

**Asymmetric Construction of Polycyclic Indole derivatives
with Different Ring Connectivity by Organocatalysis
Triggered Two-step Sequence**

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A. General information

The ^1H and ^{13}C NMR spectra were recorded at 500 MHz for ^1H and at 125 MHz for ^{13}C . The chemical shifts (δ) for ^1H and ^{13}C are given in ppm relative to residual signals of the solvents (CDCl_3 at 7.26 ppm ^1H NMR, 77.16 ppm ^{13}C NMR.). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High-resolution mass spectra (HRMS) were obtained from the Waters Q-ToF Ultima Global. X-ray data were obtained from Zhongke chemical technology service center. Optical rotations are reported as follows: $[\alpha]_D^{20}$ (c in g per 100 mL, solvent: CHCl_3).

Note: NMR signals containing common solvent contaminants were list. H_2O in CDCl_3 at 1.56 ppm ^1H NMR; ethyl acetate in CDCl_3 at 2.05 (s), 4.12 (q), 1.26 (t) ppm ^1H NMR; dichloromethane in CDCl_3 at 5.30 (s) ppm ^1H NMR; acetone in CDCl_3 at 2.17 (s) ppm ^1H NMR; diethyl ether in CDCl_3 at 1.21 (t), 3.48 (q), ppm ^1H NMR

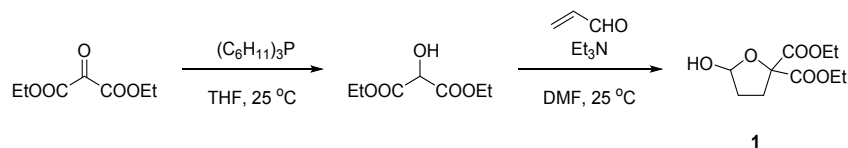
All the reactions were set up under air and using freshly distilled solvents, without any precautions to exclude moisture, unless otherwise noted open air chemistry on the bench-top. Chromatographic purification of products was accomplished using force-flow chromatography (FC) on silica gel (300-400 mesh). For thin layer chromatography (TLC) analysis throughout this work, Merck pre-coated TLC plates (silica gel 60 GF254, 0.25 mm) were used, using UV light as the visualizing agent and an phosphomolybdic acid or basic aqueous potassium permanganate (KMnO_4) as stain developing solutions. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator.

HPLC analyses on chiral stationary phase were performed on an Hitachi Chromaste. Daicel Chiralpak IA, IB, or IC columns with *n*-hexane/*i*-PrOH as the eluent were used. HPLC traces were compared to racemic samples which prepared by mixture of two enantiomeric final products obtained using (*S*) and (*R*) catalyst.

Commercial reagents and solvents were purchased from Sigma Aldrich, Fluka, and Alfa Aesar used as received, without further purification. (*E*)-2-(2-nitrovinyl)-1*H*-indoles (**2a**) were prepared from 1*H*-indole-2-carbaldehydes¹. The *tert*-butyl (*E*)-3-(2-nitrovinyl)-1*H*-indole-1-carboxylate were prepared from *tert*-butyl 3-formyl-1*H*-indole-1-carboxylate².

1. Enders, D.; Wang, C.; Yang, X.; Raabe, G., One-pot organocatalytic asymmetric synthesis of 1*H*-pyrrolo[1,2*a*]indol-3(2*H*)-ones via a Michael-hemiaminalization-oxidation sequence. *Synlett* **2011**, (4), 469-472.
2. Feng, H.-X.; Tan, R.; Liu, Y.-K., An Efficient One-Pot Approach to the Construction of Chiral Nitrogen-Containing Heterocycles under Mild Conditions. *Org. Lett.* **2015**, *17* (15), 3794-3797.

B. The synthesis of the substrate **1**



General procedure: A glass vial equipped with a magnetic stirring bar was charged with diethyl ketomalonate (8.0 mmol, 1.0 equiv) and tricyclohexyl phosphine (12.0 mmol, 1.5 equiv) in THF (15.0 mL, THF = tetrahydrofuran) at 25 °C . After the reaction was completed, solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel to provide the product diethyl 2-hydroxymalonate. Then the product diethyl 2-hydroxymalonate (8.0 mmol, 1.0 equiv) and acrolein (12.0 mmol, 1.5 equiv) were respectively dissolved in DMF (12.0 ml, DMF = N,N-dimethylformamide.) at 25 °C, and then Et₃N (0.16 mmol, 0.2 equiv, Et₃N = triethylamine) was added to the reaction mixtures at the same temperature. After the reaction was completed, water was added and the aqueous layer was extracted with ethyl acetate twice. The combined organic extracts were washed with brine, dried by Na₂SO₄, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to provide the desired product **1** (1.04 g, 56% in 2 steps).

C. Optimization of the reaction conditions

C1. Optimization of the Michael Addition

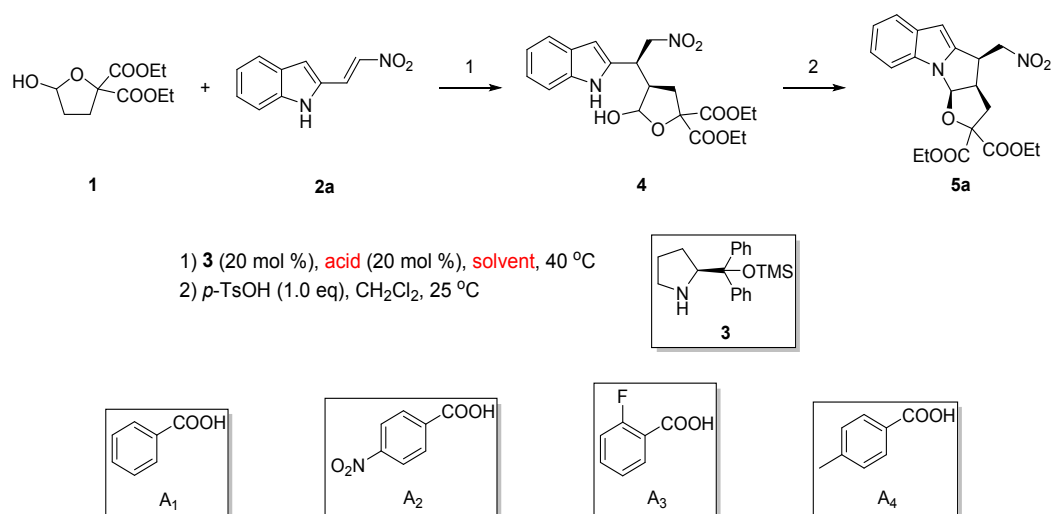
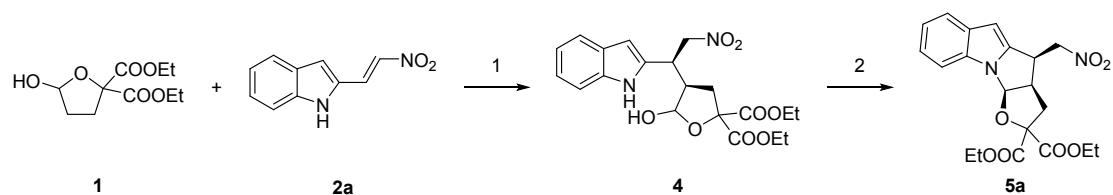


Table S1. Optimization of the Michael Addition^a

Entry	Solvent	Acid	t (h) ^b	Yield (%) ^c	ee (%) ^d	dr ^e
1	MeOH	A ₁	20	28	>99	>20:1
2	MeCN	A ₁	12	42	>99	>18:1
3	tetrahydrofuran	A ₁	12	50	>99	>20:1
4	CHCl ₃	A ₁	16	49	>99	>18:1
5	toluene	A ₁	10	70	>99	>20:1
6	toluene	A ₂	14	62	>99	>20:1
7	toluene	A ₃	14	54	>99	>20:1
8	toluene	A ₄	16	49	>99	>20:1

[a] Unless otherwise specified, all reactions were carried out using **1** (0.20 mmol, 1.0 equiv), **2a** (0.24 mmol, 1.2 equiv) in solvent (0.6 mL) with **3** (20 mol%) and **acid** (20 mol%) at 40 °C. After workup, the mixture was purified by flash chromatography on silica gel to afford **4**. Compound **4** were respectively dissolved in redistilled CH₂Cl₂ (0.10 mmol in 1 mL) at 25 °C. *p*-TsOH (1.0 eq) was added, After full conversion of the second step, the residue was purified by flash chromatography on gel to give product **5a**. [b] For the first step. [c] Isolated yield of **5a** over two steps. [d] Determined by HPLC analyses of isolated compound **5a** on chiral stationary phases. [e] Determined by ¹H NMR. MeOH = methanol; MeCN = acetonitrile; CHCl₃ = chloroform; *p*-TsOH = *p*-Toluenesulfonic acid.

Optimization of the catalyst



1) **cat.** (20 mol %), **A₁** (20 mol %), toluene, 40 °C
 2) *p*-TsOH (1.0 eq), CH₂Cl₂, 25 °C

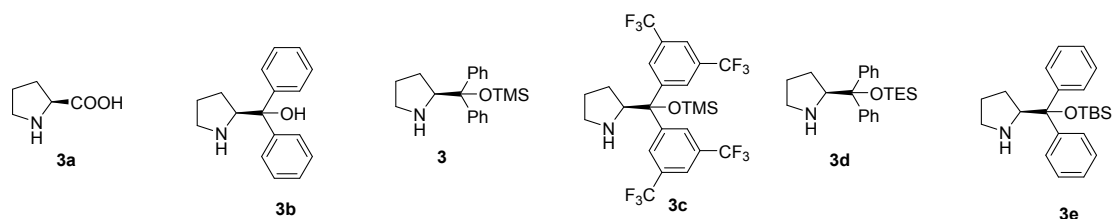


Table S2. Optimization of the catalyst ^a

Entry	Catalyst	Aci d	t (h)^b	Yield (%)^c	ee (%)^d	dr^e
1	3a	A ₁	24	32	-18	>20:1
2	3b	A ₁	12	51	92	>20:1
3	3	A ₁	10	71	>99	>20:1
4	3c	A ₁	32	49	95	>20:1
5	3d	A ₁	14	62	>99	>20:1
6	3e	A ₁	16	58	99	>20:1

[a] Unless otherwise specified, all reactions were carried out using **1** (0.20 mmol, 1.0 equiv), **2a** (0.24 mmol, 1.2 equiv) in solvent (0.6 mL) with **cat.** (20 mol%) and **acid** (20 mol%) at 40 °C. After workup, the mixture was purified by flash chromatography on silica gel to afford **4**. Compound **4** were respectively dissolved in redistilled CH₂Cl₂ (0.10 mmol in 1 mL) at 25 °C. *p*-TsOH (1.0 eq) was added, After full conversion of the second step, the residue was purified by flash chromatography on gel to give product **5a**. [b] For the first step. [c] Isolated yield of **5a** over two steps. [d] Determined by HPLC analyses of isolated compound **5a** on chiral stationary phases. TMS = trimethylsilyl; TES = triethylsilyl, TBS = *tert*-butyldimethylsilyl.

C2. Optimization of the second step

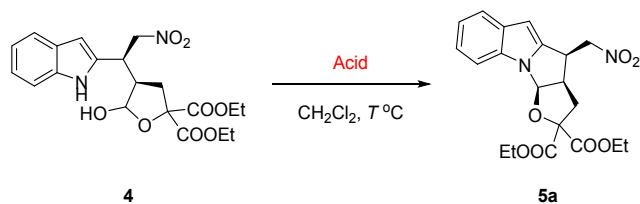


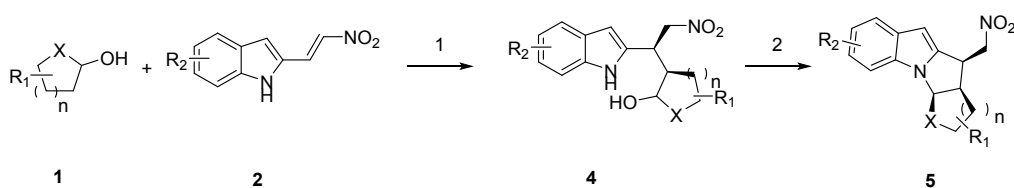
Table S3. Optimization of the second step^a

Entry	Acid	Tem (°C)	t (h)	Yield (%) ^b	ee (%) ^c
1	BF ₃ ·Et ₂ O (1.0 eq)	0	4	60	>99
2	trifluoroacetic acid (1.0 eq)	0	3	43	>99
3	triphenylphosphate (1.0 eq)	25	12	40	>99
4	methanesulfonic acid (1.0 eq)	25	0.5	29	>99
5	<i>p</i> -TsOH (1.0 eq)	0	24	64	>99
6	<i>p</i> -TsOH (0.4 eq)	25	12	65	>99
7	<i>p</i> -TsOH (0.8 eq)	25	6	69	>99
8	<i>p</i> -TsOH (1.0 eq)	25	2	76	>99

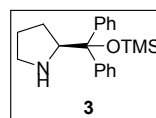
[a] Unless otherwise specified, all reactions were carried out using **4** (0.05 mmol, 1.0 equiv) in redistilled CH₂Cl₂ (1.0 mL) with **acid** at corresponding temperature. After workup, the mixture was purified by flash chromatography on silica gel to afford **5a**. [b] Isolated yield of **5a**. [c] Determined by HPLC analyses of isolated compound **5a** on chiral stationary phases. BF₃·Et₂O = boron trifluoride etherate

D. Scope of the reaction

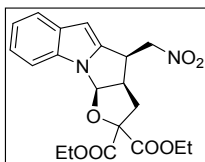
D1. Synthesis of product 5a



1) **3** (20 mol %), BA (20 mol %), toluene, 40 °C
2) *p*-TsOH (1.0 eq), CH₂Cl₂, 25 °C

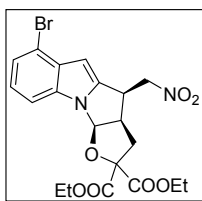


General procedure: A glass vial equipped with a magnetic stirring bar was charged with lactols **1** (0.20 mmol, 1.0 equiv), (*E*)-2-(2-nitrovinyl)-1*H*-indole **2** (0.24 mmol, 1.2 equiv), **3** (0.04 mmol, 0.2 equiv TMS = trimethylsilyl) and BA (0.04 mmol, 0.2 equiv BA = benzoic acid) in toluene (0.6 mL) at 40 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of lactols **1** (monitored by TLC analysis). After completion of the reaction, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **4**. Then, compound **4** (1.0 equiv) were respectively dissolved in anhydrous CH₂Cl₂ (0.10 mmol in 1.0 mL) at 25 °C, and *p*-TsOH (1.0 equiv) was added to the reaction mixtures. After full conversion of the second step, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 9:1 to 7:1) to give product **5**.



diethyl (3aR,4R,10aR)-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5a**)

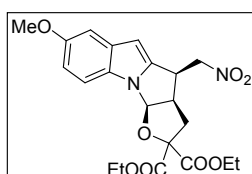
5a was obtained as a colorless oil 56.3 mg in 70% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.58 – 7.54 (m, 1H), 7.51 – 7.47 (m, 1H), 7.19 – 7.13 (m, 1H), 7.12 – 7.07 (m, 1H), 6.59 (d, $J = 5.6$ Hz, 1H), 6.09 – 6.06 (m, 1H), 5.11 (dd, $J = 14.5, 10.0$ Hz, 1H), 5.03 (dd, $J = 14.5, 5.5$ Hz, 1H), 4.30 (dq, $J = 10.8, 7.1$ Hz, 1H), 4.26 – 4.18 (m, 2H), 3.93 (dddd, $J = 11.0, 5.3, 4.8, 2.5$ Hz, 1H), 3.58 – 3.51 (m, 1H), 2.97 – 2.91 (m, 1H), 2.88 (dd, $J = 14.1, 4.2$ Hz, 1H), 2.35 (dd, $J = 14.1, 11.2$ Hz, 1H), 1.28 – 1.25 (m, 3H), 0.67 (t, $J = 7.2$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 168.0, 167.7, 139.4, 133.5, 132.0, 122.1, 121.0, 120.9, 111.3, 94.5, 92.0, 87.7, 74.1, 62.8, 62.4, 48.8, 36.8, 32.8, 14.2, 13.2 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_7^+$ 403.1500 found 403.1503. $[\alpha]_{\text{D}}^{20}$ -53.19 ($c = 1.28$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 31.84$ min, $t_{\text{minor}} = 26.49$ min, **ee >99%**. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr >20:1**.



diethyl (3aR,4R,10aR)-6-bromo-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5b**)

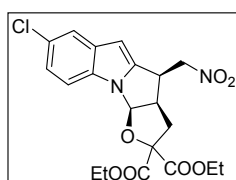
5b was obtained as a colorless oil 49.1 mg in 51% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 11/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.50 (d, $J = 8.1$ Hz, 1H), 7.27 (d, $J = 7.7$ Hz, 1H), 7.03 (t, $J = 7.9$ Hz, 1H), 6.53 (d, $J = 5.6$ Hz, 1H), 6.16 (s, 1H), 5.06 (qd, $J = 14.6, 7.7$ Hz, 2H), 4.34 – 4.16 (m, 3H), 3.99 – 3.88 (m, 1H), 3.58 (dq, $J = 10.7, 7.1$ Hz, 1H), 3.06 (dq, $J = 10.7, 7.2$ Hz, 1H), 2.83 (dd, $J = 14.1, 4.4$ Hz, 1H), 2.37 (dd, $J = 14.1, 11.0$ Hz, 1H), 1.26 (t, $J = 7.1$ Hz, 3H), 0.69 (t, $J = 7.1$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 167.7, 167.4, 139.9, 133.7, 132.1, 123.7, 122.8, 114.1, 110.3, 94.8,

92.1, 87.6, 73.6, 62.7, 62.3, 48.5, 36.7, 32.6, 14.0, 13.1 ppm. **HRMS**: $[M+H]^+$ *calcd.* For $C_{20}H_{22}BrN_2O_7^+$ 481.0605 found 481.0610. $[\alpha]_D^{20}$ -39.65 ($c = 2.04$ in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], $\lambda = 220$ nm, $t_{major} = 22.41$ min, $t_{minor} = 39.19$ min, **ee** >99%. The diastereomeric ratio was determined by 1H NMR **dr** >20:1.



diethyl (3aR,4S,10aR)-7-methoxy-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5c**)

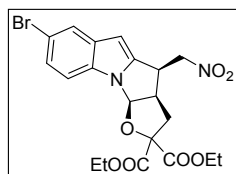
5c was obtained as a colorless oil 50.2 mg in 58% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 11/1). 1H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, $J = 8.8$ Hz, 1H), 6.97 (d, $J = 2.3$ Hz, 1H), 6.83 (dd, $J = 8.8, 2.3$ Hz, 1H), 6.56 (d, $J = 5.6$ Hz, 1H), 6.01 (s, 1H), 5.06 (ddd, $J = 20.0, 14.5, 7.7$ Hz, 2H), 4.37 – 4.14 (m, 3H), 4.00 – 3.90 (m, 1H), 3.82 (s, 3H), 3.59 (dq, $J = 10.7, 7.1$ Hz, 1H), 3.04 (dq, $J = 10.7, 7.2$ Hz, 1H), 2.88 (dd, $J = 14.1, 4.1$ Hz, 1H), 2.35 (dd, $J = 14.1, 11.2$ Hz, 1H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.74 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 167.6, 154.9, 139.9, 134.0, 127.0, 111.8, 111.8, 102.9, 94.1, 92.0, 87.5, 73.9, 62.6, 62.2, 55.8, 48.5, 36.8, 32.6, 14.0, 13.2 ppm. **HRMS**: $[M+H]^+$ *calcd.* For $C_{21}H_{25}N_2O_8^+$ 433.1605 found 433.1600. $[\alpha]_D^{20}$ -32.58 ($c = 0.83$ in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], $\lambda = 220$ nm, $t_{major} = 23.73$ min, $t_{minor} = 14.11$ min, **ee** >99%. The diastereomeric ratio was determined by 1H NMR **dr** >20:1.



diethyl (3aR,4R,10aR)-7-chloro-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5d**)

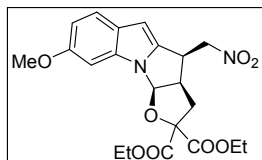
5d was obtained as a colorless oil 53.3 mg in 61% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 13/1). 1H NMR (500 MHz,

CDCl₃) δ 7.46 (t, J = 5.8 Hz, 2H), 7.12 (dd, J = 8.6, 2.0 Hz, 1H), 6.56 (d, J = 5.7 Hz, 1H), 6.02 (s, 1H), 5.04 (ddd, J = 20.2, 14.5, 7.7 Hz, 2H), 4.38 – 4.14 (m, 3H), 4.00 – 3.88 (m, 1H), 3.58 (dq, J = 10.7, 7.1 Hz, 1H), 3.05 (dq, J = 10.7, 7.2 Hz, 1H), 2.84 (dd, J = 14.1, 4.2 Hz, 1H), 2.36 (dd, J = 14.1, 11.1 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H), 0.72 (t, J = 7.1 Hz, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 167.7, 167.4, 140.8, 134.3, 130.2, 126.6, 122.2, 120.2, 112.1, 94.1, 91.9, 87.6, 73.7, 62.7, 62.3, 48.6, 36.7, 32.5, 14.0, 13.1 ppm. HRMS: [M+H]⁺ *calcd.* For C₂₀H₂₂ClN₂O₇⁺ 437.1110 found 437.1112. [α]_D²⁰ -57.38 (c = 0.68 in CHCl₃). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 220 nm, t_{major} = 37.08 min, t_{minor} = 17.11 min, **ee** >99%. The diastereomeric ratio was determined by ¹H NMR **dr** >20:1.



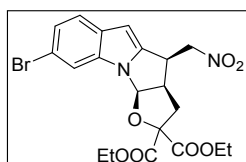
diethyl (3*aR*,4*R*,10*aR*)-7-bromo-4-(nitromethyl)-3*a*,10*a*-dihydro-4*H*-furo[3',2':4,5]pyrrolo[1,2-*a*]indole-2,2(3*H*)-dicarboxylate (**5e**)

5e was obtained as a colorless oil 54.8 mg in 57% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 13/1). ¹H NMR (500 MHz, CDCl₃) δ 7.50 (d, J = 8.1 Hz, 1H), 7.27 (d, J = 7.7 Hz, 1H), 7.03 (t, J = 7.9 Hz, 1H), 6.53 (d, J = 5.6 Hz, 1H), 6.16 (s, 1H), 5.06 (qd, J = 14.6, 7.7 Hz, 2H), 4.34 – 4.16 (m, 3H), 3.99 – 3.88 (m, 1H), 3.58 (dq, J = 10.7, 7.1 Hz, 1H), 3.06 (dq, J = 10.7, 7.2 Hz, 1H), 2.83 (dd, J = 14.1, 4.4 Hz, 1H), 2.37 (dd, J = 14.1, 11.0 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H), 0.69 (t, J = 7.1 Hz, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 167.7, 167.4, 140.6, 134.9, 130.5, 124.6, 123.3, 114.2, 112.5, 94.0, 91.9, 87.6, 73.7, 62.7, 62.3, 48.6, 36.7, 32.5, 14.0, 13.1 ppm. HRMS: [M+H]⁺ *calcd.* For C₂₀H₂₂BrN₂O₇⁺ 481.0605 found 481.0604. [α]_D²⁰ -73.38 (c = 1.22 in CHCl₃). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], λ = 220 nm, t_{major} = 24.03 min, t_{minor} = 12.66 min, **ee** = 99%. The diastereomeric ratio was determined by ¹H NMR **dr** >20:1.



diethyl (3aR,4R,10aR)-8-methoxy-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5f**)

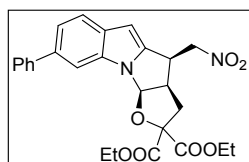
5f was obtained as a colorless oil 51.9 mg in 61% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.36 (d, J = 8.7 Hz, 1H), 7.05 (d, J = 2.1 Hz, 1H), 6.77 (dd, J = 8.7, 2.3 Hz, 1H), 6.56 (d, J = 5.6 Hz, 1H), 6.02 (s, 1H), 5.05 (ddd, J = 19.9, 14.5, 7.7 Hz, 2H), 4.36 – 4.16 (m, 3H), 3.97 – 3.90 (m, 1H), 3.86 (s, 3H), 3.62 (dq, J = 10.7, 7.1 Hz, 1H), 3.05 (dq, J = 10.7, 7.2 Hz, 1H), 2.89 (dd, J = 14.1, 4.4 Hz, 1H), 2.36 (dd, J = 14.0, 11.1 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H), 0.75 (t, J = 7.1 Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 167.7, 156.2, 137.8, 132.5, 127.3, 121.4, 111.1, 94.4, 94.3, 91.8, 87.5, 74.0, 62.6, 62.2, 55.8, 48.7, 36.6, 32.6, 14.0, 13.1 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}_8^+$ 433.1605 found 433.1601. $[\alpha]_{\text{D}}^{20}$ -48.63 (c = 2.23 in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [n -hexane/ i -PrOH = 70/30, 1 mL/min], λ = 220 nm, t_{major} = 29.87 min, t_{minor} = 12.15 min, **ee** >99%. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** >20:1.



diethyl (3aR,4R,10aR)-8-bromo-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5g**)

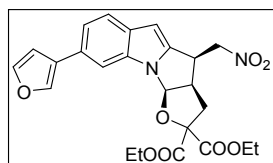
5g was obtained as a colorless oil 49.1 mg in 51% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 12/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.73 (s, 1H), 7.34 (d, J = 8.5 Hz, 1H), 7.20 (dd, J = 8.5, 1.7 Hz, 1H), 6.55 (d, J = 5.6 Hz, 1H), 6.06 (s, 1H), 5.04 (qd, J = 14.5, 7.7 Hz, 2H), 4.36 – 4.15 (m, 3H), 3.99 – 3.87 (m, 1H), 3.58 (dq, J = 10.7, 7.1 Hz, 1H), 2.99 (dq, J = 10.6, 7.2 Hz, 1H), 2.85 (dd, J = 14.1, 4.3 Hz, 1H), 2.36 (dd, J = 14.1, 11.2 Hz, 1H), 1.27 (t, J = 7.1 Hz, 3H), 0.76 (t, J = 7.2 Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 167.7, 167.4, 140.0, 132.4, 132.1, 124.1, 122.0, 115.3, 114.1, 94.6, 91.8, 87.6, 73.8, 62.7, 62.4, 48.6, 36.6, 32.4, 14.0, 13.1 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{20}\text{H}_{22}\text{BrN}_2\text{O}_7^+$ 481.0605 found 481.0606. $[\alpha]_{\text{D}}^{20}$ -68.72 (c = 1.82 in CHCl_3). The

enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], $\lambda = 220$ nm, $t_{major} = 35.60$ min, $t_{minor} = 11.45$ min, **ee** >99%. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** >20:1.



diethyl (3aR,4R,10aR)-4-(nitromethyl)-8-phenyl-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5h**)

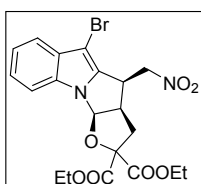
5h was obtained as a colorless oil 49.9 mg in 53% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.79 (s, 1H), 7.67 – 7.63 (m, 2H), 7.54 (d, $J = 8.3$ Hz, 1H), 7.44 (t, $J = 7.7$ Hz, 2H), 7.39 (dd, $J = 8.3, 1.5$ Hz, 1H), 7.33 (t, $J = 7.4$ Hz, 1H), 6.64 (d, $J = 5.6$ Hz, 1H), 6.10 (s, 1H), 5.09 (ddd, $J = 20.0, 14.5, 7.7$ Hz, 2H), 4.38 – 4.17 (m, 3H), 4.00 – 3.91 (m, 1H), 3.54 (dq, $J = 10.7, 7.1$ Hz, 1H), 3.01 – 2.83 (m, 2H), 2.36 (dd, $J = 14.1, 11.3$ Hz, 1H), 1.26 (t, $J = 7.1$ Hz, 3H), 0.61 (t, $J = 7.1$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 167.8, 167.6, 141.8, 140.0, 135.4, 132.6, 132.4, 128.7, 127.3, 126.8, 121.0, 120.5, 109.6, 94.3, 91.9, 87.5, 73.9, 62.6, 62.2, 48.6, 36.7, 32.6, 14.0, 13.0 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{26}\text{H}_{27}\text{N}_2\text{O}_7^+$ 479.1813 found 479.1810. $[\alpha]_{\text{D}}^{20}$ -64.67 ($c = 0.48$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 60/40, 1 mL/min], $\lambda = 220$ nm, $t_{major} = 34.42$ min, $t_{minor} = 9.23$ min, **ee** >99%. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** >20:1.



diethyl (3aR,4R,10aR)-8-(furan-3-yl)-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5i**)

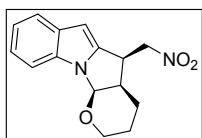
5i was obtained as a colorless oil 43.3 mg in 46% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.77 (d, $J = 0.7$ Hz, 1H), 7.67 (s, 1H), 7.48 (d, $J = 8.4$ Hz, 2H), 7.28 (dd, $J = 6.6, 1.3$ Hz, 1H), 6.78 (dd, $J = 6.4, 5.6$ Hz, 1H), 6.62 (d, $J = 5.6$ Hz, 1H), 6.08 (s, 1H), 5.08 (ddd, $J =$

20.0, 14.5, 7.7 Hz, 2H), 4.39 – 4.18 (m, 3H), 3.95 (dt, $J = 11.6, 4.9$ Hz, 1H), 3.57 (dq, $J = 10.6, 7.1$ Hz, 1H), 3.03 – 2.84 (m, 2H), 2.36 (dd, $J = 14.0, 11.2$ Hz, 1H), 1.28 (t, $J = 7.1$ Hz, 3H), 0.66 (t, $J = 7.2$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 167.8, 167.6, 164.0, 143.5, 139.7, 138.1, 132.4, 132.4, 127.1, 126.5, 121.1, 119.4, 113.7, 109.1, 108.2, 94.5, 91.9, 87.5, 73.9, 62.6, 62.3, 48.6, 36.7, 32.5, 14.0, 13.0 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{24}\text{H}_{25}\text{N}_2\text{O}_8^+$ 469.1605 found 469.1605. $[\alpha]_{\text{D}}^{20}$ -51.75 ($c = 0.72$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [n -hexane/ i -PrOH = 60/40, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 37.72$ min, $t_{\text{minor}} = 11.45$ min, **ee = 93%**. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr >20:1**.



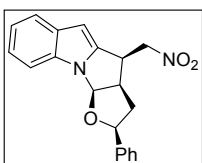
diethyl (3aR,4S,10aR)-5-bromo-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**5j**)

5j was obtained as a colorless oil 39.4 mg in 41% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 12/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.55 (d, $J = 8.0$ Hz, 1H), 7.45 (d, $J = 7.8$ Hz, 1H), 7.21 (dt, $J = 21.9, 7.3$ Hz, 2H), 6.49 (d, $J = 5.7$ Hz, 1H), 5.56 (dd, $J = 15.2, 4.0$ Hz, 1H), 5.15 (dd, $J = 15.2, 11.9$ Hz, 1H), 4.37 – 4.14 (m, 3H), 3.97 (dt, $J = 10.9, 5.1$ Hz, 1H), 3.66 – 3.54 (m, 1H), 3.18 – 3.04 (m, 1H), 2.89 (dd, $J = 14.2, 4.3$ Hz, 1H), 2.37 (dd, $J = 14.1, 11.2$ Hz, 1H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.68 (t, $J = 7.1$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 167.8, 167.4, 135.1, 132.0, 131.6, 123.2, 121.6, 119.0, 111.3, 91.9, 87.6, 83.9, 72.2, 62.7, 62.3, 48.7, 36.8, 32.4, 14.0, 13.1 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{20}\text{H}_{22}\text{BrN}_2\text{O}_7^+$ 481.0605 found 481.0601. $[\alpha]_{\text{D}}^{20}$ -12.00 ($c = 1.25$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [n -hexane/ i -PrOH = 80/20, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 24.79$ min, $t_{\text{minor}} = 11.69$ min, **ee >99%**. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr >20:1**.



(4aR,5R,11aR)-5-(nitromethyl)-3,4,4a,11a-tetrahydro-2H,5H-pyrano[3',2':4,5]pyrrolo[1,2-a]indole (**5k**)

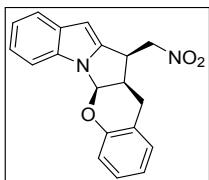
5k was obtained as a white solid 34.5 mg in 65% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 15/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.56 (d, $J = 7.9$ Hz, 1H), 7.51 (d, $J = 8.1$ Hz, 1H), 7.22 – 7.17 (m, 1H), 7.15 – 7.10 (m, 1H), 6.24 (s, 1H), 5.86 (d, $J = 4.4$ Hz, 1H), 4.87 – 4.79 (m, 1H), 4.72 (dd, $J = 13.6, 8.1$ Hz, 1H), 4.08 (q, $J = 7.3$ Hz, 1H), 3.85 – 3.77 (m, 1H), 3.70 (ddd, $J = 11.6, 8.8, 2.9$ Hz, 1H), 2.98 (ddd, $J = 12.9, 8.9, 5.6$ Hz, 1H), 2.04 – 1.95 (m, 1H), 1.72 (tdd, $J = 12.3, 5.7, 2.8$ Hz, 1H), 1.60 (ddd, $J = 13.7, 9.5, 5.0$ Hz, 2H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 139.6, 132.8, 132.5, 123.0, 120.9, 120.4, 110.3, 95.8, 84.6, 74.2, 62.8, 41.3, 38.4, 22.7, 21.2 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_3^+$ 273.1234 found 273.1240. $[\alpha]_{\text{D}}^{20}$ -125.31 ($c = 1.34$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 10.65$ min, $t_{\text{minor}} = 12.39$ min, **ee** >99%. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** >20:1.



(2S,3aR,4R,10aR)-4-(nitromethyl)-2-phenyl-2,3,3a,10a-tetrahydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole (**5l**)

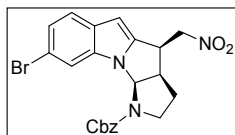
5l was obtained as a white solid 48.8 mg in 73% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.59 (dd, $J = 13.2, 8.0$ Hz, 2H), 7.23 (t, $J = 7.6$ Hz, 1H), 7.20 – 7.13 (m, 4H), 7.08 (dd, $J = 6.2, 2.6$ Hz, 2H), 6.37 (d, $J = 5.6$ Hz, 1H), 6.18 (s, 1H), 5.35 (dd, $J = 10.6, 5.2$ Hz, 1H), 4.90 (dd, $J = 13.8, 5.3$ Hz, 1H), 4.60 (dd, $J = 13.7, 10.2$ Hz, 1H), 4.33 – 4.21 (m, 1H), 3.90 (dt, $J = 12.9, 7.1$ Hz, 1H), 2.53 (ddd, $J = 12.5, 7.4, 5.4$ Hz, 1H), 1.74 (dd, $J = 22.8, 11.2$ Hz, 1H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 140.6, 138.0, 132.9, 132.4, 128.5, 127.8, 125.5, 122.0, 120.6, 120.5, 110.8, 94.9, 90.8, 84.9, 74.0, 50.5, 36.8, 36.0 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_3^+$ 335.1390 found 335.1392. $[\alpha]_{\text{D}}^{20}$ -196.17 ($c = 1.78$ in CHCl_3). The

enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], $\lambda = 220$ nm, $t_{major} = 10.90$ min, $t_{minor} = 12.35$ min, **ee** >99%. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** >20:1.



(5aR,12R,12aR)-12-(nitromethyl)-5a,12a-dihydro-12H,13H-chromeno[3',2':4,5]pyrrolo[1,2-a]indole (**5m**)

5m was obtained as a colorless oil 40.2 mg in 63% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 12/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.63 (dd, $J = 8.1, 0.6$ Hz, 1H), 7.56 (d, $J = 7.9$ Hz, 1H), 7.28 – 7.24 (m, 1H), 7.15 (ddd, $J = 22.7, 11.4, 4.1$ Hz, 4H), 6.99 – 6.93 (m, 1H), 6.83 (d, $J = 7.7$ Hz, 1H), 6.34 (d, $J = 5.9$ Hz, 1H), 6.18 (s, 1H), 4.52 – 4.43 (m, 1H), 4.30 (ddd, $J = 16.6, 13.9, 8.5$ Hz, 2H), 3.78 – 3.69 (m, 1H), 3.23 (dd, $J = 16.8, 7.3$ Hz, 1H), 2.82 (dd, $J = 16.9, 3.1$ Hz, 1H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 152.6, 140.7, 132.9, 132.4, 128.5, 128.4, 122.8, 122.2, 122.0, 121.2, 120.9, 117.9, 110.5, 96.0, 83.4, 75.6, 43.2, 37.5, 24.4 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{19}\text{H}_{17}\text{N}_2\text{O}_3^+$ 321.1234 found 321.1235. $[\alpha]_{\text{D}}^{20}$ -168.34 ($c = 3.84$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], $\lambda = 220$ nm, $t_{major} = 6.99$ min, $t_{minor} = 8.37$ min, **ee** = 98%. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** = 5:1.

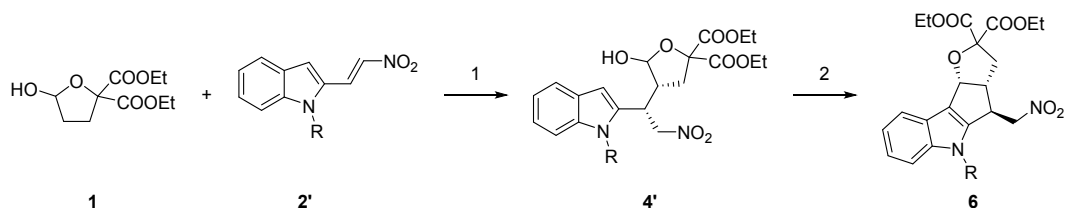


benzyl (3aR,4R,10aR)-8-bromo-4-(nitromethyl)-2,3,3a,10a-tetrahydropyrrolo[3',2':4,5]pyrrolo[1,2-a]indole-1(4H)-carboxylate (**5n**)

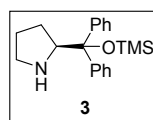
5n was obtained as a white solid 48.4 mg in 62% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.90 (s, 1H), 7.54 (d, $J = 2.8$ Hz, 1H), 7.45 (d, $J = 6.8$ Hz, 1H), 7.41 (t, $J = 7.4$ Hz, 3H), 7.39 – 7.34 (m, 2H), 7.20 (d, $J = 8.3$ Hz, 1H), 6.32 (t, $J = 8.2$ Hz, 1H), 6.15 (s, 1H), 5.43 (d, $J = 12.2$ Hz, 1H), 5.22 (d, $J = 12.1$ Hz, 1H), 4.94 (dd, $J = 13.6, 5.1$ Hz, 1H), 4.66 (dd, $J = 13.7,$

10.0 Hz, 1H), 4.23 (s, 1H), 3.66 (dd, $J = 17.4, 10.0$ Hz, 1H), 3.61 – 3.53 (m, 2H), 2.19 (dt, $J = 13.2, 6.8$ Hz, 1H), 1.80 (dt, $J = 20.9, 10.6$ Hz, 1H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 155.7, 139.3, 136.1, 132.8, 131.4, 128.7, 128.4, 128.2, 123.5, 121.7, 115.6, 114.9, 95.2, 74.5, 73.5, 67.9, 48.3, 47.4, 37.1, 25.2 ppm. **HRMS:** $[\text{M}+\text{H}]^+$ *calcd.* For $\text{C}_{22}\text{H}_{21}\text{BrN}_3\text{O}_4^+$ 470.0710 found 470.0713. $[\alpha]_{\text{D}}^{20} +61.68$ ($c = 0.89$ in CHCl_3) The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [n -hexane/ i -PrOH = 80/20, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 39.26$ min, $t_{\text{minor}} = 24.2$ min, **ee = 98%**. The diastereomeric ratio was determined by ^1H NMR **dr = 7:1**.

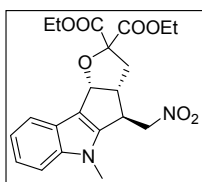
D2. Synthesis of Polycyclic Indoles via C3-Alkylation Path



1) **3** (20 mol %), BA (20 mol %), toluene, 40 °C
2) BF₃·Et₂O (1.2 eq), CH₂Cl₂, 0 °C

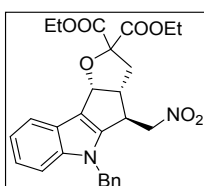


General procedure: A glass vial equipped with a magnetic stirring bar was charged with lactols **1** (0.20 mmol, 1.0 equiv), (*E*)-2-(2-nitrovinyl)-1*H*-indole **2'** (0.24 mmol, 1.2 equiv), **3** (0.04 mmol, 0.2 equiv) and BA (0.04 mmol, 0.2 equiv) in toluene (0.6 mL) at 40 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of lactols **1** (monitored by TLC analysis). After completion of the reaction, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **4'**. Then, compound **4'** (1.0 equiv) were respectively dissolved in anhydrous CH₂Cl₂ (0.10 mmol in 1 mL) at 0 °C, and BF₃·Et₂O (1.2 equiv) was added to the reaction mixtures. After full conversion of the second step, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 6:1 to 3:1) to give product **6**.



diethyl (3aR,4S,9cR)-5-methyl-4-(nitromethyl)-3a,4,5,9c-tetrahydrofuro[2',3':3,4]cyclopenta[1,2-b]indole-2,2(3H)-dicarboxylate (**6a**)

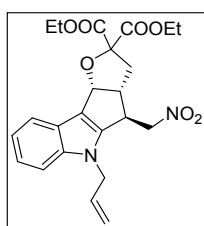
6a was obtained as a white solid 35.2 mg in 42% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.70 (d, $J = 7.9$ Hz, 1H), 7.25 – 7.18 (m, 2H), 7.18 – 7.07 (m, 1H), 6.07 (dd, $J = 6.4$, 0.8 Hz, 1H), 4.67 (dd, $J = 13.0$, 4.4 Hz, 1H), 4.41 (dd, $J = 12.9$, 9.5 Hz, 1H), 4.33 – 4.18 (m, 2H), 4.08 – 3.97 (m, 1H), 3.73 – 3.66 (m, 1H), 3.65 (s, 3H), 3.49 – 3.42 (m, 1H), 3.25 (dq, $J = 10.7$, 7.1 Hz, 1H), 2.80 (dd, $J = 13.4$, 4.7 Hz, 1H), 2.58 (dd, $J = 13.3$, 10.2 Hz, 1H), 1.26 (t, $J = 7.1$ Hz, 3H), 0.73 (t, $J = 7.1$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 169.0, 168.9, 142.7, 142.6, 123.1, 122.3, 120.4, 120.0, 118.9, 109.7, 93.4, 86.8, 83.0, 78.5, 62.2, 61.62, 52.5, 43.7, 39.7, 30.7, 14.0, 13.2 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For Chemical Formula: $\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}_7^+$ 417.1656 found 417.1660. $[\alpha]_D^{20}$ -39.33 ($c = 1.27$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [n -hexane/ i -PrOH = 80/20, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 41.69$ min, $t_{\text{minor}} = 18.87$ min, **ee = 99%**. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr >20:1**.



diethyl (3aR,4S,9cR)-5-benzyl-4-(nitromethyl)-3a,4,5,9c-tetrahydrofuro[2',3':3,4]cyclopenta[1,2-b]indole-2,2(3H)-dicarboxylate (**6b**)

6b was obtained as a colorless oil 42.1 mg in 42% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.77 – 7.72 (m, 1H), 7.37 – 7.27 (m, 3H), 7.20 – 7.12 (m, 3H), 7.08 (d, $J = 7.0$ Hz, 2H), 6.11 (dd, $J = 6.5$, 1.1 Hz, 1H), 5.29 – 5.20 (m, 2H), 4.31 (dd, $J = 13.1$, 3.7 Hz, 1H), 4.27 (dd, $J = 9.1$, 5.4 Hz, 1H), 4.25 – 4.20 (m, 1H), 4.15 (dd, $J = 13.2$, 10.2 Hz, 1H), 3.95 – 3.87 (m, 1H), 3.71 (dq, $J = 10.7$, 7.1 Hz, 1H), 3.43 (dt, $J = 10.1$, 4.9 Hz, 1H), 3.25 (dq, $J = 10.7$, 7.1 Hz, 1H), 2.78 (dd, $J = 13.5$, 4.6 Hz, 1H), 2.60 – 2.50 (m, 1H), 1.27 (d, $J = 7.1$ Hz, 3H), 0.75 (t, $J = 7.1$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 168.9, 142.5, 142.3, 136.5, 129.1, 128.1,

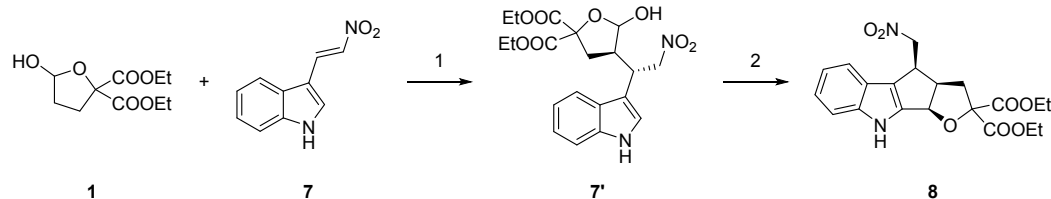
126.3, 123.3, 122.6, 120.7, 120.1, 110.2, 86.8, 83.0, 78.2, 62.2, 61.6, 52.6, 48.1, 44.0, 39.7, 14.0, 13.3 ppm. **HRMS**: $[M+H]^+$ *calcd.* For Chemical Formula: $C_{27}H_{29}N_2O_7^+$ 493.1969 found 493.1964. $[\alpha]_D^{20}$ -45.74 ($c = 0.86$ in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], $\lambda = 220$ nm, $t_{major} = 41.92$ min, $t_{minor} = 24.26$ min, **ee = 99%**. The diastereomeric ratio was determined by 1H NMR **dr >20:1**.



diethyl (3*aR*,4*S*,9*cR*)-5-allyl-4-(nitromethyl)-3*a*,4,5,9*c*-tetrahydrofuro[2',3':3,4]cyclopenta[1,2-*b*]indole-2,2(3*H*)-dicarboxylate (**6c**)

6c was obtained as a yellow oil 38.6 mg in 44% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1). 1H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, $J = 7.8$ Hz, 1H), 7.21 (q, $J = 8.0$ Hz, 2H), 7.17 – 7.12 (m, 1H), 6.11 (d, $J = 6.4$ Hz, 1H), 6.06 – 5.93 (m, 1H), 5.25 (d, $J = 10.3$ Hz, 1H), 5.02 (d, $J = 17.1$ Hz, 1H), 4.74 – 4.69 (m, 1H), 4.69 – 4.58 (m, 2H), 4.34 – 4.22 (m, 3H), 4.02 (dd, $J = 10.1, 3.4$ Hz, 1H), 3.70 (dq, $J = 10.7, 7.1$ Hz, 1H), 3.48 (dt, $J = 10.7, 5.4$ Hz, 1H), 3.23 (dq, $J = 10.7, 7.2$ Hz, 1H), 2.81 (dd, $J = 13.4, 4.5$ Hz, 1H), 2.57 (dd, $J = 13.4, 10.3$ Hz, 1H), 1.27 (s, 3H), 0.75 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 168.9, 142.2, 142.1, 132.9, 123.3, 122.5, 120.6, 120.1, 119.4, 117.4, 110.1, 86.8, 82.9, 78.4, 62.2, 61.6, 52.6, 46.9, 43.9, 39.7, 14.0, 13.2 ppm. **HRMS**: $[M+H]^+$ *calcd.* For Chemical Formula: $C_{23}H_{27}N_2O_7^+$ 443.1813 found 443.1814. $[\alpha]_D^{20}$ -25.64 ($c = 0.77$ in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], $\lambda = 210$ nm, $t_{major} = 33.55$ min, $t_{minor} = 12.99$ min, **ee = 99%**. The diastereomeric ratio was determined by 1H NMR **dr >20:1**.

D3. Optimization of the reaction conditions



1) **cat.** (20 mol %), BA (20 mol %), toluene, 40 °C
 2) *p*-TsOH (1.2 eq), CH₂Cl₂, 40 °C

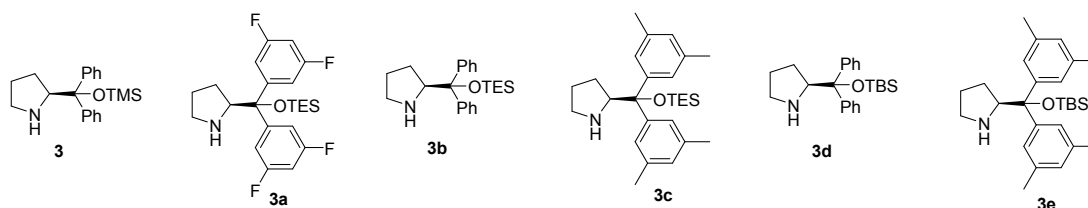
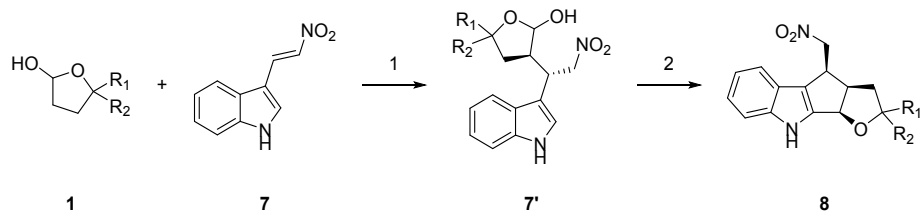


Table S4. Optimization of the reaction conditions^a

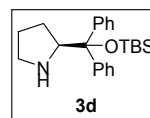
Entry	Solvent	Catalys	t (h) ^b	Yield (%) ^c	ee (%) ^d	dr ^e
		t				
1	toluene	3	64	37	73	>20:1
2	toluene	3a	NR	NR	NR	NR
3	toluene	3b	68	36	91	>20:1
4	toluene	3c	64	38	90	>20:1
5	toluene	3d	70	35	97	>20:1
6	toluene	3e	72	33	96	>20:1

[a] Unless otherwise specified, all reactions were carried out using **1** (0.20 mmol, 1.0 equiv), **7** (0.24 mmol, 1.2 equiv) in solvent (0.6 mL) with **cat.** (20 mol%) and **BA** (20 mol%) at 40 °C. After workup, the mixture was purified by flash chromatography on silica gel to afford **7'**. Compound **7'** were respectively dissolved in redistilled CH₂Cl₂ (0.10 mmol in 1 mL) at 40 °C. *p*-TsOH (1.2 eq) was added, after full conversion of the second step, the residue was purified by flash chromatography on gel to give product **8**. [b] For the first step. [c] Isolated yield of **8** over two steps. [d] Determined by HPLC analyses of isolated compound **8** on chiral stationary phases. [e] Determined by ¹H NMR. TMS = trimethylsilyl; TES = triethylsilyl, TBS = *tert*-butyldimethylsilyl.

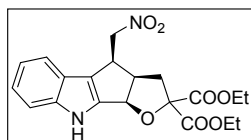
D4. Synthesis of Polycyclic Indoles via C2-Alkylation Path



1) **3d** (20 mol %), BA (20 mol %), toluene, 40 °C
2) *p*-TsOH (1.2 eq), CH₂Cl₂, 40 °C

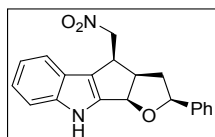


General procedure: A glass vial equipped with a magnetic stirring bar was charged with lactols **1** (0.20 mmol, 1.0 equiv), (*E*)-3-(2-nitrovinyl)-1*H*-indole **7** (0.24 mmol, 1.2 equiv), **3d** (0.04 mmol, 0.2 equiv) and BA (0.04 mmol, 0.2 equiv) in toluene (0.6 mL) at 40 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of lactols **1** (monitored by TLC analysis). After completion of the reaction, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **7'**. Then, compound **7'** (1.0 equiv) were respectively dissolved in anhydrous CH₂Cl₂ (0.10 mmol in 1.0 mL) at 40 °C, and *p*-TsOH (1.2 equiv) was added to the reaction mixtures. After full conversion of the second step, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 8:1 to 4:1) to give product **8**.



diethyl (3aR,4S,9bR)-4-(nitromethyl)-3a,4,9,9b-tetrahydrofuro[3',2':4,5]cyclopenta[1,2-b]indole-2,2(3H)-dicarboxylate (**8a**)

8a was obtained as a white solid 28.1 mg in 35% yield for two steps after column chromatography on silica gel (petroleum ether/dichloromethane = 1/3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 9.00 (s, 1H), 7.41 (d, $J = 7.9$ Hz, 1H), 7.36 (d, $J = 8.2$ Hz, 1H), 7.18 (t, $J = 7.7$ Hz, 1H), 7.10 (t, $J = 7.5$ Hz, 1H), 5.97 (d, $J = 7.0$ Hz, 1H), 4.77 (dd, $J = 13.1, 5.0$ Hz, 1H), 4.35 (dd, $J = 13.1, 9.5$ Hz, 1H), 4.26 – 4.19 (m, 2H), 4.01 (dd, $J = 9.4, 5.0$ Hz, 1H), 3.97 – 3.87 (m, 1H), 3.87 – 3.78 (m, 1H), 3.50 (dd, $J = 14.0, 6.4$ Hz, 1H), 2.80 (dt, $J = 15.4, 7.7$ Hz, 1H), 2.72 (dd, $J = 13.4, 5.7$ Hz, 1H), 1.21 (t, $J = 7.1$ Hz, 3H), 0.99 (t, $J = 7.1$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 168.6, 168.4, 142.2, 141.0, 122.9, 122.5, 120.3, 119.0, 118.1, 112.7, 87.7, 81.9, 79.4, 62.4, 62.3, 52.5, 43.7, 39.7, 13.9, 13.7 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For Chemical Formula: $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_7^+$ 403.1500 found 403.1502. $[\alpha]_{\text{D}}^{20}$ -24.71 ($c = 0.72$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 20.69$ min, $t_{\text{minor}} = 17.25$ min, **ee** = **97%**. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** >**20:1**. (The absolute configuration of compound **8a** is determined by the configuration of compound **17**.)



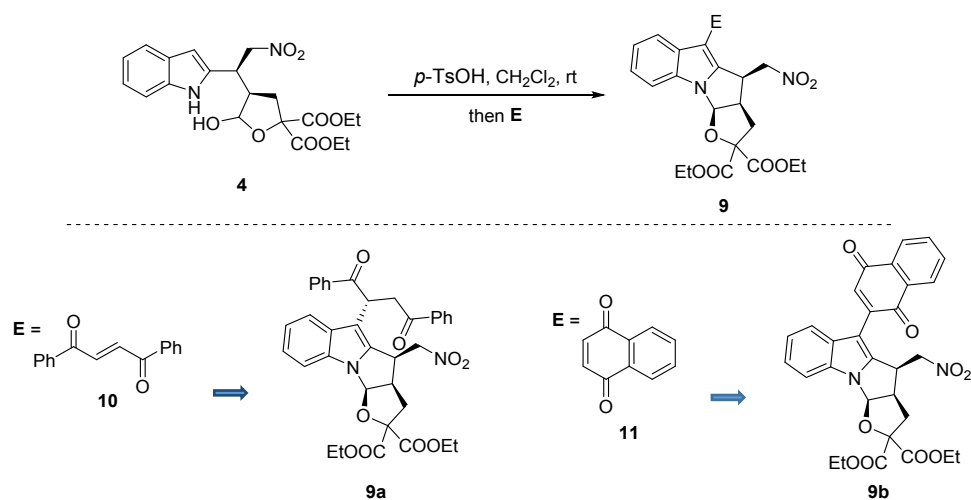
(2S,3aR,4S,9bR)-4-(nitromethyl)-2-phenyl-2,3,3a,4,9,9b-hexahydrofuro[3',2':4,5]cyclopenta[1,2-b]indole (**8b**)

8b was obtained as a white solid 26.7 mg in 40% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.59 (s, 1H), 8.39 (s, 1H), 7.41 (d, $J = 7.9$ Hz, 1H), 7.34 – 7.27 (m, 5H), 7.19 (t, $J = 5.8$ Hz, 2H), 7.12 (td, $J = 8.2, 4.5$ Hz, 1H), 5.66 (d, $J = 7.4$ Hz, 1H), 5.17 – 5.07 (m, 2H), 4.61 (dd, $J = 13.7, 10.5$ Hz, 1H), 4.27 – 4.20 (m, 1H), 3.94 (dq, $J = 11.3, 7.3$ Hz, 1H), 2.48 – 2.37 (m, 1H), 1.79 (q, $J = 11.3$ Hz, 1H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 142.9, 141.5, 140.5, 128.5, 128.1, 126.2, 126.0, 123.3, 122.5, 120.3, 118.7, 116.1, 112.5, 83.9, 79.9, 75.0, 51.6, 37.9, 37.6 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For Chemical Formula: $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_3^+$ 335.1390 found

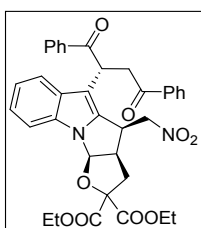
335.1386. $[\alpha]_D^{20} +13.67$ ($c = 1.8$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [n -hexane/ i -PrOH = 90/10, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 10.98$ min, $t_{\text{minor}} = 11.72$ min, **ee >99%**. The diastereomeric ratio was determined by ^1H NMR **dr = 5:1**.

E. Synthetic transformations

E1. Modification of C3 position of Indole Moiety in **4**

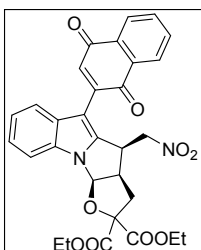


General procedure: To a suspension of **4** (1.0 equiv) were respectively dissolved in anhydrous CH₂Cl₂ (0.10 mmol in 1.0 mL) at 25 °C, and then *p*-TsOH (1.0 equiv) was added to the reaction mixtures. After the compound **4** was completely consumed (TLC control), then the **E** was added at the same temperature. After completion of the reaction, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1 to 6:1) to give the product **9**.



diethyl (3aR,4R,10aR)-5-((R)-1,4-dioxo-1,4-diphenylbutan-2-yl)-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (9a)

9a was obtained as a colorless oil 33.5 mg in 51% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.97 (dd, $J = 17.4, 7.4$ Hz, 4H), 7.62 (d, $J = 7.5$ Hz, 1H), 7.59 – 7.51 (m, 2H), 7.45 (dd, $J = 10.9, 4.2$ Hz, 3H), 7.37 (t, $J = 7.6$ Hz, 2H), 7.20 – 7.12 (m, 2H), 6.40 (d, $J = 5.9$ Hz, 1H), 5.88 (dd, $J = 14.6, 4.0$ Hz, 1H), 5.50 (t, $J = 6.2$ Hz, 1H), 5.42 – 5.34 (m, 1H), 4.27 (ddq, $J = 39.7, 10.8, 7.1$ Hz, 2H), 4.04 (s, 1H), 3.98 (dd, $J = 18.2, 7.2$ Hz, 1H), 3.88 (dt, $J = 14.3, 7.6$ Hz, 1H), 3.44 (dd, $J = 18.2, 5.8$ Hz, 1H), 3.36 (td, $J = 14.2, 6.9$ Hz, 1H), 2.98 (dd, $J = 14.1, 3.2$ Hz, 1H), 2.84 – 2.70 (m, 1H), 2.28 (dd, $J = 14.0, 11.3$ Hz, 1H), 1.27 (t, $J = 5.5$ Hz, 3H), 0.45 (t, $J = 7.0$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 199.4, 198.2, 168.2, 167.4, 136.4, 136.3, 135.9, 133.4, 133.0, 132.1, 131.7, 128.6, 128.6, 128.6, 128.2, 122.5, 121.3, 118.6, 111.3, 106.1, 91.2, 87.2, 73.5, 62.6, 62.1, 48.2, 41.5, 36.9, 32.7, 14.0, 12.8 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ calcd. For Chemical Formula: $\text{C}_{36}\text{H}_{35}\text{N}_2\text{O}_9^+$ 639.2337 found 639.2334. $[\alpha]_D^{20}$ -131 ($c = 2.16$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [n -hexane/ i -PrOH = 80/20, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 30.92$ min, $t_{\text{minor}} = 17.32$ min, **ee** >99%. The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** >20:1. (The absolute configuration of compound **9a** is derived from the the X-ray data of **5n**.)

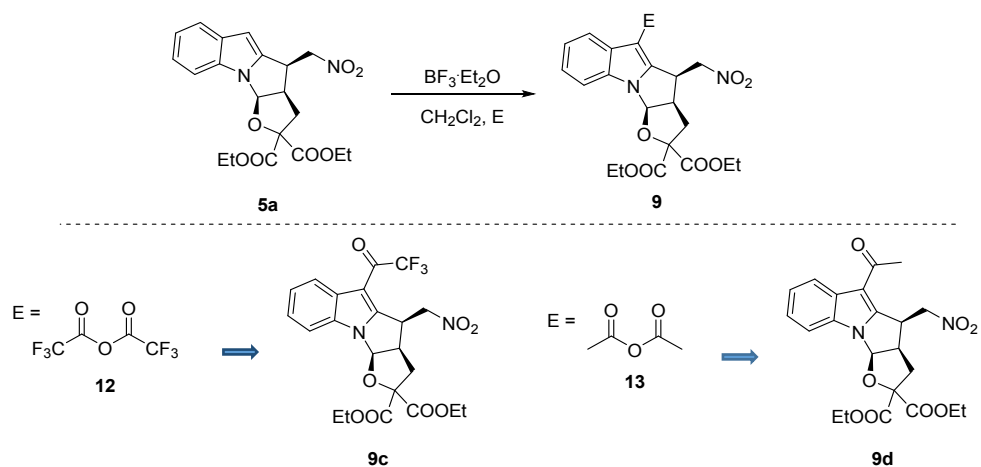


diethyl (3aR,4R,10aR)-5-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (9b)

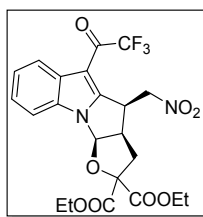
9b was obtained as a brown syrup 31.3 mg in 56% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). $^1\text{H NMR}$ (500 MHz,

CDCl₃) δ 8.13 (d, $J = 7.4$ Hz, 2H), 7.84 – 7.72 (m, 2H), 7.64 (d, $J = 8.5$ Hz, 2H), 7.28 – 7.19 (m, 3H), 6.65 (d, $J = 5.9$ Hz, 1H), 5.07 (dd, $J = 14.8, 11.3$ Hz, 1H), 4.82 – 4.74 (m, 1H), 4.64 (dd, $J = 14.9, 3.8$ Hz, 1H), 4.27 (ddq, $J = 39.6, 10.8, 7.1$ Hz, 2H), 4.17 – 4.03 (m, 1H), 3.67 – 3.59 (m, 1H), 3.12 (dq, $J = 10.6, 7.2$ Hz, 1H), 2.85 (dd, $J = 14.2, 4.0$ Hz, 1H), 2.38 (dd, $J = 14.2, 11.1$ Hz, 1H), 1.26 (s, 3H), 0.69 (t, $J = 7.1$ Hz, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 185.7, 184.8, 167.8, 167.4, 141.7, 140.9, 134.5, 134.3, 133.7, 132.2, 132.1, 132.0, 131.4, 127.1, 126.1, 123.1, 122.3, 119.2, 111.7, 101.8, 92.0, 87.6, 73.4, 62.7, 62.4, 48.3, 38.9, 32.9, 14.0, 13.1 ppm. **HRMS:** [M+H]⁺ *calcd.* For Chemical Formula: C₃₀H₂₇N₂O₉⁺ 559.1711 found 559.1709. The diastereomeric ratio was determined by ¹H NMR ***dr* >20:1**.

E2. Modification of C3 position of Indole Moiety in **5a**

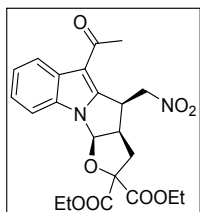


General procedure: To a suspension of **5a** (1.0 equiv) were respectively dissolved in anhydrous CH_2Cl_2 (0.10 mmol in 1.0 mL) at 0 °C, and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (1.0 equiv) was added to the reaction mixtures, then the **E** was added at the same temperature. After completion of the reaction, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1 to 6:1) to give the product **9**.



diethyl (3aR,4R,10aR)-4-(nitromethyl)-5-(2,2,2-trifluoroacetyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**9c**)

9c was obtained as a colorless oil 26.4 mg in 53% yield for one steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.91 (d, $J = 4.7$ Hz, 1H), 7.74 – 7.67 (m, 1H), 7.35 (dd, $J = 6.0, 3.0$ Hz, 2H), 6.58 (d, $J = 6.2$ Hz, 1H), 6.07 (dd, $J = 15.6, 3.7$ Hz, 1H), 5.08 (dd, $J = 15.5, 11.6$ Hz, 1H), 4.59 – 4.49 (m, 1H), 4.38 – 4.22 (m, 2H), 4.18 – 4.06 (m, 1H), 3.75 – 3.63 (m, 1H), 3.37 – 3.21 (m, 1H), 2.89 (dd, $J = 14.4, 3.9$ Hz, 1H), 2.43 (dd, $J = 14.2, 11.3$ Hz, 1H), 1.28 (t, $J = 7.1$ Hz, 3H), 0.70 (t, $J = 7.1$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 175.8, 167.7, 166.9, 151.9, 132.1, 128.3, 124.5, 124.3, 121.3, 118.0, 115.7, 112.2, 105.9, 92.5, 91.7, 87.9, 71.4, 62.9, 62.6, 48.0, 39.2, 32.7, 14.0, 13.1 ppm. **HRMS**: $[\text{M}+\text{H}]^+$ *calcd.* For Chemical Formula: $\text{C}_{22}\text{H}_{22}\text{F}_3\text{N}_2\text{O}_8^+$ 499.1323 found 499.1322. $[\alpha]_{\text{D}}^{20} +45.56$ ($c = 0.9$ in CHCl_3). The diastereomeric ratio was determined by $^1\text{H NMR}$ **dr** >20:1.

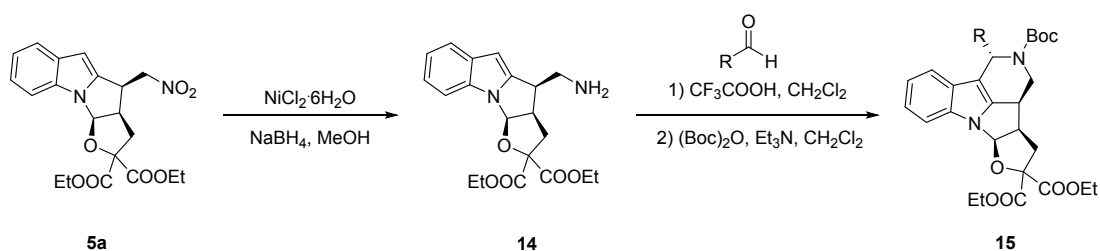


diethyl (3aR,4R,10aR)-5-acetyl-4-(nitromethyl)-3a,10a-dihydro-4H-furo[3',2':4,5]pyrrolo[1,2-a]indole-2,2(3H)-dicarboxylate (**9d**)

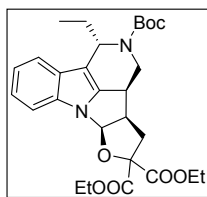
9d was obtained as a colorless oil 33.1 mg in 75% yield for one steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.83 (d, $J = 7.1$ Hz, 1H), 7.71 – 7.65 (m, 1H), 7.35 – 7.27 (m, 2H), 6.54 (d, $J = 6.1$ Hz, 1H), 6.30 (dd, $J = 15.6, 4.0$ Hz, 1H), 5.00 (dd, $J = 15.6, 11.7$ Hz, 1H), 4.46 (ddd, $J = 11.9, 8.3, 4.0$ Hz, 1H), 4.35 – 4.21 (m, 2H), 4.04 (ddd, $J = 10.9, 9.7, 6.0$ Hz, 1H), 3.67 (dq, $J = 10.8, 7.1$ Hz, 1H), 3.25 (dq, $J = 10.7, 7.1$ Hz, 1H), 2.87 (dd, $J = 14.2, 4.3$ Hz, 1H), 2.68 (s, 3H), 2.38 (dt, $J = 19.2, 9.6$ Hz, 1H), 1.28 (t, $J = 6.6$ Hz, 3H), 0.72 (t, $J = 7.1$ Hz, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 194.5, 167.7, 167.2, 146.2, 132.0, 130.2, 123.3, 123.0, 120.7, 112.1, 110.0,

92.3, 87.8, 72.1, 62.8, 62.4, 48.1, 38.5, 32.7, 31.2, 14.0, 13.1 ppm. **HRMS:** $[M+H]^+$ *calcd.* For
Chemical Formula: $C_{22}H_{25}N_2O_8^+$ 445.1605 found 445.1600. $[\alpha]_D^{20}$ +56.95 ($c = 1.08$ in
 $CHCl_3$). The diastereomeric ratio was determined by 1H NMR ***dr* >20:1**.

E3. Useful Transformations of Product **5a**

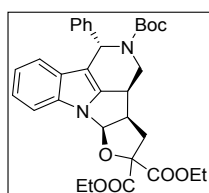


General procedure: To a suspension of **5a** (41.0 mg, 0.10 mmol, 1.0 equiv), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (28.5 mg, 0.12 mmol, 1.2 equiv.) in 1.0 mL MeOH was carefully added NaBH_4 (45.6 mg, 1.20 mmol, 12.0 equiv.) and stirred at 0°C for 1 h. The mixture was then quenched with sat. NH_4Cl and extracted with CH_2Cl_2 (3×5 mL). The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated to give a yellow oil. Subsequently, the crude intermediate was dissolved in a solution of aldehyde (0.30 mmol, 3.0 equiv) in CH_2Cl_2 , followed by adding TFA (17.0 mg, 0.15 mmol, 1.5 equiv, TFA = trifluoroacetic acid). The mixture was stirred for 12 h at room temperature. The solution was quenched with sat. NaHCO_3 and extracted with CH_2Cl_2 (3×5 mL). The combined organic phases were dried over MgSO_4 and concentrated to give a white oil. the crude intermediate was dissolved in a solution of di-*tert*-butyl dicarbonate (65.5 mg, 0.30 mmol, 3.0 equiv) in CH_2Cl_2 , followed by adding Et_3N (3.0 mg, 0.03 mmol, 0.3 equiv, Et_3N = triethylamine). After filtered and concentrated, the residue was purified by flash column chromatography to yield **15** as an brown syrup.



2-(*tert*-butyl) 5,5-diethyl (1*S*,3*aR*,3*bR*,6*aR*)-1-ethyl-3,3*a*,3*b*,6*a*-tetrahydrobenzo[*b*]furo[2,3-*e*]pyrido[3,4,5-*gh*]pyrrolizine-2,5,5(1*H*,4*H*)-tricarboxylate (**15a**)

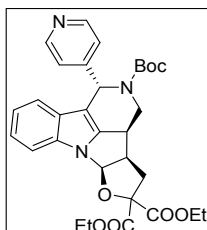
15a was obtained as a colorless oil 20.5 mg in 41% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1). ¹H NMR (500 MHz, CDCl₃) δ 7.47 (dd, *J* = 6.9, 1.6 Hz, 1H), 7.44 – 7.41 (m, 1H), 7.09 (dq, *J* = 7.2, 5.8 Hz, 2H), 6.69 (d, *J* = 4.7 Hz, 1H), 5.10 (dd, *J* = 7.8, 4.1 Hz, 1H), 4.30 – 4.17 (m, 2H), 4.05 (dd, *J* = 12.8, 7.7 Hz, 1H), 3.84 – 3.73 (m, 1H), 3.65 (dd, *J* = 12.8, 7.1 Hz, 1H), 3.57 – 3.45 (m, 2H), 3.23 (dq, *J* = 10.7, 7.1 Hz, 1H), 2.30 (ddd, *J* = 21.7, 13.9, 9.0 Hz, 2H), 2.07 – 1.98 (m, 1H), 1.87 – 1.74 (m, 1H), 1.49 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 168.5, 166.5, 155.7, 143.5, 134.3, 131.5, 120.9, 120.3, 118.6, 112.5, 109.4, 95.3, 89.0, 79.8, 62.4, 61.8, 54.0, 53.8, 42.7, 31.8, 31.6, 30.2, 28.5, 14.0, 13.4, 10.0 ppm. HRMS: [M+H]⁺ *calcd.* For Chemical Formula: C₂₈H₃₇N₂O₇⁺ 513.2595 found 513.2597. [α]_D²⁰ -68.68 (*c* = 1.43 in CHCl₃). The diastereomeric ratio was determined by ¹H NMR *dr* >20:1.



2-(*tert*-butyl) 5,5-diethyl (1*S*,3*aR*,3*bR*,6*aR*)-1-phenyl-3,3*a*,3*b*,6*a*-tetrahydrobenzo[*b*]furo[2,3-*e*]pyrido[3,4,5-*gh*]pyrrolizine-2,5,5(1*H*,4*H*)-tricarboxylate (**15b**)

15b was obtained as a colorless oil 25.2 mg in 46% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1). ¹H NMR (500 MHz, CDCl₃) δ 7.44 (dd, *J* = 15.5, 7.8 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.11 – 7.02 (m, 2H), 6.73 (d, *J* = 4.7 Hz, 1H), 6.06 (s, 1H), 4.44 (s, 1H), 4.25 (dddd, *J* = 25.0, 10.7, 7.1, 3.6 Hz, 2H), 3.88 – 3.79 (m, 1H), 3.70 – 3.62 (m, 2H), 3.53 (tt, *J* = 13.9, 5.2 Hz, 1H), 3.06 (dq, *J* = 14.7, 7.2 Hz, 1H), 2.47 (dd, *J* = 13.9, 6.8 Hz, 1H), 2.32 (dd, *J* = 13.9, 10.4 Hz, 1H), 1.29 – 1.24 (m, 11H), 0.87 (t, *J* = 7.1 Hz, 3H) ppm. ¹³C NMR (125

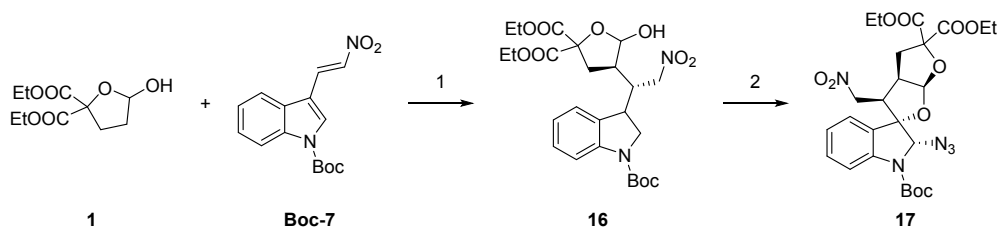
MHz, CDCl₃) δ 168.4, 166.6, 156.1, 145.1, 142.9, 134.5, 130.6, 128.3, 126.3, 125.9, 121.1, 120.3, 118.4, 112.5, 108.9, 95.5, 88.9, 80.3, 62.4, 61.8, 57.1, 53.2, 43.9, 32.6, 31.5, 28.2, 14.0, 13.4 ppm. **HRMS:** [M+H]⁺ *calcd.* For Chemical Formula: C₃₂H₃₇N₂O₇⁺ 561.2595 found 561.2591. [α]_D²⁰ -33.52 (*c* = 1.26 in CHCl₃). The diastereomeric ratio was determined by ¹H NMR *dr* >20:1.



2-(*tert*-butyl) 5,5-diethyl (1*S*,3*aR*,3*bR*,6*aS*)-1-(pyridin-4-yl)-3,3*a*,3*b*,6*a*-tetrahydrobenzo[*b*]furo[2,3-*e*]pyrido[3,4,5-*gh*]pyrrolizine-2,5,5(1*H*,4*H*)-tricarboxylate (15c)

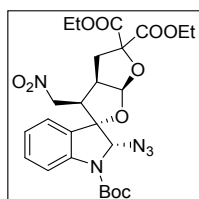
15c was obtained as a colorless oil 26.4 mg in 47% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). ¹H NMR (500 MHz, CDCl₃) δ 8.50 – 8.43 (m, 2H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 6.0 Hz, 2H), 7.07 (dtd, *J* = 14.9, 7.8, 1.1 Hz, 2H), 6.76 (d, *J* = 4.8 Hz, 1H), 5.88 (s, 1H), 4.64 (s, 1H), 4.30 – 4.19 (m, 2H), 3.89 (ddt, *J* = 10.8, 7.9, 5.4 Hz, 1H), 3.69 (dd, *J* = 15.9, 8.2 Hz, 1H), 3.58 – 3.45 (m, 2H), 2.87 (dq, *J* = 10.6, 7.1 Hz, 1H), 2.59 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.28 (dd, *J* = 14.0, 10.9 Hz, 1H), 1.25 (dd, *J* = 8.2, 6.0 Hz, 12H), 0.86 (d, *J* = 7.1 Hz, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 168.1, 166.6, 156.0, 149.8, 142.9, 134.0, 129.8, 121.4, 120.6, 120.5, 118.1, 112.6, 110.0, 95.6, 88.8, 81.0, 62.5, 61.8, 57.1, 52.6, 45.0, 32.7, 31.4, 28.1, 14.0, 13.4 ppm. **HRMS:** [M+H]⁺ *calcd.* For Chemical Formula: C₃₁H₃₆N₃O₇⁺ 562.2548 found 562.2549. [α]_D²⁰ -48.03 (*c* = 1.66 in CHCl₃). The diastereomeric ratio was determined by ¹H NMR *dr* >20:1.

E4. Synthesis of Spiro-fused 2-Azido Indoline 17 via Radical-mediated dearomatization reaction



1) **3** (20 mol %), BA (20 mol %), toluene, 25 °C
 2) Ce(NH₄)₂(NO₂)₆, NaN₃, MeCN, 0 °C

General procedure: A glass vial equipped with a magnetic stirring bar was charged with lactols **1** (0.20 mmol, 1.0 equiv), *tert-butyl* (*E*)-3-(2-nitrovinyl)-1*H*-indole-1-carboxylate **Boc-7** (0.24 mmol, 1.2 equiv), **3** (0.04 mmol, 0.2 equiv) and C₆H₅COOH (0.04 mmol, 0.2 equiv) in toluene (0.6 mL) at 25 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of lactols **1** (monitored by TLC analysis). After completion of the reaction, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to afford **16**. To a suspension of **16** (52.2 mg, 0.10 mmol), NaN₃ (9.4 mg, 0.15 mmol NaN₃ = sodium azide) in MeCN (2.0 mL) was slowly added a solution of ceric ammonium nitrate (0.08 M in acetonitrile) (3.75 mL, 0.30 mmol) under N₂ at 0 °C. Upon stirring at 0 °C for 3 h, the reaction mixture was quenched with water, extracted with ethyl acetate, washed with water, dried over MgSO₄, filtered, concentrated, and was separated by C-18 column (MeCN/H₂O = 70/30, t_R = 52 min) to give **17** as white oil (15.0 mg, 28% yield).



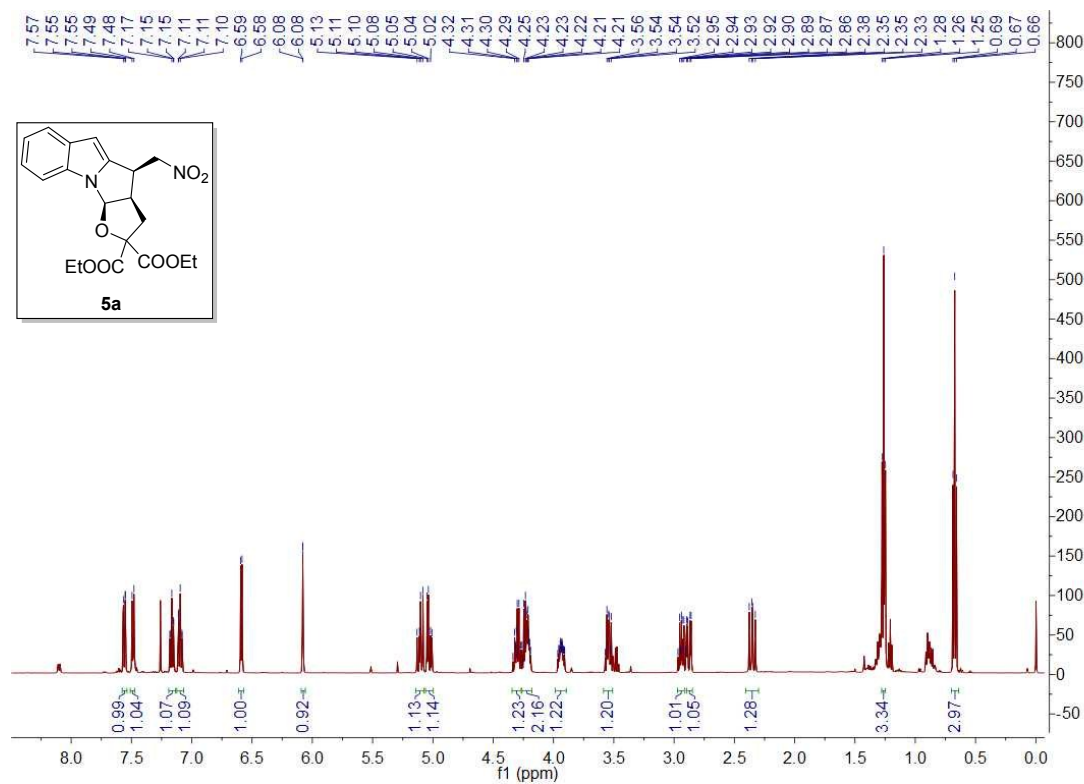
1'-(tert-butyl) 5,5-diethyl (2S,2'S,3R,3aR,6aR)-2'-azido-3-(nitromethyl)-3a,6a-dihydro-3H-spiro[furo[2,3-b]furan-2,3'-indoline]-1',5,5(4H)-tricarboxylate (17)

17 was obtained as a colorless oil 15.0 mg in 28% yield for two steps after separated by C-18 column (MeCN/H₂O = 70/30, t_R = 52 min). ¹H NMR (500 MHz, CDCl₃) δ 7.93 (s, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 6.37 (s, 1H), 6.01 (d,

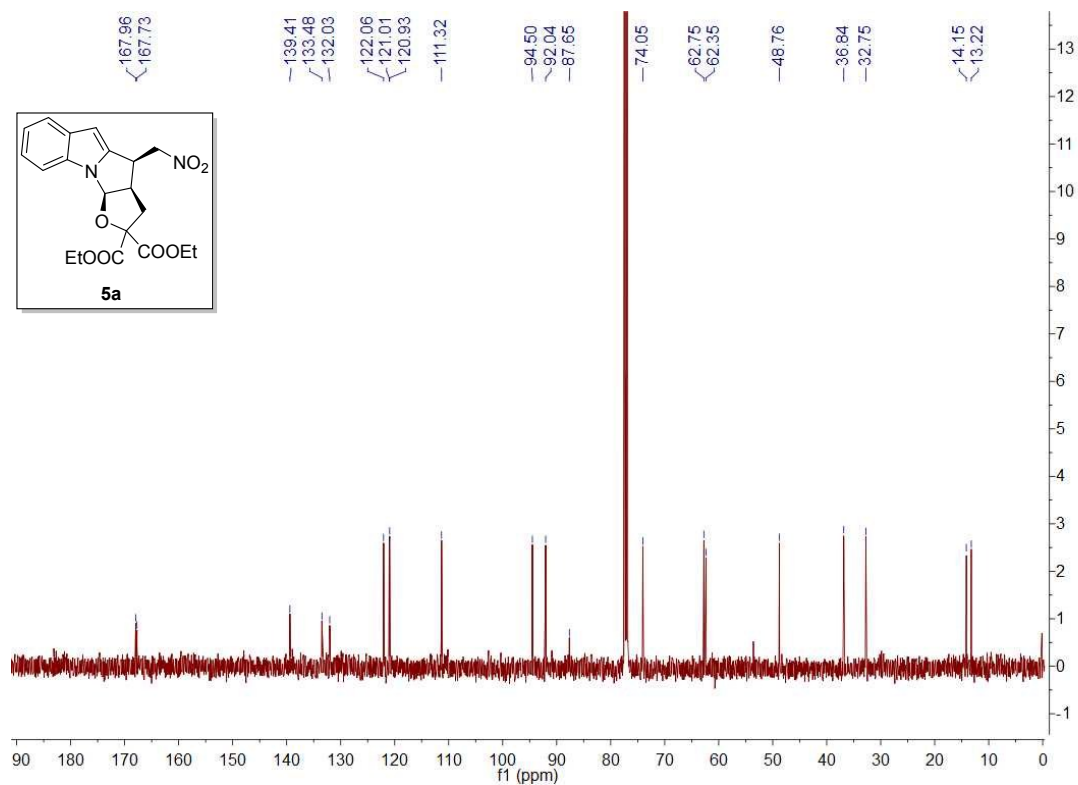
$J = 5.8$ Hz, 1H), 5.07 – 4.91 (m, 1H), 4.48 (d, $J = 14.0$ Hz, 1H), 4.38 (s, 1H), 4.32 – 4.23 (m, 3H), 3.73 – 3.59 (m, 1H), 3.54 – 3.35 (m, 1H), 2.80 (dd, $J = 13.6, 9.8$ Hz, 1H), 2.75 – 2.65 (m, 1H), 1.61 (s, 9H), 1.40 – 1.27 (m, 6H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 168.9, 167.2, 132.1, 123.8, 123.1, 116.3, 110.1, 87.2, 83.4, 80.2, 72.3, 62.7, 62.5, 45.1, 43.8, 33.1, 28.1, 14.0, 14.0 ppm. **HRMS:** $[\text{M}+\text{H}]^+$ *calcd.* For Chemical Formula: Chemical Formula: $\text{C}_{25}\text{H}_{31}\text{N}_5\text{NaO}_{10}^+$ 584.1963 found 584.1967. $[\alpha]_{\text{D}}^{20} +74.10$ ($c = 2.58$ in CHCl_3). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 75/25, 1 mL/min], $\lambda = 220$ nm, $t_{\text{major}} = 5.50$ min, $t_{\text{minor}} = 5.88$ min, **ee** >99%. The diastereomeric ratio was determined by ^1H NMR **dr** >20:1.

F. NMR spectra and HPLC traces

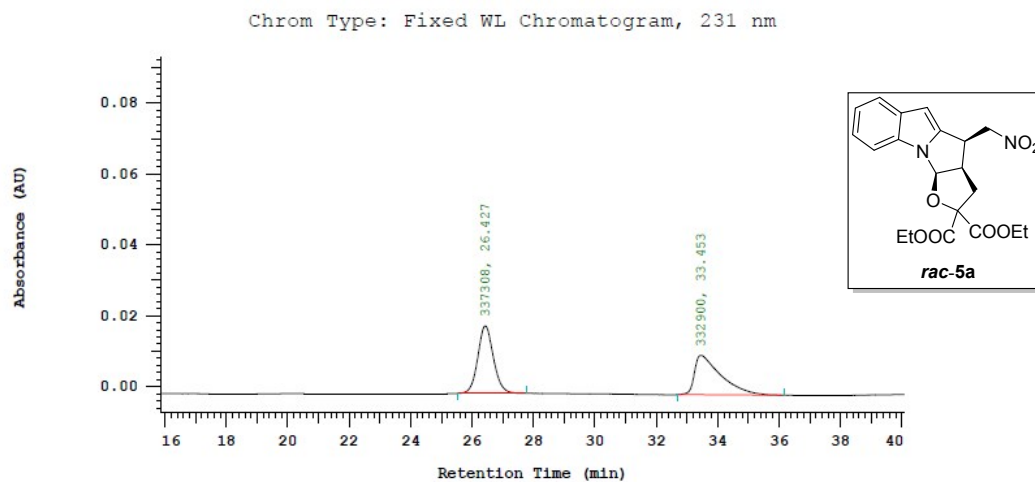
The ^1H NMR spectrum of 5a (500 MHz, CDCl_3)



The ^{13}C NMR spectrum of 5a (125 MHz, CDCl_3)



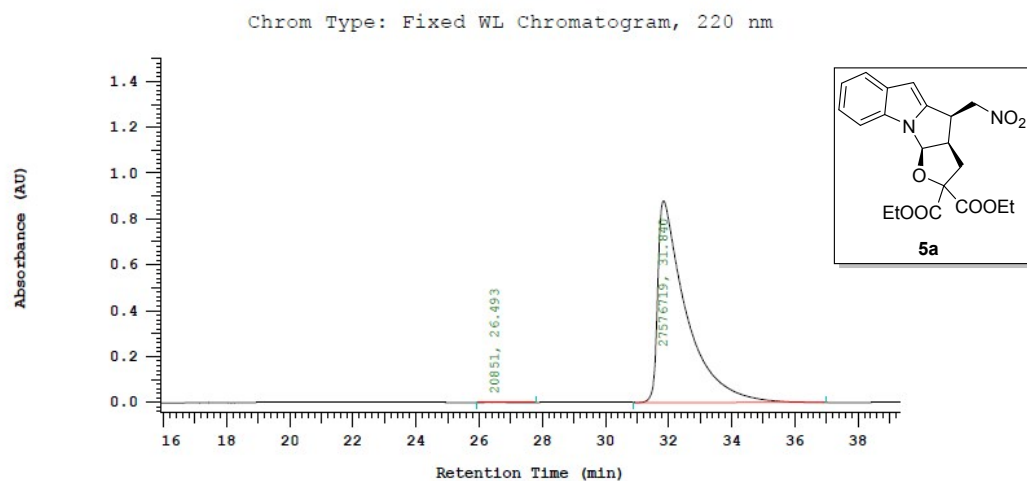
The HPLC of racemic 5a



Chrom Type: Fixed WL Chromatogram, 231 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	26.427	337308	50.329	BB
2	33.453	332900	49.671	BB
		670208	100.000	

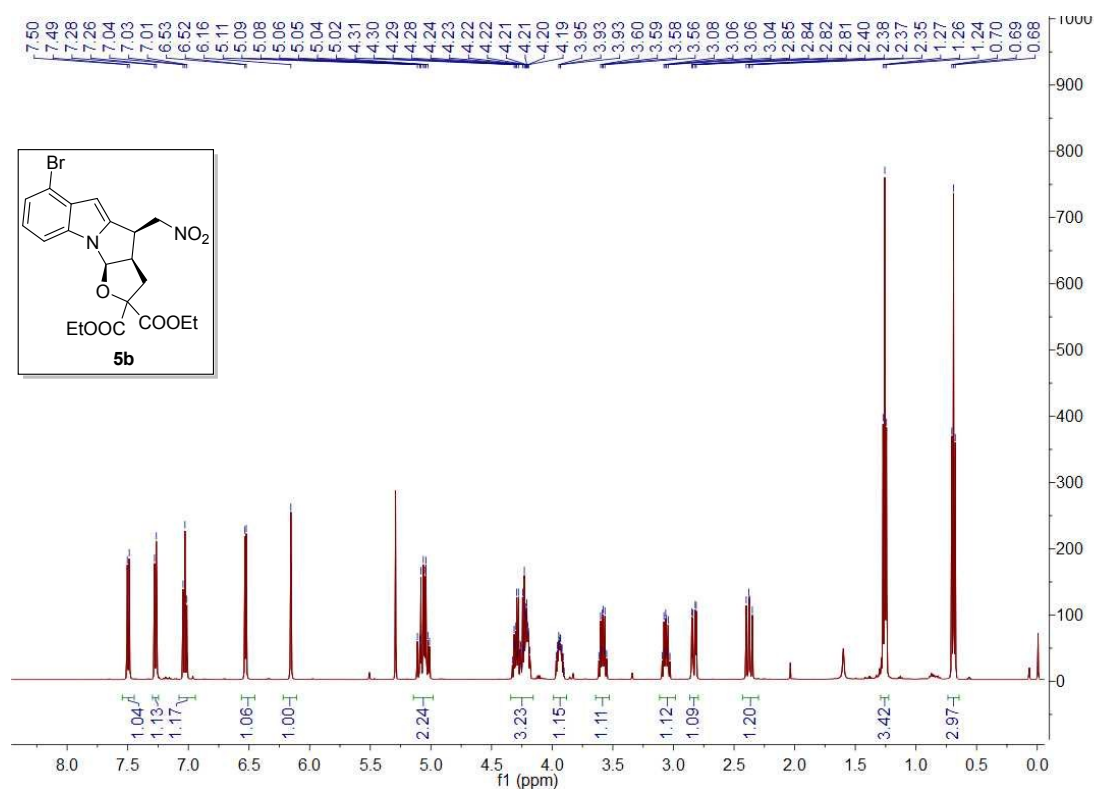
The HPLC of chiral 5a



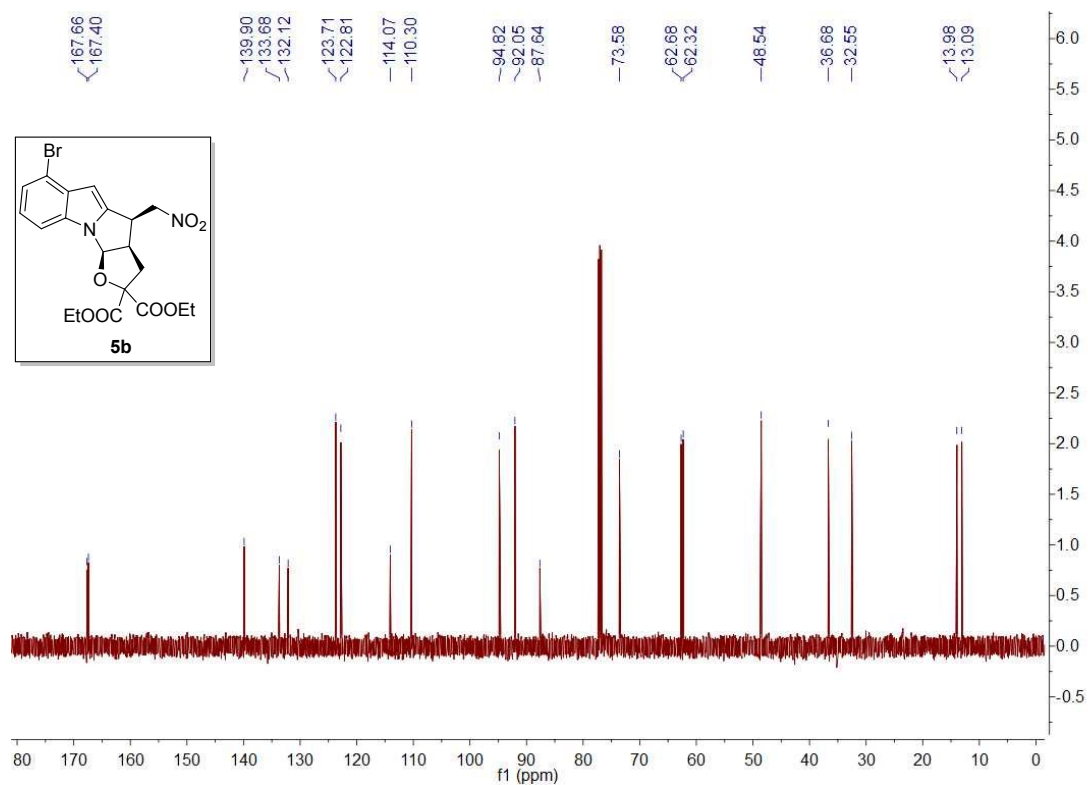
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	26.493	20851	0.076	BB
2	31.840	27576719	99.924	BB
		27597570	100.000	

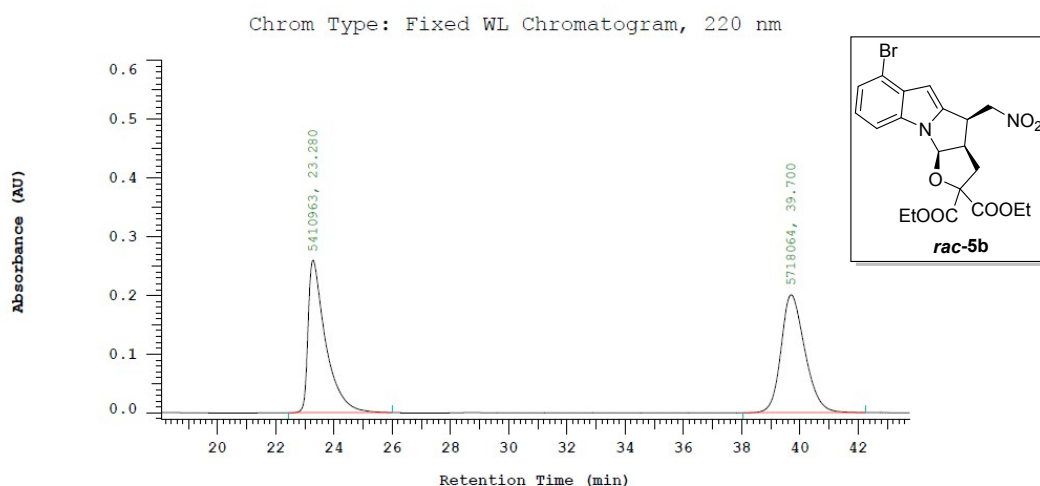
The ¹H NMR spectrum of 5b (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 5b (125 MHz, CDCl₃)



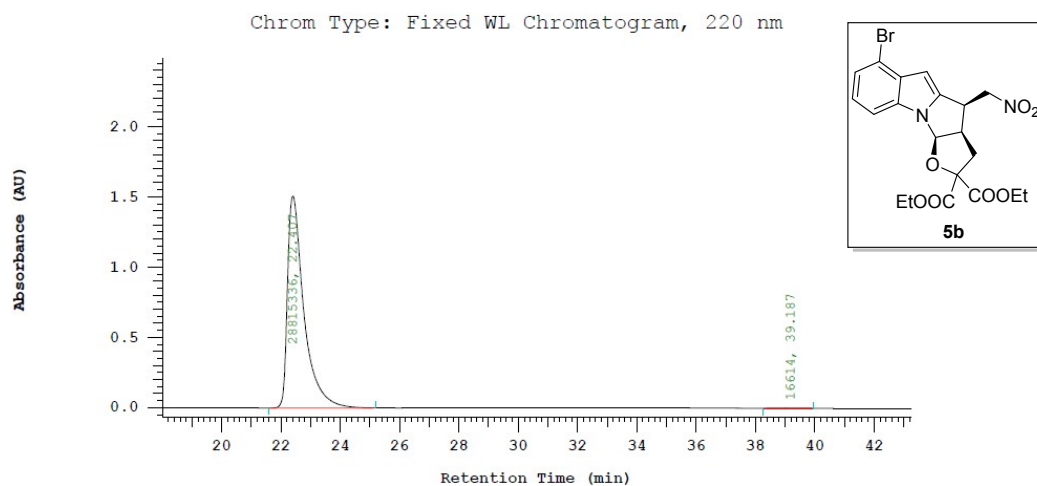
The HPLC of racemic 5b



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	23.280	5410963	48.620	BB
2	39.700	5718064	51.380	BB
		11129027	100.000	

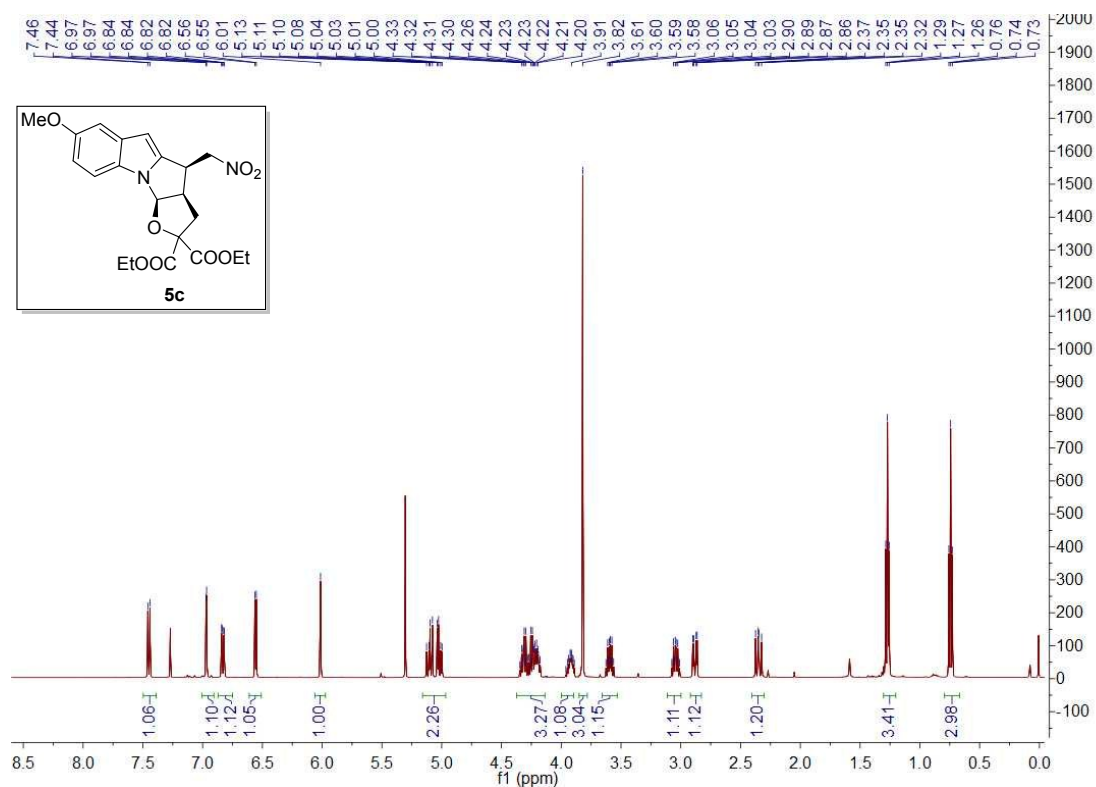
The HPLC of chiral 5b



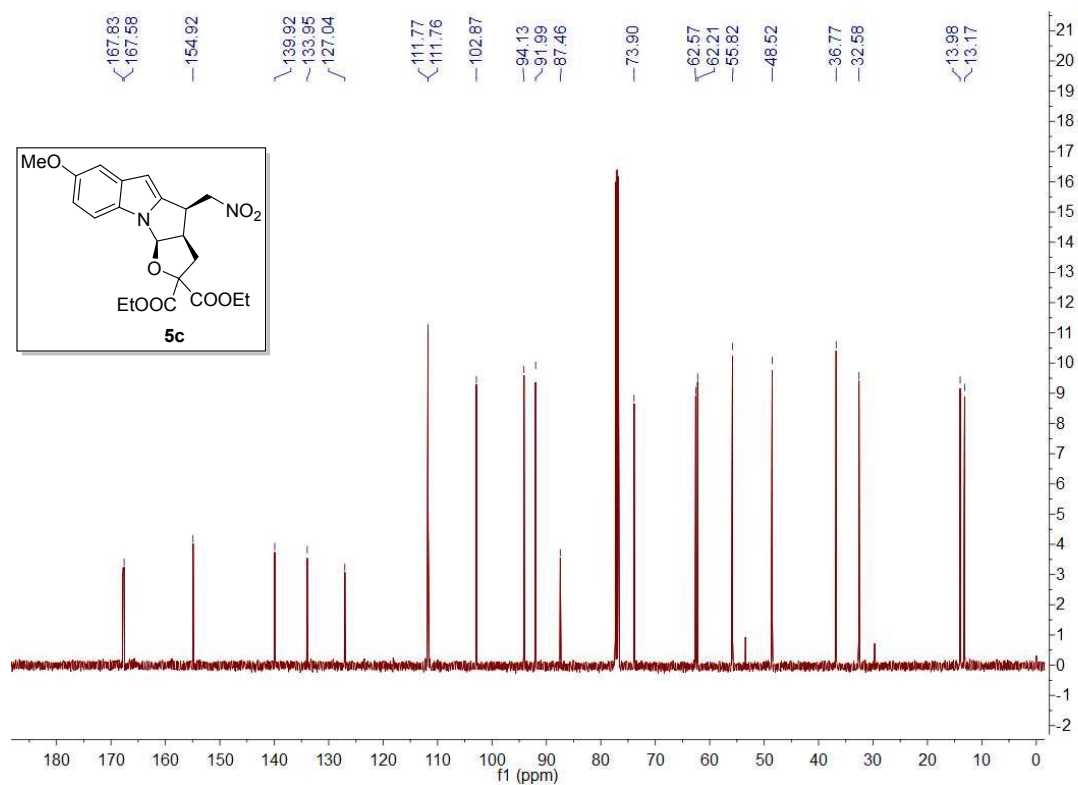
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	22.407	28815336	99.942	BB
2	39.187	16614	0.058	BB
		28831950	100.000	

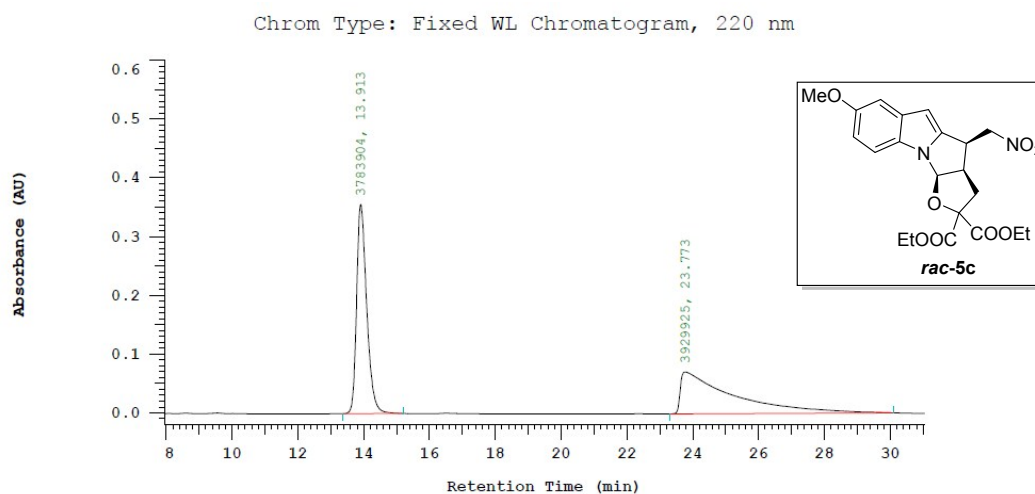
The ¹H NMR spectrum of 5c (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 5c (125 MHz, CDCl₃)



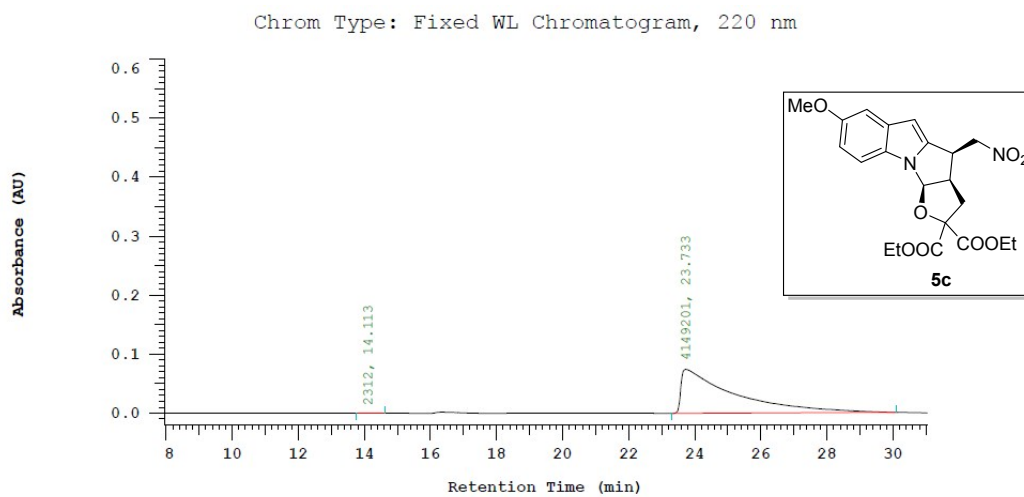
The HPLC of racemic 5c



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	13.913	3783904	49.054	BB
2	23.773	3929925	50.946	BB
		7713829	100.000	

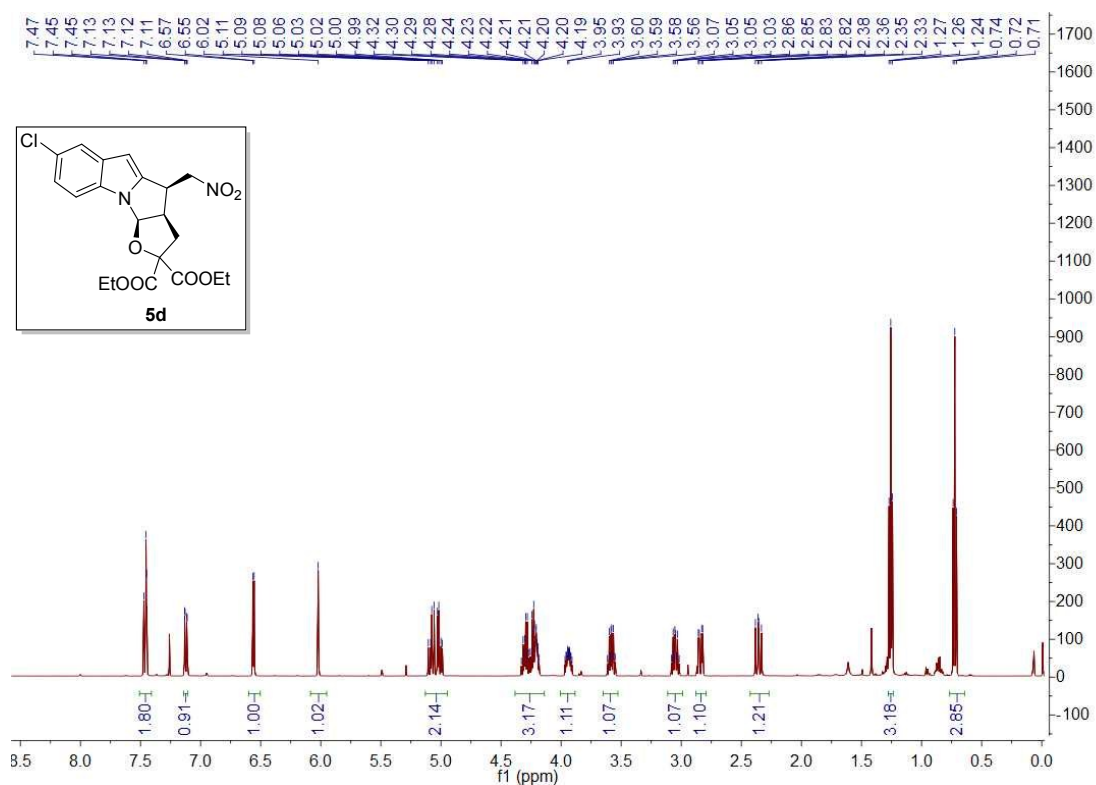
The HPLC of chiral 5c



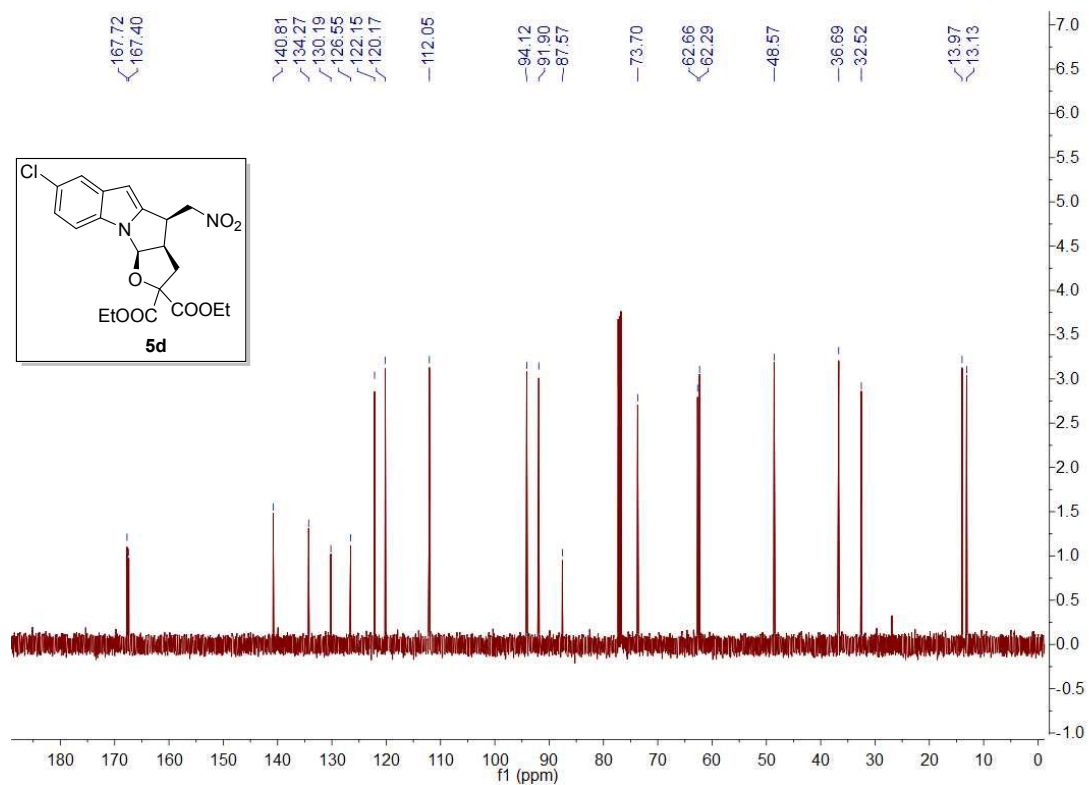
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	14.113	2312	0.056	BB
2	23.733	4149201	99.944	BB
		4151513	100.000	

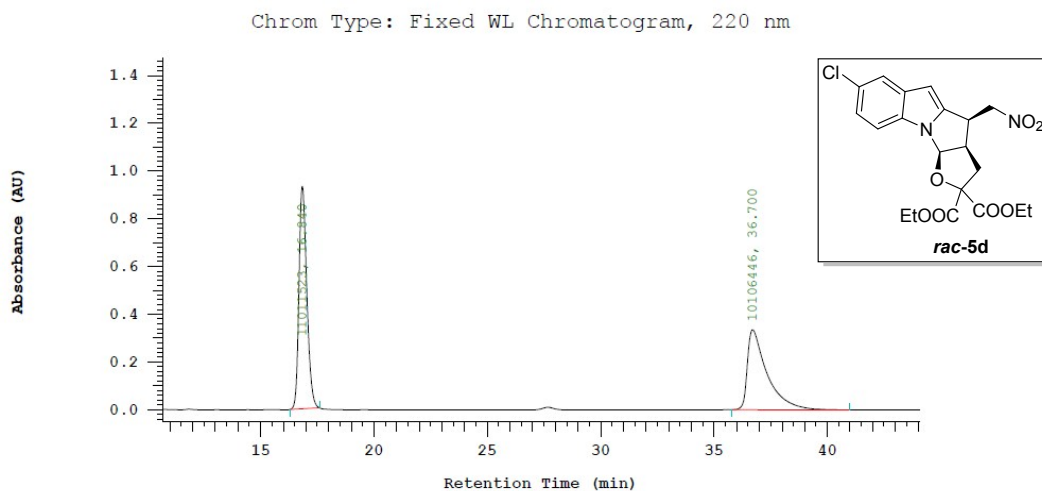
The ^1H NMR spectrum of 5d (500 MHz, CDCl_3)



The ^{13}C NMR spectrum of 5d (125 MHz, CDCl_3)



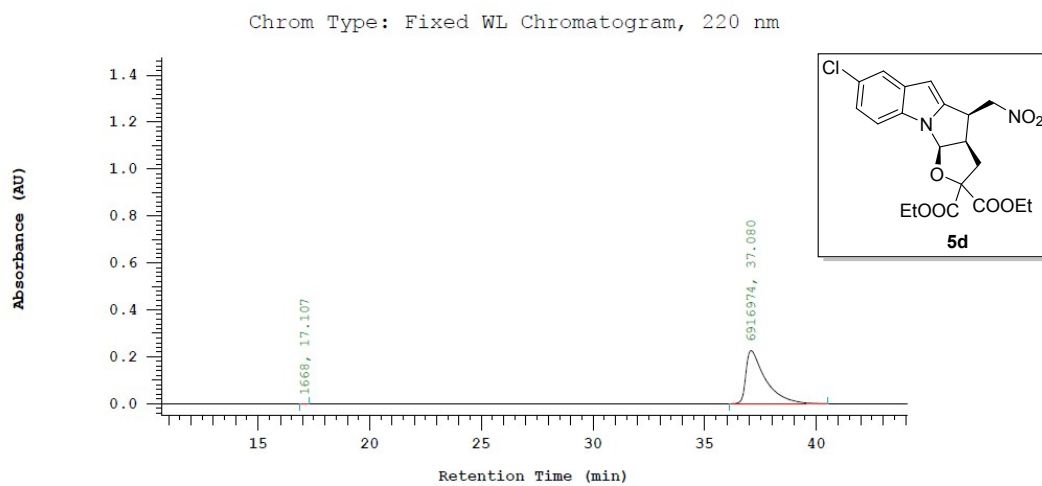
The HPLC of racemic 5d



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	16.840	11011523	52.143	BB
2	36.700	10106446	47.857	BB
		21117969	100.000	

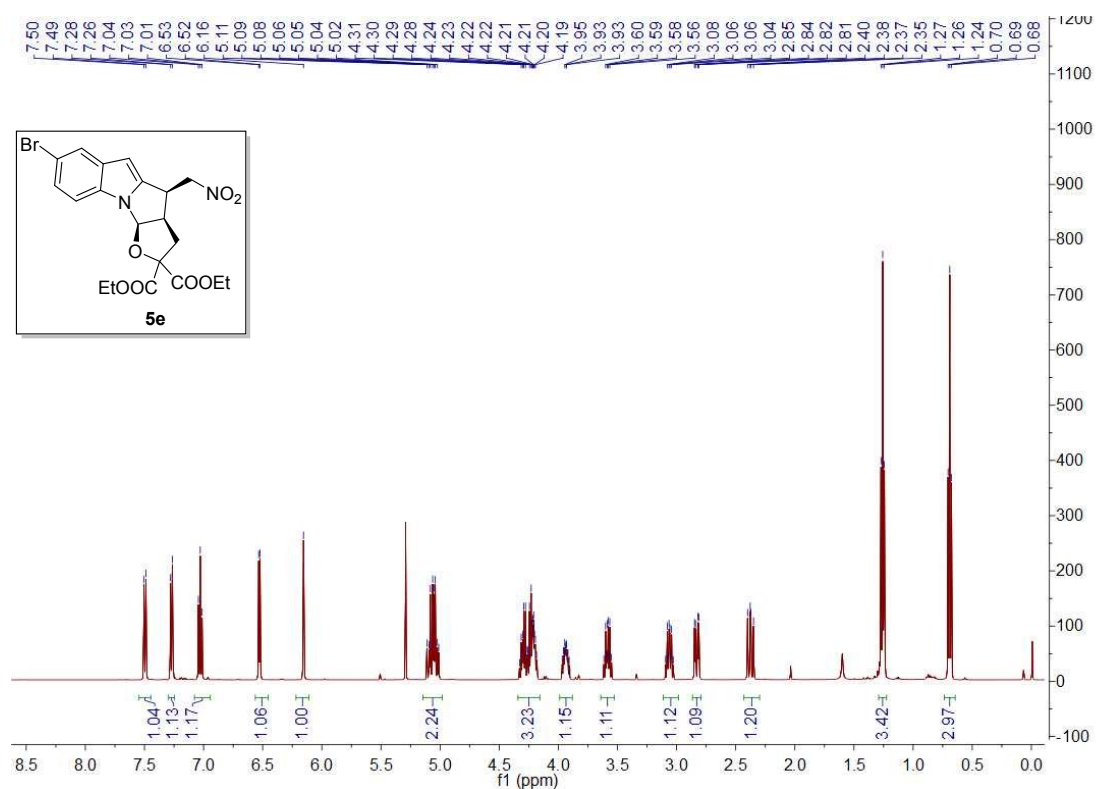
The HPLC of chiral 5d



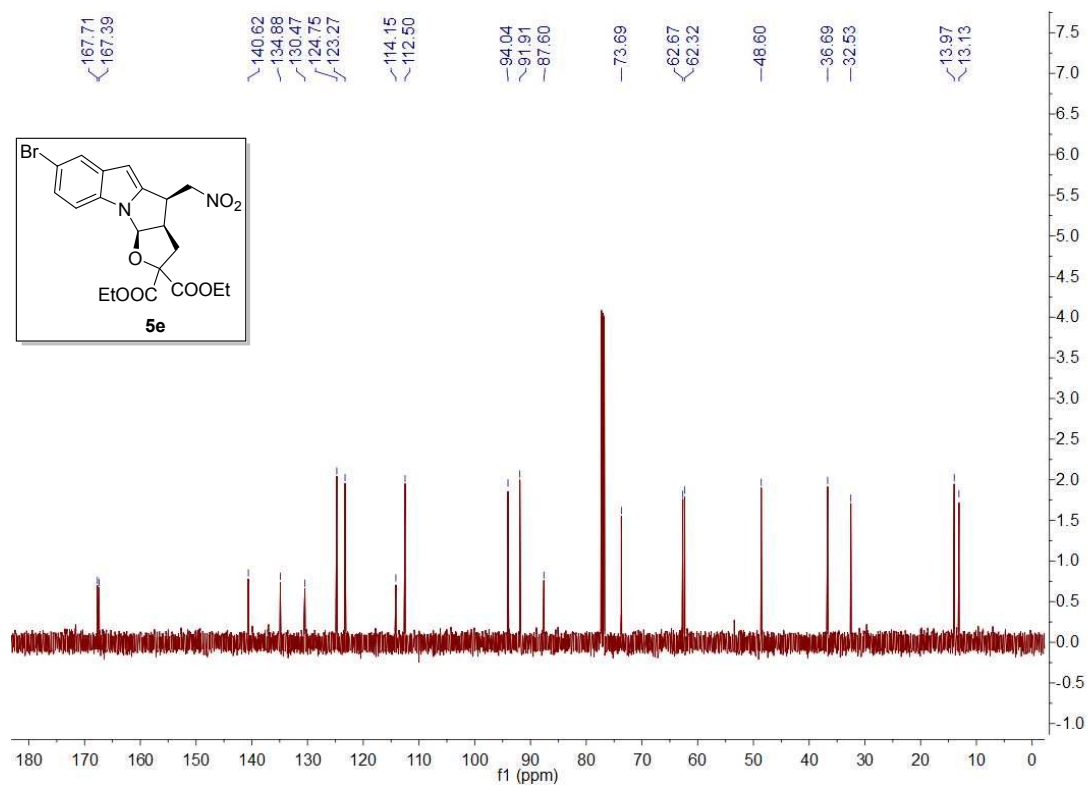
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.107	1668	0.024	BB
2	37.080	6916974	99.976	BB
		6918642	100.000	

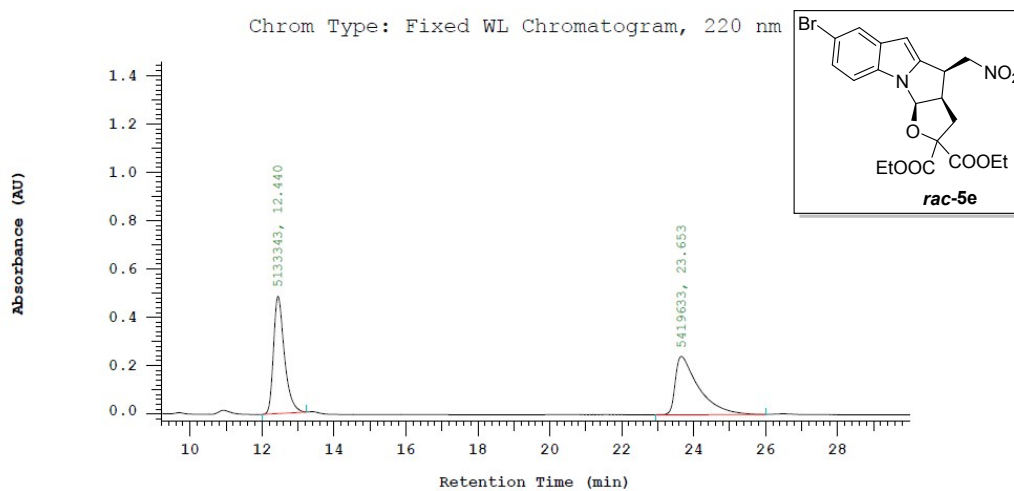
The ¹H NMR spectrum of 5e (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 5e (125 MHz, CDCl₃)



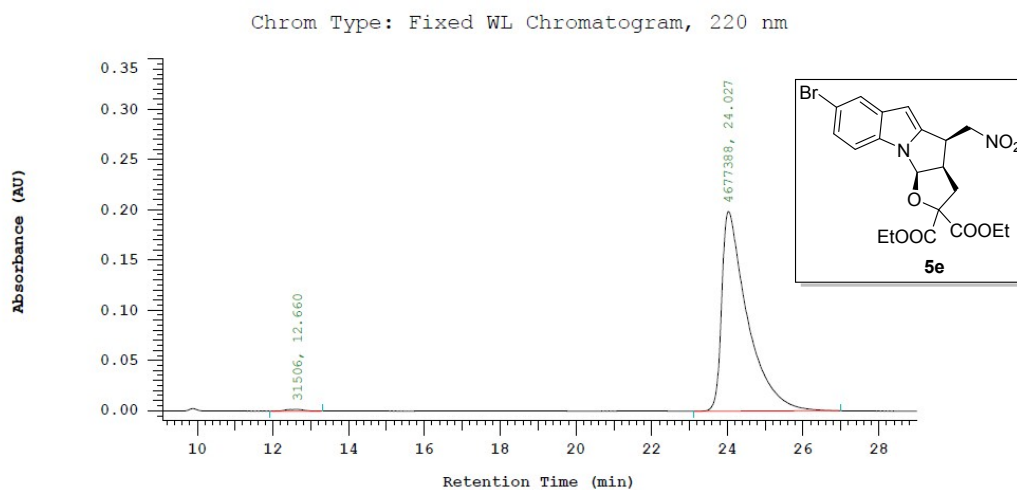
The HPLC of racemic 5e



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.440	5133343	48.644	BB
2	23.653	5419633	51.356	BB
		10552976	100.000	

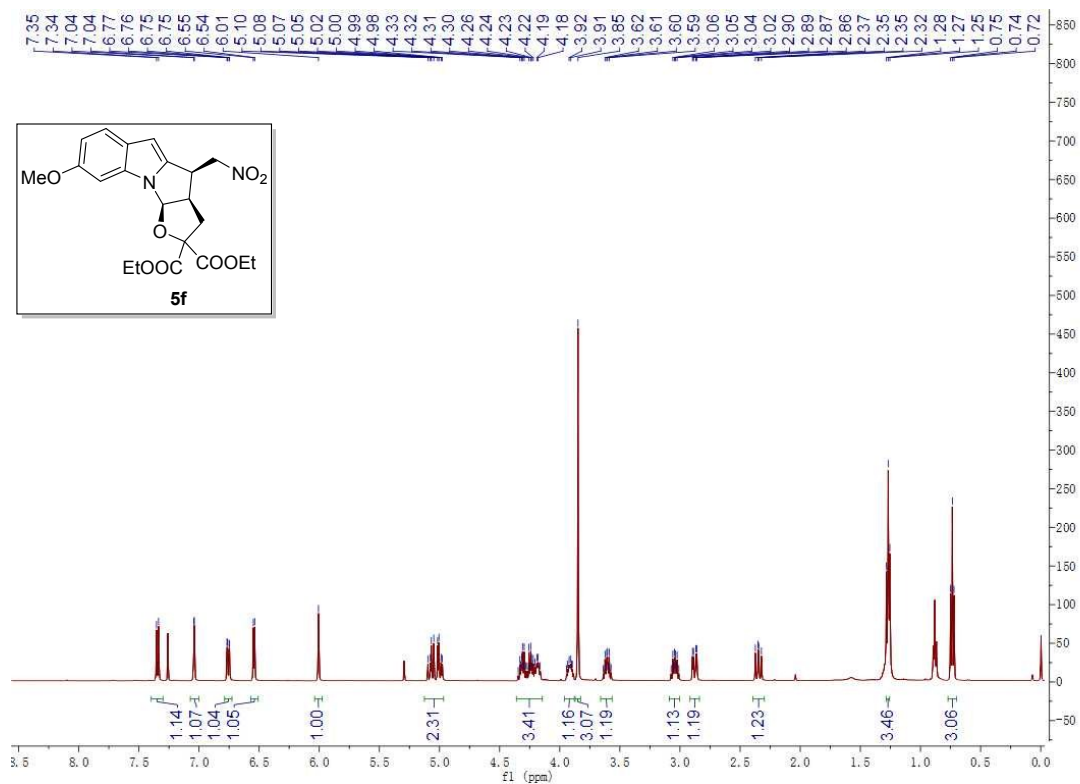
The HPLC of chiral 5e



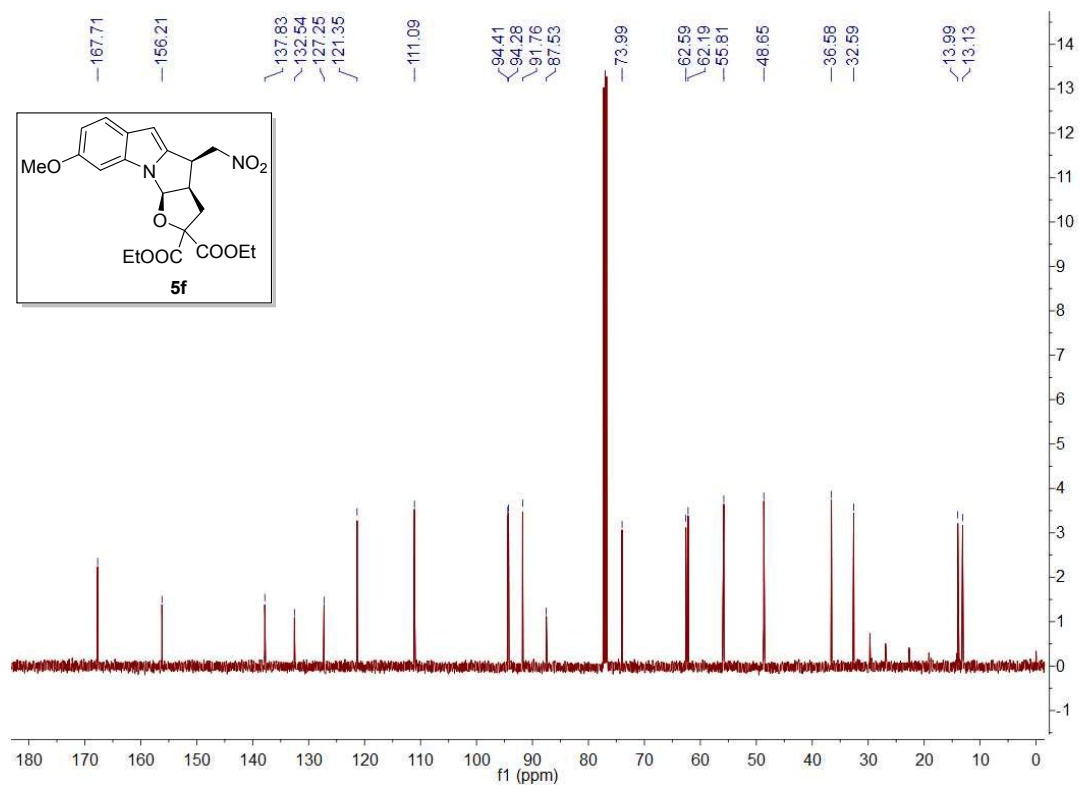
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.660	31506	0.669	BB
2	24.027	4677388	99.331	BB
		4708894	100.000	

The ¹H NMR spectrum of 5f (500 MHz, CDCl₃)

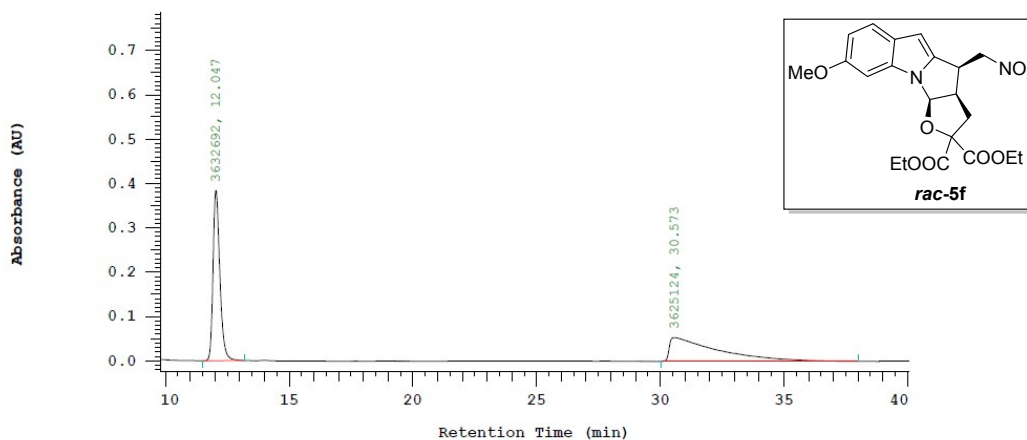


The ¹³C NMR spectrum of 5f (125 MHz, CDCl₃)



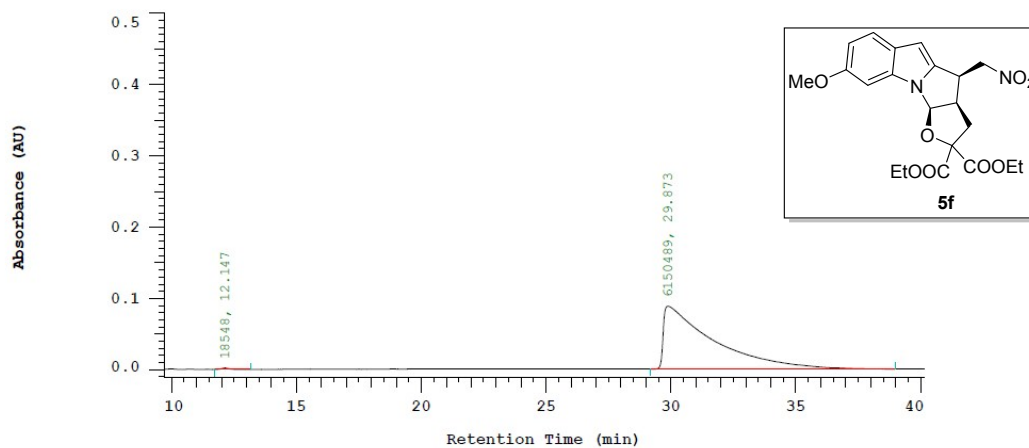
The HPLC of racemic 5f

Chrom Type: Fixed WL Chromatogram, 220 nm

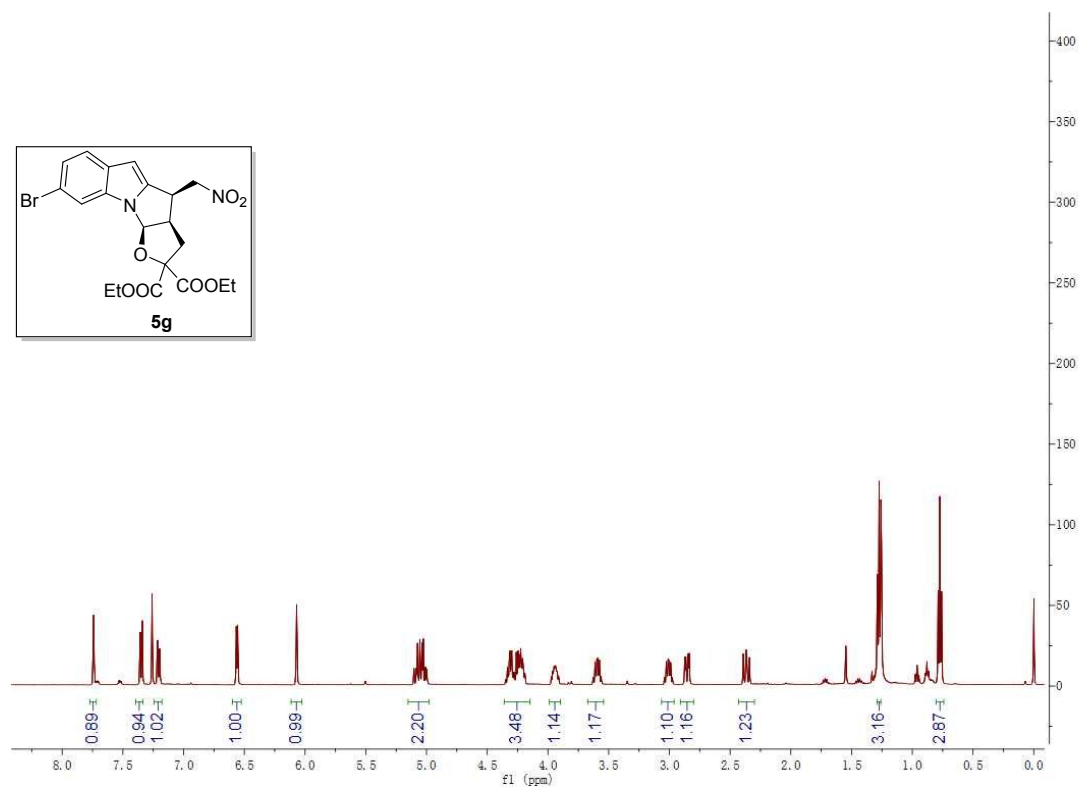


The HPLC of chiral 5f

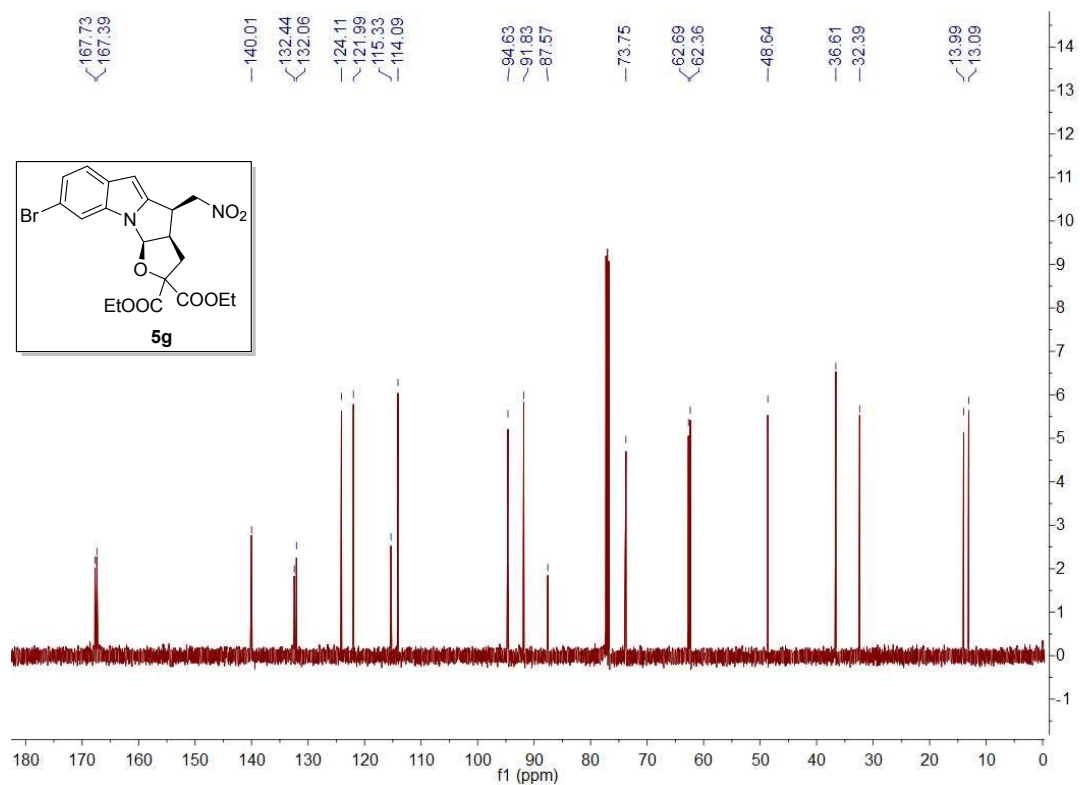
Chrom Type: Fixed WL Chromatogram, 220 nm



The ¹H NMR spectrum of 5g (500 MHz, CDCl₃)

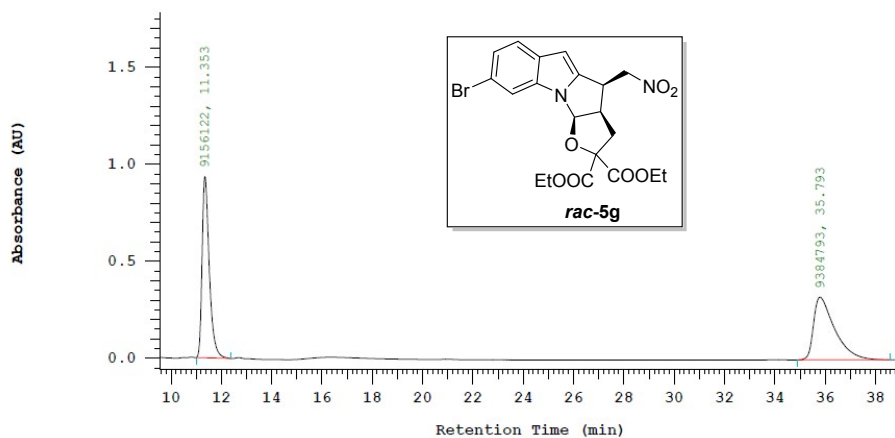


The ¹³C NMR spectrum of 5g (125 MHz, CDCl₃)



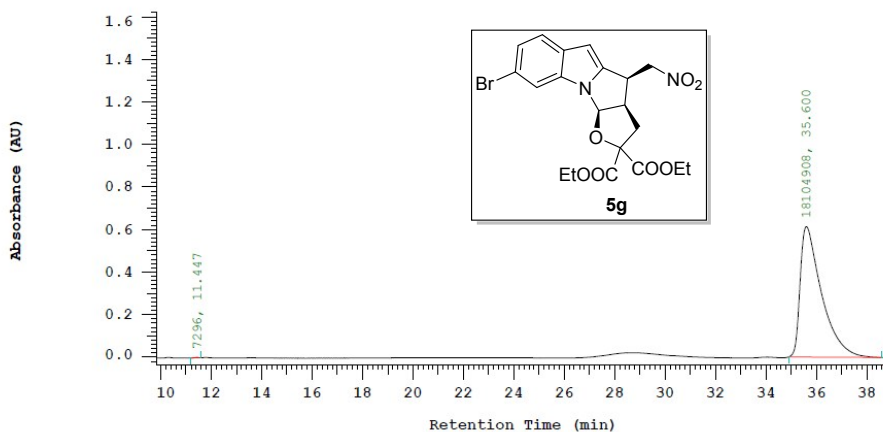
The HPLC of racemic 5g

Chrom Type: Fixed WL Chromatogram, 220 nm

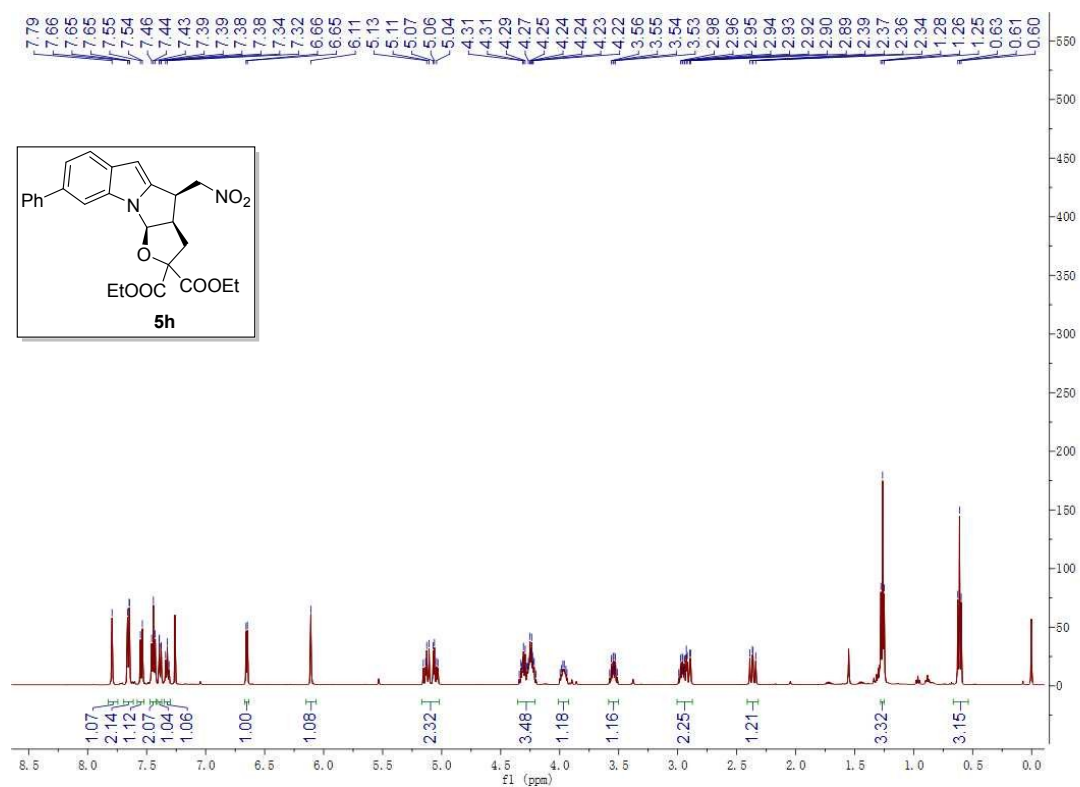


The HPLC of chiral 5g

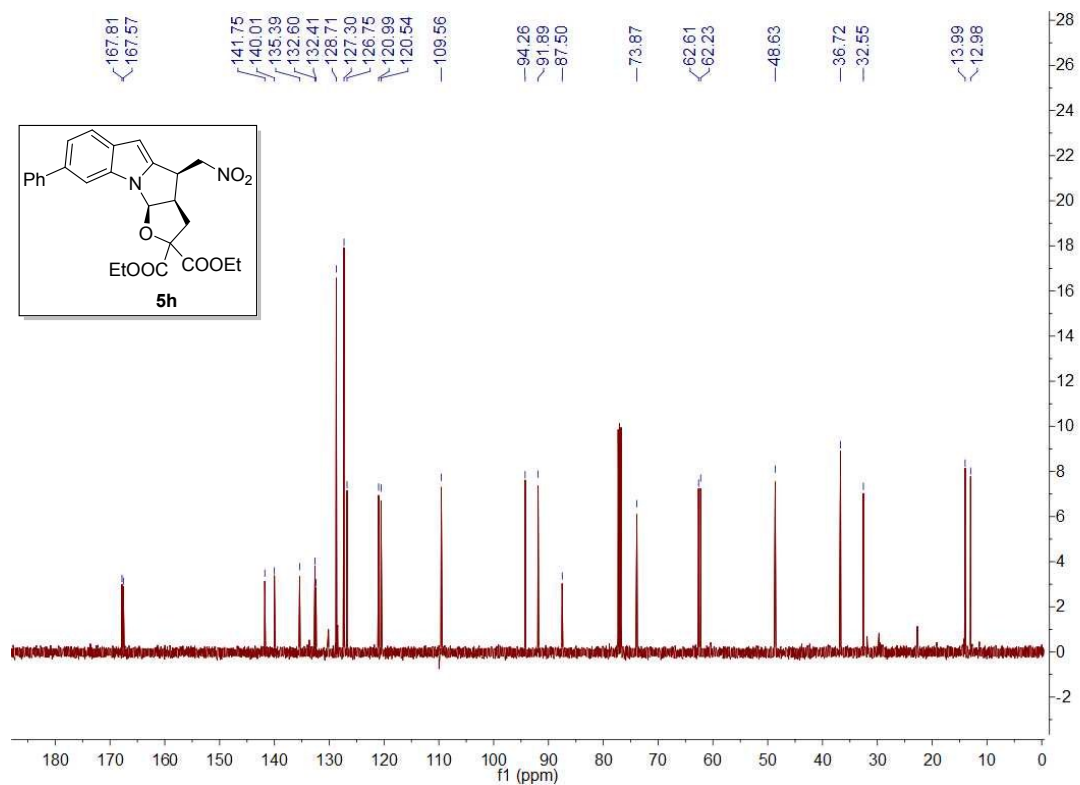
Chrom Type: Fixed WL Chromatogram, 220 nm



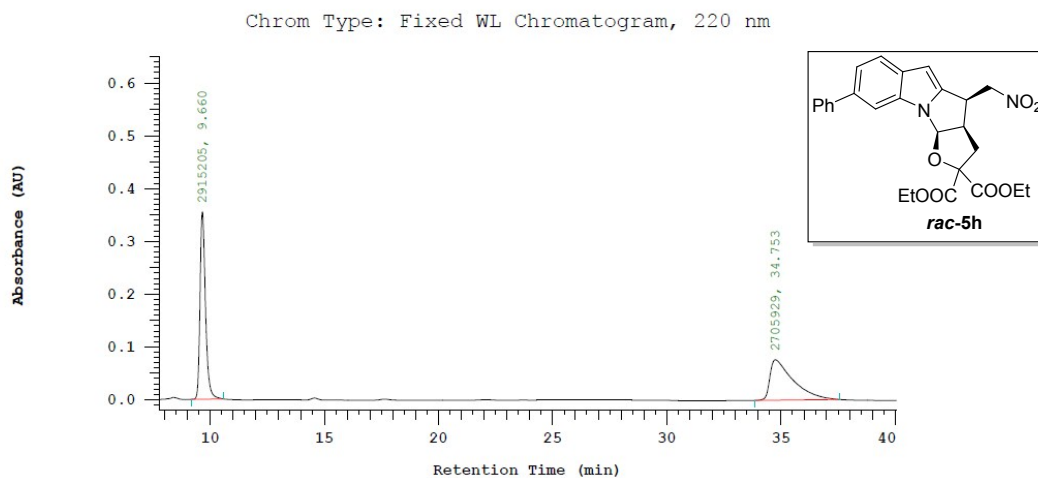
The ^1H NMR spectrum of 5h (500 MHz, CDCl_3)



The ^{13}C NMR spectrum of 5h (125 MHz, CDCl_3)



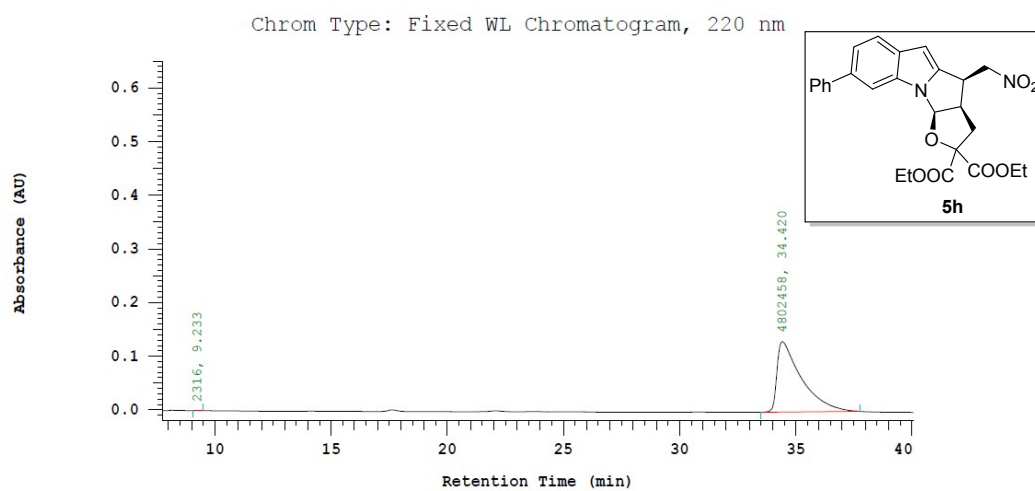
The HPLC of racemic 5h



Chrom Type: Fixed WL Chromatogram, 220 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.660	2915205	51.862	BB
2	34.753	2705929	48.138	BB
		5621134	100.000	

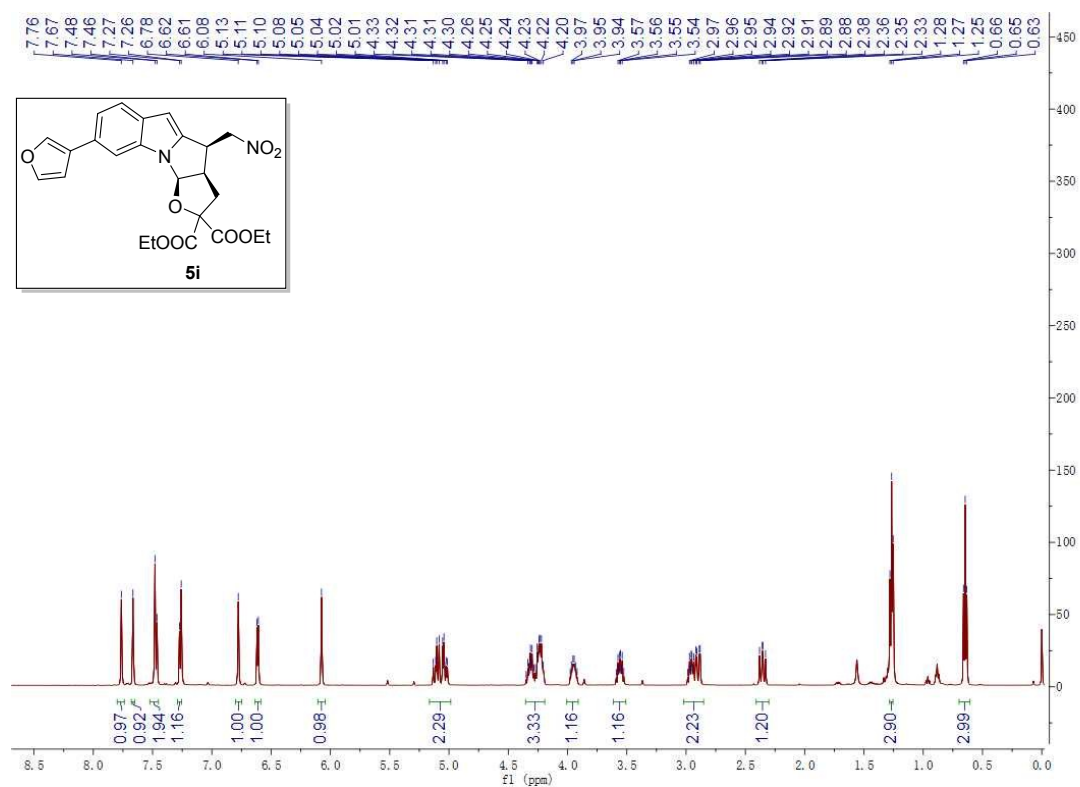
The HPLC of chiral 5h



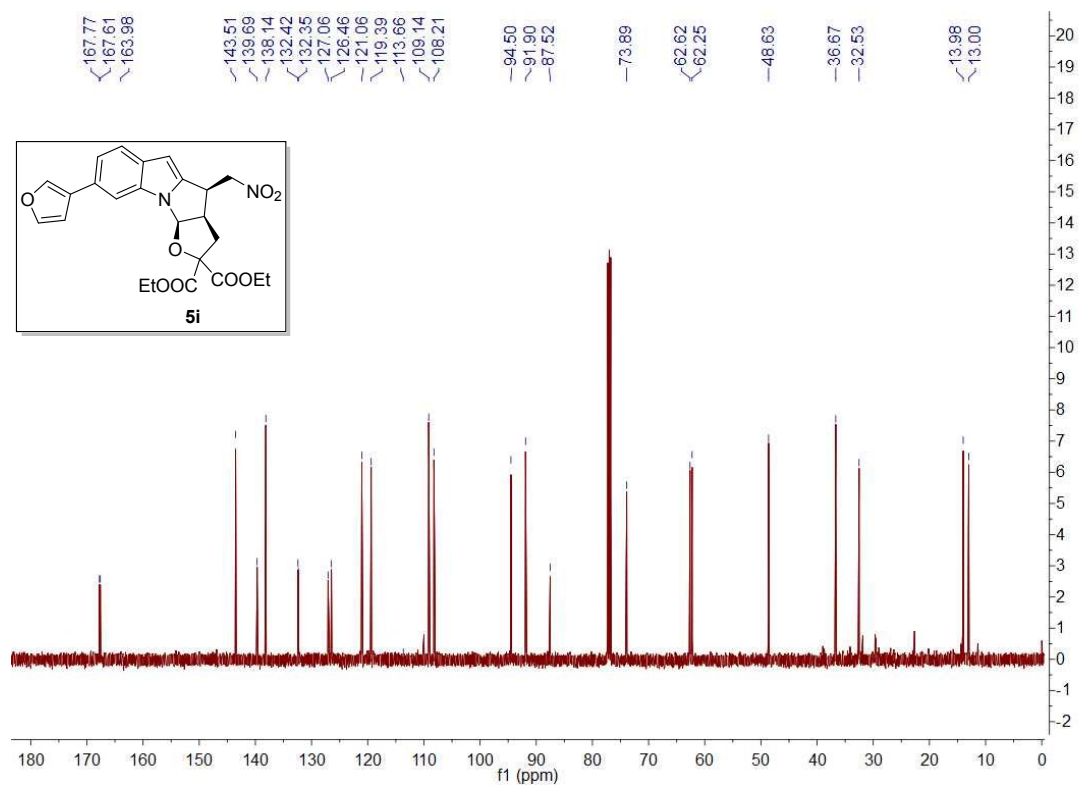
Chrom Type: Fixed WL Chromatogram, 220 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.233	2316	0.048	BB
2	34.420	4802458	99.952	BB
		4804774	100.000	

The ^1H NMR spectrum of **5i** (500 MHz, CDCl_3)

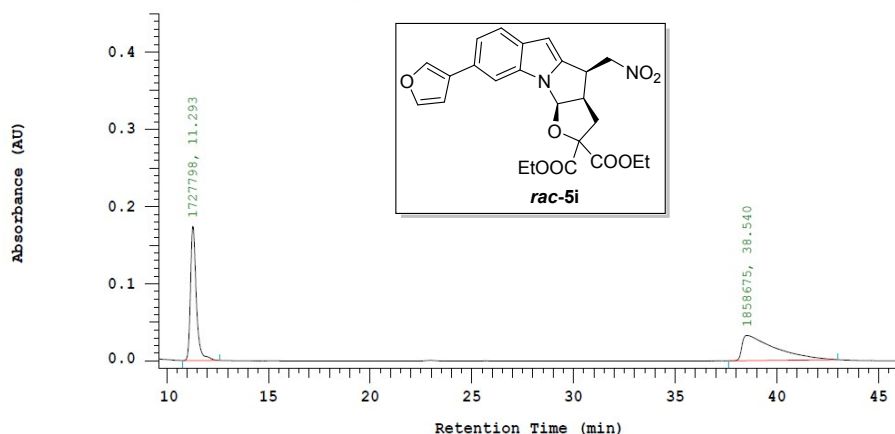


The ^{13}C NMR spectrum of **5i** (125 MHz, CDCl_3)



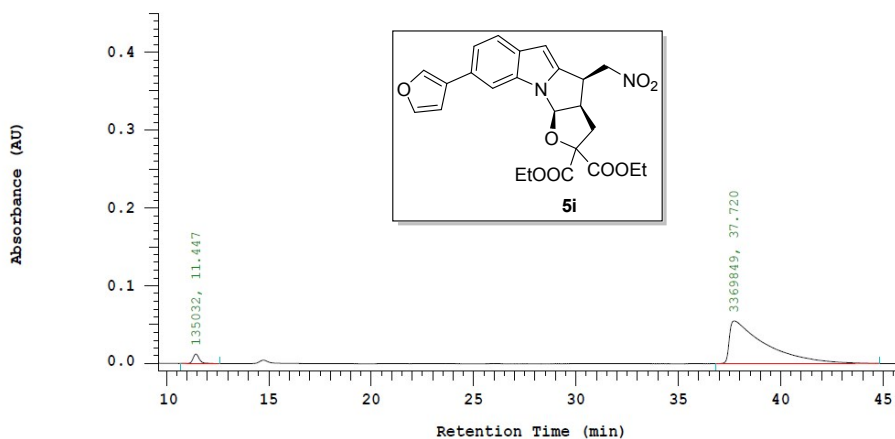
The HPLC of racemic 5i

Chrom Type: Fixed WL Chromatogram, 220 nm

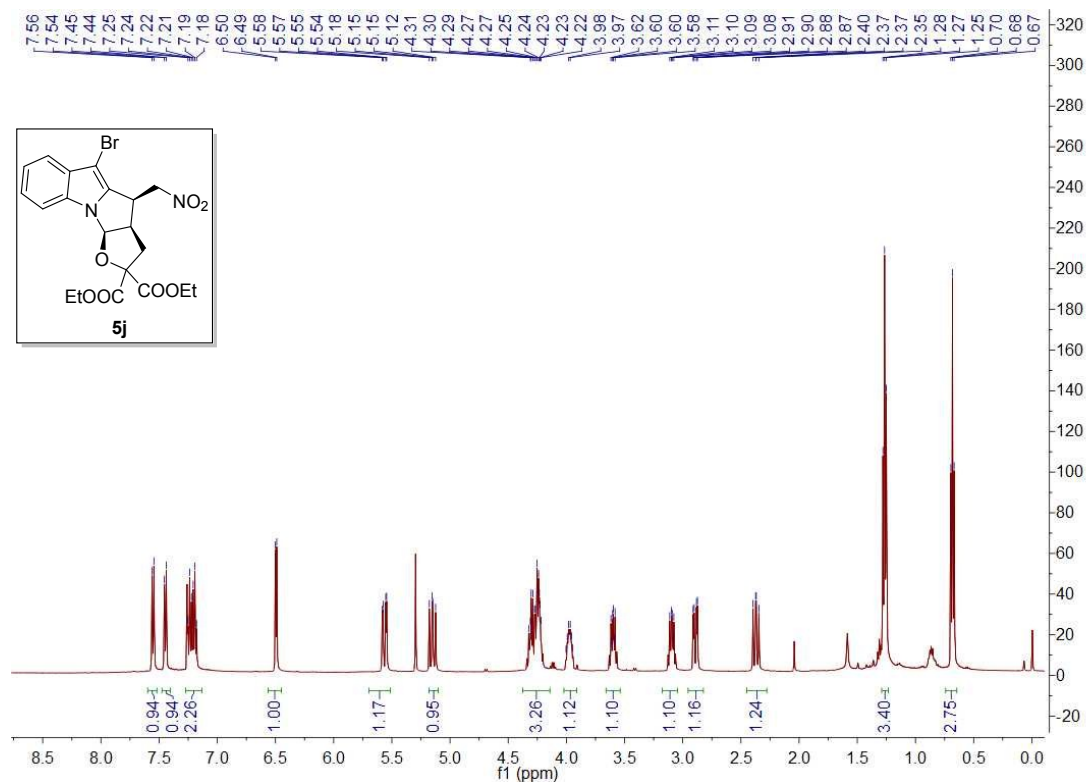


The HPLC of chiral 5i

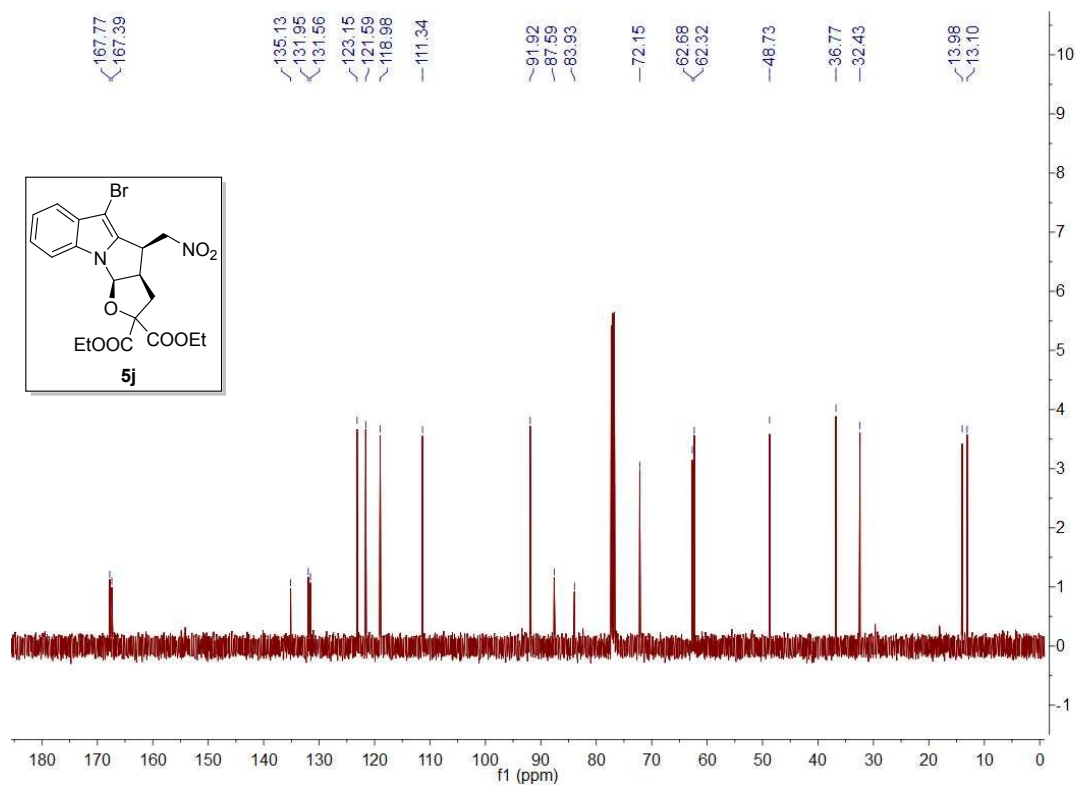
Chrom Type: Fixed WL Chromatogram, 220 nm



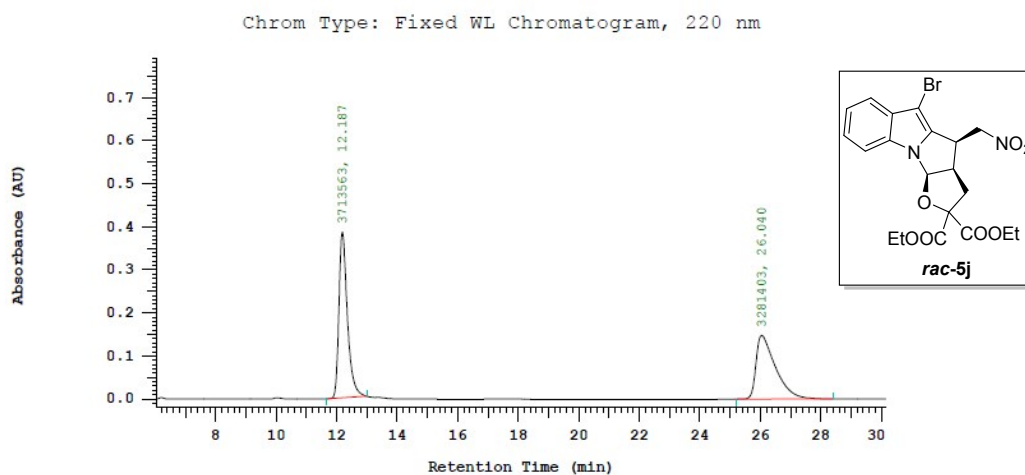
The ¹H NMR spectrum of 5j (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 5j (125 MHz, CDCl₃)



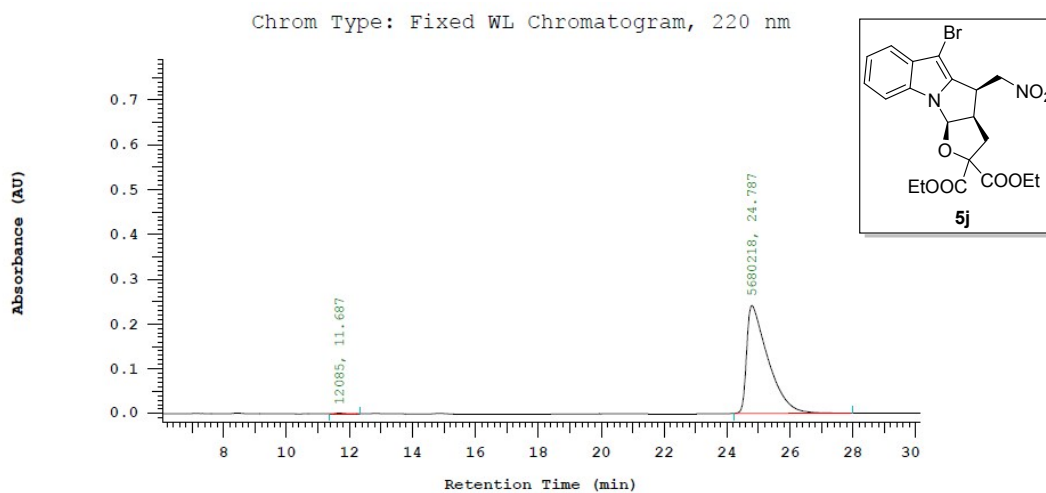
The HPLC of racemic 5j



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.187	3713563	53.089	BB
2	26.040	3281403	46.911	BB
		6994966	100.000	

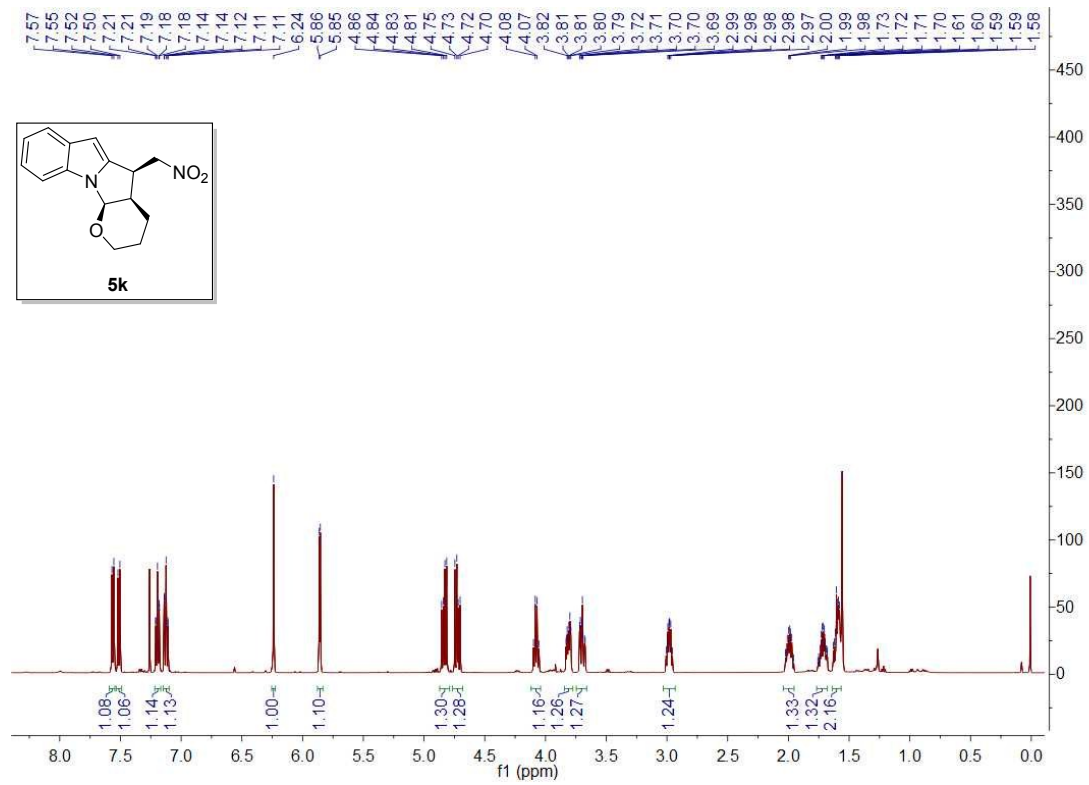
The HPLC of chiral 5j



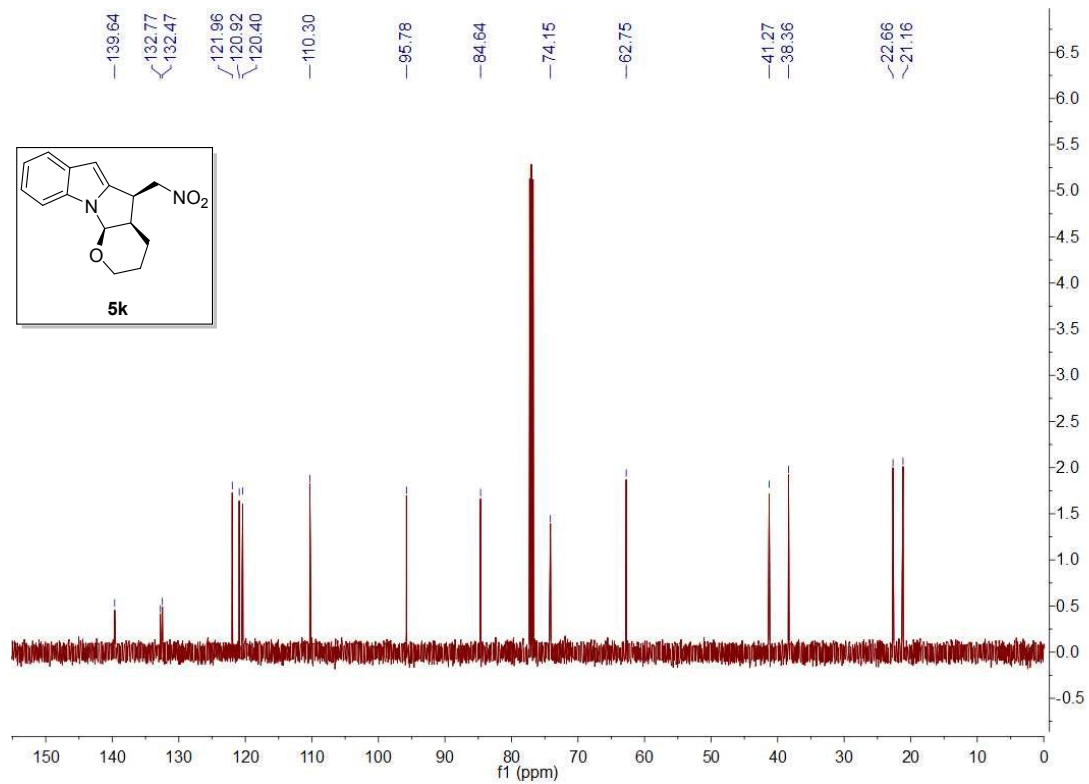
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.687	12085	0.212	BB
2	24.787	5680218	99.788	BB
		5692303	100.000	

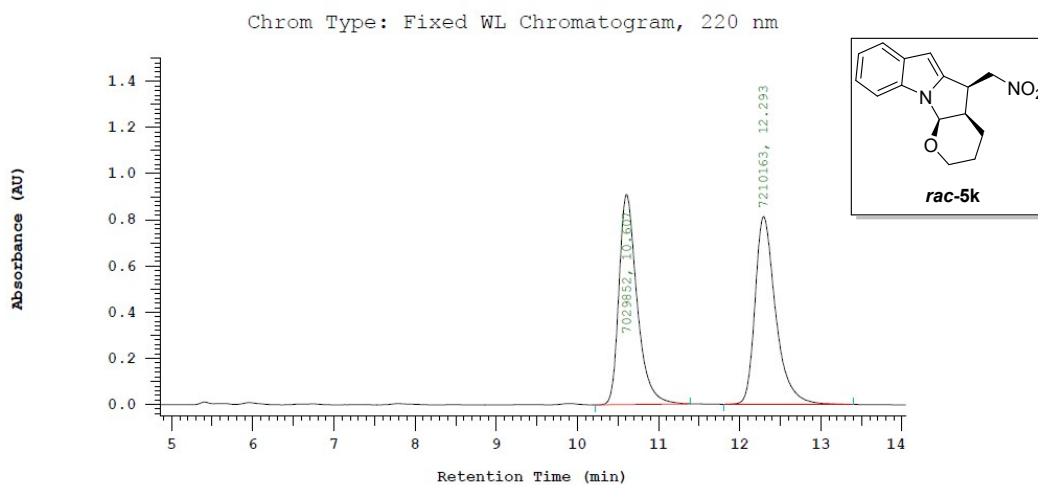
The ¹H NMR spectrum of 5k (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 5k (125 MHz, CDCl₃)



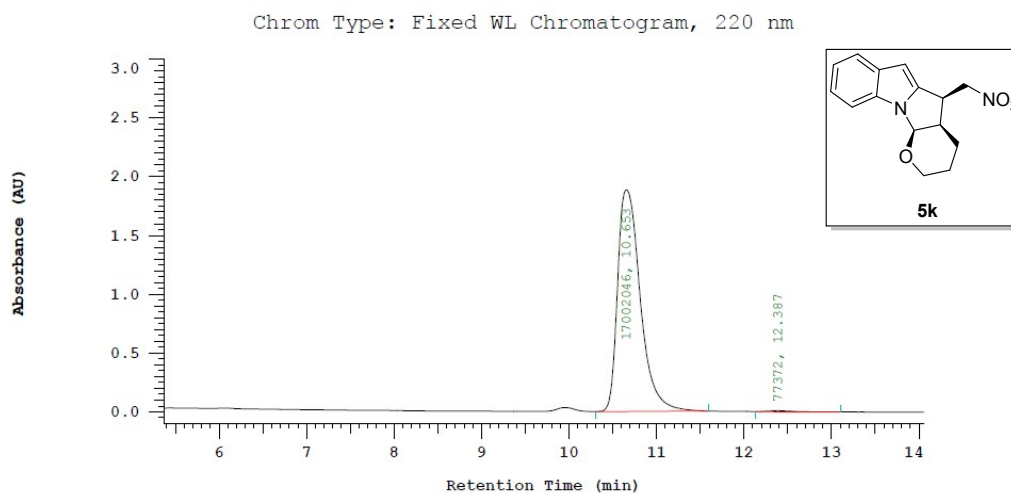
The HPLC of racemic 5k



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.607	7029852	49.367	BB
2	12.293	7210163	50.633	BB
		14240015	100.000	

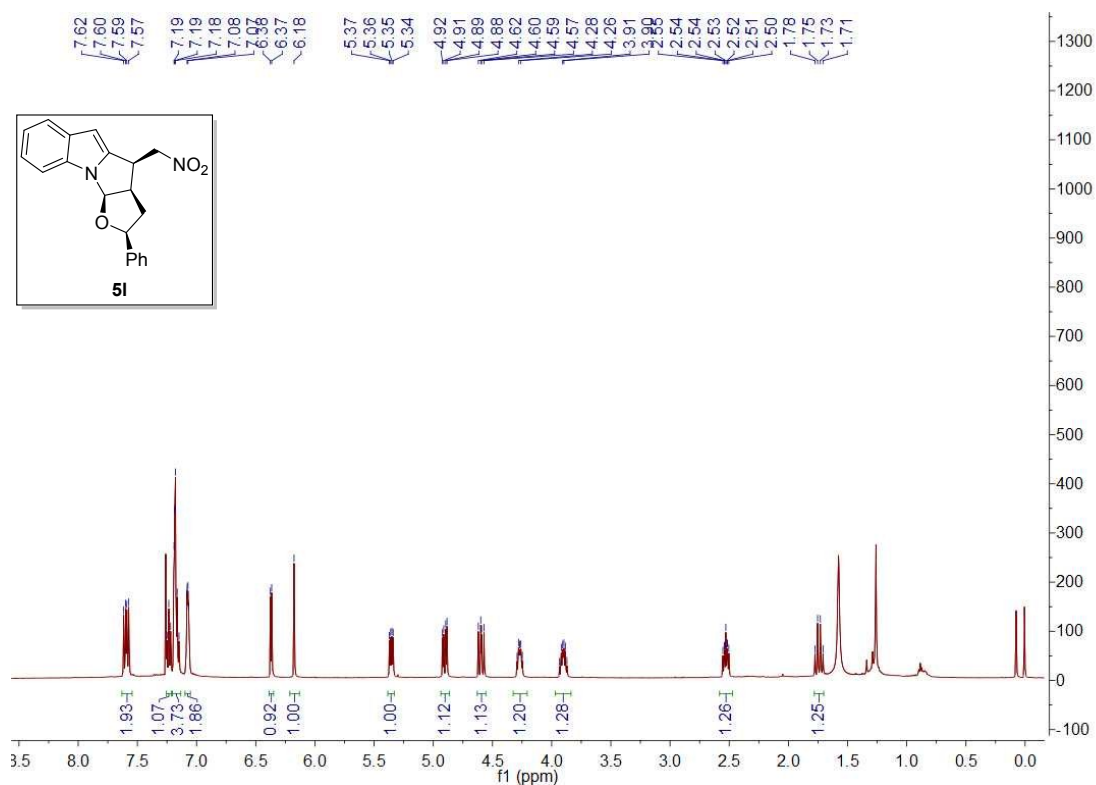
The HPLC of chiral 5k



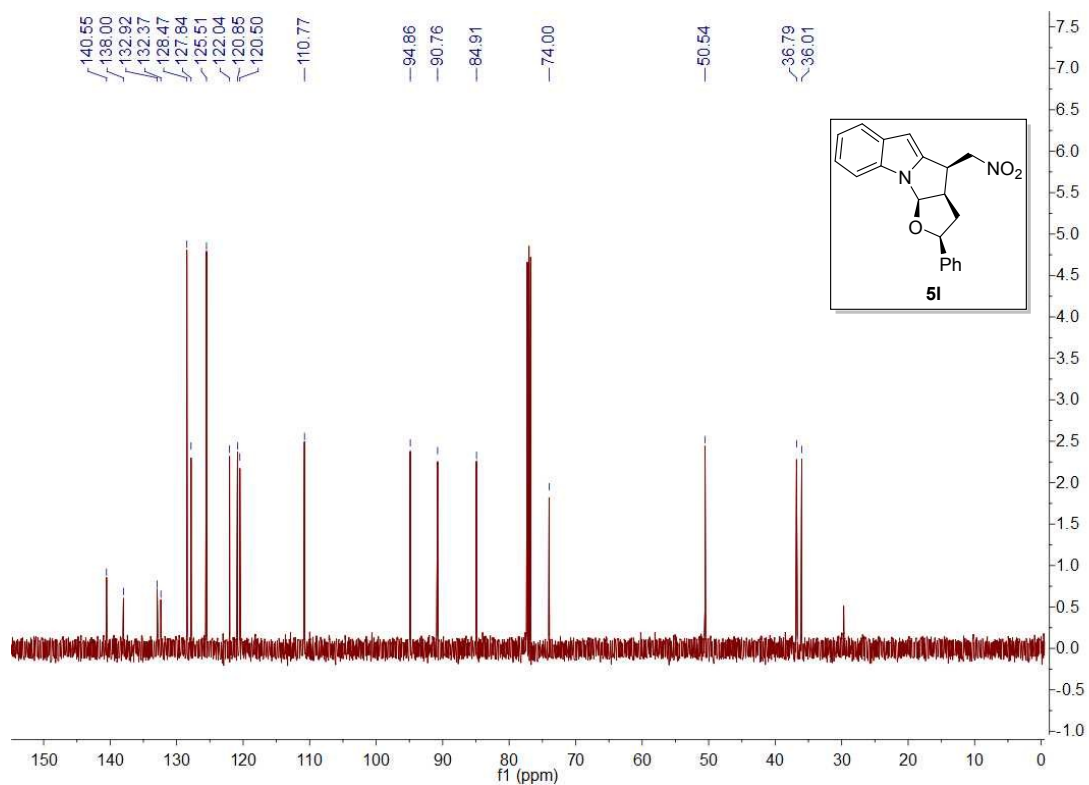
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.653	17002046	99.547	BB
2	12.387	77372	0.453	BB
		17079418	100.000	

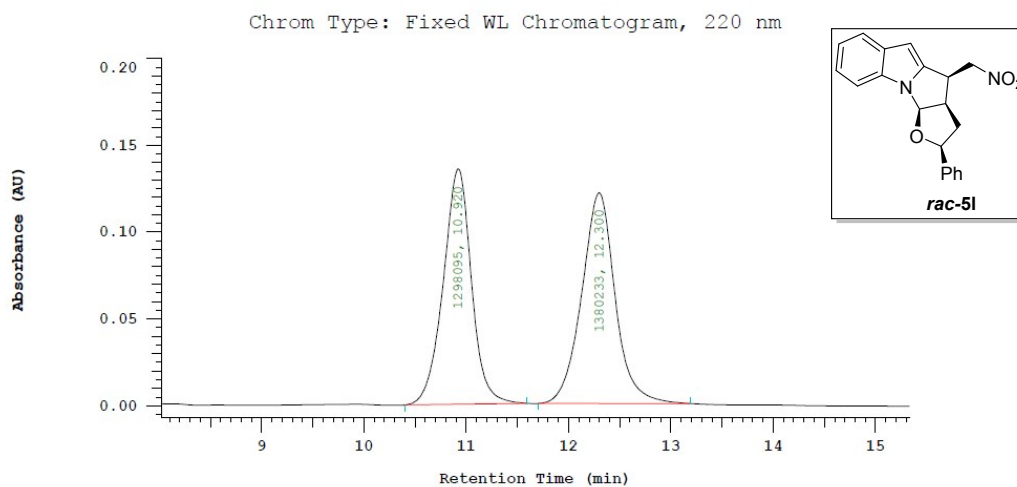
The ^1H NMR spectrum of 5I (500 MHz, CDCl_3)



The ^{13}C NMR spectrum of 5I (125 MHz, CDCl_3)



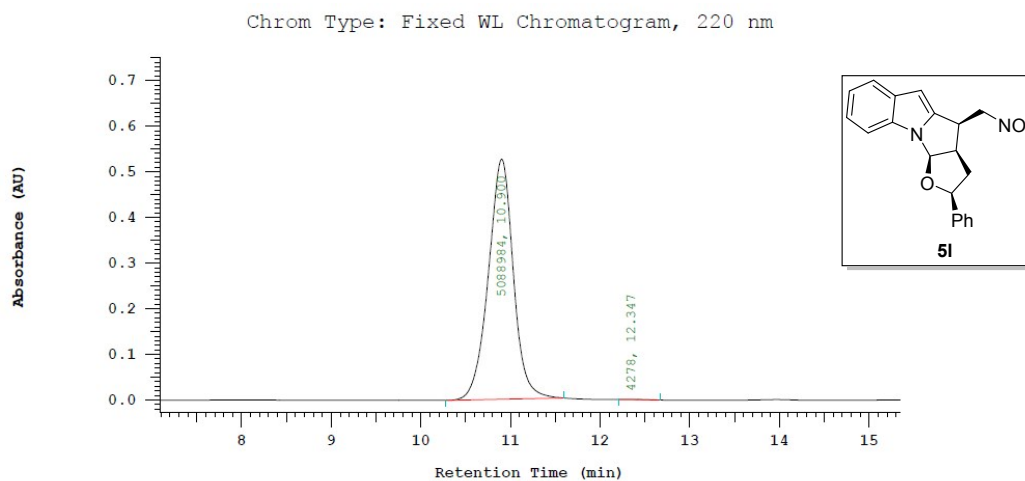
The HPLC of racemic 5I



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.920	1298095	48.467	BB
2	12.300	1380233	51.533	BB
		2678328	100.000	

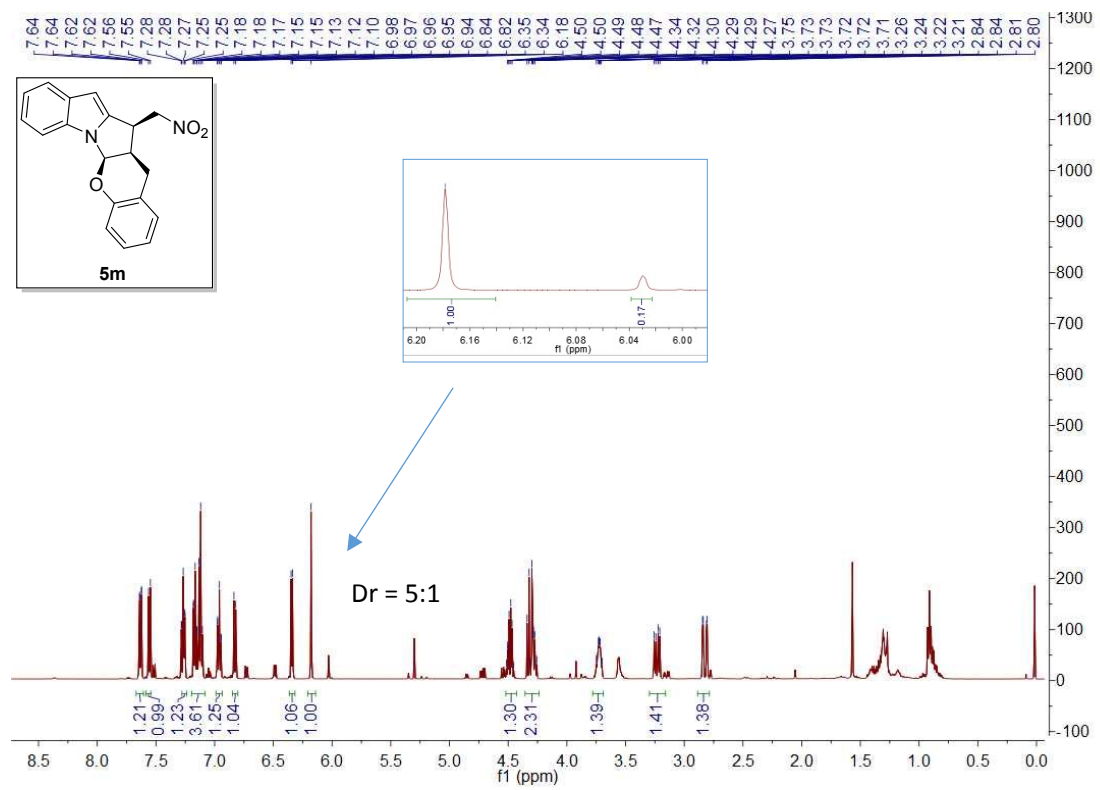
The HPLC of chiral 5I



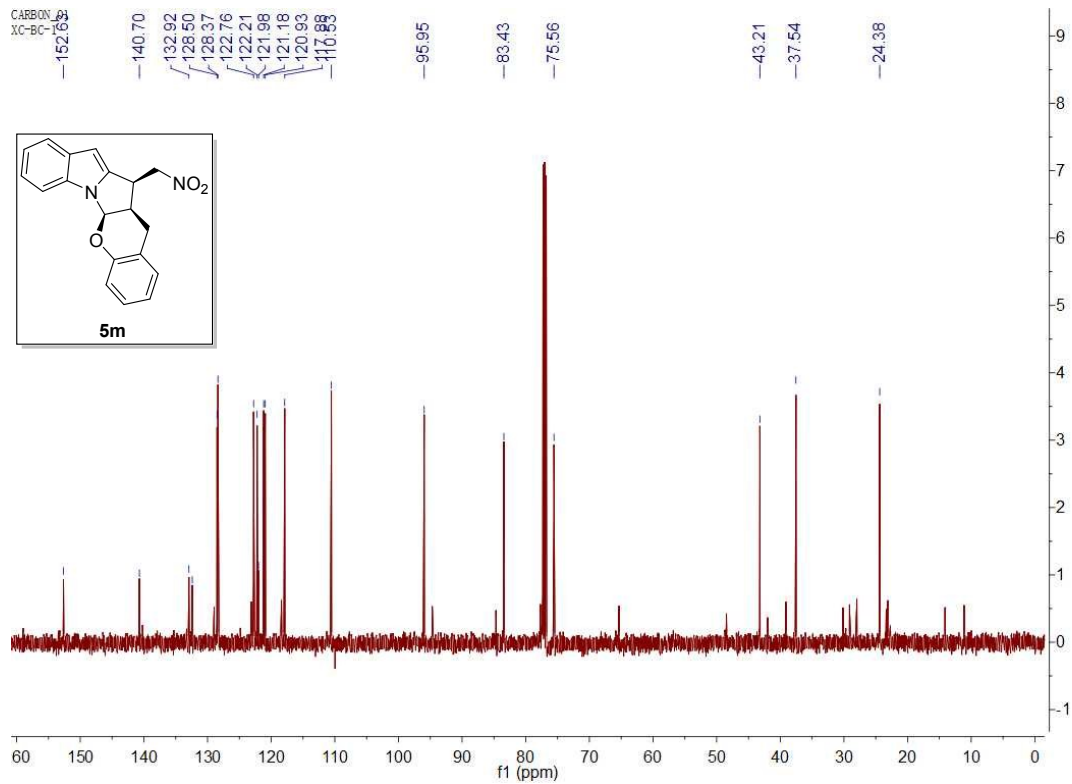
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.900	5088984	99.916	BB
2	12.347	4278	0.084	BB
		5093262	100.000	

The ¹H NMR spectrum of 5m (500 MHz, CDCl₃)

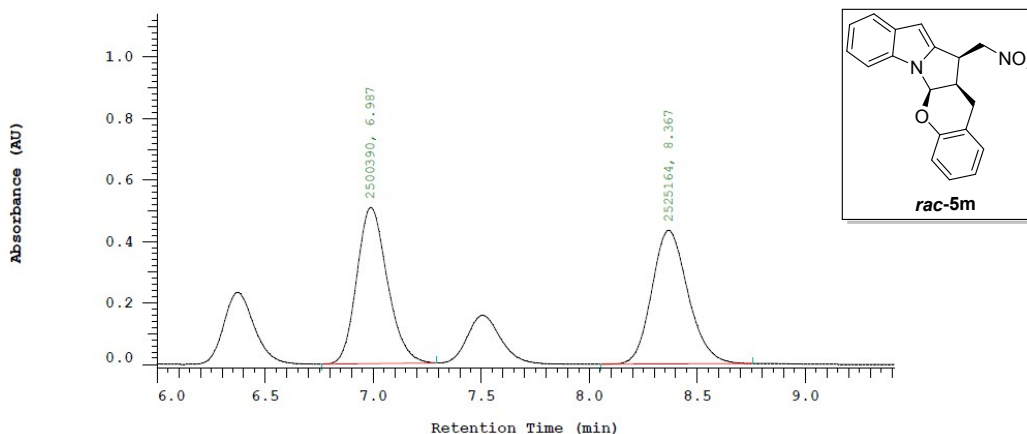


The ¹³C NMR spectrum of 5m (125 MHz, CDCl₃)



The HPLC of racemic 5m

Chrom Type: Fixed WL Chromatogram, 220 nm



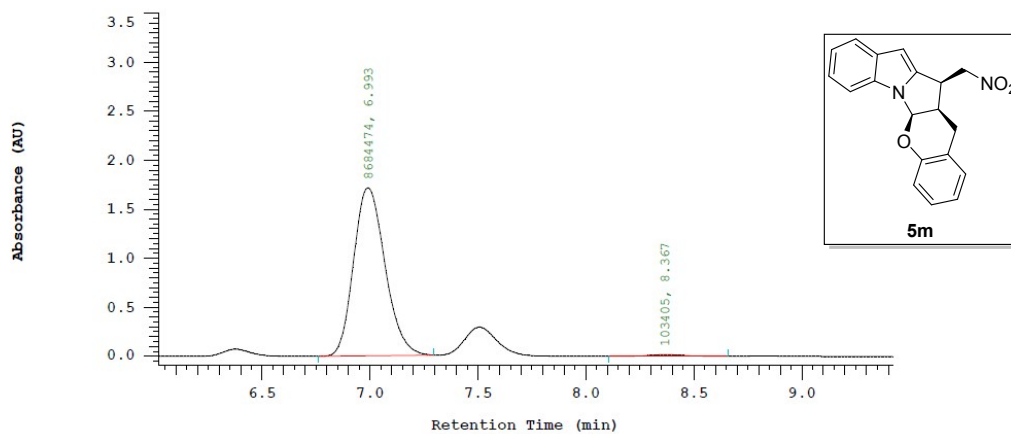
Chrom Type: Fixed WL Chromatogram, 220 nm

Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.987	2500390	49.754	BB
2	8.367	2525164	50.246	BB
		5025554	100.000	

The HPLC of chiral 5m

Chrom Type: Fixed WL Chromatogram, 220 nm

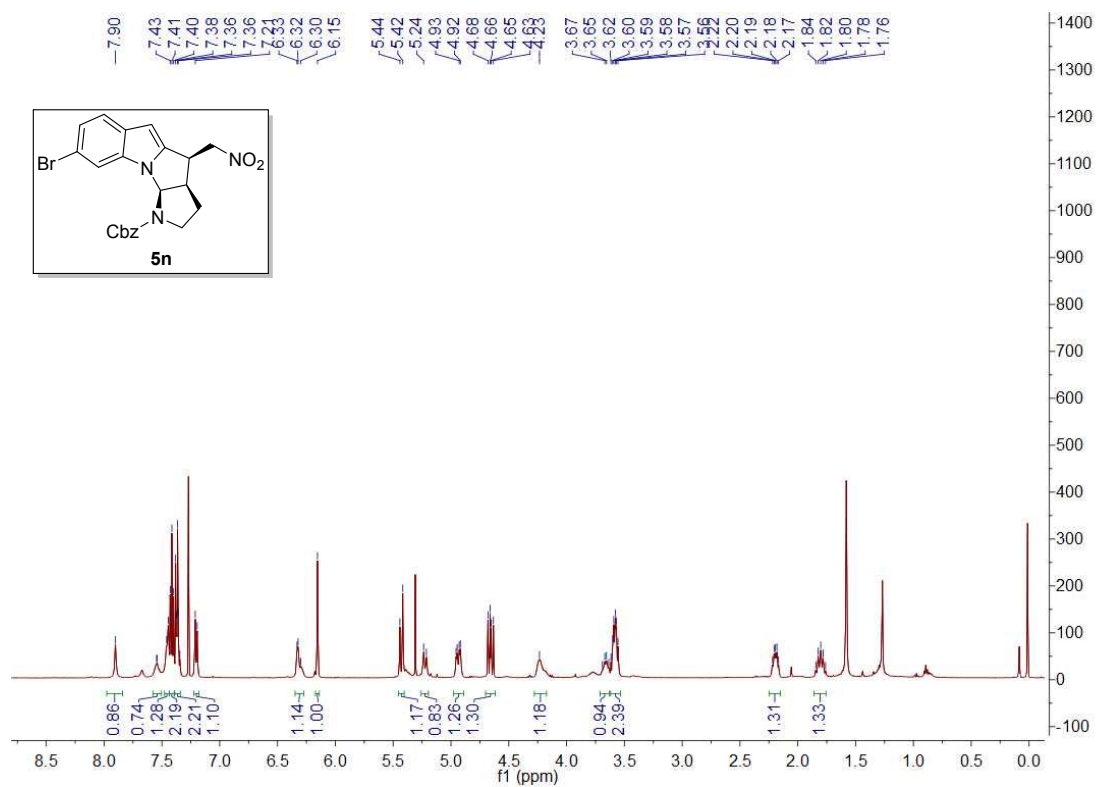


Chrom Type: Fixed WL Chromatogram, 220 nm

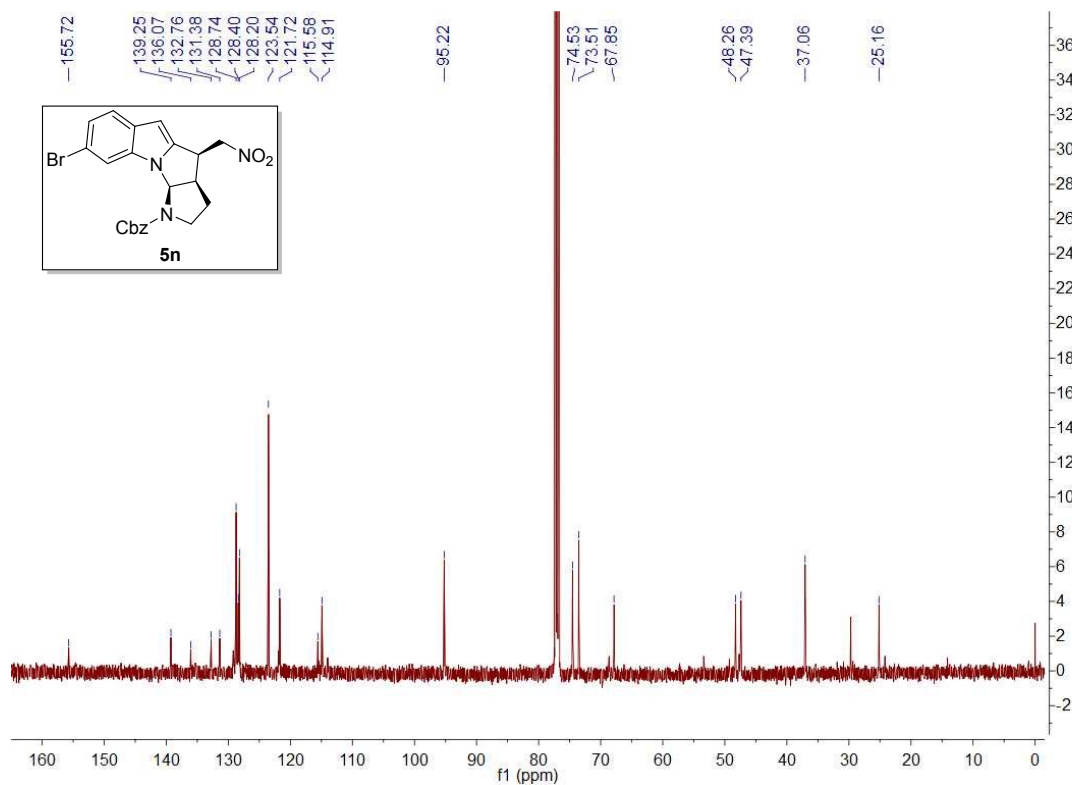
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.993	8684474	98.823	BB
2	8.367	103405	1.177	BB
		8787879	100.000	

The ^1H NMR spectrum of 5n (500 MHz, CDCl_3)

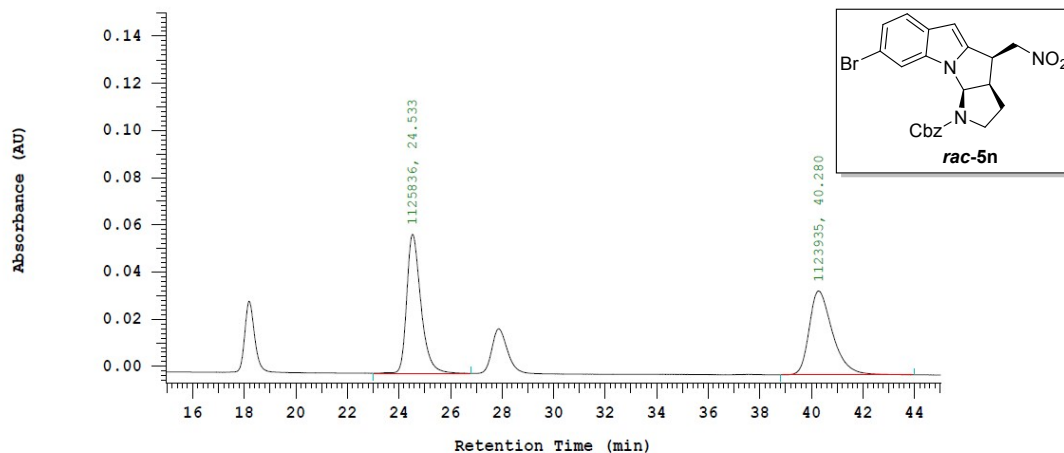


The ^{13}C NMR spectrum of 5n (125 MHz, CDCl_3)



The HPLC of racemic 5n

Chrom Type: Fixed WL Chromatogram, 220 nm



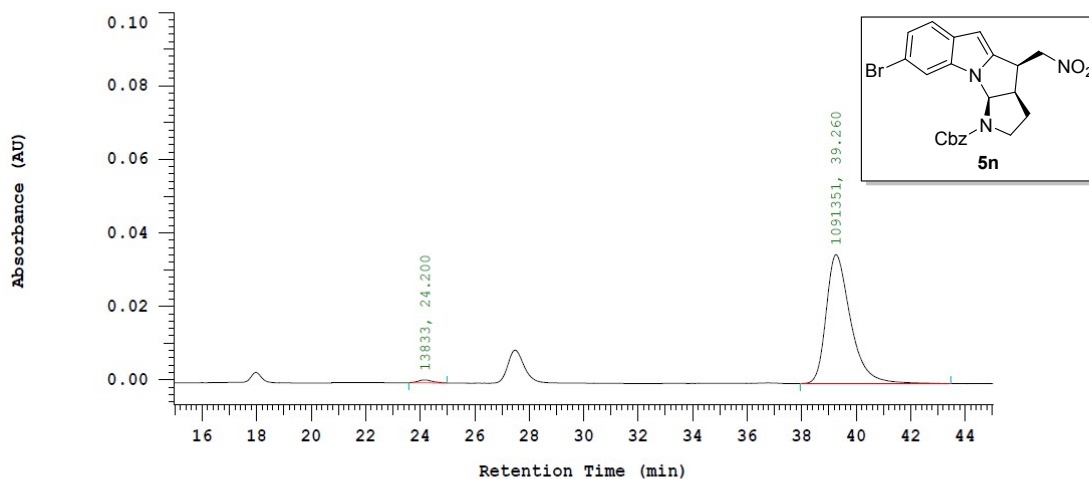
Chrom Type: Fixed WL Chromatogram, 220 nm

Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	24.533	1125836	50.042	BB
2	40.280	1123935	49.958	BB
		2249771	100.000	

The HPLC of chiral 5n

Chrom Type: Fixed WL Chromatogram, 220 nm

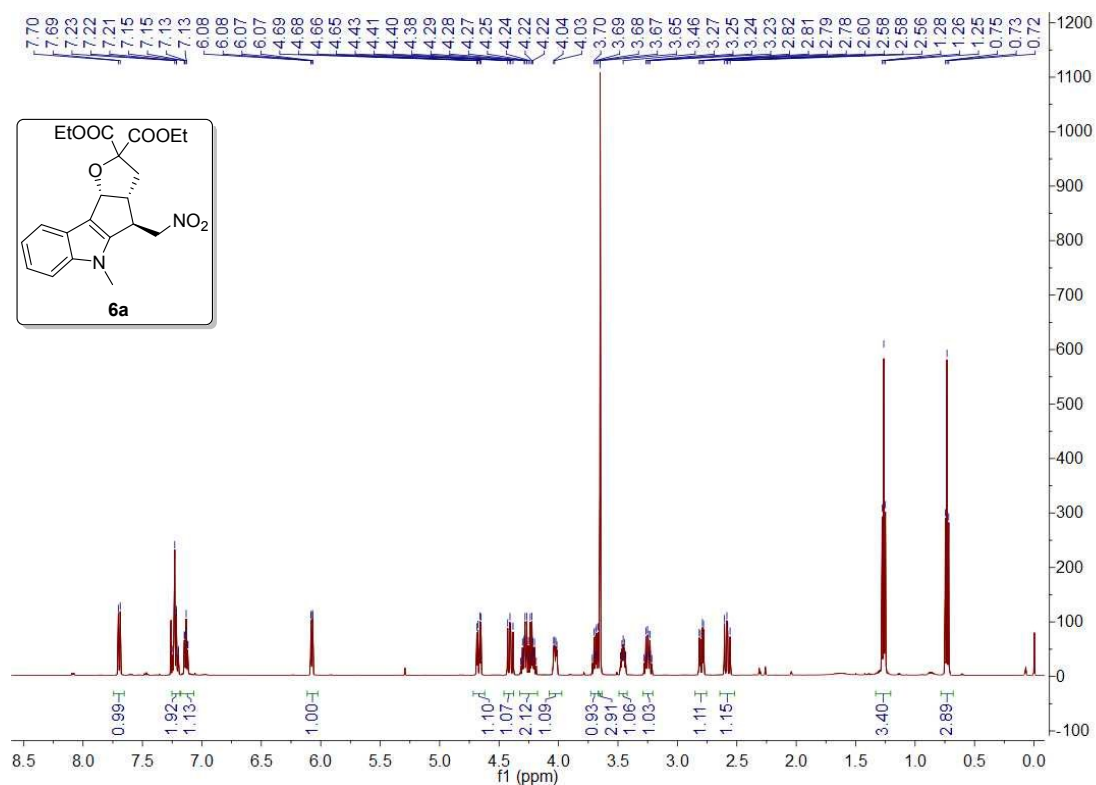


Chrom Type: Fixed WL Chromatogram, 220 nm

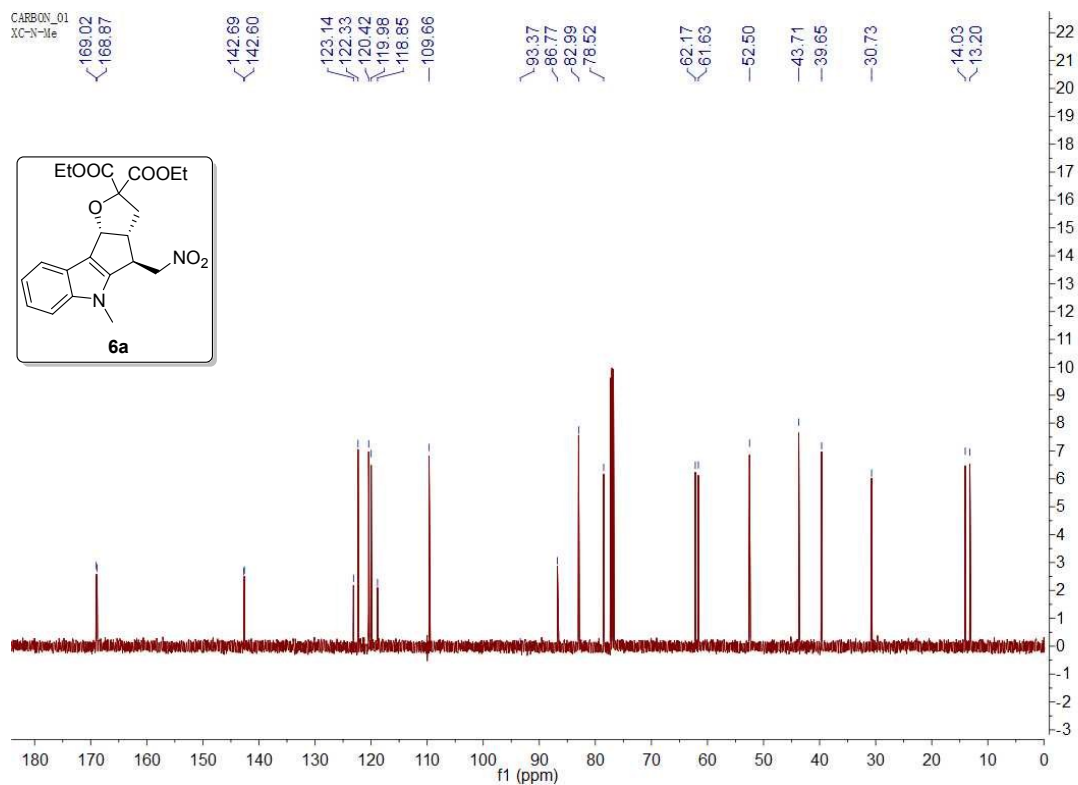
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	24.200	13833	1.252	BB
2	39.260	1091351	98.748	BB
		1105184	100.000	

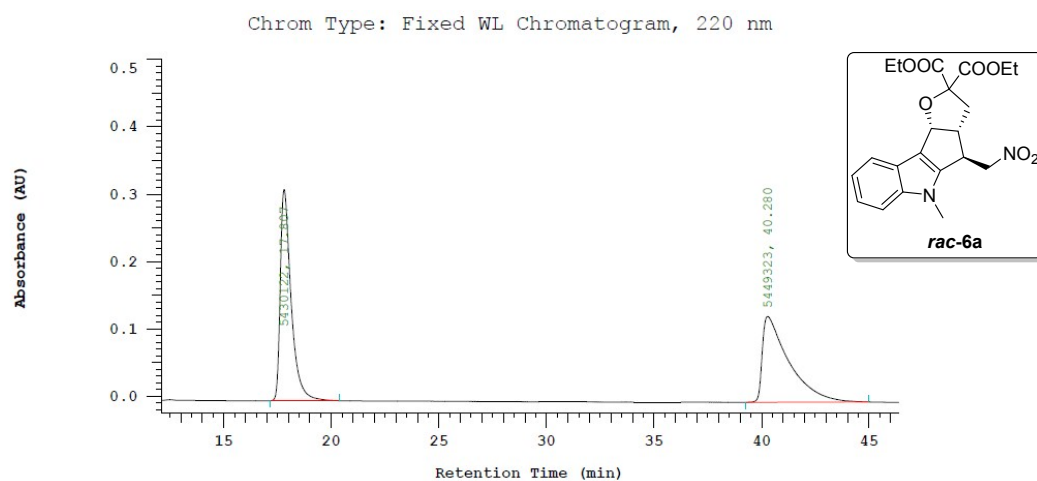
The ¹H NMR spectrum of 6a (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 6a (125 MHz, CDCl₃)



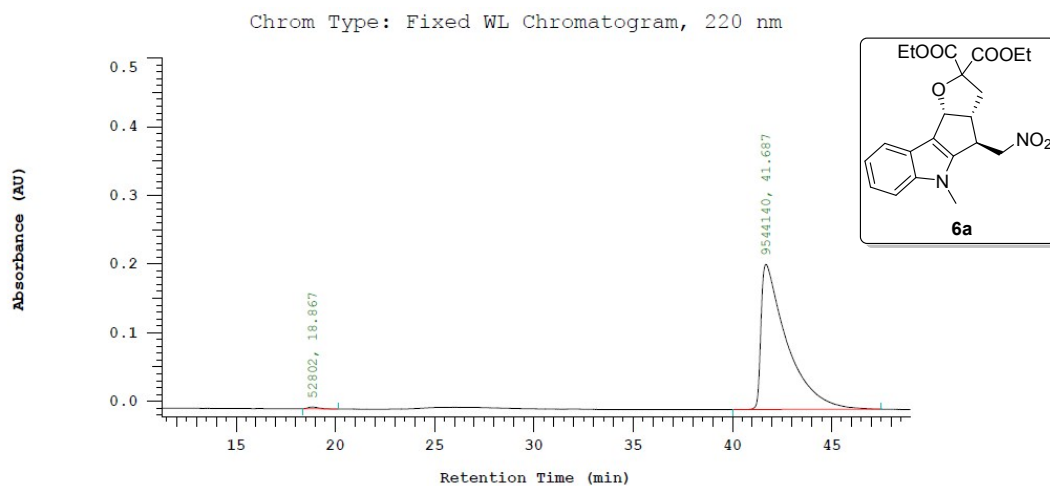
The HPLC of racemic 6a



Chrom Type: Fixed WL Chromatogram, 220 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.807	5430122	49.912	BB
2	40.280	5449323	50.088	BB
		10879445	100.000	

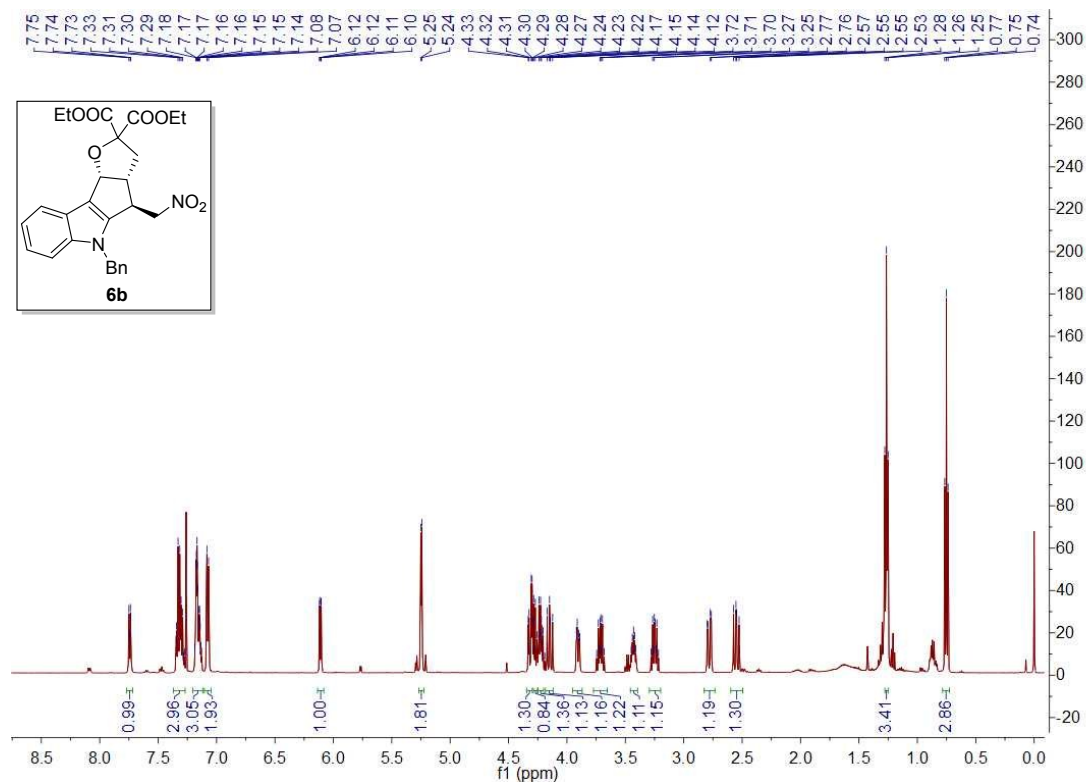
The HPLC of chiral 6a



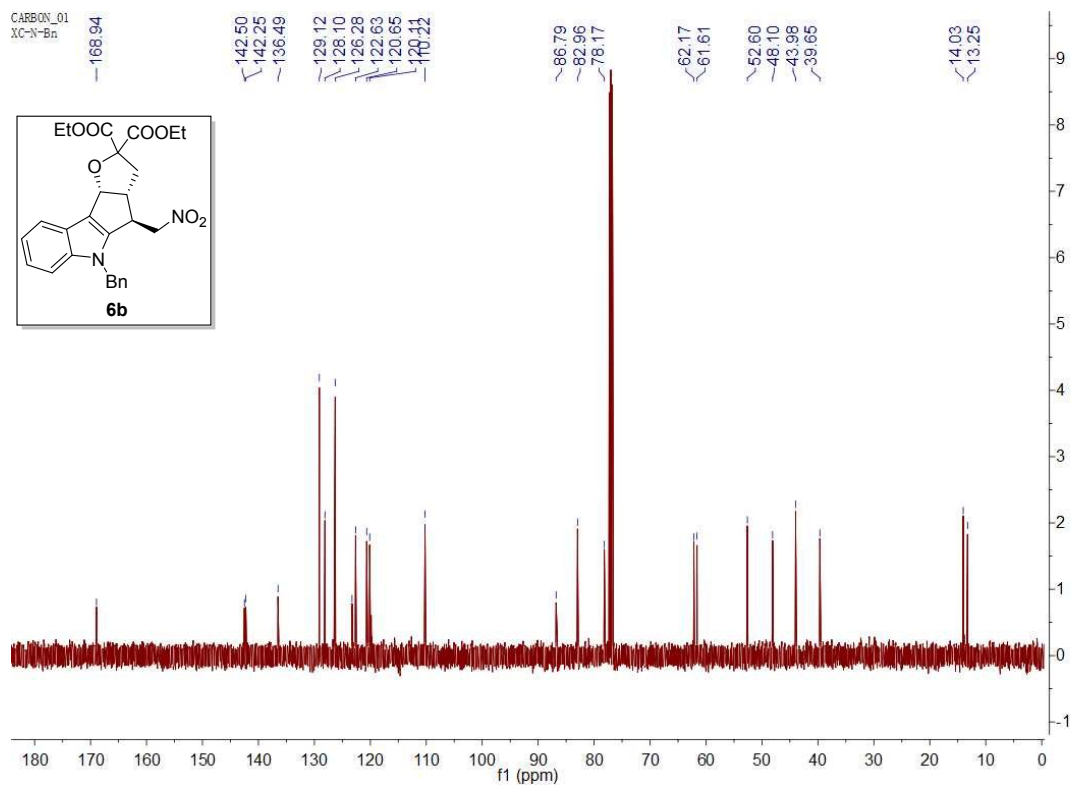
Chrom Type: Fixed WL Chromatogram, 220 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	18.867	52802	0.550	BB
2	41.687	9544140	99.450	BB
		9596942	100.000	

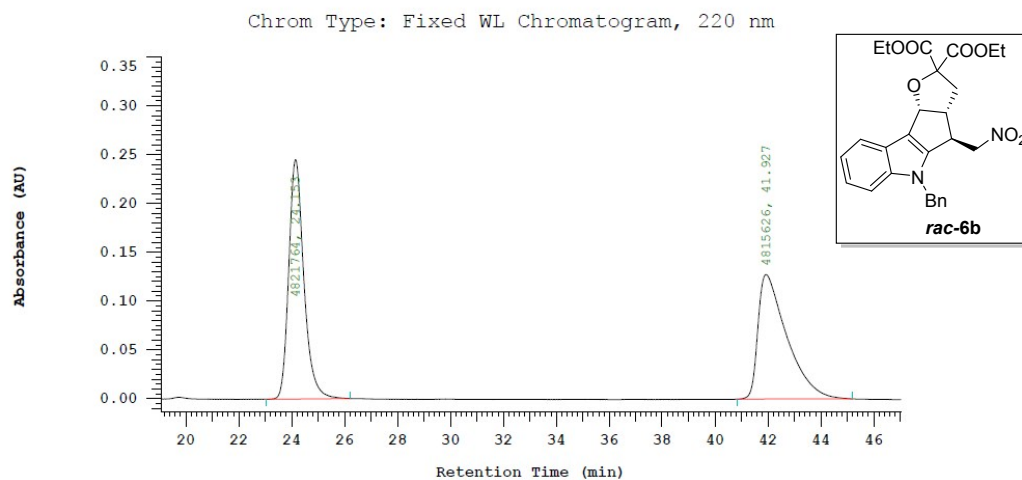
The ¹H NMR spectrum of 6b (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 6b (125 MHz, CDCl₃)



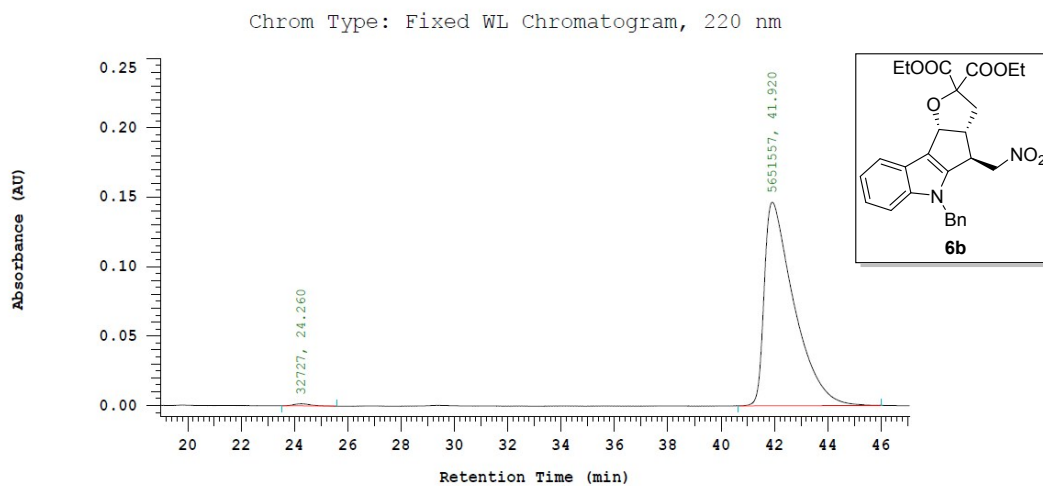
The HPLC of racemic 6b



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	24.153	4821764	50.032	BB
2	41.927	4815626	49.968	BB
		9637390	100.000	

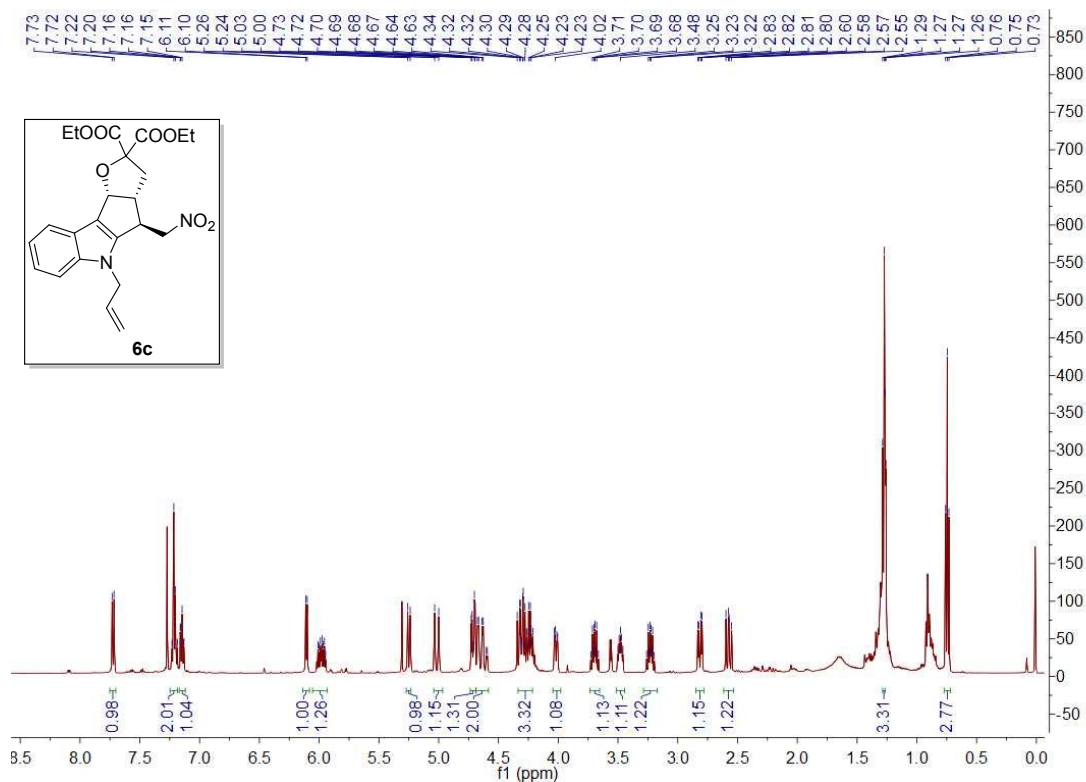
The HPLC of chiral 6b



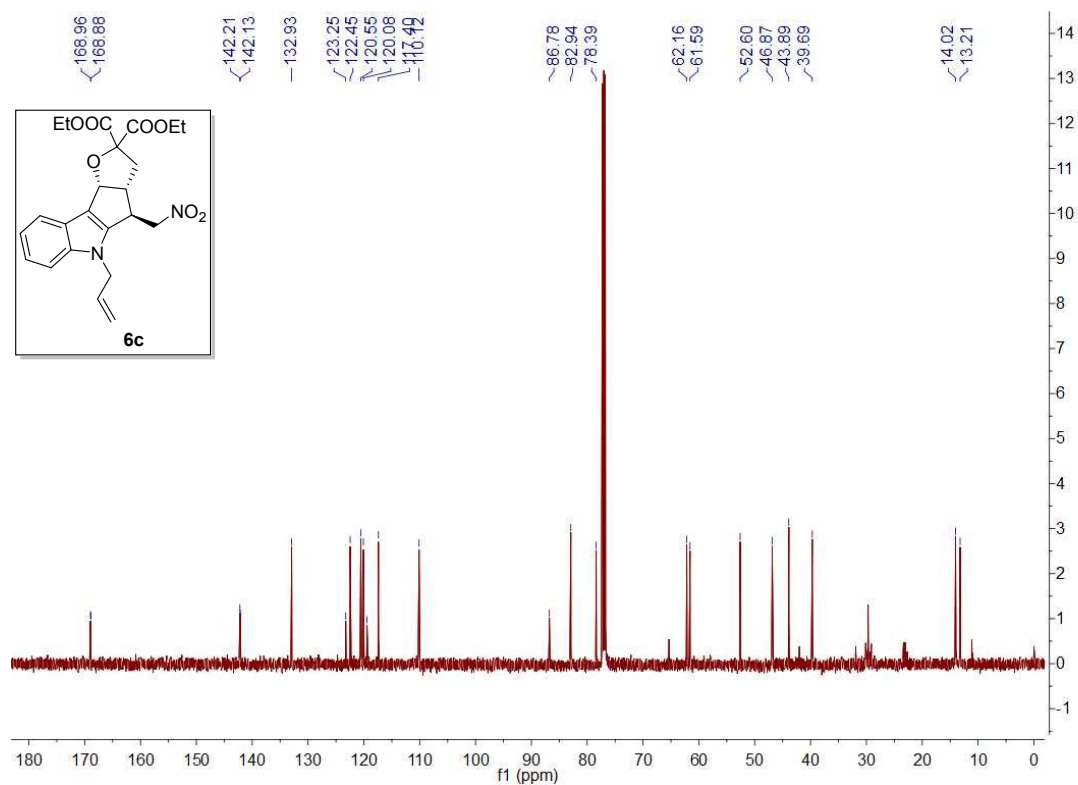
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	24.260	32727	0.576	BB
2	41.920	5651557	99.424	BB
		5684284	100.000	

The ¹H NMR spectrum of 6c (500 MHz, CDCl₃)

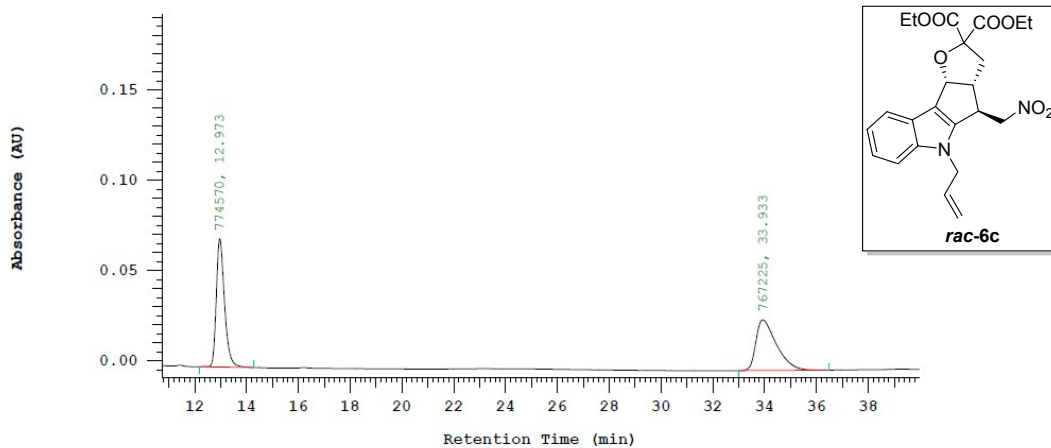


The ¹³C NMR spectrum of 6c (125 MHz, CDCl₃)



The HPLC of racemic 6c

Chrom Type: Fixed WL Chromatogram, 230 nm



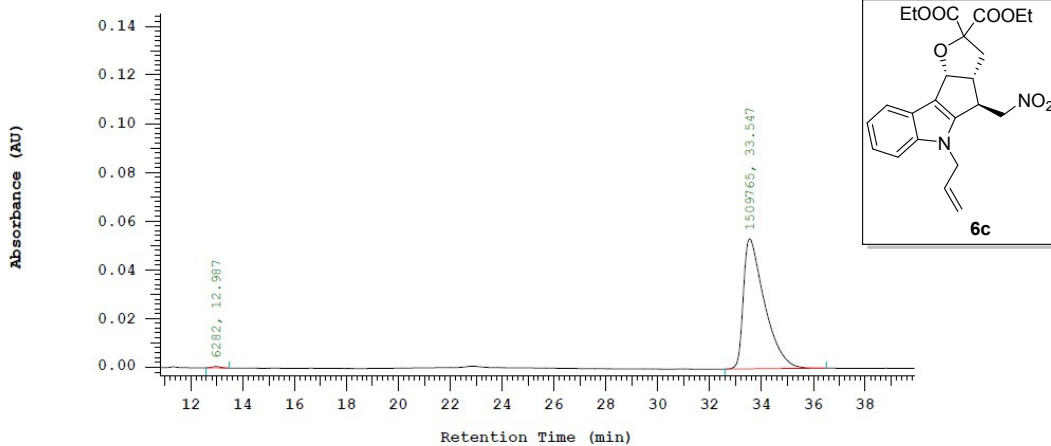
Chrom Type: Fixed WL Chromatogram, 230 nm

Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.973	774570	50.238	BB
2	33.933	767225	49.762	BB
		1541795	100.000	

The HPLC of chiral 6c

Chrom Type: Fixed WL Chromatogram, 230 nm

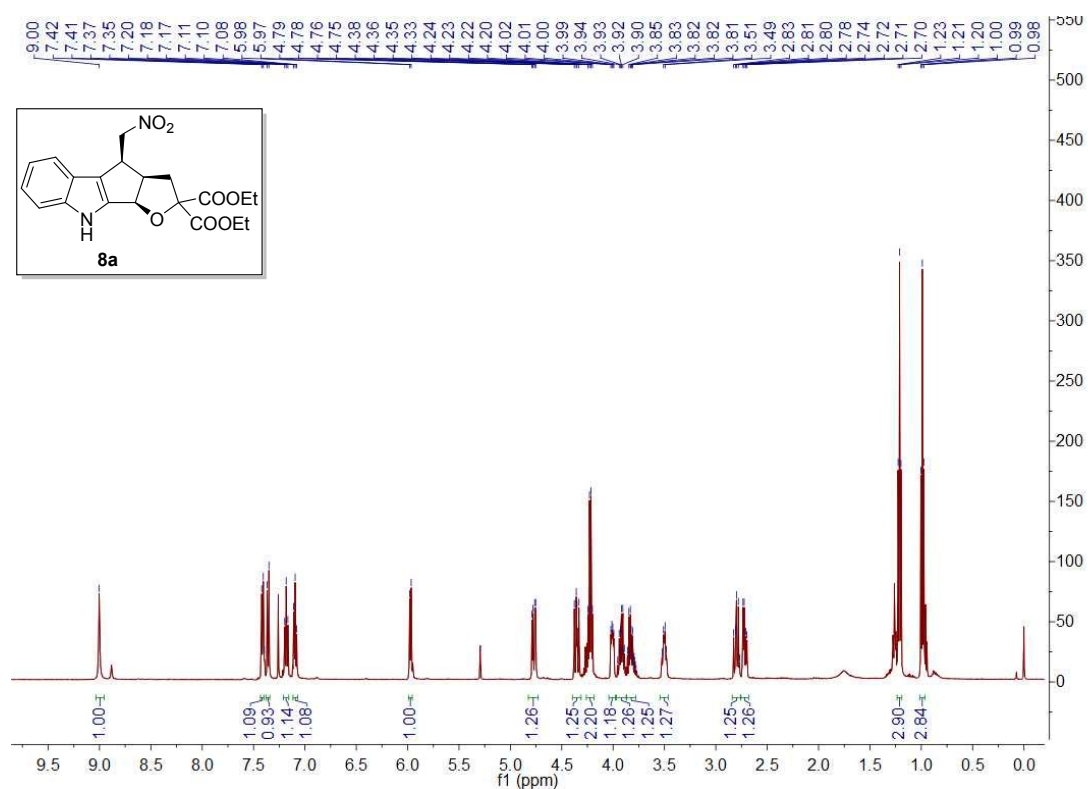


Chrom Type: Fixed WL Chromatogram, 230 nm

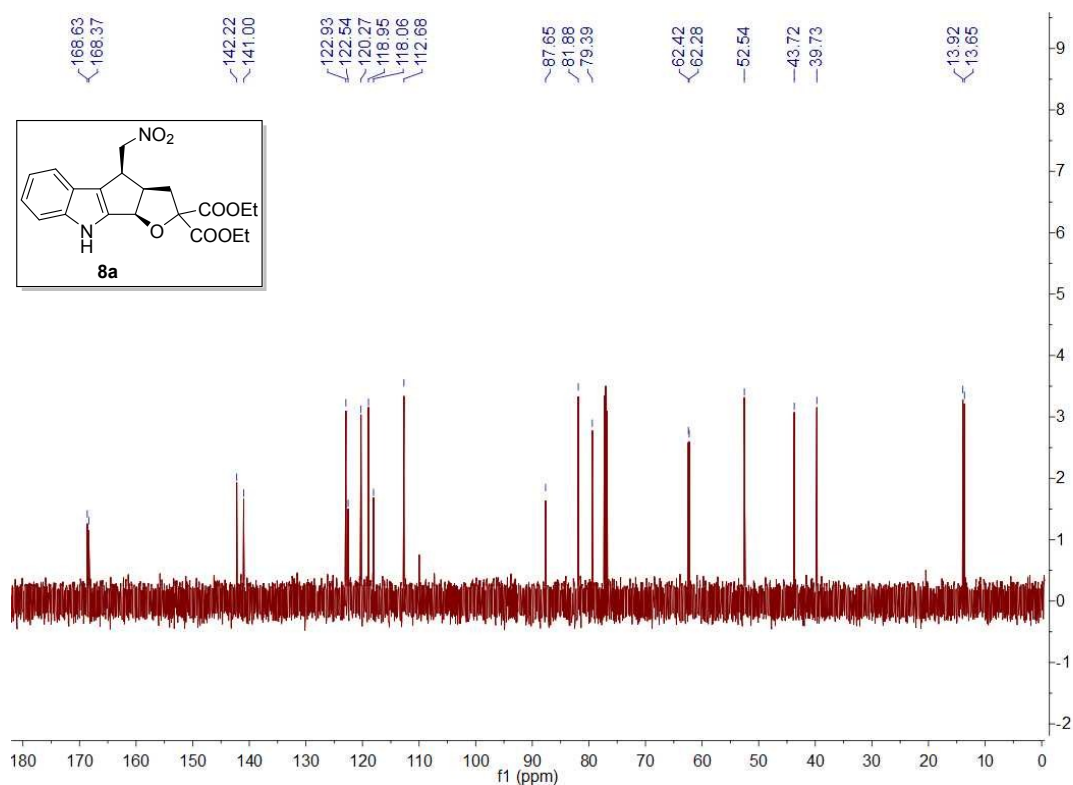
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.987	6282	0.414	BB
2	33.547	1509765	99.586	BB
		1516047	100.000	

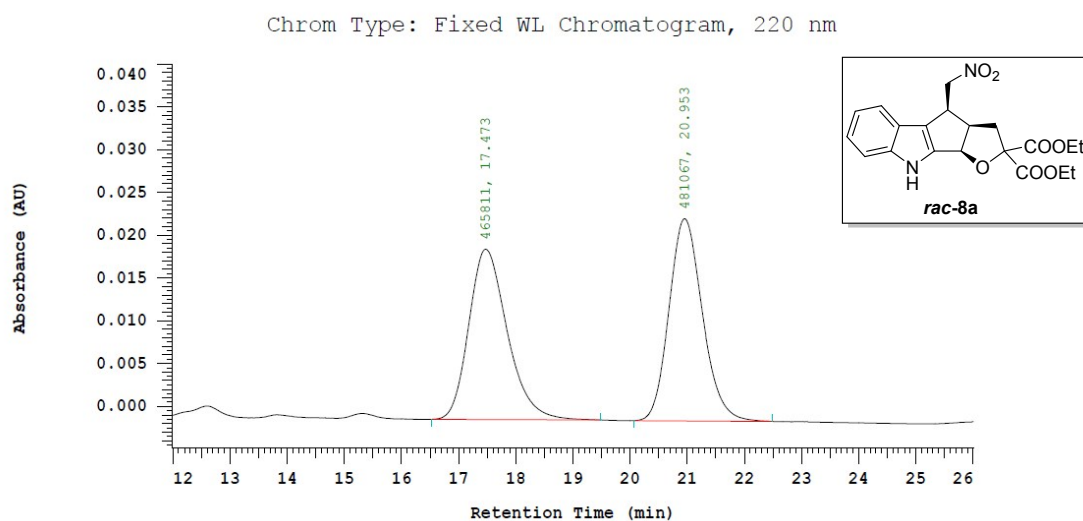
The ¹H NMR spectrum of 8a (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 8a (125 MHz, CDCl₃)



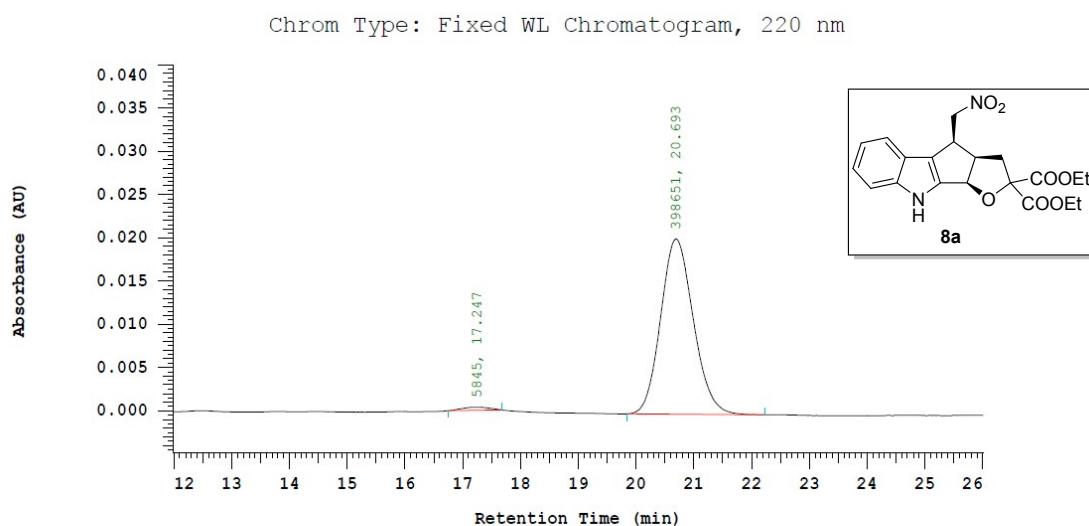
The HPLC of racemic 8a



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.473	465811	49.194	BB
2	20.953	481067	50.806	BB
		946878	100.000	

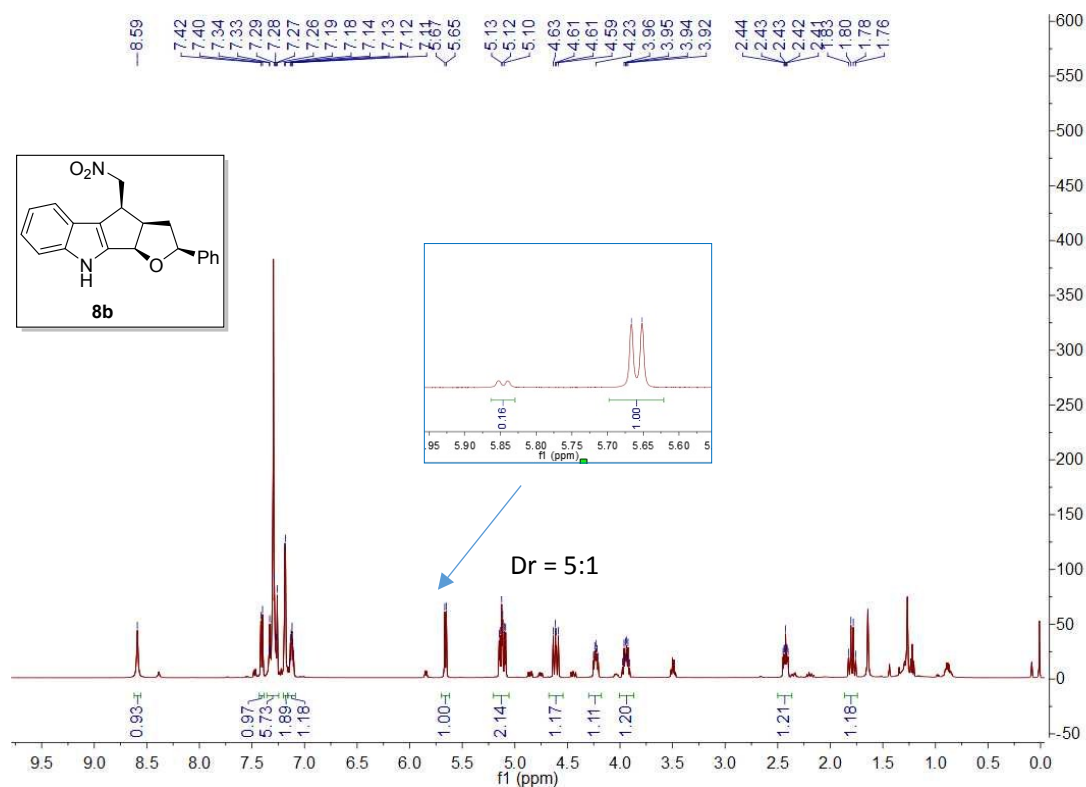
The HPLC of chiral 8a



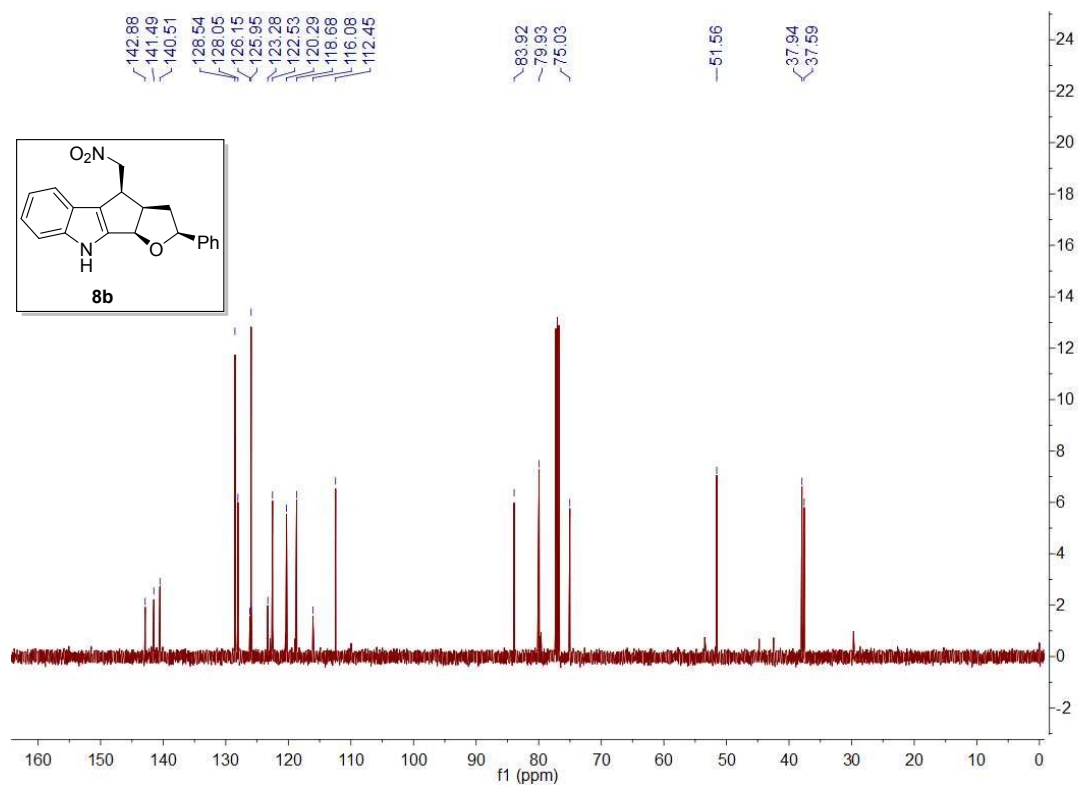
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.247	5845	1.445	BB
2	20.693	398651	98.555	BB
		404496	100.000	

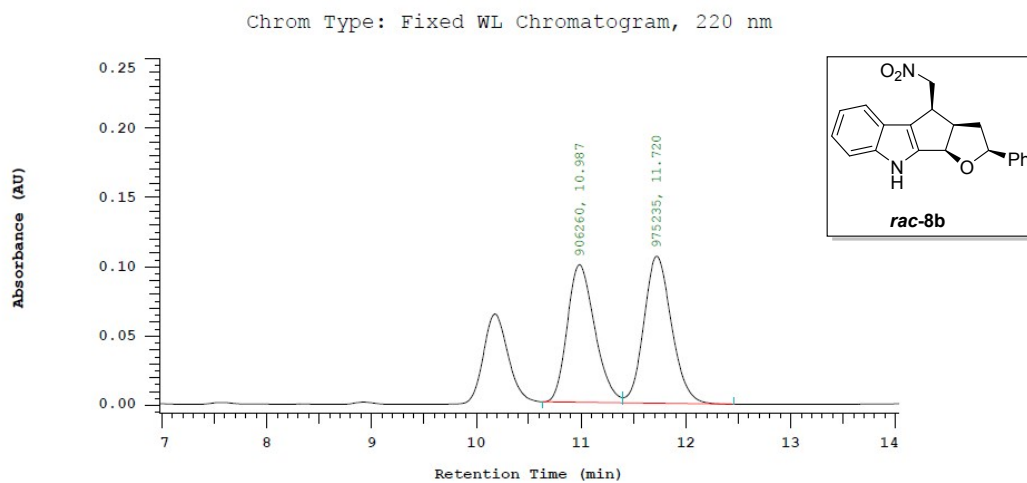
The ^1H NMR spectrum of **8b** (500 MHz, CDCl_3)



The ^{13}C NMR spectrum of **8b** (125 MHz, CDCl_3)



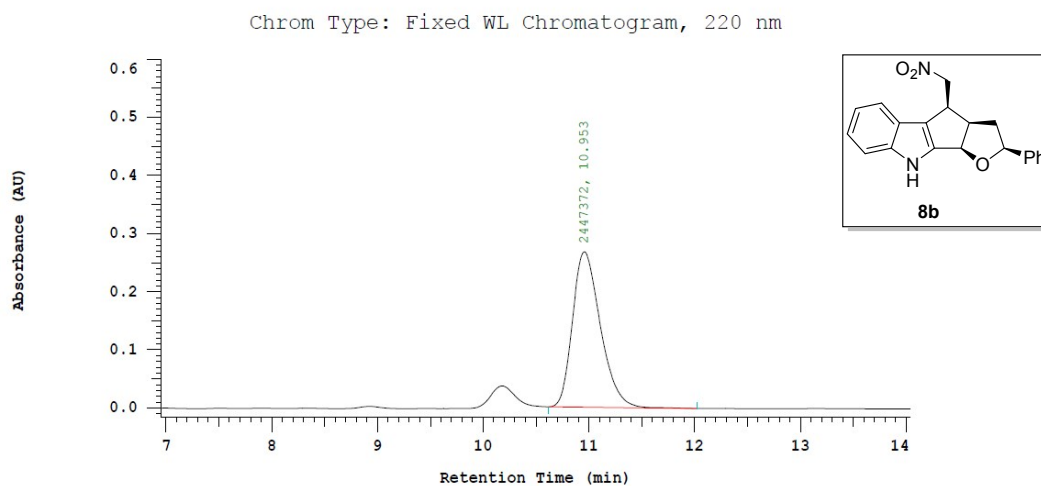
The HPLC of racemic 8b



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.987	906260	48.167	BV
2	11.720	975235	51.833	VB
		1881495	100.000	

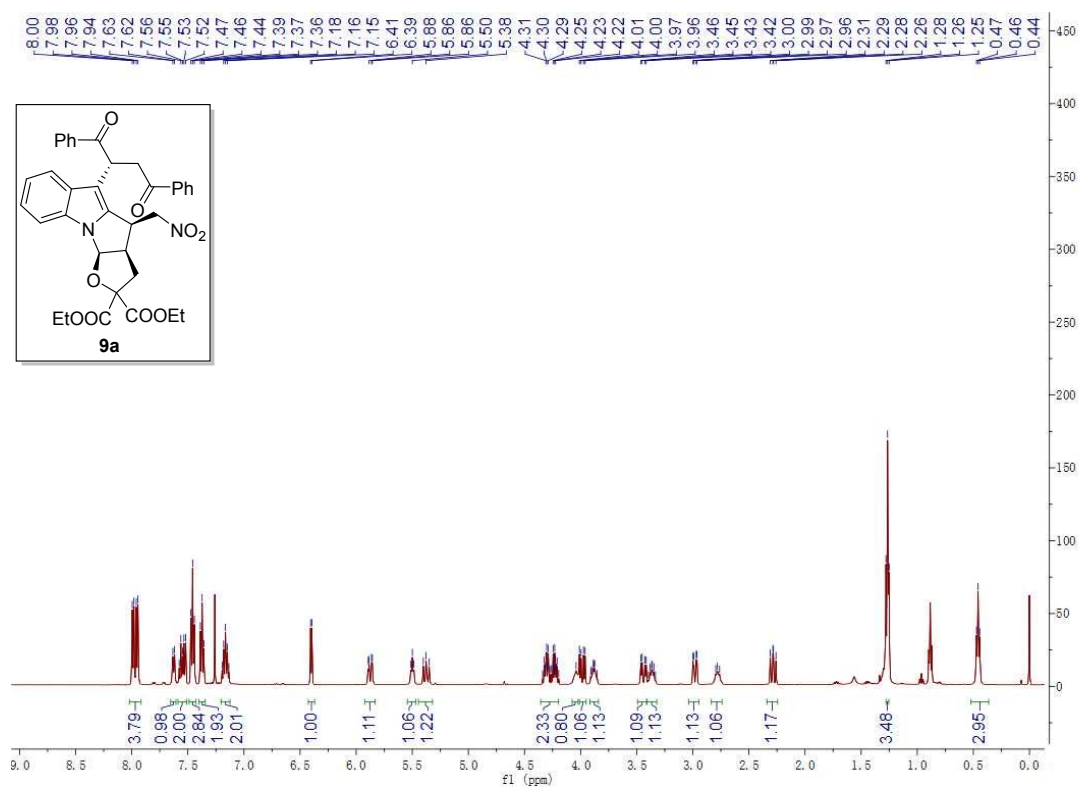
The HPLC of chiral 8b



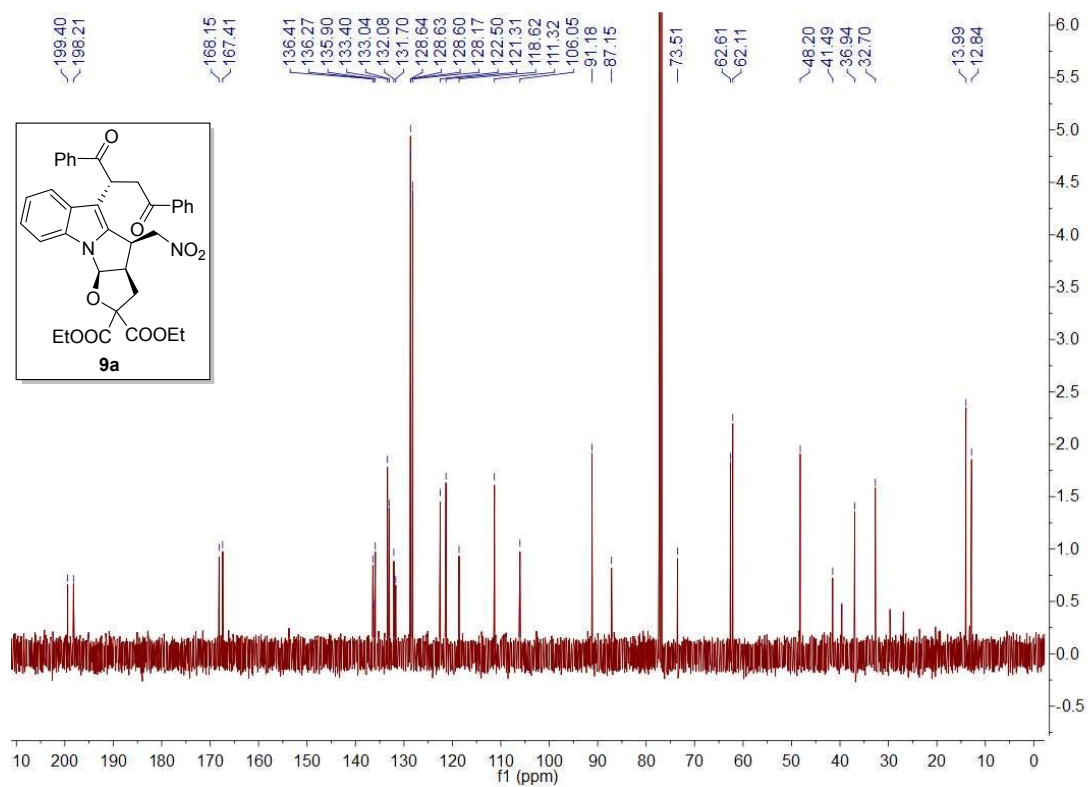
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.953	2447372	100.000	BB
		2447372	100.000	

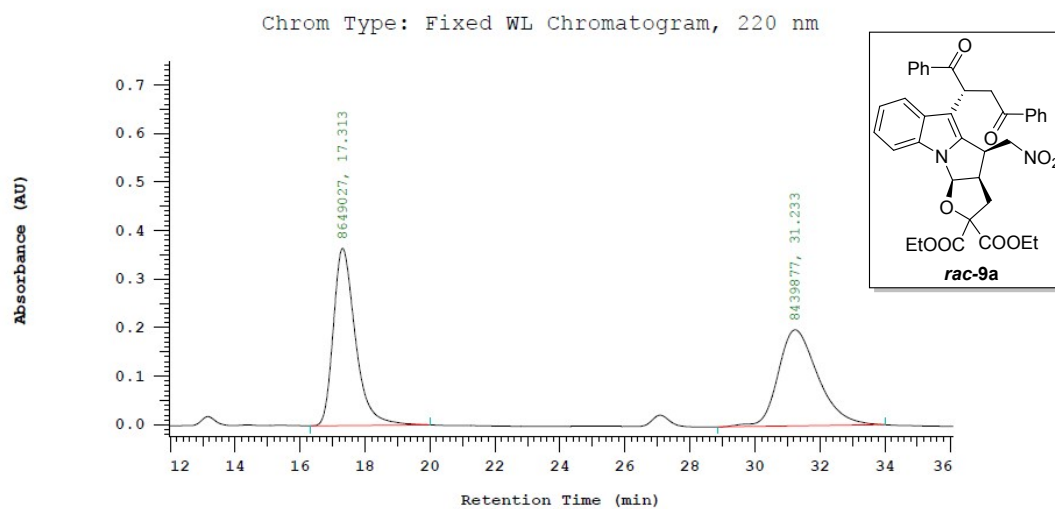
The ^1H NMR spectrum of **9a** (500 MHz, CDCl_3)



The ^{13}C NMR spectrum of **9a** (125 MHz, CDCl_3)



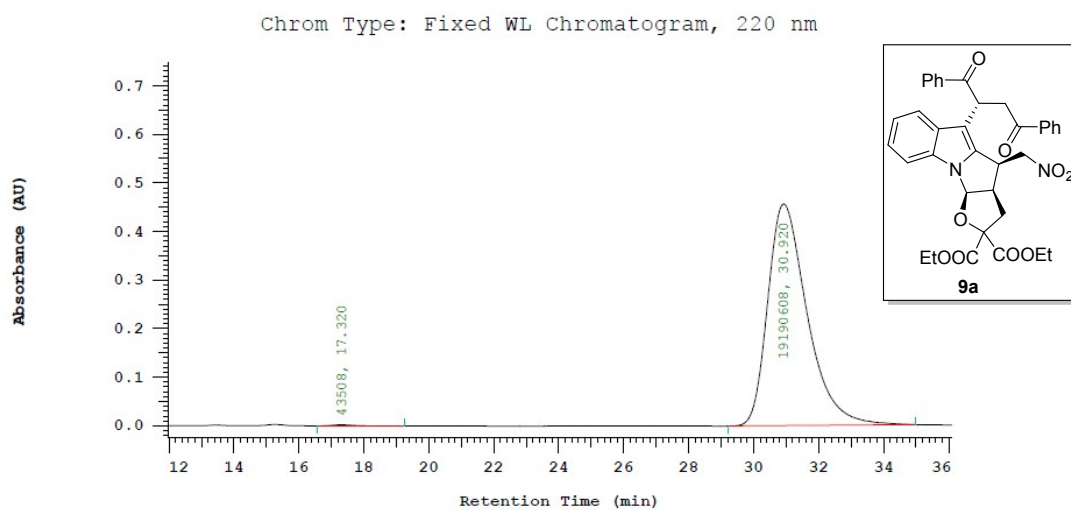
The HPLC of racemic 9a



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.313	8649027	50.612	BB
2	31.233	8439877	49.388	BB
		17088904	100.000	

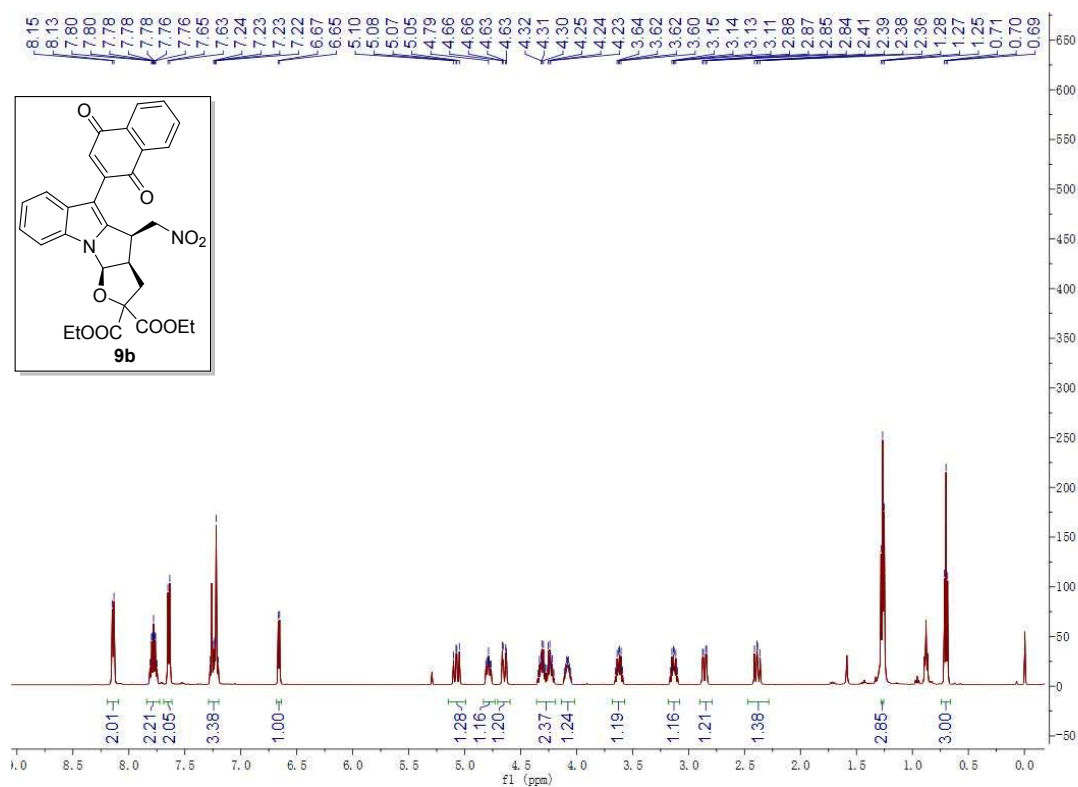
The HPLC of chiral 9a



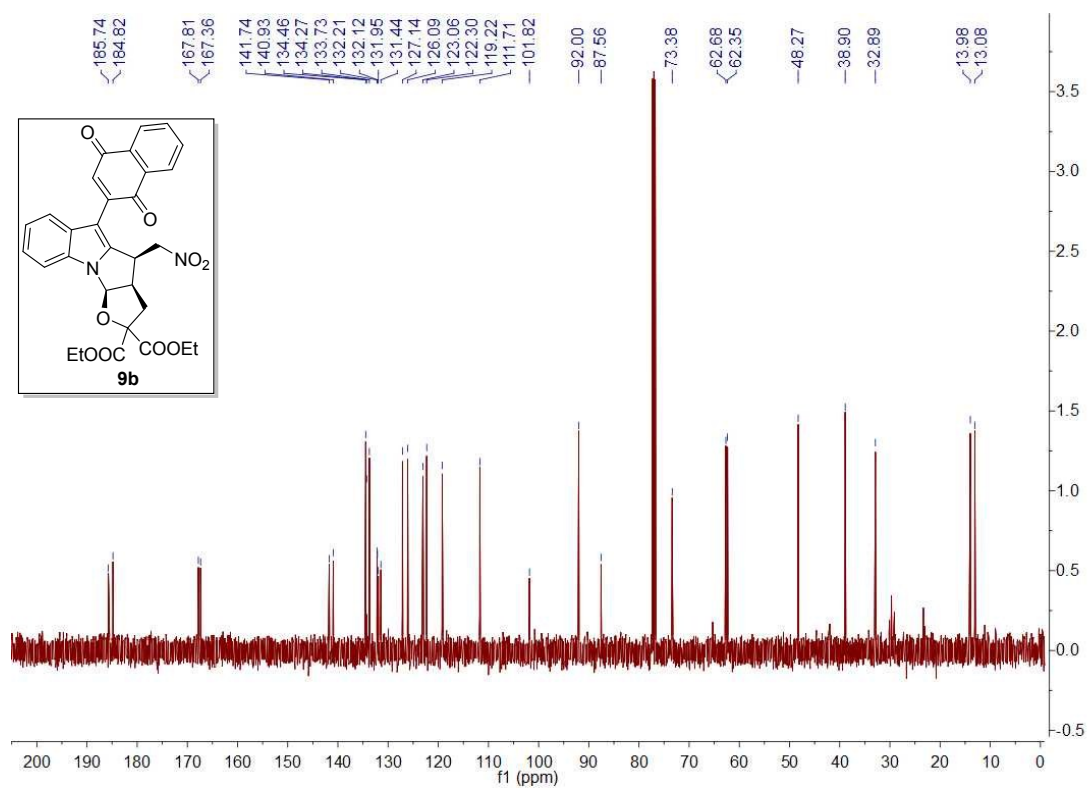
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.320	43508	0.226	BB
2	30.920	19190608	99.774	BB
		19234116	100.000	

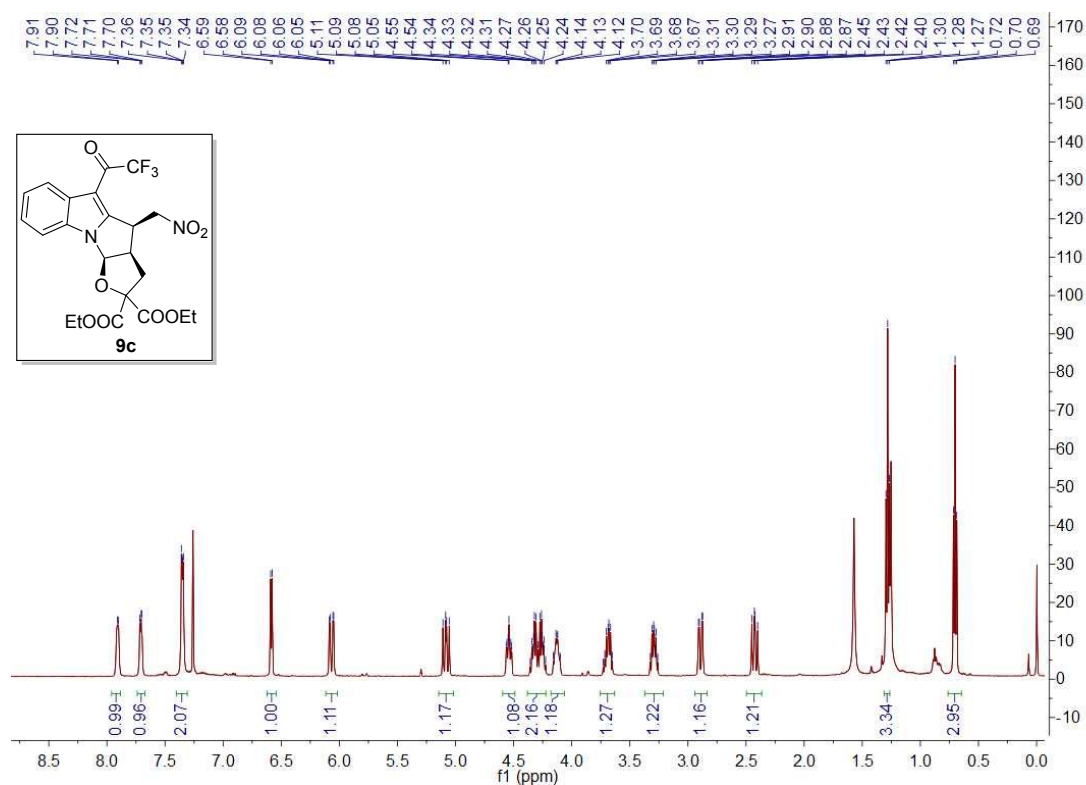
The ¹H NMR spectrum of 9b (500 MHz, CDCl₃)



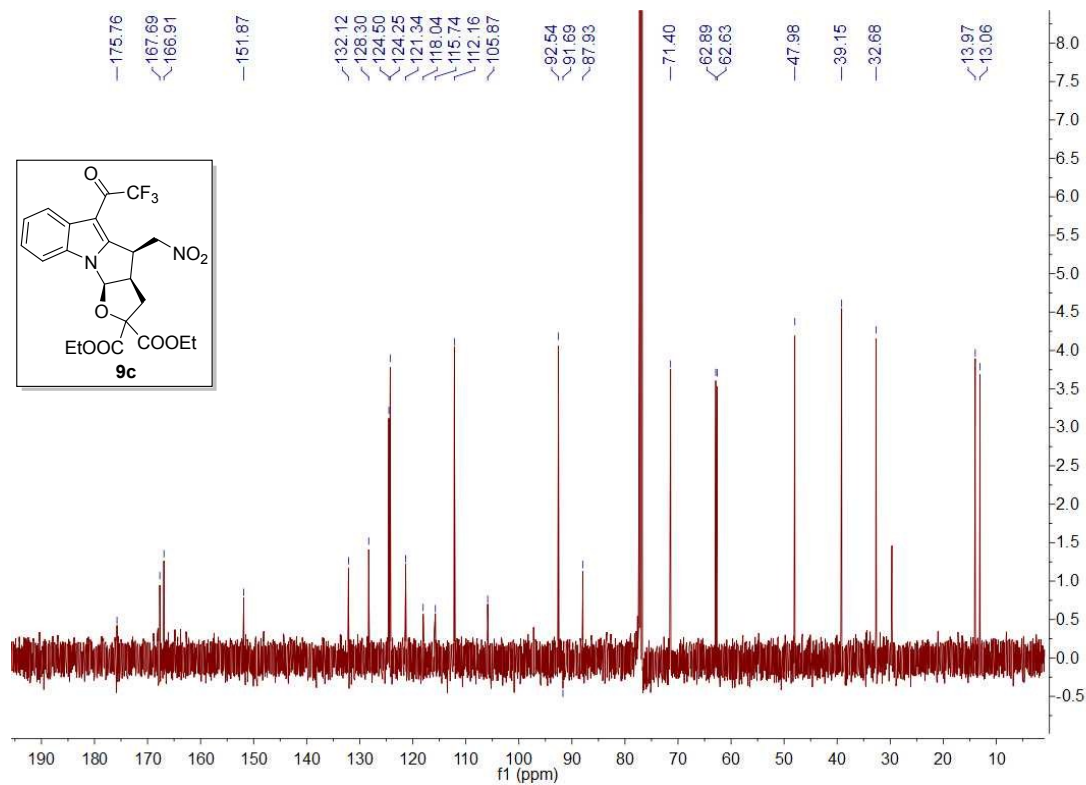
The ¹³C NMR spectrum of 9b (125 MHz, CDCl₃)



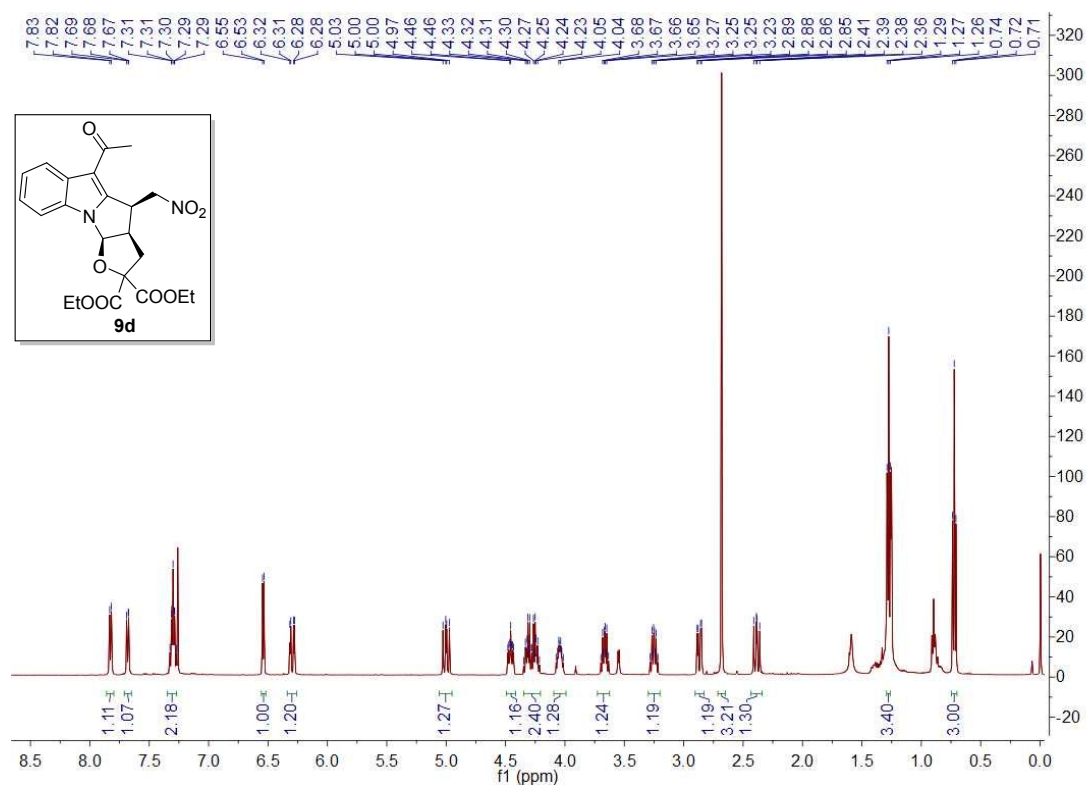
The ¹H NMR spectrum of 9c (500 MHz, CDCl₃)



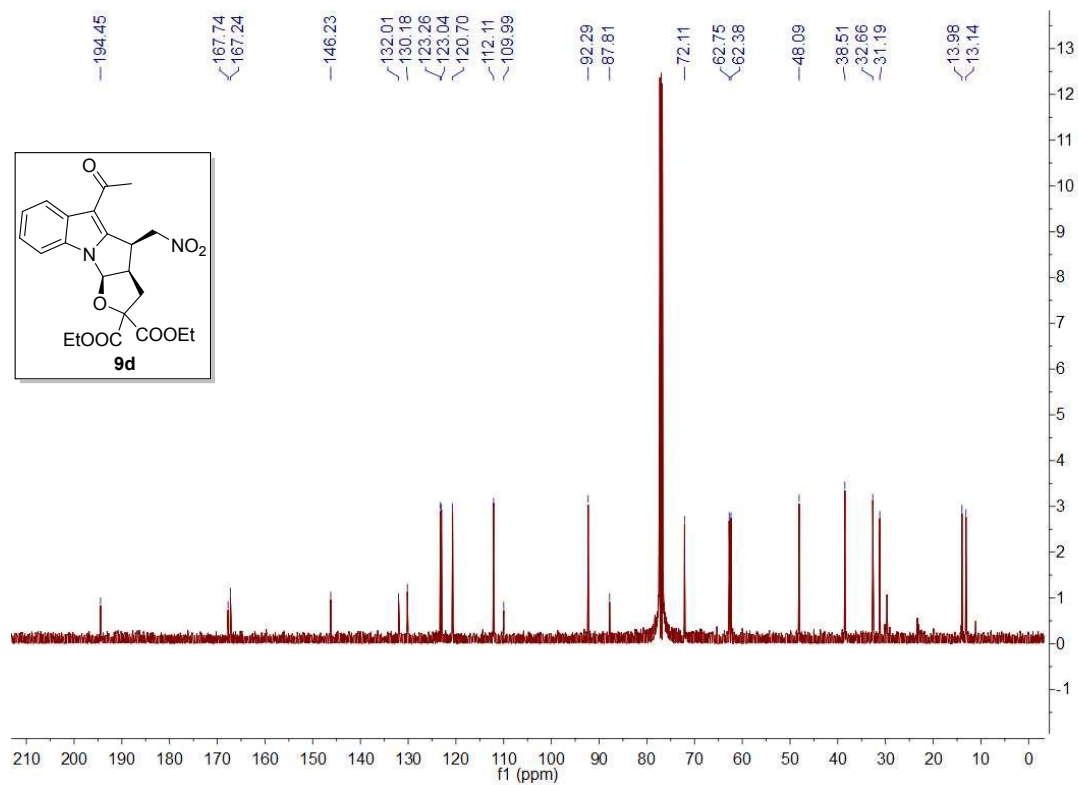
The ¹³C NMR spectrum of 9c (125 MHz, CDCl₃)



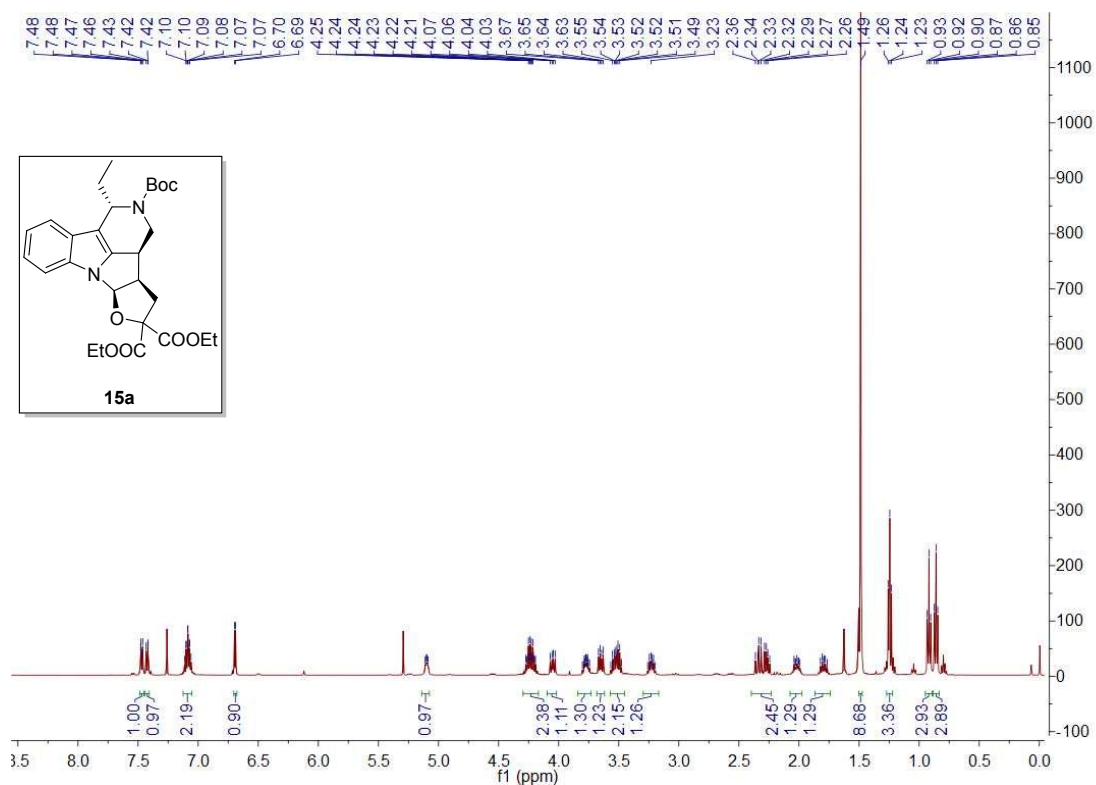
The ¹H NMR spectrum of 9d (500 MHz, CDCl₃)



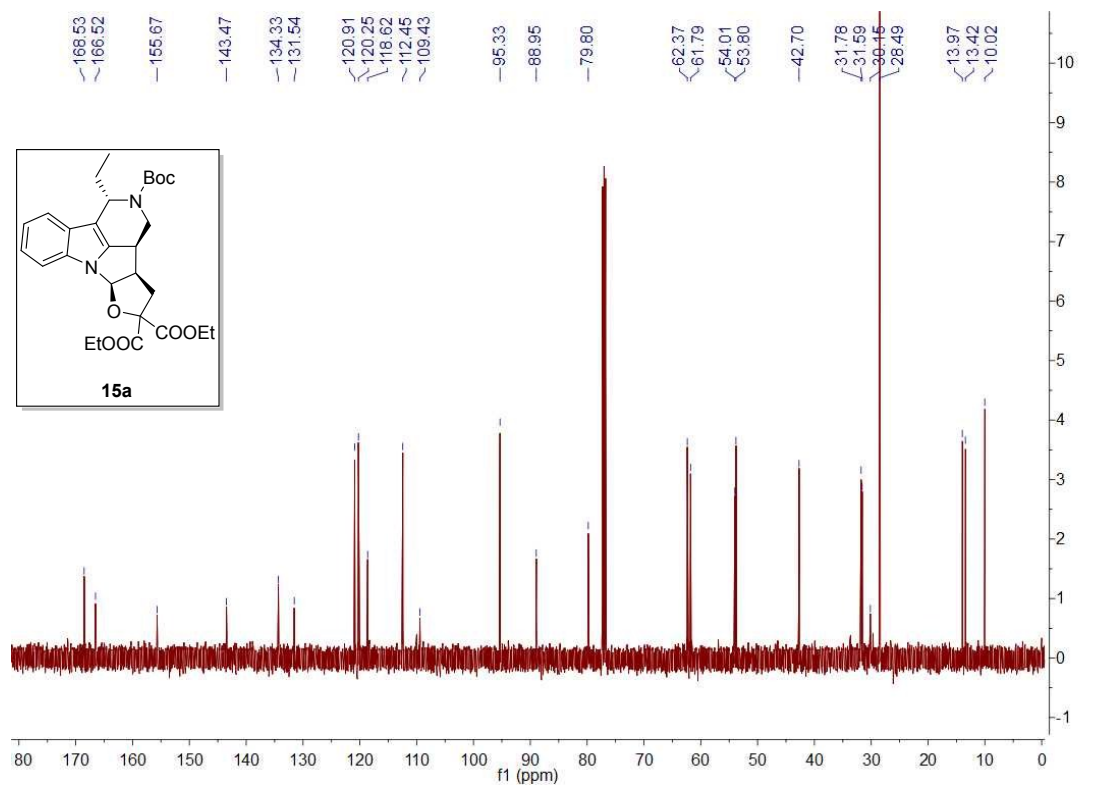
The ¹³C NMR spectrum of 9d (125 MHz, CDCl₃)



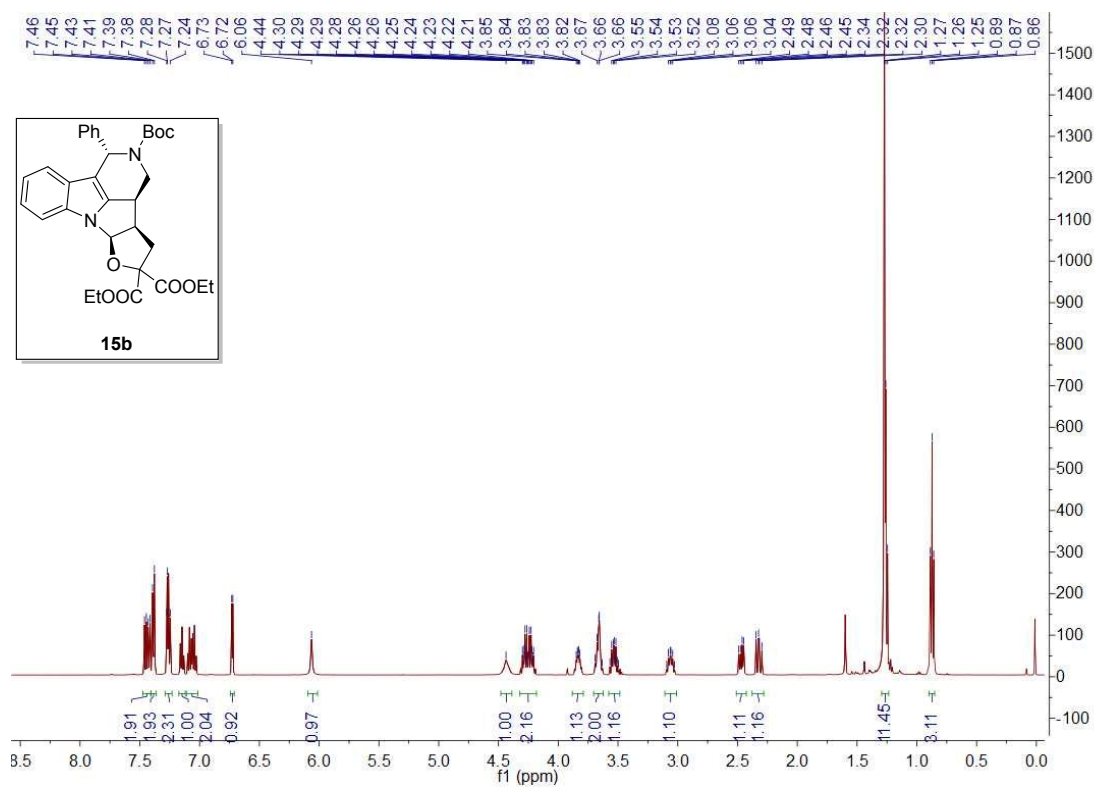
The ¹H NMR spectrum of 15a (500 MHz, CDCl₃)



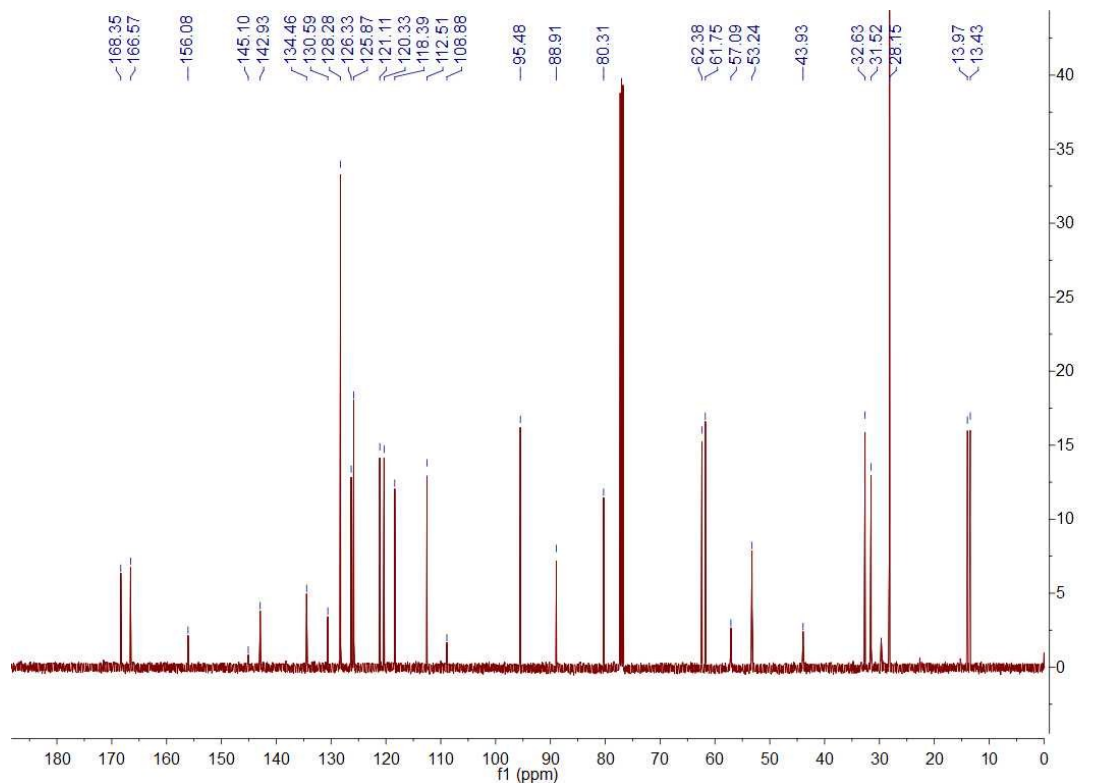
The ¹³C NMR spectrum of 15a (125 MHz, CDCl₃)



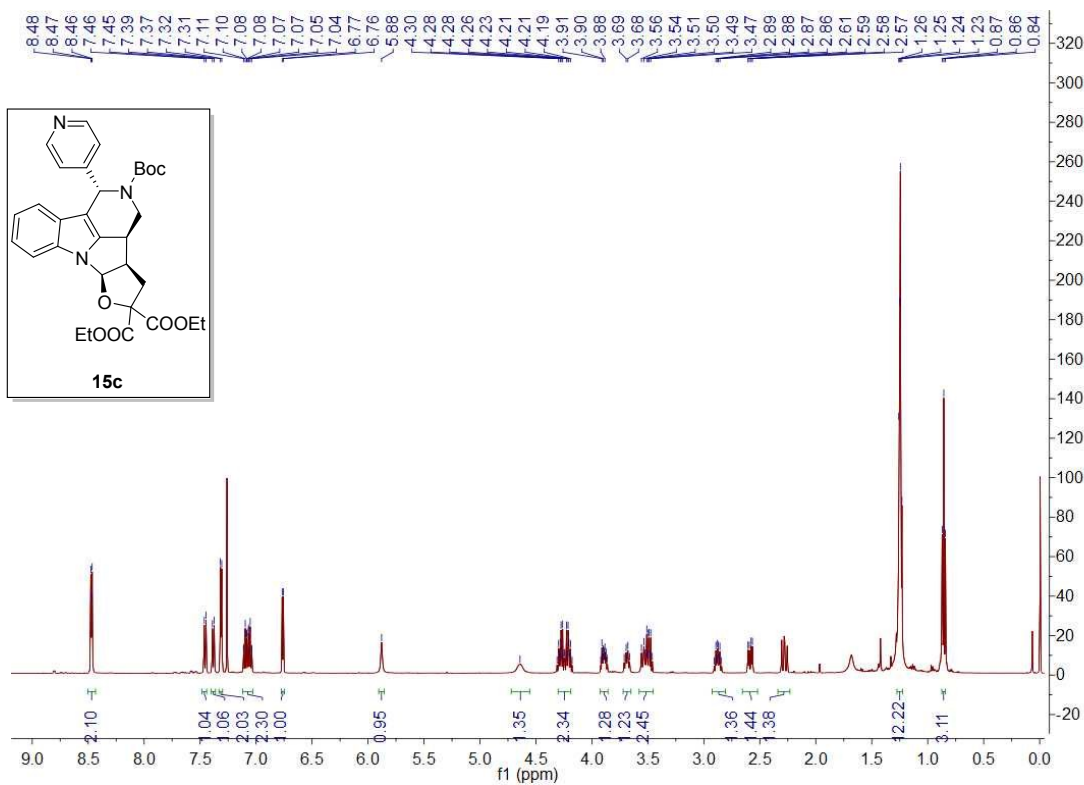
The ¹H NMR spectrum of 15b (500 MHz, CDCl₃)



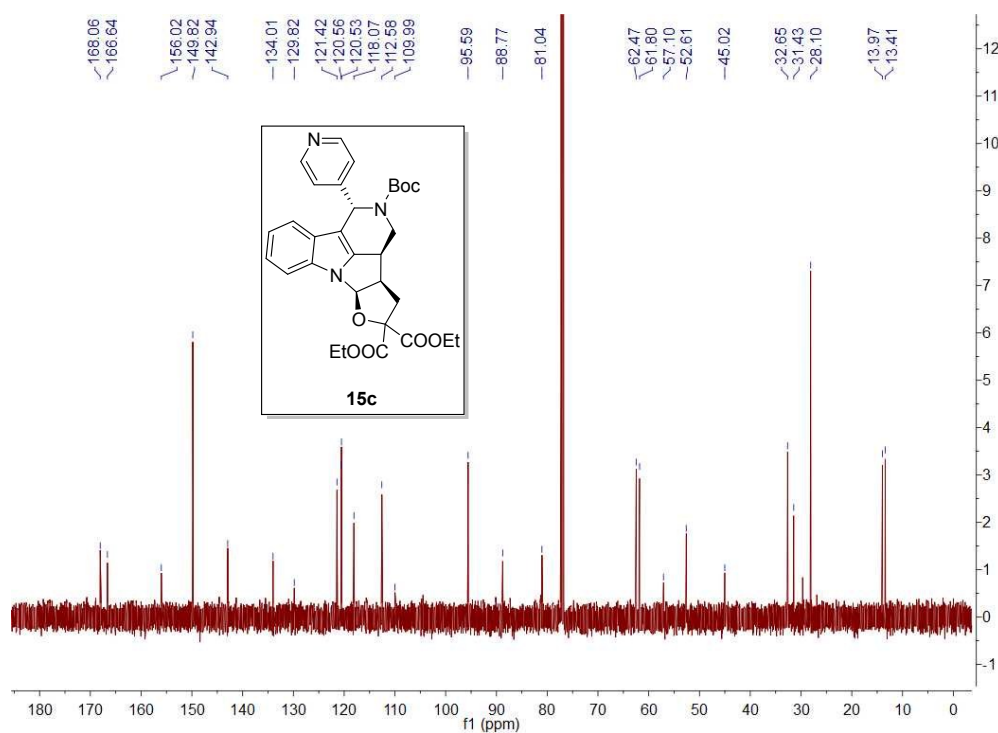
The ¹³C NMR spectrum of 15b (125 MHz, CDCl₃)



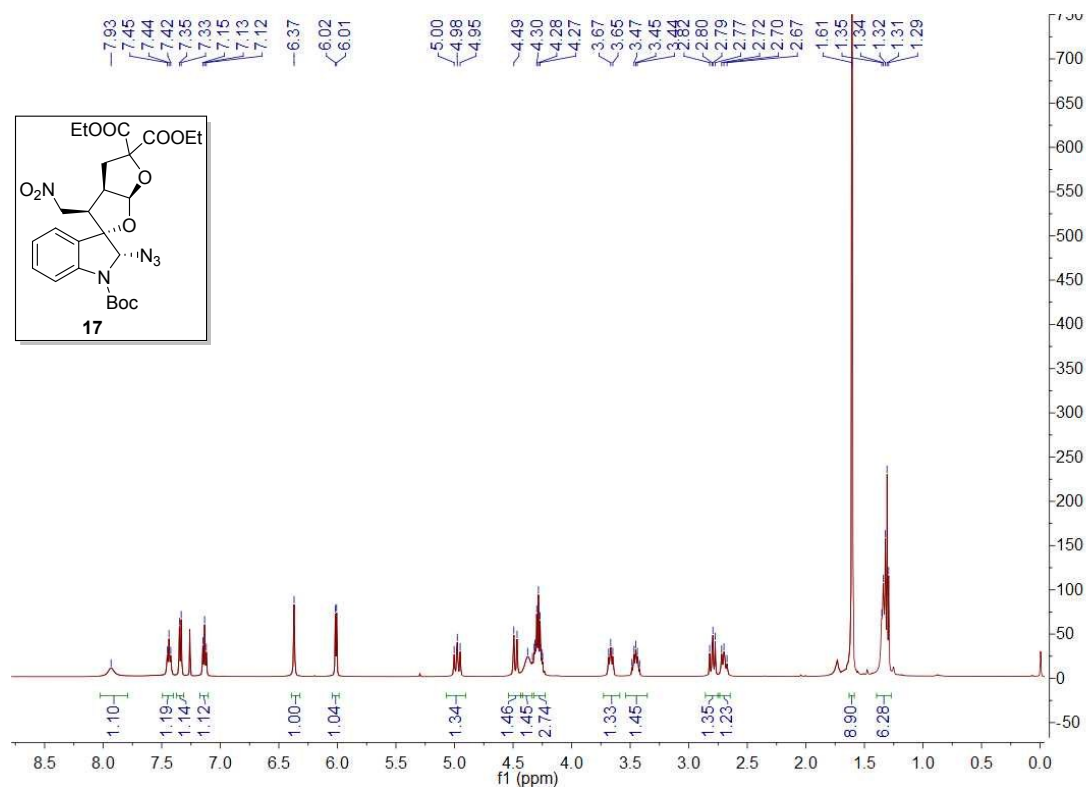
The ^1H NMR spectrum of **15c** (500 MHz, CDCl_3)



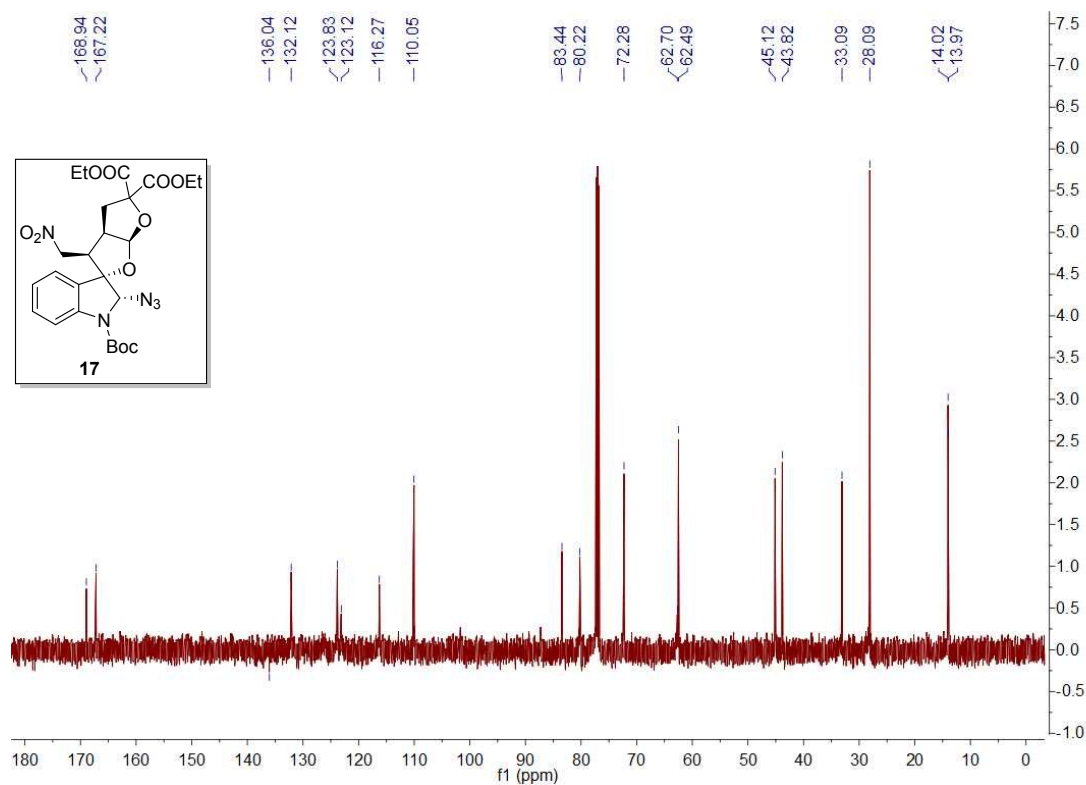
The ^{13}C NMR spectrum of **15c** (125 MHz, CDCl_3)



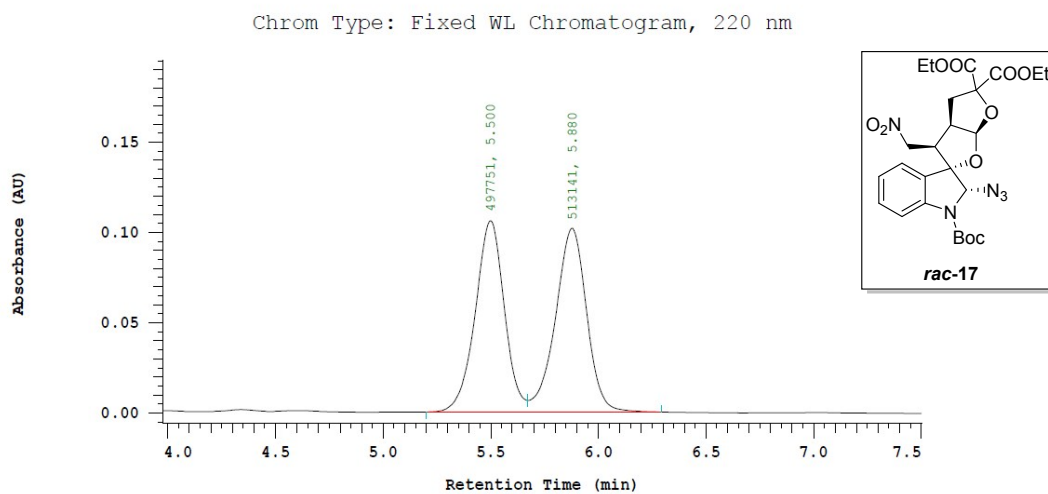
The ¹H NMR spectrum of 17 (500 MHz, CDCl₃)



The ¹³C NMR spectrum of 17 (125 MHz, CDCl₃)



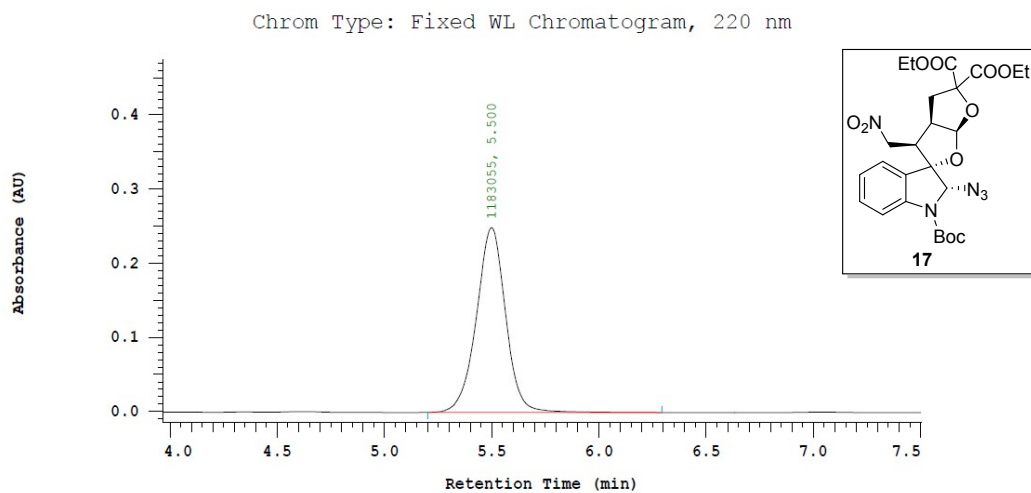
The HPLC of racemic 17



Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.500	497751	49.239	BV
2	5.880	513141	50.761	VB
		1010892	100.000	

The HPLC of chiral 17



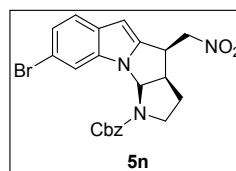
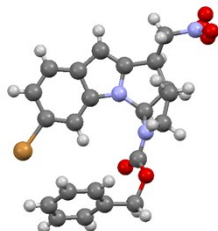
Chrom Type: Fixed WL Chromatogram, 220 nm
 Peak Quantitation: AREA
 Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.500	1183055	100.000	BB
		1183055	100.000	

G. Single crystal X-Ray diffraction data

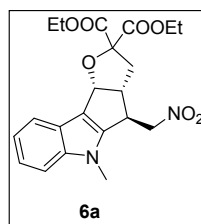
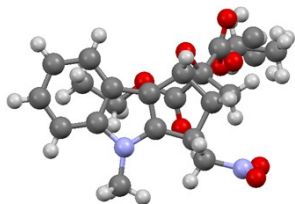
[CCDC 1877710-1877711 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.]

Absolute configuration of **5n** - CCDC 1877710



Bond precision:	C-C = 0.0060 Å	Wavelength=0.71073	
Cell:	a=9.2282 (14) alpha=90	b=9.1743 (14) beta=109.724 (3)	c=12.829 (2) gamma=90
Temperature:	120 K		
	Calculated	Reported	
Volume	1022.4 (3)	1022.4 (3)	
Space group	P 21	P 1 21 1	
Hall group	P 2yb	P 2yb	
Moiety formula	C22 H20 Br N3 O4	C22 H20 Br N3 O4	
Sum formula	C22 H20 Br N3 O4	C22 H20 Br N3 O4	
Mr	470.31	470.31	
Dx, g cm ⁻³	1.528	1.528	
Z	2	2	
Mu (mm ⁻¹)	2.045	2.045	
F000	480.0	480.0	
F000'	479.63		
h, k, lmax	11, 11, 16	11, 11, 16	
Nref	4674 [2483]	4202	
Tmin, Tmax		0.570, 0.746	
Tmin'			
Correction method=	# Reported T Limits: Tmin=0.570 Tmax=0.746		
AbsCorr =	MULTI-SCAN		
Data completeness=	1.69/0.90	Theta(max) = 27.485	
R(reflections)=	0.0326 (3248)	wR2(reflections)= 0.0730 (4202)	
S =	0.839	Npar= 289	

Absolute configuration of **6a** - 1877711



Bond precision: C-C = 0.0057 Å

Wavelength=0.71073

Cell: a=9.6264 (13) b=10.8580 (14) c=11.2163 (14)
 alpha=90 beta=113.736 (2) gamma=90
 Temperature: 120 K

	Calculated	Reported
Volume	1073.2 (2)	1073.2 (2)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C21 H24 N2 O7	C21 H24 N2 O7
Sum formula	C21 H24 N2 O7	C21 H24 N2 O7
Mr	416.42	416.42
Dx, g cm ⁻³	1.289	1.289
Z	2	2
Mu (mm ⁻¹)	0.097	0.097
F000	440.0	440.0
F000'	440.25	
h, k, lmax	12, 14, 14	12, 14, 14
Nref	4985 [2624]	4646
Tmin, Tmax		0.681, 0.746
Tmin'		

Correction method= # Reported T Limits: Tmin=0.681 Tmax=0.746
 AbsCorr = MULTI-SCAN

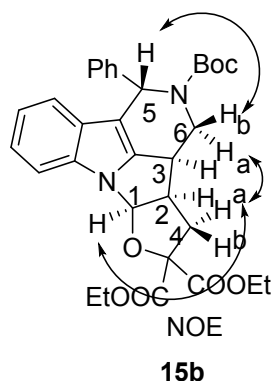
Data completeness= 1.77/0.93 Theta(max)= 27.607

R(reflections)= 0.0496 (3074) wR2(reflections)= 0.1161 (4646)

S = 1.057

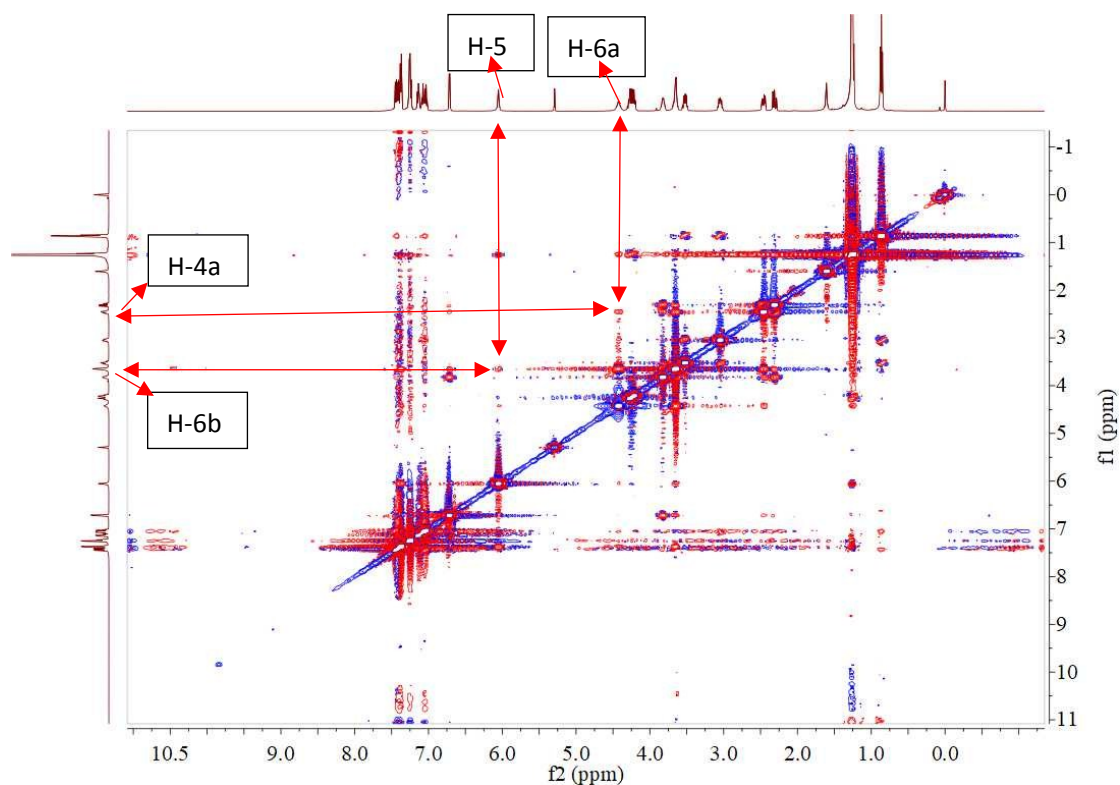
Npar= 304

H. Absolute configuration of 15b

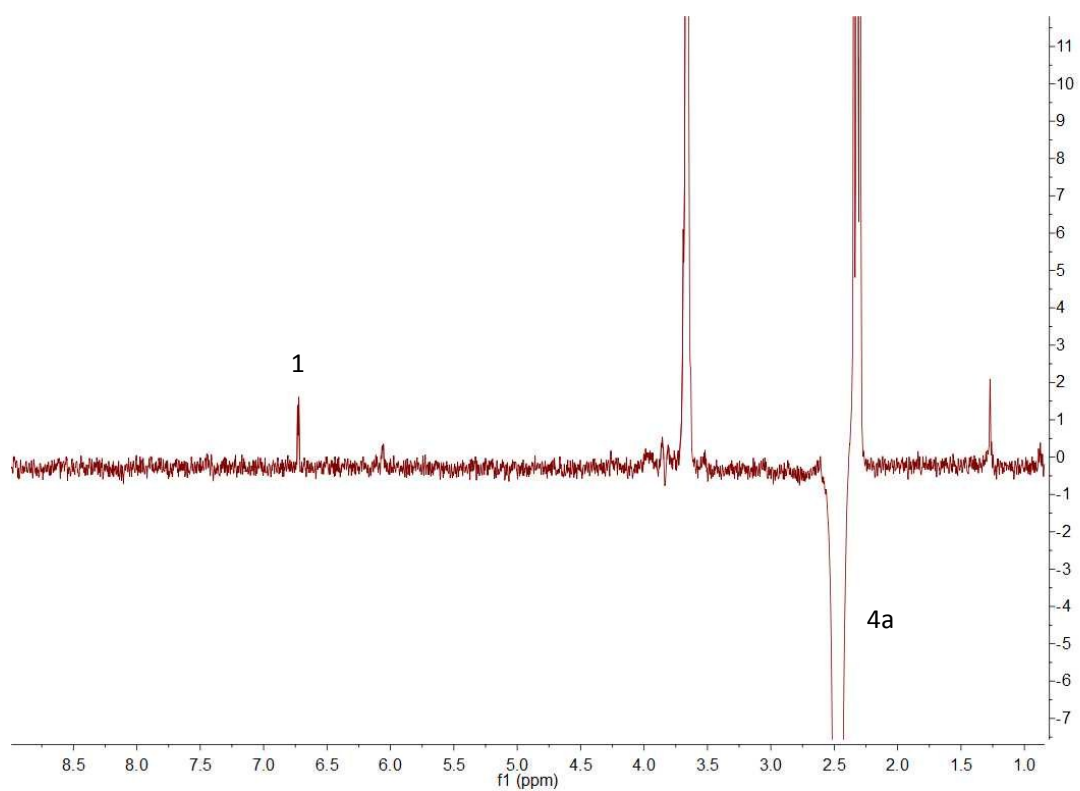


The NOE correlation of H-1/H-4a and the NOESY correlation of H-4a/H-6a indicated they are on the same side. The NOESY correlations of H-5/H-6b indicated that they are on the opposite side. The absolute configurations of C-1, C-2, C-3 were the same as **5n**. Thus, the absolute configurations of compound **5n** were determined as 1*R*, 2*R*, 3*R*, 5*S* respectively.

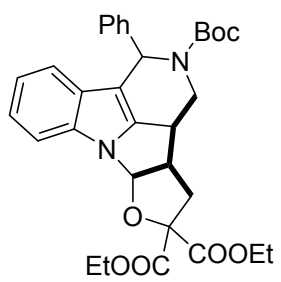
The NOESY analysis of compound 15b



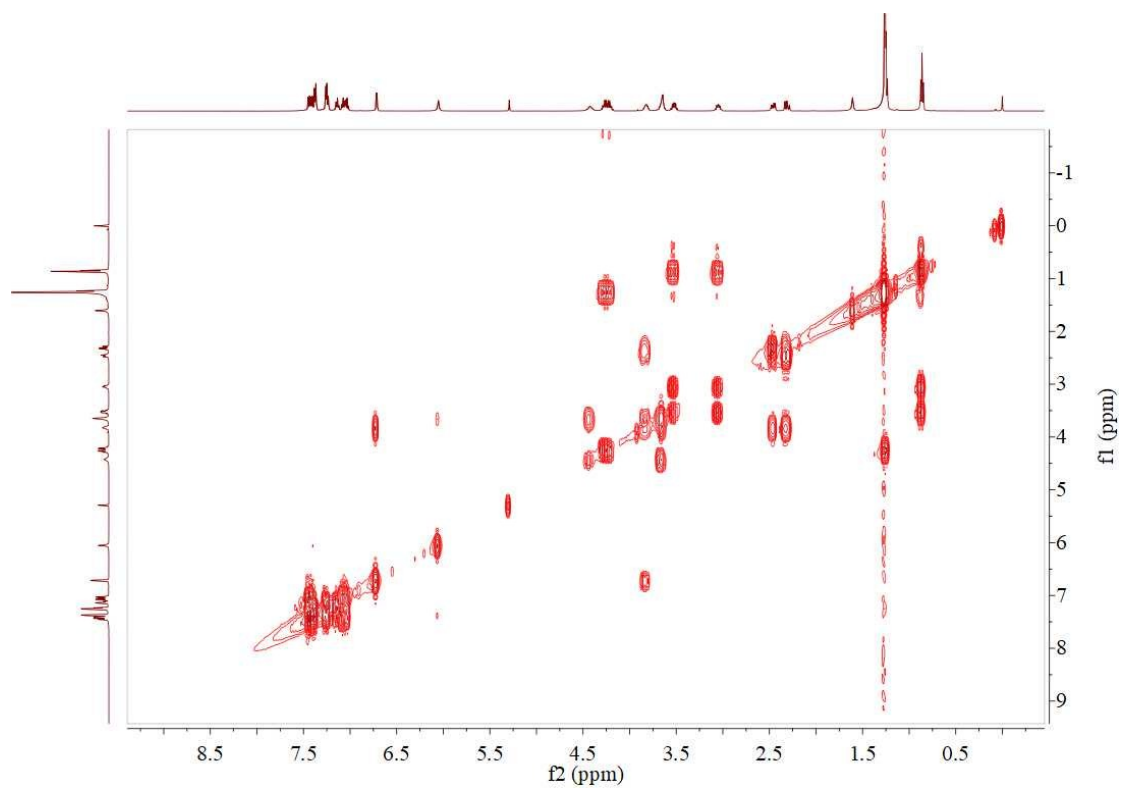
The NOE analysis of compound 15b



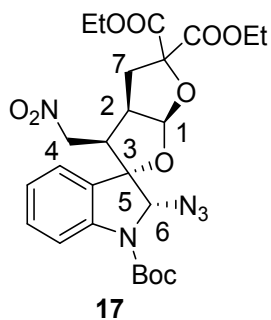
The gCOSY analysis of compound **15b**



Key COSY correlations of **15b**

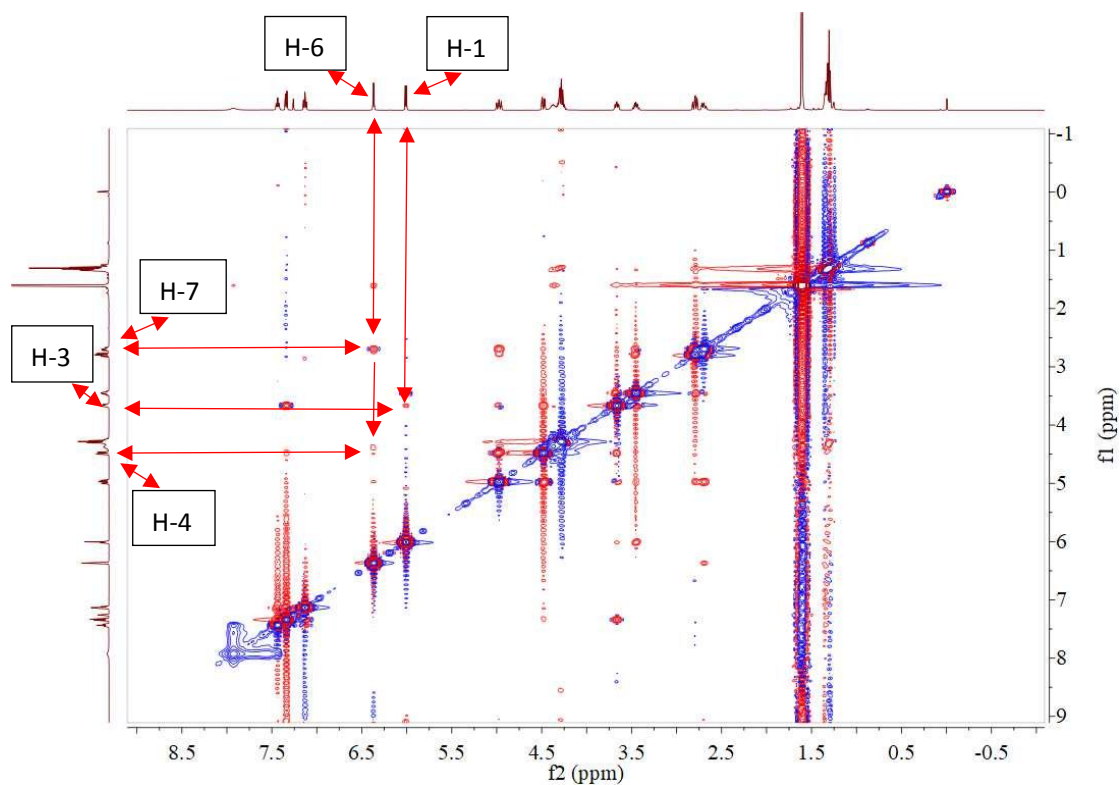


I. Absolute configuration of 17

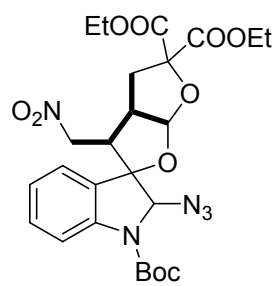


The large coupling constant (5.9 Hz) between H-1 and H-2 and NOESY correlation of H-1 and H-3 indicated that they are on the same side. While the NOESY correlations of H-6, H-4 and H-7 indicated that H-6 are on the other side. Thus, the relative configurations of compound 17 were determined as 1*R*, 2*R*, 3*R*, 5*S*, 6*S*. The absolute configuration of C-2 could be determined as R by the X-ray data of 5n. So the absolute configurations of compound 17 were determined as 1*R*, 2*R*, 3*R*, 5*S*, 6*S* respectively.

The NOE analysis of compound 17



The gCOSY analysis of compound 17



Key COSY correlations of 17

