Supporting Information

Iridium-Catalyzed Asymmetric Hydrogenation of Tetrahydro-*γ*-Carboline: A Versatile Approach to Chiral *cis*-Hexahydro-*γ*-Carboline Derivatives Compatible with C6-Substituted Carbolines

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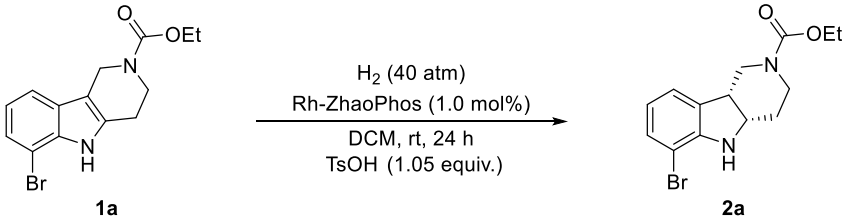
Table of Contents

I General Information

Unless extra indicated, the raw materials used in this article are commercially available. All reactions and manipulations involving air or humidity-sensitive compounds are carried out in the glove box. Unless otherwise specified, oil baths are used for heating in the reaction. Reactions were detected and analyzed by TLC, and fluorescence was observed with ultraviolet light (254 nm). In the NMR hydrogen spectroscopy, the chemical shift value of deuterated chloroform-*d* was used as a reference of 7.26 ppm to calibrate the chemical shift of the compounds. In the NMR carbon spectrum, the chemical shift of deuterated chloroform was used as a reference of 77.00 ppm or the chemical shift of deuterated DMSO-*d* of 39.50 ppm as a reference. The following letters indicate the splitting of multiple peaks: S-single peak, D-double peak, DD-double doublet, T-triplet peak, Q-quadruple peak, M-multiple peak.The determination of the enantiomer excess percentage of the compounds was performed using chiral HPLC analysis using Agilent. HPLC analysis of compounds was performed in OD-3, OD-H and AD-3 (polysaccharide derivative normal-phase coated chiral column) columns using hexane and isopropanol as eluents.

II Optimization of Reaction Conditions

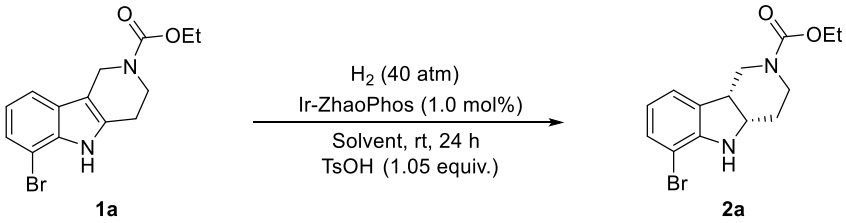
Table S1: The research of different [Rh]-salts [a]



Entry	[Rh]-salt	Yield (%) [b]	ee (%) [c]
1	$Rh(NBD)_2BF_4$	0	--
2	$[Rh(COD)Cl]_2$	0	--
3	$Rh(COD)_2BF_4$	0	--
4	$[RhOAc]_2$	0	--

[a] **1a** (0.1 mmol, 1.0 equiv.), TsOH (0.105 mmol, 1.05 equiv.), [Rh]-salt (1 mol%), ZhaoPhos(1.05 mol%),DCM (0.1 M), 25 °C, H_2 (40 atm),stir for 24 h; [b] **^{1}H NMR** yield, Trimethoxybenzene was used as the internal standard; [c] The ee (%) was determined by HPLC.

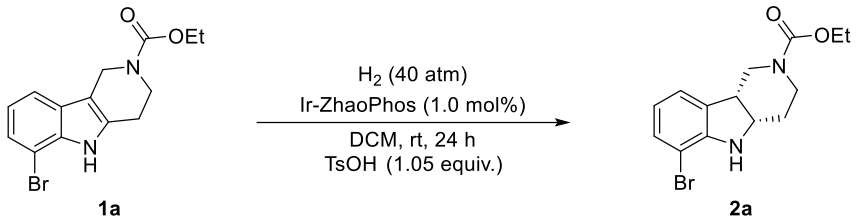
Table S2: The effect of different solvents [a]



Entry	Solvent	Yield (%) [b]	ee (%) [c]
1	DCM	70	69
2	DCE	72	67
3	EtOAc	51	40
4	EtOH	Trace	--
5	MeOH	Trace	--
6	HFIP	0	--
7	THF	Trace	--
8[d]	DCM	N.P.	--

[a] **1a** (0.1 mmol, 1.0 equiv.), TsOH (0.105 mmol, 1.05 equiv.), $[Ir(COD)Cl]_2$ (0.5 mol%), ZhaoPhos (1.05 mol%), Solvent (0.1 M), 25 °C, H_2 (40 atm), stir for 24 h; [b] **^{1}H NMR** yield, Trimethoxybenzene was used as the internal standard; [c] The ee (%) was determined by HPLC; [d] BINAP ligand was used instead of ZhaoPhos.

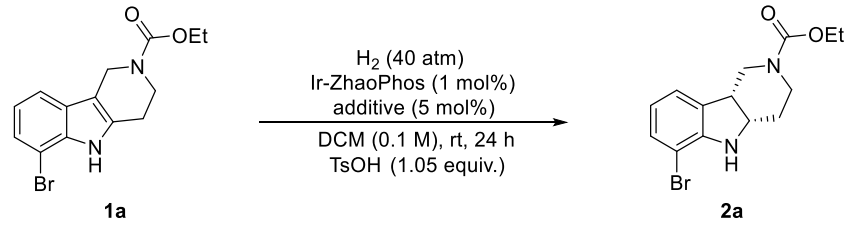
Table S3: The effect of different concentration [a]



Entry	Concentration	Yield (%) [b]	ee (%) [c]
1	DCM (0.1 M)	71	69
2	DCM (0.05 M)	57	69
3[d]	DCM (0.05 M)	83	49
4	DCM (0.2 M)	40	68

[a] **1a** (0.1 mmol,1.0 equiv.), TsOH (0.105 mmol,1.05 equiv.), $[Ir(COD)Cl]_2$ (0.5 mol%), ZhaoPhos (1.05 mol%), 25 °C, H_2 (40 atm),stir for 24 h; [b] **^{1}H NMR** yield, Trimethoxybenzene was used as the internal standard; [c] The ee (%) was determined by HPLC; [d] N-Me-ZhaoPhos ligand was used instead of ZhaoPhos.

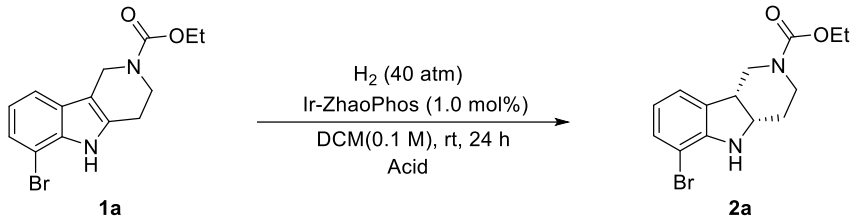
Table S4: The effect of salt additives [a]



Entry	Additive	Yield (%) [b]	ee (%) [c]
1	$Fe(OTf)_2$	28	69
2	$Sm(OTf)_3$	15	69
3	$AgNO_3$	0	--
4	$AgSbF_6$	0	--
5	AgOTf	0	--
6	$AgMeSO_3$	0	--

[a] **1a** (0.1 mmol,1.0 equiv.), TsOH (0.105 mmol,1.05 equiv.), $[Ir(COD)Cl]_2$ (0.5 mol%), ZhaoPhos (1.05 mol%), additive (5 mol%), DCM (0.1 M), 25 °C, H_2 (40 atm),stir for 24 h; [b] **^{1}H NMR** yield, Trimethoxybenzene was used as the internal standard; [c] The ee (%) was determined by HPLC.

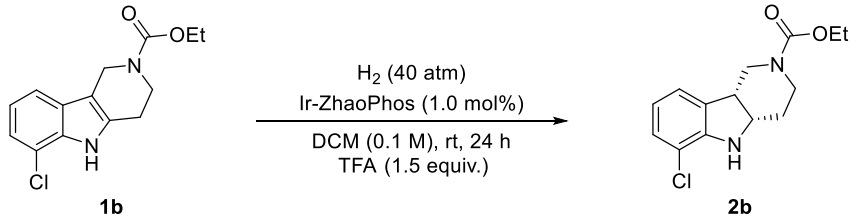
Table S5: The effect of acid additives [a]



Entry	Acid	Yield (%) [b]	ee (%) [c]
1	no TsOH	0	--
2	TsOH	84	65
3	TFA	27	72
4[d]	TFA	24	75
5	TfOH	trace	--
6	MsOH	47	57

[a] **1a** (0.1 mmol,1.0 equiv.), Acid (0.15 mmol,1.50 equiv.), $[Ir(COD)Cl]_2$ (0.5 mol%), ZhaoPhos (1.05 mol%), DCM (0.1 M), 25 °C, H_2 (40 atm), stir for 24 h; [b] **^{1}H NMR** yield, Trimethoxybenzene was used as the internal standard; [c] The ee (%) was determined by HPLC; [d] TFA (0.105 mmol,1.05 equiv.).

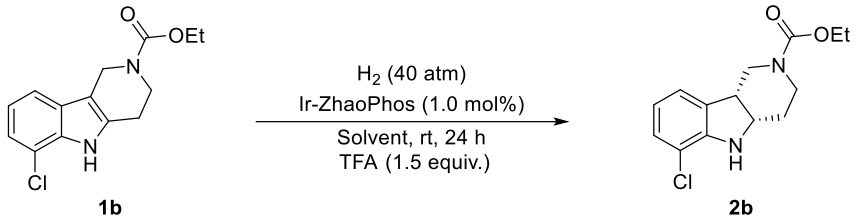
Table S6: Preliminary attempts at chlorinated substrates (**1b**) [a]



Entry	Deviation	Yield (%) [b]	ee (%) [c]
1	none	30	84
2	TsOH (1.5 equiv.)	91	65
3[d]	TsOH (1.5 equiv.)	96	52
4[e]	DCM (0.15 M)	33	80
5[f]	DCM (0.05 M)	17	78
6[g]	TFA and TsOH	28	77

[a] **1b** (0.1 mmol,1.0 equiv.), TFA (0.15 mmol,1.50 equiv.), $[Ir(COD)Cl]_2$ (0.5 mol%), ZhaoPhos (1.05 mol%), DCM (0.1 M), 25 °C, H_2 (40 atm), stir for 24 h; [b] **^{1}H NMR** yield, Trimethoxybenzene was used as the internal standard; [c] The ee (%) was determined by HPLC; [d] N-Me-ZhaoPhos ligand was used instead of ZhaoPhos; [e] DCM (0.15 M); [f] DCM (0.05 M); [g] TFA (0.15 mmol,1.5 equiv.) and TsOH (0.15 mmol,1.5 equiv.) were involved in reaction at the same time.

Table S7: Re-optimization of the reaction solvent [a]

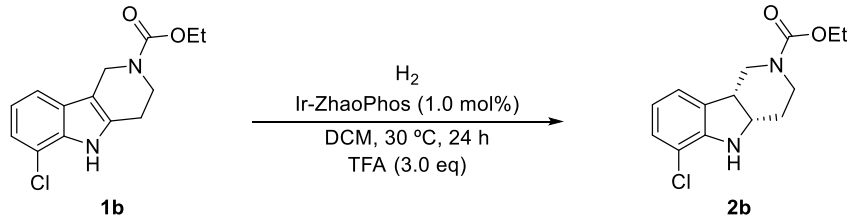


1b **2b**

Entry	Solvent	Yield (%) [b]	ee (%) [c]
1	DCE	17	85
2	THF	Trace	--
3	1,4-dioxane	Trace	--
4	EtOAc	Trace	--
5	MeCN	0	--

[a] **1b** (0.1 mmol,1.0 equiv.), TFA (0.15 mmol,1.50 equiv.), $[Ir(COD)Cl]_2$ (0.5 mol%), ZhaoPhos (1.05 mol%), Solvent (0.1 M), 25 °C, H_2 (40 atm), stir for 24 h; [b] **^{1}H NMR** yield, Trimethoxybenzene was used as the internal standard; [c] The ee (%) was determined by HPLC.

Table S8: The effect of temperature and pressure [a]

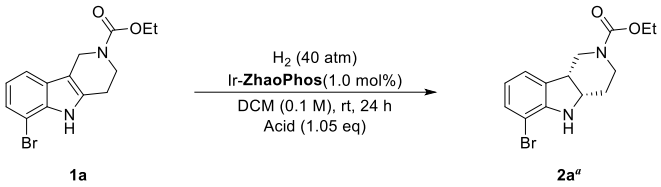


1b **2b**

Entry	Pressure	Yield (%) [b]	ee (%) [c]
1	H_2 (40 atm)	57	87
2	H_2 (65 atm)	57	85
3	H_2 (80 atm)	58	84
4[d]	H_2 (80 atm)	64	78

[a] **1b** (0.1 mmol,1.0 equiv.), TFA (0.30 mmol,3.0 equiv.), $[Ir(COD)Cl]_2$ (0.5 mol%), ZhaoPhos (1.05 mol%), DCM (0.1 M), 25 °C, stir for 24 h; [b] **^{1}H NMR** yield, Trimethoxybenzene was used as the internal standard; [c] The ee (%) was determined by HPLC; [d] The reaction temperature is 50 °C.

Table S9: Optimization of the Reaction Conditions of **1a**[a]

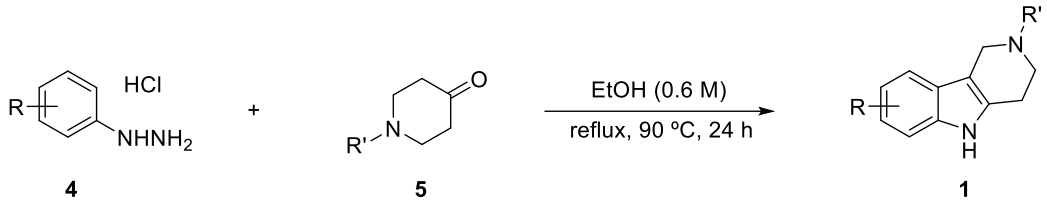


entry	acid	deviation	conv.[b] (%)	ee [c] (%)
1	TsOH	none	79	73
2	TsOH	$Rh(NBD)_2BF_4$	N.R.	/
3	TsOH	$[Rh(COD)Cl]_2$	N.R.	/
4	TsOH	DCE	72	67
5	TsOH	EtOAc	51	40
6	TsOH	THF	trace	/
7	TsOH	HFIP	N.R.	/
8	TsOH	$Fe(OTf)_2$	28	69
9	TsOH	$Sm(OTf)_3$	15	69
10	TsOH	AgOTf	trace	/
11	no TsOH	none	N.R.	/
12[d]	TsOH	none	84	65
13[d]	TFA	none	27	72
14[d]	TfOH	none	trace	/
15[d]	MsOH	none	47	57
16[e]	TFA	none	45	84

[a]Unless otherwise specified, the reactions were conducted using **1a** (0.1 mmol) in 1.0 mL of solvent, 100 μL Ir-ZhaoPhos solution (0.01 M, $[Ir(COD)Cl]_2$/(S,R)-ZhaoPhos = 1/2.1), Acid (1.05 eq). [b]The conversions were determined by ^1H NMR. [c]The ee was determined by performing chiral HPLC. [d]1.5 eq acid was used. [e]3.0 eq TFA was used.

III Experimental Section

1. General procedure for synthesis of tetrahydro-*γ*-carboline 1



4 **5** **1**

Phenylhydrazine substrate **4** and piperidone **5** used are commercially available raw materials. Phenyl hydrochloride **4** (20 mmol, 1.0 equiv.) was added to a 100 mL dry three-mouth flask filled with stirred magnets, followed by a reflux tube mounted on the three-mouth flask, the equipment was replaced three times in an argon atmosphere, then absolute ethanol (0.6 M) was added to the reaction flask through a syringe, piperidone **5** (20 mmol, 1.0 equiv.) was added to the vial through a syringe under stirring conditions, and the reaction tube was then transferred to 90 °C and maintained at this temperature for one day. Until the white solid turbidity appears in the reaction bottle, the reaction is cooled to room temperature and slowly quenched with water. After washing the white solids with n-hexane, the organic phase was concentrated under vacuum. The residue was purified by silica gel chromatography (EtOAc /petroleum ether) to afford the product **1**.

2. General procedure for hydrogenation of 1.

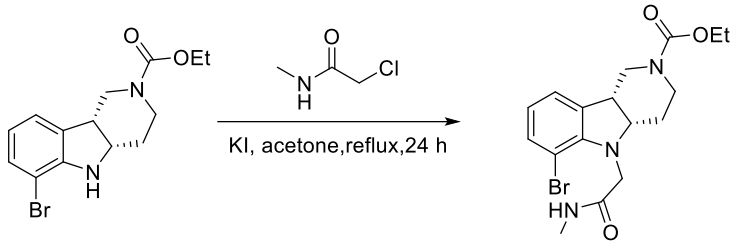
1.0 equivalent **1** was selected as the substrate, 0.5 mol% 1,5-cyclooctadiene iridium chloride dimer ($[Ir(COD)Cl]_2$) was used as the metal catalyst, 1.05 mol% 4-F-Ph-ZhaoPhos was used as the ligand, 3.0 equivalent trifluoroacetic acid (TFA) was used as the acid additive in the reaction system, and dichloromethane (DCM, 0.1 M) was selected as the reaction solvent. The reaction was carried out at room temperature for 24 hours in a hydrogen atmosphere at 40 atmospheres. After the reaction, slowly open the gas valve of the high-pressure reactor, carefully release the high-pressure hydrogen in the system, and after the pressure gauge pointer is zero, open the reactor and take out the ampoule containing the reactants. The reaction was quenched with a saturated sodium bicarbonate solution and extracted with ethyl acetate or methylene chloride, followed by drying with anhydrous sodium sulfate. The organic phase is concentrated by the rotary evaporator, and then the concentrated organic phase is added with dilute hydrochloric acid for pickling, the product is easy to become salt in the hydrochloric acid solution, the aqueous phase is transferred after pickling, and the pH of the system

is adjusted to alkaline by adding sodium hydroxide solution or saturated sodium bicarbonate solution, and the water is extracted with ethyl acetate or dichloromethane, and the product can be obtained after concentrating the organic phase. Due to the similarity and polarity of the raw material and product in the ethyl acetate/petroleum ether system, the product **2** can also be purified by silica gel chromatography separation (PE/EtOAc v/v = 2:1). The absolute configuration can be determined by comparing the optical rotation of compound **2j** with the value reported in the literature[1]. The configurations of the other chiral products were then assigned by analogy.

3. General procedure for synthesis of compound *rac*-2

1 (0.2 mmol, 1.0 equiv.) was added to a 25 mL dry Shrek reaction tube equipped with a stirred magnet, then the reaction tube was replaced three times under argon atmosphere, 1.0 mL of dichloromethane (DCM) was added to the reaction tube through a syringe, and then trifluoroacetic acid (2 mmol, 10.0 equiv.) was slowly added to the reaction tube through a syringe, stirred until the raw material was completely dissolved, and triethylsilane (0.6 mmol, 3.0 equiv.), place the reaction at room temperature for 12 h. After the reaction, trifluoroacetic acid was neutralized with saturated sodium bicarbonate aqueous solution, then organic phase was extracted by dichloromethane, the organic phase was dried with anhydrous sodium sulfate, and the residue was purified by silica gel chromatography (PE/EtOAc v/v = 5:1) to obtain racemic product ***rac*-2.** Some of the low-reactive substrates are hydrogenated using two equal amounts of enantiomer metal ligand complexes to obtain racemic products, so there may be several samples that are not completely racemic and two enantiomers are not equal (50/50).

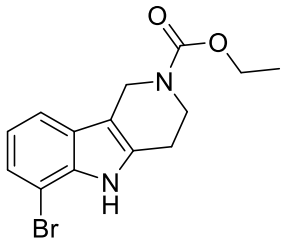
4. General procedure for synthesis of Compound 3a



2a **3a**

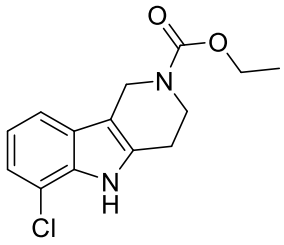
In argon atmosphere, to a solution of **2a** (790 mg, 2 mmol) in acetone (15 mL) were added 2-chloro-N-methylacetamide (258 mg, 2.4 mmol), KI (166 mg, 1 mmol), and K_2CO_3 (413 mg, 3 mmol). The reaction mixture was heated at 70 °C for 24 h, cooled to room temperature, and then the solid was removed by filtration through celite, and the filtrate was concentrated under vacuum. The residue was dissolved in CH_2Cl_2, washed by saturated NaCl, and then was dried over anhydrous Na2SO4, and the filtrate was concentrated under vacuum to give crude product **3a**. The residue was purified by silica gel flash column chromatography (EA) to give the compound **3a**. $[\alpha]_D^{25}$ + 21.3 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 6.4 Hz, 1H), 6.73 (t, *J* = 7.6 Hz, 1H), 4.39 (d, *J* = 17.9 Hz, 1H), 4.09 (s, 2H), 3.99 – 3.14 (m, 8H), 2.91 (d, *J* = 4.9 Hz, 3H), 2.02 – 1.90 (m, 1H), 1.89 – 1.77 (m, 1H), 1.23 (s, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.5, 155.7, 134.3, 133.6, 123.4, 122.5, 104.9, 65.6, 61.5, 55.3, 43.5, 40.9, 39.9, 26.1, 14.6 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AD-3 column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 7.941 min (*S*, *R*) (major), 11.994 min (*R*, *S*) (minor). HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{17}H_{22}BrN_3O_3^+$: 396.0917, found: 396.0918.

5. Characterization date of 1, 2 and 3a



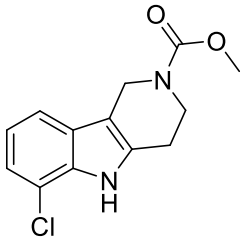
1a

Ethyl 6-bromo-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1a): The procedure was followed using 2-bromobenzazine hydrochloride (**4a**, 4.44 g, 20 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 3.0 mL, 20 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1a** as a white solid (5.41 g, 84% yield). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.15 (s, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 4.67 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 2H), 2.88 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 156.1, 134.5, 132.8, 126.7, 123.9, 120.8, 116.7, 108.5, 104.3, 61.6, 41.1, 23.3, 14.7 ppm. HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{17}BrN_2O_2^+$: 323.0390, found: 323.0388.



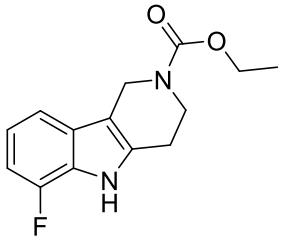
1b

Ethyl 6-chloro-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1b): The procedure was followed using 2-chlorobenzazine hydrochloride (**4b**, 3.56 g, 20 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 3.0 mL, 20 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1b** as a white solid (4.50 g, 81% yield). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.19 (s, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.8 Hz, 1H), 4.68 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 2H), 2.88 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 156.1, 133.1, 127.0, 121.0, 120.4, 116.2, 108.4, 61.6, 41.1, 23.4, 14.7 ppm. HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{15}ClN_2O_2^+$: 279.0895, found: 279.0892.



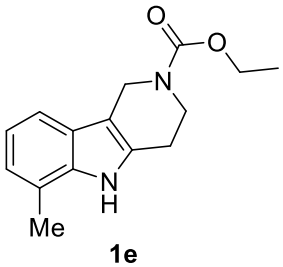
1c

Methyl 6-chloro-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1c): The procedure was followed using 2-chlorobenzazine hydrochloride (**4c**, 3.56 g, 20 mmol, 1.0 equiv.) and N-methoxycarbonyl-4-piperidone (**5c**, 3.14 g, 20 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1c** as a white solid (3.60 g, 70% yield). **^{1}H NMR** (600 MHz, Chloroform-d) δ 8.13 (s, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.15 (d, J = 7.6 Hz, 1H), 7.04 (t, J = 7.8 Hz, 1H), 4.67 (s, 2H), 3.89 (s, 2H), 3.77 (s, 3H), 2.88 (s, 2H) ppm. **^{13}C NMR** (151 MHz, Chloroform-d) δ 156.5, 133.1, 126.9, 121.1, 120.5, 116.1, 52.8, 41.2, 23.3 ppm. HRMS (ESI/ion trap) m/z: [M + H]+ calcd for C13H13ClN2O2^{+} : 265.0738, found: 265.0736.



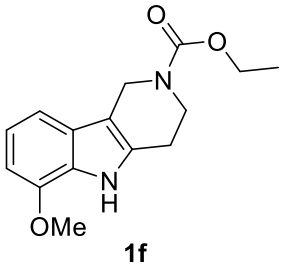
1d

Ethyl 6-fluoro-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1d): The procedure was followed using 2-fluorobenzazine hydrochloride (**4d**, 3.24 g, 20 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 3.0 mL, 20 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1d** as a white solid (2.83 g, 54% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.16 (s, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.01 (td, *J* = 7.9, 4.8 Hz, 1H), 6.87 (dd, *J* = 11.2, 7.9 Hz, 1H), 4.68 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 2H), 2.87 (t, *J* = 5.8 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6) δ 155.1, 150.1, 147.7, 134.0, 129.0, 123.3 (d, *J* = 13.1 Hz), 119.0 (d, *J* = 6.3 Hz), 113.5 (d, *J* = 2.2 Hz), 106.7, 105.7 (d, *J* = 16.3 Hz), 60.9, 40.9, 23.2, 14.6 ppm. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -135.12 ppm.



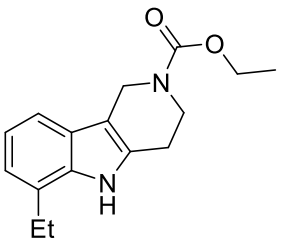
1e

Ethyl 6-methyl-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1e): The procedure was followed using *o*-tolylhydrazine hydrochloride (**4e**, 3.16 g, 20 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 3.0 mL, 20 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1e** as a white solid (4.79 g, 93% yield). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.11 (s, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.1 Hz, 1H), 4.72 (d, *J* = 8.3 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.89 (q, *J* = 10.9, 8.7 Hz, 2H), 2.87 (t, *J* = 5.6 Hz, 2H), 2.49 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 156.2, 135.3, 131.7, 124.9, 122.2, 119.7, 115.1, 107.5, 61.5, 41.3, 23.3, 16.6, 14.7 ppm. HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{18}N_2O_2^+$: 259.1441, found: 259.1439.



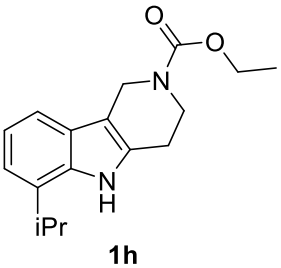
1f

Ethyl 6-methoxy-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1f): The procedure was followed using 2-methoxybenzazine hydrochloride (**4f**, 1.74 g, 10 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 1.5 mL, 10 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1f** as a white solid (1.86 g, 68% yield). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.24 (s, 1H), 7.08 (d, *J* = 7.9 Hz, 1H), 7.03 (t, *J* = 7.8 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.69 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.95 (s, 3H), 3.88 (s, 2H), 2.83 (t, *J* = 5.8 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 156.2, 145.7, 131.5, 126.7, 126.0, 120.0, 110.4, 107.5, 101.9, 61.5, 55.3, 41.3, 23.3, 14.7 ppm. HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{18}N_2O_3^+$: 275.1390, found: 275.1387.



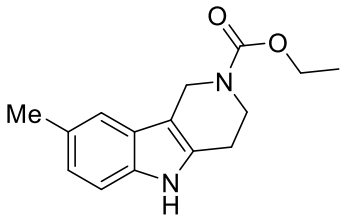
1g

Ethyl 6-ethyl-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1g): The procedure was followed using 2-ethylbenzazine hydrochloride (**4g**, 1.7 g, 10 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 1.5 mL, 10 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1g** as a white solid (2.06 g, 76% yield). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.46 (s, 1H), 7.36 (s, 1H), 7.13 (s, 1H), 7.07 (s, 1H), 4.77 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.93 (s, 2H), 2.92 – 2.87 (m, 4H), 1.40 (t, *J* = 7.6 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 156.2, 134.6, 131.6, 126.3, 125.1, 120.2, 119.7, 115.1, 107.3, 61.5, 41.3, 24.0, 23.3, 14.6, 13.9 ppm. HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{20}N_2O_2^+$: 273.1598, found: 273.1595.



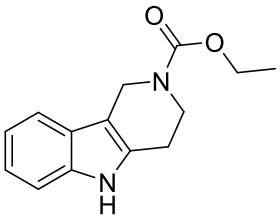
1h

Ethyl 6-isopropyl-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1h): The procedure was followed using 2-isopropylbenzazine hydrochloride (**4h**, 1.86 g, 10 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 1.5 mL, 10 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1h** as a white solid (1.4 g, 49% yield). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.16 (s, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 6.9 Hz, 1H), 7.08 (d, *J* = 6.9 Hz, 1H), 4.72 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 2H), 3.24 (p, *J* = 6.6 Hz, 1H), 2.89 (t, *J* = 5.1 Hz, 2H), 1.40 (d, *J* = 6.9 Hz, 6H), 1.33 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 156.2, 134.0, 131.5, 131.0, 125.3, 119.9, 117.7, 115.1, 107.6, 61.5, 41.3, 29.3, 23.4, 22.7, 14.7 ppm. HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{17}H_{22}N_2O_2^+$: 287.1754, found: 287.1751.



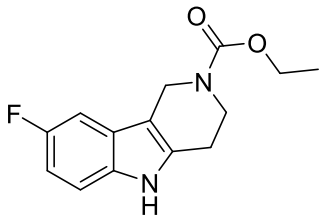
1i

Ethyl 8-methyl-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1i): The procedure was followed using *p*-tolylbenzazine hydrochloride (**4i**, 1.58 g, 10 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 1.5 mL, 10 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1i** as a white solid (2.45 g, 95% yield). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.76 (s, 1H), 7.20 – 7.18 (m, 2H), 6.89 – 6.84 (m, 1H), 4.57 (s, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.75 (t, J = 5.5 Hz, 2H), 2.78 (t, J = 5.5 Hz, 2H), 2.36 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, DMSO-d_6) δ 155.2, 134.2, 132.5, 127.0, 125.4, 122.1, 116.9, 110.6, 105.0, 60.8, 41.00, 22.9, 21.2, 14.7 ppm.



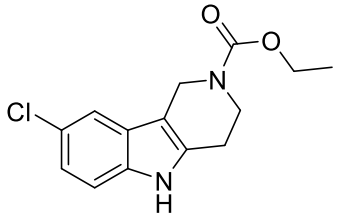
1j

Ethyl 1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1j): The procedure was followed using benzazine hydrochloride (**4j**, 1.44 g, 10 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 1.5 mL, 10 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1j** as a white solid (2.14 g, 88% yield). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.87 (brs, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 7.6 Hz, 1H), 7.11 (t, J = 7.4 Hz, 1H), 4.70 (s, 2H), 4.20 (q, J = 7.1 Hz, 2H), 3.88 (s, 2H), 2.85 (s, 2H), 1.31 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 156.3, 134.7, 133.0, 126.8, 124.1, 120.9, 116.8, 108.5, 104.4, 61.8, 41.3, 23.5, 14.9 ppm.



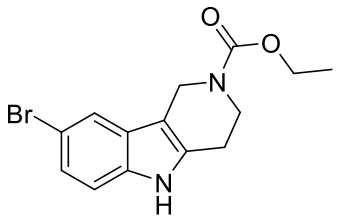
1k

Ethyl 8-fluoro-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1k): The procedure was followed using 4-fluorobenzazine hydrochloride (**4k**, 1.62g, 10 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 1.5 mL, 10 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1k** as a white solid (2.38 g, 91% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.94 (s, 1H), 7.21 (dd, *J* = 8.8, 4.3 Hz, 1H), 7.09 (dd, *J* = 9.4, 2.5 Hz, 1H), 6.89 (td, *J* = 9.1, 2.5 Hz, 1H), 4.65 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 2H), 2.84 (t, *J* = 5.8 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6) δ 156.7 (d, *J* = 231.0 Hz), 155.1, 134.8, 132.5, 125.3 (d, *J* = 10.1 Hz), 111.7 (d, *J* = 9.8 Hz), 108.4 (d, *J* = 25.8 Hz), 105.9, 102.3 (d, *J* = 23.4 Hz), 60.9, 40.9, 23.0, 14.6 ppm. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -124.38 ppm.



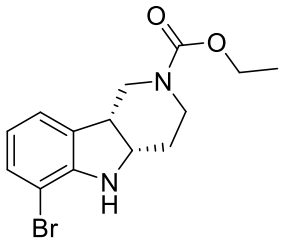
1l

Ethyl 8-chloro-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1l): The procedure was followed using 4-chlorobenzazine hydrochloride (**4l**, 1.78 g, 10 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 1.5 mL, 10 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1l** as a white solid (2.36 g, 85% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.03 (s, 1H), 7.41 (s, 1H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.10 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.64 (s, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 2H), 2.83 (t, *J* = 5.7 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6) δ 155.1, 134.3, 126.2, 123.2, 120.4, 116.7, 112.3, 105.6, 60.8, 40.8, 22.8, 14.6 ppm.



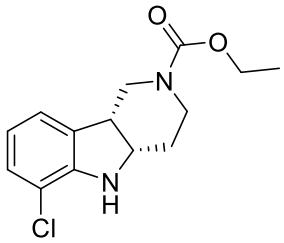
1m

Ethyl 8-bromo-1,3,4,5-tetrahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (1m): The procedure was followed using 4-bromobenzazine hydrochloride (**4m**, 2.21 g, 10 mmol, 1.0 equiv.) and N-ethoxycarbonyl-4-piperidone (**5**, 1.5 mL, 10 mmol, 1.0 equiv.). Purification using condition of silica gel chromatography afforded product **1m** as a white solid (2.16 g, 67% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.02 (s, 1H), 7.57 (s, 1H), 7.23 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.17 (d, *J* = 8.6 Hz, 1H), 4.64 (s, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 2H), 2.83 (t, *J* = 5.8 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6) δ 155.1, 134.5, 126.9, 123.0, 119.7, 112.8, 111.1, 105.5, 60.9, 40.8, 22.8, 14.6 ppm.



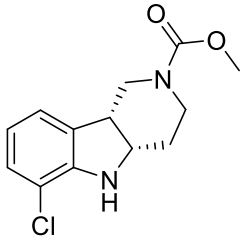
2a

Ethyl (4a*S*,9b*R*)-6-bromo-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2a): The procedure was followed using **1a** (32 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2a** as an oily yellow solid (29.8 mg, 92% yield). $[\alpha]_D^{25}$ + 55.0 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.19 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 6.59 (t, *J* = 7.6 Hz, 1H), 4.16 – 4.08 (m, 2H), 4.03 (q, *J* = 5.5 Hz, 1H), 4.00 – 3.72 (m, 2H), 3.61 – 3.53 (m, 1H), 3.48 – 3.21 (m, 3H), 1.95 – 1.87 (m, 1H), 1.83 – 1.74 (m, 1H), 1.25 (brs, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.6, 149.3, 131.5, 130.5, 123.0, 120.1, 103.7, 61.3, 56.9, 43.6, 41.8, 39.6, 27.8, 14.7 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak OD-3 column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 7.961 min (*S*, *R*) (major), 12.177 min (*R*, *S*) (minor). HRMS (ESI/ion trap) *m*/*z*: [M + H]$^+$ calcd for $C_{14}H_{17}BrN_2O_2^+$: 325.0546, found: 325.0545.



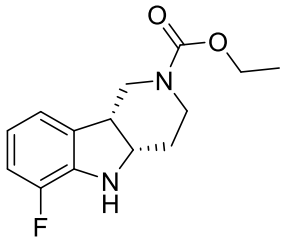
2b

Ethyl (4aS,9bR)-6-chloro-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2b): The procedure was followed using **1b** (28 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2b** as an oily yellow solid (24.3 mg, 87% yield). $[\alpha]_D^{25}$ + 41.3 (*c* 0.3, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.04 (d, *J* = 8.1 Hz, 1H), 7.00 (d, *J* = 7.3 Hz, 1H), 6.66 (t, *J* = 7.7 Hz, 1H), 4.18 – 4.08 (m, 2H), 4.03 (dt, *J* = 9.6, 4.9 Hz, 1H), 3.94 – 3.17 (m, 6H), 1.96 – 1.88 (m, 1H), 1.83 – 1.74 (m, 1H), 1.25 (brs, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.6, 147.8, 131.7, 127.7, 122.4, 119.7, 115.3, 61.3, 57.3, 43.6, 41.6, 39.6, 27.8, 14.7 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 9.468 min (*S*, *R*) (major), 12.566 min (*R*, *S*) (minor). HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{17}ClN_2O_2^+$: 281.1051, found: 281.1048.



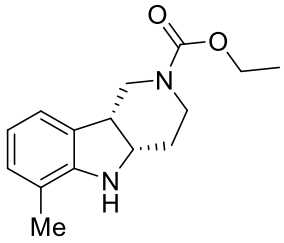
2c

Methyl (4aS,9bR)-6-chloro-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2c): The procedure was followed using **1c** (26.4 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2c** as an oily yellow solid (25 mg, 95% yield). $[\alpha]_D^{25}$ + 66.5 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.05 (d, *J* = 8.1 Hz, 1H), 7.00 (s, 1H), 6.66 (t, *J* = 7.6 Hz, 1H), 4.12 – 3.95 (m, 2H), 3.94 – 3.75 (m, 1H), 3.69 (s, 3H), 3.59 (s, 1H), 3.48 – 3.40 (m, 1H), 3.40 – 3.21 (m, 2H), 1.92 (s, 1H), 1.85 – 1.75 (m, 1H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 156.0, 147.8, 131.6, 127.8, 122.5, 119.8, 115.4, 57.2, 52.6, 43.8, 41.6, 39.7, 27.9 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 12.083 min (*S*, *R*) (major), 16.736 min (*R*, *S*) (minor). HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{13}H_{15}ClN_2O_2^+$: 267.0895, found: 267.0893.



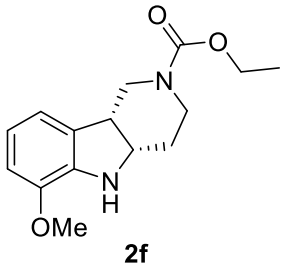
2d

Ethyl (4aS,9bR)-6-fluoro-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2d): The procedure was followed using **1d** (26 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2d** as an oily yellow solid (23.7 mg, 90% yield). $[\alpha]_D^{25}$ + 52.5 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.92 (d, *J* = 7.3 Hz, 1H), 6.84 (t, 1H), 6.67 (td, *J* = 7.8, 4.6 Hz, 1H), 4.13 (qq, *J* = 7.2, 3.6 Hz, 2H), 4.04 (dt, *J* = 7.1, 4.9 Hz, 1H), 3.97 – 3.70 (m, 2H), 3.63 – 3.54 (m, 1H), 3.50 – 3.40 (m, 1H), 3.31 (brs, 2H), 1.92 (ddt, *J* = 14.2, 9.4, 4.6 Hz, 1H), 1.79 (dq, *J* = 14.4, 4.9 Hz, 1H), 1.29 – 1.23 (m, 3H) ppm. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.6, 150.5, 148.1, 137.6 (d, *J* = 12.7 Hz), 133.8, 119.6 (d, *J* = 19.8 Hz), 114.6 (d, *J* = 17.4 Hz), 61.2, 58.2, 43.6, 41.2, 39.6, 27.9, 14.7 ppm. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -135.4 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AD-3 column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 6.770 min (*R*, *S*) (minor), 7.625 min (*S*, *R*) (major).



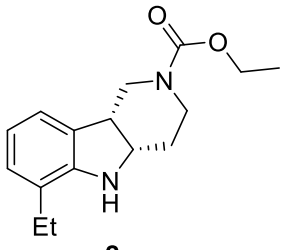
2e

Ethyl (4aS,9bR)-6-methyl-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2e): The procedure was followed using **1e** (25.8 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2e** as an oily yellow solid (24.7 mg, 95% yield). $[\alpha]_D^{25}$ + 29.9 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.99 (d, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.68 (t, *J* = 7.4 Hz, 1H), 4.19 – 4.08 (m, 2H), 3.98 (dt, *J* = 7.3, 4.9 Hz, 1H), 3.95 – 3.73 (m, 1H), 3.65 – 3.12 (m, 5H), 2.14 (s, 3H), 1.92 (td, *J* = 9.4, 4.7 Hz, 1H), 1.82 – 1.76 (m, 1H), 1.26 (s, 1H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.6, 149.3, 129.4, 128.9, 121.6, 119.1, 61.2, 57.2, 43.9, 41.1, 39.7, 28.1, 16.7, 14.7 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 90:10, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 14.152 min (*S*, *R*) (major), 15.283 min (*R*, *S*) (minor). HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{18}N_2O_2^+$: 261.1598, found: 261.1595.



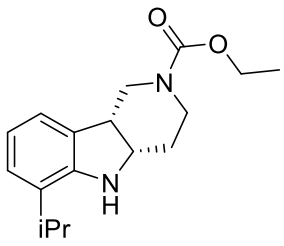
2f

Ethyl (4aS,9bR)-6-methoxy-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2f): The procedure was followed using **1f** (27 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2f** as an oily yellow solid (20 mg, 73% yield). $[\alpha]_D^{25}$ + 7.9 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.80 (d, *J* = 7.3 Hz, 1H), 6.73 (t, *J* = 7.7 Hz, 1H), 6.69 (d, *J* = 7.7 Hz, 1H), 4.17 – 4.09 (m, 2H), 4.06 – 3.88 (m, 2H), 3.83 (s, 3H), 3.82 – 3.56 (m, 2H), 3.48 – 3.38 (m, 1H), 3.36 – 3.04 (m, 2H), 1.95 – 1.87 (m, 1H), 1.84 – 1.74 (m, 1H), 1.26 (brs, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.6, 145.6, 139.6, 131.5, 119.7, 116.7, 109.8, 77.6 – 76.3 (m), 61.2, 57.9, 55.3, 44.0, 41.4, 39.7, 28.0, 14.7 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 10.443 min (*S*, *R*) (major), 20.118 min (*R*, *S*) (minor). HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{20}N_2O_3^+$: 277.1547, found: 277.1544.



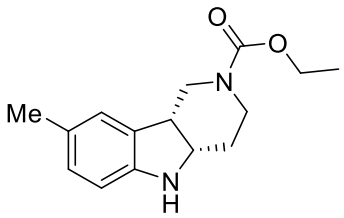
2g

Ethyl (4aS,9bR)-6-ethyl-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2g): The procedure was followed using **1g** (27 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2g** as an oily yellow solid (24.6 mg, 90% yield). $[\alpha]_D^{25}$ + 30.3 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.00 (d, *J* = 7.3 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.73 (t, *J* = 7.4 Hz, 1H), 4.18 – 4.08 (m, 2H), 3.98 (dt, *J* = 7.4, 5.0 Hz, 1H), 3.94 – 3.18 (m, 6H), 2.49 (q, *J* = 7.6 Hz, 2H), 1.91 (ddt, *J* = 14.0, 9.3, 4.7 Hz, 1H), 1.80 – 1.74 (m, 1H), 1.31 – 1.20 (m, 6H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.6, 148.6, 129.4, 126.8, 125.3, 121.6, 119.1, 61.1, 57.2, 43.8, 41.1, 39.7, 28.1, 23.9, 14.7, 13.2 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 90:10, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 10.727 min (*R*, *S*) (minor), 13.120 min (*S*, *R*) (major). HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{22}N_2O_2^+$: 275.1754, found: 275.1751.



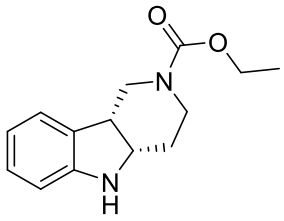
2h

Ethyl (4aS,9bR)-6-isopropyl-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2h): The procedure was followed using **1h** (28 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2h** as an oily yellow solid (22 mg, 77% yield). $[\alpha]_D^{25}$ + 13.6 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.01 – 6.98 (m, 2H), 6.75 (t, *J* = 7.5 Hz, 1H), 4.13 (qq, *J* = 10.6, 7.1 Hz, 2H), 3.97 (dt, *J* = 7.3, 5.1 Hz, 1H), 3.94 – 3.20 (m, 6H), 2.81 (hept, *J* = 6.9 Hz, 1H), 1.95 – 1.87 (m, 1H), 1.80 – 1.73 (m, 1H), 1.30 – 1.22 (m, 9H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.7, 148.1, 130.1, 124.1, 121.6, 119.3, 61.2, 57.2, 43.8, 41.2, 39.9, 28.9, 28.2, 22.2, 22.2, 14.8 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 90:10, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 6.447 min (*S*, *R*) (major), 7.545 min (*R*, *S*) (minor). HRMS (ESI/ion trap) *m*/*z*: $[M + H]^+$ calcd for $C_{17}H_{24}N_2O_2^+$: 289.1911, found: 289.1907.



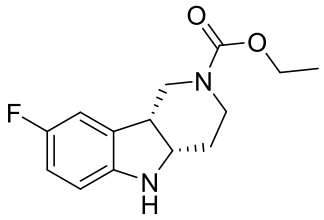
2i

Ethyl (4aS,9bR)-8-methyl-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2i): The procedure was followed using **1i** (26 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2i** as an oily yellow solid (25.7 mg, 99% yield). $[\alpha]_D^{25}$ + 53.9 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.95 (s, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.58 (d, *J* = 7.8 Hz, 1H), 4.21 – 4.05 (m, 2H), 3.98 – 3.91 (m, 1H), 3.87 – 3.10 (m, 6H), 2.25 (s, 3H), 1.88 (tt, *J* = 9.3, 4.7 Hz, 1H), 1.82 – 1.67 (m, 1H), 1.32 – 1.22 (m, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.6, 148.3, 130.3, 128.3, 124.9, 109.9, 61.2, 57.6, 43.9, 40.9, 39.8, 28.0, 20.8, 14.7 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 5.821 min (*S*, *R*) (major), 9.116 min (*R*, *S*) (minor).



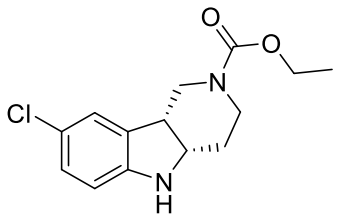
2j

Ethyl (4aS,9bR)-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2j): The procedure was followed using **1j** (24 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2j** as an oily yellow solid (23 mg, 95% yield). $[\alpha]_D^{25}$ + 75.0 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.13 (d, *J* = 7.2Hz, 1H), 7.05 (td, *J* = 7.6, 1.2 Hz, 1H), 6.73 (td, *J* = 7.4, 0.8 Hz, 1H), 6.66 (d, *J* = 7.8Hz, 1H), 4.20 – 4.06 (m, 2H), 3.97 (dt, *J* = 6.8, 4.9 Hz, 1H), 3.96 – 3.64 (m, 2H), 3.63 – 3.53 (m, 1H), 3.49 – 3.11 (m, 3H), 1.90 (ddt, *J* = 14.1, 9.3, 4.6 Hz, 1H), 1.76 (ddd, *J* = 14.4, 9.3, 5.3 Hz, 1H), 1.26 (t, *J* =6.6 Hz, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.7, 150.9, 130.1, 128.1, 124.3, 119.1, 110.0, 61.3, 57.5, 43.9, 41.0, 39.8, 28.1, 14.8 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak OD-3 column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 10.812 min (*R*, *S*) (minor), 11.642 min (*S*, *R*) (major).



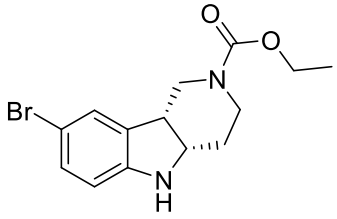
2k

Ethyl (4aS,9bR)-8-fluoro-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2k): The procedure was followed using **1k** (26 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2k** as an oily yellow solid (23 mg, 87% yield). $[\alpha]_D^{25}$ + 60.0 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.85 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.74 (td, *J* = 8.9, 2.6 Hz, 1H), 6.56 (dd, *J* = 8.5, 4.3 Hz, 1H), 4.20 – 4.05 (m, 2H), 4.02 – 3.93 (m, 1H), 3.93 – 3.67 (m, 1H), 3.69 – 3.11 (m, 5H), 1.94 – 1.82 (m, 1H), 1.77 – 1.68 (m, 1H), 1.35 – 1.17 (m, 3H) ppm. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 157.0 (d, *J* = 236.0 Hz), 155.6, 146.7, 114.0 (d, *J* = 23.3 Hz), 111.7 (d, *J* = 24.0 Hz), 110.2 (d, *J* = 8.0 Hz), 61.3, 58.0, 43.6, 41.1, 39.7, 27.9, 14.7 ppm. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -125.6 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 9.008 min (*R*, *S*) (minor), 14.061 min (*S*, *R*) (major).



2l

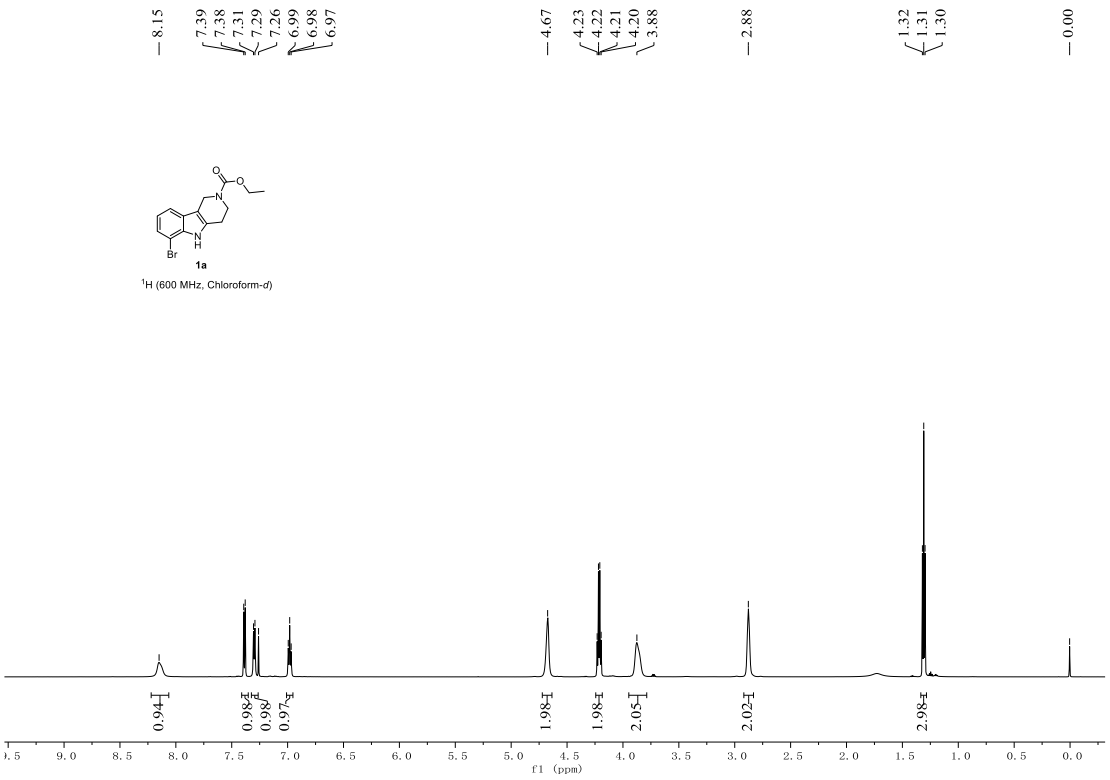
Ethyl (4aS,9bR)-8-chloro-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2l): The procedure was followed using **1l** (27.8 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2l** as an oily yellow solid (27 mg, 98% yield). $[\alpha]_D^{25}$ + 31.0 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.07 (d, *J* = 2.1 Hz, 1H), 6.99 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.55 (d, *J* = 8.2 Hz, 1H), 4.21 – 4.04 (m, 2H), 4.02 – 3.93 (m, 1H), 3.93 – 3.63 (m, 2H), 3.59 – 3.10 (m, 4H), 1.94 – 1.82 (m, 1H), 1.72 (s, 1H), 1.25 (s, 3H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 155.5, 149.3, 131.6, 127.7, 124.4, 123.4, 110.6, 61.3, 57.7, 43.4, 41.0, 39.7, 27.8, 14.6 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 85:15, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 9.429 min (*R*, *S*) (minor), 19.070 min (*S*, *R*) (major).

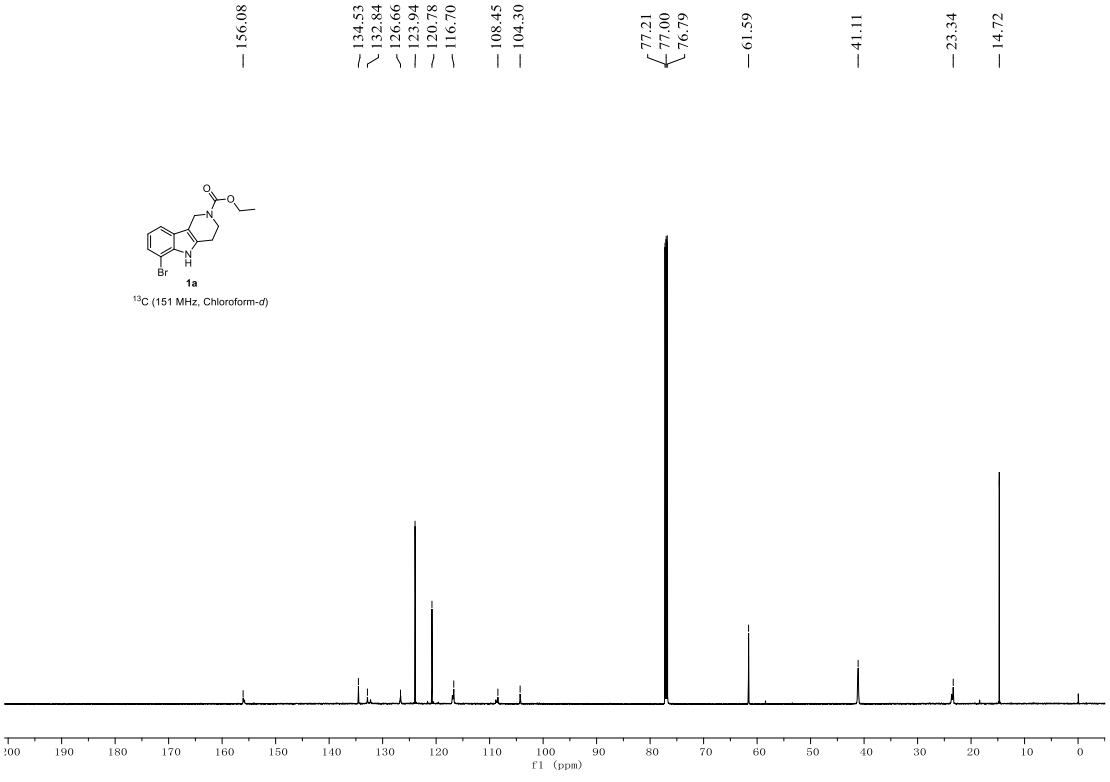


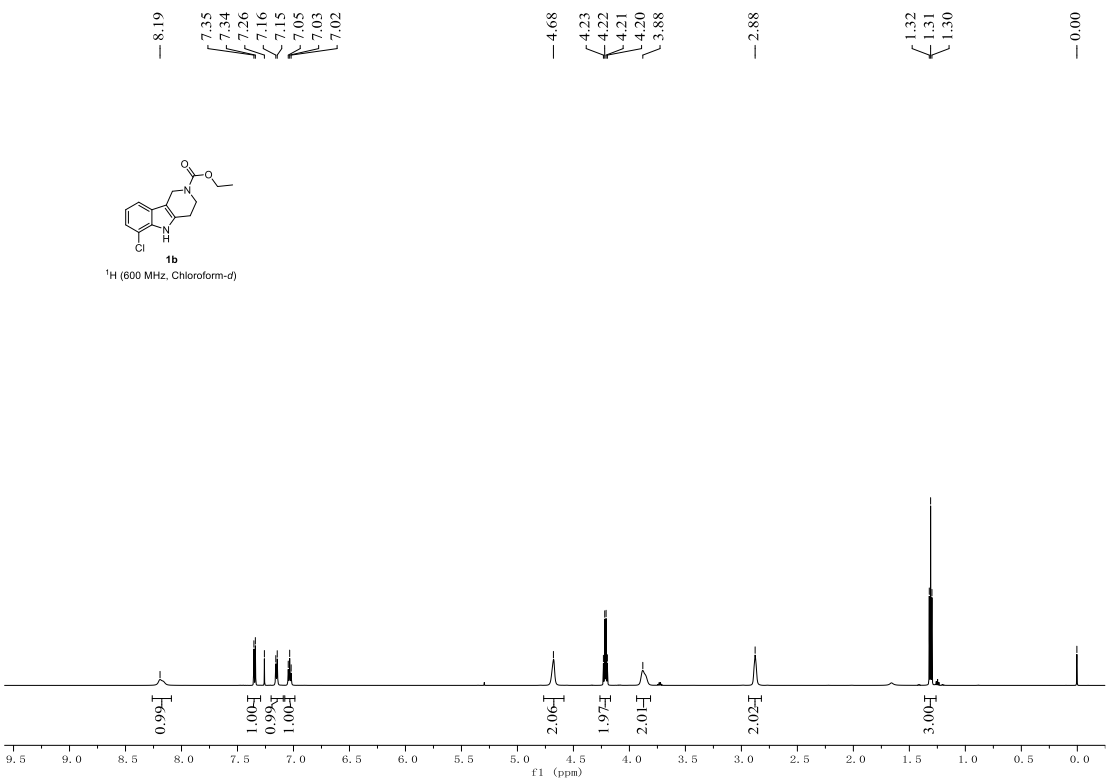
2m

Ethyl (4aS,9bR)-8-bromo-1,3,4,4a,5,9b-hexahydro-*2H*-pyrido[4,3-*b*]indole-2-carboxylate (2m): The procedure was followed using **1m** (32 mg, 0.1 mmol, 1.0 equiv.) under H_2 (40 atm). Purification using condition of silica gel chromatography afforded product **2m** as an oily yellow solid (28.7 mg, 89% yield). $[\alpha]_D^{25}$ + 21.0 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 2.0 Hz, 1H), 7.13 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.52 (d, *J* = 8.2 Hz, 1H), 4.19 – 4.07 (m, 2H), 4.01 – 3.95 (m, 1H), 3.92 – 3.64 (m, 2H), 3.62 – 3.10 (m, 4H), 1.93 – 1.84 (m, 1H), 1.70 (s, 1H), 1.34 – 1.20 (m, 3H) ppm. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.5, 149.8, 132.2, 130.6, 127.2, 111.2, 110.4, 61.3, 57.6, 43.4, 41.0, 39.6, 27.8, 14.7 ppm. The enantiomeric excess was determined by HPLC analysis on Daicel Chiralcel OD-H column (0.46 × 25 cm), Hexane/^{i}PrOH = 80:20, flow rate = 1.0 mL/min, λ = 254 nm, t_R: 7.589 min (*R*, *S*) (minor), 14.031 min (*S*, *R*) (major).

VI NMR Spectrum



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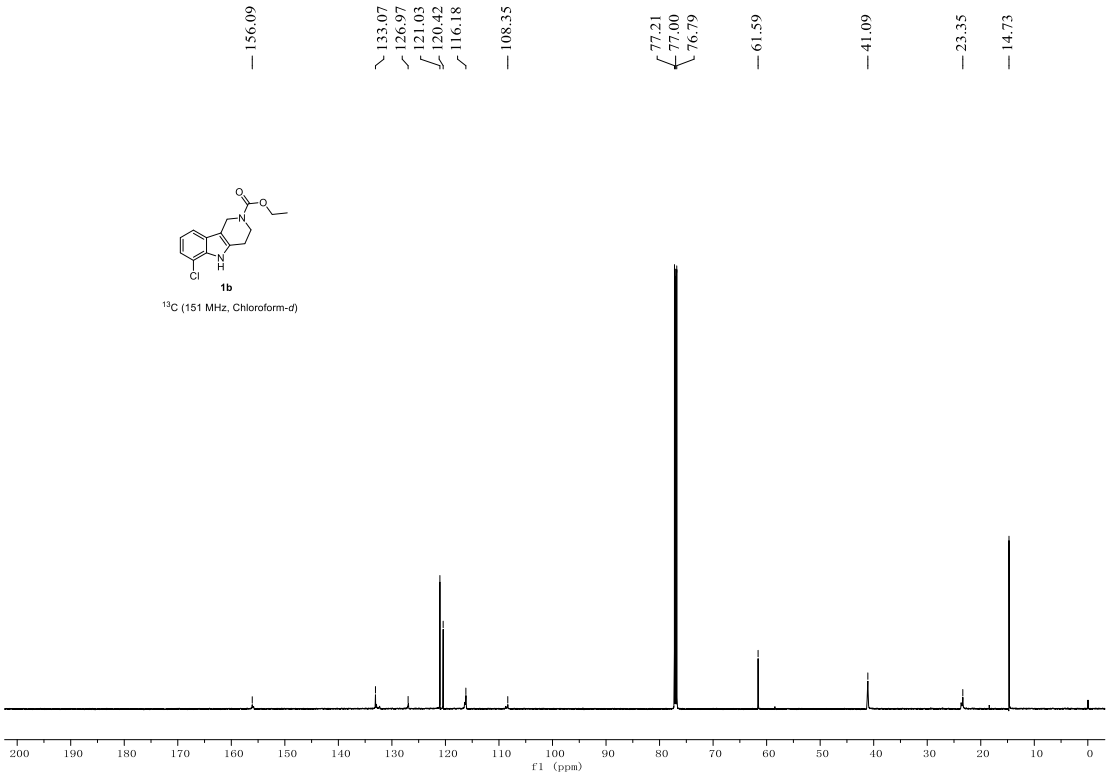
7.35
7.34
7.26
7.16
7.15
7.05
7.03
7.02
4.68
4.23
4.22
4.21
4.20
3.88
2.88
1.32
1.31
1.30
0.00
1b
1H (600 MHz, Chloroform-d)
0.99
1.00
0.99
1.00
2.06
1.97
2.01
2.02
3.00
f1 (ppm)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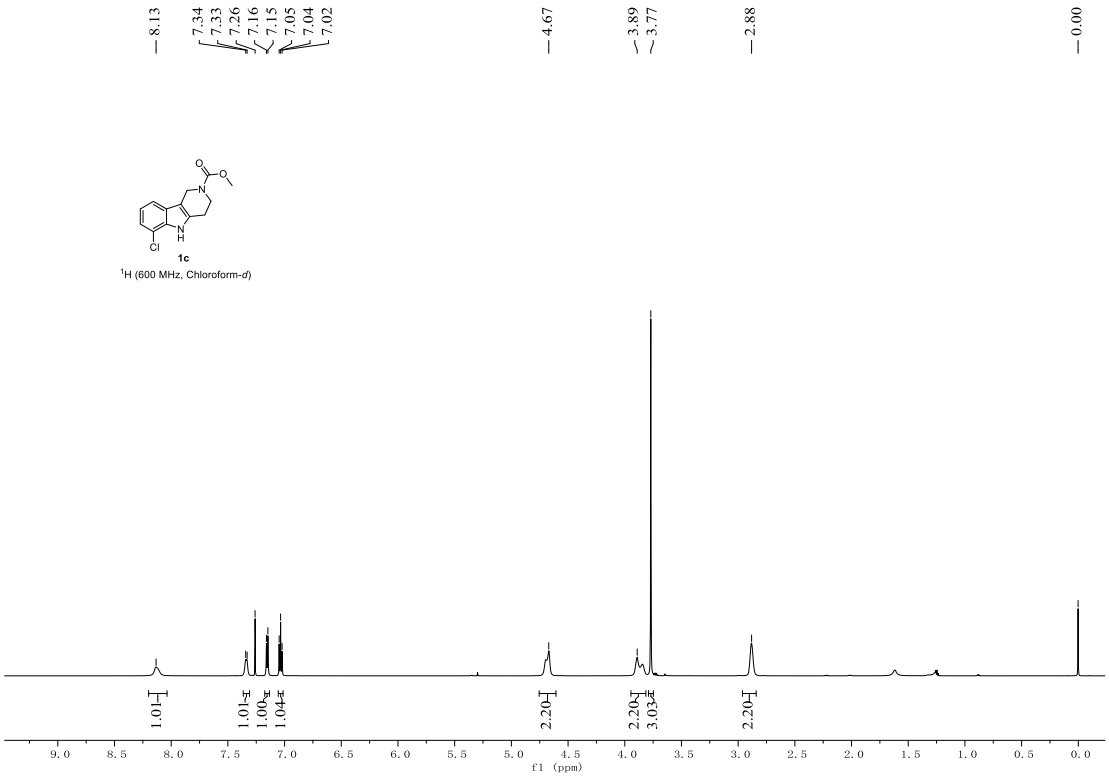
133.07
126.97
121.03
120.42
116.18
108.35
77.21
77.00
76.79
61.59
41.09
23.35
14.73
1b
13C (151 MHz, Chloroform-d)
f1 (ppm)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7.02
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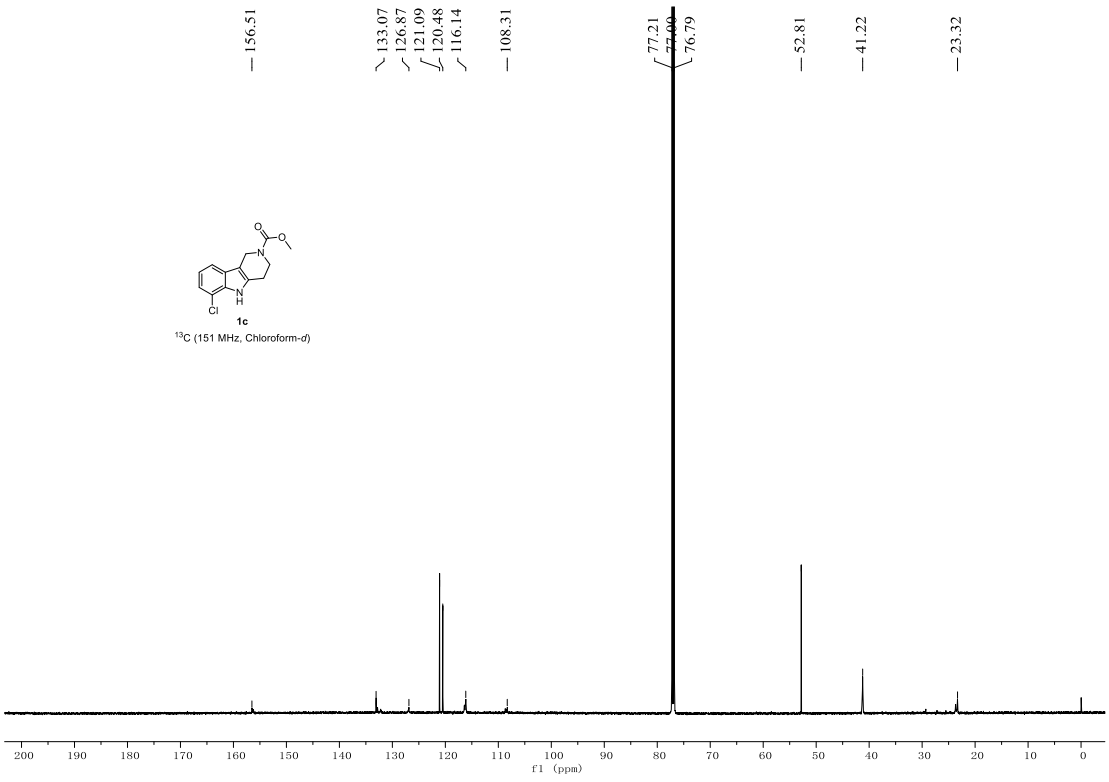
2.88
0.00
1c
1H (600 MHz, Chloroform-d)
1.01
1.01
1.00
1.04
2.20
2.20
3.03
2.20
f1 (ppm)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126.87
121.09
120.48
116.14
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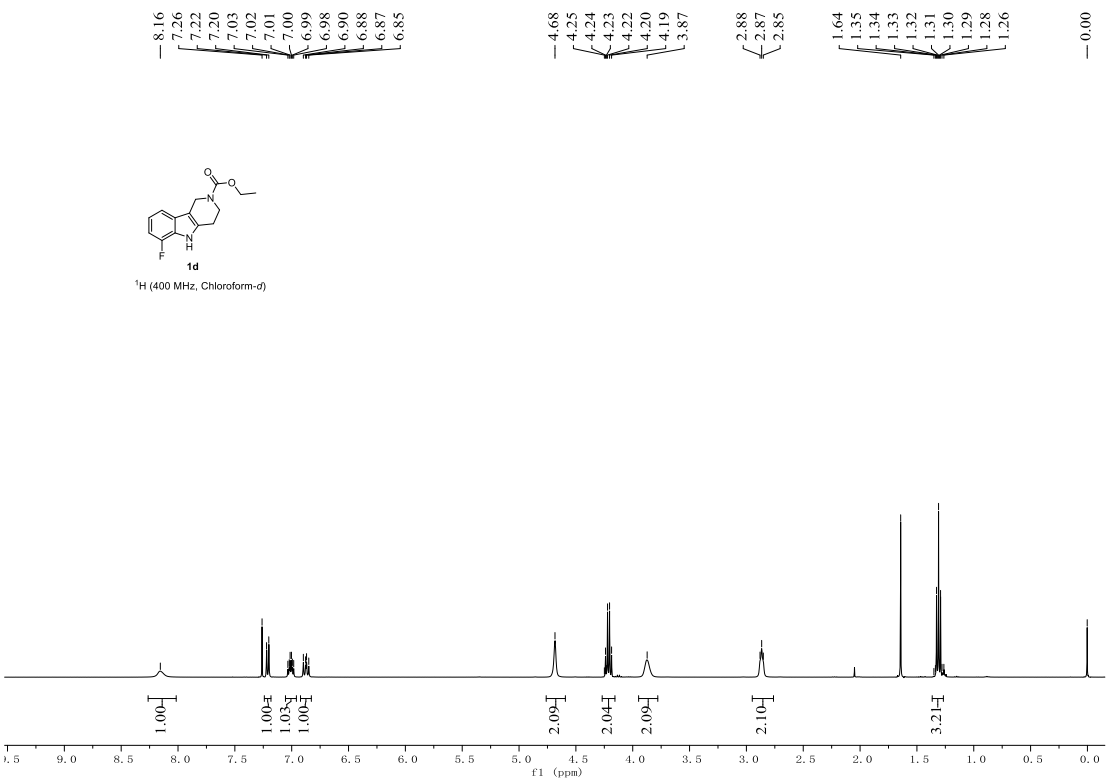
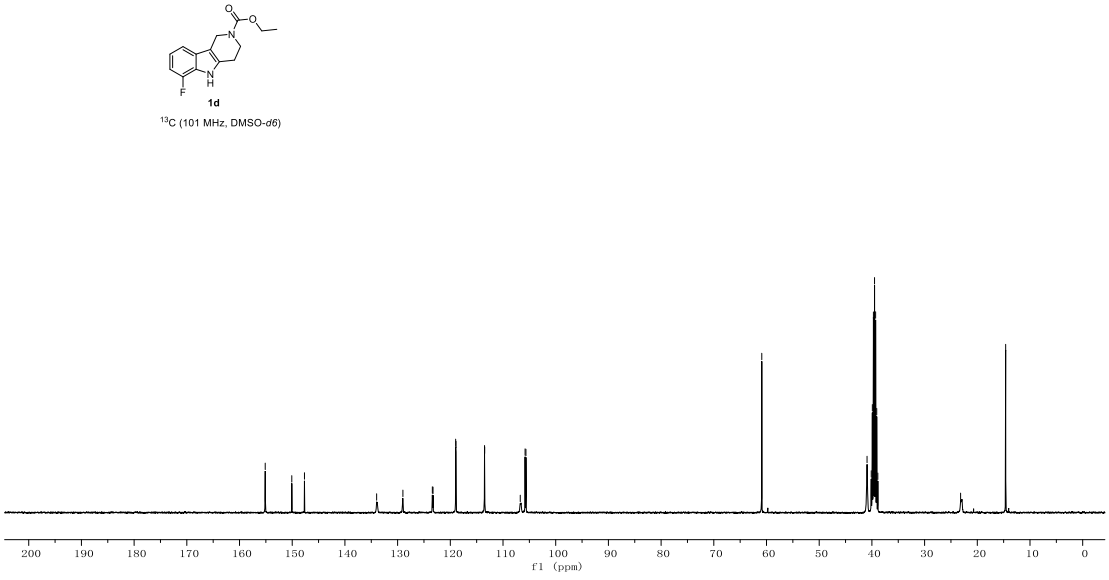
77.00
76.79
52.81
41.22
23.32
1c
13C (151 MHz, Chloroform-d)
f1 (ppm)



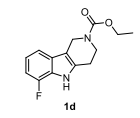
1d

^{1}H (400 MHz, Chloroform-*d*)



1d

^{13}C (101 MHz, DMSO-*d6*)

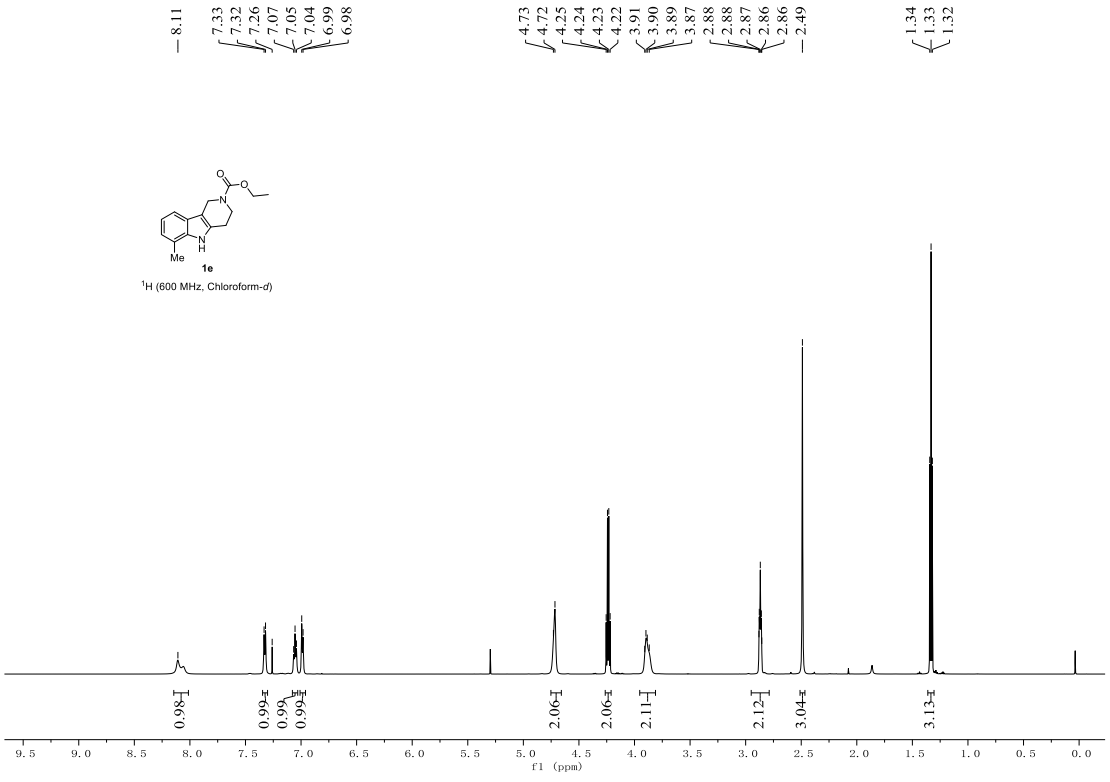


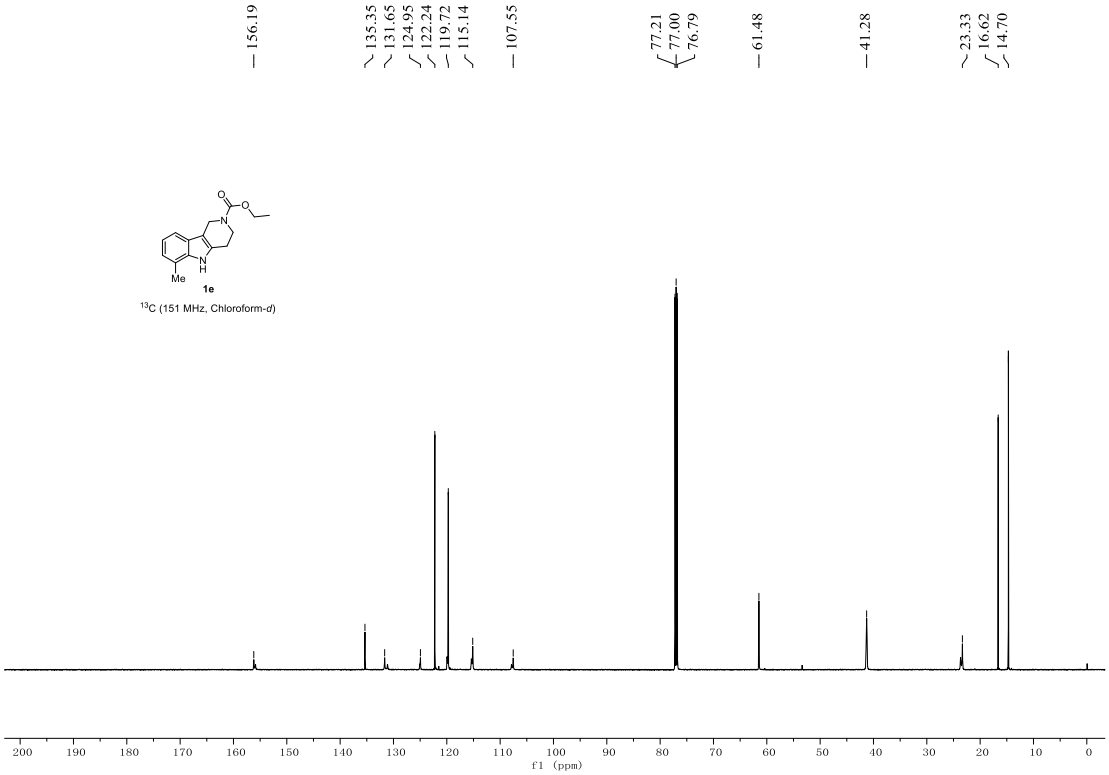
1d

^{19}F (376 MHz, Chloroform-*d*)

1e

^{1}H (600 MHz, Chloroform-*d*)

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122.24
119.72
115.14
107.55
77.21
77.00
76.79
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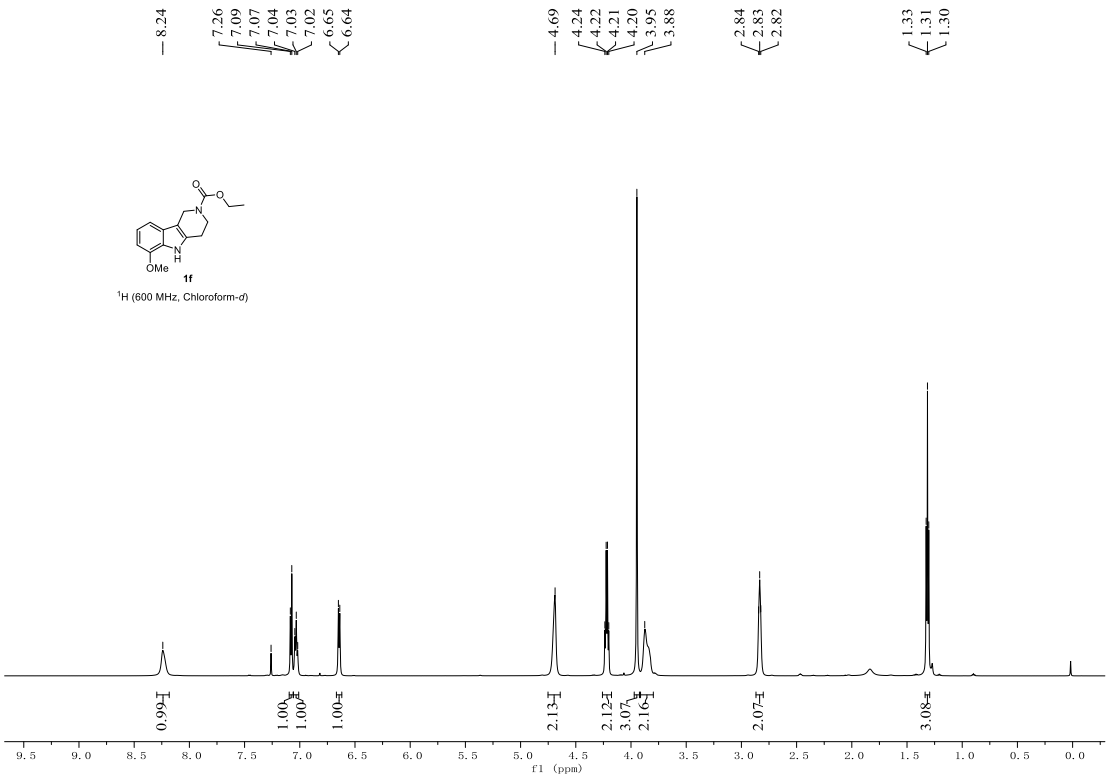
41.28
23.33
16.62
14.70
Me
1e
13C (151 MHz, Chloroform-d)
f1 (ppm)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6.64
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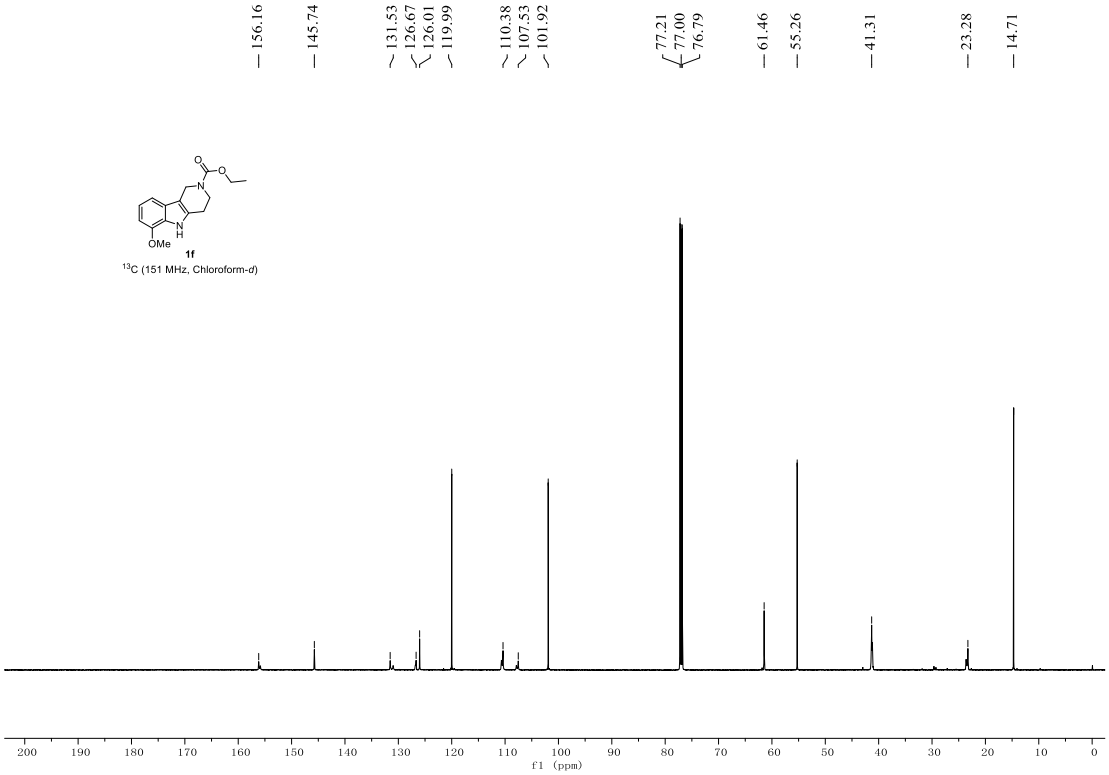
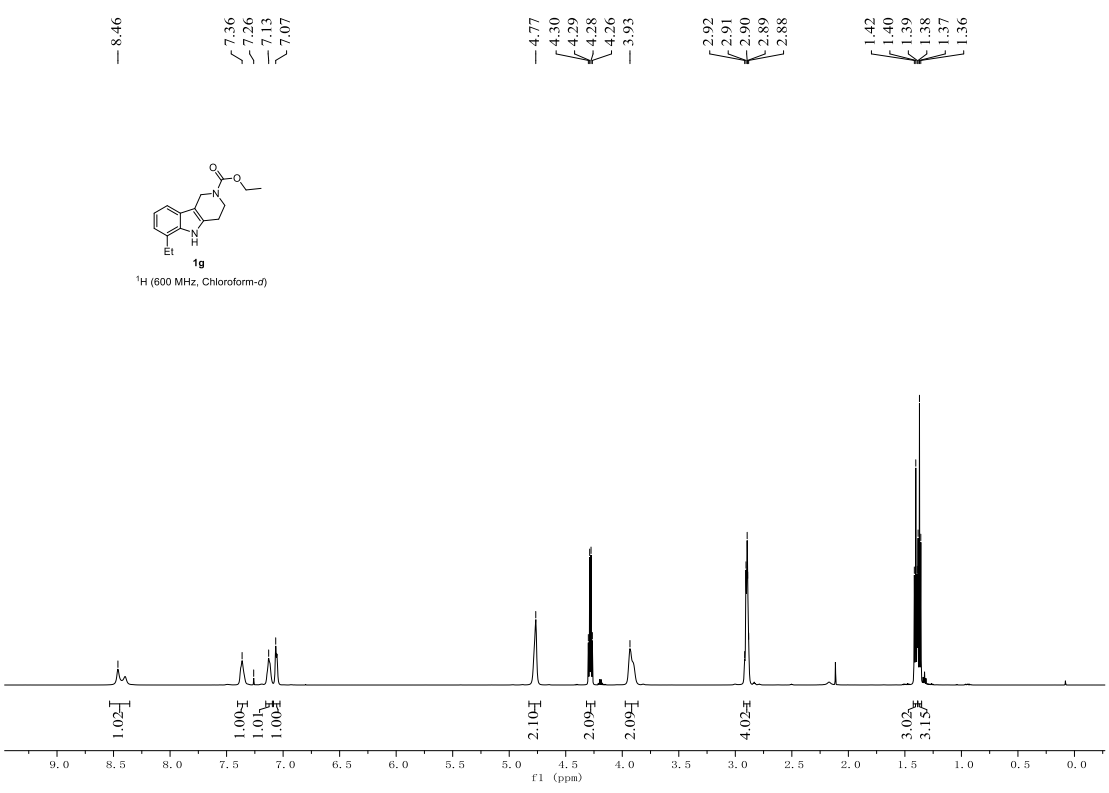
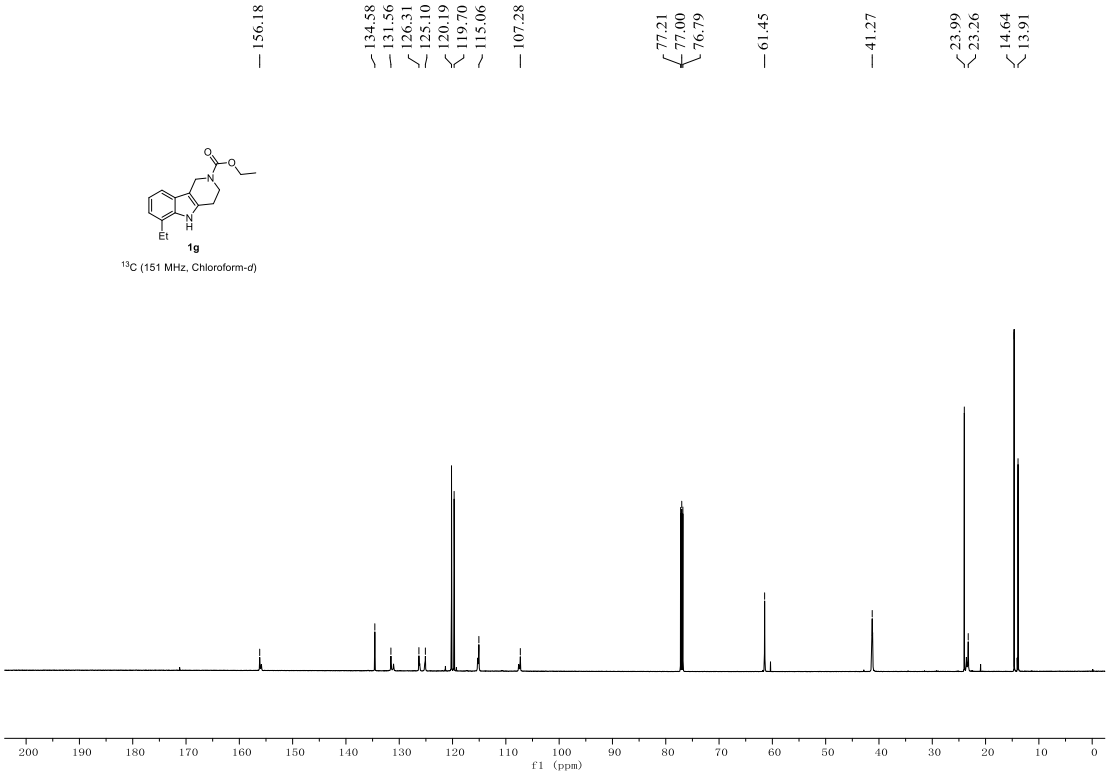
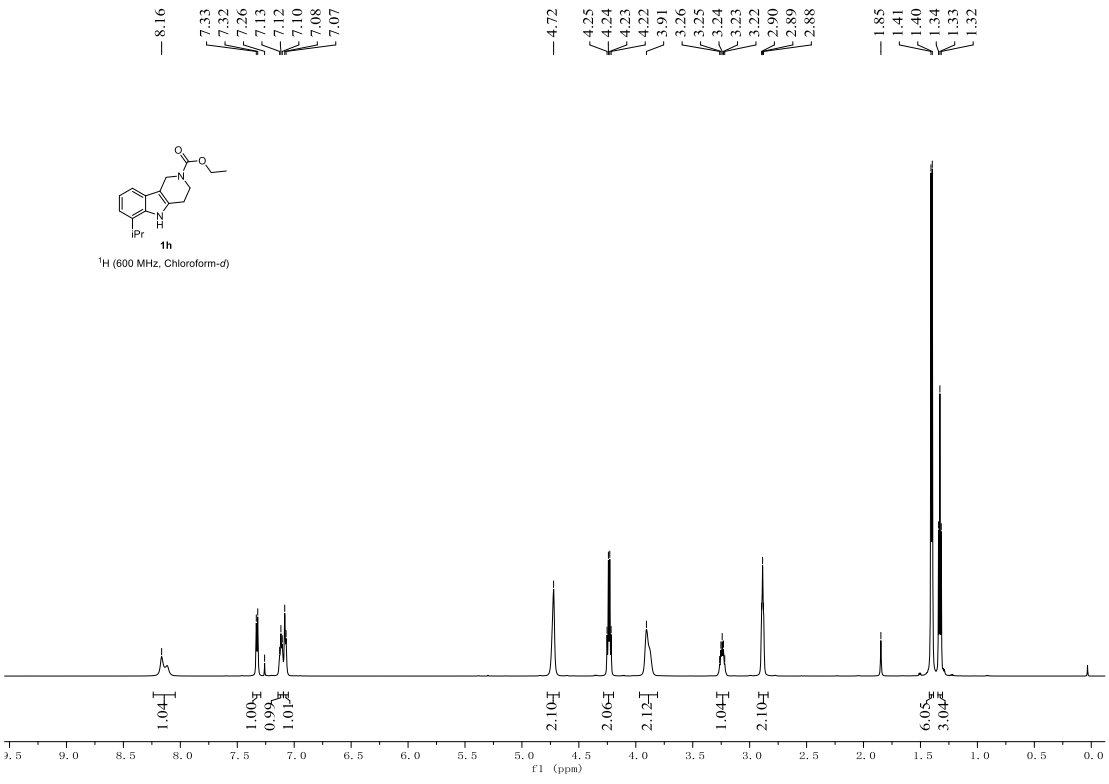
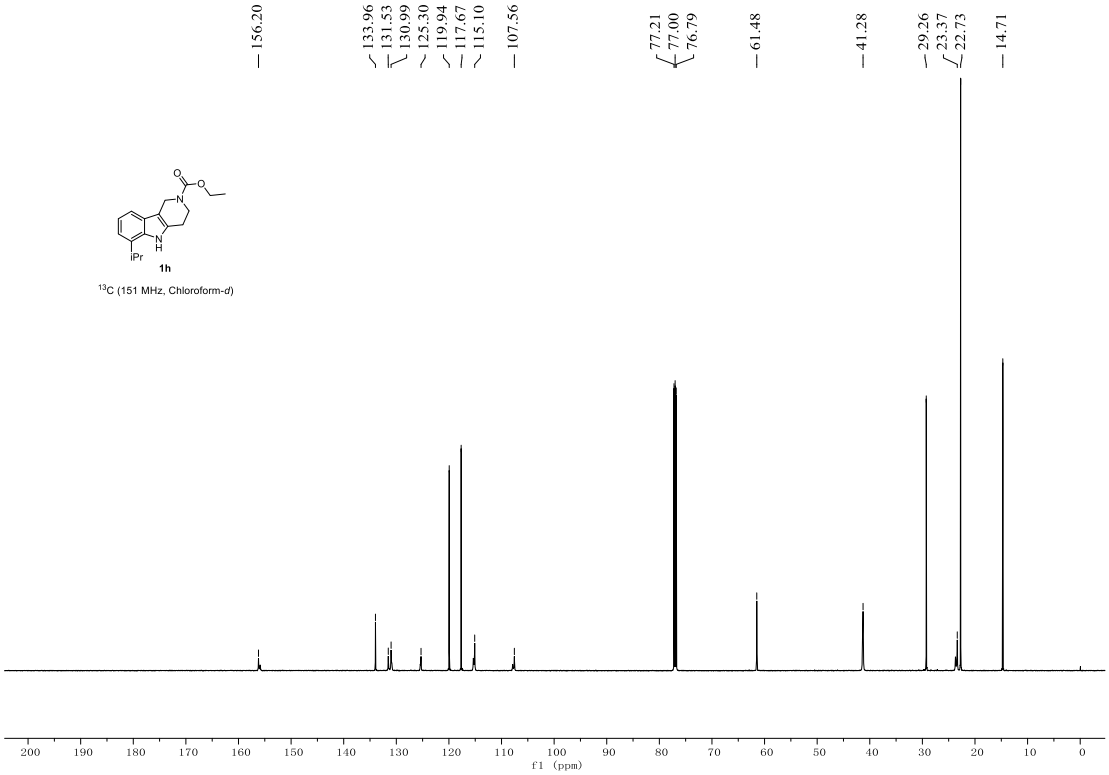
4.20
3.95
3.88
2.84
2.83
2.82
1.33
1.31
1.30
OMe
1f
1H (600 MHz, Chloroform-d)
0.99
1.00
1.00
1.00
2.13
2.12
3.07
2.16
2.07
3.08
f1 (ppm)

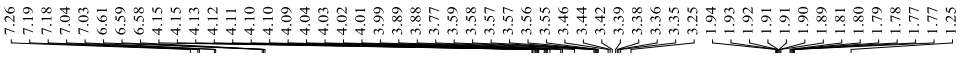

156.16
145.74
131.53
126.67
126.01
119.99
110.38
107.53
101.92
77.21
77.00
76.79
61.46
55.26
41.31
23.28
14.71
OMe
1f
13C (151 MHz, Chloroform-d)
f1 (ppm)

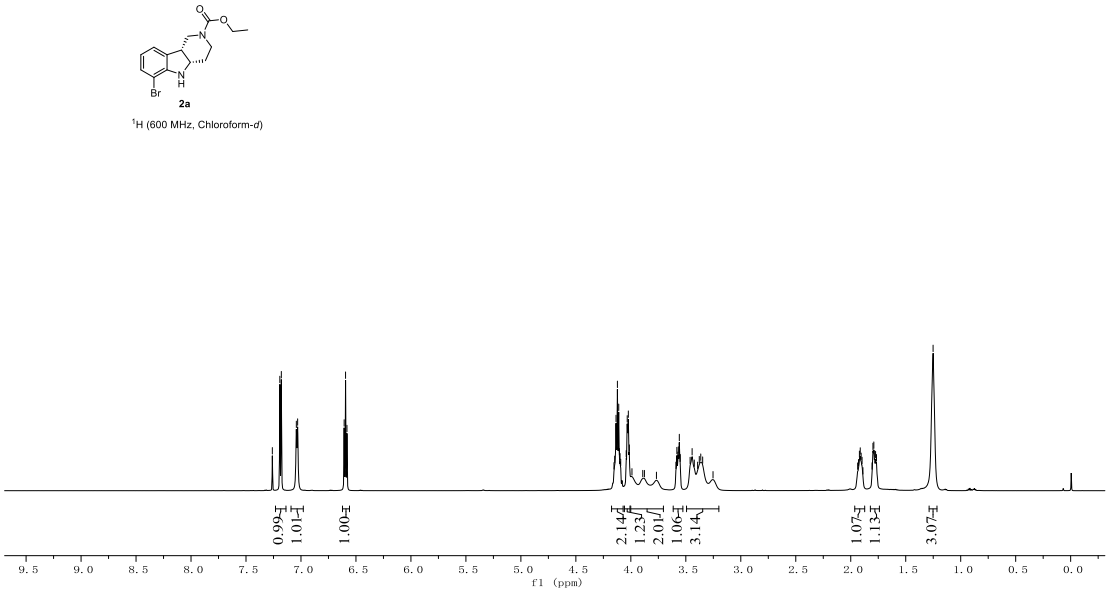

8.46
7.36
7.26
7.13
7.07
4.77
4.30
4.29
4.28
4.26
3.93
2.92
2.91
2.90
2.89
2.88
1.42
1.40
1.39
1.38
1.37
1.36
Et
1g
1H (600 MHz, Chloroform-d)
1.02
1.00
1.01
1.00
2.10
2.09
2.09
4.02
3.02
3.15
f1 (ppm)

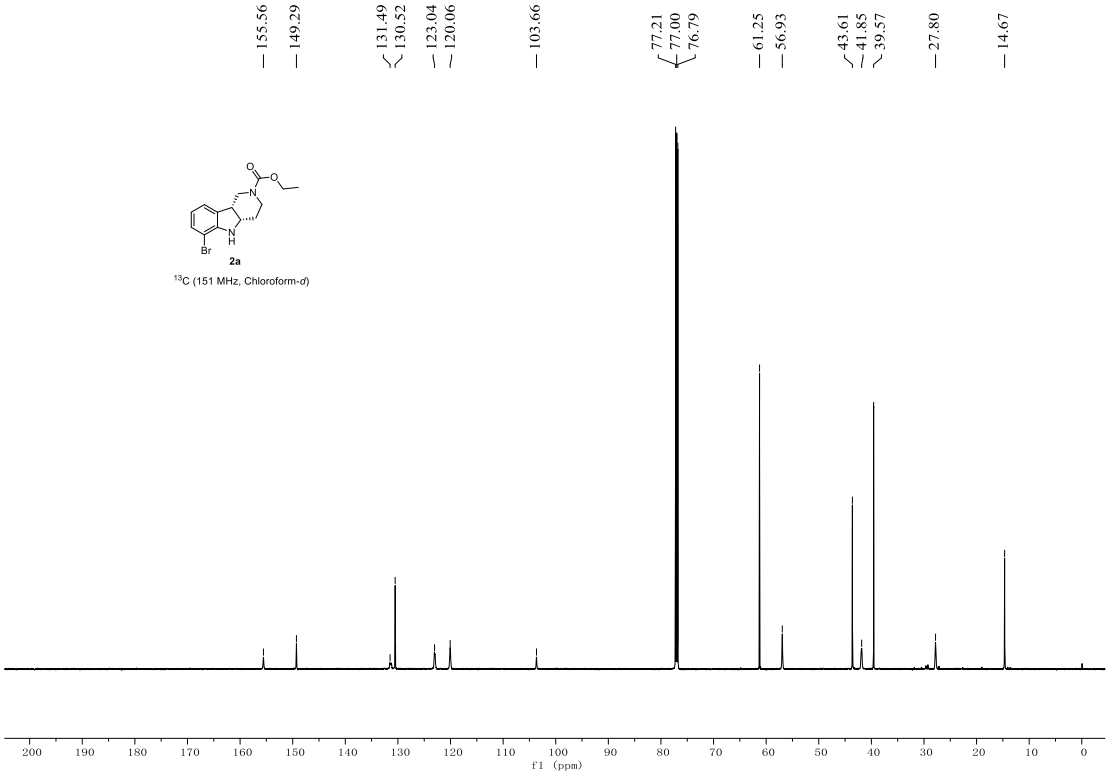

156.18
134.58
131.56
126.31
125.10
120.19
119.70
115.06
107.28
77.21
77.00
76.79
61.45
41.27
23.99
23.26
14.64
13.91
Et
1g
13C (151 MHz, Chloroform-d)
f1 (ppm)

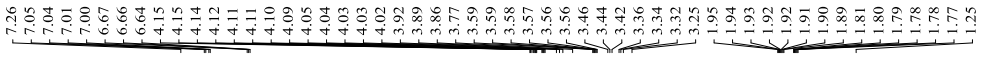

8.16
7.33
7.32
7.26
7.13
7.12
7.10
7.08
7.07
4.72
4.25
4.24
4.23
4.22
3.91
3.26
3.25
3.24
3.23
3.22
2.90
2.89
2.88
1.85
1.41
1.40
1.34
1.33
1.32
iPr
1h
1H (600 MHz, Chloroform-d)
1.04
1.00
0.99
1.01
2.10
2.06
2.12
1.04
2.10
6.05
3.04
f1 (ppm)


156.20
133.96
131.53
130.99
125.30
119.94
117.67
115.10
107.56
77.21
77.00
76.79
61.48
41.28
29.26
23.37
22.73
14.71
iPr
1h
13C (151 MHz, Chloroform-d)
f1 (ppm)


7.26
7.19
7.18
7.04
7.03
6.61
6.59
6.58
4.15
4.15
4.13
4.12
4.11
4.10
4.10
4.09
4.04
4.03
4.02
4.01
3.99
3.89
3.88
3.77
3.59
3.58
3.57
3.57
3.56
3.55
3.46
3.44
3.42
3.39
3.38
3.36
3.35
3.25
1.94
1.93
1.92
1.91
1.91
1.90
1.89
1.81
1.80
1.79
1.78
1.77
1.77
1.25


Br
2a
1H (600 MHz, Chloroform-d)
0.99
1.01
1.00
2.14
1.23
2.01
1.06
3.14
1.07
1.13
3.07
f1 (ppm)


155.56
149.29
131.49
130.52
123.04
120.06
103.66
77.21
77.00
76.79
61.25
56.93
43.61
41.85
39.57
27.80
14.67
Br
2a
13C (151 MHz, Chloroform-d)
f1 (ppm)


7.26
7.05
7.04
7.01
7.00
6.67
6.66
6.64
4.15
4.15
4.14
4.12
4.11
4.11
4.10
4.09
4.05
4.04
4.03
4.03
4.02
3.92
3.89
3.86
3.77
3.59
3.59
3.58
3.57
3.56
3.56
3.46
3.44
3.42
3.36
3.34
3.32
3.25
1.95
1.94
1.93
1.92
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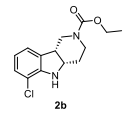
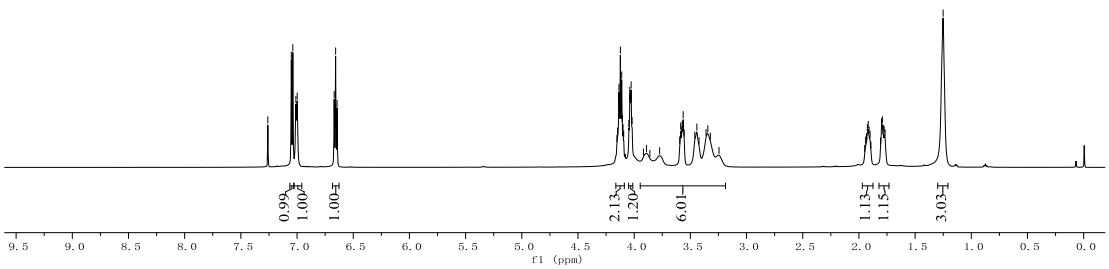
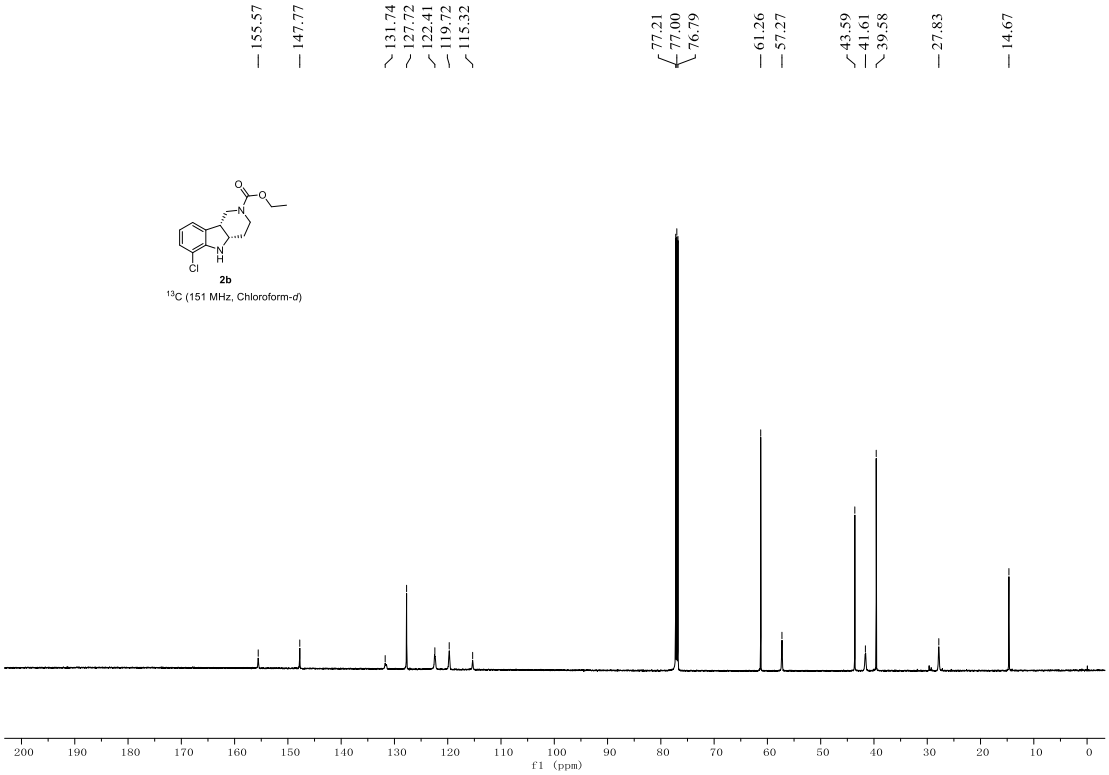
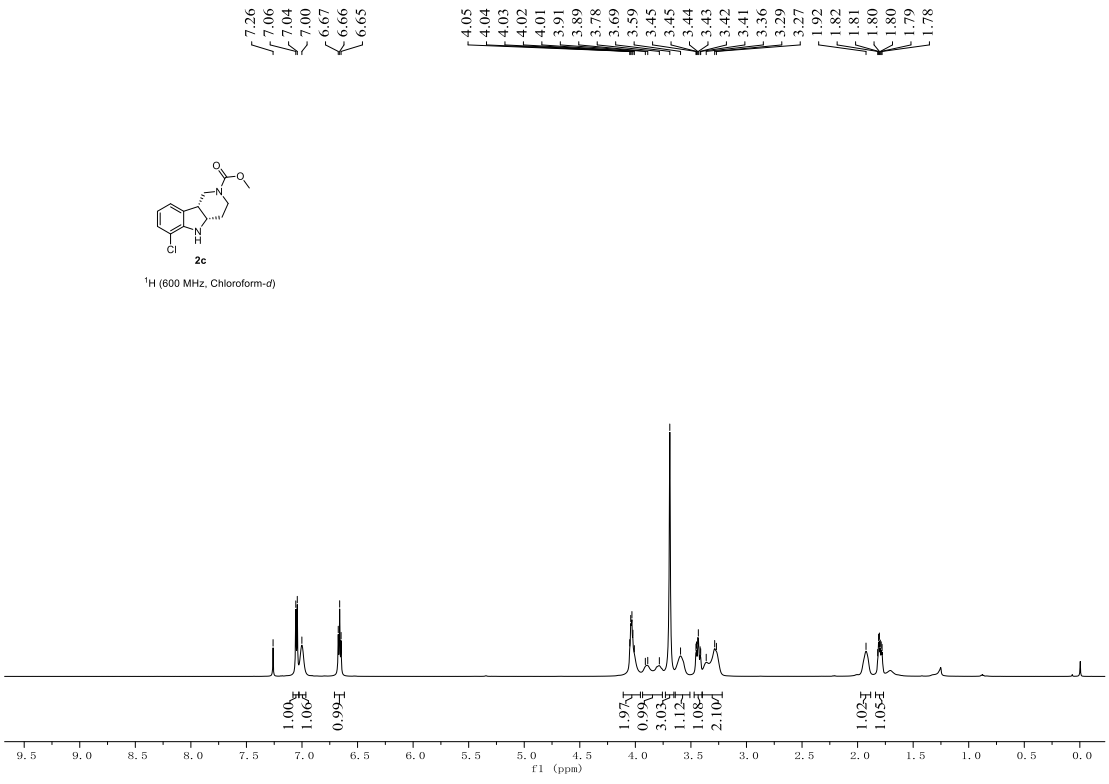
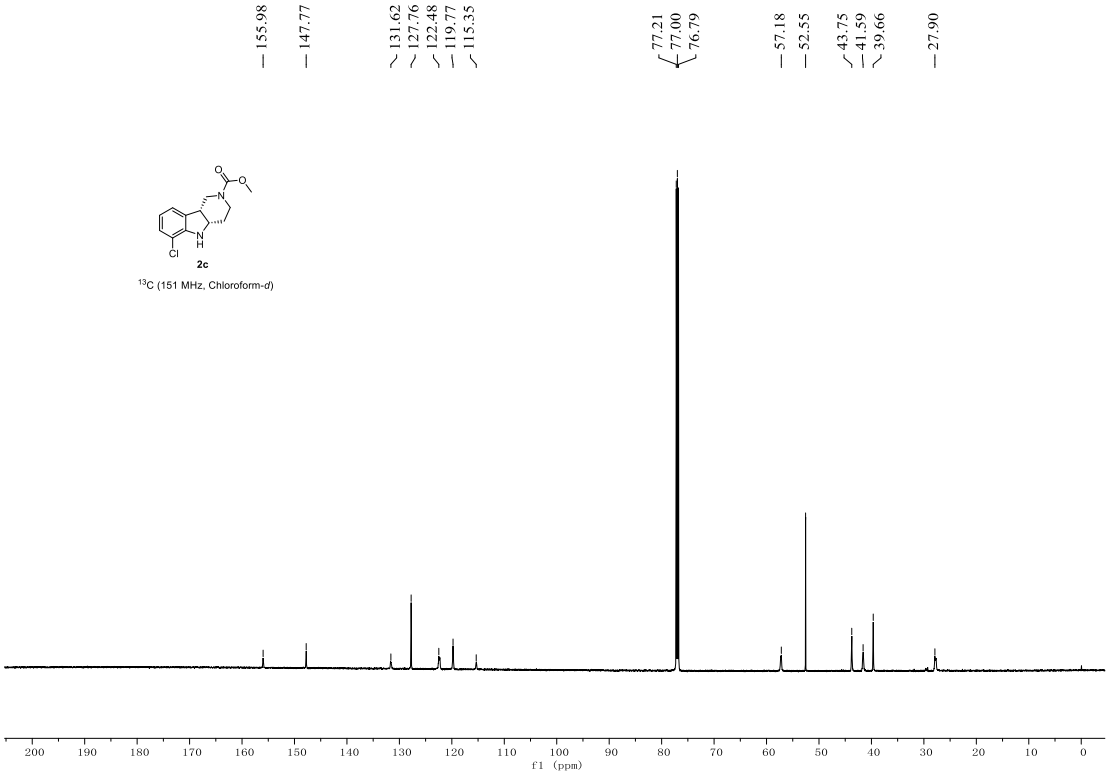
1.91
1.90
1.89
1.81
1.80
1.79
1.78
1.78
1.77
1.25

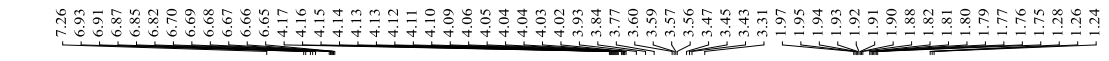

Cl
2b
1H (600 MHz, Chloroform-d)

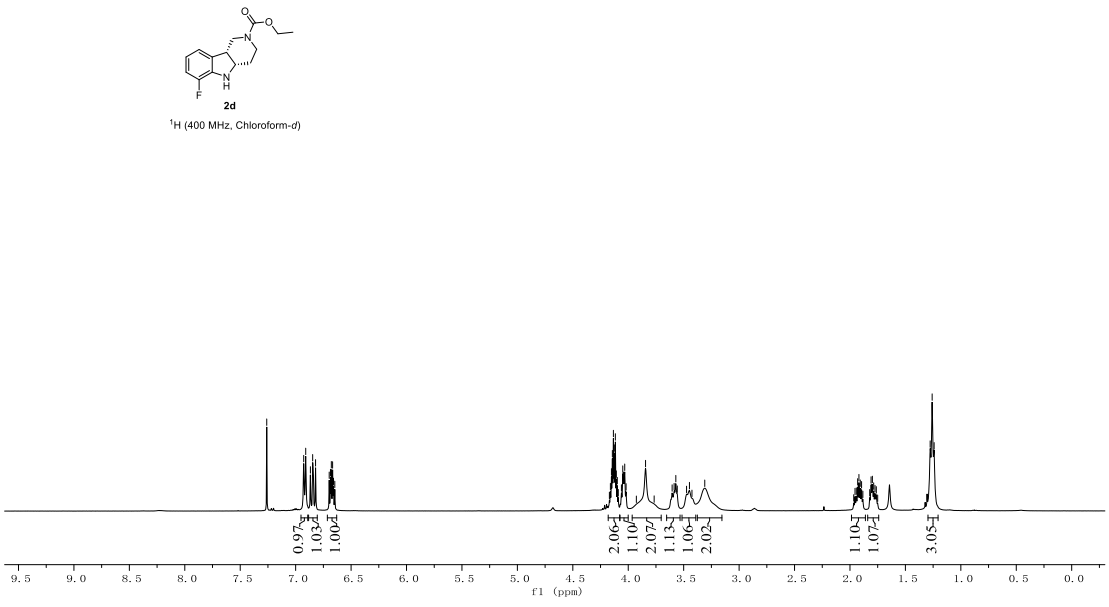

0.99
1.00
1.00
2.13
1.20
6.01
1.13
1.15
3.03
f1 (ppm)

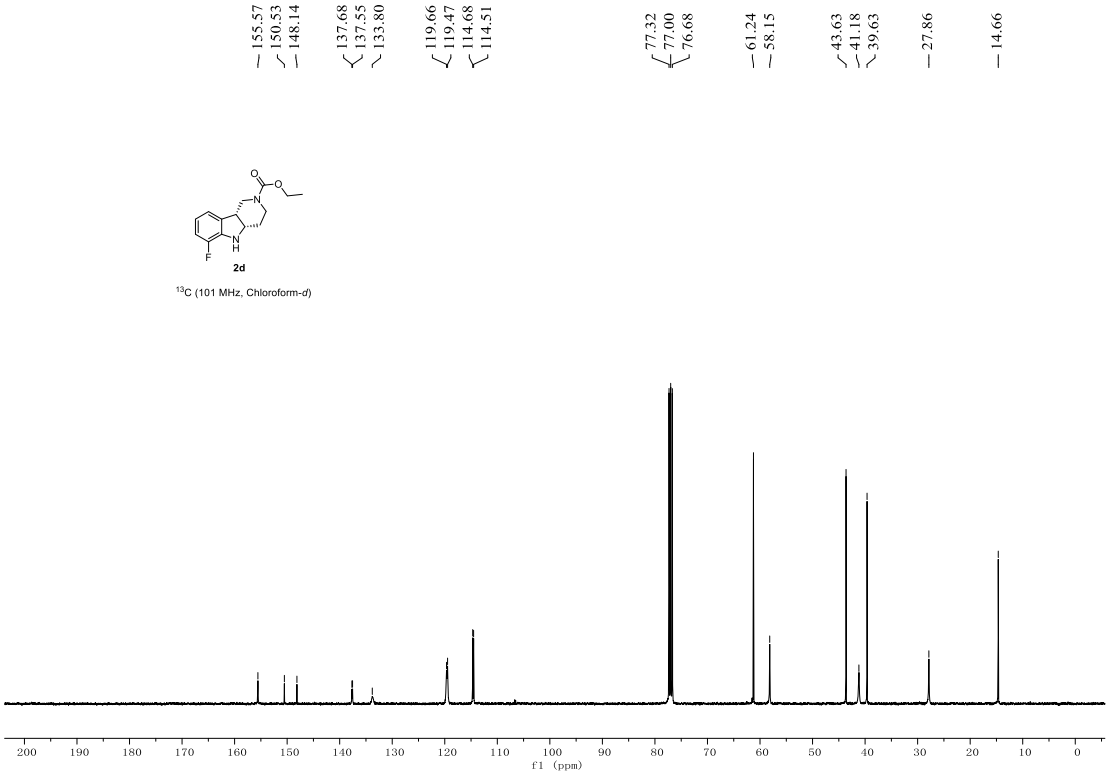

155.57
147.77
131.74
127.72
122.41
119.72
115.32
77.21
77.00
76.79
61.26
57.27
43.59
41.61
39.58
27.83
14.67
2b
13C (151 MHz, Chloroform-d)
f1 (ppm)

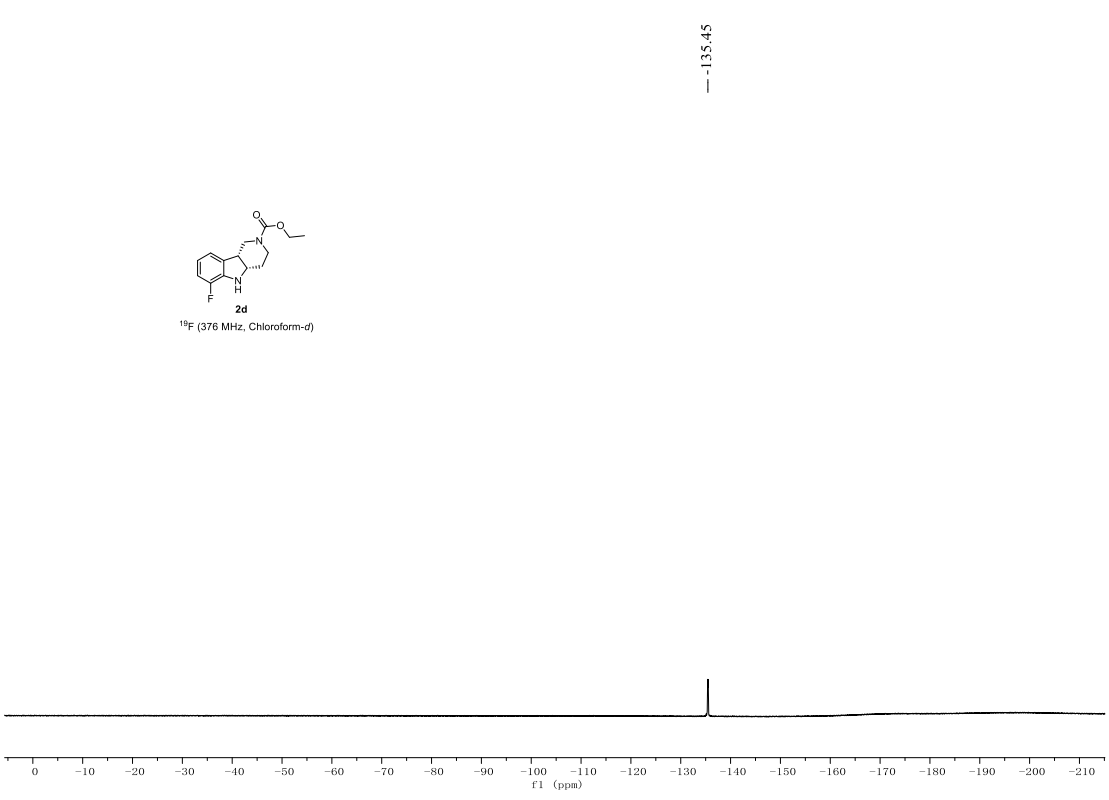

7.26
7.06
7.04
7.00
6.67
6.66
6.65
4.05
4.04
4.03
4.02
4.01
3.91
3.89
3.78
3.69
3.59
3.45
3.45
3.44
3.43
3.42
3.41
3.36
3.29
3.27
1.92
1.82
1.81
1.80
1.80
1.79
1.78
2c
1H (600 MHz, Chloroform-d)
1.00
1.06
0.99
1.97
0.99
3.03
1.12
1.08
2.10
1.02
1.05
f1 (ppm)

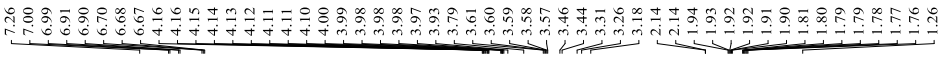

155.98
147.77
131.62
127.76
122.48
119.77
115.35
77.21
77.00
76.79
57.18
52.55
43.75
41.59
39.66
27.90
Cl
2c
13C (151 MHz, Chloroform-d)
f1 (ppm)

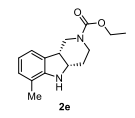

7.26
6.93
6.91
6.87
6.85
6.82
6.70
6.69
6.68
6.67
6.66
6.65
4.17
4.16
4.15
4.14
4.13
4.13
4.12
4.11
4.10
4.09
4.06
4.05
4.04
4.04
4.03
4.02
3.93
3.84
3.77
3.60
3.59
3.57
3.56
3.47
3.45
3.43
3.31
1.97
1.95
1.94
1.93
1.92
1.91
1.90
1.88
1.82
1.81
1.80
1.79
1.77
1.76
1.75
1.28
1.26
1.24


F
2d
1H (400 MHz, Chloroform-d)
0.97
1.03
1.00
2.06
1.10
2.07
1.13
1.06
2.02
1.10
1.07
3.05
f1 (ppm)


155.57
150.53
148.14
137.68
137.55
133.80
119.66
119.47
114.68
114.51
77.32
77.00
76.68
61.24
58.15
43.63
41.18
39.63
27.86
14.66
2d
13C (101 MHz, Chloroform-d)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

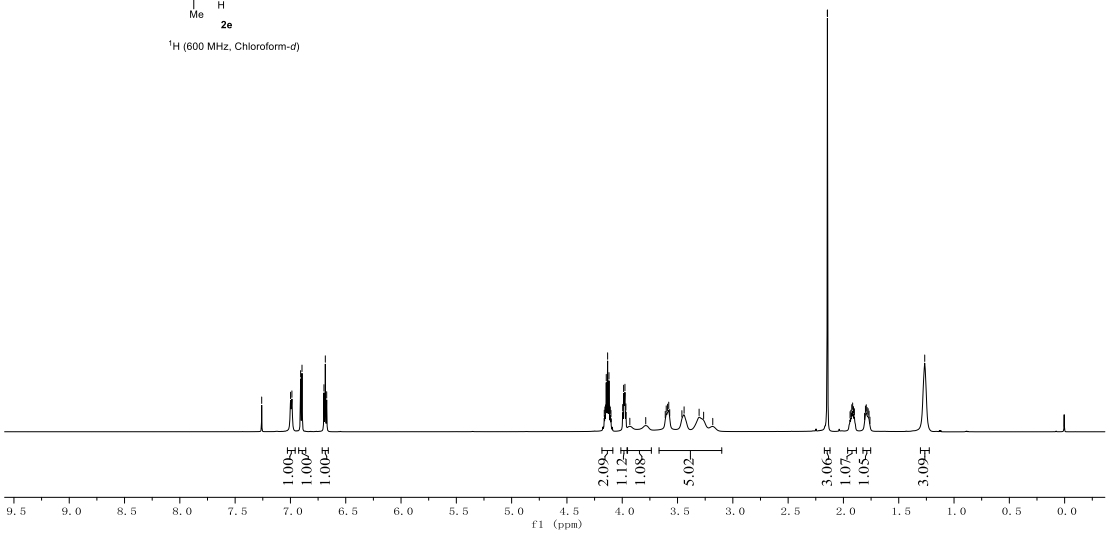

-135.45
2d
19F (376 MHz, Chloroform-d)
0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

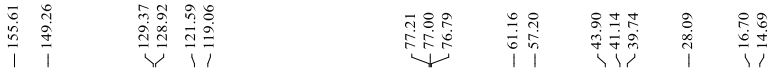


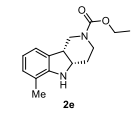


2e

^{1}H (600 MHz, Chloroform-*d*)

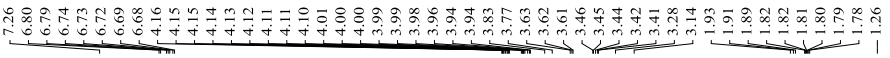


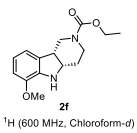




2e

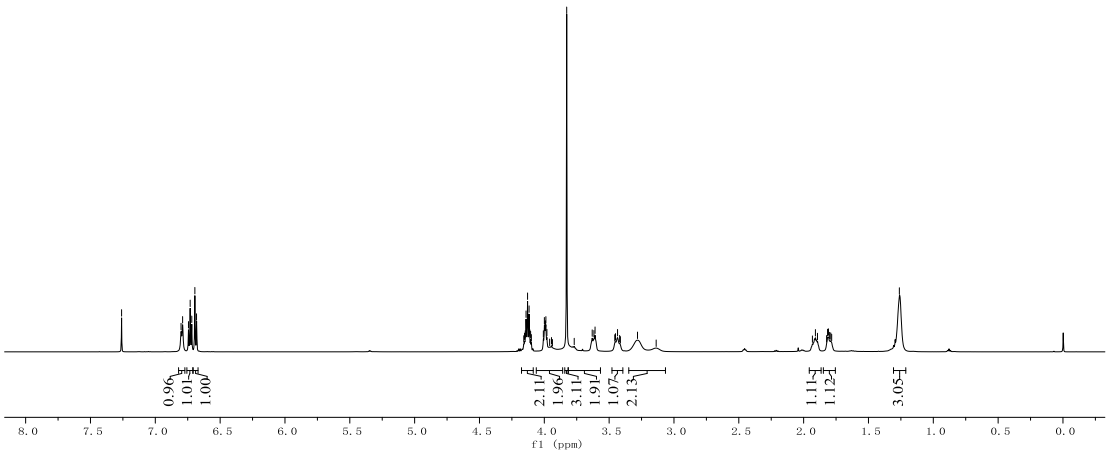
^{13}C (151 MHz, Chloroform-*d*)

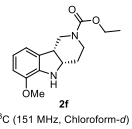




2f

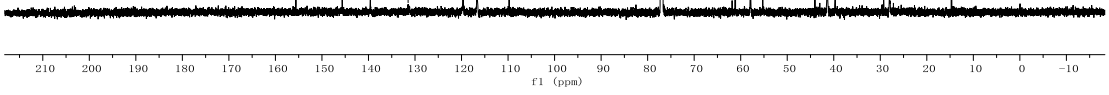
^{1}H (600 MHz, Chloroform-*d*)

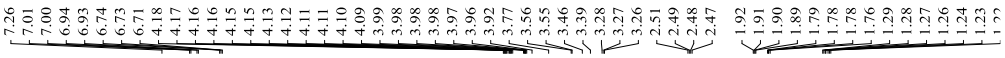


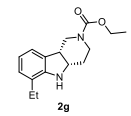


2f

^{13}C (151 MHz, Chloroform-*d*)

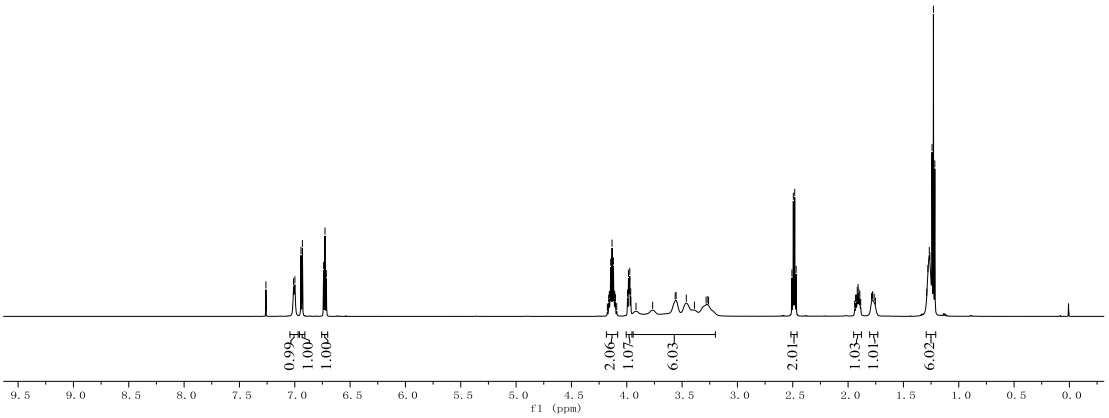


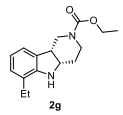




2g

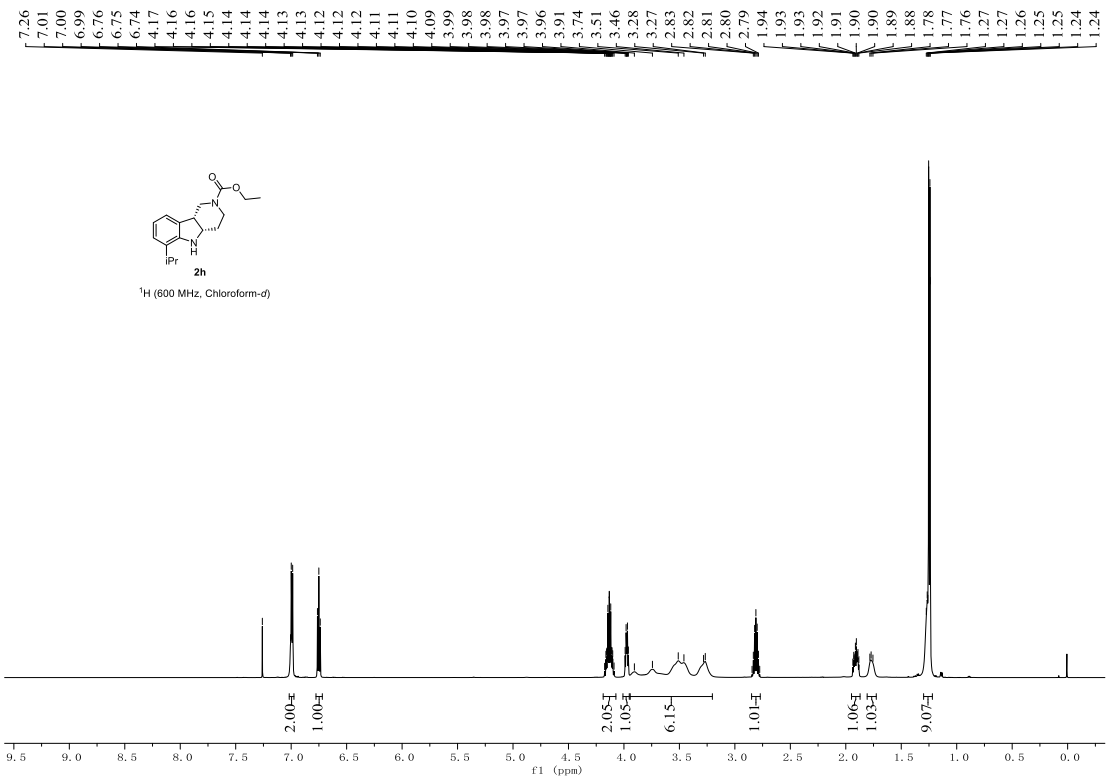
^{1}H (600 MHz, Chloroform-*d*)

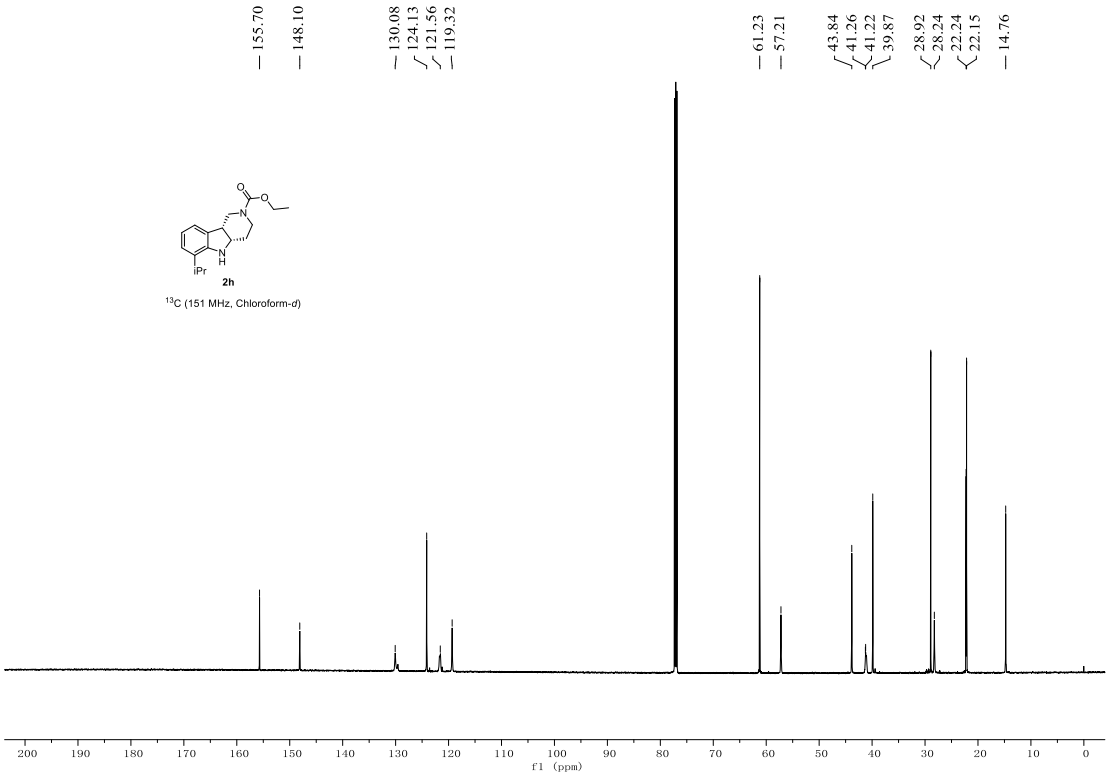


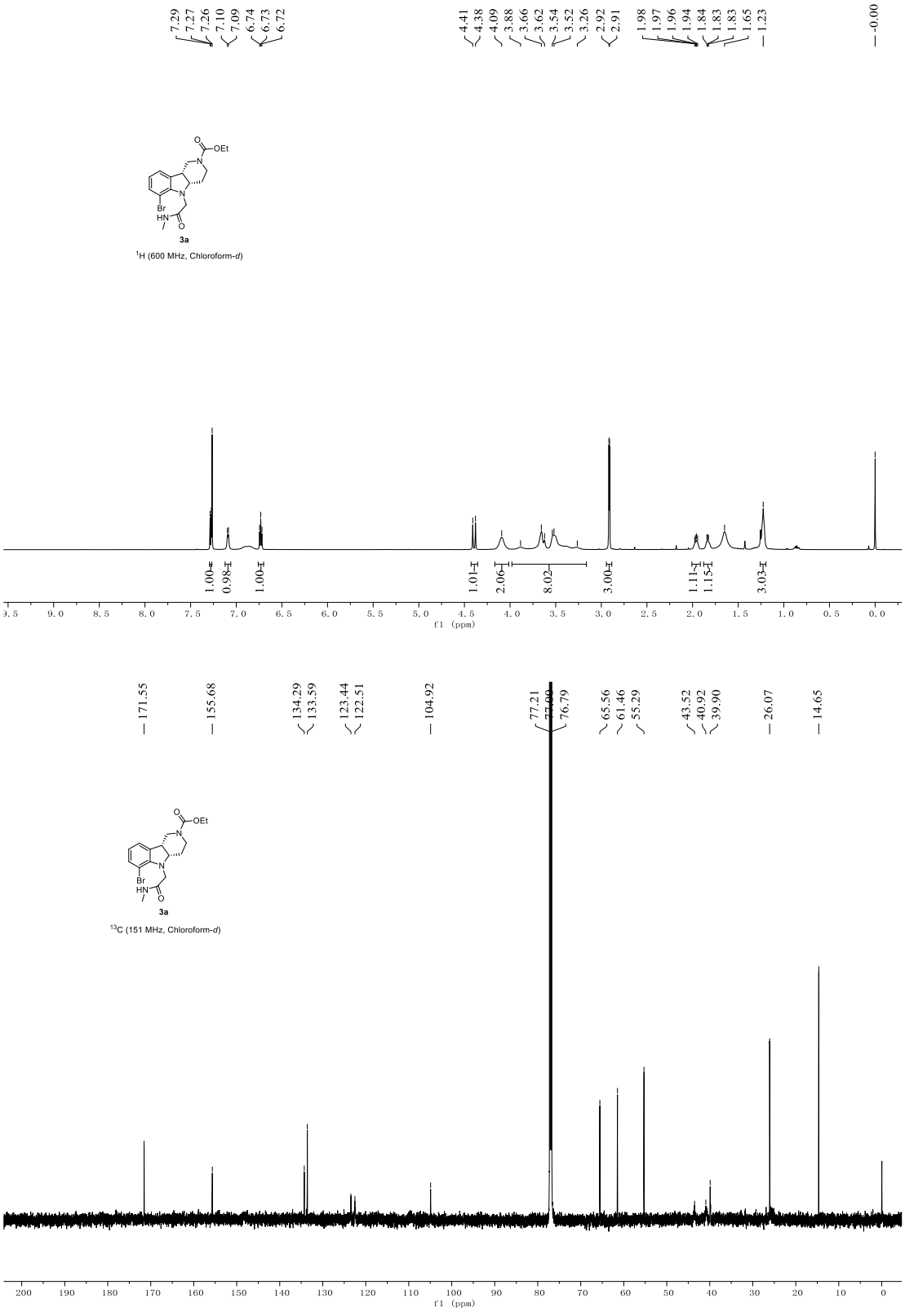


2g

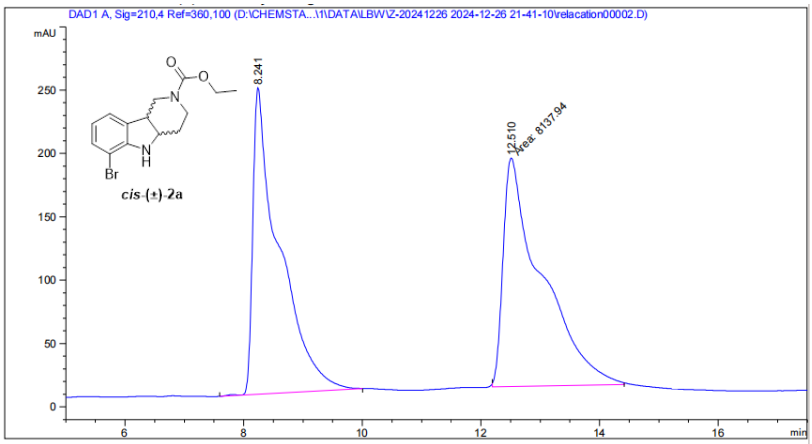
^{13}C (151 MHz, Chloroform-*d*)


7.26 7.01 7.00 6.99 6.76 6.75 6.74 4.17 4.16 4.16 4.15 4.14 4.14 4.14 4.13 4.12 4.12 4.12 4.11 4.11 4.10 4.09 3.99 3.98 3.98 3.97 3.97 3.96 3.91 3.74 3.51 3.46 3.28 3.27 2.83 2.82 2.81 2.80 2.79 1.94 1.93 1.93 1.92 1.91 1.90 1.90 1.89 1.88 1.78 1.77 1.76 1.27 1.27 1.26 1.25 1.25 1.24 1.24
iPr
N
H
O
O
2h
1H (600 MHz, Chloroform-d)
2.00
1.00
2.05
1.05
6.15
1.01
1.06
1.03
9.07
f1 (ppm)


155.70 148.10 130.08 124.13 121.56 119.32 61.23 57.21 43.84 41.26 41.22 39.87 28.92 28.24 22.24 22.15 14.76
iPr
N
H
O
O
2h
13C (151 MHz, Chloroform-d)
f1 (ppm)


7.29
7.27
7.26
7.10
7.09
6.74
6.73
6.72
4.41
4.38
4.09
3.88
3.66
3.62
3.54
3.52
3.26
2.92
2.91
1.98
1.97
1.96
1.94
1.84
1.83
1.83
1.65
1.23
-0.00
OEt
Br
HN
3a
1H (600 MHz, Chloroform-d)
1.00
0.98
1.00
1.01
2.06
8.02
3.00
1.11
1.15
3.03
f1 (ppm)
171.55
155.68
134.29
133.59
123.44
122.51
104.92
77.21
77.00
76.79
65.56
61.46
55.29
43.52
40.92
39.90
26.07
14.65
OEt
Br
HN
3a
13C (151 MHz, Chloroform-d)
f1 (ppm)

V Chiral HPLC analysis

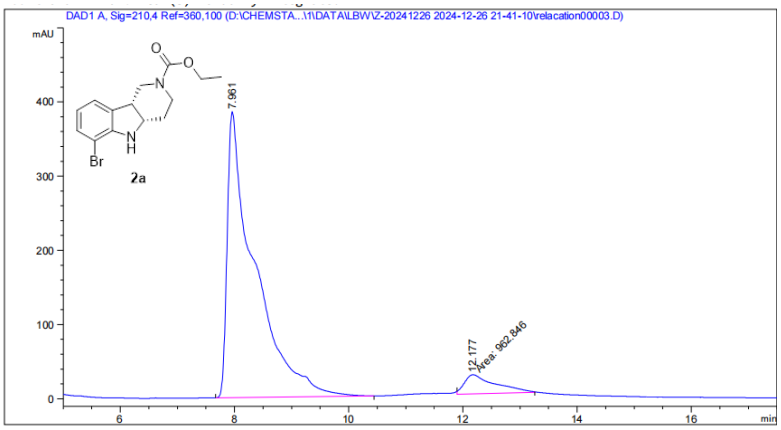



```
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.241 BB    0.4050 7443.57373  241.86877  47.7718
   2  12.510 MM    0.7522 8137.93750  180.31686  52.2282
```

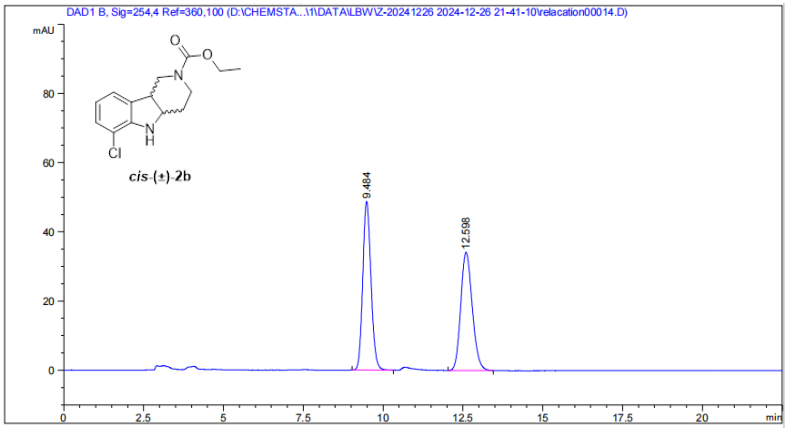



```
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.961 BB    0.4346 1.28227e4   384.99167  93.0155
   2  12.177 MM    0.6223  962.84650   25.78707   6.9845
```

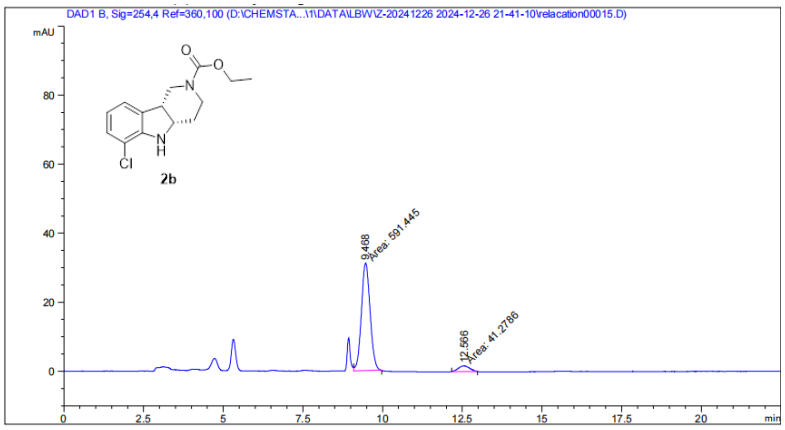



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.484 BB    0.2771  872.78882   48.69948  50.4419
   2  12.598 BB    0.3926  857.49628   34.19510  49.5581
```

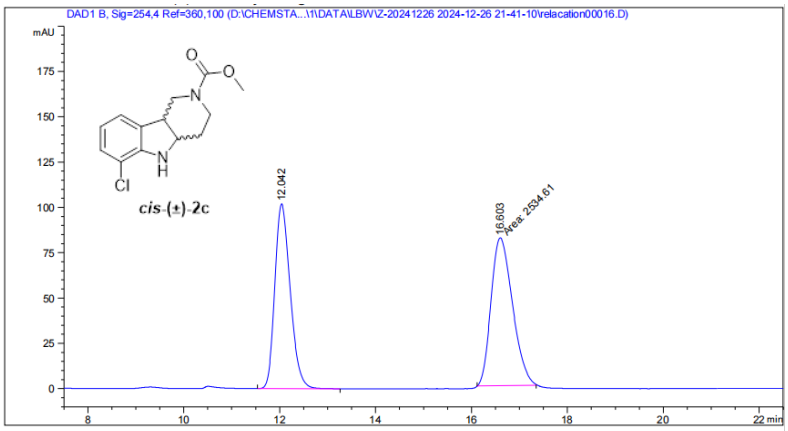



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.468 MM    0.3168  591.44482   31.11912  93.4760
   2  12.566 MM    0.4141   41.27860    1.66140   6.5240
```

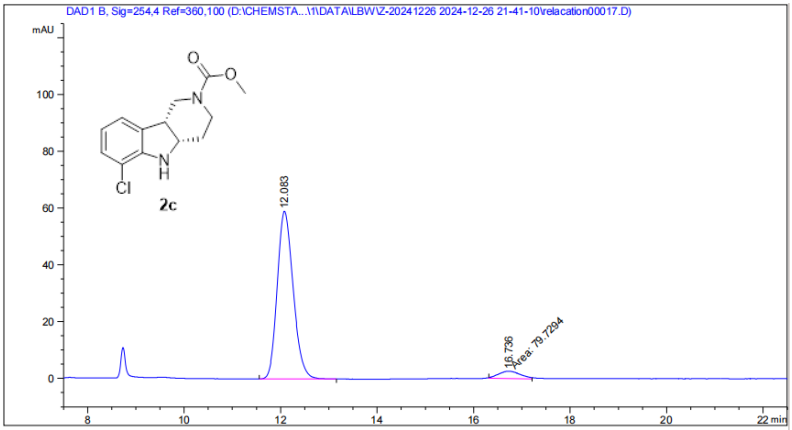



```
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.042 BB    0.3444 2275.42896  101.95937  47.3059
   2  16.603 MM    0.5173 2534.60815   81.66407  52.6941
```

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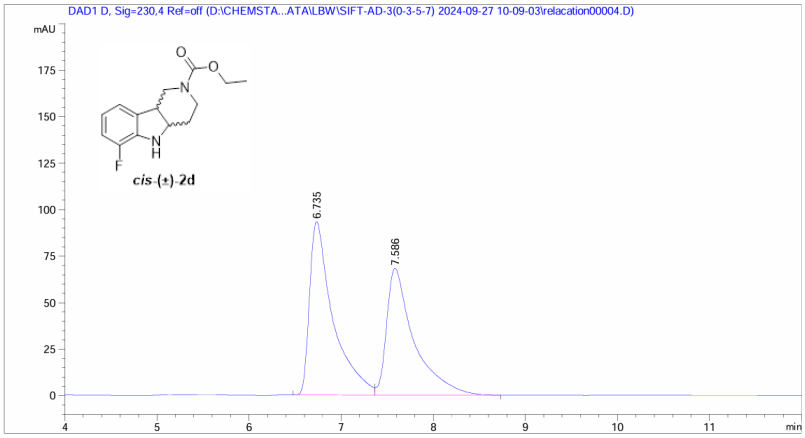
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.083 BB    0.3540 1357.79626   59.09912  94.4537
   2  16.736 MM    0.5219   79.72942    2.54598   5.5463
```

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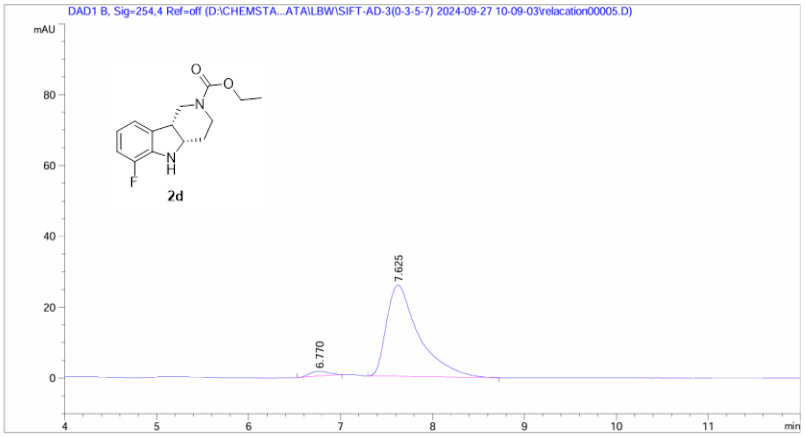
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=230,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.735 BV    0.2521 1645.23657   93.11320  53.9597
   2   7.586 VB    0.2944 1403.77051   68.11860  46.0403
```

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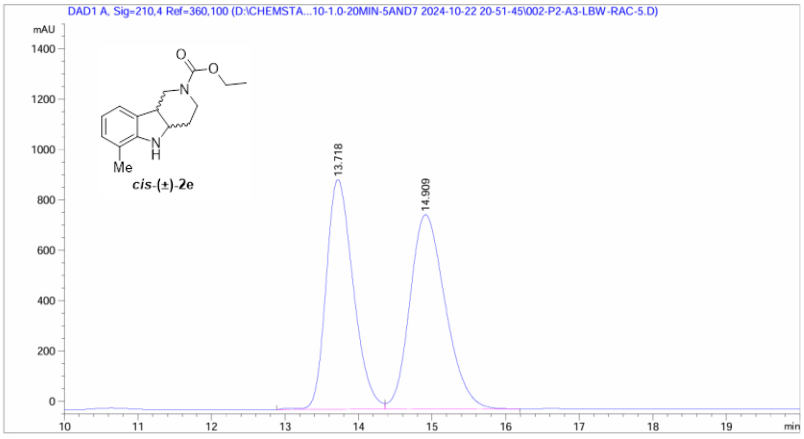
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.770 BB    0.2318   19.52233    1.34097   3.0163
   2   7.625 BB    0.3580  627.69568   25.78396  96.9837
```

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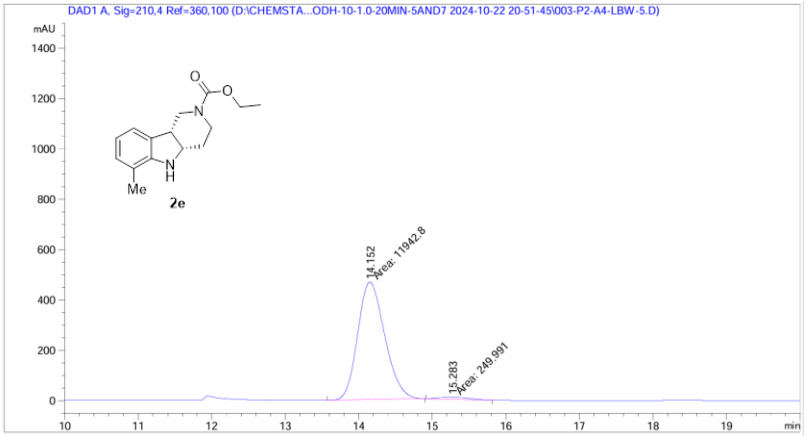
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  13.718 VV R  0.3960 2.33852e4   913.19647  47.4302
   2  14.909 VB    0.5211 2.59192e4   773.09369  52.5698
```

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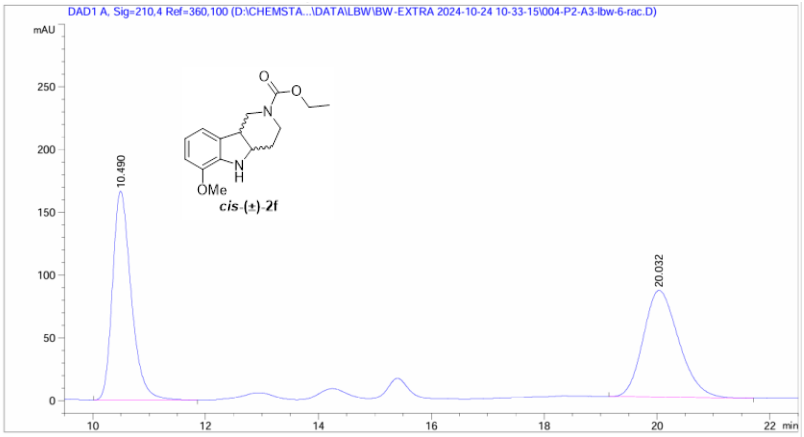
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.152 MM    0.4263 1.19428e4   466.88077  97.9497
   2  15.283 MM    0.4582  249.99060    9.09393   2.0503
```

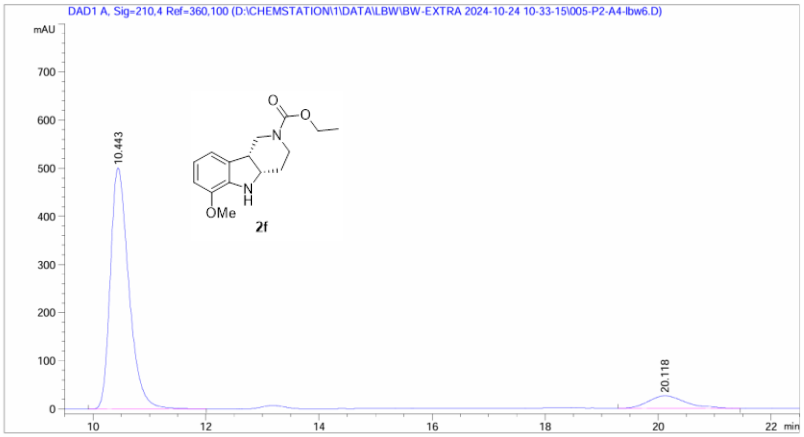



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.490 BB    0.3526 3834.98730  166.54272  50.7891
   2  20.032 BB    0.6653 3715.82153   85.12731  49.2109
```

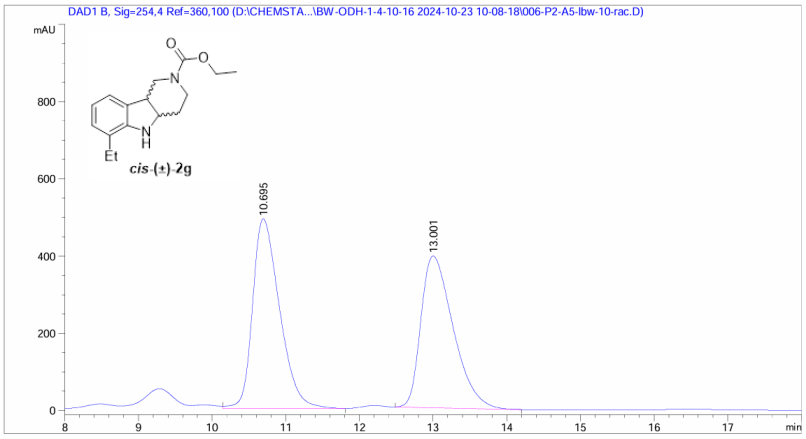



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.443 BB    0.3483 1.14382e4   501.19318  90.5835
   2  20.118 BB    0.6272 1189.04028   25.92179   9.4165
```

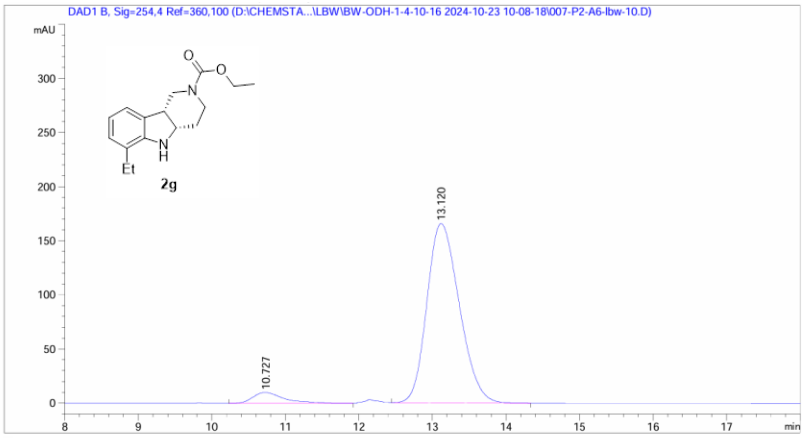



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|---------|---------|--------|
   1  10.695 VB    0.3892 1.25151e4   491.31598  51.1826
   2  13.001 BB    0.4708 1.19368e4   392.49207  48.8174
```

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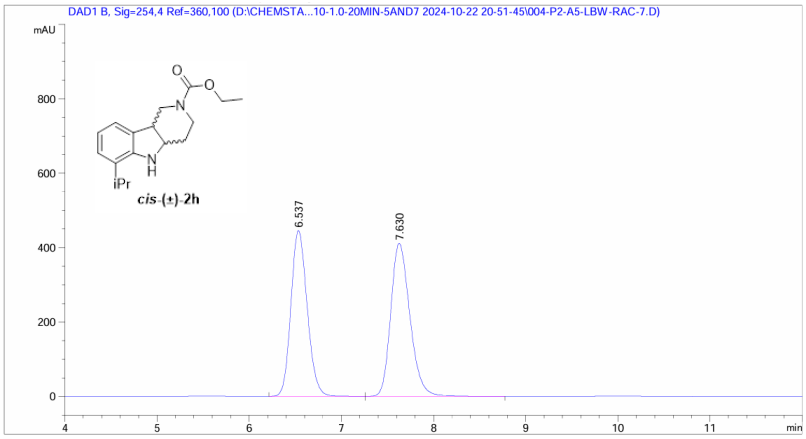
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|---------|---------|--------|
   1  10.727 BB    0.4465  305.14499   10.15657   5.6793
   2  13.120 BB    0.4791 5067.76758  165.57484  94.3207
```

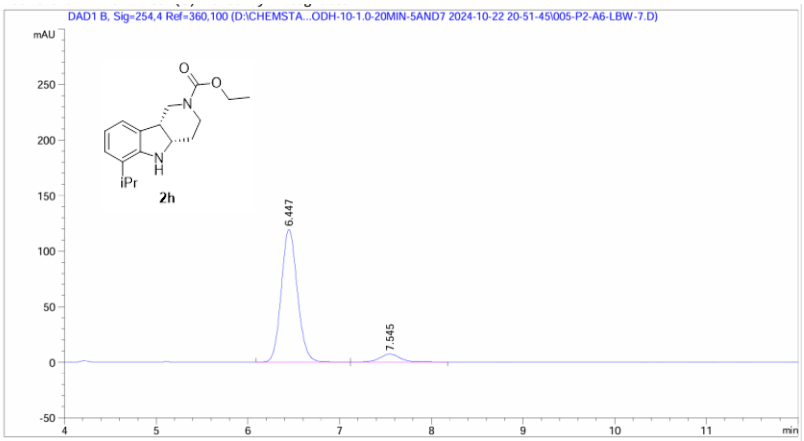



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.537 BB    0.1908 5444.59473  444.97366  47.8712
   2   7.630 BB    0.2244 5928.82080  410.85803  52.1288
```

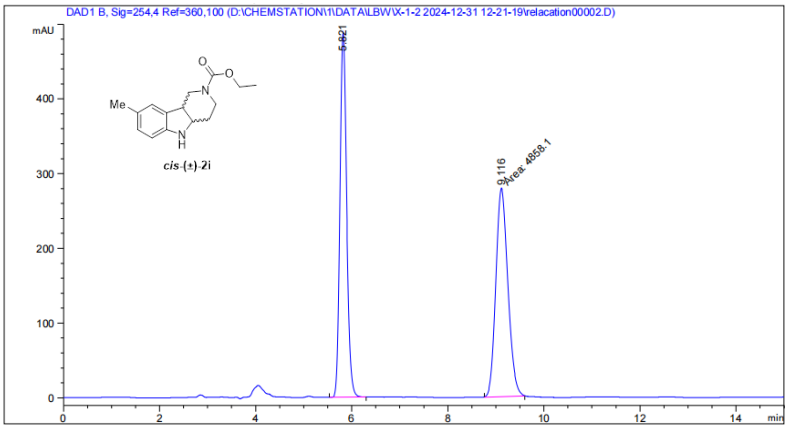



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.447 BB    0.1881 1455.00330  119.44545  92.6716
   2   7.545 BB    0.2367  115.06023    7.26898   7.3284
```

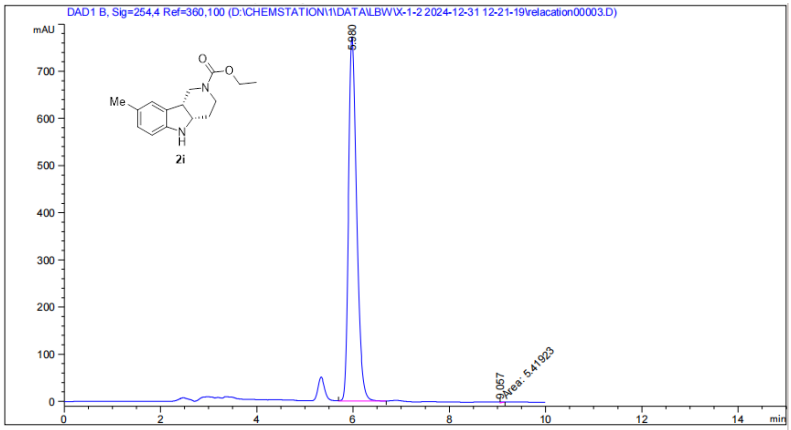



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.821 BB    0.1507 4708.04346  487.27863  49.2157
   2   9.116 MM    0.2900 4858.10449  279.16730  50.7843
```

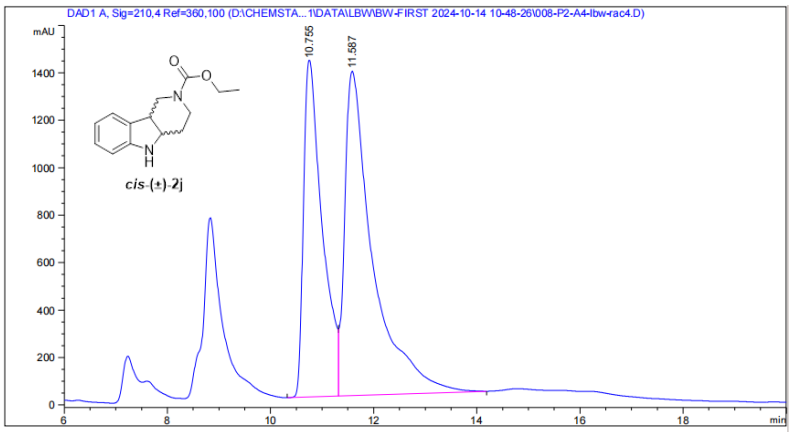



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.980 VB    0.1788 9030.05566  769.91046  99.9400
   2   9.057 MM    0.0386    5.41923    2.29465   0.0600
```

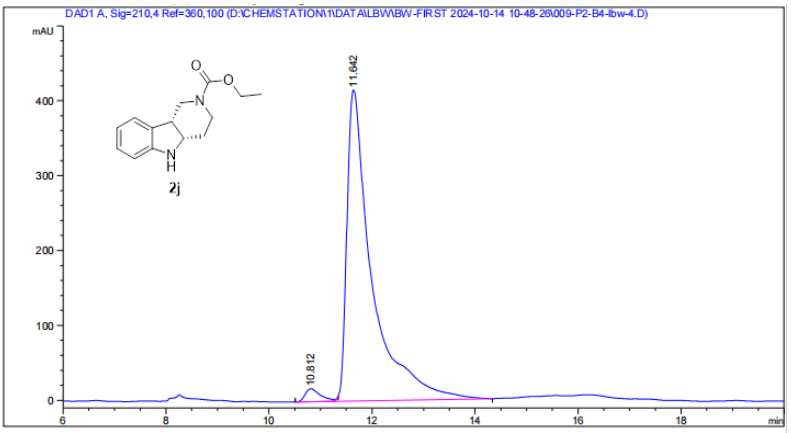



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.755 BV    0.3629 3.56388e4  1419.48975  40.7334
   2  11.587 VB    0.5345 5.18540e4  1367.06140  59.2666
```

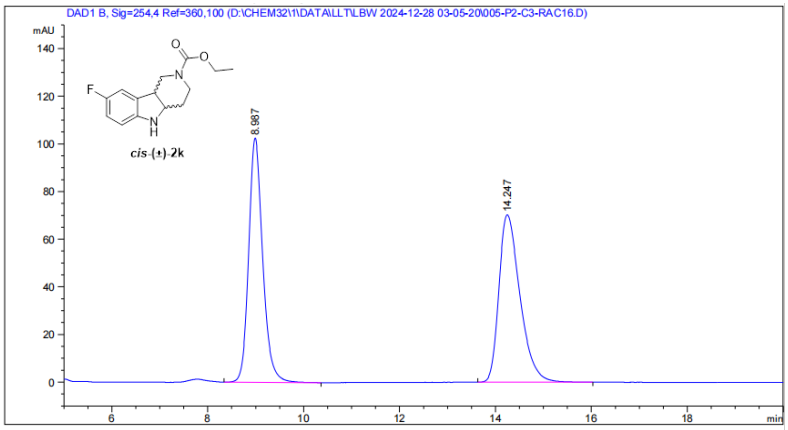



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.812 BV E  0.3071  362.35873   17.39060   2.5340
   2  11.642 VB R  0.4737 1.39374e4   415.10941  97.4660
```

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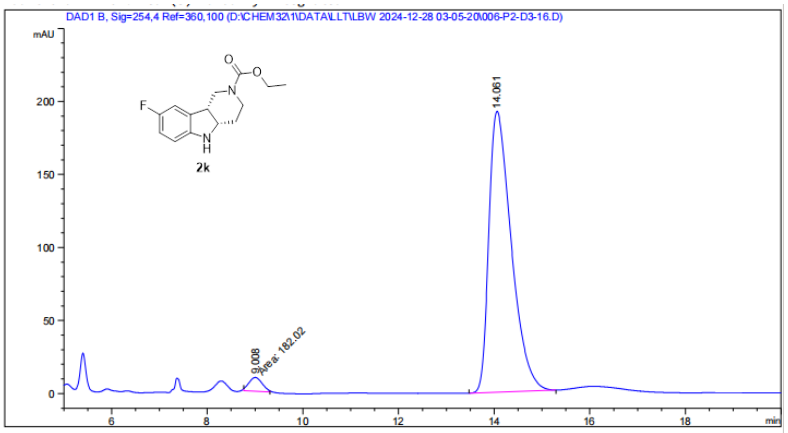
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.987 BB    0.3085 2079.96948  102.58839  49.2834
   2  14.247 BB    0.4654 2140.45679   70.25659  50.7166
```

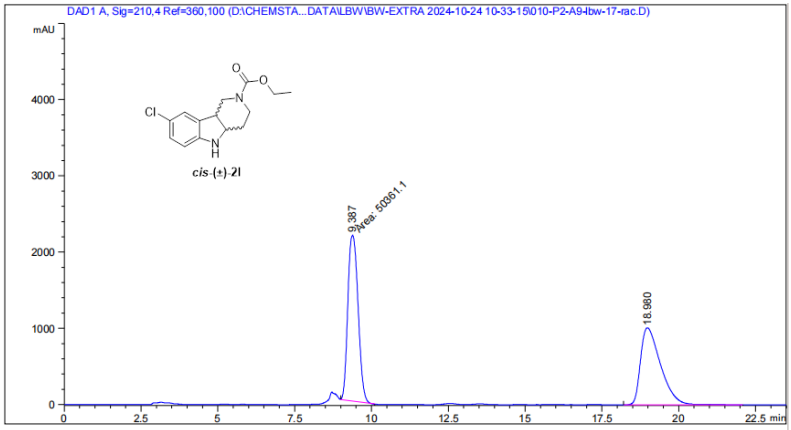



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.008 MM    0.3192  182.01999    9.50399   2.8305
   2  14.061 BB    0.5011 6248.73242  192.28784  97.1695
```

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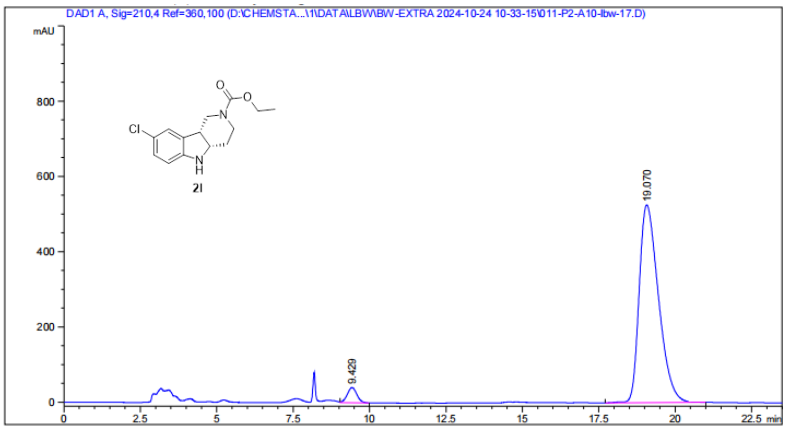
=====================================================================
                       Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.387 MM    0.3861 5.03611e4  2174.05957  52.4675
   2  18.980 BB    0.6770 4.56242e4  1010.02954  47.5325
```

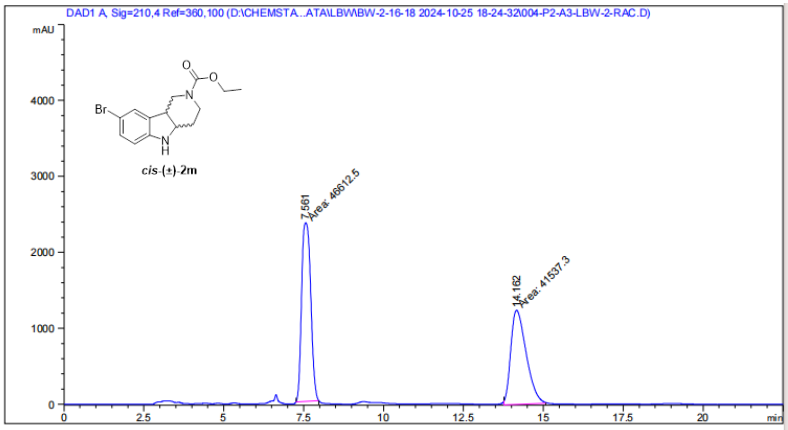



```
=====================================================================
                       Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.429 VB    0.3395  876.73853   40.35099   3.6601
   2  19.070 BB    0.6702 2.30770e4   525.60742  96.3399
```

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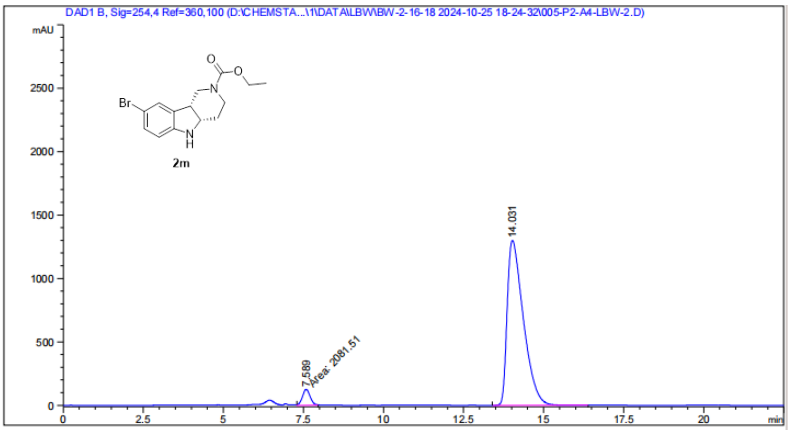
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.561 MM    0.3303 4.66125e4  2351.97534  52.8787
   2  14.162 MM    0.5588 4.15373e4  1238.78174  47.1213
```

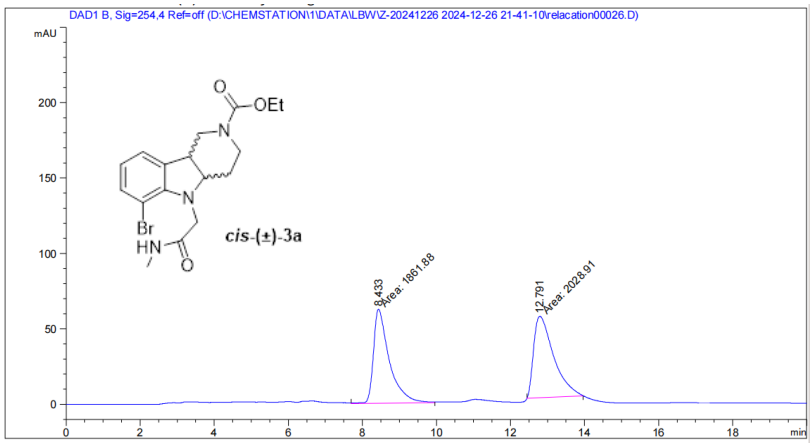



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.589 MM    0.2776 2081.50562  124.97233   4.3649
   2  14.031 BB    0.5334 4.56057e4  1299.62354  95.6351
```

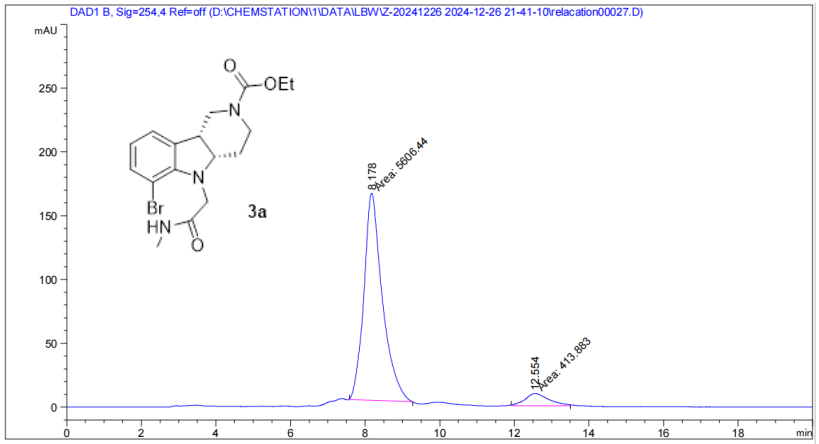



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.433 MM    0.4968 1861.88293   62.45689  47.8536
   2  12.791 MM    0.6262 2028.90869   54.00057  52.1464
```




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.178 MM    0.5756 5606.44092  162.34908  93.1252
   2  12.554 MM    0.7290  413.88312    9.46211   6.8748
```

VI References

1) Zheng, L.-S.; Yin, C.; Wang, F. Enantioselective synthesis of cis-hexahydro-γ-carboline derivatives via Ir-catalyzed asymmetric hydrogenation. *Chem. Commun.* 2022, **58**, 3286-3289.