Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Enantioselective organocatalytic sequential Michael-cyclization of functionalized nitroalkanes to 2-hydroxycinnamaldehydes: Synthesis of benzofused dioxa[3.3.1] and oxa[4.3.1] methylene-bridged compounds

Chen-Jun Peng,[a] Jun-Ping Pei,[a] Ying-Han Chen,[a] Zhi-Yong Wu,[a] Ming Liu[a,b] and Yan-Kai Liu*[a,b]

[a]Key Laboratory of Marine Drugs, Chinese Ministry of Education, School of Medicine and Pharmacy, Ocean University of China, Qingdao 266003, China.

[b]Laboratory for Marine Drugs and Bioproducts of Qingdao National Laboratory for Marine Science and Technology, Qingdao 266003, China.

Email: liuyankai@ouc.edu.cn (Y.-K. Liu)

Supporting Information

Contents

A. General information

The ^{1}H and ^{13}C NMR spectra were recorded at 500 MHz for ^{1}H and at 125 MHz for ^{13}C. The chemical shifts (δ) for ^{1}H and ^{13}C are given in ppm relative to residual signals of the solvents ($CDCl_3$ at 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR. *d6*-DMSO at 2.50 ppm ^{1}H NMR, 39.52 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 was obtained from Zhongke chemical technology service center. Optical rotations are reported as follows: $[\alpha]_D^{20}$ (c in g per 100 mL, solvent: $CHCl_3$, MeOH).

Note: NMR signals containing common solvent contaminants were list. H_2O in $CDCl_3$ at 1.56 ppm ^{1}H NMR, and in *d6*-DMSO at 3.33 ppm ^{1}H NMR; Ethyl acetate in $CDCl_3$ at 2.05 (s), 4.12 (q), 1.26 (t) ppm ^{1}H NMR; Dichloromethane in $CDCl_3$ at 5.30 (s) ppm ^{1}H 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, IC, or chiral-N(s)(2) 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.

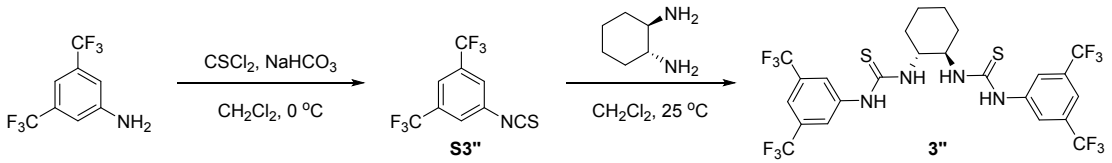
Commercial reagents and solvents were purchased from Sigma Aldrich, Fluka, and Alfa Aesar used as received, without further purification. The 2-hydroxycinnamaldehydes **1** were prepared according to the literature procedures.[1] All 1-nitromethylcycloalcohols were prepared from cyclic ketones according to the literature procedures.[2] 2-nitroethanol **2f** and 2-nitropropan-1-ol **2u** were purchased.

[1] Sun X-L; Chen Y-H; Zhu D-Y; Zhang Y; Liu Y-K. Org. Lett. **2016**, *18*, 864.

[2] Mo-Hui Wei, Yi-Rong Zhou, Liang-Hu Gu, Fan Luo, Fang-Lin Zhang. Tetrahedron Letters. **2013**, *54*, 2546.

B. Preparation of substrates

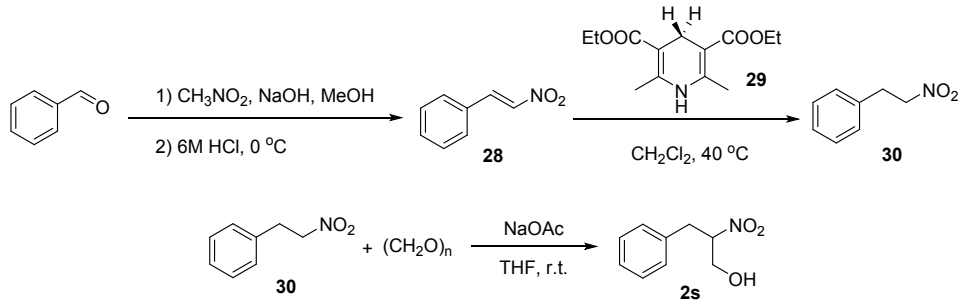
B1. Preparation of 3″



To a solution of 3,5-bis(trifluoromethyl)aniline (3 mL, 20 mmol, 1.0 equiv.) and saturated sodium bicarbonate solution (40 mL) in CH_2Cl_2 (40 mL) was added thiophosgene $CSCl_2$ (1.7 mL, 22 mmol, 1.1 equiv.) very slowly at 0 °C. The reaction was stirred at 0 °C for about 2 h (monitored by TLC). The reaction mixture was extracted three times with CH_2Cl_2 and the combined organic layers were washed with saturated sodium chloride solution. The organic layer was dried with anhydrous Na_2SO_4 and the solvent was evaporated. The product was purified by column chromatography on a silica gel (petroleum ether) to afford the desired product **S3″** as a yellow oil (2.4 g).

To a solution of **S3″** (2.4 g, 8.9 mmol, 2.5 equiv.) in CH_2Cl_2 (5 mL) was added (1*R*,2*R*)-cyclohexane-1,2-diamine (405 mg, 3.5 mmol, 1.0 equiv.) at 25 °C. The reaction was stirred at 25 °C for about 12 h until the consumption of (1*R*,2*R*)-cyclohexane-1,2-diamine (monitored by TLC). Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) to give product **3″** (1.2 g, 23% yield over two steps).

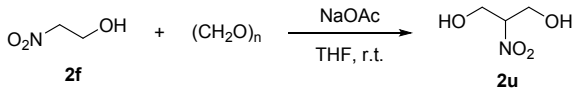
B2. Preparation of 2-nitro-3-phenylpropan-1-ol 2s



To a solution of benzaldehyde (1.8 mL, 18 mmol, 1.0 equiv.) and nitromethane (1.1 mL, 20 mmol, 1.1 equiv.) in MeOH (5 mL) was added NaOH (1.1 g, 27 mmol, 1.5 equiv.) in MeOH (5 mL) at 0 °C. The reaction was stirred at 0 °C for 2 h until the consumption of benzaldehyde (monitored by TLC). After that, pour the reaction mixture into 6M HCl solution at 0 °C and white precipitation started to form. **28** (1.6 g, 60% yield) could be afforded as a yellow solid by recrystallization with EtOH. To a solution of **28** (298 mg, 2 mmol, 1.0 equiv.) in CH_2Cl_2 (3 mL) was added **29** (608 mg, 2.4 mmol, 1.2 equiv.) and the reaction was refluxed at 40 °C for 48 h. The solvent was evaporated and the product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 80/1) to afford the desired product **30** as a yellow oil (272 mg, 90% yield).

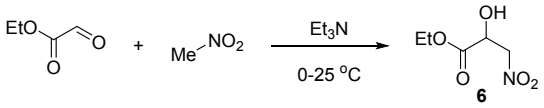
To a solution of **30** (272 mg, 1.8 mmol, 1.0 equiv.) in THF (3 mL) was added NaOAc (44 mg, 0.54 mmol, 0.3 equiv.) and paraformaldehyde (49 mg, 1.6 mmol, 0.9 equiv.) at room temperature. The reaction was stirred at room temperature until completion of the reaction. The reaction mixture was extracted three times with ethyl acetate and the combined organic layers were washed with saturated sodium chloride solution. The organic layer was dried with anhydrous Na_2SO_4 and then the solvent was evaporated. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 5/1) to afford the desired product **2s** as a white solid (222 mg, 68% yield).

B3. Preparation of 2-nitropropane-1,3-diol 2u



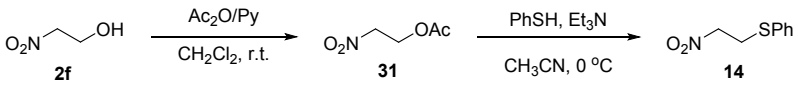
To a solution of 2−nitroethanol (0.43 mL, 6 mmol, 1.0 equiv.) in THF (10 mL) was added NaOAc (148 mg, 1.8 mmol, 0.3 equiv.) and paraformaldehyde (180 mg, 6 mmol, 1.0 equiv.) at room temperature. The reaction was stirred at room temperature until completion of the reaction. The reaction mixture was extracted three times with ethyl acetate and the combined organic layers were washed with saturated sodium chloride solution. The organic layer was dried with anhydrous Na_2SO_4 and then the solvent was evaporated. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 1.5/1) to afford the desired product **2u** as a yellow oil (300 mg, 41% yield).

B4. Preparation of ethyl 2-hydroxy-3-nitropropanoate 6



To a solution of ethyl 2-oxoacetate (1 mL, 5 mmol, 1.0 equiv.) in nitromethane (10 mL) was added Et_3N (0.35 mL, 2.5 mmol, 0.5 equiv.) at 0 °C. The reaction was stirred at 25 °C until completion of the reaction. Then the solvent nitromethane was evaporated. The residue was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 4/1) to afford the desired product **6** as a white solid (643 mg, 79% yield).

B5. Preparation of (2-nitroethyl)(phenyl)sulfane 14

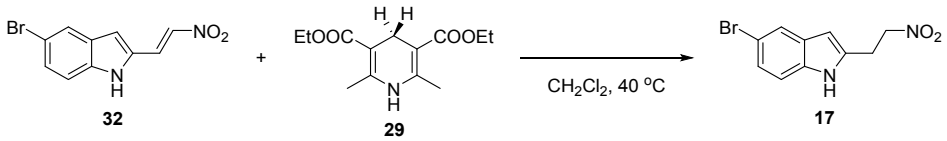


To a solution of 2−nitroethanol (0.36 mL, 5 mmol, 1.0 equiv.) and acetic anhydride (0.52 mL, 5.5 mmol, 1.1 equiv.) in CH_2Cl_2 (8 mL) was added pyridine (0.45 mL, 5.5

mmol, 1.1 equiv.). The reaction was stirred under nitrogen atmosphere at room temperature. After 7 h, the reaction mixture was poured into 1M HCl and the aqueous phase was extracted with dichloromethane. The combined organic layers were washed with 1M HCl for three times. The organic layer was washed with saturated sodium chloride solution and was dried with anhydrous Na_2SO_4 and then the solvent was evaporated. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 5/1) to afford the desired product **31** as a colorless oil (542 mg, 81% yield).

To a solution of **31** (542 mg, 4 mmol, 1.0 equiv.) and thiophenol (0.42 mL, 4 mmol, 1.0 equiv.) in acetonitrile (6 mL) was added Et_3N (0.57 mL, 4 mmol, 1.0 equiv.) at 0 ^oC. The reaction was stirred at 0 ^oC for 30min. The reaction mixture was poured into 1M HCl at 0 ^oC and the aqueous phase was extracted with ethyl acetate . The combined organic layers were washed with 1M HCl for three times. The organic layer was washed with saturated sodium chloride solution and was dried with anhydrous Na_2SO_4 and then the solvent was evaporated. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 100/1-30/1) to afford the desired product **14** as a colorless oil (608 mg, 82% yield).

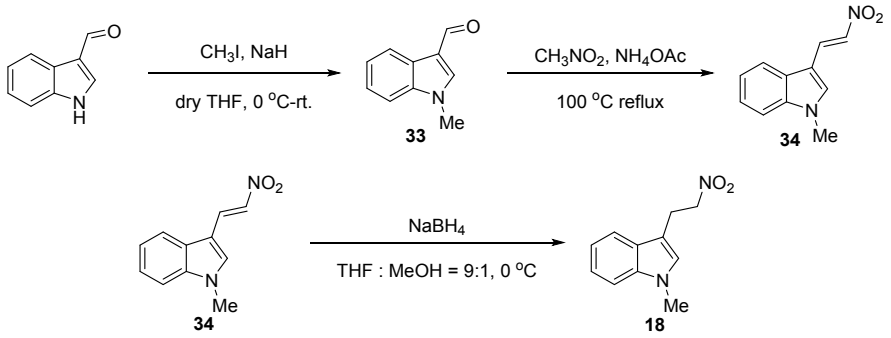
B6. Preparation of 5-bromo-2-(2-nitroethyl)-1H-indole 17



The synthetic method of **32** is the same as that of **34**.

To a solution of **32** (200 mg, 0.75 mmol, 1.0 equiv.) in CH_2Cl_2 (3 mL) was added **29** (190 mg, 0.75 mmol, 1.0 equiv.) and the reaction was refluxed at 40 ^oC for 6 days. The solvent was evaporated and the product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 6/1-4/1) to afford the desired product **17** as a red oil (141.4 mg, 70% yield).

B7. Preparation of 1-methyl-3-(2-nitroethyl)-1H-indole 18



To a solution of sodium hydride (560 mg, 14 mmol, 2.0 equiv.) in dry THF (10 mL) was added indole-3-carboxaldehyde (1 g, 7 mmol, 1.0 equiv.) at 0 °C in nitrogen atmosphere. The reaction was stirred at room temperature for 1 h and iodomethane (872 μL, 14 mmol, 2.0 equiv.) was added to the reaction. The reaction was stirred at room temperature until completion of the reaction. The mixture was quenched with sat. NH_4Cl and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was evaporated. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 2/1) to afford the desired product **33**. To a solution of **33** (1.14g, 7 mmol, 1.0 equiv.) in nitromethane (8 mL) was added ammonium acetate (270 mg, 3.5 mmol, 0.5 equiv.) and the reaction was refluxed at 100 °C for 1 h. The reaction mixture was recrystallized with ethanol and the desired product **34** was obtained as a yellow solid (1.3g, 93% yield for 2 steps).

To a solution of **34** (300 mg, 1.5 mmol, 1.0 equiv.) in mixed solvent (THF/ MeOH = 9/1, 3 mL) was added sodium borohydride (84 mg, 2.2 mmol, 1.5 equiv.) at 0 °C and the reaction was stirred at room temperature overnight. The mixture was quenched with sat. NH_4Cl and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was evaporated. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 15/1) to afford the desired product **18** as a yellow oil (134.4 mg, 44% yield).

C. Optimization of the reaction conditions

C1. Optimization of the Michael Addition

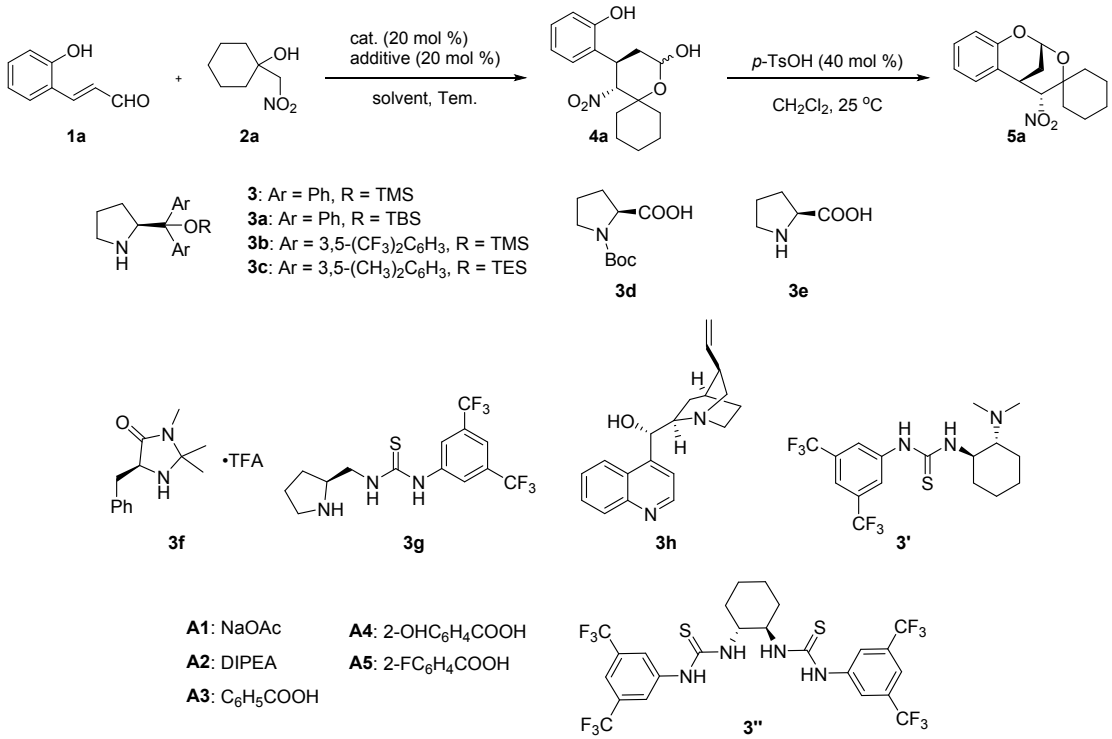


Table S1. Optimization of the Michael Addition[a]

Entry	Cat.	additive	Solvent	Tem (°C)	t(d)[b]	Yield (%)[c]	ee (%)[d]	dr[e]
1	**3**	/	$CHCl_3$	25	1	55	71	>20:1
2	**3**	/	$CHCl_3$	0	3	69	87	>20:1
3	**3a**	/	$CHCl_3$	0	3	66	87	>20:1
4	**3b**	/	$CHCl_3$	0-60	3	trace	5	>20:1
5	**3c**	/	$CHCl_3$	0	3	trace	87	>20:1
6	**3d**	/	$CHCl_3$	0	3	/	/	/

7	**3e**	/	$CHCl_3$	0	3	/	/	/
8	**3f**	/	$CHCl_3$	0-40	3	/	/	/
9	**3g**	/	$CHCl_3$	0-40	3	/	/	/
10	**3′**	/	$CHCl_3$	0	3	/	/	/
11	**3+3h**	/	$CHCl_3$	0	3	51	86	>20:1
12	**3+3′**	/	$CHCl_3$	0	3	trace	87	>20:1
13	**3′+3e**	/	$CHCl_3$	0	3	44	18	>20:1
14	**3**	/	toluene	0	3	54	83	>20:1
15	**3**	/	CH_2Cl_2	0	3	trace	84	>20:1
16	**3**	/	DCE	0	3	42	83	>20:1
17	**3**	/	TCE	0	3	trace	83	>20:1
18	**3**	/	Benzotrifluoride	0	3	39	76	>20:1
19	**3**	/	Bromobenzene	0	3	53	79	>20:1
20	**3**	/	MTBE	0	3	44	82	>20:1
21	**3**	/	CH_3CN	0	3	57	76	>20:1
22	**3**	/	Et_2O	0	3	57	80	>20:1
23	**3**	/	THF	0	3	14	79	>20:1
24	**3**	/	EA	0	3	44	77	>20:1
25	**3**	/	Acetone	0	3	29	76	>20:1

26	**3**	**A1**	$CHCl_3$	0	3	trace	86	>20:1
27	**3**	**A2**	$CHCl_3$	0	3	53	84	>20:1
28	**3**	**A3**	$CHCl_3$	0	3	trace	87	>20:1
29	**3**	**A4**	$CHCl_3$	0	3	/	/	/
30	**3**	**A5**	$CHCl_3$	0	3	32	86	>20:1
31	**3**	**3″**	$CHCl_3$	0	3	71	91	>20:1

[a] Unless otherwise specified, all reactions were carried out using **2a** (0.05 mmol, 1.0 equiv.), **1a** (0.06 mmol, 1.2 equiv.) in solvent (0.2 mL) with **cat.** (20 mol %) and additive (20 mol %) at 0 °C. After workup, the mixture was purified by flash chromatography on silica gel to afford **4a**. Compound **4a** was dissolved in redistilled CH_2Cl_2 (0.05 mmol in 0.3 mL) at 25 °C. *p*-TsOH (40 mol %) 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 ^{1}H NMR.

TMS = trimethylsilyl

TBS = (1,1-Dimethylethyl)dimethylsilyl

TES = triethylsilyl

DIPEA = N,N-Diisopropylethylamine

p-TsOH = *p*-Toluenesulfonic acid.

DCE = 1,2-dichloroethane

TCE = 1,1,2,2-tetrachloroethane

MTBE = tert-Butyl methyl ether

THF = tetrahydrofuran

EA = ethyl acetate

C2. Optimization of the one-pot reaction

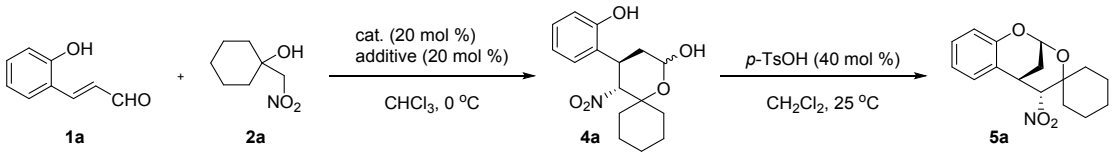


Table S2. Optimization of the one-pot reaction[a]

Entry	Cat.	additive	t(d)[b]	Yield (%)[c]	ee (%)[d]	dr[e]
1	**3**	/	3.5	73	79	>20:1
2	**3a**	/	3.5	69	81	>20:1
3	**3**	**3″**	3.5	66	79	>20:1

[a] Unless otherwise specified, all reactions were carried out using **2a** (0.05 mmol, 1.0 equiv.), **1a** (0.06 mmol, 1.2 equiv.) in $CHCl_3$ (0.2 mL) with **3** (20 mol %) and additive (20 mol %) at 0 °C for 3 days. Then *p*-TsOH (40 mol %) was added to the reaction mixture at 25 °C. After workup, the mixture was purified by flash chromatography on silica gel to afford **5a**. [b] For the two steps. [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.

TMS = trimethylsilyl *p*-TsOH = *p*-Toluenesulfonic acid.

TBS = (1,1-Dimethylethyl)dimethylsilyl

D. Scope of the reaction 1

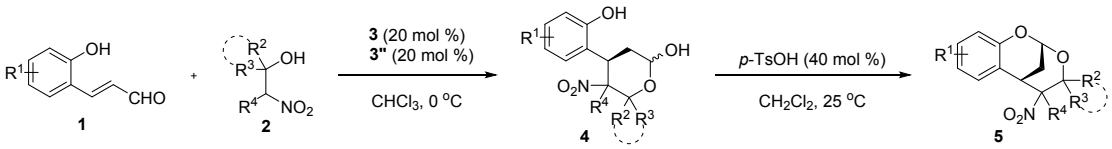
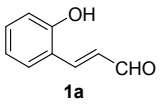
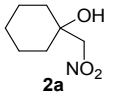
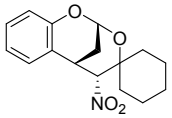
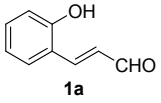
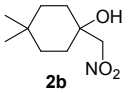
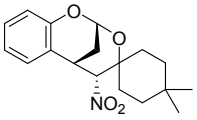
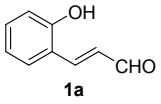
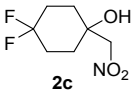
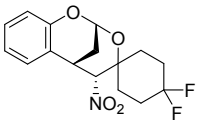
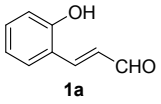
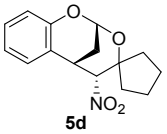
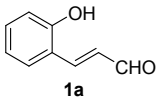
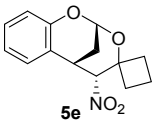
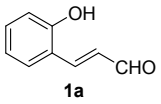
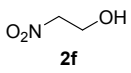
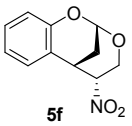
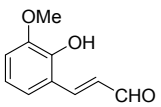
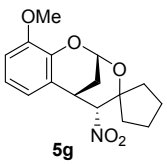
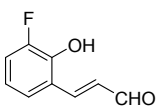
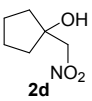
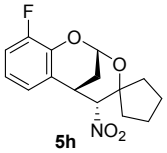
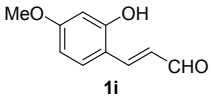


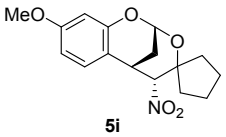
Table S3. Substrates correspond to the products

1	2	5
 **1a**	 **2a**	 **5a**
 **1a**	 **2b**	 **5b**
 **1a**	 **2c**	 **5c**
 **1a**	 **2d**	 **5d**
 **1a**	 **2e**	 **5e**
 **1a**	 **2f**	 **5f**
 **1g**	 **2d**	 **5g**
 **1h**	 **2d**	 **5h**

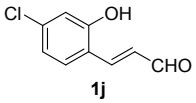


1i

2d

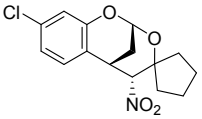


5i

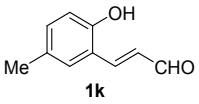


1j

2d

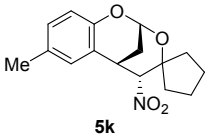


5j

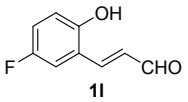


1k

2d

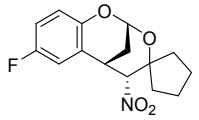


5k

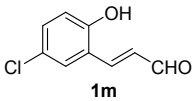


1l

2d

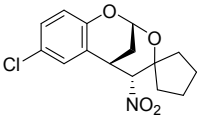


5l

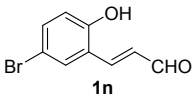


1m

2d

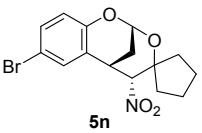


5m

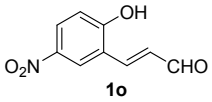


1n

2d

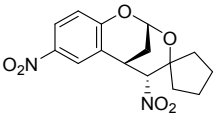


5n

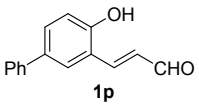


1o

2d

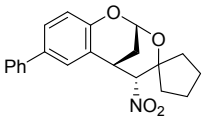


5o

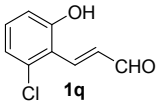


1p

2d

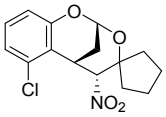


5p

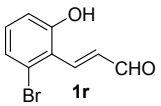


1q

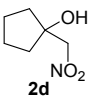
2d



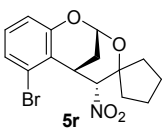
5q



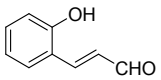
1r



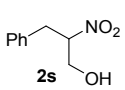
2d



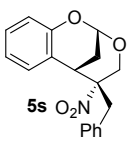
5r



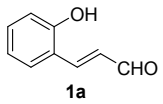
1a



2s

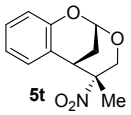


5s

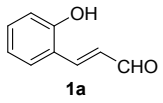


1a

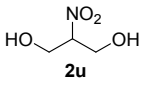
2t



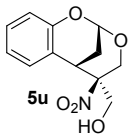
5t



1a

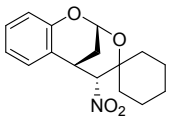


2u



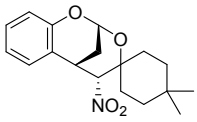
5u

General procedure: A glass vial equipped with a magnetic stirring bar was charged with 1-nitromethylcycloalcohols **2** (0.20 mmol, 1.0 equiv.), different substituted 2-hydroxycinnamaldehydes **1** (0.24 mmol, 1.2 equiv.), **3** (0.04 mmol, 0.2 equiv.) and **3″** (0.04 mmol, 0.2 equiv.) in $CHCl_3$ (0.5 mL) at 0 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of **2** (monitored by TLC analysis). After completion of the reaction, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5/1 to 1.5/1) to afford **4** as intermediate. Then, compound **4** (1.0 equiv.) was respectively dissolved in anhydrous CH_2Cl_2 (0.10 mmol in 0.5 mL) at 25 °C and *p*-TsOH (0.4 equiv.) was added to the reaction mixture. After full conversion of the second step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 100/1 to 4/1) to give product **5** for NMR and HPLC analysis.



5a

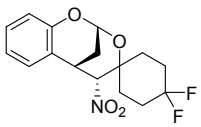
5a was obtained as a white solid 40.8 mg in 71% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 60/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26 (dd, J = 7.6, 2.5 Hz, 2H), 6.93 (t, J = 7.5 Hz, 1H), 6.82 (d, J = 8.1 Hz, 1H), 5.74 (s, 1H), 4.72 (d, J = 3.6 Hz, 1H), 3.63 (d, J = 2.9 Hz, 1H), 2.17 (dt, J = 13.2, 2.3 Hz, 1H), 2.04 – 1.91 (m, 2H), 1.86 – 1.59 (m, 5H), 1.56– 1.47 (m, 2H), 1.36 – 1.28 (m, 1H), 1.03 (qt, J = 13.2, 4.0 Hz, 1H), 0.82 (td, J = 13.6, 3.6 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.5, 131.7, 129.7, 121.9, 120.5, 115.7, 93.6, 91.4, 75.2, 40.0, 31.5, 30.7, 30.6, 25.4, 21.6, 21.4 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{16}H_{18}NO_4^-$ 288.1241, found 288.1237. **$[\alpha]_D^{20}$** 40.28 (c = 2.08 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], λ = 210 nm, t_{major} = 8.03 min, t_{minor} = 7.35 min, **ee** = **91%**. The enantiomeric excess after recrystallization was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 6.91 min, t_{minor} = 6.33 min, **ee** = **97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



5b

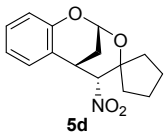
5b was obtained as a white solid 40.2 mg in 63% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 60/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27 (dd, J = 26.1, 7.8 Hz, 2H), 6.93 (t, J = 7.5 Hz, 1H), 6.81 (d, J = 8.1 Hz, 1H), 5.72 (s, 1H), 4.72 (d, J = 3.4 Hz, 1H), 3.68 (s, 1H), 2.26 – 2.12 (m, 2H), 2.05 – 1.98 (m, 1H), 1.80 – 1.63 (m, 2H), 1.50 (dd, J = 13.5, 3.0 Hz, 1H), 1.34 (dd, J = 14.3, 3.1 Hz, 1H), 1.17 (dd, J = 13.1, 1.7 Hz, 1H), 1.06 (td, J = 14.0, 3.5 Hz, 1H), 0.98 (dd, J = 13.2, 2.6 Hz, 1H), 0.89 (s, 3H), 0.76 (s, 3H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.4, 131.6, 129.5, 121.7, 120.4, 115.5, 92.9, 91.2, 75.0, 36.1, 34.1, 34.0,

32.4, 31.3, 30.4, 29.3, 26.1, 23.8 ppm. **HRMS**: [M-H]$^-$ *calcd*. For $C_{18}H_{22}NO_4^-$ 316.1554, found 316.1548. **$[\alpha]_D^{20}$** 45.66 (*c* = 1.46 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], λ = 210 nm, t_{major} = 6.24 min, t_{minor} = 5.71 min, **ee** = **88%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



5c

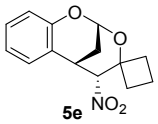
5c was obtained as a colorless oil 46 mg in 71% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.5 Hz, 2H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 5.74 (s, 1H), 4.80 (d, *J* = 3.5 Hz, 1H), 3.74 (s, 1H), 2.37 – 2.14 (m, 4H), 2.05 (ddd, *J* = 13.3, 3.8, 1.9 Hz, 1H), 1.96 (t, *J* = 11.4 Hz, 1H), 1.76 (dd, *J* = 7.7, 2.4 Hz, 2H), 1.61 – 1.54 (m, 1H), 1.29 – 1.23 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.2, 131.6, 129.9, 121.1, 120.8, 115.6, 91.3, 91.2, 73.3, 36.7, 36.6, 31.2, 30.3, 29.5, 29.3, 29.1, 26.6, 26.5 ppm. **HRMS**: [M-H]$^-$ *calcd*. For $C_{16}H_{16}F_2NO_4^-$ 324.1053, found 324.1056. **$[\alpha]_D^{20}$** 29.79 (*c* = 1.65 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], λ = 210 nm, t_{major} = 8.57 min, t_{minor} = 7.88 min, **ee** = **85%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



5d

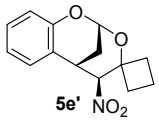
5d was obtained as a white solid 47.4 mg in 86% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 50/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 1H), 7.17 – 7.12 (m, 1H), 6.91 (t, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 5.66 (s, 1H), 4.94 (d, *J* = 3.3 Hz, 1H), 3.86 (d, *J* = 2.7 Hz, 1H), 2.24 (dt, *J* = 13.1, 2.4 Hz, 1H), 2.11 (ddd, *J* = 13.2, 9.6, 6.3 Hz, 2H), 1.88 (dd, *J*

= 13.3, 4.7 Hz, 1H), 1.82 – 1.72 (m, 1H), 1.72 – 1.60 (m, 2H), 1.52 (ddd, *J* = 15.0, 7.3, 3.7 Hz, 1H), 1.46 – 1.36 (m, 1H), 1.32 (ddd, *J* = 13.2, 9.0, 5.0 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.2, 130.5, 129.6, 120.8, 120.7, 116.0, 91.6, 90.1, 84.2, 42.4, 33.6, 32.1, 30.5, 26.7, 23.4 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{16}NO_4^-$ 274.1085, found 274.1090. **$[\alpha]_D^{20}$** 16.59 (*c* = 0.67 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 210 nm, t_{major} = 7.85 min, t_{minor} = 7.40 min, **ee** = **93%**. The enantiomeric excess after recrystallization was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 210 nm, t_{major} = 7.99 min, t_{minor} = 7.47 min, **ee >99%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr*** **>20:1**.



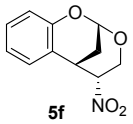
5e

5e was obtained as a white solid 32 mg in 61% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 60/1-40/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 1H), 7.14 (dd, *J* = 7.6, 1.4 Hz, 1H), 6.91 (td, *J* = 7.5, 0.9 Hz, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 5.66 (s, 1H), 4.72 (d, *J* = 3.0 Hz, 1H), 3.74 (d, *J* = 2.7 Hz, 1H), 2.61 – 2.48 (m, 1H), 2.34 – 2.13 (m, 3H), 2.09 (ddd, *J* = 13.2, 4.0, 1.9 Hz, 1H), 1.76 (ddq, *J* = 10.7, 8.3, 5.3 Hz, 2H), 1.55 – 1.40 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.1, 130.8, 129.7, 120.9, 120.1, 116.1, 92.1, 89.9, 60.5, 34.1, 32.3, 31.3, 30.4, 13.8 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{14}H_{14}NO_4^-$ 260.0928, found 260.0933. **$[\alpha]_D^{20}$** 11.86 (*c* = 1.18 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 98/2, 1 mL/min], λ = 210 nm, t_{major} = 14.04 min, t_{minor} = 13.17 min, **ee** = **95%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr*** **>20:1**.



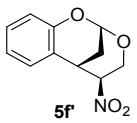
5e'

5e′ was obtained as a white solid 10 mg in 19% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 60/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.18 (m, 2H), 6.96 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 8.1 Hz, 1H), 5.75 (s, 1H), 4.91 (d, J = 2.6 Hz, 1H), 3.62 (s, 1H), 2.60 (dt, J = 13.6, 2.5 Hz, 1H), 2.32 (dd, J = 22.5, 9.7 Hz, 1H), 2.18 – 2.00 (m, 2H), 1.86 – 1.78 (m, 1H), 1.73 (ddd, J = 14.5, 10.1, 5.1 Hz, 1H), 1.54 – 1.40 (m, 1H), 1.08 (ddt, J = 12.9, 8.7, 4.2 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.9, 129.9, 128.4, 121.6, 121.2, 116.8, 92.7, 89.2, 73.7, 35.9, 33.9, 32.6, 22.8, 12.8 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{14}H_{14}NO_4^-$ 260.0928, found 260.0924. **$[\alpha]_D^{20}$** 71.17 (c = 2.39 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 7.47 min, t_{minor} = 5.99 min, **ee** = **98%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



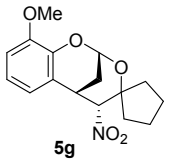
5f

5f was obtained as a white solid 10 mg in 23% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1-10/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 (d, J = 1.7 Hz, 1H), 6.96 (dd, J = 11.9, 4.7 Hz, 2H), 6.90 (t, J = 7.4 Hz, 1H), 5.58 (s, 1H), 4.80 (ddd, J = 11.2, 5.1, 3.9 Hz, 1H), 4.16 (dd, J = 12.0, 5.2 Hz, 1H), 3.94 (d, J = 2.2 Hz, 1H), 3.88 (t, J = 11.6 Hz, 1H), 2.26 (dt, J = 13.4, 2.3 Hz, 1H), 2.11 (ddd, J = 13.4, 3.9, 1.9 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.8, 152.1, 130.1, 129.6, 121.6, 115.7, 91.1, 81.0, 57.9, 33.0, 28.8 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{11}H_{10}NO_4^-$ 220.0615, found 220.0618. **$[\alpha]_D^{20}$** -40.39 (c = 0.29 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 8.64 min, t_{minor} = 7.66 min, **ee** = **98%**. The diastereomeric ratio was determined by NMR, ***dr* >20:1**.



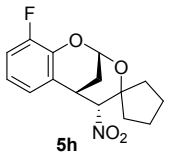
5f′

5f′ was obtained as a white solid 26.2 mg in 59% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 60/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 1H), 7.19 (dd, J = 7.8, 1.4 Hz, 1H), 7.02 – 6.95 (m, 2H), 5.64 (s, 1H), 4.51 (d, J = 14.1 Hz, 1H), 4.30 (d, J = 0.9 Hz, 1H), 4.00 – 3.88 (m, 2H), 2.36 (dt, J = 13.7, 2.4 Hz, 1H), 1.84 (ddd, J = 13.7, 2.0, 1.2 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 129.8, 128.7, 121.5, 116.3, 92.4, 82.7, 58.8, 31.3, 24.6 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{11}H_{10}NO_4^-$ 220.0615, found 220.0613. **$[\alpha]_D^{20}$** -25.53 (c = 0.75 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak ID column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 12.21 min, t_{minor} = 10.70 min, **ee = 95%**. The diastereomeric ratio was determined by NMR, ***dr* >20:1**.



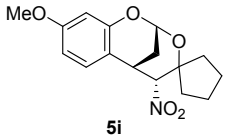
5g

5g was obtained as a white solid 36 mg in 59% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1-8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.90 – 6.83 (m, 2H), 6.74 (dd, J = 5.7, 3.4 Hz, 1H), 5.78 (d, J = 0.9 Hz, 1H), 4.92 (d, J = 3.3 Hz, 1H), 3.88 (s, 4H), 2.23 (dt, J = 13.1, 2.5 Hz, 1H), 2.14 – 2.02 (m, 2H), 1.91 – 1.82 (m, 1H), 1.75 (dd, J = 13.5, 7.5 Hz, 1H), 1.72 – 1.65 (m, 1H), 1.65 – 1.58 (m, 1H), 1.56 – 1.48 (m, 1H), 1.43 – 1.30 (m, 2H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.5, 142.8, 122.3, 121.7, 120.6, 111.6, 91.9, 90.2, 84.4, 56.1, 42.7, 33.7, 32.1, 30.5, 26.9, 23.6 ppm. **HRMS**: $[M+Na]^+$ *calcd*. For $C_{16}H_{19}NNaO_5^+$ 328.1155, found 328.1151. **$[\alpha]_D^{20}$** -22.27 (c = 1.43 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 210 nm, t_{major} = 17.01 min, t_{minor} = 15.65 min, **ee = 94%**. The diastereomeric ratio was determined by NMR, ***dr* >20:1**.



5h

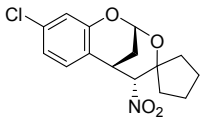
5h was obtained as a white solid 38 mg in 65% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 30/1-20/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.07 (ddd, J = 10.6, 8.2, 1.4 Hz, 1H), 6.94 (d, J = 7.7 Hz, 1H), 6.85 (td, J = 8.0, 4.9 Hz, 1H), 5.76 (s, 1H), 4.94 (d, J = 3.4 Hz, 1H), 3.92 (d, J = 2.6 Hz, 1H), 2.27 (dt, J = 13.3, 2.5 Hz, 1H), 2.17 – 2.06 (m, 2H), 1.94 – 1.85 (m, 1H), 1.81 – 1.60 (m, 3H), 1.58 – 1.49 (m, 1H), 1.45 – 1.36 (m, 1H), 1.32 (ddd, J = 20.0, 10.1, 5.5 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 151.7, 149.8, 125.7, 125.6, 123.4, 120.5, 120.4, 116.3, 116.2, 91.8, 90.0, 84.5, 42.6, 33.8, 31.8, 31.8, 30.4, 26.9, 23.6 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{15}FNO_4^-$ 292.0991, found 292.0992. **$[\alpha]_D^{20}$** 21.87 (c = 1.45 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak Chiral-NS (2) column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 210 nm, t_{major} = 12.14 min, t_{minor} = 11.49 min, **ee = 94%**. The diastereomeric ratio was determined by NMR, ***dr* >20:1**.



5i

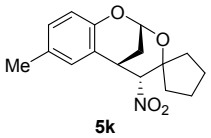
5i was obtained as a white solid 18 mg in 29% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 50/1-20/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.04 (d, J = 8.5 Hz, 1H), 6.49 (dd, J = 8.5, 2.5 Hz, 1H), 6.40 (d, J = 2.5 Hz, 1H), 5.63 (d, J = 0.8 Hz, 1H), 4.90 (d, J = 3.2 Hz, 1H), 3.81 (d, J = 3.0 Hz, 1H), 3.78 (s, 3H), 2.21 (dt, J = 13.1, 2.5 Hz, 1H), 2.16 – 2.04 (m, 2H), 1.87 (ddd, J = 12.2, 5.2, 3.4 Hz, 1H), 1.81 – 1.71 (m, 1H), 1.70 – 1.59 (m, 2H), 1.56 – 1.48 (m, 1H), 1.45 – 1.31 (m, 2H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.1, 154.2, 131.2, 113.1, 107.3, 101.3, 91.8, 90.3, 84.4, 55.4, 42.5, 33.9, 31.6, 30.9, 26.8, 23.5 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{16}H_{18}NO_5^-$ 304.1190, found 304.1182. **$[\alpha]_D^{20}$** -27.15 (c = 1.33 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], λ = 210 nm, t_{major} = 8.37 min, t_{minor} = 7.06 min, **ee** = **92%**. The diastereomeric ratio was determined by NMR, ***dr*** **>20:1**.



5j

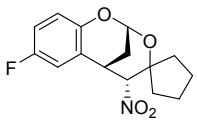
5j was obtained as a yellow oil 32 mg in 52% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 30/1-20/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.10 (d, J = 8.2 Hz, 1H), 6.90 (dd, J = 8.2, 1.0 Hz, 1H), 6.87 (s, 1H), 5.65 (s, 1H), 4.93 (d, J = 3.1 Hz, 1H), 3.83 (d, J = 2.3 Hz, 1H), 2.23 (d, J = 13.2 Hz, 1H), 2.18 – 2.10 (m, 1H), 2.05 (ddd, J = 13.3, 3.6, 1.4 Hz, 1H), 1.88 (dd, J = 9.9, 8.2 Hz, 1H), 1.77 – 1.60 (m, 3H), 1.56 – 1.46 (m, 1H), 1.46 – 1.37 (m, 1H), 1.35 – 1.28 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.8, 135.0, 131.5, 121.0, 119.5, 116.2, 91.6, 89.9, 84.2, 42.3, 33.7, 31.5, 30.3, 26.6, 23.3 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{15}ClNO_4^-$ 308.0695, found 308.0699. **$[\alpha]_D^{20}$** -14.27 (c = 1.19 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 210 nm, t_{major} = 9.99 min, t_{minor} = 7.88 min, **ee** = **91%**. The diastereomeric ratio was determined by NMR, ***dr*** **>20:1**.



5k

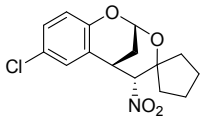
5k was obtained as a white solid 40.8 mg in 71% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 30/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.05 (dd, J = 8.3, 1.8 Hz, 1H), 6.92 (d, J = 1.5 Hz, 1H), 6.73 (d, J = 8.3 Hz, 1H), 5.63 (d, J = 0.8 Hz, 1H), 4.92 (d, J = 3.3 Hz, 1H), 3.82 (d, J = 3.0 Hz, 1H), 2.27 (s, 3H), 2.22 (dt, J = 13.1, 2.5 Hz, 1H), 2.12 – 2.04 (m, 2H), 1.90 – 1.83 (m, 1H), 1.80 – 1.74 (m, 1H), 1.72 – 1.60 (m, 2H), 1.56 – 1.49 (m, 1H), 1.44 – 1.32 (m, 2H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 151.0, 130.7, 130.3, 130.0, 120.5, 115.7,

91.6, 90.2, 84.1, 42.5, 33.7, 32.1, 30.7, 26.7, 23.4, 20.5 ppm. **HRMS**: [M-H]$^-$ *calcd*. For $C_{16}H_{18}NO_4^-$ 288.1241, found 288.1248. **$[\alpha]_D^{20}$** 29.37 (*c* = 0.96 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], λ = 210 nm, t_{major} = 7.25 min, t_{minor} = 6.13 min, **ee** = **85%**. The diastereomeric ratio was determined by NMR, ***dr*** **>20:1**.



5l

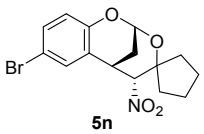
5l was obtained as a white solid 38 mg in 65% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 30/1-20/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.99 – 6.88 (m, 2H), 6.77 (dd, *J* = 8.9, 4.7 Hz, 1H), 5.63 (d, *J* = 1.0 Hz, 1H), 4.91 (d, *J* = 3.4 Hz, 1H), 3.82 (d, *J* = 3.1 Hz, 1H), 2.26 – 2.10 (m, 2H), 2.05 (ddd, *J* = 13.2, 4.2, 2.0 Hz, 1H), 1.90 – 1.83 (m, 1H), 1.79 – 1.59 (m, 3H), 1.55 – 1.49 (m, 1H), 1.47 – 1.33 (m, 1H), 1.27 (ddd, *J* = 15.7, 8.0, 3.0 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.7, 155.8, 149.5, 122.0, 117.1, 117.0, 116.9, 116.9, 116.7, 116.5, 91.7, 90.0, 84.4, 42.6, 33.8, 32.0, 30.4, 26.7, 23.5 ppm. **HRMS**: [M-H]$^-$ *calcd*. For $C_{15}H_{15}FNO_4^-$ 292.0991, found 292.0993. **$[\alpha]_D^{20}$** 8.50 (*c* = 1.57 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], λ = 210 nm, t_{major} = 7.73 min, t_{minor} = 7.05 min, **ee** = **92%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



5m

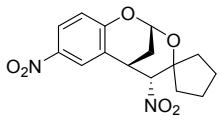
5m was obtained as a white solid 30 mg in 48% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 30/1-15/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 2H), 6.78 (d, *J* = 8.6 Hz, 1H), 5.65 (d, *J* = 1.0 Hz, 1H), 4.92 (d, *J* = 3.4 Hz, 1H), 3.82 (d, *J* = 3.0 Hz, 1H), 2.23 (dt, *J* = 13.3, 2.5 Hz, 1H), 2.20 – 2.13 (m, 1H), 2.05 (ddd, *J* = 13.3, 4.2, 2.0 Hz, 1H), 1.91 – 1.85 (m, 1H), 1.77 –

1.60 (m, 3H), 1.53 (ddd, J = 15.3, 7.3, 3.6 Hz, 1H), 1.45 – 1.38 (m, 1H), 1.31 (ddd, J = 12.1, 8.6, 3.3 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.0, 130.4, 129.8, 125.7, 122.6, 117.4, 91.8, 89.9, 84.4, 42.5, 33.8, 31.9, 30.4, 26.7, 23.5 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{15}ClNO_4^-$ 308.0695, found 308.0690. **$[\alpha]_D^{20}$** 55.19 (c = 1.11 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [n-hexane/i-PrOH = 95/5, 1 mL/min], λ = 210 nm, t_{major} = 9.53 min, t_{minor} = 8.59 min, **ee** = **93%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



5n

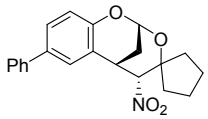
5n was obtained as a white solid 42 mg in 59% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 2H), 6.73 (d, J = 8.6 Hz, 1H), 5.65 (s, 1H), 4.92 (d, J = 3.3 Hz, 1H), 3.82 (d, J = 3.0 Hz, 1H), 2.31 – 2.09 (m, 2H), 2.04 (ddd, J = 13.3, 4.1, 2.0 Hz, 1H), 1.93 – 1.83 (m, 1H), 1.80 – 1.59 (m, 3H), 1.56 – 1.49 (m, 1H), 1.48 – 1.36 (m, 1H), 1.36 – 1.23 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.6, 133.3, 132.7, 123.1, 117.9, 112.9, 91.7, 89.9, 84.4, 42.5, 33.8, 31.8, 30.3, 26.7, 23.5 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{15}BrNO_4^-$ 352.0190, found 352.0194. **$[\alpha]_D^{20}$** 64.83 (c = 1.89 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], λ = 210 nm, t_{major} = 8.77 min, t_{minor} = 7.87 min, **ee** = **93%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



5o

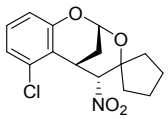
5o was obtained as a white solid 20 mg in 31% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1). **^{1}H NMR** (500

MHz, $CDCl_3$) δ 8.21 (d, J = 2.6 Hz, 1H), 8.17 (dd, J = 9.0, 2.7 Hz, 1H), 6.95 (d, J = 9.0 Hz, 1H), 5.76 (s, 1H), 5.01 (d, J = 3.3 Hz, 1H), 3.93 (d, J = 2.8 Hz, 1H), 2.32 (dt, J = 13.5, 2.3 Hz, 1H), 2.29 – 2.19 (m, 1H), 2.08 (ddd, J = 13.5, 4.0, 1.9 Hz, 1H), 1.98 – 1.89 (m, 1H), 1.71 – 1.61 (m, 3H), 1.56 – 1.50 (m, 1H), 1.46 – 1.34 (m, 1H), 1.28 – 1.22 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.7, 127.5, 125.8, 121.8, 116.8, 110.1, 92.3, 89.6, 84.6, 42.3, 33.7, 31.7, 30.1, 26.6, 23.4 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{15}N_2O_6^-$ 319.0936, found 319.0934. **$[\alpha]_D^{20}$** 105.07 (c = 0.81 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], λ = 210 nm, t_{major} = 21.01 min, t_{minor} = 18.43 min, **ee = 87%**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



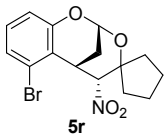
5p

5p was obtained as a white solid 40.6 mg in 58% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 50/1-20/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 – 7.53 (m, 2H), 7.51 (dd, J = 8.4, 2.3 Hz, 1H), 7.47 – 7.38 (m, 3H), 7.35 – 7.28 (m, 1H), 6.92 (d, J = 8.4 Hz, 1H), 5.70 (d, J = 1.1 Hz, 1H), 4.98 (d, J = 3.3 Hz, 1H), 3.92 (d, J = 3.1 Hz, 1H), 2.27 (dt, J = 13.2, 2.5 Hz, 1H), 2.21 – 2.08 (m, 2H), 1.98 – 1.86 (m, 1H), 1.79 (dt, J = 8.0, 6.8 Hz, 1H), 1.76 – 1.61 (m, 2H), 1.54 (ddd, J = 11.7, 7.6, 3.5 Hz, 1H), 1.48 – 1.35 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.8, 140.3, 133.9, 129.2, 128.8, 128.4, 126.9, 126.8, 121.2, 116.3, 91.8, 90.2, 84.3, 42.5, 33.8, 32.2, 30.6, 26.7, 23.4 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{21}H_{20}NO_4^-$ 350.1398, found 350.1395. **$[\alpha]_D^{20}$** 112.91 (c = 1.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 98/2, 1 mL/min], λ = 204 nm, t_{major} = 13.12 min, t_{minor} = 10.33 min, **ee = 87%**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



5q

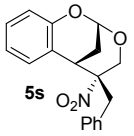
5q was obtained as a white solid 38 mg in 59% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 40/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.20 (t, J = 8.1 Hz, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 5.67 (s, 1H), 5.10 (d, J = 3.1 Hz, 1H), 4.25 (d, J = 2.0 Hz, 1H), 2.28 (d, J = 13.3 Hz, 1H), 1.97 (dd, J = 13.3, 1.6 Hz, 1H), 1.93 – 1.66 (m, 5H), 1.60 (dd, J = 15.5, 6.9 Hz, 1H), 1.53 – 1.44 (m, 1H), 1.34 – 1.26 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.4, 134.9, 129.9, 122.1, 119.6, 115.1, 92.0, 90.0, 83.9, 41.8, 33.7, 30.7, 30.1, 26.9, 23.0 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{15}ClNO_4^-$ 308.0695, found 308.0690. **$[\alpha]_D^{20}$** 106.36 (c = 1.44 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 7.23 min, t_{minor} = 6.24 min, **ee** = **92%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



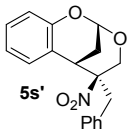
5r

5r was obtained as a white solid 55 mg in 78% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 60/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 (dd, J = 8.0, 1.2 Hz, 1H), 7.13 (t, J = 8.1 Hz, 1H), 6.84 (dd, J = 8.2, 0.8 Hz, 1H), 5.65 (d, J = 1.4 Hz, 1H), 5.09 (d, J = 3.4 Hz, 1H), 4.24 (d, J = 3.1 Hz, 1H), 2.27 (dd, J = 9.2, 6.7 Hz, 1H), 1.97 (ddd, J = 13.3, 3.9, 2.2 Hz, 1H), 1.94 – 1.64 (m, 5H), 1.64 – 1.53 (m, 1H), 1.52 – 1.42 (m, 1H), 1.33 – 1.21 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.5, 130.3, 125.4, 121.2, 115.8, 92.1, 90.1, 83.8, 41.8, 33.6, 32.3, 30.8, 26.9, 23.0 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{15}BrNO_4^-$ 352.0190, found 352.0188. **$[\alpha]_D^{20}$** 118.10 (c = 1.90 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 210 nm, *tmajor*= 8.86 min, *tminor*= 7.29 min, **ee** = **93%**. The

enantiomeric excess after recrystallization was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 210 nm, t_{major} = 7.81 min, t_{minor} = 6.31 min, **ee >99%**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

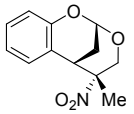


5s was obtained as a white solid 16.3 mg in 26% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 30/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 1H), 7.30 – 7.22 (m, 4H), 7.07 – 6.99 (m, 2H), 6.88 (dd, *J* = 7.4, 1.9 Hz, 2H), 5.62 (d, *J* = 1.6 Hz, 1H), 4.25 (dd, *J* = 13.7, 1.3 Hz, 1H), 3.94 (s, 1H), 3.66 (d, *J* = 13.7 Hz, 1H), 3.29 (d, *J* = 14.3 Hz, 1H), 2.76 (d, *J* = 14.3 Hz, 1H), 2.11 (dt, *J* = 13.9, 2.4 Hz, 1H), 1.95 – 1.87 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.8, 132.4, 130.7, 130.0, 129.3, 128.8, 128.0, 121.0, 120.9, 116.3, 91.8, 91.6, 61.9, 42.7, 37.1, 26.5 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{18}NO_4^+$ 312.1230, found 312.1233. **$[\alpha]_D^{20}$** -44.55 (*c* = 1.24 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 85/15, 1 mL/min], λ = 210 nm, t_{major} = 8.62 min, t_{minor} = 6.88 min, **ee** = **85%**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



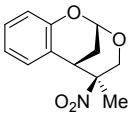
5s′ was obtained as a white solid 11.4 mg in 18% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 60/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (pd, *J* = 4.5, 1.8 Hz, 3H), 7.25 – 7.18 (m, 1H), 7.17 – 7.11 (m, 2H), 6.99 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.89 (ddd, *J* = 11.1, 8.4, 4.5 Hz, 2H), 5.65 (s, 1H), 3.91 – 3.80 (m, 2H), 3.73 (s, 1H), 3.61 (d, *J* = 13.8 Hz, 1H), 3.41 (d, *J* = 13.8 Hz, 1H), 2.61 (dt, *J* = 13.7, 2.6 Hz, 1H), 2.04 (ddd, *J* = 13.8, 3.4, 1.7 Hz, 1H) ppm. **^{13}C NMR**

(101 MHz, $CDCl_3$) δ 154.7, 133.4, 129.9, 129.8, 129.6, 128.9, 128.0, 121.5, 120.9, 115.6, 91.4, 89.7, 58.5, 40.2, 37.6, 27.0 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{18}NO_4^+$ 312.1230, found 312.1228. $\mathbf{[\alpha]_D^{20}}$ 2.90 (c = 0.82 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 85/15, 1 mL/min], λ = 210 nm, t_{major} = 8.30 min, t_{minor} = 7.61 min, **ee** = **82%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



5t

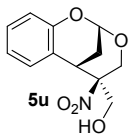
5t was obtained as a white solid 16 mg in 34% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 100/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 1H), 7.13 (dd, J = 7.8, 1.4 Hz, 1H), 6.99 – 6.92 (m, 2H), 5.60 (d, J = 1.7 Hz, 1H), 4.49 (dd, J = 13.7, 1.4 Hz, 1H), 3.80 (s, 1H), 3.51 (d, J = 13.7 Hz, 1H), 2.15 (dt, J = 13.8, 2.4 Hz, 1H), 1.93 – 1.84 (m, 1H), 1.35 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.8, 130.5, 129.7, 121.0, 120.8, 116.1, 91.8, 88.2, 63.4, 36.1, 26.3, 22.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{12}H_{14}NO_4^+$ 236.0917, found 236.0922. $\mathbf{[\alpha]_D^{20}}$ 49.12 (c = 0.13 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 210 nm, t_{major} = 6.82 min, t_{minor} = 6.24 min, **ee** = **98%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



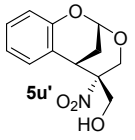
5t'

5t′ was obtained as a white solid 21 mg in 45% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 30/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 1H), 6.91 (dtd, J = 14.9, 7.9, 1.2 Hz, 3H), 5.56 (s, 1H), 4.06 (d, J = 12.1 Hz, 1H), 3.79 (dd, J = 12.1, 0.9 Hz, 1H), 3.59 (s, 1H), 2.39 (dt, J = 13.7, 2.6 Hz, 1H), 1.96 (ddd, J = 13.7, 3.5, 1.8 Hz, 1H), 1.89 (s, 3H) ppm. **^{13}C NMR**

(101 MHz, $CDCl_3$) δ 154.6, 129.8, 129.5, 121.4, 120.8, 115.6, 91.3, 85.8, 62.4, 37.7, 26.5, 23.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{12}H_{14}NO_4^+$ 236.0917, found 236.0920. $\mathbf{[\alpha]_D^{20}}$ -75.44 (c = 0.63 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 210 nm, t_{major} = 7.48 min, t_{minor} = 6.17 min, **ee** = **93%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



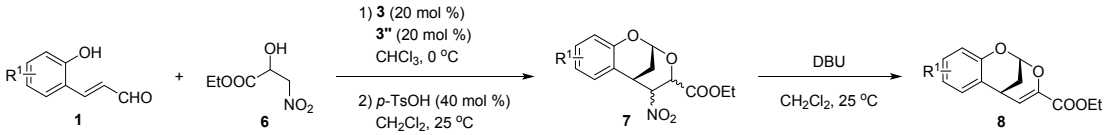
5u was obtained as a white solid 10 mg in 20% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 2H), 7.02 – 6.91 (m, 2H), 5.64 (d, J = 1.7 Hz, 1H), 4.56 (dd, J = 13.7, 1.4 Hz, 1H), 3.99 (s, 1H), 3.74 (dd, J = 11.9, 5.6 Hz, 1H), 3.62 (dd, J = 17.6, 8.8 Hz, 2H), 2.18 (dt, J = 13.9, 2.4 Hz, 1H), 1.99 – 1.84 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.9, 154.7, 130.0, 129.9, 121.2, 116.2, 92.2, 91.9, 65.1, 60.8, 32.2, 25.9 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{12}H_{14}NO_5^+$ 252.0866, found 252.0864. $\mathbf{[\alpha]_D^{20}}$ -2.72 (c = 0.34 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 210 nm, t_{major} = 10.37 min, t_{minor} = 9.23 min, **ee** = **88%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



5u′ was obtained as a white solid 10 mg in 20% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 1H), 6.91 (ddd, J = 21.5, 11.4, 5.7 Hz, 3H), 5.58 (s, 1H), 4.34 – 4.16 (m, 2H), 4.05 (d, J = 12.5 Hz, 1H), 3.90 (d, J = 12.5 Hz, 1H), 3.81 (s, 1H), 2.55 – 2.37 (m, 1H), 2.32 (dt, J = 13.8, 2.5 Hz, 1H), 2.03 – 1.91 (m, 1H) ppm.

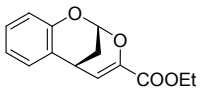
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 130.0, 129.1, 121.5, 120.0, 115.7, 91.2, 89.6, 63.9, 58.3, 33.8, 26.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{12}H_{14}NO_5^+$ 252.0866, found 252.0860. **$[\alpha]_D^{20}$** -53.74 (*c* = 0.19 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 210 nm, t_{major} = 9.50 min, t_{minor} = 8.13 min, **ee** = **90%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.

E. Scope of the reaction 2



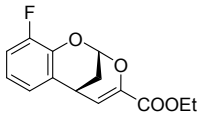
General procedure: A glass vial equipped with a magnetic stirring bar was charged with **6** (0.24 mmol, 1.2 equiv.), different substituted 2-hydroxycinnamaldehydes **1** (0.20 mmol, 1.0 equiv.), **3** (0.04 mmol, 0.2 equiv.) and **3″** (0.04 mmol, 0.2 equiv.) in $CHCl_3$ (0.5 mL) at 0 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of **1** (monitored by TLC analysis). After completion of the reaction, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3/1 to 2/1) to afford the intermediate. Then, the intermediate (1.0 equiv.) was respectively dissolved in anhydrous CH_2Cl_2 (0.10 mmol in 0.5 mL) at 25 °C and *p*-TsOH (0.4 equiv.) was added to the reaction mixture. After full conversion of the second step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 to 8/1) to give product **7**.

At last, compound **7** (1.0 equiv.) was respectively dissolved in CH_2Cl_2 (0.10 mmol in 0.5 mL) at 25 °C and DBU (1.2 equiv.) was added to the reaction mixture. After full conversion of the third step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 to 5/1) to give product **8** for NMR and HPLC analysis.



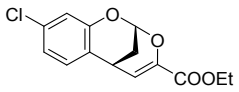
8a

8a was obtained as a white solid 30 mg in 61% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 – 7.03 (m, 2H), 6.99 – 6.84 (m, 2H), 6.41 (dd, J = 7.1, 1.4 Hz, 1H), 6.16 (d, J = 1.9 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.59 – 3.47 (m, 1H), 2.15 – 1.99 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 151.8, 141.8, 128.1, 127.3, 125.5, 121.2, 116.6, 115.0, 92.4, 61.4, 26.5, 24.8, 14.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{14}H_{15}O_4^+$ 247.0965, found 247.0967. **$[\alpha]_D^{20}$** 88.68 (c = 0.57 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], λ = 210 nm, t_{major} = 9.59 min, t_{minor} = 8.72 min, **ee** = **95%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



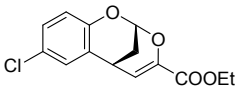
8b

8b was obtained as a white solid 16.8 mg in 32% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.97 – 6.90 (m, 1H), 6.83 (ddd, J = 12.2, 10.4, 5.5 Hz, 2H), 6.41 (dd, J = 7.1, 1.5 Hz, 1H), 6.25 (dd, J = 3.9, 2.0 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.58 (dd, J = 4.3, 2.6 Hz, 1H), 2.13 (ddd, J = 13.2, 3.3, 2.0 Hz, 1H), 2.06 (ddd, J = 13.2, 4.1, 2.3 Hz, 1H), 1.30 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.1, 142.0, 128.2, 122.2, 121.1, 121.0, 115.2, 115.0, 114.4, 92.2, 61.5, 26.1, 24.6, 14.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{14}H_{14}FO_4^+$ 265.0871, found 265.0869. **$[\alpha]_D^{20}$** 45.86 (c = 1.34 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], λ = 210 nm, t_{major} = 9.71 min, t_{minor} = 8.94 min, **ee** = **93%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



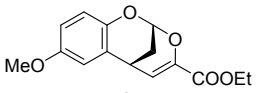
8c

8c was obtained as a white solid 11 mg in 20% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1-5/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.00 (d, J = 8.1 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 6.87 (dd, J = 8.0, 2.0 Hz, 1H), 6.38 (dd, J = 7.1, 1.6 Hz, 1H), 6.15 (q, J = 2.0 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.56 – 3.47 (m, 1H), 2.12 (ddd, J = 13.2, 3.3, 2.0 Hz, 1H), 2.02 (ddd, J = 13.1, 4.1, 2.3 Hz, 1H), 1.30 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.1, 152.5, 141.8, 133.2, 127.9, 124.1, 121.4, 117.0, 114.5, 92.2, 61.5, 26.0, 24.7, 14.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{14}H_{14}ClO_4^+$ 281.0575, found 281.0579. **$[\alpha]_D^{20}$** 56.36 (c = 0.51 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], λ = 204 nm, t_{major} = 7.28 min, t_{minor} = 6.83 min, **ee** = **85%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



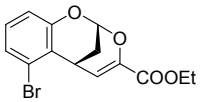
8d

8d was obtained as a colorless oil 12 mg in 21% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 – 7.04 (m, 2H), 6.87 (d, J = 8.3 Hz, 1H), 6.38 (dd, J = 7.1, 1.5 Hz, 1H), 6.15 (dd, J = 3.8, 1.9 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.54 – 3.46 (m, 1H), 2.11 (ddd, J = 13.2, 3.2, 2.0 Hz, 1H), 2.02 (ddd, J = 13.2, 4.1, 2.2 Hz, 1H), 1.30 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.1, 150.5, 142.1, 139.7, 128.0, 127.0, 125.9, 117.9, 114.2, 92.3, 61.5, 26.3, 24.5, 14.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{14}H_{14}ClO_4^+$ 281.0575, found 281.0570. **$[\alpha]_D^{20}$** 164.42 (c = 0.47 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 230 nm, t_{major} = 7.39 min, t_{minor} = 6.54 min, **ee** = **91%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.



8e

8e was obtained as a colorless oil 26.4mg in 48% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.86 (d, J = 8.8 Hz, 1H), 6.69 (dd, J = 8.8, 3.0 Hz, 1H), 6.63 (d, J = 3.0 Hz, 1H), 6.40 (dd, J = 7.1, 1.4 Hz, 1H), 6.13 (q, J = 2.0 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.75 (s, 3H), 3.47 (ddd, J = 7.2, 4.6, 2.7 Hz, 1H), 2.15 – 1.97 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4, 153.8, 145.6, 142.0, 126.1, 117.1, 114.6, 113.4, 112.4, 92.4, 61.4, 55.8, 26.8, 24.8, 14.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{15}H_{17}O_5^+$ 277.1071, found 277.1067. **$[\alpha]_D^{20}$** 136.94 (c = 1.10 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 230 nm, t_{major} = 8.84 min, t_{minor} = 7.74 min, **ee** = **92%**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

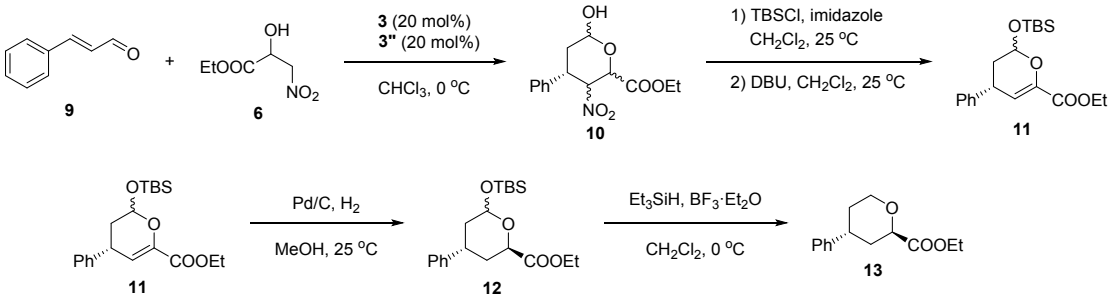


8f

8f was obtained as a colorless oil 28.4 mg in 44% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1-15/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 (dd, J = 7.9, 1.1 Hz, 1H), 6.99 (t, J = 8.1 Hz, 1H), 6.90 (d, J = 8.1 Hz, 1H), 6.47 (dd, J = 7.2, 1.5 Hz, 1H), 6.15 (dd, J = 3.9, 2.0 Hz, 1H), 4.35 – 4.16 (m, 2H), 4.00 (ddd, J = 7.3, 4.6, 2.8 Hz, 1H), 2.12 (ddd, J = 13.2, 3.3, 2.1 Hz, 1H), 2.01 (ddd, J = 13.2, 4.1, 2.3 Hz, 1H), 1.30 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.1, 153.1, 142.6, 128.6, 125.6, 124.9, 122.3, 116.0, 113.1, 92.3, 61.5, 25.9, 24.6, 14.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{14}H_{14}BrO_4^+$ 325.0070, found 325.0071. **$[\alpha]_D^{20}$** 149.82 (c = 1.08 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], λ = 204 nm, t_{major} = 9.35 min, t_{minor} = 8.43 min, **ee** = **90%**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

F. Other reactions

F1. Synthesis of 13

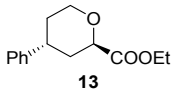


A glass vial equipped with a magnetic stirring bar was charged with ethyl 2-hydroxy-3-nitropropanoate **6** (0.20 mmol, 1.0 equiv.), cinnamaldehyde **9** (0.24 mmol, 1.2 equiv.), **3** (0.04 mmol, 0.2 equiv.) and **3″** (0.04 mmol, 0.2 equiv.) in $CHCl_3$ (1 mL) at 0 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of **6** (monitored by TLC analysis). After completion of the reaction, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3/1 to 1.5/1) to afford **10** as intermediate.

Compound **10** (1.0 equiv.) was dissolved in CH_2Cl_2 (0.10 mmol in 0.5 mL). Imidazole (3.0 equiv.) and TBSCl (2.0 equiv.) were added to the reaction mixture at 0 °C and the reaction was kept at 25 °C until the consumption of **10**. After full conversion of the second step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10/1) to give the intermediate. The intermediate (1.0 equiv) was dissolved in CH_2Cl_2 (0.10 mmol in 0.5 mL) at 25 °C and DBU (1.2 equiv.) was added to the reaction mixture. After full conversion of the third step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 100/1) to give product **11**.

Hydrogenate a solution of **11** (57 mg, 0.16 mmol) in MeOH (2 mL) at atmospheric pressure using 10% Pd/C (6 mg) as the catalyst. And the reaction mixture was stirred at 25 °C. After completion of the reaction, filter the catalyst and the solvent was

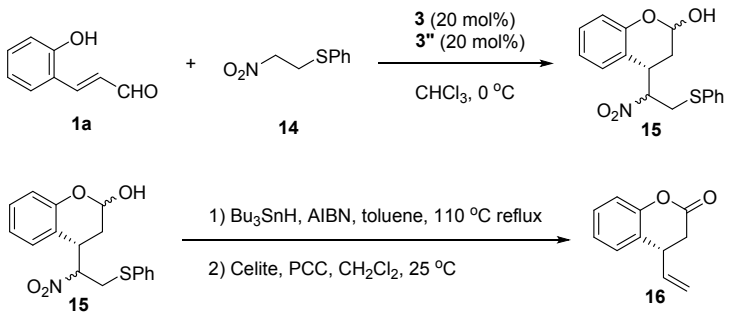
removed under vacuum. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 100/1-60/1) to afford the desired product **12**. To a solution of **12** (0.065 mmol, 1.0 equiv.) and triethylsilane (0.20 mmol, 3.0 equiv.) in anhydrous CH_2Cl_2 (0.5 mL) was added $BF_3 \cdot Et_2O$ (0.1 mmol, 1.5 equiv.) at 0 °C. The reaction was stirred at 0 °C for 1 h. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 10/1) to afford the desired product **13** for NMR and HPLC analysis.



13

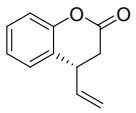
13 was obtained as a colorless oil 12 mg in 26% yield for five steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 2H), 7.23 (dd, J = 10.3, 4.6 Hz, 3H), 4.33 – 4.19 (m, 3H), 4.11 (dd, J = 11.7, 2.3 Hz, 1H), 3.63 (td, J = 11.8, 2.5 Hz, 1H), 2.86 (tt, J = 12.1, 3.8 Hz, 1H), 2.20 (ddt, J = 13.1, 3.8, 2.1 Hz, 1H), 1.88 (dtd, J = 16.4, 12.1, 4.5 Hz, 1H), 1.82 – 1.69 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.3, 144.7, 128.7, 126.7, 126.7, 76.6, 68.3, 61.2, 41.5, 36.3, 32.6, 14.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{14}H_{19}O_3^+$ 235.1329, found 235.1326. **$[\alpha]_D^{20}$** -83.28 (c = 0.42 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 19.83 min, t_{minor} = 17.89 min, **ee** = **95%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.

F2. Synthesis of 16



A glass vial equipped with a magnetic stirring bar was charged with (2-nitroethyl) (phenyl) sulfane **14** (0.24 mmol, 1.2 equiv.), 2-hydroxycinnamaldehyde **1a** (0.20 mmol, 1.0 equiv.), **3** (0.04 mmol, 0.2 equiv.) and **3″** (0.04 mmol, 0.2 equiv.) in $CHCl_3$ (0.5 mL) at 0 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of **1a** (monitored by TLC analysis). After completion of the reaction, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 8/1 to 5/1) to afford **15** as intermediate.

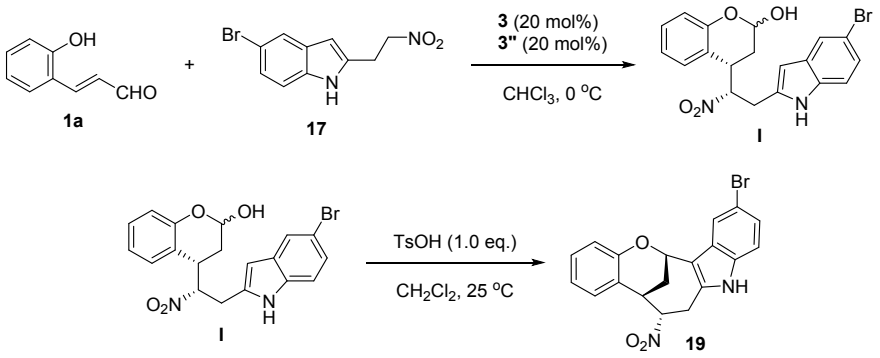
Then, compound **15** (1.0 equiv.) was dissolved in toluene (0.10 mmol in 1.0 mL). AIBN (1.0 equiv.), Bu_3SnH (3.5 equiv.) were added to the reaction mixture and the resulting reaction mixture was kept under vigorous stirring at 110 °C until the consumption of **15** (monitored by TLC analysis).After full conversion of the second step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to get the intermediate. At last, the intermediate (1.0 equiv.) was dissolved in CH_2Cl_2 (0.10 mmol in 0.5 mL) at 25 °C. Celite and PCC (3.0 equiv.) were added to the reaction mixture. After full conversion of the third step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 25/1) to give product **16** for NMR and HPLC analysis.



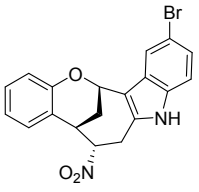
16

16 was obtained as a colorless oil 6.8 mg in 20% yield for three steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 25/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (td, J = 7.8, 1.6 Hz, 1H), 7.21 (d, J = 6.3 Hz, 1H), 7.14 (td, J = 7.5, 1.1 Hz, 1H), 7.08 (d, J = 8.1 Hz, 1H), 5.85 (ddd, J = 17.1, 10.2, 6.9 Hz, 1H), 5.24 (d, J = 10.2 Hz, 1H), 5.11 (d, J = 17.1 Hz, 1H), 3.74 (q, J = 6.6 Hz, 1H), 2.89 (dd, J = 15.8, 5.8 Hz, 1H), 2.78 (dd, J = 15.8, 7.2 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.7, 151.4, 136.8, 128.8, 127.7, 124.6, 124.6, 117.8, 117.1, 38.8, 34.9 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{11}H_{11}O_2^+$ 175.0754, found 175.0757. **$[\alpha]_D^{20}$** -57.42 (c = 0.56 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AD-H column [*n*-hexane/*i*-PrOH = 98/2, 1 mL/min], λ = 204 nm, t_{major} = 10.18 min, t_{minor} = 9.35 min, **ee** = **97%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.

F3. Synthesis of 19



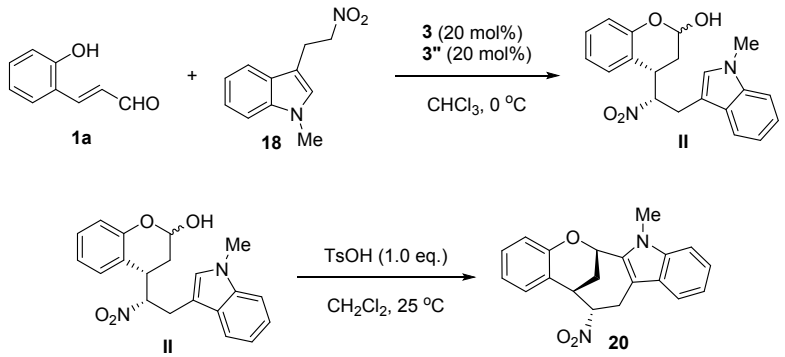
A glass vial equipped with a magnetic stirring bar was charged with 5-bromo-2-(2-nitroethyl)-1H-indole **17** (0.20 mmol, 1.0 equiv.), 2-hydroxycinnamaldehyde **1a** (0.24 mmol, 1.2 equiv.), **3** (0.04 mmol, 0.2 equiv.) and **3″** (0.04 mmol, 0.2 equiv.) in $CHCl_3$ (0.5 mL) at 0 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of **17** (monitored by TLC analysis). After completion of the reaction, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3/1 to 2/1) to afford **I** as intermediate. Then, compound **I** (1.0 equiv.) was dissolved in anhydrous CH_2Cl_2 (0.10 mmol in 0.5 mL) at 25 °C and *p*-TsOH (1.0 equiv.) was added to the reaction mixture. After full conversion of the second step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10/1) to give product **19** for NMR and HPLC analysis.



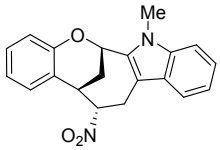
19

19 was obtained as a yellow solid 15.4 mg in 19% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.84 (d, J = 1.4 Hz, 1H), 7.28 (dd, J = 8.6, 1.7 Hz, 1H), 7.15 (dd, J = 12.0, 5.1 Hz, 2H), 6.85 (t, J = 7.4 Hz, 1H), 6.80 (dd, J = 7.7, 1.5 Hz, 1H), 6.76 (d, J = 8.2 Hz, 1H), 5.74 (d, J = 4.8 Hz, 1H), 4.91 – 4.80 (m, 1H), 4.31 (d, J = 6.8 Hz, 1H), 3.36 (dd, J = 15.7, 12.5 Hz, 1H), 3.19 (dd, J = 15.7, 2.6 Hz, 1H), 2.88 (ddd, J = 14.2, 6.8, 5.4 Hz, 1H), 2.38 (d, J = 14.3 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.7, 154.2, 133.2, 130.5, 130.1, 129.6, 129.5, 125.5, 120.6, 120.4, 118.1, 117.0, 113.9, 112.1, 86.8, 65.1, 37.4, 30.9, 28.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{16}BrN_2O_3^+$ 399.0339, found 399.0341. **$[\alpha]_D^{20}$** 159.63 (c = 0.67 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 230 nm, t_{major} = 7.55 min, t_{minor} = 6.43 min, **ee** = **98%**. The diastereomeric ratio was determined by NMR ***dr*** **>20:1**.

F4. Synthesis of 20



A glass vial equipped with a magnetic stirring bar was charged with 5-bromo-2-(2-nitroethyl)-1H-indole **18** (0.20 mmol, 1.0 equiv.), 2-hydroxycinnamaldehyde **1a** (0.24 mmol, 1.2 equiv.), **3** (0.04 mmol, 0.2 equiv.) and **3″** (0.04 mmol, 0.2 equiv.) in $CHCl_3$ (0.5 mL) at 0 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of **18** (monitored by TLC analysis). After completion of the reaction, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5/1 to 3/1) to afford **II** as intermediate. Then, compound **II** (1.0 equiv.) was dissolved in anhydrous CH_2Cl_2 (0.10 mmol in 0.5 mL) at 25 °C and *p*-TsOH (1.0 equiv.) was added to the reaction mixture. After full conversion of the second step, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40/1) to give product **20** for NMR and HPLC analysis.

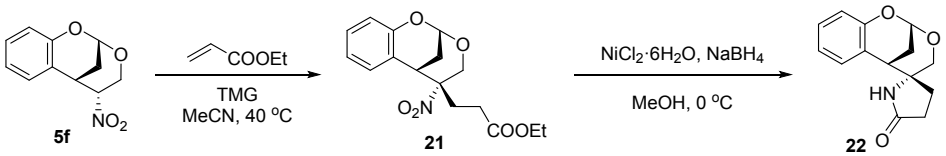


20

20 was obtained as a yellow solid 17.8 mg in 27% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 40/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 1H), 7.29 – 7.21 (m, 3H), 7.14 – 7.04 (m, 2H), 6.90 (dd, J = 10.8, 4.2 Hz, 1H), 6.76 (d, J = 8.2 Hz, 1H), 5.79 (d, J = 3.3 Hz, 1H), 5.14 (ddd, J = 10.6, 5.2, 2.3 Hz, 1H), 3.86 (d, J = 8.6 Hz, 4H), 3.62 (dd, J = 15.2, 10.6 Hz, 1H), 3.52 (dd, J = 15.2, 5.2 Hz, 1H), 2.98 (d, J = 15.2 Hz, 1H), 2.69 (ddd, J = 15.2, 6.7, 4.8 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.8, 137.1, 132.7, 129.4, 128.7, 126.4, 123.4, 122.8, 121.7, 119.5, 118.3, 117.7, 109.3, 107.5, 92.0, 67.5, 35.1, 30.2, 25.5, 25.3 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{20}H_{19}N_2O_3^+$ 335.1390, found 335.1393. **$[\alpha]_D^{20}$** 151.39 (c = 0.83 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 230 nm, t_{major} = 10.39 min, t_{minor} = 9.61 min, **ee** = **98%**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

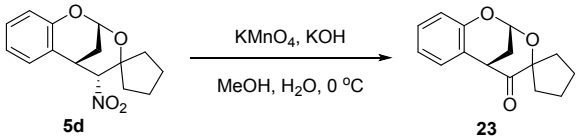
G. Synthetic transformation

(2*R*,2'*S*,6'*S*)-4'*H*,6'*H*-spiro[pyrrolidine-2,5'-[2,6]methanobenzo[*d*][1,3]dioxocin]-5-one (22)



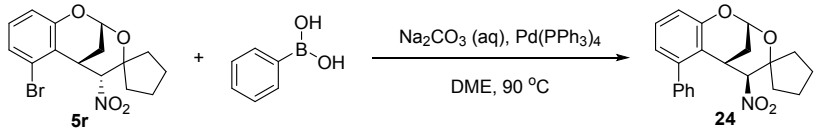
To a solution of **5f** (44 mg, 0.2 mmol) and ethyl acrylate (43 μL, 0.4 mmol) in anhydrous MeCN (1.0 mL) was added tetramethylguanidine (25 μL, 0.2 mmol) at room temperature. The reaction was stirred at 40 °C for 24 h before the solvent was removed under vacuum. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 15/1) to afford the desired product **21** as a colorless oil (52 mg, 81% yield). To a suspension of **21** (52 mg, 0.162 mmol) and $NiCl{\cdot}6H_2O$ (46 mg, 0.19 mmol) in methanol (1.5 mL) was added $NaBH_4$ (92 mg, 2.43 mmol) at 0 °C and the mixture was stirred at 0 °C for 1 h, after which the mixture was quenched with sat. NH_4Cl at 0 °C and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was evaporated. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 2/1 to CH_2Cl_2/MeOH = 20/1) to afford the desired product **22** as a white solid (39.5 mg, 99% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.24 (t, J = 7.7 Hz), 7.05 (d, J = 7.2 Hz), 6.92 (t, J = 7.8 Hz), 5.53 (s), 5.20 (s), 3.42 (d, J = 11.8 Hz), 3.31 (d, J = 11.7 Hz), 2.86 (s), 2.56 – 2.42 (m), 2.28 (d, J = 13.4 Hz), 2.11 – 2.01 (m), 1.92 (d, J = 13.1 Hz) ppm. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.4, 155.0, 129.5, 129.2, 122.3, 121.2, 116.0, 91.7, 64.8, 59.0, 40.0, 30.2, 29.8, 26.3 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{14}H_{16}NO_3^+$ 246.1125, found 246.1121. **$[\alpha]_D^{20}$** -36.86 (c = 1.67 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AD-H column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 210 nm, t_{major} = 9.93 min, t_{minor} = 9.11 min, **ee** = **89%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

(2'*R*,6'*S*)-spiro[cyclopentane-1,4'-[2,6]methanobenzo[*d*][1,3]dioxocin]-5'(6'H)-on (23)



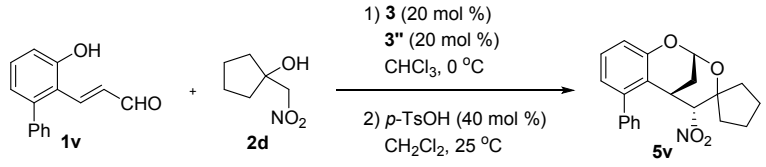
To a suspension of **5d** (34.6 mg, 0.12 mmol) and KOH (8.4 mg, 0.14 mmol) in methanol (0.5 mL) was added $KMnO_4$ (15.8 mg, 0.1 mmol) in H_2O (0.5 mL) at 0 °C. The reaction was stirred at 0 °C for 10 minutes , after which the mixture was quenched with sat. NH_4Cl at 0 °C and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was evaporated. The residue was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 30/1) to afford the desired product **23** as a white solid (20.8 mg, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 1H), 7.19 – 7.12 (m, 1H), 6.92 (t, J = 7.0 Hz, 2H), 5.83 (d, J = 1.5 Hz, 1H), 3.74 (s, 1H), 2.46 (dt, J = 13.6, 2.5 Hz, 1H), 2.33 (ddd, J = 13.6, 3.3, 1.9 Hz, 1H), 2.23 – 2.08 (m, 1H), 1.91 – 1.65 (m, 4H), 1.63 – 1.47 (m, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.1, 152.3, 129.6, 128.9, 121.6, 118.3, 116.9, 91.6, 89.3, 43.5, 41.9, 41.0, 26.5, 25.5, 25.3 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{15}H_{17}O_3^+$ 245.1172, found 245.1178. **$[\alpha]_D^{20}$** -242.99 (c = 0.74 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak Chiral-MJ (2) column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 9.66 min, t_{minor} = 7.66 min, **ee** = **88%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr*** **>20:1**.

(2'*R*,5'*S*,6'*S*)-5'-nitro-7'-phenyl-5',6'-dihydrospiro[cyclopentane-1,4'-[2,6]methanobenzo[*d*][1,3]dioxocine] (24)

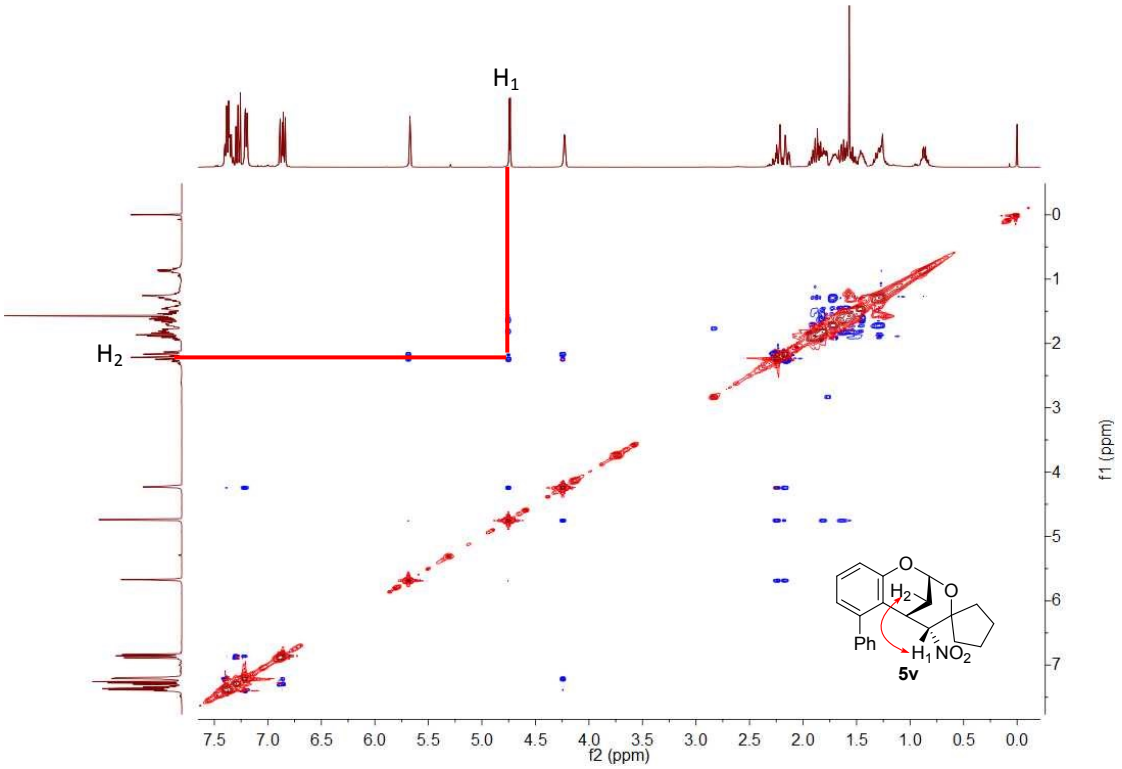


In a glass vial equipped with a magnetic stirring bar, the **5r** (35.4 mg, 0.1 mmol), phenylboronic acid (18.3 mg, 0.15 mmol) and $Pd(PPh_3)_4$ (5.8 mg, 0.005 mmol) in DME (0.5 mL) were added. Aqueous Na_2CO_3 (0.52 mmol, 2 M, 0.26 mL) was added under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 15 min and then at 90 °C for another 12 h. After being cooled to room temperature, the solvent was removed under vacuum and the residue was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was evaporated. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 100/1) to afford the desired product **24** as a white solid (16.7 mg, 48% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 – 7.40 (m, 3H), 7.33 – 7.23 (m, 3H), 6.90 (t, J = 7.3 Hz, 2H), 5.80 (s, 1H), 4.58 (s, 1H), 3.93 (s, 1H), 3.57 (s, 1H), 2.82 (dt, J = 13.6, 2.7 Hz, 1H), 1.94 – 1.84 (m, 2H), 1.82 – 1.66 (m, 3H), 1.59 – 1.44 (m, 3H), 1.17 – 1.04 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.7, 142.4, 139.1, 129.1, 128.7, 128.7, 127.9, 122.6, 120.2, 116.0, 92.3, 90.8, 80.6, 40.6, 39.6, 28.7, 25.0, 22.7, 22.7 ppm. **HRMS**: $[M-H]^-$ *calcd*. For $C_{21}H_{20}NO_4^-$ 350.1398, found 350.1401. **$[\alpha]_D^{20}$** 106.14 (c = 0.83 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 98/2, 1 mL/min], λ = 204 nm, t_{major} = 5.94 min, t_{minor} = 5.34 min, **ee = 92%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* = 12.5:1**.

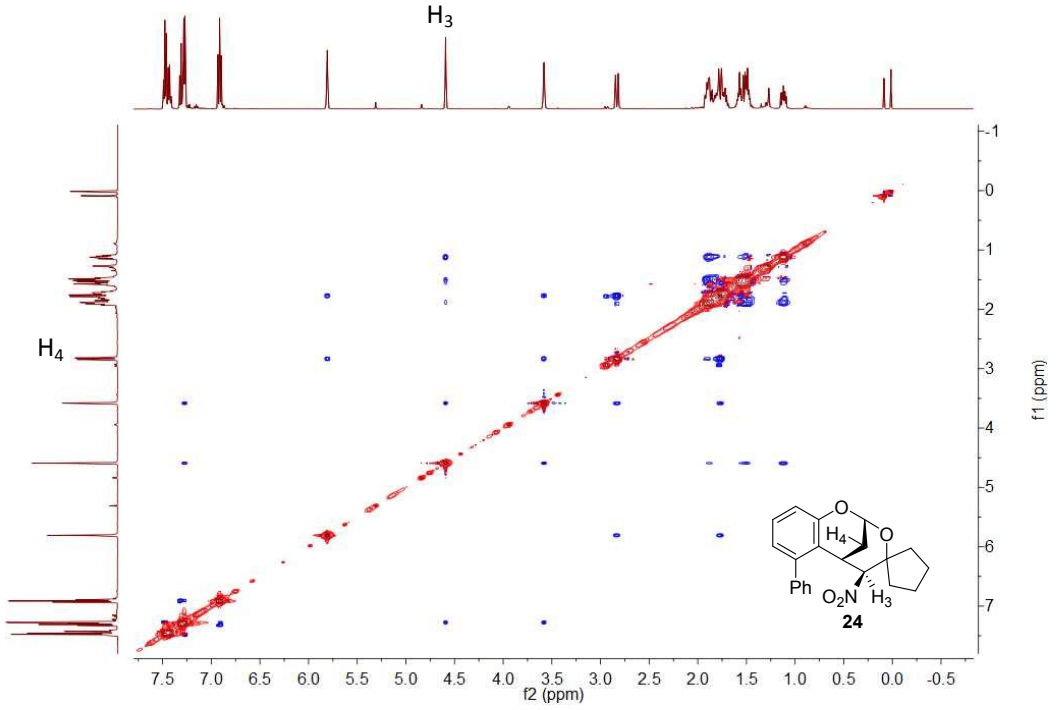
The absolute configuration of the nitro stereocenter in compound **24** was confirmed by the following method. First, following the general procedure, product **5v** was obtained by the reaction of **1v** and **2d**. It was found that compounds **5v** and **24** showed different TLC behaviour, which indicated that these two compounds are diastereoisomers. Then, the relative configuration of **5v** was confirmed by NOESY, which was matched with the configuration of **5k**.



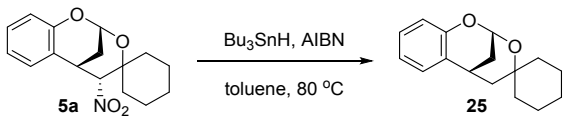
The NOSEY spectrum of 5v (500 MHz, $CDCl_3$)



The NOSEY spectrum of 24 (500 MHz, $CDCl_3$)

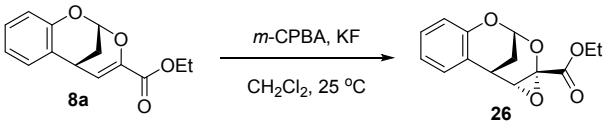


(2'*S*,6'*S*)-5',6'-dihydrospiro[cyclohexane-1,4'-[2,6]methanobenzo[*d*][1,3]dioxocine] (25)



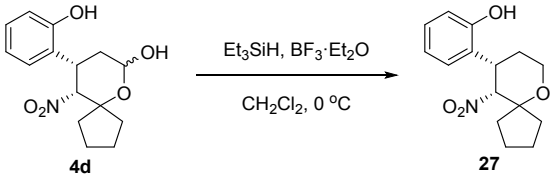
To a solution of **5a** (40 mg, 0.14 mmol) and Tributyltin Hydride (48 μL, 0.18 mmol) in toluene (1 mL) was added AIBN (4.5 mg, 0.028 mmol) at room temperature. The reaction was stirred at 80 °C for 7 hours before the solvent was removed under vacuum. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 100/1-60/1) to afford the desired product **25** as a brown oil (20 mg, 59% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 1H), 7.15 (dd, J = 7.9, 1.4 Hz, 1H), 6.97 – 6.85 (m, 2H), 5.92 (d, J = 1.6 Hz, 1H), 3.69 (s, 1H), 2.41 (dt, J = 13.7, 2.5 Hz, 1H), 2.31 (ddd, J = 13.7, 3.3, 2.0 Hz, 1H), 1.76 (dd, J = 14.3, 3.7 Hz, 1H), 1.70 – 1.60 (m, 4H), 1.58 – 1.51 (m, 1H), 1.46 – 1.32 (m, 2H), 1.31 – 1.04 (m, 3H), 0.92 – 0.79 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.9, 152.3, 129.6, 129.0, 121.5, 118.2, 117.1, 91.4, 81.0, 43.2, 36.9, 35.7, 25.8, 24.8, 20.9, 20.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{16}H_{21}O_2^+$ 245.1536, found 245.1530. **$[\alpha]_D^{20}$** -144.38 (c = 1.48 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IA column [*n*-hexane/*i*-PrOH = 98/2, 1 mL/min], λ = 204 nm, t_{major} = 6.67 min, t_{minor} = 5.77 min, **ee = 85%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

ethyl (1a*R*,3*R*,9*S*,9a*R*)-9,9a-dihydro-1a*H*-3,9-methanobenzo[*d*]oxireno[2,3-*g*][1,3]dioxocine-1a-carboxylate (26)



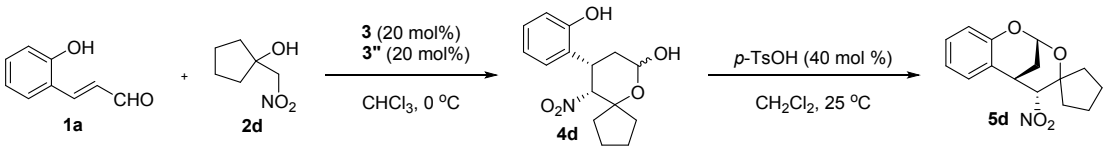
KF (35 mg, 0.6 mmol) was added to a solution of *m*-chloroperoxybenzoic acid (62 mg, 0.30 mmol) in anhydrous CH_2Cl_2 (1.5 ml) and the suspension was maintained at room temperatme with stirring. After 30 min **8a** (30 mg, 0.12 mmol) was added and the mixtme was stirred for 5 days. The insoluble complexes were then filtered off, and the solvent was removed under vacuum. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 10/1) to afford the desired product **26** as a white solid (14 mg, 44% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 (td, J = 8.1, 1.5 Hz, 1H), 7.16 (dd, J = 7.4, 1.3 Hz, 1H), 6.99 – 6.92 (m, 2H), 5.64 (s, 1H), 4.25 – 4.15 (m, 2H), 3.73 (d, J = 1.5 Hz, 1H), 3.52 (d, J = 1.8 Hz, 1H), 2.58 – 2.48 (m, 1H), 1.81 – 1.72 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.6, 152.3, 129.5, 128.3, 121.4, 121.3, 117.0, 91.4, 77.3, 62.7, 61.5, 28.2, 23.4, 14.0 ppm. **HRMS**: $[M+Na]^+$ *calcd*. For $C_{14}H_{14}NaO_5^+$ 285.0733, found 285.0729. **$[\alpha]_D^{20}$** 62.41 (c = 1.08 in $CHCl_3$). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak OD-H column [*n*-hexane/*i*-PrOH = 80/20, 1 mL/min], λ = 210 nm, t_{major} = 10.12 min, t_{minor} = 9.27 min, **ee** = **89%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

2-((9*S*,10*R*)-10-nitro-6-oxaspiro[4.5]decan-9-yl)phenol (27)



To a solution of **4d** (29.3 mg, 0.1 mmol) and triethylsilane (47.8 μL, 0.3 mmol) in anhydrous CH_2Cl_2 (1.0 mL) was added $BF_3{\cdot}Et_2O$ (18.5 μL, 0.15 mmol) at 0 °C. The reaction was stirred at 0 °C for 1 h before the solvent was removed under vacuum. The product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 5/1) to afford the desired product **27** as a white solid (17.5 mg, 63% yield). **^{1}H NMR** (500 MHz, DMSO) δ 9.79 (s, 1H), 7.08 (t, J = 7.7 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.86 – 6.81 (m, 1H), 6.75 (t, J = 7.5 Hz, 1H), 4.97 (d, J = 3.9 Hz, 1H), 3.94 (dd, J = 11.8, 4.6 Hz, 1H), 3.79 (td, J = 12.2, 2.2 Hz, 1H), 3.72 (dt, J = 13.5, 3.9 Hz, 1H), 3.35 (s, 1H), 2.69 (qd, J = 13.0, 5.2 Hz, 1H), 2.32 – 2.22 (m, 1H), 1.81 – 1.71 (m, 1H), 1.70 – 1.57 (m, 4H), 1.54 – 1.46 (m, 1H), 1.41 (d, J = 12.9 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, DMSO) δ 154.8, 128.1, 126.6, 125.0, 119.1, 114.7, 89.8, 83.0, 61.0, 37.2, 33.8, 32.1, 23.8, 22.6, 22.3 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{15}H_{20}NO_4^+$ 278.1387, found 278.1392. **$[\alpha]_D^{20}$** 117.72 (c = 0.58 in MeOH). The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 7.82 min, t_{minor} = 6.93 min, **ee = 97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

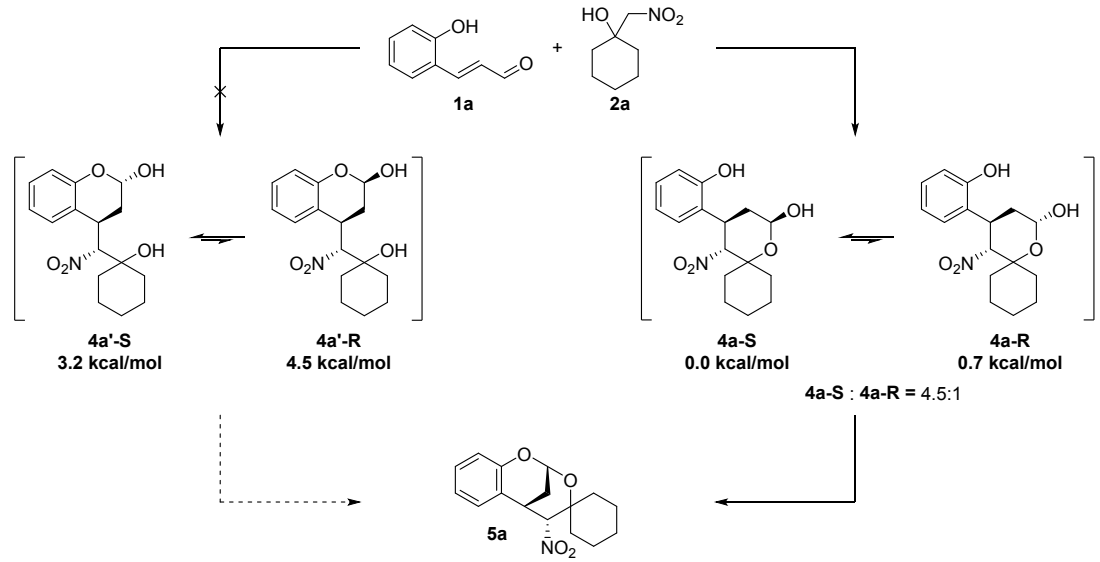
H. Scale-up synthesis of 5d

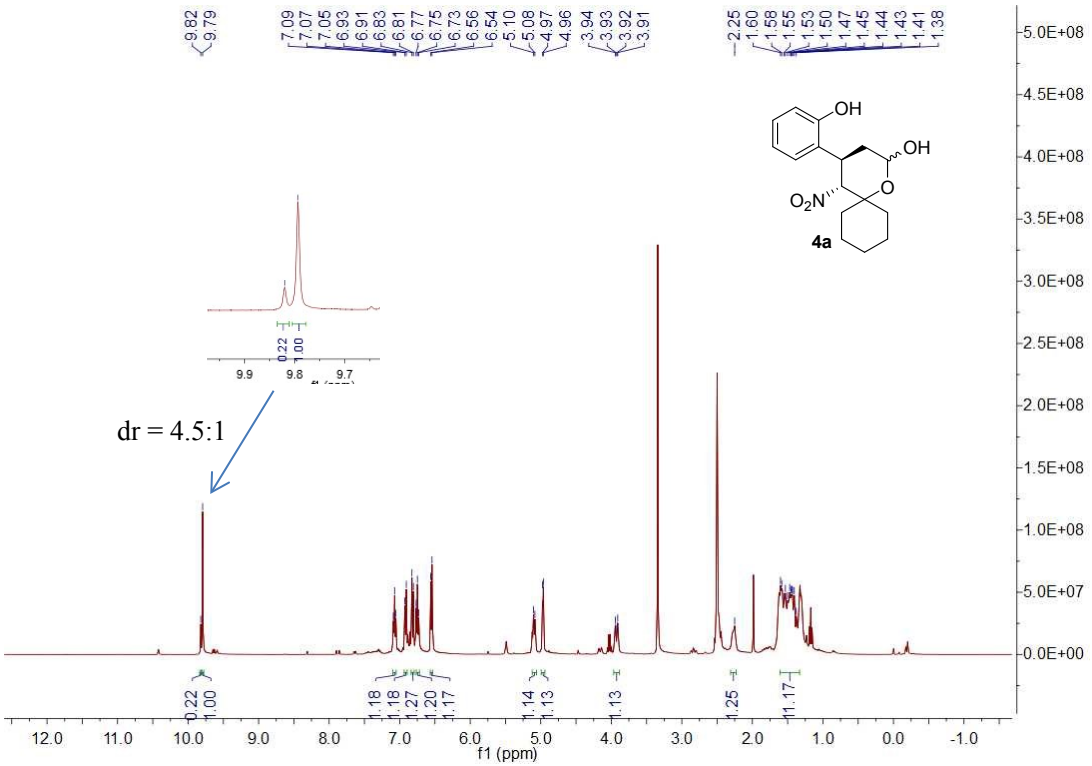


A glass vial equipped with a magnetic stirring bar was charged with 1-nitromethylcycloalcohol **2d** (290.3 mg, 2 mmol, 1.0 equiv.), 2-hydroxycinnamaldehyde **1a** (356 mg, 2.4 mmol, 1.2 equiv.), **3** (130 mg, 0.4 mmol, 0.2 equiv.) and **3''** (263mg, 0.4 mmol, 0.2 equiv.) in $CHCl_3$ (5 mL) at 0 °C. The resulting reaction mixture was kept under vigorous stirring until the consumption of **2d** (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 = 4/1 to 3/1) to afford **4d** as a red solid (586 mg). Then the second step was performed. Compound **4d** (586 mg, 2 mmol, 1.0 equiv.) was dissolved in anhydrous CH_2Cl_2 (10 mL) at 25 °C and *p*-TsOH (0.4 equiv.) was added to the reaction mixture. 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 = 60/1 to 50/1) to give product **5d** (457 mg, 83% yield over two steps, 93% ee, *dr* >20:1).

I. NMR analysis and computational studies for the reaction pathway

NMR analysis





^{1}H NMR (400 MHz, DMSO) δ 9.82 (s, 1H), 9.79 (s, 1H), 7.07 (t, J = 7.4 Hz, 1H), 6.92 (d, J = 7.7 Hz, 1H), 6.82 (d, J = 8.1 Hz, 1H), 6.74 (d, J = 7.4 Hz, 1H), 6.55 (d, J

= 6.7 Hz, 1H), 5.09 (d, *J* = 7.8 Hz, 1H), 4.97 (d, *J* = 4.0 Hz, 1H), 3.93 (dd, *J* = 10.1, 3.7 Hz, 1H), 2.25 (s, 1H), 1.61 – 1.33 (m, 11H) ppm. **MS**: $[M-H]^-$ *calcd*. For $C_{16}H_{20}NO_5^-$ 306.13, found 306.11.

Computational details

In order to investigate the intermediates which formed through catalyzed Michael addition, the energies of different proposed structures were calculated with DFT computations. The DFT calculations were performed with Gaussian 09. Geometry optimizations were carried out at the B3LYP-D3 level of theory with the 6-31G(d) basis set. Vibrational frequencies were computed at the same level to verify that the optimized structures are local minimums and to evaluate zero-point vibrational energies (ZPVE) and thermal corrections at 298 K. Solvent effects in chloroform were evaluated at the more accurate B3LYP-D3/6-311+G(d,p) level with the SMD model.

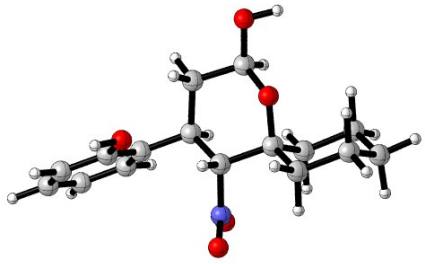


Figure S1. Lowest energy geometry of (2*S*,4*R*,5*R*)-4-(2-hydroxyphenyl)-5-nitro-1-oxaspiro[5.5] undecan-2-ol (**4a-S**)

G (chloroform) = -1053.197097 Hartree

C	3.717989	-0.289194	-1.301038
C	2.224055	-0.625093	-1.185718
C	1.653035	-0.143962	0.167837
C	2.445075	-0.790314	1.317717
C	3.948328	-0.492533	1.211926
C	4.513906	-0.920385	-0.149628
H	2.087842	-1.709676	-1.253150
H	1.666982	-0.201663	-2.027212
H	3.847601	0.800797	-1.280979
H	4.097616	-0.639205	-2.268562

H	2.270471	-1.872237	1.298694
H	2.047734	-0.415600	2.267788
H	4.479026	-1.002562	2.025027
H	4.104154	0.583853	1.350874
H	4.461088	-2.015763	-0.237659
H	5.574290	-0.648703	-0.224364
C	0.120809	-0.398641	0.338916
H	-0.136683	-0.218538	1.380877
C	-0.367265	1.950734	-0.382958
C	-0.752591	0.471603	-0.584950
H	-0.514103	0.191359	-1.615662
C	-2.236756	0.213959	-0.387146
C	-3.005795	-0.283923	-1.443983
C	-2.888668	0.446705	0.838838
C	-4.372660	-0.532030	-1.314051
C	-4.256930	0.201801	0.981412
C	-4.998968	-0.285292	-0.093559
H	-4.938122	-0.920380	-2.155588
H	-4.736415	0.392258	1.940206
H	-6.061642	-0.473931	0.030392
O	-0.368151	-2.246543	-1.038153
O	-0.204951	-2.586164	1.108115
N	-0.186080	-1.861274	0.116257
H	-2.510210	-0.492025	-2.388275
O	-2.134258	0.916078	1.887942
H	-2.695680	0.991448	2.674823
H	-0.638775	2.286474	0.620524
O	1.837703	1.270578	0.352848
C	1.132193	2.137482	-0.537029
H	1.452613	1.923985	-1.571994

H	-0.897681	2.575037	-1.109336
O	1.452982	3.447124	-0.177736
H	2.421306	3.519904	-0.193861

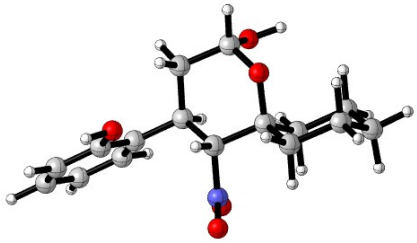


Figure S2. Lowest energy geometry of (2*R*,4*R*,5*R*)-4-(2-hydroxyphenyl)-5-nitro-1-oxaspiro[5.5]undecan-2-ol (**4a-R**)

G (chloroform) = - 1053.196027 Hartree

C	-3.750115	0.133736	1.191867
C	-2.248523	-0.189833	1.185090
C	-1.661712	-0.109200	-0.242456
C	-2.443527	-1.053495	-1.174710
C	-3.950245	-0.754227	-1.166053
C	-4.525666	-0.803490	0.256008
H	-2.107519	-1.210455	1.558039
H	-1.707308	0.475631	1.859186
H	-3.904820	1.171452	0.867121
H	-4.133296	0.060296	2.216811
H	-2.263134	-2.086001	-0.854609
H	-2.040424	-0.954772	-2.189117
H	-4.467356	-1.471992	-1.814544
H	-4.115104	0.242459	-1.592535
H	-4.457820	-1.831432	0.642178
H	-5.590697	-0.539675	0.245776
C	-0.133326	-0.421938	-0.312999
H	0.132368	-0.595144	-1.354567
C	0.418100	1.999107	-0.450694

H	0.968488	2.828710	0.003044
C	0.750766	0.686804	0.284529
H	0.471270	0.808519	1.333225
C	2.229992	0.344452	0.243442
C	2.922031	0.099443	-0.957244
C	2.955099	0.253629	1.436229
C	4.284075	-0.212508	-0.951081
C	4.315507	-0.054817	1.455863
H	2.428294	0.418190	2.372002
C	4.981151	-0.288984	0.253742
H	4.794352	-0.396730	-1.895166
H	4.845496	-0.119275	2.401265
H	6.039303	-0.534985	0.246463
O	0.135450	-2.749997	-0.331695
O	0.354338	-1.733217	1.582888
N	0.150570	-1.741136	0.370525
O	2.213931	0.175740	-2.135093
H	2.794410	-0.076068	-2.869731
C	-1.073341	2.293214	-0.384337
H	-1.343457	3.091616	-1.089208
H	0.713750	1.925453	-1.500070
O	-1.857841	1.199459	-0.829311
O	-1.371050	2.686778	0.941461
H	-2.331008	2.820687	0.991598

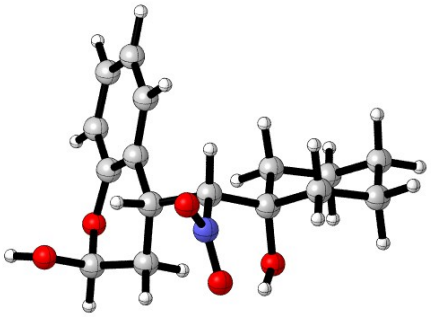


Figure S3. Lowest energy geometry of (2*S*,4*R*)-4-((*R*)-(1-hydroxycyclohexyl)(nitro) methyl)chroman-2-ol (**4a′-S**)

G (chloroform) = -1053.19198 Hartree

C	2.242033	-2.320264	1.810192
C	1.462917	-1.177001	1.649400
C	1.604744	-0.330322	0.541272
C	2.619264	-0.641226	-0.380979
C	3.400680	-1.791794	-0.236392
C	3.206092	-2.637142	0.850017
H	2.096748	-2.957367	2.677517
H	0.722407	-0.943850	2.409089
H	4.159884	-1.991354	-0.986152
H	3.816164	-3.529842	0.955645
O	2.912470	0.140413	-1.474307
C	0.760240	0.926907	0.346174
H	1.158495	1.674927	1.045193
C	0.937199	1.487335	-1.075868
H	0.392997	0.881958	-1.801330
H	0.549390	2.507452	-1.134989
C	2.405181	1.476025	-1.451660
C	-0.728588	0.733762	0.759585
H	-0.756211	0.261460	1.740080
C	-1.732581	-0.025859	-0.164468
C	-3.117440	-0.074474	0.534488

C	-1.232790	-1.460956	-0.419373
C	-4.132499	-0.888694	-0.278764
H	-2.999788	-0.520829	1.532309
H	-3.490870	0.946387	0.680864
C	-2.251520	-2.276984	-1.228977
H	-0.276452	-1.421554	-0.947793
H	-1.042908	-1.951256	0.543470
C	-3.621806	-2.311589	-0.540228
H	-5.092339	-0.911686	0.251499
H	-4.302222	-0.380886	-1.235755
H	-1.864855	-3.293627	-1.370552
H	-2.352707	-1.827735	-2.223785
H	-3.536022	-2.848918	0.416719
H	-4.342442	-2.869119	-1.151253
O	-1.859116	0.576197	-1.450182
H	-2.036595	1.521957	-1.296339
O	-1.162433	2.522465	2.225661
O	-1.695458	2.817122	0.139238
N	-1.249984	2.132735	1.070486
H	2.561766	1.823681	-2.480197
O	3.105478	2.266596	-0.524489
H	4.051142	2.192370	-0.731524

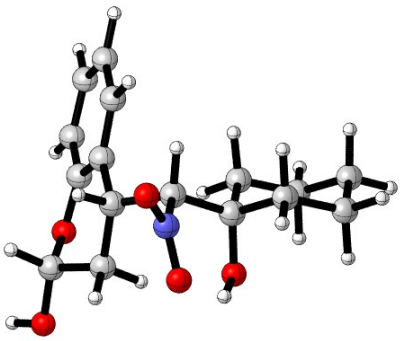


Figure S4. Lowest energy geometry of (2*R*,4*R*)-4-((*R*)-(1-hydroxycyclohexyl)(nitro) methyl)chroman-2-ol (**4a′-R**)

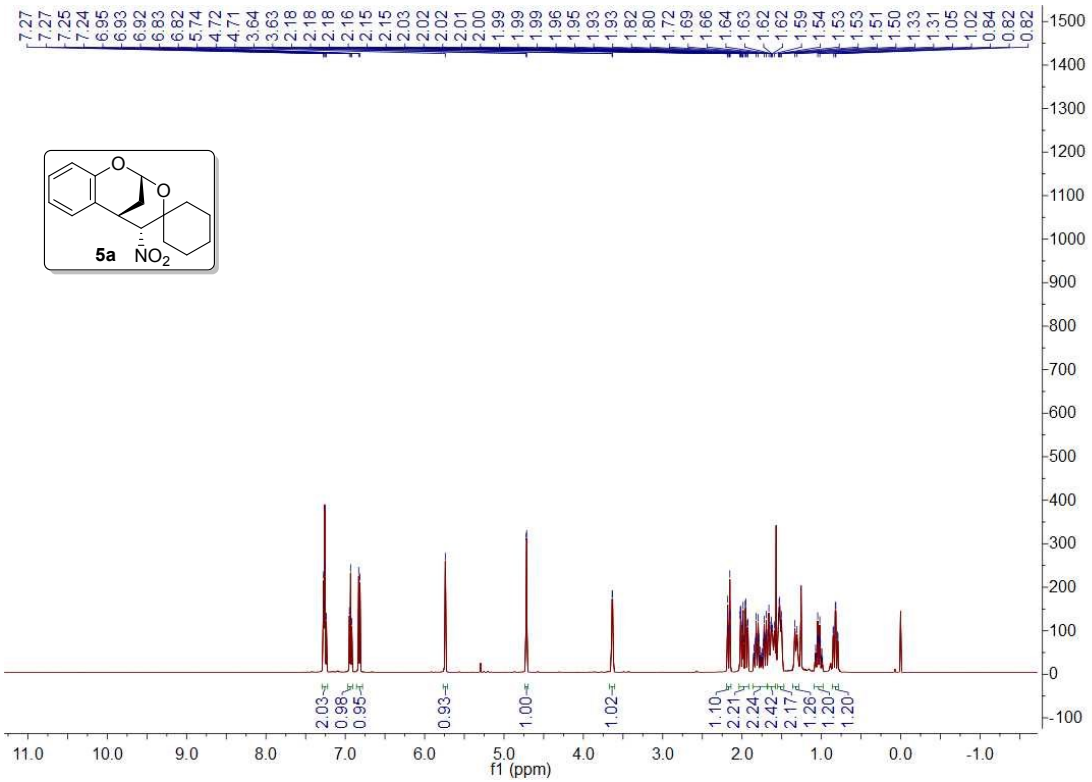
G (chloroform) = -1053.189983 Hartree

C	2.216876	2.462476	-1.781613
C	1.446786	1.302913	-1.750601
C	1.596036	0.342143	-0.740425
C	2.608526	0.553582	0.212786
C	3.380703	1.720898	0.197634
C	3.176260	2.679236	-0.788016
H	2.069163	3.190940	-2.573263
H	0.707229	1.146596	-2.531716
H	4.138307	1.843200	0.965217
H	3.777782	3.583909	-0.793327
O	2.893372	-0.352271	1.198805
C	0.729372	-0.914822	-0.676588
H	1.022534	-1.538039	-1.534602
C	0.993554	-1.719000	0.610132
H	0.471607	-1.279468	1.460803
H	0.645965	-2.749632	0.500243
C	2.471556	-1.703496	0.930387
H	3.077557	-2.065132	0.079384
C	-0.782156	-0.613772	-0.921172
H	-0.868051	-0.006807	-1.821228
C	-1.669640	0.045759	0.182666

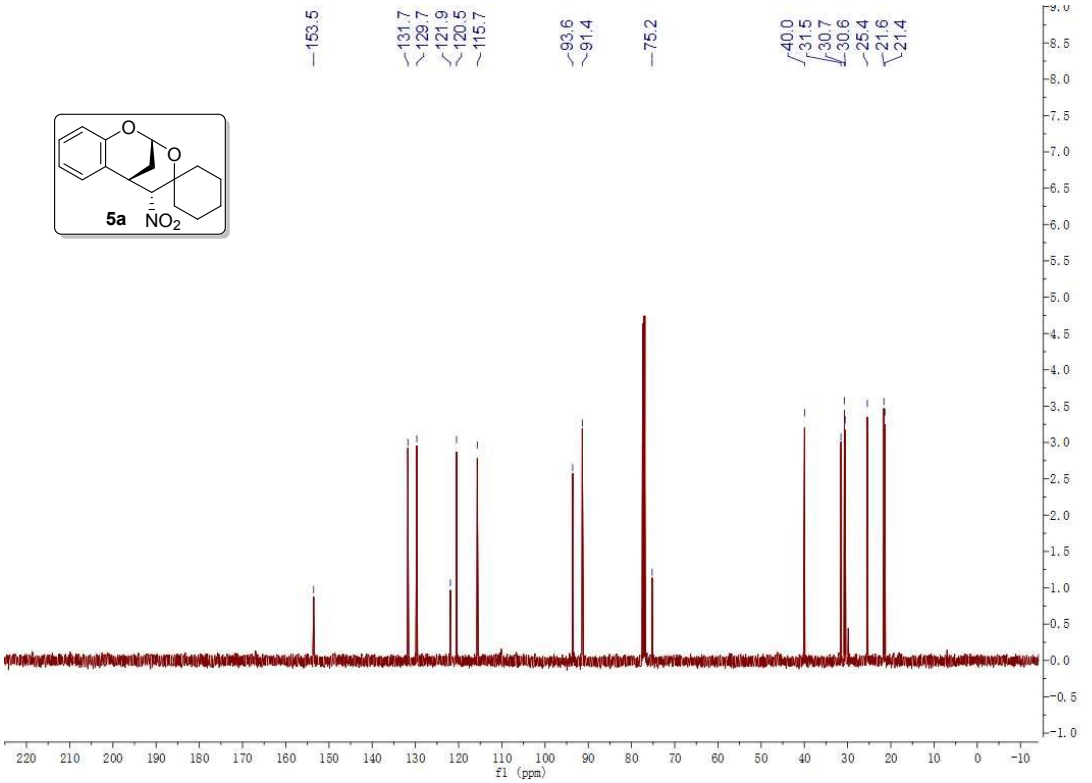
C	-3.103931	0.234366	-0.381681
C	-1.085767	1.415424	0.579776
C	-4.010862	0.968171	0.614814
H	-3.048523	0.804307	-1.320328
H	-3.534106	-0.744648	-0.624633
C	-1.999634	2.155081	1.568397
H	-0.097217	1.269228	1.022303
H	-0.944848	2.020922	-0.324322
C	-3.417372	2.326698	1.008754
H	-5.009568	1.091465	0.178510
H	-4.121835	0.345728	1.510780
H	-1.556427	3.130490	1.803333
H	-2.040780	1.584854	2.503647
H	-3.384061	2.979710	0.123175
H	-4.060785	2.825199	1.744264
O	-1.717420	-0.718634	1.383547
H	-1.965198	-1.625348	1.127334
O	2.692757	-2.449456	2.078866
H	3.634962	-2.377618	2.302739
O	-1.370114	-2.182856	-2.571443
O	-1.813073	-2.719828	-0.512315
N	-1.385674	-1.939919	-1.372784

J. NMR spectra and HPLC analyses

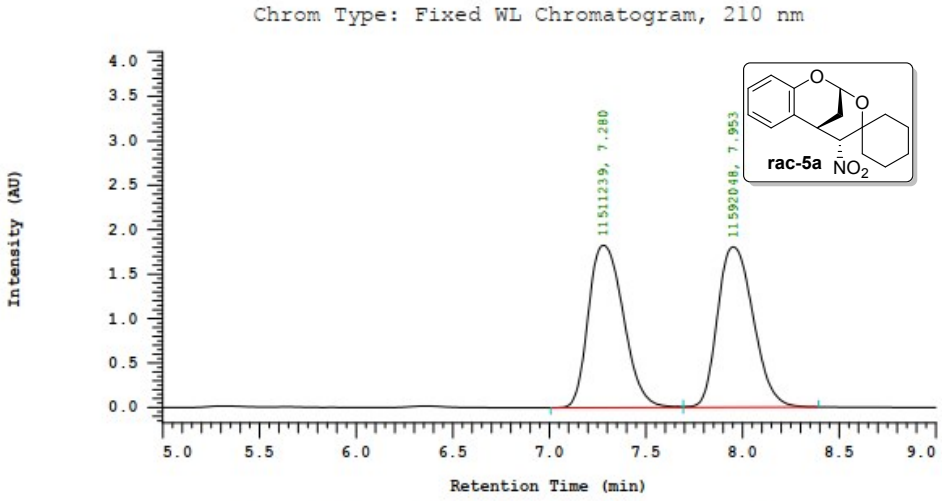
The ^{1}H NMR spectrum of 5a (500 MHz, $CDCl_3$)



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



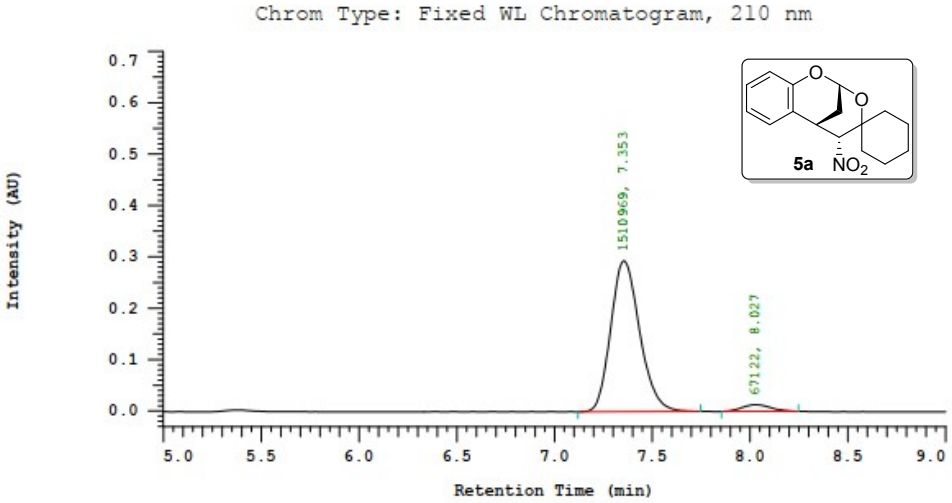
The HPLC of racemic 5a



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.280	11511239	49.825	BV
2	7.953	11592048	50.175	VB
		23103287	100.000	

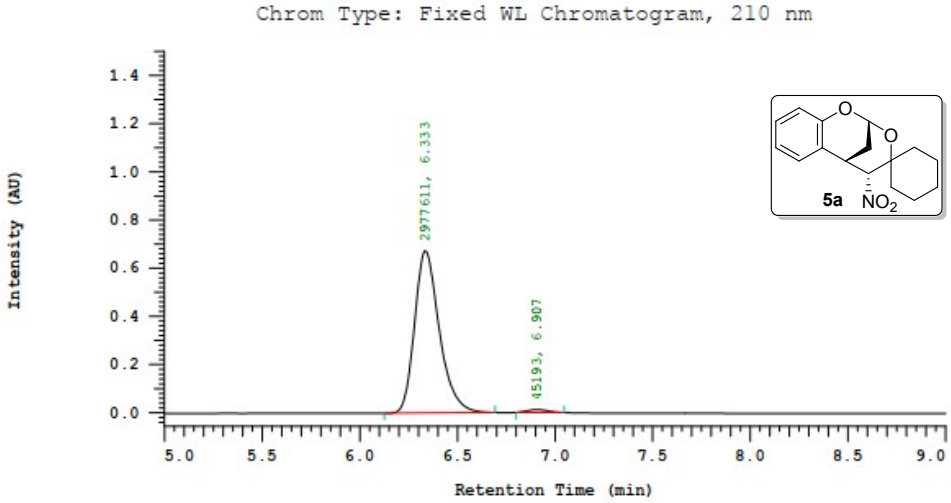
The HPLC of chiral 5a



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.353	1510969	95.747	BB
2	8.027	67122	4.253	BB
		1578091	100.000	

The HPLC of chiral 5a after recrystallization



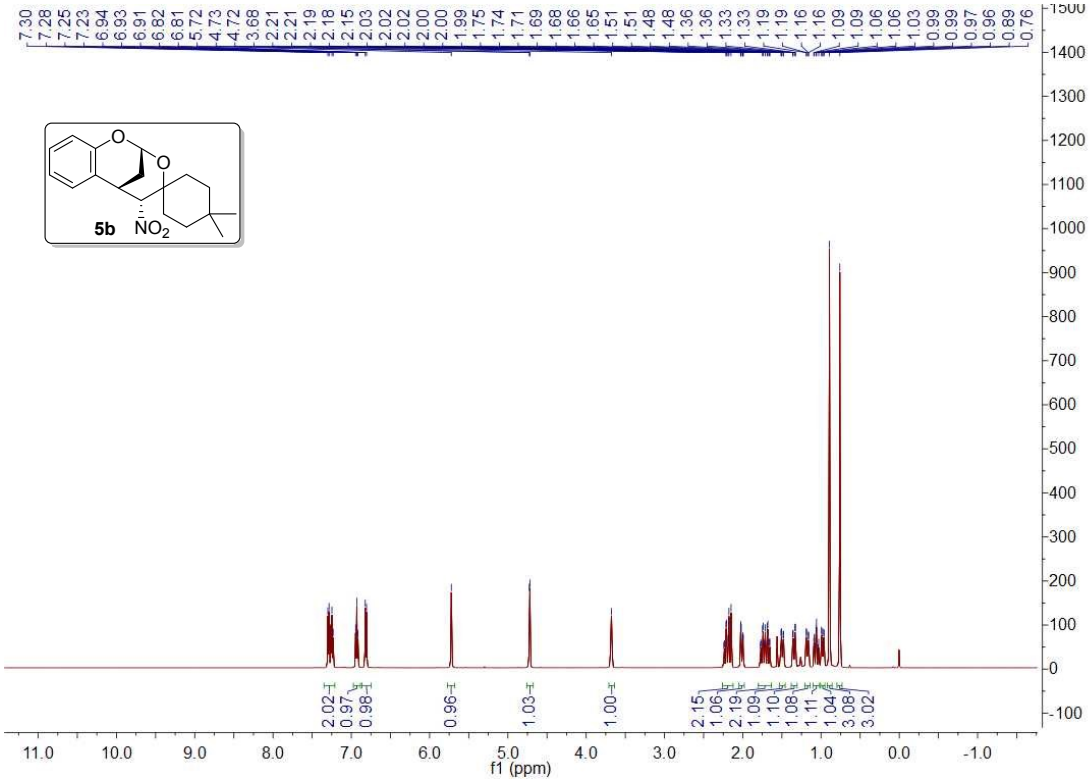
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

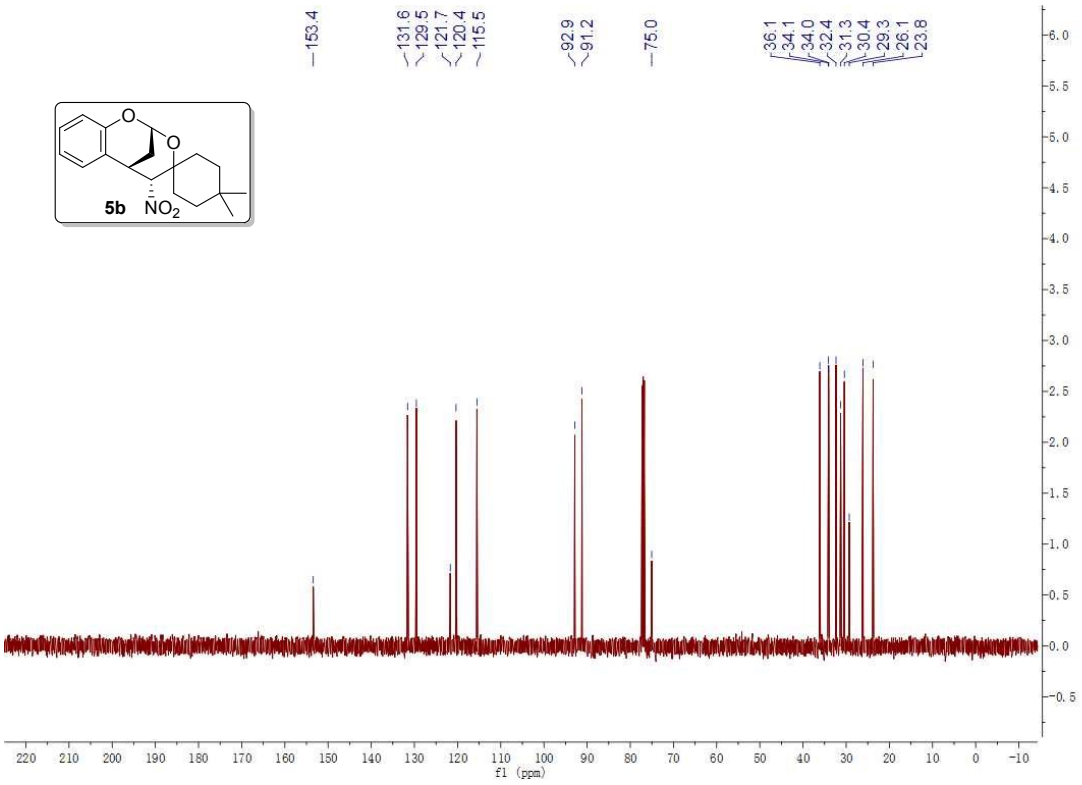
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.333	2977611	98.505	BB
2	6.907	45193	1.495	BB
		3022804	100.000	

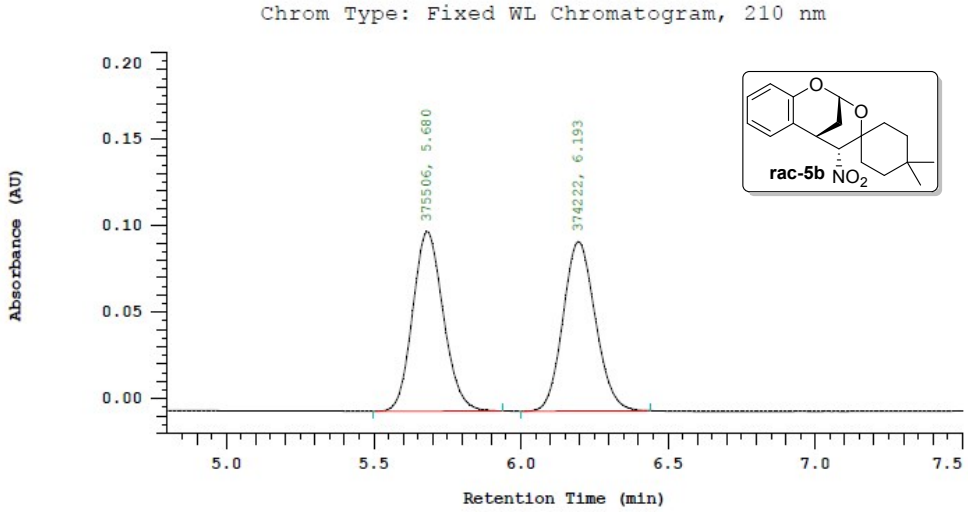
The ^{1}H NMR spectrum of 5b (500 MHz, $CDCl_3$)



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



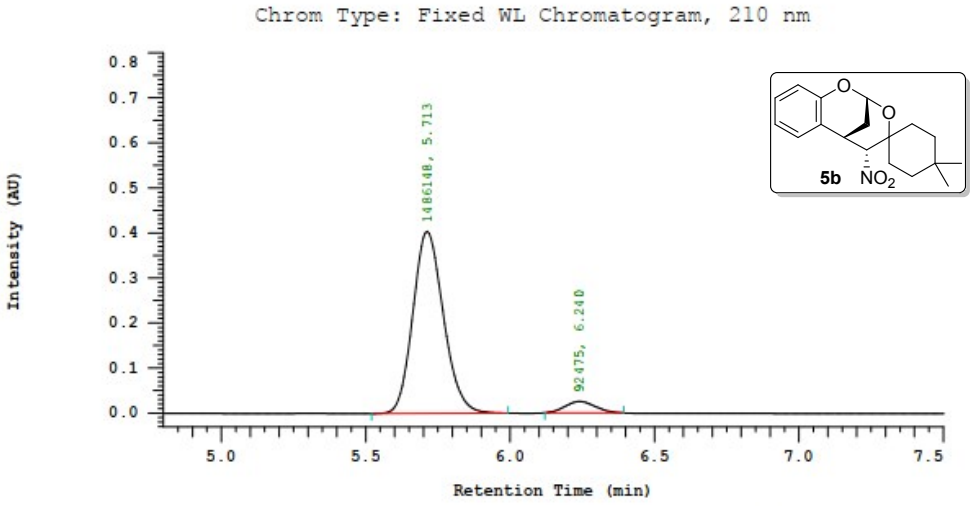
The HPLC of racemic 5b



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.680	375506	50.086	BB
2	6.193	374222	49.914	BB
		749728	100.000	

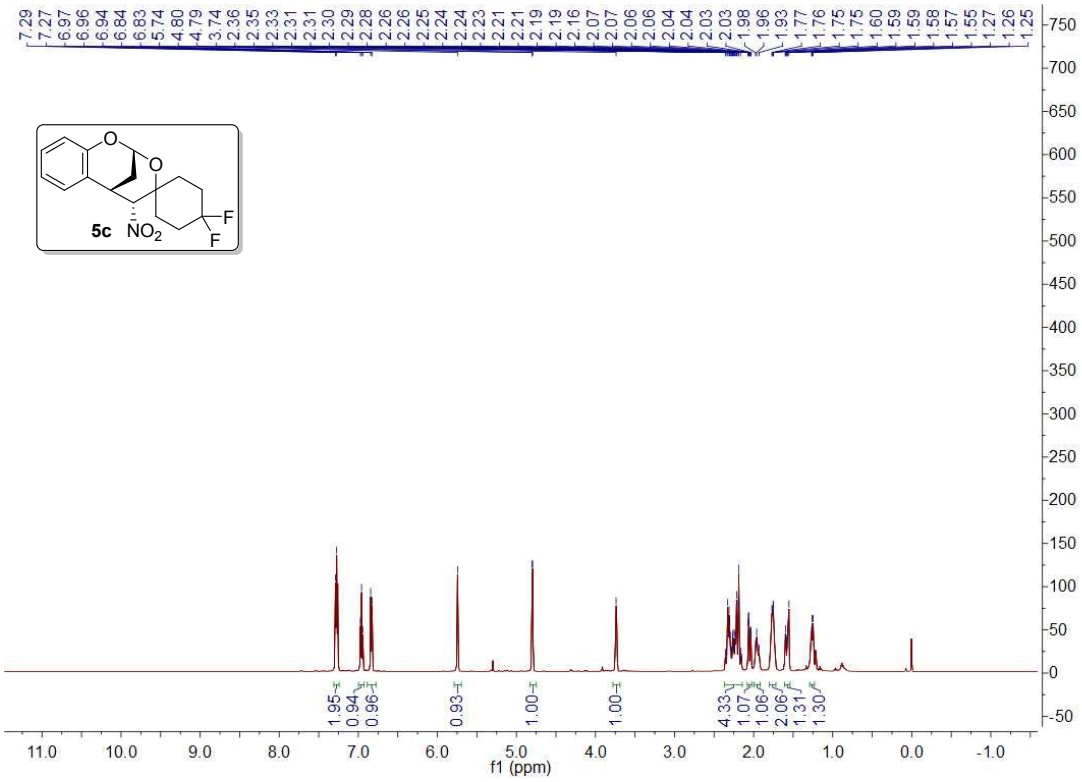
The HPLC of chiral 5b



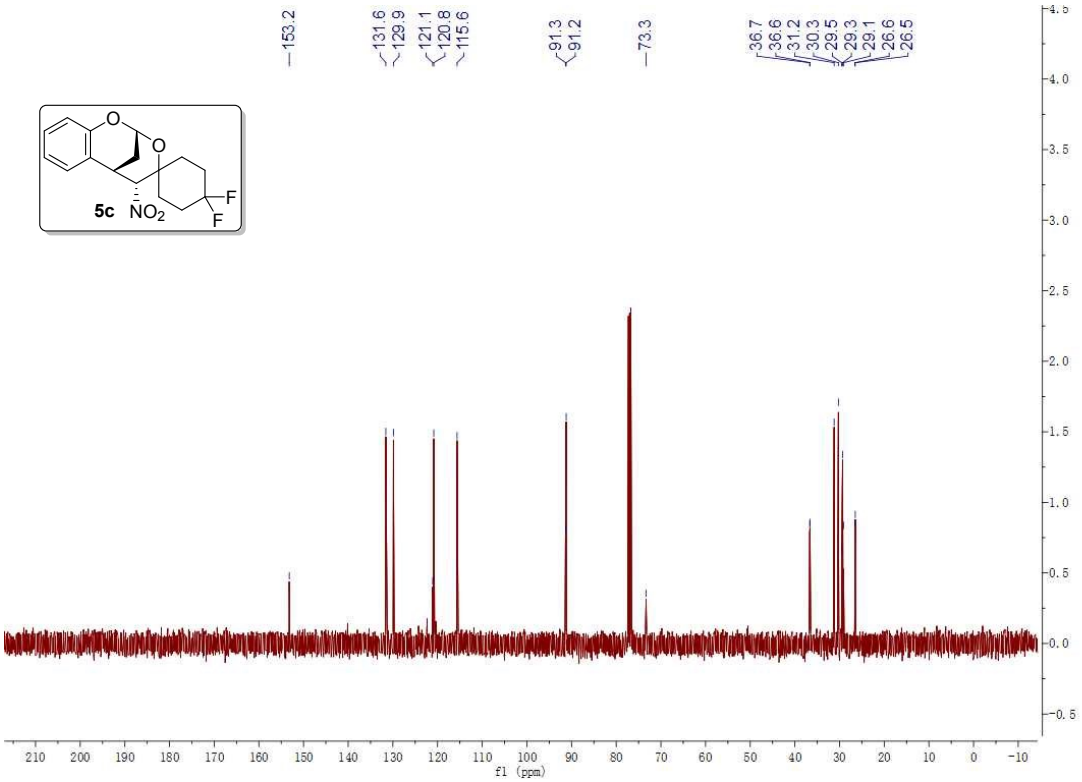
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.713	1486148	94.142	BB
2	6.240	92475	5.858	BB
		1578623	100.000	

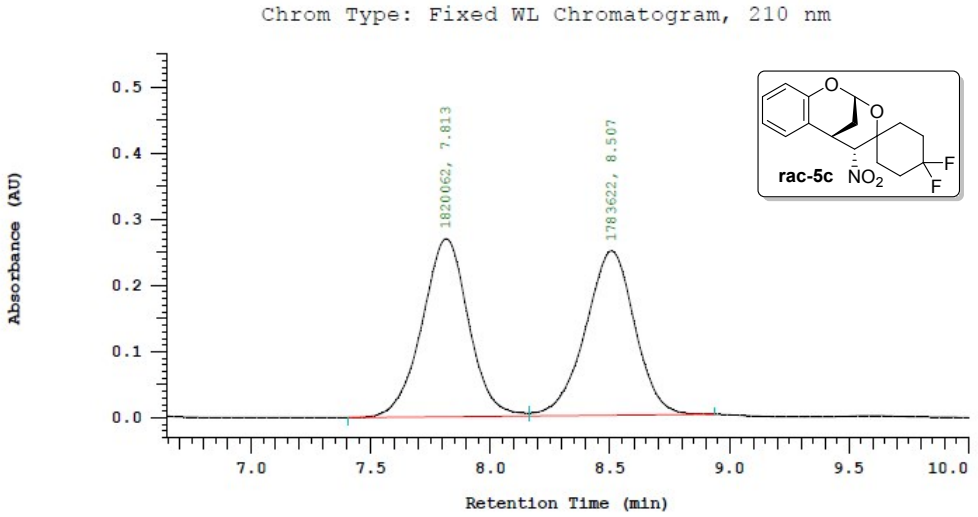
The ^{1}H NMR spectrum of 5c (500 MHz, $CDCl_3$)



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



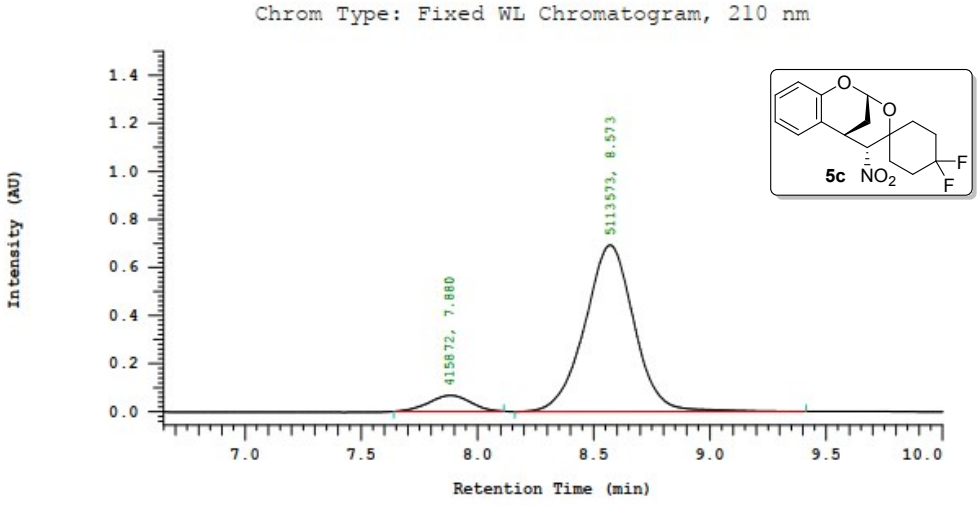
The HPLC of racemic 5c



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.813	1820062	50.506	BV
2	8.507	1783622	49.494	VB
		3603684	100.000	

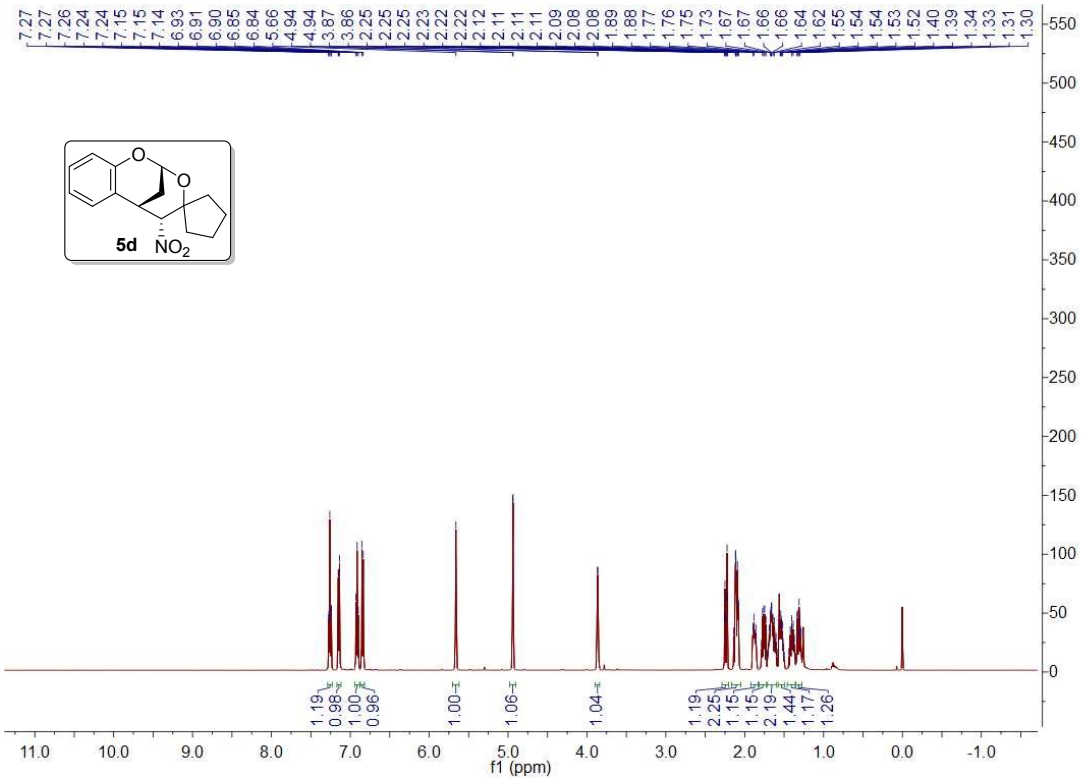
The HPLC of chiral 5c



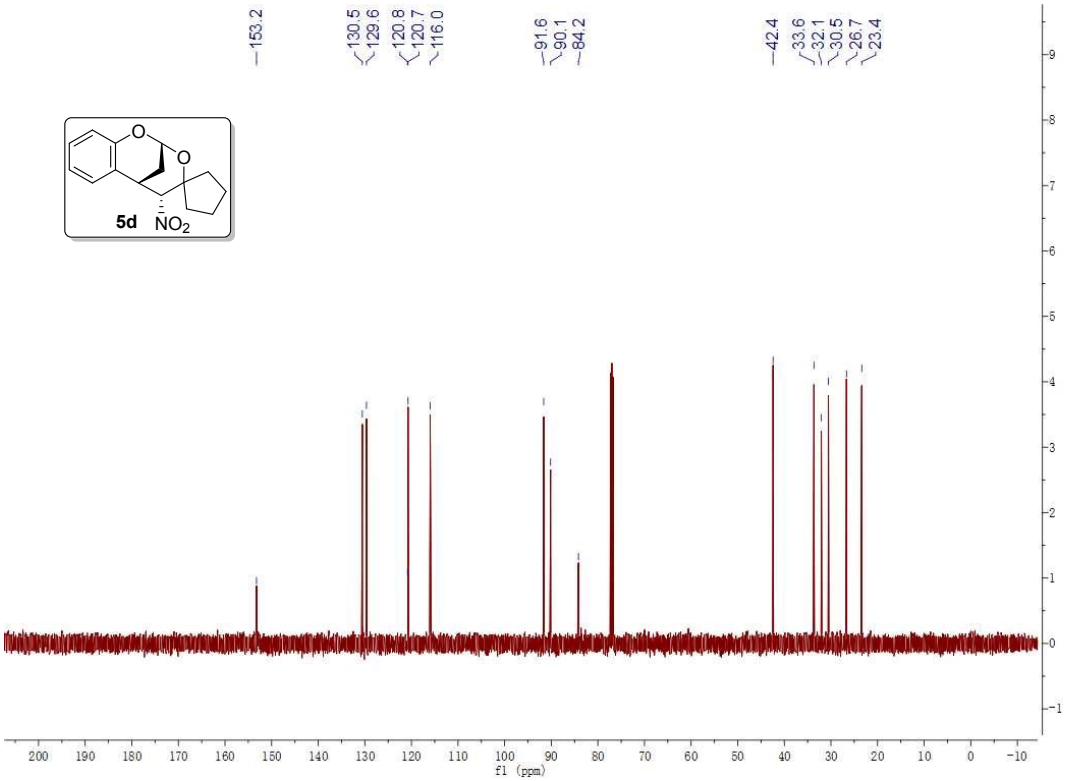
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.880	415872	7.521	BB
2	8.573	5113573	92.479	BB
		5529445	100.000	

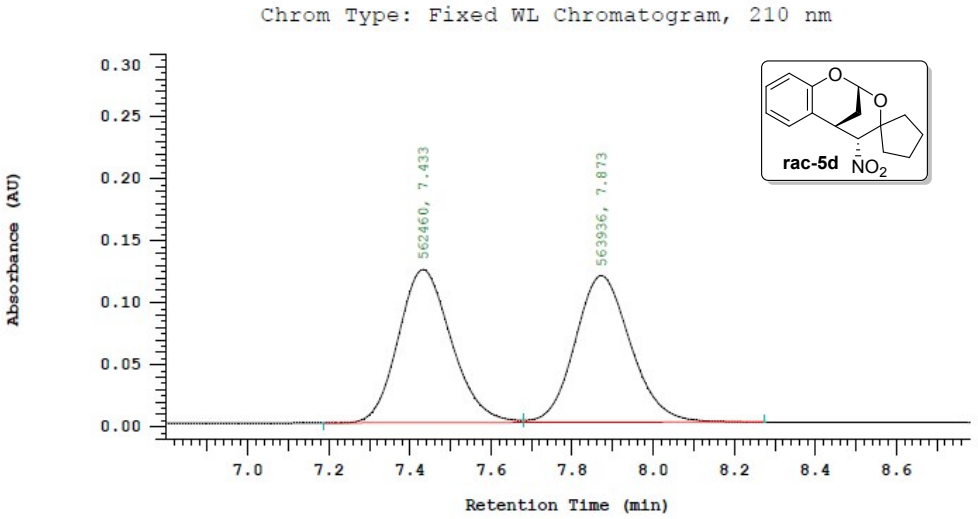
The ^{1}H NMR spectrum of 5d (500 MHz, $CDCl_3$)



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



The HPLC of racemic 5d



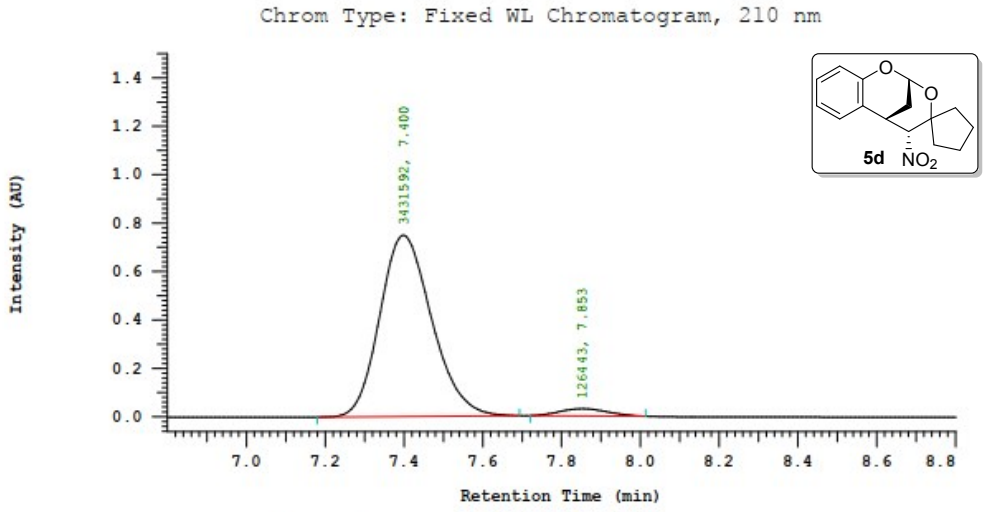
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.433	562460	49.934	BV
2	7.873	563936	50.066	VB
		1126396	100.000	

The HPLC of chiral 5d



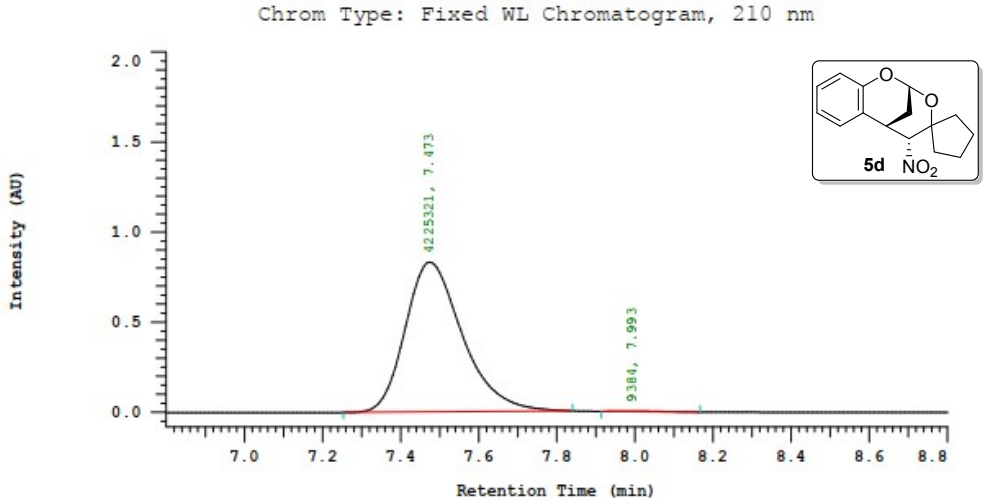
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.400	3431592	96.446	BB
2	7.853	126443	3.554	BB
		3558035	100.000	

The HPLC of chiral 5d after recrystallization



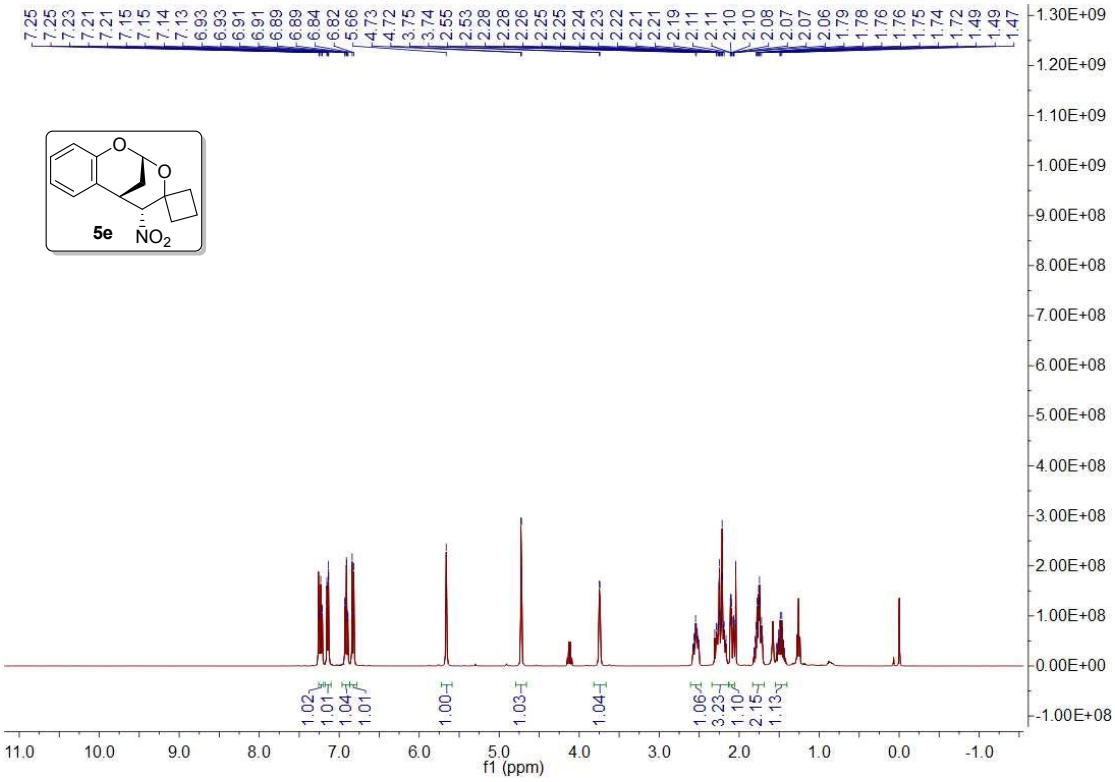
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

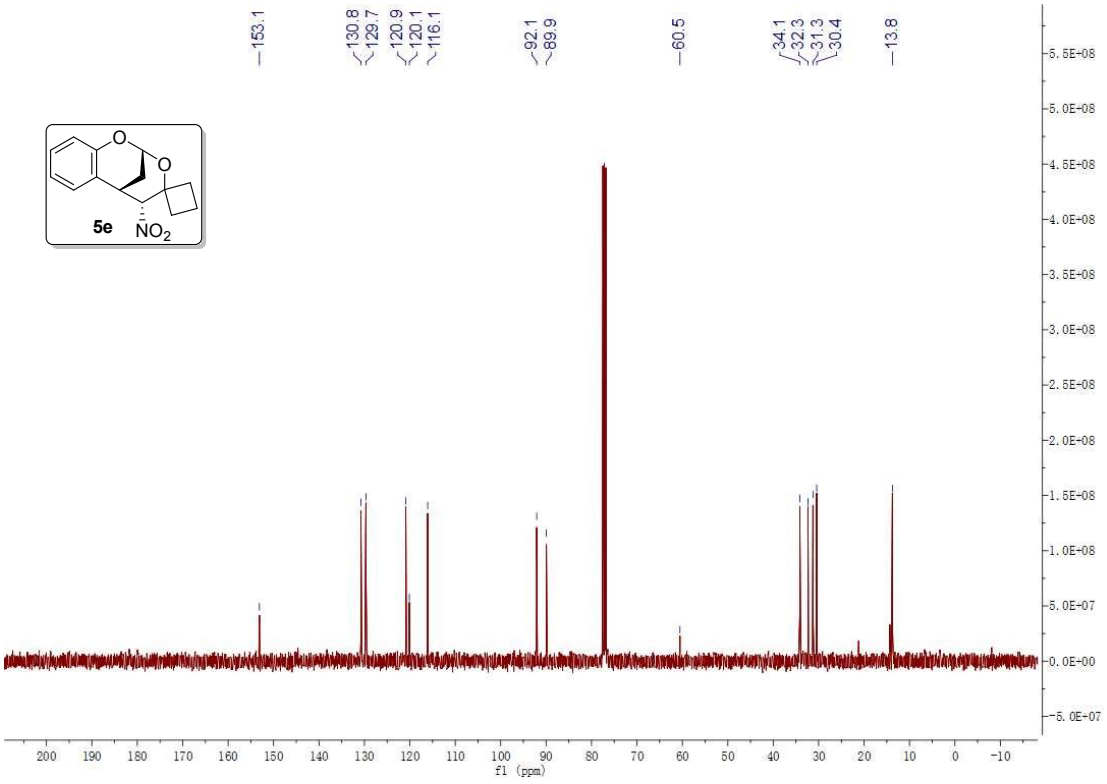
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.473	4225321	99.778	BB
2	7.993	9384	0.222	BB
		4234705	100.000	

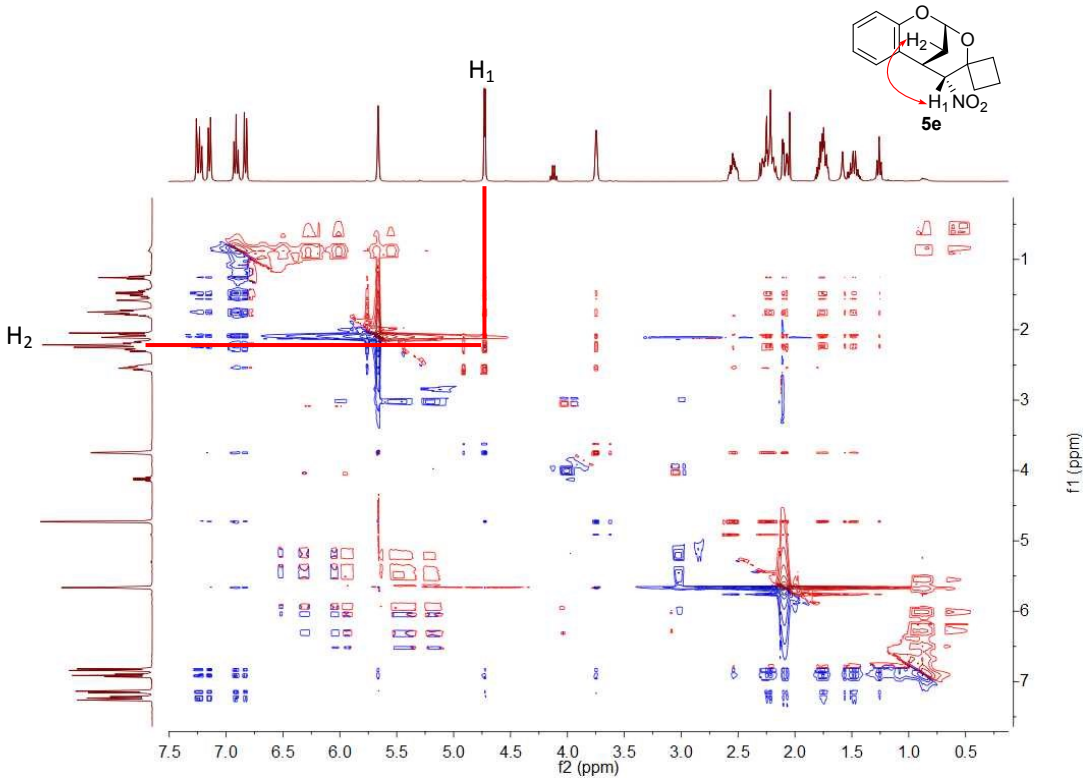
The ^{1}H NMR spectrum of 5e (400 MHz, $CDCl_3$)



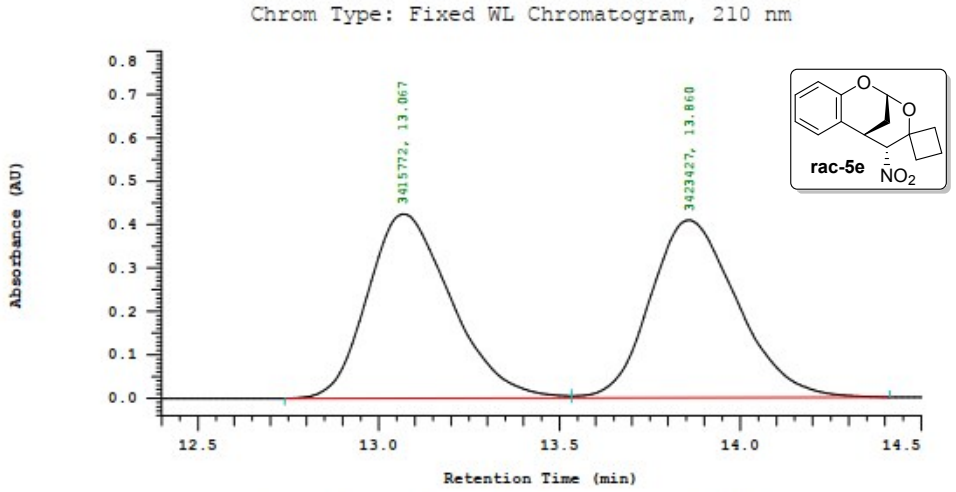
The ^{13}C NMR spectrum of 5e (101 MHz, $CDCl_3$)



The NOSEY spectrum of 5e (400 MHz, $CDCl_3$)



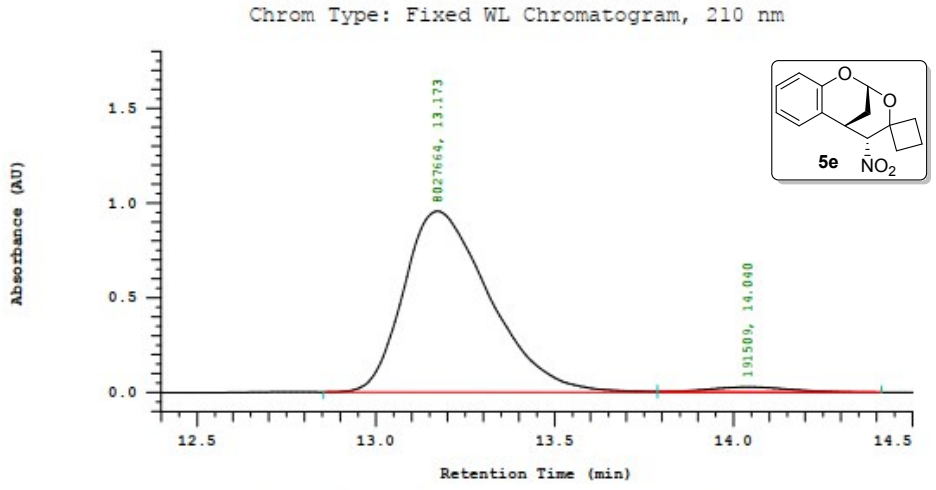
The HPLC of racemic 5e



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	13.067	3415772	49.944	BV
2	13.860	3423427	50.056	VB
		6839199	100.000	

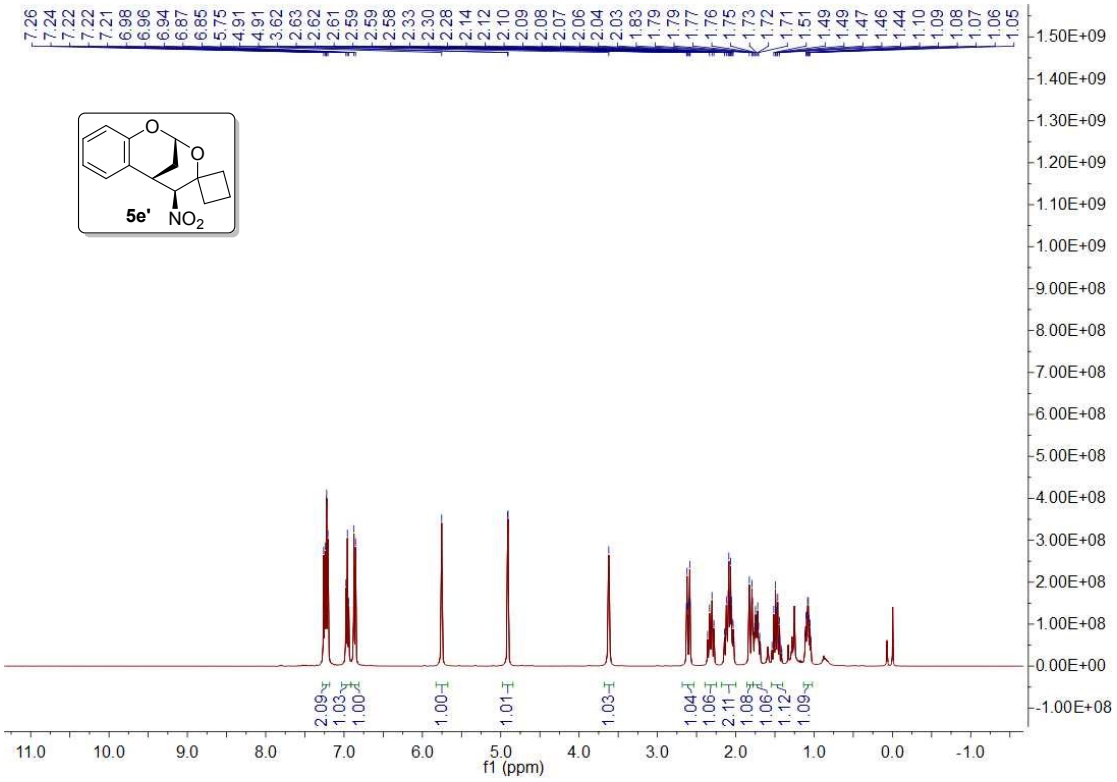
The HPLC of chiral 5e



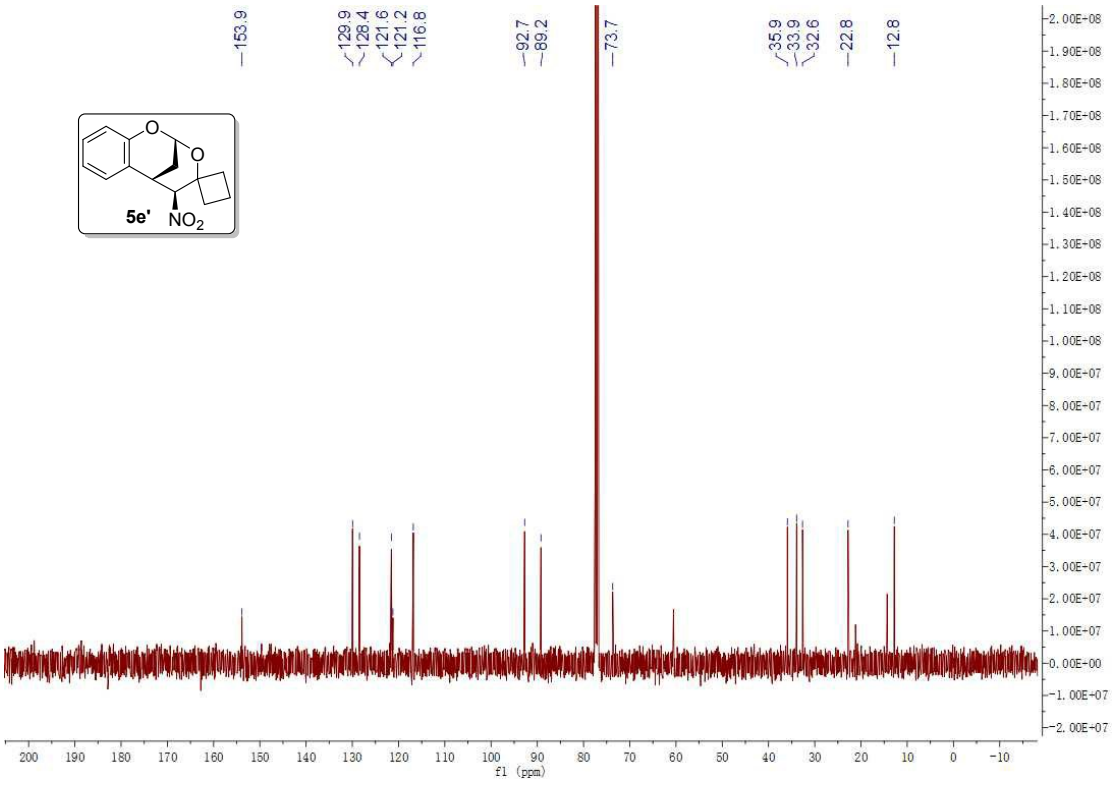
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	13.173	8027664	97.670	BV
2	14.040	191509	2.330	TBB
		8219173	100.000	

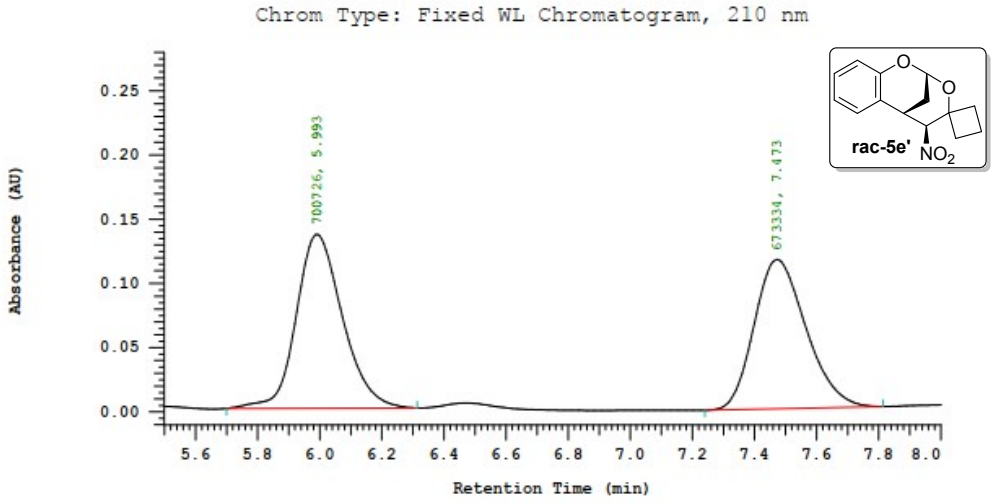
The ^{1}H NMR spectrum of 5e' (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5e' (101 MHz, $CDCl_3$)



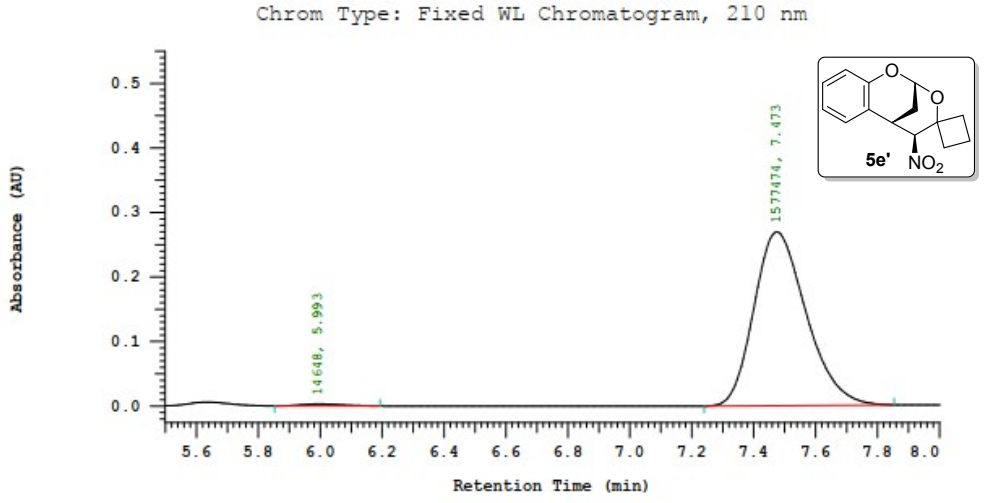
The HPLC of racemic 5e’



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.993	700726	50.997	BB
2	7.473	673334	49.003	BB
		1374060	100.000	

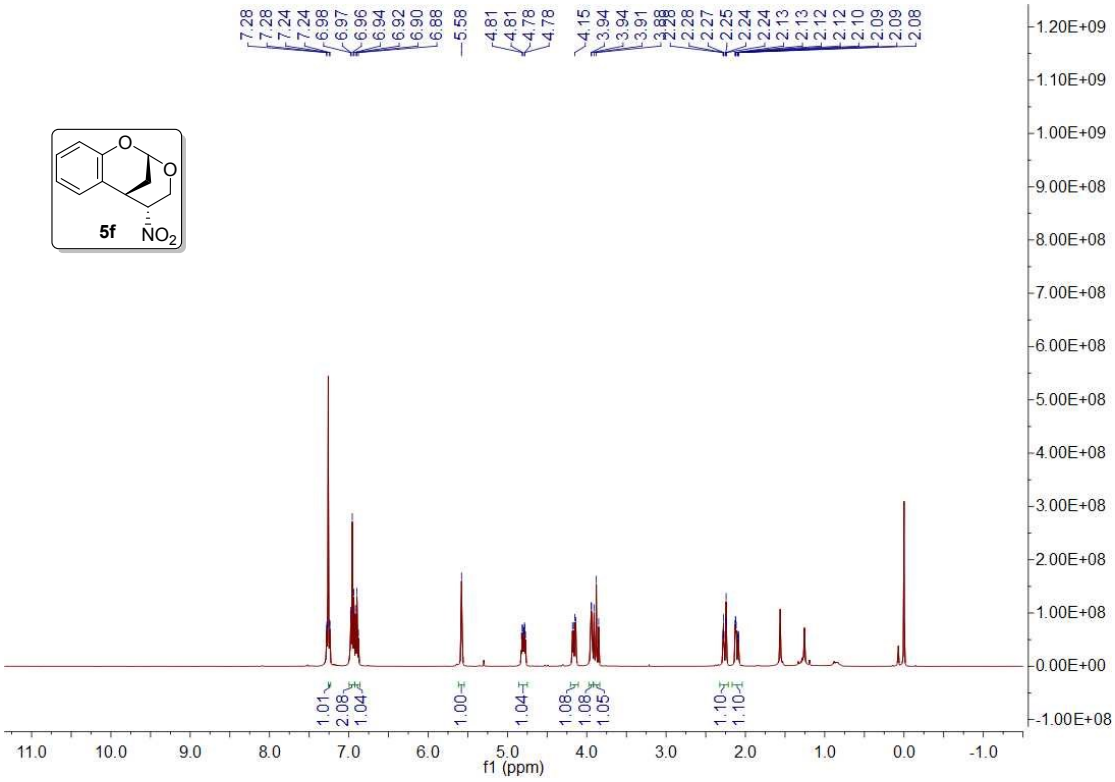
The HPLC of chiral 5e’



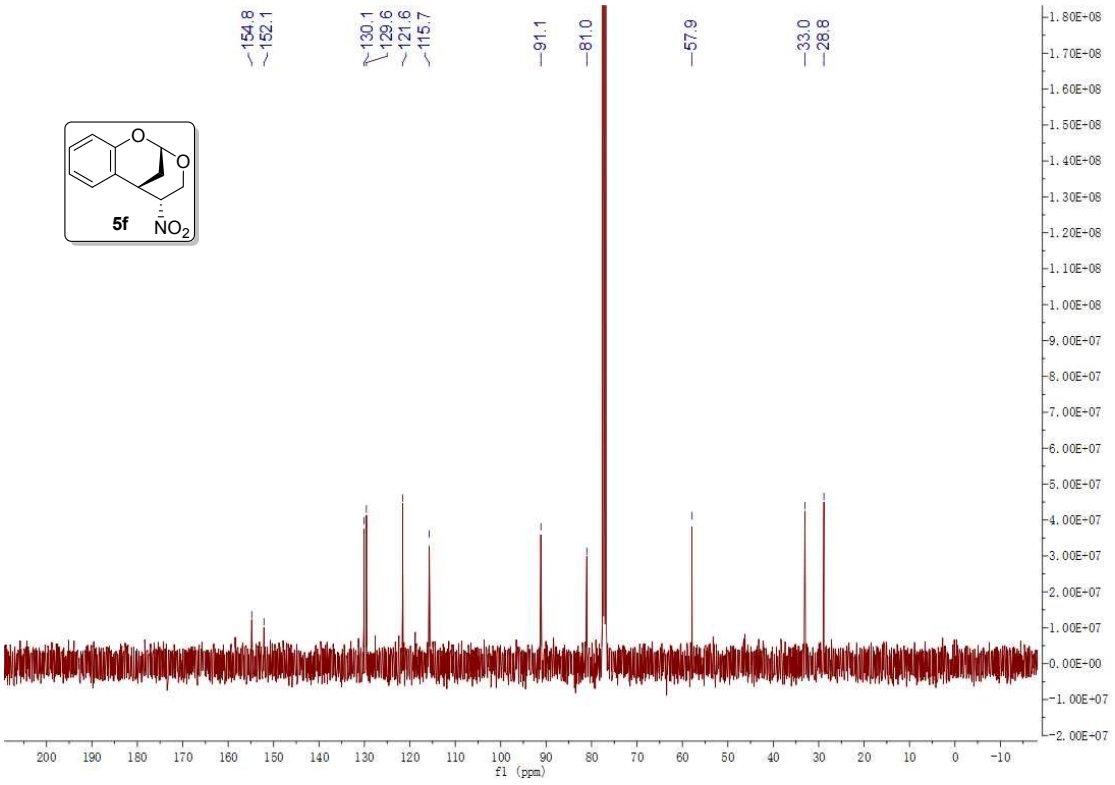
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.993	14648	0.920	BB
2	7.473	1577474	99.080	BB
		1592122	100.000	

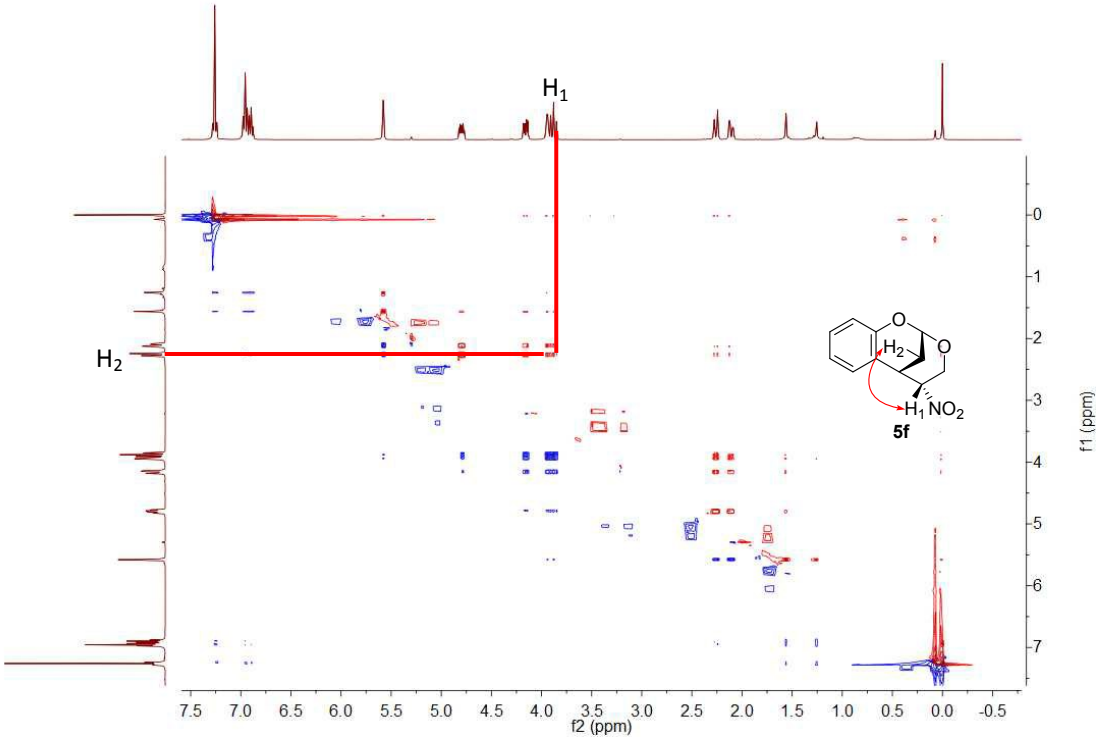
The ^{1}H NMR spectrum of 5f (400 MHz, $CDCl_3$)



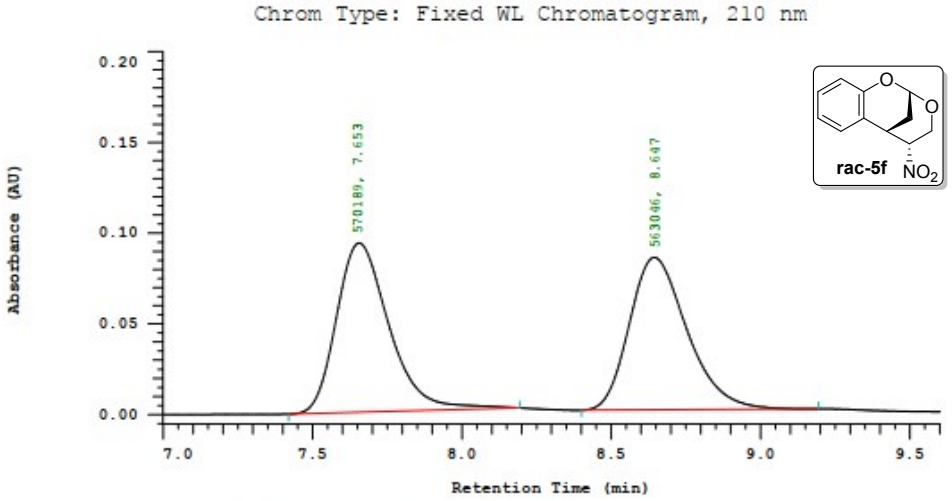
The ^{13}C NMR spectrum of 5f (101 MHz, $CDCl_3$)



The NOSEY spectrum of 5f (400 MHz, $CDCl_3$)



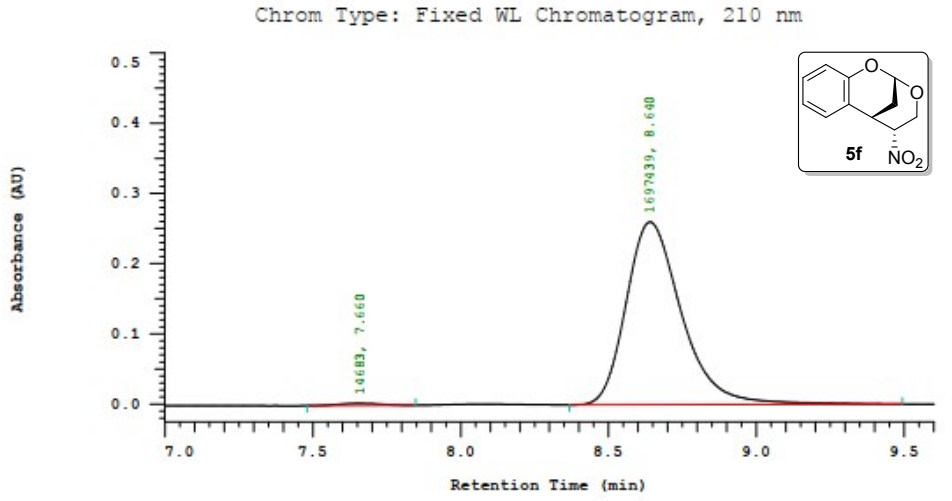
The HPLC of racemic 5f



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.653	570189	50.315	BB
2	8.647	563046	49.685	BB
		1133235	100.000	

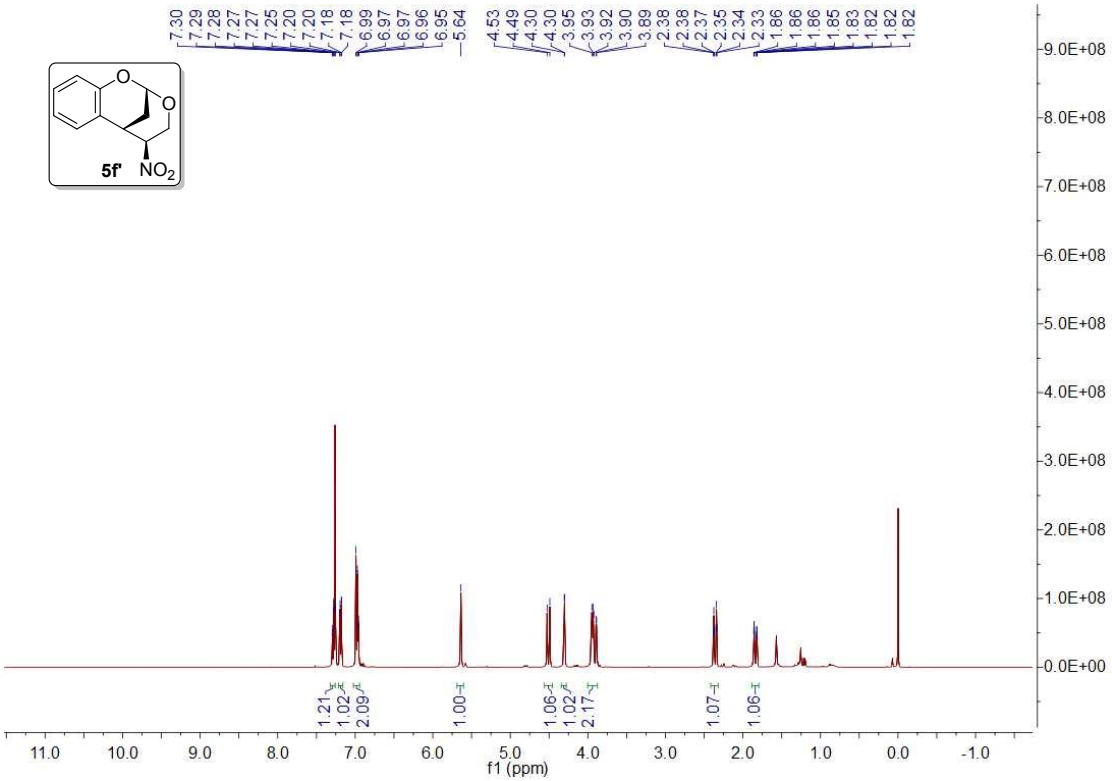
The HPLC of chiral 5f



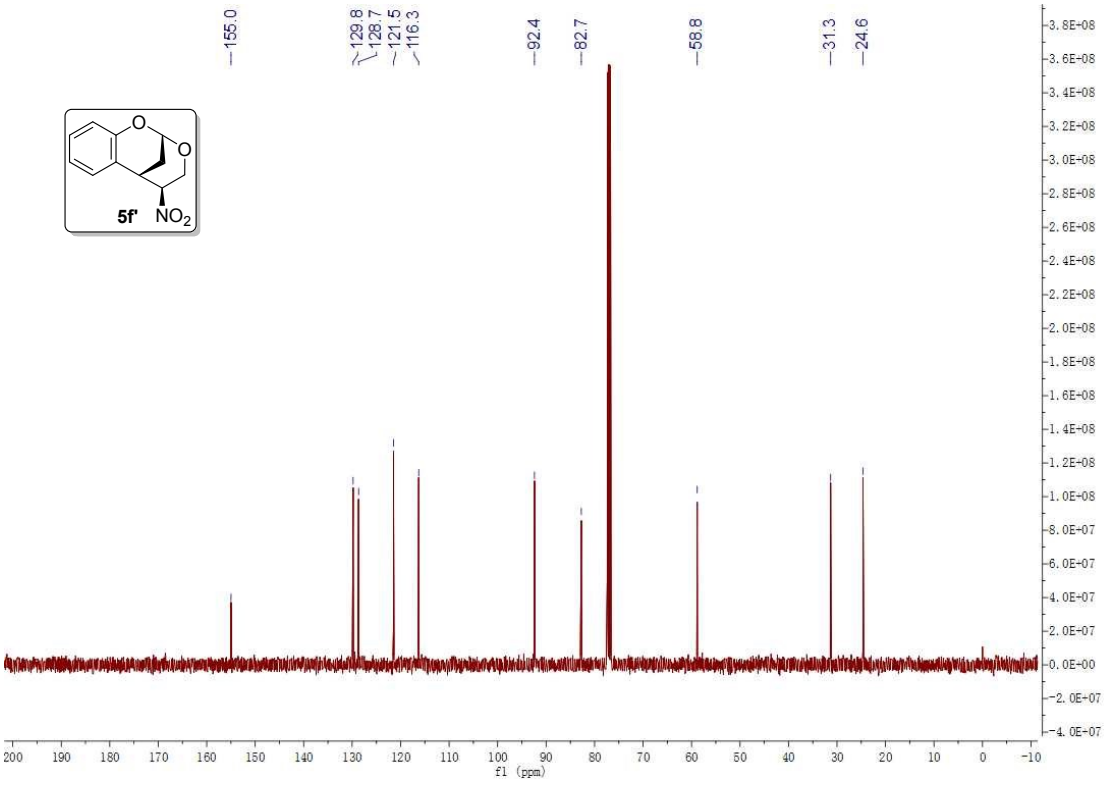
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.660	14683	0.858	BB
2	8.640	1697439	99.142	BB
		1712122	100.000	

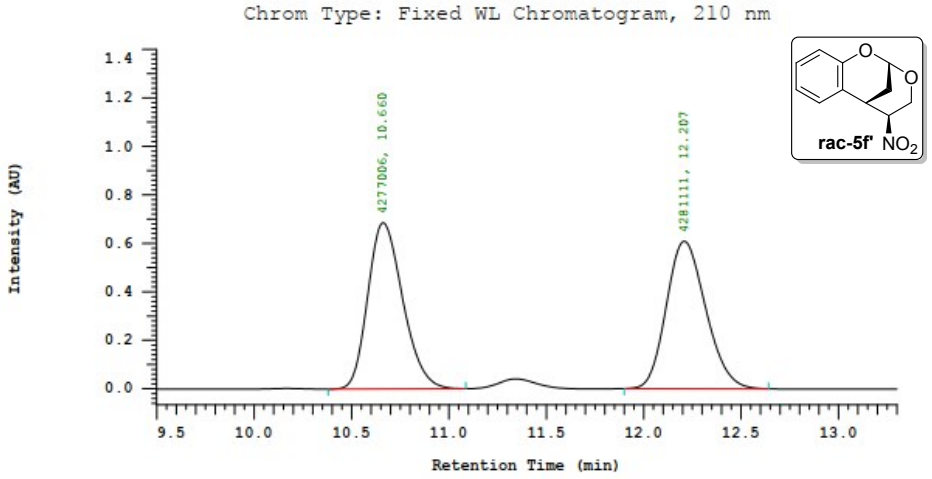
The ^{1}H NMR spectrum of 5f' (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5f' (101 MHz, $CDCl_3$)



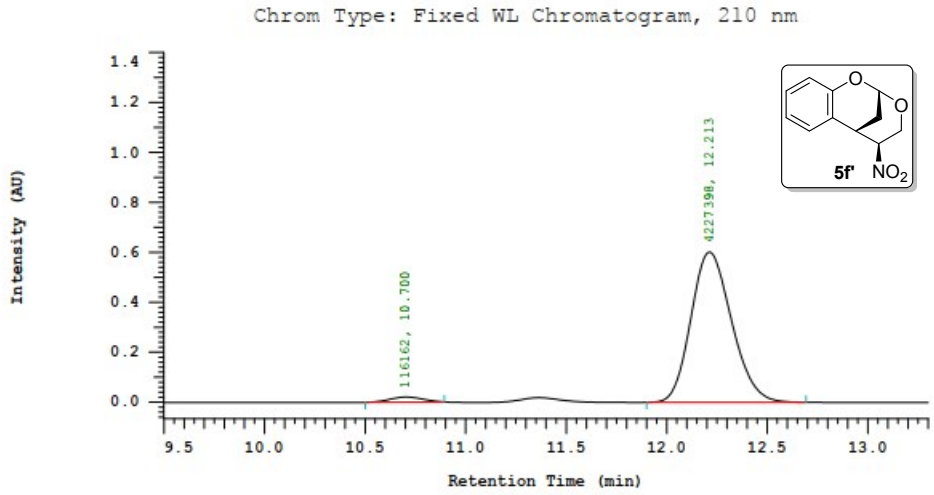
The HPLC of racemic 5f'



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.660	4277006	49.976	BB
2	12.207	4281111	50.024	BB
		8558117	100.000	

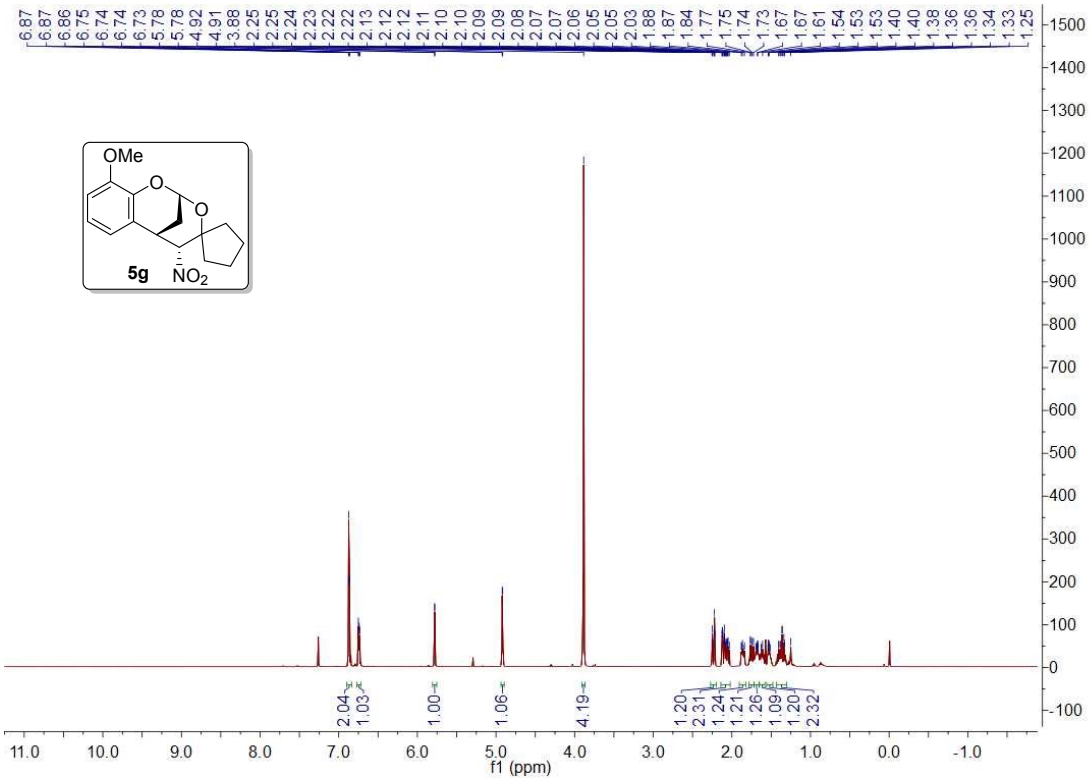
The HPLC of chiral 5f'



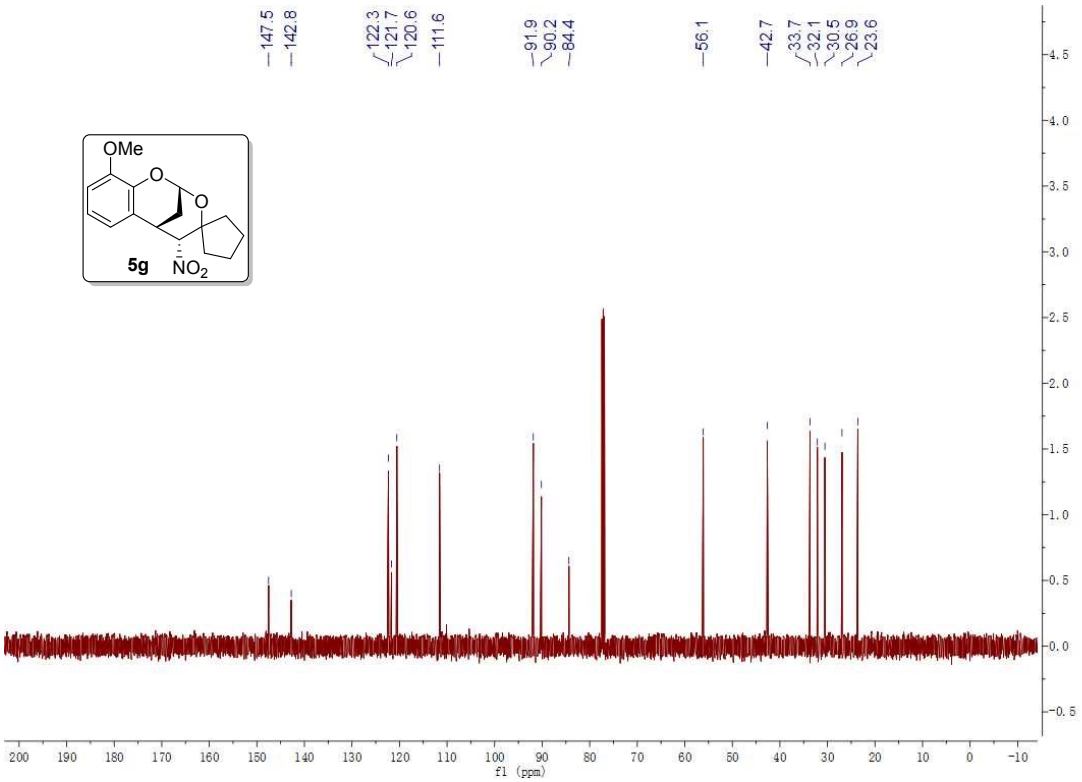
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.700	116162	2.674	BB
2	12.213	4227398	97.326	BB
		4343560	100.000	

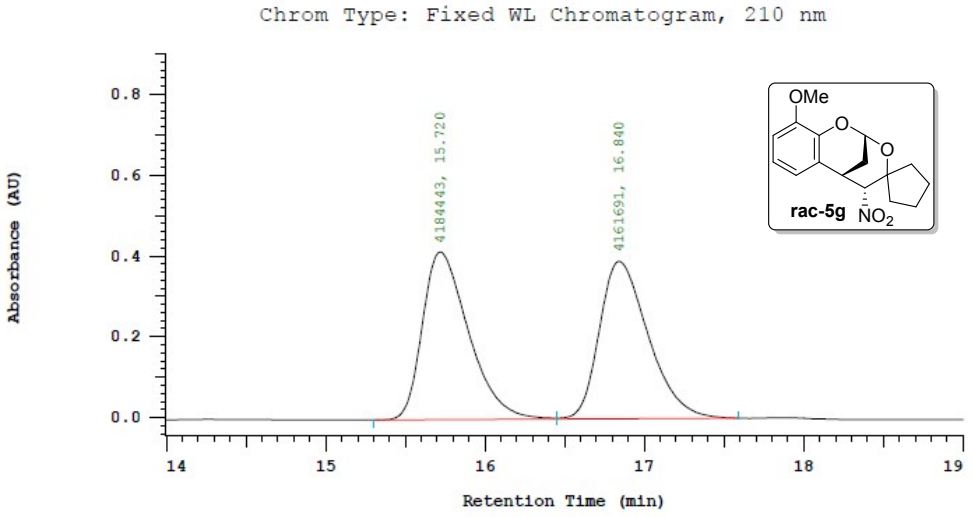
The ^{1}H NMR spectrum of 5g (500 MHz, $CDCl_3$)



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



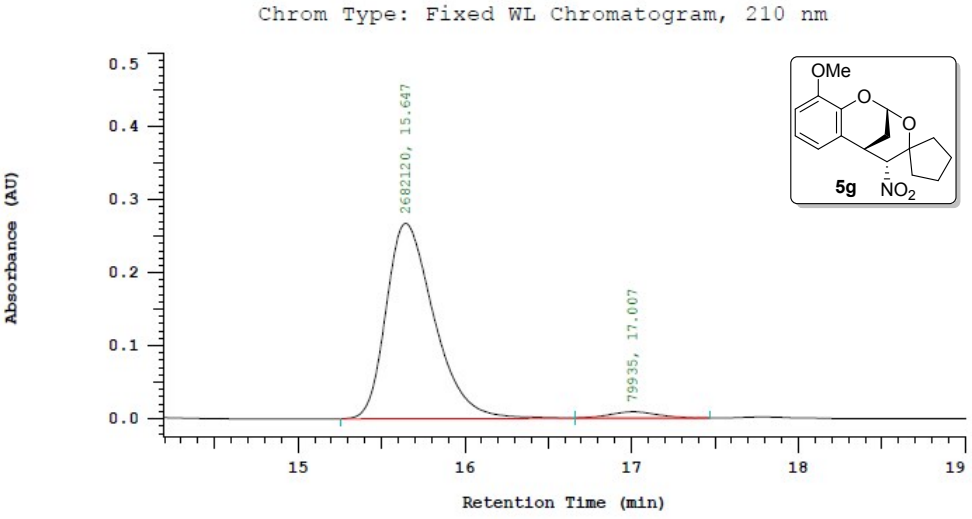
The HPLC of racemic 5g



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	15.720	4184443	50.136	BV
2	16.840	4161691	49.864	VB
		8346134	100.000	

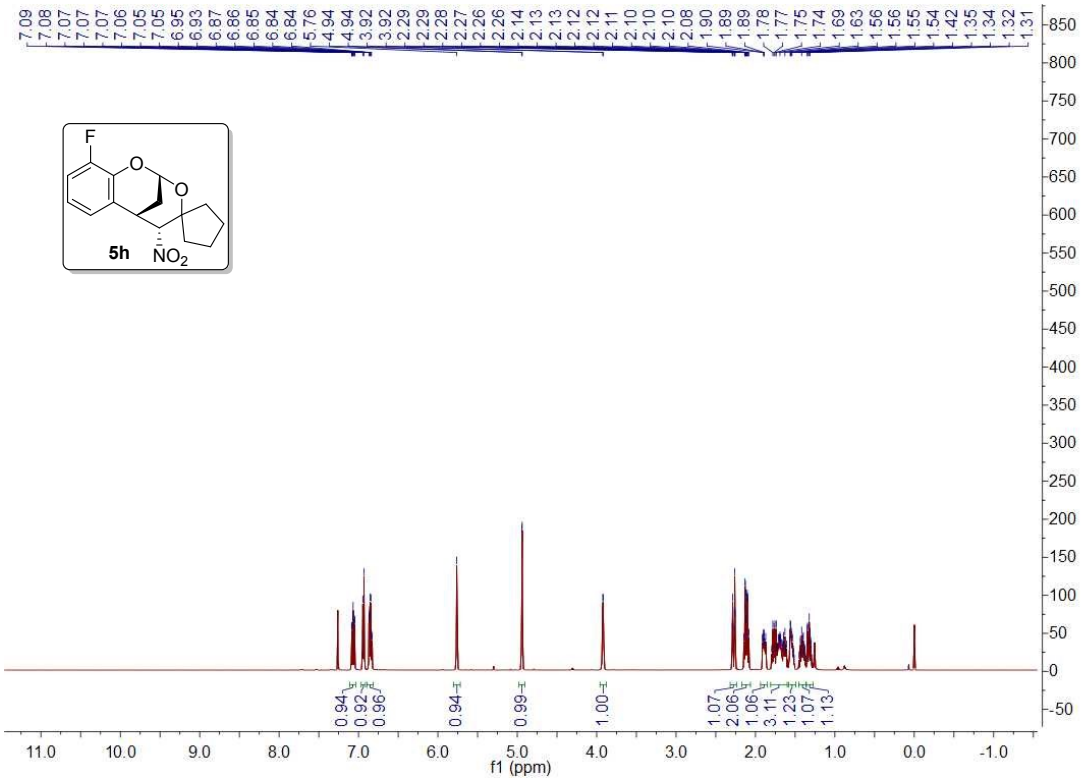
The HPLC of chiral 5g



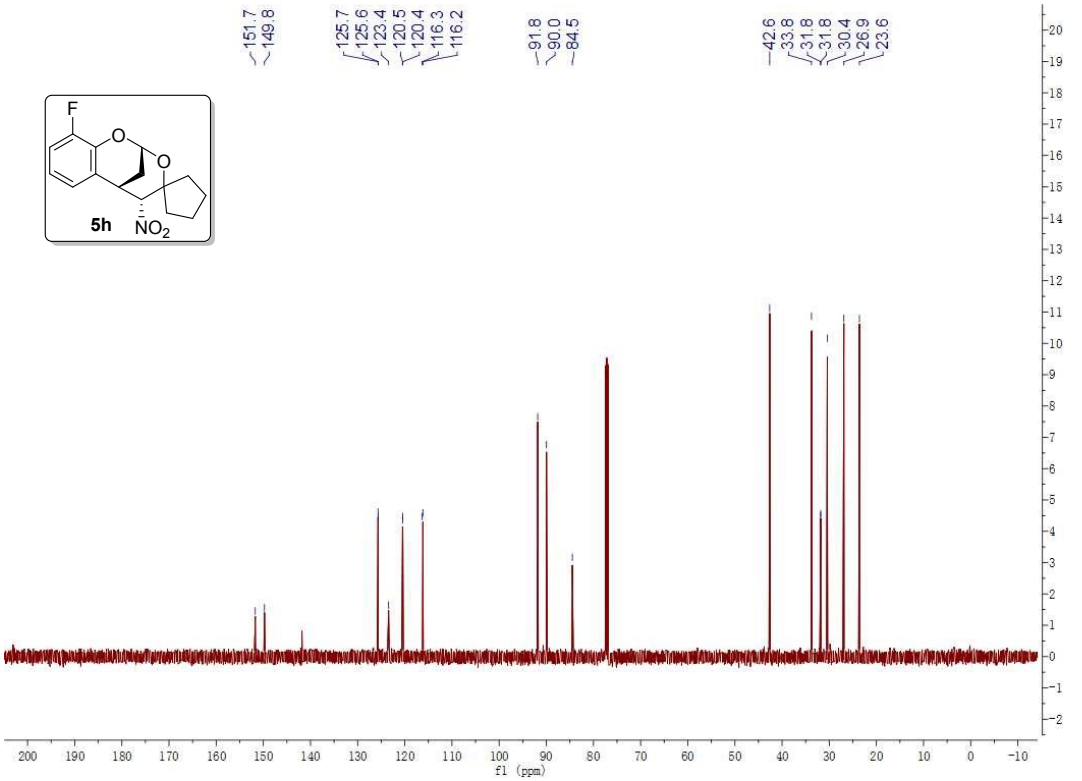
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	15.647	2682120	97.106	BV
2	17.007	79935	2.894	TBB
		2762055	100.000	

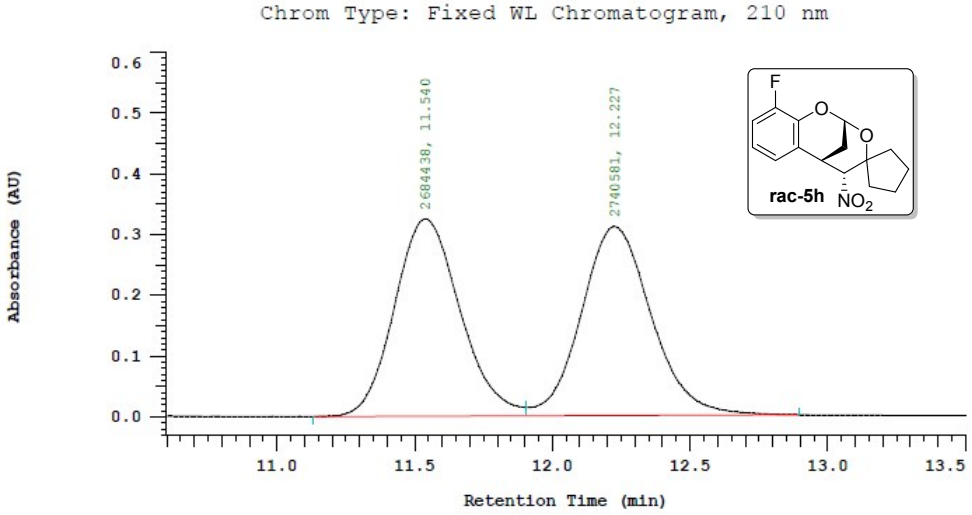
The ^{1}H NMR spectrum of 5h (500 MHz, $CDCl_3$)



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



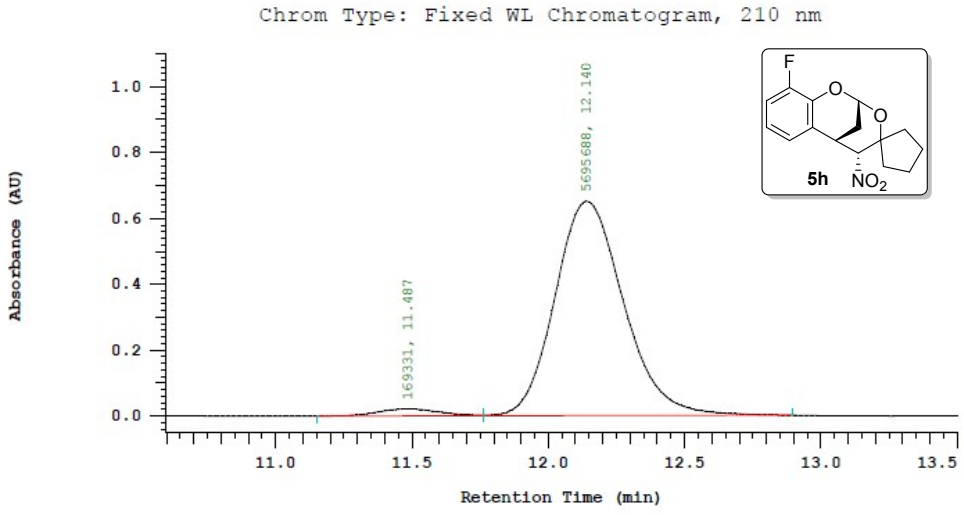
The HPLC of racemic 5h



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.540	2684438	49.483	BV
2	12.227	2740581	50.517	VB
		5425019	100.000	

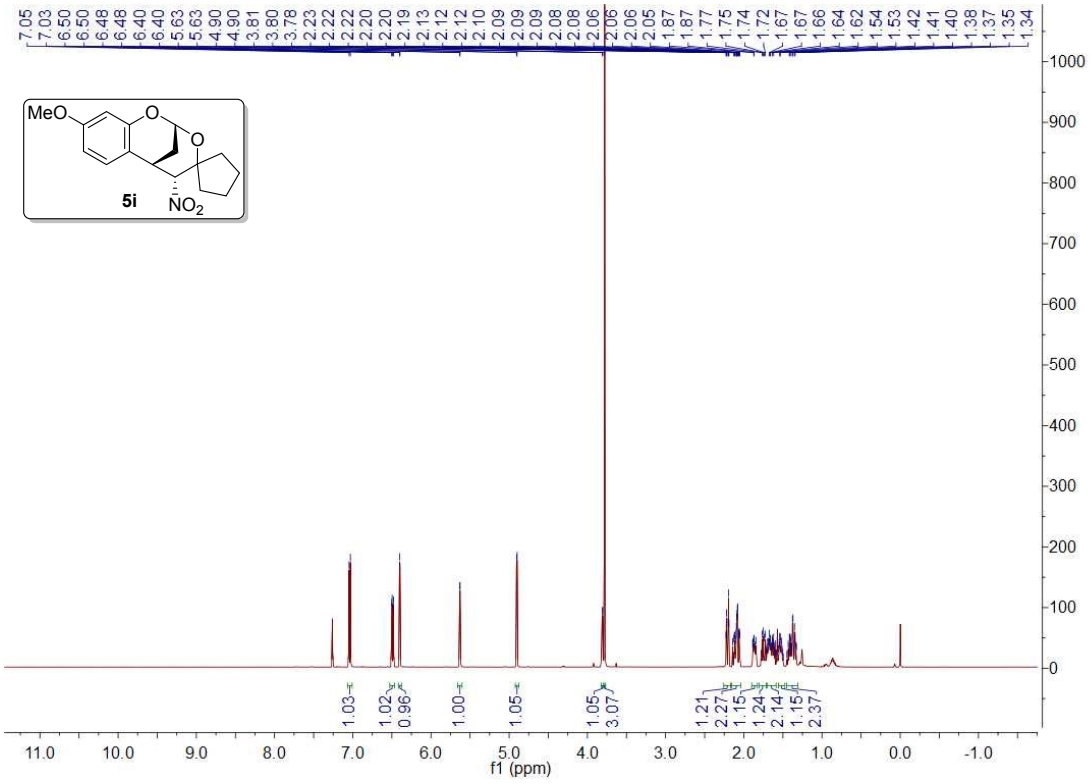
The HPLC of chiral 5h



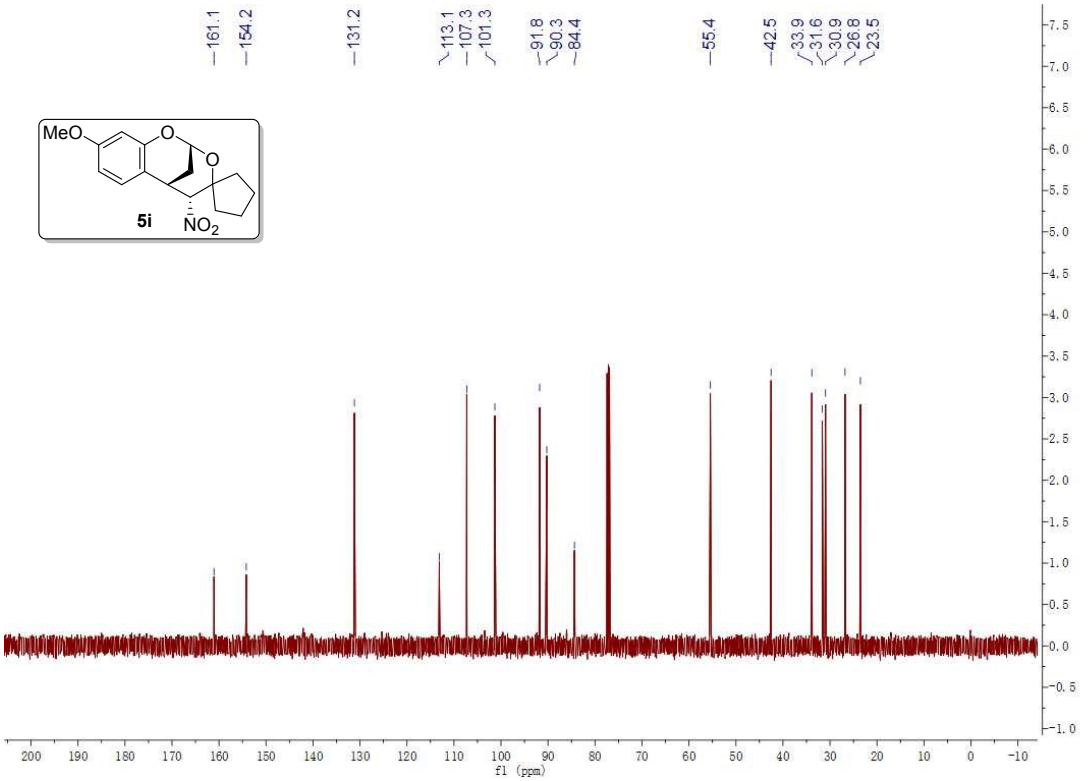
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.487	169331	2.887	BV
2	12.140	5695688	97.113	VB
		5865019	100.000	

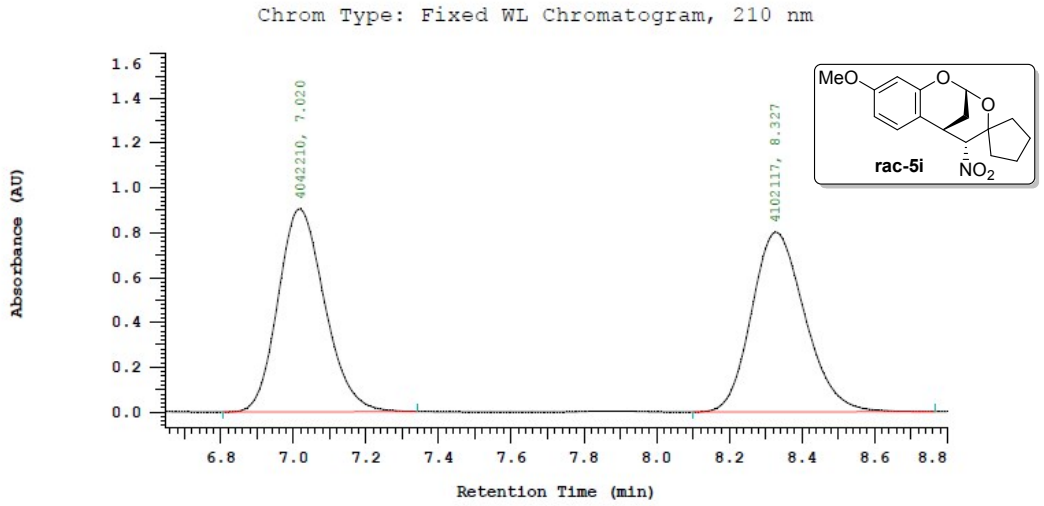
The ^{1}H NMR spectrum of 5i (500 MHz, $CDCl_3$)



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



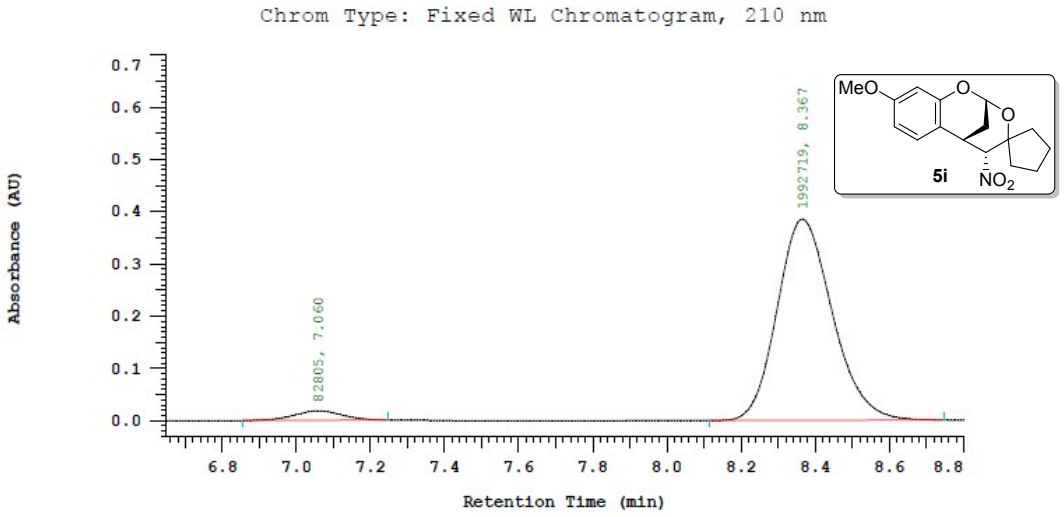
The HPLC of racemic 5i



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.020	4042210	49.632	BB
2	8.327	4102117	50.368	BB
		8144327	100.000	

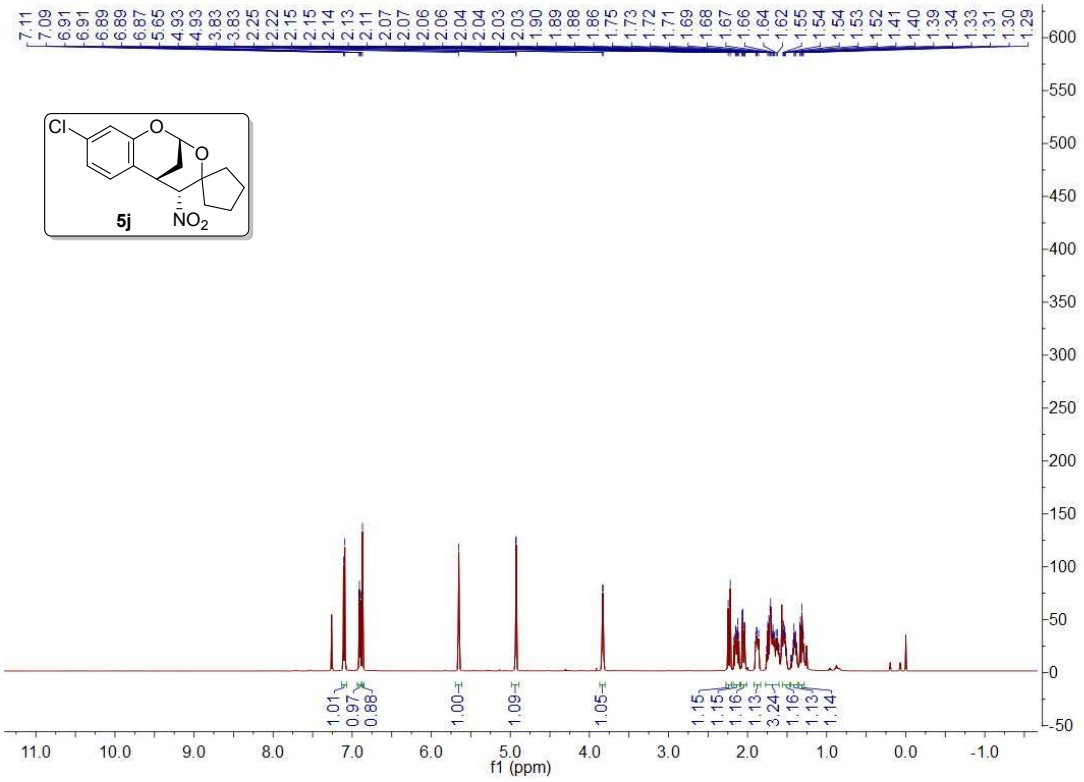
The HPLC of chiral 5i



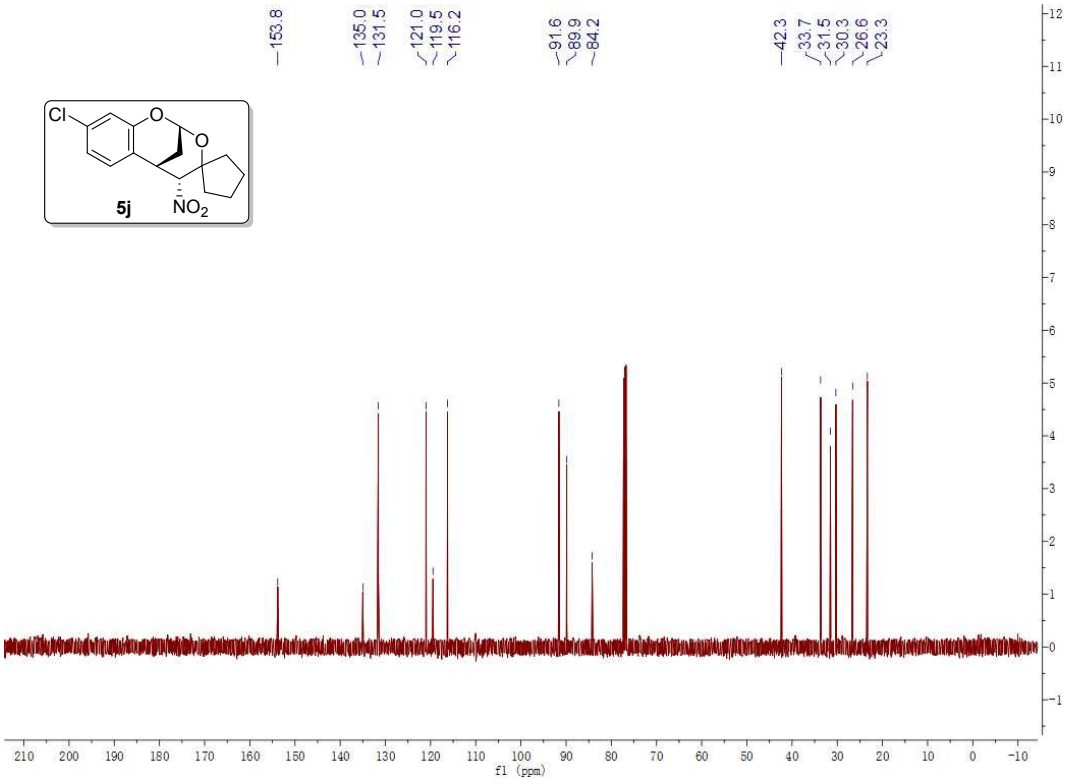
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.060	82805	3.990	BB
2	8.367	1992719	96.010	BB
		2075524	100.000	

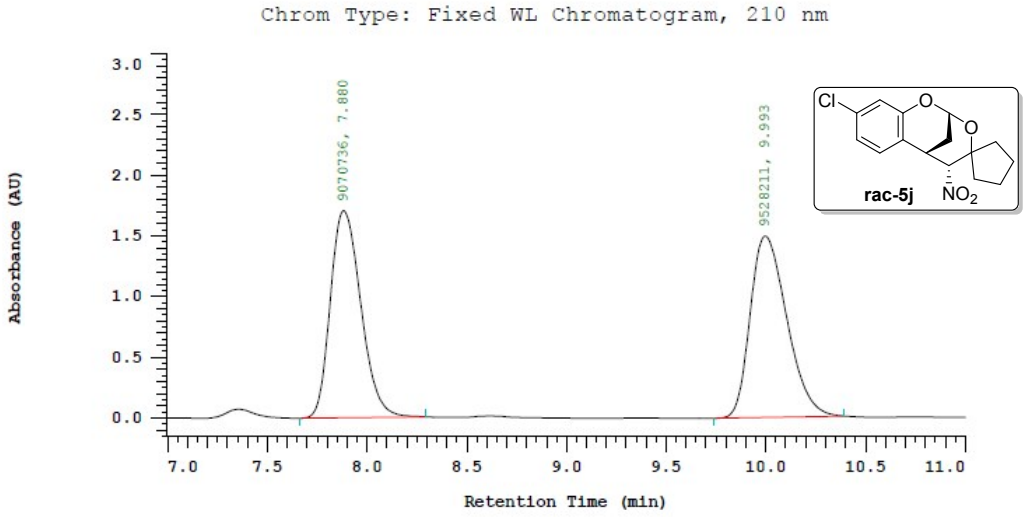
The ^{1}H NMR spectrum of 5j (500 MHz, $CDCl_3$)



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



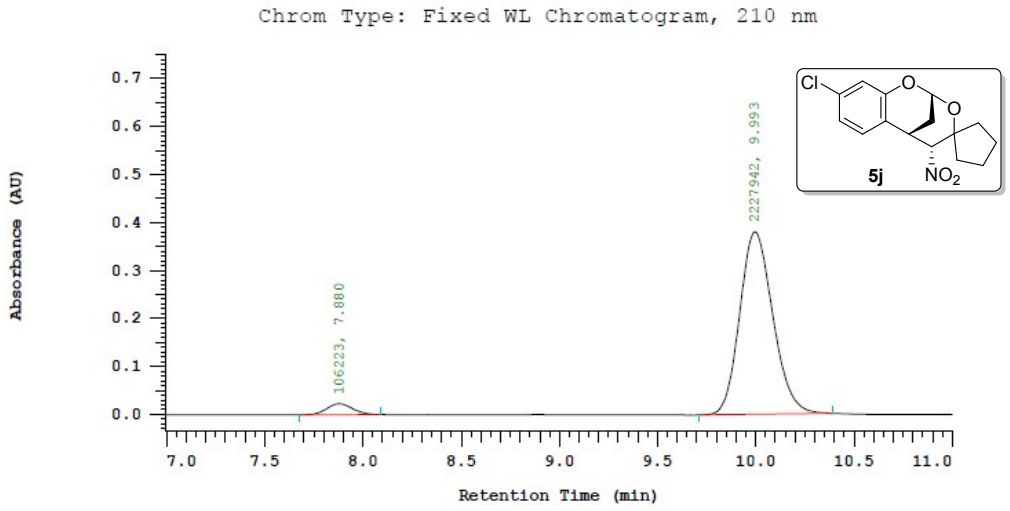
The HPLC of racemic 5j



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.880	9070736	48.770	BB
2	9.993	9528211	51.230	BB
		18598947	100.000	

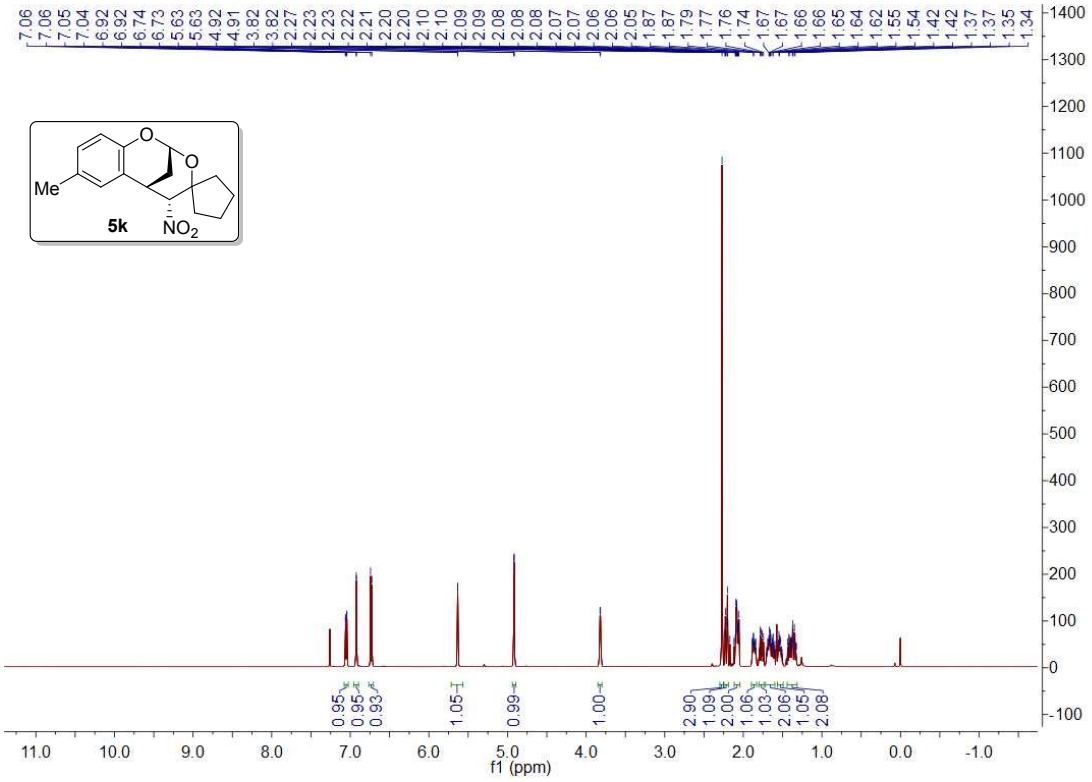
The HPLC of chiral 5j



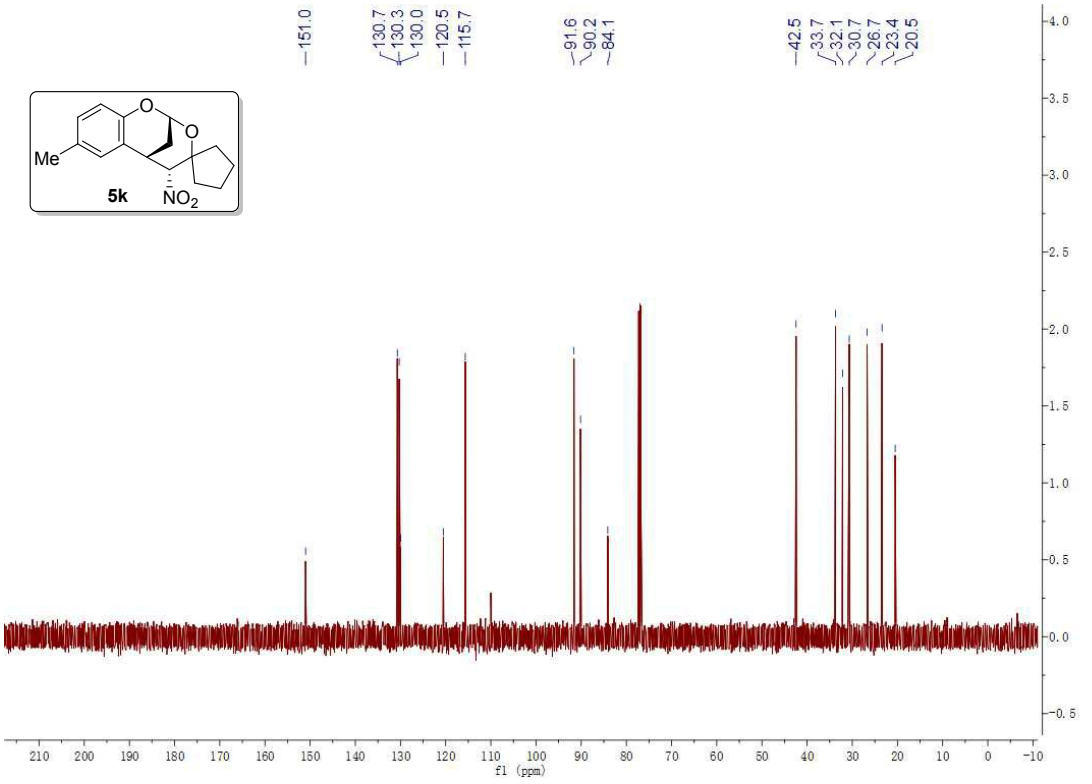
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.880	106223	4.551	BB
2	9.993	2227942	95.449	BB
		2334165	100.000	

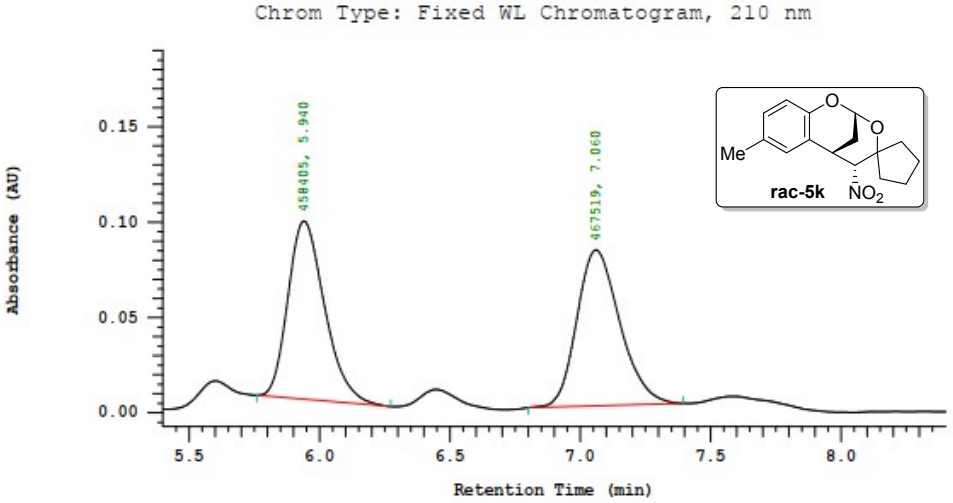
The ^{1}H NMR spectrum of 5k (500 MHz, $CDCl_3$)



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



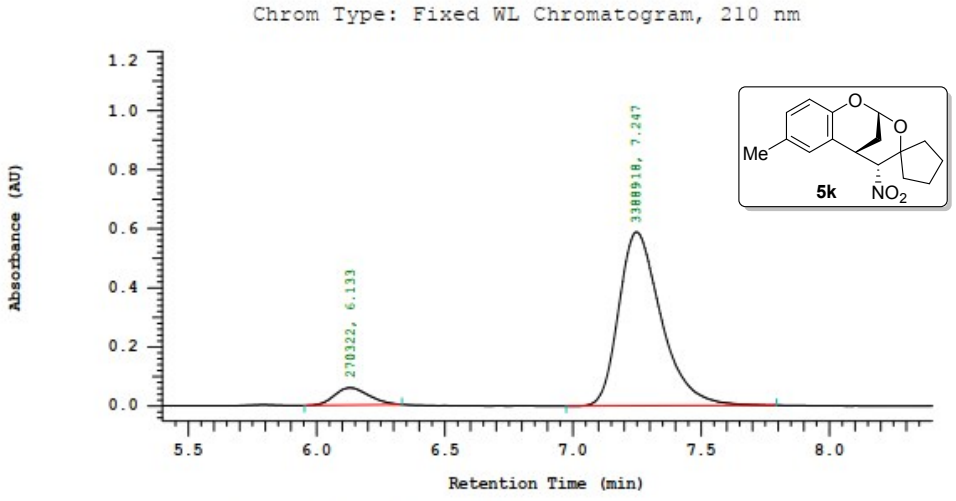
The HPLC of racemic 5k



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.940	458405	49.508	BB
2	7.060	467519	50.492	BB
		925924	100.000	

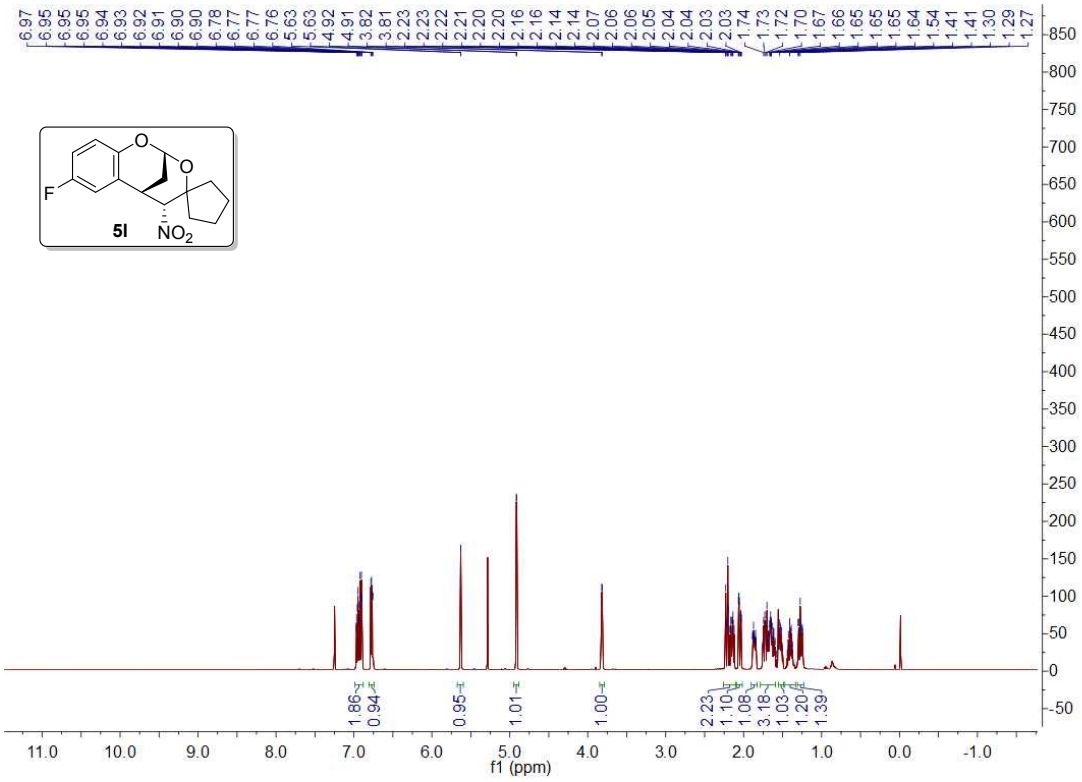
The HPLC of chiral 5k



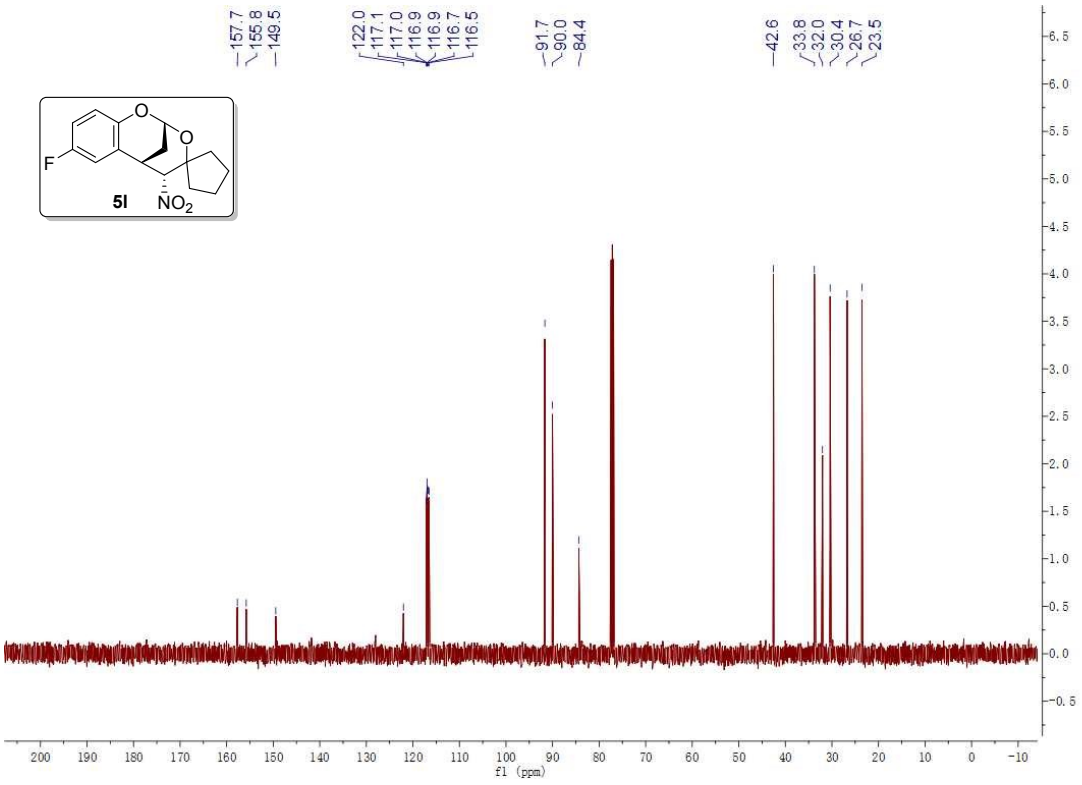
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.133	270322	7.387	BB
2	7.247	3388918	92.613	BB
		3659240	100.000	

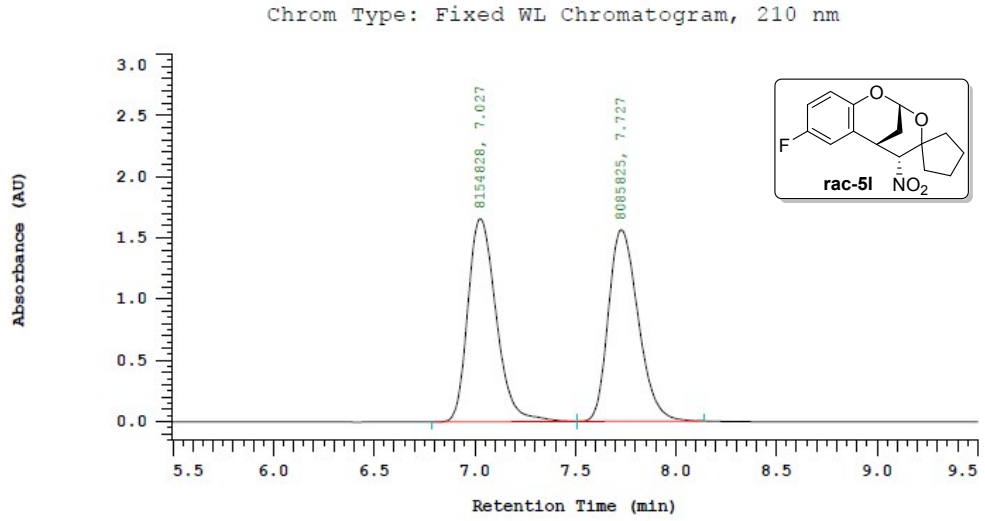
The ^{1}H NMR spectrum of 5l (500 MHz, $CDCl_3$)



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



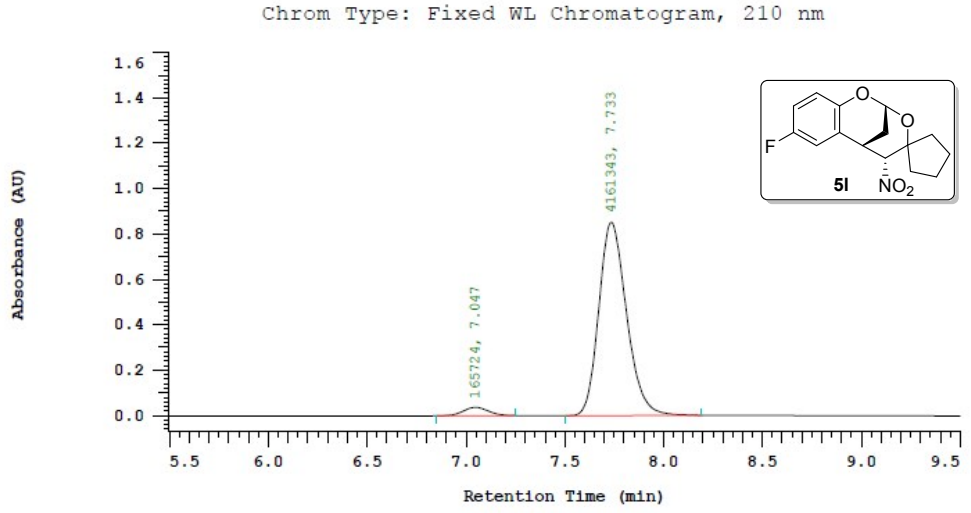
The HPLC of racemic 5l



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.027	8154828	50.212	BV
2	7.727	8085825	49.788	VB
		16240653	100.000	

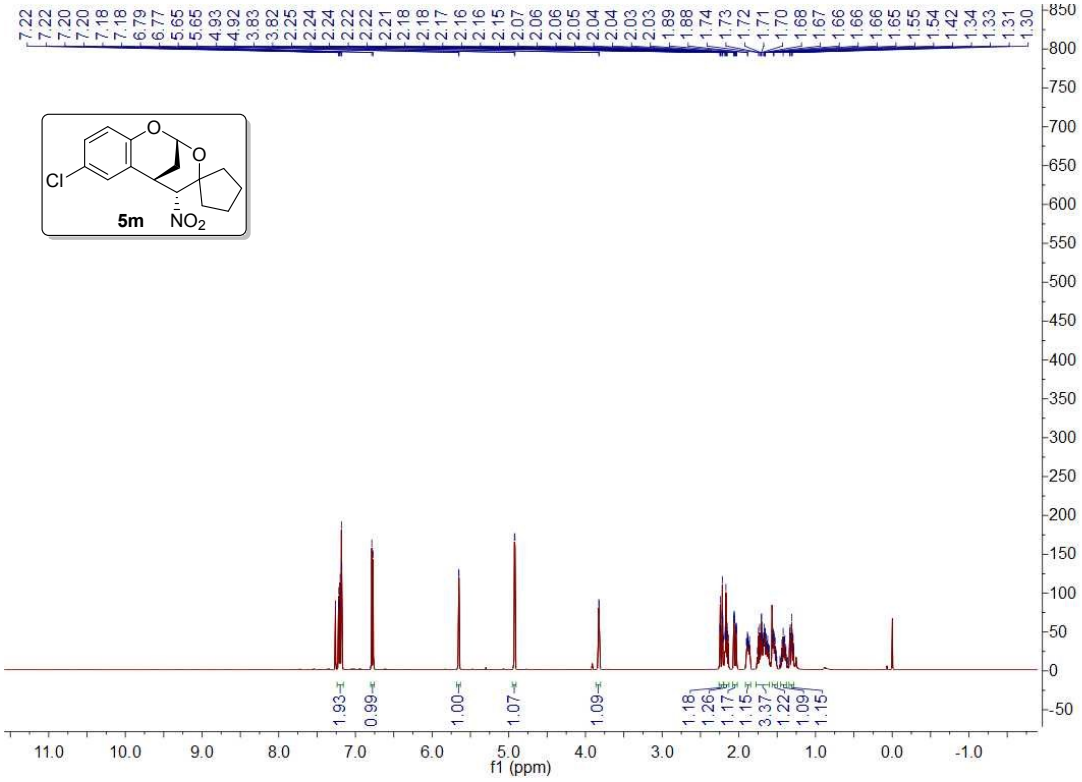
The HPLC of chiral 5l



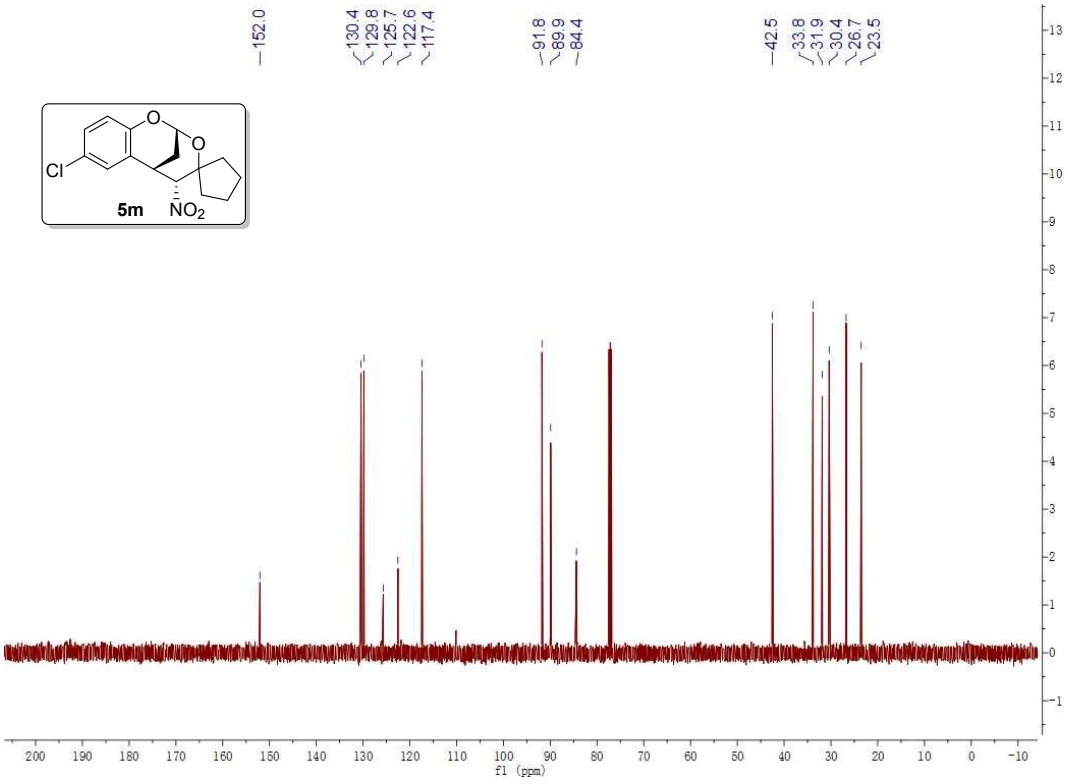
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.047	165724	3.830	BB
2	7.733	4161343	96.170	BB
		4327067	100.000	

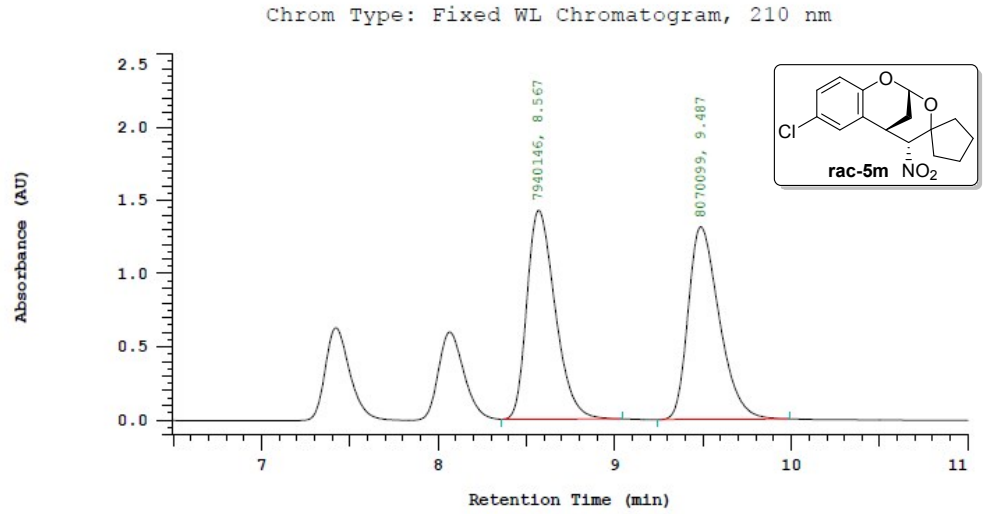
The ^{1}H NMR spectrum of 5m (500 MHz, $CDCl_3$)



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



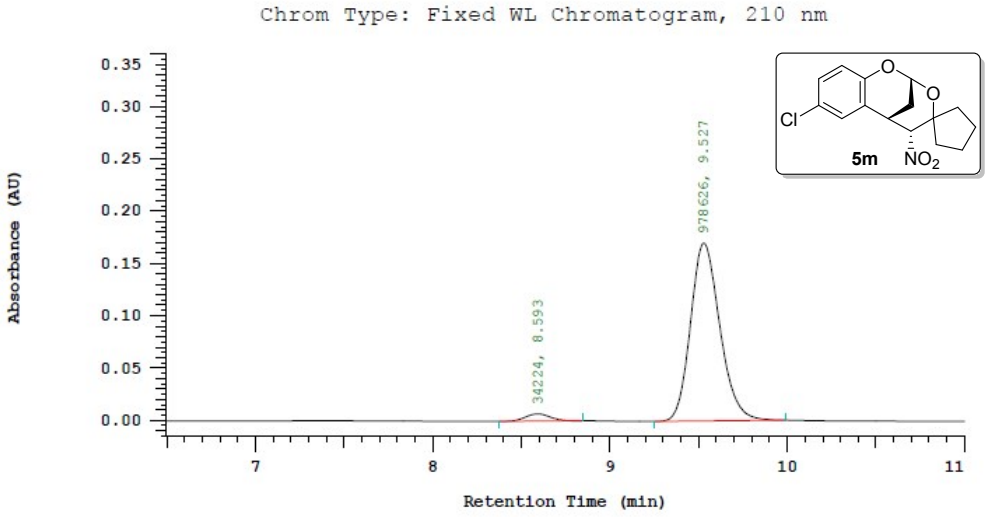
The HPLC of racemic 5m



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.567	7940146	49.594	BB
2	9.487	8070099	50.406	BB
		16010245	100.000	

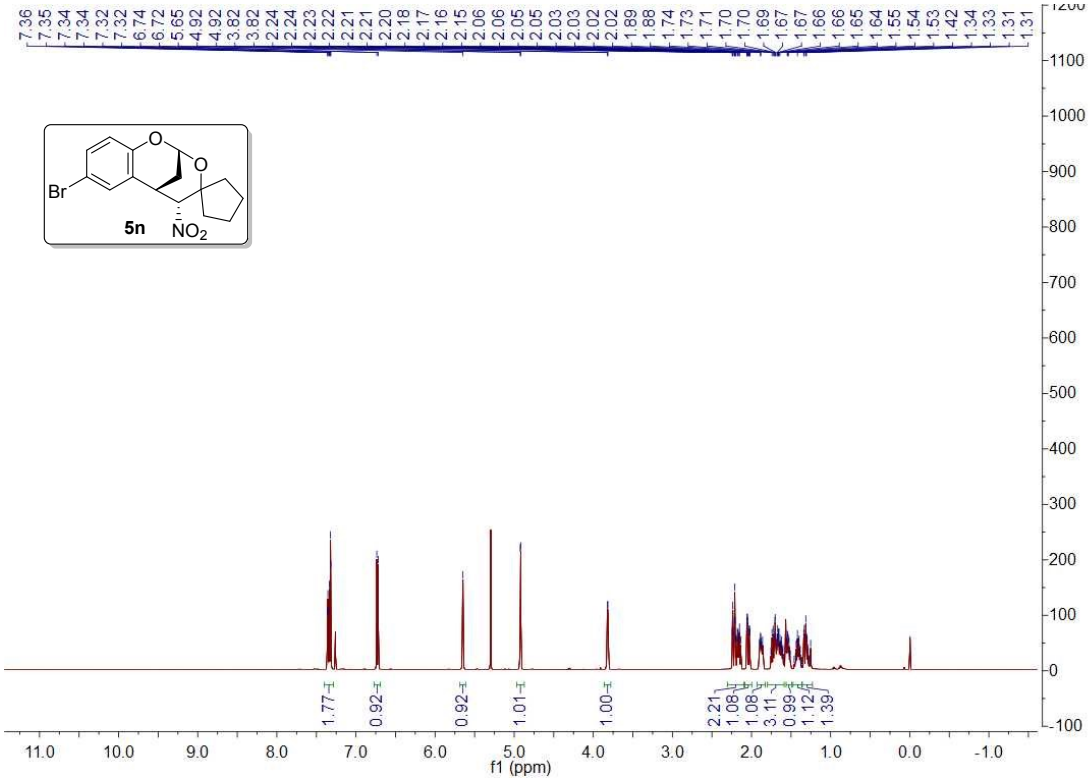
The HPLC of chiral 5m



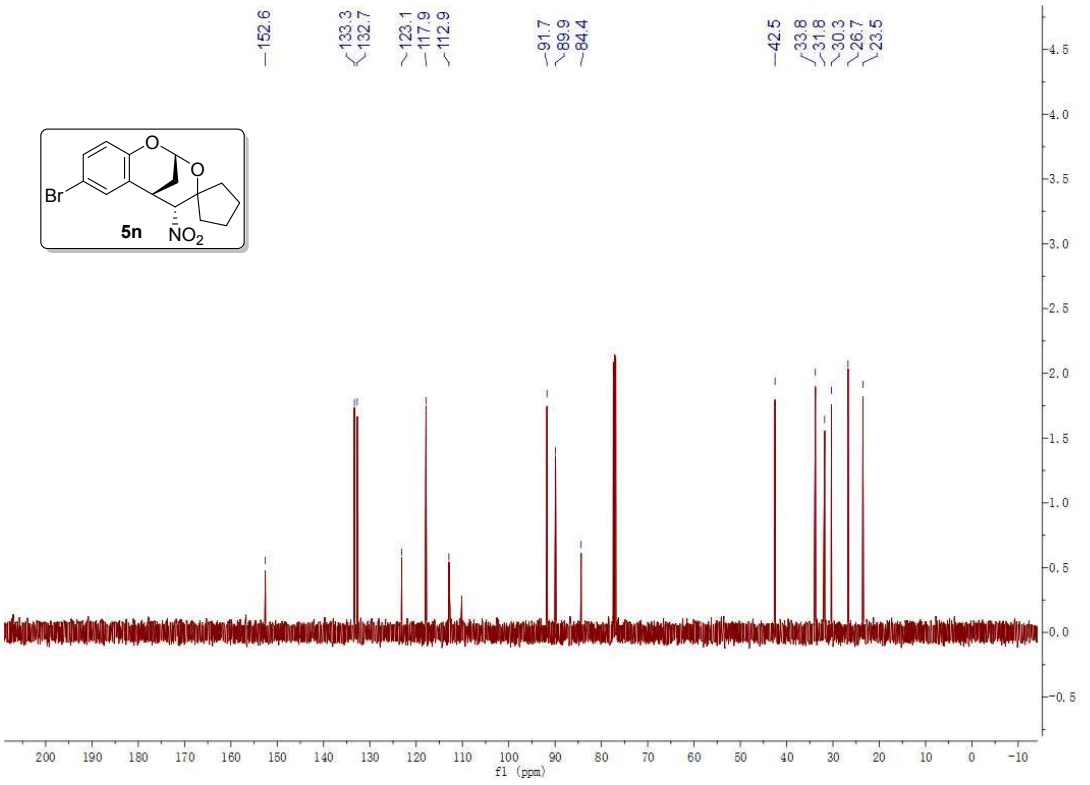
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.593	34224	3.379	BB
2	9.527	978626	96.621	BB
		1012850	100.000	

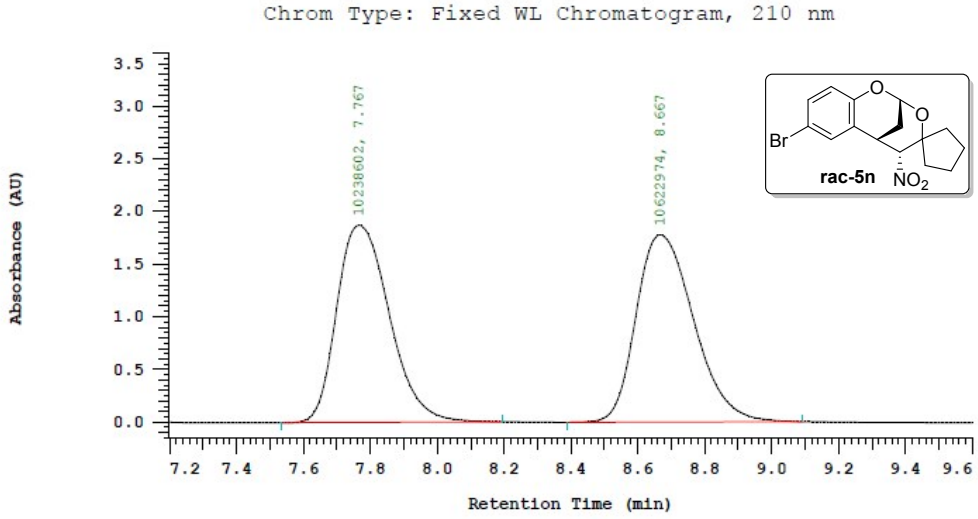
The ^{1}H NMR spectrum of 5n (500 MHz, $CDCl_3$)



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



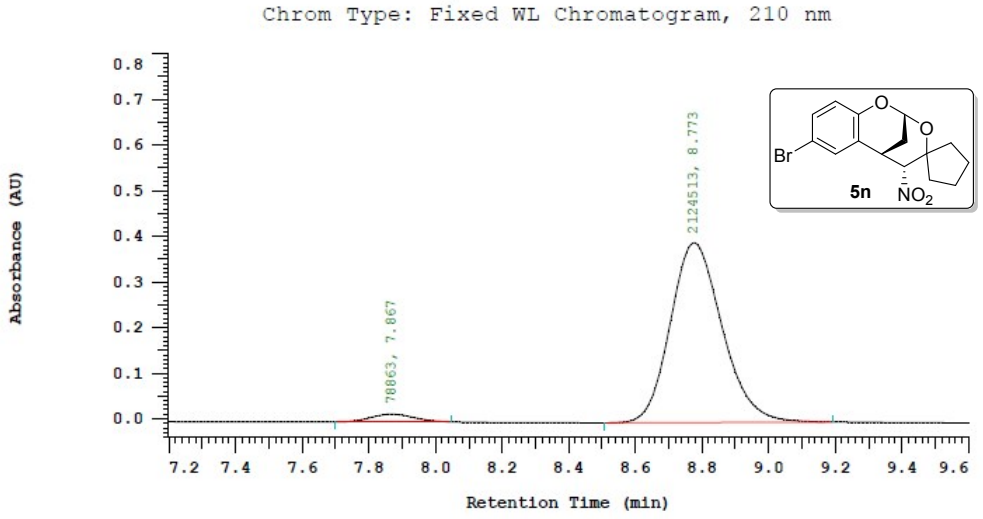
The HPLC of racemic 5n



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.767	10238602	49.079	BB
2	8.667	10622974	50.921	BB
		20861576	100.000	

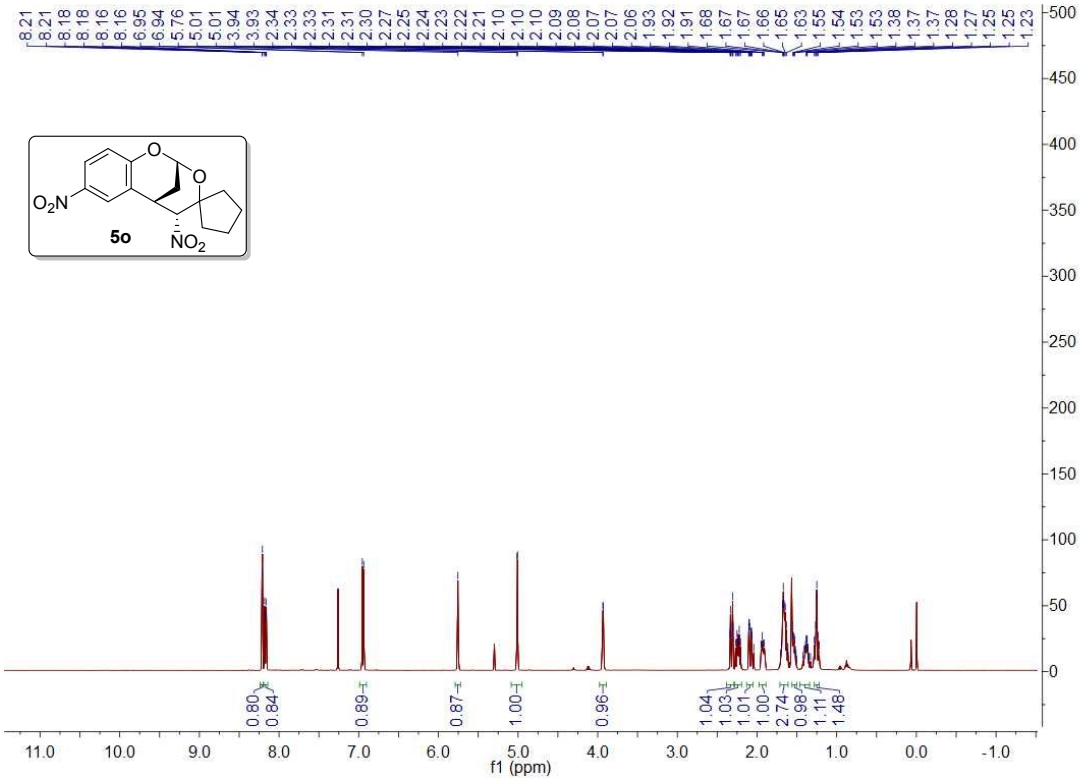
The HPLC of chiral 5n



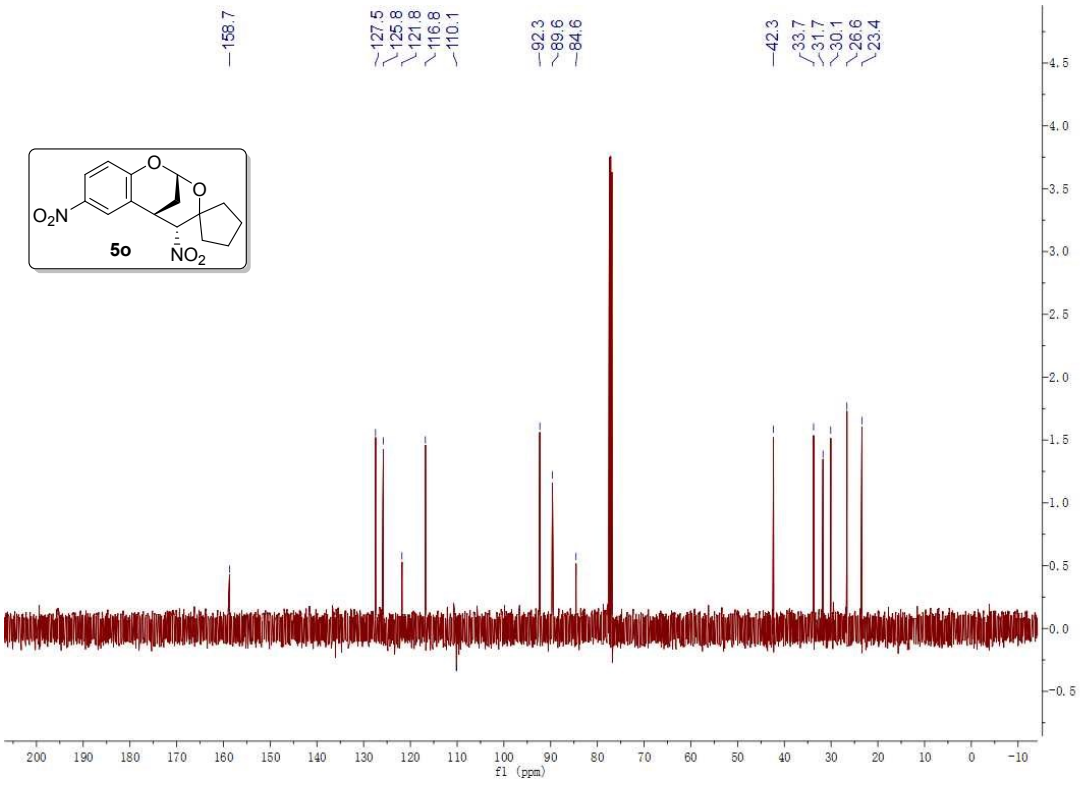
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.867	78863	3.579	BB
2	8.773	2124513	96.421	BB
		2203376	100.000	

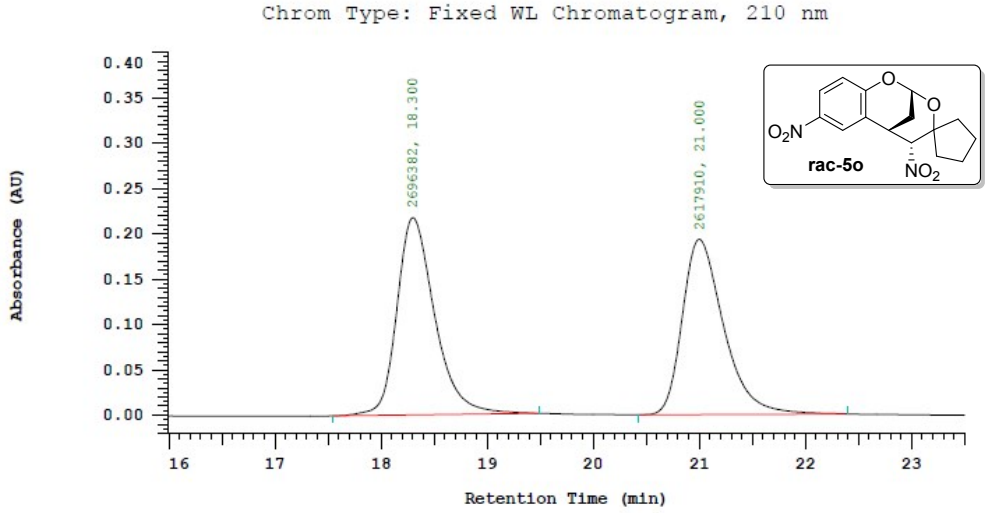
The ^{1}H NMR spectrum of 5o (500 MHz, $CDCl_3$)



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



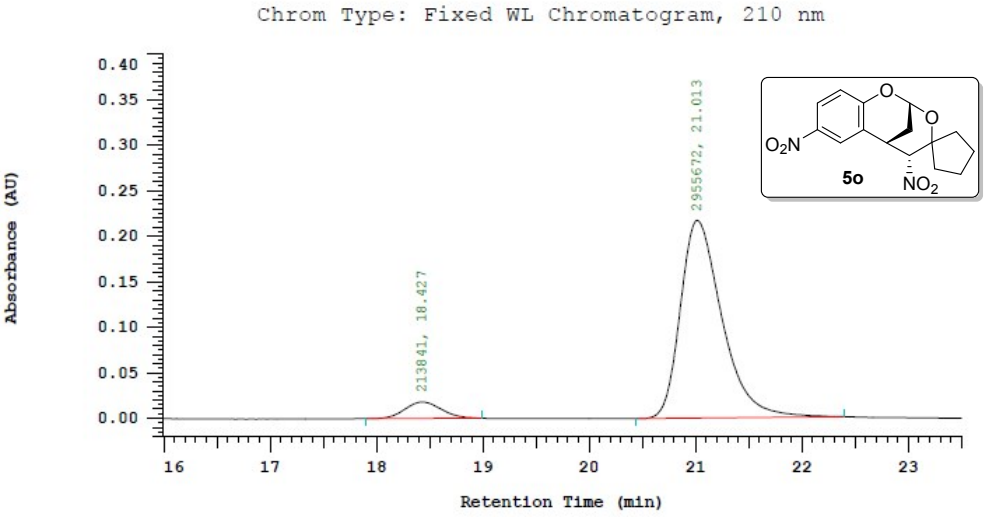
The HPLC of racemic 5o



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	18.300	2696382	50.738	BB
2	21.000	2617910	49.262	BB
		5314292	100.000	

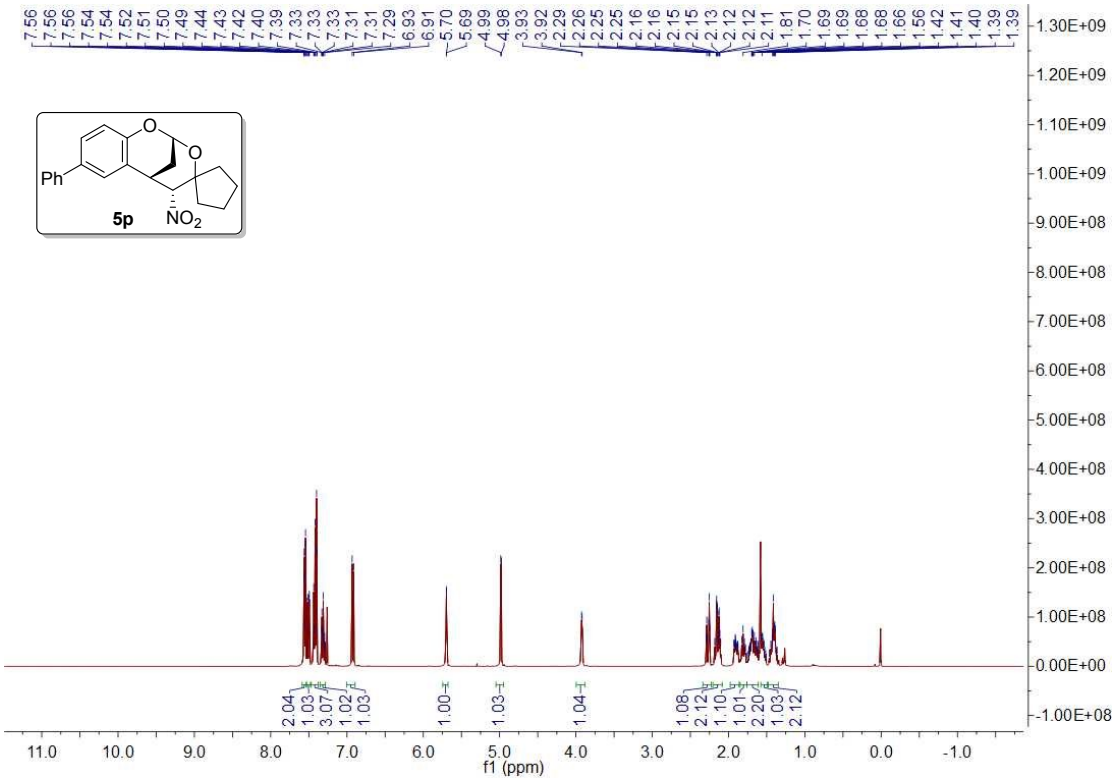
The HPLC of chiral 5o



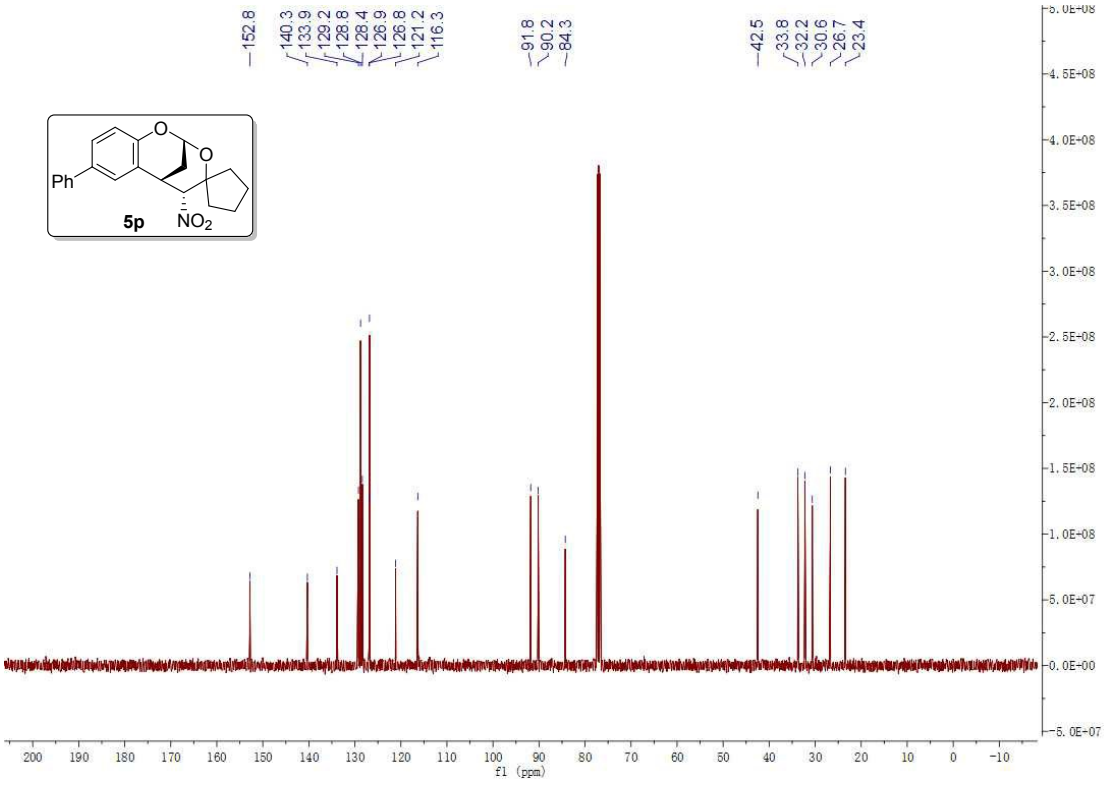
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	18.427	213841	6.747	BB
2	21.013	2955672	93.253	BB
		3169513	100.000	

The ^{1}H NMR spectrum of 5p (400 MHz, $CDCl_3$)

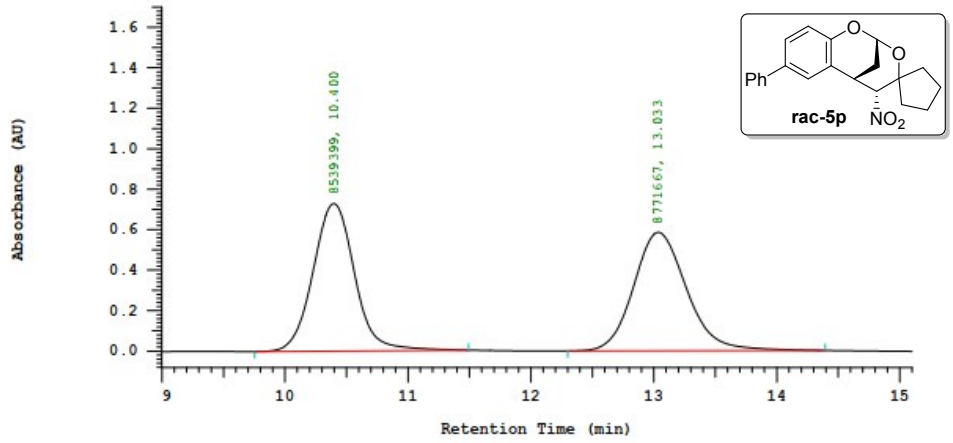


The ^{13}C NMR spectrum of 5p (101 MHz, $CDCl_3$)



The HPLC of racemic 5p

Chrom Type: Fixed WL Chromatogram, 204 nm



Chrom Type: Fixed WL Chromatogram, 204 nm

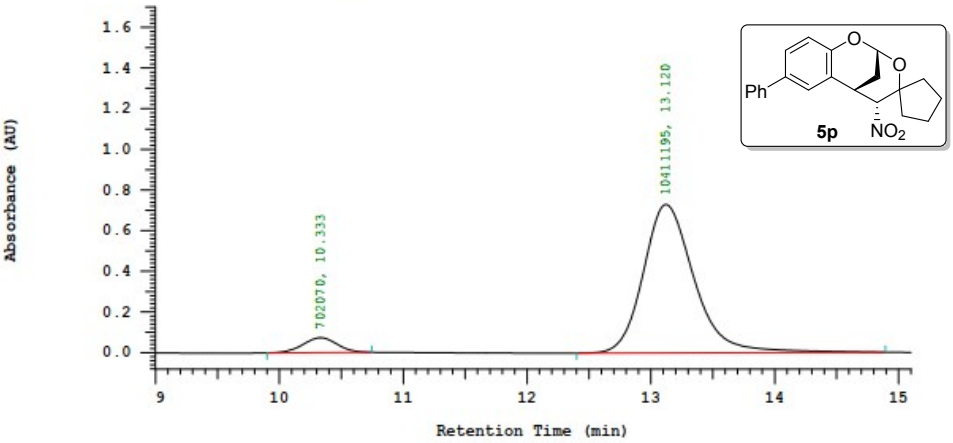
Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.400	8539399	49.329	BB
2	13.033	8771667	50.671	BB
		17311066	100.000	

The HPLC of chiral 5p

Chrom Type: Fixed WL Chromatogram, 204 nm



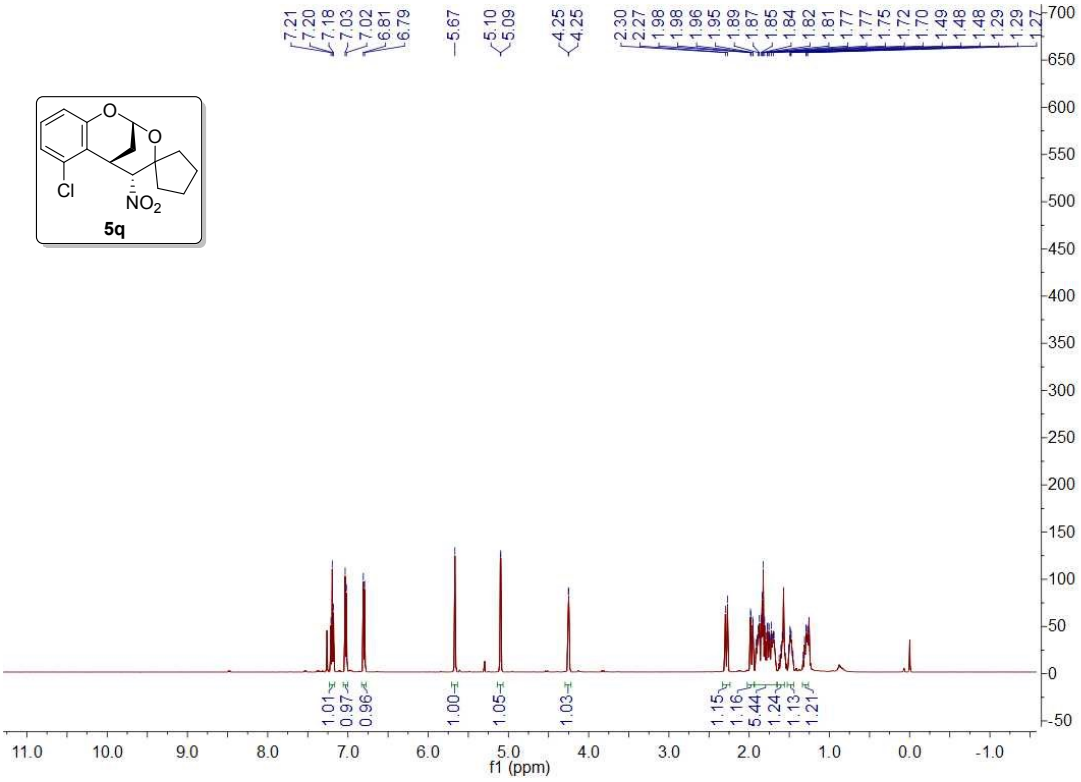
Chrom Type: Fixed WL Chromatogram, 204 nm

Peak Quantitation: AREA

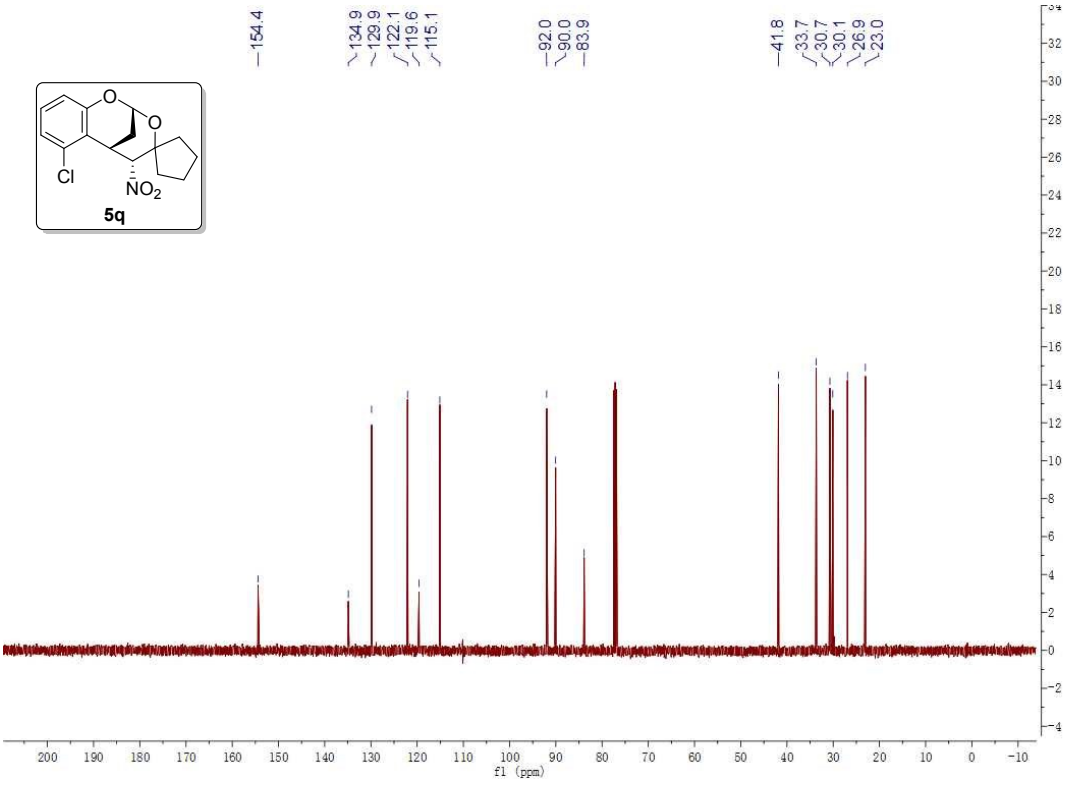
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.333	702070	6.317	BB
2	13.120	10411195	93.683	BB
		11113265	100.000	

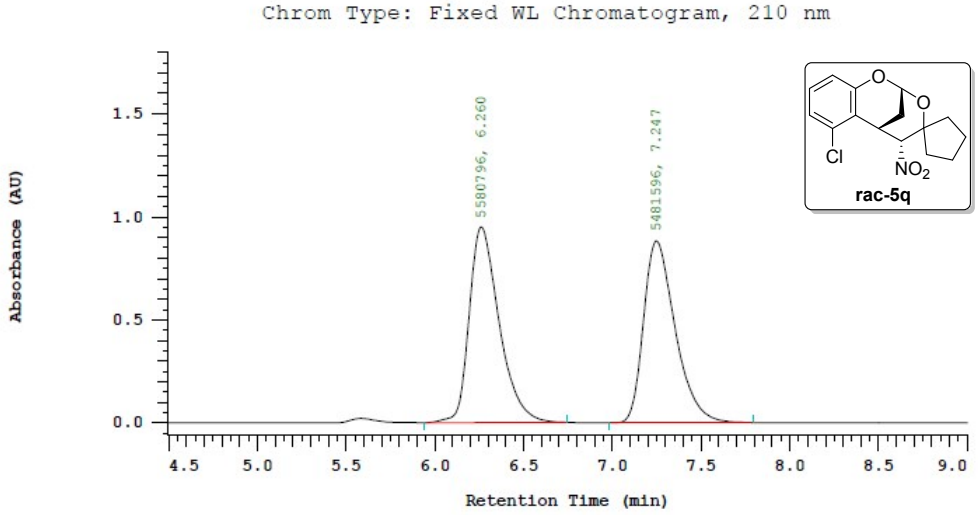
The ^{1}H NMR spectrum of 5q (500 MHz, $CDCl_3$)



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



The HPLC of racemic 5q



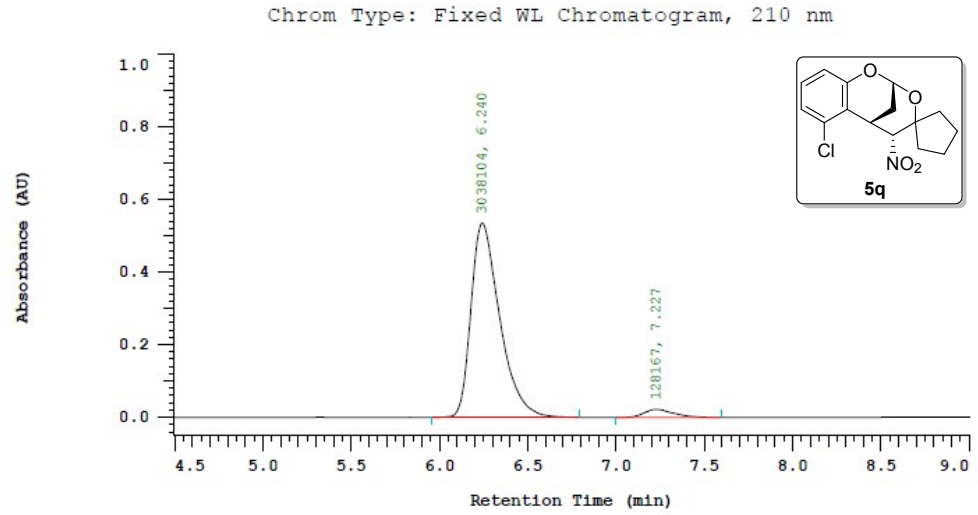
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.260	5580796	50.448	BB
2	7.247	5481596	49.552	BB
		11062392	100.000	

The HPLC of chiral 5q



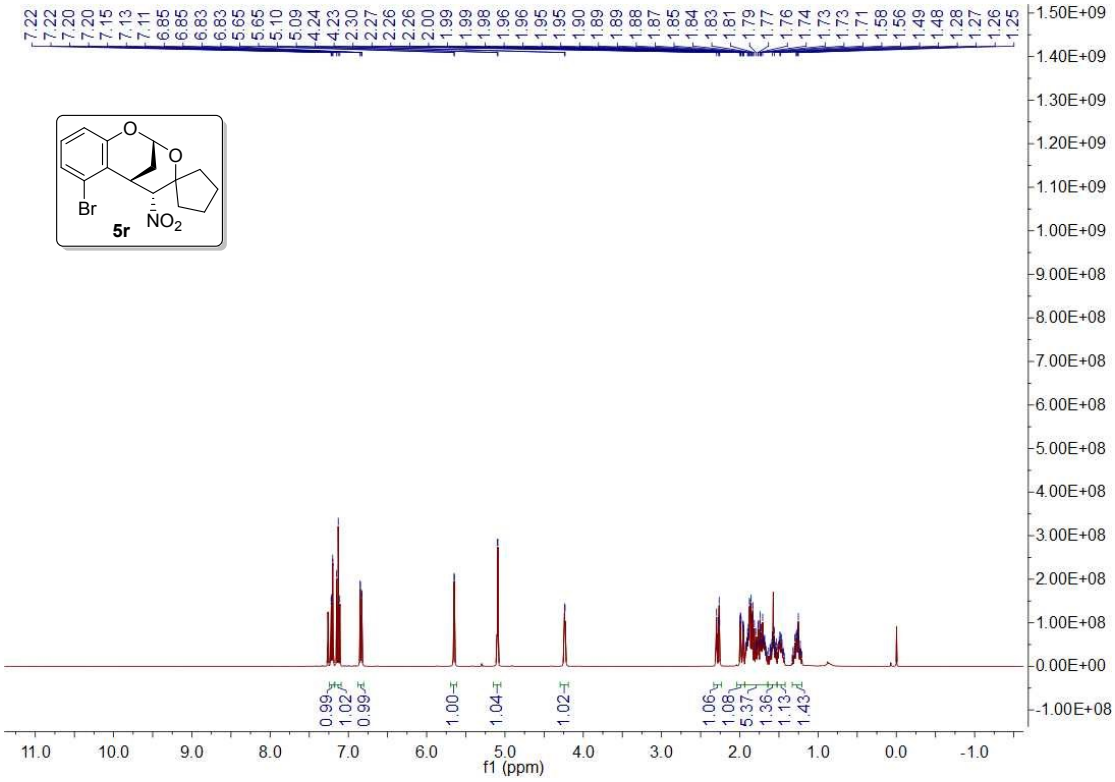
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

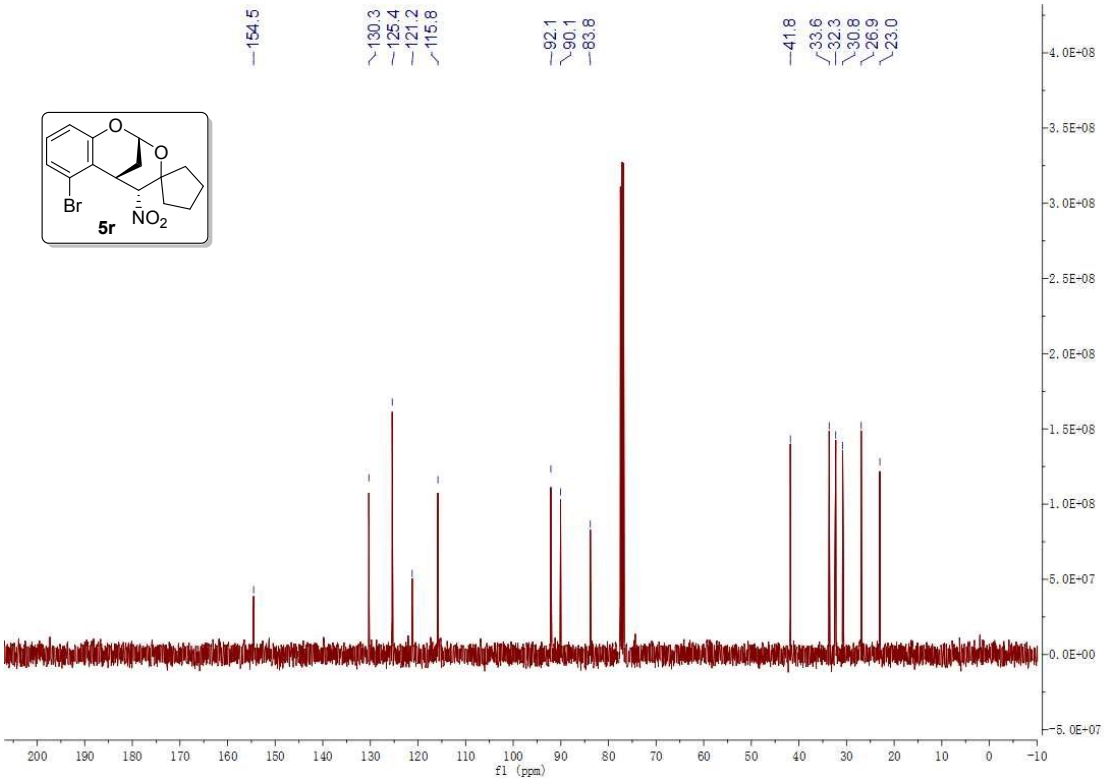
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.240	3038104	95.952	BB
2	7.227	128167	4.048	BB
		3166271	100.000	

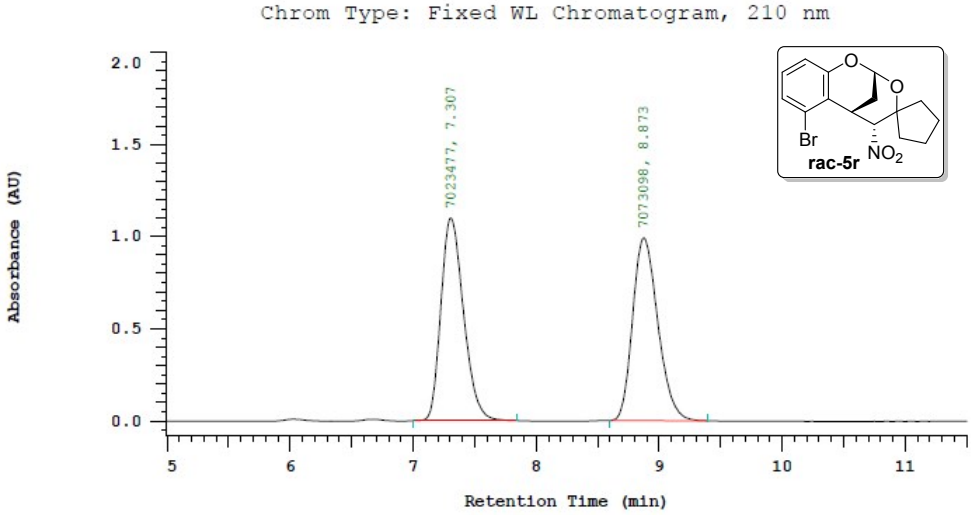
The ^{1}H NMR spectrum of 5r (500 MHz, $CDCl_3$)



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



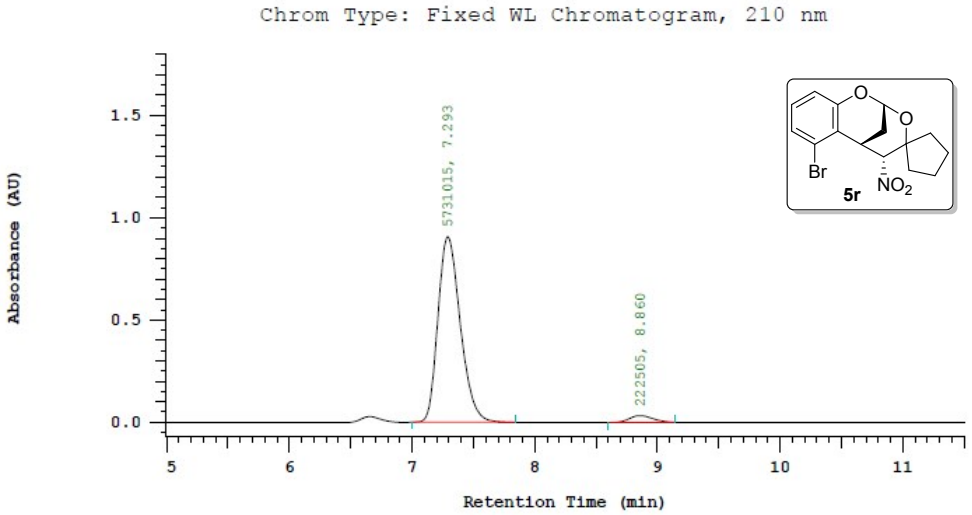
The HPLC of racemic 5r



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.307	7023477	49.824	BB
2	8.873	7073098	50.176	BB
		14096575	100.000	

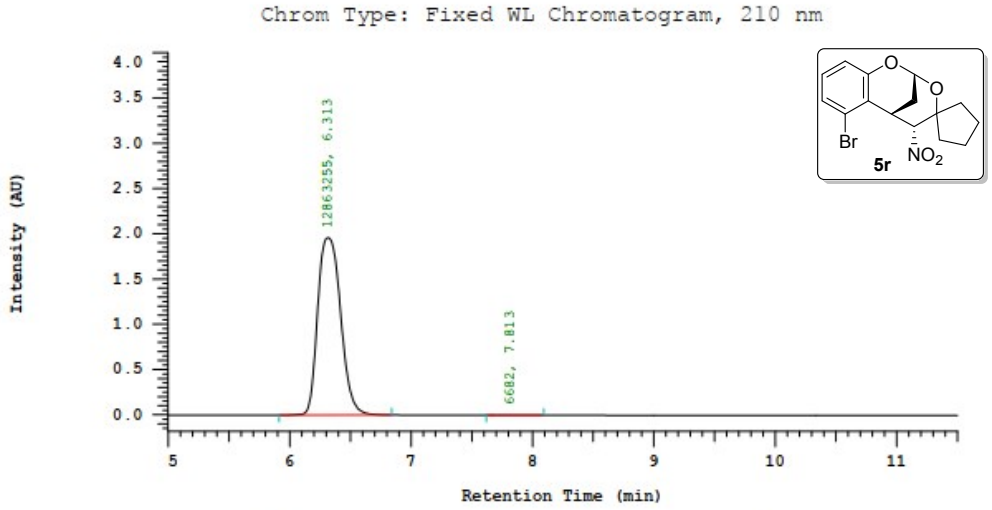
The HPLC of chiral 5r



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.293	5731015	96.263	BB
2	8.860	222505	3.737	BB
		5953520	100.000	

The HPLC of chiral 5r after recrystallization



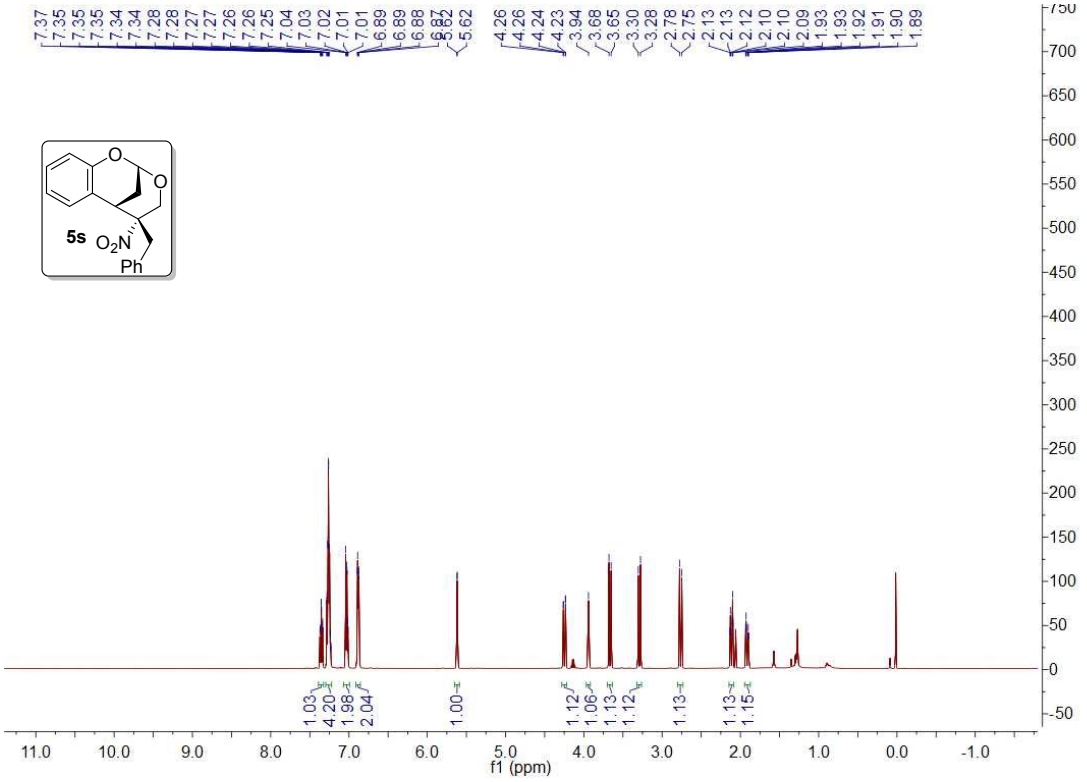
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

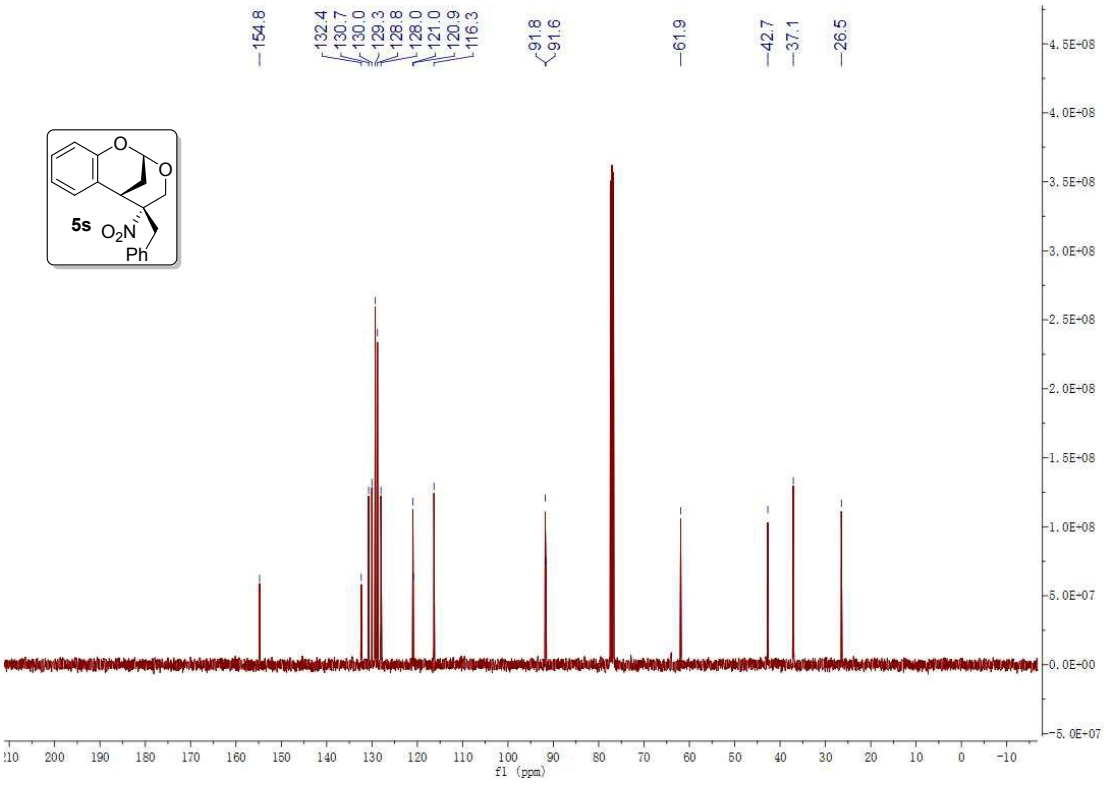
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.313	12863255	99.948	BB
2	7.813	6682	0.052	BB
		12869937	100.000	

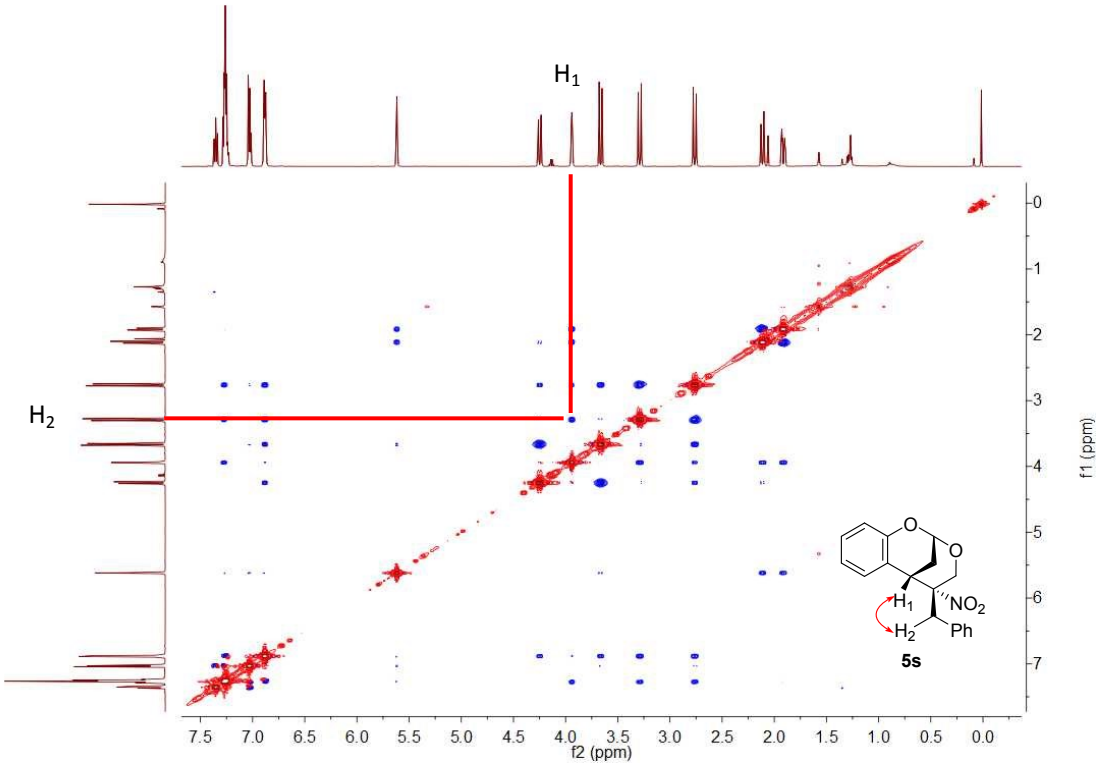
The ^{1}H NMR spectrum of 5s (500 MHz, $CDCl_3$)



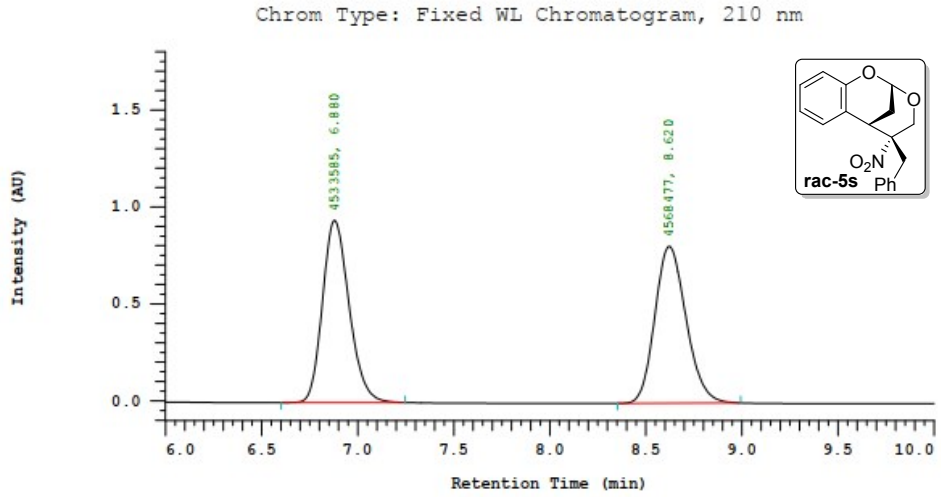
The ^{13}C NMR spectrum of 5s (101 MHz, $CDCl_3$)



The NOSEY spectrum of 5s (500 MHz, $CDCl_3$)



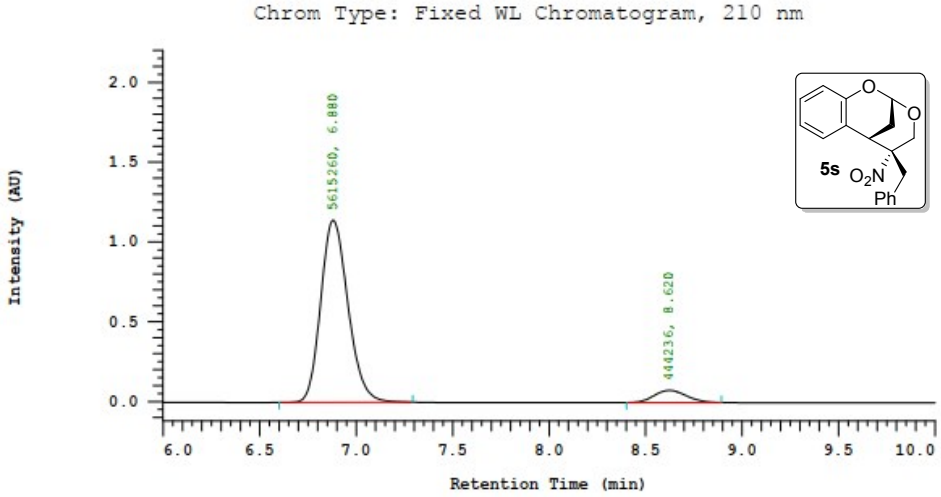
The HPLC of racemic 5s



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.880	4533585	49.808	BB
2	8.620	4568477	50.192	BB
		9102062	100.000	

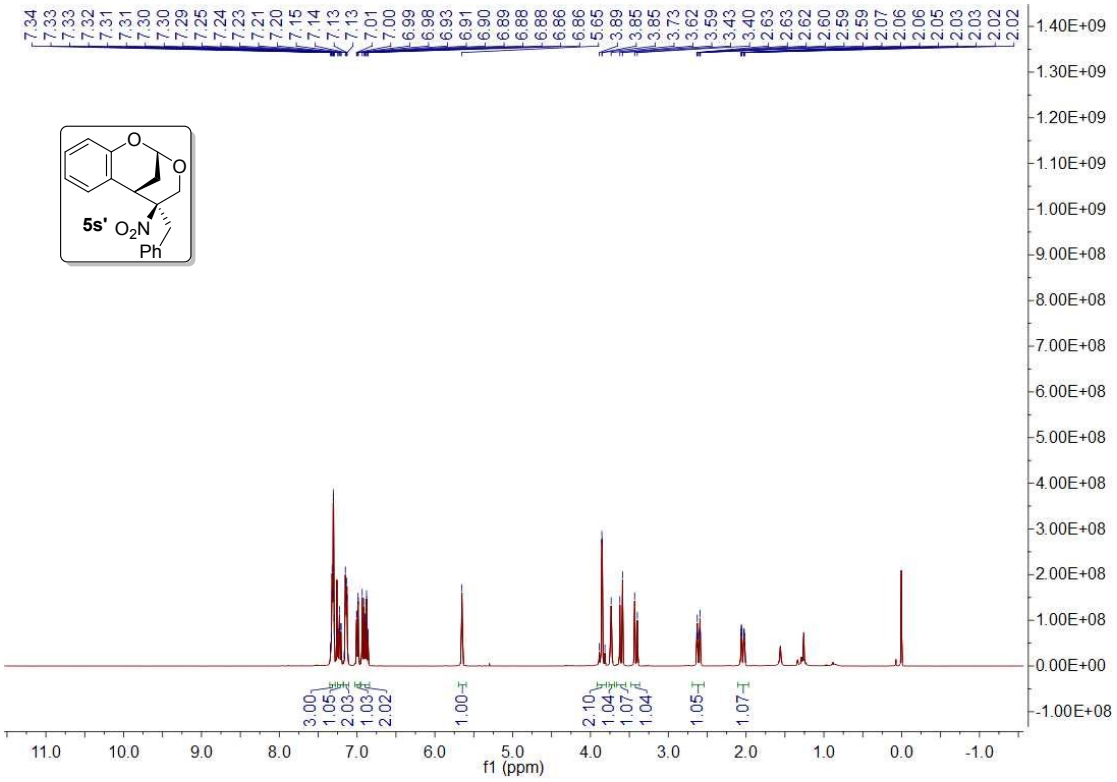
The HPLC of chiral 5s



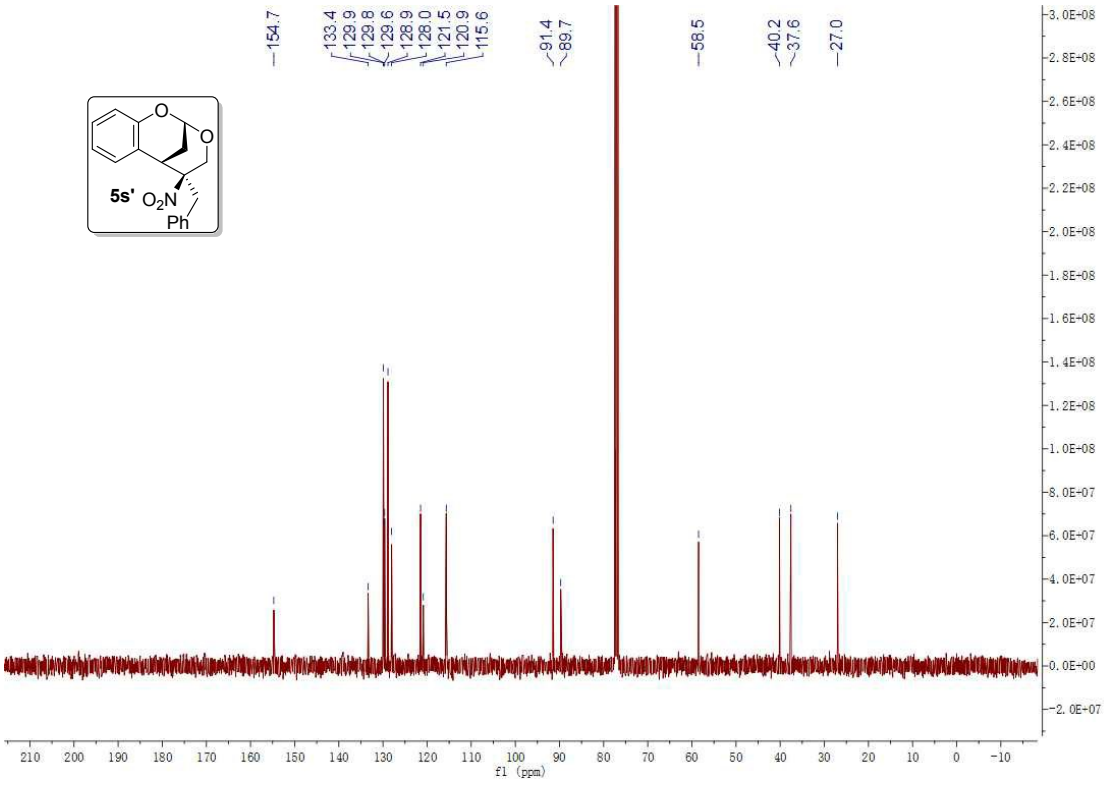
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.880	5615260	92.669	BB
2	8.620	444236	7.331	BB
		6059496	100.000	

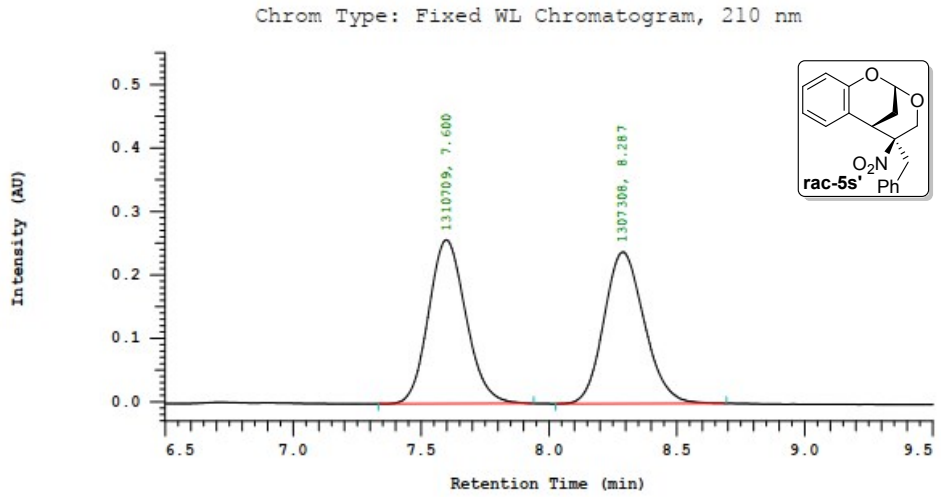
The ^{1}H NMR spectrum of 5s' (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5s' (101 MHz, $CDCl_3$)



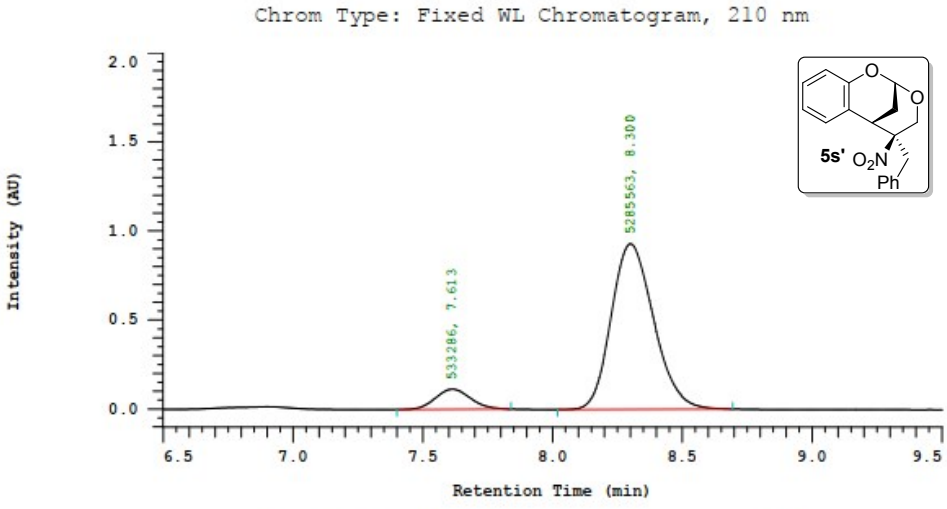
The HPLC of racemic 5s'



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.600	1310709	50.065	BB
2	8.287	1307308	49.935	BB
		2618017	100.000	

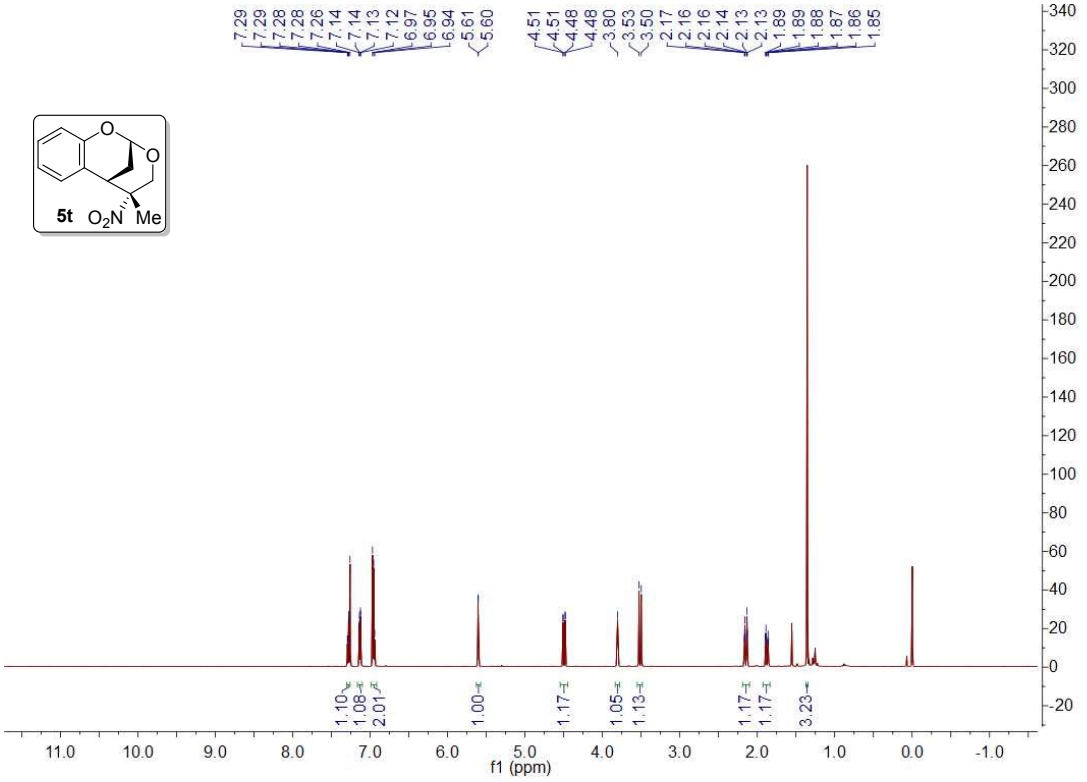
The HPLC of chiral 5s'



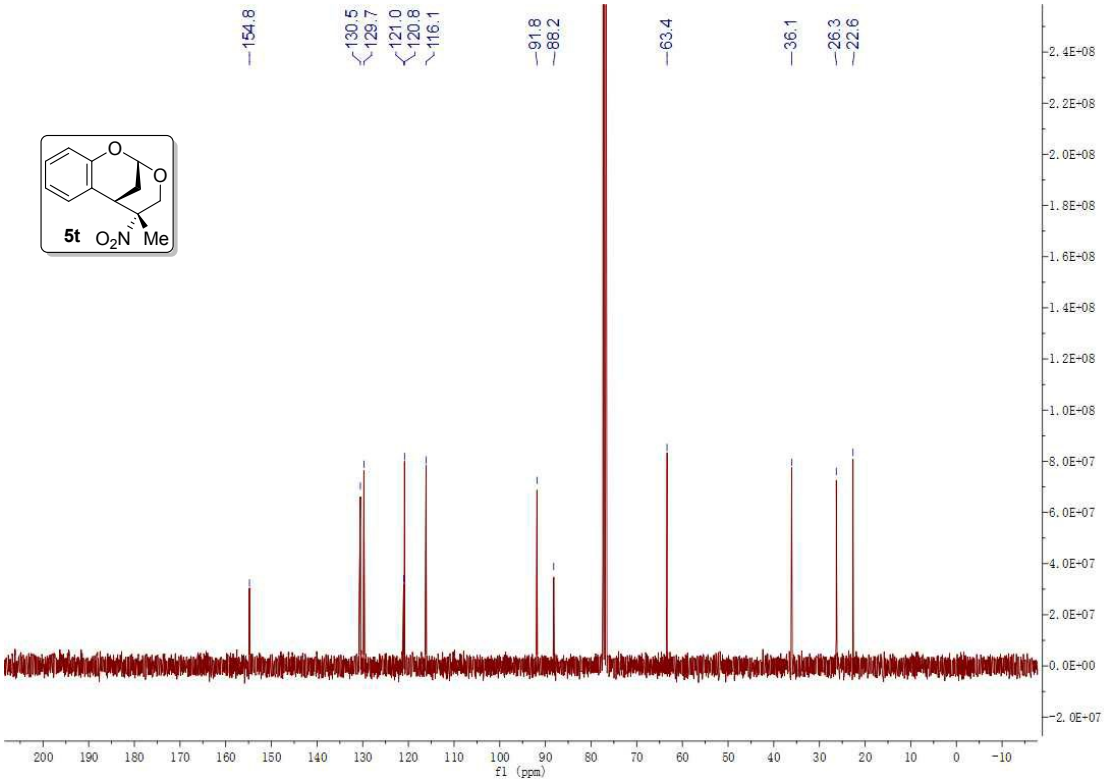
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.613	533286	9.165	BB
2	8.300	5285563	90.835	BB
		5818849	100.000	

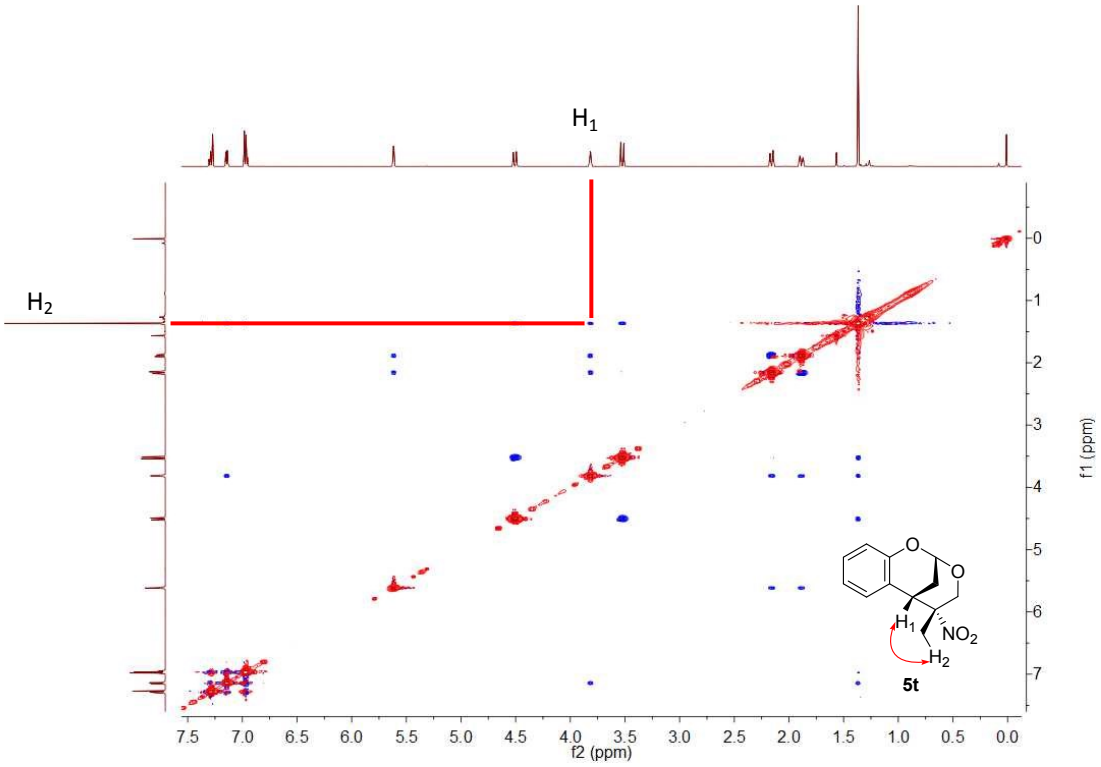
The ^{1}H NMR spectrum of 5t (500 MHz, $CDCl_3$)



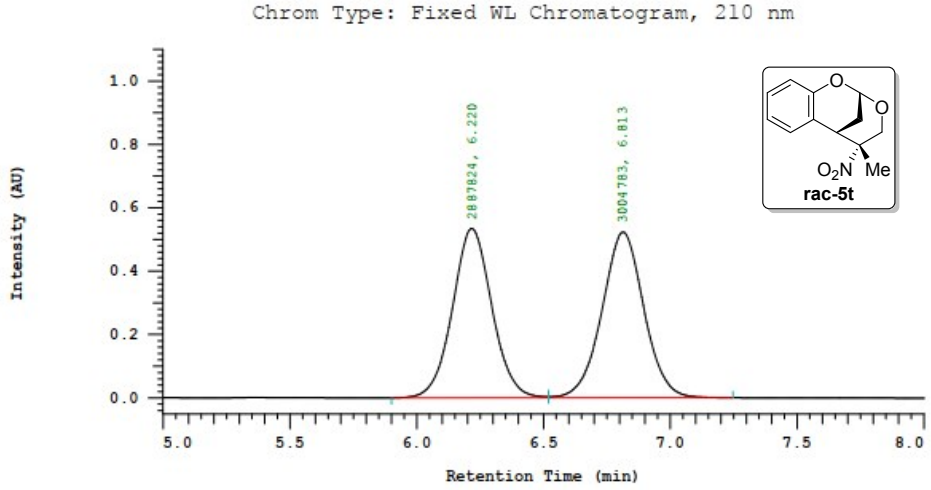
The ^{13}C NMR spectrum of 5t (101 MHz, $CDCl_3$)



The NOSEY spectrum of 5t (500 MHz, $CDCl_3$)



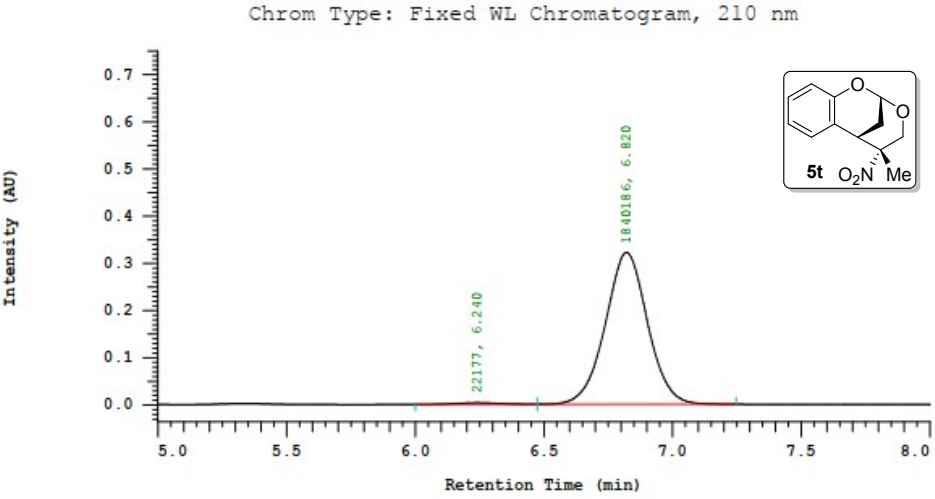
The HPLC of racemic 5t



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.220	2887824	49.008	BV
2	6.813	3004783	50.992	VB
		5892607	100.000	

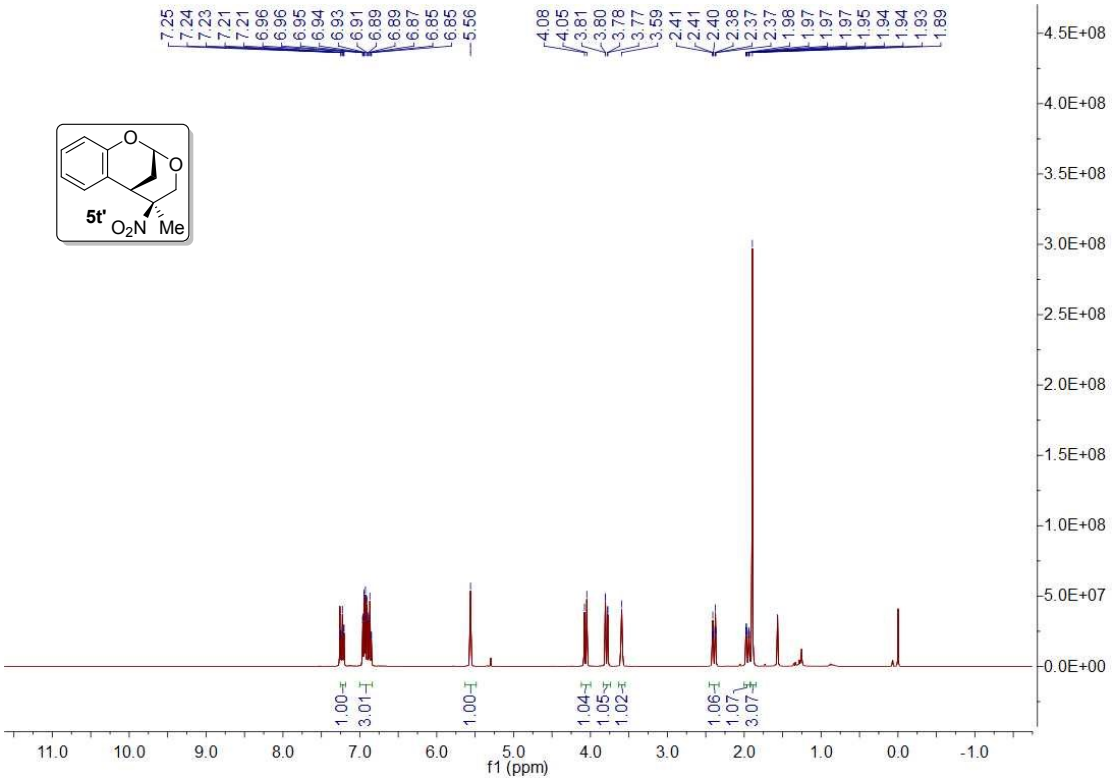
The HPLC of chiral 5t



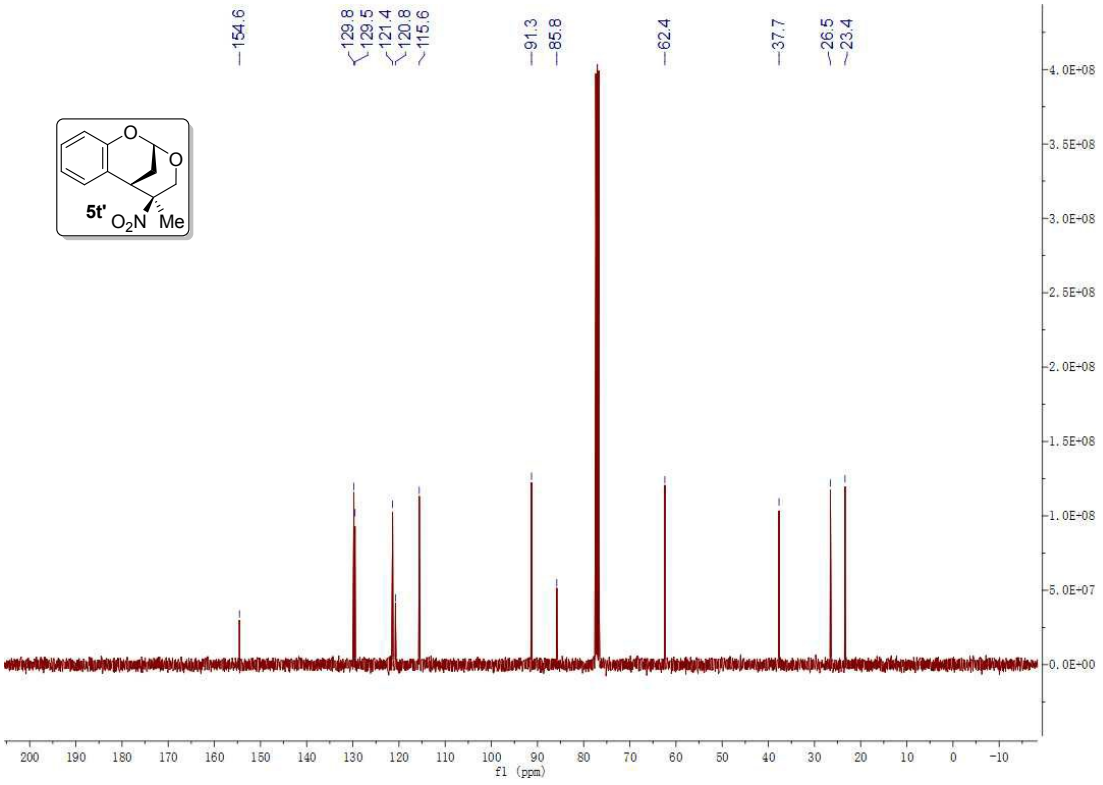
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.240	22177	1.191	BV
2	6.820	1840186	98.809	VB
		1862363	100.000	

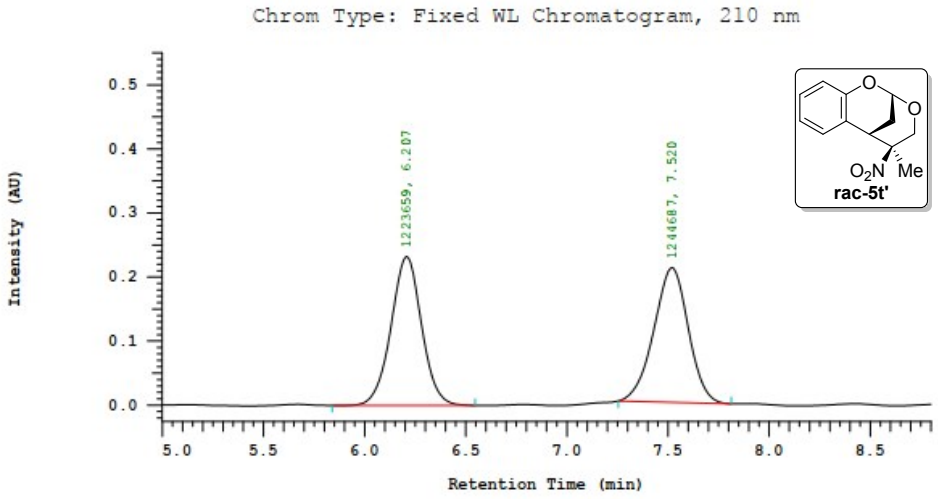
The ^{1}H NMR spectrum of 5t' (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5t' (101 MHz, $CDCl_3$)



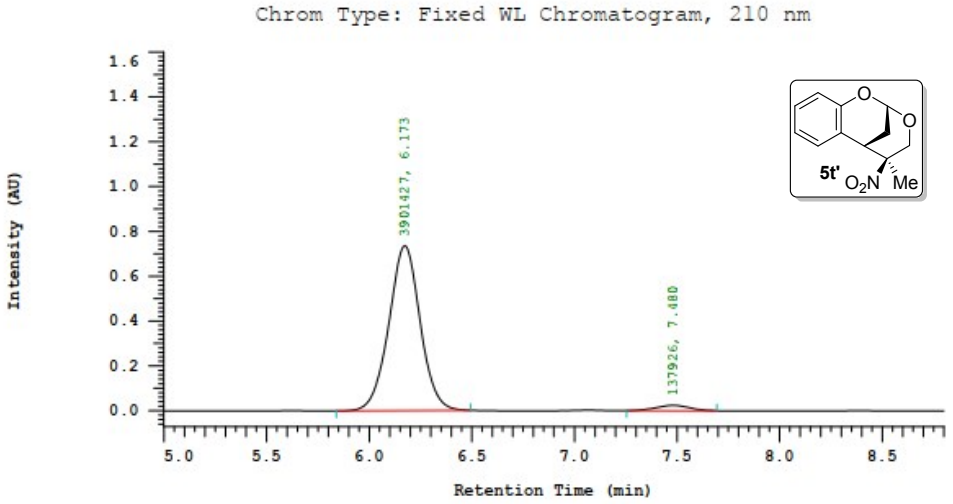
The HPLC of racemic 5t’



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.207	1223659	49.574	BB
2	7.520	1244687	50.426	BB
		2468346	100.000	

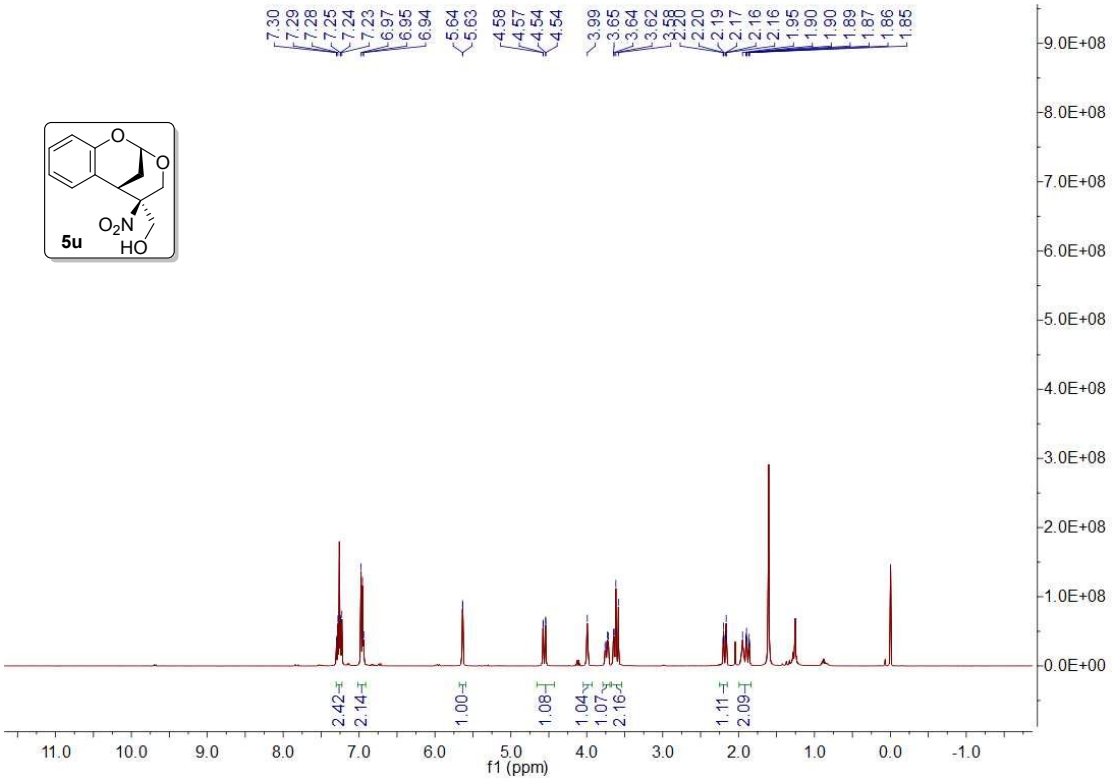
The HPLC of chiral 5t’



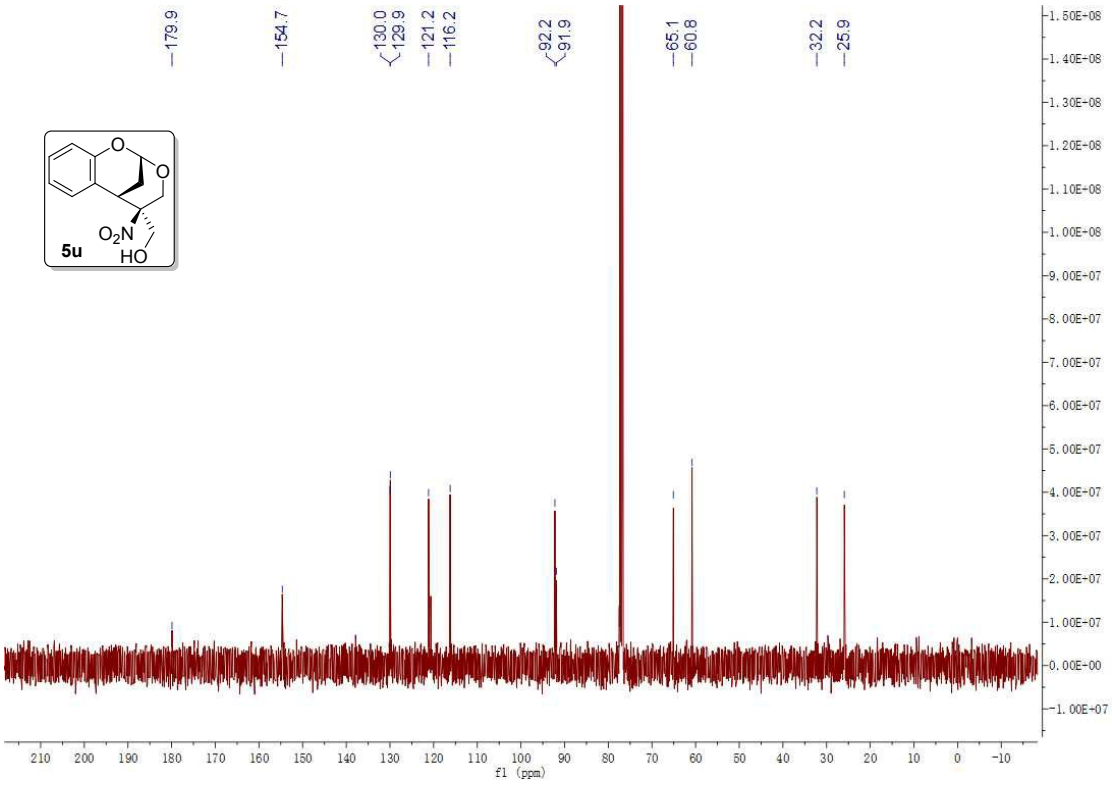
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.173	3901427	96.585	BB
2	7.480	137926	3.415	BB
		4039353	100.000	

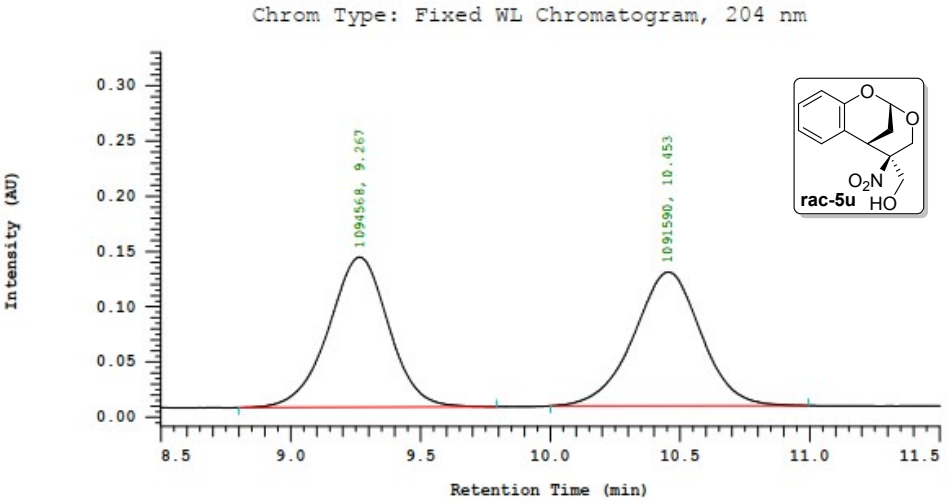
The ^{1}H NMR spectrum of 5u (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5u (101 MHz, $CDCl_3$)



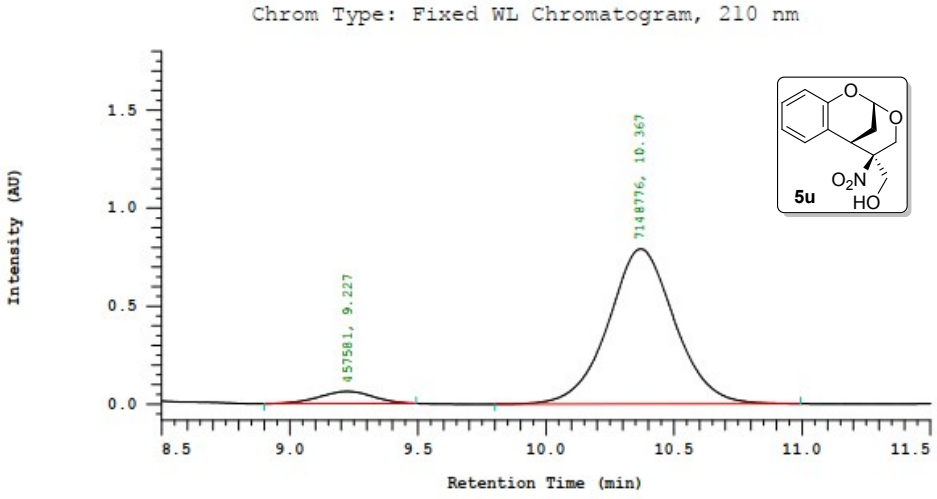
The HPLC of racemic 5u



Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.267	1094568	50.068	BB
2	10.453	1091590	49.932	BB
		2186158	100.000	

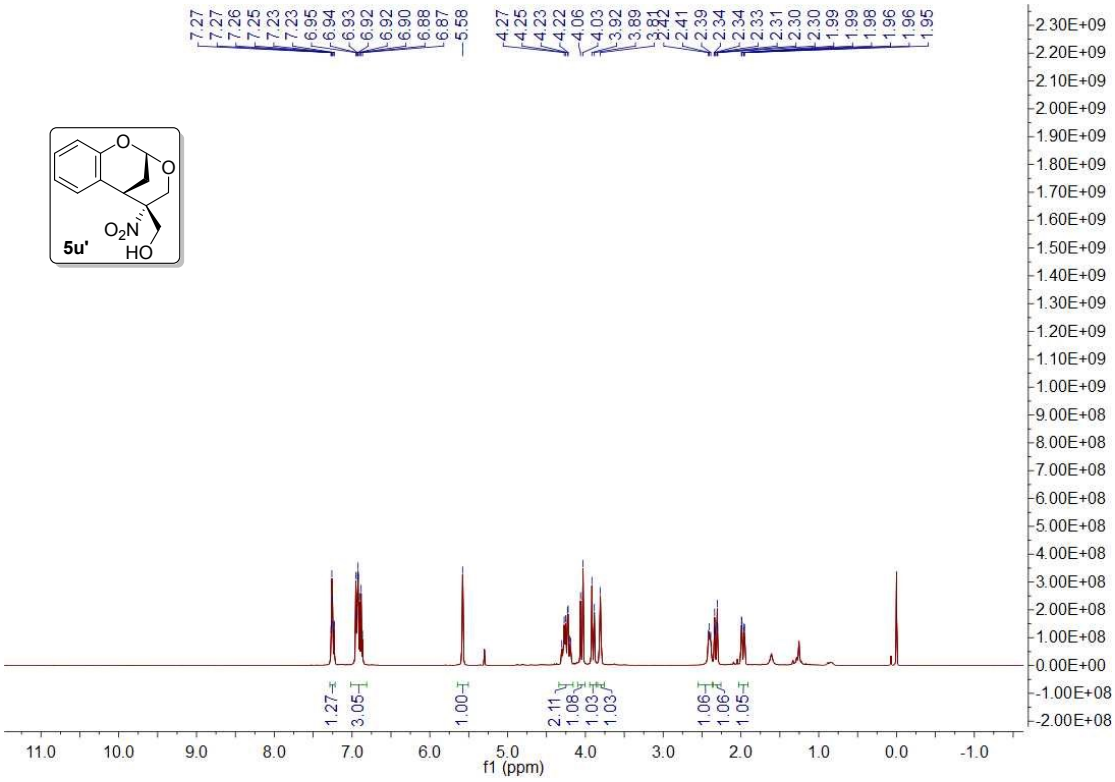
The HPLC of chiral 5u



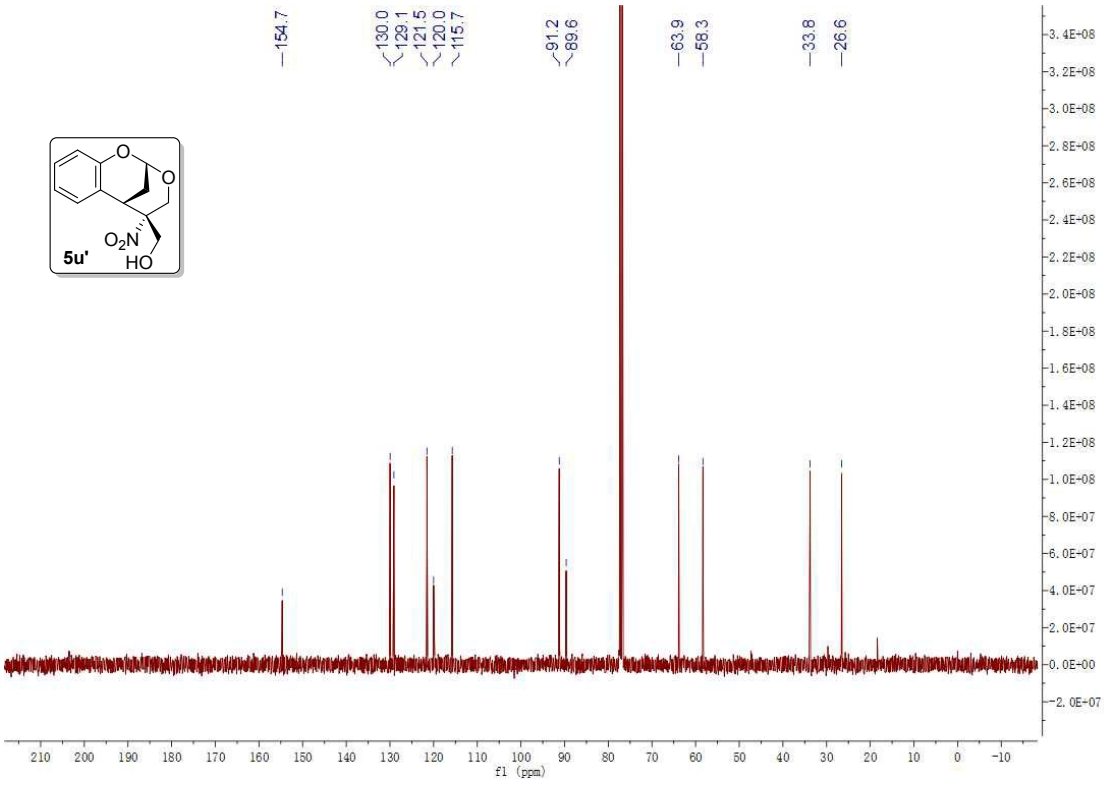
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.227	457581	6.016	BB
2	10.367	7148776	93.984	BB
		7606357	100.000	

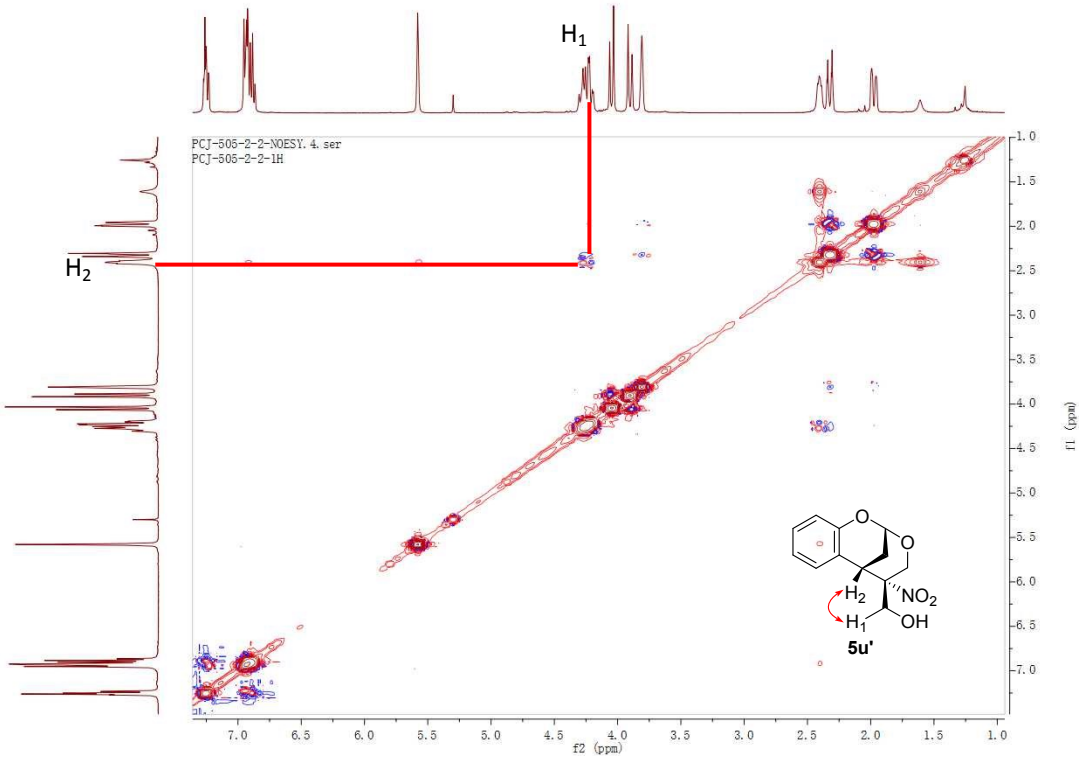
The ^{1}H NMR spectrum of 5u' (400 MHz, $CDCl_3$)



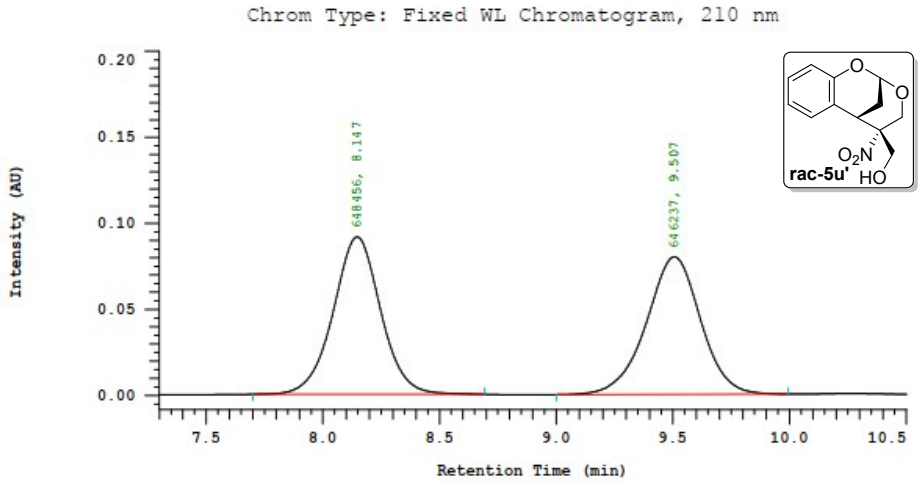
The ^{13}C NMR spectrum of 5u' (101 MHz, $CDCl_3$)



The NOSEY spectrum of 5u' (400 MHz, $CDCl_3$)



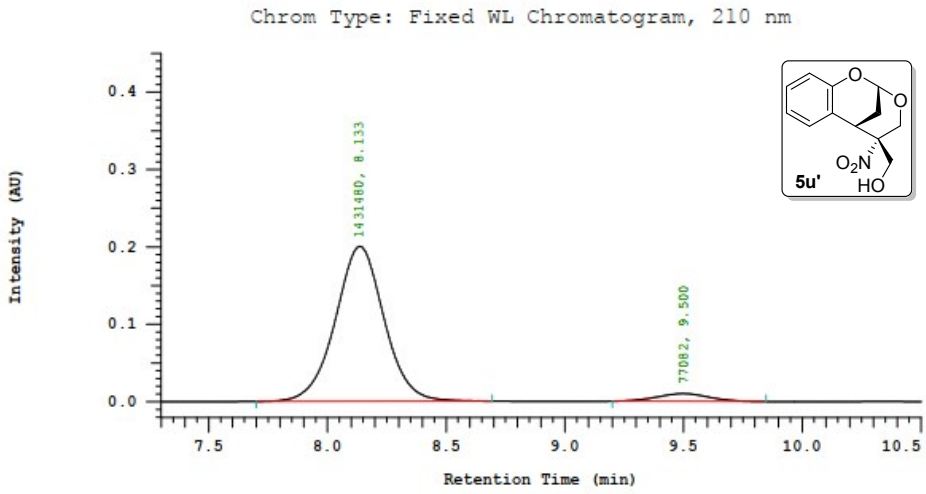
The HPLC of racemic 5u’



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.147	648456	50.086	BB
2	9.507	646237	49.914	BB
		1294693	100.000	

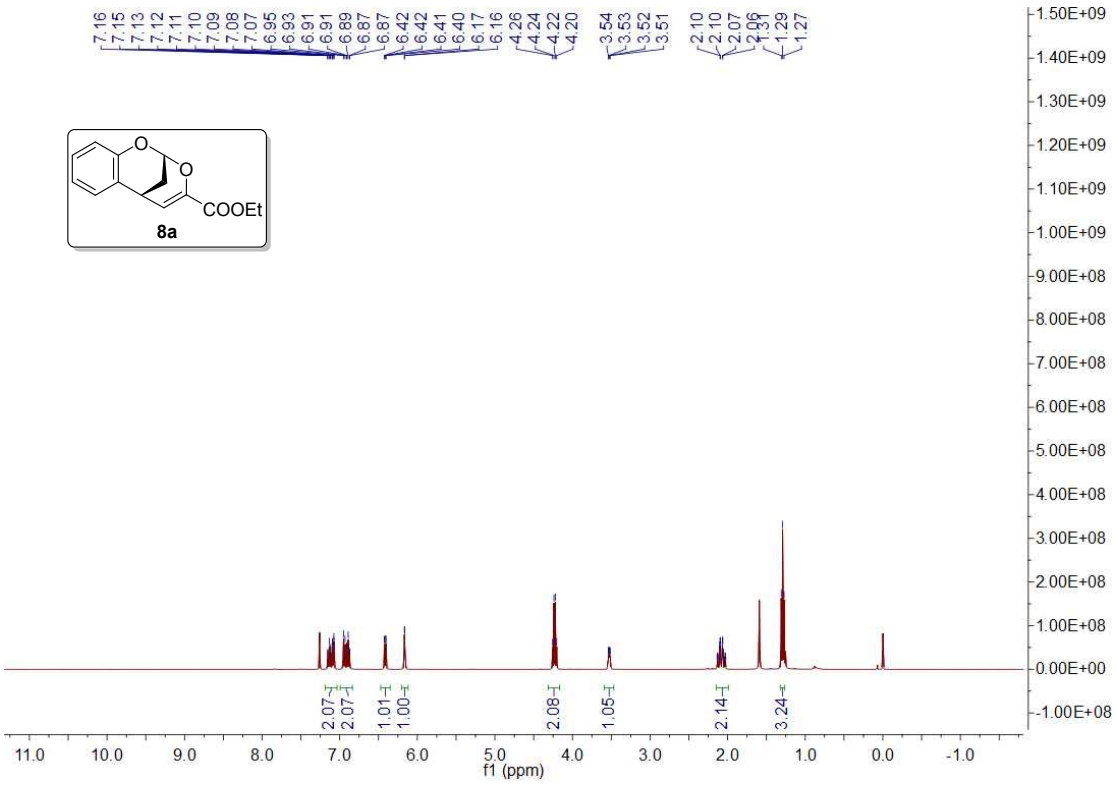
The HPLC of chiral 5u’



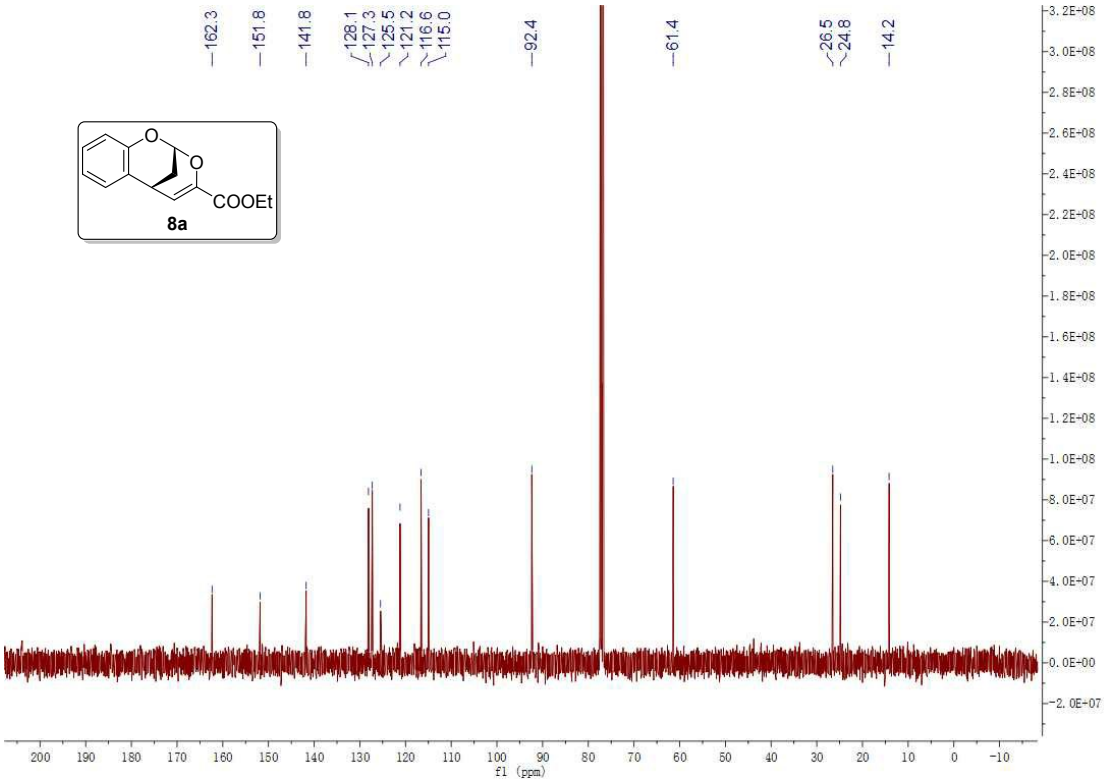
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.133	1431480	94.890	BB
2	9.500	77082	5.110	BB
		1508562	100.000	

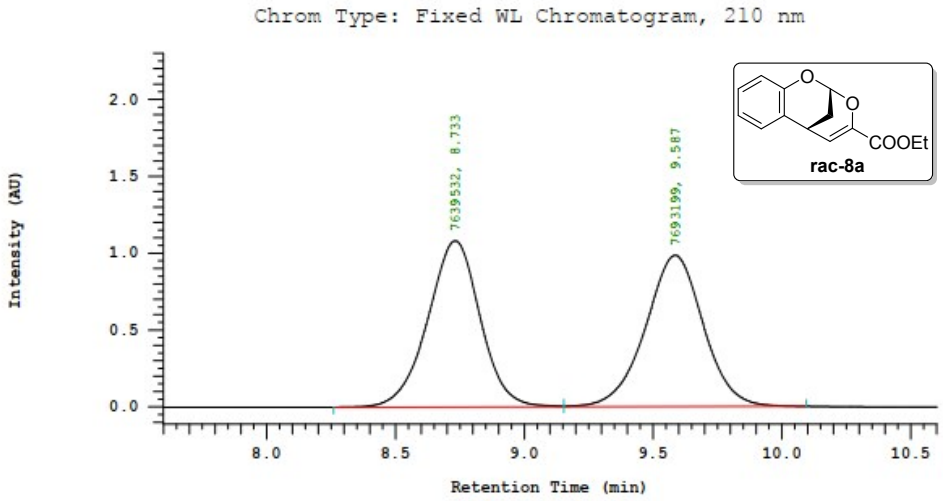
The ^{1}H NMR spectrum of 8a (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 8a (101 MHz, $CDCl_3$)



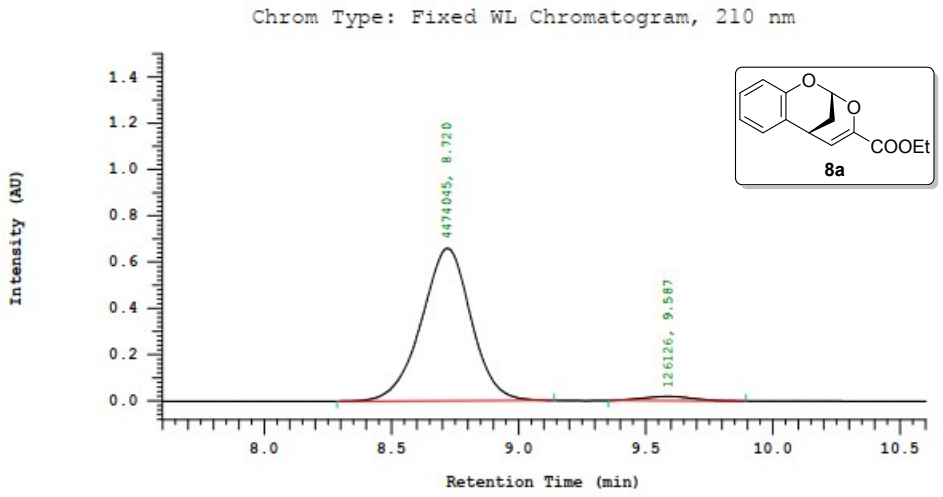
The HPLC of racemic 8a



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.733	7639532	49.825	BV
2	9.587	7693199	50.175	VB
		15332731	100.000	

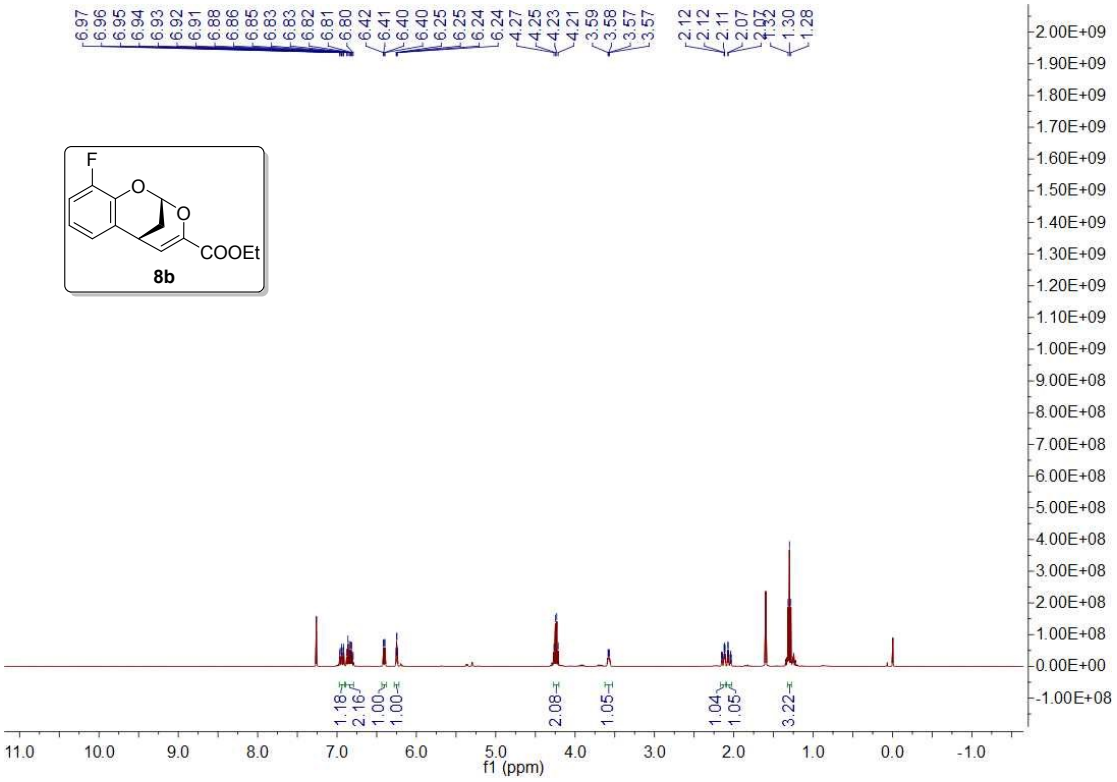
The HPLC of chiral 8a



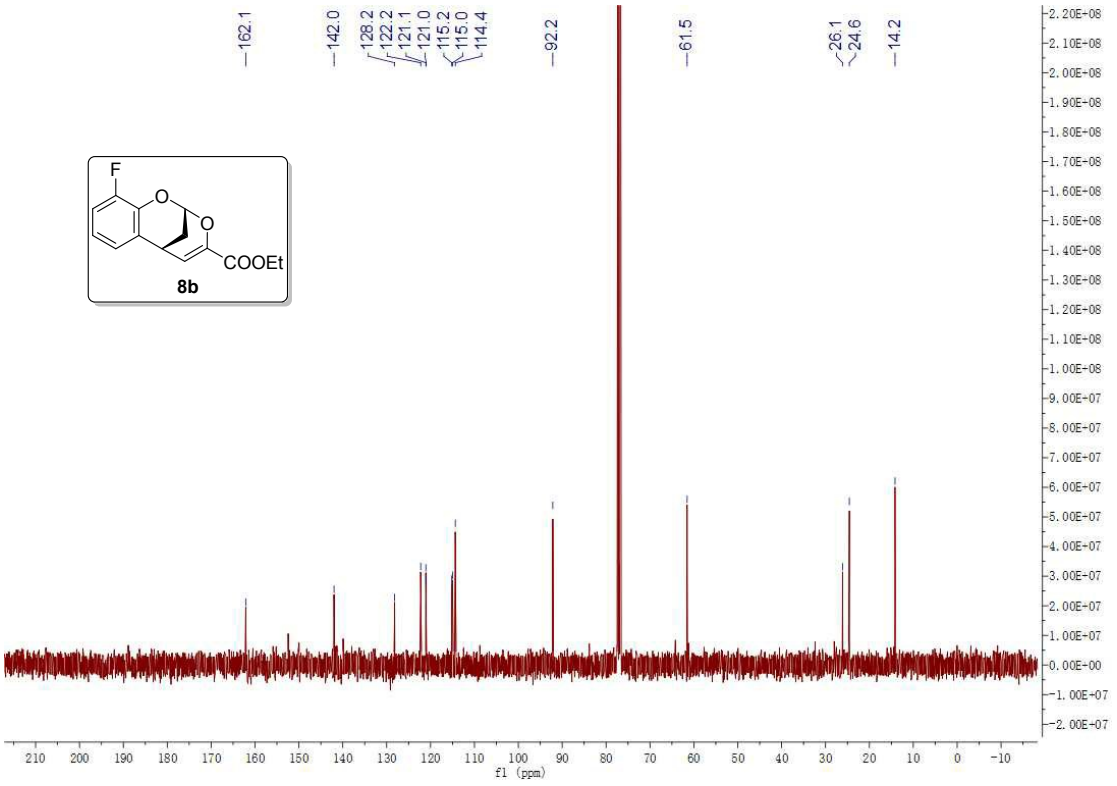
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.720	4474045	97.258	BB
2	9.587	126126	2.742	BB
		4600171	100.000	

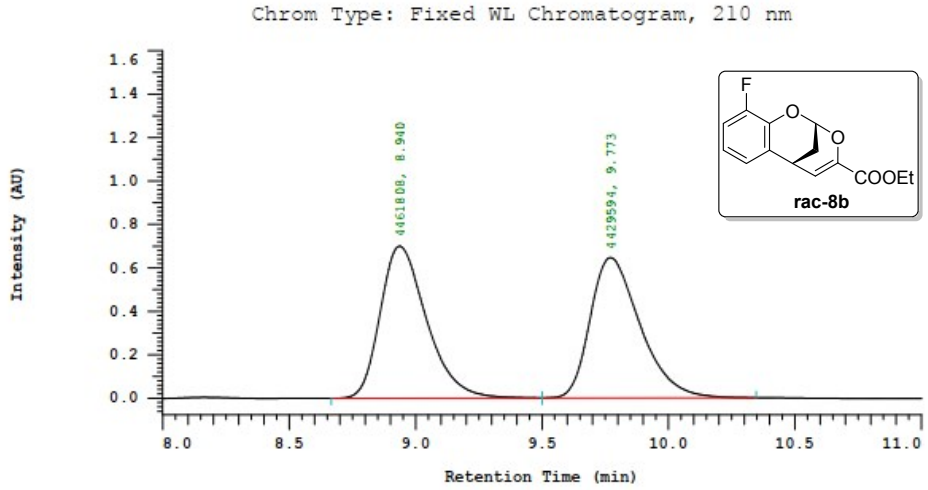
The ^{1}H NMR spectrum of 8b (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 8b (101 MHz, $CDCl_3$)



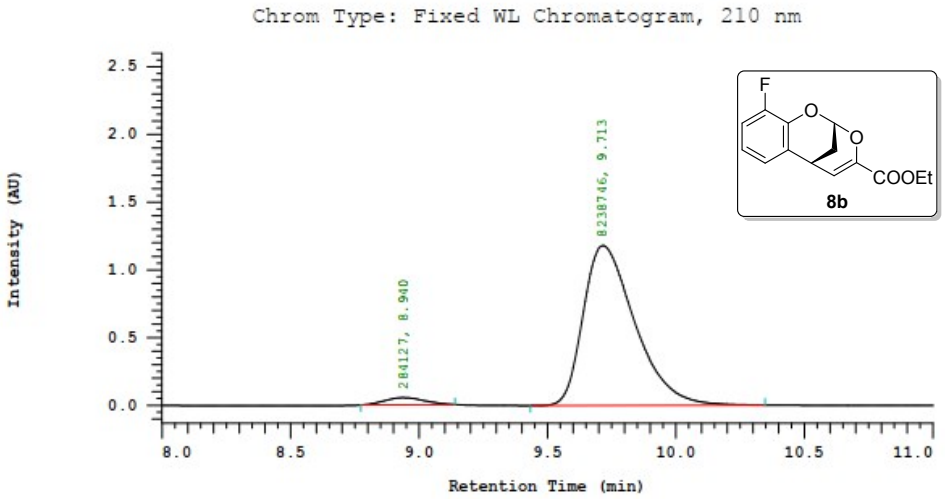
The HPLC of racemic 8b



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.940	4461808	50.181	BV
2	9.773	4429594	49.819	VB
		8891402	100.000	

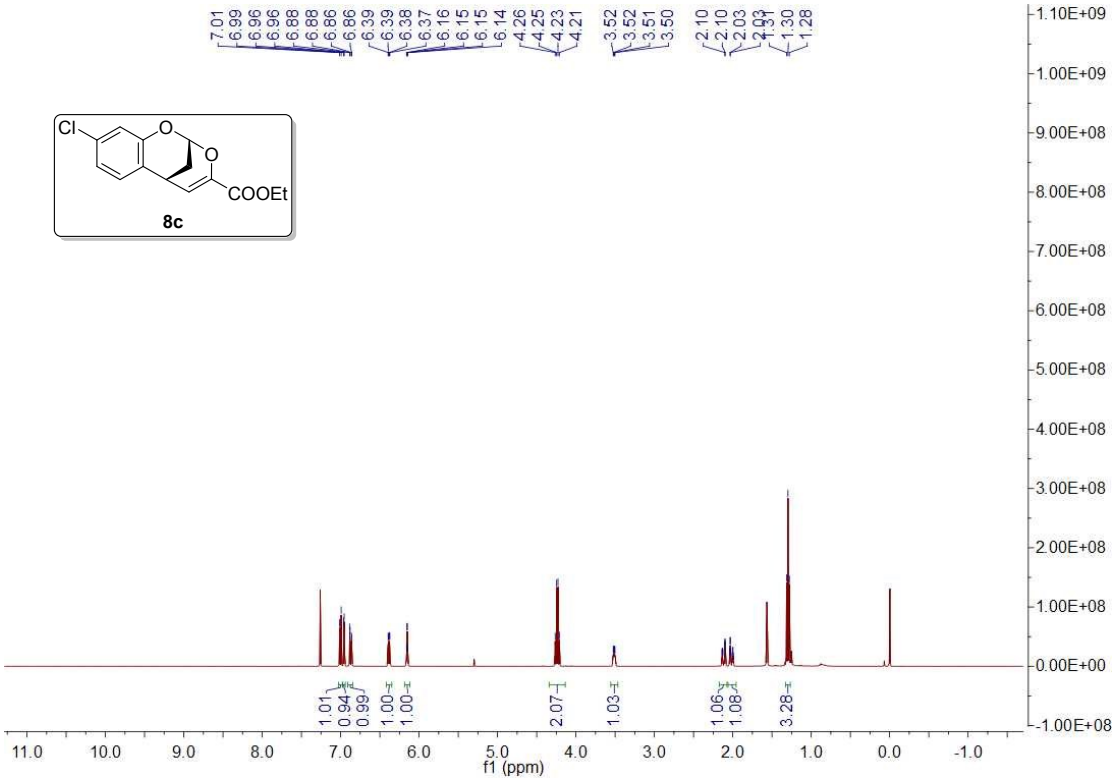
The HPLC of chiral 8b



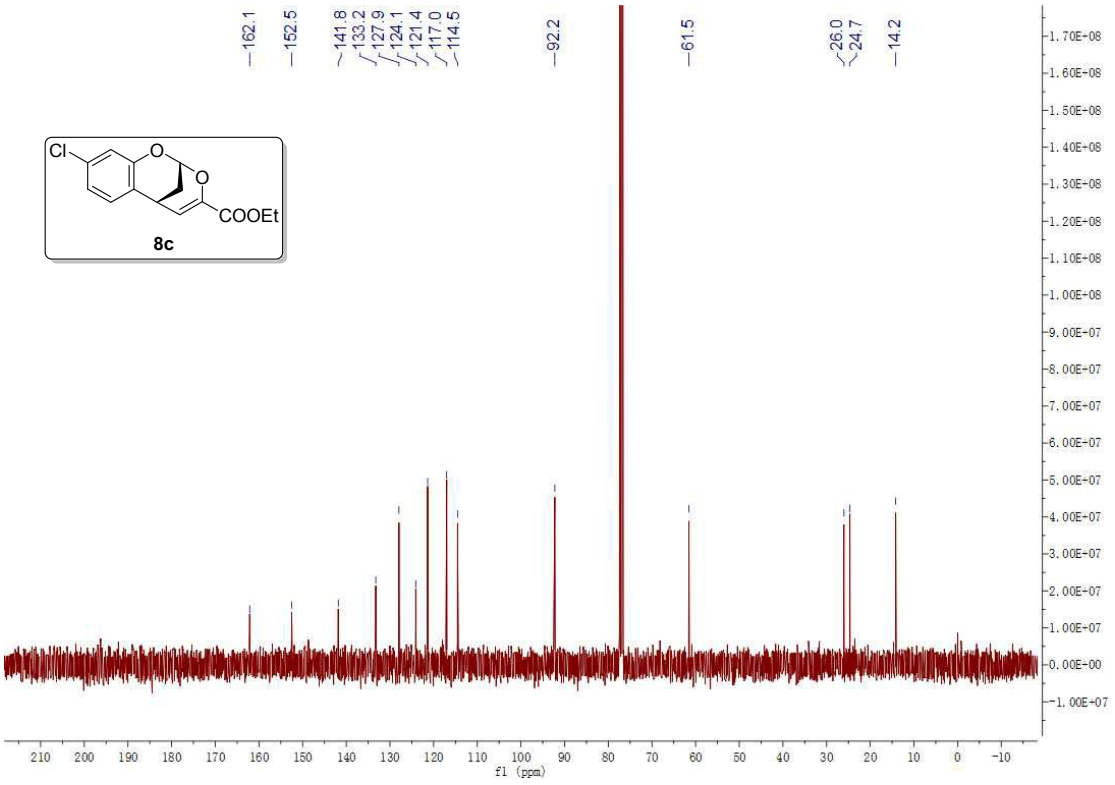
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.940	284127	3.334	BB
2	9.713	8238746	96.666	BB
		8522873	100.000	

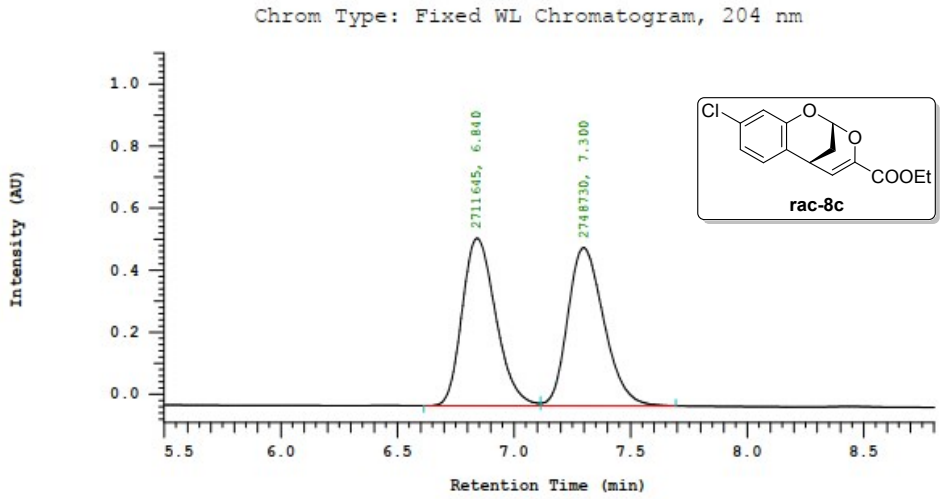
The ^{1}H NMR spectrum of 8c (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 8c (101 MHz, $CDCl_3$)



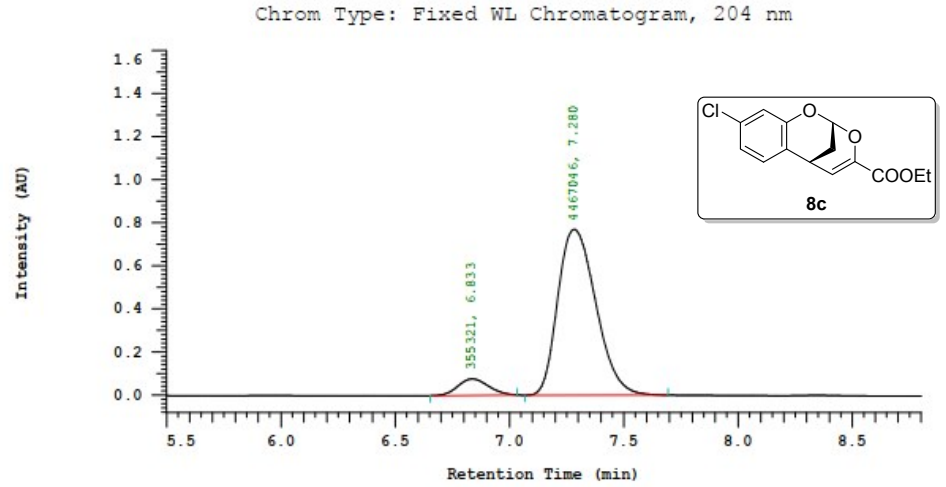
The HPLC of racemic 8c



Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.840	2711645	49.660	BV
2	7.300	2748730	50.340	VB
		5460375	100.000	

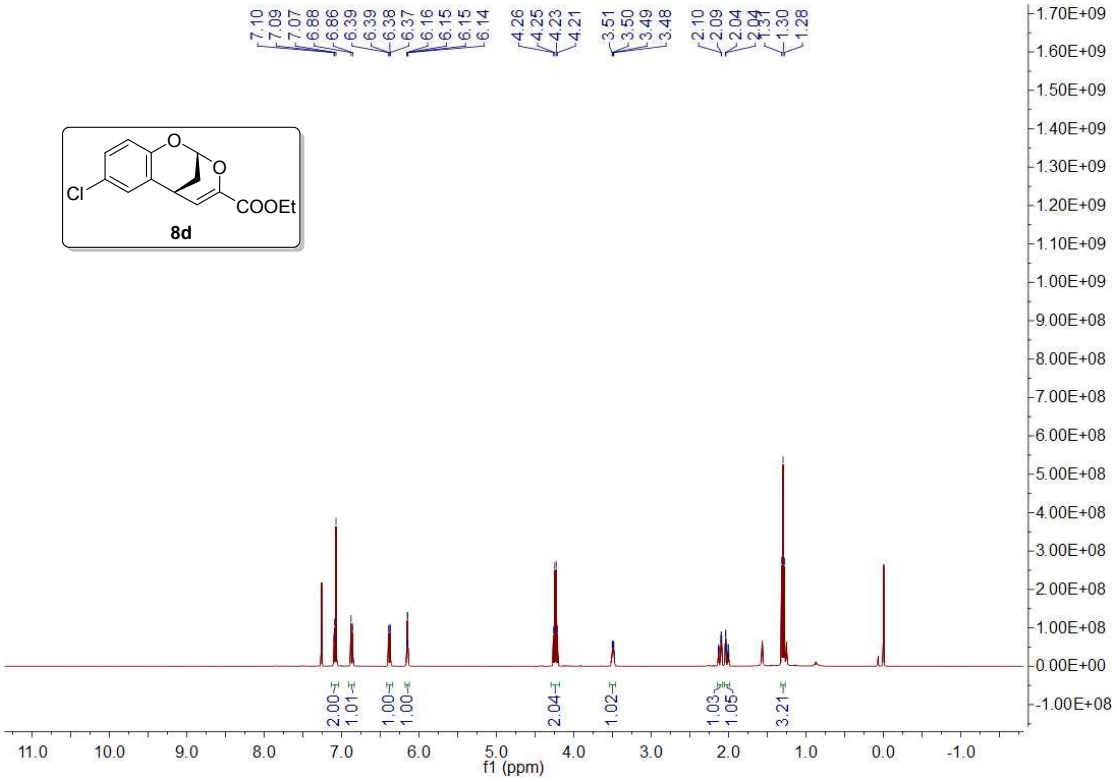
The HPLC of chiral 8c



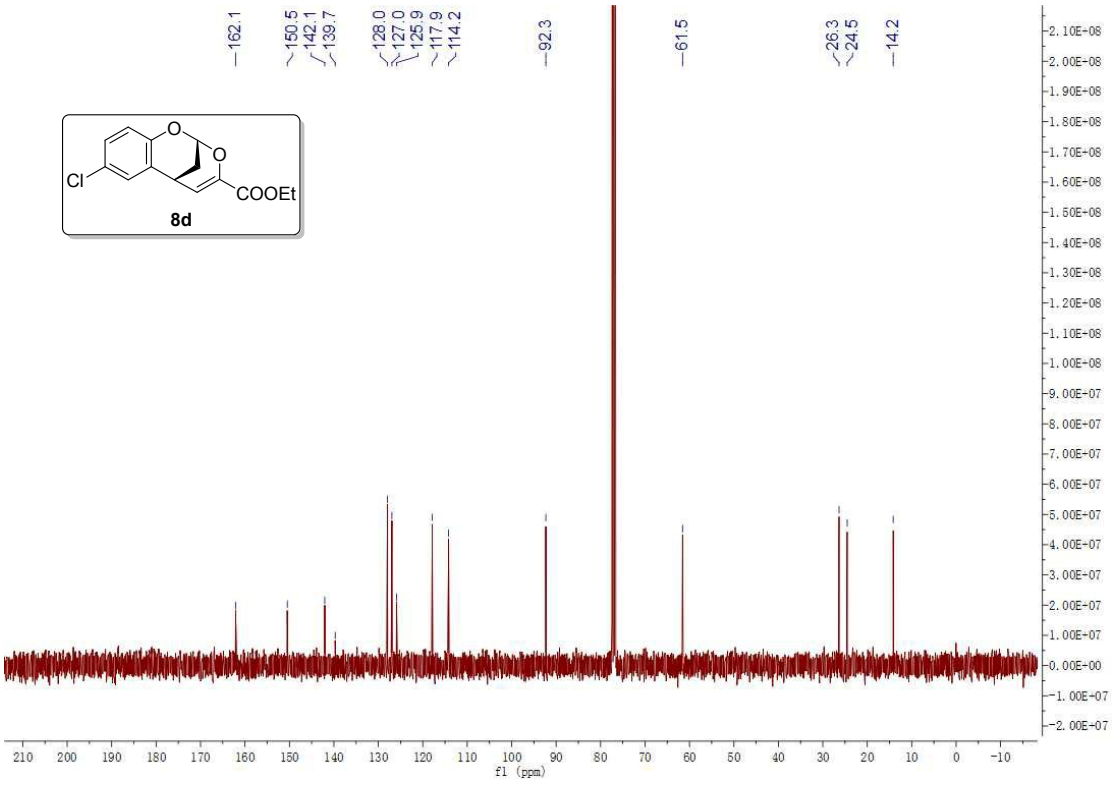
Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.833	355321	7.368	BB
2	7.280	4467046	92.632	BB
		4822367	100.000	

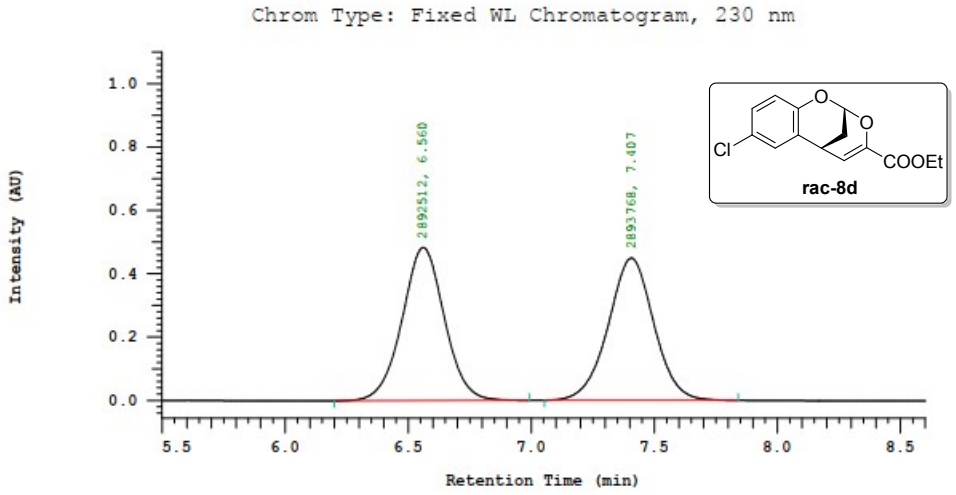
The ^{1}H NMR spectrum of 8d (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 8d (101 MHz, $CDCl_3$)



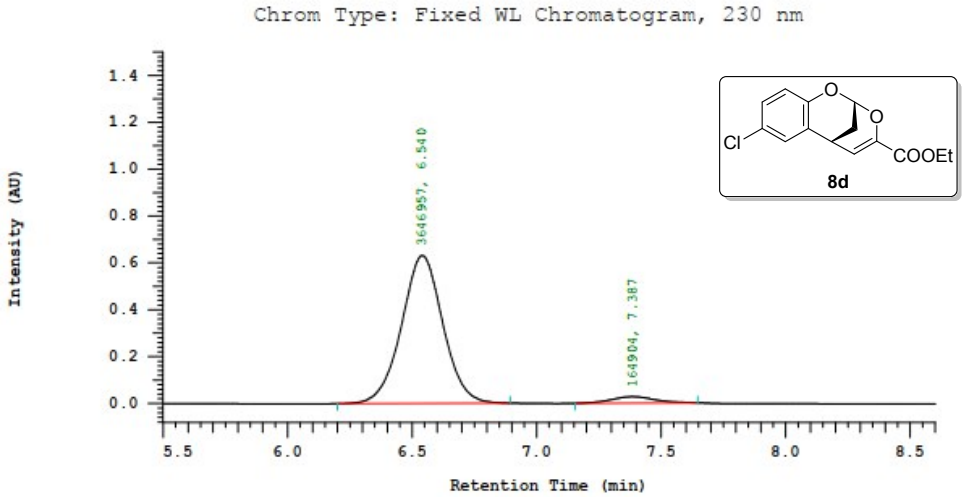
The HPLC of racemic 8d



Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.560	2892512	49.989	BB
2	7.407	2893768	50.011	BB
		5786280	100.000	

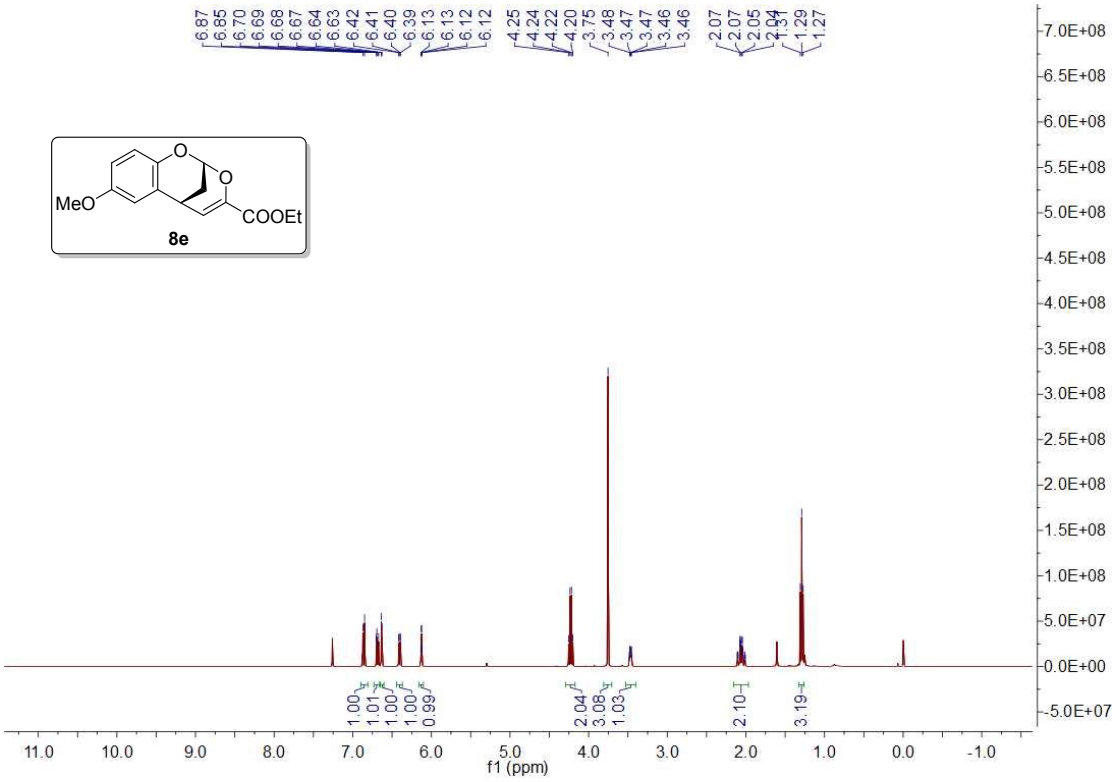
The HPLC of chiral 8d



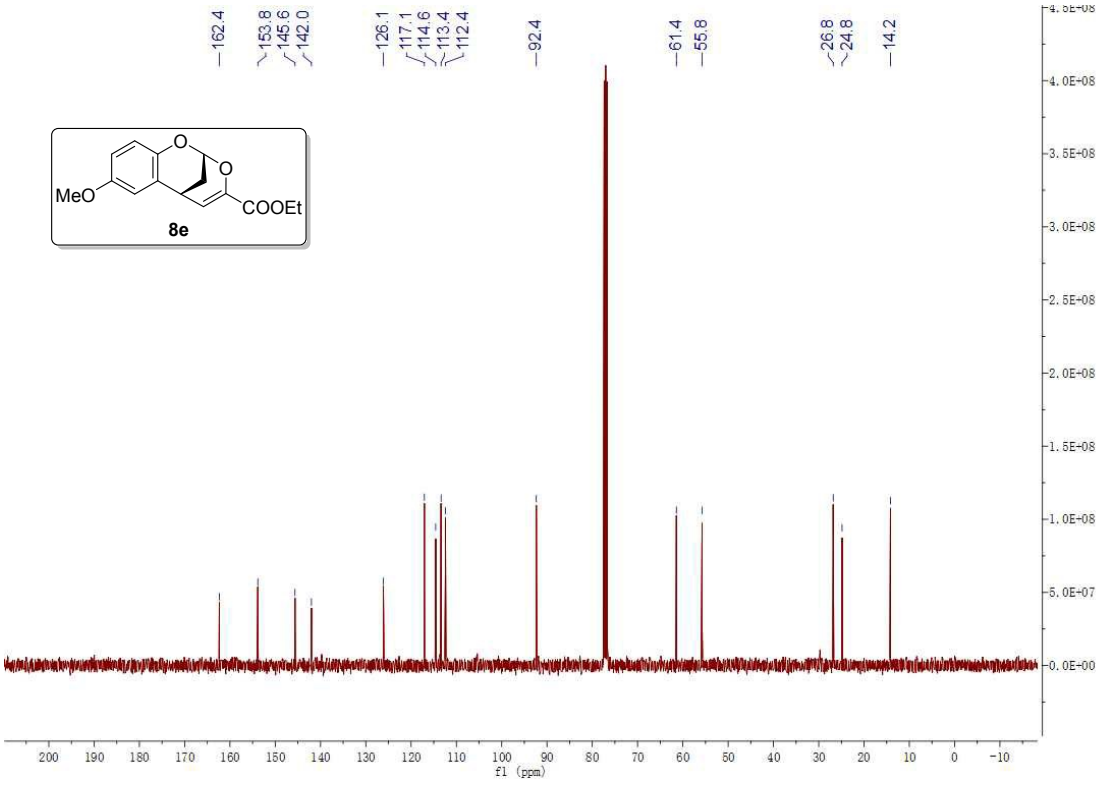
Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.540	3646957	95.674	BB
2	7.387	164904	4.326	BB
		3811861	100.000	

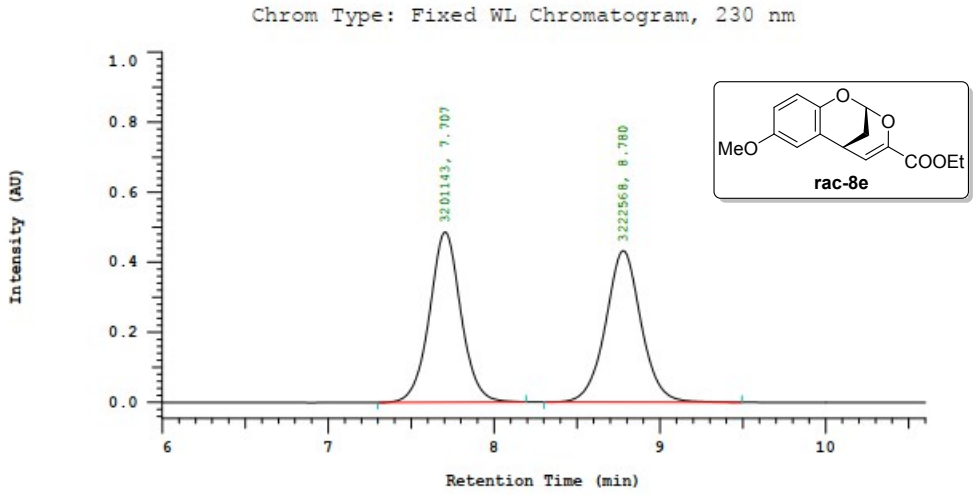
The ^{1}H NMR spectrum of 8e (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 8e (101 MHz, $CDCl_3$)



The HPLC of racemic 8e



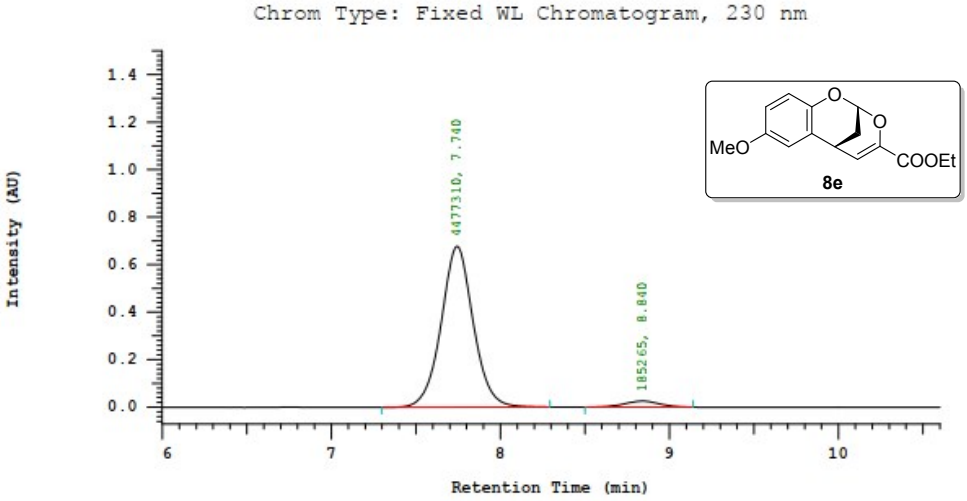
Chrom Type: Fixed WL Chromatogram, 230 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.707	3201143	49.833	BB
2	8.780	3222568	50.167	BB
		6423711	100.000	

The HPLC of chiral 8e



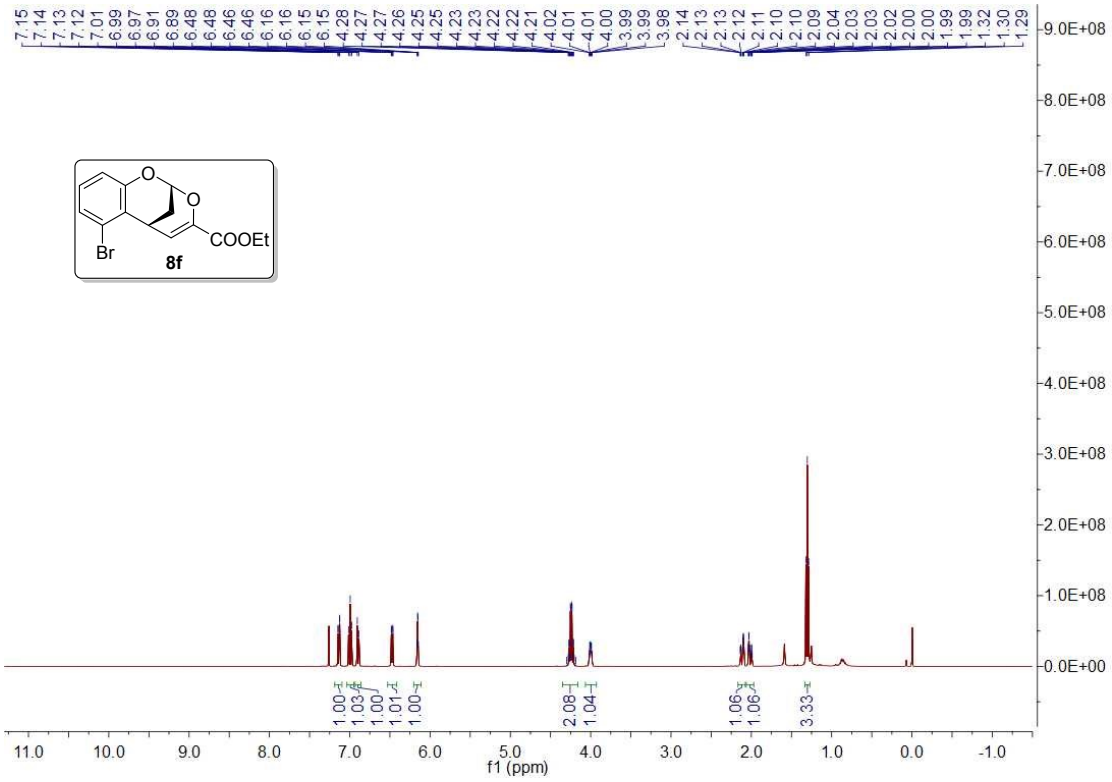
Chrom Type: Fixed WL Chromatogram, 230 nm

Peak Quantitation: AREA

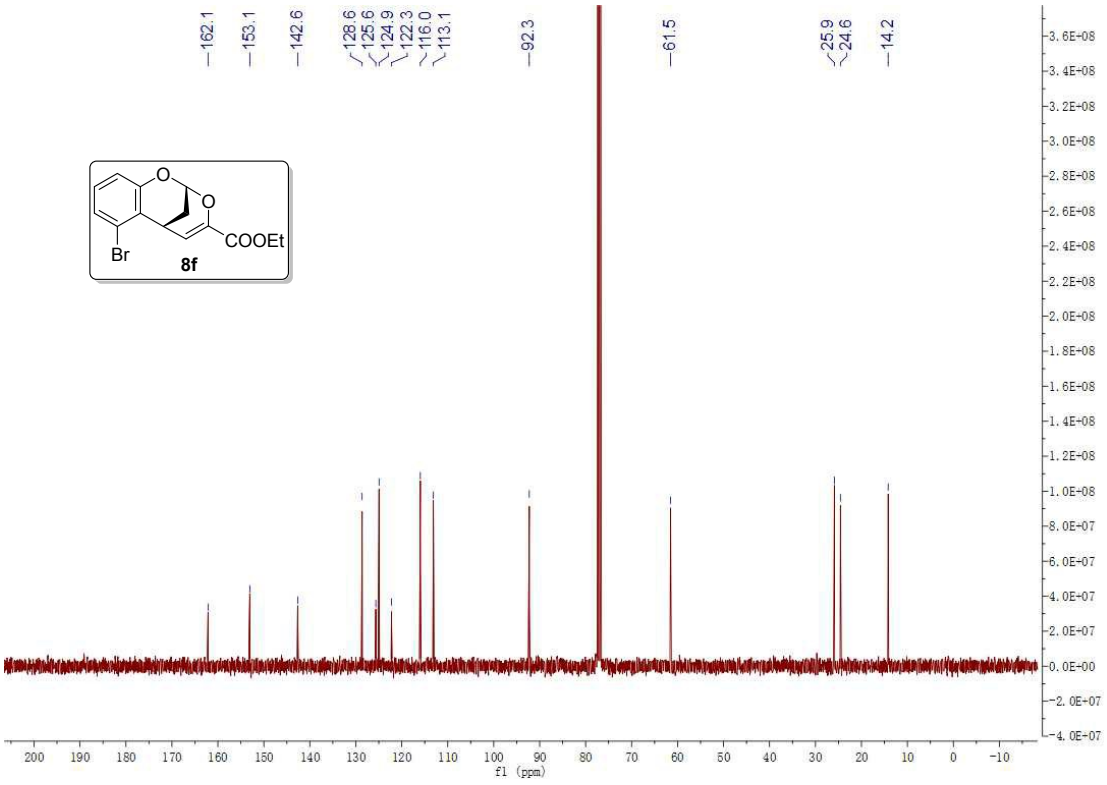
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.740	4477310	96.027	BB
2	8.840	185265	3.973	BB
		4662575	100.000	

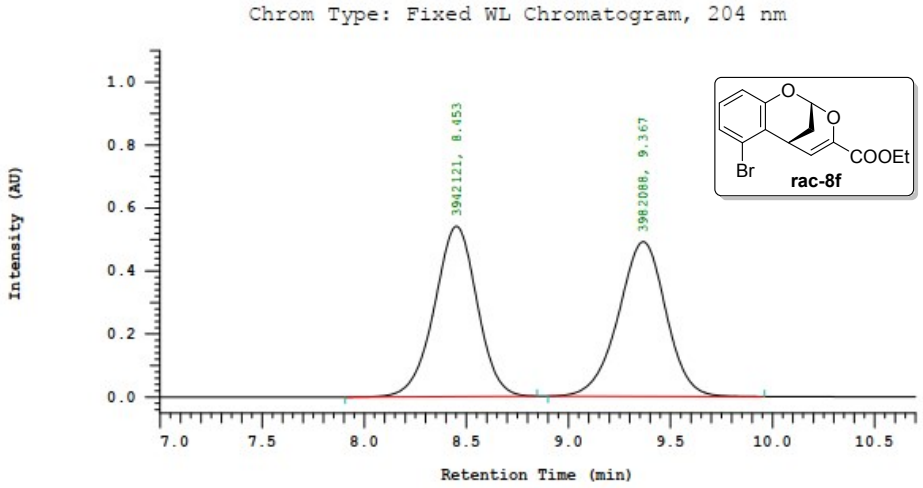
The ^{1}H NMR spectrum of 8f (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 8f (101 MHz, $CDCl_3$)



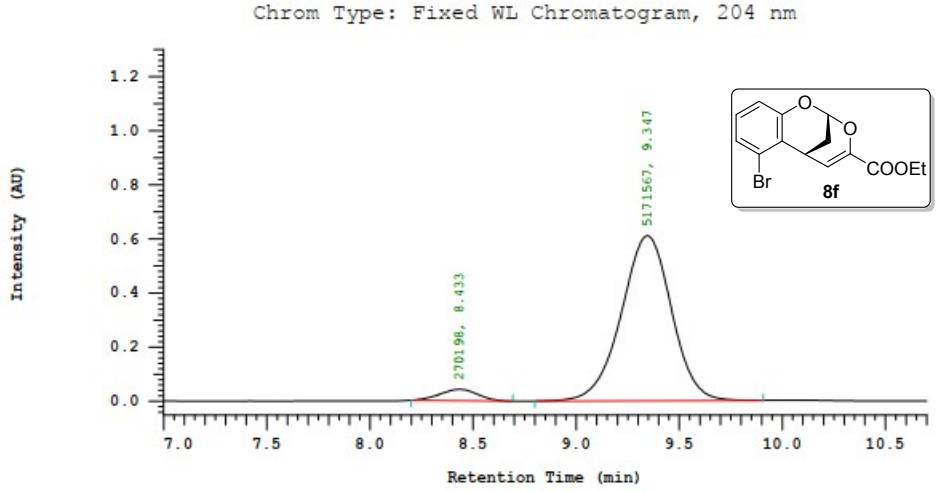
The HPLC of racemic 8f



Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.453	3942121	49.748	BB
2	9.367	3982088	50.252	BB
		7924209	100.000	

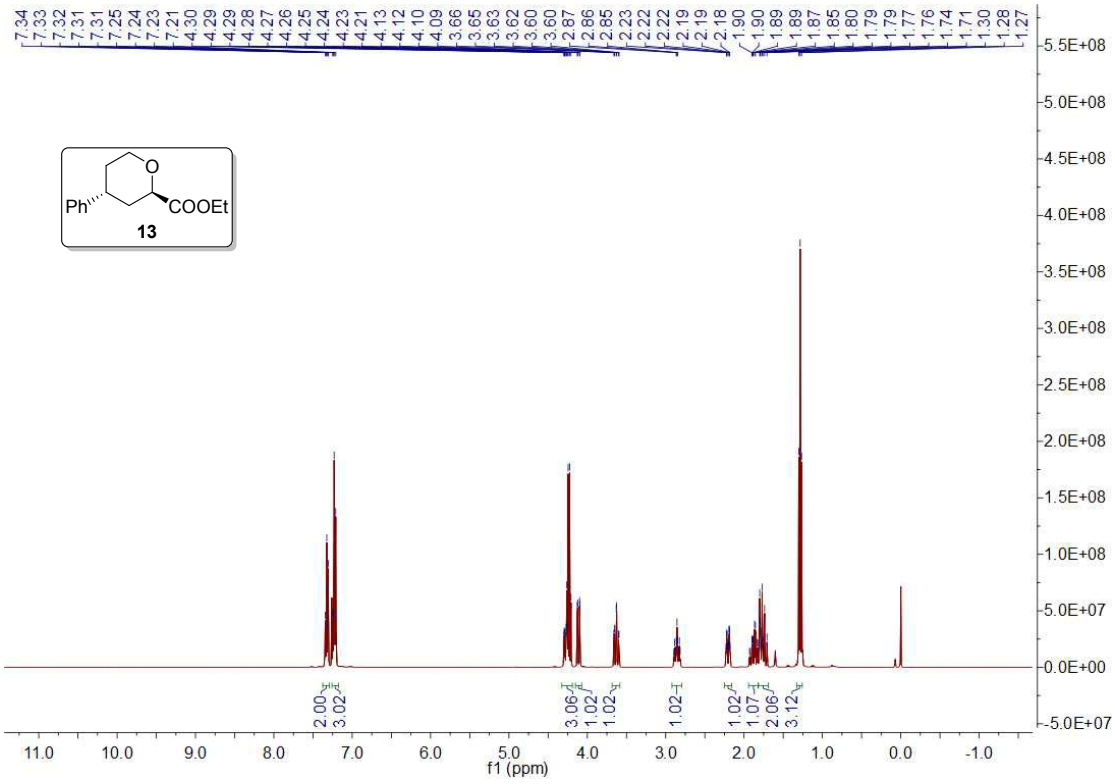
The HPLC of chiral 8f



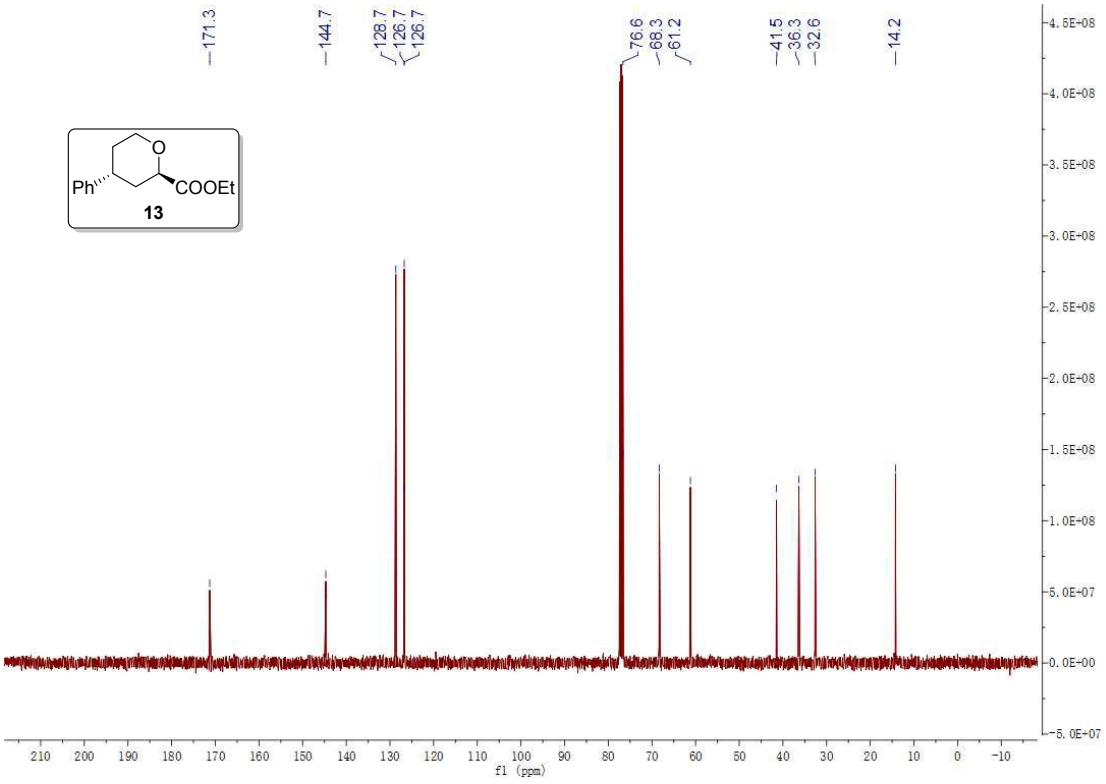
Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	8.433	270198	4.965	BB
2	9.347	5171567	95.035	BB
		5441765	100.000	

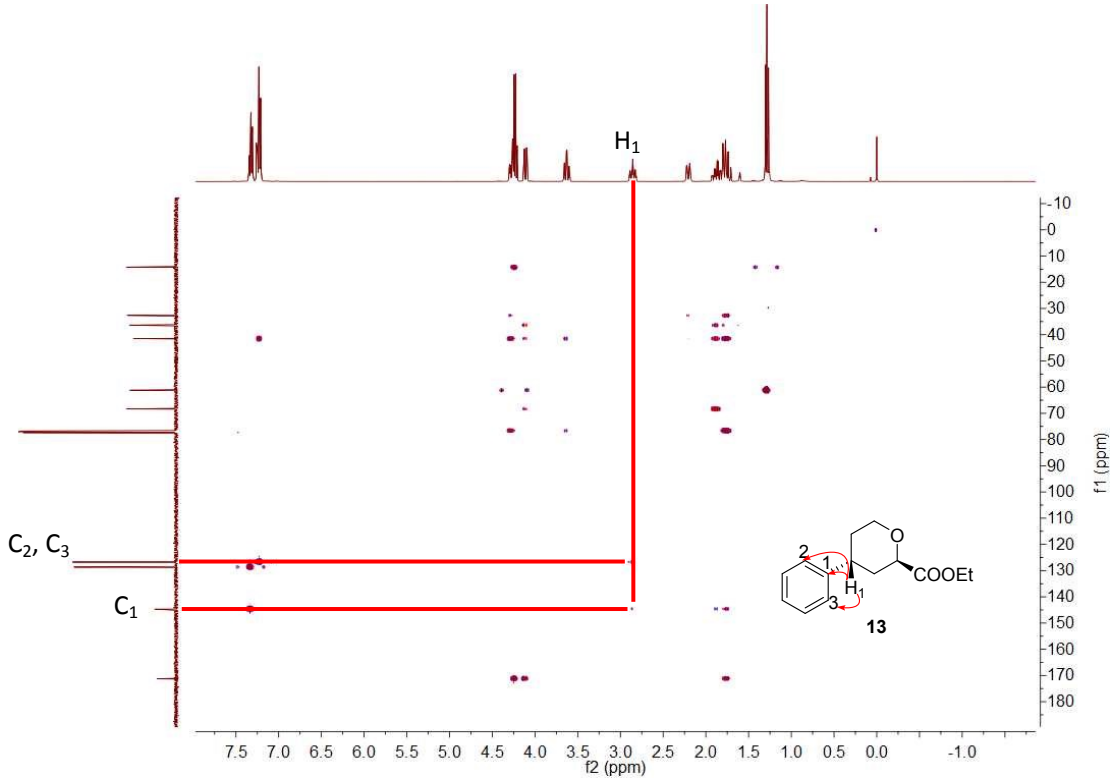
The ^{1}H NMR spectrum of 13 (400 MHz, $CDCl_3$)



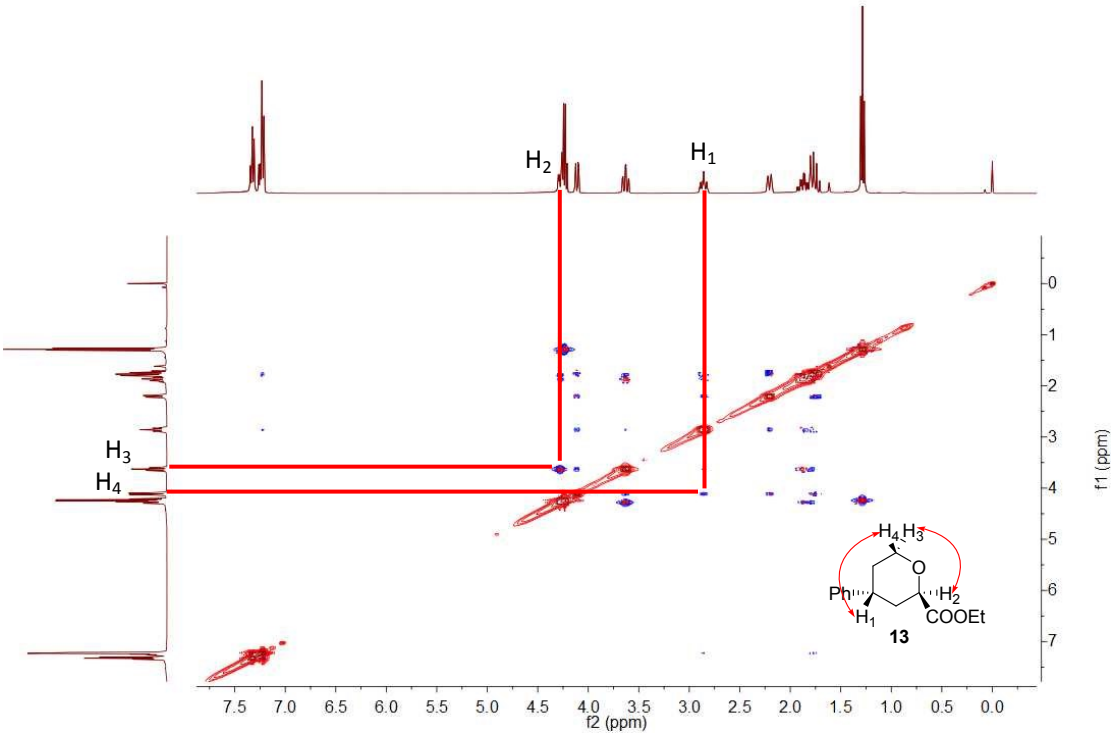
The ^{13}C NMR spectrum of 13 (101 MHz, $CDCl_3$)



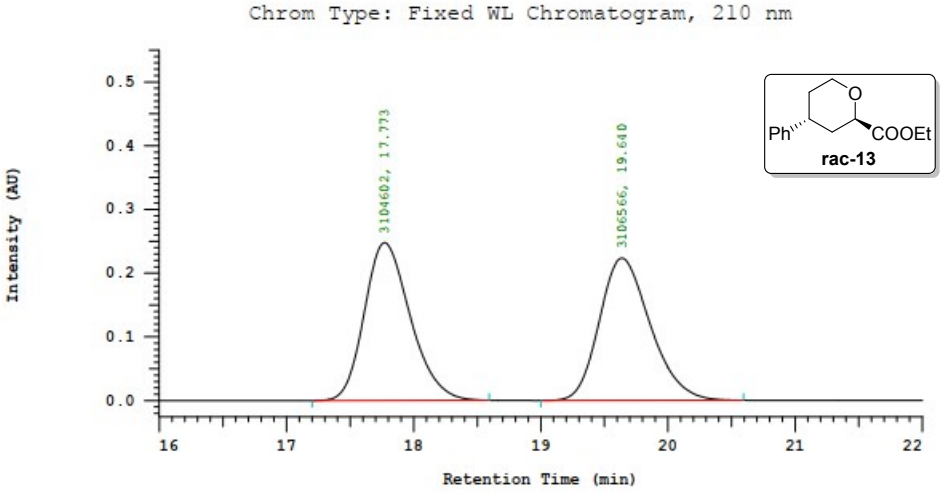
The HMBC spectrum of 13 (500 MHz, $CDCl_3$)



The NOSEY spectrum of 13 (400 MHz, $CDCl_3$)



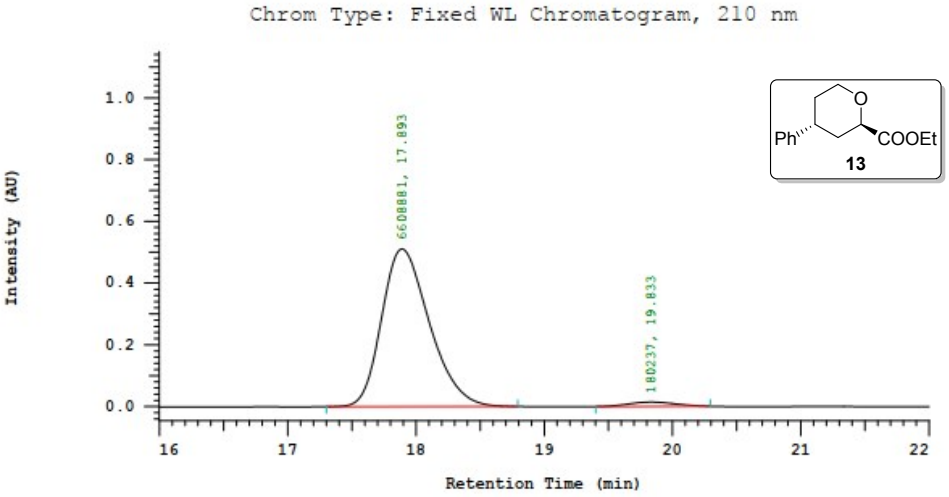
The HPLC of racemic 13



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.773	3104602	49.984	BB
2	19.640	3106566	50.016	BB
		6211168	100.000	

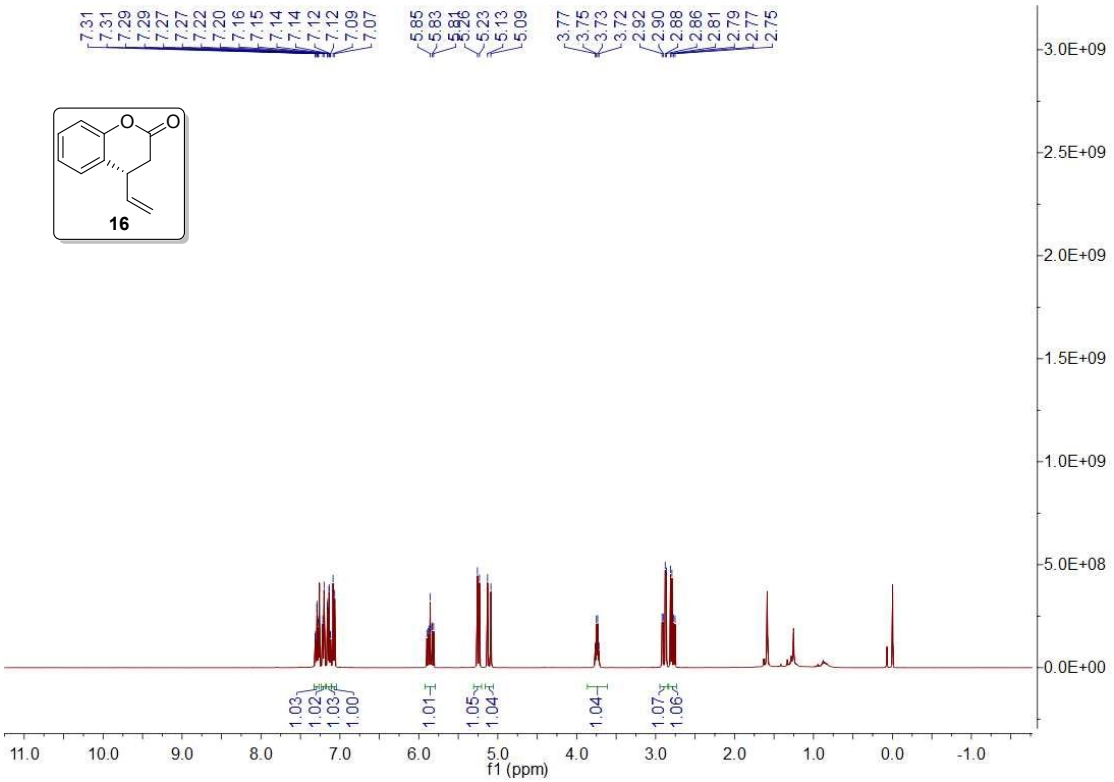
The HPLC of chiral 13



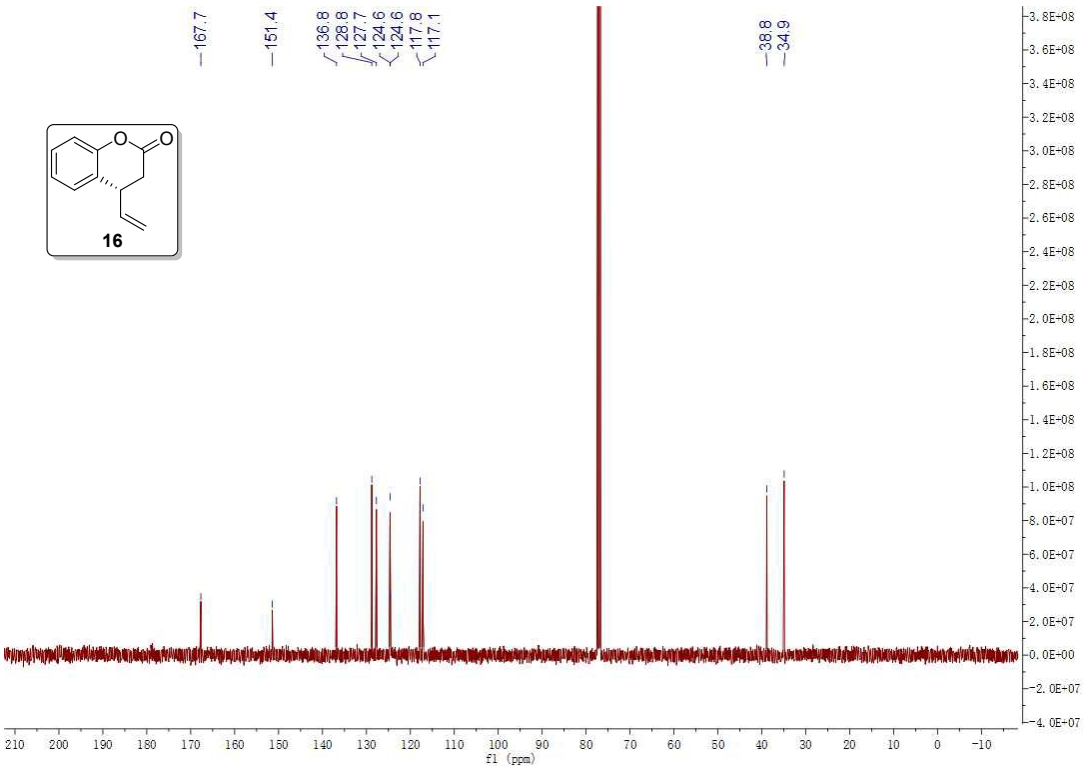
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.893	6608881	97.345	BB
2	19.833	180237	2.655	BB
		6789118	100.000	

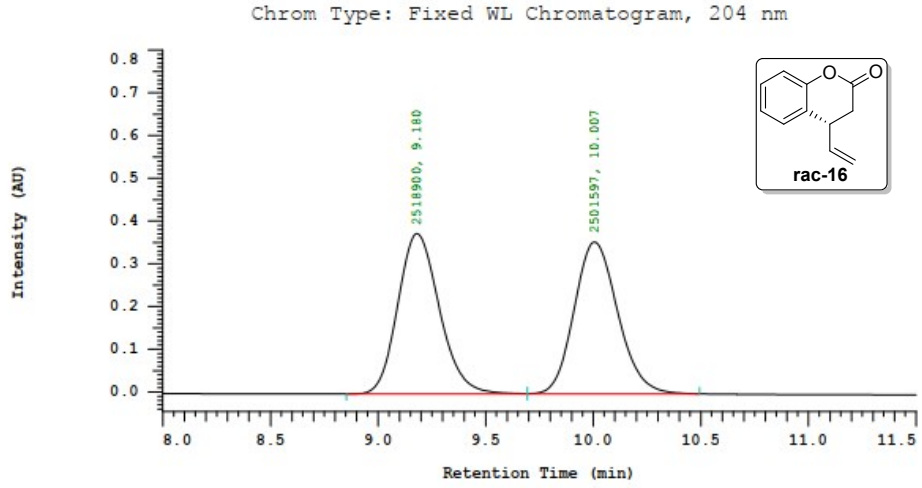
The ^{1}H NMR spectrum of 16 (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 16 (101 MHz, $CDCl_3$)



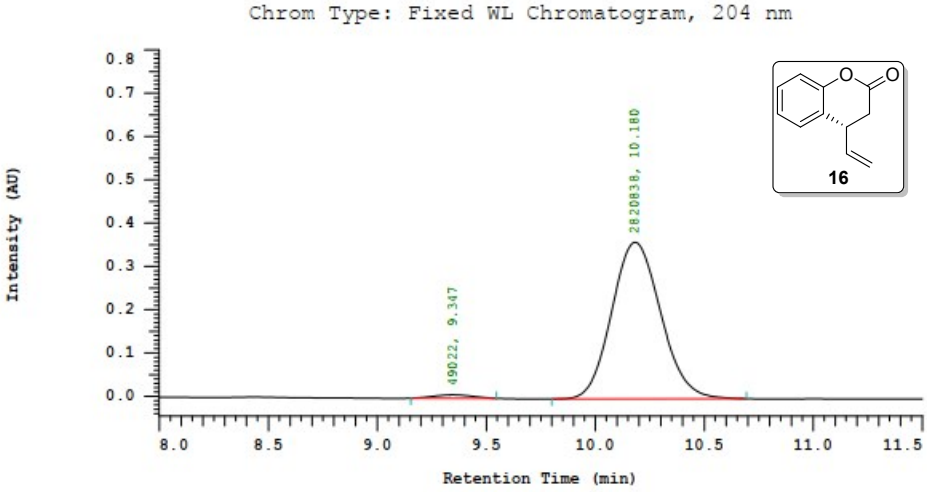
The HPLC of racemic 16



Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.180	2518900	50.172	BV
2	10.007	2501597	49.828	VB
		5020497	100.000	

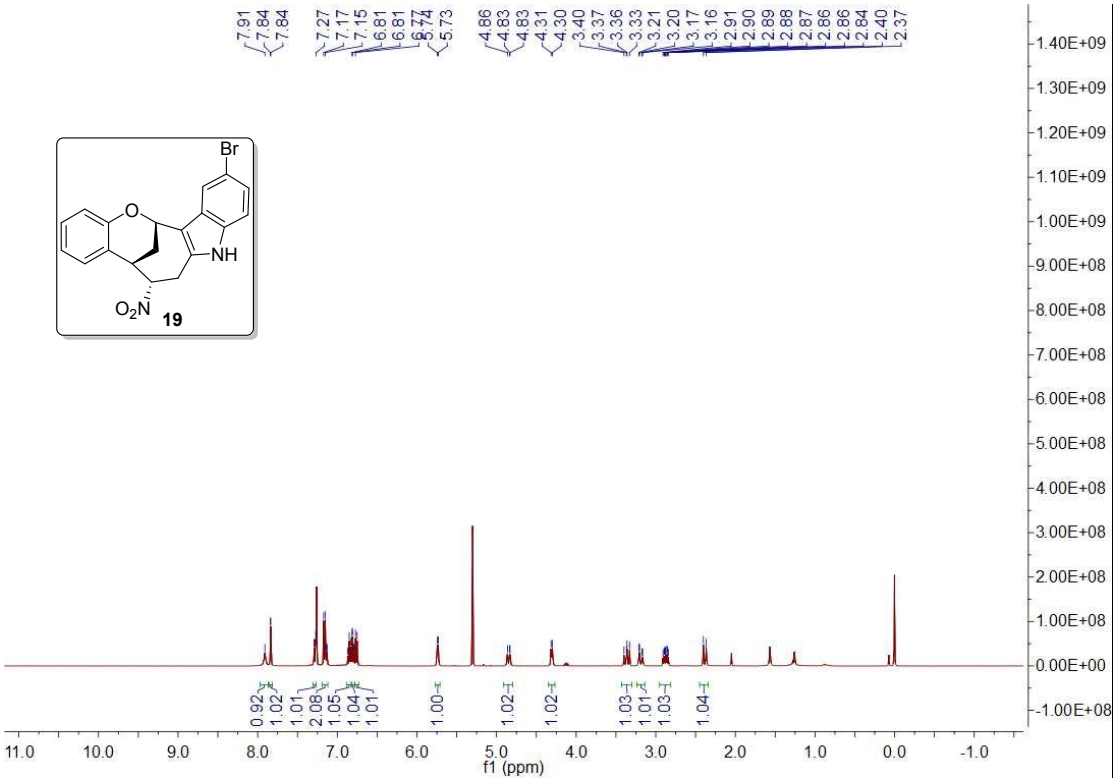
The HPLC of chiral 16



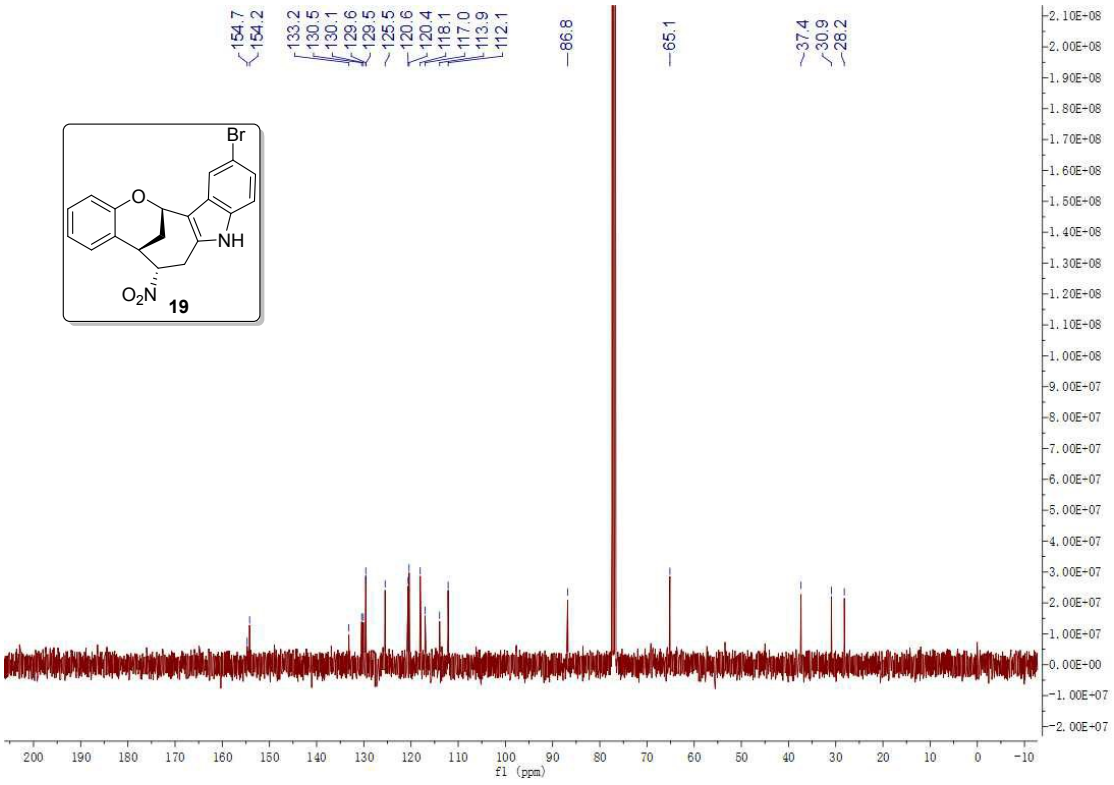
Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.347	49022	1.708	BB
2	10.180	2820838	98.292	BB
		2869860	100.000	

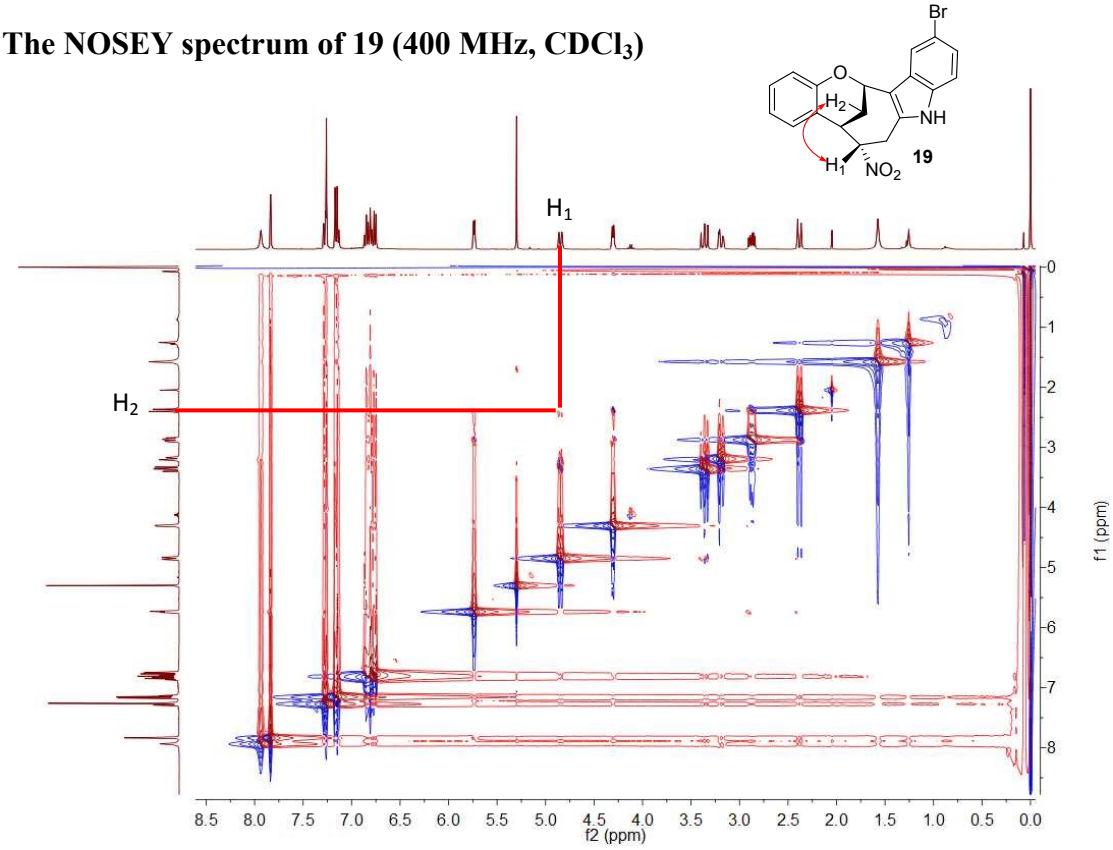
The ^{1}H NMR spectrum of 19 (400 MHz, $CDCl_3$)



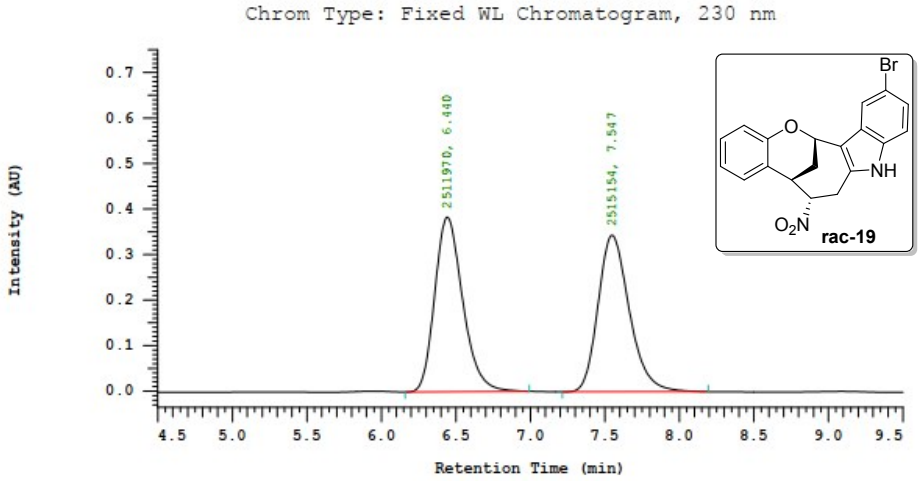
The ^{13}C NMR spectrum of 19 (101 MHz, $CDCl_3$)



The NOSEY spectrum of 19 (400 MHz, $CDCl_3$)



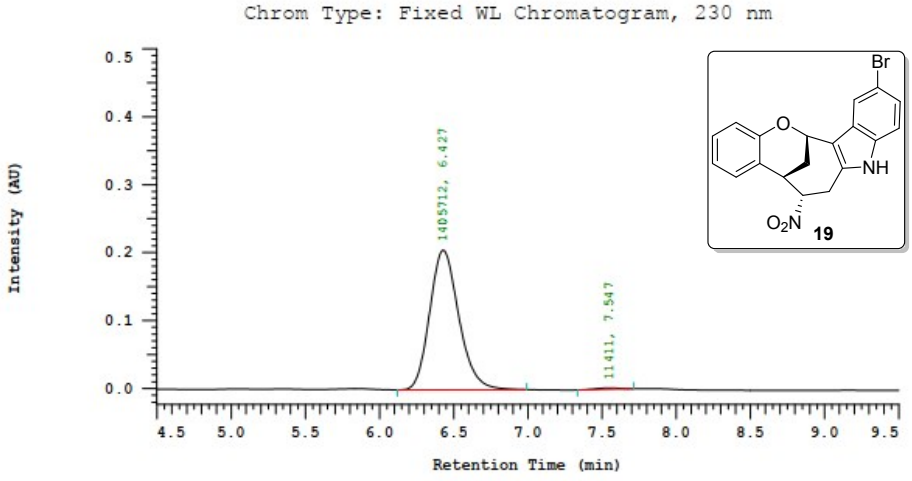
The HPLC of racemic 19



Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.440	2511970	49.968	BB
2	7.547	2515154	50.032	BB
		5027124	100.000	

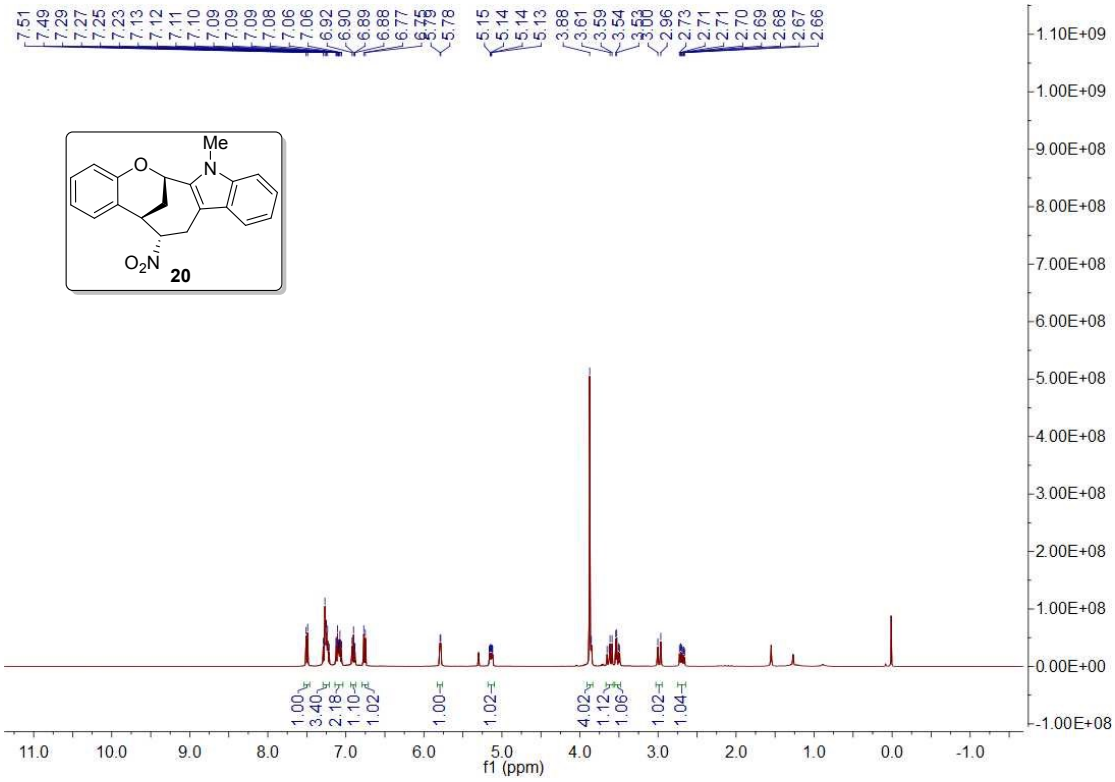
The HPLC of chiral 19



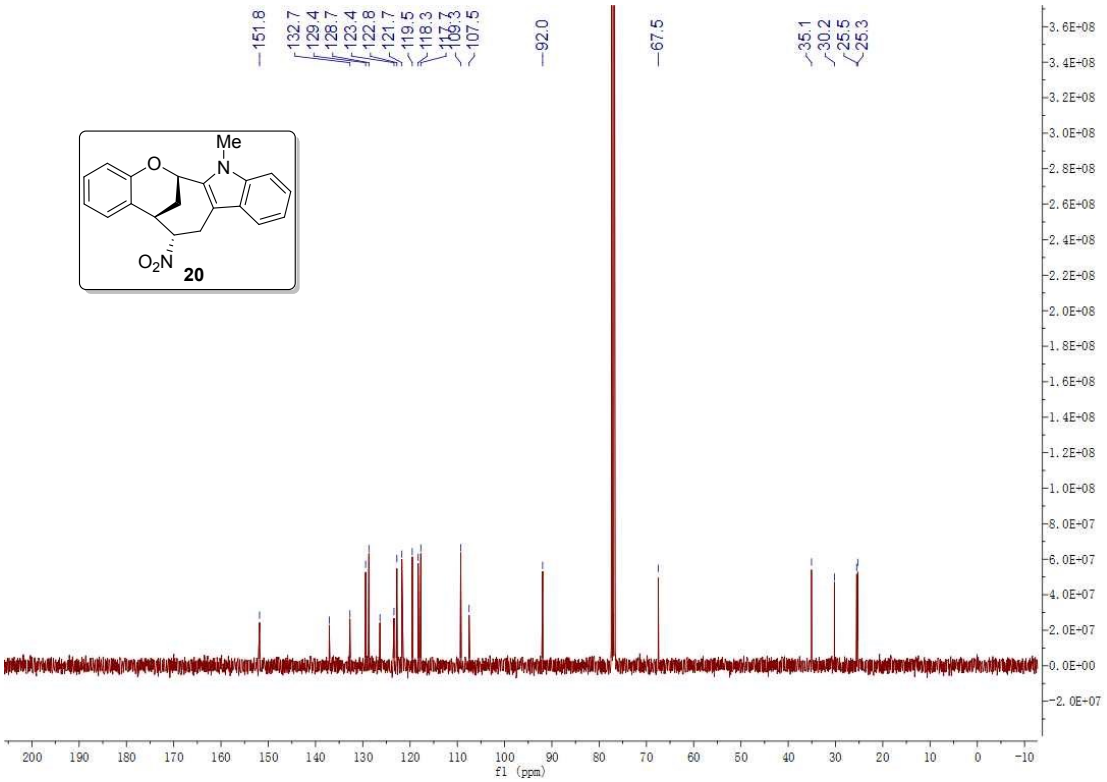
Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.427	1405712	99.195	BB
2	7.547	11411	0.805	BB
		1417123	100.000	

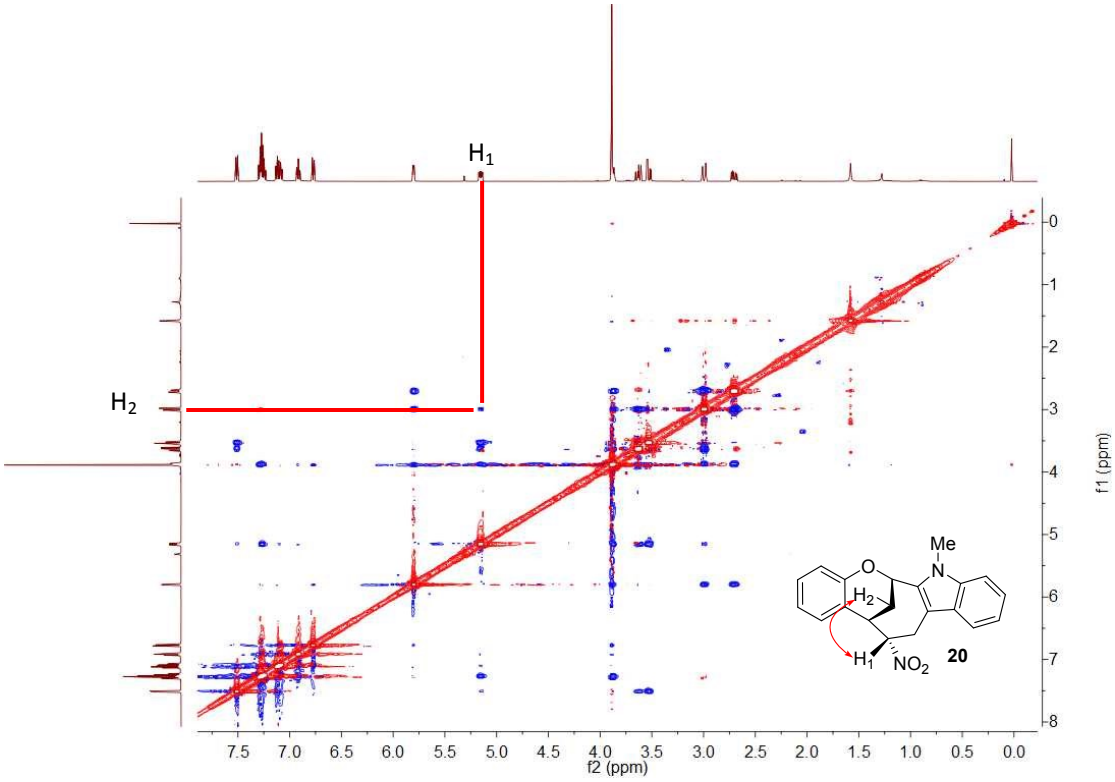
The ^{1}H NMR spectrum of 20 (400 MHz, $CDCl_3$)



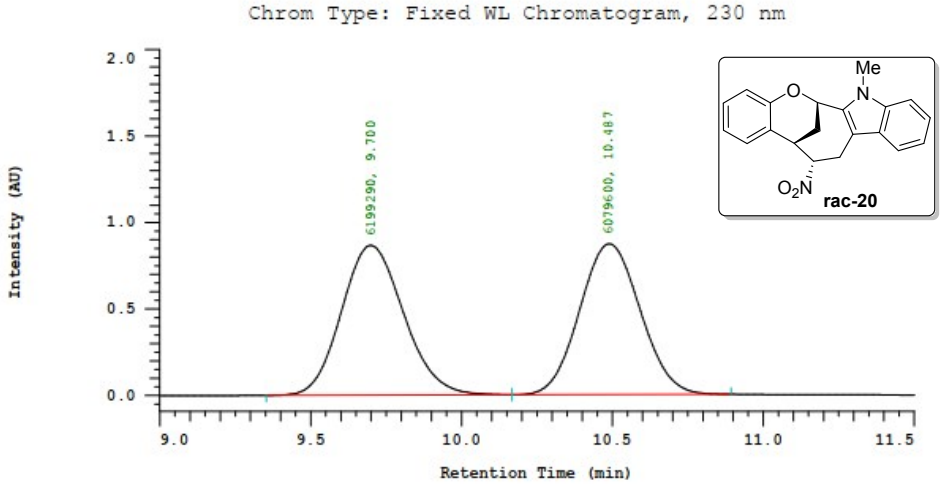
The ^{13}C NMR spectrum of 20 (101 MHz, $CDCl_3$)



The NOSEY spectrum of 20 (500 MHz, $CDCl_3$)



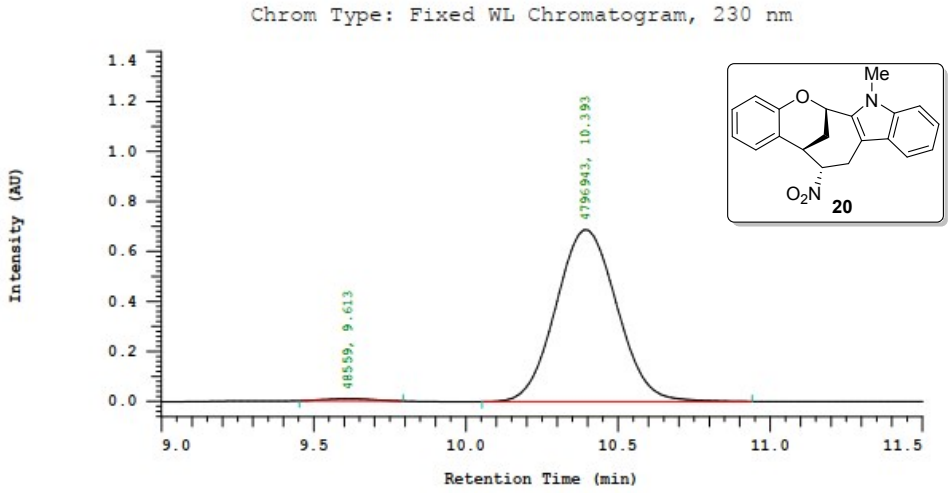
The HPLC of racemic 20



Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.700	6199290	50.487	BV
2	10.487	6079600	49.513	VB
		12278890	100.000	

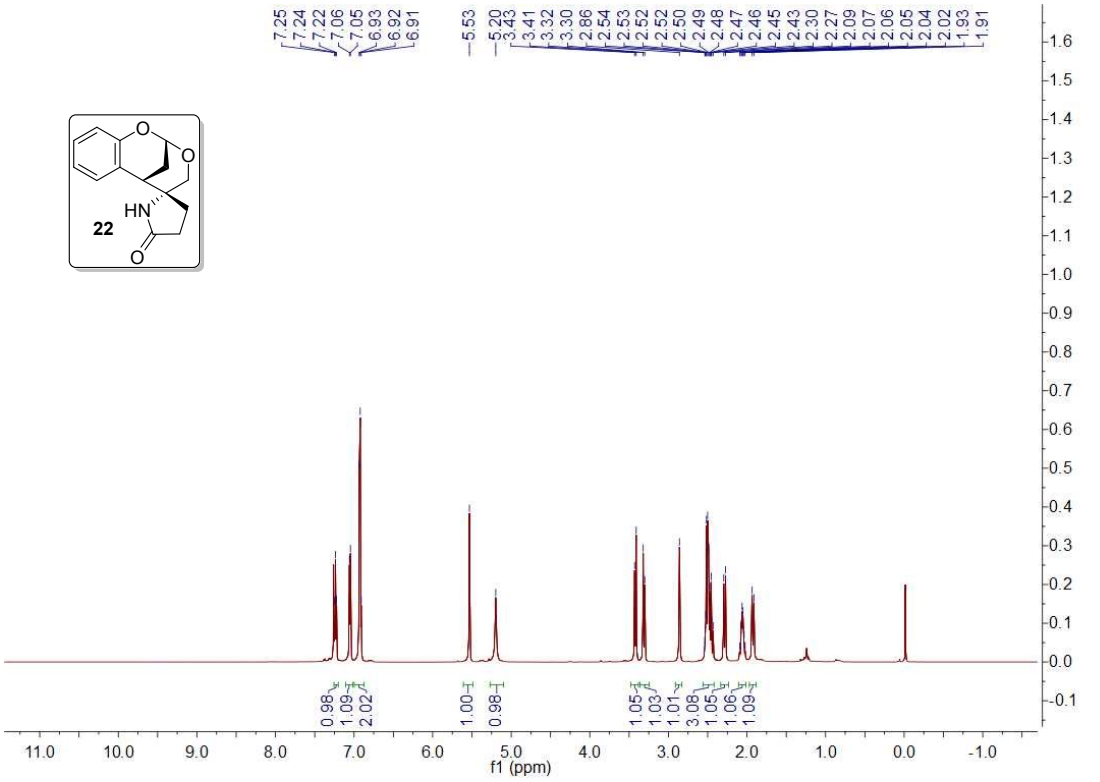
The HPLC of chiral 20



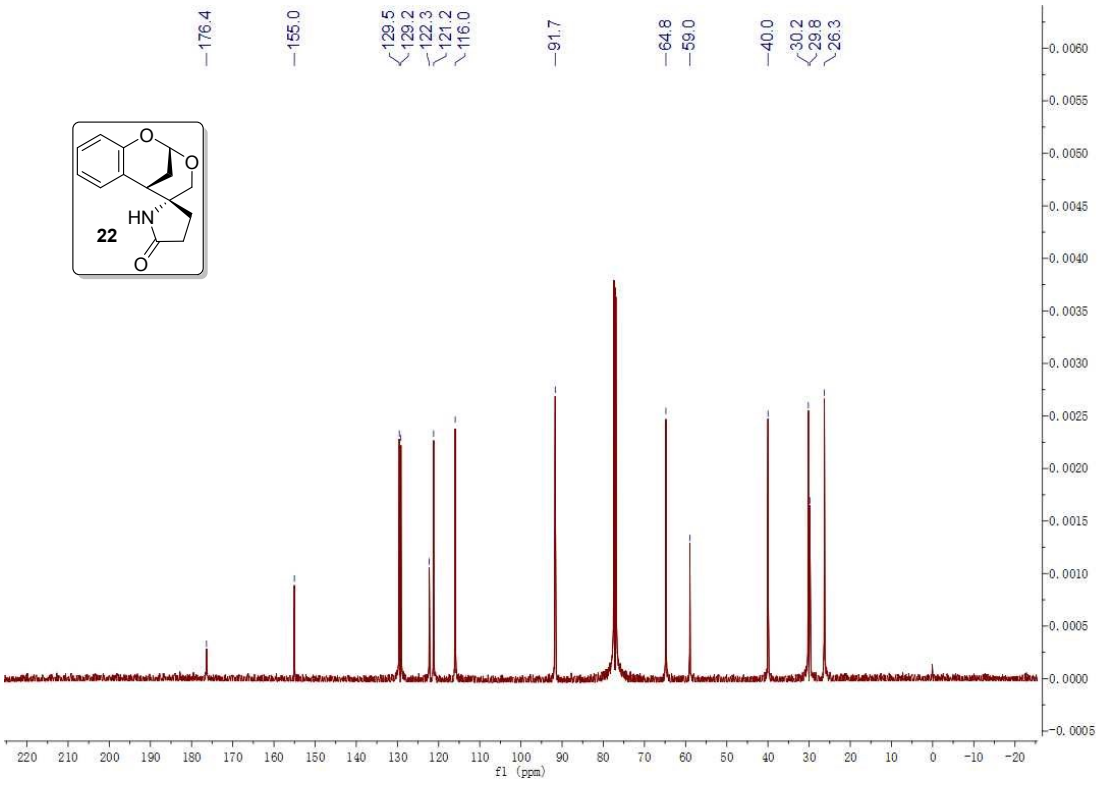
Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.613	48559	1.002	BB
2	10.393	4796943	98.998	BB
		4845502	100.000	

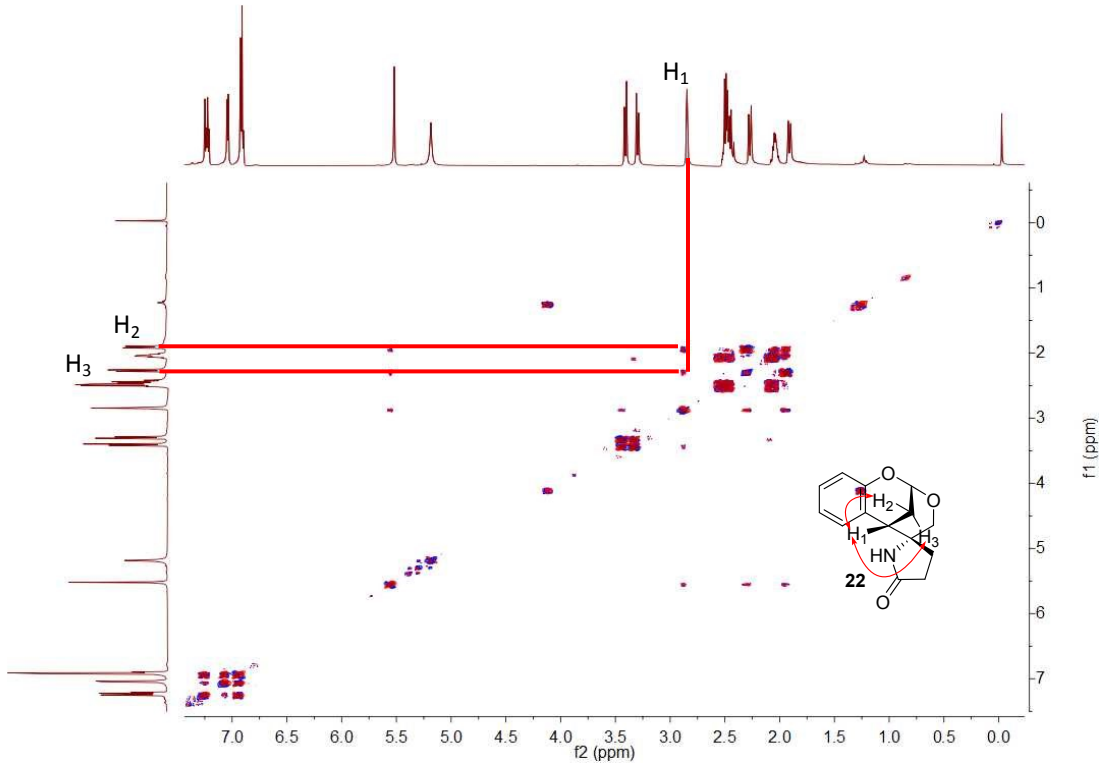
The ^{1}H NMR spectrum of 22 (600 MHz, $CDCl_3$)



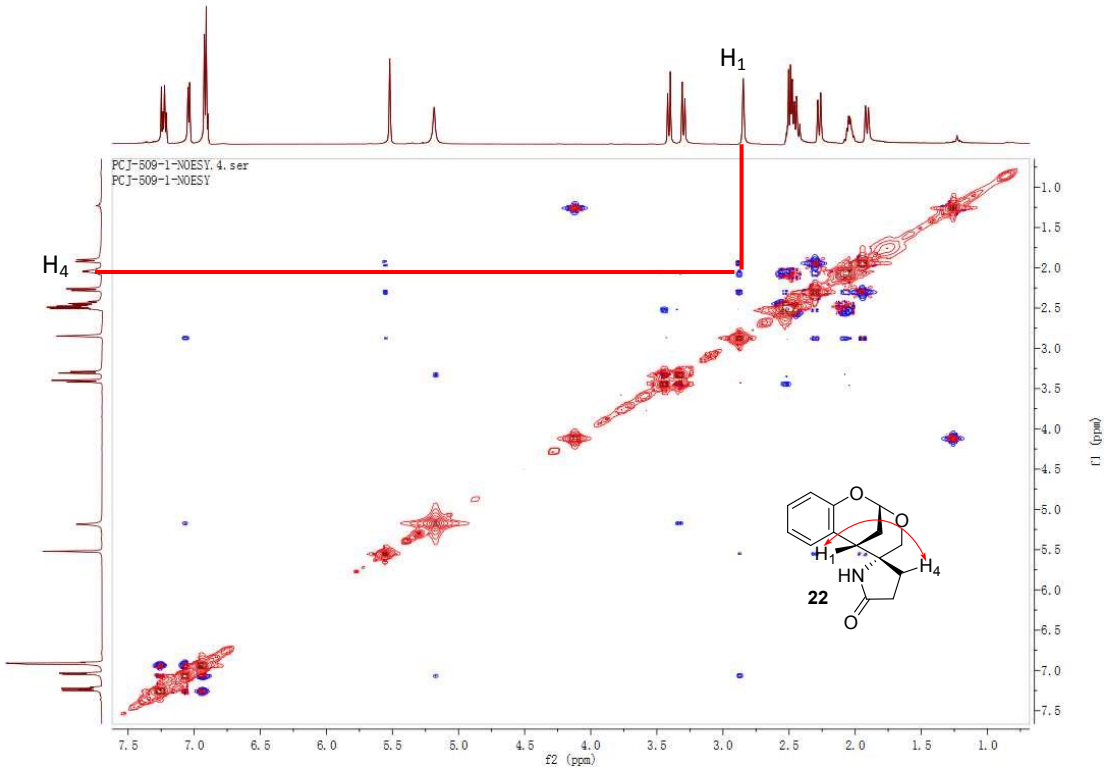
The ^{13}C NMR spectrum of 22 (151 MHz, $CDCl_3$)



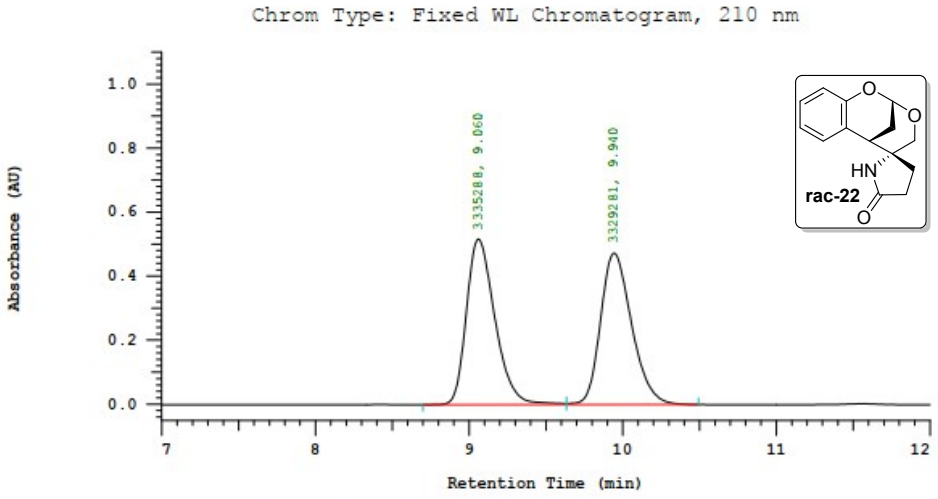
The ^{1}H-^{1}H COSY spectrum of 22 (500 MHz, $CDCl_3$)



The NOSEY spectrum of 22 (400 MHz, $CDCl_3$)



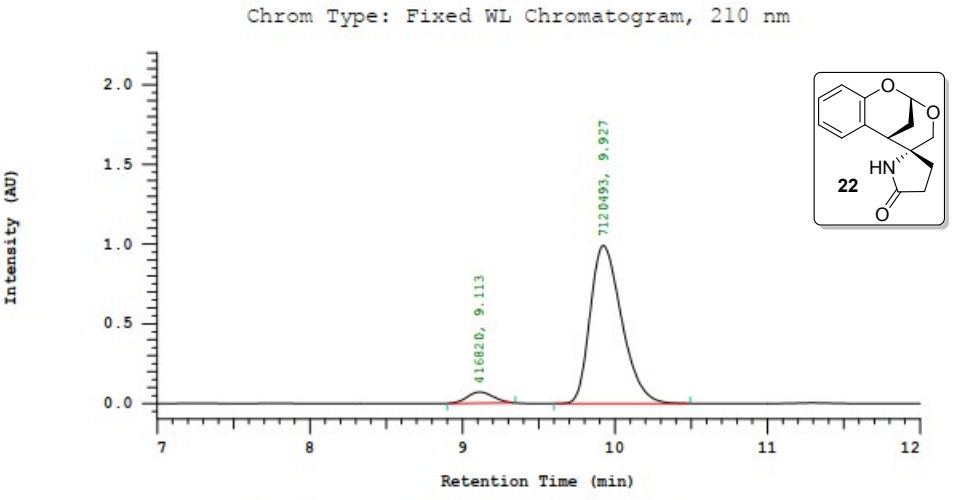
The HPLC of racemic 22



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.060	3335288	50.045	BV
2	9.940	3329281	49.955	VB
		6664569	100.000	

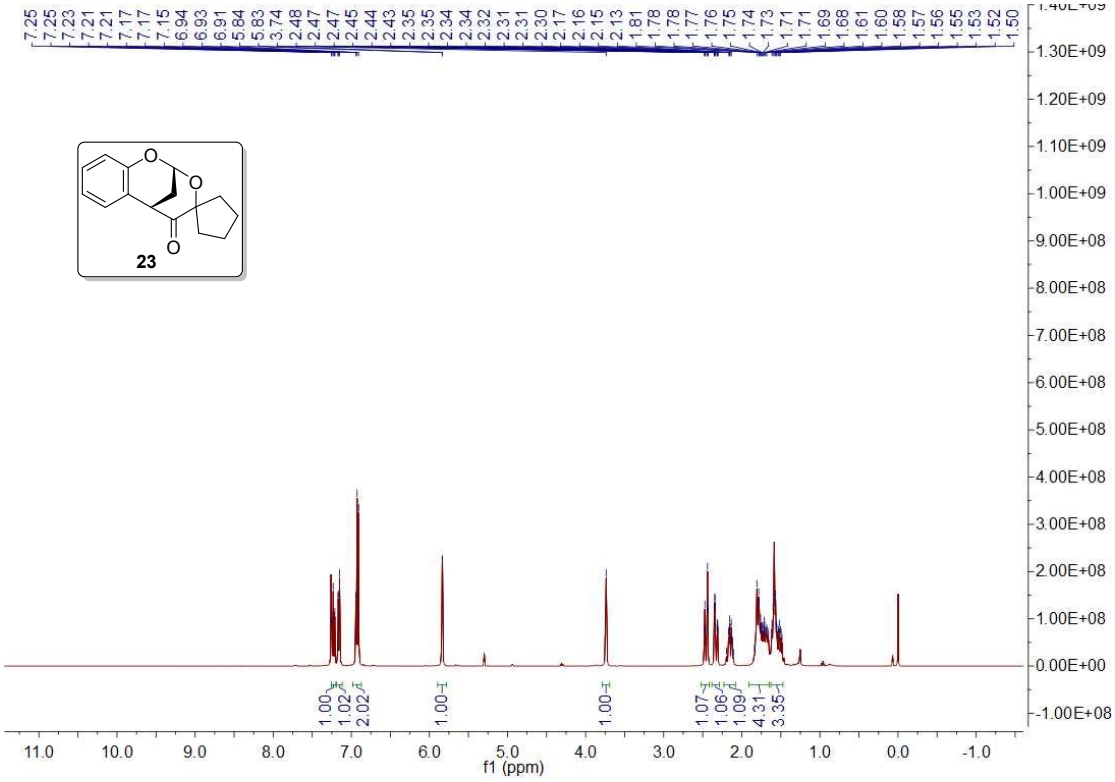
The HPLC of chiral 22



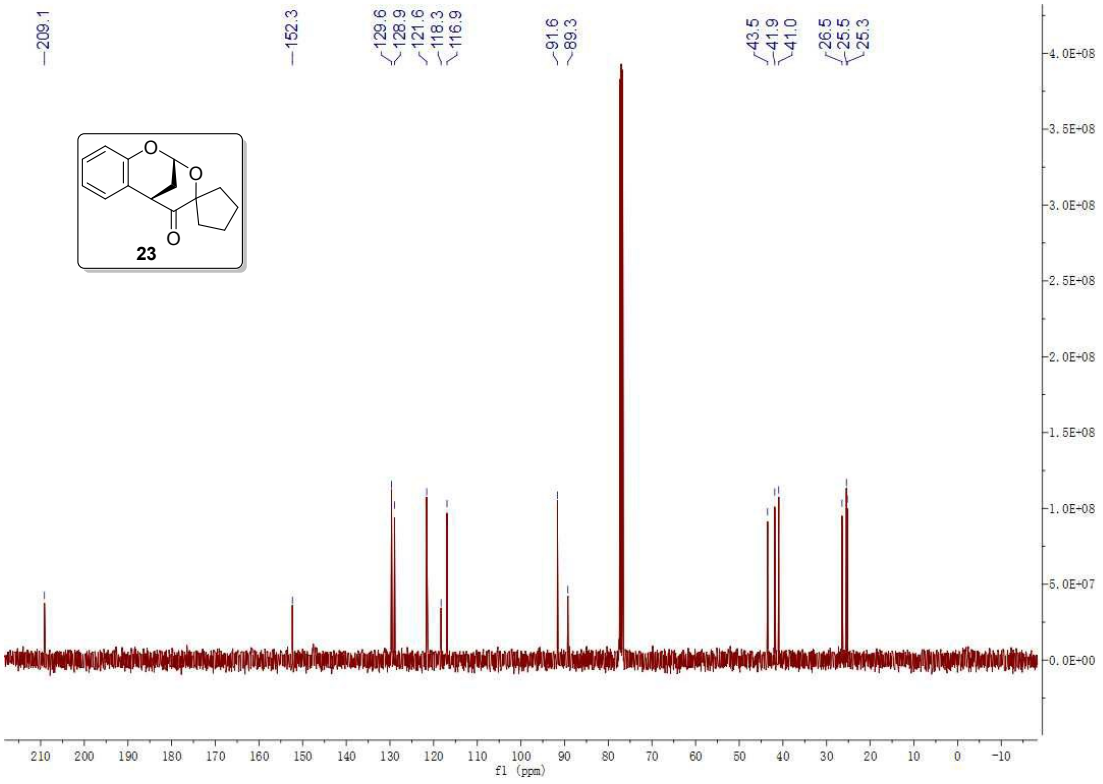
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.113	416820	5.530	BB
2	9.927	7120493	94.470	BB
		7537313	100.000	

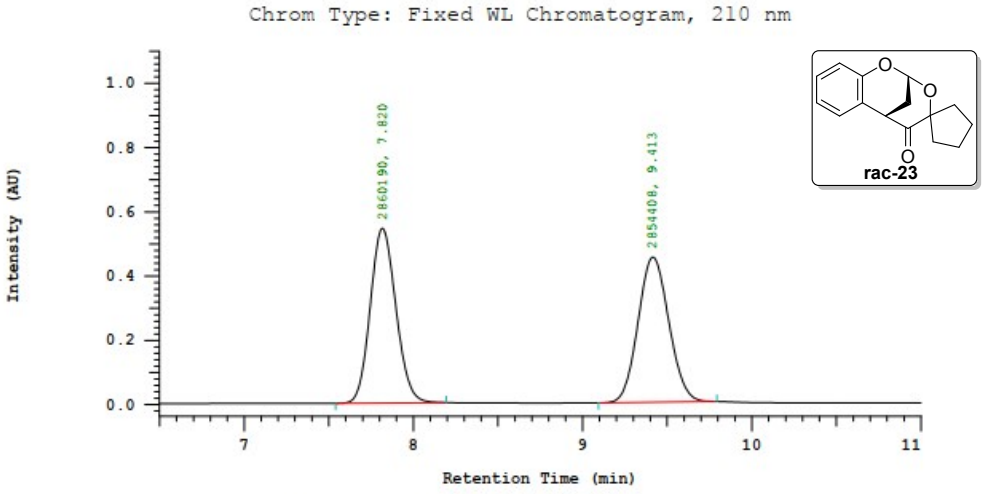
The ^{1}H NMR spectrum of 23 (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 23 (101 MHz, $CDCl_3$)



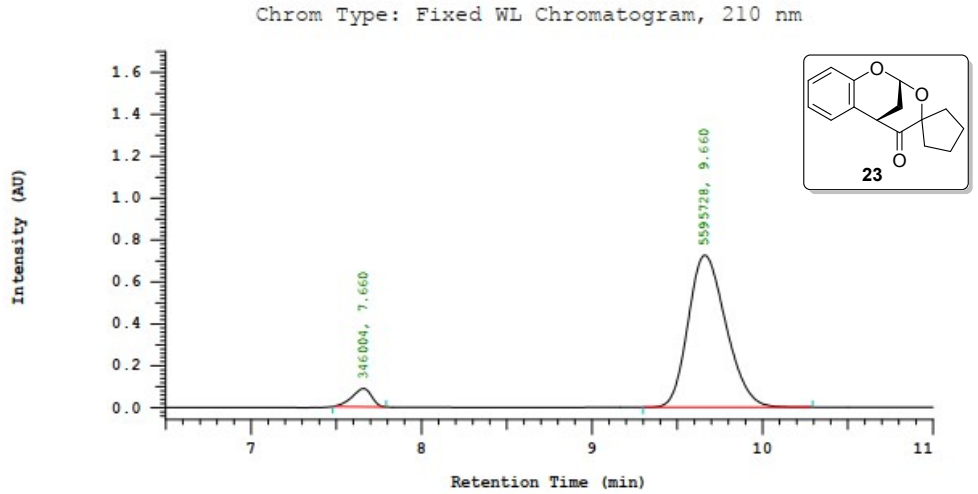
The HPLC of racemic 23



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.820	2860190	50.051	BB
2	9.413	2854408	49.949	BB
		5714598	100.000	

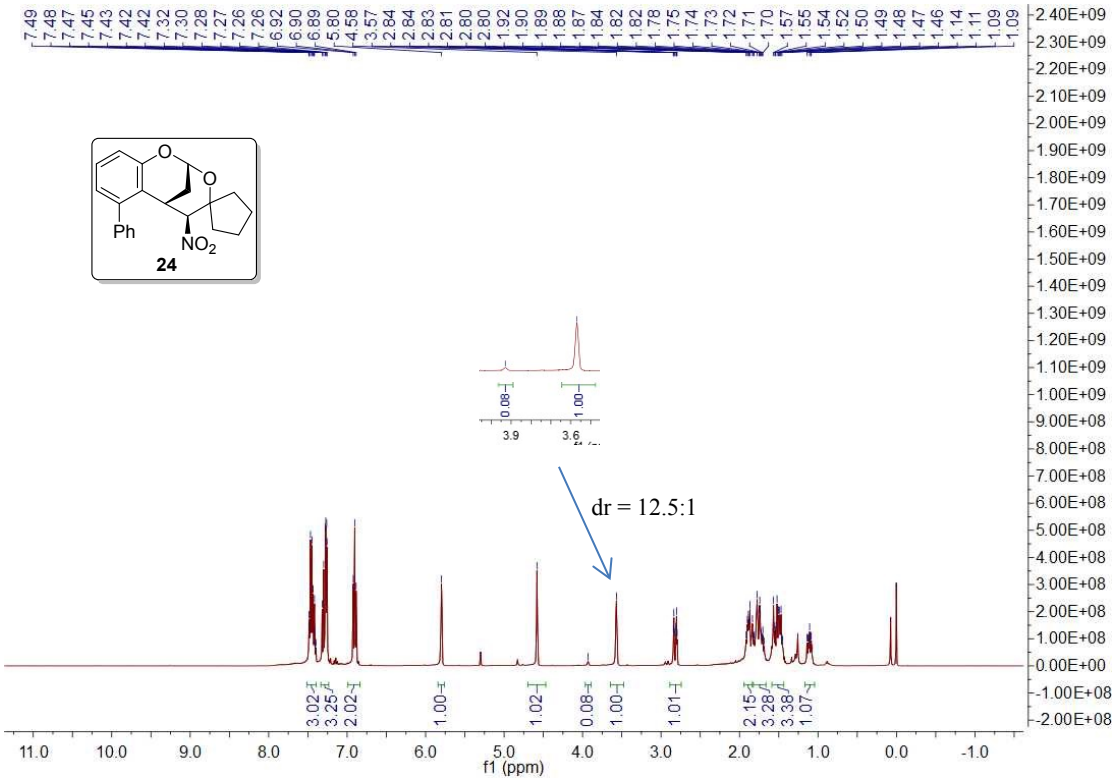
The HPLC of chiral 23



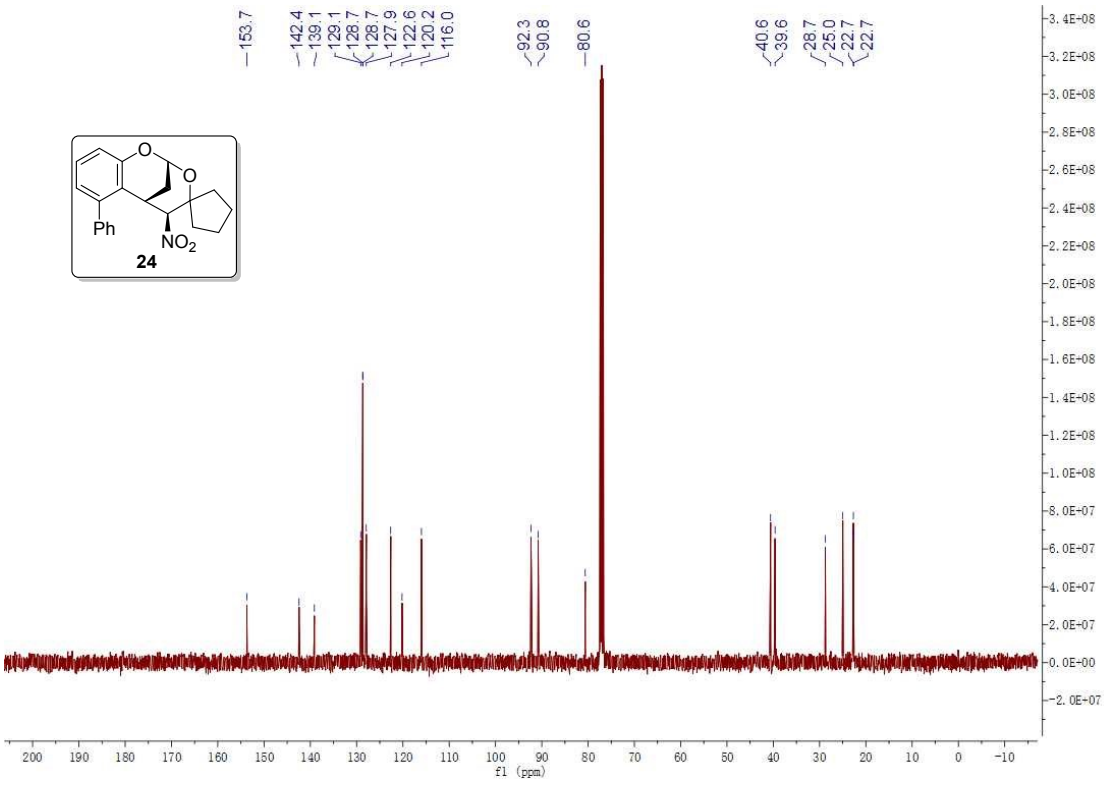
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.660	346004	5.823	BB
2	9.660	5595728	94.177	BB
		5941732	100.000	

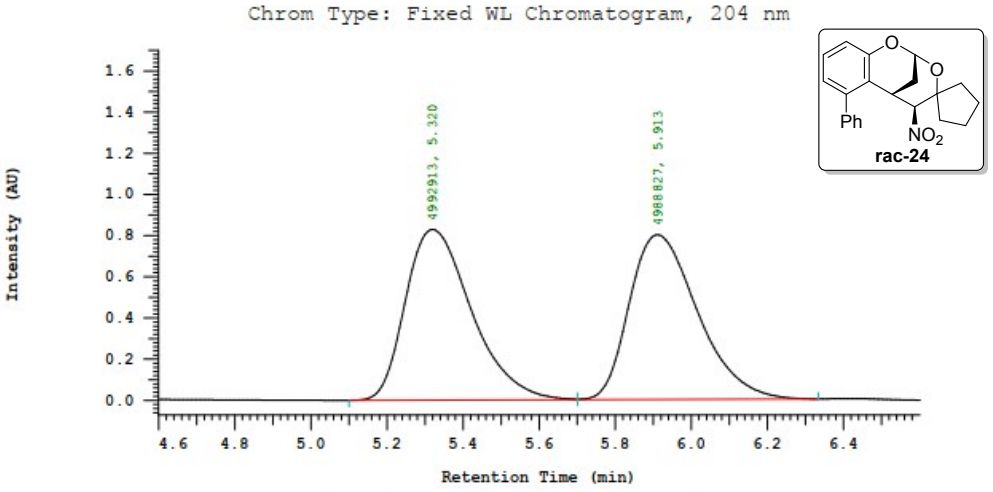
The ^{1}H NMR spectrum of 24 (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 24 (101 MHz, $CDCl_3$)



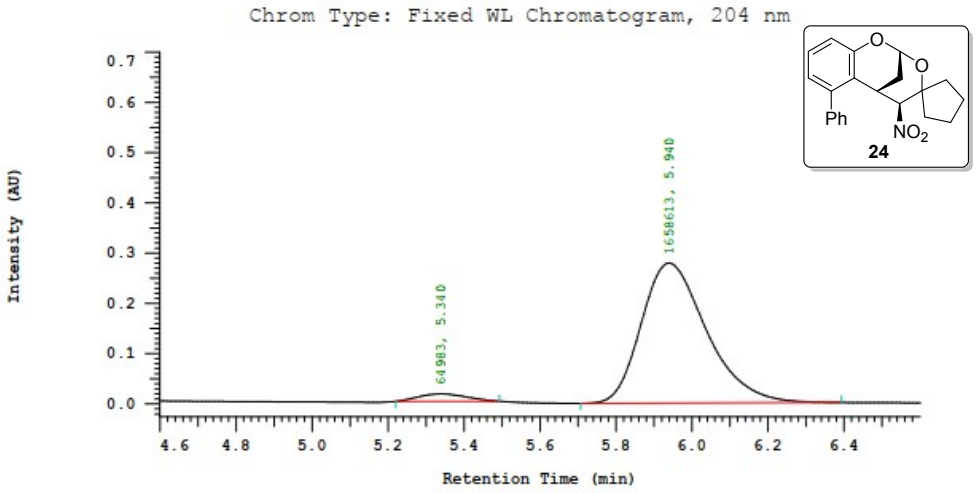
The HPLC of racemic 24



Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.320	4992913	50.020	BV
2	5.913	4988827	49.980	VB
		9981740	100.000	

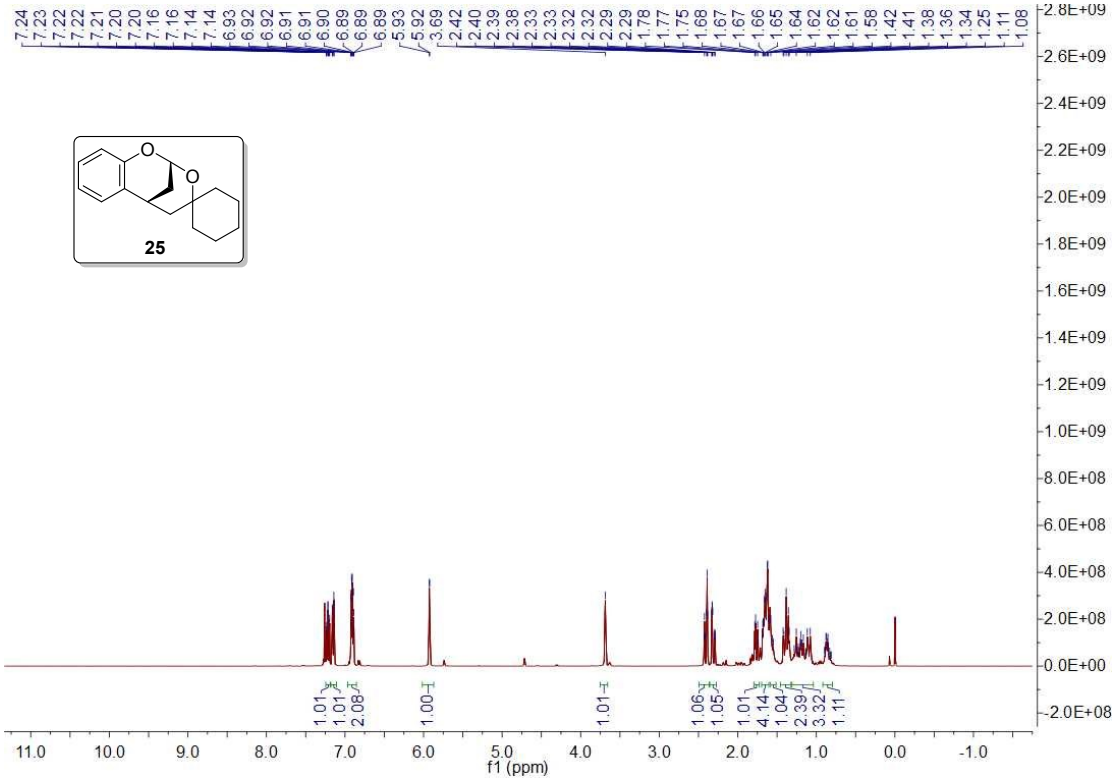
The HPLC of chiral 24



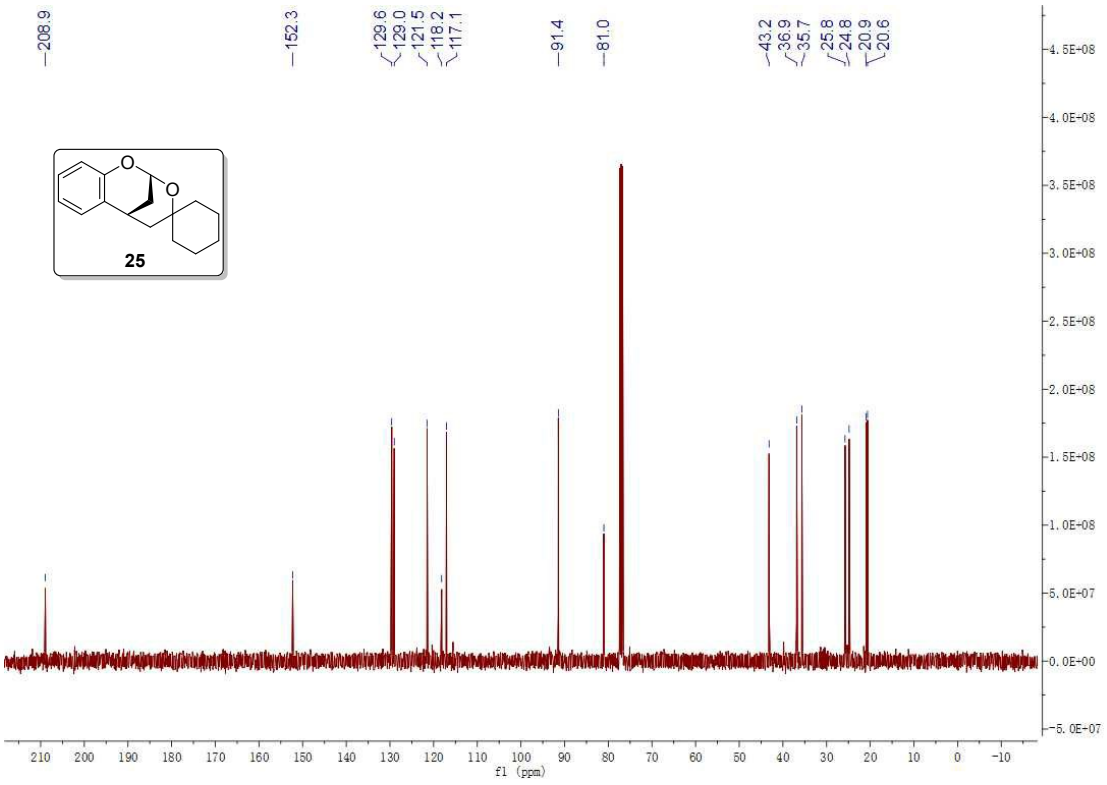
Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.340	64983	3.770	BB
2	5.940	1658613	96.230	BB
		1723596	100.000	

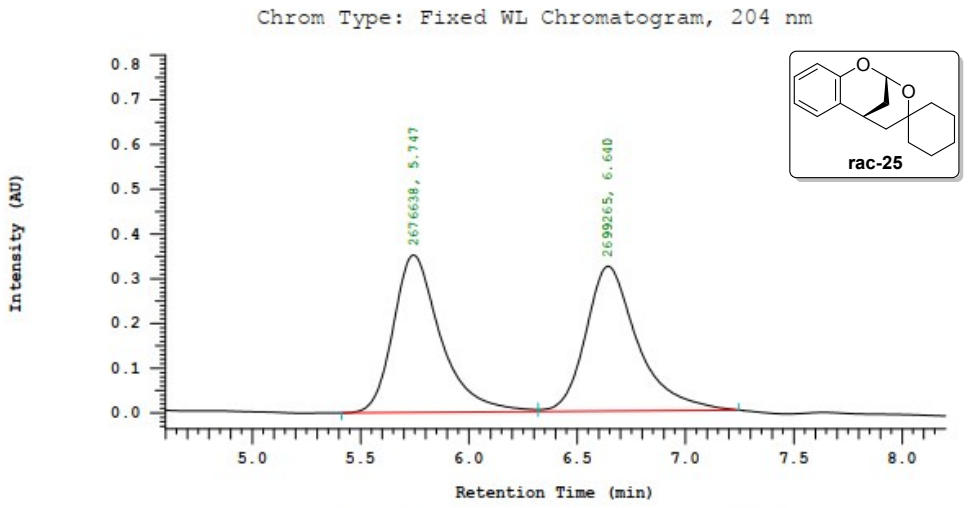
The ^{1}H NMR spectrum of 25 (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 25 (101 MHz, $CDCl_3$)



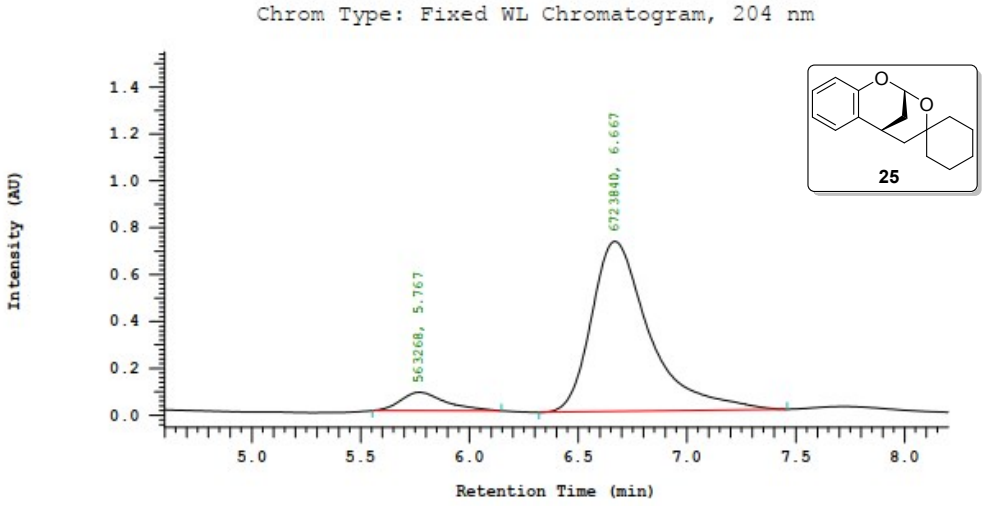
The HPLC of racemic 25



Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.747	2676638	49.790	BV
2	6.640	2699265	50.210	VB
		5375903	100.000	

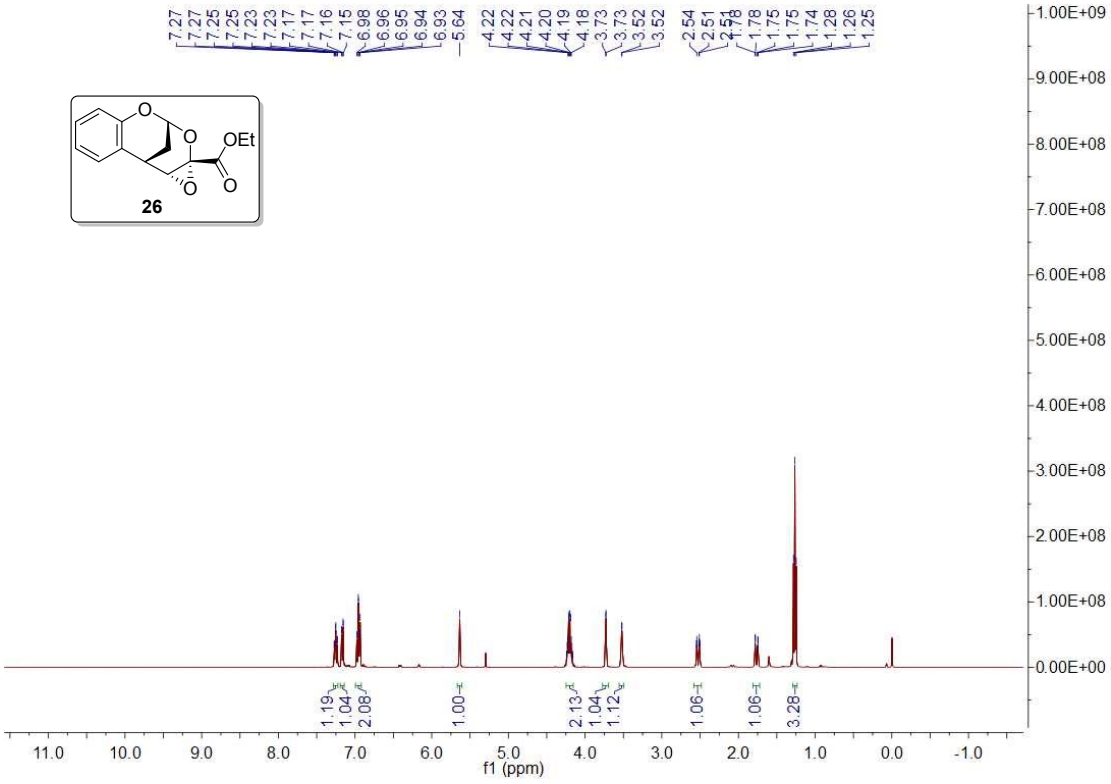
The HPLC of chiral 25



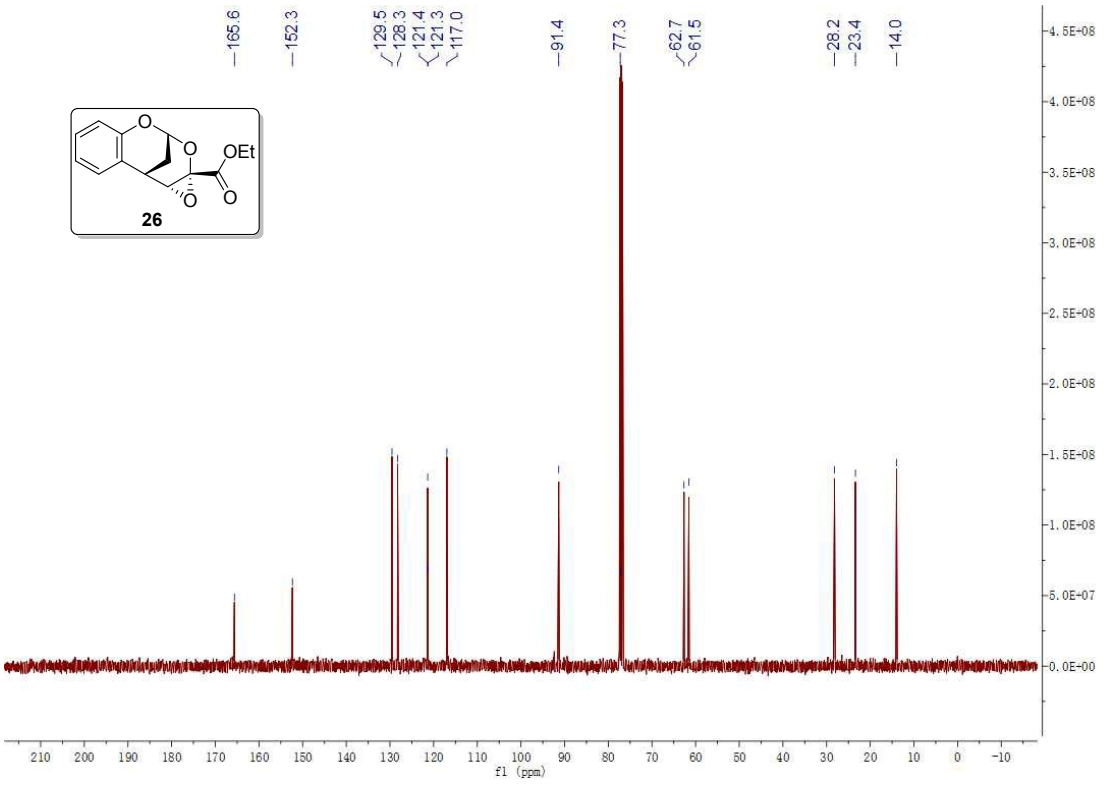
Chrom Type: Fixed WL Chromatogram, 204 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.767	563268	7.730	BB
2	6.667	6723840	92.270	BB
		7287108	100.000	

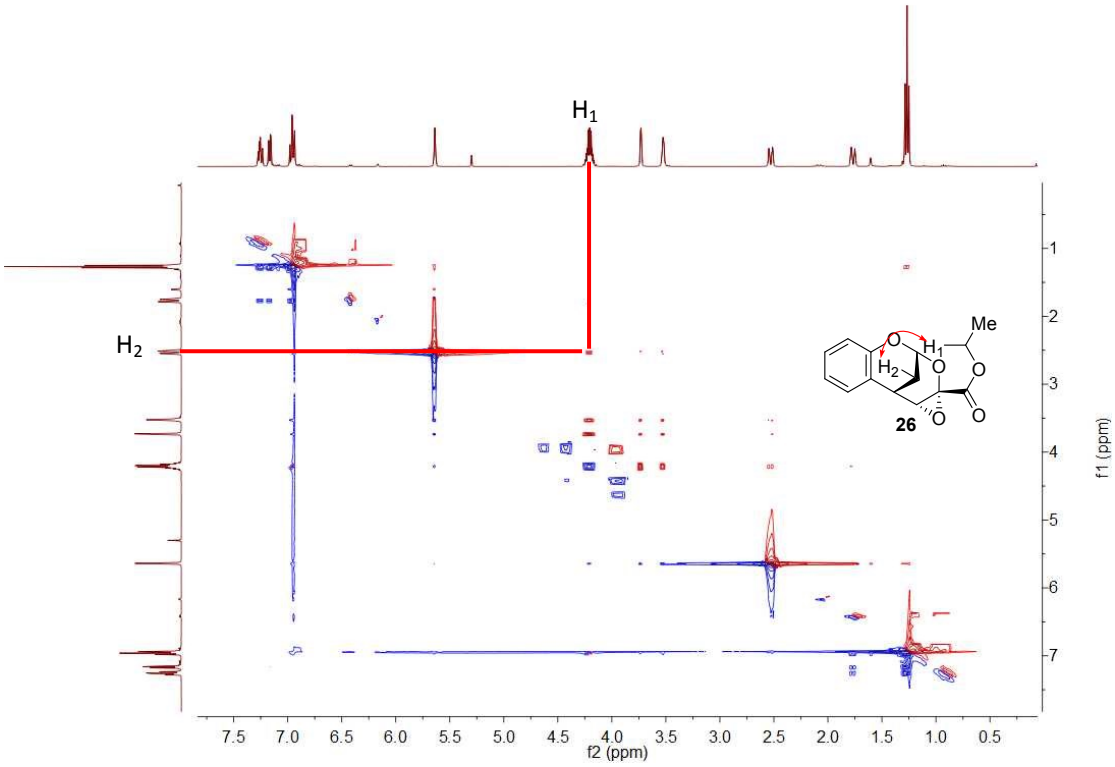
The ^{1}H NMR spectrum of 26 (400 MHz, $CDCl_3$)



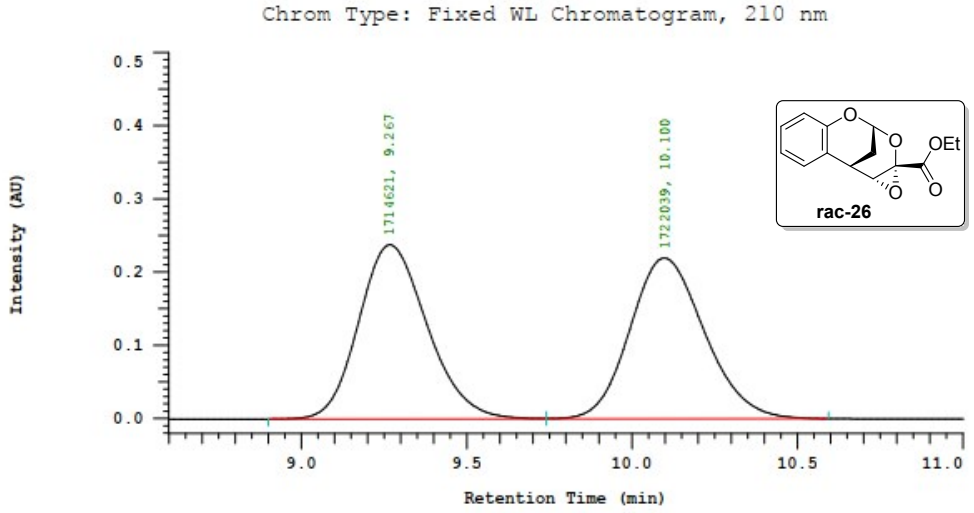
The ^{13}C NMR spectrum of 26 (101 MHz, $CDCl_3$)



The NOSEY spectrum of 26 (400 MHz, $CDCl_3$)



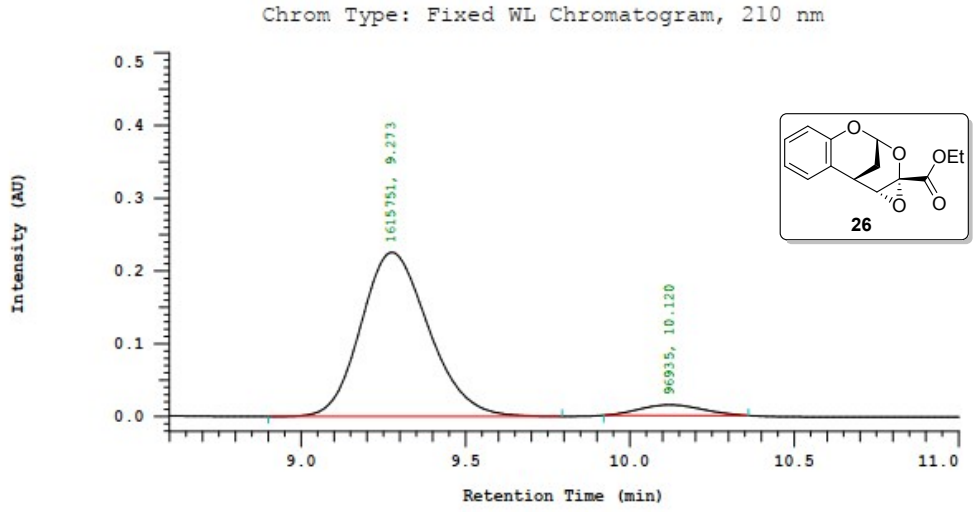
The HPLC of racemic 26



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.267	1714621	49.892	BV
2	10.100	1722039	50.108	VB
		3436660	100.000	

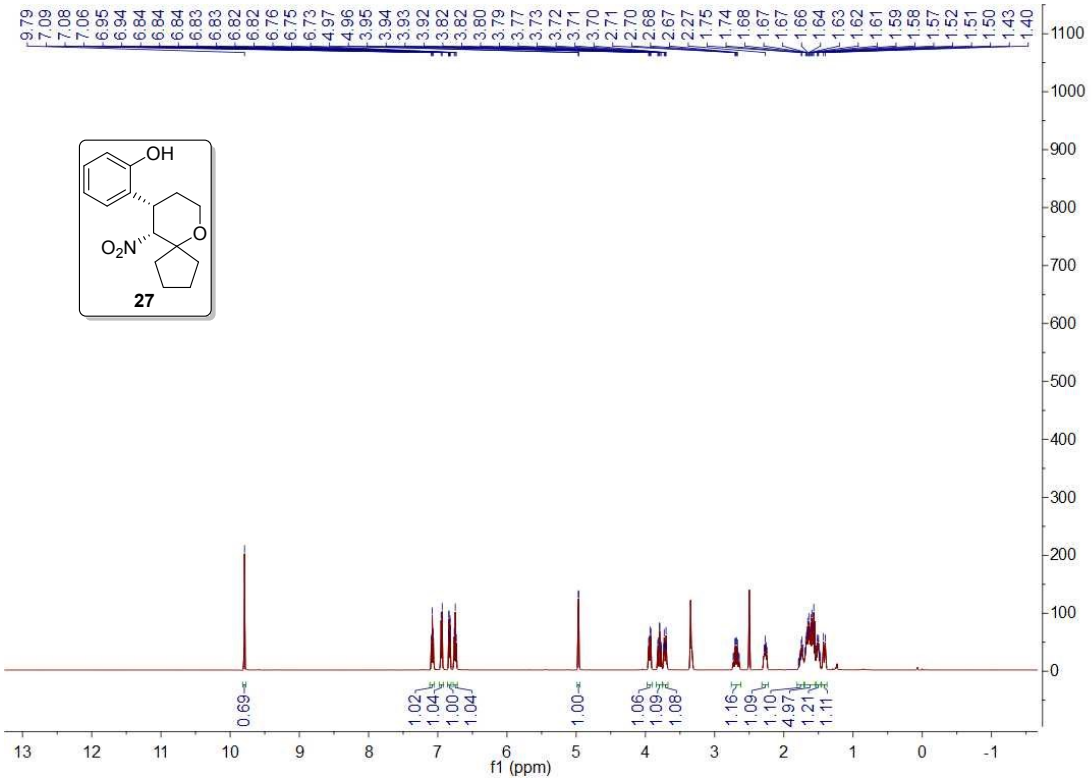
The HPLC of chiral 26



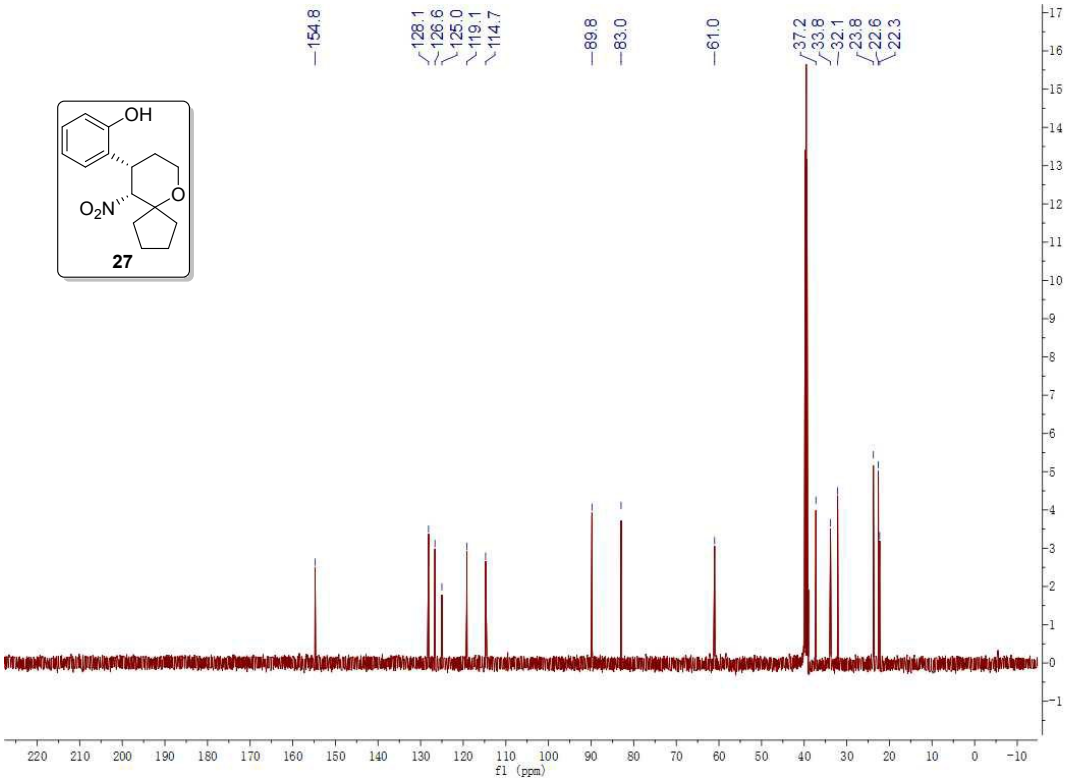
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.273	1615751	94.340	BB
2	10.120	96935	5.660	BB
		1712686	100.000	

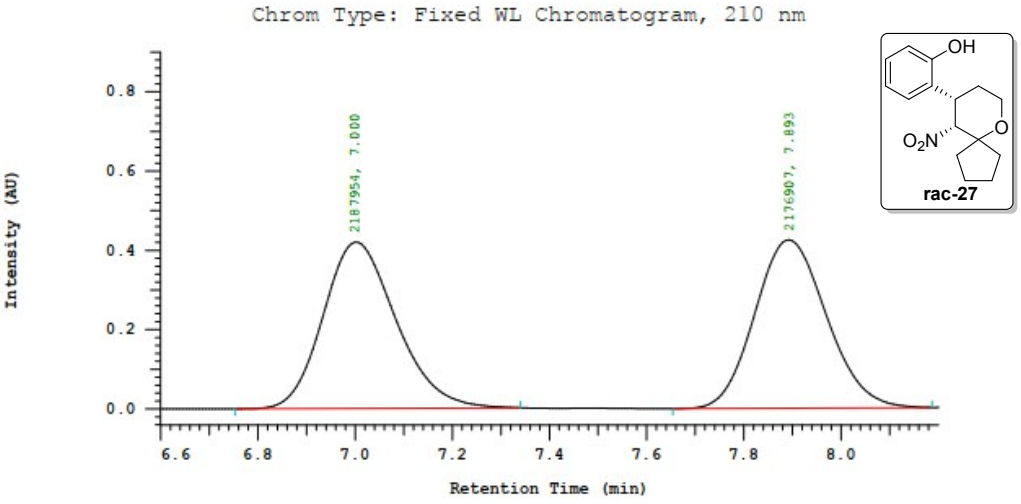
The ^{1}H NMR spectrum of 27 (500 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 27 (125 MHz, $CDCl_3$)



The HPLC of racemic 27



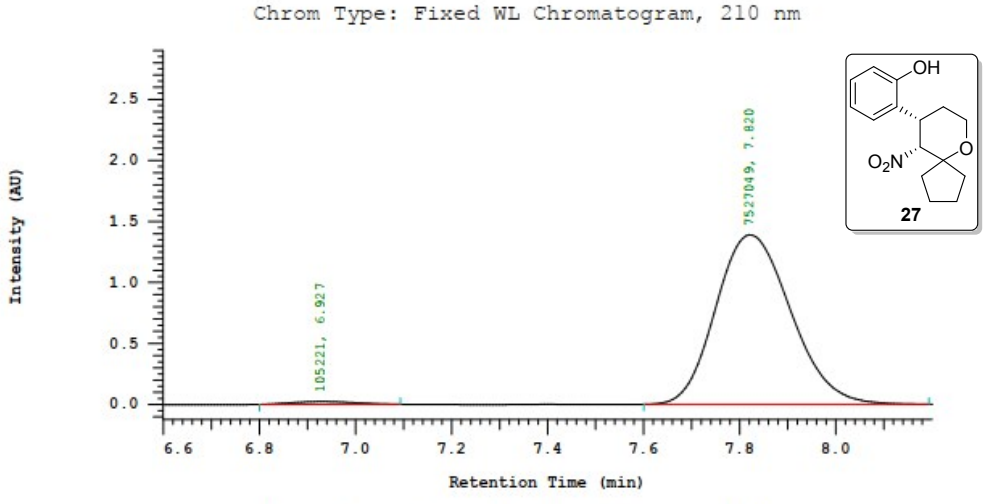
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.000	2187954	50.127	BB
2	7.893	2176907	49.873	BB
		4364861	100.000	

The HPLC of chiral 27



Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

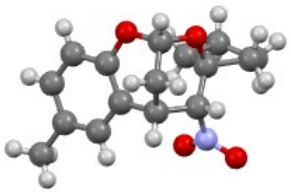
Calculation Method: AREA%

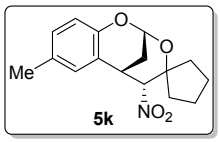
No.	RT	Area	Area %	BC
1	6.927	105221	1.379	BB
2	7.820	7527049	98.621	BB
		7632270	100.000	

K. Single crystal X-Ray diffraction data

CCDC 2072646 contains 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 **5k** - CCDC 2072646





Bond precision: C-C = 0.0052 A Wavelength=1.54184

Cell: a=7.2163(4) b=10.5180(4) c=19.1890(7)
alpha=90 beta=90 gamma=90
Temperature: 293 K

	Calculated	Reported
Volume	1456.47(11)	1456.47(10)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C16 H19 N O4	?
Sum formula	C16 H19 N O4	C16 H19 N O4
Mr	289.32	289.32
Dx,g cm-3	1.319	1.319
Z	4	4
Mu (mm-1)	0.780	0.780
F000	616.0	616.0
F000'	617.98	
h,k,lmax	8,12,22	8,12,22
Nref	2617[1532]	2616
Tmin,Tmax	0.823,0.849	0.829,1.000
Tmin'	0.823	

Correction method= # Reported T Limits: Tmin=0.829 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.71/1.00 Theta(max)= 67.248

R(reflections)= 0.0448(2138) wR2(reflections)= 0.1290(2616)

S = 1.036 Npar= 192
