Supporting Information for

Asymmetric Oxidative Rearrangement of Tetrahydro-β-Carbolines Catalyzed by Anionic Stereogenic-at-Cobalt(III) Complexes

Bin-Bin Song, Zhen-Jiang Yu, Zi-Mu Liu, Qiongqiong Zhu, Hua-Jie Jiang*, Chuan-Zhi Yao*, and Jie Yu*

Department of Applied Chemistry, Anhui Province Engineering Laboratory for Green Pesticide Development and Application, and Anhui Province Key Laboratory of Crop Integrated Pest Management, Hefei, Anhui 230036, P. R. China

*E-mail: jieyu@ahau.edu.cn; jianghj@ahau.edu.cn; ychzh@ahau.edu.cn.

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1. Introduction

1.1. General Data

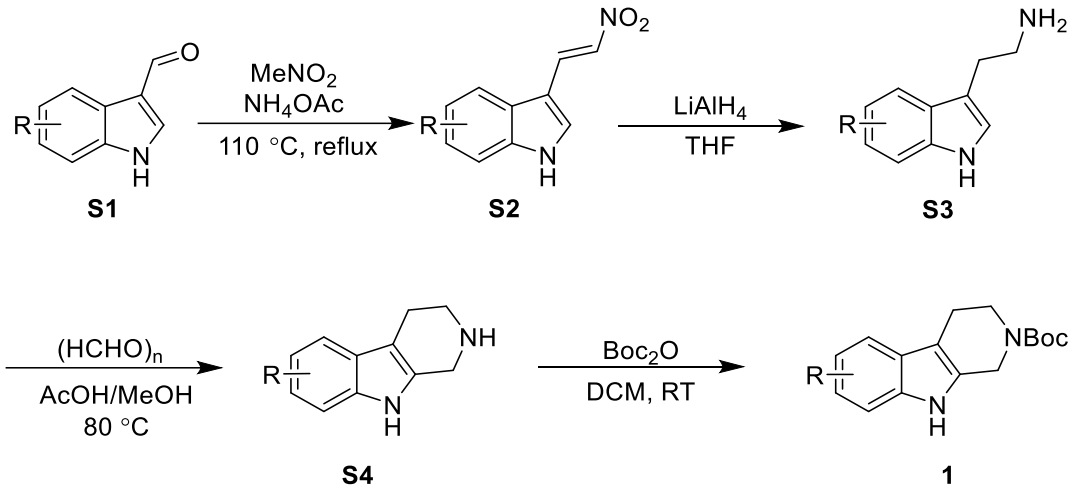
^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on an Agilent 600 NMR or Bruker-400 (or 500) MHz spectrometer at 600 MHz, 151 or 126 MHz, and 564 or 376 MHz using $CDCl_3$ as solvent, respectively. ^{1}H NMR data are reported as follows: δ, chemical shift; coupling constants (*J* are given in Hertz, Hz) and integration. Abbreviations to denote the multiplicity of a particular signal were s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Melting points were measured on a digital melting point apparatus and the temperature was uncorrected. High resolution mass spectrometric measurements (HRMS) were performed by the Waters Xevo G2-XS TOF (ESI Source). HPLC analysis was performed on Waters-Breeze (2487 Dual λ Absorbance Detector and 1525 Binary HPLC Pump, UV detection monitored at 254 nm). Chiralpak AD, AS, OJ, and OD columns were purchased from Daicel Chemical Industries, Ltd. Optical rotations were recorded on an Anton Paar MCP-100 polarimeter. Analytical-grade solvents for the column chromatography and commercially available reagents were used as received. *m*-Chloroperoxybenzoic acid was purified prior to use.

1.2. Materials

Analytical-grade solvents were used for column chromatography, and all commercially available reagents were used as received unless otherwise noted. *m*-CPBA was purified prior to use, and chloroform was distilled and dried before use. Catalysts (Λ-**1a** to Λ-**1e**) are known compounds and were synthesized according to the reported literature procedures.[1] Indoles **1a**–**1g** and **1l**–**1w** are known compounds and were prepared following previously reported procedures,[2–4] with their spectral data consistent with those reported in the literature. Indoles **1h**–**1k** and **1x** are new compounds and were synthesized according to the reported procedure.[2–4].

2. General Procedure for the Preparation of Substrates

2.1 General Procedure for Preparation of Substrates 1a-1m



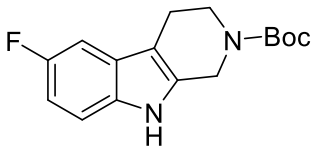
Step 1: Procedure for the synthesis of **S2**: To a solution of **S1** (1.0 equiv, 10 mmol) in nitromethane (15 mL) was added ammonium acetate (1.54 g, 2.0 equiv, 20 mmol). The reaction mixture was heated at 110 °C in an oil bath under reflux for 3 h. After cooling to room temperature, the organic layer was separated, and the aqueous phase was extracted with DCM (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting crude nitroolefin **S2** was used directly in subsequent transformations without further purification.

Step 2: Procedure for the synthesis of **S3**: $LiAlH_4$ (1.9 g, 5.0 equiv, 50 mmol) was dissolved in anhydrous THF (to give a 2.5 M solution), and the corresponding nitroolefin **S2** was added dropwise at 0 °C. The reaction mixture was heated under reflux in an oil bath for 5 h and then allowed to cool to room temperature. The reaction was carefully quenched by the sequential addition of H_2O (1 mL) and 10% aqueous NaOH (2 mL) at 0 °C. The resulting mixture was filtered through Celite and washed with ethyl acetate (3 × 50 mL). The filtrate was concentrated under reduced pressure to afford the desired product **S3**.

Step 3: Procedure for the synthesis of **S4**: To a solution of substituted tryptamine **S3** (1.0 equiv, 10 mmol) in a mixture of AcOH/MeOH (v/v = 2:5, 28 mL) was added paraformaldehyde (360 mg, 1.2 equiv, 12 mmol). The reaction mixture was heated at 80 °C for 3 h and then cooled to 0 °C. The mixture was basified to pH 9–10 by the sequential addition of saturated aqueous NaOH and $NaHCO_3$

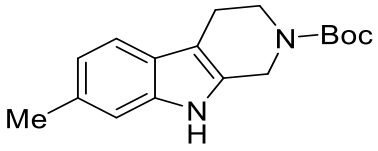
solutions (NaOH to pH 4–5, followed by $NaHCO_3$ to pH 8, and finally a few drops of NaOH to adjust the pH to 9–10). The resulting mixture was extracted with DCM (3 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude amine **S4**.

Step 4: Procedure for the synthesis of **1**: At 0 °C, Boc_2O (2.18 g, 1.0 equiv, 10 mmol) was added to a solution of the crude amine **S4** in DCM (15 mL). The reaction mixture was allowed to warm to room temperature and stirred at this temperature, with the reaction progress monitored by TLC. Upon completion (≈2 h), saturated aqueous $NaHCO_3$ (15 mL) was added. The layers were separated, and the aqueous phase was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the resulting crude residue by silica gel flash column chromatography (gradient elution with EtOAc in petroleum ether) afforded substrates **1a**–**1m**.



1h

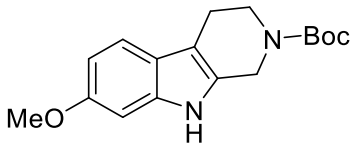
***tert*-Butyl 6-fluoro-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-b]indole-2-carboxylate 1h:** yield: 42% (1.218 g); (Flash column chromatography eluent, petrol ether/EtOAc = 3/1); yellow solid, m.p. 68.3-69.1 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.23 – 7.19 (m, 1H), 7.11 (d, *J* = 9.4 Hz, 1H), 6.91 – 6.85 (m, 1H), 4.72 – 4.57 (m, 2H), 3.80 – 3.72 (m, 2H), 2.75 (t, *J* = 5.8 Hz, 2H), 1.55 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.0 (d, *J* = 234.8 Hz), 155.6, 132.8, 127.5, 111.5, 109.7 (d, *J* = 25.2 Hz), 103.2, 80.5, 60.6, 42.7, 41.4, 28.7, 21.5, 14.3; ^{19}F NMR (565 MHz, $CDCl_3$) δ -124.90 ppm; **HRMS (ESI)** calculated for $C_{16}H_{20}FN_2O_2$ $[M+H]^+$: 291.1509, found: 291.1510.



1i

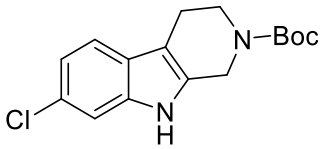
***tert*-Butyl 7-methyl-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-b]indole-2-carboxylate 1i**: yield: 45% (1.287 g); (Flash column chromatography eluent, petrol ether/EtOAc = 3/1); white solid. m.p. 103.7-

104.8 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.38 – 7.34 (m, 1H), 7.09 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 4.63 (s, 2H), 3.76 (s, 2H), 2.79 (s, 2H), 2.45 (s, 3H), 1.53 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.5, 136.8, 131.5, 130.1, 125.0, 121.2, 117.6, 111.1, 80.2, 42.8, 41.9, 28.8, 28.2, 21.6; **HRMS (ESI)** calculated for $C_{17}H_{23}N_2O_2$ $[M+H]^+$: 287.1760, found: 287.1763.



1j

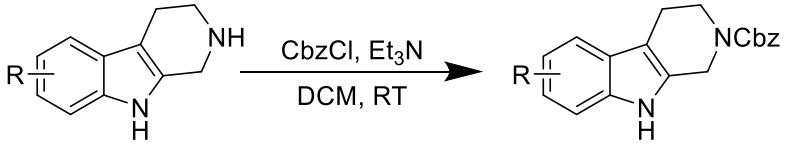
***tert*-Butyl 7-methoxy-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-b]indole-2-carboxylate 1j**: yield: 45% (1.431 g); (Flash column chromatography eluent, petrol ether/EtOAc = 3/1); white solid, m.p. 185.7-186.8 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.34 (d, *J* = 8.6 Hz, 1H), 6.83 (d, *J* = 2.3 Hz, 1H), 6.79 – 6.73 (m, 1H), 4.66 – 4.54 (m, 2H), 3.83 (s, 3H), 3.78 – 3.72 (m, 2H), 2.78 – 2.73 (m, 2H), 1.53 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.3, 137.1, 129.5, 121.6, 118.5, 109.0, 95.2, 80.2, 55.6, 42.7, 41.5, 28.6, 21.6.; **HRMS (ESI)** calculated for $C_{17}H_{22}N_2NaO_4$ $[M+Na]^+$: 325.1528, found: 325.1531.



1k

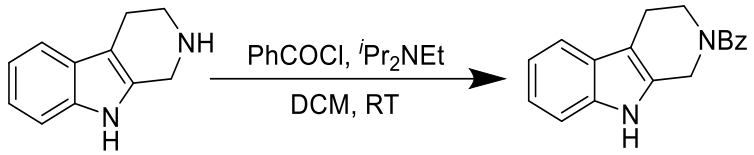
***tert*-Butyl 7-chloro-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate 1k**: yield: 45% (1.377 g); (Flash column chromatography eluent, petrol ether/EtOAc = 3/1); white solid, m.p. 196.7-197.8 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.28 (s, 1H), 7.11 – 7.01 (m, 1H), 4.65 (s, 2H), 3.76 (s, 2H), 2.76 (s, 2H), 1.54 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.6, 136.7, 131.6, 127.4, 125.8, 120.1, 118.8, 111.0, 108.6, 80.5, 42.6, 41.3, 28.6, 21.5; **HRMS (ESI)** calculated for $C_{16}H_{20}ClN_2O_2$ $[M+H]^+$: 307.1213, found: 307.1216.

2.2 General Procedure for Preparation of Substrates 1n-1r



S4 **1**

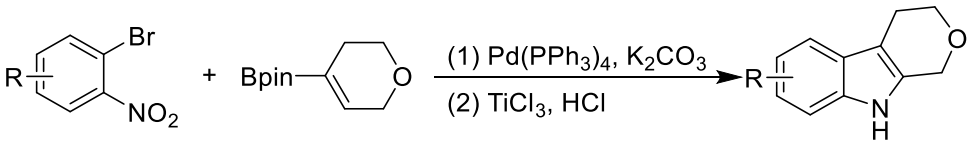
At 0 °C, to a solution of the crude amine **S4** in DCM (15 mL) was added Et_3N (1.4 mL, 1.0 equiv, 10 mmol) and CbzCl (1.5 mL, 1.05 equiv, 10.5 mmol). The resulting mixture was allowed to warm to room temperature and stirred at the same temperature. The reaction progress was monitored by TLC. Upon completion (~ 2 h), a solution of saturated aqueous solution of $NaHCO_3$ (15 mL) was added. The layers were separated, and the aqueous layer was extracted with ethyl acetate (30 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification of the resulting crude residue via silica gel flash column chromatography (gradient eluent: EtOAc in petrol ether) afforded the substrate **1o-1r**. The spectral data of **1o-1r** have been reported in previous literatures[2-4].



S4 **1n**

To a solution of **S4** (0.86 g, 5.0 mmol) in DCM (20 mL) was added $^{i}Pr_2NEt$ (0.97 g, 1.5 equiv, 7.5 mmol) and benzoyl chloride (0.89 g, 1.5 equiv, 7.5 mmol) at 0 °C under N_2. The resulting mixture was allowed to warm to room temperature and stirred at the same temperature. The reaction progress was monitored by TLC. Upon completion (~3 h), the solvent was evaporated to give the crude product, which was purified by flash column chromatography on silica gel (eluent: hexanes/DCM = 1:1 to 1:2) to afford pure **1n** as a brown solid. The spectral data of **1n** have been reported in previous literature[2].

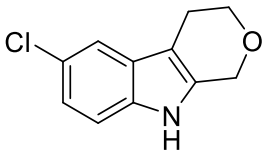
2.3 General Procedure for Preparation of Substrates 1s-1x



S5 **1**

To a solution of **S5** (1.0 equiv, 10 mmol) and 1-cyclohexen-1-yl-boronic acid pinacol ester (2.5 g, 1.2 equiv, 12 mmol) in a mixed solvent of toluene, EtOH, and H_2O (v/v/v = 5:2:1, 64 mL) were added $Pd(PPh_3)_4$ (1.16 g, 10 mol%, 1 mmol) and K_2CO_3 (5.5 g, 4.0 equiv, 40 mmol). The resultant mixture was then purged with N_2 and heated to 90 °C. The reaction progress was monitored by TLC. Upon completion (~24 h), the reaction mixture was cooled to room temperature and diluted with water (20 mL) and ethyl acetate (20 mL). The layers were separated, and the aqueous layer was extracted with

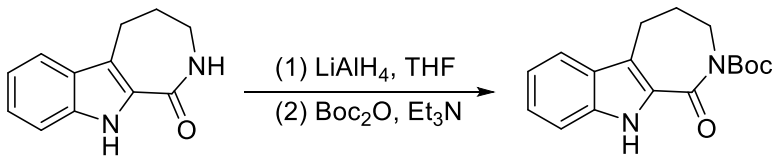
ethyl acetate (20 mL × 3). The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated. The residue was dissolved in acetonitrile (40 mL) and water (40 mL). A solution of $TiCl_3$ (15-20% in 30% hydrochloric acid, 40 mL) was added. The mixture was stirred at room temperature and the progress was monitored by TLC. Upon completion (~5 h), the mixture was extracted with ethyl acetate (20 mL × 3). The combined organic layers were washed with a saturated aqueous $NaHCO_3$ solution and brine, then dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel to afford pure **1s-1x**. The spectral data of **1s-1w** have been reported in previous literatures[2-4].



1u

6-Chloro-1,3,4,9-tetrahydropyrano[3,4-b]indole 1u: yield: 65% (1.346 g); (Flash column chromatography eluent, petrol ether/EtOAc = 3/1); yellow solid, m.p. 116.7-117.8 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.24 – 7.19 (m, 1H), 7.17 – 7.11 (m, 1H), 6.93 – 6.86 (m, 1H), 4.82 – 4.78 (m, 2H), 4.06 – 4.00 (m, 2H), 2.84 – 2.75 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 134.7, 133.2, 132.2, 130.5, 128.4, 125.4, 121.9, 117.7, 112.0, 107.5, 75.2, 65.5, 63.6, 29.8, 25.0, 22.1; **HRMS (ESI)** calculated for $C_{11}H_{11}ClNO$ $[M+H]^+$: 208.0529, found: 208.0521.

2.4 General Procedure for Preparation of Substrates 1y



1y

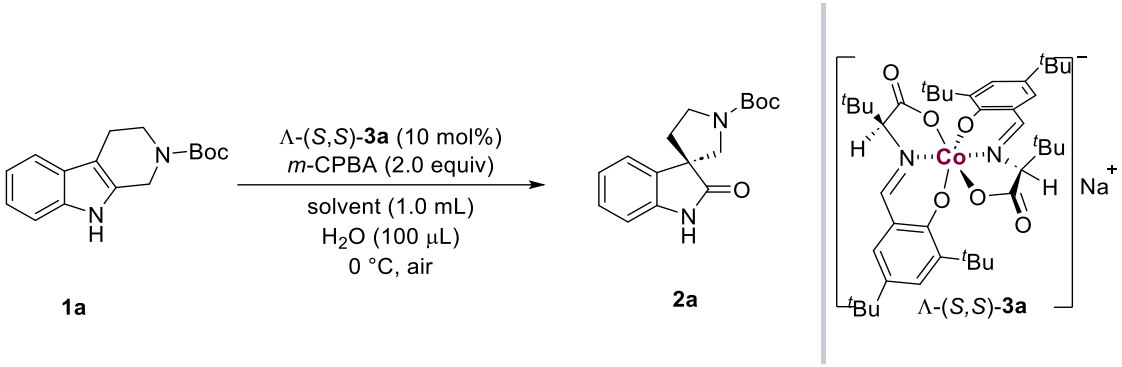
Under N_2 at room temperature, to a solution of 3,4,5,10-tetrahydroazepino[3,4 b]indol-1(2*H*)-one[5] (1.0 g, 5.0 mmol) in anhydrous THF (40 mL) was added $LiAlH_4$ (1.0 g, 5.0 equiv, 25.0 mmol). The mixture was heated to 90 ℃ and stirred for 6 h before it was cooled to 0 ℃ and treated successively with water (1 mL), a saturated aqueous NaOH solution (1 mL), and water (3.0 mL). This mixture was stirred for a few minutes and filtered. The filtrate was concentrated in vacuo to give the crude amine.

The crude amine was redissolved in DCM (20 mL). To this solution were added Boc_2O (1.09 g, 1.0

equiv, 5.0 mmol) and Et_3N (505 mg, 1.0 equiv, 5.0 mmol). The mixture was stirred at room temperature, and the reaction progress was monitored by TLC. Upon completion (~ 2 h), the solvent was evaporated, and the residue was purified by column chromatography on silica gel (eluent: hexanes/ethyl acetate = 5:1) to afford the pure indole **1y** as a white solid (428 mg, 30% yield for two steps). Due to the substitution pattern of the amide functionality, this compound is a mixture of two conformational isomers. The spectral data of **1y** have been reported in previous literatures[2].

3. Optimization of reaction conditions

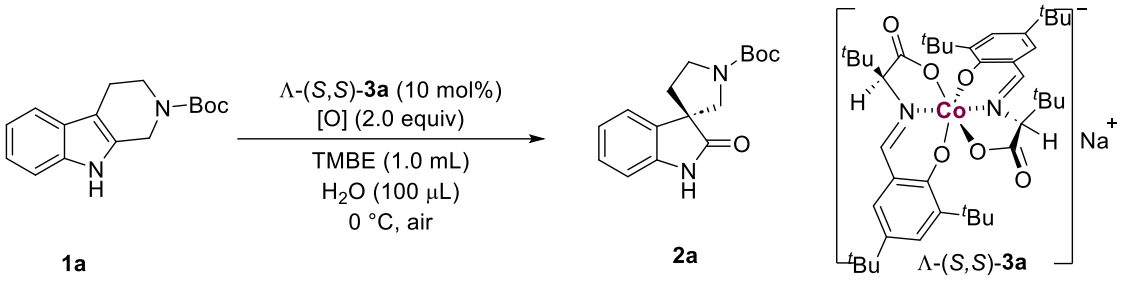
Table S1. Optimization for solvent[a].



entry	solvent	yield (%)[b]	e.r.[c]
1	THF	40	55.5:45.5
2	$CHCl_3$	62	69:31
3	Et_2O	59	67.5:32.5
4	EtOAc	60	61.5:38.5
5	DCM	42	74:26
6	CH_3CN	43	63:37
7	TBME	60	82.5:17.5
8	1,4-dioxane	63	67.5:32.5
9	Tol	20	61:39
10	Acetone	40	65:35

[a] The reactions were carried out with **1a** (0.1 mmol), H_2O (100 μL), Λ-(*S,S*)-**3a** (10 mol%), and *m*-CPBA (0.2 mmol) in solvent (1.0 mL) at 0 °C. [b] Isolated yields were based on **1a**. [c] The e.r. values were determined by chiral stationary HPLC.

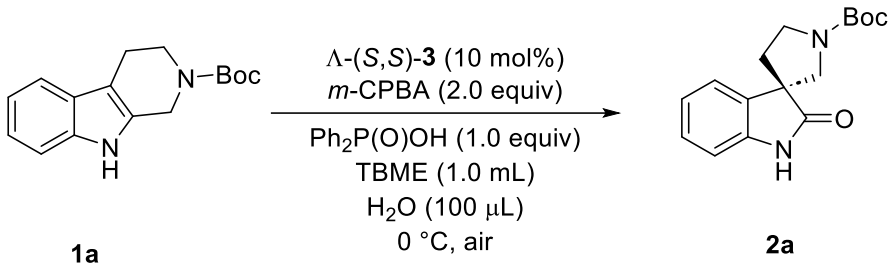
Table S2. Optimization for oxidant reagent[a].



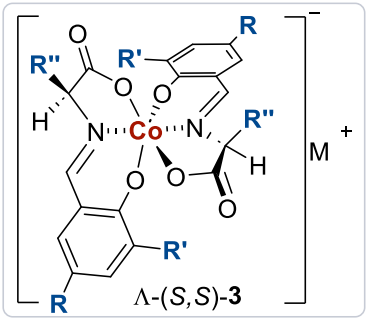
entry	oxidant	yield (%)[b]	e.r.[c]
1	NCS	83	53.5:46.5
2	NBS	78	76:24
3	NIS	82	68:32
4	I_2	80	56.5:43.5
5	*m*-CPBA	60	82.5:17.5

[a] The reactions were carried out with **1a** (0.1 mmol), H_2O (100 μL), Λ-(*S,S*)-**3a** (10 mol%), and [O] (0.2 mmol) in TBME (1.0 mL) at 0 °C. [b] Isolated yields were based on **1a**. [c] The e.r. values were determined by chiral stationary HPLC.

Table S3. Optimization for chiral catalyst[a].



1a **2a**

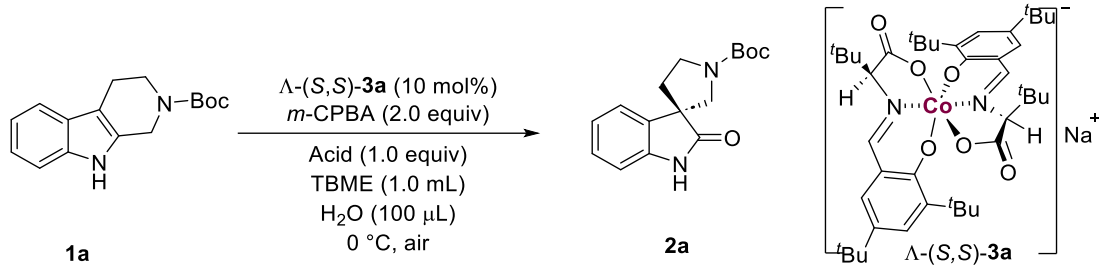


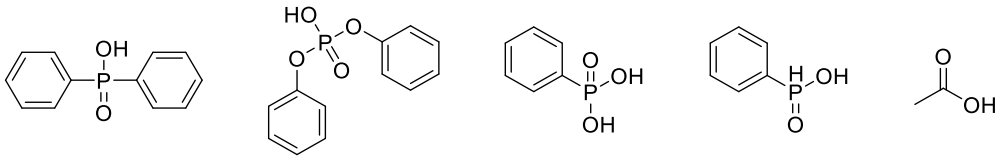
3a, R = R' = R'' = ^{t}Bu, M = Na;
3b, R = R' = R'' = ^{t}Bu, M = H;
3c, R = R' = ^{t}Bu, R'' = ^{i}Pr, M = Na;
3d, R = R' = ^{t}Bu, R'' = ^{i}Pr, M = H;
3e, R = R' = ^{t}Amyl, R'' = ^{i}Pr, M = Na;
3f, R = R' = ^{t}Amyl, R'' = ^{t}Bu, M = Na;
3g, R = R' = ^{t}Amyl, R'' = ^{t}Bu, M = H;
3h, R = R' = ^{t}Amyl, R'' = ^{t}Bu, M = Cs;

entry	**3**	yield (%)[b]	e.r.[c]
1	Λ-(*S*, *S*)-**3a**	56	90:10
2	Λ-(*S*, *S*)-**3b**	65	83.5:16.5
3	Λ-(*S*, *S*)-**3c**	52	89:11
4	Λ-(*S*, *S*)-**3d**	65	83.5:16.5
5	Λ-(*S*, *S*)-**3e**	36	86:14
6	Λ-(*S*, *S*)-**3f**	58	86:14
7	Λ-(*S*, *S*)-**3g**	58	85.5:14.5
8	Λ-(*S*, *S*)-**3h**	58	78.5:21.5

[a] The reactions were carried out with **1a** (0.1 mmol), H_2O (100 μL), $Ph_2P(O)OH$ (0.1 mmol), Λ-(*S, S*)-**3** (10 mol%), and *m*-CPBA (0.2 mmol) in TBME (1.0 mL) at 0 °C. [b] Isolated yields were based on **1a**. [c] The e.r. values were determined by chiral stationary HPLC.

Table S4. Optimization for acid[a].

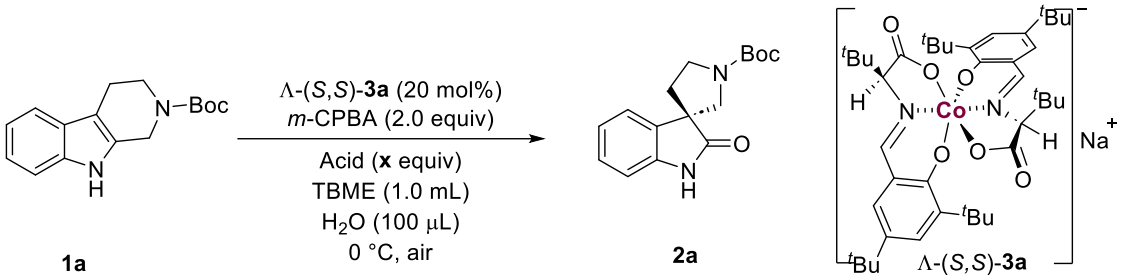




entry	acid	yield (%)[b]	e.r.[c]
1	**4a**	52	90:10
2	**4b**	40	61:39
3	**4c**	59	55:45
4	**4d**	32	67:33
5	**4e**	56	90:10

[a] The reactions were carried out with **1a** (0.1 mmol), H_2O (100 μL), Λ-(*S, S*)-**3a** (10 mol%), acid (0.1 mmol) and *m*-CPBA (0.2 mmol) in TBME (1.0 mL) at 0 °C. [b] Isolated yields were based on **1a**. [c] The e.r. values were determined by chiral stationary HPLC.

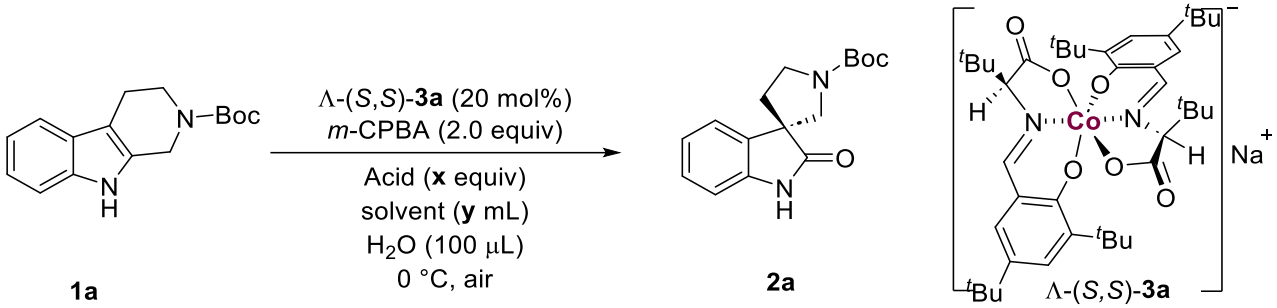
Table S5. Optimization for the equivalent of chiral catalysts and acid[a].



entry	Acid	x	yield (%)[b]	e.r.[c]
1	**4a**	0.2	65	92:8
2	**4a**	0.5	63	92:8
3	**4a**	0.7	65	94:6
4	**4a**	1.0	65	92:8
5	**4e**	1.0	60	91.5:8.5
6	**4e**	5.0	63	92:8
7	**4e**	10.0	68	94:6
8	**4e**	15.0	65	91.5:8.5

[a] The reactions were carried out with **1a** (0.1 mmol), H_2O (100 μL), Λ-(*S, S*)-**3a** (20 mol%), acid (**x** mmol), and *m*-CPBA (0.2 mmol) in TBME (1.0 mL) at 0 °C. [b] Isolated yields were based on **1a**. [c] The e.r. values were determined by chiral stationary HPLC.

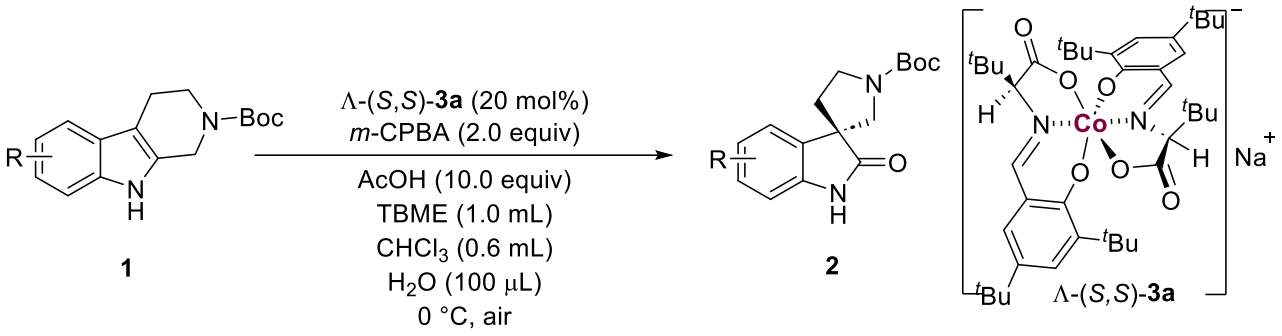
Table S6. Optimization for mixed solvent[a].



entry	Acid	x	Solvent	y	yield (%)[b]	e.r.[c]
1	**4a**	0.7	TBME/Tol (5:1)	1.2	62	91:9
2	**4a**	0.7	TBME/DCM (5:1)	1.2	60	90:10
3	**4a**	0.7	TBME/$CHCl_3$ (5:1)	1.2	63	91:9
4	**4e**	10.0	TBME/Tol (5:1)	1.2	70	92.5:7.5
5	**4e**	10.0	TBME/DCM (5:1)	1.2	73	92.5:7.5
6	**4e**	10.0	TBME/$CHCl_3$ (5:1)	1.2	66	93:7
7	**4e**	10.0	TBME/$CHCl_3$ (5:2)	1.4	65	93.5:6.5
8	**4e**	10.0	TBME/$CHCl_3$ (5:3)	1.6	68	94.5:5.5

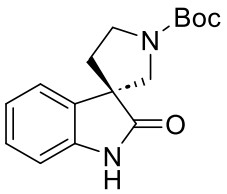
[a] The reactions were carried out with **1a** (0.1 mmol), H_2O (100 μL), Λ-(*S, S*)-**3a** (20 mol%), acid (**x** mmol), and *m*-CPBA (0.2 mmol) in TBME/Solvent (**y** mL) at 0 °C. [b] Isolated yields were based on **1a**. [c] The e.r. values were determined by chiral stationary HPLC.

4. Experimental Procedures of Asymmetric Reaction and Characterization Data



General Procedure:

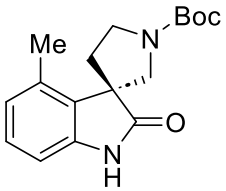
At room temperature, a 10 mL vial was charged with Λ-(*S,S*)-**3a** (16 mg, 20 mol%), H_2O (100 μL), AcOH (60 μL), and indole **1** (0.10 mmol), after which a mixed solvent of TBME/$CHCl_3$ (1.6 mL, v/v = 5:3) was added. The resulting mixture was cooled to 0 °C and stirred for 20 min, followed by the addition of *m*-CPBA (34.5 mg, 2.0 equiv, 0.20 mmol). The reaction mixture was stirred at 0 °C, and the progress of the reaction was monitored by TLC. Upon completion, the reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ solution (3 mL). The mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography afforded the pure product. Note: Compounds **2a–2m** were observed as a mixture of slowly interconverting rotamers in solution due to restricted rotation around the N–C(O) bond of the Boc carbamate. Accordingly, duplicated and/or broadened signals are observed in the ^1H and ^{13}C NMR spectra recorded at room temperature.



2a

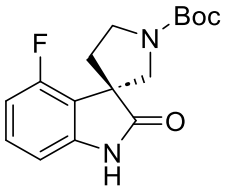
***tert*-Butyl (*R*)-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2a**: yield: 68% (19.6 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; brown oil; $[\alpha]_D^{20} = -21.2$ (c 0.13 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.38/8.28 (s, 1H), 7.26 – 7.15 (m, 2H), 7.09 – 7.01 (m, 1H), 6.97 – 6.89 (m, 1H), 3.88 – 3.75 (m, 2H), 3.74 – 3.66 (m, 1H), 3.66 – 3.54 (m, 1H), 2.45 –

2.37 (m, 1H), 2.12 – 2.04 (m, 1H), 1.51/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.2, 154.6, 140.2, 133.2, 128.5, 123.0, 110.2, 80.0, 54.3, 53.0, 45.3, 36.5, 35.7, 28.6; **HRMS (ESI)** calculated for $C_{16}H_{20}N_2NaO_3$ $[M+Na]^+$: 311.1472, found: 311.1475; **Enantiomeric ratio**: 94.5:5.5, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 8.80 min (minor), t_R = 12.25 min (major). The absolute configuration of **2a** was assigned by comparison of its optical rotation with the reported literature data[2].



2b

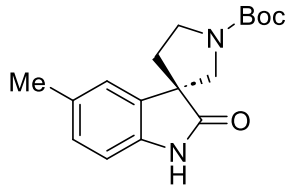
***tert*-Butyl (*R*)-4-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2b:** yield: 60% (18.1 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = −20.8 (c 0.08 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.58/8.46 (s, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.86 – 6.80 (m, 1H), 6.78 – 6.70 (m, 1H), 3.89 – 3.71 (m, 4H), 2.46 – 2.38 (m, 1H), 2.35 (s, 3H), 2.26 – 2.16 (m, 1H), 1.50/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 182.2, 154.2, 141.0, 134.6, 128.5, 125.5, 107.9, 79.9, 52.0, 45.7, 34.0, 29.8, 28.6, 18.0; **HRMS (ESI)** calculated for $C_{17}H_{22}N_2NaO_3$ $[M+Na]^+$: 325.1528, found: 325.1530; **Enantiomeric ratio**: 80.5:19.5, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 8.95 min (minor), t_R = 11.95 min (major).



2c

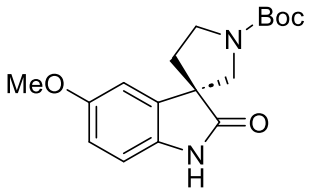
***tert*-Butyl (*R*)-4-fluoro-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2c:** yield: 62% (19.0 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = −15.3 (c 0.12 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.87/7.80 (s, 1H), 7.23 – 7.17 (m, 1H), 6.78 – 6.64 (m, 2H), 3.88 – 3.83 (m, 1H), 3.83 – 3.76 (m, 2H), 3.76 – 3.71 (m, 1H), 2.43 – 2.37 (m, 1H), 2.37 – 2.32 (m, 1H), 1.50/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.4, 158.9 (d, *J* = 247.5 Hz), 154.4, 142.6, 130.5, 110.5 (d, *J* = 21.2 Hz), 106.3 (d, *J* = 3.8 Hz), 79.9, 53.0, 52.5, 45.5, 34.9,

29.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.99 ppm; **HRMS (ESI)** calculated for $C_{16}H_{19}FN_2NaO_3$ $[M+Na]^+$: 329.1277, found: 329.1281; **Enantiomeric ratio**: 94.5:5.5, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 8.06 min (minor), t_R = 13.57 min (major).



2d

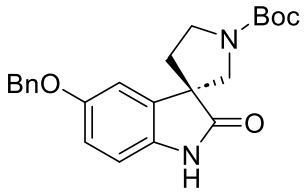
***tert*-Butyl (*R*)-5-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2d**: yield: 62% (18.7 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = −21.4 (c 0.18 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.75/8.65 (s, 1H), 7.09 – 6.94 (m, 2H), 6.87 – 6.77 (m, 1H), 3.88 – 3.75 (m, 2H), 3.73 – 3.65 (m, 1H), 3.65 – 3.53 (m, 1H), 2.44 – 2.39 (m, 1H), 2.32 (s, 3H), 2.10 – 2.02 (m, 1H), 1.52/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.5, 154.7, 137.8, 133.4, 132.7, 128.8, 123.6, 109.9, 80.0, 54.6, 53.6, 45.6, 36.5, 28.7, 21.3; **HRMS (ESI)** calculated for $C_{17}H_{22}N_2NaO_3$ $[M+Na]^+$: 325.1528, found: 325.1533; **Enantiomeric ratio**: 93:7, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 7.95 min (minor), t_R = 12.23 min (major).



2e

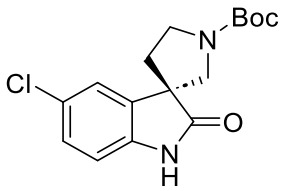
***tert*-Butyl (*R*)-5-methoxy-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2e**: yield: 65% (20.7 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = -38.8 (c 0.092 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.78/8.70 (s, 1H), 6.87 – 6.82 (m, 1H), 6.80 – 6.75 (m, 2H), 3.89 – 3.81 (m, 1H), 3.77 (s, 3H), 3.76 – 3.69 (m, 2H), 3.64 – 3.52 (m, 1H), 2.43 – 2.38 (m, 1H), 2.08 – 2.02 (m, 1H), 1.54/1.45 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.1, 156.4, 154.5, 134.6, 133.5, 112.9, 110.5, 110.2, 80.0, 56.0, 54.5, 45.3, 36.5, 35.7, 28.6; HRMS (ESI) calculated for $C_{17}H_{22}N_2NaO_4$ $[M+Na]^+$: 341.1477, found: 341.1477; **Enantiomeric ratio**: 91:9, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T

= 30 °C, λ = 254 nm): t_R = 12.30 min (minor), t_R = 18.42 min (major).



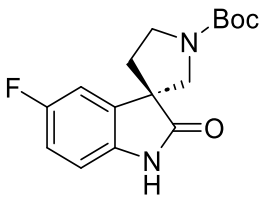
2f

***tert*-Butyl (*R*)-5-(benzyloxy)-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2f**: yield: 58% (22.9 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = −27.3 (c 0.10 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.04/7.96 (s, 1H), 7.47 – 7.23 (m, 5H), 6.93 – 6.75 (m, 3H), 5.01 (s, 2H), 3.82 – 3.66 (m, 4H), 2.45 – 2.37 (m, 1H), 2.07 – 2.00 (m, 1H), 1.51/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.0, 155.5, 154.5, 136.9, 134.6, 133.9, 128.7, 128.2, 127.7, 114.0, 111.3, 110.5, 80.0, 71.0, 54.5, 53.0, 45.3, 35.6, 29.7; **HRMS (ESI)** calculated for $C_{23}H_{26}N_2NaO_4$ $[M+Na]^+$: 417.1790, found: 417.1795; **Enantiomeric ratio**: 89:11, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 13.62 min (minor), t_R = 14.64 min (major).



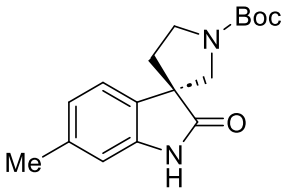
2g

***tert*-Butyl (*R*)-5-chloro-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2g**: yield: 68% (21.9 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = −16.5 (c 0.21 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.20/8.14 (s, 1H), 7.25 – 7.11 (m, 2H), 6.88 – 6.81 (m, 1H), 3.90 – 3.81 (m, 1H), 3.76 – 3.69 (m, 2H), 3.65 – 3.53 (m, 1H), 2.45 – 2.39 (m, 1H), 2.07 (m, 1H), 1.52/1.47 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.9, 154.5, 138.9, 134.8, 134.5, 128.5, 123.4, 111.3, 80.3, 54.4, 53.9, 45.4, 35.6, 28.6; **HRMS (ESI)** calculated for $C_{16}H_{19}ClN_2NaO_3$ $[M+Na]^+$: 345.0982, found: 345.0986; **Enantiomeric ratio**: 92.5:7.5, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 7.70 min (minor), t_R = 13.57 min (major).



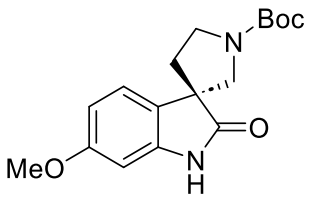
2h

***tert*-Butyl (*R*)-5-fluoro-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2h**: yield: 63% (19.1 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −9.0 (c 0.21 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.43/8.37 (s, 1H), 6.98 – 6.82 (m, 3H), 3.91 – 3.75 (m, 2H), 3.74 – 3.70 (m, 1H), 3.65 – 3.53 (m, 1H), 2.46 – 2.39 (m, 1H), 2.10 – 2.04 (m, 1H), 1.51/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.2, 159.5 (d, *J* = 242.0 Hz), 154.5, 136.2, 115.0 (d, *J* = 23.1 Hz), 110.9 (d, *J* = 7.8 Hz), 80.2, 59.6, 54.2 (d, *J* = 48.0 Hz), 45.3, 38.3, 28.6; ^{19}F NMR (565 MHz, $CDCl_3$) δ -119.58 ppm; **HRMS (ESI)** calculated for $C_{16}H_{19}FN_2NaO_3$ $[M+Na]^+$: 329.1277, found: 329.1281; **Enantiomeric ratio**: 94:6, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 8.08 min (minor), t_R = 14.03 min (major).



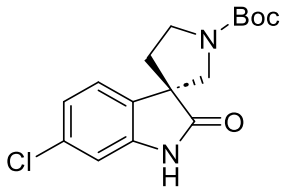
2i

***tert*-Butyl (*R*)-6-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2i**: yield: 60% (18.1 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −9.5 (c 0.25 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.75/8.65 (s, 1H), 7.09 – 6.94 (m, 2H), 6.87 – 6.77 (m, 1H), 3.88 – 3.75 (m, 2H), 3.73 – 3.65 (m, 1H), 3.65 – 3.53 (m, 1H), 2.44 – 2.39 (m, 1H), 2.32 (s, 3H), 2.10 – 2.02 (m, 1H), 1.52/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.9, 154.6, 140.4, 138.8, 130.3, 123.6, 122.6, 111.1, 80.0, 54.6, 53.3, 45.6, 36.6, 28.7, 21.7; HRMS (ESI) calculated for $C_{17}H_{22}N_2NaO_3$ $[M+Na]^+$: 325.1528, found: 325.1533; **Enantiomeric ratio**: 92:8, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 10.47 min (minor), t_R = 19.04 min (major).



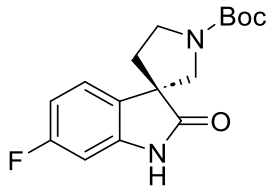
2j

***tert*-Butyl (*R*)-6-methoxy-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2j**: yield: 60% (19.1 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −12.5 (c 0.15 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.75/8.65 (s, 1H), 7.10 – 7.02 (m, 1H), 6.58 – 6.50 (m, 2H), 3.90 – 3.81 (m, 1H), 3.79 (s, 3H), 3.75 – 3.65 (m, 2H), 3.60 – 3.49 (m, 1H), 2.42 – 2.32 (m, 1H), 2.08 – 2.00 (m, 1H), 1.50/1.45 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.5, 160.4, 154.6, 141.3, 125.1, 107.6, 97.6, 80.0, 55.7, 54.1, 53.0, 52.1, 45.6, 36.6, 29.8; HRMS (ESI) calculated for $C_{17}H_{22}N_2NaO_4$ $[M+Na]^+$: 341.1477, found: 341.1481; **Enantiomeric ratio**: 80:20, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 13.42 min (minor), t_R = 21.21 min (major).



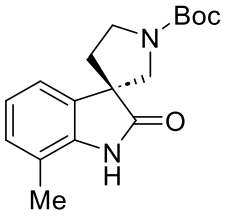
2k

***tert*-Butyl (*R*)-6-chloro-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2k**: yield: 60% (19.4 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −11.0 (c 0.14 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.31/8.25 (s, 1H), 7.13 – 6.98 (m, 2H), 6.94 (s, 1H), 3.88 – 3.78 (m, 1H), 3.78 – 3.64 (m, 2H), 3.63 – 3.50 (m, 1H), 2.44 – 2.37 (m, 1H), 2.07 – 2.02 (m, 1H), 1.51/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.3, 154.6, 141.4, 134.3, 131.5, 123.8, 123.0, 110.9, 80.3, 54.4, 53.2, 45.2, 35.6, 28.6; HRMS (ESI) calculated for $C_{16}H_{19}ClN_2NaO_3$ $[M+Na]^+$: 345.0982, found: 345.0980; **Enantiomeric ratio**: 90:10, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 9.97 min (minor), t_R = 21.17 min (major).



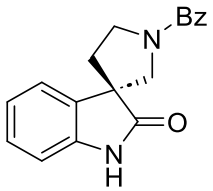
2l

***tert*-Butyl (*R*)-6-fluoro-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2l**: yield: 62% (19.0 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −14.8 (c 0.19 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.44/8.37 (s, 1H), 7.15 – 7.06 (m, 1H), 6.79 – 6.57 (m, 2H), 3.88 – 3.78 (m, 1H), 3.77 – 3.64 (m, 2H), 3.62 – 3.51 (m, 1H), 2.45 – 2.36 (m, 1H), 2.07 – 2.01 (m, 1H), 1.51/1.46 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.7, 163.0 (d, *J* = 245.6 Hz), 154.6, 141.7, 128.3 (d, *J* = 72.7 Hz), 123.9, 109.3 (d, *J* = 22.6 Hz), 98.9 (d, *J* = 27.1 Hz), 80.2, 54.5, 52.2, 45.2, 35.7, 28.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.68 ppm; **HRMS (ESI)** calculated for $C_{16}H_{19}FN_2NaO_3$ $[M+Na]^+$: 329.1277, found: 329.1280; **Enantiomeric ratio**: 89:11, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 8.92 min (minor), t_R = 19.49 min (major)



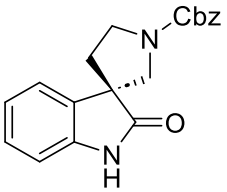
2m

***tert*-Butyl (*R*)-7-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2m**: yield: 60% (18.1 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −9.3 (c 0.13 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.59/8.53 (s, 1H), 7.10 – 6.94 (m, 3H), 3.87 – 3.75 (m, 2H), 3.73 – 3.66 (m, 1H), 3.64 – 3.53 (m, 1H), 2.45 – 2.38 (m, 1H), 2.29 (s, 3H), 2.13 – 2.05 (m, 1H), 1.51/1.45 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.8, 154.6, 139.0, 132.8, 129.8, 123.1, 120.2, 119.7, 80.0, 54.6, 54.0, 45.6, 36.6, 28.7, 16.6; **HRMS (ESI)** calculated for $C_{17}H_{22}N_2NaO_3$ $[M+Na]^+$: 325.1528, found: 325.1533; **Enantiomeric ratio**: 92:8, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 6.78 min (minor), t_R = 7.27 min (major).



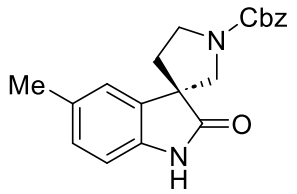
2n

(*R*)-1'-Benzoylspiro[indoline-3,3'-pyrrolidin]-2-one 2n: yield: 58% (17.0 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −5.6 (c 0.06 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.81 – 7.78 (m, 1H), 7.67 – 7.63 (m, 2H), 7.49 – 7.45 (m, 1H), 7.42 – 7.37 (m, 4H), 7.18 – 7.14 (m, 1H), 3.81 (q, *J* = 6.5 Hz, 2H), 3.45 (t, *J* = 6.8 Hz, 2H), 2.10 (s, 1H), 2.04 (s, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.8, 168.0, 137.7, 134.4, 132.9, 131.7, 130.1, 128.7, 127.9, 127.0, 121.6, 112.7, 46.2, 41.6, 29.8, 24.0; **HRMS (ESI)** calculated for $C_{18}H_{16}N_2NaO_2$ $[M+Na]^+$: 315.1109, found: 315.1112; **Enantiomeric ratio**: 86:14, determined by HPLC (Daicel Chirapak OD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 23.62 min (minor), t_R = 28.59 min (major).



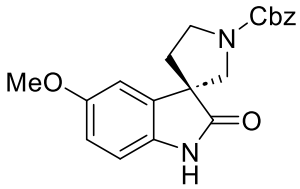
2o

Benzyl (*R*)-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2o: yield: 63% (20.3 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −11.6 (c 0.17 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.98/8.94 (s, 1H), 7.44 – 7.40 (m, 1H), 7.40 – 7.37 (m, 1H), 7.35 – 7.27 (m, 3H), 7.25 – 7.21 (m, 1H), 7.17 – 7.12 (m, 1H), 7.06 – 7.00 (m, 1H), 6.96 – 6.92 (m, 1H), 5.21 – 5.15 (m, 2H), 3.95 – 3.89 (m, 1H), 3.85 – 3.79 (m, 2H), 3.71 – 3.63 (m, 1H), 2.47 – 2.41 (m, 1H), 2.15 – 2.10 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.3, 178.2, 154.9, 140.3, 136.8, 132.7, 128.6, 128.1, 127.9, 123.1, 122.8, 110.3, 67.2, 60.6, 54.1, 53.4, 45.9, 36.4, 29.7; **HRMS (ESI)** calculated for $C_{19}H_{18}N_2NaO_3$ $[M+Na]^+$: 345.1215, found: 345.1218; **Enantiomeric ratio**: 90:10, determined by HPLC (Daicel Chirapak OD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 15.42 min (minor), t_R = 21.02 min (major).



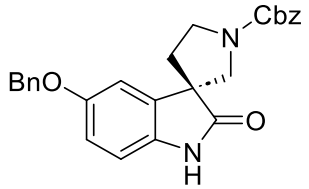
2p

Benzyl (*R*)-5-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2p: yield: 52% (17.5 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −15.9 (c 0.28 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.88/8.83 (s, 1H), 7.50 – 7.37 (m, 2H), 7.37 – 7.25 (m, 3H), 7.03 (d, *J* = 7.9 Hz, 1H), 6.99 – 6.92 (m, 1H), 6.85 – 6.79 (m, 1H), 5.26 – 5.16 (m, 2H), 3.97 – 3.90 (m, 1H), 3.86 – 3.78 (m, 2H), 3.71 – 3.62 (m, 1H), 2.45 – 2.40 (m, 1H), 2.30 (s, 3H), 2.12 – 2.07 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.1, 178.1, 154.9, 137.7, 136.7, 132.9, 132.6, 128.9, 128.6, 128.1, 127.9, 123.6, 110.0, 67.2, 54.5, 53.5, 45.9, 36.4, 29.7, 21.2; **HRMS (ESI)** calculated for $C_{20}H_{20}N_2NaO_3$ $[M+Na]^+$: 359.1372, found: 359.1375; **Enantiomeric ratio**: 90:10, determined by HPLC (Daicel Chirapak OD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 13.44 min (minor), t_R = 18.55 min (major).



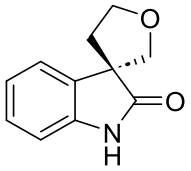
2q

Benzyl (*R*)-5-methoxy-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2q: yield: 68% (24.0 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = −32.4 (c 0.24 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.45/8.42 (s, 1H), 7.48 – 7.18 (m, 5H), 6.87 – 6.80 (m, 1H), 6.79 – 6.69 (m, 2H), 5.23 – 5.11 (m, 2H), 3.91 (m, 1H), 3.87 – 3.77 (m, 2H), 3.75 (s, 3H), 3.70 – 3.62 (m, 1H), 2.47 – 2.39 (m, 1H), 2.13 – 2.06 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.8, 156.4, 154.9, 136.9, 136.7, 134.0, 133.4, 128.7, 128.1, 127.9, 112.8, 110.6, 110.2, 67.2, 55.9, 54.2, 53.6, 45.4, 36.5, 29.8; **HRMS (ESI)** calculated for $C_{20}H_{20}N_2NaO_4$ $[M+Na]^+$: 375.1321, found: 375.1324; **Enantiomeric ratio**: 89.5:10.5, determined by HPLC (Daicel Chirapak OD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 18.67 min (minor), t_R = 27.89 min (major).



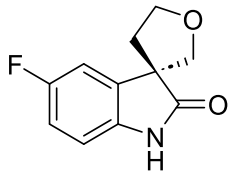
2r

Benzyl (*R*)-5-(benzyloxy)-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate 2r: yield: 62% (26.6 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = −17.6 (c 0.14 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.63/8.58 (s, 1H), 7.38 – 7.30 (m, 5H), 7.29 (s, 1H), 7.28 – 7.27 (m, 1H), 7.26 – 7.17 (m, 3H), 6.80 – 6.69 (m, 3H), 5.14 – 5.06 (m, 2H), 4.92 (s, 2H), 3.90 – 3.77 (m, 1H), 3.77 – 3.65 (m, 2H), 3.63 – 3.54 (m, 1H), 2.40 – 2.31 (m, 1H), 2.05 – 1.95 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.8, 177.7, 155.5, 154.8, 136.9, 134.1, 133.9, 133.6, 128.8, 128.6, 128.2, 127.9, 127.7, 114.1, 111.4, 110.5, 71.0, 67.2, 54.5, 45.8, 35.6, 29.7; **HRMS (ESI)** calculated for $C_{26}H_{24}N_2NaO_4$ $[M+Na]^+$:451.1634, found: 451.1634; **Enantiomeric ratio**: 83.5:16.5, determined by HPLC (Daicel Chirapak OD, isopropanol / hexane = 20/80, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 12.93 min (minor), t_R = 17.19 min (major).



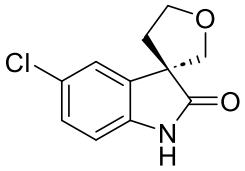
2s

(*R*)-4,5-Dihydro-2H-spiro[furan-3,3'-indolin]-2'-one 2s: yield: 65% (12.3 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = +14.0 (c 0.10 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.23 (t, *J* = 7.7 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.7 Hz, 1H), 4.25 – 4.19 (m, 2H), 4.08 (d, *J* = 8.6 Hz, 1H), 3.96 (d, *J* = 8.5 Hz, 1H), 2.58 – 2.52 (m, 1H), 2.22 – 2.16 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.5, 140.4, 134.2, 128.3, 123.1, 123.0, 110.1, 69.2, 54.9, 38.8; **HRMS (ESI)** calculated for $C_{11}H_{12}NO_2$ $[M+H]^+$: 190.0868, found: 190.0872; **Enantiomeric ratio**: 92.5:7.5, determined by HPLC (Daicel Chirapak AS, isopropanol / hexane = 40/60, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 38.85 min (minor), t_R = 52.37 min (major).



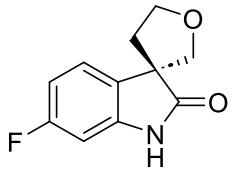
2t

(*R*)-5'-Fluoro-4,5-dihydro-2H-spiro[furan-3,3'-indolin]-2'-one 2t: yield: 62% (12.8 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = +16.6 (c 0.18 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.04 – 7.00 (m, 1H), 6.95 – 6.90 (m, 1H), 6.90 – 6.86 (m, 1H), 4.24 – 4.18 (m, 2H), 4.05 (d, *J* = 8.6 Hz, 1H), 3.95 (d, *J* = 8.6 Hz, 1H), 2.59 – 2.52 (m, 1H), 2.21 – 2.15 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.3, 159.6 (d, *J* = 241.1 Hz), 136.2, 135.9 (d, *J* = 8.0 Hz), 114.6 (d, *J* = 23.7 Hz), 111.1 (d, *J* = 25.0 Hz), 110.7 (d, *J* = 8.1 Hz), 69.08, 55.50, 38.65; ^{19}F NMR (565 MHz, $CDCl_3$) δ -119.66 ppm; **HRMS (ESI)** calculated for $C_{11}H_{11}FNO_2$ $[M+H]^+$: 208.0774, found: 208.0777; **Enantiomeric ratio**: 90:10, determined by HPLC (Daicel Chirapak OJ, isopropanol / hexane = 20/80, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 6.52 min (major), t_R = 7.78 min (minor).



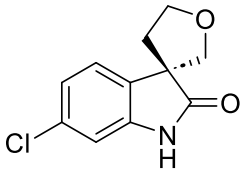
2u

(*R*)-5'-Chloro-4,5-dihydro-2H-spiro[furan-3,3'-indolin]-2'-one 2u: yield: 60% (13.4 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; **$[\alpha]_D^{20}$** = +26.7 (c 0.08 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.17 (s, 1H), 7.28 – 7.26 (m, 1H), 7.23 – 7.18 (m, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 4.25 – 4.16 (m, 2H), 4.04 (d, *J* = 8.6 Hz, 1H), 3.95 (d, *J* = 8.6 Hz, 1H), 2.59 – 2.53 (m, 1H), 2.20 – 2.15 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 180.9, 138.8, 136.0, 132.2, 128.2, 123.6, 111.1, 69.1, 55.2, 38.7; **HRMS (ESI)** calculated for $C_{11}H_{11}ClNO_2$ $[M+H]^+$: 224.0478, found: 224.0482; **Enantiomeric ratio**: 87:13, determined by HPLC (Daicel Chirapak OJ, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 9.77 min (major), t_R = 12.77 min (minor).



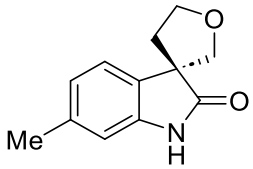
2v

(*R*)-6'-Fluoro-4,5-dihydro-2H-spiro[furan-3,3'-indolin]-2'-one 2v: yield: 60% (12.6 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = +12.6 (c 0.09 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.23 – 7.18 (m, 1H), 6.76 – 6.69 (m, 2H), 4.23 – 4.18 (m, 2H), 4.05 (d, *J* = 8.6 Hz, 1H), 3.93 (d, *J* = 8.6 Hz, 1H), 2.57 – 2.51 (m, 1H), 2.19 – 2.13 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.9, 162.9 (d, *J* = 245.2 Hz), 141.7 (d, *J* = 11.8 Hz), 129.5 (d, *J* = 3.1 Hz), 124.0 (d, *J* = 9.6 Hz), 109.4 (d, *J* = 22.5 Hz), 98.9 (d, *J* = 27.4 Hz), 69.1, 54.5, 38.7; ^{19}F NMR (565 MHz, $CDCl_3$) δ -112.18 ppm; **HRMS (ESI)** calculated for $C_{11}H_{11}FNO_2$ $[M+H]^+$: 208.0774, found: 208.0773; **Enantiomeric ratio**: 82:18, determined by HPLC (Daicel Chirapak OJ, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 10.72 min (major), t_R = 12.23 min (minor).



2w

(*R*)-6'-Chloro-4,5-dihydro-2H-spiro[furan-3,3'-indolin]-2'-one 2w: yield: 65% (14.5 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = +11.8 (c 0.10 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.05 – 7.01 (m, 1H), 6.99 – 6.95 (m, 1H), 4.23 – 4.19 (m, 2H), 4.04 (d, *J* = 8.6 Hz, 1H), 3.93 (d, *J* = 8.6 Hz, 1H), 2.57 – 2.51 (m, 1H), 2.19 – 2.13 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.5, 141.5, 134.0, 132.6, 123.9, 123.1, 110.8, 77.0, 69.1, 54.7, 38.7; **HRMS (ESI)** calculated for $C_{11}H_{11}ClNO_2$ $[M+H]^+$: 224.0478, found: 224.0482; **Enantiomeric ratio**: 85:15, determined by HPLC (Daicel Chirapak OJ, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 12.24 min (major), t_R = 14.97 min (minor).

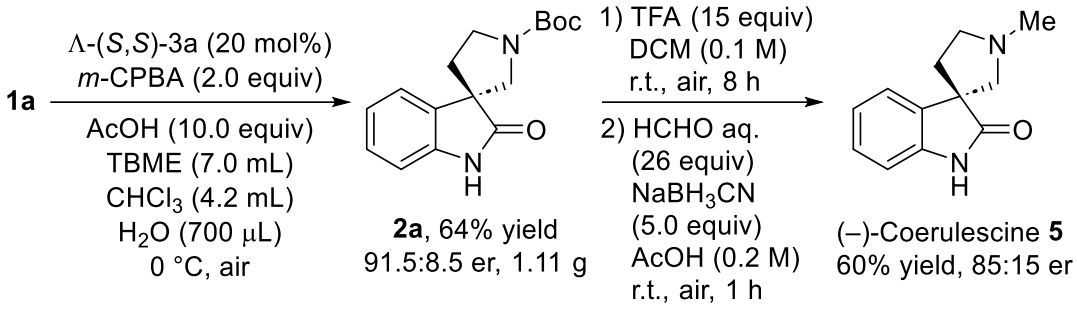


2x

(*R*)-6'-Methyl-4,5-dihydro-2H-spiro[furan-3,3'-indolin]-2'-one 2x: yield: 60% (12.2 mg); flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; colorless oil; $[\alpha]_D^{20}$ = +3.2 (c 0.18 CH_2Cl_2); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.74 (s, 1H), 4.22 – 4.18 (m, 2H), 4.05 (d, *J* = 8.5 Hz, 1H), 3.93 (d, *J* = 8.5 Hz, 1H), 2.55 – 2.50 (m, 1H), 2.35 (s, 3H), 2.18 – 2.13 (m, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 181.9, 140.5, 138.5, 131.2, 123.6, 122.7, 111.0, 69.2, 54.7, 38.8, 21.7; **HRMS (ESI)** calculated for $C_{12}H_{14}NO_2$ $[M+H]^+$: 204.1025, found: 204.1027; **Enantiomeric ratio**: 86.5:13.5, determined by HPLC (Daicel Chirapak AD, isopropanol / hexane = 10/90, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 9.69 min (minor), t_R = 10.32 min (major).

5. Synthetic Applications and Mechanistic Experiments

5.1 Gram-scale reaction and the synthesis of (–)-Coerulescine

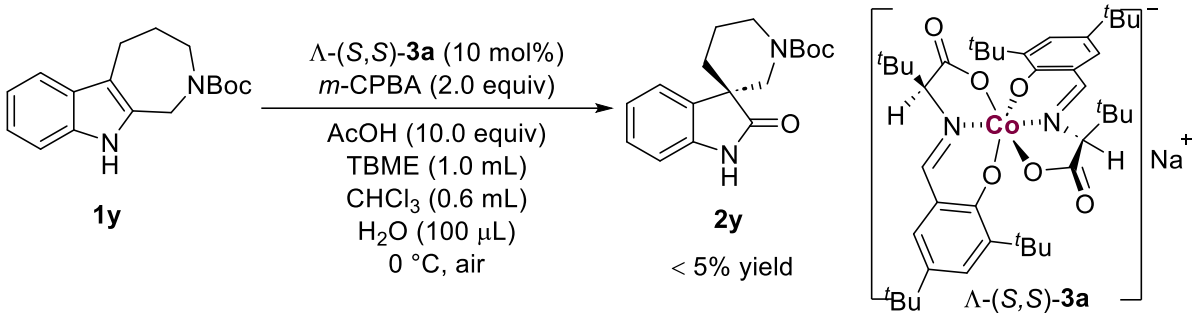


In a 50 mL tube equipped with a magnetic stirring bar, indole **1a** (6.0 mmol, 1.0 equiv), Λ-(*S,S*)-**3a** (960 mg, 20 mol%), H_2O (700 μL), AcOH (60 mmol, 10.0 equiv), and a mixed solvent of TBME/$CHCl_3$ (11.2 mL, v/v = 5:3) were combined. The resulting mixture was cooled to 0 °C and stirred for 20 min, followed by the addition of *m*-CPBA (2.42 g, 12 mmol, 2.0 equiv). The reaction mixture was stirred at the same temperature, and the reaction progress was monitored by TLC. Upon completion, the reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with ethyl acetate (3 × 15 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography afforded the pure product **2a** in 64% yield (1.11 g, 91.5:8.5 er).

To a solution of **2a** (57.6 mg, 0.20 mmol, 1.0 equiv) in anhydrous DCM (0.1 M) was added TFA (0.2 mL, 15 equiv). The reaction mixture was stirred at room temperature for 8 h, then diluted with DCM (5 mL) and H_2O (1 mL). The mixture was basified to pH 9–10 with 2 N aqueous NaOH and extracted with DCM. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to afford the crude amine. The crude amine was dissolved in AcOH (0.2 M), and aqueous formaldehyde solution (37 wt%, 0.40 mL) and $NaBH_3CN$ (63 mg, 5.0 equiv, 1.0 mmol) were added sequentially. The resulting mixture was stirred at room temperature for 1 h, then diluted with ethyl acetate (2 mL) and basified to pH 9–10 with 2 N aqueous NaOH. The mixture was extracted with ethyl acetate, and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Purification of the residue by preparative TLC (eluent: DCM/MeOH = 9:1) afforded (–)-Coerulescine **5** as a colorless wax in 60% overall yield (24.2 mg, 85:15 er).

(–)-Coerulescine 5: yield: 60% (24.2 mg); flash column chromatography eluent, DCM/MeOH = 9/1; colorless oil; $[\alpha]_D^{20}$ = +12.6 (c 0.1 CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.40 (d, *J* = 7.4 Hz, 1H), 7.23 – 7.14 (m, 1H), 7.08 – 7.01 (m, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 3.05 – 2.99 (m, 1H), 2.91 – 2.84 (m, 2H), 2.83 – 2.76 (m, 1H), 2.46 (s, 3H), 2.44 – 2.36 (m, 1H), 2.14 – 2.08 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.8, 140.2, 136.2, 127.9, 123.5, 123.0, 109.6, 66.5, 56.9, 53.8, 42.0, 38.1; **HRMS (ESI)** calculated for $C_{12}H_{15}N_2O$ $[M+H]^+$: 203.1184, found: 203.1189; **Enantiomeric ratio**: 85:15, determined by HPLC (Daicel Chirapak AS, isopropanol / hexane = 30/70, flow rate = 1.0 mL/min, T = 30 °C, λ = 254 nm): t_R = 8.96 min (major), t_R = 14.01 min (minor).

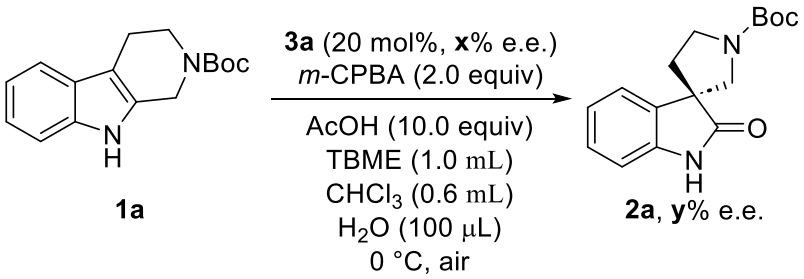
5.2 Synthesis of seven-membered ring substrates 2y



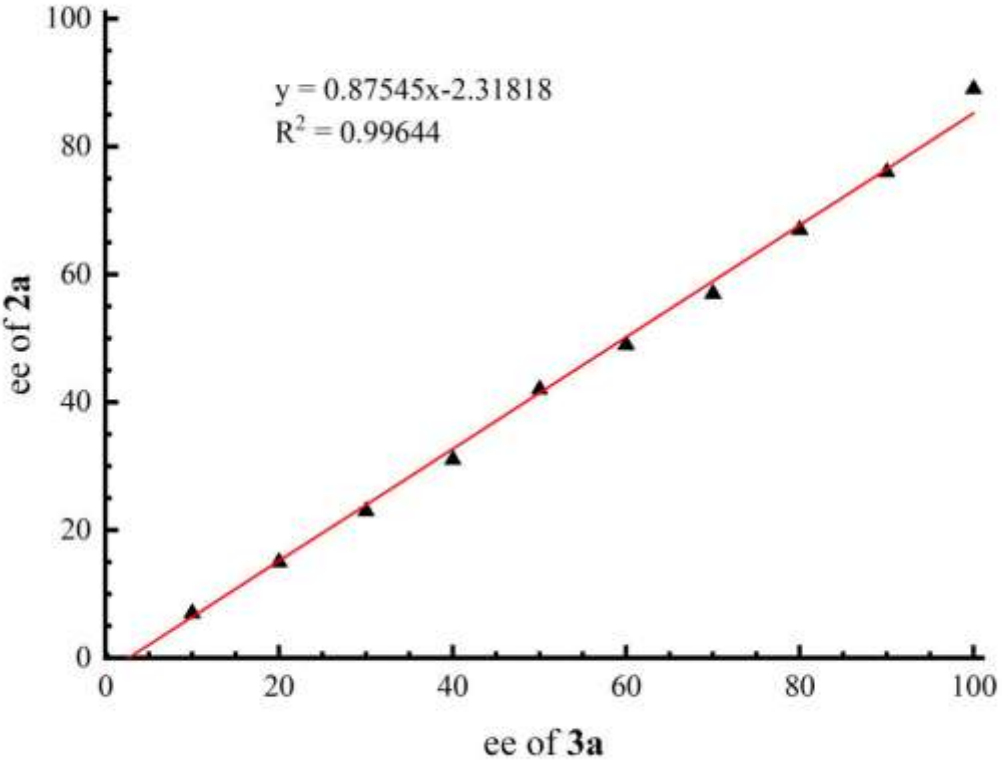
At room temperature, a 10 mL vial was charged with Λ-(*S,S*)-**3a** (16 mg, 20 mol%), H_2O (100 μL), AcOH (60 μL), and indole **1y** (0.10 mmol), after which a mixed solvent of TBME/$CHCl_3$ (1.6 mL, v/v = 5:3) was added. The resulting mixture was cooled to 0 °C and stirred for 20 min, followed by the addition of *m*-CPBA (34.5 mg, 2.0 equiv, 0.20 mmol). The reaction mixture was stirred at 0 °C, and the progress of the reaction was monitored by TLC. Unfortunately, according to TLC monitoring, only a trace amount of the desired product was observed, corresponding to a yield of less than 5%.

5.3 Non-Linear Effects

The standard reaction of **1a** showed a linear correlation between the enantiomeric excess (ee) of the product and that of the catalyst, which is consistent with the proposed enantiodetermining transition state involving a single catalyst molecule acting in a bifunctional manner.

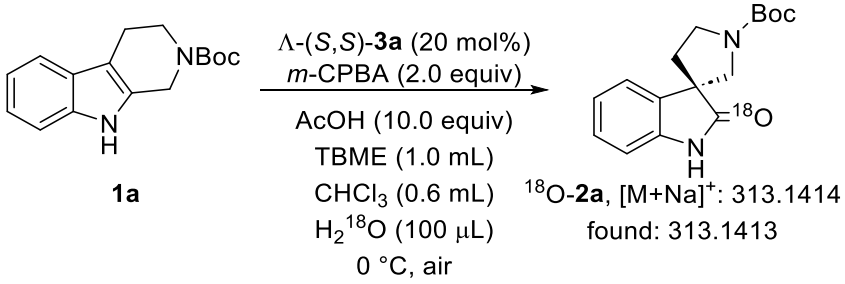


entry	Δ-**3a** (mg)	Λ-**3a** (mg)	ee of **3a** (%)	yield of **2a** (%)	ee of **2a** (%)
1	2.5	47.5	90	62	76
2	5.0	45.0	80	60	67
3	7.5	42.5	70	60	57
4	10.0	40.0	60	62	49
5	12.5	37.5	50	64	42
6	15.0	35.0	40	60	31
7	17.5	32.5	30	58	23
8	20.0	30.0	20	60	15
9	22.5	27.5	10	60	7
10	25	25	0	62	0
11	--	50	100	62	89
12	50	--	--	60	89



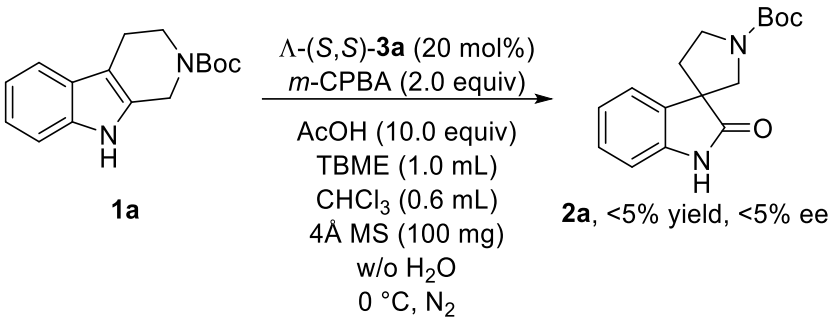
At room temperature, a 10 mL vial was charged with scalemic catalyst **3a** (16 mg, 20 mol%), H_2O (100 μL), AcOH (60 μL), and indole **1** (0.10 mmol), after which a mixed solvent of TBME/$CHCl_3$ (1.6 mL, v/v = 5:3) was added. The resulting mixture was cooled to 0 °C and stirred for 20 min, followed by the addition of *m*-CPBA (34.5 mg, 2.0 equiv, 0.20 mmol). The reaction mixture was stirred at 0 °C, and the reaction progress was monitored by TLC. Upon completion, the reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography afforded the pure product.

5.4 Isotopic labeling experiment

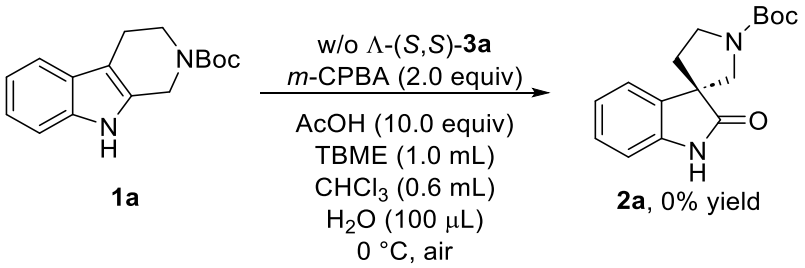


In a 10 mL tube equipped with a magnetic stirring bar, indole 1a (0.10 mmol, 1.0 equiv), Λ-(*S,S*)-**3a** (16 mg, 20 mol%), $H_2{}^{18}O$ (100 μL), AcOH (60 μL, 10.0 equiv), and dry TBME (1.0 mL) were combined under a nitrogen atmosphere. The resulting mixture was cooled to 0 °C and stirred for 20 min, followed by the addition of *m*-CPBA (34.5 mg, 2.0 equiv, 0.20 mmol). The reaction mixture was stirred at the same temperature, and the reaction progress was monitored by TLC. Upon completion, the reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography afforded the pure product ^{18}O-**2a**.

5.5 Control Experiment



In a 10-mL tube equipped with a magnetic stirring bar was charged with indole **1a** (0.1 mmol, 1.0 equiv), Λ-(*S, S*)-**3a** (16 mg, 20 mol%), AcOH (60 μL, 10.0 equiv), 4 Å MS (100 mg) and TBME/$CHCl_3$ (1.6 mL, v/v = 5:3) under the nitrogen atmosphere. The mixture was cooled to 0 °C and stirred for 20 min followed by addition of *m*-CPBA (34.5 mg, 2.0 equiv, 0.2 mmol). The mixture was stirred at the same temperature, and the reaction progress was monitored by TLC. The reaction was quenched by addition of a saturated aqueous $Na_2S_2O_3$ solution. Next, the mixture was extracted with ethyl acetate. The combined organic layers were washed by saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was subjected to silica gel column chromatography to afford the pure product.



In a 10-mL tube equipped with a magnetic stirring bar was charged with indole **1a** (0.1 mmol, 1.0 equiv), AcOH (60 μL, 10.0 equiv), and TBME/$CHCl_3$ (1.6 mL, v/v = 5:3) under the nitrogen atmosphere. The mixture was cooled to 0 °C and stirred for 20 min followed by addition of *m*-CPBA (34.5 mg, 2.0 equiv, 0.2 mmol). The mixture was stirred at the same temperature, and the reaction progress was monitored by TLC and no target product was detected.

6. References

[1] (a) J. Yu, H.-J. Jiang, Y. Zhou, S.-W. Luo and L.-Z. Gong, *Angew. Chem. Int. Ed.*, 2015, **54**, 11209–11213; (b) H.-J. Jiang, K. Liu, J. Yu, L. Zhang and L.-Z. Gong, *Angew. Chem. Int. Ed.*, 2017, **56**, 11931–11935; (c) H.-J. Jiang, X.-M. Zhong, J. Yu, Y. Zhang, X. Zhang, Y.-D. Wu and L.-Z. Gong, *Angew. Chem. Int. Ed.*, 2019, **58**, 1803–1807; (d) T.-T. Sun, K. Liu, S.-X. Zhang, C.-R. Wang, C.-Z. Yao and J. Yu, *Synlett*, 2021, **32**, 701–707.

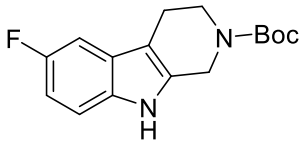
[2] C. Qian, P. Li and J. Sun, *Angew. Chem. Int. Ed.*, 2021, **60**, 5871–5875.

[3] H. Gao, X. Yang and L. Shi, *Org. Chem. Front.*, 2025, **12**, 3848–3855.

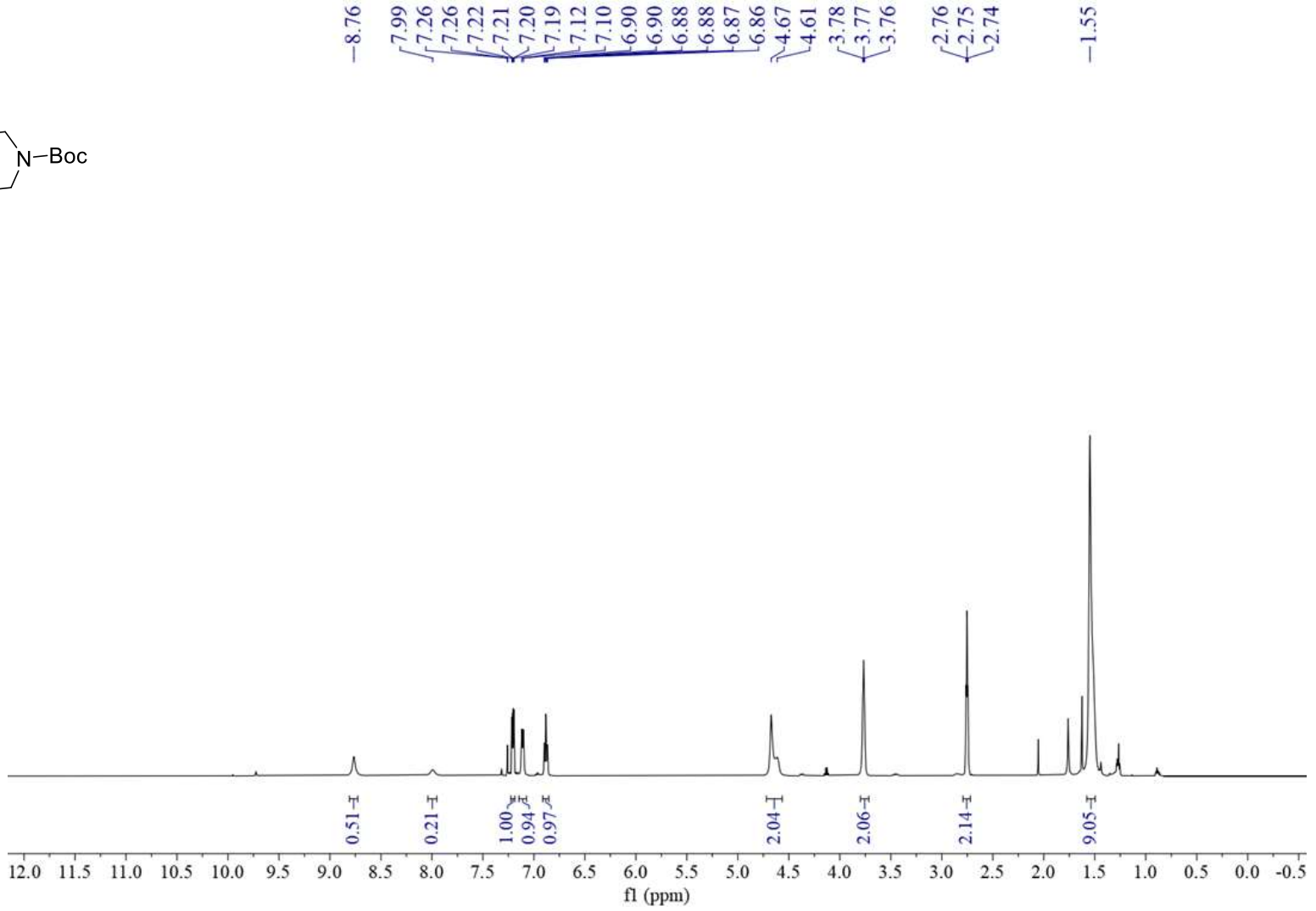
[4] X. Tan, Z. Zhou, M. Shao and J. Sun, *Angew. Chem. Int. Ed.*, 2025, e202510078.

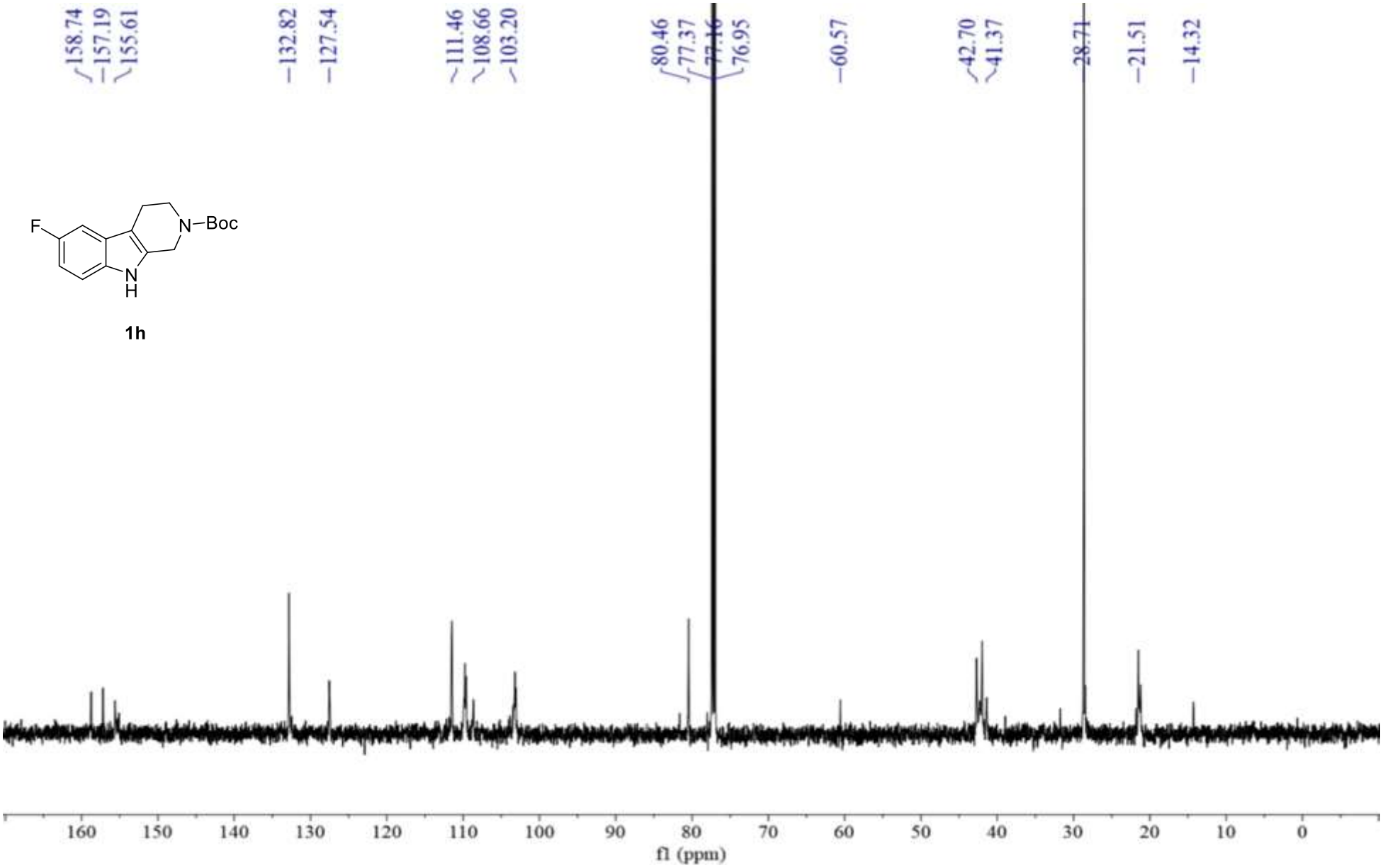
[5] B. Jackson and J. Hester, *J. Org. Chem.*, 1970, **35**, 875–883.

7. NMR Spectra and HPLC Chromatograms



1h

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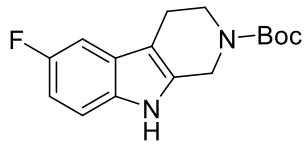
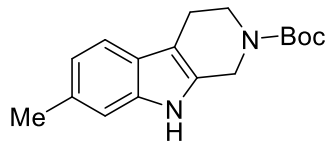
157.19
155.61
132.82
127.54
111.46
108.66
103.20
80.46
77.37
77.16
76.95
60.57
42.70
41.37
28.71
21.51
14.32
F
N–Boc
N
H
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1h


F
N–Boc
N
H

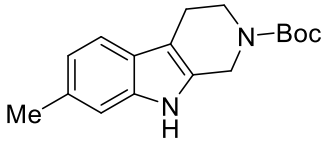
1h

-124.90
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


N–Boc
Me
N
H

1i

8.15
7.77
7.36
7.35
7.26
7.09
6.94
6.93
4.63
3.76
2.79
2.45
1.53
0.45
0.30
1.00
1.00
1.08
2.03
2.03
2.04
3.04
9.15
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


N–Boc
Me
N
H

1i

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136.78
131.45
130.08
125.01
121.20
117.65
111.06
80.18
77.37
77.16
76.95
42.77
41.88
28.77
21.61
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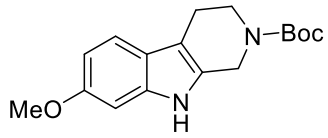
f1 (ppm)


N–Boc
MeO
N
H

1j

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7.26
6.83
6.83
6.78
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6.75
4.63
4.58
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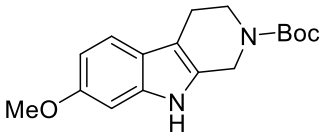
3.76
3.76
3.75
2.77
2.77
2.76
2.76
2.75
2.75
2.74
2.74
1.54
1.53
1.52
1.51
1.50
1.50
1.07
1.07
1.00
1.15
2.15
3.01
2.13
2.03
9.05
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


N–Boc
MeO
N
H

1j

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137.12
129.50
121.62
118.52
108.97
95.20
80.21
77.37
77.16
76.95
55.60
42.71
41.46
28.64
21.61
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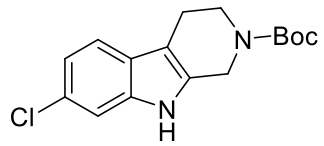
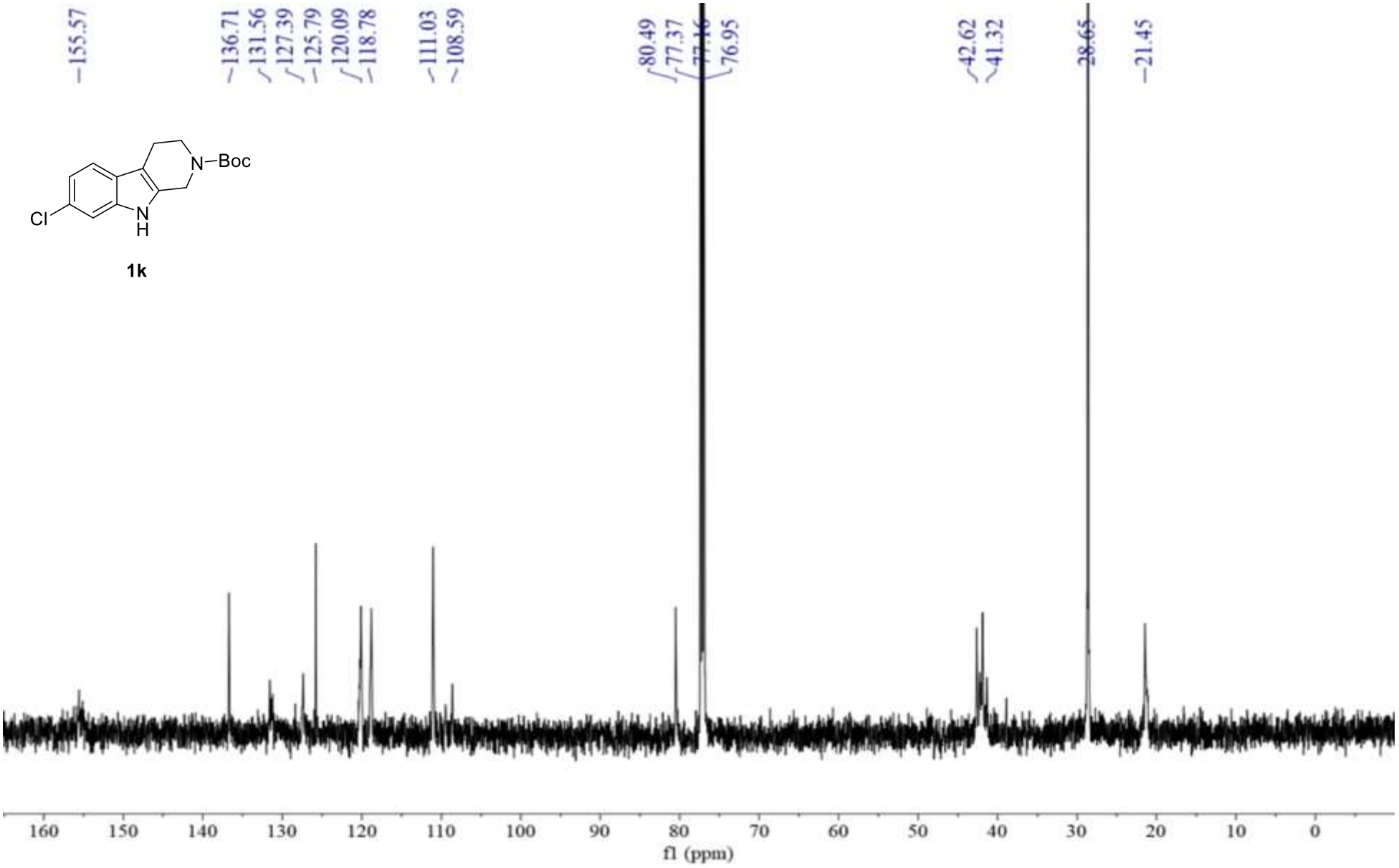
f1 (ppm)


N–Boc
Cl
N
H

1k

8.72
7.37
7.35
7.28
7.26
7.06
7.05
4.65
3.76
2.76
1.54
0.49
0.25
1.00
0.94
0.98
1.99
2.01
2.03
9.04
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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42.62
41.32
28.65
21.45
N–Boc
Cl
N
H
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100
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80
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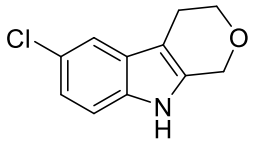
40
30
20
10
0
f1 (ppm)

1k


Cl
O
N
H

1u

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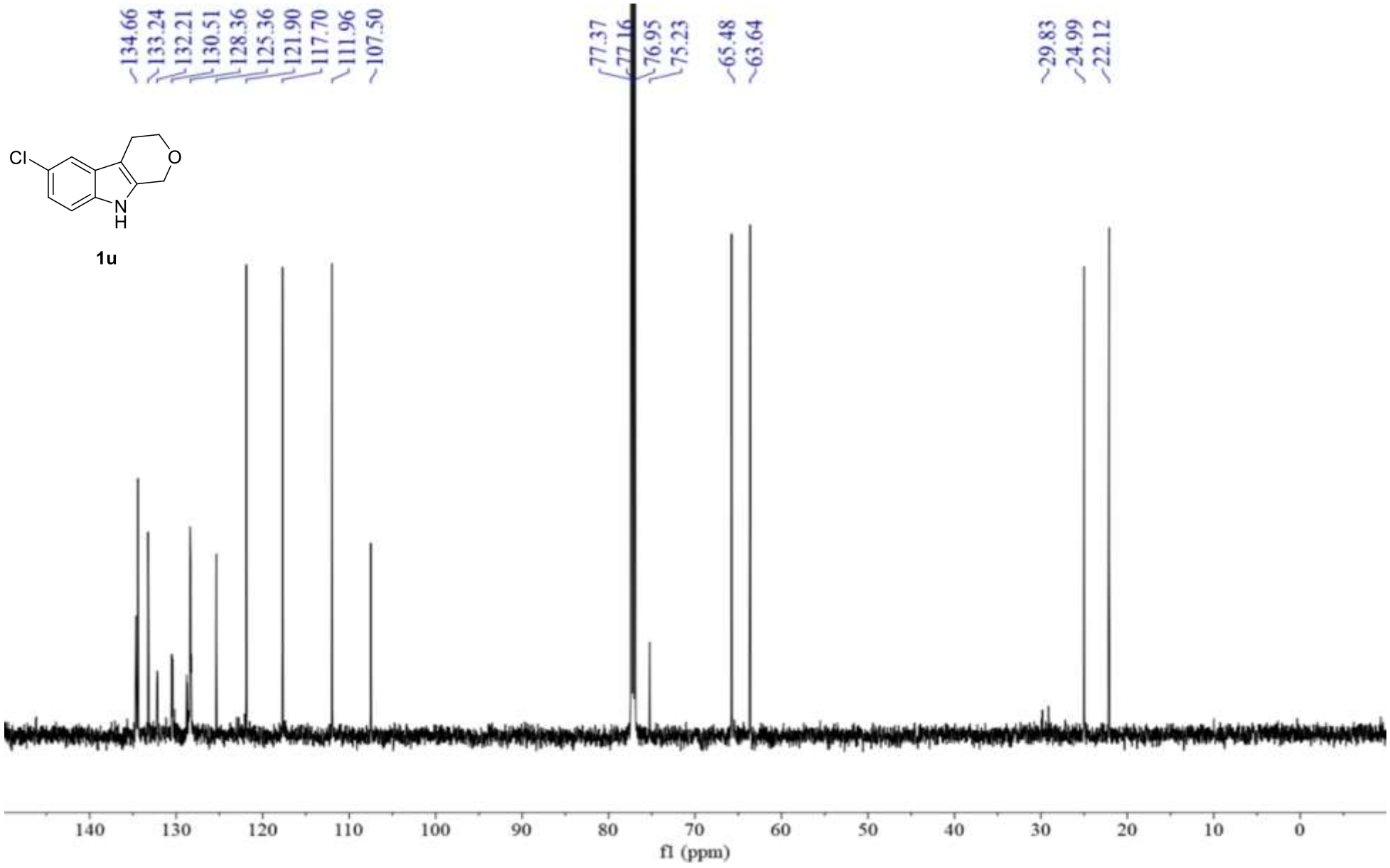
7.26
7.23
7.22
7.20
7.19
7.15
7.15
7.13
7.12
6.92
6.92
6.90
6.89
6.88
6.87
4.80
4.80
4.80
4.05
4.03
4.02
2.82
2.81
2.81
2.80
2.80
2.79
2.79
0.92
1.00
1.00
1.00
2.00
2.05
2.09
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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76.95
75.23
65.48
63.64
29.83
24.99
22.12
Cl
O
N
H
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130
120
110
100
90
80
70
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40
30
20
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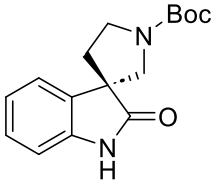
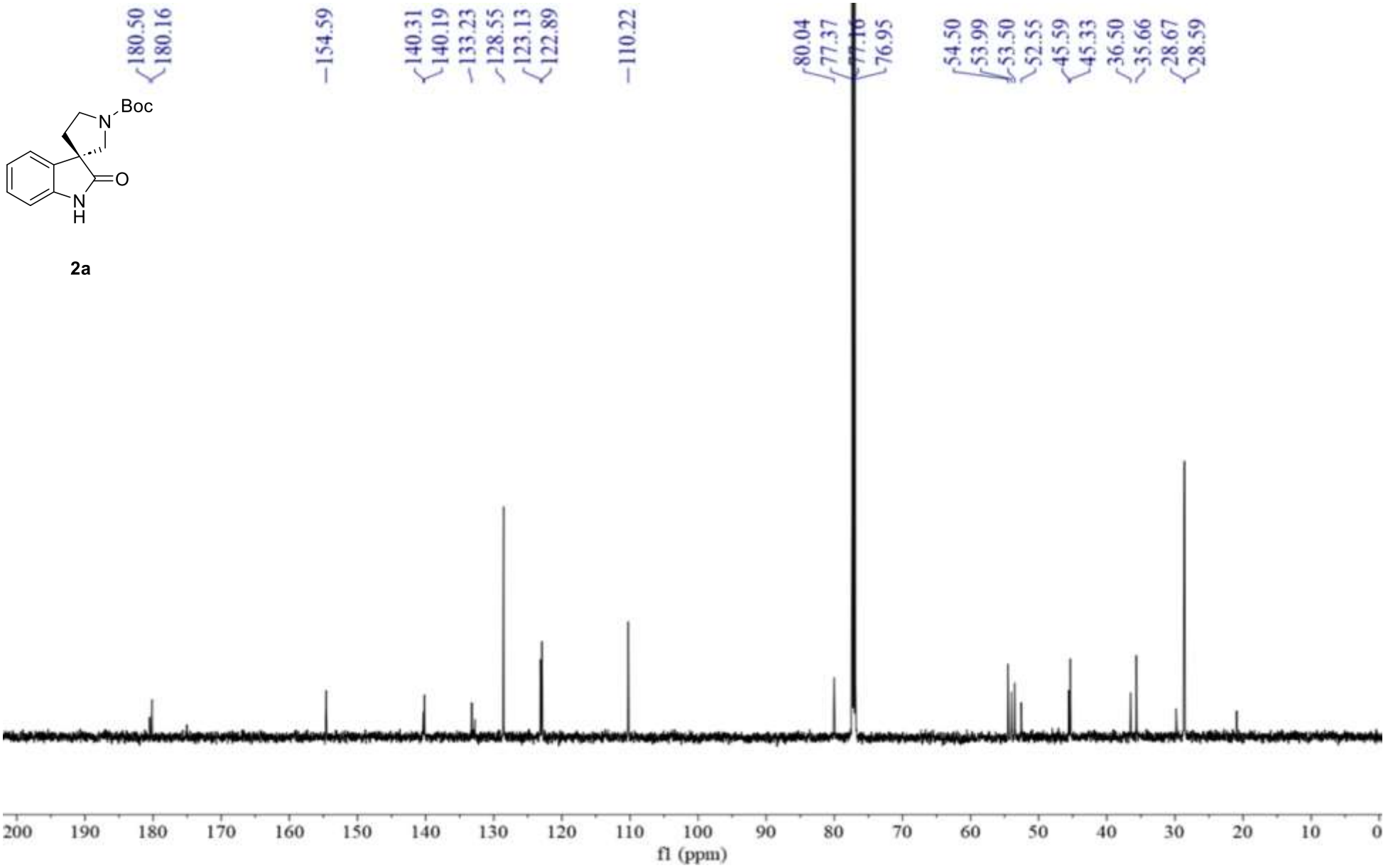
0
f1 (ppm)


Boc
N
O
N
H

2a

8.38
8.28
7.26
7.25
7.23
7.20
7.19
7.06
6.94
6.93
3.86
3.84
3.81
3.79
3.77
3.76
3.73
3.71
3.65
3.63
3.57
3.55
2.42
2.41
2.07
2.06
2.04
1.51
1.46
1.01
2.06
0.99
0.93
2.07
1.07
1.10
1.00
1.03
9.02
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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53.99
53.50
52.55
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35.66
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Boc
N
O
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H
2a
200
190
180
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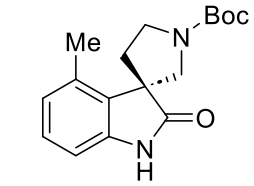
f1 (ppm)


Me
N
Boc
O
N
H

2b

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3.85
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3.82
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3.76
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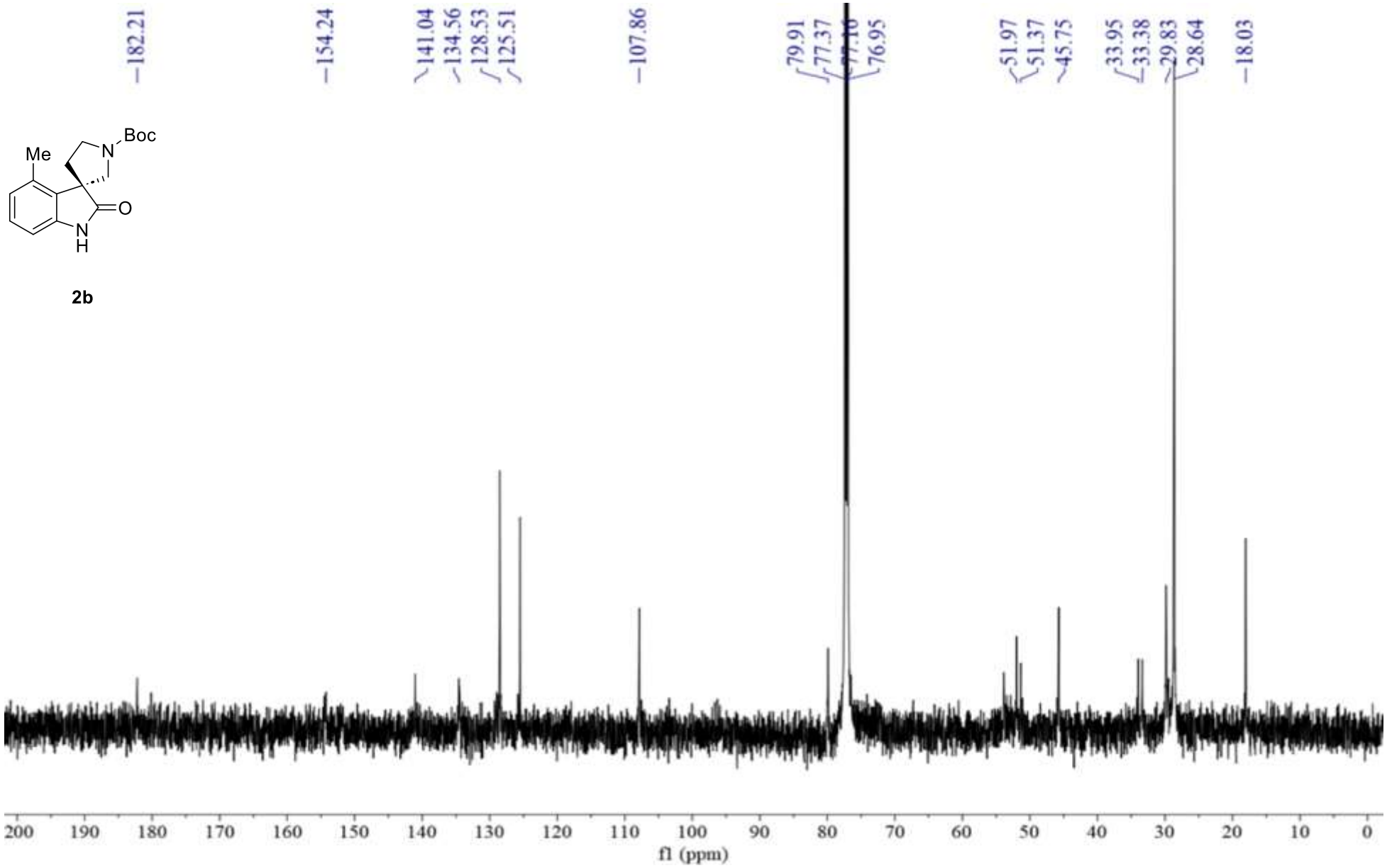
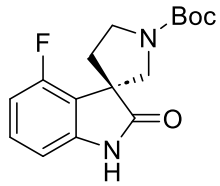
2.75
2.47
2.47
2.44
2.42
2.39
2.35
2.23
2.21
2.09
1.53
1.50
1.46
1.43
0.96
1.00
1.02
0.96
4.03
1.06
3.04
1.08
9.21
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

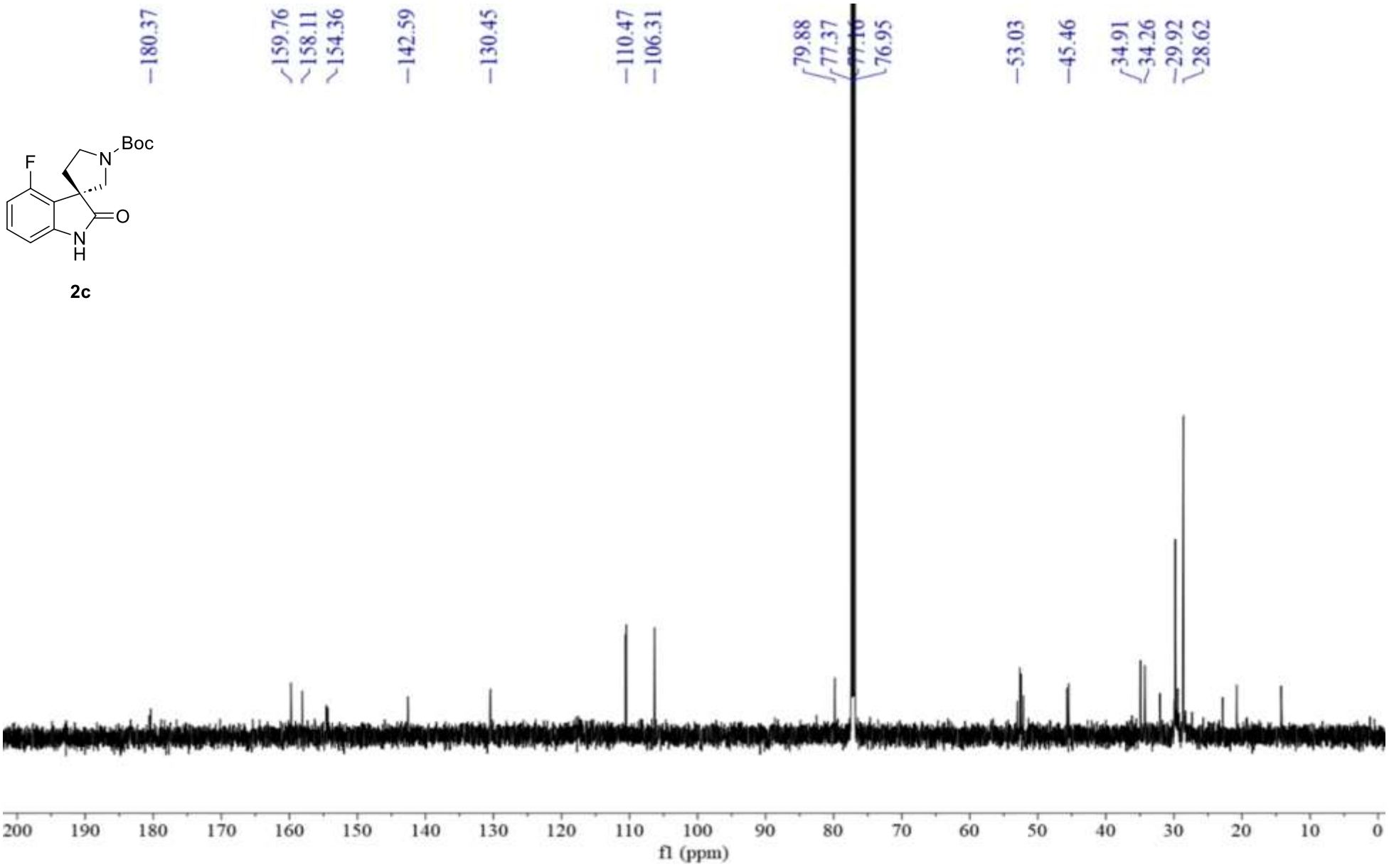

182.21
154.24
141.04
134.56
128.53
125.51
107.86
79.91
77.37
77.10
76.95
51.97
51.37
45.75
33.95
33.38
29.83
28.64
18.03
Me
N
Boc
O
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

2b


Boc
F
N
O
N
H

2c

7.87
7.80
7.26
7.21
6.76
6.75
6.73
6.72
6.70
6.69
3.87
3.85
3.83
3.81
3.78
3.77
3.76
3.75
3.73
2.39
2.38
2.36
2.35
2.34
1.50
1.46
1.02
1.00
2.16
1.04
2.09
1.09
0.91
1.19
9.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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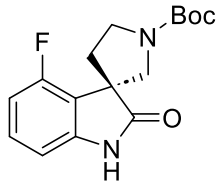
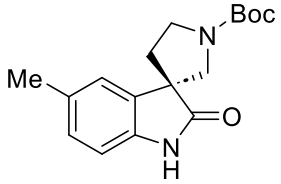
159.76
158.11
154.36
142.59
130.45
110.47
106.31
79.88
77.37
76.95
53.03
45.46
34.91
34.26
29.92
28.62
F
N
Boc
O
N
H
2c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
N
Boc
O
N
H

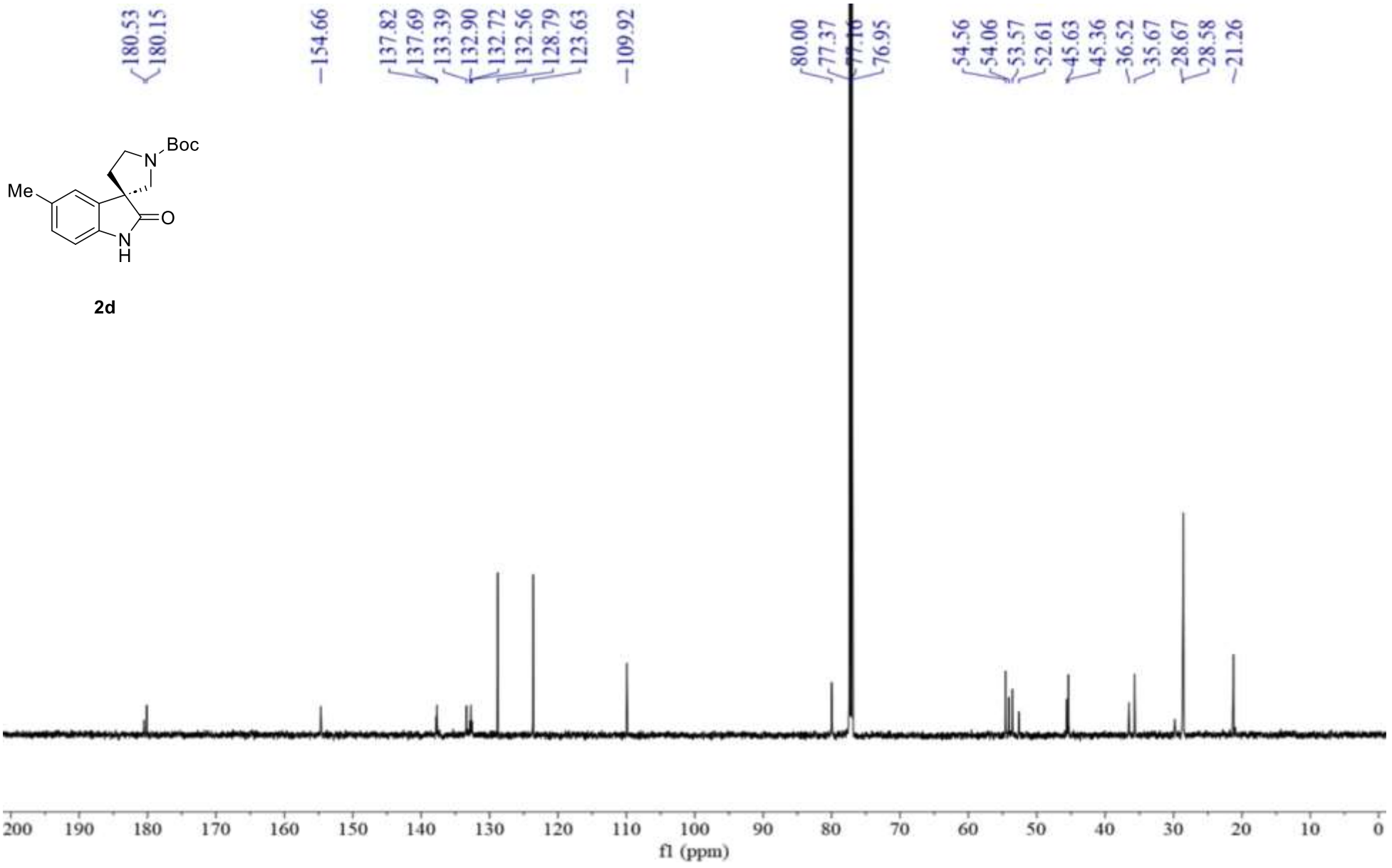
2c

-118.99
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


Boc
N
Me
O
N
H

2d

8.75
8.65
7.26
7.04
7.03
7.00
6.96
6.84
6.82
3.85
3.84
3.83
3.79
3.78
3.76
3.76
3.74
3.71
3.70
3.63
3.62
3.56
3.54
2.43
2.42
2.41
2.40
2.32
2.09
2.08
2.06
2.04
1.52
1.46
1.00
2.00
0.96
2.02
1.10
1.11
1.00
2.99
1.00
9.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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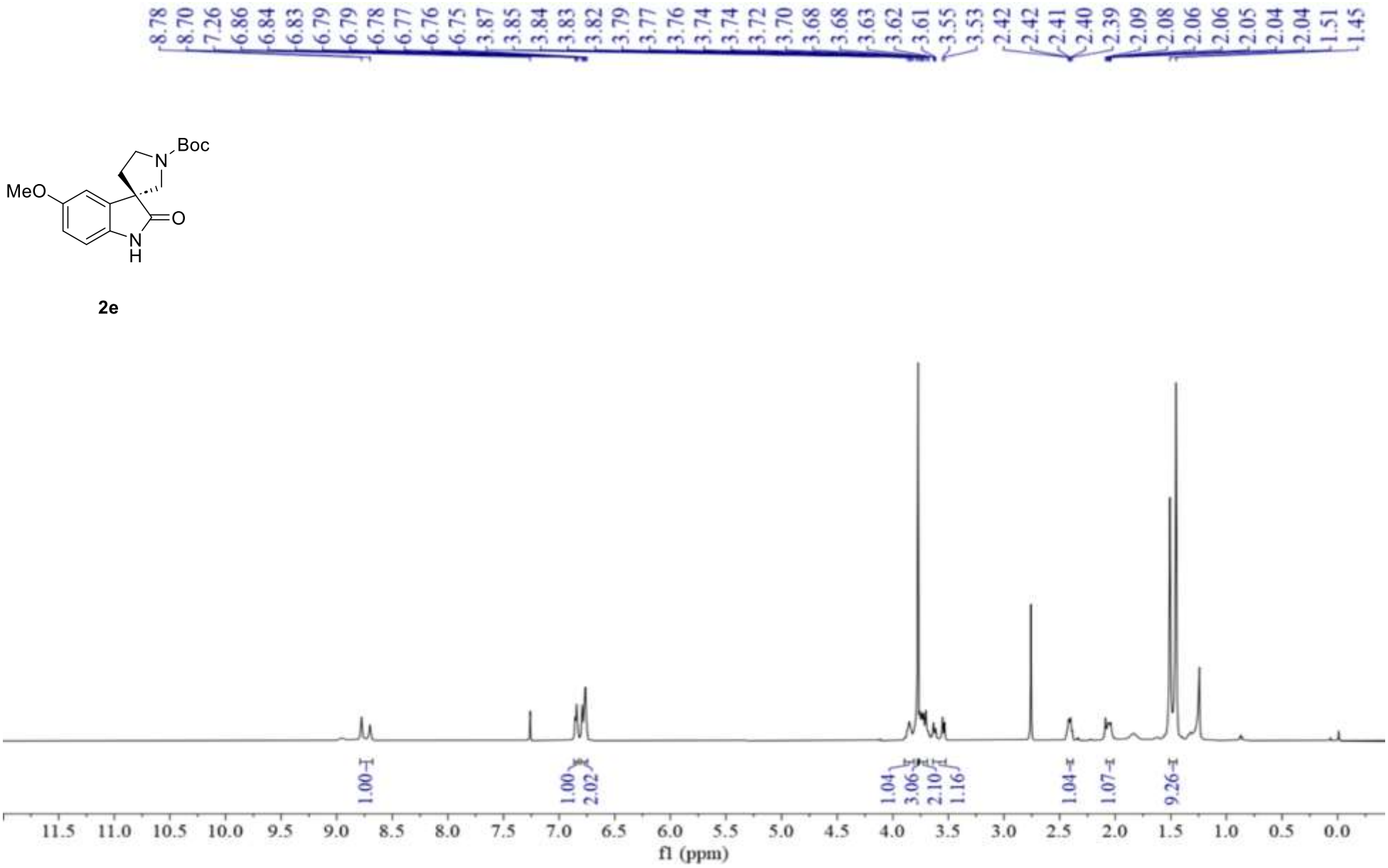
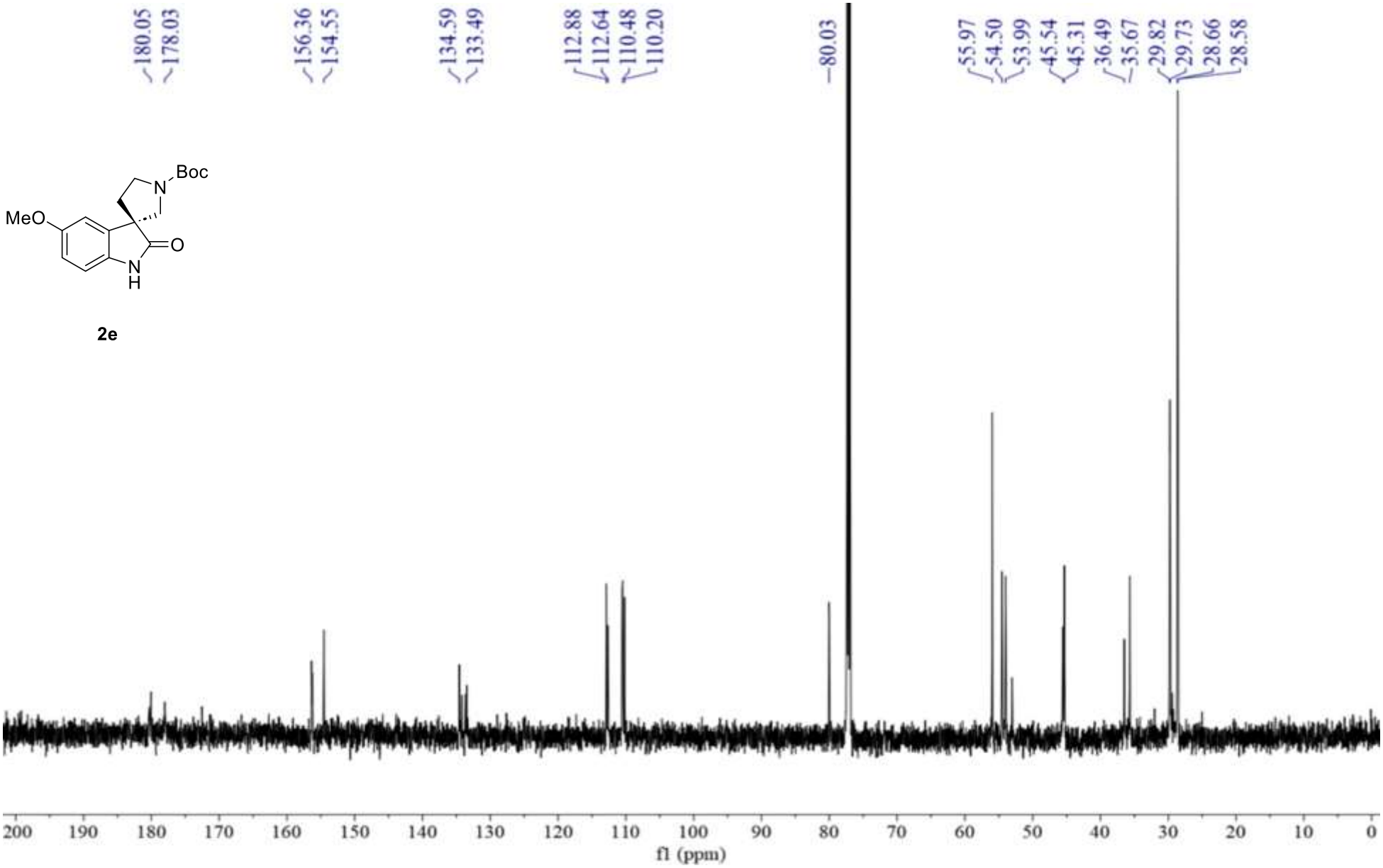
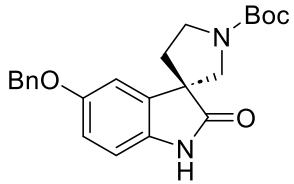
180.15
154.66
137.82
137.69
133.39
132.90
132.72
132.56
128.79
123.63
109.92
80.00
77.37
77.16
76.95
54.56
54.06
53.57
52.61
45.63
45.36
36.52
35.67
28.67
28.58
21.26
Boc
N
Me
O
N
H
2d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

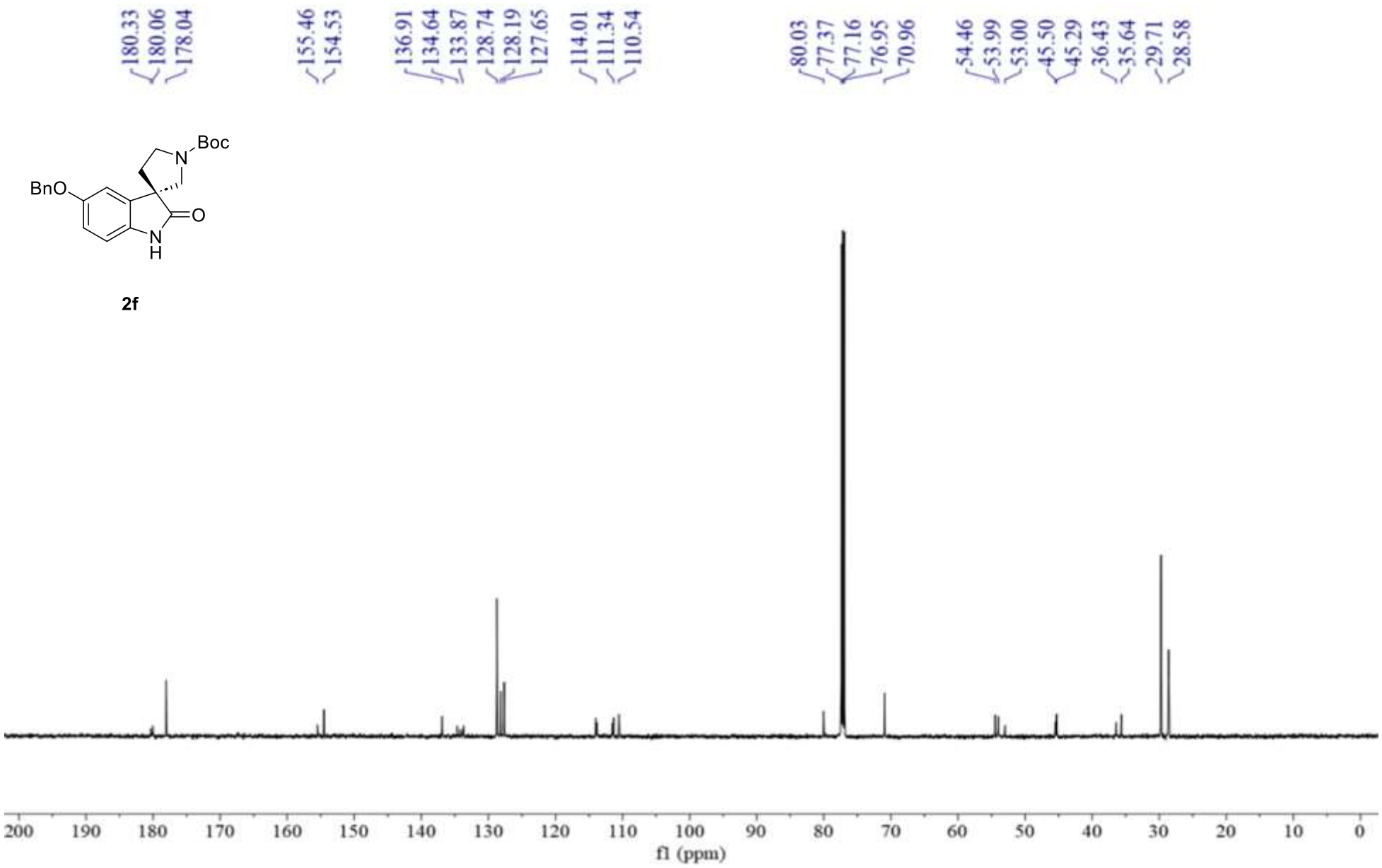

8.78
8.70
7.26
6.86
6.84
6.83
6.79
6.79
6.78
6.77
6.76
6.75
3.87
3.85
3.84
3.83
3.82
3.79
3.77
3.76
3.74
3.74
3.72
3.70
3.68
3.68
3.63
3.62
3.61
3.55
3.53
2.42
2.42
2.41
2.40
2.39
2.09
2.08
2.06
2.06
2.05
2.04
2.04
1.51
1.45
Boc
N
MeO
O
N
H
2e
1.00
1.00
2.02
1.04
3.06
2.10
1.16
1.04
1.07
9.26
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


180.05
178.03
156.36
154.55
134.59
133.49
112.88
112.64
110.48
110.20
80.03
55.97
54.50
53.99
45.54
45.31
36.49
35.67
29.82
29.73
28.66
28.58
Boc
N
MeO
O
N
H
2e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Boc
N
BnO
O
N
H

2f

8.04
7.96
7.42
7.41
7.40
7.39
7.38
7.34
7.33
7.32
7.26
6.88
6.84
6.82
6.81
5.01
3.74
3.72
3.70
3.63
3.55
2.43
2.42
2.41
2.40
2.39
2.04
1.51
1.46
1.02
4.96
2.86
1.90
2.50
1.00
1.05
9.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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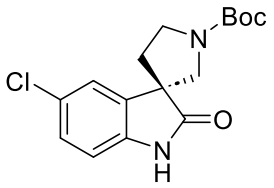
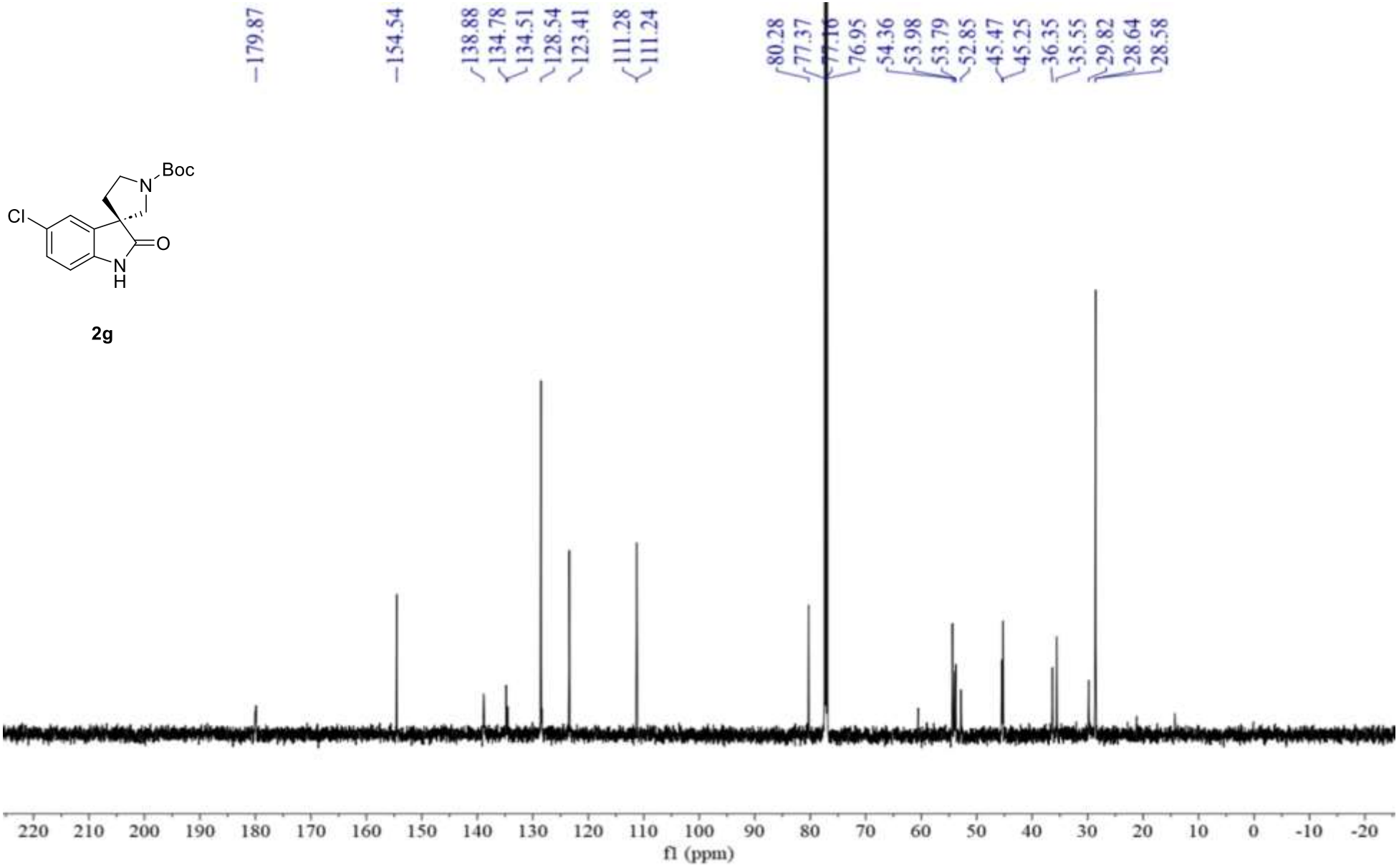
180.06
178.04
155.46
154.53
136.91
134.64
133.87
128.74
128.19
127.65
114.01
111.34
110.54
80.03
77.37
77.16
76.95
70.96
54.46
53.99
53.00
45.50
45.29
36.43
35.64
29.71
28.58
Boc
N
BnO
O
N
H
2f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

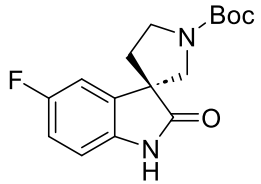

Boc
N
Cl
O
N
H

2g

9.24
9.18
7.26
7.23
7.21
7.16
7.12
6.89
6.89
6.88
6.87
3.88
3.86
3.86
3.85
3.84
3.81
3.80
3.80
3.79
3.77
3.76
3.75
3.74
3.73
3.72
3.70
3.68
3.64
3.62
3.56
3.54
2.44
2.42
2.42
2.41
2.40
2.39
2.10
2.09
2.08
2.07
2.06
2.05
2.04
2.04
1.54
1.52
1.46
1.05
0.99
0.99
1.00
1.13
2.04
1.16
1.09
1.47
8.98
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

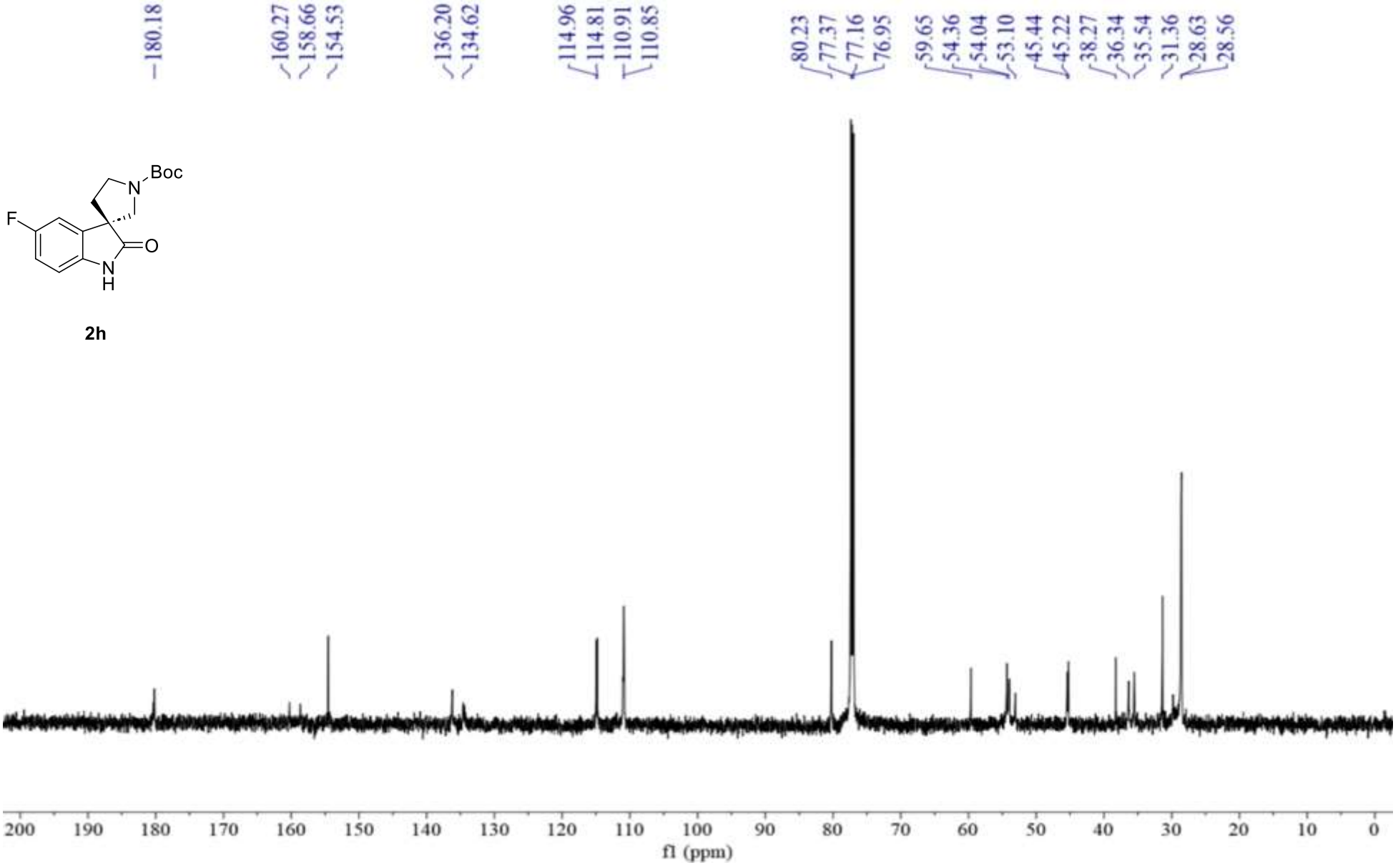

179.87
154.54
138.88
134.78
134.51
128.54
123.41
111.28
111.24
80.28
77.37
77.16
76.95
54.36
53.98
53.79
52.85
45.47
45.25
36.35
35.55
29.82
28.64
28.58
Boc
N
Cl
O
N
H
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

2g


Boc
N
F
O
N
H

2h

8.43
8.37
7.26
6.94
6.93
6.90
6.86
3.85
3.73
3.71
3.64
3.62
3.56
3.54
2.45
2.44
2.42
2.40
2.06
1.51
1.46
0.96
2.99
2.00
1.08
1.16
1.03
1.10
9.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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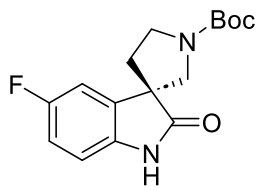
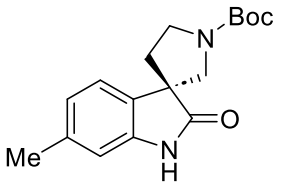
160.27
158.66
154.53
136.20
134.62
114.96
114.81
110.91
110.85
80.23
77.37
77.16
76.95
59.65
54.36
54.04
53.10
45.44
45.22
38.27
36.34
35.54
31.36
28.63
28.56
Boc
N
F
O
N
H
2h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Boc
N
F
O
N
H

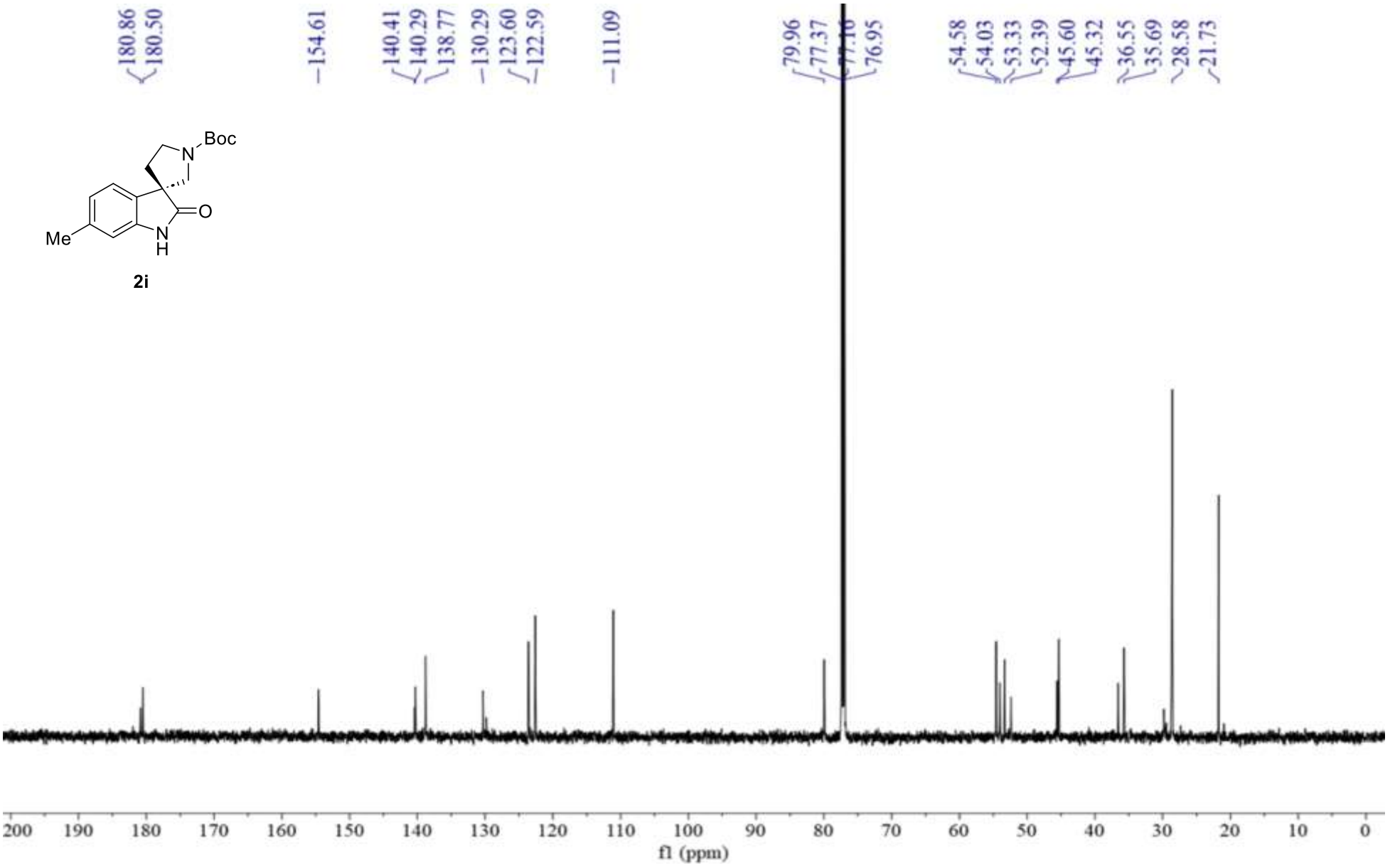
2h

-119.58
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


Boc
N
O
N
H
Me

2i

8.75
8.65
7.26
7.04
7.03
7.00
6.96
6.84
6.82
3.85
3.84
3.83
3.79
3.78
3.76
3.76
3.74
3.71
3.70
3.63
3.62
3.56
3.54
2.43
2.42
2.41
2.40
2.32
2.08
2.06
2.04
1.52
1.46
1.00
2.00
0.96
2.02
1.10
1.11
1.00
2.99
1.00
9.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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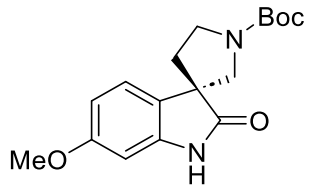
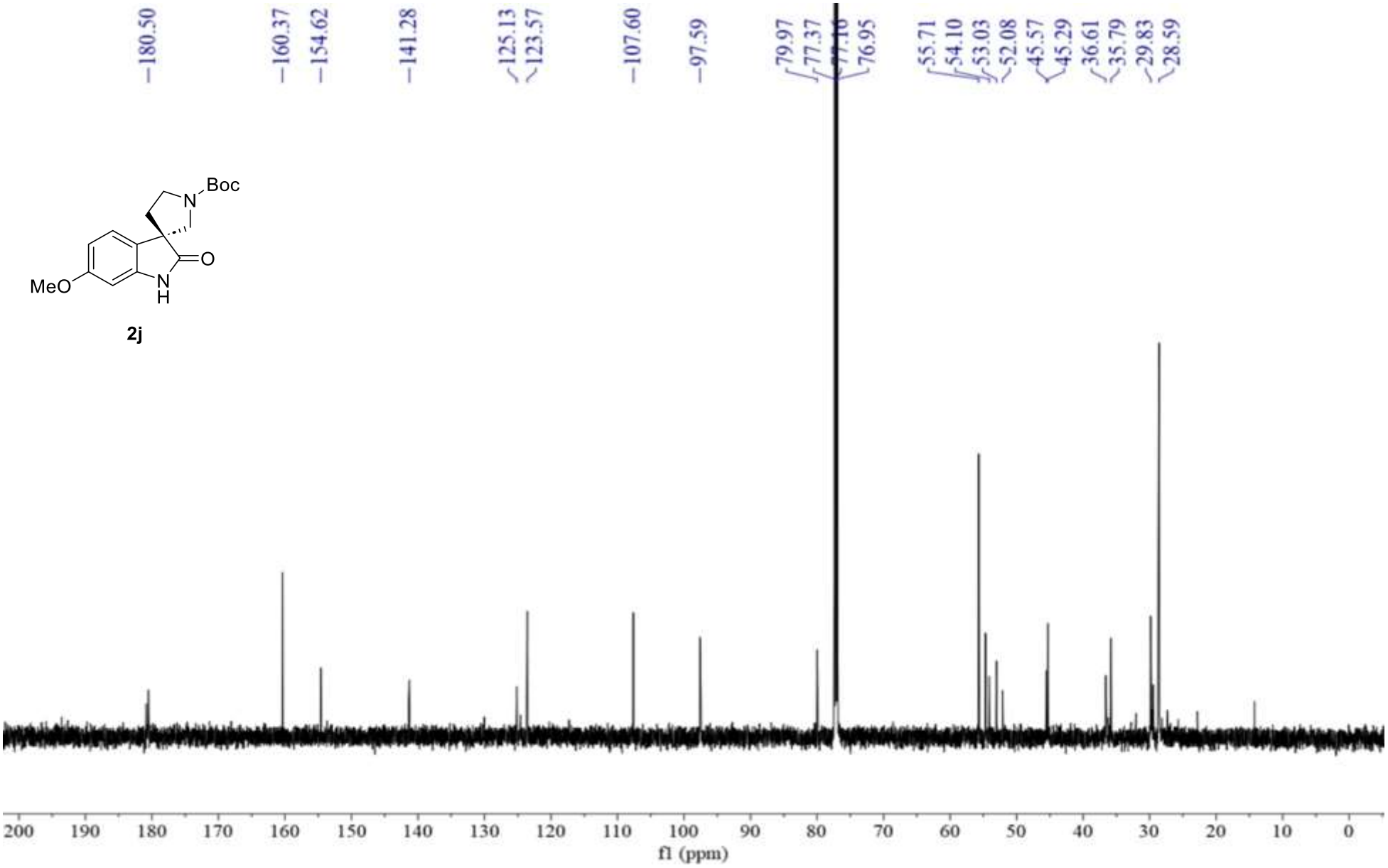
140.29
138.77
130.29
123.60
122.59
111.09
79.96
77.37
77.16
76.95
54.58
54.03
53.33
52.39
45.60
45.32
36.55
35.69
28.58
21.73
Boc
N
O
N
H
Me
2i
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Boc
N
O
MeO
N
H

2j

8.75
7.26
7.09
7.07
7.06
7.04
6.57
6.56
6.56
6.55
6.54
6.54
6.53
6.52
6.51
3.84
3.84
3.83
3.83
3.82
3.81
3.80
3.79
3.78
3.77
3.75
3.74
3.73
3.72
3.72
3.70
3.69
3.67
3.60
3.57
3.53
3.50
2.39
2.38
2.37
2.36
2.35
2.05
2.04
2.03
2.02
2.01
1.50
1.45
0.98
1.00
2.00
0.96
3.12
2.05
1.13
1.18
1.11
9.17
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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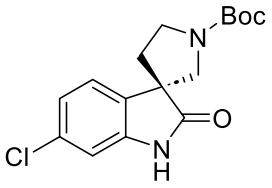
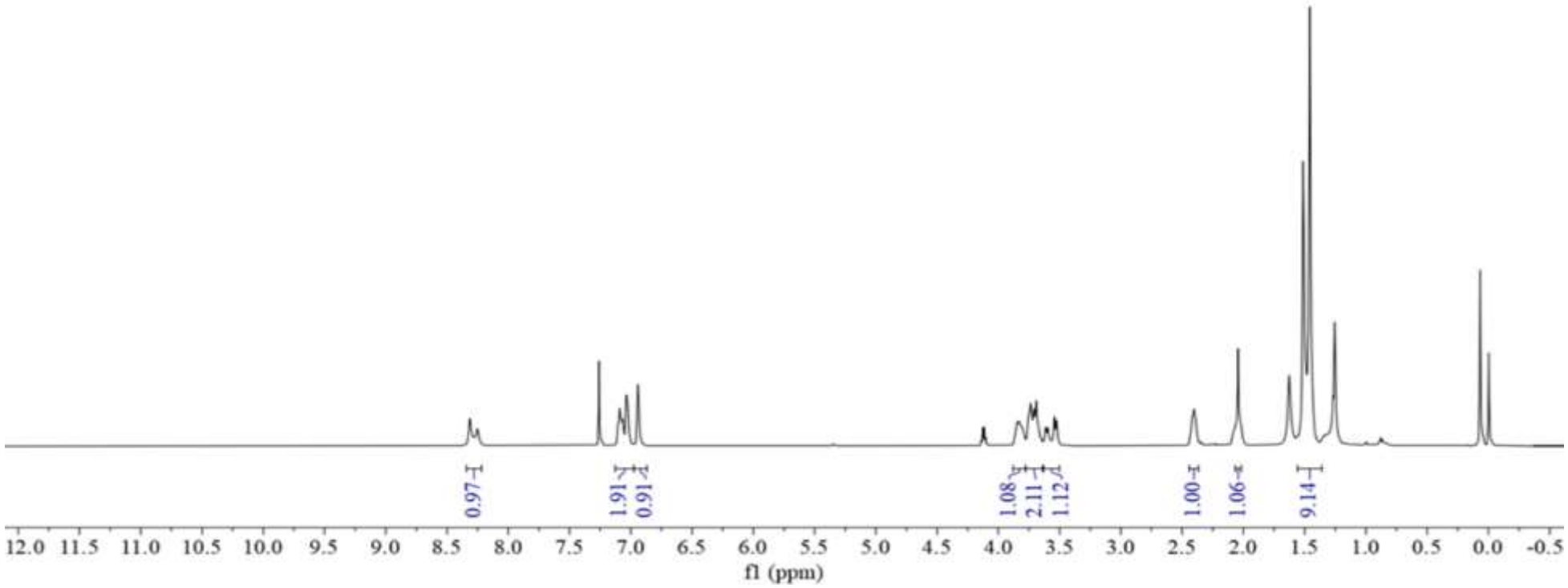
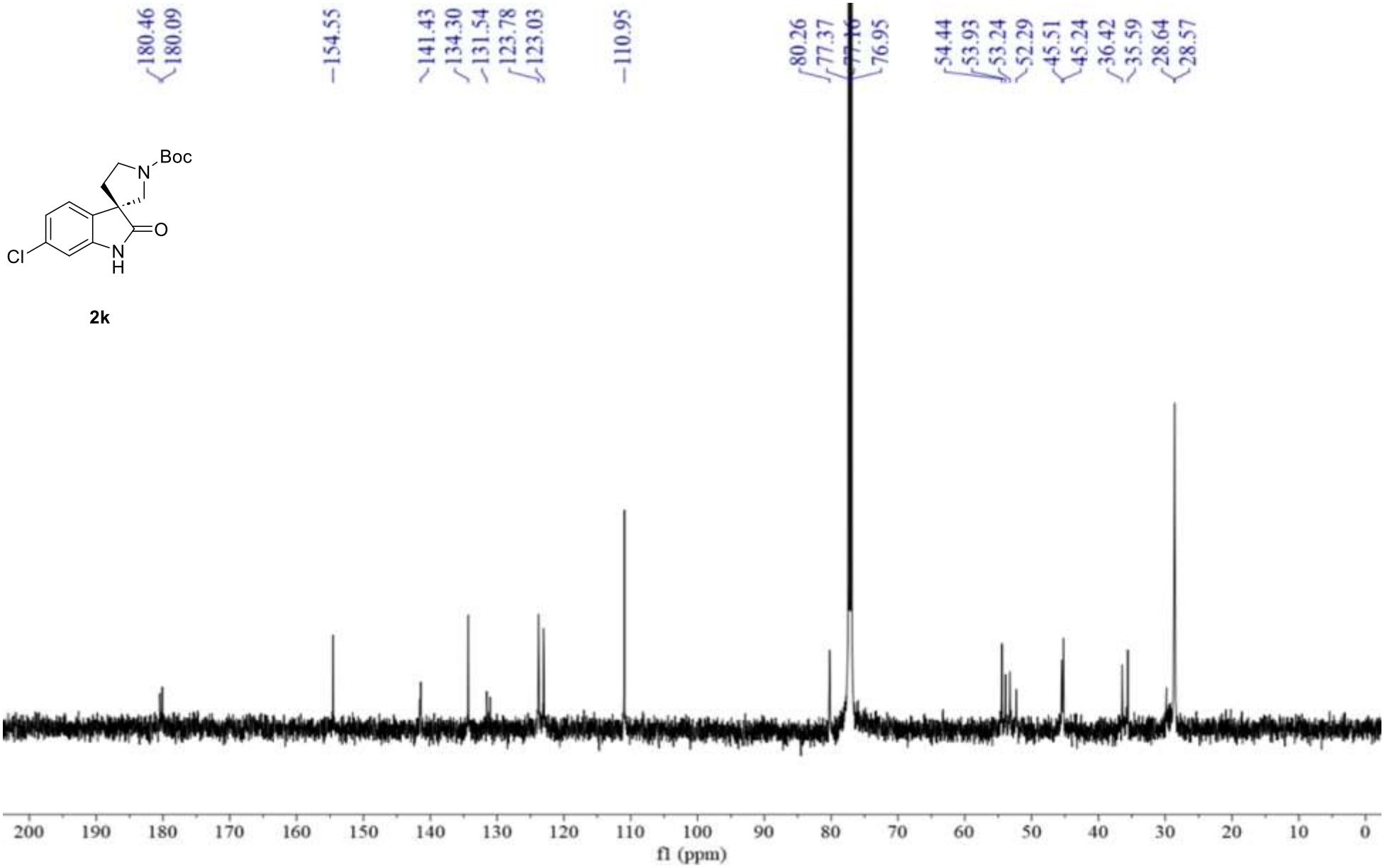
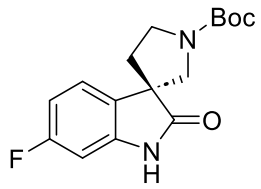
160.37
154.62
141.28
125.13
123.57
107.60
97.59
79.97
77.37
77.16
76.95
55.71
54.10
53.03
52.08
45.57
45.29
36.61
35.79
29.83
28.59
Boc
N
O
N
H
MeO
2j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Boc
N
O
Cl
N
H

2k

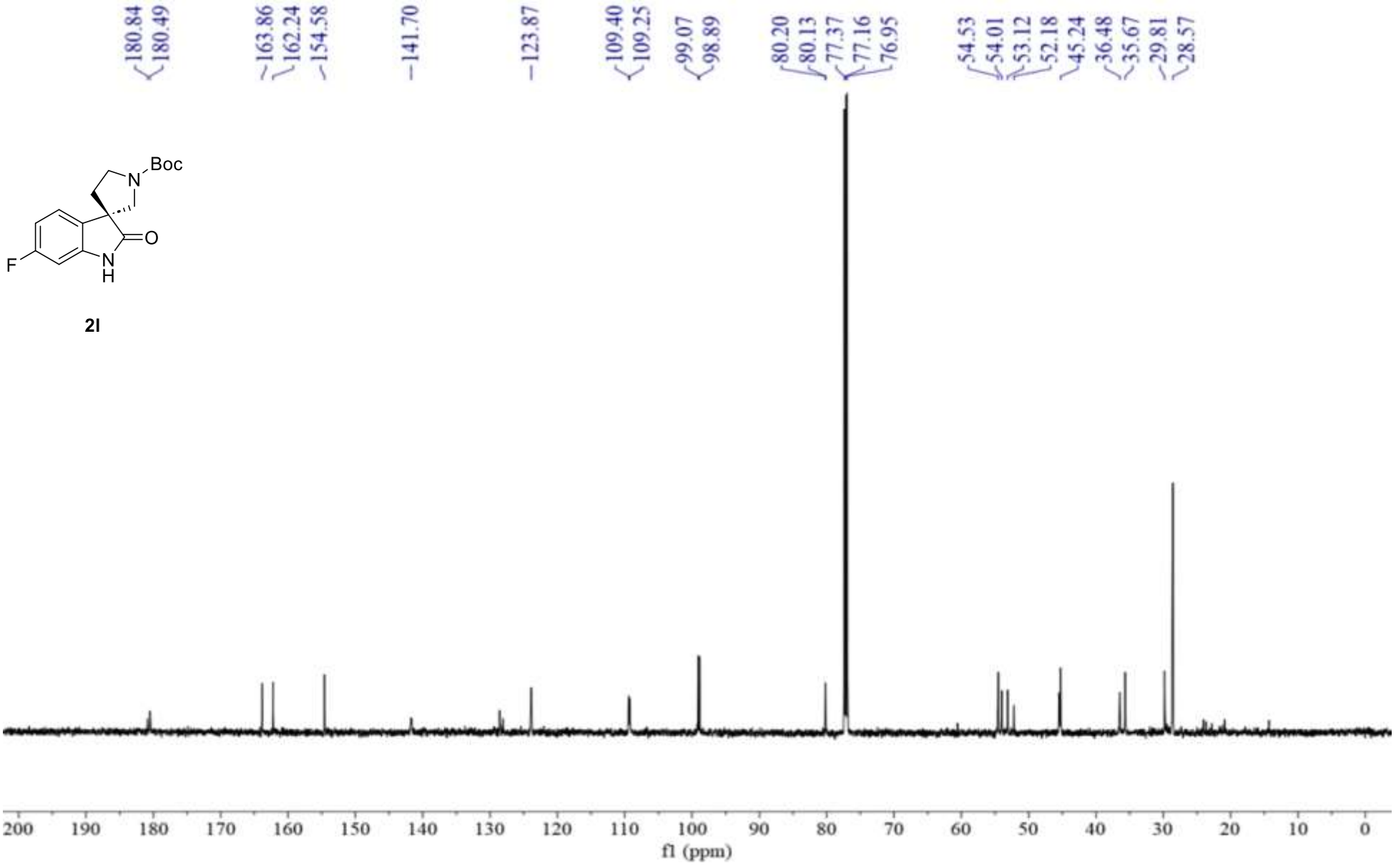

8.31
8.25
7.26
7.09
7.07
7.04
6.94
3.85
3.83
3.74
3.71
3.69
3.61
3.60
3.54
3.52
1.51
1.46
0.97
1.91
0.91
1.08
2.11
1.12
1.00
1.06
9.14
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


180.46
180.09
154.55
141.43
134.30
131.54
123.78
123.03
110.95
80.26
77.37
76.95
54.44
53.93
53.24
52.29
45.51
45.24
36.42
35.59
28.64
28.57
Boc
N
O
Cl
N
H
2k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

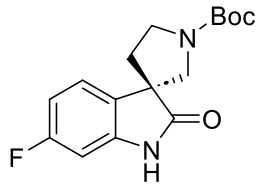

Boc
N
O
F
N
H

2l

8.44
8.37
7.26
7.12
7.11
6.74
6.68
6.67
3.85
3.81
3.75
3.74
3.71
3.69
3.61
3.59
3.54
3.52
2.41
2.39
2.07
2.04
1.51
1.46
0.97
1.00
2.02
1.11
2.08
1.06
1.07
0.99
9.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

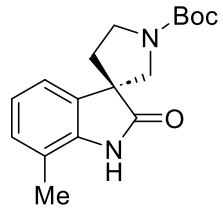

180.84
180.49
163.86
162.24
154.58
141.70
123.87
109.40
109.25
99.07
98.89
80.20
80.13
77.37
77.16
76.95
54.53
54.01
53.12
52.18
45.24
36.48
35.67
29.81
28.57
Boc
N
O
F
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

2l


Boc
N
O
F
N
H

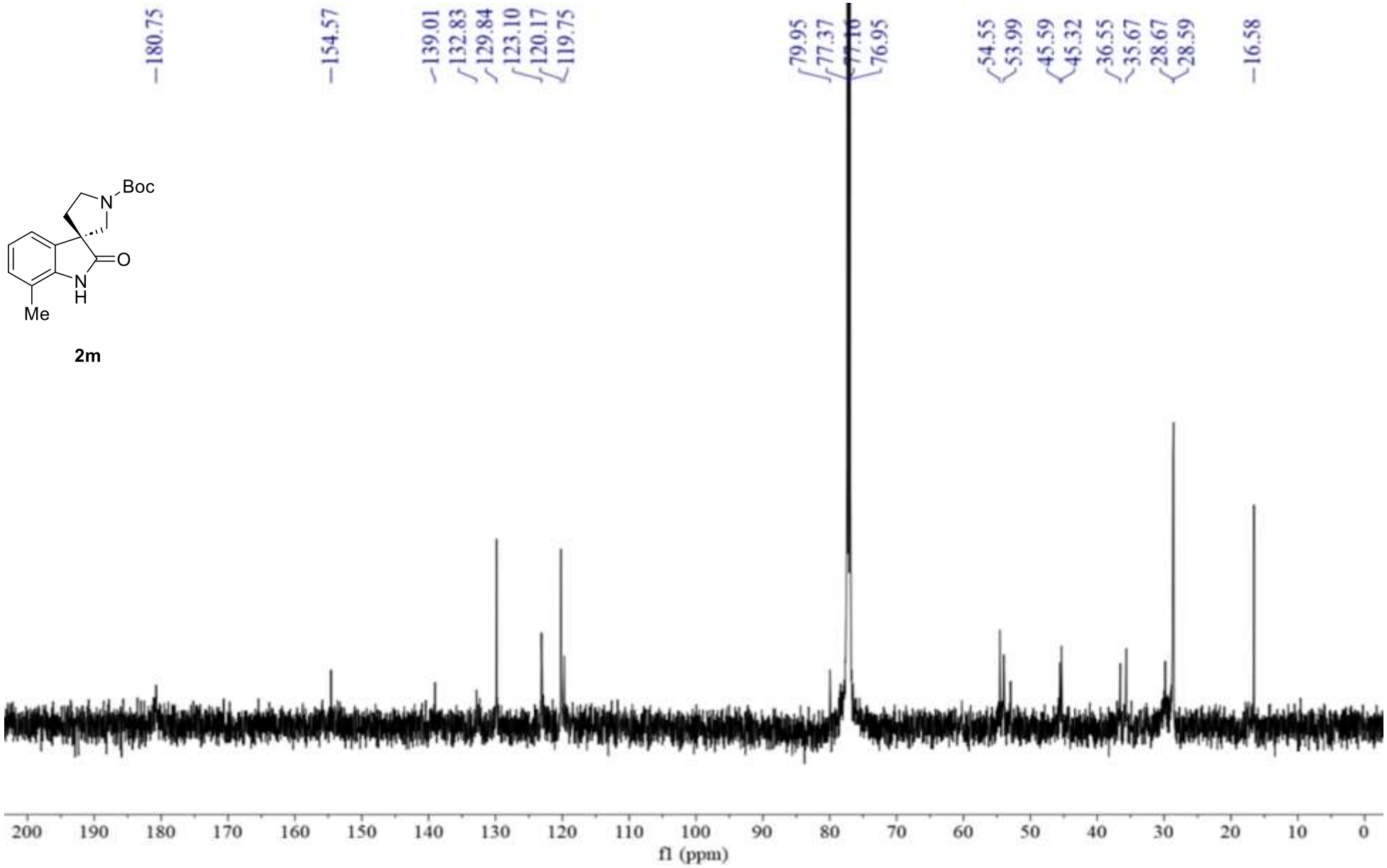
2l

-111.68
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

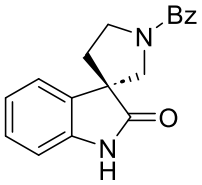

Boc
N
O
N
H
Me

2m

8.59
8.53
7.26
7.06
7.04
7.03
7.00
6.98
3.85
3.78
3.76
3.73
3.71
3.63
3.61
3.57
3.55
2.41
2.29
2.07
2.06
2.04
1.51
1.45
1.02
3.02
2.19
1.07
1.14
1.10
2.99
0.97
9.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

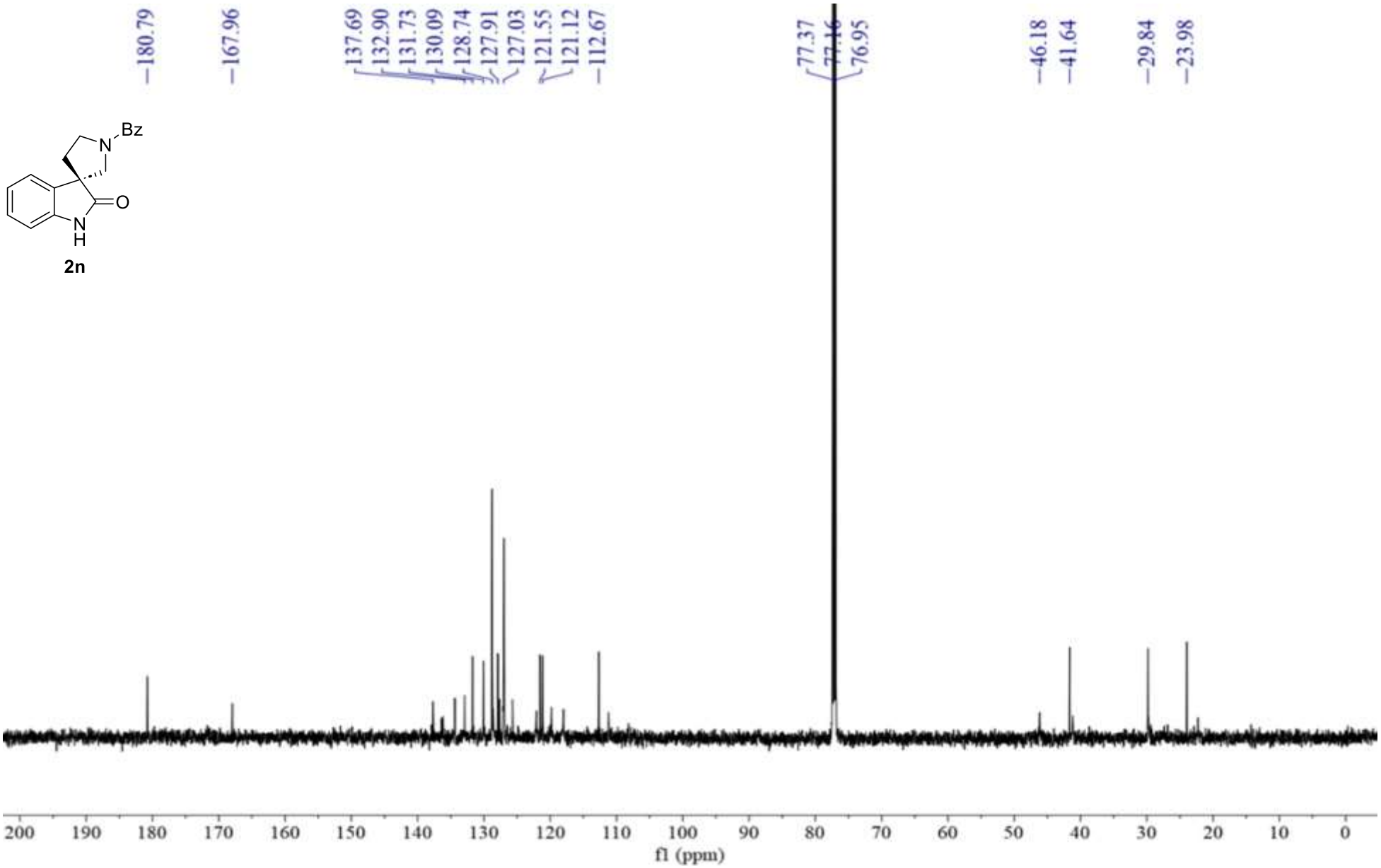

180.75
154.57
139.01
132.83
129.84
123.10
120.17
119.75
79.95
77.37
77.16
76.95
54.55
53.99
45.59
45.32
36.55
35.67
28.67
28.59
16.58
Boc
N
O
N
H
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

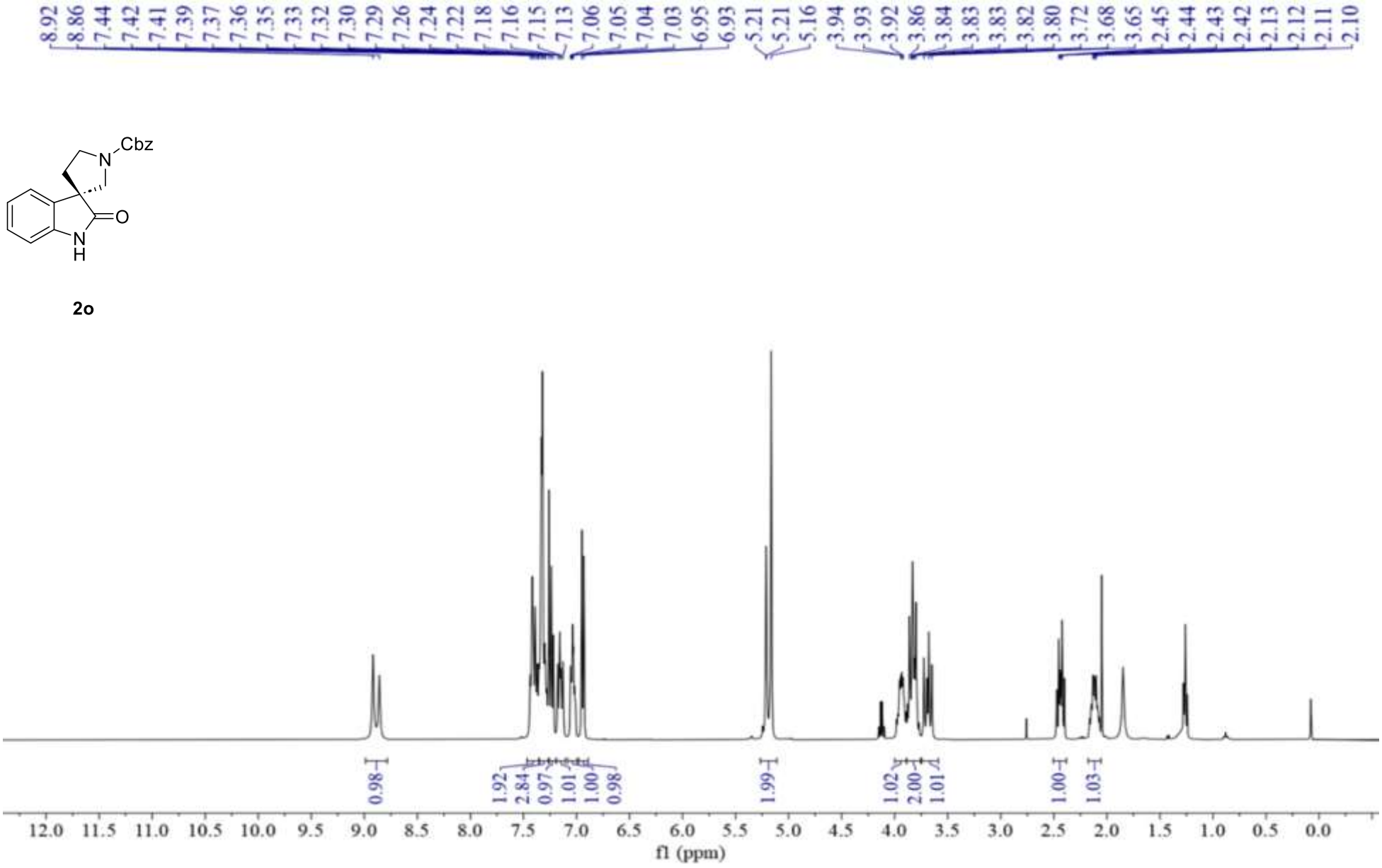
2m


Bz
N
O
N
H

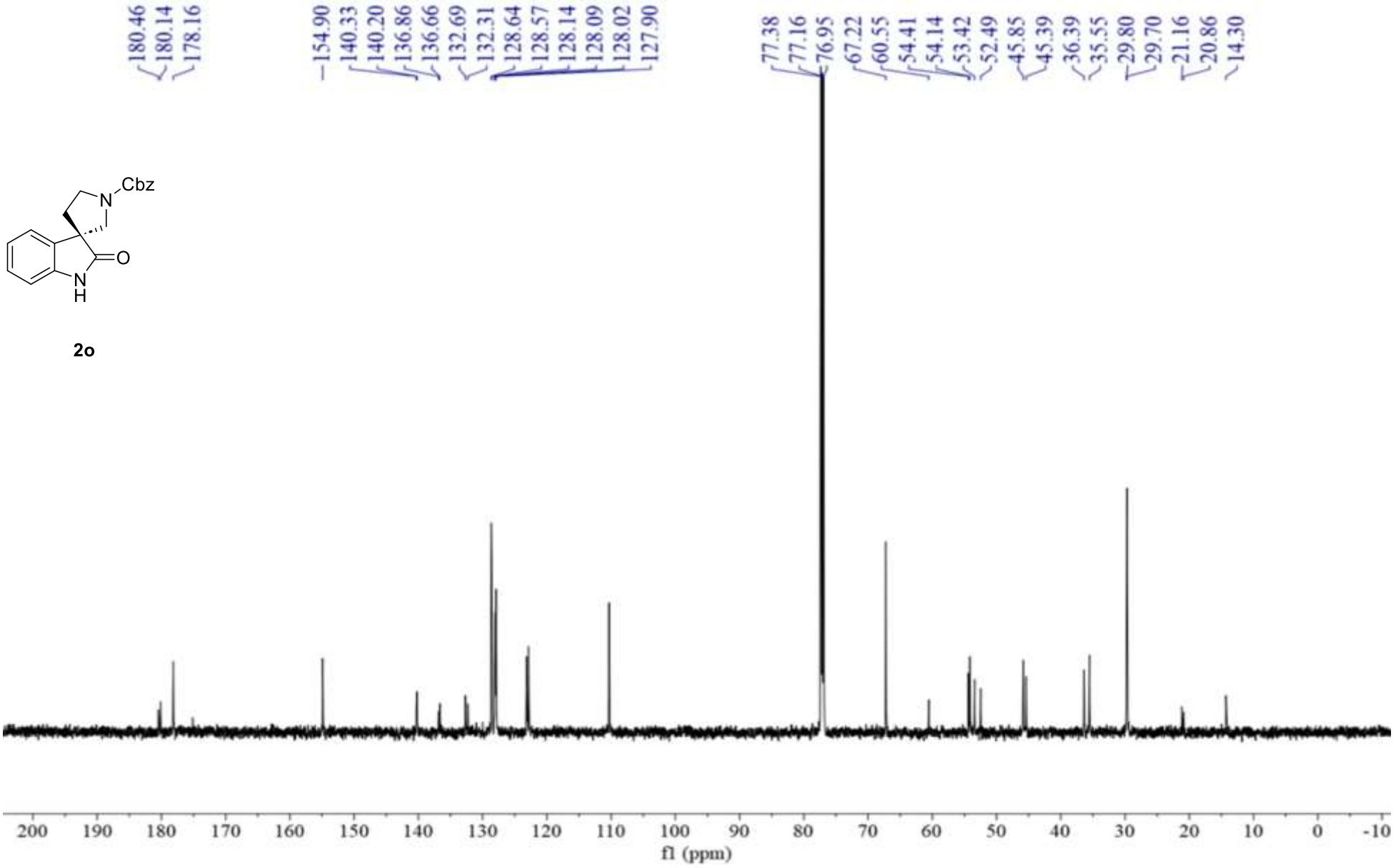
2n

9.98
9.18
7.80
7.79
7.66
7.65
7.65
7.48
7.47
7.46
7.43
7.42
7.41
7.40
7.40
7.38
7.37
7.26
7.18
7.17
7.17
7.16
7.16
7.15
7.15
3.83
3.82
3.81
3.79
3.47
3.45
3.44
2.10
2.04
1.04
0.98
1.00
2.02
1.22
4.11
1.10
2.35
2.27
0.85
0.57
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

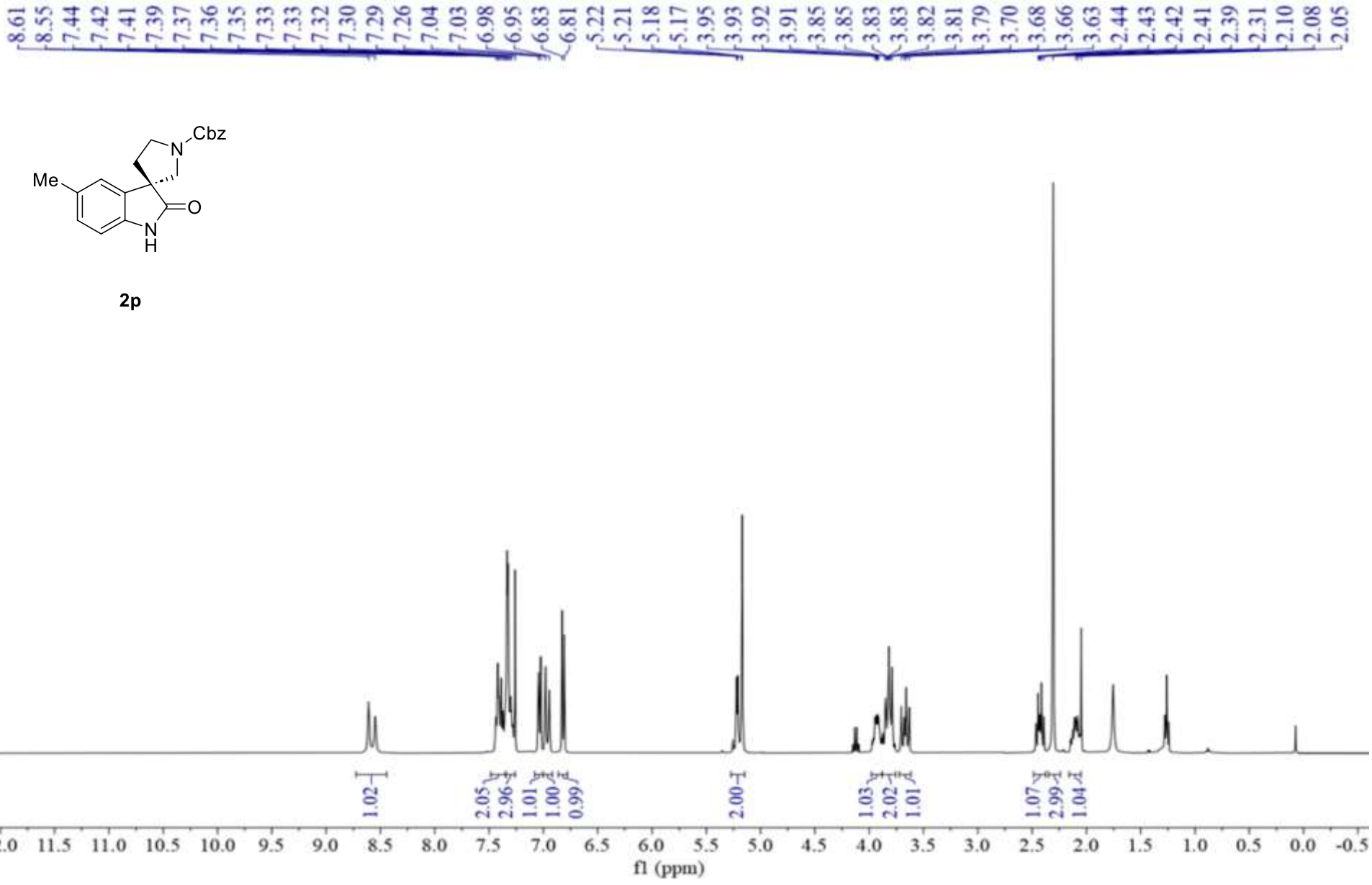

180.79
167.96
137.69
132.90
131.73
130.09
128.74
127.91
127.03
121.55
121.12
112.67
77.37
77.16
76.95
46.18
41.64
29.84
23.98
Bz
N
O
N
H
2n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.92
8.86
7.44
7.42
7.41
7.39
7.37
7.36
7.35
7.33
7.32
7.30
7.29
7.26
7.24
7.22
7.18
7.16
7.15
7.13
7.06
7.05
7.04
7.03
6.95
6.93
5.21
5.21
5.16
3.94
3.93
3.92
3.86
3.84
3.83
3.83
3.82
3.80
3.72
3.68
3.65
2.45
2.44
2.43
2.42
2.13
2.12
2.11
2.10
Cbz
N
O
N
H
0.98
1.92
2.84
0.97
1.01
1.00
0.98
1.99
1.02
2.00
1.01
1.00
1.03
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

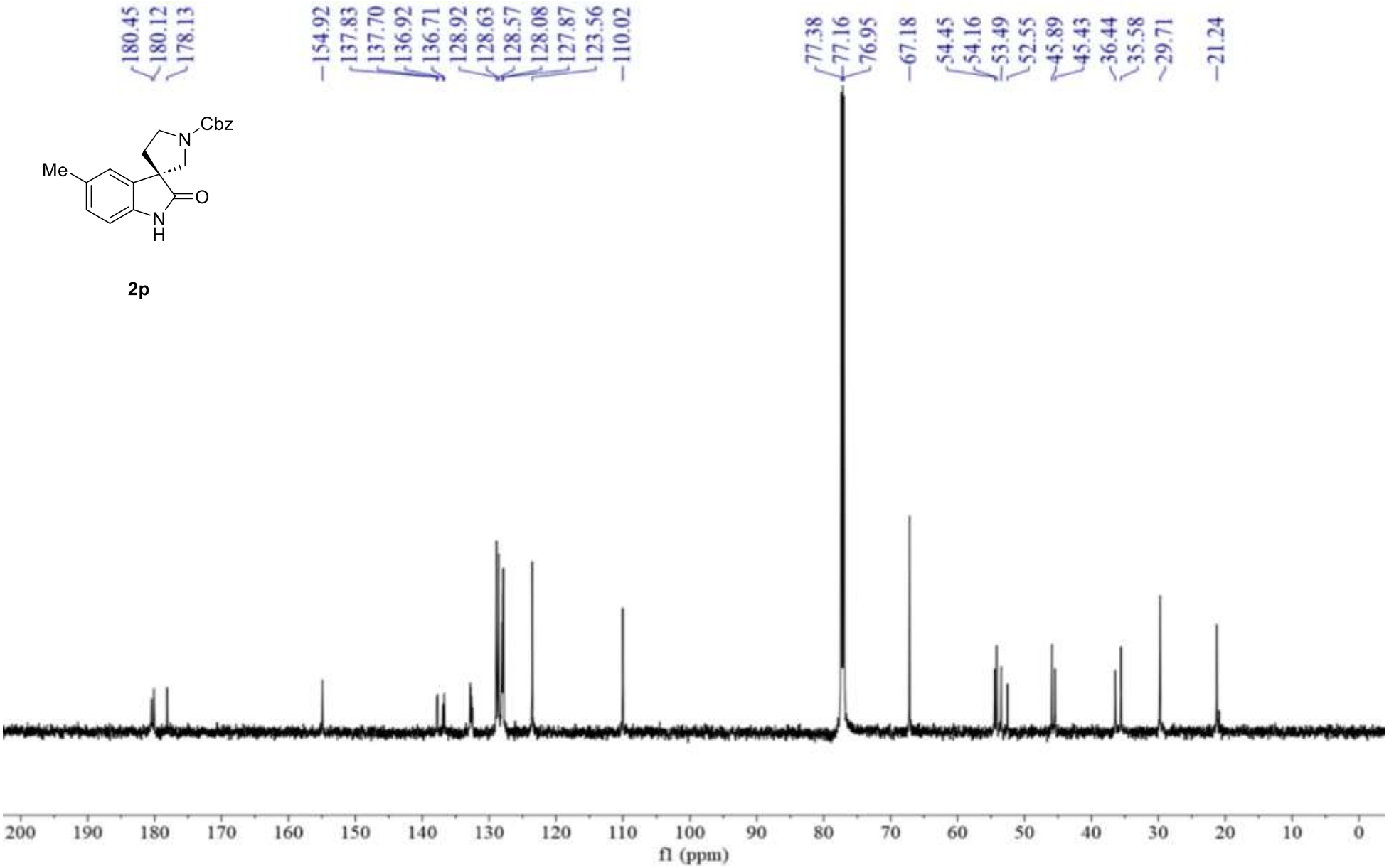
2o

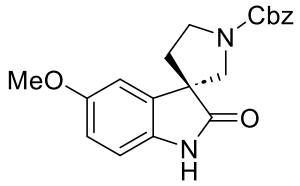

180.46
180.14
178.16
154.90
140.33
140.20
136.86
136.66
132.69
132.31
128.64
128.57
128.14
128.09
128.02
127.90
77.38
77.16
76.95
67.22
60.55
54.41
54.14
53.42
52.49
45.85
45.39
36.39
35.55
29.80
29.70
21.16
20.86
14.30
Cbz
N
O
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

2o


8.61
8.55
7.44
7.42
7.41
7.39
7.37
7.36
7.35
7.33
7.33
7.32
7.30
7.29
7.26
7.04
7.03
6.98
6.95
6.83
6.81
5.22
5.21
5.18
5.17
3.95
3.93
3.92
3.91
3.85
3.85
3.83
3.83
3.82
3.81
3.79
3.70
3.68
3.66
3.63
2.44
2.43
2.42
2.41
2.39
2.31
2.10
2.08
2.05
Cbz
N
Me
O
N
H
1.02
2.05
2.96
1.01
1.00
0.99
2.00
1.03
2.02
1.01
1.07
2.99
1.04
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

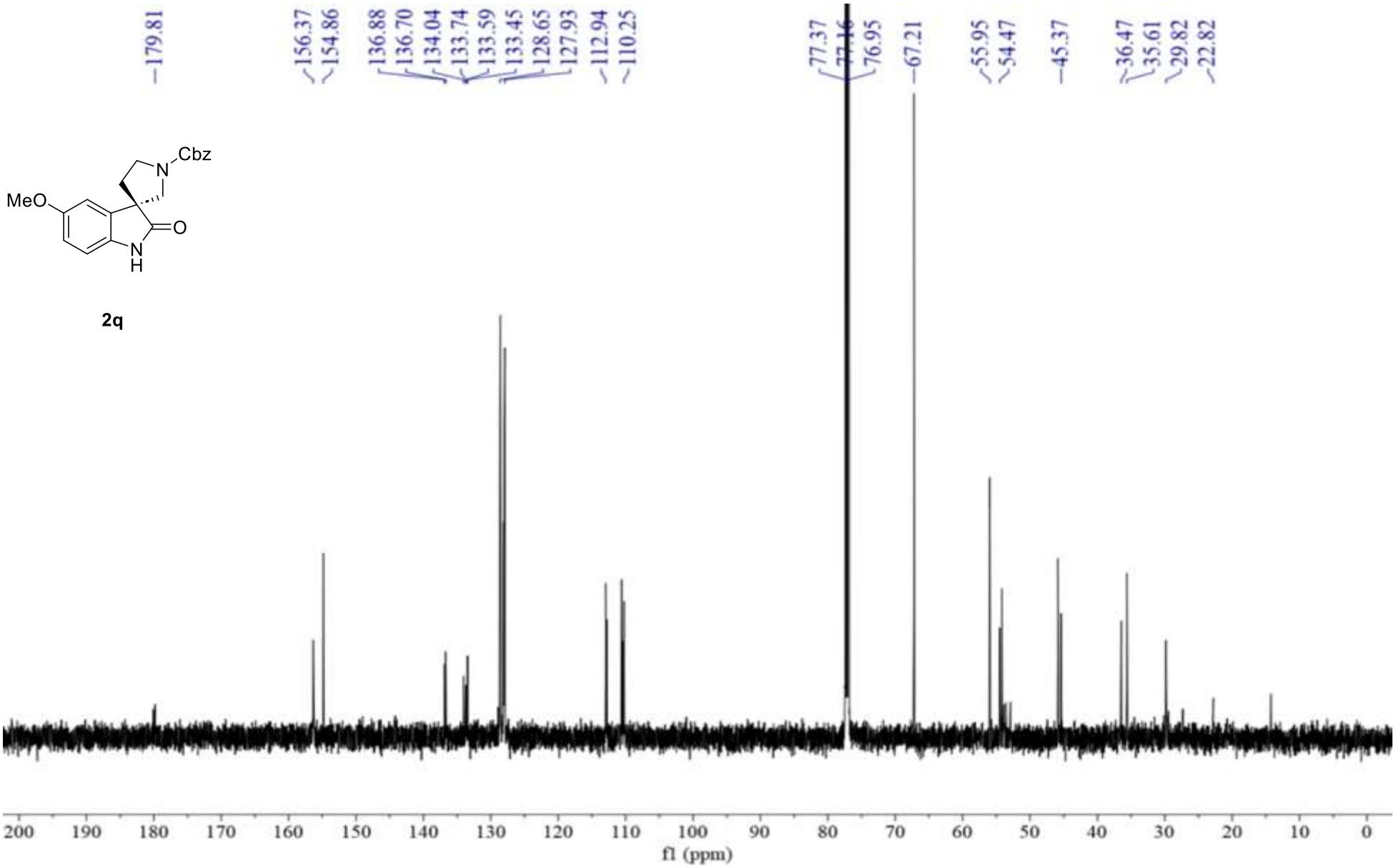
2p

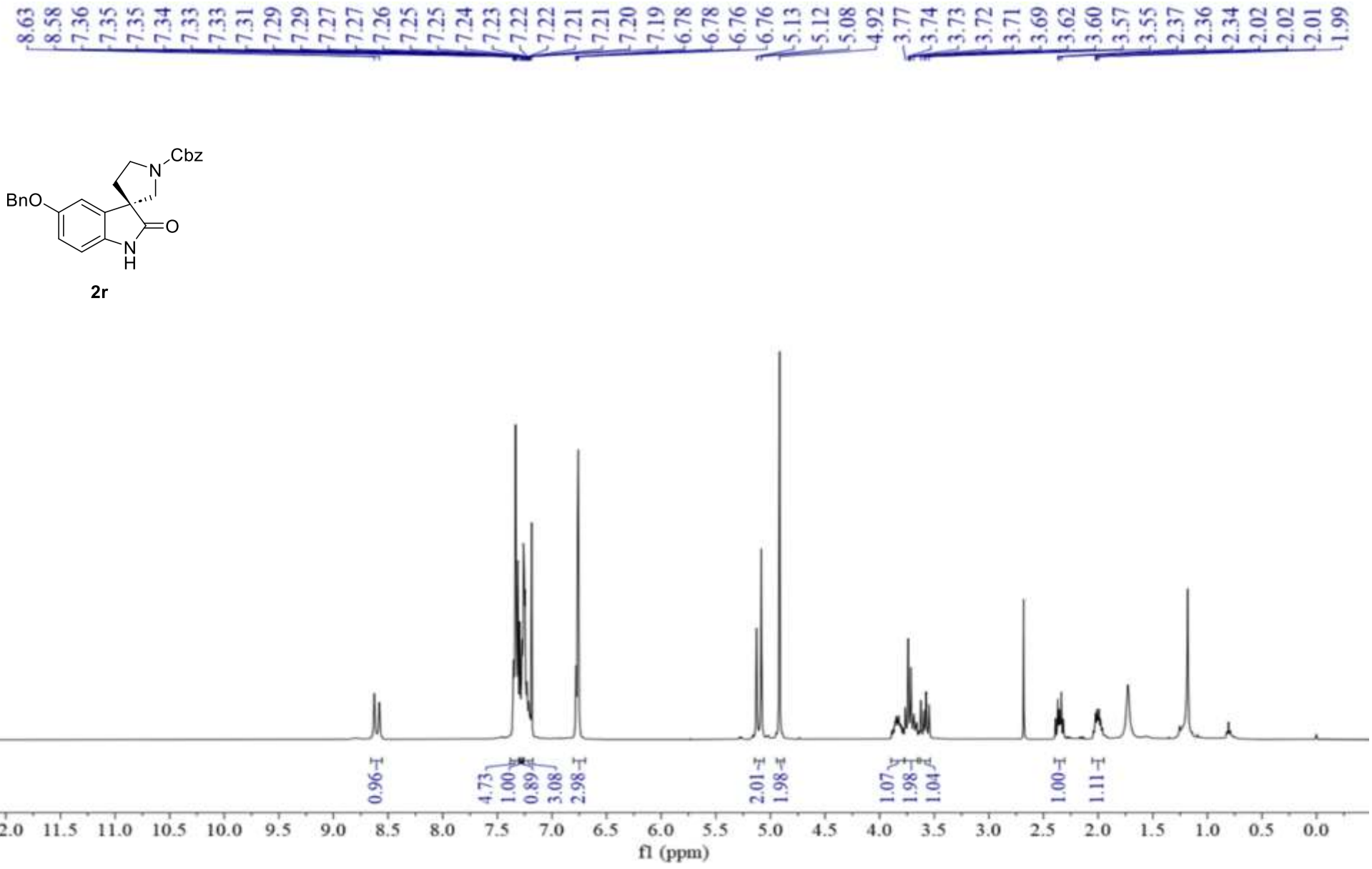

180.45
180.12
178.13
154.92
137.83
137.70
136.92
136.71
128.92
128.63
128.57
128.08
127.87
123.56
110.02
77.38
77.16
76.95
67.18
54.45
54.16
53.49
52.55
45.89
45.43
36.44
35.58
29.71
21.24
Cbz
N
Me
O
N
H
2p
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

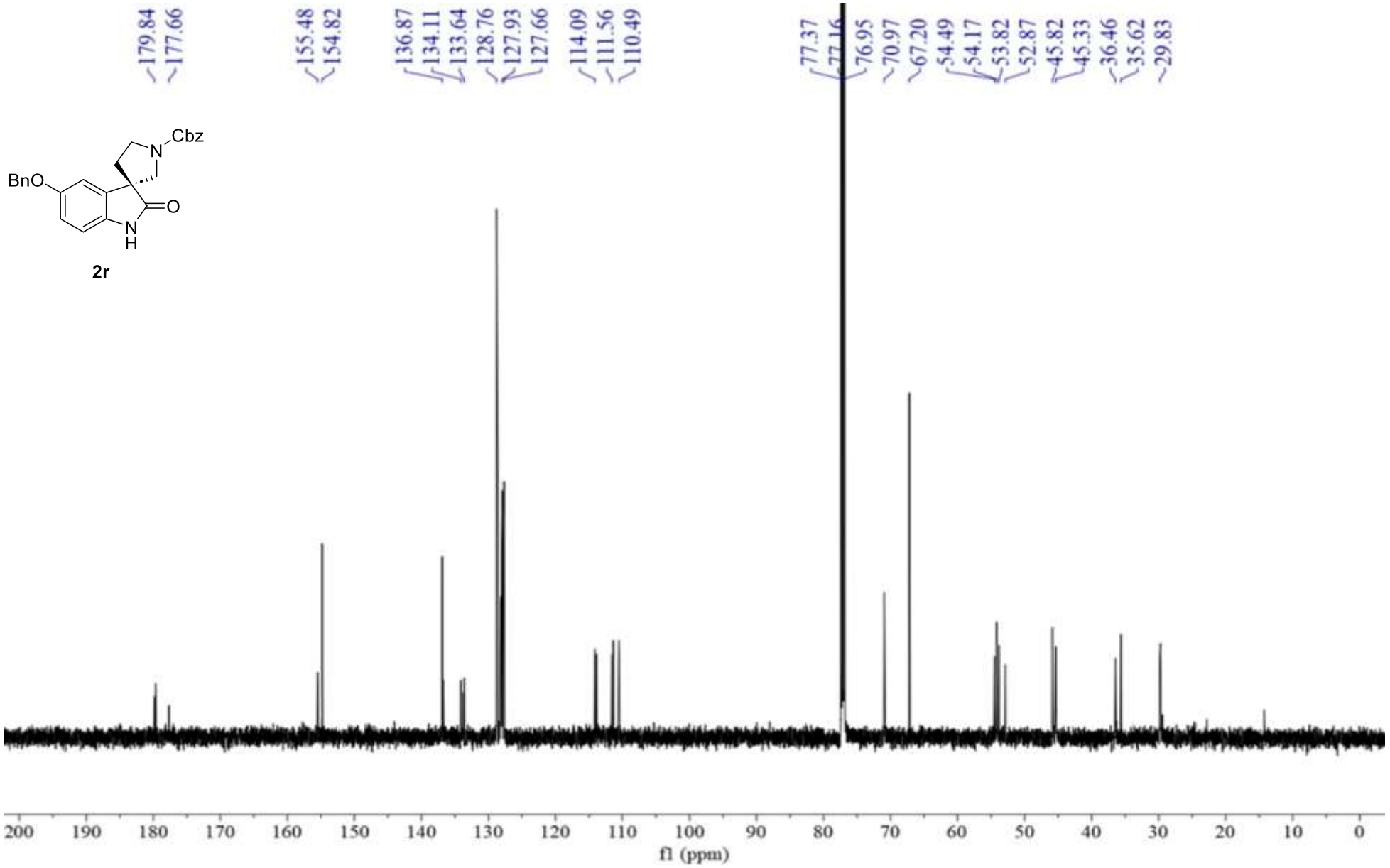

Cbz
N
MeO
O
N
H

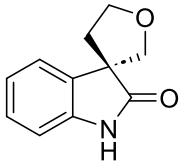
2q

8.45
8.42
7.41
7.39
7.38
7.36
7.33
7.29
7.26
6.83
6.82
6.77
6.75
5.22
5.20
5.20
5.16
3.91
3.84
3.81
3.79
3.75
3.70
3.68
3.65
3.63
2.44
2.43
2.43
2.42
2.40
2.11
2.10
2.09
2.08
2.07
1.02
4.82
0.93
1.97
2.02
1.08
2.06
3.00
1.14
1.03
1.02
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


179.81
156.37
154.86
136.88
136.70
134.04
133.74
133.59
133.45
128.65
127.93
112.94
110.25
77.37
76.95
67.21
55.95
54.47
45.37
36.47
35.61
29.82
22.82
Cbz
N
MeO
O
N
H
2q
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

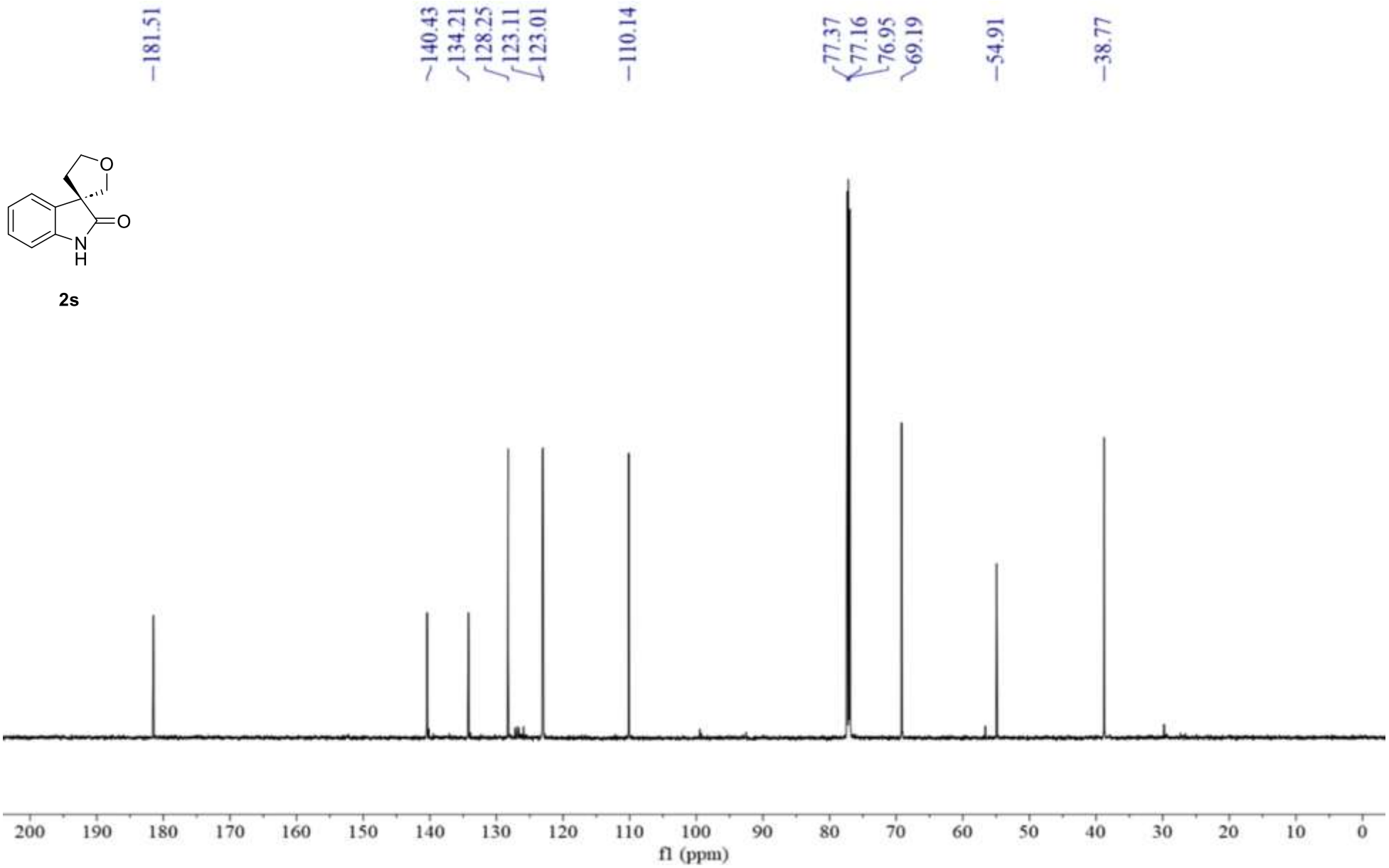

8.63
8.58
7.36
7.35
7.35
7.34
7.33
7.33
7.31
7.29
7.29
7.27
7.27
7.26
7.25
7.25
7.24
7.23
7.22
7.22
7.21
7.21
7.20
7.19
6.78
6.78
6.76
6.76
5.13
5.12
5.08
4.92
3.77
3.74
3.73
3.72
3.71
3.69
3.62
3.60
3.57
3.55
2.37
2.36
2.34
2.02
2.02
2.01
1.99
Cbz
N
BnO
O
N
H
2r
0.96
4.73
1.00
0.89
3.08
2.98
2.01
1.98
1.07
1.98
1.04
1.00
1.11
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

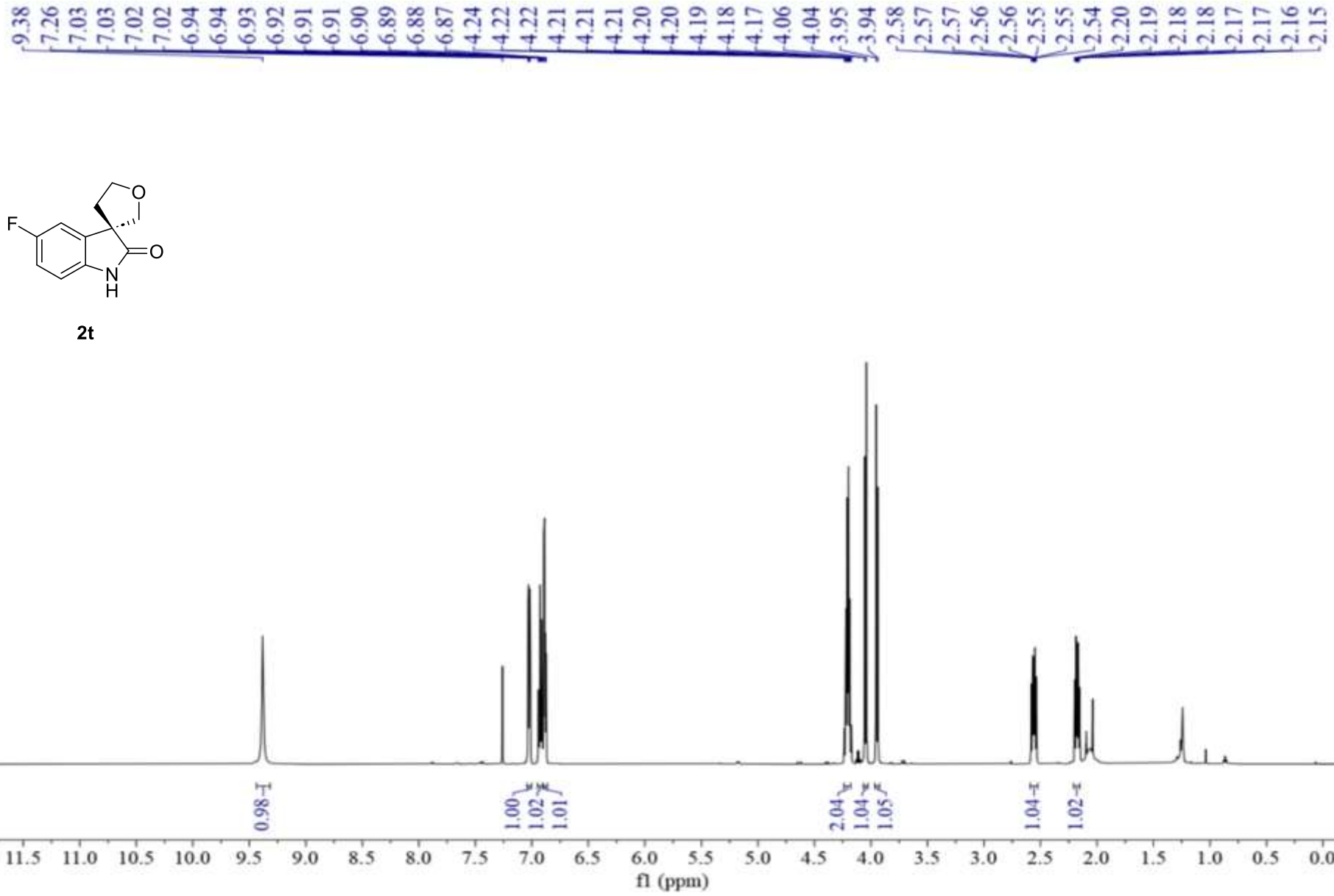

179.84
177.66
155.48
154.82
136.87
134.11
133.64
128.76
127.93
127.66
114.09
111.56
110.49
77.37
77.16
76.95
70.97
67.20
54.49
54.17
53.82
52.87
45.82
45.33
36.46
35.62
29.83
Cbz
N
BnO
O
N
H
2r
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



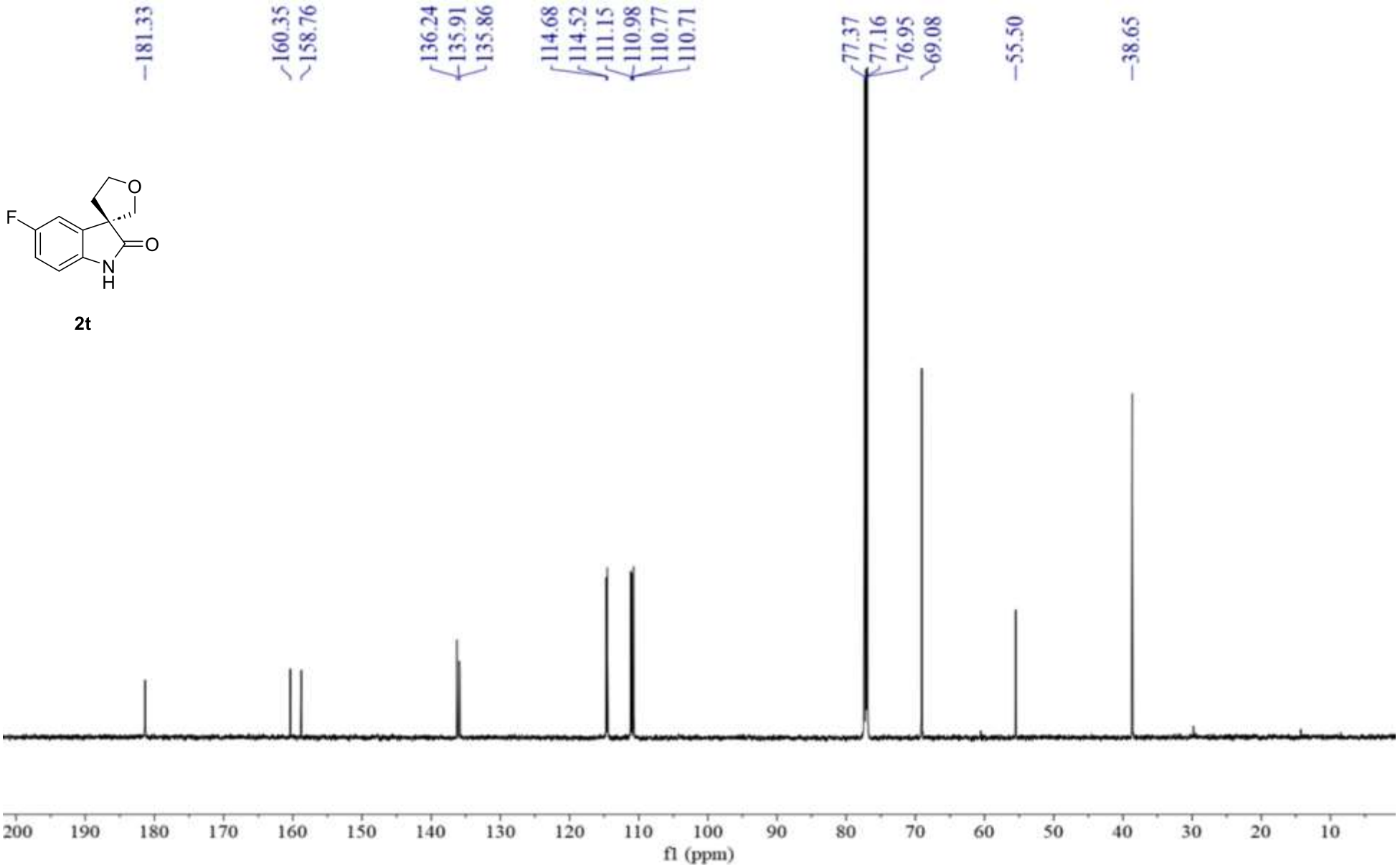
2s

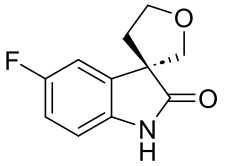
8.83
7.29
7.28
7.26
7.24
7.23
7.22
7.07
7.06
7.05
6.95
6.94
4.23
4.22
4.21
4.21
4.19
4.09
4.07
3.97
3.96
2.58
2.56
2.55
2.54
2.53
2.21
2.20
2.19
2.18
2.17
1.25
1.01
0.96
0.96
1.00
0.98
2.03
1.03
1.03
1.07
1.09
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


181.51
140.43
134.21
128.25
123.11
123.01
110.14
77.37
77.16
76.95
69.19
54.91
38.77
O
O
N
H
2s
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.38
7.26
7.03
7.03
7.02
7.02
6.94
6.94
6.93
6.92
6.91
6.91
6.90
6.89
6.88
6.87
4.24
4.22
4.22
4.21
4.21
4.21
4.20
4.20
4.19
4.18
4.17
4.06
4.04
3.95
3.94
2.58
2.57
2.57
2.56
2.56
2.55
2.55
2.54
2.20
2.19
2.18
2.18
2.17
2.17
2.16
2.15
F
O
O
N
H
0.98
1.00
1.02
1.01
2.04
1.04
1.05
1.04
1.02
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

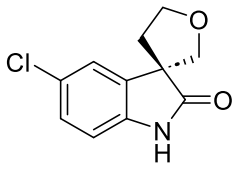
2t


181.33
160.35
158.76
136.24
135.91
135.86
114.68
114.52
111.15
110.98
110.77
110.71
77.37
77.16
76.95
69.08
55.50
38.65
F
O
O
N
H
2t
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


F
O
O
N
H

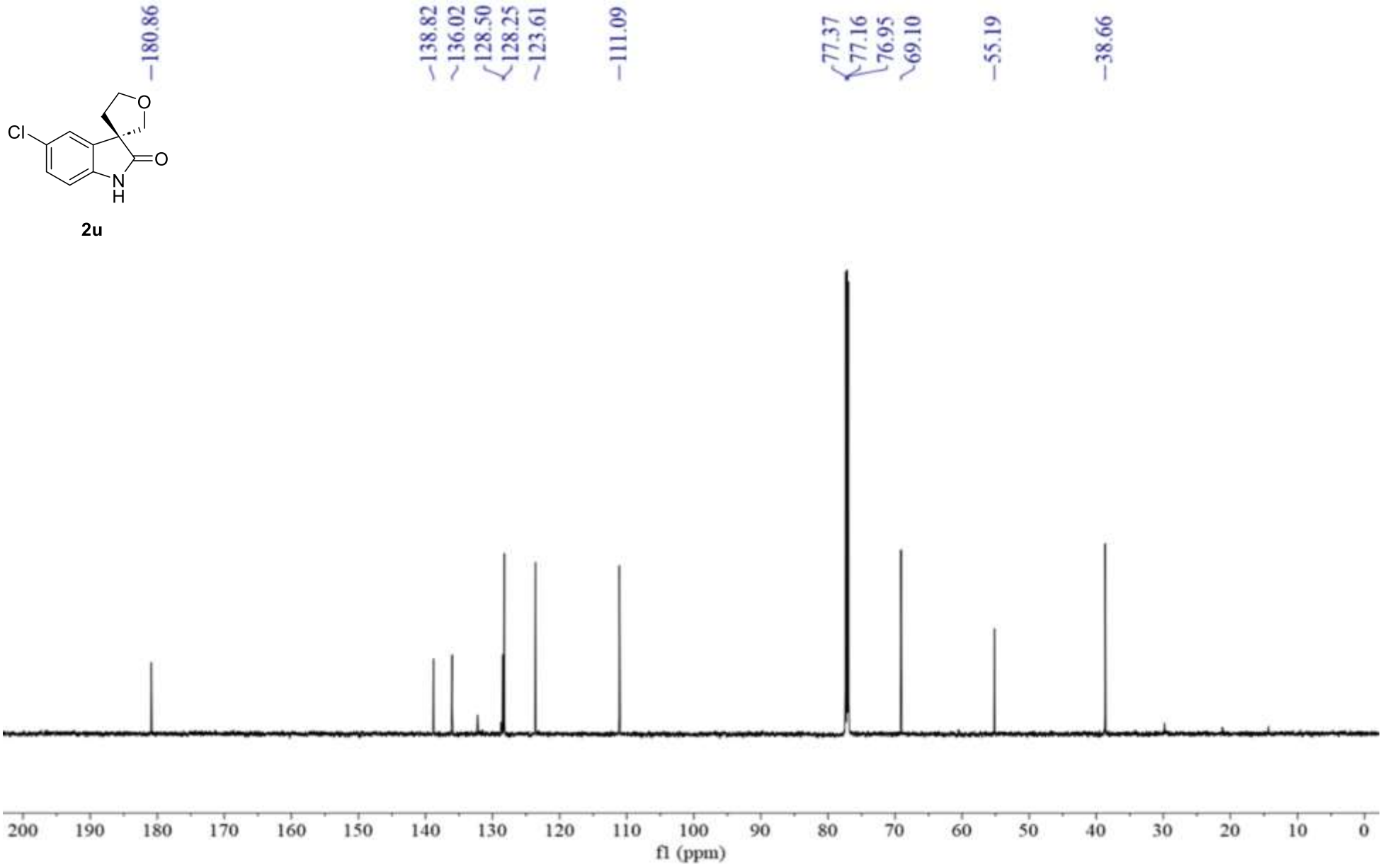
2t

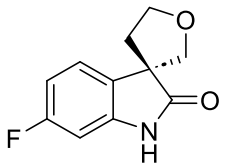
-119.66
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


Cl
O
O
N
H

2u

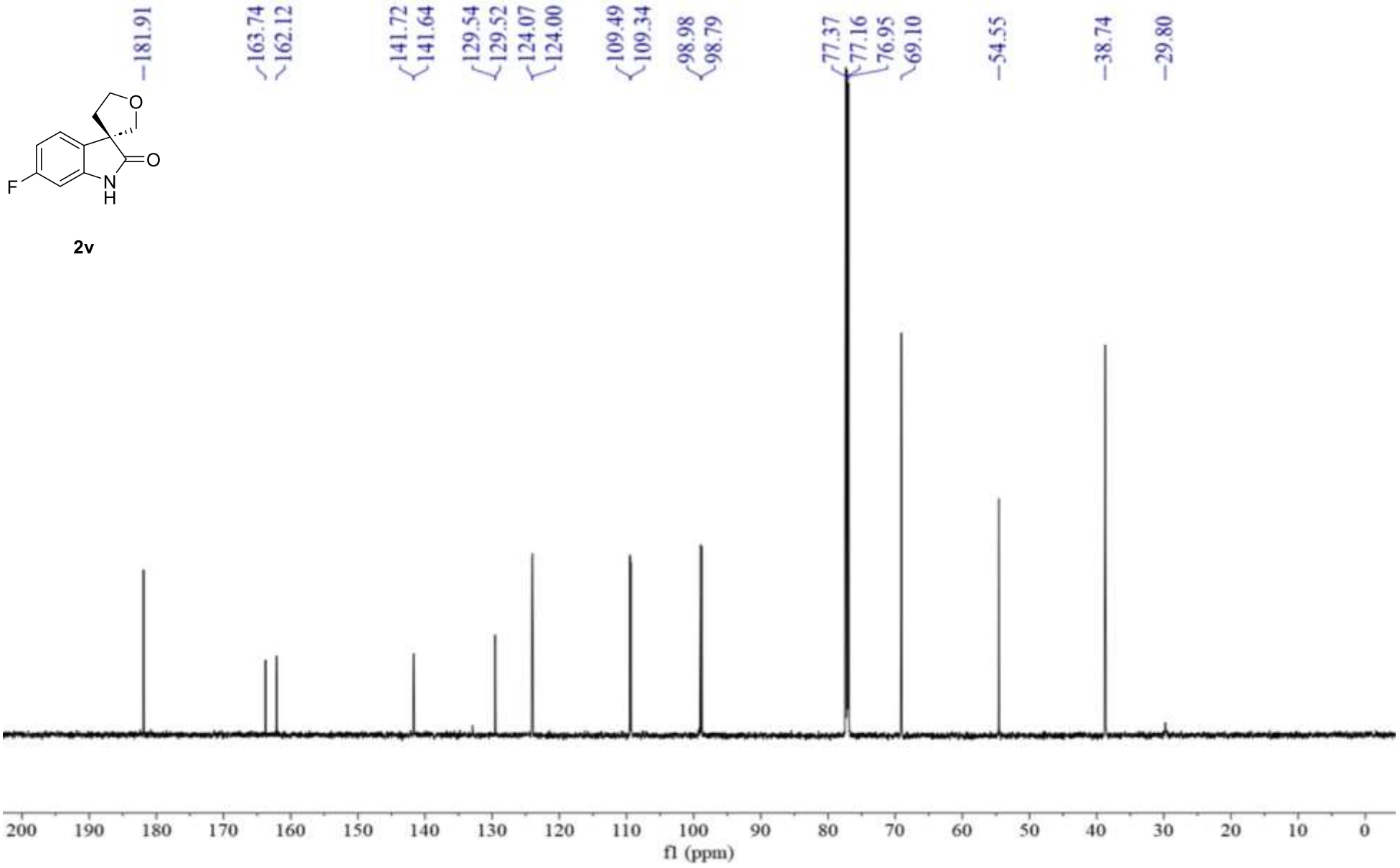
9.17
7.27
7.27
7.26
7.21
7.21
7.20
7.20
6.89
6.87
4.23
4.23
4.23
4.22
4.22
4.21
4.21
4.20
4.20
4.19
4.05
4.03
3.96
3.94
2.57
2.56
2.56
2.55
2.55
2.54
2.53
2.20
2.19
2.19
2.18
2.18
2.17
2.17
1.02
1.00
1.04
1.06
2.24
1.07
1.06
1.07
1.05
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

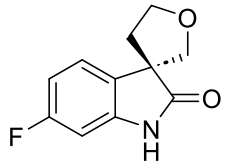

180.86
138.82
136.02
128.50
128.25
123.61
111.09
77.37
77.16
76.95
69.10
55.19
38.66
Cl
O
O
N
H
2u
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
F
N
H

2v

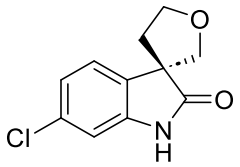
9.38
7.26
7.22
7.21
7.21
7.20
6.75
6.75
6.74
6.74
6.74
6.73
6.72
6.72
6.71
6.70
4.22
4.21
4.21
4.20
4.20
4.06
4.04
3.93
3.92
2.56
2.55
2.54
2.54
2.53
2.52
2.19
2.18
2.17
2.16
2.15
0.97
1.00
2.00
2.07
1.03
1.08
1.04
1.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


181.91
163.74
162.12
141.72
141.64
129.54
129.52
124.07
124.00
109.49
109.34
98.98
98.79
77.37
77.16
76.95
69.10
54.55
38.74
29.80
O
O
F
N
H
2v
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
F
N
H

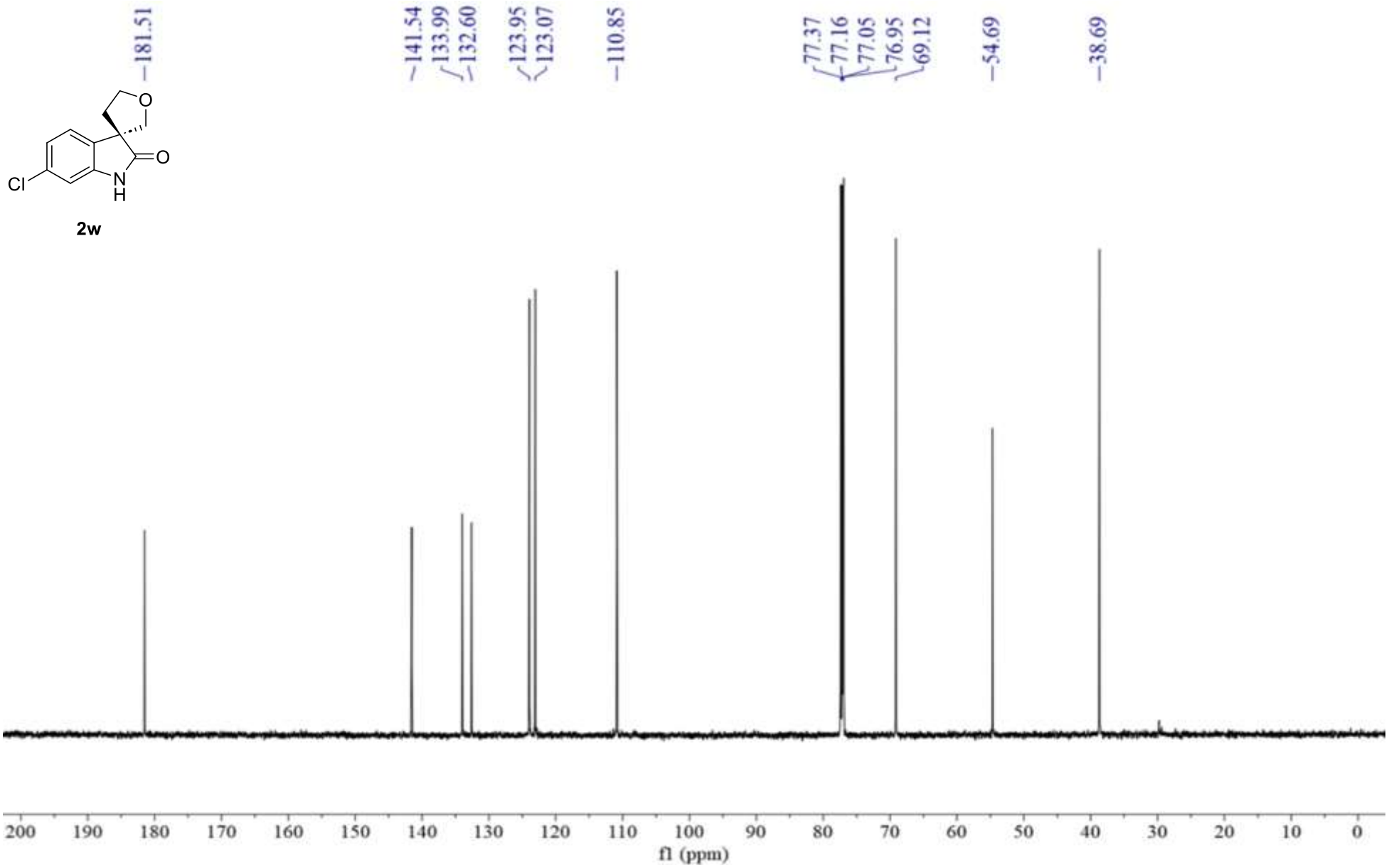
2v

-112.18
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


O
O
Cl
N
H

2w

9.48
7.26
7.20
7.18
7.03
7.03
7.02
7.02
6.98
6.98
4.22
4.22
4.21
4.21
4.21
4.20
4.19
4.05
4.04
3.94
3.92
2.57
2.55
2.54
2.54
2.53
2.53
2.52
2.18
2.17
2.16
2.15
2.14
0.96
1.00
0.96
0.94
1.98
1.01
1.01
1.03
1.05
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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133.99
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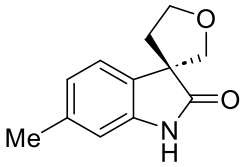
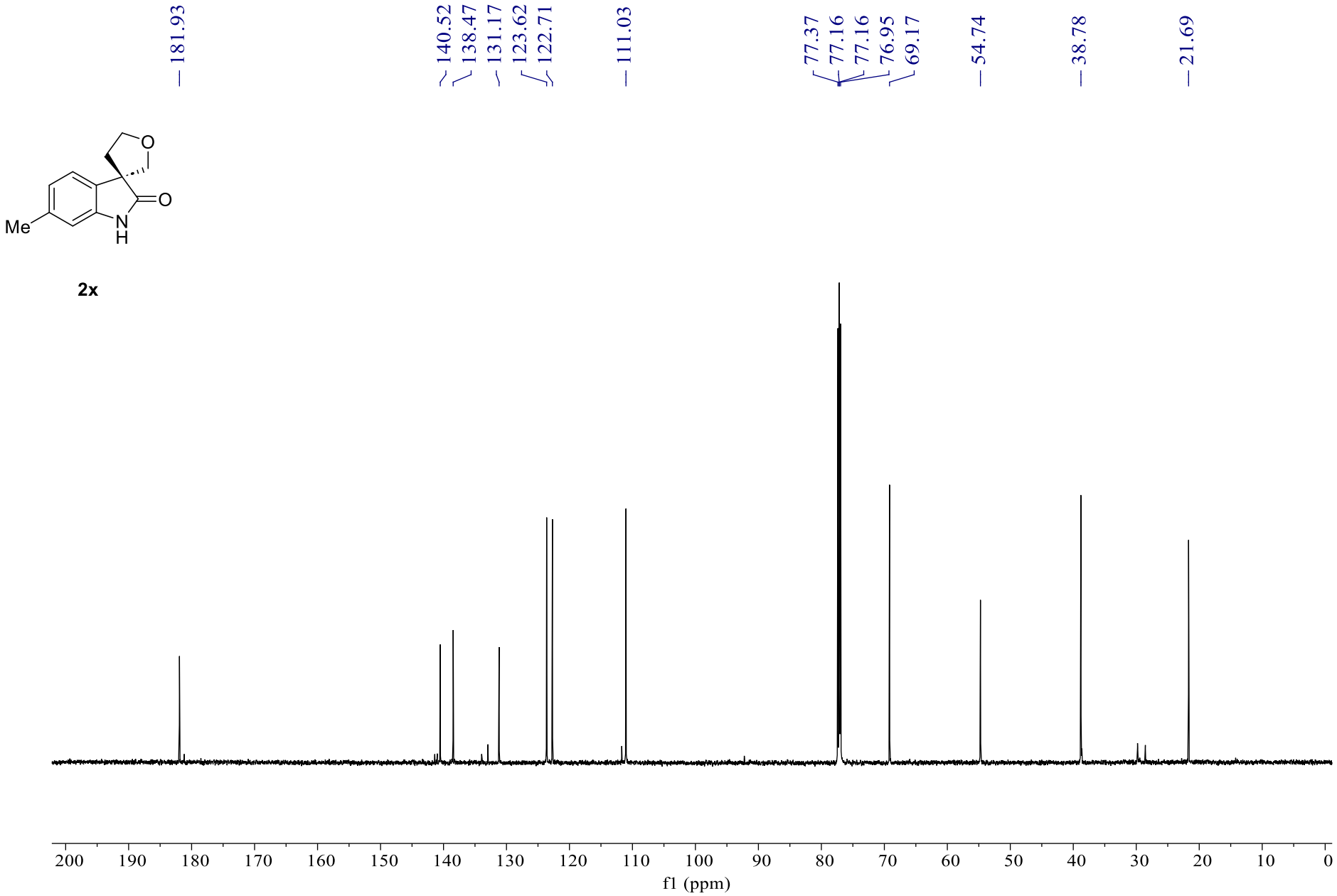
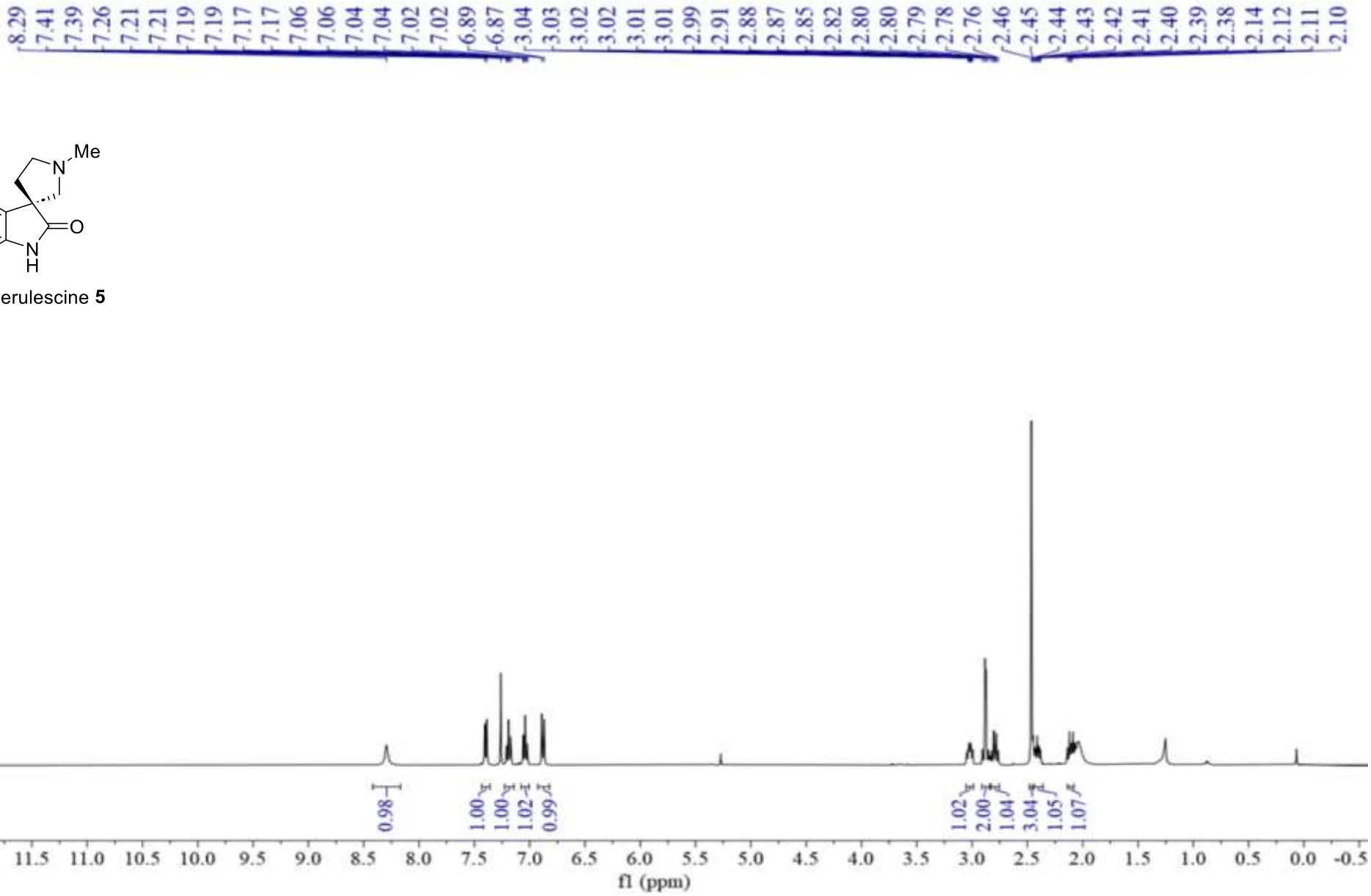
123.07
110.85
77.37
77.16
77.05
76.95
69.12
54.69
38.69
Cl
O
O
N
H
2w
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
Me
N
H

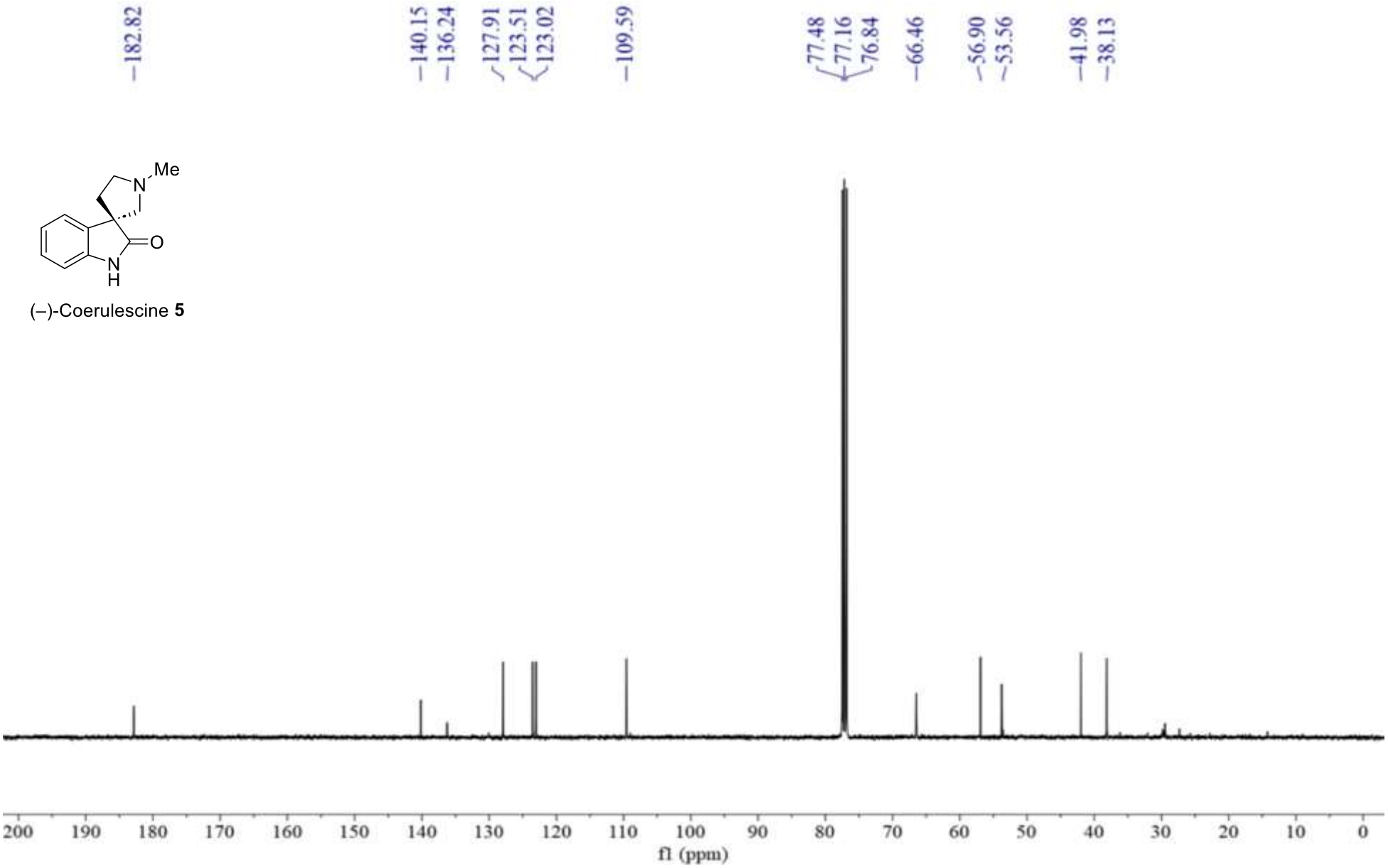
2x

7.92
7.26
7.17
7.16
6.88
6.87
6.74
4.21
4.21
4.20
4.20
4.19
4.19
4.06
4.04
3.94
3.92
2.55
2.54
2.53
2.53
2.52
2.51
2.35
2.18
2.16
2.15
2.14
2.13
0.94
0.98
1.00
1.00
2.00
1.02
0.98
1.13
3.00
1.16
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


181.93
140.52
138.47
131.17
123.62
122.71
111.03
77.37
77.16
77.16
76.95
69.17
54.74
38.78
21.69
O
O
Me
N
H
2x
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

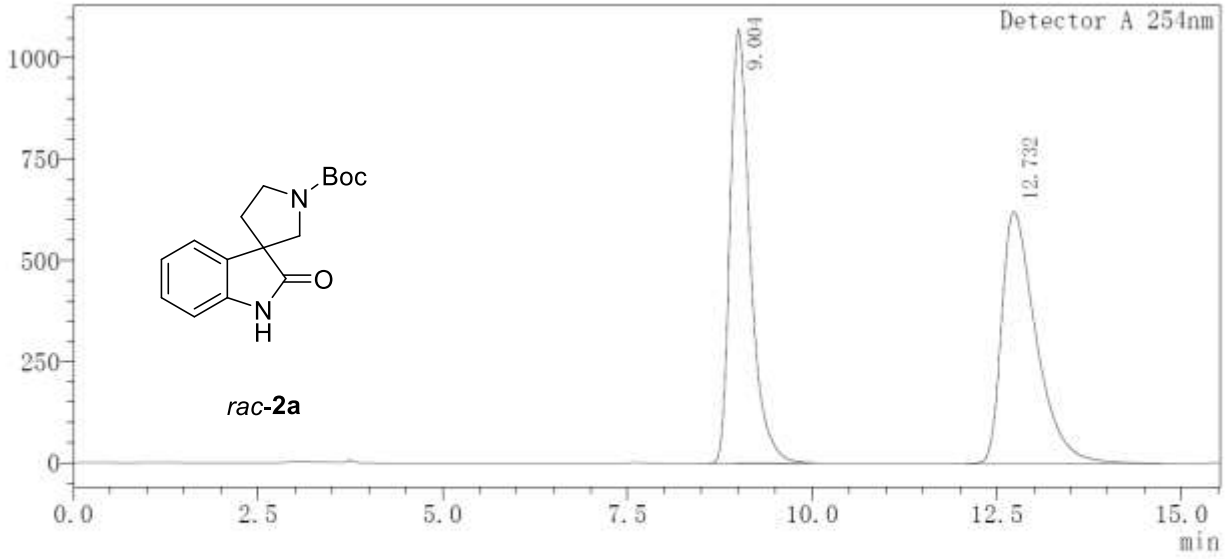


(–)-Coerulescine **5**



(–)-Coerulescine **5**

HPLC Chromatograms

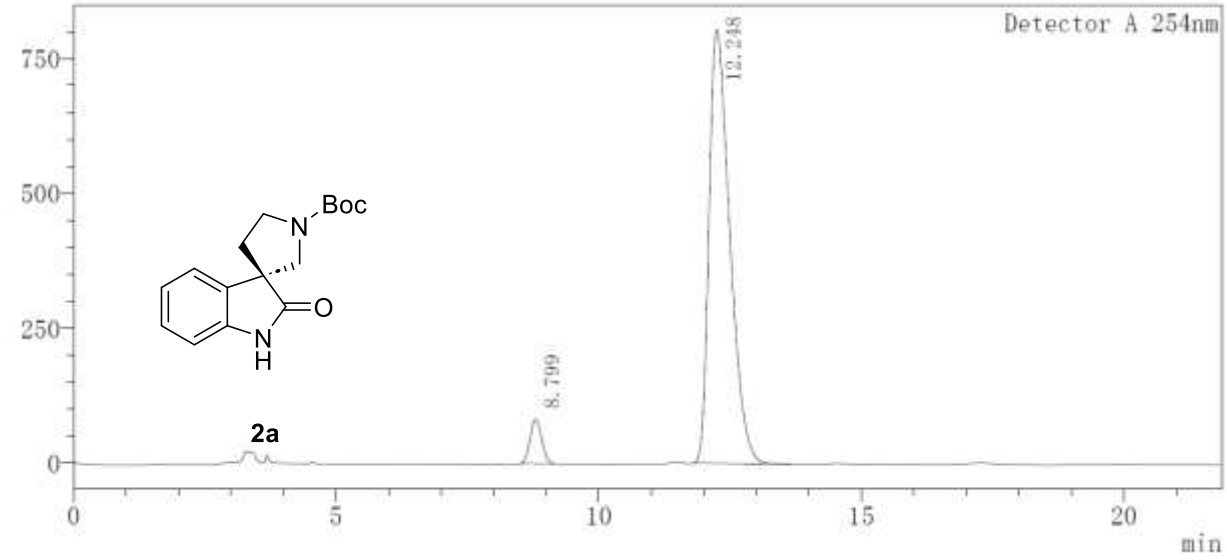


rac-**2a**

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	9.004	20411978	1072021	50.315			
2	12.732	20156246	621994	49.685			
Total		40568224	1694015				

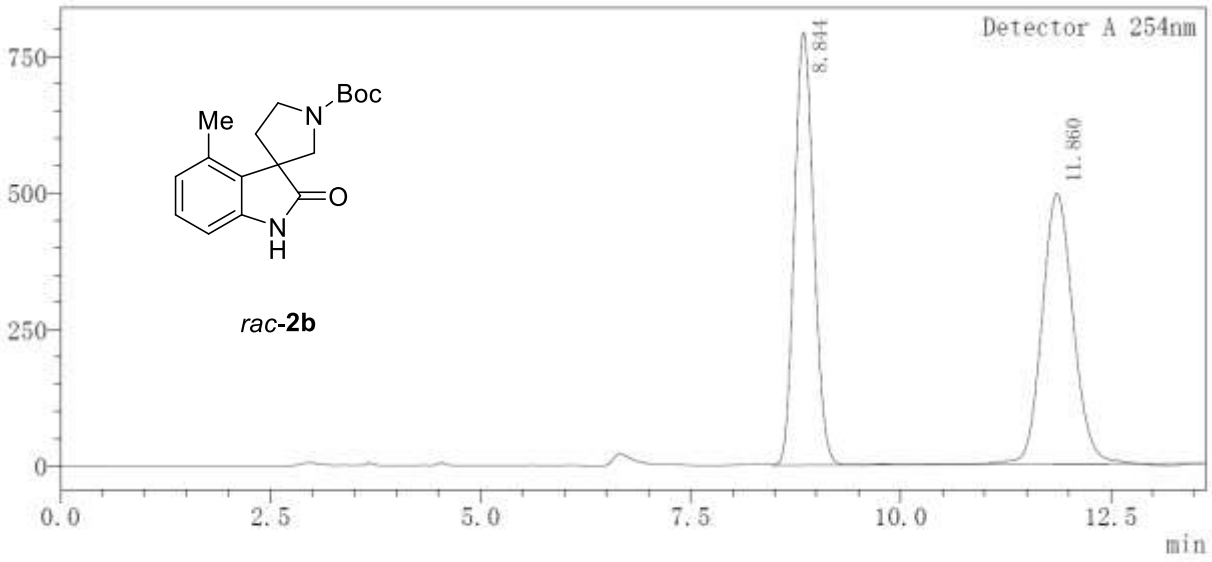


2a

〈Peak Table〉

Detector A 254nm

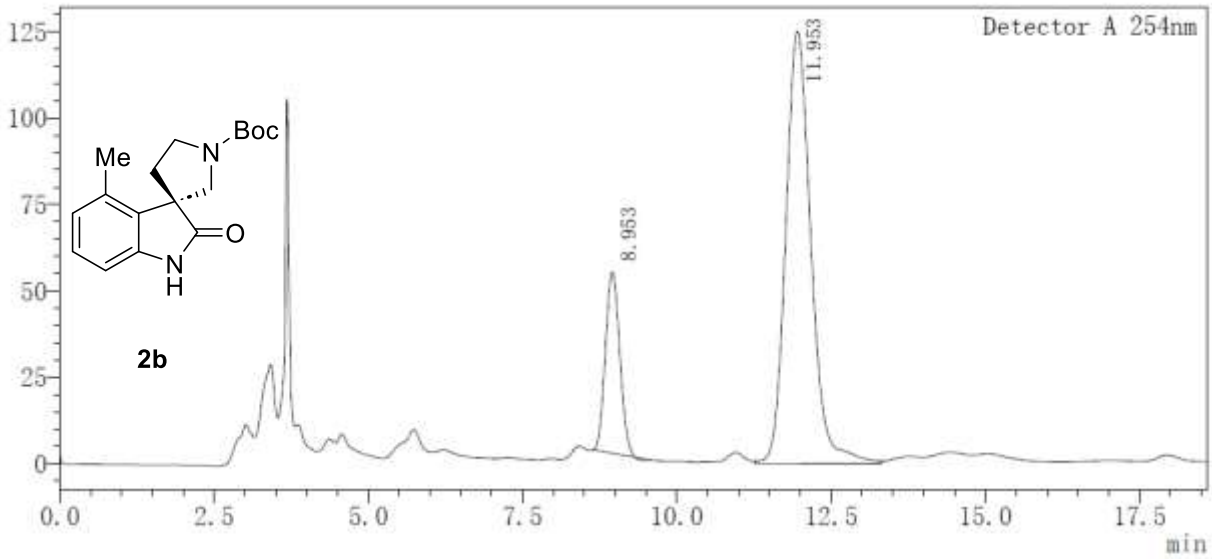
Peak	RetTime	Area	Height	Area%			
1	8.799	1253049	82099	5.374			
2	12.248	22063723	805135	94.626			
Total		23316772	887234				



〈Peak Table〉

Detector A 254nm

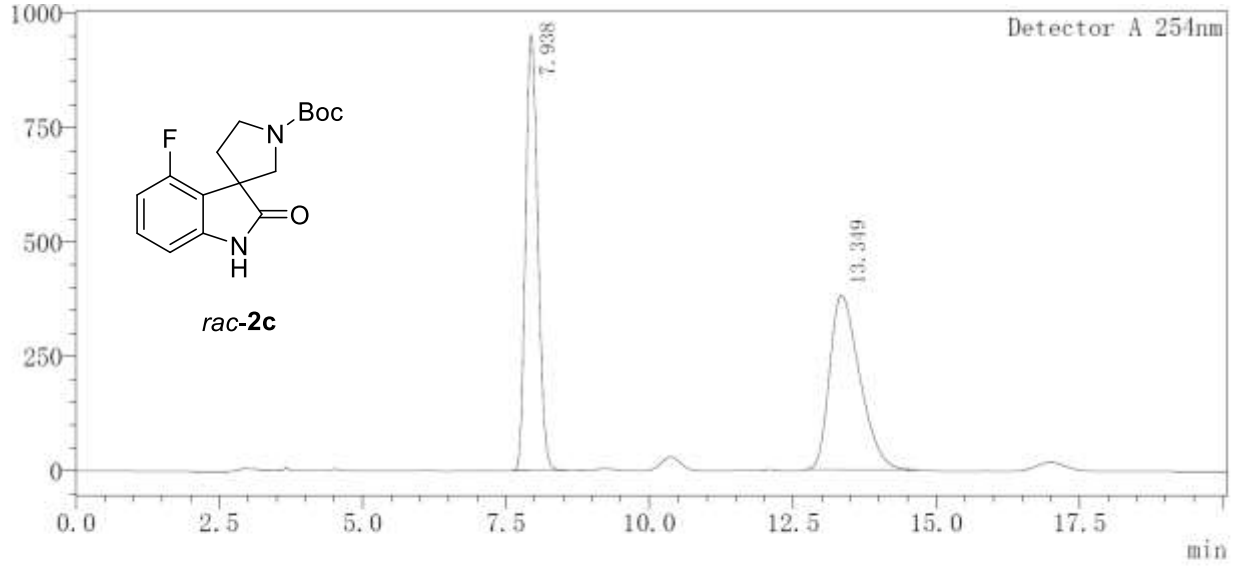
Peak	RetTime	Area	Height	Area%			
1	8.844	12727383	793260	49.995			
2	11.860	12729806	495963	50.005			
Total		25457189	1289223				



〈Peak Table〉

Detector A 254nm

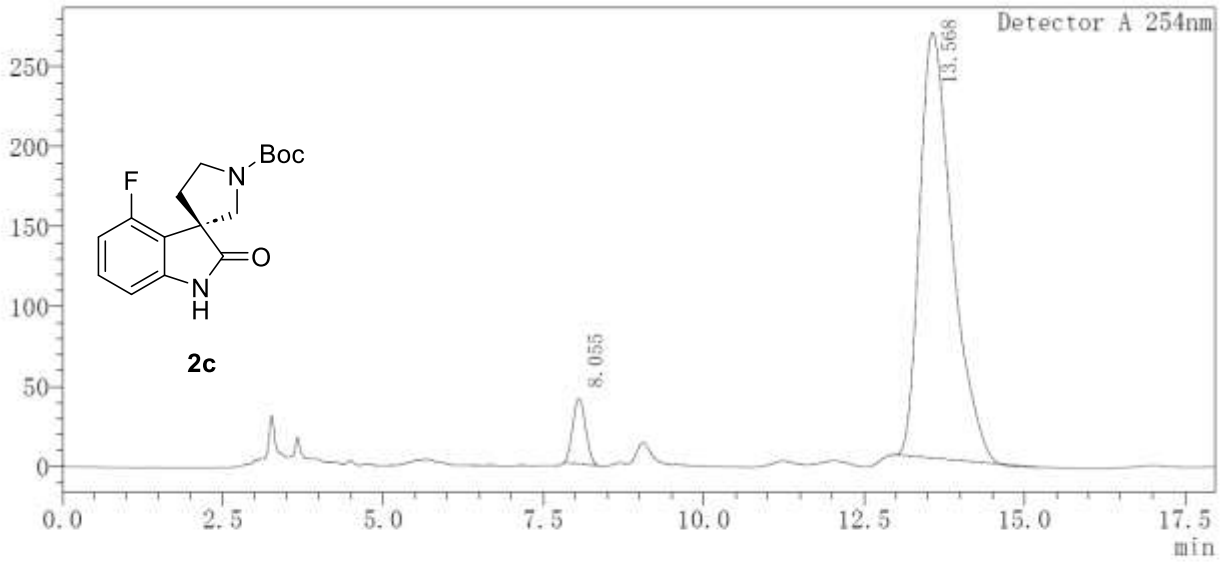
Peak	RetTime	Area	Height	Area%			
1	8.953	843272	52433	19.204			
2	11.953	3547836	124922	80.796			
Total		4391107	177355				



<Peak Table>

Detector A 254nm

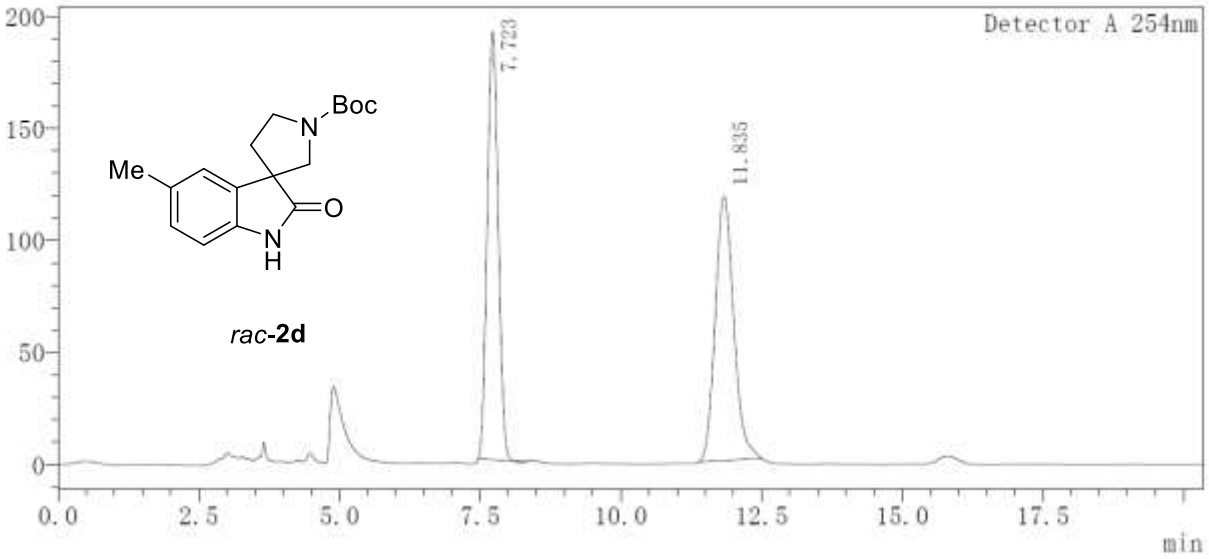
Peak	RetTime	Area	Height	Area%			
1	7.938	14111989	950901	50.326			
2	13.349	13929392	381566	49.674			
Total		28041381	1332466				



<Peak Table>

Detector A 254nm

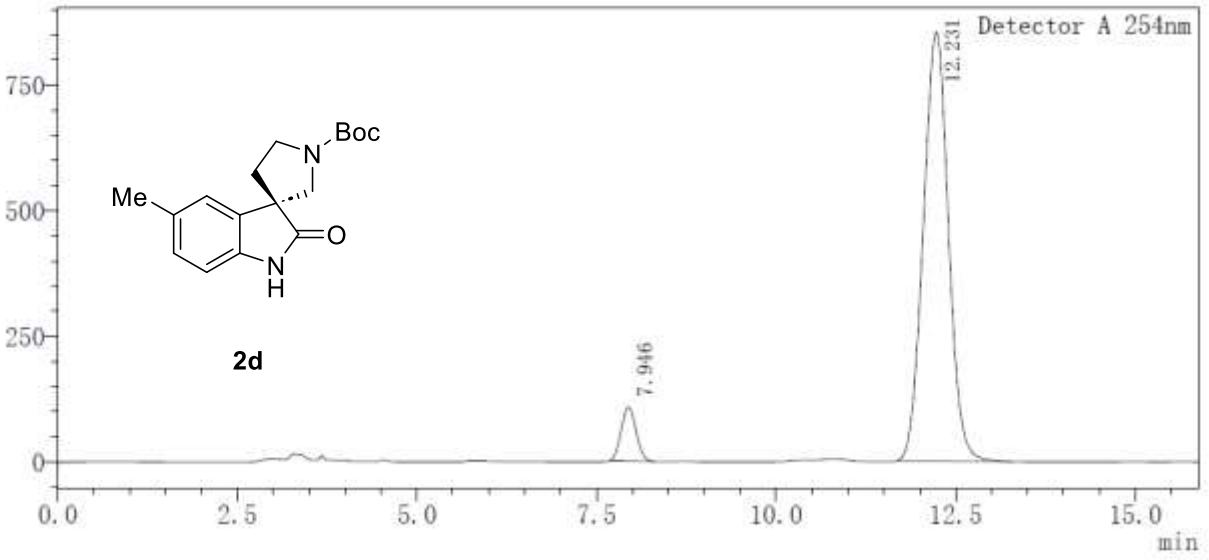
Peak	RetTime	Area	Height	Area%			
1	8.055	566588	40926	5.690			
2	13.568	9390946	266248	94.310			
Total		9957534	307174				



〈Peak Table〉

Detector A 254nm

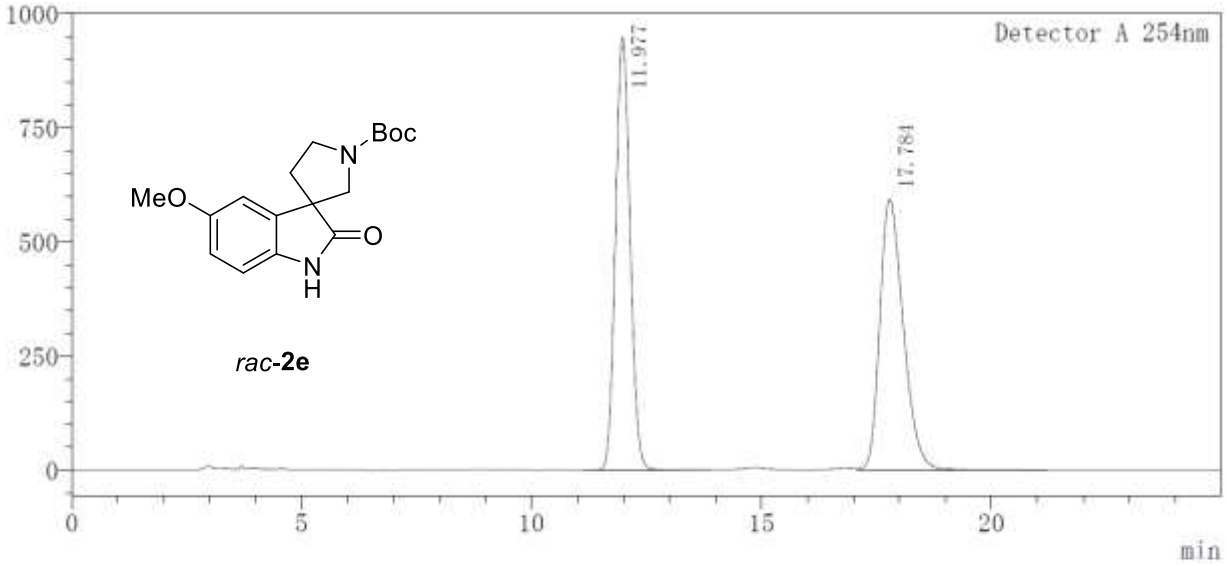
Peak	RetTime	Area	Height	Area%			
1	7.723	2595549	190942	49.155			
2	11.835	2684769	117777	50.845			
Total		5280318	308719				



〈Peak Table〉

Detector A 254nm

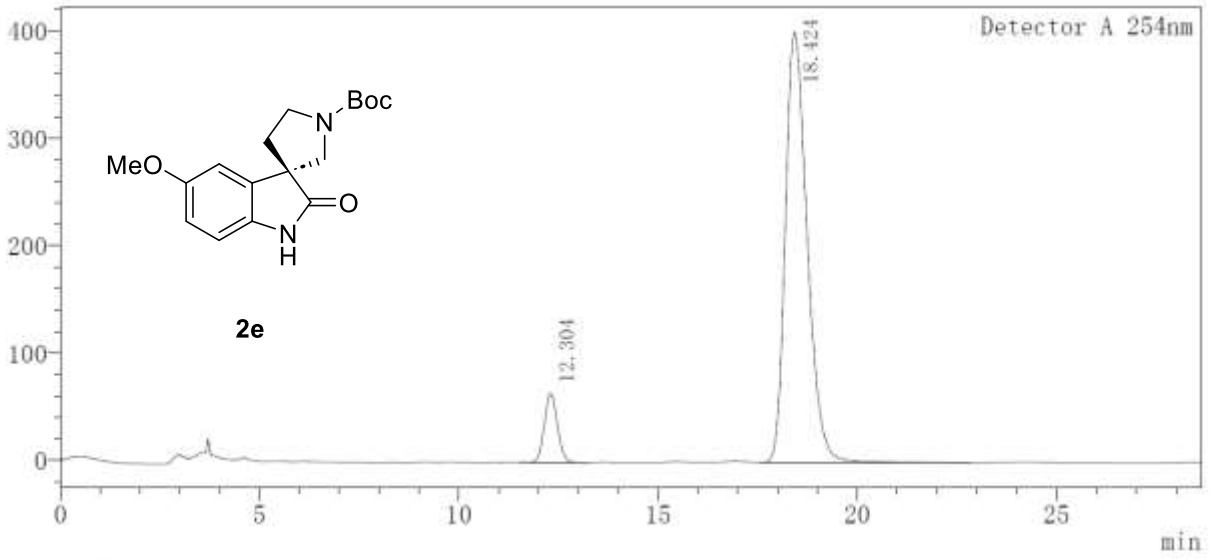
Peak	RetTime	Area	Area	Area%			
1	7.946	1540455	106785	6.915			
2	12.231	20735028	854051	93.085			
Total		22275483	960836				



〈Peak Table〉

Detector A 254nm

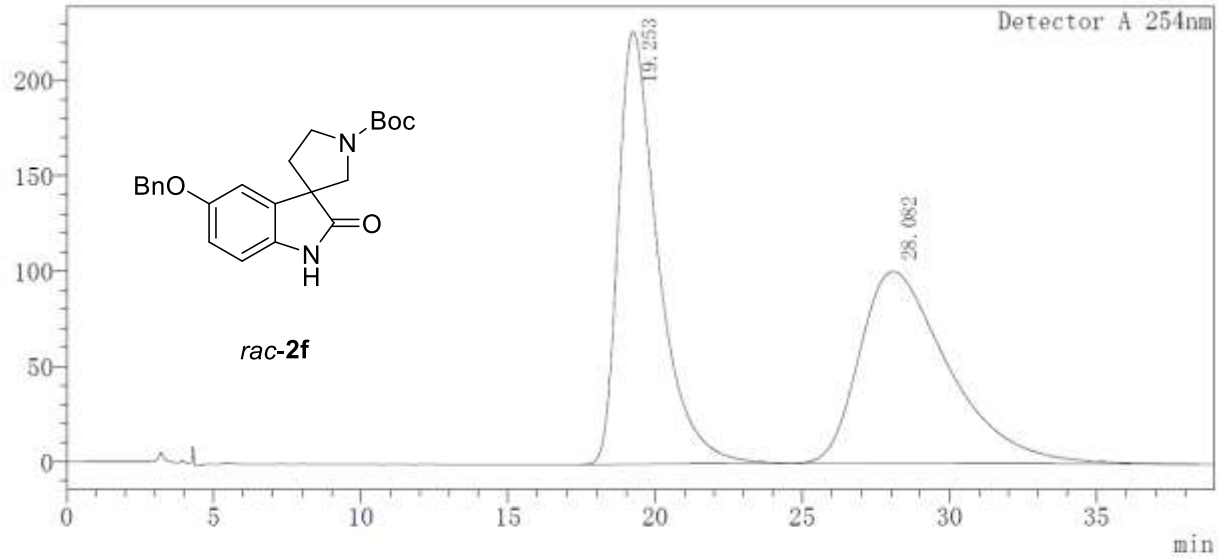
Peak	RetTime	Area	Height	Area%			
1	11.977	20942931	948641	49.860			
2	17.784	21060146	593319	50.140			
Total		42003077	1541960				



〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	12.304	1483920	64368	8.816			
2	18.424	15349008	401544	91.184			
Total		16832928	465912				

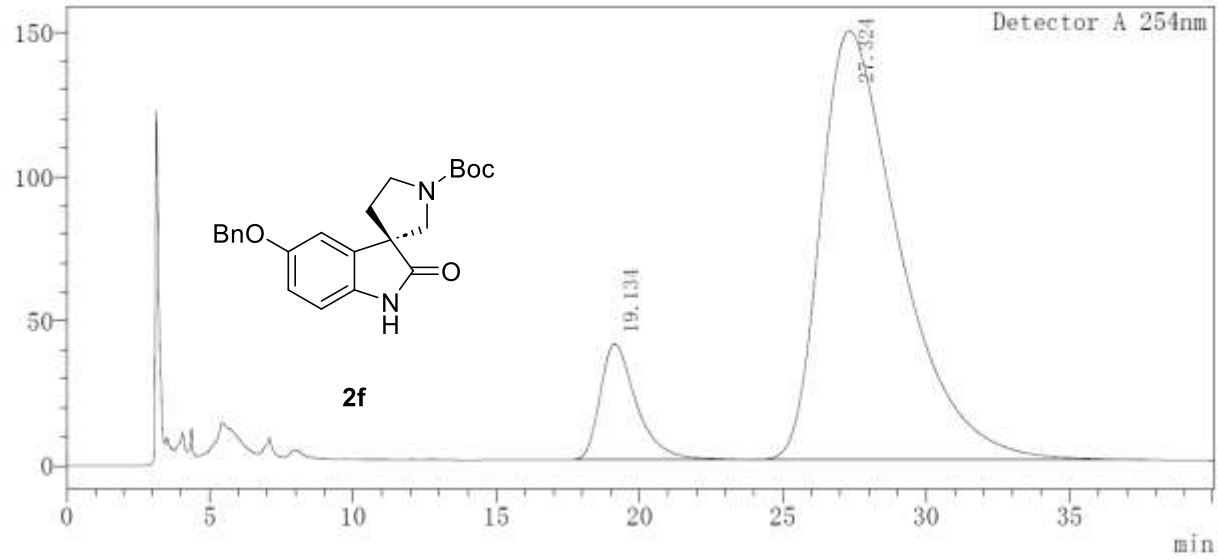


rac-**2f**

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	19.253	21327774	227211	50.088			
2	28.082	21252896	100731	49.912			
Total		42580670	327942				

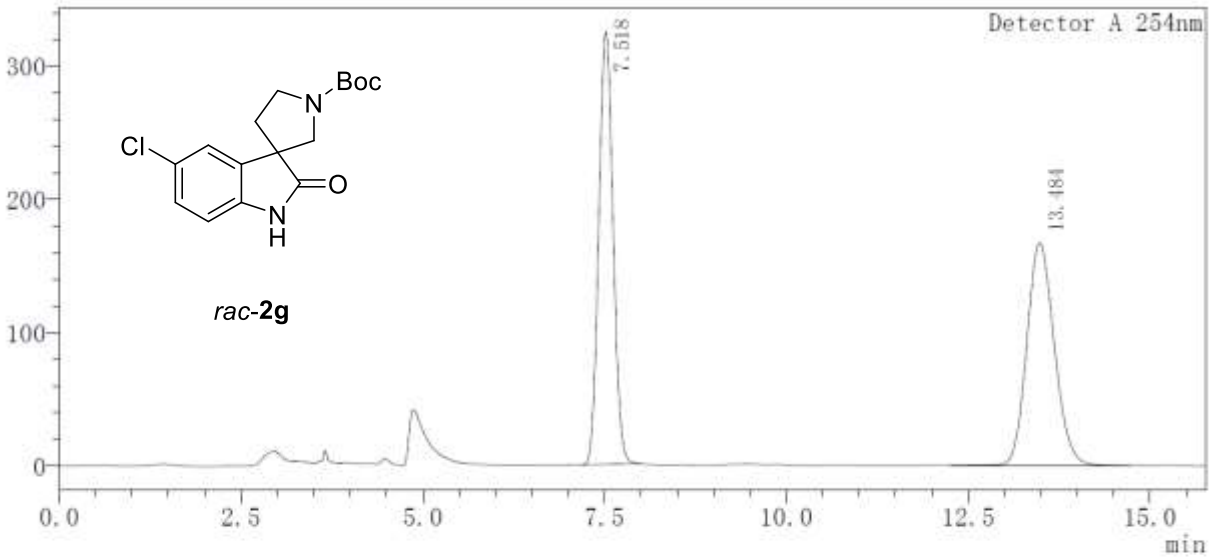


2f

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	19.134	3532845	40120	11.009			
2	27.324	28558464	148491	88.991			
Total		32091310	188611				

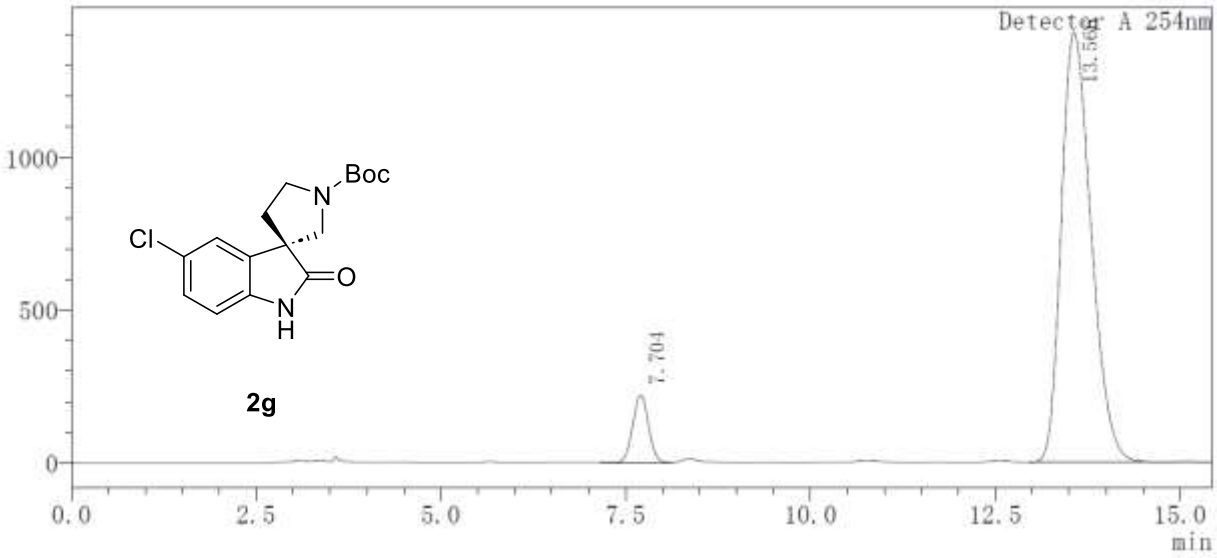


rac-**2g**

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	7.518	4431375	324567	50.024			
2	13.484	4427184	167394	49.976			
Total		8858558	491962				

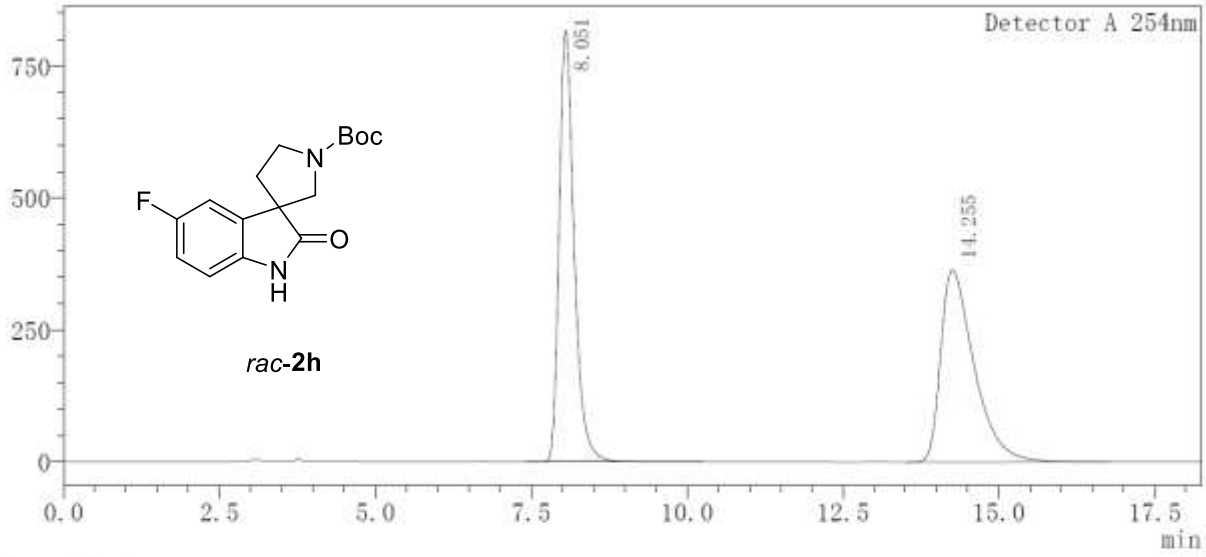


2g

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	7.704	3299672	219949	7.677			
2	13.566	39682509	1409888	92.323			
Total		42982182	1629837				

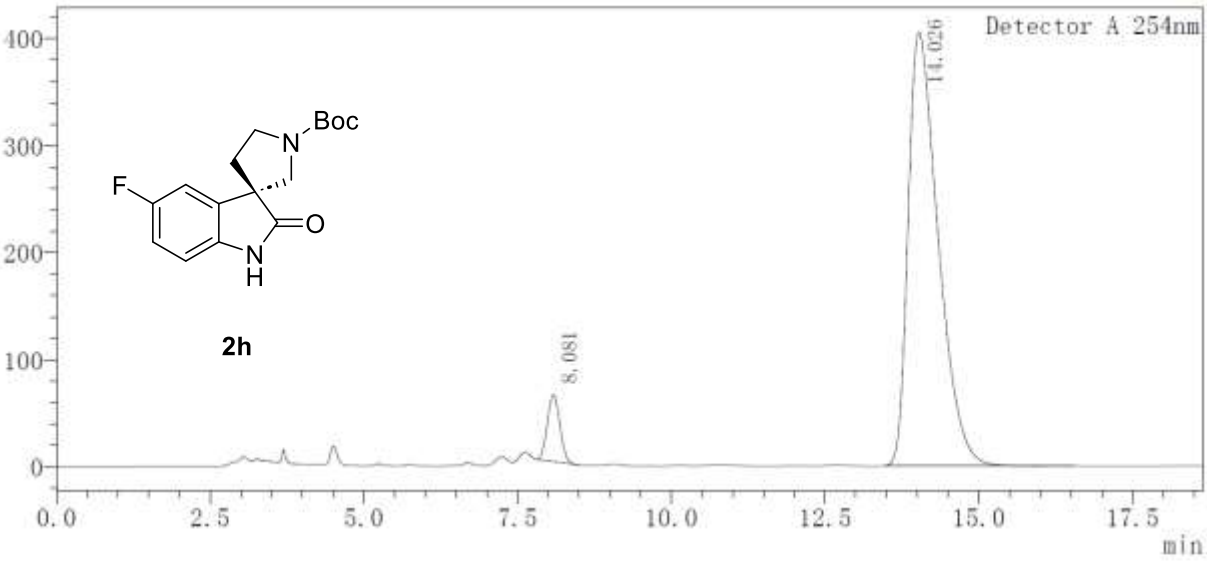


rac-**2h**

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	8.051	13703006	816734	50.260			
2	14.255	13561087	364282	49.740			
Total		27264093	1181016				

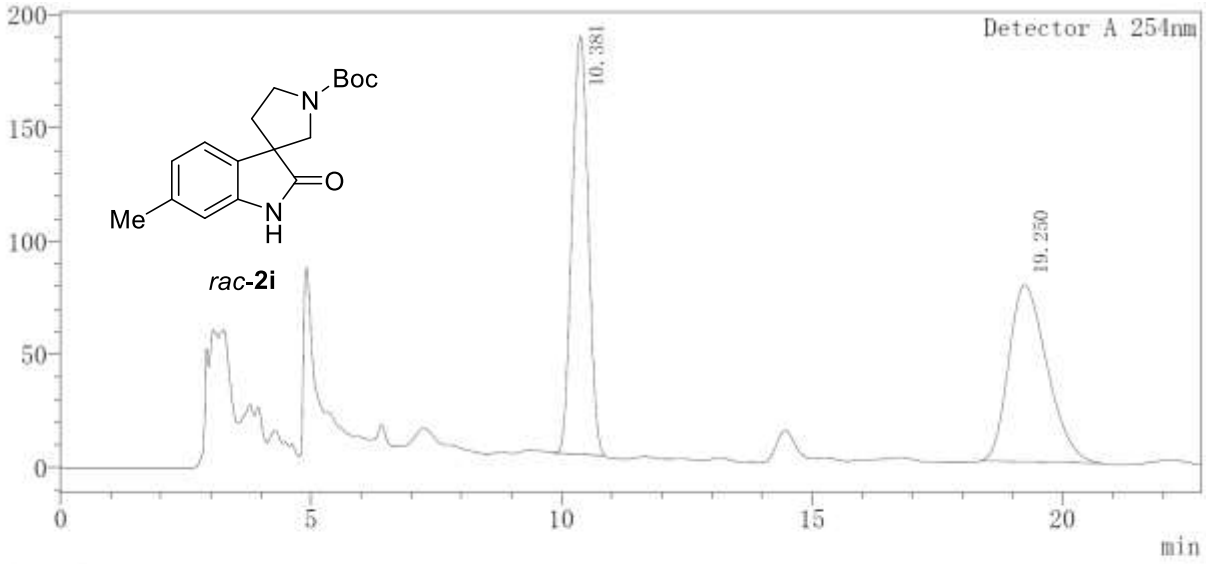


2h

〈Peak Table〉

Detector A 254nm

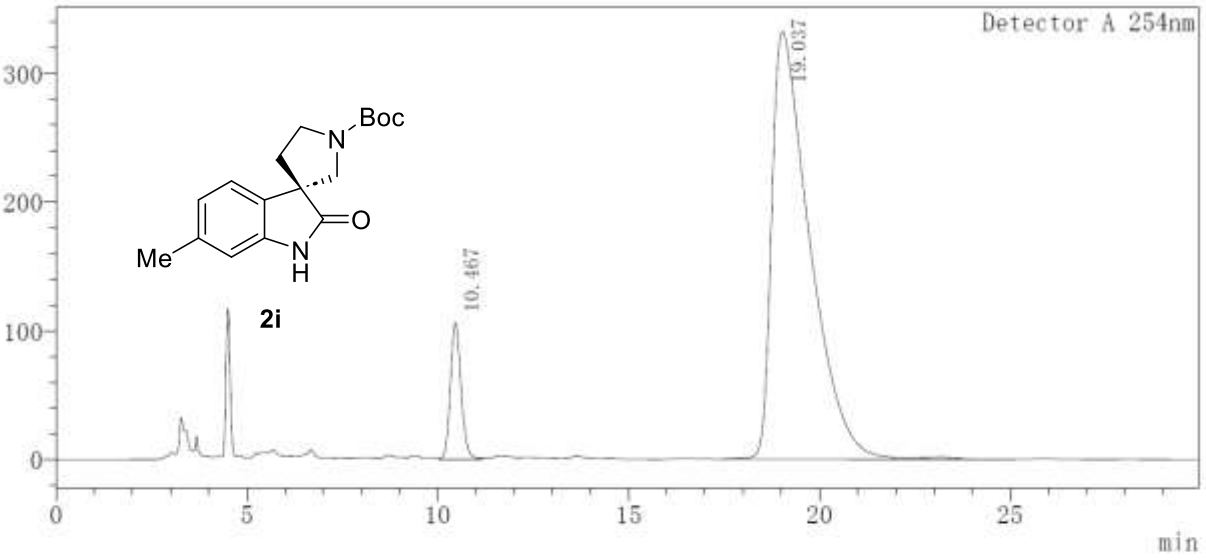
Peak	RetTime	Area	Height	Area%			
1	8.081	885917	62366	6.054			
2	14.026	13747623	405031	93.946			
Total		14633539	467397				



<Peak Table>

Detector A 254nm

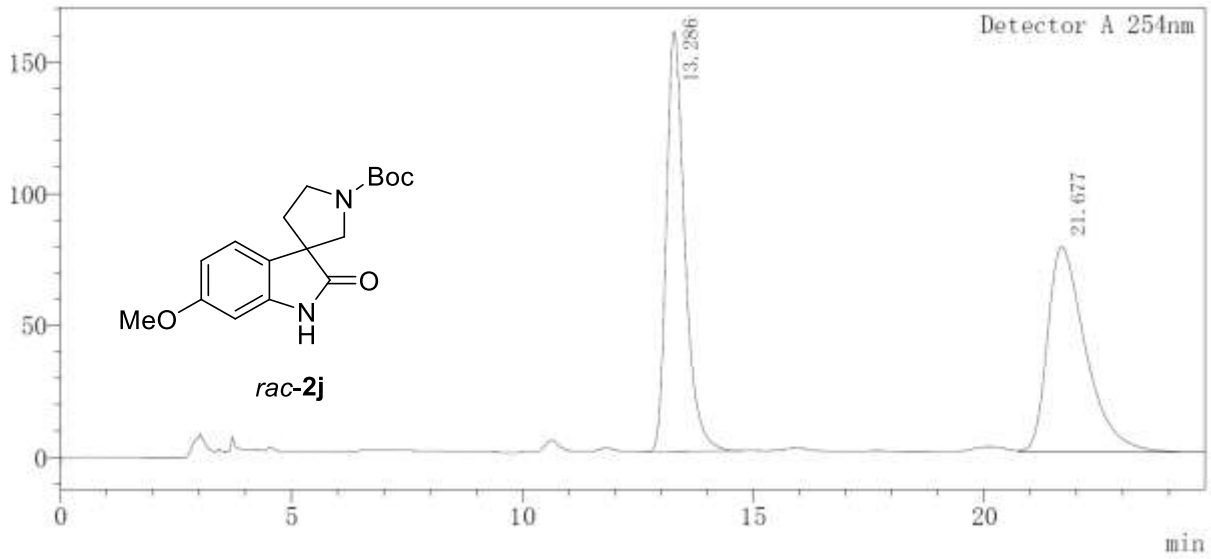
Peak	RetTime	Area	Height	Area%			
1	10.381	4015975	181874	49.092			
2	19.250	4164456	77831	50.908			
Total		8180431	259706				



<Peak Table>

Detector A 254nm

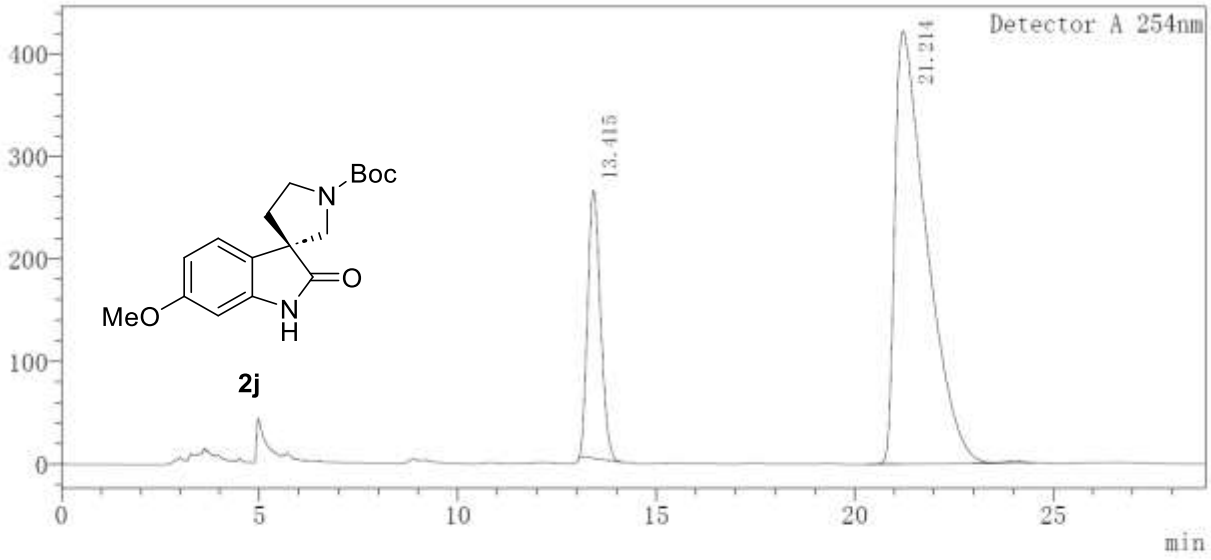
Peak	RetTime	Area	Height	Area%			
1	10.467	2053899	106244	8.209			
2	19.037	22966388	331992	91.791			
Total		25020287	438236				



<Peak Table>

Detector A 254nm

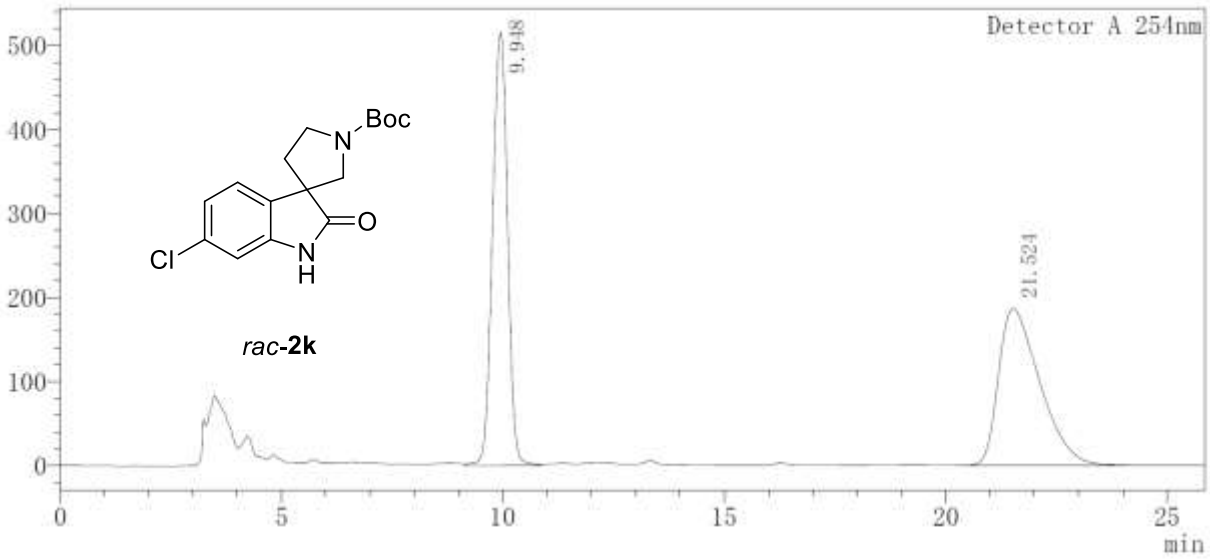
Peak	RetTime	Area	Height	Area%			
1	13.286	4427975	159413	49.594			
2	21.677	4500505	78029	50.406			
Total		8928480	237442				



<Peak Table>

Detector A 254nm

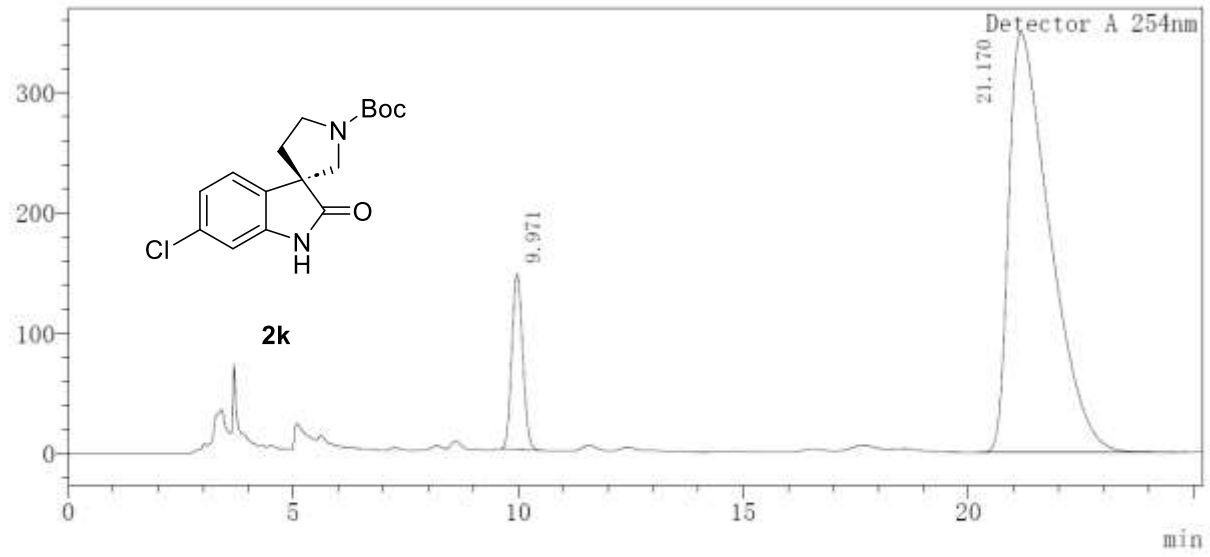
Peak	RetTime	Area	Height	Area%			
1	13.415	5875472	261088	19.985			
2	21.214	23524298	422048	80.015			
Total		29399770	683136				



<Peak Table>

Detector A 254nm

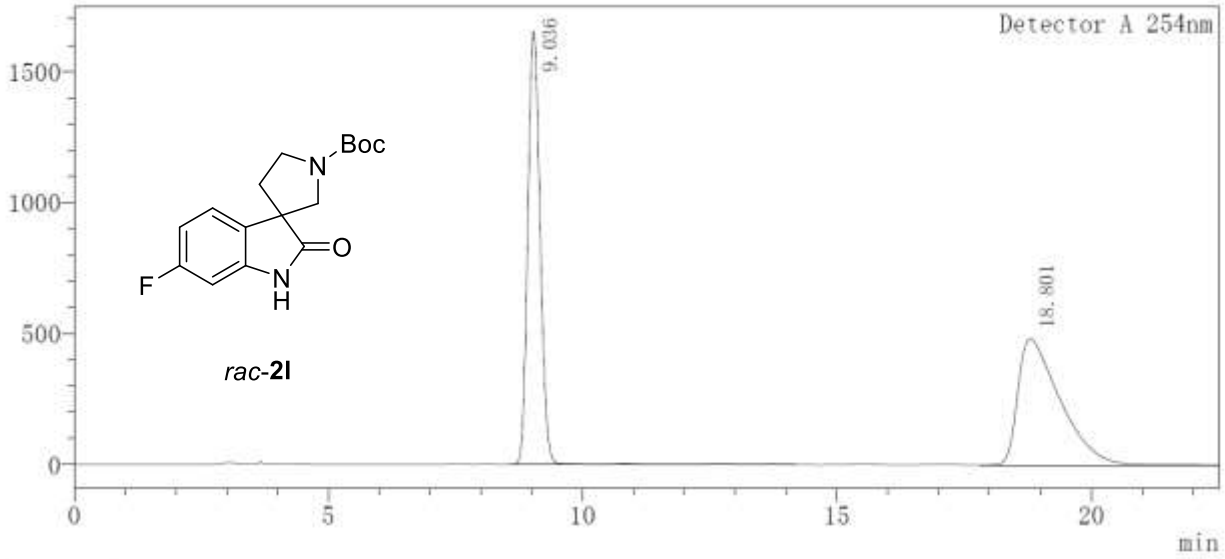
Peak	RetTime	Area	Height	Area%			
1	9.948	12209329	515595	50.167			
2	21.524	12127968	186824	49.833			
Total		24337297	702420				



<Peak Table>

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	9.971	2466042	145637	9.999			
2	21.170	22197522	349211	90.001			
Total		24663564	494847				

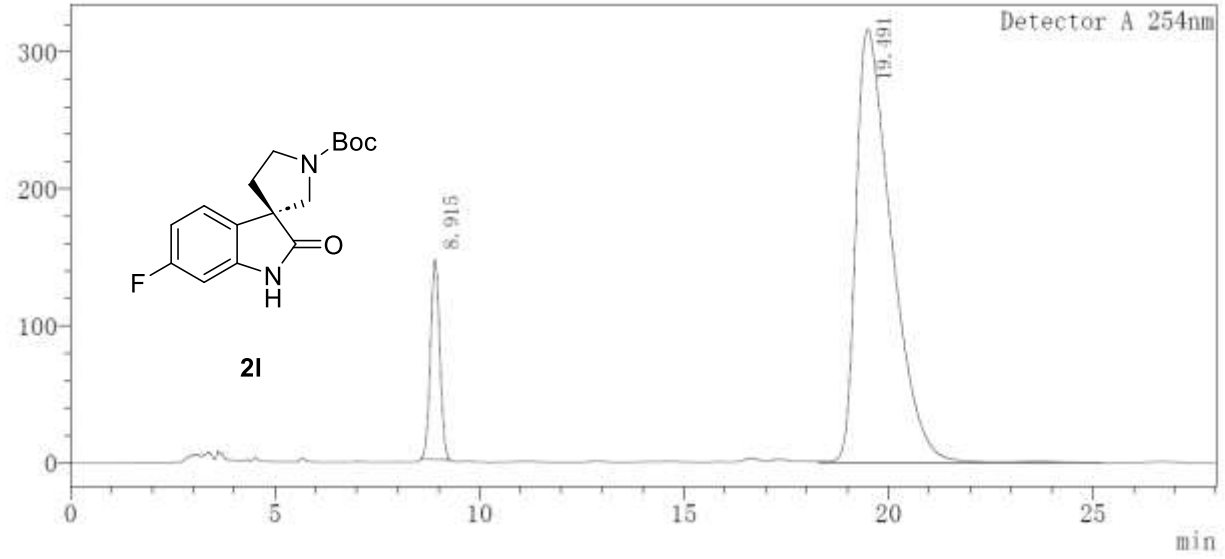


rac-**2l**

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	9.036	28086687	1654251	50.501			
2	18.801	27529883	479876	49.499			
Total		55616570	2134127				

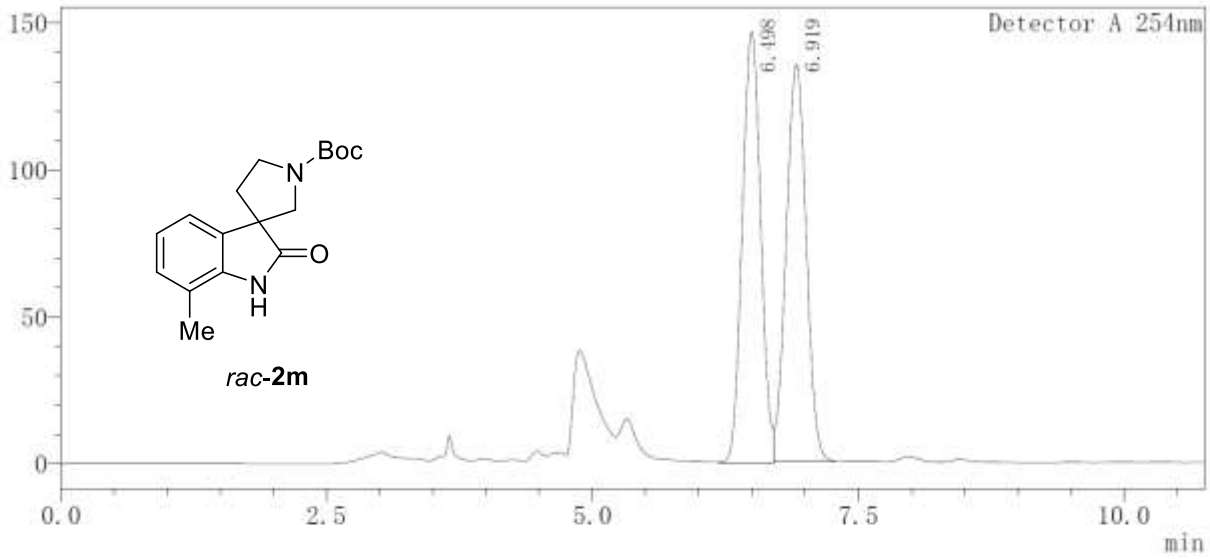


2l

〈Peak Table〉

Detector A 254nm

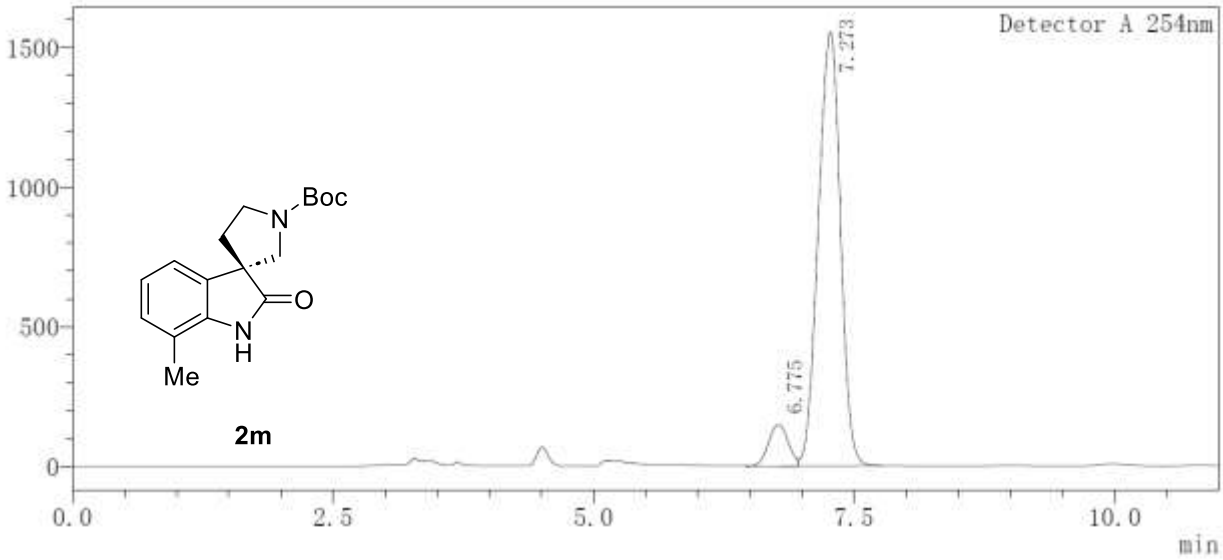
Peak	RetTime	Area	Height	Area%			
1	8.915	2316918	145684	10.791			
2	19.491	19154571	316667	89.209			
Total		21471489	462351				



<Peak Table>

Detector A 254nm

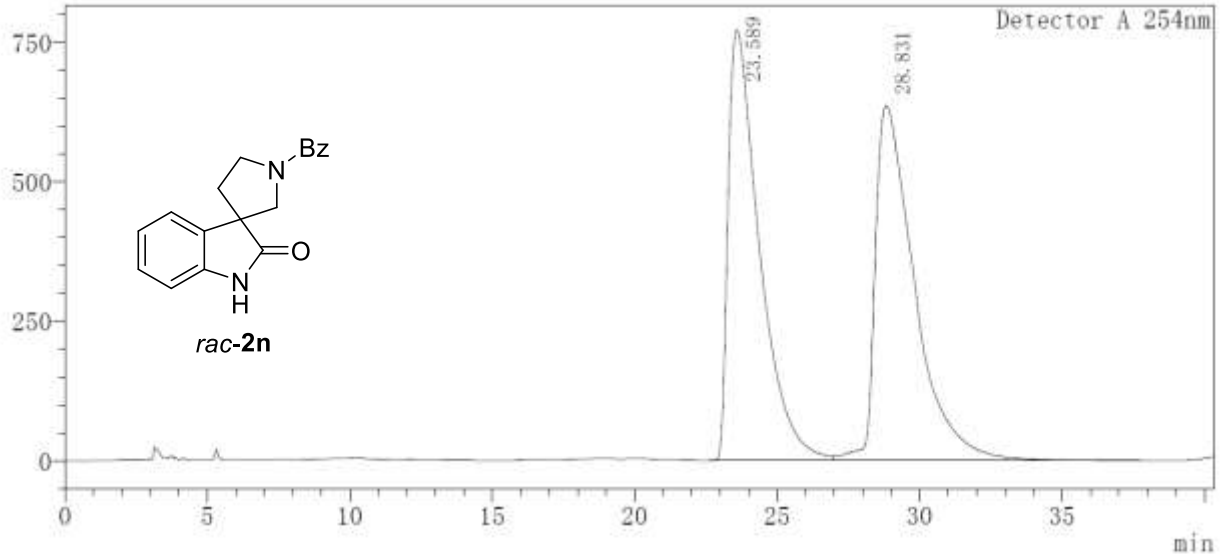
Peak	RetTime	Area	Height	Area%			
1	6.498	1769138	146932	49.950			
2	6.919	1772704	135082	50.050			
Total		3541842	282014				



<Peak Table>

Detector A 254nm

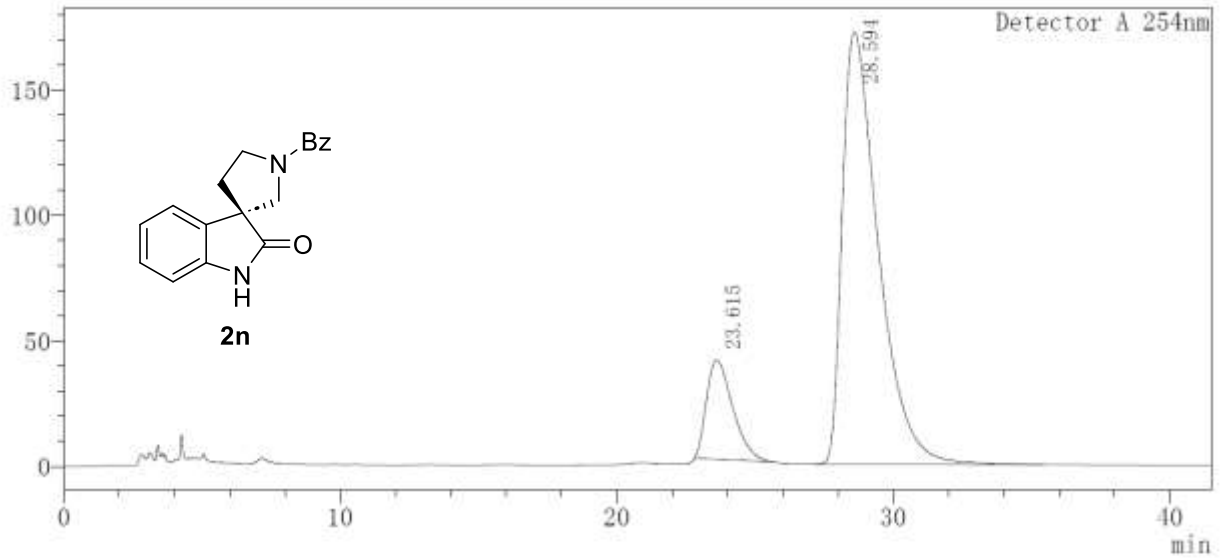
Peak	RetTime	Area	Height	Area%			
1	6.775	1981836	149620	7.946			
2	7.273	22959517	1553784	92.054			
Total		24941353	1703404				



<Peak Table>

Detector A 254nm

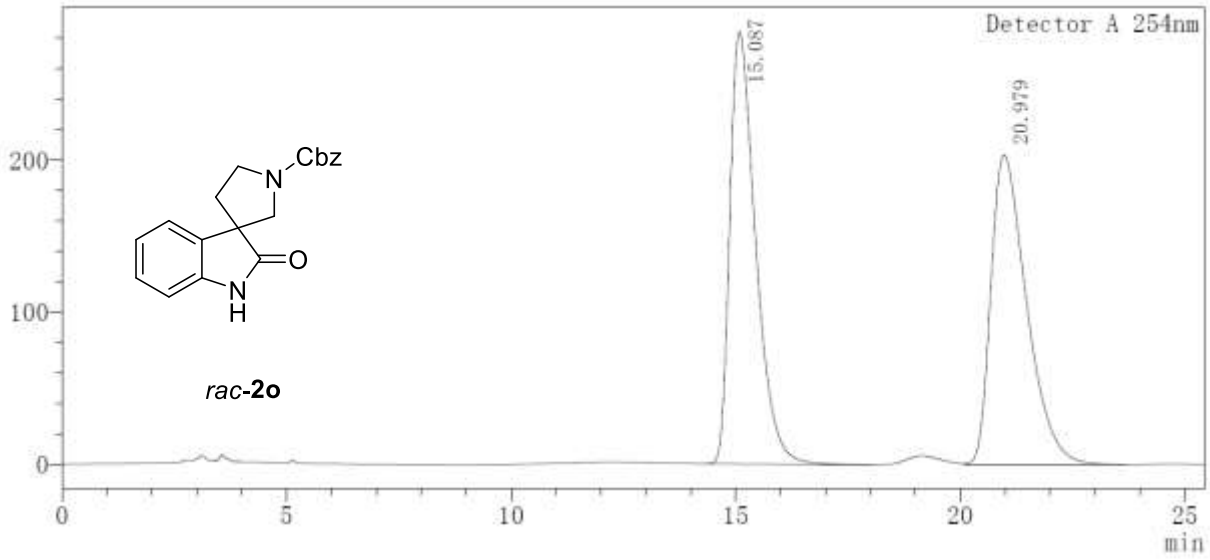
Peak	RetTime	Area	Height	Area%			
1	23.589	58921304	771817	49.042			
2	28.831	61222259	635952	50.958			
Total		120143563	1407769				



<Peak Table>

Detector A 254nm

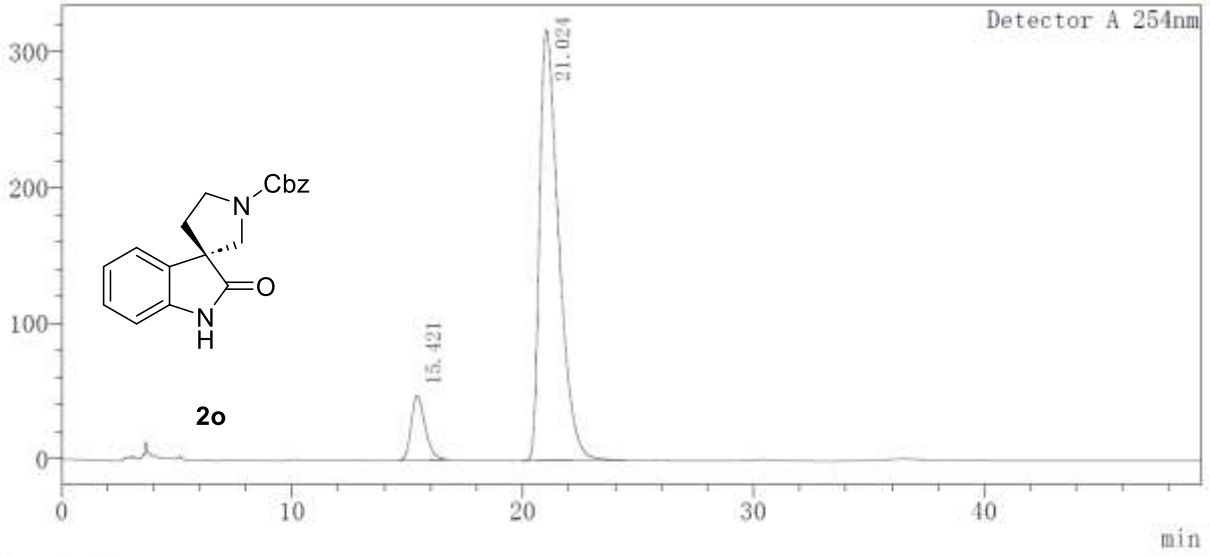
Peak	RetTime	Area	Height	Area%			
1	23.615	2611405	39473	14.296			
2	28.594	15655421	172184	85.704			
Total		18266826	211657				



〈Peak Table〉

Detector A 254nm

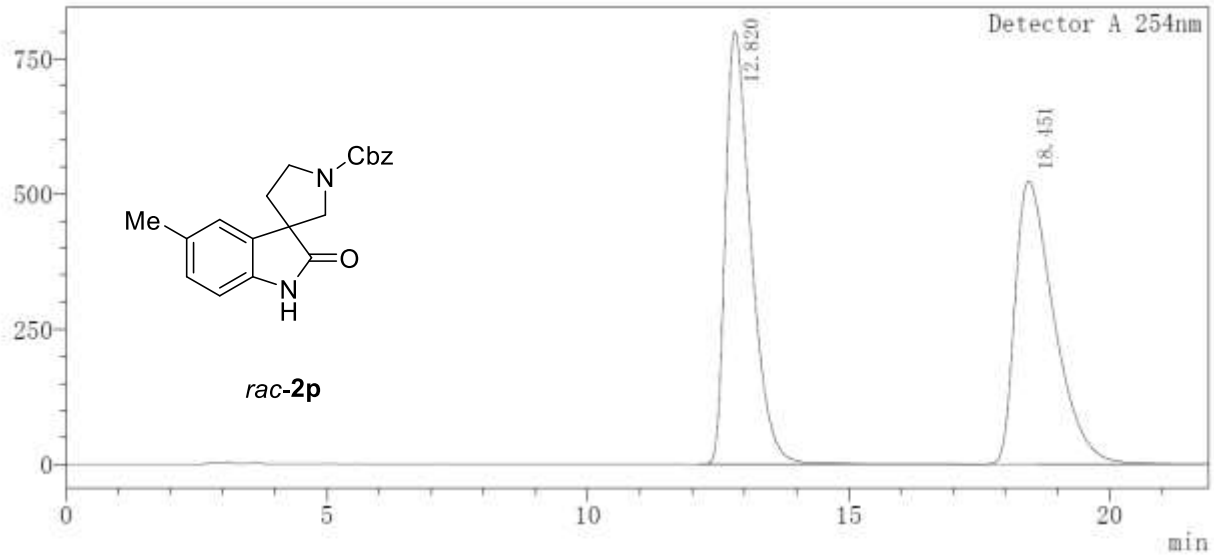
Peak	RetTime	Area	Height	Area%			
1	15.087	11349076	283672	50.179			
2	20.979	11268052	203272	49.821			
Total		22617128	486944				



〈Peak Table〉

Detector A 254nm

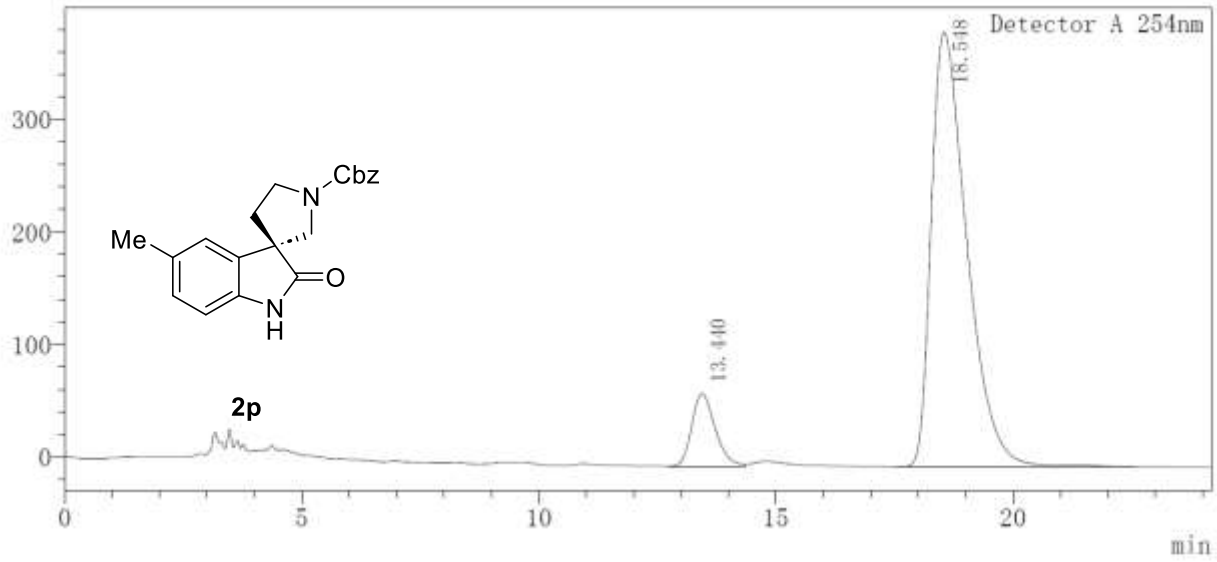
Peak	RetTime	Area	Height	Area%			
1	15.421	1964967	47483	9.686			
2	21.024	18321184	317359	90.314			
Total		20286151	364842				



<Peak Table>

Detector A 254nm

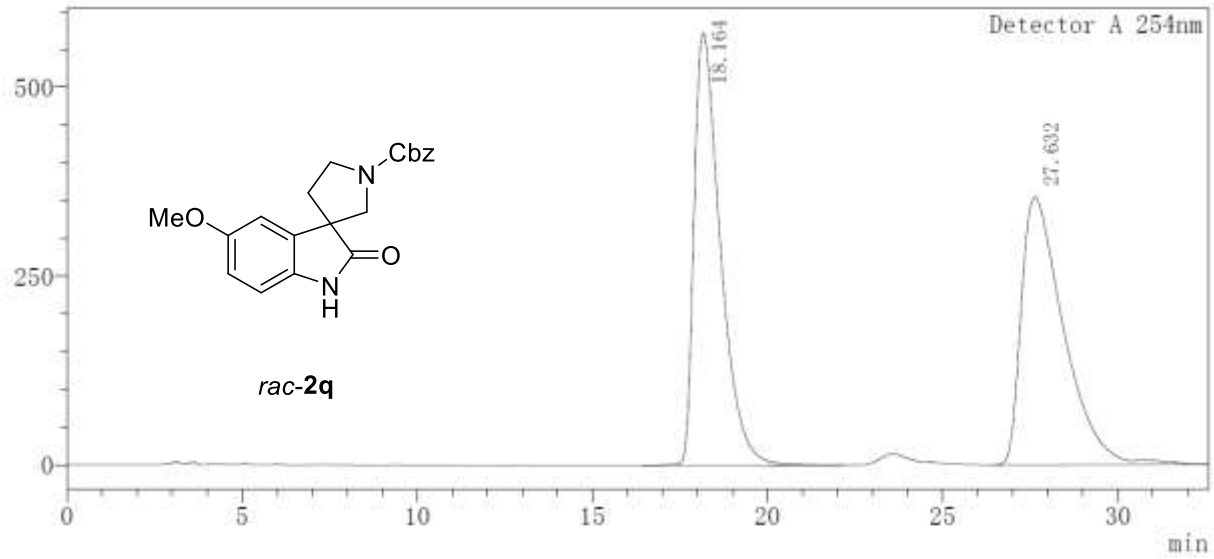
Peak	RetTime	Area	Height	Area%			
1	12.820	27445816	799769	50.264			
2	18.451	27158037	523334	49.736			
Total		54603853	1323103				



<Peak Table>

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	13.440	2210102	64604	9.853			
2	18.548	20220688	386387	90.147			
Total		22430790	450992				

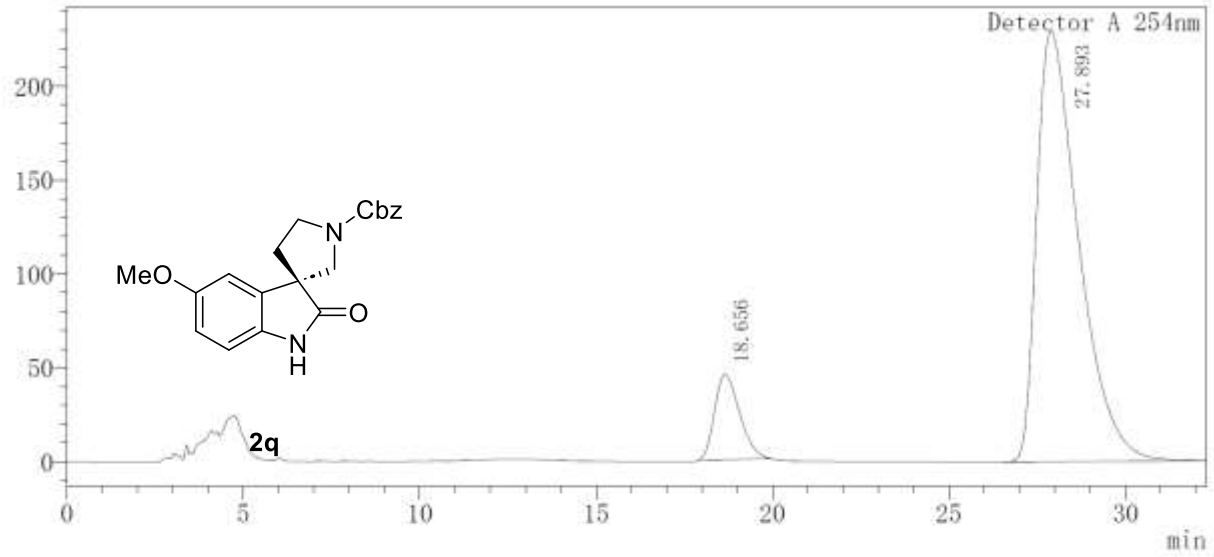


rac-**2q**

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	18.164	29966465	573000	50.060			
2	27.632	29894969	354577	49.940			
Total		59861434	927577				

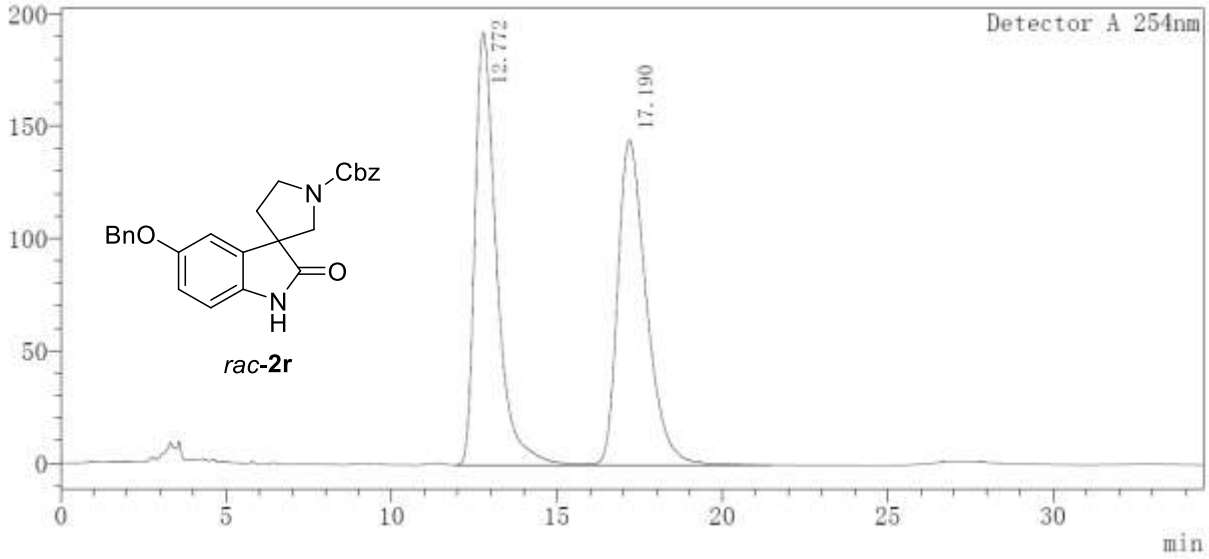


2q

〈Peak Table〉

Detector A 254nm

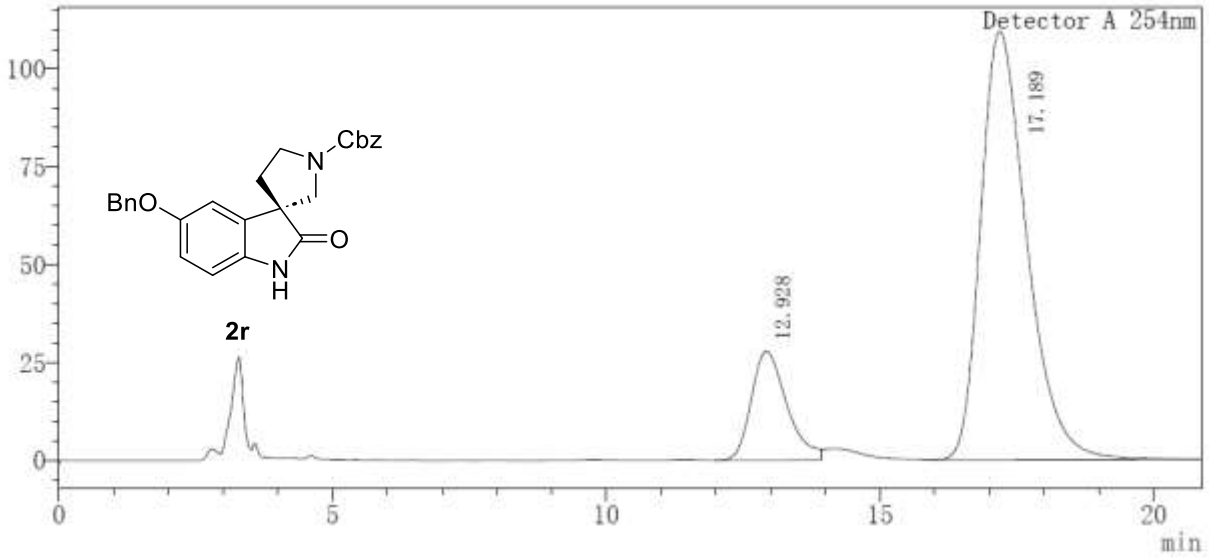
Peak	RetTime	Area	Height	Area%			
1	18.656	2235573	45268	10.554			
2	27.893	18947141	229351	89.446			
Total		21182714	274618				



〈Peak Table〉

Detector A 254nm

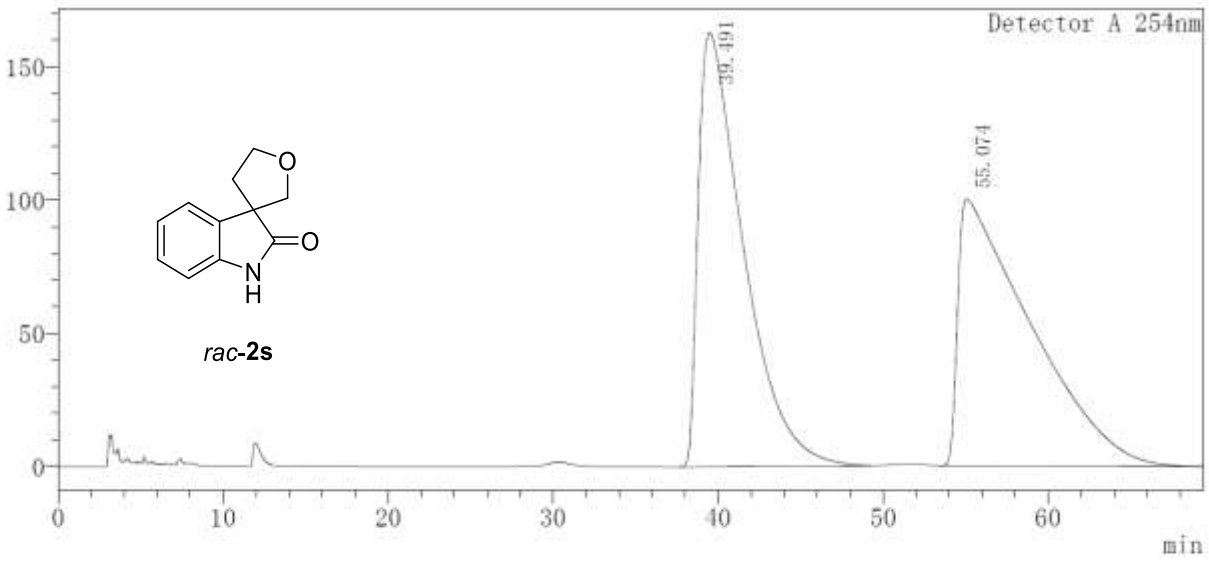
Peak	RetTime	Area	Height	Area%			
1	12.772	8748129	192375	50.157			
2	17.190	8693320	144616	49.843			
Total		17441449	336991				



〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	12.928	1257853	27862	16.377			
2	17.189	6422840	109475	83.623			
Total		7680693	137338				

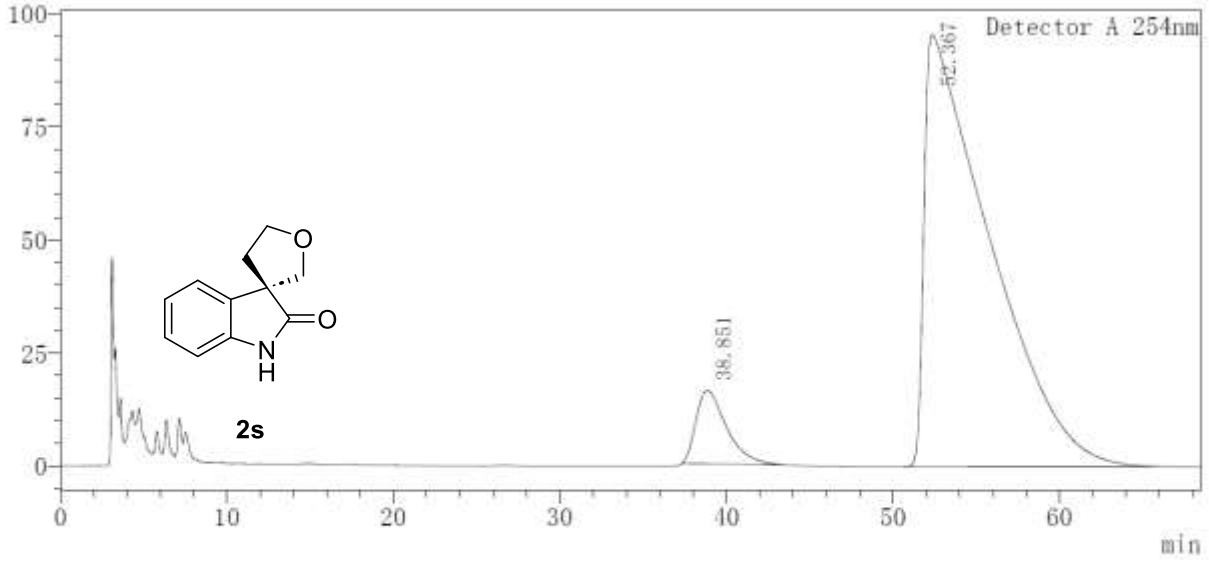


rac-**2s**

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	39.491	30885888	162602	50.114			
2	55.074	30744757	99868	49.886			
Total		61630645	262470				

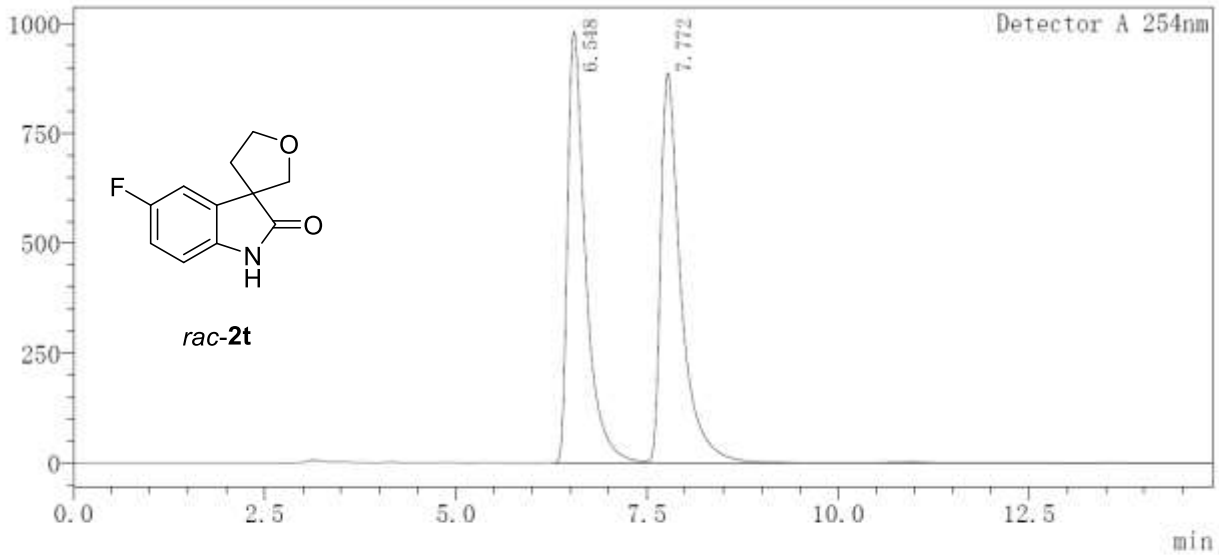


2s

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	38.851	2056003	16168	7.277			
2	52.367	26195654	95511	92.723			
Total		28251657	111679				

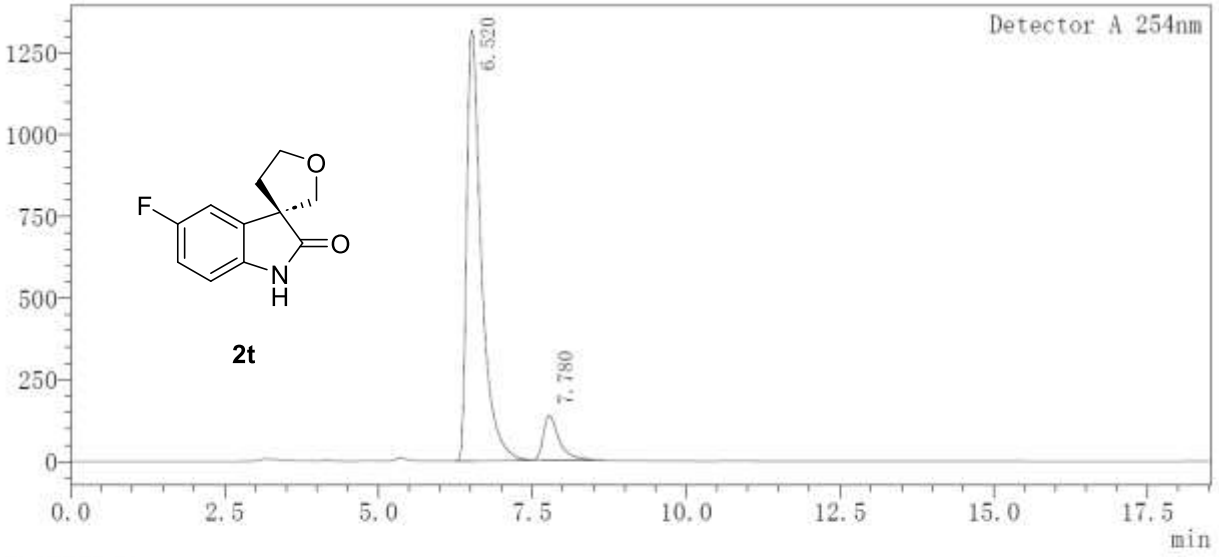


rac-**2t**

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	6.548	16034306	981155	49.342			
2	7.772	16462086	887183	50.658			
Total		32496392	1868338				

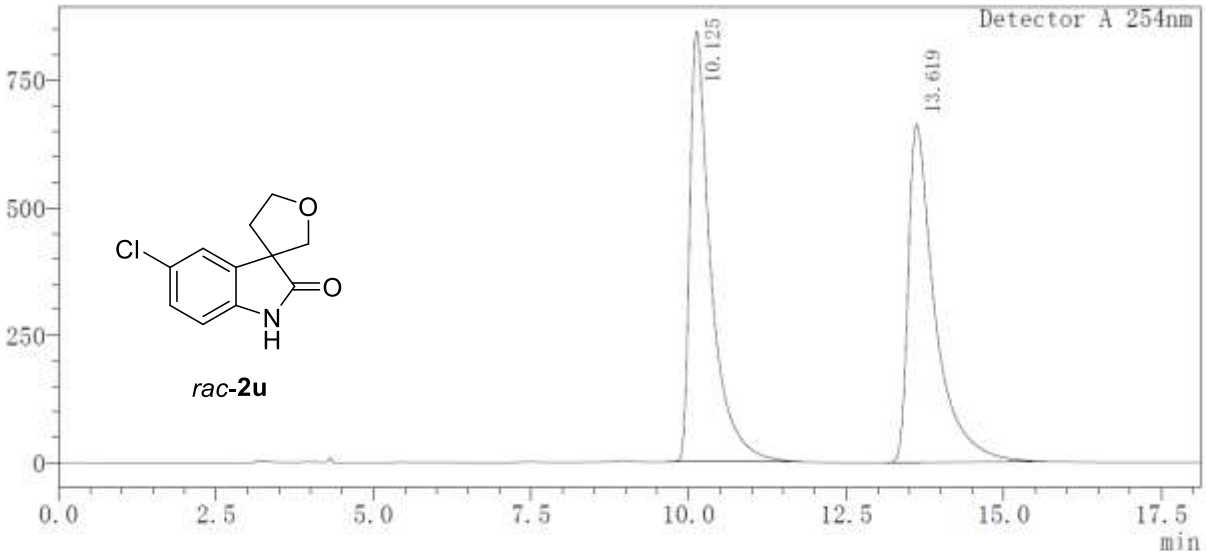


2t

〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	6.520	21867056	1319331	90.021			
2	7.780	2423877	136938	9.979			
Total		24290933	1456269				

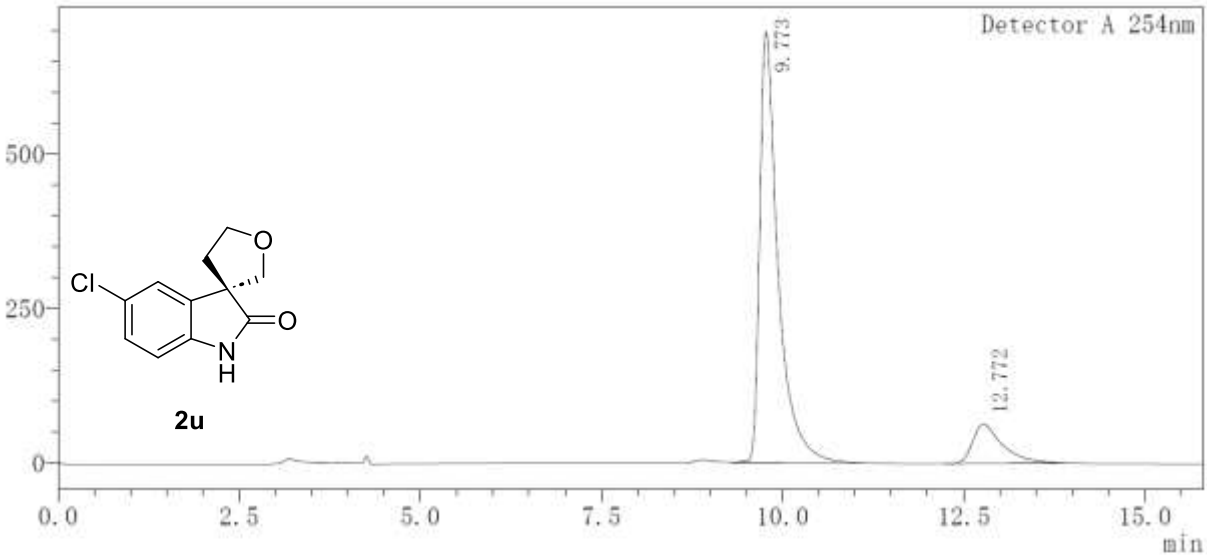


rac-**2u**

<Peak Table>

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	10.125	19642796	843182	50.149			
2	13.619	19526289	661816	49.851			
Total		39169086	1504998				

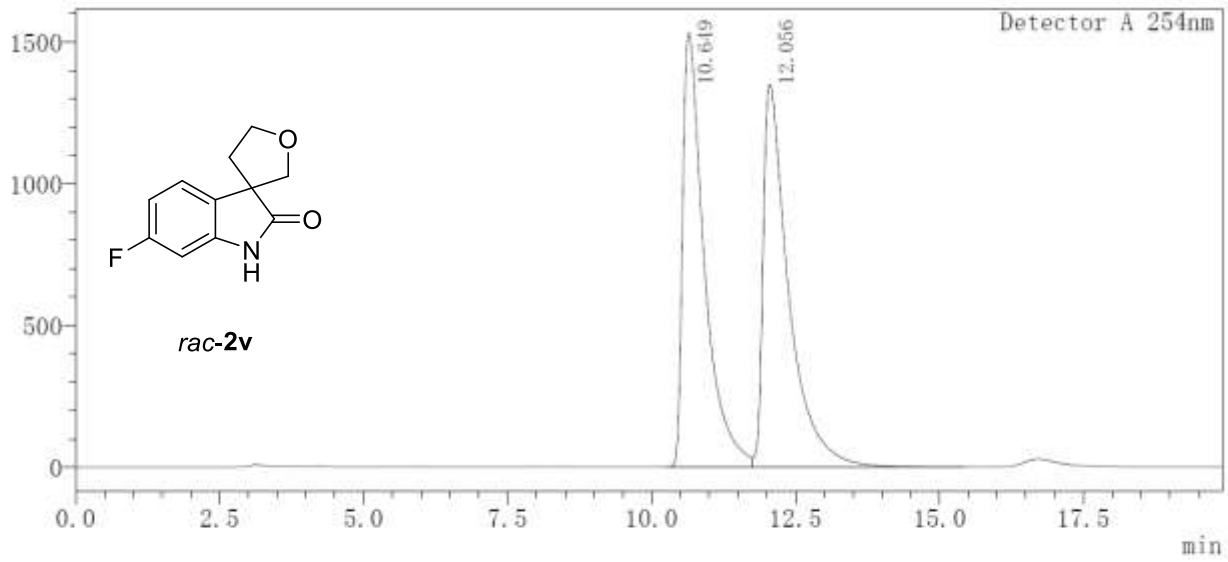


2u

<Peak Table>

Detector A 254nm

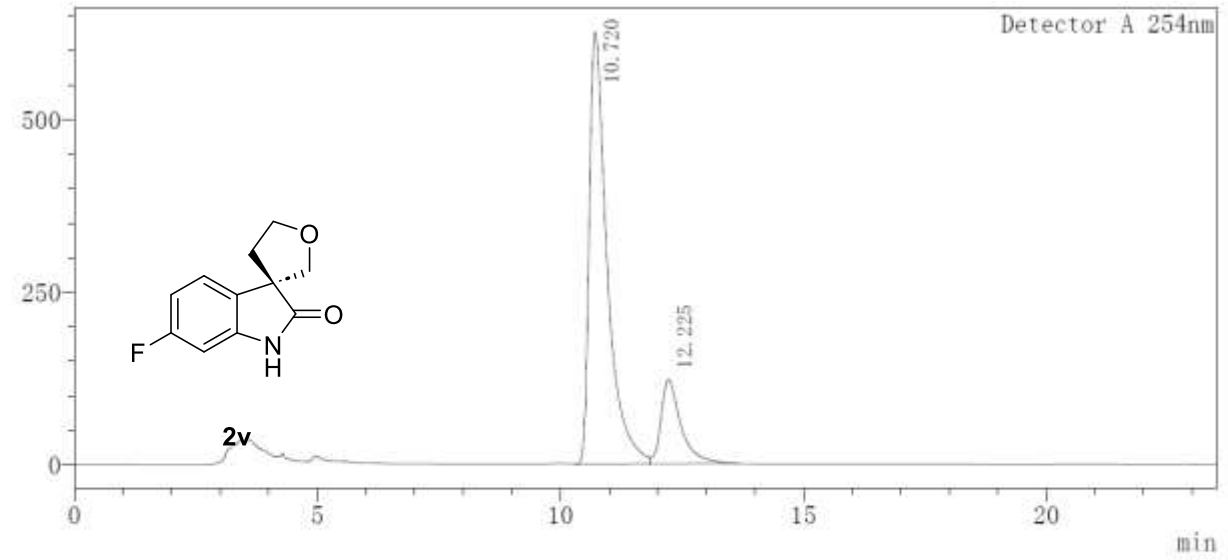
Peak	RetTime	Area	Height	Area%			
1	9.773	12371237	698285	87.091			
2	12.772	1833648	63610	12.909			
Total		14204885	761894				



〈Peak Table〉

Detector A 254nm

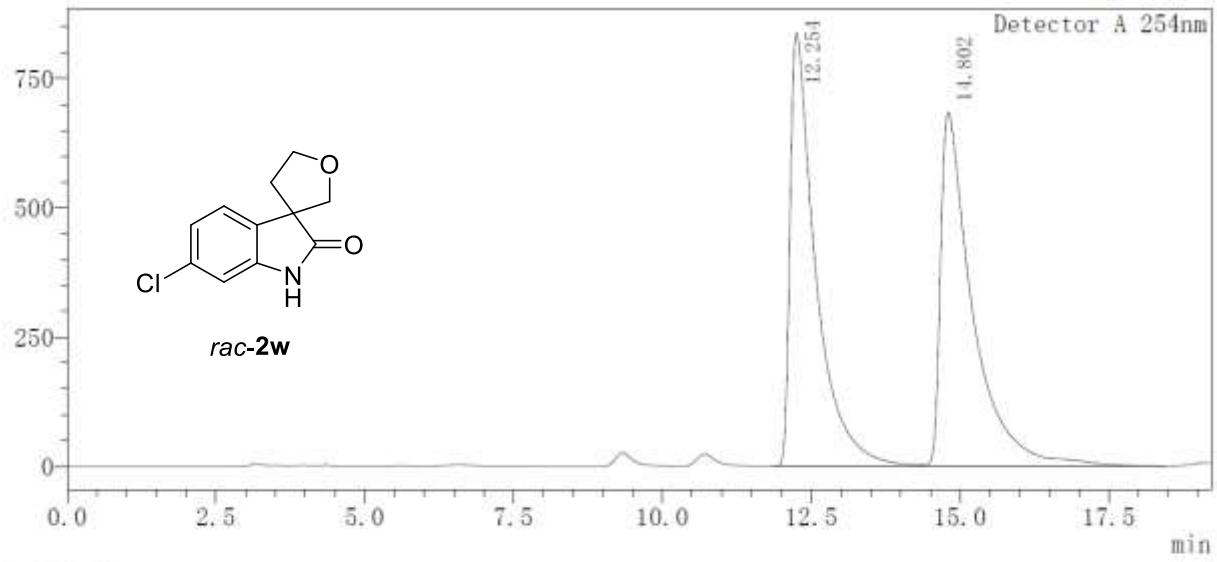
Peak	RetTime	Area	Height	Area%			
1	10.649	40085219	1531116	49.040			
2	12.056	41654035	1350983	50.960			
Total		81739254	2882099				



〈Peak Table〉

Detector A 254nm

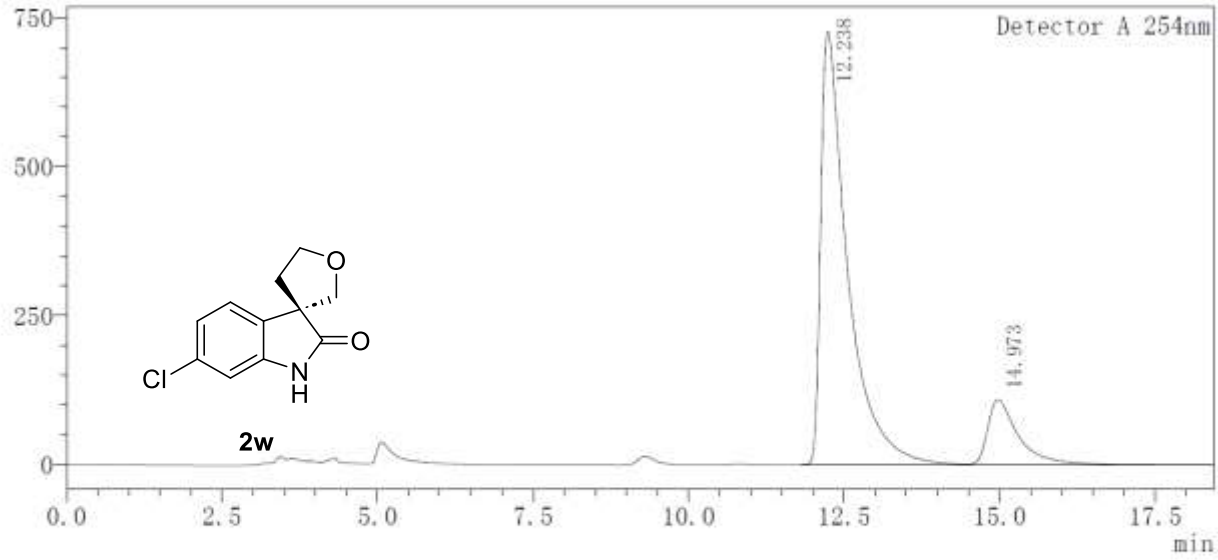
Peak	RetTime	Area	Height	Area%			
1	10.720	16014361	626116	82.017			
2	12.225	3511224	122174	17.983			
Total		19525585	748290				



〈Peak Table〉

Detector A 254nm

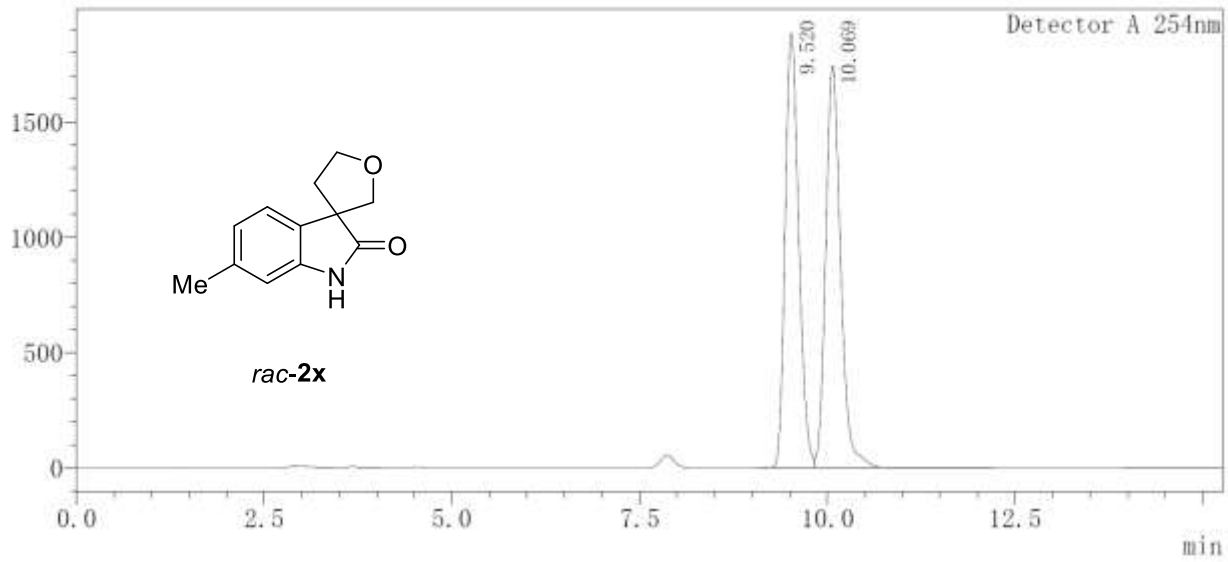
Peak	RetTime	Area	Height	Area%			
1	12.254	25102377	837638	49.448			
2	14.802	25663284	684648	50.552			
Total		50765661	1522287				



〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	12.238	21983496	727769	85.020			
2	14.973	3873479	109742	14.980			
Total		25856975	837511				

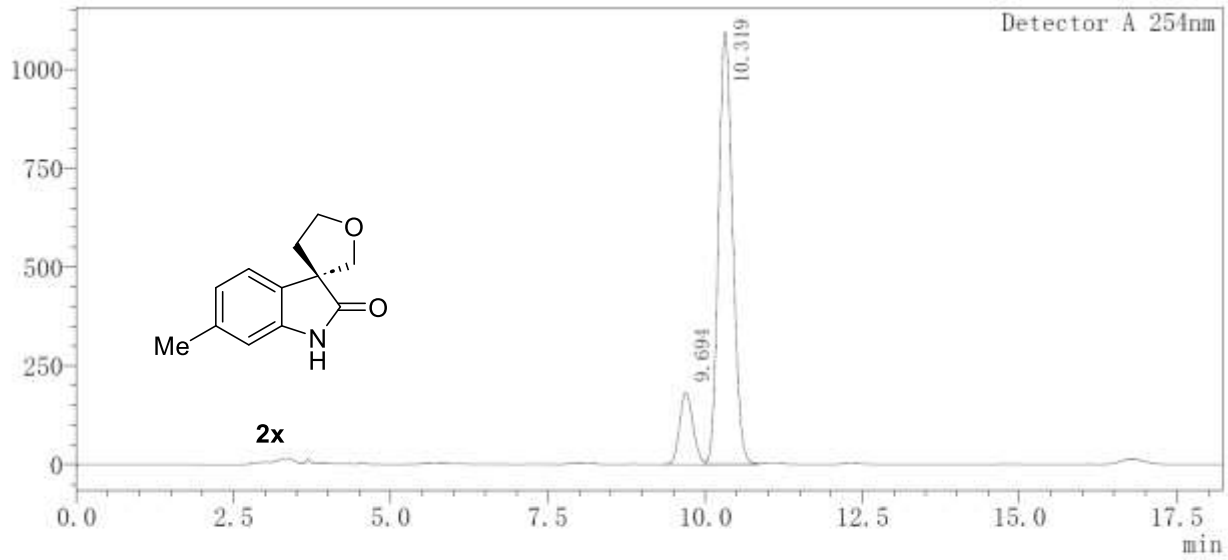


rac-**2x**

<Peak Table>

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	9.520	23740196	1884112	49.505			
2	10.069	24215246	1744193	50.495			
Total		47955442	3628306				

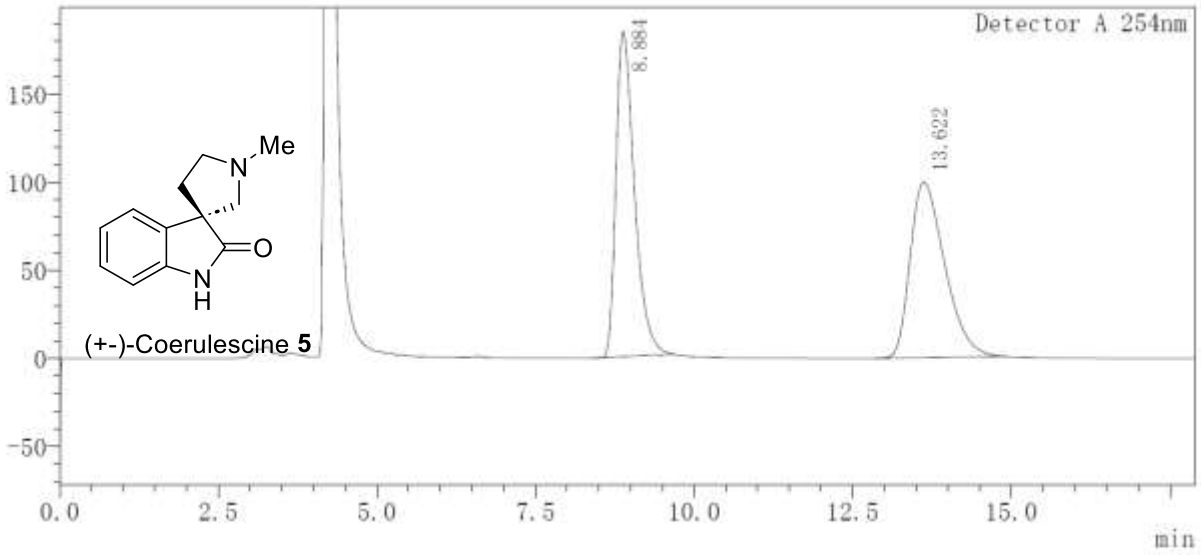


2x

<Peak Table>

Detector A 254nm

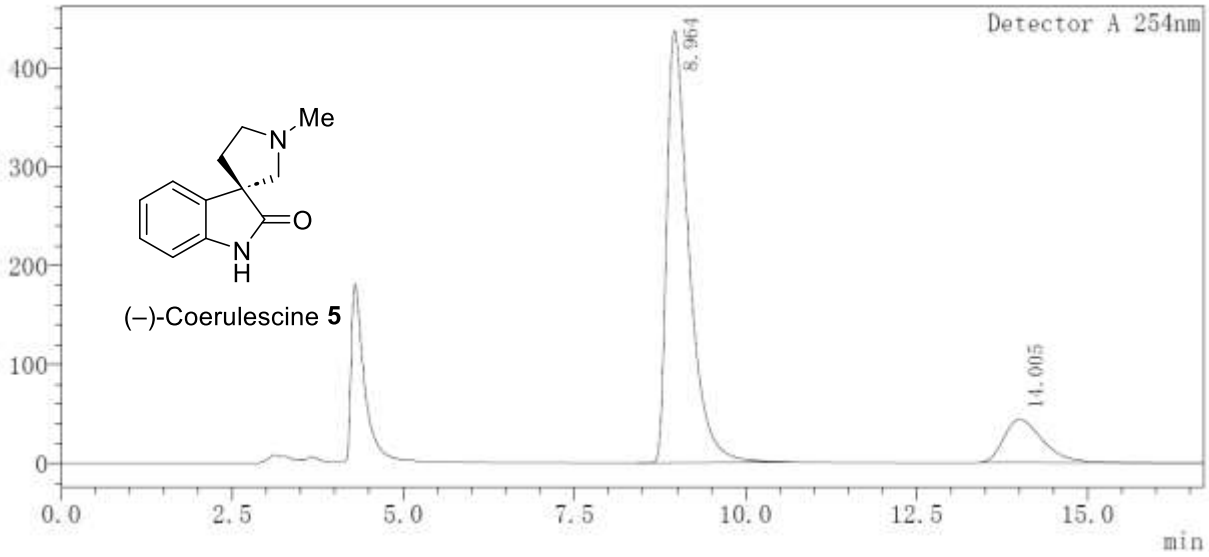
Peak	RetTime	Area	Height	Area%			
1	9.694	2708156	182664	13.660			
2	10.319	17118003	1095108	86.340			
Total		19826159	1277772				



〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	8.884	3743974	184690	49.791			
2	13.622	3775353	99574	50.209			
Total		7519327	284264				



〈Peak Table〉

Detector A 254nm

Peak	RetTime	Area	Height	Area%			
1	8.964	9854734	437217	85.085			
2	14.005	1727422	43586	14.915			
Total		11582156	480803				