Remote Stereocontrolled Asymmetric 1,6-Addition/1,4-Addition Cascade Reactions between Cyclic Dienones and 2-Indolinethiones

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A: General Remarks and Starting Materials

General Remarks

^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer (400 MHz and 100 MHz). Chemical shifts (δ) for protons are reported in parts per million (ppm) downfield from tetramethylsilane or referenced to residual solvent peak. Chemical shifts (δ) for carbon are reported in parts per million (ppm) downfield from tetramethylsilane or referenced to the carbon resonances of the solvent. Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplets, q = quartet, quint = quintet, m = multiplet), coupling constants (*J*) in Hertz (Hz), integration; "app" is used to denote the apparent splitting of a signal.

High resolution mass spectrometry (HRMS) was carried out using MicroMass GCT CA 055 instrument and recorded on a MicroMass LCTTM spectrometer.

Optical rotations were measured on an Autopol III automatic polarimeter (Rudolph Research analytical). $[\alpha]_D^T$ values are reported in 10^{-1} deg cm^2 g^{-1}; concentrations (c) are quoted in g/100 mL; D refers to the D-line of sodium (589 nm); temperatures (T) are given in degrees Celsius (°C).

Melting points were measured on a XT3A apparatus. Enantiomeric excesses were determined by HPLC analysis on an Agilent HPLC 1200 Series instrument, using the chiral stationary phase column (25 cm x 4.6 mm internal diameter, Daicel Chiralpak IA, IB, AD-H, AS-H as noted) specified in the individual experiment.

Starting Materials

All solvents and inorganic reagents were from commercial sources and used without purification unless otherwise noted. 2-Indolinethione was synthesized following literature procedure.[1-3] Different cyclic dienones were achieved according to literature procedure.[4,5]

References

[1] P. Thanigaimalai; K.-C. Lee; V. K. Sharma; N. Sharma; E. Roh; Y. Kim and S.-H. Jung, *Chem. Pharm. Bull.,* 2011, **59**, 1285-1288.

[2] T. Hino; T. Suzuki; S. Takeda; N. Kano; Y. Ishii; A. Sakai and M. Nakagawa, *Chem. Pharm. Bull.,* 1973, **21**, 2739-2748.

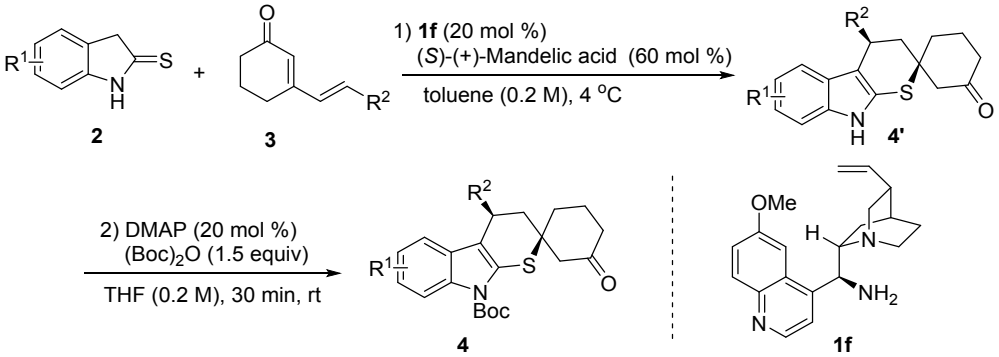
[3] T. Hino; T. Suzuki and M. Nakagawa, *Chem. Pharm. Bull.,* 1974, **22**, 1053-1060.

[4] E. Wenkert and M. K. Schorp, *J. Org. Chem.,* 1994, **59**, 1943-1944.

[5] H. Hénon; M. Mauduit and A. Alexakis, *Angew. Chem., Int. Ed.,* 2008, **47**, 9122-9124.

B: General procedure for Cascade Reactions

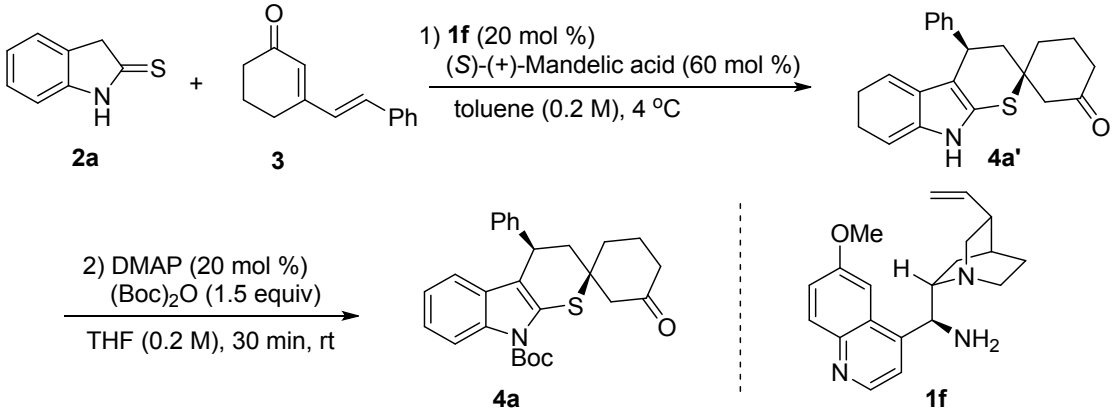
The Cascade Reactions of 2-Indolinethiones to Cyclic Dienones



Reactions were performed in toluene at 4 °C using 1.0 equiv of **2** (0.2 mmol, 0.2M), 1.5 equiv of **3**, 0.2 equiv of **1f**, and 0.6 equiv of (*S*)-(+)-mandelic acid. The reaction mixture was stirred for specified hours until fully consumption of **2** by TLC analysis. Solvent was removed under vacuum and the residue was purified by silica gel chromatography (EtOAc/PE = 1/10, 100 mL, then EtOAc/PE = 1/7, 100 mL) to deliver product **4'**.

4-Dimethylaminopyridine (DMAP, 0.2 equiv) and *di-tert*-butyl dicarbonate ($(Boc)_2O$, 1.5 equiv) were added to a solution of **4'** (1.0 equiv) in THF (0.2 M). The mixture was stirred at room temperature for 30 min. Solvent was removed under vacuum and the residue was purified by silica gel chromatography (EtOAc/PE = 1/20, 100 mL, then EtOAc/PE = 1/15, 100 mL) to afford adduct **4**.

The Experimental Procedure for The Scaled-up Reaction



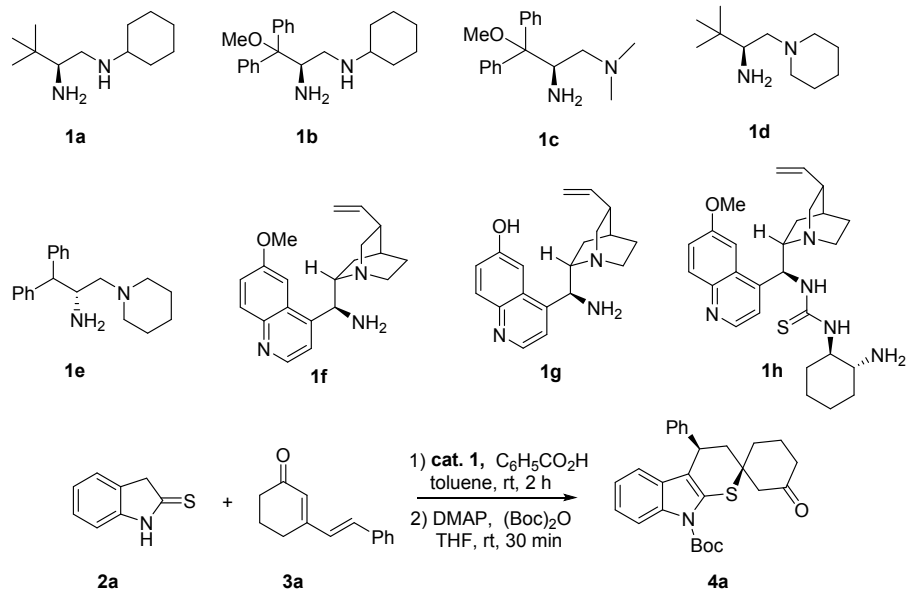
Catalyst 1f (646.4 mg, 2.0 mmol, 0.2 equiv), (S)-(+)-mandelic acid (912.9 mg, 6.0 mmol, 0.6 equiv) and 2-Indolinethione (1.49 g, 10 mmol, 1.0 equiv) were added in sequence to a solution of cyclic dienone (2.97 g, 15 mmol, 1.5 equiv) in toluene (5mL). The resulting mixture was stirred for specified hours until fully consumption of 2a by TLC analysis. Solvent was removed under vacuum and the residue was purified by silica gel chromatography (EtOAc/PE = 1/10, 100 mL, then EtOAc/PE = 1/7, 100 mL)

to deliver product 4a'.

4-Dimethylaminopyridine (DMAP, 0.2 equiv) and *di-tert*-butyl dicarbonate ($(Boc)_2O$, 1.5 equiv) were added to a solution of **4a'** (1.0 equiv) in THF (5 mL). The mixture was stirred at room temperature for 30 min. Solvent was removed under vacuum and the residue was purified by silica gel chromatography (EtOAc/PE = 1/20, 100 mL, then EtOAc/PE = 1/15, 100 mL) to afford adduct **4a** (3.13 g, 70% yield, 5/1 dr, 92% ee). The dr value is determined by 1H NMR analysis of the crude reaction mixture and the ee value is determined by HPLC analysis on chiral stationary phase.

C: Reaction Conditions Optimizing Detials

1. Optimization Studies of catalyst[a]

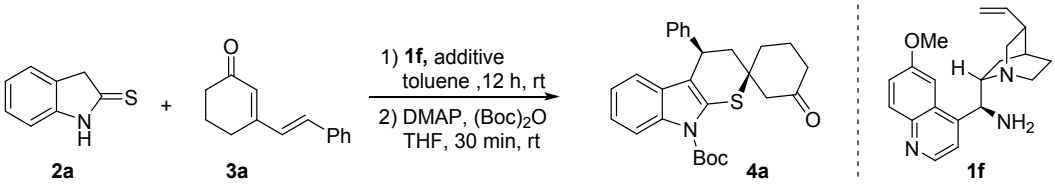


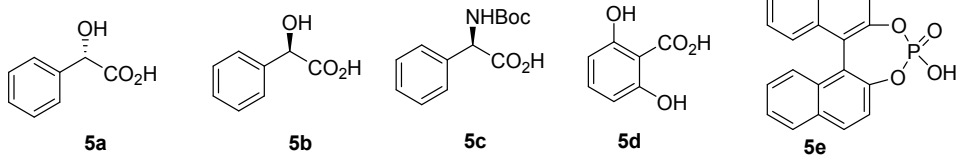
entry	cat. 1	conv (%)[b]	dr[c]	ee (%)[d]
1	**1a**	full	3/1	57
2	**1b**	full	2/1	67
3	**1c**	trace	-	-
4	**1d**	trace	-	-
5	**1e**	full	2/1	-31
6	**1f**	full	2/1	86
7	**1g**	full	3/2	83
8[f]	**1h**	47	1/1	53

[a]Reactions were performed over 2 h with **2a** (0.1 mmol, 0.2 M), **3a** (0.15 mmol), and cat. 1 (0.02 mmol), $C_6H_5CO_2H$ (0.02 mmol) in toluene at room temperature. The products, purified on silica gel in the first step, were treated with 0.2 equiv DMAP and 1.5 equiv $(Boc)_2O$ in THF

(0.2 M) at room temperature. [b]Determined by GC analysis. [c]Determined by ^{1}H NMR of the crude reaction mixture. [d]Determined by HPLC analysis on a chiral stationary phase.

2. Screening of Acids[a]



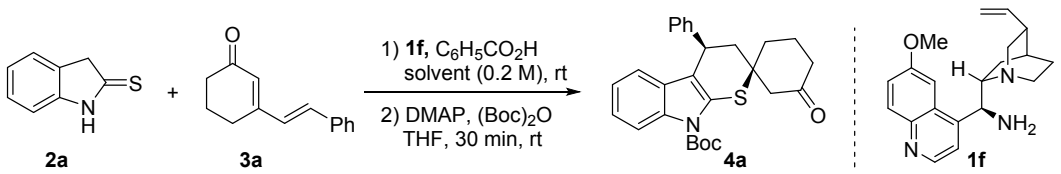


entry	additive	conv (%)[b]	dr[c]	ee (%)[d]
1	2-$NO_2C_6H_4CO_2H$	full	2/1	85
2	2-$OMeC_6H_4CO_2H$	full	2/1	87
3	2-$FC_6H_4CO_2H$	full	2/1	81
4	[e]*L*-TA	-	-	-
5	4-$OMeC_6H_4CO_2H$	full	2/1	83
6	AcOH	full	2/1	85
7	**5a**	full	4/1	92
8[f]	**5a** (10%)	57	3/1	87
9[f]	**5a** (40%)	68	4/1	93
10[f]	**5a** (60%)	72	5/1	>99
11[f]	**5a** (100%)	63	3/1	96
12	**5b**	full	3/1	89
13	**5c**	full	2/1	77
14	**5d**	full	3/1	85
15	**5e**	full	2/1	73
16	TsOH	full	2/1	63
17	TfOH	full	3/1	70
18	TCA	full	3/1	84
19	TFA	full	3/1	79
20	$C_6H_5CH_2CO_2H$	full	2/1	76

21	*o*-$OHC_6H_4CH_2CO_2H$	52	2/1	57

[a]Reactions were performed over 12 h with **2a** (0.1 mmol, 0.2 M), **3a** (0.15 mmol), and **1f** (0.02 mmol) , additive (0.02 mmol) in toluene at room temperature. The products, purified on silica gel in the first step, were treated with 0.2 equiv DMAP and 1.5 equiv $(Boc)_2O$ in THF (0.2 M) at room temperature. [b]Determined by GC analysis. [c]Determined by ^1H NMR of the crude reaction mixture. [d]Determined by HPLC analysis on a chiral stationary phase. [e]*L*-TA was *L*(-)-tartaric acid. [f]The reaction temperature was 4 °C.

3. Optimization Studies of Solvents[a]



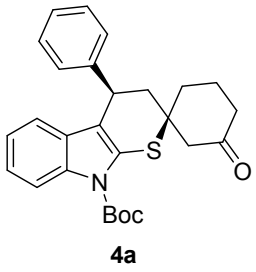
2a 3a 4a 1f

entry	solvent	conv (%)[b]	dr[c]	ee (%)[d]
1	EtOH	full	2/1	80
2	THF	full	2/1	73
3	toluene	full	2/1	85
4	MeCN	trace	-	-
5	DCM	trace	-	-

[a]Reactions were performed over 2 h with **2a** (0.1 mmol, 0.2 M), **3a** (0.15 mmol), **1f** (0.02 mmol), and $C_6H_5CO_2H$ (0.02 mmol) at room temperature. The products, purified on silica gel in the first step, were treated with 0.2 equiv DMAP and 1.5 equiv $(Boc)_2O$ in THF (0.2 M) at room temperature. [b]Determined by GC analysis. [c]Determined by ^1H NMR of the crude reaction mixture. [d]Determined by HPLC analysis on a chiral stationary phase.

D: Characterization Data of Products

4a: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

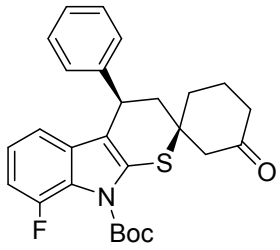


4a

The product was obtained in 72% yield, 64.4 mg, yellowish white solid. Mp 142-143 °C; $[\alpha]_D^{25}$ −158.9 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 1.99-2.07 (m, 2H), 2.11-2.20 (m, 3H), 2.27-3.32 (m, 1H), 2.33-2.39 (m, 1H), 2.47-2.53 (m, 1H), 2.57-2.61 (m, 1H), 2.77-2.81 (m, 1H), 4.13-4.17 (m, 1H), 6.55-6.57 (m, 1H), 6.88-6.92 (m, 1H), 7.08-7.13(m, 1H), 7.20-7.25 (m, 3H), 7.28-7.30 (m, 2H), 7.96-7.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.1, 37.7, 40.7, 47.7, 49.7, 50.0, 85.0, 114.5, 114.7, 119.0, 122.5, 122.9, 126.8, 128.1, 128.8, 129.5, 136.0, 143.7, 150.3, 208.1; HRMS (EI): exact mass calculated for $C_{27}H_{29}NO_3S$ $[M]^+$ require m/z =

447.1911, found m/z = 447.1912; The enantiomeric ratio was determined by Daicel Chiralpak IA, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 8.71 min (major), 12.62 min (minor), *ee* > 99%.

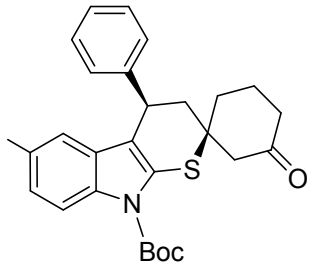
4b: *tert*-Butyl (1*R*,4'*R*)-8'-fluoro-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4b

The product was obtained in 68% yield, 62.0 mg, yellowish white solid. Mp 155-156 °C; $[\alpha]_D^{25}$ −133.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.66 (s, 9H), 2.02-2.07 (m, 2H), 2.13-2.19 (m, 3H), 2.27-2.32 (m, 1H), 2.35-2.41 (m, 1H), 2.47-2.53 (m, 1H), 2.57-2.61 (m, 1H), 2.76-2.80 (m, 1H), 4.11-4.15 (m, 1H), 6.32-6.36 (m, 1H), 6.80-6.85 (m, 2H), 7.17-7.20 (m, 2H), 7.23-7.26 (m, 2H), 7.28-7.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.1, 37.6, 40.7, 47.6, 49.7, 50.1, 85.3, 104.6, 104.8, 110.1, 114.2, 115.5, 127.1, 128.0, 128.9, 130.4, 131.4, 132.2, 143.0, 150.0, 208.0; HRMS (EI): exact mass calculated for $C_{27}H_{28}FNO_3S$ $[M]^+$ require m/z = 465.1803, found m/z = 465.1804; The enantiomeric ratio was determined by Daicel Chiralpak IA, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 10.36 min (major), 15.06 min (minor), *ee* = 93%.

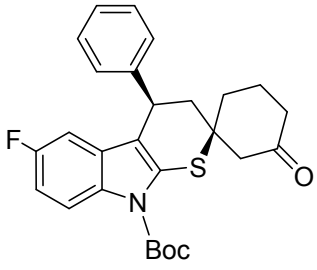
4c: *tert*-Butyl (1*R*,4'*R*)-6'-methyl-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4c

The product was obtained in 62% yield, 57.2 mg, yellowish white solid. Mp 109-110 °C; $[\alpha]_D^{25}$ −177.2 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.70 (s, 9H), 1.97-2.07 (m, 2H), 2.09-2.13 (m, 1H), 2.15 (s, 3H), 2.16-2.21 (m, 2H), 2.25-2.30 (m, 1H), 2.32-2.39 (m, 1H), 2.46-2.51 (m, 1H), 2.56-2.59 (m, 1H), 2.76-2.79 (m, 1H), 4.10-4.14 (m, 1H), 6.34-6.36 (m, 1H), 6.91-6.93 (m, 1H), 7.20-7.23 (m, 2H), 7.24-7.30 (m, 3H), 7.81-7.87 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 21.3, 28.3, 37.0, 37.7, 40.7, 47.8, 49.7, 50.0, 84.8, 114.3, 119.0, 124.1, 126.8, 127.3, 128.1, 128.7, 129.4, 129.7, 131.9, 134.1 143.7, 150.4, 208.2; HRMS (EI): exact mass calculated for $C_{28}H_{31}NO_3S$ $[M]^+$ require m/z = 461.2131, found m/z = 461.2132; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 9.15 min (major), 12.78 min (minor), *ee* > 99%.

4d: *tert*-Butyl (1*R*,4'*R*)-6'-methoxy-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

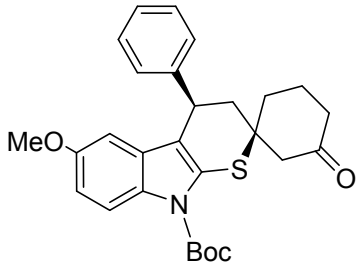


4d

The product was obtained in 65% yield, 60.5 mg, yellowish white solid. Mp 121-122 °C; $[\alpha]_D^{25}$ −154.1 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.70 (s, 9H), 2.01-2.09 (m, 2H), 2.12-2.19 (m, 3H), 2.26-2.31 (m, 1H), 2.35-2.40 (m, 1H), 2.48-2.53 (m, 1H), 2.60-2.65 (m, 1H), 2.76-

2.80 (m, 1H), 4.07-4.12 (m, 1H), 6.19-6.21 (m, 1H), 6.78-6.84 (m, 1H), 7.19-7.20 (m, 2H), 7.26-7.29 (m, 3H), 7.88-7.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.1, 37.7, 40.7, 47.7, 49.7, 50.0, 85.0, 114.5, 114.7, 119.0, 122.5, 122.9, 126.8, 128.1, 128.8, 129.5, 136.0, 143.7, 150.3, 208.1; HRMS (EI): exact mass calculated for $C_{27}H_{28}FNO_4S$ $[M]^+$ require m/z = 465.1856, found m/z = 465.1857; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 50/1, flow 0.8 mL/min, detection at 254 nm, 16.82 min (major), 27.19 min (minor), *ee* = 91%.

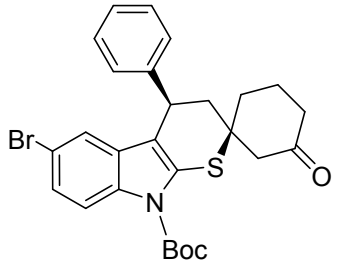
4e: *tert*-Butyl (1*R*,4'*R*)-6'-methoxy-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4e

The product was obtained in 63% yield, 60.1 mg, yellowish white solid. Mp 129-130 °C; $[\alpha]_D^{25}$ −225.8 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.70 (s, 9H), 1.99-2.09 (m, 2H), 2.12-2.20 (m, 3H), 2.27-2.32 (m, 1H), 2.34-2.39 (m, 1H), 2.48-2.54 (m, 1H), 2.59-2.62 (m, 1H), 2.79-2.82 (m, 1H), 3.48 (s, 3H), 4.09-4.13 (m, 1H), 5.99-6.00 (m, 1H), 6.68-6.71 (m, 1H), 7.22-7.24 (m, 3H), 7.27-7.30 (m, 2H), 7.81-7.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.1, 37.7, 40.7, 47.3, 49.8, 49.9, 55.2, 84.8, 102.2, 110.9, 114.2, 115.3, 126.9, 128.2, 128.8, 130.0, 130.4, 130.5, 143.5, 150.3, 155.3, 208.1; HRMS (EI): exact mass calculated for $C_{28}H_{31}NO_4S$ $[M]^+$ require m/z = 477.2021, found m/z = 477.2022; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 29.60 min (major), 33.10 min (minor), *ee* = 94%.

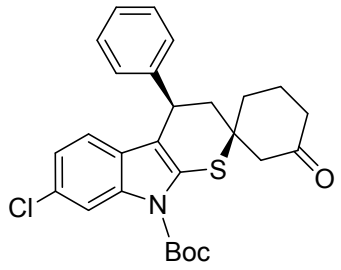
4f: *tert*-Butyl (1*R*,4'*R*)-6'-bromo-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4f

The product was obtained in 57% yield, 53.0 mg, yellowish white solid. Mp 114−115°C; $[\alpha]_D^{25}$ −60.9 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.70 (s, 9H), 2.01-2.09 (m, 2H), 2.11-2.17 (m, 3H), 2.26-2.31 (m, 1H), 2.33-2.40 (m, 1H), 2.48-2.54 (m, 1H), 2.55-2.59 (m, 1H), 2.74-2.78 (m, 1H), 4.07-4.12 (m, 1H), 6.65-6.67 (m, 1H), 7.18-7.21 (m, 3H), 7.26-7.30 (m, 3H), 7.82-7.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.1, 37.5, 40.6, 47.6, 49.7, 50.2, 85.5, 113.8, 115.9, 116.1, 121.5, 125.6, 127.1, 128.0, 128.9, 131.1, 131.2, 134.7, 142.9, 149.9, 207.8; HRMS (EI): exact mass calculated for $C_{27}H_{28}BrNO_3S$ $[M]^+$ require m/z = 525.1002, found m/z = 525.1001; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 10.33 min (major), 12.82 min (minor), *ee* = 80%.

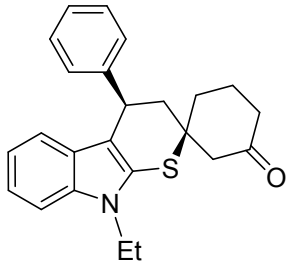
4g: *tert*-Butyl (1*R*,4'*R*)-7'-chloro-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4g

The product was obtained in 60% yield, 57.7 mg, yellowish white solid. Mp 142-143 °C; $[\alpha]_D^{25}$ −112.9 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 2.01-2.09 (m, 2H), 2.12-2.18 (m, 3H), 2.26-2.31 (m, 1H), 2.34-2.40 (m, 1H), 2.48-2.53 (m, 1H), 2.60-2.64 (m, 1H), 2.76-2.80 (m, 1H), 4.09-4.14 (m, 1H), 6.42-6.45 (m, 1H), 6.86-6.89 (m, 1H), 7.17-7.22 (m, 2H), 7.24-7.30 (m, 3H), 8.00-8.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.0, 37.6, 40.7, 47.5, 49.7, 50.2, 85.7, 114.2, 115.1, 119.5, 123.0, 127.0, 128.0, 128.8, 130.2, 136.3, 143.3, 149.9, 208.0; HRMS (EI): exact mass calculated for $C_{27}H_{28}ClNO_3S$ $[M]^+$ require m/z = 481.1541, found m/z = 481.1540; The enantiomeric ratio was determined by Daicel Chiralpak IB, *n*-Hexane/*i*PrOH = 7/3, flow 0.8 mL/min, detection at 254 nm, 11.81 min (major), 16.97 min (minor), *ee* = 97%.

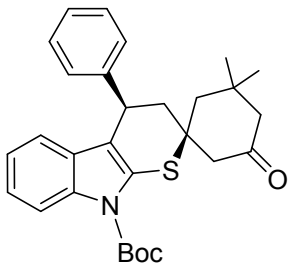
4h: (1*R*,4'*R*)-9'-ethyl-4'-phenyl-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano [2,3-*b*]indol]-3-one



4h

The product was obtained in 56% yield, 42.0 mg, yellow solid. Mp 77-78 °C; $[\alpha]_D^{25}$ −125.6 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.33 (t, J = 7.2 Hz, 3H), 2.02-2.06 (m, 1H), 2.09-2.15 (m, 2H), 2.17-2.23 (m, 2H), 2.28-2.32 (m, 1H), 2.33-2.40 (m, 1H), 2.50-2.58 (m, 2H), 2.81-2.85 (m, 1H), 4.08 (q, J_1 = 14.4 Hz, J_2 = 7.2 Hz, 2H), 4.19-4.24 (m, 1H), 6.59-6.61 (m, 1H), 6.77-6.81 (m, 1H), 7.03-7.06 (m, 1H), 7.22-7.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 15.1, 21.5, 37.5, 38.2, 38.6, 40.8, 49.4, 49.6, 52.3, 108.0, 108.2, 118.8, 118.9, 120.4, 126.6, 128.2, 128.6, 136.8, 144.7, 207.8; HRMS (EI): exact mass calculated for $C_{24}H_{25}NOS$ $[M]^+$ require m/z = 375.1701, found m/z = 375.1703; The enantiomeric ratio was determined by Daicel Chiralpak IA, *n*-Hexane/DCM = 1/1, flow 1.0 mL/min, detection at 254 nm, 11.06 min (major), 10.12min (minor), *ee* = 53%.

4i: *tert*-Butyl (1*S*,4'*R*)-3, 3-dimethyl-5-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

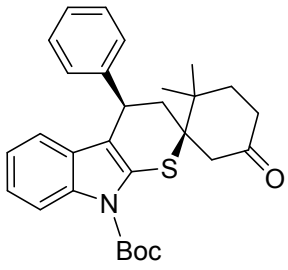


4i

The product was obtained in 72% yield, 68.4 mg, yellowish white solid. Mp 149-150 °C; $[\alpha]_D^{25}$ −199.2 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.12 (s, 3H), 1.30 (s, 3H), 1.69 (s, 9H), 1.98-2.01 (m, 1H), 2.13-2.17 (m, 1H), 2.23-2.25 (m, 2H), 2.30-2.39 (m, 2H), 2.51-2.55 (m, 1H), 2.75-2.78 (m, 1H), 4.11-4.15 (m, 1H), 6.54-6.56 (m, 1H), 6.88-6.92 (m, 1H), 7.09-7.13 (m, 1H), 7.20-7.23 (m, 3H), 7.25-7.28 (m, 2H), 8.02-8.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.1, 37.7, 40.7, 47.7, 49.7, 50.0, 85.0, 114.5, 114.7, 119.0, 122.5, 122.9, 126.8, 128.1, 128.8, 129.5, 136.0, 143.7, 150.3, 208.1; HRMS (EI): exact mass calculated for $C_{29}H_{33}NO_3S$ $[M]^+$ require m/z = 475.2201, found m/z = 475.2199; The enantiomeric ratio was determined by Daicel Chiralpak IB, *n*-Hexane/EtOH = 9/1, flow

0.8 mL/min, detection at 254 nm, 14.48 min (major), *ee* > 99%.

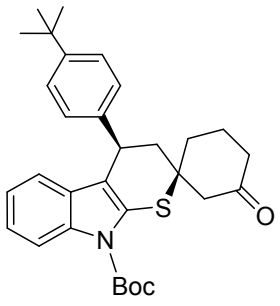
4j: *tert*-Butyl (1*R*,4'*R*)-2,2-dimethyl-5-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4j

The product was obtained in 78% yield, 74.1 mg, yellowish white solid. Mp 130-131 °C; $[\alpha]_D^{25}$ −138.3 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.26 (s, 3H), 1.39 (s, 3H), 1.72 (s, 9H), 1.82-1.89 (m, 1H), 2.08-2.17 (m, 2H), 2.22-2.27 (m, 1H), 2.37-2.45 (m, 1H), 2.51-2.57 (m, 1H), 2.72-2.76 (m, 1H), 2.84-2.88 (m, 1H), 4.09-4.13 (m, 1H), 6.53-6.55 (m, 1H), 6.88-6.92 (m, 1H), 7.07-7.11 (m, 1H), 7.21-7.22 (m, 2H), 7.25-7.29 (m, 3H), 7.95-7.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 22.4, 23.2, 27.3, 35.2, 36.0, 36.8, 40.1, 44.8, 55.5, 83.9, 112.9, 113.6, 118.0, 121.4, 121.7, 125.8, 127.2, 127.7, 128.4, 129.3, 135.0, 142.9, 149.3, 207.5; HRMS (EI): exact mass calculated for $C_{29}H_{33}NO_3S$ $[M]^+$ require m/z = 475.2243, found m/z = 475.2241; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 7.29 min (major), 8.81 min (minor), *ee* = 84%.

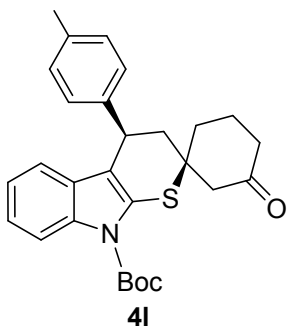
4k: *tert*-Butyl (1*R*,4'*R*)-4'-(4-(*tert*-butyl)phenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4k

The product was obtained in 65% yield, 65.4 mg, yellowish white solid. Mp 129-128 °C; $[\alpha]_D^{25}$ −201.5 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.29 (s, 9H), 1.71 (s, 9H), 2.01-2.04 (m, 2H), 2.11-2.18 (m, 3H), 2.25-2.30 (m, 1H), 2.33-2.37 (m, 1H), 2.48-2.51 (m, 1H), 2.56-2.60 (m, 1H), 2.76-2.80 (m, 1H), 4.10-4.14 (m, 1H), 6.58-6.60 (m, 1H), 6.90-6.93 (m, 1H), 7.08-7.14 (m, 3H), 7.25-7.29 (m, 2H), 7.95-7.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 29.7, 31.4, 34.5, 37.2, 40.7, 47.8, 49.7, 50.0, 85.0, 114.7, 114.8, 119.2, 122.4, 122.8, 125.6, 127.7, 129.3, 129.6, 136.0, 140.4, 149.6, 150.4, 208.2; HRMS (EI): exact mass calculated for $C_{31}H_{37}NO_4S$ $[M]^+$ require m/z = 503.2577, found m/z = 503.2579; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, 0.8 ml/min, 220 nm, flow 0.8 mL/min, detection at 254 nm, 9.44 min (major), 12.42 min (minor), *ee* = 92%.

4l: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-(*p*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

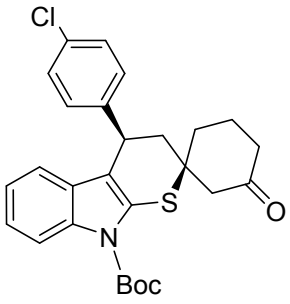


4l

The product was obtained in 60% yield, 55.3 mg, yellowish white solid. Mp 139-140 °C; $[\alpha]_D^{25}$ −249.4 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 2.01-2.09 (m, 2H), 2.12-2.18 (m, 3H), 2.24-2.29 (m, 1H), 2.32 (s, 3H), 2.35-2.39 (m, 1H), 2.47-2.52 (m, 1H), 2.56-2.60 (m, 1H), 2.76-2.80 (m, 1H), 4.09-4.14 (m, 1H), 6.59-6.61 (m, 1H),

6.90-6.93 (m, 1H), 7.09-7.12 (m, 5H), 7.95-7.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.1, 21.2, 28.3, 37.1, 37.2, 40.7, 47.8, 49.7, 50.0, 85.0, 114.7, 119.1, 122.5, 122.8, 127.9, 129.4, 129.5, 129.6, 135.9, 136.4, 140.6, 150.3, 208.2; HRMS (EI): exact mass calculated for $C_{28}H_{31}NO_3S$ $[M]^+$ require m/z = 461.2033, found m/z = 461.2031; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 8.95 min (major), *ee* > 99%.

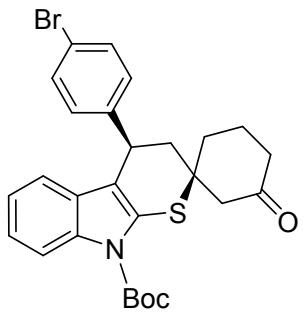
4m: *tert*-Butyl (1*R*,4'*R*)-4'-(4-chlorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4m

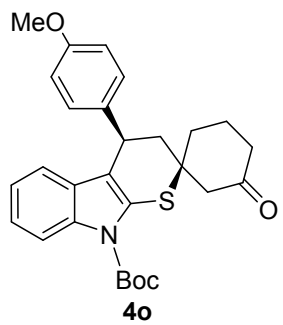
The product was obtained in 67% yield, 64.5 mg, yellowish white solid. Mp 125-126 °C; $[\alpha]_D^{25}$ −265.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 2.01-2.11 (m, 3H), 2.13-2.20 (m, 2H), 2.24-2.29 (m, 1H), 2.32-2.39 (m, 1H), 2.48-2.53 (m, 1H), 2.56-2.59 (m, 1H), 2.75-2.79 (m, 1H), 4.12-4.16 (m, 1H), 6.54-6.56 (m, 1H), 6.92-6.96 (m, 1H), 7.11-7.15 (m, 3H), 7.24-7.26 (m, 2H), 7.96-7.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.0, 37.1, 40.6, 47.5, 49.6, 50.0, 85.2, 113.9, 114.8, 118.9, 122.6, 123.0, 128.9, 129.2, 129.4, 129.7, 132.5, 135.9, 142.2, 150.3, 208.0; HRMS (EI): exact mass calculated for $C_{27}H_{28}ClNO_3S$ $[M]^+$ require m/z = 481.1544, found m/z = 481.1542; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 11.68 min (major), 15.41 min (minor), *ee* = 94%.

4n: *tert*-Butyl (1*R*,4'*R*)-4'-(4-bromophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4n

The product was obtained in 56% yield, 59.0 mg, yellowish white solid. Mp 120-121 °C; $[\alpha]_D^{25}$ −245.1 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 2.02-2.08 (m, 3H), 2.16-2.19 (m, 2H), 2.24-2.29 (m, 1H), 2.32-2.39 (m, 1H), 2.48-2.53 (m, 1H), 2.56-2.59 (m, 1H), 2.75-2.79 (m, 1H), 4.10-4.15 (m, 1H), 6.55-6.57 (m, 1H), 6.92-6.96 (m, 1H), 7.08-7.15 (m, 3H), 7.39-7.41 (m, 2H), 7.96-7.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.0, 37.2, 40.7, 47.4, 49.6, 49.9, 85.2, 113.8, 114.8, 118.9, 120.5, 122.6, 123.0, 129.2, 129.8, 131.9, 135.7, 135.9, 142.8, 150.3, 207.9; HRMS (EI): exact mass calculated for $C_{27}H_{28}BrNO_3S$ $[M]^+$ require m/z = 527.1073, found m/z = 527.1071; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 11.53 min (major), 15.26 min (minor), *ee* = 92%.

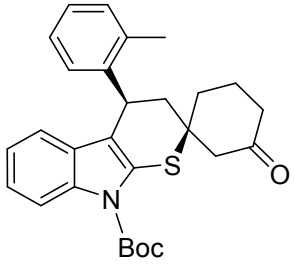


4o

4o: *tert*-Butyl (1*R*,4'*R*)-4'-(4-methoxyphenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

The product was obtained in 53% yield, 50.6 mg, yellowish white solid. Mp 145-146 ^{o}C; $[\alpha]_D^{25}$ −264.0 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 1.98-2.07 (m, 2H), 2.12-2.19 (m, 3H), 2.24-2.29 (m, 1H), 2.32-2.39 (m, 1H), 2.47-2.52 (m, 1H), 2.56-2.60 (m, 1H), 2.76-2.80 (m, 1H), 3.78 (s, 3H), 4.08-4.13 (m, 1H), 6.59-6.61 (m, 1H), 6.81-6.83 (m, 2H), 6.90-6.94 (m, 1H), 7.09-7.13 (m, 3H), 7.95-7.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 36.8, 37.1, 40.7, 47.8, 49.7, 50.0, 55.2, 85.0, 114.1, 114.7, 114.8, 119.1, 122.5, 122.8, 129.0, 129.3, 129.5, 135.6, 135.9, 150.3, 158.4, 208.2; HRMS (EI): exact mass calculated for $C_{28}H_{31}NO_4S$ $[M]^+$ require m/z = 477.2031, found m/z = 477.2029; The enantiomeric ratio was determined by Daicel Chiralpak IB, *n*-Hexane/EtOH = 9/1, flow 0.8 mL/min, detection at 254 nm, 10.07 min (major), 17.78 min (minor), *ee* = 90%.

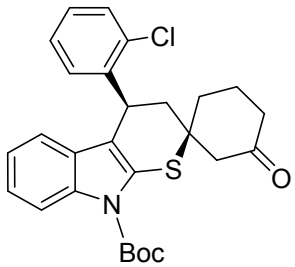
4p: *tert*-Butyl (1*R*, 4'*R*)-3-oxo-4'-(*o*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4p

The product was obtained in 52% yield, 48.0 mg, yellowish white solid. Mp 102-103 ^{o}C; $[\alpha]_D^{25}$ −230.6 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 2.03-2.10 (m, 3H), 2.15-2.20 (m, 2H), 2.25-2.30 (m, 1H), 2.32-2.39 (m, 1H), 2.48-2.49 (m, 1H), 2.53 (s, 3H), 2.60-2.64 (m, 1H), 2.79-2.83 (m, 1H), 4.43-4.44 (m, 1H), 6.43-6.45 (m, 1H), 6.88-6.92 (m, 2H), 6.99 (m, 1H), 7.08-7.12 (m, 2H), 7.22-7.23 (m, 1H), 7.96-7.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 19.3, 21.3, 28.3, 31.6, 32.7, 37.0, 40.7, 45.2, 50.0, 85.0, 114.7, 115.0, 118.8, 122.6, 122.9, 126.6, 126.8, 128.0, 129.4, 130.4, 135.0, 135.9, 141.4, 150.3, 208.2; HRMS (EI): exact mass calculated for $C_{28}H_{31}NO_3S$ $[M]^+$ require m/z = 461.2014, found m/z = 461.2013; The enantiomeric ratio was determined by Daicel Chiralpak IB, *n*-Hexane/*i*PrOH = 19/1, flow 1.0 mL/min, detection at 220 nm, 9.26 min (major), 11.51 min (minor), *ee* = 93%.

4q: *tert*-Butyl (1*R*,4'*S*)-4'-(2-chlorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

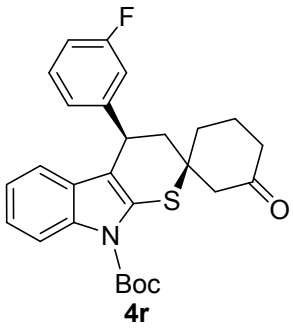


4q

The product was obtained in 55% yield, 52.9 mg, yellowish white solid. Mp 113-114 ^{o}C; $[\alpha]_D^{25}$ −186.1 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 1.99-2.12 (m, 3H), 2.15-2.18 (m, 2H), 2.27-2.32 (m, 1H), 2.34-2.40 (m, 1H), 2.49-2.53 (m, 1H), 2.56-2.59 (m, 1H), 2.76-2.79 (m, 1H), 4.14-4.18 (m, 1H), 6.57-6.59 (m, 1H), 6.89-6.96 (m, 3H), 7.01-7.03 (m, 1H), 7.11-7.14 (m, 1H), 7.22-7.26 (m, 1H), 7.96-7.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.0, 37.5, 40.7, 47.4, 49.6, 50.0, 85.2, 113.8, 114.9, 115.1, 118.8, 122.6, 123.0, 123.8, 129.2, 129.7, 130.3, 135.9, 146.4, 150.3, 161.9, 164.3, 208.0; HRMS (EI): exact mass calculated for $C_{27}H_{28}ClNO_3S$ $[M]^+$ require m/z = 481.1524, found m/z = 481.1523; The enantiomeric ratio was determined by Daicel Chiralpak IB, *n*-Hexane/*i*PrOH = 7/3, flow 0.8 mL/min, detection at 254 nm, 10.53 min (major), 8.93

min (minor), *ee* = 90%.

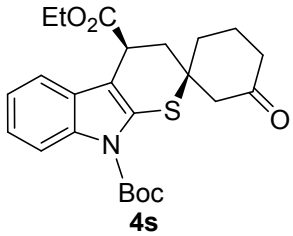
4r: *tert*-Butyl (1*R*,4'*R*)-4'-(3-fluorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4r

The product was obtained in 58% yield, 54.0 mg, yellowish white solid. Mp 99-100 °C; $[\alpha]_D^{25}$ −151.2 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.71 (s, 9H), 2.01-2.12 (m, 3H), 2.15-2.20 (m, 2H), 2.27-2.32 (m, 1H), 2.33-2.39 (m, 1H), 2.47-2.53 (m, 1H), 2.55-2.59 (m, 1H), 2.75-2.79 (m, 1H), 4.14-4.18 (m, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 6.90-6.95 (m, 3H), 7.01-7.03 (m, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 7.22-7.24 (m, 1H), 7.98 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 37.0, 37.5, 40.6, 47.4, 49.6, 50.0, 85.1, 113.8, 114.8, 115.1, 118.8, 122.6, 123.0, 123.8, 129.3, 129.7, 130.3, 135.9, 146.4, 150.3, 161.9, 164.3, 207.9; HRMS (EI): exact mass calculated for $C_{27}H_{28}FNO_3S$ $[M]^+$ require m/z = 465.1825, found m/z = 465.1823; The enantiomeric ratio was determined by Daicel Chiralpak IB, *n*-Hexane/*i*PrOH = 7/3, flow 0.8 mL/min, detection at 254 nm, 10.67 min (major), 8.97 min (minor), *ee* = 87%.

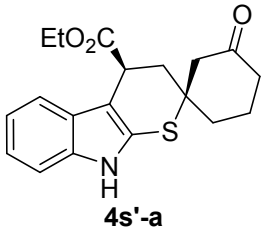
4s: *tert*-Butyl (1*R*,4'*S*)-9'-4'-ethyl-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4',9'(4'*H*)-dicarboxylate



4s

The product was obtained in 50% yield, 44.3 mg, yellowish white solid. Mp 75-76 °C; $[\alpha]_D^{25}$ −26.8 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.25 (t, *J* = 7.2 Hz, 3H), 1.68 (s, 9H), 2.03-2.10 (m, 2H), 2.13-2.24 (m, 2H), 2.31-2.39 (m, 2H), 2.42-2.45 (m, 1H), 2.45-2.51 (m, 2H), 2.62-2.65 (m, 1H), 3.89-3.93 (m, 1H), 4.20-4.23 (m, 2H), 7.14-7.23 (m, 3H), 7.98-8.00 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.2, 21.2, 28.3, 36.7, 37.8, 39.9, 40.6, 49.3, 49.5, 61.4, 85.2, 109.6, 115.0, 117.3, 122.9, 123.3, 129.2, 129.6, 135.7, 150.1, 173.6, 207.4; HRMS (EI): exact mass calculated for $C_{24}H_{29}NO_5S$ $[M]^+$ require m/z = 443.1812, found m/z = 443.1813; The enantiomeric ratio was determined by Daicel Chiralpak IB, *n*-Hexane/*i*PrOH = 19/1, flow 1.0 mL/min, detection at 254 nm, 17.37 min (major), 16.16 min (minor), *ee* = 85%.

4s'-a: **(1*S*,4'*S*)-ethyl-3-oxo-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4'-carboxylate**

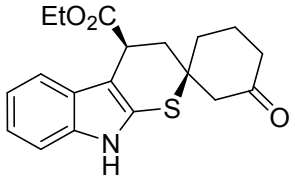


4s'-a

The product was obtained in 17% yield, 11.7 mg, yellowish white solid. Mp 105-106 °C; $[\alpha]_D^{25}$ 17.0 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.18 (t, *J* = 7.1 Hz, 3H), 1.82-1.91 (m, 2H), 1.96-2.02 (m, 2H), 2.23-2.30 (m, 2H), 2.33-2.38 (m, 1H), 2.45-2.49 (m, 1H), 2.53 (d, *J* = 14.9 Hz, 1H), 2.64 (d, *J* = 14.3 Hz, 1H), 3.95 (dd, J_1 = 9.2 Hz, J_2 = 6.3 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 6.96-7.03 (m, 2H), 7.11-7.13 (m, 1H), 7.27-7.29 (m, 1H), 8.02 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.2, 21.8, 33.9, 37.9, 40.0, 40.7, 52.0, 52.4,

61.4, 103.5, 110.4, 117.6, 119.8, 121.3, 126.6, 127.4, 136.2, 173.9, 207.8; HRMS (EI): exact mass calculated for $C_{19}H_{21}NO_3S$ $[M]^+$ require m/z = 343.1203, found m/z = 343.1202.

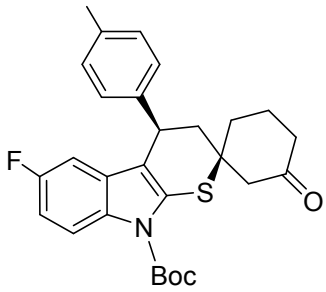
4s'-b: **(1*R*,4'*S*)-ethyl-3-oxo-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4'-carboxylate**



4s'-b

The product was obtained in 56% yield, 38.4 mg, yellowish white solid. Mp 105-106 °C; $[\alpha]_D^{25}$ -81.5 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.28 (t, *J* = 7.1 Hz, 3H), 2.03-2.11 (m, 3H), 2.19-2.22 (m, 1H), 2.30-2.38 (m, 2H), 2.45-2.55 (m, 2H), 2.67 (d, *J* = 14.5 Hz, 1H), 3.97 (dd, J_1 = 10.7 Hz, J_2 = 6.2 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 7.03-7.11 (m, 2H), 7.21 (d, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.3, 21.6, 36.8, 37.9, 40.6, 41.3, 49.6, 51.8, 61.3, 104.1, 110.4, 117.5, 119.9, 121.5, 126.0, 127.2, 136.4, 174.1, 207.5; HRMS (EI): exact mass calculated for $C_{19}H_{21}NO_3S$ $[M]^+$ require m/z = 343.1203, found m/z = 343.1202.

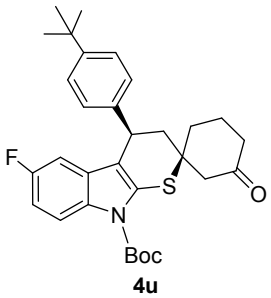
4t: *tert*-Butyl (1*R*,4'*R*)-6'-fluoro-3-oxo-4'-(*p*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4t

The product was obtained in 70% yield, 67.1 mg, yellowish white solid. Mp 124-125 °C; $[\alpha]_D^{25}$ −249.5 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.70 (s, 9H), 2.02-2.09 (m, 2H), 2.12-2.19 (m, 3H), 2.24-2.29 (m, 1H), 2.33 (s, 3H), 2.35-2.39 (m, 1H), 2.48-2.52 (m, 1H), 2.56-2.59 (m, 1H), 2.75-2.79 (m, 1H), 4.03-4.08 (m, 1H), 6.22-6.25 (m, 1H), 6.78-6.84 (m, 1H), 7.07-7.11 (m, 4H), 7.88-7.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.1, 21.2, 28.3, 37.1, 37.1, 37.7, 40.7, 47.7, 49.7, 50.1, 85.3, 104.7, 104.9, 110.3, 114.4, 115.5, 127.9, 129.6, 130.6, 131.2, 132.3, 136.6, 139.9, 150.0, 208.0; HRMS (EI): exact mass calculated for $C_{28}H_{30}FNO_3S$ $[M]^+$ require m/z = 479.1942, found m/z = 479.1943; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 8.80 min (major), 10.34 min (minor), *ee* = 84%.

4u: *tert*-Butyl (1*R*,4'*R*)-4'-(4-(*tert*-butyl)phenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

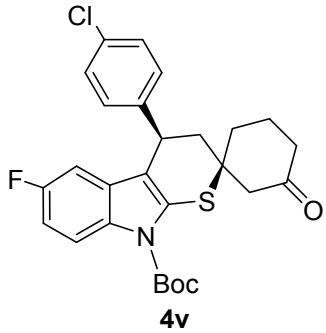


4u

The product was obtained in 72% yield, 75.1 mg, yellowish white solid. Mp 134-135 °C; $[\alpha]_D^{25}$ −230.1 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.30 (s, 9H), 1.70 (s, 9H), 2.02-2.08 (m, 2H), 2.11-2.19 (m, 3H), 2.25-2.30 (m, 1H), 2.33-2.39 (m, 1H), 2.48-2.52 (m, 1H), 2.56-2.60 (m, 1H), 2.75-2.79 (m, 1H), 4.04-4.09 (m, 1H), 6.22-6.25 (m, 1H), 6.78-6.83 (m, 1H), 7.10-7.12 (m, 2H), 7.28-7.30 (m, 2H), 7.87-7.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 31.4, 34.5, 37.0, 37.1, 40.9, 47.6, 49.7, 50.1, 85.3, 104.7, 104.9, 110.1, 114.5, 115.5, 125.7, 127.6,

130.7, 131.2, 132.2, 139.8, 149.9, 157.6, 208.0; HRMS (EI): exact mass calculated for $C_{31}H_{36}FNO_3S$ $[M]^+$ require m/z = 521.2434, found m/z = 521.2433; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 6.55 min (major), 8.48 min (minor), *ee* = 86%.

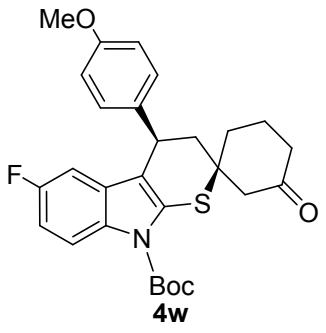
4v: *tert*-Butyl (1*R*,4'*R*)-4'-(4-chlorophenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4v

The product was obtained in 67% yield, 66.9 mg, yellowish white solid. Mp 136-137 °C; $[\alpha]_D^{25}$ −207.8 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.70 (s, 9H), 2.03-2.13 (m, 3H), 2.15-2.20 (m, 2H), 2.24-2.29 (m, 1H), 2.32-2.40 (m, 1H), 2.48-2.53 (m, 1H), 2.56-2.59 (m, 1H), 2.75-2.78 (m, 1H), 4.07-4.11 (m, 1H), 6.19-6.22 (m, 1H), 6.81-6.86 (m, 1H), 7.12-7.14 (m, 2H), 7.26-7.28 (m, 2H), 7.89-7.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 20.1, 26.4, 27.2, 36.0, 39.6, 46.4, 48.6, 49.1, 84.4, 103.6, 109.5, 112.5, 114.7, 128.0, 129.2, 130.6, 131.2, 131.7, 140.6, 148.9, 156.6, 159.0, 206.8; HRMS (EI): exact mass calculated for $C_{27}H_{27}ClFNO_3S$ $[M]^+$ require m/z = 499.1424, found m/z = 499.1423; The enantiomeric ratio was determined by Daicel Chiralpak AD-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 10.59 min (major), 12.39 min (minor), *ee* = 87%.

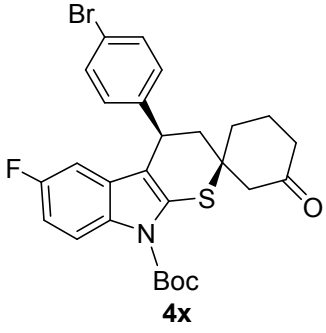
4w: *tert*-Butyl (1*R*,4'*R*)-6'-fluoro-4'-(4-methoxyphenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



4w

The product was obtained in 54% yield, 53.5 mg, yellowish white solid. Mp 104-105 °C; $[\alpha]_D^{25}$ −245.1 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.70 (s, 9H), 1.99-2.09 (m, 2H), 2.11-2.19 (m, 3H), 2.23-2.28 (m, 1H), 2.32-2.40 (m, 1H), 2.48-2.53 (m, 1H), 2.56-2.59 (m, 1H), 2.75-2.79 (m, 1H), 3.80 (s, 3H), 4.03-4.07 (m, 1H), 6.23-6.26 (m, 1H), 6.79-6.84 (m, 3H), 7.10-7.12 (m, 2H), 7.88-7.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 20.1, 27.3, 35.7, 36.0, 39.6, 46.7, 48.7, 49.1, 54.2, 84.2, 103.7, 103.9, 109.1, 113.2, 113.4, 114.4, 127.9, 129.5, 130.2, 131.2, 133.9, 149.0, 157.5, 207.0; HRMS (EI): exact mass calculated for $C_{28}H_{30}FNO_4S$ $[M]^+$ require m/z = 495.1914, found m/z = 495.1912; The enantiomeric ratio was determined by Daicel Chiralpak IB, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 14.27 min (major), *ee* > 99%.

4x: *tert*-Butyl (1*R*,4'*R*)-4'-(4-bromophenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



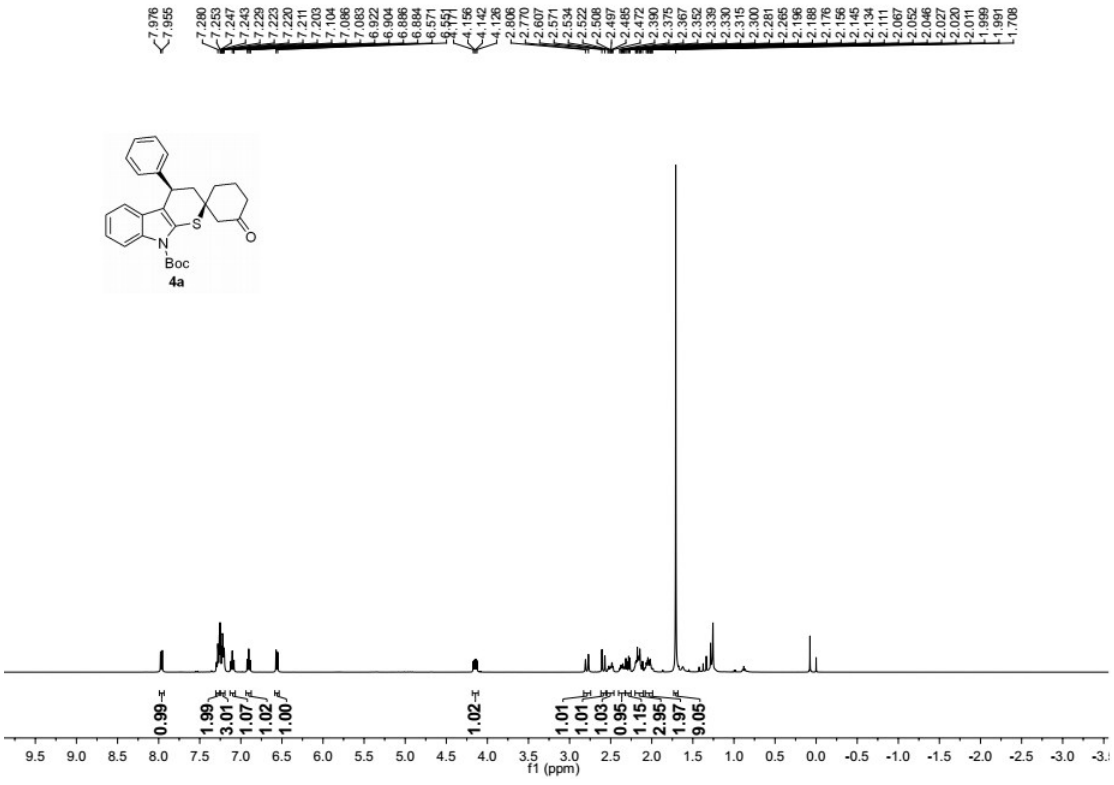
4x

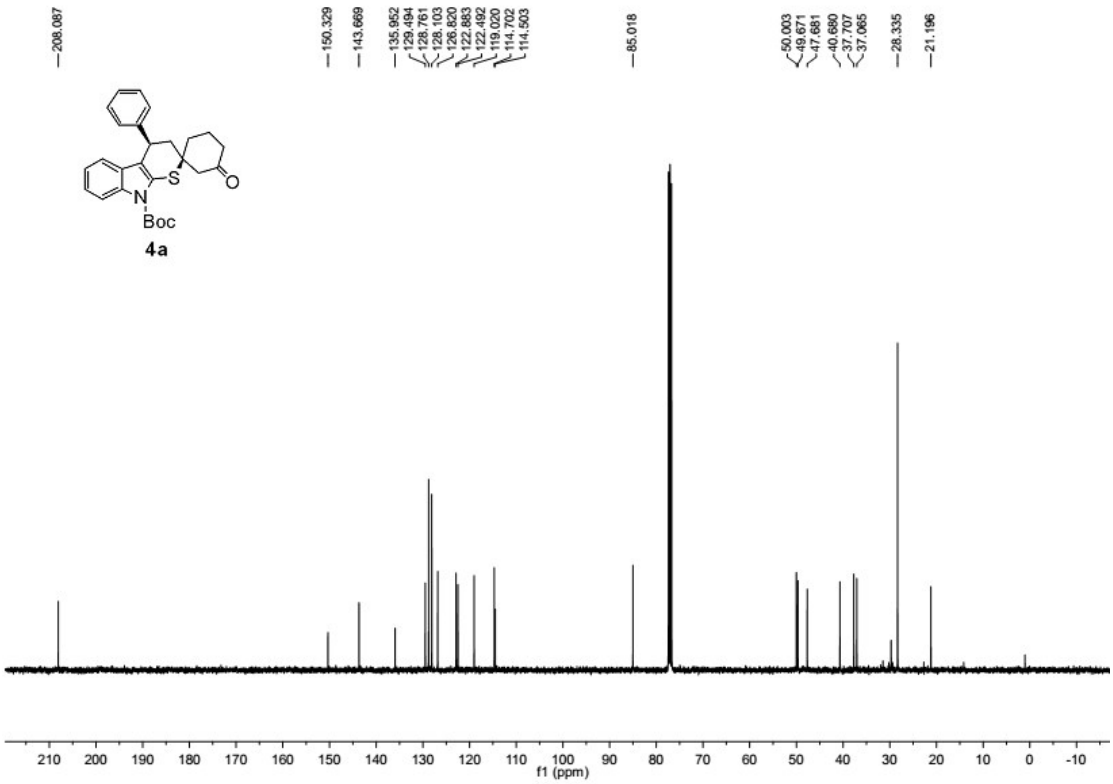
The product was obtained in 57% yield, 62.1 mg, yellowish white solid. Mp 132-133 °C; $[\alpha]_D^{25}$ −229.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.70 (s,

9H), 2.03-2.10 (m, 3H), 2.13-2.19 (m, 2H), 2.24-2.29 (m, 1H), 2.32-2.40 (m, 1H), 2.48-2.53 (m, 1H), 2.55-2.59 (m, 1H), 2.74-2.79 (m, 1H), 4.05-4.10 (m, 1H), 6.19-6.22 (m, 1H), 6.81-6.86 (m, 1H), 7.07-7.09 (m, 2H), 7.41-7.43 (m, 2H), 7.89-7.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ(ppm) 20.1, 27.2, 35.9, 36.1, 39.6, 46.4, 48.6, 49.0, 84.4, 103.6, 109.5, 112.4, 114.7, 119.8, 128.7, 129.2, 130.6, 131.0, 131.2, 141.1, 148.9, 156.6, 206.8; HRMS (EI): exact mass calculated for $C_{27}H_{27}BrFNO_3S$ $[M]^+$ require m/z = 545.0932, found m/z = 545.0933; The enantiomeric ratio was determined by Daicel Chiralpak AS-H, *n*-Hexane/*i*PrOH = 19/1, flow 0.8 mL/min, detection at 254 nm, 14.89 min (major), 16.33 min (minor), *ee* = 84%.

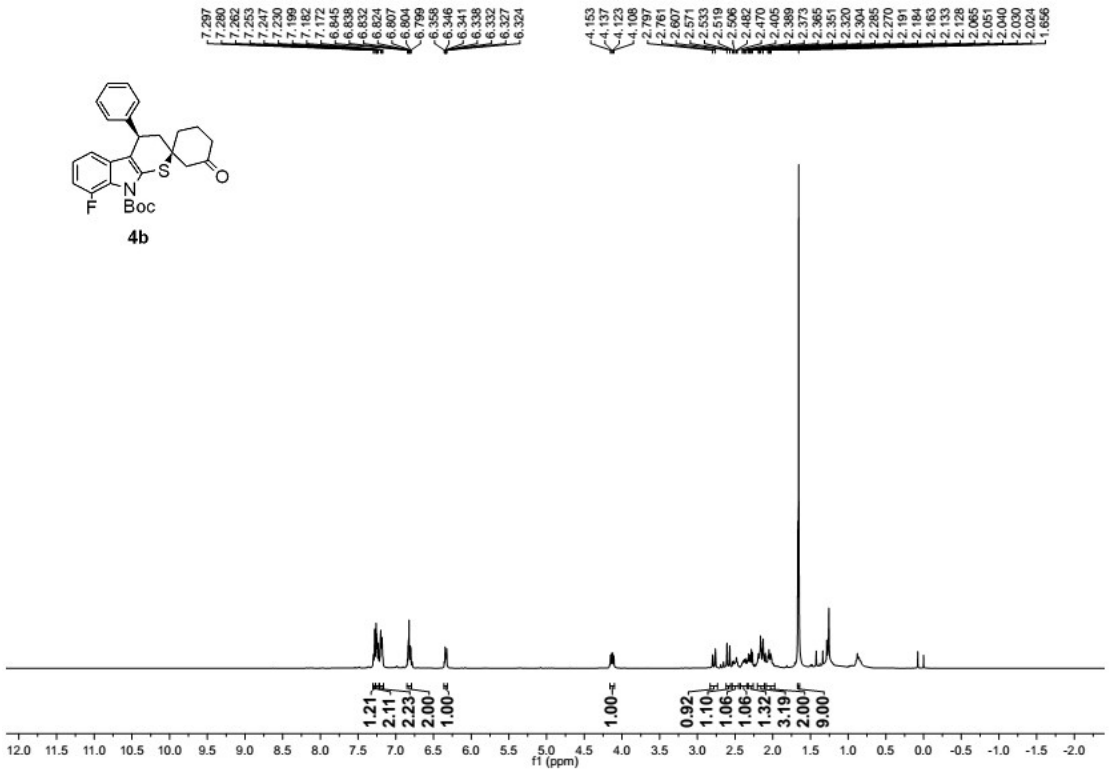
E: NMR Spectra of Products.

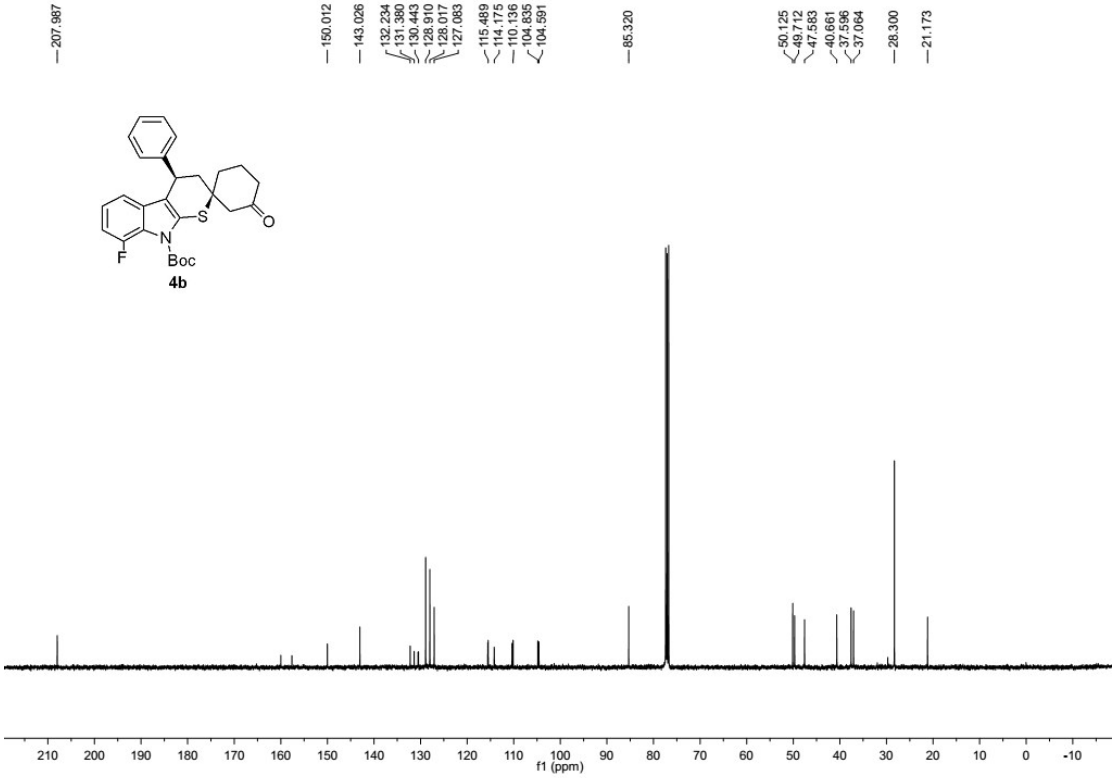
4a: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



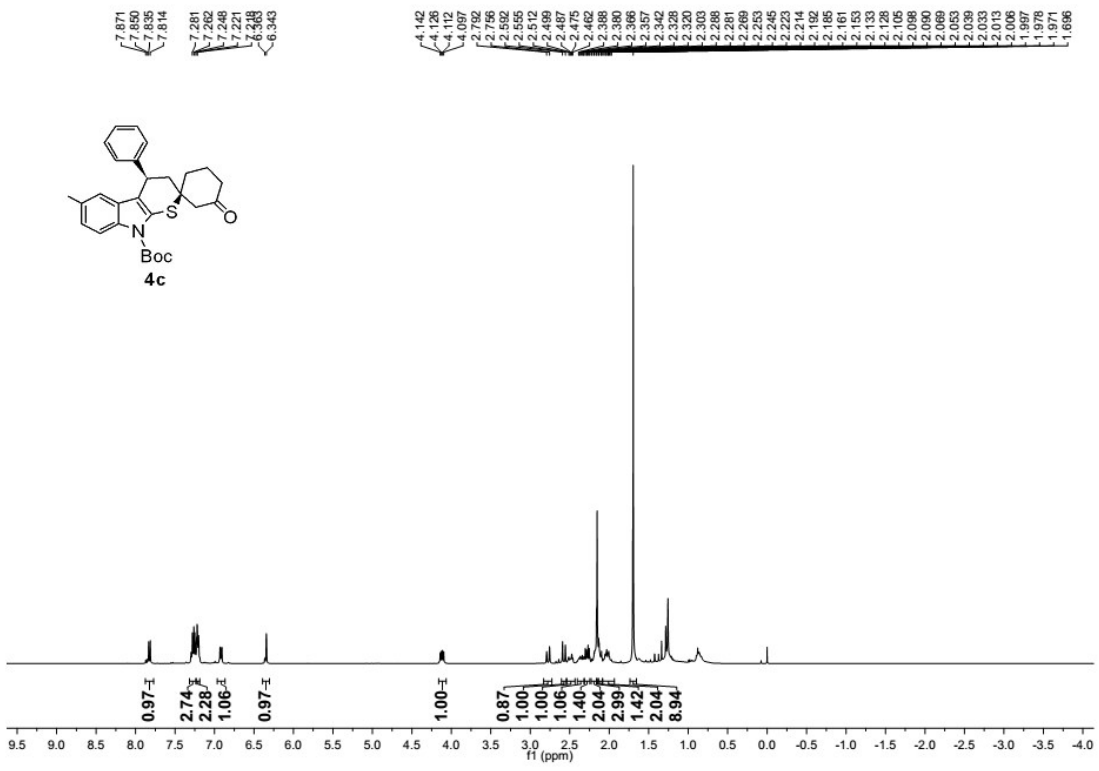


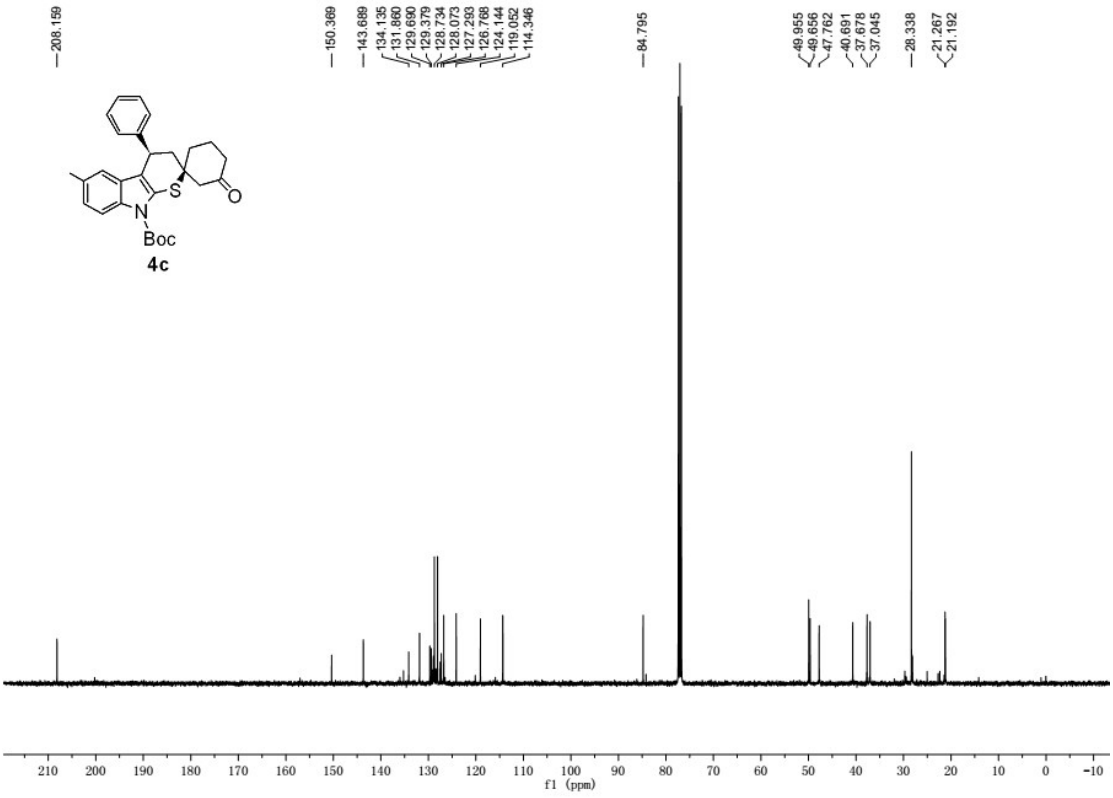
4b: *tert*-Butyl (1*R*,4'*R*)-8'-fluoro-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



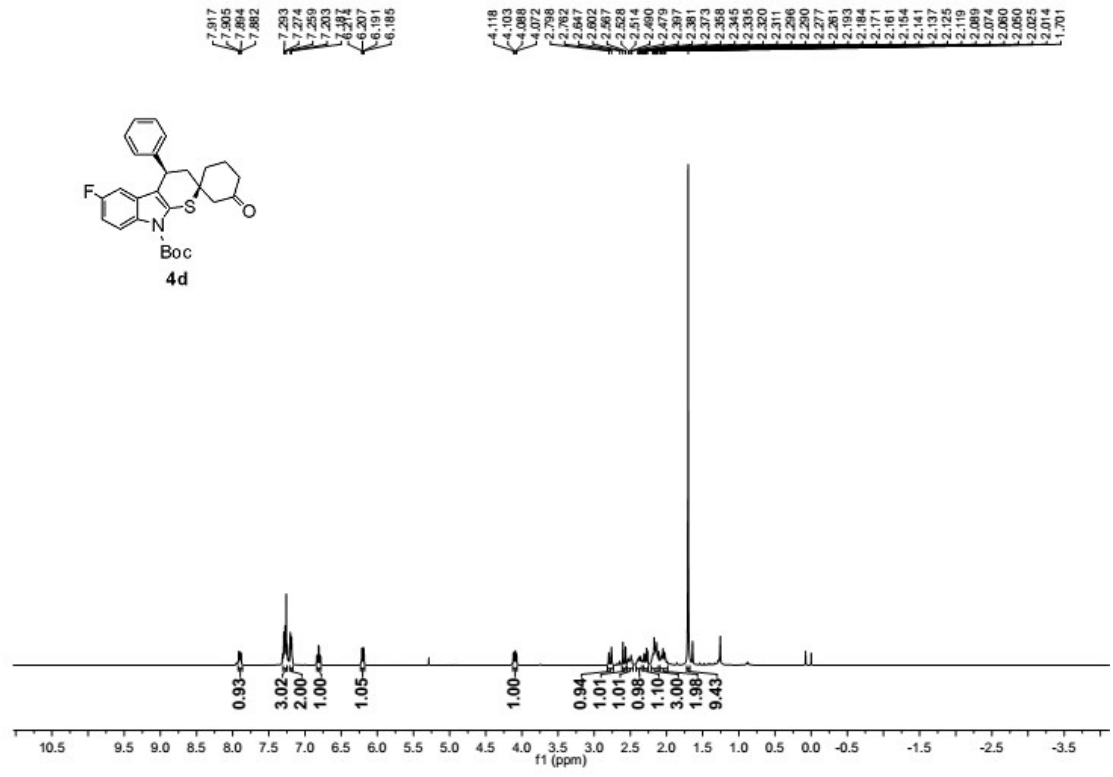


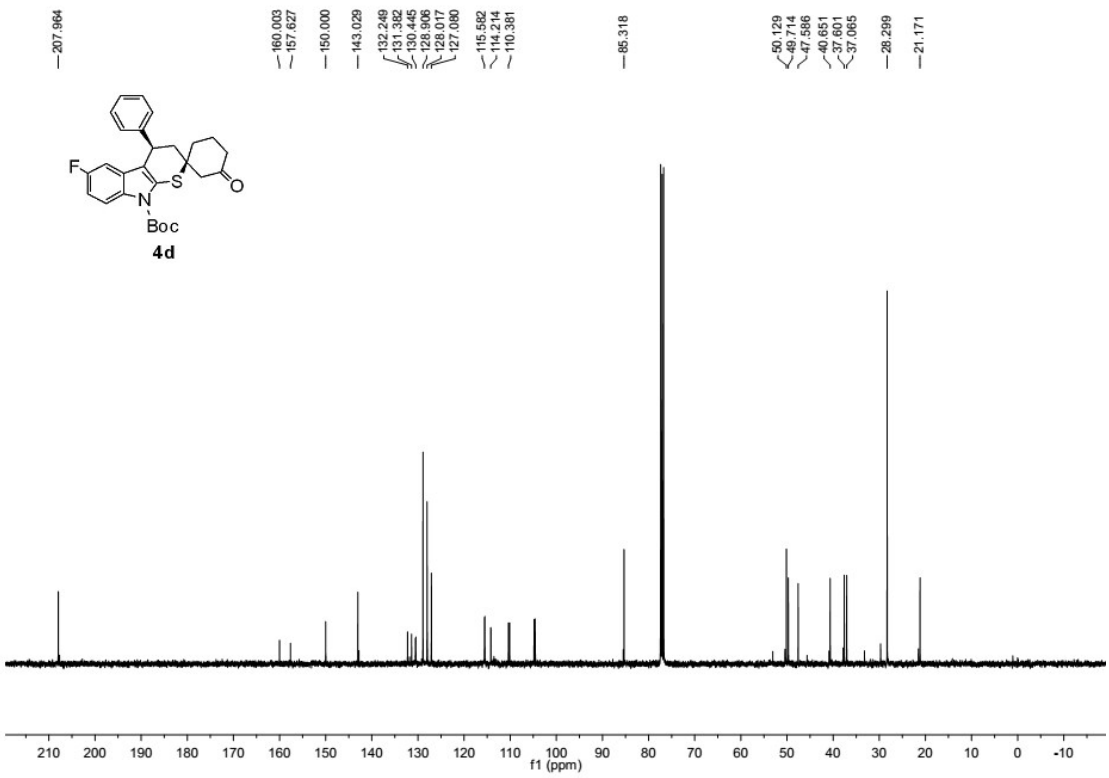
4c: *tert*-Butyl (1*R*,4'*R*)-6'-methyl-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



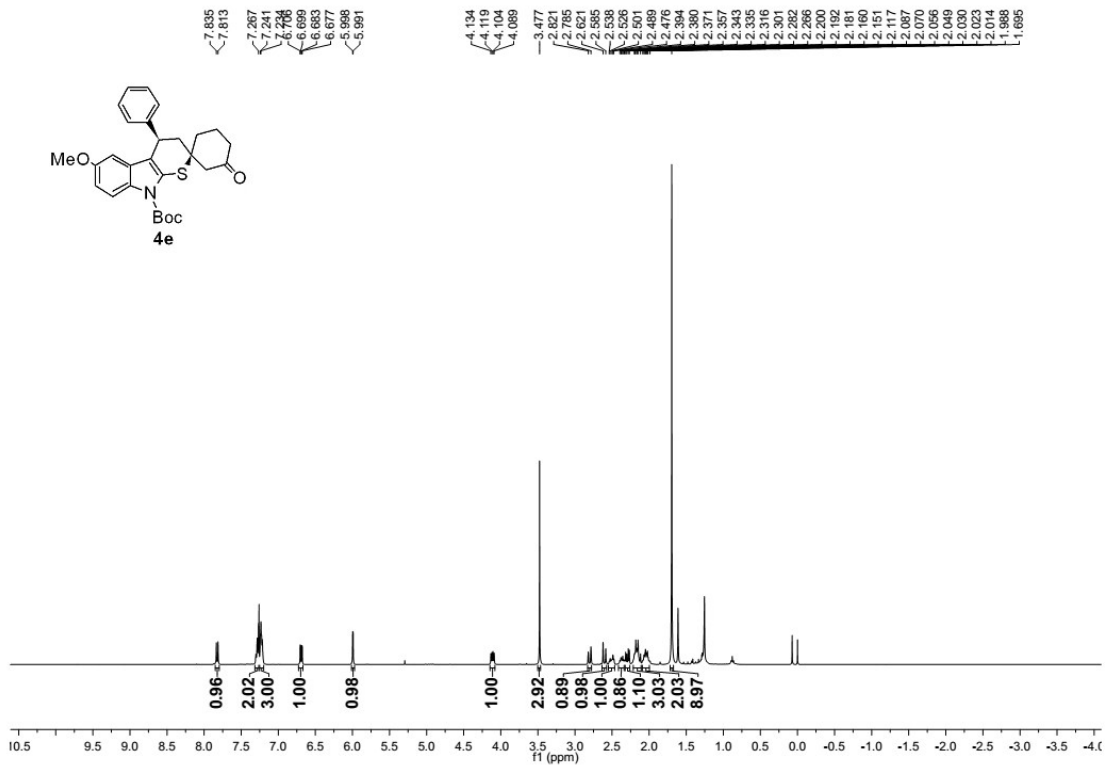


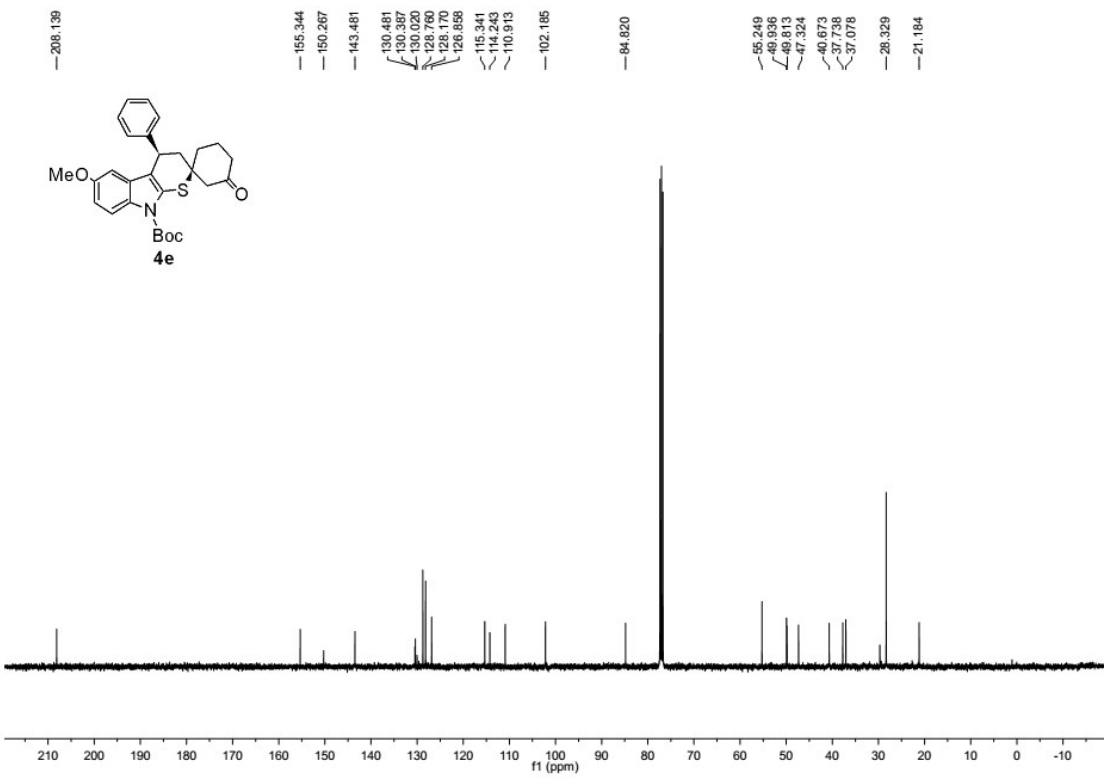
4d: *tert*-Butyl (1*R*,4'*R*)-6'-methoxy-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



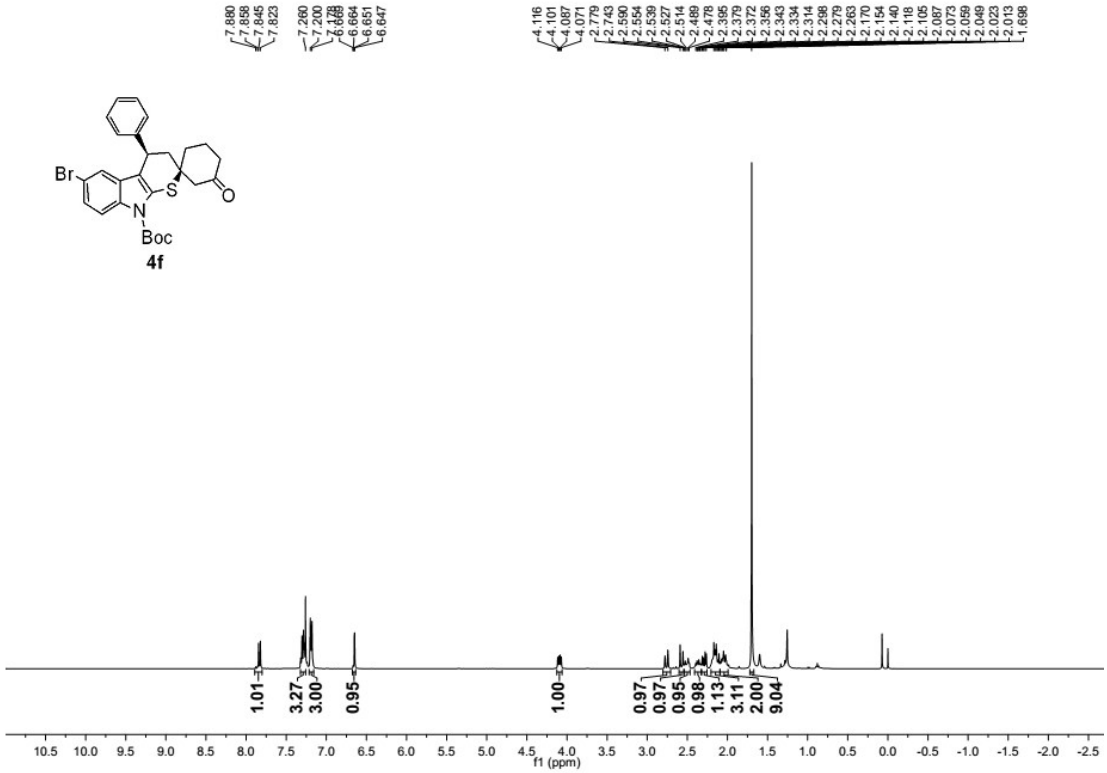


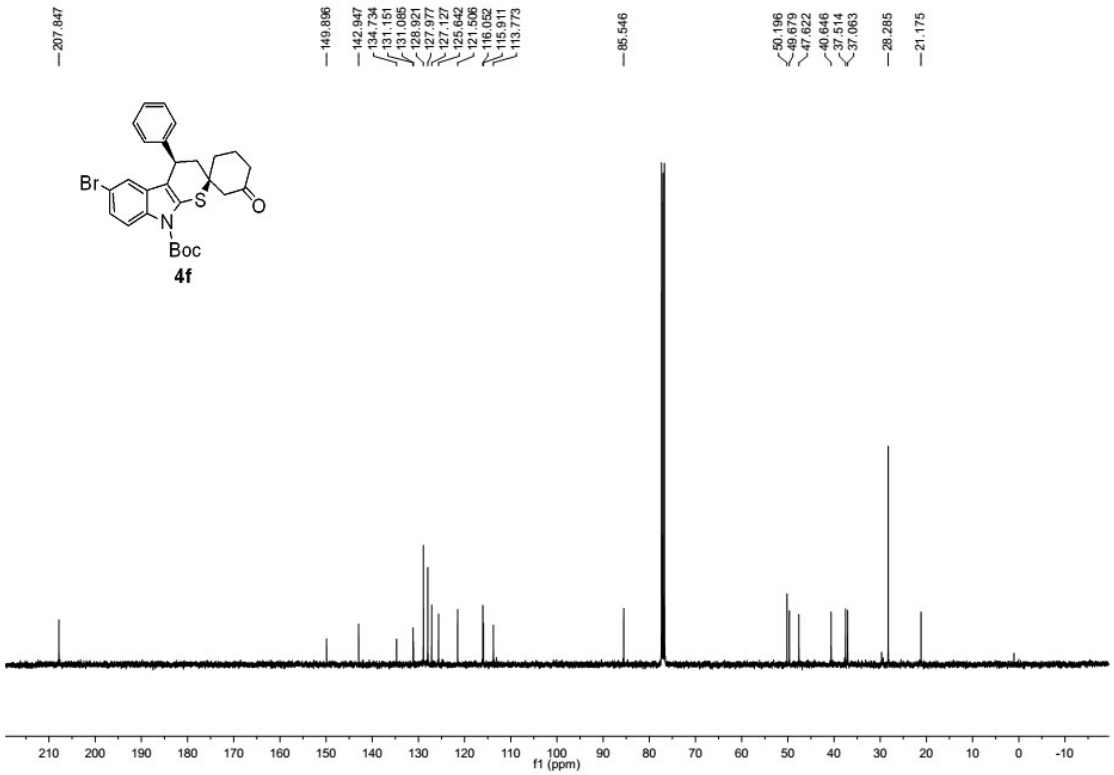
4e: *tert*-Butyl (1*R*,4'*R*)-6'-methoxy-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



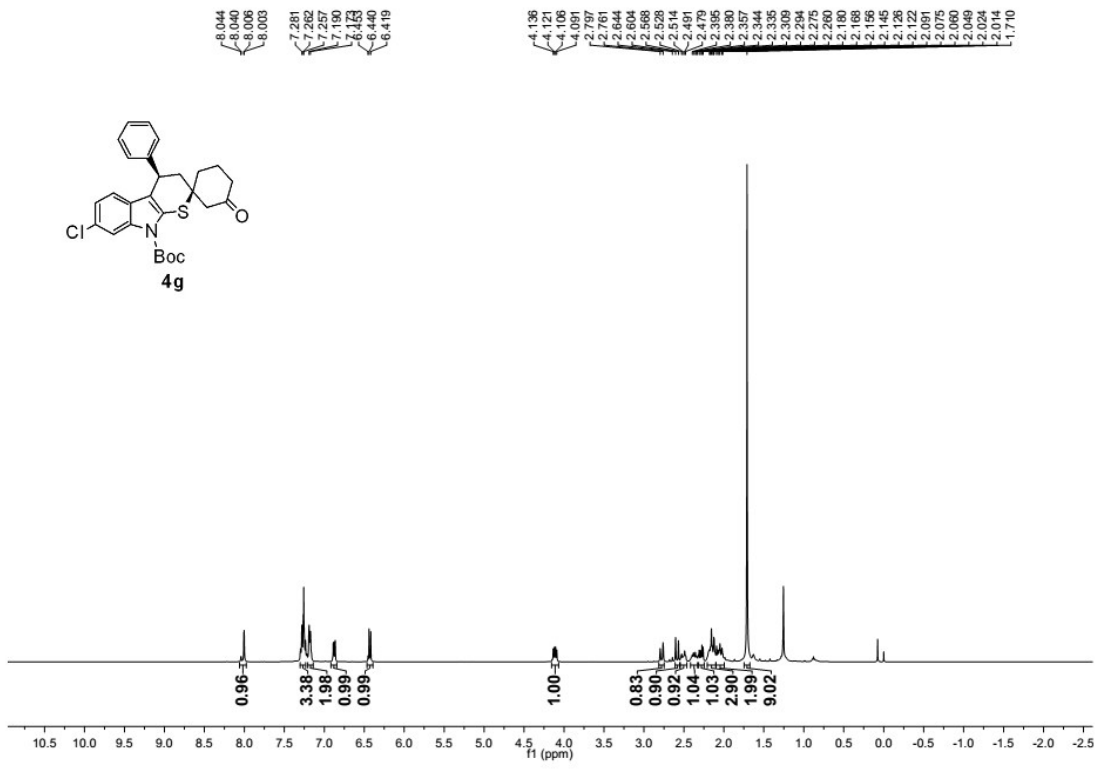


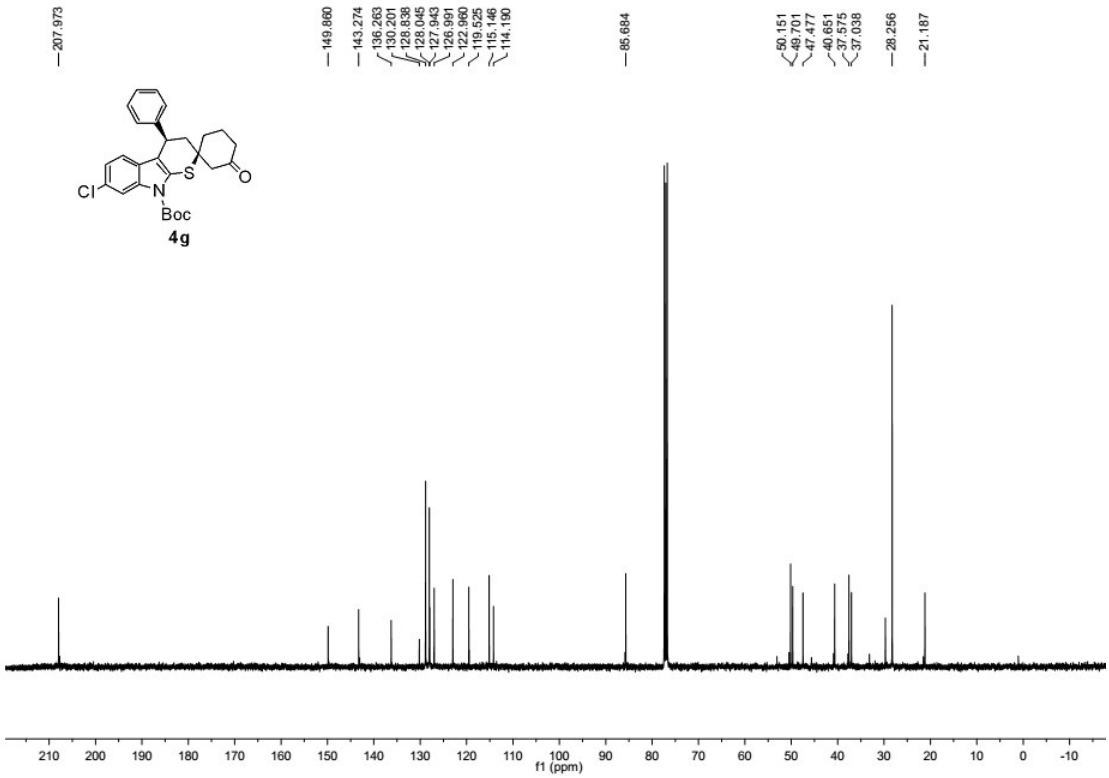
4f: *tert*-Butyl (1*R*,4'*R*)-6'-bromo-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



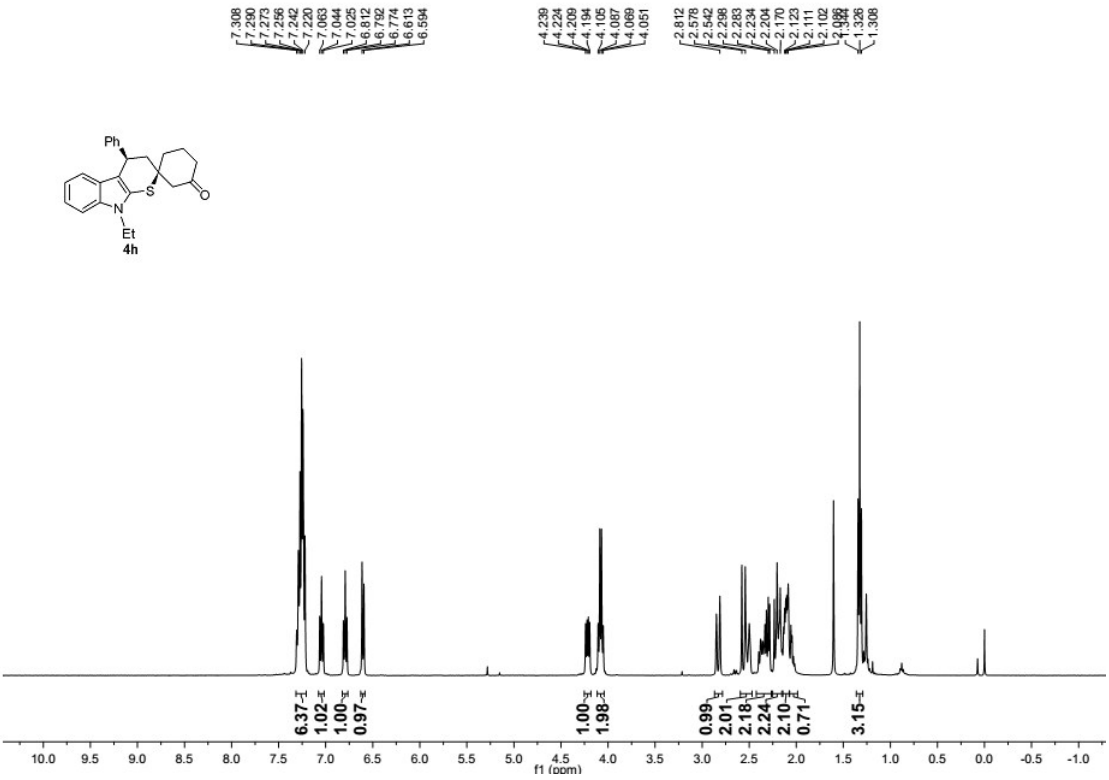


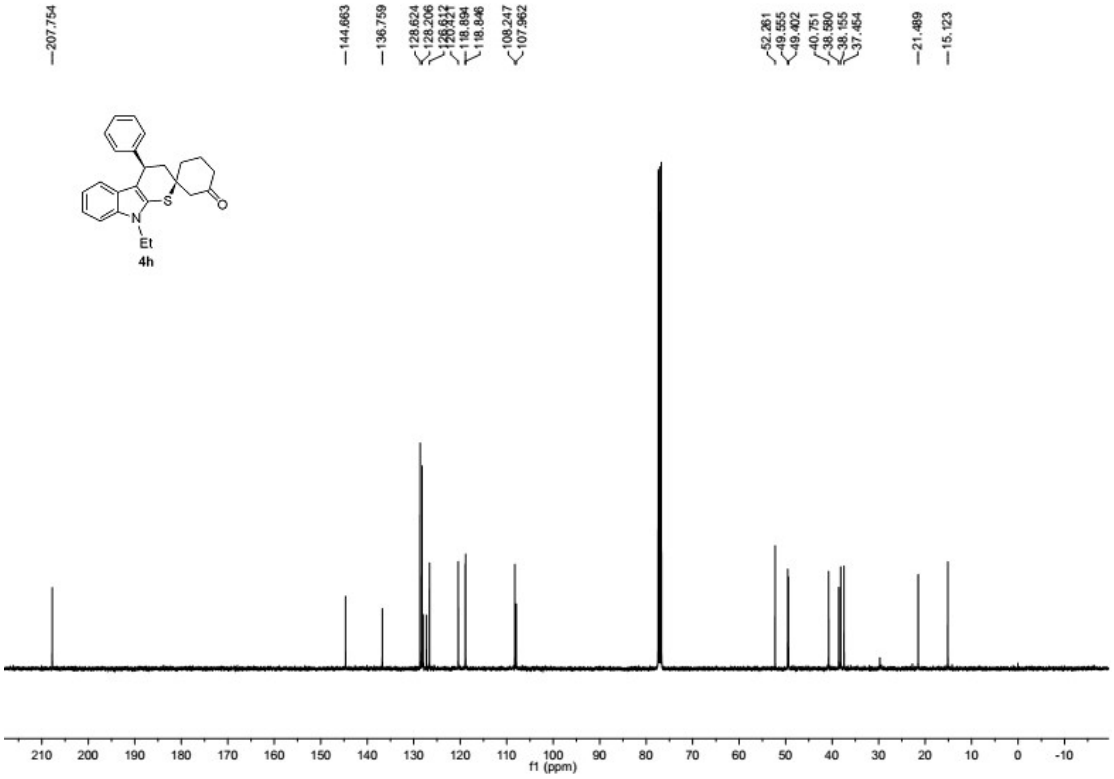
4g: *tert*-Butyl (1*R*,4'*R*)-7'-chloro-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



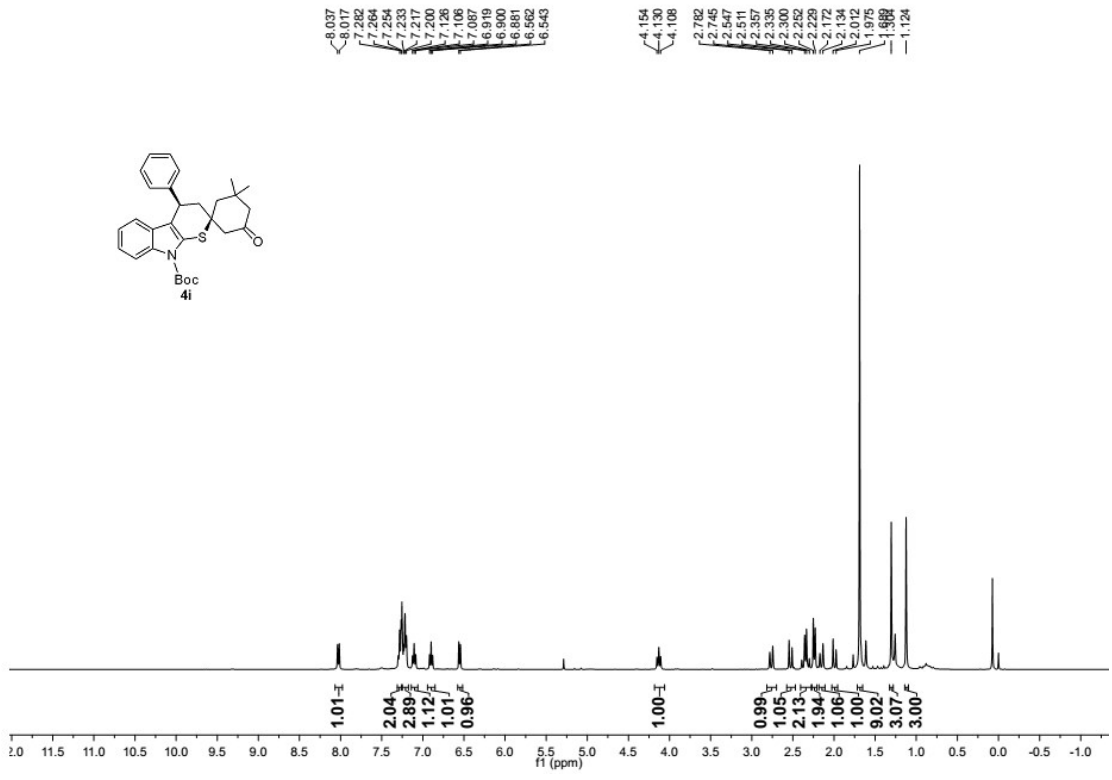


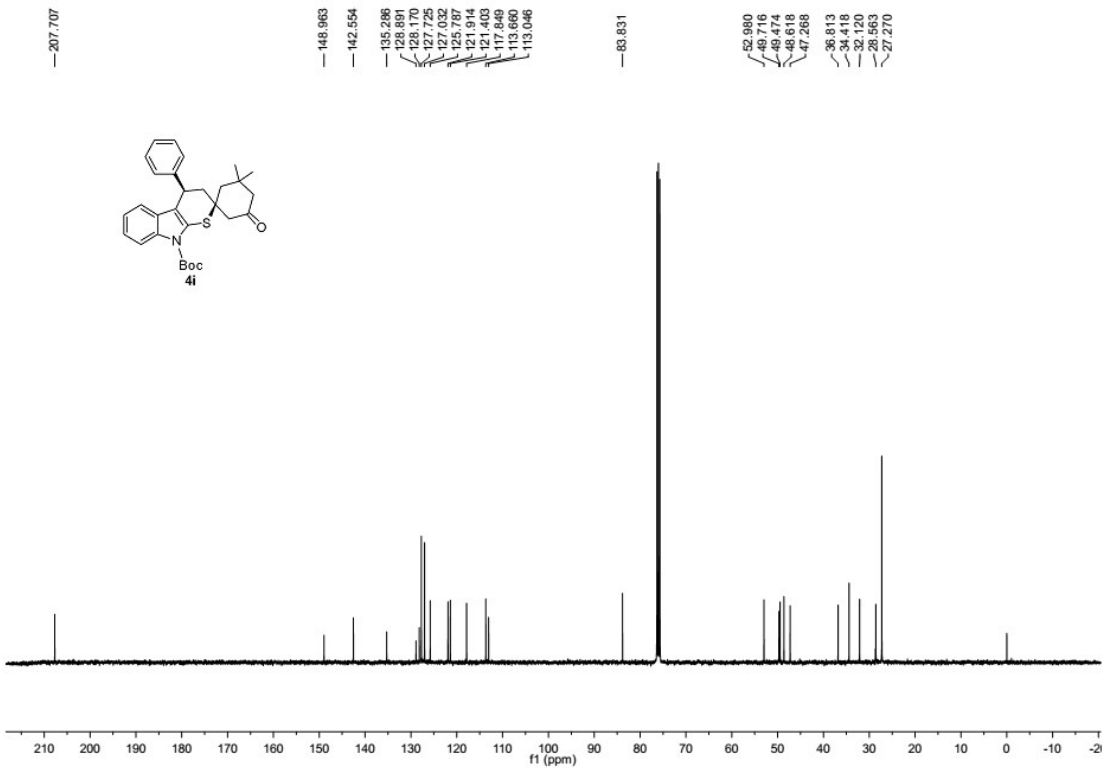
4h: (1*R*,4'*R*)-9'-ethyl-4'-phenyl-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano [2,3-*b*]indol]-3-one



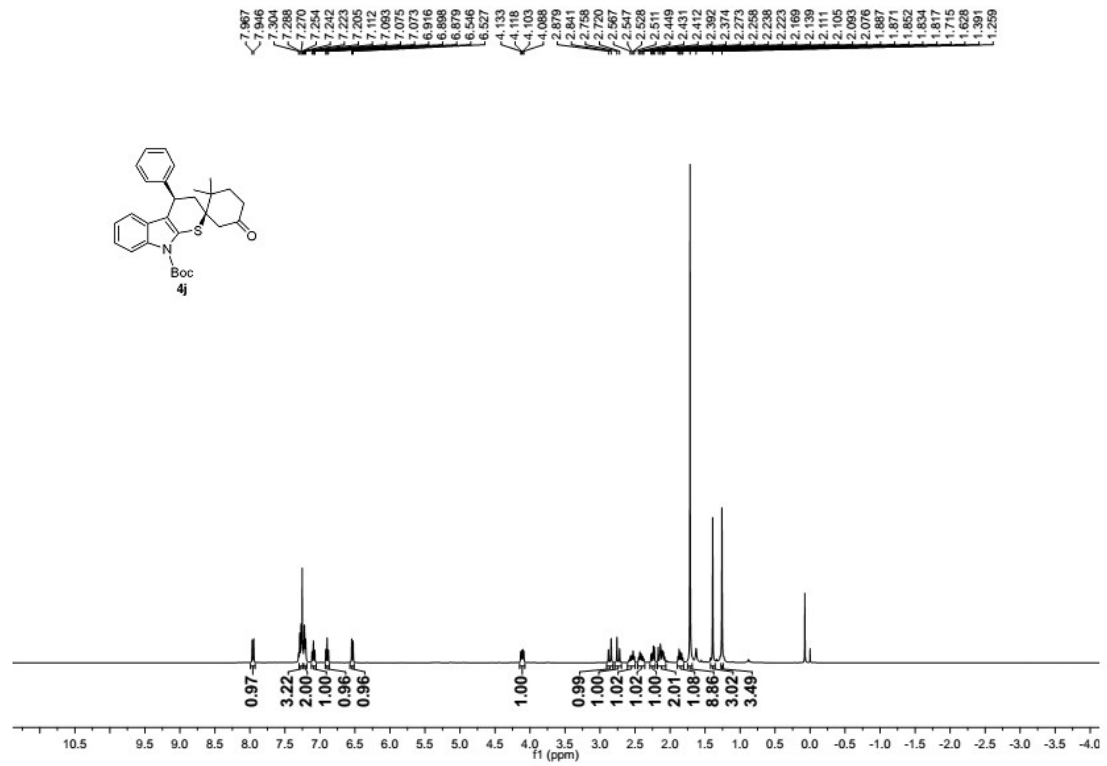


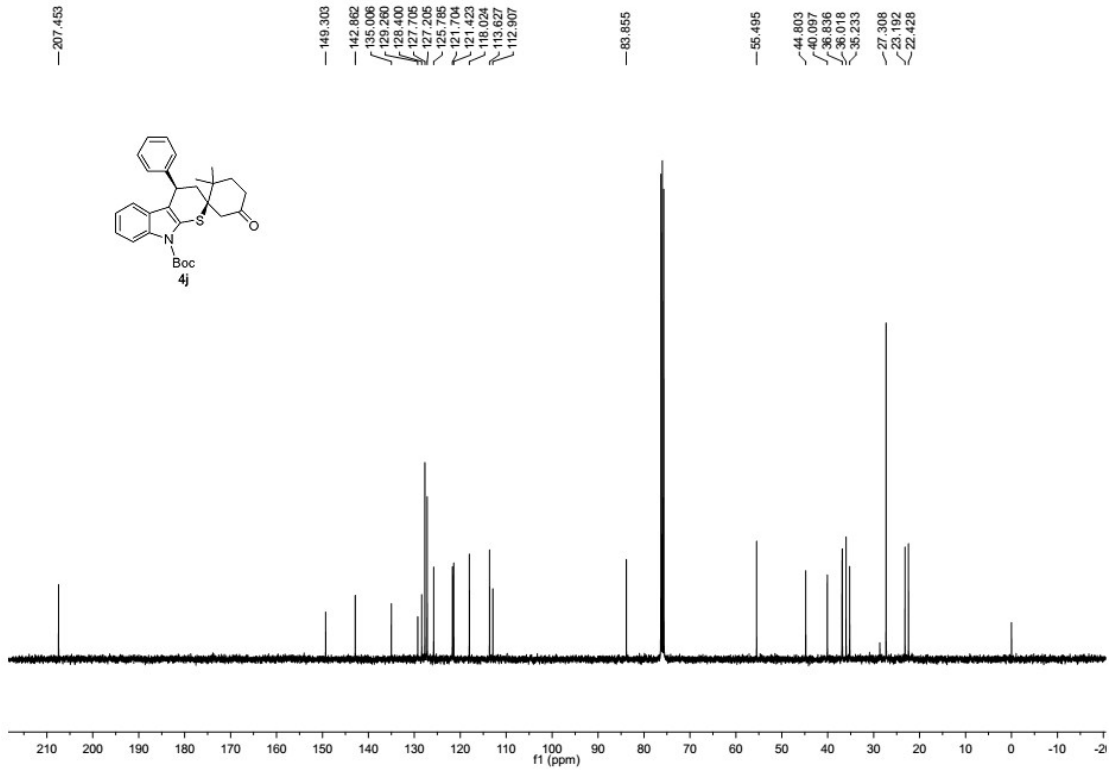
4i: *tert*-Butyl (1*S*,4'*R*)-3,3-dimethyl-5-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



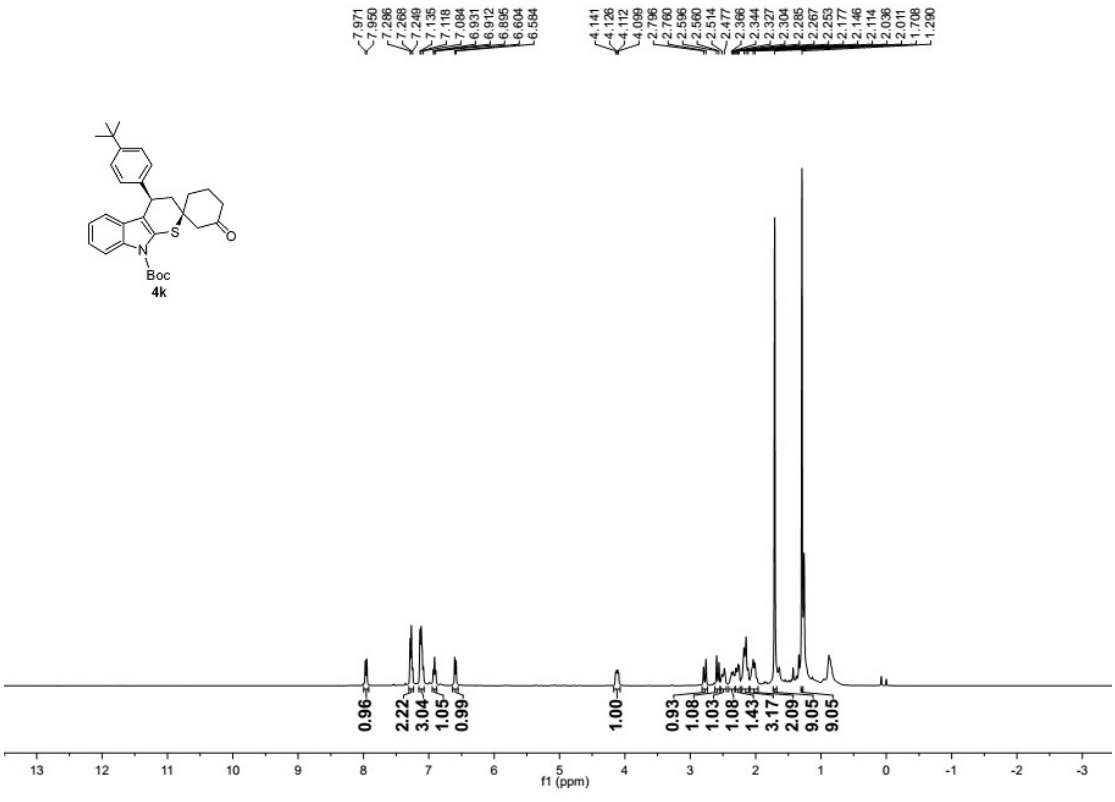


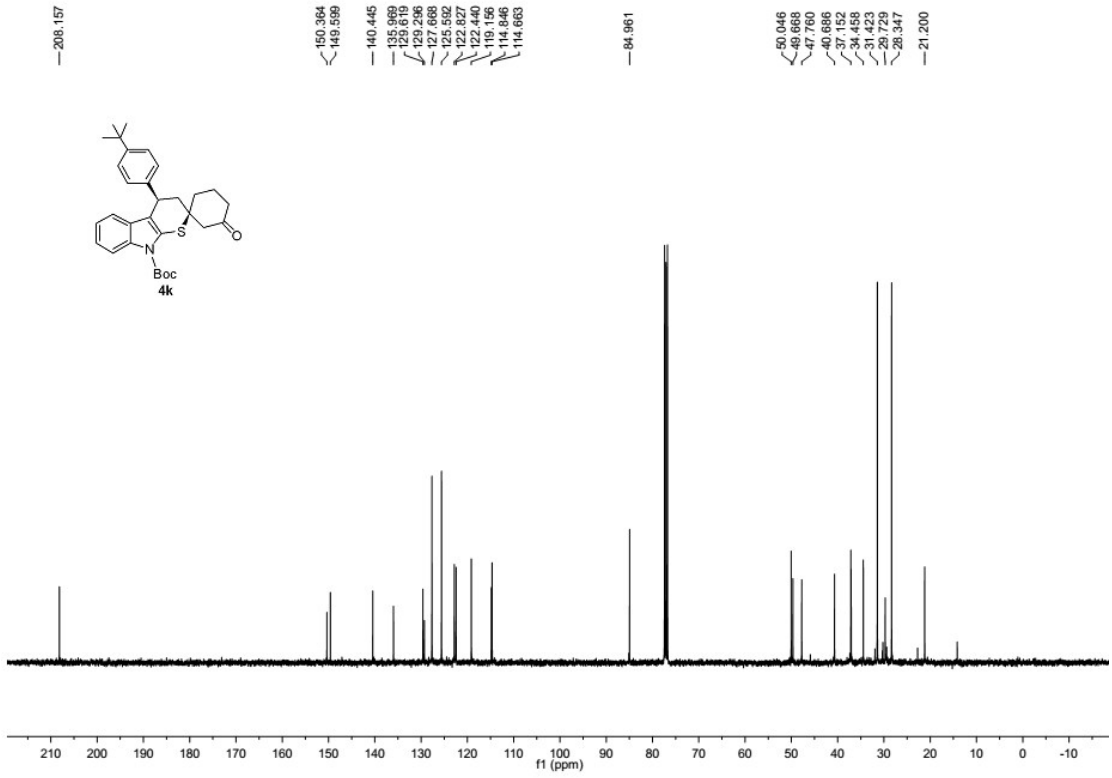
4j: *tert*-Butyl (1*R*,4'*R*)-2,2-dimethyl-5-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



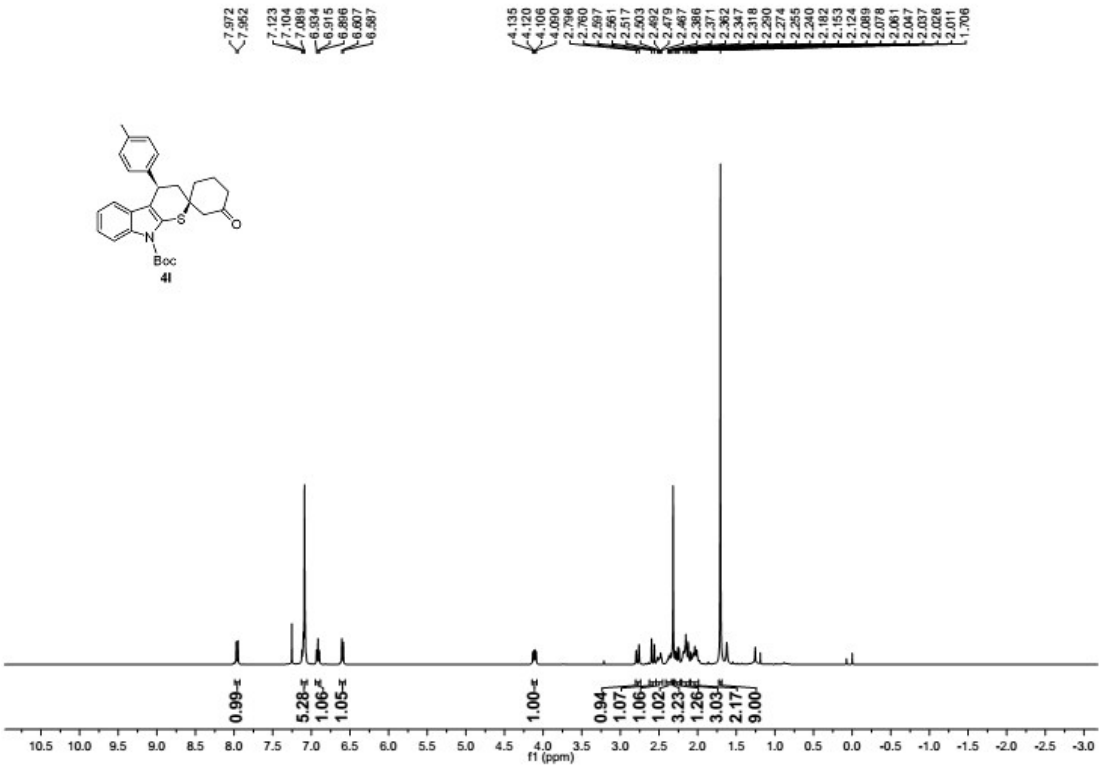


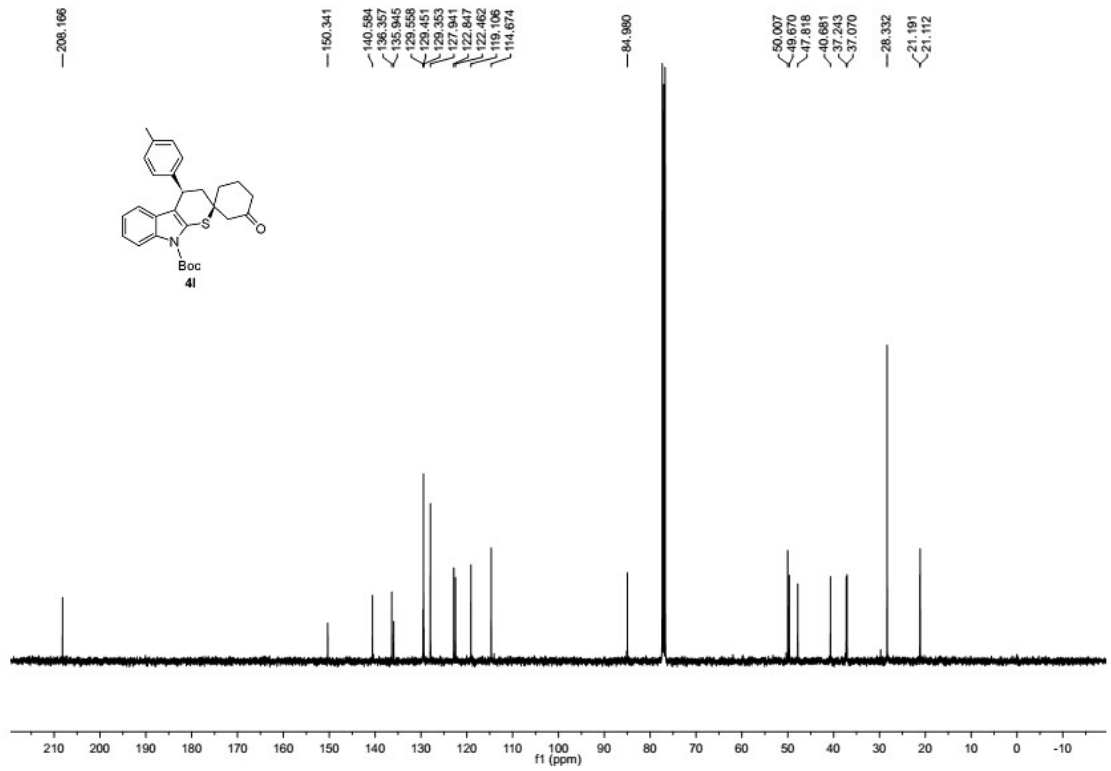
4k: *tert*-Butyl (1*R*,4'*R*)-4'-(4-(*tert*-butyl)phenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



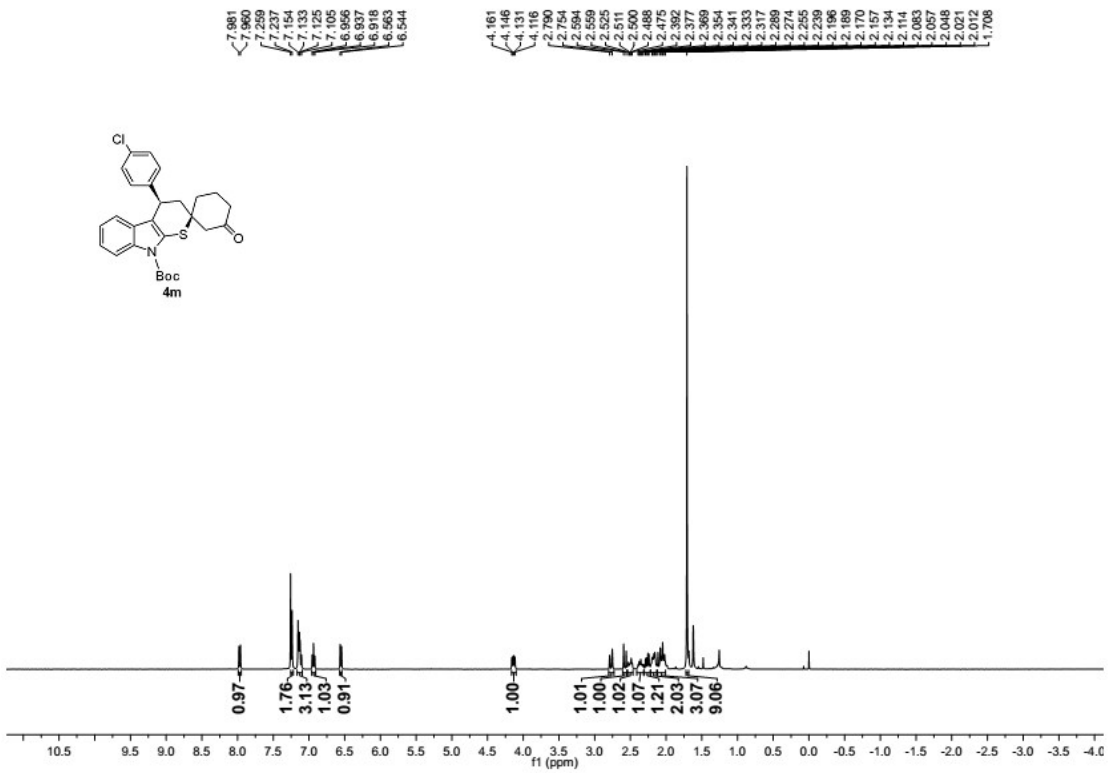


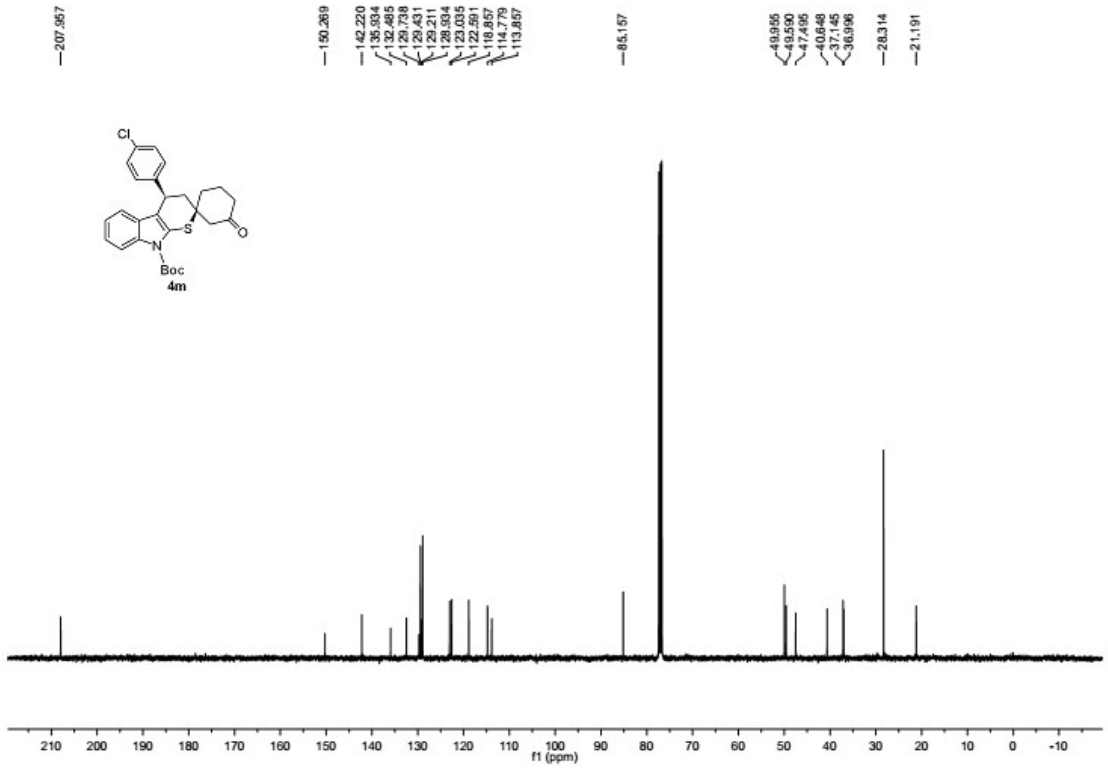
4l: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-(*p*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



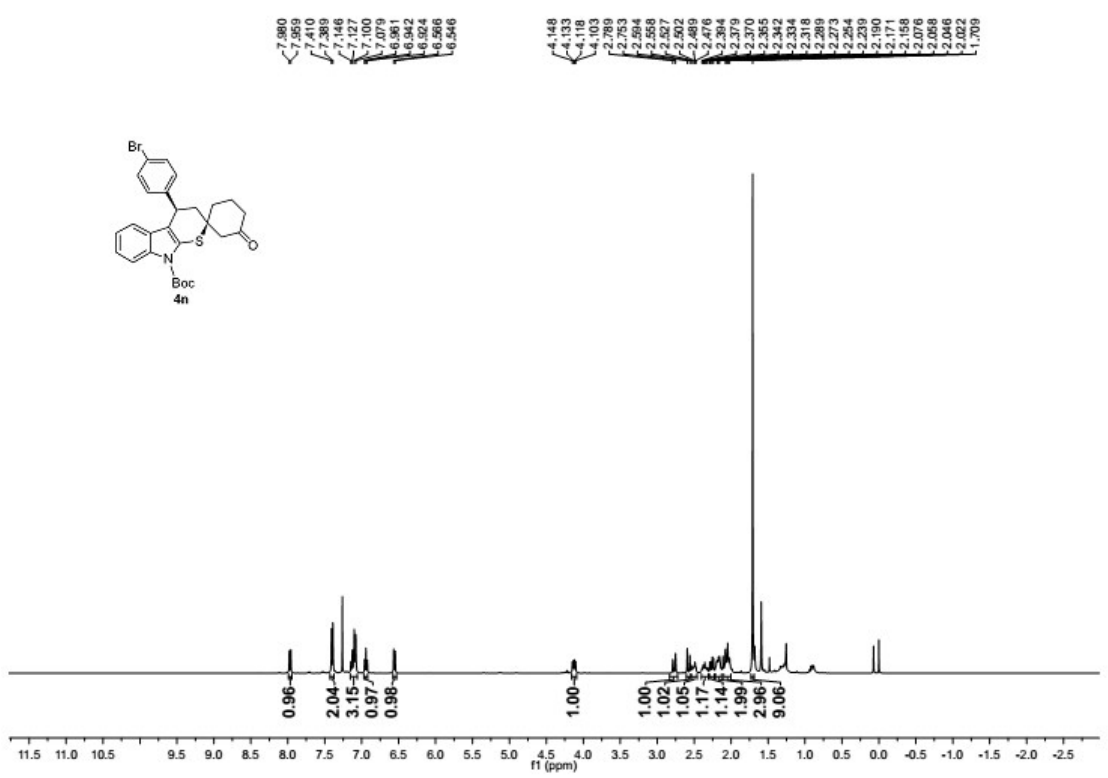


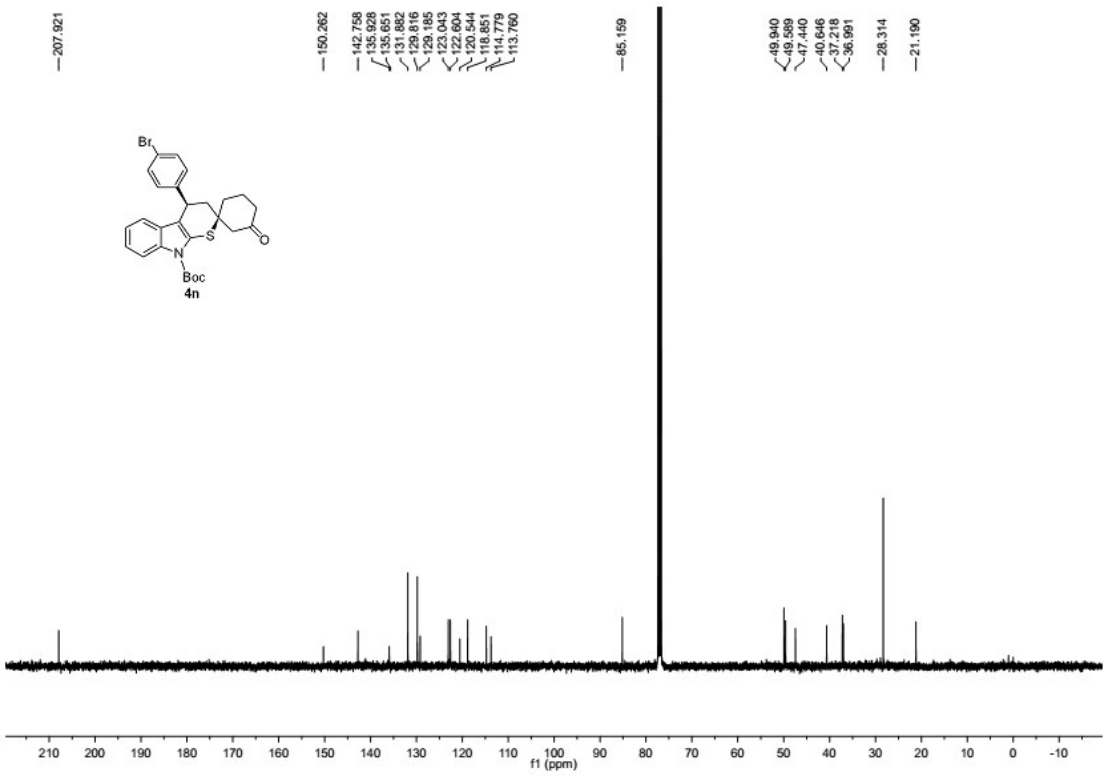
4m: *tert*-Butyl (1*R*,4'*R*)-4'-(4-chlorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



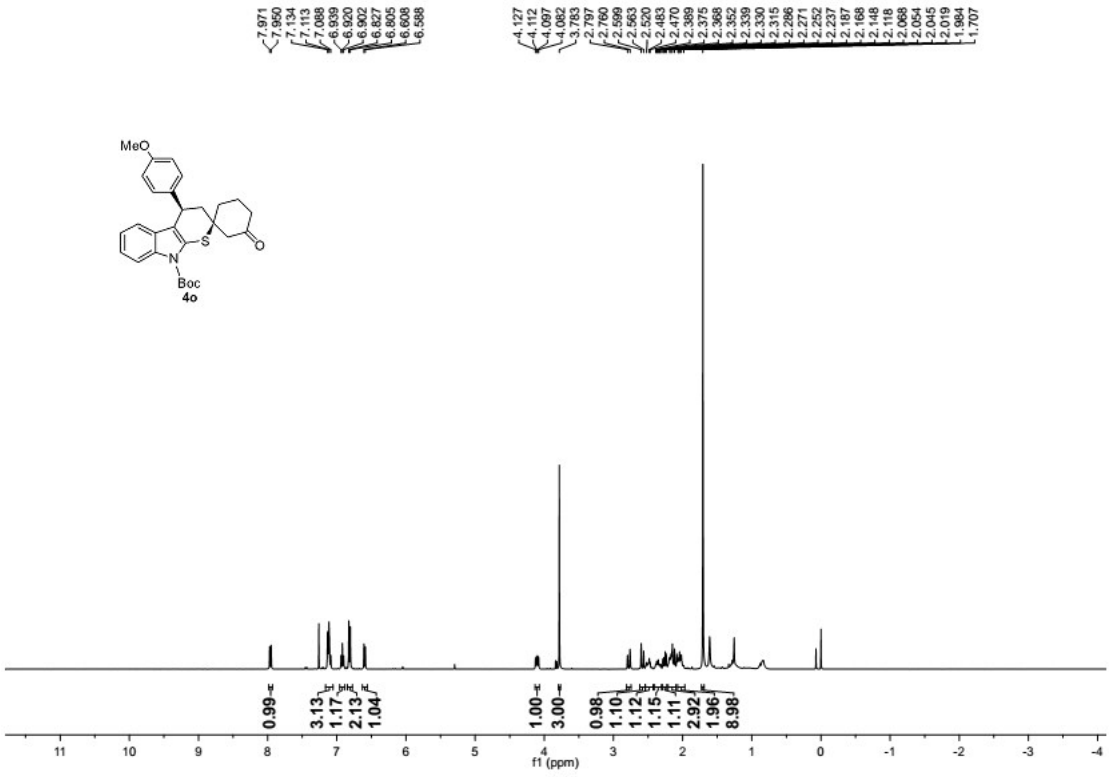


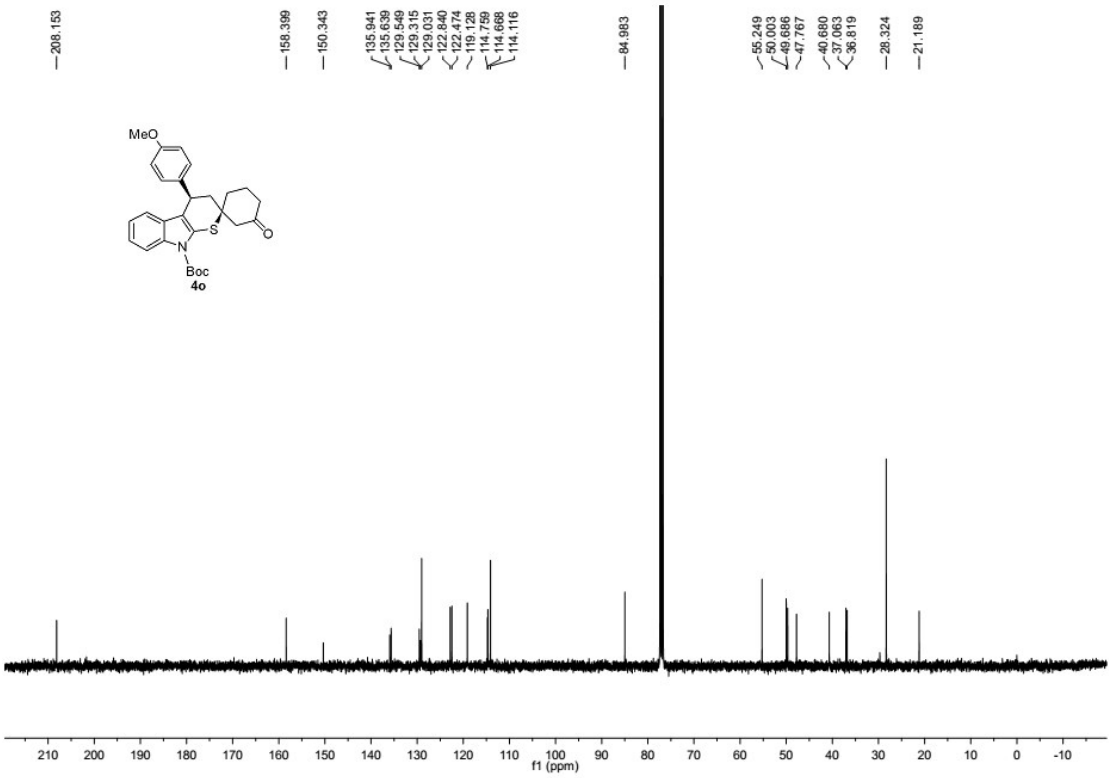
4n: *tert*-Butyl (1*R*,4'*R*)-4'-(4-bromophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



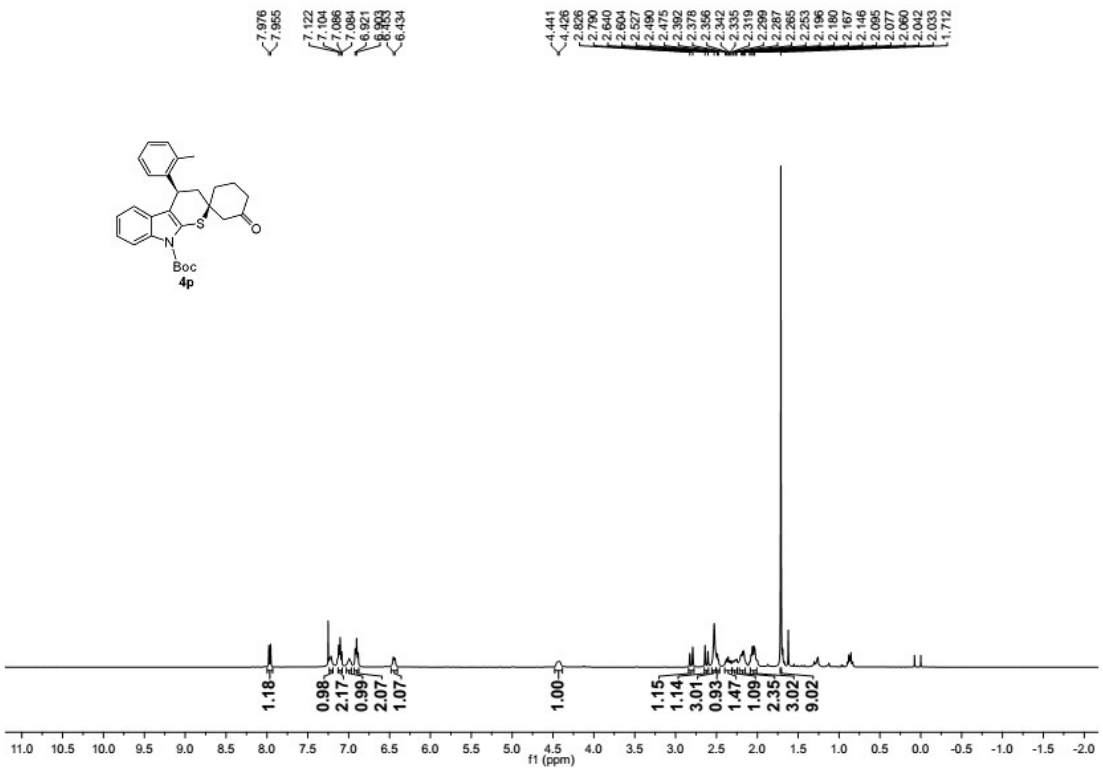


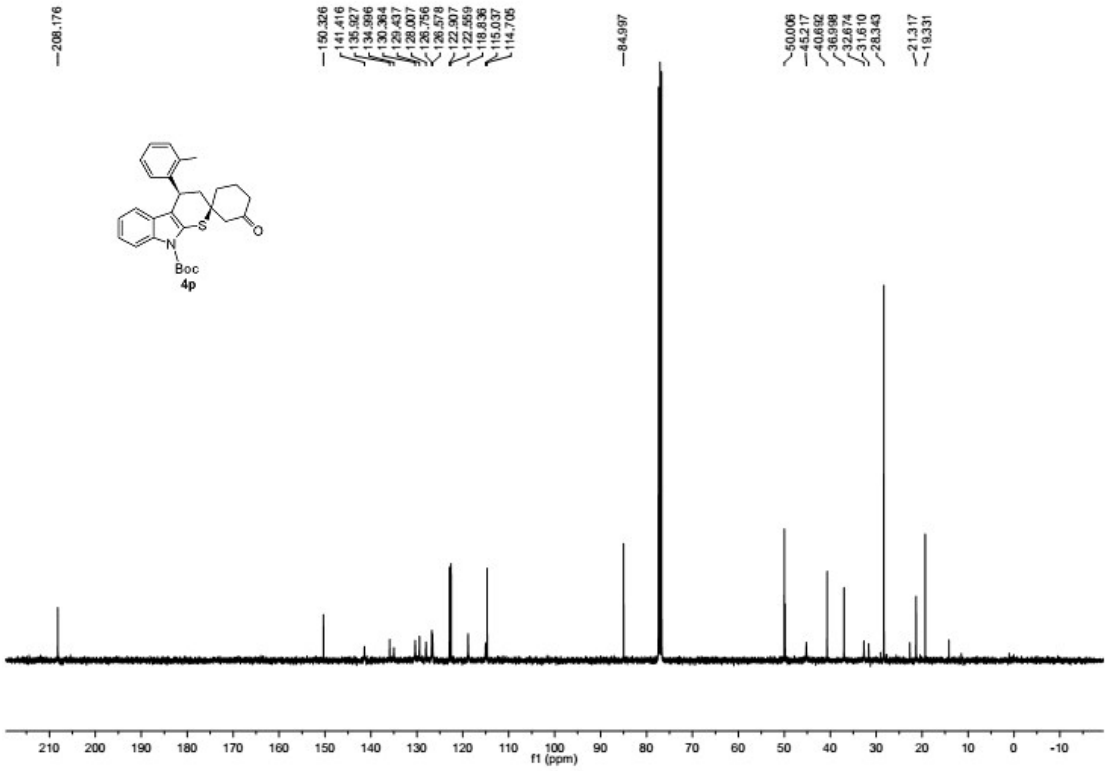
4o: *tert*-Butyl (1*R*,4'*R*)-4'-(4-methoxyphenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



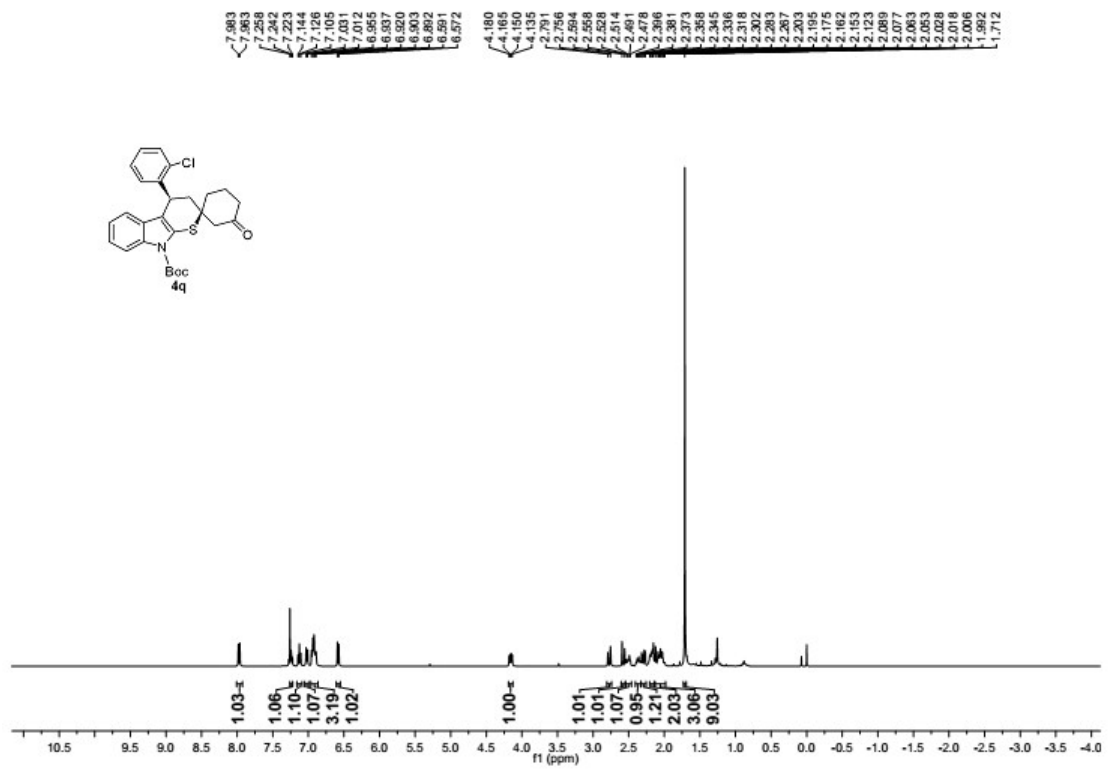


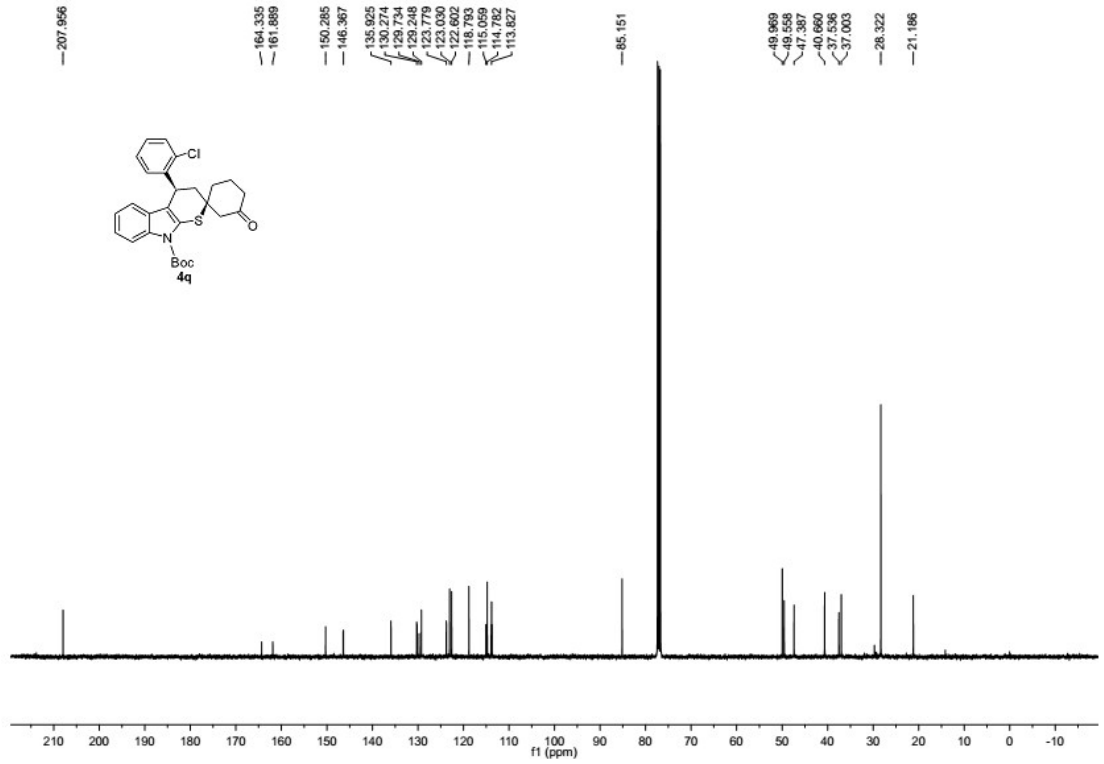
4p: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-(*o*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



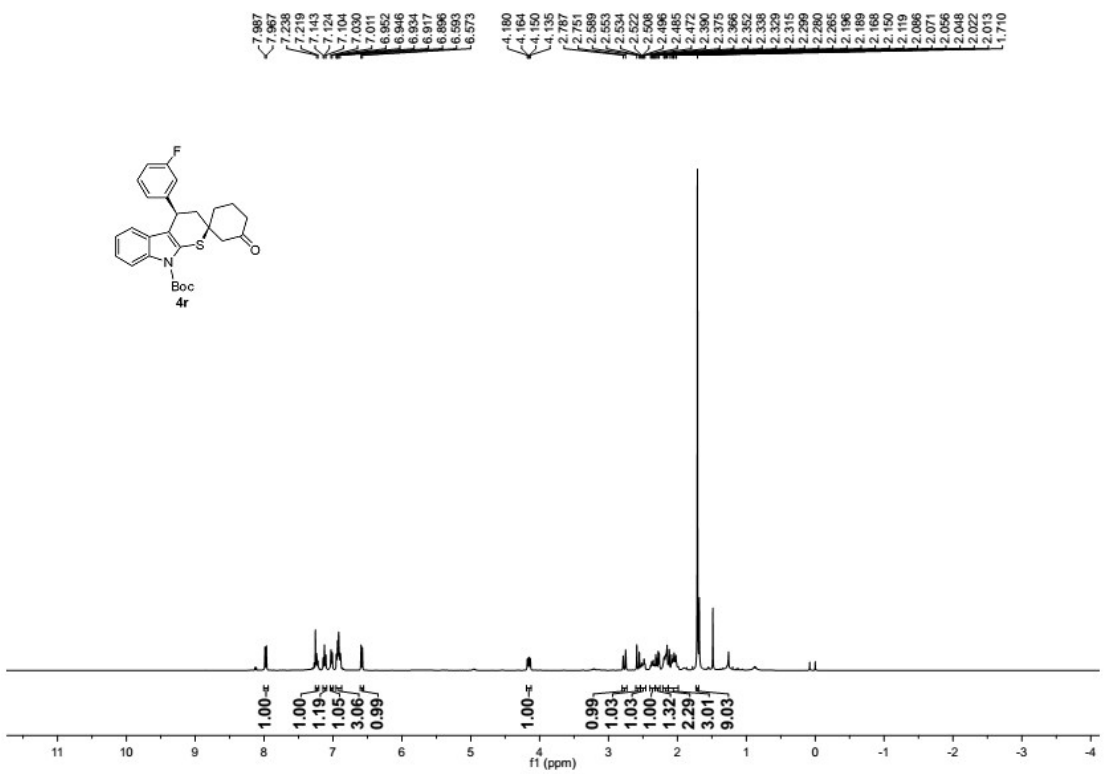


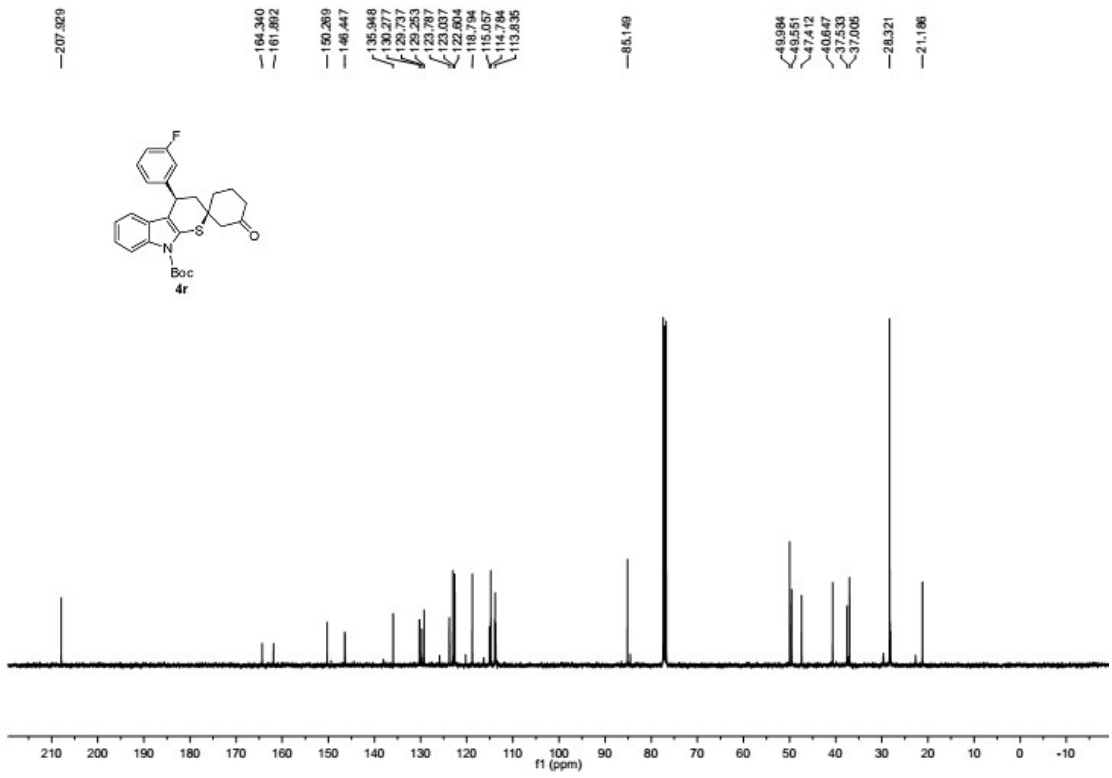
4q: *tert*-Butyl (1*R*,4'*S*)-4'-(2-chlorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



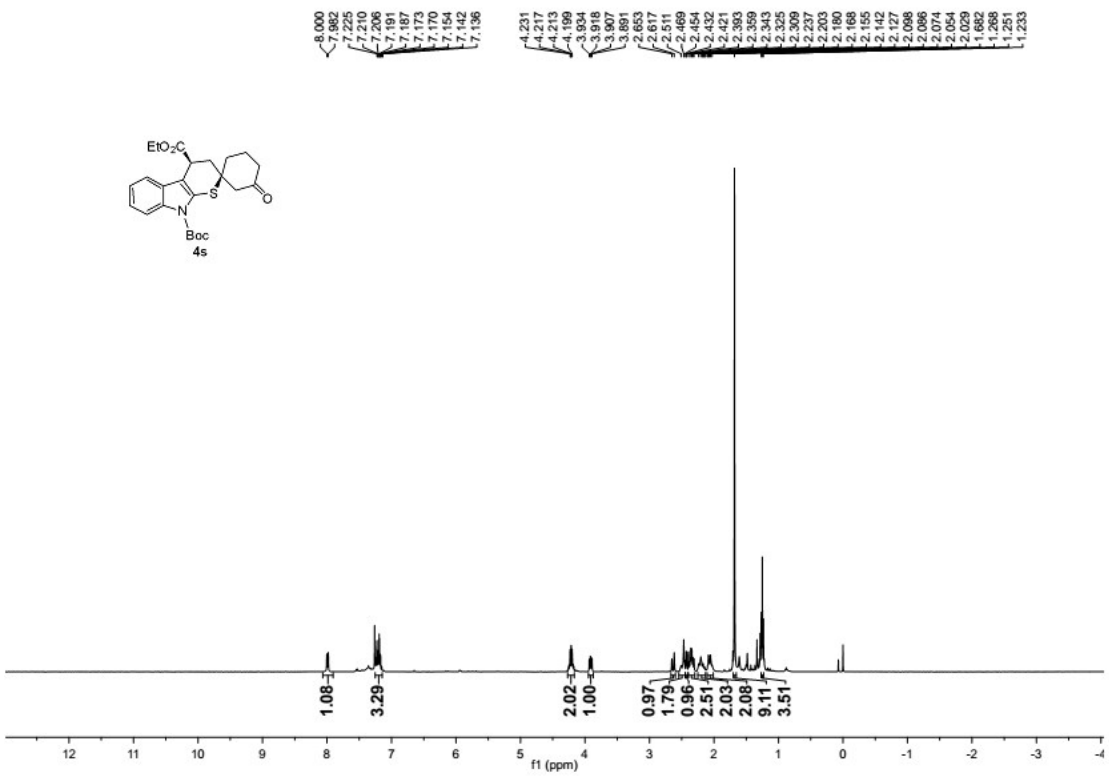


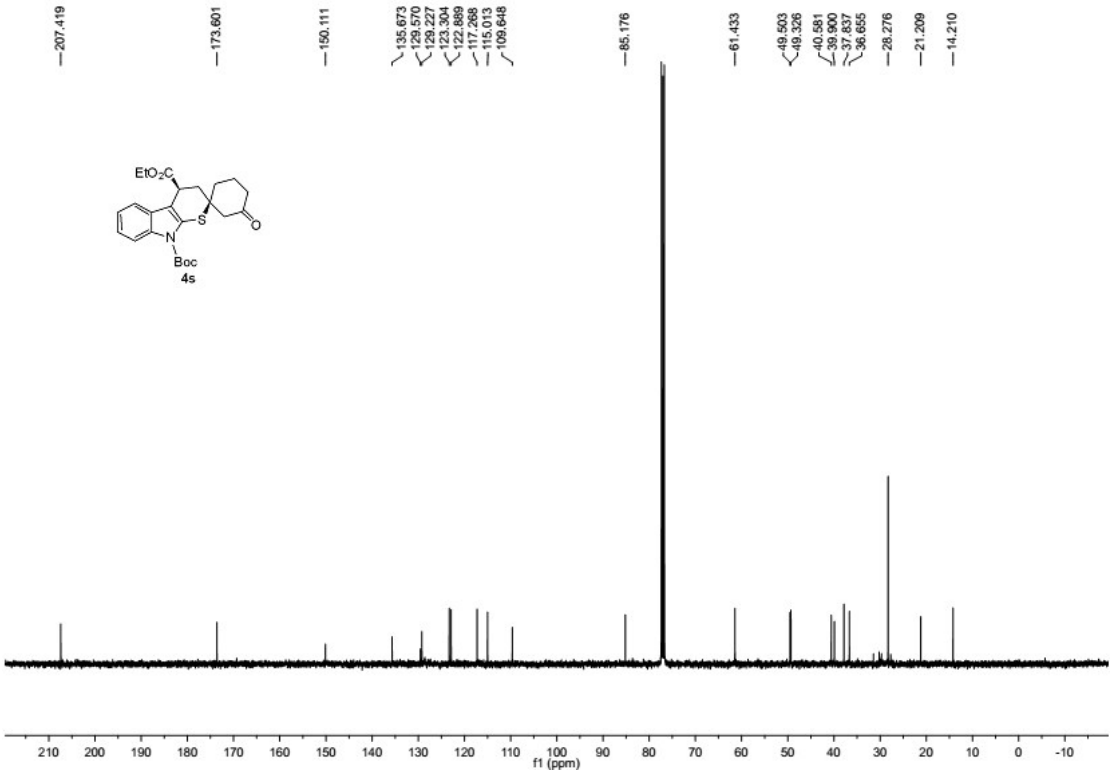
4r: *tert*-Butyl (1*R*,4'*R*)-4'-(3-fluorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



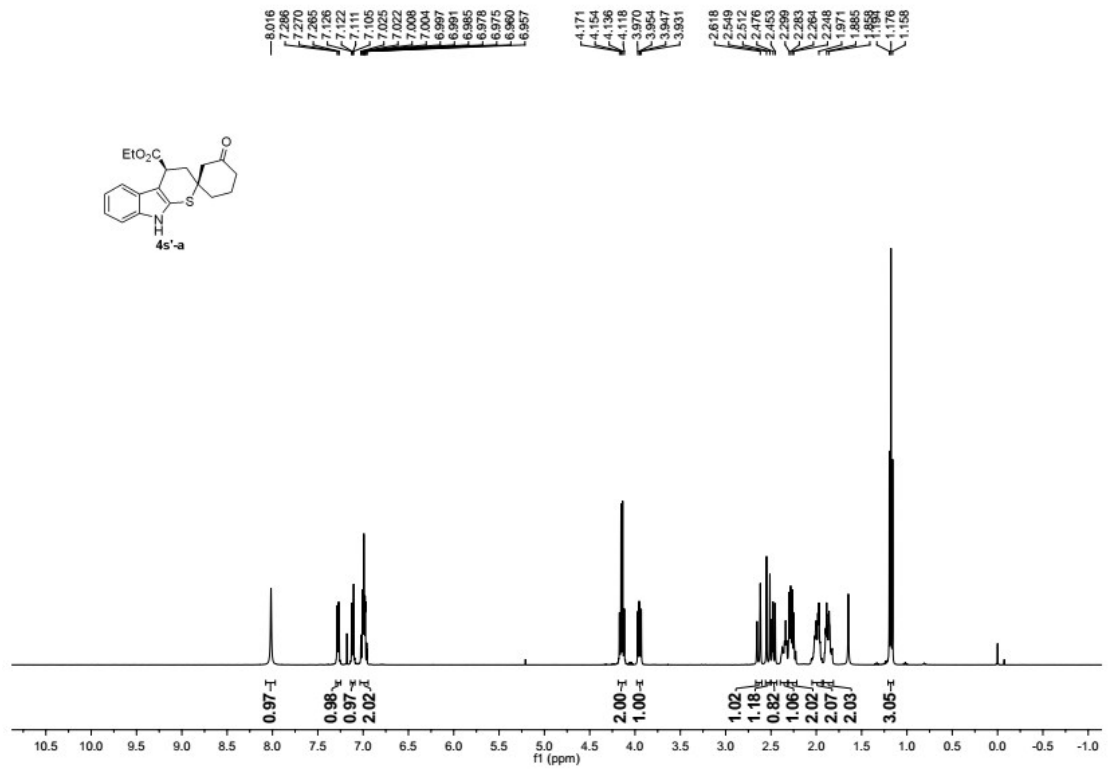


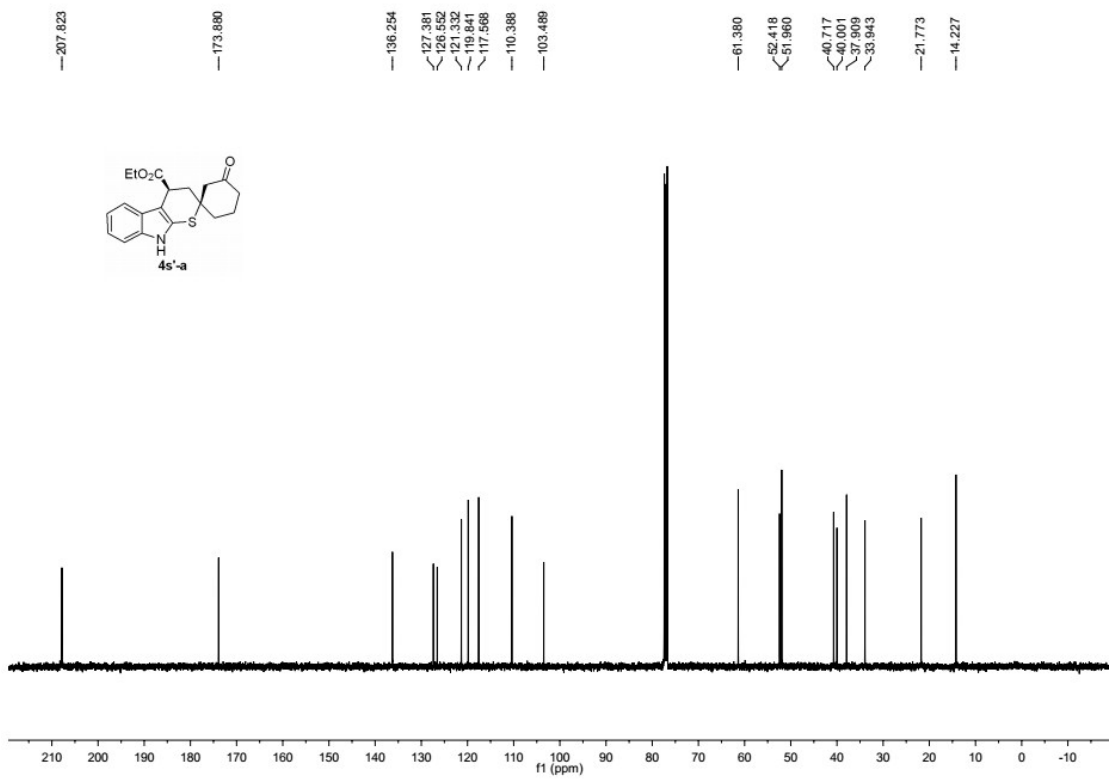
4s: *tert*-Butyl (1*R*,4'*S*)-9'-4'-ethyl-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4',9'(4'*H*)-dicarboxylate



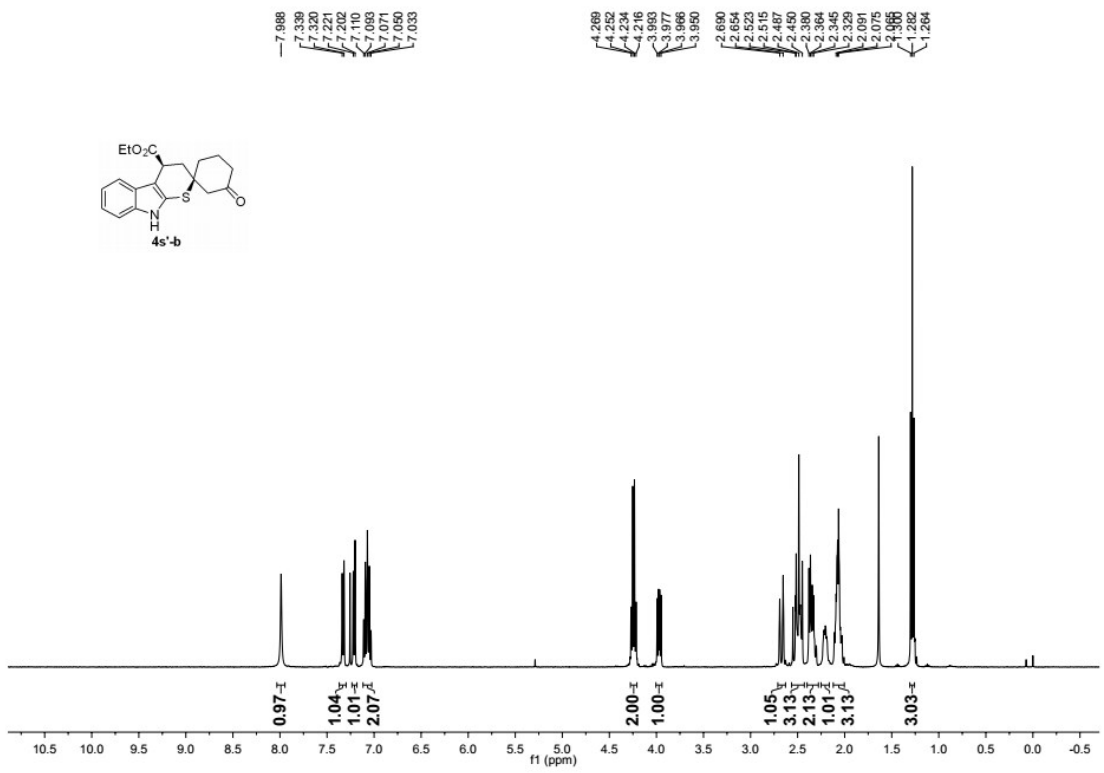


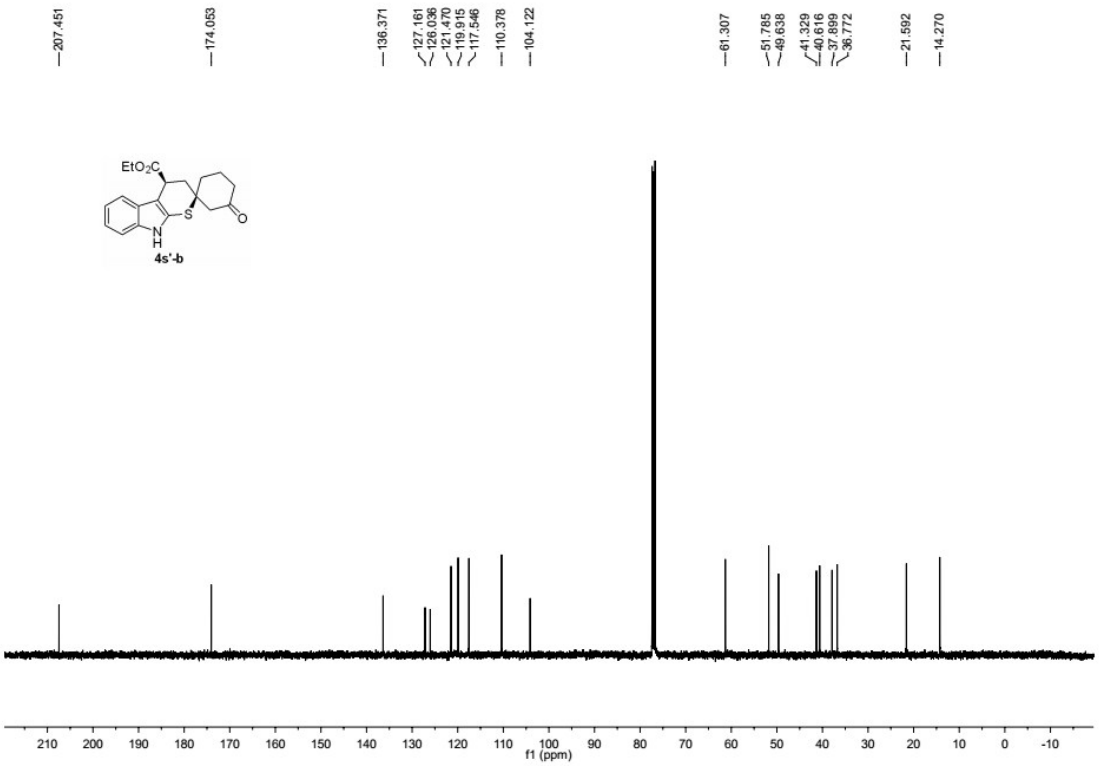
4s'-a: (1*S*,4'*S*)-ethyl-3-oxo-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4'-carboxylate



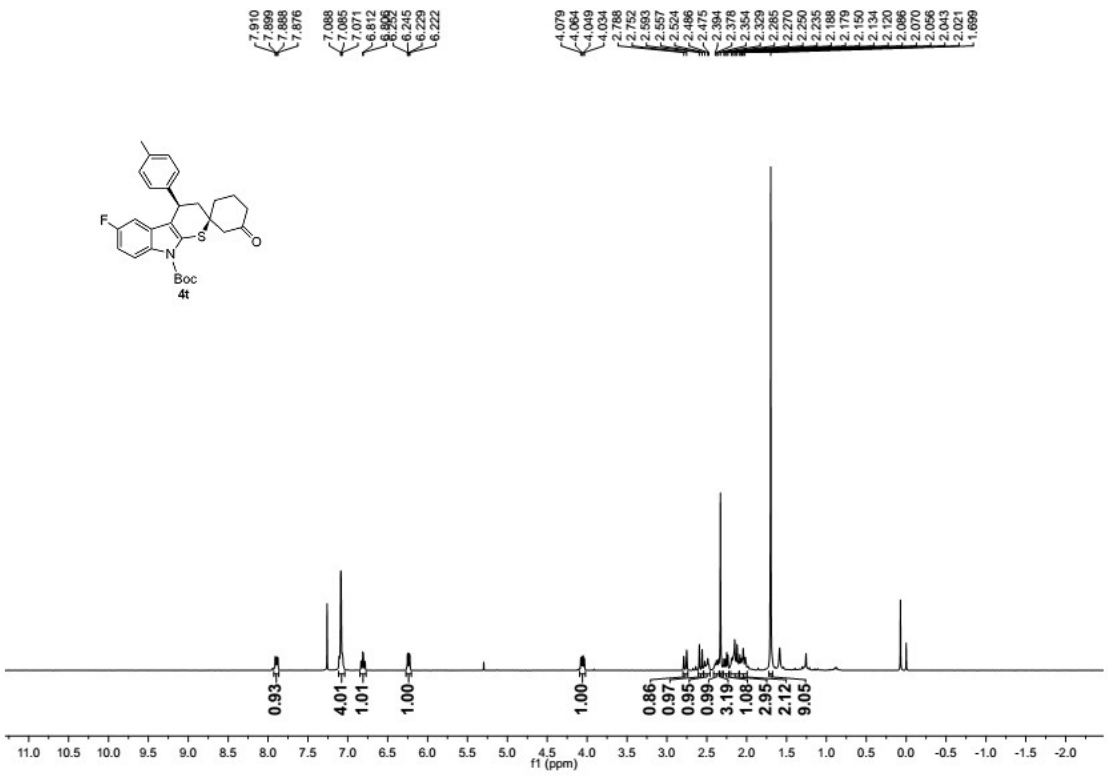


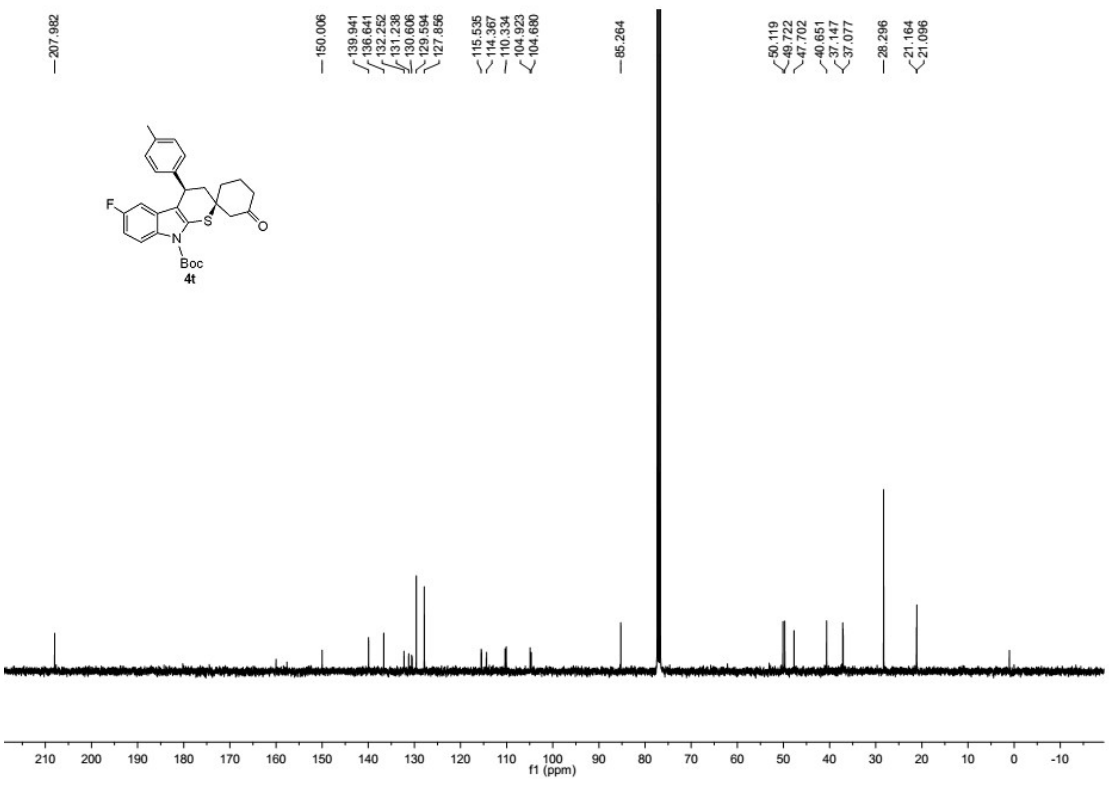
4s'-b: (1*S*,4'*S*)-ethyl-3-oxo-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4'-carboxylate



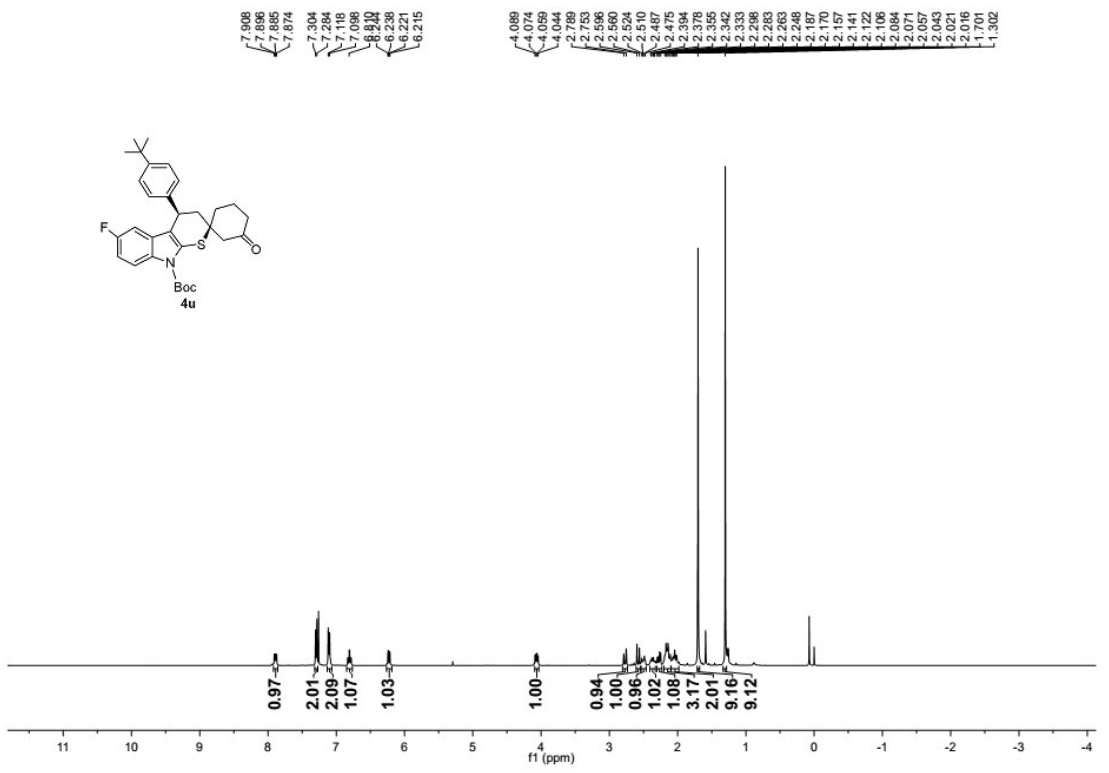


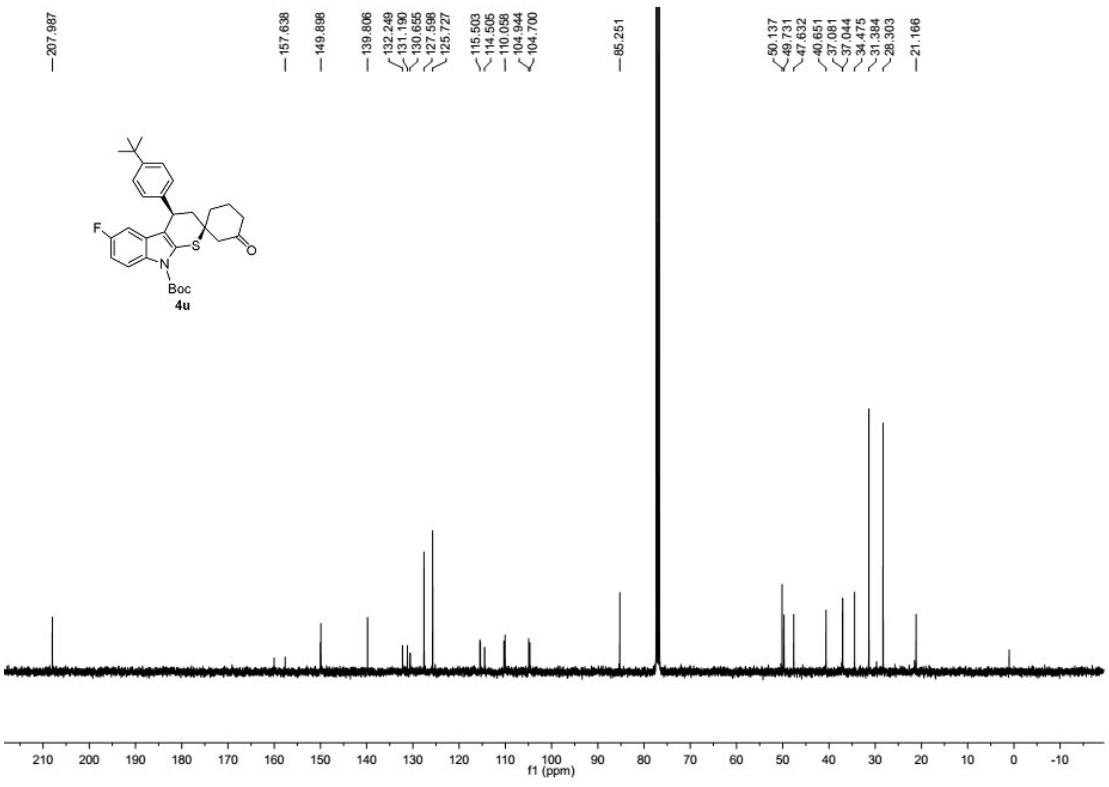
4t: *tert*-Butyl (1*R*,4'*R*)-6'-fluoro-3-oxo-4'-(*p*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



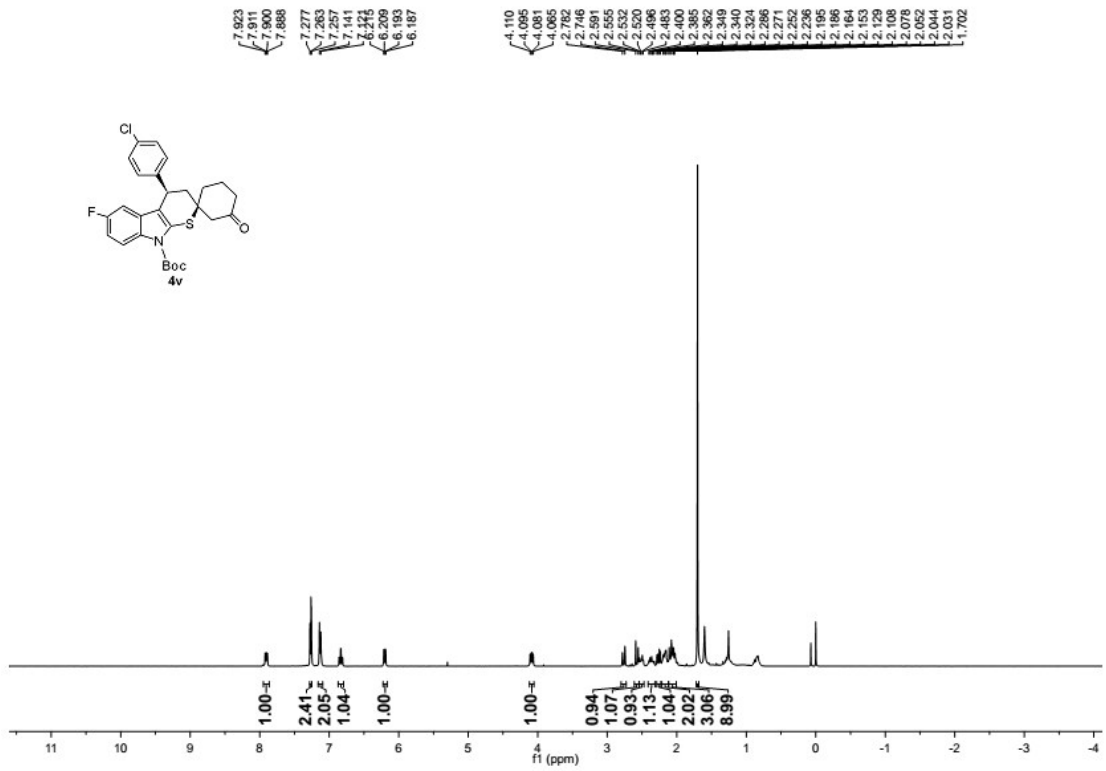


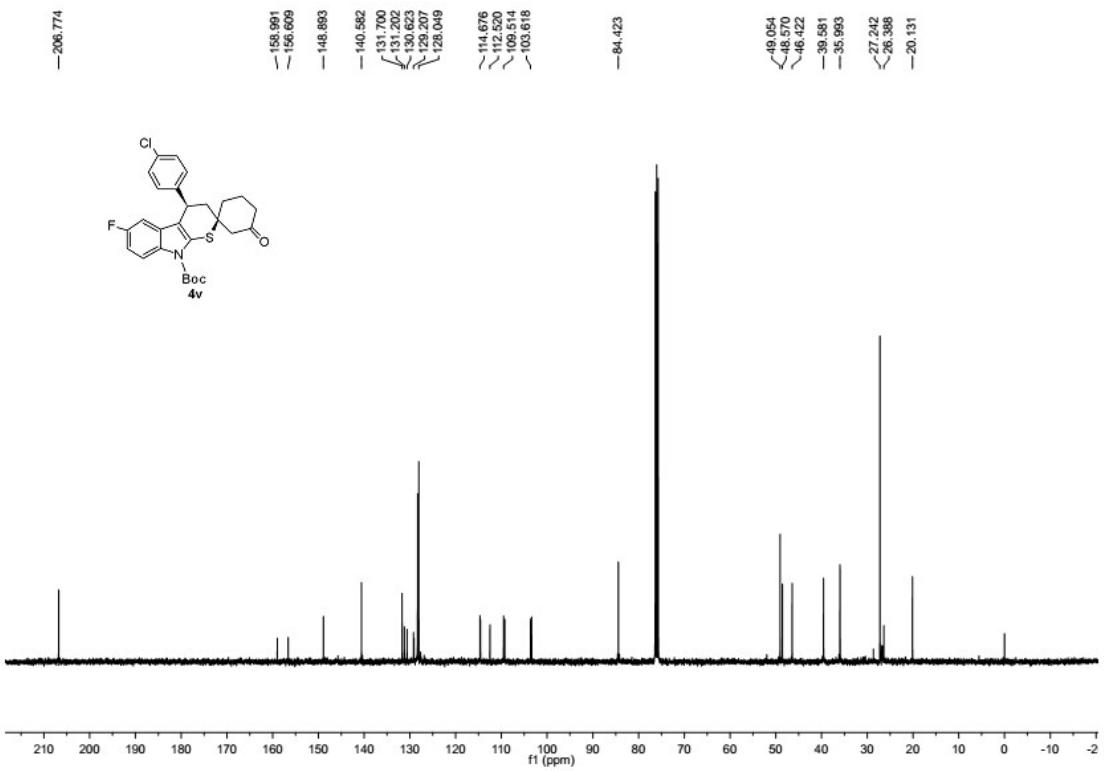
4u: *tert*-Butyl (1*R*,4'*R*)-4'-(4-(*tert*-butyl)phenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



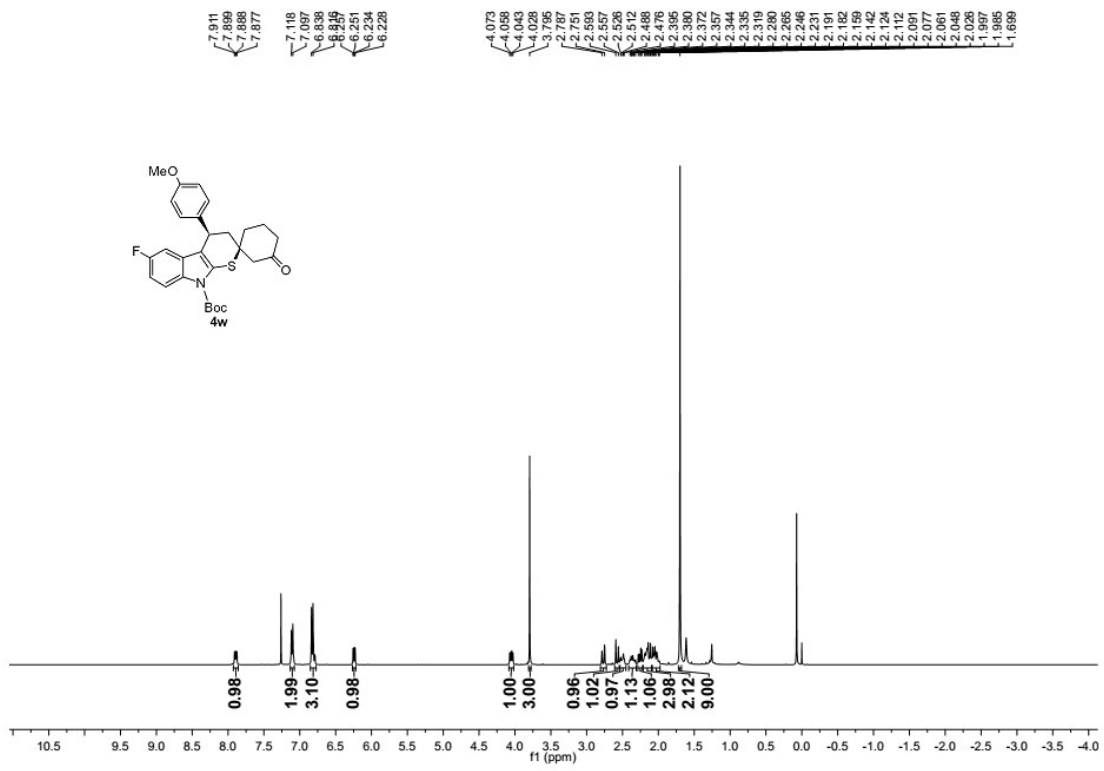


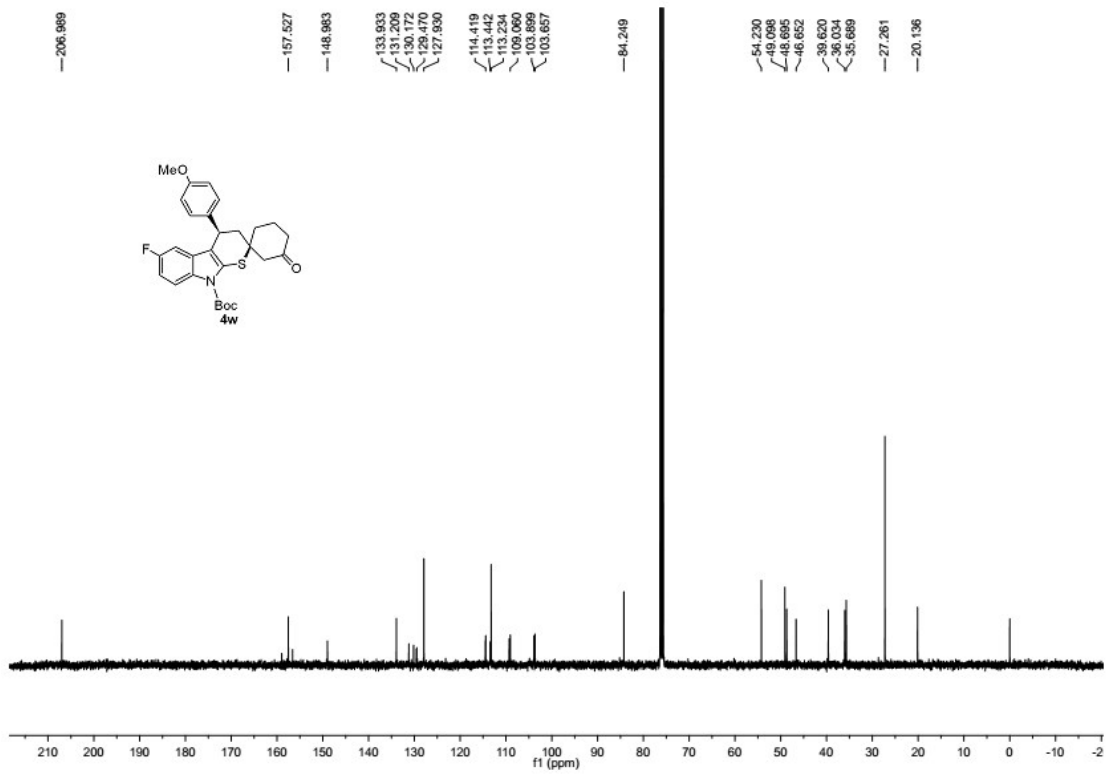
4v: *tert*-Butyl (1*R*,4'*R*)-4'-(4-chlorophenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate



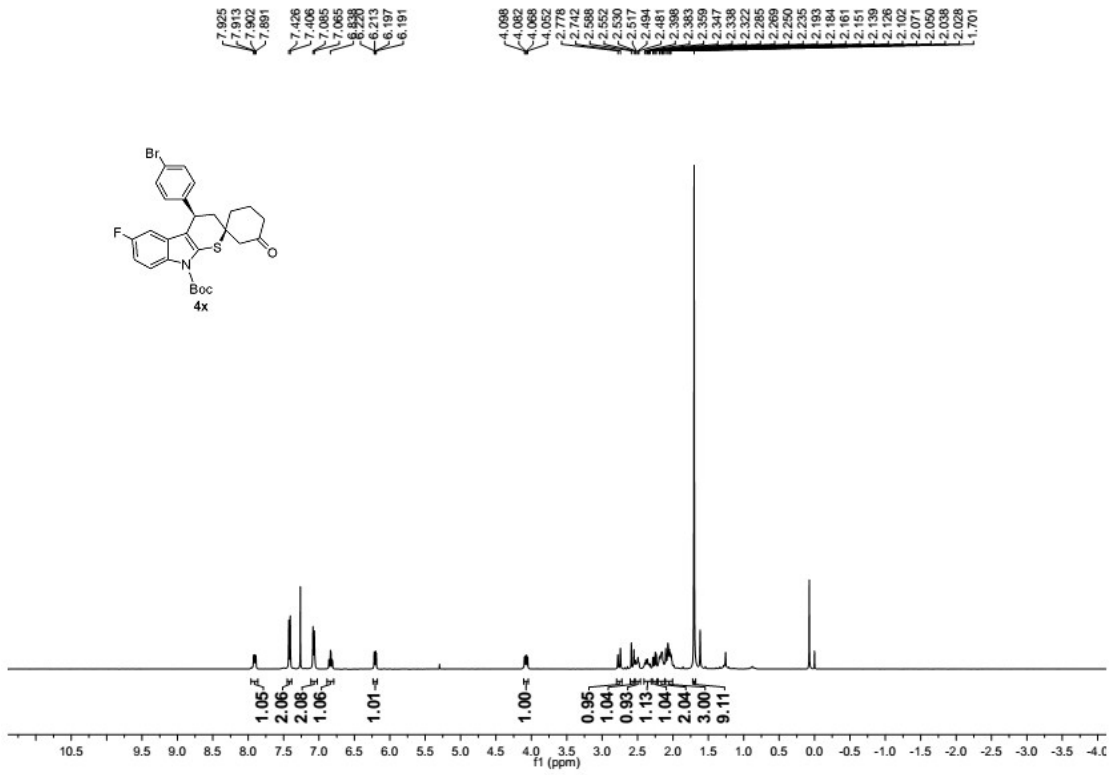


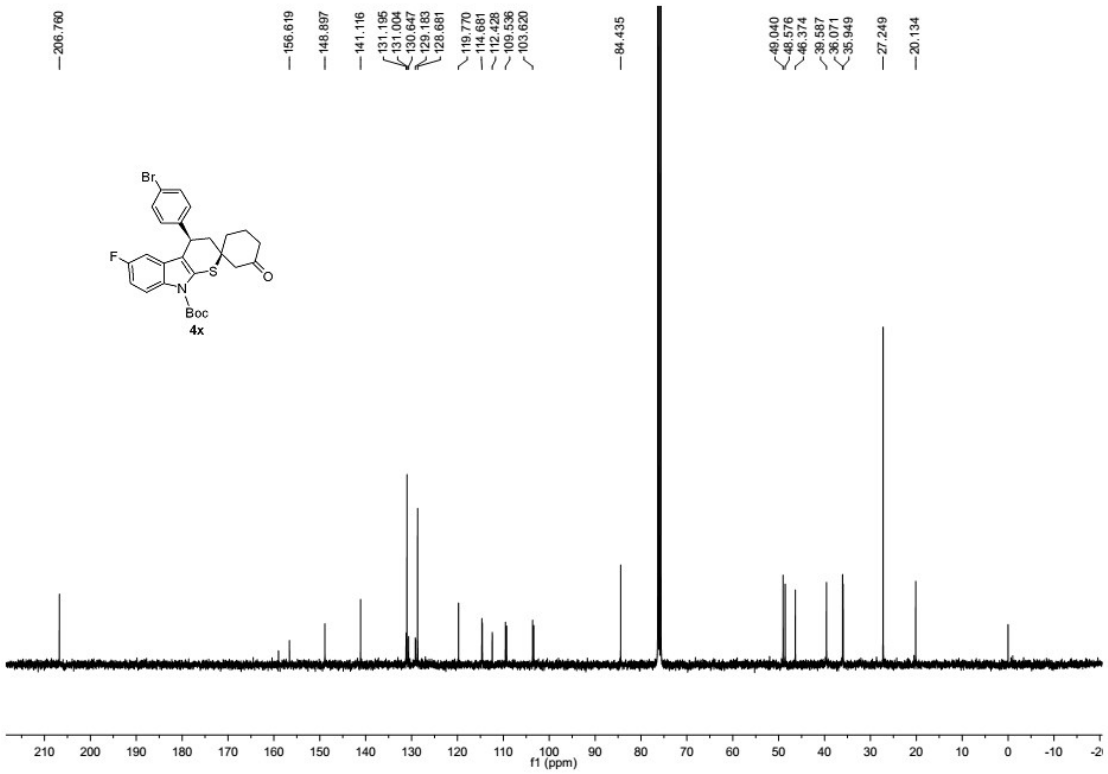
4w: *tert*-Butyl (1*R*,4'*R*)-6'-fluoro-4'-(4-methoxyphenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate





4x: *tert*-Butyl (1*R*,4'*R*)-4'-(4-bromophenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

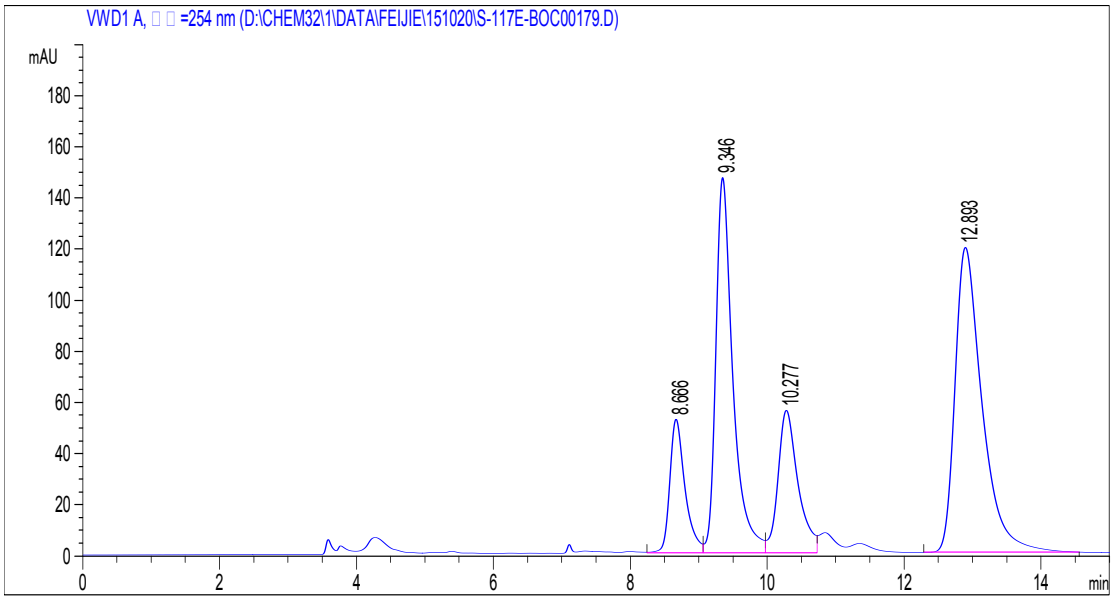




F: HPLC Charts of the Products.

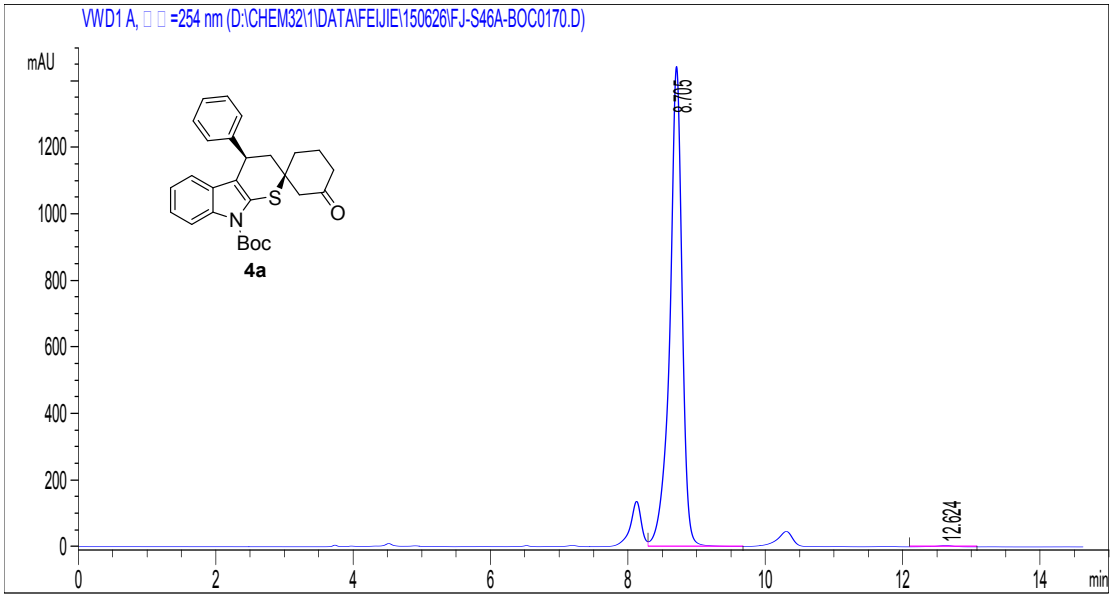
4a: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IA column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)

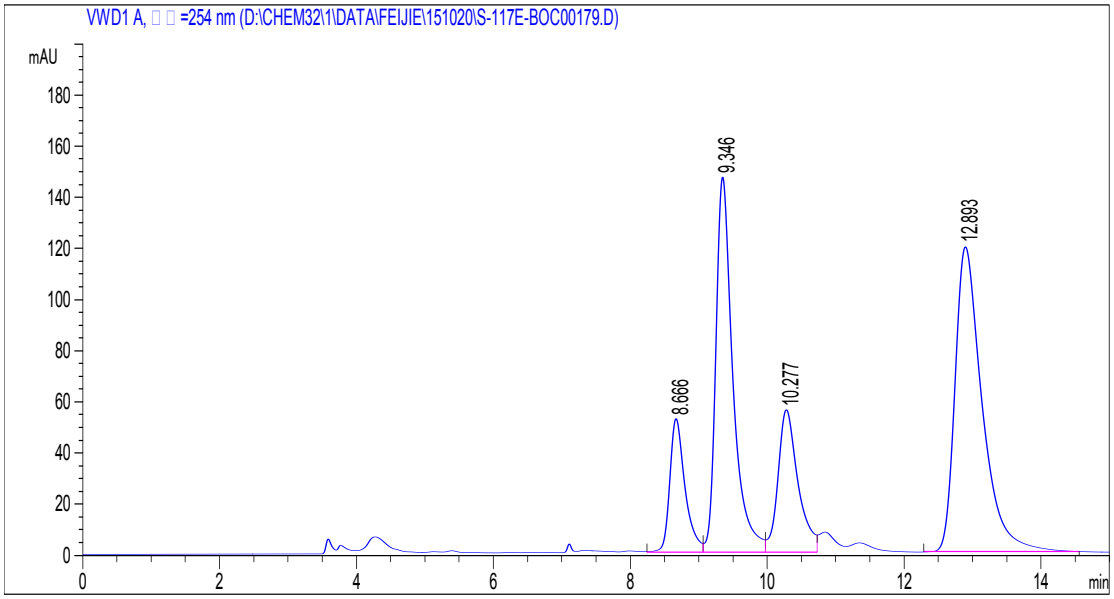
1	8.666	812.3	52.3	0.2305	0.663	10.461
2	9.346	2537.2	146.8	0.2555	0.612	32.676
3	10.277	1135.3	55.8	0.3002	0.681	14.621
4	12.893	3279.8	119.3	0.408	0.572	42.241



#	Time	Area	Height	Width	Symmetry	Area (%)
1	8.705	18039.2	1444.9	0.1835	1.19	99.559
2	12.624	79.9	4.1	0.2822	1.327	0.441

The scale-up HPLC Chart of **4a**

[IA column, 254 nm, *n*-Hexane/ *i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	8.666	812.3	52.3	0.2305	0.663	10.461
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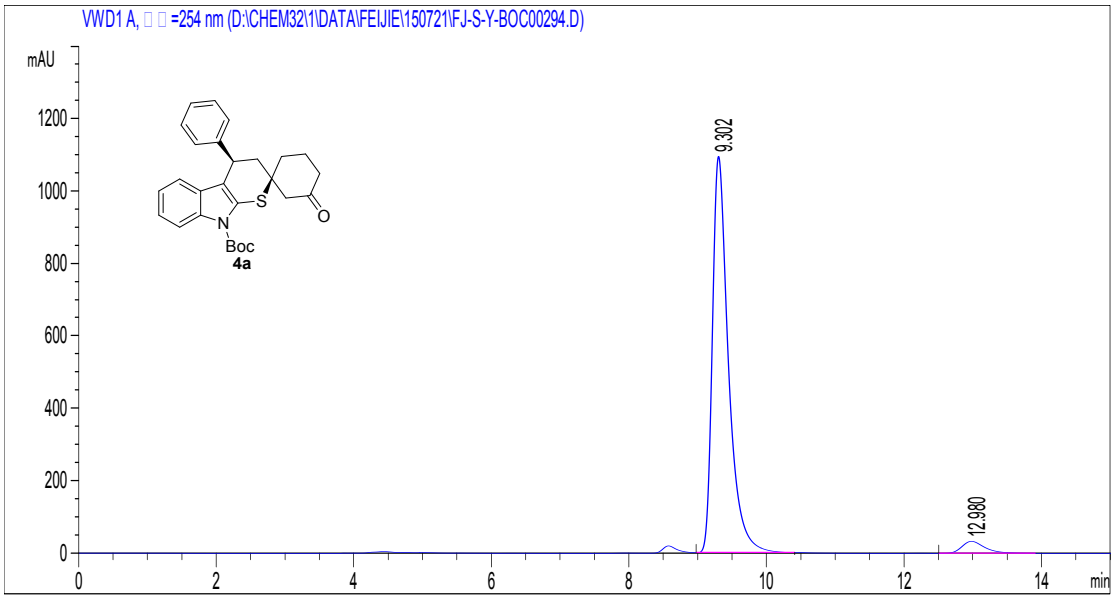
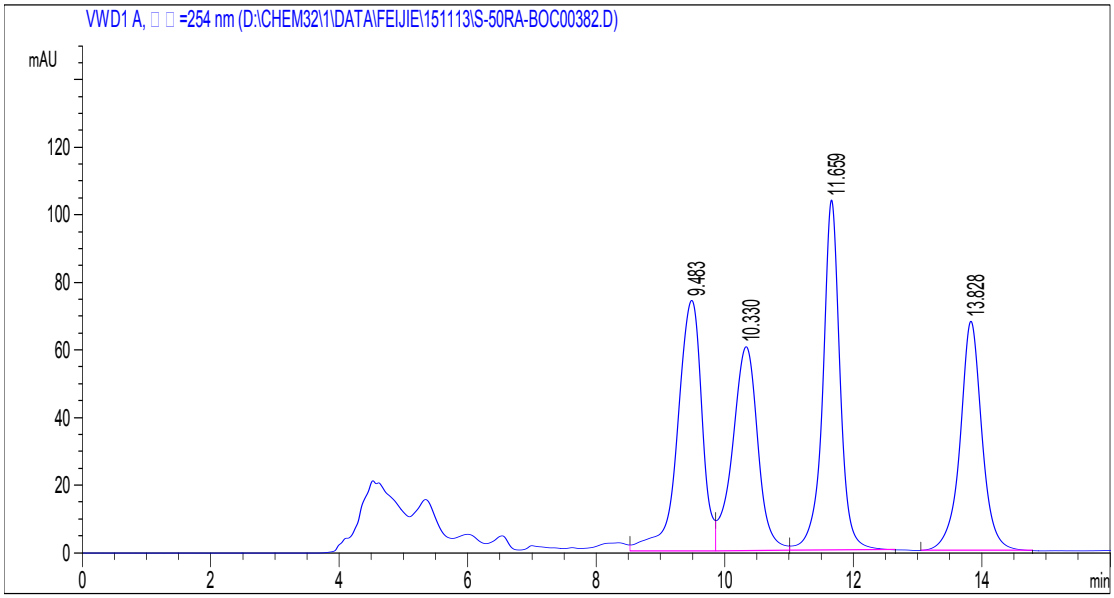
3	10.277	1135.3	55.8	0.3002	0.681	14.621
4	12.893	3279.8	119.3	0.408	0.572	42.241



#	Time	Area	Height	Width	Symmetry	Area (%)
1	9.302	17759.2	1096.1	0.2414	0.576	95.810
2	12.98	776.6	33.3	0.351	0.668	4.190

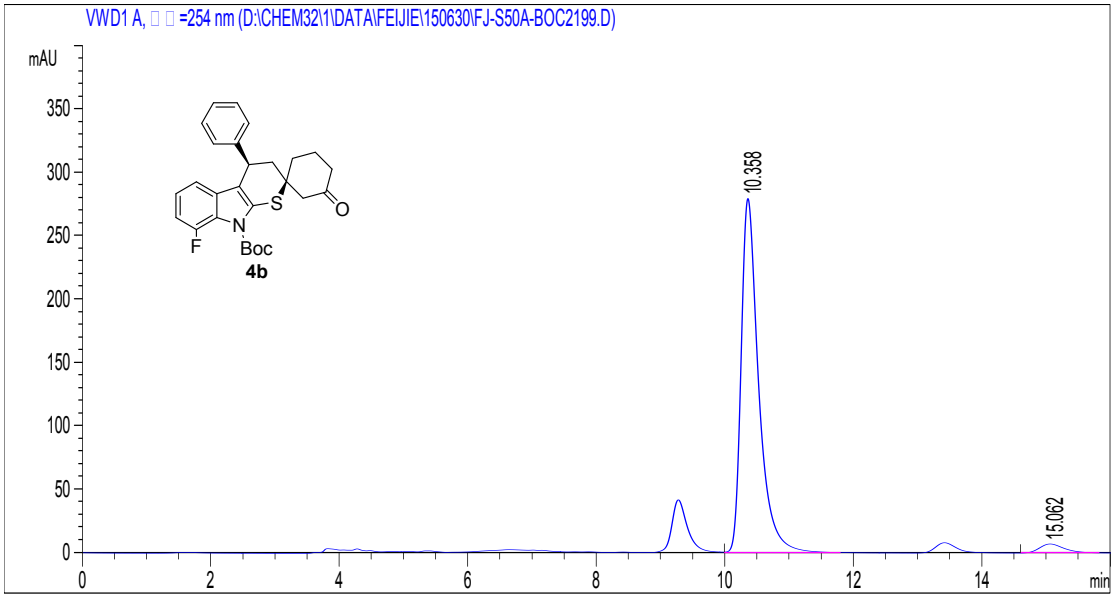
4b: *tert*-Butyl (1*R*,4'*R*)-8'-fluoro-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IA column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	9.483	1965.2	74.2	0.4154	1.376	27.473
2	10.33	1649.9	60.4	0.4193	1.116	23.065
3	11.659	1937.5	103.7	0.2777	1.004	27.085

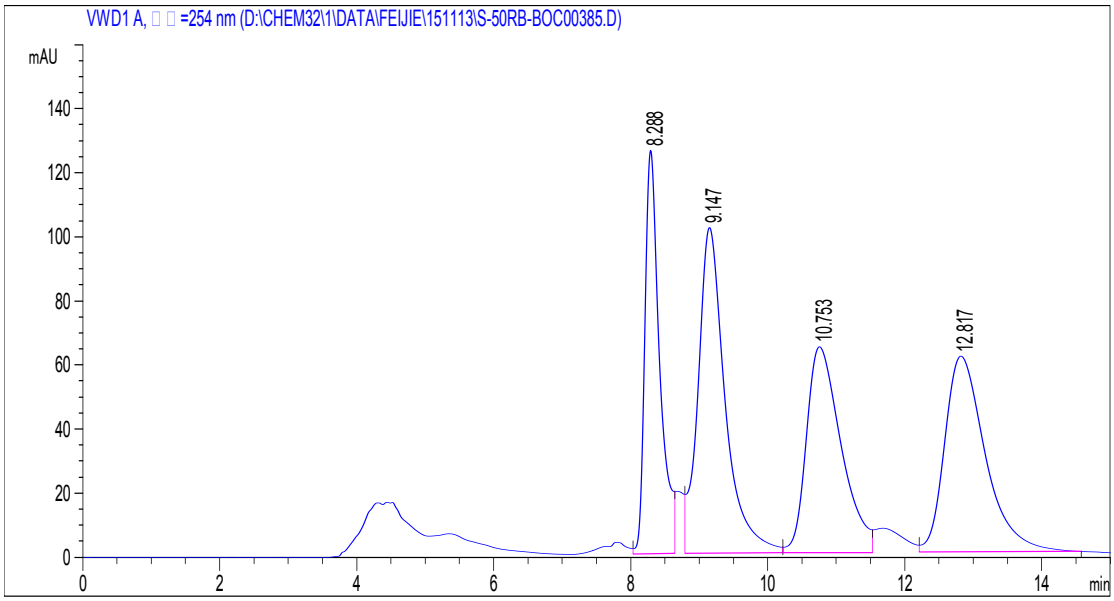
4	13.828	1600.7	67.9	0.3509	0.955	22.376



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.358	5294.1	279.5	0.2821	0.583	96.513
2	15.062	191.3	7.1	0.4048	0.705	3.487

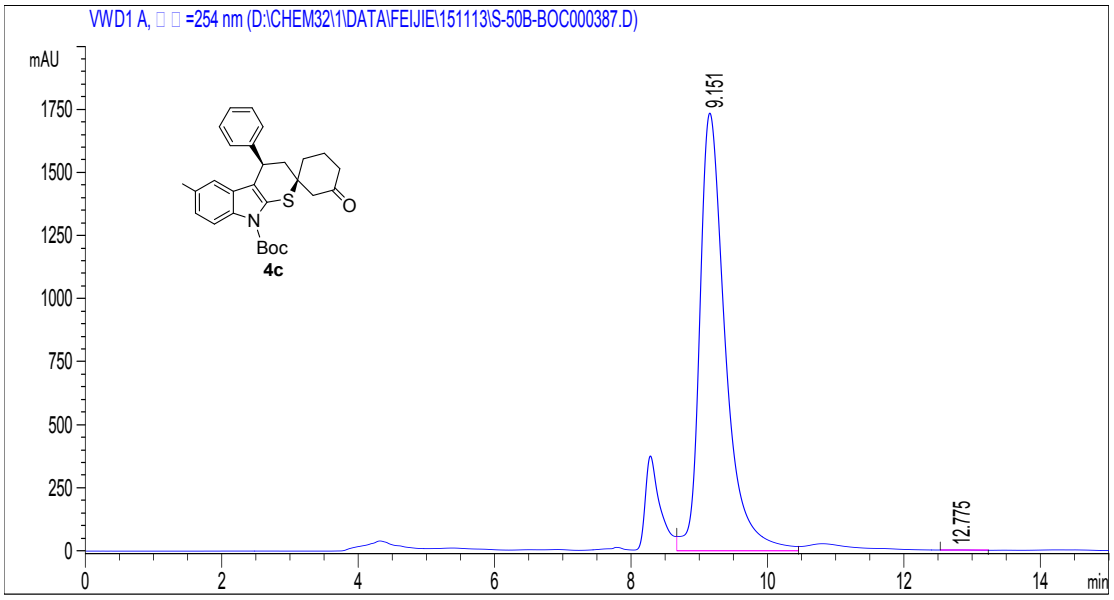
4c: *tert*-Butyl (1*R*,4'*R*)-6'-methyl-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	8.288	1889.9	126	0.2216	0.59	19.908
2	9.147	2797.1	101.8	0.4035	0.674	29.464
3	10.753	2271.7	64.4	0.5367	0.582	23.929

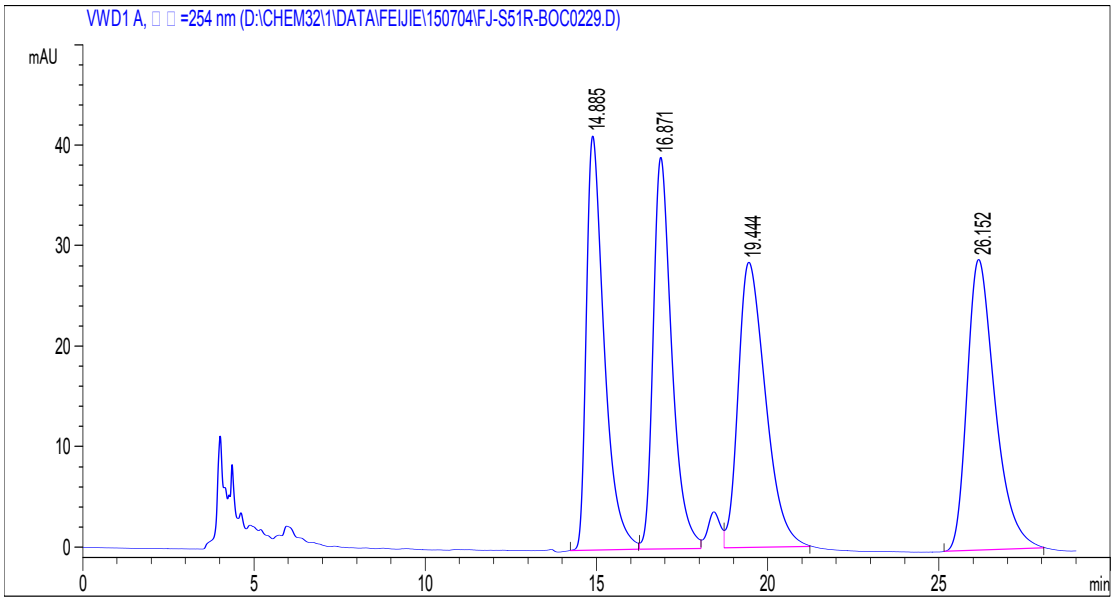
4	12.817	2534.5	61.3	0.6327	0.625	26.698



#	Time	Area	Height	Width	Symmetry	Area (%)
1	9.151	45001.7	1735.5	0.3913	0.606	99.796
2	12.775	92.2	2.6	0.4504	0.636	0.204

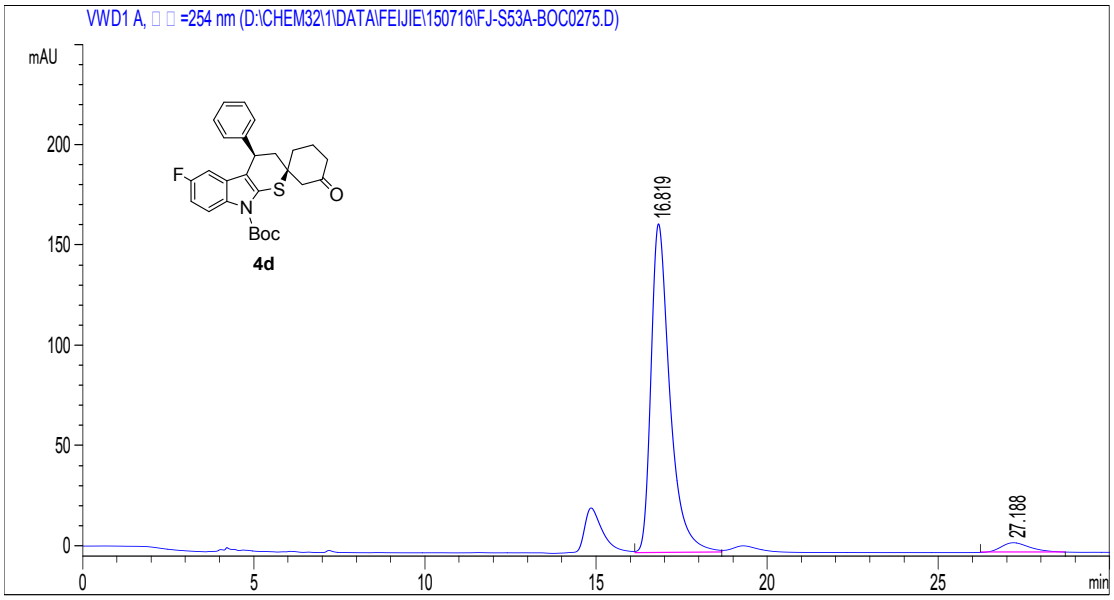
4d: *tert*-Butyl (1*R*,4'*R*)-6'-methoxy-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 50/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	14.885	1498.9	41.2	0.539	0.515	24.205
2	16.871	1473.9	39	0.5718	0.638	23.801
3	19.444	1573.4	28.4	0.8513	0.607	25.408

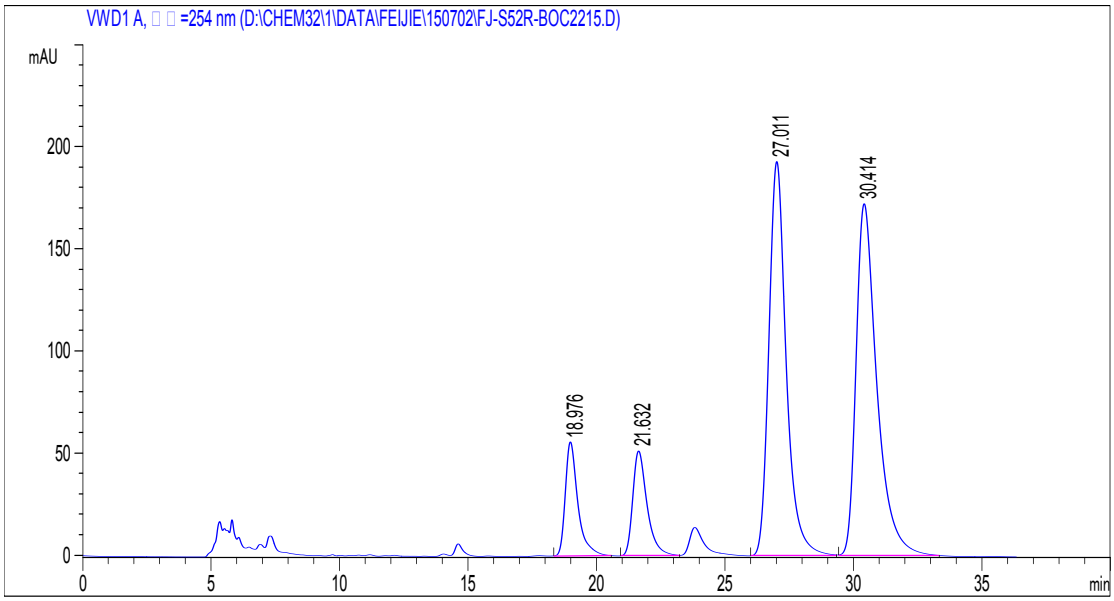
4	26.152	1646.4	29	0.848	0.659	26.586



#	Time	Area	Height	Width	Symmetry	Area (%)
1	16.819	6293	164	0.5743	0.606	95.642
2	27.188	286.7	4.8	0.8182	0.7	4.358

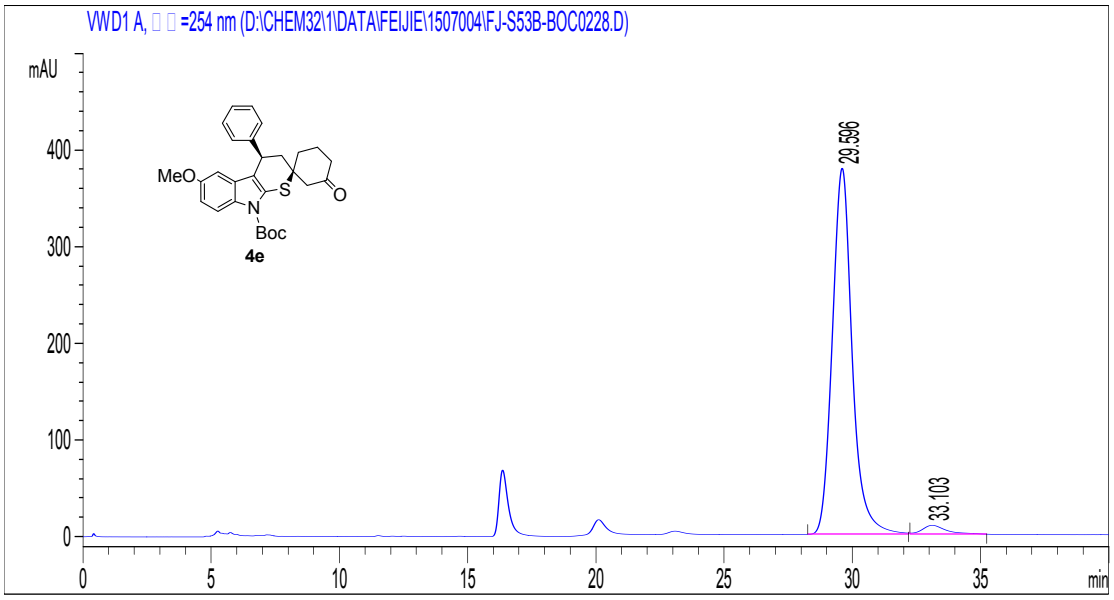
4e: *tert*-Butyl (1*R*,4'*R*)-6'-methoxy-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	18.976	1908.9	55.9	0.5046	0.629	8.423
2	21.632	1988.8	51.4	0.5828	0.642	8.775
3	27.011	9055.8	193	0.7075	0.772	39.957

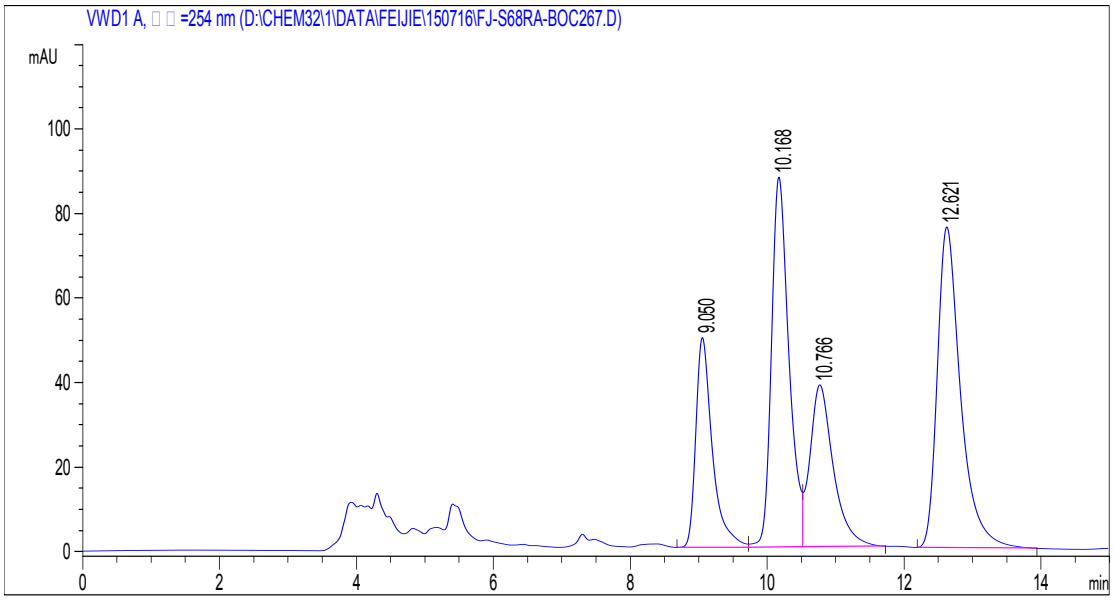
4	30.414	9710.3	172.4	0.8261	0.589	42.845



#	Time	Area	Height	Width	Symmetry	Area (%)
1	29.596	20406.6	378.9	0.8206	0.901	97.051
2	33.103	620.1	9.3	0.945	0.649	2.949

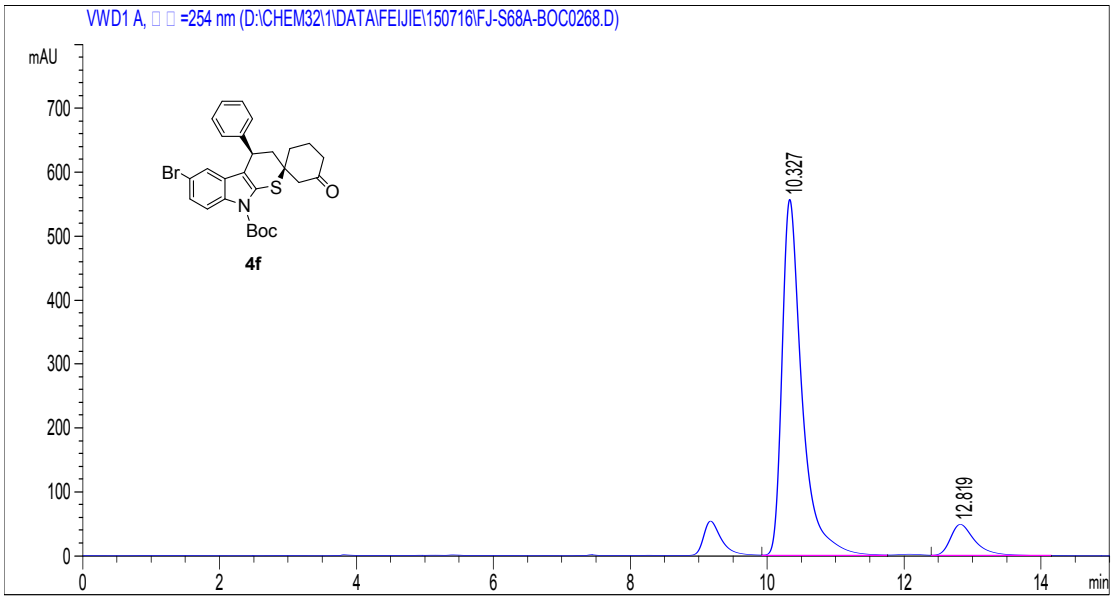
4f: *tert*-Butyl (1*R*,4'*R*)-6'-bromo-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	9.05	838.2	49.7	0.2505	0.604	16.442
2	10.168	1557	87.5	0.2672	0.702	30.541
3	10.766	909.8	38.3	0.3498	0.67	17.847

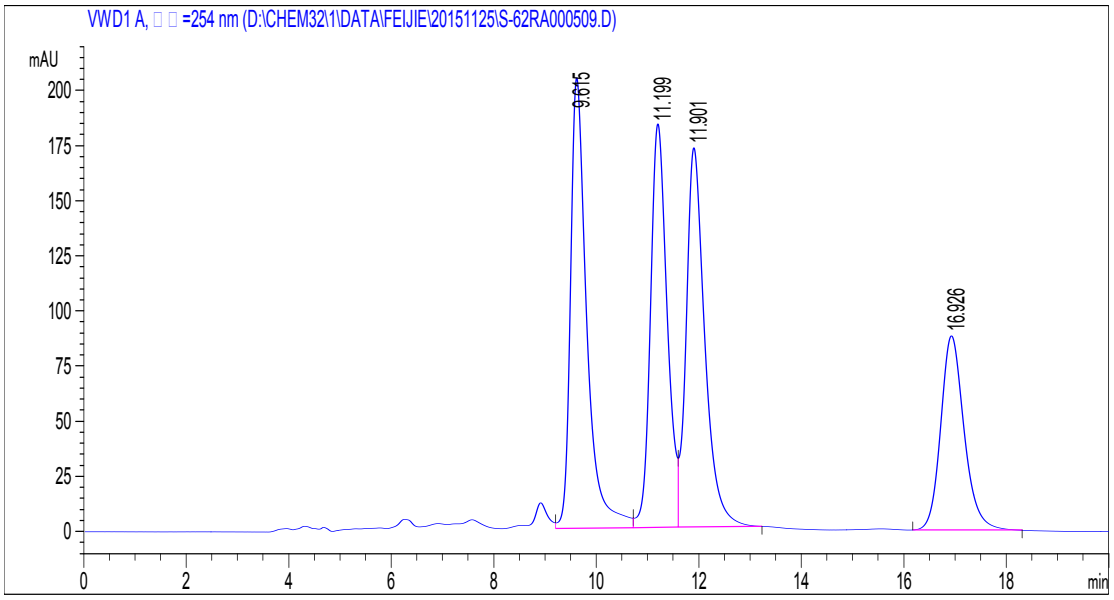
4	12.621	1792.9	75.9	0.3543	0.633	35.170



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.327	11294.8	557.3	0.3005	0.574	90.083
2	12.819	1243.5	49	0.3774	0.619	9.917

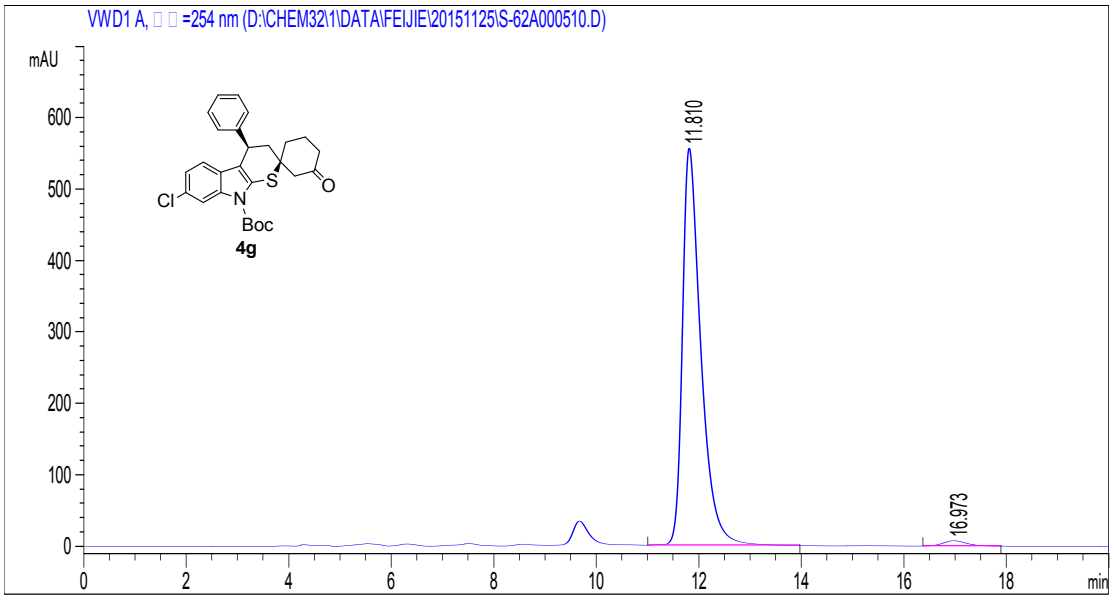
4g: *tert*-Butyl (1*R*,4'*R*)-7'-chloro-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IB column, 254 nm, *n*-Hexane/*i*PrOH = 7/3, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	9.615	4533.6	204.5	0.3285	0.563	28.644
2	11.199	4144.1	183.2	0.3425	0.777	26.184
3	11.901	4344.7	172.2	0.3745	0.655	27.451

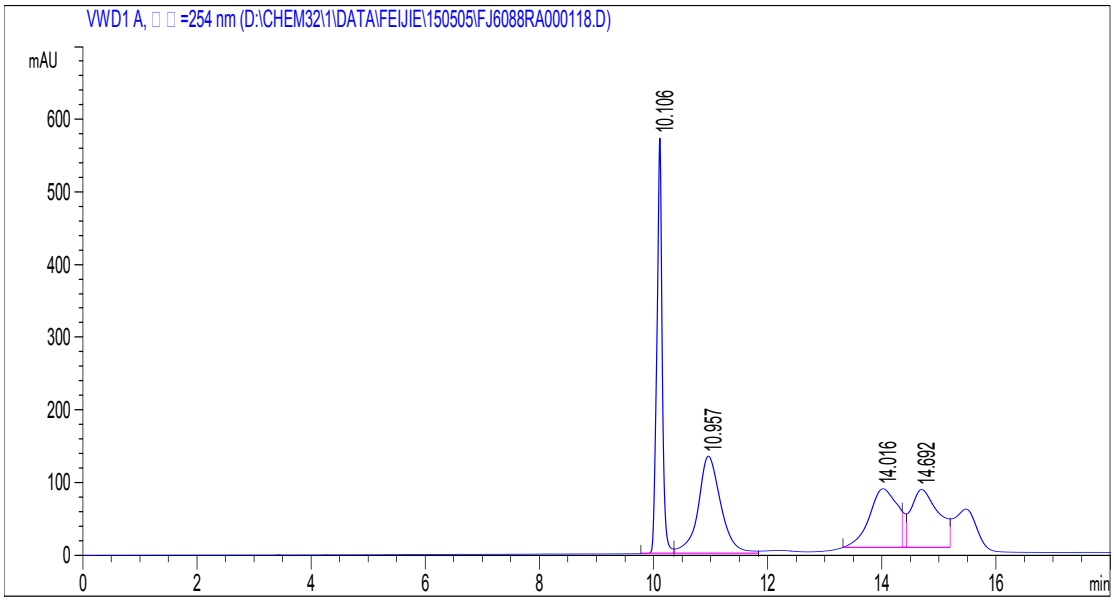
4	16.926	2804.8	88.2	0.4847	0.798	17.722



#	Time	Area	Height	Width	Symmetry	Area (%)
1	11.81	13924.2	556.2	0.3736	0.541	98.288
2	16.973	242.5	7.5	0.495	0.806	1.712

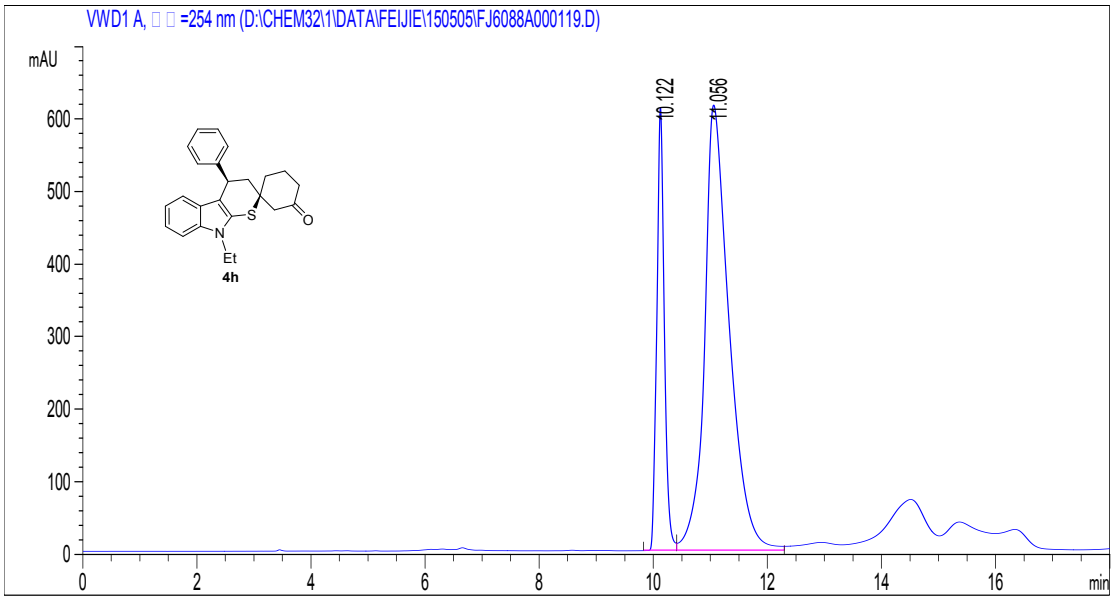
4h: (1*R*,4'*R*)-9'-ethyl-4'-phenyl-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indol]-3-one

[IA column, 254 nm, *n*-Hexane/DCM = 1/1, 1.0 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.106	3688.9	572.5	0.0912	1.123	27.967
2	10.957	3703.5	134.1	0.411	0.816	28.078
3	14.016	2920.8	80.8	0.6028	0.848	22.144

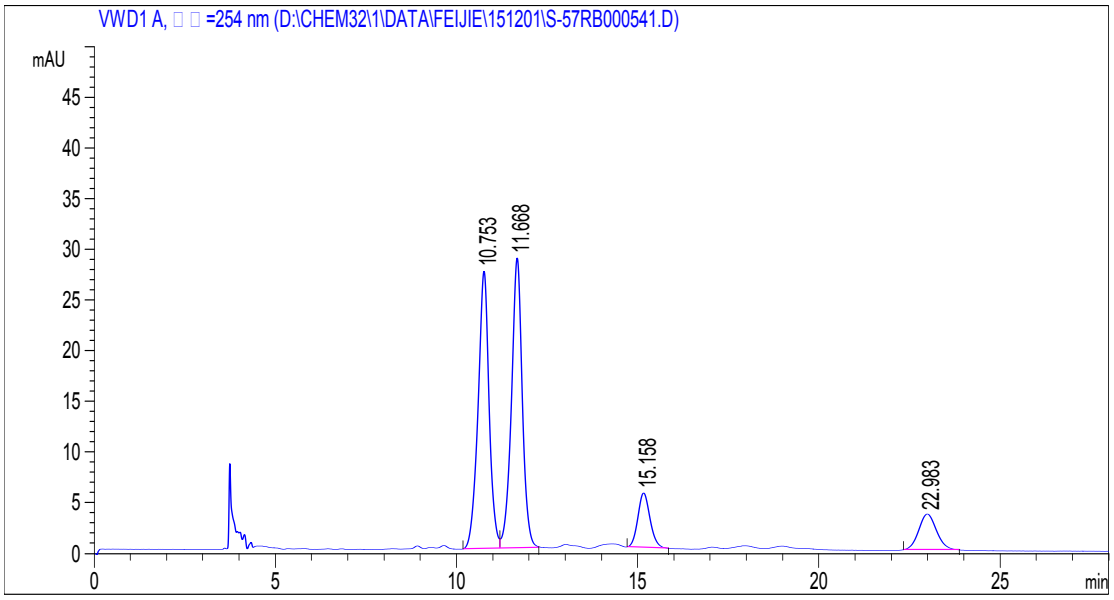
4	14.692	2876.8	79.7	0.6018	0.712	21.811



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.122	5596.4	611.4	0.133	0.869	23.221
2	11.056	18504	614.4	0.4373	0.58	76.779

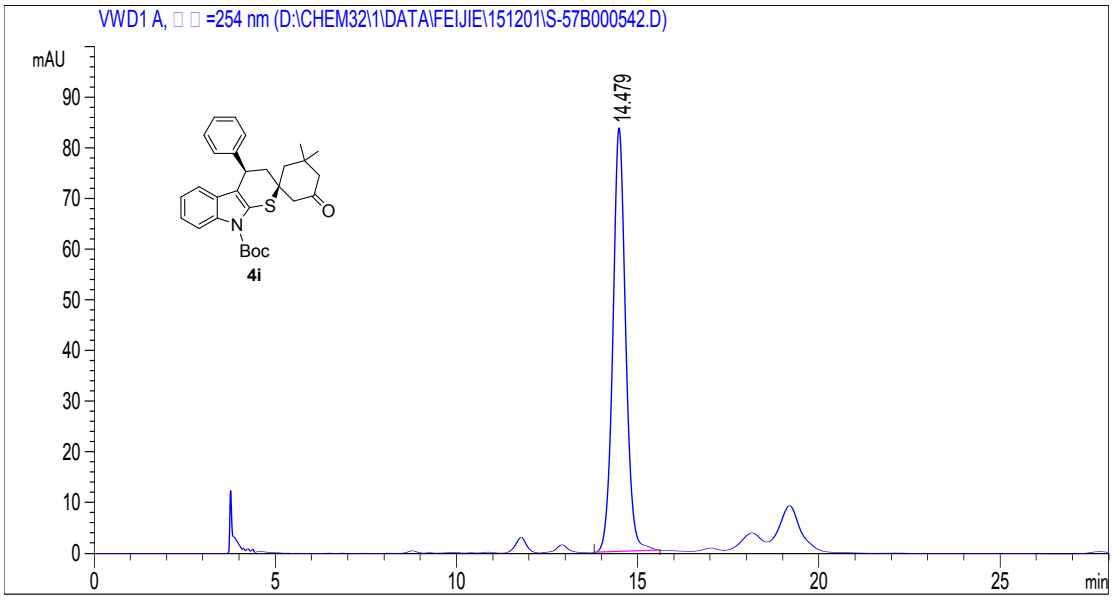
4i: *tert*-Butyl (1*S*,4'*R*)-3,3-dimethyl-5-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IB column, 254 nm, *n*-Hexane/EtOH = 9/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.753	580.7	27.4	0.3147	1.13	40.749
2	11.668	596	28.6	0.3115	1.085	41.819
3	15.158	125.3	5.4	0.3581	0.852	8.795

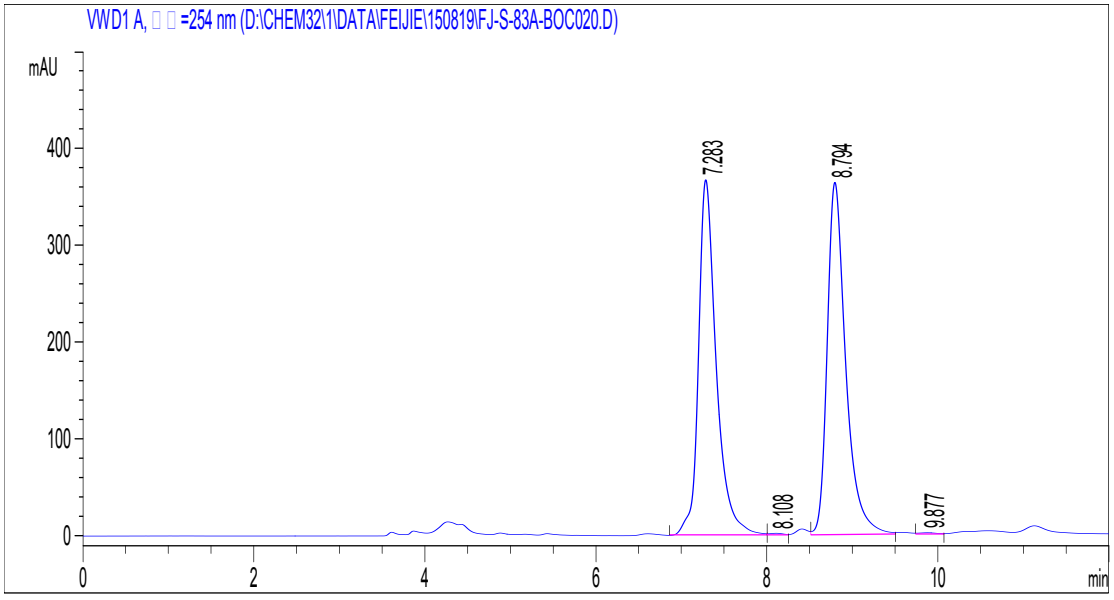
4	22.983	123.1	3.6	0.4818	0.89	8.637



#	Time	Area	Height	Width	Symmetry	Area (%)
1	14.479	2054.1	83.7	0.3709	0.885	100.000

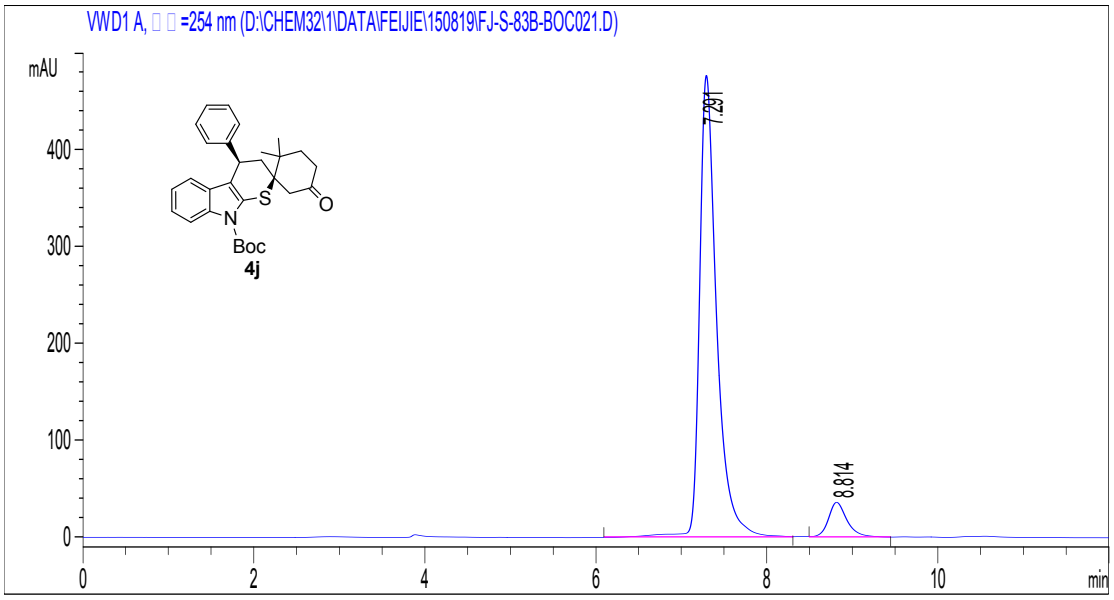
4j: *tert*-Butyl (1*R*,4'*R*)-2,2-dimethyl-5-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	7.283	5313.1	367.5	0.2138	0.654	48.902
2	8.108	21.7	1.9	0.1682	0.91	0.200
3	8.794	5500.2	364.3	0.2256	0.65	50.624

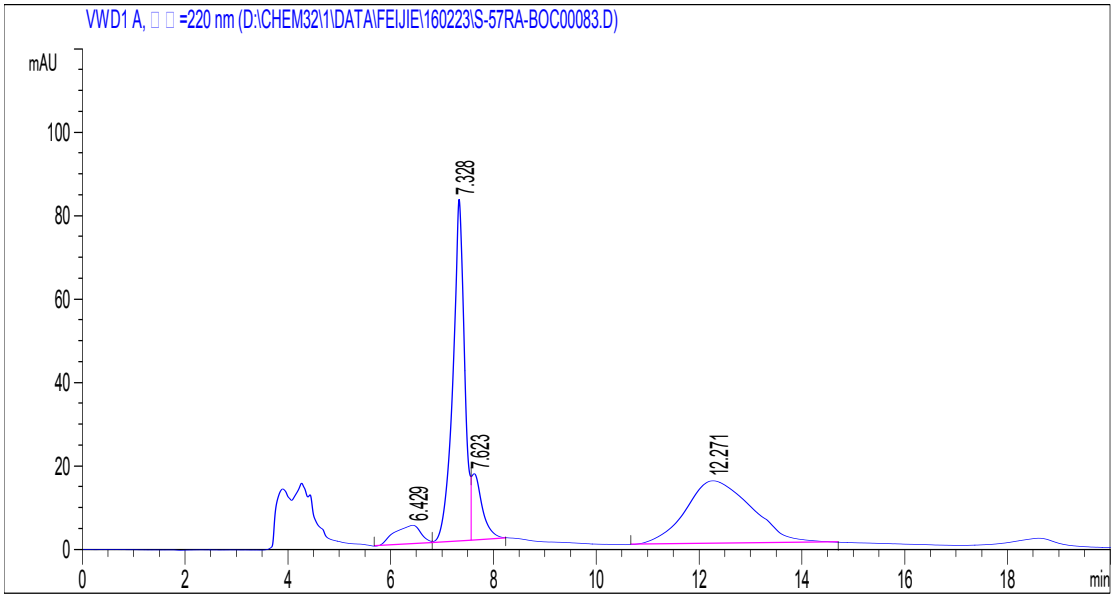
4	9.877	29.8	1.9	0.2292	0.856	0.274



#	Time	Area	Height	Width	Symmetry	Area (%)
1	7.291	6700	477.6	0.2088	0.625	92.144
2	8.814	571.2	36.4	0.2324	0.731	7.856

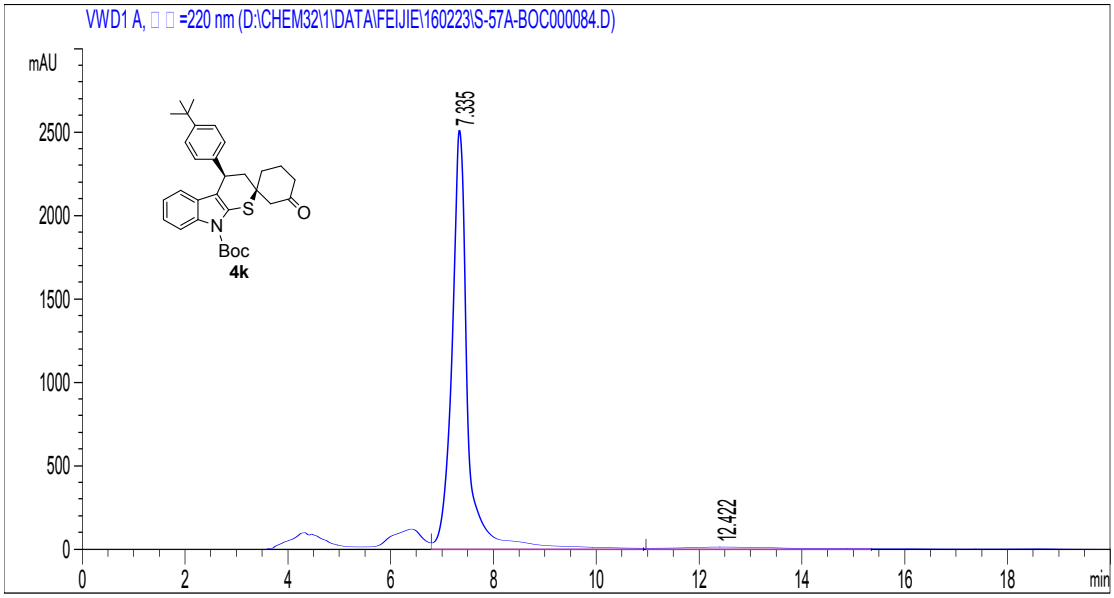
4k: *tert*-Butyl (1*R*,4'*R*)-4'-(4-(*tert*-butyl)phenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 220 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	6.429	159.4	4.4	0.482	2.239	5.244
2	7.328	1286.7	81.9	0.224	1.147	42.328
3	7.623	233.5	15.9	0.2116	0.294	7.683

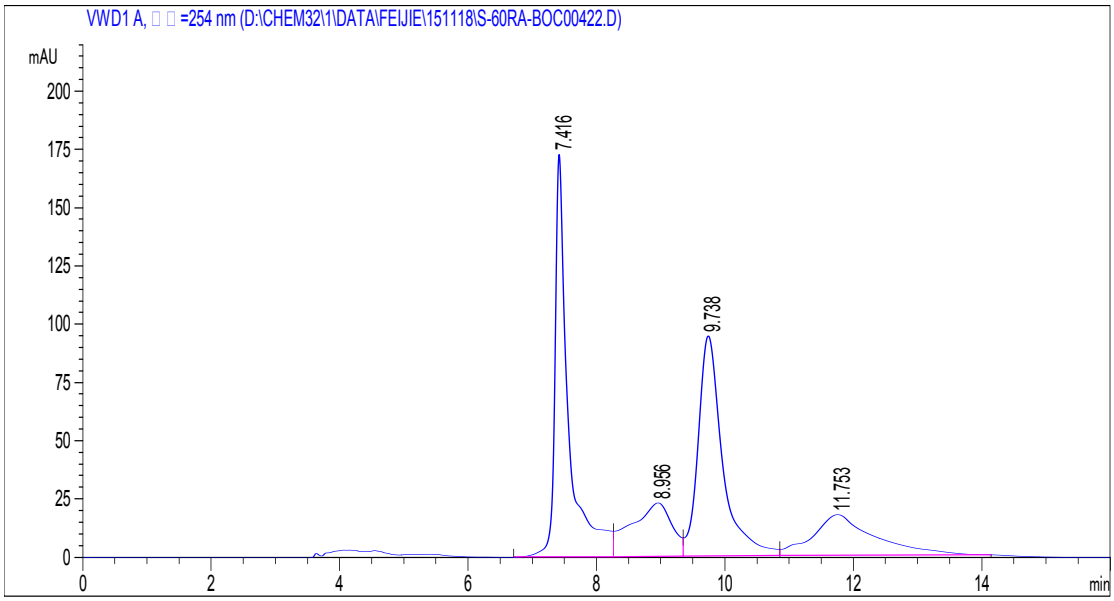
4	12.271	1360.1	15.1	1.1561	0.704	44.745



#	Time	Area	Height	Width	Symmetry	Area (%)
1	7.335	53865.5	2513.5	0.301	0.803	95.860
2	12.422	2326.1	14.4	1.9074	0.62	4.140

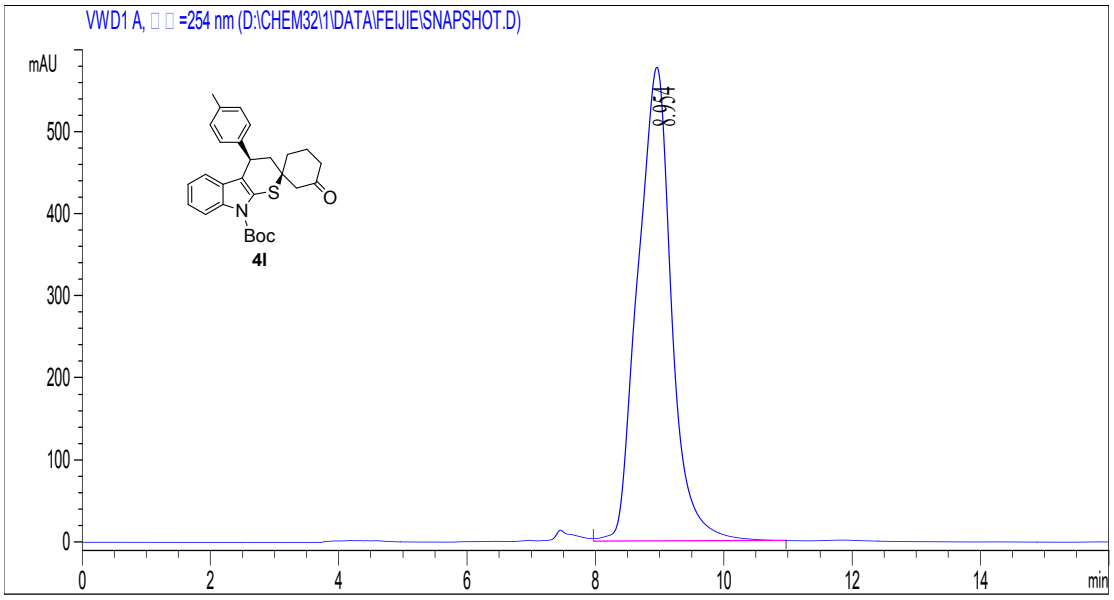
4l: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-(*p*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	7.416	2508.3	172.8	0.1999	0.421	34.680
2	8.956	1015.7	23.1	0.6064	1.895	14.043
3	9.738	2510.6	94.7	0.3923	0.647	34.712

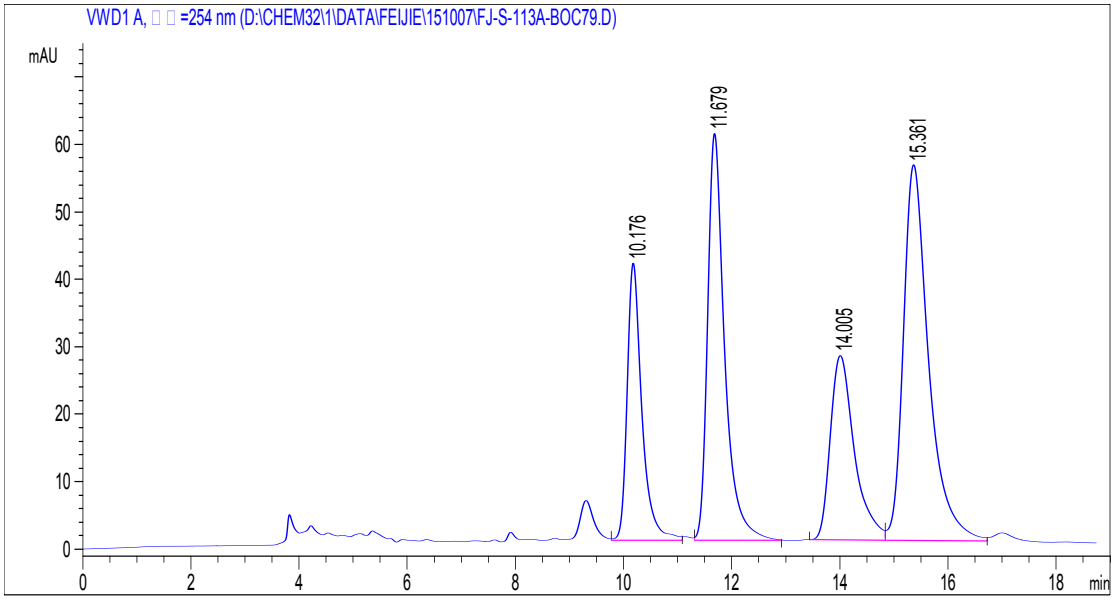
4	11.753	1198.1	17.6	0.9178	0.646	16.565



#	Time	Area	Height	Width	Symmetry	Area (%)
1	8.954	21116.4	577.7	0.5269	1.183	100.000

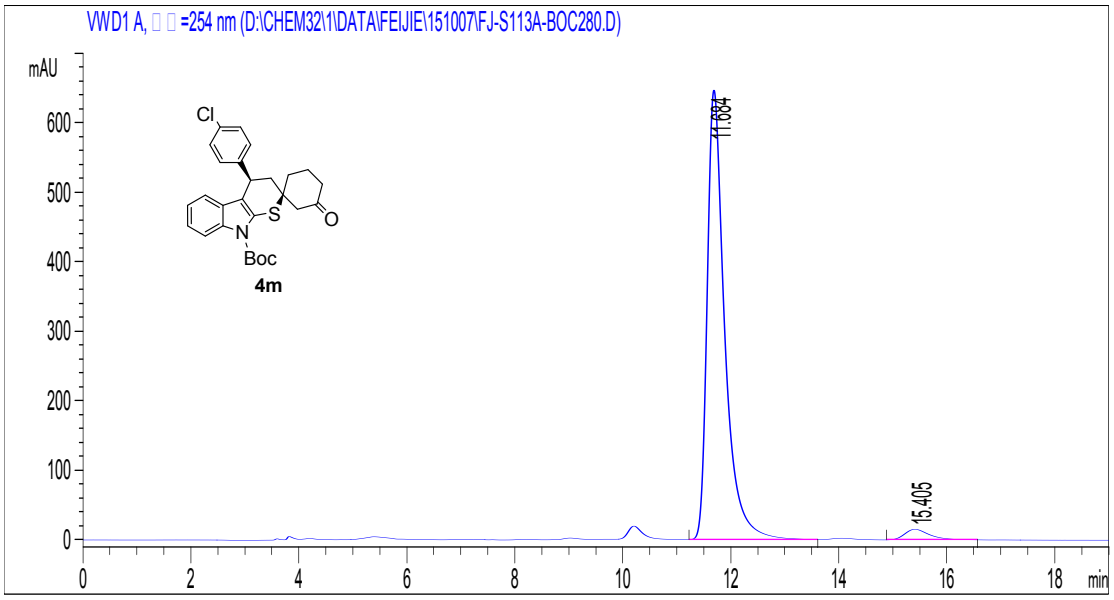
4m: *tert*-Butyl (1*R*,4'*R*)-4'-(4-chlorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.176	777.5	41.1	0.2804	0.643	16.321
2	11.679	1317.7	60.3	0.3261	0.628	27.661
3	14.005	850	27.4	0.4729	0.653	17.844

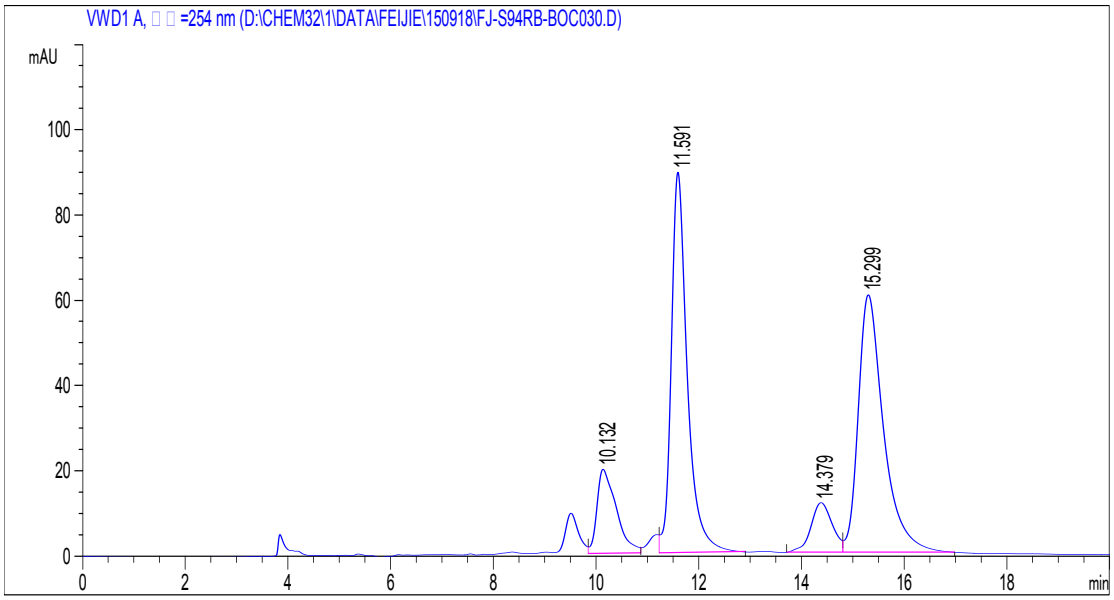
4	15.361	1818.5	55.8	0.4853	0.63	38.174



#	Time	Area	Height	Width	Symmetry	Area (%)
1	11.684	14540.3	646.6	0.3337	0.572	96.731
2	15.405	491.4	15.3	0.4803	0.639	3.269

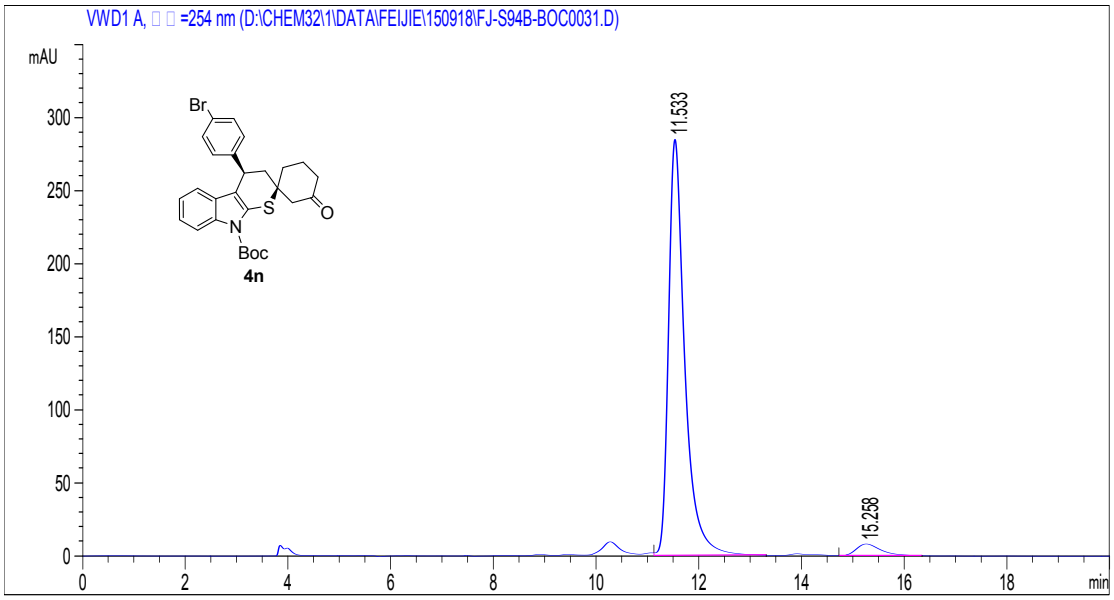
4n: *tert*-Butyl (1*R*,4'*R*)-4'-(4-bromophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.132	520.5	19.8	0.3634	0.441	10.694
2	11.591	1928.7	89.3	0.3219	0.655	39.626
3	14.379	340.2	11.7	0.4445	0.891	6.989

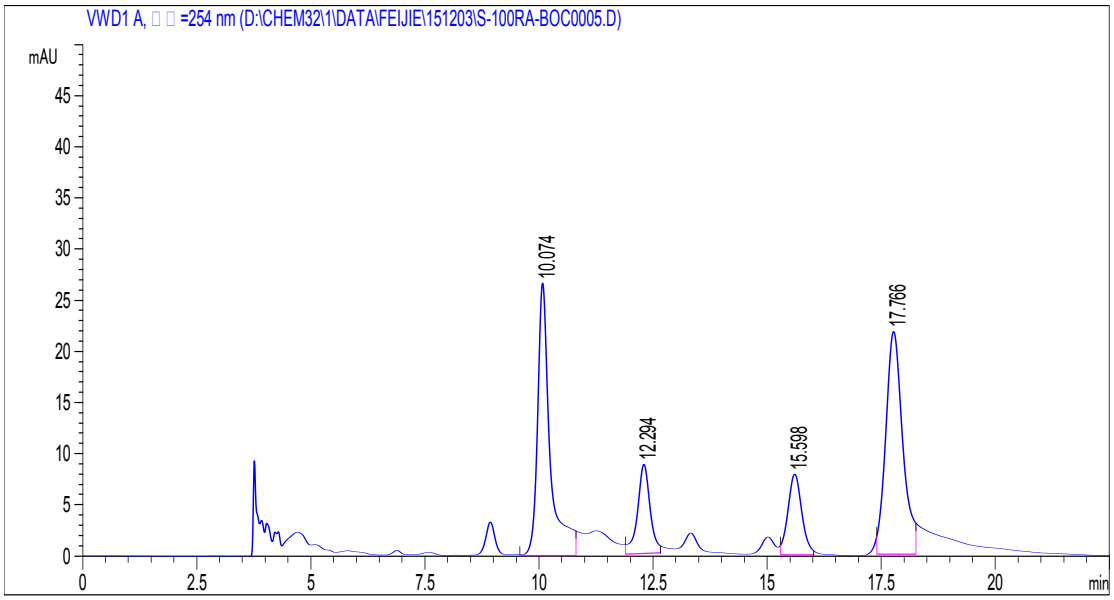
4	15.299	2077.9	60.5	0.5129	0.611	42.691



#	Time	Area	Height	Width	Symmetry	Area (%)
1	11.533	6252.9	284.8	0.3275	0.601	95.869
2	15.258	269.5	8	0.4987	0.623	4.131

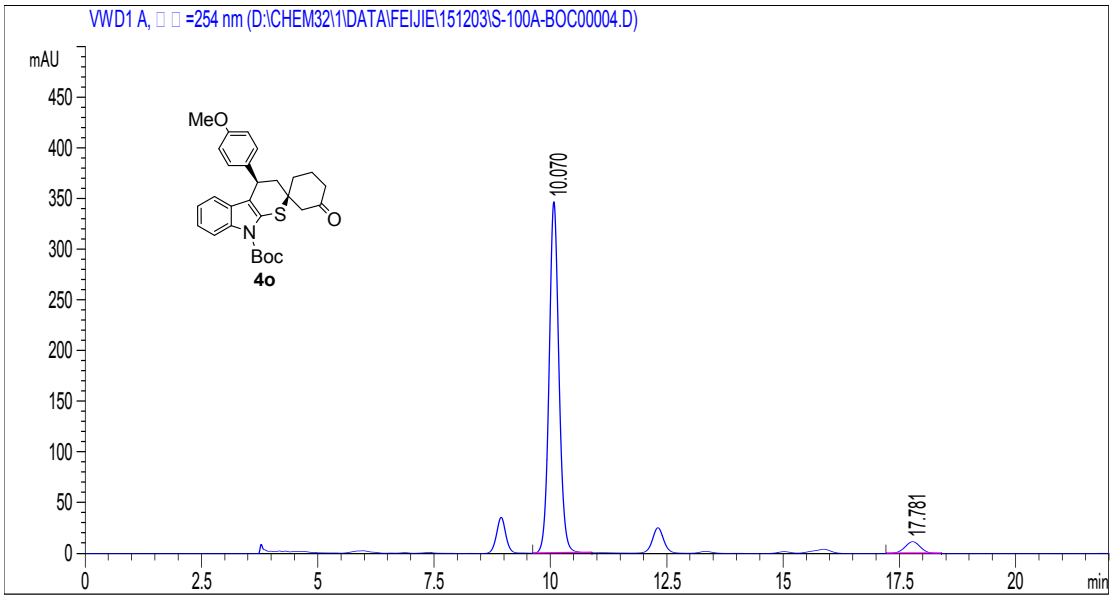
4o: *tert*-Butyl (1*R*,4'*R*)-4'-(4-methoxyphenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IB column, 254 nm, *n*-Hexane/EtOH = 9/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.074	509.1	26.7	0.3178	0.634	36.281
2	12.294	167.4	8.7	0.3189	1.013	11.928
3	15.598	167.5	7.9	0.3522	0.919	11.938

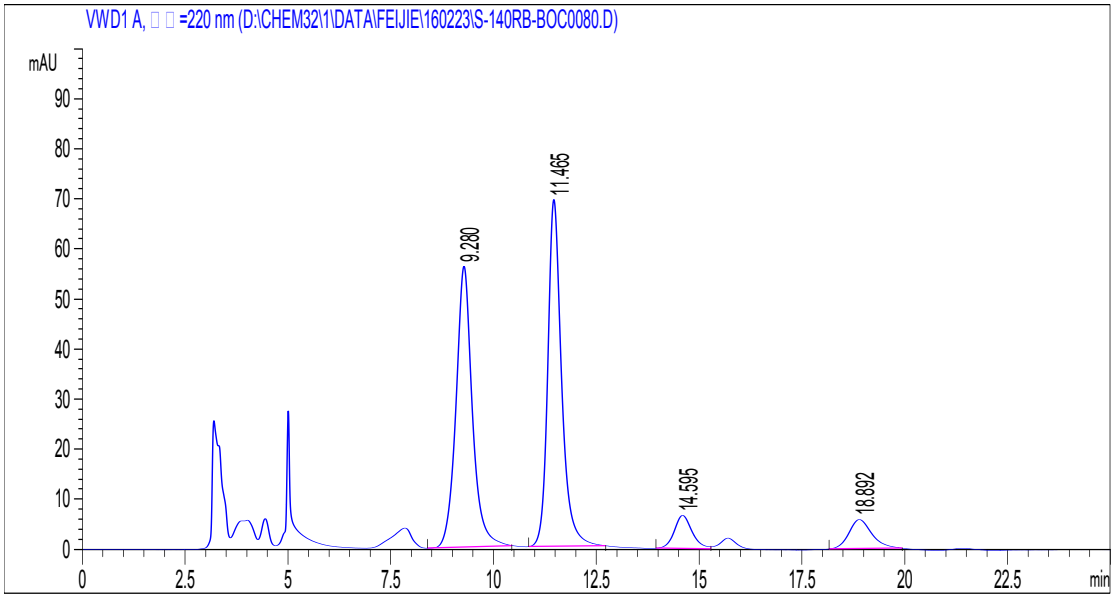
4	17.766	559.2	21.8	0.4279	0.823	39.853



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.07	5086.1	346.4	0.2237	0.895	94.861
2	17.781	275.6	11.7	0.3608	1	5.139

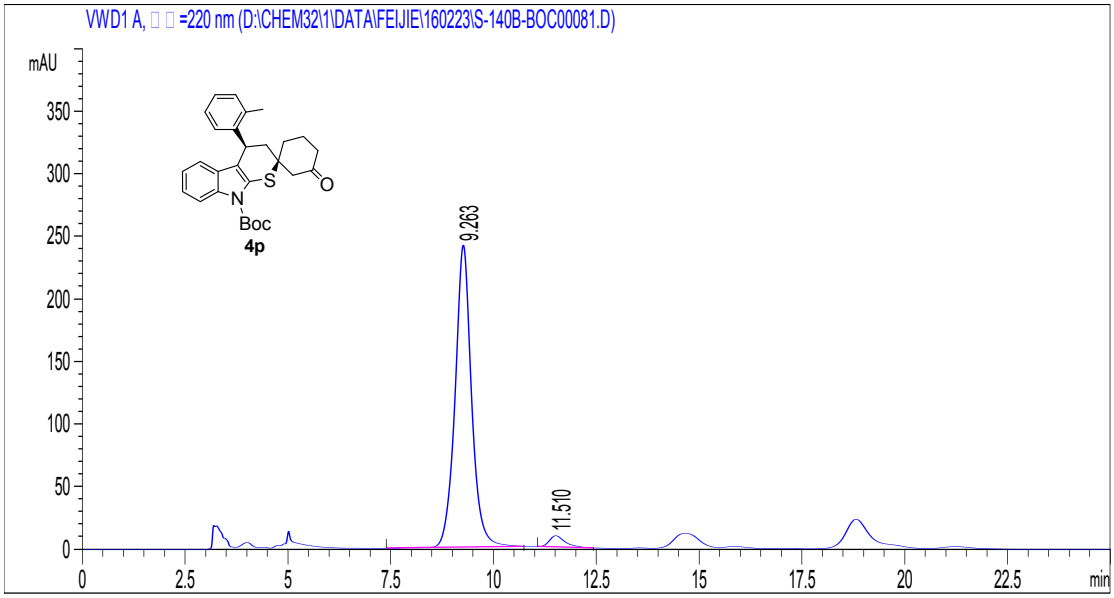
4p: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-(*o*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IB column, 220 nm, *n*-Hexane/*i*PrOH = 19/1, 1.0 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	9.28	1553.3	56.2	0.4072	0.905	43.029
2	11.465	1618.8	69.3	0.3482	0.733	44.845
3	14.595	203.8	6.7	0.4522	0.836	5.646

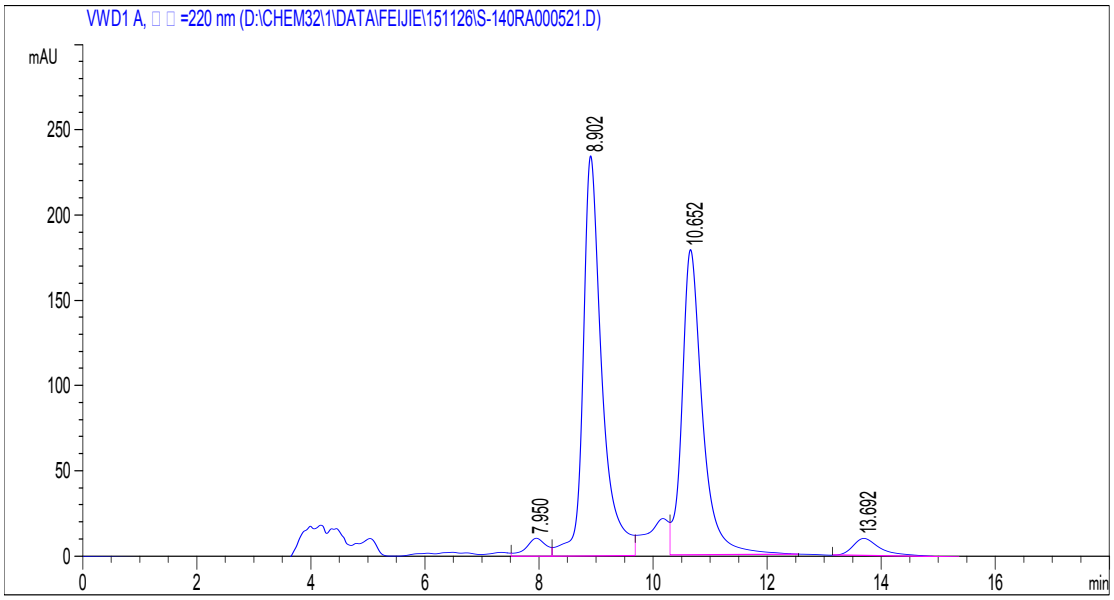
4	18.892	233.9	5.9	0.5808	0.78	6.479



#	Time	Area	Height	Width	Symmetry	Area (%)
1	9.263	6743	241.6	0.4116	0.955	96.540
2	11.51	241.6	9.1	0.3949	0.635	3.460

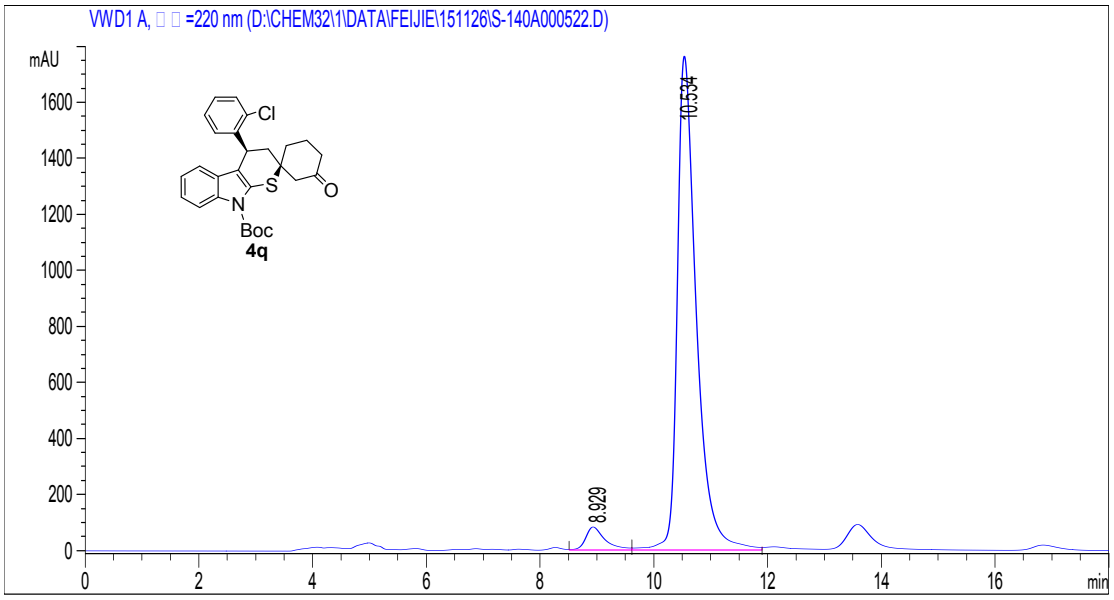
4q: *tert*-Butyl (1*R*,4'*S*)-4'-(2-chlorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IB column, 220 nm, *n*-Hexane/*i*PrOH = 7/3, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	7.95	267.3	10.7	0.3608	1.083	2.547
2	8.902	5390.6	234.8	0.3348	0.641	51.366
3	10.652	4475.6	179.3	0.367	0.649	42.647

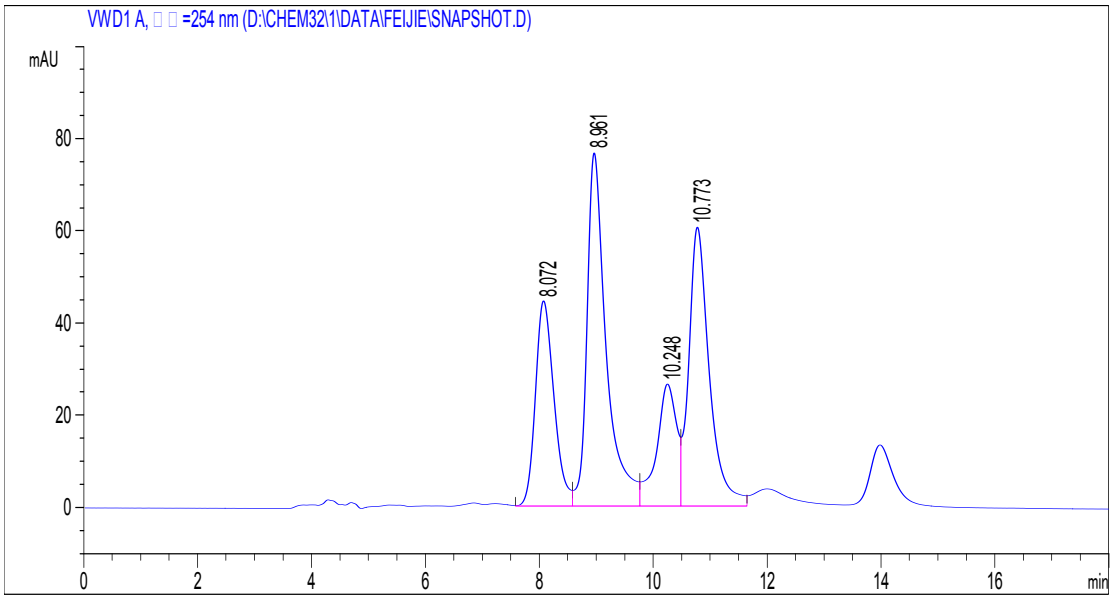
4	13.692	361.1	10.2	0.5131	0.561	3.440



#	Time	Area	Height	Width	Symmetry	Area (%)
1	8.929	2104.1	84.6	0.3601	0.583	4.855
2	10.534	41235.6	1765.2	0.3468	0.558	95.145

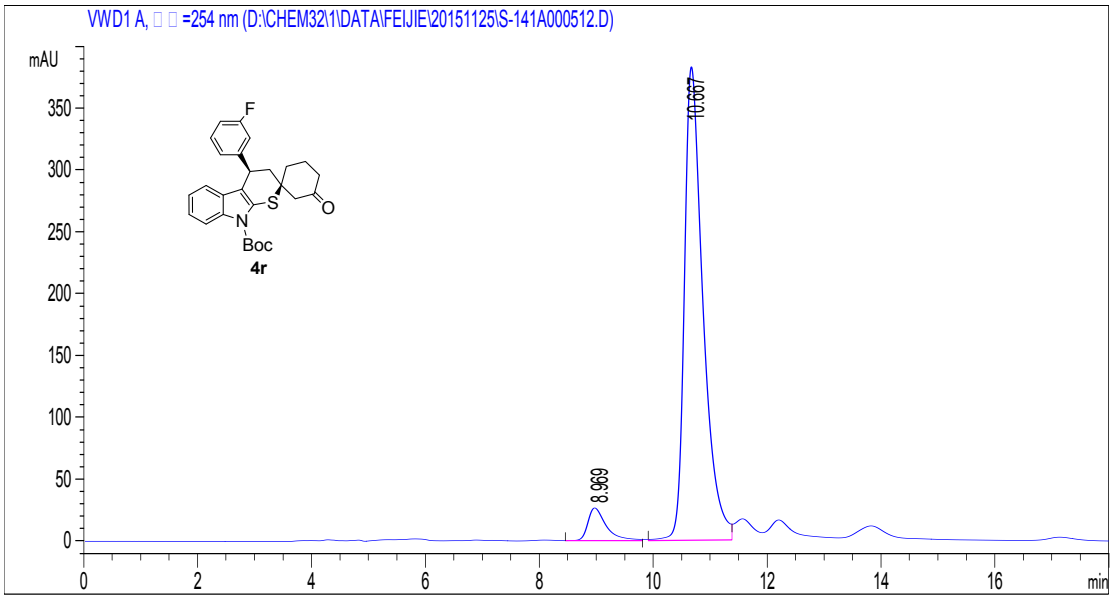
4r: *tert*-Butyl (1*R*,4'*R*)-4'-(3-fluorophenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IB column, 254 nm, *n*-Hexane/*i*PrOH = 7/3, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	8.072	1014.8	44.6	0.3456	0.739	20.343
2	8.961	1805.7	76.7	0.3431	0.553	36.198
3	10.248	651.6	26.6	0.3562	1.258	13.063

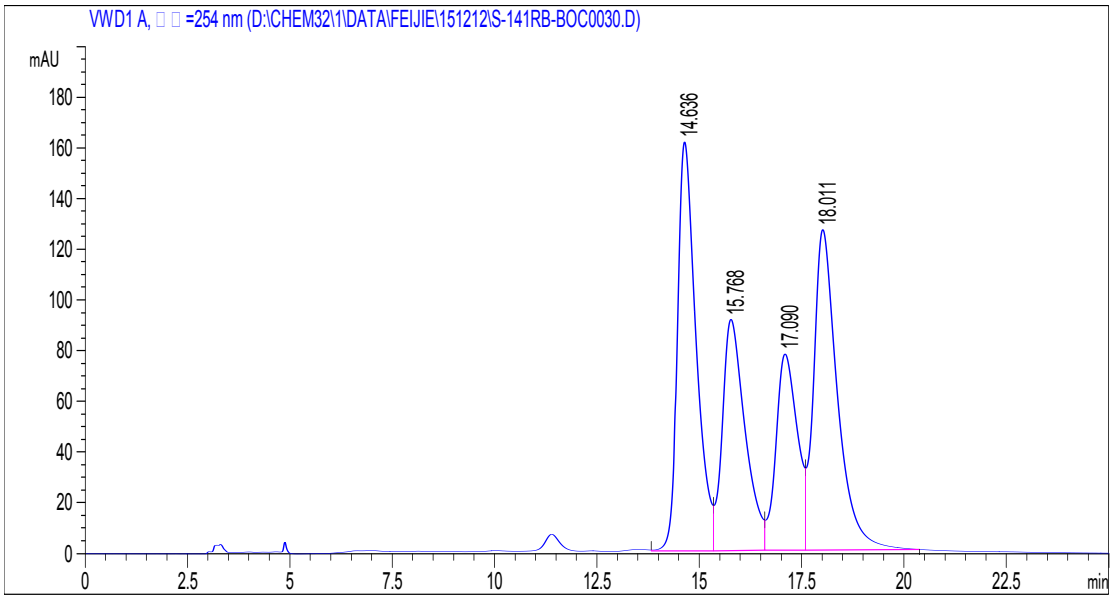
4	10.773	1516.3	60.6	0.3676	0.659	30.396



#	Time	Area	Height	Width	Symmetry	Area (%)
1	8.969	599.6	26.5	0.3335	0.548	6.433
2	10.667	8721.1	383	0.3399	0.567	93.567

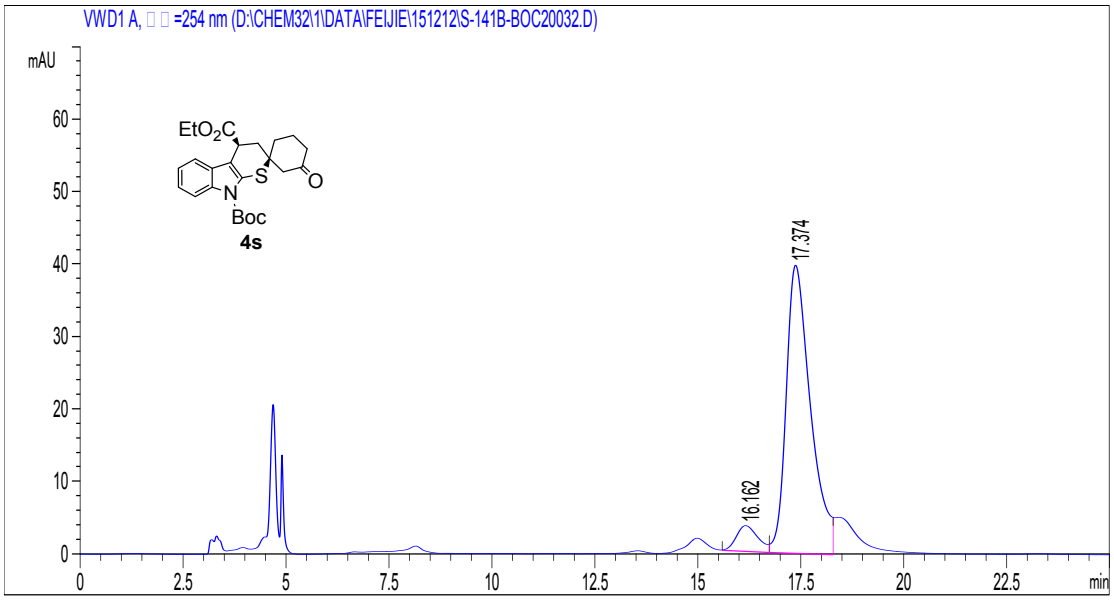
4s: *tert*-Butyl (1*R*,4'*S*)-9'-4'-ethyl-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4',9'(4'*H*)-dicarboxylate

[IB column, 254 nm, *n*-Hexaen/ *i*PrOH = 19/1, 1.0 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	14.636	5106.3	161.4	0.4725	0.591	30.754
2	15.768	3546.4	91.3	0.574	0.579	21.359
3	17.09	2829.6	77.5	0.551	0.739	17.042

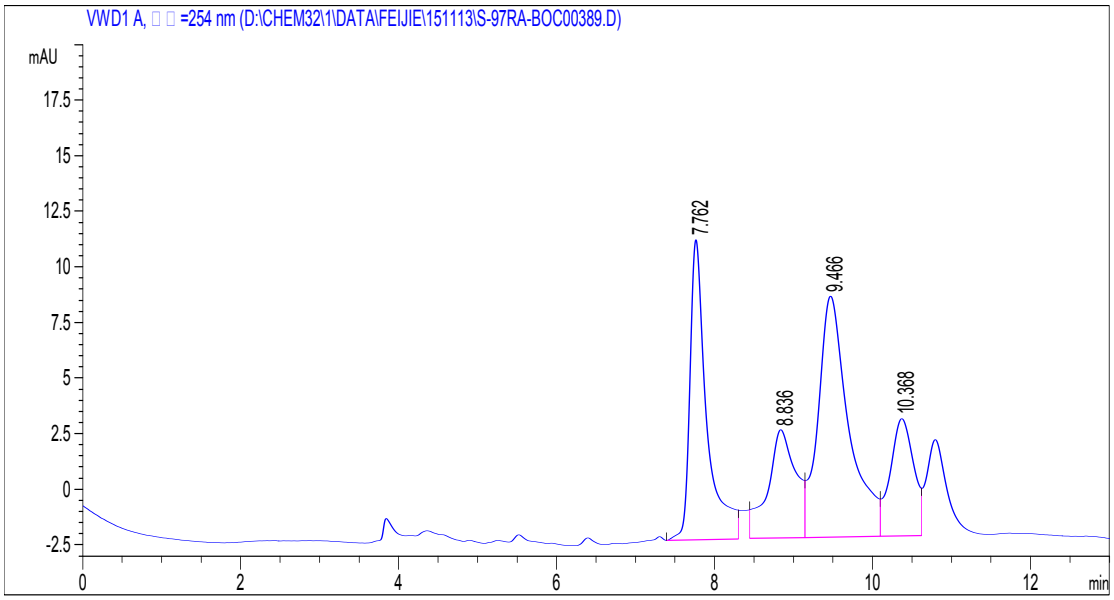
4	18.011	5121.6	126.5	0.5932	0.577	30.846



#	Time	Area	Height	Width	Symmetry	Area (%)
1	16.162	136.5	3.6	0.6241	0.733	7.687
2	17.374	1638.8	39.8	0.6859	0.613	92.313

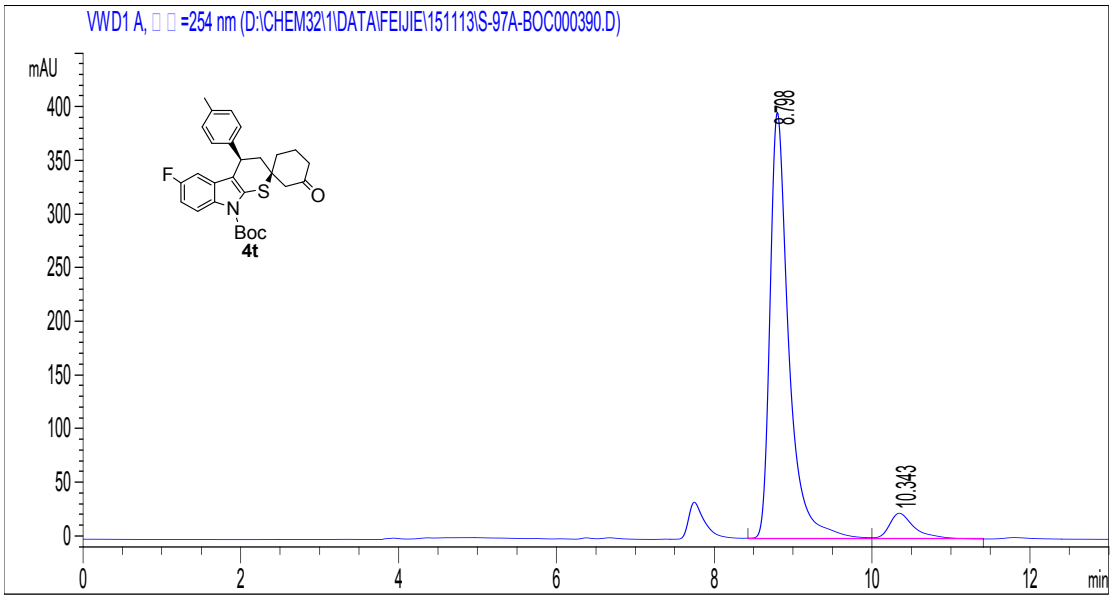
4t: *tert*-Butyl (1*R*,4'*R*)-6'-fluoro-3-oxo-4'-(*p*-tolyl)-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



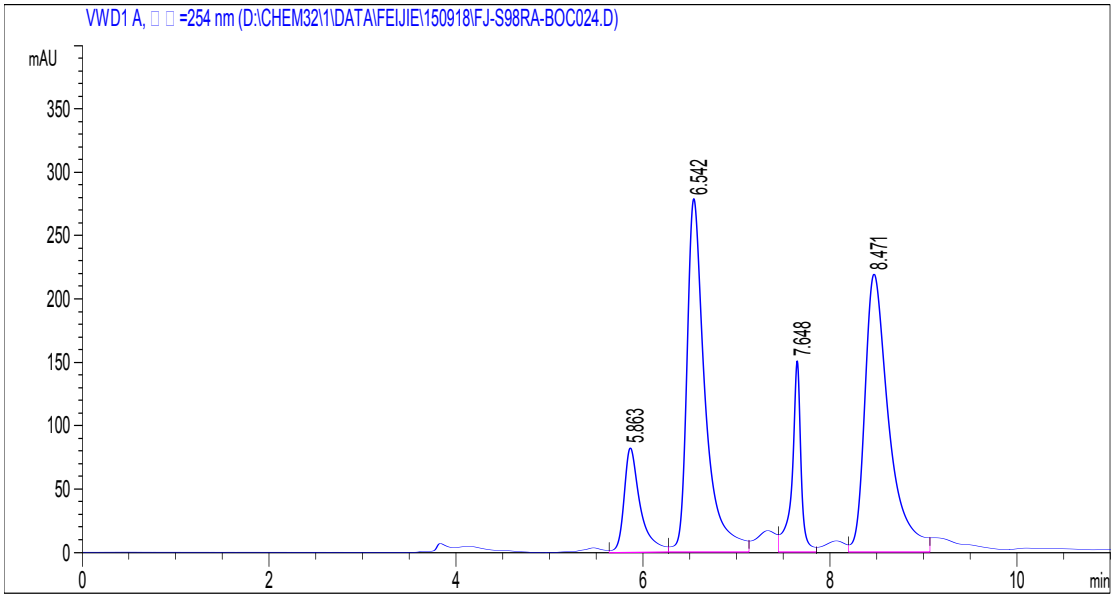
#	Time	Area	Height	Width	Symmetry	Area (%)
1	7.762	200.5	13.5	0.214	0.51	27.653
2	8.836	121.5	4.9	0.3424	0.908	16.755
3	9.466	294	10.8	0.3918	0.632	40.533

4	10.368	109.2	5.3	0.31	0.963	15.059



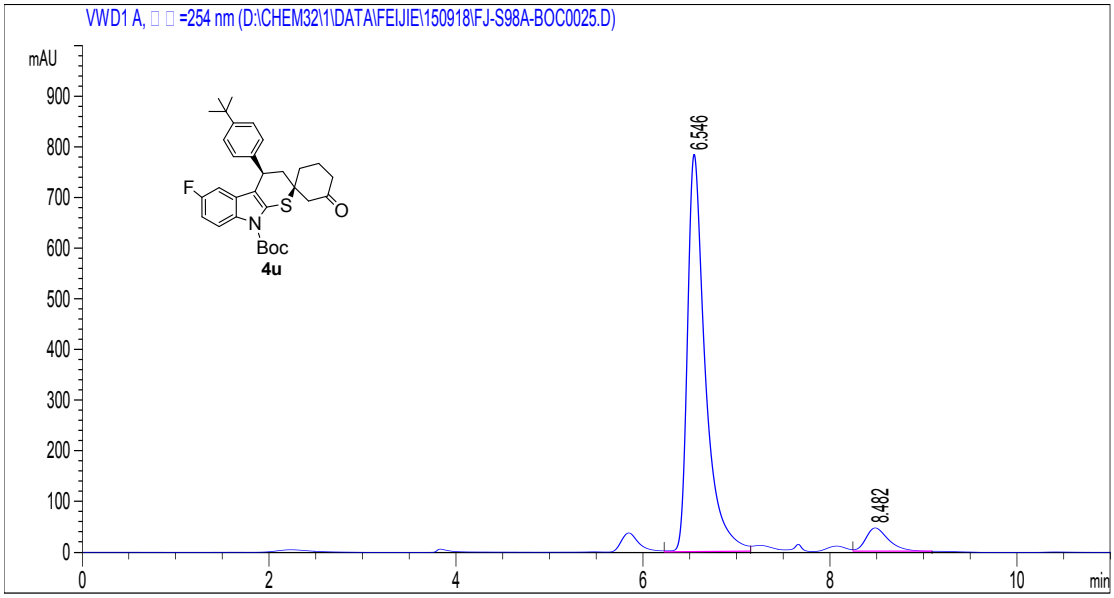
#	Time	Area	Height	Width	Symmetry	Area (%)
1	8.798	6623.1	397.8	0.2466	0.582	92.052
2	10.343	571.8	24.4	0.3438	0.583	7.948

4u: *tert*-Butyl (1*R*,4'*R*)-4'-(4-(*tert*-butyl)phenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate
[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



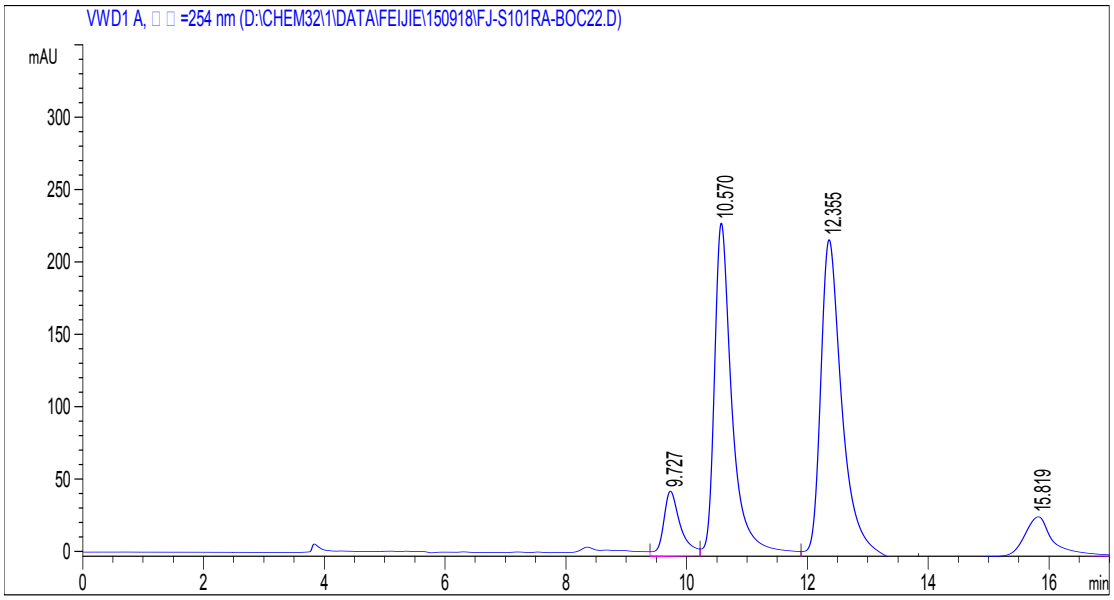
#	Time	Area	Height	Width	Symmetry	Area (%)
1	5.863	1005.9	82.8	0.1767	0.585	10.337
2	6.542	3784.4	279.3	0.1988	0.558	38.889
3	7.648	1008	151.4	0.0937	1.31	10.358

4	8.471	3933.1	219.8	0.2656	0.575	40.416



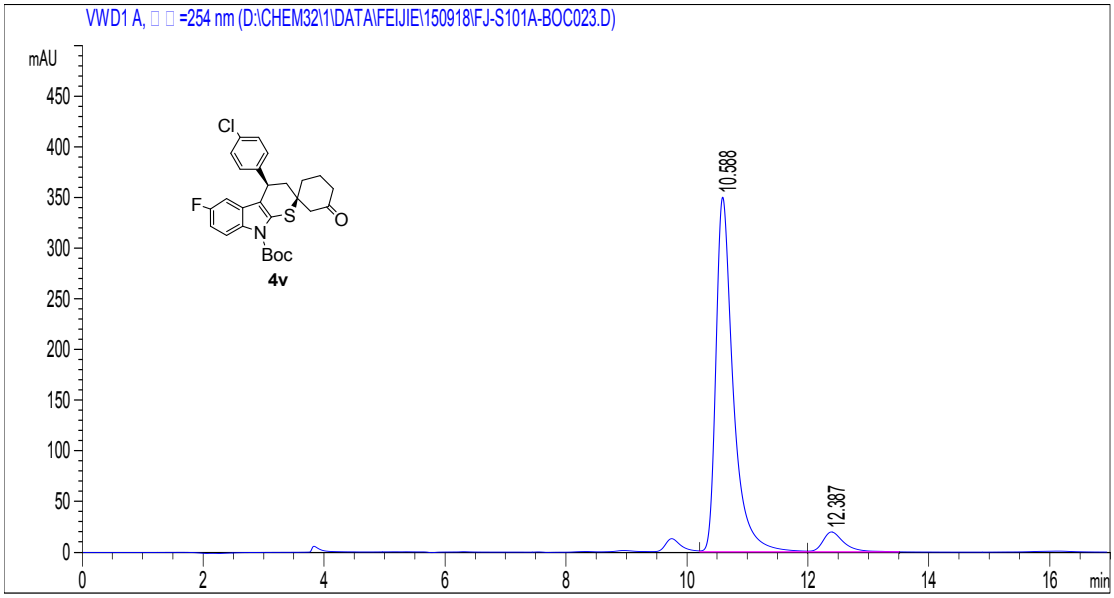
#	Time	Area	Height	Width	Symmetry	Area (%)
1	6.546	10354.4	784.6	0.1933	0.552	92.955
2	8.482	784.8	46.4	0.2557	0.664	7.045

4v: *tert*-Butyl (1*R*,4'*R*)-4'-(4-chlorophenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate
[AD-H column, 254 nm, *n*-Hexane/*i*PrOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	9.727	923.2	45.6	0.2944	0.63	7.293
2	10.570	4927.6	231.3	0.3111	0.548	38.928
3	12.355	5591.2	221.2	0.3735	0.597	44.170

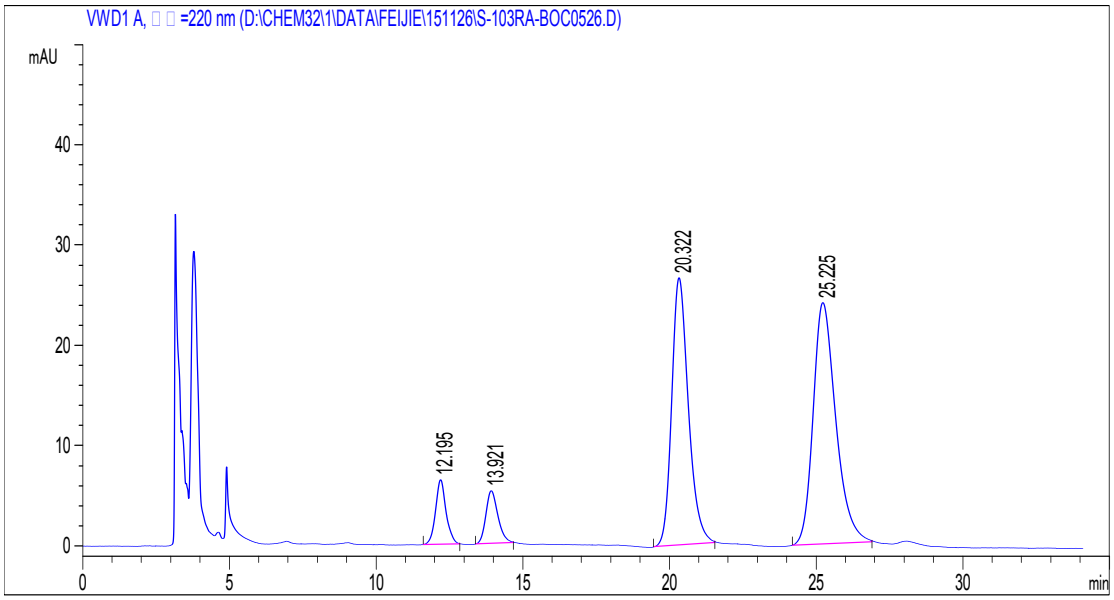
4	15.819	1216.3	29.1	0.5903	0.944	9.609



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.588	6942.7	350.2	0.2939	0.586	93.408
2	12.387	490	19.8	0.3676	0.644	6.592

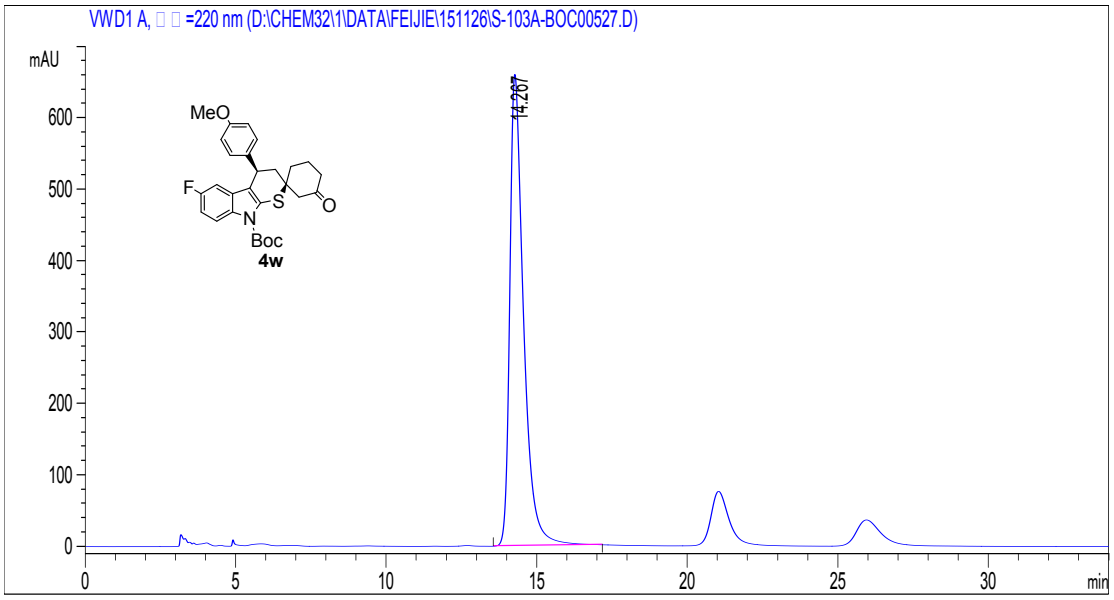
4w: *tert*-Butyl (1*R*,4'*R*)-6'-fluoro-4'-(4-methoxyphenyl)-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[IB column, 220 nm, *n*-Hexane/*i*PrOH = 19/1, 1.0 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	12.195	162.4	6.5	0.3674	0.886	6.099
2	13.921	151.9	5.3	0.4227	0.775	5.704
3	20.322	1054.3	26.7	0.5964	0.745	39.595

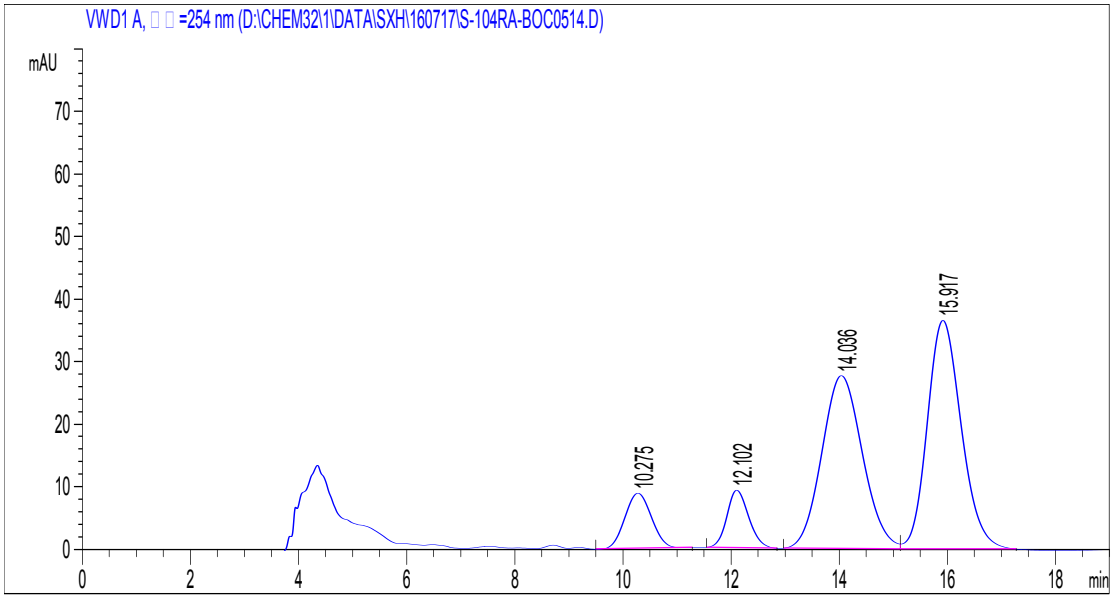
4	25.225	1294.2	24.1	0.8057	0.712	48.602



#	Time	Area	Height	Width	Symmetry	Area (%)
1	14.267	20989.2	660.3	0.4713	0.533	100.000

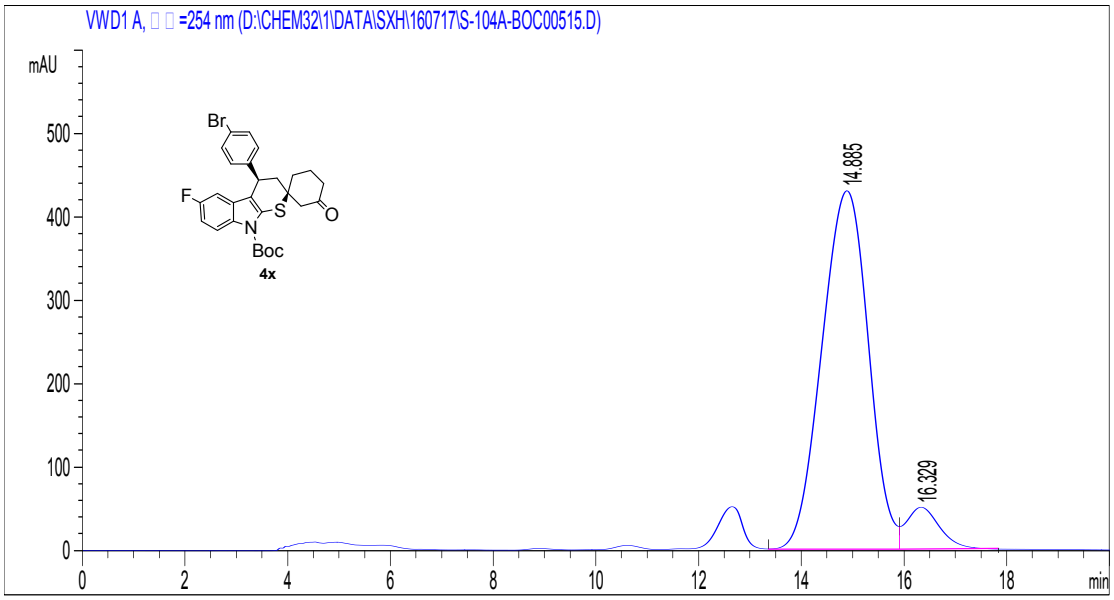
4x: *tert*-Butyl (1*R*,4'*R*)-4'-(4-bromophenyl)-6'-fluoro-3-oxo-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate

[AS-H column, 254 nm, *n*-Hexane/EtOH = 19/1, 0.8 mL/min]



#	Time	Area	Height	Width	Symmetry	Area (%)
1	10.275	303.2	8.9	0.5291	0.926	8.418
2	12.102	259.4	9.2	0.4327	0.798	7.202
3	14.036	1441.8	27.6	0.7992	0.891	40.033

4	15.917	1597.2	36.6	0.6727	0.813	44.347



#	Time	Area	Height	Width	Symmetry	Area (%)
1	14.885	27046.9	429.8	0.9861	1.122	92.210
2	16.329	2285.1	50.4	0.6779	0.725	7.790

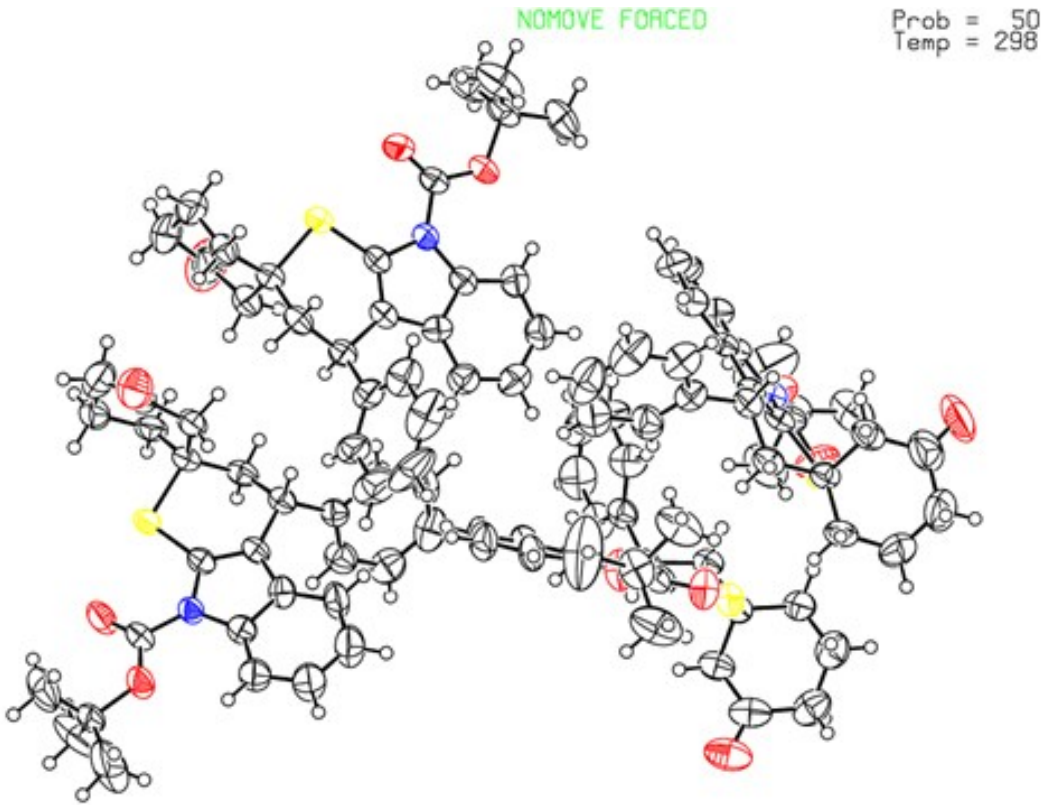
G: Determination of Absolute Configuration

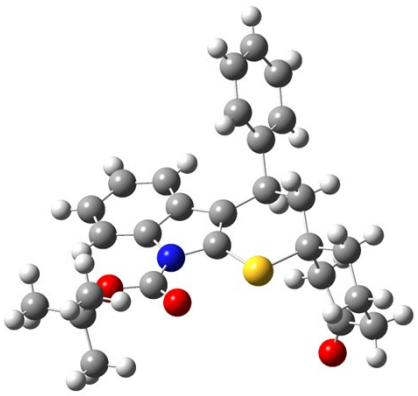
Crystal data and structure refinement for **4a**

Identification code	CCDC 1481742	
Empirical formula	$C_{27}H_{29}NO_3S$	
Formula weight	447.57	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 11.477(5) Å	α = 90°
	b = 19.264(8) Å	β = 90.732(5)°
	c = 21.970(9) Å	γ = 90°
Volume	4857(3) $Å^3$	
Z	8	
Density (calculated)	1.224 Mg/m^3	
Absorption coefficient	0.161 mm^{-1}	

F(000)	1904
Crystal size	0.400 x 0.350 x 0.300 mm^3
Theta range for data collection	1.406 to 26.999°.
Index ranges	-14<=h<=14, -20<=k<=24, -27<=l<=25
Reflections collected	23754
Independent reflections	17711 [R(int) = 0.0437]
Completeness to theta = 25.242°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.446
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	17711 / 73 / 1165
Goodness-of-fit on F2	0.873
Final R indices [I>2sigma(I)]	R_1 = 0.0512, wR_2 = 0.1162
R indices (all data)	R_1 = 0.0839, wR_2 = 0.1253
Absolute structure parameter	-0.03(7)
Extinction coefficient	n/a
Largest diff. peak and hole	0.322 and -0.237 e.$Å^{-3}$

4a: *tert*-Butyl (1*R*,4'*R*)-3-oxo-4'-phenyl-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-9'(4'*H*)-carboxylate





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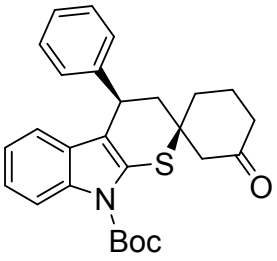
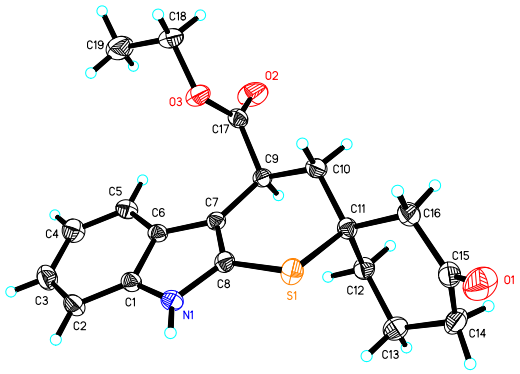


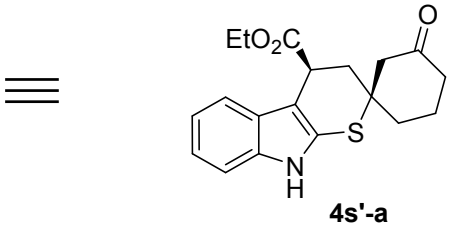
Crystal data and structure refinement for **4s'-a**

Identification code	CCDC 1495419	
Empirical formula	$C_{19}H_{21}NO_3S$	
Formula weight	343.43	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.4511(8) Å	a= 90°
	b = 8.0164(8) Å	b= 90°
	c = 28.243(3) Å	g = 90°
Volume	1687.0(3) $Å^3$	
Z	4	
Density (calculated)	1.352 Mg/m^3	
Absorption coefficient	0.209 mm^{-1}	
F(000)	728	
Crystal size	0.220 x 0.170 x 0.130 mm^3	

Theta range for data collection	2.641 to 25.996°.
Index ranges	-6<=h<=9, -9<=k<=9, -34<=l<=33
Reflections collected	10124
Independent reflections	3309 [R(int) = 0.0321]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6698
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3309 / 1 / 222
Goodness-of-fit on F^2	1.039
Final R indices [I>2sigma(I)]	R_1 = 0.0400, wR_2 = 0.0950
R indices (all data)	R_1 = 0.0434, wR_2 = 0.0974
Absolute structure parameter	0.07(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.309 and -0.145 e.Å^{-3}

4s'-a: **(1*S*,4'*S*)-ethyl-3-oxo-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4'-carboxylate**





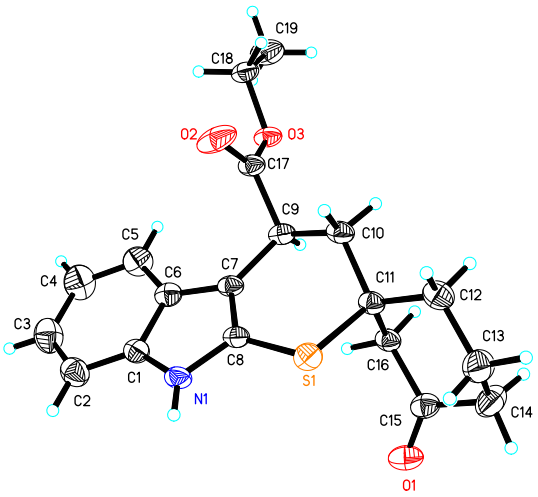
4s'-a

Crystal data and structure refinement for **4s'-b**

Identification code	CCDC 1495499	
Empirical formula	$C_{19}H_{21}NO_3S$	
Formula weight	343.43	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.8324(19) Å	a= 90°.
	b = 10.981(3) Å	b= 90°.
	c = 20.695(5) Å	g = 90°.
Volume	1779.8(7) $Å^3$	
Z	4	
Density (calculated)	1.282 Mg/m^3	
Absorption coefficient	0.198 mm^{-1}	
F(000)	728	
Crystal size	0.200 x 0.140 x 0.110 mm^3	
Theta range for data collection	1.968 to 25.493°.	

Index ranges	-8<=h<=9, -13<=k<=13, -22<=l<=25
Reflections collected	10113
Independent reflections	3313 [R(int) = 0.0382]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6729
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3313 / 0 / 222
Goodness-of-fit on F^2	1.016
Final R indices [I>2sigma(I)]	R_1 = 0.0416, wR_2 = 0.0945
R indices (all data)	R_1 = 0.0508, wR_2 = 0.0998
Absolute structure parameter	0.03(5)
Extinction coefficient	n/a
Largest diff. peak and hole	0.234 and -0.133 e.$Å^{-3}$

4s'-b: **(1*R*,4'*S*)-ethyl-3-oxo-4',9'-dihydro-3'*H*-spiro[cyclohexane-1,2'-thiopyrano[2,3-*b*]indole]-4'-carboxylate**



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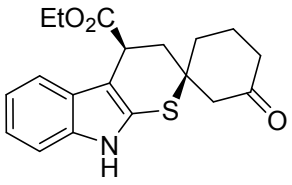

4s'-b