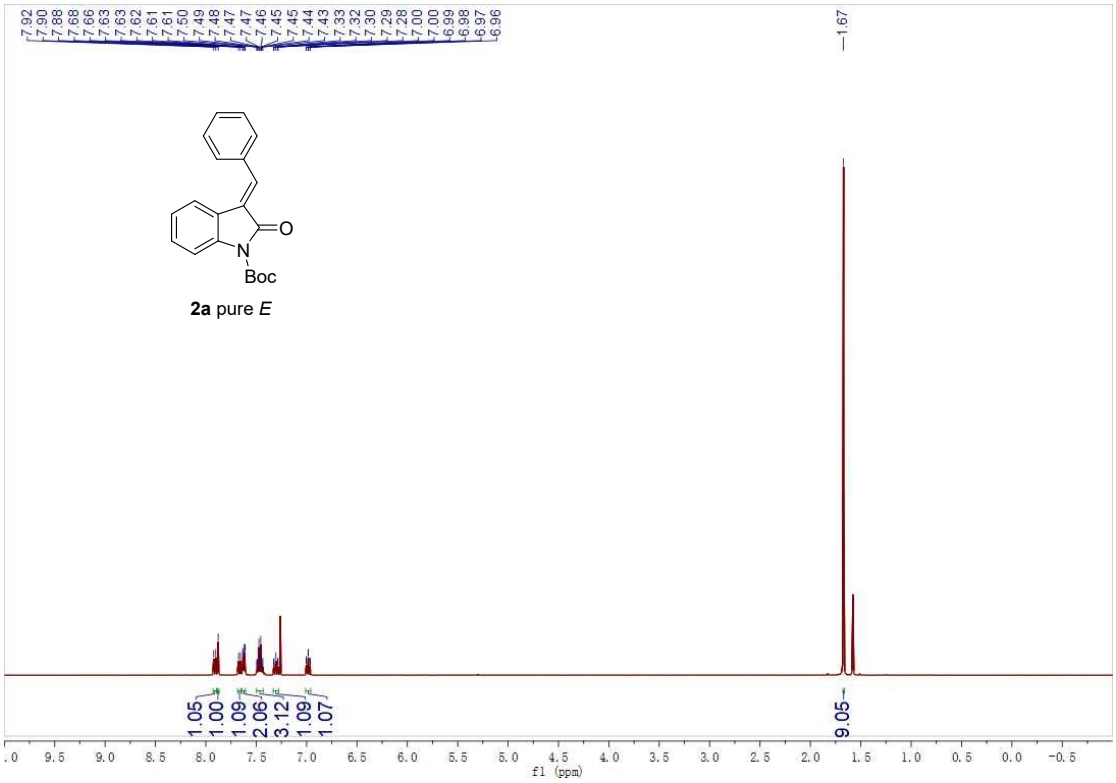
[a] Reactions were performed with **1b** (0.15 mmol), **2a** (0.1 mmol), $Pd_2(dba)_3$•$CHCl_3$ (5 mol%), and **L9** (15 mol %) in THF (1.0 mL) at 70 ºC for 48 h under an argon atmosphere.

[b] Isolated yield.

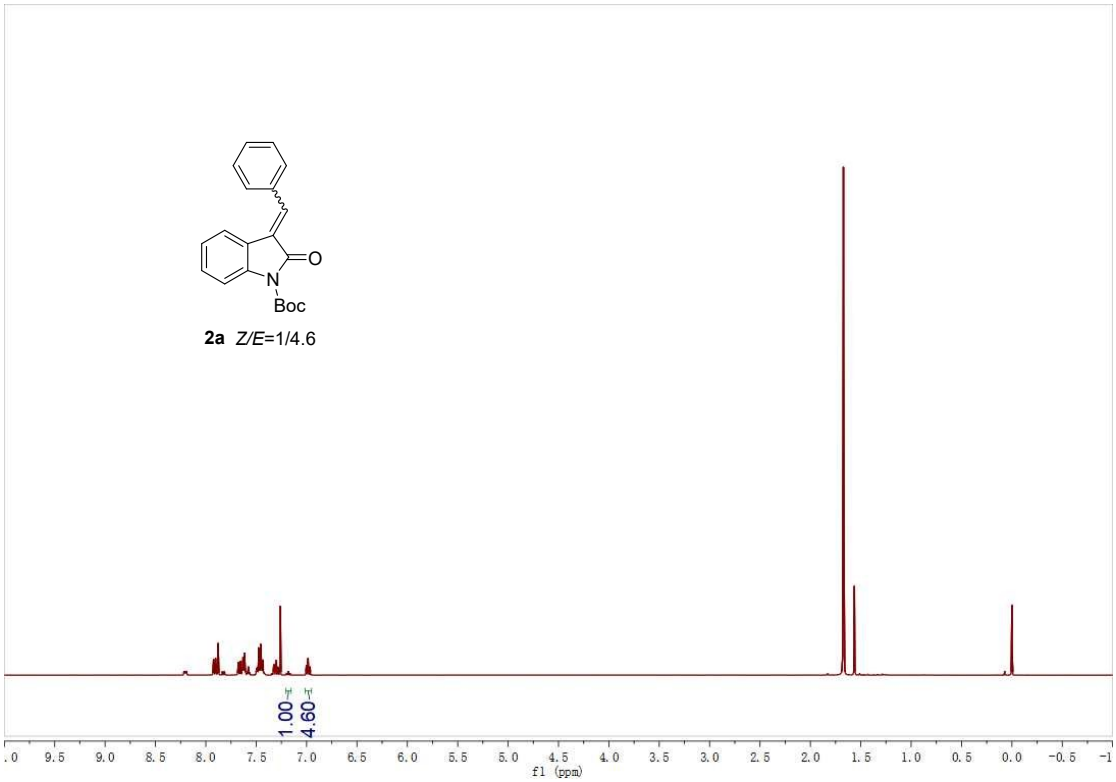
[c] *dr* values were determined by crude ^1H NMR analysis.

[d] *ee* values were determined by chiral HPLC analysis.

Figure S1. NMR spectra of **2a**



2a pure *E*



2a *Z*/*E*=1/4.6

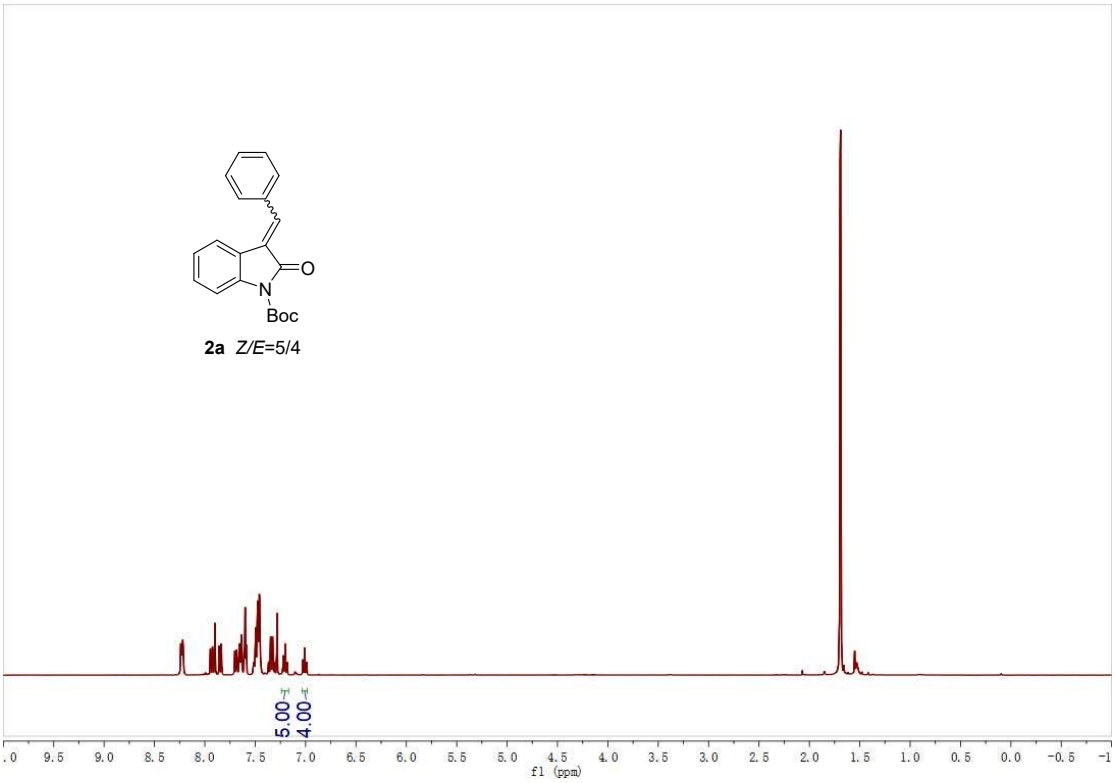
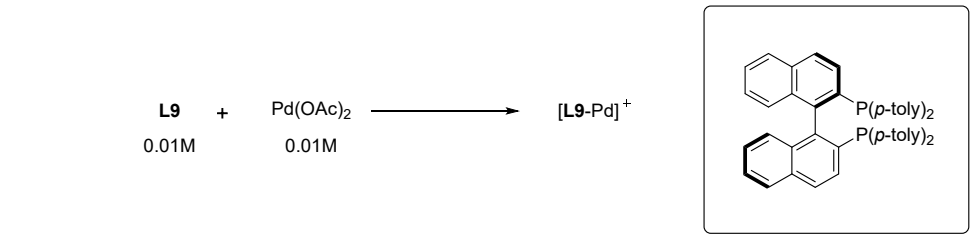
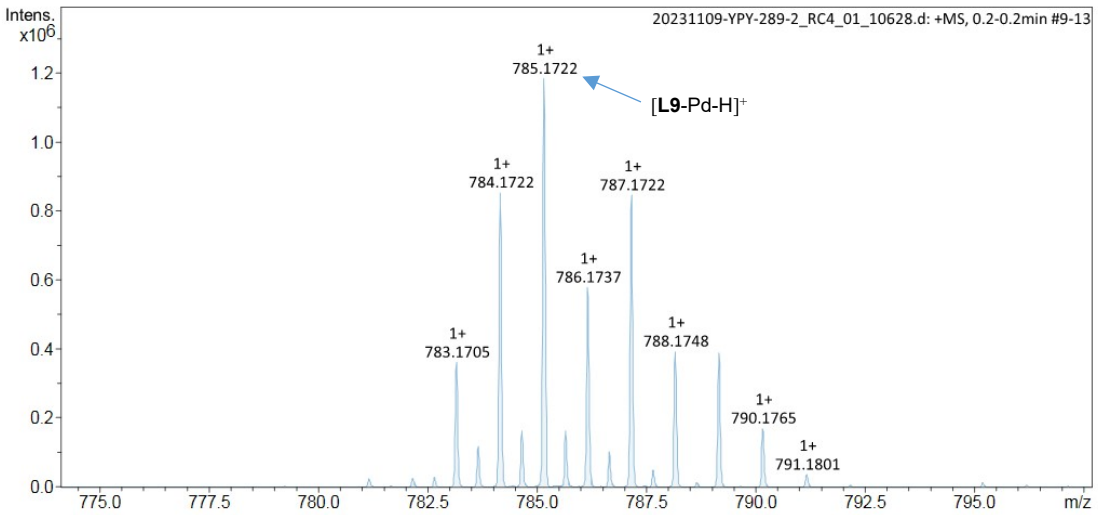


Figure S2. HRMS analysis of [Pd-**L9**]$^{+}$





2. General information

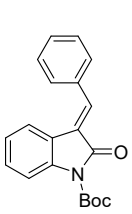
Unless otherwise noted, all reactions were carried out in oven-dried glassware under N_2 atmosphere using standard Schlenk techniques. Column chromatography was performed over silica gel (200-300 mesh). Reactions were monitored by TLC, GC-MS, and NMR. Reactions employing elevated temperatures were performed using heating mantles.

Commercial reagents were obtained from Adamas, Bide, Jiuding, Leyan, and TCI and used as received. When necessary, solvents were distilled and stored over 4Å molecular sieves.

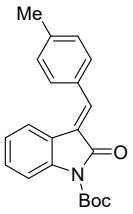
^{1}H NMR spectra were recorded with a Bruker AM400 spectrometer, and chemical shifts (in ppm) were referenced from the residual protium in $CDCl_3$ (δ = 7.26 ppm). Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qd = quartet of doublet, m = multiplet), coupling constant (s) in Hertz, integration]. ^{13}C {^{1}H} NMR spectra were obtained using the same NMR spectrometer and were calibrated with $CDCl_3$ (δ = 77.0 ppm). HRMS were recorded on a Bruker microTOF spectrometer using an electrospray ionization source (ESI). IR data were obtained with a Thermo Fisher Scientific FT-IR. Melting point (MP) was obtained with Hanon MP-430. All HPLC analyses were performed on an Agilent Technologies 1220 system with chiralcel IC HPLC column.

3. General Procedures for the Synthesis of the substrates

3.1 Preparation of 2a-2u



2a



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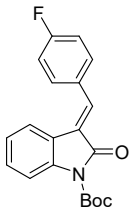

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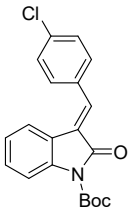

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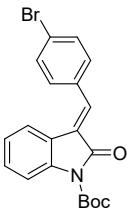

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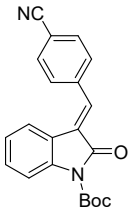

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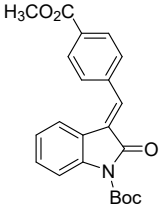

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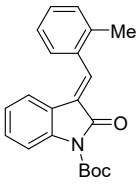

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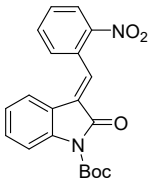

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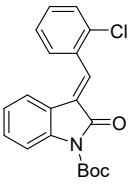

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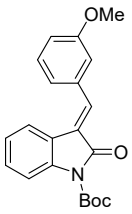

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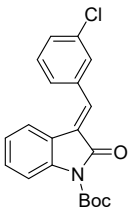

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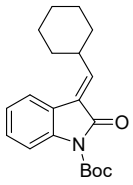

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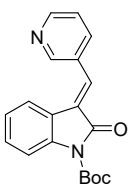

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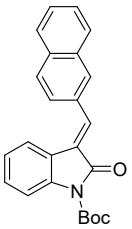

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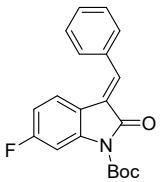

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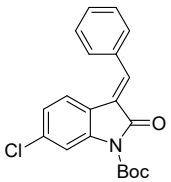

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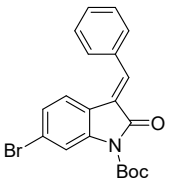

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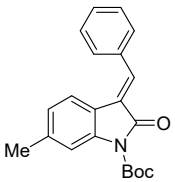

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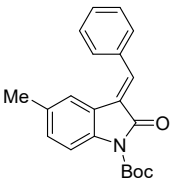

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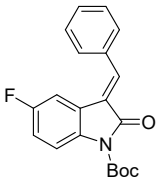

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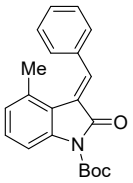

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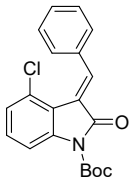

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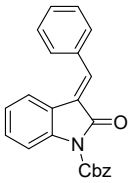
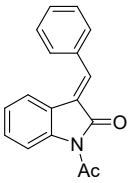
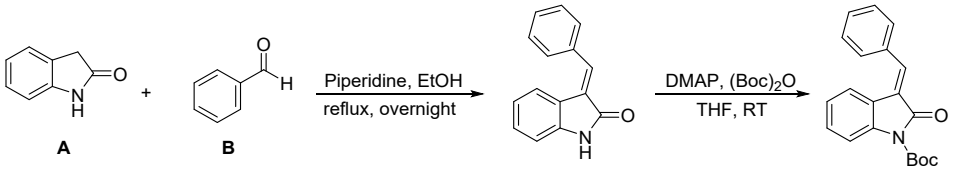


2x



2y

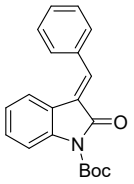
Preparation of the *N*-Boc protected Alkylidene Oxindoles[1]



A **B**

To oxindole **A** (20 mmol, 1 eq) and aldehyde **B** (24 mmol, 1.2 eq) in EtOH (30 mL) was added piperidine (2 mmol, 0.1 eq). After refluxing for 8 hours, the reaction was cooled to room temperature. Crude product was collected by flash filtration. The solid (5mmol) was dissolved by THF (50 mL), then DMAP (0.5 mmol) and $(Boc)_2O$ (7.5 mmol) were added. After stirring for 1 hour, the reaction was quenched by addition of 50 mL of cold water. The organic layer was then washed with cold water and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated. Crude product was purified by EtOH recrystallization to give the corresponding products.

2a-2u

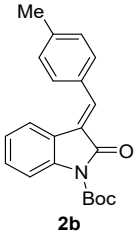


2a

***tert*-butyl (*E*)-3-benzylidene-2-oxoindoline-1-carboxylate (2a)**

Yellow solid, yield 63% (1.01 g, 3.1 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.2 Hz, 1H), 7.88 (s, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.62 (dd, J = 7.1, 1.2 Hz, 2H), 7.50 – 7.42 (m, 3H), 7.34 – 7.28 (m, 1H), 6.99 (td, J = 7.7, 1.0 Hz, 1H), 1.67 (s, 9H).



2b

***tert*-butyl (*E*)-3-(4-methylbenzylidene)-2-oxoindoline-1-carboxylate (2b)**

Yellow solid, yield 33% (0.56 g, 1.7 mmol), purified by EtOH recrystallization.

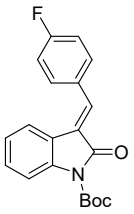
Mp 97.1 - 98.0 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.1 Hz, 1H), 7.85 (s, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.33 – 7.26 (m, 3H), 7.00 (td, J = 7.7, 1.0 Hz, 1H), 2.43 (s, 3H), 1.67 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 149.3, 140.3, 139.8, 138.7, 131.6, 129.8, 129.4, 129.3, 125.3, 123.6, 122.2, 121.7, 115.1, 84.2, 28.1, 21.6.

HRMS-ESI (positive): M = $C_{21}H_{21}NNaO_3$, calculated (M+Na) m/z: 358.1414, found: 358.1420.

IR (cm^{-1}): 3045, 2965, 1775, 1463, 1155, 746.

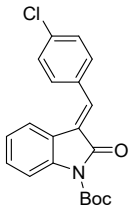


2c

***tert*-butyl (*E*)-3-(4-fluorobenzylidene)-2-oxoindoline-1-carboxylate (2c)**

Yellow solid, yield 62% (1.06 g, 3.1 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.1 Hz, 1H), 7.81 (s, 1H), 7.66 – 7.59 (m, 3H), 7.35 – 7.28 (m, 1H), 7.21 – 7.12 (m, 2H), 7.00 (td, J = 7.7, 0.9 Hz, 1H), 1.67 (s, 9H).

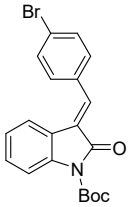


2d

***tert*-butyl (*E*)-3-(4-chlorobenzylidene)-2-oxoindoline-1-carboxylate (2d)**

Yellow solid, yield 25% (0.45 g, 1.3 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.2 Hz, 1H), 7.78 (s, 1H), 7.61 (d, J = 7.5 Hz, 1H), 7.56 (d, J = 8.4 Hz, 2H), 7.46 – 7.42 (m, 2H), 7.35 – 7.29 (m, 1H), 7.00 (td, J = 7.7, 0.9 Hz, 1H), 1.67 (s, 9H).

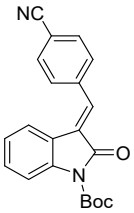


2e

***tert*-butyl (*E*)-3-(4-bromobenzylidene)-2-oxoindoline-1-carboxylate (2e)**

Yellow solid, yield 38% (0.75 g, 1.9 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.2 Hz, 1H), 7.76 (s, 1H), 7.61 (d, J = 8.4 Hz, 3H), 7.49 (d, J = 8.3 Hz, 2H), 7.35 – 7.28 (m, 1H), 7.00 (td, J = 7.7, 0.9 Hz, 1H), 1.67 (s, 9H).



2f

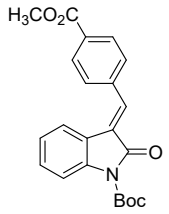
***tert*-butyl (*E*)-3-(4-cyanobenzylidene)-2-oxoindoline-1-carboxylate (2f)**

Yellow solid, yield 47% (0.82 g, 2.4 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.2 Hz, 1H), 7.80 – 7.74 (m, 3H), 7.71 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 7.5 Hz, 1H), 7.37 – 7.32 (m, 1H), 7.00 (td, J = 7.7, 0.9 Hz, 1H), 1.67 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 149.0, 140.5, 139.3, 134.7, 132.5, 131.0, 129.5, 128.3, 123.9, 122.4, 120.5, 118.3, 115.4, 112.9, 84.5, 28.0.

HRMS-ESI (positive): M = $C_{21}H_{18}N_2O_3$, calculated (M+Na) m/z: 369.1210, found: 369.1206.



2g

***tert*-butyl(*E*)-3-(4-(methoxycarbonyl)benzylidene)-2-oxoindoline-1-carboxylate (2g)**

Yellow solid, yield 53% (1.00 g, 2.6 mmol), purified by EtOH recrystallization.

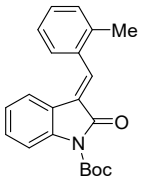
Mp 125.5 - 126.0 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.3 Hz, 2H), 7.91 (d, J = 8.2 Hz, 1H), 7.85 (s, 1H), 7.67 (d, J = 8.1 Hz, 2H), 7.54 (d, J = 7.6 Hz, 1H), 7.35 – 7.29 (m, 1H), 6.98 (td, J = 7.7, 0.9 Hz, 1H), 3.96 (s, 3H), 1.67 (d, J = 3.1 Hz, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 166.2, 149.1, 140.3, 139.2, 136.3, 131.6, 130.9, 130.5, 129.9, 129.1, 128.9, 127.5, 123.8, 122.5, 121.0, 115.3, 84.4, 52.3, 28.1.

HRMS-ESI (positive): M = $C_{22}H_{22}NO_5$, calculated (M+H) m/z: 380.1492, found: 380.1489.

IR (cm^{-1}): 3026, 2984, 1717, 1461, 1152, 780.



2h

***tert*-butyl (*E*)-3-(2-methylbenzylidene)-2-oxoindoline-1-carboxylate (2h)**

Yellow solid, yield 63% (1.06 g, 3.2 mmol), purified by EtOH recrystallization.

Mp 101.1 - 101.6 ºC.

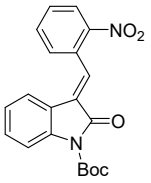
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.89 (m, 2H), 7.55 (d, J = 7.5 Hz, 1H), 7.40 – 7.35 (m, 1H), 7.35 – 7.30 (m, 3H), 7.29 (dd, J = 4.4, 3.1 Hz, 1H), 6.96 (td, J = 7.7, 0.9 Hz, 1H), 2.36 (s, 3H), 1.70 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 149.4, 139.9, 137.6, 137.3, 133.9, 130.6, 129.9, 129.6, 128.1, 126.7, 125.8, 123.8, 122.5, 121.6, 115.1, 84.2, 28.1, 19.9.

HRMS-ESI (positive): M = $C_{21}H_{21}NNaO_3$, calculated (M+Na) m/z: 358.1414,

found: 358.1409.

IR (cm^{-1}): 3012, 2985, 1724, 1460, 1152, 747.

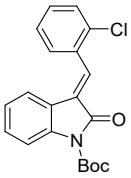


2i

***tert*-butyl (*E*)-3-(2-nitrobenzylidene)-2-oxoindoline-1-carboxylate (2i)**

Yellow solid, yield 49% (0.83 g, 2.3 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, J = 7.1, 2.5 Hz, 1H), 8.09 (s, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.74 (dd, J = 10.8, 4.1 Hz, 1H), 7.70 – 7.62 (m, 2H), 7.29 (ddd, J = 8.6, 5.3, 3.6 Hz, 1H), 6.92 – 6.84 (m, 2H), 1.67 (s, 9H).

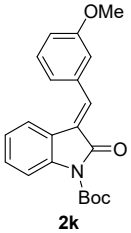


2j

***tert*-butyl (*E*)-3-(2-chlorobenzylidene)-2-oxoindoline-1-carboxylate (2j)**

Yellow solid, yield 54% (0.96 g, 2.7 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 2H), 7.66 (dd, J = 7.5, 1.6 Hz, 1H), 7.52 (dd, J = 7.9, 1.2 Hz, 1H), 7.40 (td, J = 7.7, 1.8 Hz, 1H), 7.37 – 7.28 (m, 3H), 6.95 (td, J = 7.7, 0.9 Hz, 1H), 1.67 (s, 9H).



2k

***tert*-butyl (*E*)-3-(3-methoxybenzylidene)-2-oxoindoline-1-carboxylate (2k)**

Yellow solid, yield 26% (0.46 g, 1.3 mmol), purified by EtOH recrystallization.

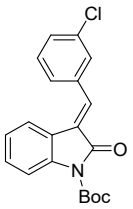
Mp 85.8 - 86.7 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.2 Hz, 1H), 7.84 (s, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.30 (t, J = 7.9 Hz, 1H), 7.20 (d, J = 7.5 Hz, 1H), 7.12 (s, 1H), 6.99 (t, J = 8.2 Hz, 2H), 3.83 (s, 3H), 1.67 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 159.7, 149.3, 140.0, 138.1, 135.9, 130.0, 129.8, 126.3, 123.7, 122.6, 121.5, 121.4, 115.7, 115.1, 114.1, 84.2, 55.3, 28.1.

HRMS-ESI (positive): M = $C_{21}H_{21}NNaO_4$, calculated (M+Na) m/z: 374.1363, found: 374.1358.

IR (cm^{-1}): 3055, 2977, 1722, 1457, 1151, 788.



2l

***tert*-butyl (*E*)-3-(3-chlorobenzylidene)-2-oxoindoline-1-carboxylate (2l)**

Yellow solid, yield 30% (0.53 g, 1.5 mmol), purified by EtOH recrystallization.

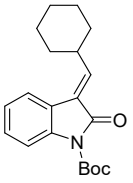
Mp 108.4 - 109.0 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.1 Hz, 1H), 7.77 (s, 1H), 7.57 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 3.0 Hz, 1H), 7.41 (dd, J = 3.8, 1.5 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.05 – 6.97 (m, 1H), 1.67 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 149.2, 140.3, 136.4, 136.0, 134.8, 130.5, 130.1, 129.7, 128.8, 127.2, 127.1, 123.8, 122.4, 121.0, 115.3, 84.4, 28.1.

HRMS-ESI (positive): M = $C_{20}H_{18}ClNNaO_3$, calculated (M+Na) m/z: 378.0867, found: 378.0875.

IR (cm^{-1}): 3060, 2965, 1775, 1463, 1155, 746.



2m

***tert*-butyl (*E*)-3-(cyclohexylmethylene)-2-oxoindoline-1-carboxylate (2m)**

White solid, yield 15% (0.24 g, 0.7 mmol), purified by EtOH recrystallization.

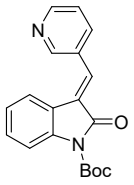
Mp 105.6 - 106.4 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 9.9 Hz, 1H), 3.02 – 2.85 (m, 1H), 1.83 (dd, *J* = 15.8, 6.8 Hz, 4H), 1.74 (d, *J* = 12.5 Hz, 1H), 1.64 (s, 9H), 1.45 – 1.25 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 149.4, 148.4, 139.4, 128.9, 124.8, 124.0, 123.0, 122.3, 115.1, 84.0, 38.0, 31.4, 28.1, 25.7, 25.4.

HRMS-ESI (positive): M = $C_{22}H_{22}NO_5$, calculated (M+H) m/z: 328.1907, found: 328.1903.

IR (cm^{-1}): 3084, 2926, 1753, 1464, 1158, 739.



2n

***tert*-butyl (*E*)-2-oxo-3-(pyridin-3-ylmethylene)indoline-1-carboxylate (2n)**

Yellow solid, yield 31% (0.50 g, 1.6 mmol), purified by EtOH recrystallization.

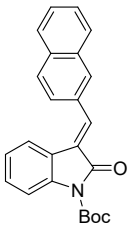
Mp 131.6 - 132.3 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 2.2 Hz, 1H), 8.67 (dd, *J* = 4.8, 1.4 Hz, 1H), 7.93 – 7.88 (m, 2H), 7.78 (s, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.42 (dd, *J* = 7.8, 4.9 Hz, 1H), 7.37 – 7.30 (m, 1H), 6.99 (td, *J* = 7.7, 0.9 Hz, 1H), 1.67 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 150.4, 149.8, 149.1, 140.4, 136.2, 133.5, 130.7, 130.7, 128.1, 123.9, 123.5, 122.2, 120.9, 115.4, 84.4, 28.1.

HRMS-ESI (positive): M = $C_{19}H_{19}N_2O_3$, calculated (M+H) m/z: 323.1390, found: 323.1382.

IR (cm^{-1}): 3055, 2975, 1721, 1459, 1154, 743.



2o

***tert*-butyl (*E*)-3-(naphthalen-2-ylmethylene)-2-oxoindoline-1-carboxylate (2o)**

Yellow solid, yield 26% (0.46 g, 1.2 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.

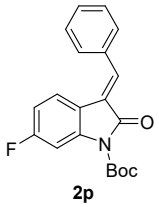
Mp 98.8 - 99.4 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.11 (s, 1H), 8.03 (s, 1H), 7.90 (ddd, *J* = 14.1, 8.9, 4.8 Hz, 4H), 7.72 (t, *J* = 7.2 Hz, 2H), 7.56 (p, *J* = 8.1 Hz, 2H), 7.32 (t, *J* = 7.9 Hz, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 1.69 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.7, 149.3, 140.1, 138.3, 133.8, 133.0, 132.1, 130.0, 129.3, 128.4, 128.4, 127.9, 127.4, 126.8, 126.2, 126.1, 123.7, 122.3, 121.6, 115.2, 84.2, 28.1.

HRMS-ESI (positive): M = $C_{24}H_{21}NNaO_3$, calculated (M+Na) m/z: 394.1414, found: 394.1411.

IR (cm^{-1}): 3052, 2976, 1717, 1462, 1159, 740.



2p

***tert*-butyl (*E*)-3-benzylidene-6-fluoro-2-oxoindoline-1-carboxylate (2p)**

Yellow solid, yield 74% (1.26 g, 3.7 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.

Mp 159.0 - 159.8 ºC.

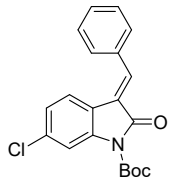
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.87 (m, 2H), 7.61 – 7.57 (m, 2H), 7.52 – 7.44 (m, 3H), 7.35 (dd, *J* = 8.8, 2.7 Hz, 1H), 7.01 (td, *J* = 8.9, 2.7 Hz, 1H), 1.66 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 159.1 (d, *J* = 241.90), 149.2, 139.8, 136.1 (d, *J* = 2.11), 134.0, 132.3, 130.2, 129.0, 128.9, 125.6 (d, *J* = 3.00), 122.7 (d, *J* = 8.95), 116.4 (d, *J* = 23.35), 116.3 (d, *J* = 7.97), 109.4 (d, *J* = 25.81), 84.4, 53.4, 28.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -118.25.

HRMS-ESI (positive): M = $C_{20}H_{18}FNNaO_3$, calculated (M+Na) m/z: 362.1163, found: 362.1163.

IR (cm^{-1}): 3063, 2986, 1721, 1466, 1145, 710.

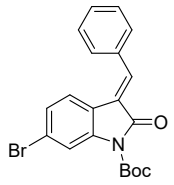


2q

***tert*-butyl (*E*)-3-benzylidene-6-chloro-2-oxoindoline-1-carboxylate (2q)**

Yellow solid, yield 70% (1.24 g, 3.5 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.55 (s, 1H), 7.52 (d, *J* = 6.8 Hz, 2H), 7.41 (q, *J* = 5.8 Hz, 3H), 7.18 (d, *J* = 8.6 Hz, 1H), 1.58 (s, 9H).

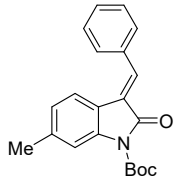


2r

***tert*-butyl (*E*)-3-benzylidene-6-bromo-2-oxoindoline-1-carboxylate (2r)**

Yellow solid, yield 68% (1.36 g, 3.4 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.80 (dd, *J* = 13.8, 5.4 Hz, 2H), 7.60 (dd, *J* = 7.1, 1.3 Hz, 2H), 7.53 – 7.46 (m, 3H), 7.42 (dd, *J* = 8.7, 2.1 Hz, 1H), 1.66 (s, 9H).



2s

***tert*-butyl (*E*)-3-benzylidene-6-methyl-2-oxoindoline-1-carboxylate(2s)**

Yellow solid, yield 75% (1.25 g, 3.5 mmol), purified by EtOH recrystallization.

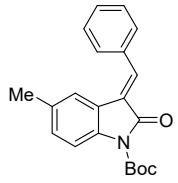
Mp 134.5 – 135.4 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 2H), 7.78 – 7.70 (m, 2H), 7.44 – 7.38 (m, 3H), 7.21 (t, *J* = 7.9 Hz, 1H), 6.97 (d, *J* = 7.7 Hz, 1H), 2.63 (s, 3H), 1.65 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 149.4, 141. 7, 139.1, 133.9, 133.1, 131.4, 129.9, 128.5, 127.9, 127.1, 126.9, 121.6, 112.6, 84.1, 28.1, 22.0.

HRMS-ESI (positive): $C_{21}H_{21}NNaO_3$, calculated (M+Na) m/z: 358.1423, found: 358.1429.

IR (cm^{-1}): 3054,1721, 1436, 1243,1121, 734.



2t

***tert*-butyl (*E*)-3-benzylidene-5-methyl-2-oxoindoline-1-carboxylate(2t)**

Yellow solid, yield 72% (1.20 g, 3.6 mmol), purified by EtOH recrystallization.

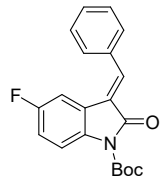
Mp 157.5 – 158.8 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.63 (dd, *J* = 7.1, 1.2 Hz, 2H), 7.50 – 7.42 (m, 4H), 7.11 (dd, *J* = 8.3, 0.9 Hz, 1H), 2.22 (s, 3H), 1.67 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 149.3, 137.9, 137.8, 134.6, 133.1, 130.6, 129.7, 129.1, 128.6, 126.2, 122.8, 121.4, 114.9, 84.0, 28.1, 21.1.

HRMS-ESI (positive): M = $C_{21}H_{21}NNaO_3$, calculated (M+Na) m/z: 358.1421, found: 358.1427.

IR (cm^{-1}): 2983,1723, 1332, 1157, 757, 697.



2u

***tert*-butyl (*E*)-3-benzylidene-5-fluoro-2-oxoindoline-1-carboxylate (2u)**

Yellow solid, yield 52% (0.88 g, 2.6 mmol), purified by EtOH recrystallization.

Mp 160.1 – 161.3 ºC.

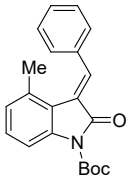
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, J = 9.7, 5.5 Hz, 2H), 7.62 – 7.55 (m, 2H), 7.52 – 7.43 (m, 3H), 7.35 (dd, J = 8.8, 2.7 Hz, 1H), 7.00 (td, J = 8.9, 2.7 Hz, 1H), 1.66 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 149.4, 141. 7, 139.1, 133.9, 133.1, 131.4, 129.9, 128.5, 127.9, 127.1, 126.9, 121.6, 112.6, 84.1, 28.1, 22.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -118.23.

HRMS-ESI (positive): M = $C_{20}H_{28}FNNaO_3$, calculated (M+Na) m/z: 362.1263, found: 362.1267.

IR (cm^{-1}): 3081,1725, 1336, 1147, 737, 621.



2v

***tert*-butyl (*E*)-3-benzylidene-4-methyl-2-oxoindoline-1-carboxylate(2v)**

Yellow solid, yield 72% (1.20 g, 3.6 mmol), purified by EtOH recrystallization.

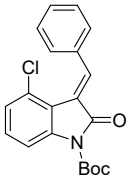
Mp 178.5 – 179.3 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.79 (d, J = 8.3 Hz, 1H), 7.63 (dd, J = 7.1, 1.2 Hz, 2H), 7.50 – 7.43 (m, 4H), 7.11 (dd, J = 8.3, 0.9 Hz, 1H), 2.22 (s, 3H), 1.67 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 149.3, 137.9, 137.8, 134.6, 133.1, 130.6, 129.7, 129.1, 128.6, 126.2, 122.8, 121.4, 114.9, 84.0, 28.1, 21.1.

HRMS-ESI (positive): M = $C_{21}H_{21}NNaO_3$, calculated (M+Na) m/z: 358.1429, found: 358.1432.

IR (cm^{-1}): 3201,1745, 1224, 1163, 734, 654.



2w

***tert*-butyl (*E*)-3-benzylidene-4-chloro-2-oxoindoline-1-carboxylate(2w)**

Yellow solid, yield 79% (1.41 g, 3.9 mmol), purified by EtOH recrystallization.

Mp 122.1 – 123.4 ºC.

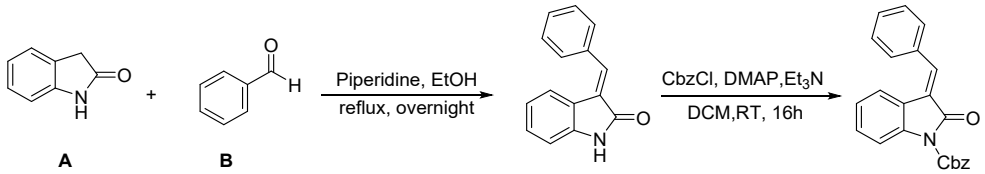
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.92 (dd, *J* = 6.5, 2.7 Hz, 2H), 7.74 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.35 (dd, *J* = 5.0, 1.8 Hz, 3H), 7.20 – 7.11 (m, 2H), 1.57 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 149.2, 143.9, 140.1, 133.5, 131.8, 130.6, 129.0, 128.5, 128.0, 126.1, 124.1, 120.2, 113.2, 84.6, 28.1.

HRMS-ESI (positive): M = $C_{20}H_{18}ClNNaO_3$, calculated (M+Na) m/z: 378.0821, found: 378.0823.

IR (cm^{-1}): 3066,1729, 1442, 1251,1130, 754.

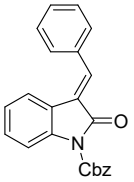
Preparation of the *N*-Cbz protected Alkylidene Oxindoles.[3]



A **B**

To oxindole **A** (20 mmol, 1 eq.) and aldehyde **B** (24 mmol, 1.2 eq.) in EtOH (30 mL) was added piperidine (2 mmol, 0.1 eq.). After refluxing for 8 hours, the reaction was cooled to room temperature. Crude product was collected by flash filtration. 4 mmol fraction of the crude benzylideneoxindole was diluted in DCM (40 mL, 0.1 M), DMAP was added portionwise (1.02 g, 2.1 mmol, 2.1 equiv.) and Et_3N (1.2 mL, 2.1 mmol, 2.1 equiv.). After 5 min, CbzCl (1.2 mL,

2.1 mmol, 2.1 equiv.) was added dropwise at 0 ºC and stirred at rt. After full consumption of the starting material, monitored by TLC (usually after 16h), the reaction was quenched with water. The organic layer was washed with 2×100 mL of water. The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (PE/EA =10/1), giving the desired *N*-Cbz protected 3-benzyloxindole in 29% yield.



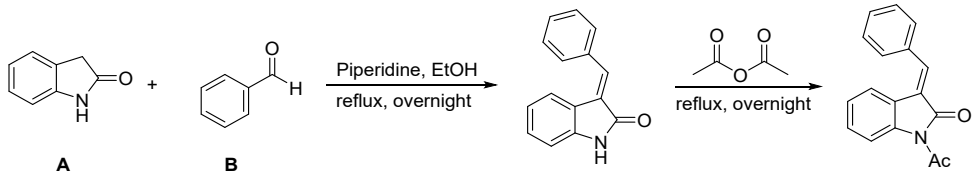
2x

benzyl (*E*)-3-benzylidene-2-oxoindoline-1-carboxylate (2x)

Yellow solid, yield 27% (0.40 g, 1.1 mmol), The crude product was purified by column chromatography (PE/EA =10/1), giving the desired *N*-Cbz protected 3-benzyloxindole. The spectroscopic data corresponds to those previously reported in the literature.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.2 Hz, 1H), 7.91 (s, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.63 (d, J = 6.6 Hz, 2H), 7.55 (d, J = 7.5 Hz, 2H), 7.50 – 7.44 (m, 3H), 7.41 (t, J = 7.4 Hz, 2H), 7.36 (d, J = 7.1 Hz, 1H), 7.33 – 7.29 (m, 1H), 7.01 (t, J = 7.7 Hz, 1H), 5.49 (s, 2H).

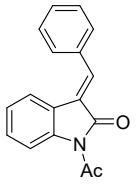
Preparation of the *N*-Ac protected Alkylidene Oxindoles.[4]



A **B**

To oxindole A (20 mmol, 1 eq.) and aldehyde B (24 mmol, 1.2 eq.) in EtOH (30 mL) was added piperidine (2 mmol, 0.1 eq.). After refluxing overnight, the reaction was cooled to room temperature. Crude product was collected by flash filtration. 4.9 mmol fraction of the crude benzylideneoxindole was diluted in acetic anhydride (24 mL) was heated to 100 ºC (bath temperature) with

stirring overnight, during which time the suspension cleared to a deep red-brown solution. The mixture was cooled and poured into 120 mL of H_2O. A yellow-orange product precipitated and was dissolved by shaking with 30 mL of MTBE/Et_2O = 1/1. The organic layer was separated, and the aqueous layer was extracted twice more with 30 mL of MTBE/Et_2O = 1/1. The combined organic extracts were washed with aqueous 2M NaOH (2 × 30 mL), H_2O (2 × 40 mL), and brine (1 × 30 mL), then dried over Na_2SO_4. Filtration and concentration under reduced pressure afforded a crude orange-red solid, which was recrystallized from EtOH, to afford the yellow needles in 38%.



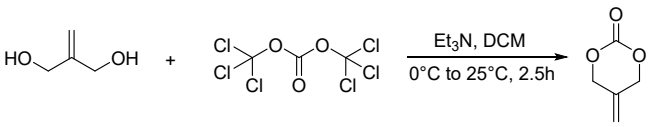
2y

(*E*)-1-acetyl-3-benzylideneindolin-2-one (2y)

Yellow needles, yield 38% (0.48 g, 1.8 mmol), purified by EtOH recrystallization. The spectroscopic data corresponds to those previously reported in the literature.[4]

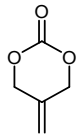
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.2 (d, J = 8.2 Hz, 1H), 7.8 (s, 1H), 7.6 (d, J = 7.8 Hz, 1H), 7.6 (d, J = 6.4 Hz, 2H), 7.4 (q, J = 5.9 Hz, 3H), 7.2 (t, J = 7.9 Hz, 1H), 6.9 (t, J = 7.6 Hz, 1H), 2.7 (s, 3H).

3.2 Preparation of 1a[5]



According to a previous reference: A solution of triphosgene (1.48 g, 5.0 mmol) in DCM (50.0 mL) was slowly added to a solution of 2-methylenepropane-1,3-diol (2.2 g, 25 mmol) and triethylamine (34.8 mL, 250 mmol) in DCM (250 mL) at 0 ºC over 30 min. The resulting mixture was stirred for 2 h while gradually raising the temperature to 20 ºC. The reaction was quenched with NH_4Cl aq and extracted with DCM. The organic layer was dried over Na_2SO_4, filtered,

and concentrated under vacuum. The residue was chromatographed on silica gel with PE/EA = 2/1 to afford a white solid (1.2 g, 42% yield).

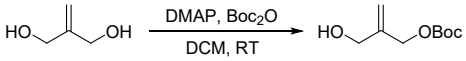


1a

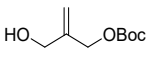
5-methylene-1,3-dioxan-2-one (1a)

White solid, yield 42% (1.2 g, 2.1 mmol), The crude product was purified by column chromatography (PE/EA = 2/1), giving the desired **1a**. The spectroscopic data corresponds to those previously reported in the literature.[5] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.32 – 5.28 (m, 2H), 4.84 (d, J = 1.2 Hz, 4H).

3.3 Preparation of 1b[6]



To a solution of freshly distilled 2-methylene propane-1,3-diol (2 g, 22.5 mmol), 4-DMAP (270 mg, 2.5 mmol) in DCM (20 mL), was added dropwise a solution of Boc_2O (0.8M in DCM, 5.7 mL) at 0 °C. After 16 h stirring at rt, the reaction mixture was quenched with HCl 1M and extracted with DCM. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (PE/EA = 4/1) afforded 1.84 g (43%) as a colourless oil.

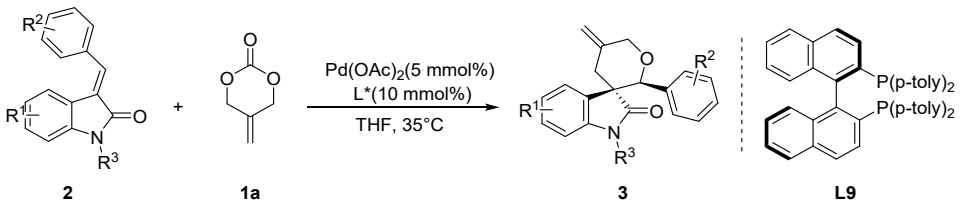


1b

***tert*-butyl (2-(hydroxymethyl)allyl) carbonate (1b)**

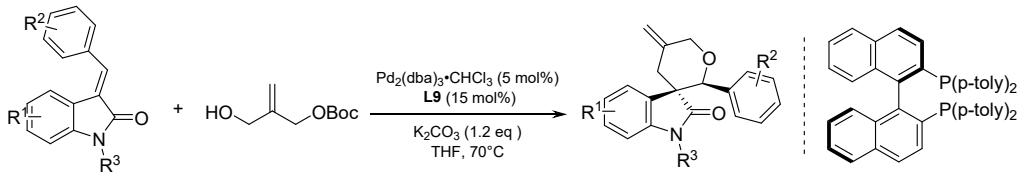
colourless oil, yield 43% (1.84 g, 9.7 mmol), The crude product was purified by column chromatography (PE/EA = 4/1), giving the desired **1b**. The spectroscopic data corresponds to those previously reported in the literature.[6] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.25 (s, 1H), 5.20 (s, 1H), 4.62 (s, 2H), 4.16 (s, 2H), 1.91 (s, 1H), 1.48 (s, 9H).

4. General procedure for the synthesis of products 3



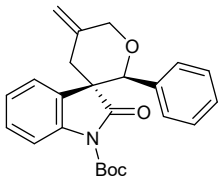
2 1a 3 L9

To an oven-dried Schlenk tube was added $Pd(OAc)_2$ (0.005 mmol), Chiral ligand **L9** (0.01 mmol) followed by the addition of THF (0.5 mL). The reaction mixture was allowed to stir for 30 mins at room temperature (25 ºC), to the reaction mixture was then added methyleneindolinones **2** (0.1 mmol), 2-Methylidenetrimethylene **1a** (0.15 mmol). The reaction mixture was allowed to stir at 35 ºC for 24 h and then directly purified by silica gel chromatography (PE/EA = 20/1 to 10/1) to provide the desired product **3**.



2 1b 3 L9

To an oven-dried Schlenk tube was added $Pd2(dba)_3•CHCl_3$ (0.005 mmol), Chiral ligand **L9** (0.015 mmol) followed by the addition of THF (0.5 mL). The reaction mixture was allowed to stir for 30 mins at room temperature (25 ºC), to the reaction mixture was then added methyleneindolinones **2** (0.1 mmol), 2-Methylidenetrimethylene **1a** (0.15 mmol), K_2CO_3 (0.12 mmol). The reaction mixture was allowed to stir at 70 ºC for 48 h and then directly purified by silica gel chromatography (PE/EA = 20/1 to 10/1) to provide the desired product **3**.



3a

***tert*-butyl(2'*S*,3*S*)-5'-methylene-2-oxo-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3a)**

Method A: **3a** (35.2 mg, 0.09 mmol) was obtained in 90% yield as a white solid. >20:1 *dr*, 90% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Method B: 35.1mg, 0.09mmol, yield 90%, >20:1 *dr*, 80% *ee.*

Mp 115.9 - 116.7°C.

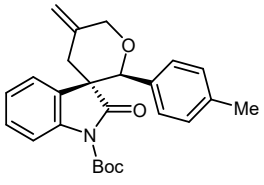
^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.67 (d, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.19 (td, *J* = 7.9, 1.3 Hz, 1H), 7.13 (dd, *J* = 10.9, 4.1 Hz, 1H), 7.06 (t, *J* = 7.2 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 2H), 6.89 (d, *J* = 7.4 Hz, 2H), 5.19 (s, 1H), 4.94 (s, 2H), 4.65 (d, *J* = 12.6 Hz, 1H), 4.46 (d, *J* = 12.6 Hz, 1H), 3.25 (d, *J* = 13.8 Hz, 1H), 2.46 (d, *J* = 13.8 Hz, 1H), 1.55 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 175.6, 148.5, 138.9, 138.2, 136.3, 128.25, 128.1, 127.8, 127.3, 126.5, 126.0, 123.6, 114.1, 113.5, 84.1, 83.7, 73.4, 54.8, 39.3, 28.0.

HRMS-ESI (positive): M = $C_{24}H_{25}NNaO_4$, calculated (M+Na) m/z: 414.1676, found: 414.1679.

IR (cm^{-1}): 3080, 1727, 1465, 1150, 750, 677.

$[\alpha]^{25}_D$ = - 62.77 (c = 0.64, $CHCl_3$).



3b

***tert*-butyl(2'*S*,3*S*)-5'-methylene-2-oxo-2'-(p-tolyl)-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3b)**

Method A: **3b** (26.6 mg, 0.066 mol) was obtained in 66% yield as a white liquid. >20:1 *dr*, 85% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Method B: 36.9mg, 0.091 mmol, yield 91%, >20:1 *dr*, 80% *ee.*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.62 (m, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.20 (td, *J* = 8.0, 1.3 Hz, 1H), 7.13 (dd, *J* = 10.9, 4.1 Hz, 1H), 6.78 (q, *J* = 8.3 Hz, 4H), 5.17 (s, 1H), 4.93 (s, 1H), 4.90 (s, 1H), 4.68 – 4.59 (m, 1H), 4.45 (d, *J* = 12.6 Hz, 1H), 3.23 (d, *J* = 13.8 Hz, 1H), 2.45 (d, *J* = 13.8 Hz, 1H), 2.16 (s, 3H), 1.55 (s, 9H).

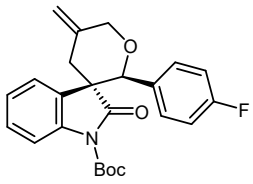
^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 148.5, 138.9, 138.2, 137.4, 133.3, 128.4, 128.0, 128.0, 126.4, 126.0, 123.6, 114.2, 113.4, 84.0, 83.7, 77.3, 77.0, 76.7, 73.4, 54.8, 39.4, 27.9, 21.0.

HRMS-ESI (positive): M = $C_{25}H_{27}NNaO_4$, calculated (M+Na) m/z: 432.1832, found: 432.1839.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 5.26 min (major), t_R = 6.43 min (minor).

IR (cm^{-1}): 2980, 1732, 1250, 1152, 754, 731.

$[\alpha]^{25}_D$ = - 60.35 (c = 0.35, $CHCl_3$).



3c

***tert*-butyl(2'*S*,3*S*)-2'-(4-fluorophenyl)-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3c)**

Method A: **3c** (36.3 mg, 0.089 mmol) was obtained in 89% yield as a yellow liquid. >20:1 *dr*, 80% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Method B: 34.7mg, 0.085 mmol, yield 85%, >20:1 *dr*, 77% *ee.*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.21 (td, *J* = 7.9, 1.4 Hz, 1H), 7.12 (td, *J* = 7.5, 1.0 Hz, 1H), 6.89 – 6.83 (m, 2H), 6.71 – 6.65 (m, 2H), 5.18 (d, *J* = 1.3 Hz, 1H), 4.94 (s, 1H), 4.91 (s, 1H), 4.64 (dd, *J* = 12.6, 1.5 Hz, 1H), 4.45 (d, *J* = 12.6 Hz, 1H), 3.23 (dd, *J* = 13.8, 1.1 Hz, 1H), 2.45 (dd, *J* = 13.8, 1.5 Hz, 1H), 1.56 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 162.2, 148.4, 138.8, 137.9, 132.2, 128.3,

128.3, 128.1, 125.9, 123.7, 114.3, 114.1, 113.6, 84.3, 83.0, 73.4, 54.7, 39.3, 28.0.

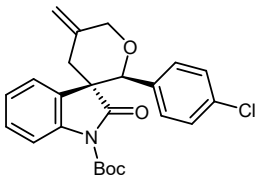
^{19}F NMR (376 MHz, $CDCl_3$) *δ* -114.09.

HRMS-ESI (positive): M = $C_{24}H_{24}FNNaO_4$, calculated (M+Na) m/z: 432.1582, found: 432.1585.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.47 min (major), t_R = 5.34 min (minor).

IR (cm^{-1}): 3076, 1733, 1251, 1152, 1090, 756.

[α]$^{25}_D$ = - 46.44 (c = 0.52, $CHCl_3$).



3d

***tert*-butyl(2'*S*,3*S*)-2'-(4-chlorophenyl)-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3d)**

Method A: **3d** (38.4 mg, 0.09 mmol) was obtained in 90% yield as a white solid. >20:1 *dr*, 87% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Method B: 38.6mg, 0.091mmol, yield 91%, >20:1 *dr*, 80% *ee.*

Mp 117.6 - 118.6°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.63 (d, *J* = 7.4 Hz, 1H), 7.48 (d, *J* = 8.1 Hz, 1H), 7.22 (dd, *J* = 11.3, 4.4 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.18 (s, 1H), 4.93 (s, 1H), 4.91 (s, 1H), 4.64 (d, *J* = 12.6 Hz, 1H), 4.45 (d, *J* = 12.6 Hz, 1H), 3.23 (d, *J* = 13.8 Hz, 1H), 2.45 (d, *J* = 13.8 Hz, 1H), 1.56 (s, 9H).

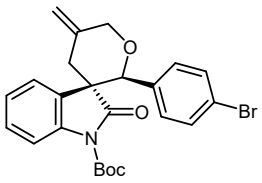
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 175.5, 148.3, 138.8, 137.8, 134.9, 133.6, 128.3, 127.9, 127.5, 125.9, 123.8, 114.3, 113.8, 84.4, 82.9, 73.4, 54.6, 39.3, 29.7, 28.0.

HRMS-ESI (positive): M = $C_{24}H_{24}ClNNaO_4$, calculated (M+Na) m/z: 448.1286, found: 448.1281.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.66 min (major), t_R = 5.82 min (minor).

IR (cm^{-1}): 2985, 1724, 1293, 1150, 756, 733.

$[\alpha]^{25}_D$ = - 51.00 (c = 0.68, $CHCl_3$).



3e

***tert*-butyl(2'*S*,3*S*)-2'-(4-bromophenyl)-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3e)**

Method A: **3e** (39.7 mg, 0.084 mmol) was obtained in 84% yield as a white solid. >20:1 *dr*, 87% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Method B: 30.7mg, 0.065 mmol, yield 65%, >20:1 *dr*, 78% *ee.*

Mp 126.8 - 127.4°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.63 (d, *J* = 6.9 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.24 – 7.19 (m, 1H), 7.12 (t, *J* = 7.4 Hz, 3H), 6.78 (d, *J* = 8.5 Hz, 2H), 5.18 (s, 1H), 4.93 (s, 1H), 4.89 (s, 1H), 4.63 (d, *J* = 12.7 Hz, 1H), 4.44 (d, *J* = 12.6 Hz, 1H), 3.22 (d, *J* = 13.8 Hz, 1H), 2.45 (d, *J* = 13.8 Hz, 1H), 1.56 (s, 9H).

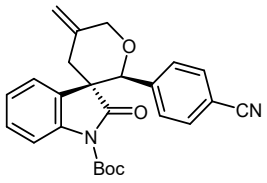
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 175.5, 148.3, 138.8, 137.7, 135.5, 130.4, 128.3, 128.2, 127.8, 125.9, 123.8, 121.9, 114.3, 113.8, 84.4, 83.0, 73.4, 54.6, 39.4, 28.0.

HRMS-ESI (positive): M = $C_{24}H_{24}BrNNaO_4$, calculated (M+Na) m/z: 492.0781, found: 492.0791.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.80 min (major), t_R = 6.08 min (minor).

IR (cm^{-1}): 2977, 1732, 1250, 1147, 752, 731.

$[\alpha]^{25}_D$ = - 46.63 (c = 0.73, $CHCl_3$).



3f

***tert*-butyl(2'*S*,3*S*)-2'-(4-cyanophenyl)-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3f)**

3f (36.6 mg, 0.088 mmol) was obtained in 88% yield as a white solid. >20:1 *dr*, 75% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 65.1 - 66.2°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.20 (td, *J* = 7.9, 1.4 Hz, 1H), 7.11 (td, *J* = 7.6, 1.0 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 2H), 5.20 (s, 1H), 4.98 (s, 1H), 4.95 (s, 1H), 4.65 (dd, *J* = 12.6, 1.4 Hz, 1H), 4.45 (d, *J* = 12.6 Hz, 1H), 3.23 (dd, *J* = 13.8, 0.9 Hz, 1H), 2.46 (dd, *J* = 13.8, 1.4 Hz, 1H), 1.56 (s, 9H).

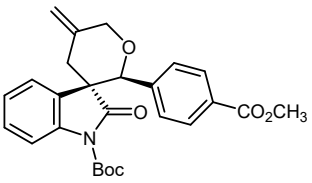
^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 148.2, 141.7, 138.5, 137.2, 131.0, 128.5, 127.3, 127.2, 125.8, 123.9, 118.5, 114.3, 114.1, 111.5, 84.6, 82.6, 73.2, 54.5, 39.4, 27.9.

HRMS-ESI (positive): M = $C_{25}H_{24}N_2NaO_4$, calculated (M+Na) m/z: 439.1628, found: 439.1628.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 10.68 min (major), t_R = 12.49 min (minor).

IR (cm^{-1}): 3081, 1751, 1251, 1149, 1092, 756.

$[\alpha]^{25}_D$ = - 42.04 (c = 0.66, $CHCl_3$).



3g

***tert*-butyl(2'*S*,3*S*)-2'-(4-(methoxycarbonyl)phenyl)-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3g)**

3g (37.8 mg, 0.084 mmol) was obtained in 84% yield as a white liquid. >20:1

dr, 85% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.69 – 7.62 (m, 3H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.18 (td, *J* = 7.9, 1.5 Hz, 1H), 7.11 (td, *J* = 7.5, 1.1 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 2H), 5.19 (s, 1H), 4.99 (s, 1H), 4.94 (s, 1H), 4.65 (dd, *J* = 12.6, 1.3 Hz, 1H), 4.45 (d, *J* = 12.6 Hz, 1H), 3.81 (s, 3H), 3.24 (d, *J* = 13.8 Hz, 1H), 2.45 (dd, *J* = 13.8, 1.3 Hz, 1H), 1.54 (s, 9H).

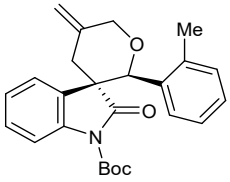
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 175.4, 166.7, 148.3, 141.5, 138.6, 137.6, 129.4, 128.6, 128.3, 127.7, 126.5, 125.9, 123.8, 114.2, 113.8, 84.4, 83.0, 73.3, 54.6, 52.0, 39.4, 27.9.

HRMS-ESI (positive): M = $C_{26}H_{27}NNaO_6$, calculated (M+Na) m/z: 472.1731, found: 472.1719.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 10.12 min (major), t_R = 14.07 min (minor).

IR (cm^{-1}): 2980, 1732, 1250, 1152, 754, 731.

$[\alpha]^{25}_D$ = - 42.6 (c = 0.77, $CHCl_3$).



3h

***tert*-butyl(2'*S*,3*S*)-5'-methylene-2-oxo-2'-(o-tolyl)-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3h)**

Method A: **3h** (21.9 mg, 0.054 mmol) was obtained in 54% yield as a yellow solid. >20:1 *dr*, 92% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 141.5 - 142.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.75 (d, *J* = 7.3 Hz, 1H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.32 – 7.22 (m, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.02 – 6.89 (m, 2H), 6.69 – 6.58 (m, 1H), 6.39 (d, *J* = 7.9 Hz, 1H), 5.21 (s, 1H), 5.19 (s, 1H), 4.97 (s, 1H), 4.64 (d, *J* = 12.7 Hz, 1H), 4.49 (d, *J* = 12.7 Hz, 1H), 3.29 (d, *J* = 13.9 Hz, 1H), 2.51 (t, *J* = 12.2 Hz, 1H), 2.38 (s, 3H), 1.50 (s, 9H).

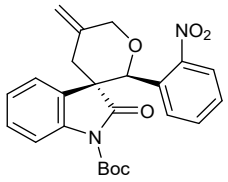
^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 148.5, 139.3, 138.4, 135.3, 134.3, 129.9, 128.5, 128.3, 127.8, 127.1, 126.3, 124.7, 123.7, 114.2, 113.4, 83.8, 79.5, 77.3, 77.0, 76.7, 73.8, 53.9, 39.6, 27.9, 19.9.

HRMS-ESI (positive): M = $C_{25}H_{27}NNaO_4$, calculated (M+Na) m/z: 428.1832, found: 428.1827.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.36 min (major), t_R = 4.75 min (minor).

IR (cm^{-1}): 3073, 1734, 1282, 1152, 751, 732.

$[\alpha]^{25}_D$ = - 26.44 (c = 0.40, $CHCl_3$).



3i

***tert*-butyl(2'*S*,3*S*)-5'-methylene-2'-(2-nitrophenyl)-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3i)**

3i (39.5 mg, 0.08 mmol) was obtained in 91% yield as a white solid. >20:1 *dr*, 80% *ee,* purified by silica gel column chromatography (PE/EA = 10/1).

Mp 119.0 - 119.5°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.64 (dd, *J* = 11.6, 4.6 Hz, 2H), 7.29 – 7.21 (m, 2H), 7.16 (td, *J* = 7.6, 1.0 Hz, 1H), 7.10 – 7.04 (m, 1H), 6.82 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.90 (s, 1H), 5.22 (s, 1H), 4.97 (s, 1H), 4.68 (d, *J* = 12.7 Hz, 1H), 4.59 (d, *J* = 12.8 Hz, 1H), 3.24 (dd, *J* = 13.9, 0.9 Hz, 1H), 2.48 (dd, *J* = 13.8, 1.0 Hz, 1H), 1.59 (s, 9H).

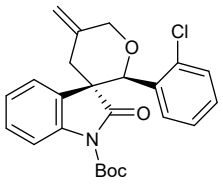
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 148.7, 148.5, 139.1, 137.6, 131.2, 129.7, 129.0, 128.7, 128.6, 127.6, 126.1, 123.8, 123.7, 114.4, 114.0, 84.4, 73.7, 54.3, 40.0, 27.8.

HRMS-ESI (positive): M = $C_{24}H_{24}N_2NaO_6$, calculated (M+Na) m/z: 459.1527, found: 459.1522.

HPLC (IC, *n*-hex/2-propanol = 80/20, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 10.53 min (major), t_R = 15.27 min (minor).

IR (cm^{-1}): 3078, 2980, 1727, 1534, 1152, 788, 692.

$[\alpha]^{25}_D$ = + 152.87 (c = 0.64, $CHCl_3$).



3j

***tert*-butyl(2'*R*,3*S*)-2'-(2-chlorophenyl)-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3j)**

3j (36.6 mg, 0.086 mmol) was obtained in 86% yield as a white solid. >20:1 *dr*, 60% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 134.8 - 135.9°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.72 (dd, J = 7.5, 0.8 Hz, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.27 (td, J = 7.9, 1.3 Hz, 1H), 7.18 (dtd, J = 8.3, 7.8, 0.9 Hz, 2H), 7.01 (td, J = 7.9, 1.6 Hz, 1H), 6.76 – 6.68 (m, 1H), 6.45 (dd, J = 8.0, 1.4 Hz, 1H), 5.51 (s, 1H), 5.19 (s, 1H), 4.99 (s, 1H), 4.66 – 4.58 (m, 1H), 4.51 (d, J = 12.7 Hz, 1H), 3.33 (d, J = 14.0 Hz, 1H), 2.51 (dd, J = 14.0, 1.0 Hz, 1H), 1.52 (s, 9H).

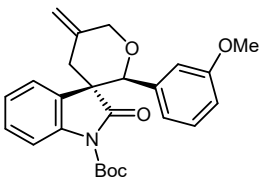
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 174.0, 148.7, 139.4, 138.3, 133.8, 132.7, 129.2, 128.9, 128.9, 128.5, 128.2, 126.2, 125.7, 123.7, 114.3, 113.6, 84.0, 79.1, 73.8, 53.6, 39.3, 28.0.

HRMS-ESI (positive): M = $C_{24}H_{24}ClNNaO_4$, calculated (M+Na) m/z: 448.1286, found: 448.1279.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.96 min (major), t_R = 6.16 min (minor).

IR (cm^{-1}): 3075, 1721, 1283, 1152, 845, 755.

$[\alpha]^{25}_D$ = - 10.38 (c = 0.68, $CHCl_3$).



3k

***tert*-butyl(2'*S*,3*S*)-2'-(3-methoxyphenyl)-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3k)**

Method A: **3k** (31.4 mg, 0.075 mmol) was obtained in 75% yield as a white solid. >20:1 *dr*, 86% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Method B: 38.3mg, yield 91%, >20:1 *dr*, 80% *ee.*

Mp 146.6 - 147.6°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.82 (d, *J* = 8.1 Hz, 1H), 7.47 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.31 (td, *J* = 8.1, 1.4 Hz, 1H), 7.10 (td, *J* = 7.6, 0.9 Hz, 1H), 5.02 (d, *J* = 1.2 Hz, 1H), 4.70 (s, 1H), 4.42 (dd, *J* = 12.3, 1.7 Hz, 1H), 4.18 (d, *J* = 12.3 Hz, 1H), 3.69 (d, *J* = 6.0 Hz, 1H), 2.92 (d, *J* = 13.4 Hz, 1H), 2.17 (dd, *J* = 13.4, 1.7 Hz, 1H), 1.64 (s, 9H), 1.55 – 1.43 (m, 4H), 1.16 (d, *J* = 10.4 Hz, 1H), 1.07 – 0.83 (m, 6H).

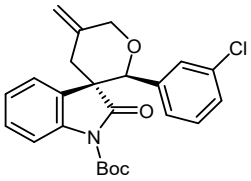
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 176.4, 149.1, 138.4, 138.3, 129.5, 127.9, 125.9, 123.9, 114.6, 112.7, 85.3, 84.4, 72.9, 52.6, 43.0, 40.7, 29.7, 29.0, 28.1, 26.1, 26.0, 25.8.

HRMS-ESI (positive): M = $C_{25}H_{27}NNaO_5$, calculated (M+Na) m/z: 444.1781, found: 444.1790.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 6.42 min (major), t_R = 8.28 min (minor).

IR (cm^{-1}): 3071, 1729, 1297, 1150, 1094, 755.

$[\alpha]^{25}_D$ = - 62.89 (c = 0.66, $CHCl_3$).



3l

***tert*-butyl(2'*S*,3*S*)-2'-(3-chlorophenyl)-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3l)**

3l (31.2 mg, 0.073 mmol) was obtained in 73% yield as a white solid. >20:1 *dr*, 83% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 129.5 - 130.4°C.

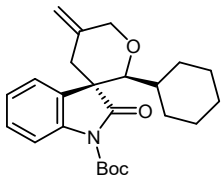
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.4 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.20 (dd, J = 11.3, 4.3 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.92 (t, J = 7.8 Hz, 2H), 6.79 (d, J = 7.7 Hz, 1H), 5.19 (s, 1H), 4.94 (s, 1H), 4.90 (s, 1H), 4.64 (d, J = 12.6 Hz, 1H), 4.44 (d, J = 12.6 Hz, 1H), 3.22 (d, J = 13.8 Hz, 1H), 2.45 (d, J = 13.8 Hz, 1H), 1.57 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 148.5, 138.7, 138.4, 137.7, 133.2, 128.5, 128.3, 127.9, 127.8, 126.7, 125.8, 124.6, 123.8, 114.1, 113.7, 84.3, 82.8, 73.3, 54.6, 39.2, 27.9.

HRMS-ESI (positive): M = $C_{24}H_{24}ClNNaO_4$, calculated (M+Na) m/z: 448.1286, found: 448.1279.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.31 min (major), t_R = 5.13 min (minor).

IR (cm^{-1}): 2979, 1732, 1253, 1148, 754, 730.



3m

***tert*-butyl(2'*S*,3*S*)-2'-cyclohexyl-5'-methylene-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3m)**

3m (32.3 mg, 0.081mmol) was obtained in 81% yield as a white liquid. >20:1 *dr*, 70% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.47 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.31 (td, *J* = 8.1, 1.4 Hz, 1H), 7.10 (td, *J* = 7.6, 0.9 Hz, 1H), 5.02 (d, *J* = 1.2 Hz, 1H), 4.70 (s, 1H), 4.42 (dd, *J* = 12.3, 1.7 Hz, 1H), 4.18 (d, *J* = 12.3 Hz, 1H), 3.69 (d, *J* = 6.0 Hz, 1H), 2.92 (d, *J* = 13.4 Hz, 1H), 2.17 (dd, *J* = 13.4, 1.7 Hz, 1H), 1.64 (s, 9H), 1.55 – 1.43 (m, 4H), 1.16 (d, *J* = 10.4 Hz, 1H), 1.07 – 0.83 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 149.1, 138.4, 138.3, 129.5, 127.9, 125.9, 123.9, 114.6, 112.7, 85.3, 84.4, 72.9, 52.6, 43.0, 40.7, 29.7, 29.0, 28.1, 26.1,

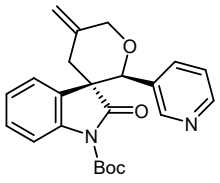
26.0, 25.8.

HRMS-ESI (positive): M = $C_{24}H_{31}NNaO_4$, calculated (M+Na) m/z: 420.2145, found: 420.2145.

HPLC (IC, *n*-hex/2-propanol = 99/1, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.67 min (major), t_R = 5.11 min (minor).

IR (cm^{-1}): 3550, 2927, 1733, 1283, 1152, 756.

[α]$^{25}_{D}$ = - 33.08 (c = 0.64, $CHCl_3$).



3n

***tert*-butyl(2'*S*,3*S*)-5'-methylene-2-oxo-2'-(pyridin-3-yl)-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3n)**

3n (36.1 mg, 0.092 mmol) was obtained in 92% yield as a white solid. >20:1 *dr*, 82% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 91.5 - 92.4°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.30 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.18 (d, *J* = 1.9 Hz, 1H), 7.65 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.20 (td, *J* = 7.9, 1.4 Hz, 1H), 7.14 (dt, *J* = 14.2, 4.6 Hz, 2H), 6.90 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.19 (s, 1H), 4.94 (s, 2H), 4.64 (d, *J* = 12.7 Hz, 1H), 4.44 (d, *J* = 12.6 Hz, 1H), 3.22 (d, *J* = 13.8 Hz, 1H), 2.47 (d, *J* = 13.8 Hz, 1H), 1.55 (s, 9H).

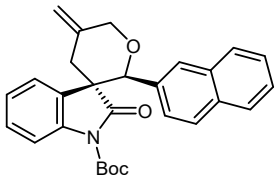
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 175.0, 149.2, 148.3, 148.0, 138.7, 137.5, 134.0, 132.0, 128.5, 127.4, 125.9, 123.9, 122.2, 114.3, 113.9, 84.4, 81.5, 73.3, 54.5, 39.3, 27.9.

HRMS-ESI (positive): M = $C_{23}H_{25}N_2O_4$, calculated (M+H) m/z: 393.1809, found: 393.1806.

HPLC (IC, *n*-hex/2-propanol = 99/1, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 15.77 min (minor), t_R = 16.84 min (major).

IR (cm^{-1}): 2979, 1756, 1283, 1152, 1092, 776.

[α]$^{25}_{D}$ = - 52.04 (c = 0.53, $CHCl_3$).



3o

***tert*-butyl(2'*S*,3*S*)-5'-methylene-2'-(naphthalen-2-yl)-2-oxo-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3o)**

Method A: **3o** (41.4 mg, 0.094 mmol) was obtained in 94% yield as a white solid. >20:1 *dr*, 86% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Method B: 40.2mg, yield 91%, >20:1 *dr*, 80% *ee.*

Mp 83.0 - 84.2°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.72 (m, 1H), 7.68 – 7.59 (m, 2H), 7.48 – 7.42 (m, 2H), 7.40 – 7.31 (m, 3H), 7.16 (dd, *J* = 5.5, 3.6 Hz, 2H), 6.98 (dd, *J* = 8.7, 0.9 Hz, 1H), 5.22 (s, 1H), 5.13 (s, 1H), 4.97 (s, 1H), 4.71 (d, *J* = 12.5 Hz, 1H), 4.53 (d, *J* = 12.6 Hz, 1H), 3.32 (d, *J* = 13.7 Hz, 1H), 2.50 (d, *J* = 13.7 Hz, 1H), 1.43 (s, 9H).

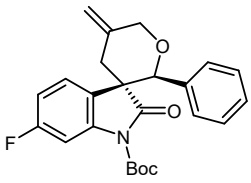
^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 148.3, 138.8, 138.1, 133.9, 132.8, 132.4, 128.2, 128.1, 128.0, 127.3, 126.8, 126.0, 125.8, 125.6, 124.1, 123.6, 114.2, 113.5, 84.0, 83.8, 73.5, 54.9, 39.5, 27.8.

HRMS-ESI (positive): M = $C_{28}H_{27}NNaO_4$, calculated (M+Na) m/z: 464.1832, found: 464.1846.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 6.81 min (major), t_R = 7.65 min (minor).

IR (cm^{-1}): 3054, 1728, 1280, 1147, 1049, 741.

$[\alpha]^{25}_D$ = - 1.05 (c = 0.71, $CHCl_3$)



3p

***tert*-butyl(2'*S*,3*S*)-6-fluoro-5'-methylene-2-oxo-2'-phenyl-5',6'-dihydro-**

2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3p)

3p (37.5 mg, 0.092 mmol) was obtained in 92% yield as a white solid. >20:1 *dr*, 84% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 116.3 - 117.5°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.42 (ddd, *J* = 11.0, 8.6, 3.6 Hz, 2H), 7.09 – 7.04 (m, 1H), 7.02 (t, *J* = 7.4 Hz, 2H), 6.93 – 6.85 (m, 3H), 5.21 (s, 1H), 4.98 – 4.90 (m, 2H), 4.64 (d, *J* = 12.6 Hz, 1H), 4.44 (d, *J* = 12.6 Hz, 1H), 3.24 (d, *J* = 13.8 Hz, 1H), 2.44 (d, *J* = 13.8 Hz, 1H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 175.1, 160.4, 158.0, 148.4, 137.6, 136.1, 134.8, 130.0 (d, *J* = 8.86 Hz), 127.9, 127.4, 126.3, 115.2 (d, *J* = 7.96 Hz), 114.4, 114.1 (d, *J* = 106.48 Hz), 114.0, 113.3, 84.2, 83.5, 73.3, 54.9, 39.1, 27.4.

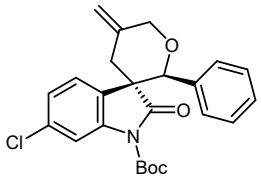
^{19}F NMR (376 MHz, $CDCl_3$) *δ* -118.26.

HRMS-ESI (positive): M = $C_{24}H_{24}FNNaO_4$, calculated (M+Na) m/z: 432.1582, found: 432.1576.

HPLC (IC, *n*-hex/2-propanol = 80/20, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.35 min (major), t_R = 4.96 min (minor).

IR (cm^{-1}): 3077, 1728, 1242, 1148, 1047, 706.

$[\alpha]^{25}_D$ = - 57.21 (c = 0.75, $CHCl_3$).



3q

***tert*-butyl(2'*S*,3*S*)-6-chloro-5'-methylene-2-oxo-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3q)**

3q (31.4 mg, 0.074 mmol) was obtained in 74% yield as a yellow solid. >20:1 *dr*, 80% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 124.8 - 125.7°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.63 (d, *J* = 2.0 Hz, 1H), 7.41 (d, *J* = 8.7 Hz, 1H), 7.16 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.08 – 6.99 (m, 3H), 6.90 (d, *J* = 7.4 Hz, 2H),

5.23 (s, 1H), 4.98 (s, 1H), 4.91 (s, 1H), 4.66 (d, *J* = 12.6 Hz, 1H), 4.44 (d, *J* = 12.6 Hz, 1H), 3.24 (d, *J* = 13.9 Hz, 1H), 2.44 (d, *J* = 13.8 Hz, 1H), 1.54 (s, 9H).

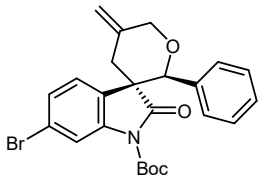
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 174.9, 148.3, 137.5, 137.4, 136.0, 130.0, 129.2, 128.1, 128.0, 127.4, 126.3, 125.9, 115.3, 114.1, 84.4, 83.6, 73.4, 54.8, 39.0, 27.9.

HRMS-ESI (positive): M = $C_{24}H_{24}ClNNaO_4$, calculated (M+Na) m/z: 448.1286, found: 448.1294.

HPLC (IC, *n*-hex/2-propanol = 80/20, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.29 min (major), t_R = 4.82 min (minor).

IR (cm^{-1}): 3059, 1729, 1250, 1149, 1090, 742.

$[\alpha]^{25}_D$ = - 14.76 (c = 0.39, $CHCl_3$).



3r

***tert*-butyl(2'*S*,3*S*)-6-bromo-5'-methylene-2-oxo-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3r)**

Method A: **3r** (44.5mg, 0.094 mmol) was obtained in 94% yield as a white solid. >20:1 *dr*, 80% *ee,* purified by silica gel column chromatography (PE/EA = 15/1).

Method B: 34.9mg, 0.074 mmol, yield 74%, >20:1 *dr*, 80% *ee.*

Mp 136.1 - 137.7°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.77 (d, *J* = 1.7 Hz, 1H), 7.33 (dt, *J* = 8.7, 5.2 Hz, 2H), 7.10 – 7.05 (m, 1H), 7.03 (t, *J* = 7.3 Hz, 2H), 6.89 (d, *J* = 7.0 Hz, 2H), 5.22 (s, 1H), 4.98 (s, 1H), 4.91 (s, 1H), 4.66 (d, *J* = 12.6 Hz, 1H), 4.44 (d, *J* = 12.6 Hz, 1H), 3.23 (d, *J* = 13.8 Hz, 1H), 2.44 (d, *J* = 13.9 Hz, 1H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 174.7, 148.2, 137.9, 137.4, 135.9, 131.0, 130.3, 128.7, 128.0, 127.4, 126.3, 116.8, 115.7, 114.1, 84.4, 83.6, 73.3, 54.7, 39.0, 27.9.

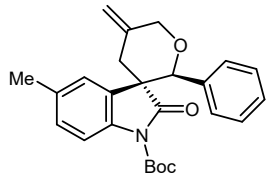
HRMS-ESI (positive): M = $C_{24}H_{24}BrNNaO_4$, calculated (M+Na) m/z: 492.0781,

found: 492.0773.

HPLC (IC, *n*-hex/2-propanol = 80/20, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 4.34 min (major), t_R = 4.86 min (minor).

IR (cm^{-1}): 3055, 1732, 1249, 1148, 1090, 747 cm^{-1};

[α]$^{25}_D$ = - 0.34 (c = 0.82, $CHCl_3$).



3t

***tert-butyl*(2'*S*,3*S*)-5-methyl-5'-methylene-2-oxo-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate(3t)**

3t (28.9 mg, 0.071 mmol) was obtained in 71% yield as a yellow liquid. >20:1 *dr*, 80% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.47 (d, *J* = 0.7 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.09 – 7.03 (m, 1H), 7.03 – 6.97 (m, 3H), 6.88 (d, *J* = 7.2 Hz, 2H), 5.19 (d, *J* = 1.1 Hz, 1H), 4.95 (s, 1H), 4.92 (s, 1H), 4.66 (dd, *J* = 12.6, 1.3 Hz, 1H), 4.46 (d, *J* = 12.6 Hz, 1H), 3.24 (d, *J* = 14.7 Hz, 1H), 2.45 (dd, *J* = 13.8, 1.3 Hz, 1H), 2.37 (s, 3H), 1.54 (s, 9H).

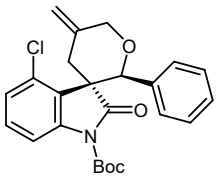
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 175.7, 148.5, 138.2, 136.5, 136.3, 133.2, 128.5, 128.3, 128.2, 127.8, 127.3, 126.5, 126.5, 113.9, 113.4, 83.9, 83.8, 73.4, 54.72, 39.3, 28.0, 21.2.

HRMS-ESI (positive): M = $C_{25}H_{27}NNaO_4$, calculated (M+Na) m/z: 428.1864, found: 428.1866.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 5.34 min (major), t_R = 6.32 min (minor).

IR (cm^{-1}): 2979, 1731, 1277, 1153, 908, 732.

[α]$^{25}_D$ = - 59.12 (c = 0.43, $CHCl_3$).



3w

***tert*-butyl(2'*S*,3*S*)-4-chloro-5'-methylene-2-oxo-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3w)**

3w (25.6 mg, 0.062 mmol) was obtained in 62% yield as a white solid. >20:1 *dr*, 11% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 142.8 – 143.7 °C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.50 (dd, *J* = 6.7, 2.4 Hz, 1H), 7.15 – 7.06 (m, 3H), 7.03 (d, *J* = 4.4 Hz, 4H), 5.43 (s, 1H), 5.18 (s, 1H), 5.00 (s, 1H), 4.69 (dd, *J* = 12.8, 1.3 Hz, 1H), 4.41 (d, *J* = 12.7 Hz, 1H), 3.80 (dd, *J* = 14.8, 1.1 Hz, 1H), 2.56 (dd, *J* = 14.7, 1.2 Hz, 1H), 1.52 (s, 9H).

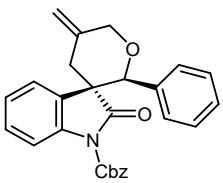
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 172.6, 148.6, 141.3, 138.0, 136.2, 129.8, 129.8, 128.1, 127.4, 126.4, 125.5, 124.9, 113.2, 112.3, 84.2, 79.4, 72.6, 54.7, 34.6, 23.0.

HRMS-ESI (positive): M = $C_{24}H_{24}ClNNaO_4$, calculated (M+Na) m/z: 448.1298, found: 448.1297.

HPLC (IC, *n*-hex/2-propanol = 80/20, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 15.51 min (minor), t_R = 35.44 min (major).

IR (cm^{-1}): 2983, 1733, 1304, 1129, 1071, 734.

$[\alpha]^{25}_D$ = - 1.67 (c = 0.06, $CHCl_3$).



3x

benzyl(2'*S*,3*S*)-5'-methylene-2-oxo-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (3x)

3x (26.7 mg, 0.063 mmol) was obtained in 63% yield as a yellow solid. >20:1

dr, 86% *ee,* purified by silica gel column chromatography (PE/EA = 10/1).

Mp 113.5 - 114.2°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.68 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.35 (m, 5H), 7.18 (dtd, *J* = 22.9, 7.6, 1.3 Hz, 2H), 7.05 – 6.99 (m, 1H), 6.89 (dt, *J* = 8.5, 4.7 Hz, 4H), 5.35 (q, *J* = 12.5 Hz, 2H), 5.20 (s, 1H), 4.95 (d, *J* = 3.8 Hz, 2H), 4.66 (dd, *J* = 12.6, 1.3 Hz, 1H), 4.47 (d, *J* = 12.6 Hz, 1H), 3.26 (dd, *J* = 13.8, 0.9 Hz, 1H), 2.48 (dd, *J* = 13.8, 1.4 Hz, 1H).

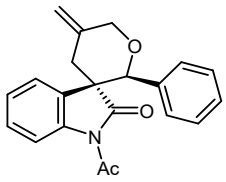
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 175.3, 150.1, 138.4, 137.9, 136.2, 135.0, 128.6, 128.4, 128.3, 127.9, 127.9, 127.4, 126.4, 126.0, 124.0, 114.3, 113.6, 83.7, 73.4, 68.3, 54.9, 39.5.

HRMS-ESI (positive): M = $C_{24}H_{24}ClNO_4$, calculated (M+H) m/z: 426.1700, found: 426.1702.

HPLC (IC, *n*-hex/2-propanol = 80/20, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 7.03 min (major), t_R = 11.75 min (minor).

IR (cm^{-1}): 3030, 1782, 1232, 1152, 767, 693.

$[\alpha]^{25}_D$ = - 67.11 (c = 0.43, $CHCl_3$).



3y

(2'*S*,3*S*)-1-acetyl-5'-methylene-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-2-one (3u)

3y (22.0 mg, 0.066 mmol) was obtained in 66% yield as a white solid. >20:1 *dr*, 87% *ee,* purified by silica gel column chromatography (PE/EA = 20/1).

Mp 65.1 - 66.2°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.89 (dd, *J* = 8.0, 0.7 Hz, 1H), 7.70 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.26 – 7.15 (m, 2H), 7.10 – 7.04 (m, 1H), 6.99 (dd, *J* = 10.2, 4.6 Hz, 2H), 6.85 (d, *J* = 7.2 Hz, 2H), 5.21 (d, *J* = 1.2 Hz, 1H), 4.96 (s, 1H), 4.93 (s, 1H), 4.67 (dd, *J* = 12.7, 1.4 Hz, 1H), 4.48 (d, *J* = 12.6 Hz, 1H), 3.23 (dd, *J* = 13.7, 1.1 Hz, 1H), 2.53 (d, *J* = 9.8 Hz, 3H), 2.48 (dd, *J* = 13.8, 1.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 170.2, 139.2, 137.7, 136.1, 128.3, 128.2, 127.4, 126.4, 125.8, 124.4, 115.6, 113.8, 83.9, 73.5, 54.8, 39.5, 26.5.

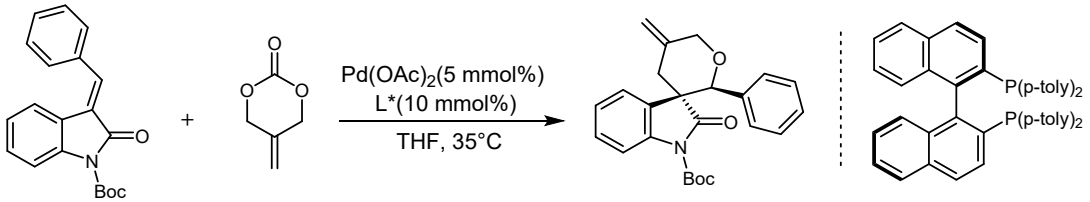
HRMS-ESI (positive): M = $C_{21}H_{20}NO_3$, calculated (M+H) m/z: 334.1438, found: 334.1444.

HPLC (IC, *n*-hex/2-propanol = 80/20, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 5.54 min (major), t_R = 5.95 min (minor).

IR (cm^{-1}): 3075, 1745, 1270, 1195, 1097, 722.

$[\alpha]^{25}_D$ = - 32.42 (c = 0.33, $CHCl_3$).

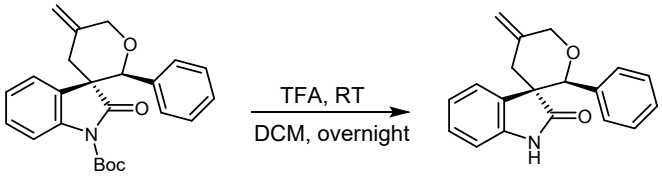
5. Scaled-up Synthesis of the Product 3a



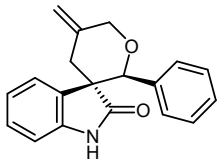
2a **1a** **3a** **L9**

To an oven-dried Schlenk tube was added $Pd(OAc)_2$ (0.2 mmol), Chiral ligand **L9** (0.4 mmol) followed by the addition of THF (20 mL). The reaction mixture was allowed to stir for 30 mins at room temperature (25 °C), to the reaction mixture was then added methyleneindolinones **2a** (40 mmol), 2-Methylidenetrimethylene **1a** (60 mmol). The reaction mixture was allowed to stir at 35 °C for 24 h and then directly purified by silica gel chromatography (PE/EA = 20/1 to 10/1) to provide the desired product **3a** in 89% yield (1.39g, 34.8 mmol) with 87% *ee* and > 20:1 *dr*.

6. Transformations of the Product 3a[7, 8]



A sealed tube was charged with chiral **3a** (0.2 mmol, 78.4 mg), trifluoroacetic acid (TFA, 1 mL) and dichloromethane (3 mL). The reaction mixture was stirred at ambient temperature until the reaction was judged to be completed by TLC analysis. 50 mL H_2O was added, and the mixture was extracted by DCM (40 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by chromatography on silica gel (PE/EA = 4/1) to afford the desired product **4a**.



4a

(2'*S*,3*S*)-5'-methylene-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-2-one (4a)

4a (55.7 mg, 0.192 mmol) was obtained in 96% yield as a white solid. >20:1 *dr*, 86% *ee,* purified by silica gel column chromatography (PE/EA = 4/1).

Mp 146.5 - 147.8°C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.24 (s, 1H), 7.64 (d, *J* = 7.4 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.09 – 7.01 (m, 2H), 6.97 (td, *J* = 6.1, 3.9 Hz, 4H), 6.60 (d, *J* = 7.7 Hz, 1H), 5.18 (s, 1H), 4.95 (s, 1H), 4.92 (s, 1H), 4.64 (d, *J* = 12.5 Hz, 1H), 4.45 (d, *J* = 12.5 Hz, 1H), 3.18 (d, *J* = 13.6 Hz, 1H), 2.40 (d, *J* = 13.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 178.8, 139.9, 138.4, 136.7, 129.8, 127.9, 127.7, 127.3, 126.8, 126.5, 121.8, 113.3, 109.2, 83.0, 82.9, 73.3, 55.1, 39.3.

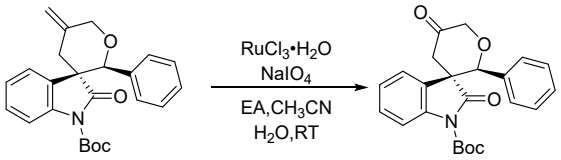
HRMS-ESI (positive): M = $C_{19}H_{18}NO_2$, calculated (M+H) m/z: 292.1332, found:

292.1327.

HPLC (AD-H, *n*-hex/2-propanol = 95/5, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 14.49 min (major), t_R = 15.49 min (minor).

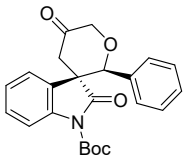
IR (cm^{-1}): 3181, 1704, 1469, 1094, 753, 681.

$[\alpha]^{25}_D$ = - 3.33(c = 1.12, $CHCl_3$).



3a **5a**

A solution of $NaIO_4$ (85 mg, 0.4 mmol) in water (0.6 mL) was added to a solution of $RuCl_3 \cdot H_2O$ (3.1 mg, 15 mol%) in MeCN (0.8 mL). This mixture was stirred 2 minutes and then a solution of the **3a** (0.1 mmol) in EA (0.8 mL) was added. The mixture was stirred for 10 minutes until TLC indicates complete consumption of the starting material. $MgSO_4$ was added and the resulting heterogeneous mixture was washed with EA, and finally evaporated under reduced pressure. Purified by flash chromatography on silica gel with PE/EA (4/1) as the solvent give a white solid **5a**.



5a

***tert*-butyl(2'*S*,3*S*)-2,5'-dioxo-2'-phenyl-5',6'-dihydro-2'*H*,4'*H*-spiro[indoline-3,3'-pyran]-1-carboxylate (5a)**

5a (18,8 mg, 0.096 mmol) was obtained in 48% yield as a colourless oil, >20:1 *dr*, 85% *ee,* purified by silica gel column chromatography (PE/EA = 5/1).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.46 (d, *J* = 8.1 Hz, 1H), 7.37 (d, *J* = 7.3 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.20 – 7.09 (m, 2H), 7.04 (t, *J* = 7.6 Hz, 2H), 6.89 (d, *J* = 7.5 Hz, 2H), 5.20 (s, 1H), 4.57 (d, *J* = 16.3 Hz, 1H), 4.46 (d, *J* = 16.2 Hz, 1H), 3.42 (d, *J* = 16.7 Hz, 1H), 2.66 (d, *J* = 16.6 Hz, 1H), 1.53 (s, 9H).

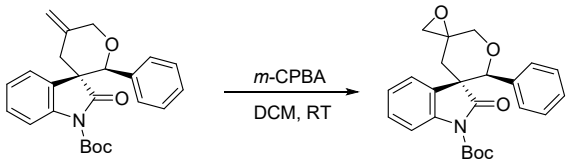
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 203.9, 174.0, 148.1, 139.0, 134.5, 129.1, 128.4, 127.5, 127.0, 126.4, 124.8, 124.4, 114.6, 84.5, 83.1, 75.5, 56.3, 44.6, 27.9.

HRMS-ESI (positive): M = $C_{23}H_{23}NNaO_5$, calculated (M+Na) m/z: 416.1459, found: 416.1468.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 13.32 min (major), t_R = 23.26 min (minor).

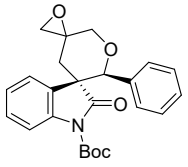
IR (cm^{-1}): 2979, 1733, 1252, 1152, 751, 715.

$[\alpha]^{25}_D$ = - 55.13 (c = 0.23, $CHCl_3$).



3a **6a**

To a solution of **3a** (0.10 mmol, 1.0 equiv.) in dichloromethane (2 mL) was added the dichloromethane solution of *m*-CPBA (0.30 mmol, 0.30 M, 1.0 mL) dropwise at 0°C under nitrogen. The reaction mixture was sealed under nitrogen and allowed to warm to room temperature and stir for 24 hours. The reaction was then quenched with saturated $NaHCO_3$ solution and extracted with dichloromethane. The combined organic phase was collected and dried with Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel chromatography (PE/EA = 5/1) to afford a white solid.



6a

***tert*-butyl(2'*S*,3*S*)-2-oxo-2'-phenyl-2'*H*,4'*H*,6'H-dispiro[indoline-3,3'-pyran-5',2''-oxirane]-1-carboxylate (6a)**

6a (18.5 mg, 0.138 mmol) was obtained in 69% yield as a white solid. 2:1 *dr*, 86% *ee,* purified by silica gel column chromatography (PE/EA = 5/1).

Mp 123.7 - 124.8°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.3, 1.0 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.14 (m, 2H), 7.10 – 7.04 (m, 1H), 7.01 (t, *J* = 7.4 Hz, 2H), 6.93 (d, *J* = 7.3 Hz, 2H), 4.93 (s, 1H), 4.23 (dd, *J* = 11.7, 1.8 Hz, 1H), 3.82 (dd,

J = 11.7, 1.8 Hz, 1H), 3.10 (d, *J* = 4.9 Hz, 1H), 3.06 (d, *J* = 13.3 Hz, 1H), 2.80 (dd, *J* = 4.9, 1.8 Hz, 1H), 1.61 – 1.57 (m, 1H), 1.56 (d, *J* = 3.9 Hz, 9H).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.15 – 8.07 (m, 1H), 7.43 – 7.37 (m, 1H), 7.24 – 7.15 (m, 2H), 7.07 (t, *J* = 7.2 Hz, 1H), 7.01 (t, *J* = 7.4 Hz, 2H), 6.93 (d, *J* = 7.3 Hz, 2H), 4.87 (s, 1H), 4.42 (d, *J* = 12.8 Hz, 1H), 3.85 (dd, *J* = 12.8, 2.3 Hz, 1H), 3.18 (d, *J* = 14.5 Hz, 1H), 2.81 (d, *J* = 4.1 Hz, 1H), 2.74 (d, *J* = 4.1 Hz, 1H), 1.55 (s, 9H).

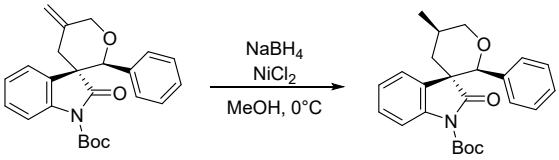
^{13}C NMR (100 MHz, $CDCl_3$) *δ* 174.5, 148.4, 139.0, 135.5, 128.5, 128.0, 127.7, 127.4, 126.4, 125.4, 123.9, 114.6, 84.4, 84.0, 72.7, 56.8, 55.8, 52.5, 37.7, 27.9.

HRMS-ESI (positive): M = $C_{24}H_{25}NNaO_5$, calculated (M+Na) m/z: 430.1625, found: 430.1619.

HPLC (IC, *n*-hex/2-propanol = 90/10, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 9.39 min (major), t_R = 13.97 min (minor).

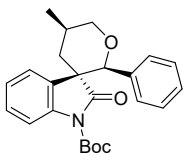
IR (cm^{-1}): 2924, 1732, 1299, 1153, 1118, 714.

$[\alpha]^{25}_D$ = - 60.56 (c = 0.23, $CHCl_3$).



3a **7a**

In a reaction tube with a magnetic stirring bar, the solution of **3a** (0.1 mmol, 1.0 equiv.) and $NiCl_2$(0.1 mmol, 1.0 equiv.) in MeOH (4.0 mL) was obtained, and then, $NaBH_4$(1.0 mmol, 10 equiv.) was slowly added at 0°C. After stirring for 2 h at 0°C, the reaction was quenched by adding NH_4Cl (*aq*). The mixture was extracted with DCM (5 mL × 3), and the combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified using flash column chromatography on silica gel (PE/EA = 5/1) to afford product **7a**.



7a

***tert*-butyl(2'*S*,3*S*,5'*R*)-5'-methyl-2-oxo-2'-phenyl-5',6'-dihydro-2'H,4'H-spiro[indoline-3,3'-pyran]-1-carboxylate (7a)**

7a (23.9 mg, 0.123 mmol) was obtained in 61% yield as a colourless oil, >20:1 *dr*, 86% *ee,* purified by silica gel column chromatography (PE/EA = 5/1).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.57 – 7.52 (m, 1H), 7.48 – 7.42 (m, 1H), 7.11 – 7.03 (m, 2H), 7.01 – 6.96 (m, 5H), 5.09 (s, 1H), 4.25 (dd, *J* = 10.5, 5.9 Hz, 1H), 3.88 (dd, *J* = 10.6, 7.4 Hz, 1H), 2.62 (dh, *J* = 13.9, 7.0 Hz, 1H), 2.44 (dd, *J* = 13.9, 5.1 Hz, 1H), 1.77 (dd, *J* = 14.0, 8.9 Hz, 1H), 1.61 (s, 9H), 1.14 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 178.1, 148.8, 138.8, 137.4, 130.2, 127.7, 127.3, 127.3, 125.8, 125.5, 123.8, 114.2, 84.1, 80.7, 73.7, 54.3, 38.5, 28.1, 24.7, 19.1.

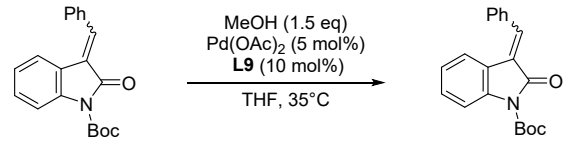
HRMS-ESI (positive): M = $C_{24}H_{27}NNaO_4$, calculated (M+Na) m/z: 416.1832, found: 416.1829.

HPLC (IC, *n*-hex/2-propanol = 95/5, flow rate = 1.0 mL/min, I = 254 nm, T = 25 ºC) t_R = 6.02 min (major), t_R = 6.69 min (minor).

IR (cm^{-1}): 2928, 1733, 1287, 1152, 1065, 752.

$[\alpha]^{25}_D$ = - 56.34 (c = 0.42, $CHCl_3$).

7. Isomerization of methyleneindodonone



pure *E* or *Z*/*E*: 5/4 *Z*/*E*: 1/4.6

To an oven-dried Schlenk tube was added $Pd(OAc)_2$ (0.005 mmol), Chiral ligand **L9** (0.01 mmol) followed by the addition of THF (0.5 mL). The reaction mixture was allowed to stir for 30 mins at room temperature (25 ºC), to the reaction mixture was then added methyleneindolinone (pure *E* or *Z*/*E* = 5/4, 0.1 mmol), MeOH (0.15 mmol). The reaction mixture was allowed to stir at 35 ºC for 24 h and then directly purified by silica gel chromatography (PE/EA = 20/1 to 10/1) to provide the product methyleneindolinone (*Z*/*E*=1/4.6**)**.

8. Crystal data for enantiopure products 3a

Preparations: Compound **3a** (20.0 mg) was dissolved in n-Hexane / isopropanol =1 (10.0 mL) in a vial. The vial was properly sealed with parafilm and kept at 25 ºC to allow the slow evaporation of the solvent until a single crystal was obtained. The crystals were subjected for single crystal XRD to determine the absolute configuration of **3a**.

Methods: The data set was collected by a Bruker D8 VENTURE with MetalJet source at 173 K equipped with micro-focus Ga radiation source (Kα = 1.34138 Å). Applied with face-indexed numerical absorption correction, the structure solution and refinement were processed by SHELXTL program package.

Date of 3a: CCDC 2302972 contains the supplementary crystallographic data, and can be obtained via www.ccdc.cam.ac.uk/conts/retrieving.html.

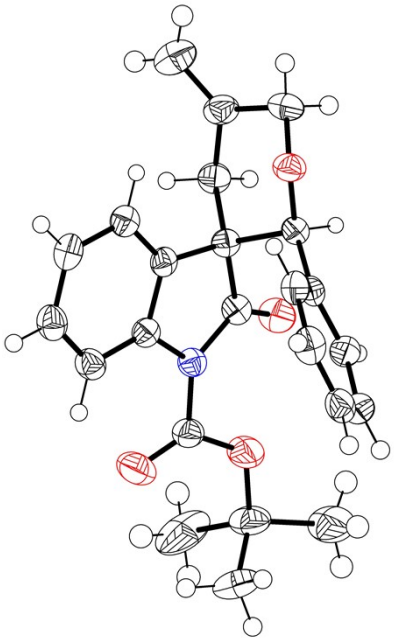


Figure S3. Single crystal structure 3a (ellipsoid contour probability 50%).

Table 1. Crystal data and structure refinement for **3a**.

Identification code	**3a**
Empirical formula	$C_{24}H_{25}NO_4$
Formula weight	391.45
Temperature	173(2) K
Wavelength	1.34139 Å
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 8.0358(3) Åa= 90°. b = 10.9125(4) Åb= 90.7150(10)°. c = 12.2549(5) Åg = 90°.
Volume	1074.56(7) $Å^3$
Z	2
Density (calculated)	1.210 Mg/m^3
Absorption coefficient	0.422 mm^{-1}
F(000)	416
Crystal size	0.210 x 0.180 x 0.140 mm^3
Theta range for data collection	4.788 to 54.927°.
Index ranges	-9<=h<=9, -13<=k<=13, -14<=l<=14
Reflections collected	15052
Independent reflections	4049 [R(int) = 0.0239]
Completeness to theta = 53.594°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.864 and 0.753
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4049 / 44 / 297
Goodness-of-fit on F^2	1.059
Final R indices [I>2sigma(I)]	R1 = 0.0295, wR2 = 0.0780
R indices (all data)	R1 = 0.0305, wR2 = 0.0793
Absolute structure parameter	0.09(5)
Extinction coefficient	0.0100(14)
Largest diff. peak and hole	0.321 and -0.186 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)for **3a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	7467(2)	4947(2)	2412(1)	30(1)
O(1)	7654(2)	3126(1)	3413(1)	43(1)
O(2)	5305(2)	5546(1)	5769(1)	37(1)
O(3)	7054(2)	3393(2)	1264(1)	55(1)

O(4)	7997(3)	5164(2)	603(1)	75(1)
C(1)	7502(2)	4226(2)	3367(2)	32(1)
C(2)	5541(2)	4811(2)	4829(2)	31(1)
C(3)	7295(2)	5078(2)	4337(2)	30(1)
C(4)	8628(2)	4803(2)	5224(2)	36(1)
C(5)	8205(3)	5403(2)	6292(2)	41(1)
C(6)	6441(3)	5196(2)	6626(2)	45(1)
C(7)	7408(2)	6327(2)	3831(2)	29(1)
C(8)	7488(2)	6215(2)	2701(2)	30(1)
C(9)	7605(2)	7225(2)	2026(2)	36(1)
C(10)	7648(2)	8373(2)	2516(2)	40(1)
C(11)	7586(2)	8506(2)	3641(2)	37(1)
C(12)	7462(2)	7477(2)	4306(2)	33(1)
C(13)	4126(2)	5046(2)	4031(2)	30(1)
C(14)	3221(2)	6132(2)	4051(2)	36(1)
C(15)	1963(3)	6340(2)	3281(2)	44(1)
C(16)	1612(2)	5470(2)	2491(2)	43(1)
C(17)	2485(3)	4381(2)	2479(2)	44(1)
C(18)	3734(3)	4164(2)	3250(2)	37(1)
C(19)	9266(3)	6059(3)	6880(2)	56(1)
C(20)	7535(3)	4523(2)	1334(2)	37(1)
C(21)	7263(3)	2684(2)	243(2)	51(1)
C(22)	6381(17)	3221(9)	-729(11)	58(2)
C(23)	9030(20)	2488(19)	143(13)	104(6)
C(24)	6220(30)	1507(10)	507(9)	85(3)

9. Reference

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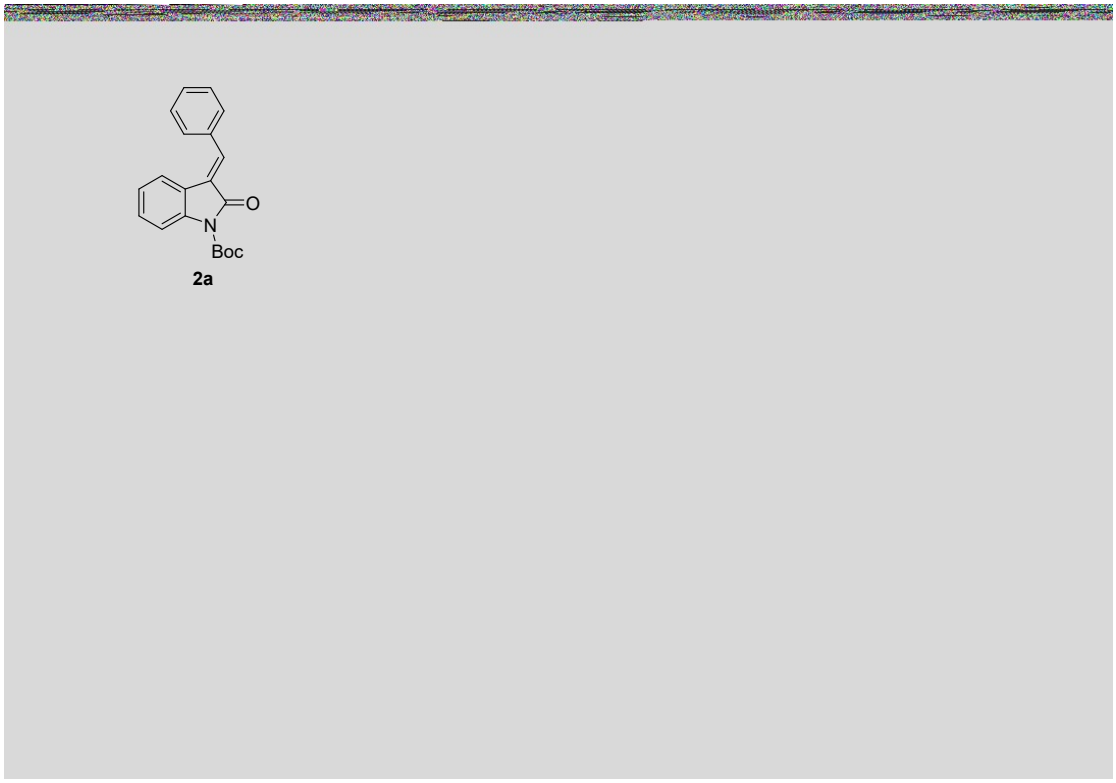
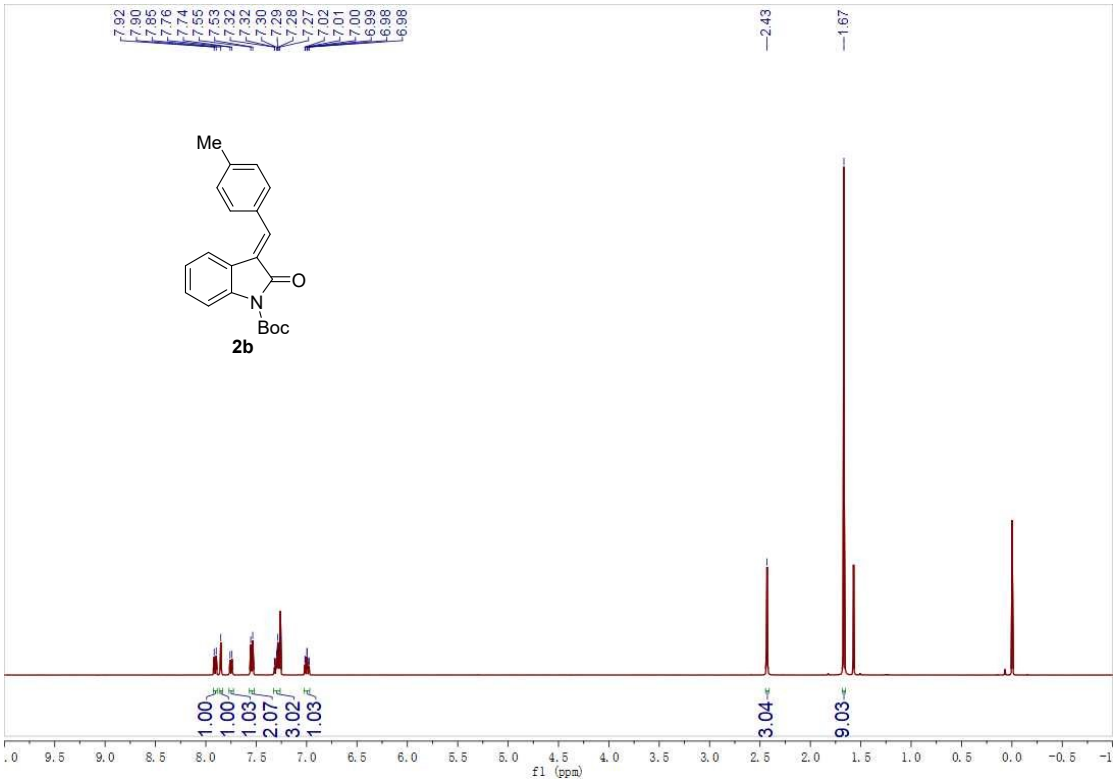
10. NMR spectra of representative compounds

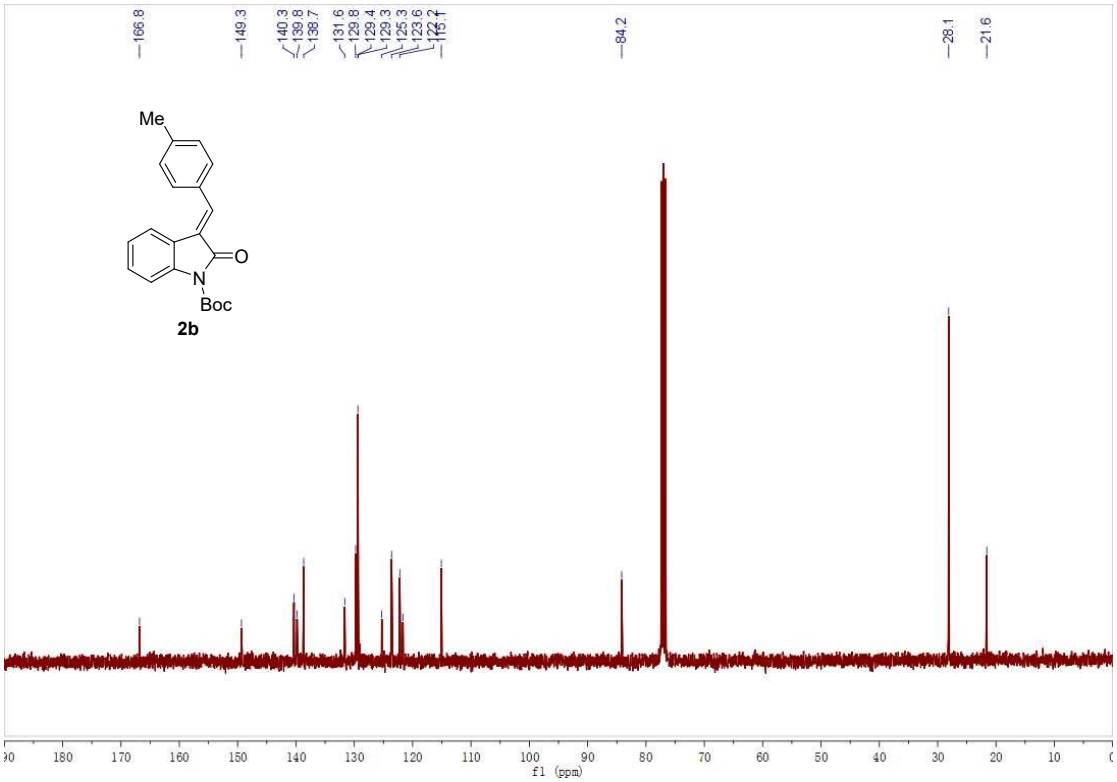
^{1}H NMR of **2a** (400 MHz, $CDCl_3$)



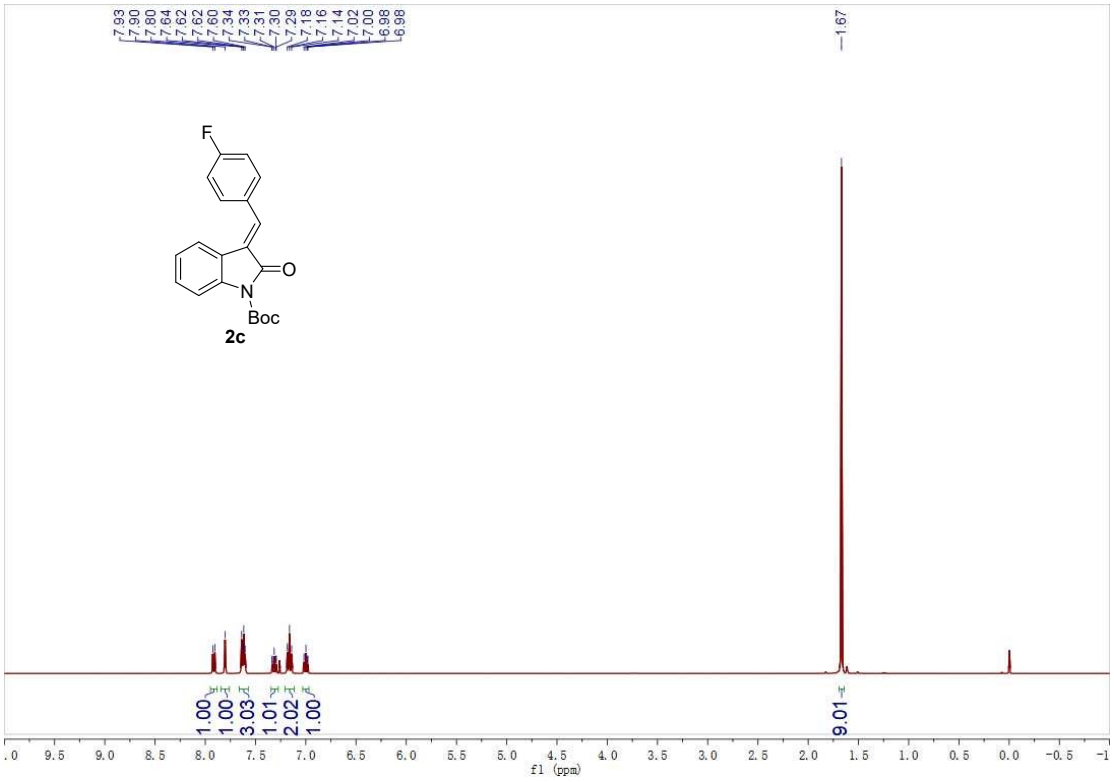
^{1}H NMR of **2b** (400 MHz, $CDCl_3$)



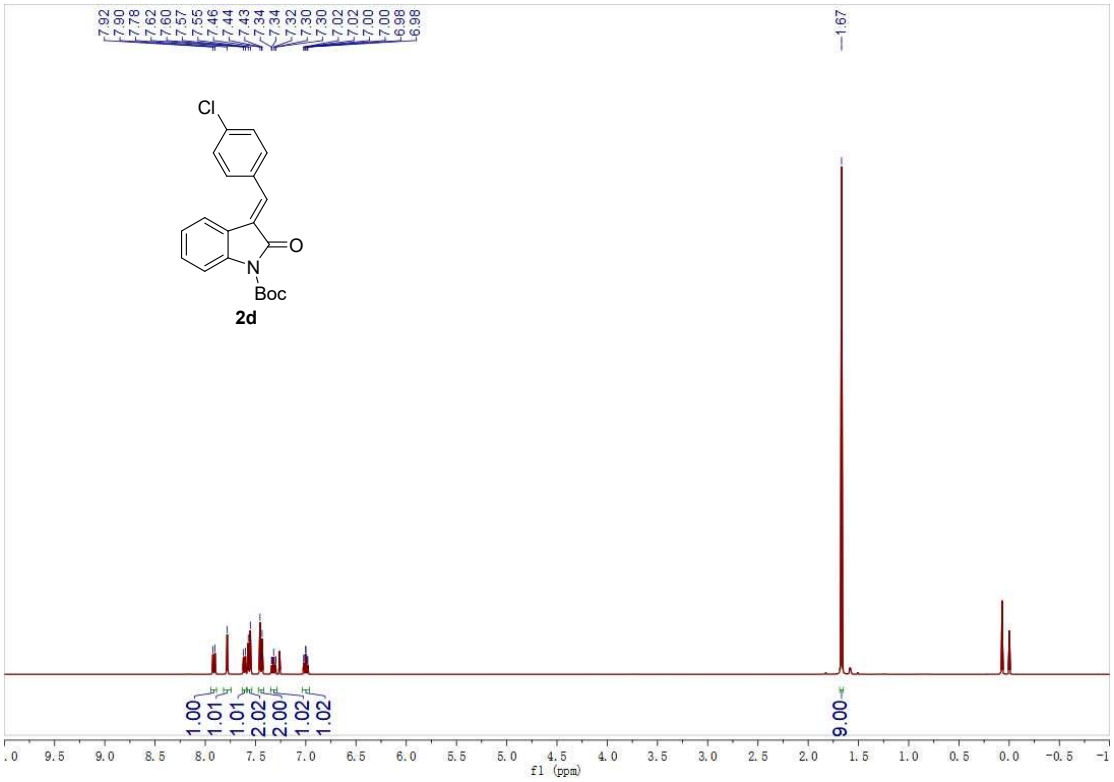
^{13}C {^{1}H} NMR of **2b** (100 MHz, $CDCl_3$)



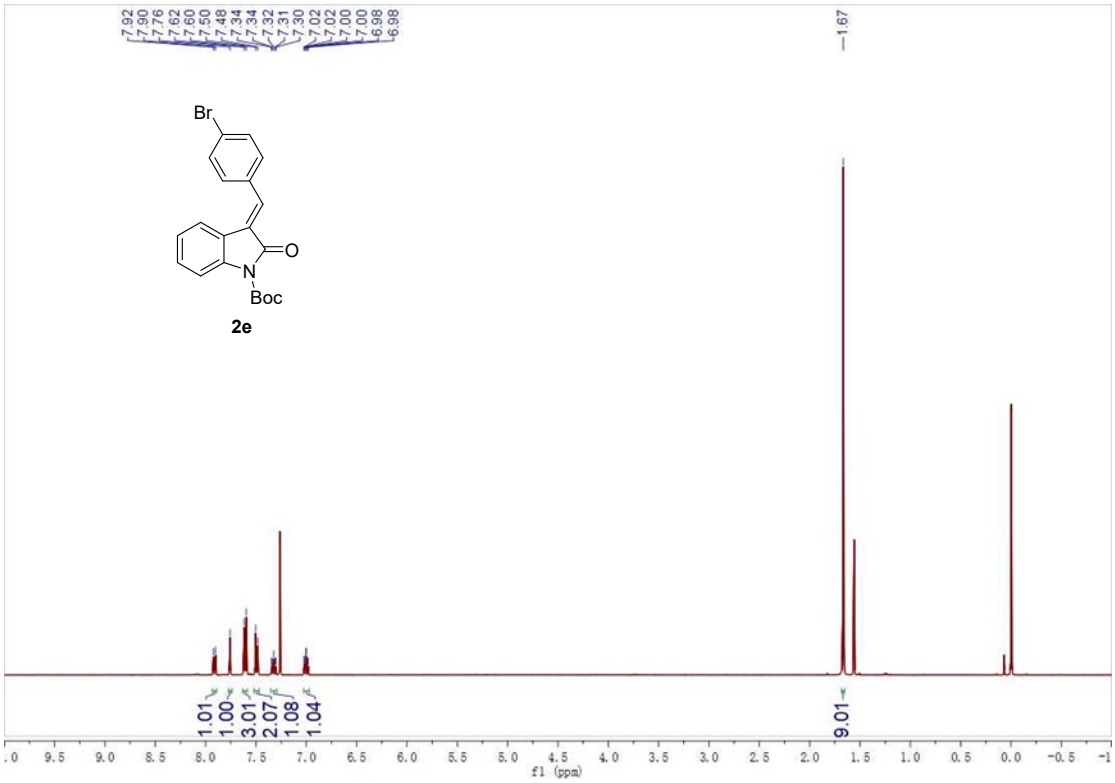
^{1}H NMR of **2c** (400 MHz, $CDCl_3$)



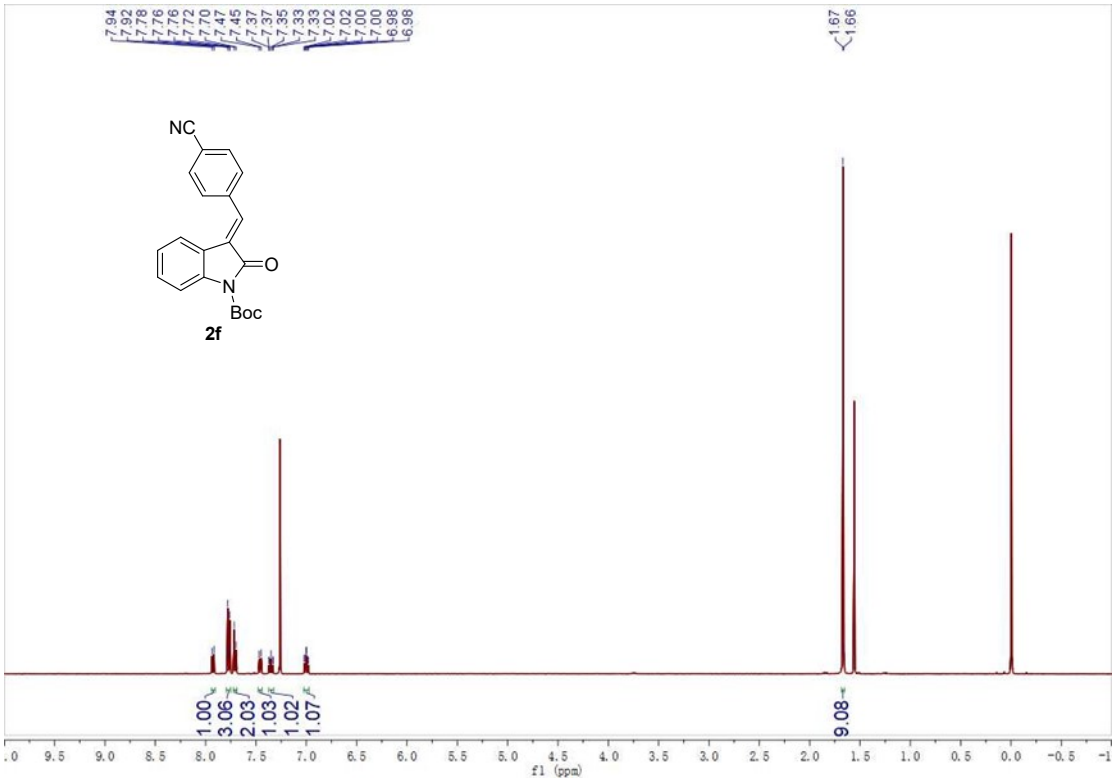
^{1}H NMR of **2d** (400 MHz, $CDCl_3$)



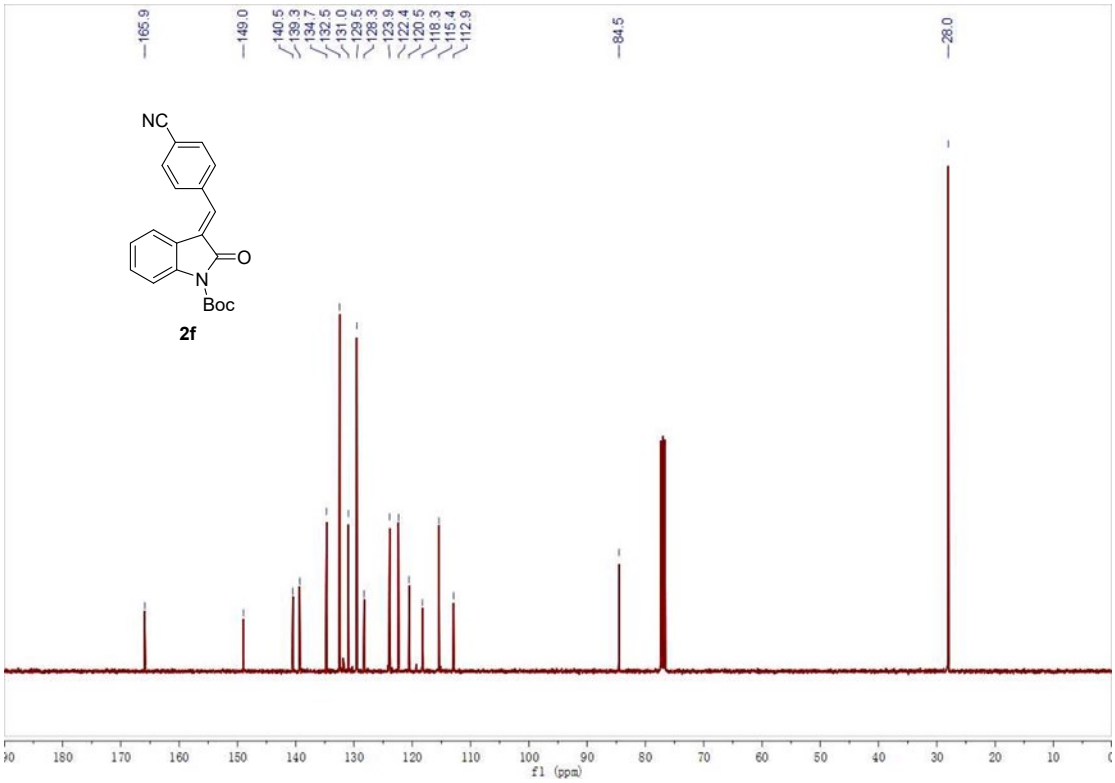
^{1}H NMR of **2e** (400 MHz, $CDCl_3$)



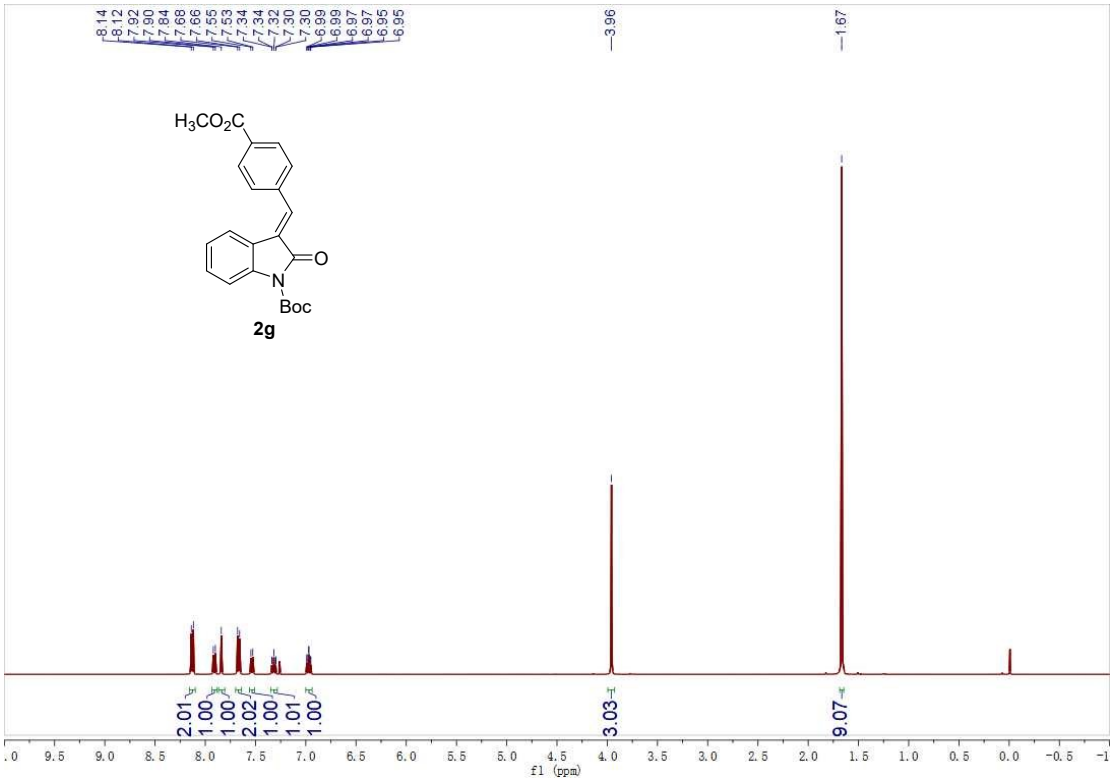
^{1}H NMR of **2f** (400 MHz, $CDCl_3$)



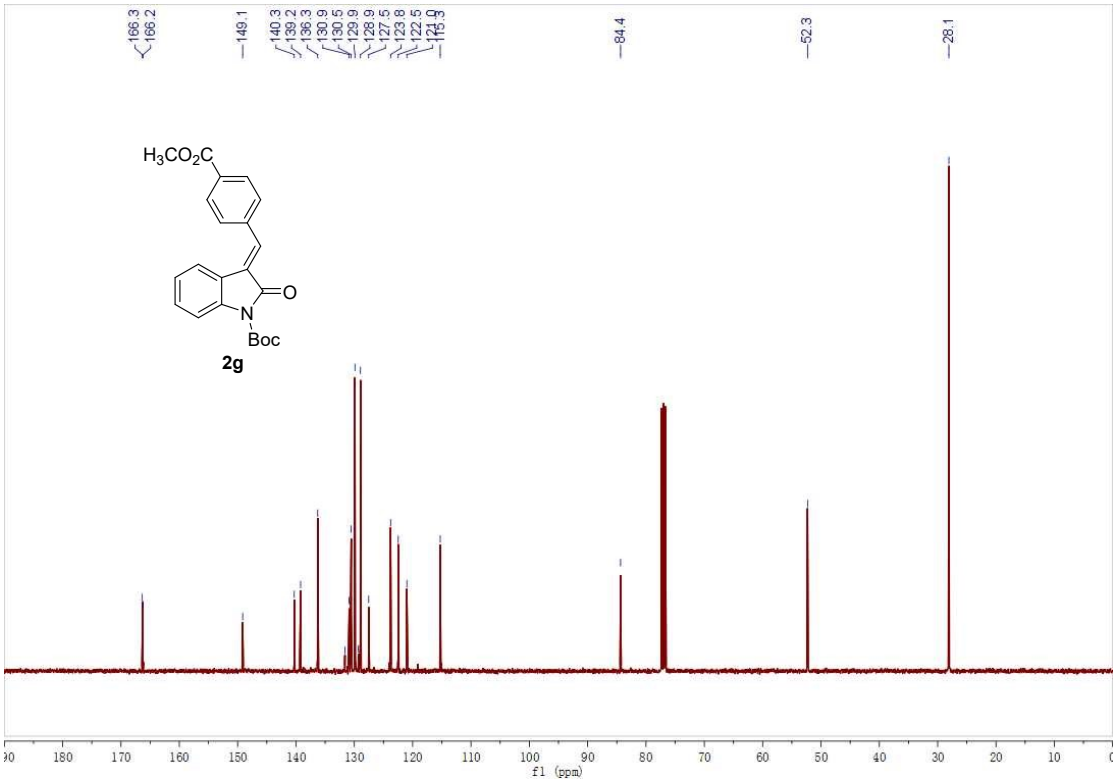
^{13}C {^{1}H} NMR of **2f** (100 MHz, $CDCl_3$)



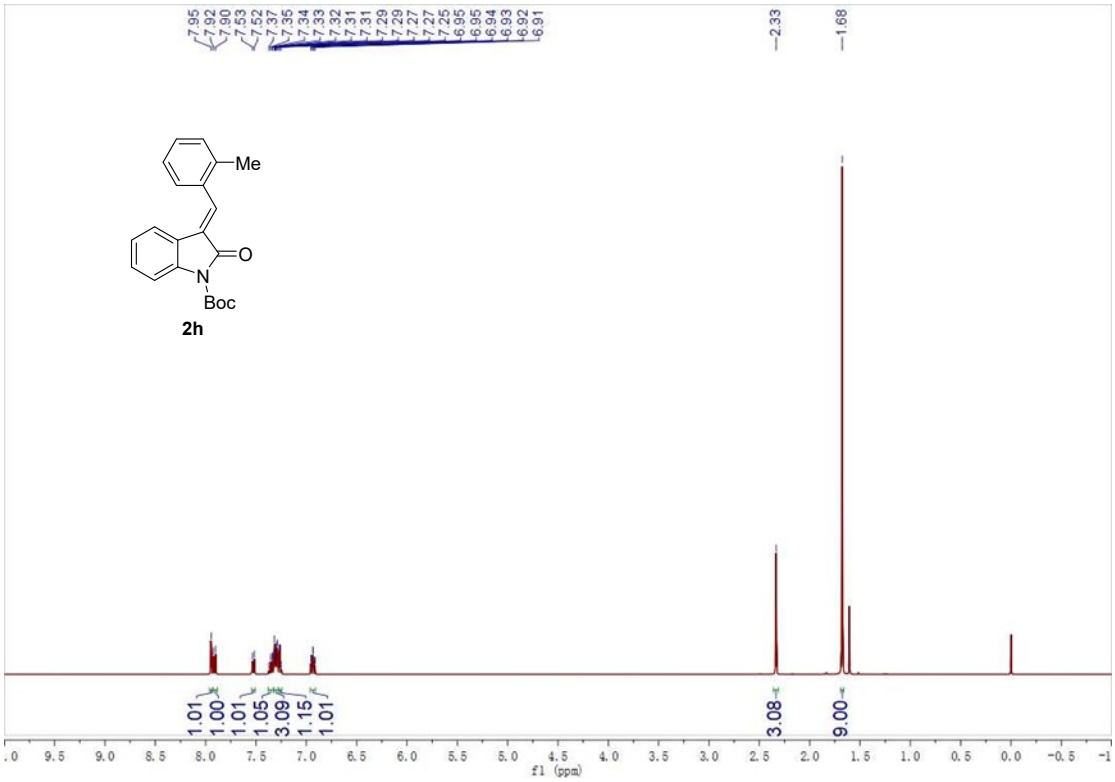
^{1}H NMR of **2g** (400 MHz, $CDCl_3$)



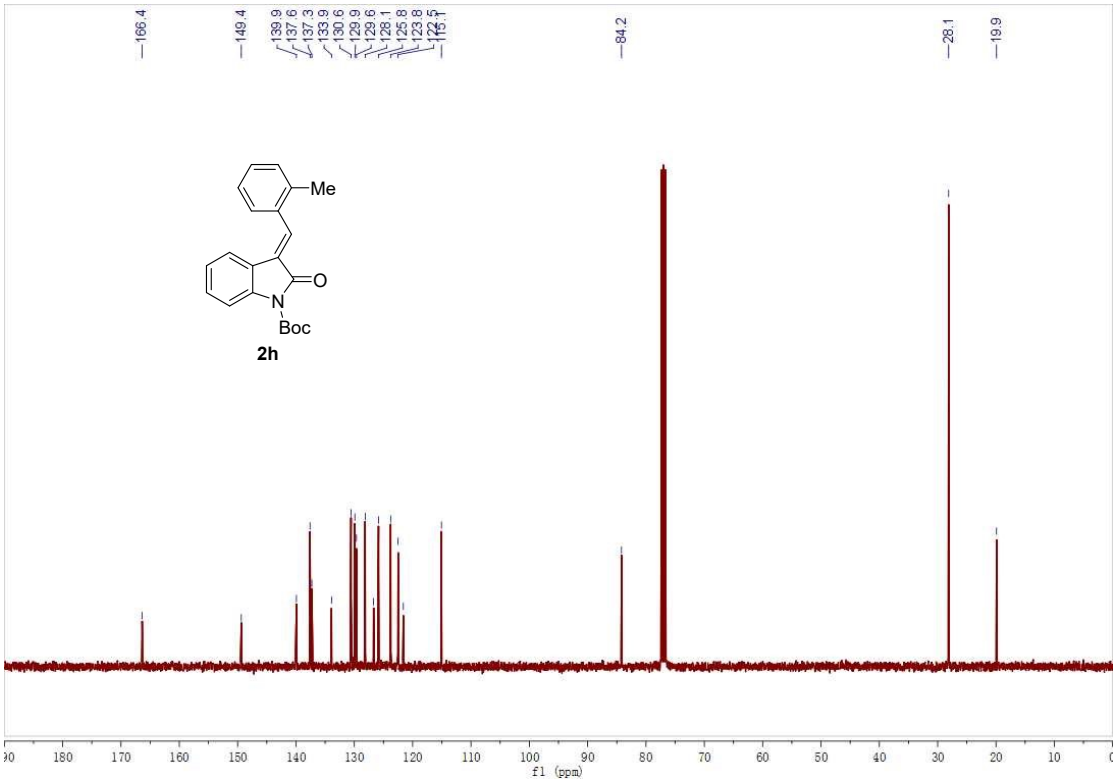
^{13}C {^{1}H} NMR of **2g** (100 MHz, $CDCl_3$)



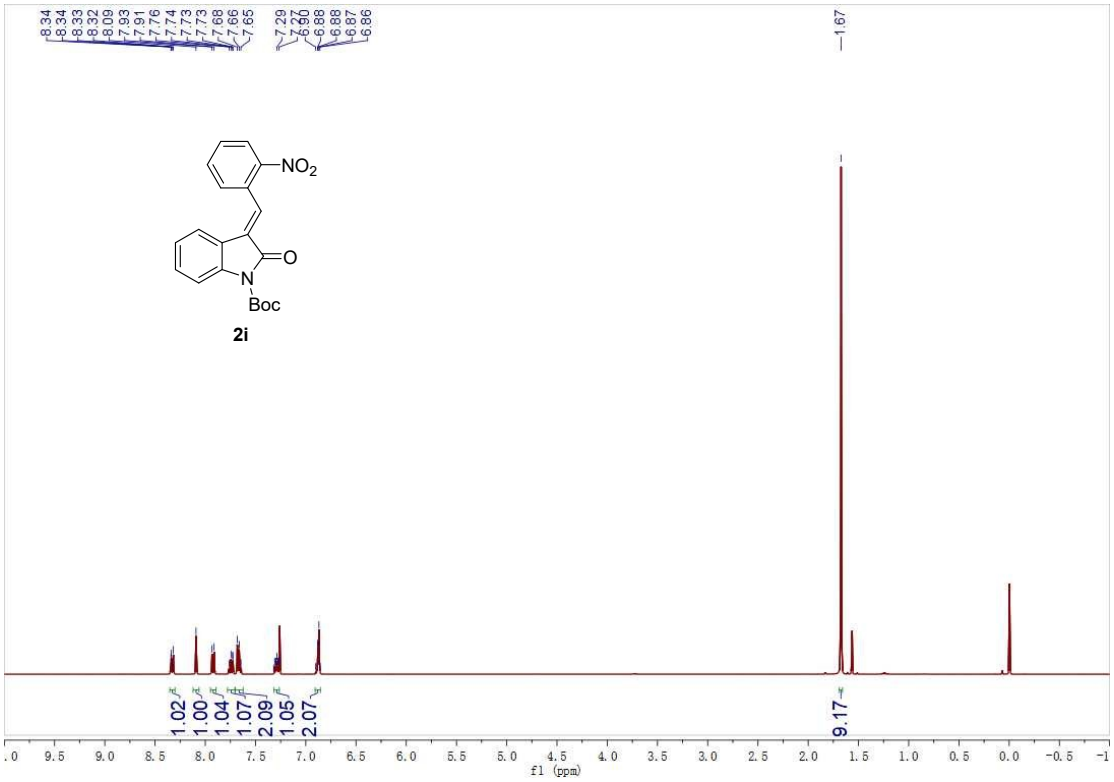
^{1}H NMR of **2h** (400 MHz, $CDCl_3$)



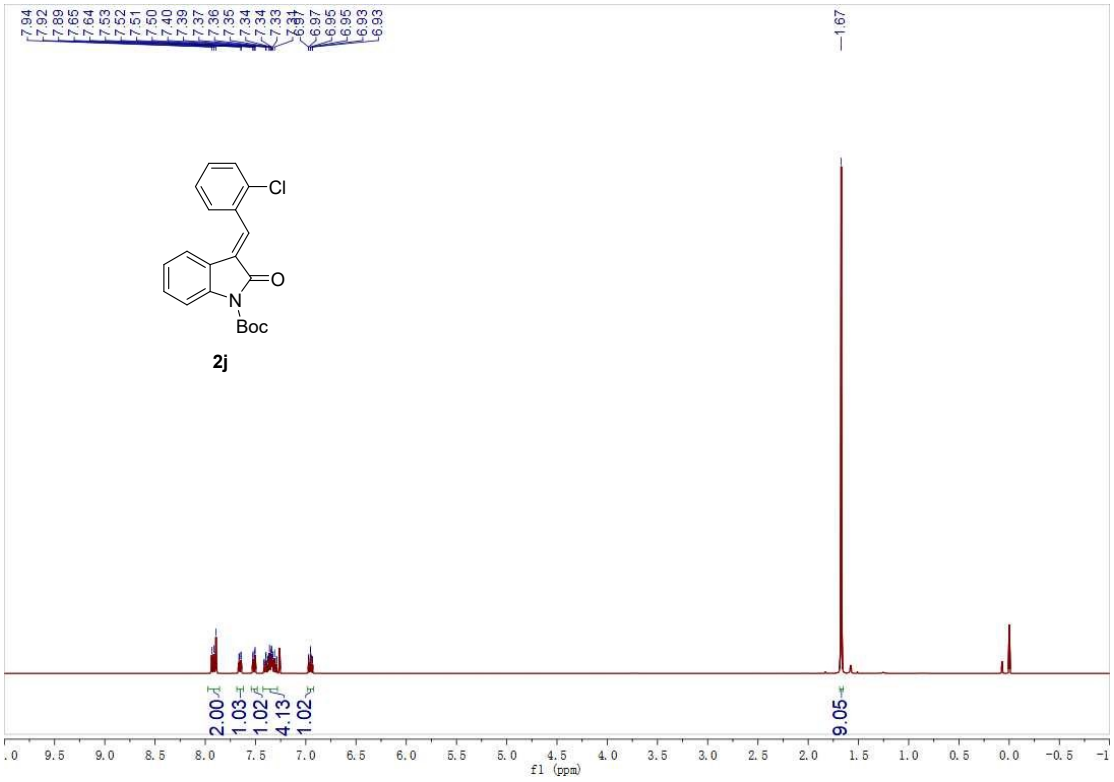
^{13}C {^{1}H} NMR of **2h** (100 MHz, $CDCl_3$)



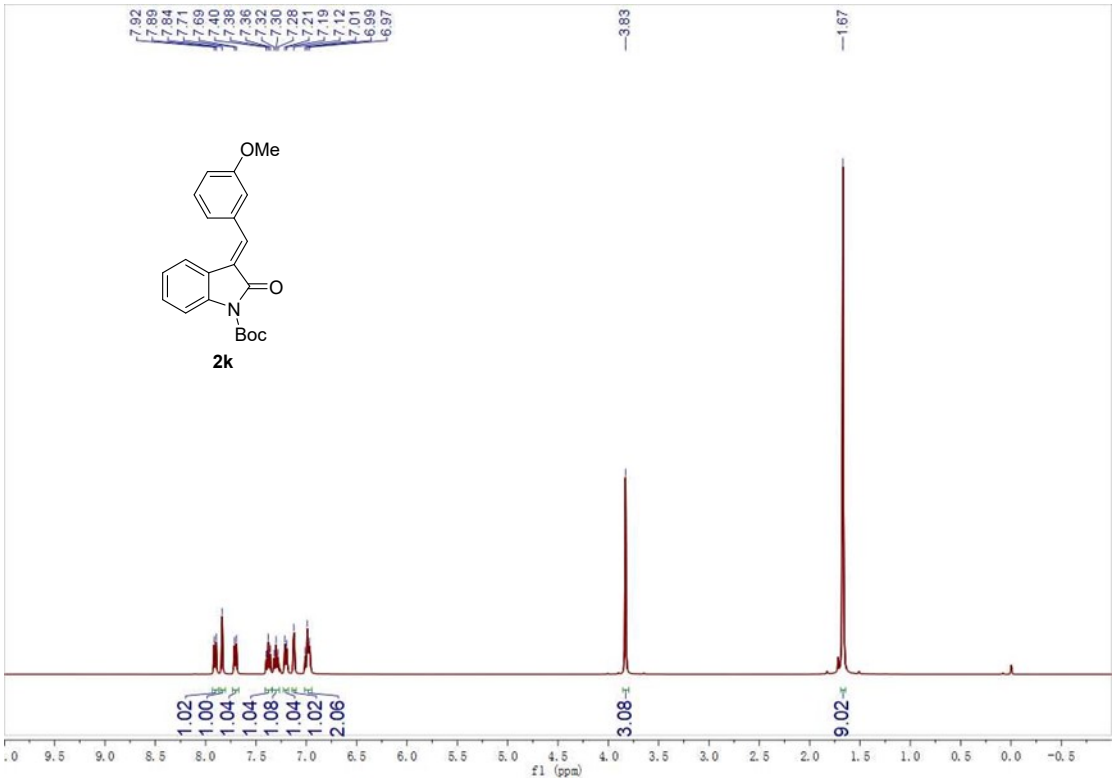
^{1}H NMR of **2i** (400 MHz, $CDCl_3$)



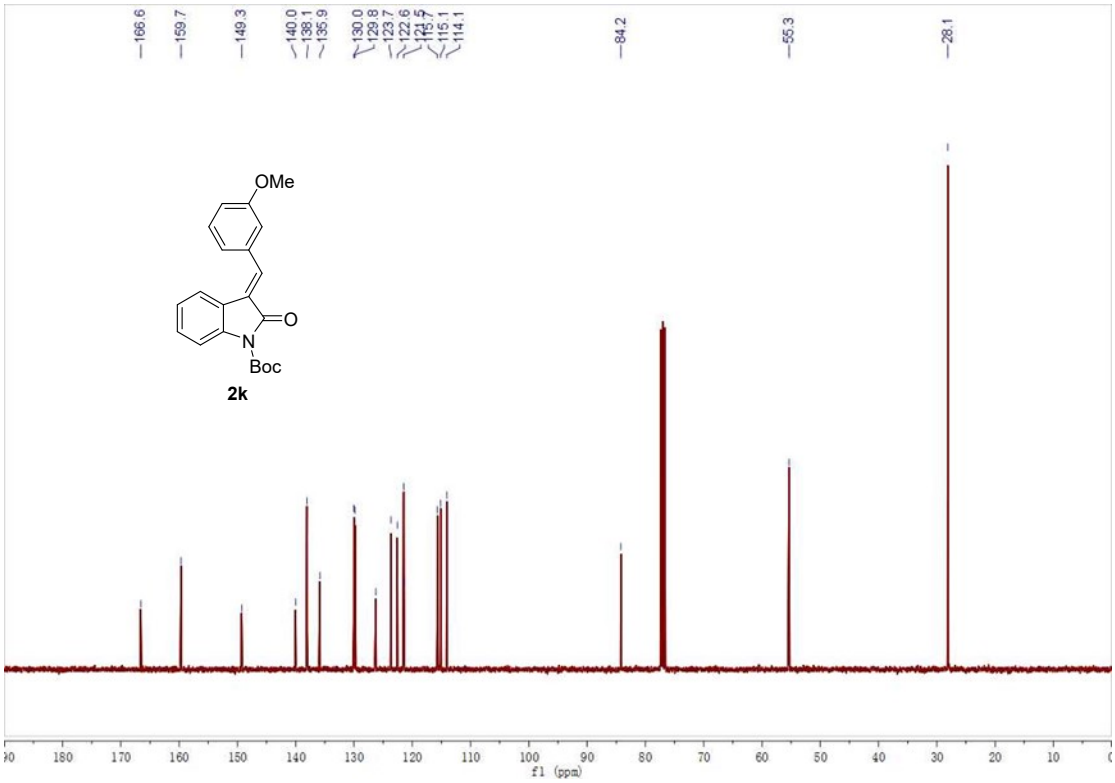
^{1}H NMR of **2j** (400 MHz, $CDCl_3$)



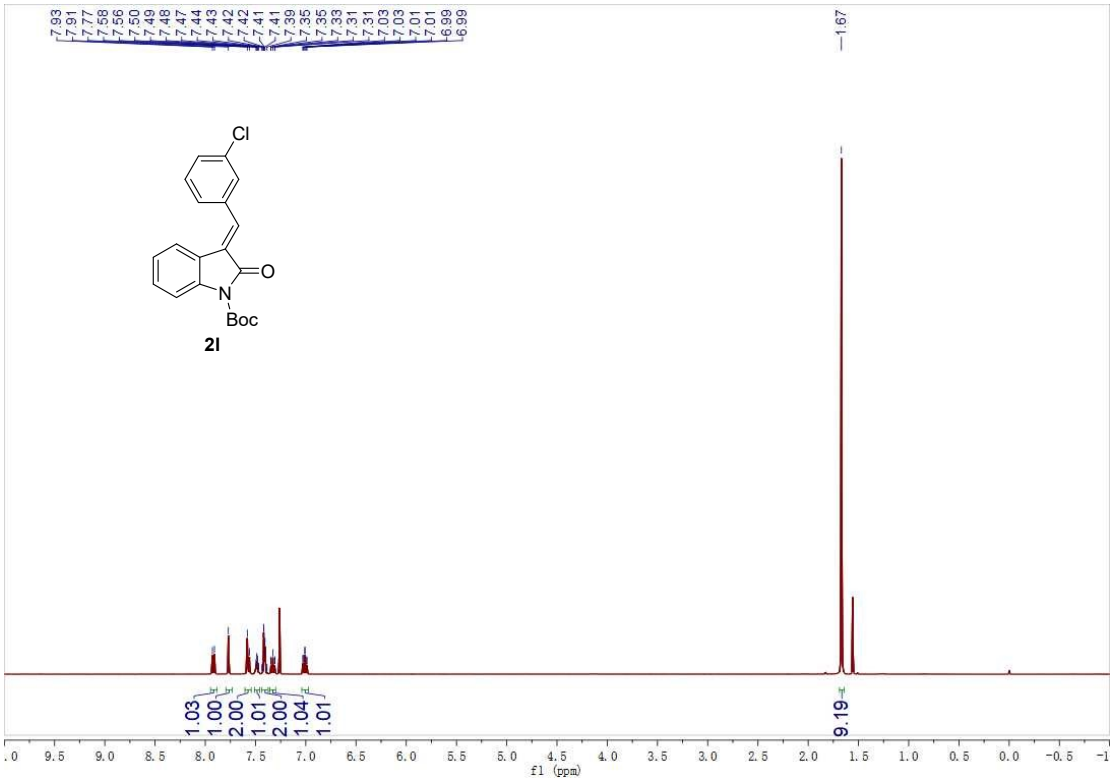
^{1}H NMR of **2k** (400 MHz, $CDCl_3$)



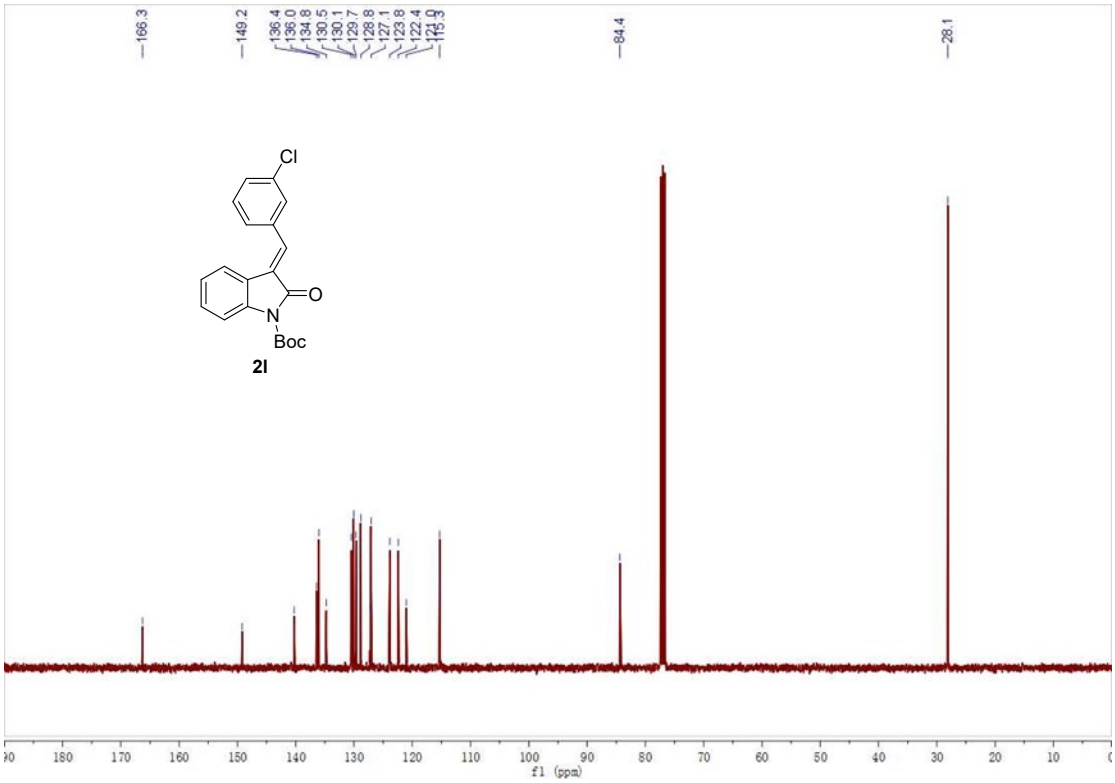
^{13}C {^{1}H} NMR of **2k** (100 MHz, $CDCl_3$)



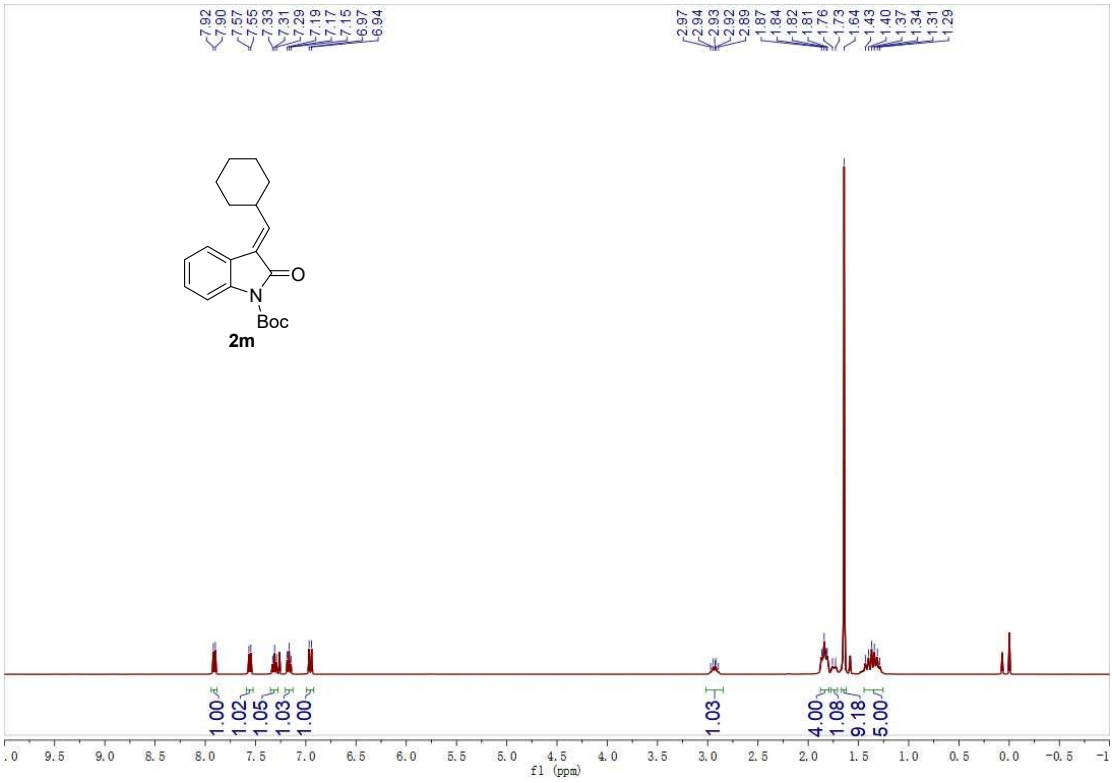
^{1}H NMR of **2l** (400 MHz, $CDCl_3$)



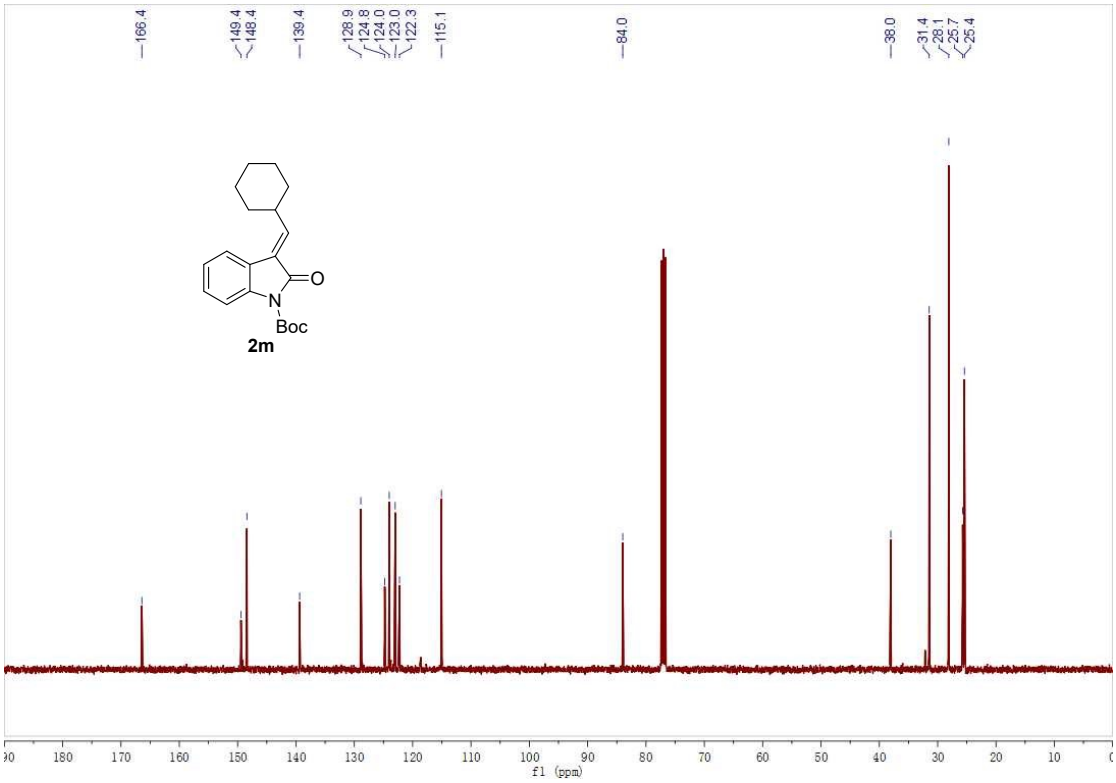
^{13}C {^{1}H} NMR of **2l** (100 MHz, $CDCl_3$)



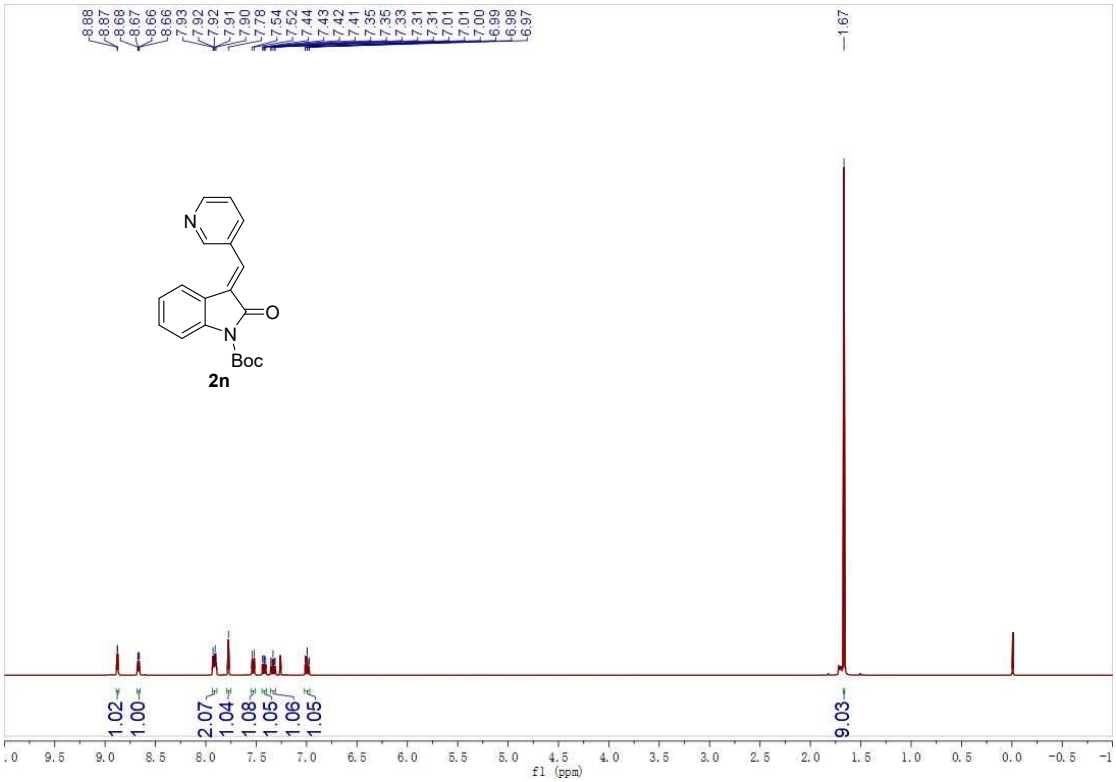
^{1}H NMR of **2m** (400 MHz, $CDCl_3$)



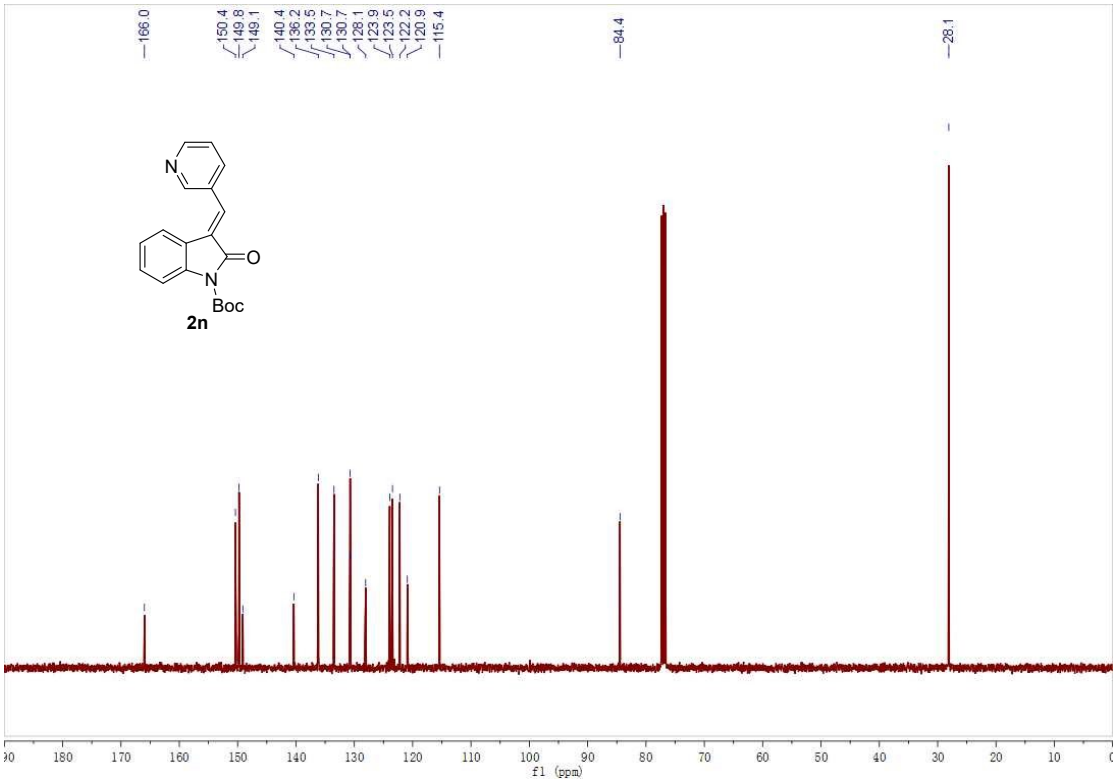
^{13}C {^{1}H} NMR of **2m** (100 MHz, $CDCl_3$)



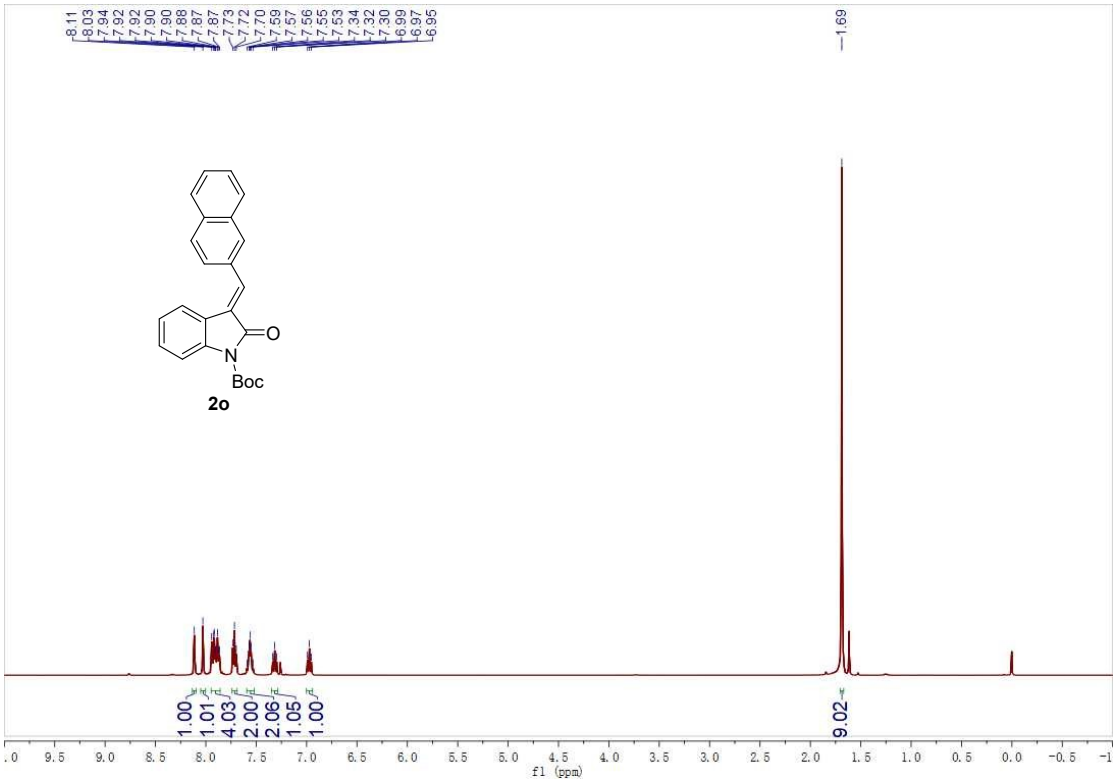
^{1}H NMR of **2n** (400 MHz, $CDCl_3$)



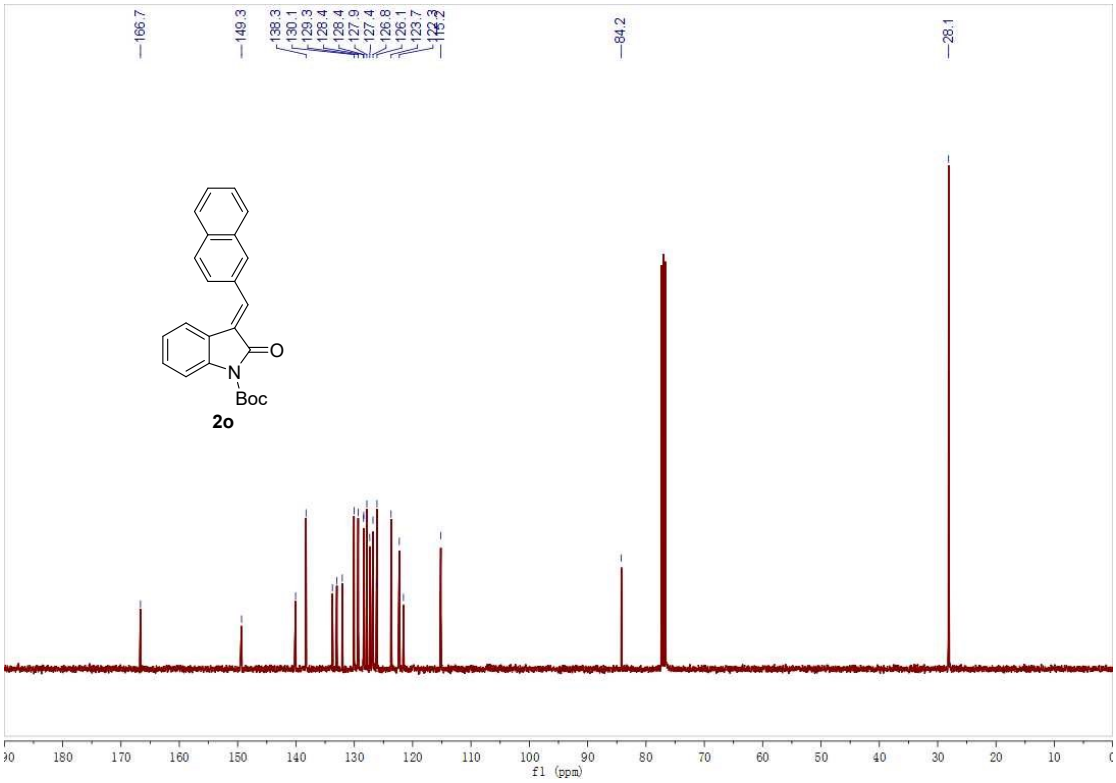
^{13}C {^{1}H} NMR of **2n** (100 MHz, $CDCl_3$)



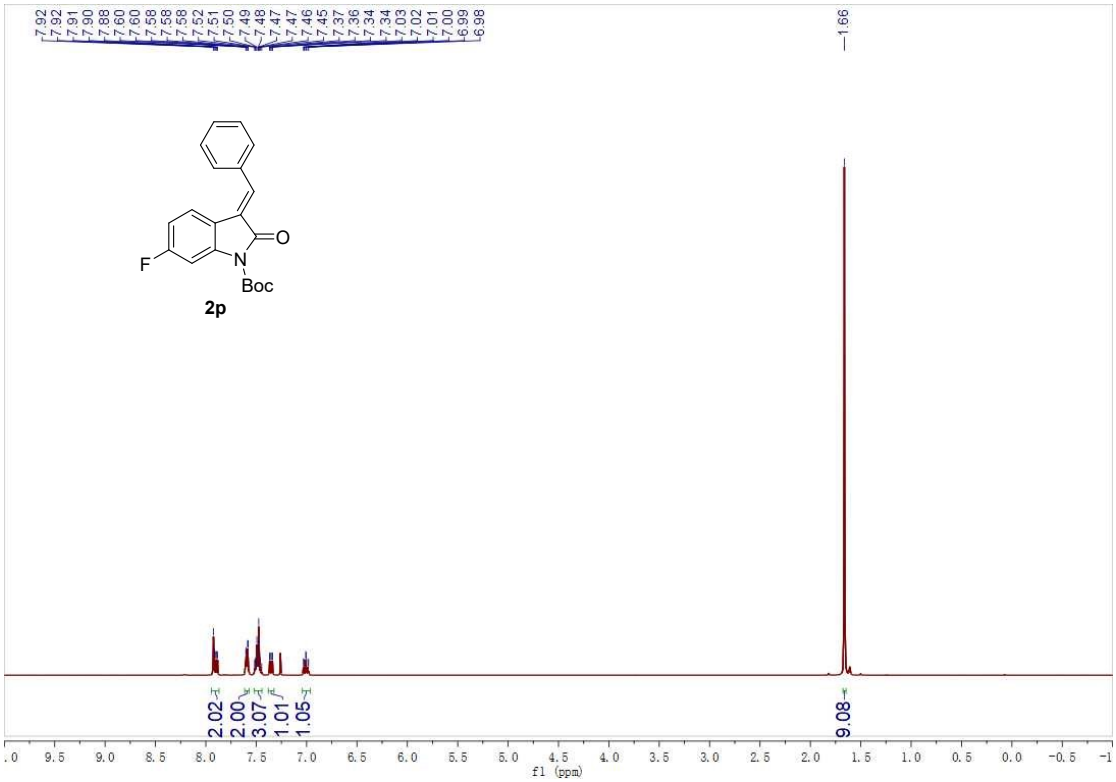
^{1}H NMR of **2o** (400 MHz, $CDCl_3$)



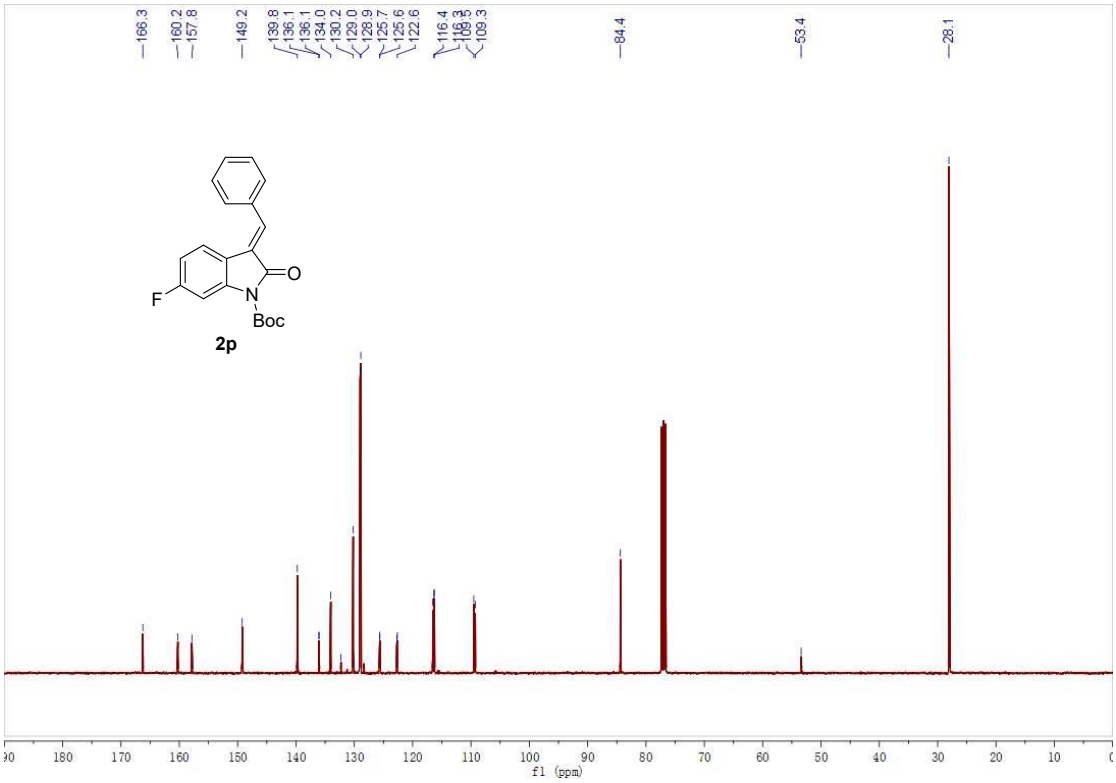
^{13}C {^{1}H} NMR of **2o** (100 MHz, $CDCl_3$)



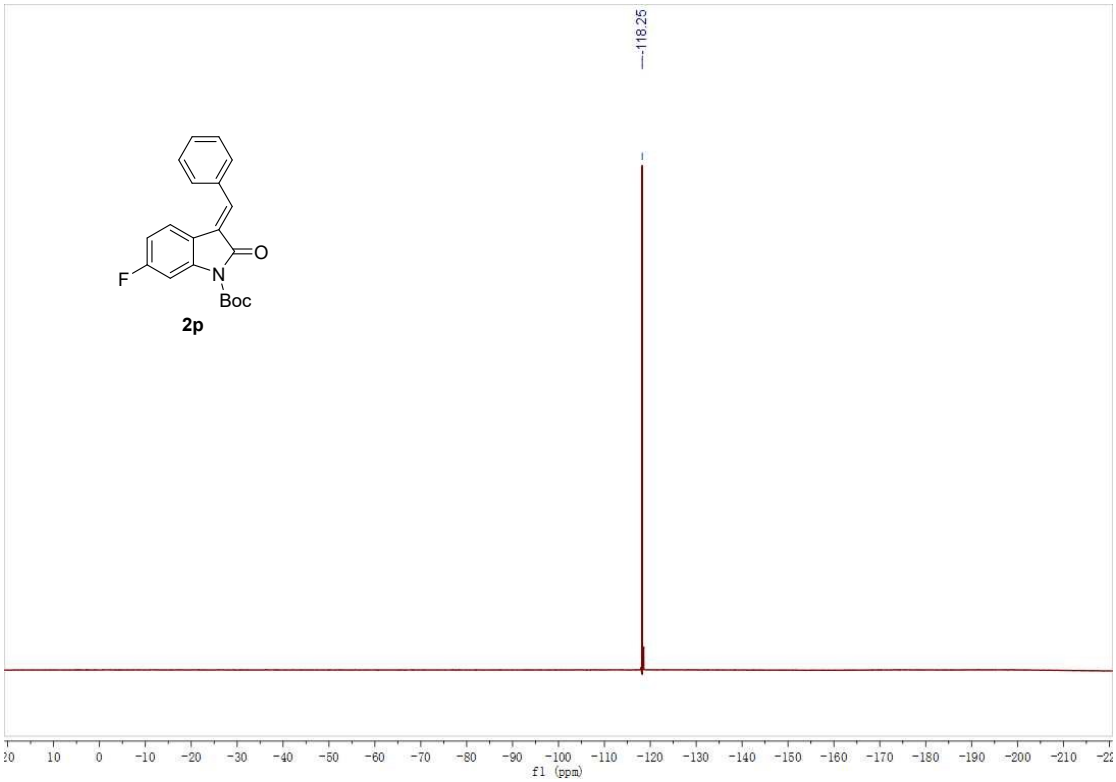
^{1}H NMR of **2p** (400 MHz, $CDCl_3$)



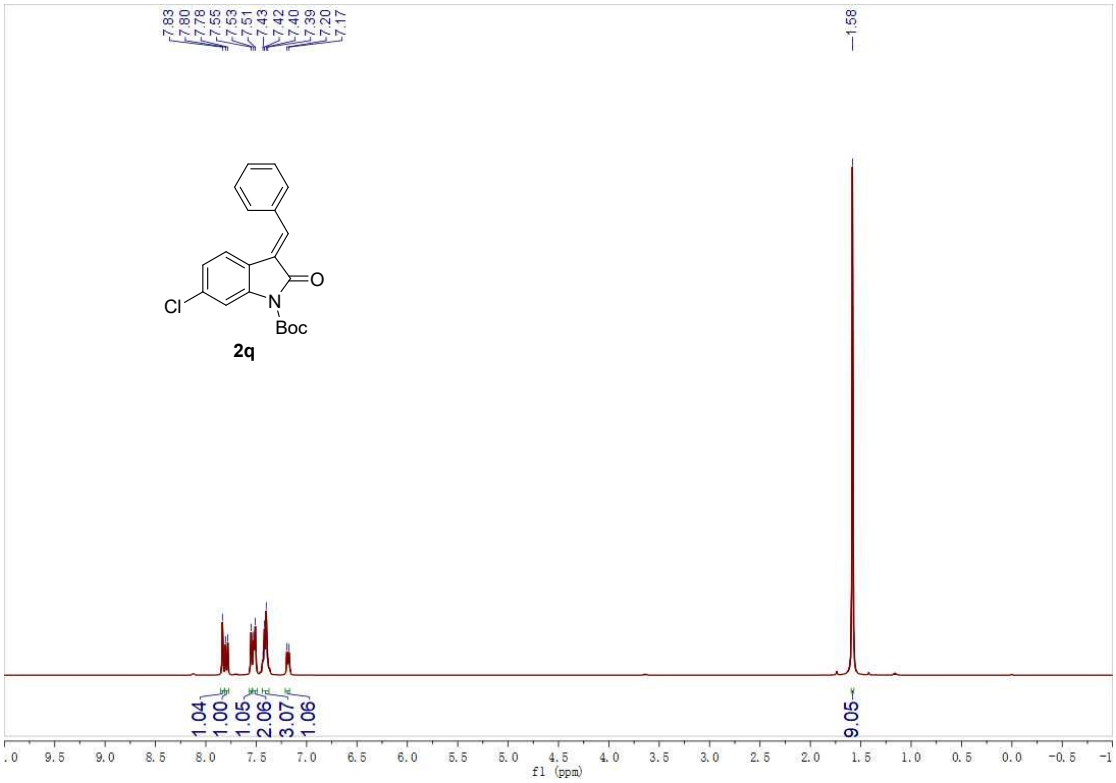
^{13}C {^{1}H} NMR of **2p** (100 MHz, $CDCl_3$)



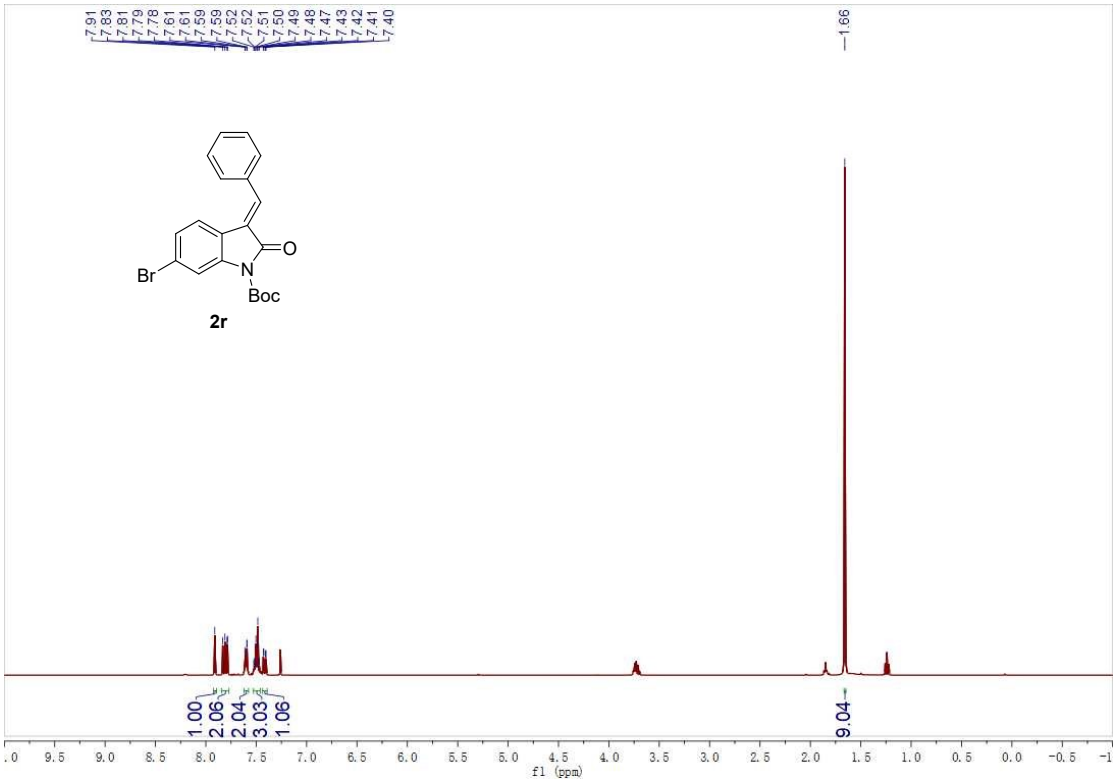
^{19}F NMR of **2p** ($CDCl_3$)



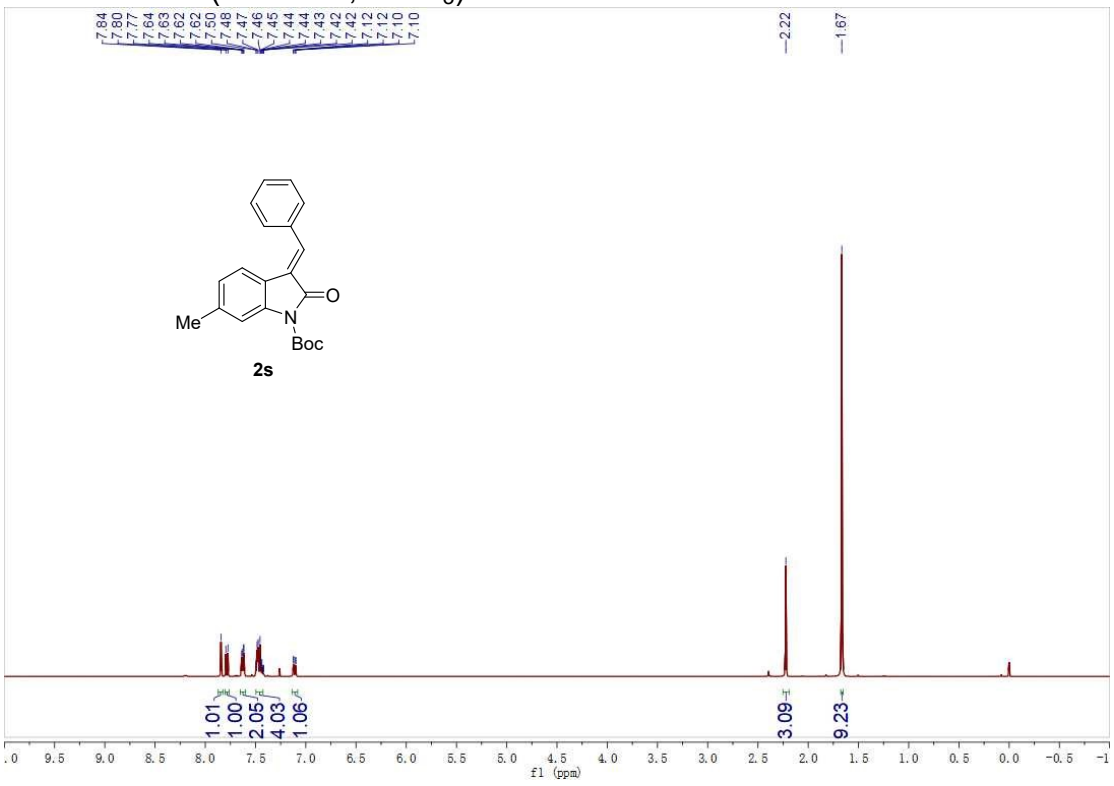
^{1}H NMR of **2q** ($CDCl_3$)



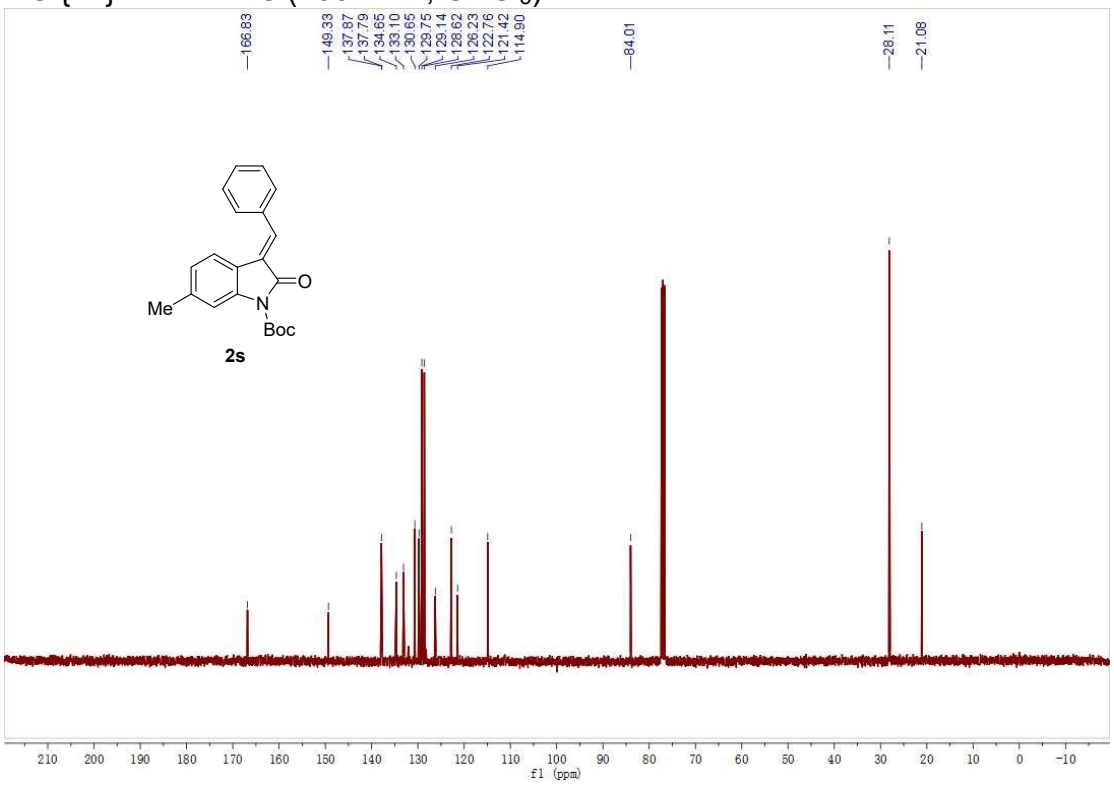
^{1}H NMR of **2r** (400 MHz, $CDCl_3$)



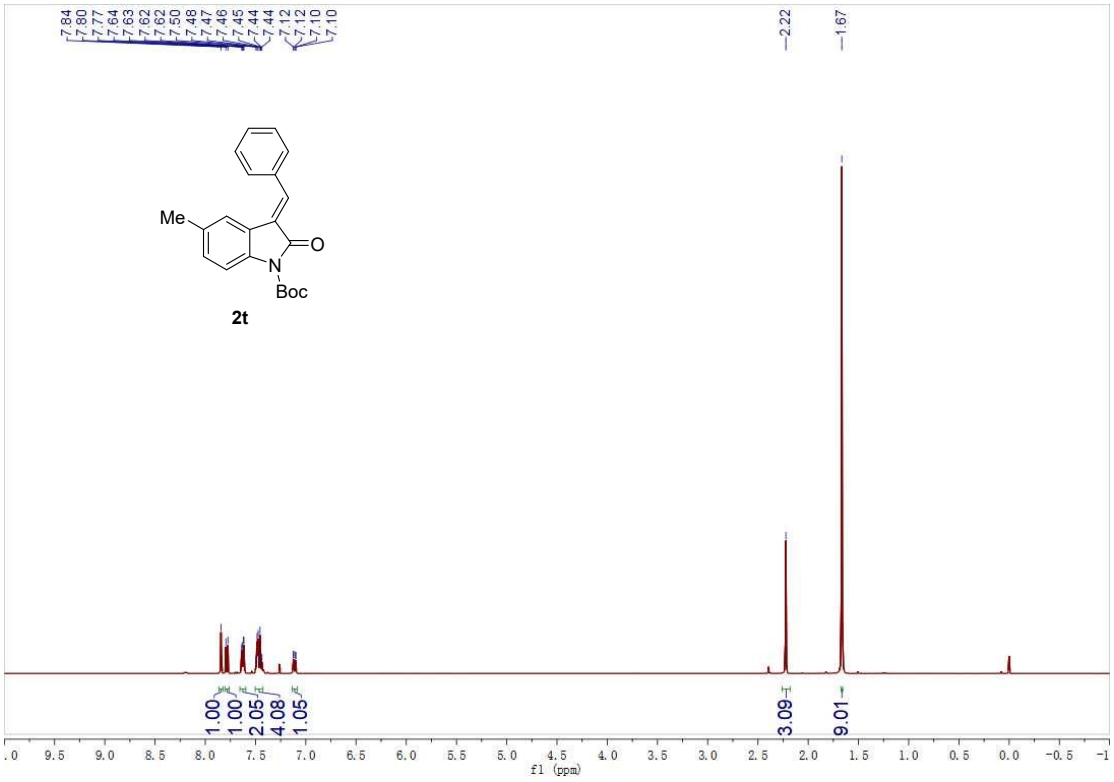
^{1}H NMR of **2s** (400 MHz, $CDCl_3$)



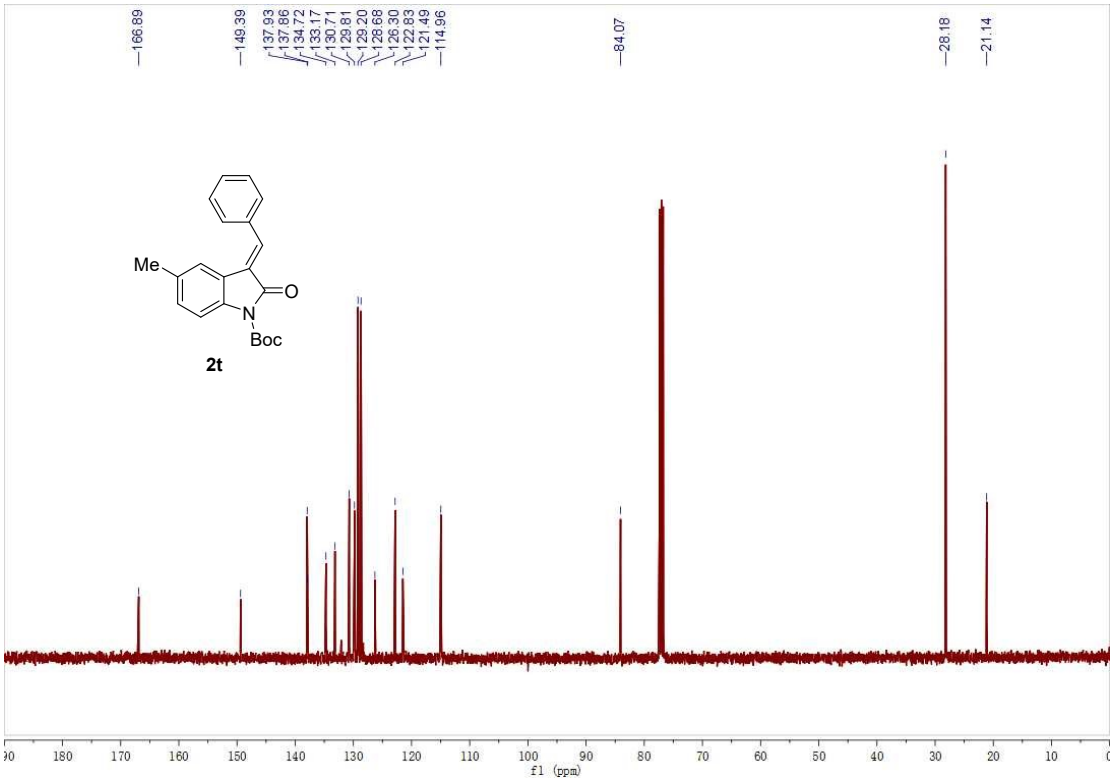
^{13}C {^{1}H} NMR of **2s** (100 MHz, $CDCl_3$)



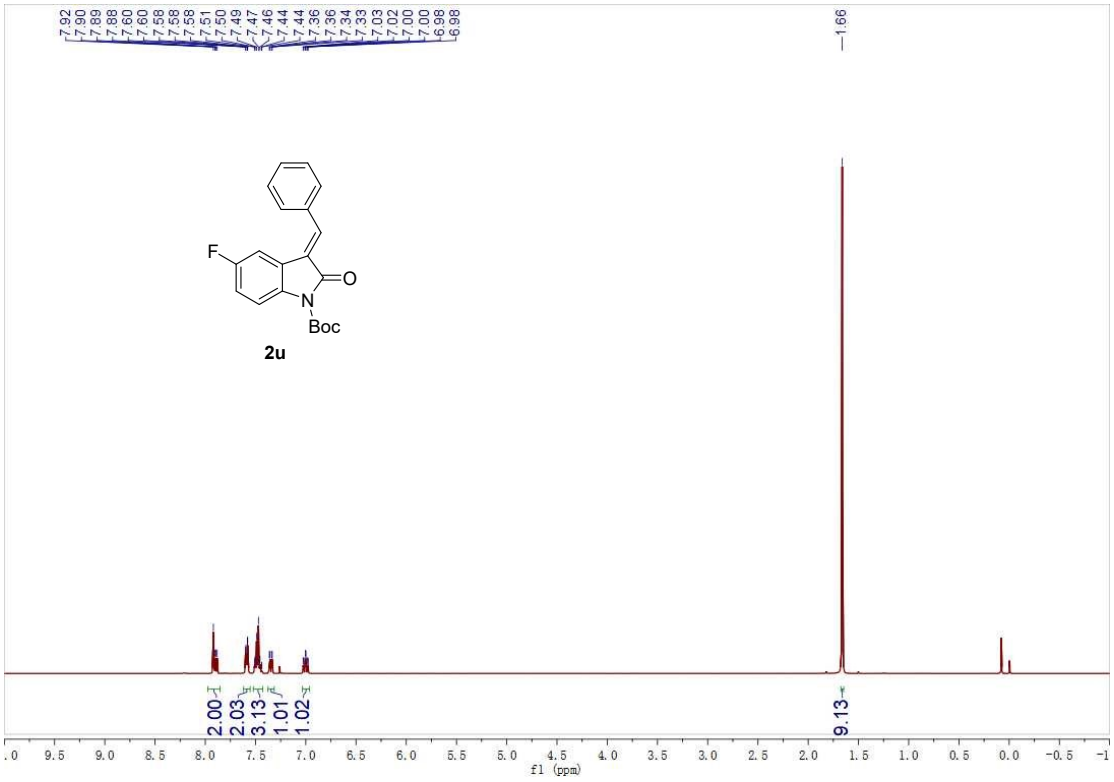
^{1}H NMR of **2t** (400 MHz, $CDCl_3$)



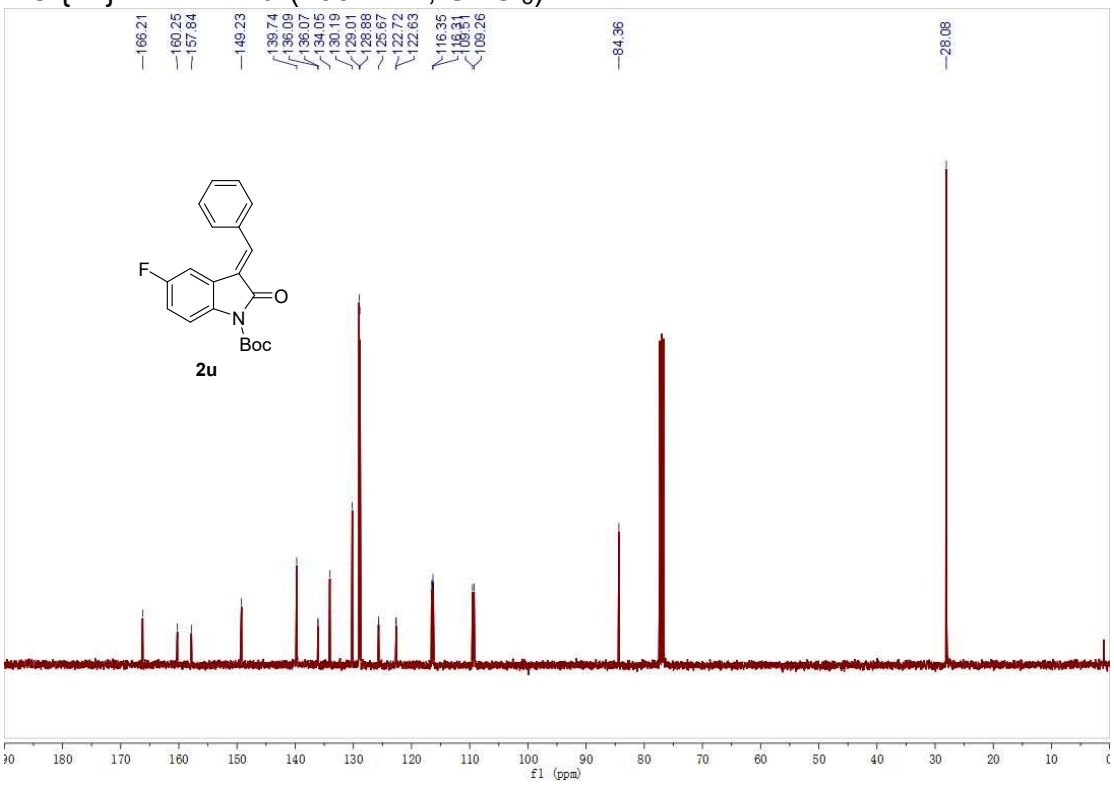
^{13}C {^{1}H} NMR of **2t** (100 MHz, $CDCl_3$)



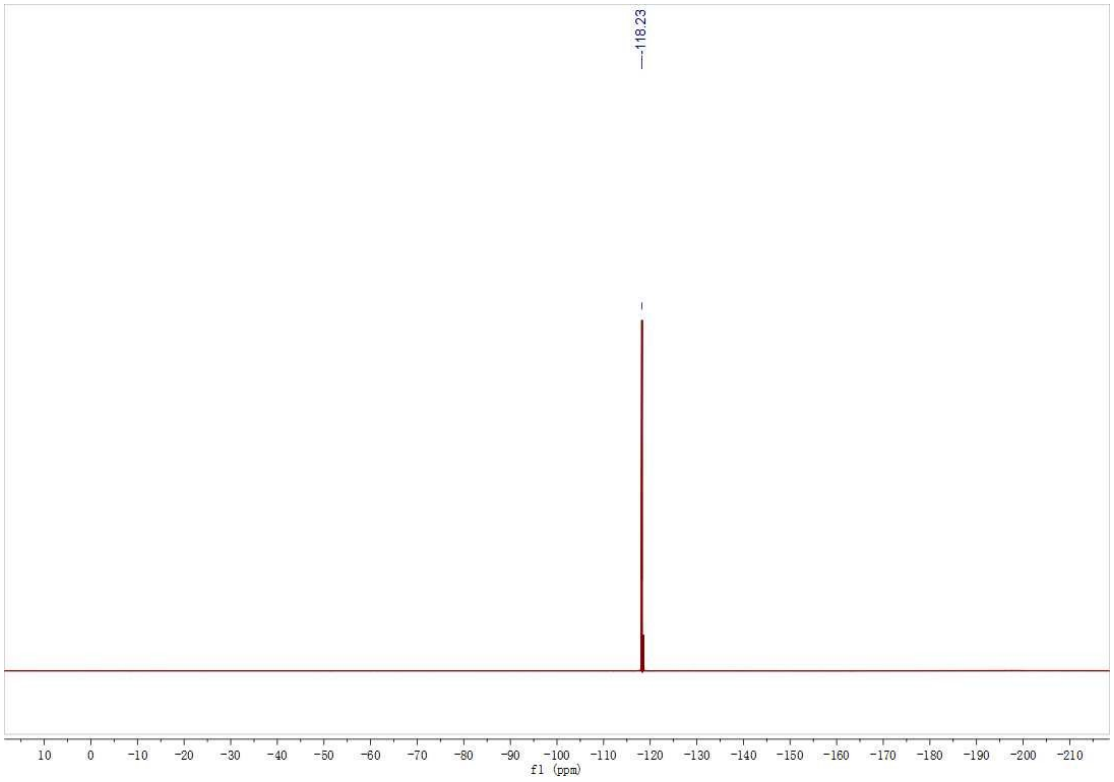
^{1}H NMR of **2u** (400 MHz, $CDCl_3$)



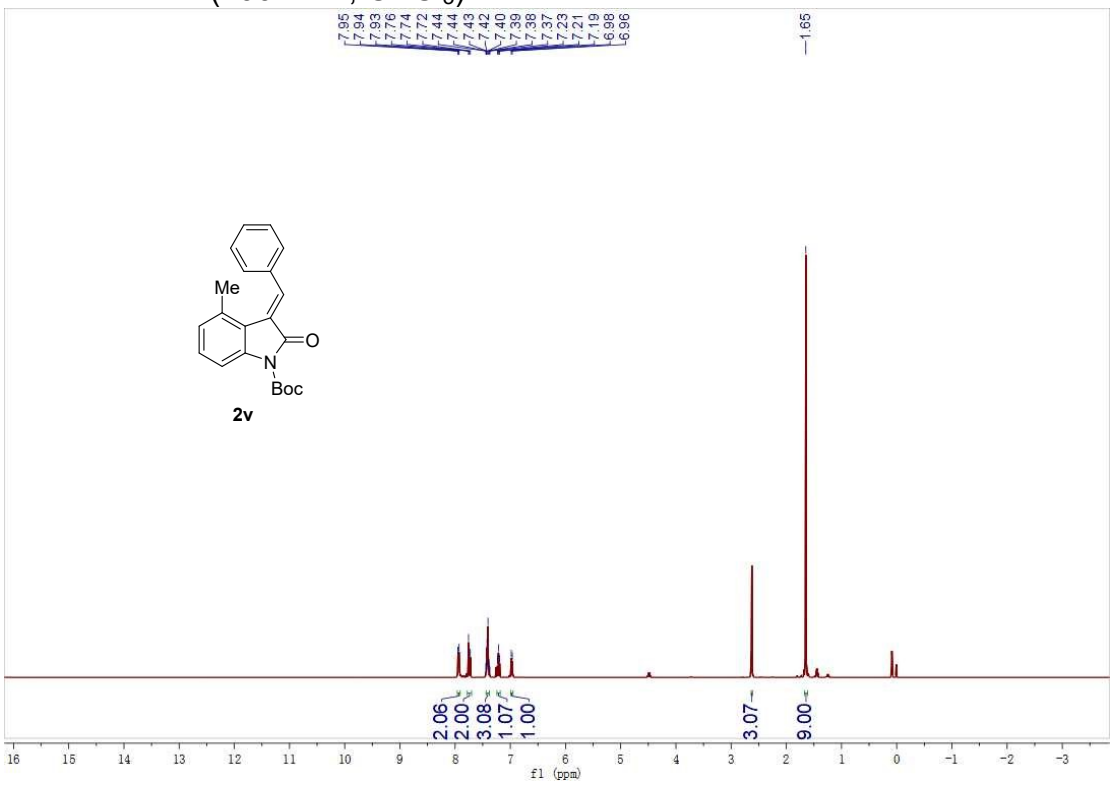
^{13}C {^{1}H} NMR of **2u** (100 MHz, $CDCl_3$)



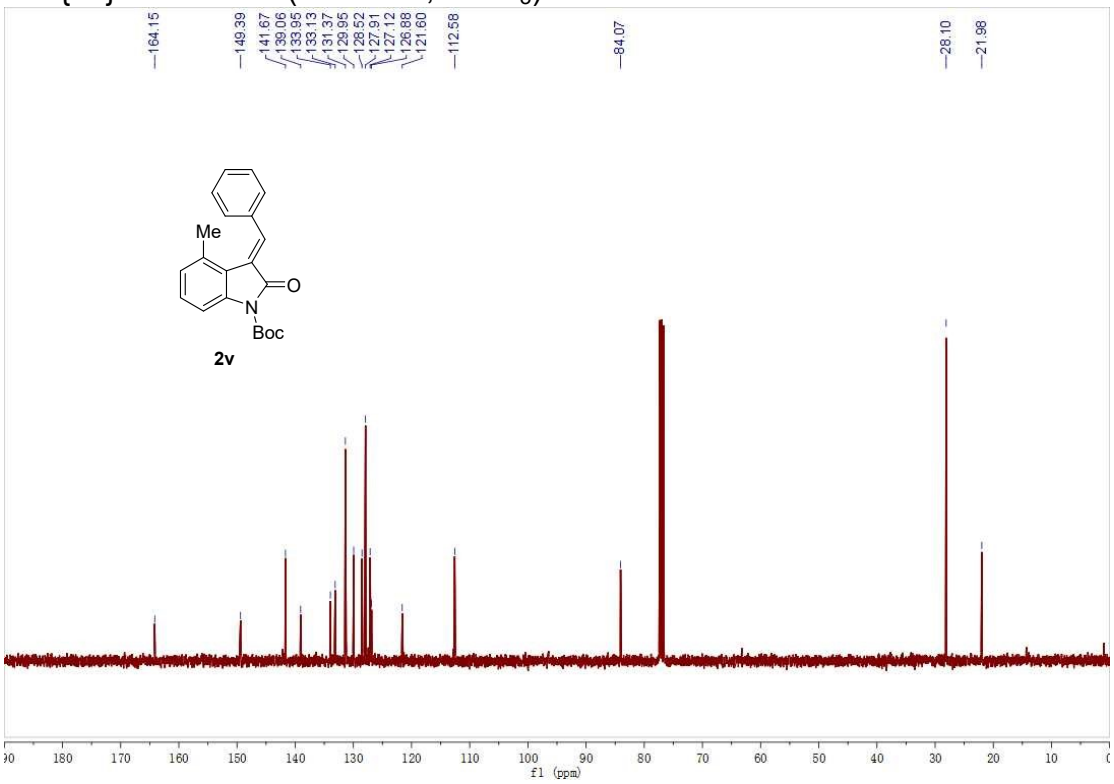
^{19}F NMR of **2u** (376 MHz, $CDCl_3$)



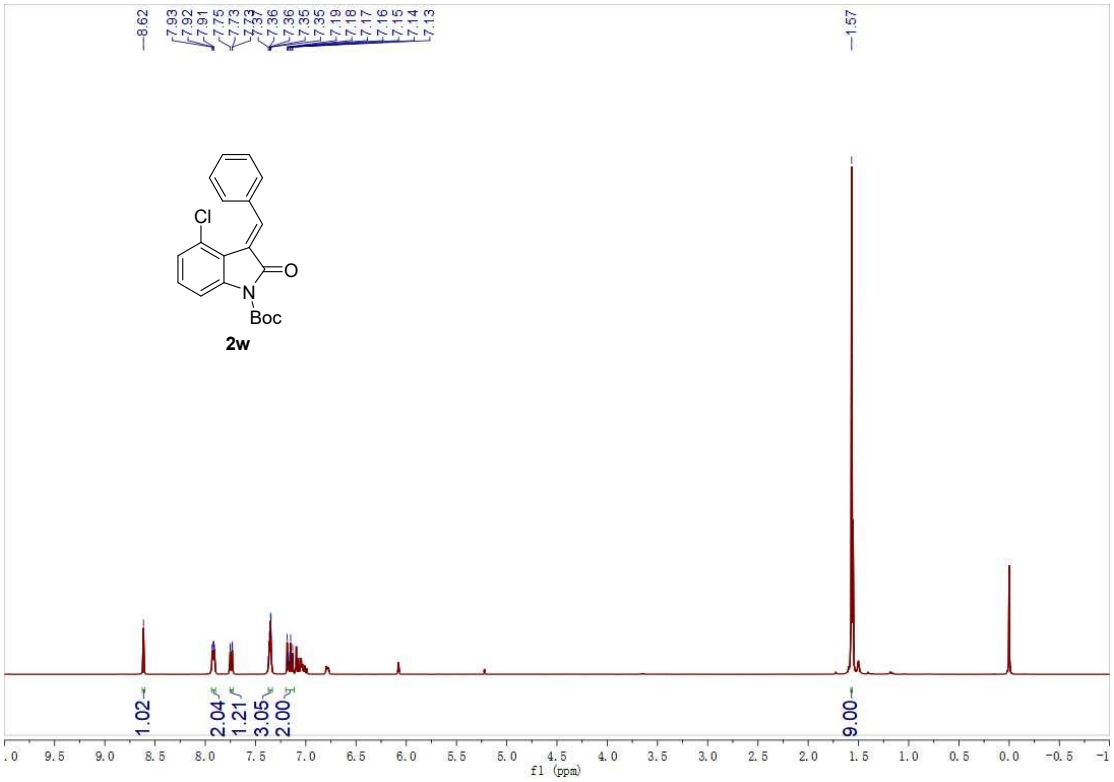
^{1}H NMR of **2v** (400 MHz, $CDCl_3$)



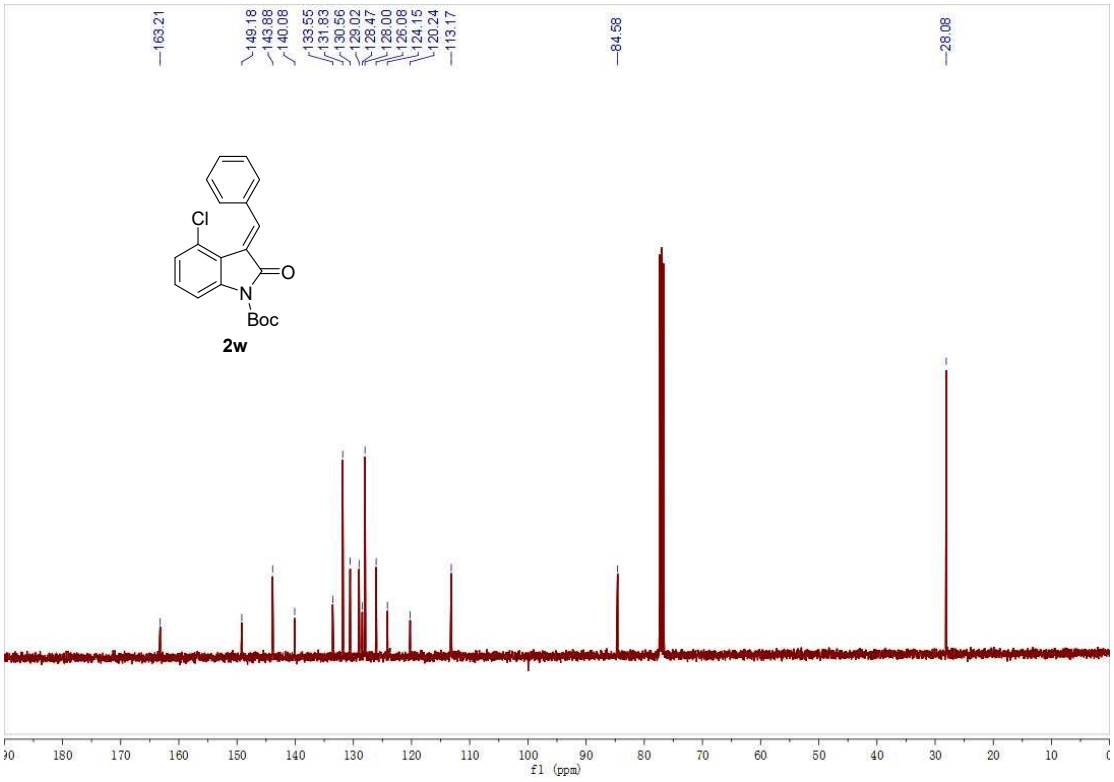
^{13}C {^{1}H} NMR of **2v** (100 MHz, $CDCl_3$)



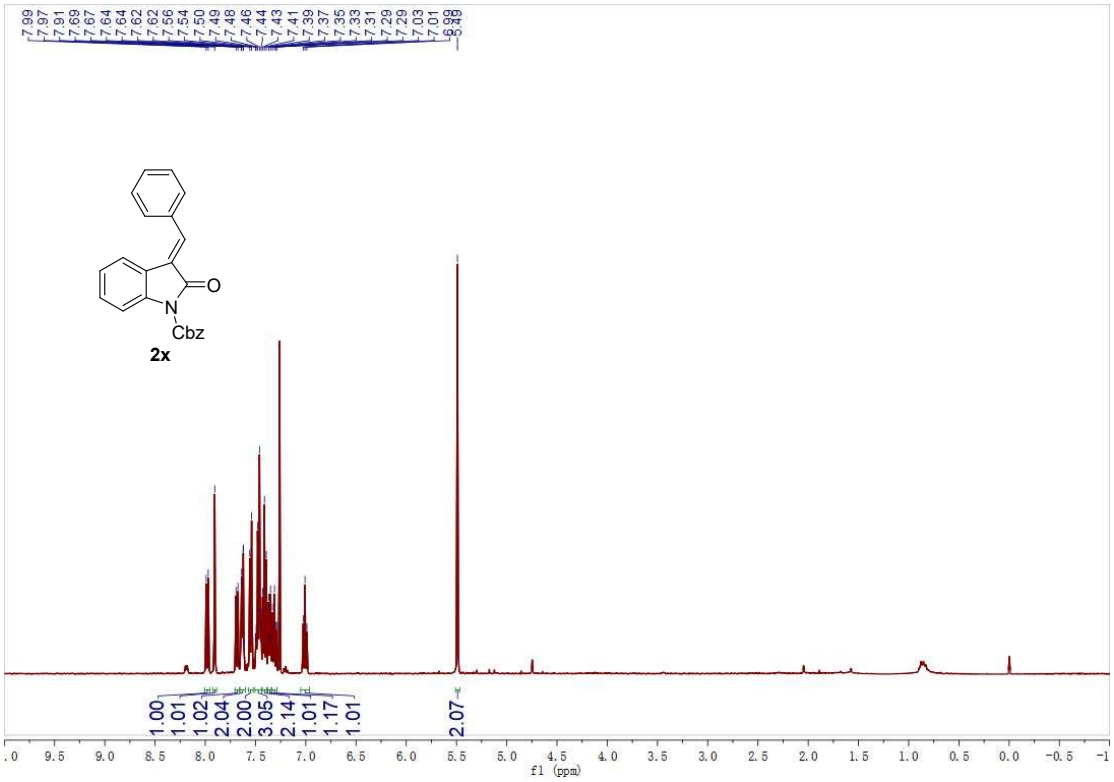
^{1}H NMR of **2w** (400 MHz, $CDCl_3$)



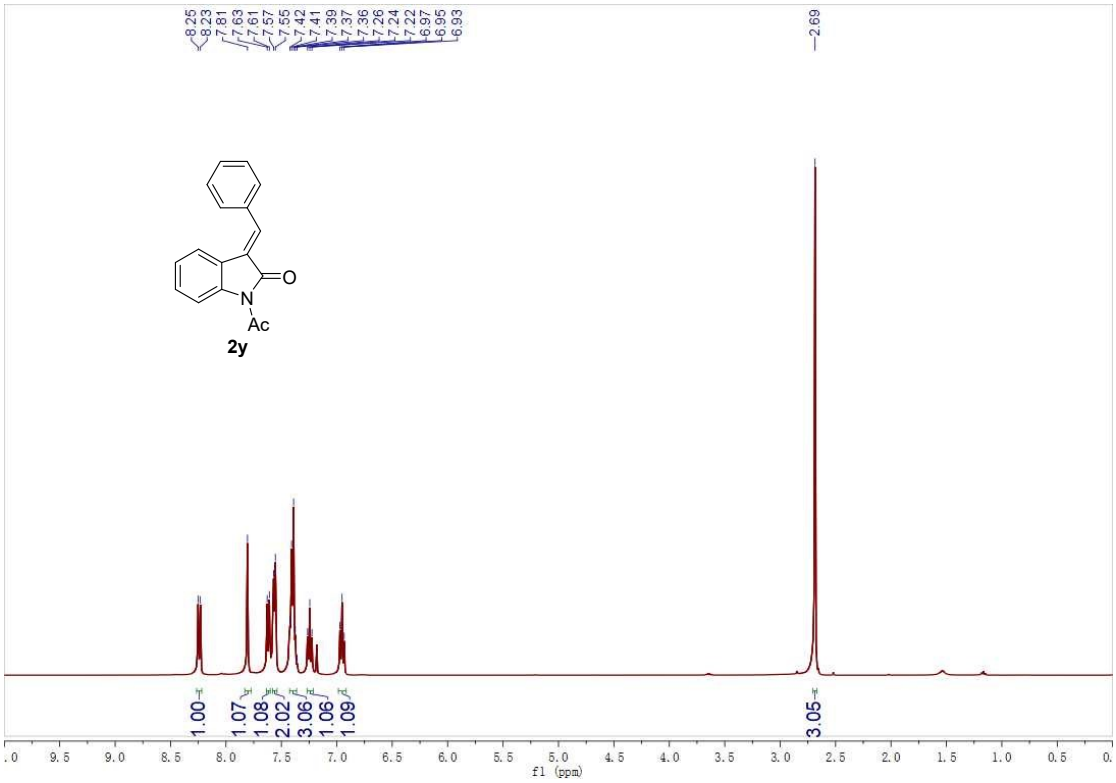
^{13}C {^{1}H} NMR of **2w** (100 MHz, $CDCl_3$)



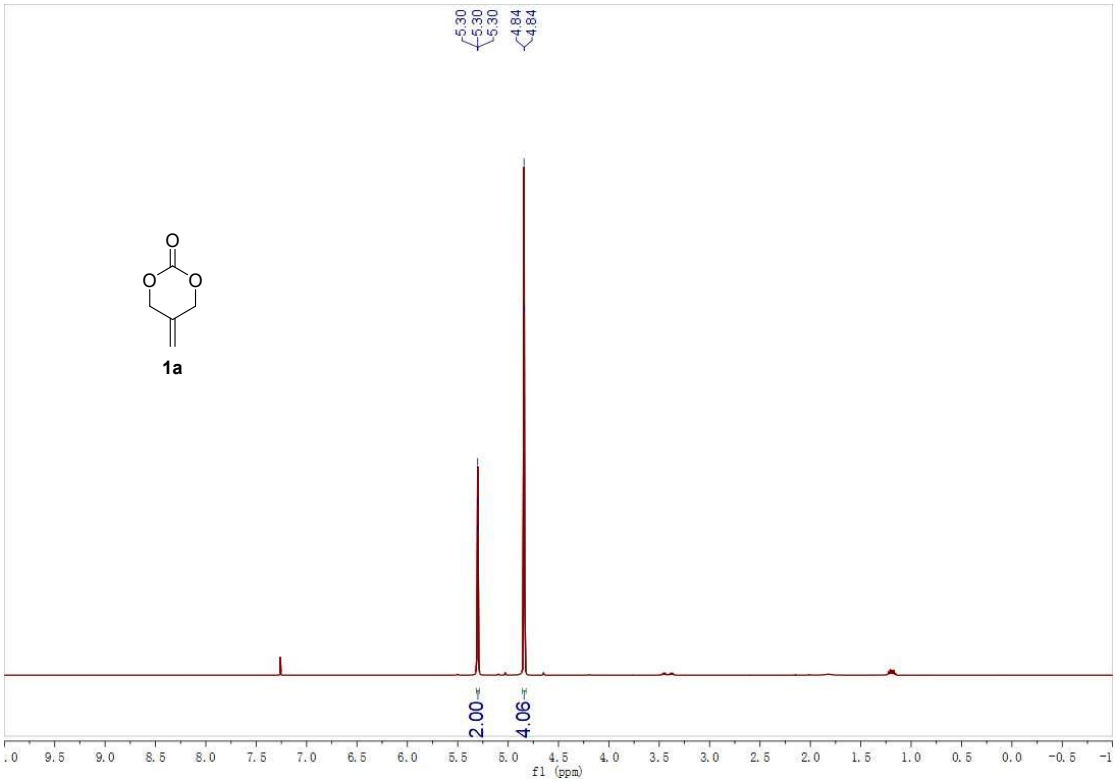
^{1}H NMR of **2x** (400 MHz, $CDCl_3$)



^{1}H NMR of **2y** (400 MHz, $CDCl_3$)

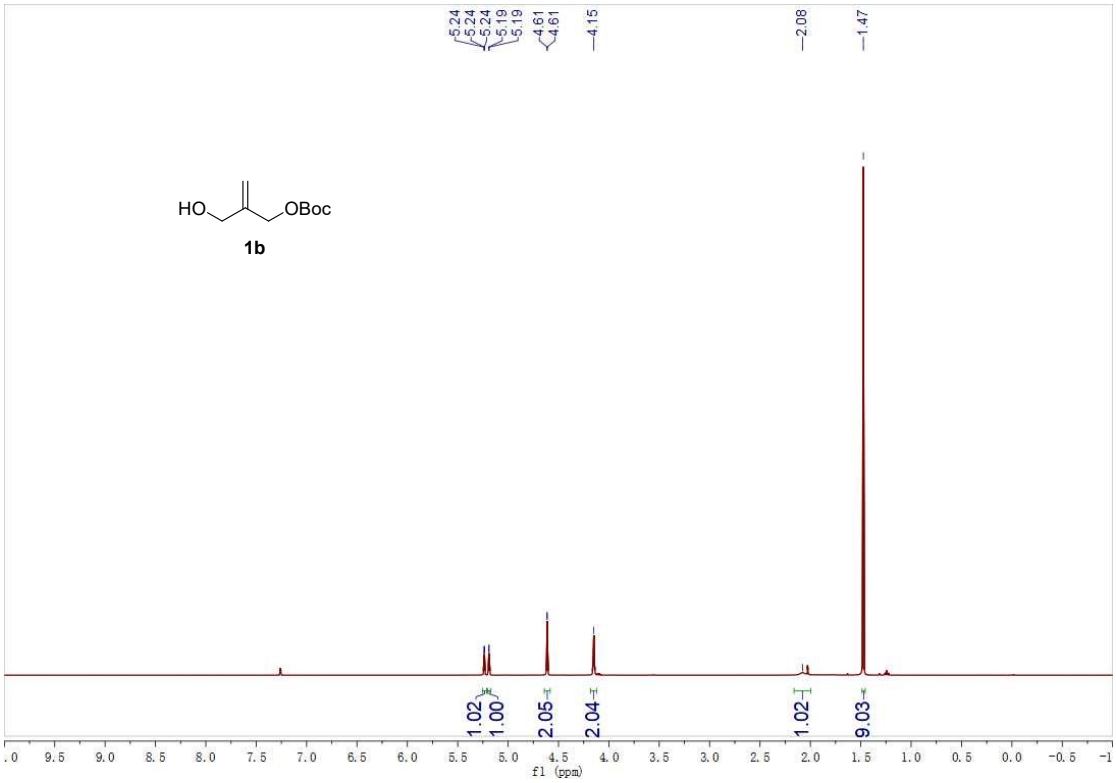


^{1}H NMR of **1a** (400 MHz, $CDCl_3$)



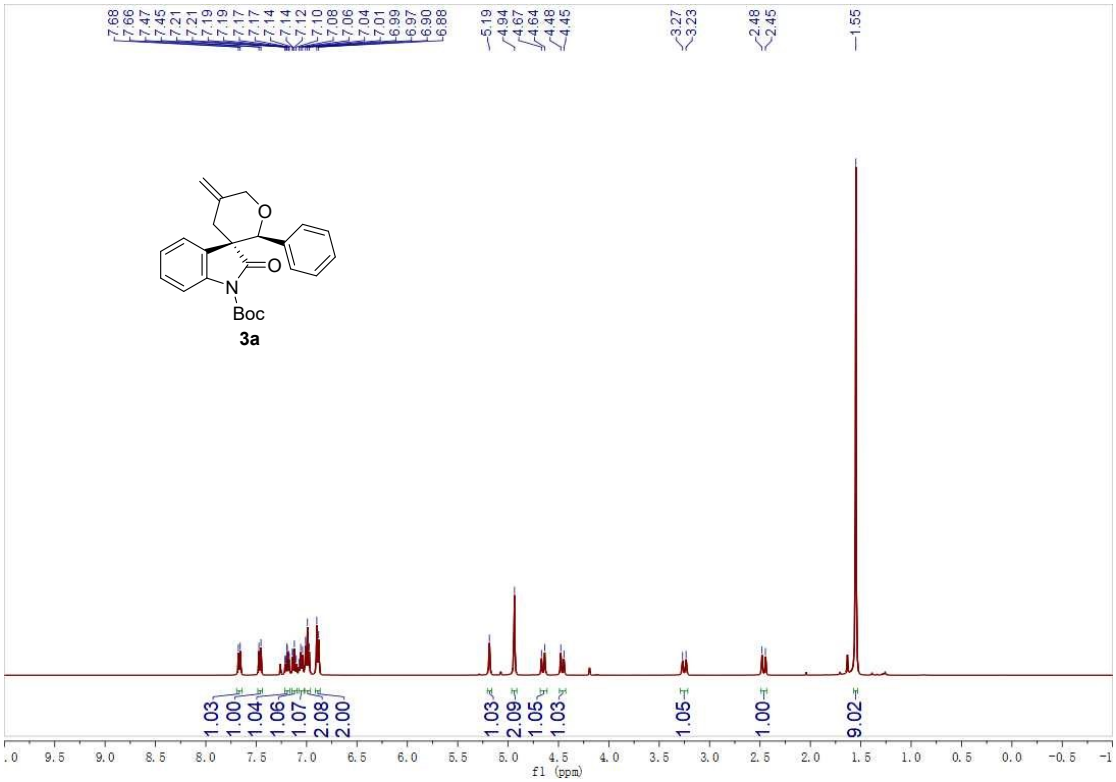
1a

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

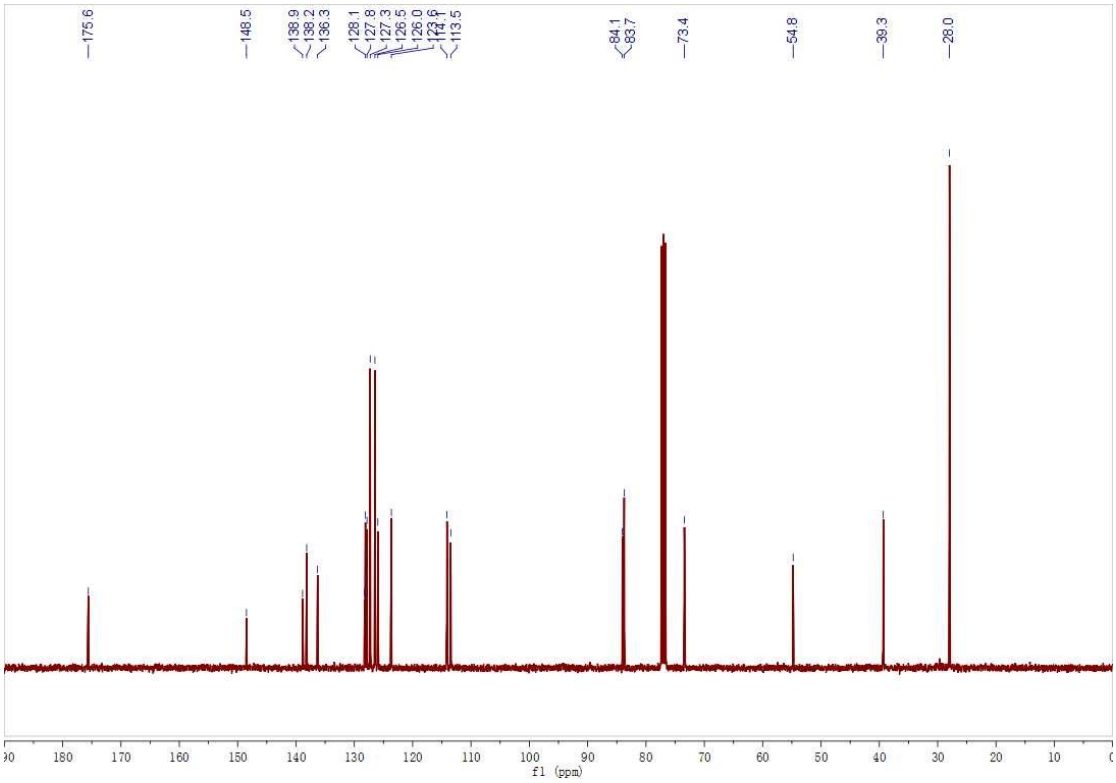


1b

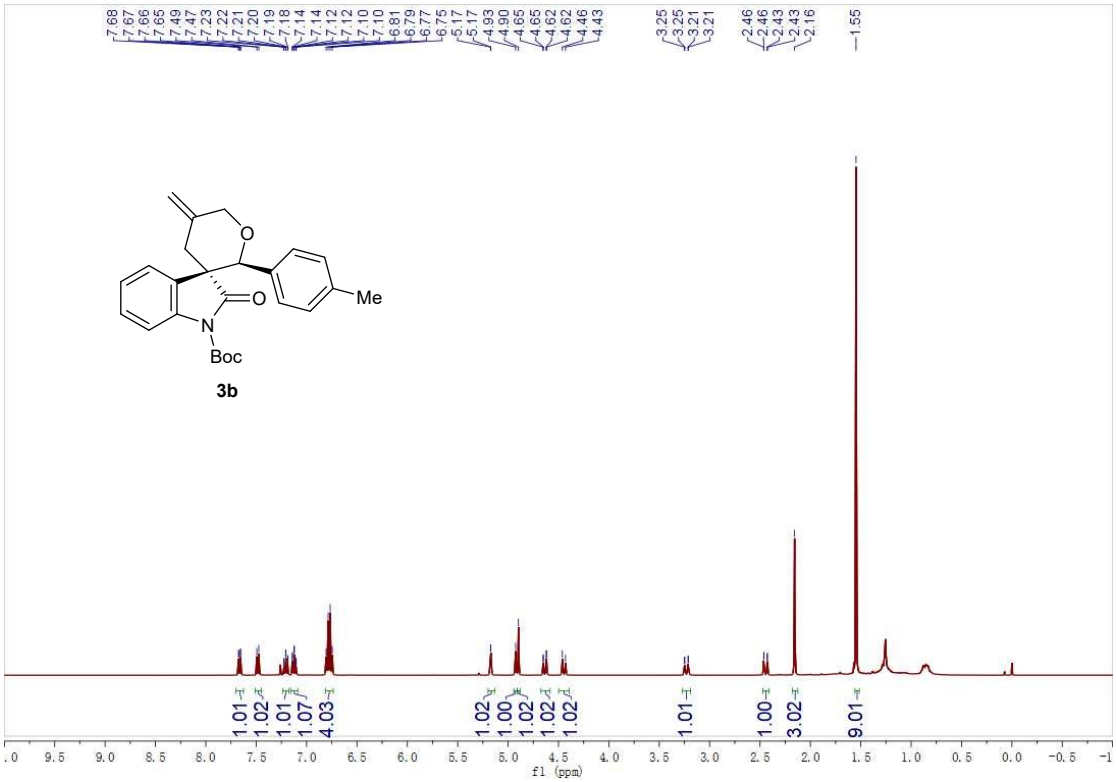
^{1}H NMR of **3a** (400 MHz, $CDCl_3$)



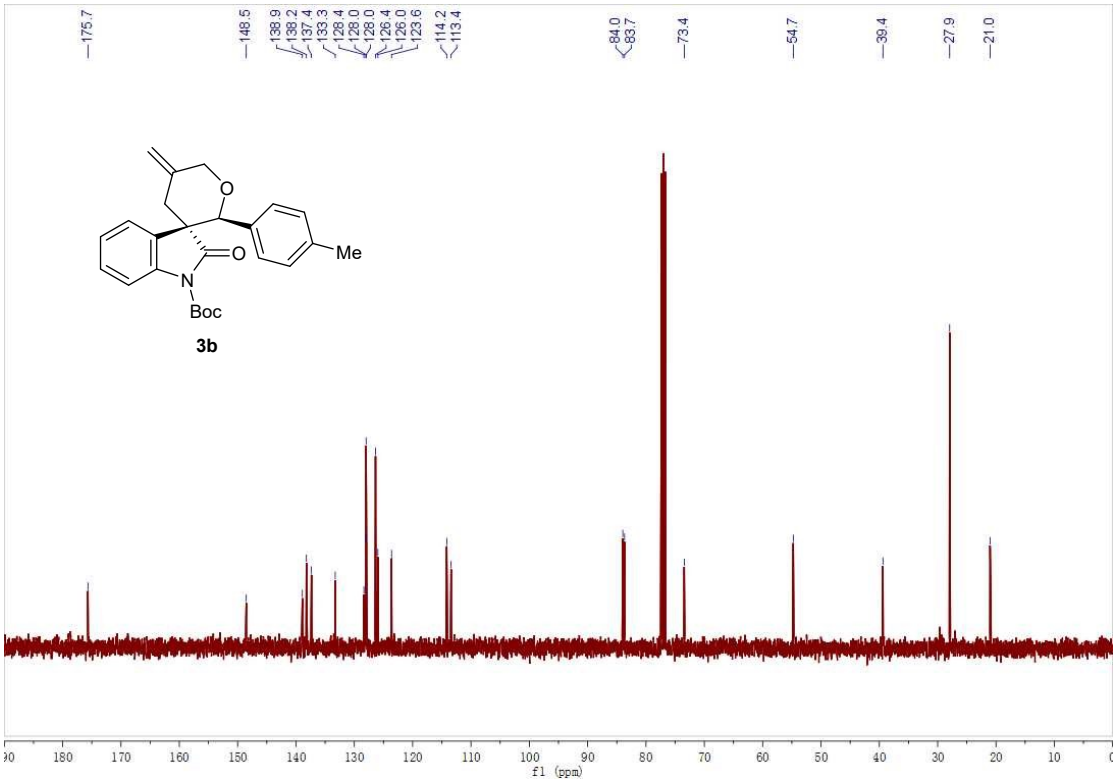
^{13}C {^{1}H} NMR of **3a** (100 MHz, $CDCl_3$)



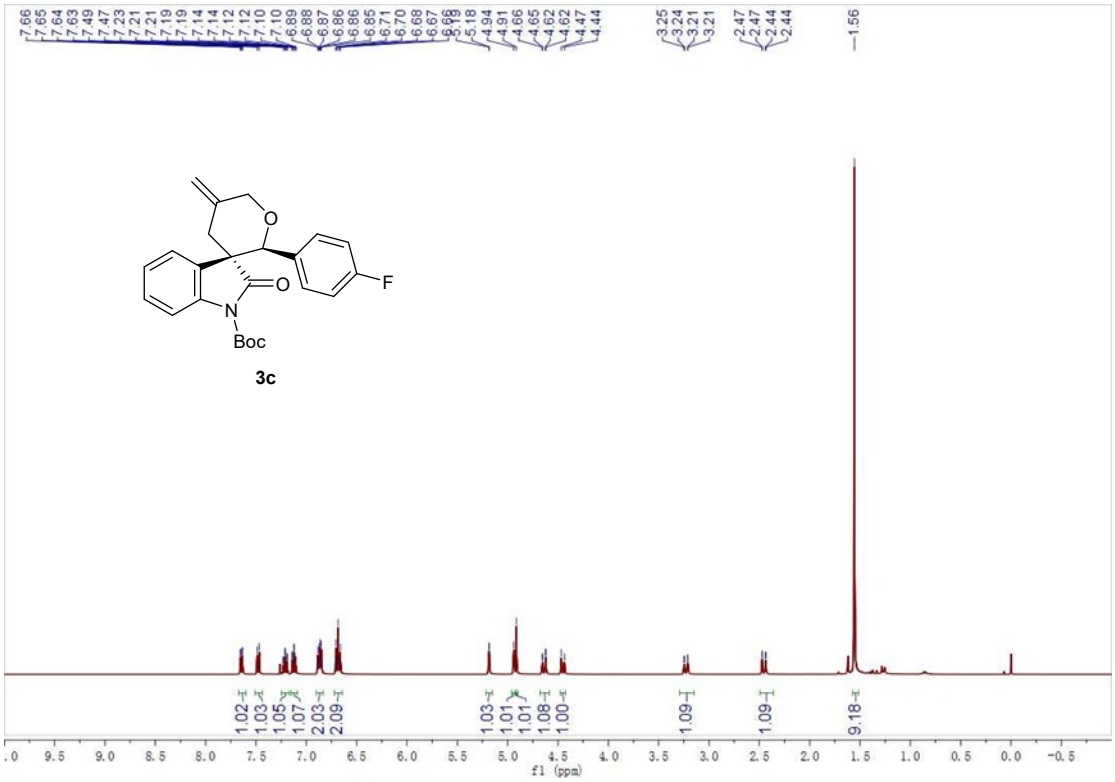
^{1}H NMR of **3b** (400 MHz, $CDCl_3$)



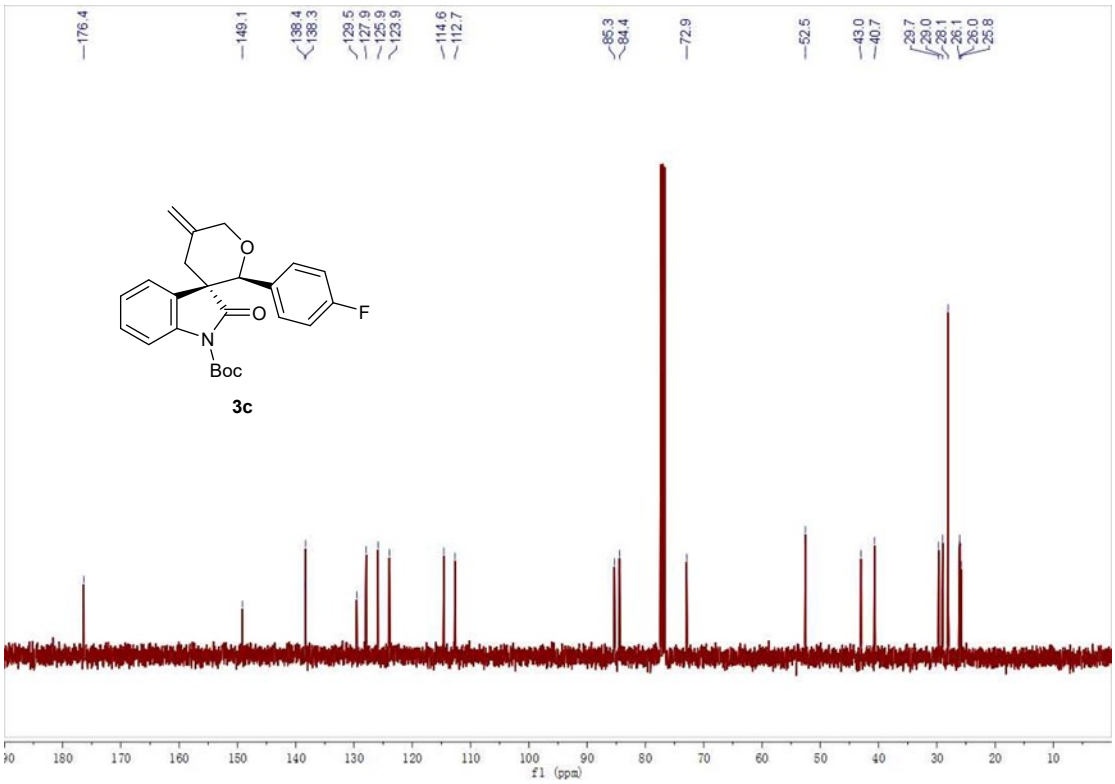
^{13}C {^{1}H} NMR of **3b** (100 MHz, $CDCl_3$)



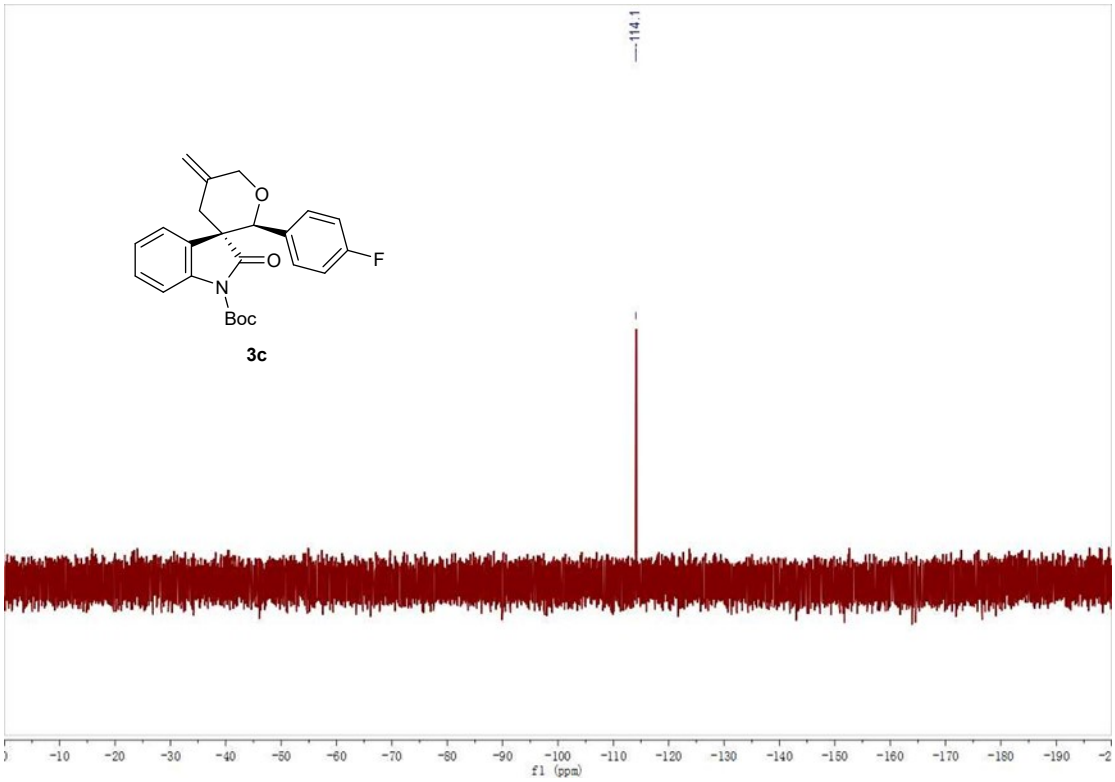
^{1}H NMR of **3c** (400 MHz, $CDCl_3$)



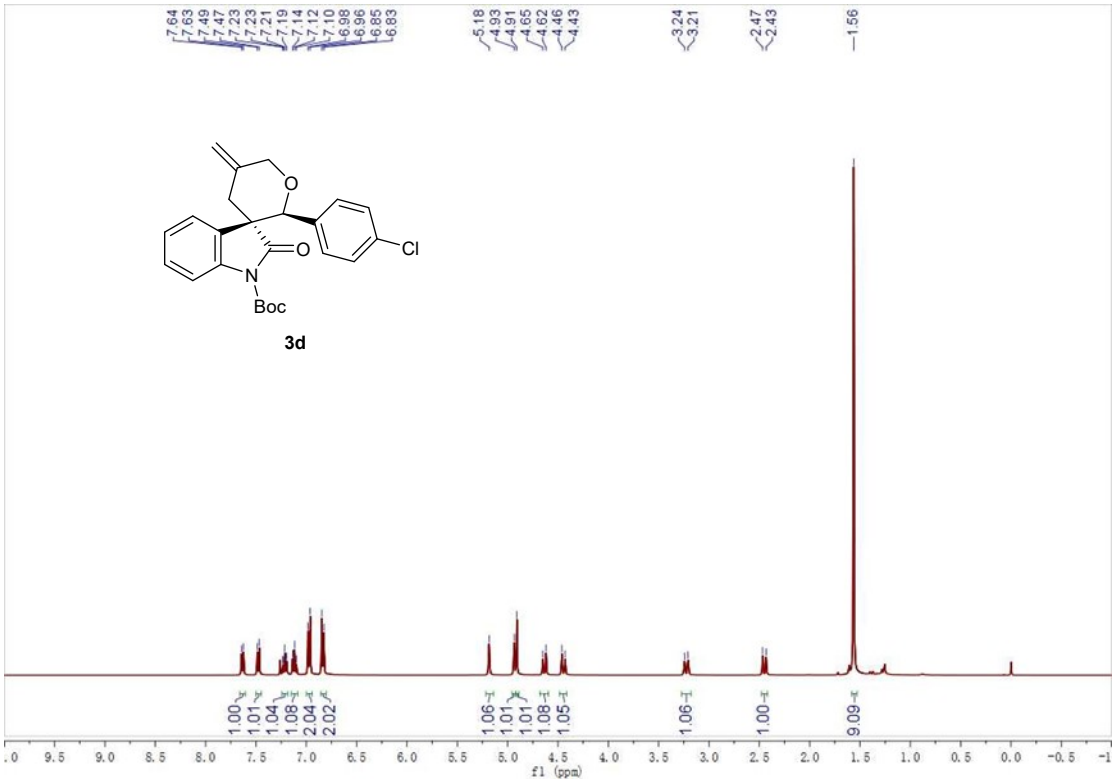
^{13}C {^{1}H} NMR of **3c** (100 MHz, $CDCl_3$)



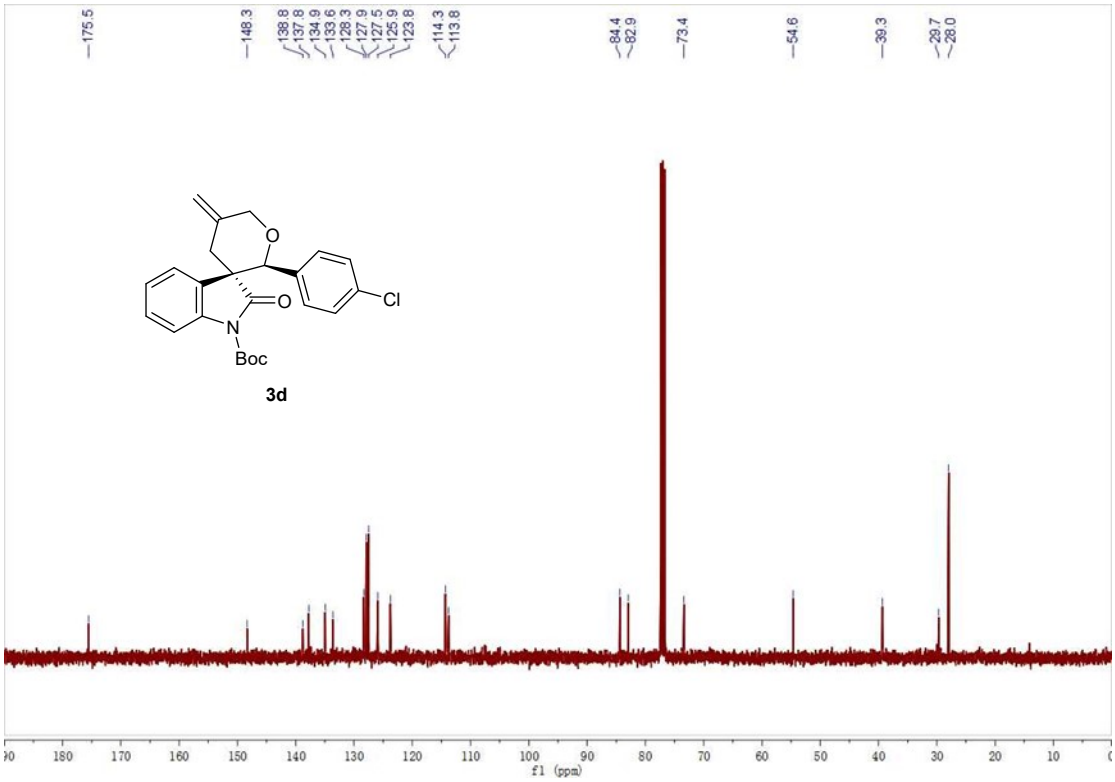
^{19}F NMR of **3c** (376 MHz, $CDCl_3$)



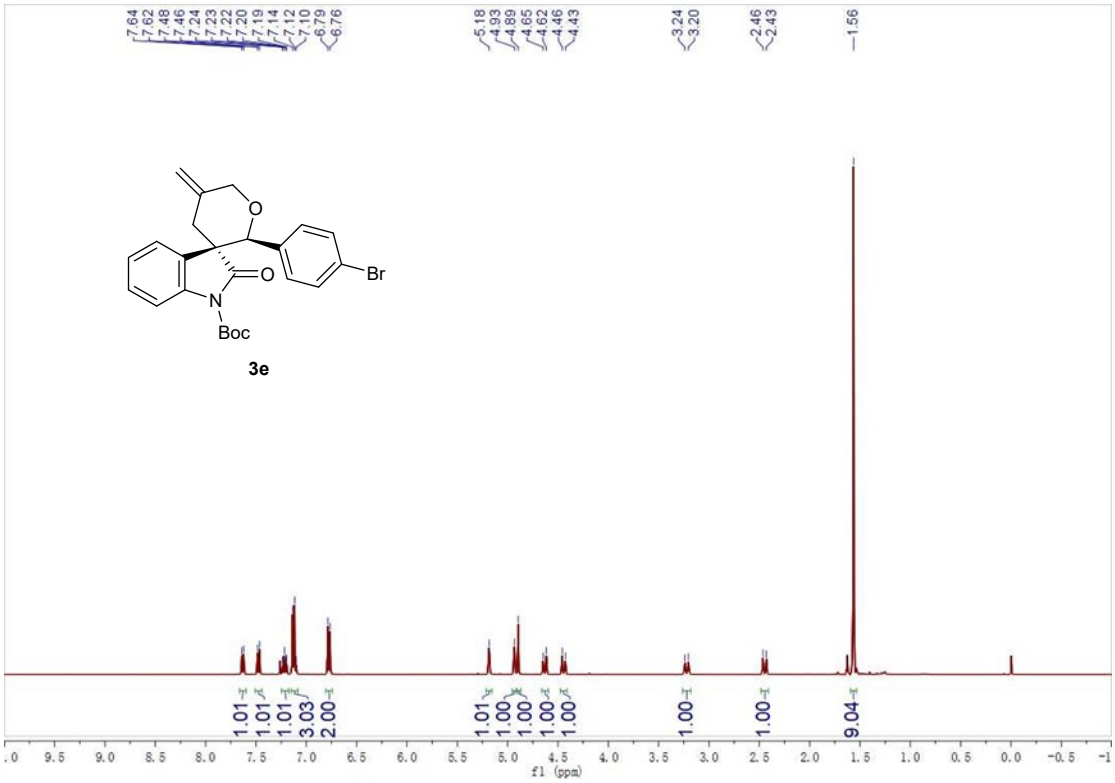
^{1}H NMR of **3d** (400 MHz, $CDCl_3$)



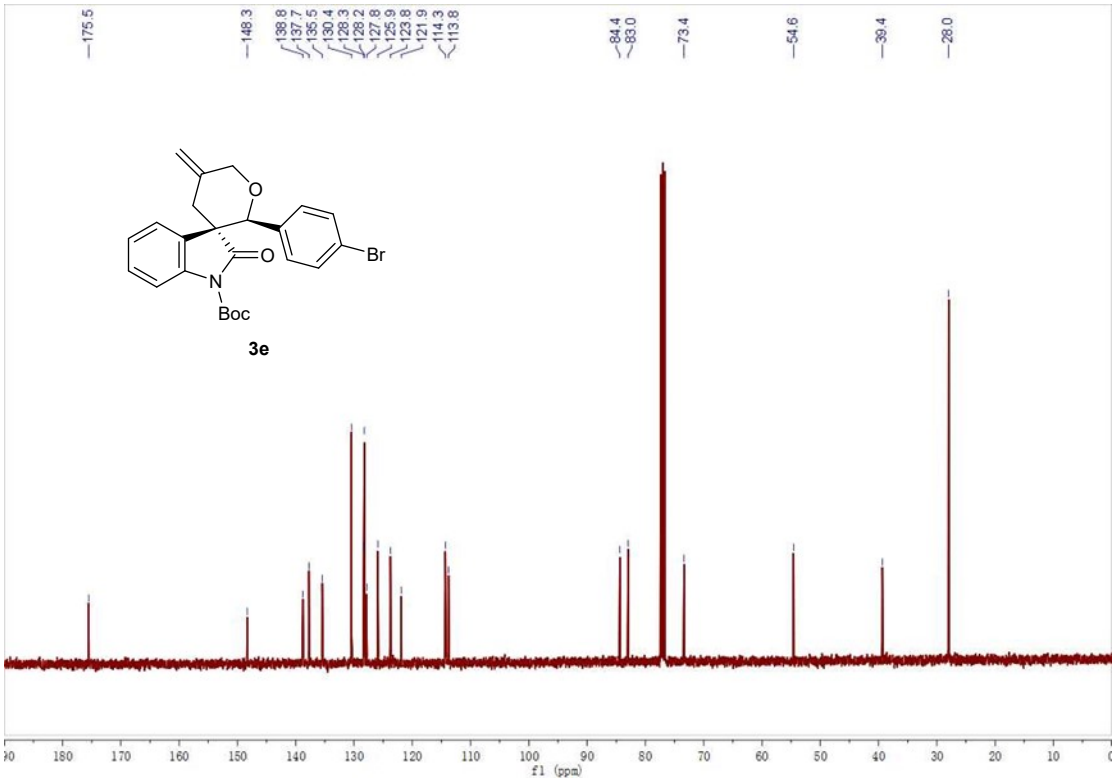
^{13}C {^{1}H} NMR of **3d** (100 MHz, $CDCl_3$)



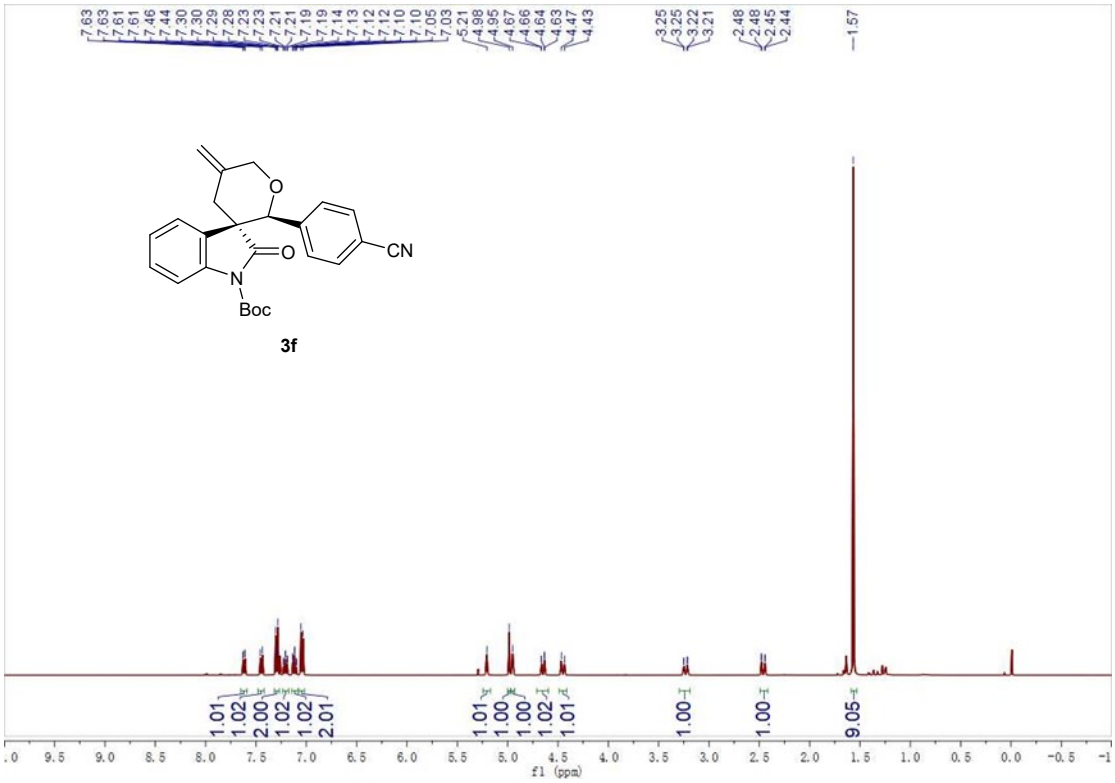
^{1}H NMR of **3e** (400 MHz, $CDCl_3$)



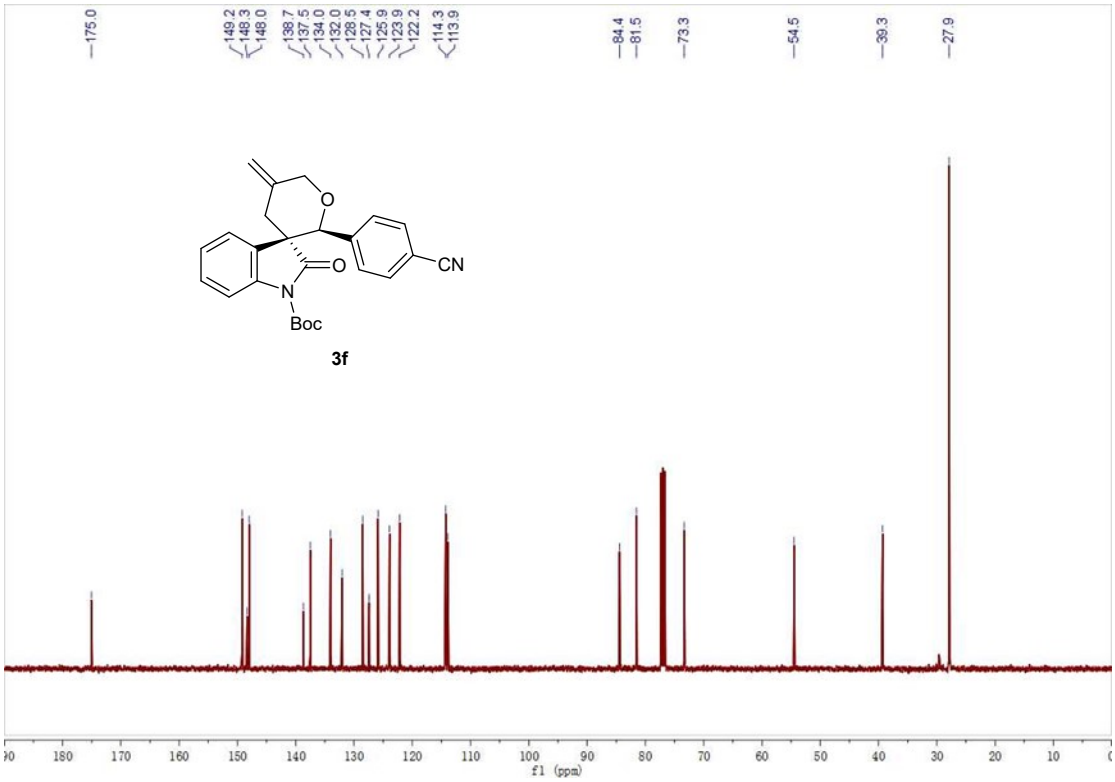
^{13}C {^{1}H} NMR of **3e** (100 MHz, $CDCl_3$)



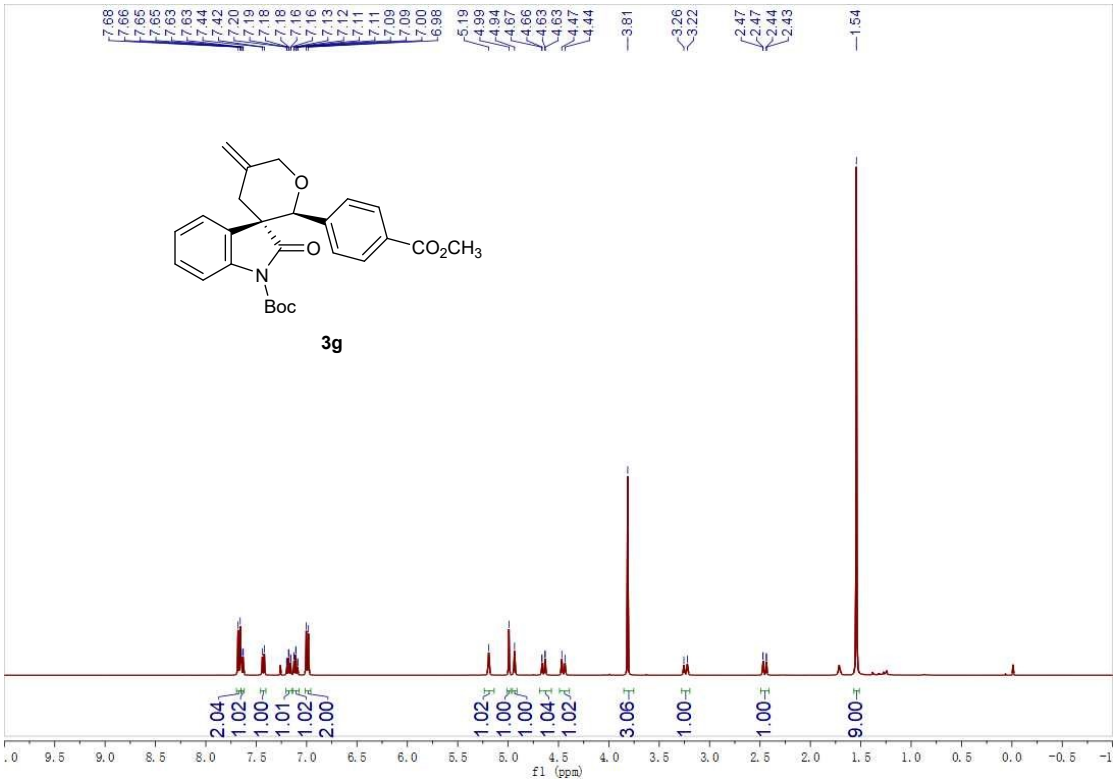
^{1}H NMR of **3f** (400 MHz, $CDCl_3$)



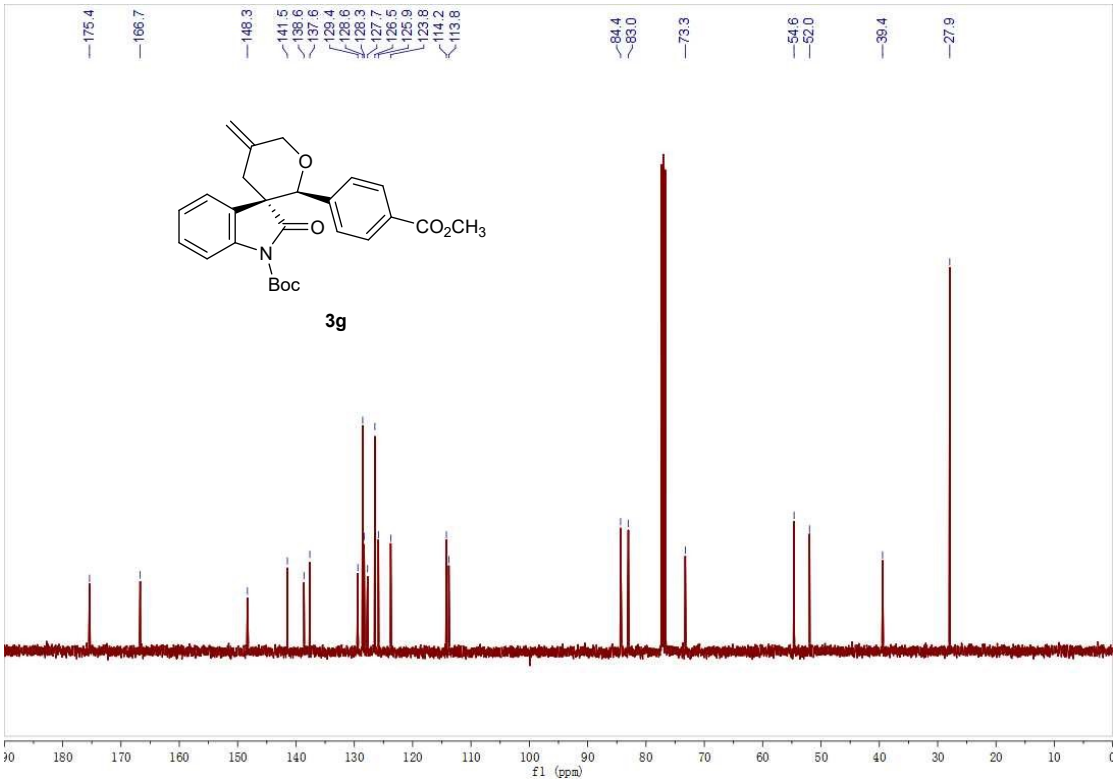
^{13}C {^{1}H} NMR of **3f** (100 MHz, $CDCl_3$)



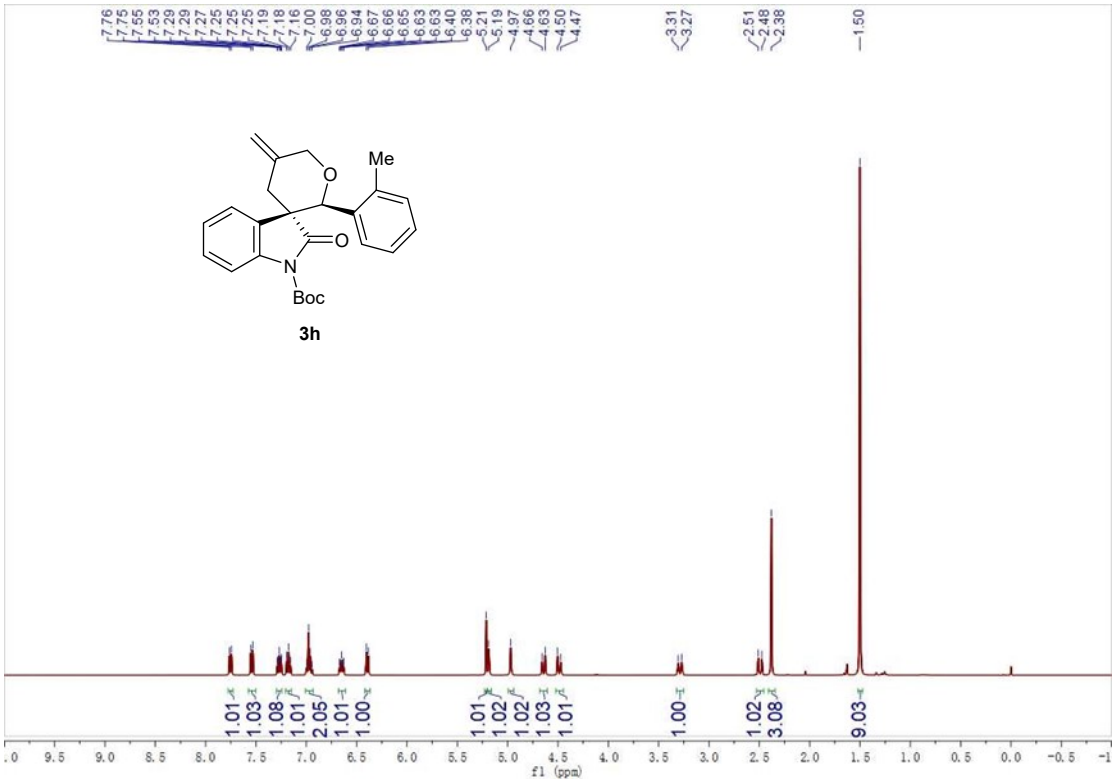
^{1}H NMR of **3g** (400 MHz, $CDCl_3$)



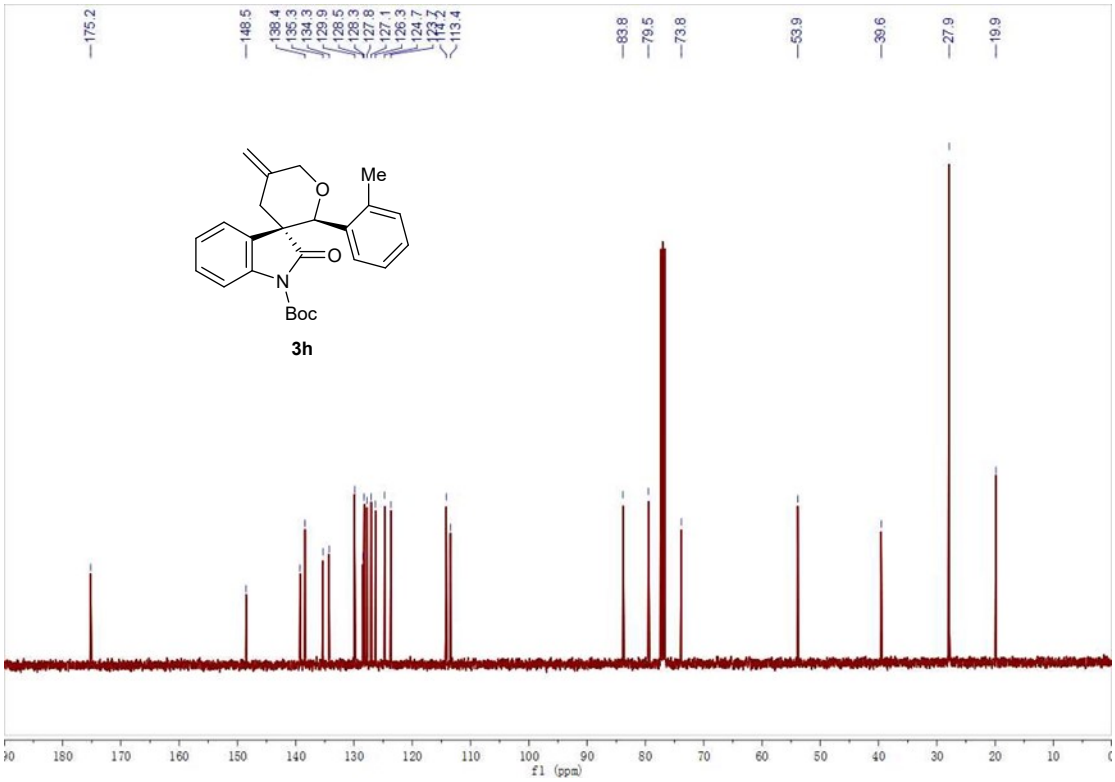
^{13}C {^{1}H} NMR of **3g** (100 MHz, $CDCl_3$)



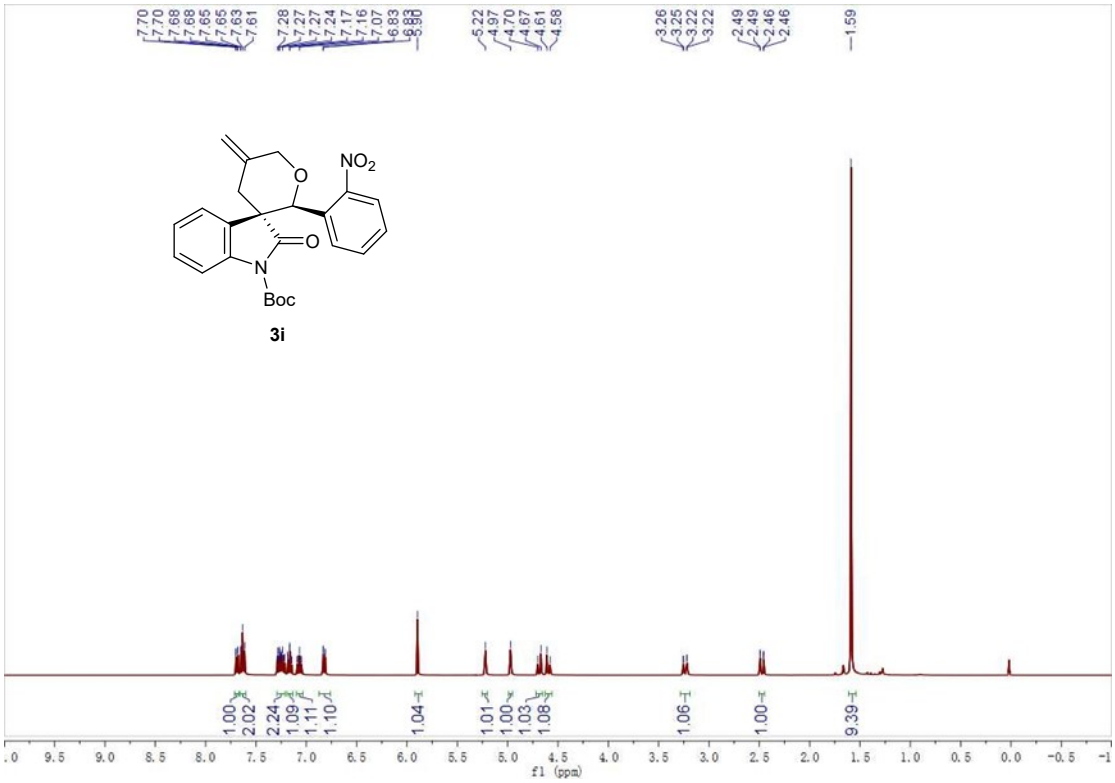
^{1}H NMR of **3h** (400 MHz, $CDCl_3$)



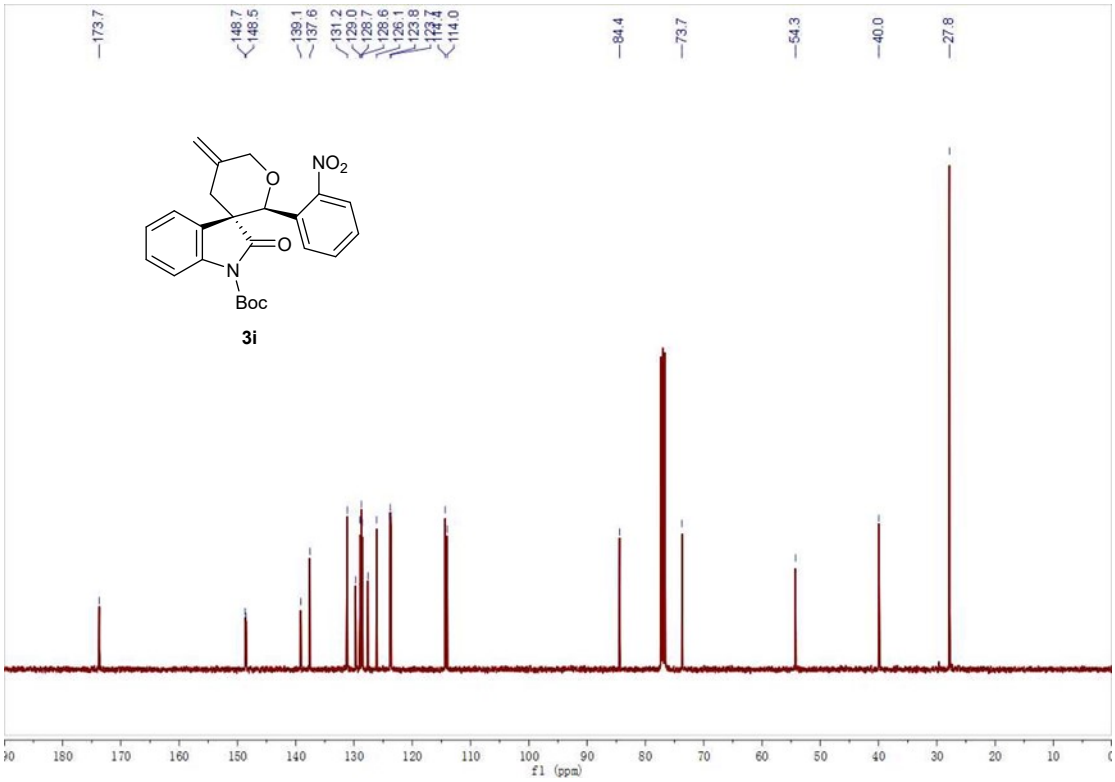
^{13}C {^{1}H} NMR of **3h** (100 MHz, $CDCl_3$)



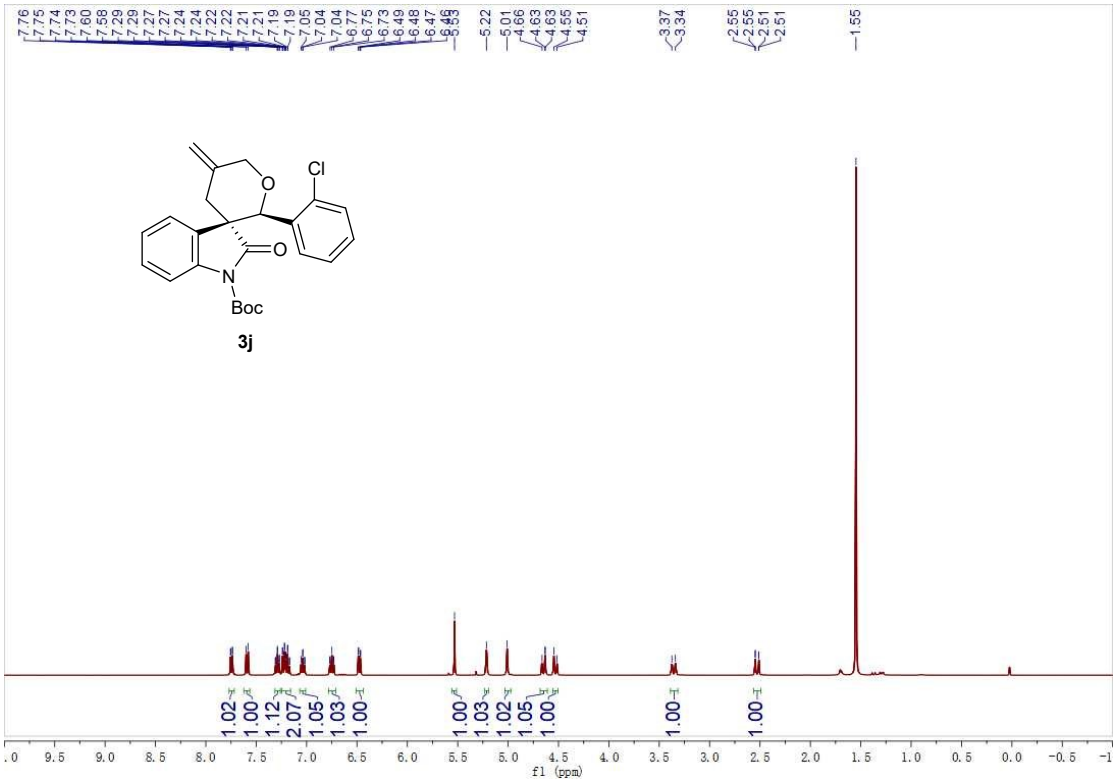
^{1}H NMR of **3i** (400 MHz, $CDCl_3$)



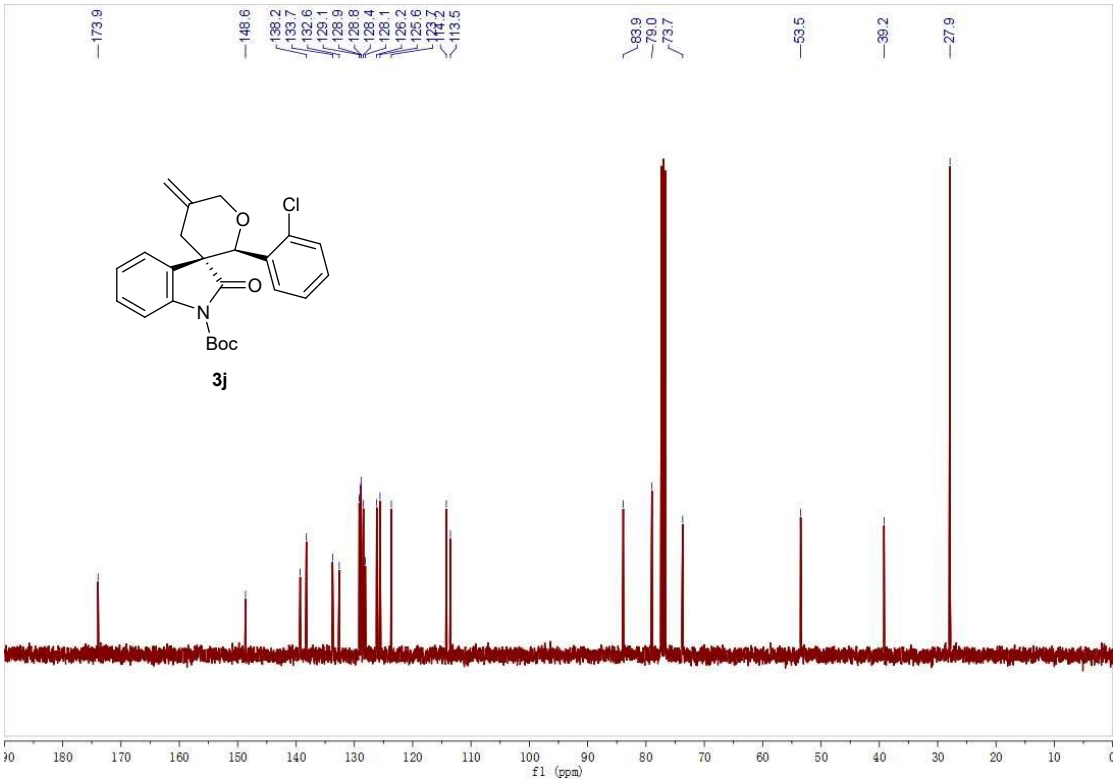
^{13}C {^{1}H} NMR of **3i** (100 MHz, $CDCl_3$)



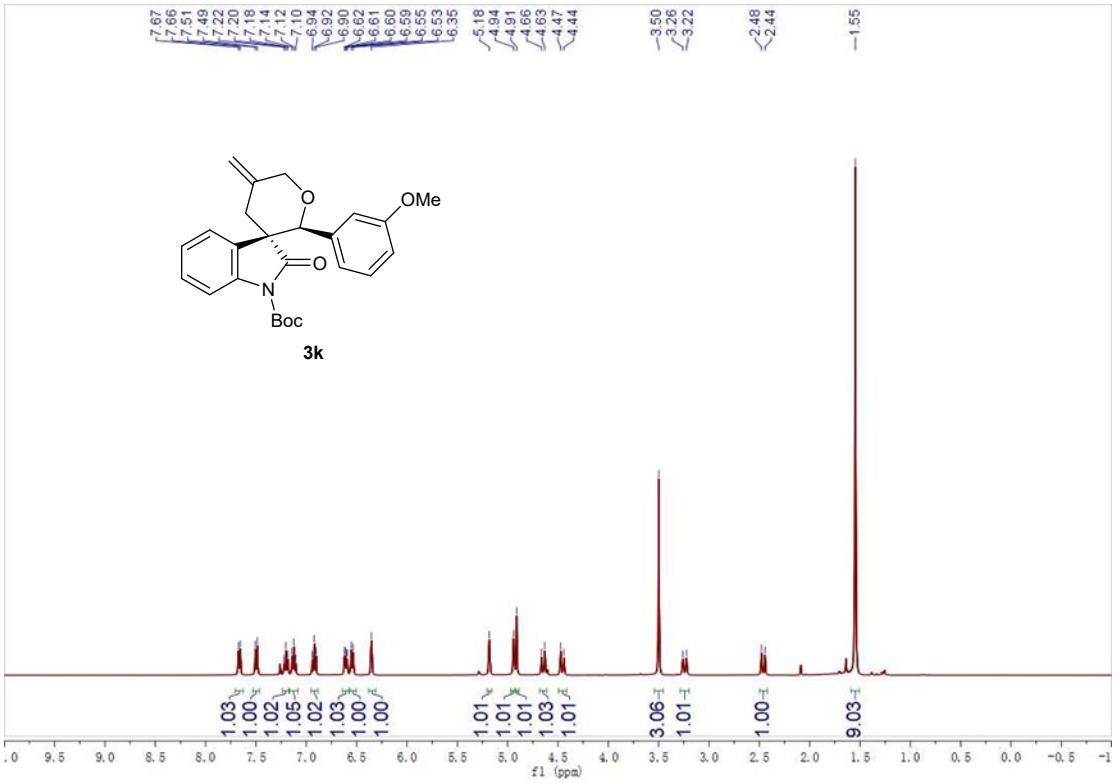
^{1}H NMR of **3j** (400 MHz, $CDCl_3$)



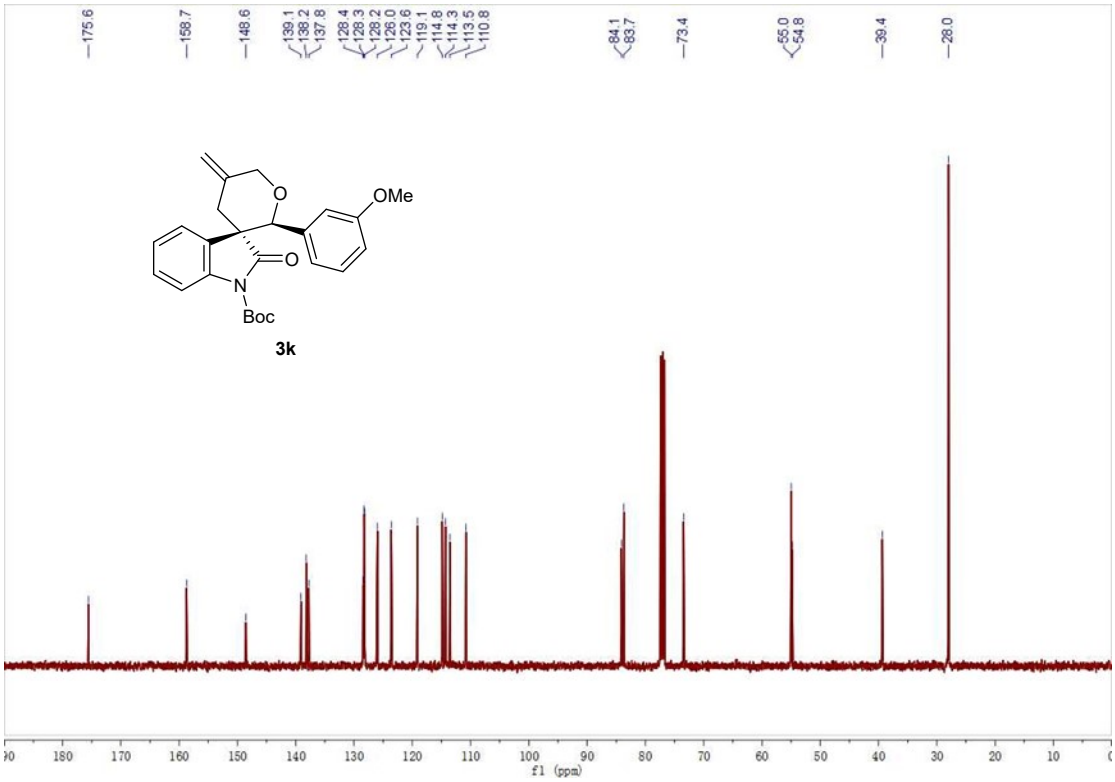
^{13}C {^{1}H} NMR of **3j** (100 MHz, $CDCl_3$)



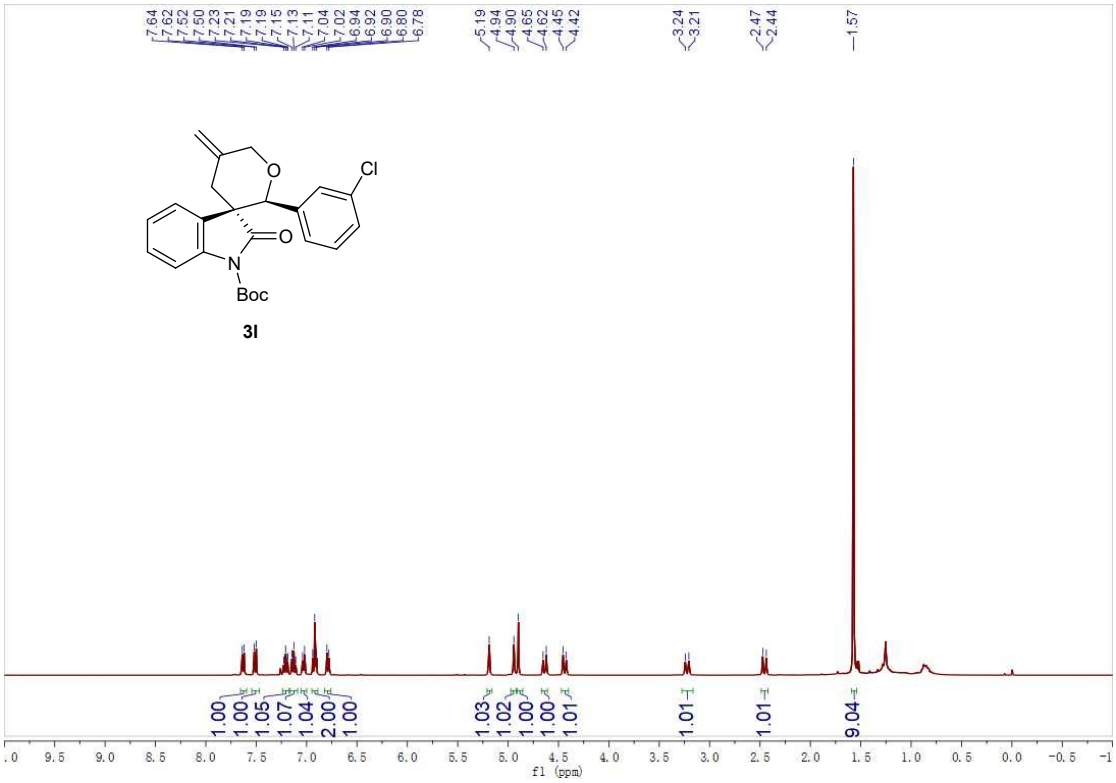
^{1}H NMR of **3k** (400 MHz, $CDCl_3$)



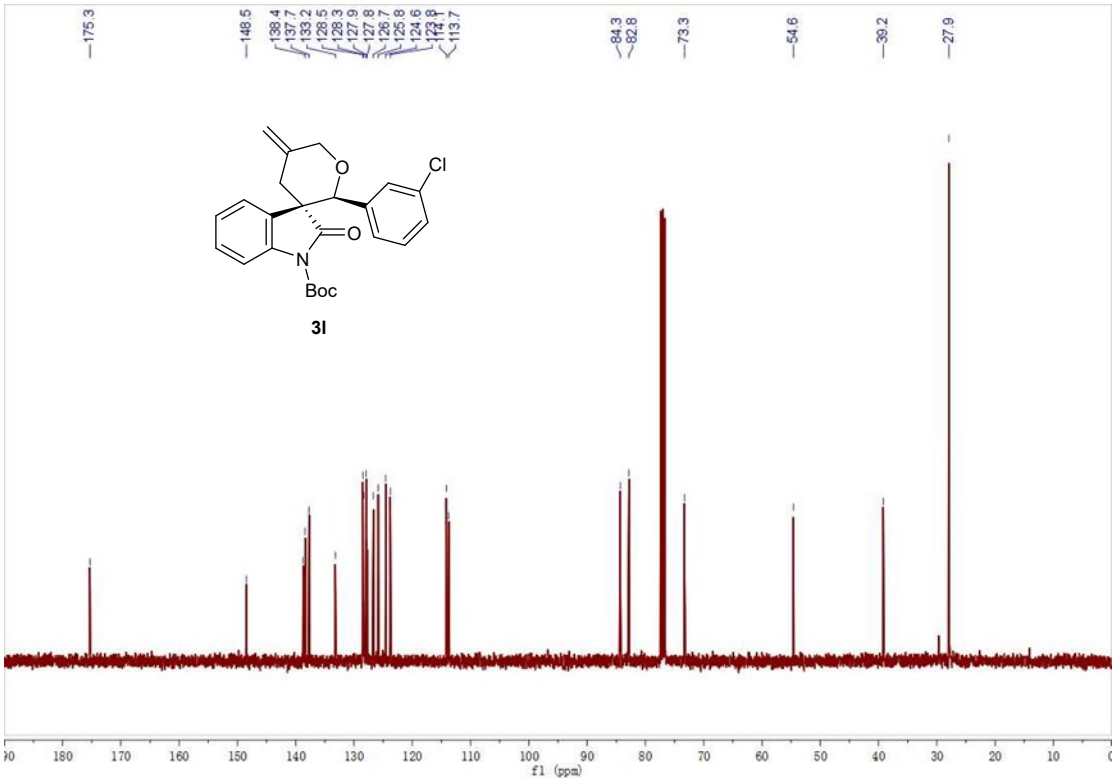
^{13}C {^{1}H} NMR of **3k** (100 MHz, $CDCl_3$)



^{1}H NMR of **3l** (400 MHz, $CDCl_3$)

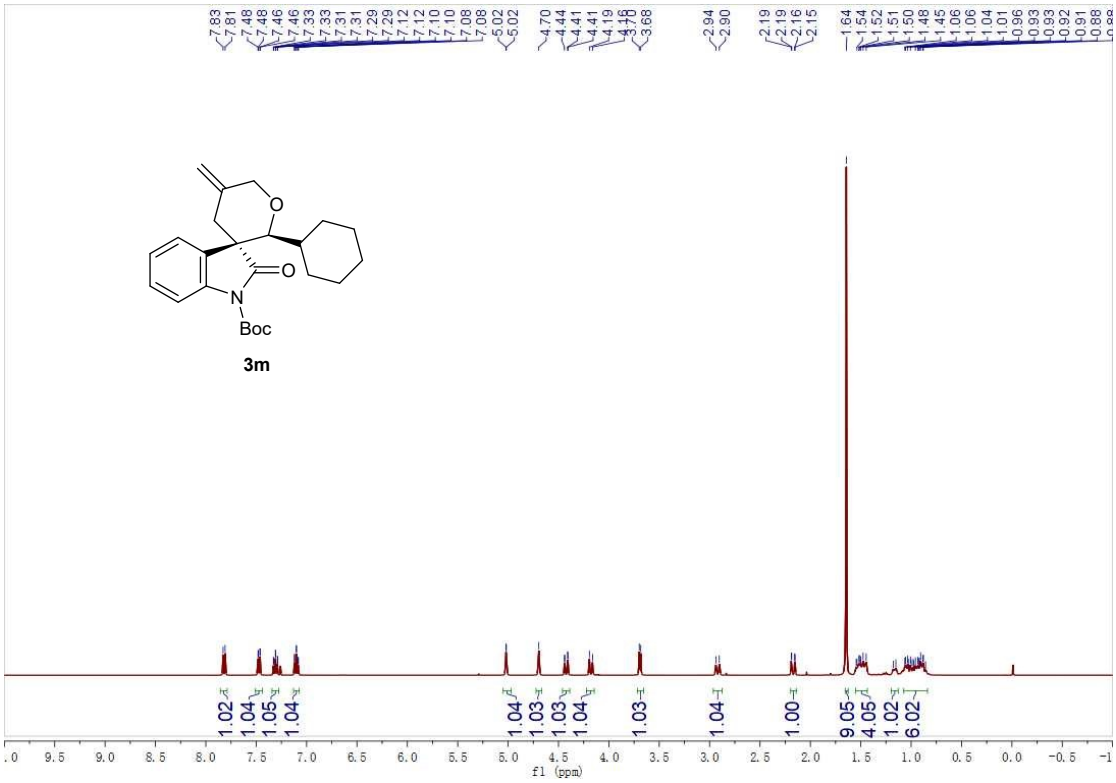


^{13}C {^{1}H} NMR of **3l** (100 MHz, $CDCl_3$)



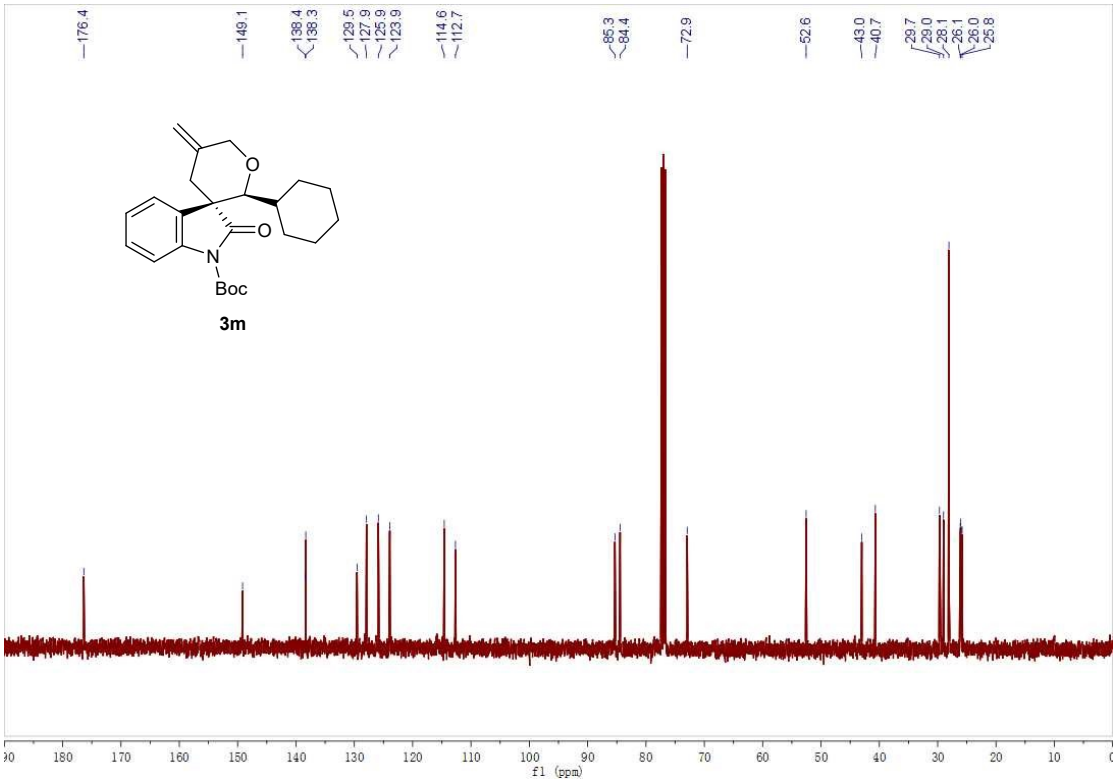
3l

^{1}H NMR of **3m** (400 MHz, $CDCl_3$)

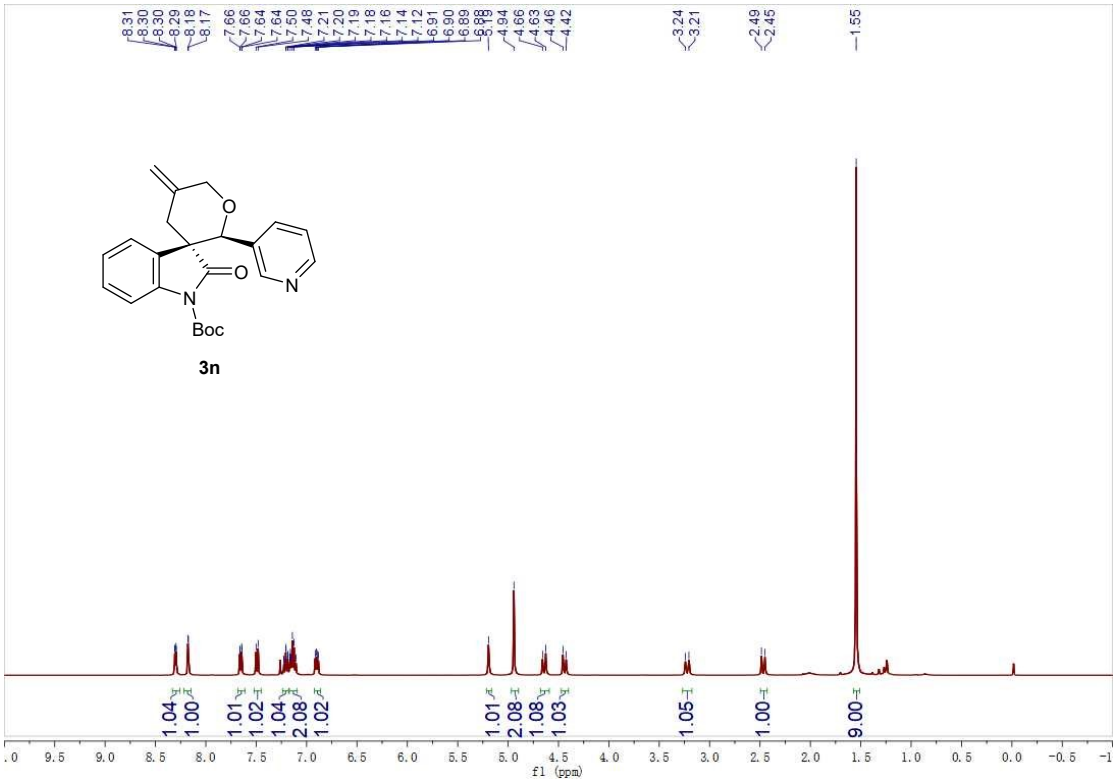


3m

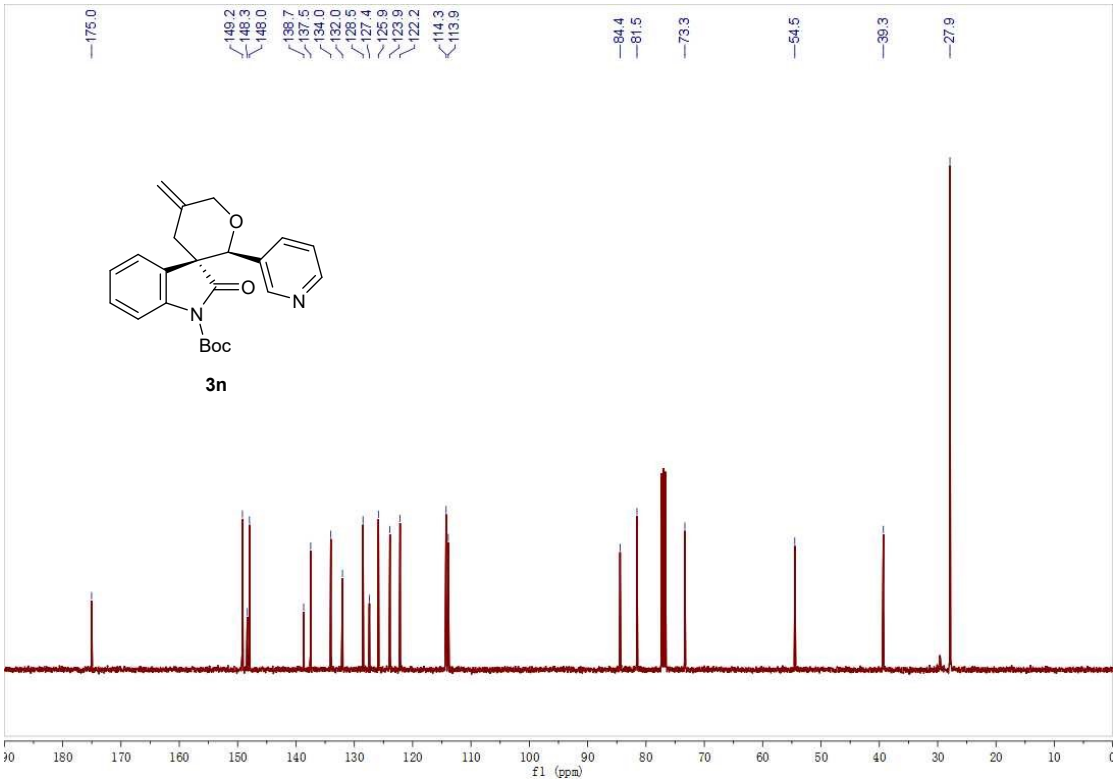
^{13}C {^{1}H} NMR of **3m** (100 MHz, $CDCl_3$)



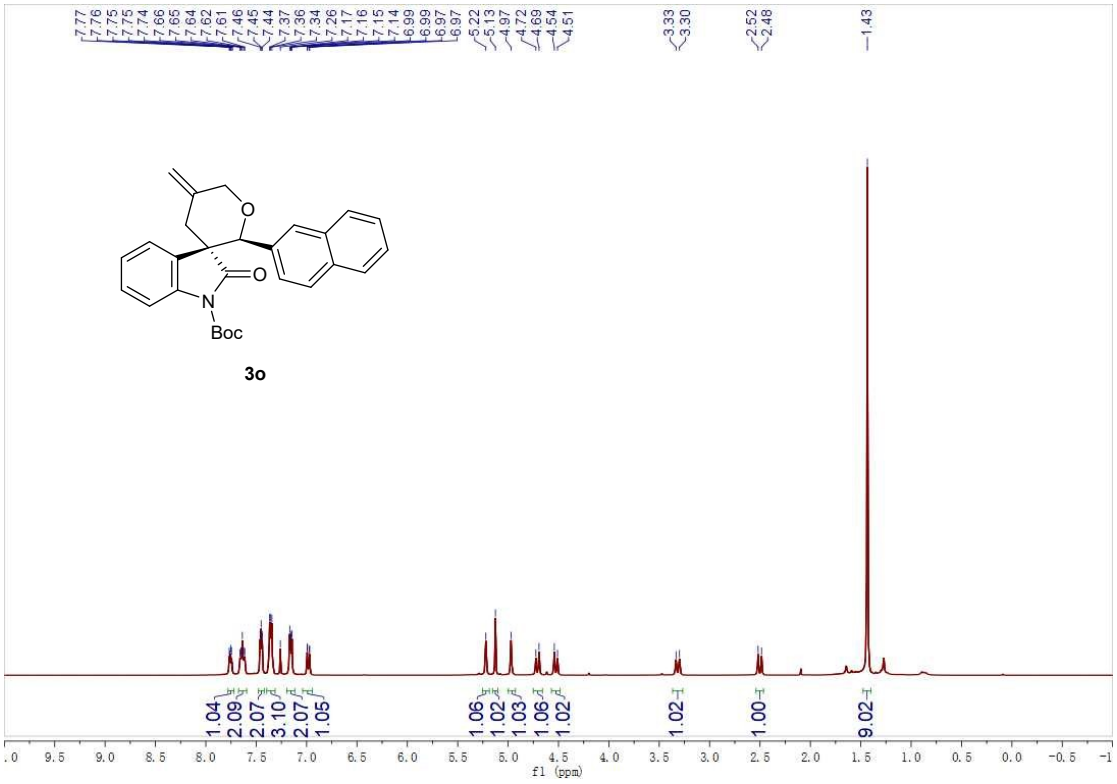
^{1}H NMR of **3n** (400 MHz, $CDCl_3$)



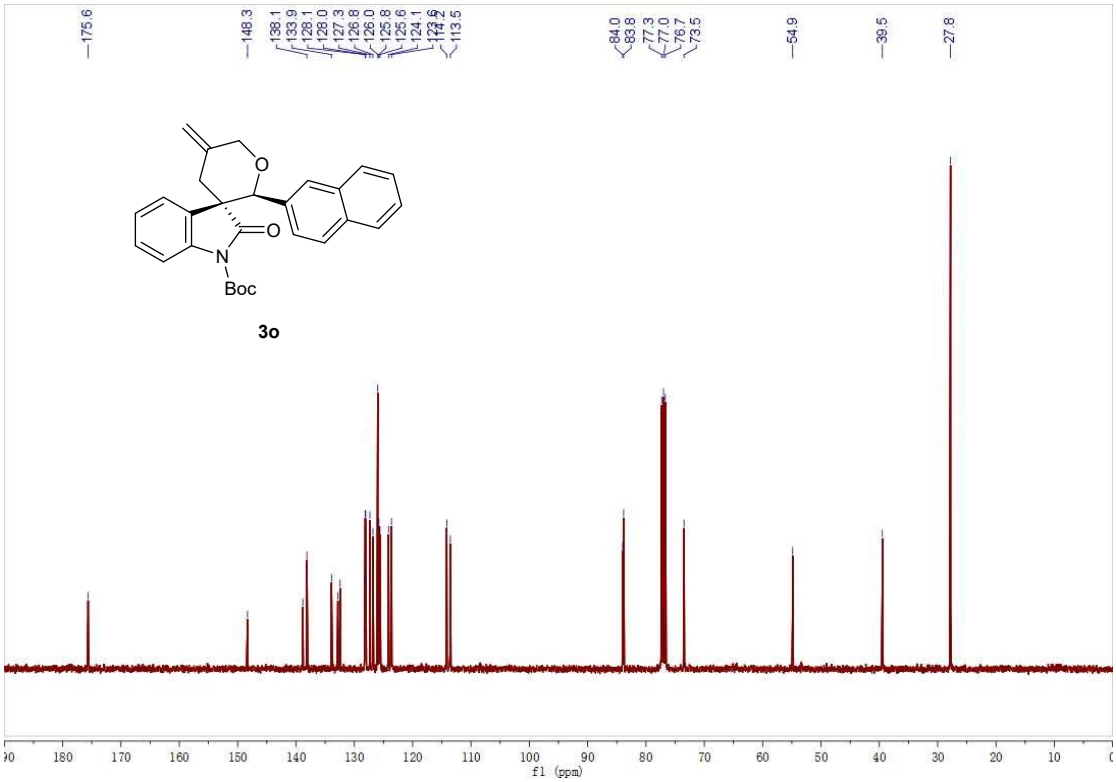
^{13}C {^{1}H} NMR of **3n** (100 MHz, $CDCl_3$)



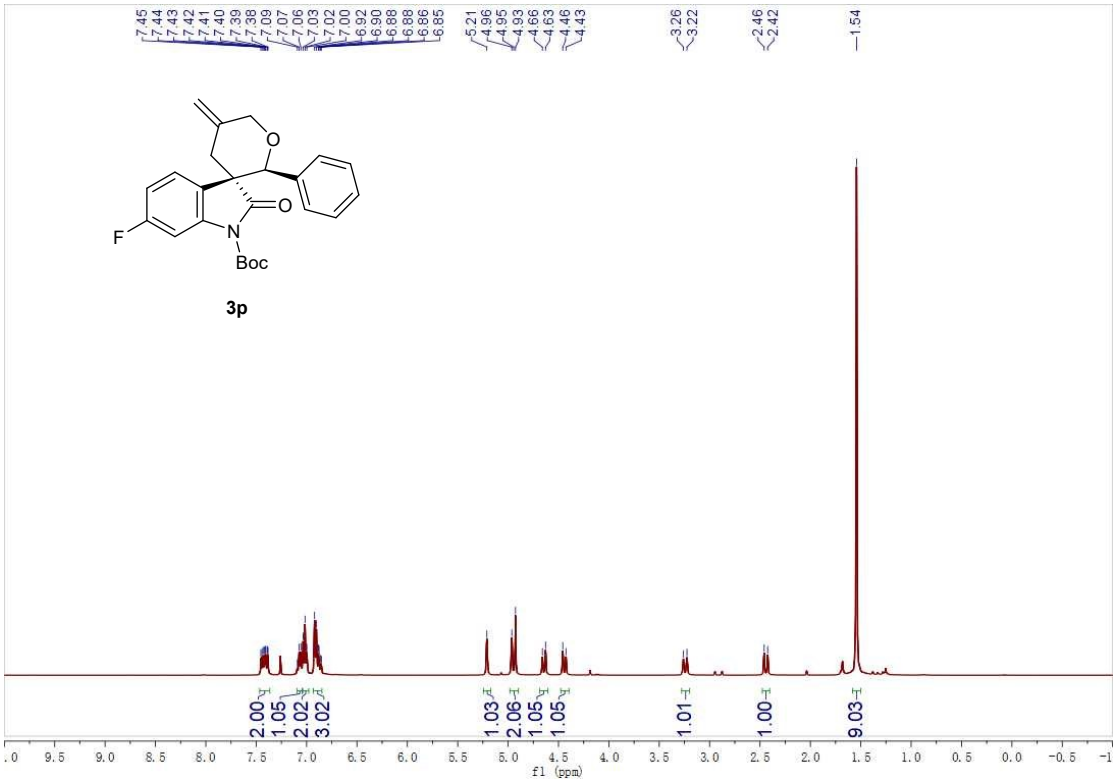
^{1}H NMR of **3o** (400 MHz, $CDCl_3$)



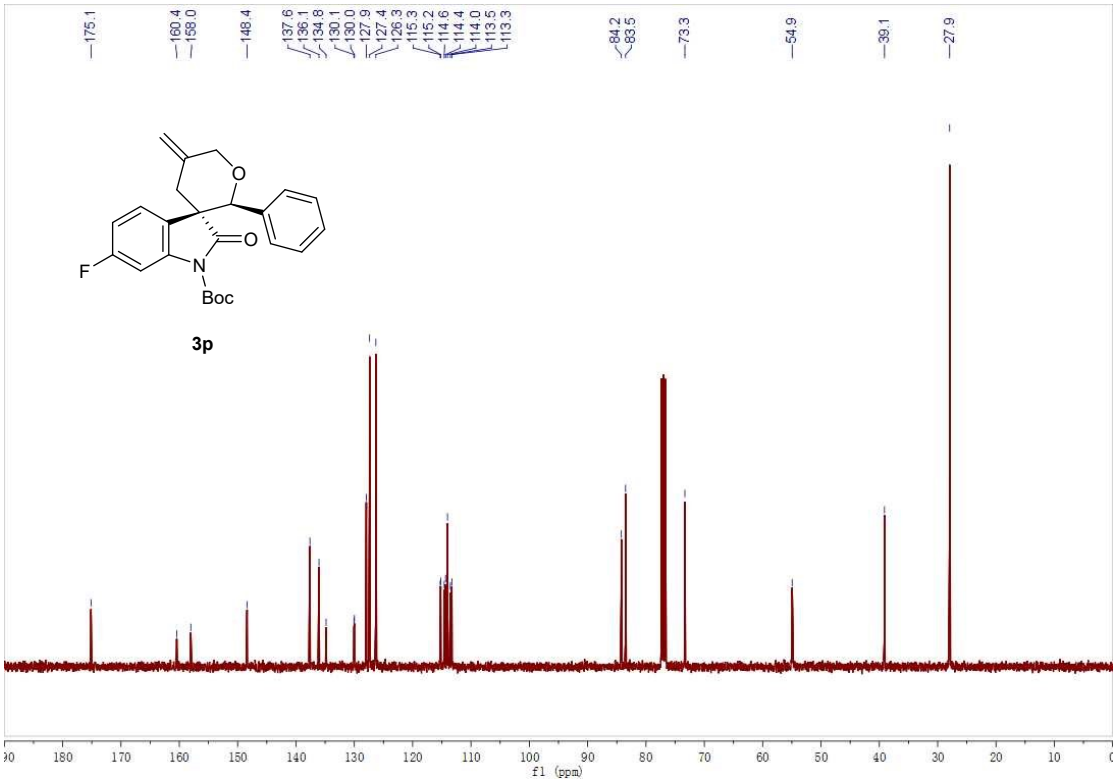
^{13}C {^{1}H} NMR of **3o** (100 MHz, $CDCl_3$)



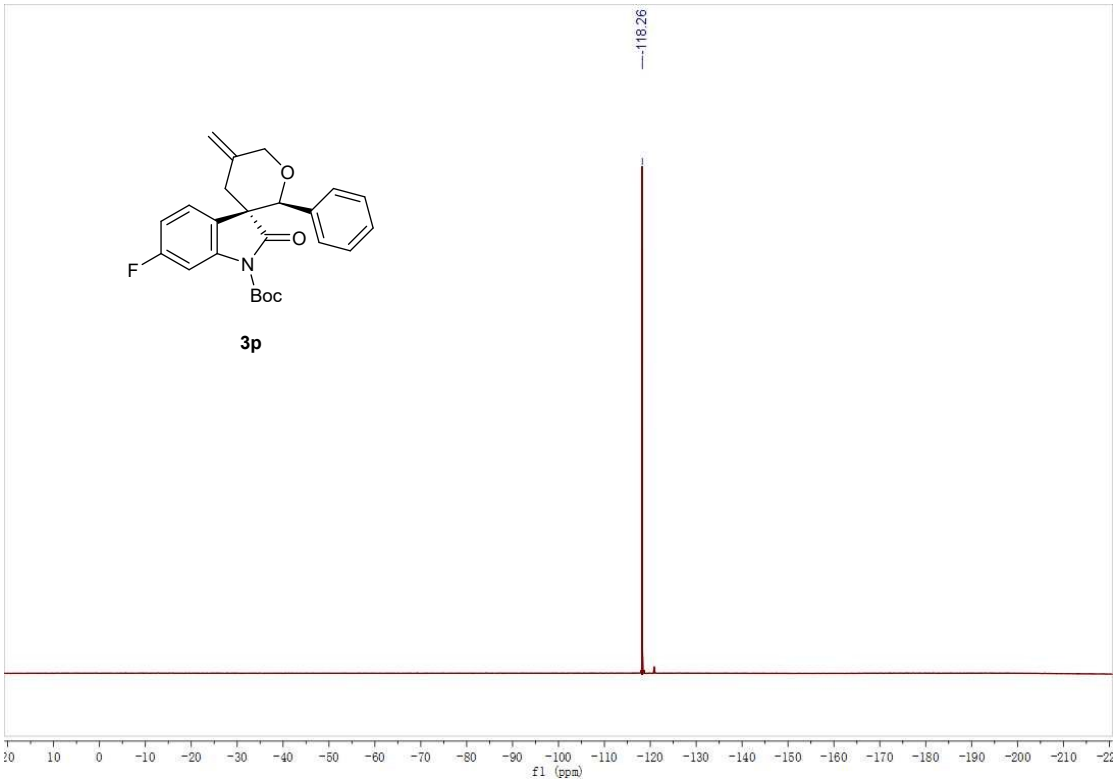
^{1}H NMR of **3p** (400 MHz, $CDCl_3$)



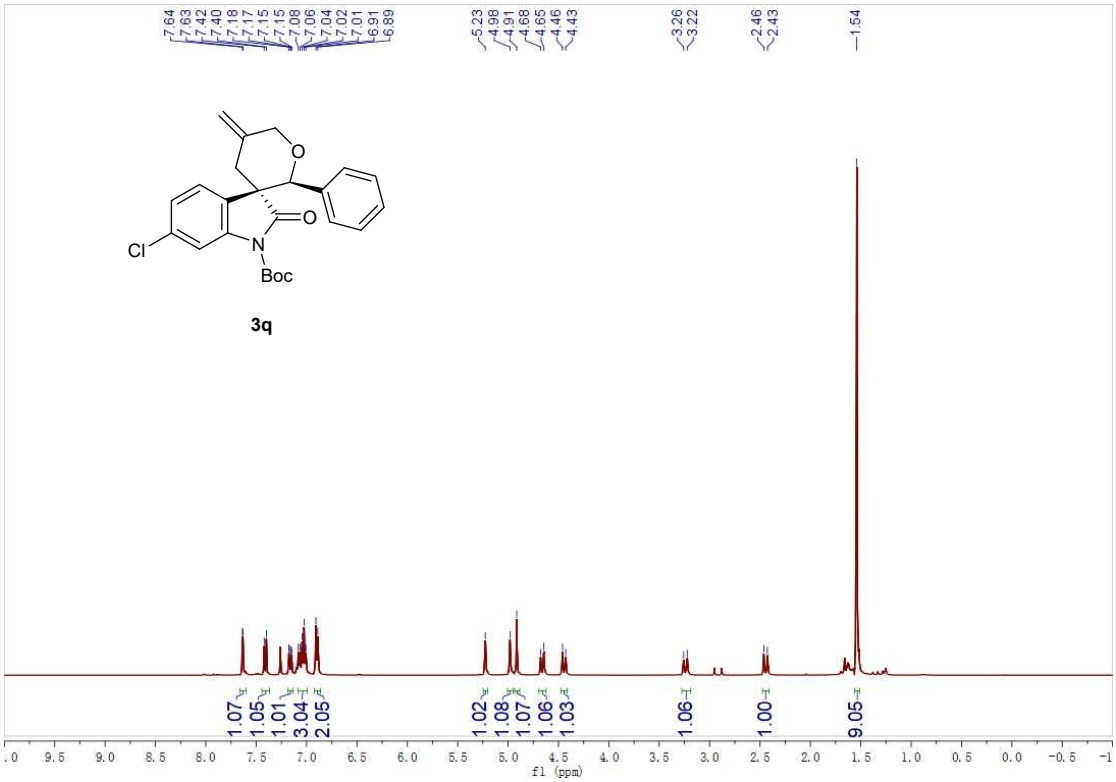
^{13}C {^{1}H} NMR of **3p** (100 MHz, $CDCl_3$)



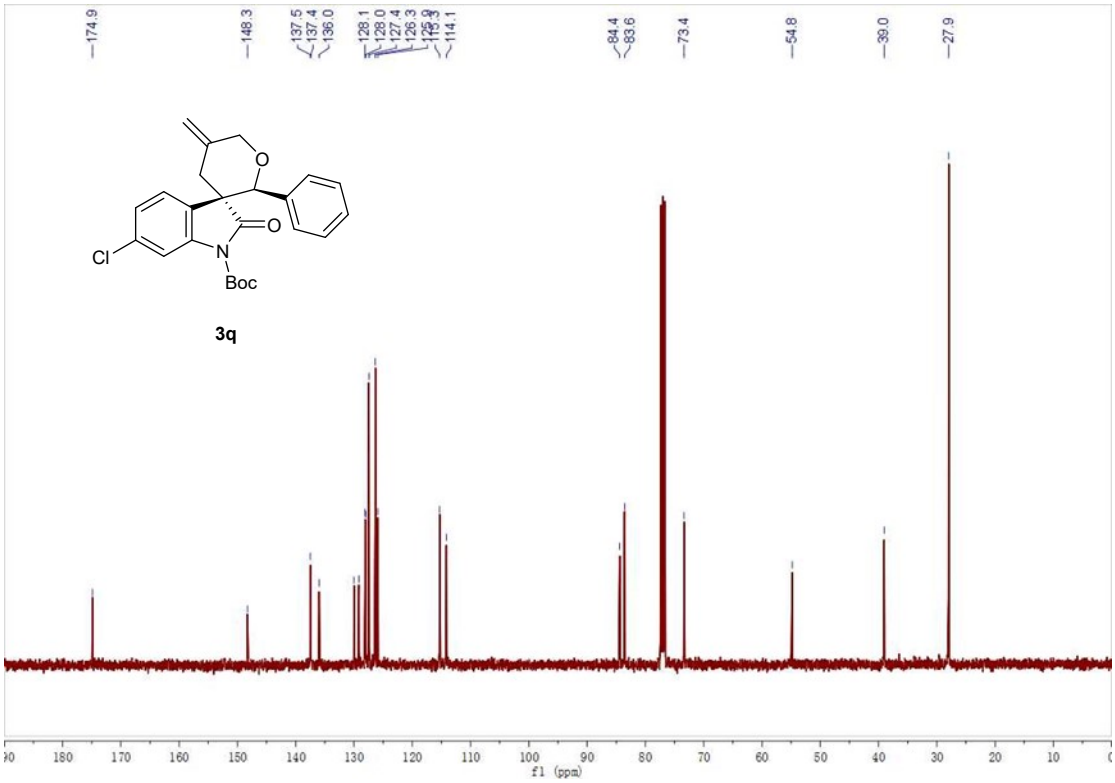
^{19}F NMR of **3p** (376 MHz, $CDCl_3$)



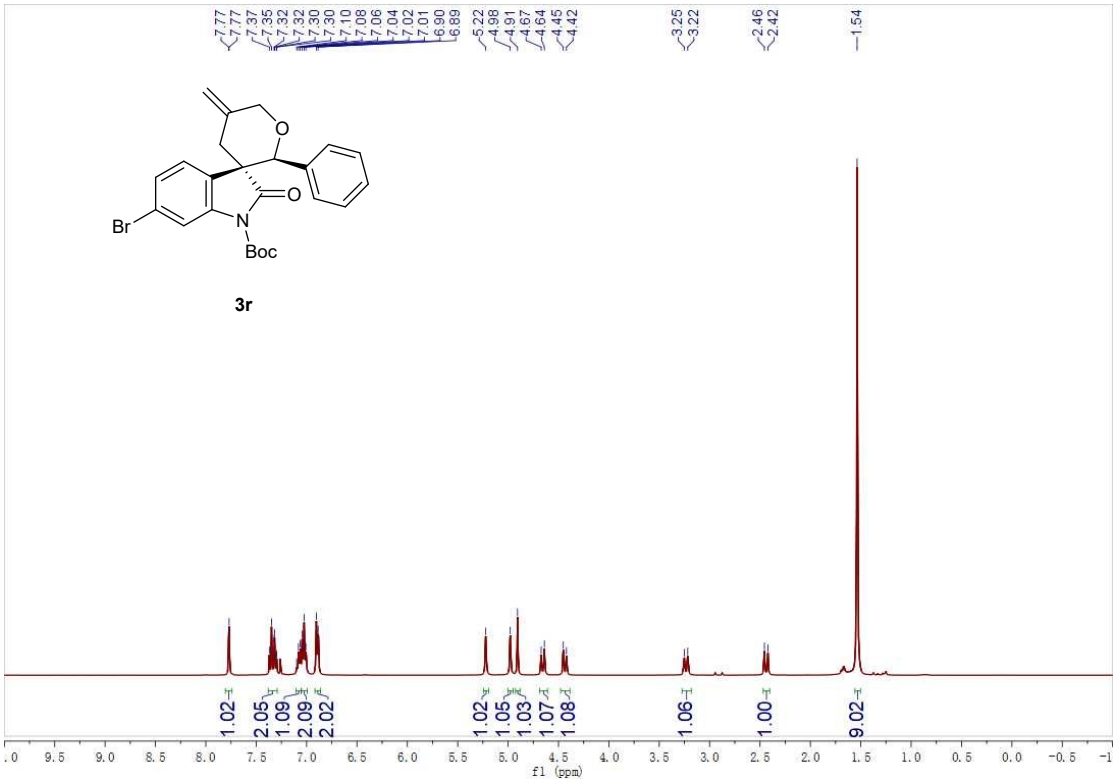
^{1}H NMR of **3q** (400 MHz, $CDCl_3$)



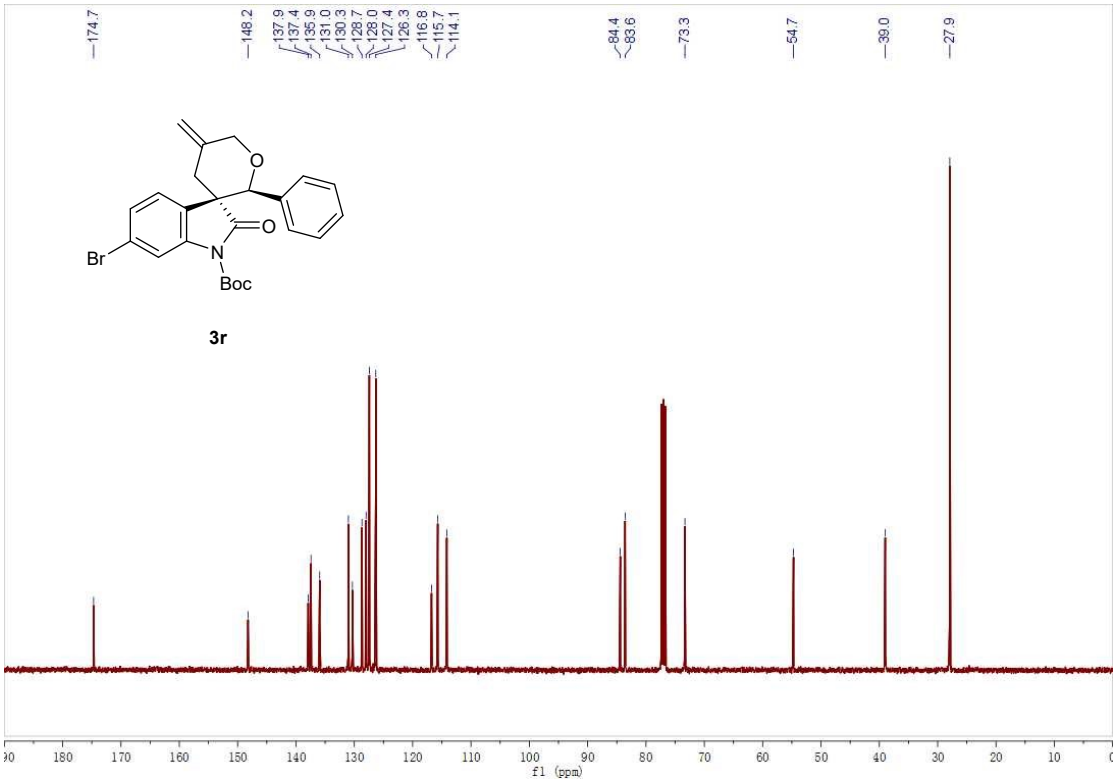
^{13}C {^{1}H} NMR of **3q** (100 MHz, $CDCl_3$)



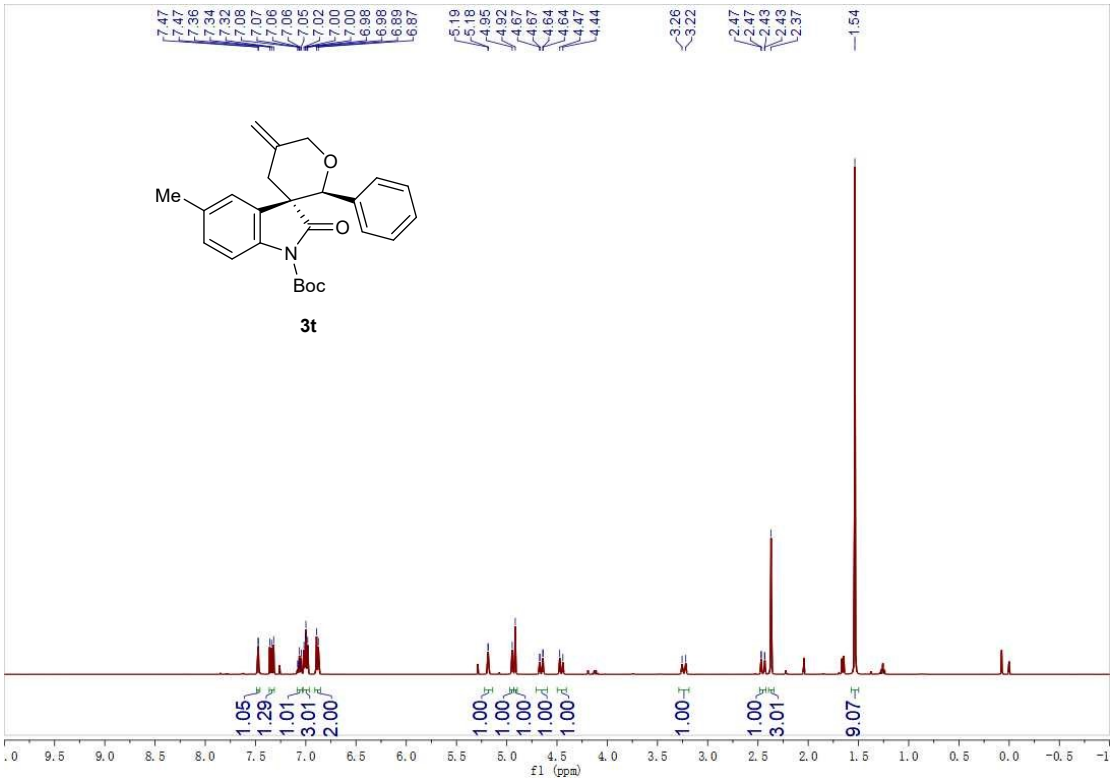
^{1}H NMR of **3r** (400 MHz, $CDCl_3$)



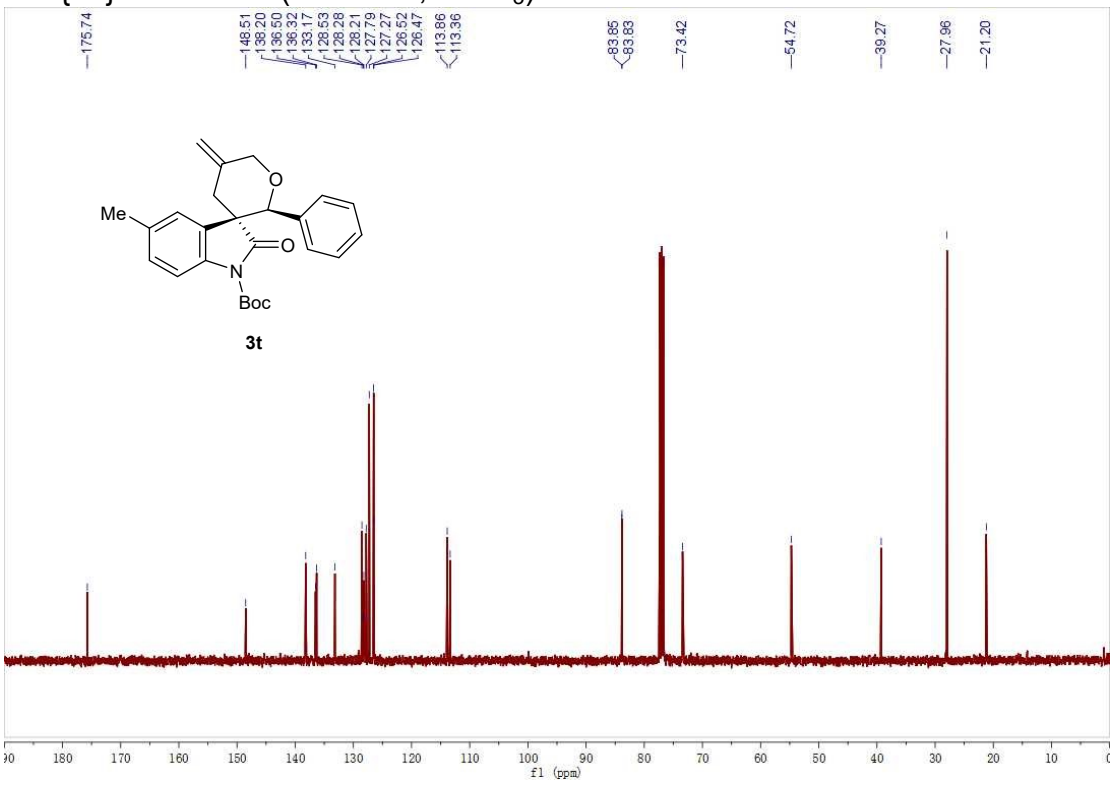
^{13}C {^{1}H} NMR of **3r** (100 MHz, $CDCl_3$)



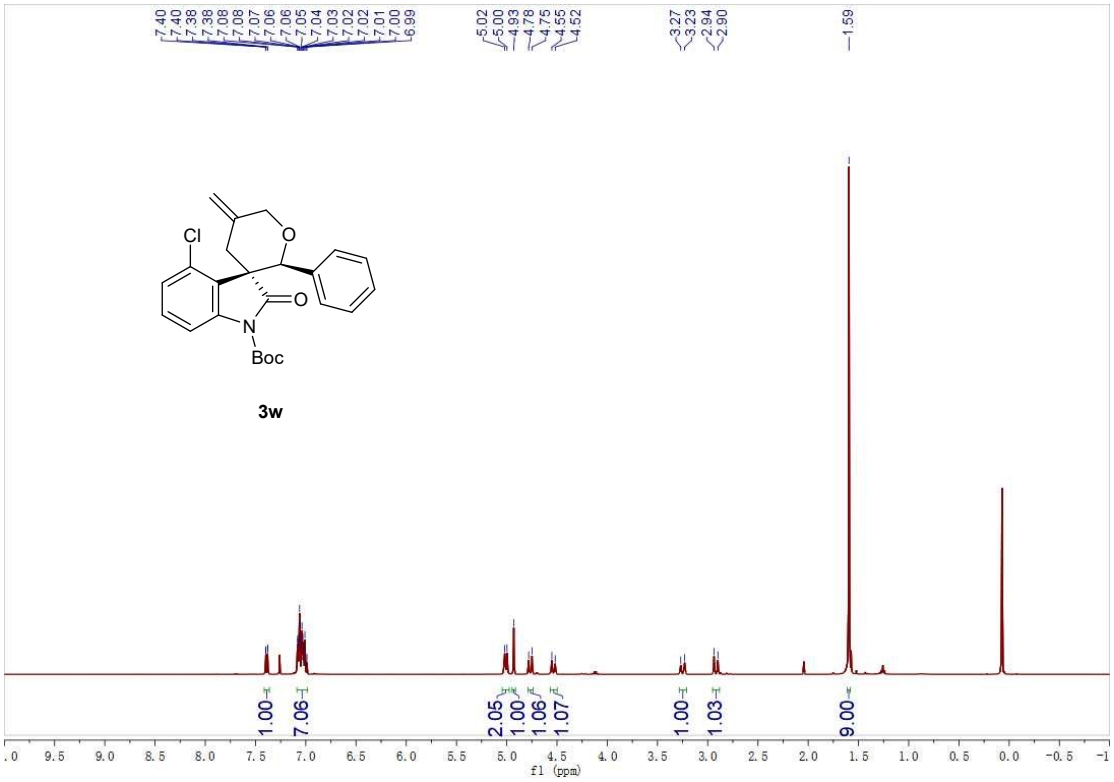
^{1}H NMR of **3t** (400 MHz, $CDCl_3$)



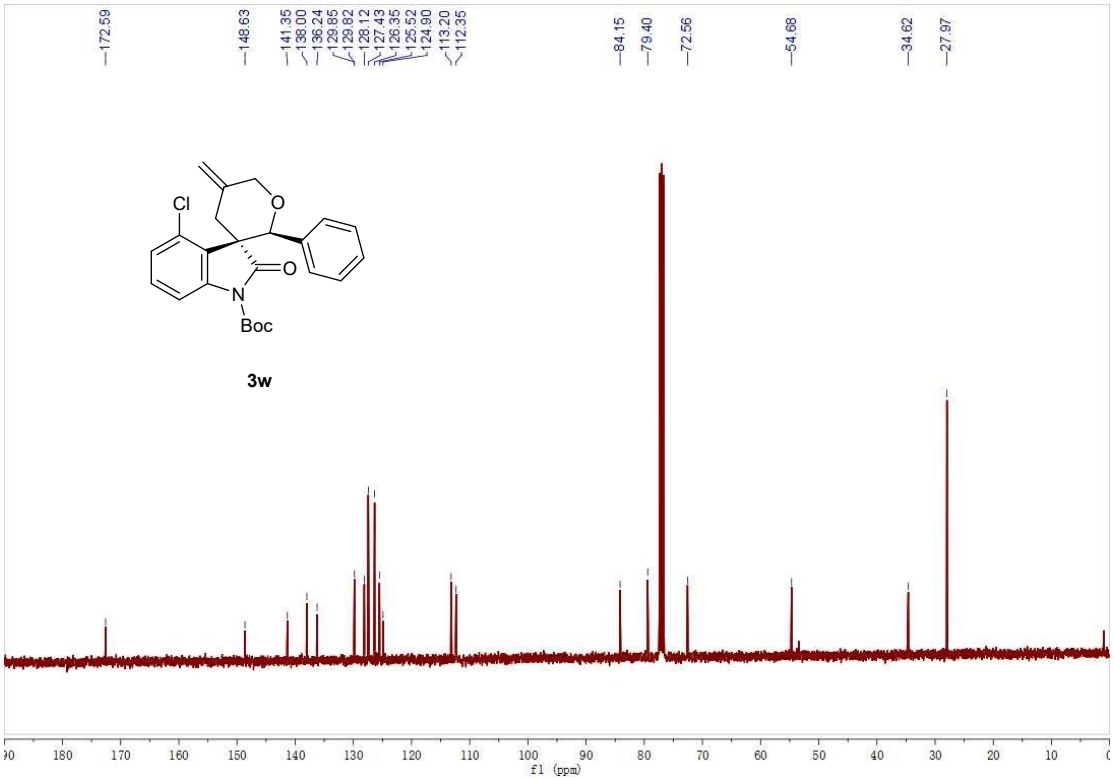
^{13}C {^{1}H} NMR of **3t** (100 MHz, $CDCl_3$)



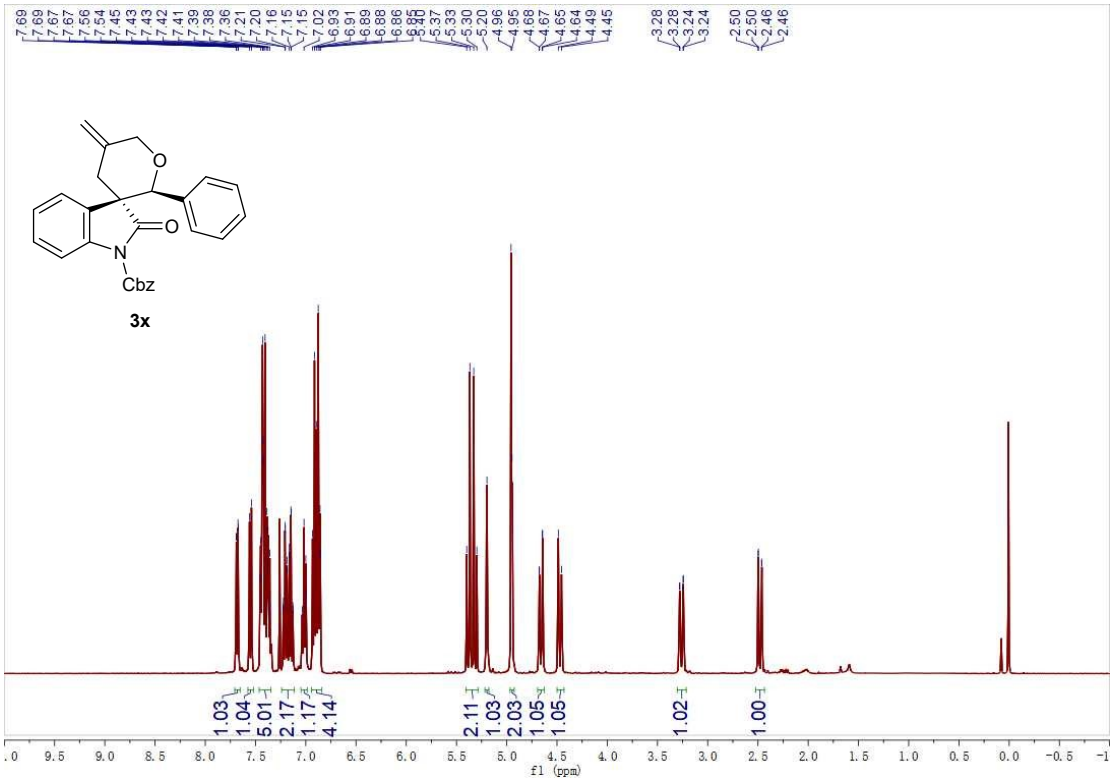
^{1}H NMR of **3w** (400 MHz, $CDCl_3$)



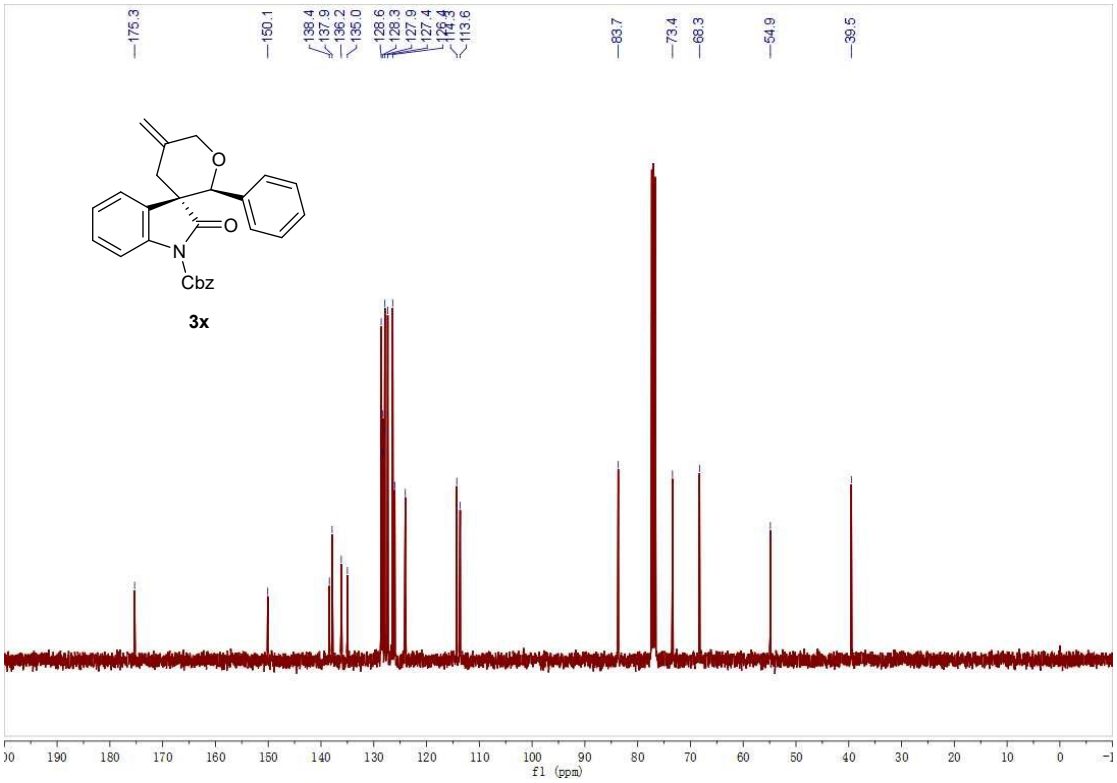
^{13}C {^{1}H} NMR of **3w** (100 MHz, $CDCl_3$)



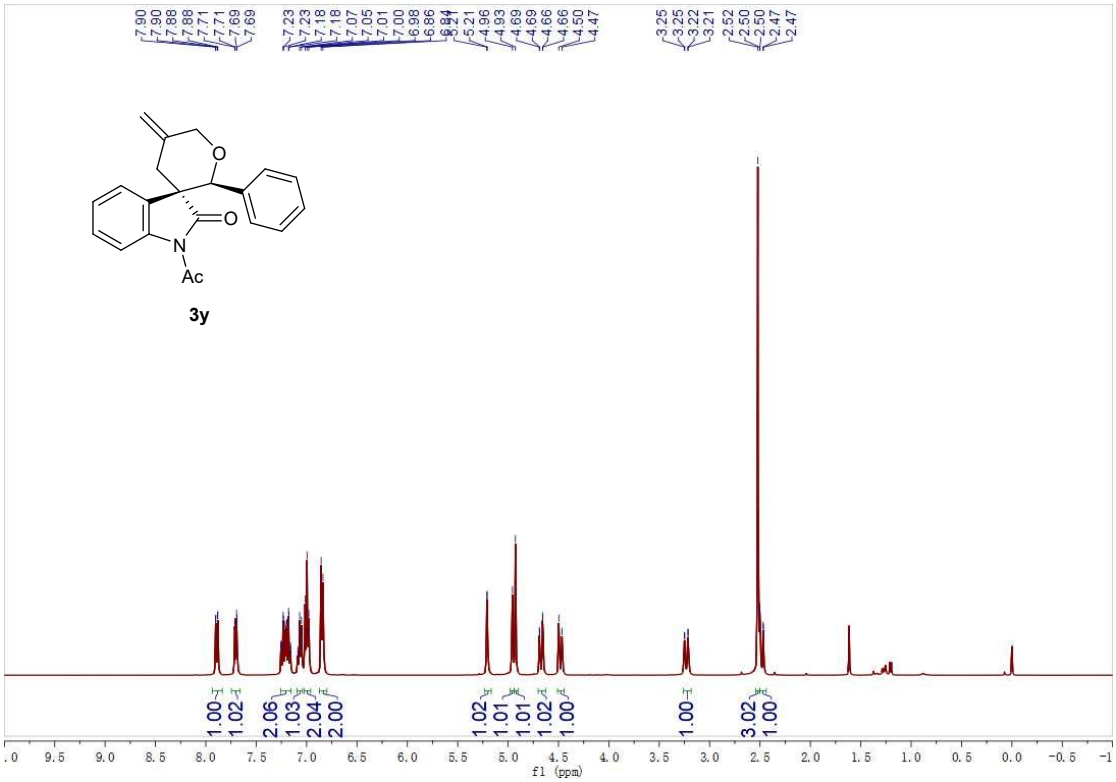
^{1}H NMR of **3x** (400 MHz, $CDCl_3$)



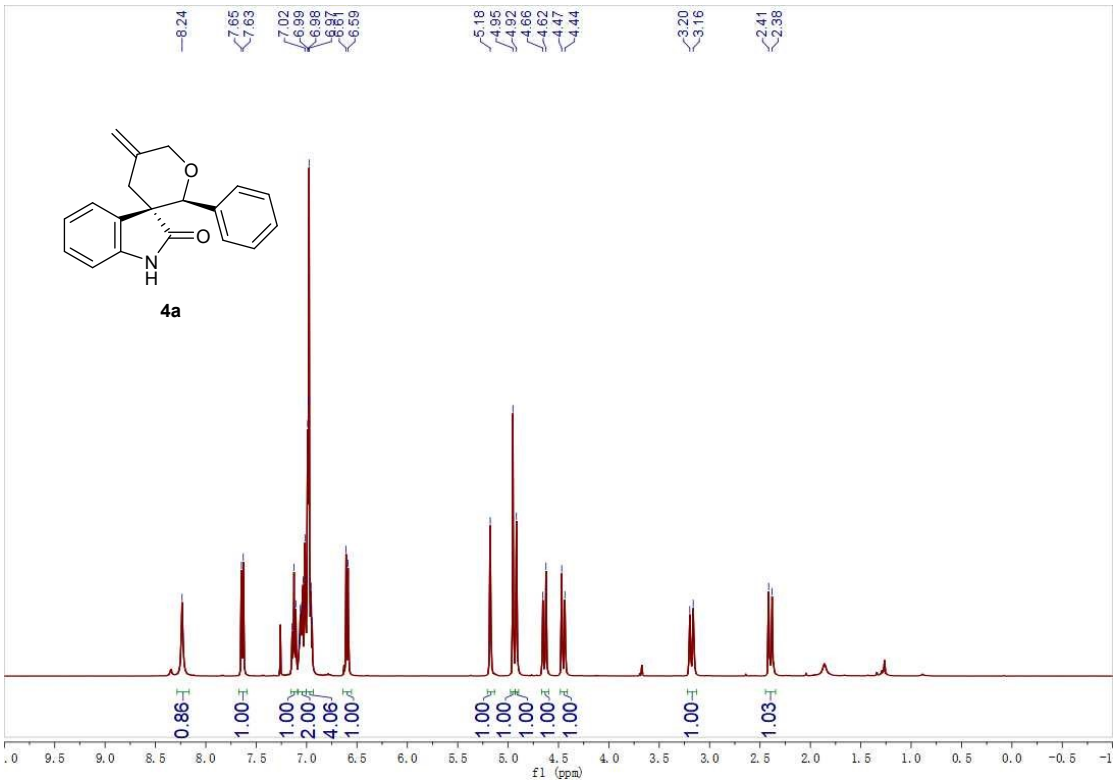
^{13}C {^{1}H} NMR of **3x** (100 MHz, $CDCl_3$)



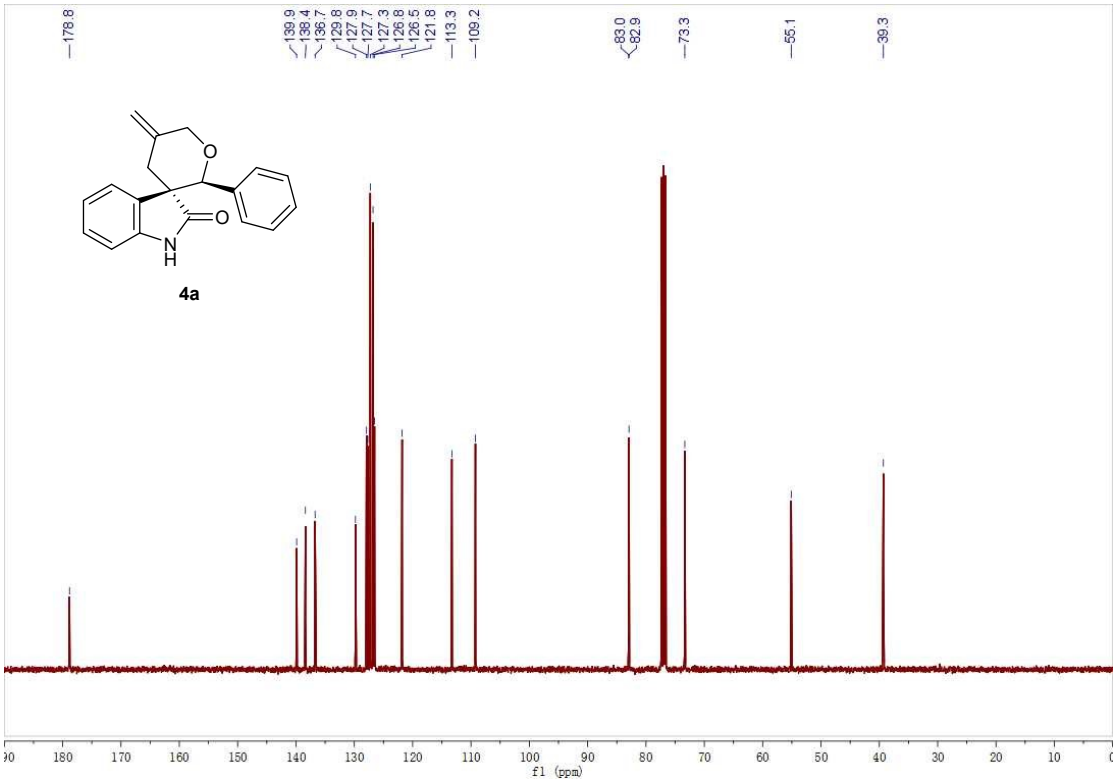
^{1}H NMR of **3y** (400 MHz, $CDCl_3$)



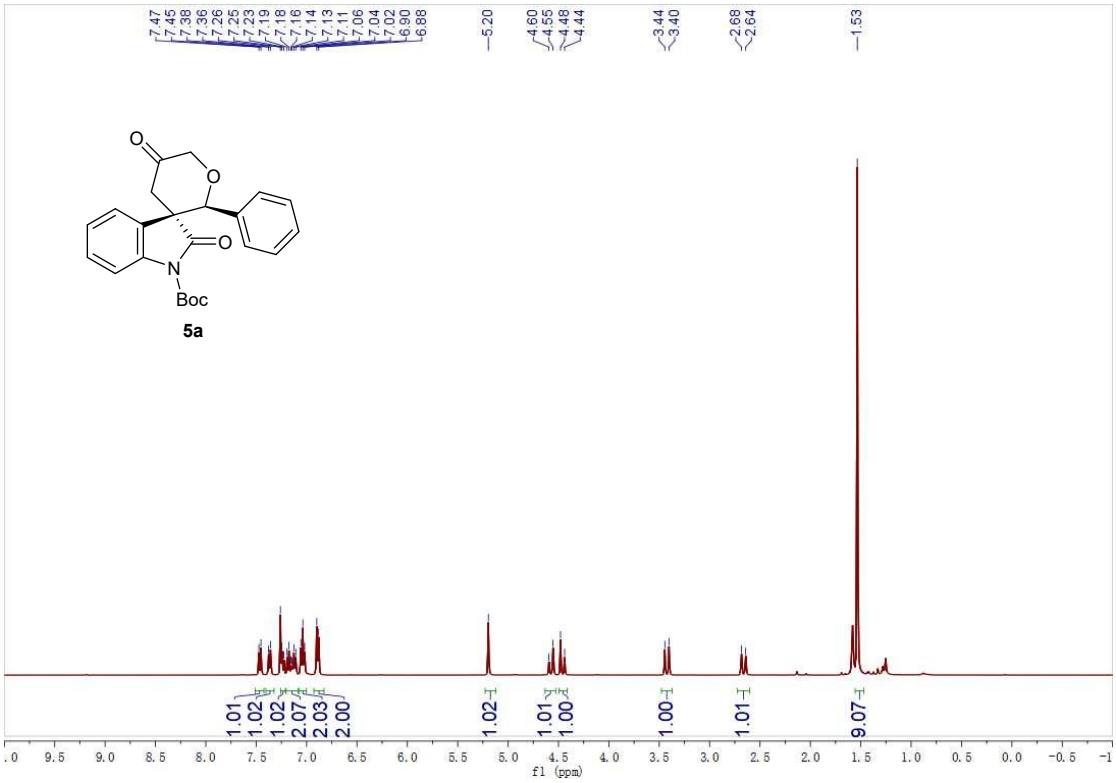
^{1}H NMR of **4a** (400 MHz, $CDCl_3$)



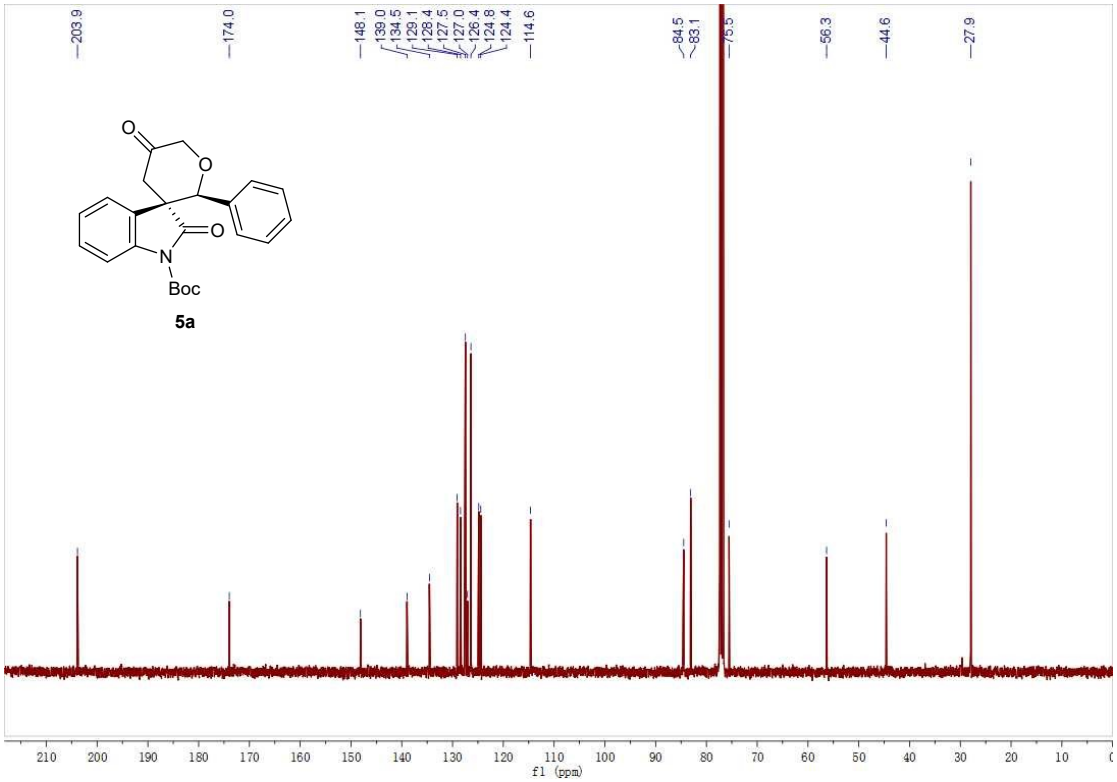
^{13}C {^{1}H} NMR of **4a** (100 MHz, $CDCl_3$)



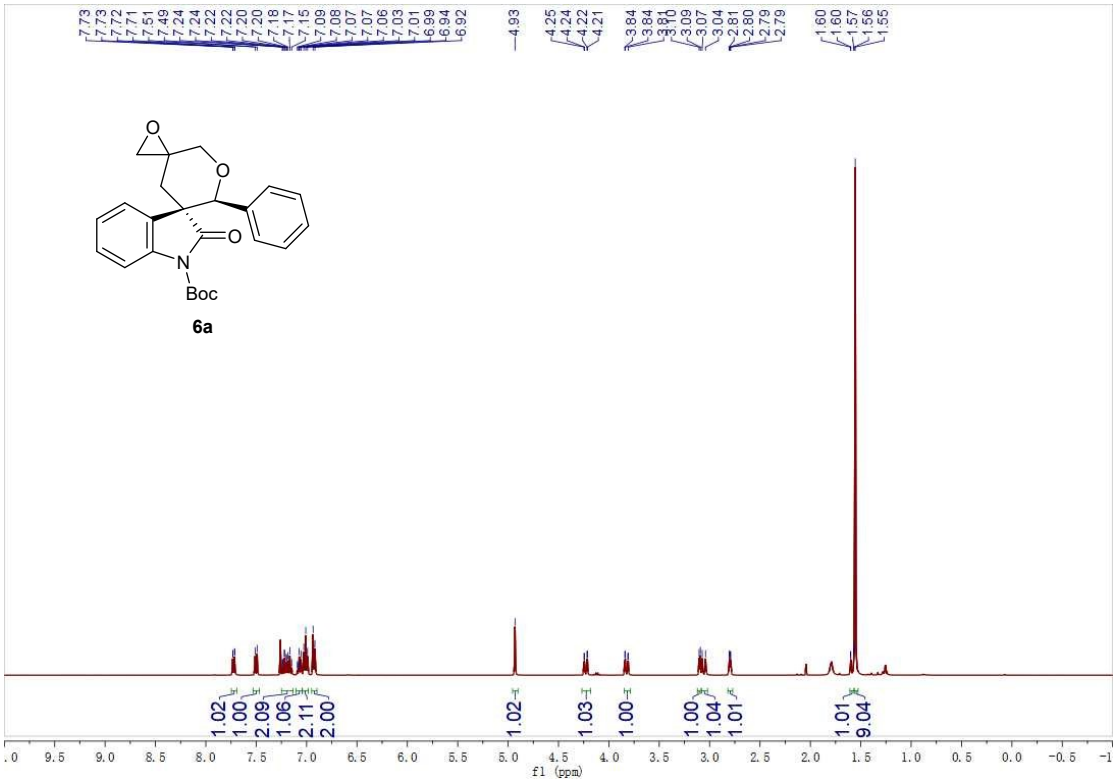
^{1}H NMR of **5a** (400 MHz, $CDCl_3$)

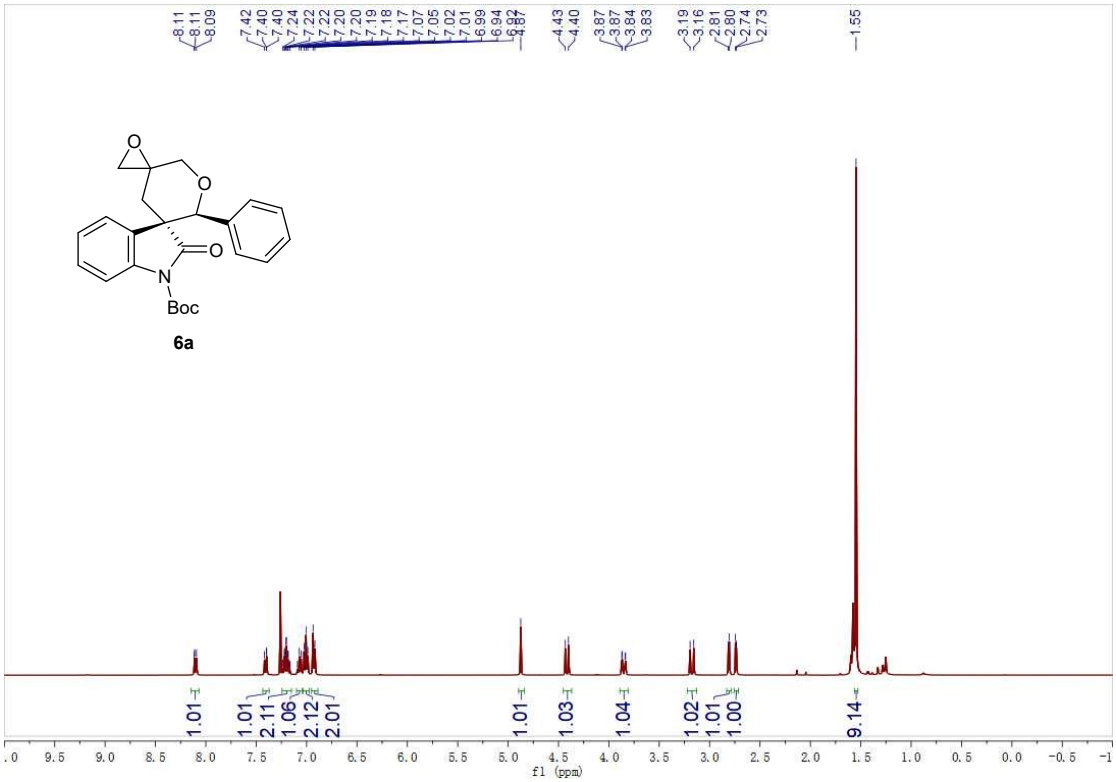


^{13}C {^{1}H} NMR of **5a** (100 MHz, $CDCl_3$)

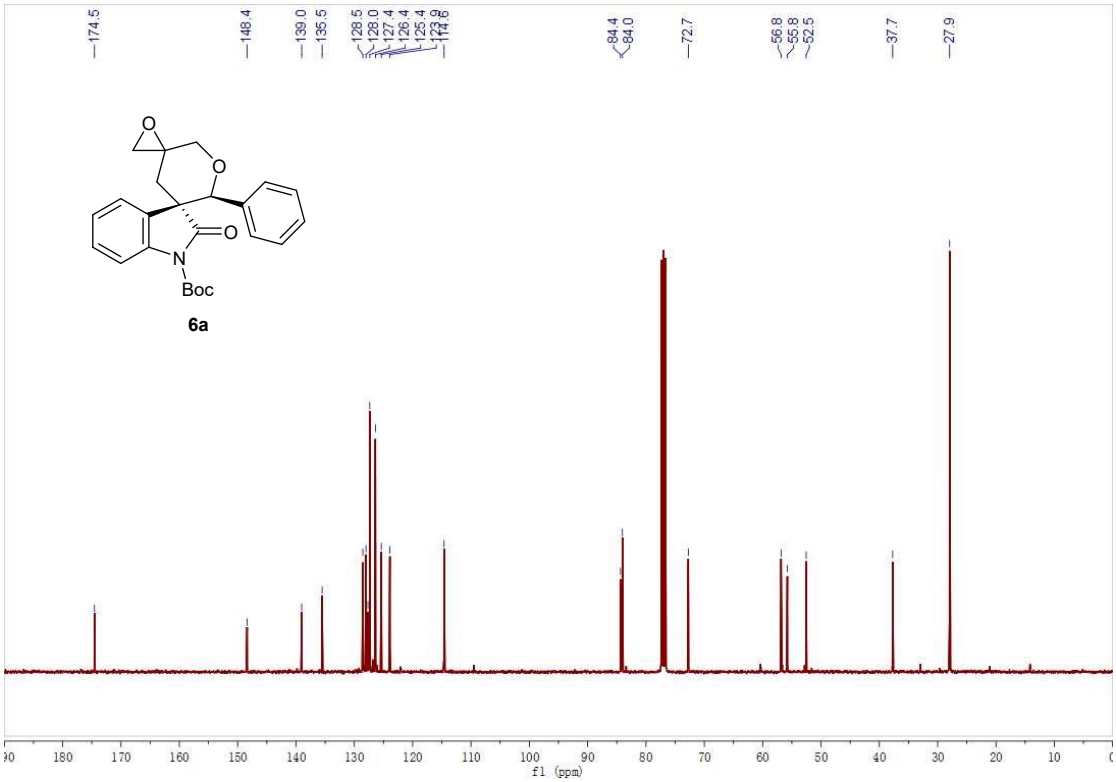


^{1}H NMR of **6a** (400 MHz, $CDCl_3$)

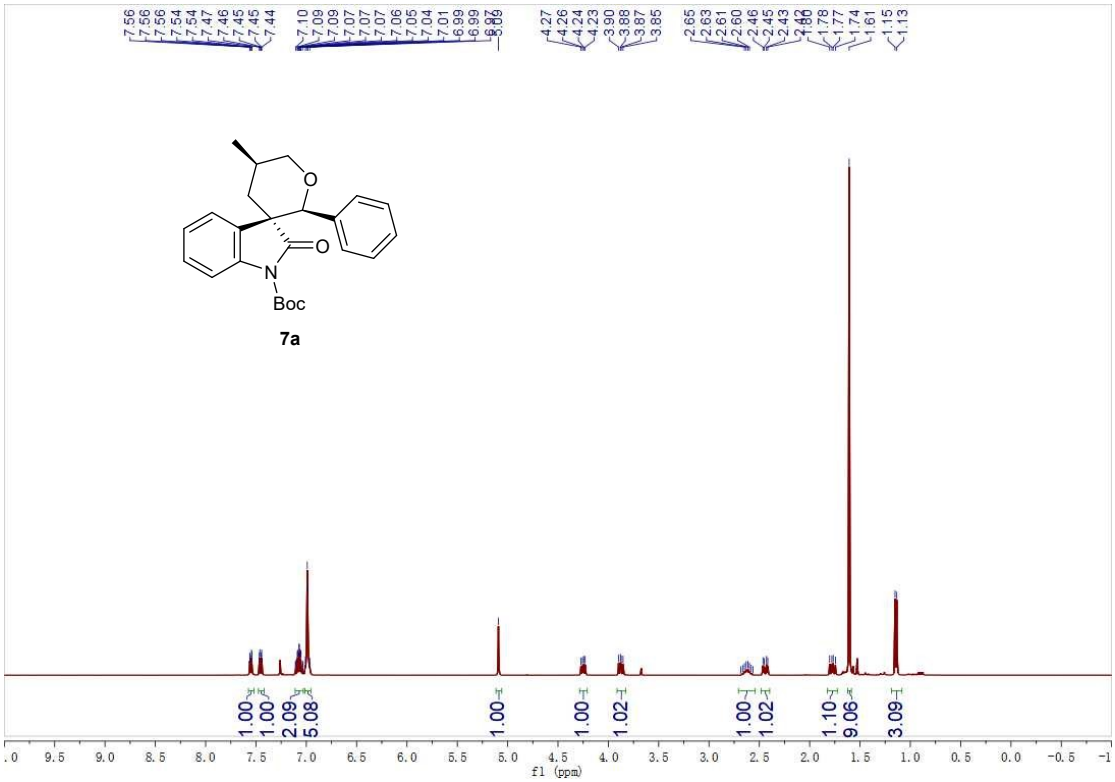




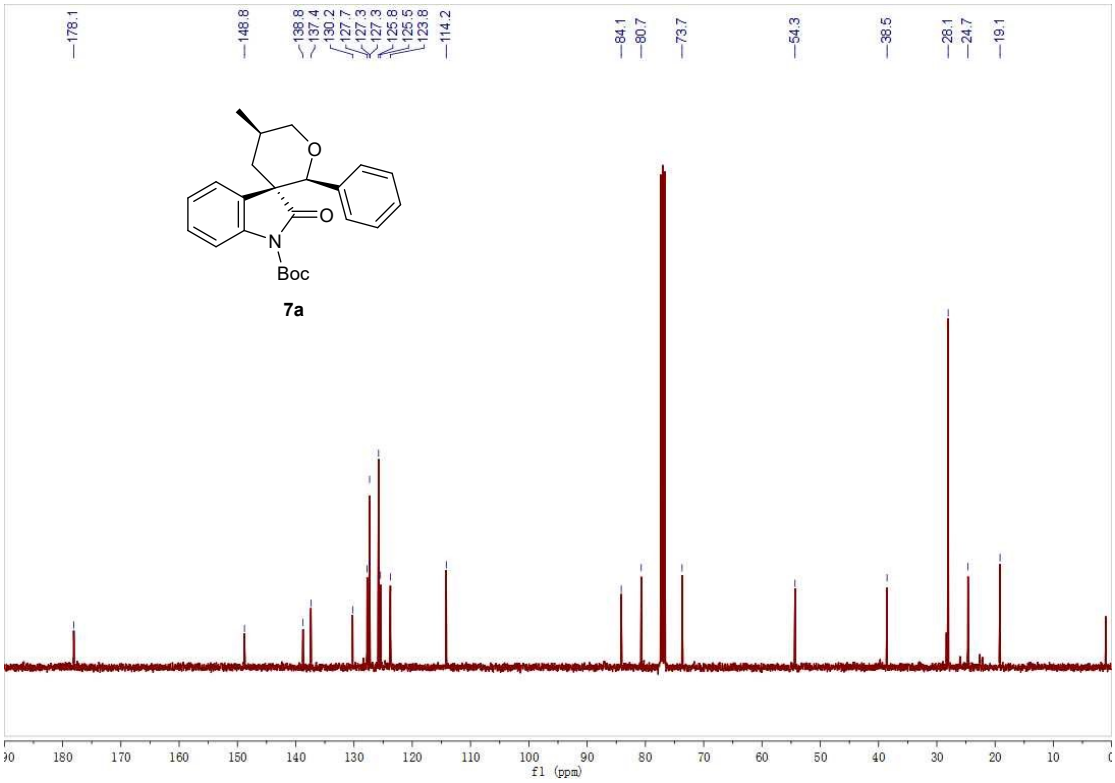
^{13}C {^{1}H} NMR of **6a** (100 MHz, $CDCl_3$)

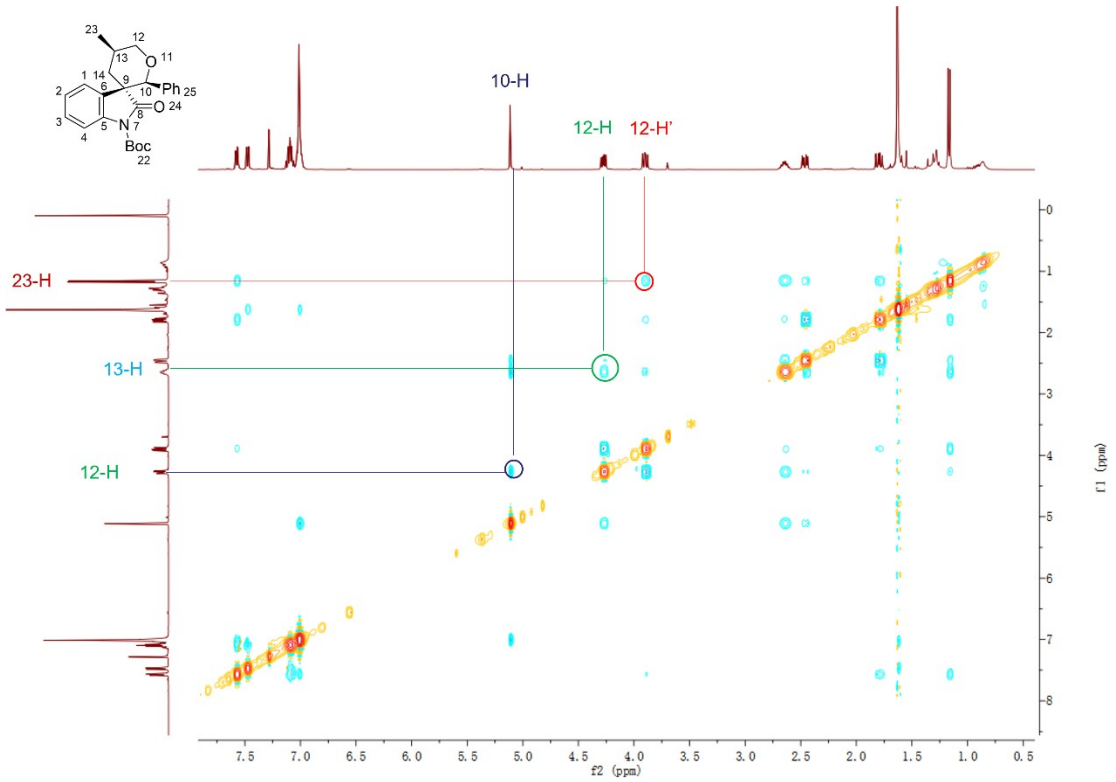


^{1}H NMR of **7a** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR of **7a** (100 MHz, $CDCl_3$)

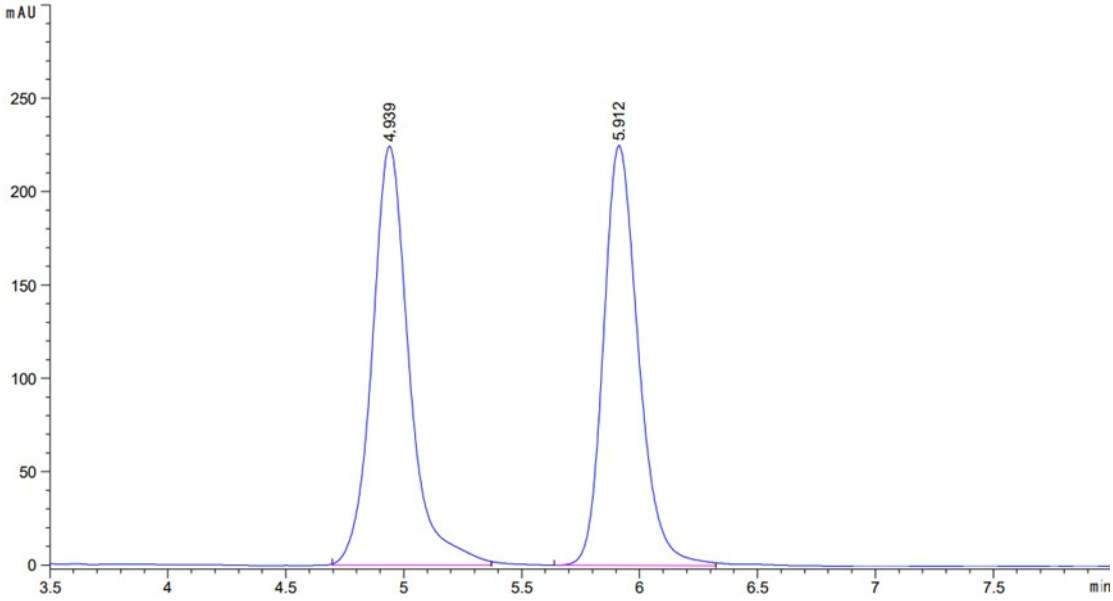



10-H
12-H
12-H'
23-H
13-H
12-H
Boc
Ph
f2 (ppm)
f1 (ppm)

11. HPLC chromatograms of representative compounds

3a

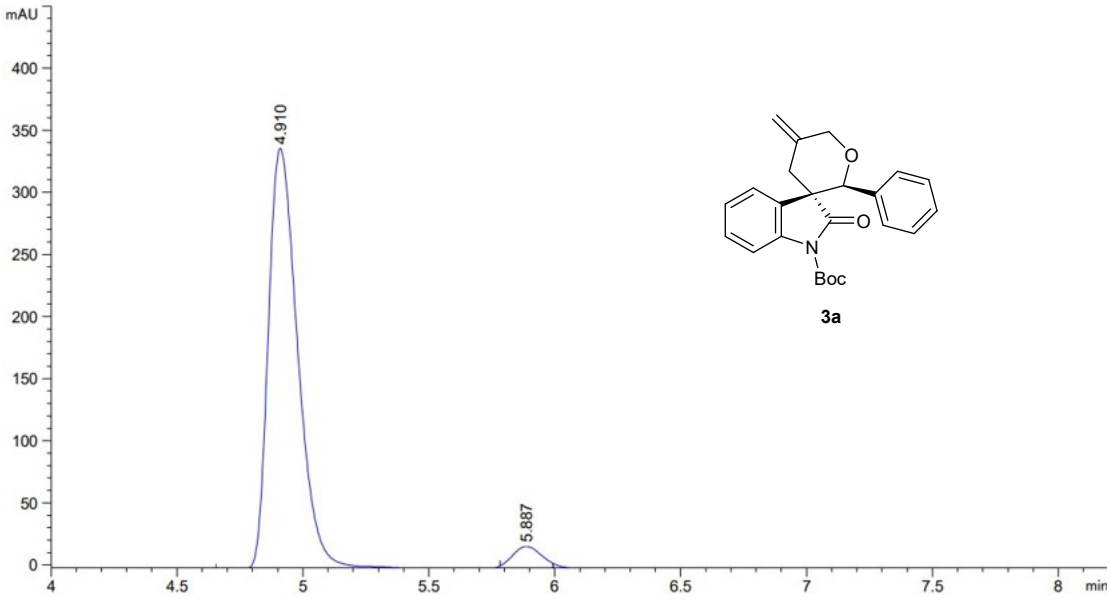
racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.939	FM	0.1818	2448.62134	224.42850	51.4055
2	5.912	MF	0.1716	2314.71997	224.85594	48.5945

chiral:

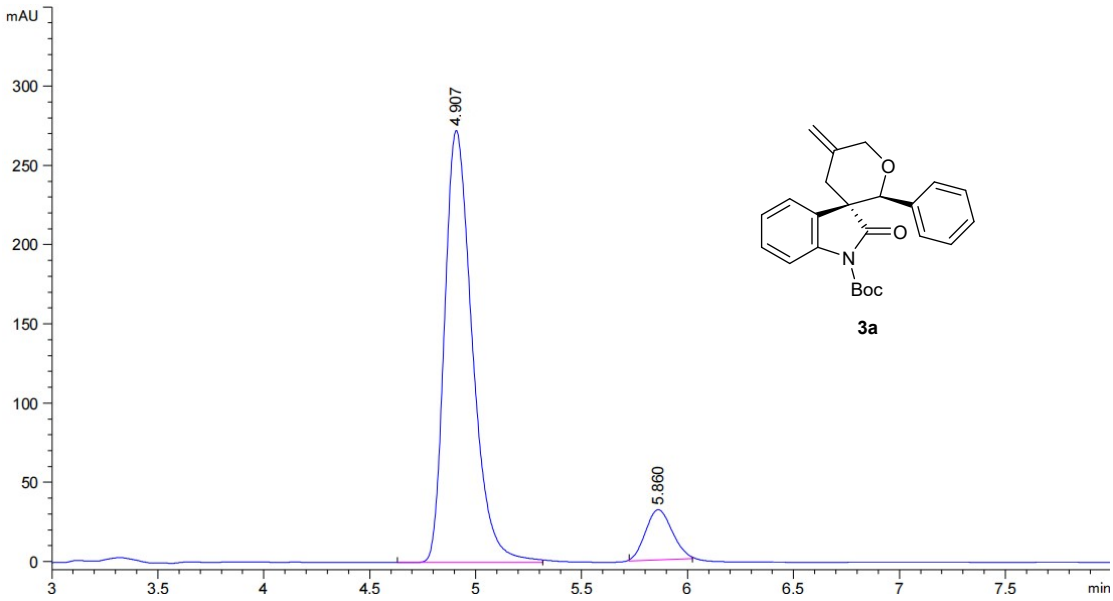
Method A



3a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.910	MF	0.1350	2746.08789	338.96597	94.8419
2	5.887	MF	0.1350	149.35091	18.44167	5.1581

Method B

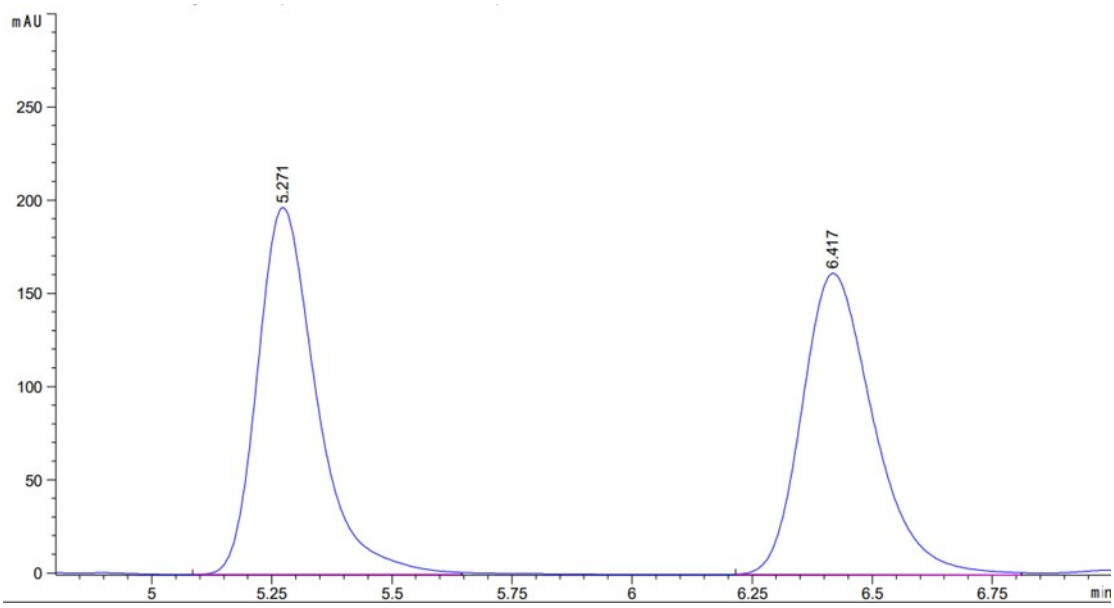


3a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.907	MF	0.1511	2471.22974	272.64468	89.8946
2	5.860	MM	0.1454	277.80167	31.85209	10.1054

3b

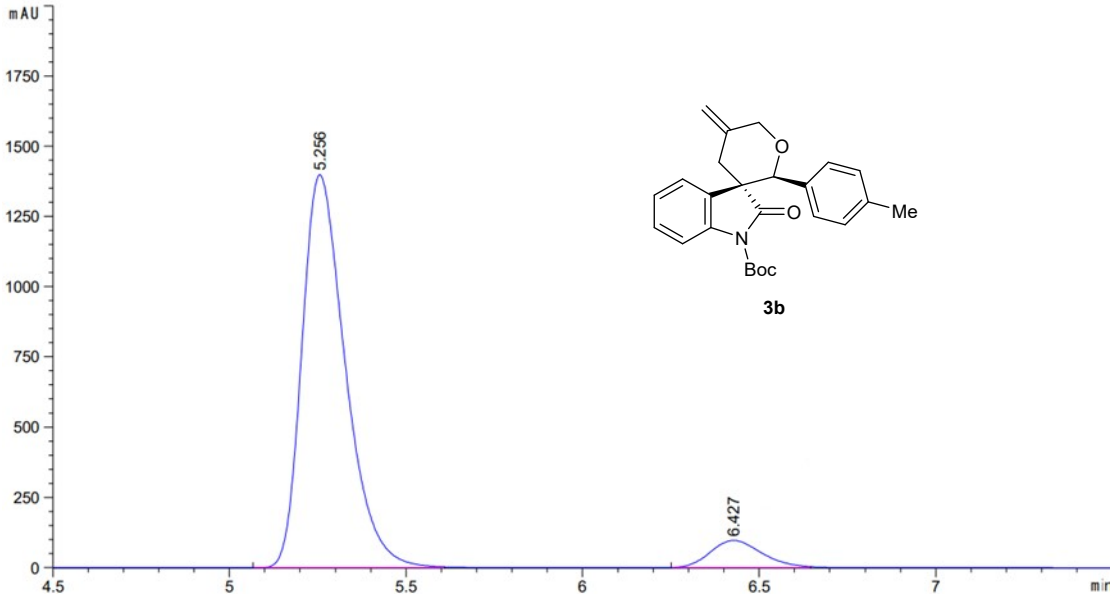
racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.271	MF	0.1420	1676.79724	196.83427	50.1362
2	6.417	MM	0.1721	1667.68677	161.52570	49.8638

chrial:

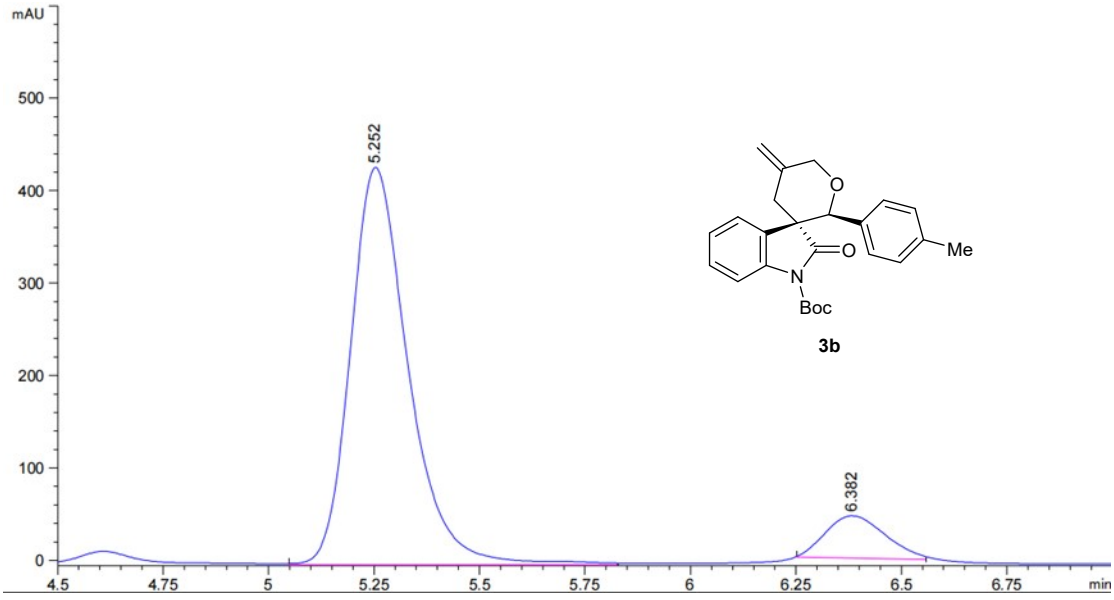
Method A



3b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.256	MF	0.1420	1.19249e4	1399.35156	92.3073
2	6.427	MF	0.1702	993.80249	97.29763	7.6927

Method B

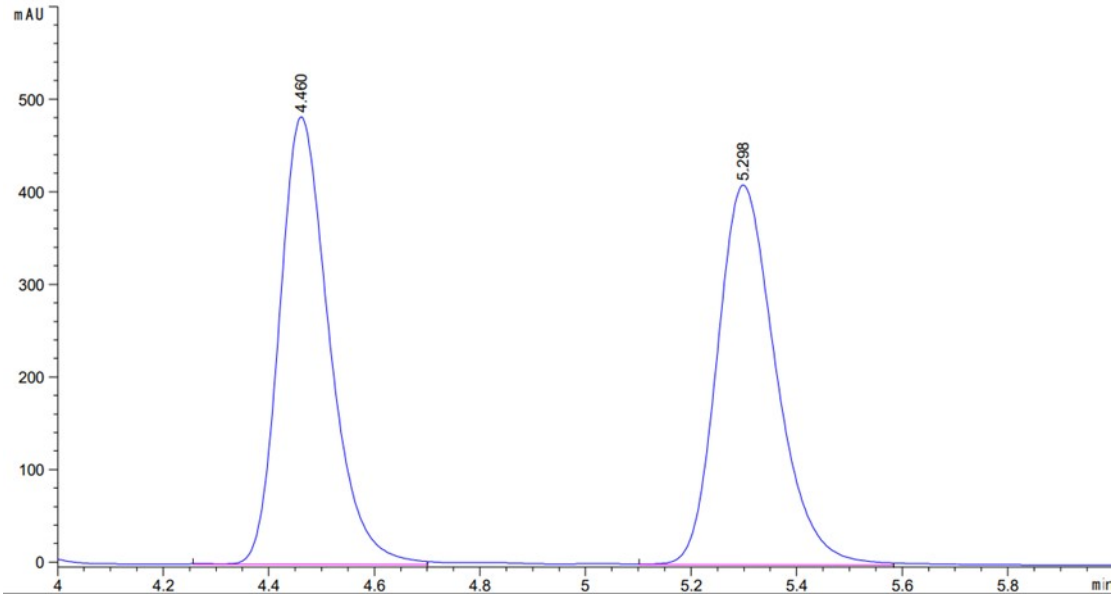


3b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.252	MM	0.1587	4095.69214	430.03888	90.1235
2	6.382	MM	0.1636	448.84137	45.71336	9.8765

3c

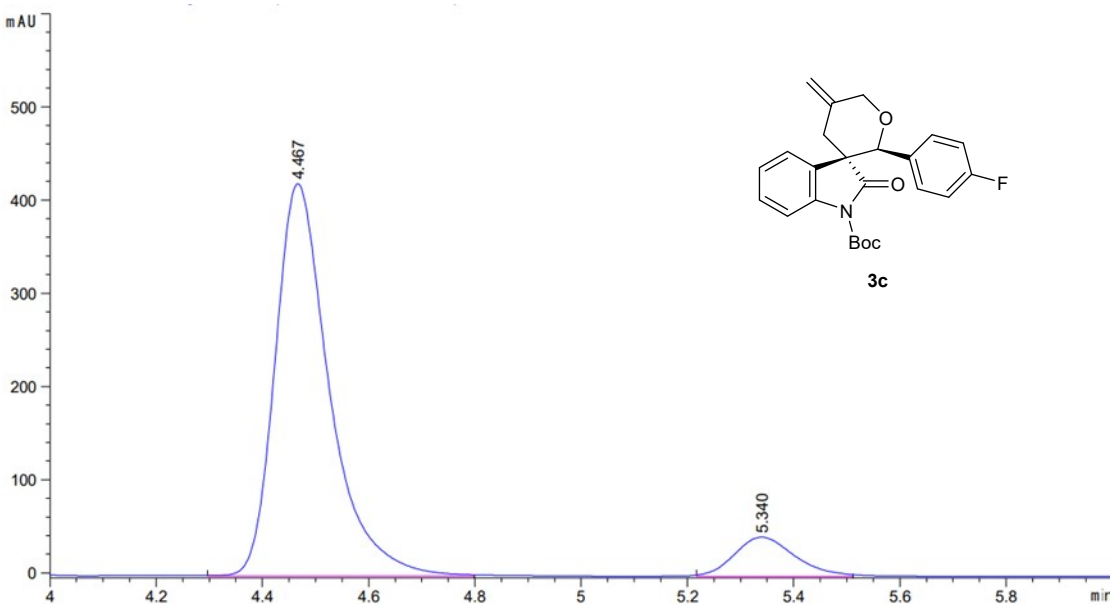
racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.460	FM	0.1092	3167.48315	483.52481	50.0110
2	5.298	MF	0.1286	3166.09058	410.27994	49.9890

chrial:

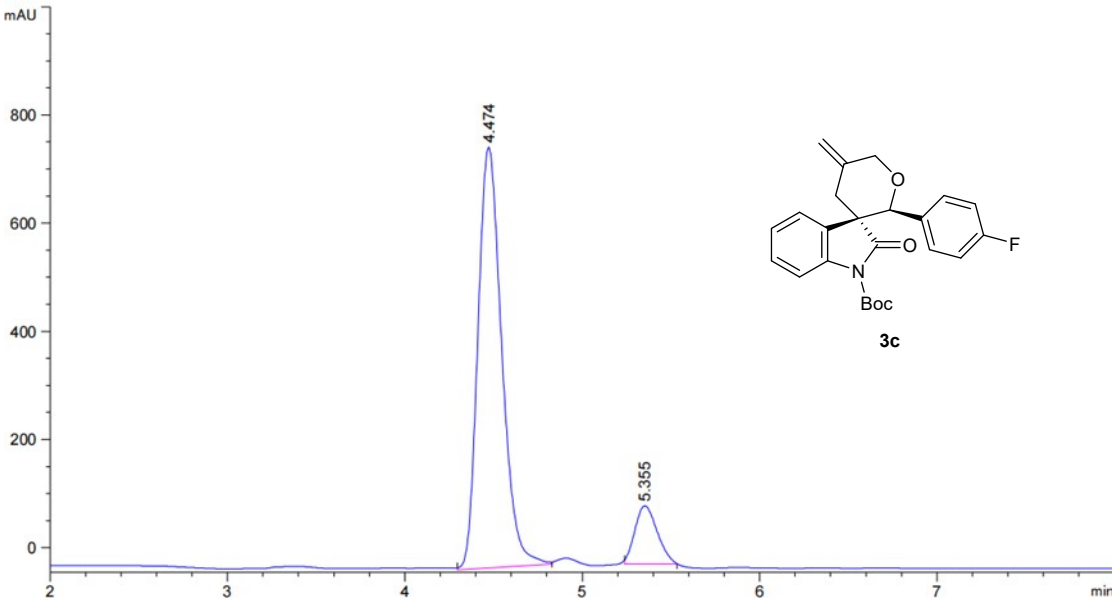
Method A



3c

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.467	FM	0.1179	2977.93018	420.90634	90.0624
2	5.340	MF	0.1306	328.58804	41.92053	9.9376

Method B

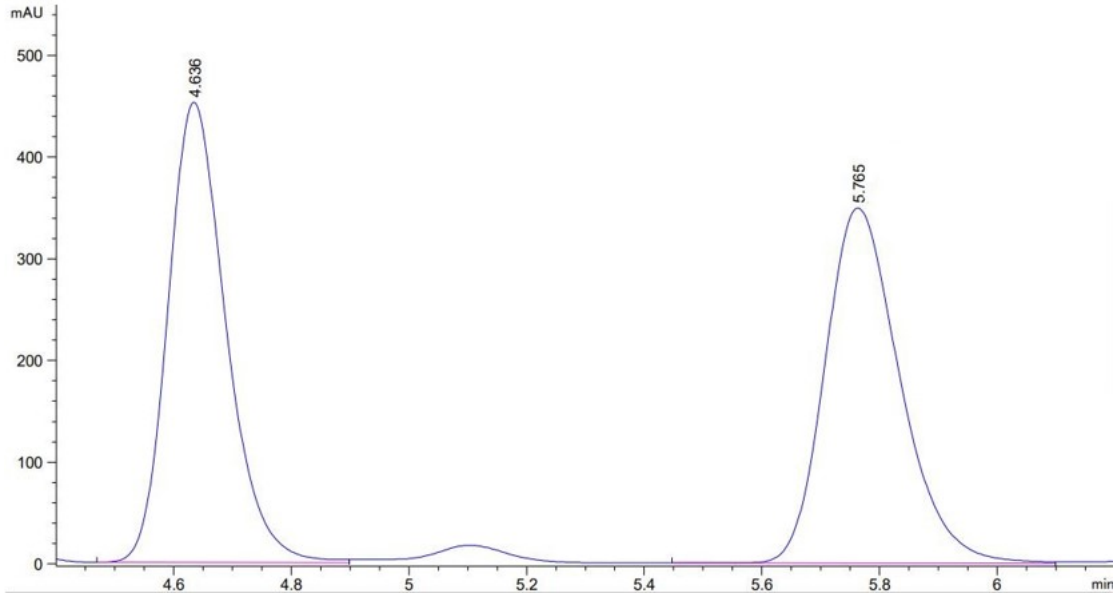


3c

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.474	MM	0.1548	7225.14209	777.66626	88.4157
2	5.355	MM	0.1464	946.64447	107.80237	11.5843

3d

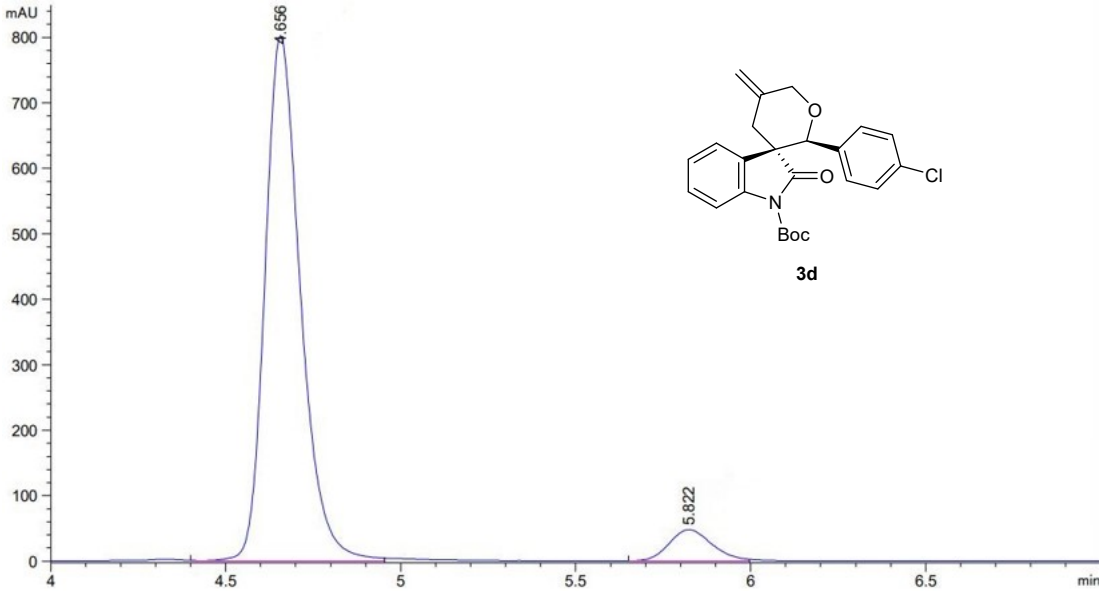
racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.636	MF	0.1141	3099.31250	452.80240	50.1061
2	5.765	MF	0.1473	3086.18164	349.22672	49.8939

chrial:

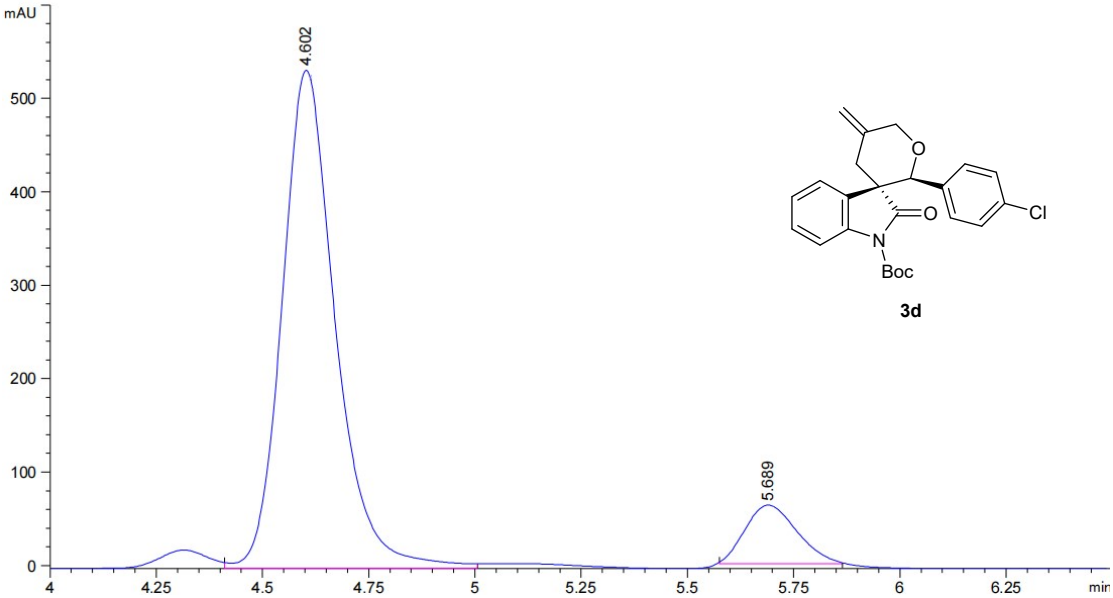
Method A



3d

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.656	MF	0.1170	5631.16650	801.85394	93.2837
2	5.822	MF	0.1422	405.43326	47.53395	6.7163

Method B

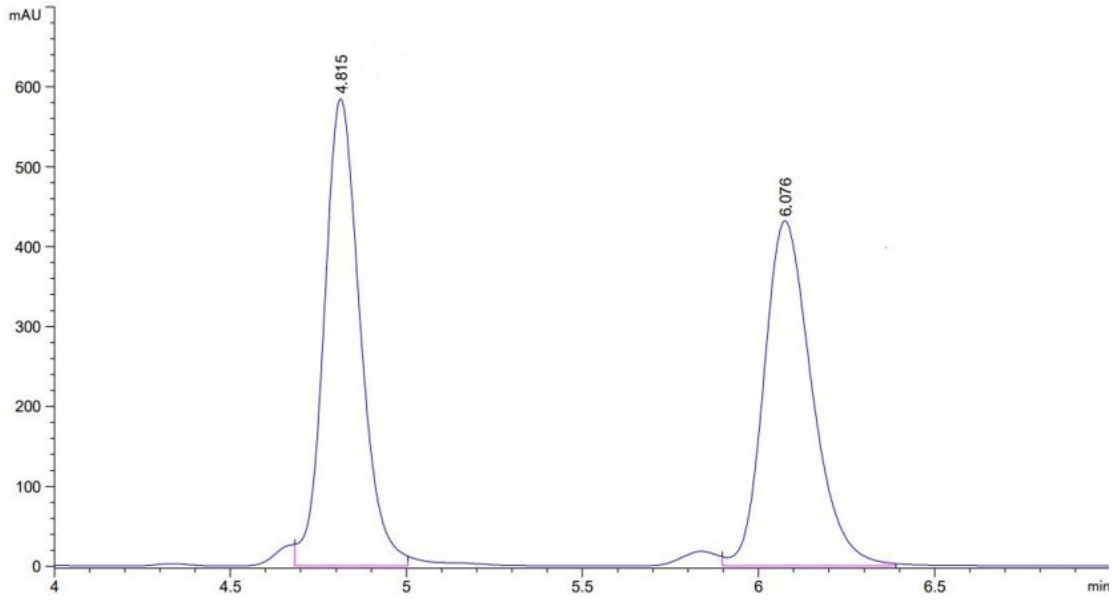


3d

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.602	MM	0.1444	4615.93359	532.86615	89.7104
2	5.689	MM	0.1410	529.43555	62.58767	10.2896

3e

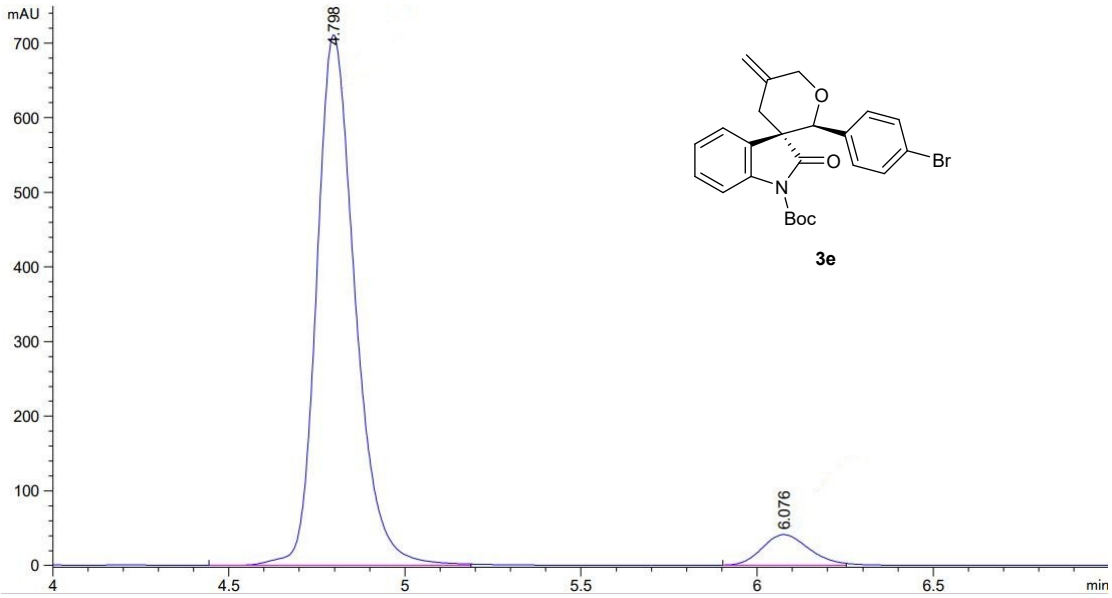
racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.815	MF	0.1183	4150.43066	584.70441	50.4205
2	6.076	FM	0.1576	4081.19800	431.68158	49.5795

chrial:

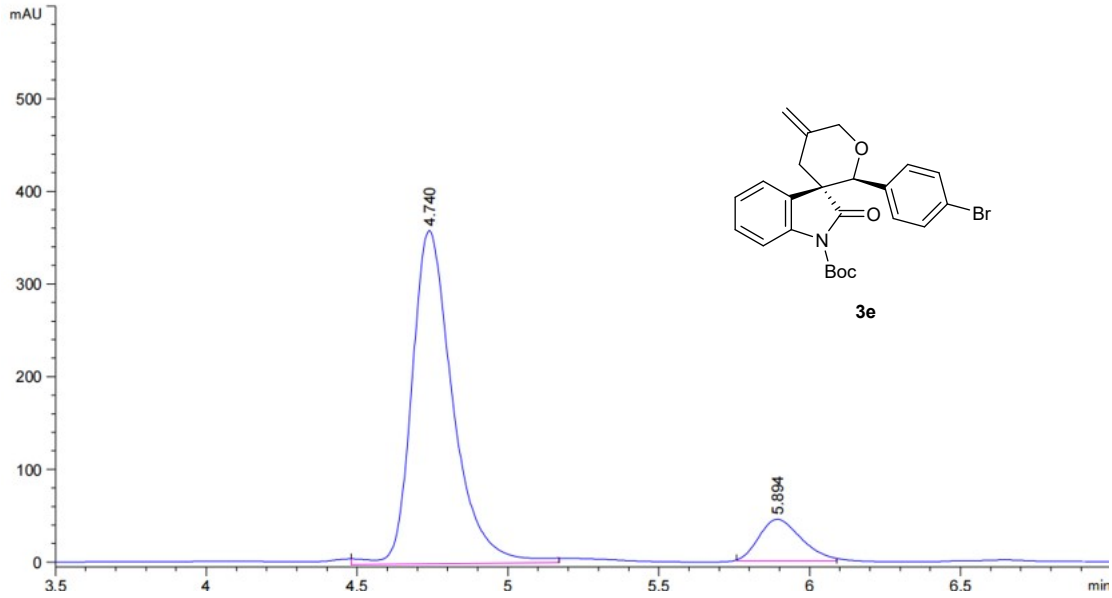
Method A



3e

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.798	MF	0.1264	5391.36816	710.97644	93.3965
2	6.076	MF	0.1542	381.18967	41.19269	6.6035

Method B

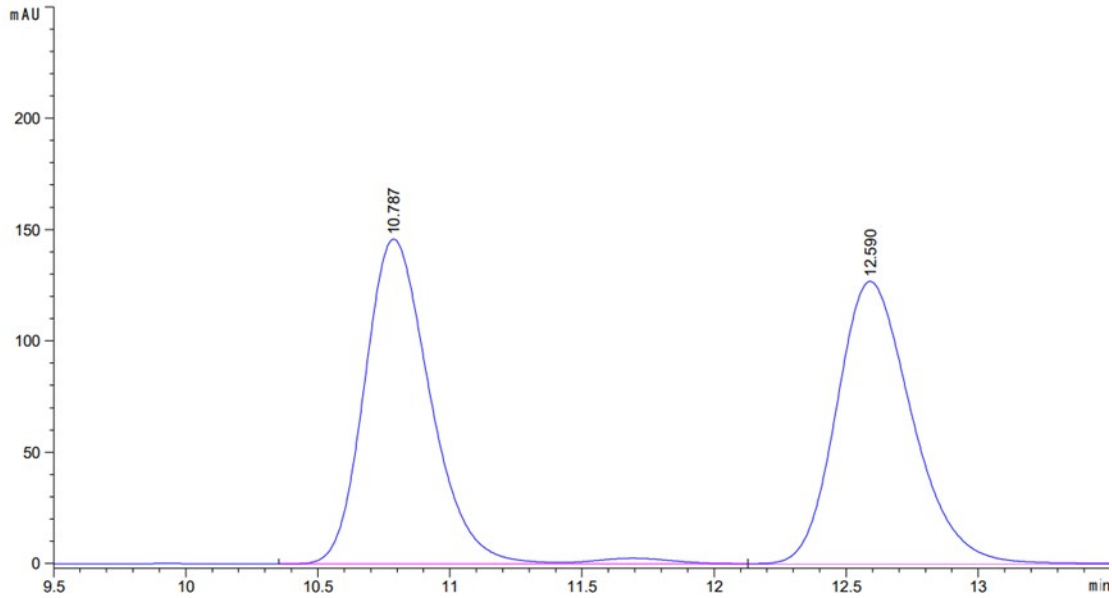


3e

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.740	FM	0.1572	3390.49072	359.40253	88.7679
2	5.894	MF	0.1609	429.01086	44.43409	11.2321

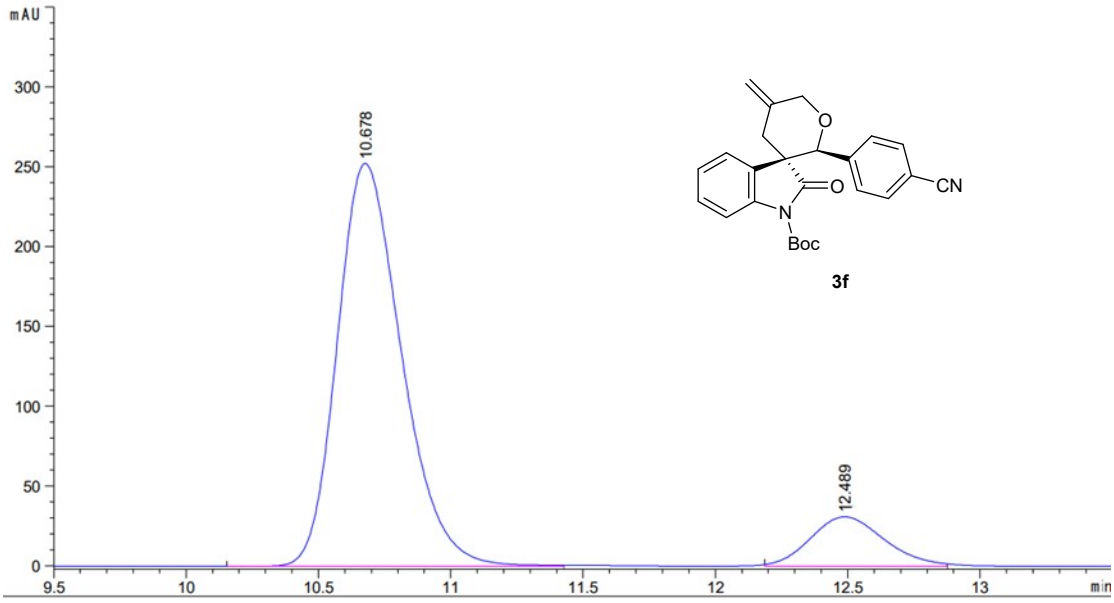
3f

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.787	BV R	0.2637	2551.31860	145.84697	50.4063
2	12.590	VB	0.3049	2510.19287	126.80631	49.5937

chrial:

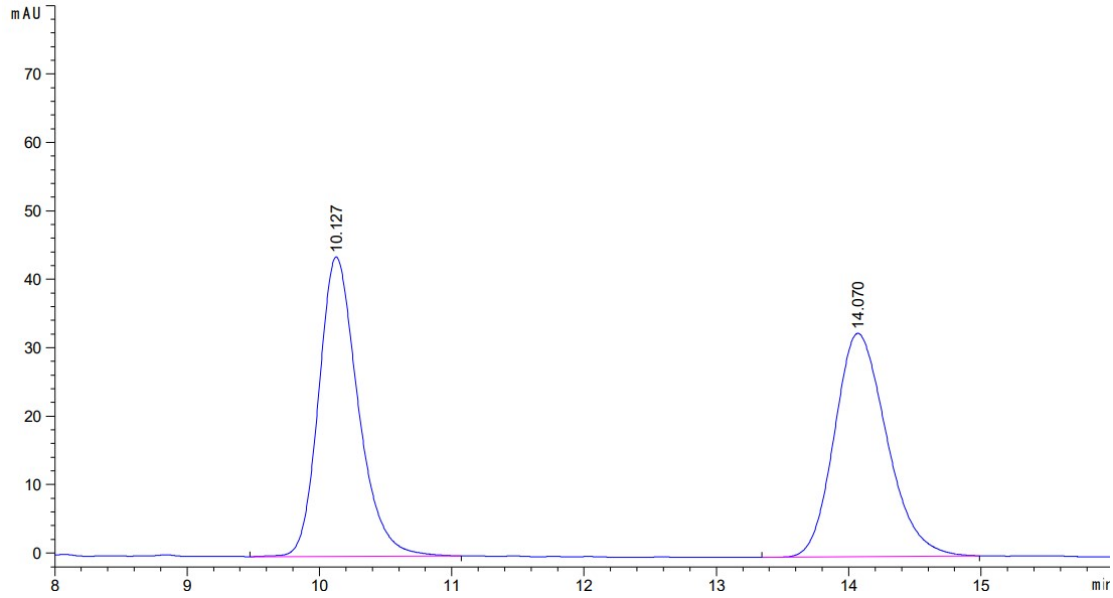


3f

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.678	MF	0.2819	4267.26563	252.25377	87.6869
2	12.489	MF	0.3235	599.21228	30.87482	12.3131

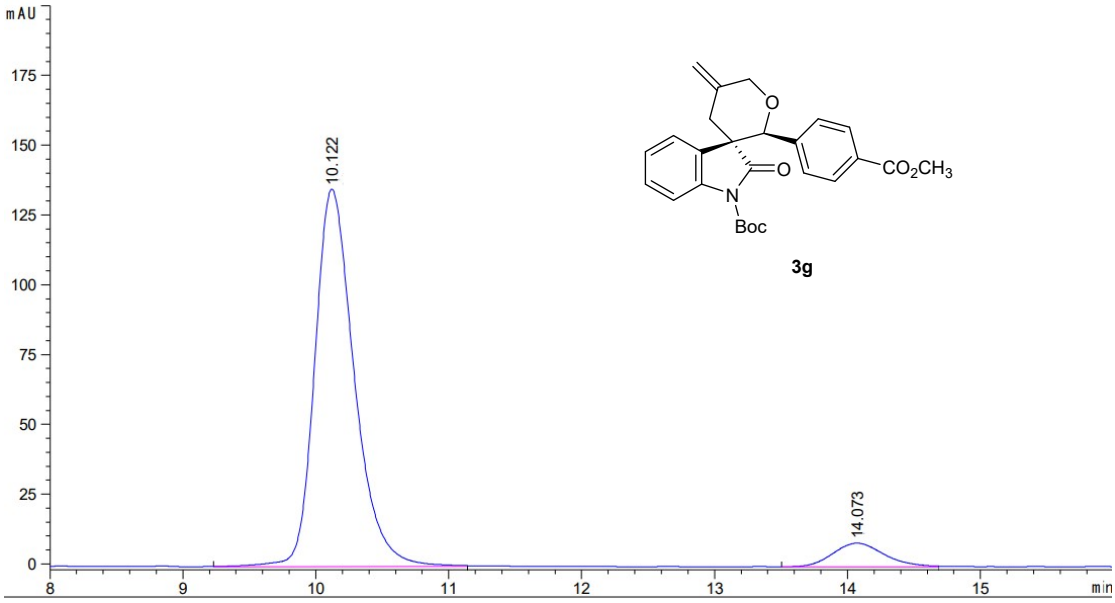
3g

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.127	BB	0.3135	901.66119	43.74352	50.2035
2	14.070	BB	0.4268	894.35260	32.62625	49.7965

chrial:

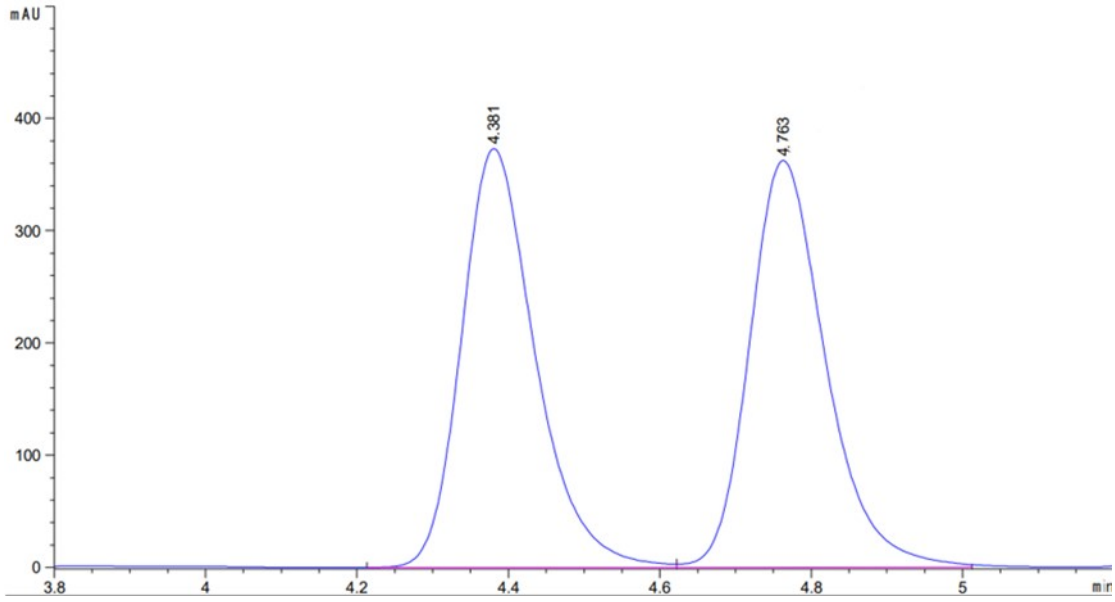


3g

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.122	FM	0.3447	2795.11108	135.13371	92.5022
2	14.073	MF	0.4462	226.55896	8.46265	7.4978

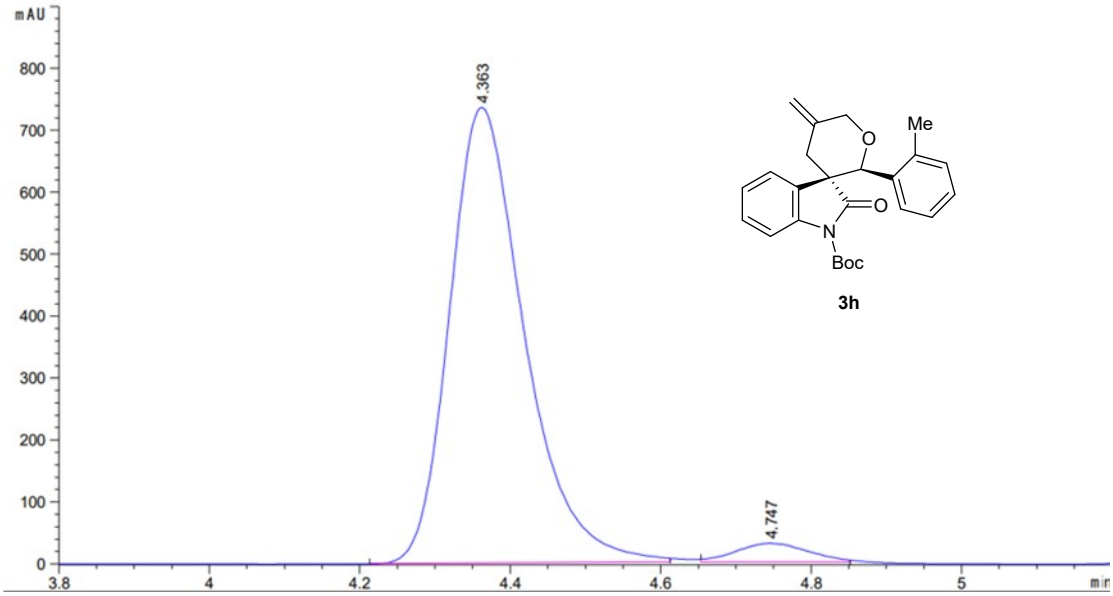
3h

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.381	BV	0.1030	2523.75049	372.90582	49.9783
2	4.763	MF	0.1161	2525.94385	362.55124	50.0217

chiral:

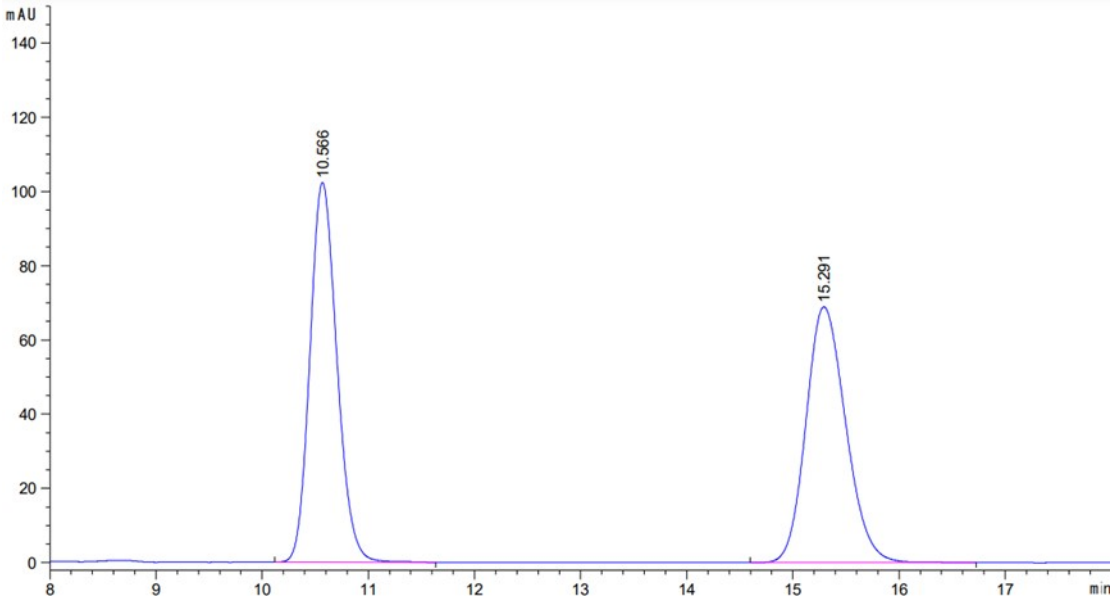


3h

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.363	MM	0.1150	5076.57715	735.67627	96.1865
2	4.747	MM	0.1114	201.27271	30.10432	3.8135

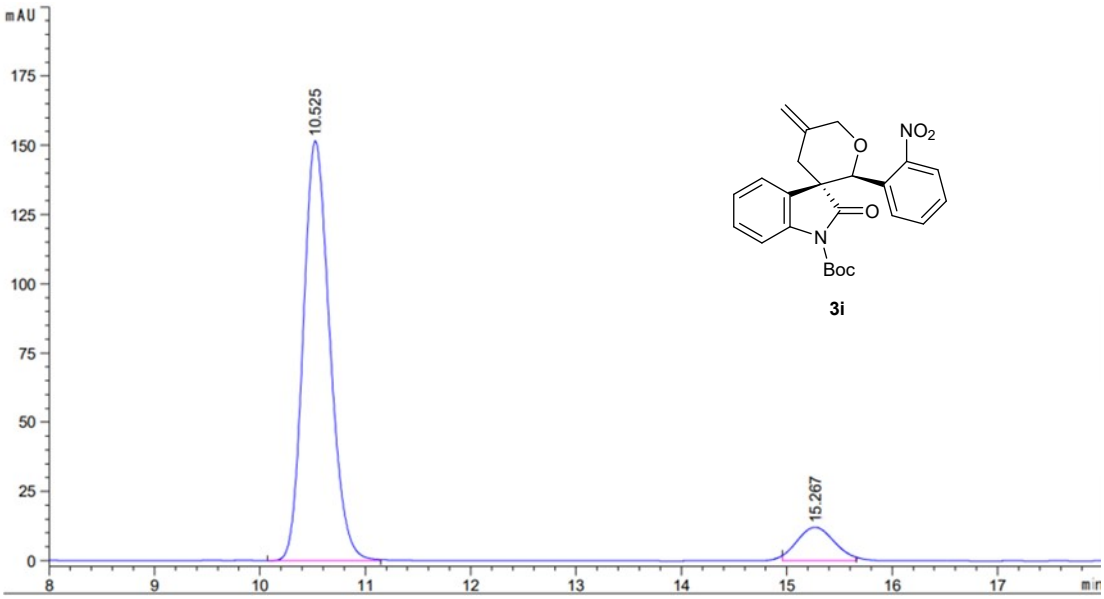
3i

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.566	BB	0.2728	1804.48987	102.31963	50.1090
2	15.291	BB	0.4031	1796.63831	68.92859	49.8910

chiral:

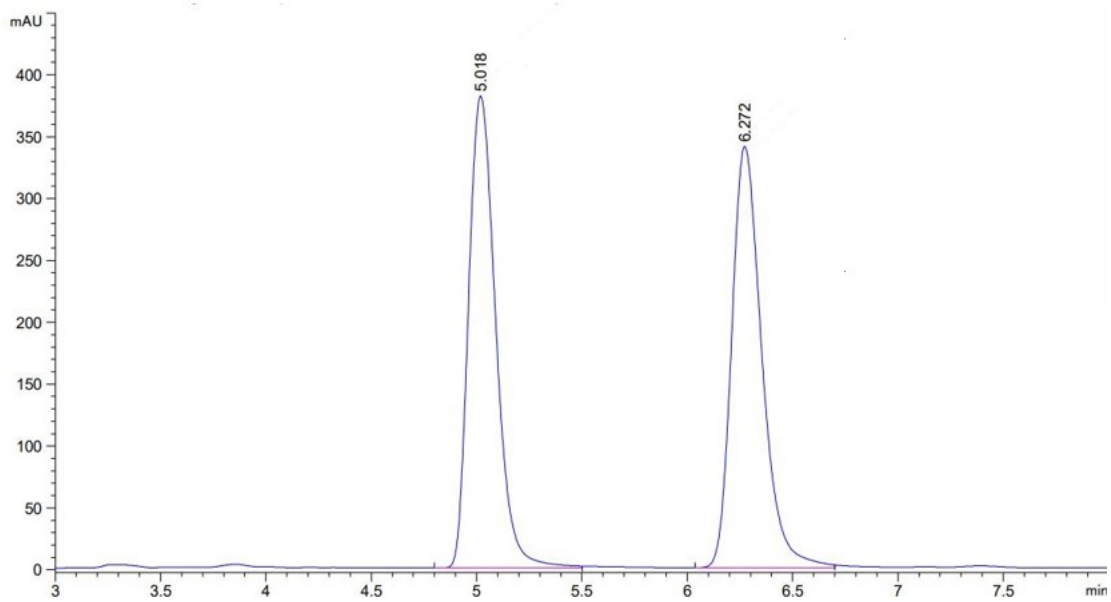


3i

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.525	MF	0.2907	2643.95239	151.55995	89.9066
2	15.267	FM	0.4084	296.82452	12.11333	10.0934

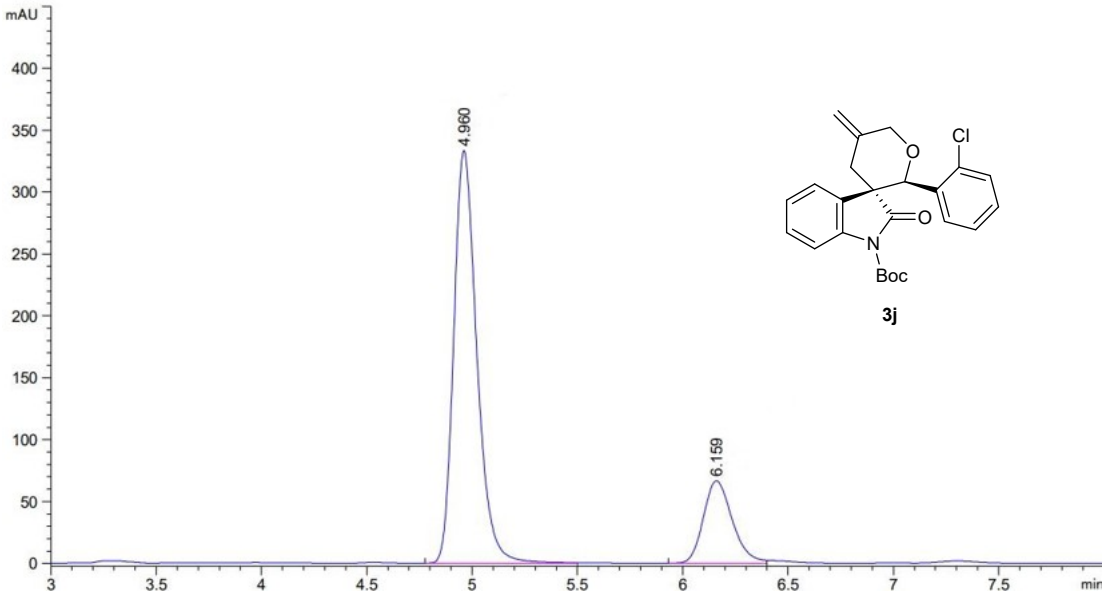
3j

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.018	MF	0.1484	3394.32471	381.14948	50.0631
2	6.272	MF	0.1657	3385.76489	340.45746	49.9369

chiral:

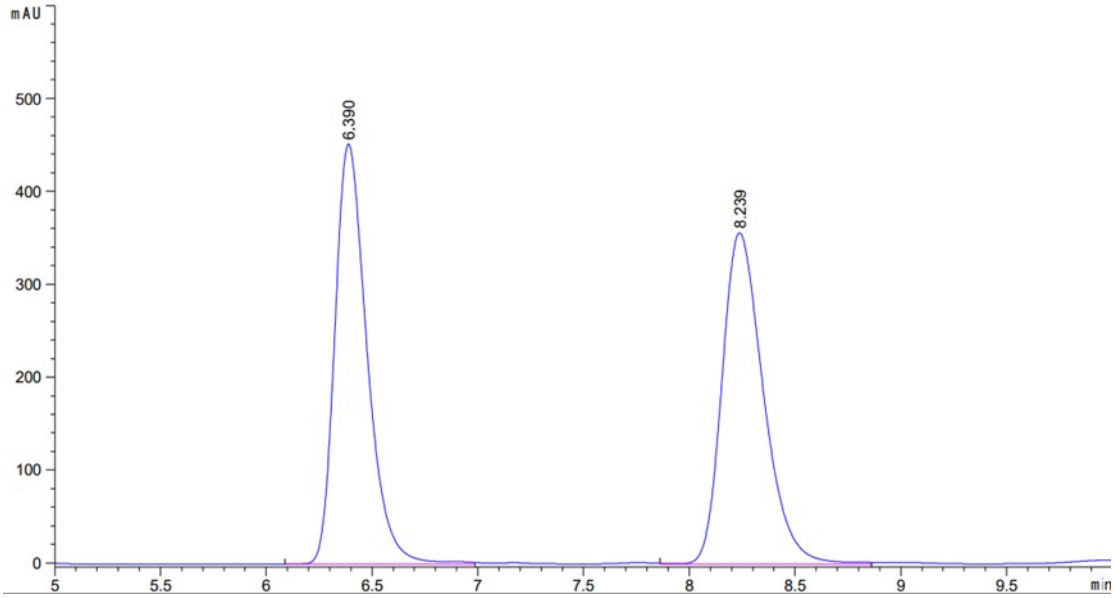


3j

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.960	MF	0.1269	2538.50366	333.29126	80.0148
2	6.159	MF	0.1590	634.04077	66.47869	19.9852

3k

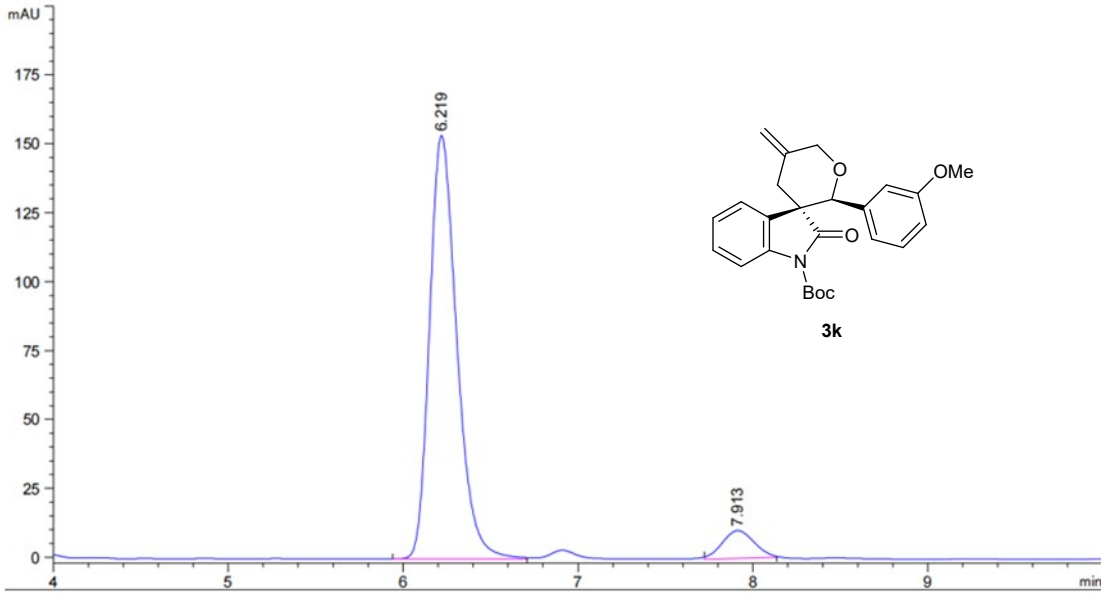
racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.390	MF	0.1759	4772.33252	452.06946	49.6762
2	8.239	FM	0.2263	4834.54492	356.12601	50.3238

chiral:

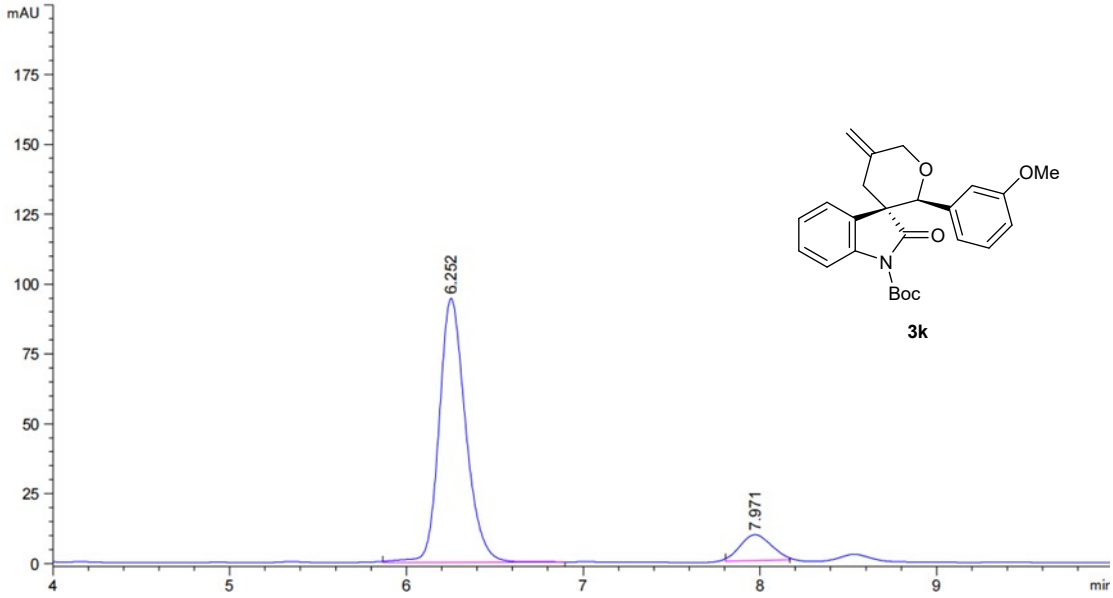
Method A



3k

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.219	MF	0.1803	1660.34692	153.51534	92.8530
2	7.913	MM	0.2116	127.79876	10.06773	7.1470

Method B

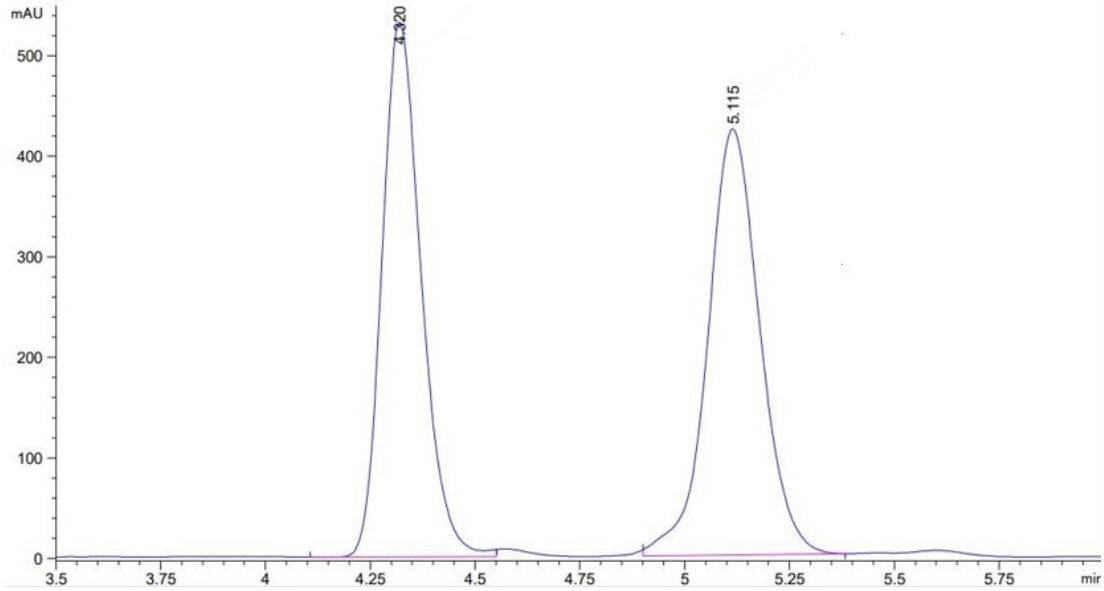


3k

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.252	FM	0.1737	984.78021	94.47954	89.7507
2	7.971	MM	0.2031	112.45901	9.23032	10.2493

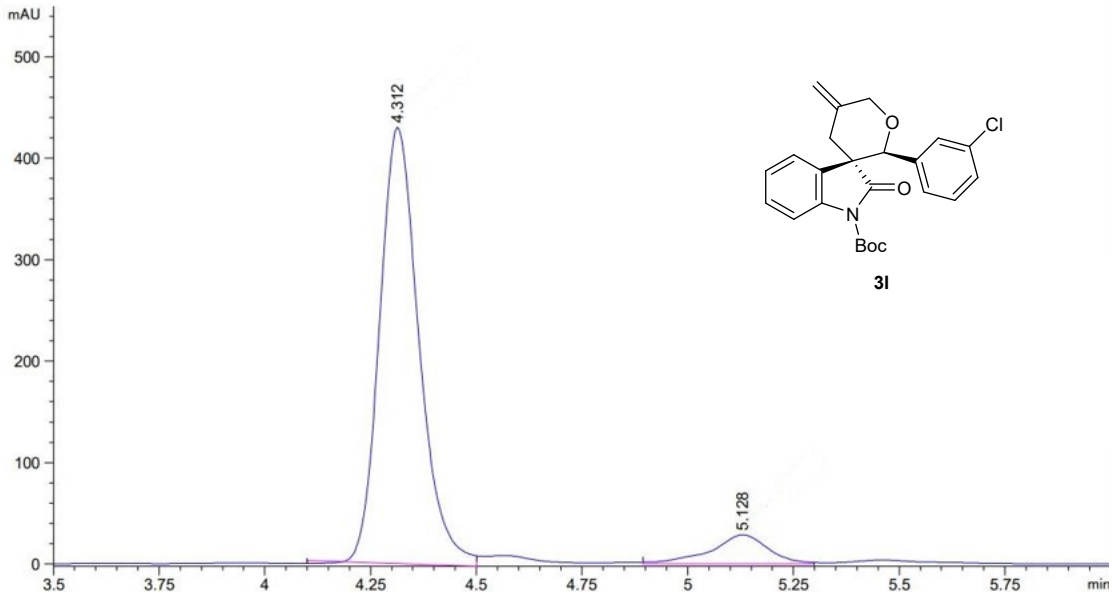
3l

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.320	MF	0.1087	3466.08203	531.61023	48.6680
2	5.115	FM	0.1438	3655.80835	423.76486	51.3320

chiral:

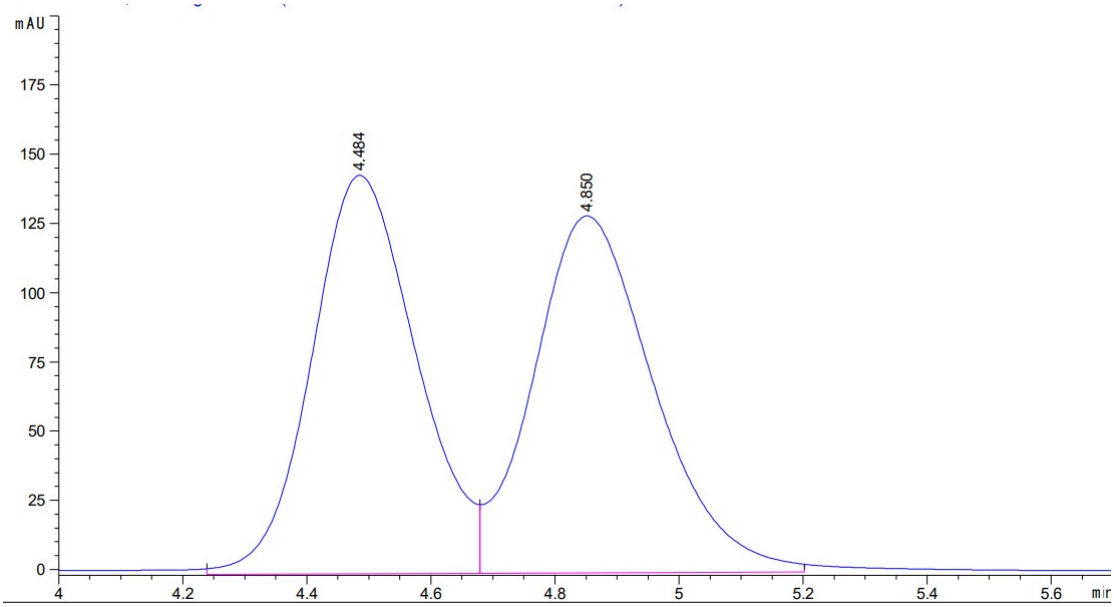


3l

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.312	MF	0.1079	2783.65063	430.07074	91.2482
2	5.128	MF	0.1566	266.98697	28.42067	8.7518

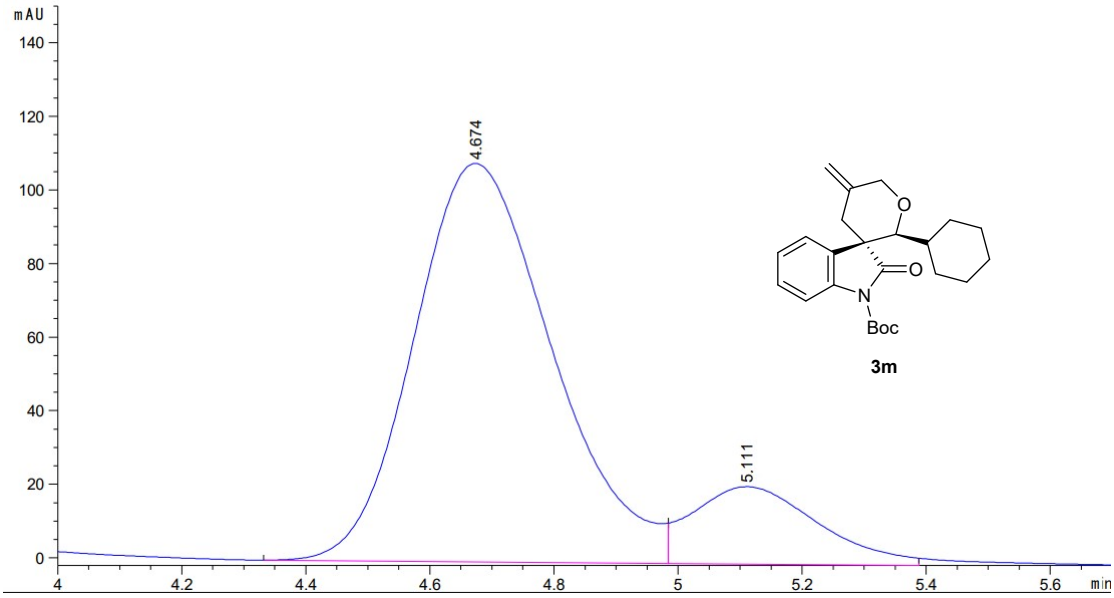
3m

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.484	FM	0.1959	1691.66370	143.92958	49.3367
2	4.850	MF	0.2246	1737.15332	128.92233	50.6633

chrial:

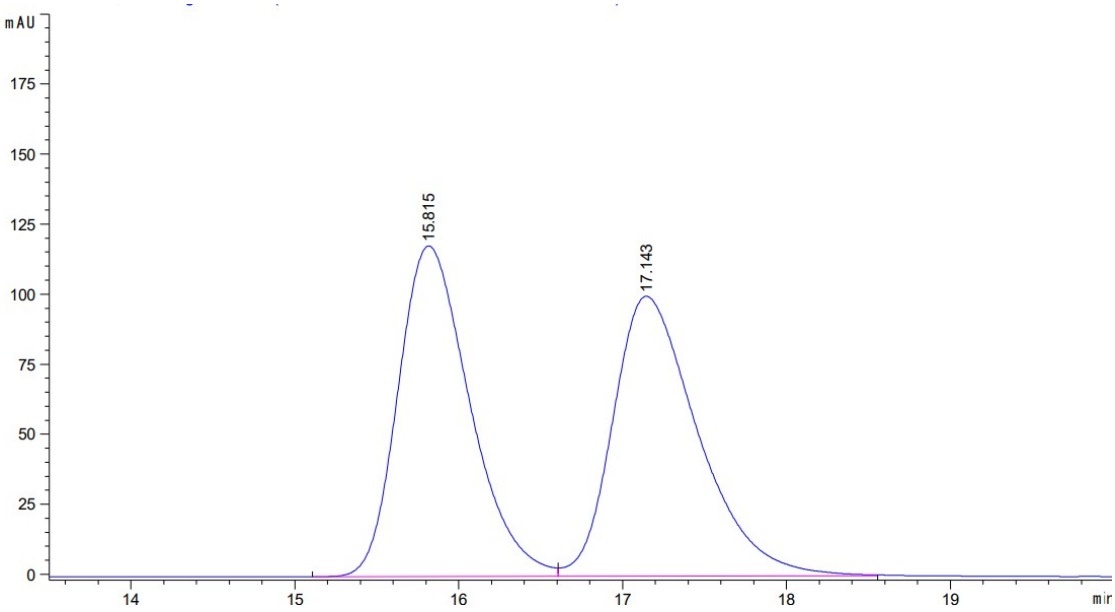


3m

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.674	MF	0.2582	1676.73083	108.24329	85.1371
2	5.111	MF	0.2325	292.71674	20.98120	14.8629

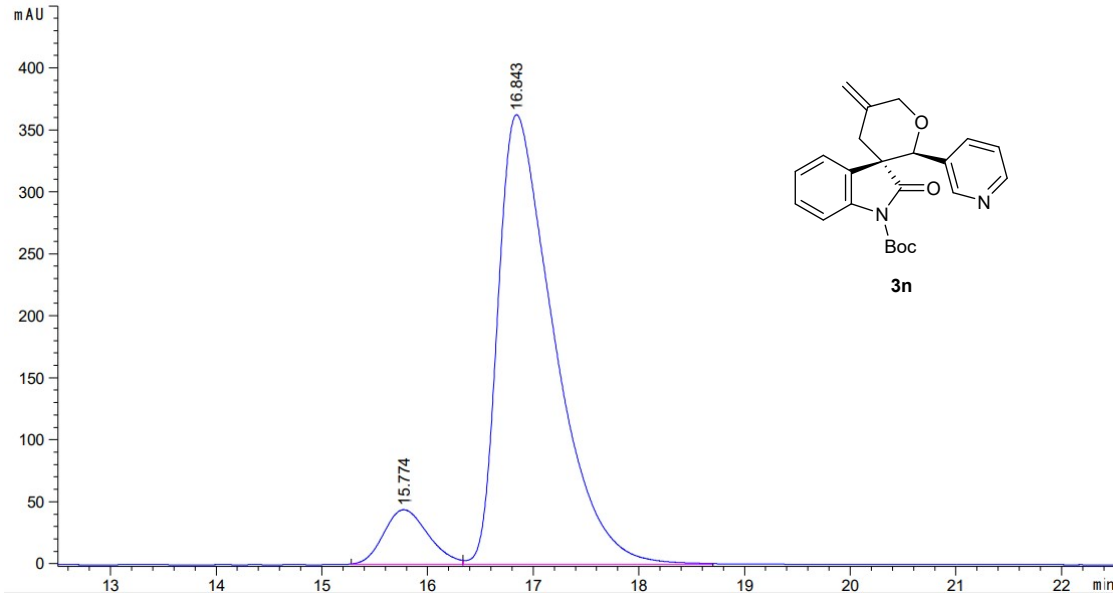
3n

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.815	FM	0.5063	3586.72461	118.06325	49.8241
2	17.143	MF	0.6022	3612.05396	99.96513	50.1759

chrial:

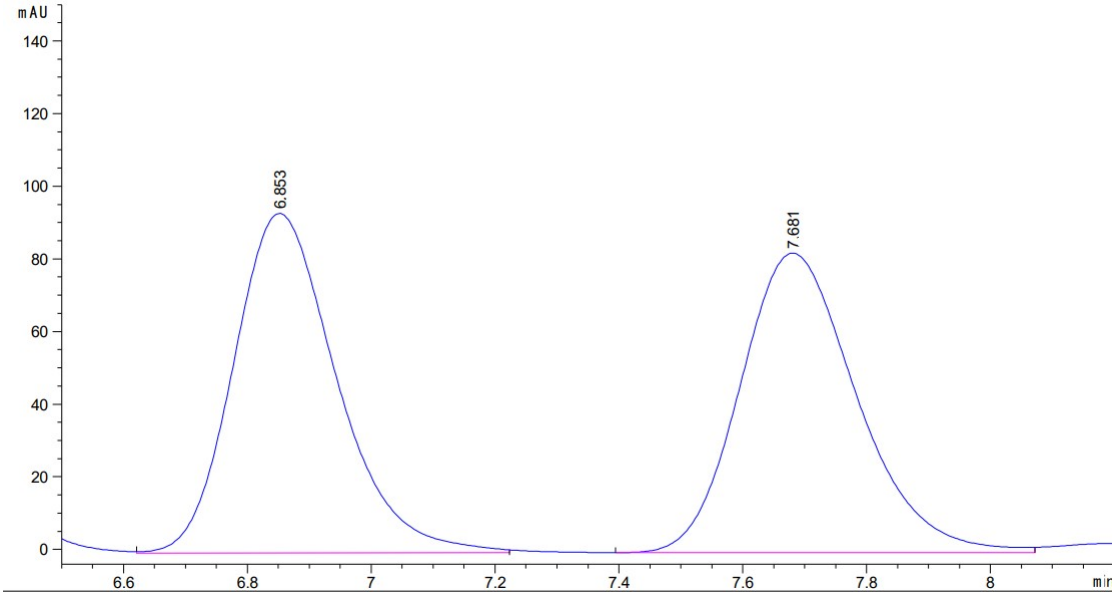


3n

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.774	FM	0.4903	1304.78638	44.35469	8.9091
2	16.843	MF	0.6127	1.33408e4	362.91104	91.0909

3o

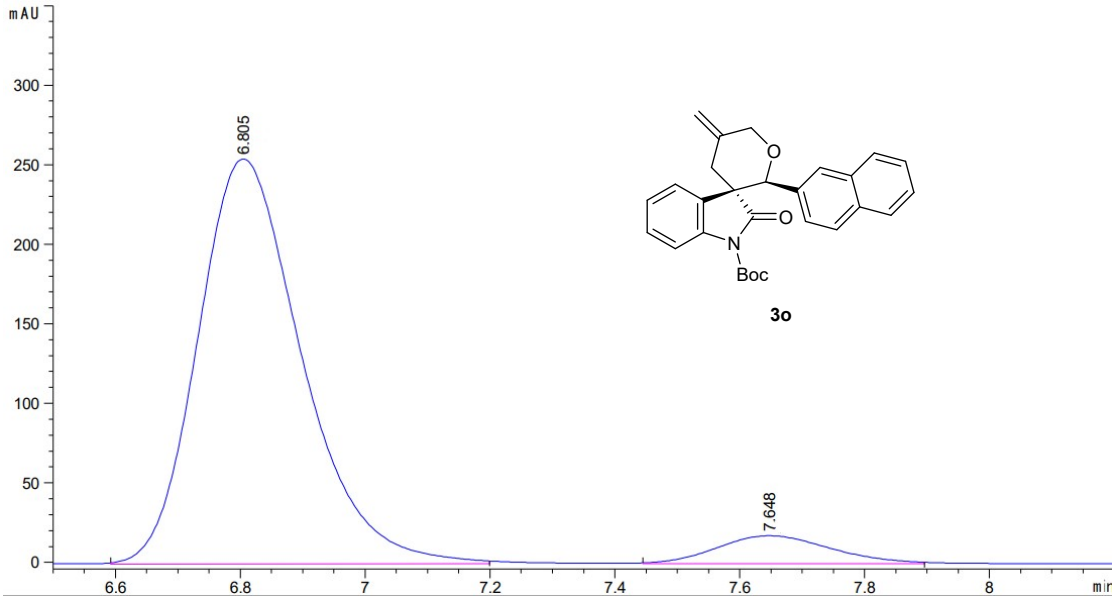
racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.853	MF	0.1926	1080.77502	93.51992	50.0747
2	7.681	MF	0.2177	1077.55017	82.50919	49.9253

chrial:

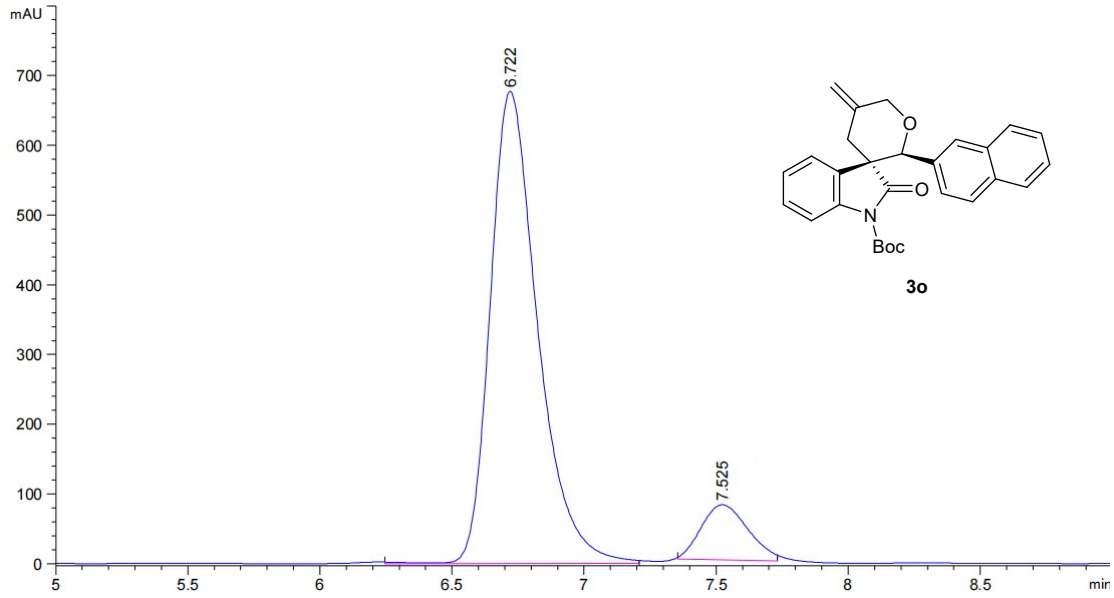
Method A



3o

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.805	FM	0.1923	2938.55200	254.70947	92.9167
2	7.648	MF	0.2124	224.01491	17.57987	7.0833

Method B

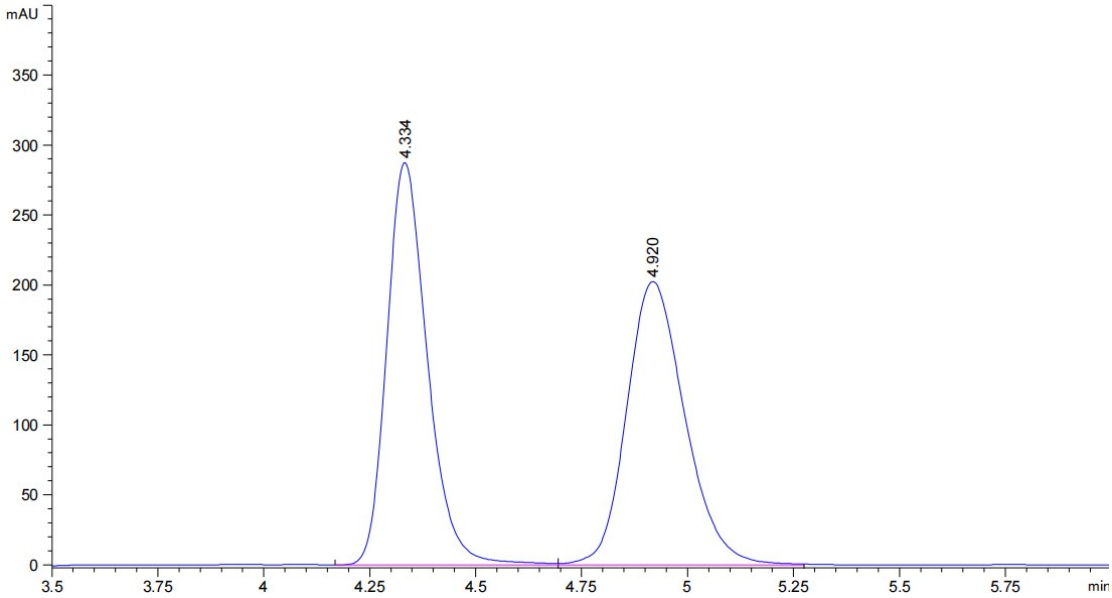


3o

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.722	FM	0.2081	8452.79004	677.01843	89.7647
2	7.525	MF	0.2039	963.81470	78.78664	10.2353

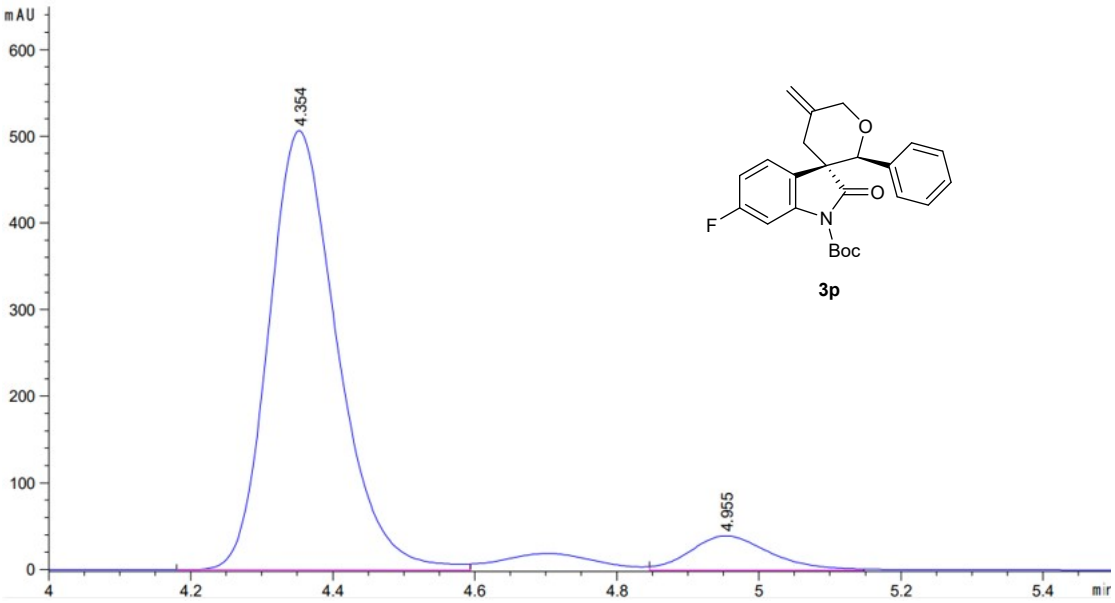
3p

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.334	BV	0.1016	1913.91492	287.58292	49.7356
2	4.920	MF	0.1591	1934.26672	202.67398	50.2644

chrial:

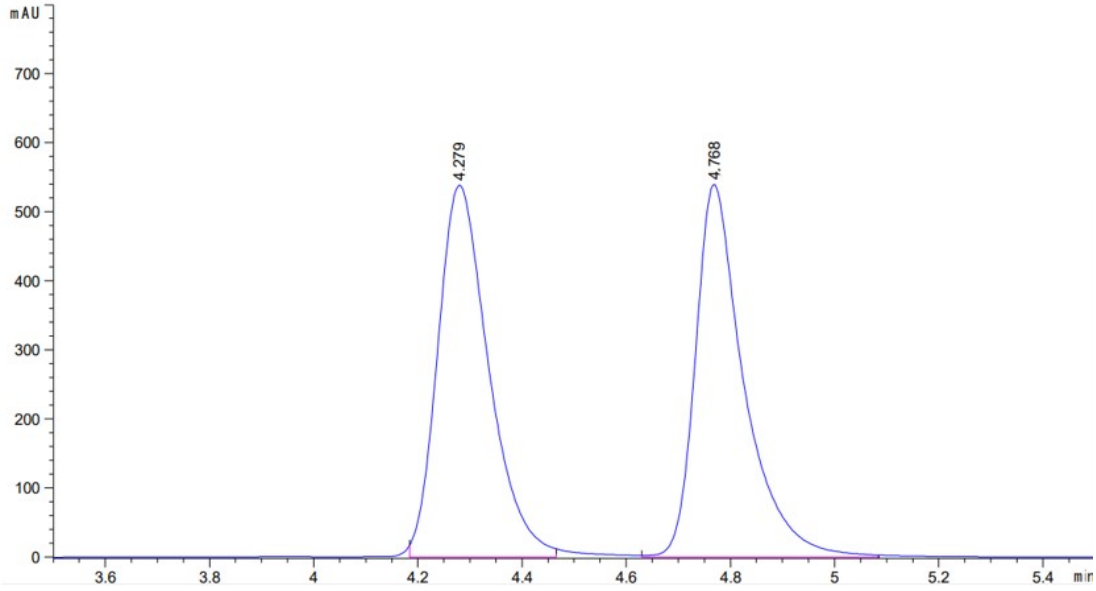


3p

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.354	MF	0.1115	3390.38428	506.95749	91.8004
2	4.955	MF	0.1288	302.82993	39.19435	8.1996

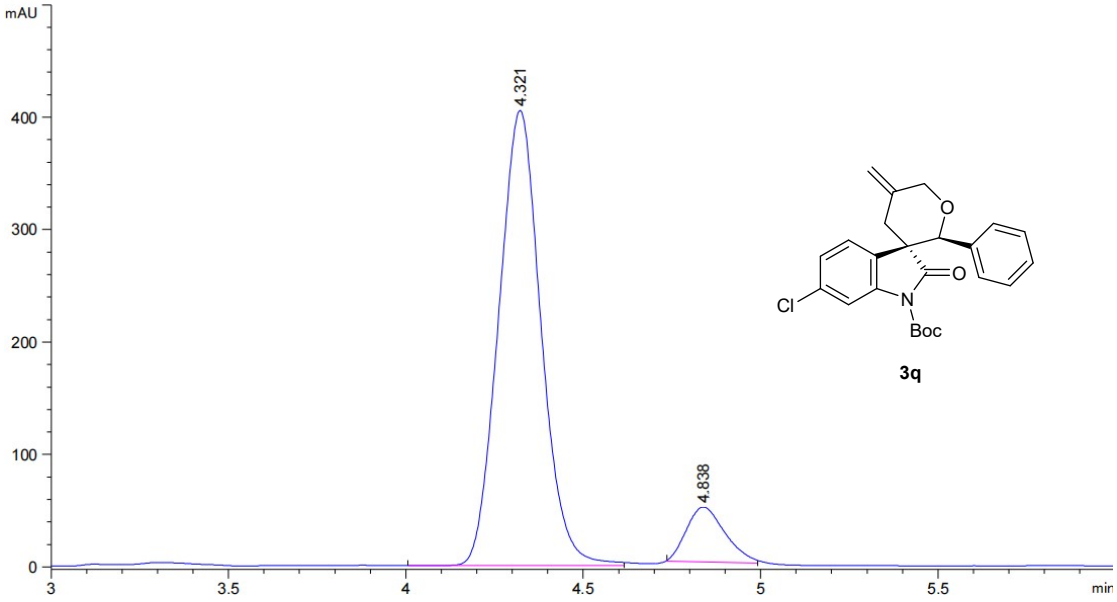
3q

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.279	FM	0.1127	3642.46069	538.86841	50.9848
2	4.768	MF	0.1080	3501.74316	540.24469	49.0152

chrial:

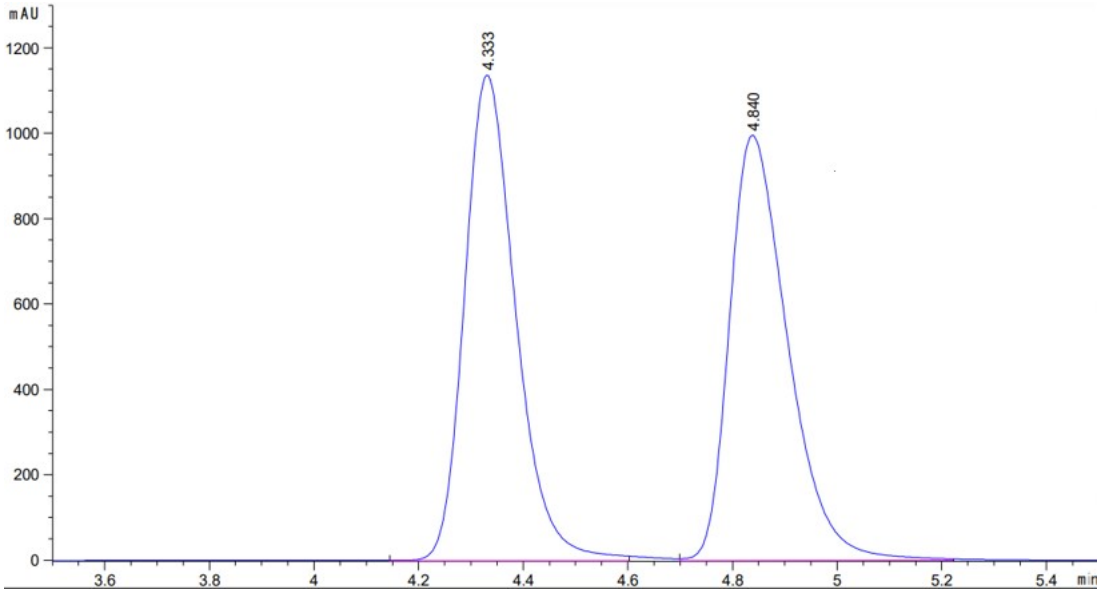


3q

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.321	MF	0.1380	3352.76489	404.91397	90.1157
2	4.838	FM	0.1257	367.74765	48.75218	9.8843

3r

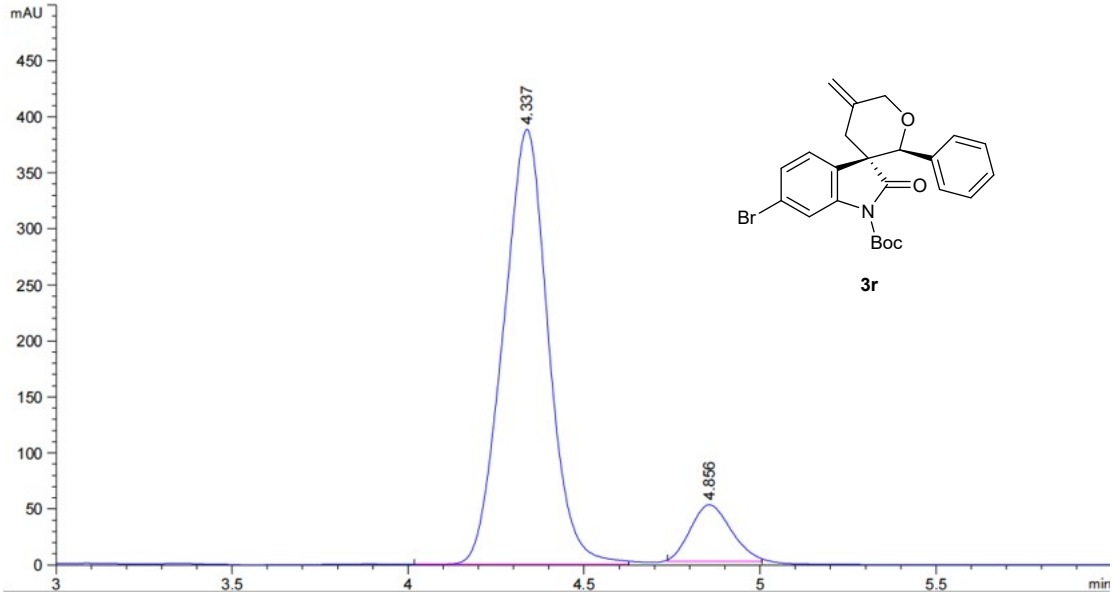
racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.333	MF	0.1133	7734.58838	1137.72021	50.0703
2	4.840	MF	0.1290	7712.86328	996.29578	49.9297

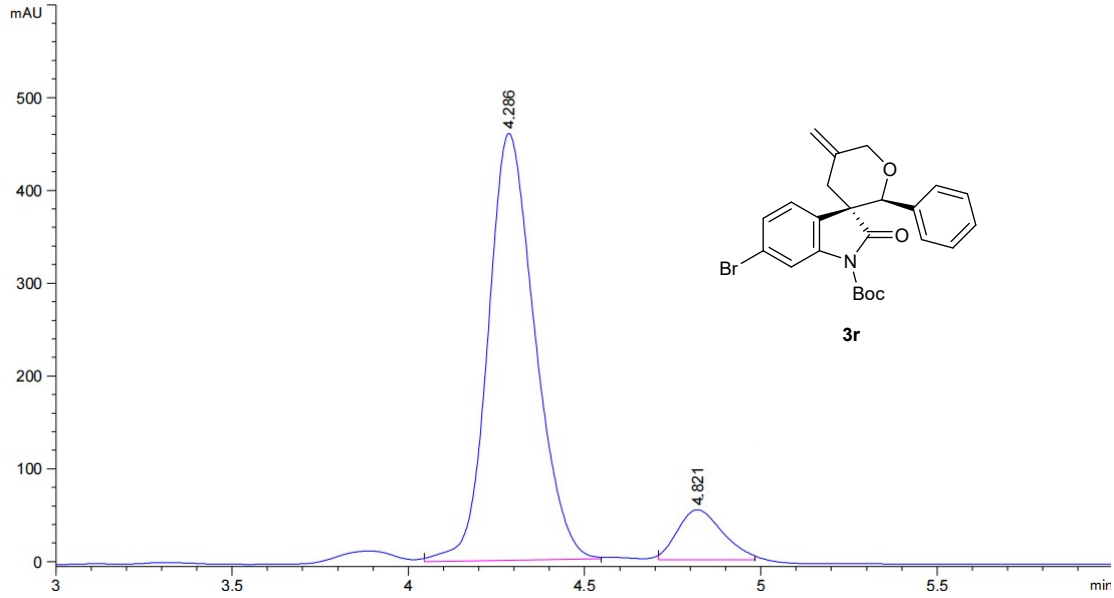
chrial:

Method A



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.337	MM	0.1453	3362.88330	385.71609	89.7244
2	4.856	MF	0.1298	385.13297	49.46754	10.2756

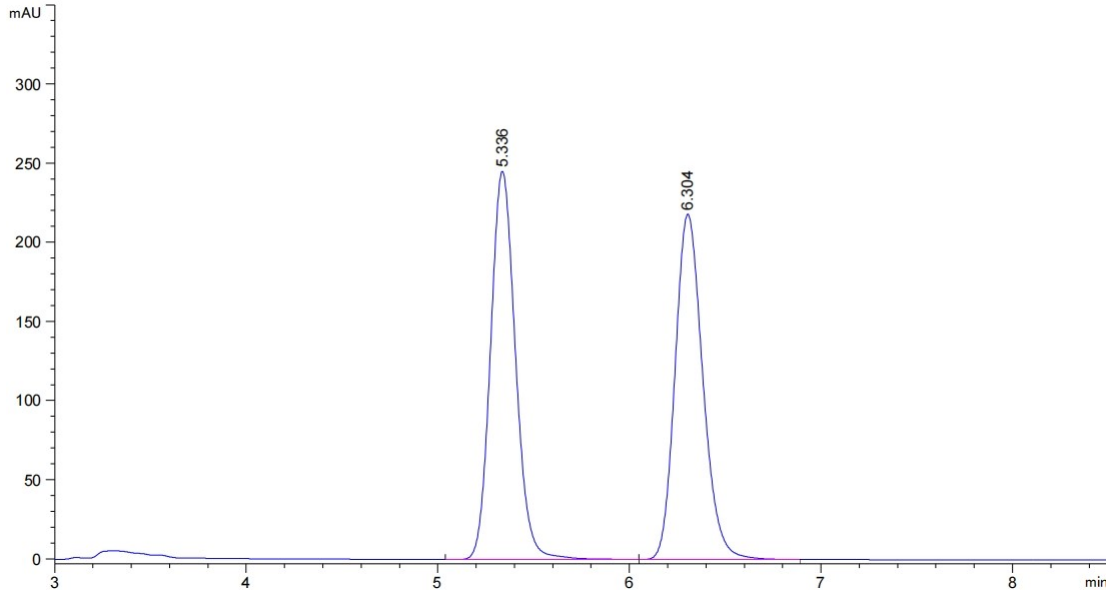
Method B



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.286	MM	0.1534	4235.17236	460.00714	89.8424
2	4.821	MM	0.1482	478.83002	53.84668	10.1576

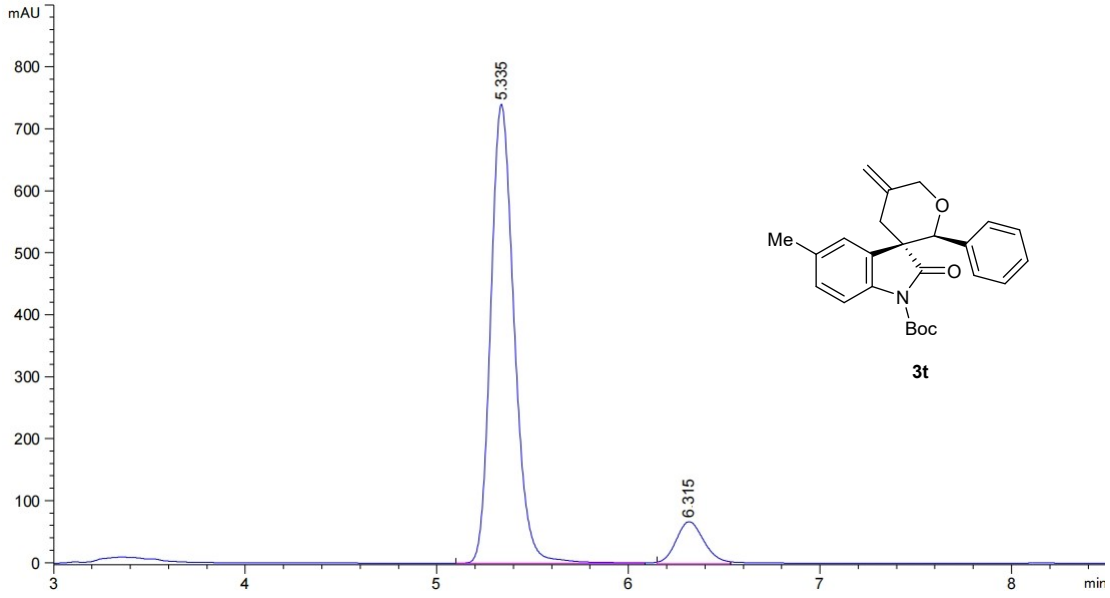
3t

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.336	BB	0.1402	2211.37769	245.35794	50.1717
2	6.304	BB	0.1555	2196.23975	218.14024	49.8283

chrial:

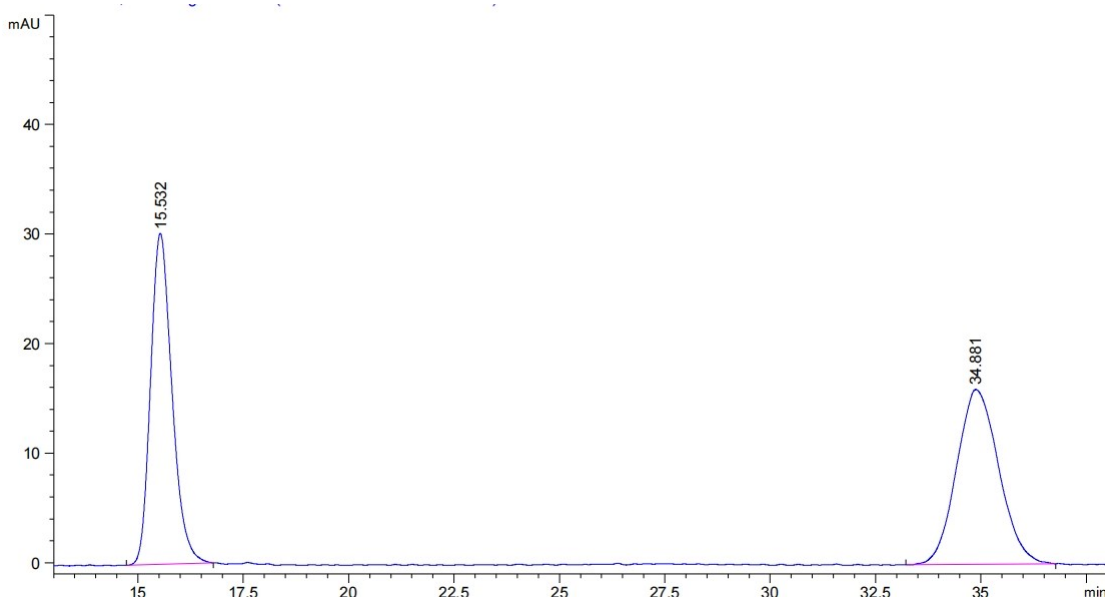


3t

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.335	BV	0.1310	6278.23535	740.13330	89.9620
2	6.315	MF	0.1711	700.52844	68.24059	10.0380

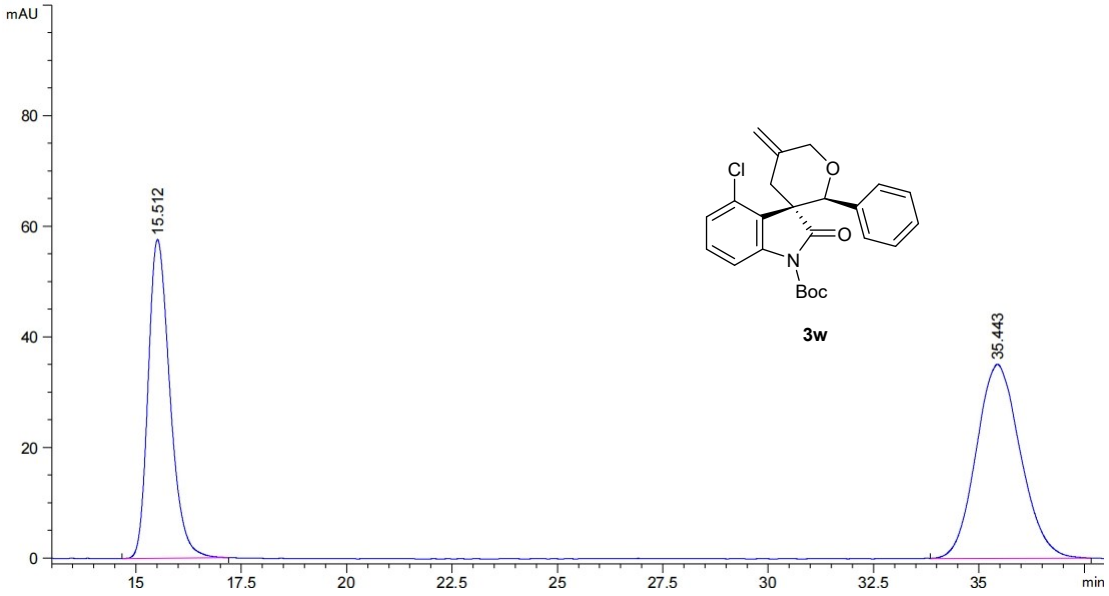
3w

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.532	BB	0.5410	1067.05676	30.21641	49.0000
2	34.881	BB	1.0302	1110.60901	15.95357	51.0000

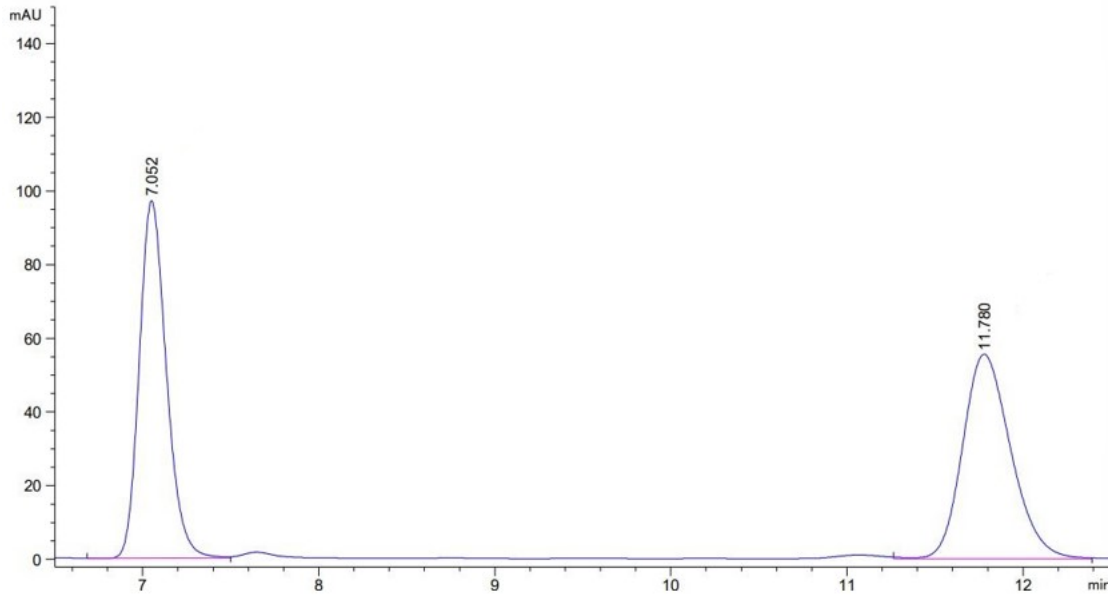
chrial:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.512	BB	0.5561	2070.10693	57.62291	44.7898
2	35.443	BB	1.0853	2551.72290	35.05412	55.2102

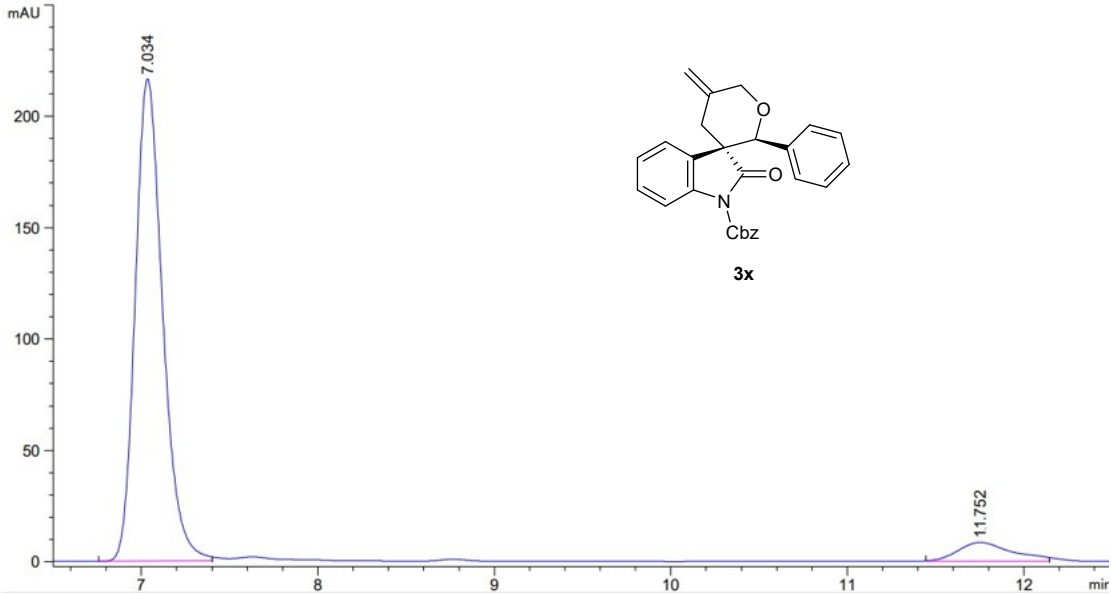
3x

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.052	MF	0.1781	1037.28943	97.06059	49.6258
2	11.780	FM	0.3164	1052.93311	55.46993	50.3742

chrial:

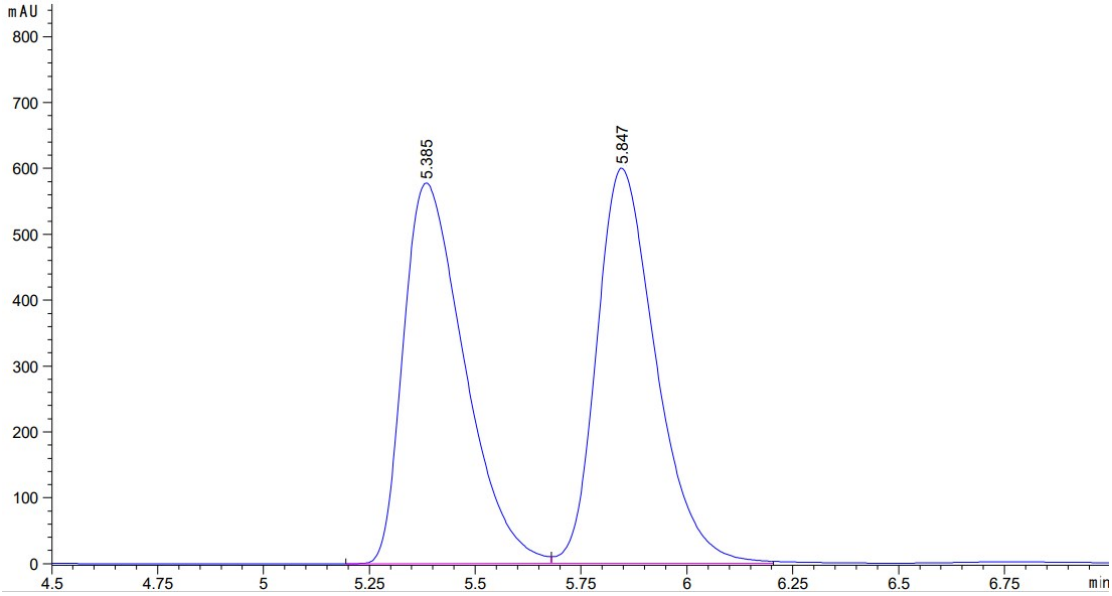


3x

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.034	MF	0.1794	2330.57617	216.48880	92.7029
2	11.752	MF	0.3593	183.45044	8.50857	7.2971

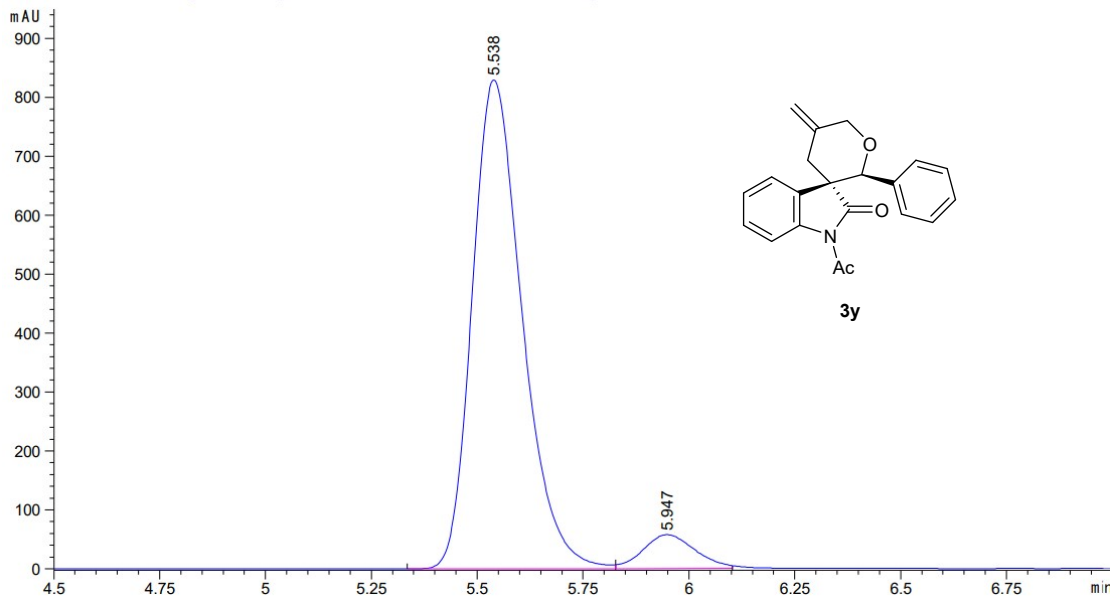
3y

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.385	BV	0.1544	5762.96240	577.64154	49.7649
2	5.847	MF	0.1615	5817.40771	600.16779	50.2351

chrial:

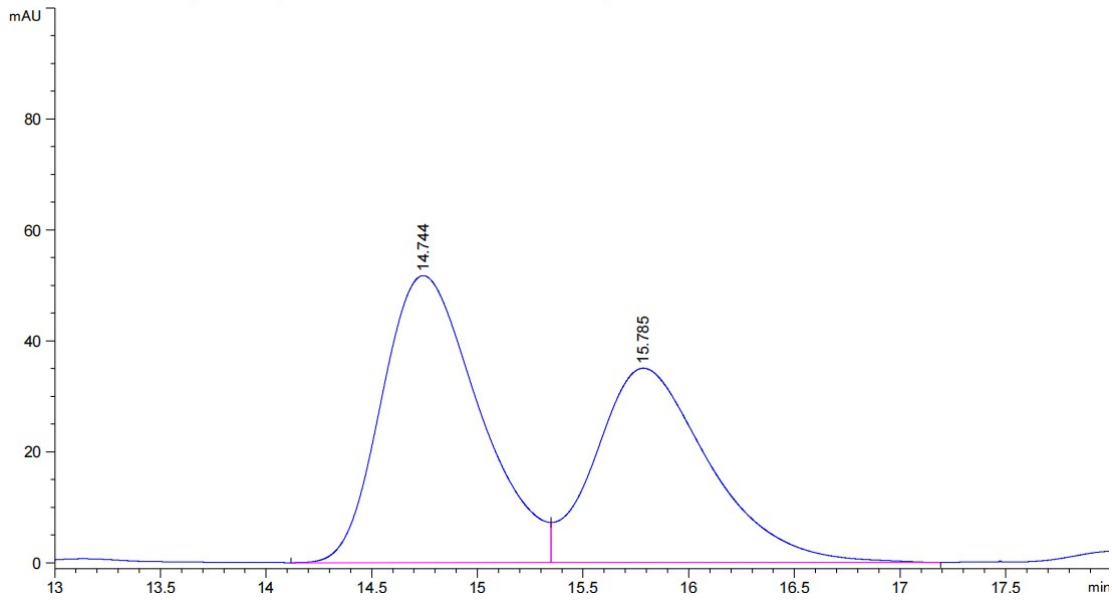


3y

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.538	FM	0.1364	6787.28564	829.41815	93.2710
2	5.947	MF	0.1420	489.66843	57.45892	6.7290

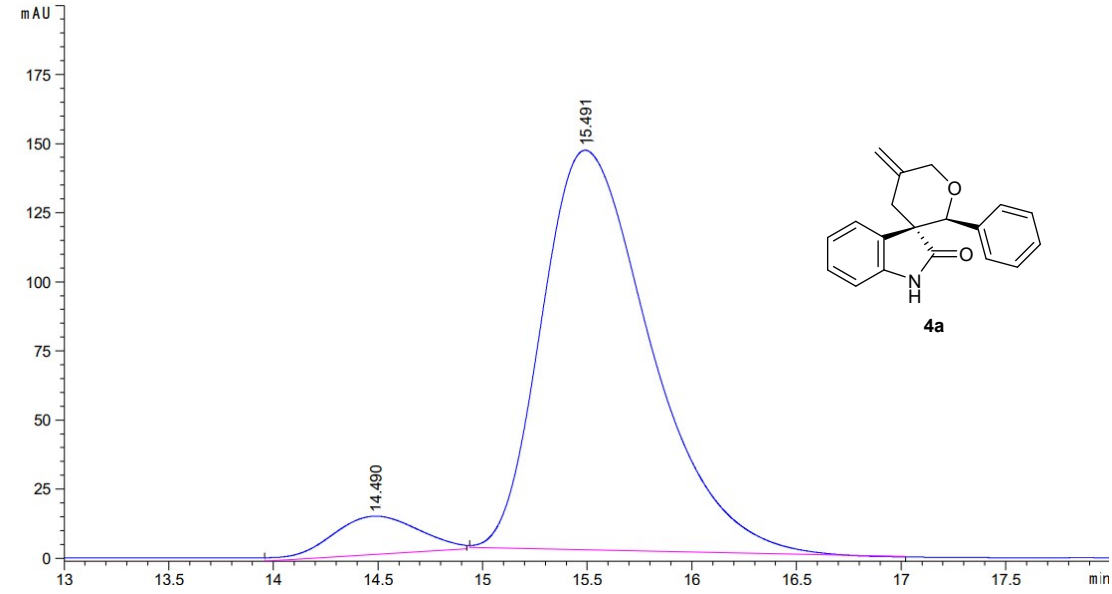
4a

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BV	0.4900	1655.19580	51.70258	55.8251
2	15.785	VB	0.5448	1309.77087	35.02126	44.1749

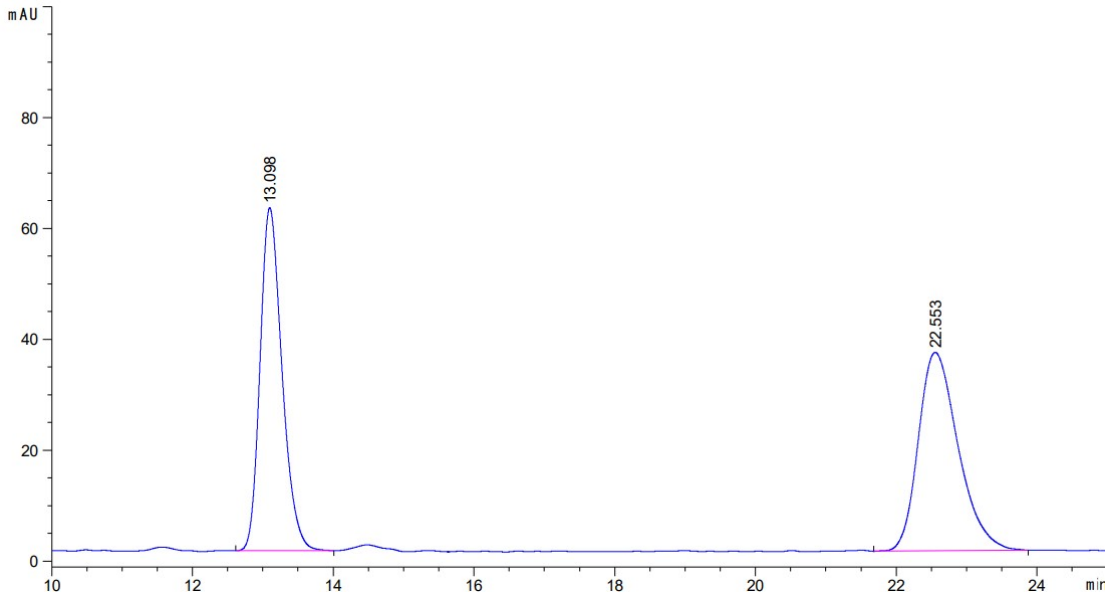
chrial:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.490	MM	0.4835	399.73343	13.77929	7.1178
2	15.491	MM	0.6015	5216.21094	144.52611	92.8822

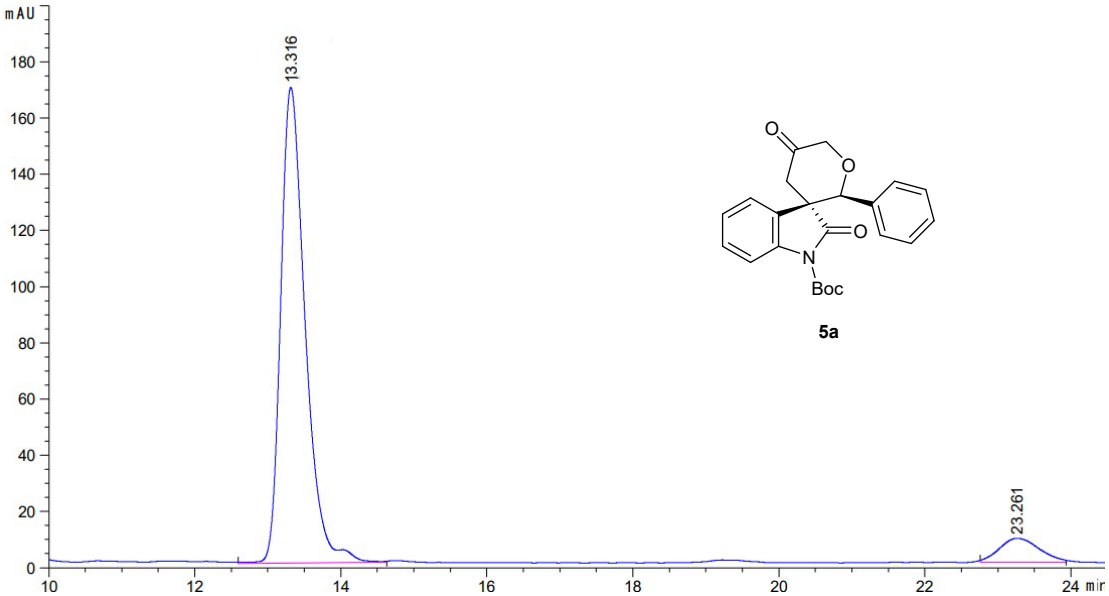
5a

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.098	BB	0.3288	1340.18835	61.83987	48.7690
2	22.553	BB	0.5880	1407.84644	35.78169	51.2310

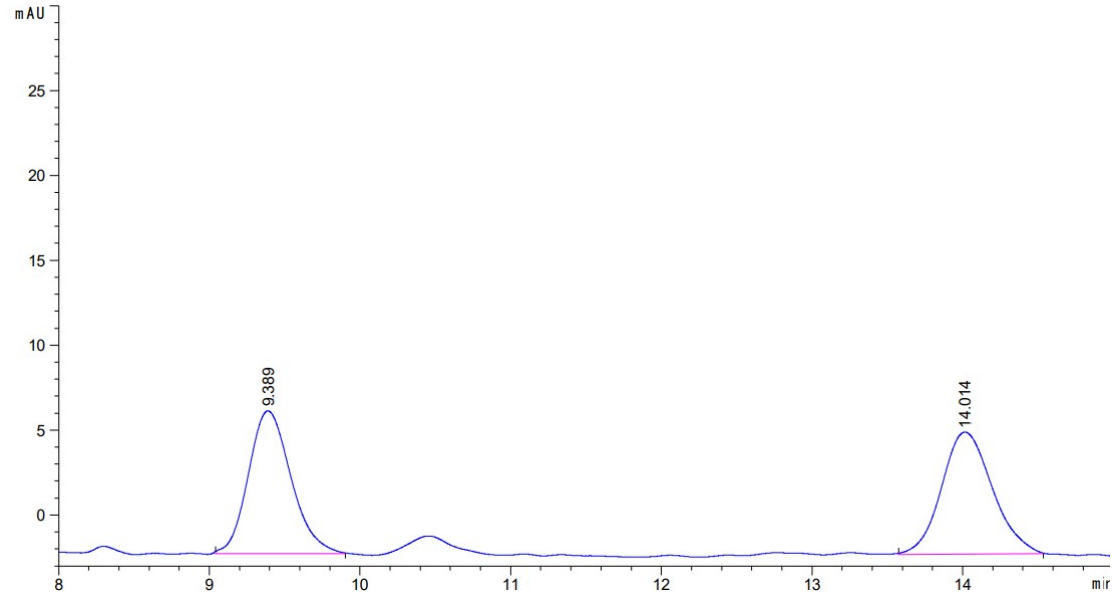
chrial:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.316	MM	0.3885	3946.72461	169.31685	92.3644
2	23.261	MM	0.6358	326.26807	8.55324	7.6356

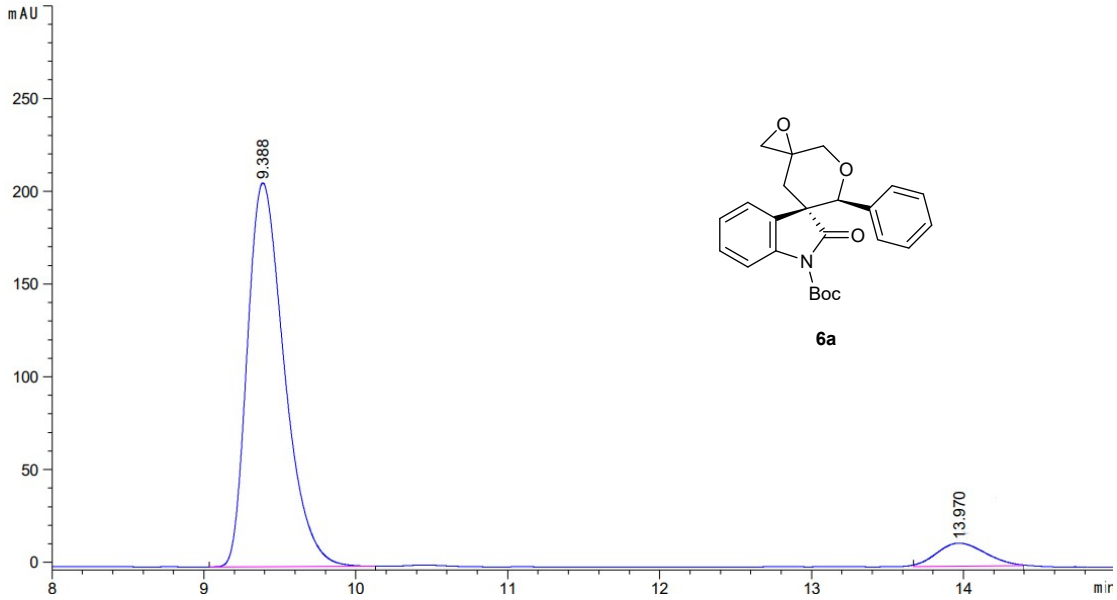
6a

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.389	MM	0.3281	165.63104	8.41306	49.5591
2	14.014	MM	0.3907	168.57825	7.19210	50.4409

chrial:

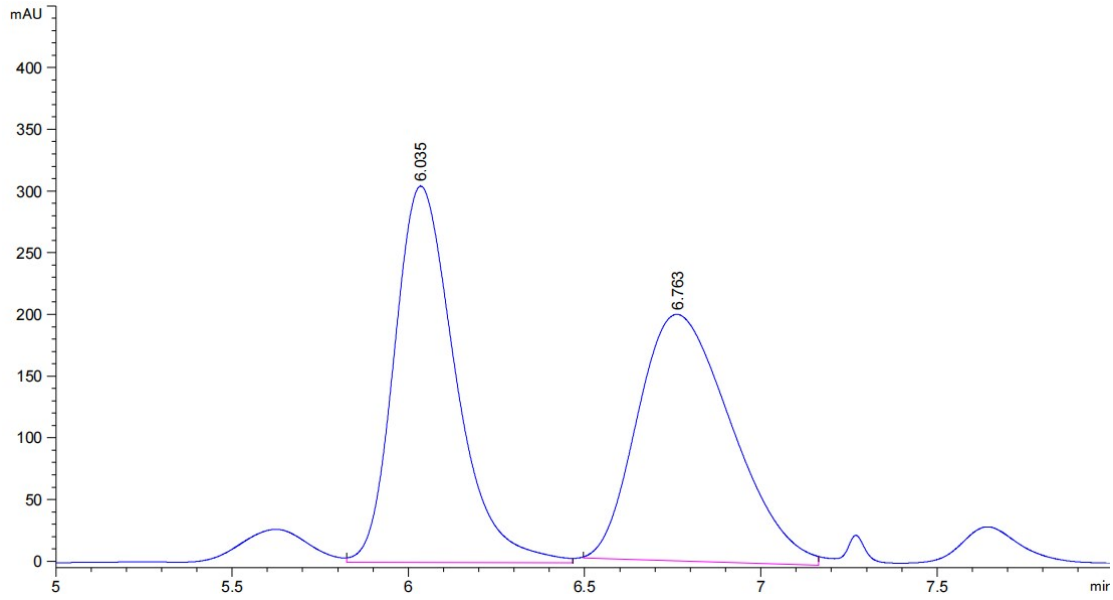


6a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.388	BB	0.2610	3492.31396	206.86449	92.8108
2	13.970	MM	0.3577	270.51639	12.60367	7.1892

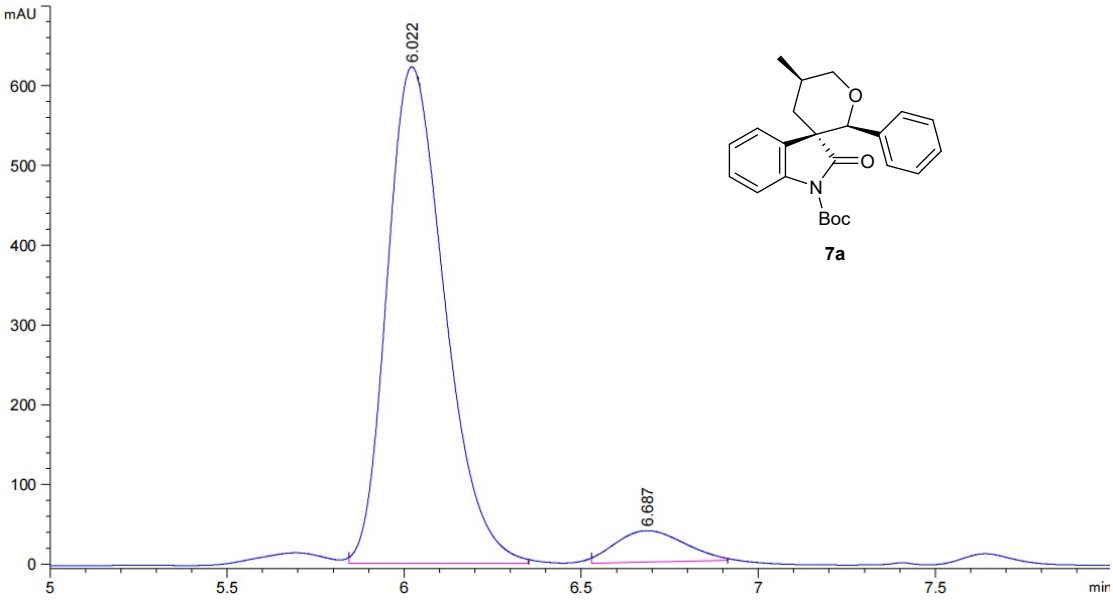
7a

racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.035	FM	0.2007	3672.75806	305.01614	49.8565
2	6.763	MM	0.3083	3693.89746	199.69498	50.1435

chrial:



7a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.022	MM	0.1882	7029.52002	622.37854	92.9785
2	6.687	MM	0.2247	530.84863	39.36784	7.0215